# Part I. Synthesis of Naturally Occurring Cyclobutanes *via* Stereoselective Photocycloadditions

# Part II. Development of Photocatalytic Net-Oxidative Transformations using Copper(II) Salts as Terminal Oxidants

By

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Under the supervision of Professor Tehshik P. Yoon
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Among many unique transformations accessible using photochemical activation, the [2+2] photocycloaddition of olefins has had the largest impact on total synthesis. However, relatively few asymmetric total syntheses of natural products involving an enantioselective [2+2] photocycloaddition have been reported to date. This is due in part to the difficulty of conducting enantioselective [2+2] photocycloaddition reactions. Recent work in the Yoon lab has focused on developing enantioselective [2+2] photocycloadditions using a dual catalysis approach. The work presented herein will describe the use of chiral Lewis acid catalysts to enable highly enantioselective photocycloadditions and further application of this strategy toward natural product synthesis.

Photoredox catalysis is a powerful strategy to generate radical and radical ion intermediates under exceptionally mild conditions. However, the development of photocatalytic oxidation reactions has been much more challenging compared to redox-neutral and net reductive transformations due to the lack of generally applicable terminal oxidants that are compatible with photoredox conditions. This thesis describes the use of copper(II) salts as terminal oxidants for robust photocatalytic oxidation reactions.

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**Table of Contents**

**List of Scheme**

**Chapter 1**

**List of Figures**

**Chapter 1**



**Chapter 2**



**Chapter 3**

**List of Tables**

**Chapter 1**



**Chapter 2**



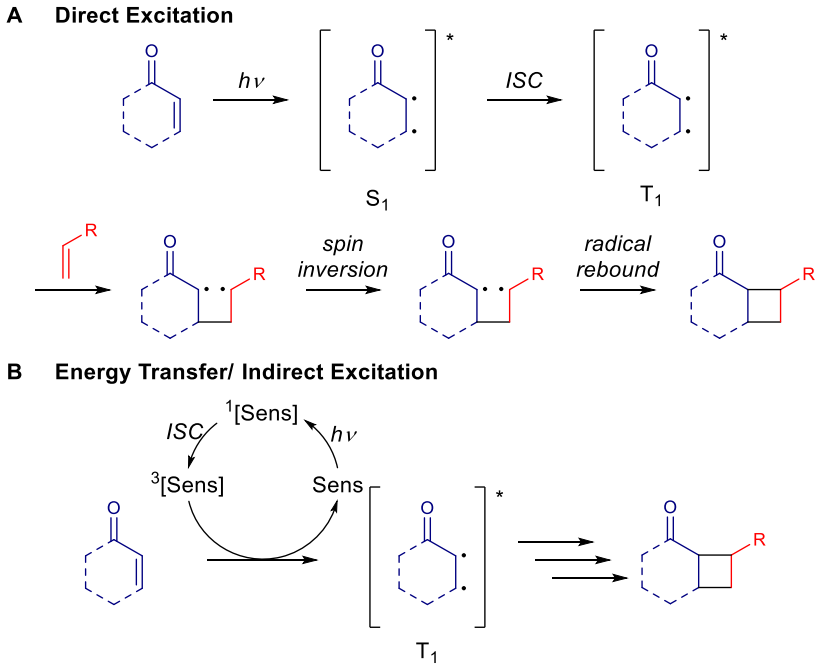
**Chapter 3**

# Chapter 1. Stereoselective [2+2] Photochemical Cycloadditions as Key Steps in Asymmetric Syntheses of Naturally Occurring Cyclobutanes

## 1.1 Introduction

The synthesis of natural products has long inspired innovation in organic chemistry. The synthetic challenge of constructing complex, structurally diverse molecular frameworks has motivated the expansion of the state-of-the-art methodologies as well as the discovery of fundamentally new reactions.[1–6] The use of photochemical transformations in total synthesis has emerged as an important strategy in total synthesis, particularly within the past few decades. A distinguishing characteristic of photochemical reactions is the involvement of highly energetic electronically excited intermediates that are produced when an organic substrate absorbs a photon. The resulting excited state intermediates enable new reaction pathways that cannot be accessed by conventional thermal methods.[7–10]

Among many unique transformations that are accessible using photochemical activation, the [2+2] photocycloaddition of olefins has arguably had the largest impact on total synthesis.[11] This reaction has been employed as a key step in hundreds of natural product syntheses over the last 40 years.[7–10] The most commonly utilized [2+2] photocycloadditions proceed *via* photoexcitation of an *α,β*-unsaturated carbonyl compound in the presence of a photochemically inactive alkene. Typically, direct excitation is applied to excite the enone, which populates the triplet state ($T_1$) by rapid intersystem crossing (ISC) from the first excited singlet state ($S_1$). The enone $T_1$ is long-lived and is capable of interacting with a photochemically inactive alkene to generate a triplet 1,4-biradical. After spin inversion to the $S_1$ state, radical rebound provides the desired cyclobutane (**Scheme 1.1.A**).[12] Triplet sensitizers can also be utilized in cases where direct excitation is either inefficient or impractical. Ketone (e.g., acetone, benzophenone, acetophenone) and transition metal photocatalysts are commonly employed triplet sensitizers. In this reaction pathway, photoexcitation of the triplet sensitizer (Sens) produces its $T_1$ state; the photoexcited sensitizer then undergoes energy transfer to populate the enone $T_1$, thereby entering into the same mechanism for the direct excitation manifold (**Scheme 1.1.B**).[13]




**Scheme 1.1.** Prototypical [2+2] photocycloadditions reaction pathways

Nevertheless, relatively few asymmetric total syntheses of natural products that involve a stereocontrolled [2+2] photocycloaddition have been reported to date. This is due in part to the difficulty of conducting enantioselective [2+2] photocycloaddition reactions. In modern synthetic chemistry, a wide range of chiral catalysts have been developed that can exert control over the stereochemical behavior of many key reactive intermediates. However, most photochemical reactions, including [2+2] photocycloadditions, involve remarkably reactive excited-state intermediates that generally react rapidly without additional activators or catalysts. This factor has complicated the development of enantioselective [2+2] photocycloaddition reactions. Thus, the characteristically low activation barriers associated with photochemical reactions have challenged the design of asymmetric catalytic strategies that can successfully outcompete direct, racemic background photoreactions.[14–18]

Stereoselective photochemical reactions have generally required the substrate molecule to reside in a chiral environment prior to the photoexcitation step. To this end, there have been two strategies applied to the asymmetric synthesis of cyclobutane-containing natural products: substrate-controlled

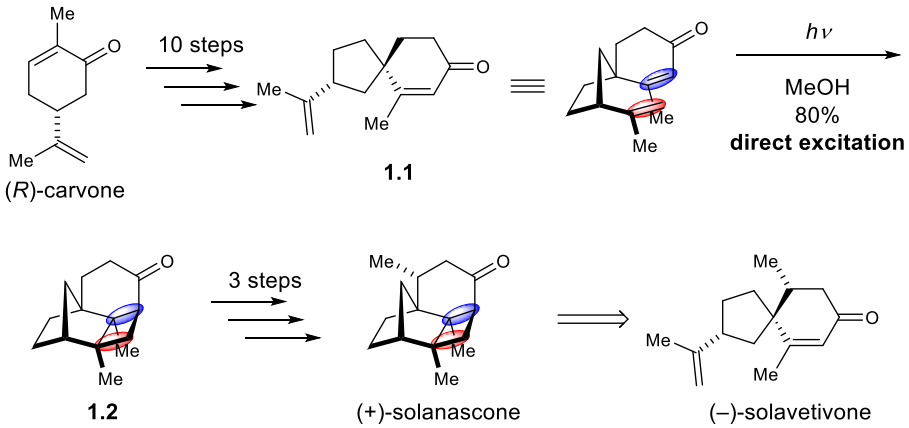
photocycloadditions and catalyst-controlled photocycloadditions. This chapter will discuss asymmetric total syntheses of naturally occurring cyclobutanes that have been accomplished by both strategies.

## 1.2 Substrate-Controlled Stereoselective [2+2] Photocycloaddition in Total Synthesis

### 1.2.1 Intramolecular [2+2] Photocycloaddition

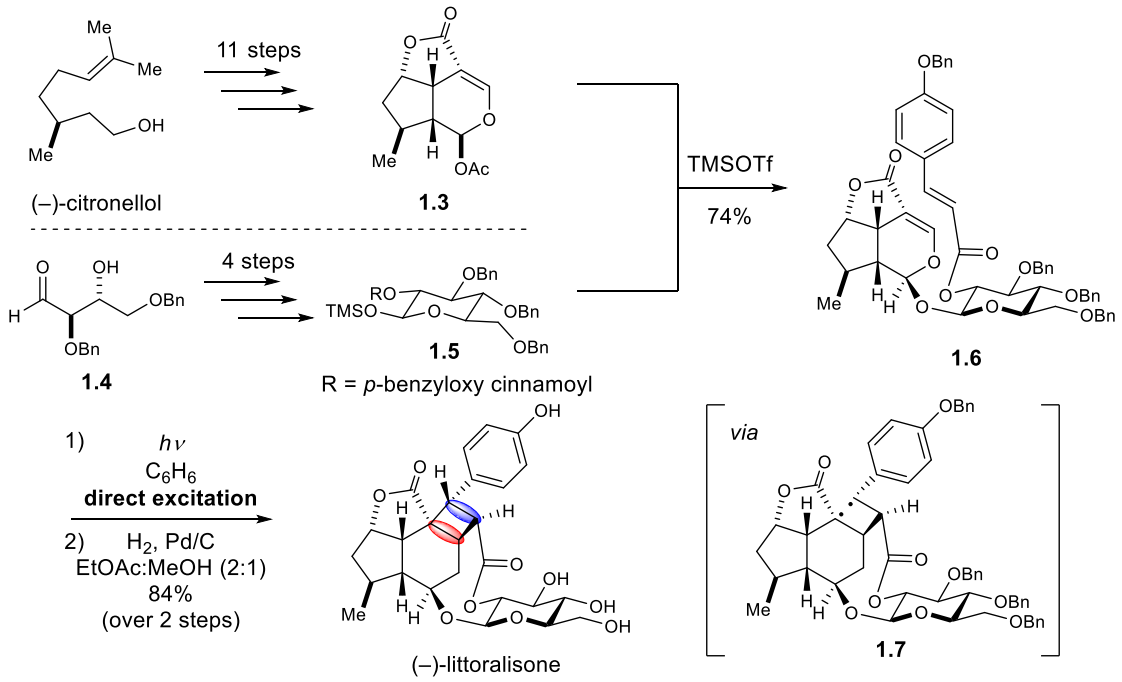
The most common strategy that has been utilized to achieve stereoselective [2+2] photocycloadditions in total synthesis is the strategic design of a chiral substrate featuring stereogenic units that can control the stereochemical outcome of the transformation. This strategy is particularly powerful for the construction of annulated cyclobutane-containing natural products that are synthesized *via* intramolecular [2+2] photocycloadditions. The added conformational rigidity imparted by preexisting ring structures provides a powerful basis for highly stereoselective reactions, as the two reacting olefins can be locked in a proximal configuration. This strategy is also frequently utilized in Nature: chiral photosubstrates have been identified in the biosynthesis of a range of biologically active compounds that proceed by [2+2] photocycloadditions.

(+)-Solanascone is a sesquiterpene initially isolated by Fujimori in 1978 from *Nicotiana. tabacum* cv. Burley.[19] It features a unique tetracyclo[5.3.1.1.$^{1,4}$.0$^{5,11}$]dodecane carbon framework. Its biogenic precursor is believed to be the bicyclic terpene (–)-solavetivone. Inspired by this biosynthetic hypothesis, Srikrishna attempted to synthesize (+)-solanascone *via* a biomimetic intramolecular [2+2] photocycloaddition of (–)-solavetivone. Unfortunately, the synthesis of (–)-solavetivone was not successful. Therefore, the authors synthesized enone **1.1**, which is a simplified substrate featuring the bicyclic scaffold of solavetivone, in ten steps from (*R*)-carvone. Direct irradiation of this intermediate generated cyclobutane **1.2** in 80% yield. Cyclobutane **1.2** was further elaborated into (+)-solanascone in three steps. The high stereoselectivity in the photocycladdition step was a consequence of the conformationally restricted and preorganized photosubstrate **1.1**, which underwent stereoselective intramolecular [2+2] photocycloaddition to furnish **1.2** as a single product.[20]

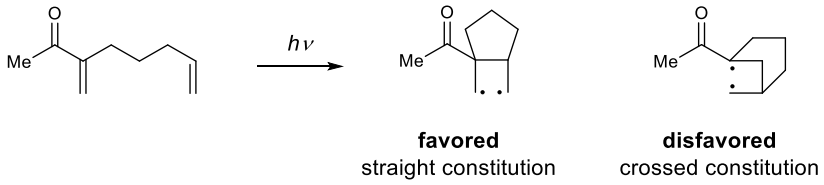



**Scheme 1.2.** Intramolecular [2+2] photocycloaddition in the synthesis of (+)-solanascone

In the asymmetric total synthesis of (–)-littoralisone, MacMillan applied an intramolecular [2+2] photocycloaddition of the enantiopure substrate **1.6** to afford cyclobutane (–)-littoralisone after hydrogenolysis. The prerequisite glucose-tethered diene **1.6** was accessed by coupling enantiomerically pure lactone **1.3** and cinnamate-functionalized glucoside **1.5**, which were synthesized from commercially available (–)-citronelleol and aldol adduct **1.4**, respectively. Presumably, the first bond formation of conformationally restricted tethered diene **1.6** in the photocycloaddition step generated the *cis*-fused 1,4-biradical **1.7**, which subsequently underwent the second bond formation to furnish the desired benzyl-protected (–)-littoralisone exclusively.[21] Diastereocontrol in the second bond forming event is enabled by the placement of the benzyloxyphenyl group toward the substantially less hindered face.



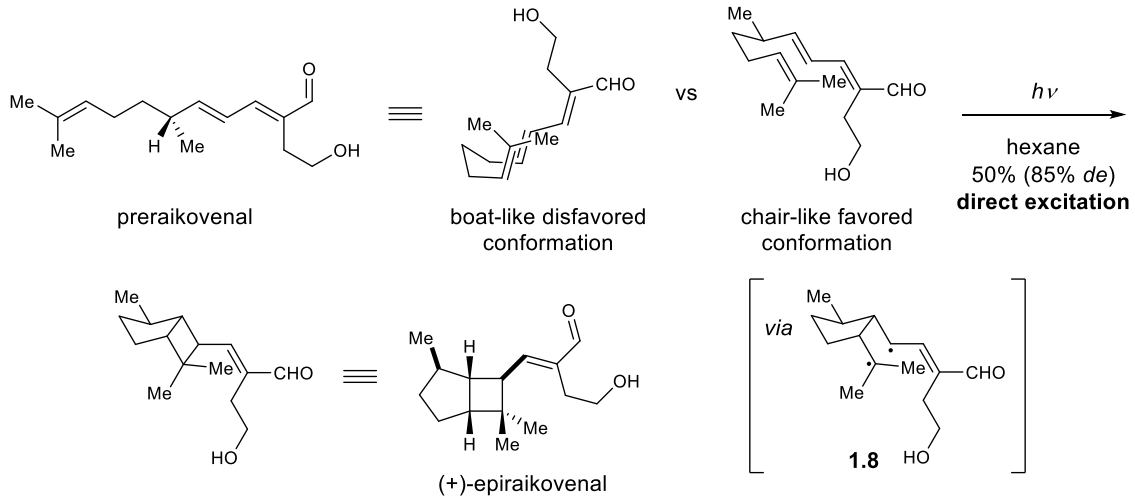

**Scheme 1.3.** Intramolecular [2+2] photocycloaddition in the synthesis of (–)-littoralisone




**Scheme 1.4.** Intermediates of straight and crossed [2+2] photocycloaddition products

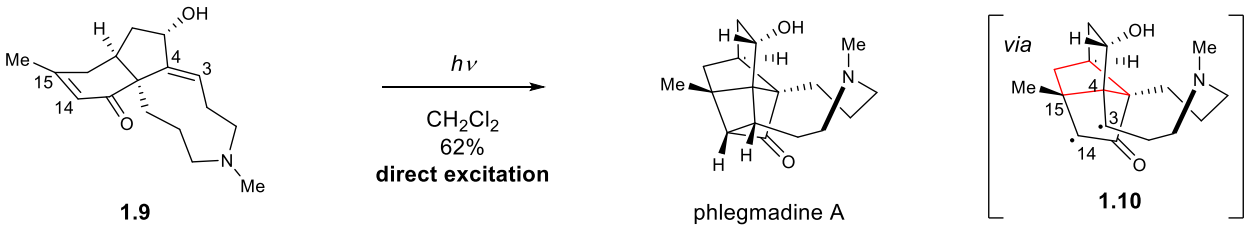
In addition to excellent levels of stereoselectivity in the synthesis of annulated cyclobutanes, regioselectivity is also controllable and predictable in intramolecular photocylcoadditions. In 1967, Shinivasan and Hammond reported [2+2] photocycloaddition reactions of substrates bearing a three-atom tether between the reacting olefins. In these seminal studies, the *straight constitutional* products are observed with high selectivity over the *crossed constitutional* isomer. The structures of these two possible products suggest that they result from a kinetic preference for formation of a five-membered ring in the intermediate 1,4-diradical (**Scheme 1.4**).[22–24] This observation has been termed the rule of five and has been used as a powerful tool for predicting both the regioselectivity and stereoselectivity of photocycloadditions in the asymmetric syntheses of cyclobutane-containing natural products.

As one example, Pietra and co-workers proposed that (+)-epiraikovenal could be accessed from a linear precursor called preraikovenal, which was co-isolated from the same source. The authors anticipated that preraikovenal would react in chair-like favored conformation as it shown in **Scheme 1.5**. In this favored conformation, the first bond forming event would result in biradical **1.8**, as predicted by the rule of five. The diastereoselectivity of the second bond-forming step was then predicted by assuming that the bulky acryloyl substituent on the C-5 radical center would prefer to occupy the less-hindered convex orientation. Indeed, [2+2] photocycloaddition of preraikovenal furnished the expected (+)-epiraikovenal as the major diastereomer in good chemical yield with high diastereo- and regioselectivity.[25]



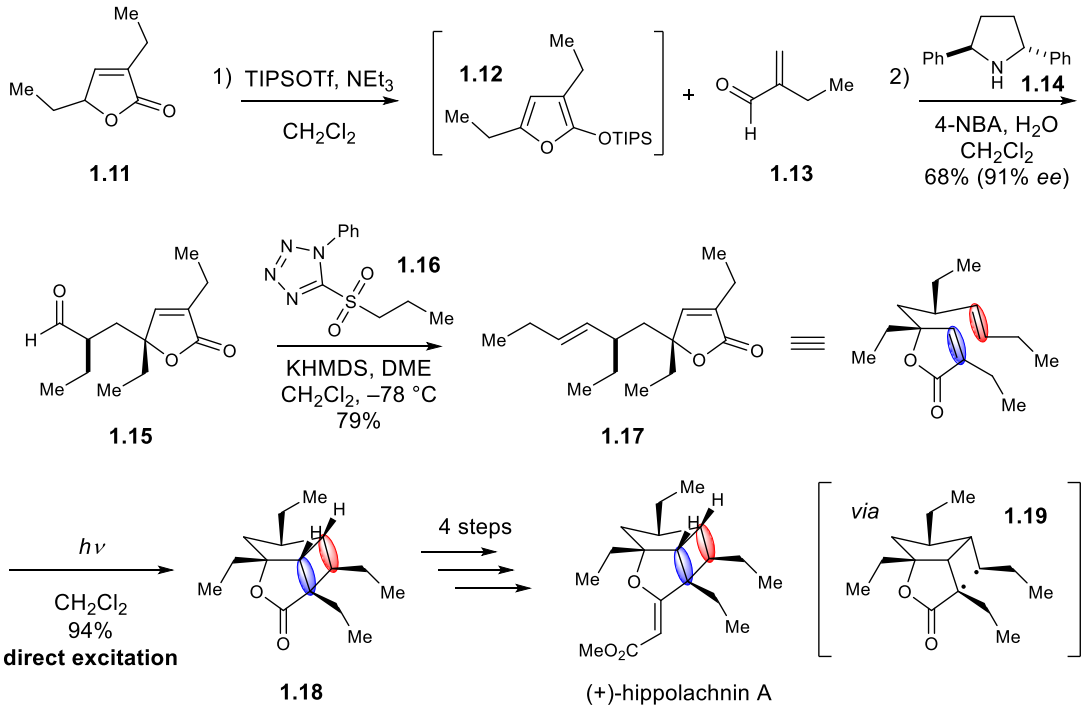

**Scheme 1.5.** Intramolecular [2+2] photocycloaddition in the total synthesis of (+)-epiraikovenal

The predicting power of the rule of five also has been applied in the synthesis of phlegmadine A. It is a *Lycopodium* alkaloid with a unique cyclobutane core and featuring a complex tetracyclo[4.2.2.0$^{3,8}$.$^{03,10}$]decane carbon framework. This compound was isolated by Zhao and Zhou from the *Phlegmariurus phlegmaria*, a traditional Chinese medicinal plant. The authors proposed that its natural precursor might be enone **1.9** and planned a biomimetic synthesis of phlegmadine A. The first bond forming event was expected between C4 and C15 to generate biradical intermediate **1.10**, which would be the result of a kinetic preference for the formation of a five-membered ring. Subsequently, conformationally locked biradical **1.10** was predicted to undergo radical rebound to furnish phlegmadine A. Indeed, irradiation of enone **1.9** produced phlegmadine A in 62% as a single product.[26]



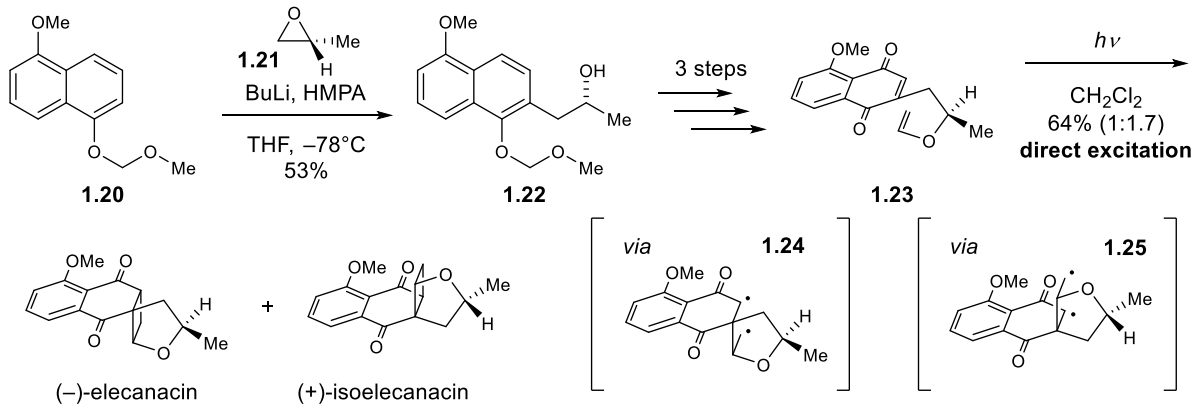

**Scheme 1.6.** Intramolecular [2+2] photocycloaddition in the total synthesis of phlegmadine A

Hippolachnin A is one of the most well-known members of the family of the *Plakortin* polyketides. This natural product contains a highly strained, bowl-shaped 5/5/4 tricyclic core with six consecutive stereogenic centers, four of which bear an ethyl substituent projected toward the convex face of the molecule. This fascinating molecular architecture along with its associated promising biological profile has stimulated extensive interests from the synthetic community.[27] Consequently, several elegant total syntheses of hippolachnin A have been reported;[28–33] however, only a few of these syntheses have been conducted in an enantioselective fashion. In 2017, Wu designed a racemic synthesis featuring (±)-**1.17** as a key intermediate;[31] Enders and Tang subsequently reported an asymmetric route to **1.17** involving enantioselective Mukaiyama–Michael addition of silyloxyfuran **1.12** to **1.13** controlled by chiral diphenylpyrrolidine catalyst **1.14**. Next, a Julia–Kocienski olefination transformed aldehyde **1.15** exclusively to the desired 1,2-disubstituted *E*-olefin **1.17**. The regioselectivity of the intramolecular [2+2] photocycloaddition of **1.17** was consistent with the rule of five. The stereoselectivity of the reaction could be rationalized by considering a stepwise mechanism involving 1,4-biradical intermediate **1.19**. The stereoselectivity of the ring-closure step was rationalized by examining the thermodynamically more stable conformer **1.19** wherein the ethyl substituent on the C-10 radical center is projected toward the less hindered convex face. The resulting cyclobutane **1.18** was subsequently converted to (+)-hippolachnin A in four steps.[34]



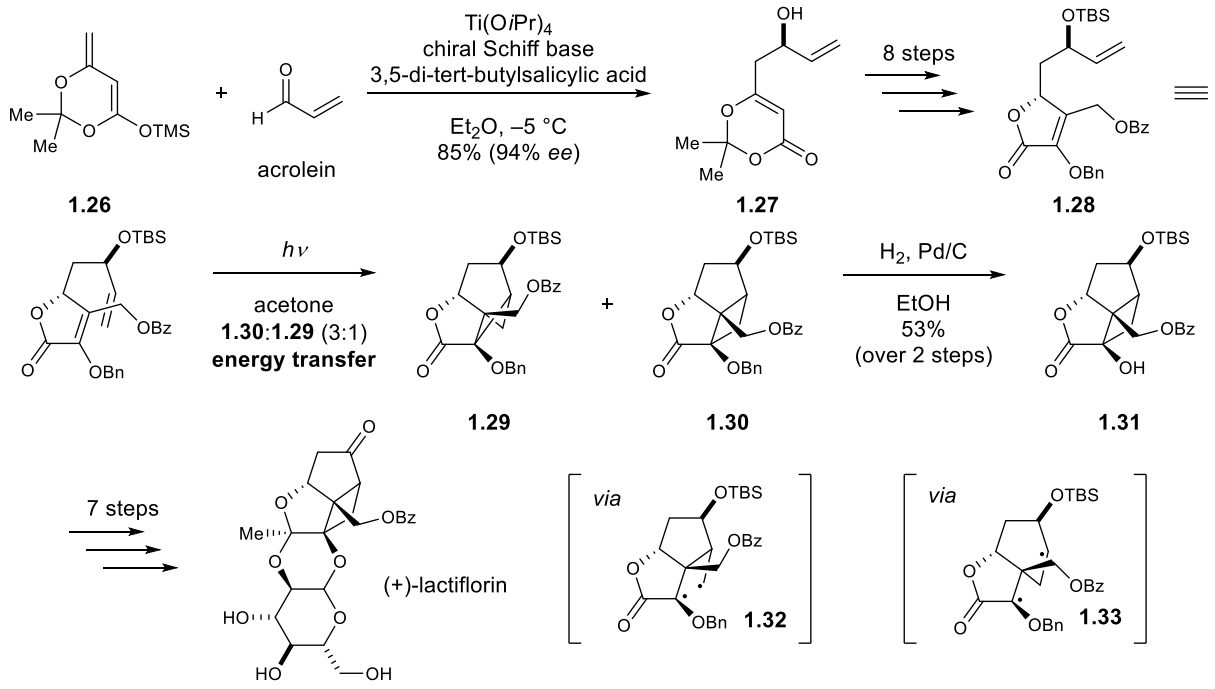

**Scheme 1.7.** Intramolecular [2+2] photocycloaddition in the total synthesis of (+)-hippolachnin A

Another application of the rule of five is found in the synthesis of (–)-elecanacin. Here, Wege recognized the tethered diene **1.23** as a potential intermediate in the synthesis of the natural product *via* intramolecular [2+2] photocycloaddition. The chirality of **1.23** was introduced by direct metalation and subsequent addition to enantiopure epoxide **1.21**. The further deprotection-oxidation-vinylation sequence of enantiopure **1.22** afforded the photosubstrate **1.23.** While **1.23** failed to provide the desired facial discrimination, the regioselectivity of the intramolecular [2+2] photocycloaddition was consistent with the rule of five, resulting in the formation of (–)-elecanacin and (+)-isoelecanacin *via* the biradical intermediates **1.24** and **1.25**, respectively.[35]



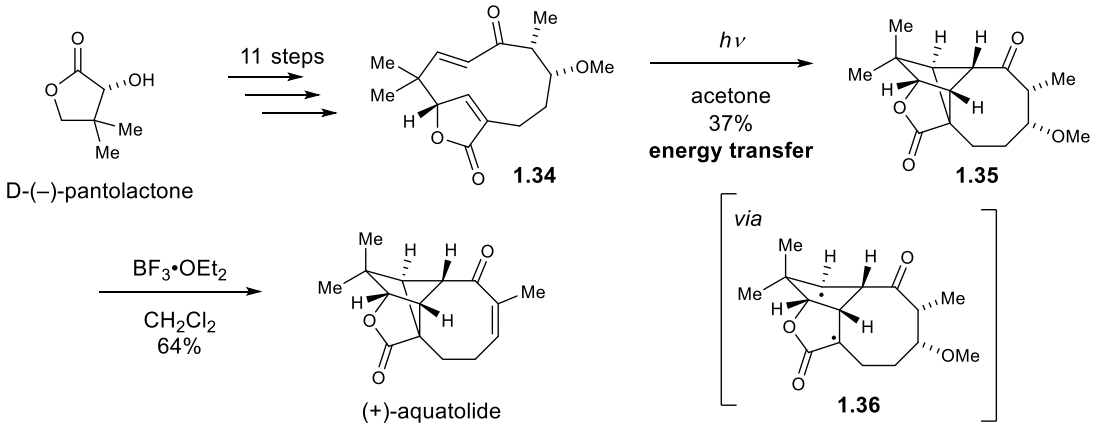

**Scheme 1.8.** Intramolecular [2+2] photocycloaddition in the total synthesis of (–)-elecanacin

Bach utilized an intramolecular [2+2] photocycloaddition as the key step in the asymmetric synthesis of the annulated cyclobutane (+)-lactriflorin. It was hypothesized that a three-atom tether between the reacting olefins in photochemically active alkene **1.28** would enable a regioselective and stereoselective intramolecular [2+2] photocycloaddition to afford cyclobutane **1.30**, a key intermediate in the synthesis. Introducing the chirality of the desired furanone photosubstrate **1.28** for the [2+2] photocycloaddition was secured from acrolein by a catalytic, enantioselective Mukaiyama aldol addition with enoxy silane **1.26**. Further manipulations completed the synthesis of furanone **1.28** in eight steps. Unexpectedly, acetone-sensitized [2+2] photocycloaddition of furanone **1.28** produced a 3:1 mixture of the regioisomeric photoadducts **1.30** and **1.29**, favoring the constitutional isomer predicted by the rule of five but nevertheless producing the opposite connectivity as a major side product. This unexpected regioselectivity is consistent with previous studies, demonstrating that the primarily formed 1,4-biradical **1.32** may revert to the starting material to form **1.33** if the subsequent ring closure is thermodynamically unfavorable.[36] Nevertheless, debenzylation *via* hydrogenolysis of the straight product (**1.30**) yielded the cyclobutane **1.31**, which was elaborated into (+)-lactiflorin in seven additional steps.[37]



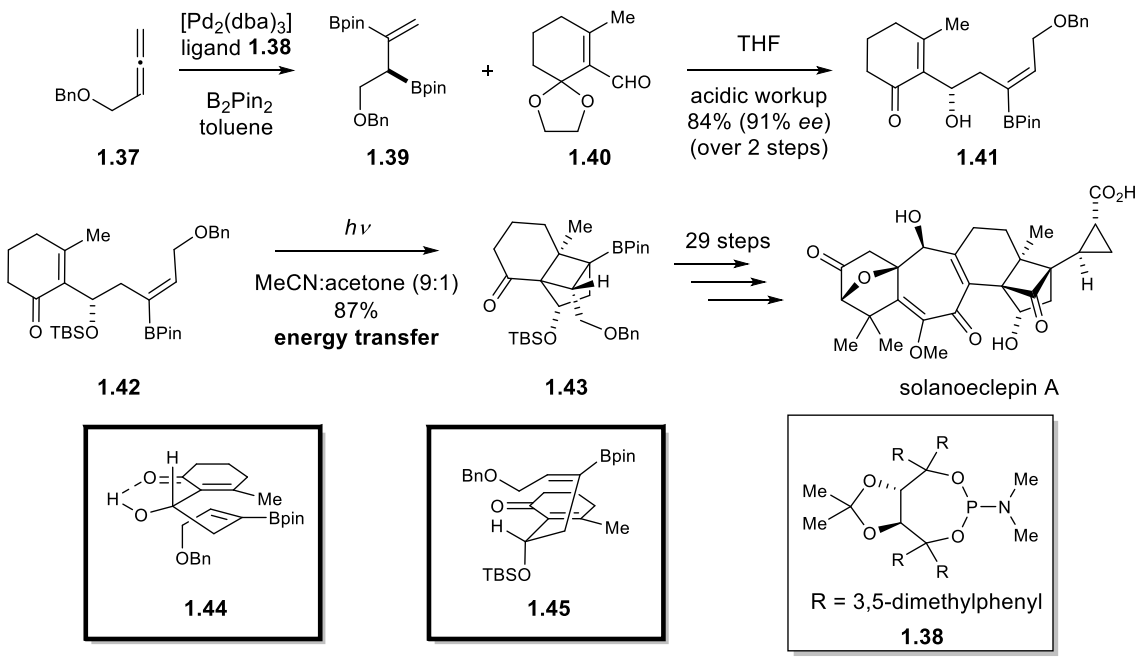

**Scheme 1.9.** Intramolecular [2+2] photocycloaddition in the total synthesis of (+)-lactiflorin

In substrates that contain two-atom tethers between reacting olefins, the rule of five predicts that a crossed reaction geometry should be favored. Takao has applied this strategy to the synthesis of (+)-aquatolide, in which intramolecular [2+2] photocycloaddition of photochemically active alkene **1.34** serves as the key step. The stereocenter at the 5-position of the photoactive lactone, derived from the chiral pool, controls the facial selectivity of the initial bond formation, forming cycloadduct **1.35** as a single isomer after sensitized cycloaddition. Lewis acid promoted elimination affords (+)-aquatolide.[38]




**Scheme 1.10.** Intramolecular [2+2] photocycloaddition in the total synthesis of (+)-aquatolide

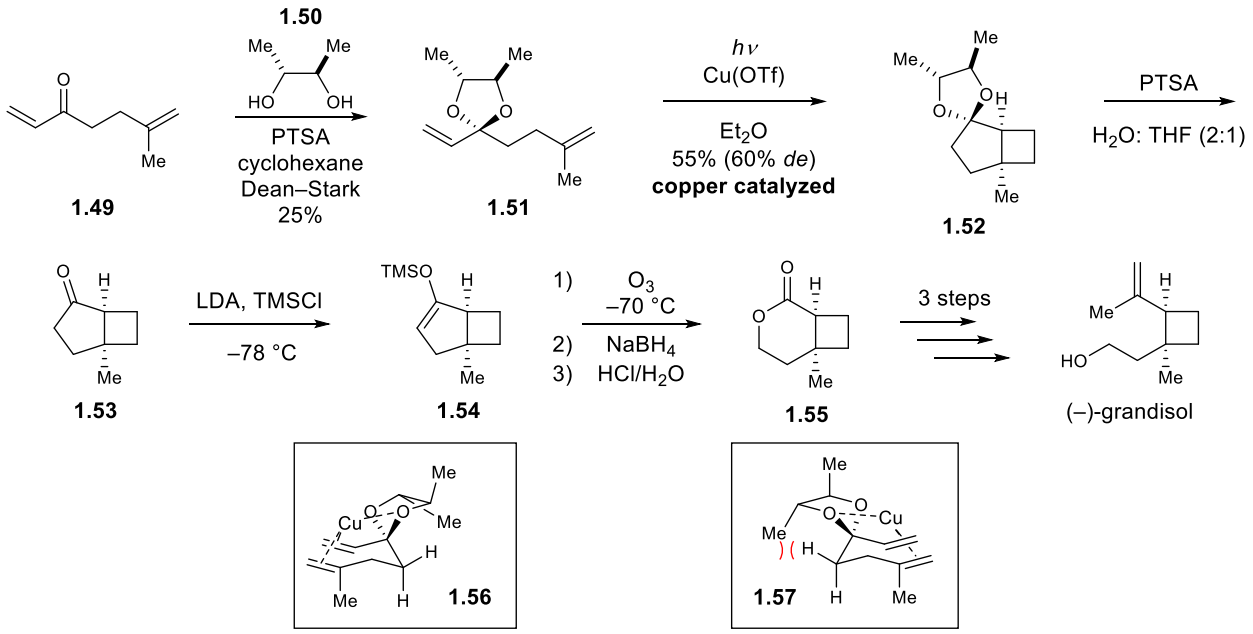
A similar crossed [2+2] photocycloaddition features as the key step in the synthesis of the complex terpenoid solanoeclepin A. Initially isolated by Mulder in 1986, the unique structural challenge in its synthesis is the highly strained and stereochemically dense tricyclo[5.2.1.$0^{1,6}$]decane framework bearing three consecutive quaternary stereocenters. Hiemstra's enantioselective synthesis of solanoeclepin A featured a Pd-catalyzed enantioselective diboration of allene **1.37** to afford diboronate **1.39**, providing **1.41** after allylation of aldehyde **1.40**. Unfortunately, the [2+2] photocycloaddition of (±)-**1.41** produces the undesired facial selectivity, likely due to a hydrogen-bonding interaction between the enone and the free hydroxyl group, resulting in a preference for conformer **1.44**. TBS-protection of the alcohol disrupts this hydrogen-bonding interaction and enabled a regio- and stereoselective acetone-sensitized [2+2] photocycloaddition of **1.42** to afford densely-substituted cyclobutane **1.43**, completing a formal synthesis of solanoeclepin A.[39]




**Scheme 1.11.** Intramolecular [2+2] photocycloaddition in the total synthesis of solanoeclepin A

Stereoselective intramolecular [2+2] photocycloaddition reactions have been exploited in the assembly of non-annulate cyclobutane natural products; such as sceptrin and grandisol. Mattay developed an alternative strategy using a Cu-catalyzed intramolecular [2+2] photocycloaddition to construct the

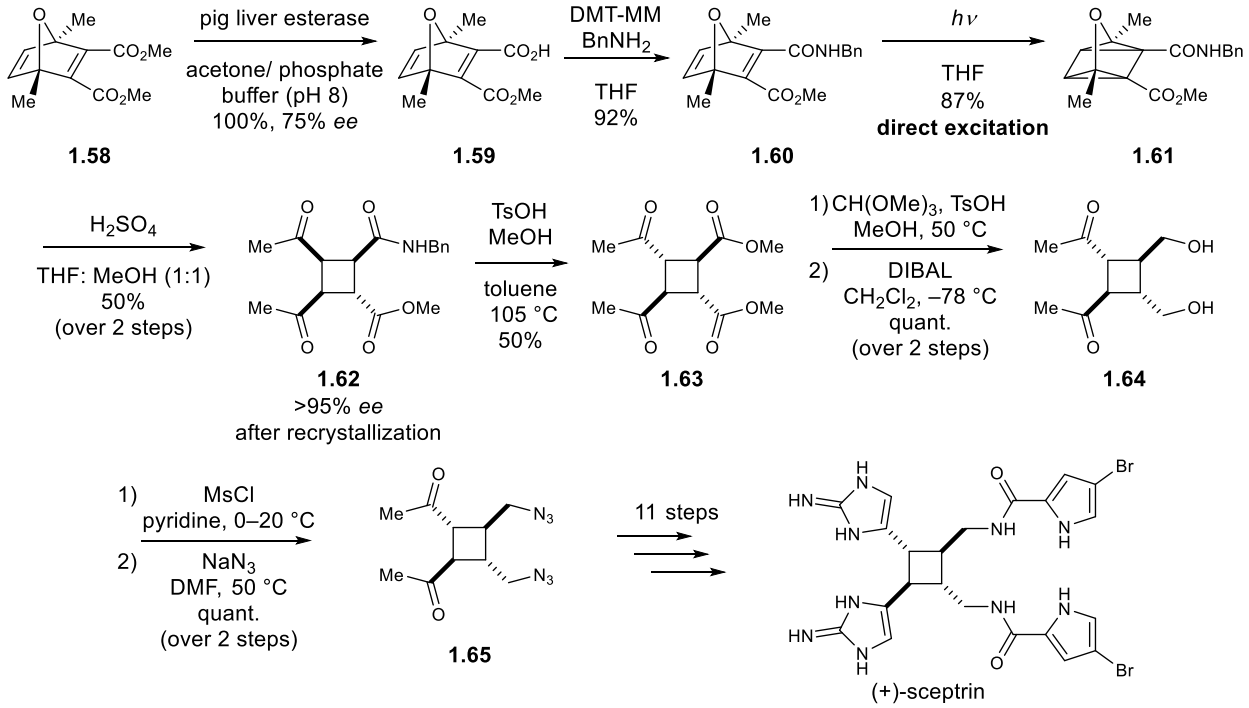
enantiopure cyclobutane core **1.52**. Cu-catalyzed [2+2] photocycloaddition reactions are uniquely suited for the synthesis of cyclobutanes from simple, unconjugated alkenes, as the key MLCT transition occurs at significantly lower wavelengths than the direct photoexcitation of simple olefins.[40,41] Here, D-(–)-2,3-butanediol **1.50** was employed as a chiral auxiliary to provide a basis for stereoselectivity in the [2+2] photocycloaddition. Enantiopure diene **1.51** underwent a Cu-catalyzed intramolecular [2+2] photocycloaddition to give cyclobutane **1.52** in 55% yield and 60% de *via* conformer **1.56**. The authors speculated that the modest stereoselectivity results from an unfavorable steric interaction between the methyl group and hydrogen in **1.57**. Cleavage of the auxiliary group by acid-catalyzed hydrolysis yielded the cyclobutyl ketone **1.53**, which was subsequently converted into (–)-grandisol in three steps.[42] Ghosh and co-workers later reported the total synthesis of both enantiomers of grandisol using a different chiral auxiliary to afford better diastereoselectivity.[43]




**Scheme 1.12.** Stereoselective intermolecular [2+2] photocycloaddition in the total synthesis of (–)-grandisol enabled by a chiral auxiliary

The first asymmetric synthesis of both enantiomers of sceptrin was reported by Baran. Baran utilized a nonobvious intramolecular [2+2] photocycloaddition beginning with enantiopure oxanorbornadiene substrate **1.60**. This compound was prepared by enzymatic desymmetrization of *meso*-diester **1.58** to afford

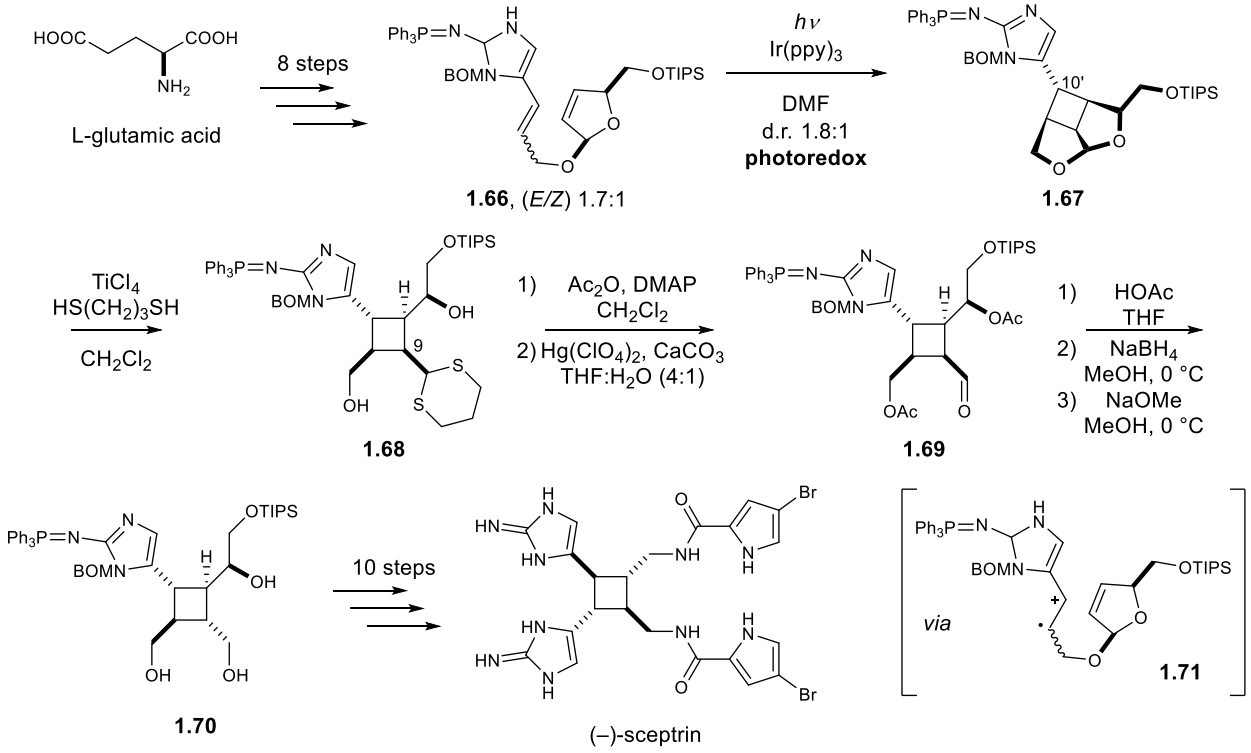
carboxylic acid intermediate **1.59** in 75% *ee*. Subsequent coupling with benzyl amine furnished amide **1.60**, which undergoes direct photocycloaddition to afford oxaquadricyclane **1.61**. Treatment with $H_2SO_4$ in THF/ MeOH (1:1) enabled production of cyclobutane **1.62** in 50% overall yield and 75% *ee*. An epimerization-esterification sequence set the desired all-*trans* stereochemistry. Protection of the ketone of **1.63** as the corresponding methyl ketals and subsequent ester reduction furnished diol **1.64**, which was converted into **1.65** by mesylation and displacement with sodium azide. The synthesis of (+)-sceptrin was completed in an additional 11 steps. A similar approach was also applied in the synthesis of (–)-sceptrin.[44]




**Scheme 1.13.** Substrate-controlled, stereoselective [2+2] photocycloaddition in the synthesis of (+)-sceptrin

Following this initial report, Baran and Chen described an alternative intramolecular [2+2] photocycloaddition strategy. Inspired by Molinski and Romo's proposed mechanism for the biogenic dimerization of hymenidin involving enzymatic single-electron transfer, the authors evaluated the possibility of using a photoredox method to effect a similar transformation (**Scheme 1.17**). Their strategy begins with the synthesis of **1.66** in eight steps from L-glutamic acid, which provided the initial source of stereochemical information. Irradiation of a solution of **1.66** with a catalytic amount of $Ir(ppy)_3$ afforded

stereochemically well-defined cyclobutane **1.67** *via* radical cation **1.71**. However, only a modest 1.8:1 diastereomeric ratio at C10' was observed, indicative of a weak preference in the second bond-forming step in the [2+2] cycloaddition reaction. Nonetheless, annulated cyclobutane **1.67** was further elaborated to provide the requisite all-*trans* configuration of the central cyclobutane core **1.70**. Transthioketalization of **1.67** deconstructed the fused-ring system to reveal the cyclobutane core (**1.68**). Acetylation of the hydroxyl group and hydrolysis of the dithiane group of **1.68** afforded *trans-cis-cis* cyclobutane **1.69**. The requisite all-*trans* configuration was furnished by epimerization of the C9 stereogenic center. Subsequent reduction of the aldehyde and acetate deprotection provided triol **1.70**. To complete the synthesis of sceptrin, the alcohols were converted to the desired amides, and partially protected diol was converted to the desired aminoimidazole.[45]



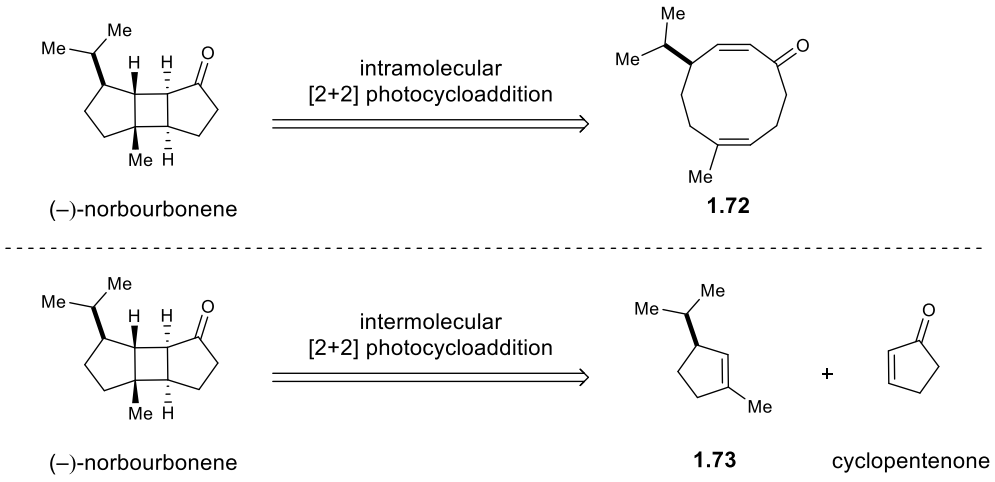

**Scheme 1.14.** Intramolecular [2+2] photocycloaddition in the synthesis of (–)-sceptrin

Given these studies, it is clear that a wide range of enantiopure natural products that can be accessed by the stereoselective intramolecular [2+2] photocycloadditions of enantioenriched, tethered dienes. This powerful synthetic tool has been extremely beneficial in the syntheses of natural products that contain

annulated cyclobutanes because the tether chain becomes structurally incorporated into the final product. Because the empirical rule of five has proven to have reliable predictive power, the design of the enantiopure diene substrates required for the synthesis of annulated cyclobutanes has been relatively straightforward. Additionally, this strategy has been used for the synthesis of monocyclic natural products with properly designed ring-cleavage steps. However, the multi-step syntheses of the photosubstrates and the necessity for further manipulations to cleave the tethering moiety can complicate total synthesis.

### 1.2.2 Intermolecular [2+2] Photocycloaddition

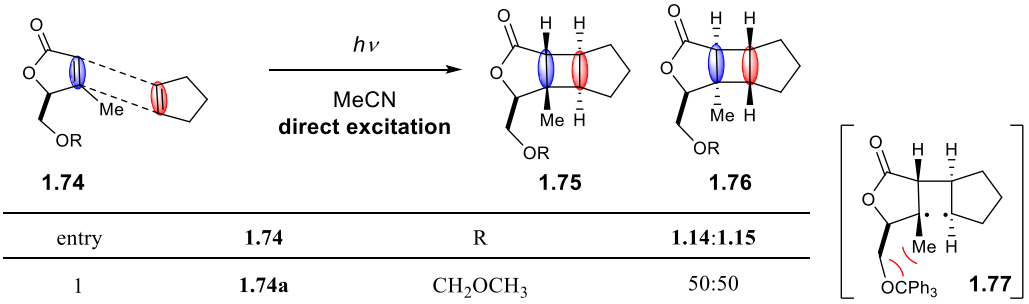
In principle, intermolecular [2+2] photocycloadditions should undoubtably be the best strategy for simple naturally occurring cyclobutanes as this strategy would enable the convergent assembly of elaborate structures from simpler alkene synthons. This approach has been successful towards the asymmetric syntheses of a broad range of naturally occurring annulated cyclobutanes. This has been particularly true for certain classes of annulated cyclobutanes that would be more challenging to synthesize *via* intramolecular [2+2] photocycloadditions. For instance, while (–)-norbourbonene could be synthesized from tethered diene **1.72** *via* intramolecular [2+2] photocycloaddition, a linear synthesis of **1.72** would pose a greater synthetic challenge than **1.73** and cyclopentenone, which are obvious synthons for the intermolecular reaction. Moreover, intermolecular reactions provide greater synthetic flexibility if the initially designed synthetic strategy is not suitable as each coupling partner is relatively easy to modify.




**Scheme 1.15.** Possible routes towards the synthesis of (–)-norbourbonene

In 1992, Wickberg realized the [2+2] photocycloaddition of enantiomerically pure alkene **1.73** and cyclopentenone. This reaction established a short route towards (–)-norbourbonene and demonstrated the high stereoselectivities that can be achieved in such reactions. Nevertheless, the regioselectivity was poor; a 1:1 mixture of (–)-norbourbonene and its constitutional isomer were formed. Furthermore, a challenging purification resulted in only 2% of isolated yield of the pure natural product.[46]

An alternate strategy toward (–)-nornourbonene was reported by Koga. Enantiomerically pure butenolide **1.74c**, which can be synthesized from commercially available **1.78** in three steps, was employed in a stereoselective photocycloaddition with cyclopentene **1.53** to construct the 4/5 bicyclic core. To develop this synthesis, the authors systematically studied butanolides featuring a range of protecting groups (**1.74a–d**) to understand the factors that control the stereoselectivity of the [2+2] photocycloaddition (Table 1.1). In these studies, stereoselectivity was found to increase with the steric profile of the protecting group, albeit only to a modest degree (entry 1–3). An improvement in stereoselectivity was also observed when the reaction was performed at a lower temperature (entry 4). Interestingly, poor selectivity was observed using a trityl protecting group. The authors speculated that the severe steric repulsions between β-methyl and trityl groups in *cis* arrangement could destabilize **1.75** during the second bond forming event causing **1.77** to revert to olefin and **1.74d**.[47]



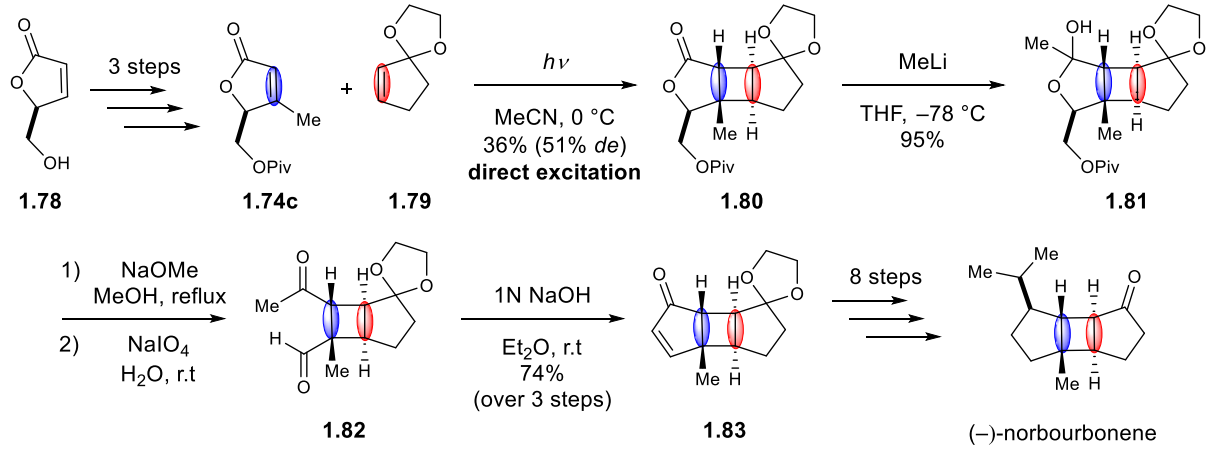

**1.74** **1.75** **1.76** **1.77**

| entry | 1.74 | R | 1.14:1.15 |
|---|---|---|---|
| 1 | **1.74a** | $CH_2OCH_3$ | 50:50 |
| 2 | **1.74b** | $COCH(CH_3)_2$ | 62:38 |
| 3 | **1.74c** | $CO(CH_3)_3$ | 71:29 |
| 4[a] | **1.74c** | $CO(CH_3)_3$ | 79:21 |
| 5[a] | **1.74d** | $CPh_3$ | 60:40 |

a) The reaction was carried out at –30 °C.

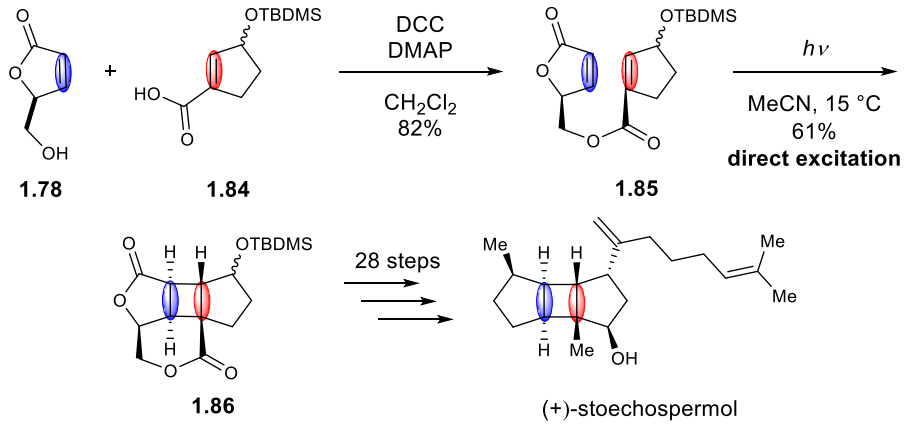
**Table 1.1.** Probing steric effect on diastereoselectivity in the [2+2] photocycloaddition

In efforts to extend this model study to total synthesis, intermolecular [2+2] photocycloaddition with **1.74c** and **1.79** resulted in only moderate stereo- and regioselectivity (Scheme 1.16). Nonetheless, after recrystallization of **1.80**, nucleophilic addition of MeLi afforded tertiary alcohol **1.81**, which was subsequently elaborated to generate keto-aldehyde **1.82**. A subsequent intramolecular aldol condensation of **1.82** showed the feasibility of this strategy to access cis, anti, cis-tricyclo[5,3,0,$0^{2,6}$]decane core **1.83** in enantioenriched form. From this intermediate, further manipulations provided access to (–)-β-bourbonene and (–)-norbourbonone in eight steps.[47,48]



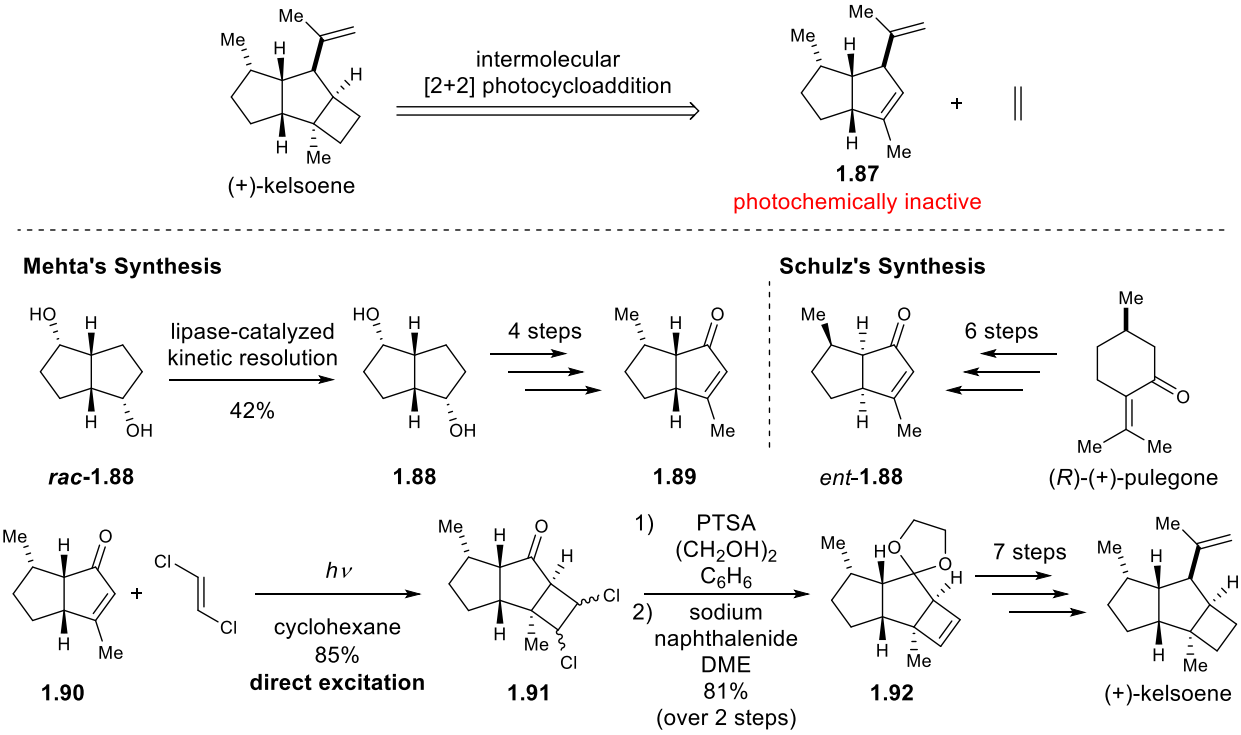

**Scheme 1.16.** Stereoselective intermolecular [2+2] photocycloaddition in the total synthesis of (–)-norbourbonene enable by a chiral auxiliary

Both of the intermolecular approaches to the synthesis of norbourbonene suffered from poor regiocontrol. As demonstrated in the preceding section, intramolecular [2+2] photocycloadditions enforce high regioselectivity *via* the rule of five. Inspired by this, Koga's group demonstrated that both stereo- and regioselectivity can be improved in the key intramolecular [2+2] photocycloaddition step by utilizing a temporary tether **1.85** to render the reaction intramolecular, generating **1.86** (Scheme 1.17). The application of this strategy to the construction of a tricyclo[5,3,0,$0^{2,6}$]decane core was exemplified in the synthesis of (+)-stoechospermol. Thus, that artificial tethering of two components can address regio- and stereoselectivity problems at the expense of requiring additional steps.[49]



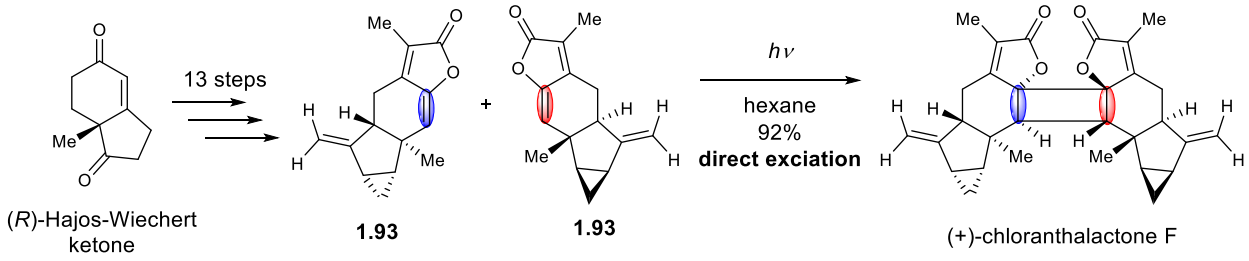

**Scheme 1.17.** Intramolecular [2+2] photocycloaddition in the total synthesis of (–)-stoechospermol

The structure of (+)-kelsoene suggests; an obvious disconnection involving an intermolecular [2+2] photocycloaddition between **1.87** and ethylene. However, because both fragments are photochemically inactive, Mehta and Schulz independently identified an alternative strategy (Scheme 1.18). Both groups synthesized photochemically active enone **1.88** and *ent*-**1.88**, respectively, and demonstrated access to the tricyclo-[5,3,0,$0^{2,5}$]decane **1.92** *via* a diastereoselective [2+2] photocycloaddition to construct **1.91**.[50,51] In Mehta's synthesis, diol **1.88**, which is easily obtainable from *rac*-**1.88** *via* enzymatic kinetic resolution, was used as a chiral building block to synthesize (+)-kelsoene. Further manipulations of diol **1.88** resulted in enantiomerically pure enone **1.89**, which underwent a facially selective [2+2] photocycloaddition with *trans*-1,2-dichloroethylene to furnish only desired *cis*, *anti*, *cis*-tricyclo[5,3,0,$0^{2,5}$]decane **1.92** following reductive dehalogenation.[50] The authors also applied a similar strategy toward the asymmetric total synthesis of sesquiterpene (–)-sulcatine G, which contains the same 4-5-5 linearly fused tricyclic core.[52]



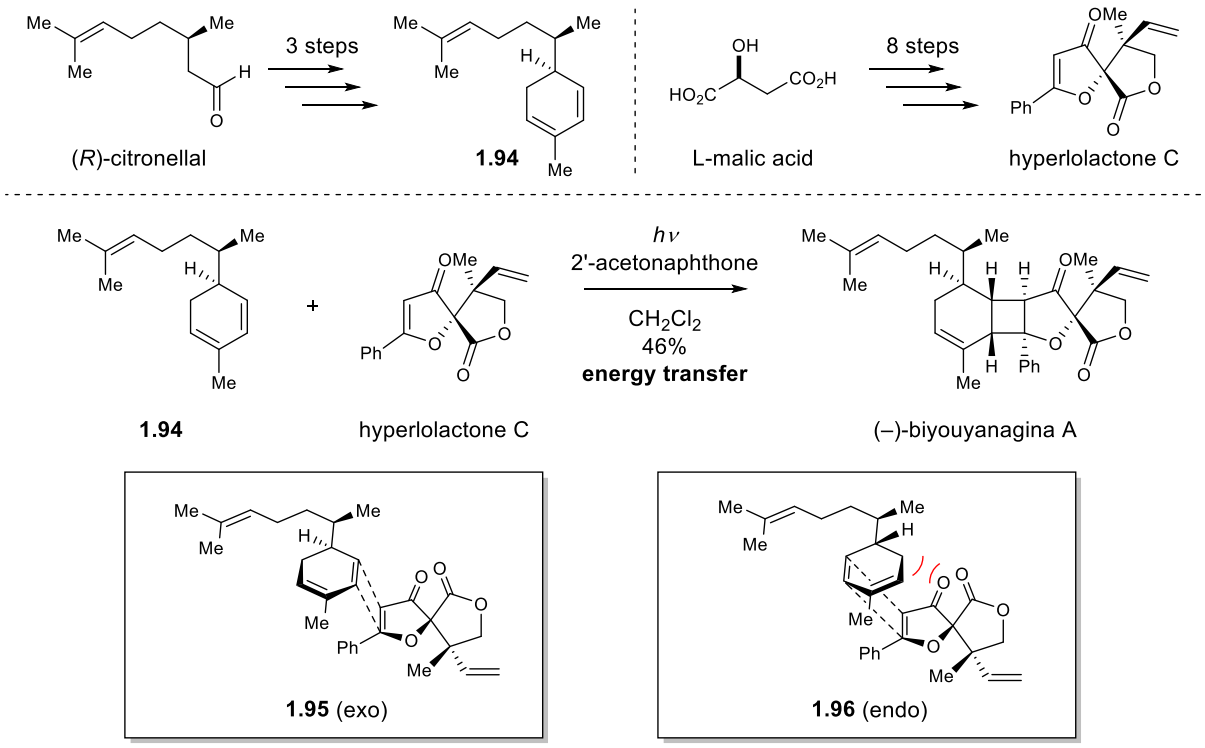

**Scheme 1.18.** Stereoselective intermolecular [2+2] photocycloaddition in the total synthesis of (+)-kelsoene

Intermolecular [2+2] photocycloadditions have also been implicated in biosynthetic pathways. One example of a biomimetic homodimerization can be found in Zhao's total synthesis of (+)-chloranthalactone F. The dimer is proposed to form biogenetically through an intermolecular [2+2] cycloaddition of enantiopure enol lactone **1.93** (Scheme 1.19). To test this hypothesis, the stereochemically-defined enol lactone **1.93** was synthesized from the enantiopure (*R*)-Hajos–Wiechert ketone. Irradiation of this photosubstrate indeed produced the desired dimer (+)-chloranthalactone F in 92% yield *via* regio- and stereoselective homodimerization.[53]



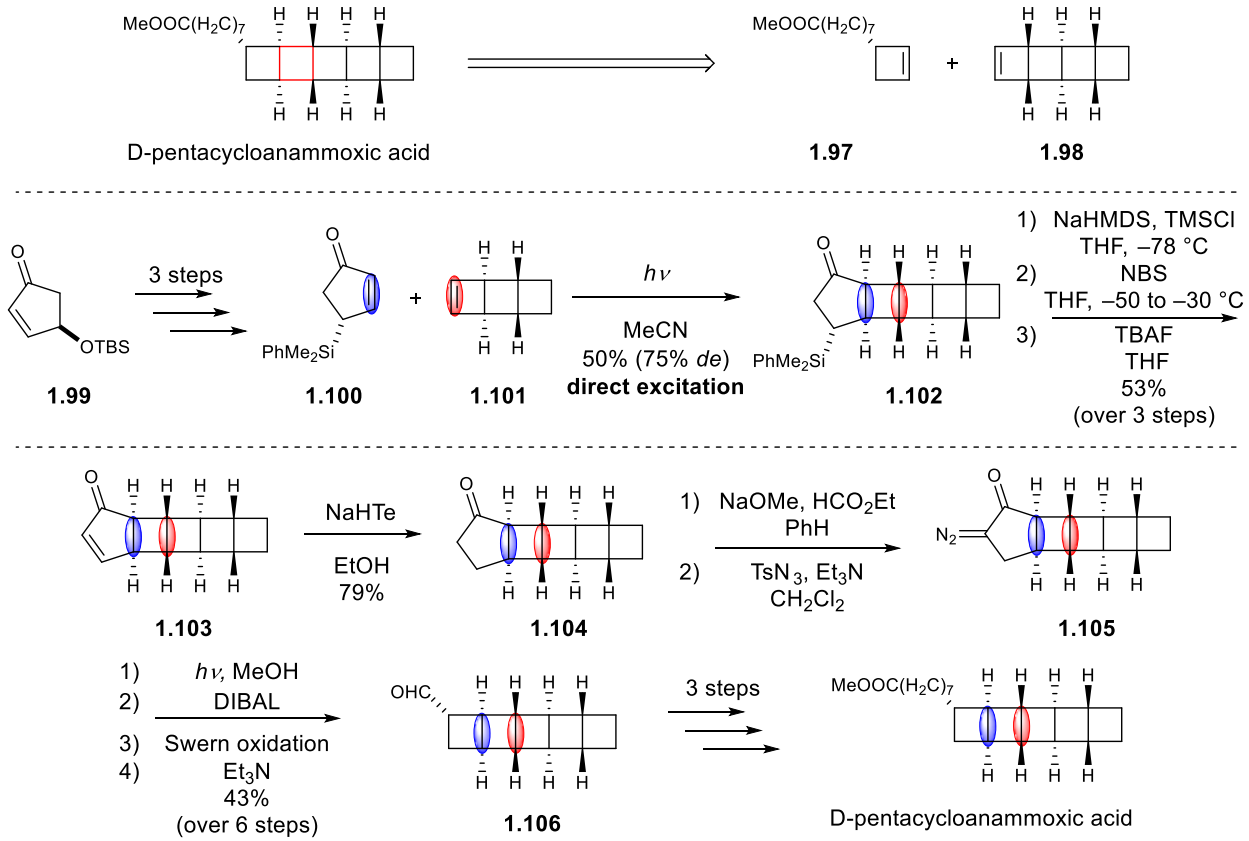

**Scheme 1.19.** Stereoselective intermolecular [2+2] photocycloaddition in the total synthesis of (+)-chloranthalactone F

A bioinspired intermolecular [2+2] photocycloaddition was also employed in the synthesis of (–)-biyouyanagina A. This annulated cyclobutane natural product has been proposed to biosynthetically arise from diene **1.94** and hyperlolactone C *via* a [2+2] photocycloaddition. To test this hypothesis, enantiopure alkene coupling partner **1.94** was synthesized from (*R*)-citronellal. The other photocycloaddition coupling component, hyperlolactone C, was synthesized starting from L-malic acid. The key acetonapthone-sensitized [2+2] photoinduced cycloaddition between the enantiopure fragments **1.94** and hyperlolactone C proceeded with high chemo-, regio-, and stereoselectivity, generating the desired cyclobutane (–)-biyouyanagin as the sole product. The authors speculated that high stereoselectivity is driven from steric constraints. The *exo* arrangement (**1.95**) should be favored over the *endo* arrangement (**1.96**) due to steric clash between the lactone and cyclohexadiene groups.[54] This result suggests that the stereoselectivity of intermolecular [2+2] photocycloadditions could be enhanced when both coupling partners are stereochemically well-defined.




**Scheme 1.20.** Stereoselective intermolecular [2+2] photocycloaddition in the total synthesis of (+)-biyouyanagina A

In the total synthesis of D-pentacycloanammoxic acid, a simple disconnection might involve a substrate-controlled stereoselective [2+2] photocycloaddition between enantiopure cyclobutene **1.97** and achiral cyclobutene **1.98** (Scheme 1.21). However, no methods to access **1.97** in enantioenriched form are available. Thus, Corey prepared photochemically active enone **1.100** from commercially available enantiopure cyclic enone **1.99**. The synthetic sequence involved a diastereoselective conjugate dimethylphenylsilylation, silyl deprotection, and alcohol dehydration. UV irradiation of this photosubstrate in the presence of cyclobutene **1.101** resulted in a [2+2] photocycloaddition, producing the desired diastereomer as the major product in 50% with 75% *de*. Treatment of **1.102** with NaHMDS followed by TMSCl generated the corresponding silyl enol ether, which was converted into enone **1.104** by an α-bromination-deprotection-reduction sequence. Subsequently, ketone **1.104** was further elaborated to the *exo* aldehyde **1.106** by the following transformations: (1) α-diazoketone formation using the Regitz method, (2) the pentacyclic ladderane methyl esters formation (*exo* + *endo*) by photoinduced Wolff ring contraction and trapping with methanol, (3) conversion of the ester group into an aldehyde by a reduction-oxidation sequence, (4) equilibration of the mixture (*exo* + *endo*) to the *exo* aldehyde. Further manipulations of **1.106** resulted in D-pentacycloanammoxic acid in three subsequent steps.[55]




**Scheme 1.21.** Stereoselective intermolecular [2+2] photocycloaddition in the total synthesis of D-pentacycloanammoxic acid enabled by a chiral auxiliary

Indeed, stereoselective intermolecular [2+2] photocycloadditions have been successfully applied in a wide range of annulated-cyclobutane-containing natural products that can be disconnected to simpler alkenes, where at least one alkene is chiral. However, a large portion of naturally occurring cyclobutanes (Figure 1.1) are most simplistically derived from achiral alkene subunits, rendering substrate-controlled stereoselective [2+2] photocycloadditions inherently impossible. Thus, the use of chiral auxiliaries has been explored to overcome this inherent problem. In this regard, grandisol has become an important benchmark target by which the viability of new diastereoselective [2+2] photocycloadditions utilizing chiral auxiliaries can be validated.

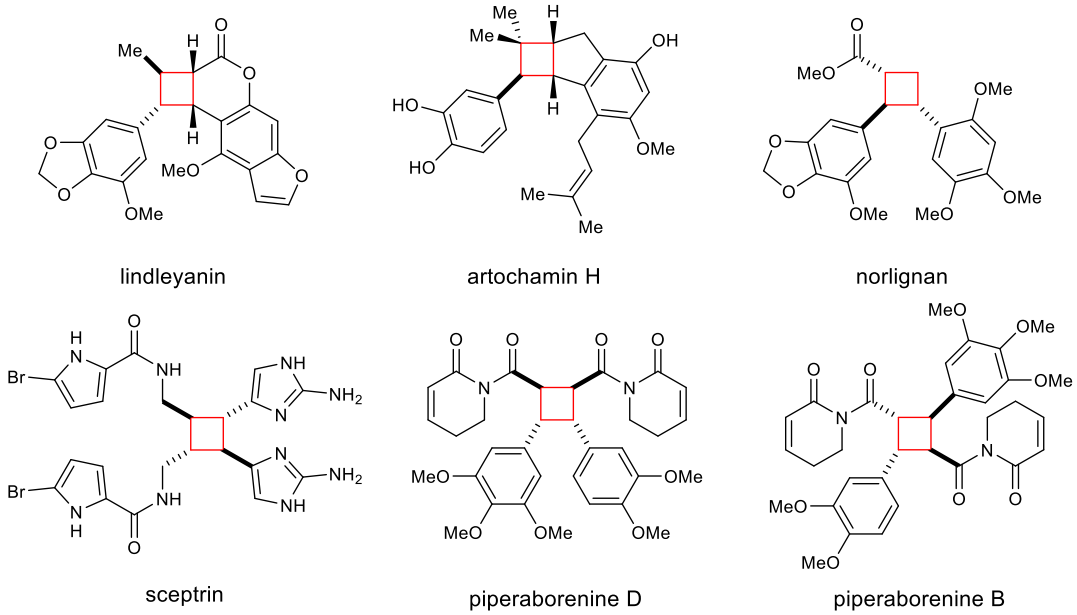
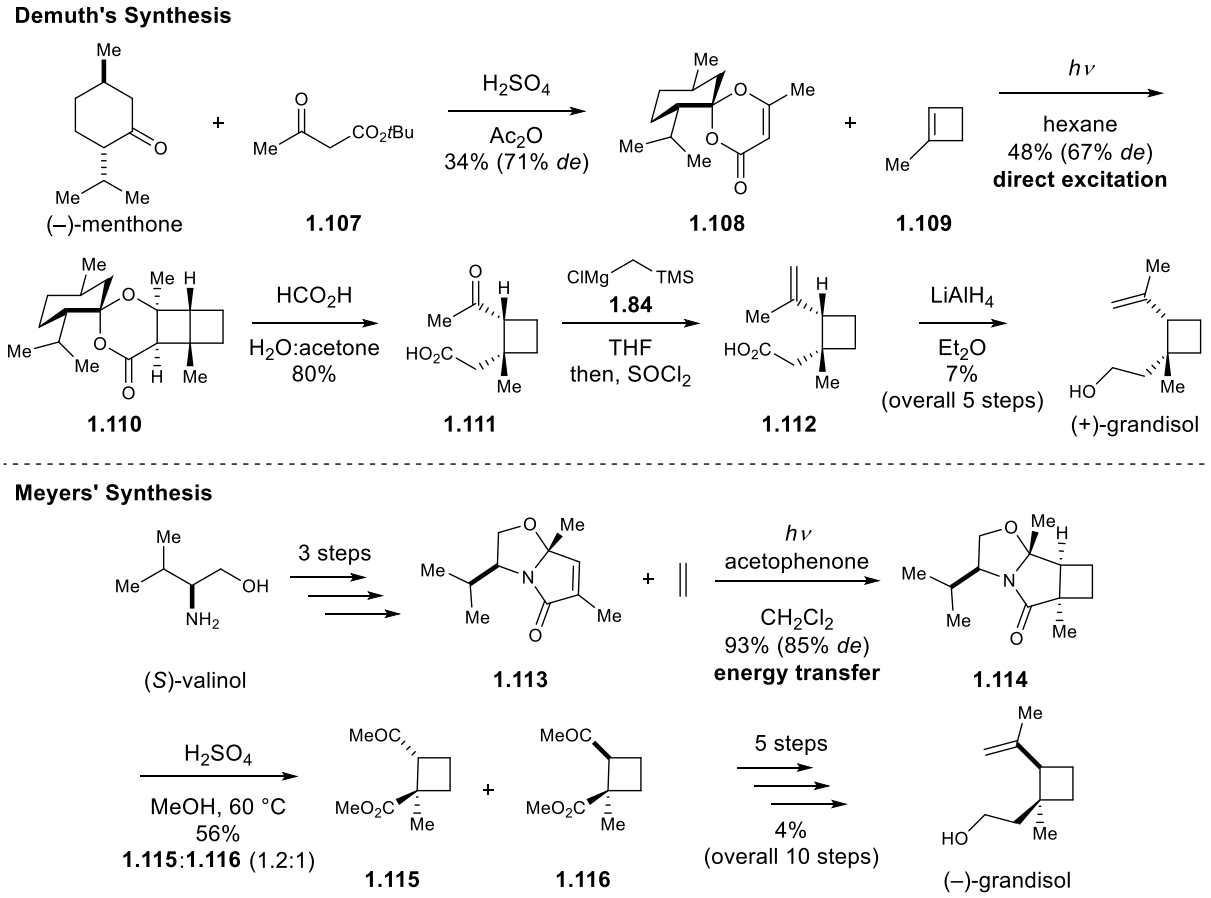


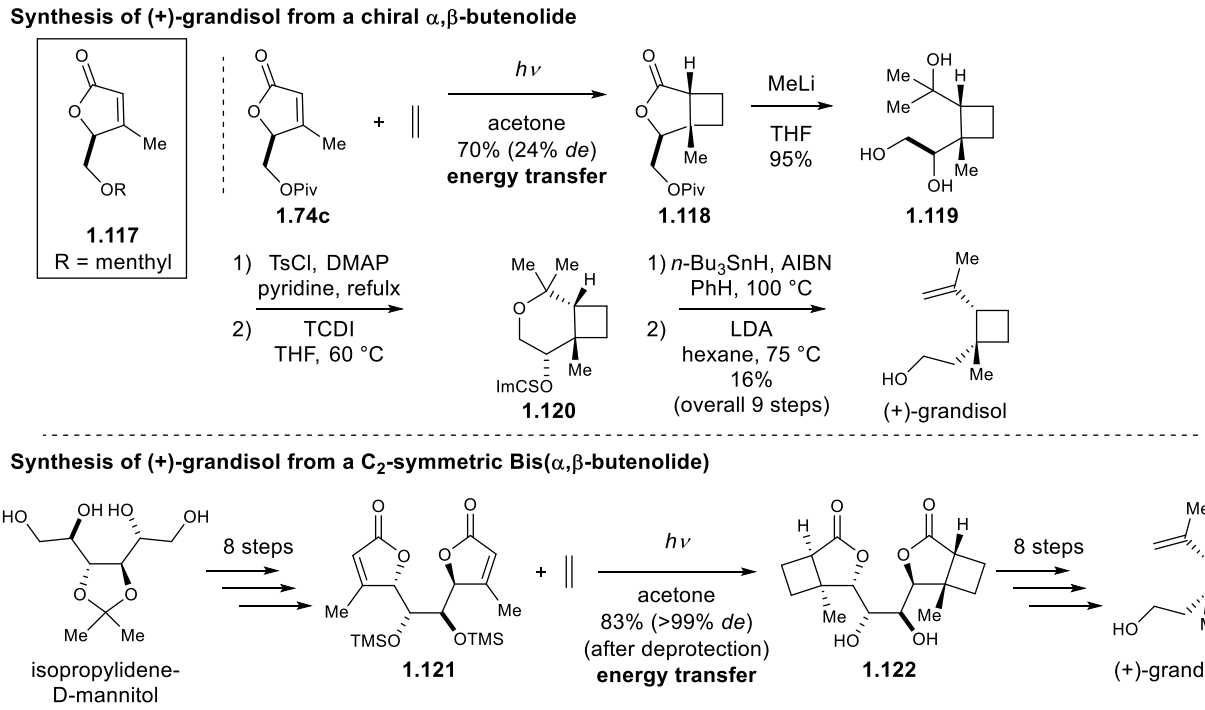

**Figure 1.1.** Representative monocyclic cyclobutane natural products

In 1986, the group of Demuth and Meyers independently synthesized grandisol in enantioenriched form leveraging a key asymmetric [2+2] photocycloaddition (Scheme 1.22). Initial attempts by Demuth employed (–)-menthone as a chiral auxiliary, which provided good stereocontrol for intermolecular photocycloaddition with 1-methylcyclobutene at –78 °C. Since 1-methylcyclobutene is unsymmetrical, this strategy suffered from poor regioselectivity. Nevertheless, after separation of the constitutional isomers and diastereomers, treatment of the desired isomer **1.110** with formic acid removed the auxiliary group to afford **1.111**, which was converted into (+)-grandisol by a methylenation-reduction sequence.[56] In Meyers' synthesis, (*S*)-valinol was employed as a chiral auxiliary, which provided much higher diasterecontrol utilizing an acetophenone-sensitized photocycloaddition with ethylene. However, the conditions used to remove the auxiliary induced epimerization to afford the desired diastereomer **1.116** as the minor product. Nevertheless, **1.116** was further elaborated to (–)-grandisol in five steps.[57] Although the proof of concept of this approach was established, the overall yields suffered from poor regioselectivity in Demuth's synthesis and facile epimerization in Meyers' synthesis.



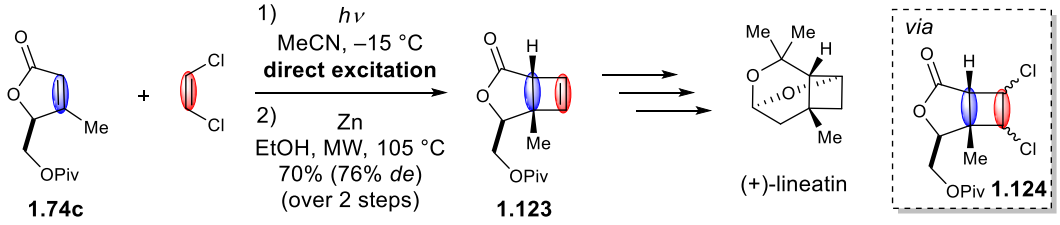

**Scheme 1.22.** Stereoselective intermolecular [2+2] photocycloaddition in the total synthesis of grandisol enabled by a chiral auxiliary

In the 1990's, the groups of Scharf and Font independently synthesized (+)-grandisol using a strategy to avoid the previously reported complications. Enantiopure 5-substitued 4-methyl-2(5*H*)-furanone **1.74c**, derived from commercially available **1.78** in three steps, was employed to control stereoselectivity for acetone-sensitized [2+2] photocycloaddition with ethylene (Scheme 1.23). Unfortunately, irradiation of **1.117** afforded the desired **1.118** with poor facial selectivity. Nonetheless, reaction of **1.118** with MeLi yielded the triol **1.119**, which underwent subsequent cyclization and thiocarbonylation to **1.120**. Barton-McCombie deoxygenation and base-catalyzed ring opening afforded (+)-grandisol.[58] A similar strategy has been applied by Scharf using menthyl protected butanolide **1.117**, which provided similar diastereocontrol as **1.74c**.[59] Although these routes provide higher overall yields by avoiding regioselectivity and epimerization, **1.74c** and **1.117** failed to provide good facial selectivity.




**Scheme 1.23.** Stereoselective intermolecular [2+2] photocycloaddition in the total synthesis of grandisol enabled by chiral butenolides

In 1999, Font's group reported a full study on the stereoselective [2+2] photocycloaddition of the butanolide fragment, which included their efforts to improve the facial discrimination. They found that while $C_2$-symmetric bis-butenolides **1.121** resulted in improved selectivity, this strategy yielded a substantially longer synthesis owing to installing and removing of the auxiliary group. More recently, in 2004, Alibes and Font disclosed that **1.74c** exhibits better selectivity when treated with (Z)-1,2-dichloroehtylene (**Scheme 1.24**). This strategy was employed for the synthesis of (+)-lineatin which is structurally and biologically related to grandisol.[61]

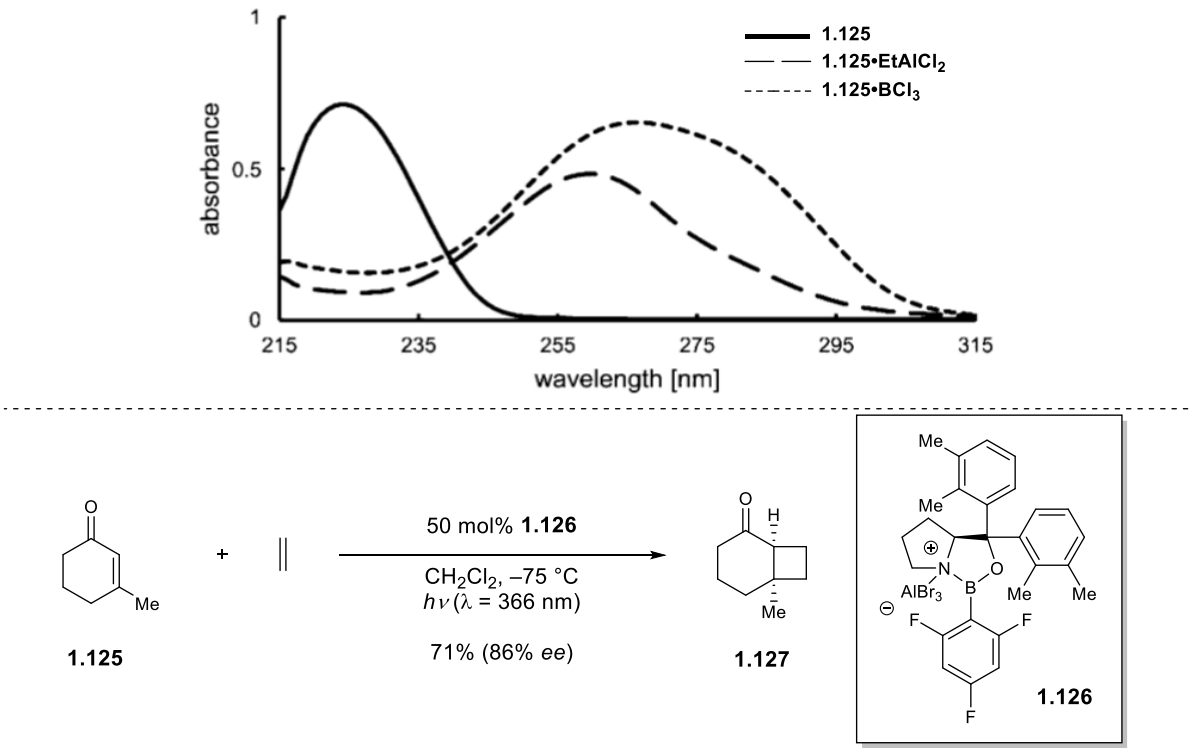



**Scheme 1.24.** Stereoselective intermolecular [2+2] photocycloaddition in the total synthesis of (+)-lineatin enabled by a chiral butanolide

## 1.3 Catalyst-Controlled Stereoselective [2+2] Photocycloaddition in Total Synthesis

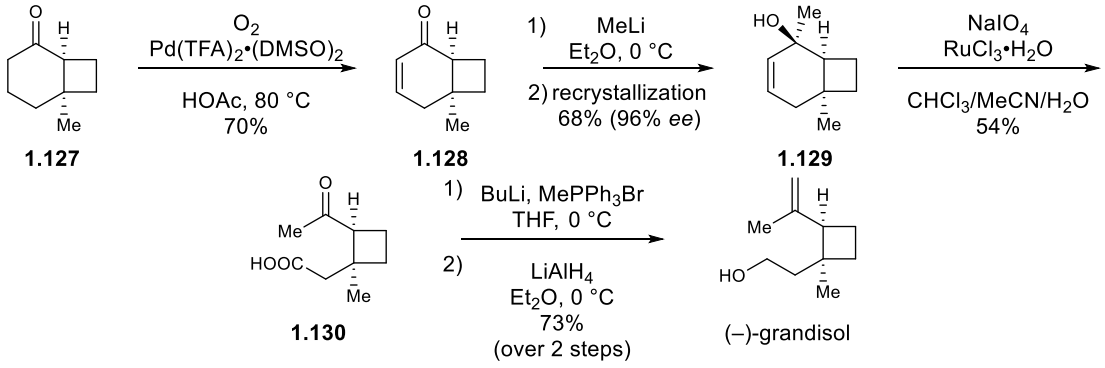
Although there are numerous elegant asymmetric syntheses of natural products wherein substrate-controlled stereoselective [2+2] photocycloadditions have been applied as a key step, this strategy has been mainly applied toward the synthesis of annulated-cyclobutane-containing natural products. A large portion of naturally occurring cyclobutanes that are not annulated (Figure 1.1) and could be concisely synthesized *via* catalyst-controlled enantioselective [2+2] photocycloaddition of two achiral alkenes. Successful implementations of substrate-controlled [2+2] photocycloaddition reactions in total syntheses of such natural products has been demonstrated using chiral auxiliaries. However, this strategy often results in longer syntheses due to the construction and subsequent removal of chiral auxiliaries which could be avoided by utilizing catalyst-controlled strategies. This gap in methodology has been identified by the synthetic community and has recently become the focus of study. As such, general catalyst-controlled enantioselective [2+2] photocycloaddition strategies that can be applied toward total synthesis have begun to emerge in recent years.

The key to achieving high sterecontrol in a [2+2] photocycloaddition is ensuring that the reaction occurs exclusively within a chiral environment. This simplest approach towards stereocontrol involves catalyst-enabled photoexcitation, which precludes uncatalyzed, racemic background reactivity. Bach has reported the enantioselective intramolecular [2+2] photocycloaddition of cyclic enone **1.125** using chiral oxazaborolidine Lewis acid **1.126** (Scheme 1.25). In this report, the absorbance properties of **1.125** undergo a bathochromic shift in the presence of either $EtAlCl_2$ or $BCl_3$. Because it was expected that **1.126** would exert an even stronger bathochromic shift than $BCl_3$. Thus, the authors hypothesized that the chiral Lewis acid-bound substrate complex would be selectively irradiated at long wavelengths to accomplish an enantioselective [2+2] photocycloaddition. Indeed, irradiation of **1.125** at 366 nm in the presence of chiral Lewis acid **1.126** produced cyclobutane **1.127** in excellent yield and enantioselectivity. A subsequent



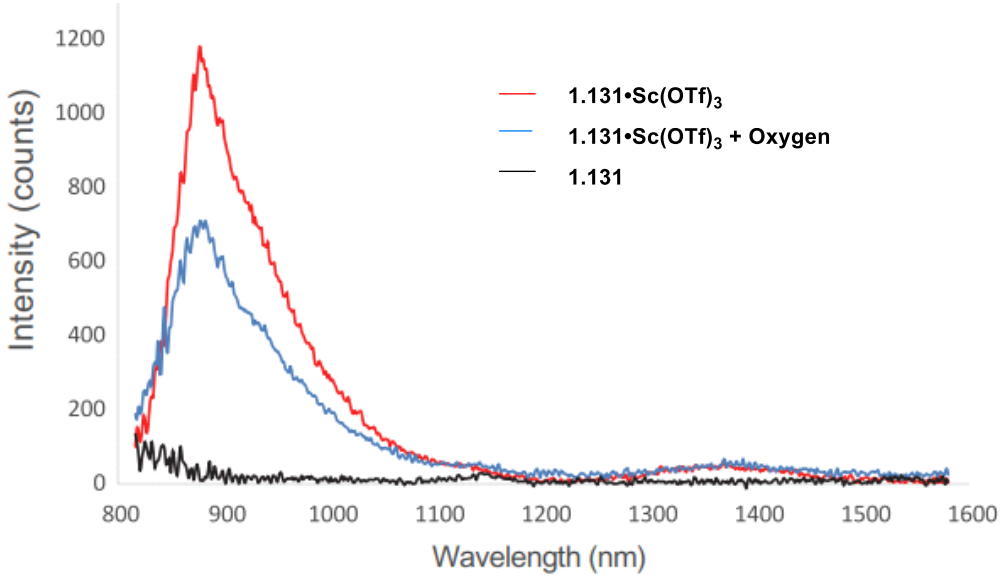

**Scheme 1.25.** Enantioselective [2+2] photocycloaddition enabled by selective irradiation

Saegusa oxidation of cycloadduct **1.127** afforded enone **1.128**, which was converted to allylic alcohol **1.129** by stereoselective methylation. At this stage, enantiopurity could be enhanced by recrystallization. Oxidative cleavage of alkene **1.129** produced ketone **1.130**, which was subsequently converted into (–)-grandisol *via* an olefination/reduction sequence. Starting from 3-methyl-2-cyclohexenone, this synthesis occurred in only six steps with an overall yield of 13% and thus represents a concise route to the enantiopure natural product.[62]



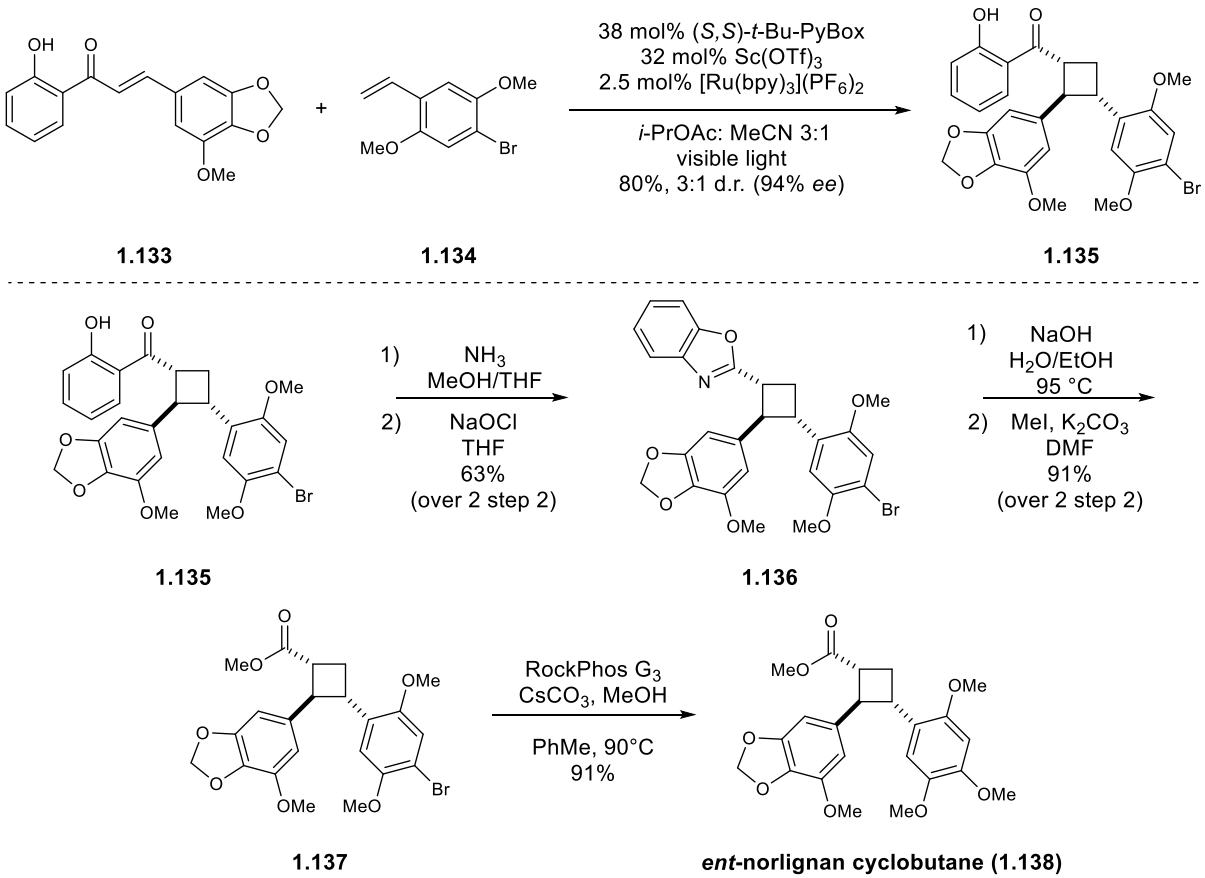

**Scheme 1.26.** Enantioselective [2+2] photocycloaddition in the total synthesis of (–)-grandisol

A complementary enantioselective [2+2] photocycloaddition strategy was developed by Yoon. Here, the authors discovered that the triplet energy of chalcone **1.131** (45 kcal/mol) is lowered in the presence of Lewis acids. Upon coordination of $Sc(OTf)_3$, a significant bathochromic shift in the emission of the chalcone to 876 nm indicates that the triplet energy of the **1.131**•$Sc(OTf)_3$ complex is reduced to 33 kcal/mol, consistent with a computational prediction (Scheme 1.27). Notably, the emission feature at 876 nm is partially quenched in the presence of oxygen, consistent with emission from a triplet state. Taking an advantage of this dramatic bathochromic shift, the authors developed a successful enantioselective [2+2] photocycloaddition between **1.131** and butadiene *via* catalyzed triplet energy transfer to a chiral Sc•**1.131** complex catalyzed by $[Ru(bpy)_3](PF_6)_2$ ($E_T$ = 46 kcal/mol). In this reaction, the phenol moiety serves as an auxiliary group to form a chelate with Lewis acid, thereby enforcing high enantioselectivity.[63]




**Scheme 1.27.** Enantioselective [2+2] photocycloaddition enabled by selective triplet energy transfer

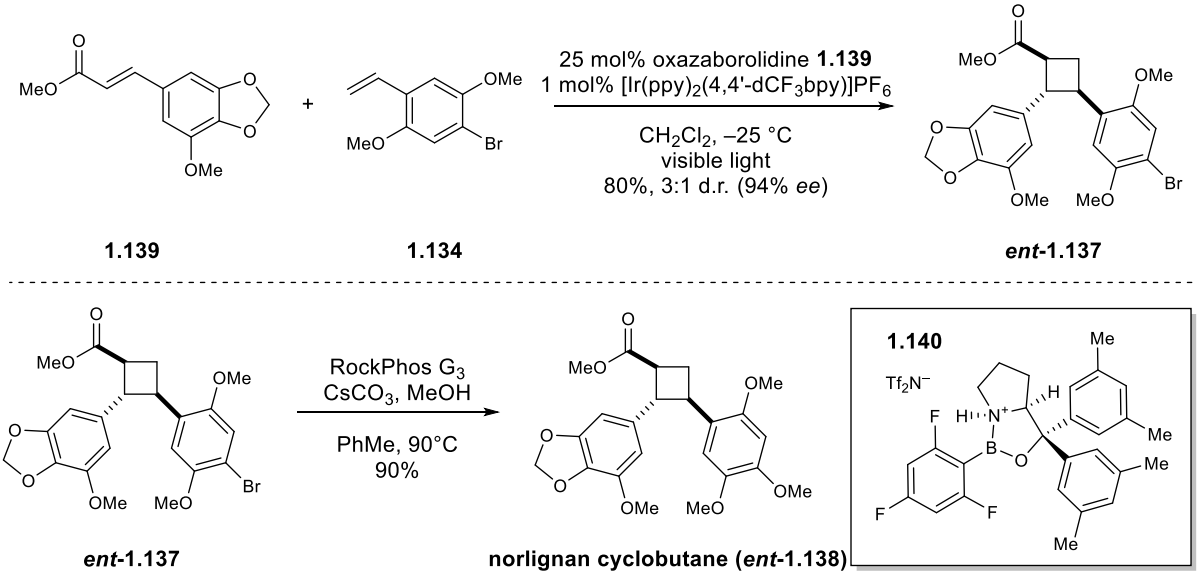
The authors envisioned this strategy could be utilized in the total synthesis of norlignan natural product **1.135** (Scheme 1.28). Thus, the cycloaddition of two achiral synthons **1.133** and **1.134** afforded cyclobutane **1.135** in 80% with 94% *ee*. Brominated styrene **1.134** was used because the fully elaborated styrene for the norlignan underwent deleterious acid-catalyzed polymerization. A subsequent condensation-*N*-chlorination-Beckmann rearrangement sequence provided benzoxazole **1.136**, which could be further converted to methyl ester **1.137** *via* hydrolysis and methylation. Elaboration to the reported structure of the natural product was accomplished by a Pd-catalyzed Buchwald aryl etherification.[64] This study demonstrated the overall feasibility of utilizing a catalyst-controlled enantioselective [2+2] photocycloaddition for the total synthesis of a cyclobutane natural product.




**Scheme 1.28.** Enantioselective [2+2] photocycloaddition in the total synthesis of *ent*-norlignan cyclobutane (**1.138**)

Because this strategy required an auxiliary group for a good chiral induction, Yoon and co-workers were inspired to develop an alternative strategy to synthesize norlignan directly. Here, similar lowering of

triplet energy strategy by Lewis acid was applied to furnish photoadduct ***ent*-1.137** in 80% yield with 94% *ee* from two achiral synthons **1.139** and **1.134**. Interestingly, thorough mechanistic studies showed that the rate of energy transfer could also be accelerated by increase in electronic coupling between the triplet donor and acceptor. Nevertheless, a subsequent Pd-catalyzed Buchwald etherification provided norlignan cyclobutane (***ent*-1.138**) in 91% yield.[65] The ability to synthesize an enantiopure cyclobutane natural product in only two steps with an overall yield of 54% from two appropriate alkene fragments clearly highlights the powerful features of catalyst-controlled enantioselective [2+2] photocycloaddition.




**Scheme 1.29.** Enantioselective [2+2] photocycloaddition in the total synthesis of norlignane cyclobutane (***ent*-1.138**)

## 1.4 Conclusions and Outlook

The purpose of this review has been to highlight some of the accomplishments that have been presented in asymmetric synthesis of cyclobutane natural products using [2+2] photocycloaddition. Both intra- and intermolecular substrate-controlled [2+2] photocycloadditions have proven to be highly useful for construction of annulated cyclobutane natural products. Moreover, these strategies have been extended to the synthesis of monocyclic natural products. However, these strategies require the use of chiral auxiliaries or complex biased intramolecular systems, which result in substantially increased longest linear sequences (LLS). Recent advances gaining absolute control over the products formed from an excited state [2+2]

photocycloaddition display great promise in the field of cyclobutane synthesis. These methods enable retrosynthetic disconnections previously viewed as not viable pathways. Utilizing catalyst control to drive reaction outcomes will massively decrease the synthetic barrier to cyclobutane natural products, eliminating the need for chiral auxiliaries and complex biased intramolecular systems. In the future, it will expand our classical chemical toolbox by offering improved LLS and overall yield for naturally occurring cyclobutane products.

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# Chapter 2. Catalytic Enantioselective Photochemical [2+2] Cycloadditions as Valuable for the Synthesis of Naturally Occurring Cyclobutanes

Portions of this work have previously been published.

Miller, Z. D.; Lee, B. J.; Yoon, T. P. "Enantioselective Crossed Photocycloadditions of Styrenic Olefins by Lewis Acid Catalyzed Triplet Sensitization" *Angew. Chem., Int. Ed.* **2017**, *56*, 11891−11895.

Daub, M. E.; Jung, H.; Lee, B. J.; Won, J.; Baik, M.-H.; Yoon, T. P. "Enantioselective [2 + 2] Cycloadditions of Cinnamate Esters: Generalizing Lewis Acid Catalysis of Triplet Energy Transfer" *J. Am. Chem. Soc.* **2019**, *141*, 9543−9547.

## 2.1 Introduction

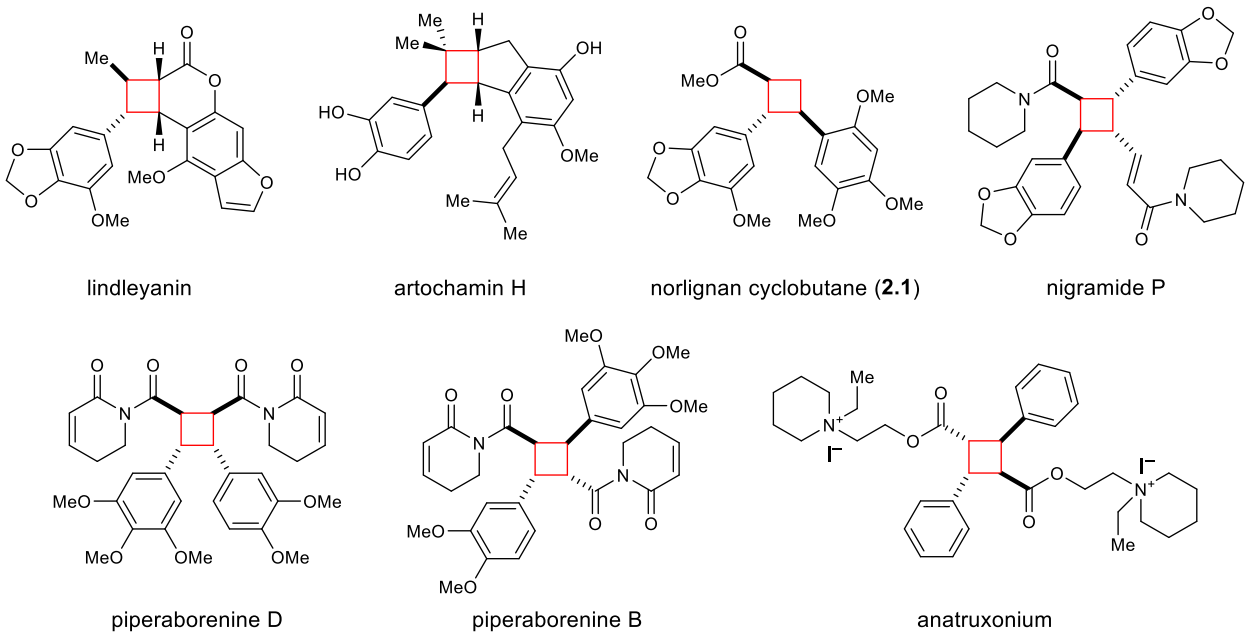
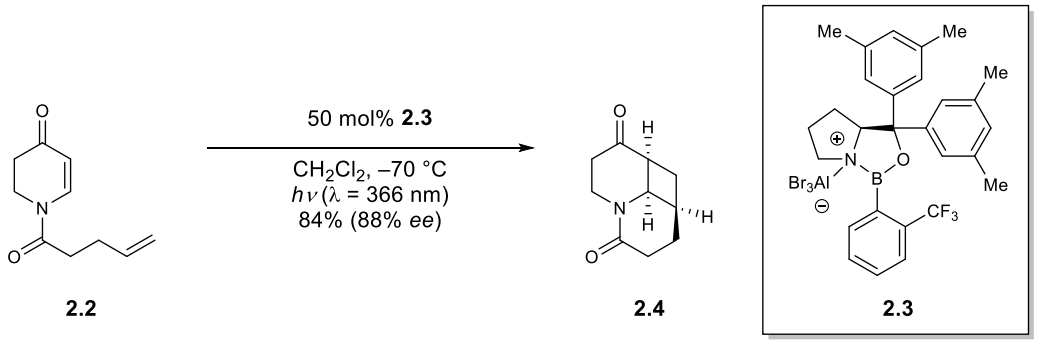



**Figure 2.1.** Representative cyclobutane natural products

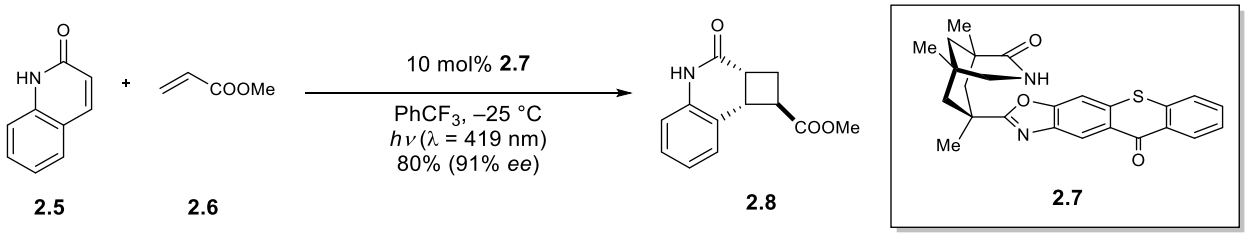
Cyclobutanes represent a structural motif found in over 2,000 natural products, many of which possess interesting biological activities.[1–4] As shown in Figure 2.1, naturally occurring cyclobutanes commonly feature dense substitution patterns with high degree of stereochemical complexity. Moreover, diarylcyclobutanes feature prominently as key structure elements of a significant subset of these compounds.[2,3] The most direct synthetic strategies for these scaffolds would involve the homo- or cross-[2+2] photocycloaddition of two alkenes. However, useful asymmetric photochemical methods involving the union of two alkenes remain scarce. As mentioned in the preceding chapter, one significant challenge is suppressing racemic background reactivity while enabling a reaction to occur exclusively in the chiral environment of a stereodifferentiating catalyst.[5] In addition, the short lifetimes of excited state intermediates in solution are problematic due to the existence of numerous potential deactivation and vibrational relaxation pathways.[6] As a consequence, there are only a limited number of highly enantioselective photochemical reactions that have been reported to date.[7–16]

Prior to 2016, only three mechanistically distinct strategies to conduct highly enantioselective [2+2] cycloaddition reactions had been reported. First, Bach demonstrated that chiral oxazaborolidine Lewis acids could stabilize excited state intermediates while significantly altering the absorptive properties of cyclic enones (Scheme 2.1).[10] This strategy effectively avoids racemic background pathways as the light energy channeled only to the chiral absorbing entity upon irradiation with a monochromatic light source. Although this strategy accomplished enantioinduction, only a relatively small set of substrates underwent Lewis acid promoted spectral shift sufficient for high enantioselectivity, and this methodology has not been applied to an intermolecular reaction.



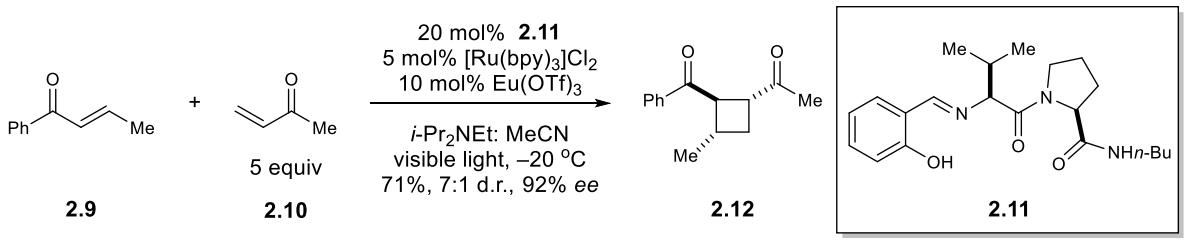

**Scheme 2.1.** Enantioselective [2+2] photocycloaddition *via* selective excitation

Second, the application of a chiral triplet sensitizer to asymmetric intermolecular [2+2] photocycloadditions has also been successfully developed (Scheme 2.2).[16] In this case, chiral triplet sensitizer **2.7** preassociates with quinolone (**2.5**) to give a bound complex where one enantioface is shielded by the planar thioxanthone. The thioxanthone moiety of the complex also acts as a light-harvesting antenna, which transmits the triplet energy to the bound quinolone to promote an intermolecular asymmetric [2+2] photocycloaddition with electron-deficient alkenes. However, this reaction was limited to quinolone substrates, required large excesses (50 equivalents) of the acceptor, and was limited in the alkene scope.



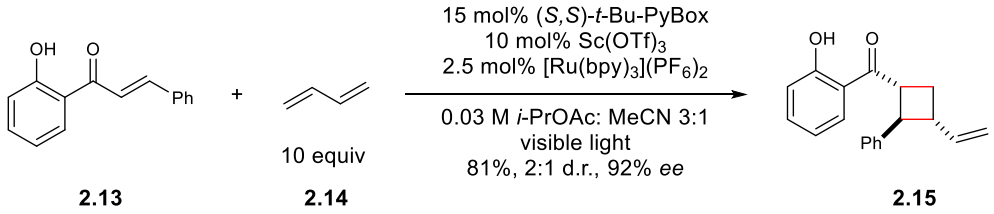
**Scheme 2.2.** Enantioselective [2+2] photocycloaddition catalyzed by chiral triplet sensitizer **2.7**

Third, our group developed the first example of asymmetric [2+2] photocycloaddition using acyclic enone substrates, relying on the chemistry of photogenerated radical anions (Scheme 2.3).[11] Chiral Lewis acid can change the redox properties of *trans*-crotonophenone (**2.9**), resulting in the selective reduction of the catalyst-bound substrate by $[Ru(bpy)_3]Cl_2$ upon irradiation. However, this strategy required crotonophenone substrates, and thus was not applicable to the synthesis of diarylcyclobutanes. Therefore, even though a variety of strategies have been developed, thus far they lack synthetic generality and thus have not been widely applied to the synthesis of cyclobutane natural products.




**Scheme 2.3.** Enantioselective [2+2] photocycloaddition *via* selective reduction

In 2016, our group developed an alternative strategy that relies on the ability of chiral Lewis acids to selectively lower the triplet energy of an enone substrate through coordination, which facilitates exergonic energy transfer from a racemic photosensitizer.[6] As shown in scheme **2.4**, the photosensitizer $[Ru(bpy)_3](PF_6)_2$ harvests visible light energy and transfers triplet energy, while the Lewis acid catalyst selectively "turns on" an asymmetric pathway and controls the facial selectivity in the bond-forming steps. Importantly, each co-catalyst operates in tandem without any deleterious effect on the other. This strategy effectively avoids the racemic background pathway as the energy transfer is only thermodynamically feasible with the catalyst-bound complex. The application of this dual catalysis strategy enabled intermolecular enantioselective [2+2] photocycloaddition of acyclic enones such as **2.13**. With the goal of adapting this strategy to the asymmetric synthesis of diarylcyclobutane natural products, we wondered if a wider range of alkenes could be used directly to access the scaffolds shown in Figure 2.1.




**2.13** **2.14** **2.15**

**Scheme 2.4.** Enantioselective [2+2] photocycloaddition *via* selective energy transfer

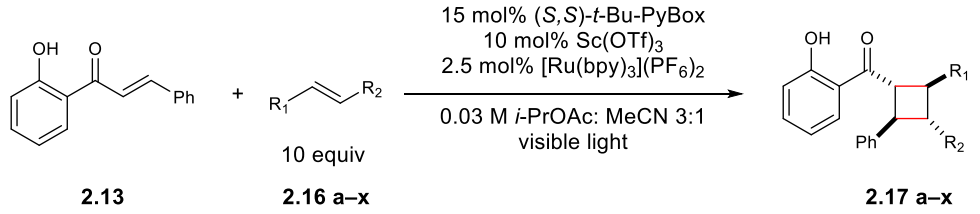
## 2.2 Results and Discussion

The enantioselective intermolecular photocycloaddition of chalcone **2.13** was chosen as a model system for the initial evaluation of coupling partners, utilizing the optimal conditions from Scheme **2.4**. To directly access structures similar to lindleyanin,[17] we chose coumarin (**2.16a**) as the first alkene substrate. Unfortunately, only trace amounts of **2.17a** were observed. On the other hand, [2+2] photocycloaddition of chalcone **2.13** with electron-rich chromene **2.16b** afforded the desired diastereomer **2.17b** as the major product, which upon oxidation would provide lindleyanin-like core **2.17a**. The structurally similar indene **2.16c**, which would form a cyclobutane that resembles artochamin H[18] provided the desired product **2.17c** in 89% yield with 3:1 d.r. It is important to note that diastereoselectivity of **2.17b** and **2.17c** are significantly different despite their structural similarity. Next, to access structures analogous to norlignan cyclobutane (**2.1**),[19] we explored a styrene (**2.16d**) as an alkene partner. Pleasingly, the desired [2+2] photocycloaddition afforded **2.17d** in excellent yield and modest diastereoselectivity. As shown in figure **2.1**, the vast majority of naturally occurring cyclobutanes are truxillate and truxinate products. Thus, we explored a methyl cinnamate **2.16e** as a coupling partner. Unfortunately, electron-poor **2.16e** did not give any desired product. Although β-methyl styrene (**2.16f**) furnished the desired diastereomer **2.17f** as the major product, conversion of **2.17f** to **2.17e** was not obvious.

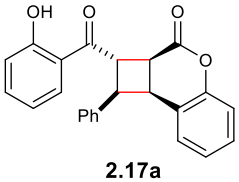
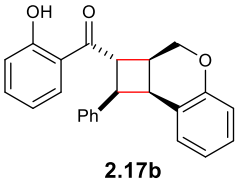
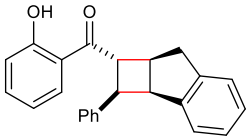
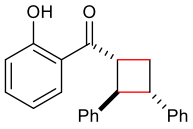
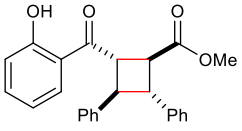
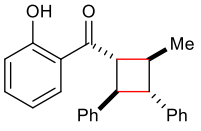
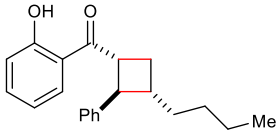
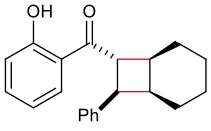
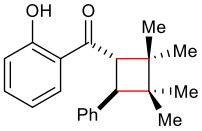
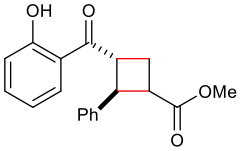
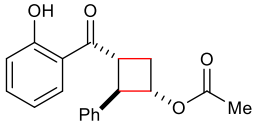
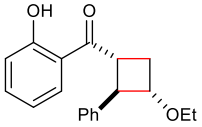
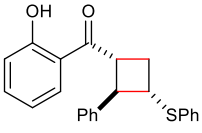
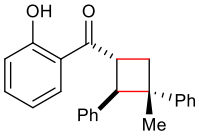
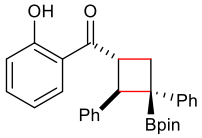
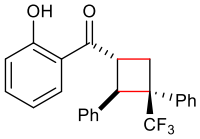
We also screened other coupling partners to investigate what features were responsible for good reactivity. Unactivated linear and cyclic alkenes (**2.16g**–**2.16i**) did not give any desired product. Using electron-poor methyl acrylate **2.16j**, only trace amounts of [2+2] product **2.17j** were formed. On the other hand, we observed no clear trend in reactivity by varying electron-rich alkene coupling partners (**2.16k**–**2.16m**). Although vinyl acetate **2.16k** only gave trace amounts of [2+2] product and ethyl vinyl ether **2.16l**

underwent polymerization instead of reacting with **2.13**, phenyl vinyl sulfide **2.16m** gave exclusively the [2+2] product with good yield. We next explored sterically hindered 1,1-disubstitued alkenes (**2.16n**–**2.16p**) to evaluate the steric effect on the reactivity. Interestingly, sterically crowded α- methyl styrene **2.16n** showed excellent reactivity, while sterically similar, but electronically more deficient styrenes **2.16o** and **2.16p** showed poor reactivity.

**Table 2.1.** Screen of alkene coupling partners for [2+2] photocycloaddition[a]

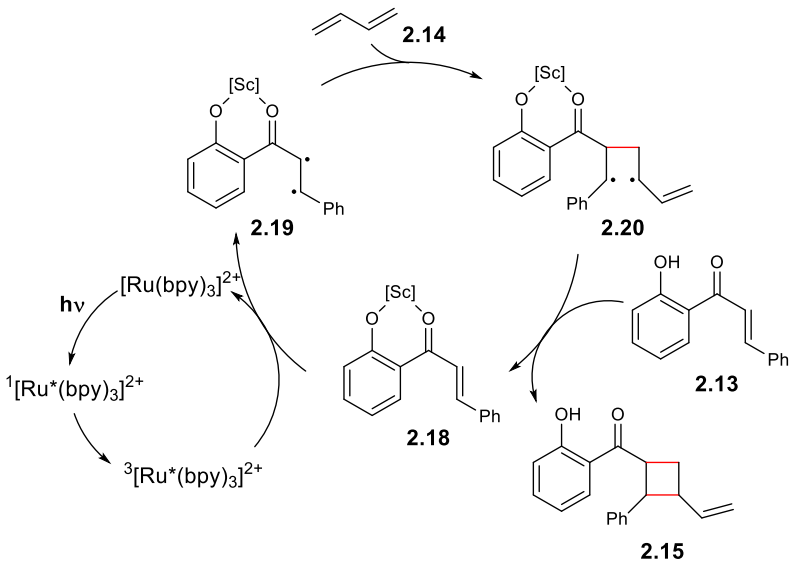



**2.13** **2.16 a–x** **2.17 a–x**

| | | | |
|---|---|---|---|
|  **2.17a** trace [2+2] |  **2.17b** 97%, >10:1 d.r. |  **2.17c** 89%, 3:1 d.r. |  **2.17d** 88%, 2:1 d.r. |
|  **2.17e** 0% |  **2.17f** 58%, 16:3:2:1 d.r. |  **2.17g** 0% |  **2.17h** 0% |
|  **2.17i** 0% |  **2.17j** trace [2+2] |  **2.17k** 0% |  **2.17l** 0% |
|  **2.17m** 86%, 1:1 d.r. |  **2.17n** 83%, 2:1 d.r. |  **2.17o** trace |  **2.17p** 0% |

a) Yields determined by $^{1}$H NMR analysis using phenanthrene as a calibrated internal standard.

In order to rationalize the results of the alkene screen we considered a mechanism based upon the previously proposed mechanism of triplet-state enone-alkene cycloadditions (Scheme 2.5). We speculated that the first bond formation was between the α-position of the enone and the terminal position of butadiene (**2.14)** to afford an intermediate biradical **2.20**. This key step was consistent with the empirical results of the alkene screen: alkene coupling partners that undergo productive [2+2] photocycloaddition would form stabilized 1,4-biradical intermediates such as **2.20**. Although there were some alkenes (**2.16a**, **2.16e**, **2.16o**, and **2.16p**) that would form equally stable 1,4-biradical intermediates, they nevertheless did not form the desired cyclobutanes. This trend could be explained by considering the degree of polarity matching between the coupling partners. We speculated that electrophilic α-carbonyl radical of **2.19** would preferentially react with electron-rich alkenes over electron-deficient alkenes. Therefore, highly electron-deficient alkenes would not participate in [2+2] photocycloaddition due to this electronic mismatch.

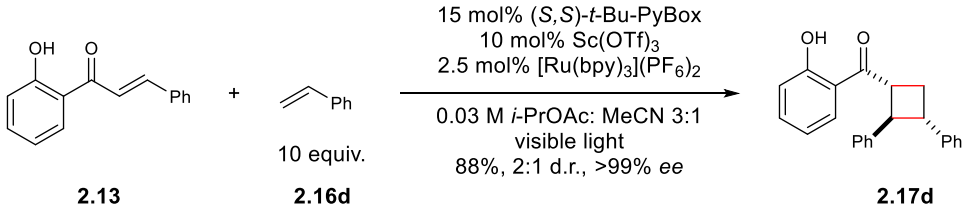



**Scheme 2.5.** Proposed mechanism of cycloadditions featuring Lewis acid catalyzed triplet sensitization

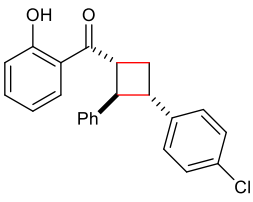
As an initial exploration of synthetic utility, we became interested in determining the scope of the enantioselective catalytic transformation with a sterically and electronically diverse range of styrenes. Styrenes bearing substituents at all positions of the aromatic ring reacted smoothly and with high ee values (**2.17q**–**2.17aa**). A variety of electron-withdrawing substituents on the styrene were readily

tolerated. These included an ester group (**2.17t**) whose Lewis basicity did not interfere with the action of the chiral Sc Lewis acid, and potentially UV-sensitive halide substituents (**2.17q**, **2.17r**, **2.17x**, **2.17z**) which

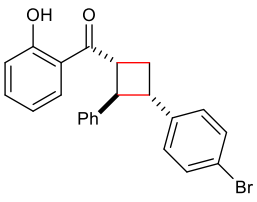
**Table 2.2.** Reaction scope with respect to styrenes[a]



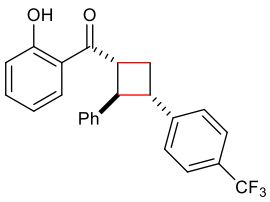

**2.13** **2.16d** **2.17d**



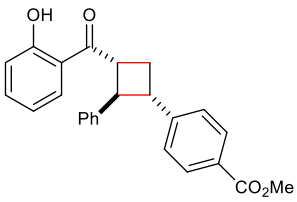
**2.17q** 97%, 3:1 d.r.
96% ee



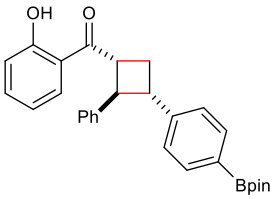
**2.17r** 91%, 2:1 d.r.
95% ee



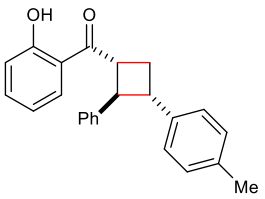
**2.17s** 91%, 2:1 d.r.
95% ee



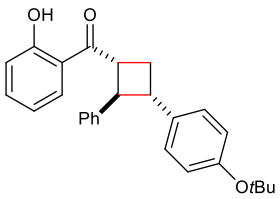
**2.17t** 77%, 2:1 d.r.
99% ee



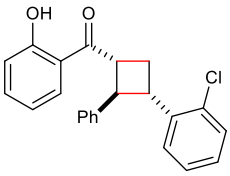
**2.17u** 87%, 2:1 d.r.
93% ee



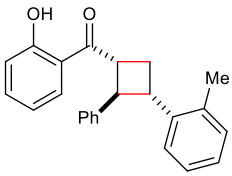
**2.17v** 86%, 2:1 d.r.
92% ee



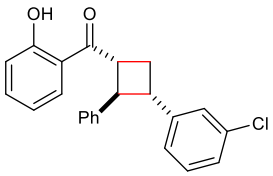
**2.17w** 87%, 2:1 d.r.
94% ee



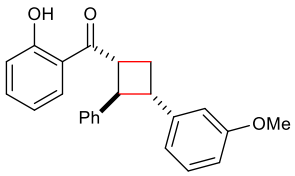
**2.17x** 82%, 4:1 d.r.
94% ee



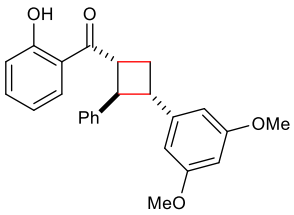
**2.17y** 87%, 2:1 d.r.
93% ee



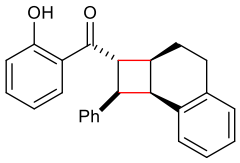
**2.17z** 82%, 4:1 d.r.
94% ee



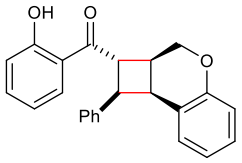
**2.17aa** 92%, 2:1 d.r.
93% ee



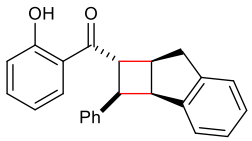
**2.21ab** 86%, 2:1 d.r.
90% ee



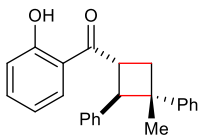
**2.17ac** 94%, >10:1 d.r.
96% ee



**2.17b** 97%, >10:1 d.r.
98% ee



**2.17c** 89%, 3:1 d.r.,
93% ee



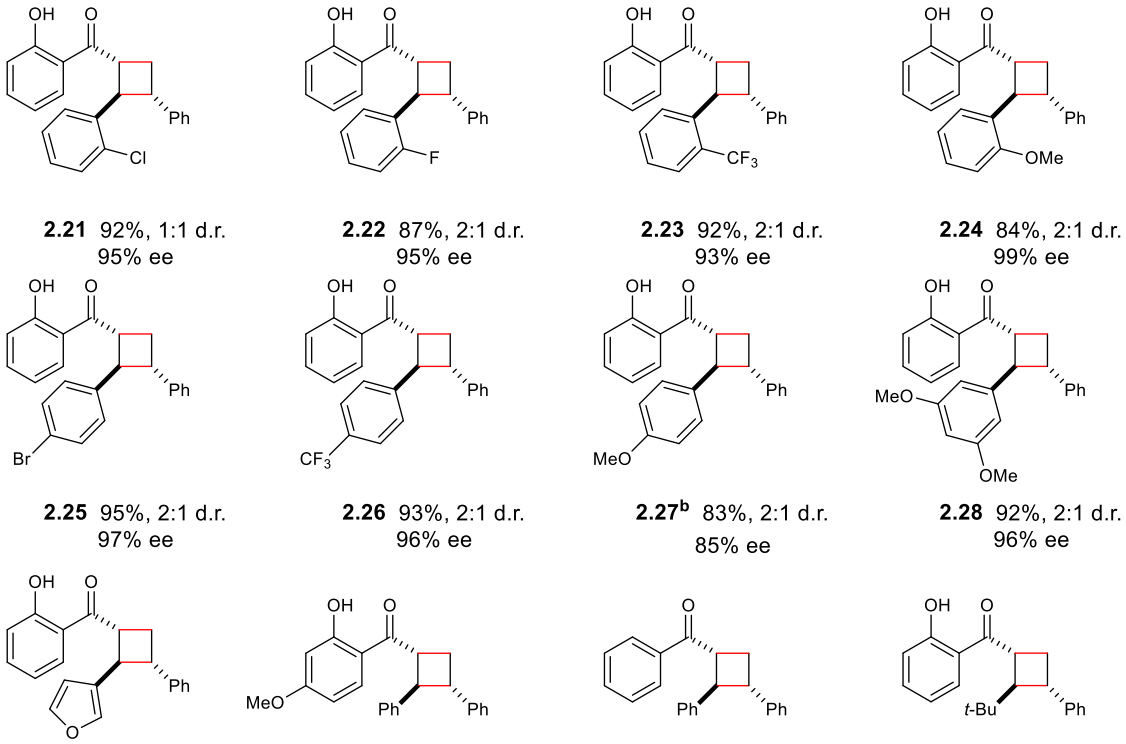
**2.17n** 83%, 2:1 d.r.
96% ee

a) Yields of isolated products are the averaged results of two reproducible experiments. Diastereomeric ratio were determined by 1H NMR analysis of the unpurified reaction mixtures. Enantiomeric excesses for the major diastereomer were determined by chiral-phase SFC.

survived irradiation without homolytic degradation. A boronate ester moiety was also readily tolerated (**2.17u**), providing a versatile handle for subsequent derivatization of the cycloadduct. A variety of electron-donating substituents could also be incorporated on all positions of the styrene ring (**2.17w**, **2.17aa**, **2.17ab**). Substituents on the styryl double bond were also tolerated (**2.17ac**, **2.17b**, **2.17c**, **2.17n**).

Next, we varied the structures of the 2-hydroxy chalcones. Chalcones bearing electronically varied β-aryl groups were readily tolerated and reacted with high ee values (**2.21**–**2.29**). As we observed in our study of cycloadditions with dienes, electron-rich 2'-hydroxychalcones exhibited modest levels of background cycloaddition with near-UV irradiation, a feature which can lead to diminished ee values using a broad-spectrum CFL light source.[6] Thus, while the β-*p*-methoxyphenyl cycloadduct **2.27** was formed with relatively modest ee value using the standard protocol (70% ee), the selectivity could be improved to 85% ee by irradiation with a monochromatic blue LED. The 2-acylphenol moiety of the substrate could be modified without eroding the high degree of enantioselectivity and reactivity (**2.30**). However, the chelating phenolyl moiety was required for optimal results. The unsubstituted chalcone itself provided low yields and low ee values (**2.31**), which was suggestive of a diminished propensity to bind to the Lewis acid and thus poorer organization of this monodentate substrate around the $Sc^{III}$ center. Finally, replacement of the β-aryl moiety with an aliphatic group afforded no reactivity (**2.32**). Presumably, the less extensive conjugation of this substrate shifts the triplet energy of its Lewis acid complex outside of the range accessible by using $Ru(bpy)_3^{2+}$ as a triplet sensitizer.

**Table 2.3.** Reaction scope with respect to chalcones[a]




**2.21** 92%, 1:1 d.r.
95% ee

**2.22** 87%, 2:1 d.r.
95% ee

**2.23** 92%, 2:1 d.r.
93% ee

**2.24** 84%, 2:1 d.r.
99% ee

**2.25** 95%, 2:1 d.r.
97% ee

**2.26** 93%, 2:1 d.r.
96% ee

**2.27**[b] 83%, 2:1 d.r.
85% ee

**2.28** 92%, 2:1 d.r.
96% ee

**2.29** 42%, 2:1 d.r.
94% ee

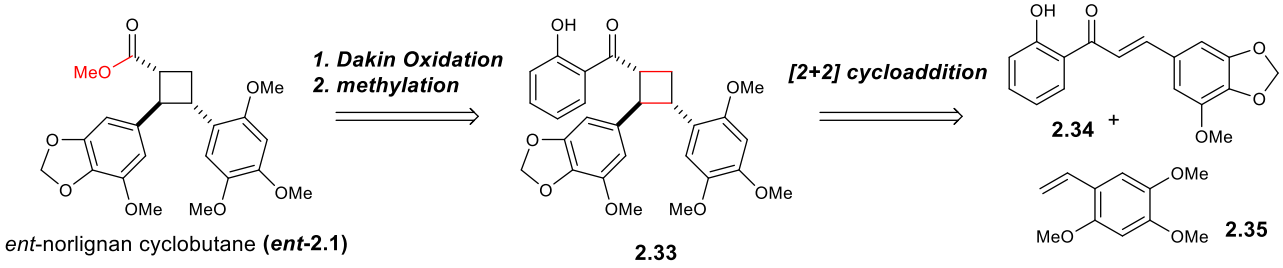
**2.30** 95%, 2:1 d.r.
90% ee

**2.31**[c] 18%, 2:1 d.r.
17% ee

**2.32**[c] 0%

a) Yields of isolated products are the averaged results of two reproducible experiments. Diastereomeric ratio were determined by 1H NMR analysis of the unpurified reaction mixtures. Enantiomeric excesses for the major diastereomer were determined by chiral-phase SFC. b) Reaction was irradiated with monochromatic high-intensity blue LED. c) Yields determined by 1H NMR analysis using phenanthrene as a calibrated internal standard.

Having shown that this strategy could tolerate a wide range of styrenes and chalcones, we anticipated that the direct synthesis of *ent*-norlignan cyclobutane (***ent*-2.1**) could be feasible *via* our newly developed enantioselective [2+2] photocycloaddition followed by cleaving the phenol auxiliary group (Scheme 2.6).

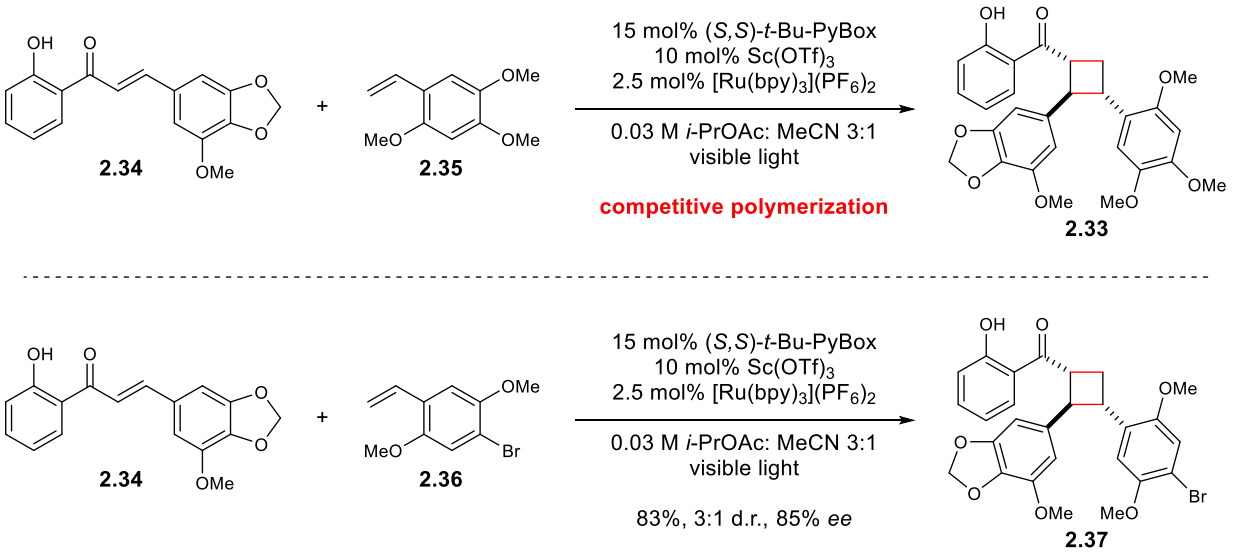



*ent*-norlignan cyclobutane (***ent*-2.1**)

**2.33**

**Scheme 2.6.** Retrosynthetic analysis of *ent*-norlignan cyclobutane (***ent*-2.1**)

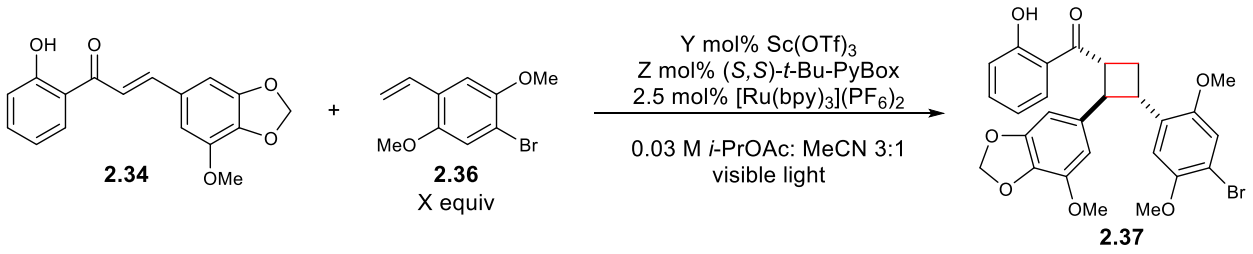
Under the standard [2+2] photocycloaddition conditions with **2.34** and the tri-methoxylated styrene **2.35** *en route* to cyclobuatne ***ent*-2.1**, it was found that the styrene undergoes polymerization. We hypothesized that the significantly less activated brominated analogue **2.36** would undergo the desired cycloaddition with **2.37** without polymerization. Indeed, **2.36** underwent cycloaddition with a good yield but disappointingly 85% ee. Unfortunately, unlike the simpler example, changing the light source to a monochromatic blue LED did not improve the enantioselectivity.




**Scheme 2.7.** Initial attempt to construct the cyclobutane core *via* [2+2] photocycloaddition

We speculated that this might be a consequence of a competitive racemic pathway; indeed, when the Lewis acid was omitted from this reaction, the racemic cycloadduct was formed in 25% yield without any remaining starting material. We hypothesized that this background reactivity could be minimized by adding more chiral Lewis acid if the intrinsic enantioselectivity was high. To confirm this hypothesis, an experiment with a stoichiometric amount of Lewis acid was conducted and revealed its high enantioselectivity by affording cyclobutane **2.37** in 95% ee (entry 3). It is noteworthy that 4 equivalents of **2.36** could be used instead of 10 equivalents without having any deleterious effect on yield or enantioselectivity (entry 2). With further optimization, we found that 30 mol% of $Sc(OTf)_3$ and 36 mol% of (*S*,*S*)-*t*-Bu-PyBox with 1.5 equivalents of **2.36** could be used without sacrificing high enantioselectivity (entry 4–7). It is important to mention that 32 mol% of $Sc(OTf)_3$ and 38 mol% of (*S*,*S*)-*t*-Bu-PyBox with

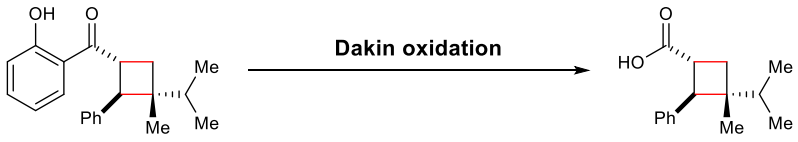
1.5 equivalents of **2.36** were used for the isolation scale experiment (entry 8) due to irreproducibility in enantioselectivity (from 91% ee to 93% ee).




| Entry | **Equivalencies 2.36** | **$Sc(OTf)_3$ loading (Y mol%)** | **Pybox loading (Z mol%)** | NMR yield (%) | ee (%) |
|---|---|---|---|---|---|
| 1 | 10 | 10 | 15 | 83 | 85 |
| 2 | 4 | 10 | 15 | 85 | 84 |
| 3 | 4 | 100 | 150 | 85 | 95 |
| 4 | 4 | 50 | 75 | - | 94 |
| 5 | 4 | 30 | 45 | - | 91 |
| 6 | 1.5 | 30 | 45 | - | 94 |
| 7 | 1.5 | 30 | 36 | - | 93 |
| 8 | 1.5 | 32 | 38 | 80 (isolated) | 94 |

**Table 2.4.** Effort towards preventing Lewis-acid-free sensitization

Next, we explored Dakin oxidation followed by methylation to transform the auxiliary group to the desired methyl ester group. Dakin oxidation of cyclobutane **2.38** was chosen as a model system for initial evaluation of reaction conditions because of the easy separation between the two diastereomers and the highly efficient preparation of this model reagent. Previous reports from our lab employed 3 equivalents of 3-chloroperbenzoic acids and 1 equivalent of trifluoroacetic acid to oxidize the electron-rich phenyl group on stereoenriched aryl cyclopentyl ketones.[20] We speculated that this would be a good starting point. Surprisingly, the reaction did not proceed at all after seven days (entry 1). We examined stronger oxidizing agents (entry 2), $Sc(OTf)_3$ as a Lewis acid catalyst (entry 3),[21] and nucleophilic oxidation conditions (entry 4). These all gave no desired product. Finally, we tried strongly acidic conditions using sulfuric acid as solvent, which gave moderate yield and maintained good ee in the formation of **2.39** (entry 5).[22] However, this reaction could not be applied in the total synthesis of **2.37** due to the strongly acidic conditions.

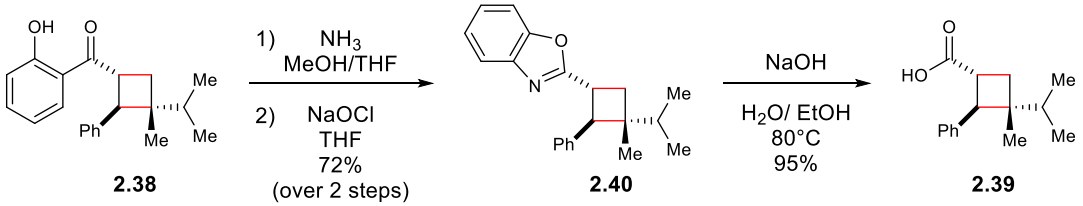



**2.38** **2.39**

| Entry | ***oxidizing agent*** | ***catalyst*** | Remaining SM | NMR yield (%) |
|---|---|---|---|---|
| 1 | *m*-CPBA | TFA | - | 0% |
| 2 | $CF_3CO_3H$ | TFA | 93% | 0% |
| 3 | *m*-CPBA | $Sc(OTf)_3$ | 62% | 0% |
| 4 | $H_2O_2$ | NaOH | 93% | 0% |
| 5 | $CH_3CO_3H$ (10 equiv.) | $H_2SO_4$ | 0% | 66%, 94% *ee* |

**Table 2.5.** Dakin oxidation condition screen

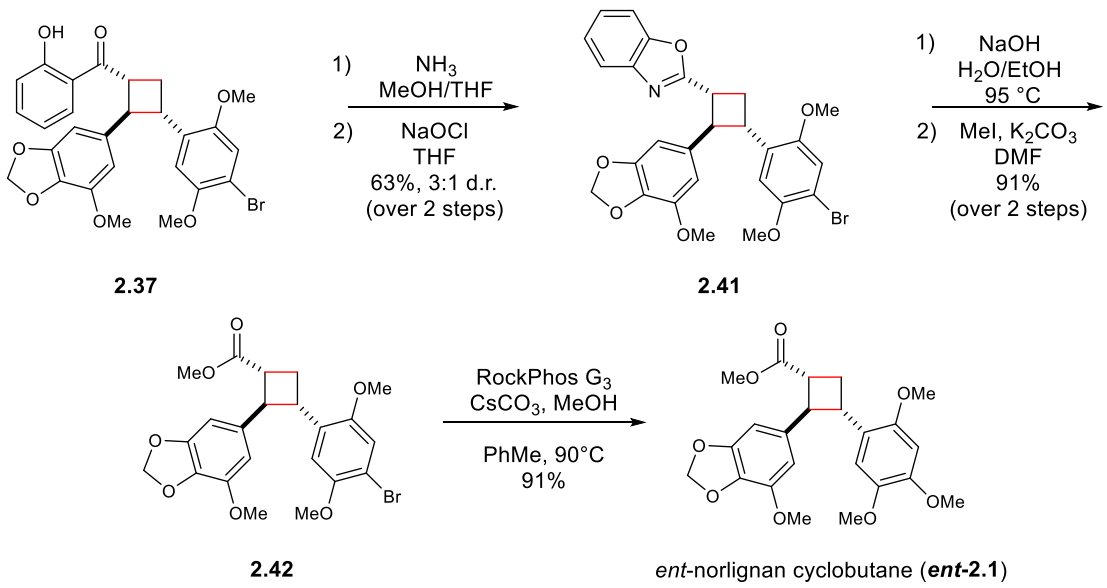
As a result, alternative disconnections to cleave an auxiliary group were evaluated. Recently, Merck reported a method to convert 2'-hydroxyaryl ketimines to benzoxazoles using bleach as a chlorinating reagent.[23] We hypothesized that this protocol could be used to convert **2.38** to benzoxazole **2.40**, which could further be hydrolyzed to cyclobutane carboxylic acid **2.39**. Indeed, treatment of **2.38** with 10 equivalents of $NH_3$ in methanol followed by Beckmann rearrangement with 3 equivalents of NaOCl in isopropanol afforded **2.40** in 72% yield and 92% ee. The benzoxazole was further converted to carboxylic acid **2.39** in 95% yield *via* base-promoted hydrolysis.




**2.38** **2.40** **2.39**

**Scheme 2.8.** An alternative strategy to access **2.39**

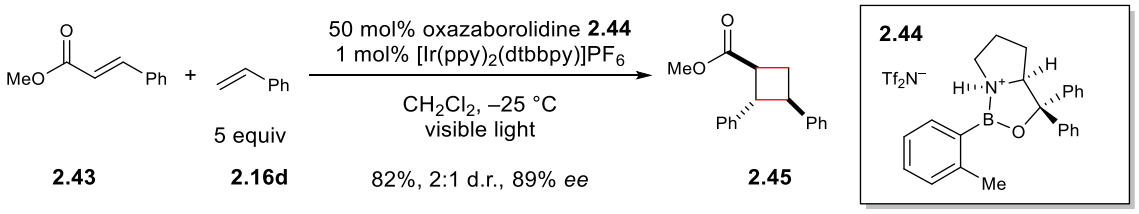
With the promising cleavage strategy in hand, we adapted this one-pot method for the conversion of 2'-hydroxyaryl ketone **2.37** into benzoxazoles **2.41**. At this point, the diastereomers could be easily separated by chromatography. A subsequent hydrolysis/methylation sequence afforded the corresponding methyl ester **2.42** in 91% yield. Finally, the synthesis of the enantiomer of the cyclobutane natural product **2.1** was accomplished by a Pd-catalyzed Buchwald etherification.[24]




**Scheme 2.9.** Synthesis of *ent*-nolignan cyclobutane (***ent*-2.1**)

Although our method has proven to be applicable to the concise synthesis of a cyclobutane natural product, the requirement for a chelating auxiliary hydroxylaryl group represented a significant synthetic limitation. The asymmetric synthesis of the *ent*-norlignan (***ent*-2.1**) required only five steps, but three were required to modify an auxiliary group to the requisite methyl ester. Because of this inefficiency, we were interested in developing an alternative method with cinnamate esters that would enable a more direct route toward the class of chiral cyclobutane natural products. We hypothesized that other Lewis acids would lower the triplet energies of cinnamate esters to suppress the racemic background reactivity and the appropriate selection of Lewis acid would provide a well-organized, highly enantiodifferentiating transition state to give high enantioselectivity. In particular, colleague Dr. Mary Beth Daub was interested in evaluating oxazaborolidine catalysts as a Lewis acid co-catalyst, because these are among the most successful chiral Lewis acids for asymmetric transformations of α,β-unsaturated carbonyl compounds.[25] Indeed, the protonated version of commercially available oxazaborolidine catalyst **2.44** immediately gave a promising result. Irradiation of methyl cinnamate **2.43** with styrene **2.16d** in the presence of 1 mol% $[Ir(ppy)_2(dtbbpy)]PF_6$ and 50 mol% of chiral oxazaborolidine **2.49a** furnished the desired cyclobutane adduct **2.45** in 82% yield with 89% ee. After further optimization, Dr. Daub found that the optimized

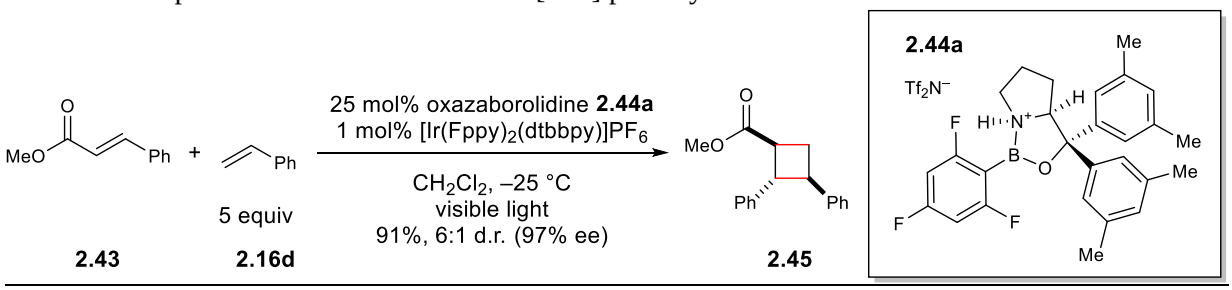
conditions were as follows: 1.0 equivalent **2.43**, 5.0 equivalents **2.16d**, 25 mol % oxazaborolidine **2.44a**, and 1 mol % $[Ir(Fppy)_2(dtbbpy)]PF_6$ are combined in $CH_2Cl_2$ (0.1 M) under $N_2$ in a sealed vial at –25 °C.



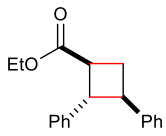

**Scheme 2.10.** Initial result of enantioselective [2+2] photocycloaddition of methyl cinnamate (**2.43**)

With the optimal reaction conditions in hand, Dr. Mary Beth Daub and the writer next evaluated the scope of the reaction. The yield and ee of the cycloaddition were insensitive to the identity of the ester moiety (**2.45**–**2.48**), and cinnamate esters with electronically and sterically varied β-aryl substituents were competent substrates (**2.50**–**2.52**). Moreover, methyl (*E*)-3-(thiophen-2-yl)acrylate underwent the desired cycloaddition to furnish cyclobutane **2.53**, suggesting that heterocycles could be tolerated. However, methyl crotonate did not give any desired product **2.49**, presumably due to its higher triplet energy compared to the more extended π system of methyl cinnamate **2.43**. As we had observed in the asymmetric [2+2] photocycloaddition of 2'-hydroxychalcones, electron-donating and electron-withdrawing substituents at all positions on styrene were tolerated (**2.54**–**2.57**). It is noteworthy that highly electron-rich styrenes underwent acid-promoted polymerization instead of the desired cycloaddition as we had observed in the previous method.

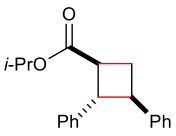
**Table 2.6.** Scope studies for enantioselective [2+2] photocycloadditions of cinnamate esters[a]



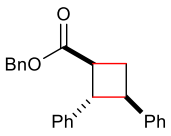

**2.43** **2.16d** **2.45**



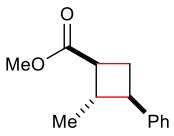

**2.46** 94%, 6:1 d.r.
98% ee



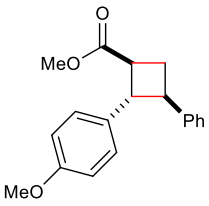

**2.47** 96%, 7:1 d.r.
97% ee



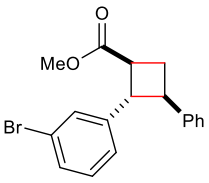

**2.48** 86%, 6:1 d.r.
97% ee



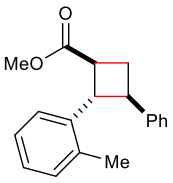

**2.49** 0%



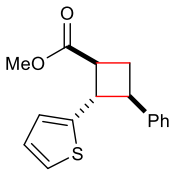

**2.50** 76%, >20:1 d.r.
97% ee



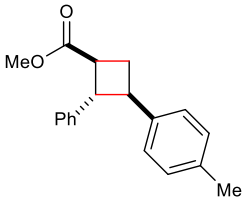

**2.51** 82%, 5:1 d.r.
95% ee



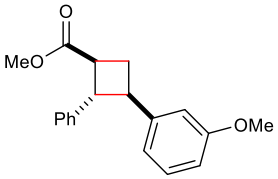

**2.52** 96%, 9:1 d.r.
99% ee



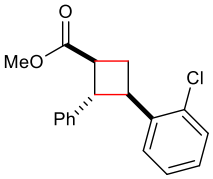

**2.53** 68%, 4:1 d.r.
93% ee



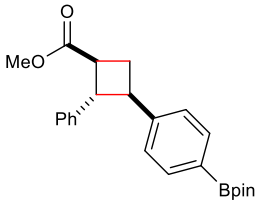

**2.54** 76%, 5:1 d.r.
96% ee




**2.55** 67%, 6:1 d.r.
90% ee




**2.56** 78%, 9:1 d.r.
96% ee

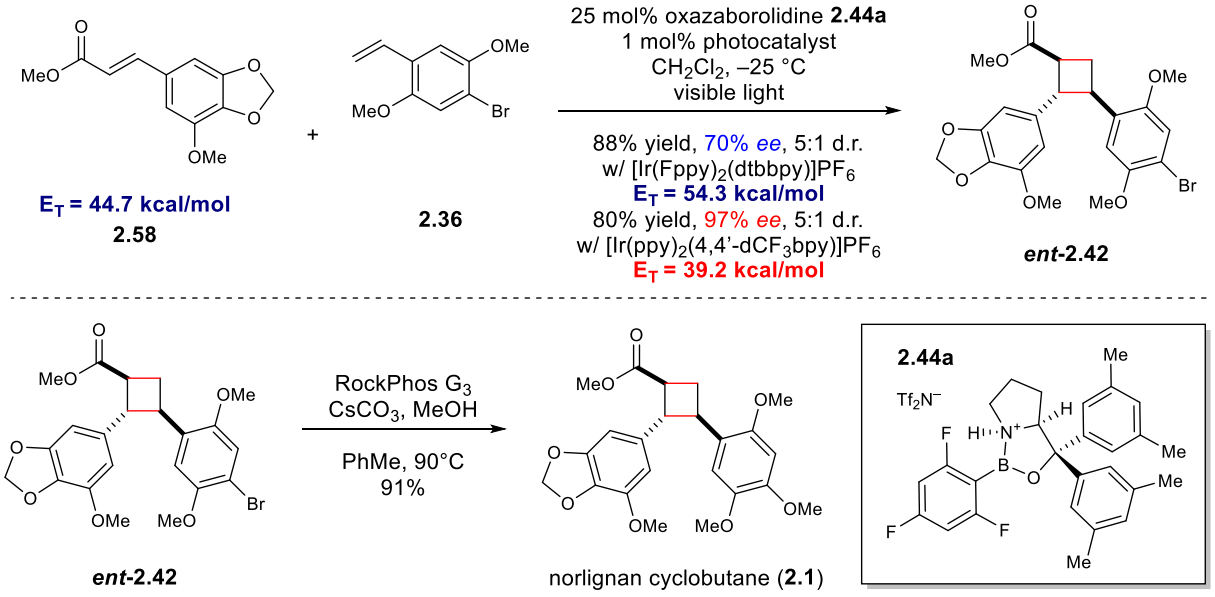



**2.57** 77%, 6:1 d.r.
92% ee

a) Diastereomeric ratio were determined by 1H NMR analysis of the unpurified reaction mixtures. Enantiomeric excesses for the major diastereomer were determined by chiral-phase HPLC or SFC.

As mentioned above, one important goal of this project was to demonstrate that enantioselective [2+2] photocycloaddition is a viable strategy for the synthesis of naturally occurring cyclobutanes. In this regard, we developed a concise, two-step synthesis of norlignan utilizing this newly developed strategy. Because the scope is very similar to the previous strategy, the key [2+2] cycloaddition step was conducted using the same styrene **2.36**. Interestingly, the cycloaddition between **2.58** and **2.36** under standard conditions gave good yields of ***ent*-2.42** but low stereocontrol (70% ee). A control reaction suggested that there was a significant racemic background reaction (82% yield in the absence of Lewis acid). The higher level of

racemic background reactivity was rationalized by calculating the triplet energy of the cinnamate ester **2.58**, which was estimated to be 44.7 kcal/mol (calculation was conducted by colleague Hoimin Jung). We hypothesized that this background process could be minimized by further tuning the photocatalyst. Gratifyingly, we found that $[Ir(ppy)_2(4,4'\text{-}dCF_3bpy)]PF_6$ ($E_T$ = 39.2 kcal/mol)[26] afforded the desired cyclobutane ***ent*-2.42** in 97% ee. These experiments confirmed that the rate of energy transfer could be accelerated by increasing the thermodynamic driving force for energy transfer through stabilizing the triplet state of the organic substrate. Subsequent Pd-catalyzed Buchwald etherification afforded natural product **2.1** in two steps with 54% overall yield.




**Scheme 2.11.** Synthesis of natural product **2.1**

## 2.3 Conclusions and Outlook

Although the most direct route to synthesize naturally occurring cyclobutanes is *via* stereoselective intermolecular [2+2] photocycloaddition of two achiral alkenes, this route has rarely been pursued due to the lack of general strategies. The primary challenge of suppressing a racemic background reactivity in order to induce high enantioselectivity has been addressed with several different approaches. However, none of them is applicable toward the synthesis of diarylcyclobutane-containing natural product owing to the limitations in substrate scopes. We have demonstrated that stereoselective [2+2] photocycloaddition of

two simple alkenes is a viable pathway to synthesize naturally occurring cyclobutanes *via* Lewis-acid-catalyzed selective triplet energy transfer mechanism. More importantly, this straightforward retrosynthetic analysis allowed access to norlignan cyclobutane (**2.1**) in only two steps with 54% overall yield. From a broader perspective, these results were fascinating because they enabled retrosynthetic disconnections previously viewed as unviable pathways for a certain class of cyclobutane natural products. As a result, this dual-catalysis approach will inspire synthetic chemists to revisit enantioselective [2+2] photocycloaddition as a potential solution to synthesize structurally unique bioactive cyclobutane compounds.

## 2.4 Contributions

Regarding respective contributions for the enantioselective [2+2] photocycloaddition reaction with chalcone **2.13** and styrene **2.16d**, it was co-discovered by Dr. Travis Blum and Dr. Zachary Miller. It was at this point that the writer joined the project and explored the substrate scope and other coupling partners with colleague Dr. Zachary Miller. The writer discovered and optimized the auxiliary cleavage step. Following this discovery, the writer discovered and optimized the key [2+2] photocycloaddition toward natural product ***ent*-2.1**. The writer designed the retrosynthetic analysis of ***ent*-2.1** and accomplished the total synthesis.

Regarding respective contributions for the enantioselective [2+2] photocycloaddition reaction with cinnamate **2.43** and styrene **2.16d**, it was discovered and optimized by Dr. Mary Beth Daub. It was at this point that the writer joined the project and helped to finish the substrate scope. The writer optimized and conducted the [2+2] photocycloaddition for the total synthesis of **2.1**.

## 2.5 Experimental

### 2.5.1 General Experimental Information

#### 2.5.1.1 Reagent Preparation for the Chalcone Project

MeCN solvent was purified by elution through alumina as described by Grubbs.[27] *i*-PrOAc and all solvents used for chromatography were used as received. A 23W (1200 lumens) SLI Lighting Mini-Lynx compact fluorescent light bulb (CFL) or a 15 W Eagle Light PAR38 blue LED flood light (500 lumens) was used for all photochemical reactions as noted. Flash column chromatography was performed with Silicycle 40–

63Å silica (230–40 mesh). All commercially available olefinic coupling partners were purified by distillation prior to use. (*S*,*S*)-*t*-BuPyBox was prepared according to a literature method.[28] $Ru(bpy)_3(PF_6)_2$ was prepared according to a previously reported method.[29] The 2'-hydroxychalcones were synthesized according to a known procedure and were purified by recrystallization prior to use.[30] Methyl 4-vinylbenzoate,[31] 3,5-dimethoxy styrene,[32] and 4-phenyl vinylboronic acid[33] were prepared as previously described. 2-*H*-Chromene was synthesized via dehydration of racemic 2-chromanol according to a published procedure.[34]

#### 2.5.1.2 Reagent Preparation for the Methyl Cinnamate Project

All reactions were performed under an inert atmosphere of nitrogen using oven-dried or flame-dried glassware and Teflon® coated stir bars. Solvents were dried by passage through columns of activated alumina. A 15W Eagle Light PAR38 blue LED flood light (500 lumens) or a Kessil H150 Blue LED light were used for all photochemical reactions as noted. All commercially available aldehydes and olefinic coupling partners were purified by distillation prior to use, and all other reagents were prepared using known literature procedures. Reactions were monitored by thin-layer chromatography (TLC) performed on 250 μm silica gel 60 plates with 254 nm fluorescent indicator from EMD Chemicals using UV light as a visualizing agent and ceric ammonium molybdate and heat as developing agents. Flash chromatography was performed with Silicycle 40–63Å silica (230–40 mesh).

#### 2.5.1.3 Product Characterization

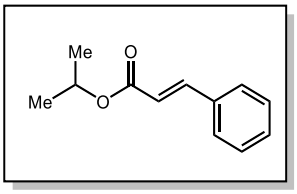
NMR spectra were recorded on a Bruker Avance-400, Avance-500, or Avance-600 MHz spectrometer with DCH, Prodigy, BBFO+, or TCI-F probes. Chemical shifts are reported in parts per million and are internally referenced to tetramethyl silane (0.00 ppm) or the residual protio-solvent peak ($CDCl_3$: 7.26 ppm for $^1H$ NMR and 77.16 ppm for $^{13}C$ NMR). $^{19}F\{^1H\}$ spectra were absolute referenced to the corresponding $^1H$ spectra using the method described by Harris. Data are reported as follows: chemical shift, multiplicity (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sext = sextet, sept = septet, m = multiplet, br = broad), coupling constant(s) in Hz, integration. NMR spectra were obtained at 298 K unless otherwise noted. FT-IR spectra were recorded on a Bruker Alpha Platinum spectrometer and are

reported in terms of frequency of absorption ($cm^{-1}$). Optical rotations were measured with a Rudolph Research Autopol III polarimeter operating on the sodium D-line (589 nm) using a 50 mm path-length cell and are reported as: $[\alpha]_D^T$ (concentration in g/100 mL,solvent). Analytical chiral HPLC or chiral SFC were performed with a Waters Alliance system HPLC using Daicel CHIRALPAK® columns (4.6 mm x 25 cm) and Chromasolv®-grade methanol, *i*-PrOH, EtOH, or 25% *i*-PrOH in hexanes. High resolution mass spectra (HRMS) were recorded on a Thermo Q Exactive™ Plus using ESI-TOF (electrospray ionization-time of flight). Melting points (mp) are uncorrected and were measured on a Mel-Temp II melting point apparatus.

### 2.5.2 Synthesis of Cinnamic Esters

**General Procedure A: Synthesis of Cinnamic Esters by Acylation of Alcohols**

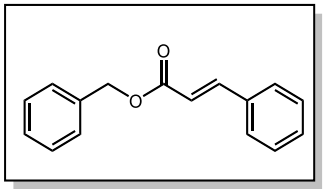
To a solution of cinnamoyl chloride (1 equiv) in $CH_2Cl_2$ (0.5 M) at 0 ˚C in an ice bath was added triethylamine (2.2 equiv) dropwise *via* syringe followed by the alcohol (1.1 equiv). After five minutes, the solution was allowed to warm to room temperature. After 17 h, 1 M HCl was added to the reaction mixture, and the aqueous layer was extracted three times with $CH_2Cl_2$. The combined organic extracts were washed with water, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography, yielding the desired cinnamic ester.




**Isopropyl cinnamate (2.47a):**

The title compound was prepared according to General Procedure A using cinnamoyl chloride (1.00 g, 6.00 mmol), triethylamine (1.84 mL, 13.20 mmol), 2-propanol (0.51 mL, 6.60 mmol), and $CH_2Cl_2$ (12 mL). The crude material was purified by flash chromatography ($SiO_2$, 3% EtOAc:hexanes) to afford isopropyl cinnamate (611.0 mg, 54%) as a colorless oil. The spectral data for this compound are consistent with those reported in the literature.[35] $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.67 (d, $J$ = 16.0 Hz, 1H), 7.55–7.50 (m, 2H), 7.41– 7.36 (m, 3H), 6.42 (d, $J$ = 16.0 Hz, 1H), 5.14 (sept, $J$ = 6.3 Hz, 1H), 1.32 (d, $J$ = 6.4 Hz, 6H);

$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 166.5, 144.3, 134.5, 130.1, 128.0, 118.8, 67.8, 22.0.

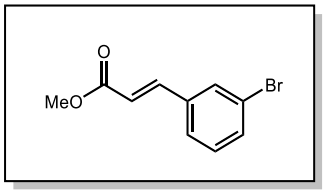


**Benzyl cinnamate (2.48a):**

The title compound was prepared according to General Procedure A using cinnamoyl chloride (0.956 g, 5.74 mmol), triethylamine (1.76 mL, 12.62 mmol), benzyl alcohol (0.65 mL, 6.31 mmol), and $CH_2Cl_2$ (11.5 mL). The crude material was purified by flash chromatography ($SiO_2$, 3% EtOAc:hexanes) to afford benzyl cinnamate (1.146 g, 84%) as a white solid. The spectral data for this compound are consistent with those reported in the literature.[1] $^1$H NMR ($CDCl_3$, 400 MHz) 7.73 (d, $J$ = 16.0 Hz, 1H), 7.56–7.49 (m, 2H), 7.45– 7.31 (m, 8H), 6.49 (d, $J$ = 16.0 Hz, 1H), 5.26 (s, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 166.8, 145.2, 136.1, 136.0, 134.3, 130.4, 128.9, 128.6, 128.29, 128.26, 128.1, 117.9, 66.4.

**General Procedure B: Synthesis of Cinnamic Esters by Wittig Olefination**

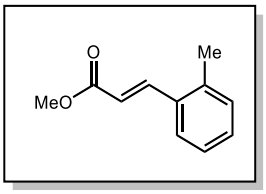
To a solution of freshly distilled aldehyde (1 equiv) in $CH_2Cl_2$ (0.2 M) at 0 ˚C in an ice bath was added methyl (triphenylphosphoranylidene)acetate (1.5 equiv) in one portion. After thirty minutes, the reaction mixture was allowed to warm to room temperature. After 19 h, the solvent was removed *in vacuo*, and the crude residue was purified by flash column chromatography, yielding the desired cinnamic ester.



**Methyl (*E*)-3-(3-bromophenyl)acrylate (2.51a):**

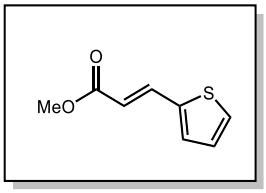
The title compound was prepared according to General Procedure B using 3-bromobenzaldehyde (0.64 mL, 5.49 mmol), methyl (triphenylphosphoranylidene)acetate (2.71 g, 8.11 mmol), and $CH_2Cl_2$ (27 mL). The crude material was purified by flash chromatography ($SiO_2$, 5% EtOAc:hexanes) to afford methyl (*E*)- 3-(3-bromophenyl)acrylate (1.25 g, 96%) as a white solid. The spectral data for this compound are consistent with those reported in the literature.[36] $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.67 (s, 1H), 7.61 (d, $J$ = 16.0 Hz,

1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 7.9 Hz, 1H), 6.43 (d, *J* = 16.0 Hz, 1H), 3.81 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 167.0, 143.1, 136.5, 133.1, 130.7, 130.4, 126.7, 123.0, 119.3, 51.9.



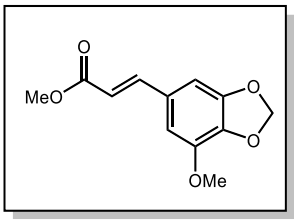

**Methyl (*E*)-3-(*o*-tolyl)acrylate (2.52a):**

The title compound was prepared according to General Procedure B using *o*-tolualdehyde (0.69 mL, 5.97 mmol), methyl (triphenylphosphoranylidene)acetate (3.01 g, 9.00 mmol), and $CH_2Cl_2$ (30 mL). The crude material was purified by flash chromatography ($SiO_2$, 5% EtOAc:hexanes) to afford methyl (*E*)- 3-(*o*-tolyl)acrylate (823 mg, 78%) as a colorless oil. The spectral data for this compound are consistent with those reported in the literature.[37] $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.98 (d, *J* = 15.9 Hz, 1H), 7.55 (d, *J* = 7.2 Hz, 1H), 7.31–7.24 (m, 1H), 7.23–7.18 (m, 1H), 6.36 (d, *J* = 15.9 Hz, 1H), 3.81 (s, 3H), 2.44 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 167.5, 142.5, 137.7, 133.4, 130.8, 130.0, 126.4, 126.3, 118.8, 51.7, 19.8.




**Methyl (*E*)-3-(thiophen-2-yl)acrylate (2.53a):**

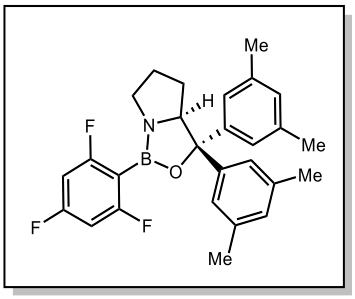
The title compound was prepared according to General Procedure B using 2-thiophenecarboxaldehyde (0.56 mL, 6.00 mmol), methyl (triphenylphosphoranylidene)acetate (3.01 g, 9.00 mmol), and $CH_2Cl_2$ (30 mL). The crude material was purified by flash chromatography ($SiO_2$, 5% EtOAc:hexanes) to afford methyl (*E*)- 3-(thiophen-2-yl)acrylate (951 mg, 94%) as a white solid. The spectral data for this compound are consistent with those reported in the literature.[38] $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.79 (d, *J* = 15.7 Hz, 1H), 7.37 (d, *J* = 5.0 Hz, 1H), 7.25 (d, *J* = 3.6 Hz, 1H), 7.05 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.24 (d, *J* = 15.7 Hz, 1H), 3.79 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 167.3, 139.5, 137.3, 130.9, 128.4, 128.1, 116.5, 51.7.




**Methyl (*E*)-3-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)acrylate (2.58):**

The title compound was prepared according to General Procedure B using 5-methoxypiperonal (1.00 g, 5.57 mmol), methyl (triphenylphosphoranylidene)acetate (2.79 g, 8.35 mmol), and $CH_2Cl_2$ (28 mL). The crude material was purified by flash chromatography ($SiO_2$, Gradient 15 to 20% EtOAc:hexanes) to afford methyl (*E*)-3-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)acrylate (1.23 g, 93%) as a white solid (mp 100–101 ˚C). $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.57 (d, $J$ = 15.9 Hz, 1H), 6.75 (s, 1H), 6.70 (s, 1H), 6.28 (d, $J$ = 15.9 Hz, 1H), 6.02 (s, 2H), 3.92 (s, 3H), 3.80 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 167.5, 149.3, 144.6, 143.7, 137.4, 129.2, 116.3, 109.1, 102.0, 101.3, 56.6, 51.7; IR (thin film) $\nu$ 3070, 3004, 2950, 2904, 2845, 1705, 1636, 1623, 1603, 1508, 1449, 1429, 1277, 1168, 1135, 1093, 1041, 978, 924, 828 cm$^{-1}$; HRMS (ESI) $m$ / z calcd for $C_{12}H_{12}O_5H$ $(M + H)^+$ 237.0758, found 237.0754.

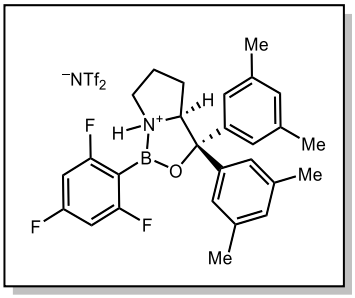
### 2.5.3 Synthesis of Oxazaborolidine 2.44a




**Oxazaborolidine Precursor 2.S1:**

The following procedure was adapted from Bach *et al*.[13] A 25 mL round-bottom flask was charged with 2,4,6-trifluorophenylboronic acid (1.00 equiv) and equipped with a Dean–Stark apparatus. The apparatus was purged with $N_2$ and a solution of (*S*)- bis(3,5-dimethylphenyl)(pyrrolidin-2-yl)methanol (1.00 equiv, 0.1 M in PhMe) was added to the 25 mL round-bottom flask. Additional toluene was added to the reaction mixture to bring the concentration to 0.02 M, and the Dean–Stark apparatus was filled with toluene. The reaction mixture was heated to reflux (Bath Temperature: 148 ˚C). After three hours, the Dean–Stark trap

was drained and half of the toluene in the reaction vessel was removed by distillation. The Dean– Stark apparatus was refilled with toluene, and the volume of toluene that was distilled from the reaction mixture was replenished. The procedure was repeated again after refluxing for 3 hours. After 16 hours, the toluene was distilled from the reaction mixture to a volume of ~1 mL. After allowing to cool to room temperature, the Dean–Stark apparatus was quickly removed under flow of nitrogen and replaced with a septum, and the remaining toluene was removed *in vacuo*. The oxazaborolidine was dissolved in $CH_2Cl_2$ (0.15 M) and used directly. The oxazaborolidine was freshly prepared for each photochemical reaction. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.10 (s, 2H), 6.98 (s, 2H), 6.80 (s, 1H), 6.76 (s, 1H), 6.56 (dd, *J* = 9.1, 7.2 Hz, 2H), 4.47 (dd, *J* = 10.1, 5.6 Hz, 1H), 3.21 (dt, *J* = 10.6, 7.3 Hz, 1H), 3.08 (ddd, *J* = 10.8, 91, 5.2 Hz, 1H), 2.22 (s, 6H), 2.20 (s, 6H), 1.80–1.69 (m, 2H), 1.66–1.58 (m, 1H), 0.85 (dq, *J* = 12.2, 9.8 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 165.5 (ddd, *J* = 249.5, 16.8, 15.0 Hz), 163.5 (dt, *J* = 250.5, 15.8 Hz), 146.1, 142.4, 136.5, 136.0, 127.9, 127.3, 123.1, 123.0, 103.4–102.2 (m),[6] 99.1–98.7 (m), 87.7, 72.3, 42.0, 29.5, 25.4, 20.54, 20.49; $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ –96.9 (d, *J* = 8.3 Hz, 2F), –105.8 (t, *J* = 8.3 Hz, 1F); $^{11}$B NMR (128 MHz, $CDCl_3$) $\delta$ 29.8 (br s).




**Oxazaborolidine 2.44a:**

A solution of oxazaborolidine precursor **S6** (1.2 equiv, 0.15 M in $CH_2Cl_2$) was cooled to –40 ˚C. A solution of trifluoromethanesulfonimide (1.0 equiv, 0.5 M solution in $CH_2Cl_2$) was added dropwise *via* syringe. After 30 min at –40 ˚C, oxazaborolidine **6f** was used directly in the enantioselective [2+2] photocycloaddition.

### 2.5.4 Synthesis of Cyclobutanes

**General Procedure A: Enantioselective [2+2] Photocycloaddition of 2'-Hydroxychalcones**

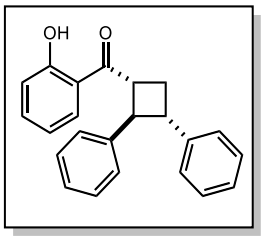
In an oven-dried 6 dram vial were combined 2'-hydroxychalcone (1.0 equiv.), $Sc(OTf)_3$ (0.10 equiv.), (*S*,*S*)-*t*-BuPyBox (0.15 equiv.), and $Ru(bpy)_3(PF_6)_2$ (0.025 equiv.). A magnetic stir bar was added, and the contents were dissolved in 3:1 *i*-PrOAc:MeCN (12 mL). To this solution was added the styrene (10 equiv.) by syringe under air, the vial was sealed with a Teflon-lined cap and stirred under 23W CFL (or a 15W blue LED when mentioned) irradiation for 20 h at rt, unless a longer irradiation time is required as determined by TLC. Upon complete consumption of starting material, the reaction mixture was filtered through a plug of silica (eluting with 100% $Et_2O$). The filtrate was then concentrated *in vacuo* and the crude material was purified by flash-column chromatography to afford analytically pure material. The isolated yields represent the summation of both major and minor diastereomeric cycloadducts. Unless otherwise noted, characterization data and enantiomeric excesses are reported for the major isomer and minor isomer.

**General Procedure B: Enantioselective [2+2] Photocycloaddition of 2'-Hydroxychalcones**

In an oven-dried 6 dram vial were combined 2'-hydroxychalcone (1.0 equiv.), $Sc(OTf)_3$ (0.10 equiv.), (*S*,*S*)-*t*-BuPyBox (0.15 equiv.), and $Ru(bpy)_3(PF_6)_2$ (0.025 equiv.). A magnetic stir bar was added, and the contents were dissolved in 3:1 *i*-PrOAc:MeCN (12 mL). To this solution was added the styrene (10 equiv.) by syringe, the vial was sealed with a Teflon-lined cap and stirred under 23W CFL irradiation for 20 h at room temperature. The reaction progress was monitored by TLC, and at 20 h, the reaction mixture was filtered through a plug of silica (eluting with 100% $Et_2O$). The filtrate was then concentrated *in vacuo* and the crude material was purified by flash-column chromatography to afford mixtures of major and minor diastereomers and difficult to remove aldehyde oxidation byproduct by flash-column chromatography. The afforded cycloadducts and aldehydes were dissolved in EtOAc, EtOH, and $H_2O$ (9 mL, 5:3:1) and sodium bisulfite (1.0 equiv.) was added to a 3-dram vial equipped with a Teflon stir bar and sealed with a cap. The resulting solution was stirred for 12 h to afford analytically pure material. The isolated yields represent the summation of both major and minor diastereomeric cycloadducts. Unless otherwise noted, characterization data and enantiomeric excesses are reported for the major isomer and minor isomer.

**General Procedure C: Enantioselective [2+2] Photocycloaddition of Cinnamic Esters**

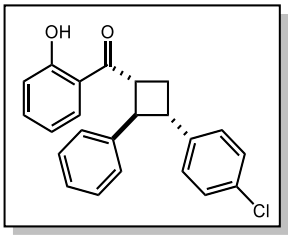
To a solution of cinnamic ester (1 equiv) and photocatalyst (1 mol%) in $CH_2Cl_2$ (0.032 M) cooled to –40 ˚C was added a pre-cooled solution of oxazaborolidine **6f** (25 mol%, 0.1 M in $CH_2Cl_2$) dropwise *via* syringe. After five minutes, styrene (5 equiv) was added dropwise *via* syringe. The reaction mixture was allowed to warm to –25 ˚C, and irradiated with a HG150 Kessil lamp at a distance of 6 cm. After 24 h, the reaction was quenched with triethylamine (0.1 mL). The reaction mixture was allowed to warm to room temperature and filtered through a pad of silica (elution with $Et_2O$). The filtrate was concentrated *in vacuo*, and the crude residue was purified using flash chromatography, yielding the desired [2+2] cycloadduct.




**((1*R*,2*R*,3*S*)-2,3-Diphenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.17d**)**:**

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 880 μL (4.0 mmol) styrene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (2.5% EtOAc:Hex). Combined yield: 210 mg of a clear oil (80%, 0.32 mmol) as a 2:1 (major:minor) mixture of diastereomers; >99% ee (Daicel CHIRALPAK® OJ-H, 5% (methanol), 4 mL/min, 221nm; $t_1$ = 12.84 min, $t_2$ = 14.15 min. Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 880 μL (4.0 mmol) 1-chloro-3-vinylbenzene. Crude d.r.: 2:1; Combined isolated yield: 118 mg of a clear oil (90%, 0.35 mmol); >99% ee.

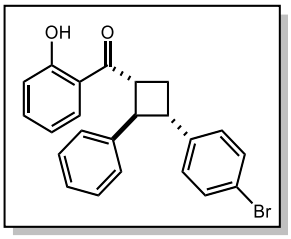
**(1*R*, 2*R*, 3*S*)** diastereomer (major) and **(1*R*, 2*R*, 3*R*)** diastereomer **(**minor) as a mixture: **$^{1}$H NMR** (500 MHz, $CDCl_3$): δ 12.41 (s, 0.73H), 12.40 (s, 0.24H), 0.75 (dd, *J* = 8.1, 1.7 Hz, 0.31H), 7.52 (dd, *J* = 8.1, 1.7 Hz, 0.82H), 7.42-7.48 (m, 1.2H), 7.26-7.33 (m, 6H), 7.20-7.25 (m, 1.65H), 7.15-7.20 (m, 0.62H), 7.00 (dd, *J* =12.5, 8.4 Hz, 1.6H), 6.95 (d, *J* = 7.93 Hz, 0.59H), 6.81 (td, *J* = 7.40, 1.40 Hz, 0.32H), 6.78 (td, *J* = 7.34, 1.40 Hz, 0.77H), 4.41 (m, 0.63H), 4.02-4.10 (m, 2H), 3.75-3.82 (m, 0.93H), 2.90-2.97 (m, 0.38H), 2.82-2.86 (m, 0.4H), 2.52-2.77 (m. 0.75H), 2.46-2.56 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 206.0, 205.5, 162.85, 162.82, 143.0, 142.0, 140.2, 139.2, 136.3, 130.1, 130.0, 128.6, 128.5, 128.01, 128.00, 127.95, 127.91, 127.0, 126.9, 126.7, 126.6, 126.3, 126.0, 118.9, 118.8, 118.6, 118.5, 118.4, 118.2, 49.2, 46.8, 46.0, 45.0, 42.7, 42.6, 41.5, 30.9, 27.5; **IR** (thin film): ν 3027, 1631, 1485, 1272 $cm^{-1}$**;** **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{23}H_{20}O_2$ requires *m/z* 327.1391, found *m/z* 327.1390; **$[\alpha]^{22}_D$** −144.0 º (*c*1.0, $CH_2Cl_2$).




**((1*R*,2*R*,3*S*)-3-(4-Chlorophenyl)-2-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.17q**)**:**

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 580 μL (4.0 mmol) 1-chloro-4-styrene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (2.5% EtOAc:Hex gradient). Combined yield: mg of a clear oil (98%, 0.39 mmol); 96% ee (Daicel CHIRALPAK® OD-H, 4% (*i*-PrOH), 4 mL/min, 221nm; $t_1$ = 14.37 min, $t_2$ = 17.71 min. Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 580 μL (4.0 mmol) 1-chloro-4-vinylbenzene. Crude d.r.: 2:1; Combined isolated yield: 142 mg of a clear oil (96%, 0.30 mmol); 95% ee. Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.37 (s, 1H), 7.50 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.44 (ddd, *J* = 8.5, 7.2, 1.6 Hz, 1H), 7.30-7.40 (m, 2H), 7.26-7.29 (m, 2H), 7.19-7.21 (m, 2H), 6.98 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.77 (ddd, *J* = 8.1, 7.3, 1.1 Hz, 1H), 4.06 (q, *J* = 8.6, 1H), 4.00 (t, *J* = 9.5, 1H) 3.76 (q, *J* = 8.6, 1H), 2.79 (dt, *J* = 10.9, 8.2 Hz, 1H), 2.47 (q, *J* = 10.2, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.3, 162.9, 141.6, 141.5, 136.5, 132.4, 103.1, 128.7, 128.6, 128.1, 127.0, 126.9, 118.8, 118.5, 118.4, 49.5, 45.8, 42.1, 30.7; **IR** (thin film): ν 3150, 1630, 1490, 1205, 523 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{23}H_{19}ClO_2$ requires *m/z* 361.1001, found *m/z* 361.1005; **$[\alpha]^{22}_D$** −132.0 º (*c*1.0, $CH_2Cl_2$).




**((1*R*,2*R*,3*S*)-3-(4-Bromophenyl)-2-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.17r**):

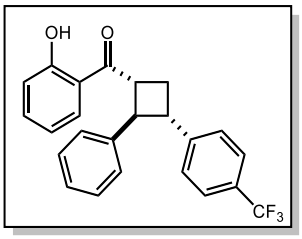
Experiment 1: Prepared according to general procedure B using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 523 µl (4.0 mmol) 1-bromo-4-vinylbenzene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 150 mg of a clear oil (92%, 0.37 mmol) as a 2:1 (major:minor) mixture of diastereomers; 95% ee (major) (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 10.66 min, $t_2$ = 11.25 min), 97% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 8.18 min, $t_2$ = 8.95 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (5% MTBE: Pent). Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 523 µL (4.0 mmol) 1-bromo-4-vinylbenzene. Crude d.r: 2:1; Combined isolated yield: 147 mg of a clear oil (90%, 0.36 mmol); 95% ee (major), 97% ee (minor).

Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.37 (s, 1H), 7.50 (dd, *J* = 8.08, 1.61 Hz, 1H), 7.41-7.45 (m, 3H), 7.30-7.33 (m, 2H), 7.24-7.27 (m, 3H), 7.14 (d, *J* = 8.43 Hz, 2H), 6.98 (dd, *J* = 8.39, 1.10 Hz 1H), 6.78 (td, *J* = 7.35, 1.11 Hz 1H), 4.05 (q, *J* = 9.13 Hz, 1H), 3.99 (t, *J* = 9.50 Hz, 1H), 3.72 (q, *J* = 9.54 Hz, 1H), 2.78 (dt, *J* = 10.79, 8.16 Hz, 1H), 2.47 (q, *J* = 10.15 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.3, 162.9, 142.1, 141.6, 136.5, 131.6, 130.1, 128.7, 128.5, 127.1, 126.9, 120.4, 118.9, 118.5, 118.4, 49.4, 45.8, 42.3, 30.7; **IR** (thin film): ν 3029, 2940, 1632, 1486, 1446 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{23}H_{19}BrO_2$ requires *m/z* 405.0496, found *m/z* 405.0498; **$[\alpha]^{22}_D$** −31.4 º (*c*1.3, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.36 (s, 1H), 7.53 (dd, *J* = 8.09, 1.68 Hz, 1H), 7.46 (ddd, *J* = 8.63, 7.22, 1.68 Hz, 1H), 7.25-7.27 (m, 2H), 7.13-7.17 (m, 2H), 7.09-7.12 (m, 1H), 7.01 (dd, *J* = 8.39, 1.21 Hz, 1H), 6.94-6.96 (m, 2H), 6.84-6.87 (m, 2H), 6.81 (ddd, *J* = 8.14, 7.17, 1.15 Hz, 1H), 4.35-4.41 (m, 2H), 4.00-4.05 (m, 1H), 2.95 (dddd, *J* = 12.06, 9.05, 5.96, 2.22 Hz, 1H) 2.75-2.81 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.8, 162.9, 139.4, 138.8, 136.4, 131.0, 129.9, 129.6, 128.2, 128.0, 126.6, 119.9, 118.9, 118.7, 118.1, 46.8, 44.4, 40.9, 27.4; **IR** (thin film): ν 3030, 2929, 1633, 1486, 1447 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{23}H_{19}BrO_2$ requires *m/z* 405.0496, found *m/z* 405.0498; **$[\alpha]^{22}_D$** −99.0 º (*c*0.61, $CH_2Cl_2$).




**(2-Hydroxyphenyl)((1*R*,2*R*,3*S*)-2-phenyl-3-(4-(trifluoromethyl)phenyl)cyclobutyl)methanone** (**2.17s**):

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 591 μL (4.0 mmol) 1-(trifluoromethyl)-4-vinylbenzene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel

(5%) MTBE:Pent). Combined yield: 147 mg of a clear oil (93%, 0.37 mmol) as a 2:1 (major:minor) mixture of diastereomers; 95% ee (major) (Daicel CHIRALPAK® AD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 5.58 min, $t_2$ = 8.63 min), 96% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 5.09 min, $t_2$ = 5.58 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (5% MTBE: Pent). Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 591 μL (4.0 mmol) 1-(trifluoromethyl)-4-vinylbenzene. Crude d.r.: 2:1; Combined isolated yield: 139 mg of a clear oil (88%, 0.35 mmol); 95% ee (major), 96% ee (minor).

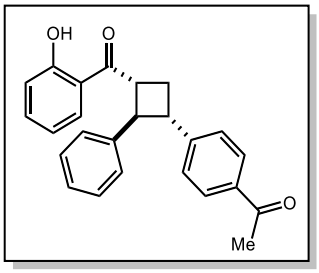
Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.36 (s, 1H), 7.56 (d, *J* = 8.09 Hz, 2H), 7.50 (dd, *J* = 8.09, 1.61 Hz, 1H), 7.44 (ddd, *J* = 8.64, 7.20, 1.66 Hz, 1H), 7.23-7.38 (m, 7H), 6.99 (dd, *J* = 8.45, 1.11 Hz, 1H), 6.78 (ddd, *J* = 8.13, 7.18, 1.16 Hz, 1H), 4.02-4.13 (m, 2H), 3.83 (q, *J* = 9.05 Hz, 1H), 2.83 (dt, *J* = 10.94, 7.90 Hz, 1H), 2.49-2.56 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.12, 162.89, 147.10, 141.42, 136.53, 130.07, 128.93 (q, *J* = 32.46 Hz), 128.79, 127.17, 127.05, 126.95, 125.47 (q, *J* = 3.78 Hz), 124.20 (q, *J* = 271.93 Hz), 118.87, 118.53, 118.41, 49.39, 45.90, 42.39, 30.40; **$^{19}$F NMR** (470 MHz, $CDCl_3$): δ –62.4; **IR** (thin film): ν 2925, 1630, 1486, 1322, 1159 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{19}F_3O_2$ requires *m/z* 395.1264, found *m/z* 395.1267; **$[\alpha]^{22}_D$** −32.0 º (*c*2.4, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.35 (s, 1H), 7.54 (dd, *J* = 8.06, 1.65 Hz, 1H), 7.46 (ddd, *J* = 8.70, 7.20, 1.66 Hz, 1H), 7.39 (d, *J* = 8.07 Hz, 2H), 7.08-7.15 (m, 5H), 7.02 (dd, *J* = 8.42, 1.11 Hz, 1H), 6.94-6.96 (m, 2H), 6.81 (ddd, *J* = 8.20, 7.17, 1.18 Hz, 1H), 4.38-4.43 (m, 2H), 4.13 (q, *J* = 9.12 Hz, 1H), 2.96-3.02 (m, 1H), 2.81-2.87 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.6, 162.9, 144.5, 138.6, 136.5, 130.0, 128.25, 128.23 (q, *J* = 32.74 Hz), 128.1, 127.9, 126.7, 124.8 (q, *J* = 3.78 Hz), 124.2 (q, *J* = 271.92 Hz), 119.0, 118.7, 118.0, 47.0, 44.4, 41.3, 27.2; **$^{19}$F NMR** (470 MHz, $CDCl_3$): δ –62.4; **IR** (thin film): ν 2927, 1633, 1486,

1324, 1159 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{19}F_3O_2$ requires *m/z* 395.1264, found *m/z* 395.1265; $[\alpha]^{22}_D$ −115.4 º (*c*0.4, $CH_2Cl_2$).




**Methyl 4-((1*S*,2*R*,3*R*)-3-(2-hydroxybenzoyl)-2-phenylcyclobutyl)benzoate** (**2.17t**):

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 649 mg (4.0 mmol) methyl 4-vinylbenzoate, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (10% MTBE:Pent). Combined yield: 119 mg of a clear oil (77%, 0.31 mmol) as a 2:1 (major:minor) mixture of diastereomers; >99% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 4 mL/min, 244 nm; $t_1$ = 6.82 min, $t_2$ = 7.21 min), 99% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 4 mL/min, 244nm; $t_1$ = 6.57 min, $t_2$ = 8.38 min).. Characterization data was obtained for the major and minor diastereomers by flash-colum chromatography (8% MTBE: Pen). Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 649 mg (4.0 mmol) methyl 4-vinylbenzoate. Crude d.r.: 2:1; Combined isolated yield: 119 mg of a clear oil (77%, 0.31 mmol); >99% ee (major), 98% ee (minor).

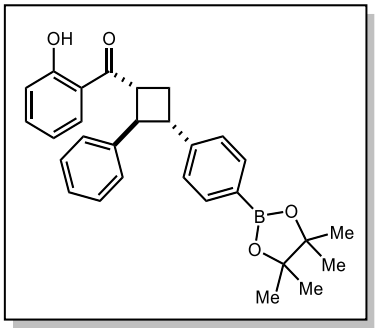
Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.36 (s, 1H), 7.98 (d, *J* = 8.30 Hz, 2H), 7.51 (dd, *J* = 8.07, 1.66 Hz, 1H), 7.44 (ddd, *J* = 8.68, 7.19, 1.66 Hz, 1H), 7.32 (m, 4H), 7.23-7.29 (m, 3H), 6.99 (dd, *J* = 8.43, 1.18 Hz, 1H),

6.78 (ddd, *J* = 8.19, 7.18, 1.18 Hz, 1H), 4.04-4.12 (m, 2H), 3.90 (s, 3H), 3.80-3.86 (m, 1H), 2.82 (dt, *J* = 11.08, 8.22 Hz, 1H), 2.53 (td, *J* = 10.89, 9.82 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.2, 166.9, 162.9, 148.3, 141.6, 136.5, 130.1, 129.9, 128.7, 128.6, 127.1, 126.9, 126.7, 118.8, 118.5, 118.4, 52.1, 49.3, 45.9, 30.5; **IR** (thin film): ν 2925, 1718, 1631, 1275 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{25}H_{22}O_4$ requires *m/z* 385.1445, found *m/z* 385.1449; **$[\alpha]^{22}_D$** −84.8 º (*c*0.21, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.36 (s, 1H), 7.82 (d, *J* = 8.27 Hz, 2H), 7.55 (dd, *J* = 8.09, 1.67 Hz, 1H), 7.46 (ddd, *J* = 8.66, 7.21, 1.65 Hz, 1H), 7.11 (m, 2H), 7.07 (m, 3H), 7.01 (dd, *J* = 8.40, 1.16 Hz, 1H), 6.95 (m, 2H), 6.82 (ddd, *J* = 8.24, 7.21, 1.21 Hz, 1H), 4.42 (m, 2H), 4.13 (m, 1H), 3.86 (s, 1H), 2.98 (m, 1H), 2.86 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.7, 167.0, 162.9, 145.9, 138.7, 136.5, 129.9, 129.3, 128.2, 127.9, 127.9, 127.8, 126.7, 119.0, 118.7, 118.1, 52.0, 47.0, 44.5, 41.5, 27.2; **IR** (thin film): ν 2925, 1718, 1632, 1276 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{25}H_{22}O_4$ requires *m/z* 385.1445, found *m/z* 385.1447; **$[\alpha]^{22}_D$** −76.6 º (*c*0.18, $CH_2Cl_2$).




**(2-hydroxyphenyl)((1R,2R,3S)-2-phenyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)cyclobutyl)methanone** (**2.17u**):

Experiment 1: Prepared according to general procedure B using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 920 μL (4.0 mmol) 4-vinylphenylboronic acid pinacol ester, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel

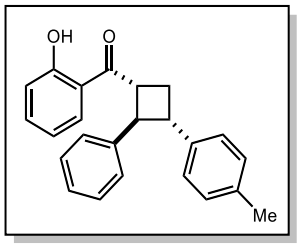
(10% MTBE:Pent). Combined yield: 160 mg of a clear oil (88%, 0.35 mmol) as a 2:1 (major:minor) mixture of diastereomers; 93% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 7.23 min, $t_2$ = 7.52 min), 97% ee (minor) (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 6.83 min, $t_2$ = 8.54 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (7% MTBE: Pent). Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 920 μL (4.0 mmol) 4-vinylphenylboronic acid pinacol ester. Crude d.r.: 1:1; Combined isolated yield: 154 mg of a clear oil (85%, 0.34 mmol); 93% ee (major), 97% ee (minor).

Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.40 (s, 1H), 7.76 (d, *J* = 8.07 Hz, 2H), 7.53 (dd, *J* = 8.06, 1.65 Hz, 1H), 7.28-7.31 (m, 4H), 7.24-7.26 (m, 2H), 7.20-7.23 (m, 1H), 6.98 (dd, *J* = 8.42,1.13 Hz, 1H), 6.78 (ddd, *J* = 8.10, 7.18, 1.15 Hz, 1H), 4.03-4.10 (m, 2H), 3.73-3.80 (m, 1H), 2.76-2.82 (m, 1H), 2.46-2.53 (m, 1H), 1.33 (s, 12H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.5, 162.8, 146.2, 141.9, 136.4, 135.0, 128.6, 126.91, 126.85, 126.2, 118.8, 118.48, 118.47, 83.7, 49.1, 45.9, 43.1, 31.0, 24.8; **$^{11}$B NMR** (160 MHz, $CDCl_3$): δ 31.7; **IR** (thin film): ν 2926, 1742, 1633, 1609, 1359 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{29}H_{31}BO_4$ requires *m/z* 452.2279, found *m/z* 452.2282; **$[\alpha]^{22}_D$** −19.46 º (*c*0.74, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.39 (s, 1H), 7.59 (d, *J* = 8.02 Hz, 2H), 7.56 (dd, *J* = 8.00, 1.66 Hz, 1H), 7.45 (ddd, *J* = 8.65, 7.16, 1.65 Hz, 1H), 7.09-7.12 (m, 2H), 7.04-7.07 (m, 1H), 6.99-7.02 (m, 3H), 6.94-6.96 (m, 2H), 6.81 (ddd *J* = 8.21, 7.20, 1.19 Hz, 1H), 4.38-4.43 (m, 2H), 4.05-4.10 (m, 1H), 2.90-2.95 (m, 1H), 2.78-2.86 (m, 1H), 1.31 (s, 12H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 206.0, 162.9, 143.7, 139.2, 136.3, 134.5, 130.0, 128.1, 128.0, 127.3, 126.4, 118.9, 118.6, 118.1, 83.65, 46.8, 44.8, 41.6, 27.6, 24.9; **$^{11}$B NMR** (160 MHz, $CDCl_3$): δ 31.4; **IR** (thin film): ν 2927, 1743, 1635, 1610, 1360 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{29}H_{31}BO_4$ requires *m/z* 452.2279, found *m/z* 452.2282; **$[\alpha]^{22}_D$** −56.0 º (*c*0.60, $CH_2Cl_2$).




**(2-Hydroxyphenyl)((1*R*,2*R*,3*S*)-2-phenyl-3-(*p*-tolyl)cyclobutyl)methanone** (**2.17v**):

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 527 μL (4.0 mmol) 1-methyl-4-vinylbenzene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 120 mg of a clear oil (88%, 0.35 mmol) as a 2:1 (major:minor) mixture of diastereomers; 92% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 6.46 min, $t_2$ = 6.81 min), 96% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 6.42 min, $t_2$ = 6.86 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (4% MTBE: Pent). Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 527 μL (4.0 mmol) 1-methyl-4-vinylbenzene. Crude d.r.: 2:1; Combined isolated yield: 115 mg of a clear oil (84%, 0.34 mmol); 92% ee (major), 96% ee (minor).

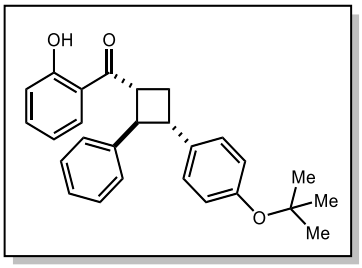
Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.42 (s, 1H), 7.53 (dd, *J* = 8.06, 1.65 Hz, 1H), 7.43 (ddd, *J* = 8.65, 7.16, 1.65 Hz, 1H), 7.26-7.31 (m, 4H), 7.20-7.23 (m, 1H), 7.18 (d, *J* = 8.03 Hz 2H), 7.12 (d, *J* = 7.87 Hz, 2H), 6.98 (dd, *J* = 8.40, 1.13 Hz 1H), 6.78 (ddd, *J* = 8.25, 7.12, 1.17 Hz 1H), 4.01-4.07 (m, 2H), 3.70-3.76 (m, 1H), 2.75-2.81 (m, 1H), 2.44-2.50 (m, 1H), 2.32 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.6, 162.8, 142.1, 140.1, 136.4, 136.2, 130.2, 129.2, 128.6, 127.0, 126.8, 126.7, 118.8, 118.53, 118.46, 49.3, 45.9, 42.5,

32.1, 21.1; **IR** (thin film): ν 2922, 1630, 1580, 1485, 1445, 1207, 1155 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{22}O_2$ requires *m/z* 341.1547, found *m/z* 341.1547; $[\alpha]^{22}_D$ −50.4 º (*c*0.79, $CH_2Cl_2$).

Minor

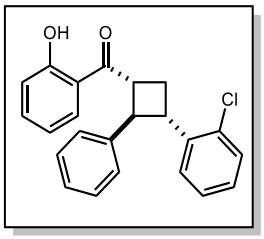
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.41 (s, 1H), 7.57 (dd, *J* = 8.09, 1.65 Hz, 1H), 7.44 (ddd, *J* = 8.65, 7.20, 1.63 Hz, 1H), 7.10-7.14 (m, 2H), 7.05-7.09 (m, 1H), 7.00 (dd, *J* = 8.41, 1.12 Hz, 1H), 6.94-6.96 (m, 4H), 6.89 (d, *J* = 8.03 Hz, 2H), 6.81 (ddd, *J* = 8.21, 7.19, 1.20 Hz, 1H), 4.35-4.44 (m, 2H), 4.02 (td, *J* = 9.02, 5.74 Hz, 1H), 2.91 (dddd, *J* = 11.93, 8.84, 6.92, 1.43 Hz, 1H), 2.78 (ddd, *J* = 11.93, 9.05, 5.80 Hz, 1H), 2.23 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 206.1, 162.8, 139.4, 137.2, 136.3, 135.5, 130.0, 128.7, 128.0, 127.97, 127.80, 126.3, 118.9, 118.6, 118.2, 46.7, 44.8, 41.1, 27.9, 21.0; **IR** (thin film): ν 2923, 1632, 1579, 1485, 1445, 1206, 1154 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{22}O_2$ requires *m/z* 341.1547, found *m/z* 341.1548; $[\alpha]^{22}_D$ −108.0 º (*c*1.2, $CH_2Cl_2$).




**((1*R*,2*R*,3*S*)-3-(4-(*tert*-Butoxy)phenyl)-2-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.17w**):

Experiment 1: Prepared according to general procedure B using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 518 μL (4.0 mmol) 1-(*tert*-butoxy)-4-vinylbenzene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (2.0-2.5% EtOAc:Hex gradient). Combined yield: 146 mg of a clear oil (91%, 0.36 mmol) as a 2:1 (major:minor) mixture of diastereomers; 96% ee (Daicel CHIRALPAK® OJ-H, gradient 5% to 20% (EtOH), 3 mL/min, 221nm; $t_1$ = 11.76 min, $t_2$ = 13.34 min. Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg

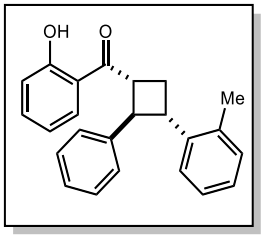
(0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 518 μL (4.0 mmol) 1-1-(*tert*-butoxy)-4-vinylbenzene. Crude d.r.: 2:1; Combined isolated yield: 132 mg of a clear oil (83%, 0.33 mmol); 91% ee. **(1*R*, 2*R*, 3*S*)** diastereomer (major) and **(1*R*, 2*R*, 3*R*)** diastereomer **(**minor) as a mixture: **$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.42 (s, 0.68H), 12.40 (s, 0.40H), 7.56 (dd, *J* = 7.9, 1.6 Hz, 0.40H), 7.51 (dd, *J* = 8.0, 1.7 Hz, 0.80H), 7.44 (dddd, *J* = 8.7, 7.2, 4.5, 1.7 Hz, 1.28H), 7.28-2.32 (m, 3.02H), 7.20-2.24 (m, 0.78H), 7.14-7.17 (m, 1.51H), 7.03-7.20 (m, 1H), 6.99 (td, *J* = 8.6, 1.1 Hz, 1.25H), 6.92 (dd, *J* = 8.3, 1.9 Hz, 1.5H), 6.89 (m, 1.45H), 6.41-6.81 (m, 1.9H), 4.42 (q, *J* = 8.8 Hz, 0.40H), 4.33 (t, *J* = 8.8 Hz, 0.40H), 3.99-4.06 (m, 1.90H), 3.75 (td, *J* = 8.6, 1.2 Hz, 0.75H), 2.88-2.96 (m, 0.40H), 2.73-2.83 (m, 1.11H), 2.44-2.51 (m, 0.75H), 1.32 (s, 6H), 1.24 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 206.1, 206.0, 162.83, 162.81, 153.9, 153.3, 142.1, 139.1, 138.0, 136.33, 136.30, 135.14, 135.13, 130.0, 128.6, 128.2, 128.1, 127.9, 127.0, 126.8, 126.3, 126.1, 124.2, 124.0, 118.9, 118.8, 118.6, 118.5, 118.4, 118.2, 78.3, 78.2, 49.4, 47.0, 46.0, 44.4, 42.0, 41.1, 31.1, 28.8, 28.7, 27.1; **IR** (thin film): ν 2926, 1609, 1254, 1117, 910 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{27}H_{28}O_3$ requires *m/z* 399.1966, found *m/z* 399.1968; **$[\alpha]^{22}_D$** −131.0 º (*c*1.0, $CH_2Cl_2$).




**((1*R*,2*R*,3*S*)-3-(2-Chlorophenyl)-2-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.17x**)**:**

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 580 μL (4.0 mmol) 1-chloro-2-styrene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (1-2.5% EtOAc:Hex gradient). Combined yield: 127 mg of a clear oil (88%, 0.35 mmol); 95% ee (Daicel CHIRALPAK® OJ-H, 5% (*i*-PrOH), 4 mL/min, 221nm; $t_1$ = 8.93 min, $t_2$ = 9.47 min. Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-

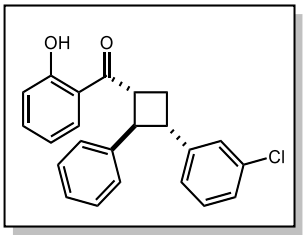
BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 580 μL (4.0 mmol) 1-chloro-2-vinylbenzene. Crude d.r.: 4:1; Combined isolated yield: 108 mg of a clear oil (76%, 0.30 mmol); 92% ee. **$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.38 (s, 1H), 7.57 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.43-7.48 (m, 2H), 7.34 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.23-7.24 (m, 2H), 7.20-7.22 (m, 1H), 7.17 (td, *J* = 7.7, 1.1 Hz, 1H), 6.99 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.81 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H), 4.32 (t, *J* = 9.7, 1H), 4.16 (td, *J* = 10.1, 8.2 Hz, 1H), 4.06 (q, *J* = 8.8 Hz, 1H), 3.04 (dt, *J* = 10.8, 8.4 Hz, 1H), 2.26 (q, *J* = 10.2 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.4, 162.8, 141.6, 140.1, 136.4, 133.6, 130.1, 129.4, 128.6, 127.83, 127.75, 127.0, 126.93, 126.90, 118.9, 118.5, 118.4, 46.5, 46.0, 39.5, 32.4; **IR** (thin film): ν 2921, 2023, 1975, 1638, 1215, 754 $cm^{-1}$**;** **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{23}H_{19}ClO_2$ requires *m/z* 361.1001, found *m/z* 361.1002; **$[\alpha]^{22}_D$** −40.0 ° (*c*0.3, $CH_2Cl_2$).




**(2-Hydroxyphenyl)((1*R*,2*R*,3*S*)-2-phenyl-3-(*o*-tolyl)cyclobutyl)methanone** (**2.17y**):

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 518 μL (4.0 mmol) 1-methyl-2-vinylbenzene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (0-10% Acetone:Hex gradient). Combined yield: 125 mg of a clear oil (91%, 0.36 mmol); 98% ee (Daicel CHIRALPAK® OD-H, 5% (*i*-PrOH), 4 mL/min, 221nm; $t_1$ = 10.10 min, $t_2$ = 11.34 min. Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 518 μL (4.0 mmol) 1-methyl-2-vinylbenzene. Crude d.r.: 2:1; Combined isolated yield: 119 mg of a clear oil (86%, 0.34 mmol); 98% ee.

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.40 (s, 1H), 7.55 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.44 (ddd, *J* = 8.6, 7.1, 1.66 Hz, 1H) 7.40 (d, *J* = 7.7 Hz, 1H) 7.29 (d, *J* = 4.3 Hz, 4H) 7.18-7.24 (m, 2H), 7.13 (m, 2H), 6.98 (dd, *J* = 8.4, 1.1 Hz, 1H) 6.79 (ddd, *J* = 8.1, 7.2, 1.2 Hz, 1H), 4.27 (t, *J* = 9.6 Hz, 1H), 4.07 (q, *J* = 8.1 Hz, 1H), 3.93 (q, *J* = 8.1 Hz, 1H), 2.88 (dt, *J* = 10.6, 8.3 Hz, 1H), 2.34 (q, *J* = 10.2 Hz, 1H), 2.25 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.5, 162.8, 142.1, 140.7, 136.4, 135.8, 130.13, 130.10, 128.6, 126.9, 126.8, 126.5, 126.2, 125.9, 118.8, 118.50, 118.47, 47.0, 46.2, 40.1, 32.0, 19.8; **IR** (thin film): ν 3028, 1633, 1487, 1284, 754 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{22}O_2$ requires *m/z* 341.1547, found *m/z* 341.1548; **$[\alpha]^{22}_D$** – 24.0 º (*c*0.3, $CH_2Cl_2$).




**((1*R*,2*R*,3*S*)-3-(4-Chlorophenyl)-2-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.17z**):

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 508 μL (4.0 mmol) 1-chloro-3-vinylbenzene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 129 mg of a clear oil (89%, 0.36 mmol) as a 2:1 (major:minor) mixture of diastereomers; 95% ee (major) (Daicel CHIRALPAK® OJ-H, gradient 5% to 30% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 9.01 min, $t_2$ = 9.74 min), 98% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 8.17 min, $t_2$ = 8.72 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (3% MTBE: Pent). Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 508

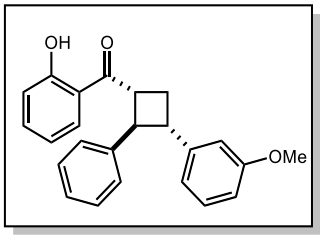
μL (4.0 mmol) 1-chloro-3-vinylbenzene. Crude d.r.: 2:1; Combined isolated yield: 128 mg of a clear oil (88%, 0.35 mmol); 95% ee (major), 98% ee (minor).

Major:

**$^{1}$H NMR** (500 MHz, $CDCl_3$): δ 12.37 (s, 1H), 7.49 (dd, *J* = 8.11, 1.51 Hz, 1H), 7.43 (ddd, *J* = 8.34, 7.21, 1.57 Hz, 1H), 7.32 (t, *J* = 7.51 Hz, 2H), 7.18-7.28 (m, 6H), 7.15 (dd, *J* = 7.53, 1.60 Hz, 1H), 6.98 (dd, *J* = 8.51, 1.06 Hz, 1H), 6.77 (td, *J* = 7.29, 1.06 Hz 1H), 4.01-4.08 (m, 2H), 3.71-3.77 (m, 1H), 2.76-2.83 (m, 1H), 2.44-2.52 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.2 162.9, 145.1, 141.5, 136.5, 134.4, 130.1, 129.8, 128.7, 127.1, 126.9, 126.8, 124.9, 118.8, 118.5, 118.4, 49.2, 45.9, 42.3, 39.7; **IR** (thin film): ν 2925, 1632, 1482, 1445, 1206, 1155 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{23}H_{19}ClO_2$ requires *m/z* 361.1001, found *m/z* 361.1005; **$[\alpha]^{22}_D$** −38.4 º (*c*3.2, $CH_2Cl_2$).

Minor:

**$^{1}$H NMR** (500 MHz, $CDCl_3$): δ 12.36 (s, 1H), 7.54 (dd, *J* = 8.09, 1.66 Hz, 1H), 7.46 (ddd, *J* = 8.61, 7.16, 1.66 Hz, 1H), 7.13-7.17 (m, 2H), 7.08-7.11 (m, 1H), 7.04-7.05 (m, 2H), 7.00-7.02 (m, 2H), 6.95-6.97 (m, 2H), 6.80-6.83 (m, 2H), 4.35-4.42 (m, 2H), 4.01-4.07 (m, 1H), 2.95 (dddd, *J* = 12.15, 8.18, 7.25, 2.48 Hz, 1H), 2.80 (ddt, *J* = 12.34, 9.23, 5.77 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.7, 162.9, 142.5, 138.7, 136.4, 133.9, 129.9, 129.1, 128.2, 128.0, 127.9, 126.6, 126.2, 126.2, 119.0, 118.6, 118.1, 47.0, 44.4, 41.1, 27.1; **IR** (thin film): ν 2924, 1632, 1482, 1446, 1207, 1156 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{23}H_{19}ClO_2$ requires *m/z* 361.1001, found *m/z* 361.1004; **$[\alpha]^{22}_D$** −81.8 º (*c*0.93, $CH_2Cl_2$).

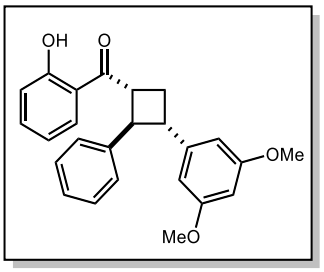



**(2-Hydroxyphenyl)((1*R*,2*R*,3*S*)-3-(3-methoxyphenyl)-2-phenylcyclobutyl)methanone** (**2.17aa**)**:**

Experiment 1: Prepared according to general procedure B using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 555 μL (4.0 mmol) 3-

vinylanisole, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (gradient 1% to 5% EtOAc:Hex). Combined yield: 129 mg of a clear oil (90%, 0.36 mmol) as a 2:1 (major:minor) mixture of diastereomers; 93% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (*i*-PrOH), 1 mL/min, 240 nm; $t_1$ = 4.5 min, $t_2$ = 5.1 min). Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 555 μL (4.0 mmol) 3-vinylanisole. Crude d.r.: 2:1; Combined isolated yield: 135 mg of a clear oil (94%, 0.38 mmol); 93% ee (major).

**(1*R*, 2*R*, 3*S*)** diastereomer (major) and **(1*R*, 2*R*, 3*R*)** diastereomer **(**minor) as a mixture: **$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.41 (s, 0.64H), 12.40 (s, 0.42H), 7.56 (dd, *J* = 8.1, 1.6 Hz, 0.46H), 7.51 (dd, *J* = 8.1, 2.6 Hz, 0.77H), 7.43 (dddd, *J* = 8.6, 7.2, 5.8, 1.6 Hz, 1.4H), 7.29 (d, *J* = 6.4 Hz, 1.5H), 7.22 (t, *J* = 7.6 Hz, 1.5H), 7.13 (dd, *J* = 8.0, 6.3 Hz, 0.96H), 7.09 – 7.04 (m, 0.93H), 7.02 – 6.95 (m, 2.1H), 6.86 (d, *J* = 7.6 Hz, 0.74H), 6.83 – 6.73 (m, 2.6H), 6.62 (dd, *J* = 8.3, 2.4 Hz, 0.90H), 6.49 (t, *J* = 2.0 Hz, 0.44H), 4.44 – 4.32 (m, 0.91H), 4.12 (dd, *J* = 14.4, 7.2 Hz, 0.24H), 4.07 – 3.98 (m, 1.8H), 3.77 (s, 1.49H), 3.77 – 3.69 (m, 1.38H), 3.62 (s, 1.36H), 2.99 – 2.84 (m, 0.48H), 2.82 – 2.72 (m, 1.3H), 2.55 – 2.39 (m, 0.65H), 1.30 – 1.21 (m, 0.56H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 206.0, 205.4, 162.8, 159.70, 159.2, 144.8, 142.0, 139.2, 136.3, 130.1, 130.0, 129.5, 128.9, 128.6, 128.0, 127.0, 126.9, 126.4, 121.5, 120.3, 119.1, 118.9, 118.8, 118.6, 118.5, 118.4, 118.1, 113.9, 112.6, 112.0, 111.7, 111.4, 55.2, 55.0, 49.1, 46.8, 45.89, 44.6, 42.7, 41.4, 30.9, 27.5; **IR** (thin film): ν 3030, 1631, 1400, 1207, 900 $cm^{-1}$; **HRMS** (ESI$^-$): $[M-H]^-$ calculated for $C_{24}H_{22}O_3$ requires *m/z* 357.1496, found *m/z* 357.1498; **$[\alpha]^{22}_D$** −92.4° (*c*1.0, $CH_2Cl_2$).




**((1*R*,2*R*,3*S*)-3-(3,5-Dimethoxyphenyl)-2-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.17ab**):

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 656 μL (4.0 mmol) 1,3-dimethoxy-5-vinylbenzene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (10% MTBE:Pent). Combined yield: 135 mg of a clear oil (87%, 0.35 mmol) as a 2:1 (major:minor) mixture of diastereomers; 91% ee (major) (Daicel CHIRALPAK® AD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 9.80 min, $t_2$ = 10.88 min), 95% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 7.80 min, $t_2$ = 8.07 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (7% MTBE: Pent). Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 656 μL (4.0 mmol) 1,3-dimethoxy-5-vinylbenzene. Crude d.r.: 2:1; Combined isolated yield: 115 mg of a clear oil (84%, 0.34 mmol); 89% ee (major), 95% ee (minor).

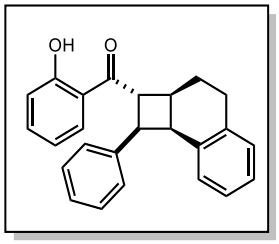
Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.40 (s, 1H), 7.52 (dd, *J* = 8.00, 1.64 Hz, 1H), 7.44 (ddd, *J* = 8.65, 7.15, 1.65 Hz, 1H), 7.27-7.32 (m, 4H), 7.21-7.24 (m, 1H), 6.98 (dd, *J* = 8.37,1.13 Hz 1H), 6.78 (ddd, *J* = 8.19, 7.18, 1.18 Hz, 1H), 6.42 (dd, *J* = 2.26, 0.61 Hz 2H), 6.33 (t, *J* = 2.29 Hz 1H), 4.00-4.07 (m, 2H), 3.76 (s, 6H), 3.68-3.74 (m, 1H), 2.75-2.81 (m, 1H), 2.45-2.51 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.4, 162.8, 160.9, 145.6, 142.0, 136.4, 130.1, 128.6, 127.0, 126.9, 118.8, 118.5, 104.9, 98.4, 55.3, 49.0, 45.8,

43.0, 30.9; **IR** (thin film): ν 2928, 1741, 1633, 1600, 1205, 1154 cm$^{-1}$; **HRMS** (ESI$^-$): [M-H]$^-$ calculated for $C_{25}H_{24}O_4$ requires *m/z* 387.1602, found *m/z* 387.1604; **[α]$^{22}_D$** −34.0 º (*c*0.30, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.38 (s, 1H), 7.55 (dd, *J* = 8.07, 1.64 Hz, 1H), 7.45 (ddd, *J* = 8.61, 7.18, 1.67 Hz, 1H), 7.13-7.17 (m, 2H), 7.08-7.12 (m, 1H), 6.99-7.01 (m, *J* = 8.51, 1.51 Hz, 3H), 6.80 (ddd, *J* = 8.13, 7.16, 1.16 Hz, 1H), 6.19 (t, *J* = 2.26 Hz, 1H), 6.12 (d, *J* = 2.50 Hz, 2H), 4.34-4.41 (m, 2H), 3.99 (ddd, *J* = 8.68, 8.13, 5.75 Hz, 1H), 3.61 (s, 6H), 2.87-2.93 (m, 1H), 2.76-2.82 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 206.0, 162.8, 160.4, 142.7, 139.2, 136.4, 130.0, 128.1, 126.5, 118.9, 118.6, 118.2, 106.3, 97.9, 55.2, 46.9, 44.6, 41.6, 27.5; **IR** (thin film): ν 2930, 1633, 1598, 1201, 1152 cm$^{-1}$; **HRMS** (ESI$^-$): [M-H]$^-$ calculated for $C_{25}H_{24}O_4$ requires *m/z* 387.1602, found *m/z* 387.1605; **[α]$^{22}_D$** −71.2 º (*c*0.70, $CH_2Cl_2$).

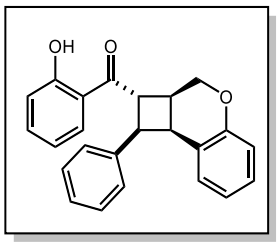



**(2-Hydroxyphenyl)((1*R*,2*R*,2a*S*,8b*R*)-1-phenyl-1,2,2a,3,4,8b-hexahydrocyclobuta[*a*]naphthalen-2-yl)methanone** (**2.17ac**)**:**

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 522 μL (4.0 mmol) 1,2-dihydronaphthalene, and an irradiation time of 20 h. The crude material resulted in >10:1 (major:minor) d.r. that was purified by flash-column chromatography on silica gel (5.0-10% Acetone:Hex gradient). Combined yield: 129 mg of a clear oil (91%, 0.36 mmol); 96% ee (Daicel CHIRALPAK® OD-H, gradient 5% to 20% (EtOH), 4 mL/min, 221nm; $t_1$ = 10.94 min, $t_2$ = 11.76 min. Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 522 μL (4.0 mmol)

1,2-dihydronaphthalene. Crude d.r.: >10:1; Combined isolated yield: 137 mg of a clear oil (97%, 0.38 mmol); 96% ee.

**$^{1}$H NMR** (500 MHz, $CDCl_3$): δ 12.53 (s, 1H), 7.47 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.40 (ddd, *J* = 8.7, 7.2, 1.7 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.06 (qq, *J* = 2.5, 1.1 Hz, 3H), 6.95 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.84 (tt, *J* = 7.3, 1.2 Hz, 1H), 6.74-6.78 (m, 2H), 6.71 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H), 6.41 (d, *J* = 7.6 hz, 1H), 4.40 (t, *J* = 9.7 Hz, 1H), 4.26 (t, *J* = 9.3, 1H), 3.86 (t, *J* = 9.0 Hz, 1H), 3.37 (tt, *J* = 8.2, 3.6 Hz, 1H), 3.19 (ddd, *J* = 17.6, 12.8, 5.3 Hz, 1H), 2.97 (ddd, *J* = 16.5, 5.2, 2.2 Hz, 1H), 1.98 (ddt, *J* = 14.2, 5.3, 2.6 Hz, 1H), 1.76 (tt, *J* = 13.4, 4.7 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.9, 162.9, 138.7, 136.6, 136.3, 134.9, 131.7, 130.1, 128.8, 128.5, 127.8, 126.5, 125.8, 119.0, 118.7, 118.4, 46.5, 45.9, 39.2, 33.9, 26.5, 23.0; **IR** (thin film): ν 2925, 1632, 1487, 1205, 1156, 754 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{25}H_{22}O_2$ requires *m/z* 353.1547, found *m/z* 353.1549; **$[\alpha]^{22}_D$** −76.0 º (*c*0.6, $CH_2Cl_2$).

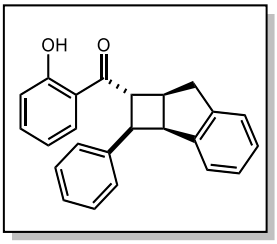



**(2-Hydroxyphenyl)((1*R*,2*S*,2a*S*,8b*S*)-1-phenyl-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[*c*]chromen-2-yl)methanone** (**2.17b**)**:**

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 529 mg (4.0 mmol) 2-*H*-chromene, and an irradiation time of 20 h. The crude material resulted in >10:1 (major:minor) d.r. that was purified by flash-column chromatography on silica gel (0%-1%-5% EtOAc:Hex gradient). Combined yield: 143 mg of a clear oil (100%, 0.4 mmol); >99% ee (Daicel CHIRALPAK® OJ-H, 8% (EtOH), 4 mL/min, 221nm; $t_1$ = 3.62 min, $t_2$ = 4.56 min. Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg

(0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 529 mg (4.0 mmol) 2-*H*-chromene. Crude d.r.: >10:1; Combined isolated yield: 132 mg of a clear oil (93%, 0.37 mmol); 97% ee.

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.41 (s, 1H), 7.56 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.41 (ddd, J = 8.6, 7.2, 1.7 Hz, 1H), 7.04-7.12 (m, 4H), 7.01 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.95 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.76-6.82 (m, 1H), 6.73 (td, *J* = 7.6, 7.0, 1.1 Hz, 1H), 6.62 (td, *J* = 7.4, 1.3 Hz, 1H), 6.36 (dd, J = 7.7, 1.5 Hz, 1H), 4.57 (t, *J* = 9.5 Hz, 1H), 4.35 (dd, *J* = 10.3, 8.8 Hz, 1H), 4.22 (dd, *J* = 11.8, 1.6 Hz, 1H), 3.86 (dd, *J* = 11.9, 2.1 Hz, 1H), 3.80 (t, *J* = 8.8 Hz, 1H), 3.35 (tt, *J* = 8.8, 1.9 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.1, 162.9, 155.6, 137.9, 136.5, 132.1, 130.5, 128.3, 127.8, 127.4, 126.8, 122.3, 121.4, 118.93, 118.90, 118.3, 117.4, 65.3, 46.0, 44.4, 36.1, 35.5; **IR** (thin film): ν 3030, 2926, 2866, 1632, 1254 $cm^{-1}$; **HRMS** ($ESI^-$): $[M+H]^+$ calculated for $C_{24}H_{20}O_3$ requires *m/z* 357.1487, found *m/z* 357.1478. **$[\alpha]^{22}_D$** −92.0 º (*c*1.0, $CH_2Cl_2$).




**(2-Hydroxyphenyl)((1*R*,2*R*,2a*R*,7a*S*)-2-phenyl-2,2a,7,7a-tetrahydro-1*H*-cyclobuta[*a*]inden-1-yl)methanone** (**2.17c**):

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 467 μL (4.0 mmol) 1*H*-indene, and an irradiation time of 20 h. The crude material resulted in a 3:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 121 mg of a clear oil (89%, 0.36 mmol) as a 3:1 (major:minor) mixture of diastereomers; 95% ee (major) (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 10.66 min, $t_2$ = 11.25 min), 92% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 8.18 min, $t_2$ = 8.95 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (5% MTBE: Pent). Experiment 2: 89.6

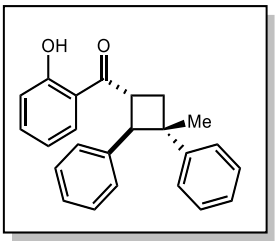
mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S,S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 467 μL (4.0 mmol) 1*H*-indene. Crude d.r.: 3:1; Combined isolated yield: 120 mg of a clear oil (88%, 0.35 mmol); 91% ee (major), 92% ee (minor).

Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.50 (s, 1H), 7.46 (dd, *J* = 8.03, 1.65 Hz, 1H), 7.39 (ddd, *J* = 8.59, 7.18, 1.68 Hz, 1H), 7.36 (d, *J* = 7.56 Hz, 1H), 7.21 (t, *J* = 7.45 Hz 1H), 7.15-7.18 (m, 3H), 6.94-6.98 (m, 2H), 6.85-6.87 (m, 2H), 6.69 (ddd, *J* = 8.17, 7.14, 1.17 Hz, 1H), 6.45 (d, *J* = 7.58 Hz, 1H), 4.36 (t, *J* = 9.31 Hz, 1H), 4.14 (t, *J* = 8.01 Hz, 1H), 4.06 (dd, *J* = 10.03, 6.59 Hz, 1H), 3.53 (q, *J* = 7.14 Hz, 1H), 3.29 (dd, *J* = 16.77, 7.66 Hz, 1H), 3.08 (d, *J* = 16.78 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.9, 162.9, 143.7, 141.4, 138.6, 136.3, 130.1, 128.3, 127.9, 127.8, 127.2, 126.7, 126.1, 125.4, 118.8, 118.7, 118.4, 50.5, 48.4, 45.7, 38.9, 37.6; **IR** (thin film): ν 3027, 2916, 1689, 1628, 1483, 1445, 1200, 1154 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{20}O_2$ requires *m/z* 339.1391, found *m/z* 339.1391; **$[\alpha]^{22}_D$** −136.6 º (*c*1.4, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 12.29 (s, 1H), 7.76 (dd, *J* = 8.03, 1.62 Hz, 1H), 7.49 (ddd, *J* = 8.66, 7.18, 1.66 Hz, 1H), 7.36-7.37 (m, 4H), 7.23-7.26 (m, 2H), 7.16-7.20 (m, 3H), 7.02 (dd, *J* = 8.48, 1.14 Hz, 1H), 6.93 (ddd, *J* = 8.23, 7.19, 1.17 Hz, 1H), 4.33 (t, *J* = 9.26 Hz, 1H), 4.12 (ddd, *J* = 8.82, 7.15, 1.03 Hz, 1H), 4.03 (t, *J* = 7.37 Hz, 1H), 3.73-3.80 (m, 1H), 3.10 (dd, *J* = 17.42, 10.14 Hz, 1H), 2.92 (dd, *J* = 17.46, 4.98 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.4, 162.5, 125.5, 144.6, 143.3, 136.3, 129.9, 128.6, 126.93, 126.89, 126.5, 126.5, 125.1, 123.6, 119.0, 118.8, 118.7, 50.1, 50.1, 46.2, 40.1, 34.3; **IR** (thin film): ν 2923, 2852, 1742, 1627, 1483, 1446, 1203 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{20}O_2$ requires *m/z* 339.1391, found *m/z* 339.1390; **$[\alpha]^{22}_D$** −111.6 º (*c*1.2, $CH_2Cl_2$); mp = 125-128 ºC.




**(2-Hydroxyphenyl)((1*R*,2*R*,3*S*)-3-methyl-2,3-diphenylcyclobutyl)methanone (2.17n):**

Experiment 1: Prepared according to general procedure A using 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 520 μL (4.0 mmol) prop-1-en-2-ylbenzene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 115 mg of a clear oil (84%, 0.34 mmol) as a 2:1 (major:minor) mixture of diastereomers; 96% ee (major) (Daicel CHIRALPAK® OD-H, 10% solvent (methanol), 4 mL/min, 221 nm; $t_1$ = 4.88 min, $t_2$ = 5.17 min), 96% ee (minor) (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 4.25 min, $t_2$ = 4.92 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (3% MTBE: Pent). Experiment 2: 89.6 mg (0.04 mmol) (*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 520 μL (4.0 mmol) prop-1-en-2-ylbenzene. Crude d.r.: 2:1; Combined isolated yield: 112 mg of a clear oil (82%, 0.33 mmol); 96% ee (major), 96% ee (minor).

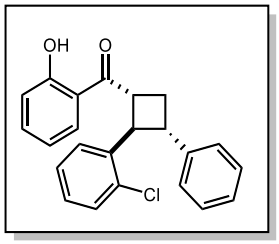
Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.33 (s, 1H), 7.75 (dd, *J* = 8.06, 1.65 Hz, 1H), 7.45 (ddd, *J* = 8.65, 7.25, 1.64 Hz, 1H), 7.25-7.36 (m, 9H), 7.21 (tt, *J* = 6.41, 1.67 Hz 1H), 6.97 (dd, *J* = 8.40, 1.17 Hz, 1H), 6.86 (ddd, *J* = 8.25, 7.21, 1.20 Hz, 1H), 4.43 (q, *J* = 9.45 Hz, 1H), 4.34 (d, *J* = 9.88 Hz, 1H), 2.73 (dd, *J* = 10.80, 9.53 Hz, 1H), 2.50 (dd, *J* = 10.79, 8.95 Hz, 1H), 1.40 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 206.0, 162.8, 150.2, 139.0, 136.3, 123.0, 128.4, 128.4, 128.2, 126.8, 126.0, 125.1, 118.8, 118.6, 118.5, 50.0, 43.6, 41.3,

37.7, 24.9; **IR** (thin film): ν 2959, 2928, 1631, 1487, 1445, 1289, 1210 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{22}O_2$ requires *m/z* 341.1547, found *m/z* 341.1547; $[\alpha]^{22}_D$ −103.4 º (*c*0.69, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.39 (s, 1H), 7.55 (dd, *J* = 8.07, 1.66 Hz, 1H), 7.43 (ddd, *J* = 8.63, 7.19, 1.65 Hz, 1H), 7.13-7.17 (m, 2H), 7.08-7.11 (m, 4H), 6.98 (ddd, *J* = 8.24, 5.32, 1.37 Hz, 3H), 6.85 (m, 2H), 6.78 (ddd, *J* = 8.24, 7.21, 1.21 Hz, 1H), 4.17 (q, *J* = 8.99 Hz, 1H), 3.96 (d, *J* = 8.88 Hz, 1H), 3.14 (dd, *J* = 11.95, 9.35 Hz, 1H), 2.57 (dd, *J* = 11.90, 8.70 Hz, 1H), 1.64 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 206.1, 162.8, 143.7, 139.4, 136.3, 130.1, 128.3, 127.9, 127.8, 127.0, 126.6, 125.8, 118.8, 118.5, 118.4, 54.7, 45.9, 42.3, 34.4, 32.2; **IR** (thin film): ν 2923, 2853, 1740, 1632, 1487, 1446, 1244, 1208 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{22}O_2$ requires *m/z* 341.1547, found *m/z* 341.1546; $[\alpha]^{22}_D$ −134.6 º (*c*0.15, $CH_2Cl_2$).




**((1*R*,2*R*,3*S*)-2-(2-Chlorophenyl)-3-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.21**)**:**

Experiment 1: Prepared according to general procedure A using 103.5 mg (0.4 mmol) (*E*)-3-(2-chlorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene, and an irradiation time of 20 h. The crude material resulted in a 1:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 133 mg of a clear oil (92%, 0.37 mmol) as a 1:1 (major:minor) mixture of diastereomers; 95% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 255 nm; $t_1$ = 7.60 min, $t_2$ = 7.97 min), 98% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 4 mL/min, 221 nm; $t_1$ = 6.57 min, $t_2$ = 8.38 min).. Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (3% MTBE: Pent). Experiment 2: 103.5 mg (0.4 mmol) (*E*)-3-(2-chlorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one, 19.2 mg (0.04 mmol)

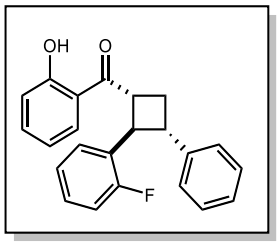
$Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene. Crude d.r.: 1:1; Combined isolated yield: 133 mg of a clear oil (92%, 0.37 mmol); 95% ee (major), 98% ee (minor).

Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.41 (s, 1H), 7.57 (dd, *J* = 7.78, 1.61 Hz, 1H), 7.42 (m, 2H), 7.28-7.33 (m, 6H), 7.16-7.23 (m, 2H), 6.97 (m, 1H), 6.72 (td, *J* = 7.64, 1.20 Hz, 1H), 4.46 (t, *J* = 9.59 Hz, 1H), 4.17 (td, *J* = 9.44, 8.32 Hz, 1H), 3.88 (td, *J* = 9.99, 8.53 Hz, 1H), 2.74 (dt, *J* = 10.92, 8.48 Hz, 1H), 2.60 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.1, 162.8, 142.8, 138.8, 136.3, 134.1, 129.9, 129.7, 128.5, 128.4, 128.2, 127.2, 126.70, 126.68, 118.8, 118.7, 118.4, 47.1, 45.0, 42.3, 29.8; **IR** (thin film): ν 2924, 1630, 1483, 1444, 1280, 1206 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{23}H_{19}ClO_2$ requires *m/z* 361.1001, found *m/z* 361.1005; **$[\alpha]^{22}_D$** −29.0 º (*c*1.0, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.31 (s, 1H), 7.75 (dd, *J* = 8.01, 1.64 Hz, 1H), 7.50 (ddd, *J* = 8.66, 7.17, 1.66 Hz, 1H), 7.18-7.20 (m, 1H), 7.13 (m, 4H), 7.01-7.07 (m, 2H), 7.00 (m, 2H), 6.94-6.97 (m, 1H), 6.92 (ddd, *J* = 8.16, 7.18, 1.15 Hz, 1H), 4.85 (t, *J* = 9.31 Hz, 1H), 4.62 (dd, *J* = 9.73, 9.19 Hz, 1H), 4.14 (td, *J* = 9.09, 4.17 Hz, 1H), 2.88 (dt, *J* = 11.89, 8.76 Hz, 1H), 2.79 (dddd, *J* = 11.89, 9.70, 4.11, 0.82 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 205.4, 162.9, 140.1, 136.7, 136.5, 134.0, 129.8, 129.3, 127.9, 127.7, 127.63, 127.59, 126.21, 126.17, 119.0, 118.8, 118.2, 42.9, 42.6, 41.3, 29.4; **IR** (thin film): ν 2924, 1632, 1482, 1445, 1280, 1207 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{23}H_{19}ClO_2$ requires *m/z* 361.1001, found *m/z* 361.1003; **$[\alpha]^{22}_D$** −64.0 º (*c*0.41, $CH_2Cl_2$).

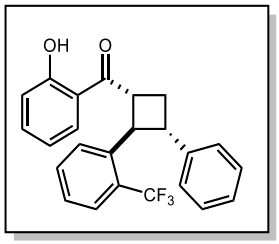



**((1*R*,2*R*,3*S*)-2-(2-Fluorophenyl)-3-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.22**)**:**

Experiment 1: Prepared according to general procedure A using 96.9 mg (0.4 mmol) (*E*)-3-(2-fluorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major;minor) mixture of inseparable diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 125 mg of a clear oil (90%, 0.36 mmol) as a 2:1 (major:minor) mixture of diastereomers; 95% ee (major) (Daicel CHIRALPAK® AD-H, 10% solvent (methanol), 5 mL/min, 221 nm; $t_1$ = 3.45 min, $t_2$ = 4.92 min). Experiment 2: 96.9 mg (0.4 mmol) (*E*)-3-(2-fluorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene. Crude d.r: 2:1; Combined isolated yield: 115 mg of a clear oil (83%, 0.33 mmol); 95% ee (major).

**(1*R*, 2*R*, 3*R*)** diastereomer (major) and **(1*R*, 2*R*, 3*S*)** diastereomer (minor) as a mixture: **$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.40 (s, 0.72H), 12.34 (s, 0.26H), 7.68 (dd, *J* = 8.08, 1.68 Hz, 0.27H), 7.54 (dd, *J* = 8.08, 1.62 Hz, 0.75H), 7.48 (ddd, *J* = 8.63, 7.17, 1.69 Hz, 0.29H), 7.44 (ddd, *J* = 8.65, 7.13, 1.65 Hz, 0.76H), 7.33-7.36 (m, 0.96H), 7.27-7.32 (m, 2.81H), 7.19-7.24 (m, 1.52H), 7.13-7.16 (m, 0.59H), 7.10-7.12 (m, 0.61H), 7.08-7.10 (m, 0.79H), 7.02-7.07 (m, 0.59H), 6.97-7.02 (m, 1.66H), 6.94 (td, *J* = 7.60, 1.98 Hz, 0.41H), 6.89 (ddt, *J* = 8.21, 7.11, 1.21 Hz, 0.55H), 6.76-6.84 (m, 1.06H), 4.73 (t, *J* = 9.01Hz, 0.27H), 4.56 (td, *J* = 8.94, 7.61Hz, 0.27H), 4.27 (q, *J* = 8.82 Hz, 0.74H), 4.21 (t, *J* = 9.46 Hz, 0.75H), 4.07 (td, *J* = 9.15, 5.26 Hz, 0.28H), 3.89 (q, *J* = 9.31 Hz, 0.74H), 2.84-2.93 (m, 0.52H), 2.81 (dt, *J* = 10.90, 8.09 Hz, 0.77H), 2.51 (q, *J* = 10.03 Hz, 0.74H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.7, 205.2, 162.9, 162.8, 161.2 (d, *J* = 246.32 Hz), 160.6 (d, *J* = 245.13 Hz), 143.0, 140.2, 136.5, 136.3, 129.9, 129.8, 129.1 (d, *J* = 4.91 Hz),

128.6 (d, *J* = 8.06 Hz), 128.49, 128.48 (d, *J* = 13.93 Hz), 128.2 (d, *J* = 4.63 Hz), 128.02 (d, *J* = 8.47 Hz), 127.97, 127.6, 126.7, 126.4 (d, *J* =15.19 Hz), 126.2, 124.3 (d, *J* = 3.51 Hz), 123.6 (d, *J* = 3.51 Hz), 119.0, 118.8, 118.7, 118.6, 118.5, 118.1, 115.8 (d, *J* = 22.22 Hz), 115.0 (d, *J* = 22.17 Hz), 44.3 (d, *J* = 2.40 Hz), 44.2, 42.9, 42.1 (d, *J* = 1.93 Hz), 41.3, 39.8 (d, *J* = 1.87 Hz), 31.0, 28.8; **$^{19}$F NMR** (470 MHz, $CDCl_3$): δ –115.6 (s, 0.28F), –115.8 (s, 0.72F); **IR** (thin film): ν 3032, 2932, 1632, 1487, 1448, 1234, 1207 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{23}H_{19}FO_2$ requires *m/z* 345.1296, found *m/z* 345.1297.




**(2-Hydroxyphenyl)((1*R*,2*R*,3*S*)-3-phenyl-2-(2-(trifluoromethyl)phenyl)cyclobutyl)methanone** (**2.23**)**:**

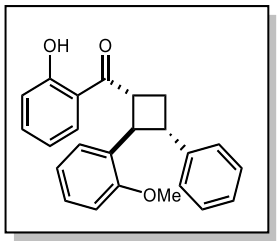
Experiment 1: Prepared according to general procedure A using 117 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-(2-(trifluoromethyl)phenyl)prop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 151 mg of a clear oil (95%, 0.38 mmol) as a 2:1 (major:minor) mixture of diastereomers; 93% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 4 mL/min, 221 nm; $t_1$ = 6.82 min, $t_2$ = 7.21 min), 99>% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 4 mL/min, 221 nm; $t_1$ = 6.57 min, $t_2$ = 8.38 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (4% MTBE: Pent). Experiment 2: 117 mg (.04 mmol) (*E*)-1-(2-hydroxyphenyl)-3-(2-(trifluoromethyl)phenyl)prop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene. Crude d.r: 2:1; Combined isolated yield: 139 mg of a clear oil (88%, 0.35 mmol); 93% ee (major), 99>% ee (minor).

Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.37 (s, 1H), 7.96 (d, *J* = 7.90 Hz, 1H), 7.69 (dd, *J* = 7.72, 1.32 Hz, 1H), 7.54 (dd, *J* = 7.93, 1.29 Hz, 1H), 7.36 (ddt, *J* = 8.81, 7.46, 1.73 Hz, 2H), 7.25-7.29 (m, 2H), 7.18-7.22 (m, 4H), 6.94 (dd, *J* = 8.41, 1.09 Hz, 1H), 6.59 (ddd, *J* = 8.15, 7.14, 1.15 Hz, 1H), 4.23 (t, 9.13 Hz, 1H), 4.15 (q, 9.22 Hz, 1H), 3.80 (q, *J* = 9.43 Hz, 1H), 2.77 (q, *J* = 10.48 Hz, 1H), 2.67 (dt, *J* = 10.99, 8.25 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 204.3, 162.8, 141.9, 140.2, 136.2, 132.3, 129.6, 128.9 (q, *J* = 29.64 Hz), 128.4, 127.1, 126.8, 126.7, 125.9 (q, *J* = 5.79 Hz), 123.7 (q, *J* = 274.33 Hz), 118.7, 118.5, 118.4, 47.4, 46.4, 44.9, 28.1; **$^{19}$F NMR** (470 MHz, $CDCl_3$): δ –58.0; **IR** (thin film): ν 3029, 2950, 1632, 1604, 1311, 1282, 1157, 1119 $cm^{-1}$; **HRMS** (EI) calculated for $[M-H]^-$ calculated for $C_{24}H_{19}F_3O_2$ requires *m/z* 395.1264, found *m/z* 395.1287; **$[\alpha]^{22}_D$** −25.4 º (*c*3.5, $CH_2Cl_2$); mp = 132-135 ºC.

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.27 (s, 1H), 7.66 (dd, *J* = 8.00, 1.64 Hz, 1H), 7.53 (dd, *J* = 7.7-, 1.52 Hz, 1H), 7.46 (ddd, *J* = 8.61, 7.17, 1.66 Hz, 1H), 7.18 (td, *J* = 7.59, 1.58 Hz, 1H), 7.13-7.16 (m, 3H), 7.03-7.08 (m, 3H), 6.98-7.01 (m, 2H), 6.86 (ddd, *J* = 8.20, 7.20, 1.18 Hz, 1H), 4.88 (t, *J* = 9.29 Hz, 1H), 4.59 (q, *J* = 9.11 Hz, 1H), 4.05 (td, *J* = 8.26, 5.87 Hz, 1H), 2.87-2.90 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 205.1, 162.9, 139.3, 137.3, 136.5, 131.0, 129.8, 128.8, 128.7 (q, 29.45 Hz), 128.1, 127.7, 126.4, 126.2, 125.8 (q, 5.91 Hz), 124.4 (q, 274.02 Hz), 118.9, 118.7, 118.2, 43.5, 42.5, 41.6, 27.7; **$^{19}$F NMR** (470 MHz, $CDCl_3$): δ –59.3; **IR** (thin film): ν 3034, 2928, 1634, 1610, 1310, 1283, 1157, 1114 $cm^{-1}$; **HRMS** (EI) calculated for $[M-H]^-$ calculated for $C_{24}H_{19}F_3O_2$ requires *m/z* 395.1264, found *m/z* 395.1285; **$[\alpha]^{22}_D$** −86.2 º (*c*1.8, $CH_2Cl_2$).

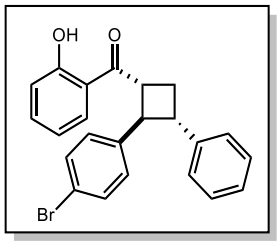



**(2-Hydroxyphenyl)((1*R*,2*R*,3*S*)-2-(2-methoxyphenyl)-3-phenylcyclobutyl)methanone** (**2.24**)**:**

Experiment 1: Prepared according to general procedure A using 102 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-(2-methoxyphenyl)prop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol)

styrene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of inseparable diastereomers that was purified by flash-column chromatography on silica gel (10% MTBE:Pent). Combined yield: 123 mg of a clear oil (86%, 0.34 mmol) as a 2:1 (major:minor) mixture of diastereomers; 99>% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 10% solvent (methanol), 5 mL/min, 221 nm; $t_1$ = 6.83 min, $t_2$ = 7.06 min), 95% ee (minor) (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 6.59 min, $t_2$ = 7.23 min). Experiment 2: 102 mg (.04 mmol) (*E*)-1-(2-hydroxyphenyl)-3-(2-methoxyphenyl)prop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene. Crude d.r: 2:1; Combined isolated yield: 116 mg of a clear oil (81%, 0.32 mmol); 99>% ee (major), 95% ee (minor).

**(1*R*, 2*R*, 3*R*)** diastereomer (major) and **(1*R*, 2*R*, 3*S*)** diastereomer (minor) as a mixture: **$^1$H NMR** (500 MHz, $C_6D_6$): δ 13.29 (s, 1H), 13.03 (s, 0.44H), 7.42-7.44 (m, 0.44H), 7.27-7.30 (m, 2H), 7.21 (dd, *J* = 7.72, 1.62 Hz, 1H), 7.11-7.14 (m, 2H), 7.25-7.29 (m, 2.78H), 6.96-7.06 (m, 6H), 6.86-6.93 (m, 2.27H), 6.84 (td, *J* = 7.49, 1.05 Hz, 1H), 6.71 (td, *J* = 7.46, 1.11 Hz, 0.44H), 6.47 (ddd, *J* = 8.22, 6.20, 2.15 Hz, 0.44H), 6.40 (ddd, *J* = 8.21, 5.53, 2.83 Hz, 1H), 6.32 (dd, *J* = 8.17, 1.07 Hz, 1H), 6.26 (dd, *J* = 8.20, 1.07 Hz, 0.44H), 4.79 (dd, 9.66, 7.95 Hz, 0.44H), 4.37 (t, 9.61 Hz, 1H), 4.26 (dtd, 9.20, 7.63, 1.22 Hz, 0.44H), 3.89 (td, 9.33, 5.68 Hz, 0.44H), 3.63-3.71 (m, 2H), 3.06 (s, 1.32H), 2.83 (s, 3H), 2.64-2.69 (m, 0.44H), 2.58 (q, 10.16 Hz, 1H), 2.42 (dddd, *J* = 11.84, 9.70, 5.77, 0.90 Hz, 0.44H), 2.22 (dt, 10.47, 8.15 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 206.5, 206.3, 162.9, 162.7, 157.2, 157.1, 143.7, 141.1, 136.27, 135.9, 130.00, 129.98, 129.9, 128.44 127.9, 127.7, 127.6, 127.50, 127.45, 127.2, 127.04, 126.96, 126.5, 125.8, 120.5, 119.9, 119.5, 119.0, 118.6, 118.6, 118.4, 118.2, 110.0, 109.8, 54.8, 54.2, 46.7, 44.01 42.6, 42.5, 41.5, 41.4, 40.2, 30.2, 28.9; **IR** (thin film): ν 2939, 1630, 1606, 1487, 1447, 1242, 1206 $cm^{-1}$; **HRMS** (EI) calculated for $[M-H]^-$ calculated for $C_{24}H_{22}O_3$ requires *m/z* 357.1496, found *m/z* 357.1495.




**((1*R*,2*R*,3*S*)-2-(4-Bromophenyl)-3-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.25**):

Experiment 1: Prepared according to general procedure A using 121 mg (0.4 mmol) (*E*)-3-(4-bromophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 156 mg of a clear oil (96%, 0.38 mmol) as a 2:1 (major:minor) mixture of diastereomers; 97% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 10.33 min, $t_2$ = 11.07 min), 97% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 10.81 min, $t_2$ = 11.33 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (3% MTBE: Pent). Experiment 2: 121.3 mg (0.4 mmol) (*E*)-3-(4-bromophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene. Crude d.r: 2:1; Combined isolated yield: 150 mg of a clear oil (92%, 0.37 mmol); 97% ee (major), 97% ee (minor).

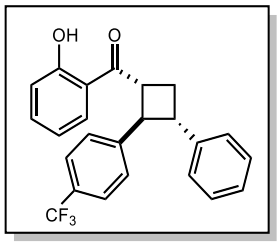
Major

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 12.34 (s, 1H), 7.54 (dd, *J* = 8.05, 1.64 Hz, 1H), 7.41-7.47 (m, 3H), 7.32 (m, 2H), 7.23 (m, 2H), 7.16 (d, *J* = 8.43 Hz, 2H), 6.99 (dd, *J* = 8.43, 1.08 Hz, 1H), 6.82 (ddd, *J* = 8.21, 7.32, 1.19 Hz, 1H), 3.97-4.06 (m, 2H), 3.69-3.75 (m, 1H), 2.80-2.85 (m, 1H), 2.49 (dd, *J* = 9.43, 8.70 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 205.2, 162.9, 142.7, 141.0, 136.5, 131.7, 130.0, 128.7, 128.6, 126.8, 126.7, 120.7, 118.9, 118.6, 118.4, 48.4, 45.9, 42.7, 31.2; **IR** (thin film): ν 3029, 2944, 1632, 1485, 1447 $cm^{-1}$;

**HRMS** (ESI$^-$): [M-H]$^-$ calculated for $C_{23}H_{19}BrO_2$ requires *m/z* 405.0496, found *m/z* 405.0492; **[α]$^{22}_D$** −27.2 º (*c*0.45, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 12.33 (s, 1H), 7.55 (dd, *J* = 8.09, 1.68 Hz, 1H), 7.47 (ddd, *J* = 8.60, 7.16, 1.69 Hz, 1H), 7.17-7.24 (m, 4H), 7.12 (m, 1H), 7.01 (m, 3H), 6.84 (ddd, *J* = 8.15, 7.16, 1.17 Hz, 1H), 6.80 (m, 2H), 4.36 (m, 2H), 4.04 (m, 1H), 2.88-2.94 (m, 1H), 2.82 (ddd, *J* = 11.74, 9.00, 6.90 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 205.6, 162.9, 139.8, 138.4, 136.5, 131.1, 129.9, 129.7, 128.2, 127.9, 126.3, 120.3, 119.0, 118.7, 118.1, 45.9, 44.8, 41.4, 27.7; **IR** (thin film): ν 3029, 2925, 1739, 1632, 1485, 1448 cm$^{-1}$; **HRMS** (ESI$^-$): [M-H]$^-$ calculated for $C_{23}H_{19}BrO_2$ requires *m/z* 405.0496, found *m/z* 405.0499; **[α]$^{22}_D$** − 122.6 º (*c*0.46, $CH_2Cl_2$).




**(2-Hydroxyphenyl)((1*R*,2*R*,3*S*)-3-phenyl-2-(4-(trifluoromethyl)phenyl)cyclobutyl)methanone** (**2.26**)**:**

Experiment 1: Prepared according to general procedure A using 117 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major;minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 150 mg of a clear oil (95%, 0.38 mmol) as a 2:1 (major:minor) mixture of diastereomers; 96% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 5.42 min, $t_2$ = 5.70 min), 99% ee (minor) (Daicel CHIRALPAK® AD-H, 10% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 3.82 min, $t_2$ = 4.95 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (3-5% MTBE: Pen). Experiment 2: 102 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg

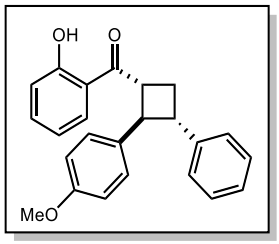
(0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene. Crude d.r: 2:1; Combined isolated yield: 142 mg of a clear oil (90%, 0.36 mmol); 96% ee (major), 99% ee (minor).

Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.32 (s, 1H), 7.55-7.58 (m, 3H), 7.47 (ddd, *J* = 8.65, 7.17, 1.66 Hz, 1H), 7.40 (d, *J* = 8.03 Hz, 2H), 7.32-7.35 (m, 2H), 7.23-7.28 (m, 3H), 7.01 (dd, *J* = 8.46, 1.16 Hz, 1H), 6.83 (ddd, *J* = 8.24, 7.21, 1.20 Hz, 1H), 4.20 (t, *J* = 9.68 Hz, 1H), 4.05 (q, *J* = 9.48 Hz, 1H), 3.78 (td, *J* = 10.02, 8.26 Hz, 1H), 2.88 (dt, *J* = 10.16, 8.43 Hz, 1H), 2.49 (q, *J* = 10.23 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.1, 162.9, 146.1, 142.5, 136.6, 129.9, 129.1 (q, *J* = 32.36 Hz), 128.7, 127.3, 126.9, 126.7, 125.6 (q, *J* = 3.78 Hz), 124.1 (q, *J* = 271.96 Hz), 119.0, 118.6, 118.3, 48.2, 45.8, 42.6, 31.8; **$^{19}$F NMR** (470 MHz, $CDCl_3$): δ –62.5; **IR** (thin film): ν 2929, 1633, 1325, 1161, 1120 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{19}F_3O_2$ requires *m/z* 395.1264, found *m/z* 395.1268; **$[\alpha]^{22}_D$** −27.8 º (*c*0.57, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.31 (s, 1H), 7.58 (dd, *J* = 8.06, 1.60 Hz, 1H), 7.48 (ddd, *J* = 8.57, 7.10, 1.65 Hz, 1H), 7.35 (d, *J* = 8.08 Hz, 2H), 7.18 (td, *J* = 7.20, 1.32 Hz, 2H), 7.09-7.12 (m, 1H), 7.01-7.04 (m, 5H), 6.86 (ddd, *J* = 8.17, 7.13, 1.15 Hz, 1H), 4.51 (t, *J* = 8.73 Hz, 1H), 4.44 (td, *J* = 8.85, 7.67 Hz, 1H), 4.09 (td, *J* = 9.19, 5.39 Hz, 1H), 2.89-2.95 (m, 1H), 2.86 (ddd, *J* = 11.96, 9.49, 5.50 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.4, 162.9, 143.5, 139.7, 136.6, 129.8, 128.5 (q, *J* = 32.34 Hz), 128.2, 128.2, 127.8, 126.4, 124.9 (q, *J* = 3.79 Hz), 124.1 (q, *J* = 271.89 Hz), 119.0, 118.8, 118.0, 45.7, 44.6, 41.5, 28.3; **$^{19}$F NMR** (470 MHz, $CDCl_3$): δ –62.4; **IR** (thin film): ν 2924, 1633, 1323, 1160, 1117 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{19}F_3O_2$ requires *m/z* 395.1264, found *m/z* 395.1265; **$[\alpha]^{22}_D$** −72.6 º (*c*1.4, $CH_2Cl_2$).




**(2-Hydroxyphenyl)((1*R*,2*R*,3*S*)-2-(4-methoxyphenyl)-3-phenylcyclobutyl)methanone** (**2.27**)**:**

Experiment 1: *Note: This reaction was performed with high-intensity blue LED.*

Prepared according to general procedure A using 102 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene, and irradiating with a blue LED for a time of 12 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (8% MTBE:Pent). Combined yield: 122 mg of a clear oil (85%, 0.34 mmol) as a 2:1 (major:minor) mixture of diastereomers; 86% ee (major) (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 9.57 min, $t_2$ = 11.53 min), 90% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 8.23 min, $t_2$ = 8.48 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (8% MTBE: Pent). Experiment 2: 102 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene. Crude d.r:. 2:1; Combined isolated yield: 116 mg of a clear oil (81%, 0.32 mmol); 83% ee (major), 90% ee (minor).

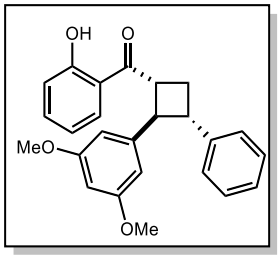
Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.45 (s, 1H), 7.53 (dd, *J* = 8.08 1.65 Hz, 1H), 7.46 (ddd, *J* = 8.65, 7.16, 1.66 Hz, 1H), 7.31-7.34 (m, 2H), 7.27-7.29 (m, 2H), 7.22-7.26 (m, 3H), 7.00 (dd, *J* = 8.39, 1.12 Hz, 1H), 6.87-6.88 (m, 2H), 6.80 (ddd, *J* = 8.18, 7.26, 1.18 Hz, 1H), 4.03 (td, *J* = 9.44, 8.03 Hz, 1H), 3.97 (t, *J* = 9.46 Hz, 1H), 3.81 (s, 3H), 3.76 (dd, *J* = 10.20, 8.50 Hz, 1H), 2.78 (dt, *J* = 10.74, 8.09 Hz, 1H), 2.54 (q, *J* = 10.17 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.6, 162,8, 158.5, 143.2, 136.3, 134.1, 130.2, 128.5,

128.1, 126.7, 126.6, 118.8, 118.6, 118.4, 114.0, 55.3, 49.2, 46.4, 42.9, 30.3; **IR** (thin film): ν 2937, 1633, 1610, 1511, 1246 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{22}O_3$ requires *m/z* 357.1496, found *m/z* 357.1500; $[\alpha]^{22}_D$ −38.2 º (*c*1.0, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.41 (s, 1H), 7.53 (dd, *J* = 8.05, 1.64 Hz, 1H), 7.44 (ddd, *J* = 8.64, 7.18, 1.63 Hz, 1H), 7.17 (dd, *J* = 8.20, 6.92 Hz, 2H), 7.10 (m, 1H), 7.00 (ddd, *J* = 8.28, 6.83, 1.36 Hz, 3H), 6.85 (m, 2H), 6.79 (ddd, *J* = 8.10, 7.15, 1.18 Hz, 1H), 6.65 (m, 2H), 4.34 (dt *J* = 9.26, 7.39 Hz, 1H), 4.29 (dd *J* = 9.47, 7.34 Hz, 1H), 4.03 (td *J* = 9.13, 5.81 Hz, 1H), 3.71 (s, 3H), 2.93 (dddd, *J* = 12.03, 8.76, 7.06, 1.31 Hz, 1H), 2.80 (ddd, *J* = 11.99, 9.09, 5.80 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 206.12, 162.83, 158.06, 140.29, 136.28, 131.37, 130.04, 129.13, 127.99, 127.95, 125.97, 118.87, 118.55, 118.23, 113.39, 55.11, 46.64, 45.33, 41.49, 26.90; **IR** (thin film): ν 2923, 1632, 1609, 1447, 1245 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{22}O_3$ requires *m/z* 357.1496, found *m/z* 357.1498; $[\alpha]^{22}_D$ −56.6 º (*c*0.64, $CH_2Cl_2$).




**((1*R*,2*R*,3*S*)-2-(3,5-Dimethoxyphenyl)-3-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.28**)**:**

Experiment 1: Prepared according to general procedure A using 113 mg (0.4 mmol) (*E*)-3-(3,5-dimethoxyphenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (7% MTBE: Pent). Combined yield: 143 mg of a clear oil (92%, 0.37 mmol) as a 2:1 (major:minor) mixture of diastereomers; 96% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 8.59 min, $t_2$ = 9.06 min), 99% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 8.84 min, $t_2$ = 9.90 min). Characterization data was obtained for the

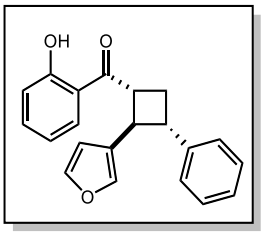
major and minor diastereomers by flash-column chromatography (7% MTBE: Pent). Experiment 2: 113.7 mg (0.4 mmol) (*E*)-3-(3,5-dimethoxyphenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene. Crude d.r: 2:1; Combined isolated yield: 142 mg of a clear oil (91%, 0.37 mmol); 96% (major), 99% ee (minor).

Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.41 (s, 1H), 7.55 (dd, *J* = 8.01, 1.66 Hz, 1H), 7.44 (ddd, *J* = 8.65, 7.22, 1.64 Hz, 1H), 7.26-7.32 (m, 4H), 7.19-7.23 (m, 1H), 6.98 (dd, *J* = 8.43, 1.18 Hz, 1H), 6.80 (ddd, *J* = 8.12, 7.22, 1.20 Hz, 1H), 6.44 (d, *J* = 2.25 Hz, 2H), 6.33 (t, *J* = 2.27 Hz, 1H), 3.97-4.05 (m, 2H), 3.73-3.78 (m, 7H), 2.77 (dt, *J* = 10.92, 7.98 Hz, 1H), 2.45-2.51 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 205.5, 162.8, 161.0, 144.5, 143.0, 136.4, 130.2, 128.5, 126.7, 126.6, 118.8, 118.4, 105.2, 98.5, 55.3, 49.6, 45.9, 42.4, 30.6; **IR** (thin film): ν 2940, 1631, 1597, 1203, 1154 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{25}H_{24}O_4$ requires *m/z* 387.1602, found *m/z* 387.1605; $[\alpha]^{22}_D$ −54.4 º (*c*4.3, $CH_2Cl_2$).

Minor

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.39 (s, 1H), 7.59 (dd, *J* = 8.07, 1.64 Hz, 1H), 7.45 (ddd, *J* = 8.67, 7.16, 1.65 Hz, 1H), 7.18-7.21 (m, 2H), 7.09-7.13 (m, 1H), 7.06 (dd, *J* = 8.04, 1.28 Hz, 2H), 7.01 (dd, *J* = 8.39, 1.13 Hz, 1H), 6.83 (ddd, *J* = 8.19, 7.17, 1.19 Hz, 1H), 6.17 (t, *J* = 2.29 Hz, 1H), 6.07 (d, *J* = 2.21 Hz, 2H), 4.35-4.41 (m, 1H), 4.32 (dd, *J* = 9.43, 7.63 Hz, 1H), 4.04 (td, *J* = 9.20, 5.76 Hz, 1H), 3.59 (s, 6H), 2.90 (dddd, *J* = 11.98, 8.78, 7.25, 1.18 Hz, 1H), 2.80 (ddd, *J* = 11.98, 9.36, 5.74 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 205.9, 162.9, 160.3, 141.6, 140.4, 136.4, 130.0, 128.1, 127.9, 126.1, 119.0, 118.6, 106.3, 98.6, 55.2, 46.9, 44.9, 41.5, 27.6; **IR** (thin film): ν 2926, 1739, 1632, 1597, 1203, 1151 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{25}H_{24}O_4$ requires *m/z* 387.1602, found *m/z* 387.1603; $[\alpha]^{22}_D$ −102.0 º (*c*1.8, $CH_2Cl_2$).




**((1*R*,2*R*,3*S*)-2-(Furan-3-yl)-3-phenylcyclobutyl)(2-hydroxyphenyl)methanone** (**2.29**)**:**

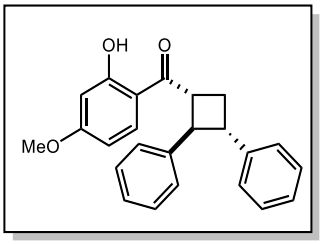
Experiment 1: Prepared according to general procedure A using 85.7 mg (0.4 mmol) (*E*)-3-(furan-3-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μl (4.0 mmol) styrene, and an irradiation time of 20 h. The crude material resulted in a 1:1 (major;minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent). Combined yield: 53.6 mg of a clear oil (42%, 0.17 mmol) as a 2:1 (major:minor) mixture of diastereomers; 94% ee (major) (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 7.34 min, $t_2$ = 7.82 min). Characterization data was obtained for the major diastereomers by flash-column chromatography (3% MTBE: Pent). Experiment 2: 85.7 mg (0.4 mmol) (*E*)-3-(furan-3-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene. Crude d.r: 1:1; Combined isolated yield: 53.5 mg of a clear oil (42%, 0.17mmol); 94% ee (major).

Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.39 (s, 1H), 7.56 (dd, *J* = 8.04, 1.63 Hz, 1H), 7.45 (ddd, *J* = 8.56, 7.15, 1.68 Hz, 1H), 7.40 (t, *J* = 1.71 Hz, 1H), 7.28-7.33 (m, 3H), 7.24-7.26 (m, 2H), 7.20-7.24 (m, 1H), 6.99 (dd, *J* = 8.44, 1.14 Hz, 1H), 6.82 (ddd, *J* = 8.21, 7.21, 1.19 Hz, 1H), 6.42 (s (broad), 1H), 3.95 (td, *J* = 9.67, 8.37 Hz, 1H), 3.80 (t, *J* = 9.52 Hz, 1H), 3.61 (td, *J* = 10.02, 8.22 Hz, 1H), 2.71-2.76 (m, 1H) 2.55 (q, *J* = 10.39 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 205.3, 162.8, 143.5, 142.8, 139.2, 136.4, 130.2, 128.5, 126.7, 126.6, 126.4, 118.8, 118.5, 118.4, 109.4, 45.9, 42.9, 41.3, 30.2; **IR** (thin film): ν 2926, 1756, 1630, 1488, 1447, 1211, 1156 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{21}H_{18}O_3$ requires *m/z* 317.1183, found *m/z* 317.1182; **$[\alpha]^{22}_D$** −46.0 º (*c*1.1, $CH_2Cl_2$).

Minor

**$^{1}$H NMR** (500 MHz, $CDCl_3$): δ 12.39 (s, 1H), 7.52 (dd, *J* = 8.08, 1.64 Hz, 1H), 7.45 (ddd, *J* = 8.59, 7.17, 1.65 Hz, 1H), 7.25-7.28 (m, 2H), 7.17-7.20 (m, 1H), 7.14 (dt, *J* = 5.16, 1.51 Hz, 3H), 7.01 (dd, *J* = 8.43, 1.14 Hz, 1H), 6.99 (m, 1H), 6.82 (ddd, *J* = 8.20, 7.18, 1.17 Hz, 1H), 5.81 (dd, *J* = 1.72, 0.86 Hz, 1H), 4.16 (ddt, *J* = 14.29, 9.06, 7.26 Hz, 1H), 3.96 (td, *J* = 9.10, 6.09 Hz, 1H), 2.90 (dddd, *J* = 12.05, 8.54, 6.27, 2.00 Hz, 1H), 2.80 (ddd, *J* = 11.55, 8.50, 6.14 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 205.8, 162.8, 142.8, 140.4, 139.7, 136.4, 130.0, 128.1, 127.9, 126.4, 123.9, 118.9, 118.6, 118.2, 110.3, 46.1, 40.8, 38.8, 26.7; **IR** (thin film): ν 2945, 1765, 1633, 1209, 1156 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{21}H_{18}O_3$ requires *m/z* 317.1183, found *m/z* 317.1182. *Note: Minor product ee was not measured due to the inability to purify the racemic minor product.*




**((1*R*,2*R*,3*S*)-2,3-Diphenylcyclobutyl)(2-hydroxy-4-methoxyphenyl)methanone** (**2.30**)**:**

Experiment 1: Prepared according to general procedure A using 102 mg (0.4 mmol) (*E*)-1-(2-hydroxy-4-methoxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene, and an irradiation time of 20 h. The crude material resulted in a 2:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (5% MTBE:Pent.). Combined yield: 136 mg of a clear oil (95%, 0.38 mmol) as a 2:1 (major:minor) mixture of diastereomers; 90% ee (major) (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent (methanol), 3 mL/min, 221 nm; $t_1$ = 8.76 min, $t_2$ = 9.23 min), 97% ee (minor) (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent (methanol), 3 mL/min, 221nm; $t_1$ = 9.52 min, $t_2$ = 9.98 min). Characterization data was obtained for the major and minor diastereomers by flash-column chromatography (2-7% MTBE: Pent). Experiment 2: 102 mg (0.4 mmol) (*E*)-1-(2-hydroxy-4-methoxyphenyl)-3-phenylprop-2-en-1-one, 19.2 mg (.04 mmol) $Sc(OTf)_3$, 20.0 mg

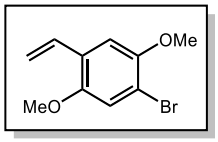
(0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 459 μL (4.0 mmol) styrene. Crude d.r.: 2:1; Combined isolated yield: 135 mg of a clear oil (94%, 0.38 mmol); 90% (major), 97% ee (minor).

Major

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.92 (s, 1H), 7.41 (d, *J* = 8.97 Hz, 1H), 7.26-7.32 (m, 8H), 7.19-7.24 (m, 2H), 6.43 (d, *J* = 2.48 Hz, 1H), 6.31 (dd, *J* = 8.95, 2.52 Hz, 1H), 4.05 (t, *J* = 9.57 Hz, 1H), 3.97 (td, *J* = 9.61, 8.25 Hz, 1H), 3.82 (s, 3H), 3.76 (td, *J* = 9.82, 8.15 Hz, 1H), 2.75 (dt, *J* = 10.94, 8.33 Hz, 1H), 2.51 (q, *J* = 10.35 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 203.5, 166.1, 165.8, 143.2, 142.2, 131.7, 128.6, 128.5, 127.0, 126.79, 126.76, 126.6, 112.7, 107.5, 100.9, 55.6, 49.4, 45.6, 42.7, 30.7; **IR** (thin film): ν 2935, 1615, 1501, 1446, 1369, 1234 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{22}O_3$ requires *m/z* 357.1496, found *m/z* 357.1498; **$[\alpha]^{22}_D$** −15.24 º (*c*0.42, $CH_2Cl_2$).

Minor

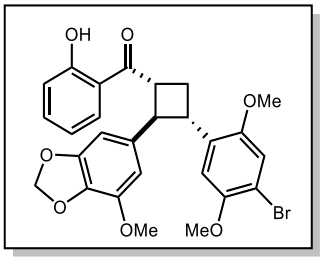
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 12.89 (s, 1H), 7.47 (d, *J* = 9.00 Hz, 1H), 7.15 (dd, *J* = 8.07, 6.72 Hz, 2H), 7.04-7.12 (m, 4H), 7.01 (dd, *J* = 7.85, 1.33 Hz, 2H), 6.92-6.94 (m, 2H), 6.45 (d, *J* = 2.49 Hz, 1H), 6.35 (dd, *J* = 8.95, 2.51 Hz, 1H), 4.32-4.39 (m, 2H), 4.06 (td, *J* = 8.98, 5.82 Hz, 1H), 3.82 (s, 3H), 2.89-2.95 (m, 1H), 2.78 (ddd, *J* = 12.06, 8.91, 5.99 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 204.1, 166.0, 165.8, 140.4, 139.4, 131.6, 128.0, 127.9, 126.3, 126.0, 112.3, 107.6, 101.1, 55.6, 47.0, 44.3, 41.5, 27.4; **IR** (thin film): ν 2921, 1624, 1502, 1451, 1370, 1236 $cm^{-1}$; **HRMS** ($ESI^-$): $[M-H]^-$ calculated for $C_{24}H_{22}O_3$ requires *m/z* 357.1496, found *m/z* 357.1498; **$[\alpha]^{22}_D$** −40.8 º (*c*0.47, $CH_2Cl_2$).




**1-Bromo-2,5-dimethoxy-4-vinylbenzene** (**2.36**)**:**

The following procedure was adapted from Kamada *et al*.[39] To a solution of methyltriphenylphosphonium bromide (9.37 g, 26.2 mmol) in THF (100 mL) at 0 ˚C was added potassium *tert*-butoxide (2.94 g, 26.2 mmol) in one portion. After thirty minutes, the reaction mixture was cool to –78 ˚C and 4-bromo-2,5-

dimethoxybenzaldehyde (4.95 g, 20.2 mmol) in THF (35 mL) was added dropwise *via* syringe. The transfer was completed with an additional two portions of THF (5 mL). After 1 h, the reaction mixture was allowed to warm to room temperature. After 1 h at room temperature, water (100 mL) was added to the reaction mixture, followed by $Et_2O$ (200 mL). The aqueous layer was extracted two times with $Et_2O$ (100 mL). The combined organic extracts were washed with water (100 mL), brine (100 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography ($SiO_2$, Gradient 0% to 6% EtOAc:hexanes) to afford the title compound (4.59 g, 94%). $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.06 (s, 1H), 7.02 (s, 1H), 6.97 (dd, $J$ = 17.5, 11.0 Hz, 1H), 5.73 (dd, $J$ = 17.5, 1.0 Hz, 1H), 5.30 (dd, $J$ = 11.0, 1.0 Hz, 1H), 3.88 (s, 3H), 3.80 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 151.2, 150.1, 131.0, 126.6, 116.6, 115.0, 111.1, 110.1, 56.9, 56.4.

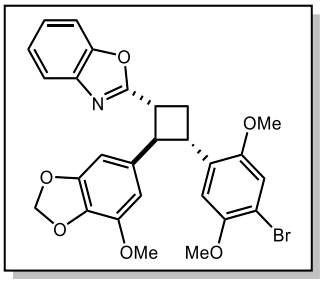



**((1*R*,2*R*,3*S*)-3-(4-Bromo-2,5-dimethoxyphenyl)-2-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)cyclobutyl) (2-hydroxyphenyl)methanone** (**2.37**)**:**

Experiment 1: Prepared according to general procedure A using 119 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)prop-2-en-1-one, 63.0 mg (0.128 mmol) $Sc(OTf)_3$, 51.2 mg (0.154 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-PrOAc:MeCN, 146 mg (0.6 mmol) 1-bromo-2,5-dimethoxy-4-vinylbenzene, and an irradiation time of 12 h. The crude material resulted in a 3:1 (major:minor) mixture of diastereomers that was purified by flash-column chromatography on silica gel (30% $Et_2O$:Pent). Combined yield: 173 mg of a clear oil (80%, 0.32 mmol) as a 3:1 (major:minor) mixture of diastereomers; 96% ee (Daicel CHIRALPAK® AD-H, gradient 5% to 50% solvent (methanol), 5 mL/min, 221nm; $t_1$ = 9.09 min, $t_2$ = 11.55 min. Experiment 2: 89.6 mg (0.4 mmol) (*E*)-1-(2-hydroxyphenyl)-3-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)prop-2-en-1-one, 19.2 mg (0.04 mmol) $Sc(OTf)_3$, 20.0 mg (0.06 mmol) (*S*,*S*)-*t*-BuPyBox, 8.7 mg (0.01 mmol) $Ru(bpy)_3(PF_6)_2$, 12 mL (3:1) *i*-

PrOAc:MeCN, 146 mg (0.6 mmol) 1-bromo-2,5-dimethoxy-4-vinylbenzene. Crude d.r.: 3:1; Combined isolated yield: 173 mg of a clear oil (80%, 0.32 mmol); 93% ee.

Major diastereomer: **$^{1}$H NMR** (500 MHz, $CDCl_3$): δ 12.38 (s, 1H), 7.55 (dd, *J* = 7.96, 1.66 Hz, 1H), 7.45 (ddd, *J* = 8.57, 7.19, 1.66 Hz, 1H), 7.01 (s, 1H), 6.99 (dd, *J* =8.45, 1.11 Hz, 1H), 6.89 (s, 1H), 6.82 (ddd, *J* = 8.11, 7.16, 1.14 Hz, 1H), 6.53 (d, *J* =1.49 Hz, 1H), 6.42 (d, *J* =1.51 Hz, 1H), 5.94 (d, *J* =1.47 Hz, 1H), 5.93 (d, *J* =1.46 Hz, 1H), 3.99-4.03 (m, 1H), 3.91-3.97 (m, 2H), 3.85 (s, 3H), 3.82 (s, 3H), 3.72 (s, 3H), 2.80 (dt, *J* = 10.63, 8.19 Hz, 1H), 7.55 (q, *J* = 10.12 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 205.6, 162.8, 151.8, 150.3, 149.1, 143.5, 136.8, 136.5, 134.0, 131.3, 130.2, 118.9, 118.5, 115.9, 112.0, 109.5, 106.7, 101.4, 100.9, 57.2, 56.6, 56.1, 47.7, 47.1, 37.2, 31.1; **IR** (thin film): ν 2997, 2941, 2843, 1630, 1491, 1445, 1209 $cm^{-1}$**; HRMS** (ESI$^-$): $[M-H]^-$ calculated for $C_{27}H_{25}BrO_7$ requires *m/z* 539.0711, found *m/z* 539.0715. An analytically pure sample of enantioenriched **47** could not be obtained; the optical rotation of the 3:1 mixture of diastereomers is $[\alpha]^{22}_{D}$ −30.8 º (*c*0.59, $CH_2Cl_2$).

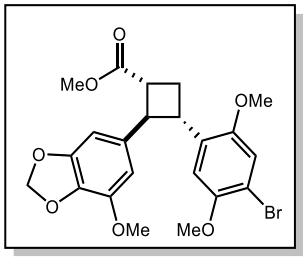



**2-((1*R*,2*R*,3*S*)-3-(4-Bromo-2,5-dimethoxyphenyl)-2-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)cyclobutyl) benzo[*d*]oxazole** (**2.41**)**:**

The combined diastereomers of cyclobutane **2.37** (150 mg, 0.28 mmol) were dissolved in 1 ml THF in an oven-dried 3-dram vial equipped with a stirbar, and 7 M methanolic ammonia (0.6 ml, 4.2 mmol) was added. The vial was sealed with a Teflon cap, and the reaction was stirred at ambient temperature for 12 h. The mixture was concentrated *in vacuo* to afford a yellow oil. This crude product was dissolved in THF (1.3 mL), and aqueous 10% NaOCl (3 equiv, 0.84 mmol) was added dropwise. After stirring for 30 min, the mixture was diluted with water and extracted with $Et_2O$ (3 x 10 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo.* The residue was purified by

flash-column chromatography on silica gel (gradient 30% to 40% $Et_2O$:pentanes) to afford 66 mg of a colorless oil (63% yield, 0.17 mmol). The major diastereomer could be isolated using the same conditions to afford 51 mg (49%, 0.13 mmol) of the title compound as a colorless oil (overall 66 mg, 63%, 0.17 mmol); 93% ee (Daicel CHIRALPAK® AD-H, gradient 5% to 50% solvent (methanol), 5 mL/min, 221 nm; $t_1$ = 9.10 min, $t_2$ = 11.93 min).

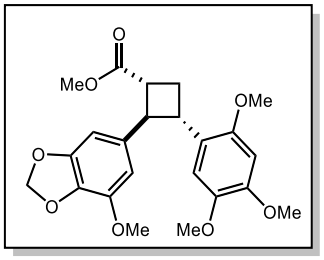
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 7.69-7.72 (m, 1H), 7.48-7.52 (m, 1H), 7.30-7.34 (m, 2H), 7.03 (s, 1H), 6.97. (s, 1H), 6.54 (d, *J* = 1.46 Hz, 1H), 6.50 (d, *J* = 1.40 Hz, 1H), 5.92 (s, 2H), 4.02 (t, 9.77 Hz, 1H), 3.92 (td, *J* = 10.23, 8.05 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.73 (s, 3H), 3.68-3.73 (m, 1H), 2.88 (dt, 10.65, 8.10 Hz, 1H), 2.53 (q, 10.35 Hz, 1H) ; **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 167.6, 151.9, 150.9, 150.3, 149.0, 143.5, 141.4, 136.5, 134.1, 131.3, 124.7, 124.3, 119.8, 116.0, 112.2, 110.5, 109.6, 106.3, 101.3, 100.8, 57.2, 56.6, 56.1, 51.4, 38.4, 38.3, 31.1; **IR** (thin film): ν 2928, 2847, 1630, 1567, 1494, 1453, 1208, 1041 $cm^{-1}$; **HRMS** ($ESI^-$): $[M+H]^+$ calculated for $C_{27}H_{24}BrNO_6$ requires *m/z* 538.0860, found *m/z* 538.0862; **$[\alpha]^{22}_D$** −38.6 º (*c*0.42, $CH_2Cl_2$).




**Methyl (1*R*,2*R*,3*S*)-3-(4-bromo-2,5-dimethoxyphenyl)-2-(7-methoxybenzo[*d*][1,3]dioxol-5-yl) cyclobutane-1-carboxylate** (**2.42**). NaOH (60 equiv, 12.0 mmol) in $H_2O$ (2.0 mL) was added to a stirring solution of cyclobutane **2.41** (1 equiv, 110 mg, 0.20 mmol, 95% ee) in EtOH (3.0 mL) in an oven-dried 3 dram vial. The vial was sealed with a Teflon cap and stirred at 95 ºC for 36 h. The reaction was quenched with 1M HCl and extracted with $Et_2O$ (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo.* The resulting residue was transferred to a 3 dram vial and dissolved in DMF (0.4 mL). $K_2CO_3$ (1.5 equiv, 0.31 mmol) was added, and the solution and stirred for 5 min. After this period, iodomethane (3.0 equiv, 0.61 mmol) was added via syringe, and the vial was sealed with a Teflon cap. The resulting solution was stirred for 1 h at room temperature. The reaction was

then slowly quenched with $H_2O$ (2 mL) and extracted with $Et_2O$ (5 mL). The organic layer was washed with $H_2O$ (2 x 2 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting residue was purified by flash column chromatography on silica gel (40% $Et_2O$:pentanes) to afford the methyl ester (89 mg, 91% yield, 0.186 mmol) as a cloudy oil; 93% ee (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent (methanol), 5 mL/min, 221 nm; $t_1$ = 5.54 min, $t_2$ = 6.50 min).

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 7.00 (s, 1H), 6.89 (s, 1H), 6.48 (d, *J* = 1.52 Hz, 1H), 6.44 (d, *J* = 1.59 Hz, 1H), 5.92 (s, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.74-3.79 (m, 2H), 3.73 (s, 3H), 3.71 (s, 3H), 3.05-3.10 (m, 1H), 2.58-2.63 (m, 1H), 2.19-2.25 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 174.6, 151.8, 150.2, 148.9, 143.4, 136.9, 133.9, 131.5, 115.9, 112.1, 109.5, 106.2, 101.3, 100.7, 57.2, 56.6, 56.1, 51.9, 49.5, 42.6, 37.5, 29.4; **IR** (thin film): ν 2996, 2948, 2843, 1727, 1630, 1493, 1435, 1207, 1040 $cm^{-1}$; **HRMS** ($ESI^-$): $[M+H]^+$ calculated for $C_{22}H_{23}BrO_7$ requires *m/z* 479.0700, found *m/z* 479.0700; **$[\alpha]^{22}_D$** +54.3° (*c*0.44, $CH_2Cl_2$).

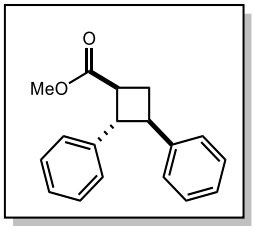



**Methyl (1*R*,2*R*,3*S*)-2-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)-3-(2,4,5-trimethoxyphenyl)cyclobutane-1-carboxylate** (***ent*-2.1**)**:**

A 8 mL screw cap vial equipped with a magnetic stir bar and was charged with the cyclobutane **2.42** (1 equiv, 70 mg, 0.15 mmol, 93% ee), $Cs_2CO_3$ (2 equiv, 12 mg, 0.29 mmol), and [(2-di-*tert*-butylphosphino-3-methoxy-6-methyl-2′,4′,6′-triisopropyl-1,1′-biphenyl)-2-(2-aminobiphenyl)]palladium(II) methanesulfonate (RockPhos Pd G3, 0.1 equiv, 12 mg, 0.015 mmol). The vial was sealed with septum, then evacuated and backfilled with nitrogen three times. Methanol (5 equiv, 0.73 mmol, 30 μL) was added by syringe, followed by toluene (1.5 mL). The vial was sealed with Teflon cap, and the reaction mixture was stirred at 90 °C for 24 h. The reaction mixture was then cooled to room temperature, diluted with 5 mL ethyl acetate, and filtered. The crude reaction mixture was concentrated *in vacuo* and purified by flash-column chromatography on silica gel (60% $Et_2O$:pentanes) to afford the product (57 mg, 91%, 0.132 mmol)

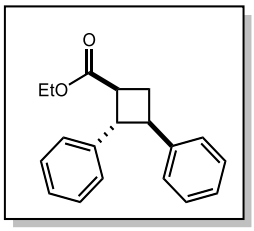
as a colorless oil; 92% ee (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent (methanol), 5 mL/min, 221 nm; $t_1$ = 4.47 min, $t_2$ = 5.20 min).

**$^1$H NMR** (500 MHz, $CDCl_3$): δ 6.88 (s, 1H), 6.49 (s, 1H), 6.49 (s, 1H), 6.46 (d, *J* = 1.44 Hz, 1H), 5.92 (s, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.75-3.79 (m, 2H), 3.731 (s, 3H), 3.729 (s, 3H), 3.02-3.07 (m, 1H), 2.55-2.59 (m, 1H), 2.21-2.28 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$): δ 174.8, 151.5, 148.8, 148.3, 143.4, 137.3, 133.8, 122.7, 111.9, 106.1, 101.3, 100.8, 97.8, 56.9, 56.54, 56.47, 56.2, 51.8, 50.0, 42.5, 37.0, 29.6; **IR** (thin film): ν 2947, 2841, 1726, 1630, 1507, 1455, 1433, 1200, 1033 $cm^{-1}$; **HRMS** ($ESI^-$): $[M+H]^+$ calculated for $C_{23}H_{26}O_8$ requires *m/z* 431.1700, found *m/z* 431.1697; **$[\alpha]^{22}_D$** +20.0° (*c*0.01, $CHCl_3$).




**Methyl (1*S*,2*S*,3*R*)-2,3-diphenylcyclobutane-1-carboxylate (2.45):**

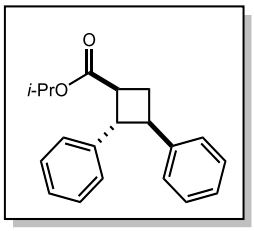
The title compound was prepared according to General Procedure C using methyl cinnamate (64.9 mg, 0.400 mmol), $[Ir(Fppy)_2(dtbpy)(PF_6)]$ (3.8 mg, 0.004 mmol), styrene (0.23 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude material resulted in a 6:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, Column 1: 2.5% MTBE:pentane, Column 2: 3% $Et_2O$:pentane). Combined yield: 97.3 mg of a clear oil (91%, 0.365 mmol); 97% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 5.20 min, $t_2$ = 6.62 min). $[\alpha]_D^{20}$ = –39.8° (c = 1.0, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.37–7.18 (m, 10H), 3.85 (t, *J* = 9.7 Hz, 1H), 3.72 (s, 3H), 3.53 (td, *J* = 10, 8.3 Hz, 1H), 3.20 (dt, *J* =9.7, 8.3 Hz, 1H), 2.63 (dt, *J* = 10.6, 8.3 Hz, 1H), 2.41 (q, *J* = 10.3 Hz, 1H); $^{13}$C NMR (126 MHz $CDCl_3$) $\delta$ 174.6, 143.2, 142.1, 128.47, 128.46, 126.8, 126.7, 126.6, 126.57, 51.9, 50.8, 43.5, 41.5, 29.6; IR (thin film) $\nu$ 3059, 3027, 2987, 2948, 1728, 1600, 1496, 1439, 1200, 1159, 1027, 751, 696 $cm^{-1}$; HRMS (ESI) *m* / z calcd for $C_{18}H_{18}O_2Na$ $(M + Na)^+$ 289.1199, found 289.1194.




**Ethyl (1*S*,2*S*,3*R*)-2,3-diphenylcyclobutane-1-carboxylate (2.46):**

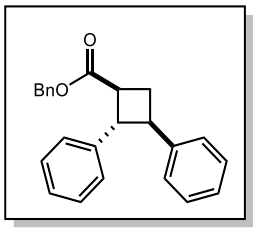
The title compound was prepared according to General Procedure C using ethyl cinnamate (70.5 mg, 0.400 mmol), $[Ir(Fppy)_2(dtbpy)(PF_6)]$ (3.8 mg, 0.004 mmol), styrene (0.23 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude material resulted in a 6:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, Column 1: 4% EtOAc:hexanes, Column 2: 4% MTBE/pentane). Combined yield: 105.3 mg of a clear oil (94%, 0.376 mmol);

98% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 4.89 min, $t_2$ = 6.09 min). $[\alpha]_D^{20}$ = –41.8° (c = 1.0, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.34–7.18 (m, 10H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.85 (t, *J* = 9.8 Hz, 1H), 3.55 (td, *J* = 9.8, 8.3 Hz, 1H), 3.17 (ap q, *J* = 9.3 Hz, 1H), 2.63 (dt, *J* = 10.6, 8.3 Hz, 1H), 2.40 (q, *J* = 10.3 Hz, 1H), 1.28 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 174.1, 143.3, 142.2, 128.4 (2C), 126.8, 126.63, 126.62, 126.5, 60.6, 50.7, 43.3, 41.8, 29.6, 14.3; IR (thin film) $\nu$ 3060, 3028, 2980, 2903, 1726, 1603, 1496, 1446, 1195, 1161, 1029, 752 cm$^{-1}$; HRMS (ESI) *m* / z calcd for $C_{19}H_{20}O_2Na$ $(M + Na)^+$ 303.1355, found 303.1352.



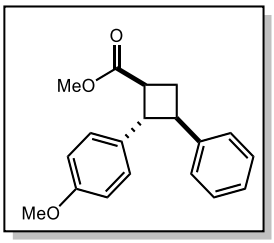

**Isopropyl (1*S*,2*S*,3*R*)-2,3-diphenylcyclobutane-1-carboxylate** (**2.47**)**:**

The title compound was prepared according to General Procedure C using isopropyl cinnamate (76.1 mg, 0.400 mmol), $[Ir(Fppy)_2(dtbpy)(PF_6)]$ (3.8 mg, 0.004 mmol), styrene (0.23 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude material resulted in a 7:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, Column 1: 4% EtOAc:hexanes, Column 2: 4% MTBE:pentane). Combined yield: 112.9 mg of a clear oil (96%, 0.384 mmol); 97% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 4.37 min, $t_2$ = 4.86 min). $[\alpha]_D^{20}$ = –41.6˚ (c = 1.0, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.34–7.18 (m, 10H), 5.06 (sept, *J* = 6.3 Hz, 1H), 3.84 (t, *J* = 9.7 Hz, 1H), 3.55 (td, *J* = 10.0, 8.3 Hz, 1H), 3.12 (td, *J* = 9.7, 8.5 Hz, 1H), 2.62 (dt, *J* = 10.3, 8.3 Hz, 1H), 2.38 (q, *J* = 10.3 Hz, 1H), 1.26 (d, *J* = 6.3 Hz, 3H) 1.25 (d, *J* = 6.3 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 173.7, 143.4, 142.3, 128.44, 128.41, 126.8, 126.61, 126.58, 126.5, 67.9, 50.6, 43.0, 42.1, 29.6, 21.87, 21.85; IR (thin film) $\nu$ 3061, 3027, 2979, 2943, 1722, 1603, 1495, 1448, 1197, 1106, 751, 696 cm$^{-1}$; HRMS (ESI) *m* / z calcd for $C_{20}H_{22}O_2Na$ $(M + Na)^+$ 317.1512, found 317.1509.




**Benzyl (1*S*,2*S*,3*R*)-2,3-diphenylcyclobutane-1-carboxylate (2.48):**

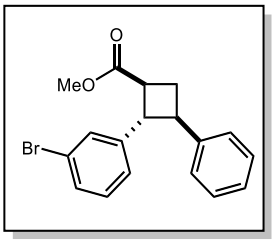
The title compound was prepared according to General Procedure C using benzyl cinnamate (95.3 mg, 0.400 mmol), [Ir(Fppy)$_2$(dtbpy)(PF$_6$)] (3.8 mg, 0.004 mmol), styrene (0.23 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude material resulted in a 6:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, Column 1: 4% EtOAc:hexanes, Column 2: 4% MTBE:pentane). Combined yield: 118.1 mg of a clear oil (86%, 0.345 mmol); 97% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 5.97 min, $t_2$ = 6.50 min). $[\alpha]_D^{20}$ = –26.0˚ (c = 1.0, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.39–7.18 (m, 15H), 5.19 (d, *J* = 12.5 Hz, 1H), 5.15 (d, *J* = 12.5 Hz, 1H), 3.86 (t, *J* = 9.8 Hz, 1H), 3.56 (q, *J* = 9.5 Hz, 1H), 3.24 (q, *J* = 9.3 Hz, 1H), 2.64 (dt, *J* = 10.7, 8.3 Hz, 1H), 2.42 (q, *J* = 10.4 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 173.9, 143.1, 142.0, 136.0, 128.54, 128.45 (2C), 128.2, 128.1, 126.8, 126.7, 126.66, 126.6, 66.4, 50.8, 43.3, 41.8, 29.5; IR (thin film) $\nu$ 3061, 3027, 2979, 2943, 1722, 1603, 1495, 1448, 1197, 1106, 751, 696 cm$^{-1}$; HRMS (ESI) *m* / z calcd for $C_{20}H_{22}O_2Na$ $(M + Na)^+$ 317.1512, found 317.1509.




**Methyl (1*S*,2*S*,3*R*)-2-(4-methoxyphenyl)-3-phenylcyclobutane-1-carboxylate (2.50):**

The title compound was prepared according to General Procedure C using methyl (*E*)-3-(4-methoxyphenyl)acrylate[40] (76.9 mg, 0.400 mmol), [Ir(Fppy)$_2$(dtbpy)(PF$_6$)] (3.8 mg, 0.004 mmol), styrene (0.23 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude

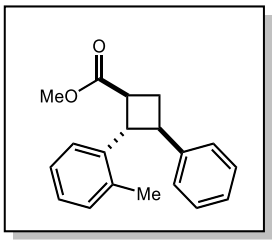
material resulted in a single diastereomer (>20:1) that was purified by flash chromatography ($SiO_2$, Column 1: 8% EtOAc:hexanes, Column 2: 10% $Et_2O$:pentane). Yield: 90.4 mg of a clear oil (76%, 0.305 mmol); 94% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 6.16 min, $t_2$ = 7.69 min). $[\square]_D^{20}$ = –46.4˚ (c = 1.0, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.33–7.28 (m, 2H), 7.27–7.23 (m, 2H), 7.23– 7.19 (m, 1H), 7.18 (ap d, *J* = 8.5 Hz, 2H), 6.84 (ap d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 3.75 (t, *J* = 9.8 Hz, 1H), 3.71 (s, 3H), 3.49 (dt, *J* = 10.0, 8.3 Hz, 1H), 3.15 (dt, *J* = 9.6, 8.3 Hz, 1H), 2.60 (td, *J* = 10.5, 8.3 Hz, 1H), 2.39 (q, *J* = 10.5 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 174.6, 158.4, 143.2, 134.2, 128.4, 127.7, 126.8, 126.5, 113.9, 55.3 51.8, 50.4, 43.7, 41.9, 29.3; IR (thin film) $\nu$ 3062, 3030, 2996, 2951, 2835, 1728, 1611, 1513, 1455, 1435, 1247, 1177, 1033, 821, 762, 665 $cm^{-1}$; HRMS (ESI) *m* / z calcd for $C_{19}H_{20}O_3Na$ $(M + Na)^+$ 319.1305, found 319.1301.




**Methyl (1*S*,2*S*,3*R*)-2-(3-bromophenyl)-3-phenylcyclobutane-1-carboxylate (2.51):**

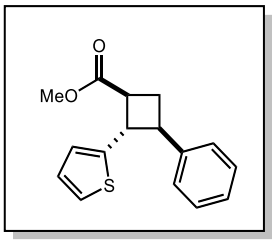
The title compound was prepared according to General Procedure C using methyl (*E*)-3-(3-bromophenyl)acrylate (96.4 mg, 0.400 mmol), $[Ir(Fppy)_2(dtbpy)(PF_6)]$ (3.8 mg, 0.004 mmol), styrene (0.23 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude material resulted in a 5:1mixture of diastereomers that was purified by flash chromatography ($SiO_2$, Column 1: 4% EtOAc:hexanes, Column 2: 4% MTBE:pentane). Yield: 113.9 mg of a clear oil (82%, 0.330 mmol); 95% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 5.39 min, $t_2$ = 7.77 min). $[\alpha]_D^{20}$ = –42.2˚ (c = 1.0, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.41 (s, 1H), 7.37–7.30 (m, 3H), 7.28–7.21 (m, 3H), 7.18–7.15 (m, 2H), 3.80 (t, *J* = 9.7 Hz, 1H), 3.73 (s, 3H), 3.51 (td, *J* = 9.8, 8.8 Hz, 1H), 3.17 (td, *J* = 9.5, 9.0 Hz, 1H), 2.64 (dt, *J* = 10.4, 8.4 Hz, 1H), 2.40 (q, *J* = 10.4 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 174.2, 144.4, 142.6, 130.1, 129.9, 129.7, 128.6, 126.76, 126.75, 125.4, 122.7, 52.0, 50.2, 43.4, 41.4, 29.6; IR (thin film) $\nu$ 3063, 3028, 2993, 2951, 1731, 2595, 1565, 1495, 1476,

1456, 1435, 1231, 1162, 1073, 1029, 780, 760, 745, 698 $cm^{-1}$; HRMS (ESI) *m* / z calcd for $C_{18}H_{17}O_2BrH$ $(M + H)^+$ 345.0485, found 345.0485.




**Methyl (1*S*,2*S*,3*R*)-3-phenyl-2-(*o*-tolyl)cyclobutane-1-carboxylate** (**2.52**)**:**

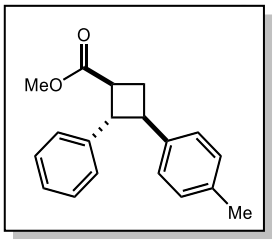
The title compound was prepared according to General Procedure C using methyl (*E*)-3-(*o*-tolyl)acrylate (70.5 mg, 0.400 mmol), $[Ir(Fppy)_2(dtbpy)(PF_6)]$ (3.8 mg, 0.004 mmol), styrene (0.23 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude material resulted in a 9:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, Column 1: 4% EtOAc:hexanes, Column 2: 6% $Et_2O$:pentane). Yield: 108.9 mg of a clear oil (97%, 0.388 mmol); 99% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 5.14 min, $t_2$ = 7.30 min). $[\alpha]_D^{20}$ = –39.0˚ (c = 1.0, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.46 (d, *J* = 7.9 Hz, 1H), 7.30–7.17 (m, 6H), 7.15–7.08 (m, 2H), 4.03 (t, *J* = 9.8 Hz, 1H), 3.68 (s, 3H), 3.59 (td, *J* = 10.0, 8.5 Hz, 1H), 3.19 (td, *J* = 9.7, 8.4 Hz, 1H), 2.62 (dt, *J* = 10.6, 8.2 Hz, 1H), 2.44 (q, *J* = 10.3 Hz, 1H), 2.10 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 174.7, 143.3, 139.7, 136.3, 130.3, 128.4, 126.7, 126.6, 126.5, 126.2, 126.1, 51.8, 48.1, 43.7, 41.8, 29.1, 19.8; IR (thin film)  3061, 3026, 2987, 2950, 1730, 1602, 1494, 1456, 1435, 1229, 1200, 1161, 1029, 753, 699 $cm^{-1}$; HRMS (ESI) *m* / z calcd for $C_{19}H_{20}O_2NH_4$ $(M + NH_4)^+$ 298.1802, found 298.1802.




**Methyl (1*S*,2*S*,3*R*)-3-phenyl-2-(thiophen-2-yl)cyclobutane-1-carboxylate** (**2.53**)**:**

The title compound was prepared according to General Procedure C using methyl (*E*)-3-(thiophen-2-

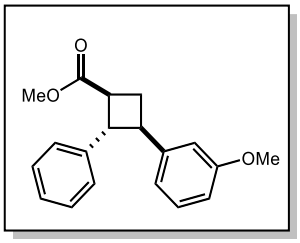
yl)acrylate (67.3 mg, 0.400 mmol), [Ir(Fppy)$_2$(dtbpy)(PF$_6$)] (3.8 mg, 0.004 mmol), styrene (0.23 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude material resulted in a 4:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, Column 1: 4% EtOAc:hexanes, Column 2: 6% $Et_2O$:pentane). Yield: 73.8 mg of a clear oil (68%, 0.271 mmol); 93% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 5.88 min, $t_2$ = 7.36 min). $[\alpha]_D^{20}$ = –39.6˚ (c = 1.0, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.34–7.29 (m, 2H), 7.29–7.25 (m, 2H), 7.25–7.20 (m, 1H), 7.18 (ap d, *J* = 5.1 Hz, 1H), 6.96–6.93 (m, 1H), 6.91–6.89 (m, 1H), 3.94 (t, *J* = 9.6 Hz, 1H), 3.72 (s, 3H), 3.55 (dt, *J* = 9.8, 8.7 Hz, 1H), 3.19 (dt, *J* = 9.4, 8.9 Hz, 1H), 2.62 (td, *J* = 10.6, 8.4 Hz, 1H), 2.41 (q, *J* = 10.4 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 174.0, 146.0, 142.4, 128.5, 126.9, 126.7, 126.67, 123.85, 123.80, 51.9, 46.7, 45.4, 43.5, 28.9; IR (thin film) $\nu$ 3063, 3026, 2989, 2950, 1729, 1602, 1496, 1456, 1435, 1227, 1199, 1160, 1086, 1029, 848, 760, 696 cm$^{-1}$; HRMS (ESI) *m* / z calcd for $C_{16}H_{16}O_2SH$ $(M + H)^+$ 273.0944, found 273.0940.




**Methyl (1*S*,2*S*,3*R*)-2-phenyl-3-(*p*-tolyl)cyclobutane-1-carboxylate** (**2.54**)**:**

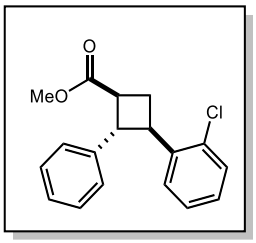
The title compound was prepared according to General Procedure C using methyl (*E*)-3-(thiophen-2-yl)acrylate (67.3 mg, 0.400 mmol), [Ir(Fppy)$_2$(dtbpy)(PF$_6$)] (3.8 mg, 0.004 mmol), 1-methyl-4-vinylbenzene (0.26 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude material resulted in a 5:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, 5% $Et_2O$:pentane). Yield: 85.6 mg of a clear oil (76%, 0.305 mmol); 96% ee (Daicel CHIRALPAK® OD-H, 1–40% IPA:hexanes over 20 min, flow rate of 1 mL/min; $t_1$ = 6.02 min, $t_2$ = 9.93 min). $[\alpha]_D^{20}$ = –31.2˚ (c = 0.25, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.31–7.28 (m, 2H), 7.25–7.22 (m, 3H), 7.19–7.17 (m, 2H), 7.18 (ap d, *J* = 7.9 Hz, 2H), 3.82 (t, *J* = 9.8 Hz, 1H), 3.72 (s, 3H), 3.48 (td, *J* = 10.1, 8.1 Hz, 1H), 3.19 (td, *J* = 9.8, 8.2 Hz, 1H), 2.60 (dt, *J* = 10.8, 8.2 Hz, 1H), 2.38 (q, *J* = 10.4 Hz, 1H), 2.32 (s, 3H); $^{13}$C NMR

(126 MHz, $CDCl_3$) $\delta$ 174.66, 142.18, 140.14, 136.16, 129.14, 128.44, 126.78, 126.64 126.58, 51.84, 50.86, 43.28, 41.35, 29.76, 21.05; IR (thin film) $\nu$ 3024, 2948, 1728, 1602, 1510, 1201, 1162, 908, 729, 697 $cm^{-1}$; HRMS (ESI) *m* / z calcd for $C_{19}H_{20}O_2Na$ $(M + Na)^+$ 303.1356, found 303.1353.



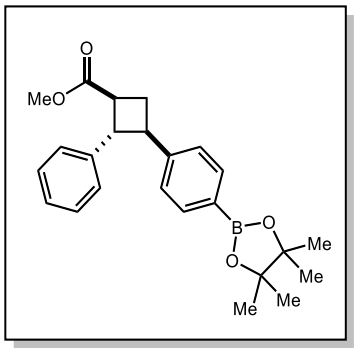

**Methyl (1*S*,2*S*,3*R*)-3-(3-methoxyphenyl)-2-phenylcyclobutane-1-carboxylate (2.55):**

The title compound was prepared according to General Procedure C using methyl cinnamate (64.9 mg, 0.400 mmol), $[Ir(Fppy)_2(dtbpy)(PF_6)]$ (3.8 mg, 0.004 mmol), 3-vinylanisole (0.28 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude material resulted in a 6:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, 6% EtOAc:hexanes). Yield: 78.9 mg of a clear oil (67%, 0.266 mmol); 90% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 6.10 min, $t_2$ = 6.90 min). $[\alpha]_D^{20}$ = –34.0˚ (c = 1.0, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.34–7.27 (m, 2H), 7.26–7.18 (m, 3H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.81 (br t, *J* = 1.9 Hz, 1H), 6.76 (dd, *J* = 8.2, 2.3 Hz, 1H), 3.84 (t, *J* = 9.8 Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 3.50 (td, *J* = 10.1, 8.2 Hz, 1H), 3.19 (td, *J* = 9.8, 8.2 Hz, 1H), 2.62 (dt, *J* = 10.7, 8.2 Hz, 1H), 2.40 (q, *J* = 10.4 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 174.5, 159.7, 144.9, 142.0, 129.5, 128.5, 126.7, 126.6, 119.2, 112.7, 111.7, 55.2, 51.9, 50.7, 43.5, 41.4, 29.6; IR (thin film) $\nu$ 3058, 3028, 2995, 2950, 2835, 1728, 1601, 1583, 1489, 1452, 1435, 1289, 1260, 1230, 1198, 1158, 1039, 774, 755, 696 $cm^{-1}$; HRMS (ESI) *m* / z calcd for $C_{19}H_{20}O_3H$ $(M + H)^+$ 297.1485, found 297.1483.



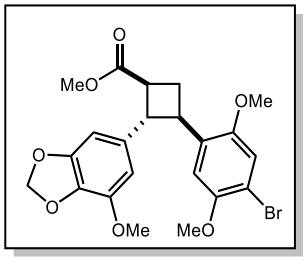

**Methyl (1*S*,2*S*,3*R*)-3-(2-chlorophenyl)-2-phenylcyclobutane-1-carboxylate (2.56):**

The title compound was prepared according to General Procedure C using methyl cinnamate (64.9 mg, 0.400 mmol), [Ir(Fppy)$_2$(dtbpy)(PF$_6$)] (3.8 mg, 0.004 mmol), 2-chlorostyrene (0.26 mL, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL). The crude material resulted in a 9:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, Column 1: 4% EtOAc:hexanes, Column 2: 0.5% EtOAc:PhMe). Yield: 93.5 mg of a clear oil (78%, 0.311 mmol); 96% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 5.08 min, $t_2$ = 7.37 min). $[\alpha]_D^{20}$ = –10.8° (c = 1.0, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.45 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.35–7.20 (m, 7H), 7.16 (td, *J* = 7.7, 1.7 Hz, 1H), 4.05 (t, *J* = 9.8 Hz, 1H), 3.95 (td, *J* = 10.2, 8.1 Hz, 1H), 3.73 (s, 3H), 3.20 (td, *J* = 9.6, 8.3 Hz, 1H), 2.83 (dt, *J* = 10.7, 8.3 Hz, 1H), 2.20 (q, *J* = 10.2 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 174.6, 141.7, 140.2, 133.6, 129.4, 128.5, 127.8, 127.7, 127.0, 126.8, 126.6, 51.9, 48.1, 42.1, 40.0, 30.4; IR (thin film) $\nu$ 3063, 3027, 2995, 2951, 1730, 1497, 1476, 1436, 1230, 1199, 1164, 1034, 752, 698 cm$^{-1}$; HRMS (ESI) *m* / z calcd for $C_{18}H_{17}ClO_2NH_4$ $(M + NH_4)^+$ 318.1255, found 318.1253.



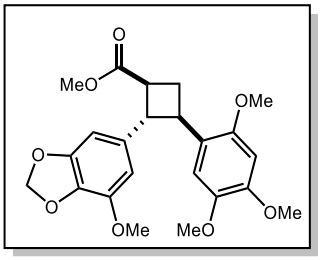

**Methyl (1*S*,2*S*,3*R*)-2-phenyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)cyclo- butane-1-carboxylate (22).** The title compound was prepared according to General Procedure C using methyl cinnamate (64.9 mg, 0.400 mmol), [Ir(Fppy)$_2$(dtbpy)(PF$_6$)] (3.8 mg, 0.004 mmol), 4-vinylphenylboronic

acid (460.2 mg, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL), an irradiation time of 76 h. The crude material resulted in a 6:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, 5% $Et_2O$: Pentane). Yield: 120.7 mg of a clear oil (77%, 0.307 mmol); 92% ee (Daicel CHIRALPAK® IC, 1–40% IPA:hexanes over 20 min, flow rate of 1 mL/min; $t_1$ = 5.91 min, $t_2$ = 6.35 min). $[\alpha]_D^{20}$ = –46.2˚ (c = 0.81, $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.77–7.75 (m, 2H), 7.30–7.27 (m, 4H), 7.23– 7.20 (m, 3H), 3.85 (t, *J* = 9.8 Hz, 1H), 3.72 (s, 3H), 3.52 (td, *J* = 10.1, 8.1 Hz, 1H), 3.22 (td, *J* = 9.9, 8.2 Hz, 1H), 2.62 (dt, *J* = 11.0, 8.3 Hz, 1H), 2.42 (q, *J* = 10.4 Hz, 1H), 1.33 (s, 12H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 174.55, 146.30, 142.00, 135.02, 128.47, 126.70, 126.54, 126.33, 83.72, 51.87, 50.68, 43.87, 41.28, 29.50, 24.85; $^{11}$B NMR (160 MHz, CDCl3): δ 30.5 (b, B); IR (thin film) $\nu$ 2380, 1730, 1608, 1492, 1441, 1396, 1357, 1322, 1267, 1144, 1088, 736, 699 cm$^{-1}$; HRMS (ESI) *m* / z calcd for $C_{24}H_{29}BO_4Na$ $(M + Na)^+$ 415.2051, found 415.2048.




**((1R,2R,3S)-3-(4-Bromo-2,5-dimethoxyphenyl)-2-(7-methoxybenzo[d][1,3]dioxol-5- yl)cyclobutyl) (2-hydroxyphenyl)methanone (*ent*-2.42):**

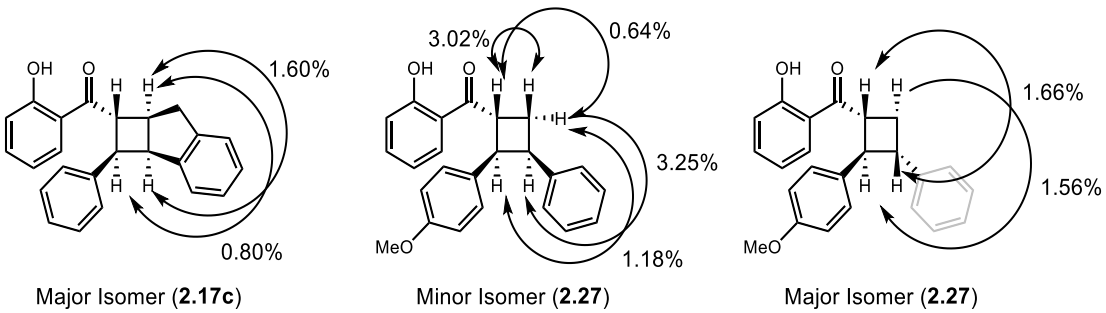
The title compound was prepared according to General Procedure C using methyl (*E*)-3-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)acrylate (94.5 mg, 0.400 mmol, $[Ir(ppy)_2(4,4'\text{-}dCF_3bpy)(PF_6)]$ (3.8 mg, 0.004 mmol), 1-bromo-2,5-dimethoxy-4-vinylbenzene (486.2 mg, 2.00 mmol), oxazaborolidine **6f** (1.0 mL, 0.100 mmol), and $CH_2Cl_2$ (12.5 mL), an irradiation time of 36 h. The crude material resulted in a 5:1 mixture of diastereomers that was purified by flash chromatography ($SiO_2$, Gradient 20% to 40% MTBE: Pentane. Yield: 151.9 mg of a cloudy oil (80%, 0.318 mmol); 97% ee (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, flow rate of 1 mL/min; $t_1$ = 9.31 min, $t_2$ = 9.93 min) $[\alpha]_D^{22}$ = –60.0˚ (c = 0.60, $CH_2Cl_2$); lit for 93% ee $[\alpha]_D^{22}$ = +54.3˚ (c = 0.44, $CH_2Cl_2$).




**Methyl (1R,2R,3S)-2-(7-methoxybenzo[d][1,3]dioxol-5-yl)-3-(2,4,5- trimethoxyphenyl)cyclobutane 1-carboxylate (2.1):**

A 8 mL screw cap vial equipped with a magnetic stir bar and was charged with the cyclobutane **25** (1 equiv, 90.0 mg, 0.188 mmol, 97% ee), Cs2CO3 (2 equiv, 133 mg, 0.376 mmol), and [(2-di-tertbutylphosphino-3-methoxy-6-methyl-2′,4′,6′-triisopropyl-1,1′-biphenyl)-2-(2-aminobiphenyl)]palladium(II) methanesulfonate (RockPhos Pd G3, 0.1 equiv, 16.0 mg, 0.0188 mmol). The vial was sealed with septum, then evacuated and backfilled with nitrogen three times. Methanol (5 equiv, 0.940 mmol, 38 µL) was added by syringe, followed by toluene (1.9 mL). The vial was sealed with Teflon cap, and the reaction mixture was stirred at 90 ºC for 24 h. The reaction mixture was then cooled to room temperature, diluted with 5 mL ethyl acetate, and filtered. The crude reaction mixture was concentrated in vacuo and purified by flash-column chromatography on silica gel (60% $Et_2O$:pentanes) to afford the product (74.6 mg, 92%, 0.173 mmol) as a colorless oil; 97% ee (Daicel CHIRALPAK® OJ-H, isocratic 40% EtOH:hexanes over 40 min,flow rate of 4 mL/min; $t_1$ = 21.3 min, $t_2$ = 24.5 min); $[\alpha]_D^{22}$ = –33.0˚ (c = 0.41, $CHCl_3$); lit for 92% ee $[\alpha]_D^{22}$ = +20.0˚ (c= 0.01, $CHCl_3$).

### 2.5.5 NOE Assignment of Relative Stereochemistry



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# Chapter 3. Site-Selective Alkoxylation of Benzylic C–H Bonds *via* Photoredox Catalysis

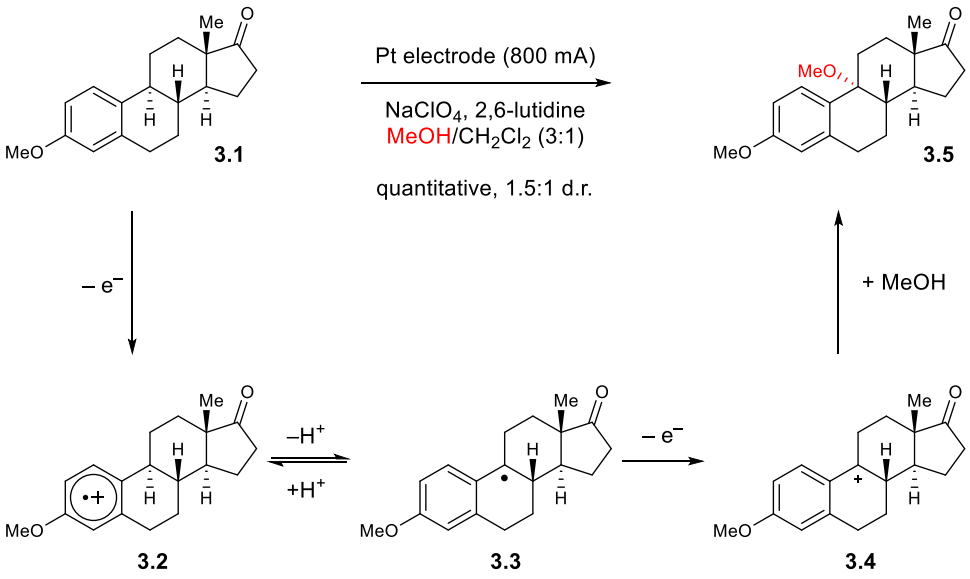
Portions of this work have previously been published:

Lee, B. J.; DeGlopper, K. S.; Yoon, T. P. "Site-Selective Alkoxylation of Benzylic C−H Bonds by Photoredox Catalysis" *Angew. Chem., Int. Ed.* **2020**, *59*, 197−202.

## 3.1 Introduction

The development of efficient methods for site-selective functionalization of $sp^3$-hybridized C–H bonds has profoundly diversified the syntheses of complex molecules.[1–3] Late-stage functionalization strategies that enable single-step incorporation of new functionality are particularly important because they allow for the rapid synthesis of structural analogues of pharmaceutical candidates in the pursuit of new chemical and biological properties.[4,5] Much of the recent work in this area has centered on the construction of C–C, C–F, and C–N bonds at aliphatic positions.[6,7] These reactions are fundamentally oxidative transformations in nature and their development has benefited from the availability of numerous electrophilic group-transfer oxidants for each of these important classes of C–H functionalizations (e.g., Selectfluor and NFSI for C–F bond formation; Michael acceptors and diazoesters for C–C bond formation; and azides, azodicarboxylic acids, hydroxylamine derivatives, and iminoiodinanes for C–N bond formation).

In contrast, few similar strategies for the site-selective alkoxylation of $sp^3$-hybridized C–H bonds have been reported to date, despite the ubiquity of C–O bonds in bioactive molecules.[8] Almost all reported methods using electrophilic group-transfer oxidants incorporate hydroxyl and ester functionalities,[9–14] consistent with the availability of the corresponding group-transfer oxidants (e.g., hydroperoxides and peroxyesters). The relative paucity of group-transfer oxidants for direct alkoxylation has significantly impeded the development of similar robust C–H alkoxylation strategies. Instead, net-oxidative strategies have been explored with appropriate terminal oxidants in the presence of more readily synthesized nucleophilic alcohols. As a result, there are numerous established methods for oxidative functionalizations of $sp^3$-hybridized C–H bonds in complex organic molecules using simple alcohols, including electrochemical oxidations,[15–19] chemical oxidations,[20–24] and transition metal catalyzed C–H alkoxylation protocols.[25–30] However, most of these strategies require solvent quantities of the alcohol coupling partner for optimal reactivity, barring a few notable examples.[29,30] This feature limits the practical scopes of these strategies to inexpensive, simple alcohols. Thus, a more synthetically general method for the coupling of alcohols is needed.




**Scheme 3.1.** Site-selective C–H methoxylation of estrone **3.1** *via* electrochemical oxidation

In 1979, Ponsold reported an electrochemical oxidation method that enabled site-selective C–H methoxylation of estrone **3.1** in nearly quantitative yield (Scheme 3.1).[16] This strategy required solvent quantities of methanol, presumably because methanol reduction at the cathode completed the electrochemical cell as methanol served as the terminal oxidant for this net-oxidative process. Ponsold proposed that anodic oxidation of estrone **3.1** afforded radical cation **3.2**. Facile deprotonation of a weakened benzylic C–H bond would afford benzylic radical intermediate **3.3**.[31,32] This radical intermediate could undergo further anodic oxidation to corresponding carbocation (**3.4**), which could then be trapped by methanol. We hypothesized that a sufficiently oxidizing photocatalyst could mimic the initial anodic oxidation and that radical oxidation and photocatalyst turnover could be accomplished in the presence of an appropriate terminal oxidant. In addition, we hypothesized that this strategy could exhibit complementary site selectivity from conventional methods, which are driven by bond dissociation energy (BDE). Importantly, because the proposed method would use an exogenous terminal oxidant rather than proton reduction to balance the redox reaction, we hypothesized that this strategy would require significantly lower loading of the alcohol partner. For this reason, we were interested in exploring the

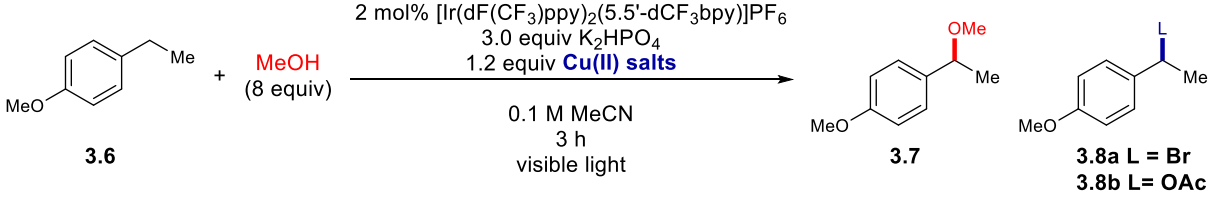
application of this strategy towards late-stage benzylic C–H alkoxylation using structurally complex alcohols.

### 3.2 Reaction Design and Optimization

We initially focused our investigation of benzylic C–H alkoxylation reactions using Cu(II) salts as terminal oxidants, was motivated by several factors. First, our laboratory and Tunge have recently demonstrated that Cu(II) salts are excellent terminal oxidants in photoredox catalysis[33,34] because they are unlikely to generate reactive open-shelled radical intermediates that are common to other classes of terminal oxidants (e.g., molecular oxygen, persulfates, and peroxides) and incompatible with highly functionalized complex organic molecules. Second, seminal studies by Kochi demonstrated that benzylic radicals could undergo rapid oxidation by Cu(II) salts to their corresponding carbocations.[35–37] Finally, Cu(II) salts are mild oxidants that are inexpensive, easily handled, and compatible with a wide range of functional groups.[38]

We initially examined to examine the reaction of easily oxidizable 4-ethylanisole (**3.6**) ($E_{p/2}$ = +1.52 V vs SCE) with methanol using [Ir(dF($CF_3$)ppy)$_2$(5.5'-d$CF_3$bpy)]$PF_6$ ($E_{1/2}$ [*$Ir^{III}$/$Ir^{II}$] = +1.68 V) as the photocatalyst, $K_2HPO_4$ as the base, and a variety of Cu(II) salts as terminal oxidants. The photocatalyst was carefully chosen to avoid overoxidation of the alkoxylated products since they would be more difficult to oxidize than the starting anisole. A screen of Cu(II) salts under these conditions revealed that nucleophilic ligands on Cu(II) promoted the formation of ligand transfer products such as **3.8a** and **3.8b** (entries 1 and 2). Fortunately, relatively less nucleophilic ligand TFA did not compete with methanol for nucleophilic substitution. Interestingly, $Cu(OTf)_2$ resulted in a slower reaction than $Cu(TFA)_2$•x$H_2O$ (entry 4). Thus, we proceeded to further optimization with $Cu(TFA)_2$•x$H_2O$.

**Table 3.1.** Evaluation of Cu(II) salts for benzylic C–H methoxylation[a]



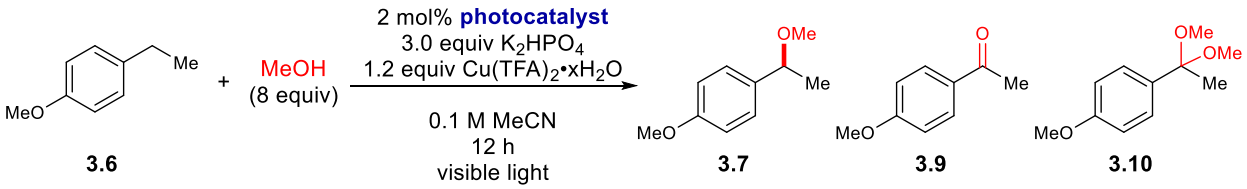

**3.6** **3.7** **3.8a L = Br** **3.8b L= OAc**

| Entry | Cu(II) salts | 3.6 (%) | 3.7 (%) | 3.8 (%) |
|---|---|---|---|---|
| 1 | $CuBr_2$ | 60 | 0 | **3.8a** = 28 |
| 2 | $Cu(OAc)_2•xH_2O$ | 55 | 11 | **3.8b** = 18 |
| 3 | $Cu(TFA)_2•xH_2O$ | 31 | 49 | - |
| 4 | $Cu(OTf)_2$ | 79 | 9 | - |

a) Yields determined by $^1$H NMR analysis using phenanthrene as a calibrated internal standard.

Next, a wide range of photocatalysts were evaluated, and it was found that [Ir(dF($CF_3$)ppy)$_2$(5.5'-d$CF_3$bpy)]$PF_6$ was the most effective and afforded the desired product (**3.7**) in 72% yield along with 9% of ketone **3.9** and 4% dimethoxylated product (**3.10**) (Table 3.1, entry 3). As expected, photocatalysts with more negative reduction potentials resulted in slower reactions (entries 1 and 2). On the other hand, strongly oxidizing photocatalysts such as [Ir(2,4-d$CF_3$($CF_3$)ppy)$_2$(5.5'-d$CF_3$bpy)]$PF_6$ provided ketone **3.9** as the major product along with **3.7** as the minor product after 12 h of irradiation (entry 4). As the photocatalyst could easily oxidize both the starting material and product, these data may suggest that selecting an appropriate photocatalyst is critical to minimize overoxidation.

**Table 3.2.** Evaluation of photocatalysts for benzylic C–H methoxylation

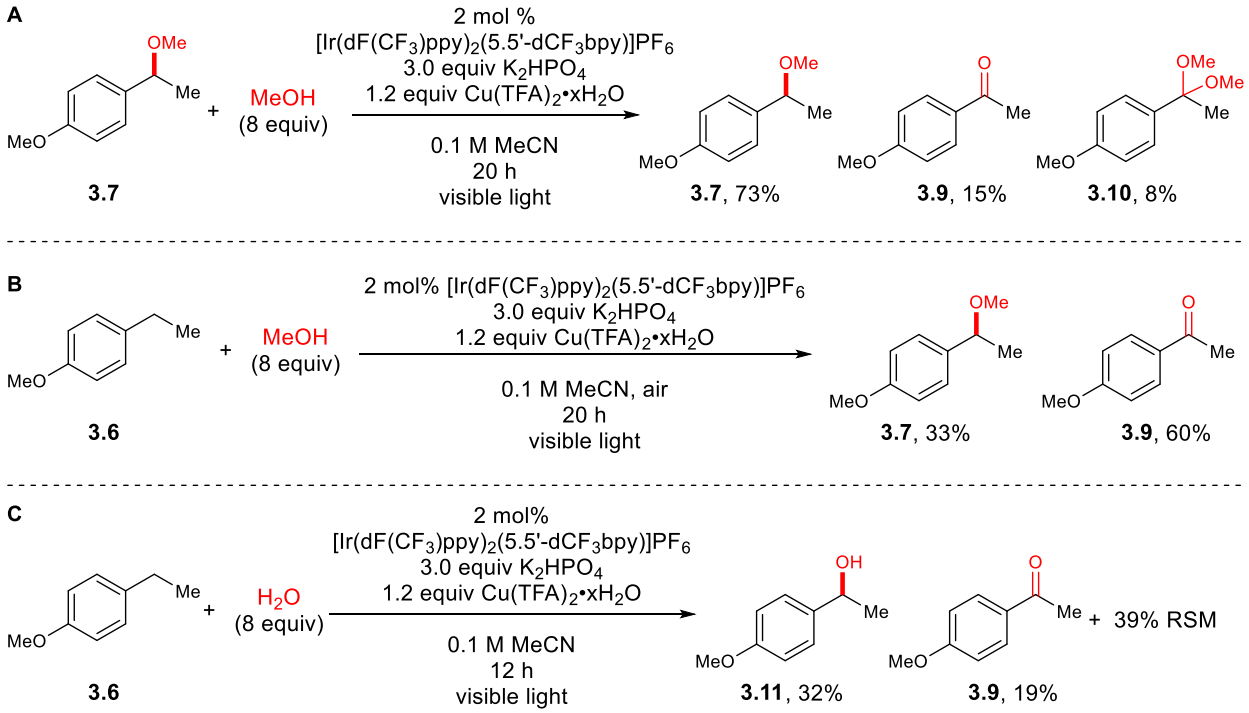



**3.6** **3.7** **3.9** **3.10**

| Entry | photocatalyst (oxidation potential) | 3.6 (%) | 3.7 (%) | 3.9 (%) | 3.10 (%) |
|---|---|---|---|---|---|
| 1 | [Ir(dF($CF_3$)ppy)$_2$(dtbbpy)]$PF_6$ **1.21 V** | 58 | 29 | 0 | 0 |
| 2 | [Ir(dF($CF_3$)ppy)$_2$(bpy)]$PF_6$ **1.32 V** | 49 | 44 | 2 | 0 |
| 3 | [Ir(dF($CF_3$)ppy)$_2$(5.5'-d$CF_3$bpy)]$PF_6$ **1.62 V** | 0 | 72 | 9 | 4 |
| 4 | [Ir(2,4-d$CF_3$($CF_3$)ppy)$_2$(5.5'-d$CF_3$bpy)]$PF_6$ **1.85 V** | 0 | 35 | 60 | 0 |

a) Yields determined by $^1$H NMR analysis using phenanthrene as a calibrated internal standard.

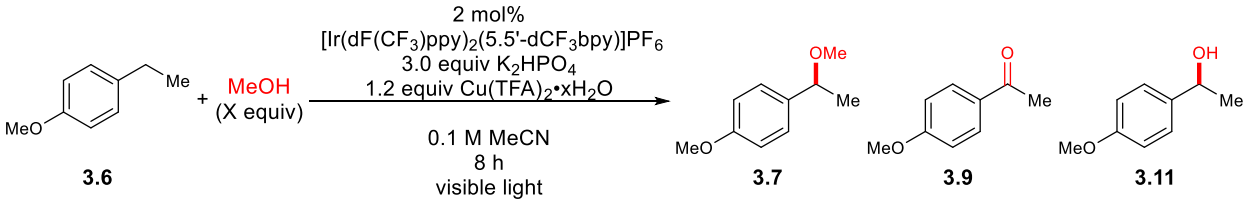
To better understand the origin of side product **3.9**, several experiments were performed. First, upon resubjection of **3.7** to reaction conditions, **3.9** was formed in 15% yield along with 8% dimethoxylated product **3.10** after 20 h of irradiation (Scheme 3.2.A). Second, we wondered if the formation of **3.9** could arise *via* trapping the intermediate benzylic radical with molecular oxygen. To test this possibility, the photoreaction was conducted open to the air; indeed, ketone **3.9** was generated in 60% yield (Scheme 3.2.B). Finally, we wondered if water from $Cu(TFA)_2 \bullet xH_2O$ could participate as a nucleophile to form the corresponding benzyl alcohol, which is known to undergo facile decomposition to form **3.9**.[39] Interestingly, when the reaction was conducted with water as a nucleophile instead of MeOH, the reaction was significantly slower than optimized conditions. Nevertheless, benzyl alcohol **3.11** and ketone **3.9** were formed in 32% and 19% yields, respectively (Scheme 3.2.C). Although control reactions suggested that all three pathways could be responsible for generation of **3.9**, the major pathway was likely the overoxidation of the desired product **3.7** as the reaction was vigorously degassed and **3.11** was not observed.




**Scheme 3.2.** Investigation of the origin of ketone **3.9**

Having identified the optimal terminal oxidant and photocatalyst, we next focused on optimizing reaction conditions using 2.0 equivalents of MeOH instead of 8.0. When the previously optimized conditions were conducted with 2.0 equivalents of MeOH, the reaction was slower and a significant amount of **3.11** was formed. We attributed this to the presence of water in the hydrate form of $Cu(TFA)_2$ salts (Table 3.3, entry 2). To address this problem, we thus prepared the anhydrous acetonitrile complex $Cu(TFA)_2$•MeCN, the use of which inhibited formation of **3.11**. Interestingly, it increased the rate of reaction as well (entry 3).

**Table 3.3.** Survey of MeOH equivalencies[a]



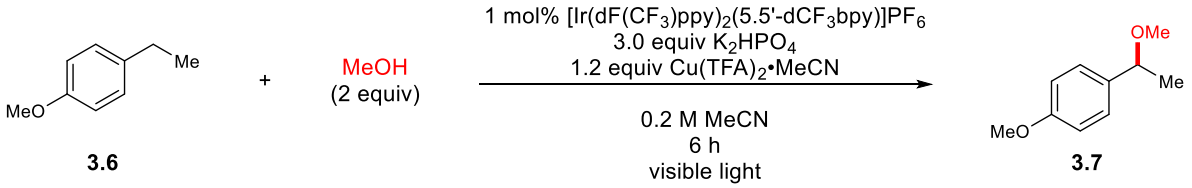

**3.6** **3.7** **3.9** **3.11**

| Entry | MeOH (X equiv) | 3.6 (%) | 3.7 (%) | 3.9 (%) | 3.11 (%) |
|---|---|---|---|---|---|
| 1 | 8.0 | 3 | 87 | 9 | 0 |
| 2 | 2.0 | 24 | 59 | 7 | 11 |
| 3[b] | 2.0 | 6 | 75 | 4 | 0 |

a) Yields determined by $^1$H NMR analysis using phenanthrene as a calibrated internal standard. b) $Cu(TFA)_2$•MeCN was used instead of $Cu(TFA)_2$•$H_2O$.

After further optimization, the optimized conditions were as follows (Table 3.4, Entry 1): 1.0 equivalent 4-ethylanisole, 2.0 equivalents methanol, 3.0 equivalents of $K_2HPO_4$, 1.2 equivalents $Cu(TFA)_2$•MeCN, and 1.0 mol % $[Ir(dF(CF_3)ppy)_2(5.5'\text{-}dCF_3bpy)]PF_6$ in degassed MeCN (0.2 M) under a nitrogen atmosphere and irradiation with 40 W blue LEDs. To demonstrate that Cu(II) salts were unique in their ability to promote this alkoxylation reaction, a wide range of other common terminal oxidants were evaluated, and none produced significant yields of **3.7** (entry 2). Finally, control experiments validated the photocatalytic nature of this reaction and the necessity of the Cu(II) oxidant; no product was observed in the absence of photocatalyst, Cu(II) terminal oxidant, or light (entries 3–5).

**Table 3.4.** Survey of other common oxidants[a]




| Entry | varaiation from standard condtions | **3.7 (%)** |
|---|---|---|
| 1 | none | 73 |
| 2 | Air, Phi(OAc)$_2$, TEMPO, $MnO_2$, $FeCl_3$, *t*-BuOOH, or benzoquinone instead of Cu(TFA)$_2$ | <10 |
| 3 | no photocatalyst | 0 |
| 4 | no Cu(TFA)$_2$•MeCN | 0 |
| 5 | no light | 0 |

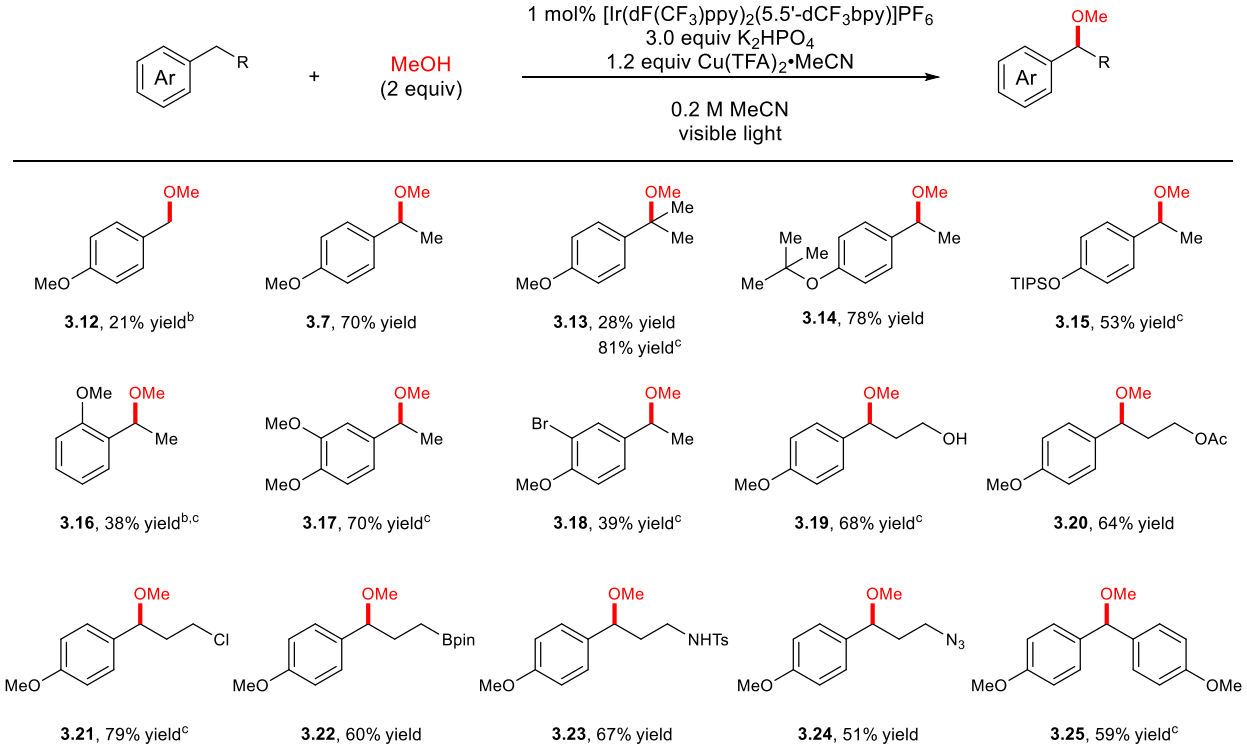
a) Yields determined by $^1$H NMR analysis using phenanthrene as a calibrated internal standard.

## 3.3 Result and Discussion

With the optimized conditions in hand, we next examined the substrate scope of this benzylic C–H methoxylation. Surprisingly, primary, secondary, and tertiary benzylic positions provided significantly different outcomes. Substrates with primary benzylic sites provided lower yield owing to the rapid formation of the overoxidation aldehyde product (Table 3.5, **3.12**). Substrates containing tertiary benzylic sites, on the other hand, required significantly longer reaction times; ether **3.13** was obtained in only 28% yield after 30 h. We hypothesized that the reaction efficiency could be improved by increasing the photon flux. Indeed, the reaction efficiency was improved by diluting the reaction mixture. However, a significant amount of the trifluoroacetoxylation product (**3.8c**) was observed. Fortunately, this problem was addressed by simply using 8 equivalents of methanol, which resulted in 81% yield in 13 h. Replacing the methoxy substituent on the arene with other electron-donating groups was also viable and produced the corresponding methoxylated adducts in moderate to good yields (**3.14** and **3.15**). *ortho*-Methoxy substituted arenes were also methoxylated in moderate yield (**3.16**). A variety of common functional groups were well tolerated. These included azides, boronic esters, esters, free alcohols, primary alkyl halides, protected alcohols, protected amines, and pyridines (**3.19**–**3.24**). A diphenylmethane derivative was also functionalized in good yield (**3.25**). All substrates that required long reaction times or that gave poor yields

using 2 equivalents MeOH gave significantly better results when 8 equivalents MeOH was used. These scope studies suggested that the presence of alkoxy substituents on the arene that could stabilize the putative quinone methide intermediate was strictly required, but a variety of electron-donating groups could be used for this purpose. Additionally, substituents on the arenes did not hamper the desired reactivity (**3.17** and **3.18**).

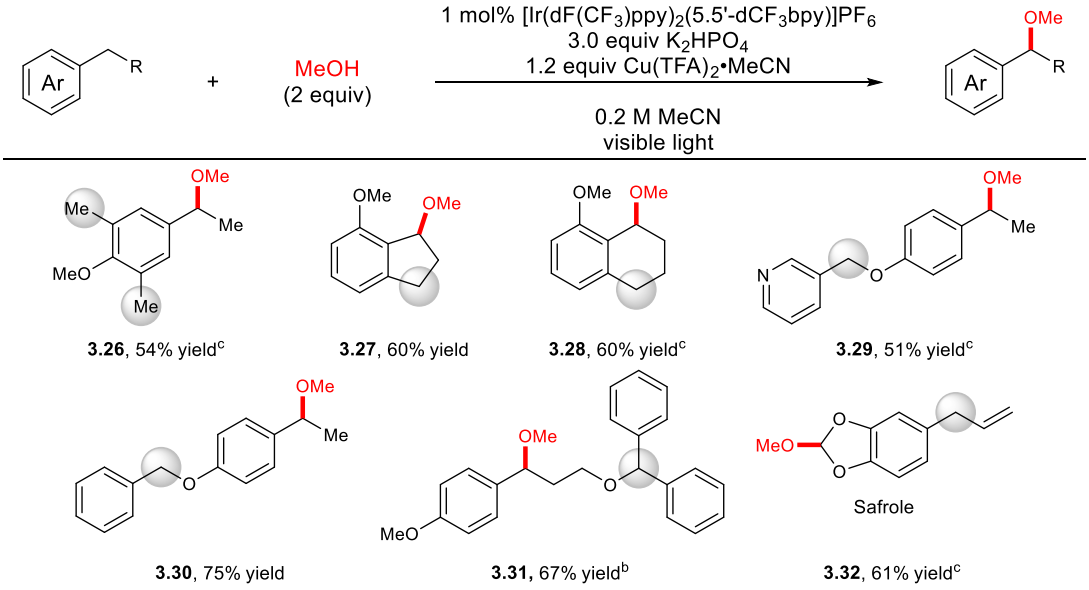
**Table 3.5.** Arene Scope for benzylic C–H methoxylation[a]




a) Yields of isolated products are the averaged results of two reproducible experiments. b) Yields determined by 1H NMR analysis using phenanthrene as a calibrated internal standard. c) Reaction conducted at 0.1 M using 8.0 equivalent methanol.

We next evaluated the site selectivity of this transformation in arene substrates containing multiple benzylic C–H bonds. In general, this reaction displayed a remarkable degree of site selectivity consistent with the predicted stability of the quinone methide intermediate (**3.26**–**3.28**). Thus, functionalization of *p*-alkoxy-activated benzylic positions is highly selective even in the presence of extremely weak benzylic C–H bonds (**3.29**–**3.31**). These results contrasted with previous methods where stereoelectronically activated sites were preferably oxidized. Interestingly, the natural product safrole was functionalized at the methylenedioxy site over the benzylic position (**3.32**).

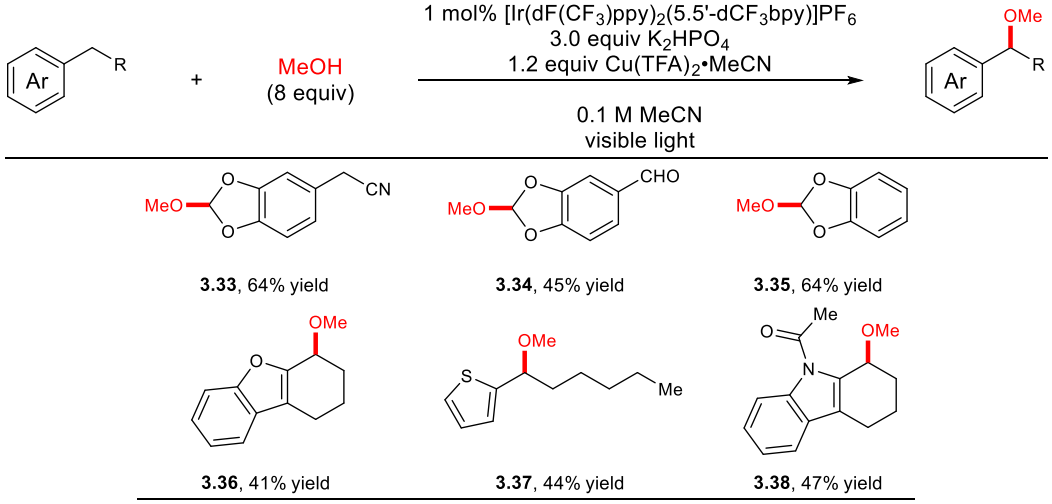
**Table 3.6.** Exploring site selectivity for benzylic C–H methoxylation[a]




a) Yields of isolated products are the averaged results of two reproducible experiments. b) Yields determined by $^1$H NMR analysis using phenanthrene as a calibrated internal standard. c) Reaction conducted at 0.1 M using 8.0 equivalent methanol.

Intrigued by this result, we further explored benzodioxazole substrates to gain insights into the generality of this transformation. A wide variety of benzodioxazoles were amenable towards the functionalization (**3.33**–**3.35**). Finally, benzylic positions of electron-rich heterocycles that are also readily oxidized by the photocatalyst could also be functionalized using this protocol (**3.36**–**3.38**).

**Table 3.7.** Arene Scope for benzylic C–H methoxylation[a]




a) Yields of isolated products are the averaged results of two reproducible experiments.

Several electron-rich arene substrates evaluated that did not undergo the desired methoxylation reaction. For instance, the easily oxidizable **3.39** did not undergo C–H alkoxylation. We hypothesized that this limitation was the result of inefficient oxidation by $Cu(TFA)_2$•MeCN. To test this hypothesis, **3.40** and **3.41**, which could generate radicals prone to oxidation, were evaluated. These substrates did not react at all, however, suggesting that these substrates did not form the corresponding radicals, likely due to the kinetically incompetent deprotonation step. To support this hypothesis, decarboxylative methoxylation was conducted in the presence of $Cu(TFA)_2$•MeCN; indeed, the desired product **3.43** formed in 21% yield (Scheme **3.3**). This suggested that radical oxidation by Cu(II) was kinetically and thermodynamically feasible.

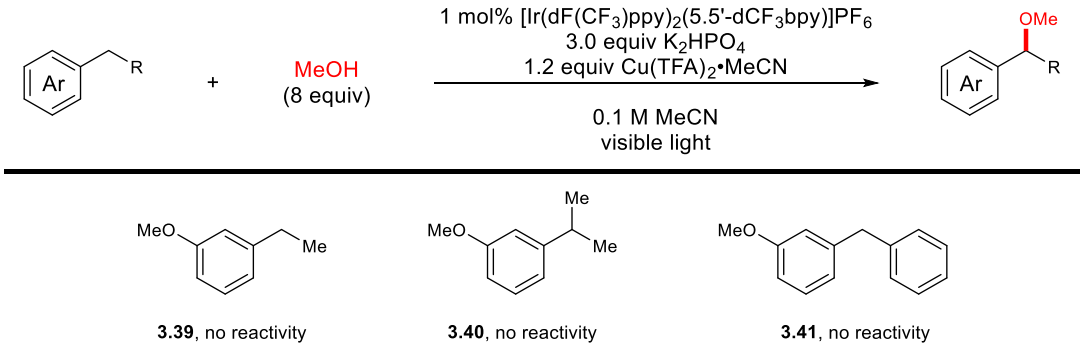
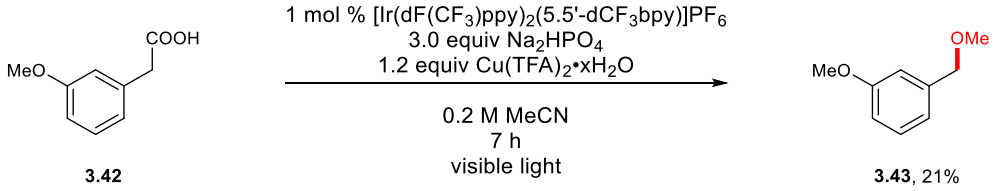


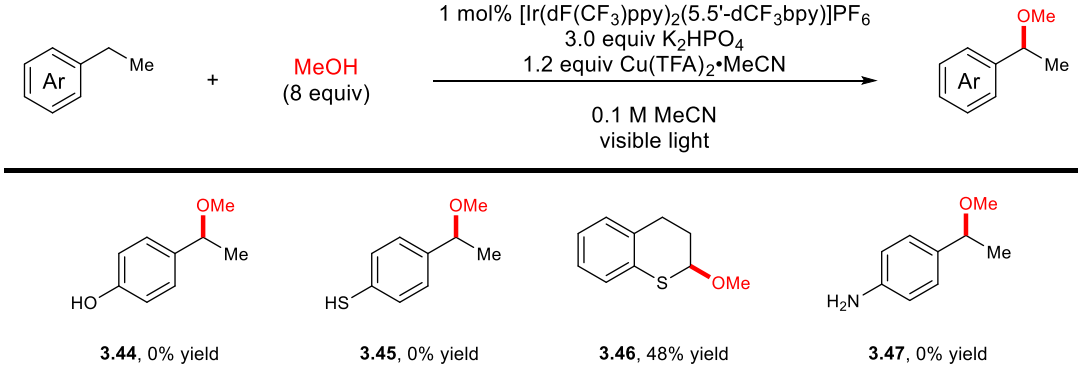

**Table 3.8.** Probing the reactivity of the *m*-methoxy arene substrates




**Scheme 3.3.** Probing the feasibility of radical oxidation by $Cu(TFA)_2$

Other electron-rich arene substrates were also examined in our studies. Phenol and thiol phenol, which contain acidic protons, did not undergo productive C–H alkoxylation (Table 3.9, **3.44** and **3.45**). Instead, the reactions turned black as soon as arene substrate was added. In contrast, thiochromane underwent C–H alkoxylation, but at the position functionalization α to the sulfur atom (**3.46**), which was consistent with

previously reported radical cation chemistry.[40] Finally, aniline was chosen as a potential candidate, but the desired **3.47** was not generated under reaction conditions.

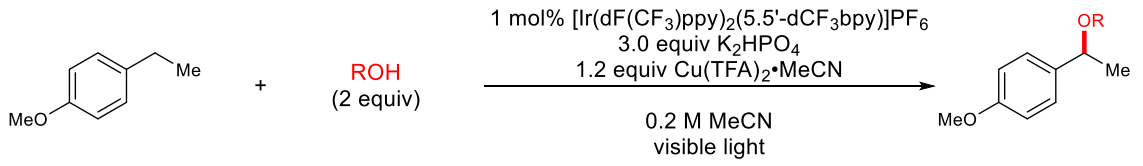


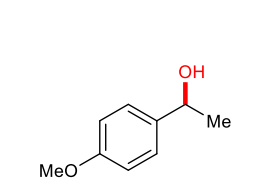

**3.44**, 0% yield **3.45**, 0% yield **3.46**, 48% yield **3.47**, 0% yield

**Table 3.9.** Probing the reactivity of other electron-rich arene substrates

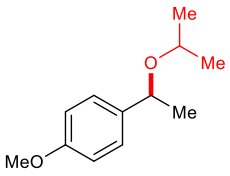
Next, we examined the scope of this reaction with regard to the nucleophilic partner. Water, unfortunately, did not deliver the desired hydroxylated product, and instead afforded ketone as the major product instead (Table 3.10, **3.11**). Alcohols of increased steric bulk reacted poorly presumably due to competitive reaction pathways such as ligand transfer and $E_1$ reaction, although the yields of these reactions can be increased by using 8 equiv of alcohol (**3.48**–**3.50**). A variety of functional groups including aldehydes, alkenes, alkynes, alcohols, primary alkyl halides, silyl groups, nitriles, sulfones, ethers, and protected amines were all tolerated and delivered the desired product in 30% to 60% yields (**3.51**–**3.62**). Because increasing steric bulk decreased the rate of the nucleophilic substitution step, an unsymmetrical 1,3-diol gave high levels of regioselectivity, reacting exclusively through the less hindered primary alcohol (**3.62**).

**Table 3.10.** Alcohol scope of benzylic C–H alkoxylation[a]

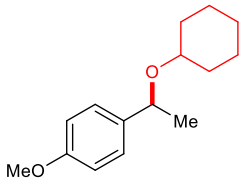


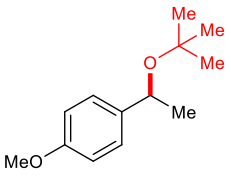

**3.11**, 23% yield[b]



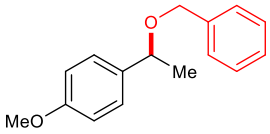

**3.48**, 55% yield
68% yield[c]



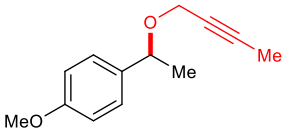

**3.49**, 52% yield
66% yield[c]



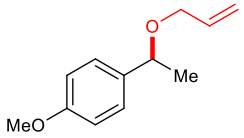

**3.50**, 23% yield
45% yield[c]



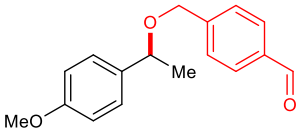

**3.51**, 56% yield



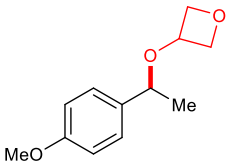

**3.52**, 53% yield



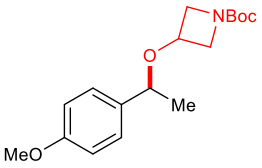

**3.53**, 58% yield



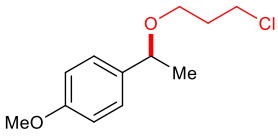

**3.54**, 43% yield



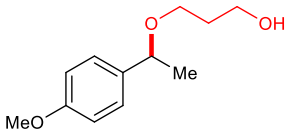

**3.55**, 30% yield



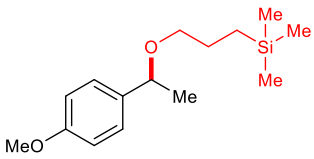

**3.56**, 35% yield



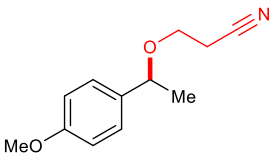

**3.57**, 52% yield



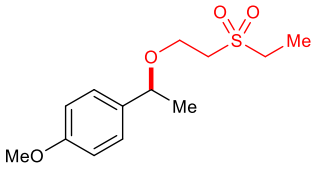

**3.58**, 47% yield



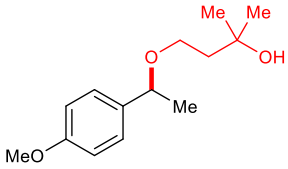

**3.59**, 48% yield




**3.60**, 49% yield




**3.61**, 43% yield



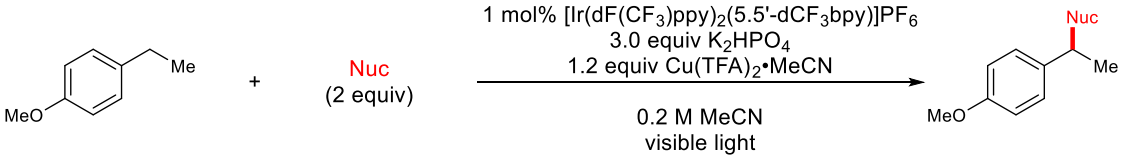

**3.62**, 62% yield

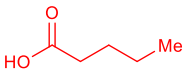
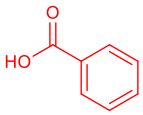
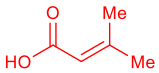
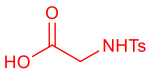
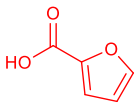
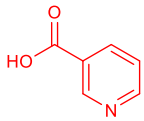
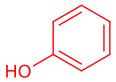
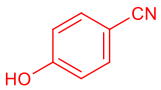
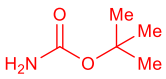
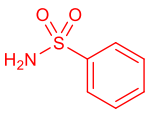
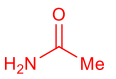
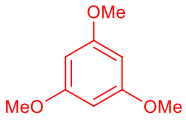
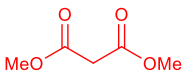
a) Yields of isolated products are the averaged results of two reproducible experiments. b) Yields determined by 1H NMR analysis using phenanthrene as a calibrated internal standard. c) Reaction conducted using 8.0 equivalent nucleophiles.

Following the promising results with alcohol nucleophiles, other classes nucleophiles were also examined (Table 3.11). Carboxylic acids reacted smoothly under the standard reaction conditions, delivering the functionalized products in good yields, including both simple aliphatic and more functionalized acids (**3.63**–**3.67**). Unfortunately, carboxylic acids with strongly coordinating functional groups (**3.68**) were not suitable reaction partners. Phenols (**3.69** and **3.70**) did not afford the functionalized

products. Next, a wide range of amine nucleophiles, including carbamates, sulfonamides, amides, and azides, were examined (**3.71**–**3.74**). Among them, only *N*-Boc carbamates (**3.71**) provided the functionalized product in modest yield, suggesting that alternate conditions might be required for the general introduction of C–N bonds using this photocatalytic strategy. Carbon-centered nucleophiles were also explored but none of them gave promising results. Nucleophiles that were easier to oxidize than the anisole unit, such as allyl silanes and trimethoxy benzene (**3.75** and **3.76**), were decomposed under the reaction conditions. Notably, *in situ* generated anionic nucleophiles (**3.77** and **3.78**) coordinated the Cu(II) salts either to make "ate"-complexes or effect ligand exchange without any observable productive reactivity.

**Table 3.11.** Other nucleophiles screen[a]

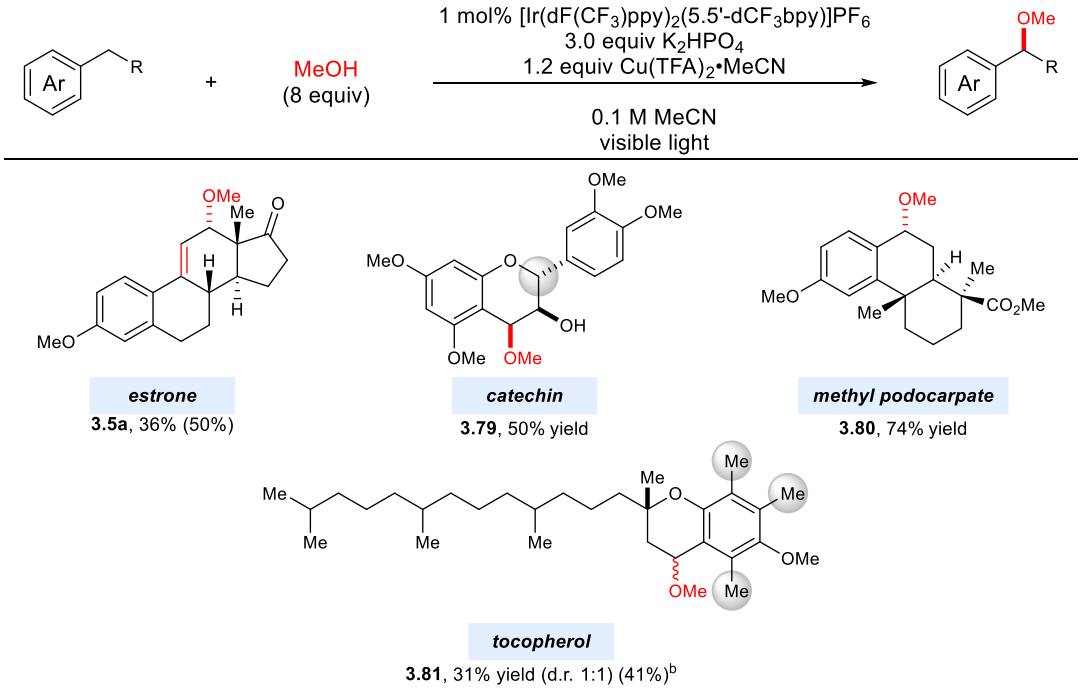



| | | | |
|---|---|---|---|
|  |  |  |  |
| **3.63**, 51% yield | **3.64**, 54% yield | **3.65**, 58% yield | **3.66**, 50% yield |
|  |  |  |  |
| **3.67**, 56% yield | **3.68**, 0% yield[b] | **3.69**, 0% yield[b] | **3.70**, 0% yield[b] |
|  |  |  | TMS–$N_3$ |
| **3.71**, 38% yield[b] | **3.72**, 0% yield[b] | **3.73**, 0% yield[b] | **3.74**, 0% yield[b] |
|  |  |  | TMS–CN |
| **3.75**, 0% yield[b] | **3.76**, 0% yield[b] | **3.77**, 0% yield[b] | **3.78**, 0% yield[b] |

a) Yields of isolated products are the averaged results of two reproducible experiments. b) Reaction conducted using 8.0 equivalent nucleophiles.

The combination of high site selectivity and broad functional group compatibility suggested to us that this method might be applicable to the late-stage diversification of complex bioactive organic compounds. Since Ponsold demonstrated that estrone **3.1** undergoes site-selective C–H alkoxylation under electrochemical method, we were interested in mimicking this reactivity with our strategy. Interestingly, **3.1** participated in oxidation-deprotonation-oxidation sequence to form the corresponding carbocation, which underwent elimination instead of alcohol substitution. Subsequent allylic C–H alkoxylation furnished the unexpected product **3.5a**. Other complicated molecules, however, exhibited the expected reactivity. Table 3.12 outlines the functionalization of a range of commercially available natural product scaffolds, all of which were selectively functionalized at the benzylic position of the most electron rich aromatic ring. No diastereoselectivity was observed in substrates without significant stereochemical bias (**3.81**), but six-membered rings with a strong preference for a single chair conformation underwent highly selective functionalization of the axial C–H bond (**3.79** and **3.80**), suggesting that the deprotonation step required the overlap of the half vacant p orbital with the scissile σ bond.

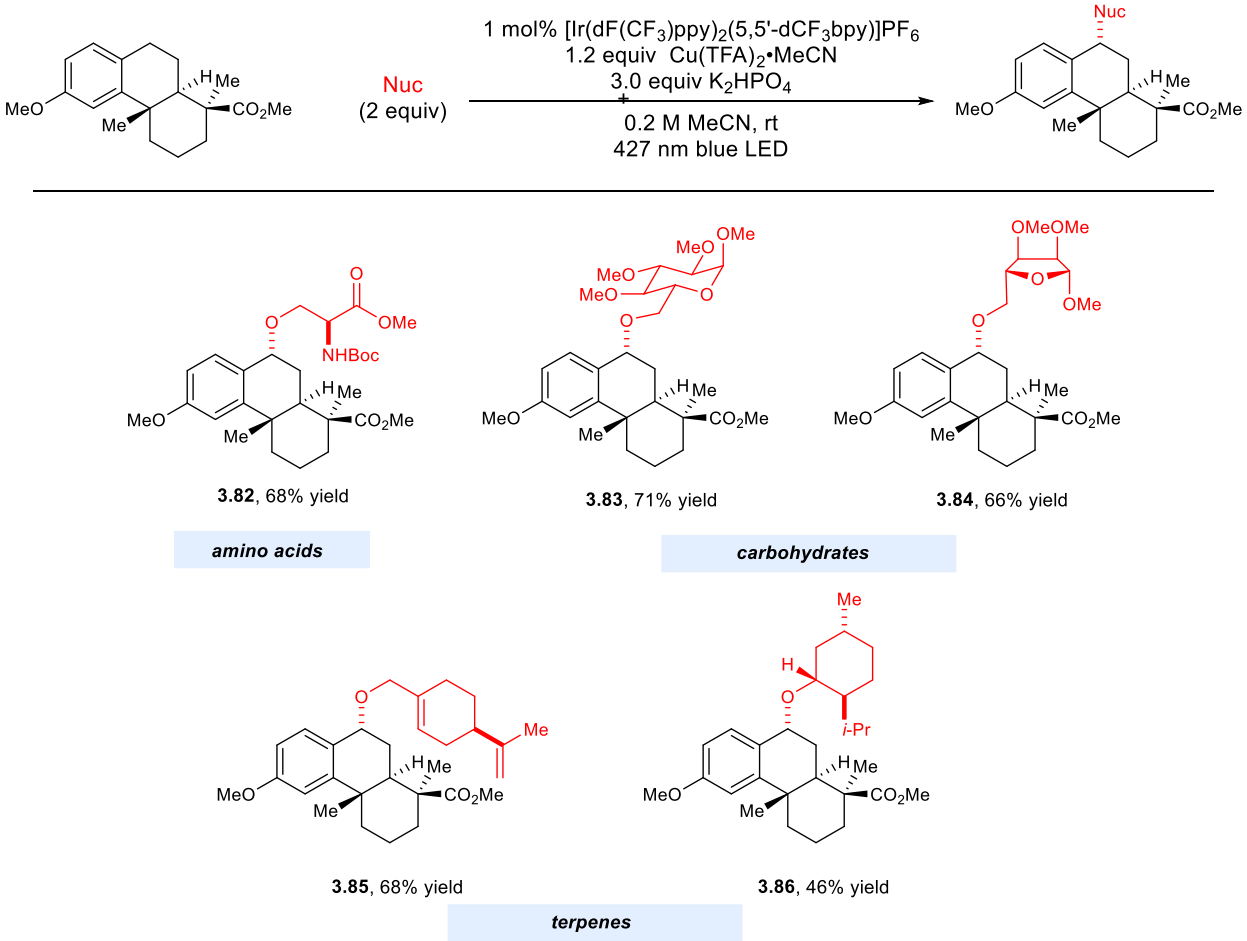
**Table 3.12.** Late stage methoxylation *via* oxidative photoredox catalysis




a) Yields of isolated products are the averaged results of two reproducible experiments. b) Reaction conducted at 0.05 M MeCN:$CH_2Cl_2$ using 8.0 equivalent methanol. RSM yield is provided in parentheses.

Given the observation that synthetically useful yields could be obtained using only two equivalents of the alcohol nucleophile, we envisioned that this method might serve to couple two high-value reaction partners. Thus, the ability to conjugate *O*-methylpodocarpate with a variety of structurally complex nucleophilic partners was evaluated. The alcohol moiety of a protected serine was readily installed in good yield (**3.82**) without competitive attack of the Boc carbamate. The reaction also incorporated protected hexose and pentose moieties (**3.83** and **3.84**) as well as primary and secondary terpene alcohols (**3.85** and **3.86**) in synthetically useful yields.

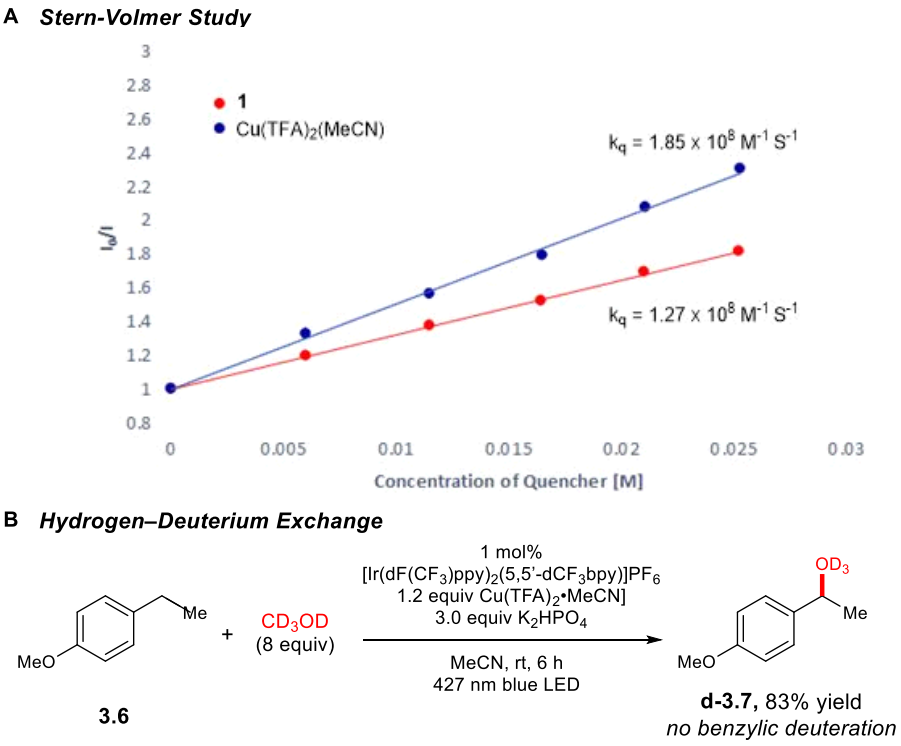
**Table 3.13.** Late stage functionalization *via* oxidative photoredox catalysis[a]




a) Yields of isolated products are the averaged results of two reproducible experiments.

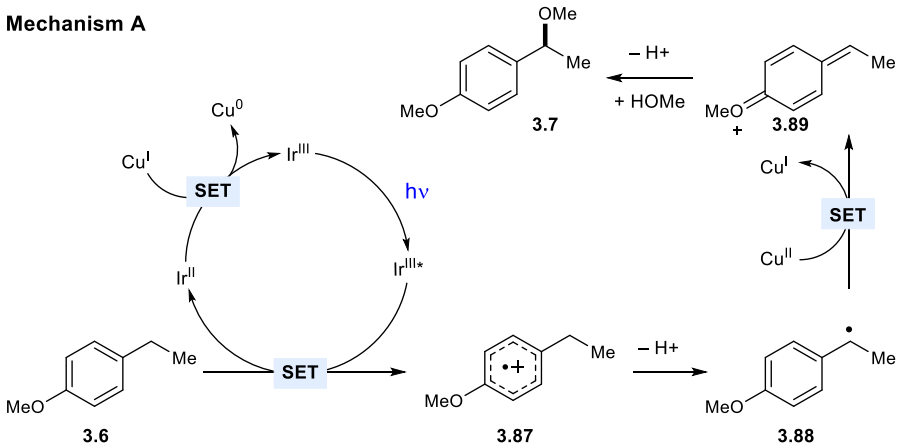
### 3.4 Mechanistic Studies

In addition to exploring the scope of this transformation, we also studied the mechanism. We first examined the nature of the initial photoinduced electron-transfer step. Cyclic voltammetry studies suggested that the excited-state reduction and oxidation potentials of the optimal photocatalyst (+1.68 V and –0.43 V vs SCE, respectively)[41] were sufficient to either oxidize **3.6** ($E_{p/2}$ = +1.52 V) or reduce $Cu(TFA)_2$•MeCN ($E_{p/2}$ = +0.38 V). To identify the kinetically competent pathway for the initial oxidation step, Stern-Volmer studies were conducted. Stern-Volmer analysis indicated that **3.6** and $Cu(TFA)_2$•MeCN could quench the photocatalysts excited state at the rate of 1.27 x $10^8$ $M^{-1}$ $s^{-1}$ and 1.85 x $10^8$ $M^{-1}$ $s^{-1}$, respectively (Scheme **3.4.A**). These experiments suggested that the arene radical cation could be generated *via* either the excited Ir*(III) photocatalyst or an Ir(IV) complex ($E_{1/2}$ = +1.94 V)[41] generated *via* oxidative quenching by $Cu(TFA)_2$•MeCN. We also examined the photocatalytic reaction of **3.6** with $CD_3OD$, which resulted in the formation of **d-3.7** in 83% yield with no incorporation of deuterium at the benzylic position (Scheme **3.4.B**). This experiment suggested that the deprotonation step was irreversible under the optimized conditions. Then, as we expected from Kochi's studies, the oxidation of electron-rich organoriadicals by Cu(II) should occur at diffusion-controlled rates.[35–37] Based on these studies and literature precendents, we proposed that both mechanisms shown in Scheme **3.5** and **3.6** could be operative.



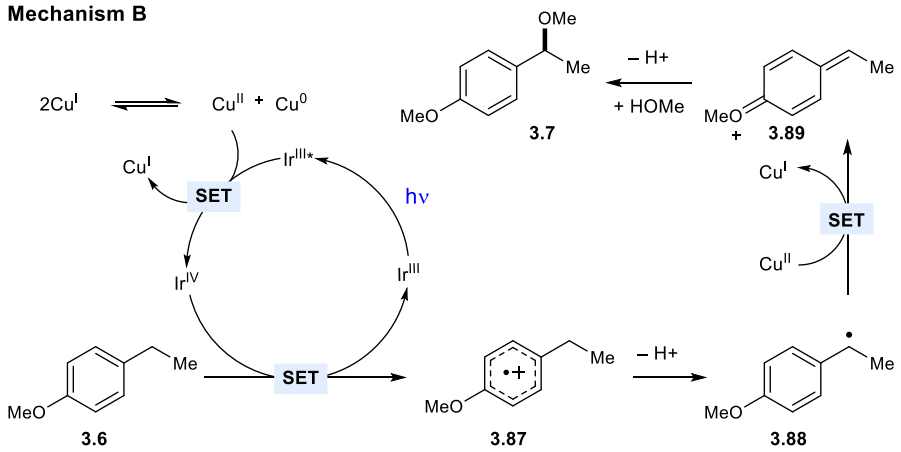

**Scheme 3.4.** Development of mechanistic hypothesis

In the first mechanistic scenario, photoexcitation of the Ir(III) catalyst that affords a long-lived triplet excited state that can oxidize **3.6** to generate arene radical cation **3.87**. Subsequent benzylic deprotonation and rapid oxidation of **3.87** by Cu(II) salts give rise to quinone methide (**3.89**). This highly electrophilic species undergoes nucleophilic attack by the alcohol coupling partner to afford the observed benzylic ether product **3.7**. It is important to note that the reaction proceeds to completion with only 1.2 equivalents of Cu(II), indicating that both oxidizing equivalents of Cu(II) are consumed in this reaction. This implies that Cu(I) might be responsible for turning over the reduced photocatalyst to the ground state to close the catalytic cycle.




**Scheme 3.5.** Proposed mechanism initiated by arene oxidation

Another possibility is that the excited-state of the photocatalyst is oxidatively quenched by Cu(II) to afford a strongly oxidizing Ir(IV) complex. Subsequent oxidation of the arene affords the arene radical cation **3.87**. In this scenario, Cu(I), the byproduct of either oxidation step, can undergo disproportionation to Cu(II) and Cu(0).




**Scheme 3.6.** Proposed mechanism initiated by copper reduction

### 3.5 Conclusions and Outlook

Inspired by the previously developed electrochemical site-selective benzylic C–H alkoxylation, we have developed a new photocatalytic strategy to introduce diverse alkoxide functionalities into complex organic molecules by direct functionalization of benzylic C–H bonds. The site selectivity and broad functional group compatibility of this method renders it applicable to late-stage functionalizations of complex bioactive compounds. More importantly, the site selectivity of this method is complementary to

conventional protocols since it is driven by the electrochemical potentials of arene substrates instead of the relative BDEs of benzylic C–H bonds. Moreover, the reaction provides synthetically useful yields using only two equivalents of alcohols in most cases. This feature distinguishes this method from the electrochemical protocol and enables the formation of new benzylic ether compounds *via* the coupling of two structurally complex reaction partners. From a broader perspective, diverting organoradical intermediates, which are readily generated by photoredox activation, towards cationic reactivity *via* in situ oxidation by Cu(II) provides new prospects for photocatalytic oxidative functionalization reactions with broad utility in synthetic and medicinal chemistry.

## 3.6 Contributions

Regarding respective contributions, the writer discovered and optimized the benzylic C–H alkoxylation. It was at this point that my colleague Kimberly DeGlopper joined the project and helped exploring the substrate scope.

## 3.7 Experimental

### 3.7.1 General Experimental Information

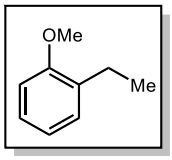
All reactions were performed under an $N_2$ atmosphere unless otherwise stated. All glassware was dried in an oven at 120 °C for at least 2 h prior to use and allowed to cool in a desiccator cabinet. MeCN, THF, $Et_2O$, DMF, toluene, and $CH_2Cl_2$ were purified by elution through alumina as described by Grubbs.[42] $Cu(TFA)_2(H_2O)_n$ was used as purchased from Alfa. All other chemicals were purchased from commercial suppliers and used as received. Flash column chromatography was performed with normal phase $SiO_2$ (Sigma-Aldrich or Macherey-Nagel, 60 Å pore size, 230-400 mesh, 40-63 µm particle size) according to the method of Still.[43] Reactions were monitored by thin-layer chromatography (Silicycle, 250 µm thickness), and visualization was accomplished with a 254 nm UV light or by staining with $KMnO_4$ solution (3.0 g of $KMnO_4$ and 20.0 g of $K_2CO_3$ in 5 mL of 5% aq. NaOH and 300 mL $H_2O$). $^1H$, $^{13}C\{^1H\}$, and $^{11}B\{^1H\}$ NMR data for all previously uncharacterized compounds were obtained using a Bruker AVANCE-400 or Bruker AVANCE-

500 spectrometer with DCH, Prodigy, or BBFO+ probes. 1H spectra were internally referenced to tetramethyl silane (0.00 ppm). $^{13}C\{^{1}H\}$ spectra were internally referenced to $CDCl_3$ (77.16 ppm). $^{1}H$ NMR spectra were tabulated as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet, br = broad), coupling constant(s), and number of protons. 13C NMR spectra were tabulated by observed peak. The spectrometers used for this work are supported by the NIH (S10 OD012245) and a generous gift from Paul J. and Margaret M. Bender. Mass spectrometry was performed with a Thermo Q ExactiveTM Plus. This instrument is supported by the NIH (S10 OD020022) and the University of Wisconsin. IR spectra were obtained using a Bruker Alpha Platinum FTIR spectrometer equipped with an attenuated total reflectance (ATR) sampling head. UV-Vis absorption spectra were acquired using a Varian Cary® 50 UV-visible spectrophotometer with a scan rate of 300 nm/min. UV-Vis emission spectra were acquired on an ISS PC1 spectrofluorimeter. Cyclic voltammograms were acquired using a Pine Research WaveNow potentiostat/galvanostat. Melting points were obtained using a Stanford Research Systems DigiMelt apparatus.

### 3.7.2 Synthesis of Arene Substrate

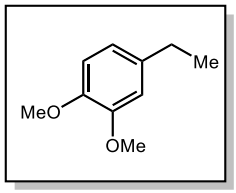
**General Procedure A: Synthesis of Arene Substrate by Reduction of Ketones**[44]

A 100-mL round-bottomed flask was charged with $PdCl_2$ (10 mol%) and the aromatic ketone (1 equiv). Under a nitrogen atmosphere, methanol (0.5 M with respect to substrate) was added, followed by PMHS (5 equiv, slow addition). The mixture was stirred at 40 ºC for 12–24 hours, monitoring for completion by TLC. After completion of the reaction, the product was dissolved in pentane and water was added. The mixture was extracted three times into an equal volume of pentane, and the combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure, and purified by column chromatography on silica gel to afford the pure product.



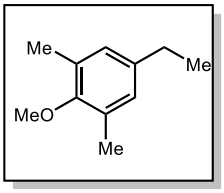

**1-Ethyl-2-methoxybenzene (3.16a)**:

Prepared according to the General Procedure A with 2'-methoxyacetophenone (1.99 g, 13.3 mmol). Following workup, the product was purified by flash column chromatography on silica gel (gradient 0% to 5% $Et_2O$/pentane) to give the title compound as a clear liquid (1.40 g, 10.3 mmol, 78%). Spectral data were consistent with those reported previously.[45]




**4-Ethyl-1,2-dimethoxybenzene (3.17a)**:

Prepared according to the General Procedure A with 3',4'-dimethoxyacetophenone (1.02 g, 5.68 mmol). Following workup, the product was purified by flash column chromatography on silica gel (gradient 0% to 10% $Et_2O$/pentane) to give the title compound as a clear liquid (828 mg, 4.98 mmol, 88%). Spectral data were consistent with those reported previously.[46]

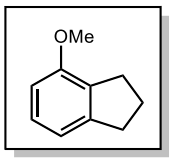



**5-Ethyl-2-methoxy-1,3-dimethylbenzene (3.26a)**:

Prepared according to the General Procedure A with 3',5'-dimethyl-4'-methoxyacetophenone (1.02 g, 5.68 mmol). Following workup, the product was purified by flash column chromatography on silica gel (gradient 0% to 5% $Et_2O$/pentane) to give the title compound as a clear liquid (858 mg, 5.23 mmol, 92%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.84 (s, 2H), 3.70 (s, 3H), 2.54 (q, *J* = 7.62 Hz, 2H), 2.27 (s, 6H), 1.20 (t, *J* = 7.60 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.25, 139.91, 130.87, 128.53, 60.11, 28.54, 16.46, 16.11;

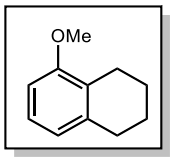
**IR** (thin film): 2961, 2930, 2868, 1483, 1455, 1222, 1140, 1016, 866 ; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{11}H_{16}O]$ requires *m/z* 165.1274, found *m/z* 165.1272.




**4-Methoxy-2,3-dihydro-1H-indene (3.27a)**:

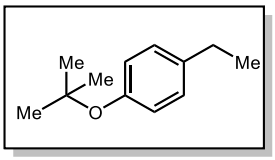
Prepared according to the General Synthesis Procedure with 7-methoxy-1-indanone (921 mg, 5.68 mmol). Following workup, the product was purified by flash column chromatography on silica gel (gradient 0% to 5% $Et_2O$/pentane) to give the title compound as a clear liquid (741 mg, 5.00 mmol, 88%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.13 (d, *J* = 7.76 Hz, 1H), 6.86 (d, *J* = 7.28 Hz, 1H), 6.67 (d, *J* = 8.05 Hz, 1H), 3.84 (s, 3H), 2.92 (t, *J* = 7.51 Hz, 2H), 2.87 (t, *J* = 7.42 Hz, 2H), 2.07 (q, *J* = 7.49 Hz, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 156.20, 146.38, 131.80, 127.61, 117.00, 107.78, 55.31, 33.37, 29.50, 25.07; **IR** (thin film): ν 2944, 2841, 1588, 1475, 1444, 1258, 1070, 764 ; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{10}H_{12}O]$ requires *m/z* 149.0961, found *m/z* 149.0959.



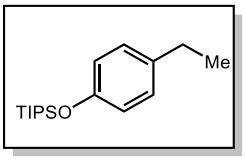

**5-Methoxy-1,2,3,4-tetrahydronaphthalene (3.28a)**:

Prepared according to the General Synthesis Procedure with 5-methoxy-1-tetralone (1.00 g, 5.68 mmol). Following workup, the product was purified by flash column chromatography on silica gel (gradient 0% to 5% $Et_2O$/pentane) to give the title compound as a clear liquid (792 mg, 4.88 mmol, 86%). Spectral data were consistent with those reported previously.[47]




**1-(tert-Butoxy)-4-ethylbenzene (3.14a)**:

A 250-mL round-bottomed flask was charged with a magnetic stir bar, 10% Pd/C (2 g), and MeOH (100 mL). The stirred solution was fitted with a hydrogen balloon and purged for 20 min. 4-*tert*-Butoxystyrene (10 mmol, 1.88 mL) was then added, and the reaction was stirred at room temperature for 12 h, at which point it was passed through a Celite plug ($Et_2O$). The solvent was removed under reduced pressure, and the resulting residue was purified by flash column chromatography on silica gel (pentane) to afford the title compound as a clear liquid (1.50 g, 8.4 mmol, 84%). Spectral data were consistent with those reported previously.[48]

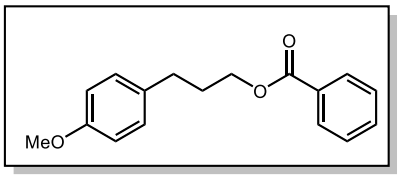



**(4-Ethylphenoxy)triisopropylsilane (3.15a)**:

A mixture of 4-ethylphenol (1.2 g, 10 mmol, 1 equiv) and imidazole (1.4 g, 20 mmol, 2 equiv) in dimethylformamide (DMF, 8.3 mL) was added dropwise into a solution of triisopropylsilyl chloride (1.9 g, 10 mmol, 1 equiv) in DMF (1.2 mL). After stirring for 12 h at room temperature, an aqueous solution of sodium bicarbonate was added to the reaction mixture, and the evolving two-phased system was separated. The aqueous phase was extracted with pentane three times, and the combined organic solutions were washed with water three times, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (pentane) to afford the product as a clear liquid (9.0 mmol, 2.5 g, 90%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.02 (d, *J* = 8.41 Hz, 2H), 6.79 (d, *J* = 8.46 Hz, 2H), 2.57 (q, *J* = 7.61 Hz, 2H), 1.21-1.28 (m, 3H), 1.20 (t, *J* = 7.60 Hz, 3H), 1.09-1.10 (m, 18H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 153.85, 137.31, 129.00, 120.19, 28.43, 26.11, 18.60, 16.17, -4.03; **IR** (thin film): ν 2962, 2893, 1608, 1507,

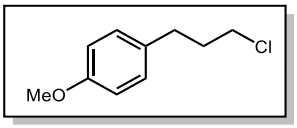
1463, 1260, 913, 882, 832, 684, 668; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{17}H_{30}OSi]$ requires *m/z* 279.2139, found *m/z* 279.2139.




**3-(4-Methoxyphenyl)propyl acetate (3.20a)**:

To a solution of benzoic acid (305 mg, 2.5 mmol, 1 equiv) in $CH_2Cl_2$ (15 mL) were added 3-(4-methoxyphenyl)-1-propanol (830 mg, 5 mmol, 2 equiv), DCC (567 mg, 2.75 mmol, 1.1 equiv), and DMAP (31 mg, 0.25 mmol, 0.1 equiv). The mixture was stirred at room temperature for 12 h. The solid was filtered, and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (10% $Et_2O$ in pentane) to afford the product as a clear liquid (603 mg, 2.23 mmol, 89%).

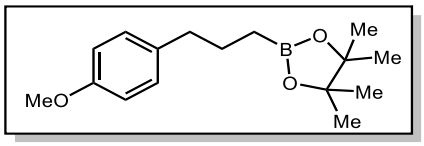
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 8.33, 1.43 Hz, 2H), 7.56 (tt, *J* = 7.52, 1.43 Hz, 1H), 7.45 (t, *J* = 7.79 Hz, 2H), 7.13 (d, *J* = 8.57 Hz, 2H), 6.84 (d, *J* = 8.59 Hz, 2H), 4.33 (t, *J* = 6.45 Hz, 2H), 3.79 (s, 3H), 2.74 (t, *J* = 7.31 Hz, 1H), 2.08 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 166.62, 157.92, 133.23, 132.88, 130.40, 129.55, 129.35, 128.35, 113.89, 64.26, 55.27, 31.38, 30.52; **IR** (thin film): ν 2949, 2837, 1715, 1609, 1510, 1452, 1270, 1243, 1110, 1030, 749; **HRMS** (ESI) $[M+NH_4]^+$ calculated for $[C_{17}H_{18}O_3]$ requires *m/z* 293.1148, found *m/z* 293.1139.




**1-(3-Chloropropyl)-4-methoxybenzene (3.21a)**:

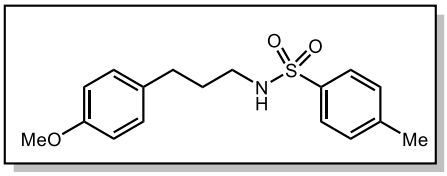
A 100-mL round-bottomed flask equipped with a stir bar was charged with $PPh_3$ (5.24 g, 20 mmol, 2 equiv) and $CCl_4$ (3.23 g, 21 mmol, 2.1 equiv) under $N_2$. Anhydrous $CH_2Cl_2$ (50 mL) was added, and the mixture was placed in an ice bath and stirred for 10 min at 0 °C. 3-(4-Methoxyphenyl)-1-propanol (1.66 g, 10 mmol, 1 equiv), diluted with $CH_2Cl_2$ (7.6 mL), was added dropwise at 0 °C. Upon addition of the alcohol, the ice bath was removed, and the reaction was stirred for 14 h at room temperature. The reaction mixture was

concentrated under reduced pressure, and the resulting residue was purified by flash column chromatography on silica gel (5% $Et_2O$ in pentane) to afford the product as a clear liquid (1.37 g, 7.40 mmol, 74%). Spectral data were consistent with those reported previously.[49]



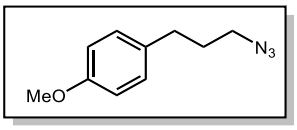

**3-(3-(4-Methoxyphenyl)propyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.22a)**:

Prepared as described by Watson. Spectral data were consistent with those reported previously.[50]




***N*-(3-(4-Methoxyphenyl)propyl)-4-methylbenzenesulfonamide (3.23a)**:

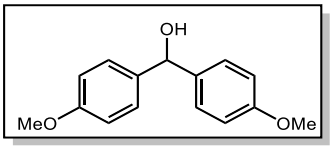
3-(4-Methoxyphenyl)propylamine (991 mg, 6.0 mmol, 1 equiv) was dissolved in $CH_2Cl_2$ and cooled to 0 °C. Triethylamine (909 mg, 9.0 mmol, 1.5 equiv) and DMAP (73 mg, 0.6 mmol, 0.1 equiv) were added. Finally, *p*-toluenesulfonyl chloride (1.26 g, 6.6 mmol, 1.1 equiv) was added portionwise. The solution was slowly warmed to room temperature and stirred for an additional 19 h. Once complete, the reaction was quenched with 1 M HCl. The aqueous layer was washed with $CH_2Cl_2$, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (gradient 50% $Et_2O$ in pentane to 100% $Et_2O$) to afford the product as a white solid (1.71 g, 5.34 mmol, 89%). Spectral data were consistent with those reported previously.[51]




**1-(3-Azidopropyl)-4-methoxybenzene (3.24a)**:

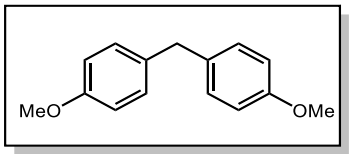
To a solution of triphenylphosphine (1.44 g, 5.5 mmol, 1.1 equiv) in 23 mL of anhydrous THF at 0 °C was added diisopropyl azodicarboxylate (1.021 g, 5.05 mmol, 1.01 equiv), followed by 3-(4-methoxyphenyl)-1-propanol (830 mg, 5.0 mmol, 1 equiv) in 12 mL of anhydrous THF, followed by diphenylphosphonic azide (2.475 g, 9.0 mmol, 1.8 equiv). The reaction was allowed to warm to room temperature and stir for 3

h. The reaction was diluted with $Et_2O$ and washed with a saturated aqueous solution of $NaHCO_3$ and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (5% $Et_2O$ in pentane) to afford the product as a pale-yellow liquid (803 mg, 4.20 mmol, 84%). Spectral data were consistent with those reported previously.[52]




**Bis(4-methoxyphenyl)methanol (3.S1)**:

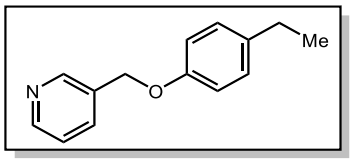
To a 100-mL nitrogen-purged round-bottomed flask containing *p*-anisaldehyde (10 mmol) in $Et_2O$ (10 mL) at 0 °C, was added 4-methoxyphenyl magnesium bromide (30 mL, 15 mmol, 1.5 equiv, 0.5 M solution in THF) dropwise over 5 min. The reaction was then allowed to warm to room temperature and left to stir overnight. A saturated aqueous solution of $NH_4Cl$ was then added slowly and stirred for a few minutes. $Et_2O$ was then added, and the layers were separated. The aqueous layer was extracted with $Et_2O$ (2x), and then the combined organic extracts were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (20% $Et_2O$ in pentane) to afford the product as a white solid (2.3 g, 9.2 mmol, 92%). Spectral data were consistent with those reported previously.[53]




**Bis(4-methoxyphenyl)methane (3.25a)**:

A 100-mL round-bottomed flask was charged with $PdCl_2$ (123 mg, 0.7 mmol, 0.1 equiv) and bis(4-methoxyphenyl)methanol (1.71 g, 7 mmol, 1 equiv). Under a nitrogen atmosphere, MeOH (14 mL) was added, followed by PMHS (0.87 mL, 2 equiv, slow addition). The mixture was stirred at 40 ºC for 12 h. After completion of the reaction, the product was dissolved in pentane, and water was added. The mixture was extracted three times into an equal volume of pentane and the combined organic layers were dried

($MgSO_4$), filtered, concentrated under reduced pressure, and purified by column chromatography on silica gel (gradient 0% to 5% $Et_2O$/pentane) to afford the pure product as a white solid (1.36 g, 5.95 mmol, 85%). Spectral data were consistent with those reported previously.[45]

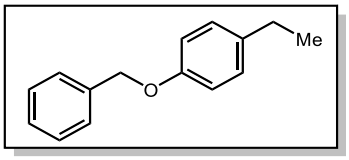



**3-((4-Ethylphenoxy)methyl)pyridine (3.29a)**:

A mixture of 4-ethylphenol (1.12 g, 9.16 mmol, 1 equiv), 3-(chloromethyl)pyridine hydrochloride (1.64 g, 10 mmol, 1 equiv), and $K_2CO_3$ (4.15 g, 30 mmol, 3 equiv) was dissolved in $CH_3CN$ (20 mL) and heated to reflux under nitrogen for 12 h. After cooling to room temperature, the reaction mixture was filtered and washed with $CH_2Cl_2$. The combined organic extracts were concentrated under reduced pressure, and the resulting residue was purified by column chromatography on silica gel (30% MTBE/pentane) to afford the pure product as a clear liquid (1.1 g, 5.0 mmol, 54%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.68 (dd, *J* = 2.16, 0.92 Hz, 1H), 8.58 (dd, *J* = 4.77, 1.68 Hz, 1H), 7.78 (dt, *J* = 8.03, 1.93 Hz, 1H), 7.32 (ddd, *J* = 7.85, 4.83, 0.88 Hz, 1H), 7.13 (d, *J* = 8.60 Hz, 2H), 6.90 (d, *J* = 8.61 Hz, 2H), 5.06 (s, 2H), 2.60 (q, *J* = 7.60 Hz, 2H), 1.21 (t, *J* = 7.60 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 156.44, 149.41, 149.04, 137.18, 135.25, 132.76, 128.85, 123.49, 114.69, 67.64, 27.99, 15.85;

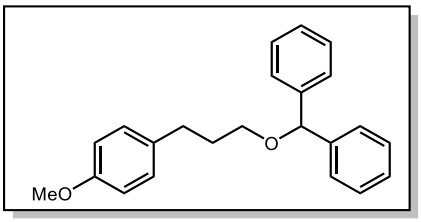
**IR** (thin film): ν 3032, 2962, 2967, 1607, 1582, 1508, 1230, 1176, 1020, 862, 708; **HRMS** (ESI) $[M–H]^+$ calculated for $[C_{14}H_{15}NO]$ requires *m/z* 212.1070, found *m/z* 212.1068.




**1-(Benzyloxy)-4-ethylbenzene (3.30a)**:

A mixture of 4-ethylphenol (1.22 g, 10 mmol, 1 equiv), benzyl bromide (1.88 g, 11 mmol, 1.1 equiv), and $CsCO_3$ (3.58 g, 11 mmol, 1.1 equiv) was dissolved in $CH_3CN$ (25 mL). The mixture was stirred at room temperature for 3 h under a nitrogen atmosphere. After 3 h, the reaction mixture was diluted with $CH_2Cl_2$. The organic solution was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and

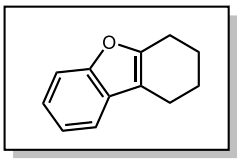
concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (pentane) to afford the pure product as a clear liquid (1.32 g, 6.2 mmol, 62%). Spectral data were consistent with those reported previously.[54]




**((3-(4-Methoxyphenyl)propoxy)methylene)dibenzene (3.31a)**:

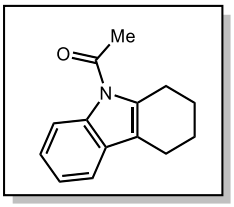
A 100-mL round-bottomed flask, equipped with a magnetic stir bar, was charged with 3-(4-methoxyphenyl)-1-1propanol (1.66 g, 10 mmol, 1 equiv) and anhydrous THF (50 mL). The mixture was cooled to 0 °C, then treated with NaH (60% dispersion in mineral oil, 600 mg, 15 mmol, 1.5 equiv). After being stirred at room temperature for 30 min, bromodiphenylmethane (2.47 g, 10 mmol, 1 equiv) was added portion-wise. The mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with $Et_2O$ and $H_2O$, and the layers were separated. The aqueous layer was extracted with $Et_2O$ (2x). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (10% $Et_2O$ in pentane) to afford the product as a clear oil (1.23 g, 3.70 mmol, 37%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.29-7.37 (m, 8H), 8.58 (dd, *J* = 4.77, 1.68 Hz, 1H), 7.22-7.26 (m, 2H), 7.08 (d, *J* = 8.58 Hz, 2H), 6.80 (d, *J* = 8.60 Hz, 2H), 5.32 (s, 1H), 3.78 (s, 3H), 3.46 (t, *J* = 6.25 Hz, 2H), 2.65-2.72 (m, 2H), 1.86-1.98 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 157.68, 142.56, 134.14, 129.35, 128.34, 127.34, 126.98, 113.69, 83.61, 68.26, 55.25, 31.75, 31.54; **IR** (thin film): ν 3059, 3028, 2936, 2857, 1608, 1508, 1450, 1243, 1178, 1098, 1069, 1031, 699; **HRMS** (ESI) $[M+NH_4]^+$ calculated for $[C_{23}H_{24}O_2]$ requires *m/z* 350.2115, found *m/z* 350.2111.



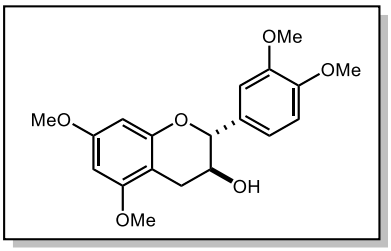
**1,2,3,4-Tetrahydrodibenzo[b,d]furan (3.36a)**:

Prepared as described by Tang. Spectral data were consistent with those reported previously.[55]



**1-(1,2,3,4-tetrahydro-9H-carbazol-9-yl)ethan-1-one (3.38a)**:

Prepared as described by Vincent. Spectral data were consistent with those reported previously.[56]



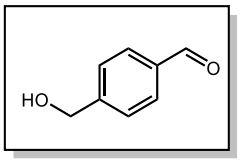
**(2R,3S)-2-(3,4-Dimethoxyphenyl)-5,7-dimethoxychroman-3-ol (3.79a)**:

A 100-mL round-bottomed flask, equipped with a magnetic stir bar, was charged with *trans*-3,3',4',5,7-pentahydroxyflavane (1.00 g, 3.44 mmol, 1 equiv), anhydrous $K_2CO_3$ (3.80 g, 27.5 mmol, 8 equiv), and anhydrous acetone (50 mL). Then MeI (1.70 mL, 27.5 mmol, 8 equiv) was added dropwise to the solution. The resulting solution was stirred for 14 days and eluted through a short pad of silica using acetone. The filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (50% $Et_2O$ in pentane) to afford the product as a white solid (703 mg, 2.03 mmol, 59%).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.96-7.01 (m, 2H), 6.89 (d, *J* = 8.19 Hz, 1H), 6.14 (d, *J* = 2.37 Hz, 1H), 6.10 (d, *J* = 2.30 Hz, 1H), 4.65 (d, *J* = 8.32 Hz, 1H), 4.05 (td, *J* = 8.77, 5.85 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.80 (s, 3H), 3.75 (s, 3H), 3.06 (dd, *J* = 16.36, 5.70 Hz, 1H), 2.58 (dd, *J* = 16.30, 9.09 Hz, 1H), 1.80 (s, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.73, 158.75, 155.31, 149.35, 149.33, 130.31, 119.97, 111.20, 109.96, 101.70, 93.01, 91.91, 81.81, 68.24, 55.97, 55.92, 55.52, 55.38, 27.6; **IR** (thin film):

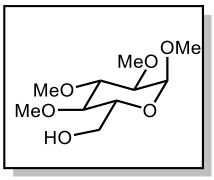
ν 3498, 3001, 2936, 3839, 1592, 1509, 1457, 1421, 1140, 1115, 1023, 730; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{19}H_{22}O_6]$ requires *m/z* 369.1309, found *m/z* 369.1307; m.p = 139–140 ºC.

### 3.7.3 Synthesis of Alcohol Coupling Partners




**4-(Hydroxymethyl)benzaldehyde (3.54a)**:

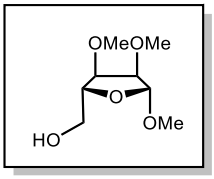
A 100-mL round-bottomed flask, equipped with a magnetic stir bar, was charged with terephthalaldehyde (1.37g, 10.2 mmol, 1.00 equiv), followed by a solution of EtOH:THF (10 mL: 30 mL). $NaBH_4$ (102.1 mg, 2.7 mmol, 0.265 equiv) was added to the solution at 0 °C, and the mixture was stirred for 30 min. Then the reaction mixture was stirred for an additional 6 h at room temperature. The reaction mixture was neutralized with 1 N HCl to pH = 5. The solution was concentrated under reduced pressure, and the resulting residue was dissolved in water. The aqueous solution was extracted three times with EtOAc (20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (50% $Et_2O$/pentane) to afford the product as a white solid (1.36 g, 9.99 mmol, 66%). Spectral data were consistent with those reported previously.[57]




**((2R,3R,4S,5R,6S)-3,4,5,6-Tetramethoxytetrahydro-2H-pyran-2-yl)methanol (3.83a)**:

To a stirred suspension of methyl-α-D-glucopyranoside (5.00 g, 25.7 mmol) in $CH_2Cl_2$ (100 mL) at room temperature was added DABCO (5.77 g, 51.4 mmol) and triphenylmethylchloride (14.3 g, 51.4 mmol). After being stirred for 24 h, the reaction mixture was concentrated under vaccum and the resulting residue

was purified by flash column chromatography on silica gel (50% EtOAc in pentane). To a solution of the tritylated product in DMF (76.0 mL) were added MeI (8.00 mL, 128 mmol) and NaH (60% in mineral oil, 3.22 g, 80.5 mmol) portion-wise at 0 °C. After being stirred for 12 h at room temperature, saturated aqueous $NH_4Cl$ was added dropwise. The mixture was extracted with EtOAc three times, washed with $H_2O$, saturated aqueous $NH_4Cl$, dried over $Na_2SO_4$, filtered, and the reaction mixture was concentrated under vacuum. The resulting residue was purified by flash column chromatography on silica gel (gradient 10% to 50% $Et_2O$ in pentane). The methylated product was dissolved in $CH_2Cl_2$ (125 mL), and $Et_3SiH$ (4.15 mL, 26.0 mmol) was added neat followed by the addition of TBSOTf (32.4 μL, 0.140 mmol). After 2 h, the yellow color disappeared, and TLC analysis indicated that the reaction was completed. Saturated aqueous $NaHCO_3$ solution (0.1 mL) was added, and the mixture was dried with $Na_2SO_4$, filtered and concentrated under vacuum. The residue was purified by silica gel chromatography (gradient 50% to 100% $Et_2O$ in pentane) to give **3.83a** as a white solid (2.60 g, 43%). Spectral data were consistent with those reported previously.[58]




**((2R,3R,4R,5R)-3,4,5-Trimethoxytetrahydrofuran-2-yl)methanol (3.84a)**:

To a stirred suspension of methyl beta-D-ribofuranoside (5.00 g, 30.5 mmol) in $CH_2Cl_2$ (100 mL) at room temperature was added DABCO (6.83 g, 60.9 mmol) and triphenylmethylchloride (17.0 g, 60.9 mmol). After being stirred for 24 h, the reaction mixture was concentrated under vacuum and the resulting residue was purified by flash column chromatography on silica gel (50% EtOAc in pentane). To a solution of the tritylated product in DMF (47.3 mL) were added MeI (5.00 mL, 82.4 mmol) and NaH (60% in mineral oil, 3.22 g, 51.5 mmol) portion-wise at 0 °C. After being stirred for 12 h at room temperature, saturated aqueous $NH_4Cl$ was added dropwise. The mixture was extracted with EtOAc three times, washed with $H_2O$, saturated aqueous $NH_4Cl$, dried over $Na_2SO_4$, filtered, and the reaction mixture was concentrated under vacuum. The resulting residue was purified by flash column chromatography on silica gel (gradient 10% to

50% $Et_2O$ in pentane). The methylated product was dissolved in $CH_2Cl_2$ (80 mL), and $Et_3SiH$ (2.60 mL, 16.6 mmol) was added neat followed by the addition of TBSOTf (21.0 μL, 0.0910 mmol). After 2 h, the yellow color disappeared, and TLC analysis indicated that the reaction was completed. Saturated aqueous $NaHCO_3$ solution (0.1 mL) was added, and the mixture was dried with $Na_2SO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel chromatography (gradient 50% to 100% EtOAc in pentane) to give **S21** as a colorless oil (1.10 g, 19%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 4.93 (s, 1H), 4.18 (dt, *J* = 6.81, 3.31 Hz, 1H), 3.98 (dd, *J* = 6.82, 4.74 Hz, 1H), 3.85 (dt, *J* = 11.9, 3.48 Hz, 1H), 3.77 (d, *J* = 4.67 Hz, 1H), 3.63 (ddd, *J* = 12.1, 8.63, 3.65 Hz, 1H), 3.52 (s, 3H), 3.45 (s, 3H), 3.44 (s, 3H), 2.10 (dd, *J* = 8.86, 3.85 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 106.03, 82.39, 82.11, 79.26, 62.92, 58.45, 58.37, 55.67;

**IR** (thin film): ν 3460, 2919, 2830, 1451, 1374, 1320 ,1189, 1131, 1091, 1043, 946, 930; **HRMS** (ESI) $[M+NH_4]^+$ calculated for $[C_8H_{16}O_5]$ requires *m/z* 210.1336, found *m/z* 210.1334.

### 3.7.4 Synthesis of $Cu_2(TFA)_4(MeCN)_2$

$CuCO_3Cu(OH)_2$ (2.21g, 10 mmol, 1 equiv) was added to a 100-mL round-bottom flask with a stirbar. A 1:1 mixture of TFA/$H_2O$ (6 mL) was added slowly, and the solution was stirred until all the copper dissolved. The reaction mixture was then evaporated under reduced pressure to afford the hydrated $Cu(TFA)_2$ as a blue solid. This material was then dissolved in 50 mL MeCN and stirred. After 1 h, 3.0 g of activated 3Å mol sieves were added, and the mixture was stirred for an additional 30 min. The reaction mixture was then filtered, and the sieves were washed with several portions of MeCN. The filtrate was evaporated under reduced pressure to afford the product as a blue-green powder (5.00 g, 15.1 mmol, 76%).[59]

### 3.7.5 Synthesis of C–H Alkoxylation Product

**General Procedure A:** A dry 20-mL Schlenk tube (1.5 cm diameter) was charged with $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol, 0.01 equiv), $K_2HPO_4$ (312 mg, 1.8 mmol, 3 equiv), and $Cu(TFA)_2(MeCN)$ (238 mg 0.72 mmol, 1.2 equiv). A stock solution containing the alkyl arene (0.6 mmol, 1 equiv) and MeOH (40 mg, 1.2 mmol, 2 equiv) in 0.9 mL MeCN was added. An additional 2.1 mL MeCN were added to rinse the wall of the Schlenk tube. The reaction was degassed by three freeze/pump/thaw cycles (4 cycles, 5 min each) under nitrogen in the dark before back filling with nitrogen. The reaction was then allowed to stir while being irradiated by a 40W Kessil Lamp PR160 (427nm). After a pre-determined time point, the reaction was eluted through a short pad of silica using $Et_2O$. After concentration under reduced pressure, the pure methoxylated alkyl arene was isolated by flash column chromatography.

**General Procedure B:** A dry 20-mL Schlenk tube (1.5 cm diameter) was charged with $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol, 0.01 equiv.), $K_2HPO_4$ (312 mg, 1.8 mmol, 3 equiv.), $Cu(TFA)_2(MeCN)$ (238 mg 0.72 mmol, 1.2 equiv), and MeOH (0.2 mL 5.0 mmol, 8 equiv.). A stock solution containing the alkyl arene (0.6 mmol, 1 equiv.) in 0.9 mL MeCN was then added. An additional 5.1 mL MeCN were added to rinse the wall of the Schlenk tube. The reaction was degassed by three freeze/pump/thaw cycles (4 cycles, 5 min each) under nitrogen in the dark before back filling with nitrogen. The reaction was then allowed to stir while being irradiated by a 40W Kessil Lamp PR160 (427nm). After a pre-determined time point, the reaction was eluted through a short pad of silica using $Et_2O$. After concentration under reduced pressure, the pure methoxylated alkyl arene was isolated by flash column chromatography.

**General Procedure C:** A dry 20-mL Schlenk tube (1.5 cm diameter) was charged with $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol, 0.01 equiv.), $K_2HPO_4$ (312 mg, 1.80 mmol, 3 equiv.), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol, 1.2 equiv.). A stock solution containing 1-ethyl-4-methoxybenzene (82 mg, 0.60 mmol, 1 equiv.) and the alcohol/ carboxylic acid (1.2 mmol, 2 equiv.) in 0.9 mL MeCN was then added. An additional 2.1 mL MeCN were added to rinse the wall of the Schlenk tube.

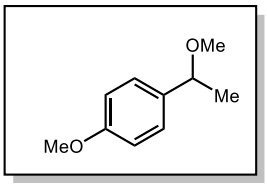
The reaction was degassed by three freeze/pump/thaw cycles (4 cycles, 5 min each) under nitrogen in the dark before back filling with nitrogen. The reaction was then allowed to stir while being irradiated by a 40W Kessil Lamp PR160 (427nm). After a pre-determined time point, the reaction was eluted through a short pad of silica using $Et_2O$. After concentration under reduced pressure, the pure product was isolated by flash column chromatography.

**General Procedure D:** A dry 20-mL Schlenk tube (1.5 cm diameter) was charged with $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol, 0.01 equiv.), $K_2HPO_4$ (312 mg, 1.80 mmol, 3 equiv.), $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol, 1.2 equiv.), and the alcohol/ carbamate (5.0 mmol, 8 equiv.). A stock solution containing 1-ethyl-4-methoxybenzene (82 mg, 0.60 mmol, 1 equiv.) in 0.9 mL MeCN was then added. An additional 2.1 mL MeCN were added to rinse the wall of the Schlenk tube. The reaction was degassed by three freeze/pump/thaw cycles (4 cycles, 5 min each) under nitrogen in the dark before back filling with nitrogen. The reaction was then allowed to stir while being irradiated by a 40W Kessil Lamp PR160 (427nm). After a pre-determined time point, the reaction was eluted through a short pad of silica using $Et_2O$. After concentration under reduced pressure, the pure product was isolated by flash column chromatography.

**General Procedure E:** A dry 20-mL Schlenk tube (1.5 cm diameter) was charged with $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (3.45 mg, 0.003 mmol, 0.01 equiv.), $K_2HPO_4$ (156 mg, 0.900 mmol, 3 equiv.), $Cu(TFA)_2(MeCN)$ (119 mg 0.360 mmol, 1.2 equiv.), and MeOH (0.10 mL 2.5 mmol, 8 equiv.). A stock solution containing the alkyl arene (0.3 mmol, 1 equiv.) in 0.9 mL MeCN was then added. An additional 5.1 mL MeCN were added to rinse the wall of the Schlenk tube. The reaction was degassed by three freeze/pump/thaw cycles (4 cycles, 5 min each) under nitrogen in the dark before back filling with nitrogen. The reaction was then allowed to stir while being irradiated by a 40W Kessil Lamp PR160 (427nm). After a pre-determined time point, the reaction was eluted through a short pad of silica using $Et_2O$. After concentration by rotary evaporation, the pure methoxylated alkyl arene was isolated by flash column chromatography.

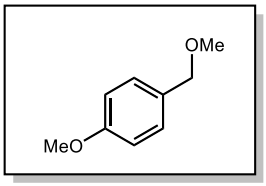
**General Procedure F:** A dry 20-mL Schlenk tube (1.5 cm diameter) was charged with $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (3.45 mg, 0.003 mmol, 0.01 equiv.), $K_2HPO_4$ (156 mg, 0.900 mmol, 3 equiv.), $Cu(TFA)_2(MeCN)$ (119 mg 0.360 mmol, 1.2 equiv.), and MeOH (0.10 mL 2.5 mmol, 8 equiv.). A stock solution containing the alkyl arene (0.3 mmol, 1 equiv.) in 0.9 mL DCM was then added. An additional 5.1 mL MeCN were added to rinse the wall of the Schlenk tube. The reaction was degassed by three freeze/pump/thaw cycles (4 cycles, 5 min each) under nitrogen in the dark before back filling with nitrogen. The reaction was then allowed to stir while being irradiated by a 40W Kessil Lamp PR160 (427nm). After a pre-determined time point, the reaction was eluted through a short pad of silica using $Et_2O$. After concentration by rotary evaporation, the pure methoxylated alkyl arene was isolated by flash column chromatography.

**General Procedure G:** A dry 20 mL Schlenk tube (1.5 cm diameter) was charged with $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)][PF_6]$ (3.45 mg, 0.00300 mmol, 0.01 equiv.), $K_2HPO_4$ (156 mg, 0.900 mmol, 3 equiv.), $Cu(TFA)_2(MeCN)$ (119 mg 0.360 mmol, 1.2 equiv.), methyl (1S,4aS,10aR)-6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (94.0 mg, 0.300 mmol, 1 equiv.) and alcohol (0.6 mmol, 2 equiv.). 1.5 mL MeCN were then added to rinse the wall of the Schlenk tube. The reaction was degassed by three freeze/pump/thaw cycles (4 cycles, 5 min each) under nitrogen in the dark before back filling with nitrogen. The reaction was then allowed to stir while being irradiated by a 40W Kessil Lamp PR160 (427nm). After a pre-determined time point, the reaction was eluted through a short pad of silica using $Et_2O$. After concentration by rotary evaporation, the pure product was isolated by flash column chromatography.



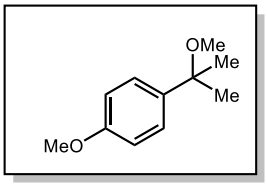

**1-Methoxy-4-(1-methoxyethyl)benzene (3.7)**

Prepared according to general procedure A using 1-ethyl-4-methoxybenzene (81.7 mg, 0.600 mmol), MeOH (40 mg, 1.2 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (5% $Et_2O$/Pentane). (6 h) Experiment 1: 73.2 mg of a clear liquid (73%, 0.440 mmol); Experiment 2: 66.8 mg of a clear liquid (67%, 0.402 mmol). Spectral data were consistent with those reported previously.[60]




**1-Methoxy-4-(methoxymethyl)benzene (3.12)**

Prepared according to general procedure B using 1-methyl-4-methoxybenzene (73.3 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was analyzed for NMR yield using phenanthrene as an internal standard. (12 h) Experiment 1: 21% yield by $^1H$ NMR. Spectral data were consistent with those reported previously.[61]

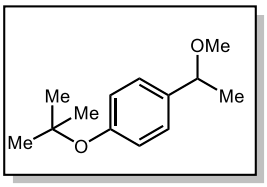



**1-Methoxy-4-(2-methoxypropan-2-yl)benzene (3.13)**

Prepared according to general procedure B using 1-isopropyl-4-methoxybenzene (90.1 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column

chromatography (5% $Et_2O$/Pentane). (13 h) Experiment 1: 87.4 mg of a clear liquid (81%, 0.486 mmol); Experiment 2: 86.7 mg of a clear liquid (80%, 0.480 mmol).

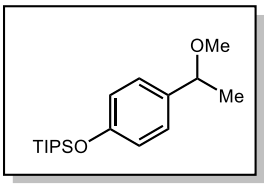
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.75 Hz, 2H), 6.88 (d, *J* = 8.76 Hz, 2H), 3.81 (s, 3H), 3.04 (s, 3H), 1.51 (s, 6H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.42, 137.86, 127.04, 113.44, 76.37, 55.23, 50.48, 27.99; **IR** (thin film): ν 2974, 2931, 1783, 1609, 1509, 1246; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{11}H_{16}O_2]$ requires *m/z* 149.0961, found *m/z* 149.0960.




**1-(*tert*-Butoxy)-4-(1-methoxyethyl)benzene (3.14)**

Prepared according to general procedure A using 1-(*tert*-butoxy)-4-ethylbenzene (107 mg, 0.600 mmol), MeOH (40 mg, 1.2 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (10% $Et_2O$/Pentane). (14 h) Experiment 1: 89.9 mg of a clear liquid (72%, 0.432 mmol); Experiment 2: 104.9 mg of a clear liquid (84%, 0.504 mmol).

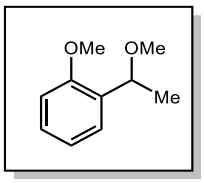
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.45 Hz, 2H), 6.96 (d, *J* = 8.51 Hz, 2H), 4.26 (q, *J* = 6.43 Hz, 1H), 3.20 (s, 3H), 1.42 (d, *J* = 6.53 Hz, 3H), 1.34 (s, 9H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 154.68, 138.14, 126.69, 124.00, 79.17, 78.27, 56.27, 28.86, 23.58; **IR** (thin film): ν 2975, 2930, 1605, 1503, 1163, 1107; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{13}H_{20}O_2]$ requires *m/z* 231.1356, found *m/z* 231.1354.




**Triisopropyl(4-(1-methoxyethyl)phenoxy)silane (3.15)**

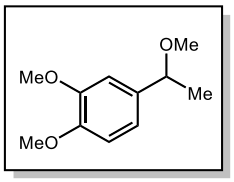
Prepared according to general procedure B using (4-ethylphenoxy)triisopropylsilane (167 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (2% $Et_2O$/Pentane). (56 h) Experiment 1: 95.2 mg of a clear liquid (52%, 0.309 mmol); Experiment 2: 99.6 mg of a clear liquid (54%, 0.323 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.49 Hz, 2H), 6.78 (d, *J* = 8.48 Hz, 2H), 4.16 (q, *J* = 6.46 Hz, 1H), 3.11 (s, 3H), 1.34 (d, *J* = 6.42 Hz, 3H), 1.14-1.22 (m, 3H), 1.02-1.03 (m, 18H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.43, 135.73, 127.33, 119.75, 79.17, 56.17, 23.65, 17.93, 12.67; **IR** (thin film): ν 2944, 2893, 2867, 1607, 1509, 1463, 1259, 1116, 911, 882, 836, 677; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{18}H_{32}O_2Si]$ requires *m/z* 331.2064, found *m/z* 331.2063.




**1-Methoxy-2-(1-methoxyethyl)benzene (3.16)**

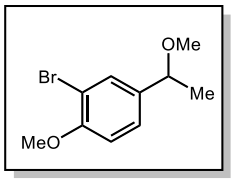
Prepared according to general procedure B using 1-ethyl-2-methoxybenzene (81.7 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was analyzed for NMR yield using phenanthrene as an internal standard. (3 d) Experiment 1: 38% yield by $^1$H NMR. Spectral data were consistent with those reported previously.[62]




**1,2-Dimethoxy-4-(1-methoxyethyl)benzene (3.17)**

Prepared according to general procedure B using 4-ethyl-1,2-dimethoxybenzene (99.7 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (20% $Et_2O$/Pentane). (7 d) Experiment 1: 83.4 mg of a clear liquid (71%, 0.425 mmol); Experiment 2: 81.1 mg of a clear liquid (69%, 0.414 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.87 (d, *J* = 1.28 Hz, 1H), 6.83-6.84 (m, 2H), 4.24 (q, *J* = 6.45, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.21 (s, 3H), 1.43 (d, *J* = 6.43 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 149.16, 136.09, 118.66, 110.80, 108.82, 79.39, 56.29, 55.85, 23.87; **IR** (thin film): ν 2972, 2931, 1597, 1511, 1259, 1026; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{11}H_{16}O_3]$ requires *m/z* 165.0910, found *m/z* 165.0909.

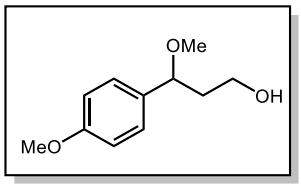



**2-Bromo-1-methoxy-4-(1-methoxyethyl)benzene (3.18)**

Prepared according to general procedure B using 2-bromo-4-ethyl-1-methoxybenzene (129 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (5% $Et_2O$/Pentane). (60 h) Experiment 1: 53.6 mg of a clear liquid (38%, 0.230 mmol); Experiment 2: 58.4 mg of a clear liquid (40%, 0.250 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 2.07 Hz, 1H), 7.21 (dd, *J* = 8.40, 2.11 Hz, 1H), 6.88 (d, *J* = 8.41 Hz, 1H), 4.22 (q, *J* = 6.45, 1H), 3.90 (s, 3H), 3.20 (s, 3H), 1.41 (d, *J* = 6.41 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.18, 137.21, 131.23, 126.31, 111.83, 111.65, 78.58, 56.40, 56.30, 23.79; **IR** (thin film):

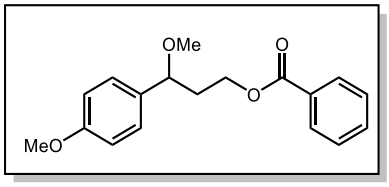
ν 2973, 2928, 1601, 1494, 1289, 1051; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{10}H_{13}BrO_2]$ requires *m/z* 212.9910, found *m/z* 212.9911.




**3-Methoxy-3-(4-methoxyphenyl)propan-1-ol (3.19)**

Prepared according to general procedure B using 3-(4-methoxyphenyl)propan-1-ol (99.7 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (60% $Et_2O$/Pentane). (10 h) Experiment 1: 77.4 mg of a clear liquid (69%, 0.416 mmol); Experiment 2: 74.1 mg of a clear liquid (66%, 0.398 mmol).

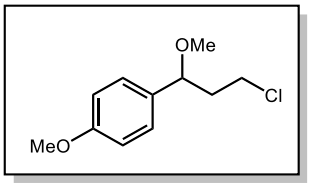
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.58 Hz, 2H), 6.90 (d, *J* = 8.64 Hz, 2H), 4.34 (dd, *J* = 8.92, 4.24 Hz, 1H), 3.81 (s, 3H), 3.74-3.77 (m, 2H), 3.20 (s, 3H), 2.78-2.80 (m, 1H), 2.01-2.08 (m, 1H), 1.80-1.86 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.20, 133.45, 127.75, 113.89, 83.31, 61.12, 56.37, 55.26, 40.36; **IR** (thin film): ν 3394, 2931, 1610, 1510, 1244, 1033; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{11}H_{16}O_3]$ requires *m/z* 165.0910, found *m/z* 165.0909.




**3-Methoxy-3-(4-methoxyphenyl)propyl benzoate (3.20)**

Prepared according to general procedure A using 3-(4-methoxyphenyl)propyl benzoate (163 mg, 0.600 mmol), MeOH (40 mg, 1.2 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (15% $Et_2O$/Pentane). (12 h) Experiment 1: 123 mg of a clear oil (62%, 0.373 mmol); Experiment 2: 127 mg of a clear oil (65%, 0.385 mmol).

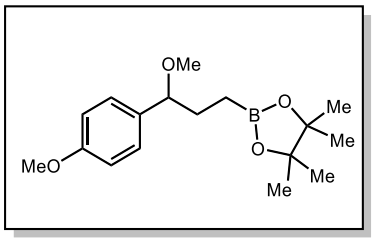
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.33, 1.43 Hz, 2H), 7.54 (tt, *J* = 7.52, 1.43 Hz, 1H), 7.43 (t, *J* = 7.78 Hz, 2H), 7.24 (d, *J* = 8.70 Hz, 2H), 6.89 (d, *J* = 8.65 Hz, 2H), 4.43 (ddd, *J* = 11.03, 7.22, 5.87 Hz, 1H), 4.26-4.33 (m, 2H), 3.79 (s, 3H), 3.20 (s, 3H), 2.27 (ddt, *J* = 14.04, 7.91, 6.05 Hz, 1H), 2.07 (ddt, *J* = 14.09, 7.24, 5.95 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 166.45, 159.25, 133.32, 132.85, 130.34, 129.52, 128.31, 127.84, 113.92, 80.32, 62.00, 56.43, 55.22, 37.15; **IR** (thin film): ν 2934, 2830, 1716, 1608, 1511, 1453, 1271, 1244, 1174, 1104, 1029, 710; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{18}H_{20}O_4]$ requires *m/z* 323.1254, found *m/z* 323.1250.




**1-(3-Chloro-1-methoxypropyl)-4-methoxybenzene (3.21)**

Prepared according to general procedure B using 1-(3-chloropropyl)-4-methoxybenzene (111 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (5% $Et_2O$/Pentane). (8 h) Experiment 1: 106 mg of a clear liquid (83%, 0.496 mmol); Experiment 2: 95.6 mg of a clear liquid (74%, 0.447 mmol).

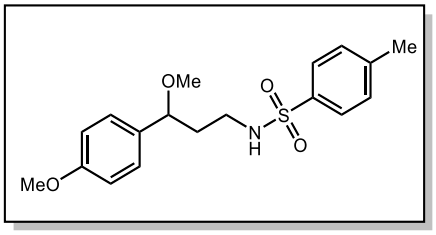
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.60 Hz, 2H), 6.90 (d, *J* = 8.62 Hz, 2H), 4.31 (dd, *J* = 8.26, 5.14 Hz, 1H), 3.81 (s, 3H), 3.68 (ddd, *J* = 10.75, 7.92, 5.65 Hz, 1H), 3.48 (dt, *J* = 10.76, 6.05 Hz, 1H), 3.20 (s, 3H), 2.24 (ddt, *J* = 14.22, 8.28, 5.91 Hz, 1H), 1.98 (dddd, *J* = 14.19, 7.92, 5.96, 5.08 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.30, 133.03, 127.85, 113.94, 79.94, 56.55, 55.28, 41.76, 40.83; **IR** (thin film): ν 2999, 2940, 2836, 1611, 1583, 1509, 1447, 1242, 1034, 814; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{11}H_{15}ClO]$ requires *m/z* 183.0571, found *m/z* 183.0573.




**2-(3-Methoxy-3-(4-methoxyphenyl)propyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.22)**

Prepared according to general procedure A using 2-(3-(4-methoxyphenyl)propyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (166 mg, 0.600 mmol), MeOH (40 mg, 1.2 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (20% $Et_2O$/Pentane). (8 h and 30 min) Experiment 1: 110 mg of a clear liquid (62%, 0.372 mmol); Experiment 2: 104 mg of a clear liquid (57%, 0.340 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.61 Hz, 2H), 6.86 (d, *J* = 8.61 Hz, 2H), 3.98 (dd, *J* = 7.36, 5.96 Hz, 1H), 3.80 (s, 3H), 3.18 (s, 3H), 1.88 (ddt, *J* = 13.97, 9.30, 7.02 Hz, 1H), 1.72 (ddt, *J* = 13.65, 9.31, 6.18 Hz, 1H), 1.23 (s, 12H), 0.69-0.82 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.89, 134.37, 127.93, 113.59, 85.14, 82.87, 56.45, 55.23, 32.39, 24.79, 7.39; **$^{11}$B NMR** (160 MHz, $CDCl_3$) δ 34.01; **IR** (thin film): ν 2977, 2929, 1610, 1510, 1243, 1143; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{17}H_{27}BO_4]$ requires *m/z* 274.1849, found *m/z* 274.1851.

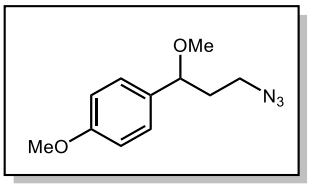



***N*-(3-Methoxy-3-(4-methoxyphenyl)propyl)-4-methylbenzenesulfonamide (3.23)**

Prepared according to general procedure A using *N*-(3-(4-methoxyphenyl)propyl)-4-methylbenzenesulfonamide (192 mg, 0.600 mmol), MeOH (40 mg, 1.2 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (60% $Et_2O$/Pentane). (12

h) Experiment 1: 146 mg of a clear oil (70%, 0.418 mmol); Experiment 2: 134 mg of a clear oil (64%, 0.384 mmol).

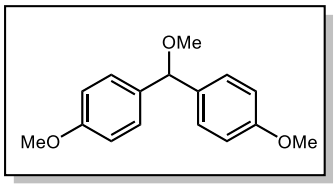
**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.26 Hz, 2H), 7.32 (d, *J* = 8.10 Hz, 2H), 7.07 (d, *J* = 8.65 Hz, 2H), 6.83 (d, *J* = 8.62 Hz, 2H), 5.24 (dd, *J* = 6.94, 4.79 Hz, 1H), 4.13 (dd, *J* = 8.39, 4.23 Hz, 1H), 3.79 (s, 3H), 3.12 (s, 3H), 2.97-3.13 (m, 1H), 3.00 (ddt, *J* = 12.43, 7.59, 4.63 Hz, 1H), 2.44 (s, 3H), 1.73-1.86 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.24, 143.24, 137.81, 129.67, 127.57, 127.17, 113.91, 82.64, 56.41, 55.27, 41.09, 36.92, 21.55; **IR** (thin film): ν 3279, 2930, 1607, 1509, 1244, 1155; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{18}H_{23}NO_4S]$ requires *m/z* 372.1240, found *m/z* 372.1236.




**1-(3-Azido-1-methoxypropyl)-4-methoxybenzene (3.24)**

Prepared according to general procedure A using 1-(3-azidopropyl)-4-methoxybenzene (115 mg, 0.600 mmol), MeOH (40 mg, 1.2 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (5% $Et_2O$/Pentane). (12 h) Experiment 1: 59.6 mg of a clear liquid (45%, 0.269 mmol); Experiment 2: 74.0 mg of a clear liquid (56%, 0.334 mmol).

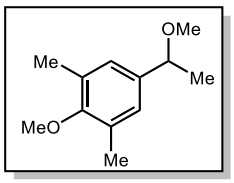
**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 4.19 (dd, *J* = 8.4, 5.1 Hz, 1H), 3.82 (s, 3H), 3.43 (ddd, *J* = 12.2, 7.7, 6.3 Hz, 1H), 3.27 (dt, *J* = 12.4, 6.3 Hz, 1H), 3.19 (s, 3H), 2.04 (ddt, *J* = 14.5, 8.4, 6.1 Hz, 1H), 1.84 (dddd, *J* = 14.1, 7.6, 6.6, 5.1 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.31, 133.13, 127.80, 113.96, 80.23, 56.44, 55.28, 48.24, 37.34; **IR** (thin film): ν 2933, 2830, 2095, 1611, 1511, 1246, 1106; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{11}H_{15}N_3O_2]$ requires *m/z* 190.0975, found *m/z* 190.0973.




**4,4'-(Methoxymethylene)bis(methoxybenzene) (3.25)**

Prepared according to general procedure B using bis(4-methoxyphenyl)methane (137 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (10% $Et_2O$/Pentane). (4 h) Experiment 1: 95.9 mg of a clear liquid (62%, 0.371 mmol); Experiment 2: 81.9 mg of a clear liquid (55%, 0.317 mmol).

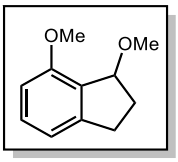
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.58 Hz, 4H), 6.85 (d, *J* = 8.73 Hz, 4H), 5.16 (s, 1H), 3.78 (s, 6H), 3.34 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.87, 134.52, 128.11, 113.73, 84.51, 56.79, 55.25; **IR** (thin film): ν 2995, 2932, 2829, 1609, 1507, 1459, 1241, 1171, 1085, 1031, 815; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{15}H_{15}O_2]$ requires *m/z* 227.1067, found *m/z* 227.1067.




**2-Methoxy-5-(1-methoxyethyl)-1,3-dimethylbenzene (3.26)**

Prepared according to general procedure B using ((3-(4-methoxyphenyl)propoxy)methylene)dibenzene (98.6 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (5% $Et_2O$/Pentane). (21 h and 30 min) Experiment 1: 62.6 mg of a clear liquid (54%, 0.322 mmol); Experiment 2: 61.2 mg of a clear liquid (53%, 0.315 mmol).

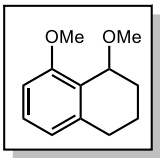
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.94 (s, 1H), 4.18 (q, *J* = 6.44 1H), 3.72(s, 3H), 3.21 (s, 3H), 2.28 (s, 6H), 1.40 (d, *J* = 6.43 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 156.23, 138.60, 130.70, 126.57, 79.27, 59.65, 56.39, 23.66, 16.19; **IR** (thin film): ν 2976, 2929, 1482, 1449, 1222, 1145, 1111, 1015; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{12}H_{18}O_2]$ requires *m/z* 217.1199, found *m/z* 217.1199.




**1,7-Dimethoxy-2,3-dihydro-1H-indene (3.27)**

Prepared according to general procedure A using 4-methoxy-2,3-dihydro-1H-indene (89.0 mg, 0.600 mmol), MeOH (40 mg, 1.2 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (10% $Et_2O$/Pentane). (28 h) Experiment 1: 63.3 mg of a clear liquid (59%, 0.355 mmol); Experiment 2: 64.8 mg of a clear liquid (61%, 0.364 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.76 Hz, 1H), 6.87 (d, *J* = 7.40 Hz, 1H), 6.71 (d, *J* = 8.15 Hz, 1H), 4.98 (dd, *J* = 6.08, 1.48 1H), 3.85 (s, 3H), 3.38 (s, 3H), 3.14 (dt, *J* = 16.28, 8.28 Hz, 1H), 2.78 (ddd, *J* = 16.03, 8.58, 2.30 Hz, 1H), 2.10-2.23 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 156.97, 147.33, 130.26, 130.19, 117.22, 108.21, 81.64, 56.42, 55.31, 31.65, 30.87; **IR** (thin film): ν 2931, 2825, 1732, 1591, 1474, 1262, 1075; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{11}H_{14}O_2]$ requires *m/z* 201.0886, found *m/z* 201.0885.

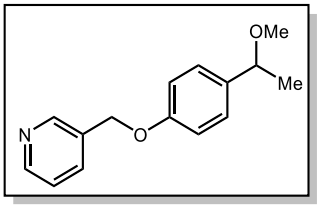



**1,8-Dimethoxy-1,2,3,4-tetrahydronaphthalene (3.28)**

Prepared according to general procedure B using 5-methoxy-1,2,3,4-tetrahydronaphthalenes (97.4 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (10% $Et_2O$/Pentane). (17 h) Experiment 1: 68.7 mg of a clear liquid (60%, 0.357 mmol); Experiment 2: 67.9 mg of a clear liquid (59%, 0.353 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.15 (t, *J* = 7.90 Hz, 1H), 6.71 (d, *J* = 7.98 Hz, 2H), 4.55 (t, *J* = 3.04 Hz, 1H), 3.85 (s, 3H), 3.45 (s, 3H), 2.77-2.87 (m, 1H), 2.66 (ddd, *J* = 17.35, 12.19, 5.96 Hz, 1H), 2.22-2.26 (m, 1H), 1.95 (dddd, *J* = 21.57, 12.93, 5.57, 2.80 Hz, 1H), 1.68-1.73 (m, 1H), 1.51 (dt, *J* = 13.71, 3.51 Hz, 1H);

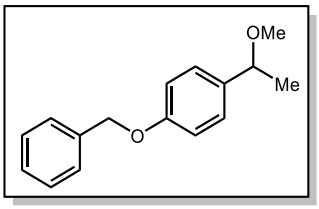
**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.32, 139.05, 128.31, 125.26, 121.39, 107.77, 70.10, 56.84, 55.60, 29.13, 26.61, 17.14; **IR** (thin film): ν 2936, 1587, 1465, 1260, 1086, 904, 726; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{11}H_{13}O]$ requires *m/z* 161.0961, found *m/z* 161.0960.




**3-((4-(1-Methoxyethyl)phenoxy)methyl)pyridine (3.29)**

Prepared according to general procedure B using 3-((4-ethylphenoxy)methyl)pyridine (128 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (40% MTBE/Pentane). (3 d) Experiment 1: 71.3 mg of a clear oil (49%, 0.293 mmol); Experiment 2: 70.4 mg of a clear oil (52%, 0.289 mmol).

**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 2.18 Hz, 1H), 8.59 (dd, *J* = 4.81, 1.64 Hz, 1H), 7.78 (dt, *J* = 7.98, 1.93 Hz, 1H), 7.33 (dd, *J* = 7.84 1H), 7.25 (d, *J* = 8.62 2H), 6.96 (d, *J* = 8.66 2H), 5.08 (s, 2H), 4.26 (q, *J* = 6.45 1H), 3.20 (s, 3H), 1.42 (d, *J* = 6.52 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 157.80, 149.46, 149.01, 136.33, 135.28, 132.57, 127.54, 123.52, 114.70, 79.06, 67.59, 56.27, 23.78; **IR** (thin film): ν 2975, 2928, 1608, 1508, 1233, 1106, 1021; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{15}H_{17}O_2N]$ requires *m/z* 244.1332, found *m/z* 244.1332.

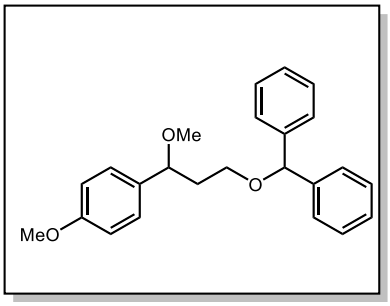



**1-(Benzyloxy)-4-(1-methoxyethyl)benzene (3.30)**

Prepared according to general procedure A using 1-(benzyloxy)-4-ethylbenzene (127 mg, 0.600 mmol), MeOH (40 mg, 1.2 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column

chromatography (7% $Et_2O$/Pentane). (8 h and 30 min) Experiment 1: 105 mg of a clear liquid (72%, 0.432 mmol); Experiment 2: 112 mg of a clear liquid (77%, 0.462 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.16 Hz, 2H), 7.37 (t, *J* = 7.32 Hz, 2H), 7.31 (t, *J* = 8.53 Hz, 1H), 7.23 (d, *J* = 8.53 2H), 6.96 (d, *J* = 8.57 2H), 5.04 (s, 2H), 4.24 (q, *J* = 6.44 1H), 3.19 (s, 3H), 1.42 (d, *J* = 6.49 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.29, 137.10, 135.85, 128.62, 127.99, 127.53, 127.49, 114.76, 79.15, 70.07, 56.28, 23.83; **IR** (thin film): ν 2974, 2926, 1608, 1507, 1227, 1106, 1019; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{16}H_{18}O_2]$ requires *m/z* 211.1117, found *m/z* 211.1116.

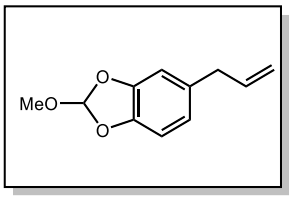



**((3-Methoxy-3-(4-methoxyphenyl)propoxy)methylene)dibenzene (3.31)**

Prepared according to general procedure A using ((3-(4-methoxyphenyl)propoxy)methylene)dibenzene (200 mg, 0.600 mmol), MeOH (40 mg, 1.2 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (10% $Et_2O$/Pentane). (21 h) Experiment 1: 46.4 mg of a clear liquid (23%, 0.128 mmol) (62% NMR yield); Experiment 2: 70.9 mg of a clear liquid (33%, 0.196 mmol) (71% NMR yield).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.29-7.35 (m, 8H), 7.21-7.25 (m, 1H), 7.19 (d, *J* = 8.60 Hz 2H), 6.86 (d, *J* = 8.69 Hz 2H), 5.29 (s, 1H), 4.32 (dd, *J* = 7.89, 5.96 Hz, 1H), 3.80 (s, 3H), 3.56 (ddd, *J* = 9.31, 7.11, 5.35 Hz, 1H), 3.37 (ddd, *J* = 9.31, 6.45, 5.53 Hz, 1H), 3.15 (s, 3H) 2.14 (dddd, *J* = 14.22, 7.81, 6.48, 5.41 Hz, 1H), 1.90 (ddt, *J* = 13.97, 7.06, 5.67 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.04, 142.52, 142.45, 133.95, 128.31, 128.30, 127.96, 127.34, 127.33, 127.00, 126.98, 113.73, 83.65, 80.33, 65.70, 56.35, 55.24, 38.35; **IR** (thin film):

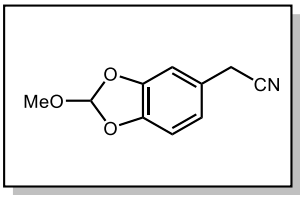
ν 3060, 2928, 2866, 1608, 1507, 1450, 1298, 1244, 1176, 1098, 1073, 1031, 830, 699; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{24}H_{26}O_3]$ requires *m/z* 385.1774, found *m/z* 385.1767.




**5-Allyl-2-methoxybenzo[d][1,3]dioxole (3.32)**

Prepared according to general procedure B using 5-allylbenzo[d][1,3]dioxole (97.4 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (Gradient 0% to 1% $Et_2O$/Pentane). (12 h) Experiment 1: 70.2 mg of a clear liquid (61%, 0.365 mmol); Experiment 2: 68.6 mg of a clear liquid (60%, 0.357 mmol).

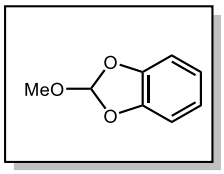
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.86 (s, 1H), 6.82 (d, *J* = 7.88 Hz 1H), 6.77 (d, *J* = 1.70 Hz 1H), 6.71 (dd, *J* = 7.87, 1.85 Hz 1H), 5.96 (ddt, *J* = 16.89, 10.15, 6.71 Hz 1H), 5.07-5.14 (m, 2H), 3.43 (s, 3H), 3.35 (dd, *J* = 6.84, 1.56 Hz 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 146.16, 144.40, 137.52, 133.97, 121.41, 119.10, 115.79, 108.66, 107.80, 49.88, 39.96; **IR** (thin film): ν2946, 2844, 1493, 1441, 1247, 1198, 1090, 1032, 908; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{11}H_{13}O_3]$ requires *m/z* 193.0859, found *m/z* 193.0861.




**2-(2-Methoxybenzo[d][1,3]dioxol-5-yl)acetonitrile (3.33)**

Prepared according to general procedure B using 2-(benzo[d][1,3]dioxol-5-yl)acetonitrile (96.7 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (Gradient 10% to 20% $Et_2O$/Pentane). (24 h) Experiment 1: 50.2 mg of a pale-yellow oil (44%, 0.263 mmol); Experiment 2: 52.1 mg of a pale-yellow oil (45%, 0.272 mmol).

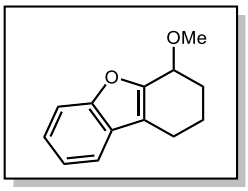
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.77-6.93 (m, 4H), 3.68 (s, 2H), 3.41 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 146.74, 145.98, 123.46, 121.39, 119.56, 117.90, 108.42, 108.09, 50.08, 23.38; **IR** (thin film): ν 2949, 2846, 2250, 1496, 1445, 1250, 1203, 1093, 1034; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{10}H_{10}O_3N]$ requires *m/z* 192.0655, found *m/z* 192.0653.




**2-Methoxybenzo[d][1,3]dioxole (3.35)**

Prepared according to general procedure B using 2-methoxybenzo[d][1,3]dioxole (73.3 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (Gradient 0% to 5% $Et_2O$/Pentane). (14 h) Experiment 1: 57.7 mg of a clear liquid (63%, 0.379 mmol); Experiment 2: 58.1 mg of a clear liquid (64%, 0.382 mmol).

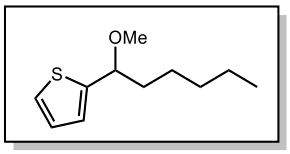
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.86-6.90 (m, 4H), 6.85 (s, 1H), 3.41 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 145.94, 121.72, 118.84, 108.28, 49.91; **IR** (thin film): ν 2948, 2842, 1482, 1238, 1202, 1238, 1092, 1035, 737; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_8H_9O_3]$ requires *m/z* 153.0546, found *m/z* 153.0545.




**4-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan (3.36)**

Prepared according to general procedure B using 1,2,3,4-tetrahydrodibenzo[b,d]furan (103 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (Gradient 2.5% to 5% $Et_2O$/Pentane). (24 h) Experiment 1: 48.9 mg of a clear oil (40%, 0.242 mmol); Experiment 2: 49.7 mg of a clear oil (41%, 0.246 mmol).

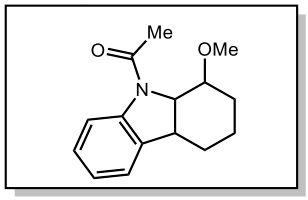
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.89 Hz, 1H), 7.46 (d, *J* = 8.08 Hz, 1H), 7.25-7.29 (m, 1H), 7.21 (td, *J* = 7.89, 1.06 Hz, 1H), 4.46 (t, *J* = 4.09 Hz, 1H), 3.56 (s, 3H), 2.74 (td, *J* = 16.57, 4.52 Hz, 1H), 2.56 (ddd, *J* = 16.45, 9.28, 5.28 Hz, 1H), 2.11-2.19 (m, 1H), 1.96-2.05 (m, 1H), 1.81-1.97 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 154.79, 152.49, 127.84, 124.32, 122.32, 119.42, 116.63, 111.41, 71.24, 57.13, 29.12, 20.67, 18.86; **IR** (thin film): ν 2931, 2863, 2821, 1451, 1366, 1185, 743; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{13}H_{14}O_2]$ requires *m/z* 171.0804, found *m/z* 171.0803.




**2-(1-methoxyhexyl)thiophene (3.37)**

Prepared according to general procedure B using 2-hexylthiophene (101 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (2.5% $Et_2O$/Pentane). (3 d) Experiment 1: 56.3 mg of a yellow oil (44%, 0.284 mmol); Experiment 2: 54.5 mg of a yellow oil (44%, 0.275 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.24-7.29 (m, 1H), 6.94-6.98 (m, 2H), 4.35 (t, *J* = 6.80 Hz 1H), 3.25 (s, 3H), 1.91 (dddd, *J* = 12.5, 9.13, 7.10, 5.30 Hz 1H), 1.67-1.76 (m, 1H), 1.36-1.45 (m, 1H), 1.22-1.32 (m, 5H), 0.81-0.91 (m, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 146.40, 126.24, 125.20, 124.76, 79.46, 56.40, 38.29, 31.62, 25.49, 22.55, 14.03; **IR** (thin film): ν 2928, 2857, 2821, 1463, 1319, 1092, 827, 696; **HRMS** (ESI) $[M\text{-}OMe]^+$ calculated for $[C_{11}H_{18}OS]$ requires *m/z* 167.0889, found *m/z* 167.0890.

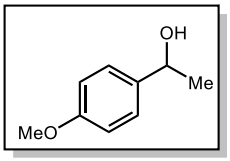



**1-(1-Methoxy-1,2,3,4-tetrahydro-9H-carbazol-9-yl)ethan-1-one (3.38)**

Prepared according to general procedure B using 1-(1,2,3,4-tetrahydro-9H-carbazol-9-yl)ethan-1-one (127 mg, 0.600 mmol), MeOH (0.2 mL, 5.0 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol),

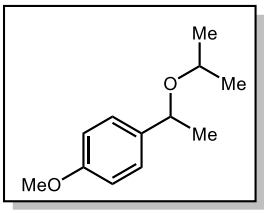
$K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (Gradient 20% to 30% $Et_2O$/Pentane). (12 h) Experiment 1: 68.1 mg of a white solid (47%, 0.280 mmol); Experiment 2: 66.6 mg of a white solid (46%, 0.274 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.39 Hz, 1H), 7.46 (dt, *J* = 7.63, 1.04 Hz, 1H), 7.32 (ddd, *J* = 7.85, 6.92, 1.05 Hz, 1H), 7.25 (t, *J* = 7.52 Hz, 1H), 4.88 (t, *J* = 3.38 Hz, 1H), 3.46 (s, 3H), 2.83 (ddd, *J* = 16.7, 5.60, 2.53 Hz, 1H), 2.78 (s, 3H), 2.57 (dddd, *J* = 16.7, 11.1, 5.91, 1.11 Hz, 1H), 2.33 (ddt, *J* = 14.0, 5.50, 2.99 Hz, 1H), 1.98 (tddd, *J* = 13.5, 11.1, 5.60, 2.74 Hz, 1H), 1.85 (dtt, *J* = 13.4, 5.37, 2.73 Hz, 1H), 1.72 (tt, *J* = 13.6, 3.26 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 169.90, 136.48, 133.96, 129.39, 125.24, 122.95, 121.51, 118.90, 115.75, 71.22, 55.96, 26.74, 26.45, 21.27, 16.98; **IR** (thin film): ν 2954, 2931, 2901, 1687, 1604, 1401, 1170, 1150, 1070, 752; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{15}H_{17}O_2N]$ requires *m/z* 266.1152, found *m/z* 266.1148; m.p = 76–77 ºC.




**1-(1-Isopropoxyethyl)-4-methoxybenzene (3.11)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (82.1 mg, 0.602 mmol), water (21.7 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). Experiment 1: 23% yield by $^1$H NMR; Experiment 2: 16% yield by $^1$H NMR. Spectral data were consistent with those reported previously.[63]

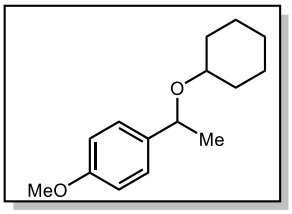



**1-(1-Isopropoxyethyl)-4-methoxybenzene (3.48)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (82.0 mg, 0.600 mmol), isopropyl alcohol (72.2 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was

purified by flash column chromatography (5% $Et_2O$/Pentane). (7 h) Experiment 1: 62.5 mg of a clear liquid (54%, 0.322 mmol); Experiment 2: 65.6 mg of a clear liquid (56%, 0.338 mmol).

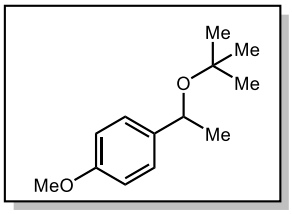
Prepared according to general procedure D using 1-ethyl-4-methoxybenzene (82.0 mg, 0.600 mmol), isopropyl alcohol (292 mg, 4.86 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (2.5 % $Et_2O$/Pentane). (8 h) Experiment 1: 79.4 mg of a clear liquid (68%, 0.409 mmol). Spectral data were consistent with those reported previously.[64]




**1-(1-(Cyclohexyloxy)ethyl)-4-methoxybenzene (3.49)**

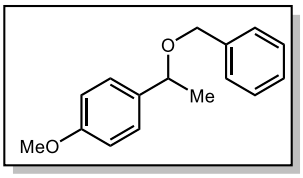
Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (82.0 mg, 0.600 mmol), cyclohexanol (121 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (5% $Et_2O$/Pentane). (7 h) Experiment 1: 70.2 mg of a clear liquid (50%, 0.300 mmol); Experiment 2: 73.9 mg of a clear liquid (53%, 0.315 mmol).

Prepared according to general procedure D using 1-ethyl-4-methoxybenzene (81.6 mg, 0.600 mmol), cyclohexanol (599 mg, 5.59 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (5% $Et_2O$/Pentane). (7 h) Experiment 1: 92.7 mg of a clear liquid (66%, 0.396 mmol). Spectral data were consistent with those reported previously.[65]



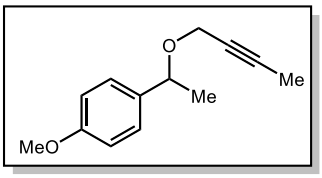

**1-(1-(*tert*-Butoxy)ethyl)-4-methoxybenzene (3.50)**

Prepared according to general procedure D using 1-ethyl-4-methoxybenzene (81.6 mg, 0.599 mmol), *tert*-butanol (356 mg, 4.81 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (2.5% $Et_2O$/Pentane). (14.5 h) Experiment 1: 57.5 mg of a clear oil (46%, 0.276 mmol); Experiment 2: 55.0 mg of a clear oil (44%, 0.264 mmol). Spectral data were consistent with those reported previously.[66]




1-(1-(Benzyloxy)ethyl)-4-methoxybenzene (3.51)

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (81.7 mg, 0.600 mmol), benzyl alcohol (130 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (1% $Et_2O$/Pentane). (12 h) Experiment 1: 811.8 mg of a clear oil (59%, 0.338 mmol); Experiment 2: 77.7 mg of a clear oil (53%, 0.321 mmol). Spectral data were consistent with those reported previously.[67]

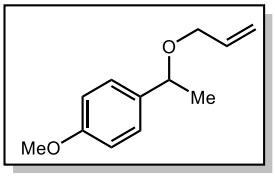



**1-(1-(But-2-yn-1-yloxy)ethyl)-4-methoxybenzene (3.52)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (81.5 mg, 0.599 mmol), 2-butyn-1-ol (83.8 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$

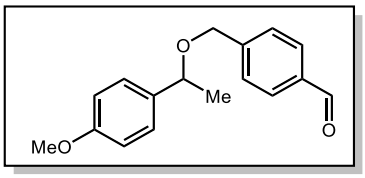
(312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (1% $Et_2O$/Pentane). (12 h) Experiment 1: 66.8 mg of a clear oil (54%, 0.327 mmol); Experiment 2: 63.1 mg of a clear oil (52%, 0.309 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.55 (q, *J* = 6.5 Hz, 1H), 3.99 (dq, *J* = 15.0, 2.4 Hz, 1H), 3.85 – 3.77 (m, 1H), 3.80 (s, 3H) 1.85 (t, *J* = 2.3 Hz, 3H), 1.45 (d, *J* = 6.5 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.1, 134.7, 127.7, 113.8, 81.9, 76.1, 75.4, 55.9, 55.3, 23.8, 3.7; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{13}H_{16}O_2]$ requires *m/z* 227.1043, found *m/z* 227.1038; **IR** (thin film): *ν* 2974, 2931, 2856, 2837, 2293, 2244, 1243, 1082, 1034, 831.




**1-(1-(Allyloxy)ethyl)-4-methoxybenzene (3.53)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (81.6 mg, 0.599 mmol), 2-propen-1-ol (73.5 mg, 1.27 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (1% $Et_2O$/Pentane). (12 h) Experiment 1: 68.0 mg of a clear oil (59%, 0.354 mmol); Experiment 2: 66.0 mg of a clear oil (57%, 0.343 mmol). Spectral data were consistent with those reported previously.[68]

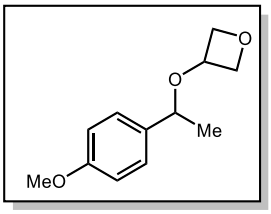



**4-((1-(4-Methoxyphenyl)ethoxy)methyl)benzaldehyde (3.54)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (81.8 mg, 0.601 mmol), 4-(hydroxymethyl)benzaldehyde (164 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material

was purified by flash column chromatography (20% MTBE/Pentane). (12 h) Experiment 1: 73.7 mg of a clear oil (45%, 0.273 mmol); Experiment 2: 66.1 mg of a clear oil (41%, 0.245 mmol).

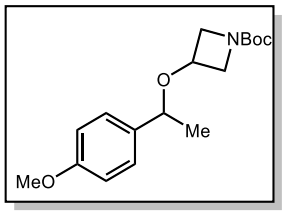
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 7.9 Hz, 2H), 7.28 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 4.53 – 4.31 (m, 3H), 3.81 (s, 3H), 1.50 (d, *J* = 6.5 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 192.0, 159.2, 146.0, 135.6, 135.2, 129.9, 127.7, 127.6, 114.0, 77.4, 69.4, 55.3, 24.1; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{17}H_{18}O_3]$ requires *m/z* 293.1148, found *m/z* 293.1146; **IR** (thin film): *ν* 2973, 2929, 2836, 2735, 1695, 1510, 1242, 1086, 830, 810.




**3-(1-(4-Methoxyphenyl)ethoxy)oxetane (3.55)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (82.0 mg, 0.600 mmol), 1,3-epoxy-2-propanol (88.9 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (20% $Et_2O$/Pentane). (8 h) Experiment 1: 36.2 mg of a clear liquid (29%, 0.174 mmol); Experiment 2: 37.1 mg of a clear liquid (30%, 0.178 mmol).

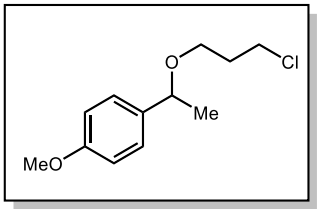
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.61 Hz 2H), 6.87 (d, *J* = 8.62 Hz 2H), 4.70 (t, *J* = 6.48 Hz 1H), 4.65 (t, *J* = 6.11 Hz 1H), 4.48 (p, *J* = 6.03 Hz 1H), 4.37-4.41 (m, 2H), 4.32 (q, *J* = 6.46 Hz 1H), 3.80 (s, 3H), 1.45 (d, *J* = 6.52 Hz 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.33, 134.80, 127.61, 113.87, 79.38, 79.19, 76.97, 70.37, 55.29, 23.53; **IR** (thin film): ν 2953, 2872, 1611, 1511, 1456, 1243, 1177, 1123, 1031, 966, 832; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{12}H_{16}O_3]$ requires *m/z* 231.0992, found *m/z* 231.0988.




***tert*-Butyl 3-(1-(4-methoxyphenyl)ethoxy)azetidine-1-carboxylate (3.56)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (81.9 mg, 0.601 mmol), 1-boc-3-hydroxyazetidine (209 mg, 1.21 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (20% $Et_2O$/Pentane). (12 h) Experiment 1: 62.0 mg of a clear liquid (34%, 0.202 mmol); Experiment 2: 66.4 mg of a clear liquid (36%, 0.216 mmol).

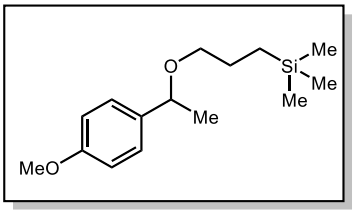
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.33 (q, *J* = 6.5 Hz, 1H), 4.13 (tt, *J* = 6.6, 4.7 Hz, 1H), 4.01 (ddd, *J* = 9.1, 6.5, 1.0 Hz, 1H), 3.86 (dd, *J* = 9.1, 4.7 Hz, 1H), 3.80 (s, 3H), 3.80 – 3.77 (m, 2H), 3.70 – 3.62 (m, 1H), 1.45 (d, *J* = 6.5 Hz, 3H), 1.41 (s, 9H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.3, 156.3, 134.6, 127.6, 113.9, 79.4, 77.3, 77.1, 76.8, 76.7, 65.6, 55.3, 28.4, 23.5; **IR** (thin film): *ν* 2974, 2932, 2881, 2837, 1697, 1402, 1365, 1244, 1156, 1115, 1080, 1034, 832; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{17}H_{25}NO_4]$ requires *m/z* 330.1676, found *m/z* 330.1672.




**1-(1-(3-Chloropropoxy)ethyl)-4-methoxy)benzene (3.57)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (81.6 mg, 0.599 mmol), 3-chloro-1-propanol (116 mg, 1.23 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (1% $Et_2O$/Pentane). (12 h) Experiment 1: 74.7 mg of a clear oil (54%, 0.327 mmol); Experiment 2: 66.5 mg of a clear oil (49%, 0.291 mmol).

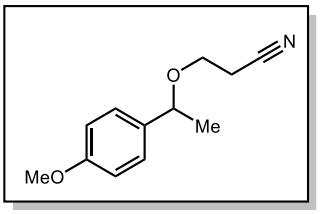
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.36 (q, *J* = 6.5 Hz, 1H), 3.80 (s, 3H), 3.70 – 3.55 (m, 2H), 3.41 – 3.35 (m, 2H), 1.98 (m, 2H), 1.42 (d, *J* = 6.4 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.0, 135.8, 127.3, 113.8, 77.7, 64.8, 55.2, 42.1, 33.0, 23.9; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{12}H_{17}ClO_2]$ required *m/z* 251.0809, found *m/z* 251.0806; **IR** (thin film): *ν* 2970, 2929, 2865, 1510, 1243, 1098, 1035, 8310.




**3-(1-(4-Methoxyphenyl)ethoxy)propyl)trimethylsilane (3.59)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (82.0 mg, 0.602 mmol), 3-(trimethylsilyl)-1-propanol (160 mg, 1.21 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (1% $Et_2O$/Pentane). (17.5 h) Experiment 1: 83.4 mg of a clear oil (52%, 0.313 mmol); Experiment 2: 70.8 mg of a clear oil (43%, 0.260 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.35 (q, *J* = 6.4 Hz, 1H), 3.80 (s, 3H), 3.22 (t, *J* = 7.2 Hz, 2H), 1.63 – 1.46 (m, 2H), 1.42 (d, *J* = 6.5 Hz, 3H), 0.41 (ddd, J = 10.0, 7.7, 4.5 Hz, 2H), -0.04 (s, 9 H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.8, 136.3, 127.3, 113.7, 77.4, 71.5, 55.2, 24.4, 24.1, 12.6, -1.7; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{15}H_{26}O_2Si]$ requires *m/z* 289.1594, found *m/z* 289.1590; **IR** (thin film): *ν* 2953, 2929, 2871, 1511, 1244, 1098, 1038, 854, 830, 734.

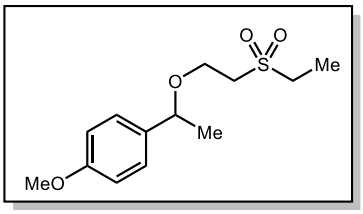



**3-(1-(4-Methoxyphenyl)ethoxy)propanenitrile (3.60)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (82.0 mg, 0.600 mmol), 2-cyanoethanol (85.3 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$

(312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (20% $Et_2O$/Pentane). (10 h) Experiment 1: 60.1 mg of a clear liquid (49%, 0.293 mmol); Experiment 2: 58.7 mg of a clear liquid (48%, 0.286 mmol).

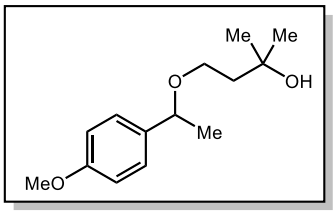
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.63 Hz 2H), 6.89 (d, *J* = 8.62 Hz 2H), 4.42 (q, *J* = 6.46 Hz 1H), 3.81 (s, 3H), 3.48 (td, *J* = 6.41, 2.1 Hz 2H), 2.54 (t, *J* = 6.41 Hz 2H), 1.45 (d, *J* = 6.41 Hz 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.28, 134.71, 127.43, 117.97, 113.99, 78.31, 62.82, 55.29, 23.85, 19.05; **IR** (thin film): ν 2973, 2931, 2875, 2252, 1611, 1511, 1455, 1243, 1097, 1031, 832; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{12}H_{15}ON]$ requires *m/z* 228.0995, found *m/z* 228.0994.




**1-(1-(2-(Ethylsulfonyl)ethoxy)ethyl)-4-methoxy)benzene (3.61)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (81.7 mg, 0.600 mmol), 2-(ethylsulfonyl)ethanol (170 mg, 1.23 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (50% $Et_2O$/Pentane). (24 h) Experiment 1: 68.5 mg of a clear oil (42%, 0.251 mmol); Experiment 2: 70.8 mg of a clear oil (43%, 0.260 mmol).

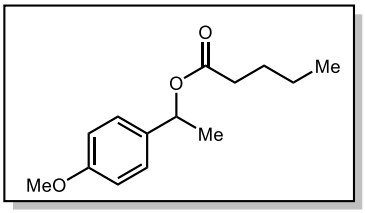
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 4.40 (q, *J* = 6.5 Hz, 1H), 3.80 (s, 3H), 3.75 – 3.61 (m, 2H), 3.22 – 3.05 (m, 4H), 1.47 – 1.37 (m, 6H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.3, 134.4, 127.4, 114.0, 78.5, 62.1, 55.3, 52.7, 49.3, 23.5, 6.6; **HRMS** (ESI) $[M+NH_4]^+$ calculated for $[C_{13}H_{20}O_4S]$ requires *m/z* 290.1421, found *m/z* 290.1419; **IR** (thin film): *ν* 2974, 2928, 2870, 1511, 1311, 1288, 1242, 1121, 1095, 1029, 833.




**4-(1-(4-Methoxyphenyl)ethoxy)-2-methylbutan-2-ol (3.62)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (81.4 mg, 0.598 mmol), 3-methyl-1,3-butanediol (127 mg, 1.22 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (50% $Et_2O$/Pentane). (13 h) Experiment 1: 87.5 mg of a clear oil (61%, 0.367 mmol); Experiment 2: 88.9 mg of a clear oil (62%, 0.373 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.35 (q, *J* = 6.4 Hz, 1H), 3.80 (s, 3H), 3.51 (t, *J* = 5.9 Hz, 2H), 1.72 (qt, *J* = 14.5, 5.8 Hz, 2H), 1.43 (d, *J* = 6.5 Hz, 3H), 1.23 (s, 3H), 1.16 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.1, 135.1, 127.4, 113.8, 78.3, 70.6, 65.8, 55.2, 41.4, 29.3, 29.2, 23.9; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{14}H_{22}O_3]$ requires *m/z* 261.1461, found *m/z* 261.1458; **IR** (thin film): *ν* 3436, 2970, 2931, 2870, 2837, 1511, 1243, 1172, 1091, 1035, 831.

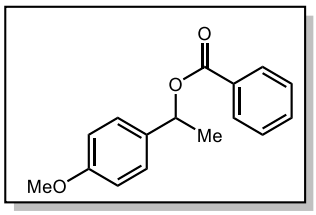



**1-(4-Methoxyphenyl)ethyl pentanoate (3.63)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (82.0 mg, 0.600 mmol), pentanoic acid (123 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (5% $Et_2O$/Pentane). (24 h) Experiment 1: 71.7 mg of a clear liquid (51%, 0.303 mmol); Experiment 2: 71.1 mg of a clear liquid (51%, 0.301 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.66 Hz 2H), 6.87 (d, *J* = 8.70 Hz 2H), 5.86 (q, *J* = 6.60 Hz 1H), 3.80 (s, 3H), 2.30 (td, *J* = 7.45, 2.16 Hz 2H), 1.55-1.64 (m, 2H), 1.51 (d, *J* = 6.58 Hz 3H), 1.33 (sext, *J* =

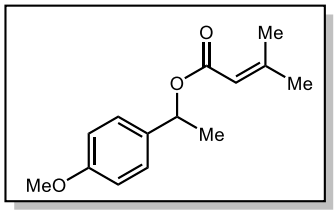
7.32 Hz 2H), 0.89 (t, *J* = 7.37 Hz 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 173.17, 159.19, 133.94, 127.54, 113.80, 71.71, 55.28, 34.39, 27.03, 22.23, 22.03, 13.72; **IR** (thin film): ν 2959, 2932, 2869, 1729, 1513, 1246, 1169, 1007, 826; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{14}H_{20}O_3]$ requires *m/z* 259.1305, found *m/z* 259.1301.




**1-(4-Methoxyphenyl)ethyl benzoate (3.64)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (82.0 mg, 0.600 mmol), benzoic acid (147 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (5% $Et_2O$/Pentane). (33 h) Experiment 1: 81.2 mg of a clear liquid (53%, 0.317 mmol); Experiment 2: 81.9 mg of a clear liquid (54%, 0.320 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 8.17, 1.42 Hz 2H), 7.51-7.58 (m, 1H), 7.43 (t, *J* = 7.77 Hz 2H), 7.39 (d, *J* = 8.66 Hz 2H), 6.90 (d, *J* = 8.64 Hz 2H), 6.10 (q, *J* = 6.57 Hz 1H), 3.80 (s, 3H), 1.66 (d, *J* = 6.57 Hz 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 165.87, 159.28, 133.86, 132.84, 130.63, 129.62, 128.30, 127.56, 113.88, 72.65, 55.28, 22.18; **IR** (thin film): ν 2977, 2933, 2837, 1712, 1610, 1512, 1244, 1029, 709; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{16}H_{16}O_3]$ requires *m/z* 279.0992, found *m/z* 279.0988.

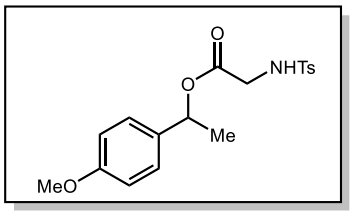



**1-(4-Methoxyphenyl)ethyl 3-methylbut-2-enoate (3.65)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (82.0 mg, 0.600 mmol), 3-methyl-2-butenoic acid (121 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol),

$K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (Gradient 5% to 10% $Et_2O$/Pentane). (24 h) Experiment 1: 91.9 mg of a clear liquid (65%, 0.392 mmol); Experiment 2: 70.2 mg of a clear liquid (50%, 0.300 mmol).

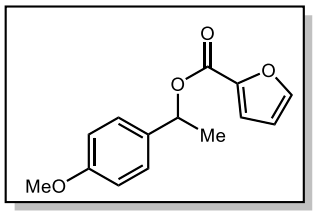
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.70 Hz 2H), 6.87 (d, *J* = 8.72 Hz 2H), 5.87 (q, *J* = 6.58 Hz 1H), 5.70 (m, 1H), 3.79 (s, 3H), 2.15 (d, *J* = 1.29 Hz 3H), 1.87 (d, *J* = 1.36 Hz 3H), 1.53 (d, *J* = 6.62 Hz 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 165.96, 159.12, 156.69, 134.30, 127.53, 116.35, 113.81, 70.97, 55.28, 27.42, 22.20, 20.22; **IR** (thin film): ν 2979, 2936, 2838, 1709, 1650, 1513, 1226, 1143, 1034, 1006, 729; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{14}H_{18}O_3]$ requires *m/z* 257.1148, found *m/z* 257.1149.




**1-(4-Methoxyphenyl)ethyl tosylglycinate (3.66)**

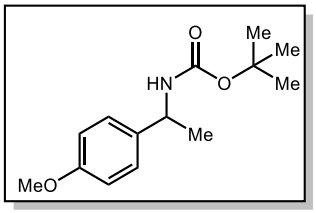
Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (82.0 mg, 0.600 mmol), *N*-(*p*-toluenesulfonyl)glycine (275 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (Gradient 50% to 75% $Et_2O$/Pentane). (34 h) Experiment 1: 113.8 mg of a pale-yellow oil (52%, 0.313 mmol); Experiment 2: 102.9 mg of a pale-yellow oil (47%, 0.283 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.35 Hz 2H), 7.25 (d, *J* = 8.82 Hz 2H), 7.19 (d, *J* = 8.70 Hz 2H), 6.86 (d, *J* = 8.73 Hz 2H), 5.76 (q, *J* = 6.60 Hz 1H), 4.98 (t, *J* = 5.49 Hz 1H), 3.80 (s, 3H), 3.80 (dd, *J* = 17.78, 5.65 Hz 1H), 3.71 (dd, *J* = 17.80, 5.31 Hz 1H), 2.40 (s, 3H), 1.45 (d, *J* = 6.58 Hz 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 168.12, 159.59, 143.78, 136.09, 132.39, 129.75, 127.69, 127.24, 113.91, 74.10, 55.30, 44.37, 21.63, 21.54; **IR** (thin film): ν 3282, 2978, 2931, 2840, 1737, 1608, 1513, 1449, 1331, 1298, 1157, 1117, 1095, 1058, 1029, 816; **HR MS** (ESI) $[M+NH_4]^+$ calculated for $[C_{18}H_{21}NO_5S]$ requires *m/z* 381.1479, found *m/z* 381.1471.



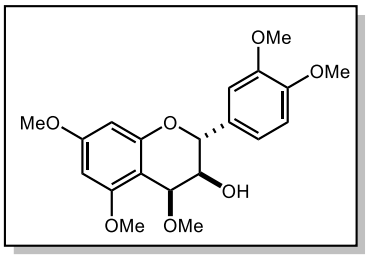

**1-(4-Methoxyphenyl)ethyl furan-2-carboxylate (3.67)**

Prepared according to general procedure C using 1-ethyl-4-methoxybenzene (81.7 mg, 0.600 mmol), 2-furoic acid (136mg, 1.21 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by flash column chromatography (10% $Et_2O$/Pentane). (24 h) Experiment 1: 83.9 mg of a clear oil (57%, 0.341 mmol); Experiment 2: 80.5 mg of a clear oil (54%, 0.327 mmol). Spectral data were consistent with those reported previously.[69]




**tert-Butyl (1-(4-methoxyphenyl)ethyl)carbamate (3.71)**

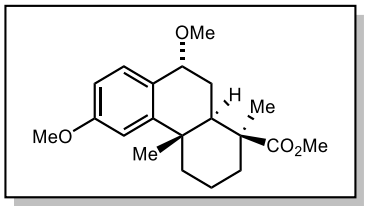
Prepared according to general procedure D using 1-ethyl-4-methoxybenzene (82.0 mg, 0.600 mmol), *tert*-butyl carbamate (141 mg, 1.20 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (6.90 mg, 0.006 mmol), $K_2HPO_4$ (312 mg, 1.80 mmol), and $Cu(TFA)_2(MeCN)$ (238 mg 0.720 mmol). The crude material was purified by iterative flash column chromatography; first condition (20% MTBE/Pentane) and second condition (20% $Et_2O$/Pentane). (6 h) Experiment 1: 57.2 mg of a white solid (38%, 0.228 mmol). Spectral data were consistent with those reported previously.[70]




**(2R,3S,4S)-2-(3,4-Dimethoxyphenyl)-4,5,7-trimethoxychroman-3-ol (3.79)**

Prepared according to general procedure E using (2R,3S)-2-(3,4-dimethoxyphenyl)-5,7-dimethoxychroman-3-ol (104 mg, 0.300 mmol), MeOH (0.10 mL, 2.5 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (3.45 mg, 0.003 mmol), $K_2HPO_4$ (156 mg, 0.900 mmol), and $Cu(TFA)_2(MeCN)$ (119 mg 0.360 mmol). The crude material was purified by flash column chromatography (Gradient 60% $Et_2O$/Pentane to $Et_2O$). (3 h) Experiment 1: 58.9 mg of a white solid (52%, 0.157 mmol); Experiment 2: 54.6 mg of a white solid (48%, 0.145 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.05 (dd, *J* = 8.22, 2.00 Hz 1H), 6.99 (d, *J* = 1.99 Hz 1H), 6.91 (d, *J* = 8.24 Hz 1H), 6.11 (d, *J* = 2.40 Hz 1H), 6.10 (d, *J* = 2.31 Hz 1H), 4.97 (d, *J* = 10.38 Hz 1H), 4.70 (d, *J* = 3.57 Hz 1H), 3.95 (ddd, *J* = 10.34, 9.36, 3.61 Hz 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.84 (s, 3H), 3.76 (s, 3H), 3.58 (s, 3H), 2.44 (d, *J* = 9.39 Hz 1H); **$^{13}$C NMR** (101 MHz, acetone-$d_6$) δ 161.79, 159.74, 156.05, 149.44, 149.18, 131.99, 120.74, 111.98, 111.40, 103.67, 93.00, 91.10, 77.03, 70.81, 70.79, 58.09, 55.24, 55.23, 55.09, 54.72; **IR** (thin film): ν 3501, 2937, 2835, 1704, 1602, 1511, 1455, 1340, 1259, 1203, 1136, 1067, 1023, 812; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{20}H_{24}O_7]$ requires *m/z* 345.1333, found *m/z* 345.1331; m.p = 133–135 ºC.

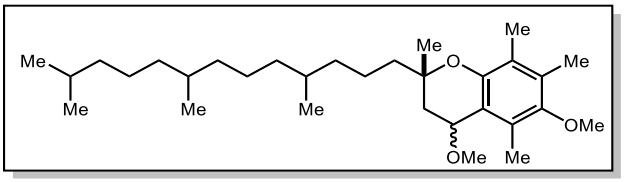



**Methyl (1S,4aS,9R,10aR)-6,9-dimethoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (3.80)**

Prepared according to general procedure E using methyl (1S,4aS,10aR)-6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (94.0 mg, 0.300 mmol), MeOH (0.10 mL, 2.5

mmol), [Ir(dF($CF_3$)ppy)$_2$(5,5'-d$CF_3$bpy)]$PF_6$ (3.45 mg, 0.00300 mmol), $K_2HPO_4$ (156 mg, 0.900 mmol), and Cu(TFA)$_2$(MeCN) (119 mg 0.360 mmol). The crude material was purified by flash column chromatography (20% $Et_2O$/Pentane). (1 hr and 30 min) Experiment 1: 71.6 mg of a clear oil (72%, 0.215 mmol); Experiment 2: 74.6 mg of a clear oil (75%, 0.224 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.44 Hz 1H), 6.79 (d, *J* = 2.56 Hz 1H), 6.74 (dd, *J* = 8.40, 2.58 Hz 1H), 4.23 (d, *J* = 2.83 Hz 1H), 3.77 (s, 3H), 3.67 (s, 3H), 3.45 (s, 3H), 2.47-2.55 (m, 1H), 2.25-2.31 (m, 1H), 2.15-2.23 (m, 1H), 1.91-2.02 (m, 3H), 1.63 (dtd, *J* = 14.21, 4.49, 4.34, 2.21 Hz, 1H), 1.44 (td, *J* = 13.33, 4.10 Hz, 1H), 1.29 (s, 3H), 1.14 (td, *J* = 13.61, 4.27 Hz 1H), 0.98 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 178.03, 159.46, 150.01, 132.13, 127.09, 111.52, 110.72, 77.14, 56.24, 55.23, 51.32, 45.50, 43.62, 38.82, 38.80, 37.34, 28.33, 24.56, 21.83, 19.91.; **IR** (thin film): ν 2943, 1724, 1609, 1497, 1462, 1270, 1223, 1144, 1076; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{20}H_{28}O_4]$ requires *m/z* 355.1880, found *m/z* 355.1874.



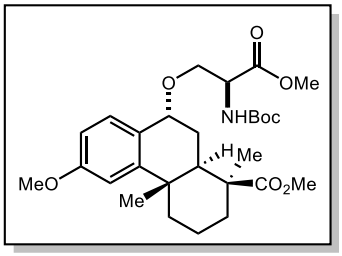

**4,6-Dimethoxy-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chromane (3.81)**

Prepared according to general procedure F using 6-methoxy-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chromane (134 mg, 0.300 mmol), MeOH (0.10 mL, 2.5 mmol), [Ir(dF($CF_3$)ppy)$_2$(5,5'-d$CF_3$bpy)]$PF_6$ (3.45 mg, 0.003 mmol), $K_2HPO_4$ (156 mg, 0.900 mmol), and Cu(TFA)$_2$(MeCN) (119 mg 0.360 mmol). The crude material was purified by flash column chromatography (Gradient 2.5% to 5% $Et_2O$/Pentane). (10 d) Experiment 1: 43.0 mg of a clear oil (30%, 0.0906 mmol) 1:1 d.r. Experiment 2: 45.6 mg of a clear oil (32%, 0.0961 mmol) 1:1 d.r.

**Major: $^1$H NMR** (500 MHz, $CDCl_3$) δ 4.28 (dd, *J* = 5.02, 2.53 Hz 1H), 3.63 (s, 3H), 3.40 (s, 3H), 2.24 (s, 3H), 2.18 (s, 3H), 2.17-2.20 (m, 1H), 2.08 (s, 3H), 1.79 (dd, *J* = 14.57, 4.96 Hz 1H), 1.57-1.66 (m, 2H), 1.44-1.54 (m, 2H), 1.19-1.45 (m, 14H), 1.01-1.18 (m, 6H), 0.87 (d, *J* = 6.61 Hz 9H), 0.85 (d, *J* = 6.74 Hz 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 149.85, 147.67, 130.55, 127.68, 123.25, 117.78, 74.74, 71.41, 60.32,

55.07, 42.96, 42.95, 39.38, 37.56, 37.46, 37.43, 37.41, 37.40, 37.38, 37.34, 37.30, 34.26, 34.22, 32.81, 32.79, 32.69, 32.67, 27.99, 24.83, 24.81, 24.46, 24.45, 23.25, 23.23, 22.73, 22.64, 20.91, 20.89, 19.76, 19.71, 19.69, 19.68, 19.64, 19.61, 12.77, 11.90, 11.41; **IR** (thin film): ν 2924, 2864, 1456, 1405, 1375, 1253, 1085, 1015, 735; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{31}H_{54}O_3]$ requires *m/z* 497.3965, found *m/z* 497.3959.

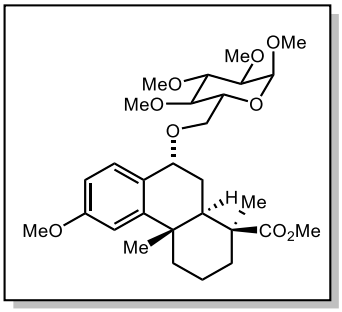
**Minor:** $^{1}$**H NMR** (500 MHz, $CDCl_3$) δ 4.28 (dd, *J* = 5.02, 2.53 Hz 1H), 3.63 (s, 3H), 3.40 (s, 3H), 2.24 (s, 3H), 2.18 (s, 3H), 2.17-2.20 (m, 1H), 2.08 (s, 3H), 1.79 (dd, *J* = 14.57, 4.96 Hz 1H), 1.57-1.66 (m, 2H), 1.44-1.54 (m, 2H), 1.19-1.45 (m, 14H), 1.01-1.18 (m, 6H), 0.87 (d, *J* = 6.61 Hz 9H), 0.85 (d, *J* = 6.74 Hz 3H); $^{13}$**C NMR** (126 MHz, $CDCl_3$) δ 149.85, 147.67, 130.55, 127.68, 123.25, 117.78, 74.74, 71.41, 60.32, 55.07, 42.96, 42.95, 39.38, 37.56, 37.46, 37.43, 37.41, 37.40, 37.38, 37.34, 37.30, 34.26, 34.22, 32.81, 32.79, 32.69, 32.67, 27.99, 24.83, 24.81, 24.46, 24.45, 23.25, 23.23, 22.73, 22.64, 20.91, 20.89, 19.76, 19.71, 19.69, 19.68, 19.64, 19.61, 12.77, 11.90, 11.41; **IR** (thin film): ν 2924, 2864, 1456, 1405, 1375, 1253, 1085, 1015, 735; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{31}H_{54}O_3]$ requires *m/z* 497.3965, found *m/z* 497.3959.




**Methyl (1S,4aS,9R,10aR)-9-((S)-2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)-6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (3.82)**

Prepared according to general procedure G using methyl (1S,4aS,10aR)-6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (94.0 mg, 0.300 mmol), methyl (*tert*-butoxycarbonyl)-L-serinate (132 mg, 0.600 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (3.45 mg, 0.00300 mmol), $K_2HPO_4$ (156 mg, 0.900 mmol), and $Cu(TFA)_2(MeCN)$ (119 mg 0.360 mmol). The crude material was purified by flash column chromatography (25% $Et_2O$/Pentane). (9 h 30 min) Experiment 1: 106.2 mg of a white solid (68%, 0.204 mmol); Experiment 2: 103.7 mg of a white solid (67%, 0.200 mmol).

**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.42 Hz 1H), 6.79 (d, *J* = 2.58 Hz 1H), 6.75 (dd, *J* = 8.42, 2.56 Hz 1H), 5.33 (d, *J* = 8.92 Hz 1H), 4.48 (dt, *J* = 9.23, 3.46 Hz 1H), 4.32 (d, *J* = 2.85 Hz 1H), 4.10 (dd, *J* = 9.25, 3.35 Hz 1H), 3.79 (s, 3H), 3.77-3.79 (m, 1H), 3.71 (s, 3H), 3.66 (s, 3H), 2.39 (dt, *J* = 14.77, 1.83 Hz 1H), 2.28 (dd, *J* = 13.67, 3.48 Hz 1H), 2.15-2.23 (m, 1H), 1.91-2.04 (m, 2H), 1.87 (dd, *J* = 12.84, 1.45 Hz 1H), 1.60-1.66 (m, 1H), 1.45 (s, 9H), 1.38-1.45 (m, 1H), 1.25 (s, 3H), 1.09 (td, *J* = 12.86, 3.57 Hz 1H), 0.95 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 177.88, 171.23, 159.56, 155.64, 150.09, 132.08, 126.54, 111.62, 110.66, 79.94, 76.26, 68.65, 55.21, 54.10, 52.40, 51.34, 45.62, 43.53, 38.84, 38.67, 37.44, 28.34, 28.24, 25.46, 21.75, 19.85; **IR** (thin film): ν 3443, 2946, 2873, 1715, 1576, 1206, 1160, 1097, 1068, 730; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{28}H_{41}NO_8]$ requires *m/z* 542.2724, found *m/z* 542.2721; m.p = 48–56 ºC.

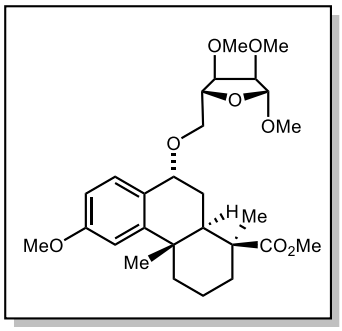



**Methyl (1S,4aS,9R,10aR)-6-methoxy-1,4a-dimethyl-9-(((2R,3R,4R,5S,6S)-3,4,5,6-tetramethoxytetrahydro-2H-pyran-2-yl)methoxy)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (3.83)**

Prepared according to general procedure G using methyl (1S,4aS,10aR)-6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (94.0 mg, 0.300 mmol), ((2R,3R,4S,5R,6S)-3,4,5,6-tetramethoxytetrahydro-2H-pyran-2-yl)methanol (142 mg, 0.600 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'-dCF_3bpy)]PF_6$ (3.45 mg, 0.00300 mmol), $K_2HPO_4$ (156 mg, 0.900 mmol), and $Cu(TFA)_2(MeCN)$ (119 mg 0.360 mmol). The crude material was purified by flash column chromatography (Gradient 50% to 75% $Et_2O$/Pentane). (10 h) Experiment 1: 113.9 mg of a white solid (71%, 0.212 mmol) 20:1 d.r.; Experiment 2: 113.2 mg of a white solid (70%, 0.211 mmol) 20:1 d.r..

**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.46 Hz 1H), 6.79 (d, *J* = 2.56 Hz 1H), 6.72 (dd, *J* = 8.42, 2.59 Hz 1H), 4.80 (d, *J* = 3.58 Hz 1H), 4.41 (t, *J* = 2.70 Hz 1H), 3.80 (dd, *J* = 10.77, 2.01 Hz 1H), 3.78 (s, 3H),

3.70 (dd, *J* = 10.75, 4.06 Hz 1H), 3.67 (s, 3H), 3.62 (s, 3H), 3.59-3.62 (m, 1H), 3.48-3.53 (m, 1H), 3.51 (s, 3H), 3.50 (s, 3H), 3.40 (s, 3H), 3.18-3.24 (m, 2H), 2.51 (dd, *J* = 13.88, 2.29 Hz 1H), 2.26-2.32 (m, 1H), 2.17-2.19 (m, 1H), 2.06 (d, *J* = 12.81 Hz 1H), 1.93-2.03 (m, 2H), 1.60-1.67 (m, 1H), 1.43 (td, *J* = 13.39, 4.13 Hz 1H), 1.30 (s, 3H), 1.14 (td, *J* = 13.56, 4.17 Hz 1H), 0.97 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 178.06, 159.44, 150.23, 132.20, 126.84, 111.18, 110.83, 97.39, 83.69, 81.78, 79.47, 76.27, 70.43, 66.75, 60.90, 60.42, 58.96, 55.21, 55.14, 51.31, 45.35, 43.66, 38.86, 38.72, 37.38, 28.36, 25.89, 21.92, 19.91; **IR** (thin film): ν 2937, 2836, 1722, 1609, 1497, 1148, 1095, 1040, 909, 728; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{29}H_{44}O_9]$ requires *m/z* 559.2878, found *m/z* 559.2868; m.p = 58–67 ºC.

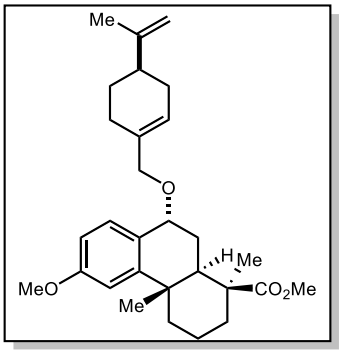



**Methyl (1S,4aS,9R,10aR)-6-methoxy-1,4a-dimethyl-9-(((2R,3S,4S,5S)-3,4,5 trimethoxytetrahydrofuran-2-yl)methoxy)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (3.84)**

Prepared according to general procedure G using methyl (1S,4aS,10aR)-6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (94.0 mg, 0.300 mmol), ((2R,3R,4R,5R)-3,4,5-trimethoxytetrahydrofuran-2-yl)methanol (116 mg, 0.600 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (3.45 mg, 0.00300 mmol), $K_2HPO_4$ (156 mg, 0.900 mmol), and $Cu(TFA)_2(MeCN)$ (119 mg 0.360 mmol). The crude material was purified by flash column chromatography (50% $Et_2O$/Pentane). (9 h 30 min) Experiment 1: 98.2 mg of a white solid (66%, 0.199 mmol); Experiment 2: 97.6 mg of a white solid (66%, 0.198 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 9.48 Hz 1H), 6.79 (d, *J* = 2.58 Hz 1H), 6.74 (dd, *J* = 8.43, 2.59 Hz 1H), 4.93 (d, *J* = 1.52 Hz 1H), 4.46-4.47 (m, 1H), 4.23 (td, *J* = 6.31, 4.36 Hz 1H), 3.84 (dd, *J* = 6.37, 4.72 Hz 1H), 3.78 (s, 3H), 3.75-3.79 (m, 1H), 3.72 (dd, *J* = 4.73, 1.43 Hz 1H), 3.66 (s, 3H), 3.62 (dd, *J* =

10.63, 6.23 Hz 1H), 3.48 (s, 3H), 3.40 (s, 3H), 3.38 (s, 3H), 2.47 (d, *J* = 12.95 Hz 1H), 2.25-2.31 (m, 1H), 2.17-2.20 (m, 1H), 1.92-2.04 (m, 3H), 1.63 (dt, *J* = 14.34, 3.54 Hz 1H), 1.42 (td, *J* = 13.37, 4.12 Hz 1H), 1.28 (s, 3H), 1.12 (td, *J* = 13.60, 4.27 Hz 1H), 0.97 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 178.03, 159.41, 150.05, 132.22, 126.97, 111.46, 110.64, 105.55, 82.20, 80.92, 80.71, 75.79, 70.21, 58.36, 58.30, 55.21, 55.15, 51.31, 45.59, 43.61, 38.88, 38.75, 37.42, 28.31, 25.68, 21.78, 19.90; **IR** (thin film): ν 2936, 2839, 1724, 1609, 1460, 1271, 1196, 1140, 1106, 1068, 1041; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{27}H_{40}O_8]$ requires *m/z* 515.2615, found *m/z* 515.2612; m.p = 102–104 ºC.

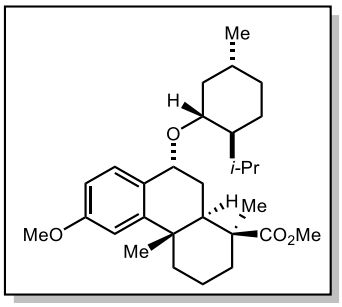



**Methyl (1S,4aS,9R,10aR)-6-methoxy-1,4a-dimethyl-9-(((R)-4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)methoxy)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (3.85)**

Prepared according to general procedure G using methyl (1S,4aS,10aR)-6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (94.0 mg, 0.300 mmol), (R)-(4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)methanol (91.3 mg, 0.600 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (3.45 mg, 0.00300 mmol), $K_2HPO_4$ (156 mg, 0.900 mmol), and $Cu(TFA)_2(MeCN)$ (119 mg 0.360 mmol). The crude material was purified by flash column chromatography (10% $Et_2O$/Pentane). (10 h) Experiment 1: 93.9 mg of a clear oil (69%, 0.207 mmol); Experiment 2: 91.6 mg of a clear oil (67%, 0.202 mmol).

**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.41 Hz 1H), 6.78 (d, *J* = 2.60 Hz 1H), 6.75 (dd, *J* = 8.44, 2.63 Hz 1H), 5.75-5.79 (m, 1H), 4.71-4.73 (m, 2H), 4.36 (dd, *J* = 2.69, 2.69 Hz 1H), 4.05 (d, *J* = 11.3 Hz 1H), 3.93 (d, *J* = 11.3 Hz 1H), 3.77 (s, 3H), 3.67 (s, 3H), 2.46 (dd, *J* = 13.96, 2.23 Hz 1H), 2.25-2.32 (m, 1H), 2.15-2.21 (m, 5H), 1.91-2.05 (m, 4H), 1.84-1.90 (m, 1H), 1.74 (s, 3H), 1.57-1.66 (m, 1H), 1.41-1.56 (m, 2H), 1.29 (s, 3H), 1.14 (td, *J* = 13.57, 4.23 Hz 1H), 0.97 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 178.06,

159.35, 150.11, 149.96, 135.03, 132.15, 127.45, 124.76, 111.63, 110.63, 108.63, 74.46, 73.24, 55.23, 51.32, 45.53, 43.68, 41.16, 38.78, 38.76, 37.37, 30.60, 28.39, 27.55, 26.97, 25.20, 21.83, 20.80, 19.93; **IR** (thin film): ν 2933, 1723, 1609, 1497, 1442, 1269, 1222, 1200, 1144, 1040, 730; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{29}H_{40}O_4]$ requires *m/z* 475.2819, found *m/z* 475.2814.



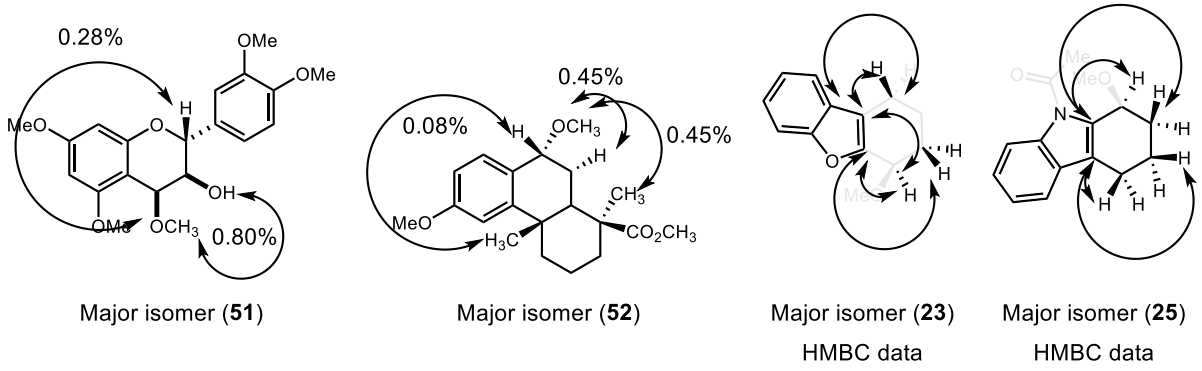

**Methyl (1S,4aS,9R,10aR)-9-(((1S,2R,5S)-2-isopropyl-5-methylcyclohexyl)oxy)-6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (3.86)**

Prepared according to general procedure G using methyl (1S,4aS,10aR)-6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (94.0 mg, 0.300 mmol), (1R,2S,5R)-2-isopropyl-5-methylcyclohexan-1-ol (93.8 mg, 0.600 mmol), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (3.45 mg, 0.00300 mmol), $K_2HPO_4$ (156 mg, 0.900 mmol), and $Cu(TFA)_2(MeCN)$ (119 mg 0.360 mmol). The crude material was purified by flash column chromatography (10% $Et_2O$/Pentane). (10 h) Experiment 1: 61.2 mg of a white solid (45%, 0.134 mmol); Experiment 2: 63.6 mg of a white solid (46%, 0.139 mmol).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.29 Hz 1H), 6.74-6.80 (m, 2H), 4.50 (dd, *J* = 4.15, 1.70 Hz 1H), 3.77 (s, 3H), 3.66 (s, 3H), 3.31 (td, *J* = 10.28, 4.16 Hz 1H), 2.43-2.47 (m, 1H), 2.39 (ddt, *J* = 14.85, 7.90, 3.93 Hz 1H), 2.24-2.31 (m, 2H), 2.18-2.24 (m, 1H), 2.06 (td, *J* = 14.23, 4.10 Hz 1H), 1.92-2.01 (m, 2H), 1.61-1.70 (m, 3H), 1.46 (td, *J* = 13.62, 4.17 Hz 1H), 1.37-1.43 (m, 1H), 1.27 (s, 3H), 1.20-1.24 (m, 1H), 1.14 (td, *J* = 13.56, 4.21 Hz 1H), 1.02-1.07 (m, 2H), 1.01 (d, *J* = 6.50 Hz 3H), 0.96 (s, 3H), 0.88-0.91 (m, 1H), 0.86 (d, *J* = 7.02 Hz 3H), 0.79 (d, *J* = 6.87 Hz 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 178.08, 159.08, 149.88, 132.11, 127.61, 112.14, 110.22, 76.51, 70.70, 55.24, 51.30, 47.98, 45.86, 43.99, 41.98, 38.80, 38.37, 37.63, 34.49, 31.71, 28.43, 27.01, 24.48, 23.07, 22.60, 21.88, 21.38, 19.88, 16.55; **IR** (thin film):

ν 2926, 2864, 1724, 1610, 1499, 1455, 1269, 1143, 1041; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{29}H_{44}O_4]$ requires *m/z* 479.3132, found *m/z* 479.3126; m.p = 62–68 ºC.

### 3.7.6 NOE Assignment of Relative Stereochemistry and Regiochemistry Assignment




Major isomer (**51**) Major isomer (**52**) Major isomer (**23**) HMBC data Major isomer (**25**) HMBC data

### 3.7.7 Stern-Volmer Experiments

Stern-Volmer experiments tracking the quenching of the phosphorescence of $[Ir(dF(CF_3)ppy)_2(5,5'dCF_3bpy)]PF_6$ (**Ir**) were conducted on an ISS PC1 Spectrofluorimeter. Rigorously degassed ($N_2$) stock solutions of each component were prepared prior to each set of experiments. The solutions were irradiated at 400 nm and luminescence was measured at 580 nm. Because $Cu(TFA)_2(MeCN)$ absorbs at 400 nm and 580 nm, **I** for Experiment 2 was normalized for an inner filter effect as described by Albinsson.[71] The solutions were loaded into quartz cuvettes and sealed under inert atmosphere using a rubber septum. The concentration of photocatalyst **Ir** was 2.6 x $10^{-5}$ M.

**Experiment 1**: Constant Iridium; Varied 1-ethyl-4-methoxybenzene

| Species | Concentration (M) |
|---|---|
| $[Ir(dF(CF_3)ppy)_2(5,5'-dCF_3bpy)]PF_6$ | 2.62E-05 |
| 1-ethyl-4-methoxybenzene | Varied |

| [1-ethyl-4-methoxybenzene] M | $I_0/I$ (1) | $I_0/I$ (2) | $I_0/I$ (3) | $I_0/I$ (average) |
|---|---|---|---|---|
| 0 | 1.00 | 1.00 | 1.00 | 1.00 |
| 0.006 | 1.18 | 1.21 | 1.19 | 1.19 |
| 0.011 | 1.34 | 1.39 | 1.37 | 1.37 |
| 0.016 | 1.51 | 1.53 | 1.51 | 1.52 |
| 0.021 | 1.71 | 1.69 | 1.67 | 1.69 |
| 0.025 | 1.84 | 1.81 | 1.79 | 1.81 |

**Table 3.14.** Relevant concentrations and tabulated quenching data for Experiment 1

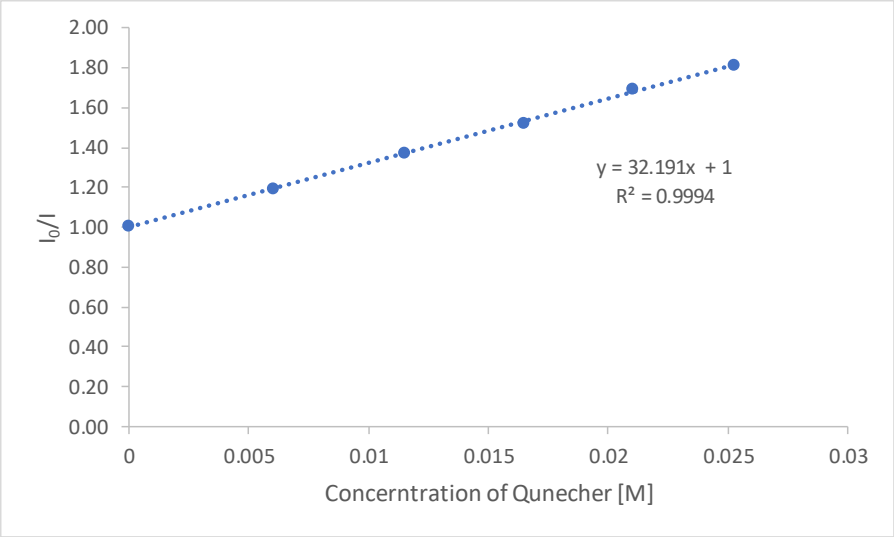



**Figure 3.1.** Graphical representation of $I_0/I$ data collected in Experiment 1

**Experiment 2**: Constant Iridium; Varied $Cu(TFA)_2(MeCN)$

| Species | Concentration (M) |
|---|---|
| $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ | 2.62E-05 |
| $Cu(TFA)_2(MeCN)$ | Varied |

| [$Cu(TFA)_2(MeCN)$] M | $I_0/I_{norm}$ (1) | $I_0/I_{norm}$ (2) | $I_0/I_{norm}$ (3) | $I_0/I_{norm}$ (average) |
|---|---|---|---|---|
| 0 | 1.00 | 1.00 | 1.00 | 1.00 |
| 0.006 | 1.31 | 1.33 | 1.30 | 1.31 |
| 0.011 | 1.58 | 1.53 | 1.54 | 1.55 |
| 0.016 | 1.83 | 1.72 | 1.76 | 1.77 |
| 0.021 | 2.12 | 1.96 | 1.99 | 2.02 |
| 0.025 | 2.35 | 2.21 | 2.25 | 2.27 |

**Table 3.15.** Relevant concentrations and tabulated quenching data for Experiment 2

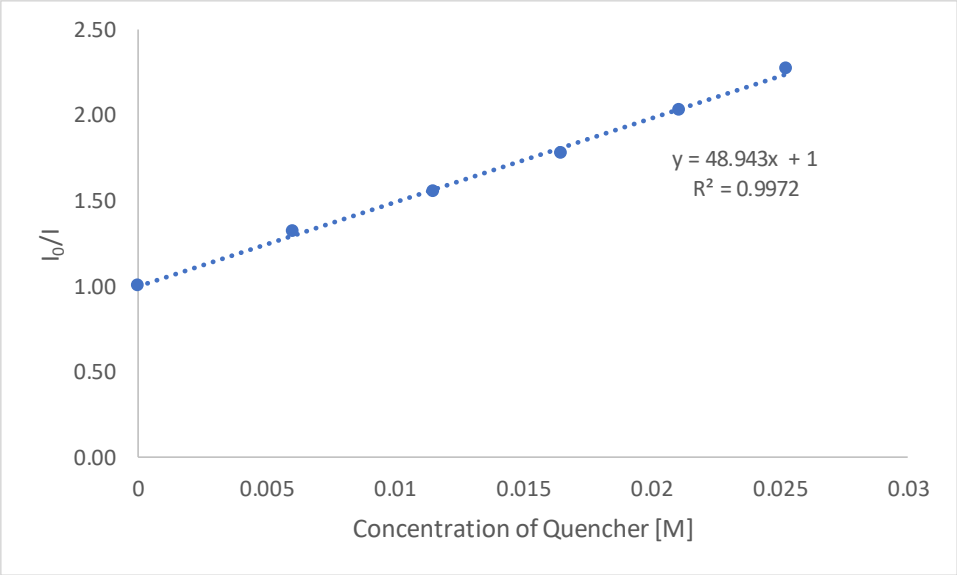



**Figure 3.2.** Graphical representation of $I_0/I_{norm}$ data collected in Experiment 2

| [Cu(TFA)$_2$(MeCN)] M | Absorbance at 400 nm | Absorbance at 580 nm |
|---|---|---|
| 0 | 0.00 | 0.00 |
| 0.006 | 0.022 | 0.043 |
| 0.011 | 0.044 | 0.080 |
| 0.016 | 0.064 | 0.11 |
| 0.024 | 0.12 | 0.17 |

**Table 3.16.** Relevant concentrations and tabulated absorbance data

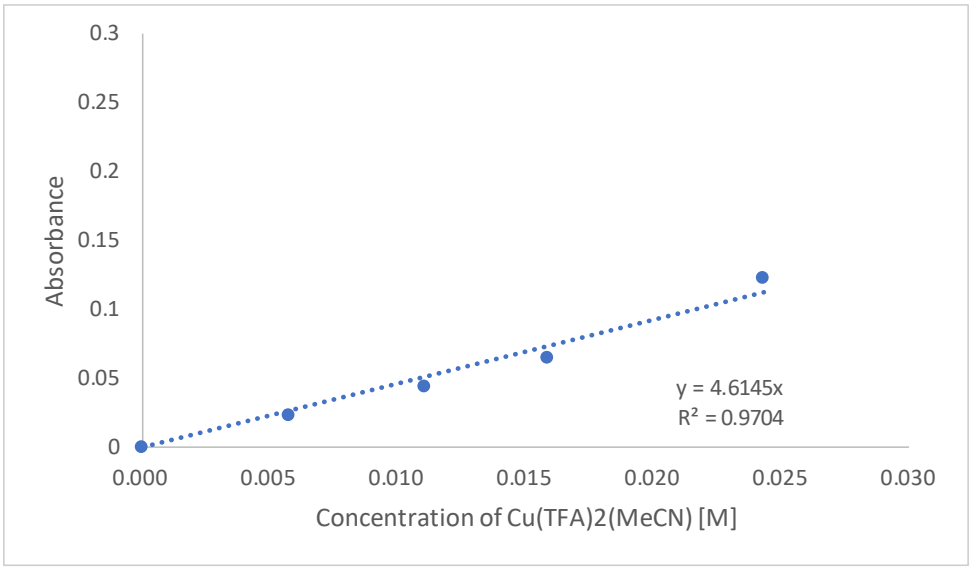



**Figure 3.3.** Graphical representation of molar absorptivity of Cu(TFA)$_2$(MeCN) at 400 nm

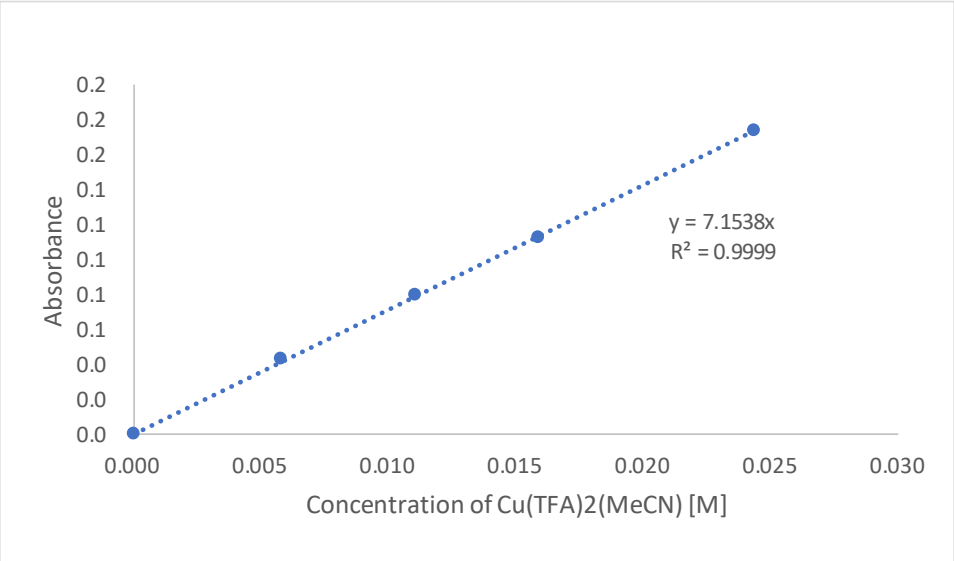



**Figure 3.4.** Graphical representation of molar absorptivity of $Cu(TFA)_2(MeCN)$ at 580 nm

### 3.7.8 Cyclic Voltammetry Data

Cyclic voltammetry experiments were performed in MeCN with analyte (1 mM) and $[(n\text{-}Bu)_4N]^+[PF6]^-$ (100 mM) using a glassy carbon working electrode, platinum wire counter electrode, a $Ag/AgNO_3$ MeCN reference electrode, and a scan rate of 50 mV/s. Ferrocene was added as an internal reference to SCE.

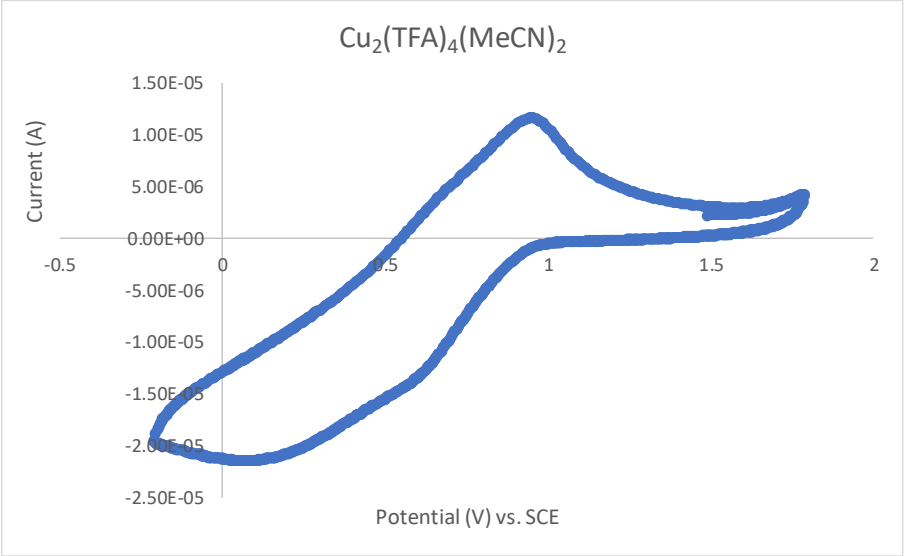



**Figure 3.5.** Cyclic voltammograms of $Cu(TFA)_2(MeCN)$

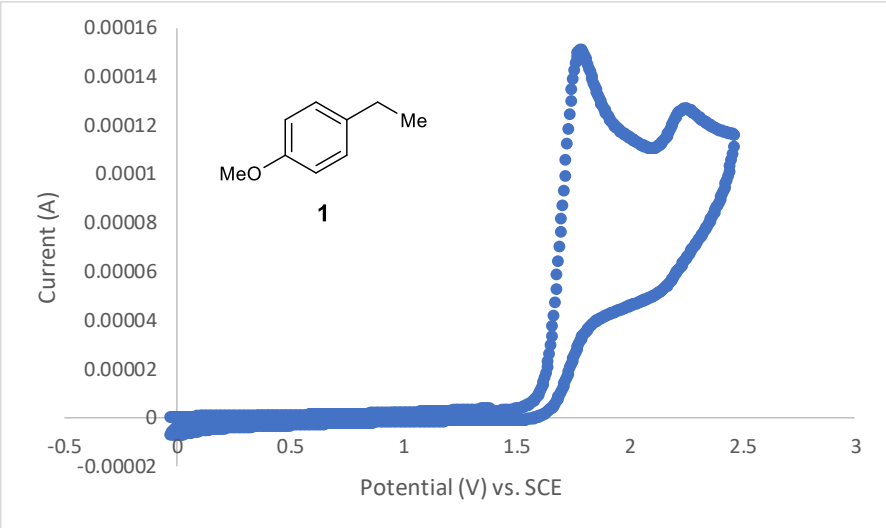



**Figure 3.6.** Cyclic voltammograms of 1-ethyl-4-methoxybenzene (**3.6**)

**Cu(TFA)$_2$(MeCN):** $Cu^{II}/Cu^{I}$ $^{+}$ $E_{p/2}$ = 0.38 V vs. SCE in MeCN

**1-ethyl-4-methoxybenzene (3.6)**: **3.6**/**3.6**$^{\bullet+}$ $E_{p/2}$ = 1.52 V vs. SCE in MeCN

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59. (a) The identity of this compound was confirmed by X-Ray crystallography. CCDC 1917423 contains the supplementary crystallographic data for this structure. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures. (b) Karpova, E. V.; Boltalin, A. I.; Zakharov, M. A.; Sorokina, N. I.; Korenev, Yu. M.; Troyanov, S. I. Z. Synthesis and Crystal Structure of Copper(II) Trifluoroacetates, $Cu_2(CF_3COO)_4 \cdot 2CH_3CN$ and $Cu(CF_3COO)_2(H_2O)_4$ *Anorg. Allg. Chem.* **1998**, *624*, 741–744.

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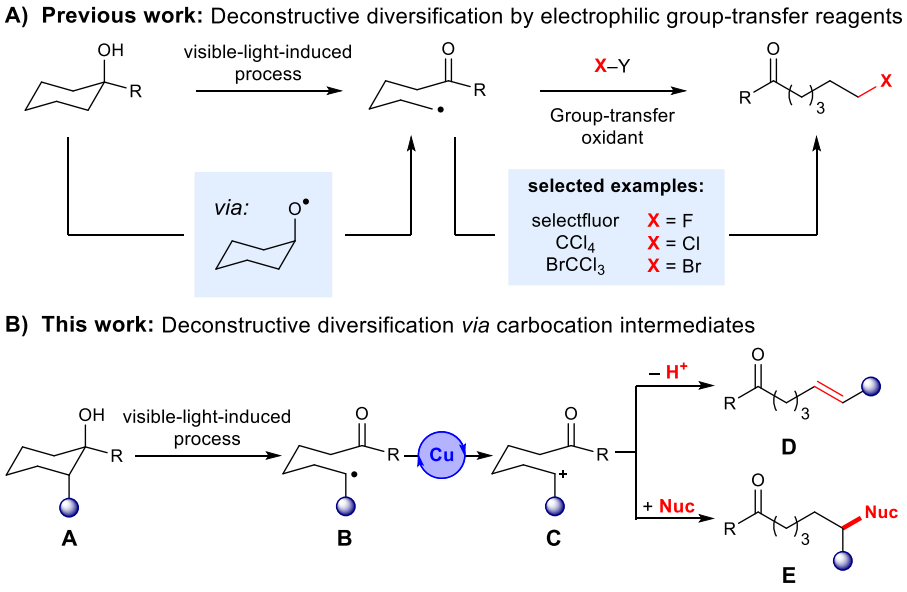
# Chapter 4. Deconstructive Diversification of Cyclic Alcohols Enabled by Oxidative Dual Photoredox Catalysis

## 4.1 Introduction

Carbon–carbon (C–C) bonds are ubiquitous in organic molecules. As such, new reactions that selectively activate and functionalize of C–C bonds have the potential to significantly impact the synthesis of organic molecules.[1–3] The development of methods to selectively deconstruct a specific C–C bond in cyclic molecules have been an area of growing interest over the past decade because they enable the rapid transformations of one molecular scaffold into another, often producing structures with very different three-dimensional geometries.[4–7] Several recent methods for the selective cleavage of C–C bonds in cyclic alcohols exploit the propensity of highly reactive oxygen-centered radicals to undergo β-scission.[7] This strategy is valuable because it results in the net remote functionalization of aldehydes and ketones, a transformation that is challenging to accomplish otherwise.[8] Visible-light-promoted methods are particularly attractive because they offer milder radical initiation conditions that do not require strong oxidants, high temperatures, or UV light irradiation.[9,10] In these methods, the ring-opening radical cascades terminate when a carbon-centered radical intermediate is trapped by electrophilic group-transfer reagents such as alkyne,[11,12] arene,[13] cyanide,[12] halogen,[12,14,15] hydrogen atom transfer reagents,[14,16] as well as azodicarboxylates,[17] Michael acceptors,[18,19] and molecular oxygen (Scheme 4.1.A).[18] The success of these strategies depends on the availability of an appropriate group-transfer oxidant. We envisioned that a strategy coupling similar radical cleavage reactions with more general terminal oxidant would enable incorporation of a wide range of functional groups that could not be accomplished using previous methods.



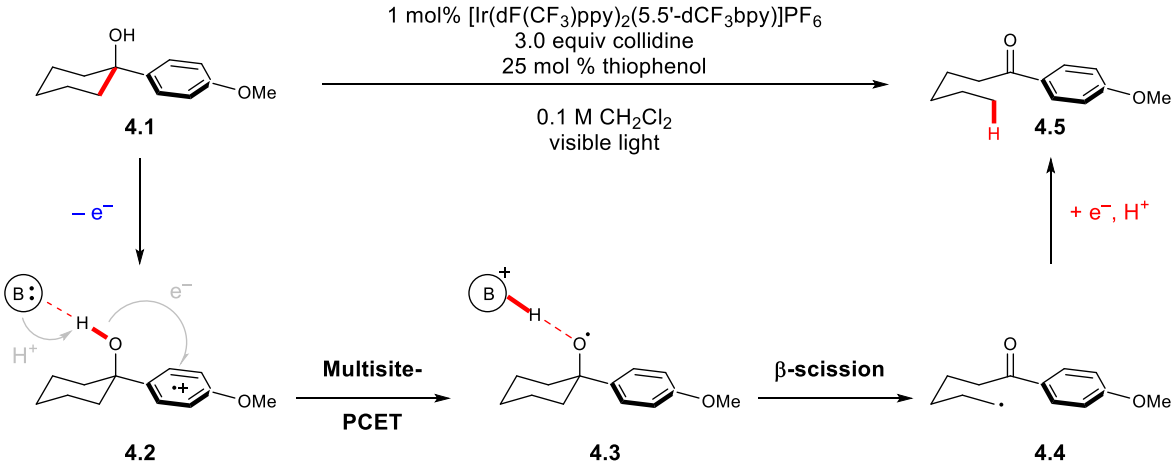

**Scheme 4.1.** Synthetic methodology design

We became interested in developing new deconstructive diversification methods based on our recent work in photocatalytic oxidative functionalization. We have demonstrated that Cu(II) salts, which are effective C($sp^3$) radical oxidants, are compatible with photocatalysis, and enable a wide range of net-oxidative photoredox transformations *via* carbocation intermediates. In these reactions, organoradical intermediates are generated by well-known photoinduced pathways and oxidized in the presence of Cu(II) salts.[20,21] We questioned whether a similar series of elementary steps could enable deconstructive diversification of cyclic alcohols (Scheme 4.1.B). In our mechanistic proposal, an alkoxy radical generated by photocatalyzed processes would undergo β-C–C scission to yield a ketone and a distal alkyl radical (**B**). Oxidation of **B** by Cu(II) would afford the corresponding carbocation intermediate (**C**). We envisioned that **C** could undergo either elimination or substitution to afford **D** and **E** respectively depending on the structural features of **C** as Kochi observed.[22] Thus, this new platform would effectively complement classical deconstructive functionalization reactions.

## 4.2 Reaction Design and Optimization

As a starting point for our investigations, we initially considered Knowles' recent reports of oxygen-centered radical initiating deconstructive functionalization of cycloalkanols. This strategy is attractive

because it operates smoothly with both strained and unstrained cycloalkanols under similar conditions as our previously developed net-oxidative photoredox transformations. In Knowles' proposed mechanism, of the electron-rich arene (**4.1**) is oxidized by the excited state photocatalyst, generating a transient radical cation (**4.2**). This intermediate undergoes intramolecular proton-coupled electron transfer (PCET), wherein deprotonation of the hydroxyl group by the Brønsted base in concert with one-electron reduction of the arene radical cation provides the key oxyl radical intermediate (**4.3**). Based on this proposal, we hypothesized that the organoradical intermediate (**4.4**) generated by β-C–C scission could be intercepted by a Cu(II) oxidant and be diverted towards oxidative elimination to an alkene.

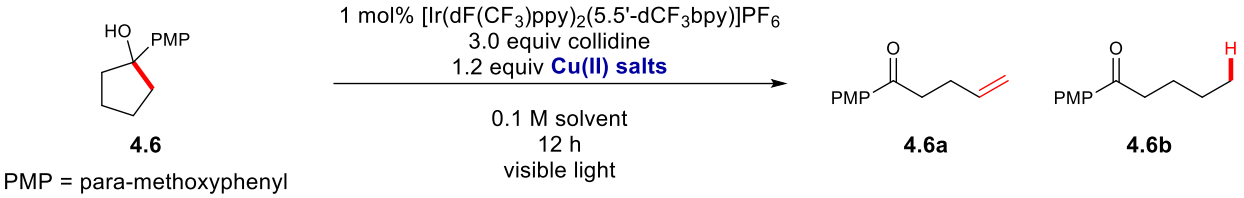



**Scheme 4.2.** Catalytic ring-opening of cyclic alcohols *via* multisite-PCET

Early attempts using the previously established O–H PCET conditions in the presence of $Cu(TFA)_2$•MeCN as a terminal oxidant resulted in only the redox-neutral deconstructive hydrogen atom transfer product (**4.6b**) with poor mass balance (entry 1). This suggested that radical initiation had occurred under these conditions, but that the radical oxidation step was challenging. To this end, we explored a wide variety of solvents (entries 1–4). A survey of solvents revealed promising reactivity in MeCN, which afforded the deconstructive elimination product **4.6a** (entry 4) along with significant amounts of the undesired non-oxidized product **4.6b** with moderate mass balance. Next, we examined alternate Cu(II) salts (entries 4–10) and found that the more basic counterions were generally more effective, with $Cu(OAc)_2$ providing alkene **4.6a** in 84% yield without any observable formation of **4.6b** (entry 9). This result was

consistent with Kochi's proposal that alkenes formation from an alkylcopper intermediate *via* synchronous loss of a β-proton with electron transfer should be more facile as the basicity of counterion increases.[22] Finally, control experiments indicated that there was no reaction in the absence of either the photocatalyst, visible light, or Cu(II) salt (entries 10–12).

**Table 4.1.** Reaction optimization[a]




**4.6** **4.6a** **4.6b**

PMP = para-methoxyphenyl

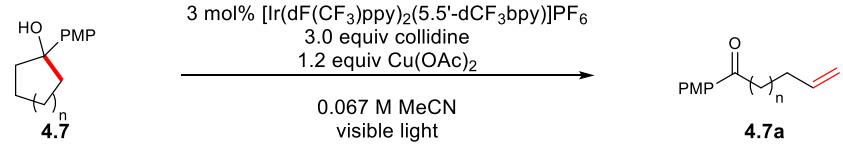
| Entry | Cu(II) salts | solvent | 4.6 (%) | 4.6a (%) | 4.6b (%) |
|---|---|---|---|---|---|
| 1 | $Cu(TFA)_2$•MeCN | $CH_2Cl_2$ | 7 | 0 | 47 |
| 2 | $Cu(TFA)_2$•MeCN | PhMe | 30 | 0 | 53 |
| 3 | $Cu(TFA)_2$•MeCN | THF | 60 | 0 | 33 |
| 4 | $Cu(TFA)_2$•MeCN | MeCN | 40 | 9 | 14 |
| 5 | $Cu(OTf)_2$ | MeCN | trace | trace | 13 |
| 6 | $CuBr_2$ | MeCN | trace | 0 | 11 |
| 7 | $CuCl_2$ | MeCN | trace | 0 | 47 |
| 8 | $CuSO_4$ | MeCN | 32 | 16 | 9 |
| 9 | $Cu(OAc)_2$ | MeCN | 13 | 84 | 0 |
| | ***chage from the optimal condtion (entry 9)*** | | | | |
| 10 | no light | | 103 | 0 | 0 |
| 11 | no photocatalyst | | 98 | 0 | 0 |
| 12 | no Cu(II) salt | | 109 | 0 | 0 |

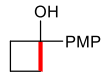
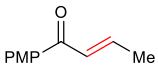
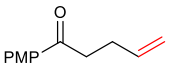
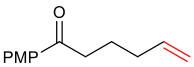
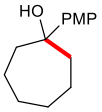
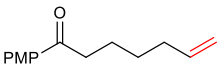
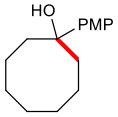
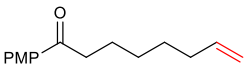
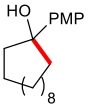
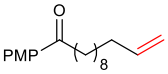
a) Yields determined by GC analysis using 1-methylnapthalene as a calibrated internal standard.

With these optimized conditions, we have commenced an evaluation the scope of the deconstructive elimination protocol. At the preparative scale the model reaction required significantly longer reaction time. Fortunately, the reaction time was shortened by simply increasing the photocatalyst loading and the photon flux, resulting in 83% isolated yield of **6a**. Cyclobutanol **8** reacted smoothly to form a β,γ-unsaturated ketone, but underwent *in situ* isomerization to form the thermodynamically more stable α,β-unsaturated ketone (**4.8a**) under the reaction conditions. Besides **8**, cyclic alcohols of various other ring sizes (5-,6-,7-,8-, and 12-membered rings) displayed the desired reactivity to access γ,δ-, δ,ε-, ε,ζ-, ζ,η-, and λ,μ-unsaturated

ketone products (**9a**–**12a**). The moderate isolated yield of **4.11a** was due to the difficult separation from the reduced product (**4.11b**).

**Table 4.2.** Exploring different ring sizes of cyclic alcohols[a]

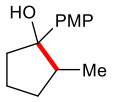
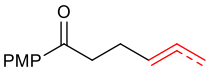
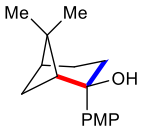
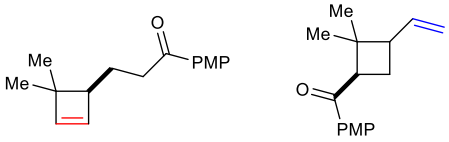


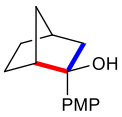
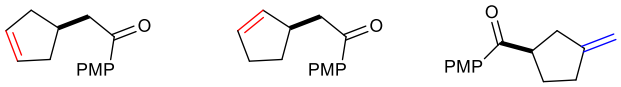

| Starting Material | Product | Starting Material | Product | Starting Material | Product |
|---|---|---|---|---|---|
|  |  |  |  |  |  |
| **4.8** | **4.8a**, 88% | **4.6** | **4.6a**, 83% | **4.9** | **4.9a**, 85% |
|  |  |  |  |  |  |
| **4.10** | **4.10a**, 77% | **4.11** | **4.11a**, 42% | **4.12** | **4.12a**, 87% |

a) Yields represent the isolated yields of products.

Unsymmetrical cyclic alcohol **4.13** underwent bond scission with high selectivity to generate the more stable radical intermediate (Table 4.3, **4.13a**). The deconstructive elimination of bridged bicycle **4.14**, exhibited the opposite selectivity in favoring the formation of the primary radical, which was consistent with the relative radical stabilization energies of primary radical and cyclobutyl radical.[23] Interestingly, for the structurally similar **4.15**, the C–C bond cleavage step occurred with poor selectivity, despite the fact that the secondary radical intermediate was significantly more stable than the competing primary radical. In addition, mixtures of constitutional isomers were observed in experiments where elimination could occur from more than one position (**4.13a** and **4.15a**). These results showed that the selectivity of C–C bond cleavage was governed by multiple factors, as opposed to solely dependent on radical stability.

**Table 4.3.** Exploring unsymmetrical cyclic alcohols[a]

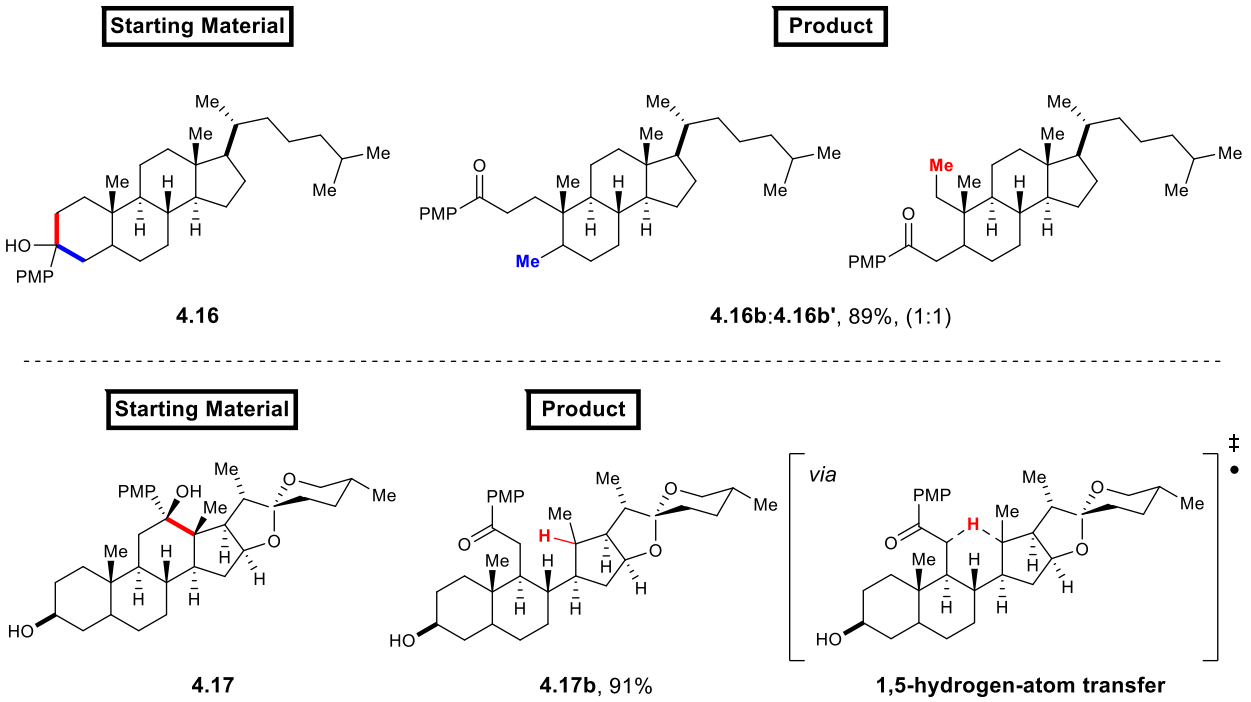
| Starting Material | Product | Starting Material | Product |
|---|---|---|---|
|  |  |  |  |
| **4.13** | **4.13a**, quant (1:1) | **4.14** | **4.14a**:**4.14a'**, 55%, (1:4) |

| Starting Material | Product |
|---|---|
|  |  |
| **4.15** | **4.15a**:**4.15a'**:**4.15a''**, 83%, (1:1:1)[b] |

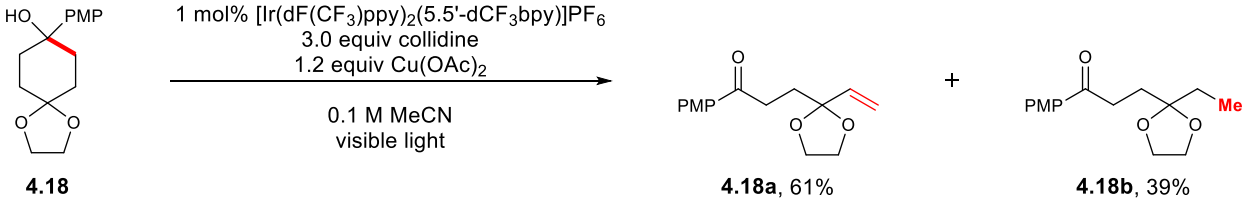
a) Reaction conditions: cyclic alcohol (0.1 mmol, 1 equivalent), [Ir(dF(CF$_3$)ppy)$_2$(5,5'-dCF$_3$bpy)]PF$_6$ (1 mol%), collidine (3 equivalent), Cu(OAc)$_2$ (1.2 equivalent), and MeCN (0.1 M) unless otherwise noted. Yields determined by $^1$H NMR analysis using 1-methylnapthelene as a calibrated internal standard. b) Reaction conditions: cyclic alcohol (0.4 mmol, 1 equivalent), [Ir(dF(CF$_3$)ppy)$_2$(5,5'-dCF$_3$bpy)]PF$_6$ (3 mol%), collidine (3 equivalents), Cu(OAc)$_2$ (1.2 equivalents), and MeCN (0.067 M). Yields represent the isolated yields of products.

Having established that relatively simple benzylic cycloalkanols were suitable substrates for this reaction, we were interested in applying this strategy to complex substrates. Interestingly, steroid-derived benzylic cycloalkanol (**4.16**) underwent redox-neutral deconstruction to afford a 1:1 mixture of **4.16b** and **4.16b'** in an excellent yield. Similar reactivity was observed with cycloalkanol **4.17** and the C–C bond scission occurred with excusive formation of the more stable tertiary radical. We hypothesized that this unexpected reactivity could be due to kinetically competitive 1,5-hydrogen-atom transfer (HAT) in these highly organized systems. We hypothesized therefore that cycloalkanol **4.18** would similarly afford a significant amount of redox-neutral deconstruction product (**4.18b**) due to the Thorpe–Ingold effect. In accordance with the hypothesis, cycloalkanol **4.18** provided a mixture of oxidation product (**4.18a**) and hydrogen atom transfer product (**4.18b**) under the reaction conditions (Scheme 4.3).

**Table 4.4.** Exploring complex cyclic alcohols[a]

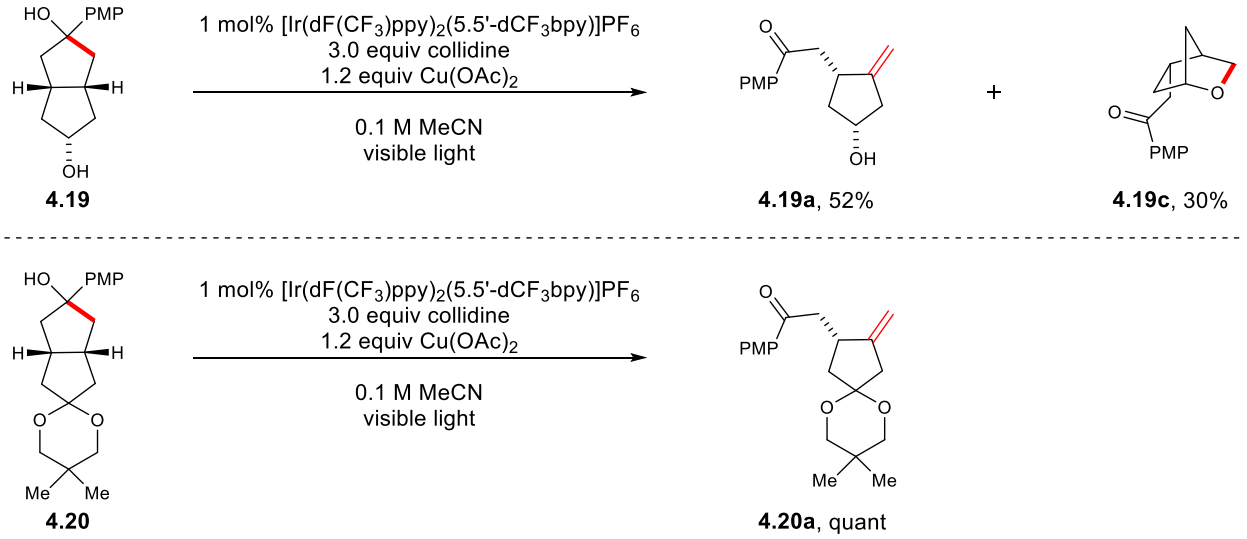



a) Reaction conditions: cyclic alcohol (0.1 mmol, 1 equivalent), $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}dCF_3bpy)]PF_6$ (1 mol%), collidine (3 equivalent), $Cu(OAc)_2$ (1.2 equivalent), and MeCN (0.067 M) unless otherwise noted. Yields determined by $^1H$ NMR analysis using 1-methylnapthelene as a calibrated internal standard.




**Scheme 4.3.** Probing a competitive 1,5-HAT pathway

Cycloalkanols **4.19** and **4.20** were then evaluated to examine the functional group tolerance of this strategy. Unexpectedly, the yield of the desired product (**4.19a**) was moderate, with significant competitive formation of a substitution product, **4.19c**. On the other hand, acetal-containing cycloalkanol **4.20** reacted smoothly to afford **4.20a** in a quantitative yield. Further studies of the functional group compatibility of this reaction are still ongoing.




**Scheme 4.4.** Exploring other classes of cyclic alcohols

To further expand the scope and utility of this methodology, we next probed whether electron-rich aryl groups other than *p*-methoxyphenyl could be accommodated as the initial site of oxidation. A range of arene-substituted cyclopentanols, including *m*-methoxyphenyl (**4.21**), benzofuran (**4.22**), benzothiophene (**4.23**), naphthalene (**4.24**), and phenol (**4.25**), could serve as efficient oxidation sites. These studies to extend the scope of electron-rich arenes are also ongoing.

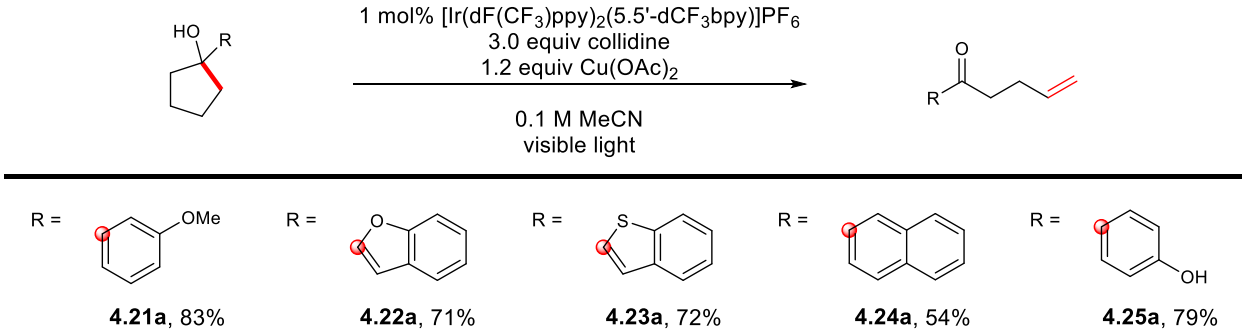
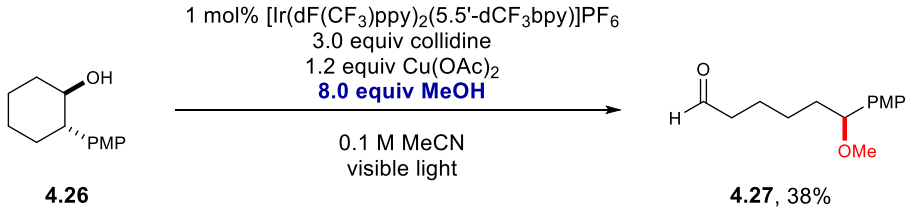



**Table 4.5.** Substrate scope

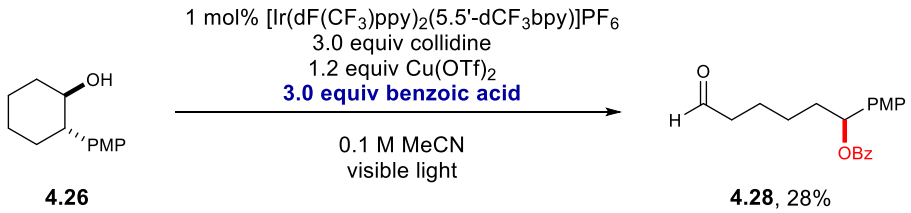
Finally, we are interested in showing that the use of Cu(II) terminal oxidants with photoredox catalysis provides a general strategy for oxidative deconstruction of cycloalkanols. Early studies by Kochi demonstrated that diverse reaction pathways were available following the Cu(II)-mediated oxidation of organoradical intermediates depending on their structural features. Oxidation of simple primary and secondary alkyl radicals by Cu(II) salts usually afforded elimination products. On the other hand, allylic

radicals selectively provided only substitution products, while benzylic, homoallylic, and tertiary radicals usually produced a mixture of elimination and substitution products. With these precedents in mind, we initiated a study on the reactivity of the easily accessible cycloalkanol **4.26** in the presence of Cu(II) salts and nucleophiles. Gratifyingly, it was found that the substitution products **4.27** and **4.28** could be formed using this platform in the presence of methanol and benzoic acid as nucleophiles, respectively. These results suggested that deconstructive substitution reactions would be compatible with a broad range of nucleophiles. Future studies will focus on optimizing the deconstructive substitution reaction conditions, investigating the reactivities of structurally different carbocations, and expanding the scope of nucleophiles.




**4.26** **4.27**, 38%

**Scheme 4.5.** Probing the reactivity of deconstructive methoxylation




**4.26** **4.28**, 28%

**Scheme 4.6.** Probing the reactivity of deconstructive benzoyloxylation

### 4.3 Conclusions and Outlook

In this section, we have demonstrated the first example of diverting alkoxy radicals generated by photocatalytic multisite-PCET toward cationic reactivity to enable remote oxidative functionalization. This strategy allows the incorporation of functional groups that were not possible with previous strategies including alkenes, ethers, and esters. Moreover, the functional groups are installed at remote position from the carbonyl, while most existing methods are only suitable for α- or β-functionalizations. From a broader perspective, these results are intriguing because they demonstrate that the organoradical intermediates that are readily generated by photoredox activation can be diverted towards elimination, substitution, and other

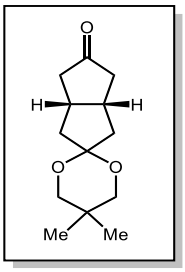
reactions typical of cationic intermediates. This combination thus provides a promising new platform to design new bond-forming oxidative functionalization reactions with broad utility in synthetic chemistry

## 4.4 Experimental

### 4.4.1 General Experimental Information

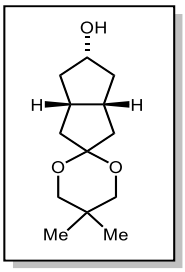
All reactions were performed under an $N_2$ atmosphere unless otherwise stated. All glassware was dried in an oven at 120 °C for at least 2 h prior to use and allowed to cool in a desiccator cabinet. MeCN, THF, $Et_2O$, DMF, toluene, and $CH_2Cl_2$ were purified by elution through alumina as described by Grubbs.[24] All other chemicals were purchased from commercial suppliers and used as received. Flash column chromatography was performed with normal phase $SiO_2$ (Sigma-Aldrich or Macherey-Nagel, 60 Å pore size, 230-400 mesh, 40-63 µm particle size) according to the method of Still.[25] Reactions were monitored by thin-layer chromatography (Silicycle, 250 µm thickness), and visualization was accomplished with a 254 nm UV light or by staining with $KMnO_4$ solution (3.0 g of $KMnO_4$ and 20.0 g of $K_2CO_3$ in 5 mL of 5% aq. NaOH and 300 mL $H_2O$) or by staining with dinitrophenylhydrazine (DNP) (12.0 g of 2,4-dinitrophenylhydrazine in 60 mL $H_2SO_4$, 80 mL $H_2O$, and 200 mL 95% EtOH). $^1H$ and $^{13}C\{^1H\}$ NMR data for all previously uncharacterized compounds were obtained using a Bruker AVANCE-400 or Bruker AVANCE-500 spectrometer with DCH, Prodigy, or BBFO+ probes. $^1H$ spectra were internally referenced to tetramethyl silane (0.00 ppm). 13C{1H} spectra were internally referenced to $CDCl_3$ (77.16 ppm). $^1H$ NMR spectra were tabulated as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet, br = broad), coupling constant(s), and number of protons. $^{13}C$ NMR spectra were tabulated by observed peak. Mass spectrometry was performed with a Thermo Q ExactiveTM Plus. IR spectra were obtained using a Bruker Alpha Platinum FTIR spectrometer equipped with an attenuated total reflectance (ATR) sampling head. Melting points were obtained using a Stanford Research Systems DigiMelt apparatus.

### 4.4.2 Synthesis of Tertiary Alcohols



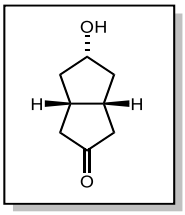
**(3aR,6aS)-5',5'-dimethyltetrahydro-1H-spiro[pentalene-2,2'-[1,3]dioxan]-5(3H)-one (4.S1)**:

Prepared as described by Wilson. Spectral data were consistent with those reported previously.[26]



**(3aR,5s,6aS)-5',5'-dimethylhexahydro-1H-spiro[pentalene-2,2'-[1,3]dioxan]-5-ol (4.S2)**:

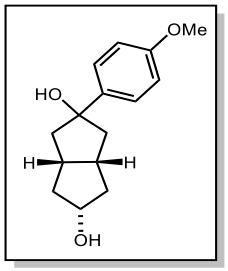
To a solution of (3aR,6aS)-5',5'-dimethyltetrahydro-1H-spiro[pentalene-2,2'-[1,3]dioxan]-5(3H)-one (**4.S1**, 3.0 g, 13 mmol, 1 equiv) in methanol (38 mL) was added sodium borohydride (1.0 g, 26 mmol, 2.0 equiv) at –45 °C. Upon addition, the reaction mixture was allowed to room temperature. After 2 hours, water (50 mL) and diethyl ether (50 mL) were added and the layers were separated. The aqueous layer was extracted with diethyl ether (2 x 50 mL), the combined organic layers were dried over sodium sulfate, filtered, and concentrated. The crude product was carried on to the next step.



**(3aR,5s,6aS)-5-hydroxyhexahydropentalen-2(1H)-one (4.S3)**:

To a solution of (3aR,5s,6aS)-5',5'-dimethylhexahydro-1H-spiro[pentalene-2,2'-[1,3]dioxan]-5-ol (**S2**, 3.0 g, 13 mmol, 1 equiv) in acetone (100 mL) and water (1.3 mL) was added *p*-toluenesulfonic acid (150 mg, 0.86 mmol, 0.065 equiv). After 3 hours, aq sat $NaHCO_3$ (50 mL) was added and the layers were separated.

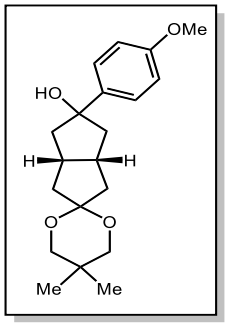
The aqueous layer was extracted with dichloromethane (5 x 20 mL), the combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The crude product was carried on to the next step.




**(2r,3aR,5s,6aS)-2-(4-methoxyphenyl)octahydropentalene-2,5-diol (4.19)**:

A flame-dried 100 mL round bottom flask was charged with a stir bar and degassed. Commercial 4-methoxyphenylmagnesium bromide solution (34 mL, 17 mmol, 2.0 equiv, 0.5 M THF solution) was syringed into the flask. (3aR,5s,6aS)-5-hydroxyhexahydropentalen-2(1H)-one (**4.S3**, 1.2 g, 8.5 mmol, 1.0 equiv) in 10 mL THF was added dropwise into the solution. The reaction was stirred at room temperature and consumption of starting material was monitored by GC. Upon completion, the reaction mixture was quenched by slow addition of ice water. The aqueous layer was extracted with ethyl acetate (3 x 10 mL) The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated. The crude product was purified by flash-column chromatography on silica gel (4:3:3, pentane: ethyl acetate: dichloromethane) to furnish (2r,3aR,5s,6aS)-2-(4-methoxyphenyl)octahydropentalene-2,5-diol **4.19** (810 mg, 38% over three steps) as a white solid.

**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.9 Hz, 2H), 4.28–4.27 (m, 1H), 3.80 (s, 3H), 2.84–2.81 (m, 2H), 2.74–2.66 (m, 2H), 2.40 (dd, *J* = 14.3, 9.4 Hz, 2H), 2.19 (ddd, *J* = 13.7, 9.3, 6.3 Hz, 2H), 2.10 (dd, *J* = 13.8, 1.8 Hz, 2H), 1.84 (dt, *J* = 13.6, 4.7 Hz, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.51, 139.27, 126.36, 113.55, 85.46, 76.16, 55.29, 48.66, 43.38, 41.76; **IR** (thin film): ν 3231, 2935, 1610, 1513, 1240, 824 ; **HRMS** (ASAP) $[M+H]^+$ calculated for $[C_{15}H_{21}O_3]$ requires *m/z* 231.1380, found *m/z* 231.1379; m.p = 116–118 °C.




**(3aR,6aS)-5-(4-methoxyphenyl)-5',5'-dimethylhexahydro-1H-spiro[pentalene-2,2'-[1,3]dioxan]-5-ol (4.20)**:

A flame-dried 100 mL round bottom flask was charged with a stir bar and degassed. Commercial 4-methoxyphenylmagnesium bromide solution (38 mL, 19 mmol, 2.0 equiv, 0.5 M THF solution) was syringed into the flask. (3aR,6aS)-5',5'-dimethyltetrahydro-1H-spiro[pentalene-2,2'-[1,3]dioxan]-5(3H)-one (**S1**, 1.3 g, 5.8 mmol, 1.0 equiv) in 10 mL THF was added dropwise into the solution. The reaction was stirred at room temperature and consumption of starting material was monitored by GC. Upon completion, the reaction mixture was quenched by slow addition of ice water. The aqueous layer was extracted with ethyl acetate (3 x 10 mL) The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated. The crude product was purified by flash-column chromatography on silica gel (7:2:1, pentane: ethyl acetate: dichloromethane) to furnish (3aR,6aS)-5-(4-methoxyphenyl)-5',5'-dimethylhexahydro-1H-spiro[pentalene-2,2'-[1,3]dioxan]-5-ol **13** (1.3 g, 71%) as a white solid.

**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H), 3.53 (s, 2H), 3.50 (s, 2H), 2.74–2.66 (m, 2H), 2.40 (s, 1H), 2.36–2.28 (m, 4H), 2.05 (dd, *J* = 13.3, 6.0 Hz, 2H), 1.96 (dd, *J* = 13.3, 3.0 Hz, 2H), 0.98 (s, 6H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.39, 139.10, 126.38, 113.43, 110.24, 84.77, 72.47, 71.70, 55.27, 47.67, 40.66, 39.58, 30.13, 22.53; **IR** (thin film): ν 3428, 2950, 2934, 1606, 1511, 1215, 1103, 823 ; **HRMS** (ESI) $[M+Na]^+$ calculated for $[C_{20}H_{28}O_3NaO]$ requires *m/z* 355.1880, found *m/z* 355.1876; m.p = 158–160 °C.

### 4.4.3 Synthesis of Alkene *via* Deconstructive Elimination

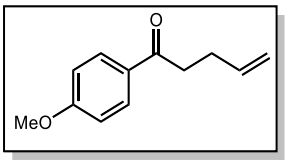
**General Synthesis Procedure A:**

A dry 6-dram vial (24 mL) outfitted with a PTFE/silicone septra was charged with [Ir(dF(CF3)ppy)2(5,5'-dCF3bpy)]PF6 (14 mg, 0.012 mmol, 0.03 equiv), $Cu(OAc)_2 \cdot H_2O$ (97 mg, 0.48 mmol, 1.2 equiv), and the relevant alcohol (0.40 mmol, 1.0 equiv). 6 mL of degassed anhydrous MeCN and redistilled collidine were added *via* syringe. The resulting mixture was stirred for a minute and was sparged with nitrogen for 10 minutes. After sparging, the puncture was sealed with electrical tape. The reaction was irradiated with two 40W Kessil Lamp PR160 (427nm) and let stir at room temperature with a fan to cool the reaction setup. After 36 hours, aq sat $NH_4Cl$ (5 mL) and ethyl acetate (12 mL) were added, the layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated. The crude product was purified by flash-column chromatography on silica gel.

**General Synthesis Procedure B:**

A dry 6-dram vial (24 mL) outfitted with a PTFE/silicone septra was charged with [Ir(dF(CF3)ppy)2(5,5'-dCF3bpy)]PF6 (14 mg, 0.012 mmol, 0.03 equiv), $Cu(OAc)_2 \cdot H_2O$ (97 mg, 0.48 mmol, 1.2 equiv), and the relevant alcohol (0.40 mmol, 1.0 equiv). 6 mL of degassed anhydrous MeCN and redistilled collidine were added *via* syringe. The resulting mixture was stirred for a minute and was sparged with nitrogen for 10 minutes. After sparging, the puncture was sealed with electrical tape. The reaction was irradiated with two 40W Kessil Lamp PR160 (427nm) and let stir at room temperature with a fan to cool the reaction setup. After 36 hours, additional [Ir(dF(CF3)ppy)2(5,5'-dCF3bpy)]PF6 (14 mg, 0.012 mmol, 0.03 equiv) and $Cu(OAc)_2 \cdot H_2O$ (97 mg, 0.48 mmol, 1.2 equiv) were added. The resulting mixture was stirred for a minute and was sparged with nitrogen for 10 minutes. After sparging, the puncture was sealed with electrical tape. The reaction was irradiated with two 40W Kessil Lamp PR160 (427nm) and let stir at room temperature with a fan to cool the reaction setup. After 36 hours, aq sat $NH_4Cl$ (5 mL) and ethyl acetate (12 mL) were added, the layers were separated, the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The

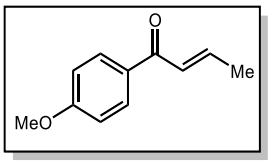
combined organic layers were dried over sodium sulfate, filtered, and concentrated. The crude product was purified by flash-column chromatography on silica gel.




**1-(4-methoxyphenyl)pent-4-en-1-one (4.6a)**:

Prepared according to general procedure A using 1-(4-methoxyphenyl)cyclopentan-1-ol (**4.6**, 77 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (5% $Et_2O$/pentane) to afford the titled compound as a colorless oil (68 mg, 89%). Note: Isolated product contains 5% reduced byproduct.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.9 Hz, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 5.91 (ddt, *J* = 16.8, 10.1, 6.5 Hz, 1H), 5.08 (dtd, *J* = 17.1, 1.7 Hz, 1H), 5.01 (dq, *J* = 10.2, 1.5 Hz, 1H), 3.87 (s, 3H), 3.02 (dd, *J* = 7.9, 6.9 Hz, 2H), 2.49 (dtt, *J* = 8.3, 6.7, 1.4 Hz, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 198.43, 163.81, 137.89, 130.69, 130.46, 115.54, 114.11, 55.85, 37.80, 28.77; **IR** (thin film): ν 3077, 2935, 2840, 1674, 1598, 1253, 1168 ; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{12}H_{15}O_2]$ requires *m/z* 191.1067, found *m/z* 191.1067.

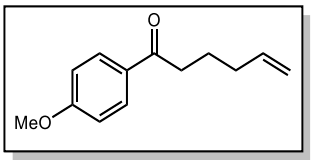



**(*E*)-1-(4-methoxyphenyl)but-2-en-1-one (4.8a)**:

Prepared according to general procedure A using 1-(4-methoxyphenyl)cyclobutan-1-ol (**4.8**, 71 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (5% $Et_2O$/pentane) to afford the titled compound as a colorless oil (62 mg, 88%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.9 Hz, 2H), 7.06 (dq, *J* = 15.2, 6.8 Hz, 1H), 6.94 (d, *J* = 8.9 Hz, 2H), 6.90 (dq, *J* = 15.2, 1.6 Hz, 1H), 3.87 (s, 3H), 1.99 (dd, *J* = 6.8, 1.6 Hz, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 188.99, 163.28, 143.91, 130.80, 127.17, 113.74, 55.46, 18.55; **IR** (thin film):

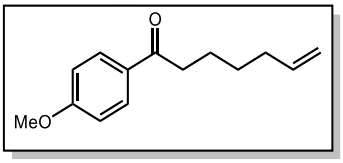
ν 2937, 1611, 1514, 1301, 1250, 1179 ; **HRMS** (ASAP) $[M+H]^+$ calculated for $[C_{11}H_{13}O_2]$ requires *m/z* 161.0961, found *m/z* 161.0963.




**1-(4-methoxyphenyl)hex-5-en-1-one (4.9a)**:

Prepared according to general procedure A using 1-(4-methoxyphenyl)cyclohexan-1-ol (**4.9**, 83 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (5% $Et_2O$/pentane) to afford the titled compound as a colorless oil (69 mg, 85%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 5.82 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.04 (dtd, *J* = 17.2, 1.7, 1.7 Hz, 1H), 4.99 (dq, *J* = 10.1, 1.5 Hz, 1H), 3.86 (s, 3H), 2.92 (t, *J* = 7.4 Hz, 2H), 2.20–2.10 (m, 2H), 1.84 (p, *J* = 7.4 Hz, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 198.85, 163.36, 138.16, 130.29, 130.20, 115.21, 113.69, 55.45, 37.40, 33.28, 23.57; **IR** (thin film): ν 3076, 2935, 1674, 1598, 1252, 1236, 1167 ; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{13}H_{17}O_2]$ requires *m/z* 205.1223, found *m/z* 205.1223.

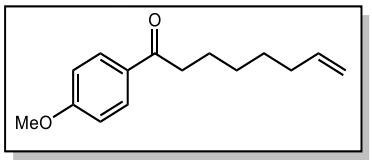



**1-(4-methoxyphenyl)hept-6-en-1-one (4.10a)**:

Prepared according to general procedure A using 1-(4-methoxyphenyl)cycloheptan-1-ol (**4.10**, 88 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (5% $Et_2O$/pentane) to afford the titled compound as a colorless oil (67 mg, 77%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 5.82 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.02 (dtd, *J* = 17.2, 1.7, 1.7 Hz, 1H), 4.95 (ddt, *J* = 10.2, 2.3, 1.3 Hz, 1H), 3.87 (s, 3H), 2.92 (t, *J* = 7.4 Hz, 2H), 2.14–2.04 (m, 2H), 1.75 (p, *J* = 7.5 Hz, 2H), 1.48 (p, *J* = 7.6 Hz, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 198.98, 163.35, 138.62, 130.32, 130.20, 114.61, 113.69, 55.46, 38.10, 33.62, 28.67, 24.08;

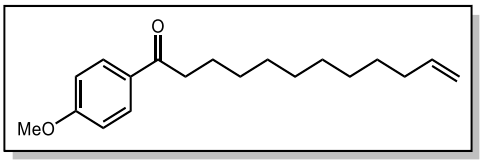
**IR** (thin film): ν 2933, 1674, 1599, 1256, 1160; **HRMS** (ASAP) $[M+H]^+$ calculated for $[C_{14}H_{19}O_2]$ requires *m/z* 219.1380, found *m/z* 219.1379.




**1-(4-methoxyphenyl)oct-7-en-1-one (4.11a)**:

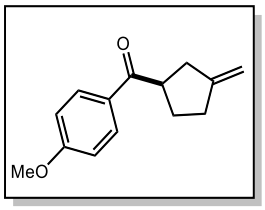
Prepared according to general procedure A using 1-(4-methoxyphenyl)cyclooctan-1-ol (**4.11**, 94 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (5% $Et_2O$/pentane) to afford the titled compound as a colorless oil (39 mg, 42%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.00 (dtd, *J* = 17.2, 1.9, 1.9 Hz, 1H), 4.96–4.91 (m, 1H), 3.87 (s, 3H), 2.91 (t, *J* = 7.4 Hz, 2H), 2.09–2.04 (m, 2H), 1.73 (p, *J* = 7.4 Hz, 2H), 1.48–1.36 (m, 4H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 199.10, 163.33, 138.94, 130.31, 130.21, 114.37, 113.68, 55.46, 38.24, 33.64, 28.91, 28.77, 24.44; **IR** (thin film): ν 3078, 3005, 2852, 1668, 1600, 1253, 1175; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{15}H_{21}O_2]$ requires *m/z* 233.1536, found *m/z* 233.1535.




**1-(4-methoxyphenyl)dodec-11-en-1-one (4.12a)**: Prepared according to general procedure A using 1-(4-methoxyphenyl)cyclododecan-1-ol (**4.12**, 117 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (5% $Et_2O$/pentane) to afford the titled compound as a white solid (101 mg, 87%).

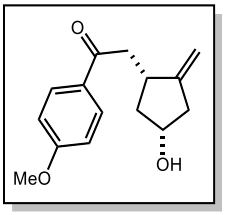
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.00 (dtd, *J* = 17.1, 1.7, 1.7 Hz, 1H), 4.93 (ddt, *J* = 10.2, 2.4, 1.2 Hz, 1H), 3.87 (s, 3H), 2.90 (t, *J* = 7.4 Hz, 2H), 2.03 (tdd, *J* = 8.0, 6.0, 1.4 Hz, 2H), 1.72 (p, *J* = 7.4 Hz, 2H), 1.41–1.26 (m, 12H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 199.25, 163.31, 139.25, 130.32, 130.25, 114.11, 113.67, 55.45, 38.33, 33.81, 29.48, 29.45, 29.12, 28.94, 24.66; **IR** (thin film): ν 2915, 2848, 1675, 1603, 1174; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{19}H_{29}O_2]$ requires *m/z* 289.2162, found *m/z* 289.2161; m.p = 52–53 °C.




**(*R*)-(4-methoxyphenyl)(3-methylenecyclopentyl)methanone (4.15a'')**:

Prepared according to general procedure A using (1*R*,2*R*,4*S*)-2-(4-methoxyphenyl)bicyclo[2.2.1]heptan-2-ol (**10**, 88 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (5% $Et_2O$/pentane) to afford the mixture of **10a**:**10a'**:**10a''** (1:1:1) as a colorless oil (72 mg, 83%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.9 Hz, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 4.90–4.89 (m, 2H), 3.87 (s, 3H), 3.77 (p, *J* = 8.2 Hz, 1H), 2.69 (ddd, *J* = 16.4, 8.6, 2.4 Hz, 1H), 2.60 (dd, *J* = 16.4, 8.2 Hz, 1H), 2.54–2.45 (m, 1H), 2.42–2.35 (m, 1H), 2.09–1.92 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 200.24, 163.40, 151.05, 130.66, 129.68, 113.76, 105.72, 55.48, 46.41, 36.64, 32.45, 30.27; **IR** (thin film): ν 2938, 1669, 1598, 1510, 1255, 1169; **HRMS** (ASAP) $[M+H]^+$ calculated for $[C_{14}H_{17}O_2]$ requires *m/z* 217.1223, found *m/z* 217.1222.

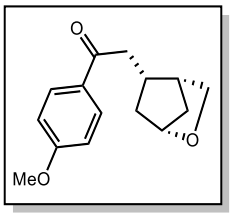



**2-((1*R*,4*R*)-4-hydroxy-2-methylenecyclopentyl)-1-(4-methoxyphenyl)ethan-1-one (*rac*-4.19a)**:

Prepared according to general procedure A using (2r,3aR,5s,6aS)-2-(4-methoxyphenyl)octahydropentalene-2,5-diol (**4.19**, 99 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (7:1.5:1.5, hexane: ethyl acetate: dichloromethane) to afford the title compound as a colorless oil (46 mg, 47%).

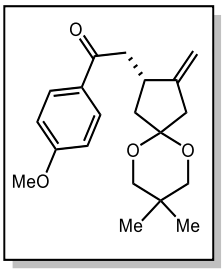
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 5.00 (d, *J* = 2.3 Hz, 1H), 4.88 (d, *J* = 2.3 Hz, 1H), 4.37–4.32 (m, 1H), 3.88 (s, 3H), 3.27 (dd, *J* = 16.9, 4.9 Hz, 1H), 3.20 (dd, *J* = 16.9, 8.4 Hz, 1H), 3.12–3.07 (m, 1H), 2.74–2.64 (m, 1H), 2.41 (ddt, *J* = 16.3, 3.8, 1.8 Hz, 1H), 2.35 (ddd,

*J* = 13.8, 8.8, 5.6 Hz, 1H), 1.89 (s, 1H), 1.54–1.44 (m, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 198.17, 163.44, 153.01, 130.38, 130.16, 113.68, 106.62, 71.81, 55.49, 43.74, 43.16, 41.76, 37.22; **IR** (thin film): ν 3349, 2933, 1672, 1623, 1599, 1257, 1170 ; **HRMS** (ASAP) $[M+H]^+$ calculated for $[C_{15}H_{19}O_3]$ requires *m/z* 247.1329, found *m/z* 247.1326.




**2-((1*R*,4*R*,5*R*)-2-oxabicyclo[2.2.1]heptan-5-yl)-1-(4-methoxyphenyl)ethan-1-one (*rac*-4.19c)**: The crude material was purified by flash-column chromatography (7:1.5:1.5, hexane: ethyl acetate: dichloromethane) to afford the title compound as a colorless oil (24 mg, 24%).

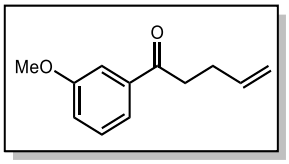
**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 4.32–4.27 (m, 1H), 3.89–3.87 (m, 1H), 3.87 (s, 3H), 3.61 (dd, *J* = 7.8, 2.3 Hz, 1H), 3.16 (dd, *J* = 16.7, 7.6 Hz, 1H), 3.10 (dd, *J* = 16.8, 6.8 Hz, 1H), 2.61–2.51 (m, 2H), 1.96 (ddd, *J* = 13.3, 11.1, 2.3 Hz, 1H), 1.82–1.76 (m, 1H), 1.62 (d, *J* = 9.9 Hz, 1H), 1.20 (ddd, *J* = 13.3, 5.5, 2.7 Hz, 1H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 198.21, 163.49, 130.28, 130.18, 113.76, 77.09, 67.35, 55.49, 41.33, 40.29, 38.61, 38.60, 33.59; **IR** (thin film): ν 2930, 1673, 1598, 1509, 1259, 1160 ; **HRMS** (ASAP) $[M+H]^+$ calculated for $[C_{15}H_{19}O_3]$ requires *m/z* 247.1329, found *m/z* 247.1327.




**(*S*)-2-(8,8-dimethyl-3-methylene-6,10-dioxaspiro[4.5]decan-2-yl)-1-(4-methoxyphenyl)ethan-1-one (*rac*-4.20a)**: Prepared according to general procedure A using (3aR,6aS)-5-(4-methoxyphenyl)-5',5'-dimethylhexahydro-1H-spiro[pentalene-2,2'-[1,3]dioxan]-5-ol (**4.20**, 129 mg, 0.40 mmol). The crude

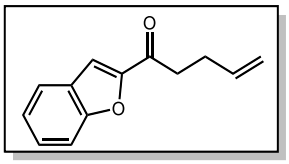
material was purified by flash-column chromatography (7:1.5:1.5, hexane: ethyl acetate: dichloromethane) to afford the title compound as a colorless oil (79 mg, 62%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 4.96 (d, *J* = 2.2 Hz, 1H), 4.88 (d, *J* = 2.2 Hz, 1H), 3.87 (s, 3H), 3.55 (d, *J* = 11.3 Hz, 1H), 3.49 (d, *J* = 11.3 Hz, 1H), 3.45 (d, *J* = 10.8 Hz, 1H), 3.44 (t, *J* = 10.9 Hz, 1H), 3.28–3.18 (m, 2H), 3.07–2.97 (m, 1H), 2.81–2.67 (m, 2H), 2.50 (ddd, *J* = 13.2, 8.3, 1.6 Hz, 1H), 1.71–1.63 (m, 1H), 1.01 (s, 3H), 0.90 (s, 3H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 197.89, 163.48, 151.14, 130.37, 130.18, 113.74, 106.89, 106.28, 72.18, 71.80, 55.48, 43.37, 43.03, 39.76, 37.36, 30.06, 22.57, 22.32; **IR** (thin film): ν 2953, 2864, 1724, 1599, 1395, 1223 ; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{20}H_{27}O_4]$ requires *m/z* 331.1904, found *m/z* 331.1901.




**1-(3-methoxyphenyl)pent-4-en-1-one (4.21a)**: Prepared according to general procedure B using 1-(3-methoxyphenyl)cyclopentan-1-ol (**4.21**, 78 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (5% $Et_2O$/pentane) to afford the titled compound as a colorless oil (64 mg, 83%).

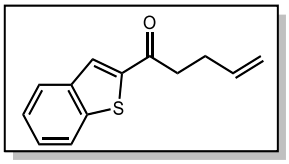
**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.54 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.49 (dd, *J* = 2.7, 1.5 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 1H), 7.11 (ddd, *J* = 8.3, 2.7, 1.0 Hz, 1H), 5.90 (ddt, *J* = 16.8, 10.1, 6.5 Hz, 1H), 5.09 (dtd, *J* = 17.1, 1.7, 1.7 Hz, 1H), 5.03–4.99 (m, 1H), 3.86 (s, 3H), 3.06 (t, *J* = 7.4 Hz, 2H), 2.53–2.45 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 199.39, 160.00, 138.48, 137.43, 129.71, 120.81, 119.60, 115.44, 112.45, 55.58, 38.01, 28.35; **IR** (thin film): ν 2941, 1684, 1597, 1582, 1261 ; **HRMS** (ASAP) $[M+H]^+$ calculated for $[C_{12}H_{15}O_2]$ requires *m/z* 191.1067, found *m/z* 191.1067.




**1-(benzofuran-2-yl)pent-4-en-1-one (4.22a)**: Prepared according to general procedure A using 1-(benzofuran-2-yl)cyclopentan-1-ol (**4.22**, 81 mg, 0.40 mmol). The crude material was purified by flash-

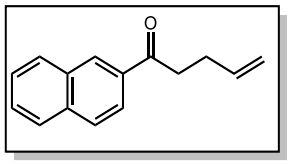
column chromatography (gradient 2.5% to 5% $Et_2O$/pentane) to afford the titled compound as a white solid (57 mg, 71%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.71 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.58 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.51 (d, *J* = 1.0 Hz, 1H), 7.48 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.31 (td, *J* = 7.5, 7.1, 1.0 Hz, 1H), 5.91 (ddt, *J* = 16.8, 10.1, 6.5 Hz, 1H), 5.12 (dtd, *J* = 17.1, 1.6, 1.6 Hz, 1H), 5.03 (dq, *J* = 10.2, 1.5 Hz, 1H), 3.06 (t, *J* = 7.7 Hz, 2H), 2.60–2.49 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 190.64, 155.63, 152.60, 136.85, 128.21, 127.07, 123.90, 123.28, 115.60, 112.64, 112.48, 38.08, 28.03; **IR** (thin film): ν 3078, 2918, 1680, 1641, 1556, 1138 ; **HRMS** (ASAP) $[M+H]^+$ calculated for $[C_{13}H_{13}O_2]$ requires *m/z* 201.0910, found *m/z* 201.0910; m.p = 43–45 °C.

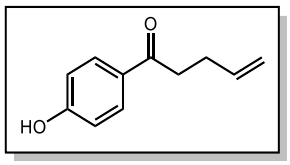



**1-(benzo[b]thiophen-2-yl)pent-4-en-1-one (4.23a)**: Prepared according to general procedure B using 1-(benzo[b]thiophen-2-yl)cyclopentan-1-ol (**4.23**, 88 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (2.5% $Et_2O$/pentane) to afford the titled compound as a white solid (62 mg, 72%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 0.8 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.47 (ddd, *J* = 8.2, 7.1, 1.4 Hz, 1H), 7.41 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 5.92 (ddt, *J* = 16.8, 10.1, 6.5 Hz, 1H), 5.12 (dtd, *J* = 17.1, 1.6, 1.6 Hz, 1H), 5.04 (ddt, *J* = 10.2, 1.4, 1.4 Hz, 1H), 3.12 (t, *J* = 7.2 Hz, 2H), 2.61–2.51 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 193.91, 143.71, 142.50, 139.15, 136.91, 128.88, 127.38, 125.90, 125.01, 123.03, 115.63, 38.44, 28.47; **IR** (thin film): ν 3072, 2920, 1662, 1642, 1518, 1164 ; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{13}H_{13}OS]$ requires *m/z* 217.0682, found *m/z* 217.0681; m.p = 56–58 °C.



**1-(naphthalen-2-yl)pent-4-en-1-one (4.24a)**: Prepared according to general procedure A using 1-(naphthalen-2-yl)cyclopentan-1-ol (**4.24**, 87 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (2.5% $Et_2O$/pentane) to afford the titled compound as a colorless oil (47 mg, 54%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.04 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 8.9z Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.60 (ddd, *J* = 8.1, 6.8, 1.4 Hz, 1H), 7.56 (ddd, *J* = 8.1, 6.8, 1.4 Hz, 1H),5.95 (ddt, *J* = 16.8, 10.1, 6.5 Hz, 1H), 5.12 (dtd, *J* = 17.1, 1.7, 1.7 Hz, 1H), 5.04 (ddt, *J* = 10.2, 1.5, 1.5 Hz, 1H), 3.21 (t, *J* = 7.3 Hz, 2H), 2.65–2.49 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 199.41, 137.37, 135.59, 134.31, 132.57, 129.65, 129.56, 128.47, 128.42, 127.80, 126.77, 123.90, 115.36, 37.85, 28.34; **IR** (thin film): ν 3059, 2976, 2916, 1678, 1627, 1231 ; **HRMS** (ESI) $[M+H]^+$ calculated for $[C_{15}H_{14}O]$ requires *m/z* 211.1117, found *m/z* 211.1117.



**1-(4-hydroxyphenyl)pent-4-en-1-one (4.25a)**: Prepared according to general procedure B using 4-(1-hydroxycyclopentyl)phenol (**4.25**, 72 mg, 0.40 mmol). The crude material was purified by flash-column chromatography (20% $Et_2O$/pentane) to afford the titled compound as a colorless oil (52 mg, 72%).

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.91 (ddt, *J* = 16.8, 10.1, 6.5 Hz, 1H), 5.17 (s, 1H), 5.08 (dtd, *J* = 17.1, 1.7 Hz, 1H), 5.01 (dq, *J* = 10.2, 1.5 Hz, 1H), 3.03 (t, *J* = 7.3 Hz, 2H), 2.53–2.42 (m, 2H); **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 197.97, 159.65, 137.44, 130.64, 130.44, 115.29, 115.21, 37.43, 28.35; **IR** (thin film): ν 3269, 3075, 1654, 1599, 1577, 1208, 1165 ; **HRMS** (ESI) $[M–H]^–$ calculated for $[C_{11}H_{11}O_2]$ requires *m/z* 175.0765, found *m/z* 175.0765.

## 4.5 References

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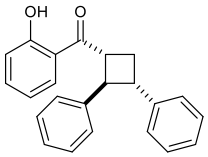
# Appendix A. $^{1}H$ and $^{13}C$ NMR Spectra for New Compounds

# List of Compounds for Chapter 2

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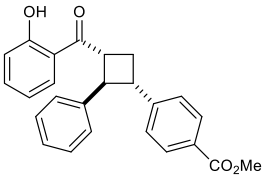


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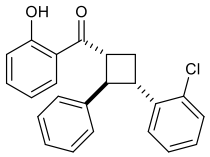


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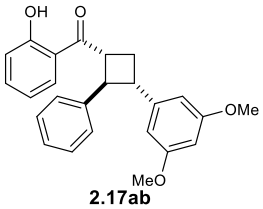


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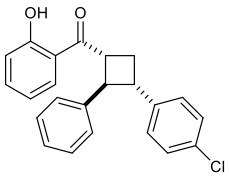


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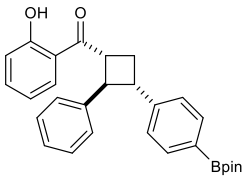


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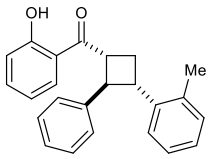


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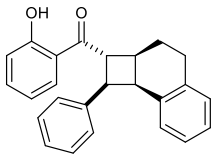


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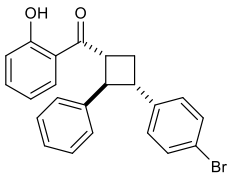


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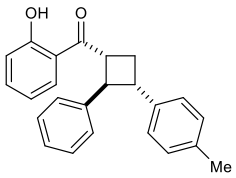


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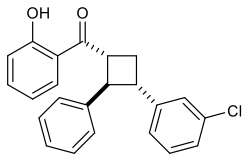


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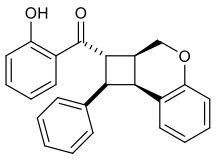


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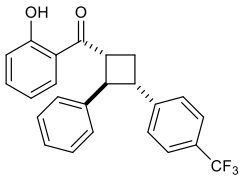


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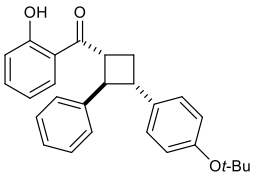


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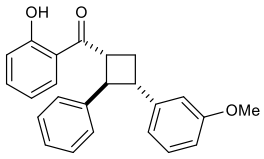


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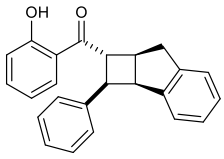
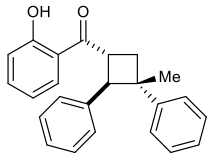



**2.17c**

# List of Compounds for Chapter 2

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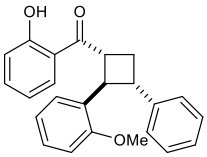


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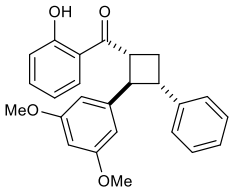
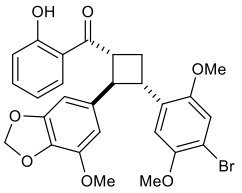
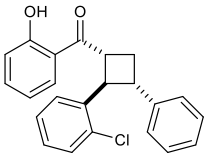


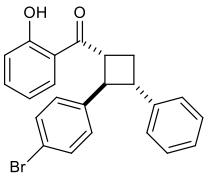

**2.28**



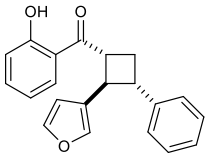

**2.37**



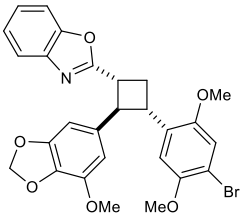

**2.21**



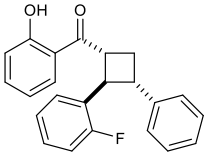

**2.25**



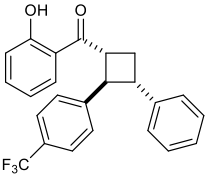

**2.29**



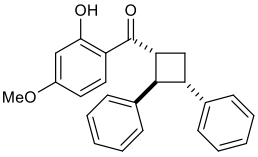

**2.41**



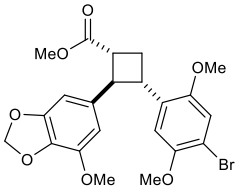

**2.22**



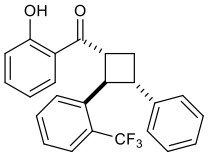

**2.26**




**2.30**




**2.42**

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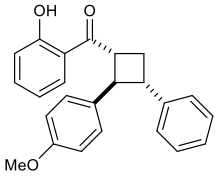


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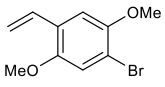
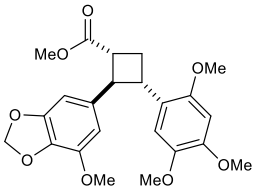
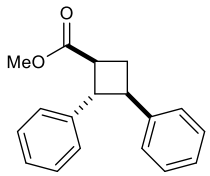



**2.36**




***ent*-2.1**

# List of Compounds for Chapter 2

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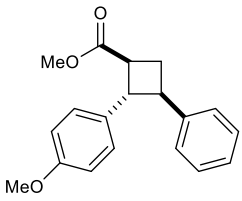


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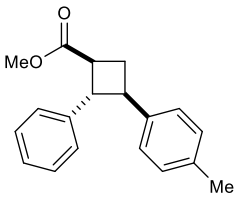


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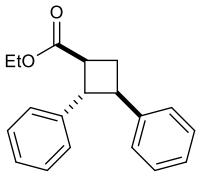


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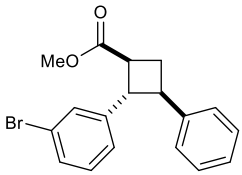
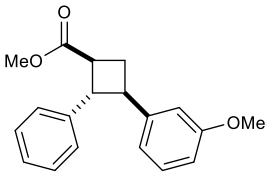



**2.51**

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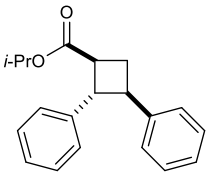


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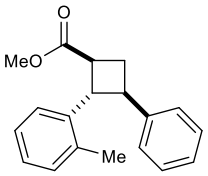


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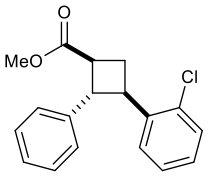


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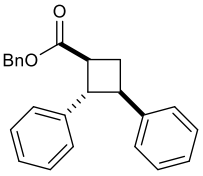
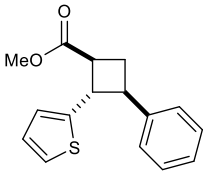



**2.48**

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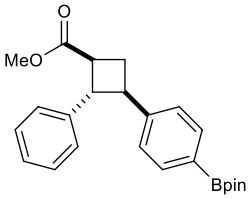
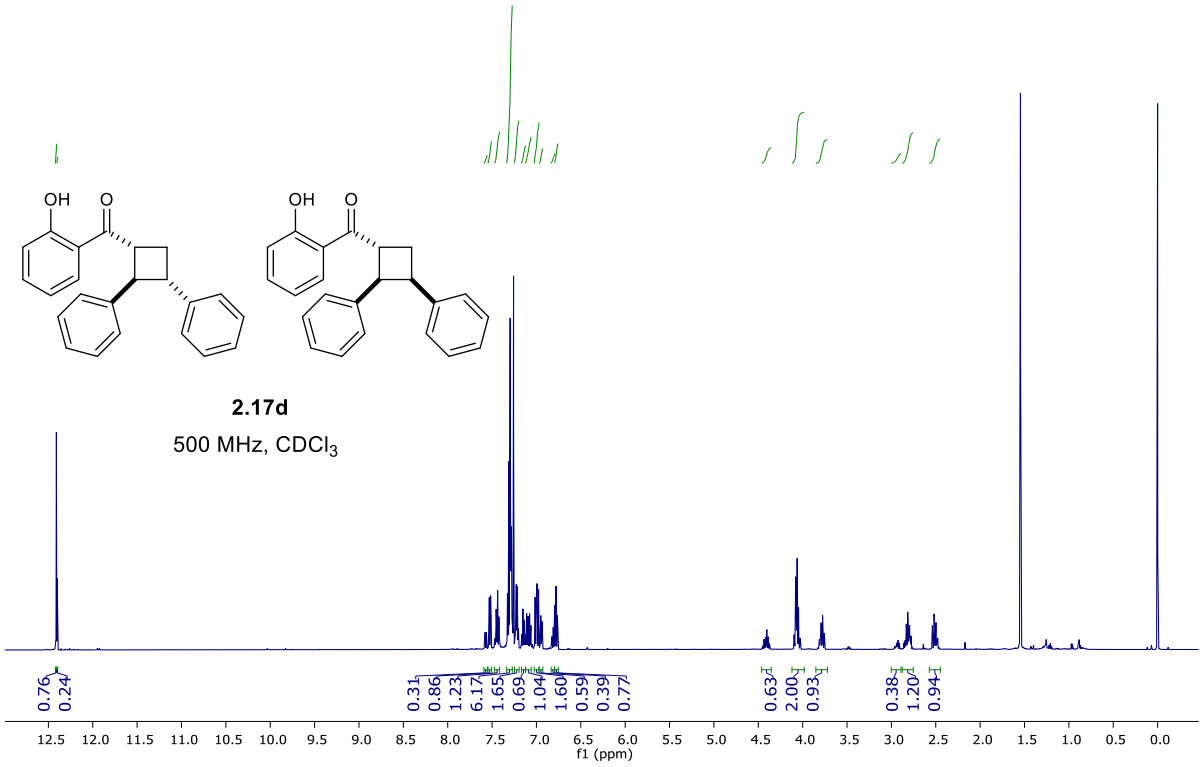
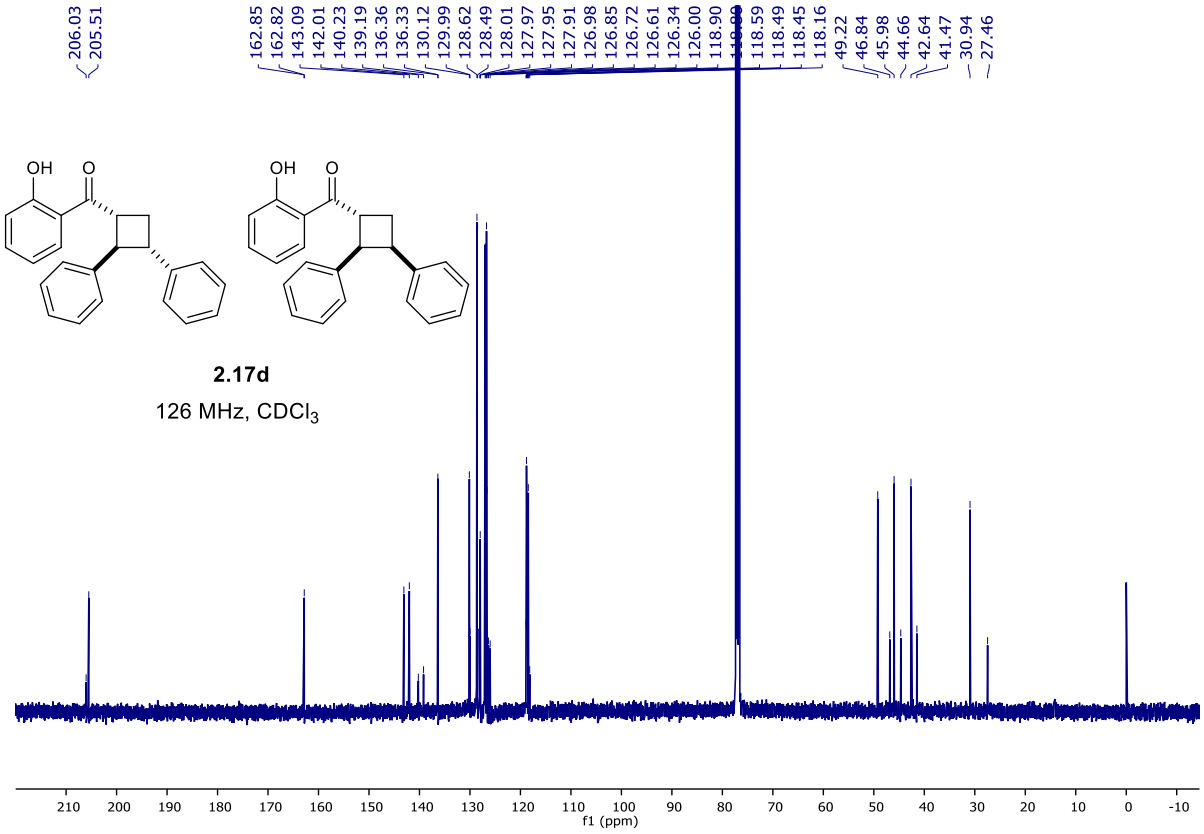
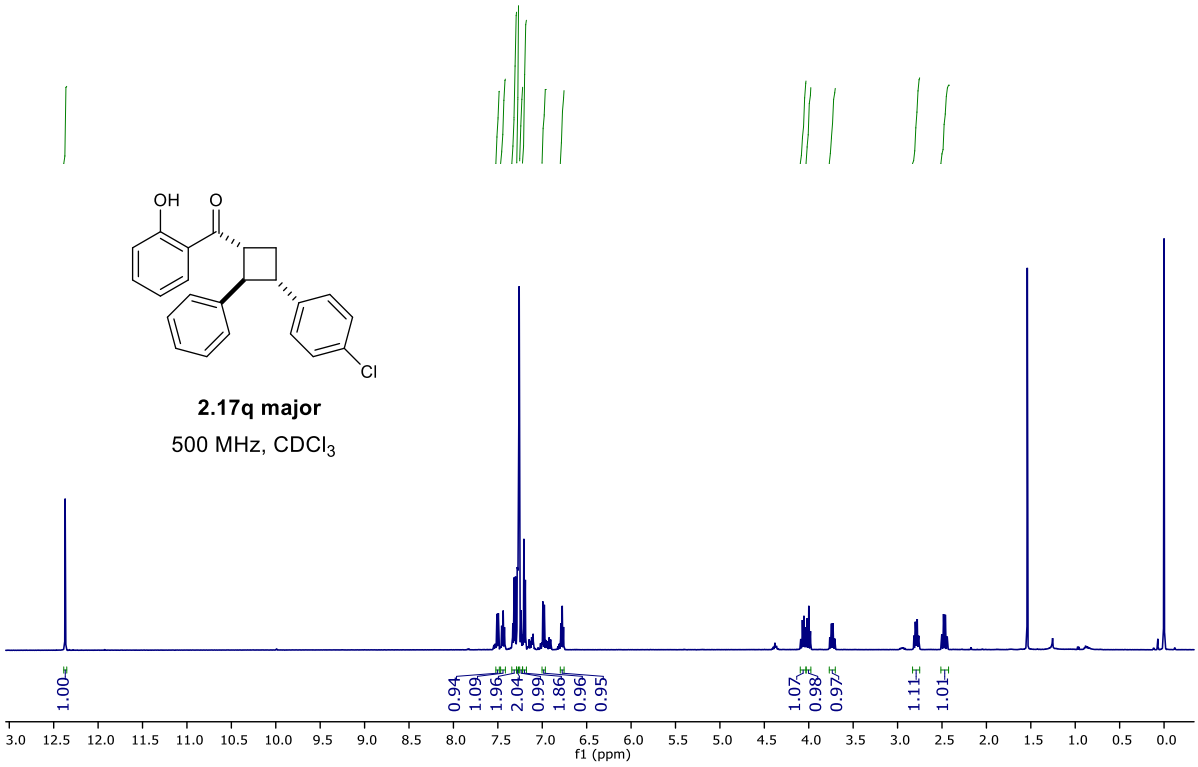
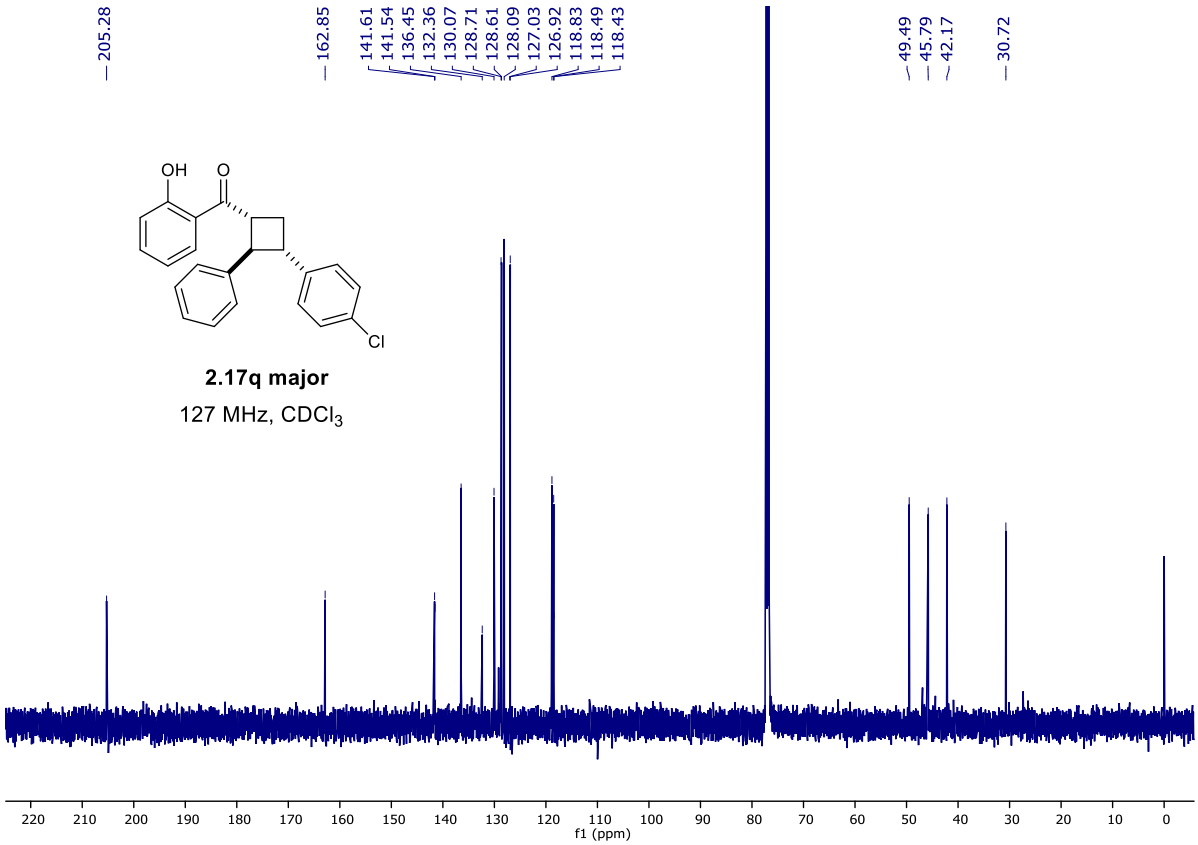


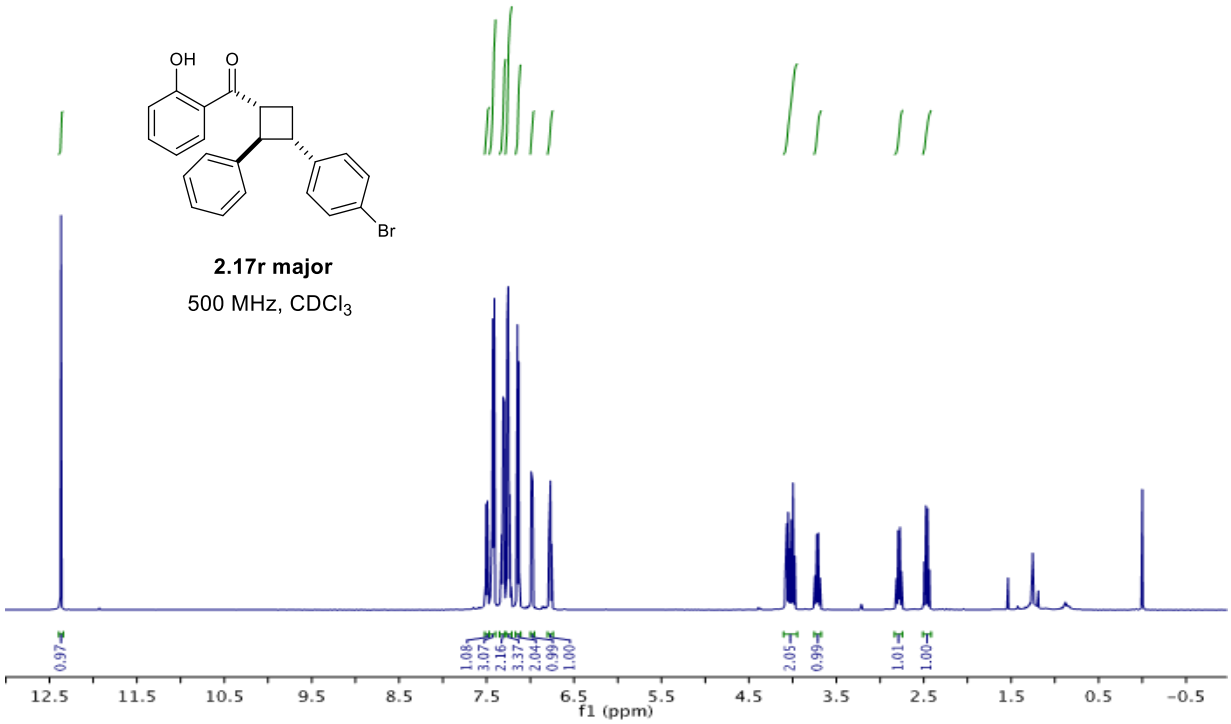

**2.57**


OH
O
OH
O
2.17d
500 MHz, CDCl3
0.76
0.24
0.31
0.86
1.23
6.17
1.65
0.69
1.04
1.60
0.59
0.39
0.77
0.63
2.00
0.93
0.38
1.20
0.94
f1 (ppm)


206.03
205.51
162.85
162.82
143.09
142.01
140.23
139.19
136.36
136.33
130.12
129.99
128.62
128.49
128.01
127.97
127.95
127.91
126.98
126.85
126.72
126.61
126.34
126.00
118.90
118.59
118.49
118.45
118.16
49.22
46.84
45.98
44.66
42.64
41.47
30.94
27.46
OH
O
OH
O
2.17d
126 MHz, CDCl3
f1 (ppm)

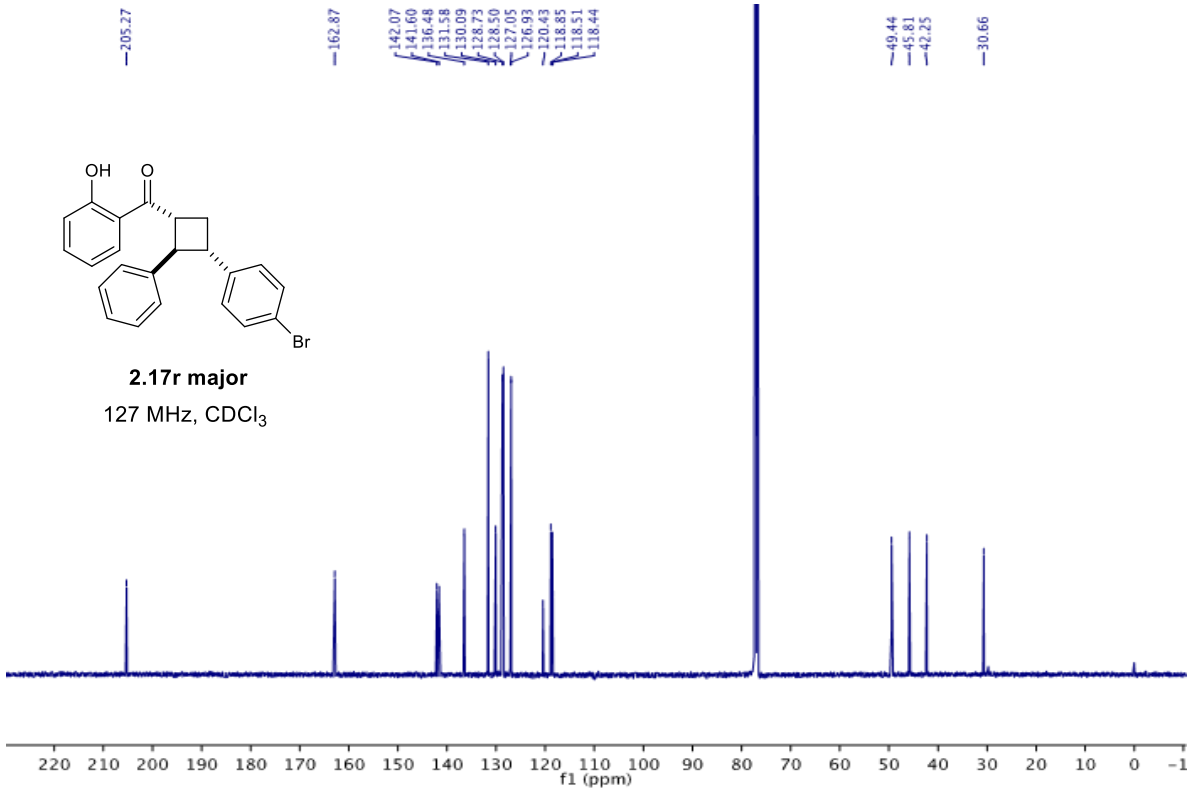

OH
O
Cl
2.17q major
500 MHz, CDCl3
1.00
0.94
1.09
1.96
2.04
0.99
1.86
0.96
0.95
1.07
0.98
0.97
1.11
1.01
f1 (ppm)


205.28
162.85
141.61
141.54
136.45
132.36
130.07
128.71
128.61
128.09
127.03
126.92
118.83
118.49
118.43
49.49
45.79
42.17
30.72
OH
O
Cl
2.17q major
127 MHz, CDCl3
f1 (ppm)



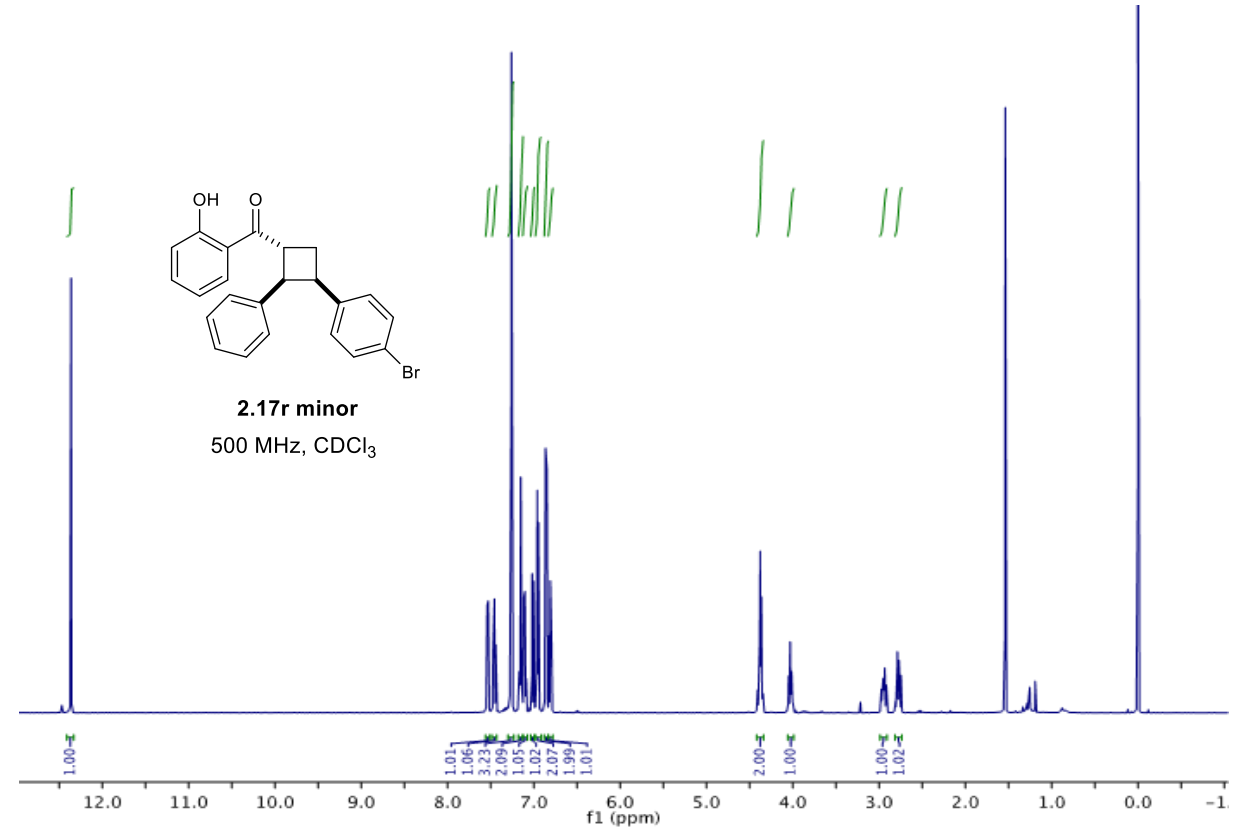

**2.17r major**

500 MHz, $CDCl_3$



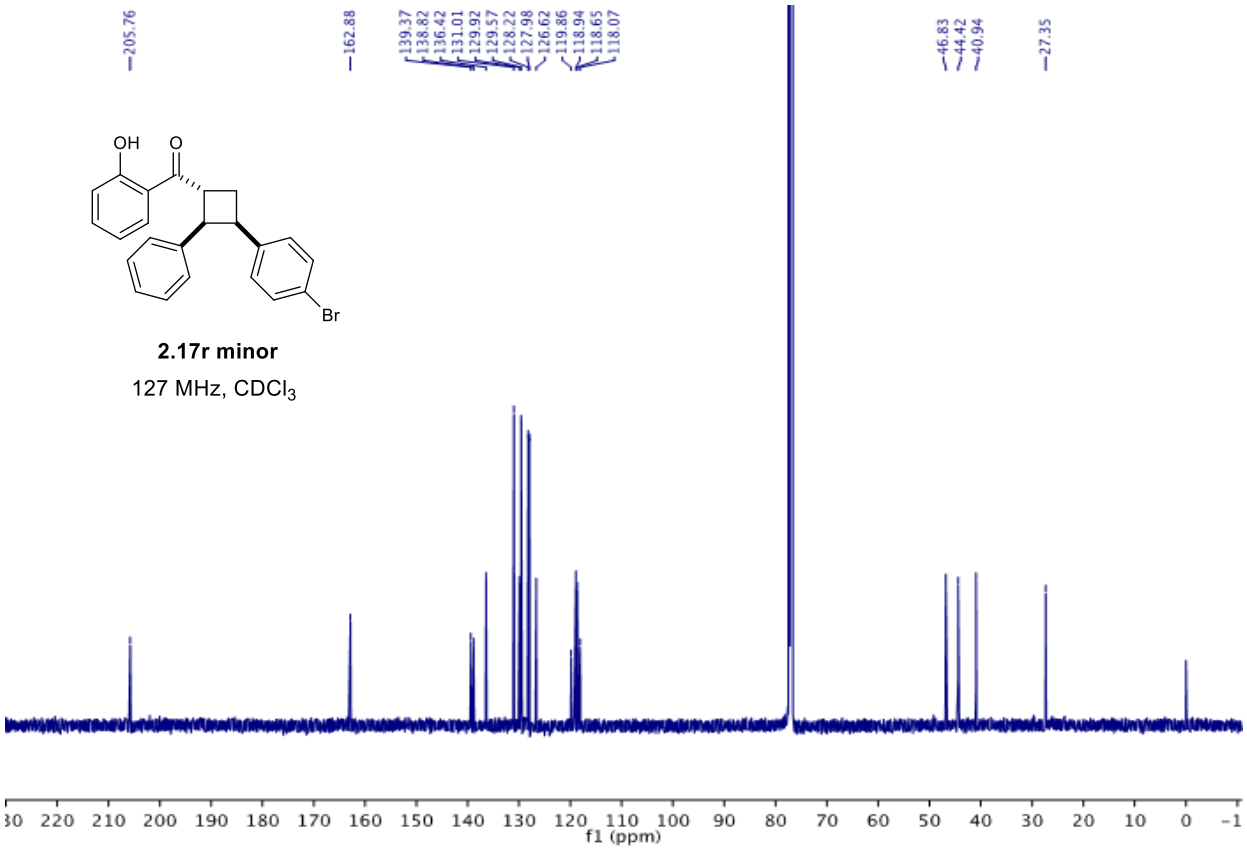

**2.17r major**

127 MHz, $CDCl_3$



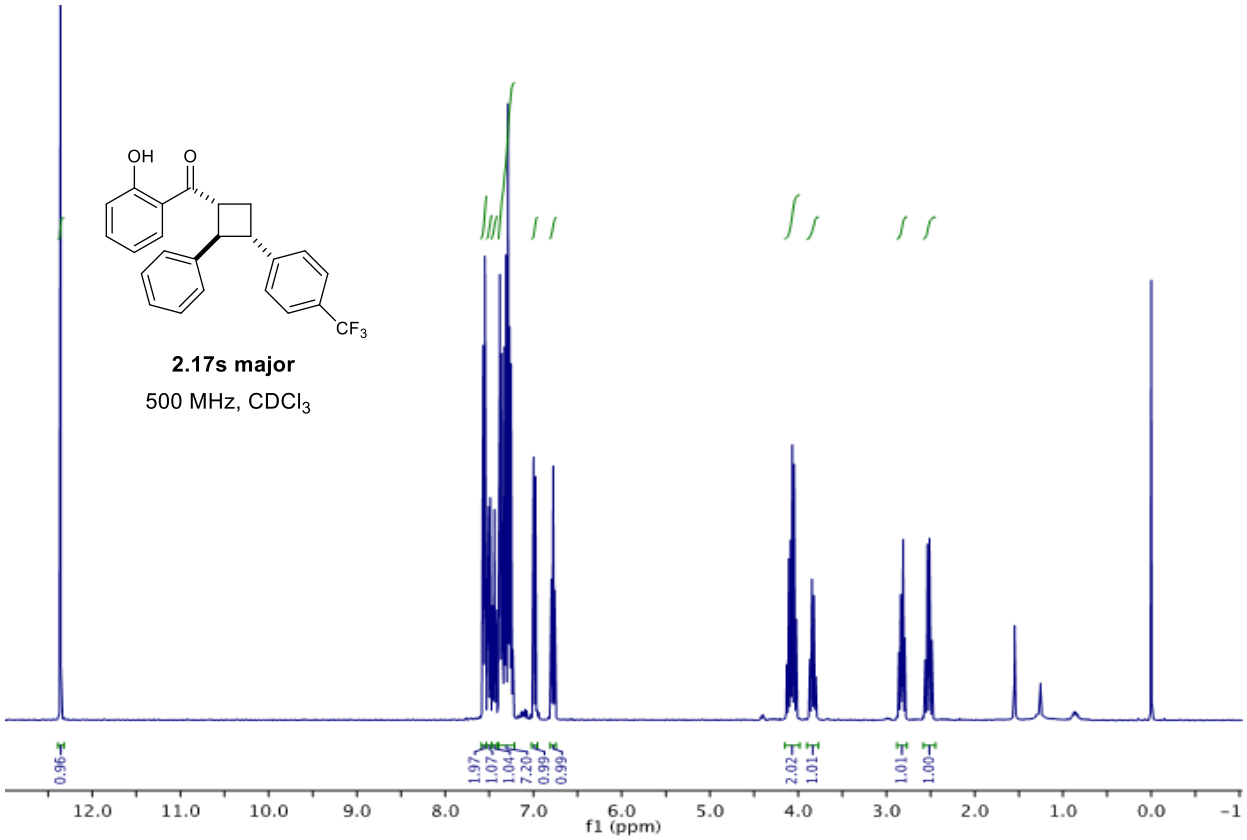

**2.17r minor**

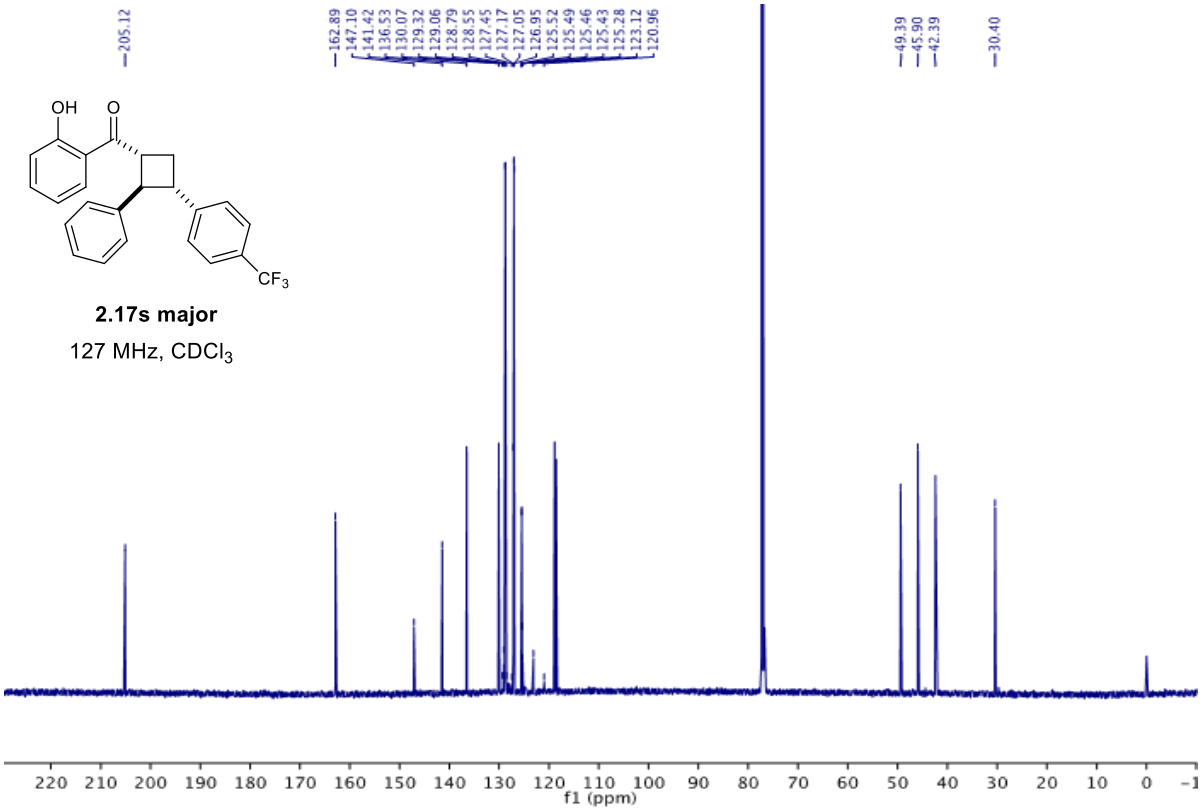
500 MHz, $CDCl_3$

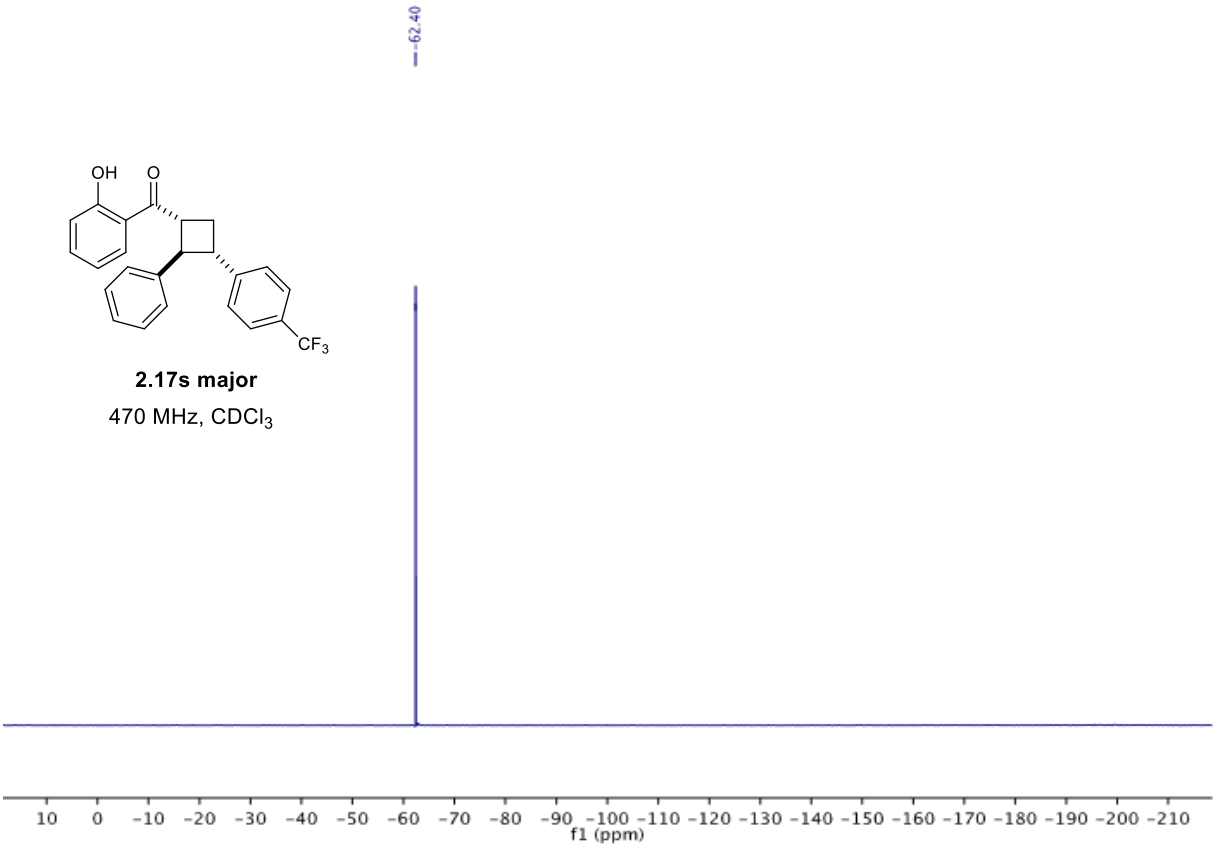



**2.17r minor**

127 MHz, $CDCl_3$

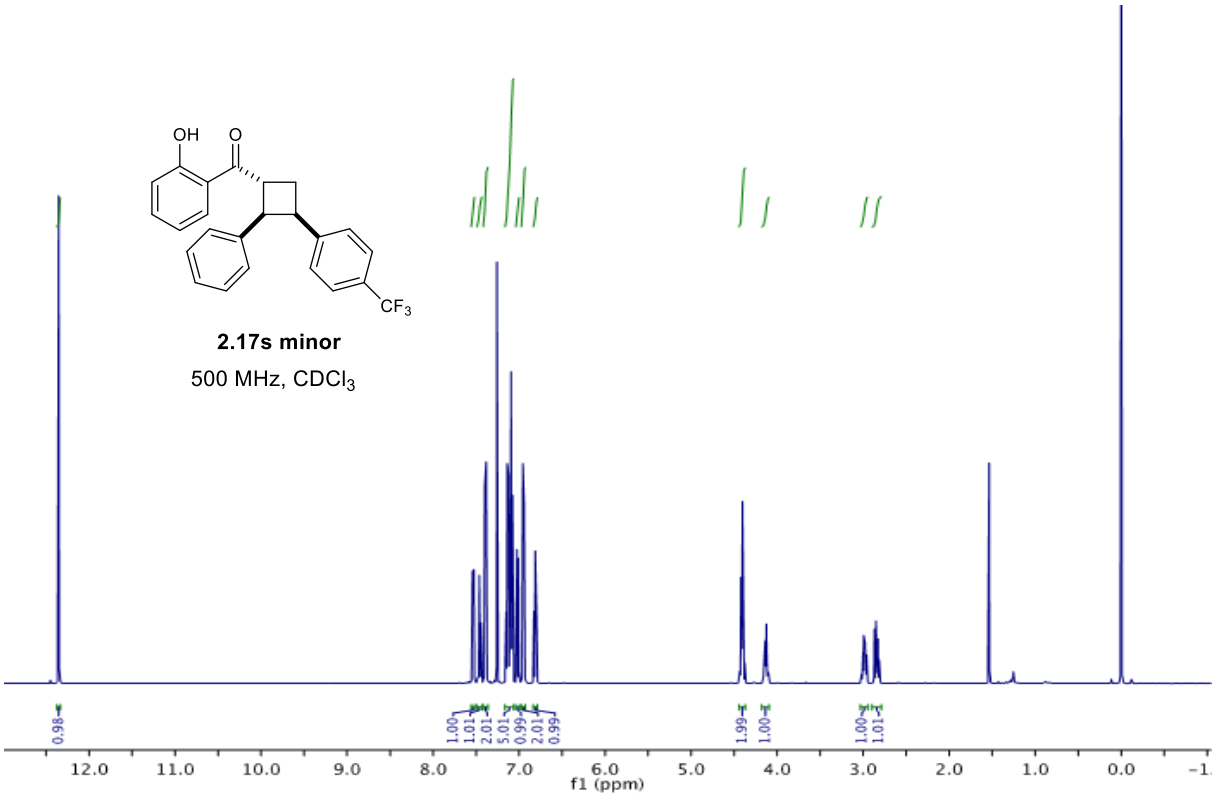

OH
O
CF3
2.17s major
500 MHz, CDCl3
0.96
1.97
1.07
1.04
7.20
0.99
0.99
2.02
1.01
1.01
1.00
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1
f1 (ppm)


205.12
162.89
147.10
141.42
136.53
130.07
129.32
129.06
128.79
128.55
127.45
127.17
127.05
126.95
125.52
125.49
125.46
125.43
125.28
123.12
120.96
49.39
45.90
42.39
30.40
OH
O
CF3
2.17s major
127 MHz, CDCl3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)



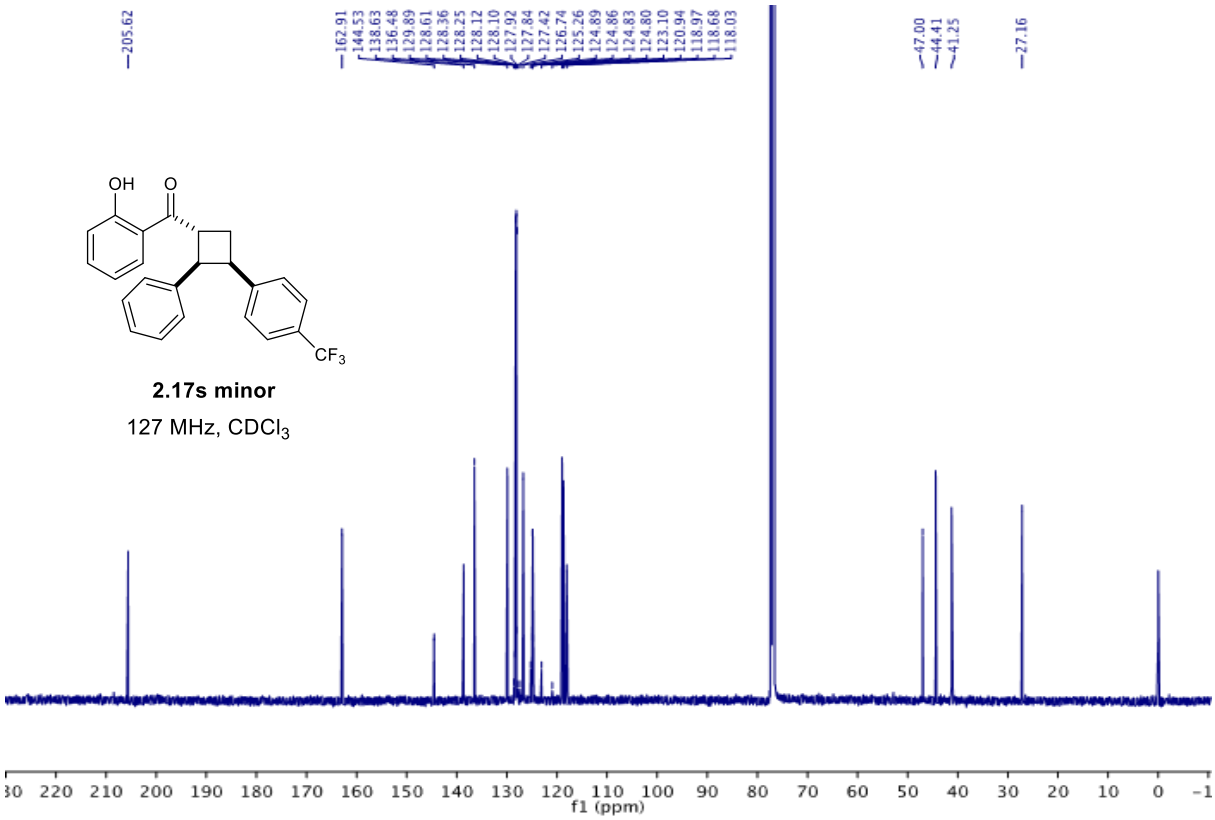

**2.17s major**

470 MHz, $CDCl_3$



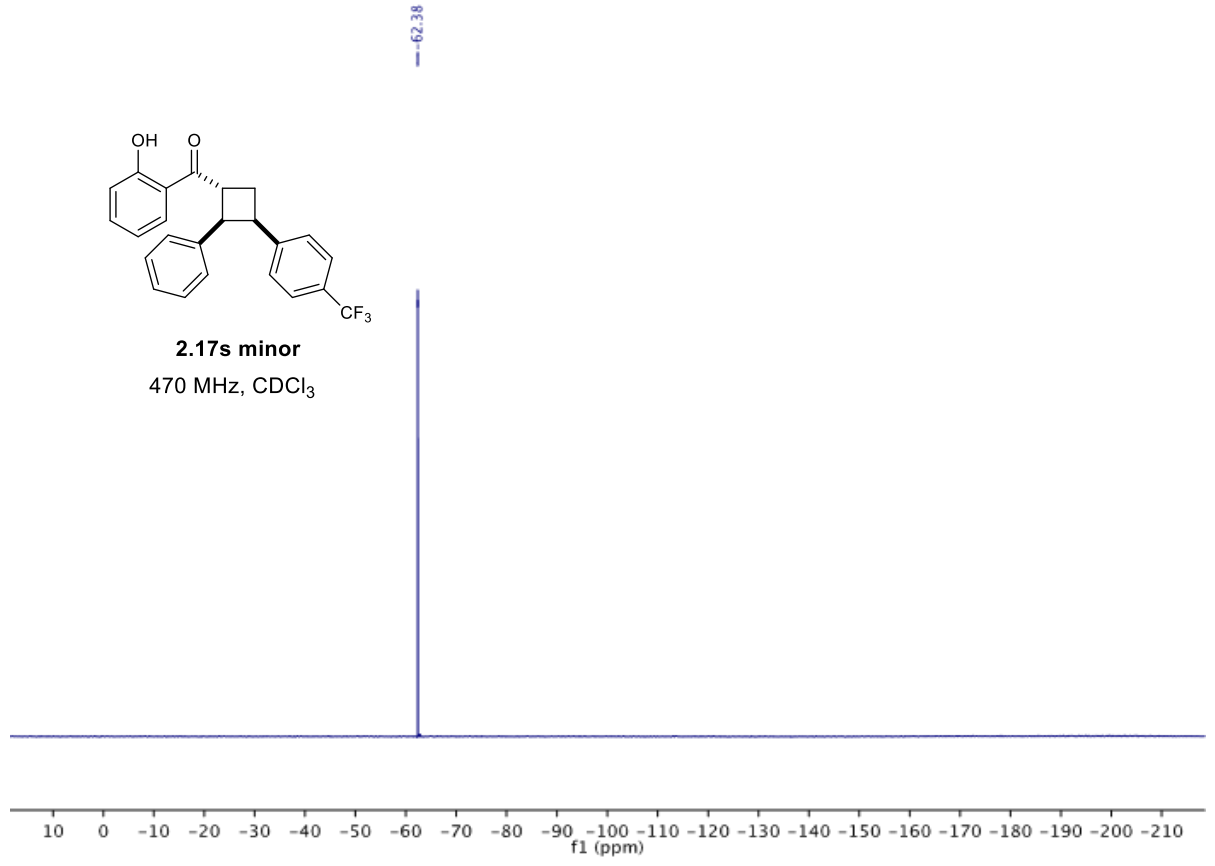

**2.17s minor**

500 MHz, $CDCl_3$



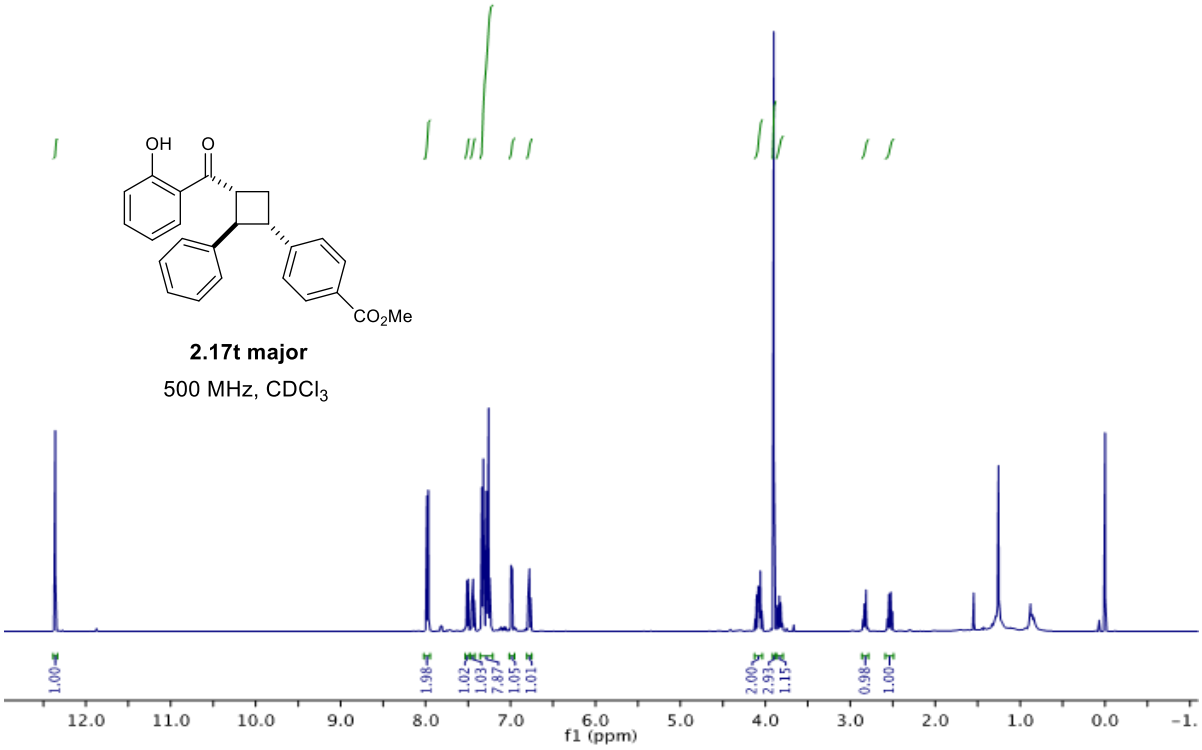

**2.17s minor**

127 MHz, $CDCl_3$



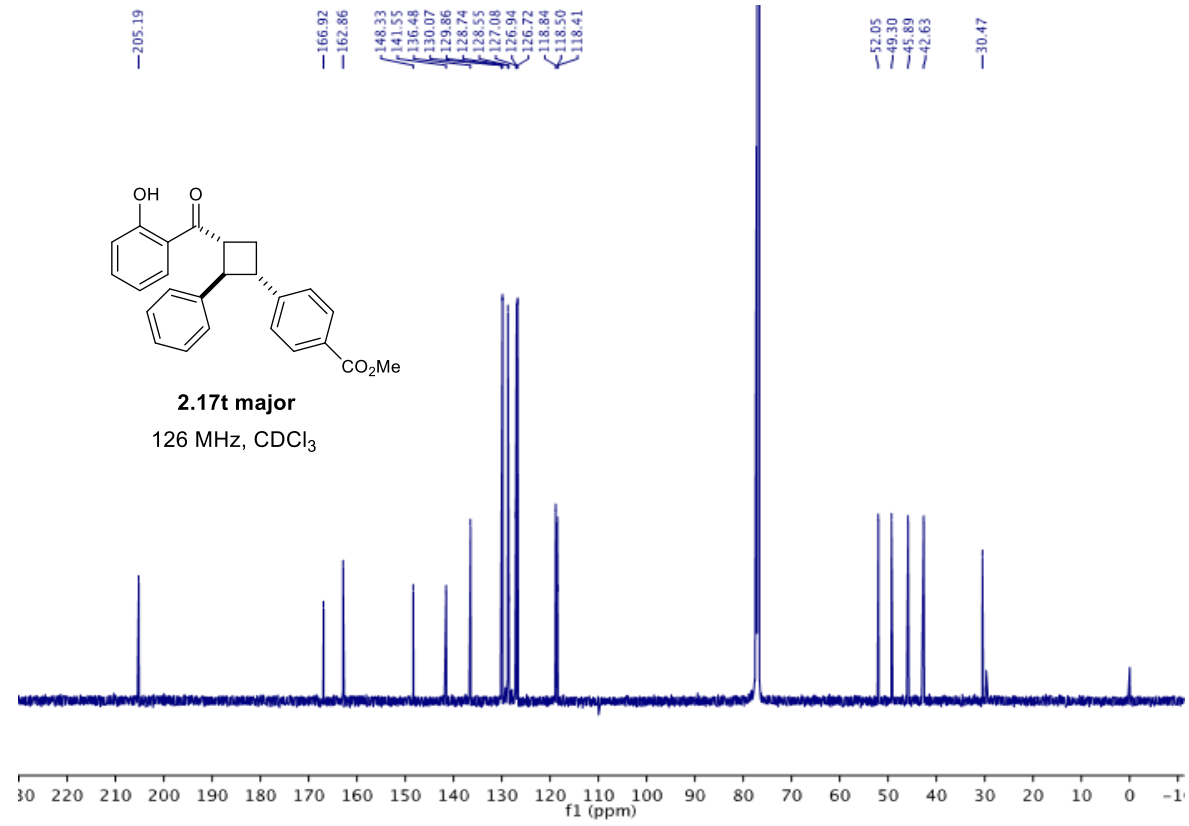

**2.17s minor**

470 MHz, $CDCl_3$



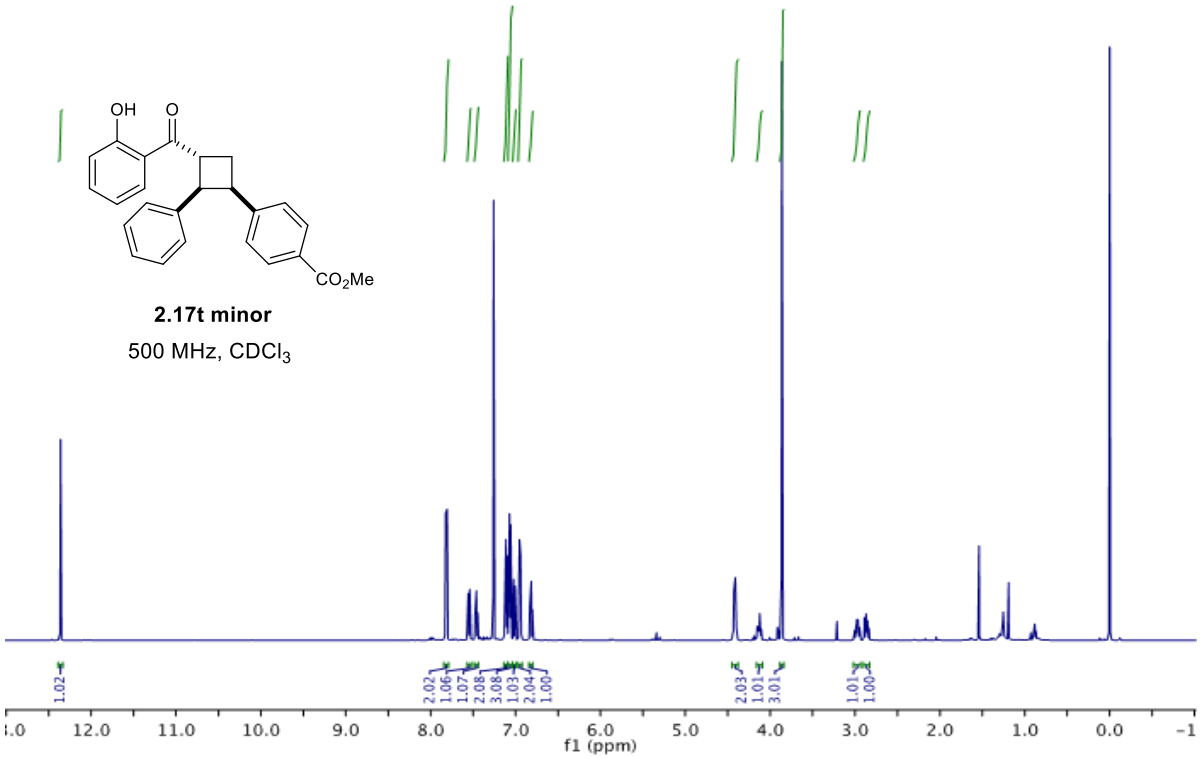

**2.17t major**

500 MHz, $CDCl_3$



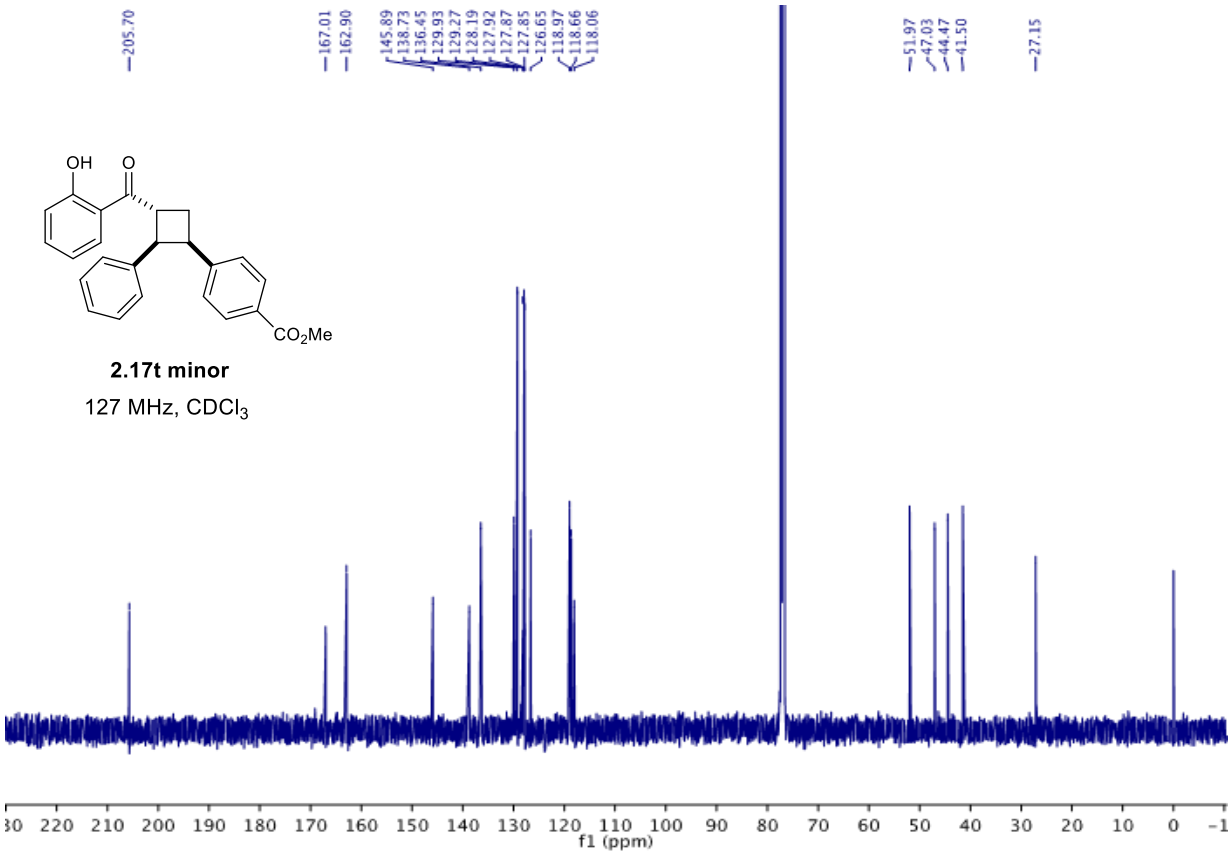

**2.17t major**

126 MHz, $CDCl_3$



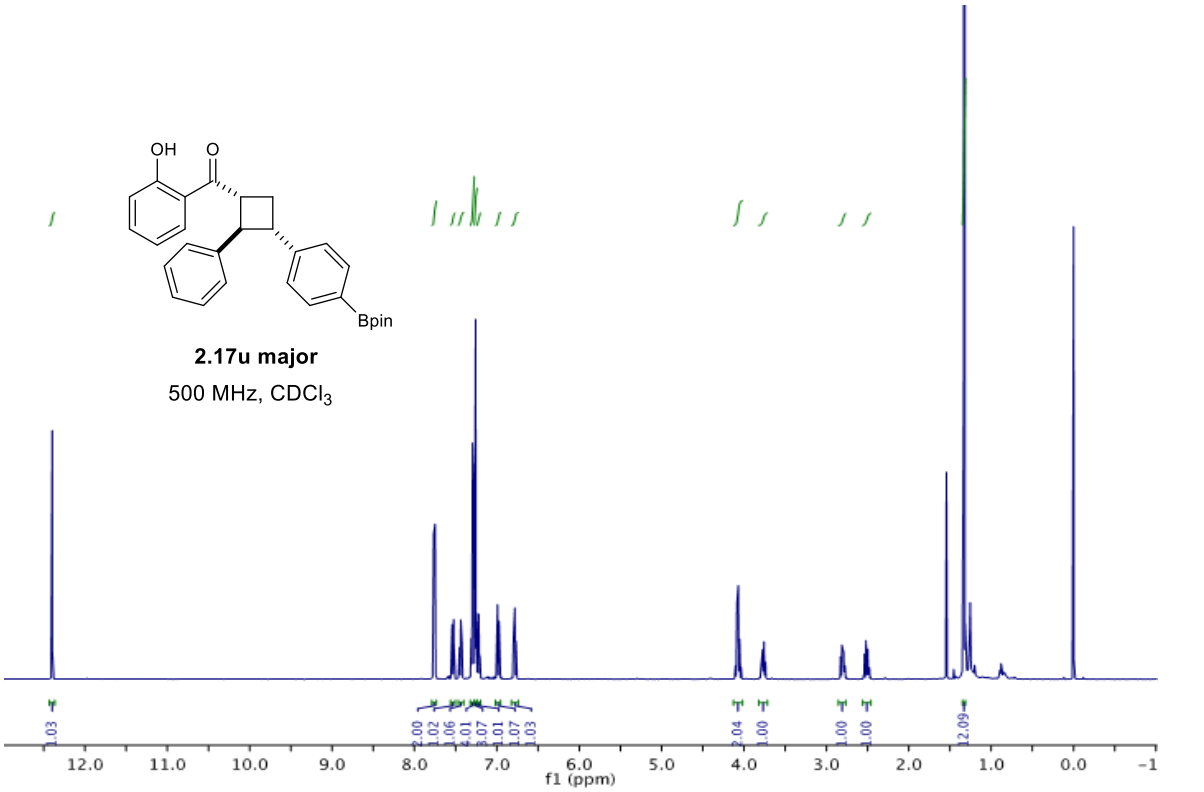

**2.17t minor**

500 MHz, $CDCl_3$



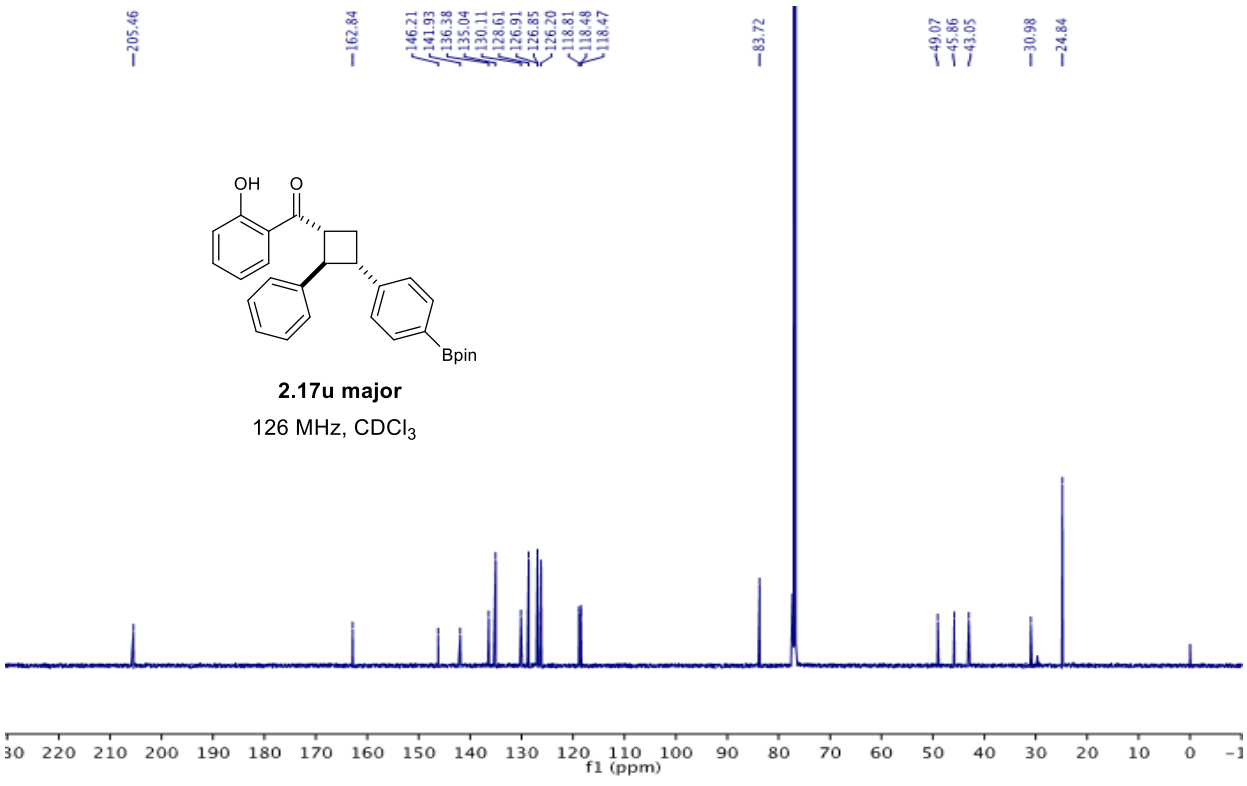

**2.17t minor**

127 MHz, $CDCl_3$



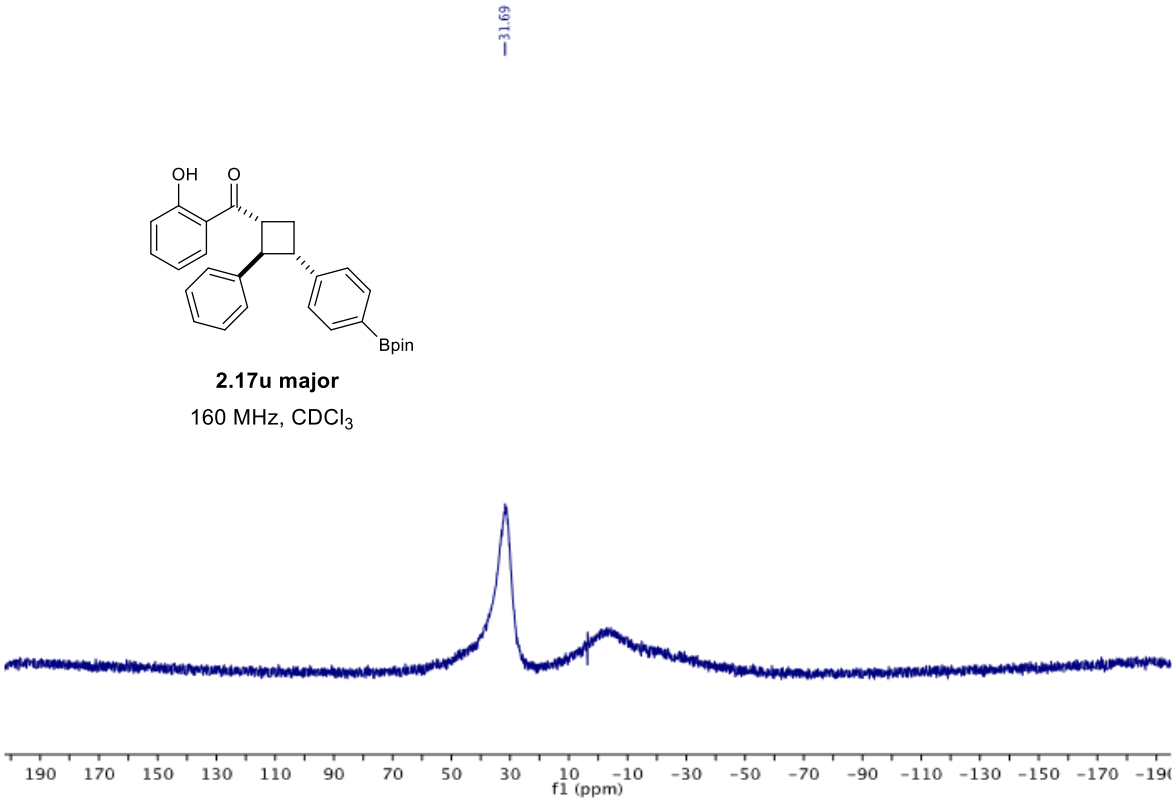

**2.17u major**

500 MHz, $CDCl_3$



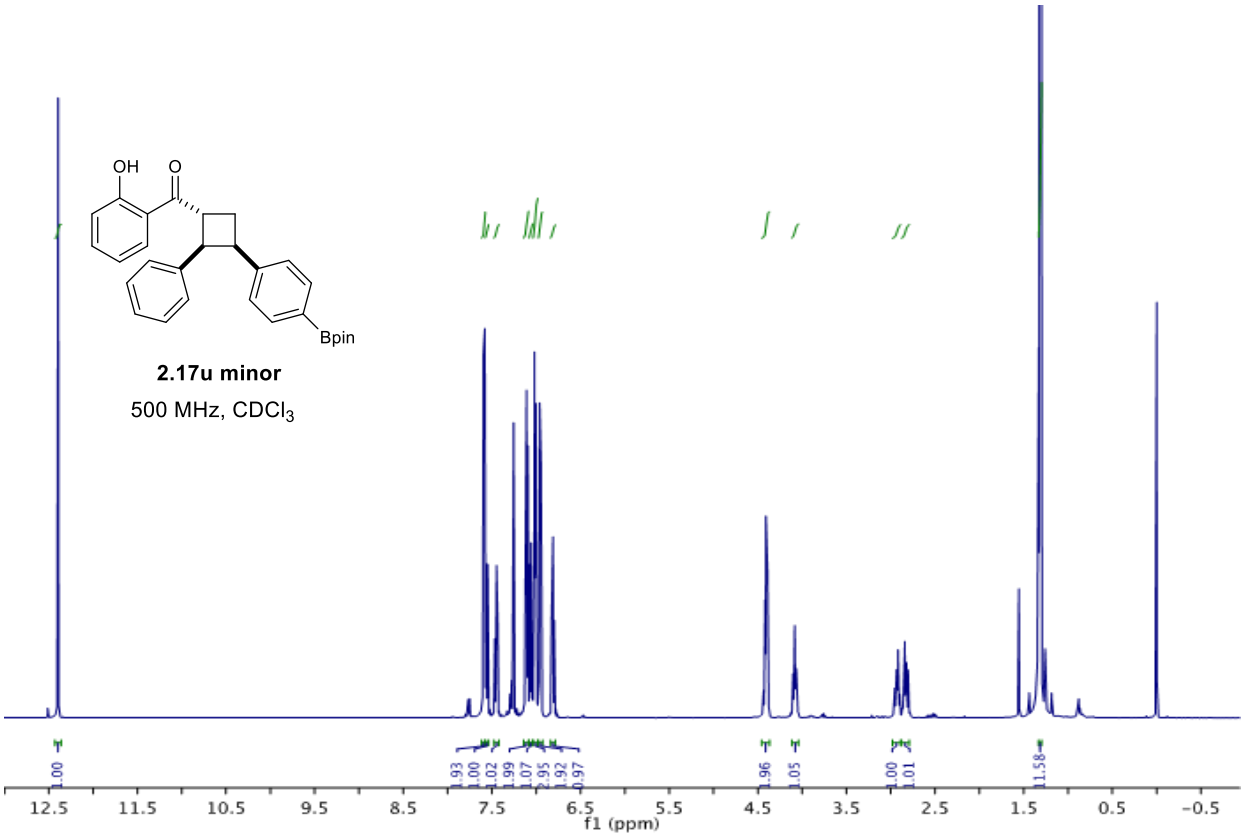

**2.17u major**

126 MHz, $CDCl_3$



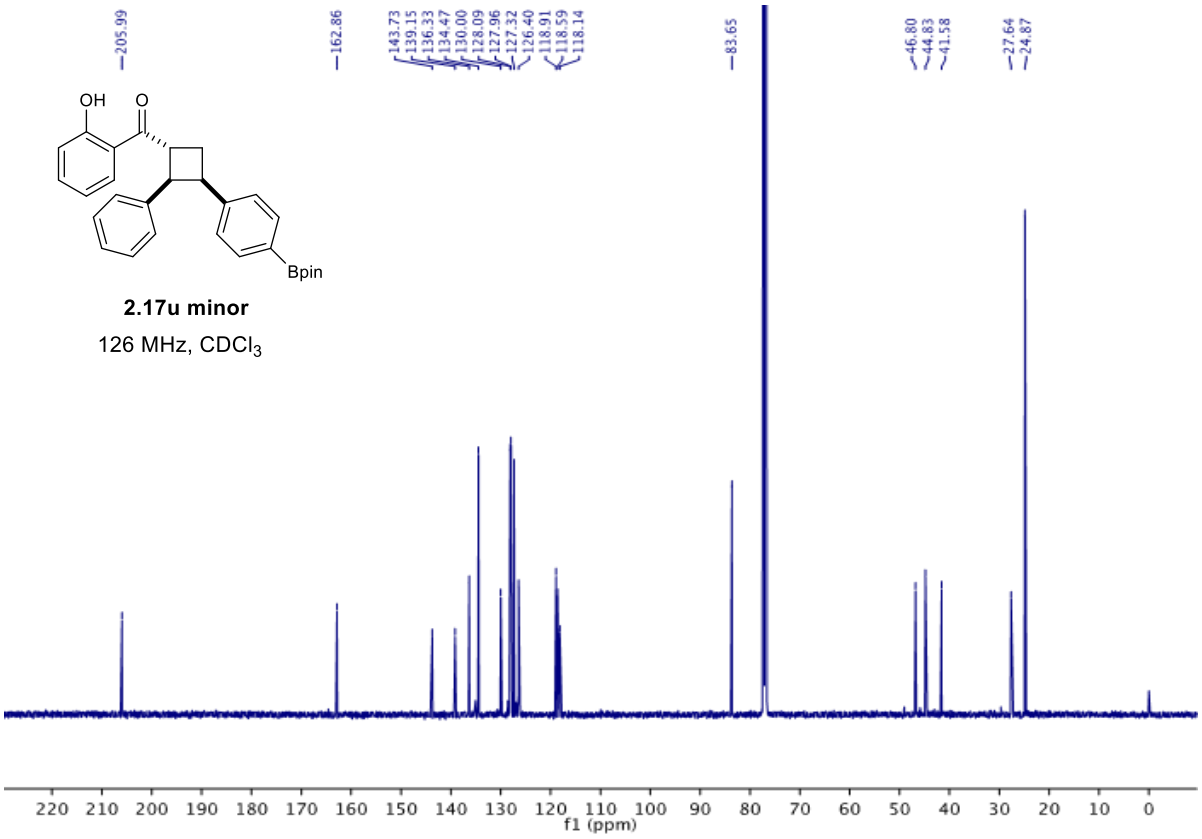

**2.17u major**

160 MHz, $CDCl_3$



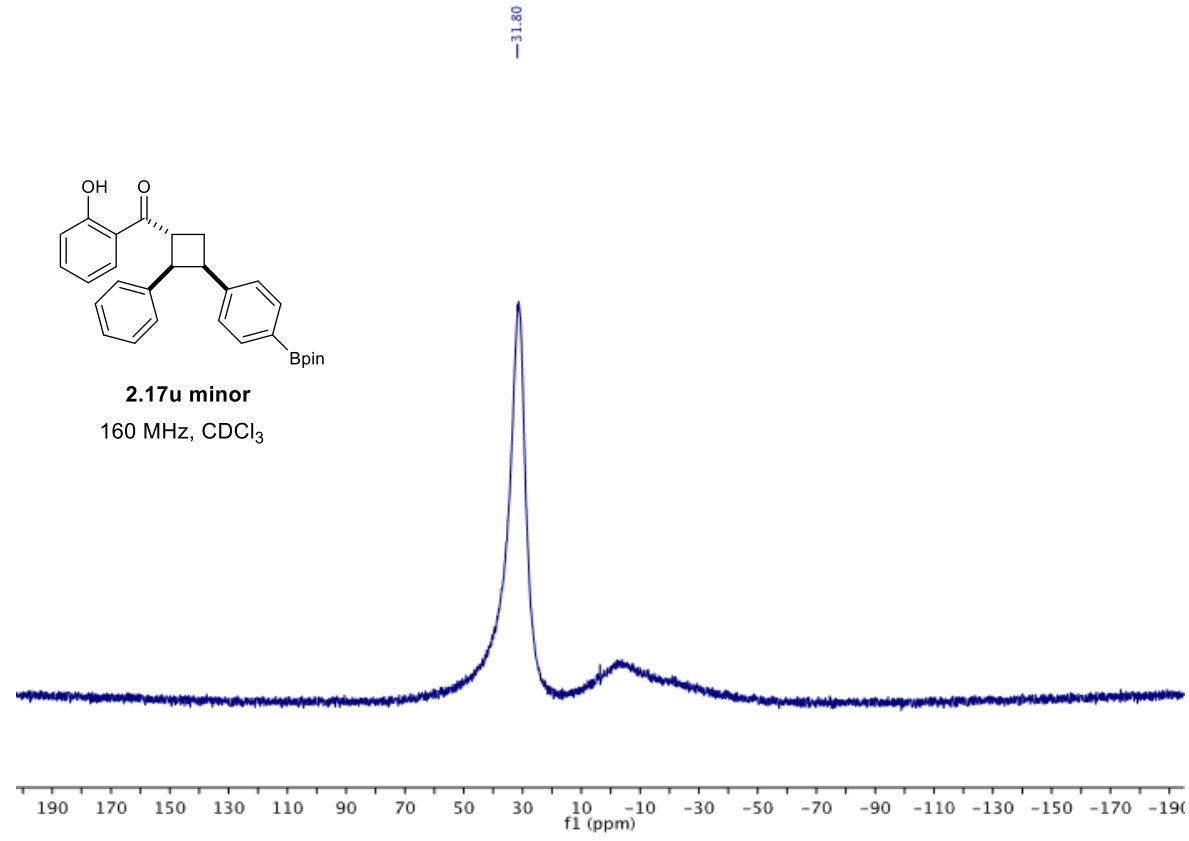

**2.17u minor**

500 MHz, $CDCl_3$



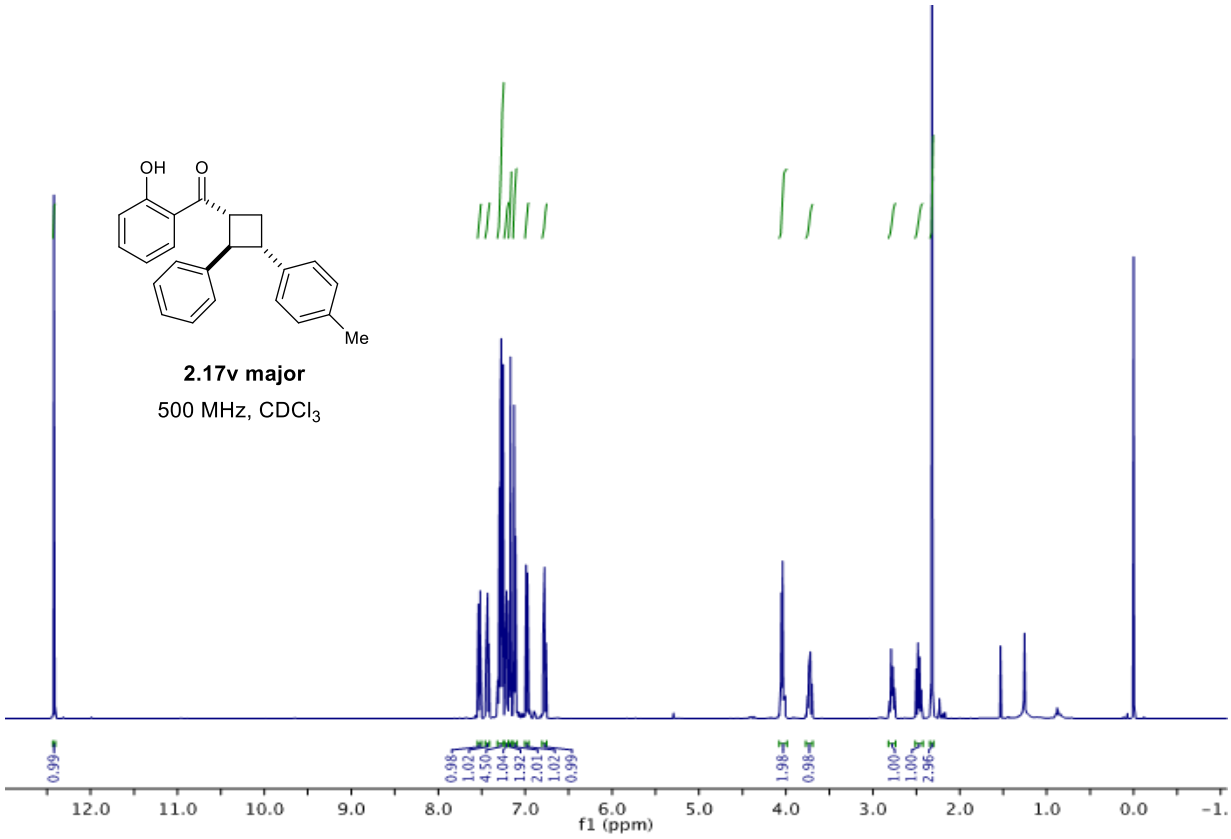

**2.17u minor**

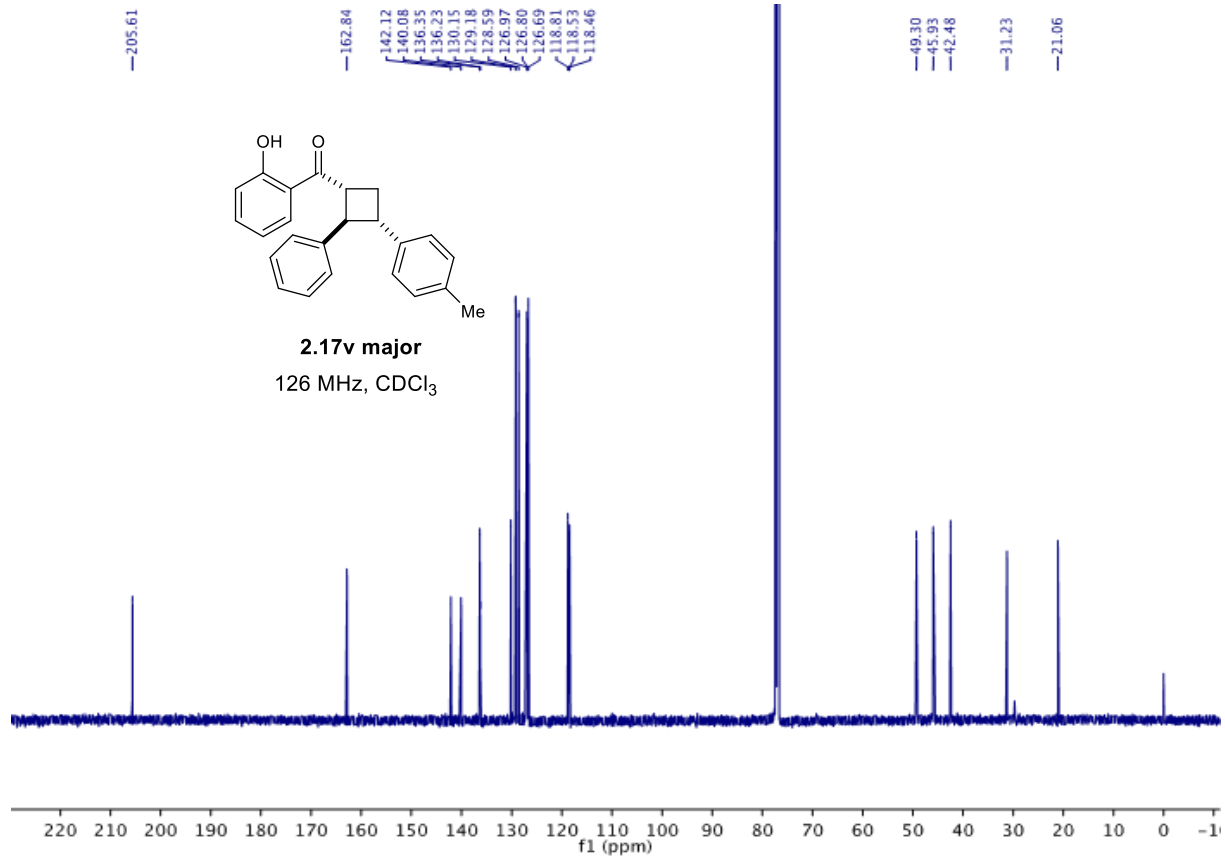
126 MHz, $CDCl_3$

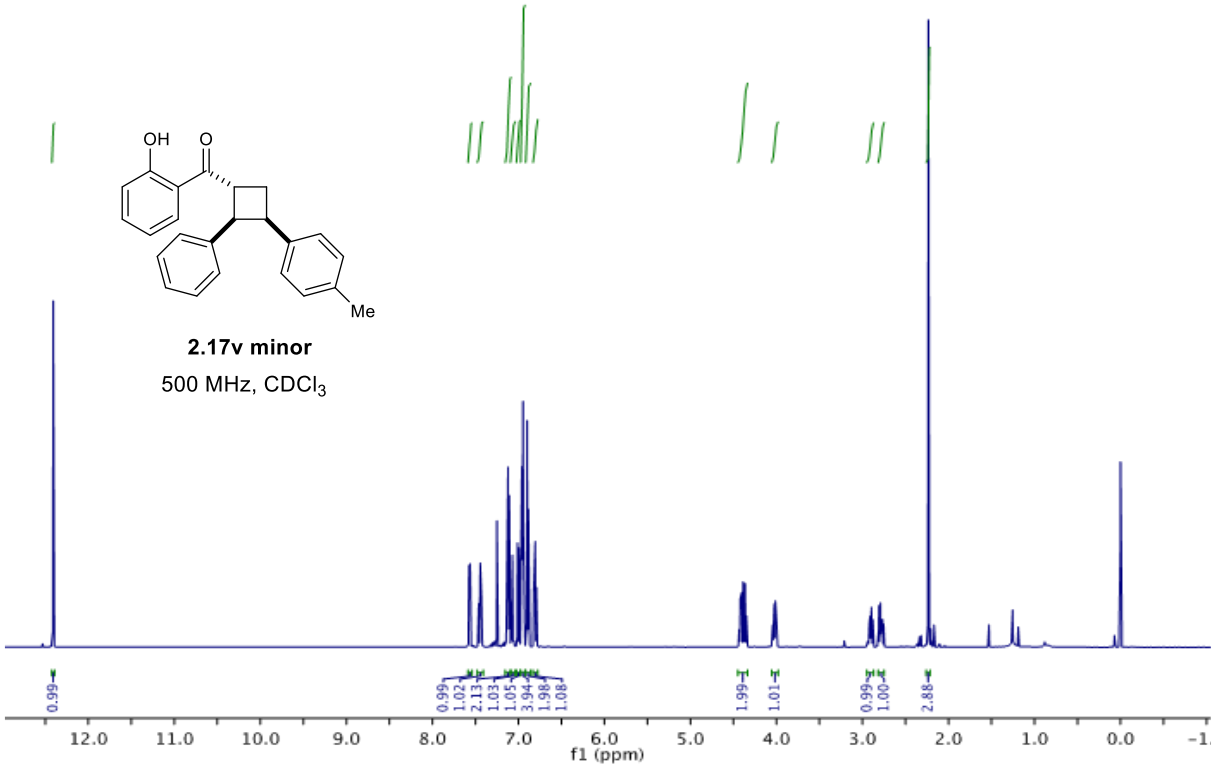



**2.17u minor**

160 MHz, $CDCl_3$

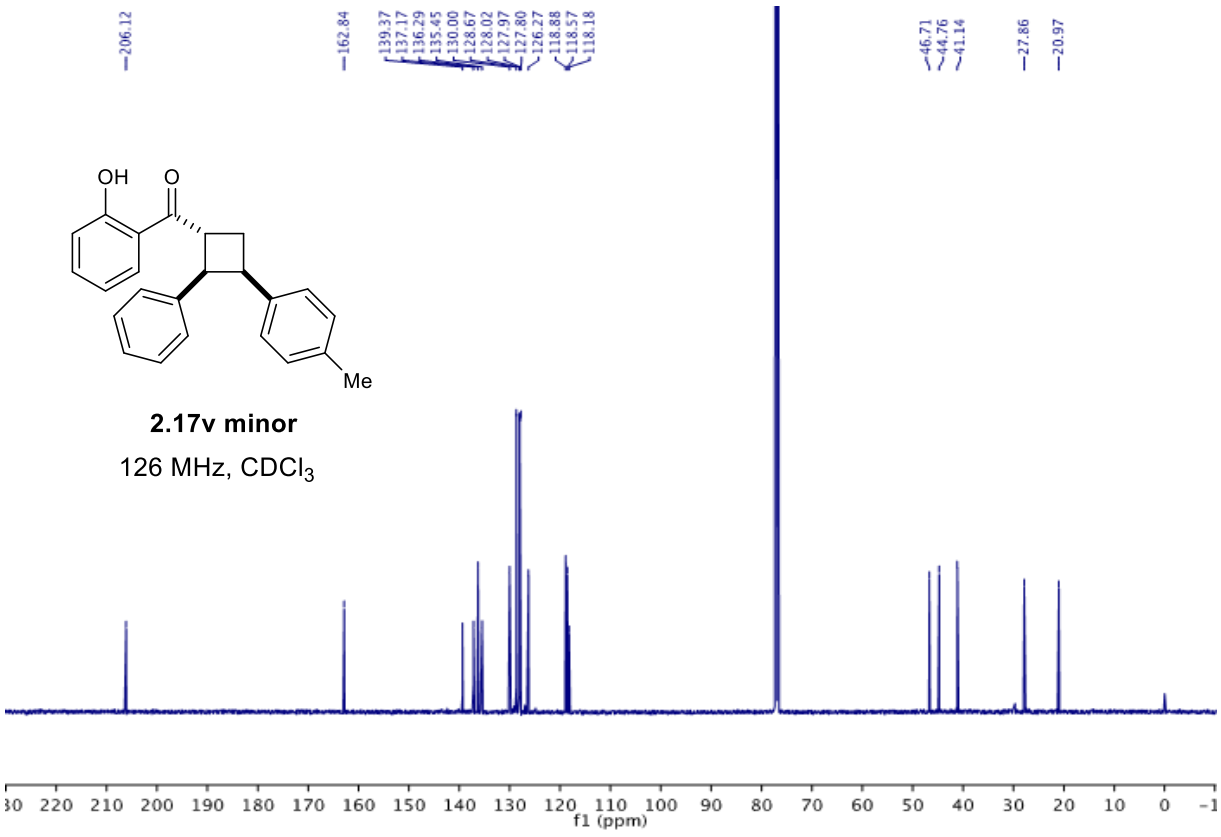

OH
O
Me
2.17v major
500 MHz, CDCl3
f1 (ppm)


205.61
162.84
142.12
140.08
136.35
136.23
130.15
129.18
128.59
126.97
126.80
126.69
118.81
118.53
118.46
49.30
45.93
42.48
31.23
21.06
OH
O
Me
2.17v major
126 MHz, CDCl3
f1 (ppm)



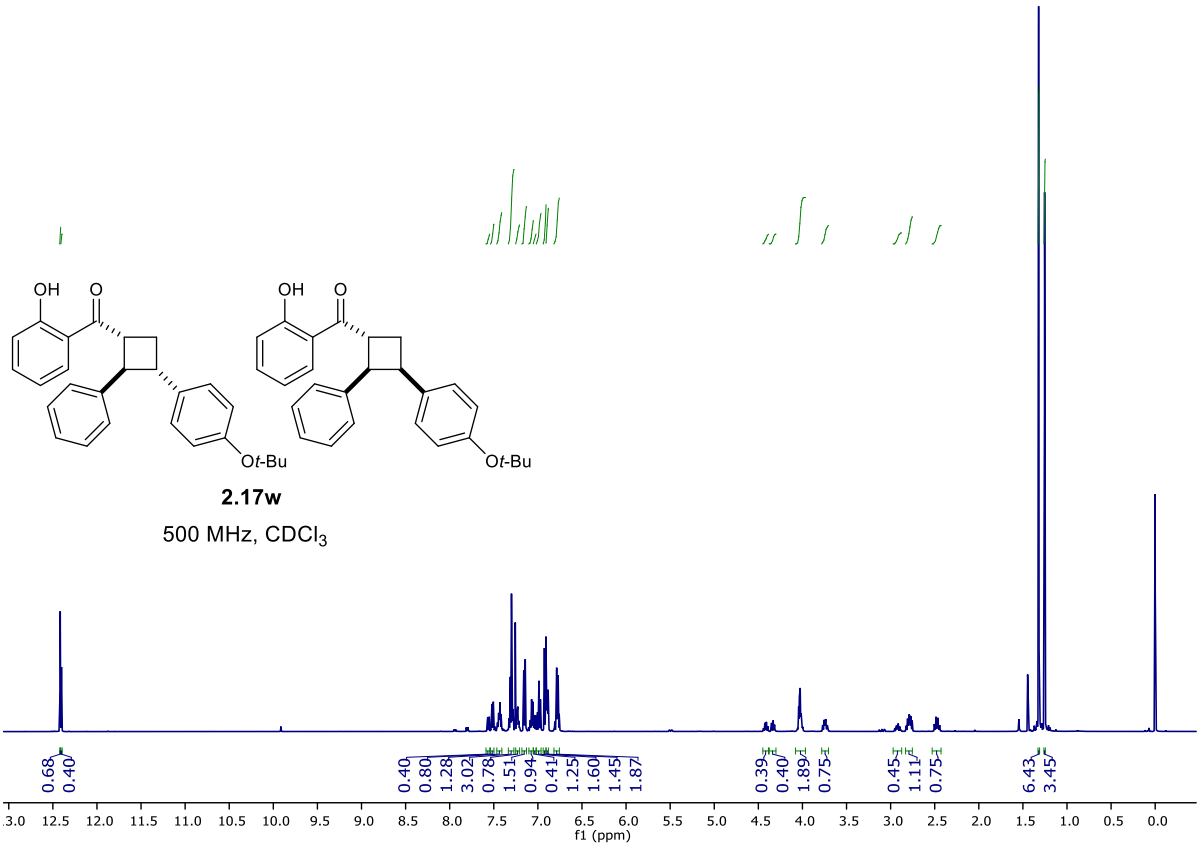

**2.17v minor**

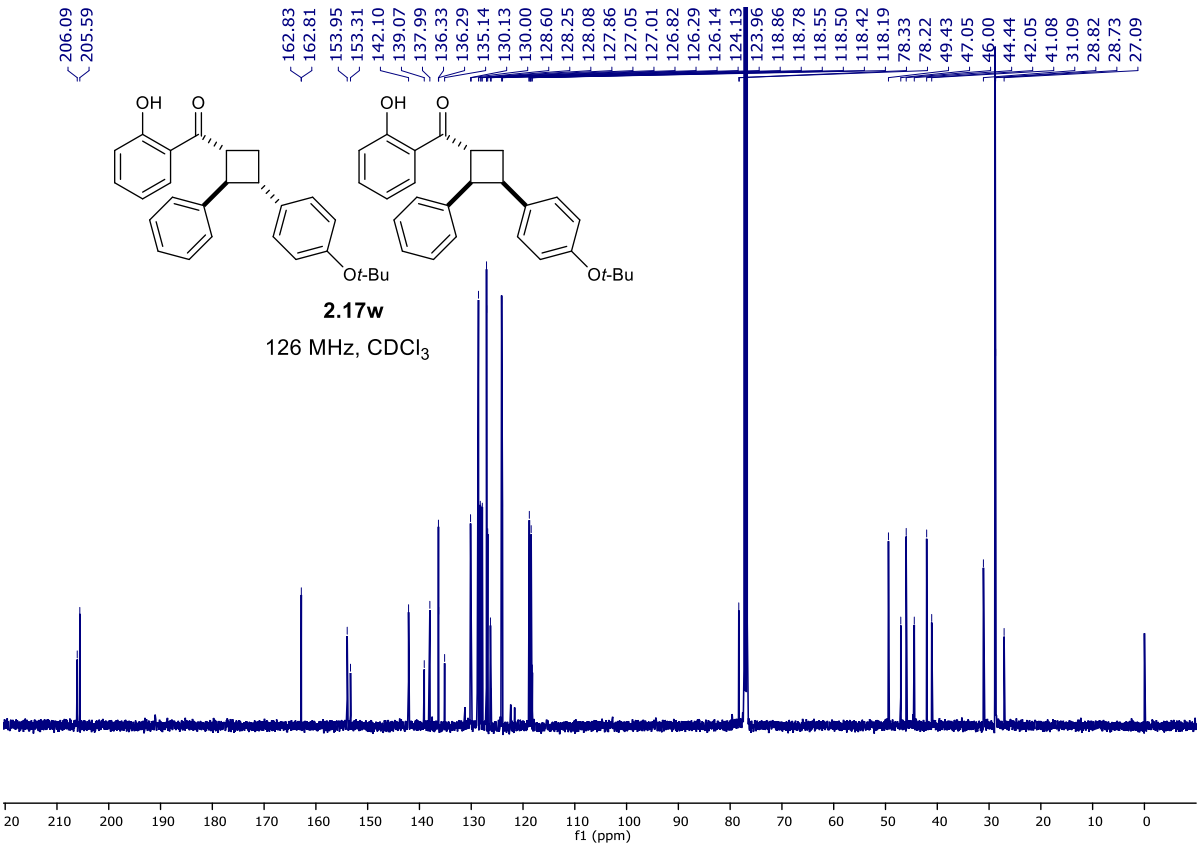
500 MHz, $CDCl_3$

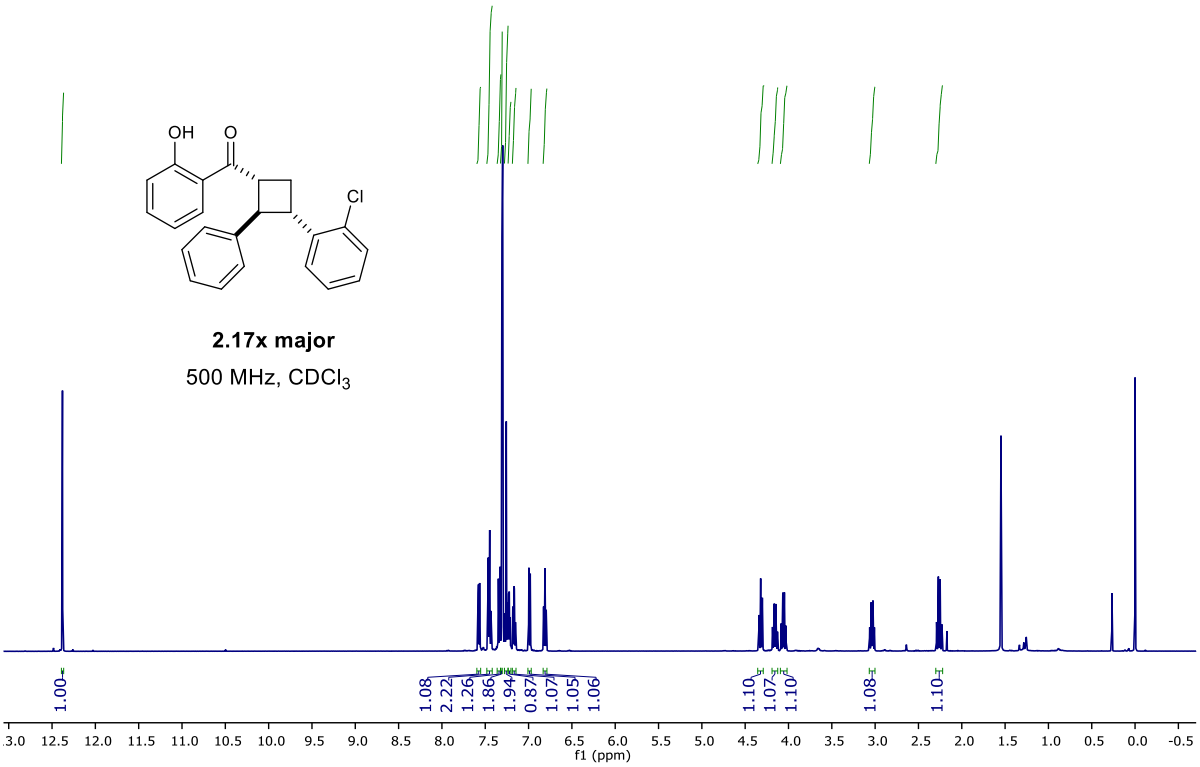


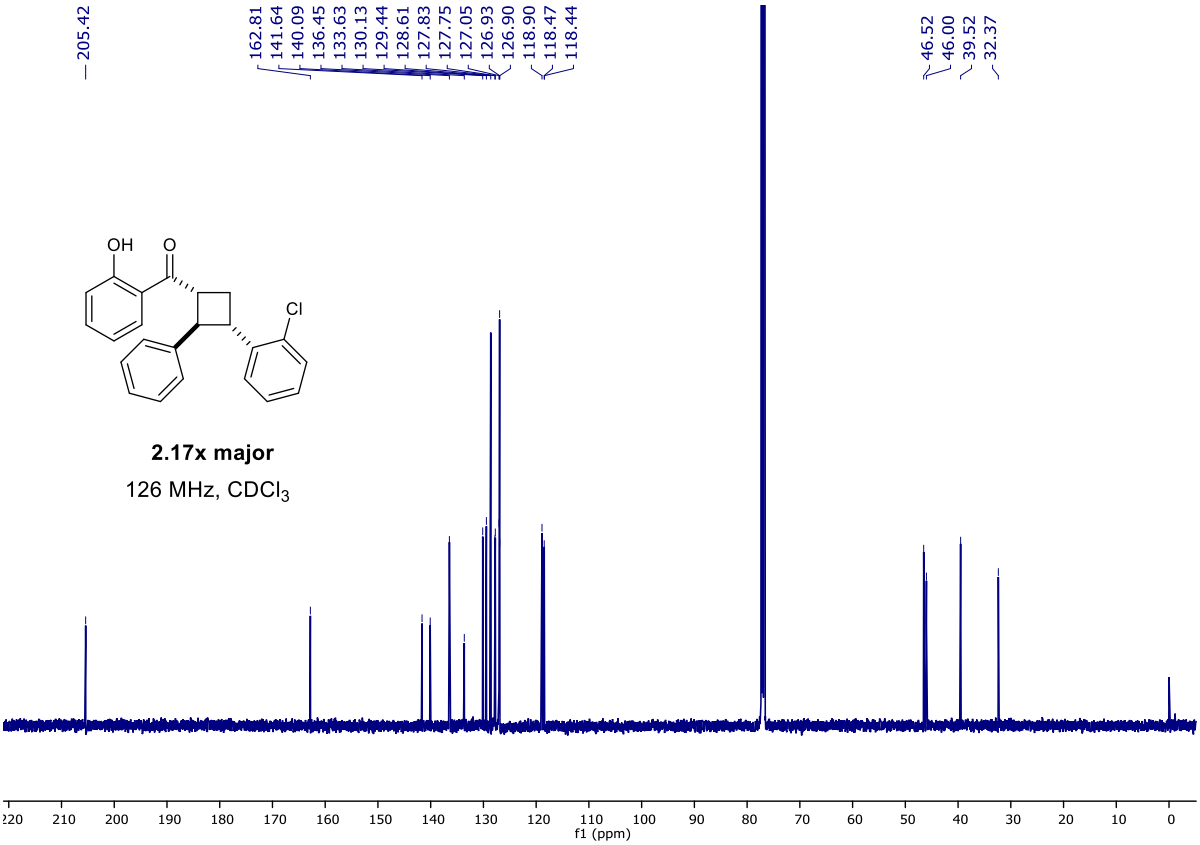

**2.17v minor**

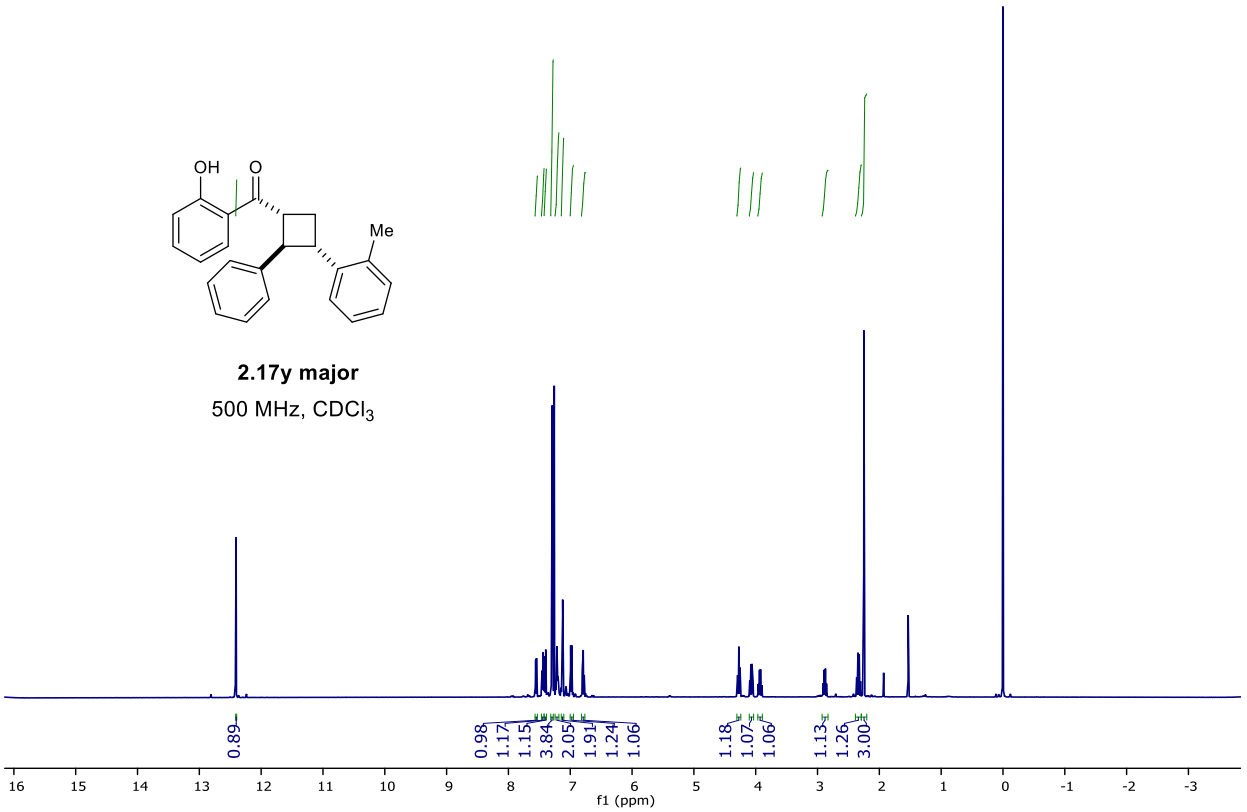
126 MHz, $CDCl_3$

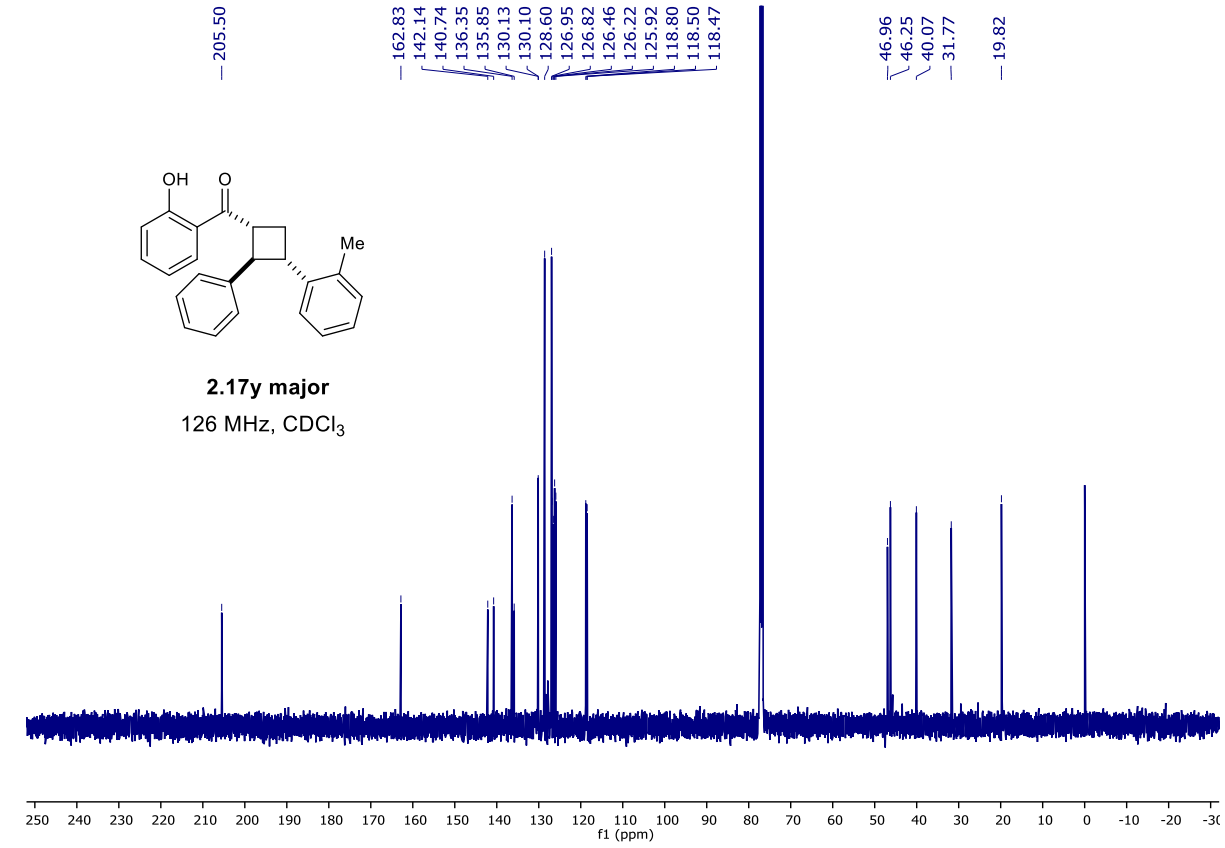

OH
O
Ot-Bu
2.17w
500 MHz, CDCl3
0.68
0.40
0.40
0.80
1.28
3.02
0.78
1.51
0.94
0.41
1.25
1.60
1.45
1.87
0.39
0.40
1.89
0.75
0.45
1.11
0.75
6.43
3.45
f1 (ppm)

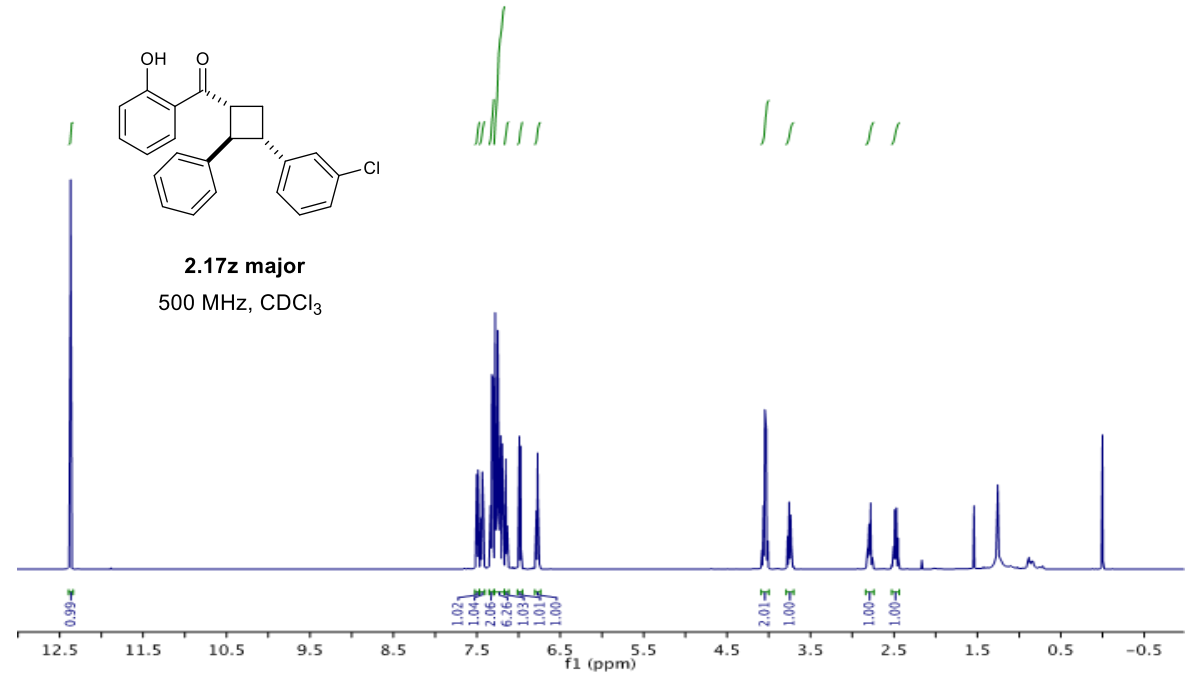

206.09
205.59
162.83
162.81
153.95
153.31
142.10
139.07
137.99
136.33
136.29
135.14
130.13
130.00
128.60
128.25
128.08
127.86
127.05
127.01
126.82
126.29
126.14
124.13
123.96
118.86
118.78
118.55
118.50
118.42
118.19
78.33
78.22
49.43
47.05
46.00
44.44
42.05
41.08
31.09
28.82
28.73
27.09
OH
O
Ot-Bu
2.17w
126 MHz, CDCl3
f1 (ppm)


OH
O
Cl
2.17x major
500 MHz, CDCl3
1.00
1.08
2.22
1.26
1.86
1.94
0.87
1.07
1.05
1.06
1.10
1.07
1.10
1.08
1.10
f1 (ppm)


205.42
162.81
141.64
140.09
136.45
133.63
130.13
129.44
128.61
127.83
127.75
127.05
126.93
126.90
118.90
118.47
118.44
46.52
46.00
39.52
32.37
OH
O
Cl
2.17x major
126 MHz, CDCl3
f1 (ppm)

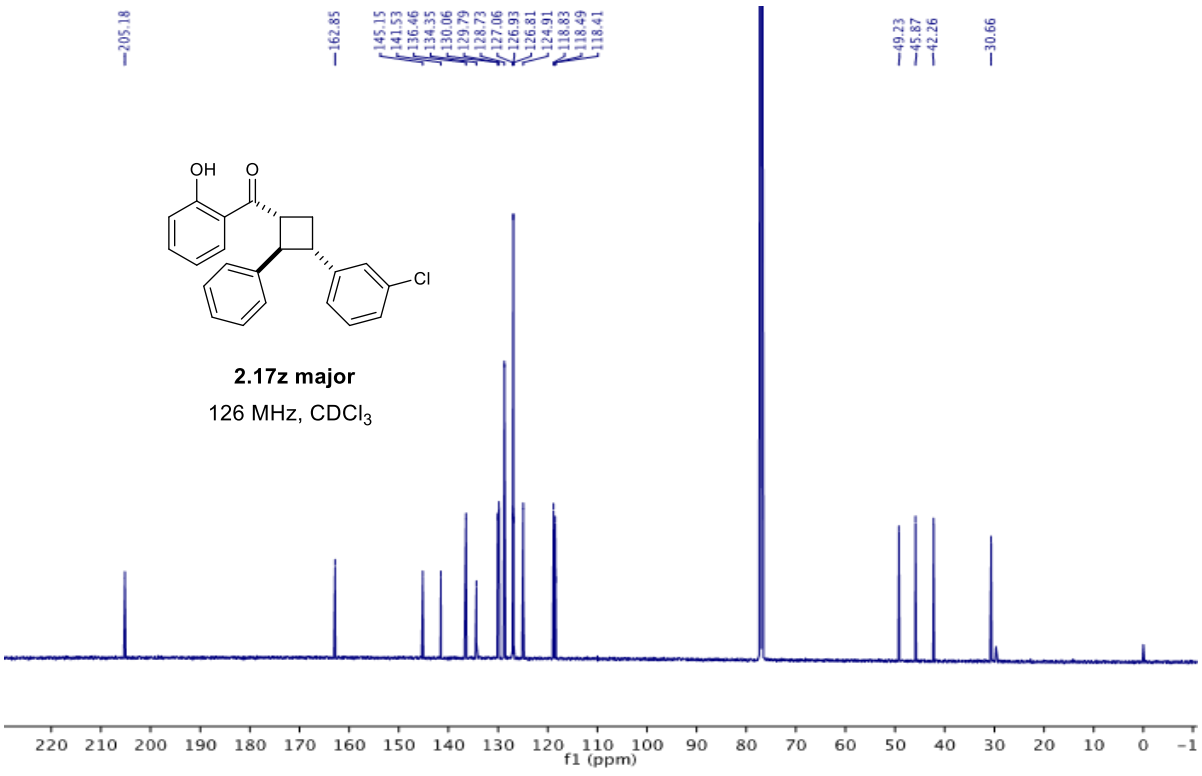

OH
O
Me
2.17y major
500 MHz, CDCl3
0.89
0.98
1.17
1.15
3.84
2.05
1.91
1.24
1.06
1.18
1.07
1.06
1.13
1.26
3.00
f1 (ppm)


205.50
162.83
142.14
140.74
136.35
135.85
130.13
130.10
128.60
126.95
126.82
126.46
126.22
125.92
118.80
118.50
118.47
46.96
46.25
40.07
31.77
19.82
OH
O
Me
2.17y major
126 MHz, CDCl3
f1 (ppm)



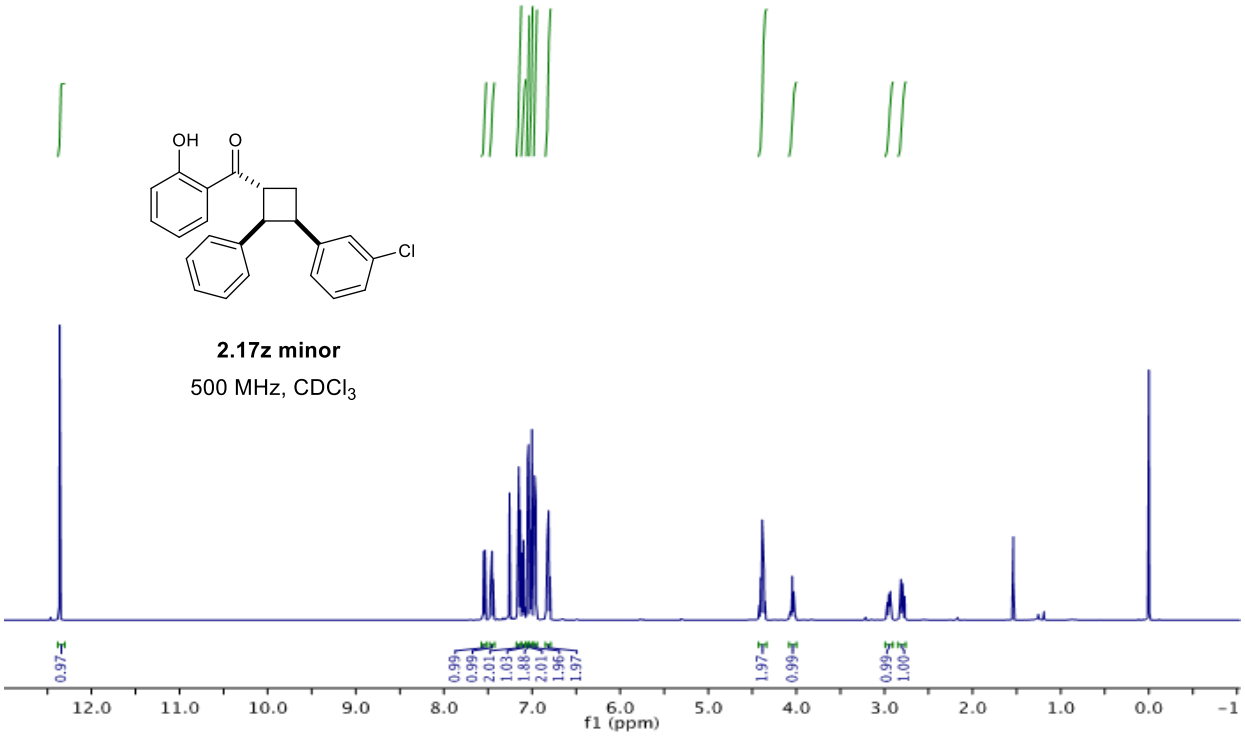

**2.17z major**

500 MHz, $CDCl_3$



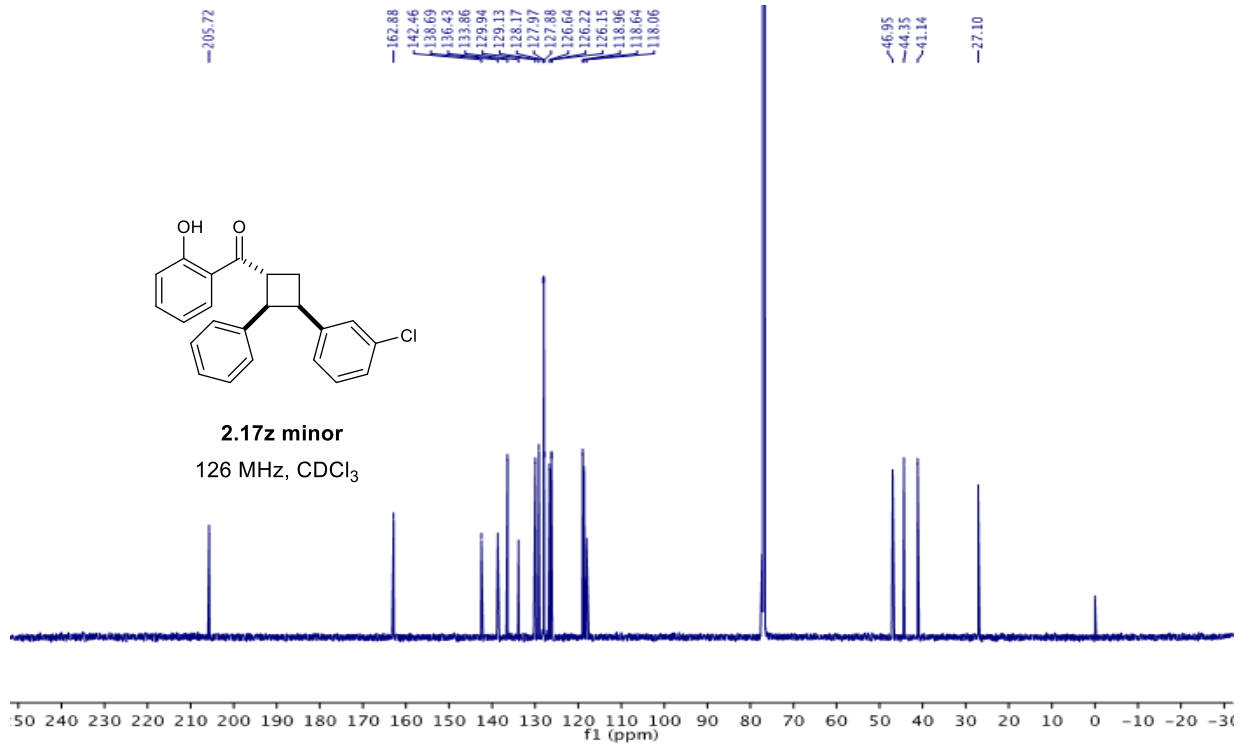

**2.17z major**

126 MHz, $CDCl_3$



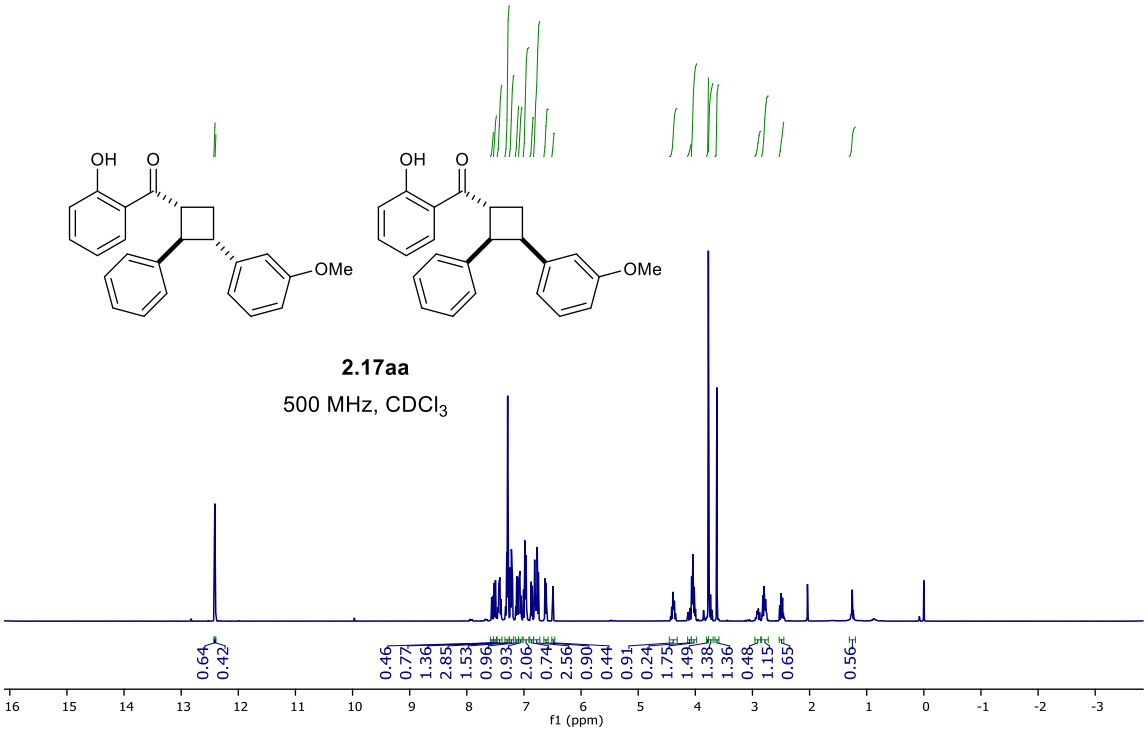

**2.17z minor**

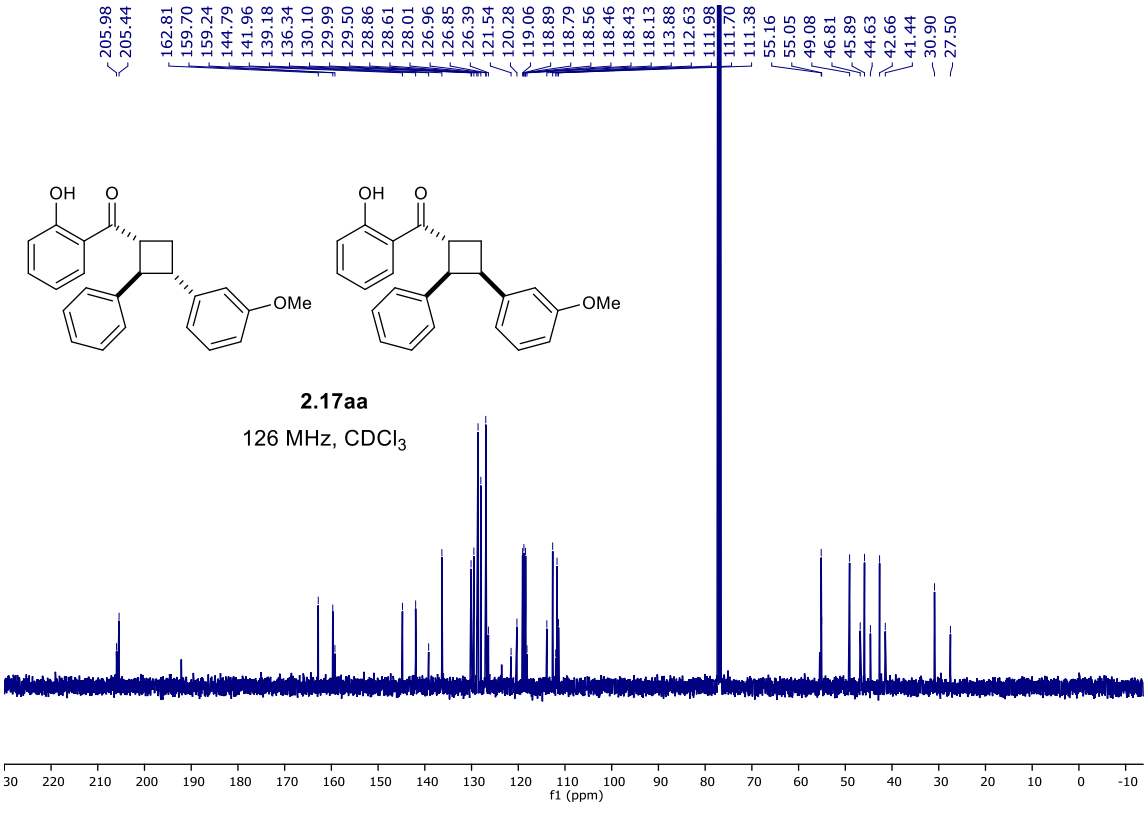
500 MHz, $CDCl_3$

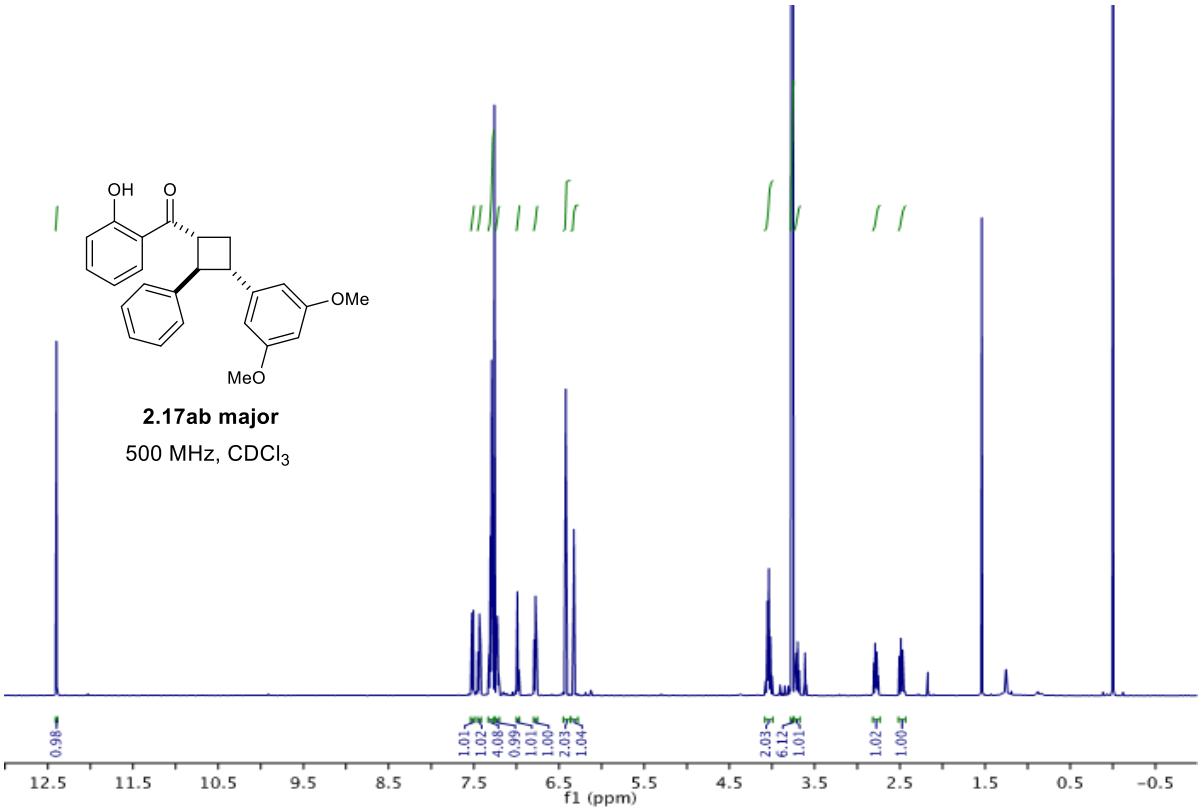


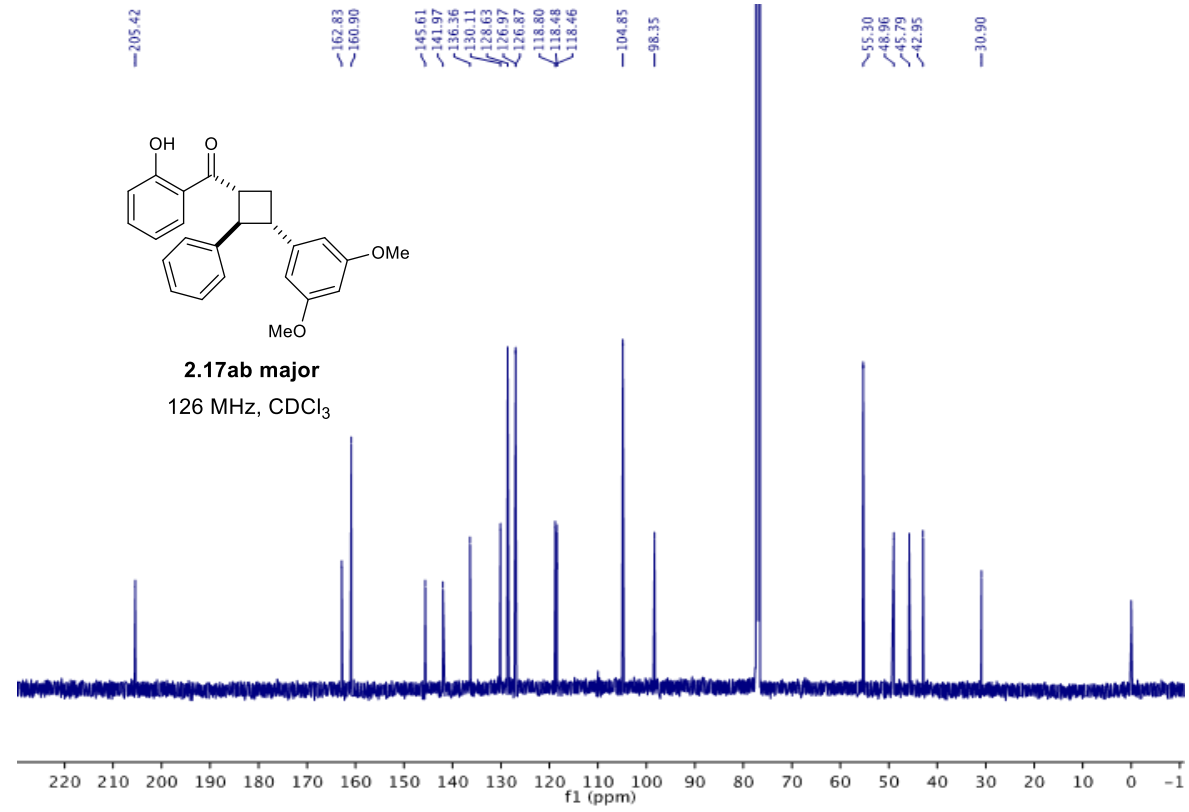

**2.17z minor**

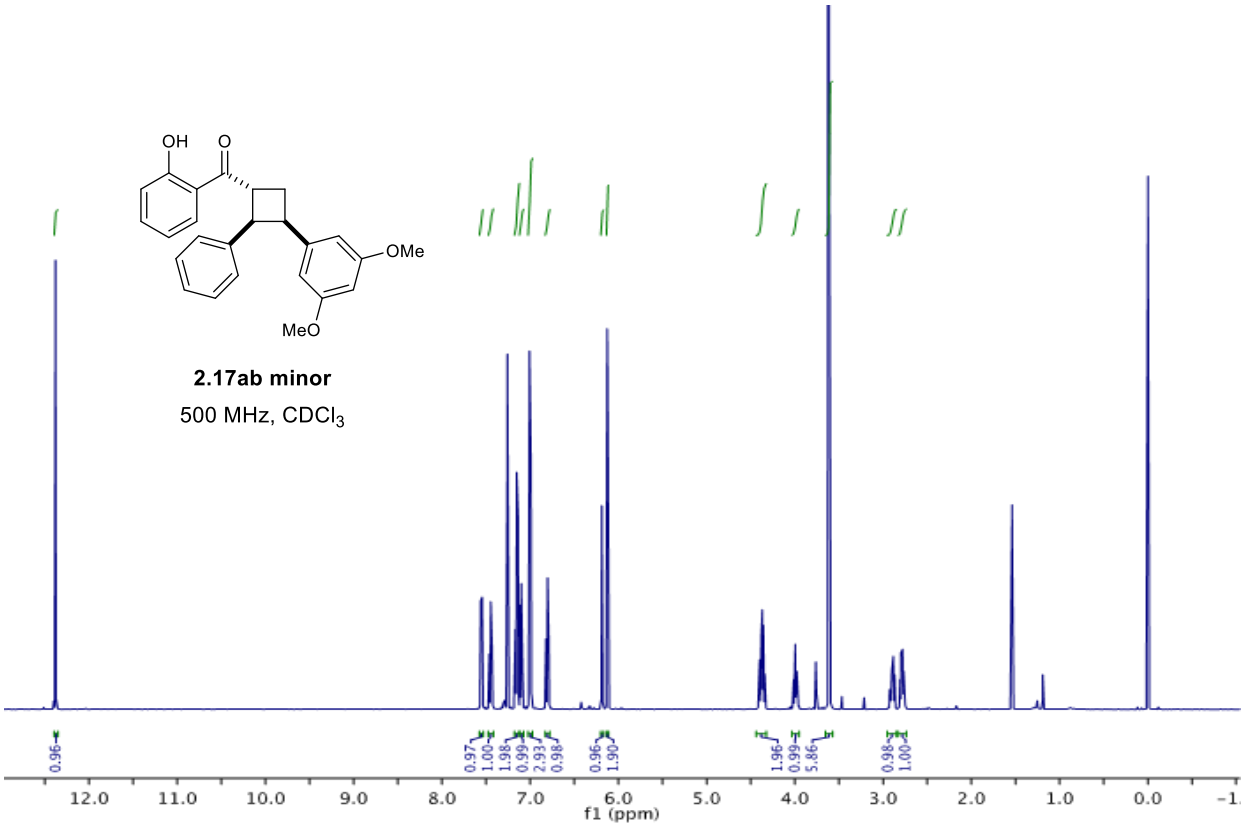
126 MHz, $CDCl_3$


OH
O
OMe
OH
O
OMe
2.17aa
500 MHz, CDCl3
0.64
0.42
0.46
0.77
1.36
2.85
1.53
0.96
0.93
2.06
0.74
2.56
0.90
0.44
0.91
0.24
1.75
1.49
1.38
1.36
0.48
1.15
0.65
0.56
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
f1 (ppm)


205.98
205.44
162.81
159.70
159.24
144.79
141.96
139.18
136.34
130.10
129.99
129.50
128.86
128.61
128.01
126.96
126.85
126.39
121.54
120.28
119.06
118.89
118.79
118.56
118.46
118.43
118.13
113.88
112.63
111.98
111.70
111.38
55.16
55.05
49.08
46.81
45.89
44.63
42.66
41.44
30.90
27.50
OH
O
OMe
OH
O
OMe
2.17aa
126 MHz, CDCl3
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

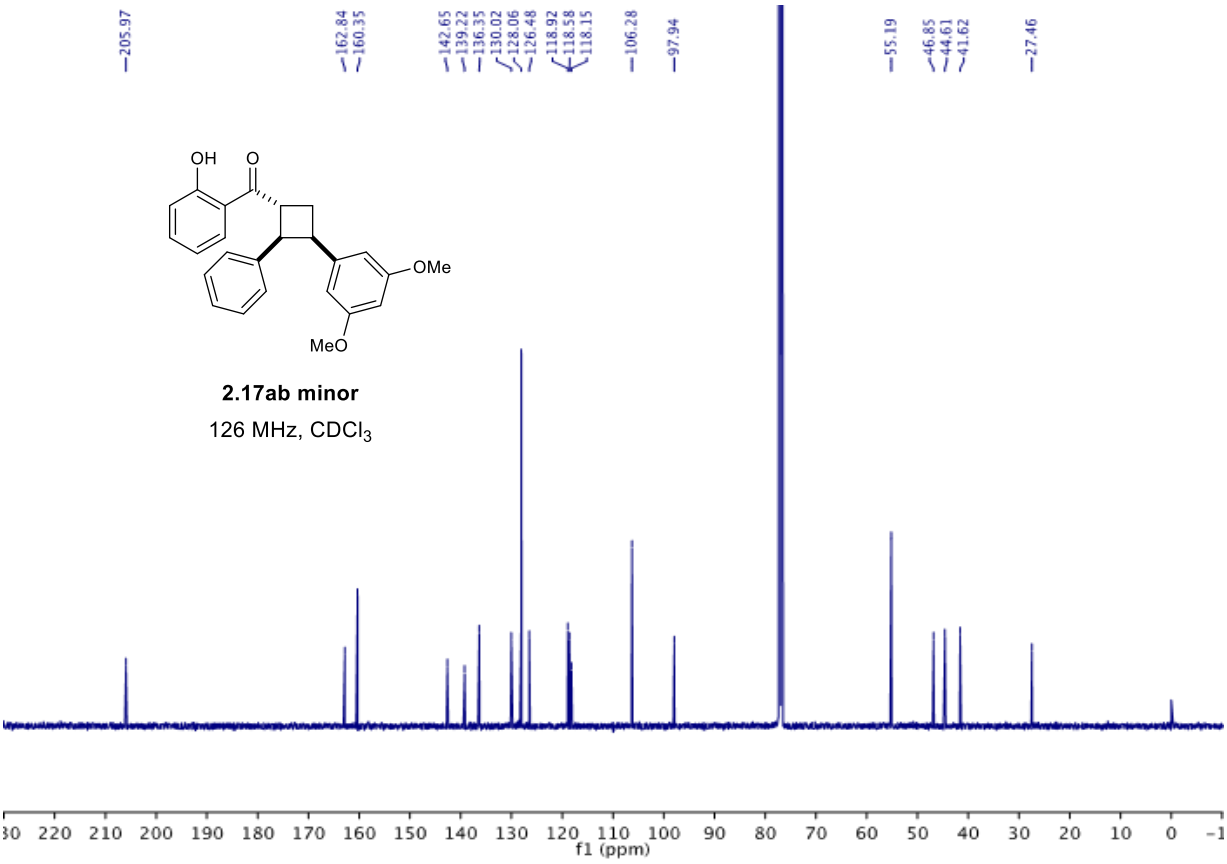

OH
O
OMe
MeO
2.17ab major
500 MHz, CDCl3
f1 (ppm)


OH
O
OMe
MeO
2.17ab major
126 MHz, CDCl3
f1 (ppm)



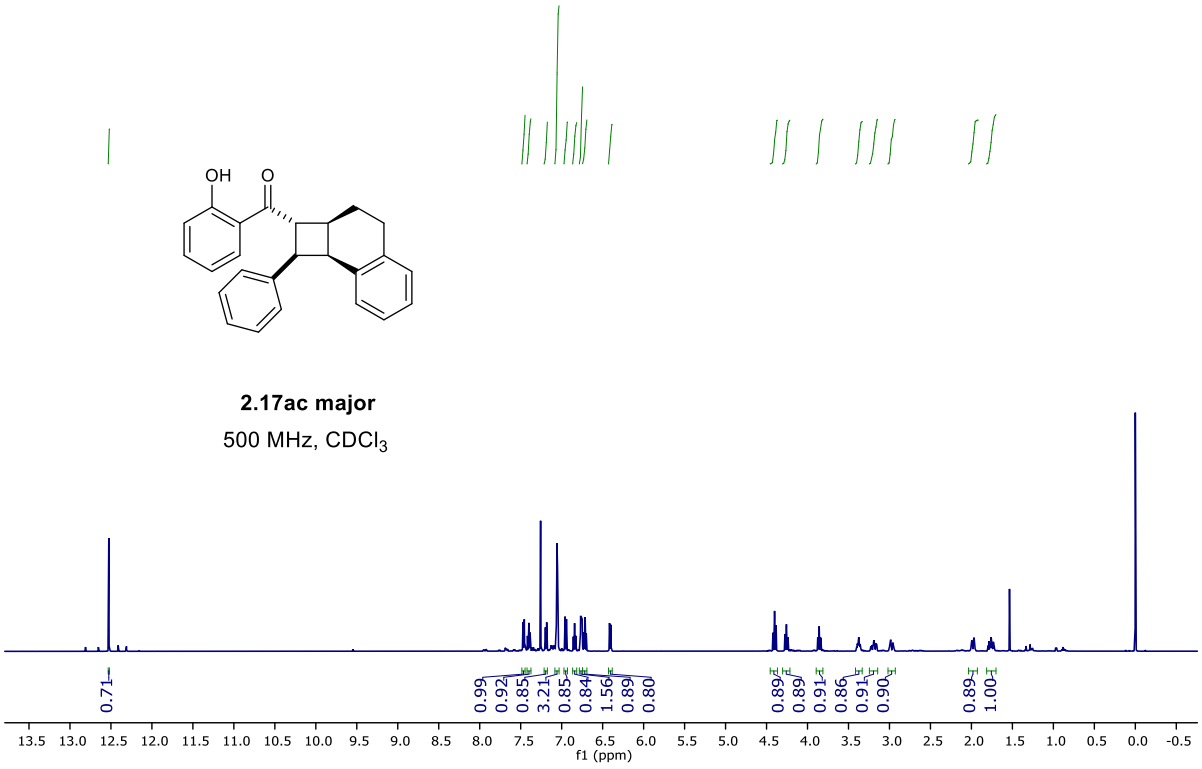

**2.17ab minor**

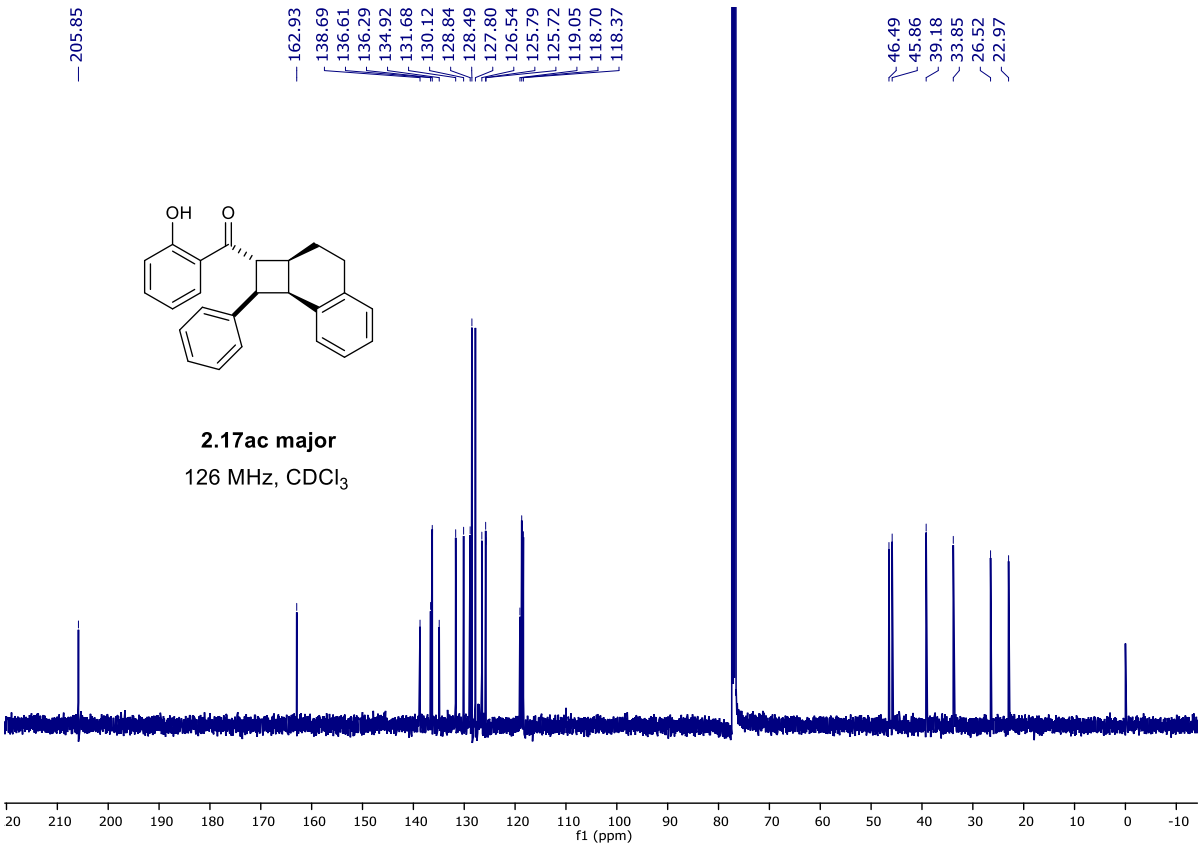
500 MHz, $CDCl_3$

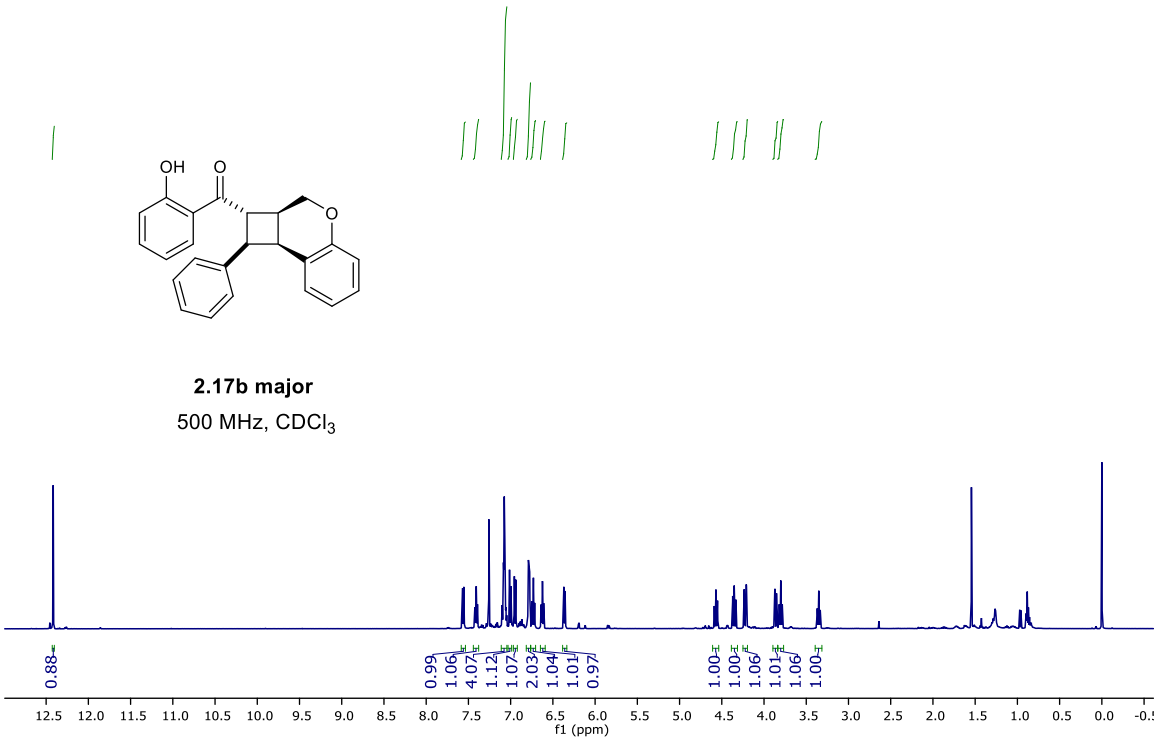



**2.17ab minor**

126 MHz, $CDCl_3$

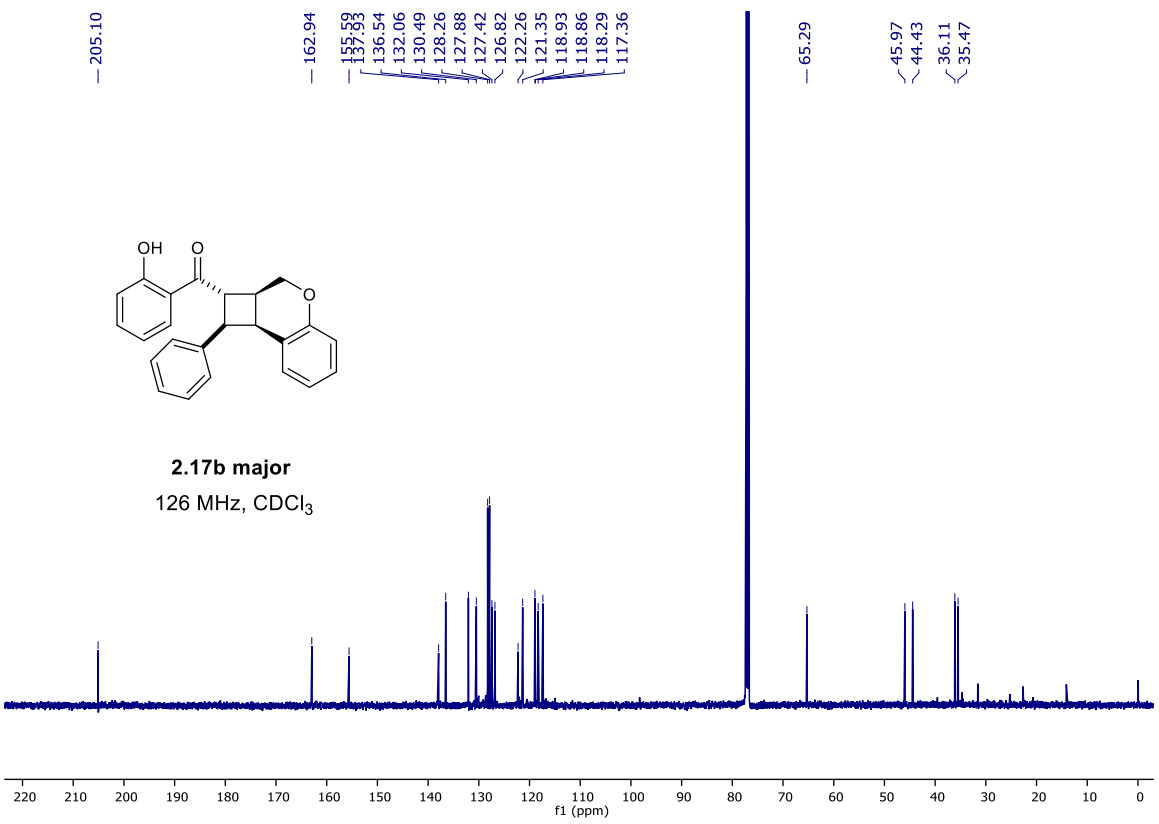

OH
O
2.17ac major
500 MHz, CDCl3
0.71
0.99
0.92
0.85
3.21
0.85
0.84
1.56
0.89
0.80
0.89
0.89
0.91
0.86
0.91
0.90
0.89
1.00
f1 (ppm)


205.85
162.93
138.69
136.61
136.29
134.92
131.68
130.12
128.84
128.49
127.80
126.54
125.79
125.72
119.05
118.70
118.37
46.49
45.86
39.18
33.85
26.52
22.97
OH
O
2.17ac major
126 MHz, CDCl3
f1 (ppm)



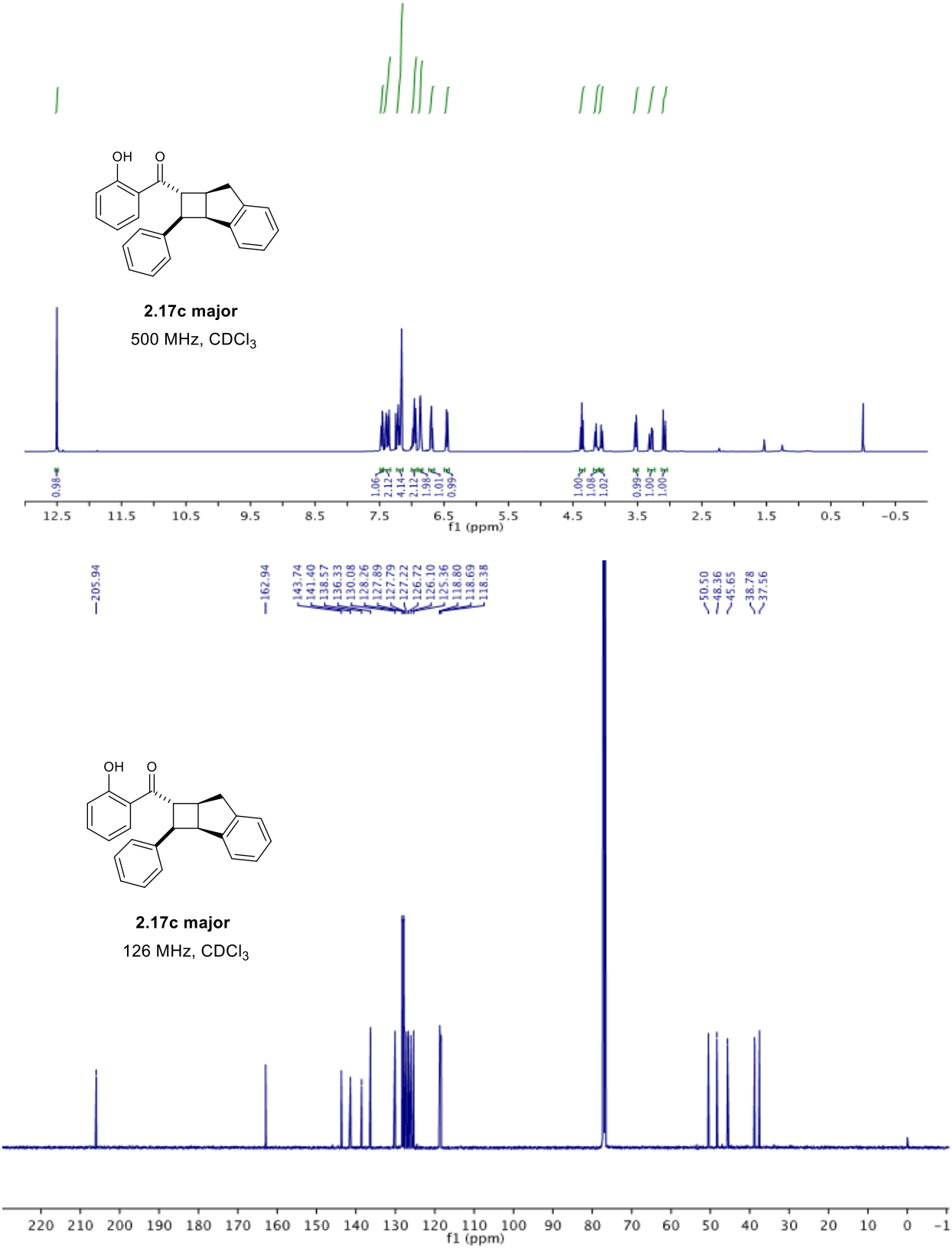

**2.17b major**

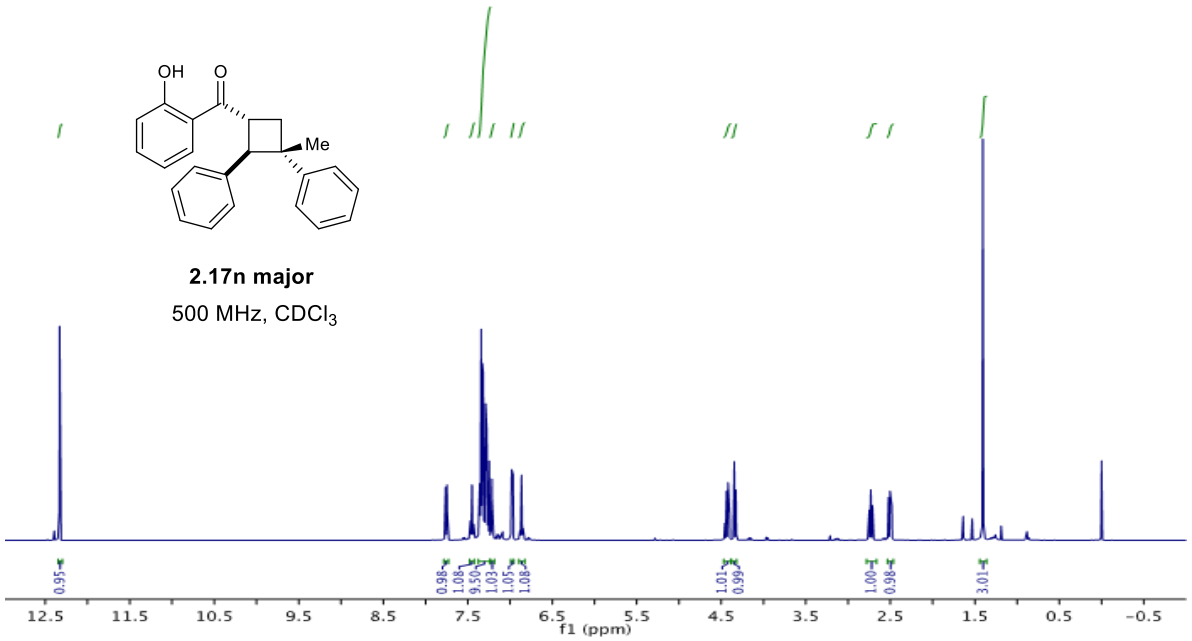
500 MHz, $CDCl_3$




**2.17b major**

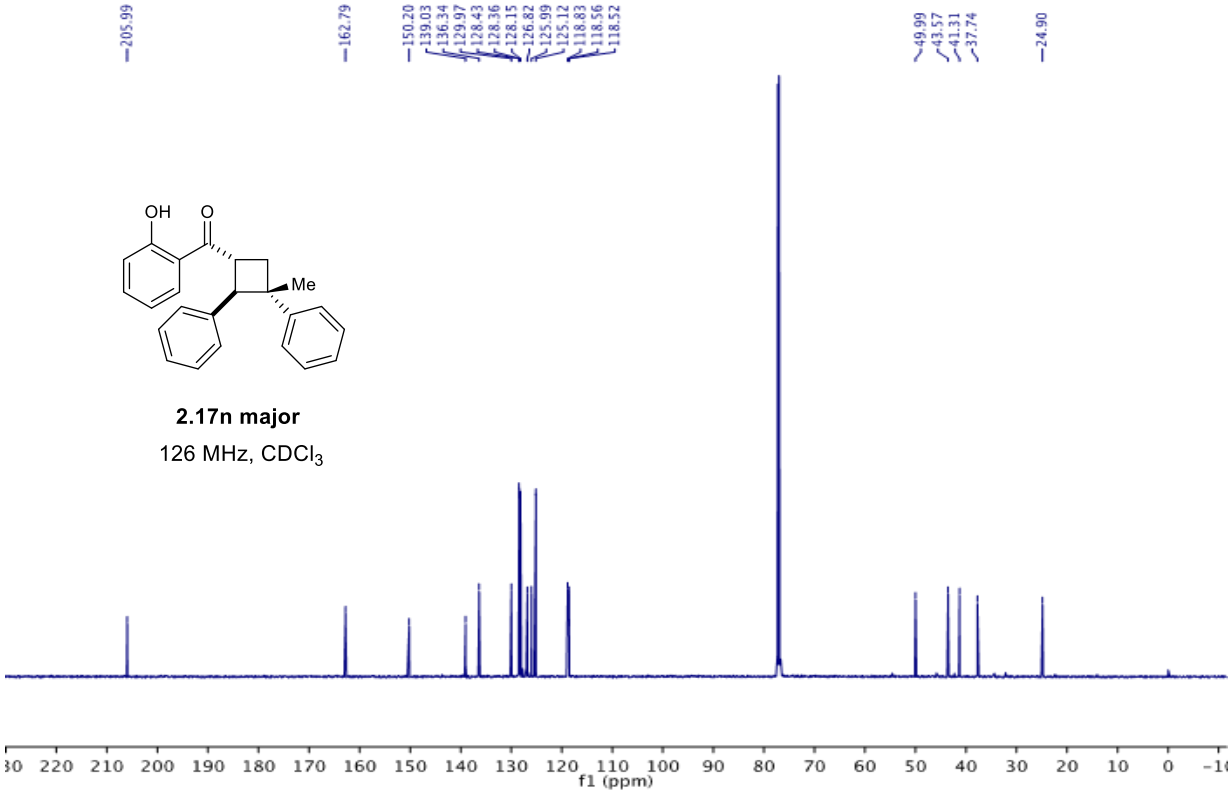
126 MHz, $CDCl_3$


OH
O
2.17c major
500 MHz, CDCl3
0.98
1.06
2.12
4.14
2.12
1.98
1.01
0.99
1.00
1.08
1.02
0.99
1.00
1.00
12.5 11.5 10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5
f1 (ppm)
205.94
162.94
143.74
141.40
138.57
136.33
130.08
128.26
127.89
127.79
127.22
126.72
126.10
125.36
118.80
118.69
118.38
50.50
48.36
45.65
38.78
37.56
OH
O
2.17c major
126 MHz, CDCl3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)



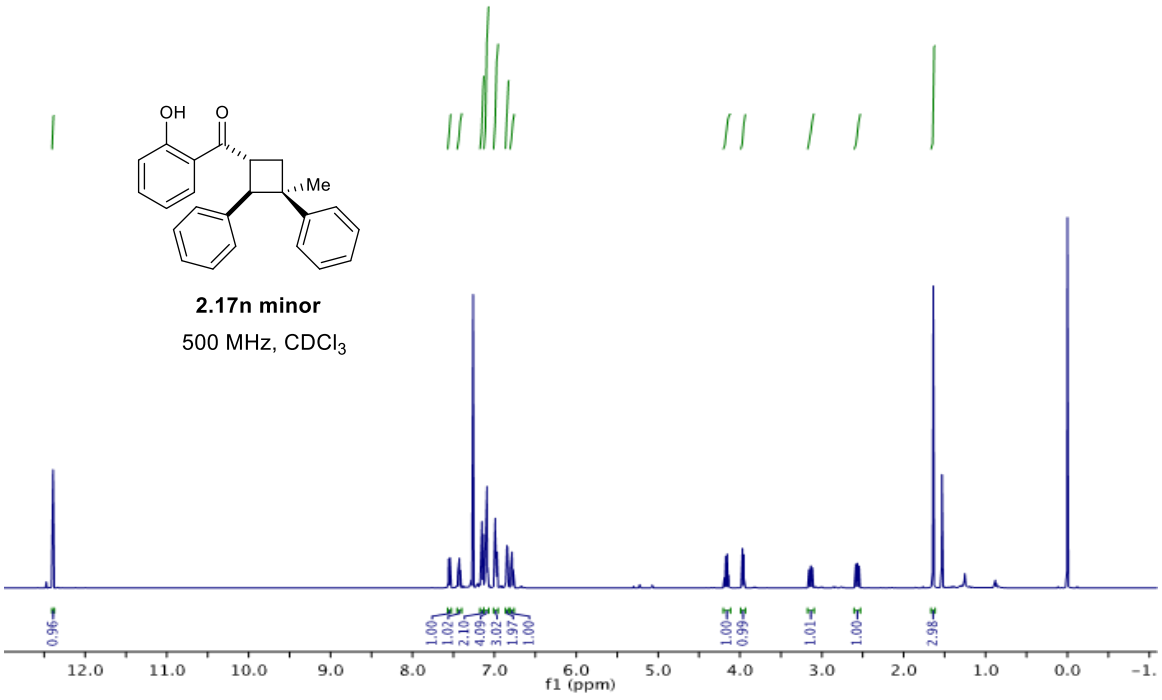

**2.17n major**

500 MHz, $CDCl_3$



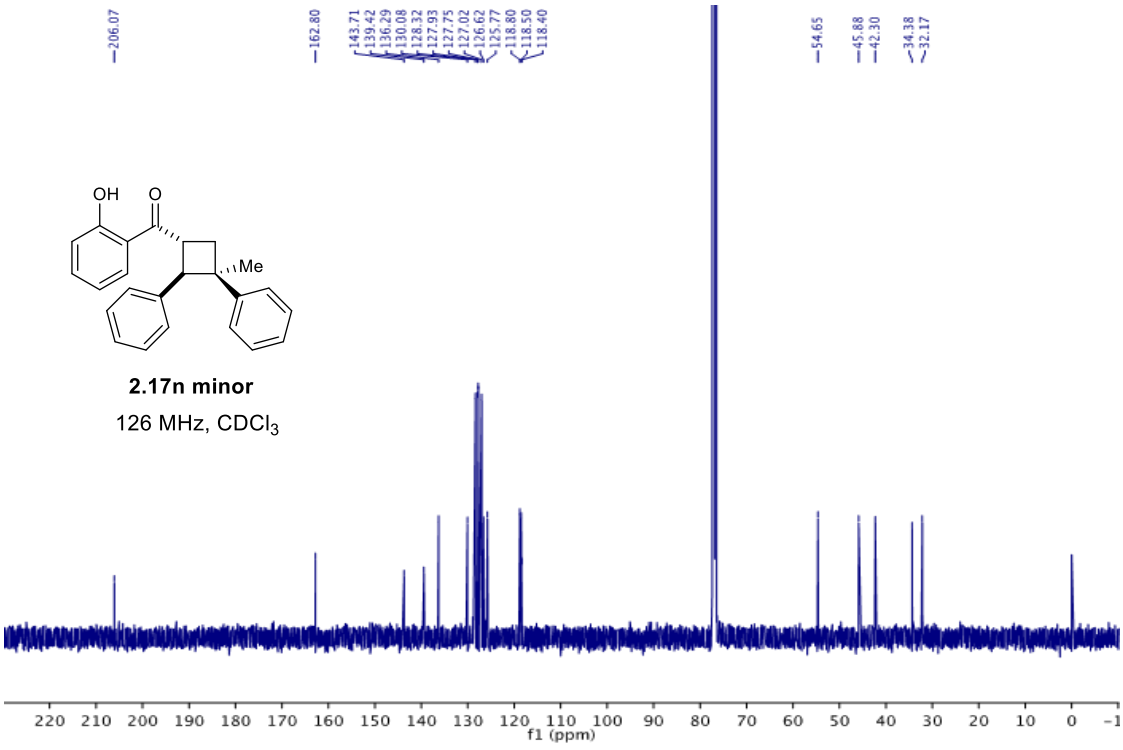

**2.17n major**

126 MHz, $CDCl_3$



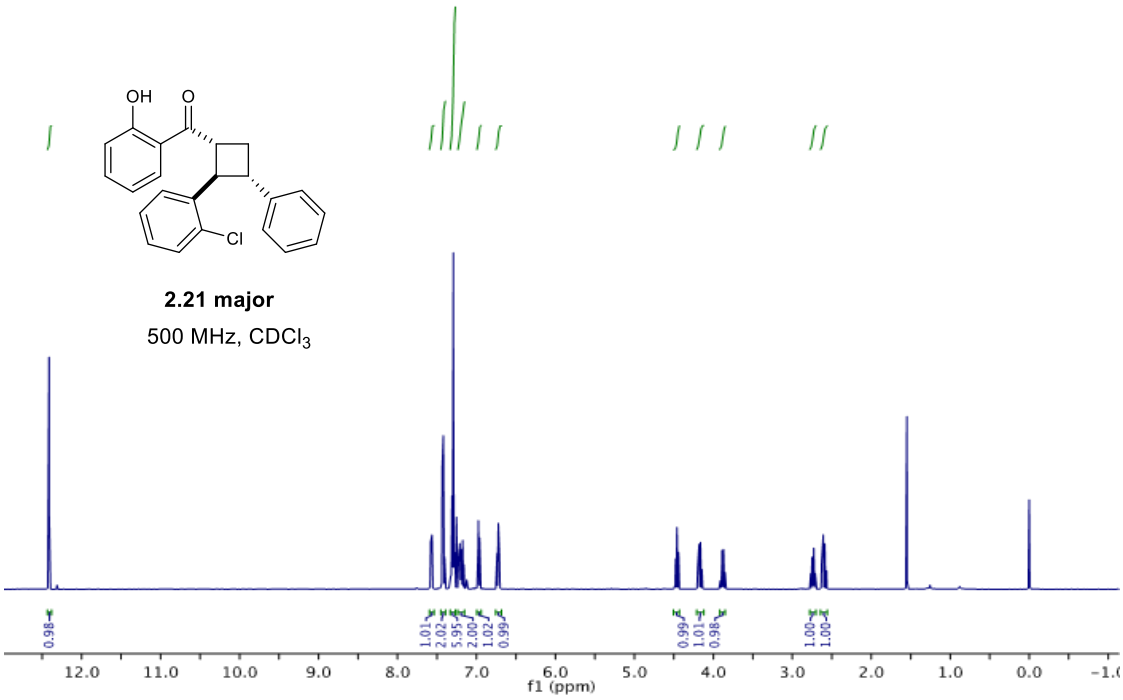

**2.17n minor**

500 MHz, $CDCl_3$



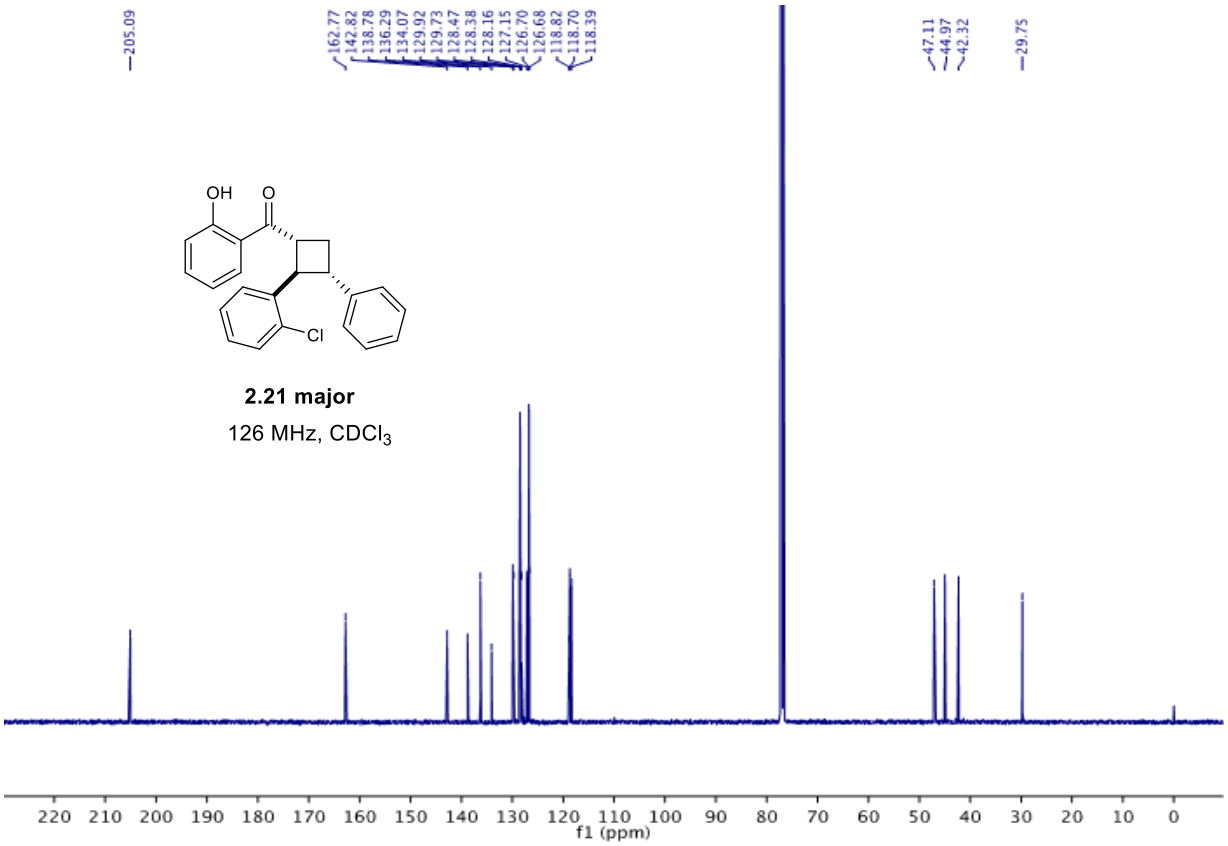

**2.17n minor**

126 MHz, $CDCl_3$



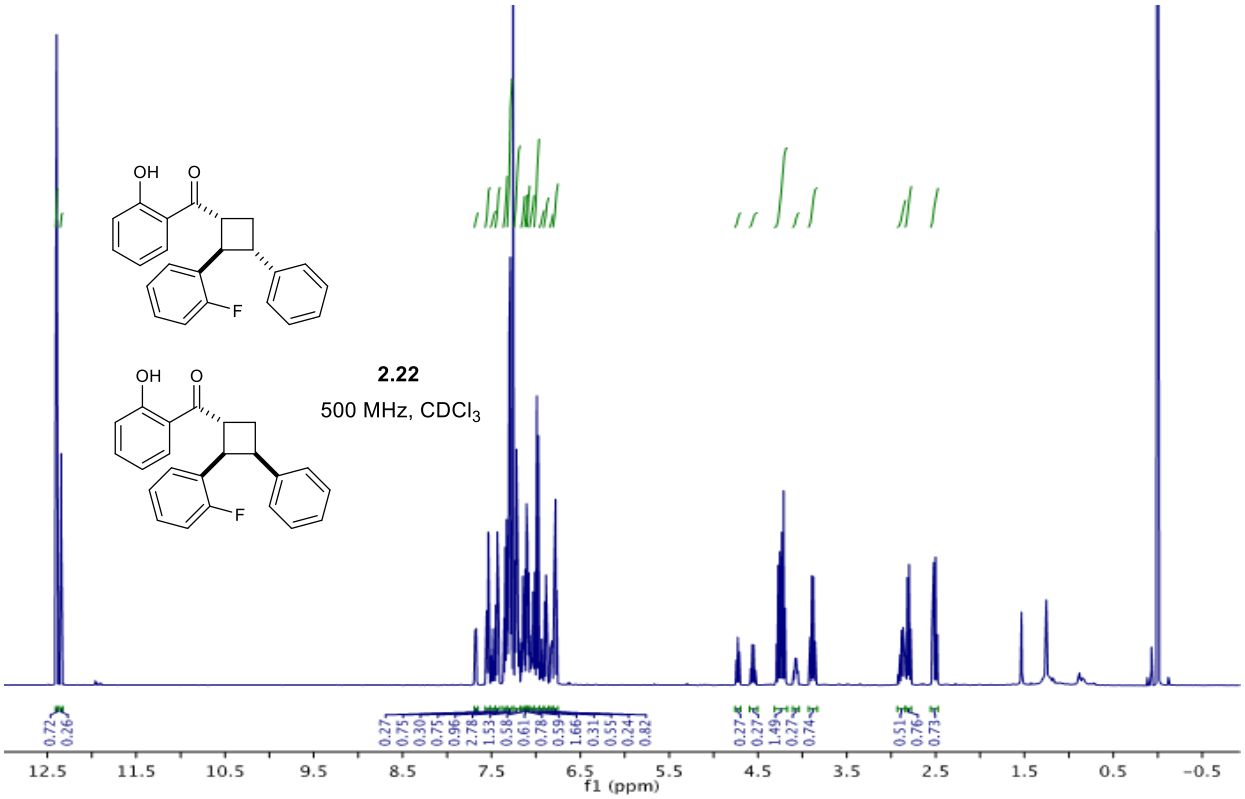

**2.21 major**

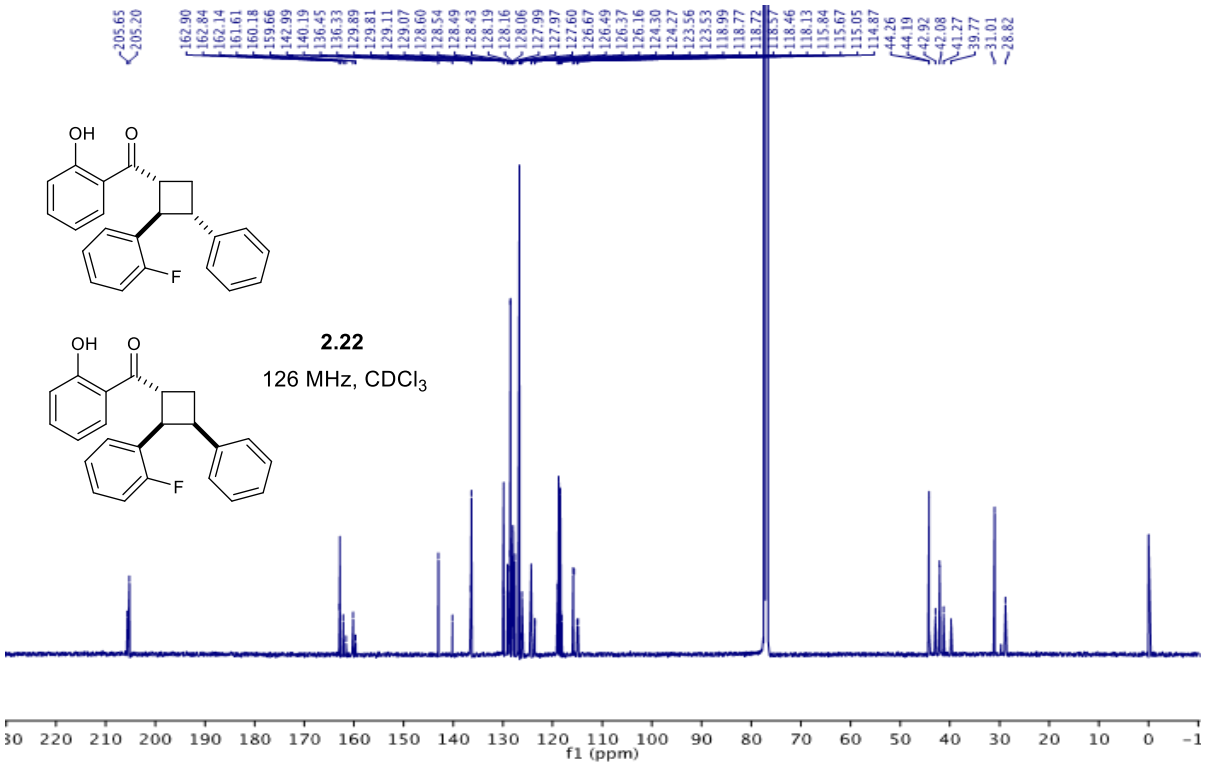
500 MHz, $CDCl_3$

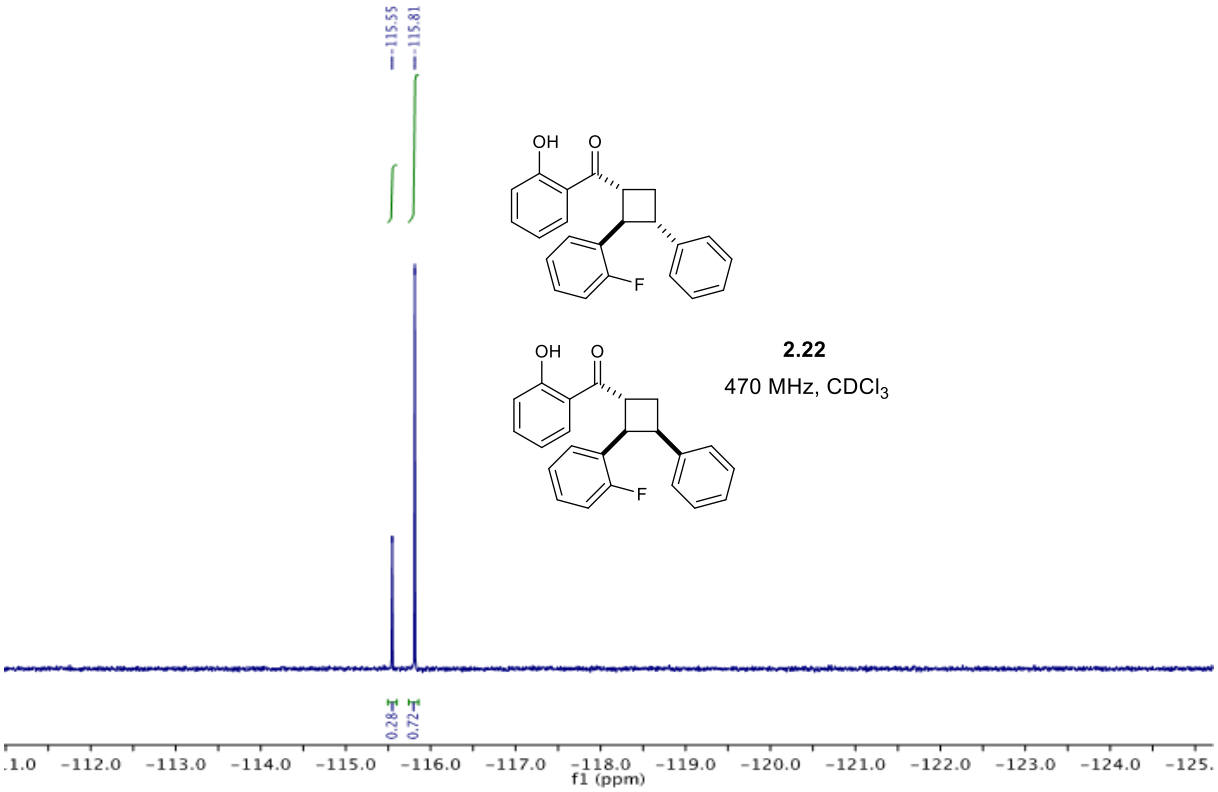



**2.21 major**

126 MHz, $CDCl_3$

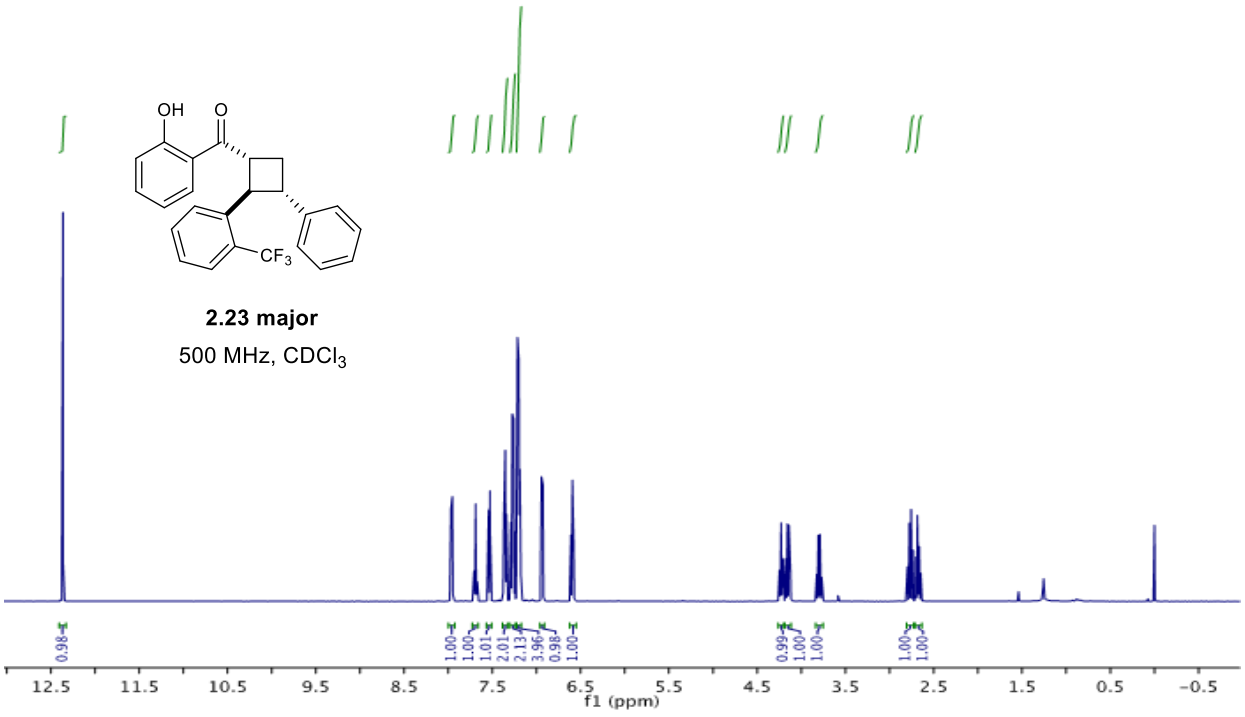

OH
O
F
2.22
500 MHz, CDCl3
f1 (ppm)


OH
O
F
2.22
126 MHz, CDCl3
f1 (ppm)



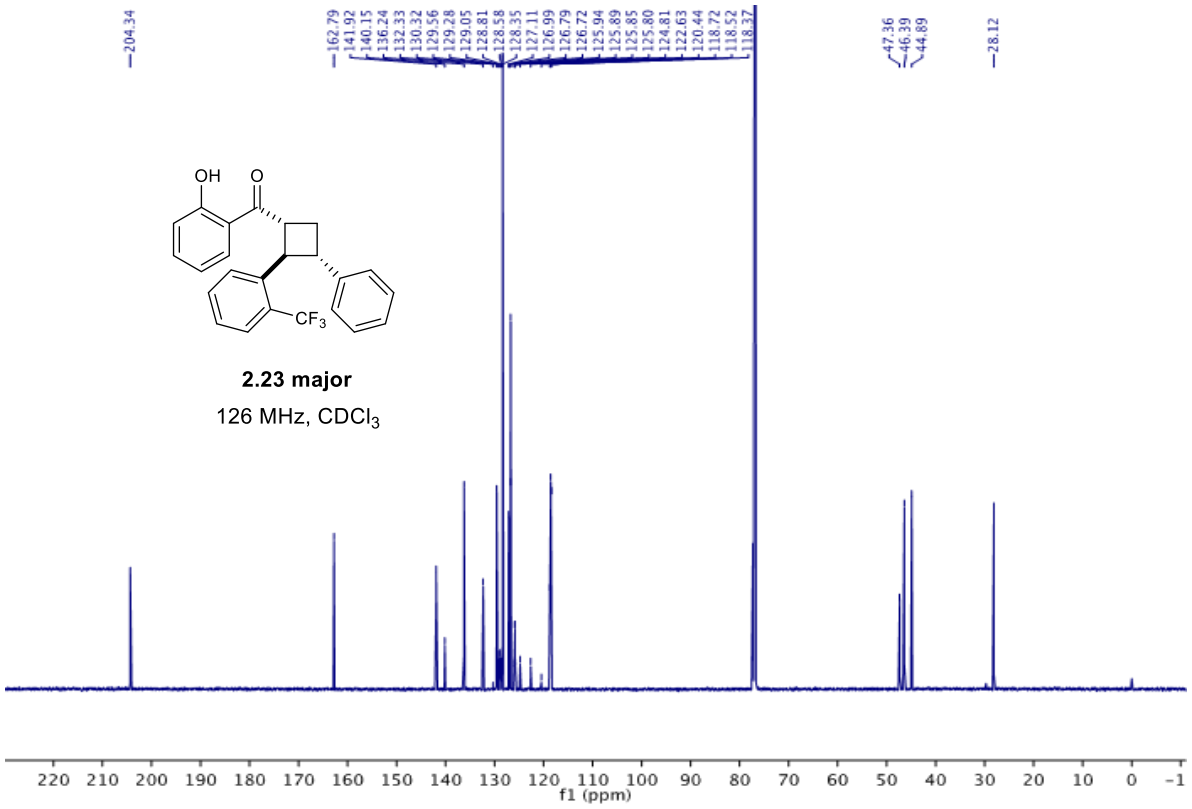

**2.22**

470 MHz, $CDCl_3$



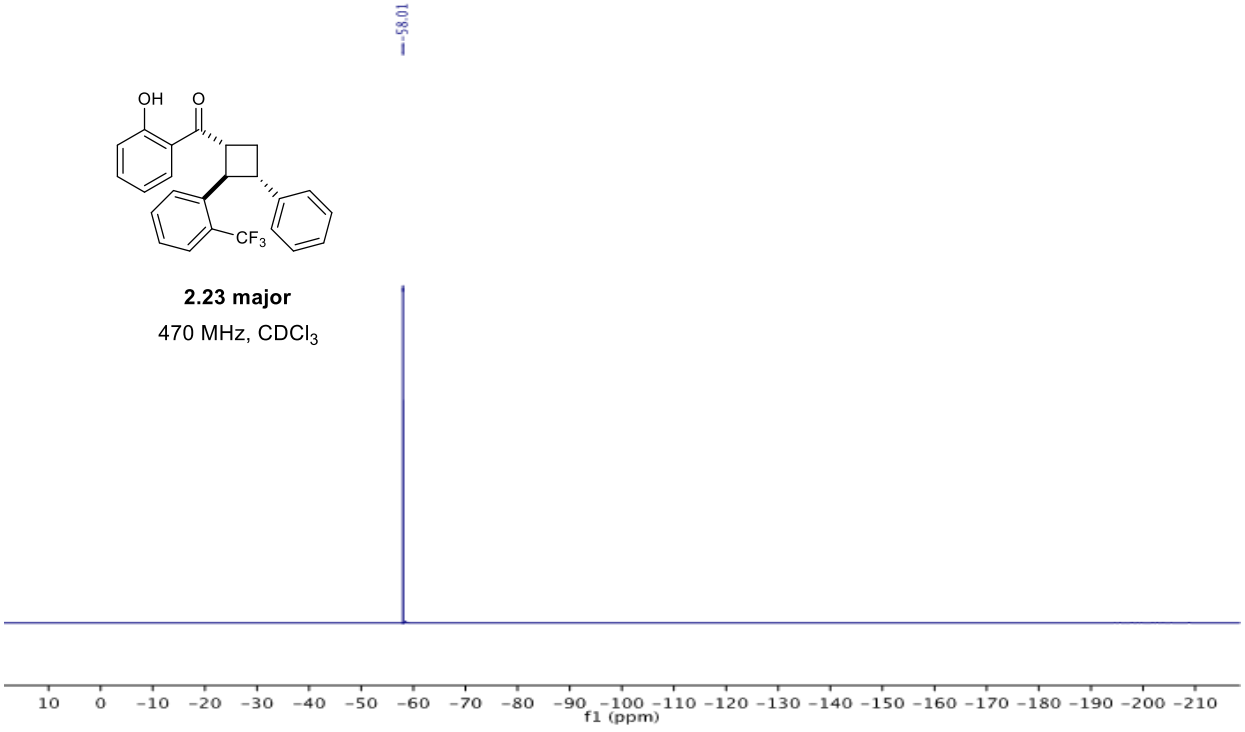

**2.23 major**

500 MHz, $CDCl_3$



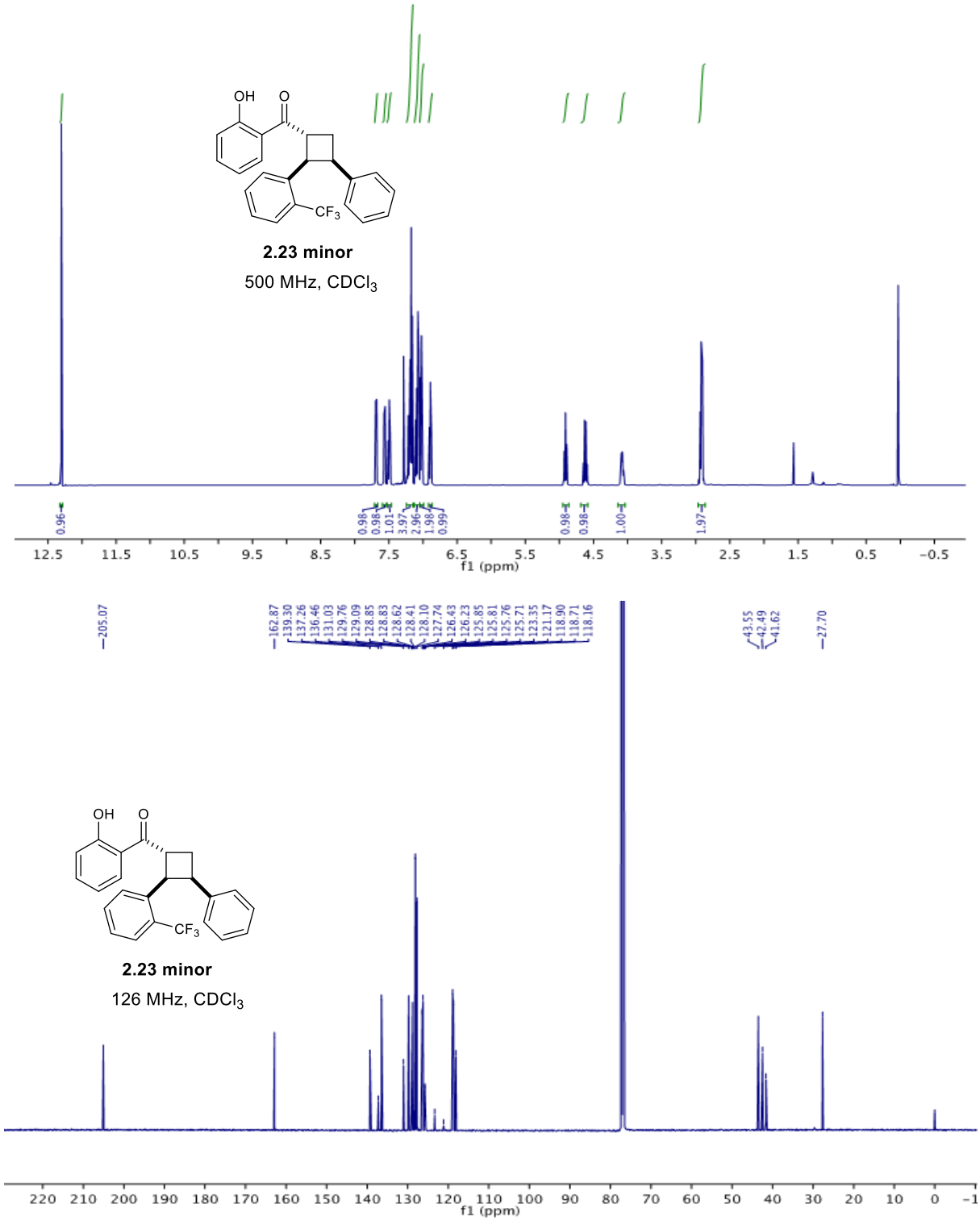

**2.23 major**

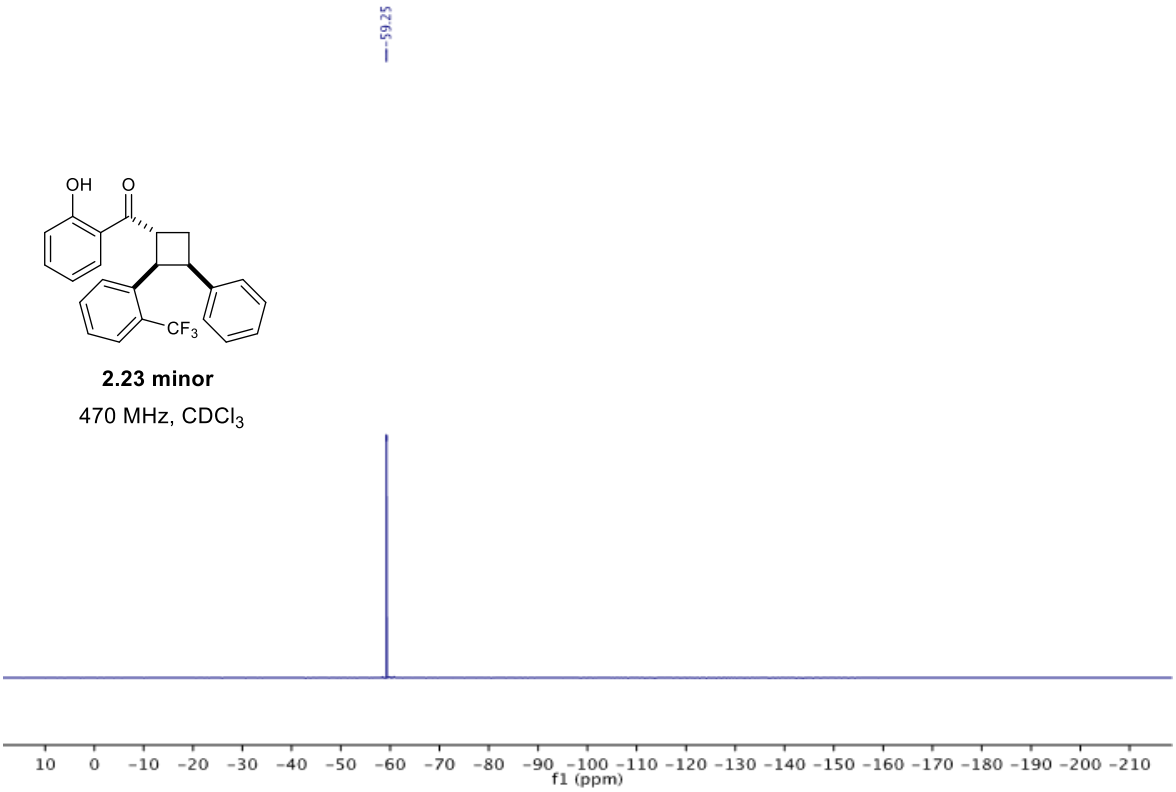
126 MHz, $CDCl_3$




**2.23 major**

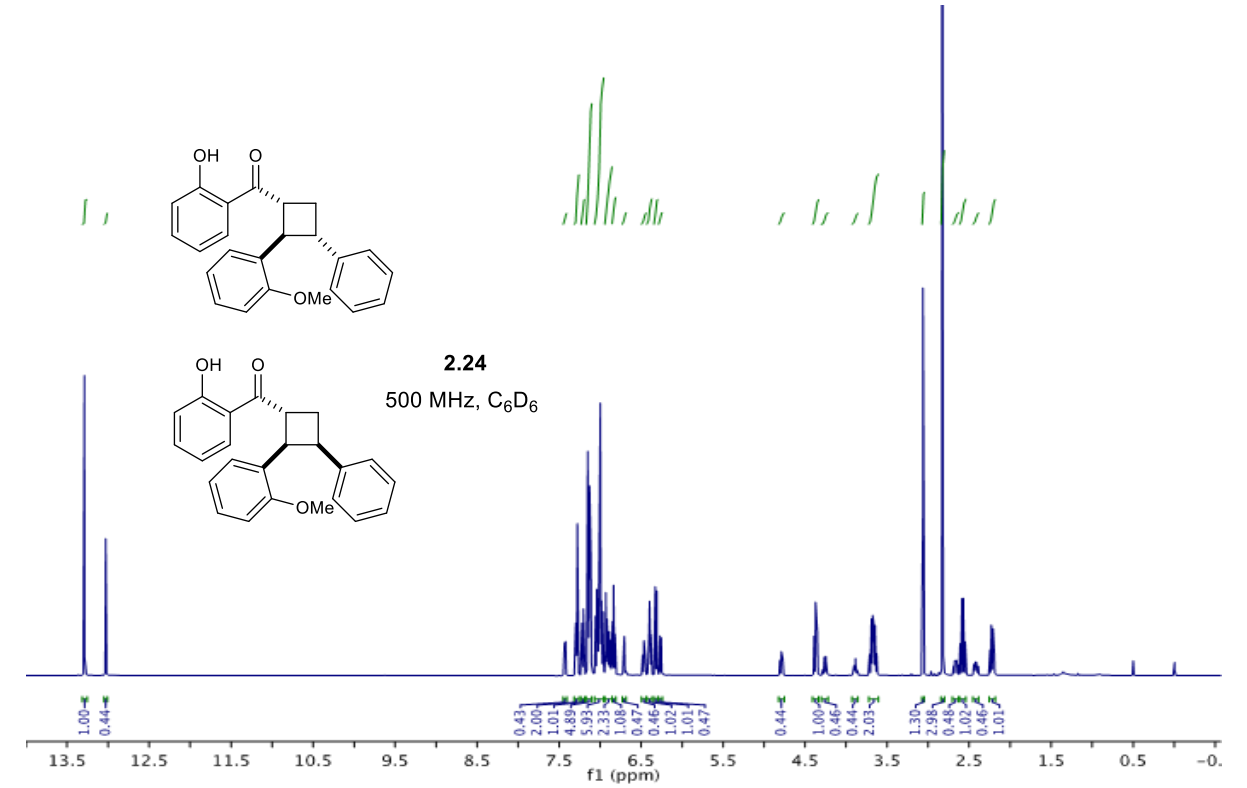
470 MHz, $CDCl_3$

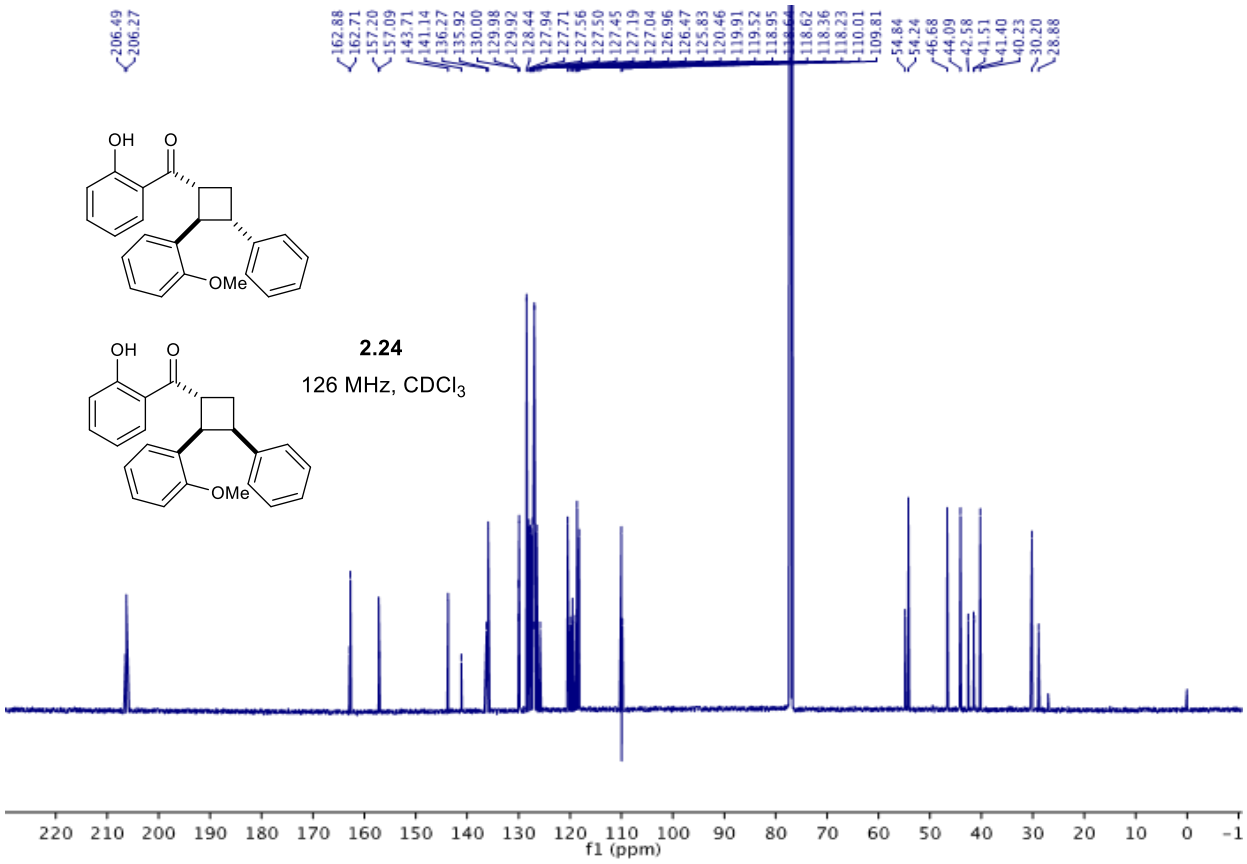

OH
O
CF3
2.23 minor
500 MHz, CDCl3
0.96
0.98
0.98
1.01
3.97
2.96
1.98
0.99
0.98
0.98
1.00
1.97
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)
205.07
162.87
139.30
137.26
136.46
131.03
129.76
129.09
128.85
128.83
128.62
128.41
128.10
127.74
126.43
126.23
125.85
125.81
125.76
125.71
123.35
121.17
118.90
118.71
118.16
43.55
42.49
41.62
27.70
OH
O
CF3
2.23 minor
126 MHz, CDCl3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

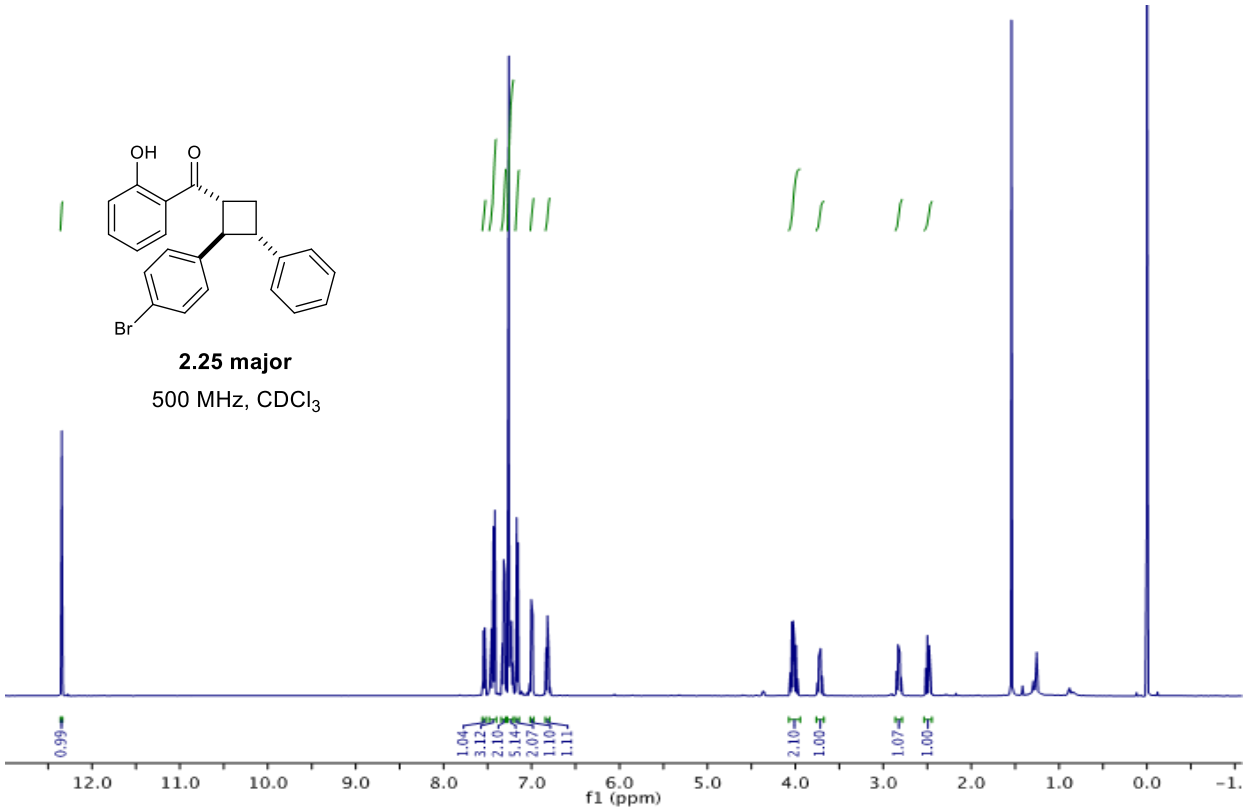



**2.23 minor**

470 MHz, $CDCl_3$

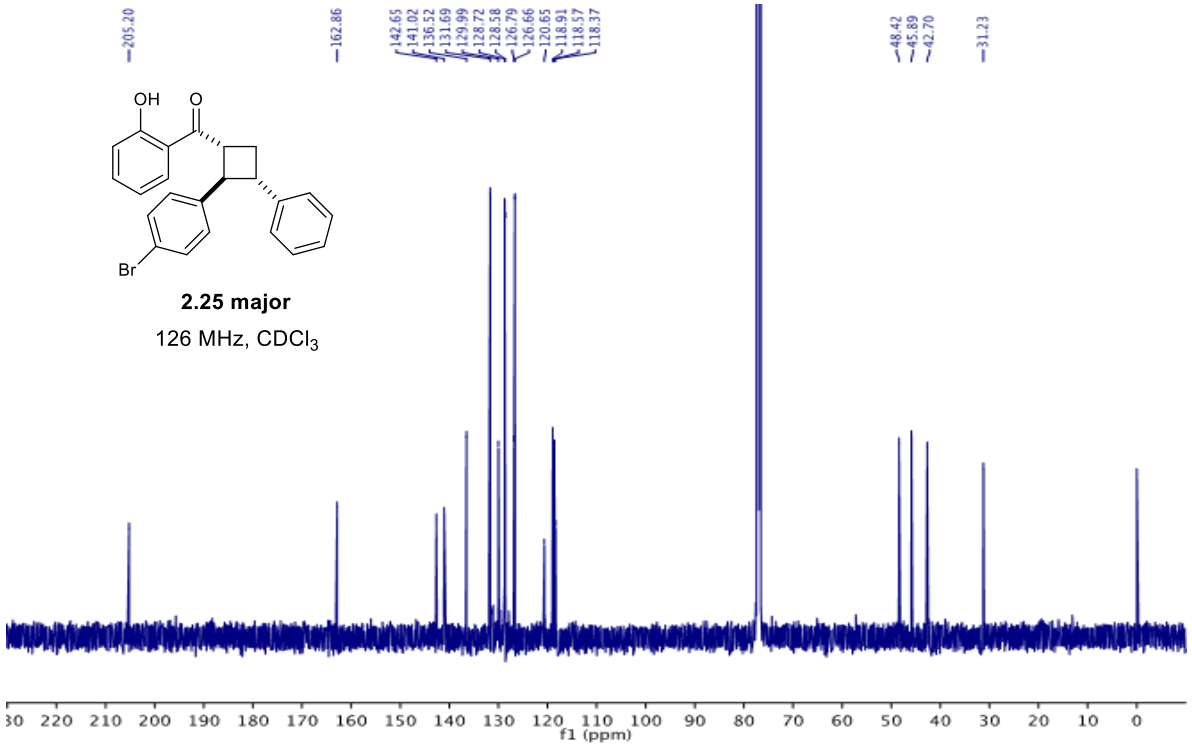

OH
O
OMe
2.24
500 MHz, C6D6
f1 (ppm)


OH
O
OMe
2.24
126 MHz, CDCl3
f1 (ppm)



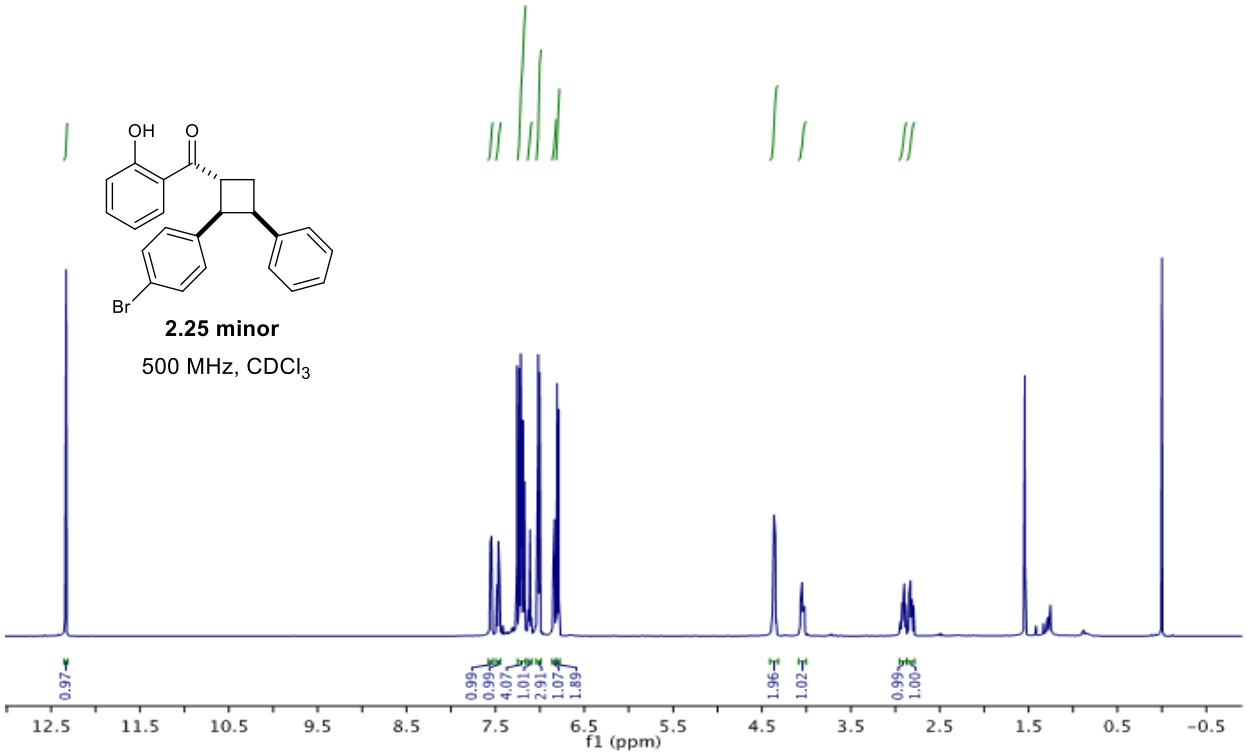

**2.25 major**

500 MHz, $CDCl_3$



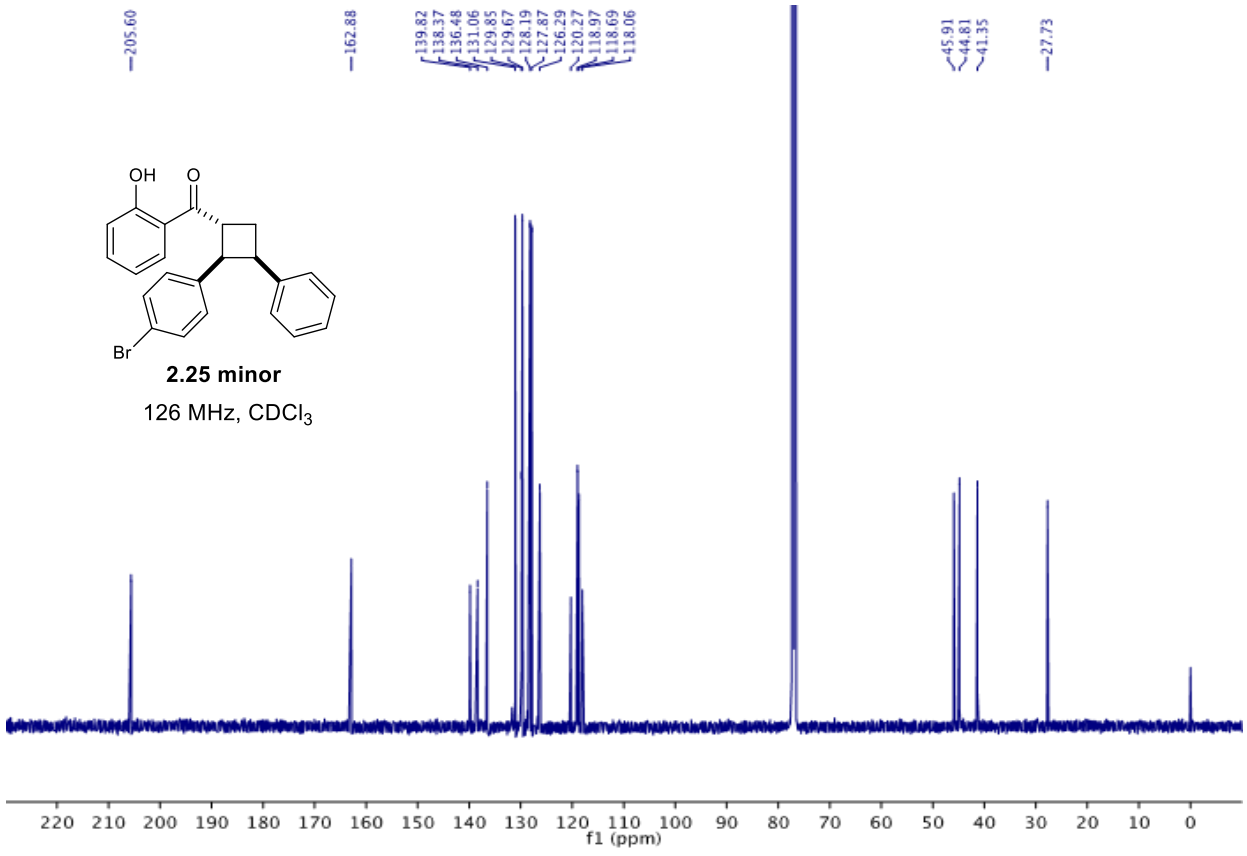

**2.25 major**

126 MHz, $CDCl_3$



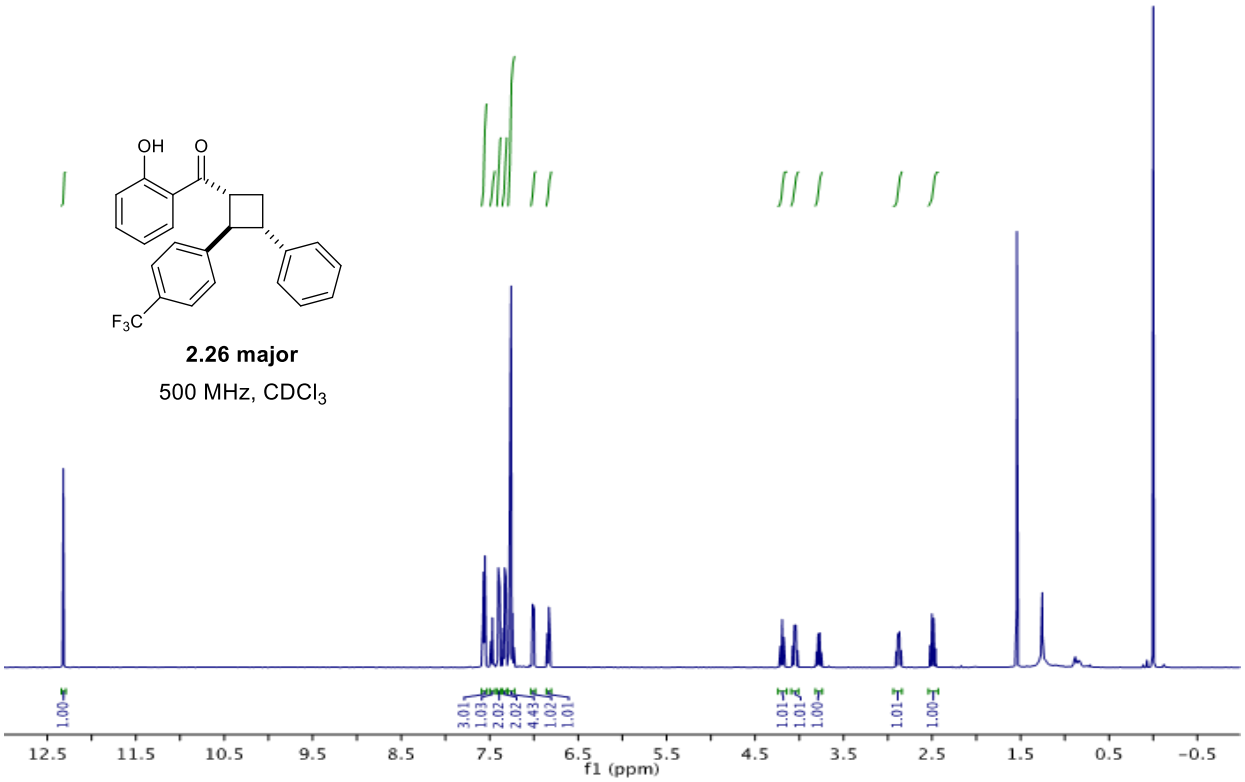

**2.25 minor**

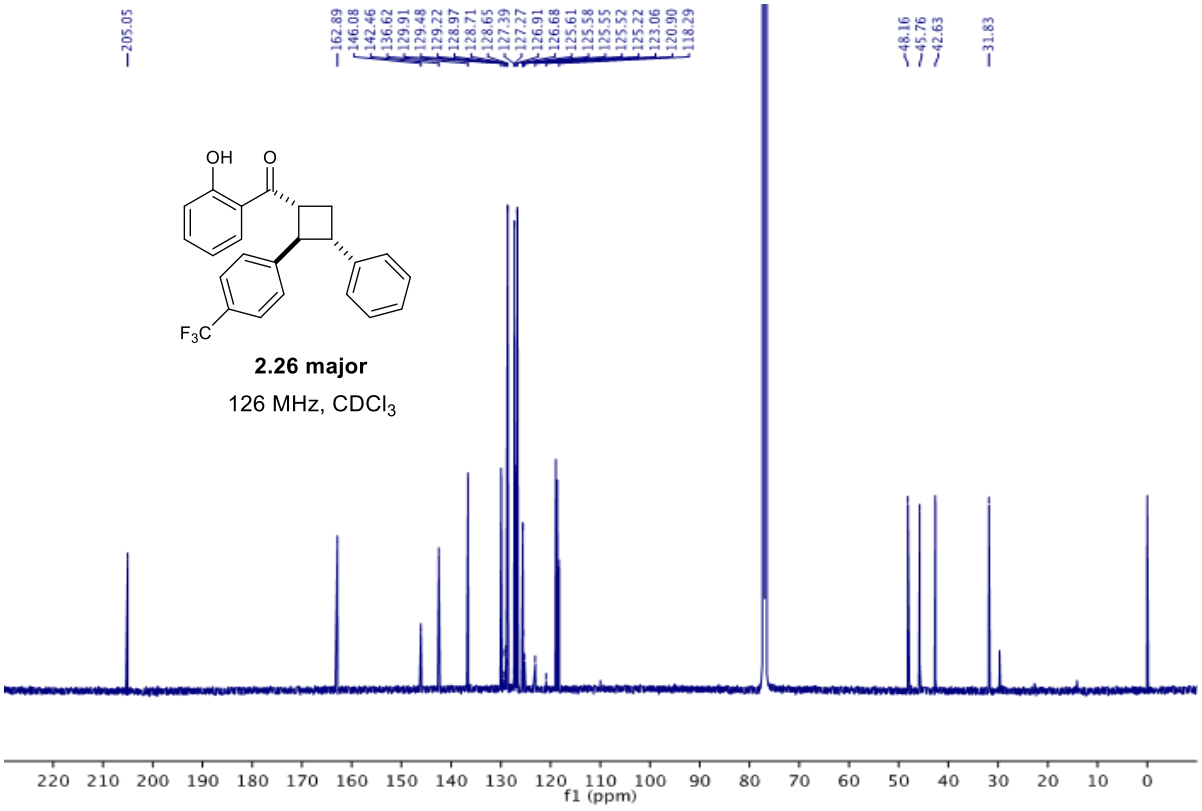
500 MHz, $CDCl_3$

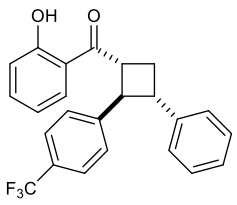



**2.25 minor**

126 MHz, $CDCl_3$


OH
O
F3C
2.26 major
500 MHz, CDCl3
1.00
3.01
1.03
2.02
2.02
4.43
1.02
1.01
1.01
1.01
1.00
1.01
1.00
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

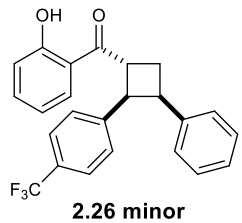

205.05
162.89
146.08
142.46
136.62
129.91
129.48
129.22
128.97
128.71
128.65
127.39
127.27
126.91
126.68
125.61
125.58
125.55
125.52
125.22
123.06
120.90
118.29
48.16
45.76
42.63
31.83
OH
O
F3C
2.26 major
126 MHz, CDCl3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)




**2.26 major**

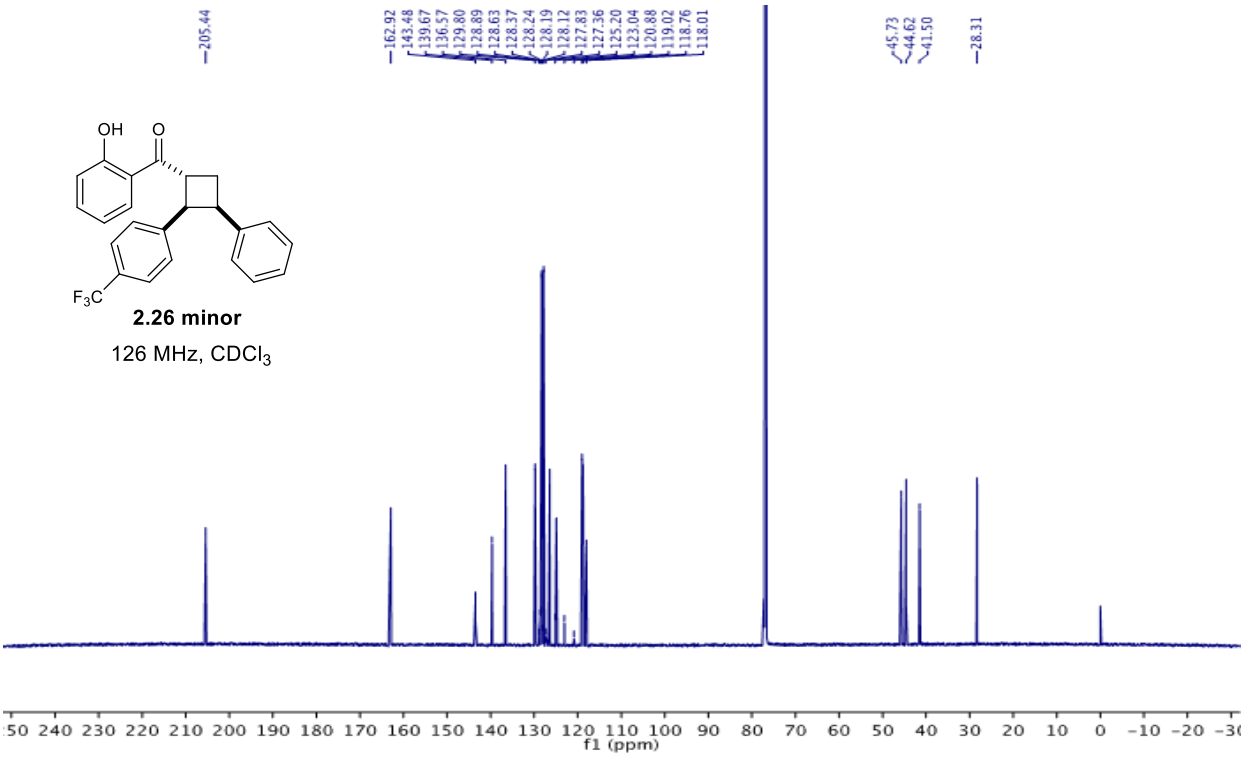
470 MHz, $CDCl_3$



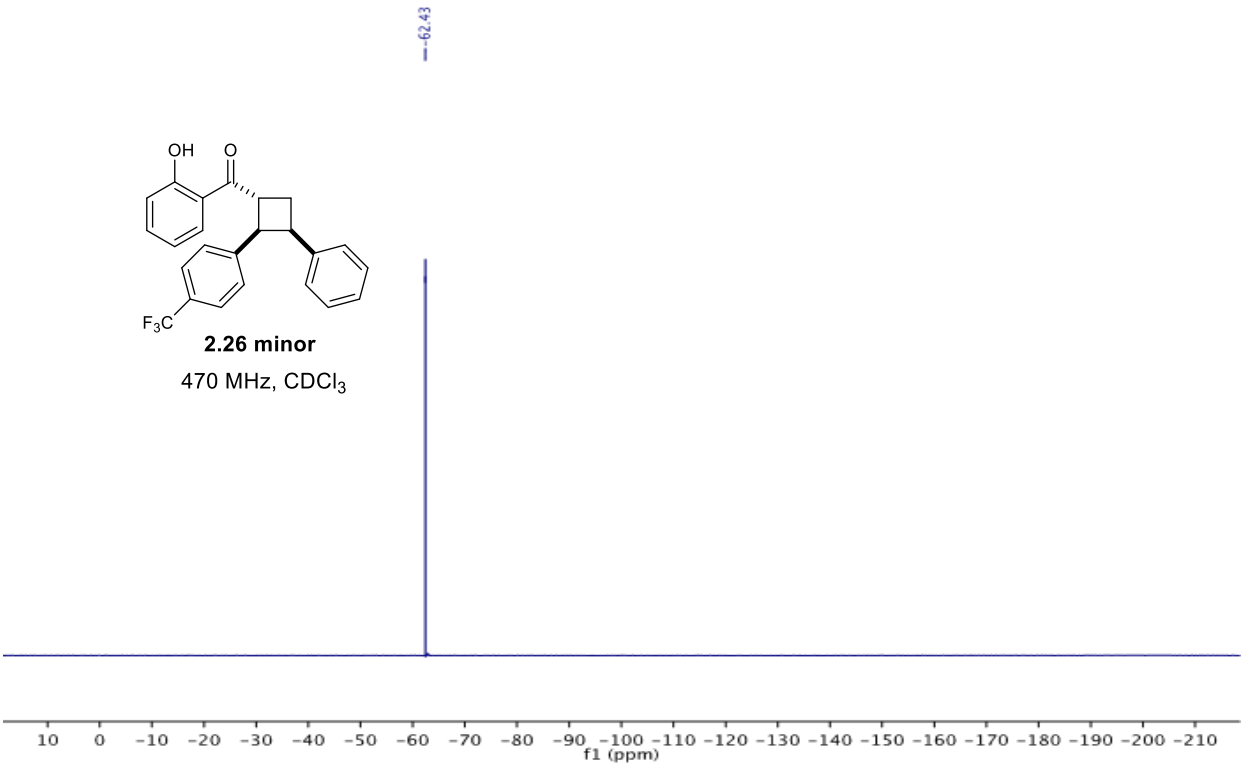

**2.26 minor**

500 MHz, $CDCl_3$



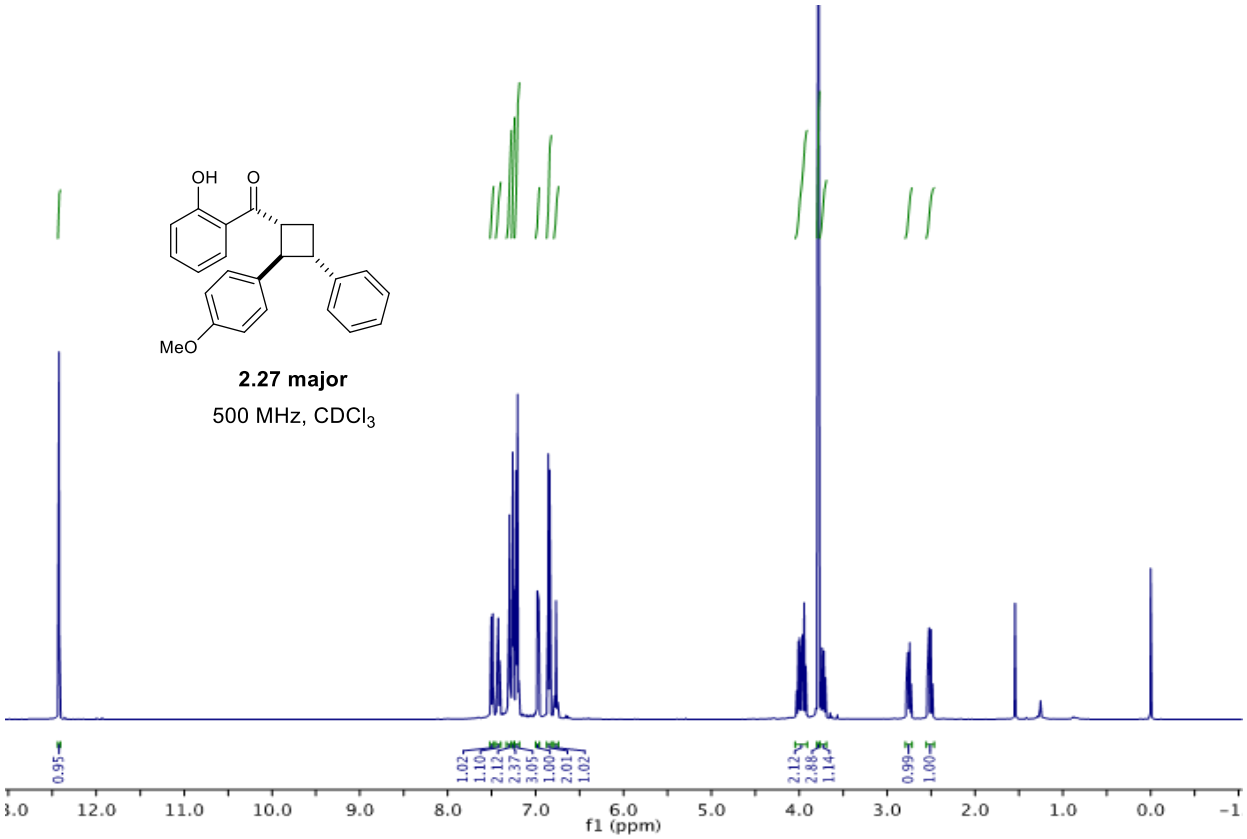

**2.26 minor**

126 MHz, $CDCl_3$



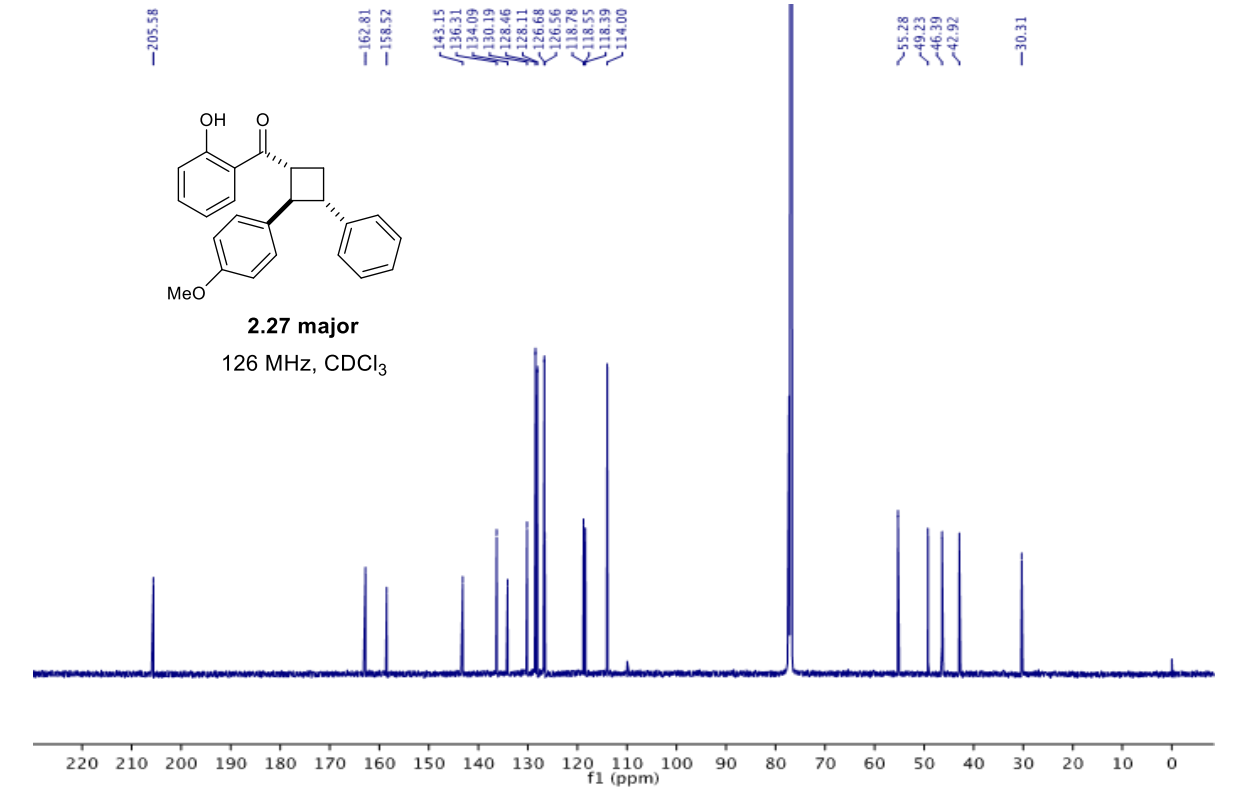

**2.26 minor**

470 MHz, $CDCl_3$



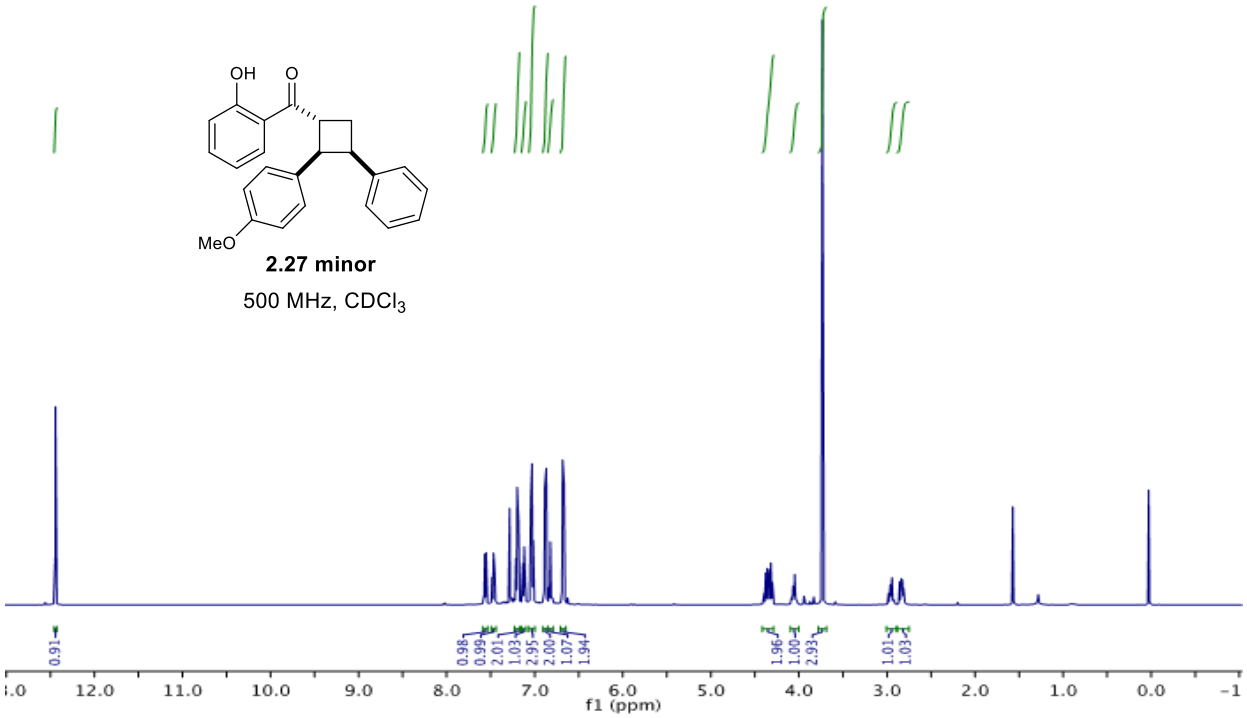

**2.27 major**

500 MHz, $CDCl_3$



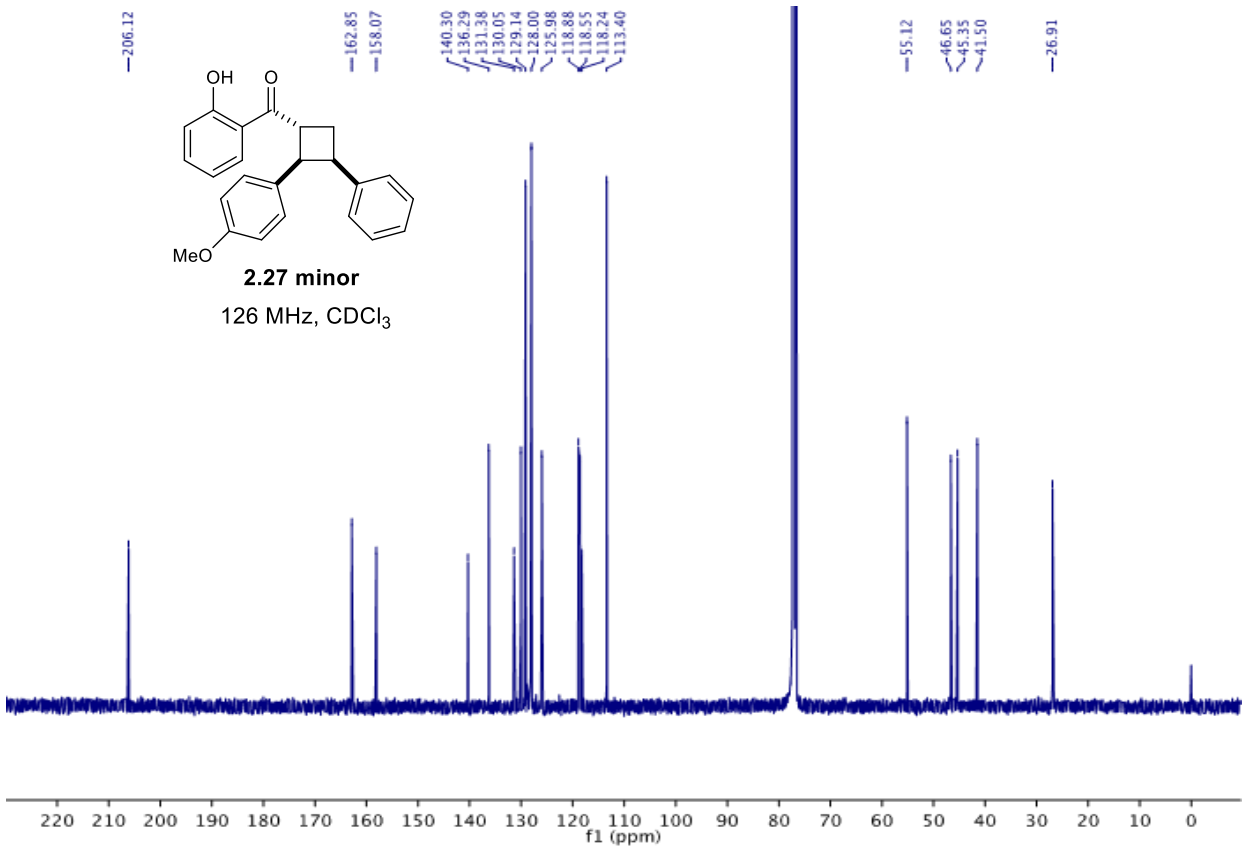

**2.27 major**

126 MHz, $CDCl_3$



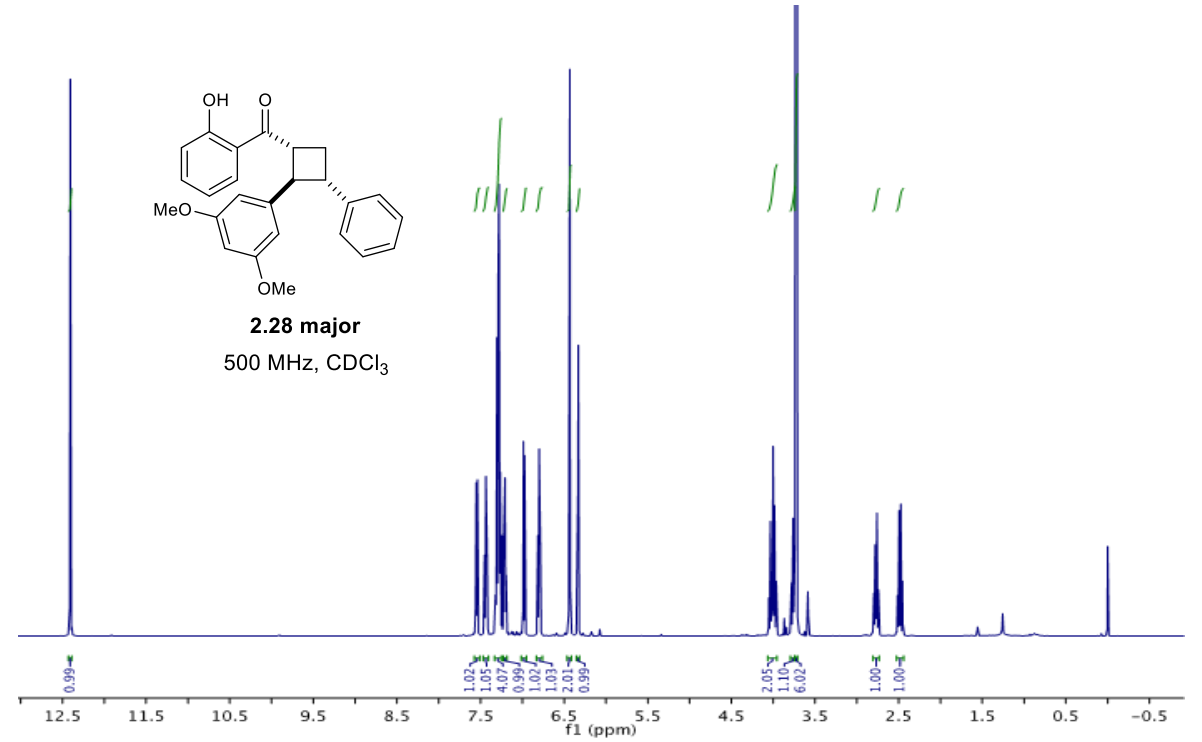

**2.27 minor**

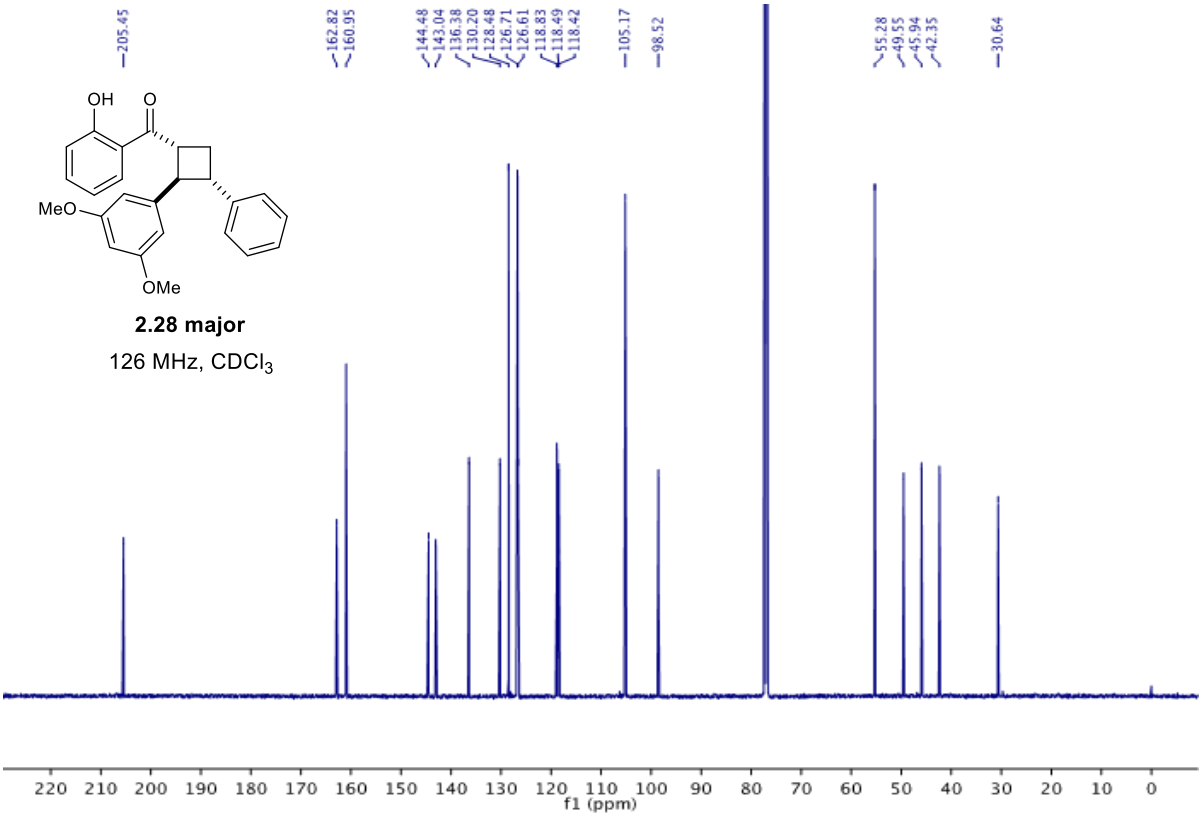
500 MHz, $CDCl_3$

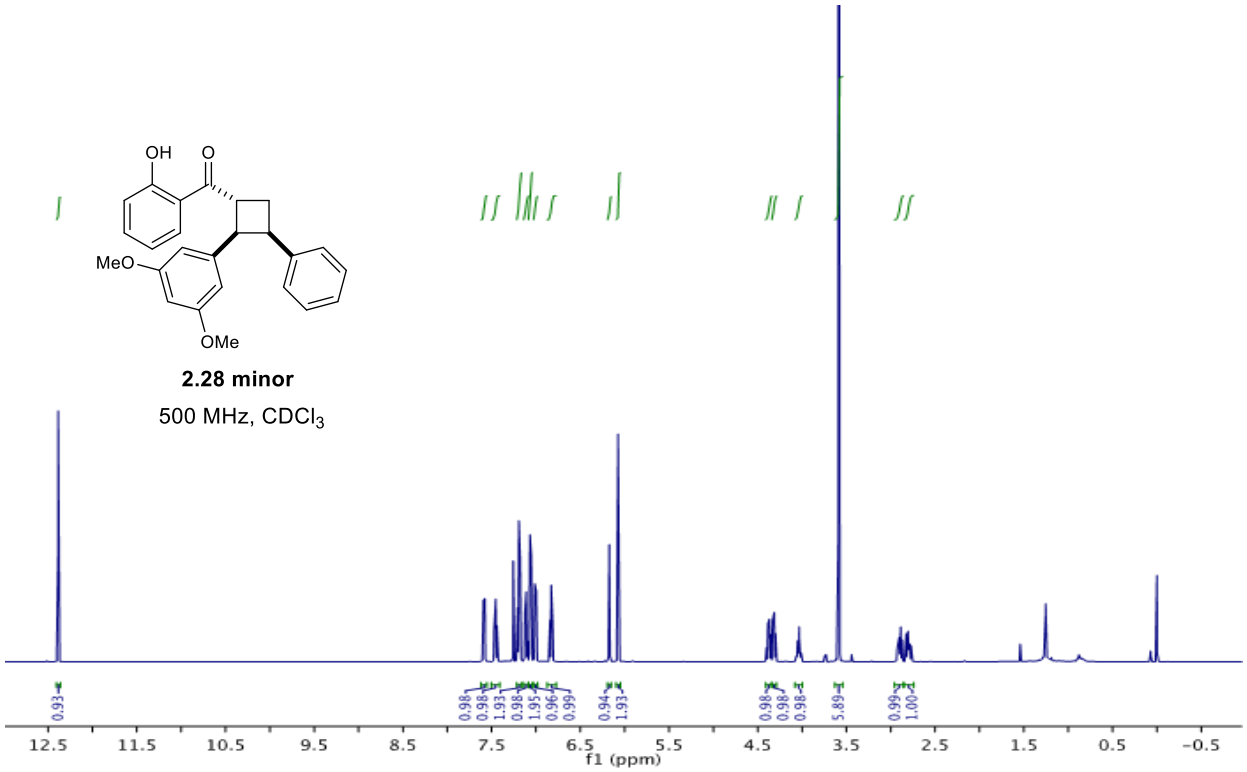



**2.27 minor**

126 MHz, $CDCl_3$

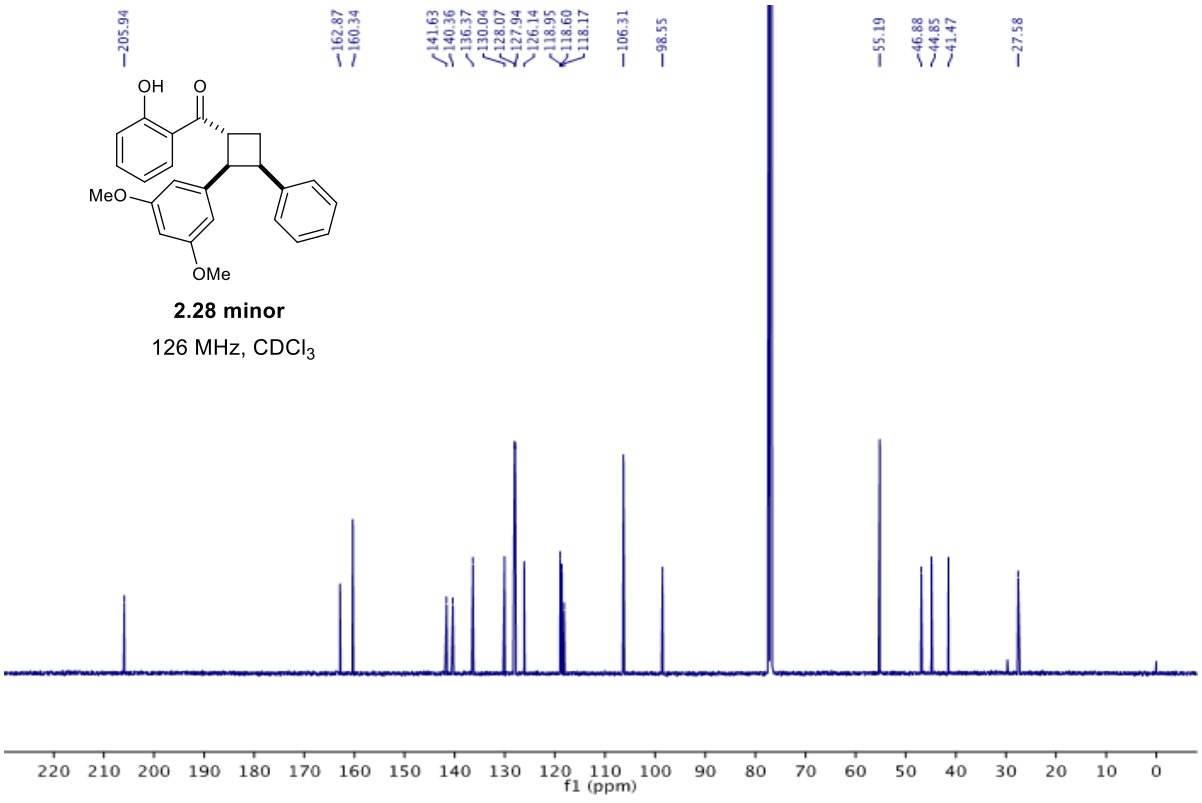

OH
O
MeO
OMe
2.28 major
500 MHz, CDCl3
f1 (ppm)


205.45
162.82
160.95
144.48
143.04
136.38
130.20
128.48
126.71
126.61
118.83
118.49
118.42
105.17
98.52
55.28
49.55
45.94
42.35
30.64
OH
O
MeO
OMe
2.28 major
126 MHz, CDCl3
f1 (ppm)



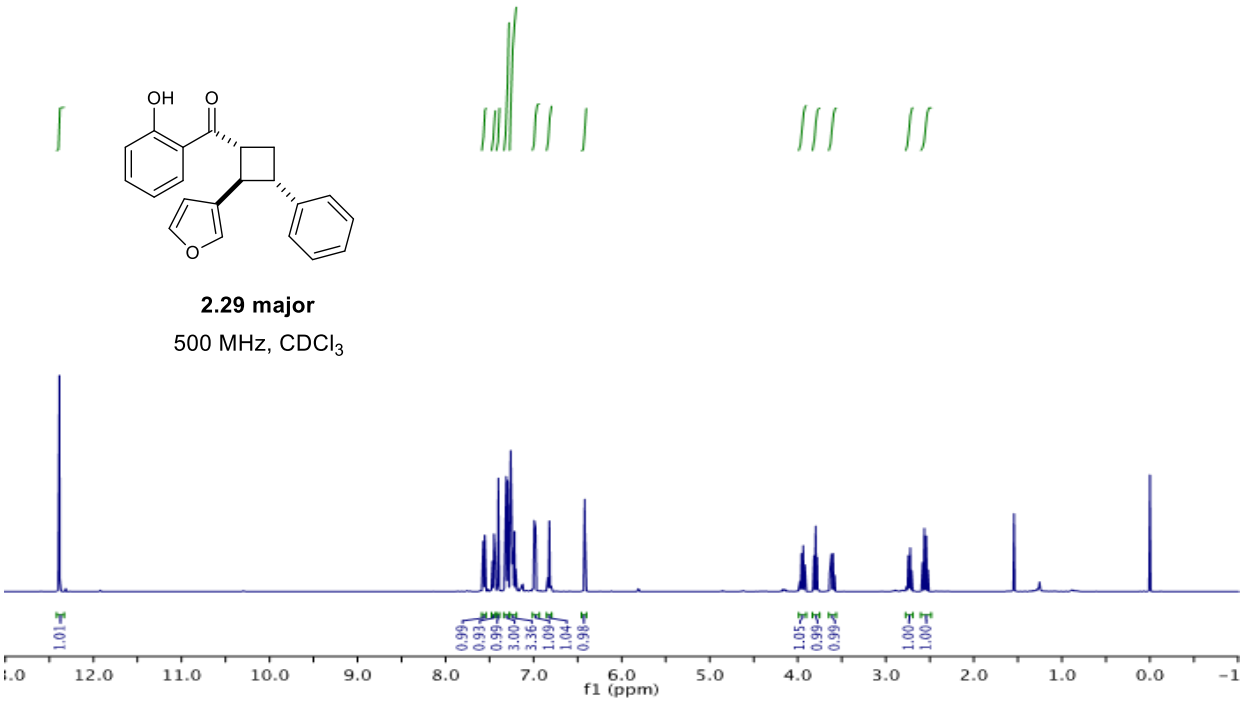

**2.28 minor**

500 MHz, $CDCl_3$



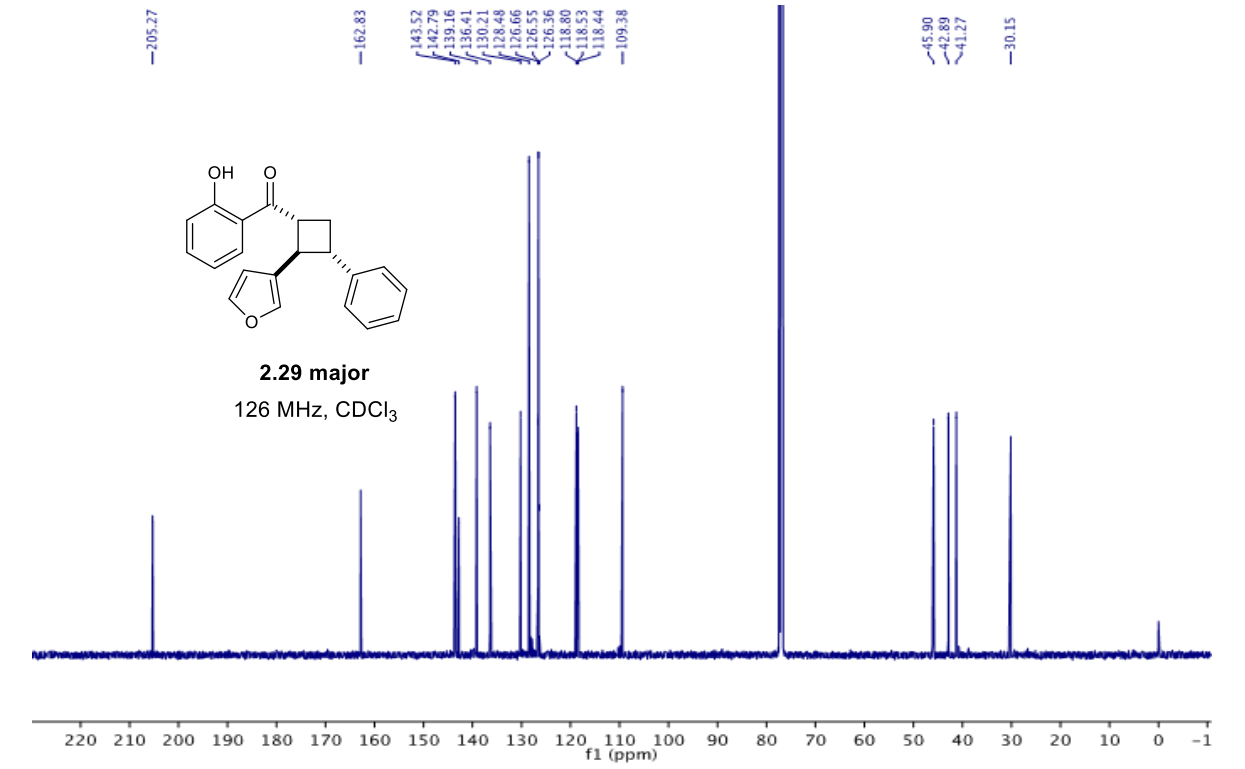

**2.28 minor**

126 MHz, $CDCl_3$



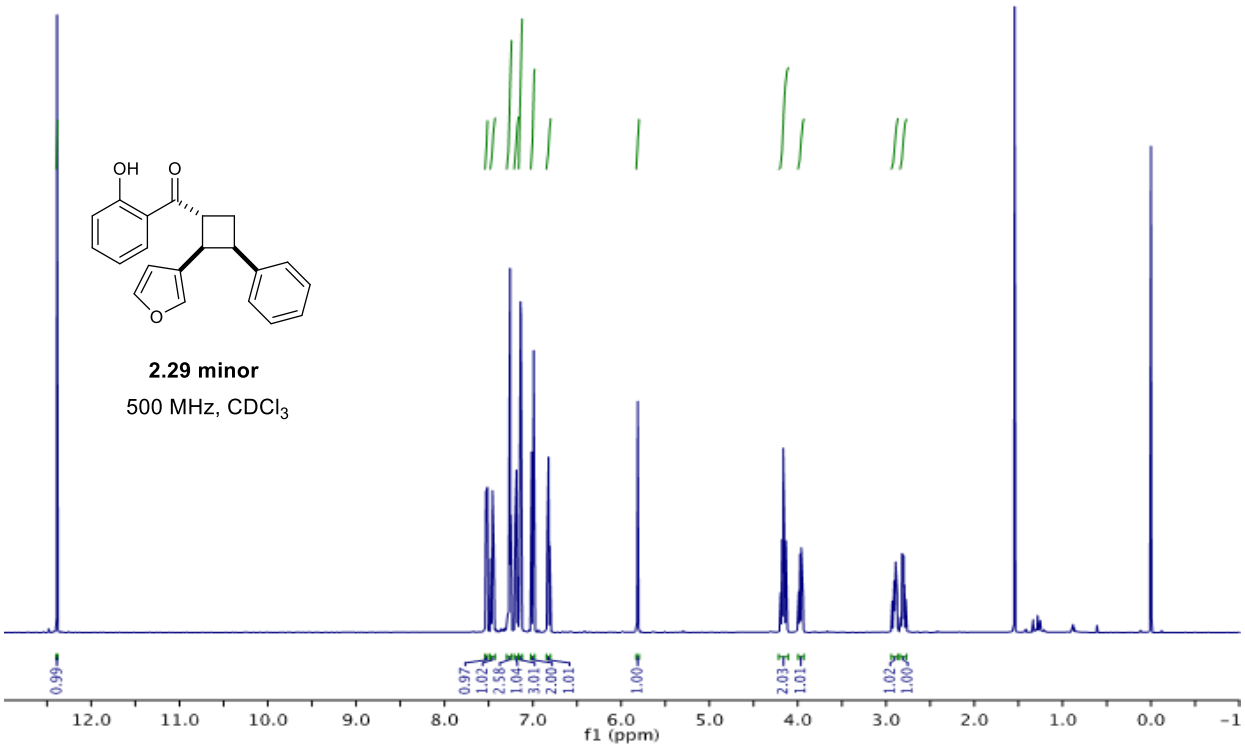

**2.29 major**

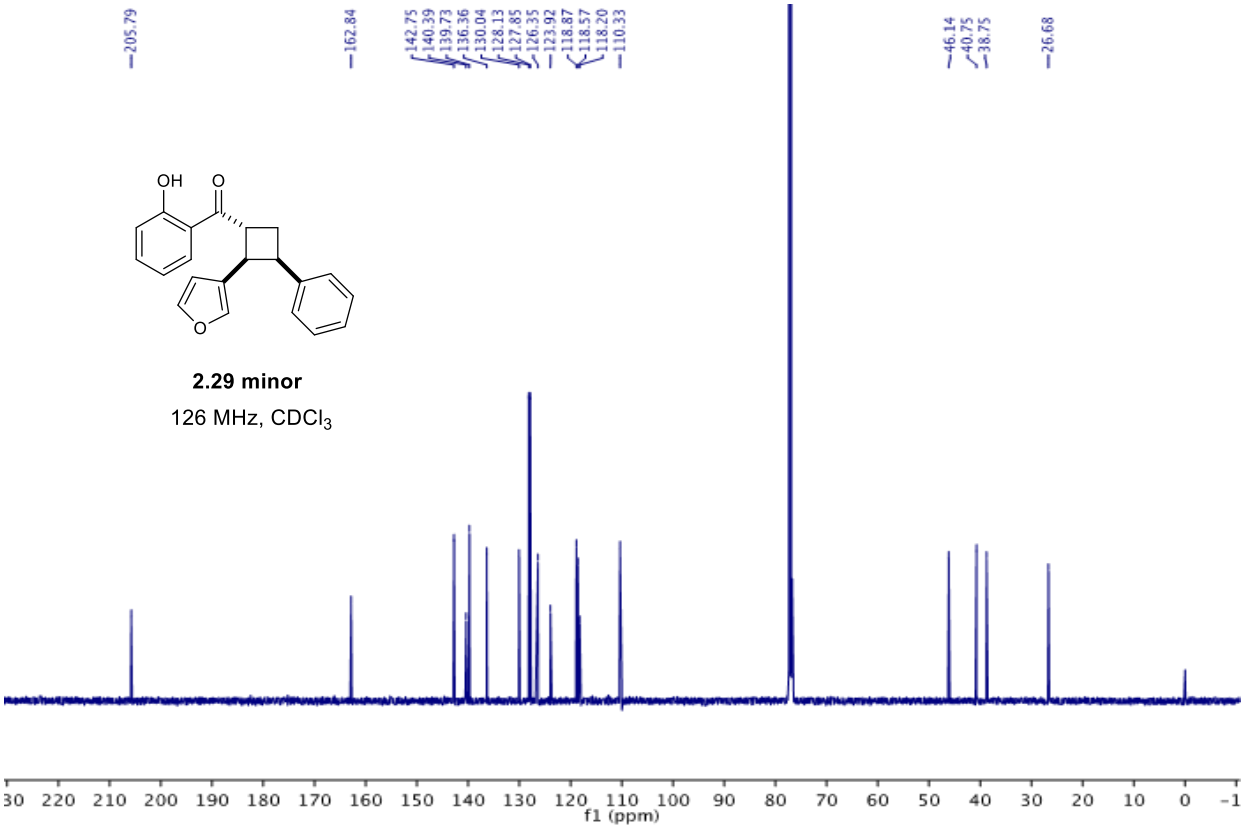
500 MHz, $CDCl_3$

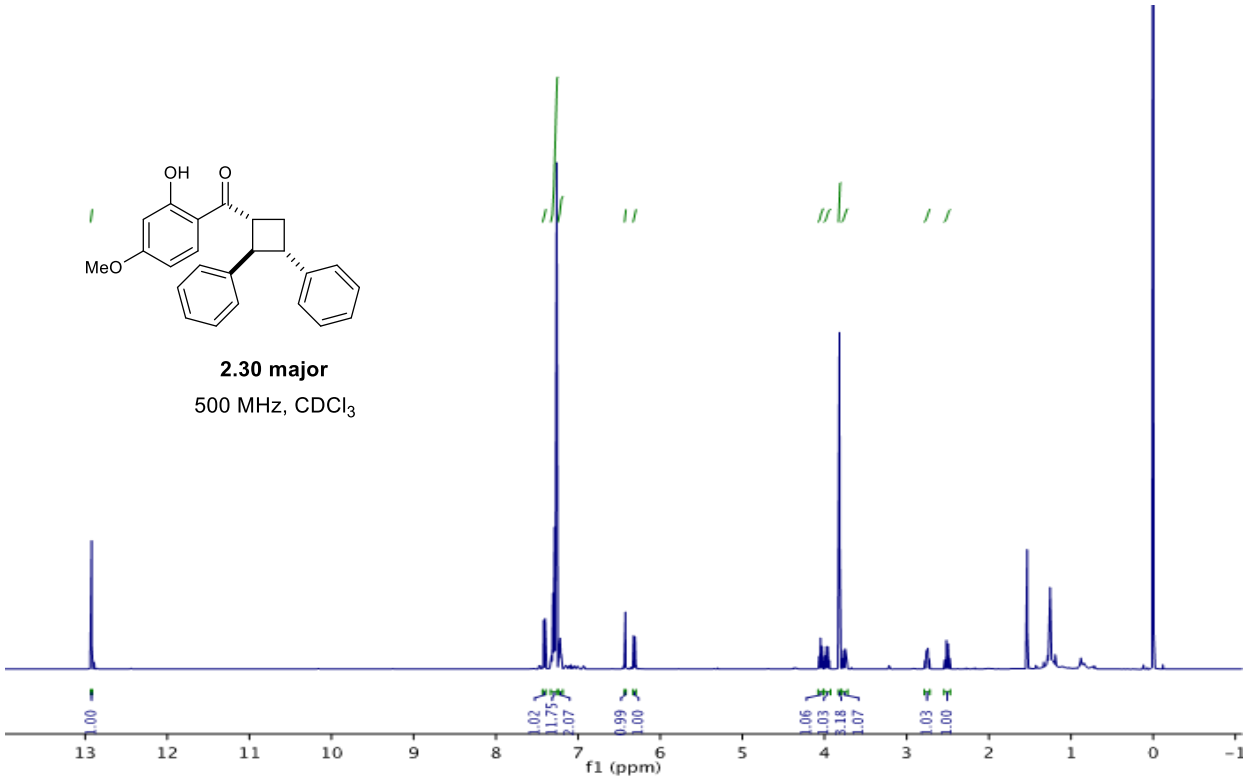



**2.29 major**

126 MHz, $CDCl_3$

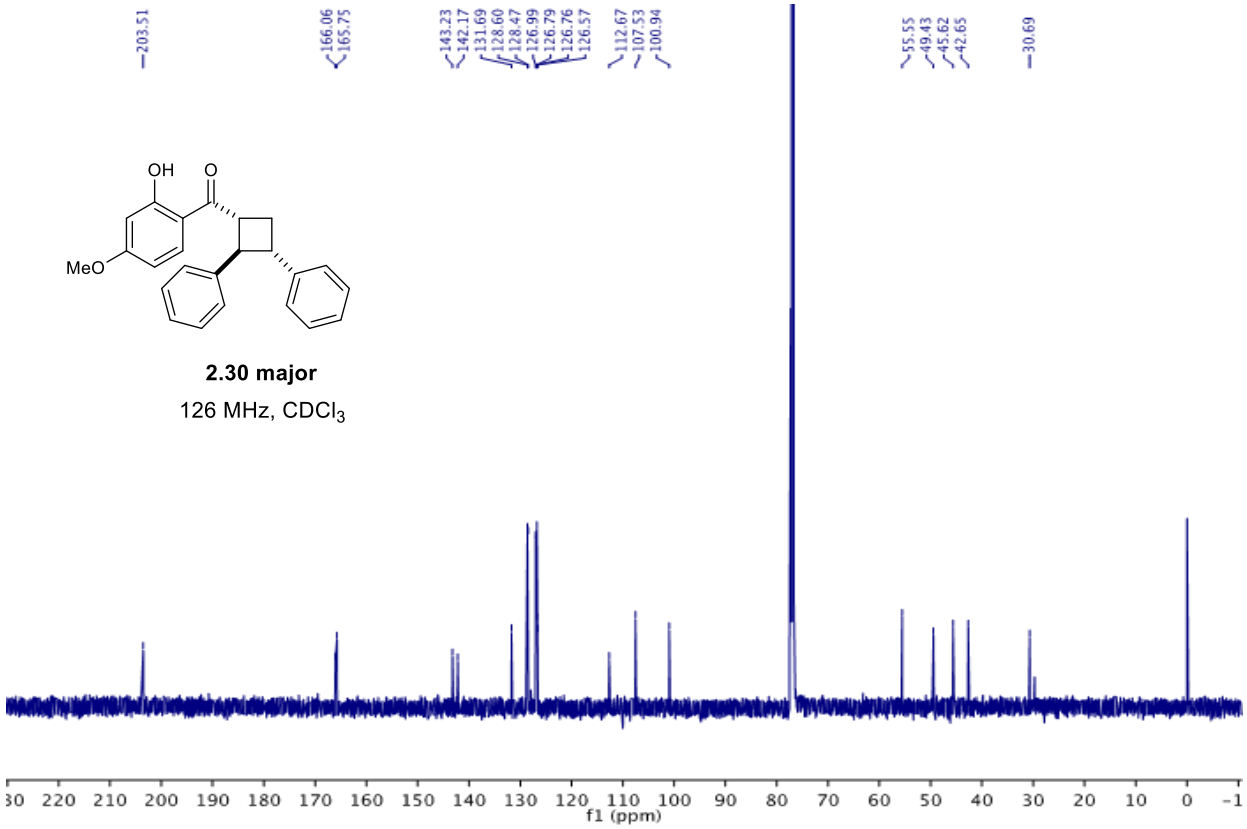

OH
O
O
2.29 minor
500 MHz, CDCl3
0.99
0.97
1.02
2.58
1.04
3.01
2.00
1.01
1.00
2.03
1.01
1.02
1.00
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1
f1 (ppm)


205.79
162.84
142.75
140.39
139.73
136.36
130.04
128.13
127.85
126.35
123.92
118.87
118.57
118.20
110.33
46.14
40.75
38.75
26.68
OH
O
O
2.29 minor
126 MHz, CDCl3
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)



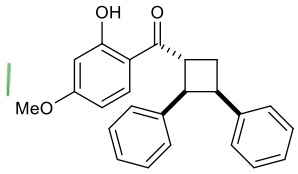

**2.30 major**

500 MHz, $CDCl_3$




**2.30 major**

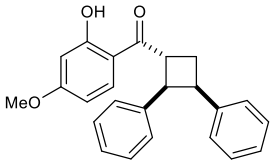
126 MHz, $CDCl_3$




**2.30 minor**

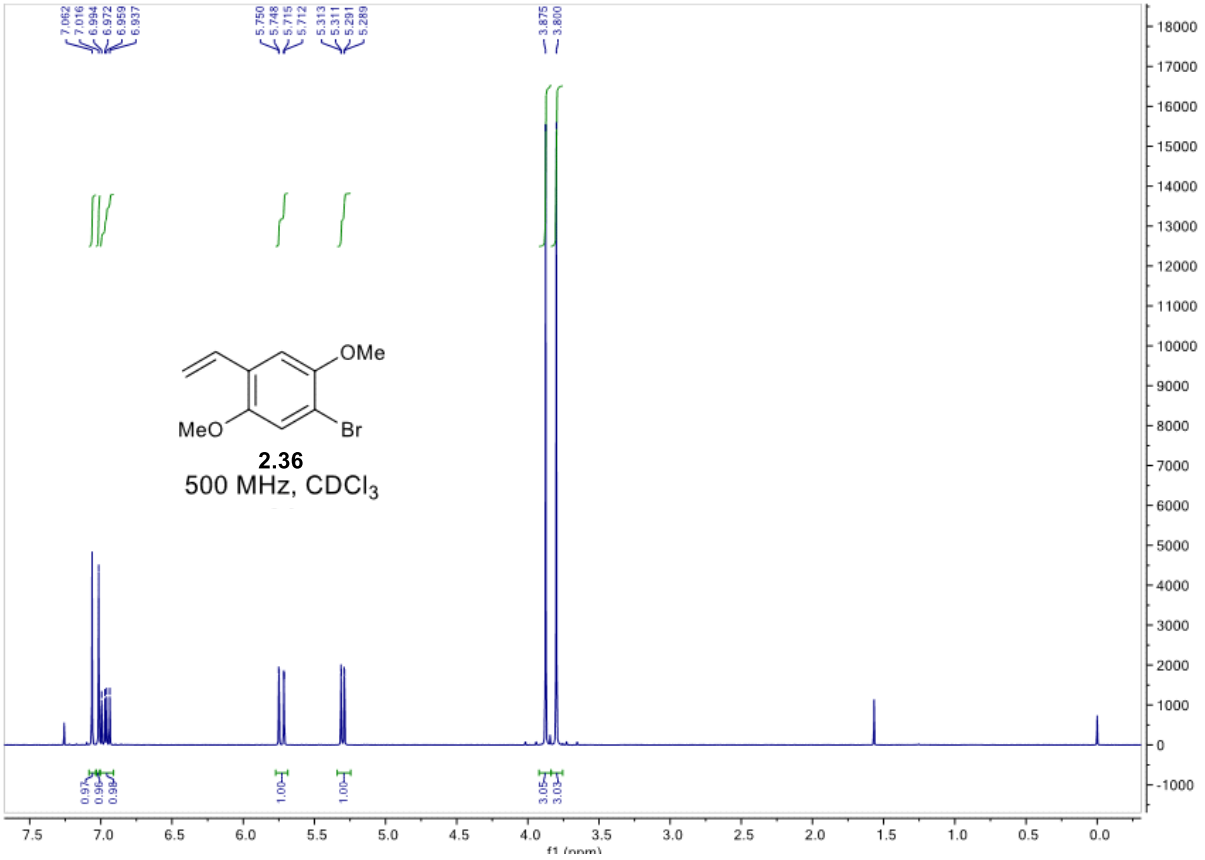
500 MHz, $CDCl_3$

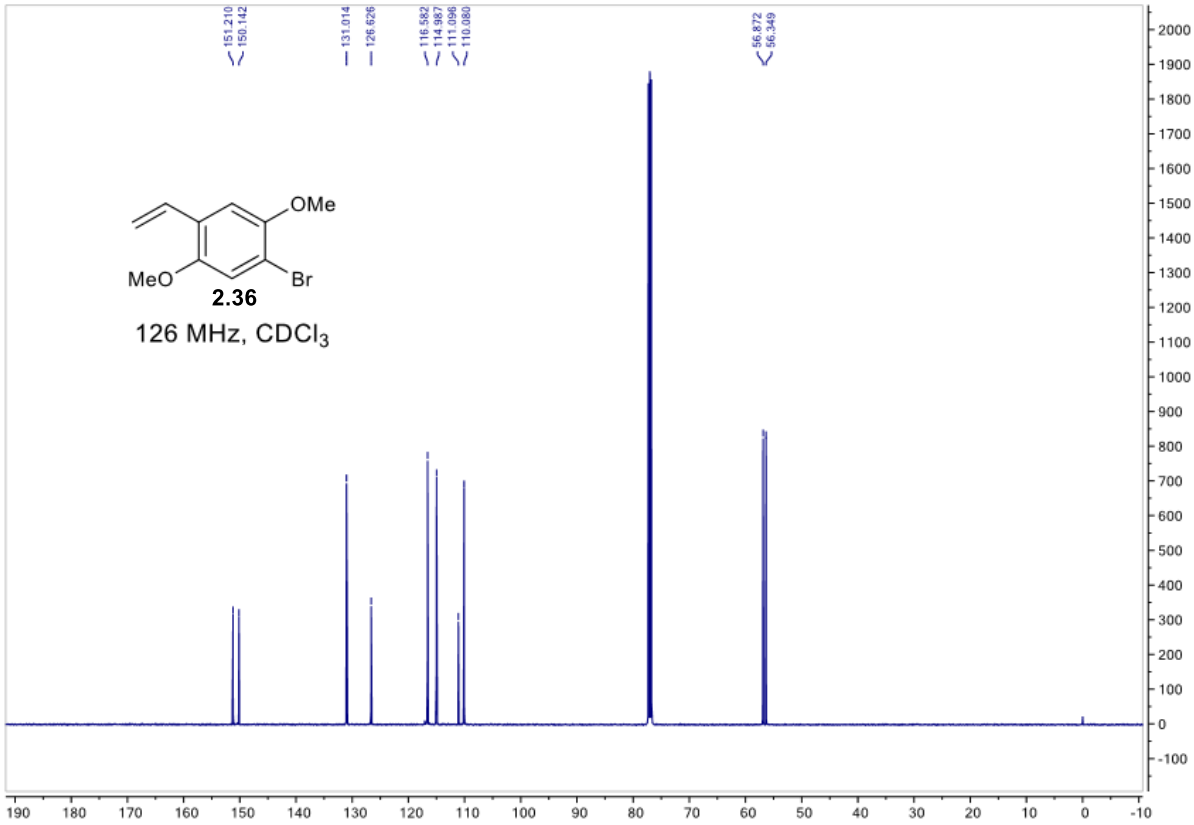


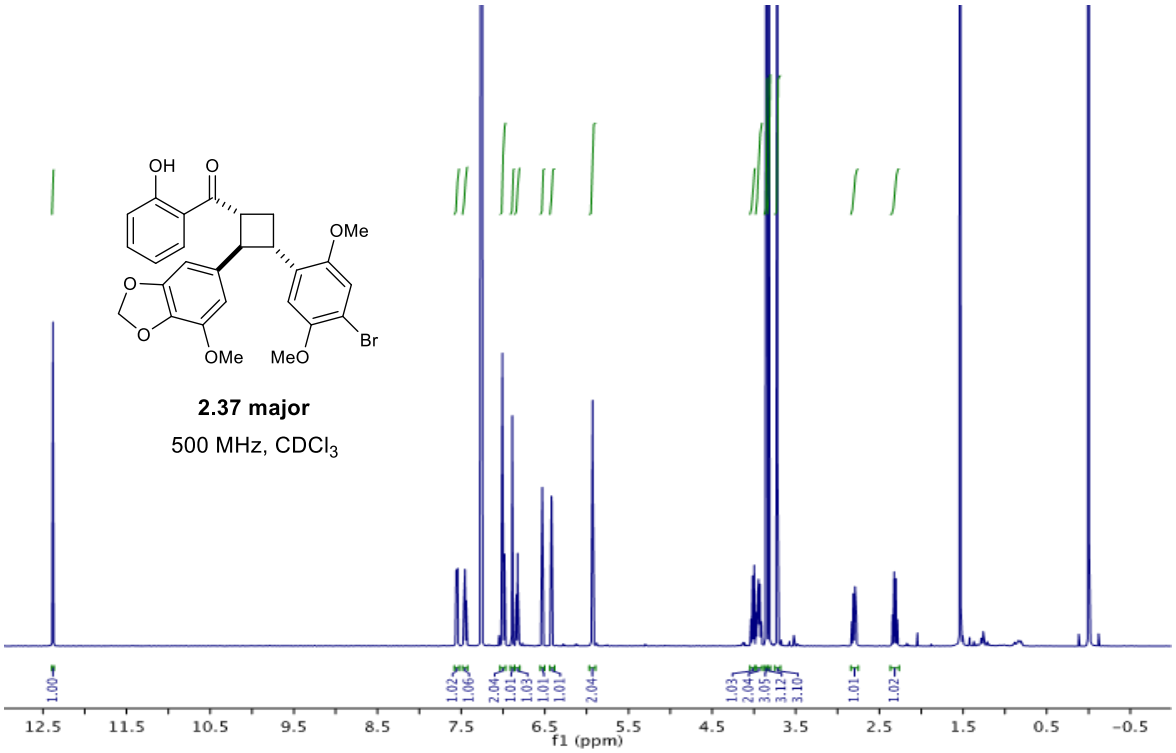




**2.30 minor**

126 MHz, $CDCl_3$

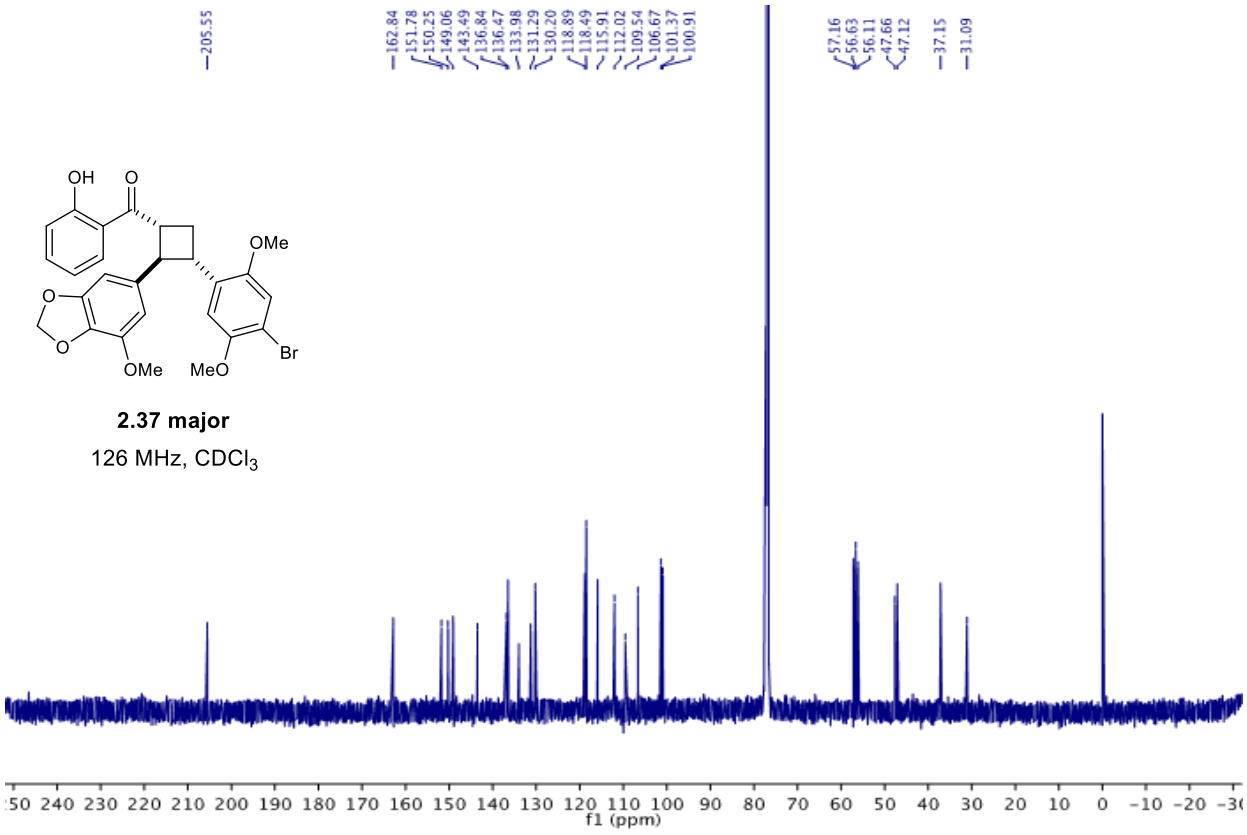

7.062
7.016
6.994
6.972
6.959
6.937
5.750
5.748
5.715
5.712
5.313
5.311
5.291
5.289
3.875
3.800
OMe
MeO
Br
2.36
500 MHz, CDCl3
0.97
0.96
0.98
1.00
1.00
3.05
3.03
f1 (ppm)


151.210
150.142
131.014
126.626
116.582
114.987
111.096
110.080
56.872
56.349
OMe
MeO
Br
2.36
126 MHz, CDCl3



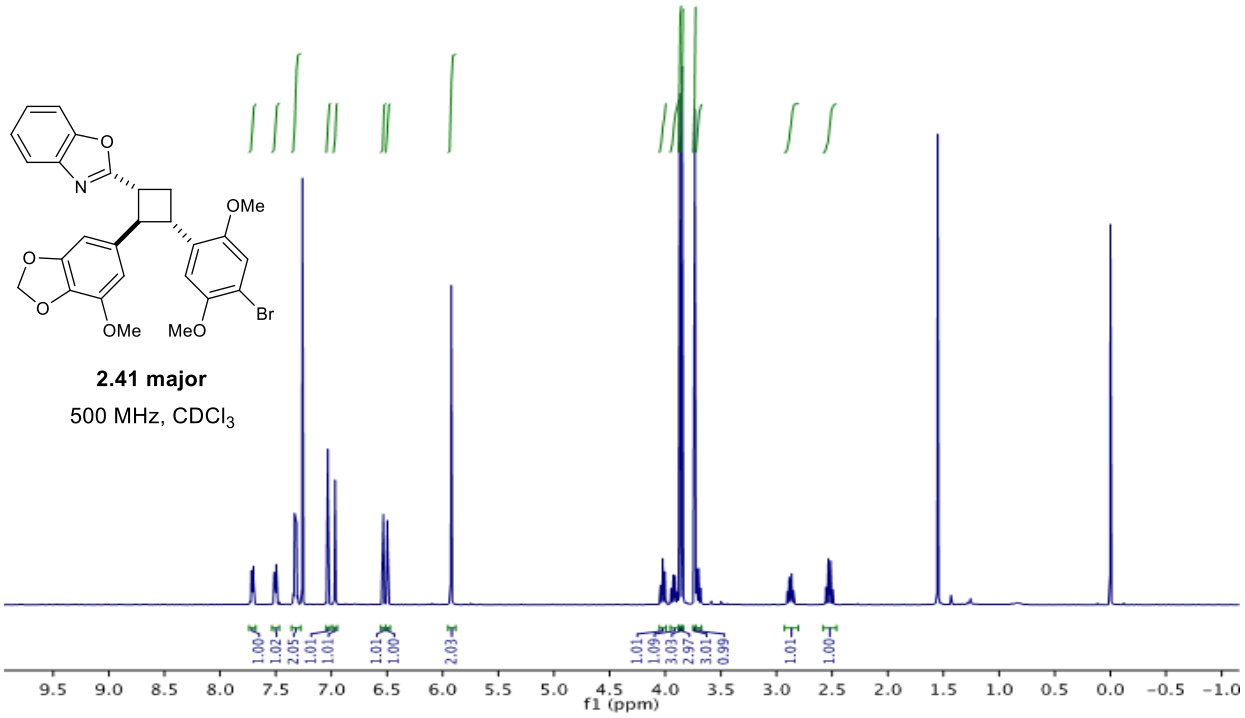

**2.37 major**

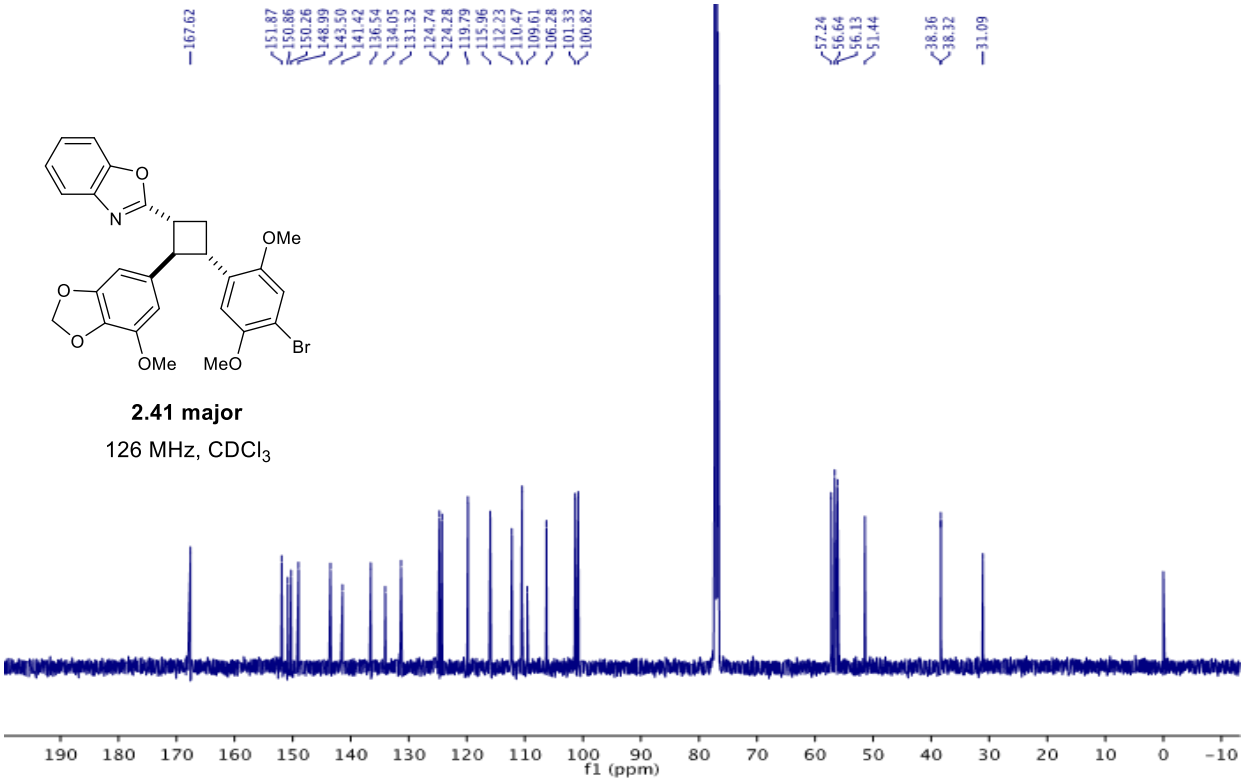
500 MHz, $CDCl_3$

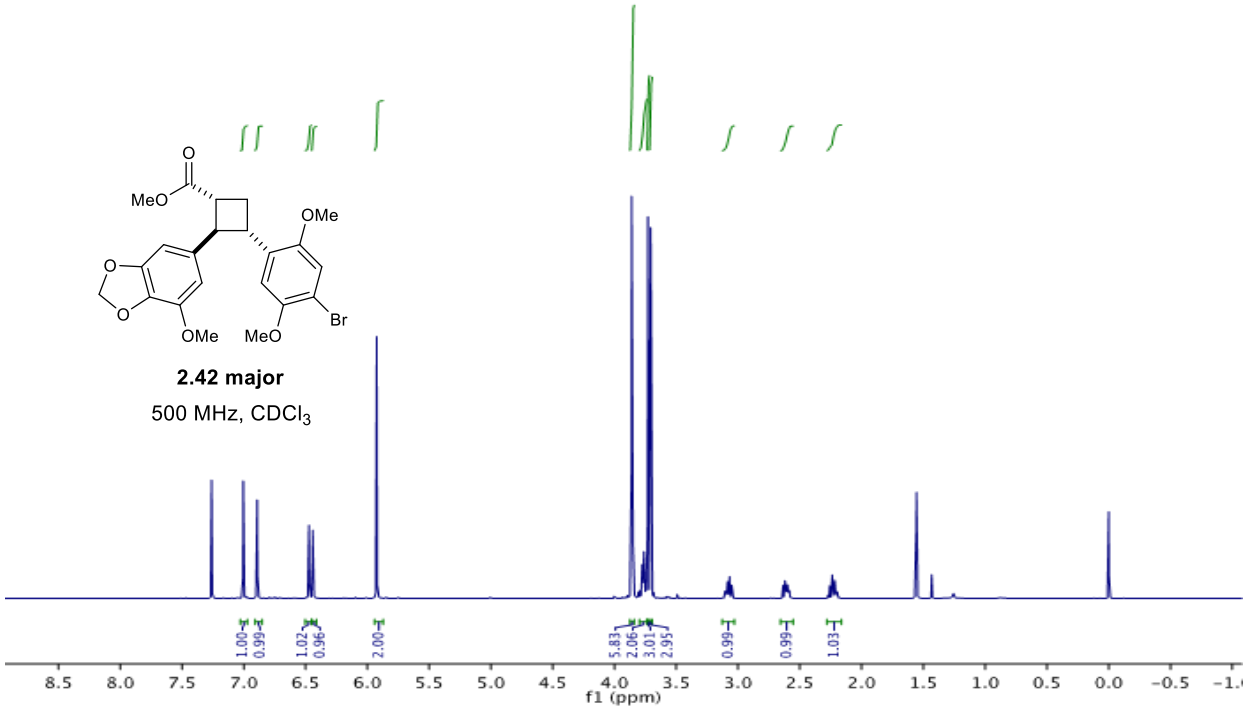


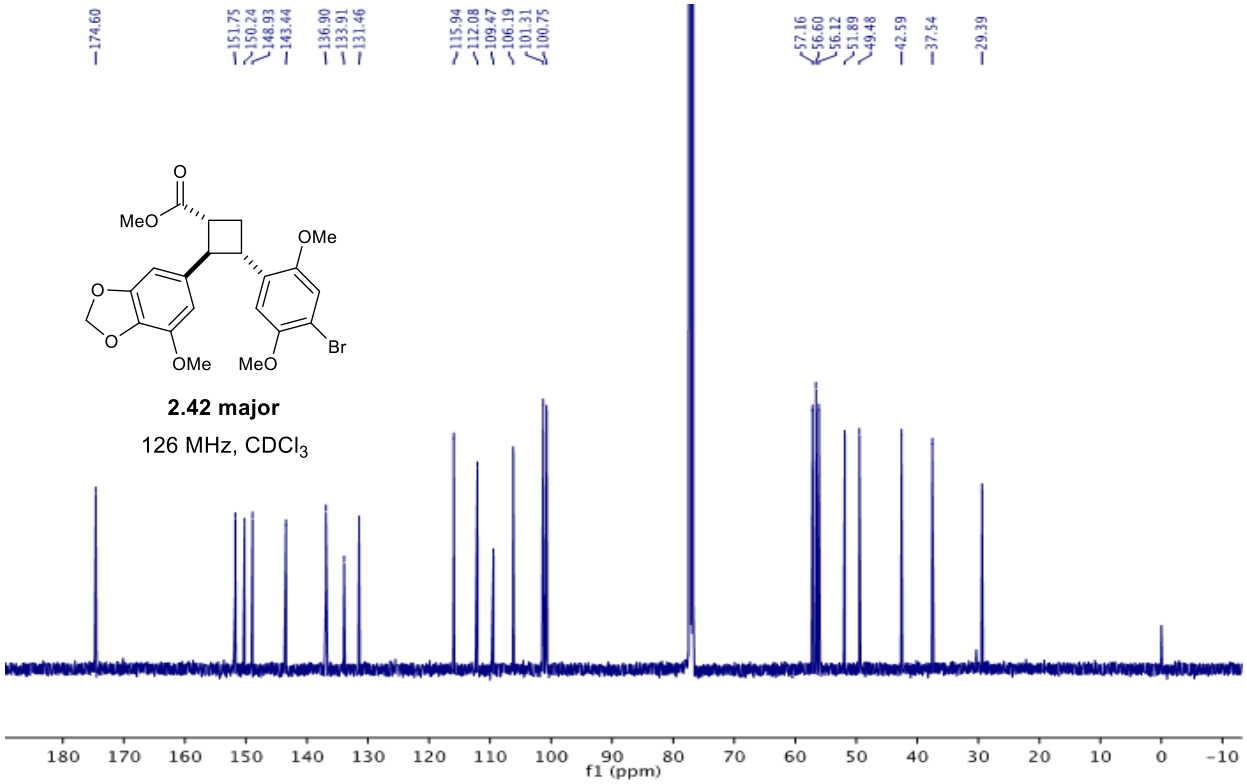

**2.37 major**

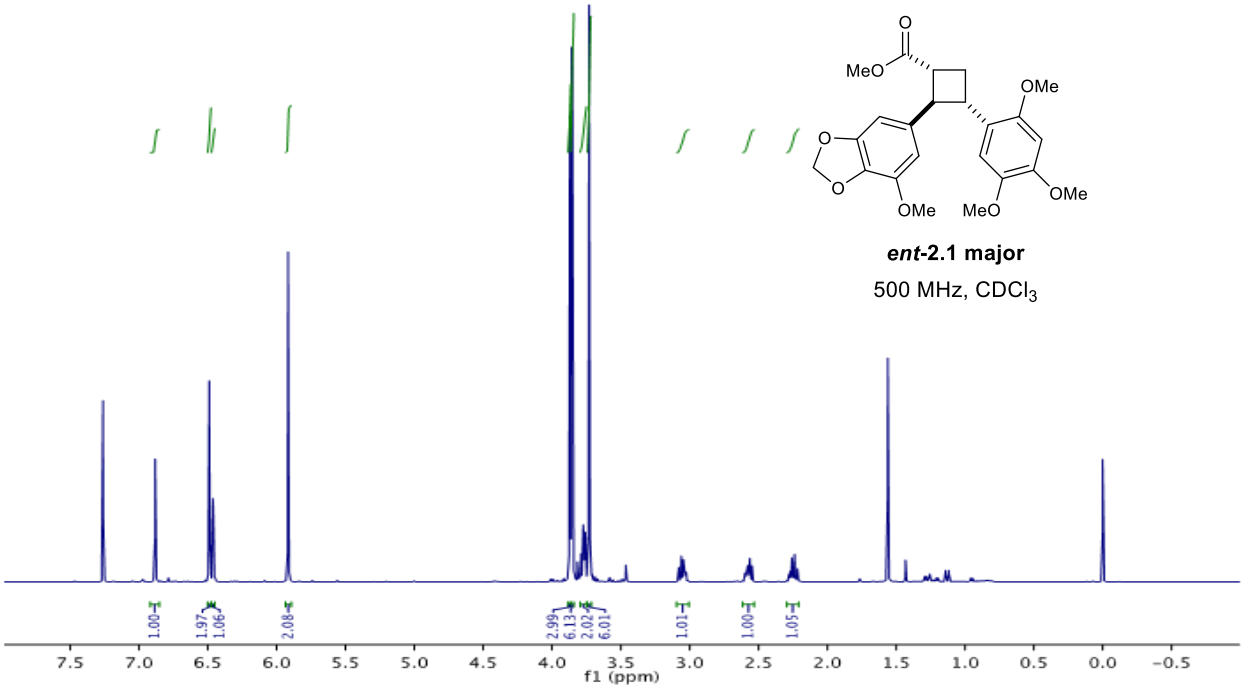
126 MHz, $CDCl_3$


OMe
OMe
MeO
Br
2.41 major
500 MHz, CDCl3
1.00
1.02
2.05
1.01
1.01
1.01
1.00
2.03
1.01
1.09
3.03
2.97
3.01
0.99
1.01
1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
f1 (ppm)


167.62
151.87
150.86
150.26
148.99
143.50
141.42
136.54
134.05
131.32
124.74
124.28
119.79
115.96
112.23
110.47
109.61
106.28
101.33
100.82
57.24
56.64
56.13
51.44
38.36
38.32
31.09
OMe
OMe
MeO
Br
2.41 major
126 MHz, CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

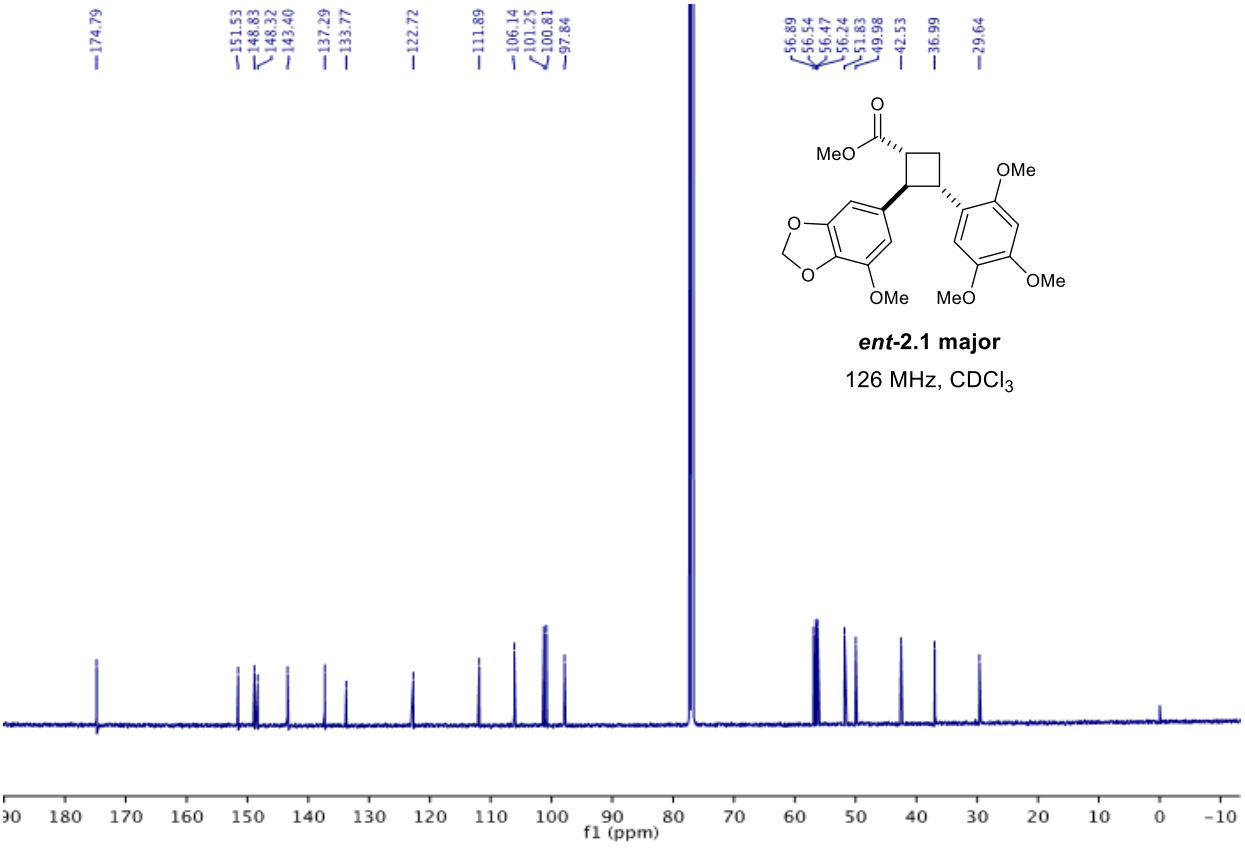

MeO
O
OMe
O
O
OMe
MeO
Br
2.42 major
500 MHz, CDCl3
1.00
0.99
1.02
0.96
2.00
5.83
2.06
3.01
2.95
0.99
0.99
1.03
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


174.60
151.75
150.24
148.93
143.44
136.90
133.91
131.46
115.94
112.08
109.47
106.19
101.31
100.75
57.16
56.60
56.12
51.89
49.48
42.59
37.54
29.39
MeO
O
OMe
O
O
OMe
MeO
Br
2.42 major
126 MHz, CDCl3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



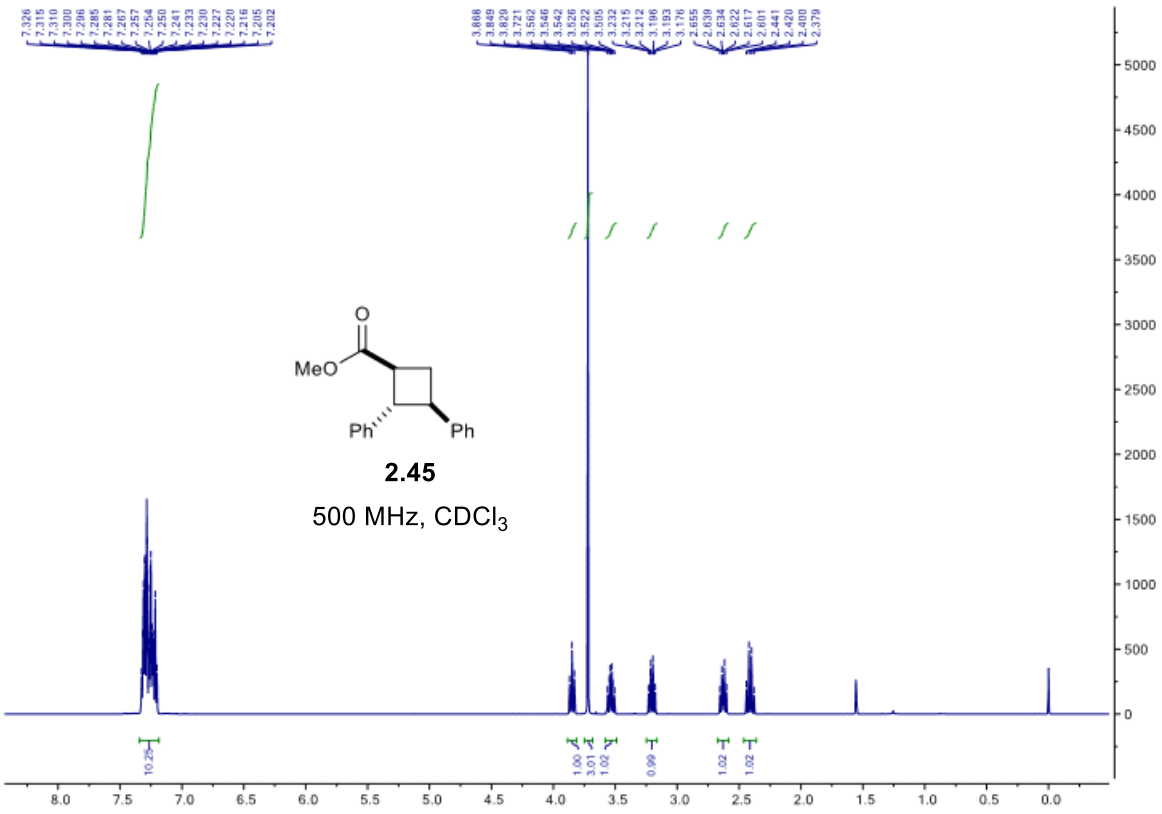

***ent*-2.1 major**

500 MHz, $CDCl_3$



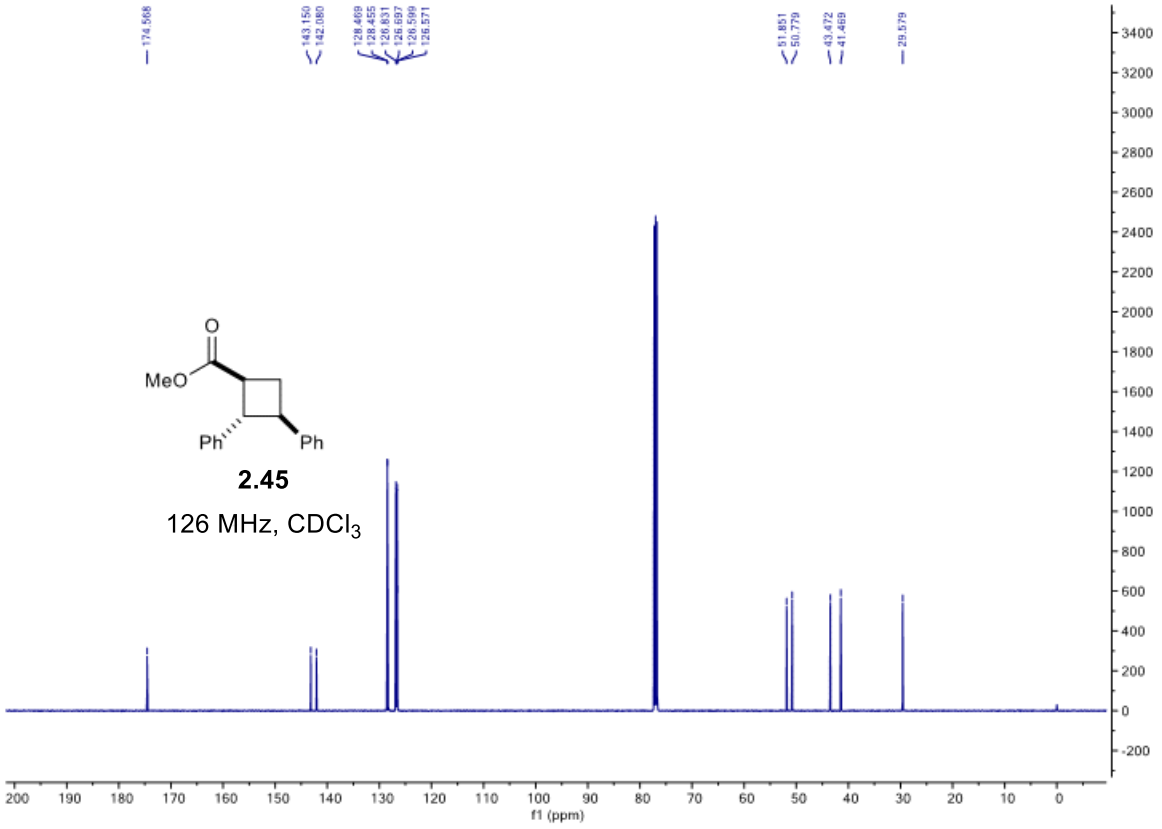

***ent*-2.1 major**

126 MHz, $CDCl_3$



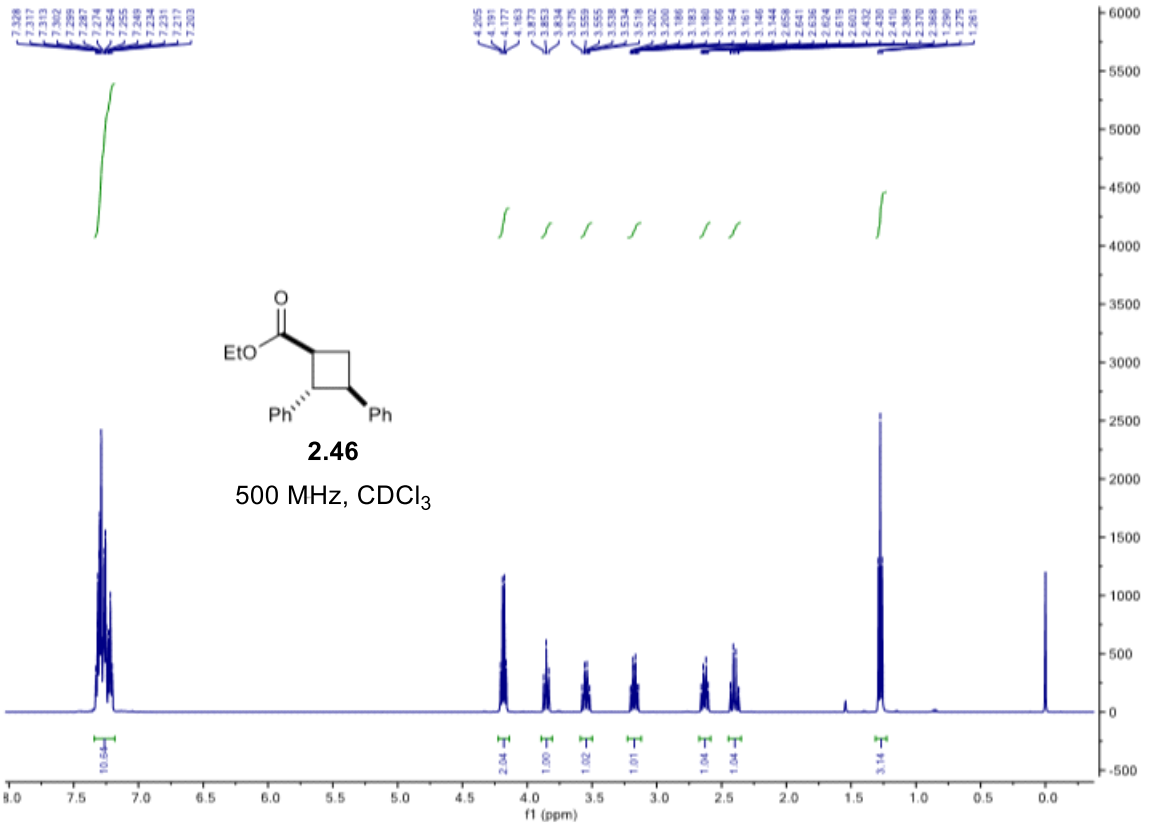

**2.45**

500 MHz, $CDCl_3$



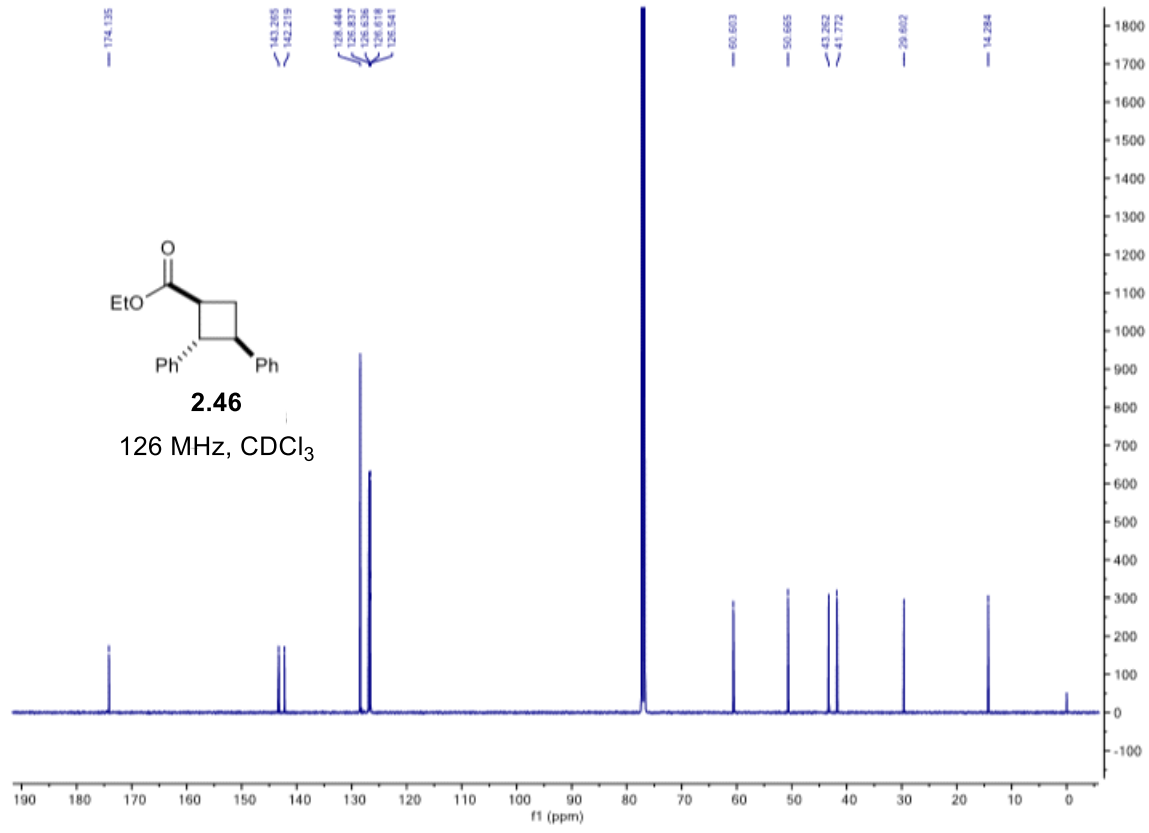

**2.45**

126 MHz, $CDCl_3$



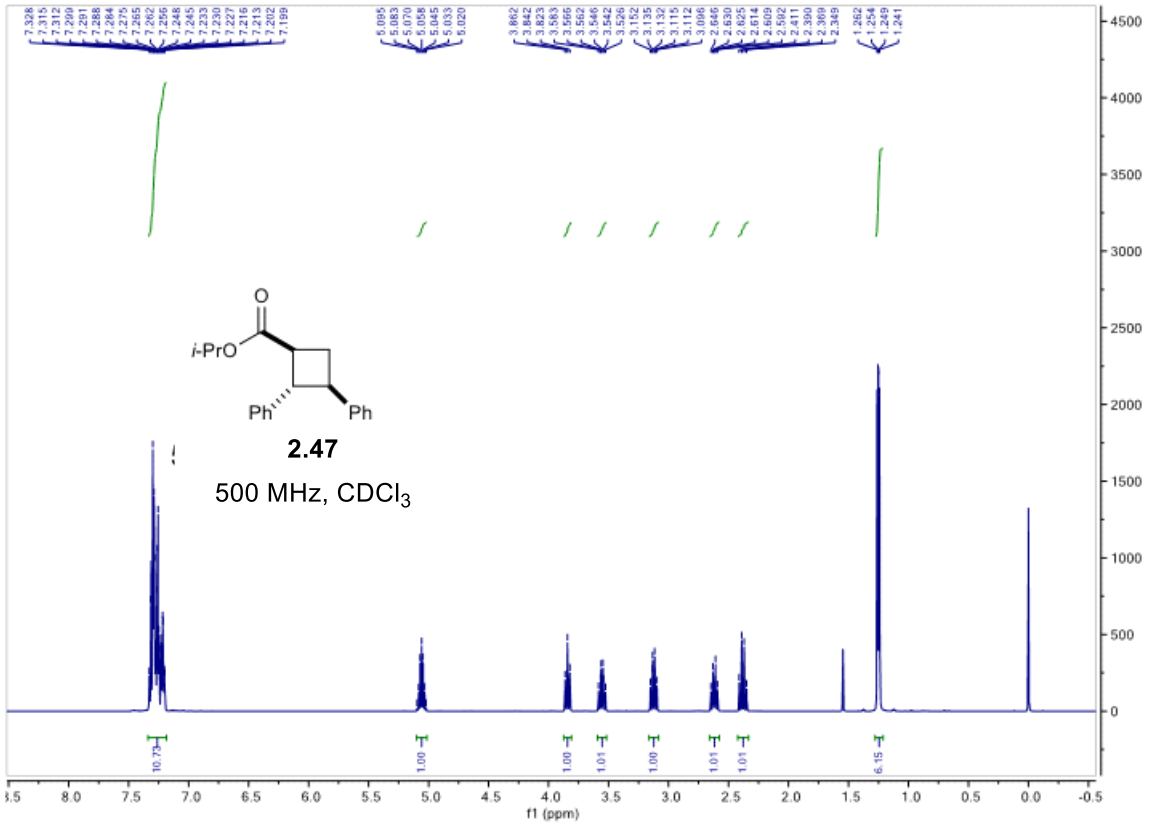

**2.46**

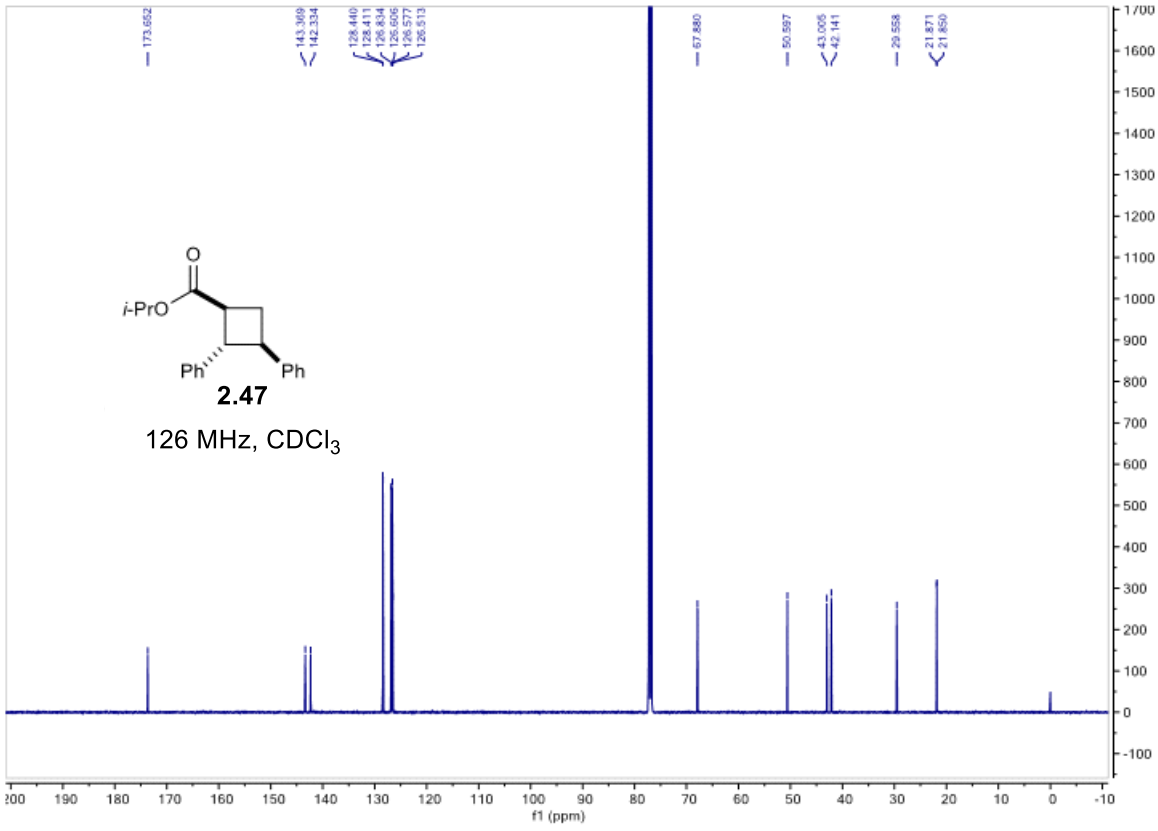
500 MHz, $CDCl_3$

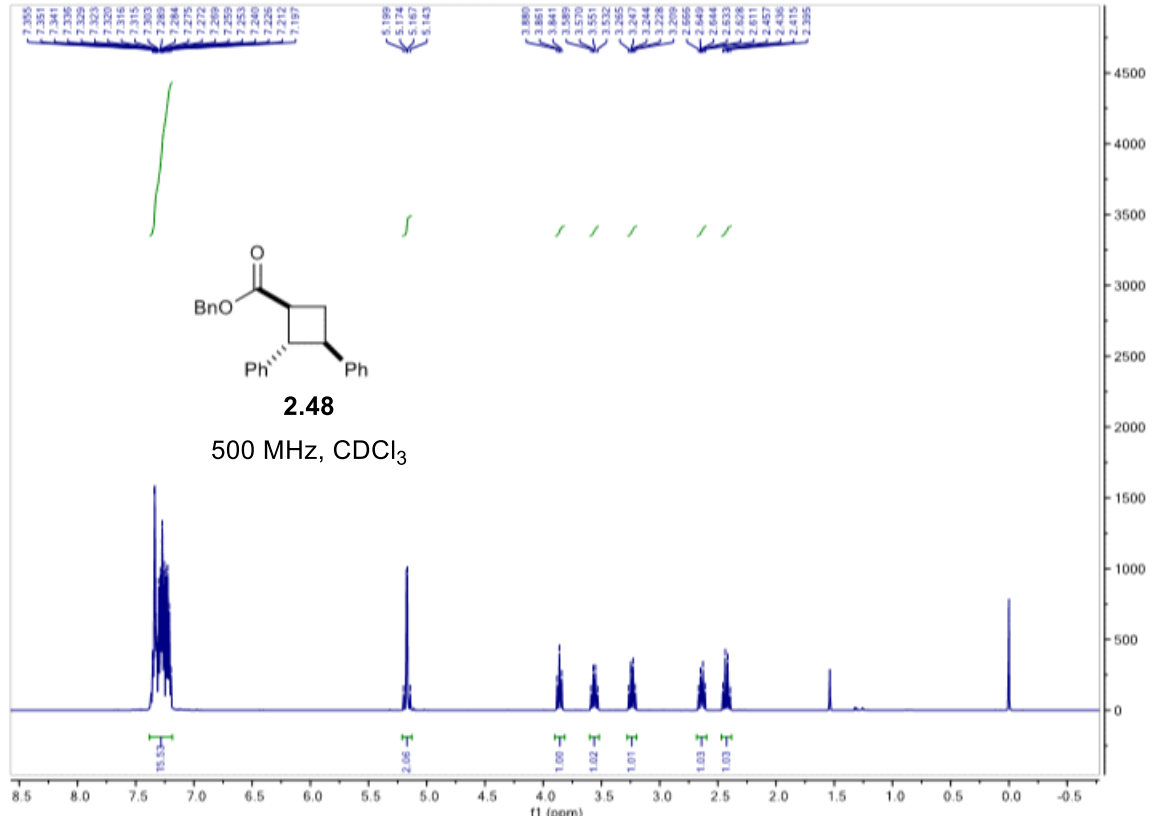



**2.46**

126 MHz, $CDCl_3$

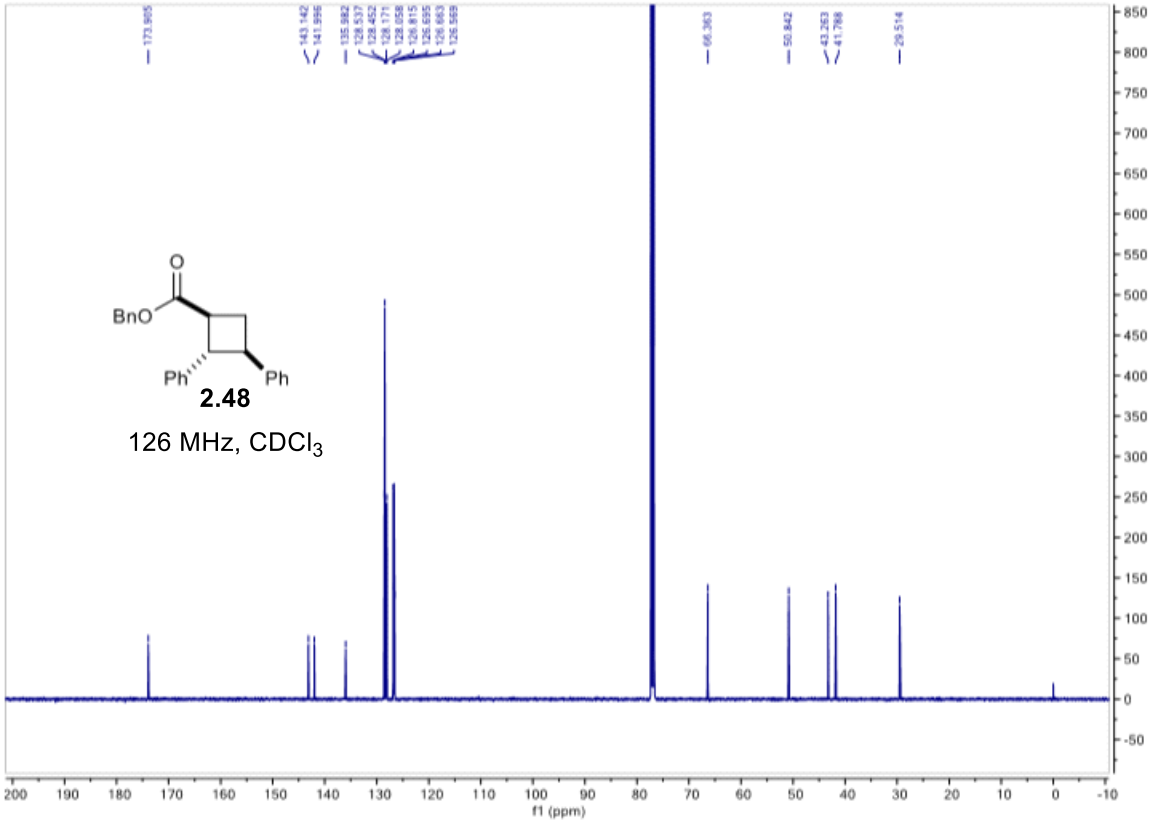

i-PrO
O
Ph
Ph
2.47
500 MHz, CDCl3
f1 (ppm)


i-PrO
O
Ph
Ph
2.47
126 MHz, CDCl3
f1 (ppm)



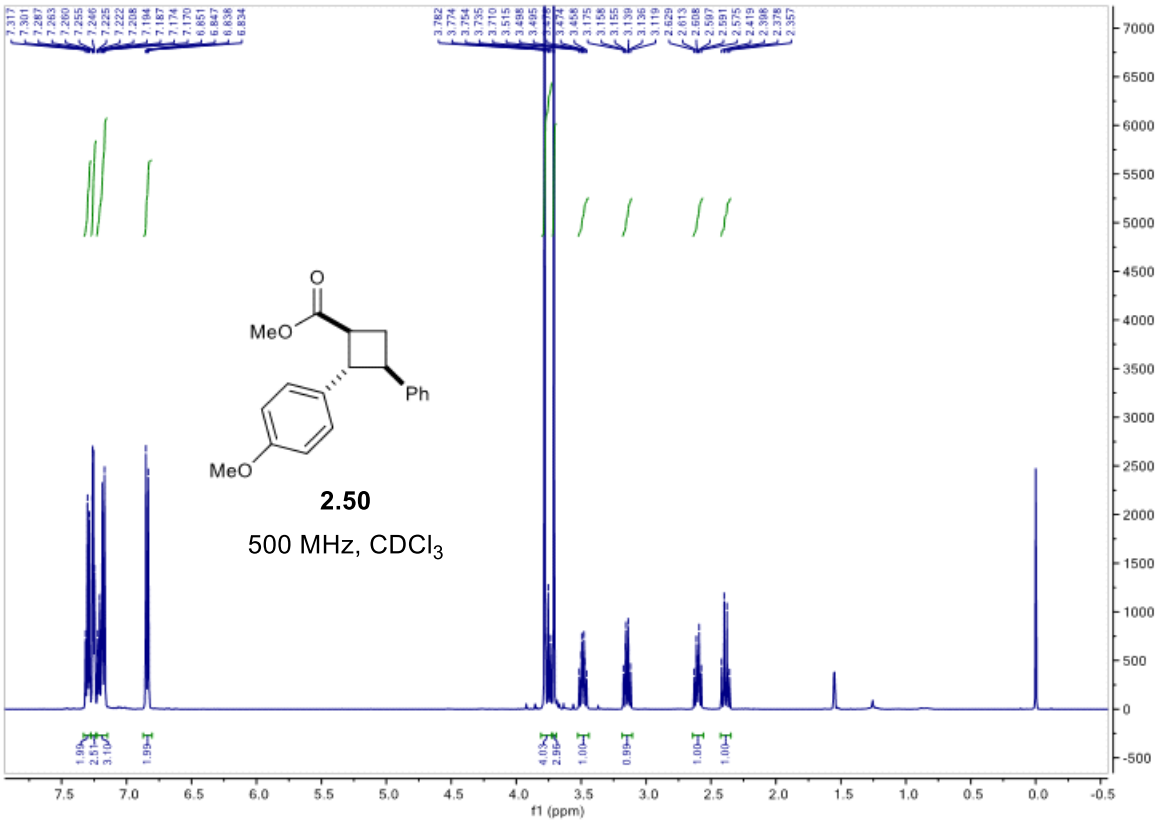

**2.48**

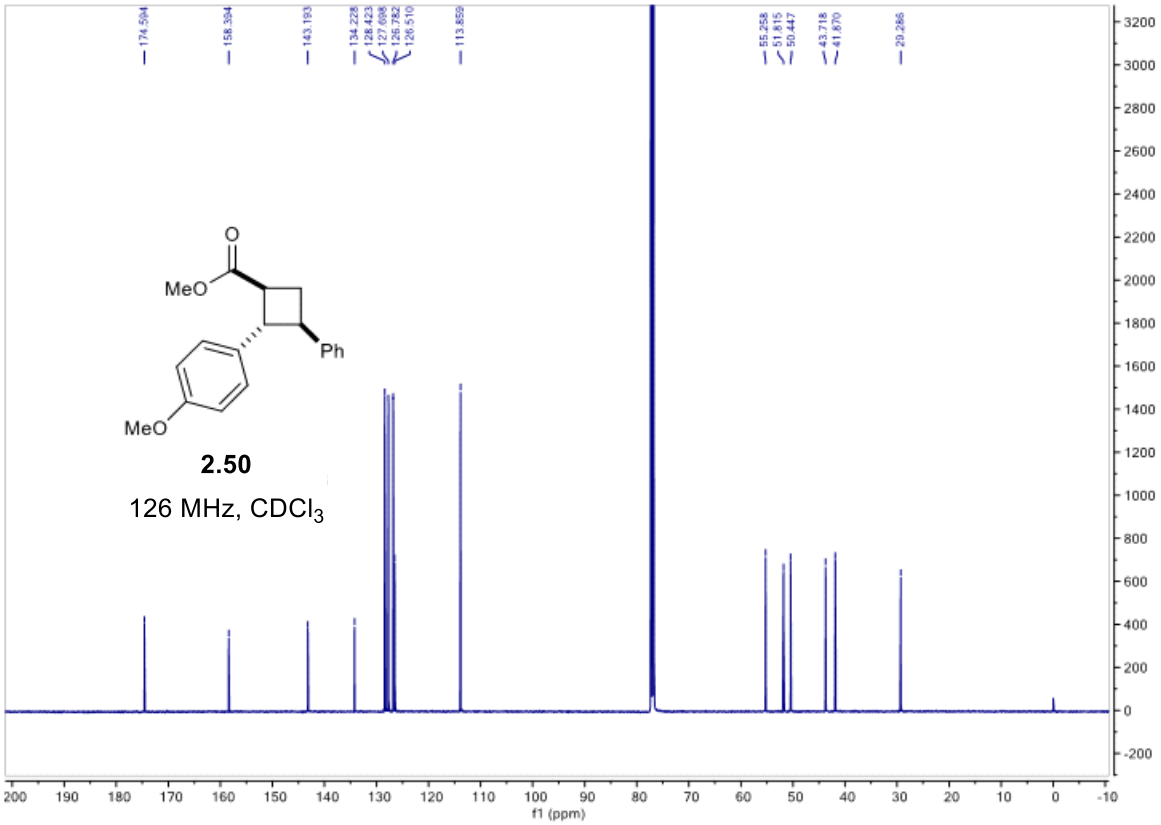
500 MHz, $CDCl_3$

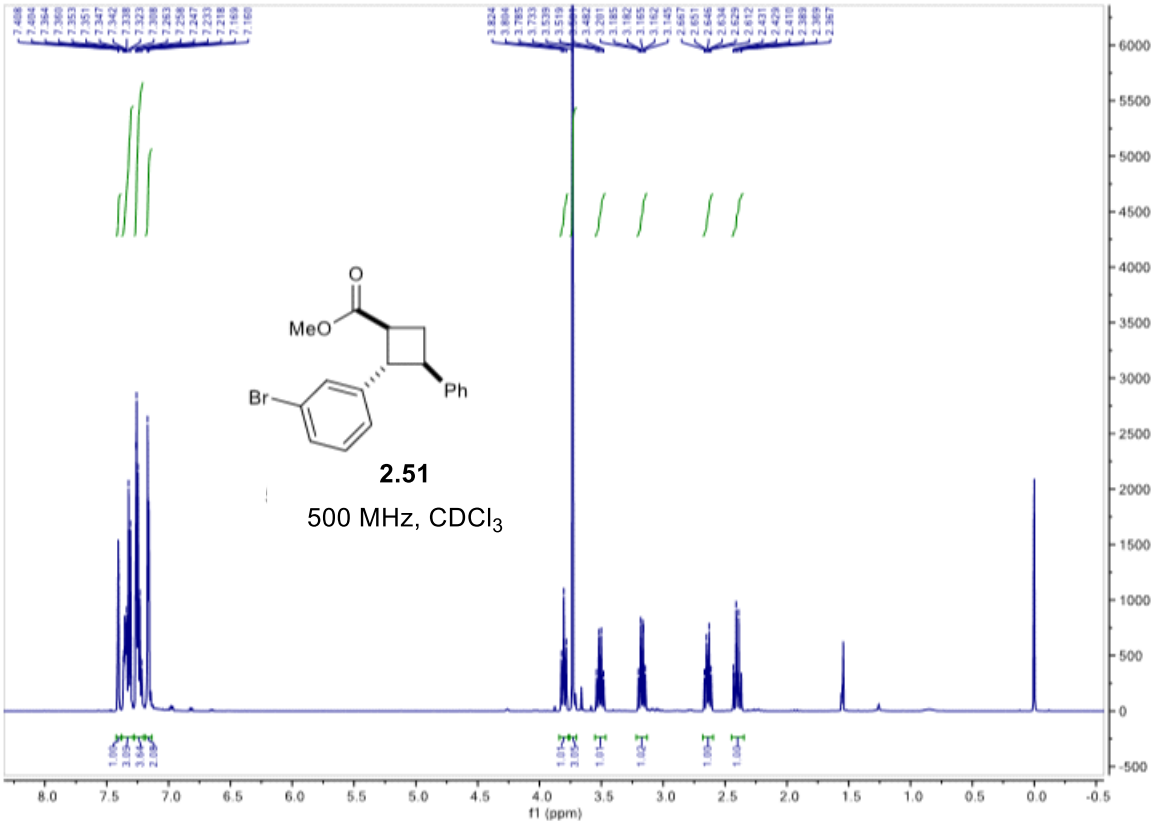



**2.48**

126 MHz, $CDCl_3$

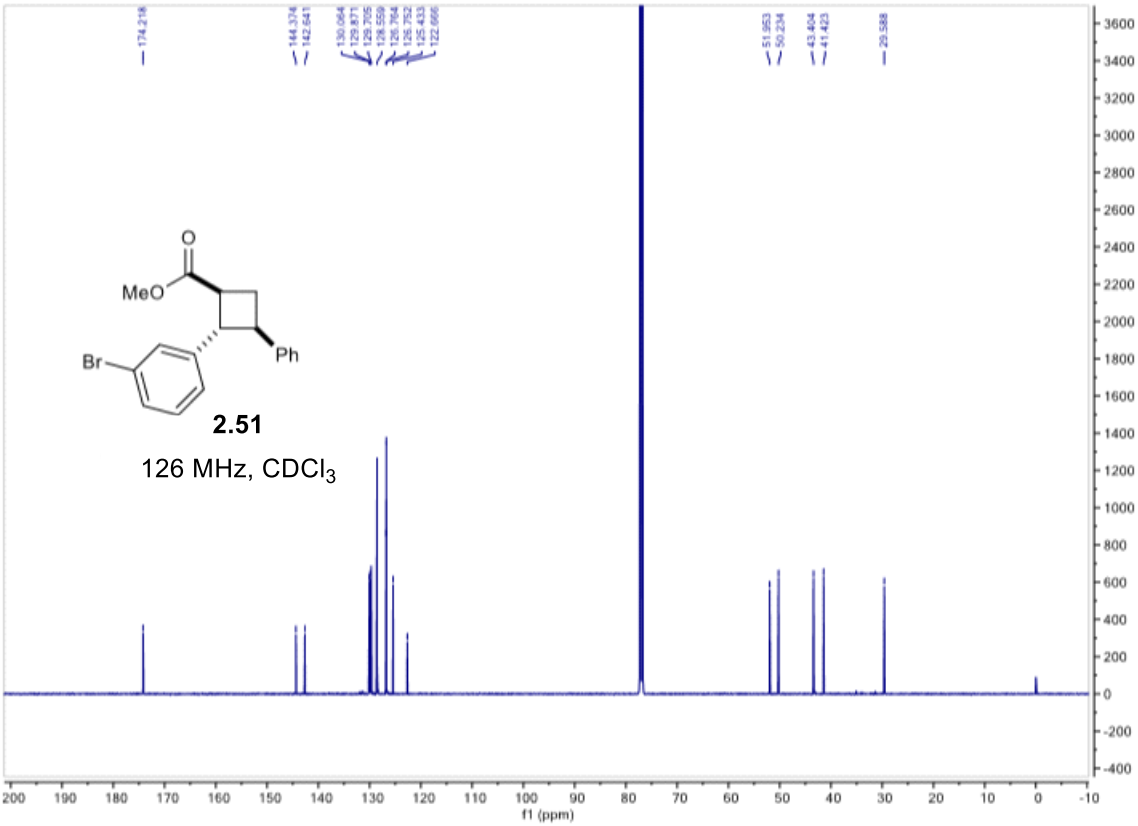

MeO
Ph
MeO
2.50
500 MHz, CDCl3
f1 (ppm)


MeO
Ph
MeO
2.50
126 MHz, CDCl3
f1 (ppm)



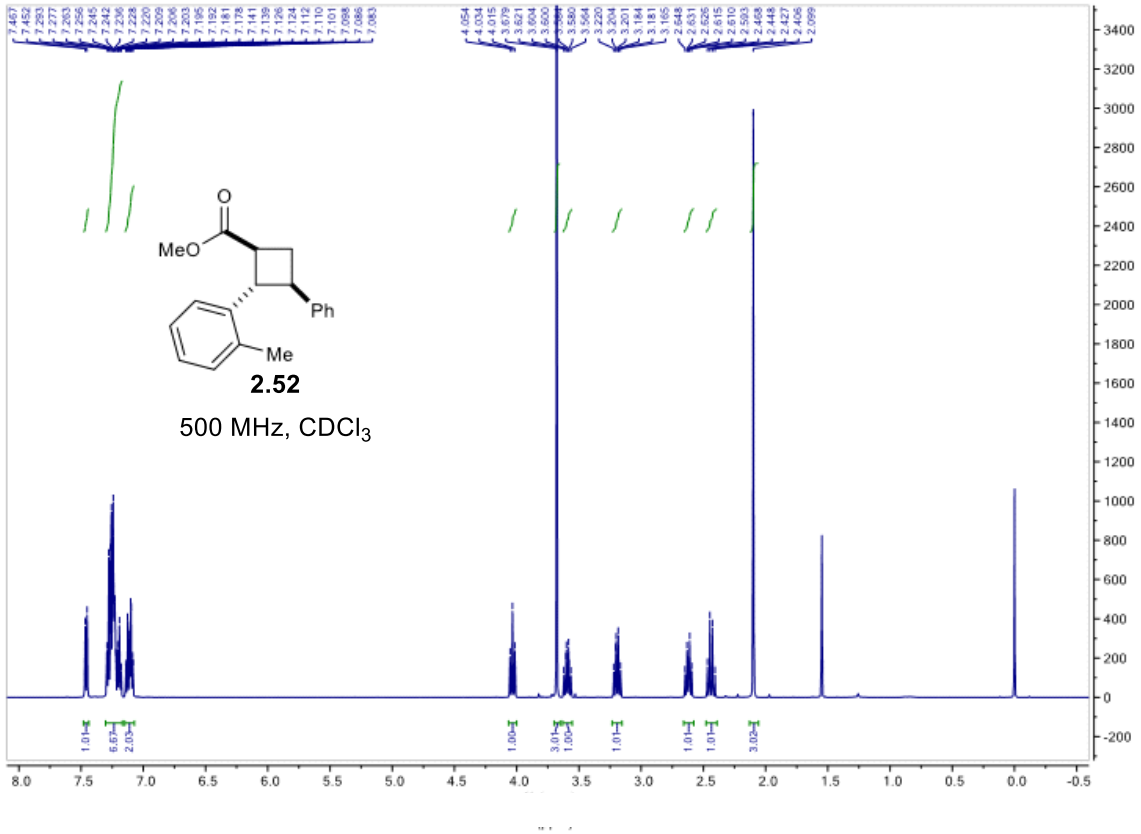

**2.51**

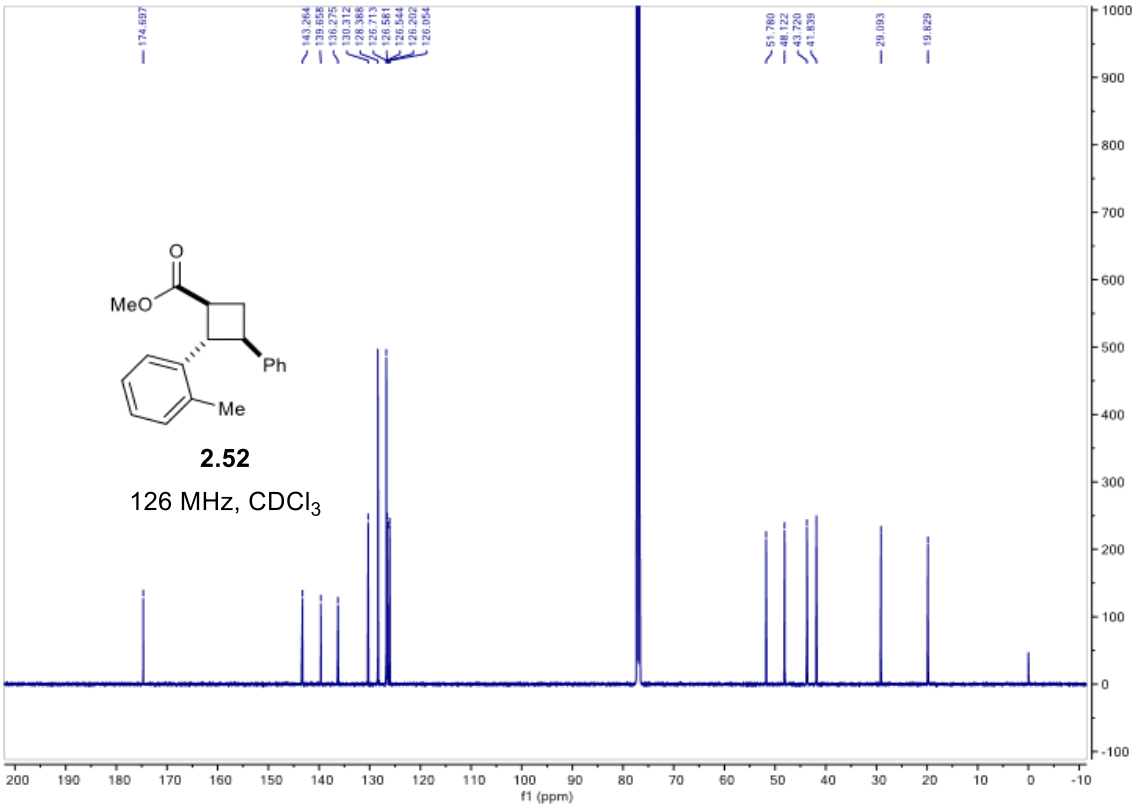
500 MHz, $CDCl_3$

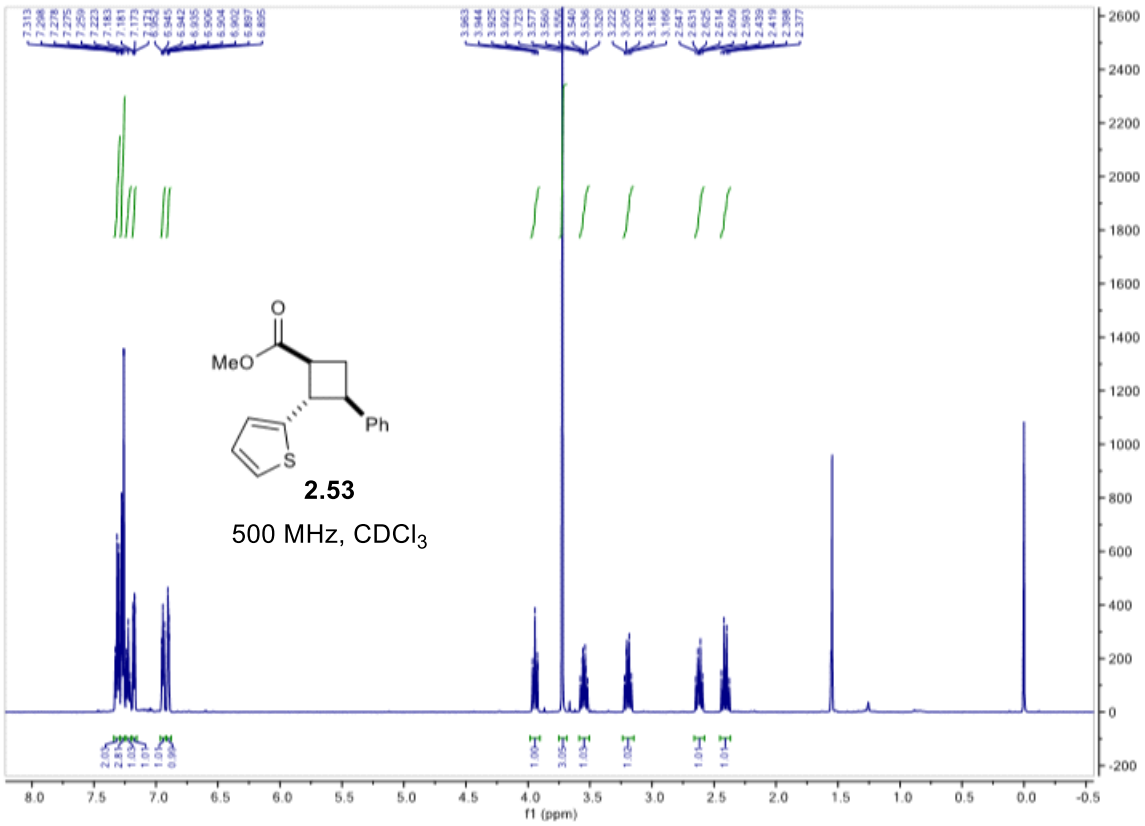


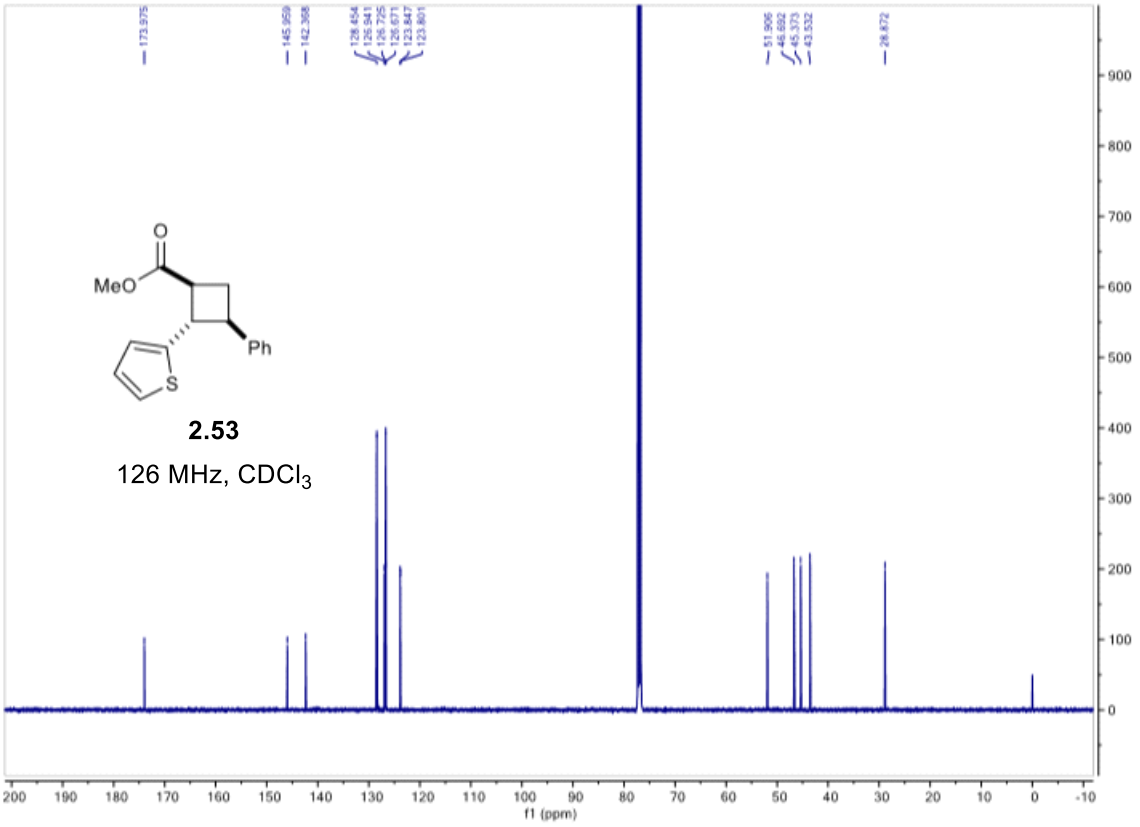

**2.51**

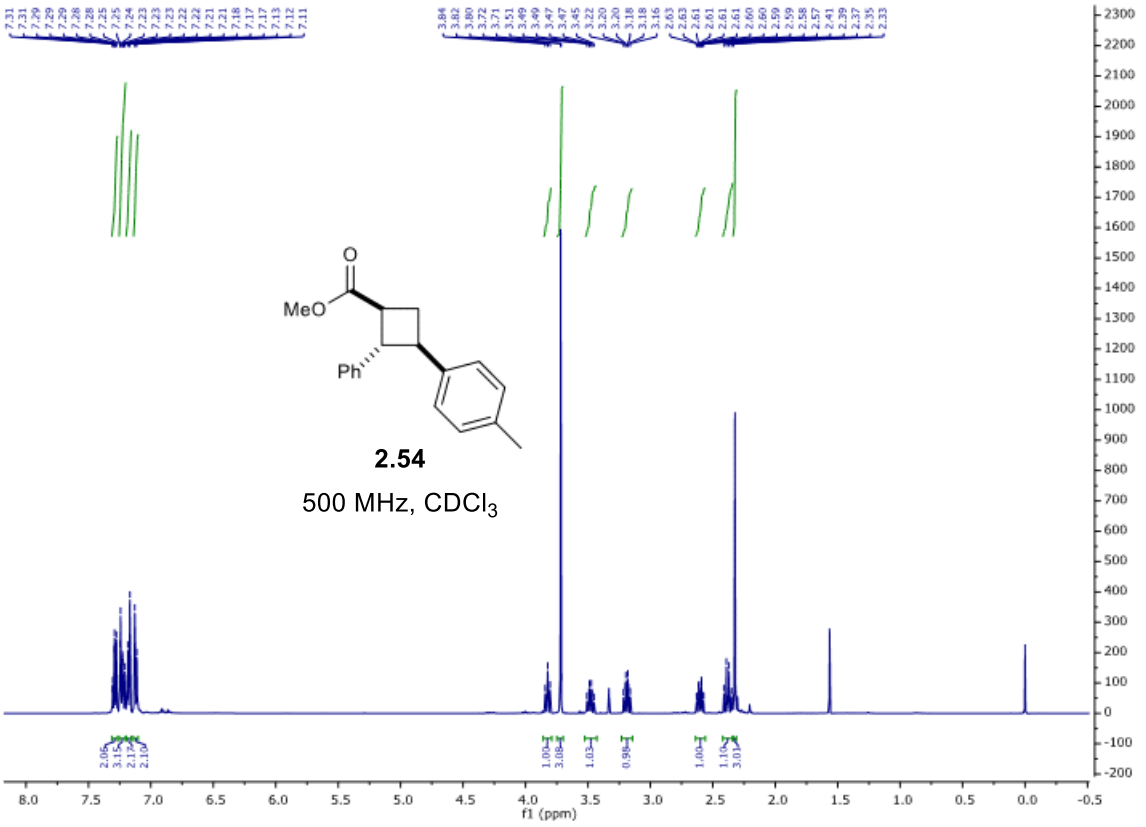
126 MHz, $CDCl_3$


MeO
O
Ph
Me
2.52
500 MHz, CDCl3


MeO
O
Ph
Me
2.52
126 MHz, CDCl3
f1 (ppm)

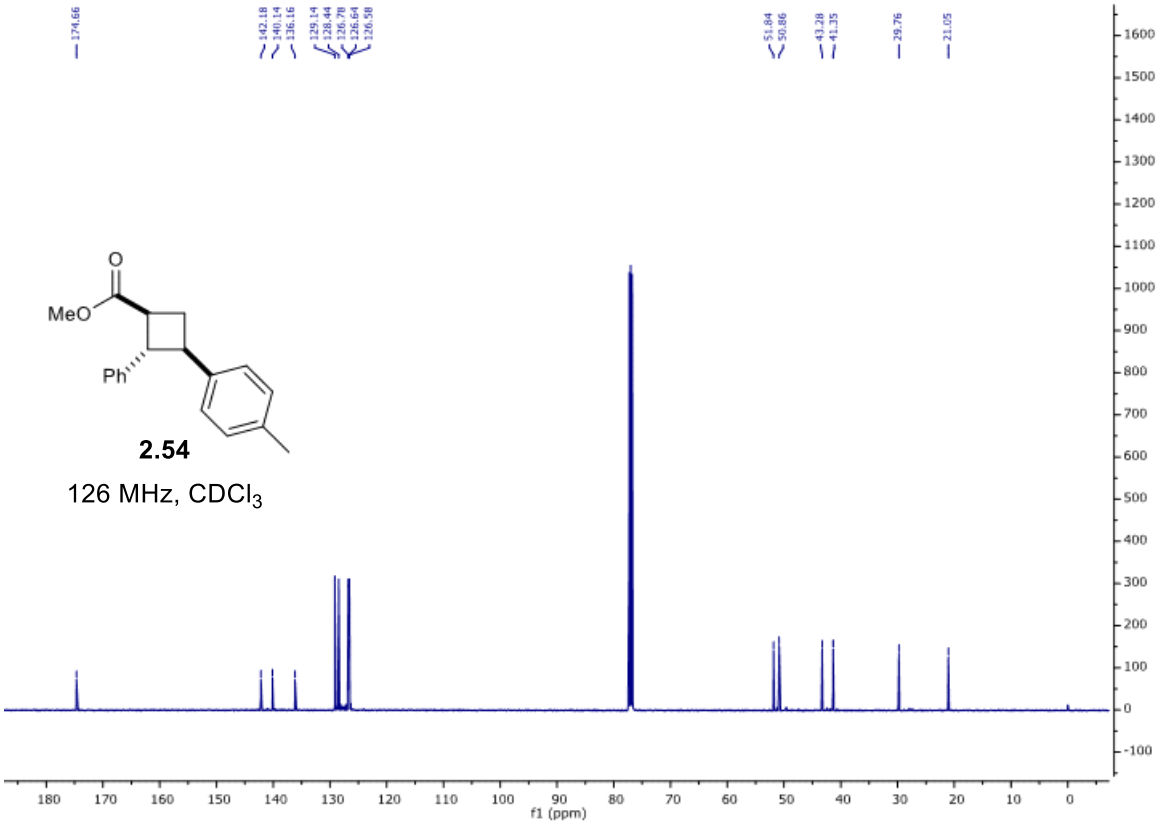

MeO
O
Ph
S
2.53
500 MHz, CDCl3
f1 (ppm)


MeO
O
Ph
S
2.53
126 MHz, CDCl3
f1 (ppm)



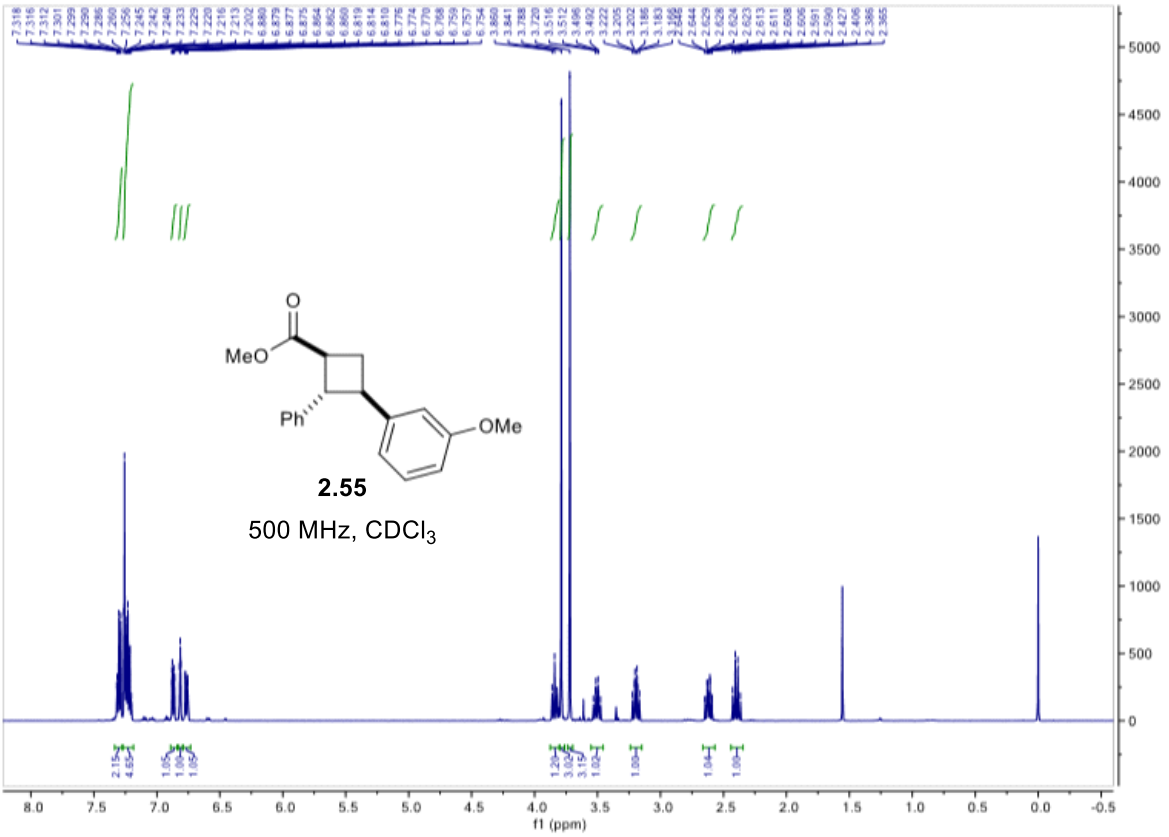

**2.54**

500 MHz, $CDCl_3$



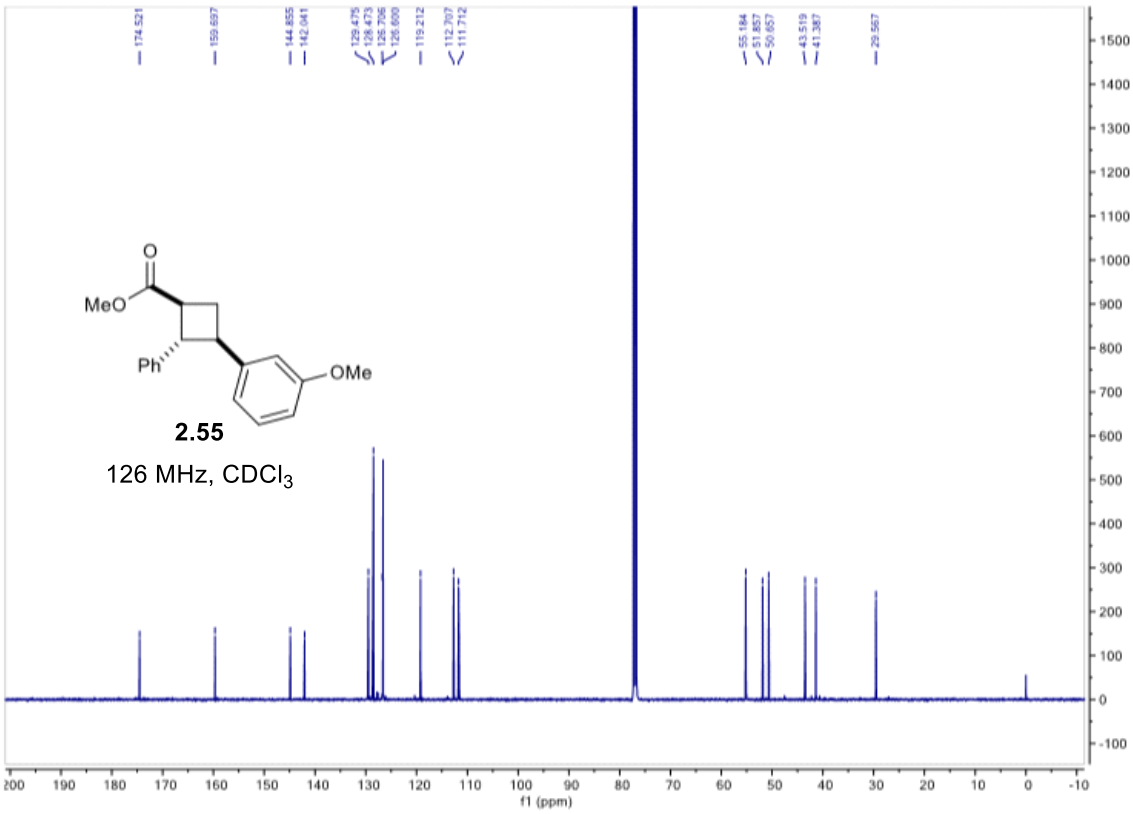

**2.54**

126 MHz, $CDCl_3$



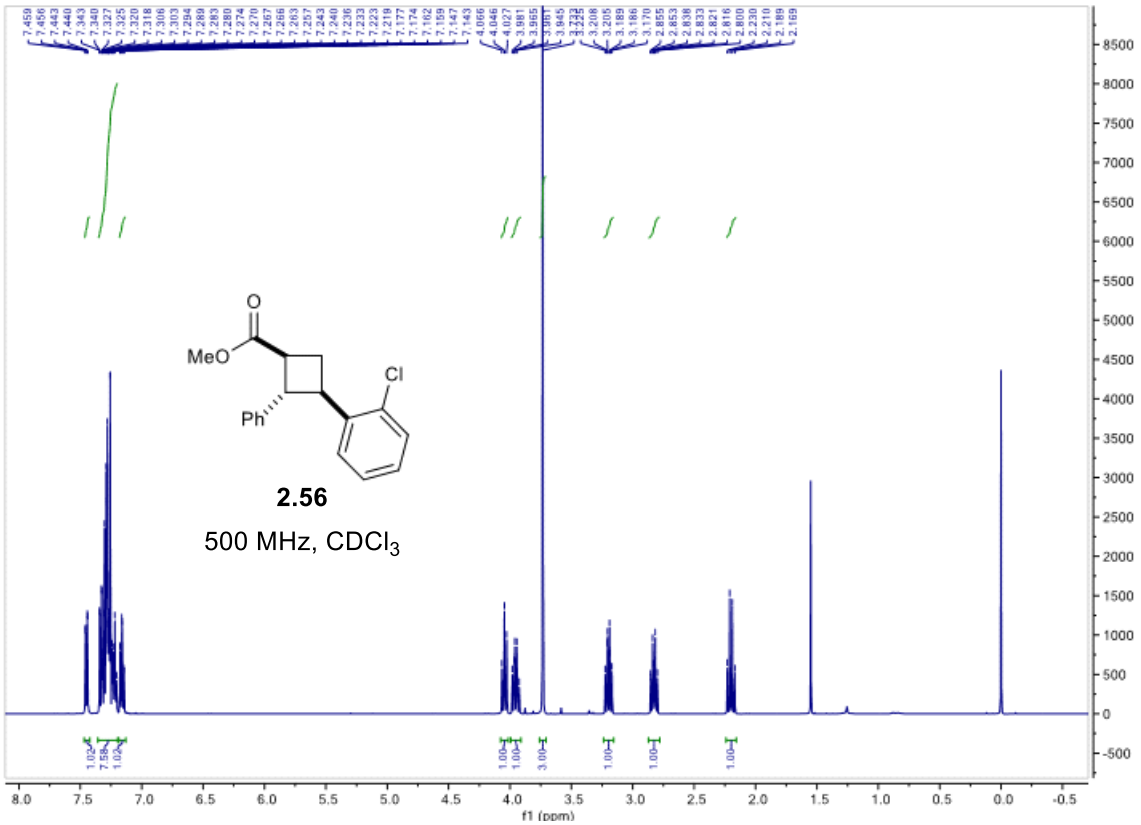

**2.55**

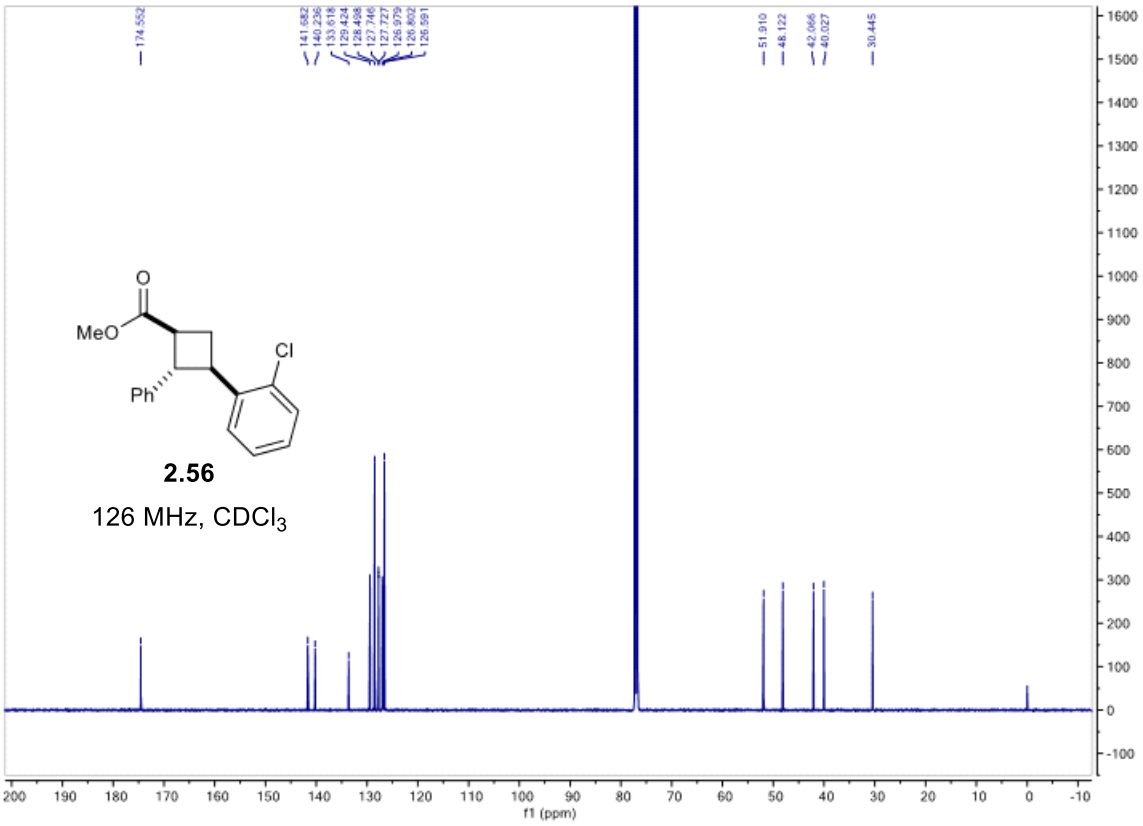
500 MHz, $CDCl_3$

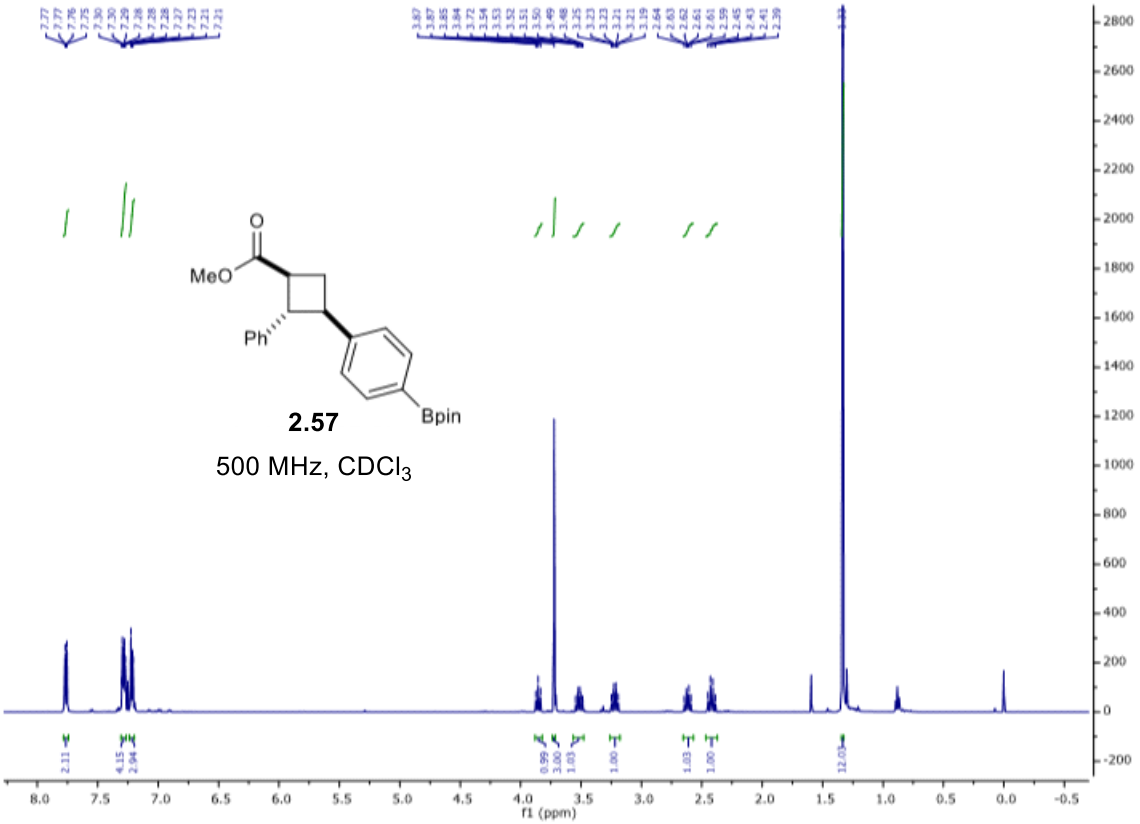



**2.55**

126 MHz, $CDCl_3$

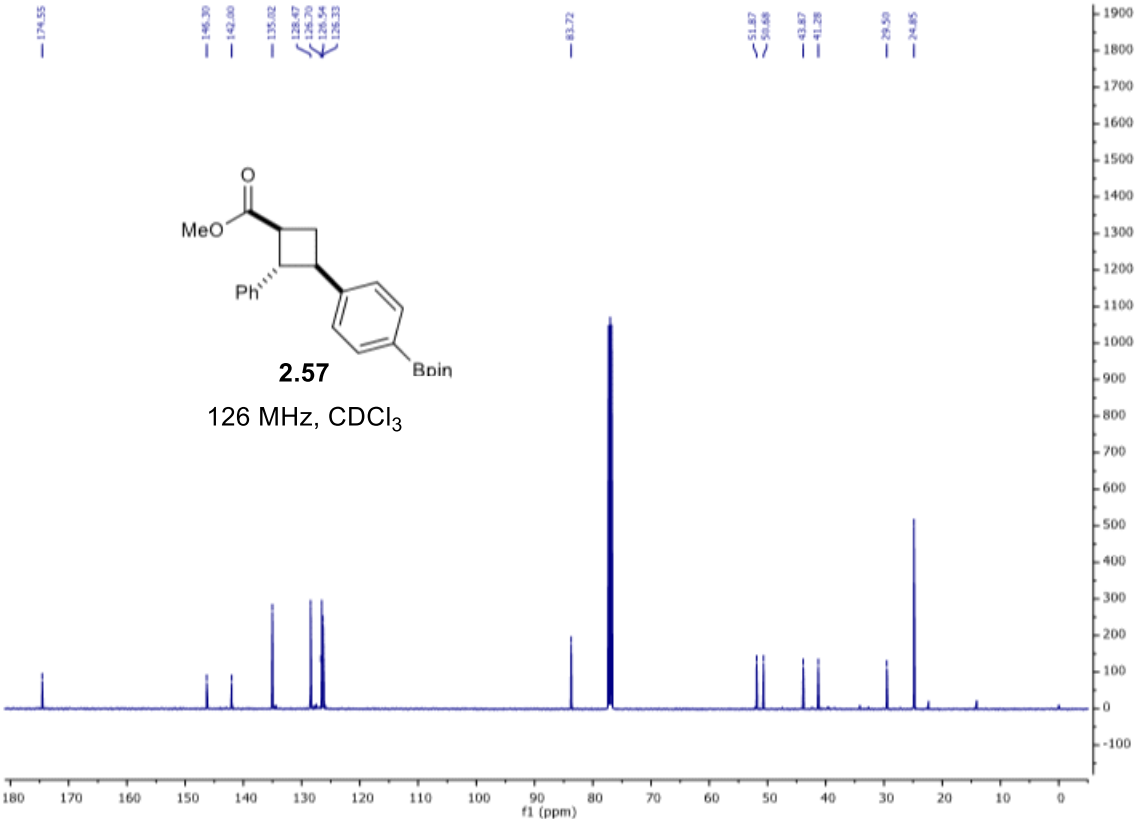

MeO
O
Cl
Ph
2.56
500 MHz, CDCl3
f1 (ppm)


MeO
O
Cl
Ph
2.56
126 MHz, CDCl3
f1 (ppm)



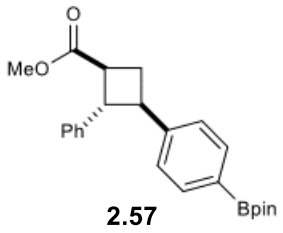

**2.57**

500 MHz, $CDCl_3$




**2.57**

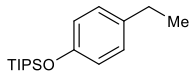
126 MHz, $CDCl_3$



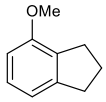

**2.57**

128 MHz, $CDCl_3$

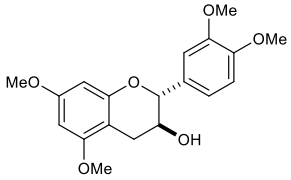
# List of Compounds for Chapter 3



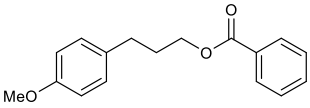

**3.15a**



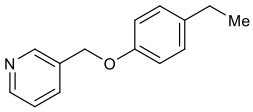

**3.27a**



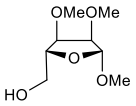

**3.79a**



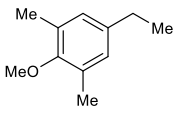

**3.20a**



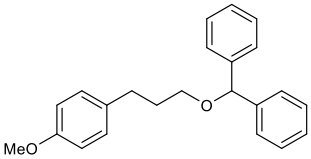

**3.29a**




**3.84a**

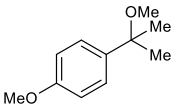



**3.26a**




**3.31a**

# List of Compounds for Chapter 3

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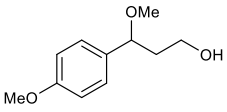


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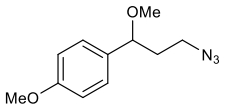


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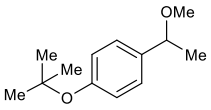


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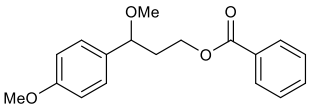


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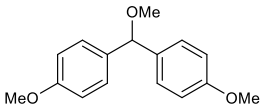


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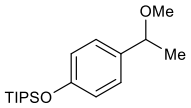


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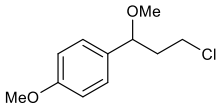


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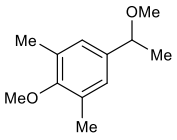


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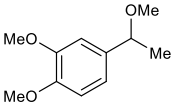


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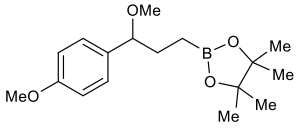


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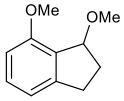


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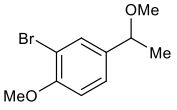


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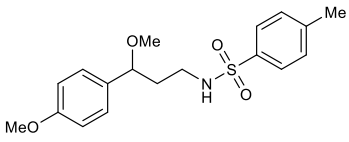


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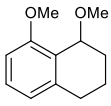
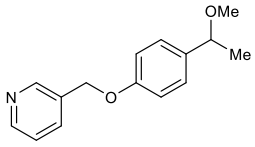



**3.28**

# List of Compounds for Chapter 3

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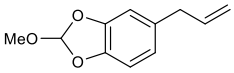
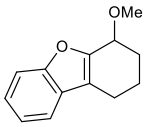
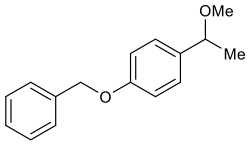



**3.32**




**3.36**

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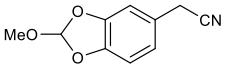


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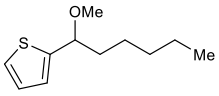


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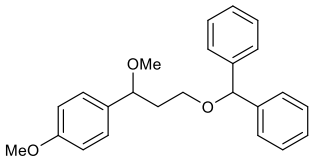


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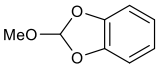


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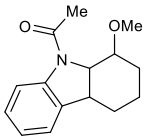
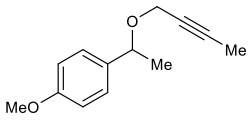



**3.38**

# List of Compounds for Chapter 3

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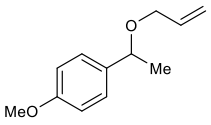


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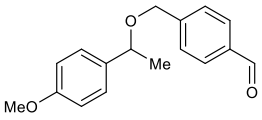


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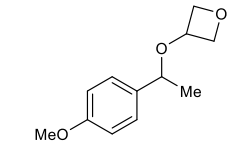


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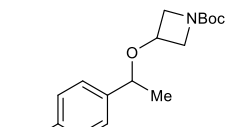


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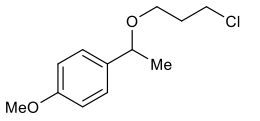


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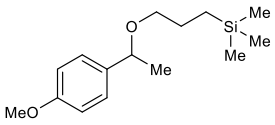
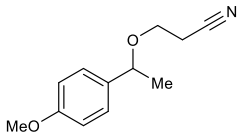



**3.59**

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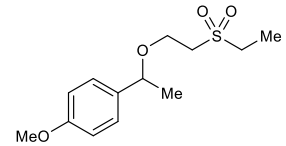


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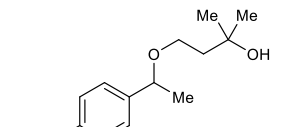
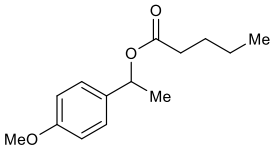



**3.62**

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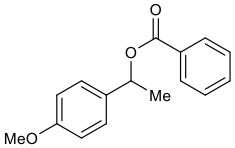


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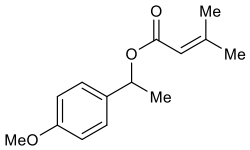
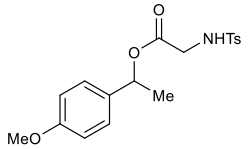
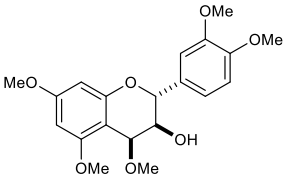



**3.65**




**3.66**

# List of Compounds for Chapter 3

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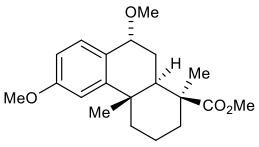
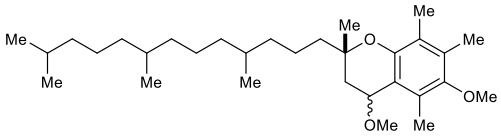



**3.80**

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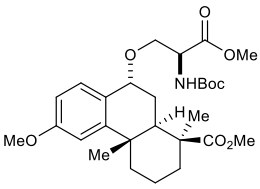
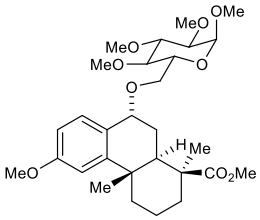



**3.82**

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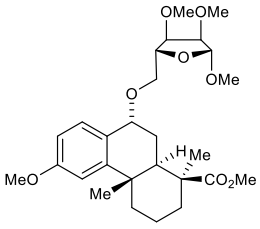
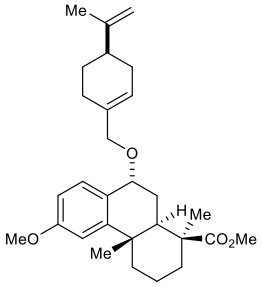



**3.84**

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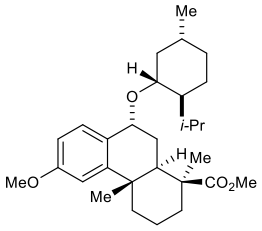
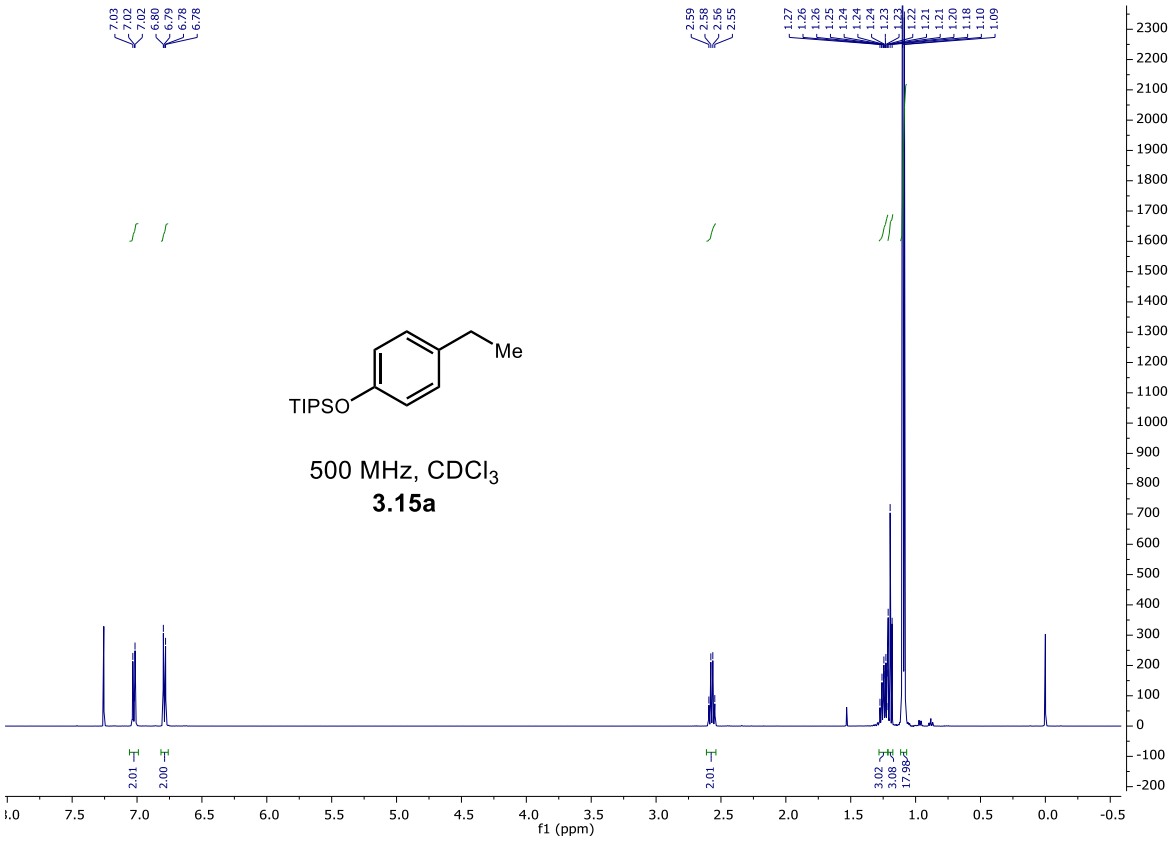
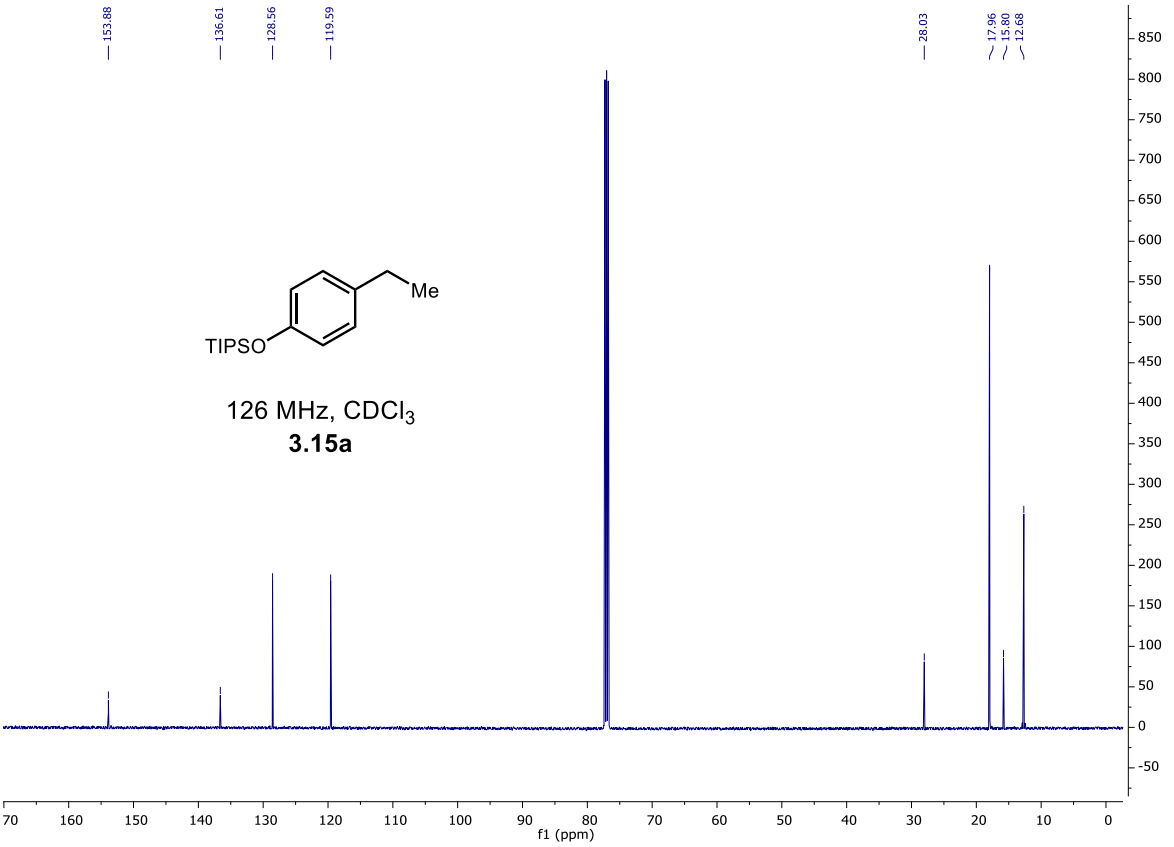
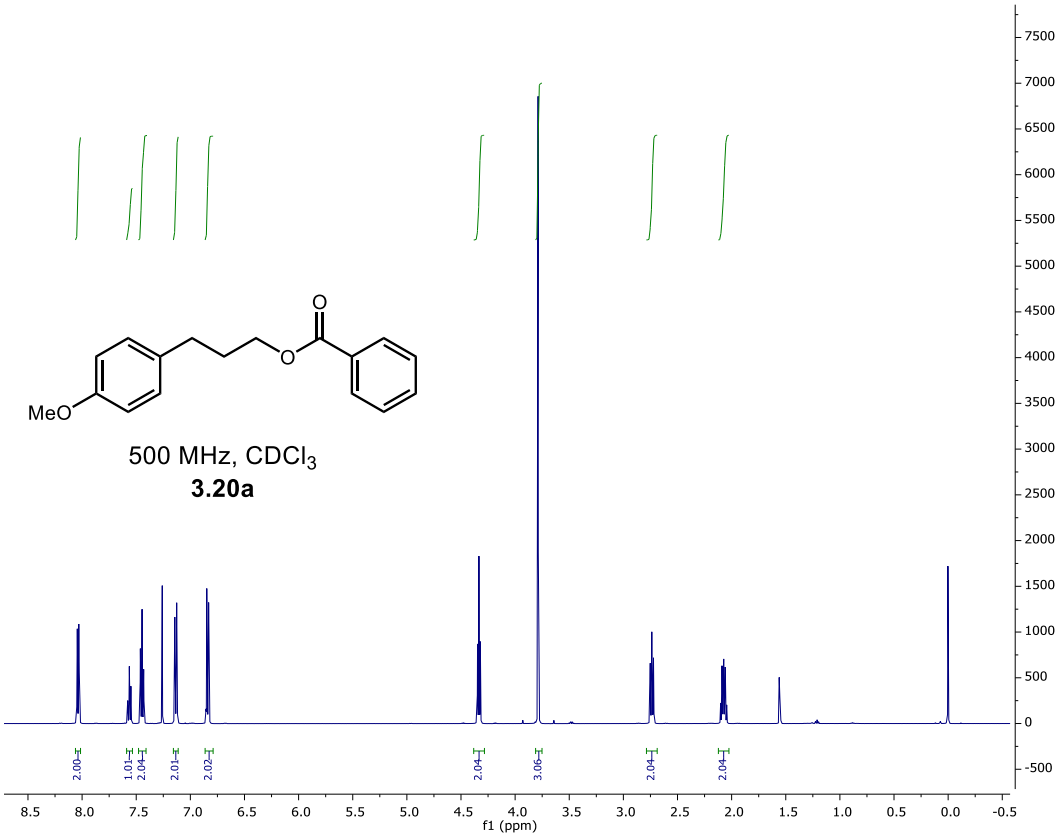
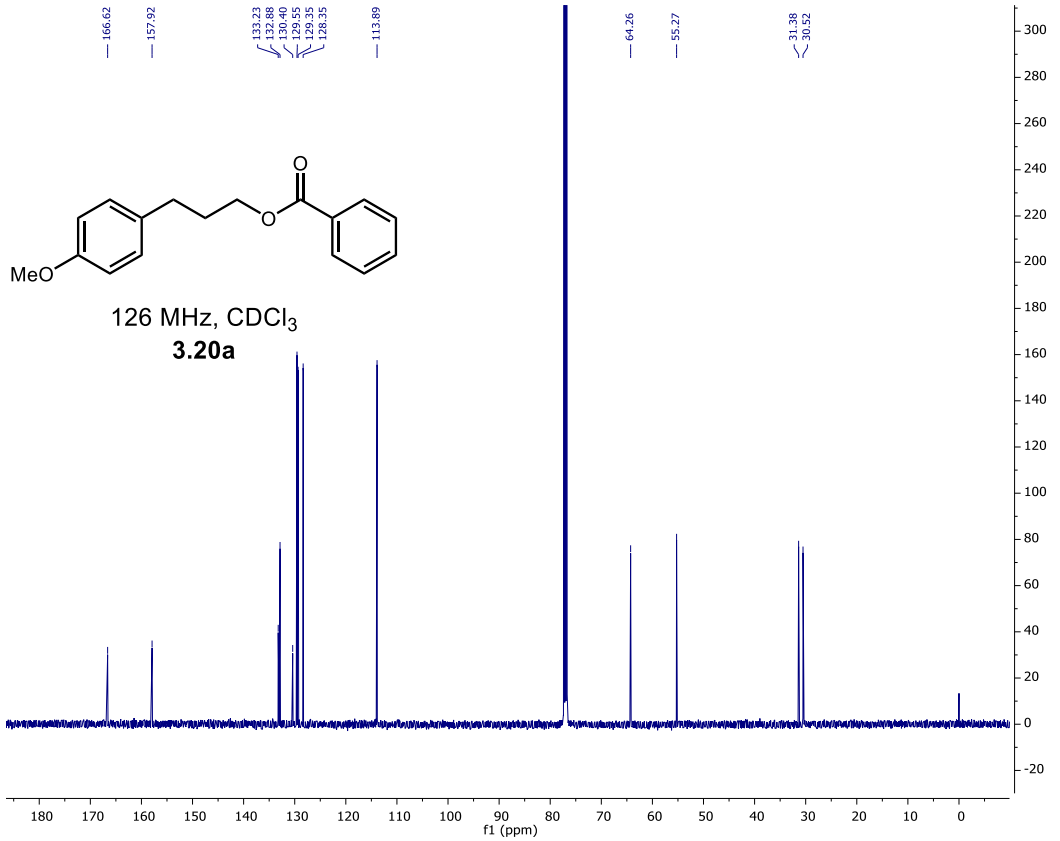


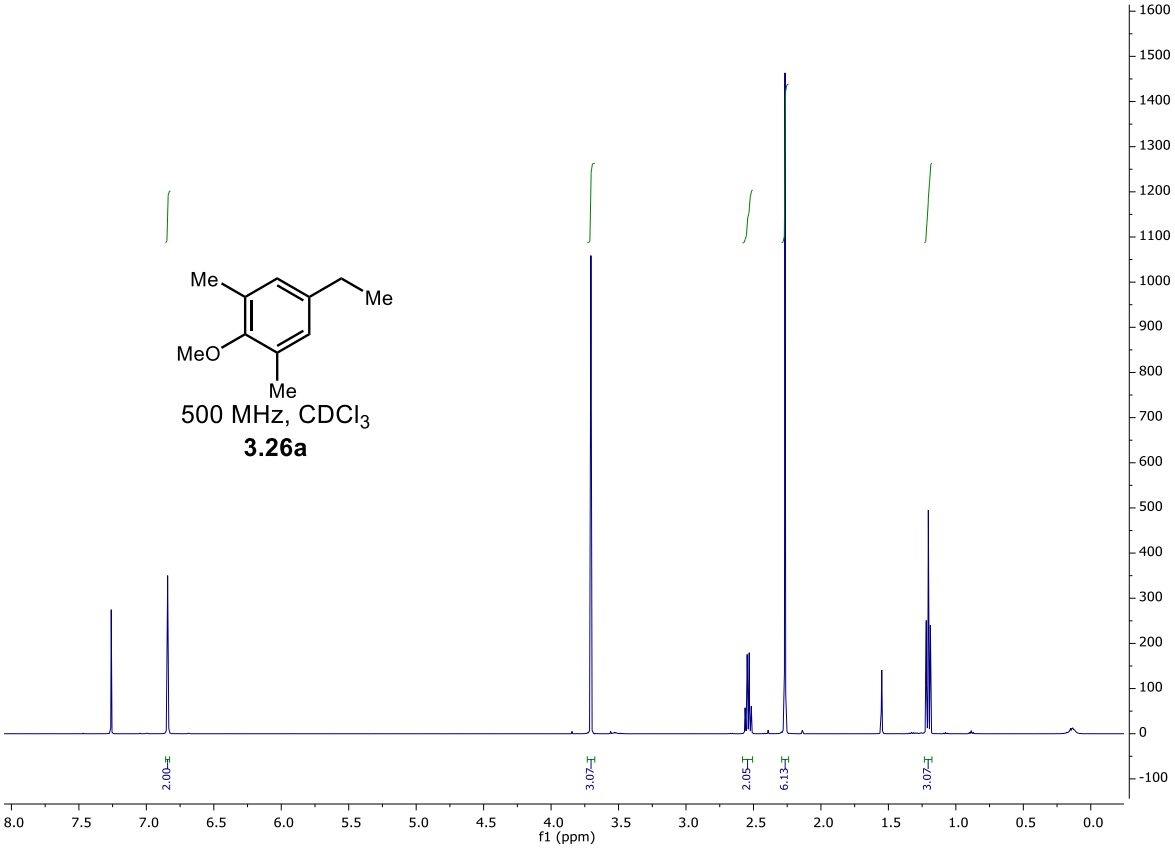

**3.86**

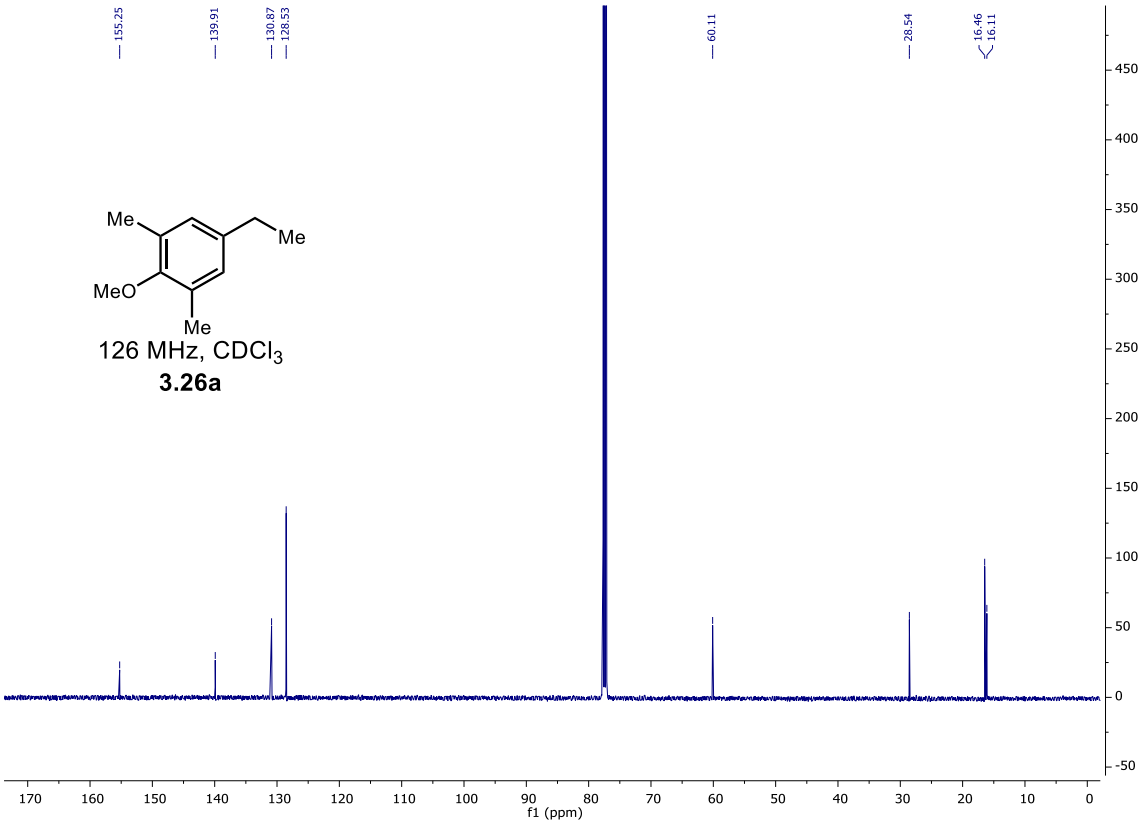

7.03
7.02
7.02
6.80
6.79
6.78
6.78
2.59
2.58
2.56
2.55
1.27
1.26
1.26
1.25
1.24
1.24
1.24
1.23
1.23
1.22
1.21
1.21
1.20
1.18
1.10
1.09
Me
TIPSO
500 MHz, CDCl3
3.15a
2.01
2.00
2.01
3.02
3.08
17.98
f1 (ppm)

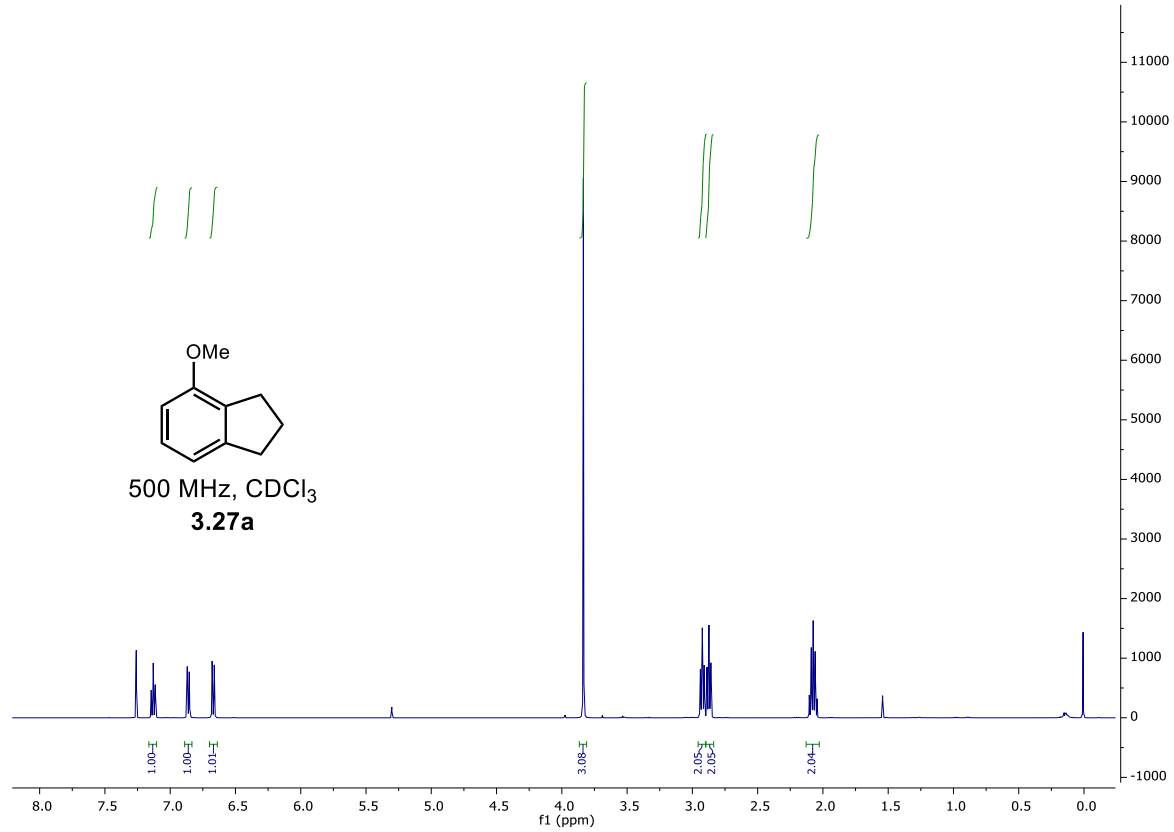

153.88
136.61
128.56
119.59
28.03
17.96
15.80
12.68
Me
TIPSO
126 MHz, CDCl3
3.15a
f1 (ppm)

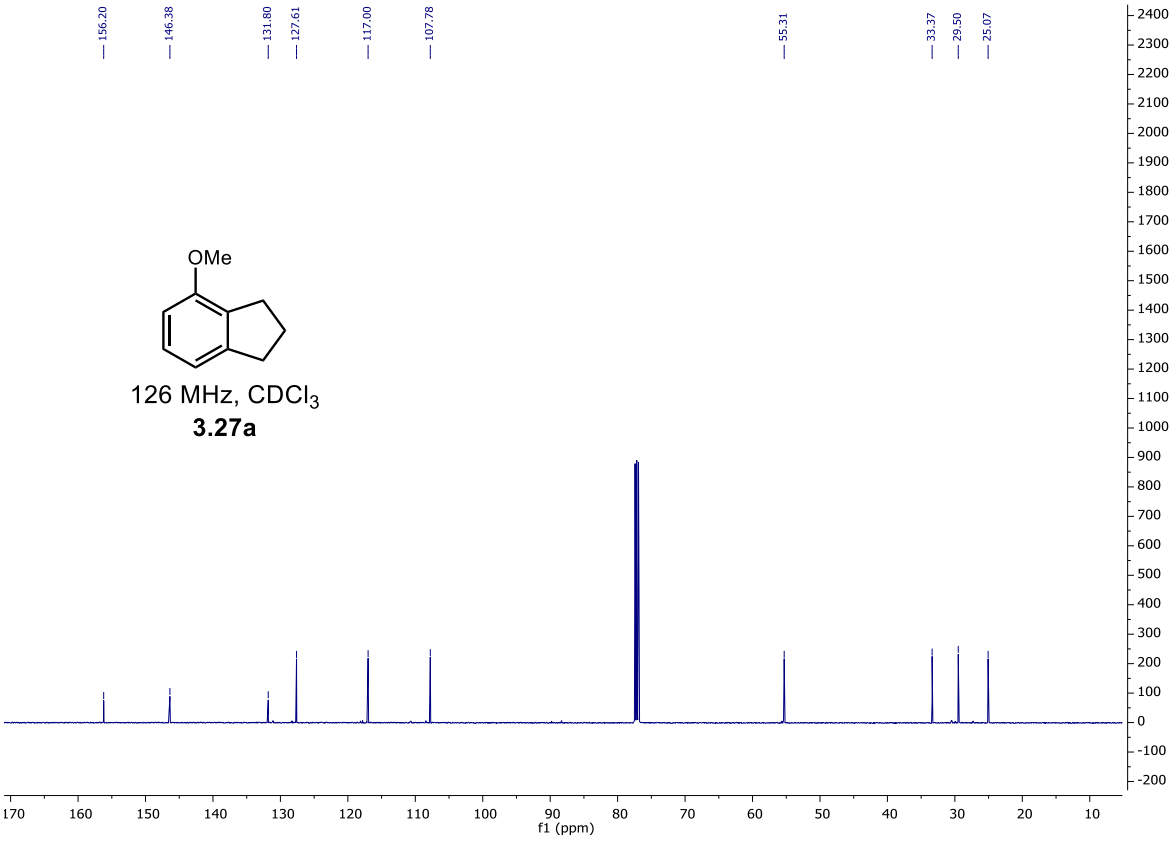

MeO
O
O
500 MHz, $CDCl_3$
**3.20a**
2.00
1.01
2.04
2.01
2.02
2.04
3.06
2.04
2.04
f1 (ppm)

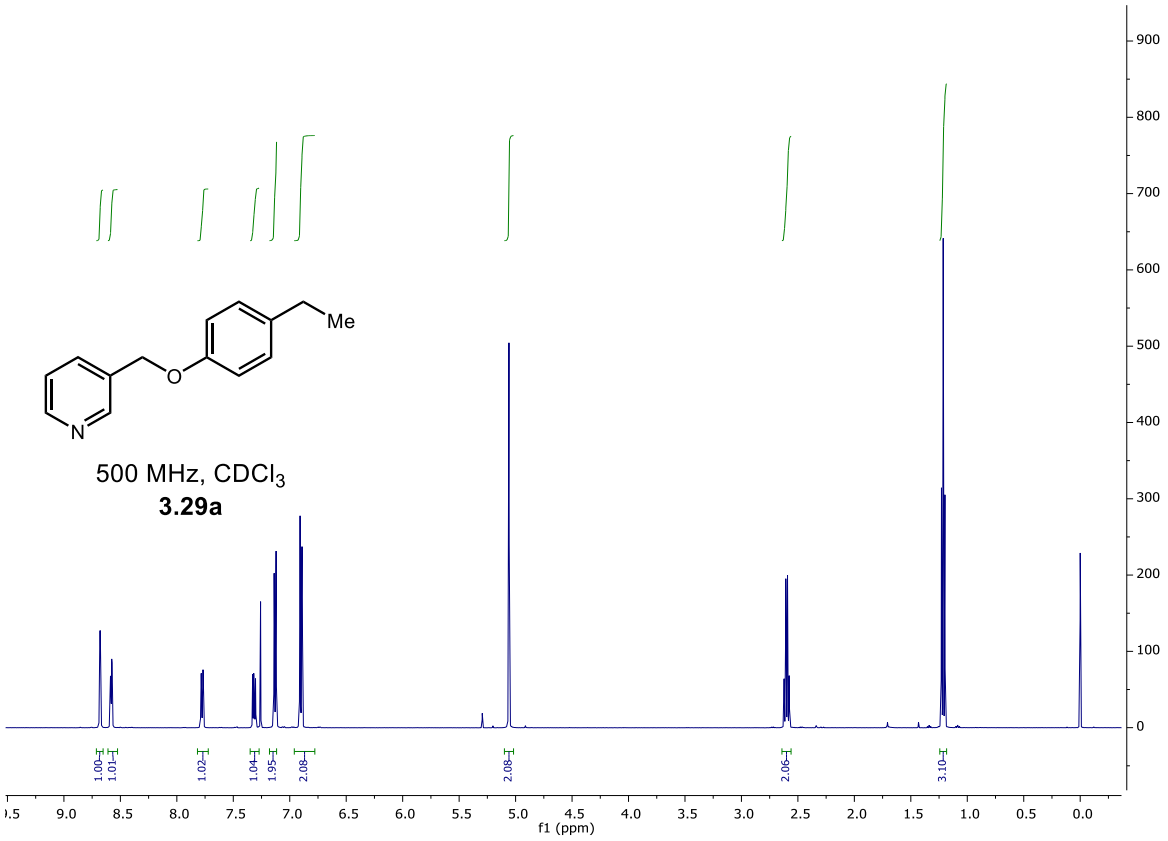

166.62
157.92
133.23
132.88
130.40
129.55
129.35
128.35
113.89
64.26
55.27
31.38
30.52
MeO
O
O
126 MHz, $CDCl_3$
**3.20a**
f1 (ppm)

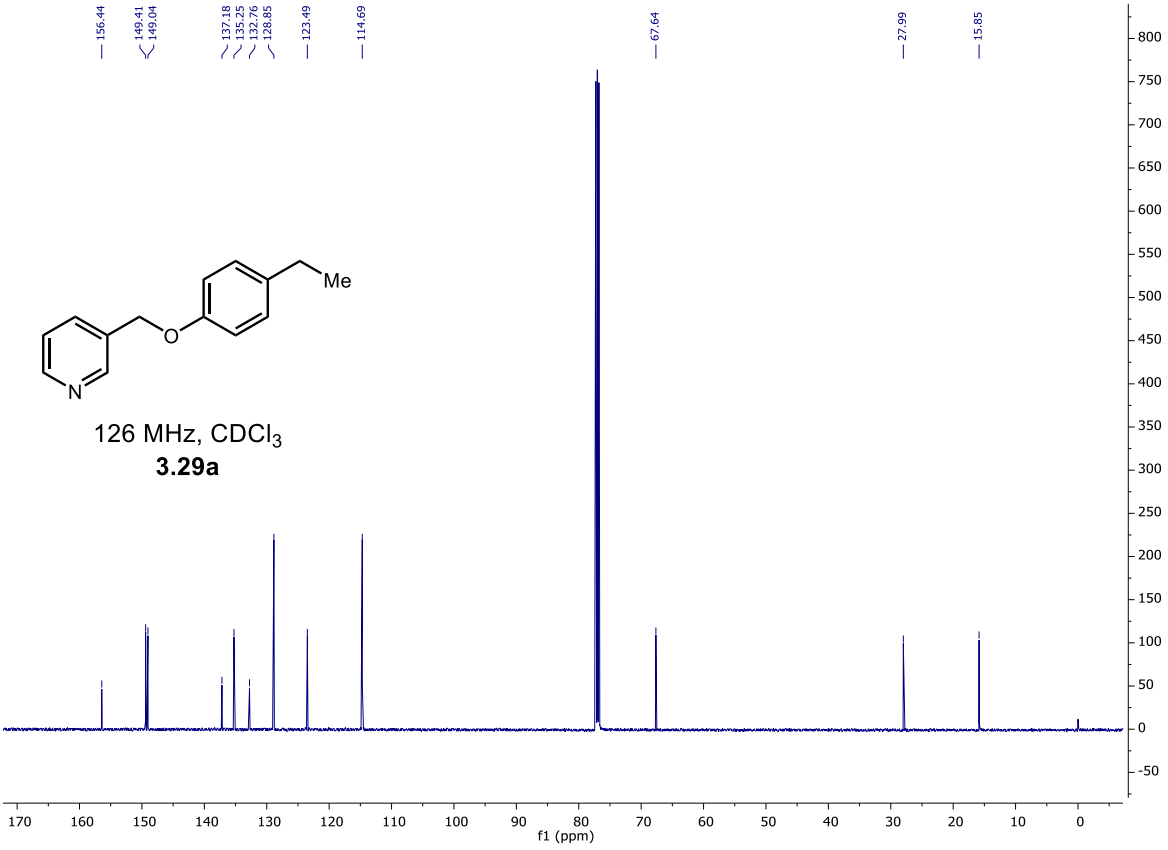

Me
Me
MeO
Me
500 MHz, CDCl3
3.26a
2.00
3.07
2.05
6.13
3.07
f1 (ppm)

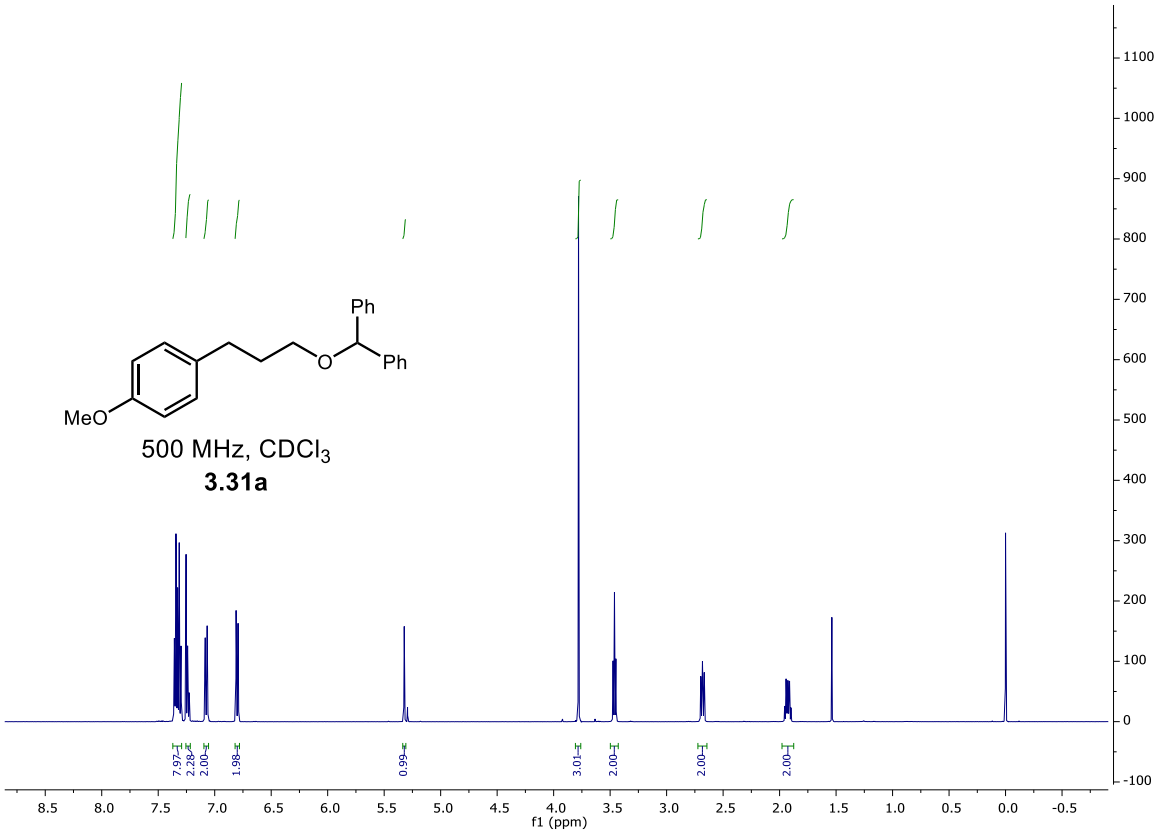

155.25
139.91
130.87
128.53
60.11
28.54
16.46
16.11
Me
Me
MeO
Me
126 MHz, CDCl3
3.26a
f1 (ppm)

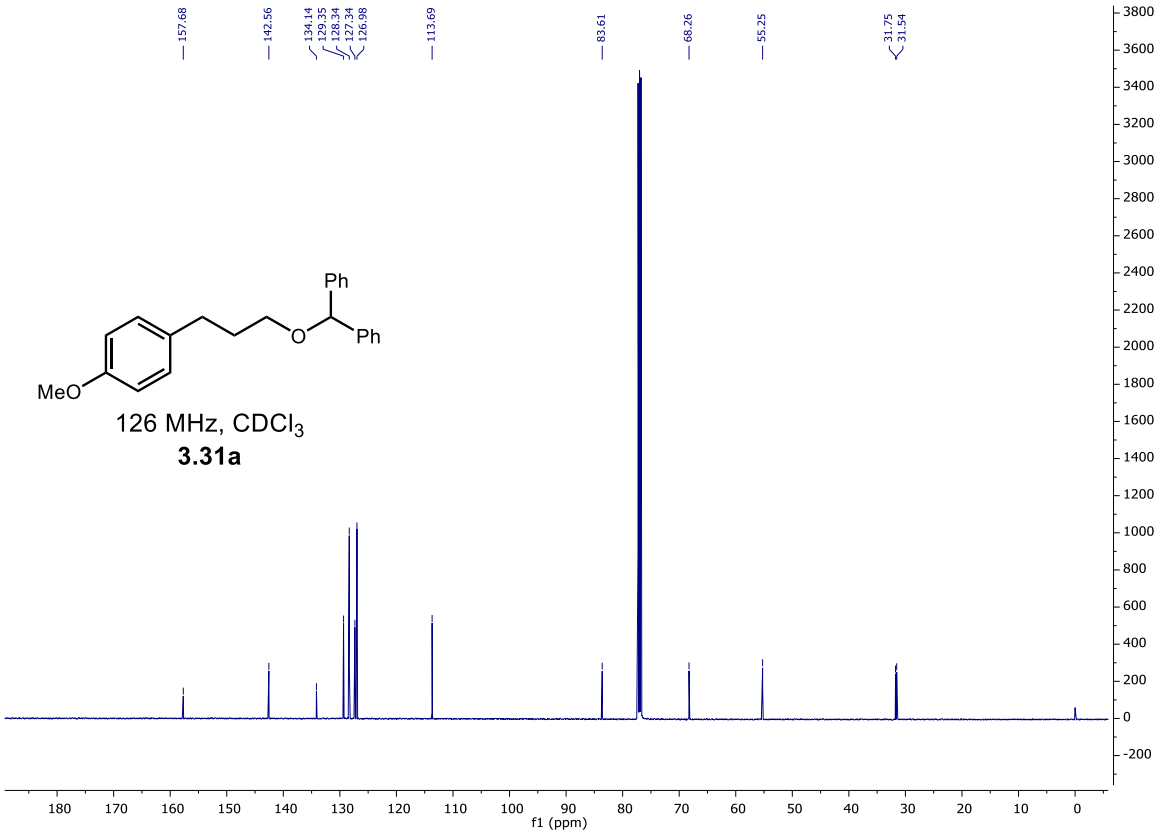

OMe
500 MHz, CDCl3
3.27a
1.00
1.00
1.01
3.08
2.05
2.05
2.04
f1 (ppm)

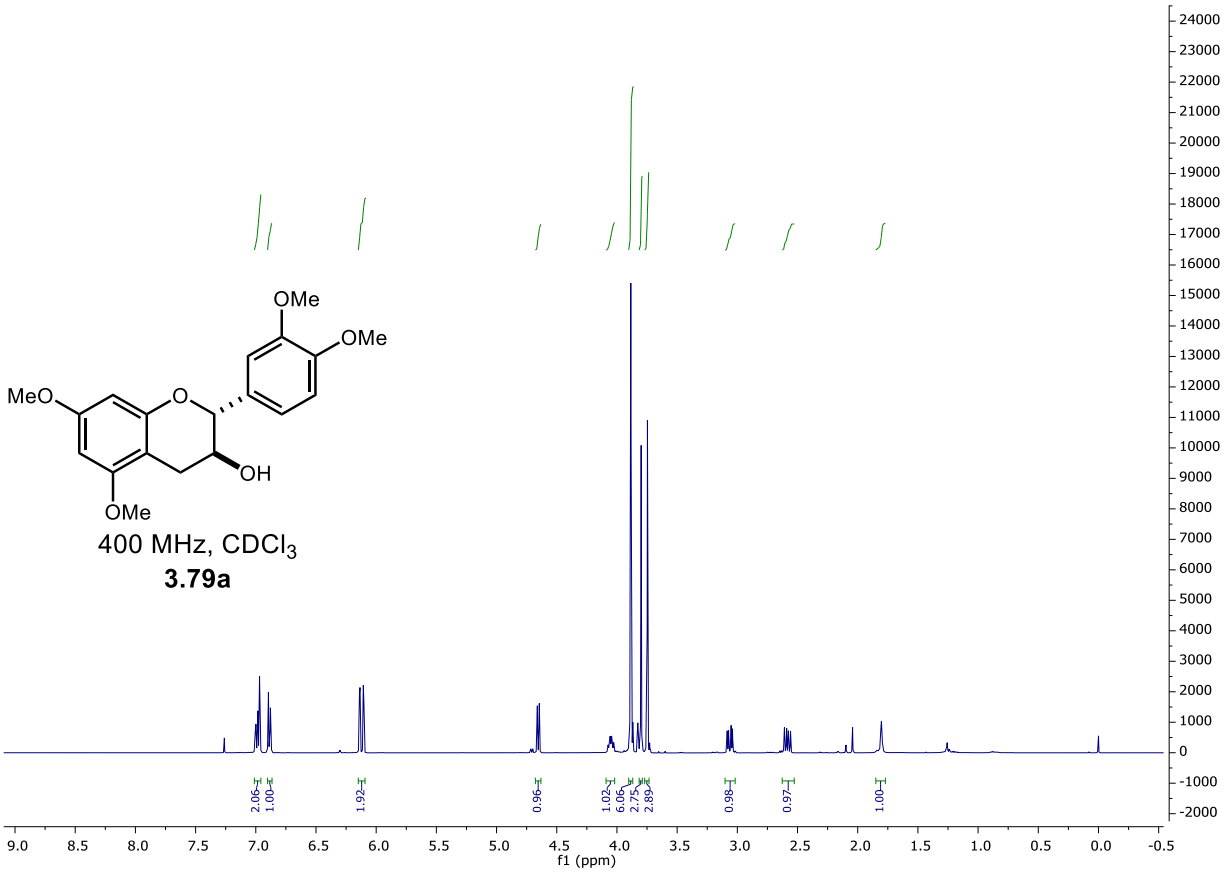

156.20
146.38
131.80
127.61
117.00
107.78
55.31
33.37
29.50
25.07
OMe
126 MHz, CDCl3
3.27a
f1 (ppm)

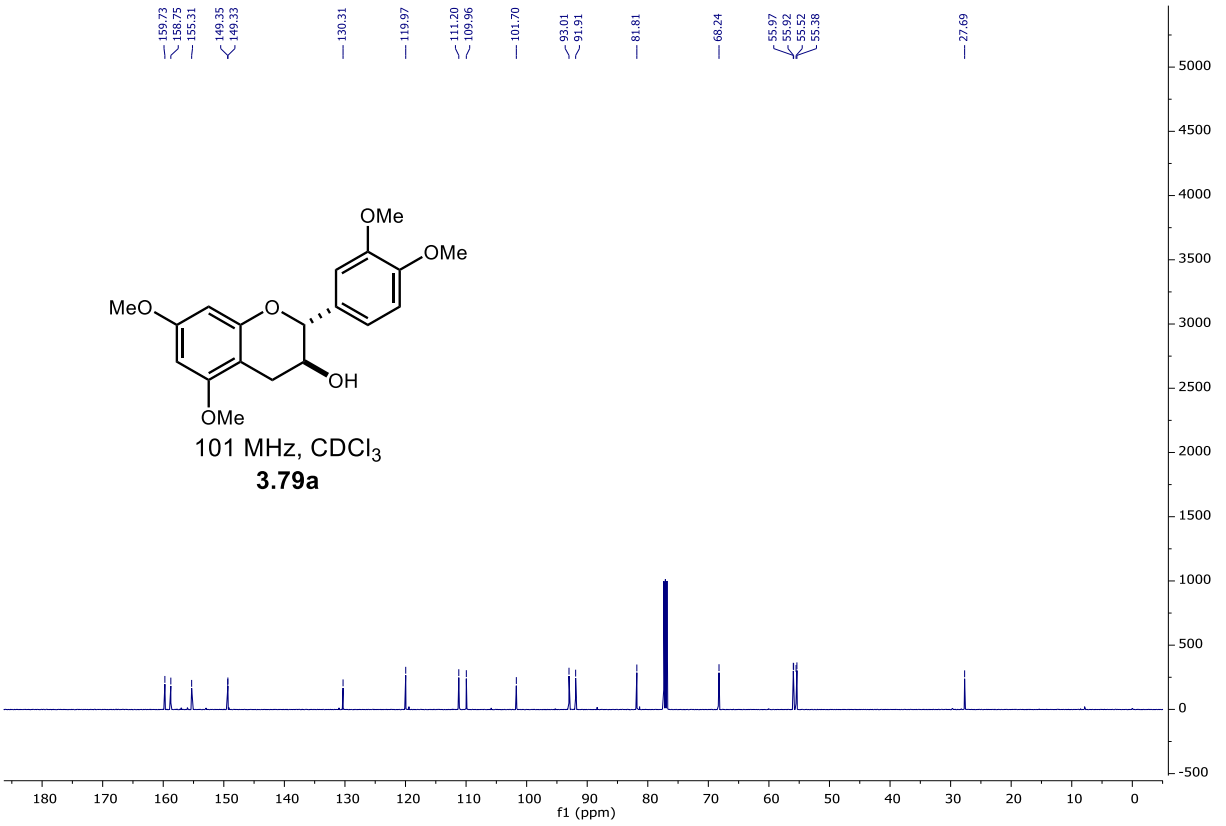

Me
O
N
500 MHz, CDCl3
3.29a
1.00
1.01
1.02
1.04
1.95
2.08
2.08
2.06
3.10
f1 (ppm)

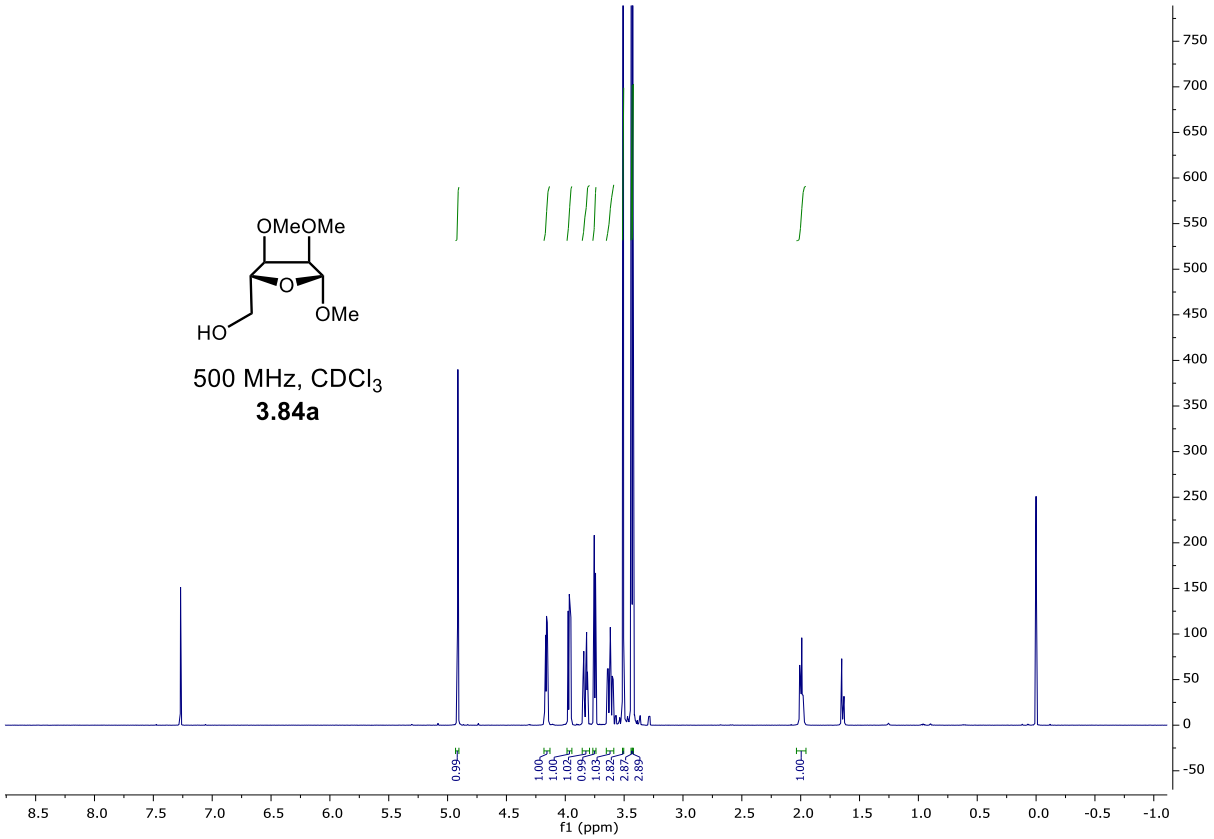

156.44
149.41
149.04
137.18
135.25
132.76
128.85
123.49
114.69
67.64
27.99
15.85
Me
O
N
126 MHz, CDCl3
3.29a
f1 (ppm)

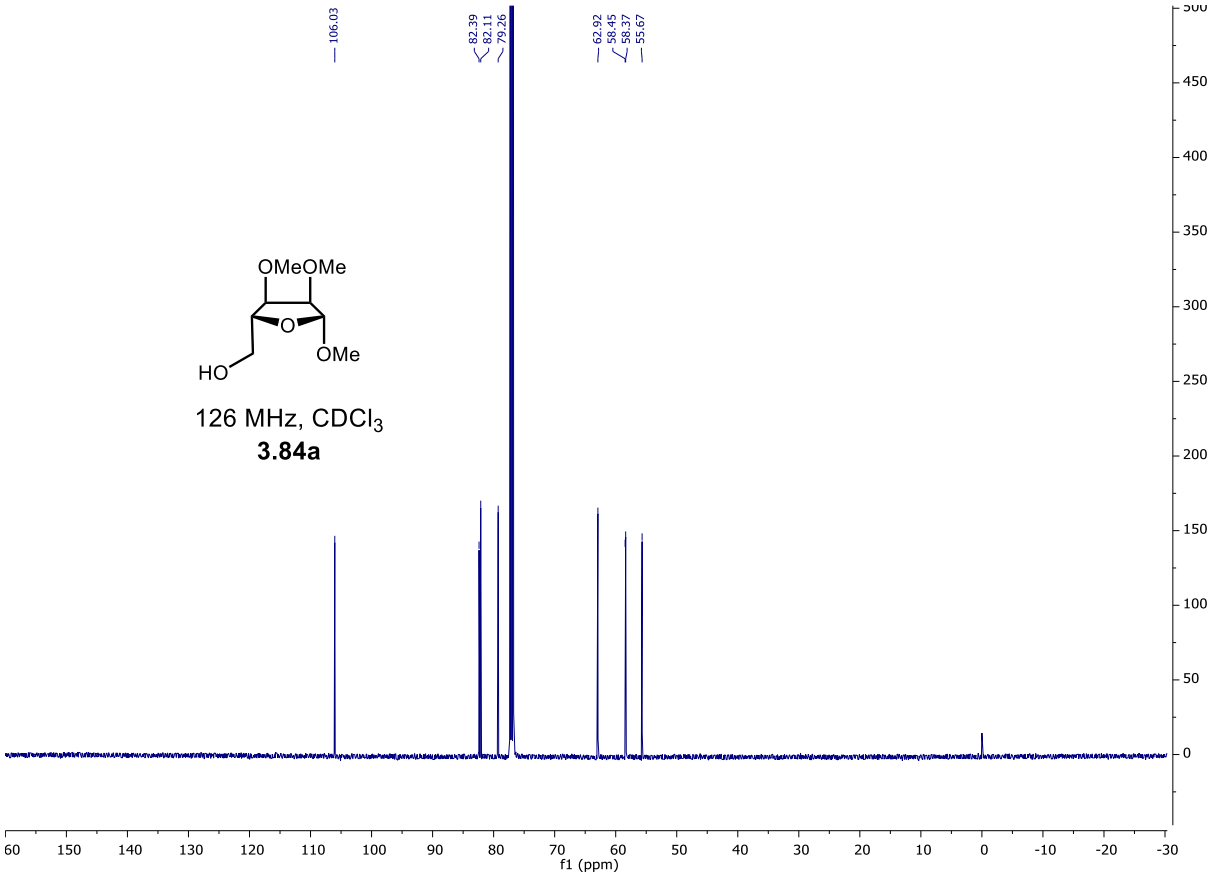

Ph
Ph
O
MeO
500 MHz, CDCl3
3.31a
7.97
2.28
2.00
1.98
0.99
3.01
2.00
2.00
2.00
f1 (ppm)

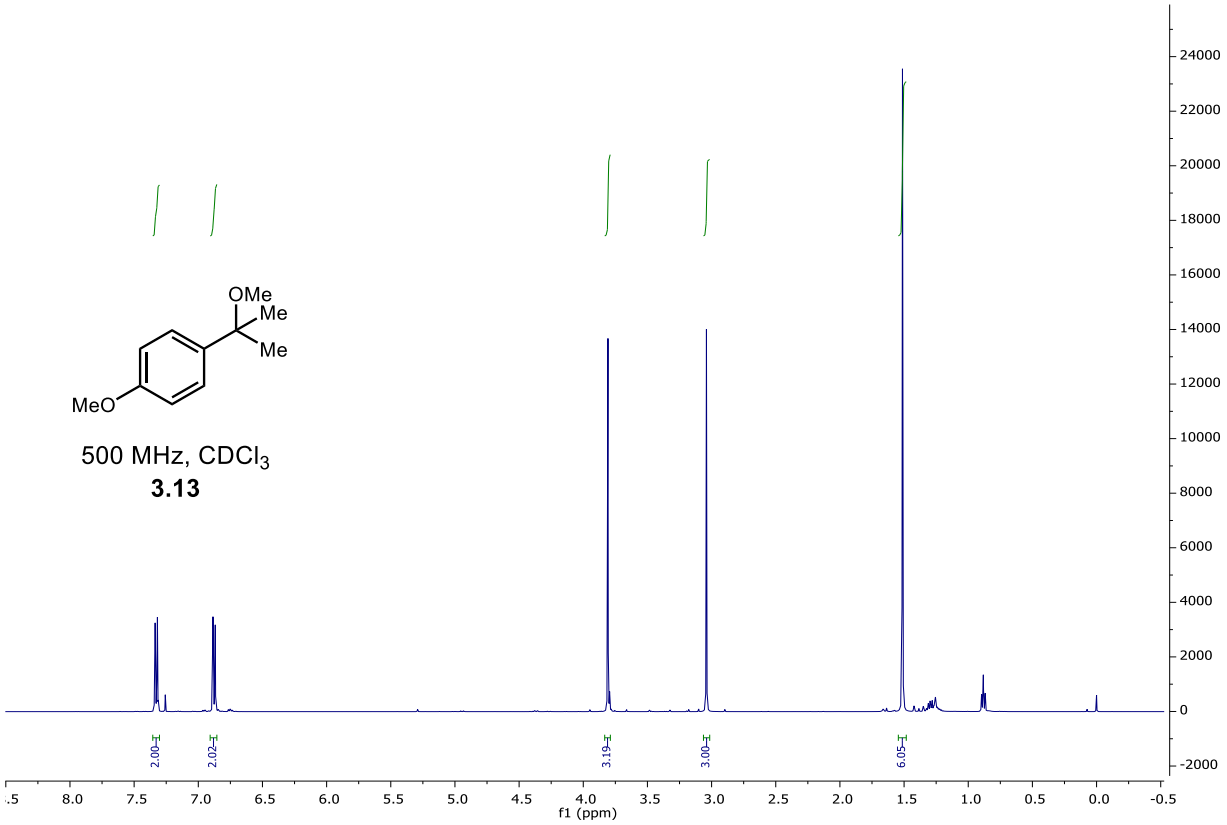

157.68
142.56
134.14
129.35
128.34
127.34
126.98
113.69
83.61
68.26
55.25
31.75
31.54
Ph
Ph
O
MeO
126 MHz, CDCl3
3.31a
f1 (ppm)

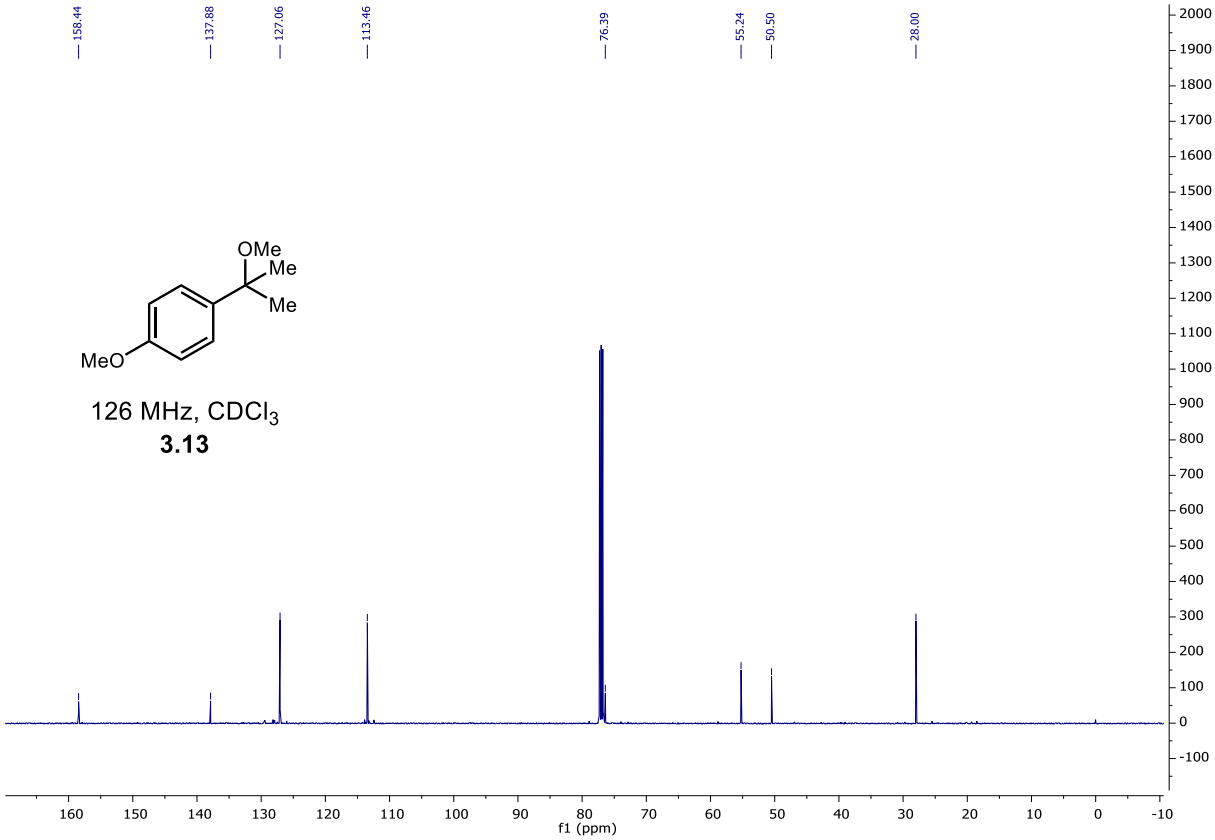

OMe
OMe
MeO
O
OH
OMe
400 MHz, CDCl3
3.79a
f1 (ppm)

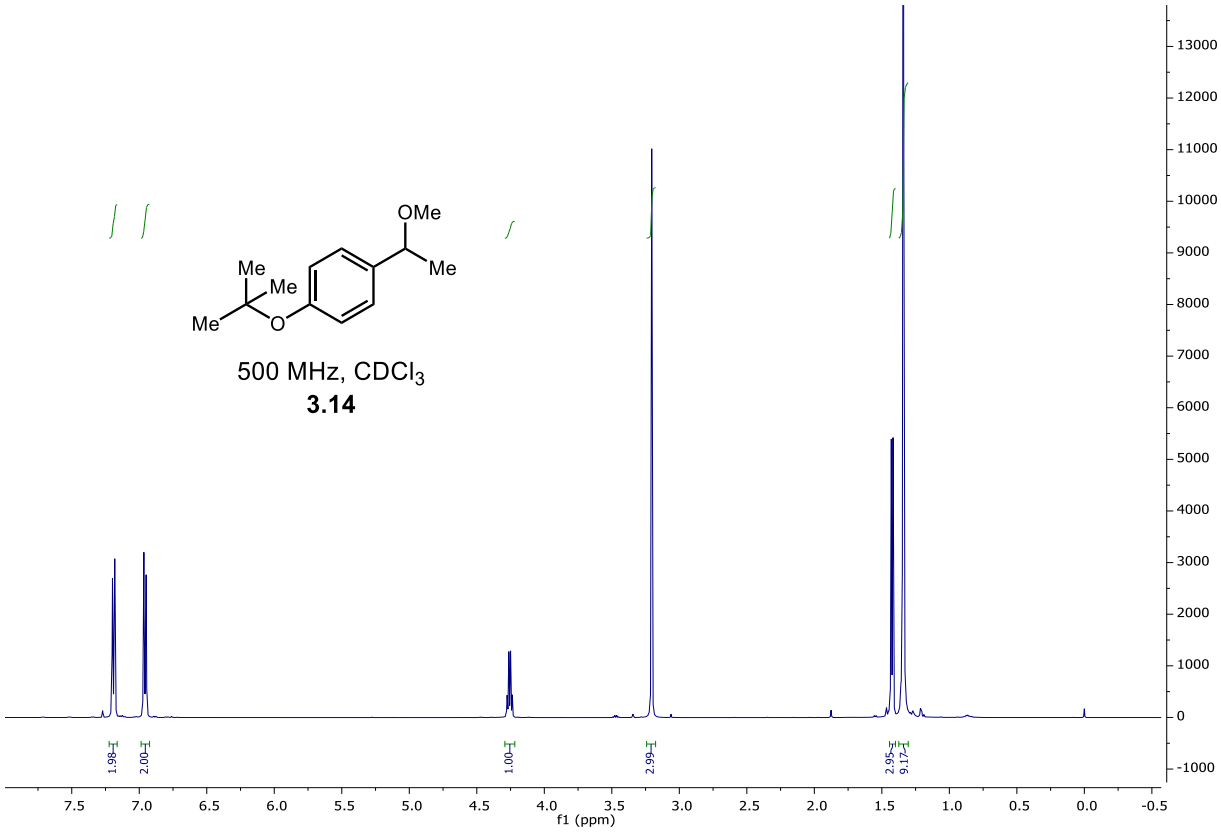

OMe
OMe
MeO
O
OH
OMe
101 MHz, CDCl3
3.79a
f1 (ppm)

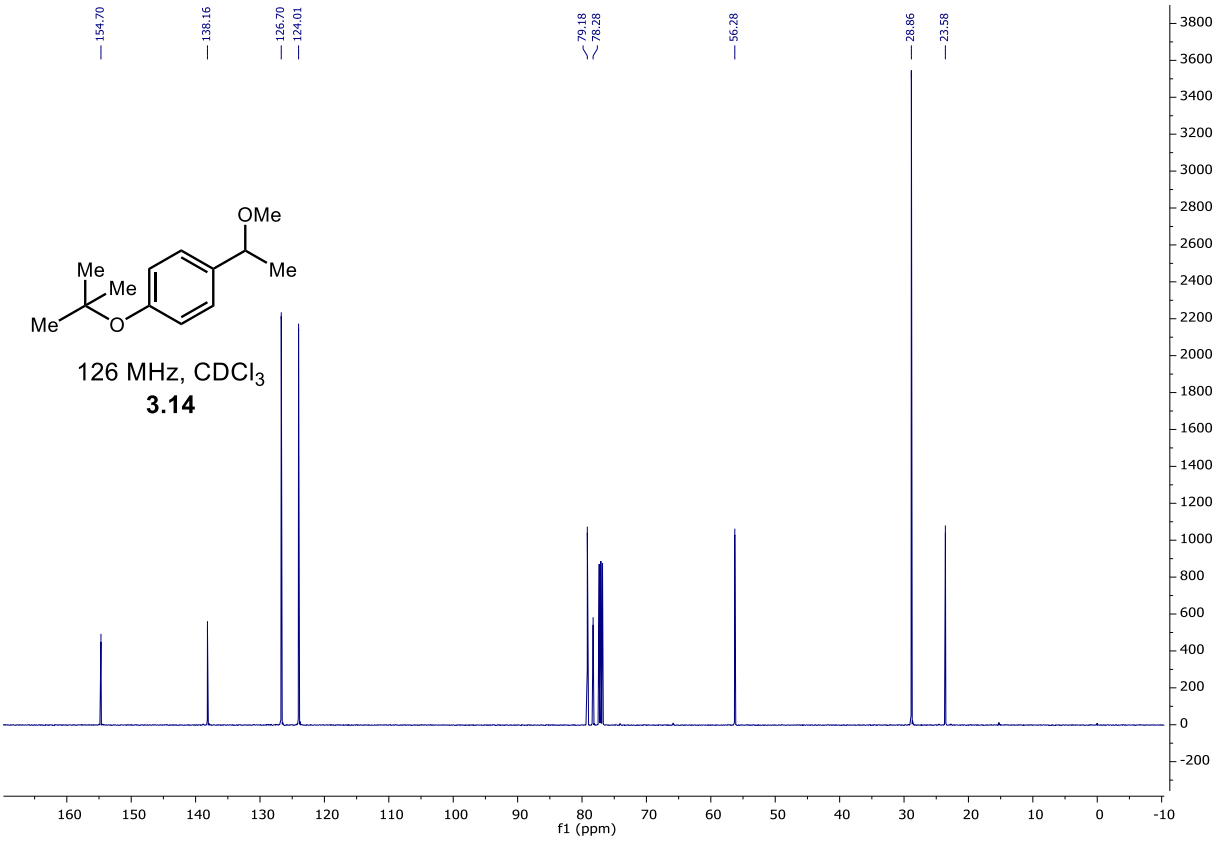

OMeOMe
O
OMe
HO
500 MHz, CDCl3
3.84a
f1 (ppm)

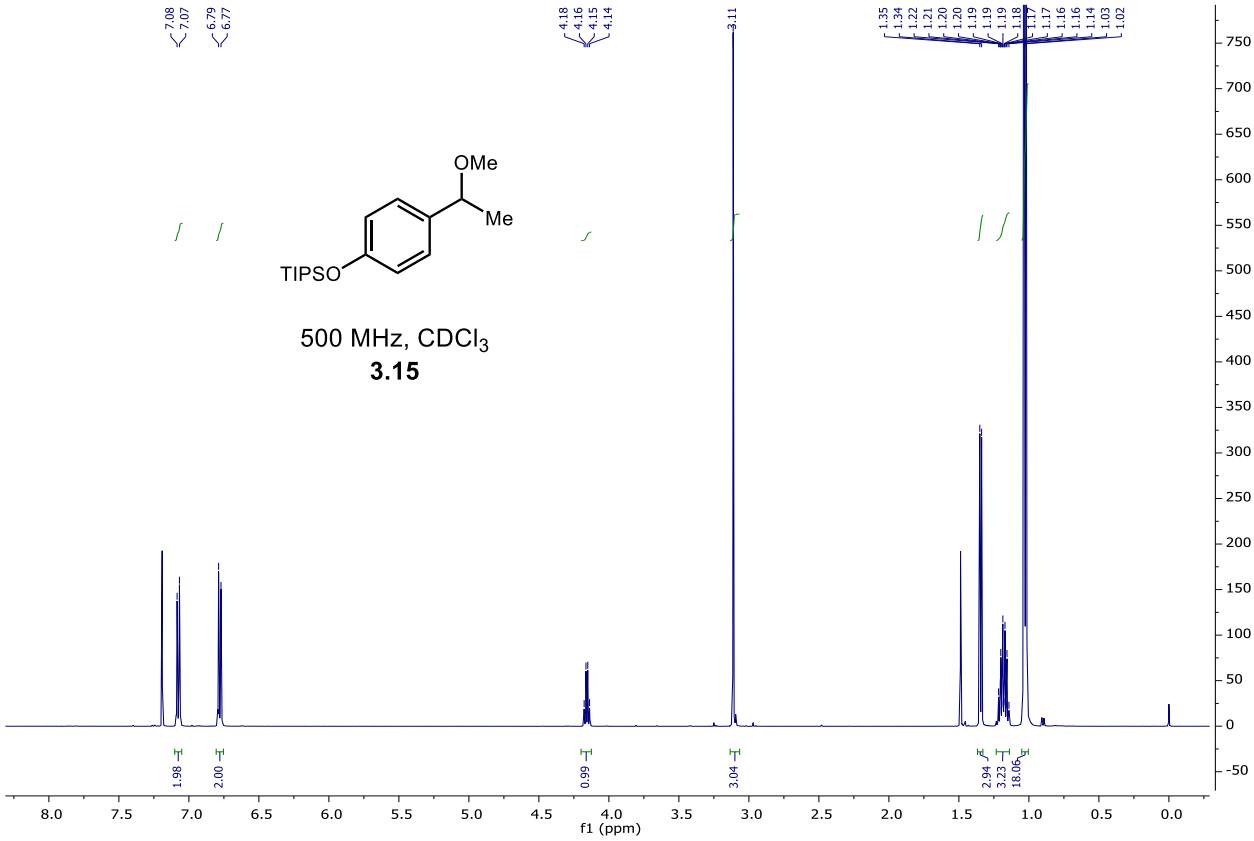

106.03
82.39
82.11
79.26
62.92
58.45
58.37
55.67
OMeOMe
O
OMe
HO
126 MHz, CDCl3
3.84a
f1 (ppm)


OMe
Me
Me
MeO
500 MHz, CDCl3
3.13
2.00
2.02
3.19
3.00
6.05
f1 (ppm)


158.44
137.88
127.06
113.46
76.39
55.24
50.50
28.00
OMe
Me
Me
MeO
126 MHz, CDCl3
3.13
f1 (ppm)

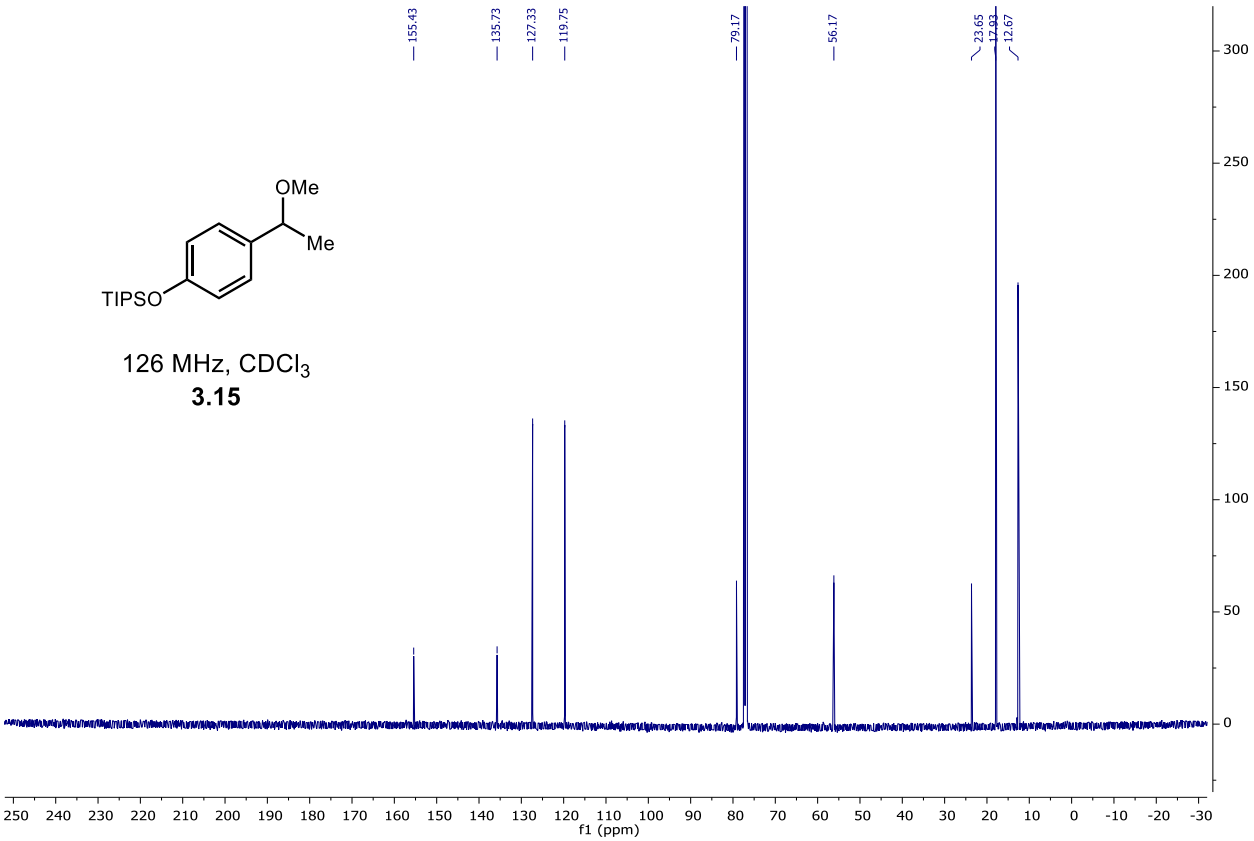

OMe
Me
Me
Me
Me
O
500 MHz, CDCl3
3.14
1.98
2.00
1.00
2.99
2.95
9.17
f1 (ppm)


154.70
138.16
126.70
124.01
79.18
78.28
56.28
28.86
23.58
OMe
Me
Me
Me
Me
O
126 MHz, CDCl3
3.14
f1 (ppm)



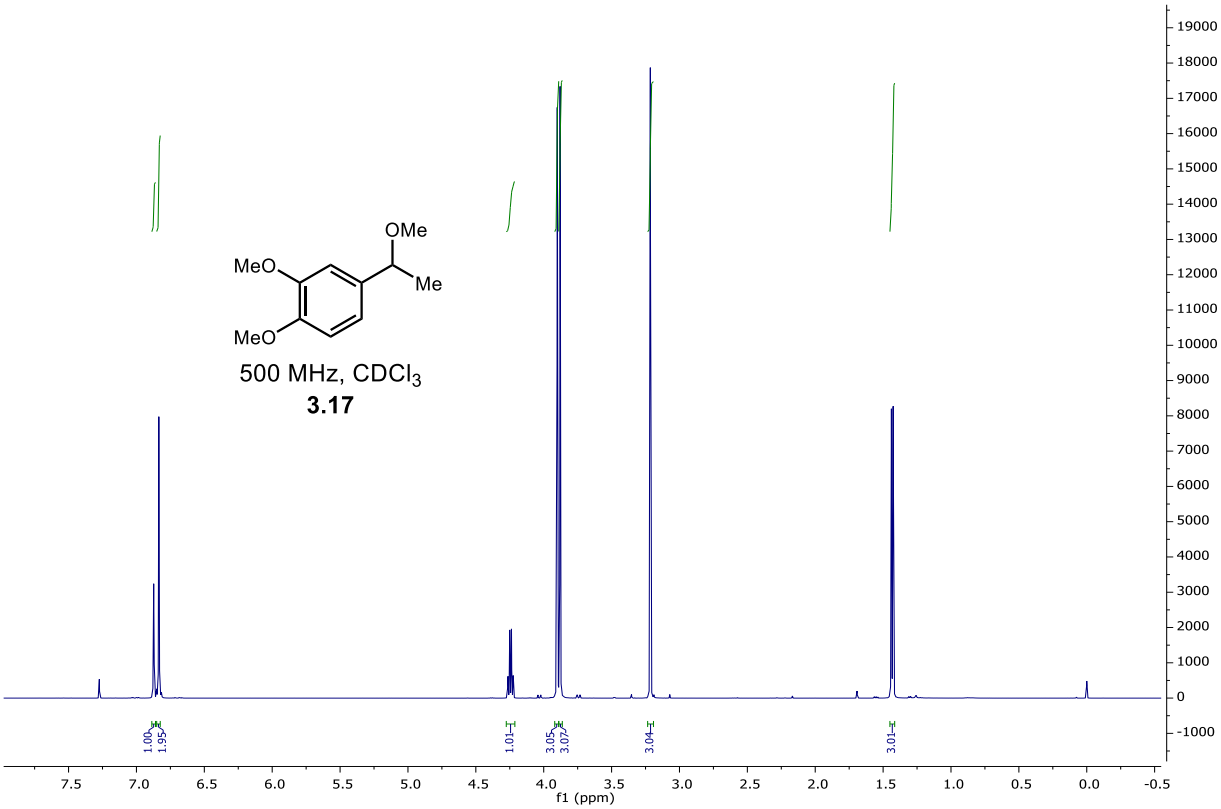

500 MHz, $CDCl_3$

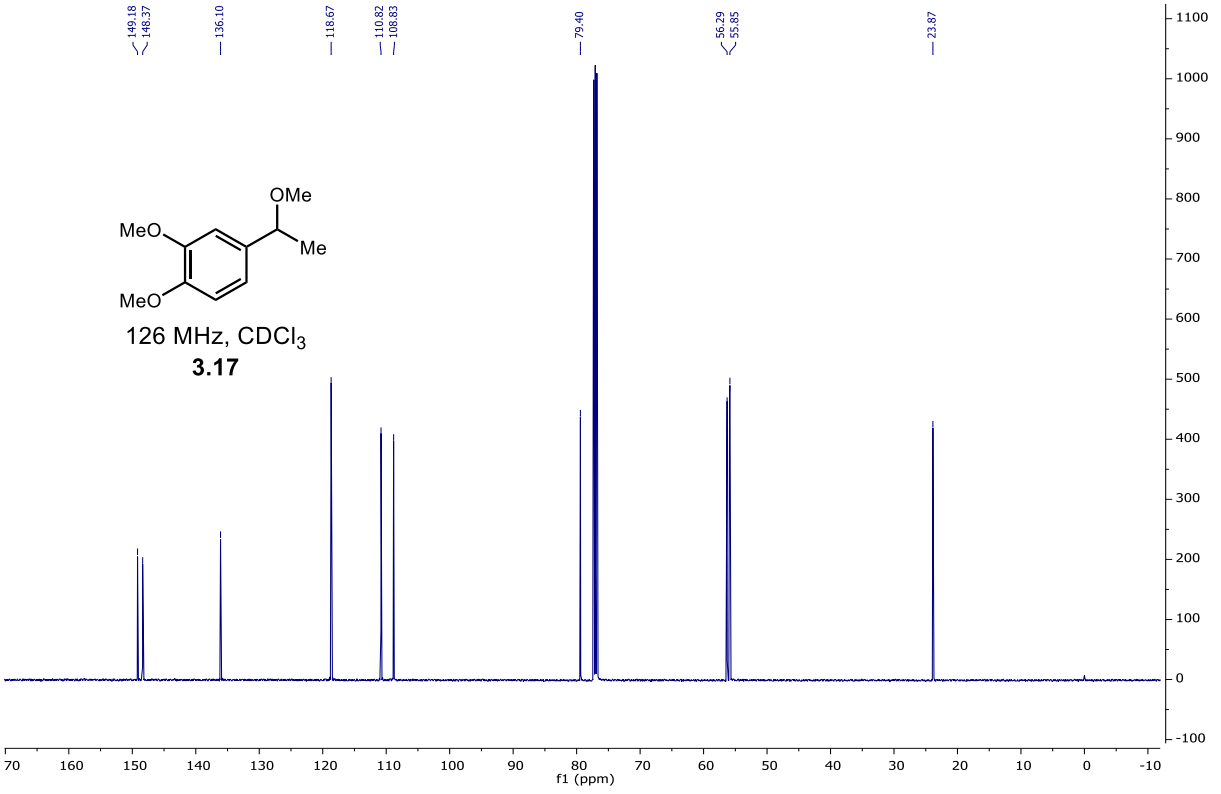
**3.15**

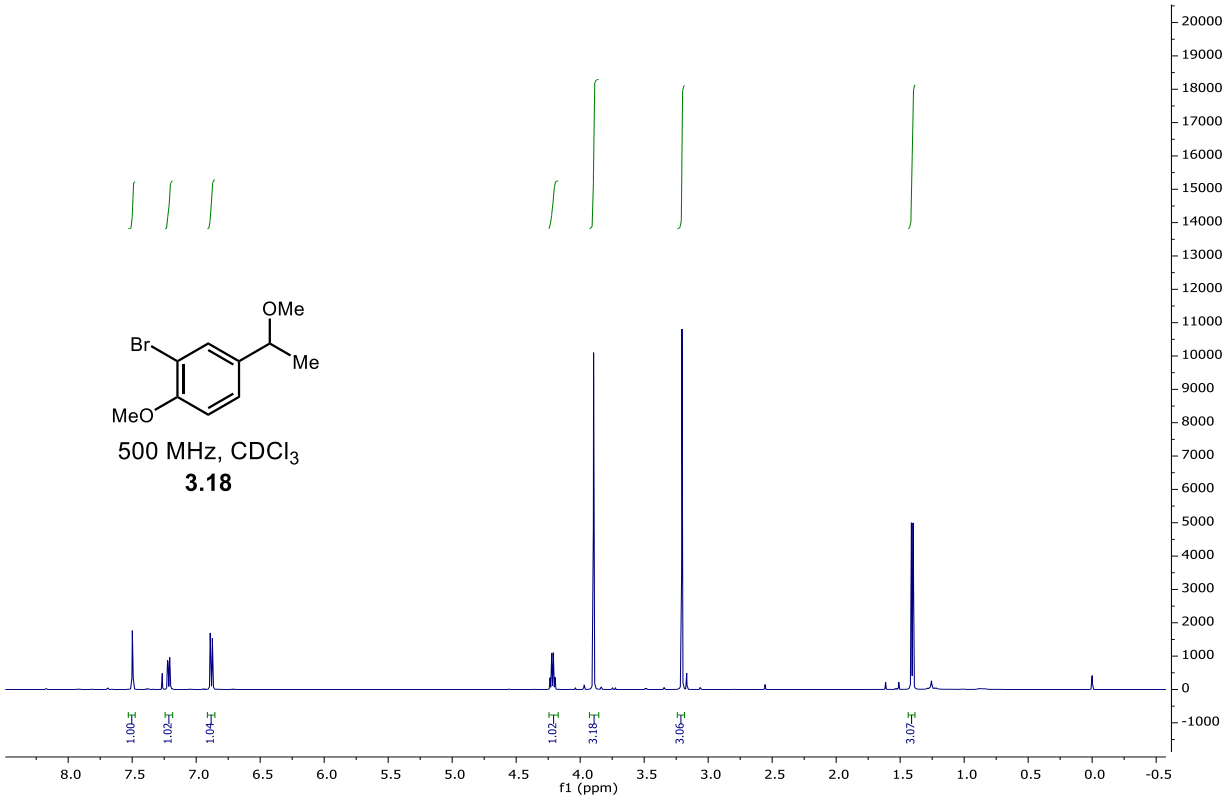


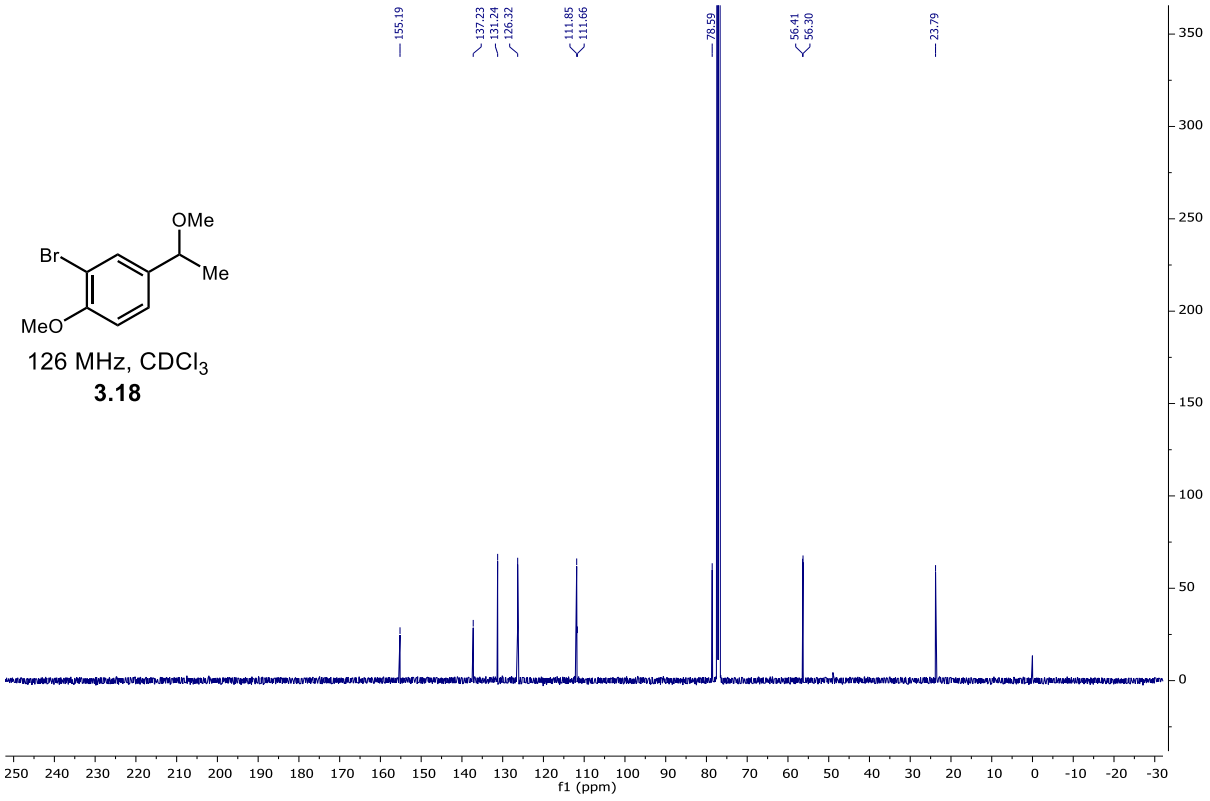

126 MHz, $CDCl_3$

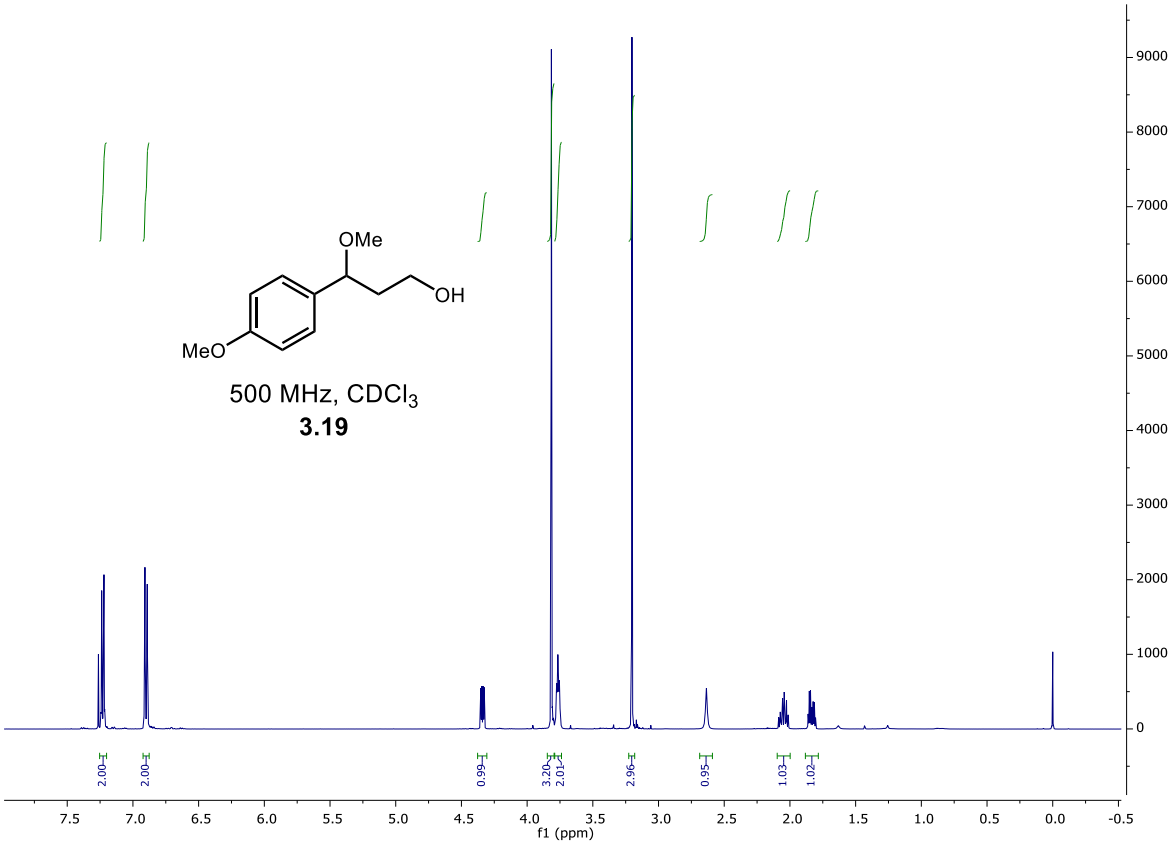
**3.15**

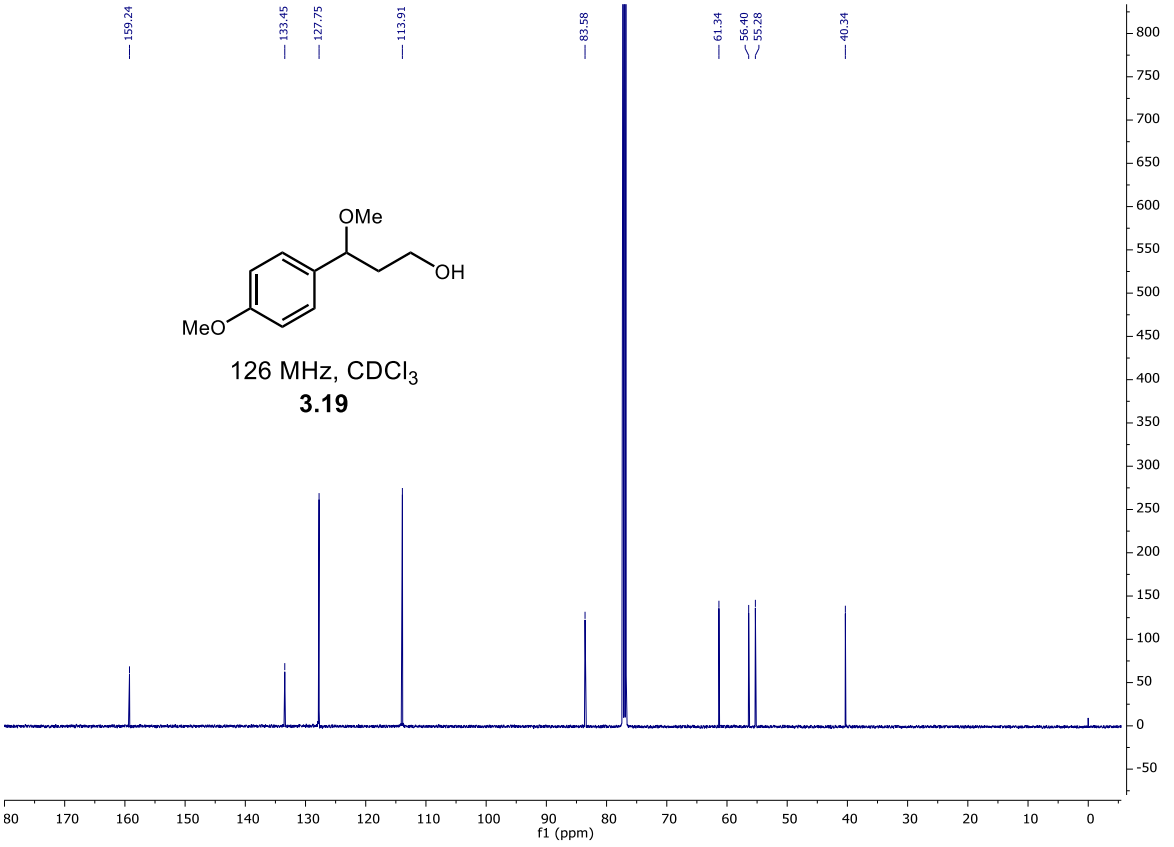

OMe
MeO
Me
MeO
500 MHz, CDCl3
3.17
1.00
1.95
1.01
3.05
3.07
3.04
3.01
f1 (ppm)

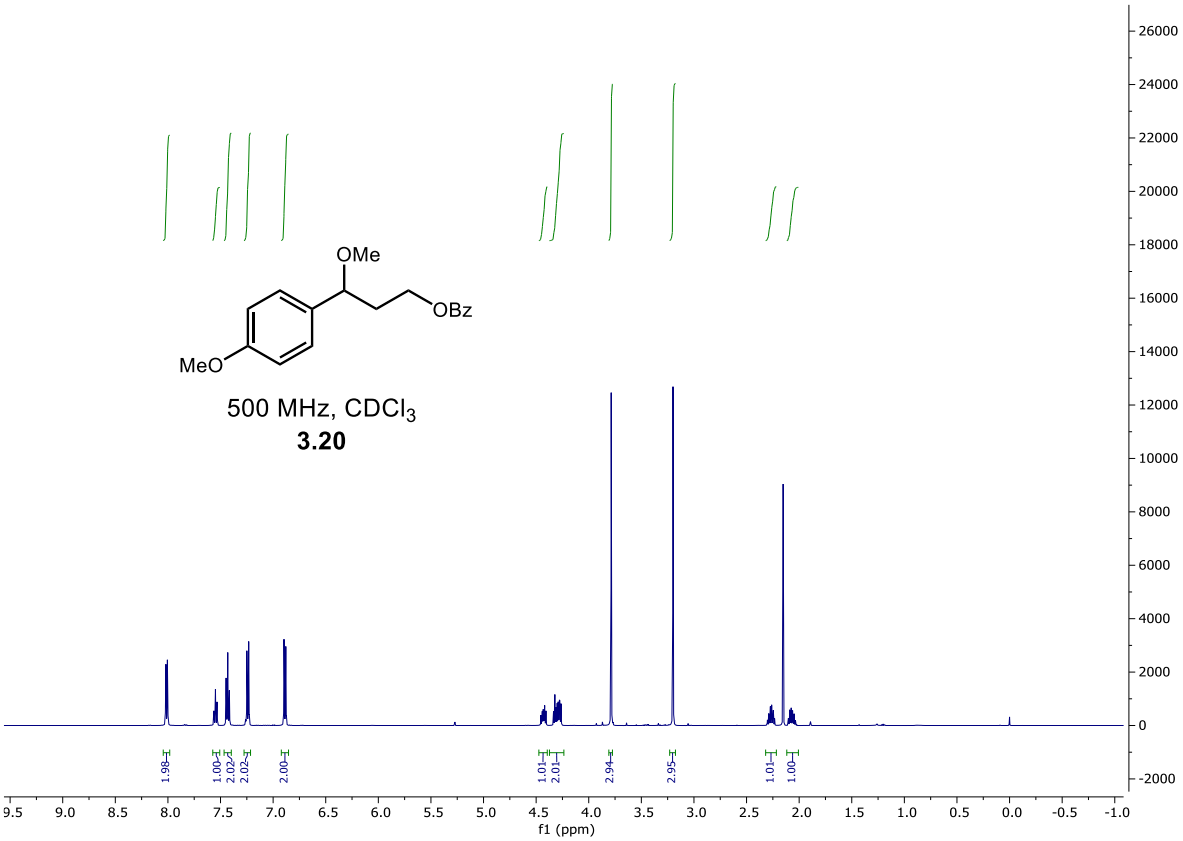

149.18
148.37
136.10
118.67
110.82
108.83
79.40
56.29
55.85
23.87
OMe
MeO
Me
MeO
126 MHz, CDCl3
3.17
f1 (ppm)

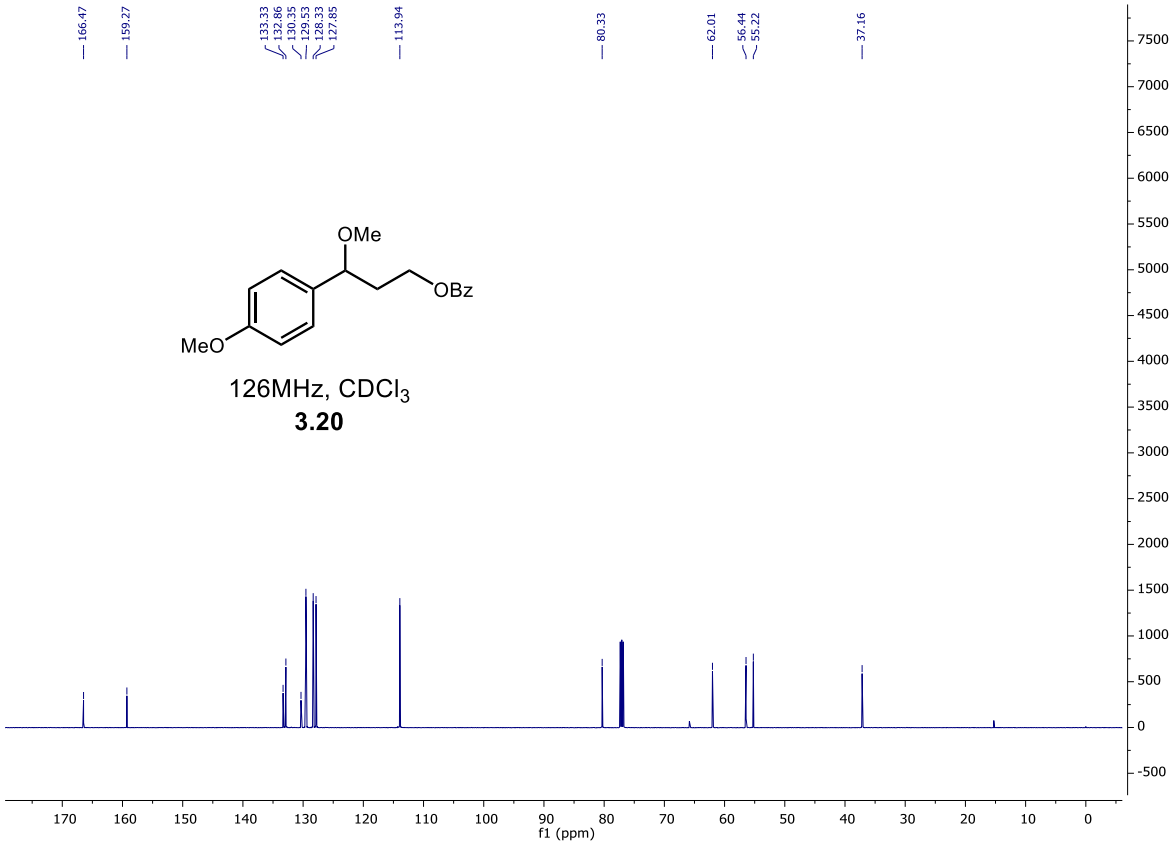

OMe
Br
Me
MeO
500 MHz, CDCl3
3.18
1.00
1.02
1.04
1.02
3.18
3.06
3.07
f1 (ppm)

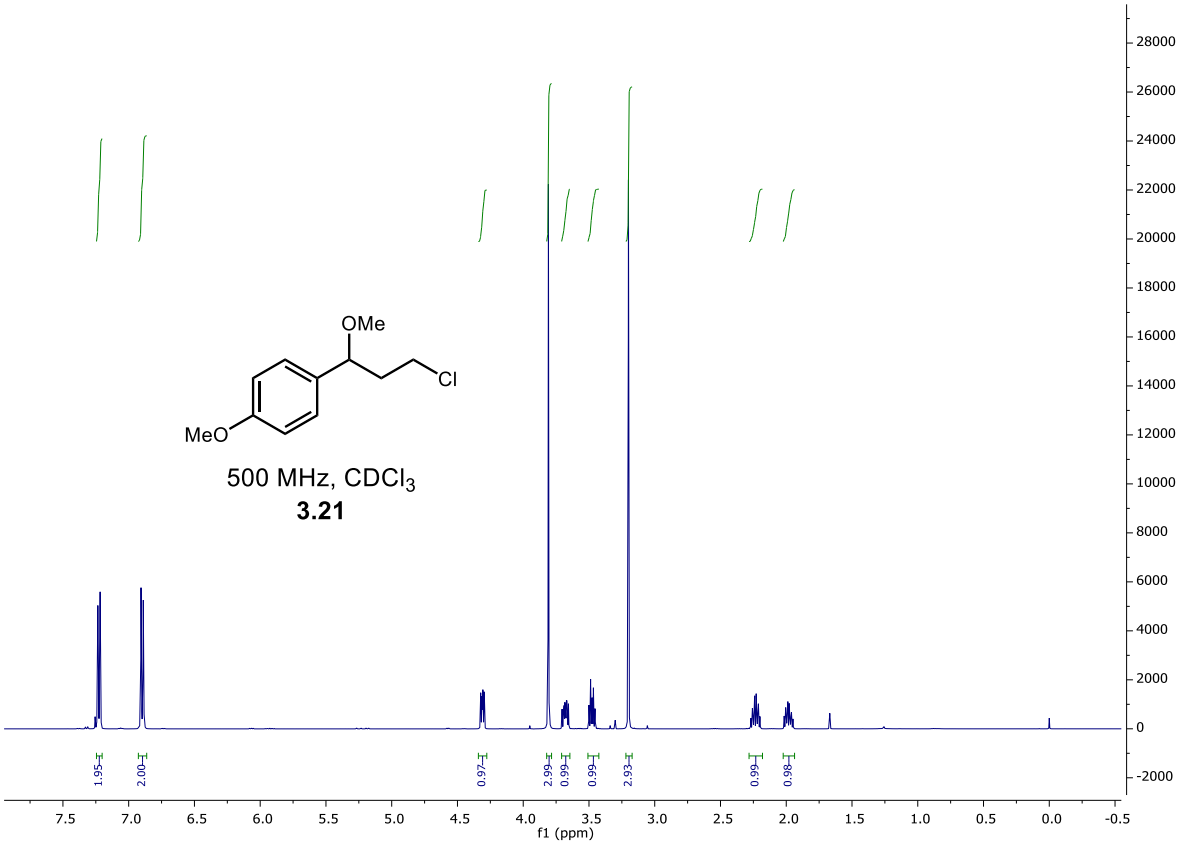

155.19
137.23
131.24
126.32
111.85
111.66
78.59
56.41
56.30
23.79
OMe
Br
Me
MeO
126 MHz, CDCl3
3.18
f1 (ppm)

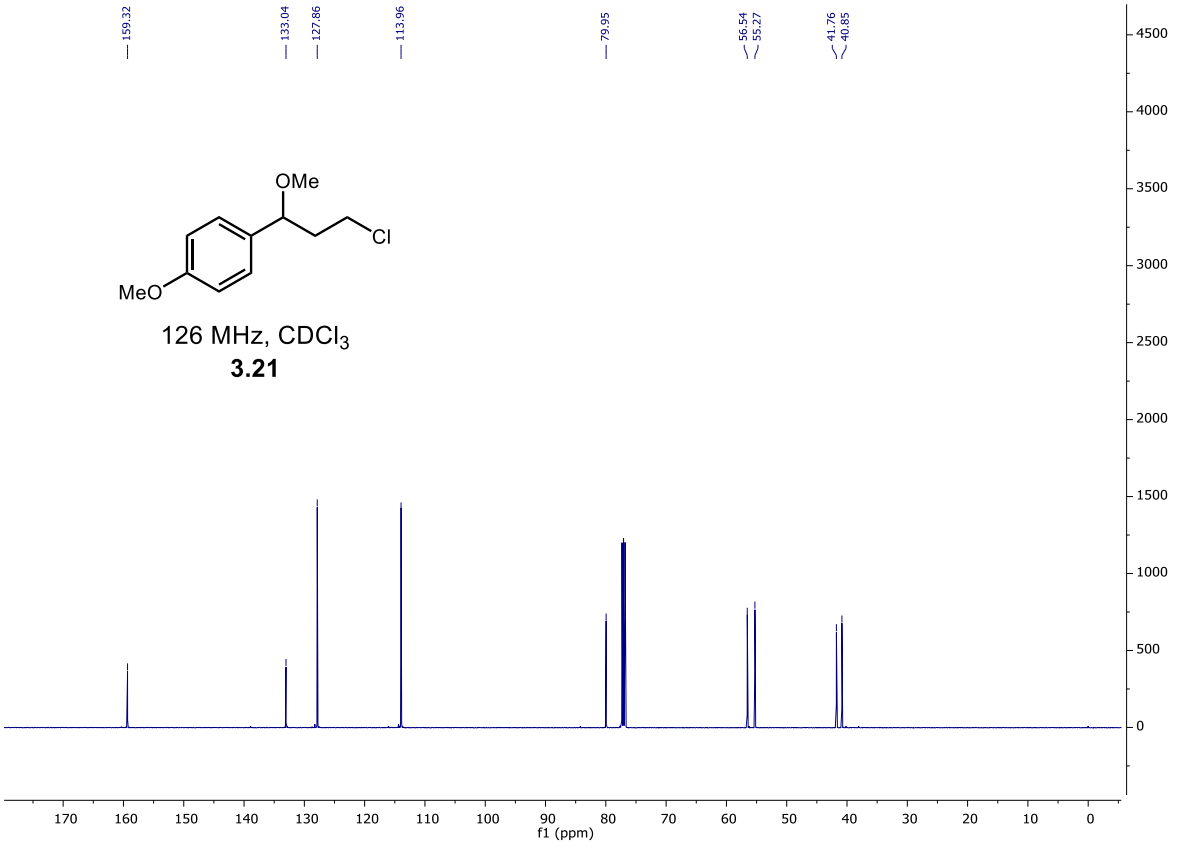

OMe
OH
MeO
500 MHz, CDCl3
3.19
2.00
2.00
0.99
3.20
2.01
2.96
0.95
1.03
1.02
f1 (ppm)

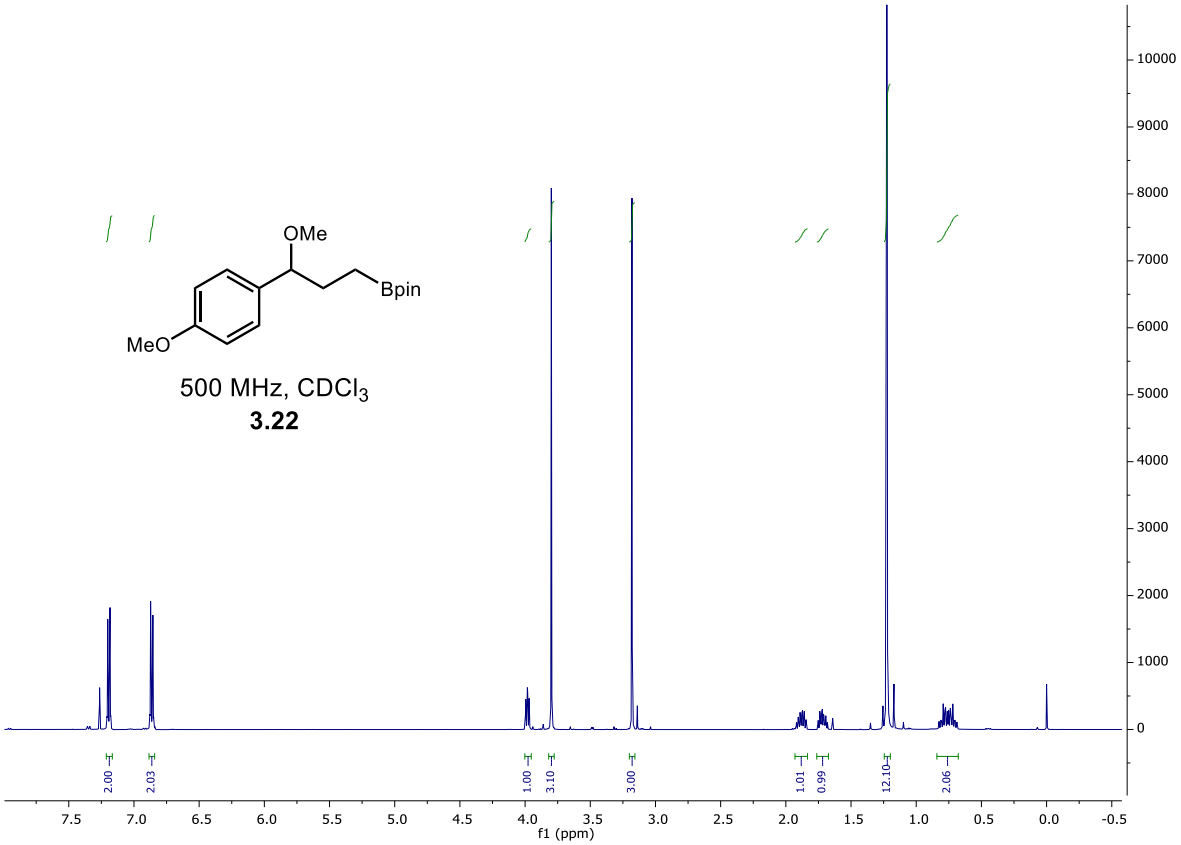

159.24
133.45
127.75
113.91
83.58
61.34
56.40
55.28
40.34
OMe
OH
MeO
126 MHz, CDCl3
3.19
f1 (ppm)

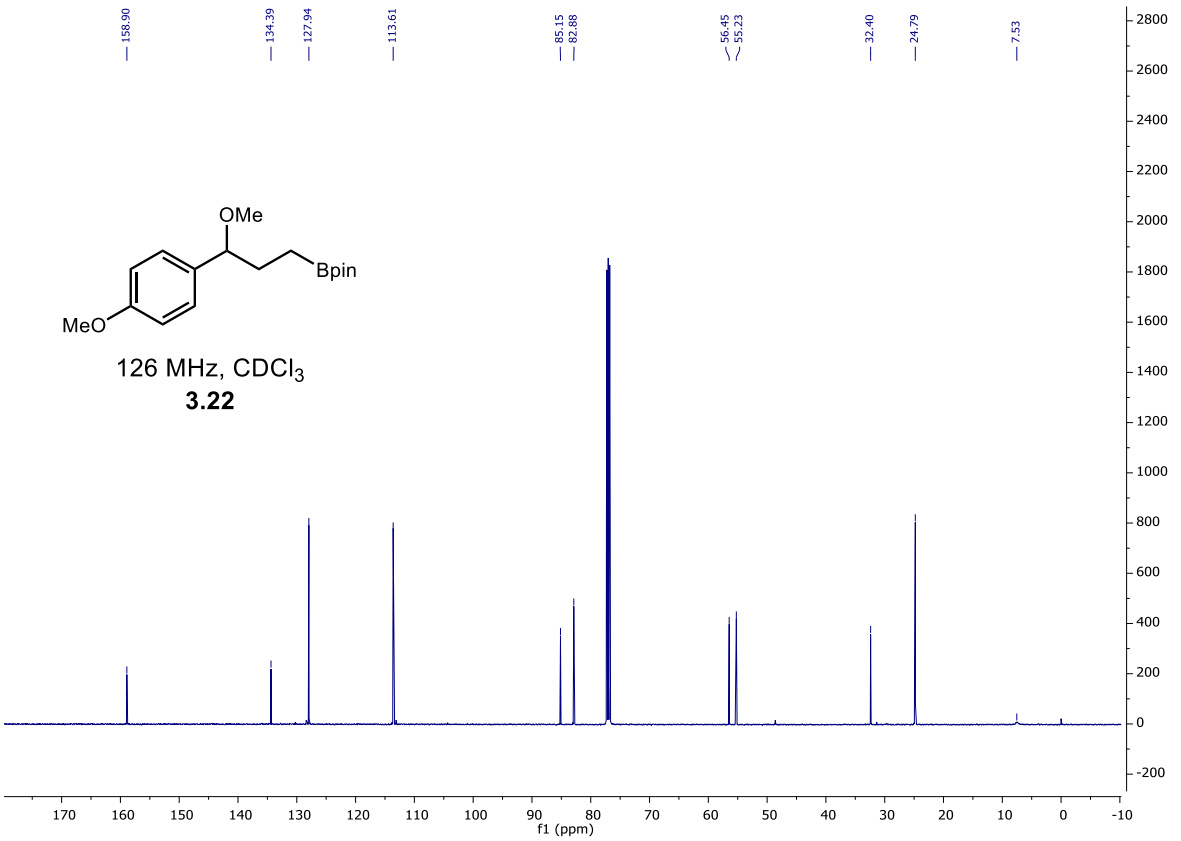

OMe
OBz
MeO
500 MHz, CDCl3
3.20
f1 (ppm)

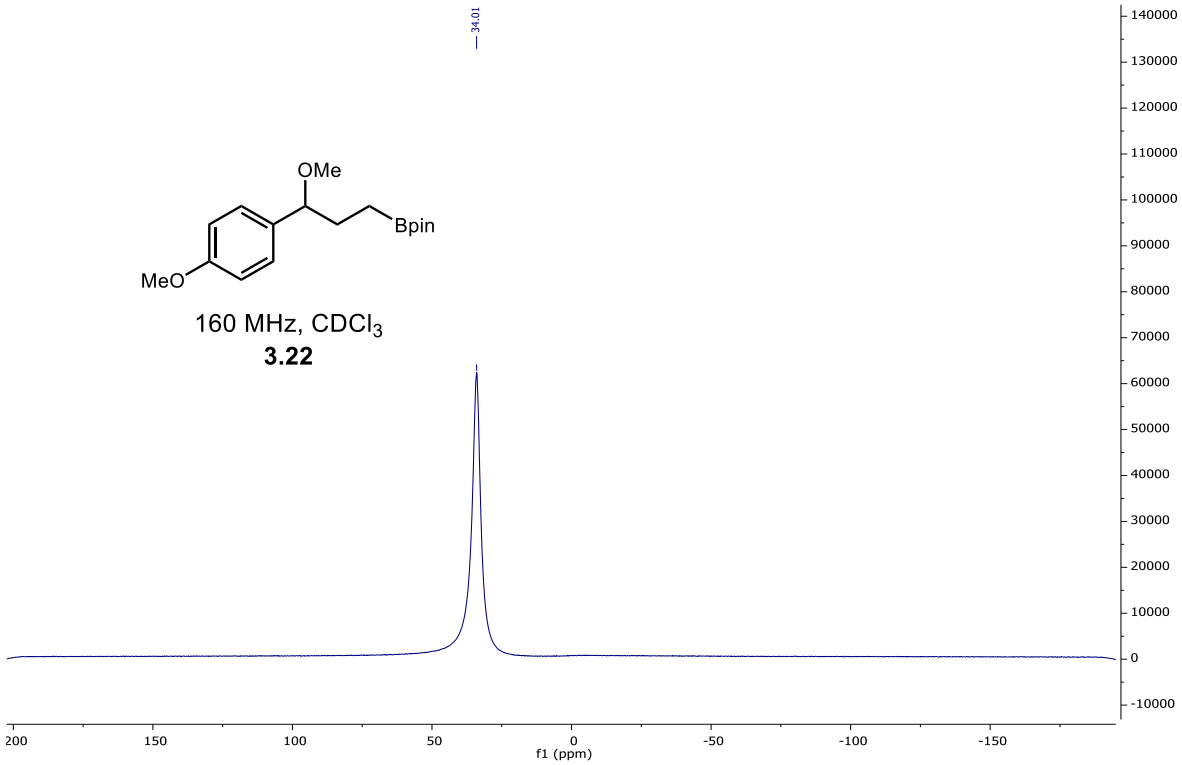

166.47
159.27
133.33
132.86
130.35
129.53
128.33
127.85
113.94
80.33
62.01
56.44
55.22
37.16
OMe
OBz
MeO
126MHz, CDCl3
3.20
f1 (ppm)

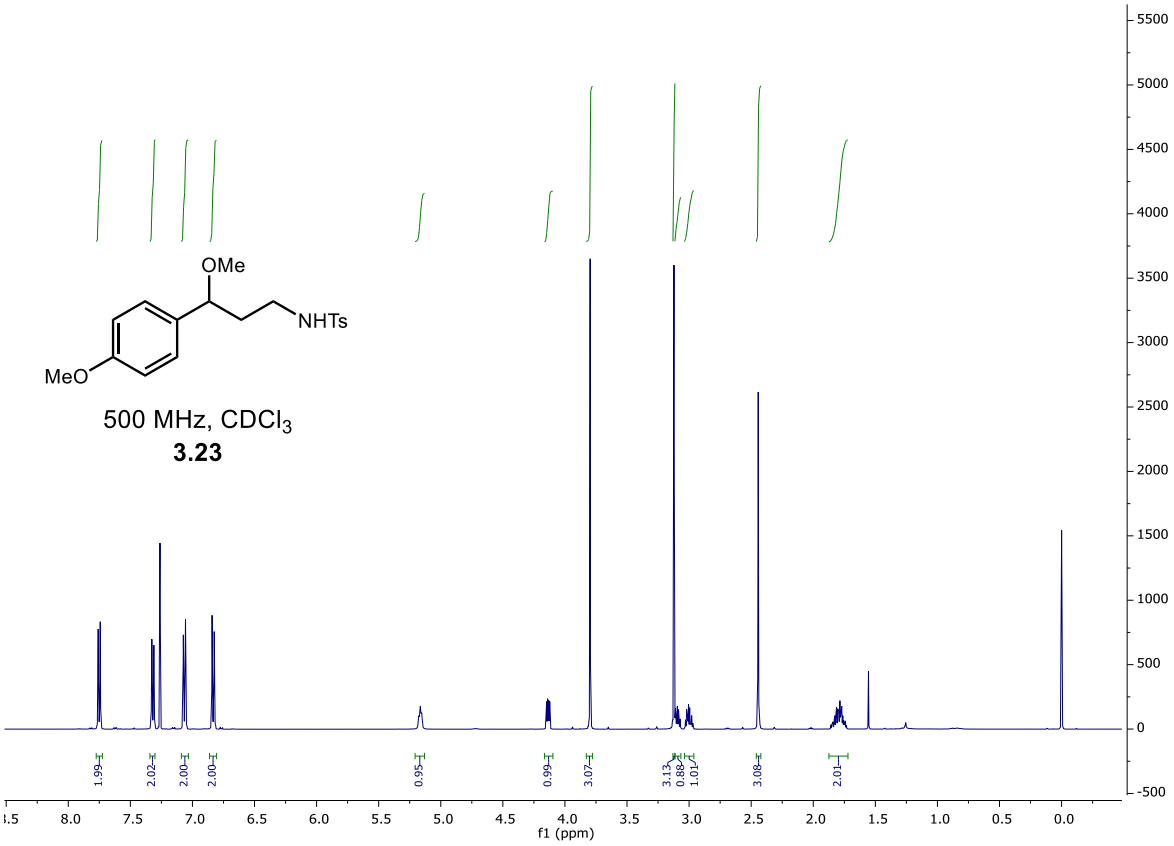

OMe
Cl
MeO
500 MHz, CDCl3
3.21
1.95
2.00
0.97
2.99
0.99
0.99
2.93
0.99
0.98
f1 (ppm)

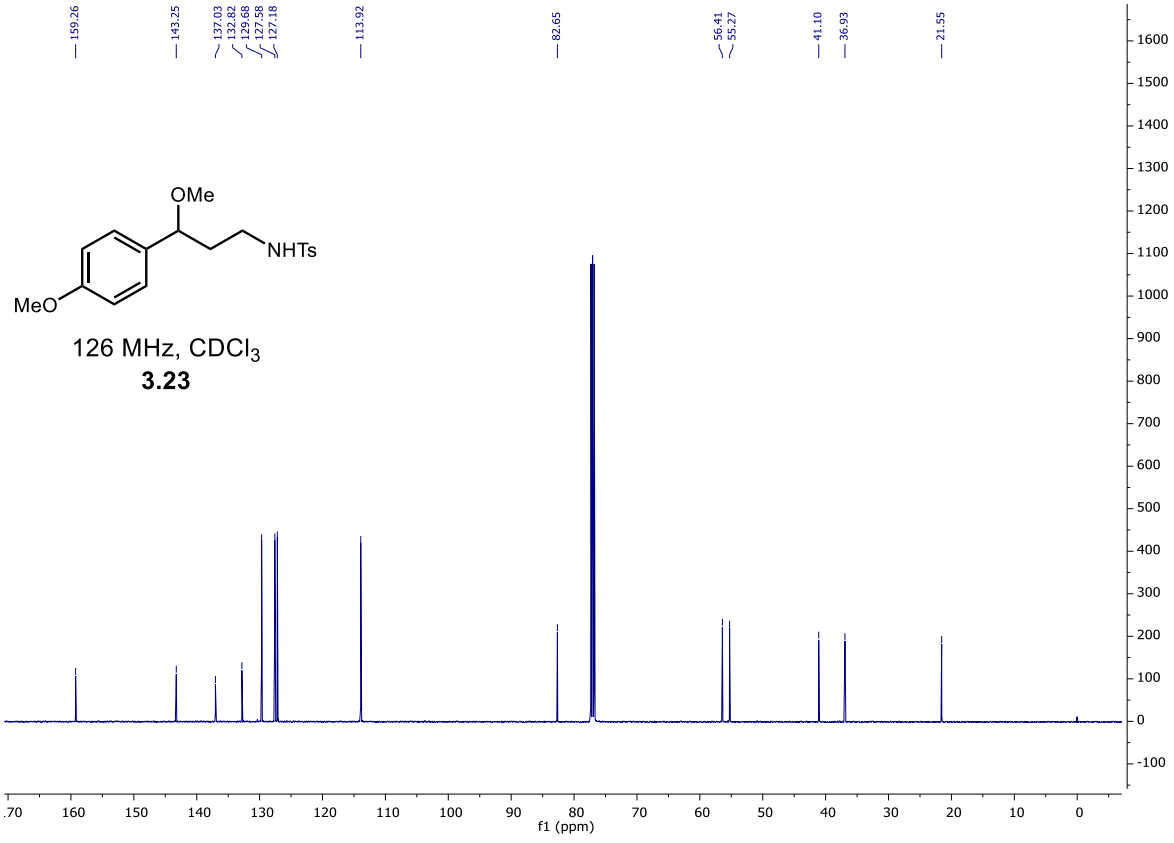

159.32
133.04
127.86
113.96
79.95
56.54
55.27
41.76
40.85
OMe
Cl
MeO
126 MHz, CDCl3
3.21
f1 (ppm)

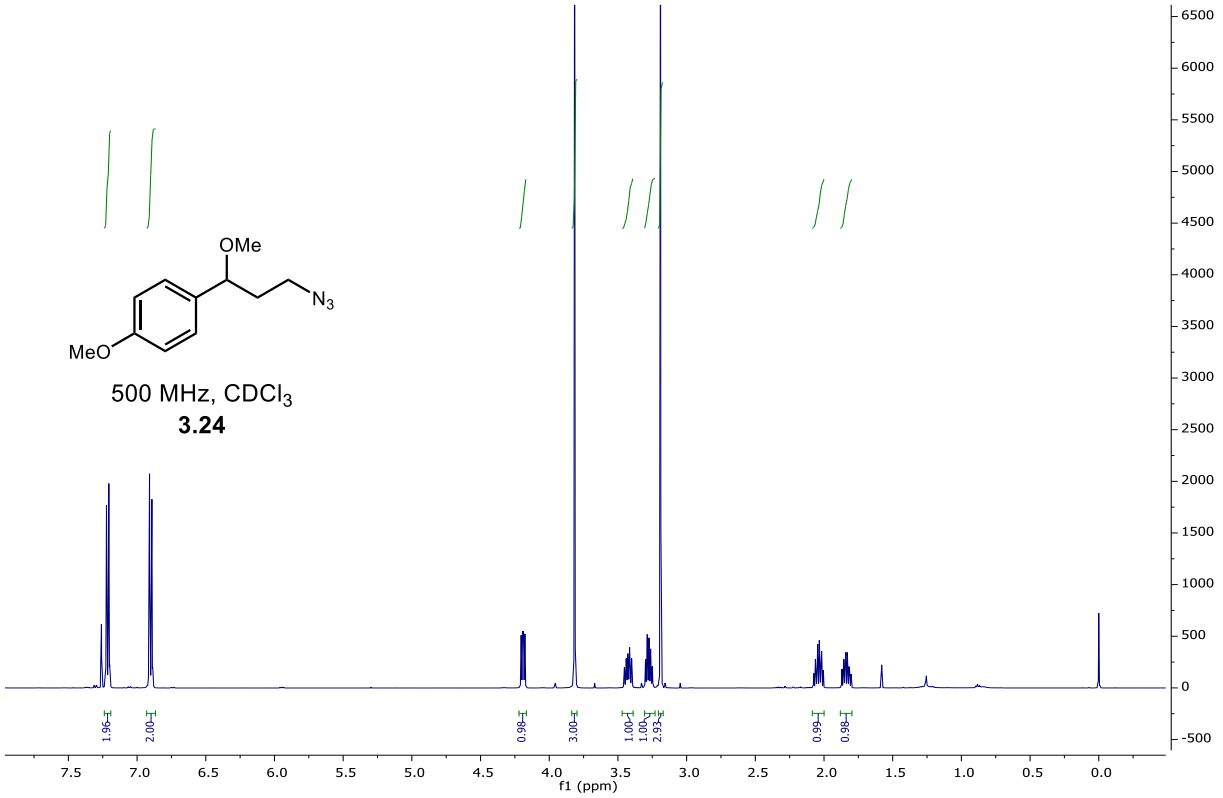

OMe
Bpin
MeO
500 MHz, CDCl3
3.22
f1 (ppm)

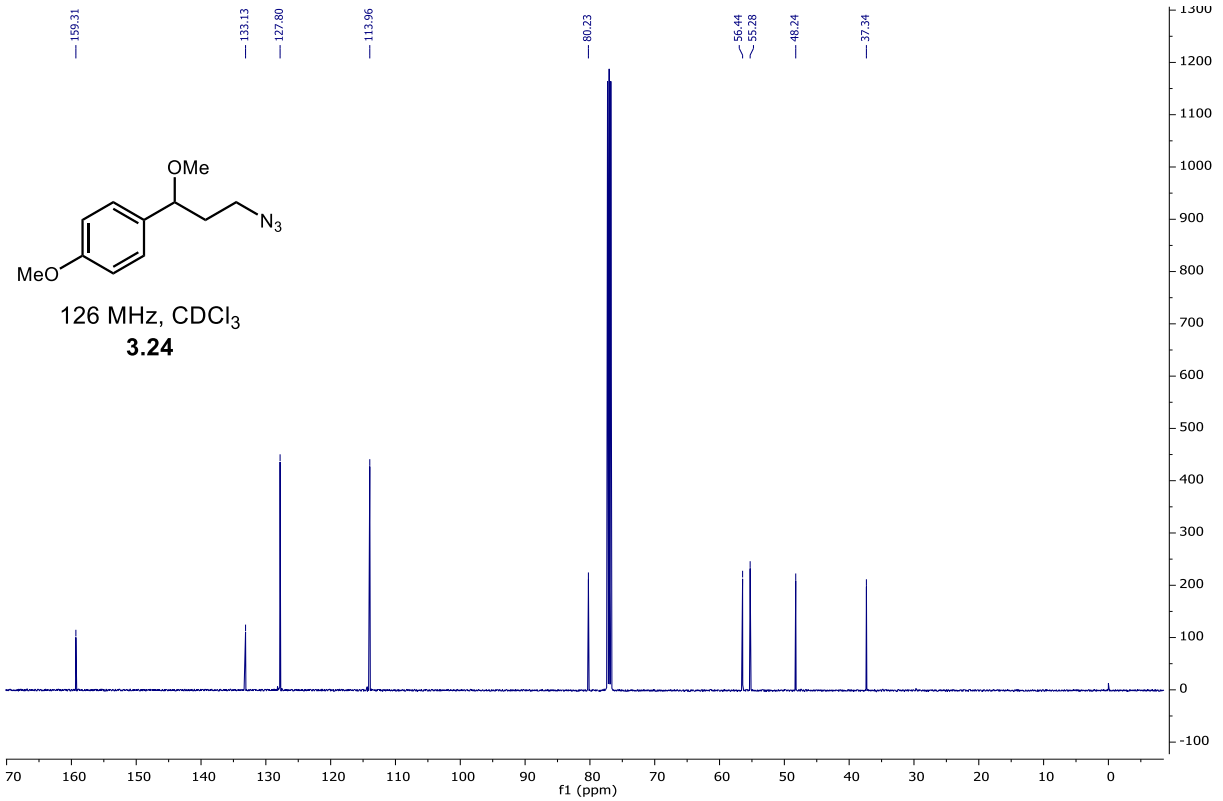

158.90
134.39
127.94
113.61
85.15
82.88
56.45
55.23
32.40
24.79
7.53
OMe
Bpin
MeO
126 MHz, CDCl3
3.22
f1 (ppm)

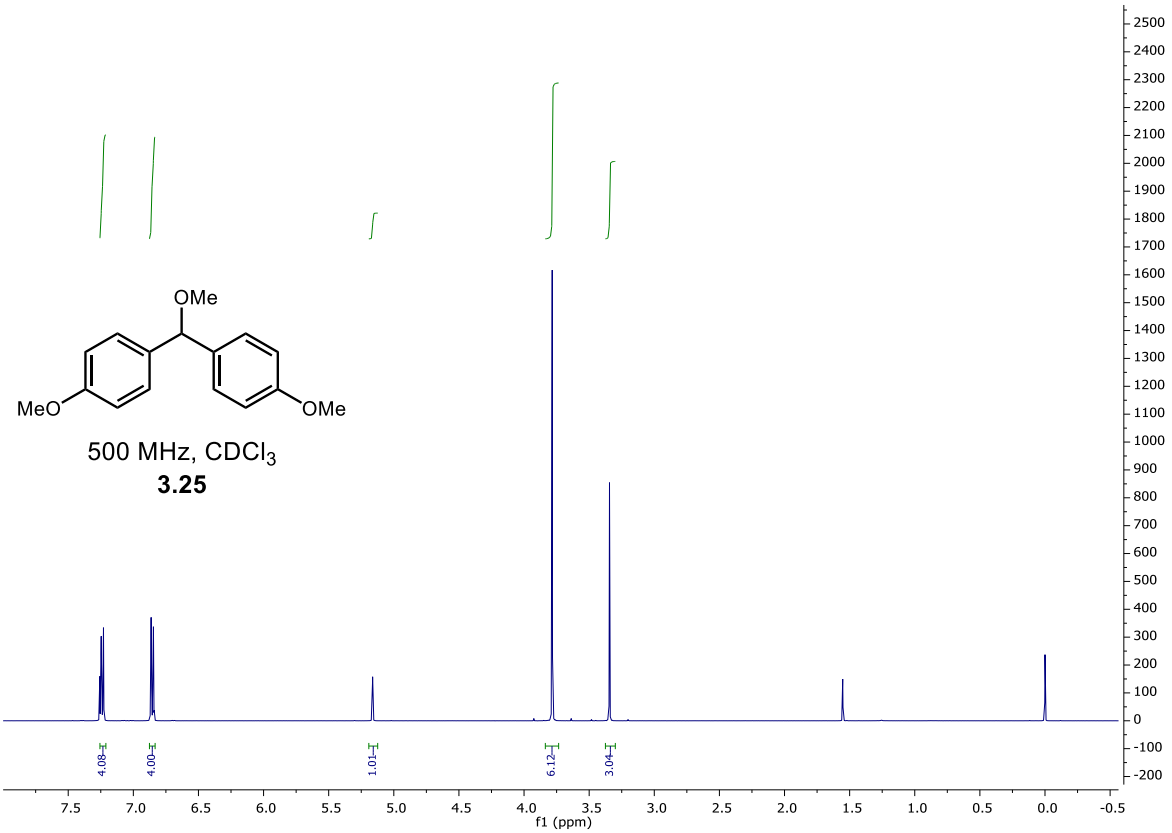

34.01
OMe
Bpin
MeO
160 MHz, CDCl3
3.22
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
200
150
100
50
0
-50
-100
-150
f1 (ppm)

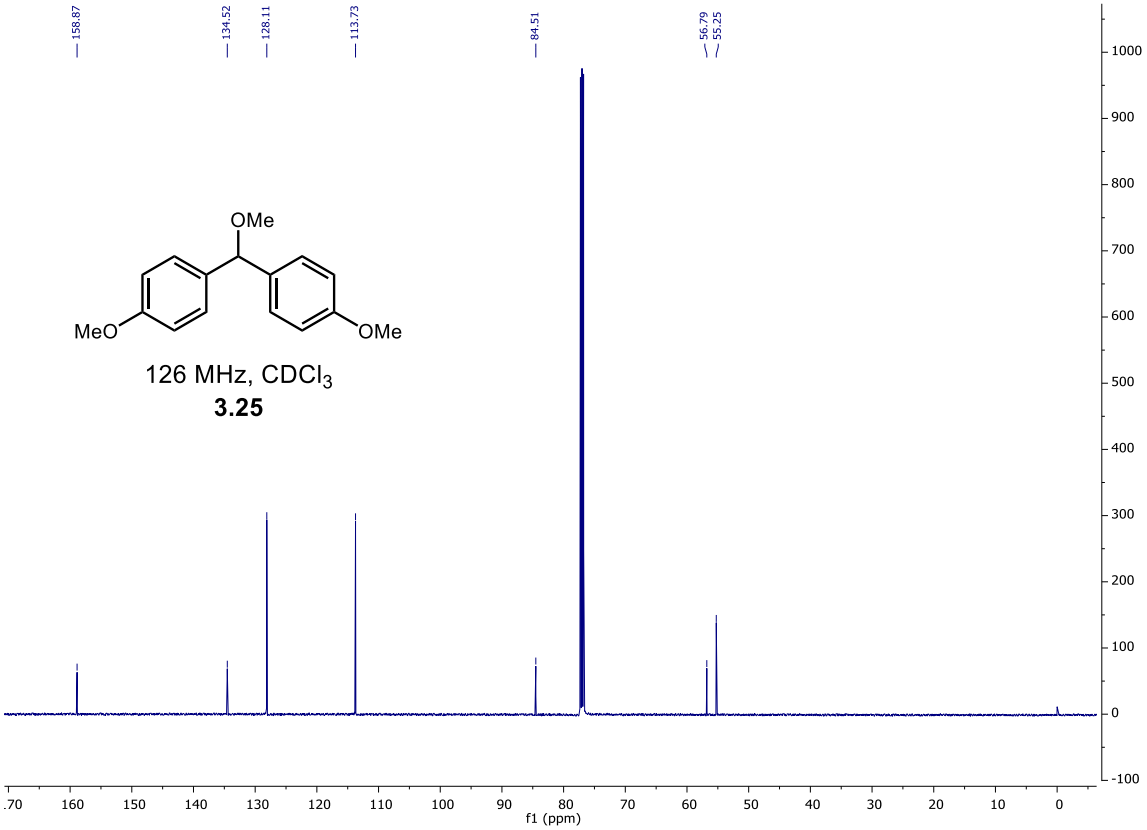

OMe
NHTs
MeO
500 MHz, CDCl3
3.23
f1 (ppm)

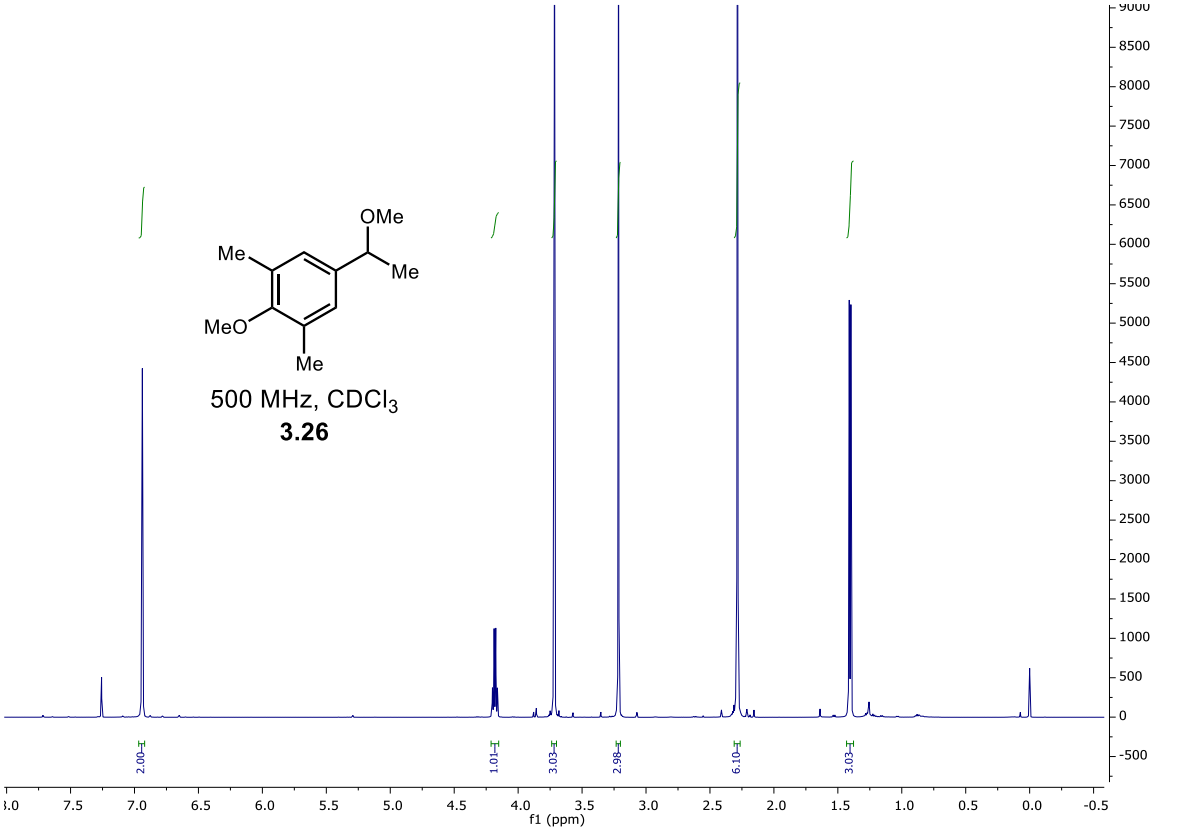

159.26
143.25
137.03
132.82
129.68
127.58
127.18
113.92
82.65
56.41
55.27
41.10
36.93
21.55
OMe
NHTs
MeO
126 MHz, CDCl3
3.23
f1 (ppm)

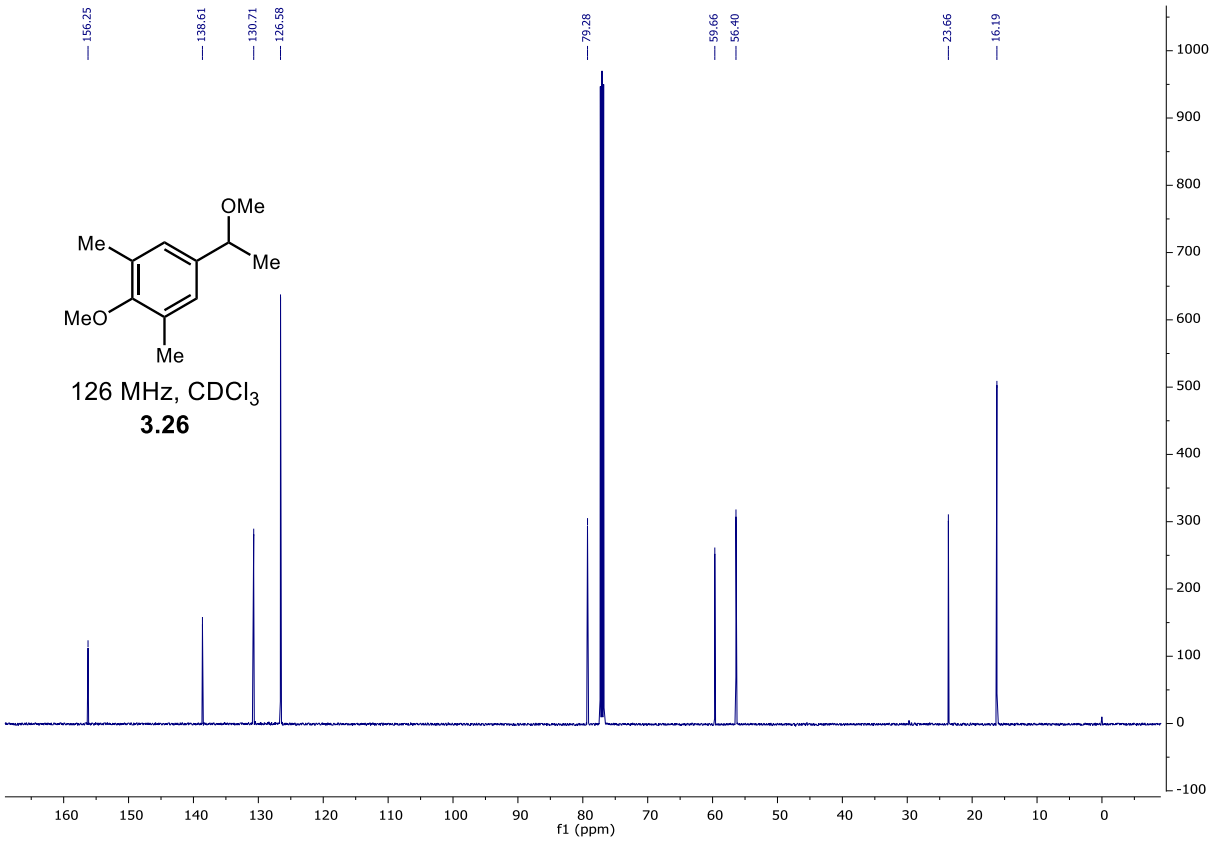

OMe
N3
MeO
500 MHz, CDCl3
3.24
1.96
2.00
0.98
3.00
1.00
1.00
2.93
0.99
0.98
f1 (ppm)

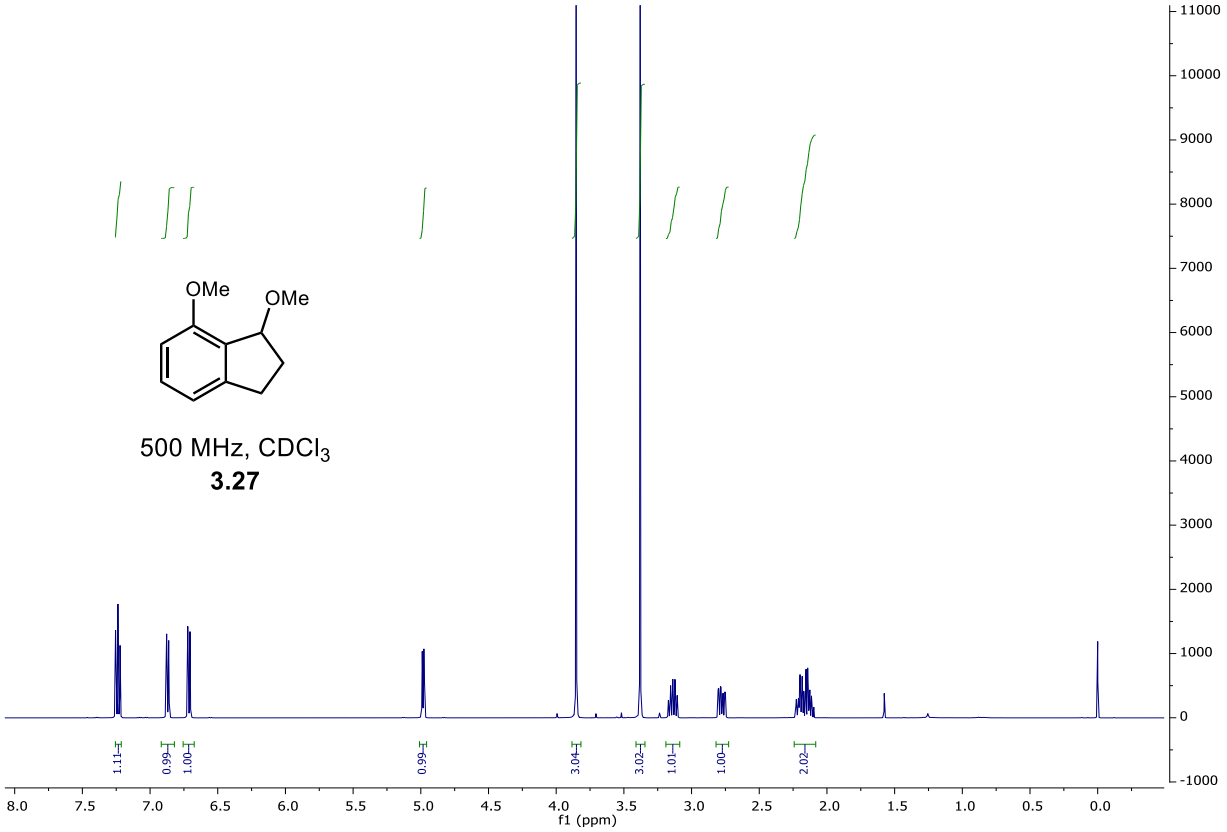

159.31
133.13
127.80
113.96
80.23
56.44
55.28
48.24
37.34
OMe
N3
MeO
126 MHz, CDCl3
3.24
f1 (ppm)

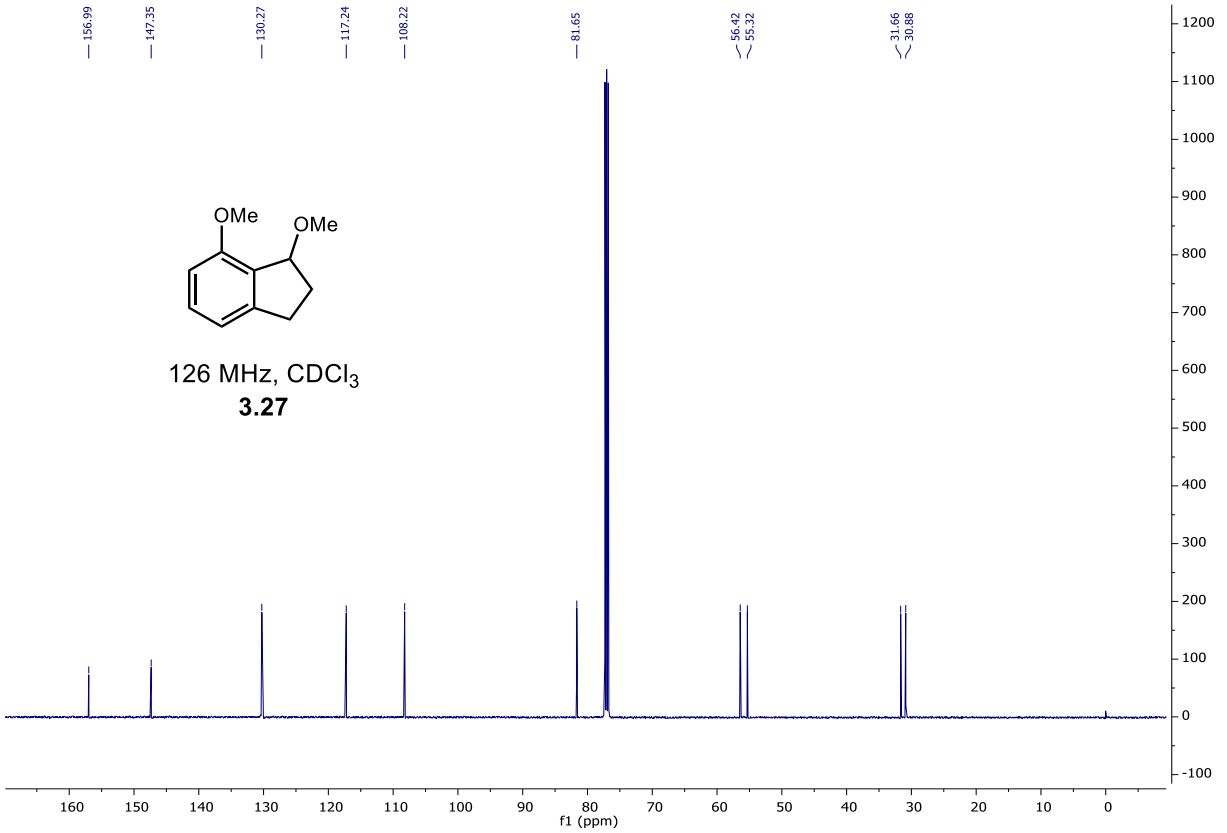

OMe
MeO
OMe
500 MHz, CDCl3
3.25
4.08
4.00
1.01
6.12
3.04
f1 (ppm)

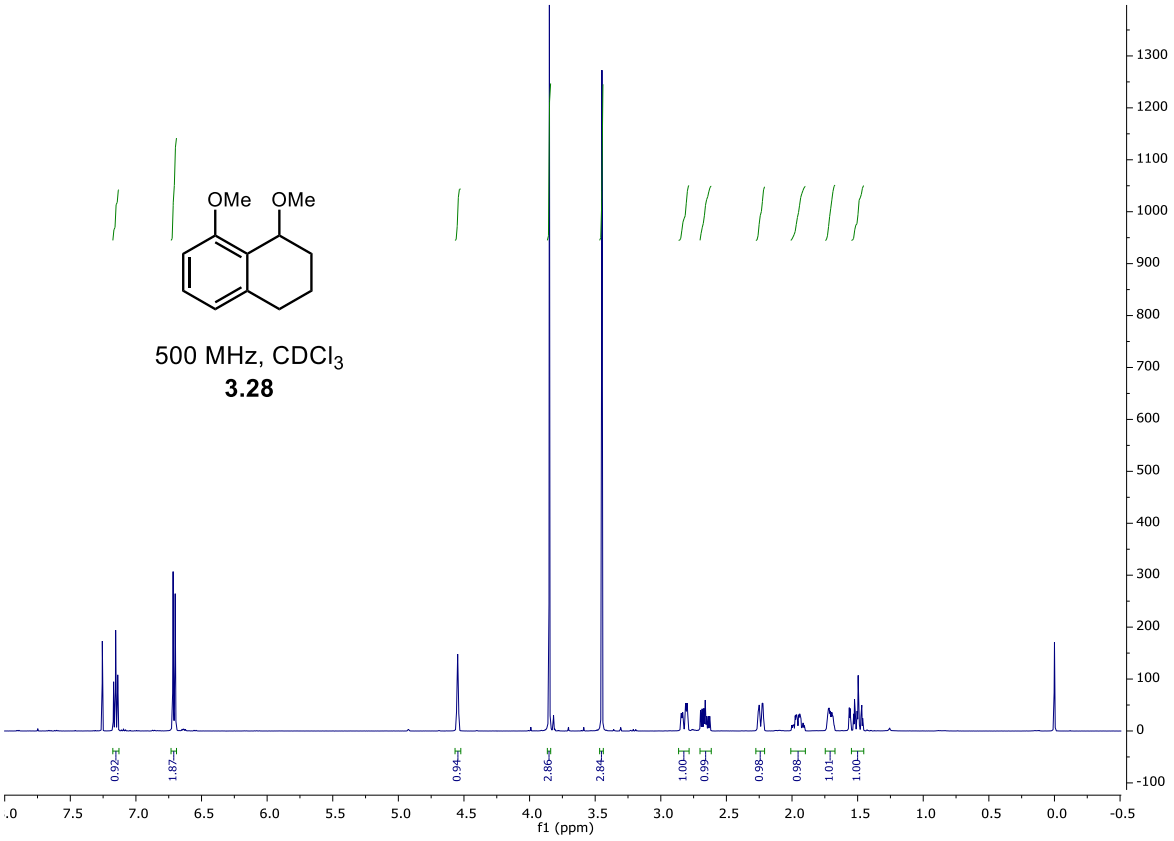

158.87
134.52
128.11
113.73
84.51
56.79
55.25
OMe
MeO
OMe
126 MHz, CDCl3
3.25
f1 (ppm)


OMe
Me
Me
MeO
Me
500 MHz, CDCl3
3.26
2.00
1.01
3.03
2.98
6.10
3.03
f1 (ppm)

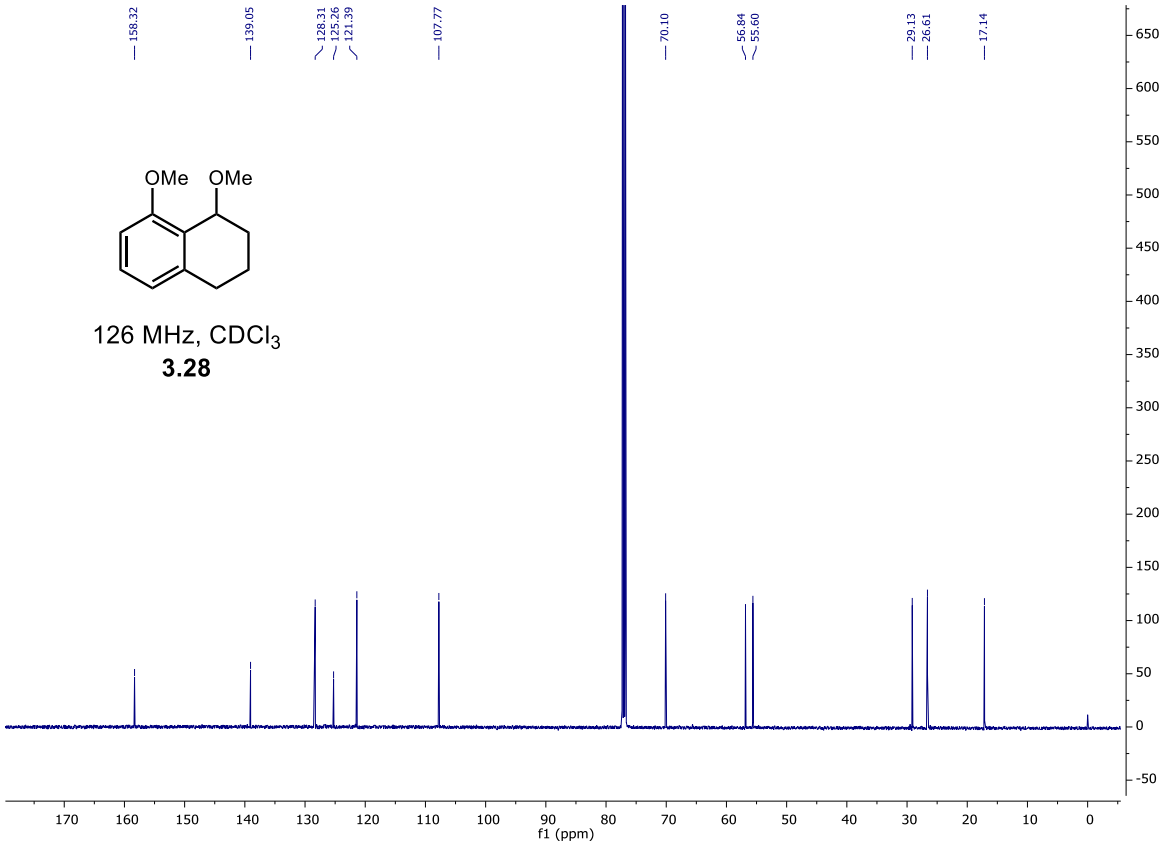

156.25
138.61
130.71
126.58
79.28
59.66
56.40
23.66
16.19
OMe
Me
Me
MeO
Me
126 MHz, CDCl3
3.26
f1 (ppm)


OMe
OMe
500 MHz, CDCl3
3.27
1.11
0.99
1.00
0.99
3.04
3.02
1.01
1.00
2.02
f1 (ppm)

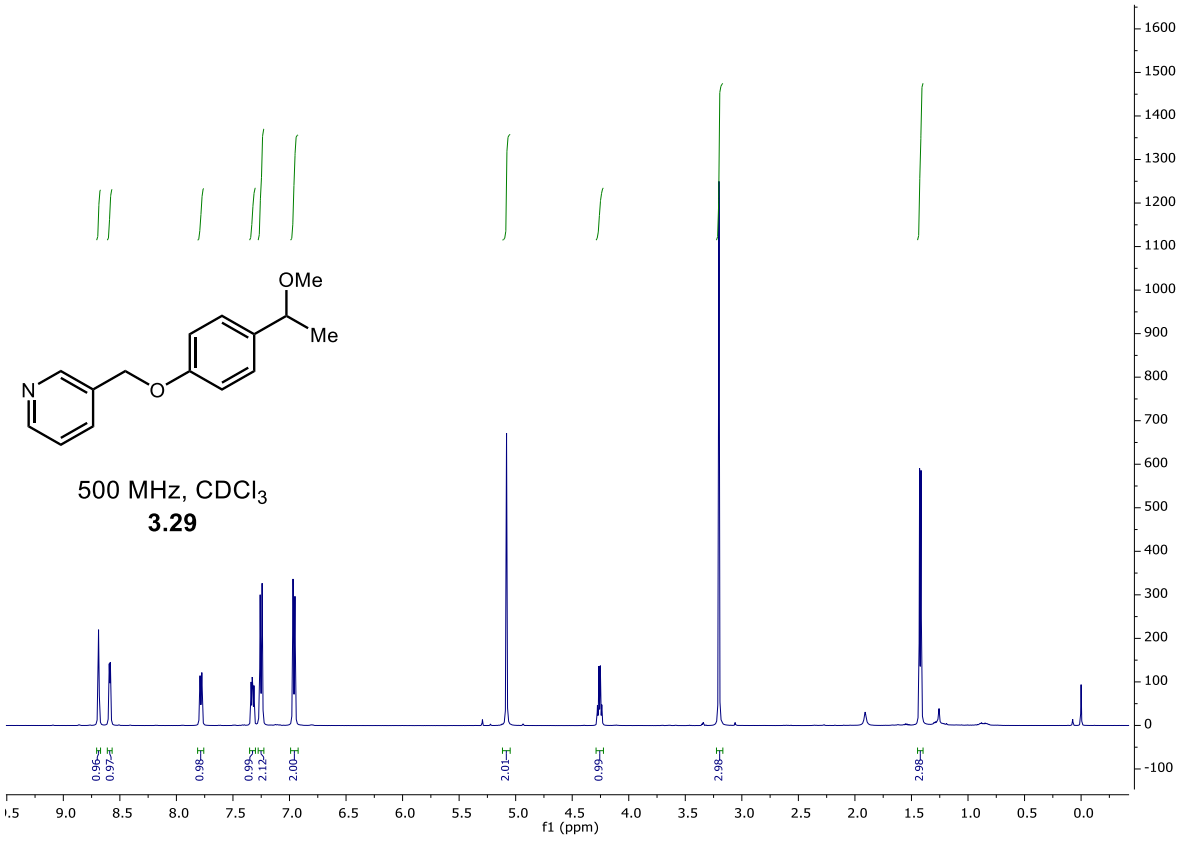

156.99
147.35
130.27
117.24
108.22
81.65
56.42
55.32
31.66
30.88
OMe
OMe
126 MHz, CDCl3
3.27
f1 (ppm)

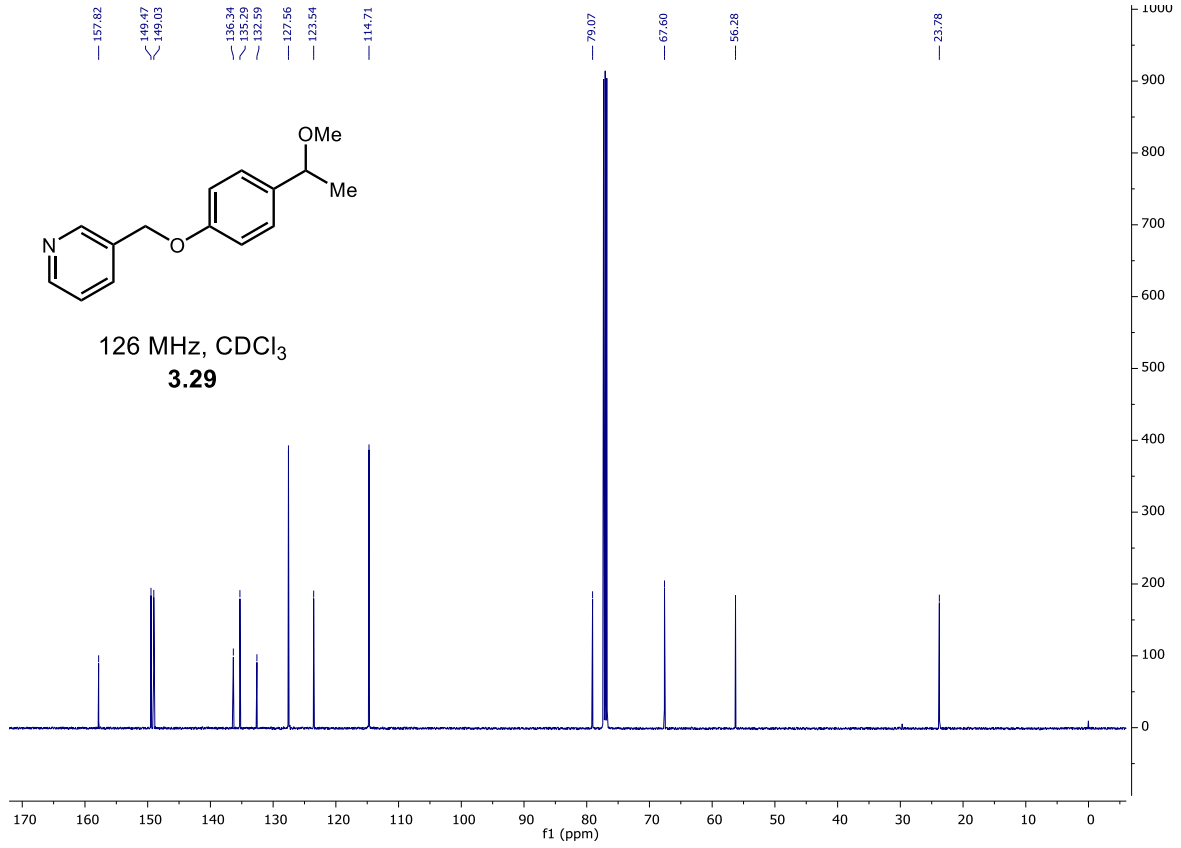


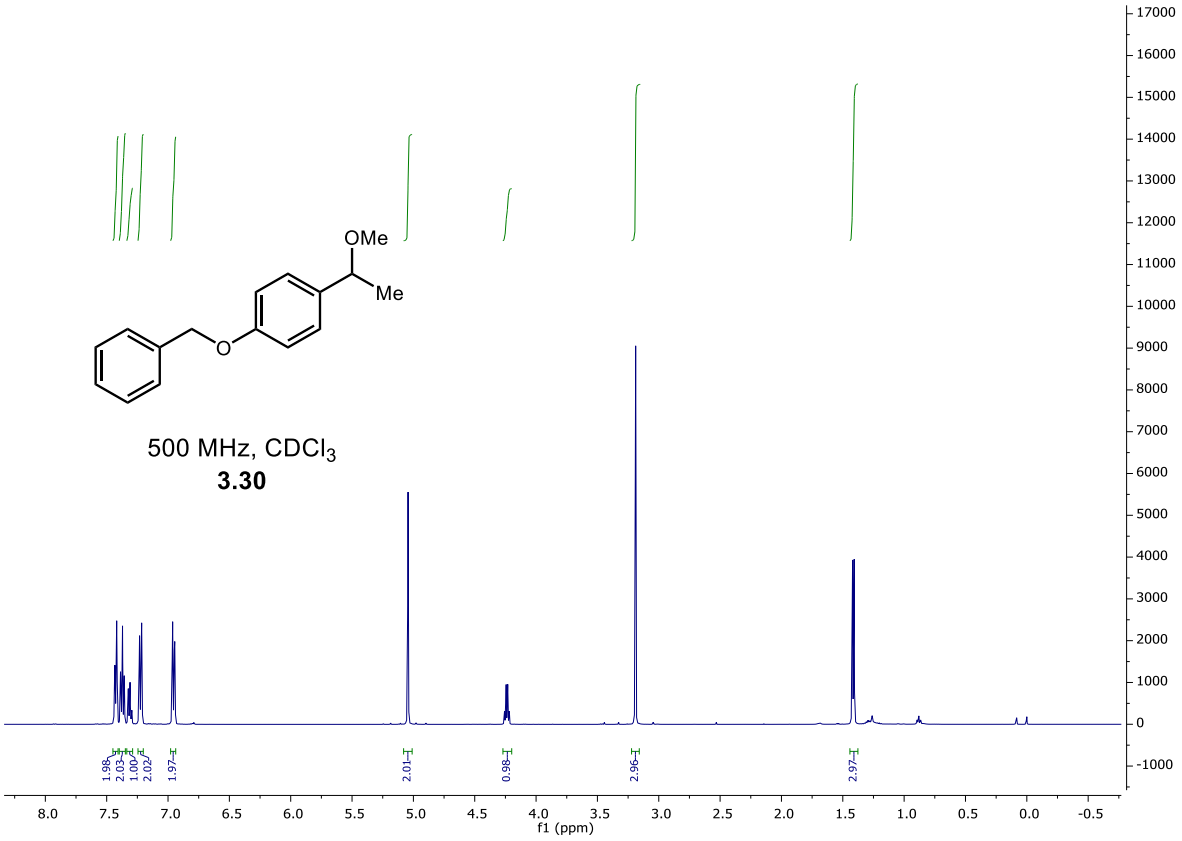

500 MHz, $CDCl_3$
**3.28**

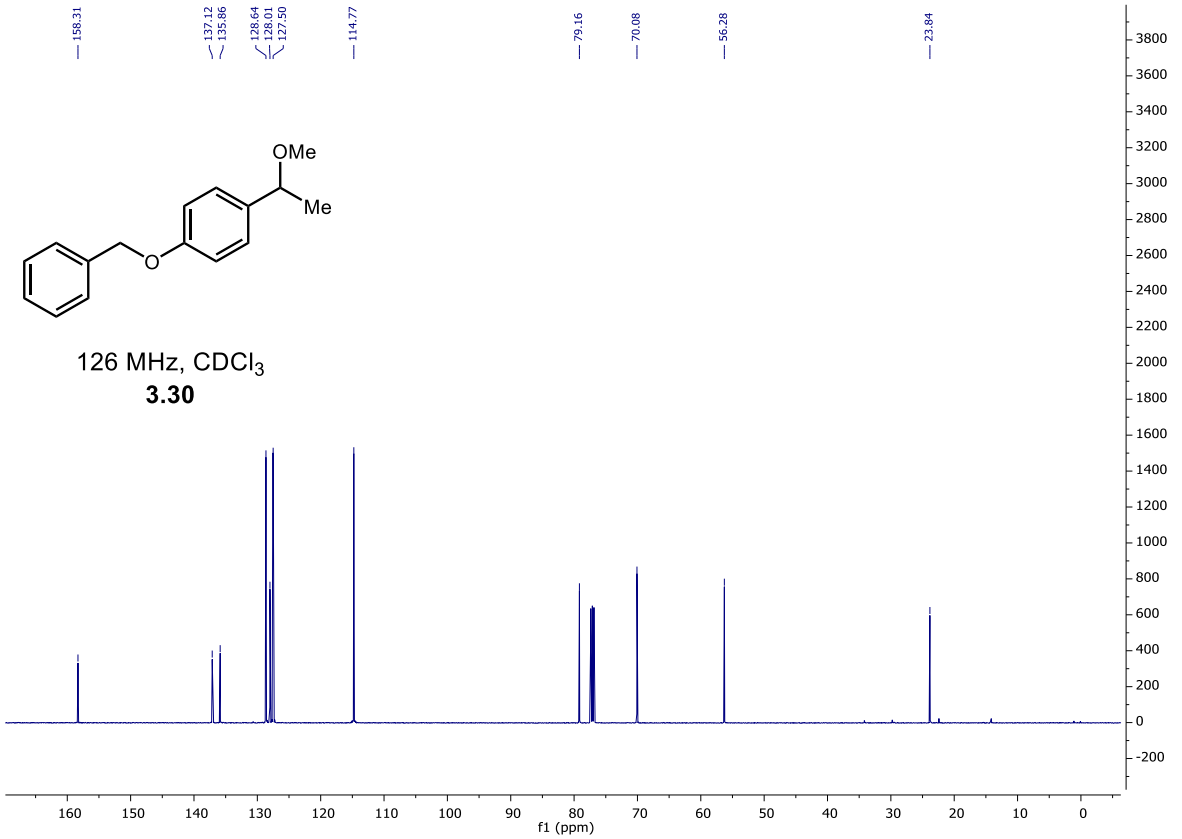


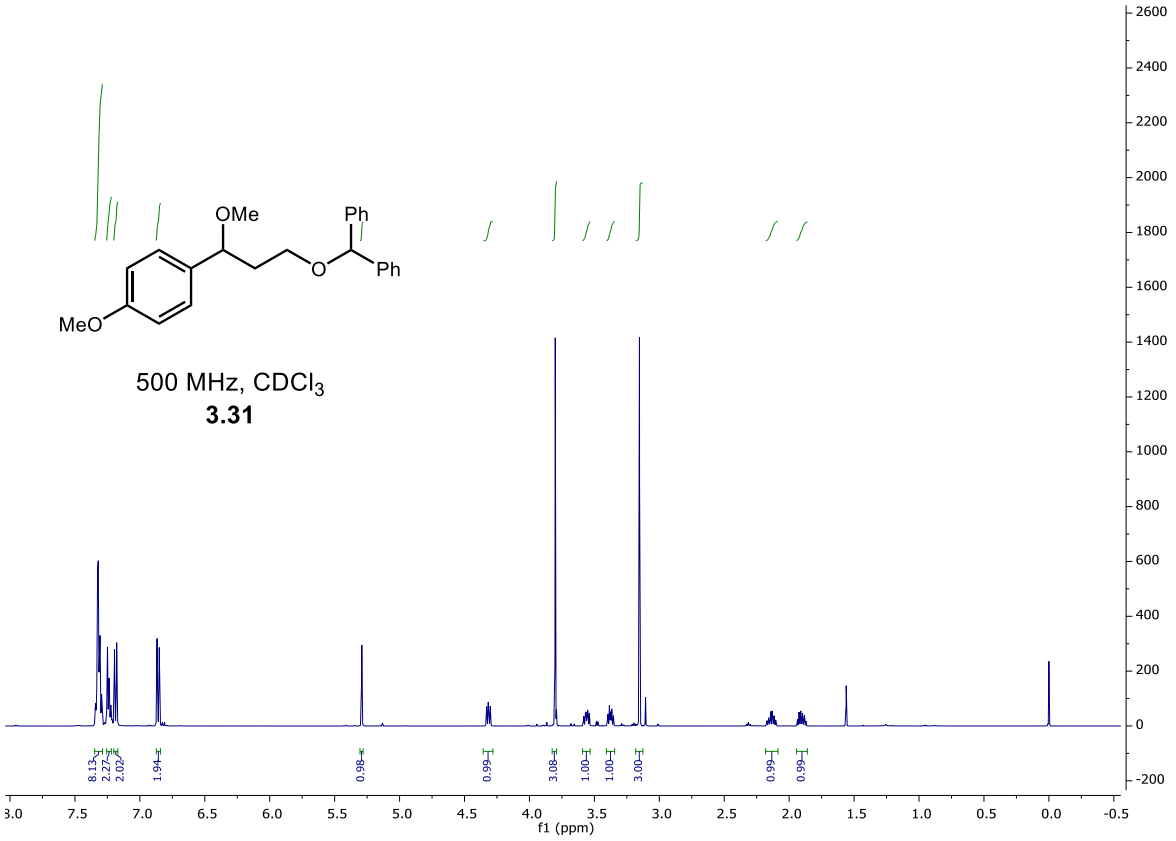

126 MHz, $CDCl_3$
**3.28**

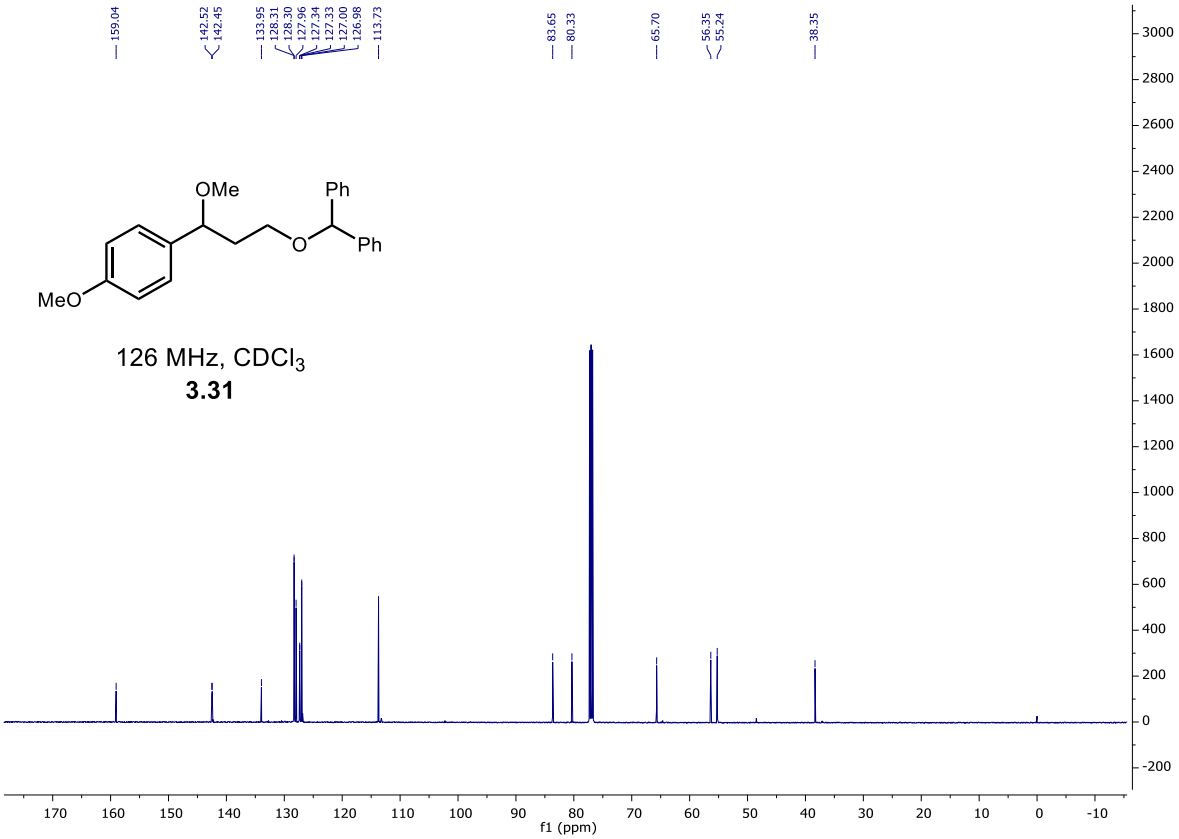

OMe
Me
N
O
500 MHz, CDCl3
3.29
0.96
0.97
0.90
0.99
2.12
2.00
2.01
0.99
2.98
2.98
f1 (ppm)

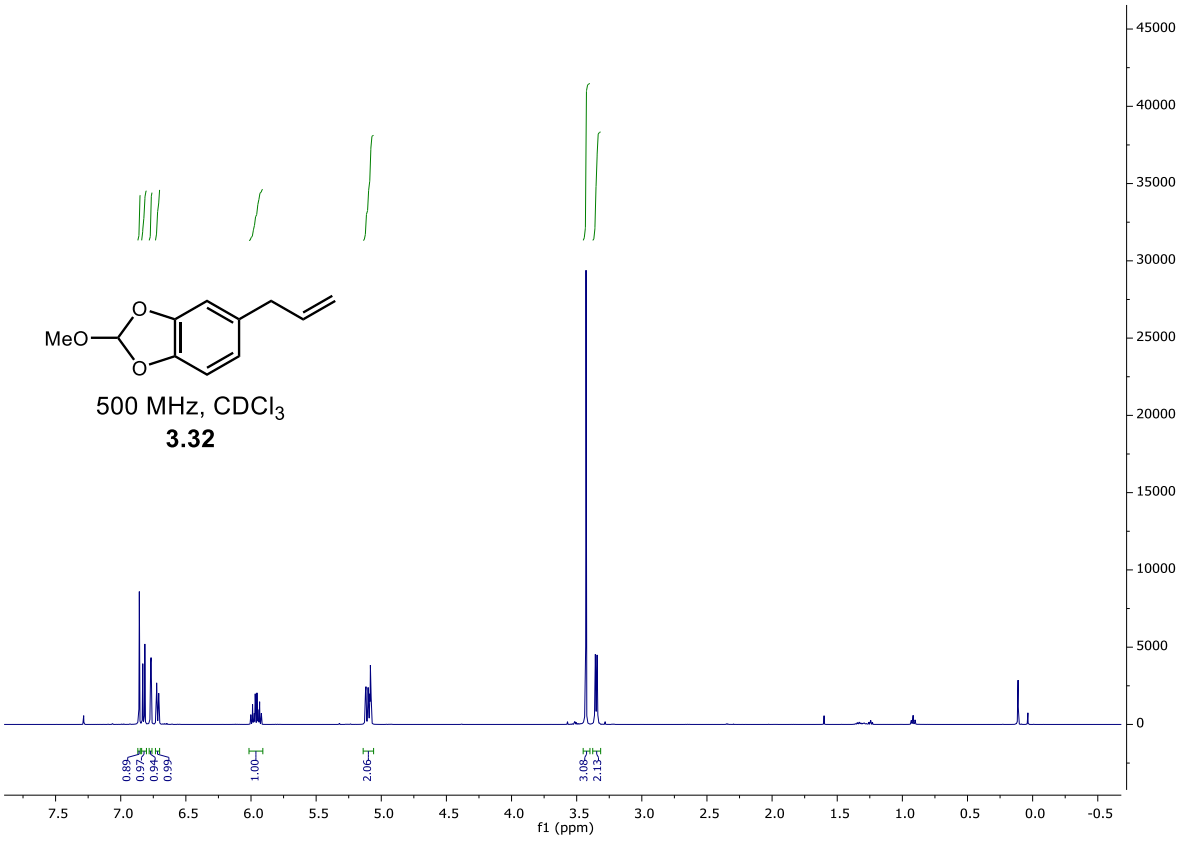

157.82
149.47
149.03
136.34
135.29
132.59
127.56
123.54
114.71
79.07
67.60
56.28
23.78
OMe
Me
N
O
126 MHz, CDCl3
3.29
f1 (ppm)

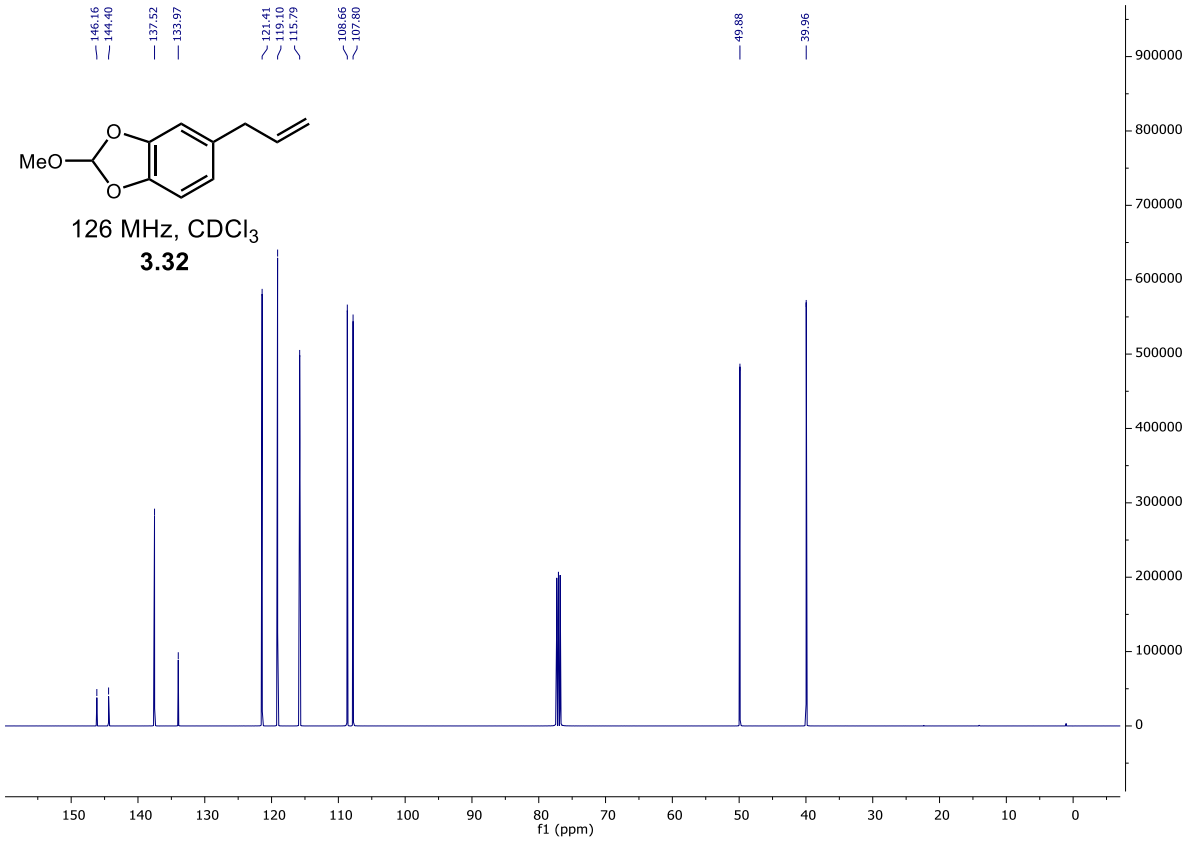

OMe
Me
O
500 MHz, CDCl3
3.30
1.98
2.03
1.00
2.02
1.97
2.01
0.98
2.96
2.97
f1 (ppm)

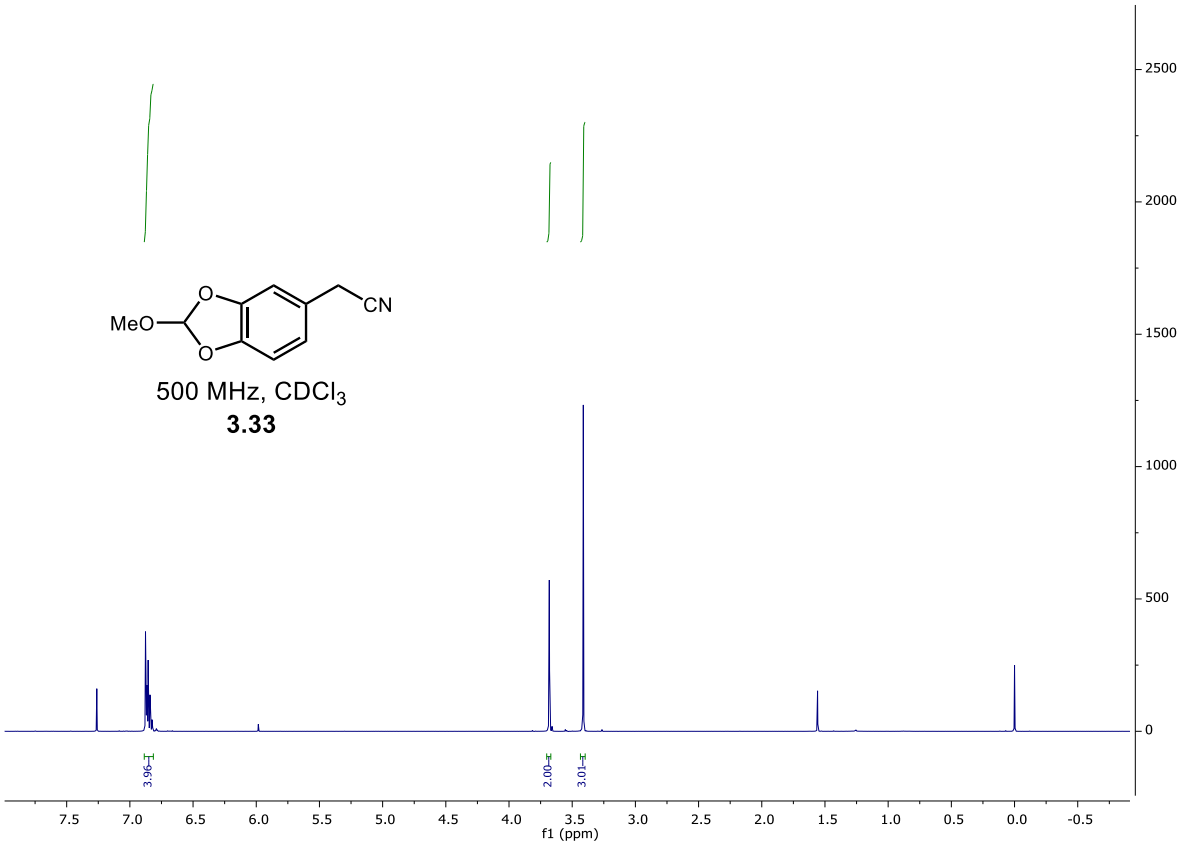

158.31
137.12
135.86
128.64
128.01
127.50
114.77
79.16
70.08
56.28
23.84
OMe
Me
O
126 MHz, CDCl3
3.30
f1 (ppm)

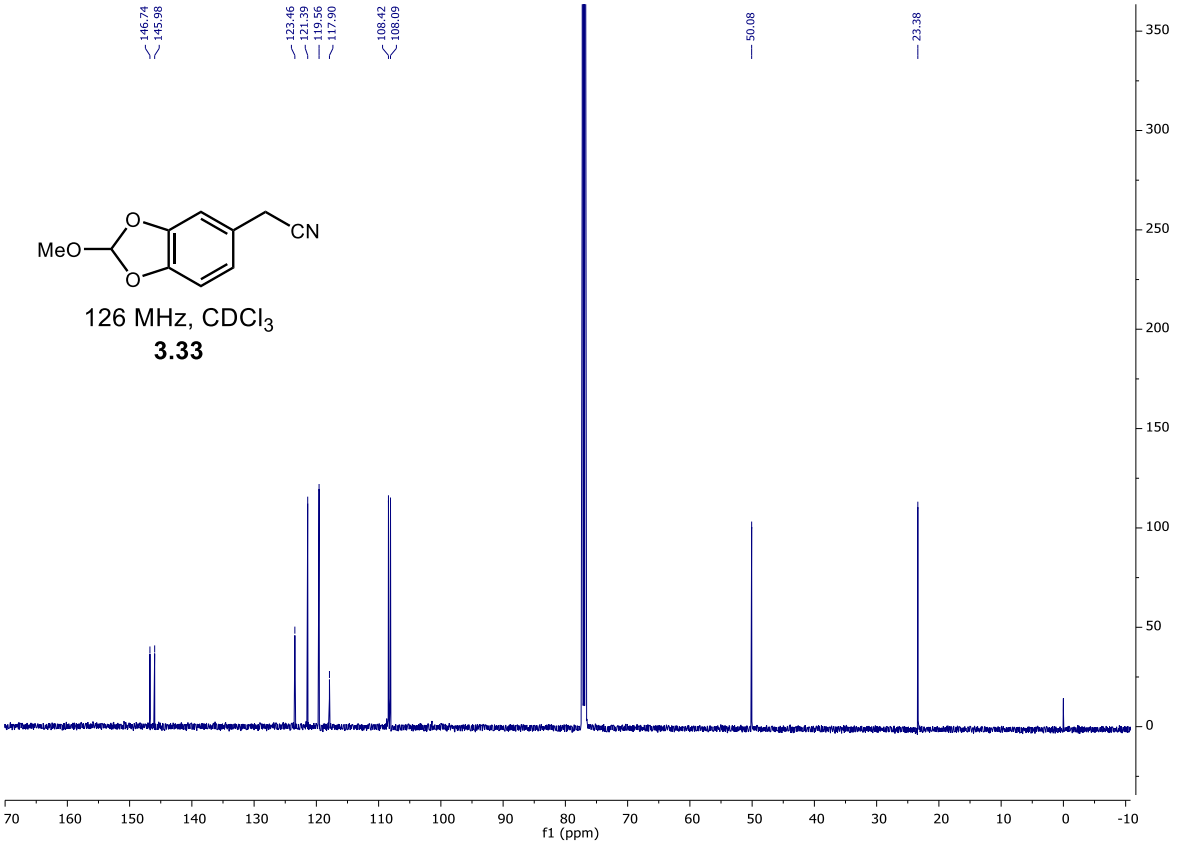

OMe
Ph
O
Ph
MeO
500 MHz, CDCl3
3.31
f1 (ppm)

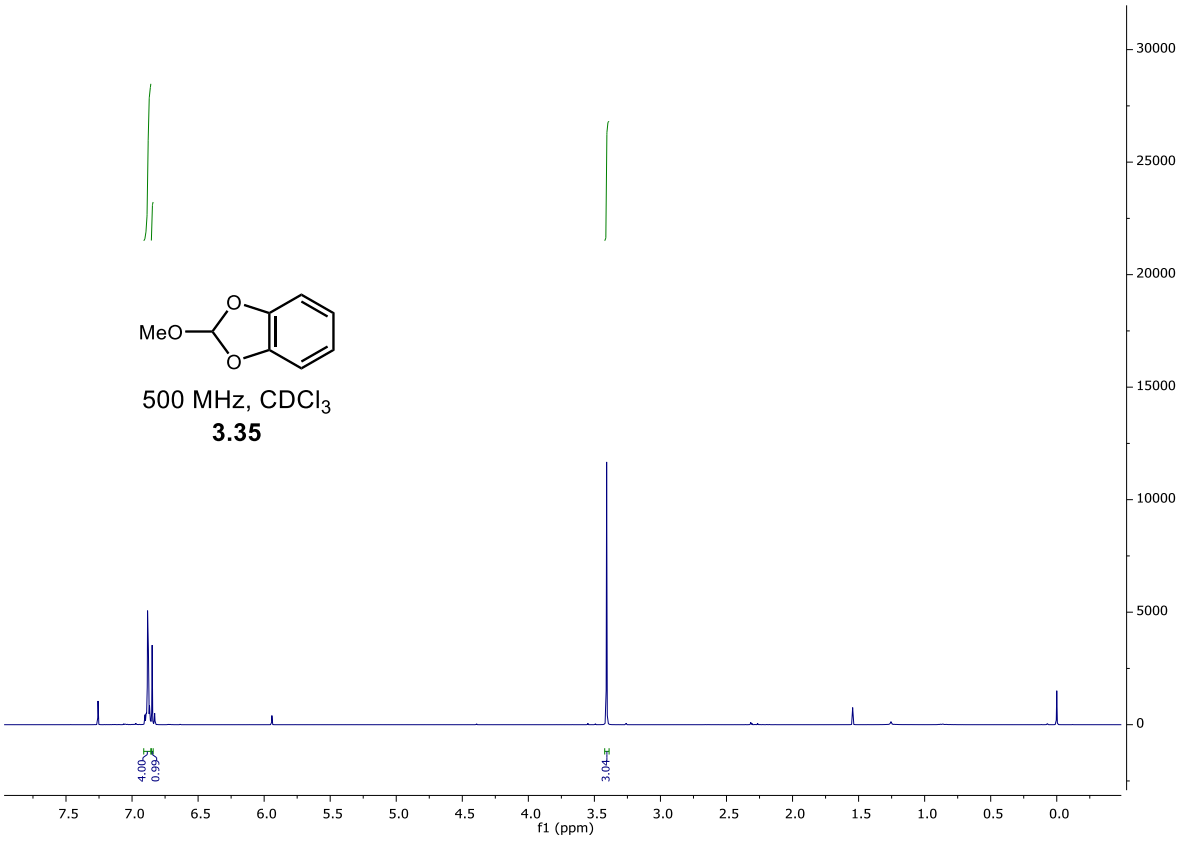

159.04
142.52
142.45
133.95
128.31
128.30
127.96
127.34
127.33
127.00
126.98
113.73
83.65
80.33
65.70
56.35
55.24
38.35
OMe
Ph
O
Ph
MeO
126 MHz, CDCl3
3.31
f1 (ppm)

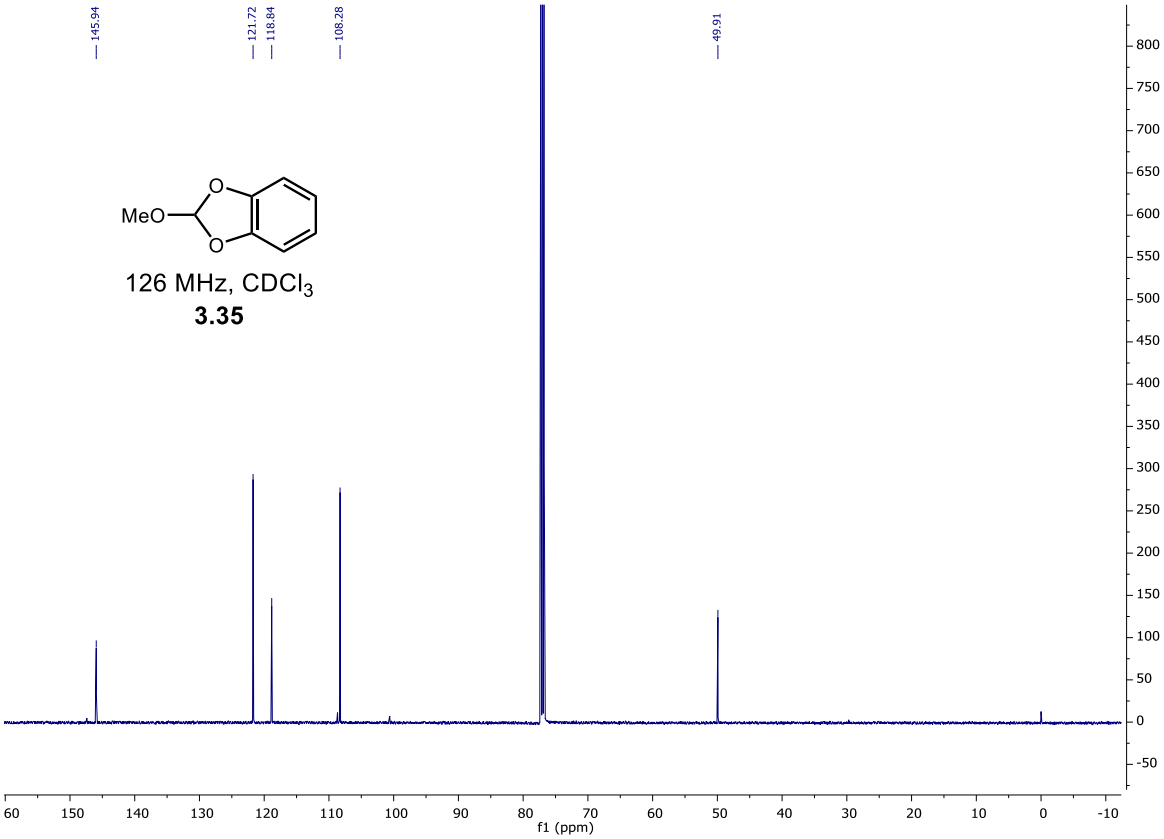

MeO
O
O
500 MHz, CDCl3
3.32
0.89
0.97
0.94
0.99
1.00
2.06
3.08
2.13
f1 (ppm)

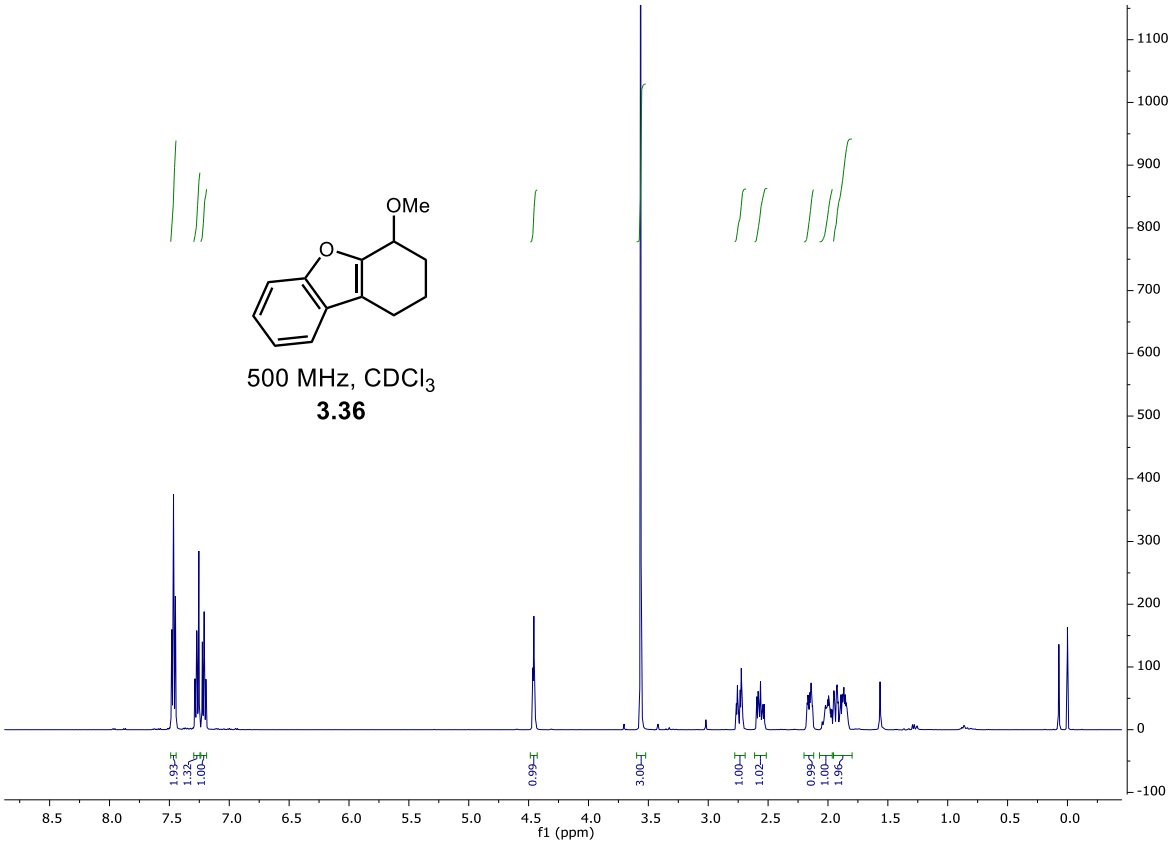

146.16
144.40
137.52
133.97
121.41
119.10
115.79
108.66
107.80
49.88
39.96
MeO
O
O
126 MHz, CDCl3
3.32
f1 (ppm)

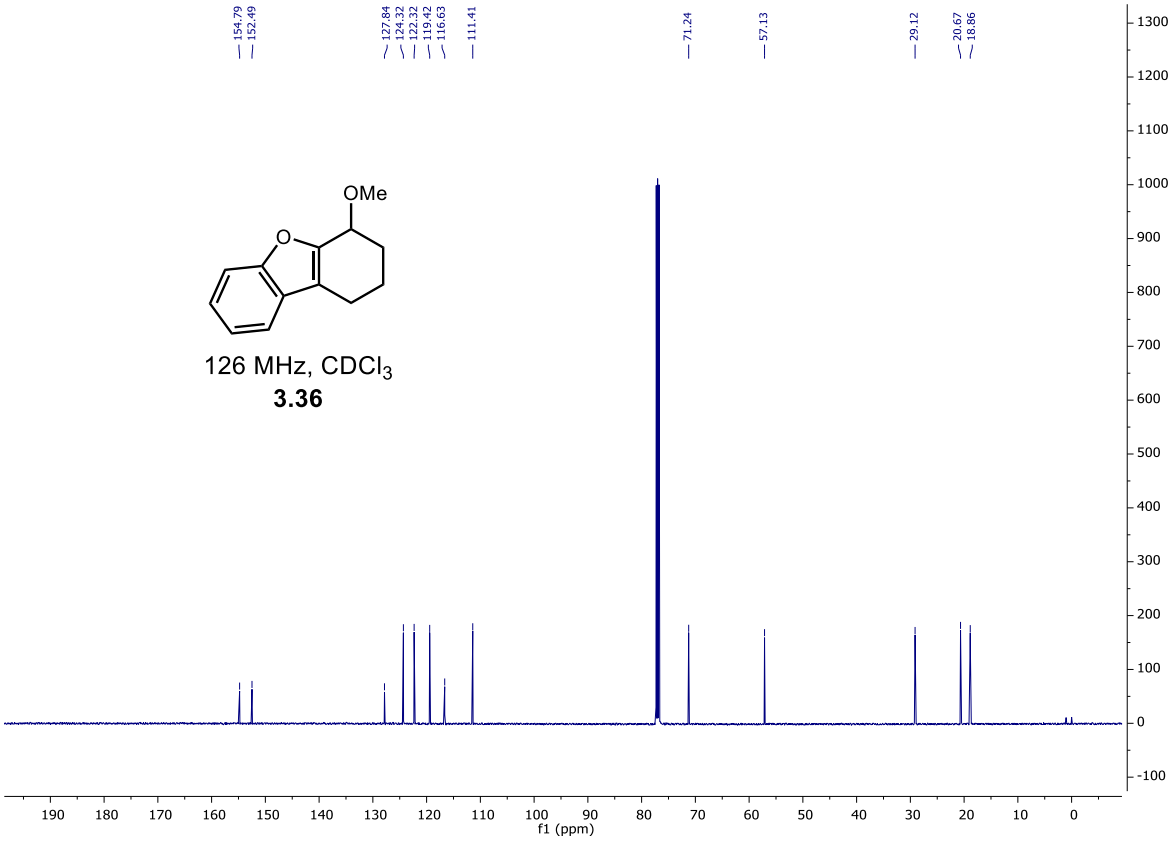

MeO
O
O
CN
500 MHz, CDCl3
3.33
3.96
2.00
3.01
f1 (ppm)

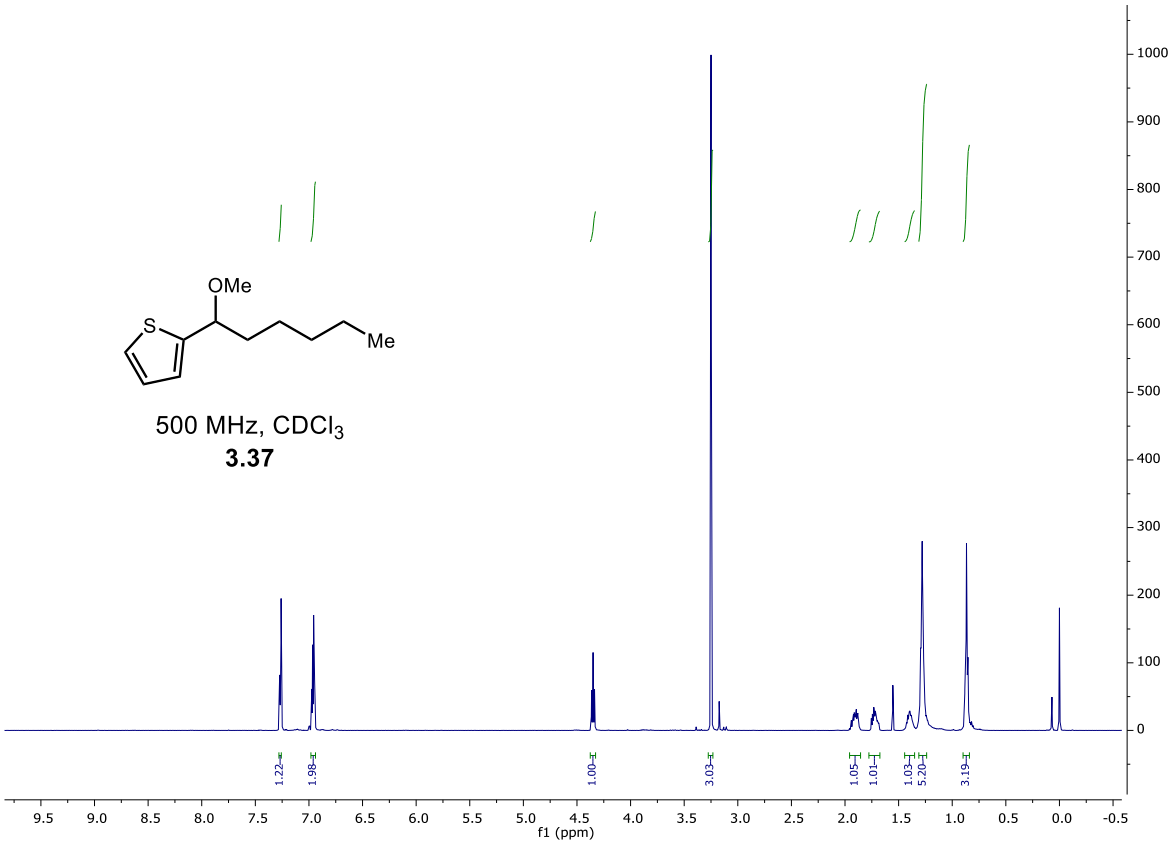

146.74
145.98
123.46
121.39
119.56
117.90
108.42
108.09
50.08
23.38
MeO
O
O
CN
126 MHz, CDCl3
3.33
f1 (ppm)

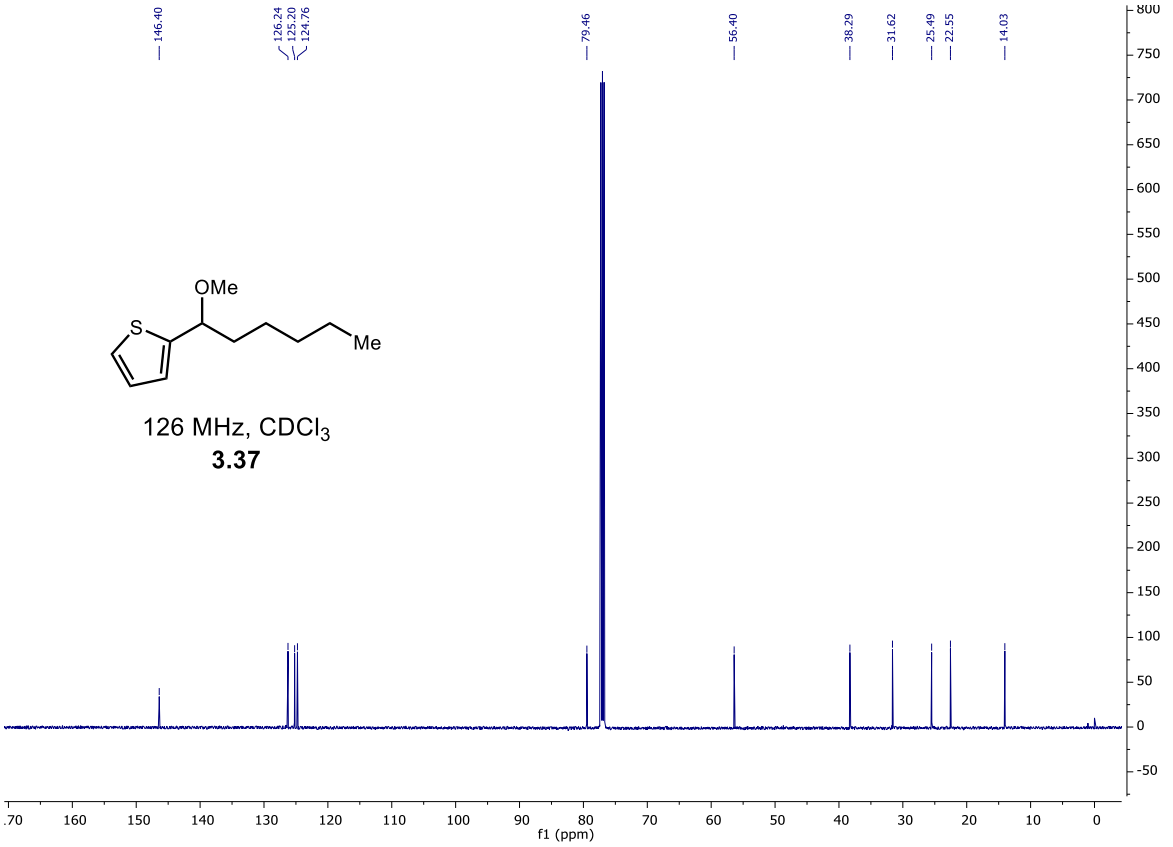

MeO
O
O
500 MHz, CDCl3
3.35
4.00
0.99
3.04
f1 (ppm)

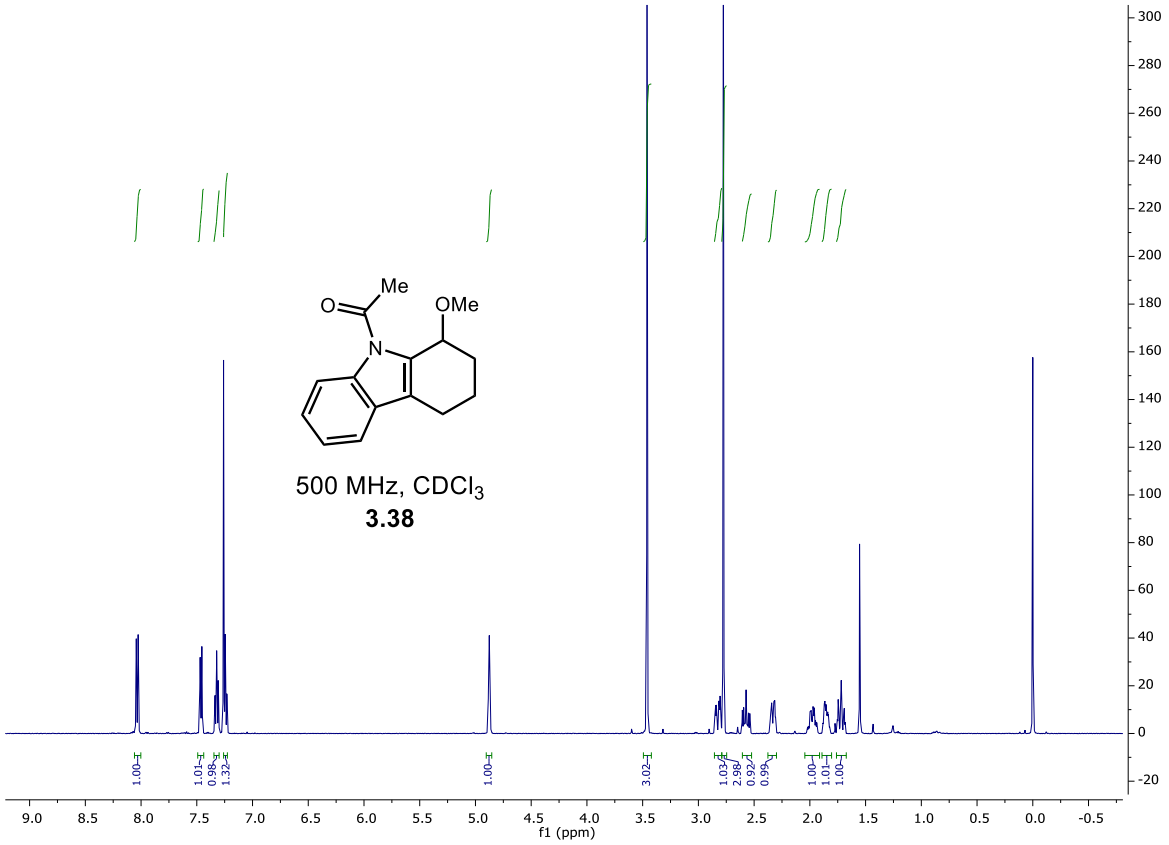

145.94
121.72
118.84
108.28
49.91
MeO
O
O
126 MHz, CDCl3
3.35
f1 (ppm)

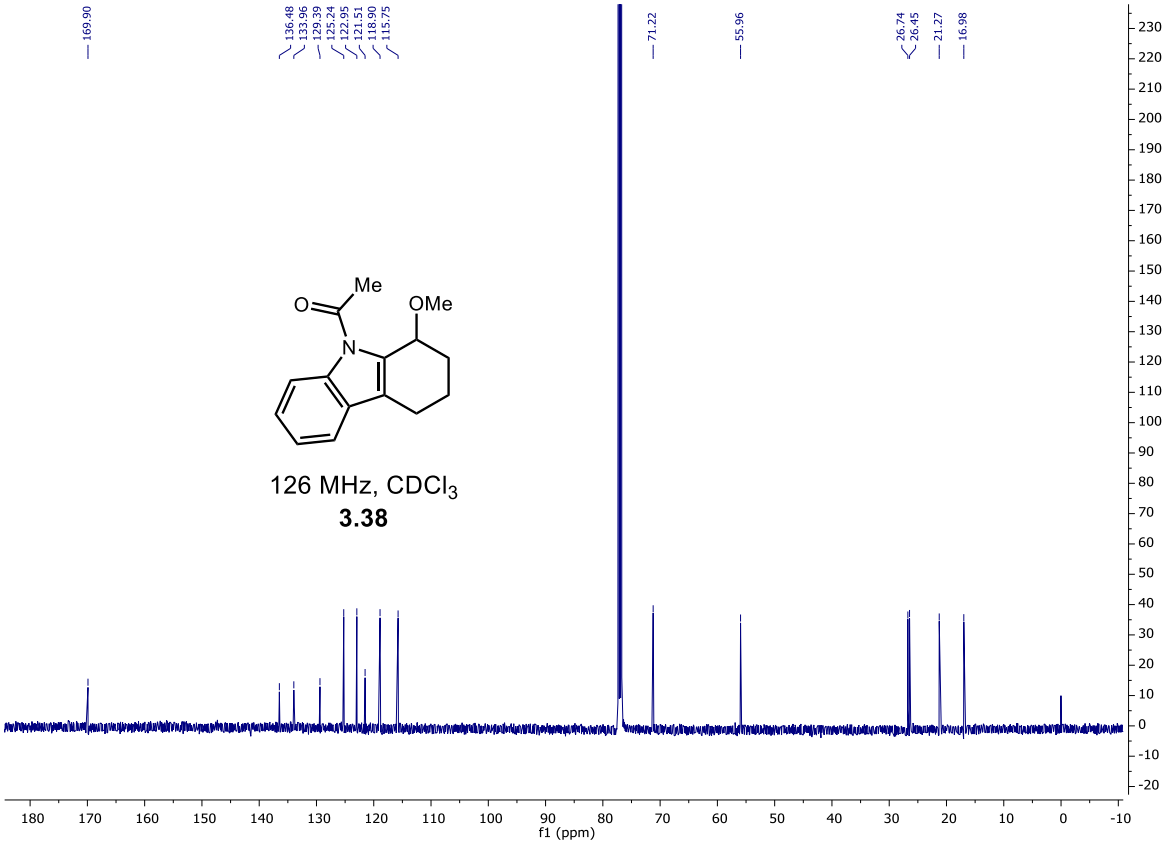

OMe
O
500 MHz, CDCl3
3.36
1.93
1.32
1.00
0.99
3.00
1.00
1.02
0.99
1.00
1.96
f1 (ppm)

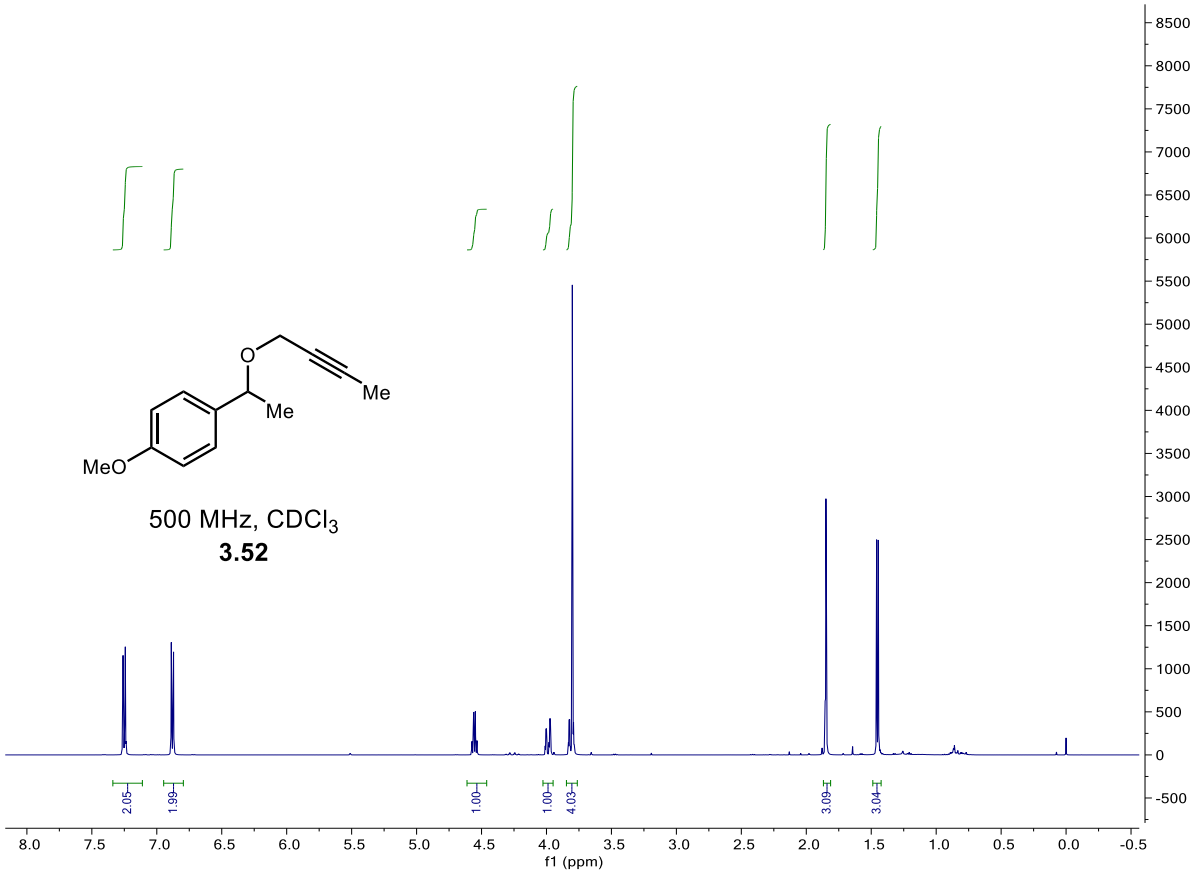

154.79
152.49
127.84
124.32
122.32
119.42
116.63
111.41
71.24
57.13
29.12
20.67
18.86
OMe
O
126 MHz, CDCl3
3.36
f1 (ppm)

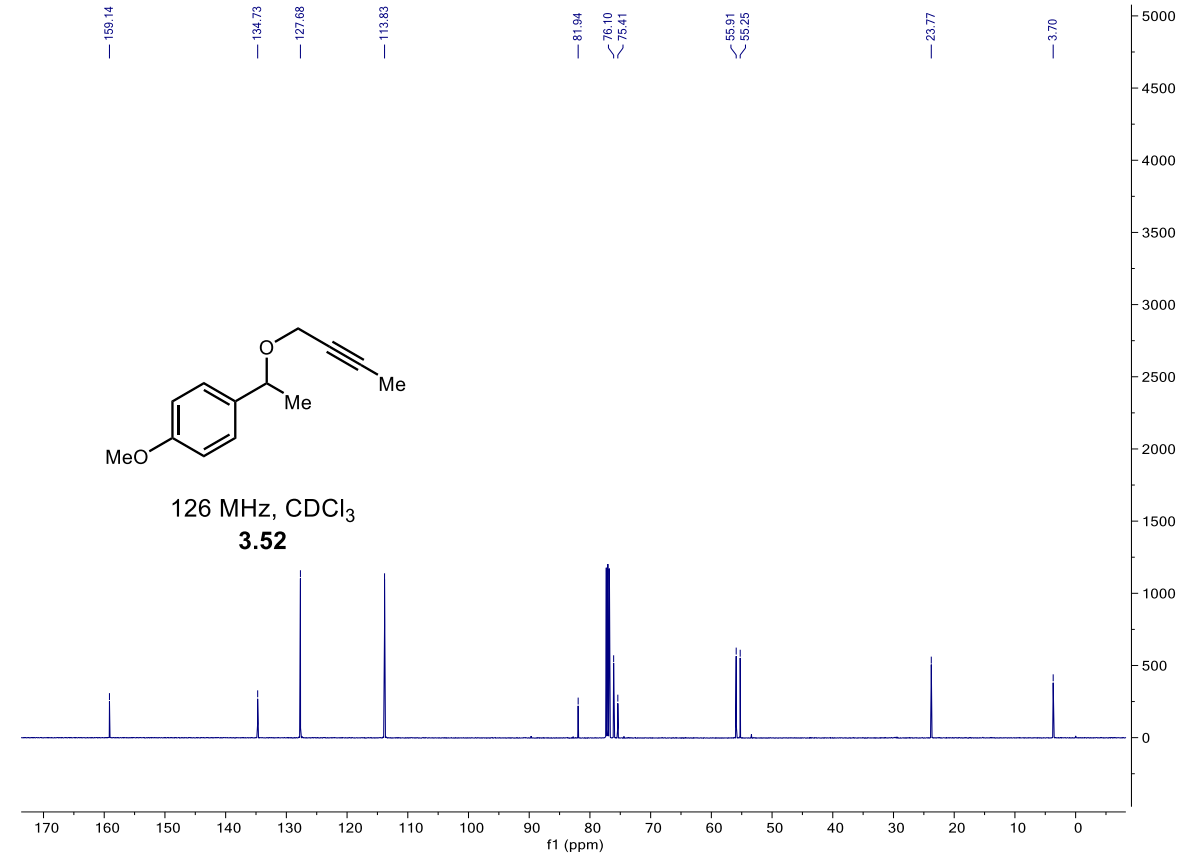

OMe
S
Me
500 MHz, CDCl3
3.37
1.22
1.98
1.00
3.03
1.05
1.01
1.03
5.20
3.19
f1 (ppm)

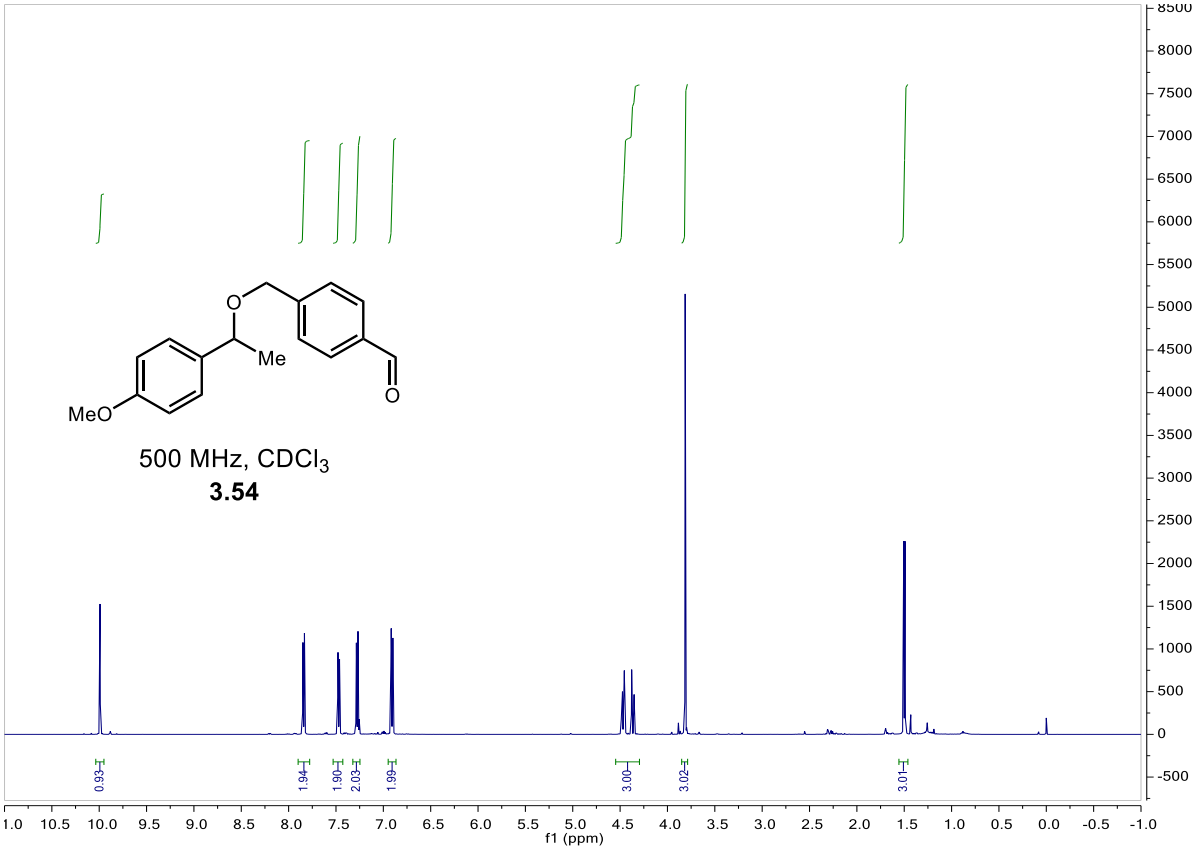

146.40
126.24
125.20
124.76
79.46
56.40
38.29
31.62
25.49
22.55
14.03
OMe
S
Me
126 MHz, CDCl3
3.37
f1 (ppm)

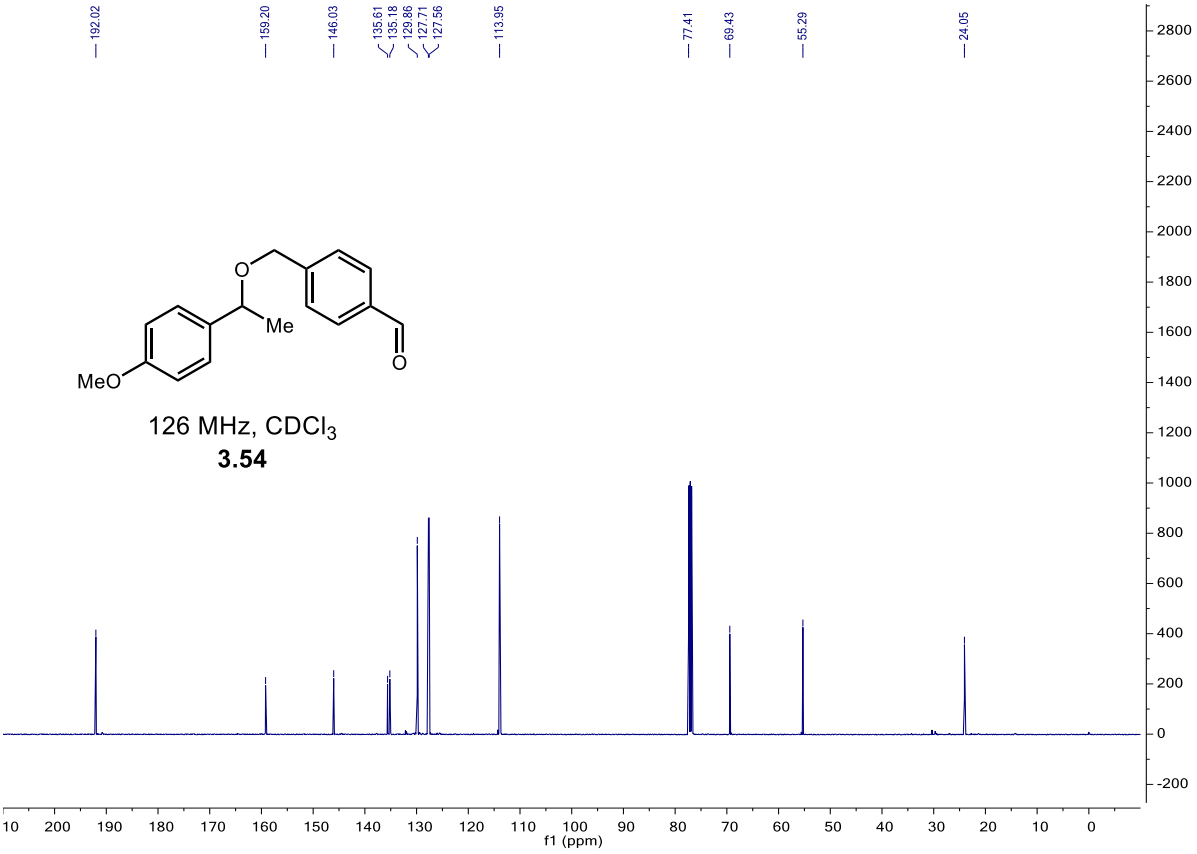

Me
O
OMe
N
500 MHz, CDCl3
3.38
f1 (ppm)

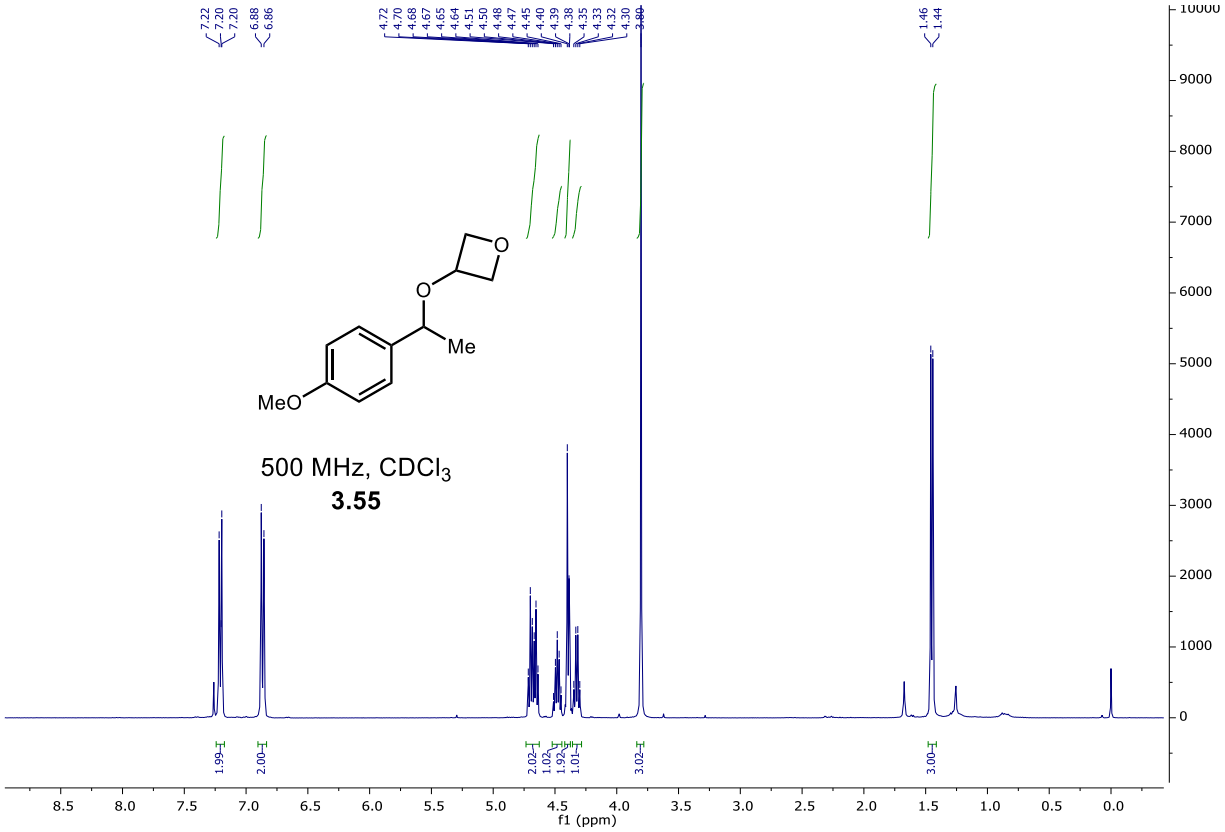

169.90
136.48
133.96
129.39
125.24
122.95
121.51
118.90
115.75
71.22
55.96
26.74
26.45
21.27
16.98
Me
O
OMe
N
126 MHz, CDCl3
3.38
f1 (ppm)

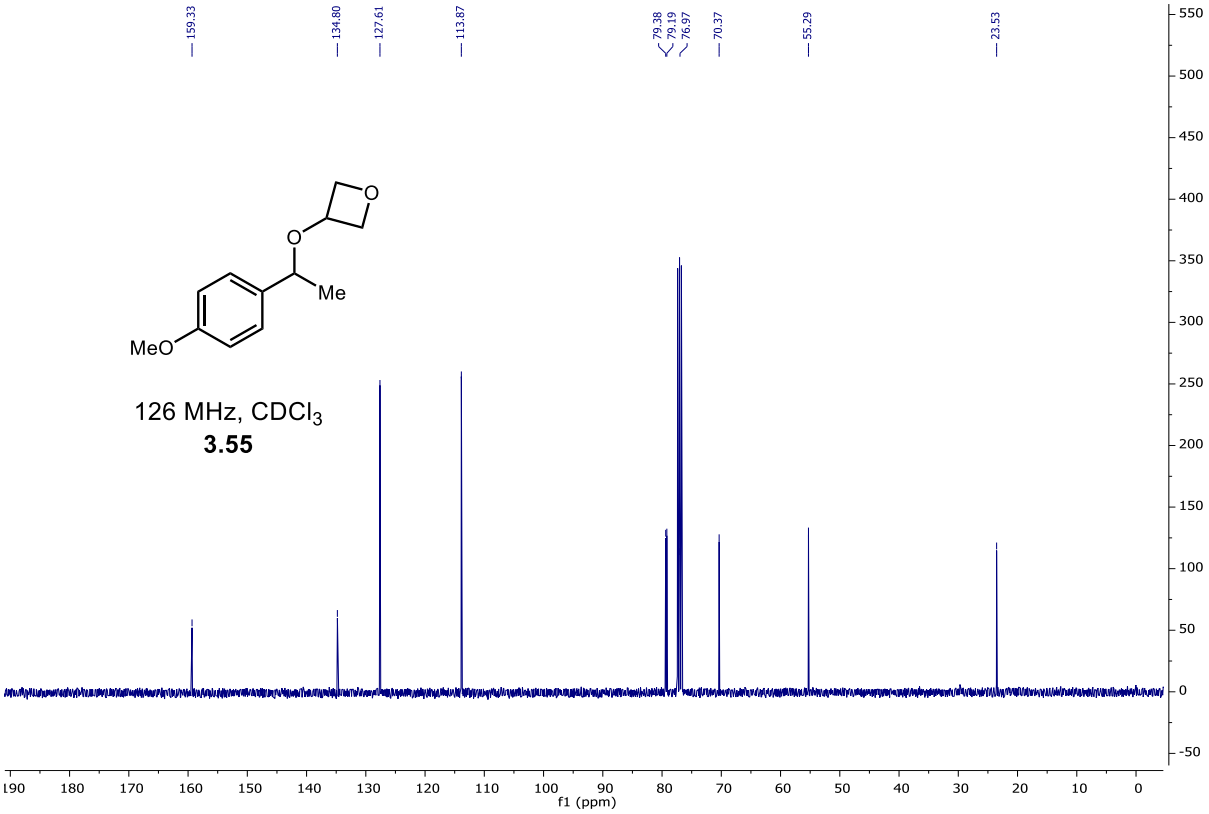

O
Me
Me
MeO
500 MHz, $CDCl_3$
**3.52**
2.05
1.99
1.00
1.00
4.03
3.09
3.04
f1 (ppm)

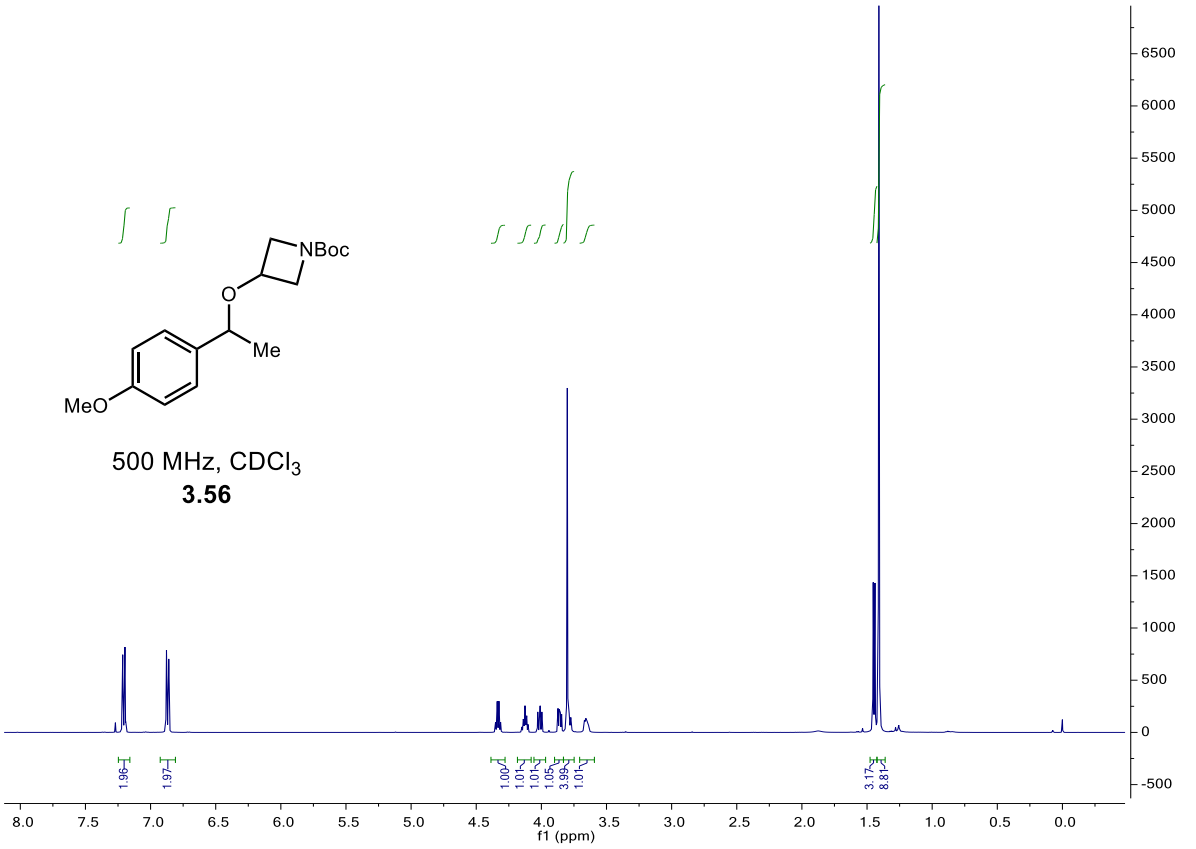

159.14
134.73
127.68
113.83
81.94
76.10
75.41
55.91
55.25
23.77
3.70
O
Me
Me
MeO
126 MHz, $CDCl_3$
**3.52**
f1 (ppm)

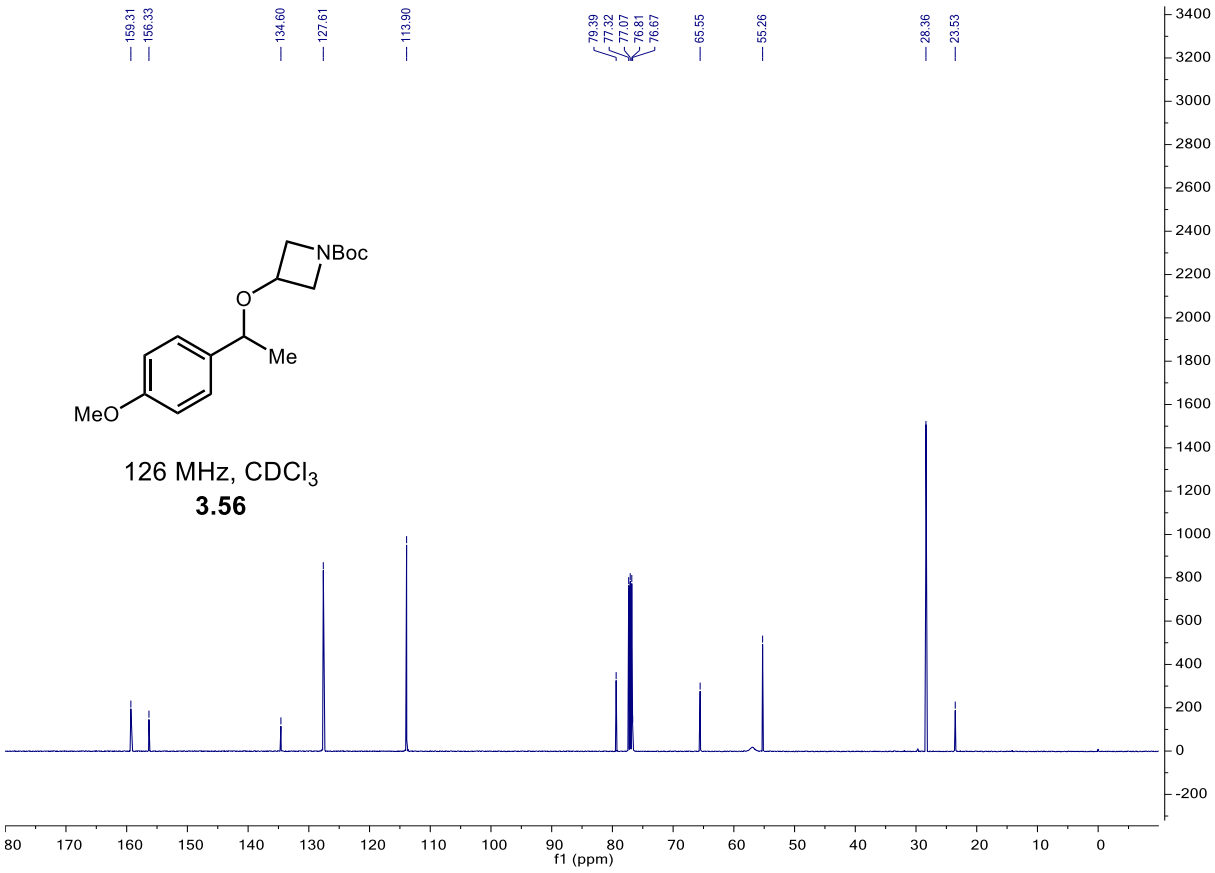

MeO
Me
O
O
500 MHz, CDCl3
3.54
0.93
1.94
1.90
2.03
1.99
3.00
3.02
3.01
f1 (ppm)

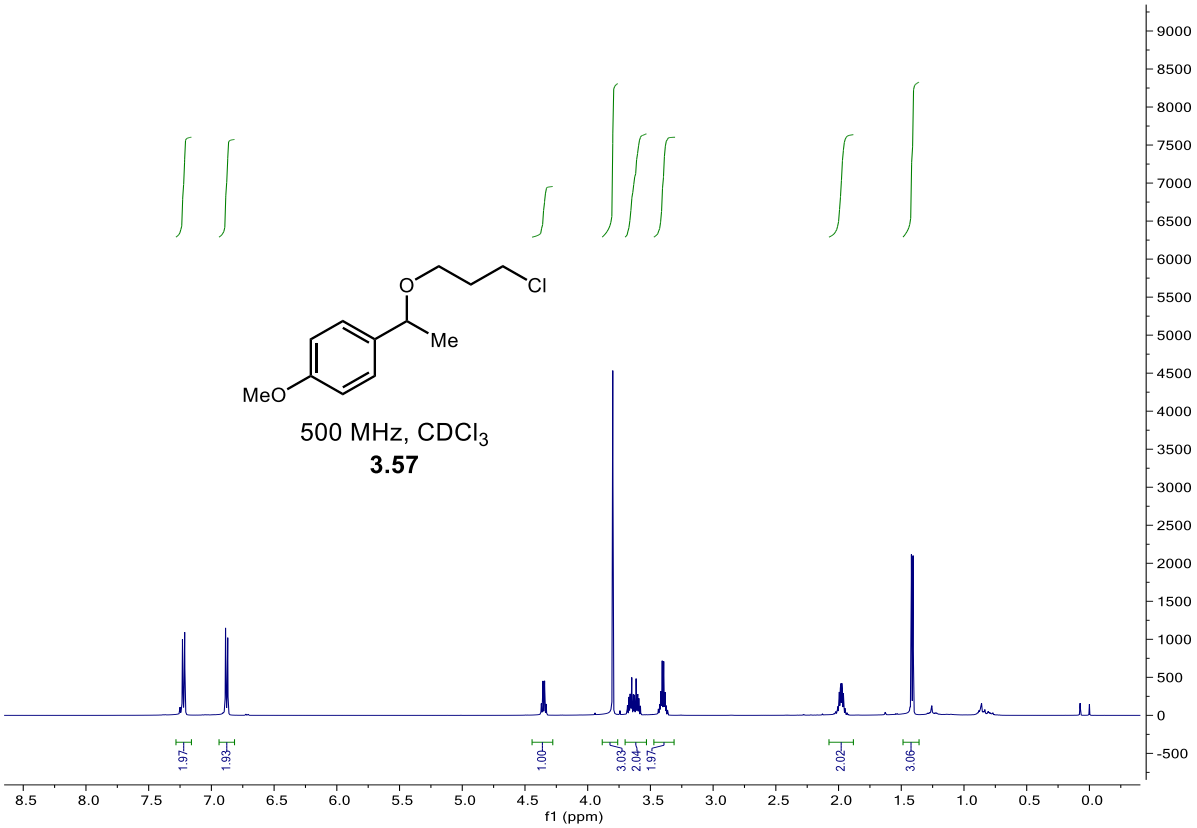

192.02
159.20
146.03
135.61
135.18
129.86
127.71
127.56
113.95
77.41
69.43
55.29
24.05
MeO
Me
O
O
126 MHz, CDCl3
3.54
f1 (ppm)

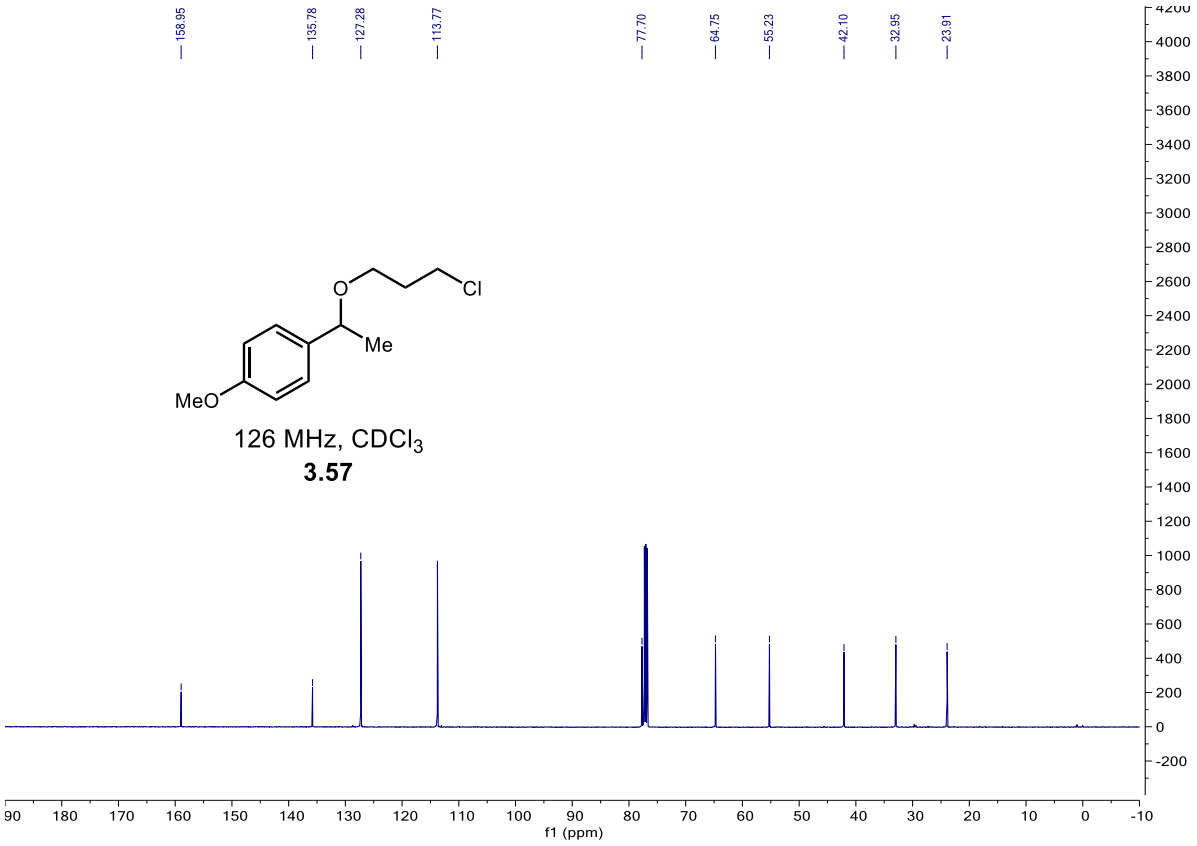

7.22
7.20
7.20
6.88
6.86
4.72
4.70
4.68
4.67
4.65
4.64
4.51
4.50
4.48
4.47
4.45
4.40
4.39
4.38
4.35
4.33
4.32
4.30
3.80
1.46
1.44
O
O
Me
MeO
500 MHz, CDCl3
3.55
1.99
2.00
2.02
1.02
1.92
1.01
3.02
3.00
f1 (ppm)

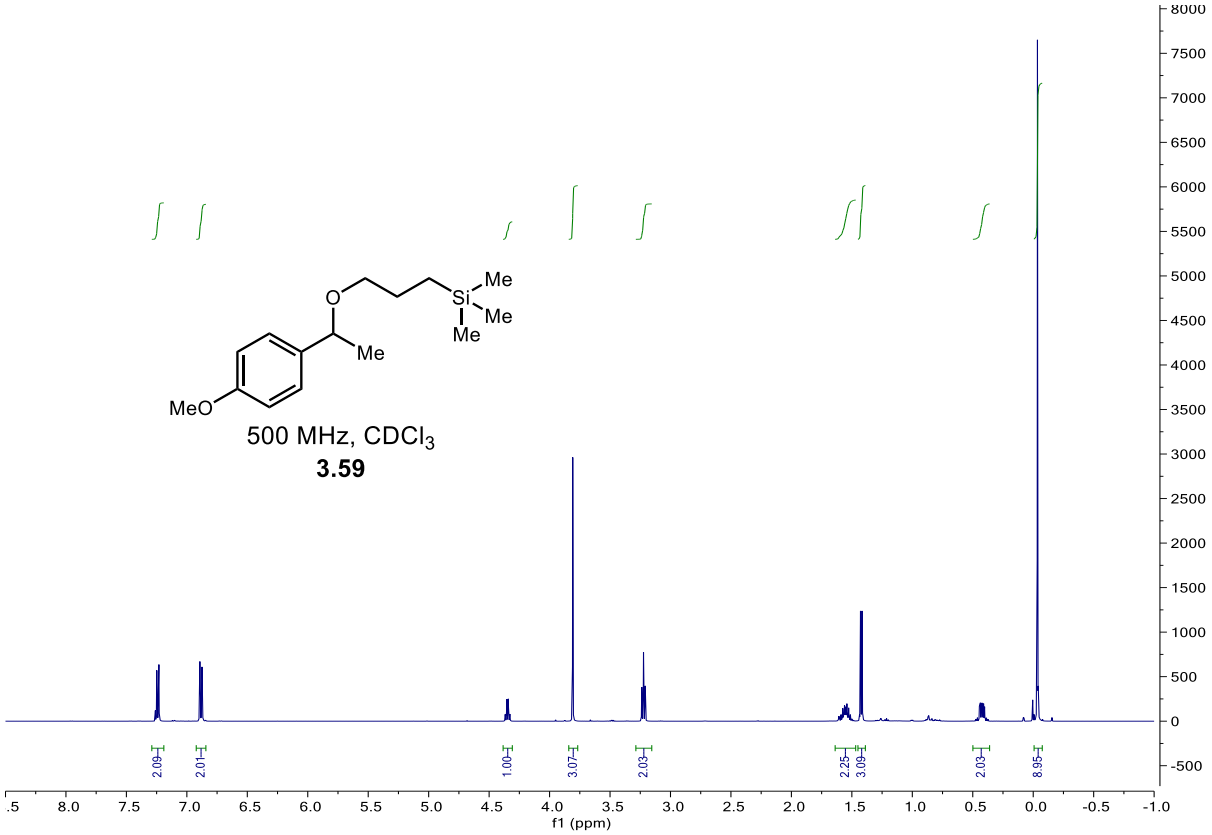

159.33
134.80
127.61
113.87
79.38
79.19
76.97
70.37
55.29
23.53
O
O
Me
MeO
126 MHz, CDCl3
3.55
f1 (ppm)

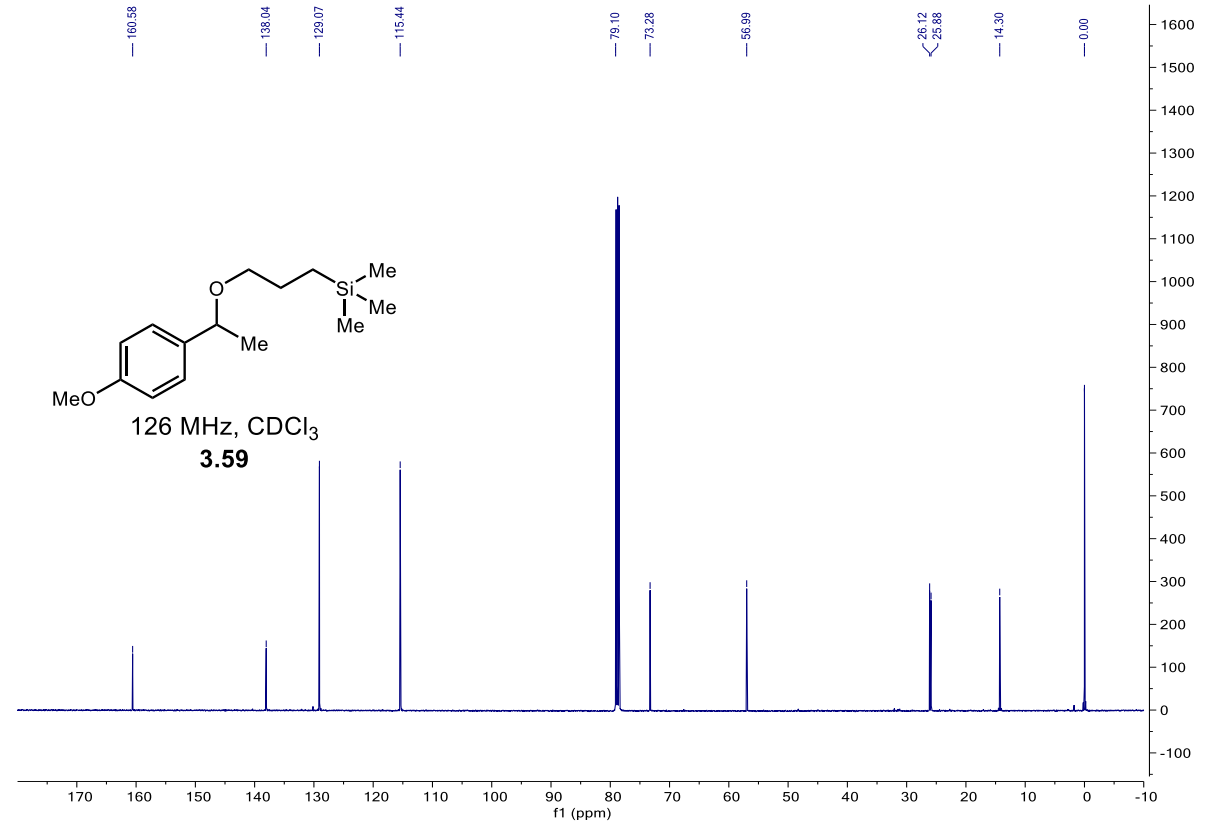

NBoc
O
Me
MeO
500 MHz, CDCl3
3.56
f1 (ppm)

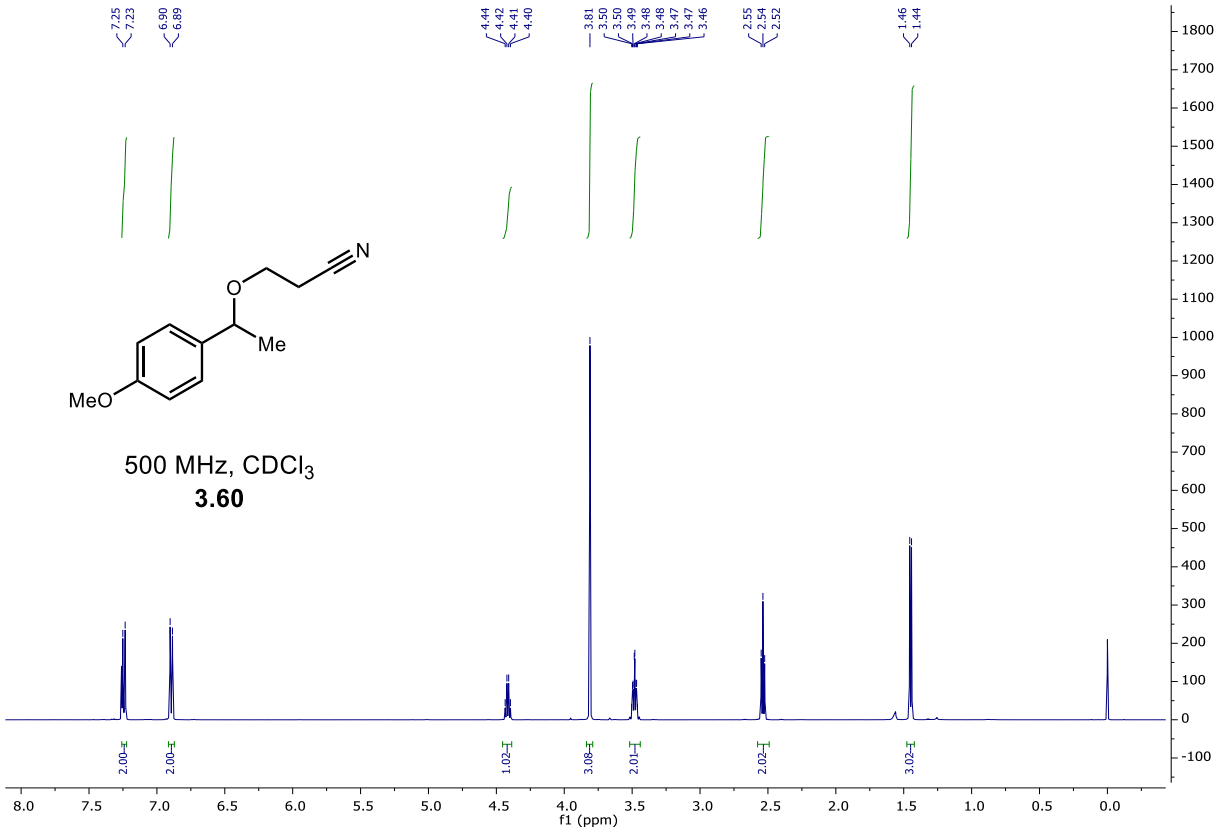

159.31
156.33
134.60
127.61
113.90
79.39
77.32
77.07
76.81
76.67
65.55
55.26
28.36
23.53
NBoc
O
Me
MeO
126 MHz, CDCl3
3.56
f1 (ppm)


O
Cl
Me
MeO
500 MHz, CDCl3
3.57
1.97
1.93
1.00
3.03
2.04
1.97
2.02
3.06
f1 (ppm)


158.95
135.78
127.28
113.77
77.70
64.75
55.23
42.10
32.95
23.91
O
Cl
Me
MeO
126 MHz, CDCl3
3.57
f1 (ppm)

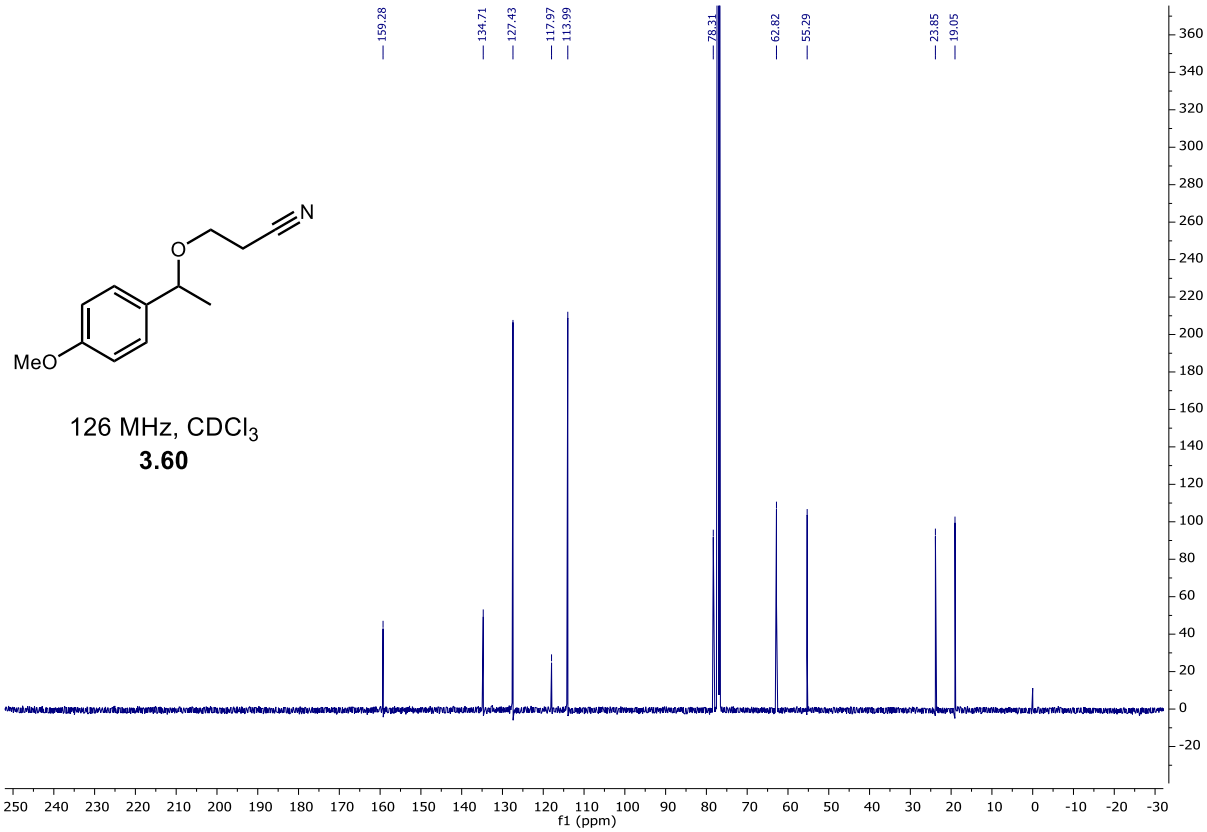

Me
O
Si
Me
Me
Me
MeO
500 MHz, CDCl3
3.59
2.09
2.01
1.00
3.07
2.03
2.25
3.09
2.03
8.95
f1 (ppm)


160.58
138.04
129.07
115.44
79.10
73.28
56.99
26.12
25.88
14.30
0.00
O
Si
Me
Me
Me
Me
MeO
126 MHz, CDCl3
3.59
f1 (ppm)



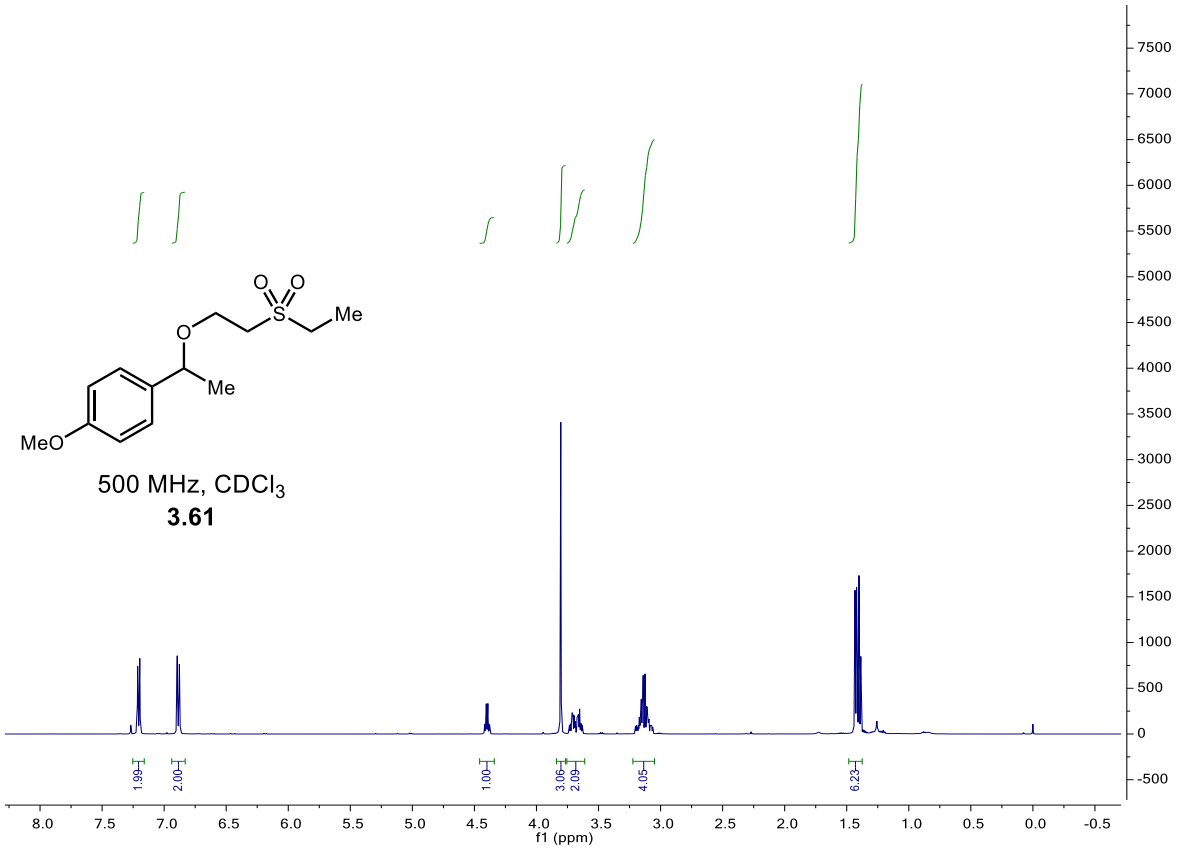

500 MHz, $CDCl_3$

**3.60**



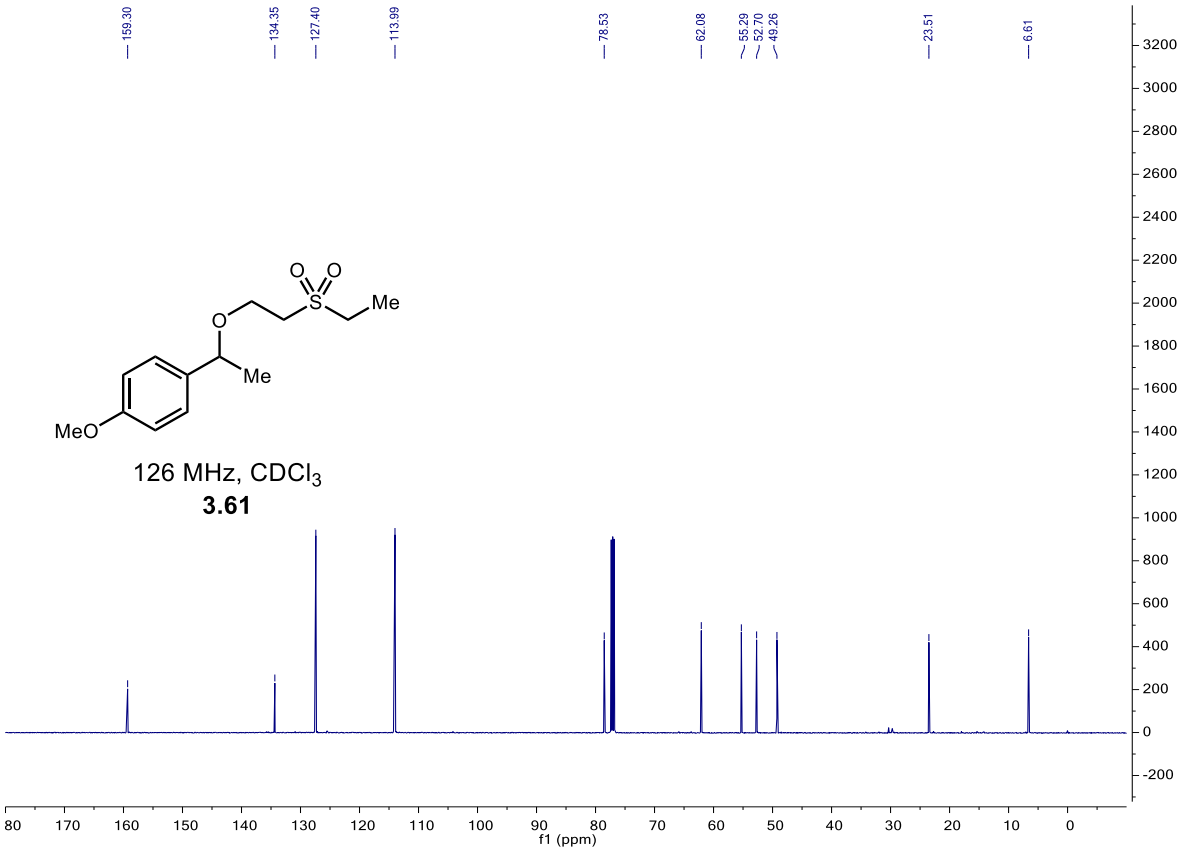

126 MHz, $CDCl_3$

**3.60**



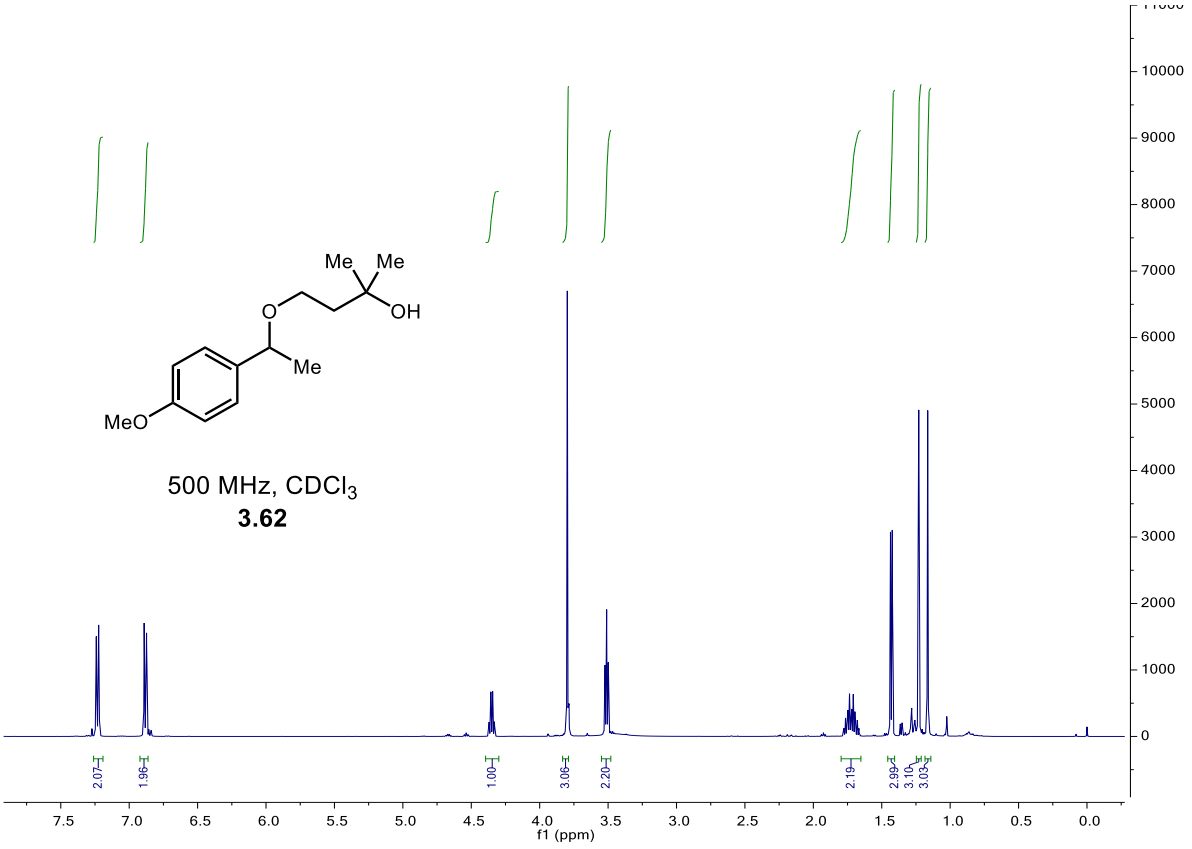

500 MHz, $CDCl_3$

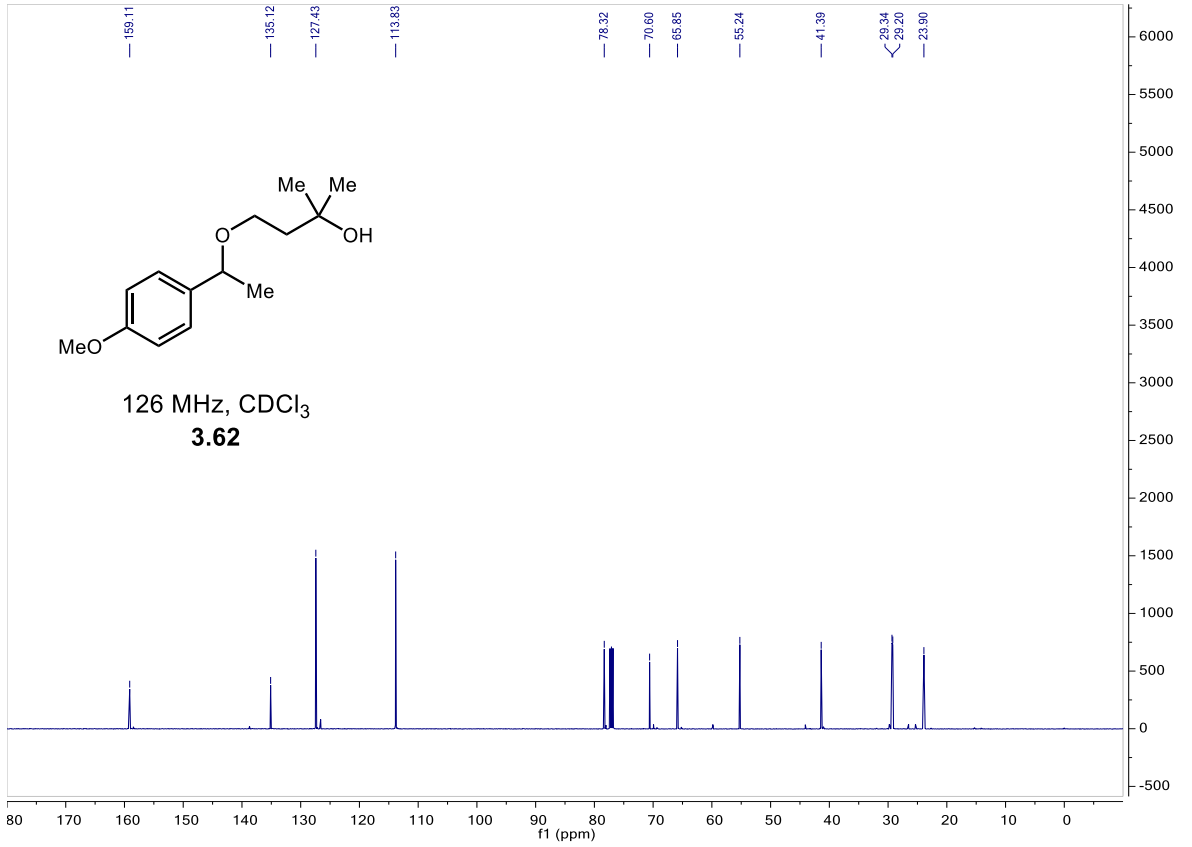
**3.61**

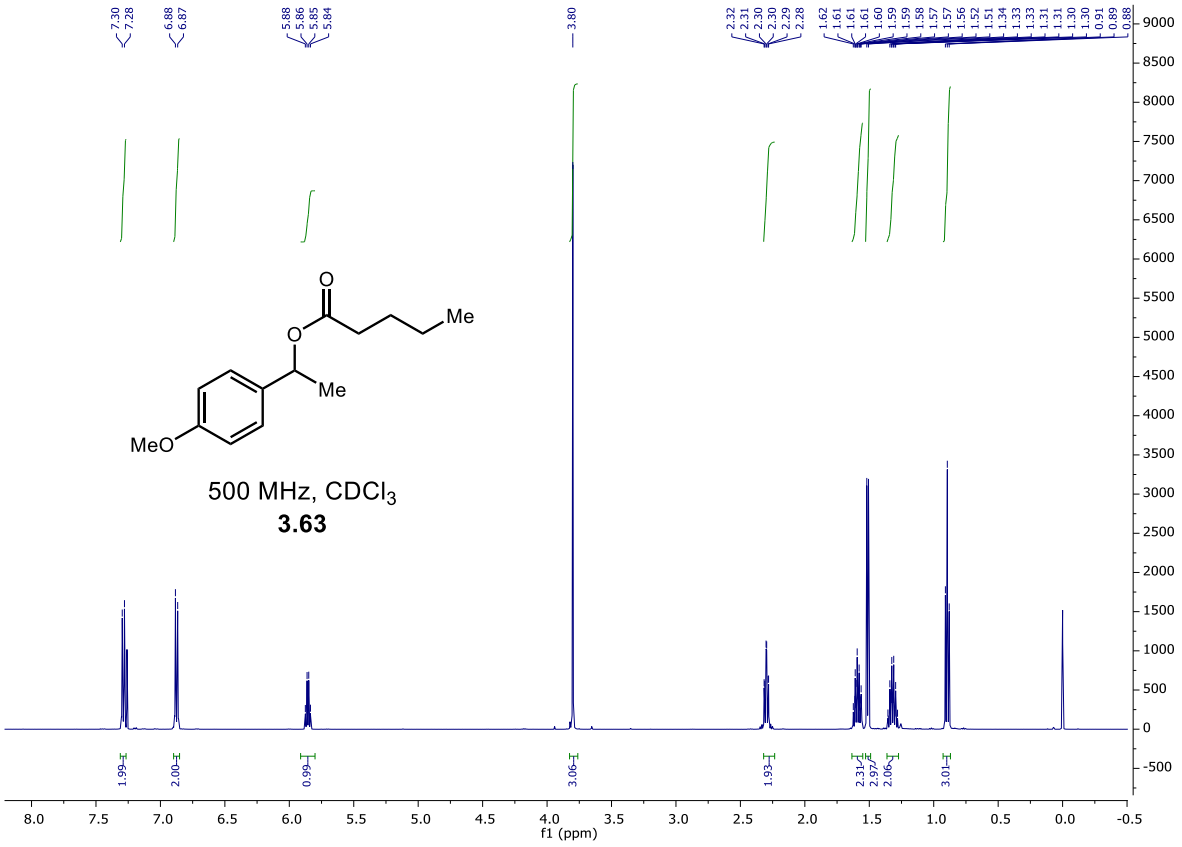


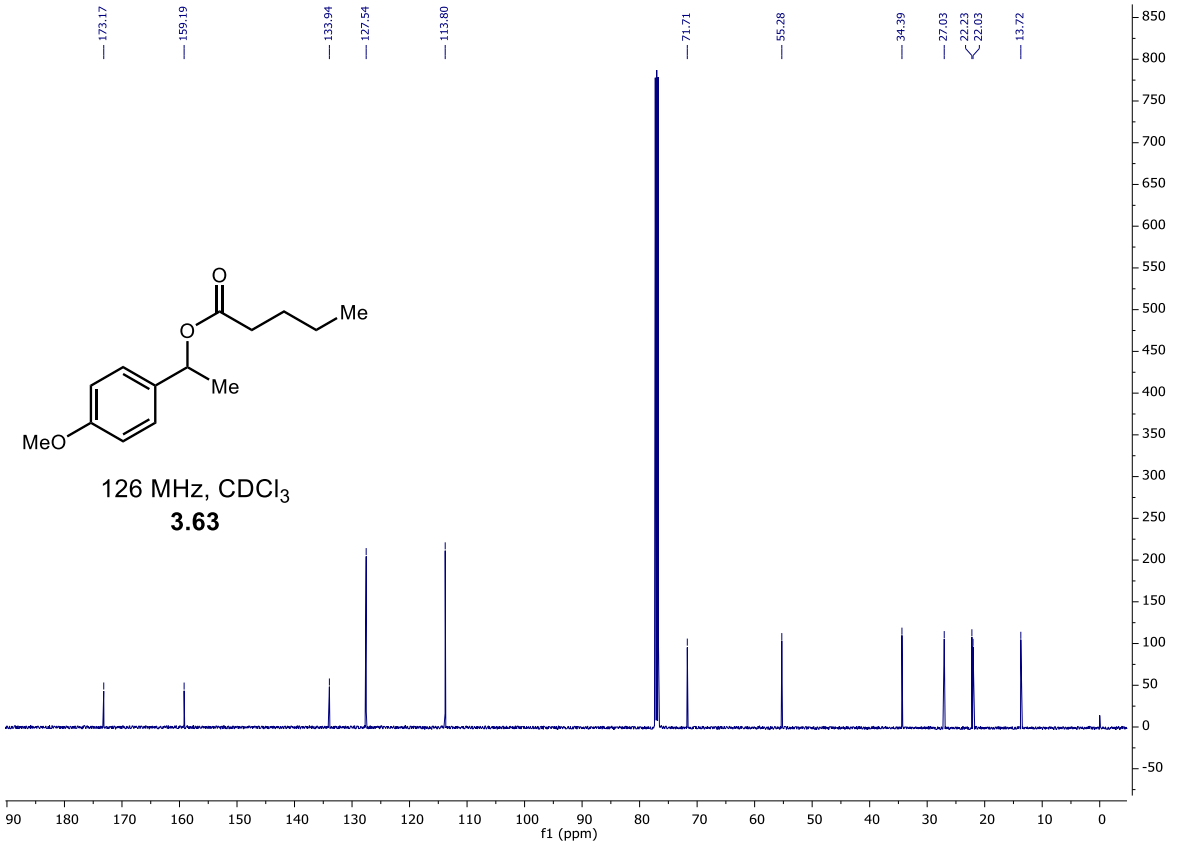

126 MHz, $CDCl_3$

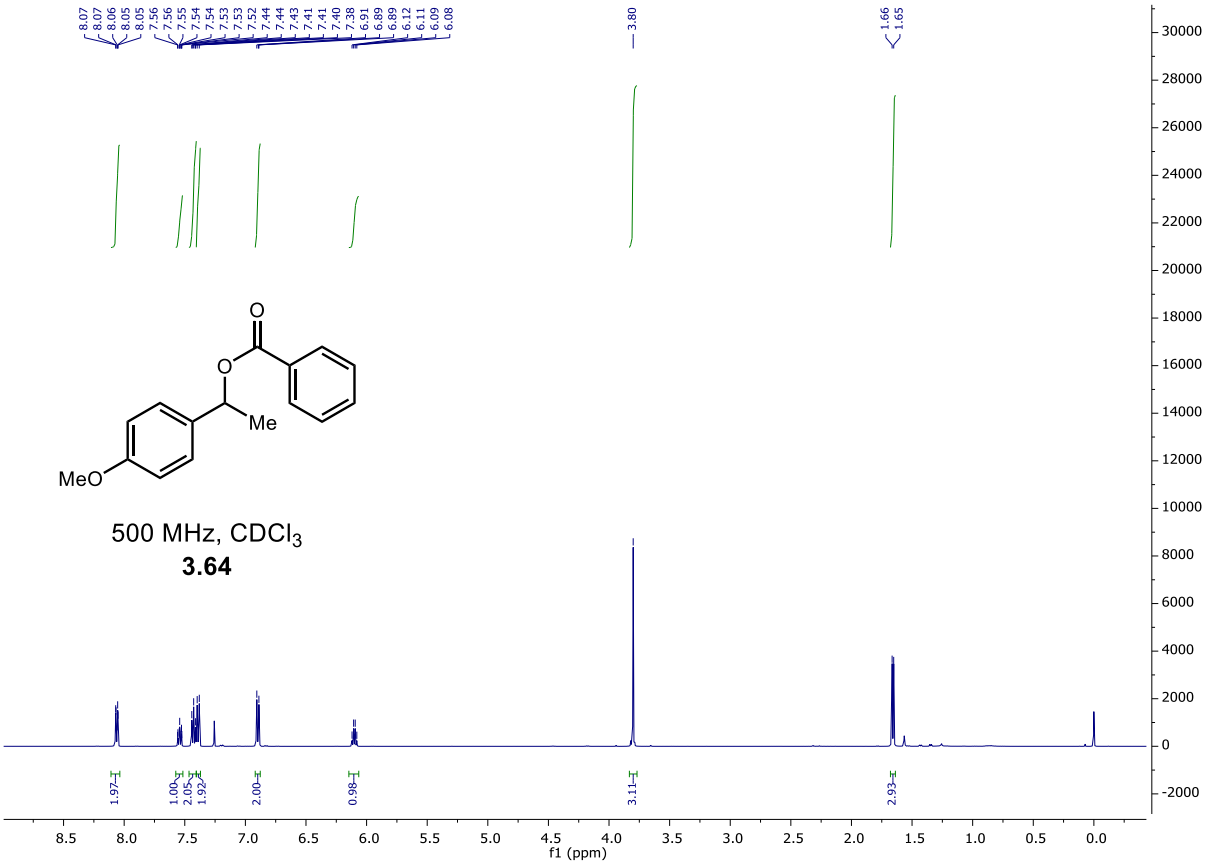
**3.61**

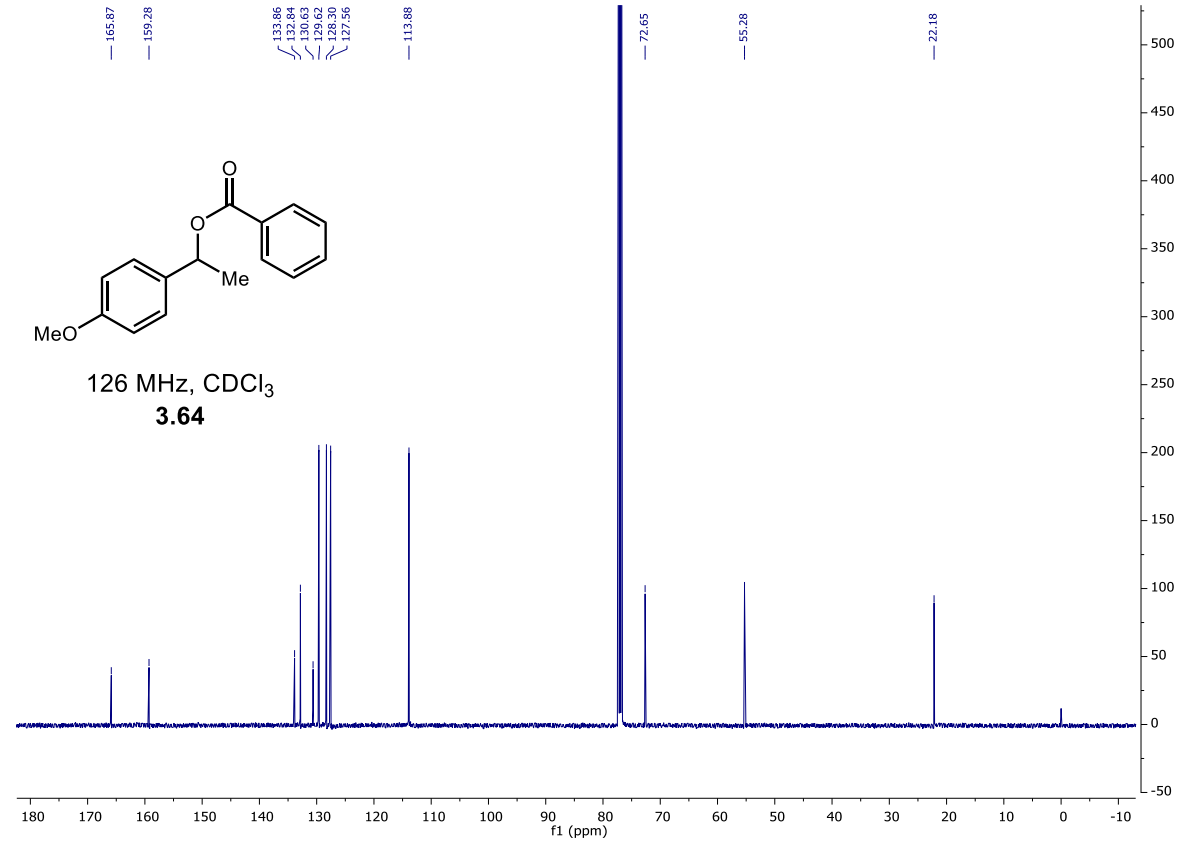

Me
Me
OH
O
Me
MeO
500 MHz, CDCl3
3.62
2.07
1.96
1.00
3.06
2.20
2.19
2.99
3.10
3.03
f1 (ppm)

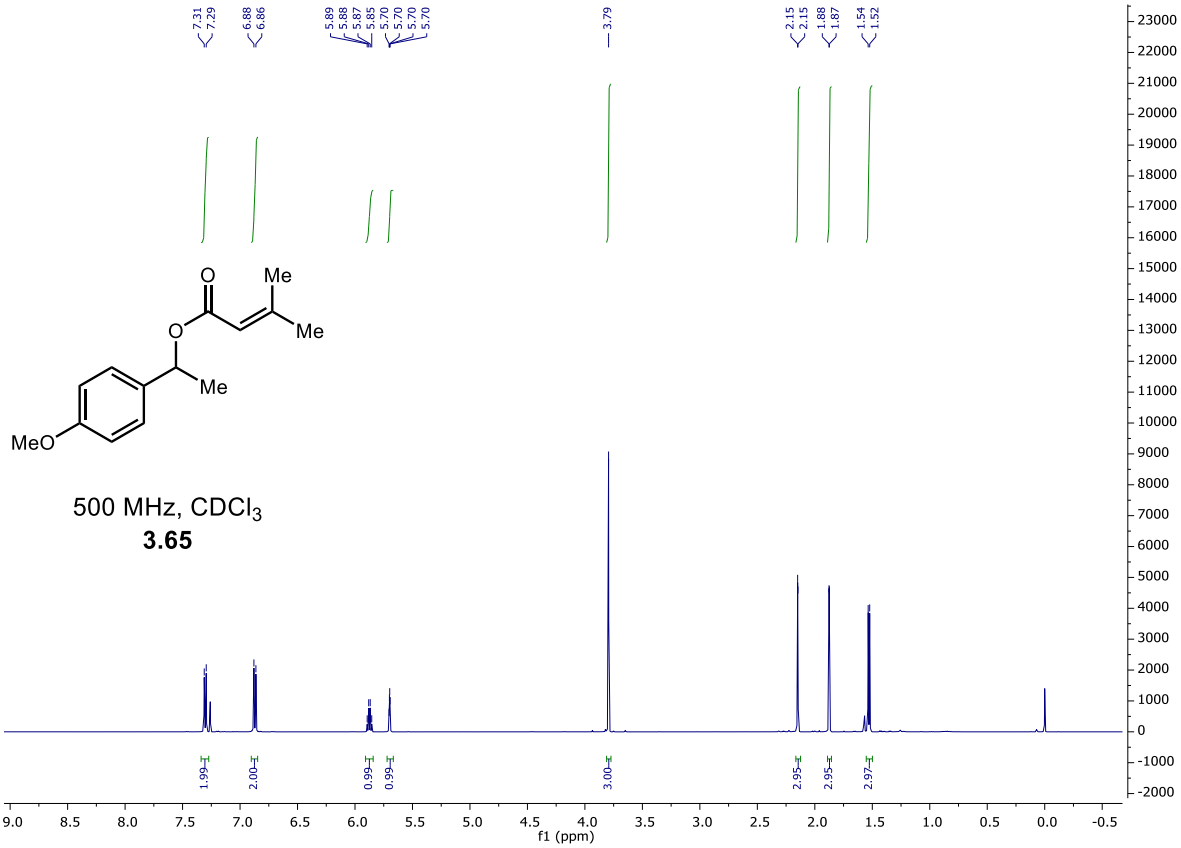

159.11
135.12
127.43
113.83
78.32
70.60
65.85
55.24
41.39
29.34
29.20
23.90
Me
Me
OH
O
Me
MeO
126 MHz, CDCl3
3.62
f1 (ppm)

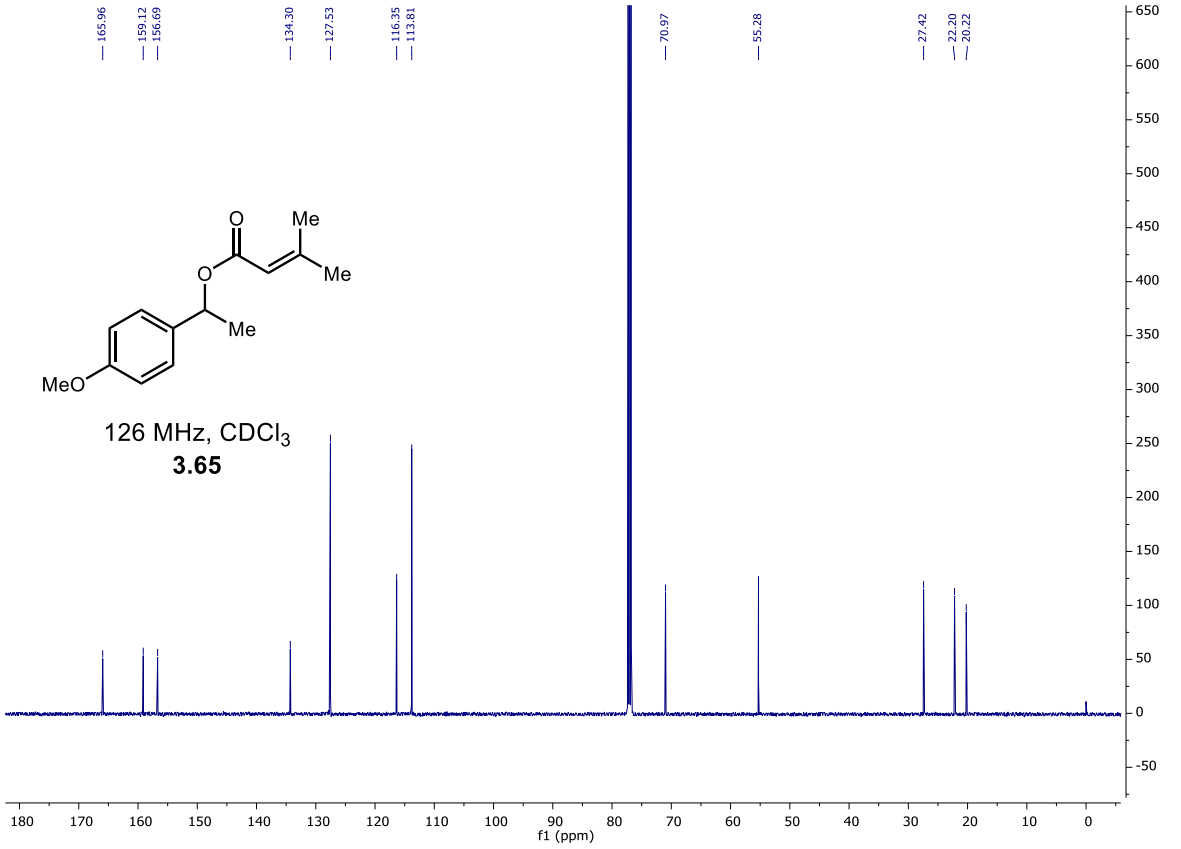

7.30
7.28
6.88
6.87
5.88
5.86
5.85
5.84
3.80
2.32
2.31
2.30
2.30
2.29
2.28
1.62
1.61
1.61
1.61
1.60
1.59
1.59
1.58
1.57
1.57
1.56
1.52
1.51
1.34
1.33
1.33
1.31
1.31
1.30
1.30
0.91
0.89
0.88
O
O
Me
Me
MeO
500 MHz, CDCl3
3.63
1.99
2.00
0.99
3.06
1.93
2.31
2.97
2.06
3.01
f1 (ppm)

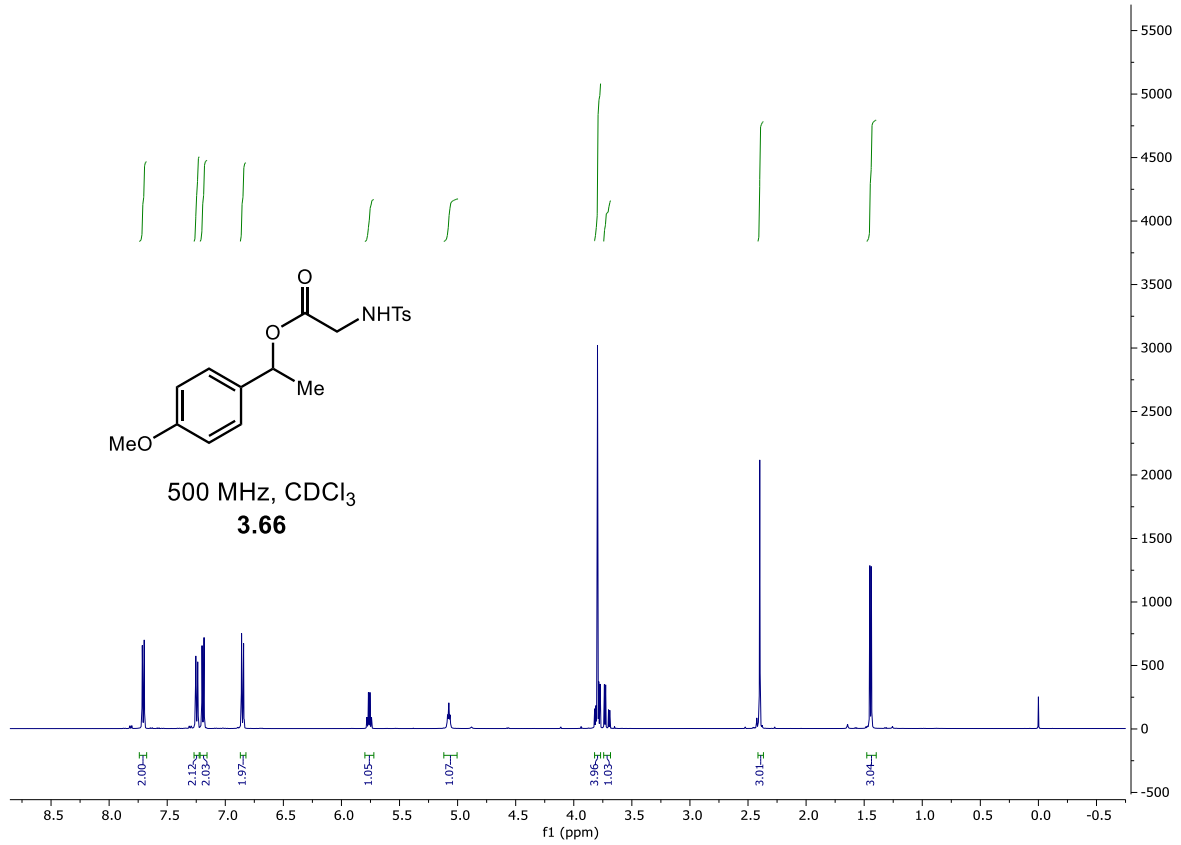

173.17
159.19
133.94
127.54
113.80
71.71
55.28
34.39
27.03
22.23
22.03
13.72
O
O
Me
Me
MeO
126 MHz, CDCl3
3.63
f1 (ppm)

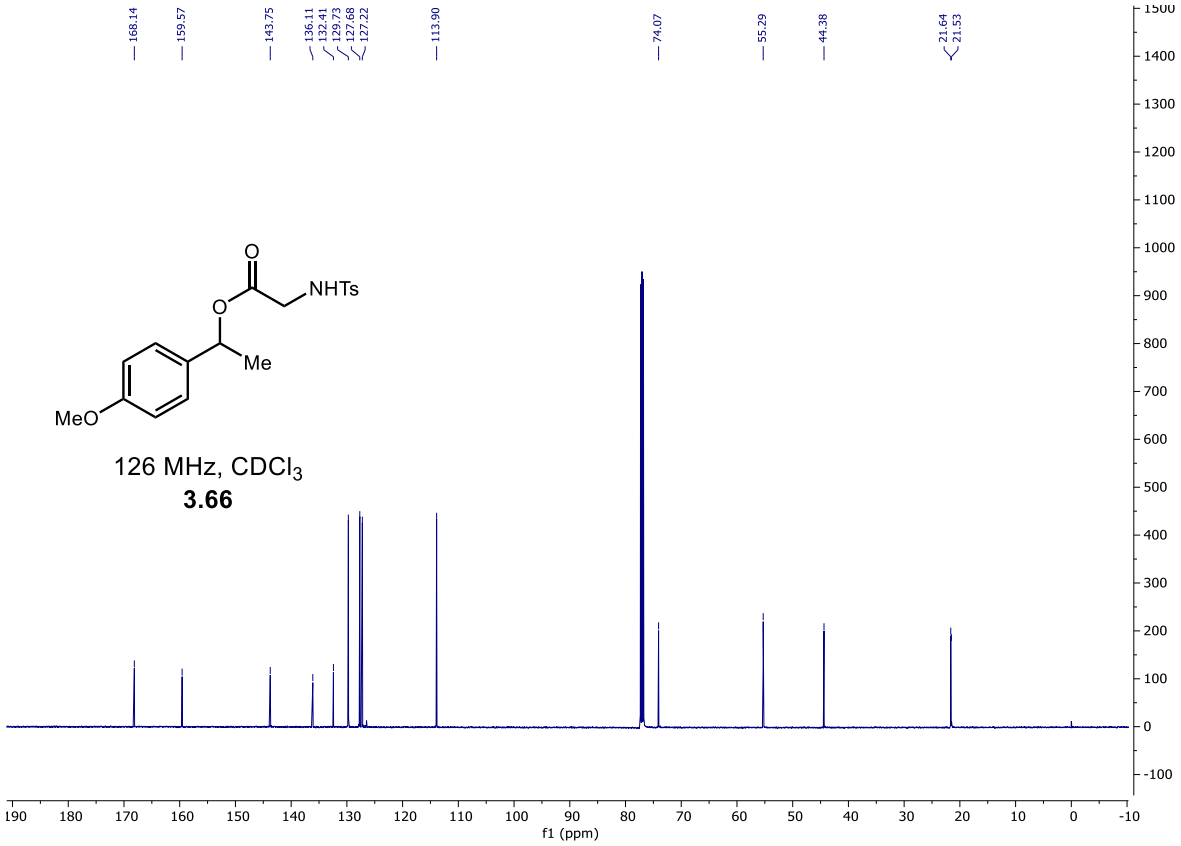

8.07
8.07
8.06
8.05
8.05
7.56
7.56
7.55
7.54
7.54
7.53
7.53
7.52
7.44
7.44
7.43
7.41
7.41
7.40
7.38
6.91
6.89
6.89
6.12
6.11
6.09
6.08
3.80
1.66
1.65
O
O
Me
MeO
500 MHz, CDCl3
3.64
1.97
1.00
2.05
1.92
2.00
0.98
3.11
2.93
f1 (ppm)

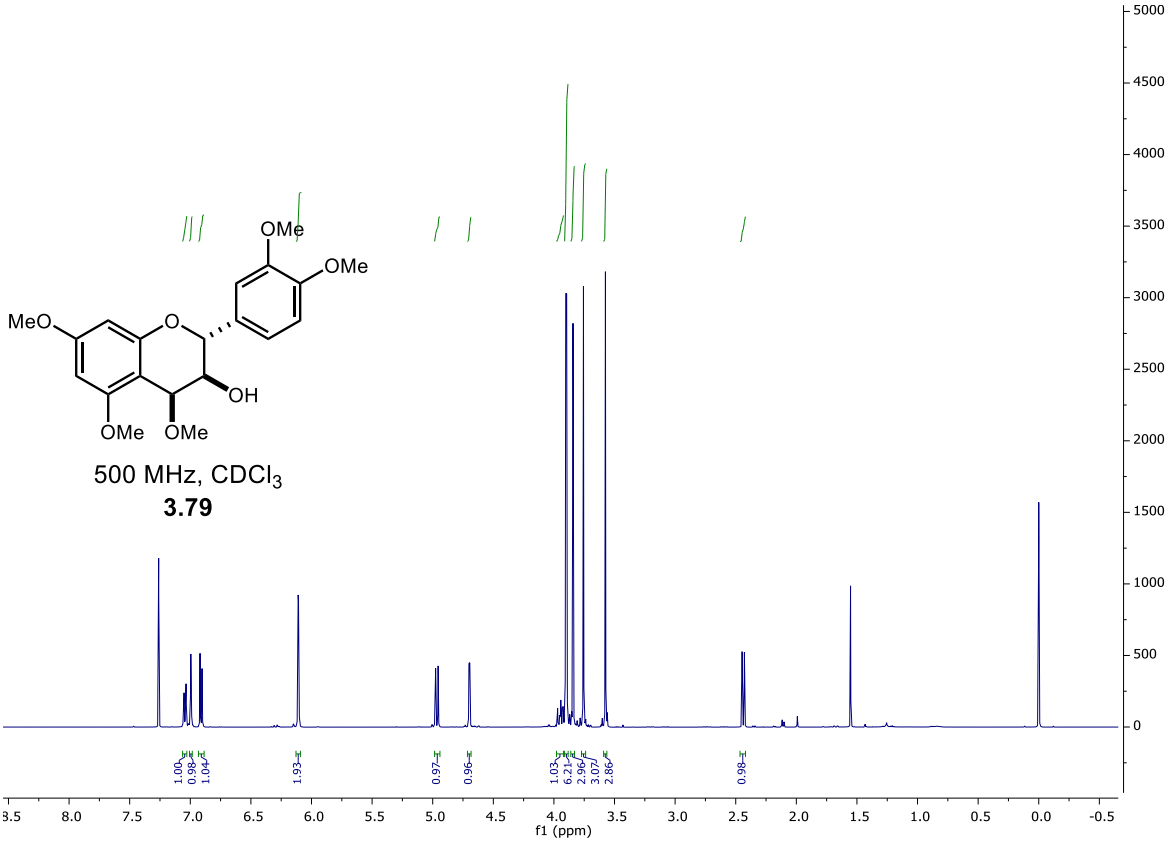

165.87
159.28
133.86
132.84
130.63
129.62
128.30
127.56
113.88
72.65
55.28
22.18
O
O
Me
MeO
126 MHz, CDCl3
3.64
f1 (ppm)

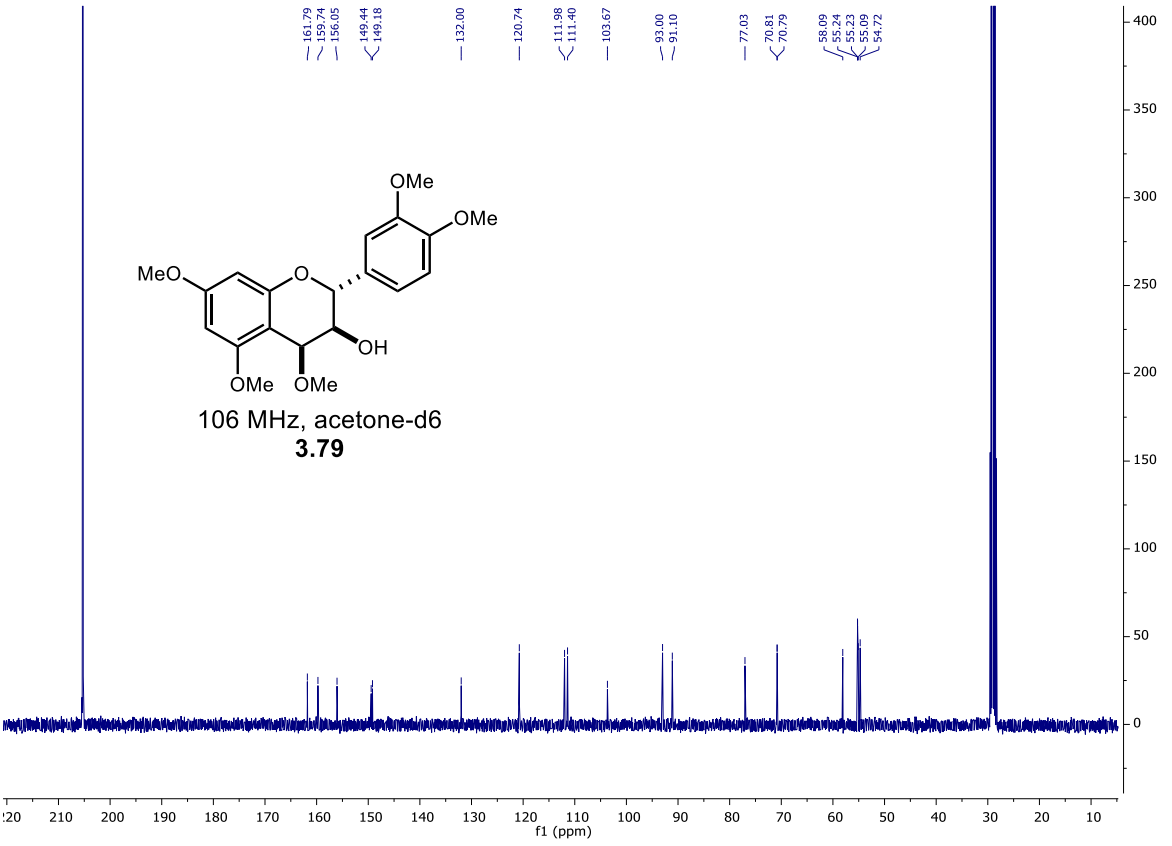

7.31
7.29
6.88
6.86
5.89
5.88
5.87
5.85
5.70
5.70
5.70
5.70
3.79
2.15
2.15
1.88
1.87
1.54
1.52
O
Me
O
Me
Me
MeO
500 MHz, CDCl3
3.65
1.99
2.00
0.99
0.99
3.00
2.95
2.95
2.97
f1 (ppm)

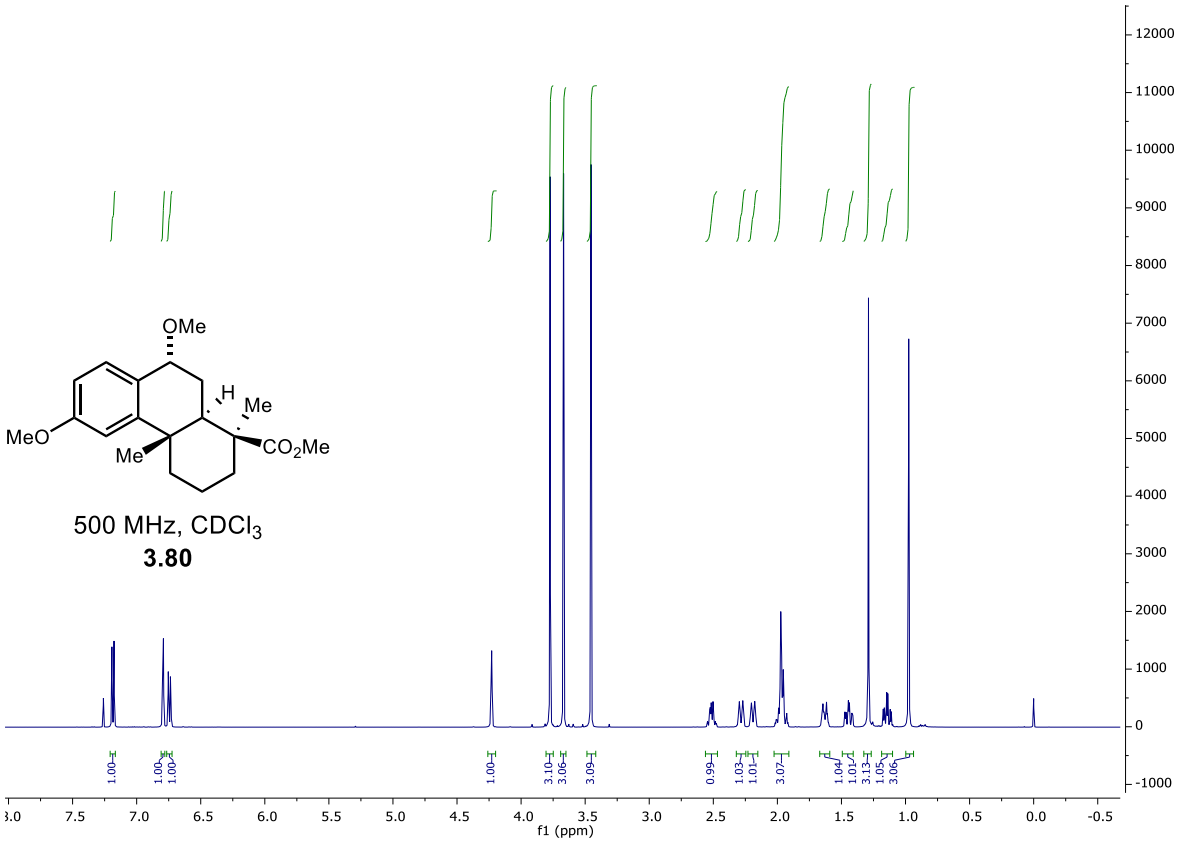

165.96
159.12
156.69
134.30
127.53
116.35
113.81
70.97
55.28
27.42
22.20
20.22
O
Me
O
Me
Me
MeO
126 MHz, CDCl3
3.65
f1 (ppm)

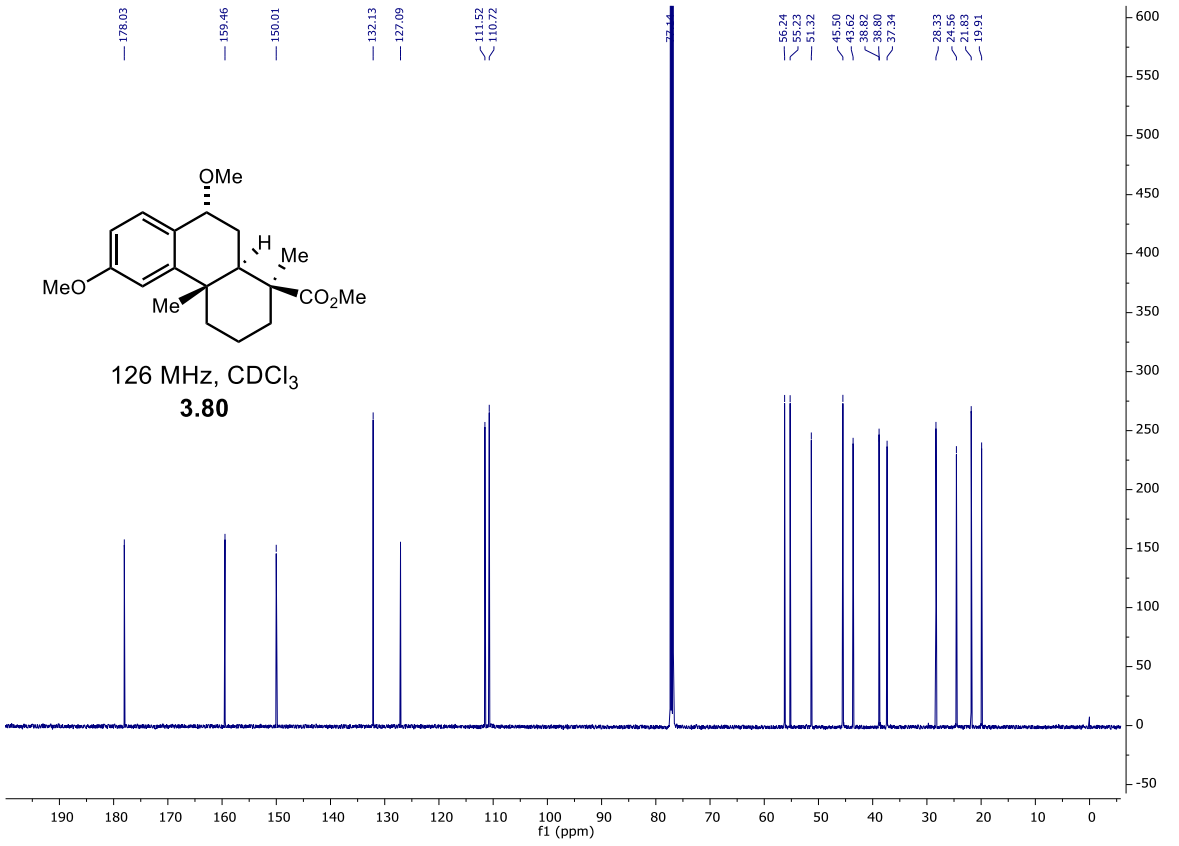

O
NHTs
O
Me
MeO
500 MHz, CDCl3
3.66
f1 (ppm)

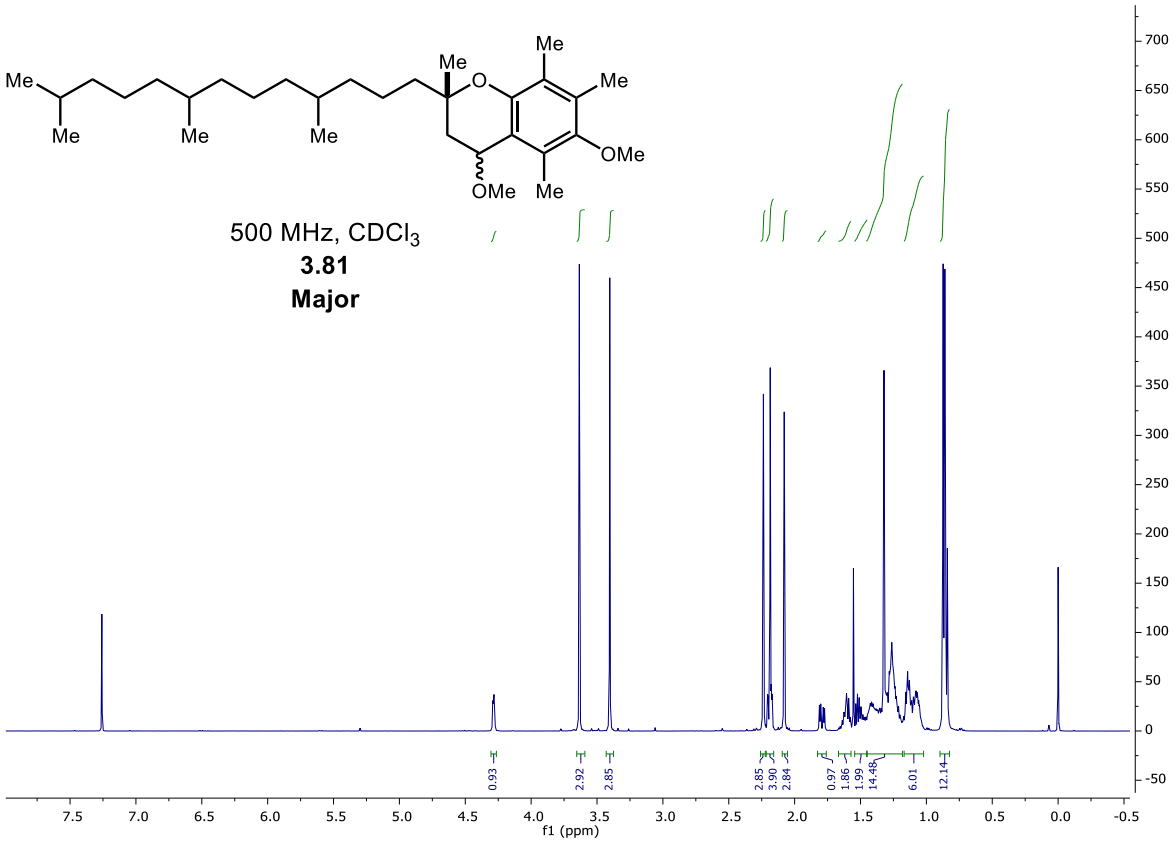

168.14
159.57
143.75
136.11
132.41
129.73
127.68
127.22
113.90
74.07
55.29
44.38
21.64
21.53
O
NHTs
O
Me
MeO
126 MHz, CDCl3
3.66
f1 (ppm)

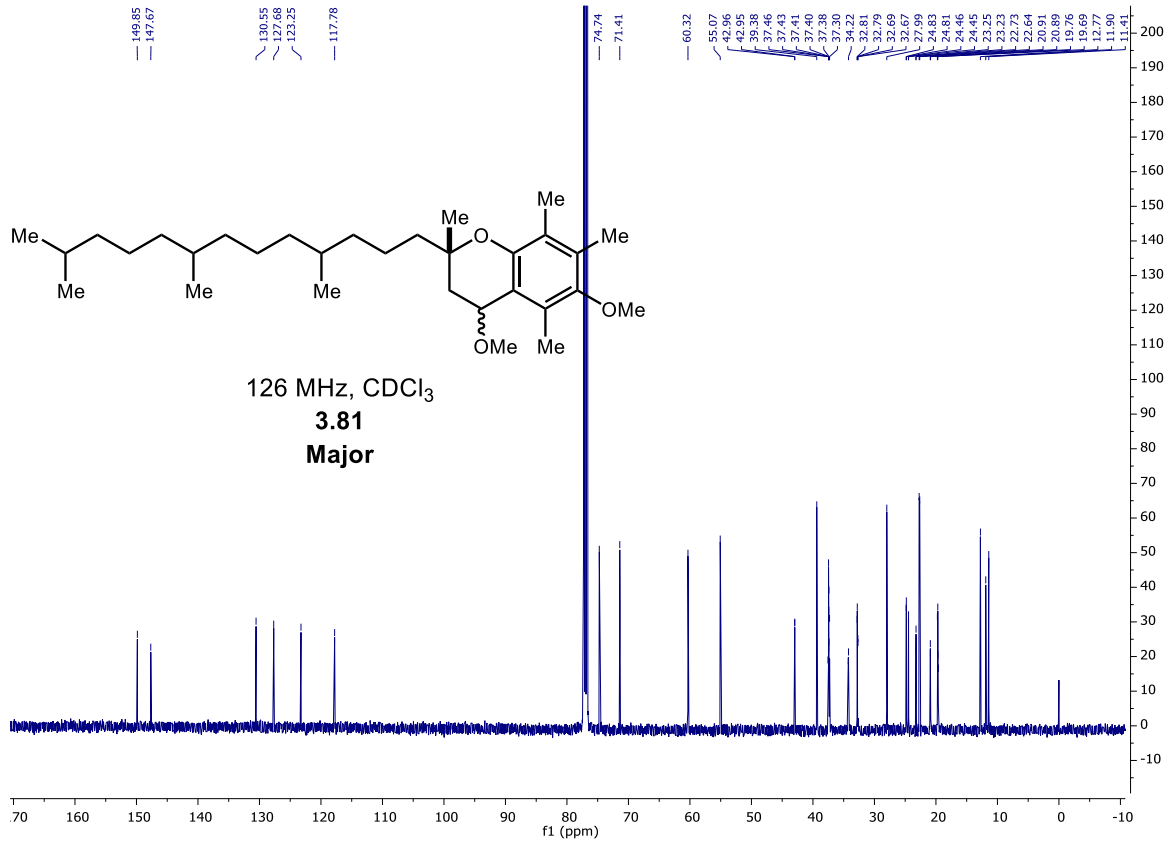

OMe
OMe
MeO
O
OH
OMe
OMe
500 MHz, CDCl3
3.79
f1 (ppm)

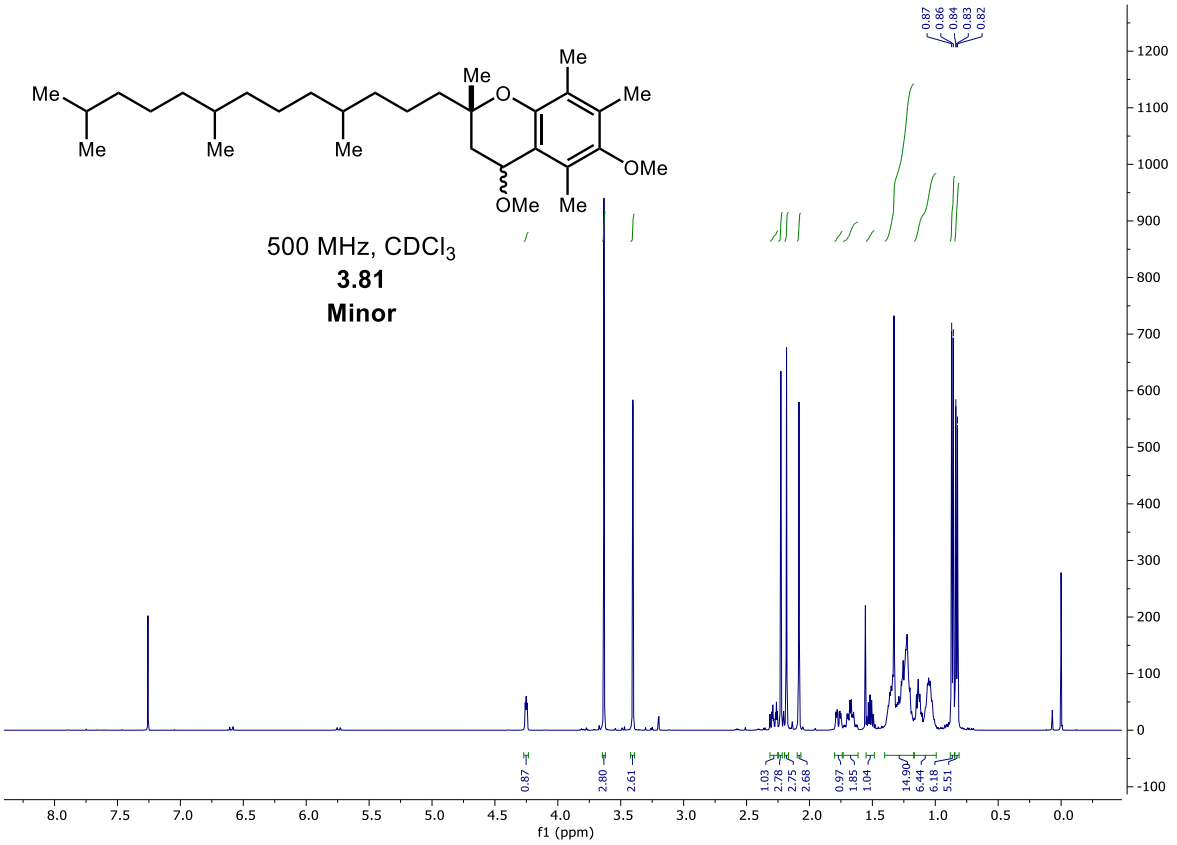

161.79
159.74
156.05
149.44
149.18
132.00
120.74
111.98
111.40
103.67
93.00
91.10
77.03
70.81
70.79
58.09
55.24
55.23
55.09
54.72
OMe
OMe
MeO
O
OH
OMe
OMe
106 MHz, acetone-d6
3.79
f1 (ppm)

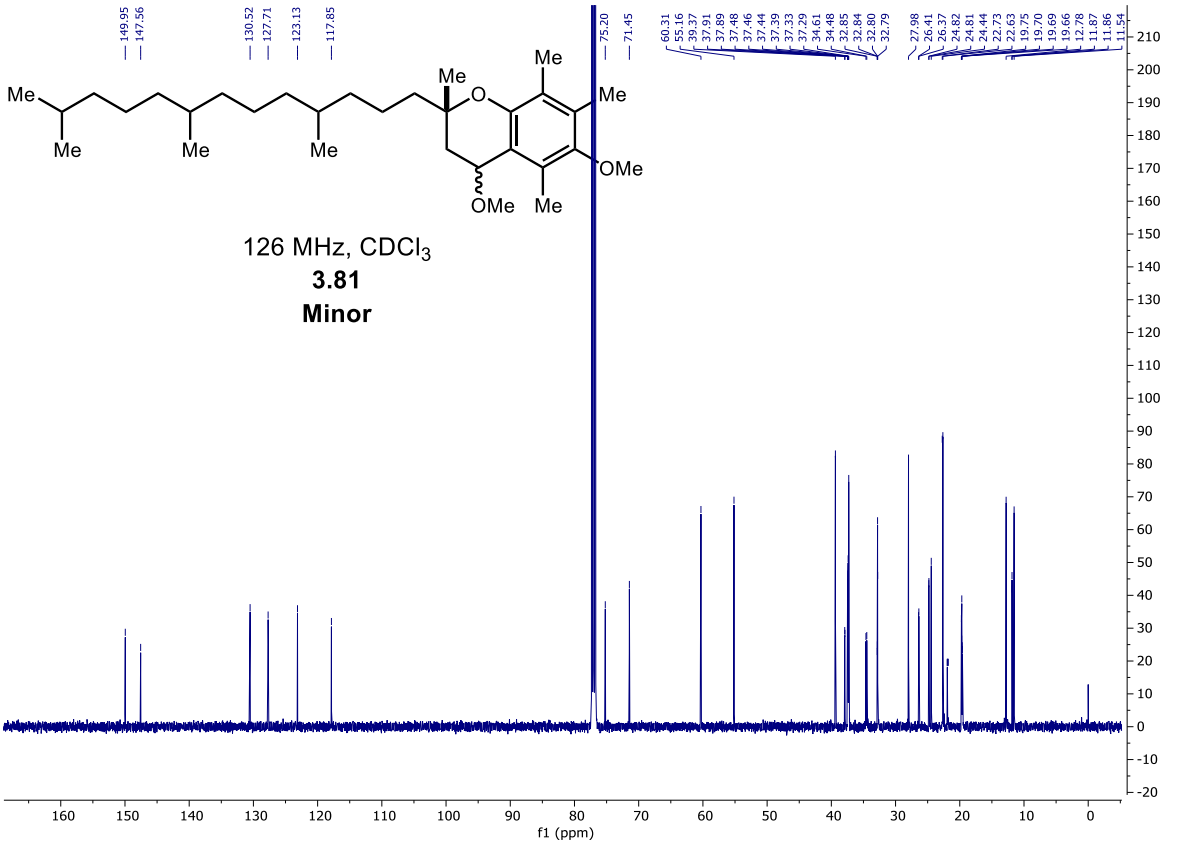

OMe
H
Me
MeO
Me
CO2Me
500 MHz, CDCl3
3.80
f1 (ppm)

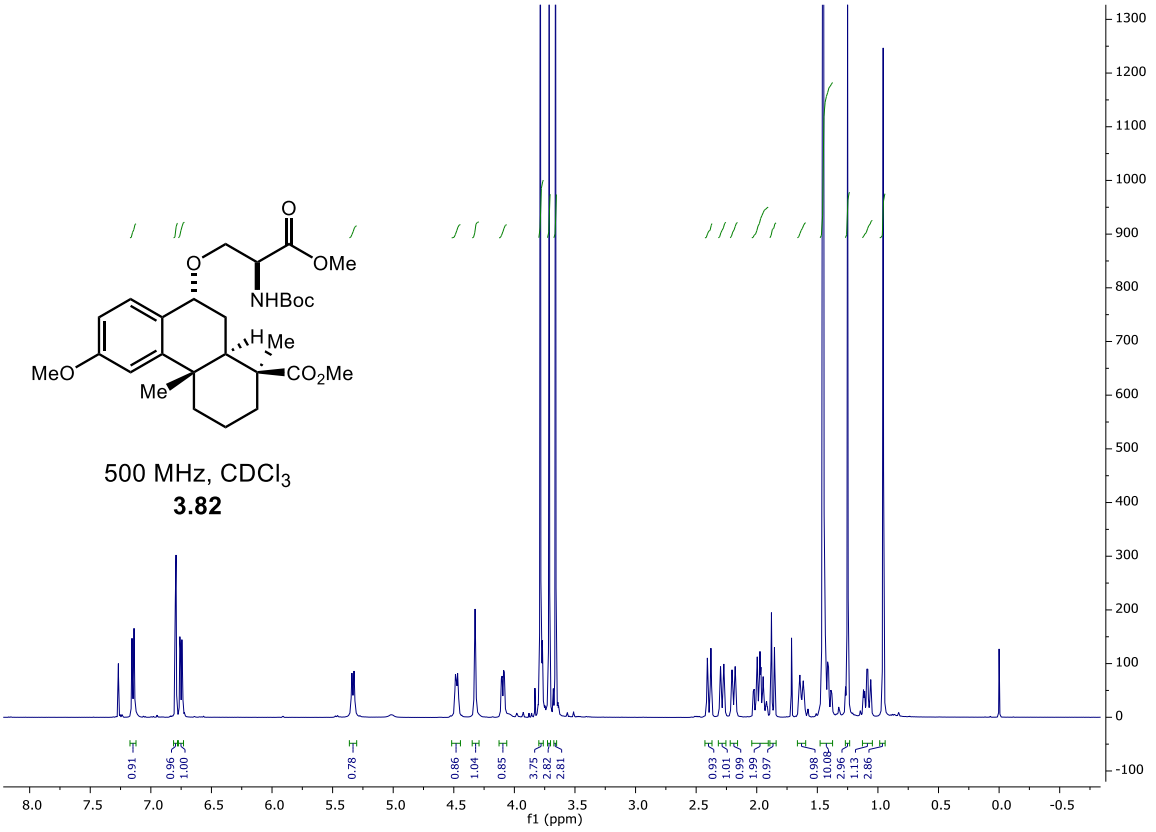

178.03
159.46
150.01
132.13
127.09
111.52
110.72
56.24
55.23
51.32
45.50
43.62
38.82
38.80
37.34
28.33
24.56
21.83
19.91
OMe
H
Me
MeO
Me
CO2Me
126 MHz, CDCl3
3.80
f1 (ppm)

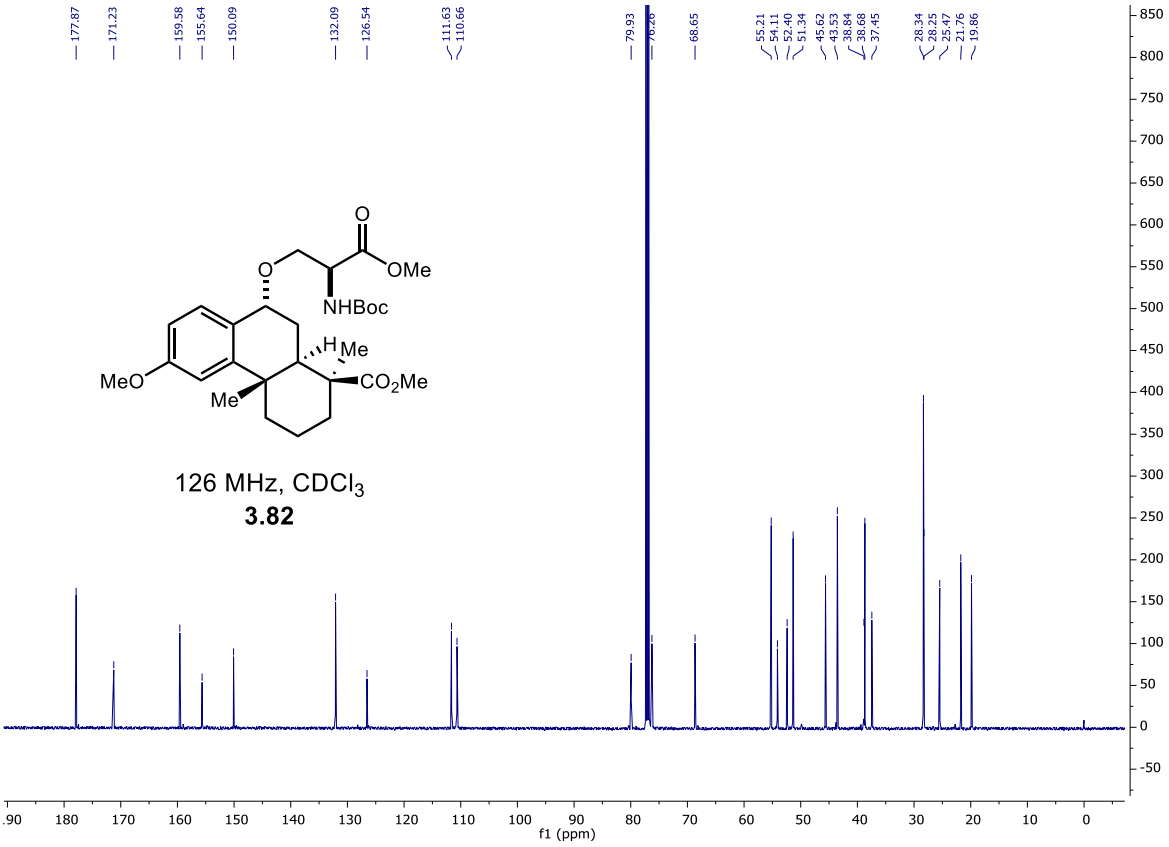

Me
Me
Me
Me
Me
Me
O
Me
OMe
OMe
Me
500 MHz, CDCl3
3.81
Major
f1 (ppm)

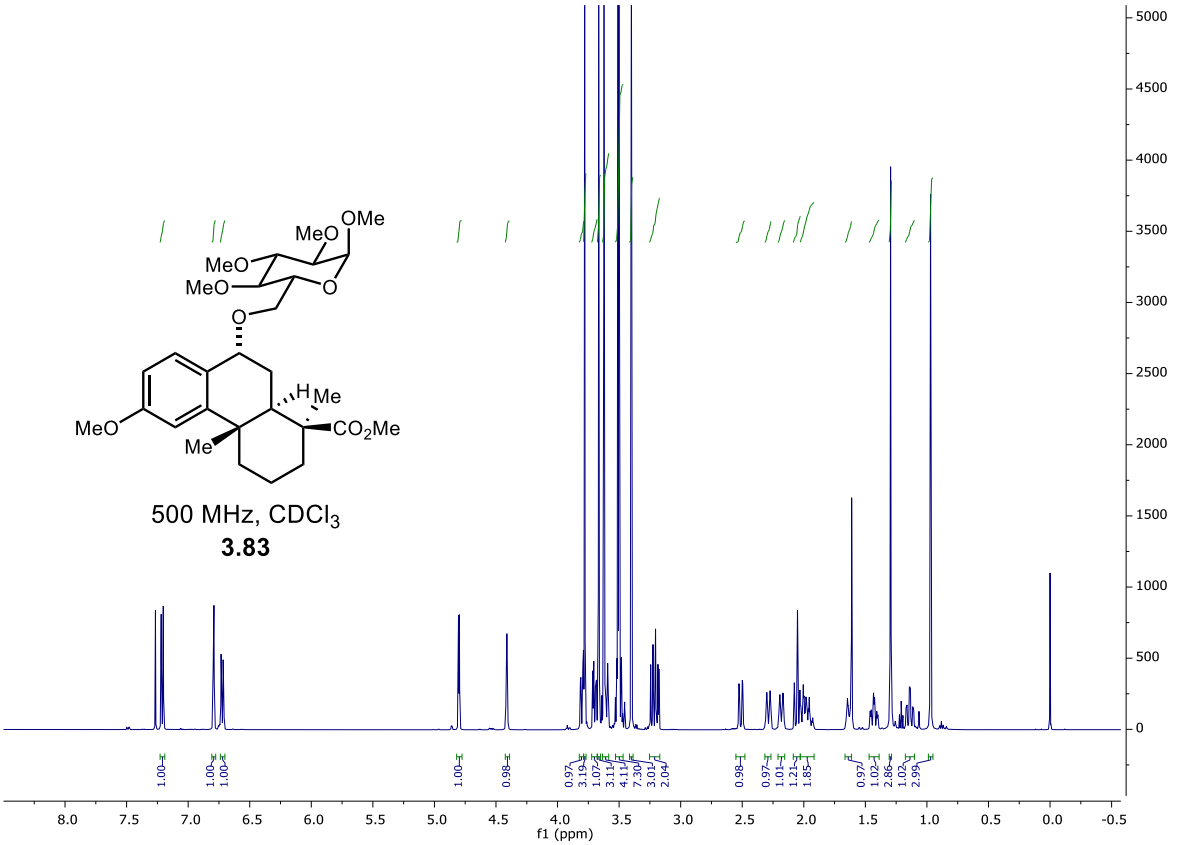

Me
Me
Me
Me
Me
Me
O
Me
OMe
OMe
Me
126 MHz, CDCl3
3.81
Major
f1 (ppm)


500 MHz, CDCl3
3.81
Minor
f1 (ppm)


126 MHz, CDCl3
3.81
Minor
f1 (ppm)


500 MHz, CDCl3
3.82
f1 (ppm)

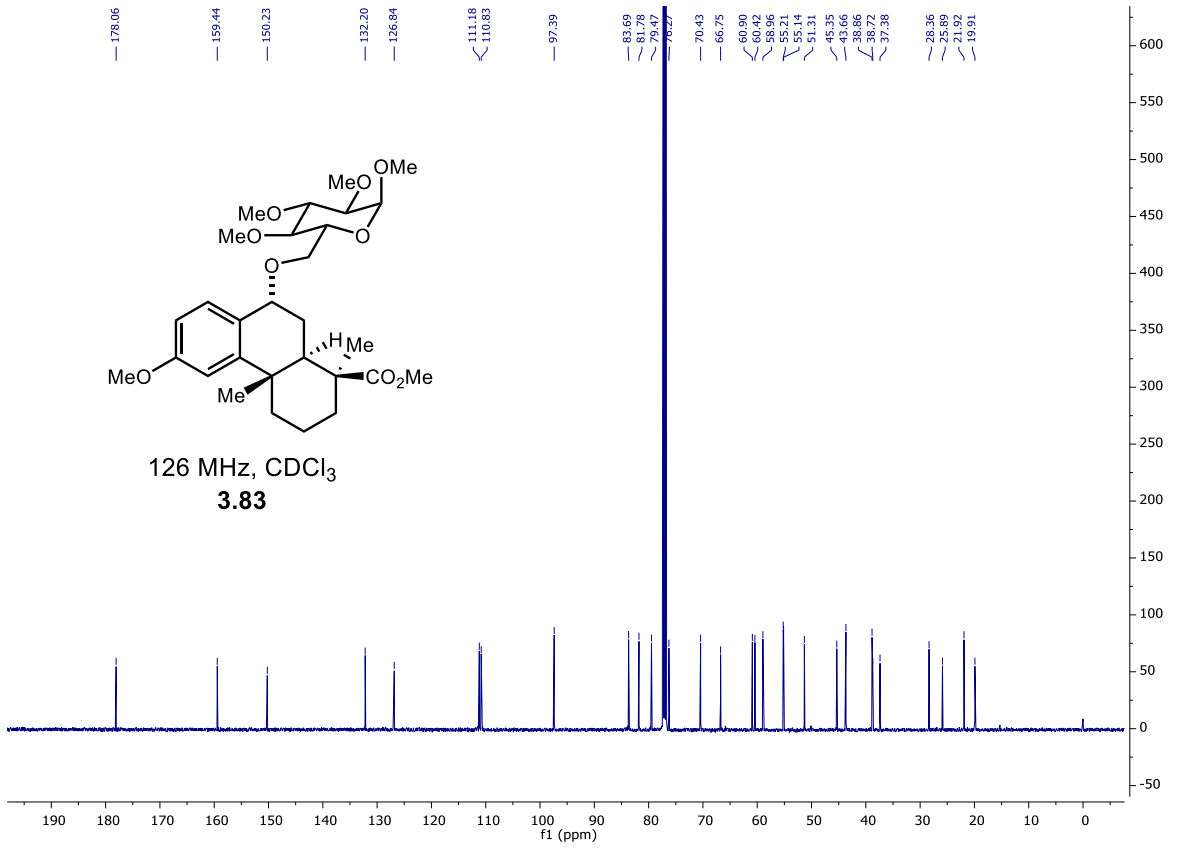

126 MHz, CDCl3
3.82
f1 (ppm)




500 MHz, $CDCl_3$

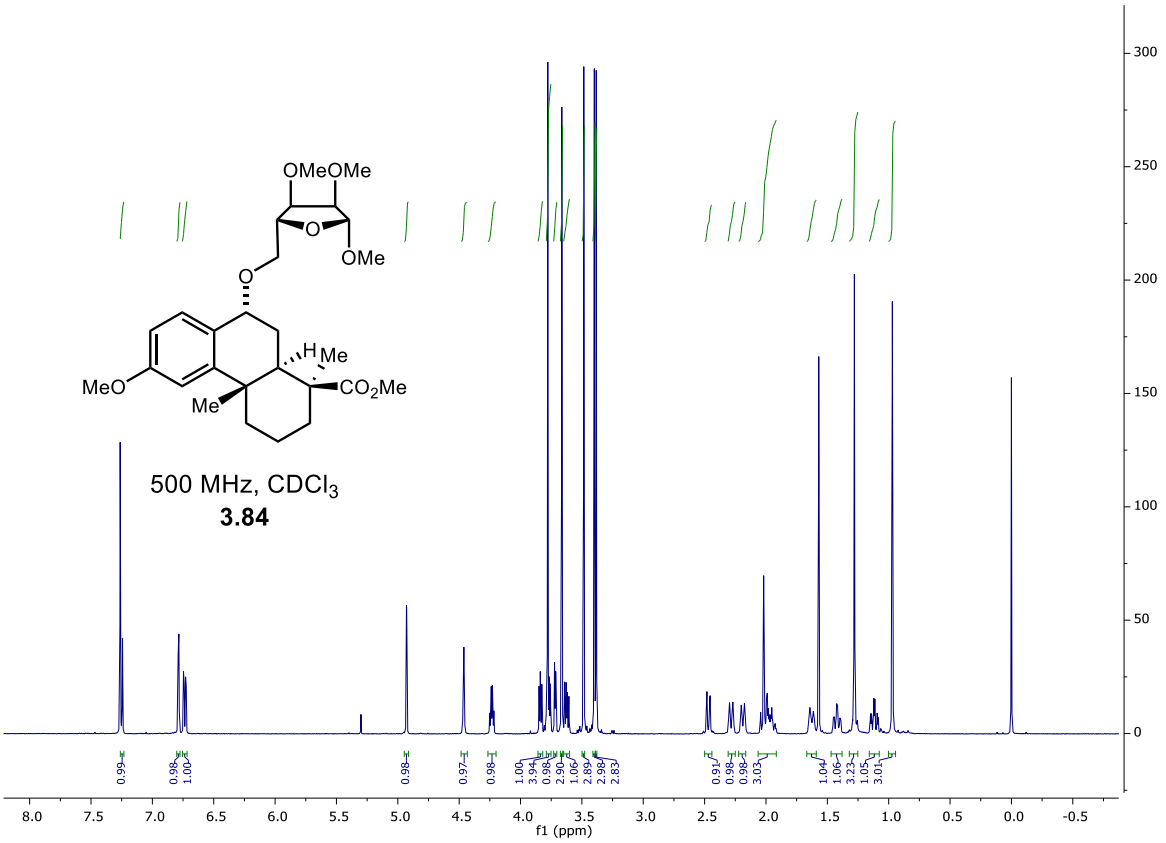
**3.83**

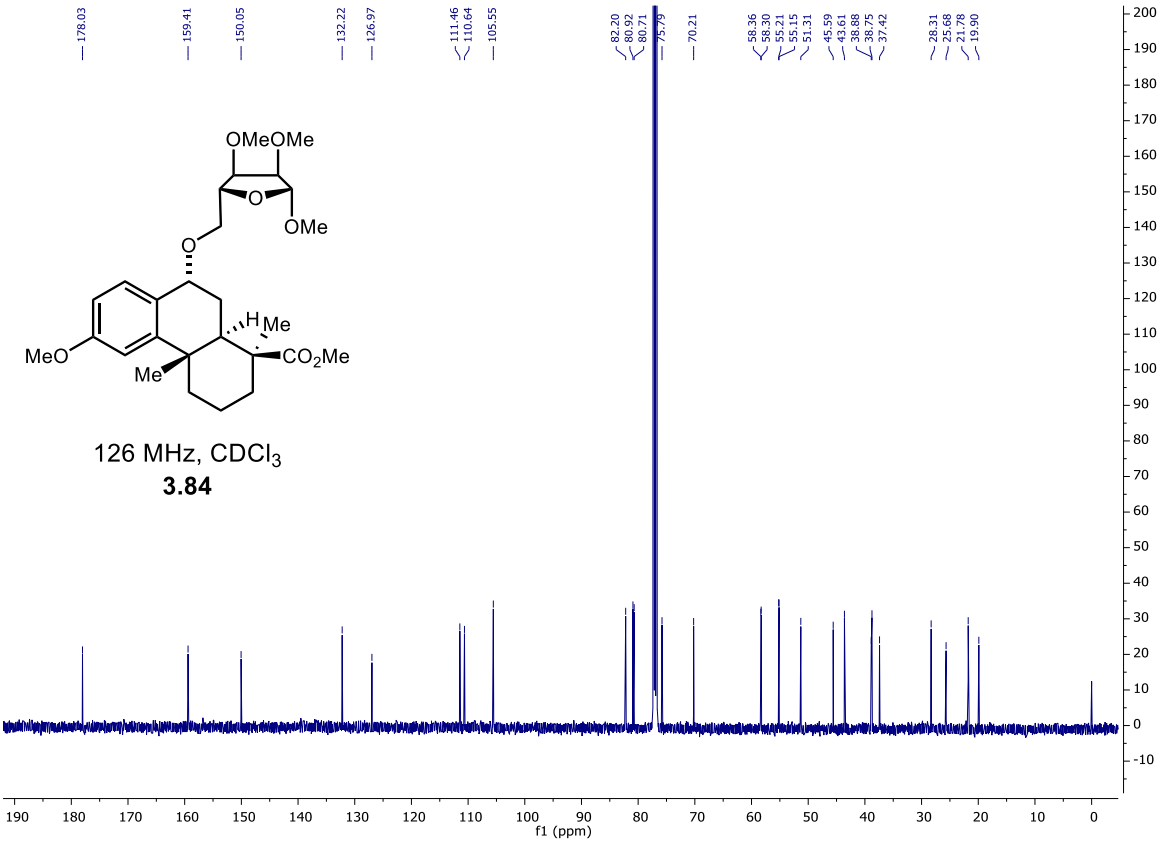
I

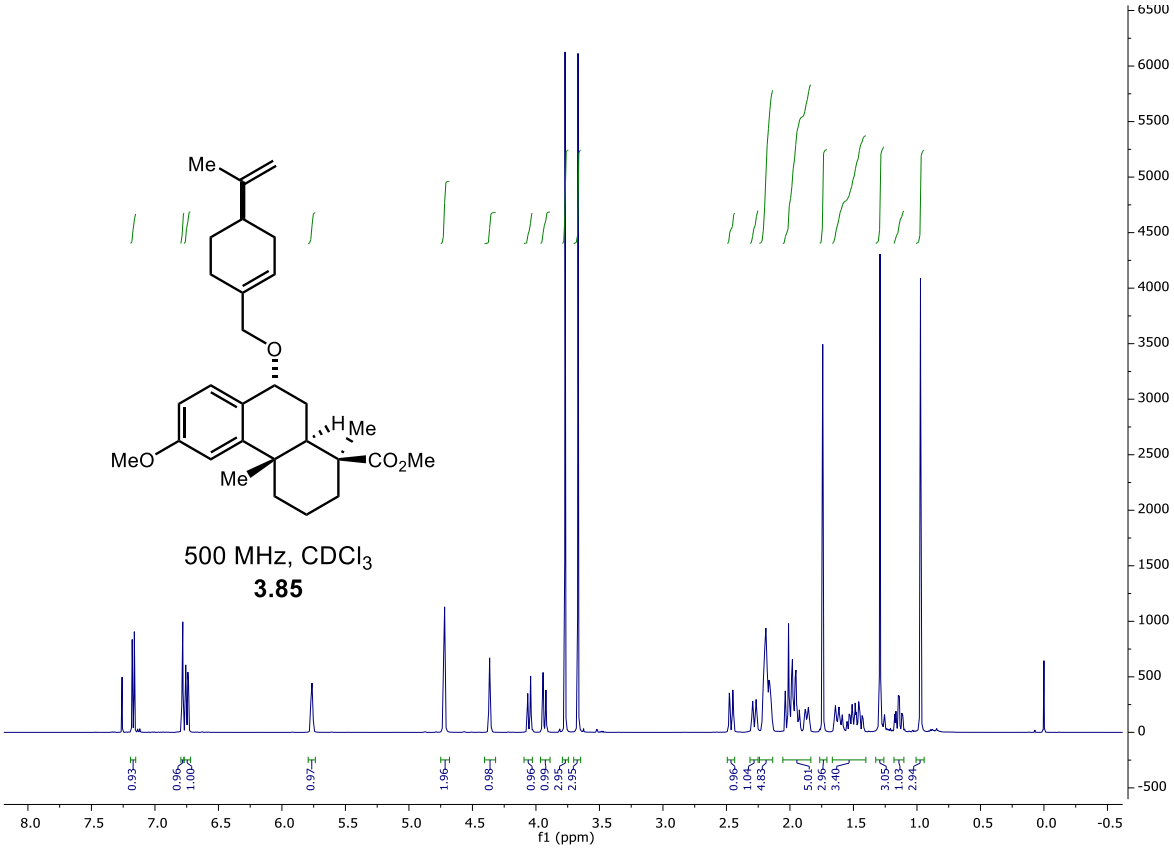


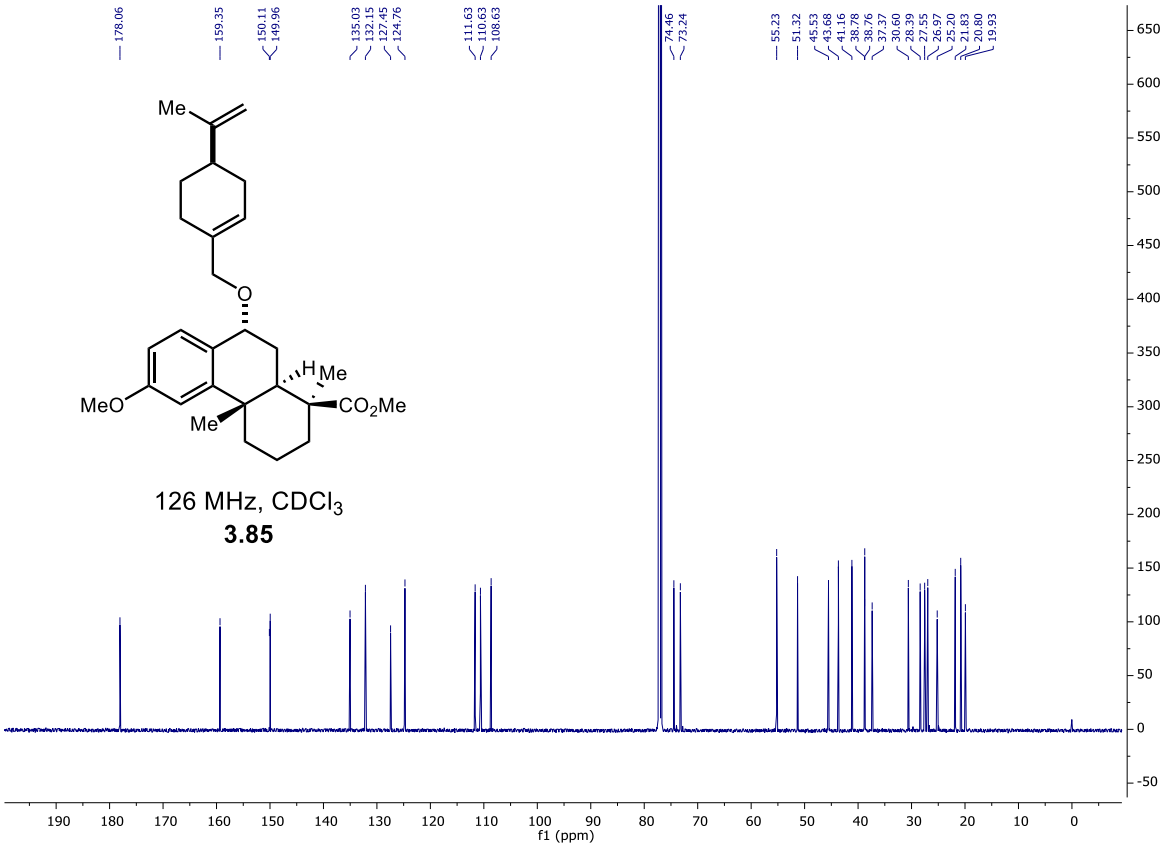

126 MHz, $CDCl_3$

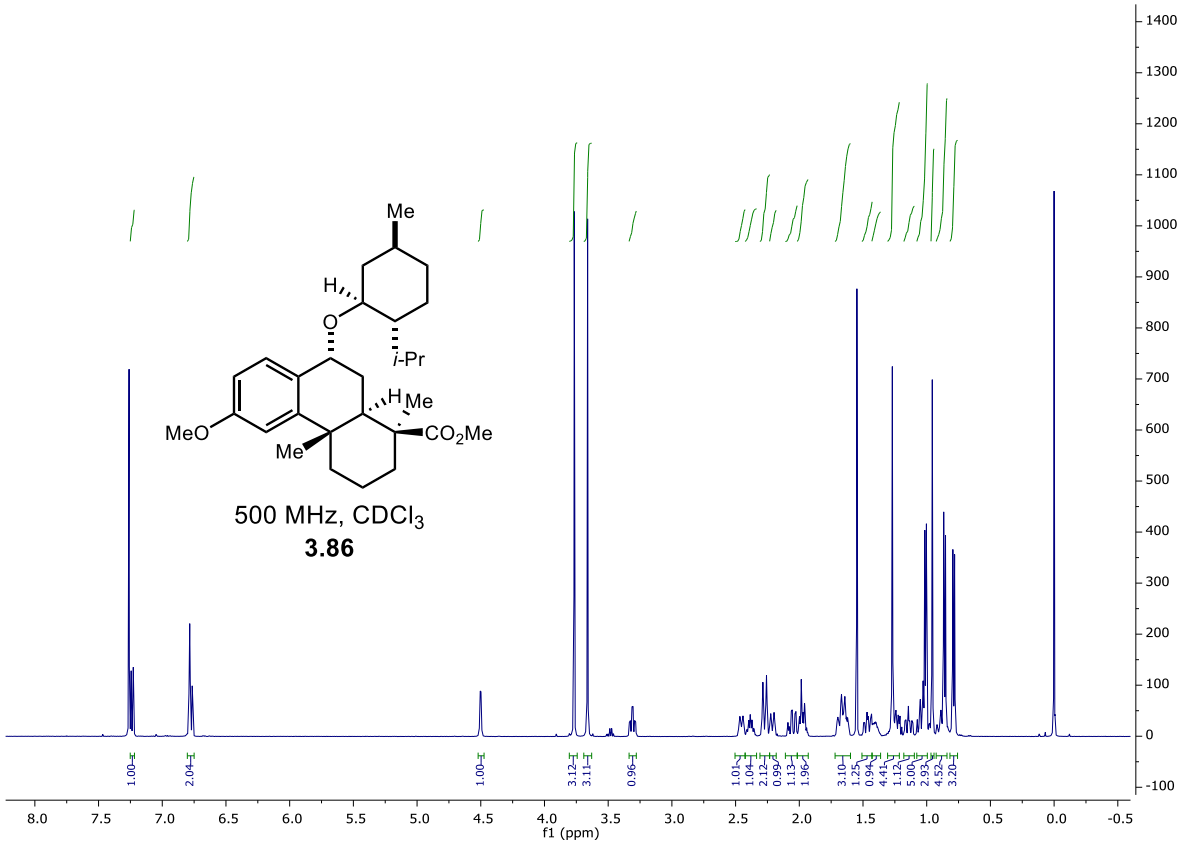
**3.83**

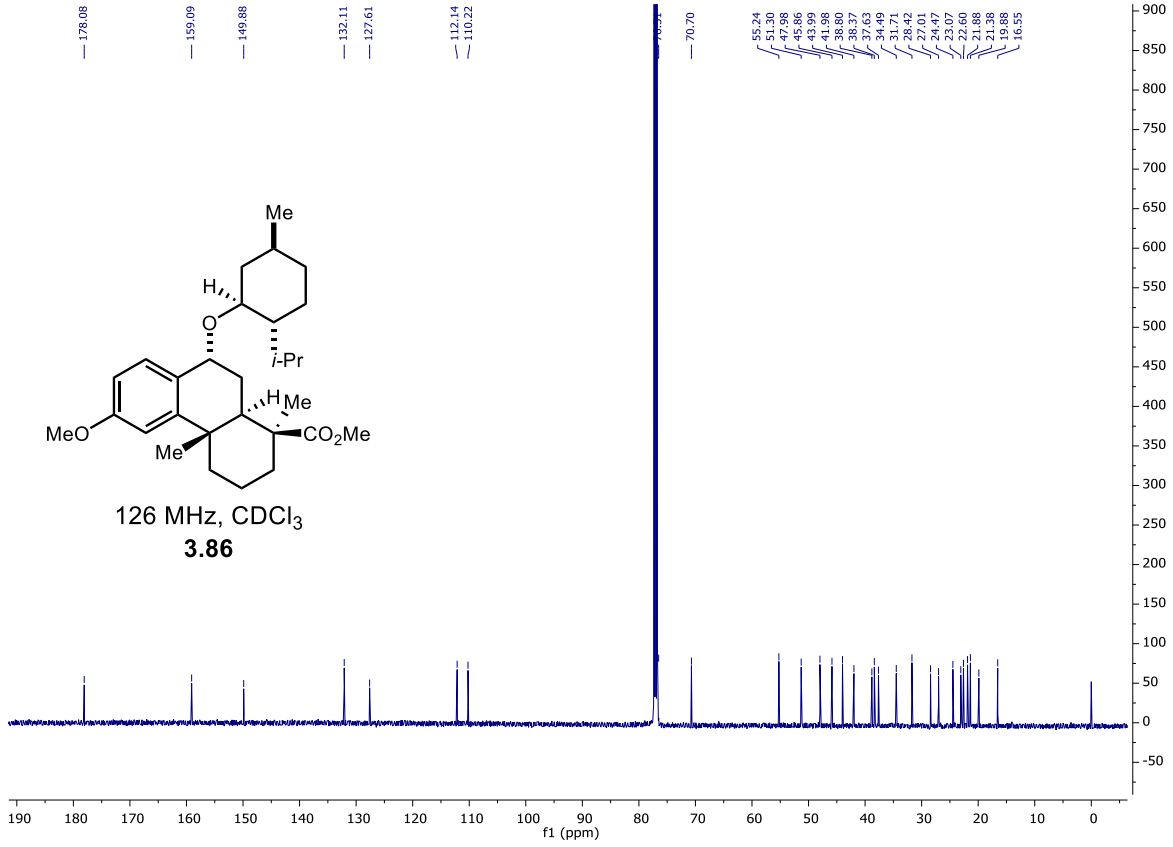

OMeOMe
O
OMe
O
H
Me
MeO
CO2Me
Me
500 MHz, CDCl3
3.84
f1 (ppm)


178.03
159.41
150.05
132.22
126.97
111.46
110.64
105.55
82.20
80.92
80.71
75.79
70.21
58.36
58.30
55.21
55.15
51.31
45.59
43.61
38.88
38.75
37.42
28.31
25.68
21.78
19.90
OMeOMe
O
OMe
O
H
Me
MeO
CO2Me
Me
126 MHz, CDCl3
3.84
f1 (ppm)

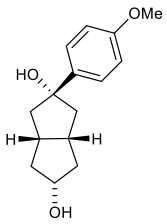

Me
O
H
Me
MeO
CO2Me
Me
500 MHz, CDCl3
3.85
f1 (ppm)


178.06
159.35
150.11
149.96
135.03
132.15
127.45
124.76
111.63
110.63
108.63
74.46
73.24
55.23
51.32
45.53
43.68
41.16
38.78
38.76
37.37
30.60
28.39
27.55
26.97
25.20
21.83
20.80
19.93
Me
O
H
Me
MeO
CO2Me
Me
126 MHz, CDCl3
3.85
f1 (ppm)

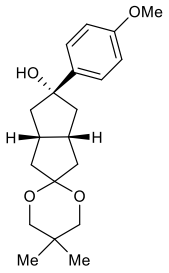

Me
H
O
i-Pr
H
Me
MeO
CO2Me
Me
500 MHz, CDCl3
3.86
f1 (ppm)


Me
H
O
i-Pr
H
Me
MeO
CO2Me
Me
126 MHz, CDCl3
3.86
f1 (ppm)

# List of Compounds for Chapter 4

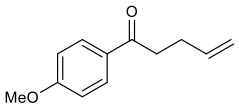



**4.19**

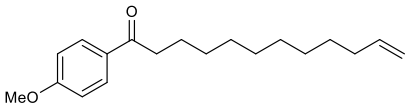



**4.20**

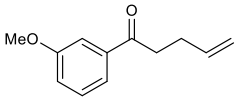
# List of Compounds for Chapter 4



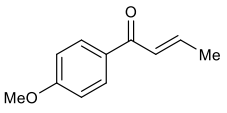

**4.6a**



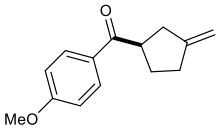

**4.12a**



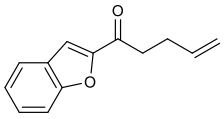

**4.21a**



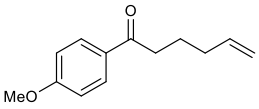

**4.8a**



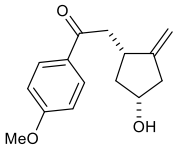

**4.15a''**



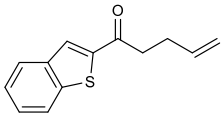

**4.22a**



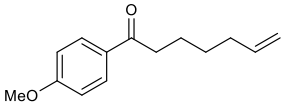

**4.9a**



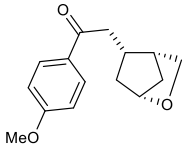

**4.19a**



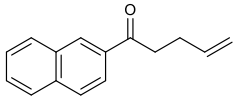

**4.23a**



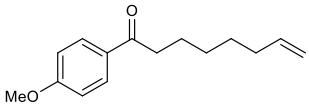

**4.10a**



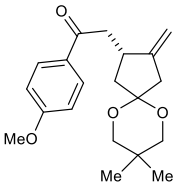

**4.19c**



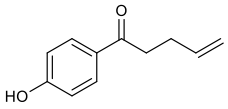

**4.24a**



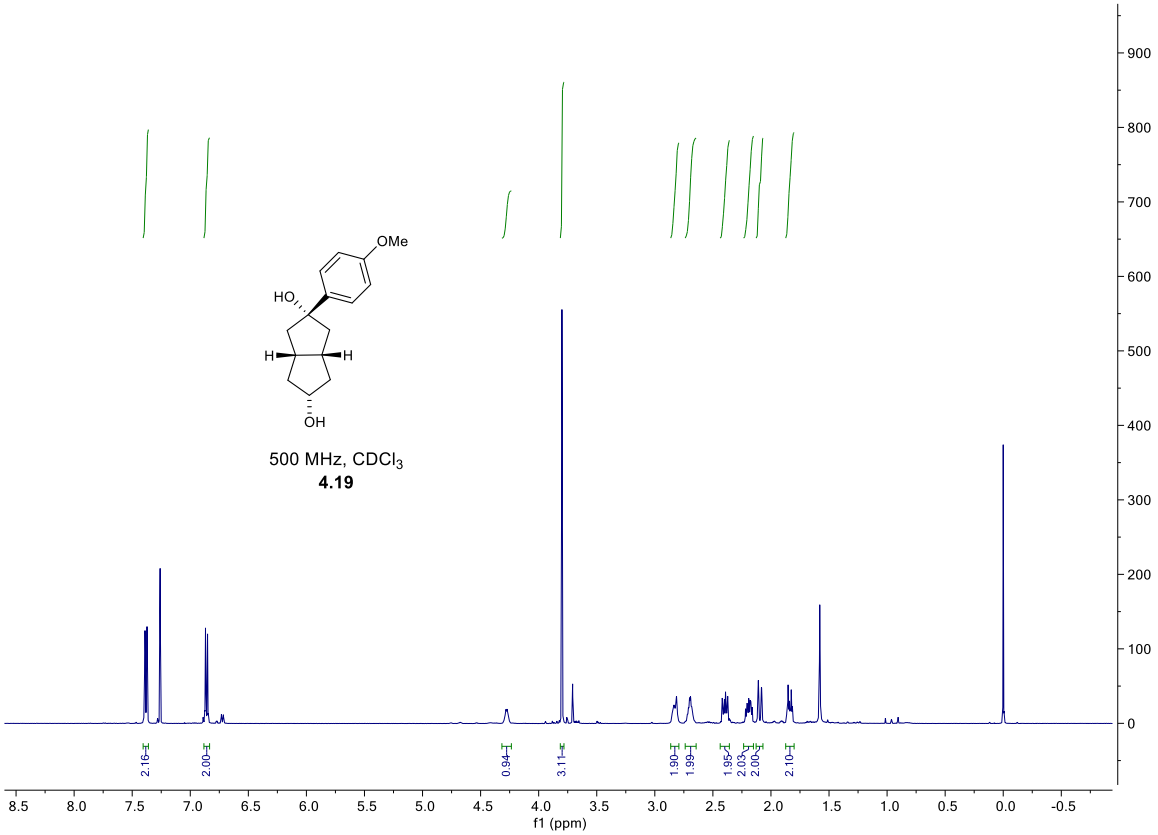

**4.11a**

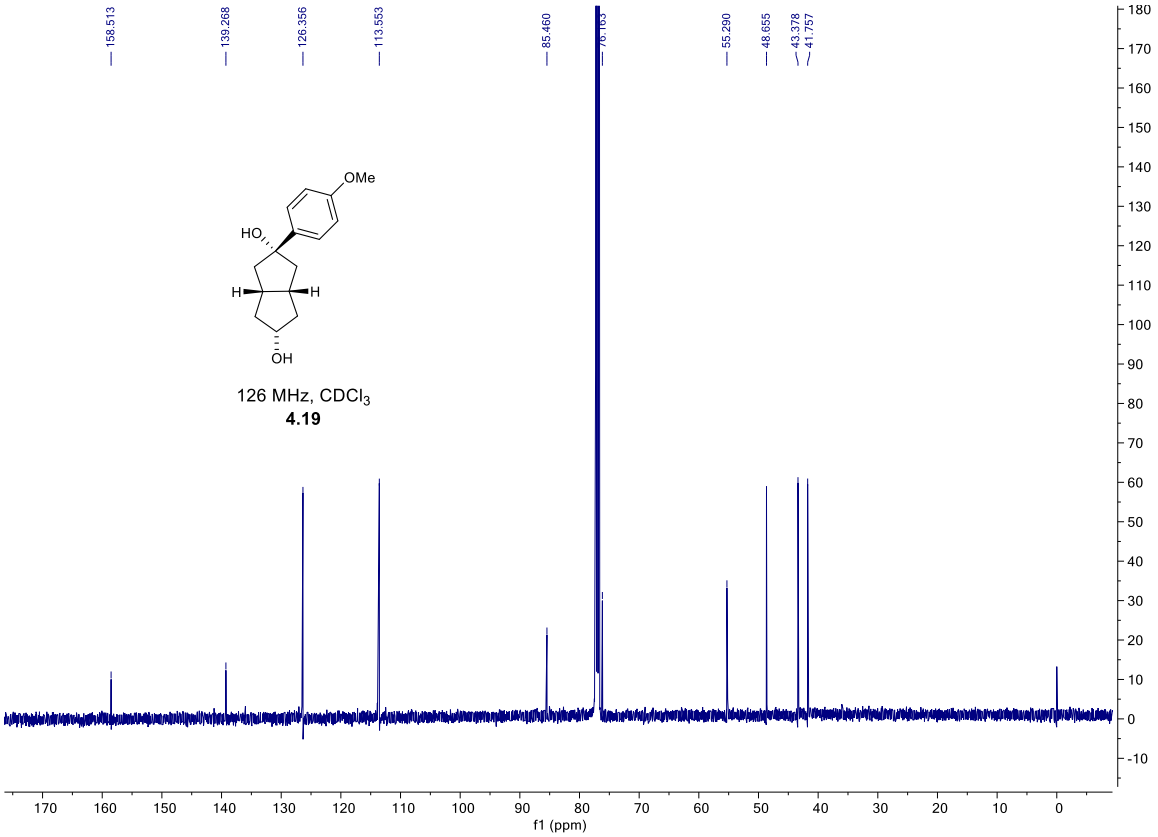


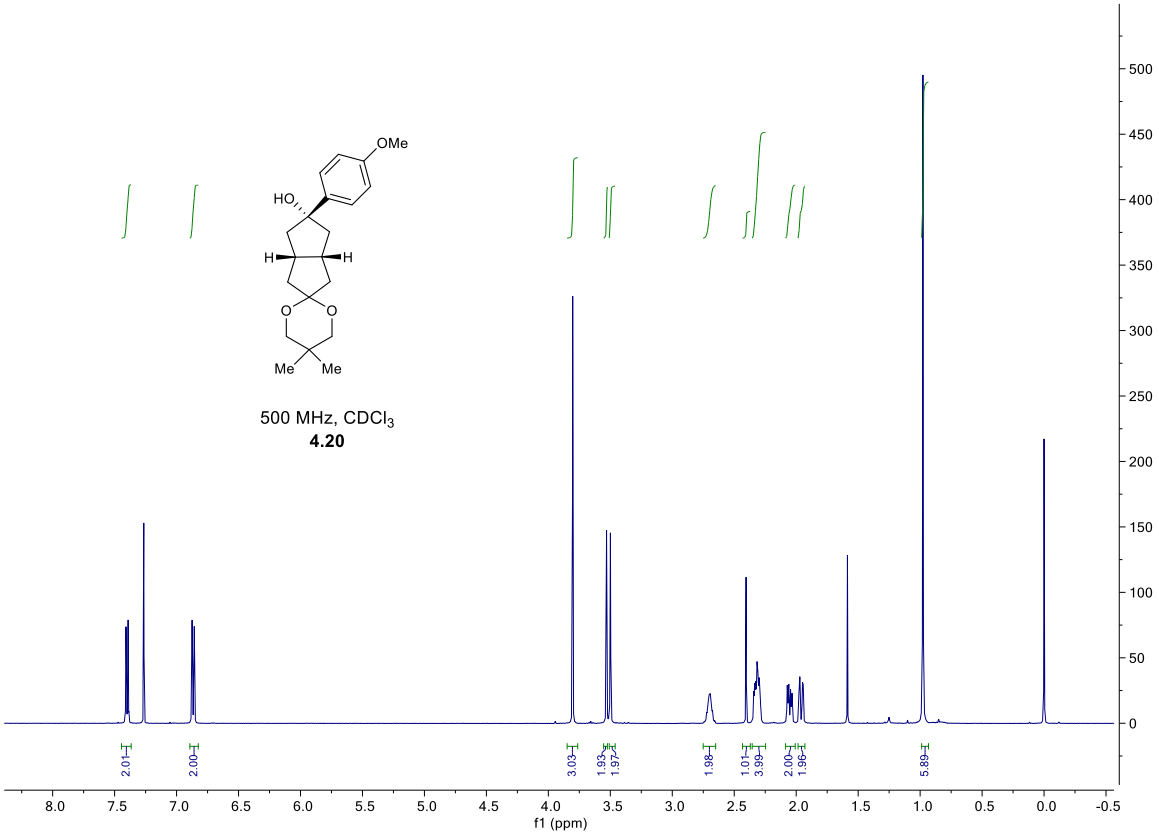

**4.20a**

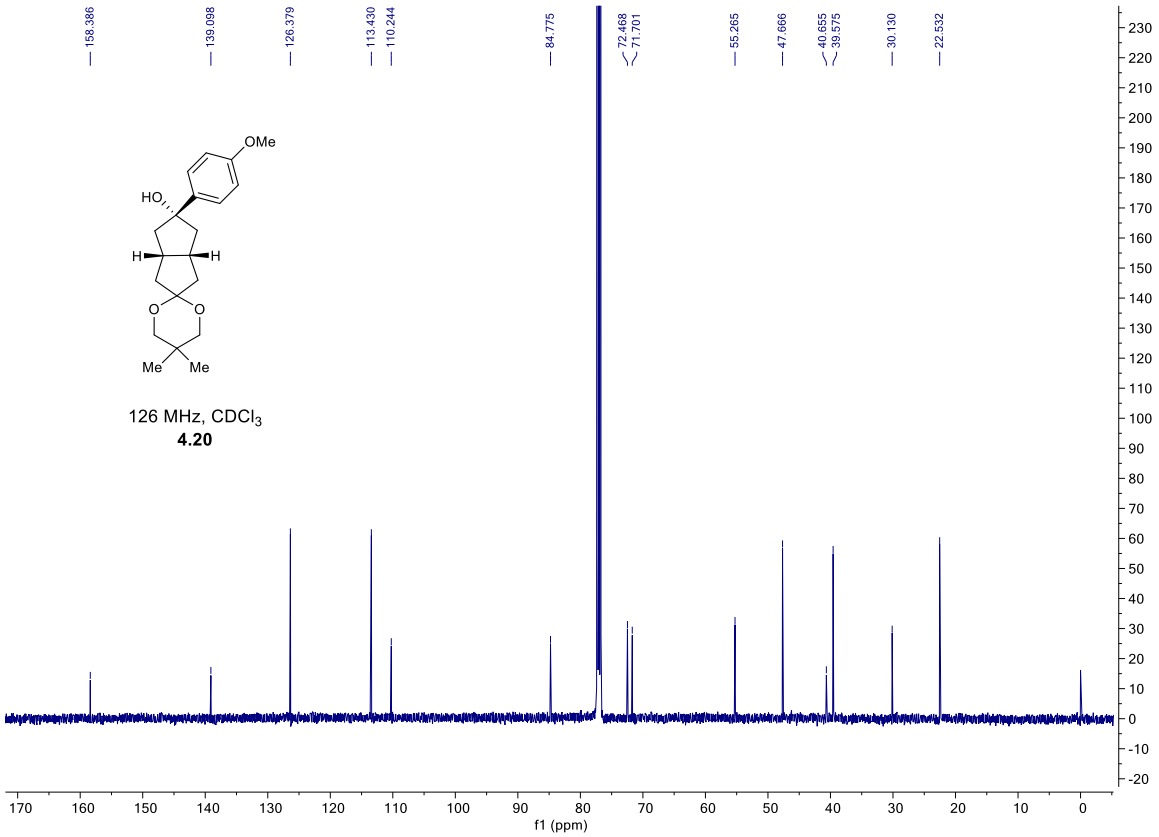


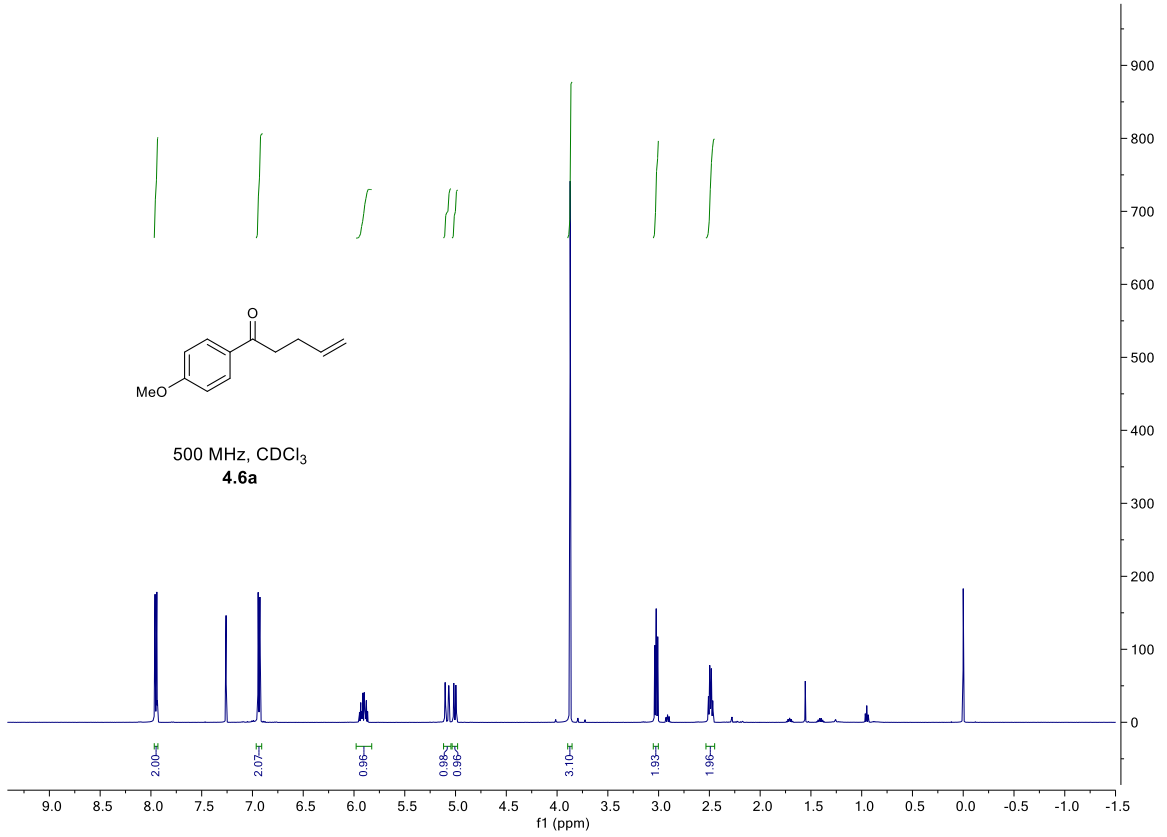

**4.25a**

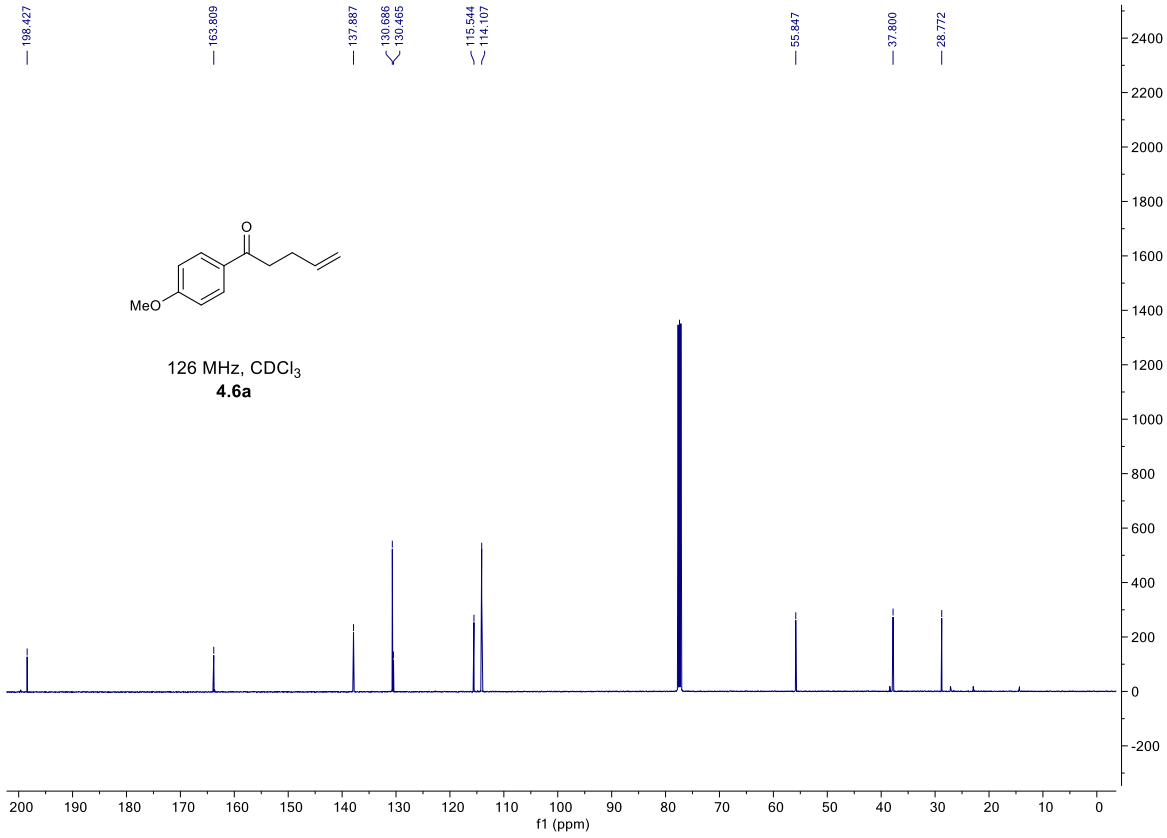

OMe
HO
H
H
OH
500 MHz, CDCl3
4.19
2.16
2.00
0.94
3.11
1.90
1.99
1.95
2.03
2.00
2.10
f1 (ppm)

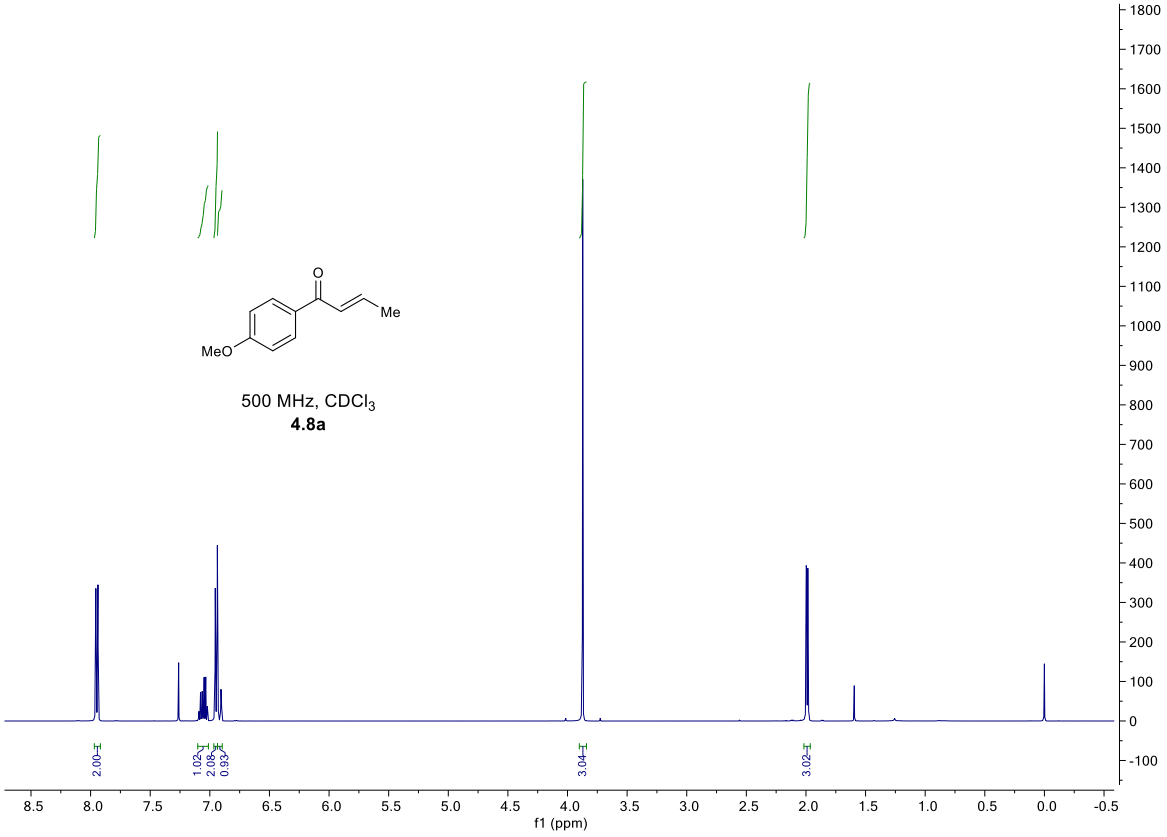

158.513
139.268
126.356
113.553
85.460
76.163
55.290
48.655
43.378
41.757
OMe
HO
H
H
OH
126 MHz, CDCl3
4.19
f1 (ppm)

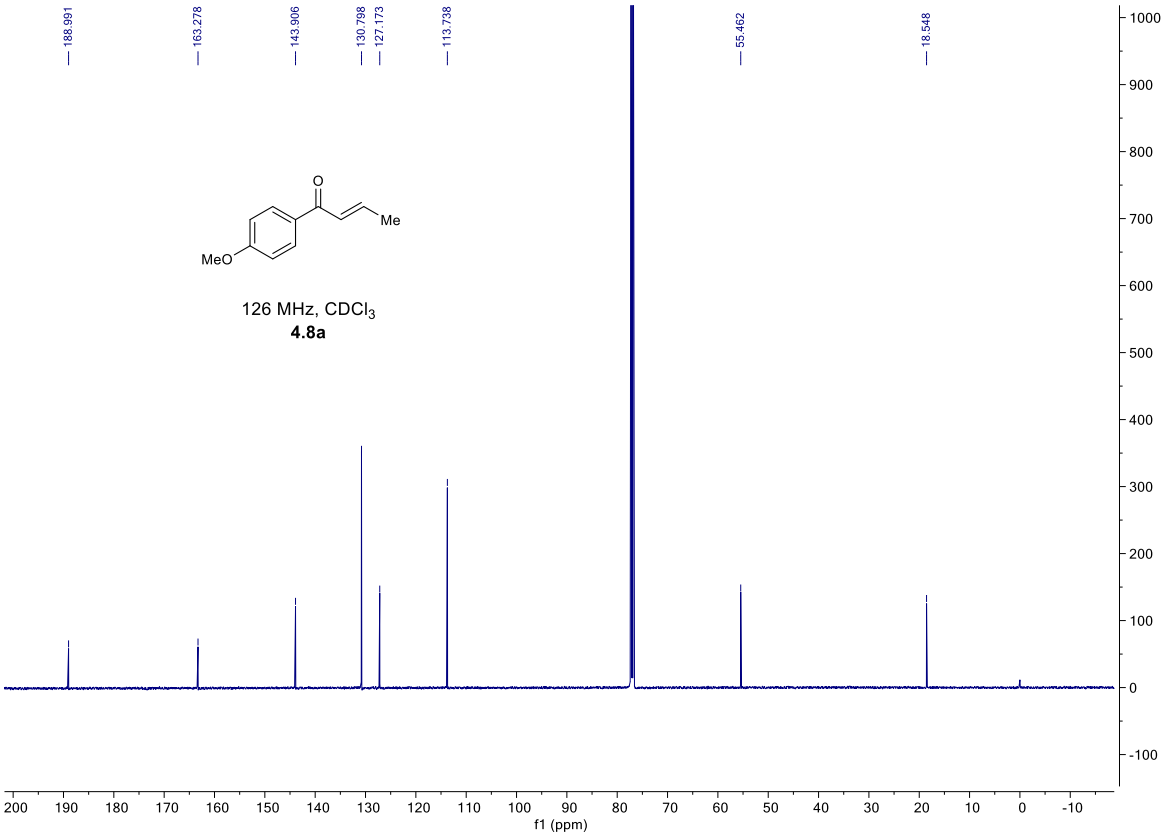

OMe
HO
H
H
O
O
Me
Me
500 MHz, CDCl3
4.20
2.01
2.00
3.03
1.93
1.97
1.98
1.01
3.99
2.00
1.96
5.89
f1 (ppm)

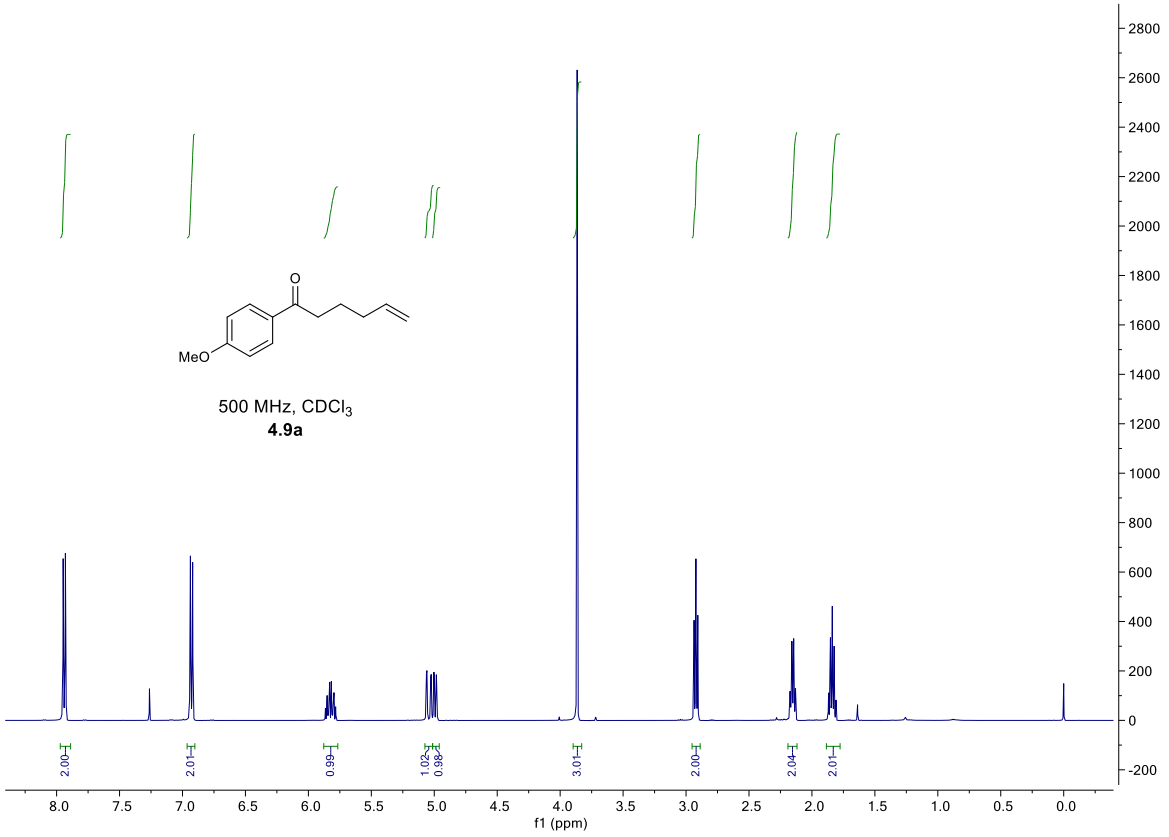

158.386
139.098
126.379
113.430
110.244
84.775
72.468
71.701
55.265
47.666
40.655
39.575
30.130
22.532
OMe
HO
H
H
O
O
Me
Me
126 MHz, CDCl3
4.20
f1 (ppm)

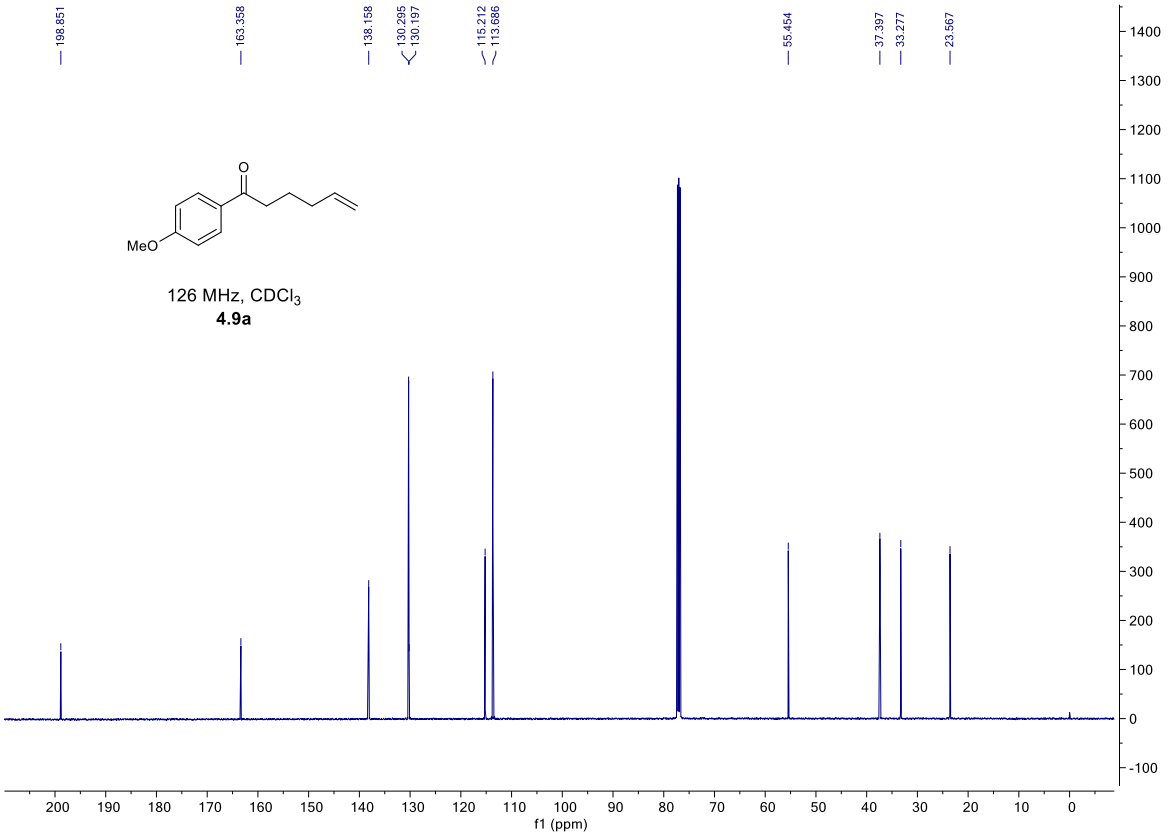

MeO
O
500 MHz, CDCl3
4.6a
2.00
2.07
0.96
0.98
0.96
3.10
1.93
1.96
f1 (ppm)

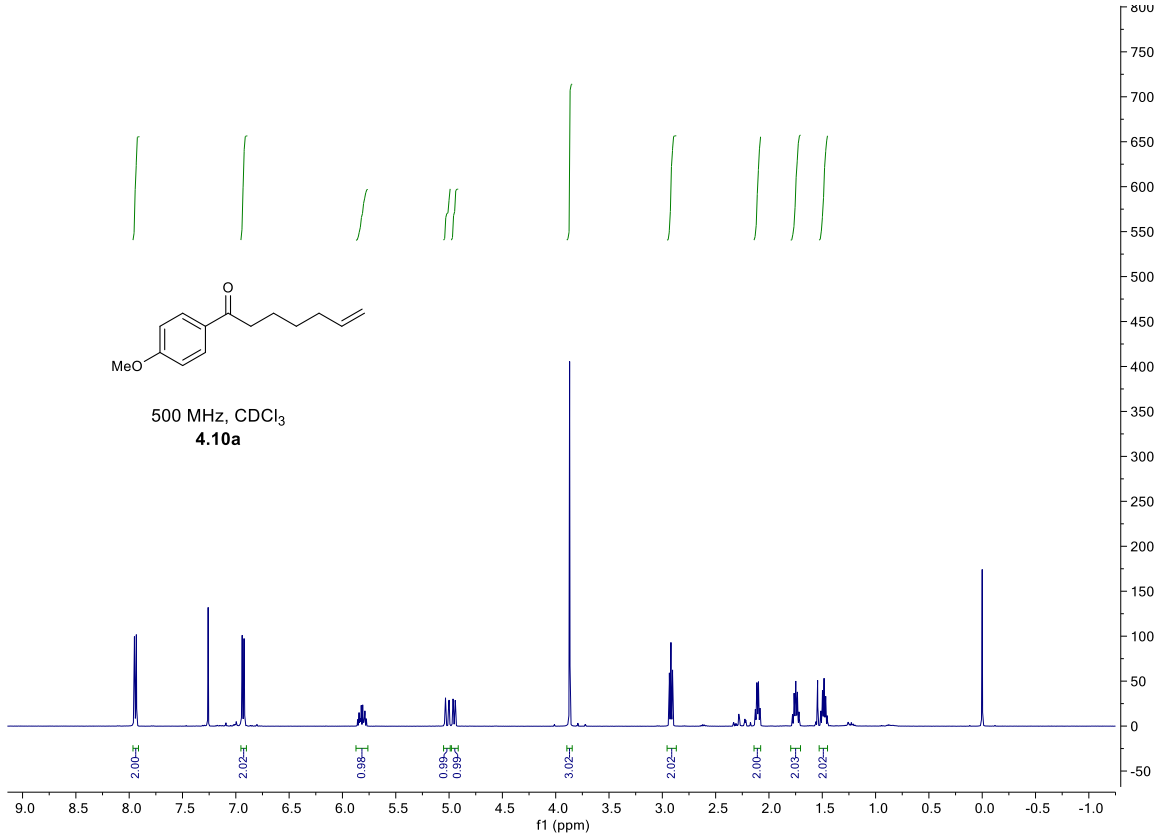

198.427
163.809
137.887
130.686
130.465
115.544
114.107
55.847
37.800
28.772
MeO
O
126 MHz, CDCl3
4.6a
f1 (ppm)

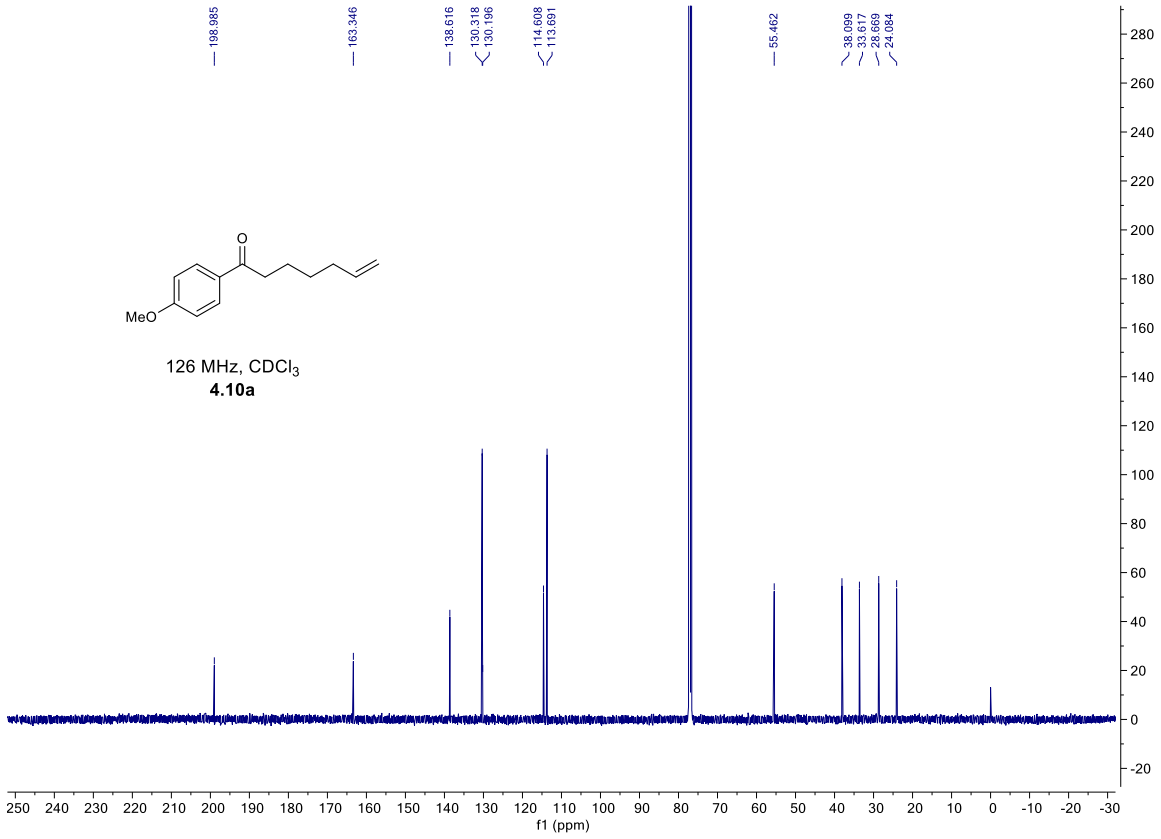

O
Me
MeO
500 MHz, CDCl3
4.8a
2.00
1.02
2.08
0.93
3.04
3.02
f1 (ppm)

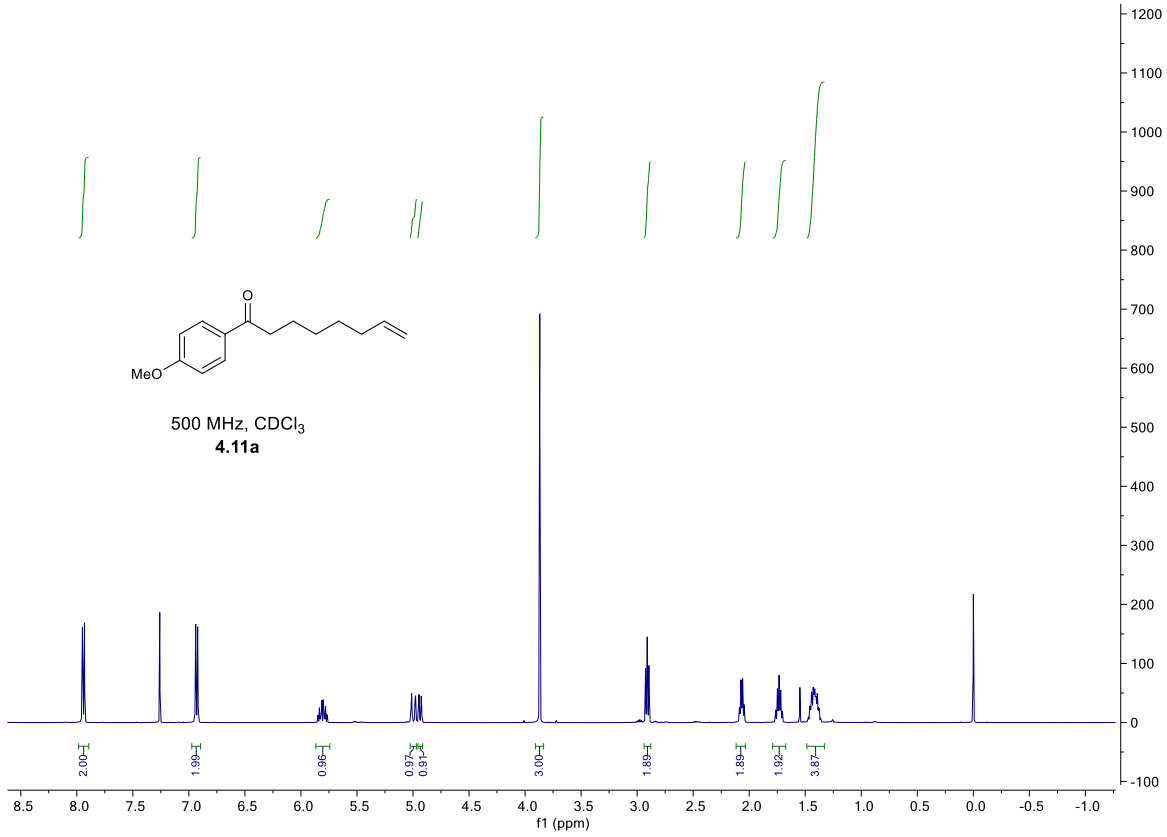

188.991
163.278
143.906
130.798
127.173
113.738
55.462
18.548
O
Me
MeO
126 MHz, CDCl3
4.8a
f1 (ppm)

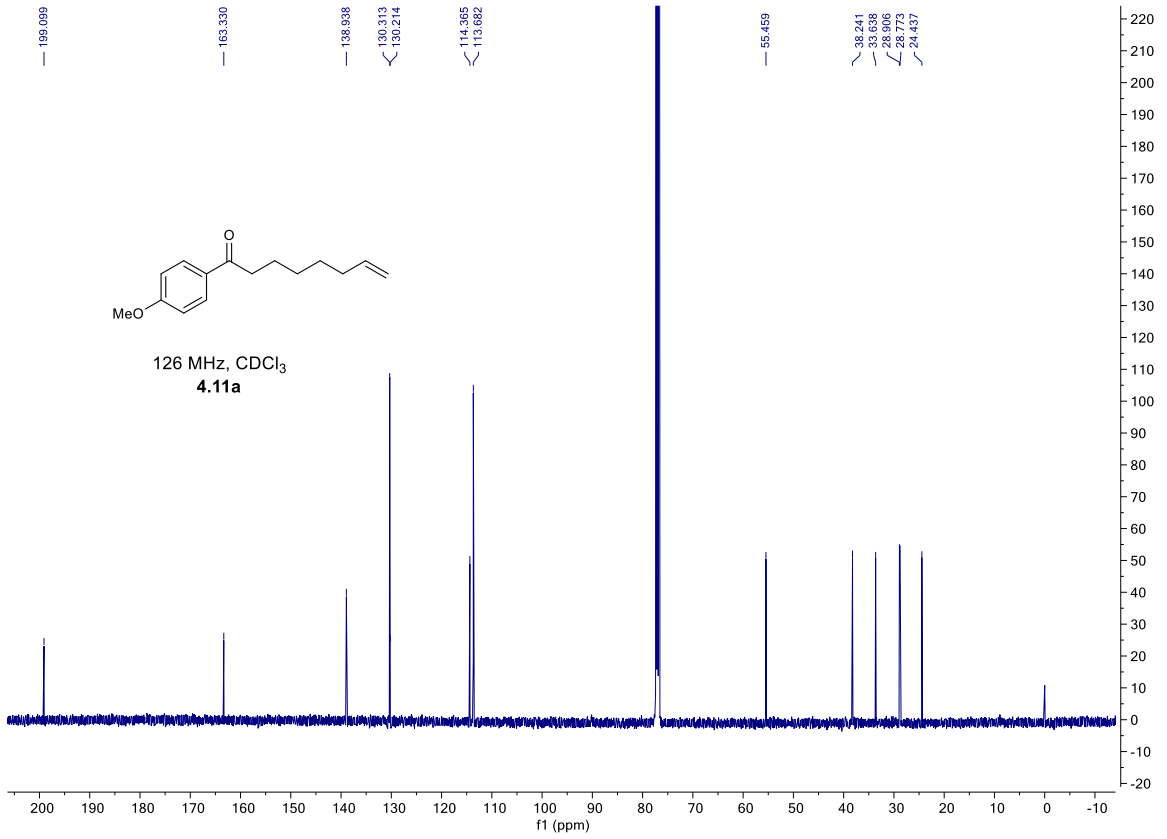

MeO
O
500 MHz, CDCl3
4.9a
2.00
2.01
0.99
1.02
0.98
3.01
2.00
2.04
2.01
f1 (ppm)

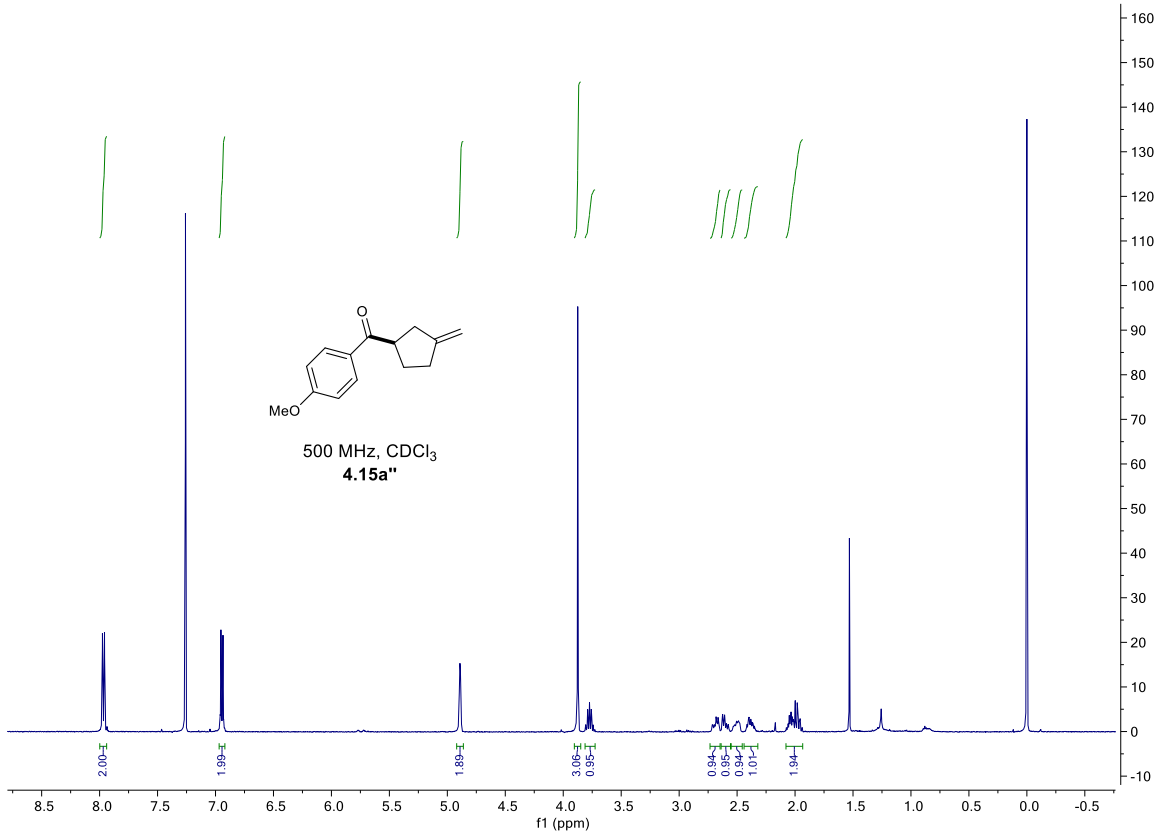

198.851
163.358
138.158
130.295
130.197
115.212
113.686
55.454
37.397
33.277
23.567
MeO
O
126 MHz, CDCl3
4.9a
f1 (ppm)

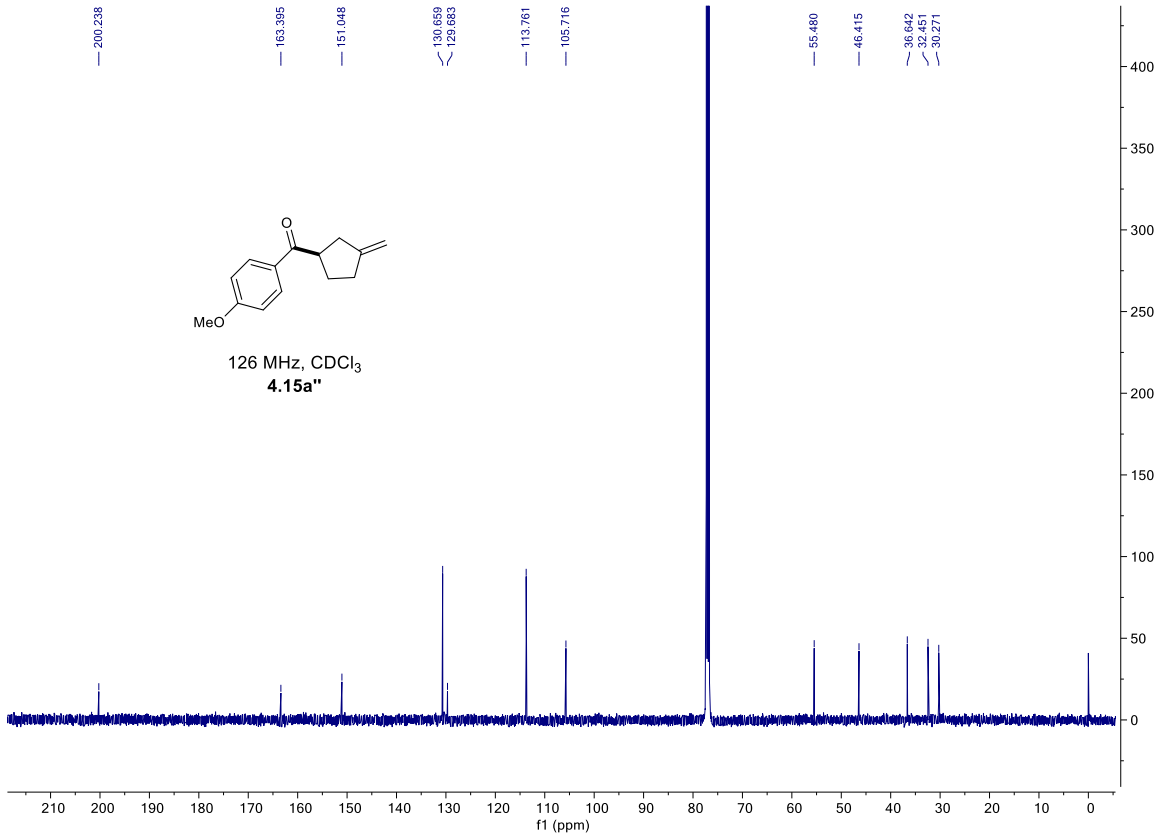

MeO
O
500 MHz, CDCl3
4.10a
2.00
2.02
0.98
0.99
0.99
3.02
2.02
2.00
2.03
2.02
f1 (ppm)

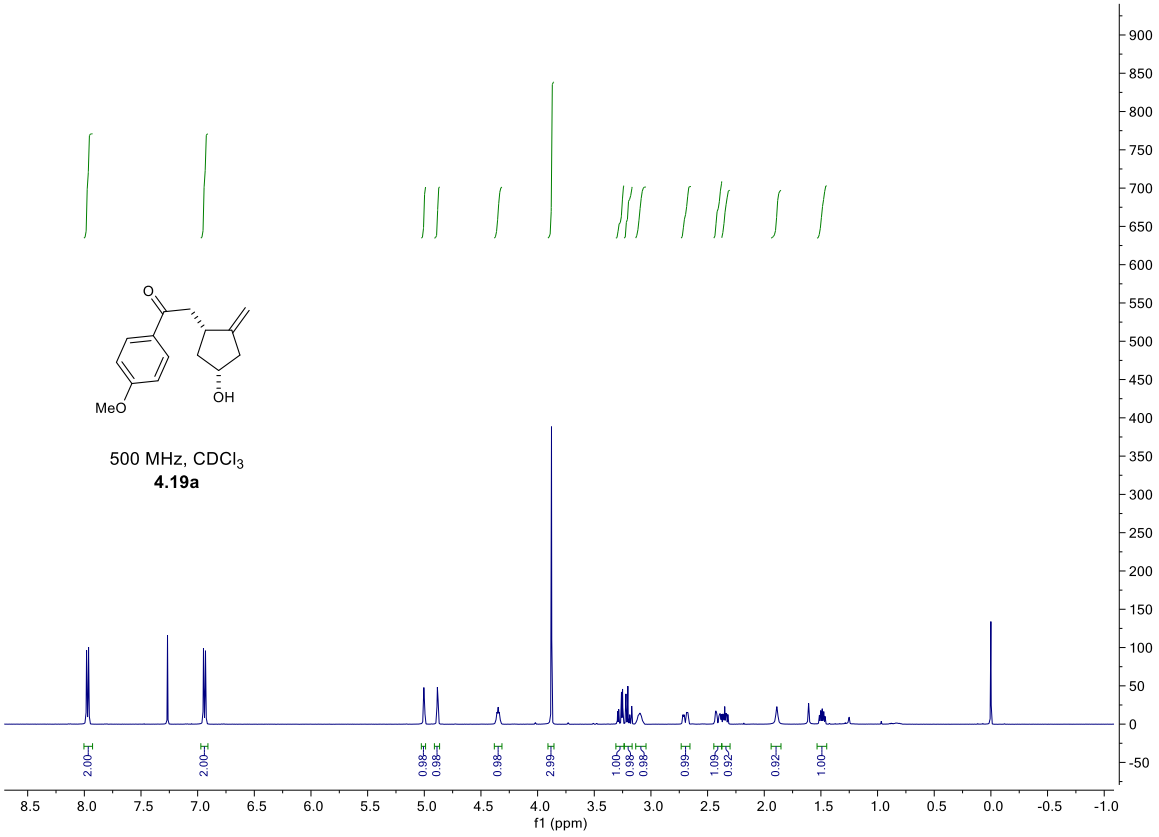

198.985
163.346
138.616
130.318
130.196
114.608
113.691
55.462
38.099
33.617
28.669
24.084
MeO
O
126 MHz, CDCl3
4.10a
f1 (ppm)

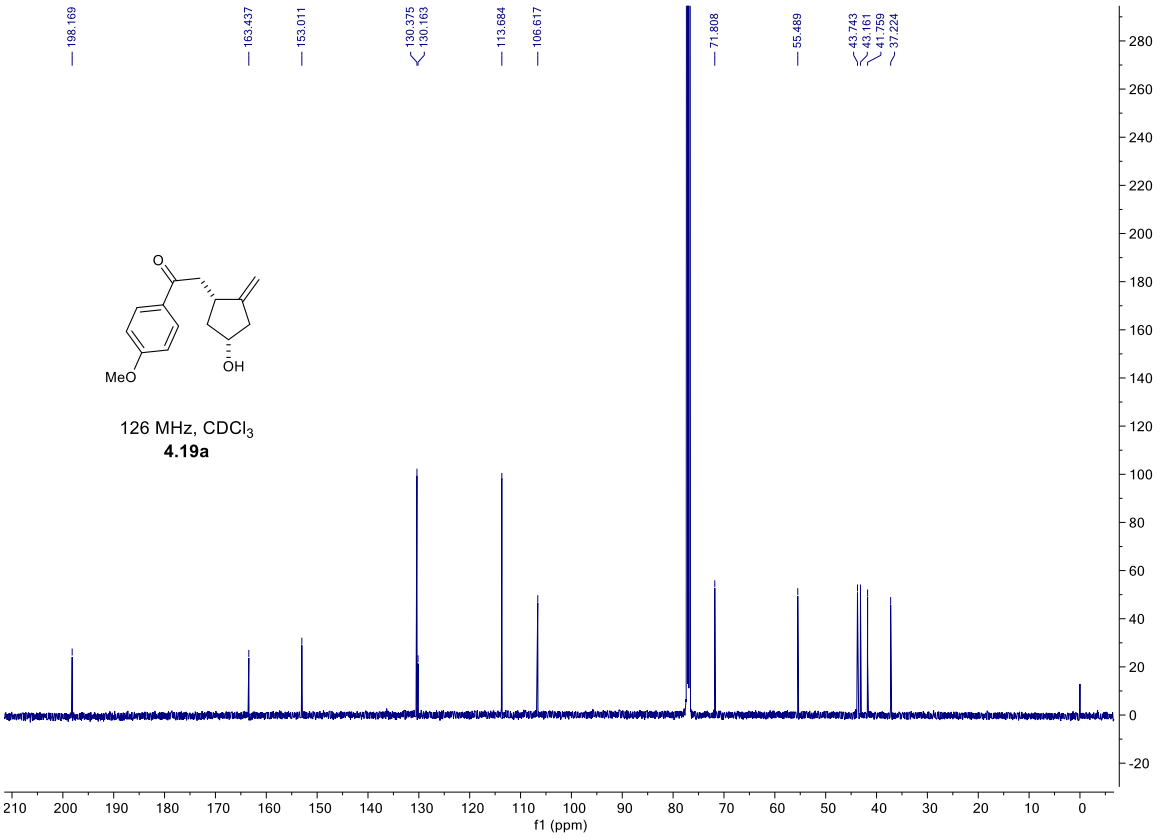

MeO
O
500 MHz, CDCl3
4.11a
2.00
1.99
0.96
0.97
0.91
3.00
1.89
1.89
1.92
3.87
f1 (ppm)

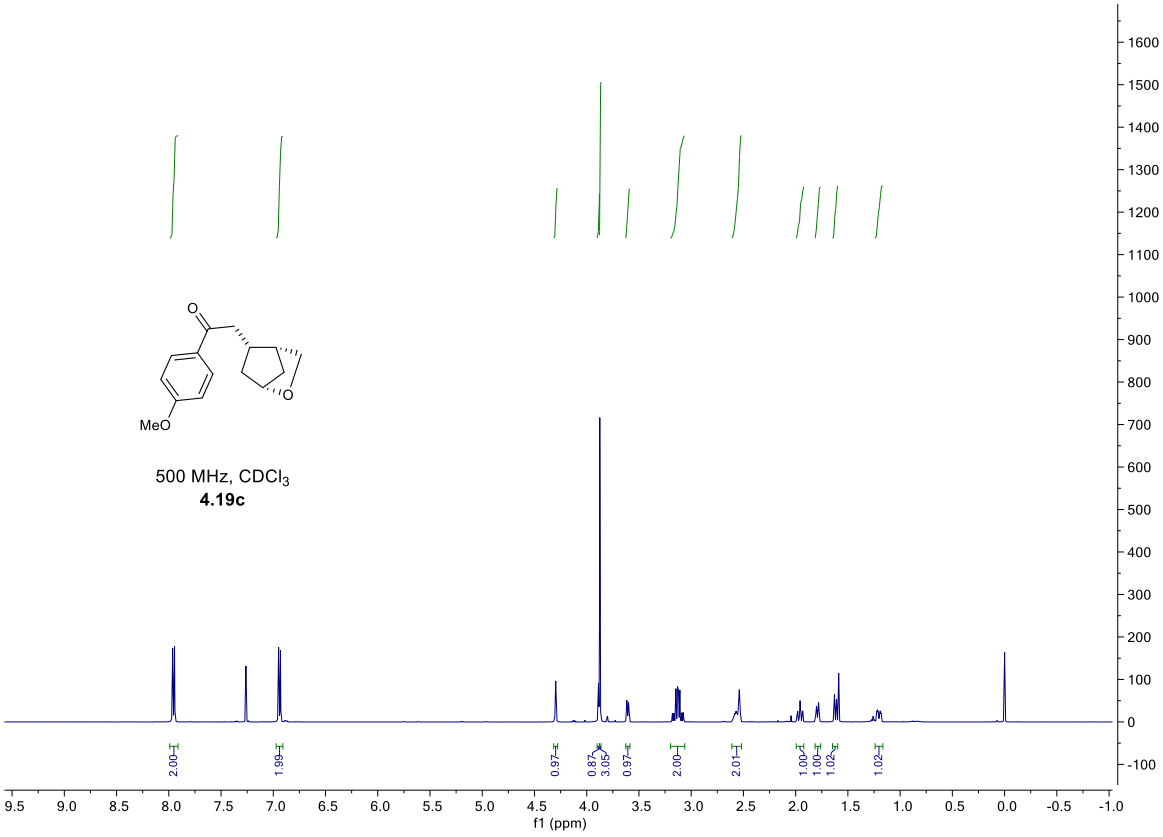

199.099
163.330
138.938
130.313
130.214
114.365
113.682
55.459
38.241
33.638
28.906
28.773
24.437
MeO
O
126 MHz, CDCl3
4.11a
f1 (ppm)

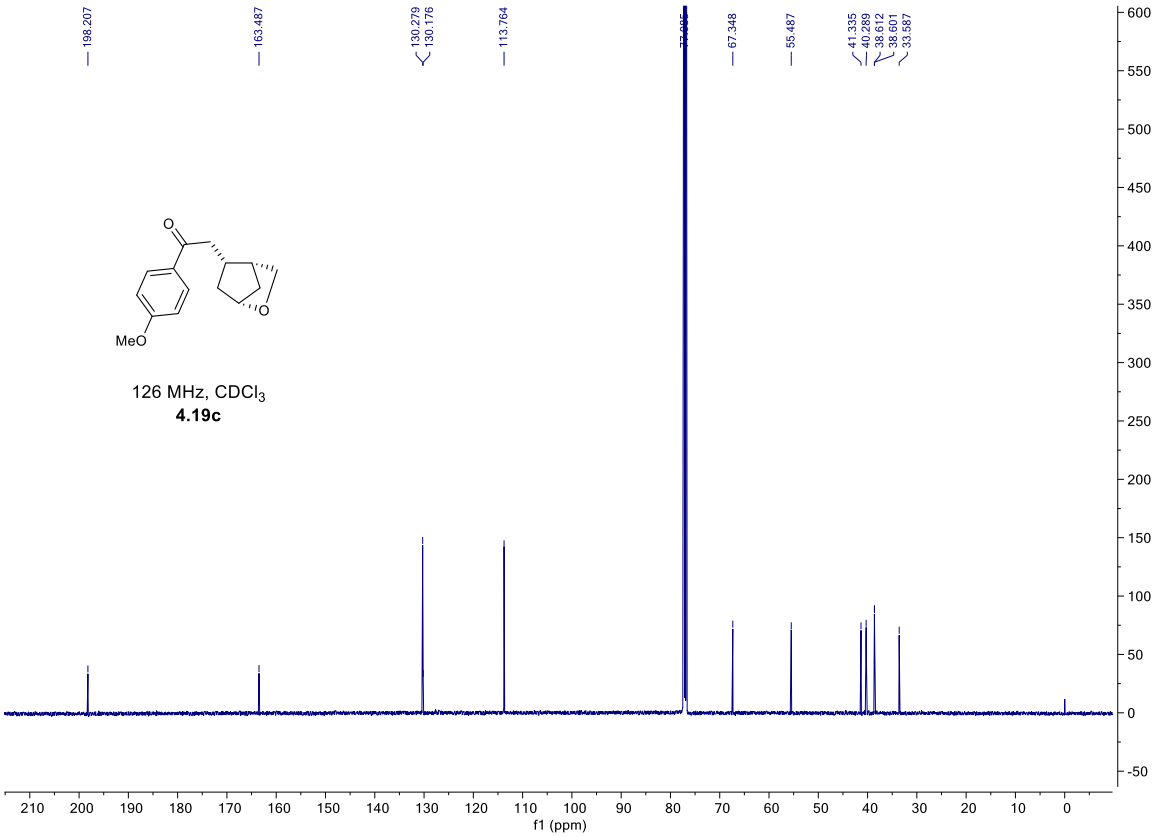

MeO
500 MHz, CDCl3
4.15a''
2.00
1.99
1.89
3.06
0.95
0.94
0.95
0.94
1.01
1.94
f1 (ppm)

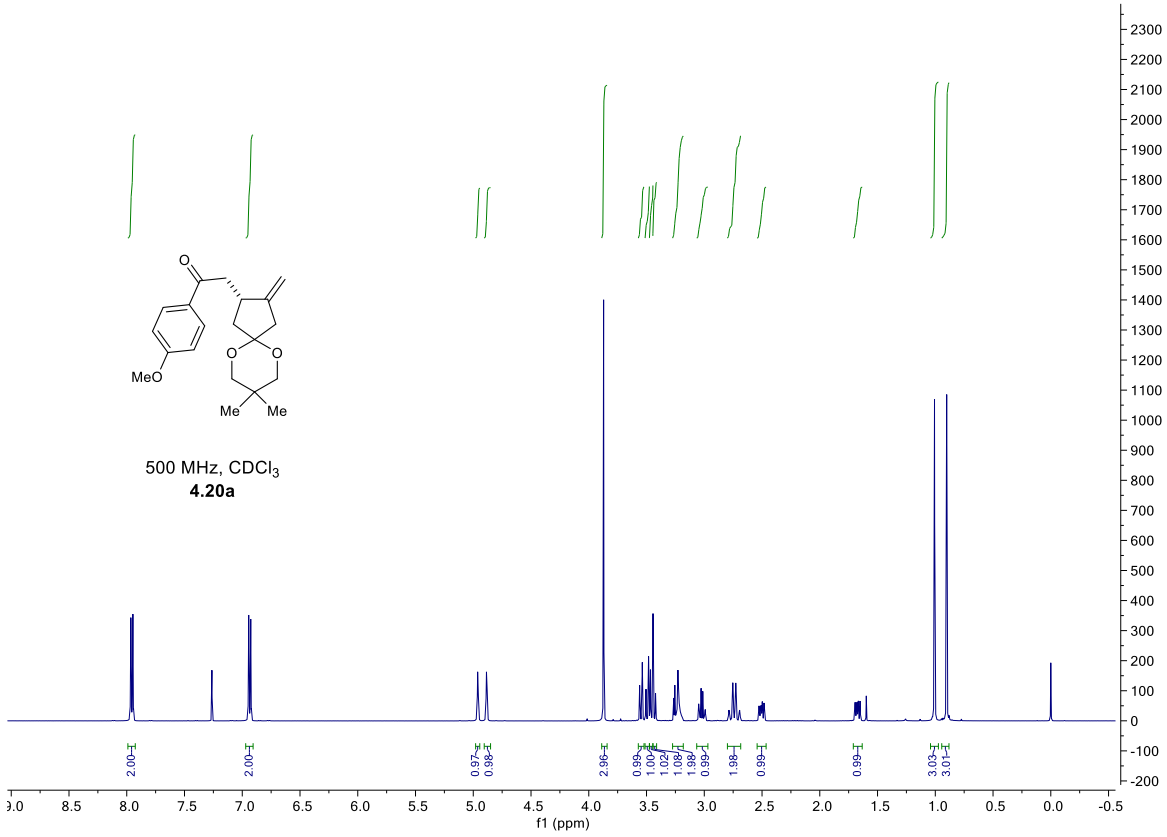

200.238
163.395
151.048
130.659
129.683
113.761
105.716
55.480
46.415
36.642
32.451
30.271
MeO
126 MHz, CDCl3
4.15a''
f1 (ppm)

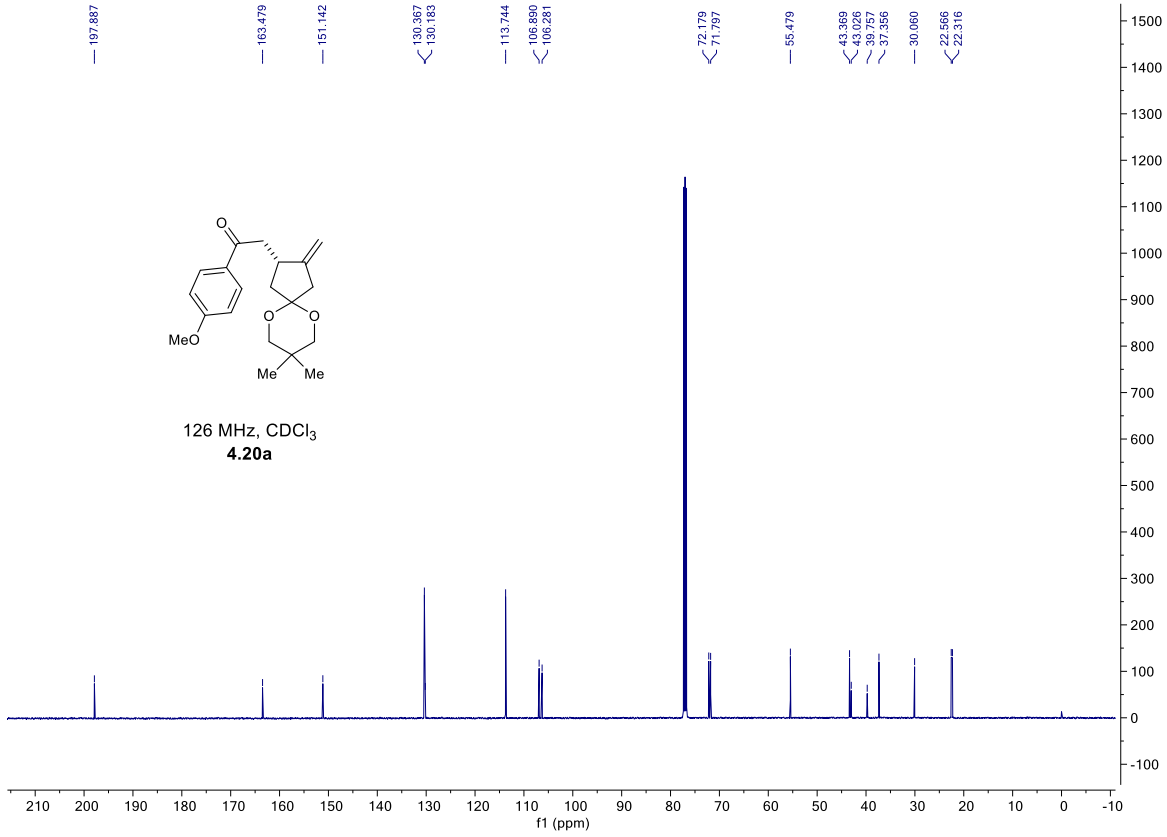

MeO
OH
500 MHz, CDCl3
4.19a
f1 (ppm)

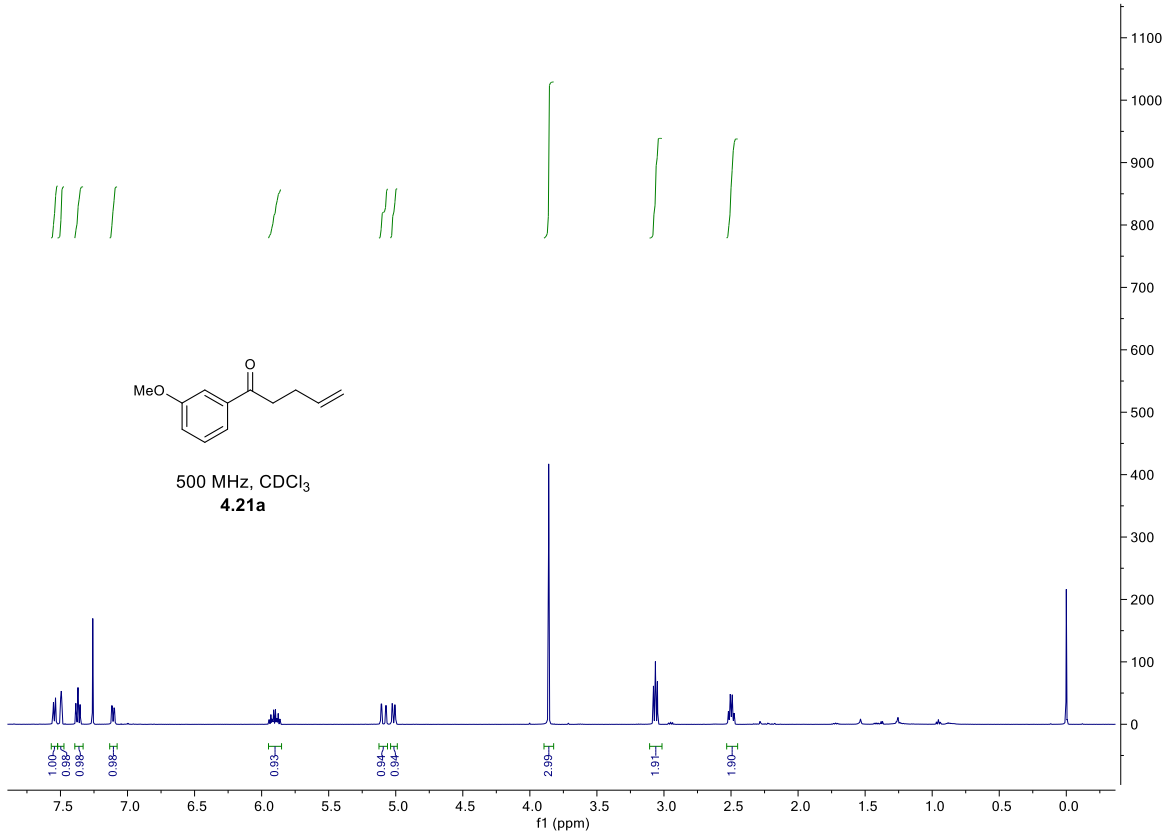

198.169
163.437
153.011
130.375
130.163
113.684
106.617
71.808
55.489
43.743
43.161
41.759
37.224
MeO
OH
126 MHz, CDCl3
4.19a
f1 (ppm)

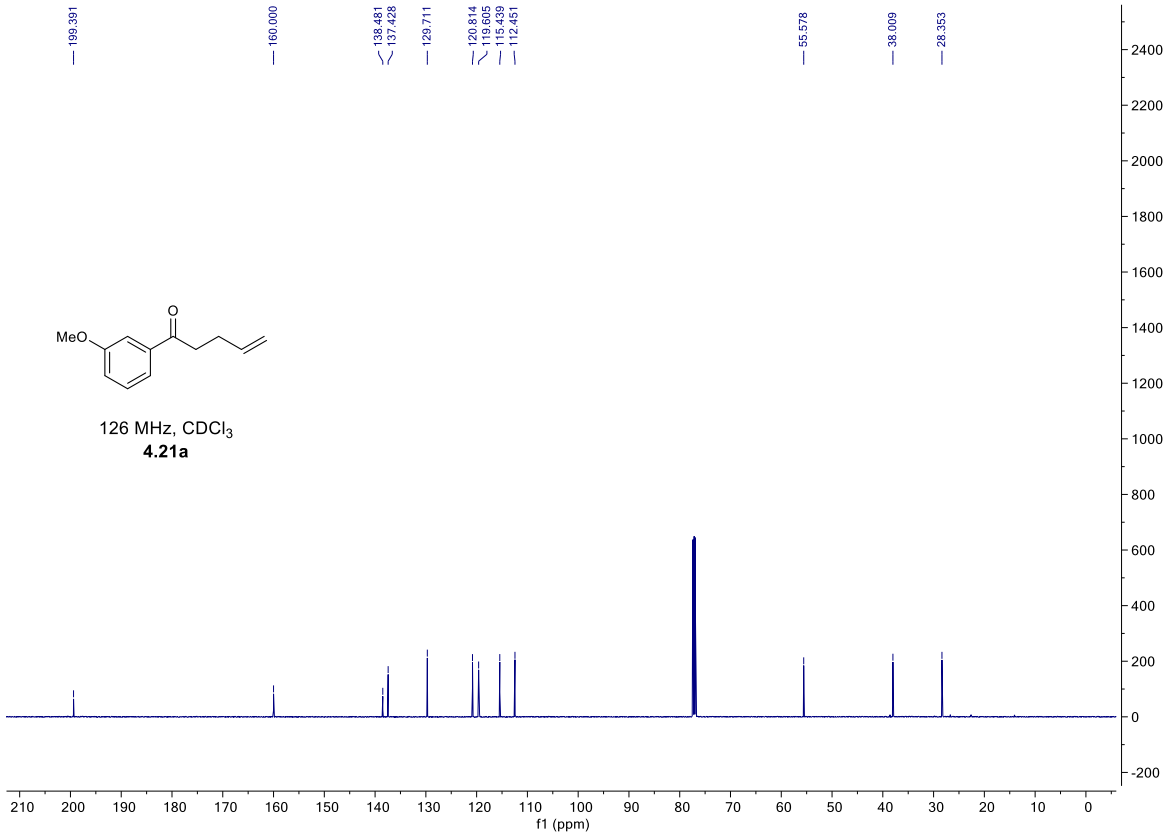

MeO
O
O
500 MHz, CDCl3
4.19c
2.00
1.99
0.97
0.87
3.05
0.97
2.00
2.01
1.00
1.00
1.02
1.02
f1 (ppm)

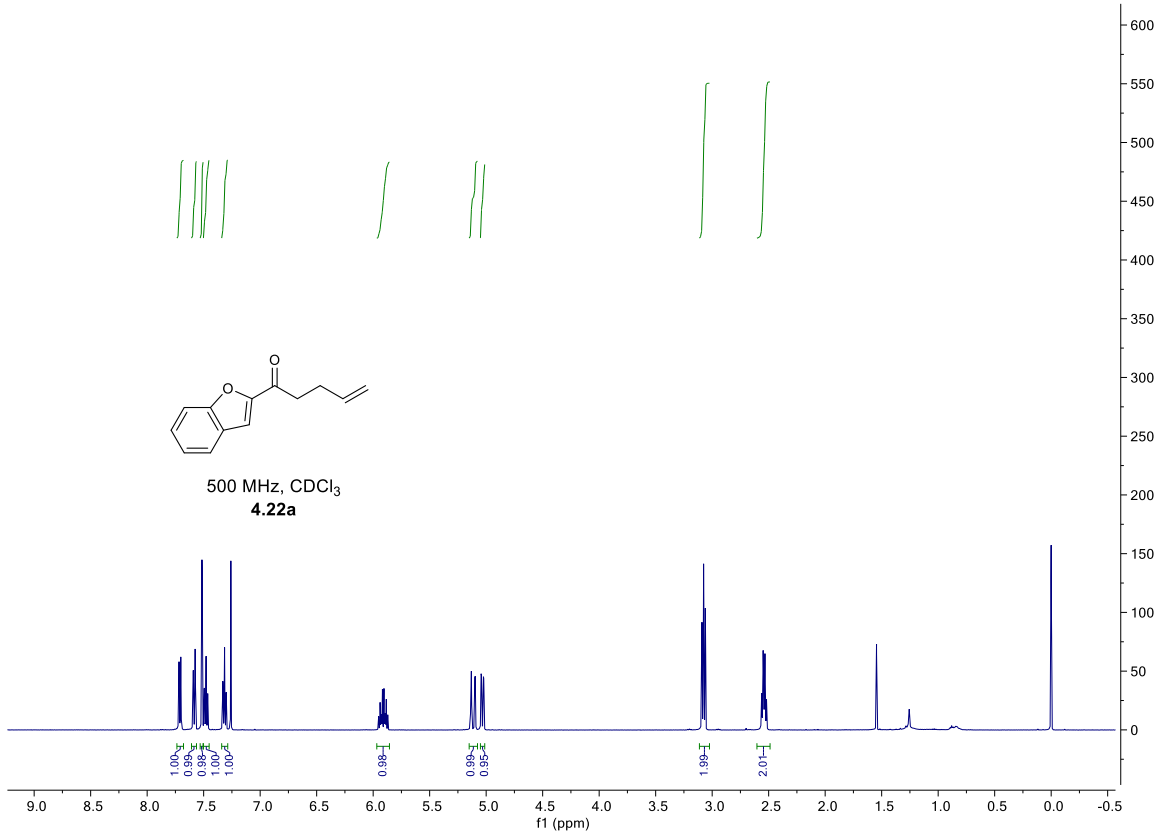

198.207
163.487
130.279
130.176
113.764
67.348
55.487
41.335
40.289
38.612
38.601
33.587
MeO
O
O
126 MHz, CDCl3
4.19c
f1 (ppm)

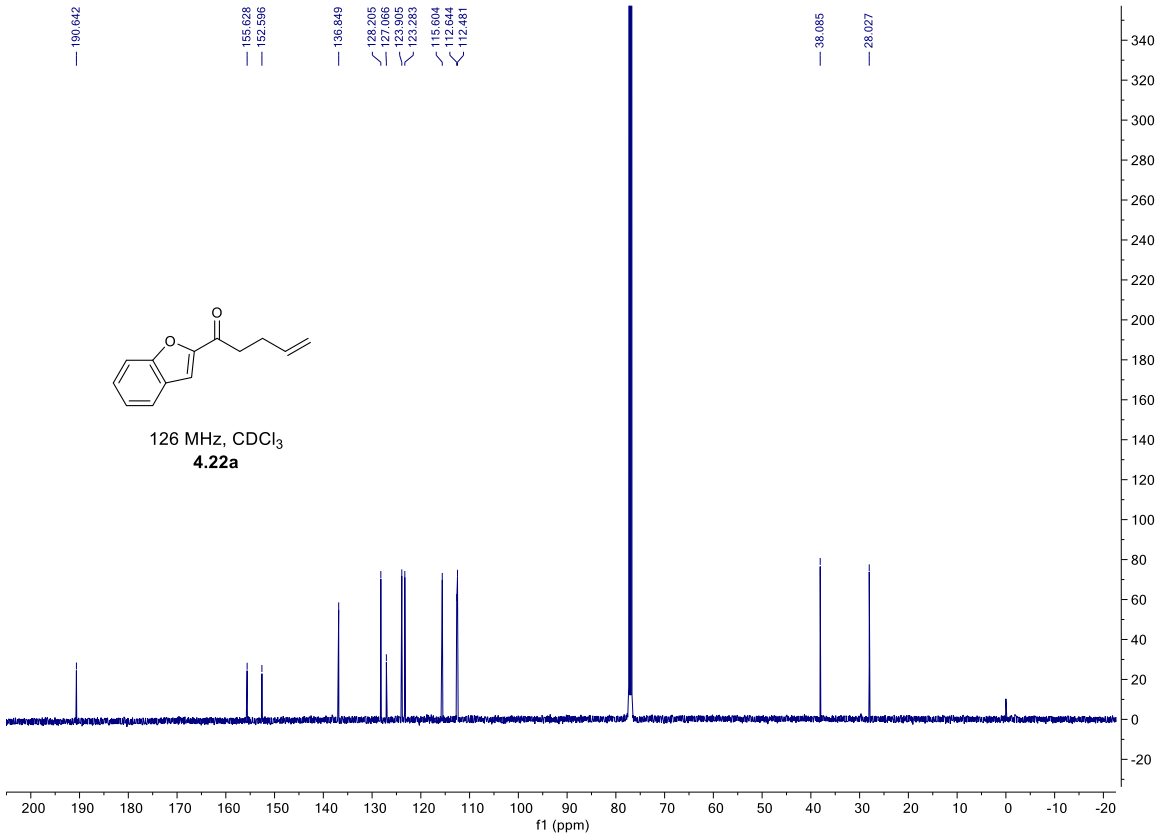

MeO
Me
Me
500 MHz, CDCl3
4.20a
f1 (ppm)

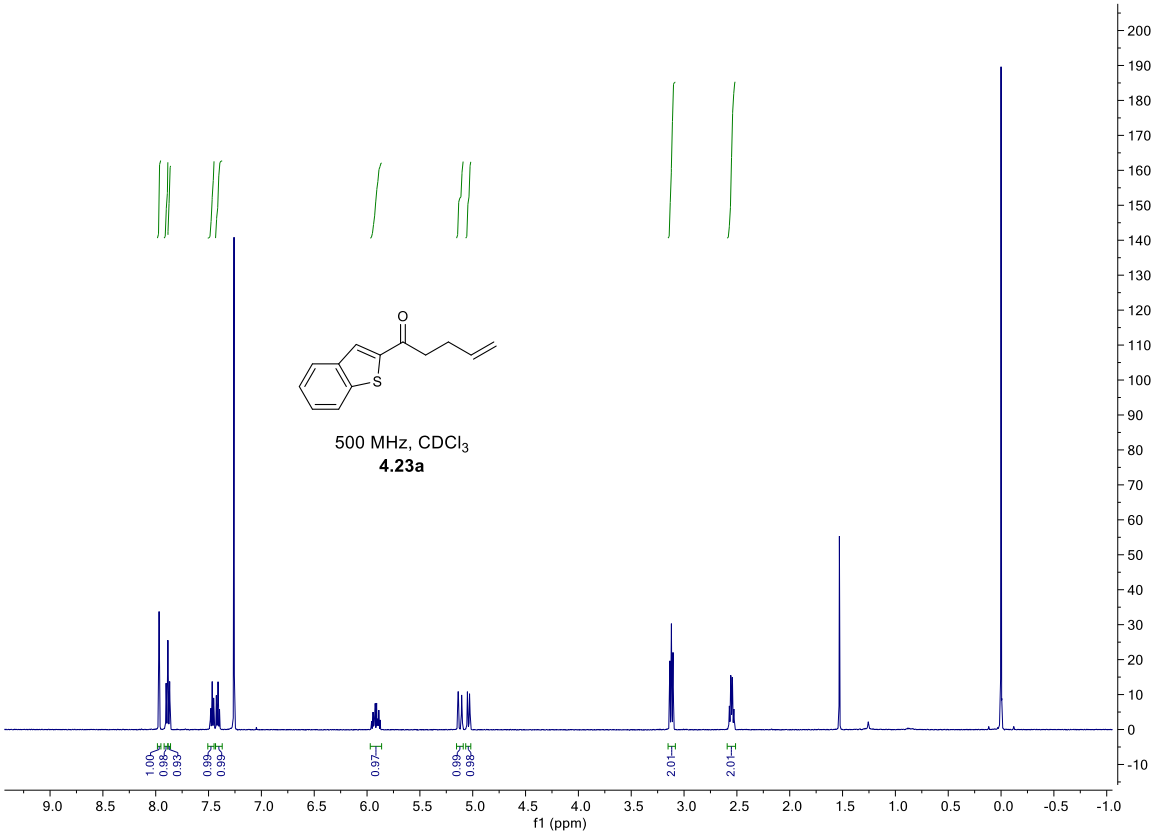

197.887
163.479
151.142
130.367
130.183
113.744
106.890
106.281
72.179
71.797
55.479
43.369
43.026
39.757
37.356
30.060
22.566
22.316
MeO
Me
Me
126 MHz, CDCl3
4.20a
f1 (ppm)

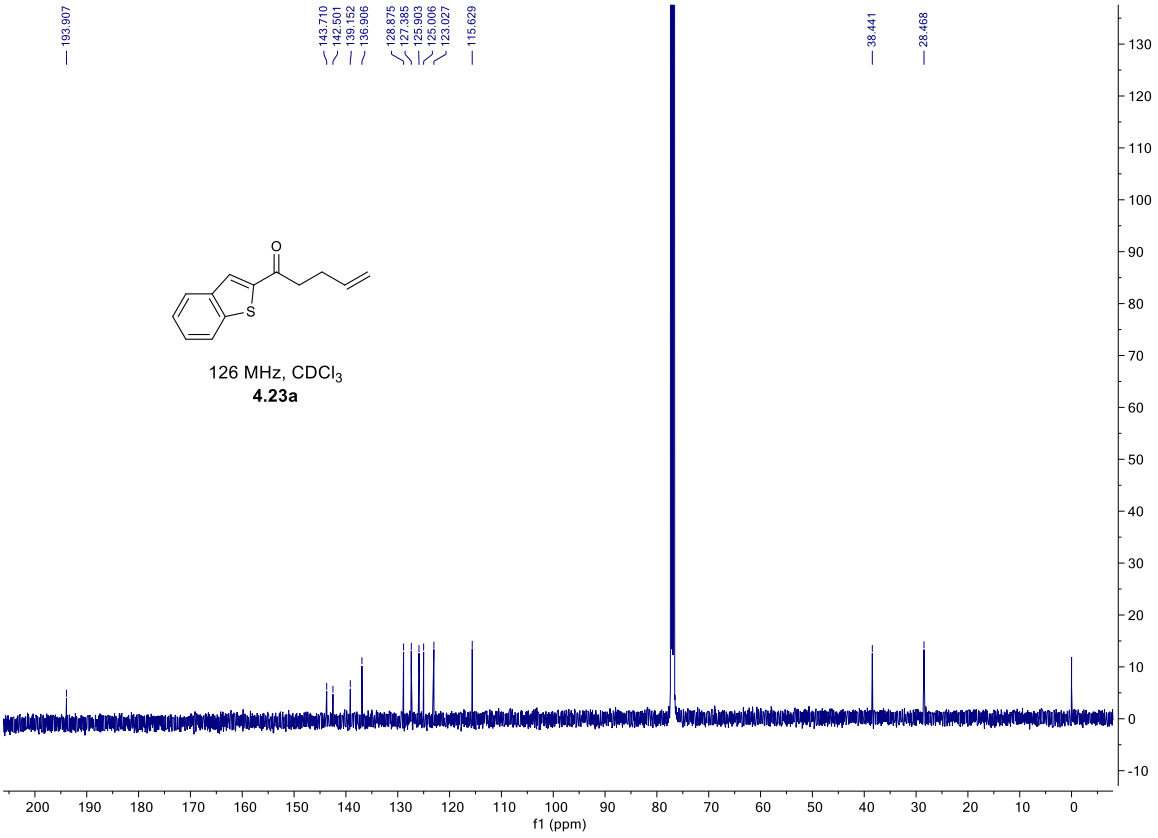

MeO
O
500 MHz, CDCl3
4.21a
1.00
0.98
0.98
0.98
0.93
0.94
0.94
2.99
1.91
1.90
f1 (ppm)

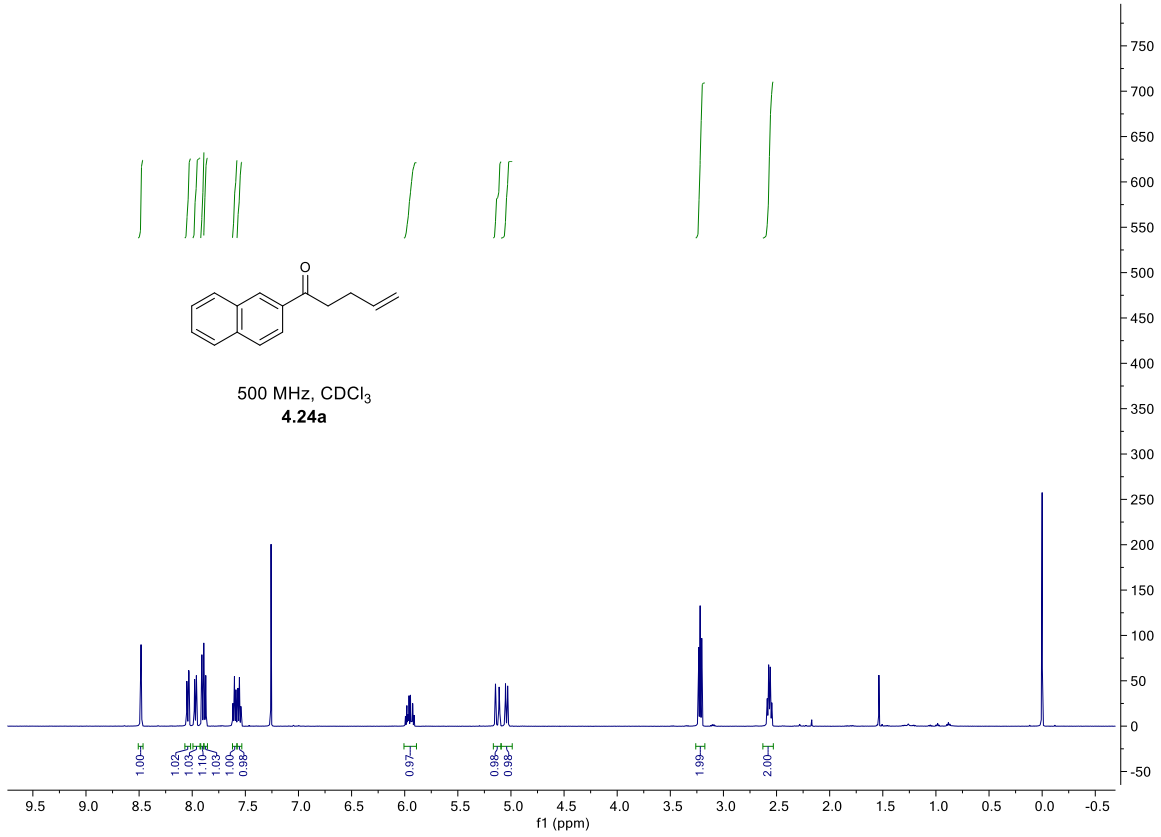

199.391
160.000
138.481
137.428
129.711
120.814
119.605
115.439
112.451
55.578
38.009
28.353
MeO
O
126 MHz, CDCl3
4.21a
f1 (ppm)

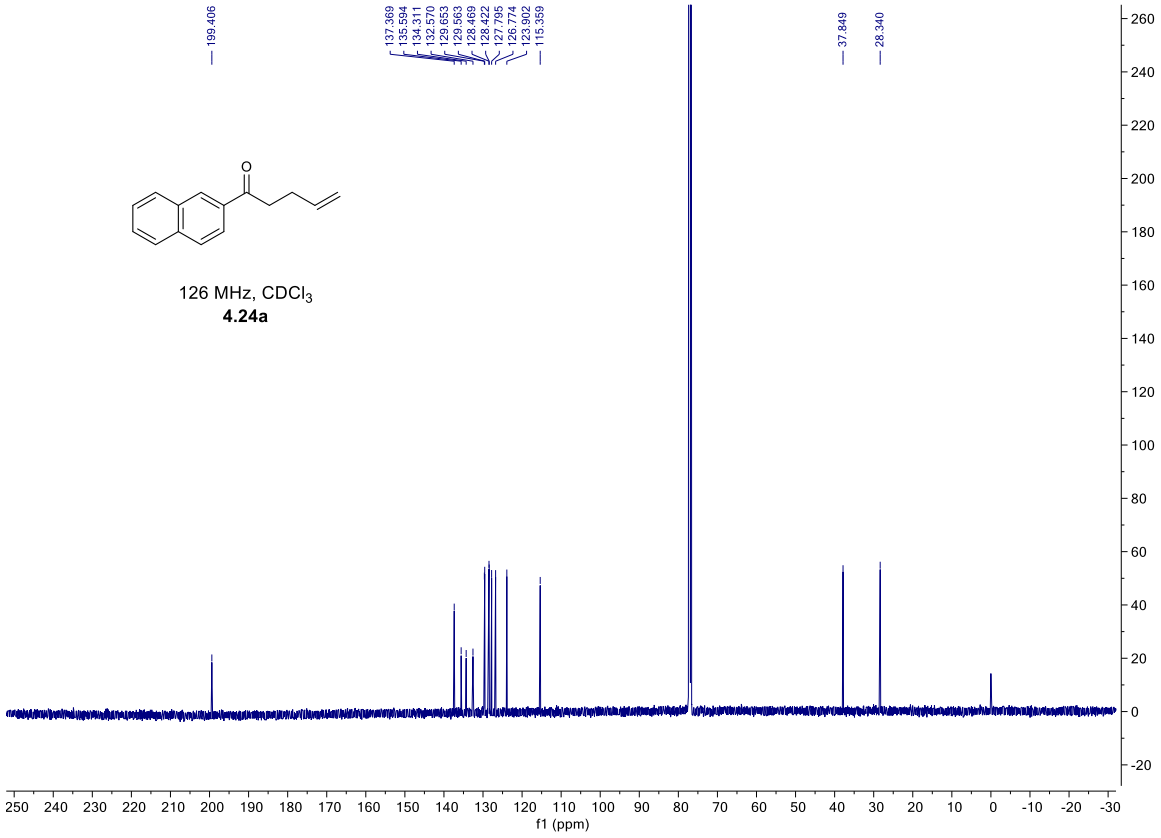

500 MHz, CDCl3
4.22a
1.00
0.99
0.98
1.00
1.00
0.98
0.99
0.95
1.99
2.01
f1 (ppm)

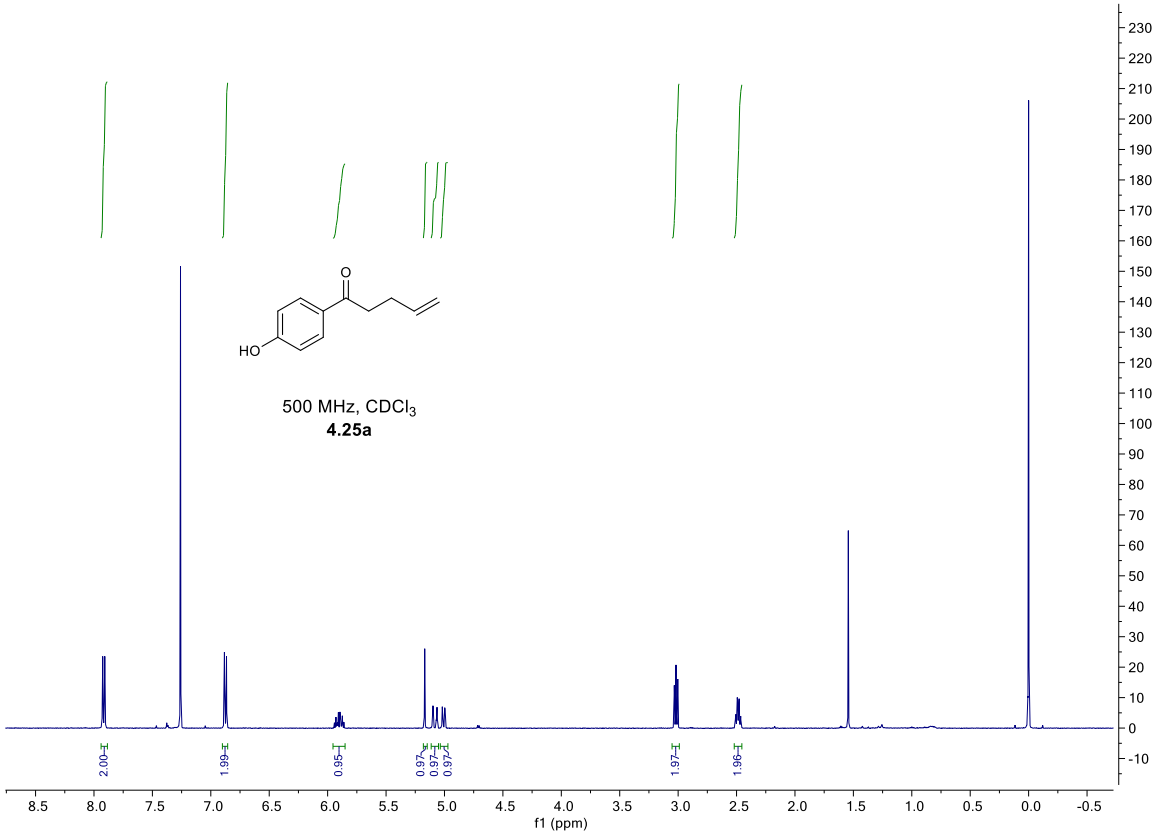

190.642
155.628
152.596
136.849
128.205
127.066
123.905
123.283
115.604
112.644
112.481
38.085
28.027
126 MHz, CDCl3
4.22a
f1 (ppm)

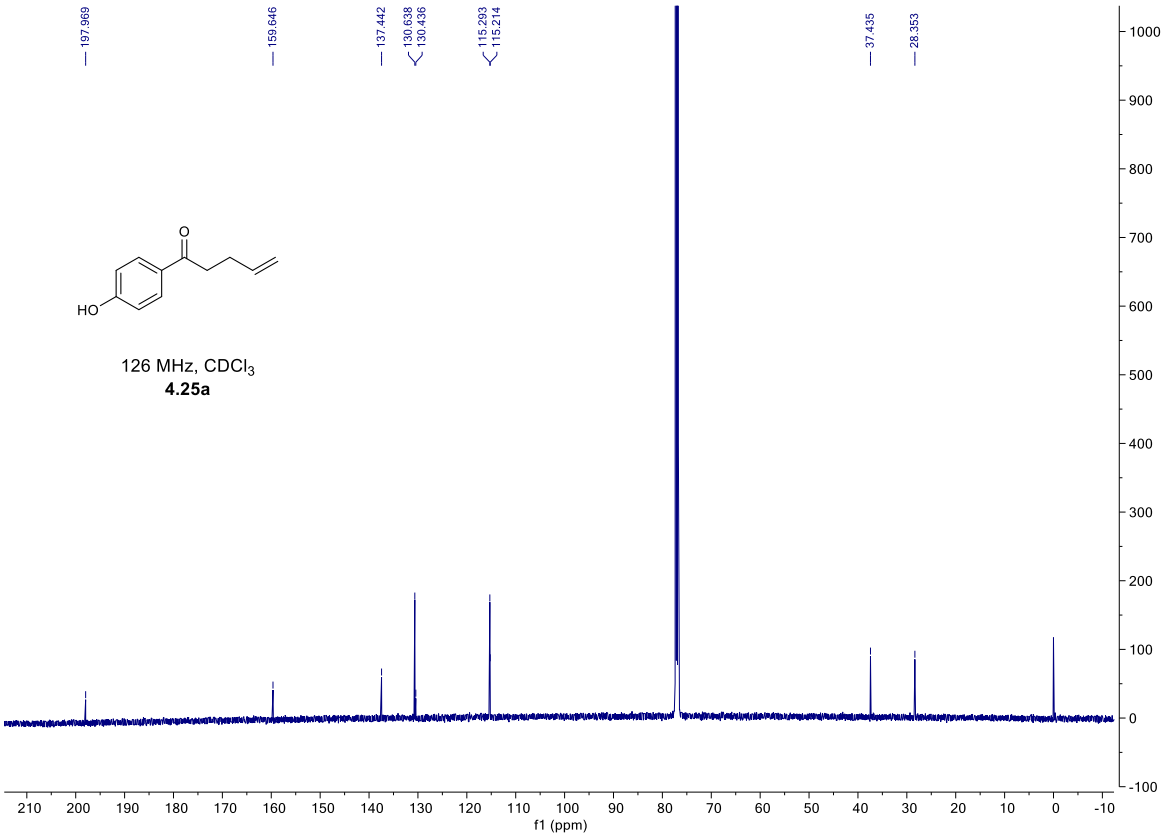

500 MHz, CDCl3
4.23a
f1 (ppm)


193.907
143.710
142.501
139.152
136.906
128.875
127.385
125.903
125.006
123.027
115.629
38.441
28.468
126 MHz, CDCl3
4.23a
f1 (ppm)


500 MHz, CDCl3
4.24a
f1 (ppm)

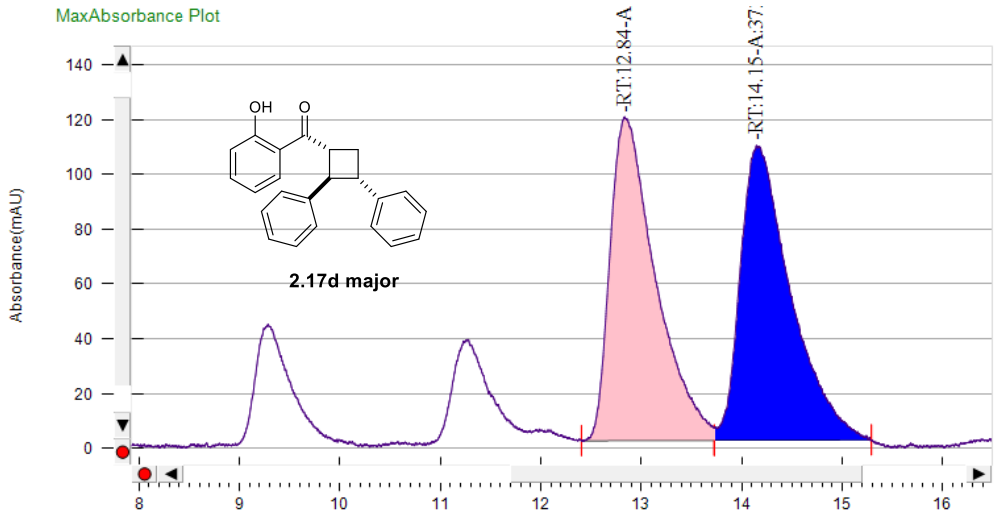

199.406
137.369
135.594
134.311
132.570
129.653
129.563
128.469
128.422
127.705
126.774
123.902
115.359
37.849
28.340
126 MHz, CDCl3
4.24a
f1 (ppm)


HO
O
500 MHz, CDCl3
4.25a
2.00
1.99
0.95
0.97
0.97
0.97
1.97
1.96
f1 (ppm)


197.969
159.646
137.442
130.638
130.436
115.293
115.214
37.435
28.353
HO
O
126 MHz, CDCl3
4.25a
f1 (ppm)

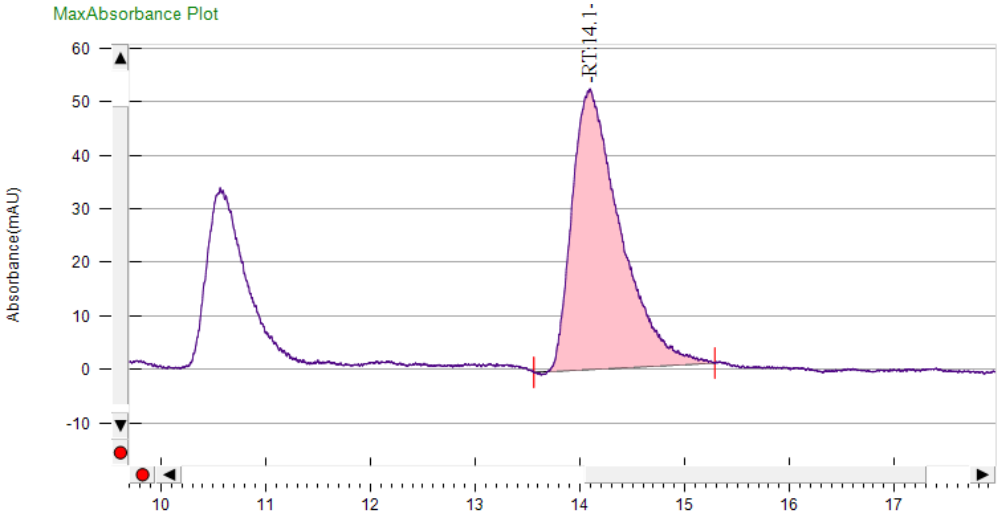
# Appendix B. SFC and HPLC Traces for New Compounds (Chapter 2)

Racemic (Daicel CHIRALPAK® OJ-H, 5%, 4mL/min, MeOH)



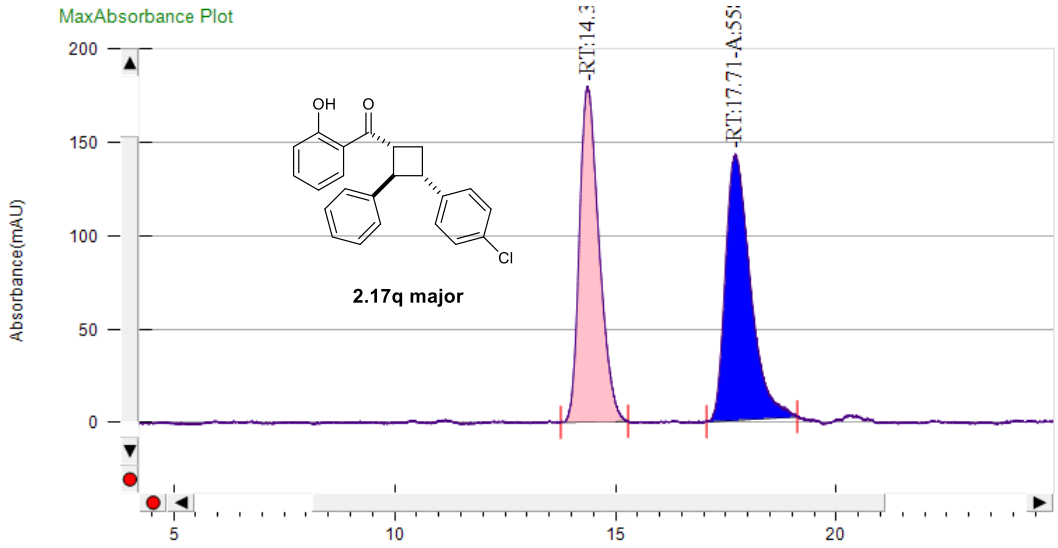

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.7875 | 3707.4144 | 12.84 | 118.0972 |
| **2** | 50.2125 | 3739.0657 | 14.15 | 107.5346 |
| **Total:** | 100 | | | |

Enantioenriched



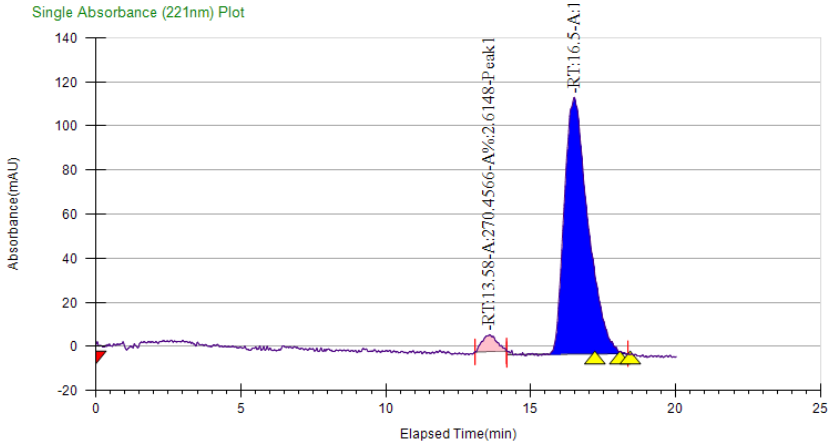

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 100 | 1671.6753 | 14.1 | 52.4308 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, 4% solvent, 4mL/min, *i*-PrOH)



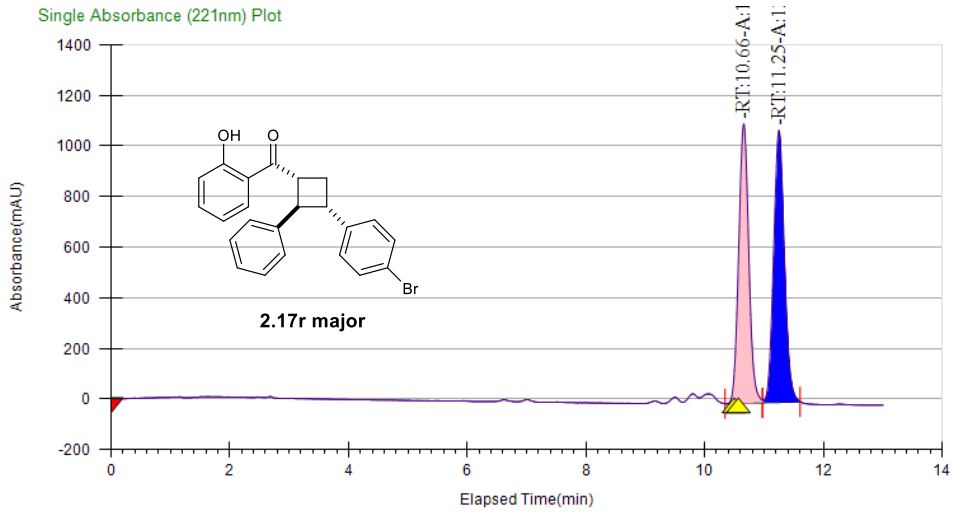

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.7286 | 5529.4179 | 14.37 | 179.8854 |
| **2** | 50.2714 | 5589.7793 | 17.71 | 142.5365 |
| **Total:** | 100 | | | |

Enantioenriched



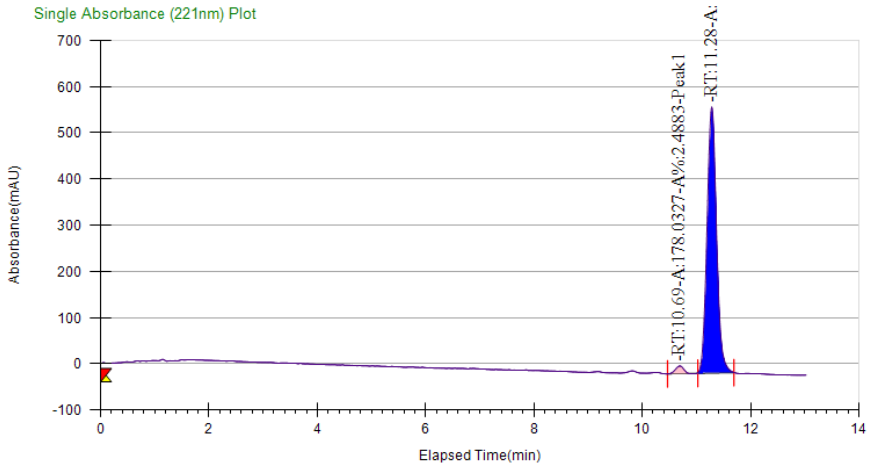

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 2.6148 | 270.4566 | 13.58 | 7.6175 |
| **2** | 97.3852 | 10072.7344 | 16.6 | 116.498.75 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



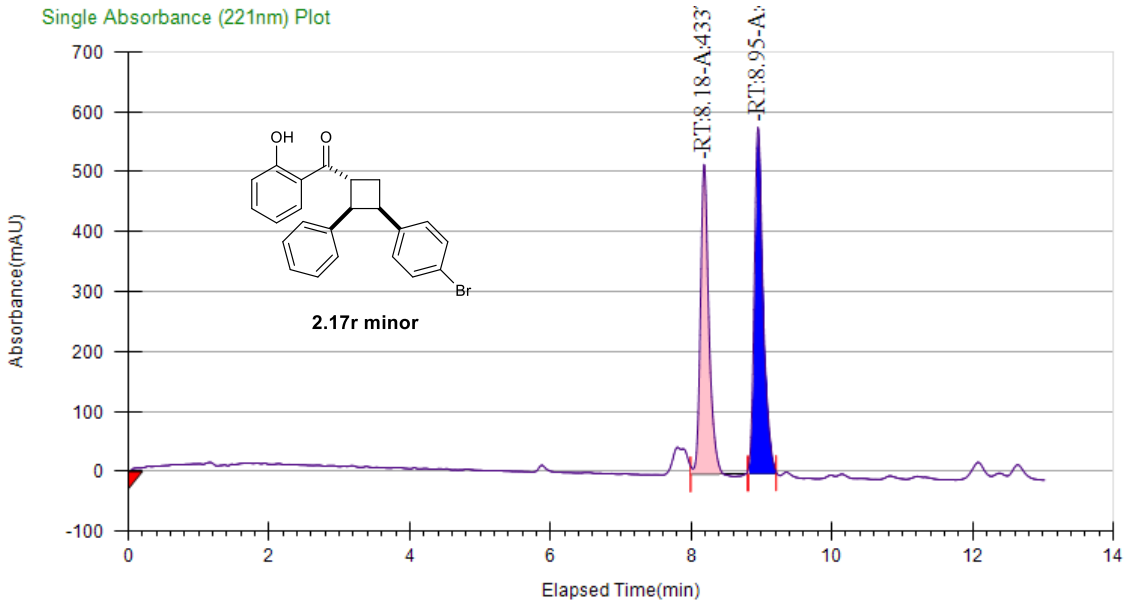

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.1058 | 13034.5907 | 10.66 | 1105.3647 |
| **2** | 50.8942 | 13509.2918 | 11.25 | 1076.6149 |
| **Total:** | 100 | | | |

Enantioenriched



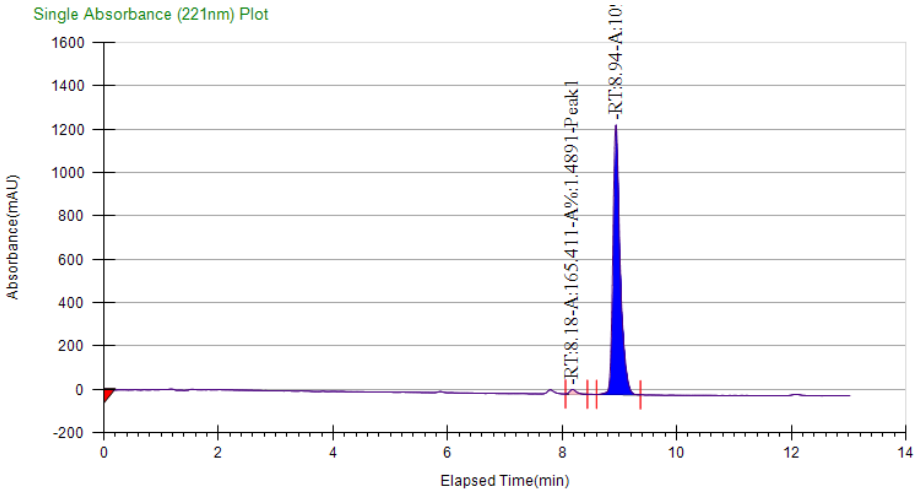

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 2.4883 | 178.0327 | 10.69 | 16.6534 |
| **2** | 97.5117 | 6976.8204 | 11.28 | 576.4619 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



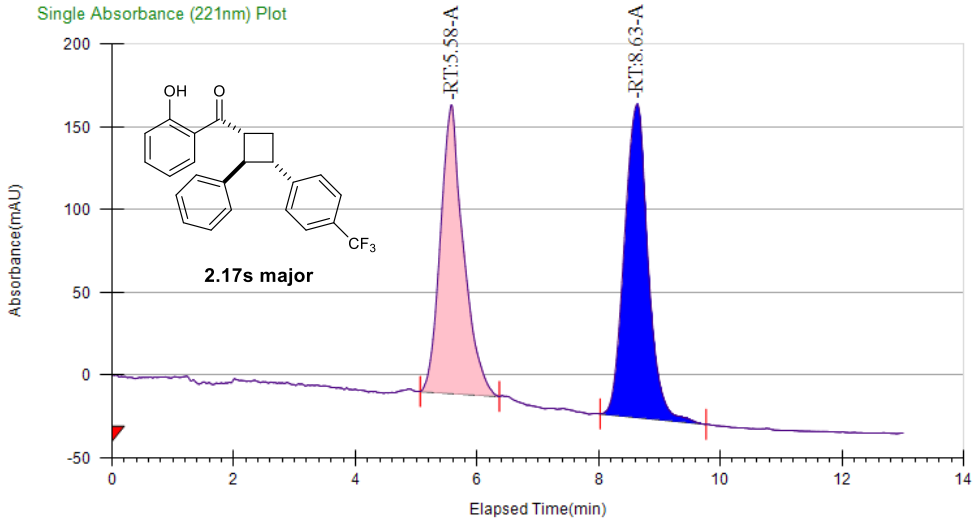

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 46.534 | 4337.4207 | 8.18 | 517.076 |
| **2** | 53.466 | 4983.5408 | 8.95 | 577.8244 |
| **Total:** | 100 | | | |

Enantioenriched



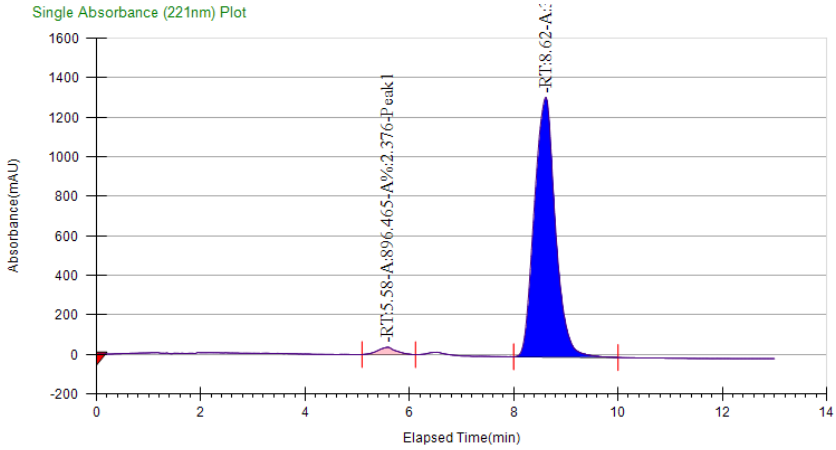

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 1.4891 | 165.411 | 8.18 | 21.3928 |
| **2** | 98.5109 | 10942.448 | 8.94 | 1243.22 |
| **Total:** | 100 | | | |

Racemic Major (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



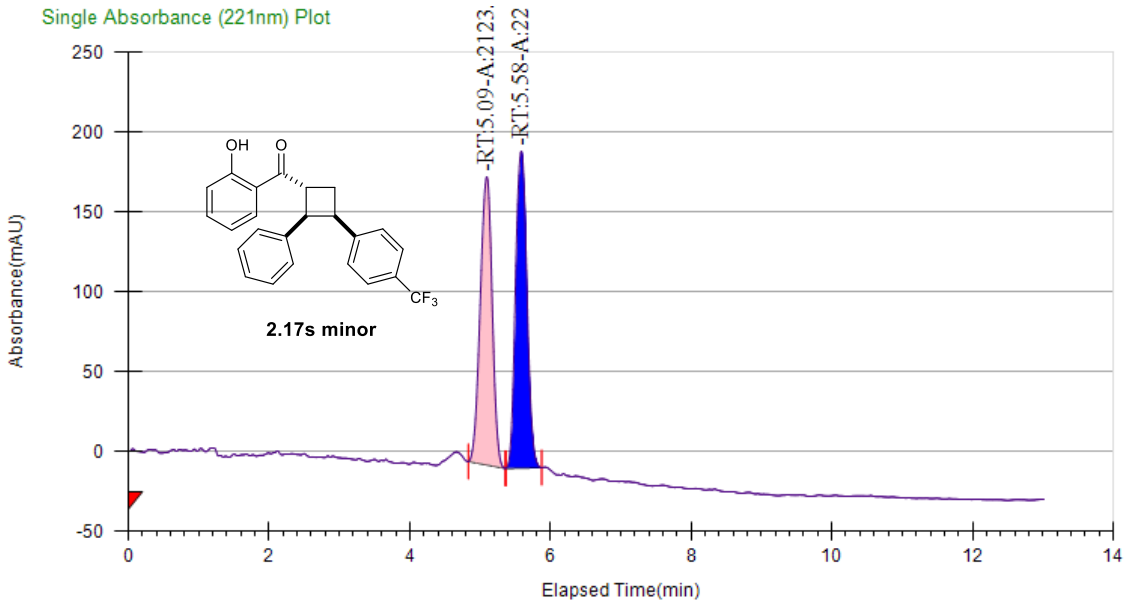

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 47.3652 | 4581.0326 | 5.58 | 174.1974 |
| **2** | 52.6348 | 5090.6955 | 8.63 | 189.2235 |
| **Total:** | 100 | | | |

Enantioenriched



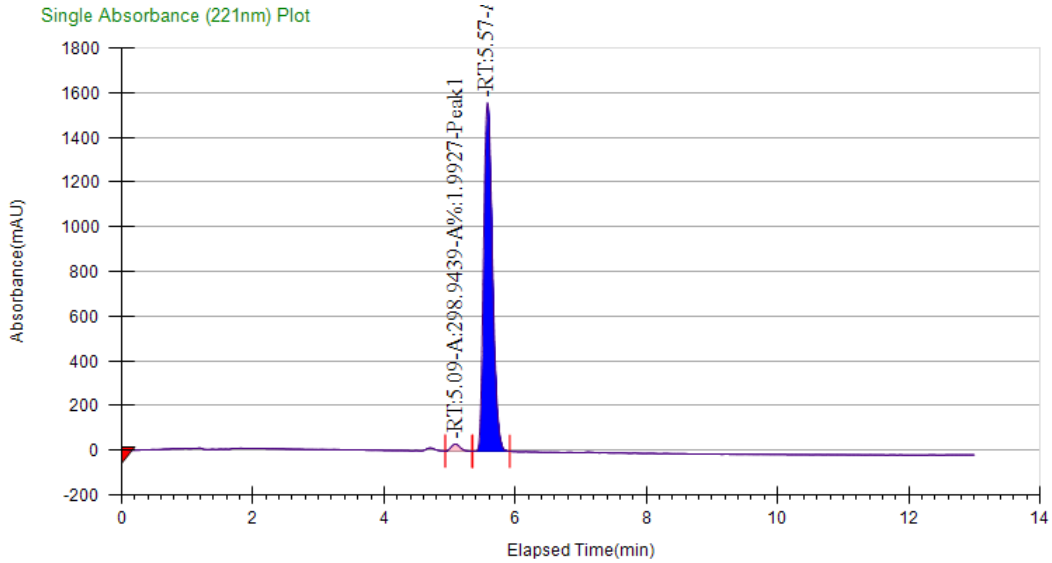

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| 1 | 2.376 | 896.465 | 5.58 | 37.0757 |
| 2 | 97.624 | 36833.4576 | 8.62 | 1313.7311 |
| Total: | 100 | | | |

Racemic Minor (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



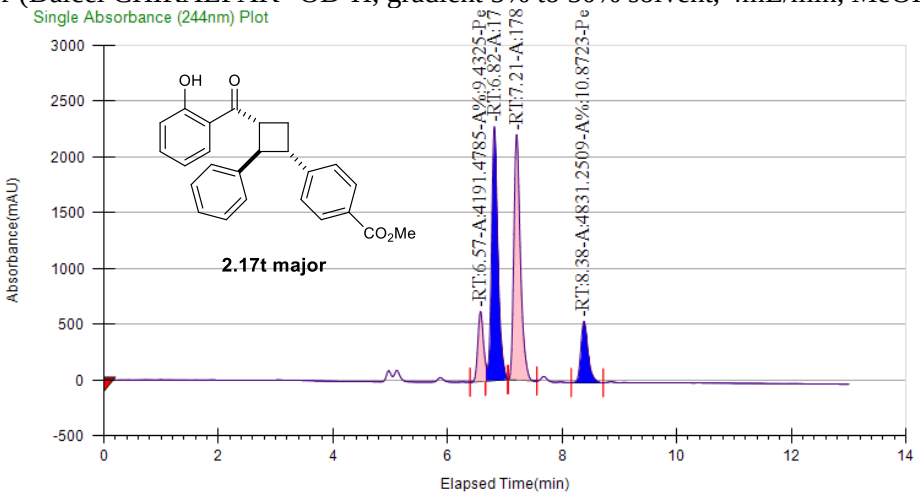

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 48.8741 | 2123.9534 | 5.09 | 180.4009 |
| **2** | 51.1259 | 2221.8143 | 5.58 | 198.4785 |
| **Total:** | 100 | | | |

Enantioenriched



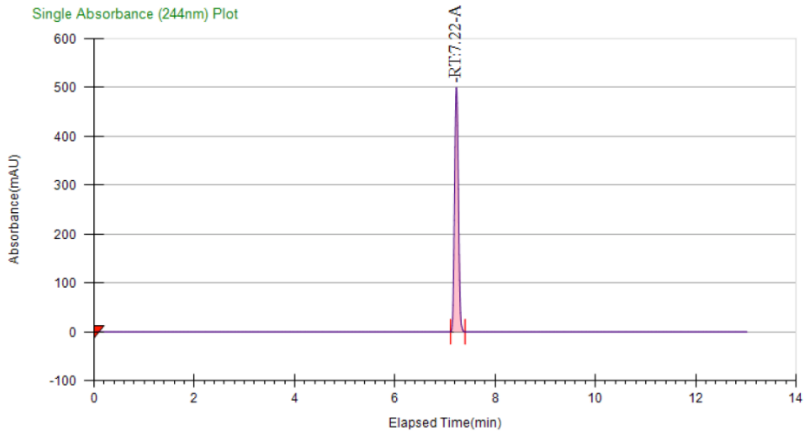

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 1.9927 | 298.9439 | 5.09 | 31.7482 |
| **2** | 98.0073 | 14703.1726 | 5.57 | 1558.4802 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 4mL/min, MeOH)



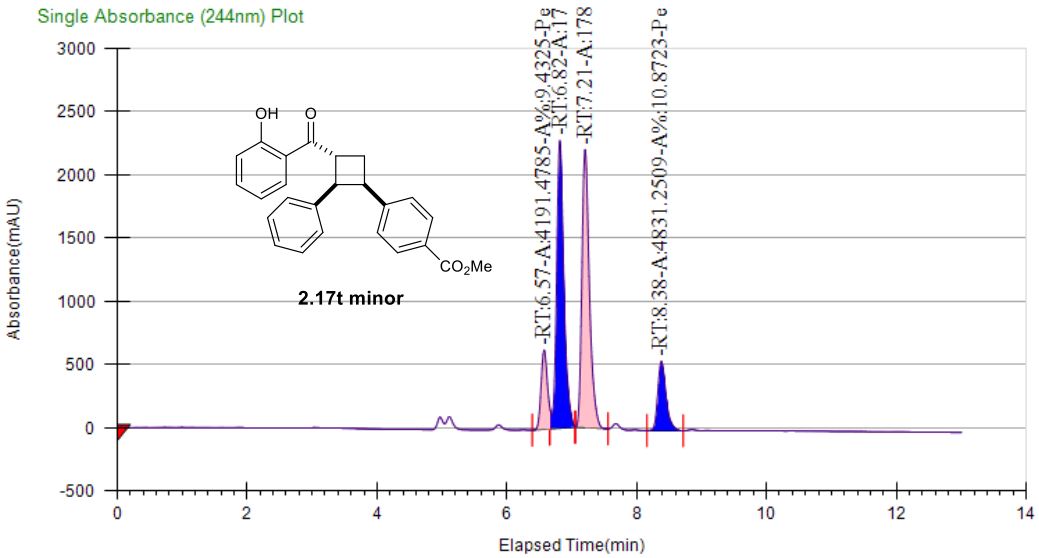

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 39.5762 | 17586.2782 | 6.82 | 2277.0791 |
| **2** | 40.119 | 17827.4566 | 7.21 | 2200.6461 |
| **Total:** | 79.6952 | | | |

Enantioenriched major



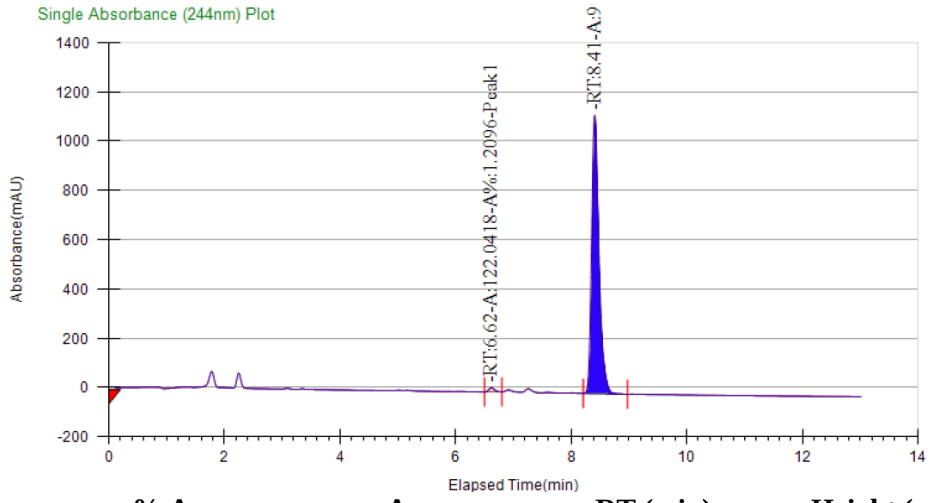

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 100 | 2691.0174 | 7.22 | 500.0744 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 4mL/min, MeOH)



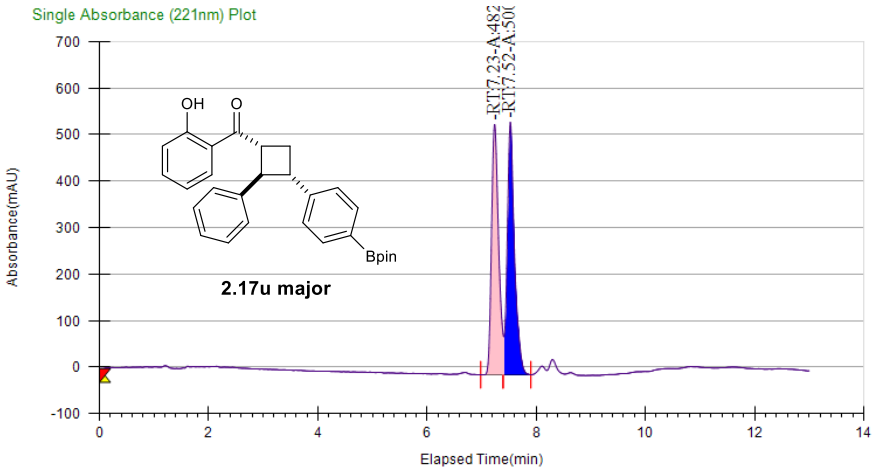

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 9.4325 | 4191.4785 | 6.57 | 629.3558 |
| **2** | 10.8723 | 4831.2509 | 8.38 | 547.3199 |
| **Total:** | 20.3048 | | | |

Enantioenriched minor



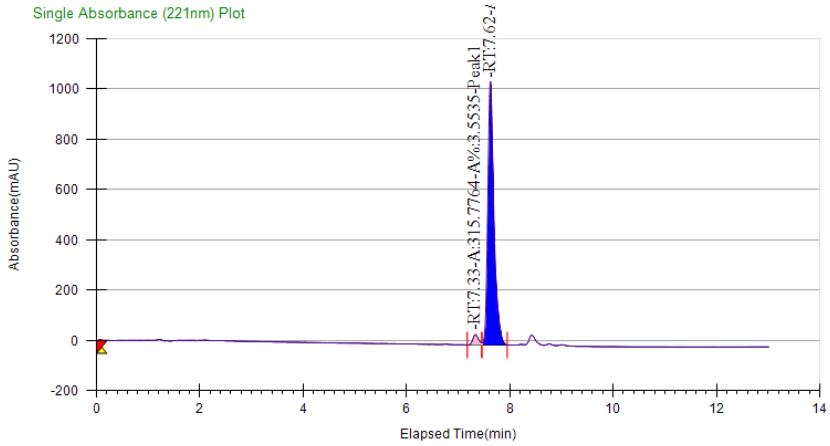

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 1.2096 | 122.0418 | 6.62 | 17.6761 |
| **2** | 98.7904 | 9967.4278 | 8.41 | 1131.4049 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



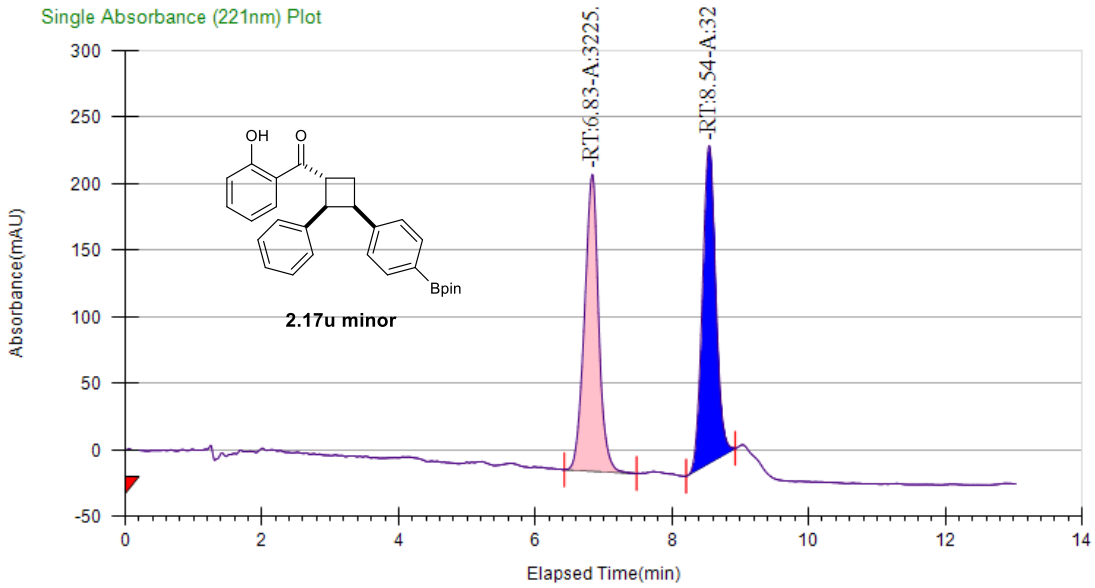

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.0807 | 4825.7754 | 7.23 | 538.509 |
| **2** | 50.9193 | 5006.5471 | 7.52 | 543.4495 |
| **Total:** | 100 | | | |

Enantioenriched



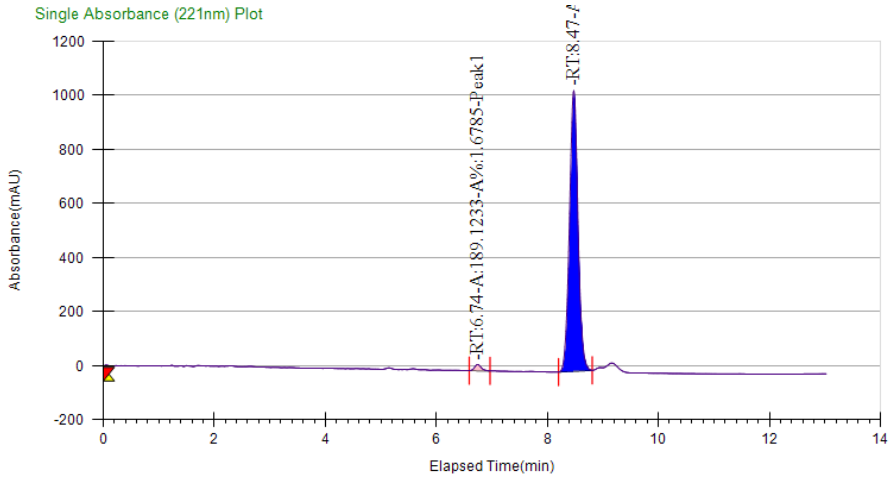

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 3.5535 | 315.7764 | 7.33 | 41.1704 |
| **2** | 96.4465 | 8570.5033 | 7.62 | 1048.6558 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



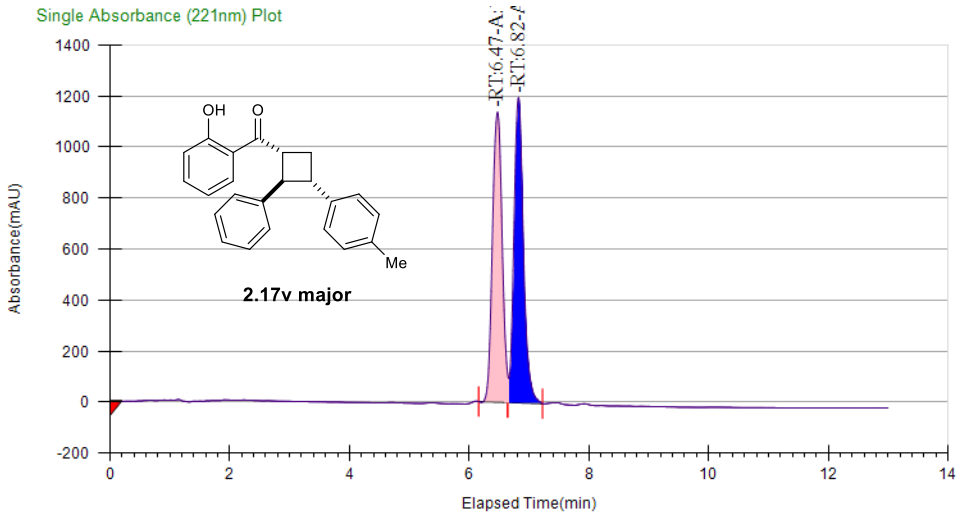

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.8965 | 3225.3079 | 6.83 | 223.1916 |
| **2** | 50.1035 | 3238.6897 | 8.54 | 238.9765 |
| **Total:** | 100 | | | |

Enantioenriched



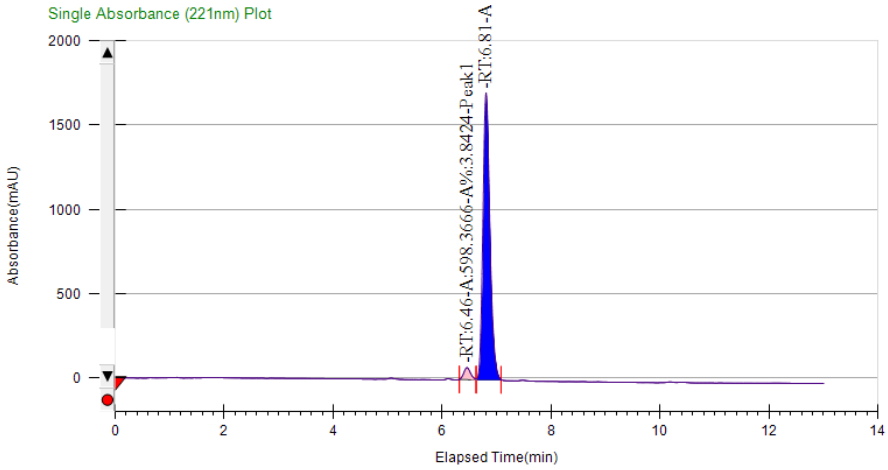

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 1.6785 | 189.1233 | 6.74 | 23.1428 |
| **2** | 98.3215 | 11078.1634 | 8.47 | 1039.5681 |
| **Total:** | 100 | | | |

**Racemic Major** (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



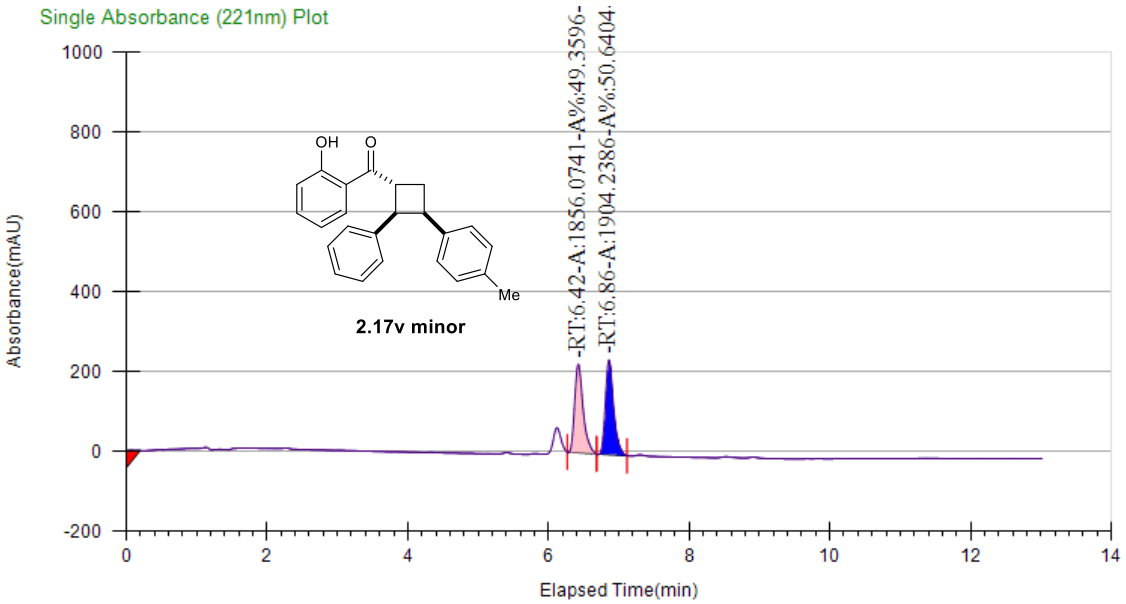

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.0856 | 12749.9725 | 6.47 | 1138.5262 |
| **2** | 50.9144 | 13224.9866 | 6.82 | 1198.9806 |
| **Total:** | 100 | | | |

Enantioenriched



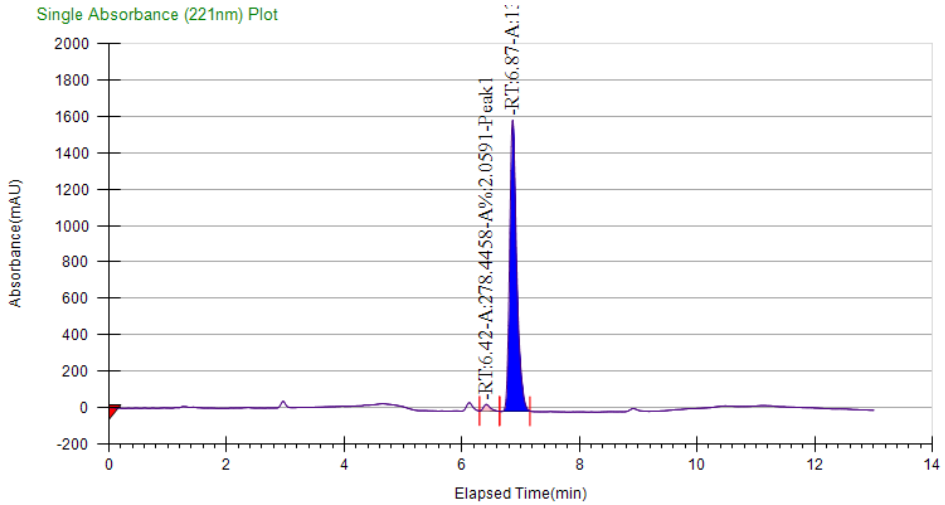

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 3.8424 | 598.3666 | 6.46 | 70.1314 |
| **2** | 96.1576 | 14974.4432 | 6.81 | 1701.0395 |
| **Total:** | 100 | | | |

Racemic Minor (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



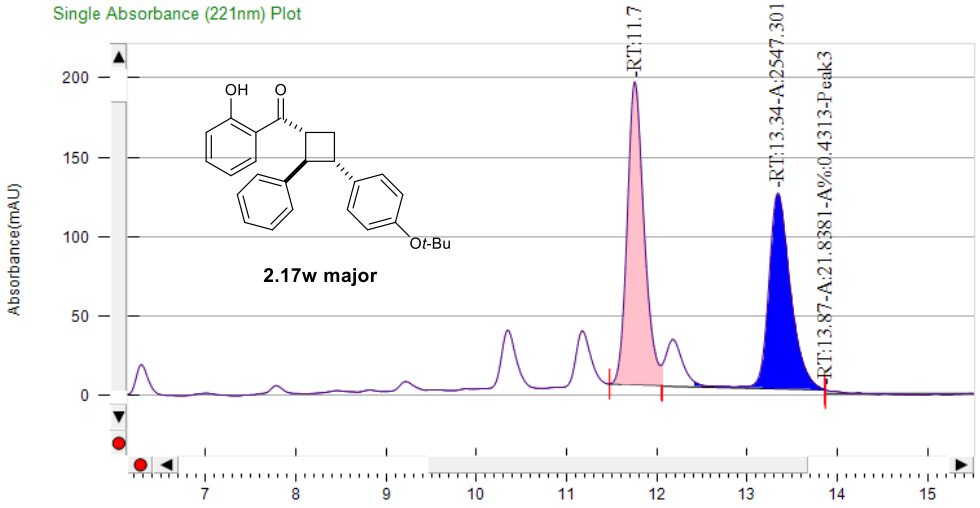

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.3596 | 1856.0741 | 6.42 | 221.6817 |
| **2** | 50.6404 | 1904.2386 | 6.86 | 237.0265 |
| **Total:** | 100 | | | |

Enantioenriched



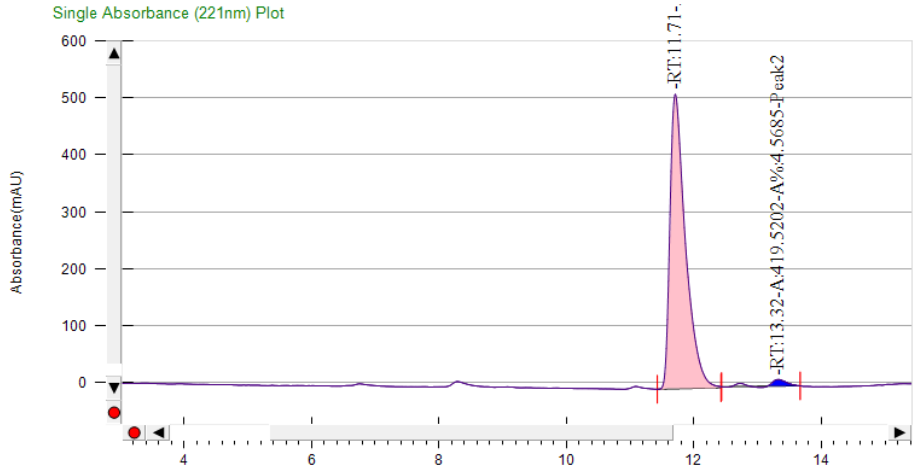

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 2.0591 | 278.4458 | 6.42 | 35.9941 |
| **2** | 97.9409 | 13244.4581 | 6.87 | 1598.0748 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OJ-H, gradient 5% to 20% solvent, 3mL/min, EtOH)



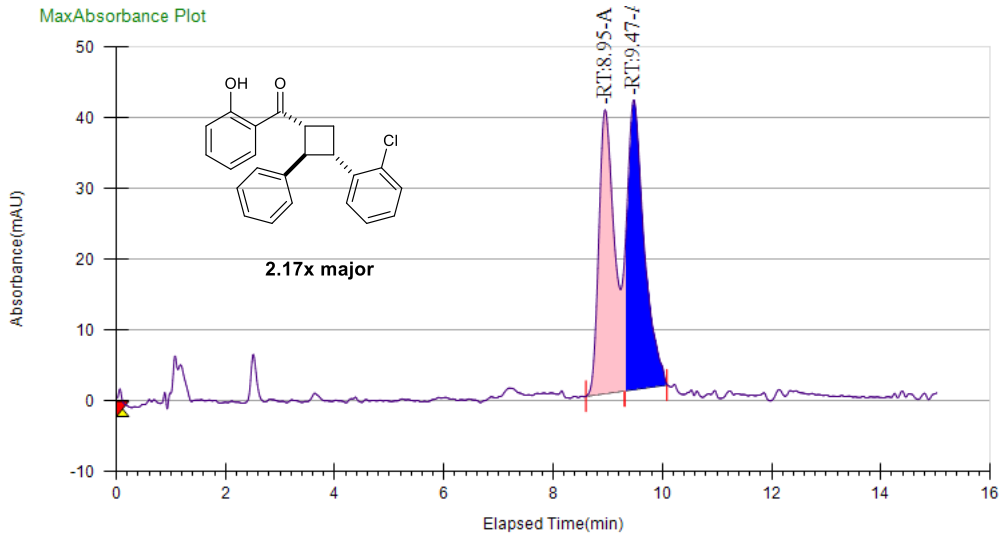

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.2547 | 2493.6706 | 11.76 | 179.8854 |
| **2** | 50.314 | 2547.3013 | 13.34 | 142.5365 |
| **Total:** | 100 | | | |

Enantioenriched



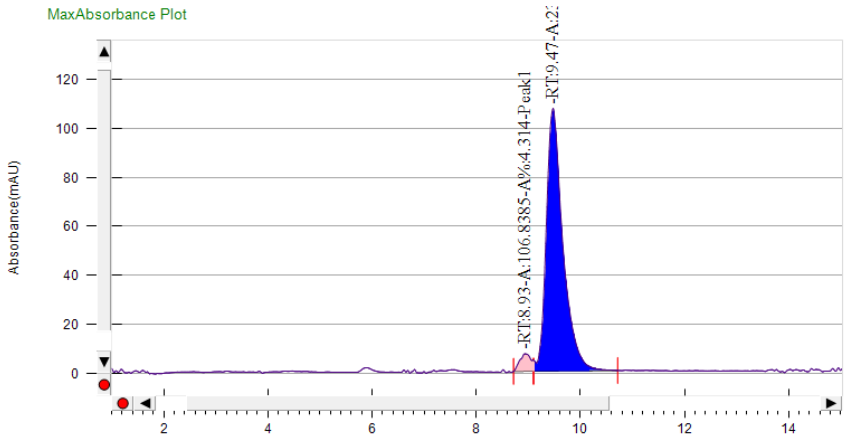

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 95.4315 | 8763.379 | 11.71 | 516.9567 |
| **2** | 4.5685 | 419.5202 | 13.32 | 12.1619 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OJ-H, gradient 8% solvent, 4mL/min, *i*-PrOH)



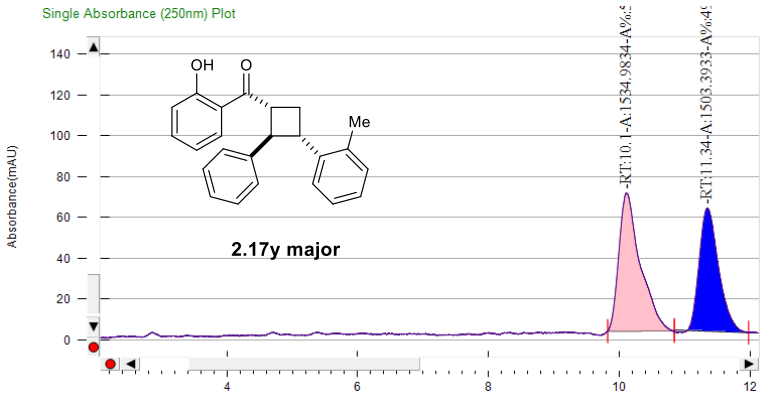

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.1768 | 827.9576 | 8.95 | 40.1003 |
| **2** | 50.8232 | 855.6774 | 9.47 | 40.944 |
| **Total:** | 100 | | | |

Enantioenriched



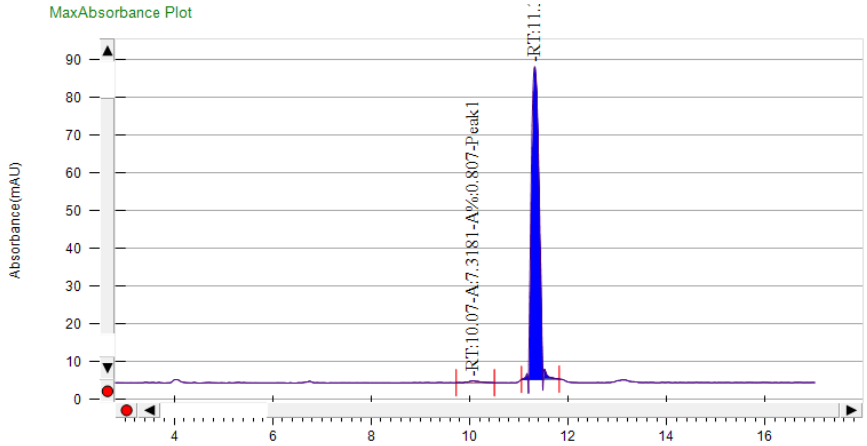

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 4.314 | 106.8385 | 8.93 | 7.1215 |
| **2** | 95.686 | 2369.7084 | 9.47 | 107.3582 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, 5% solvent, 4mL/min, MeOH)



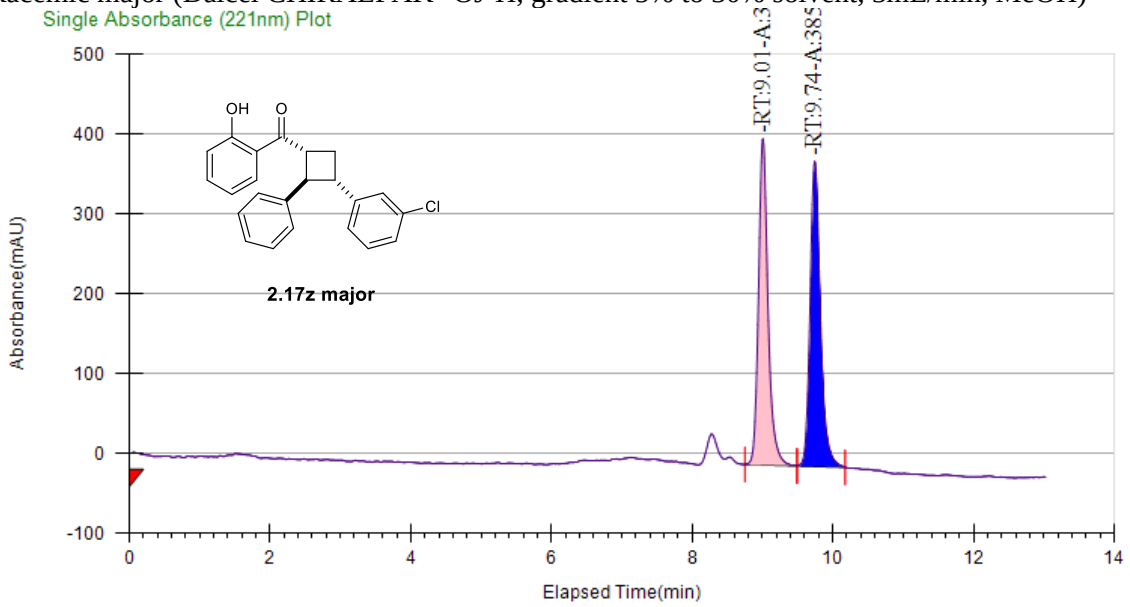

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 50.5199 | 1534.9834 | 10.10 | 67.5418 |
| **2** | 49.4801 | 1503.3933 | 11.34 | 59.9921 |
| **Total:** | 100 | | | |

Enantioenriched



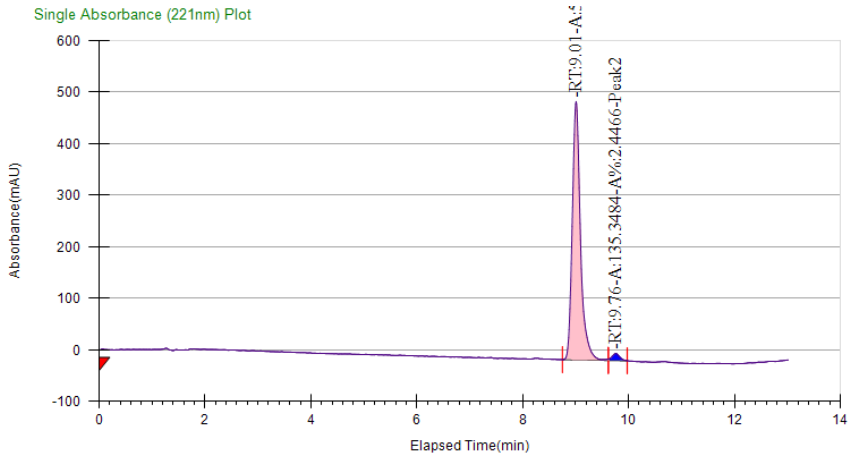

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 0.807 | 7.3181 | 10.07 | 0.4862 |
| **2** | 99.193 | 899.5306 | 11.32 | 82.8245 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OJ-H, gradient 5% to 30% solvent, 3mL/min, MeOH)



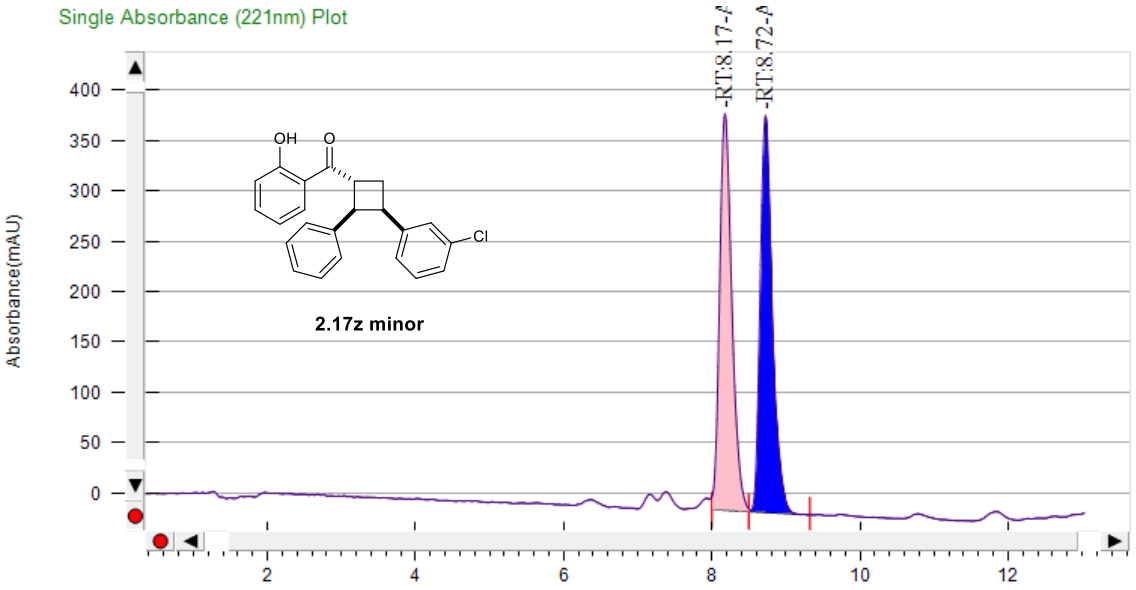

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.9153 | 3844.9529 | 9.01 | 408.6361 |
| **2** | 50.0847 | 3857.9964 | 9.74 | 382.2292 |
| **Total:** | 100 | | | |

Enantioenriched



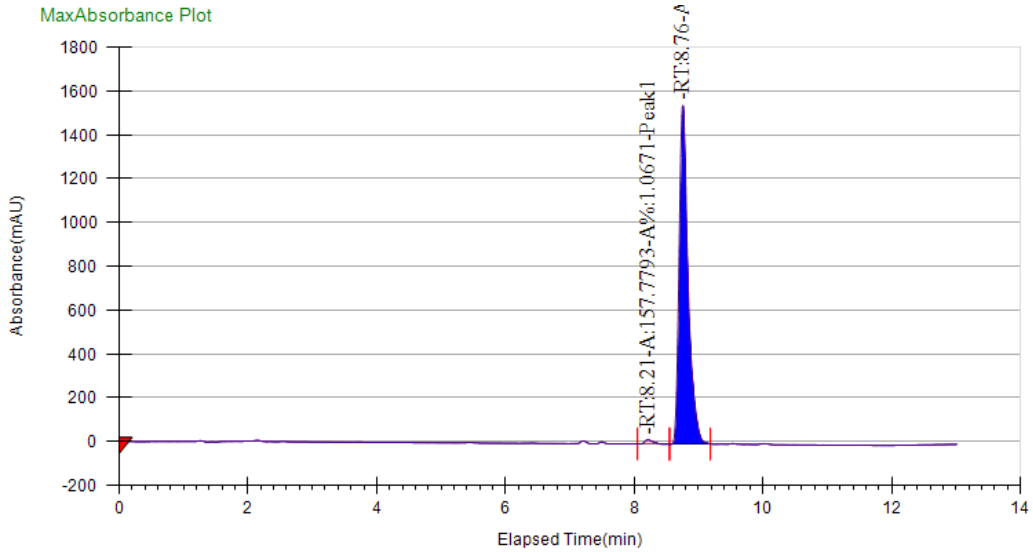

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 97.5534 | 5396.649 | 9.01 | 501.678 |
| **2** | 2.4466 | 135.3484 | 9.76 | 13.7496 |
| **Total:** | 100 | | | |

Racemic Minor (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent, 3mL/min, MeOH)



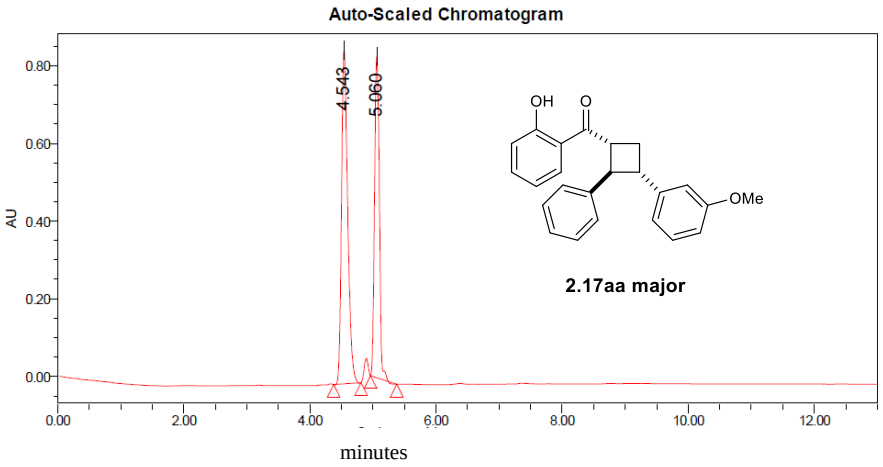

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 50.3382 | 4514.6738 | 8.17 | 392.9181 |
| **2** | 49.6618 | 4454.0071 | 8.72 | 393.2688 |
| **Total:** | 100 | | | |

Enantioenriched



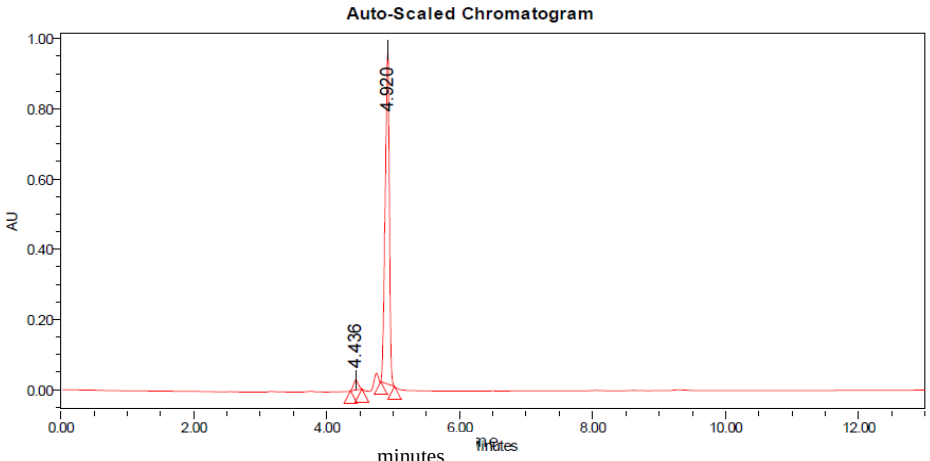

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 1.0671 | 157.7793 | 8.21 | 18.5973 |
| **2** | 98.9329 | 14628.4976 | 8.76 | 1544.3644 |
| **Total:** | 100 | | | |

Racemic Major (HPLC Diacel CHIRALPAK® OD-H, gradient 5% to 50%, 1.0 mL/min, *i*-POH)



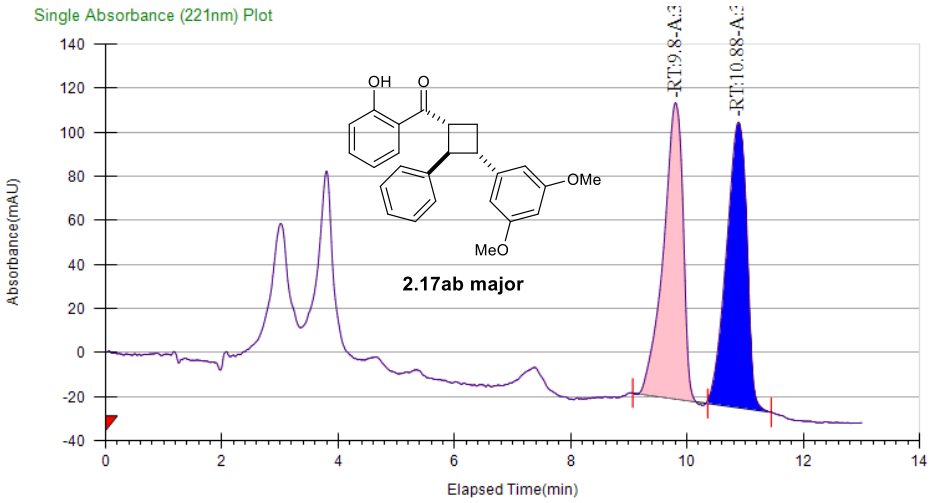

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 56.88 | 5817316 | 4.543 | 858949 |
| **2** | 43.12 | 4410435 | 5.060 | 826491 |
| **Total:** | 100 | | | |

Enantioenriched



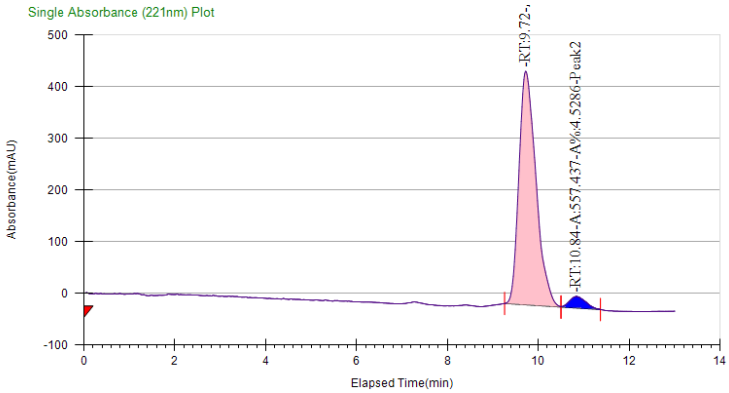

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 3.28 | 139474 | 4.436 | 27652 |
| **2** | 96.72 | 4115063 | 4.920 | 950656 |
| **Total:** | 100 | | | |

Racemic Major (Daicel CHIRALPAK® AD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



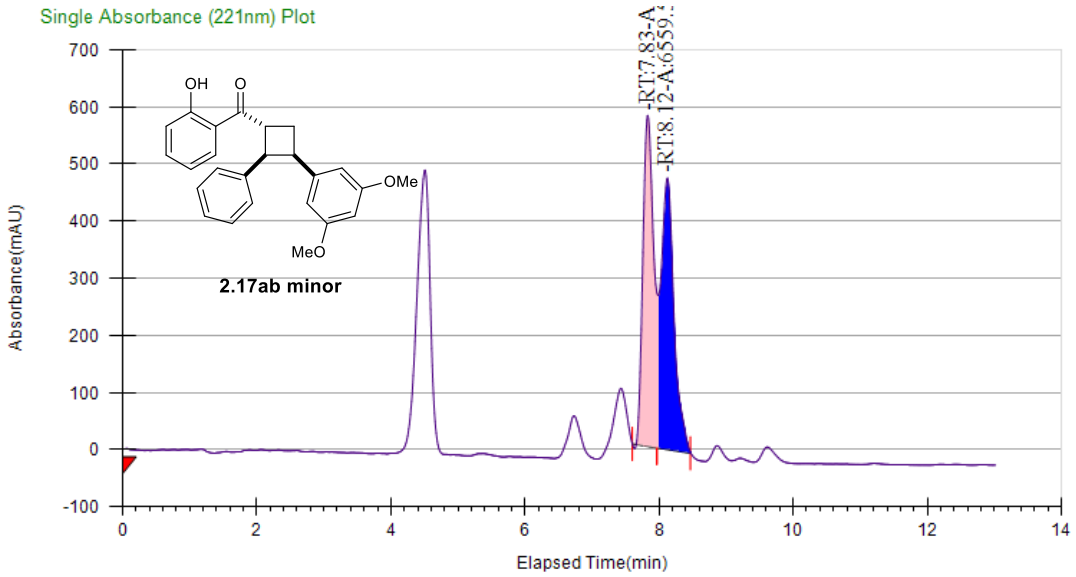

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 50.1274 | 3156.7943 | 9.80 | 134.4165 |
| **2** | 49.8726 | 3140.7476 | 10.88 | 129.6566 |
| **Total:** | 100 | | | |

Enantioenriched



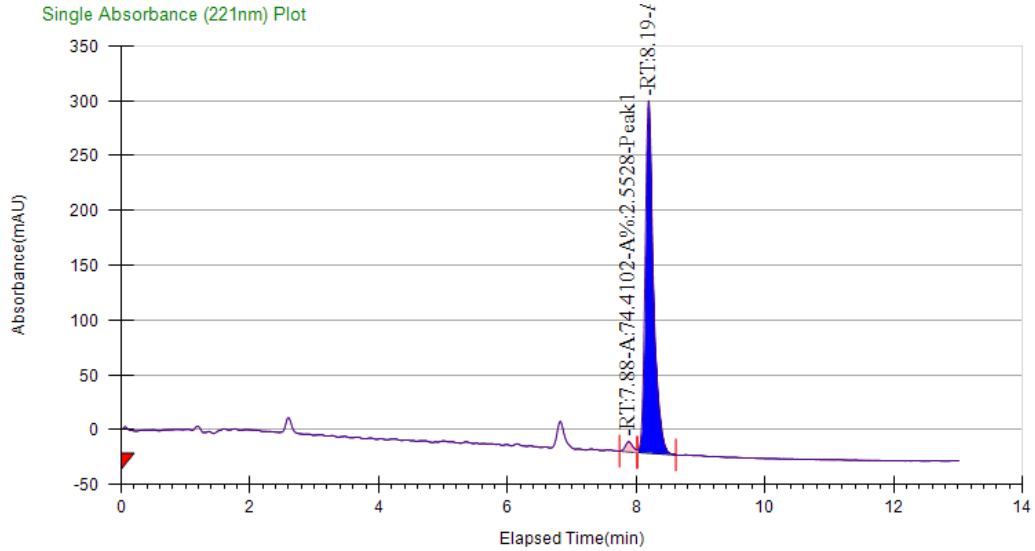

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 95.4714 | 11751.773 | 9.72 | 452.1229 |
| **2** | 4.5286 | 557.437 | 10.84 | 22.4322 |
| **Total:** | 100 | | | |

Racemic Minor (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



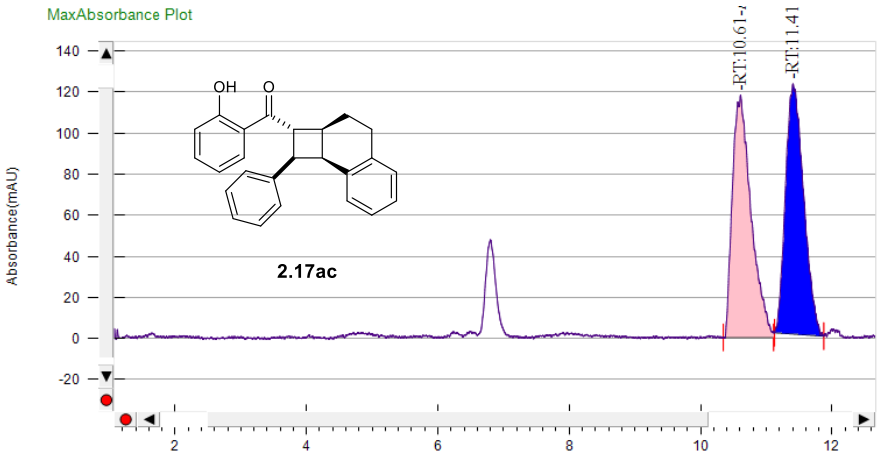

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.3431 | 6389.4617 | 7.83 | 580.0454 |
| **2** | 50.6569 | 6559.574 | 8.12 | 475.688 |
| **Total:** | 100 | | | |

Enantioenriched



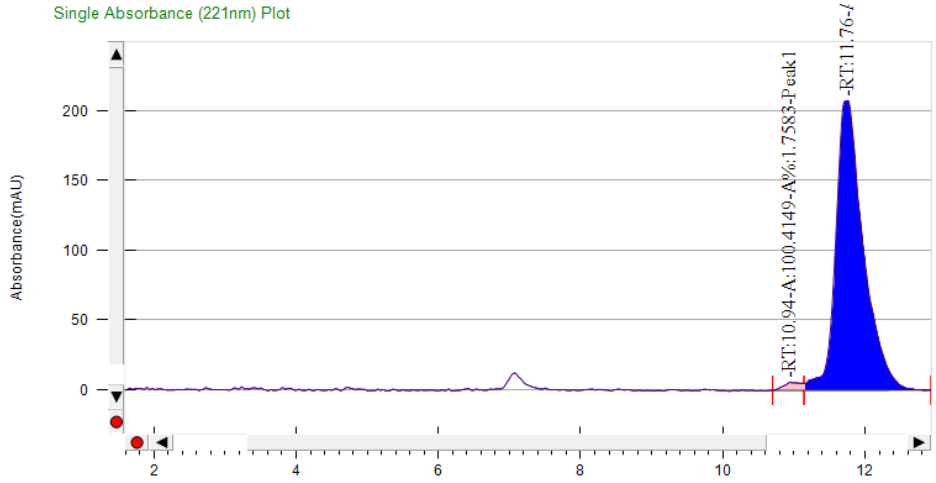

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 2.5528 | 74.4102 | 7.88 | 9.1454 |
| **2** | 97.4472 | 2840.3943 | 8.19 | 321.557 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, 5% solvent, 4mL/min, MeOH)



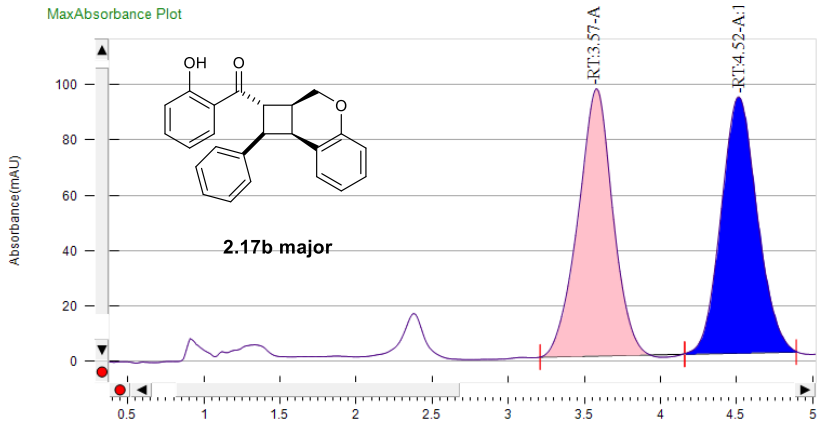

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.9517 | 2320.9759 | 10.61 | 117.9311 |
| **2** | 50.0483 | 2325.469 | 11.41 | 121.7574 |
| **Total:** | 100 | | | |

Enantioenriched



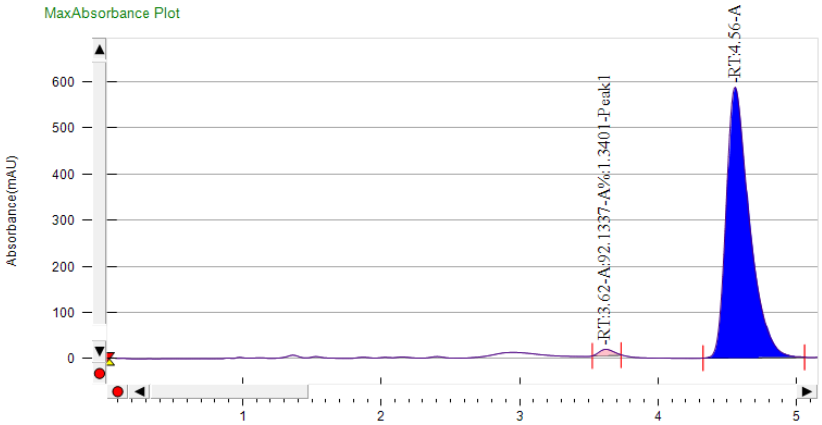

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 1.7583 | 100.4149 | 10.94 | 5.7411 |
| **2** | 98.2417 | 5610.6081 | 11.76 | 207.6382 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OJ-H, 8% solvent, 4mL/min, EtOH)



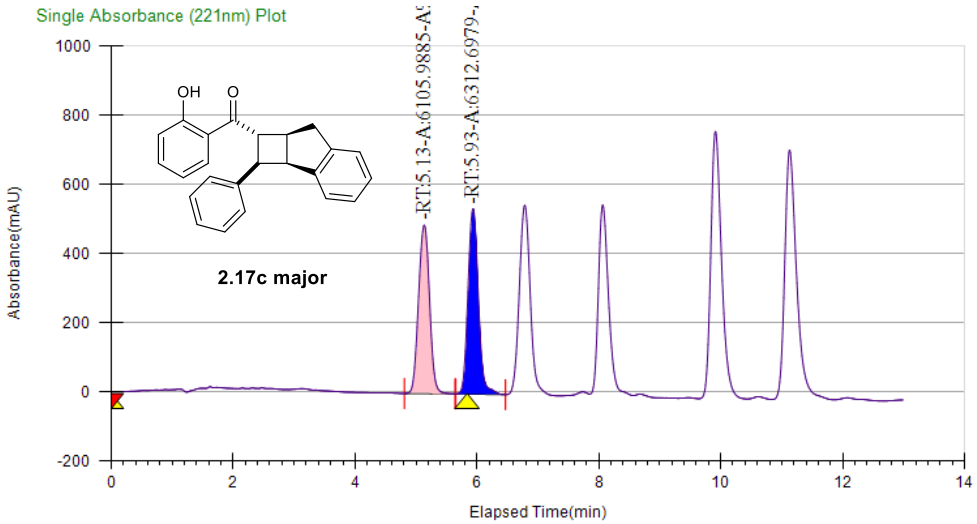

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 50.143 | 1522.143 | 3.57 | 96.4856 |
| **2** | 49.857 | 1514.2131 | 4.52 | 92.6366 |
| **Total:** | 100 | | | |

Enantioenriched



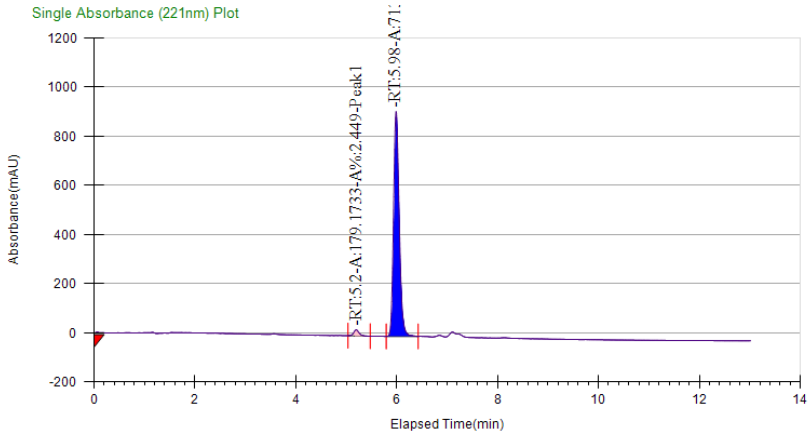

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 1.3401 | 92.1337 | 3.62 | 13.5844 |
| **2** | 98.6599 | 6783.0615 | 4.56 | 586.6628 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



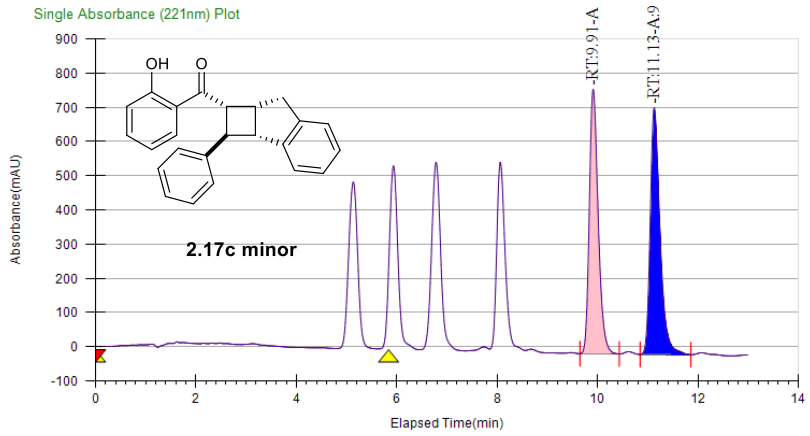

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.1677 | 6105.9885 | 5.13 | 487.4281 |
| **2** | 50.8323 | 6312.6979 | 5.93 | 536.1499 |
| **Total:** | 100 | | | |

Enantioenriched



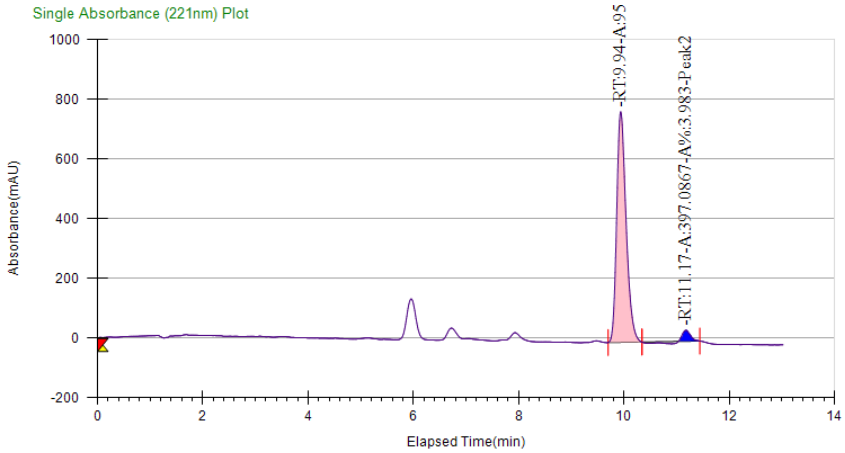

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 2.449 | 179.1733 | 5.2 | 24.4964 |
| **2** | 97.551 | 7137.1244 | 5.98 | 915.5062 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



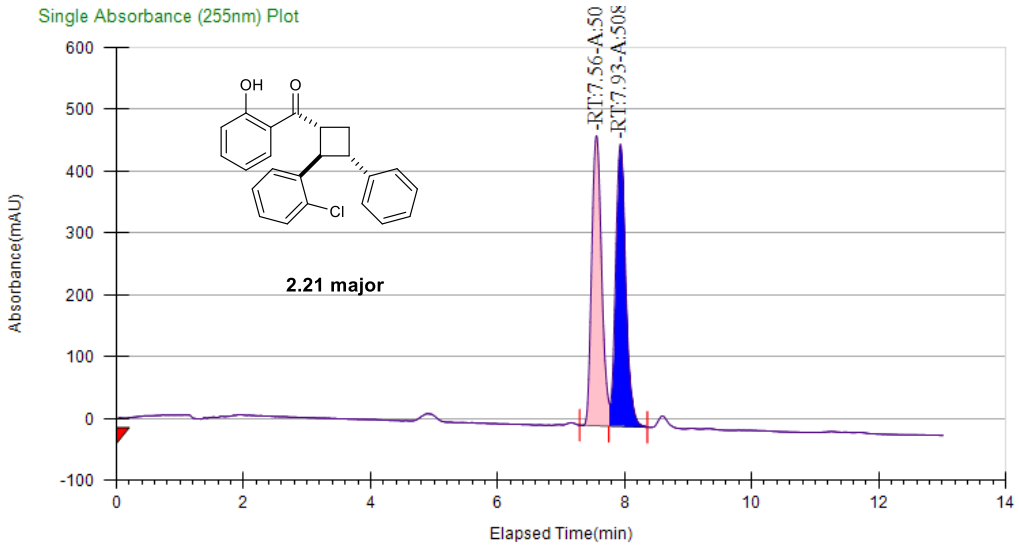

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.1479 | 9439.695 | 9.91 | 772.6613 |
| **2** | 50.8521 | 9767.0223 | 11.13 | 720.8943 |
| **Total:** | 100 | | | |

Enantioenriched



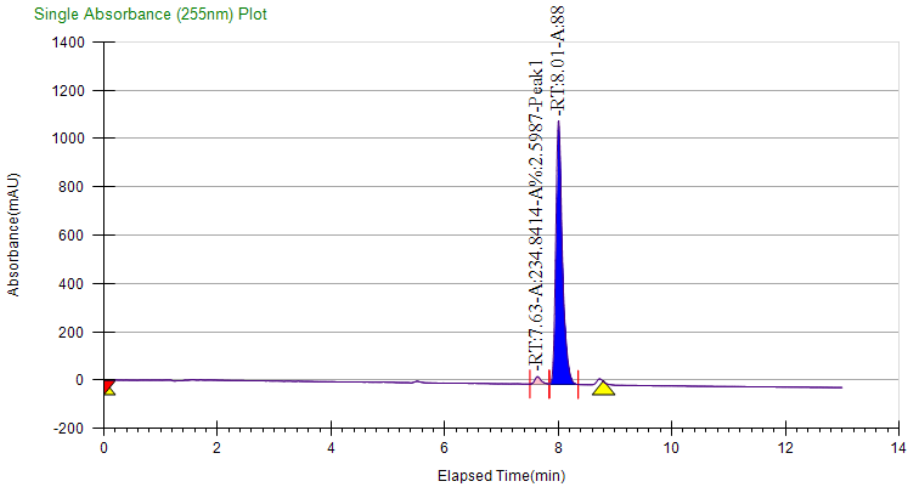

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 96.017 | 9572.3269 | 9.94 | 772.7114 |
| **2** | 3.983 | 397.0867 | 11.17 | 36.8096 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



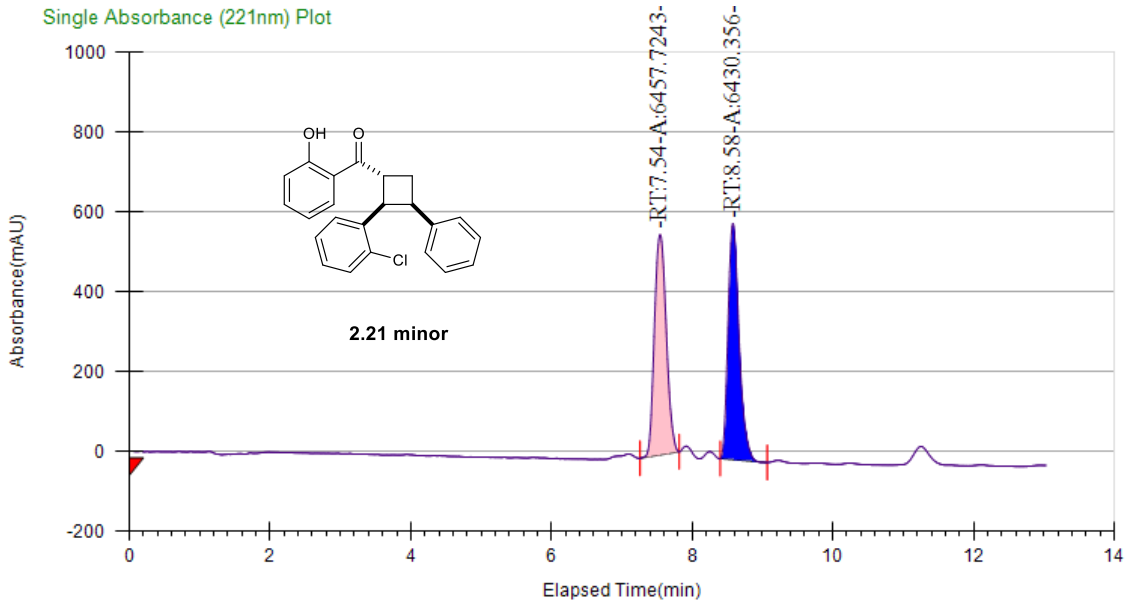

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.9724 | 5079.7714 | 7.56 | 469.423 |
| **2** | 50.0276 | 5085.3852 | 7.93 | 456.6474 |
| **Total:** | 100 | | | |

Enantioenriched



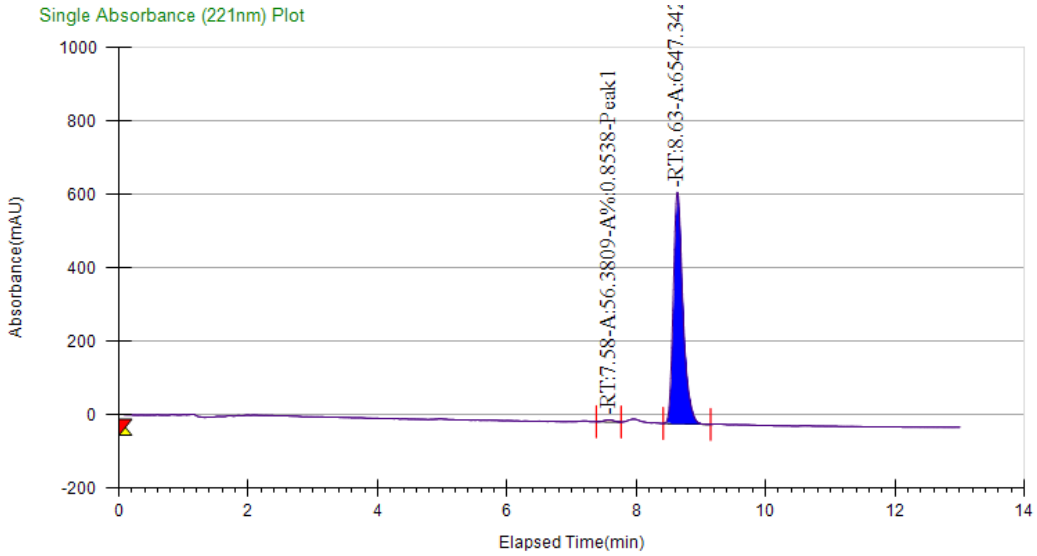

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 2.5987 | 234.8414 | 7.63 | 30.8885 |
| **2** | 97.4013 | 8802.0297 | 8.01 | 1091.9955 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



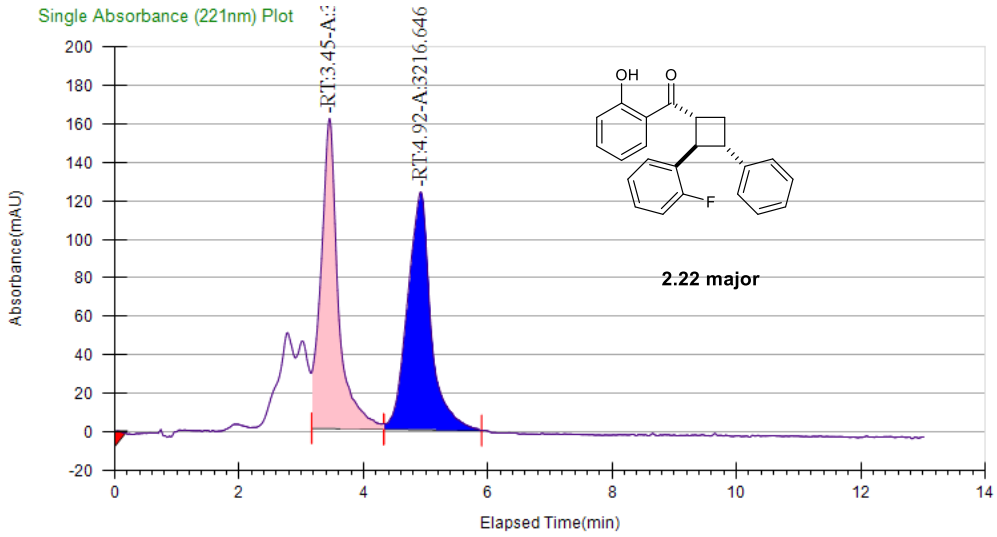

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 50.1062 | 6457.7243 | 7.54 | 551.7267 |
| **2** | 49.8938 | 6430.356 | 8.58 | 591.785 |
| **Total:** | 100 | | | |

Enantioenriched



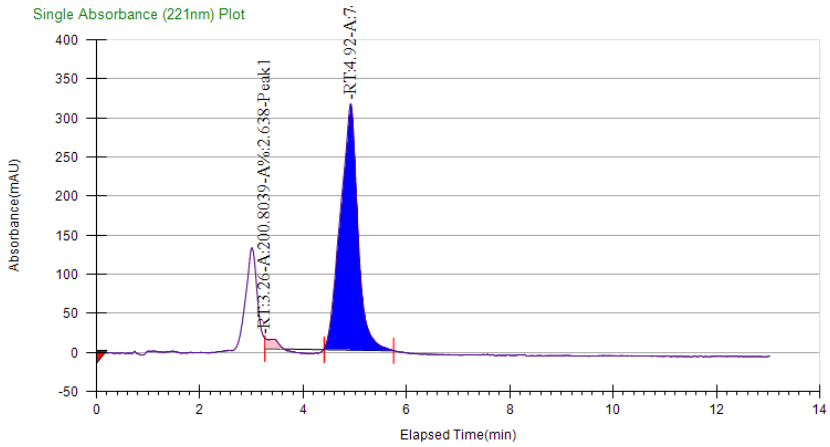

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 0.8538 | 56.3809 | 7.58 | 5.6836 |
| **2** | 99.1462 | 6547.3426 | 8.63 | 630.1889 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® AD-H, 10% solvent, 5mL/min, MeOH)



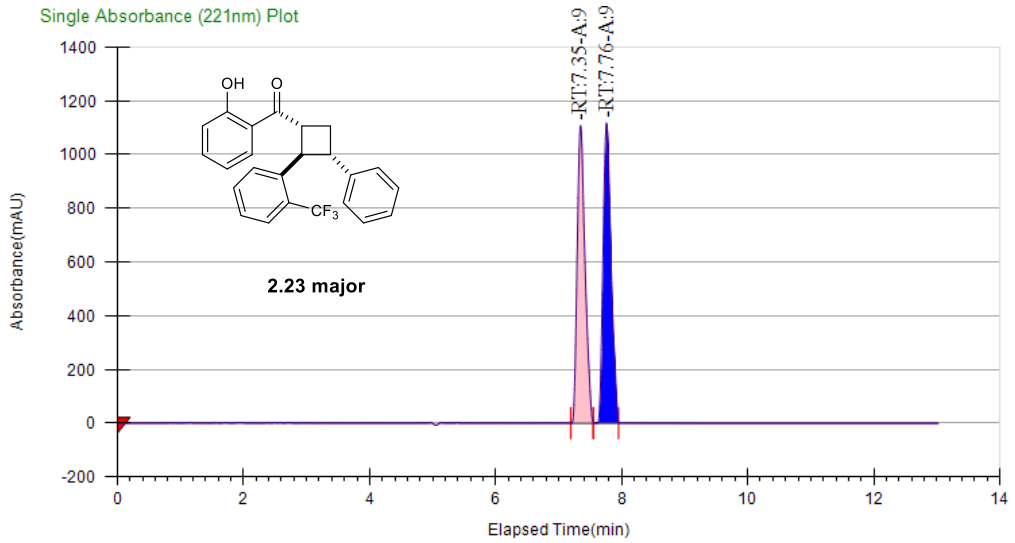

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.3695 | 3136.5272 | 3.45 | 160.7936 |
| **2** | 50.6305 | 3216.6466 | 4.92 | 123.5008 |
| **Total:** | 100 | | | |

Enantioenriched



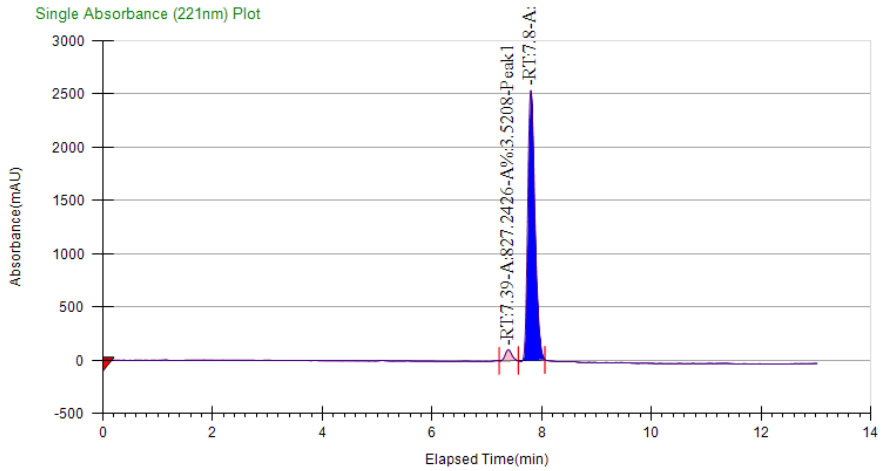

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 2.638 | 200.8039 | 3.26 | 13.4436 |
| **2** | 97.362 | 7411.2632 | 4.92 | 315.2173 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent, 3mL/min, *i*-PrOH)



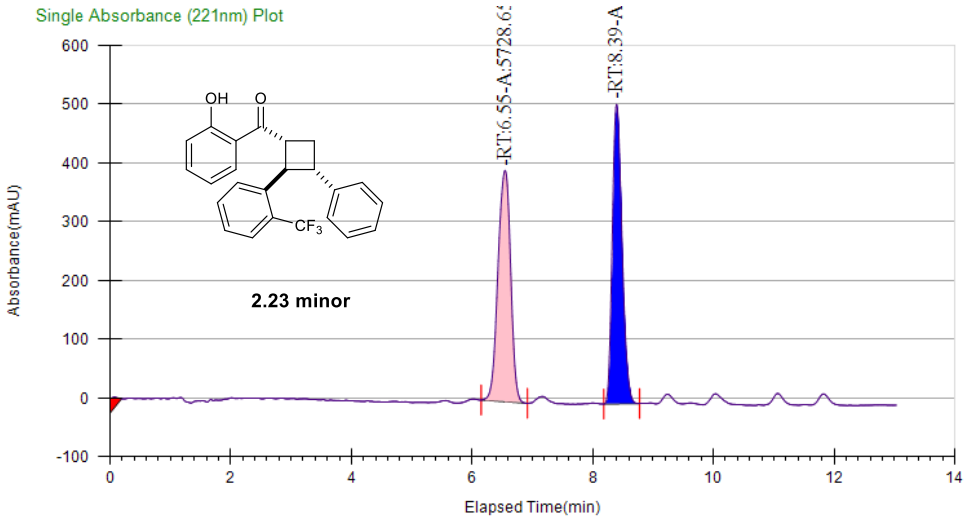

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.5086 | 9549.7725 | 7.35 | 1107.93 |
| **2** | 50.4914 | 9739.3422 | 7.76 | 1117.7942 |
| **Total:** | 100 | | | |

Enantioenriched



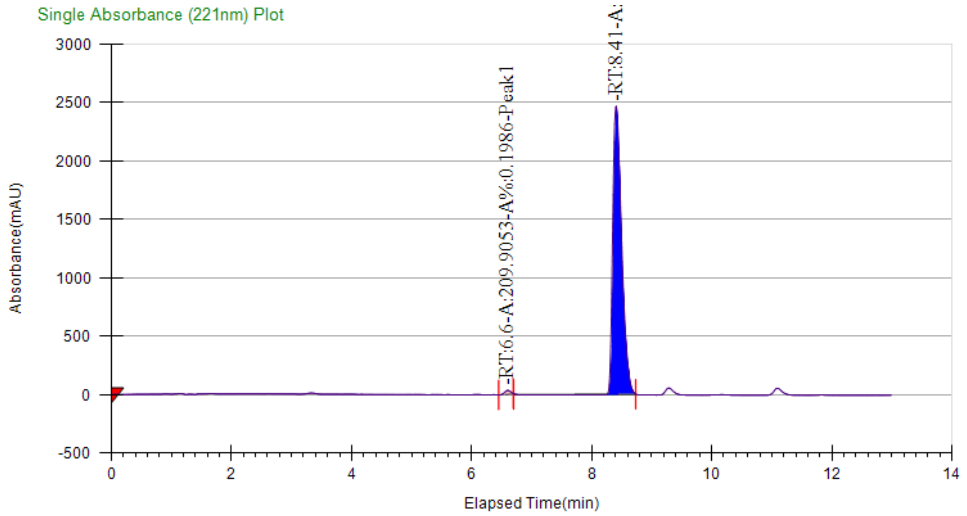

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 3.5208 | 827.2426 | 7.39 | 103.0428 |
| **2** | 96.4792 | 22668.9212 | 7.8 | 2533.7806 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent, 3mL/min, *i*-PrOH)



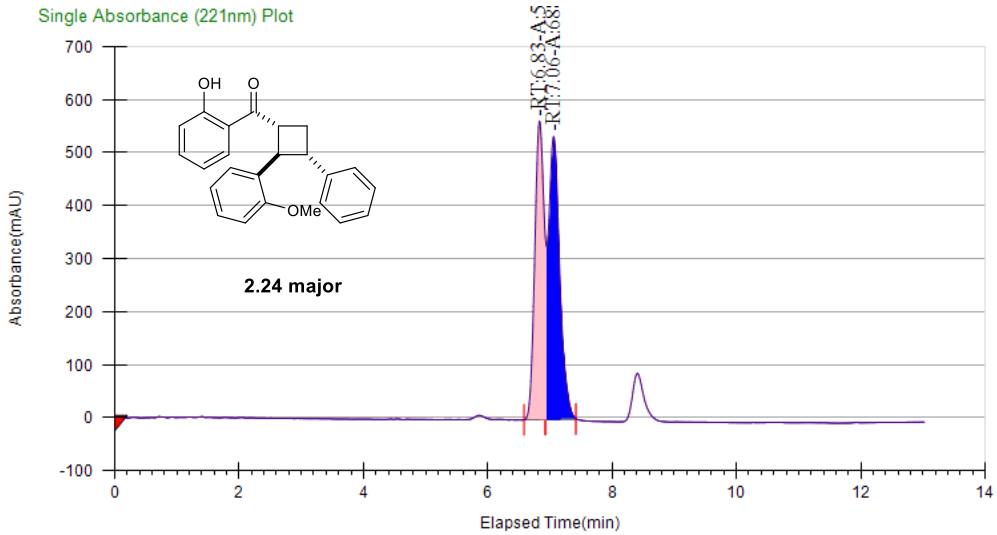

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 50.2268 | 5728.6539 | 6.55 | 393.9662 |
| **2** | 49.7732 | 5676.9107 | 8.39 | 510.1907 |
| **Total:** | 100 | | | |

Enantioenriched



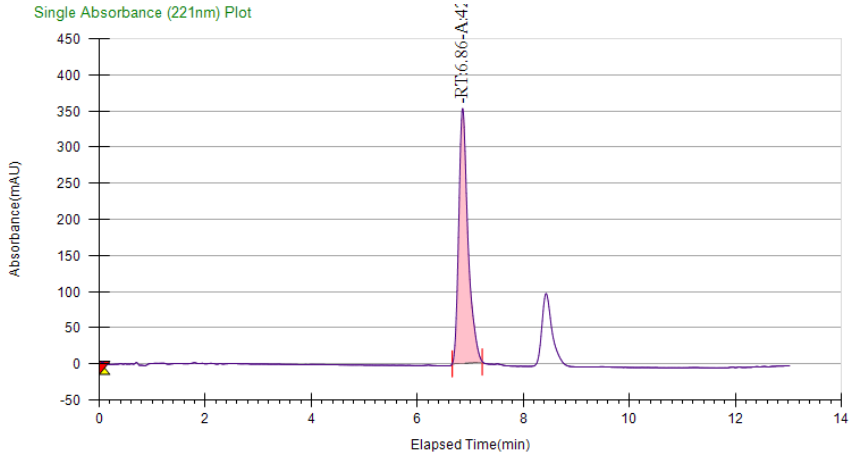

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 0.1986 | 209.9053 | 6.6 | 31.8131 |
| **2** | 99.8014 | 105479.4374 | 8.41 | 2469.035 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, gradient 5% to 10% solvent, 5mL/min, MeOH)



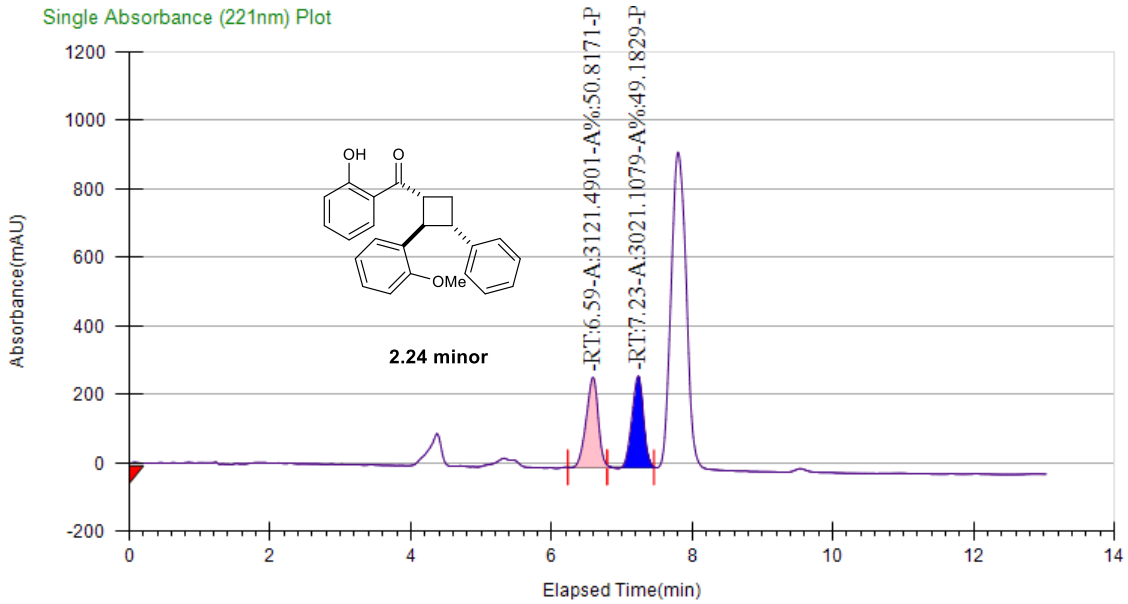

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 45.3103 | 5702.9392 | 6.83 | 563.5417 |
| **2** | 54.6897 | 6883.4585 | 7.06 | 534.1561 |
| **Total:** | 100 | | | |

Enantioenriched



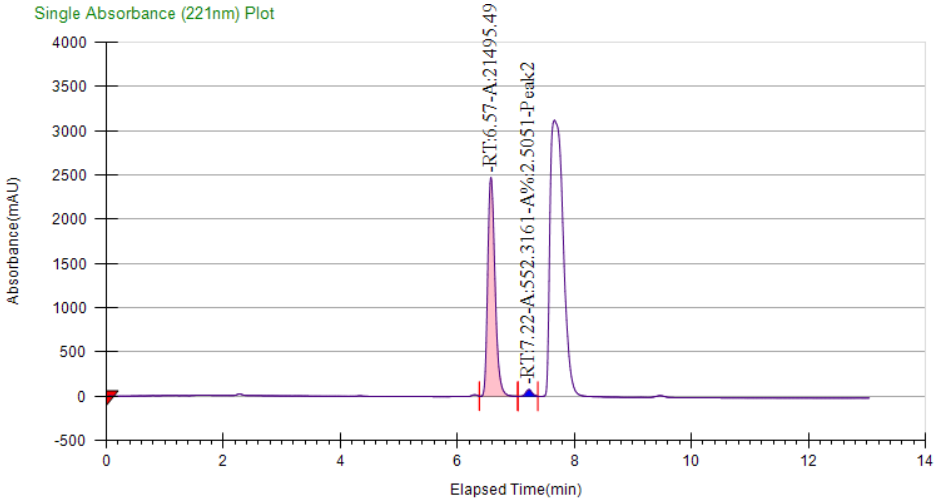

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 100 | 4278.3986 | 6.86 | 352.443 |
| **2** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



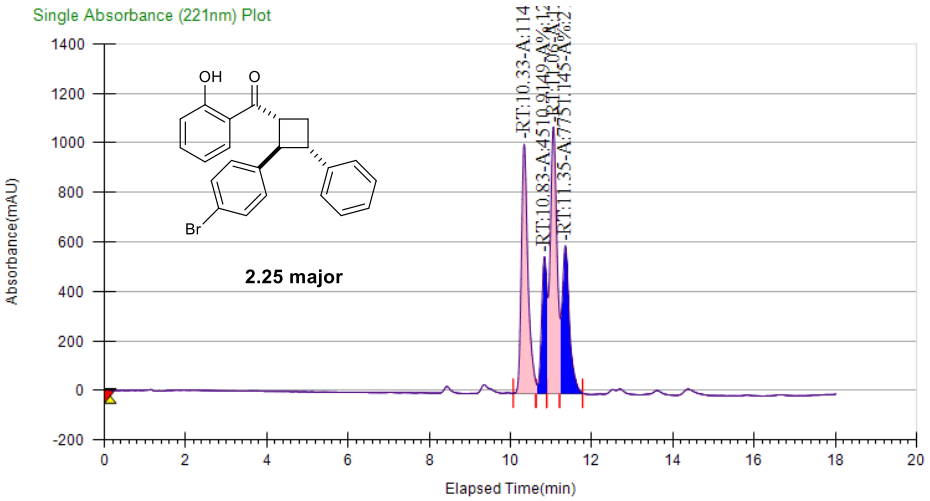

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 50.8171 | 3121.4901 | 6.59 | 263.1416 |
| **2** | 49.1829 | 3021.1079 | 7.23 | 267.2794 |
| **Total:** | 100 | | | |

Enantioenriched



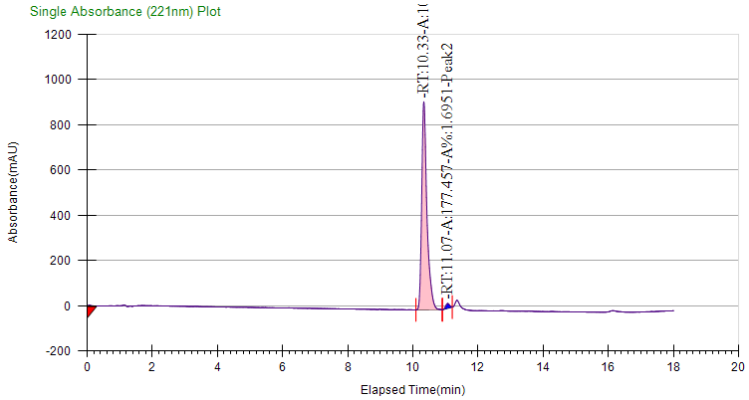

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 97.4949 | 21495.4904 | 6.57 | 2472.5916 |
| **2** | 2.5051 | 552.3161 | 7.22 | 75.118 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent, 3mL/min, MeOH)



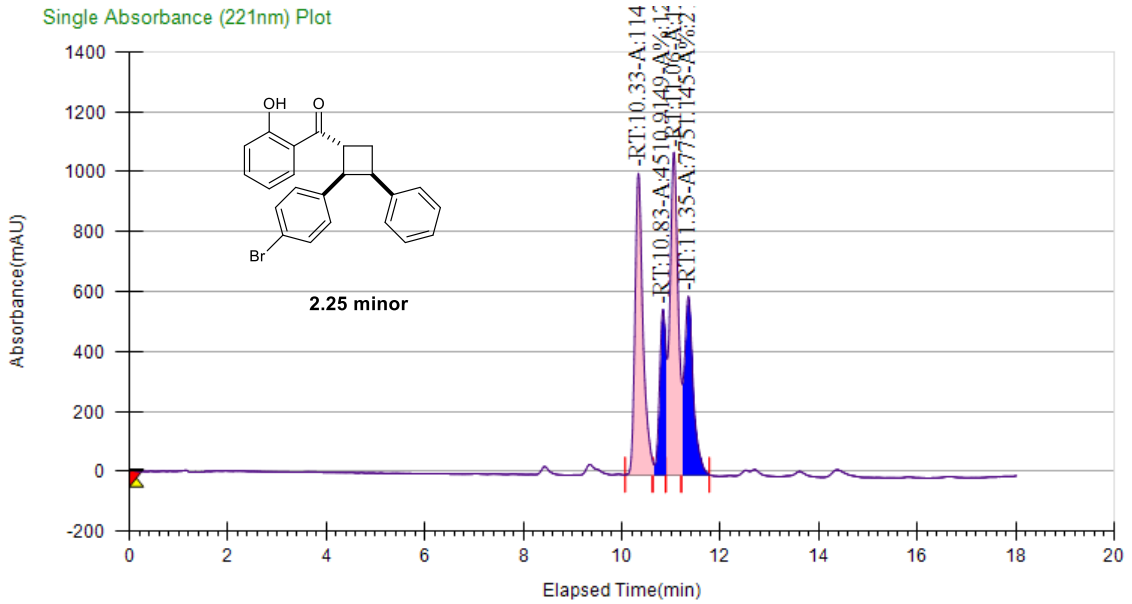

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 31.4778 | 11414.7962 | 10.33 | 1006.6565 |
| **2** | 34.7079 | 12586.1361 | 11.06 | 1077.0668 |
| **Total:** | 66.1857 | | | |

Enantioenriched



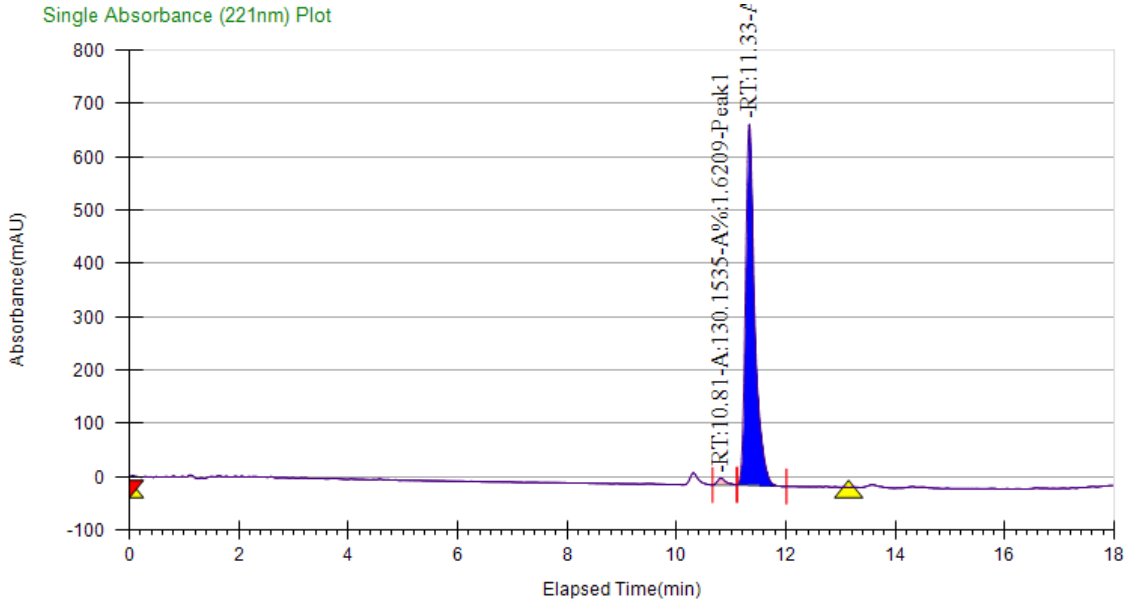

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 98.3049 | 10291.3946 | 10.33 | 920.5649 |
| **2** | 1.6951 | 177.457 | 11.07 | 21.7303 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent, 3mL/min, MeOH)



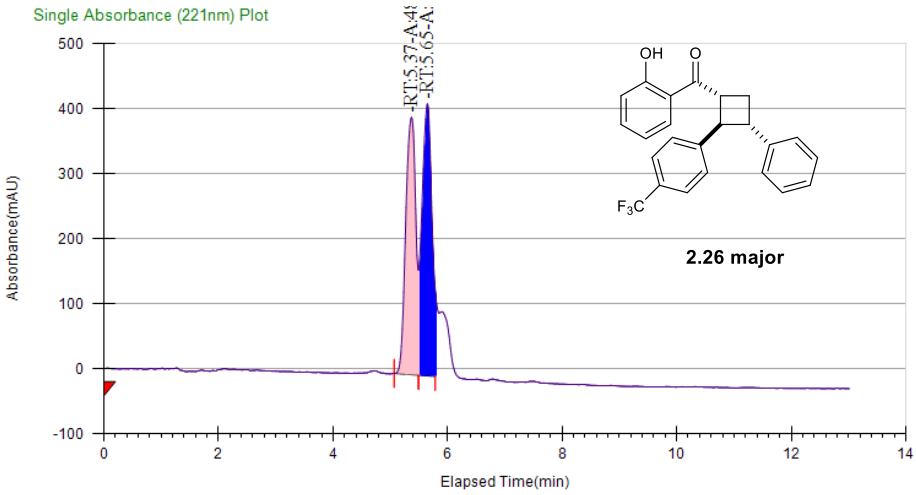

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 12.4394 | 4510.9149 | 10.83 | 551.6176 |
| **2** | 21.3748 | 7751.145 | 11.35 | 596.3708 |
| **Total:** | 33.8142 | | | |

Enantioenriched



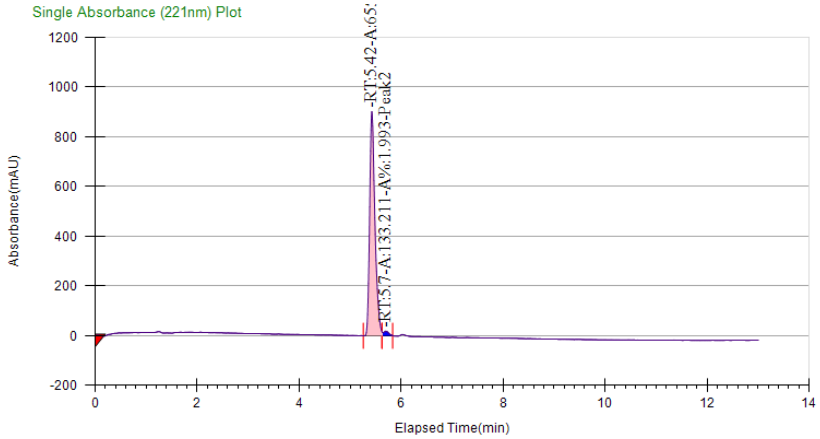

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 1.6209 | 130.1535 | 10.81 | 12.6662 |
| **2** | 98.3791 | 7899.6095 | 11.33 | 676.5947 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



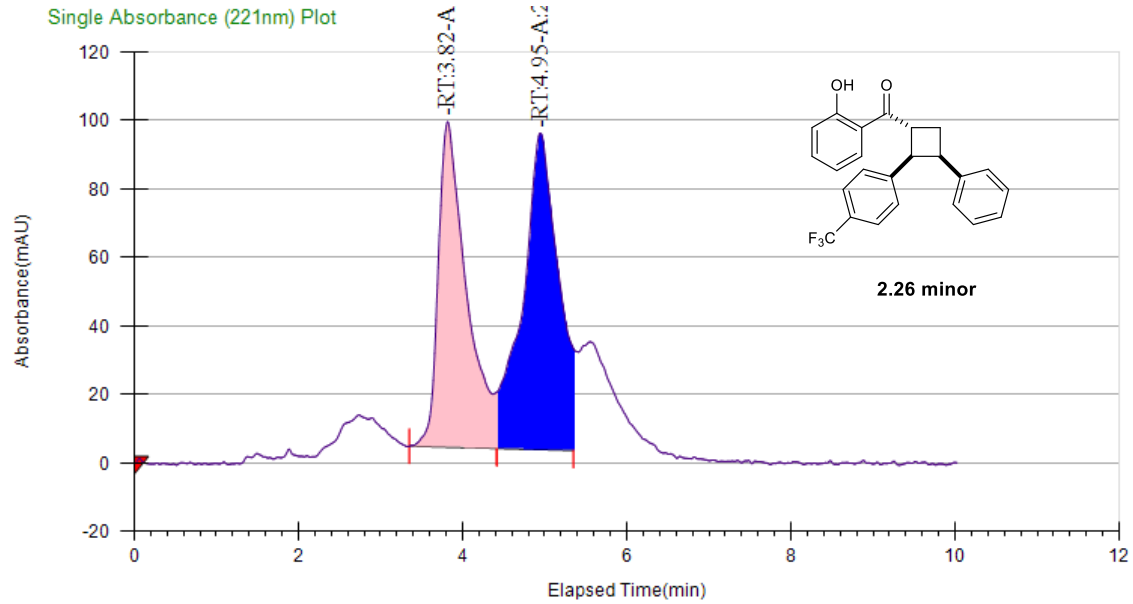

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.4213 | 4866.2668 | 5.37 | 395.717 |
| **2** | 50.5787 | 4980.2338 | 5.65 | 418.4816 |
| **Total:** | 100 | | | |

Enantioenriched



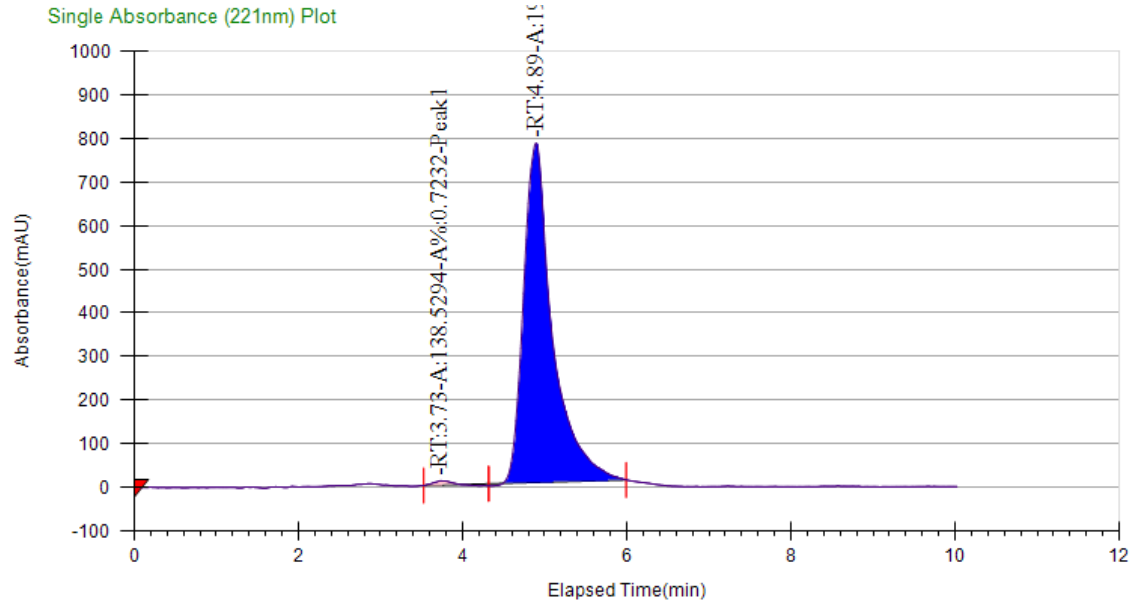

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 98.007 | 6550.7836 | 5.42 | 903.0529 |
| **2** | 1.993 | 133.211 | 5.7 | 18.5133 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® AD-H, 10% solvent, 3mL/min, MeOH)



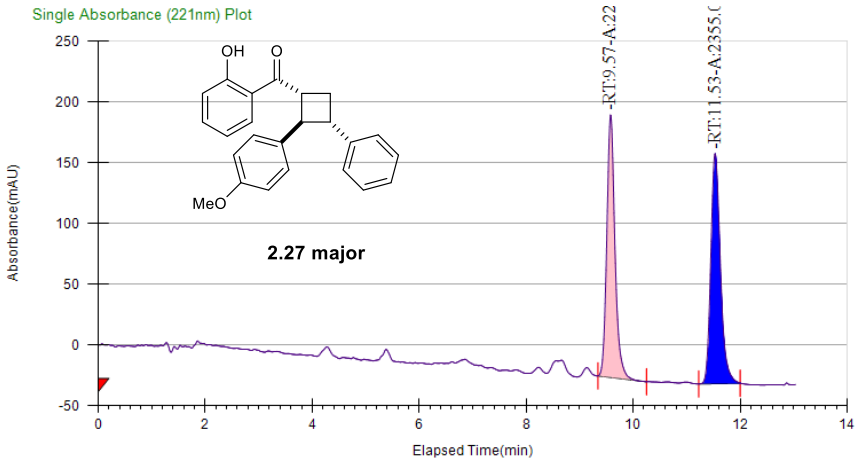

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 45.1168 | 2294.1088 | 3.82 | 95.1046 |
| **2** | 54.8832 | 2790.7169 | 4.95 | 92.466 |
| **Total:** | 100 | | | |

Enantioenriched



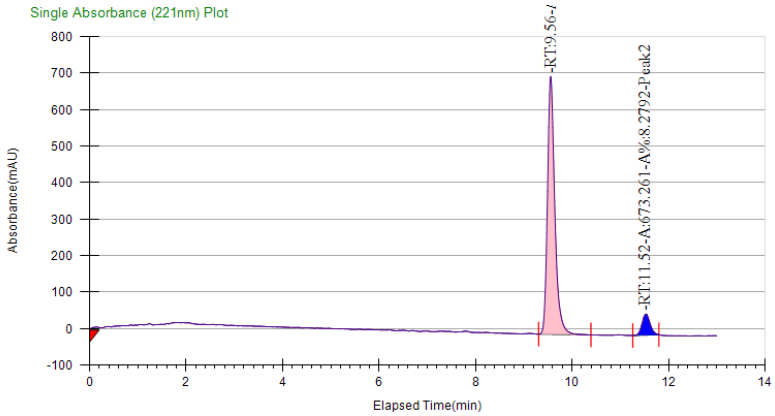

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 0.7232 | 138.5294 | 3.73 | 9.6379 |
| **2** | 99.2768 | 19015.6269 | 4.89 | 777.9112 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



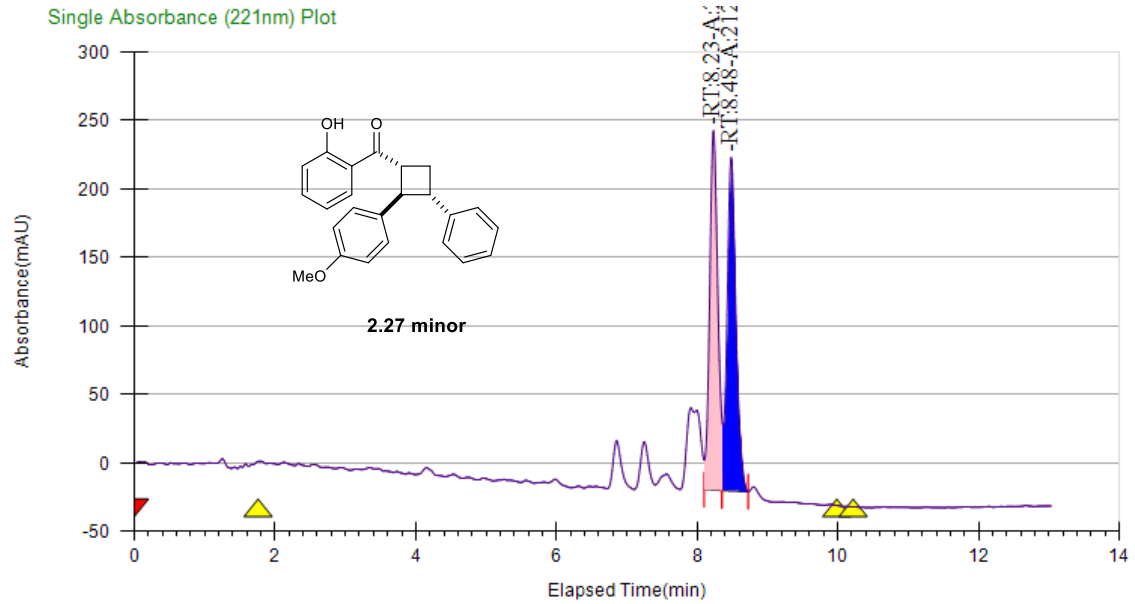

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.2645 | 2286.7551 | 9.57 | 216.0194 |
| **2** | 50.7355 | 2355.0348 | 11.53 | 189.2991 |
| **Total:** | 100 | | | |

Enantioenriched



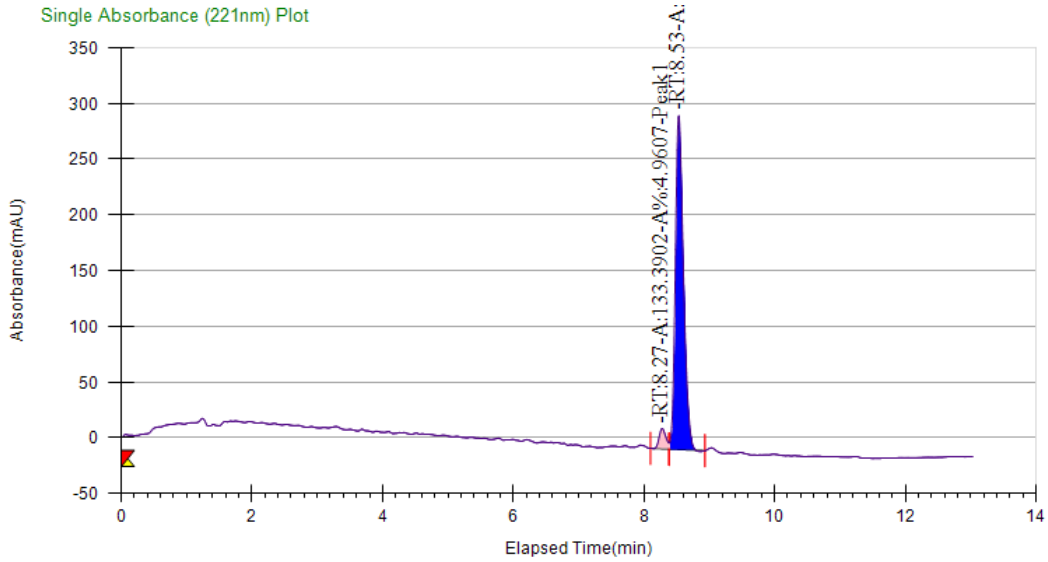

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 91.7208 | 7458.6698 | 9.56 | 706.6145 |
| **2** | 8.2792 | 673.261 | 11.52 | 57.6095 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OD-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



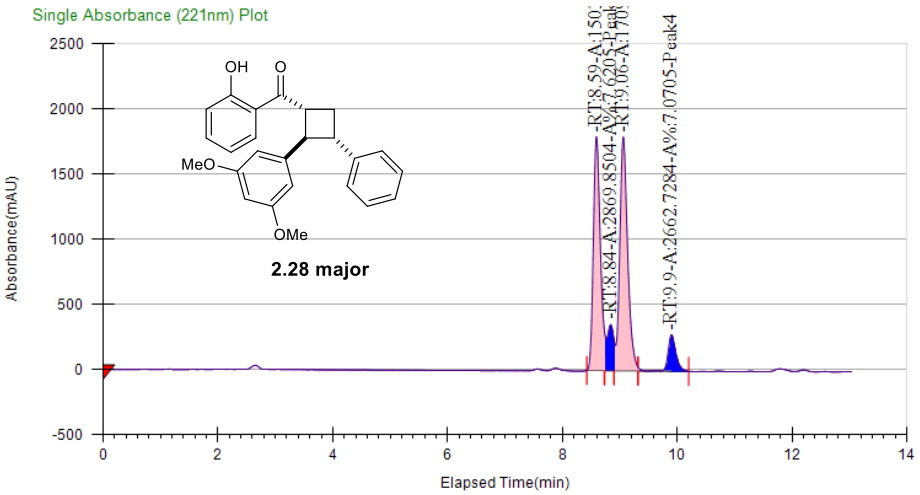

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.8254 | 2106.5121 | 8.23 | 262.7497 |
| **2** | 50.1746 | 2121.274 | 8.48 | 243.5976 |
| **Total:** | 100 | | | |

Enantioenriched



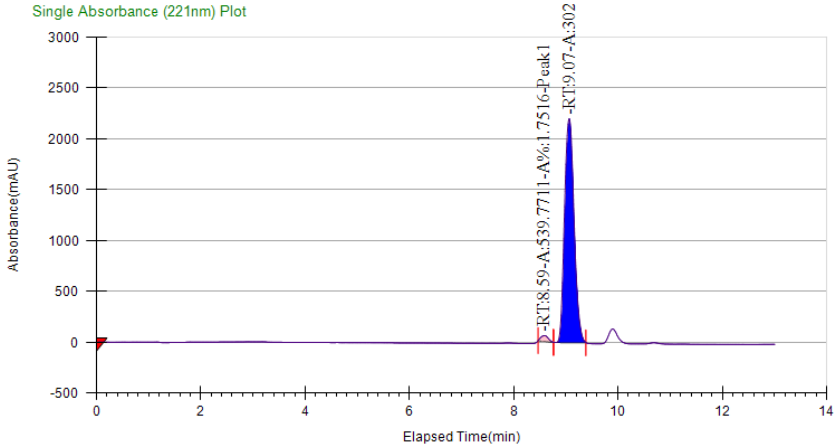

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 4.9607 | 133.3902 | 8.27 | 18.2082 |
| **2** | 95.0393 | 2555.5319 | 8.53 | 299.8399 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent, 3mL/min, MeOH)



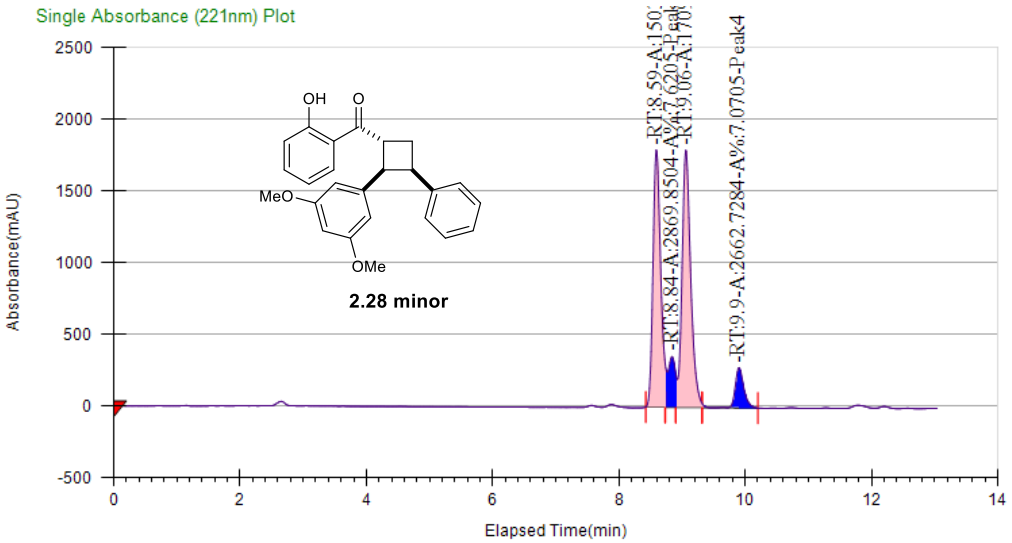

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 39.9261 | 15036.0748 | 8.59 | 1794.0823 |
| **2** | 45.383 | 17091.1487 | 9.06 | 1793.8418 |
| **Total:** | 85.3091 | | | |

Enantioenriched



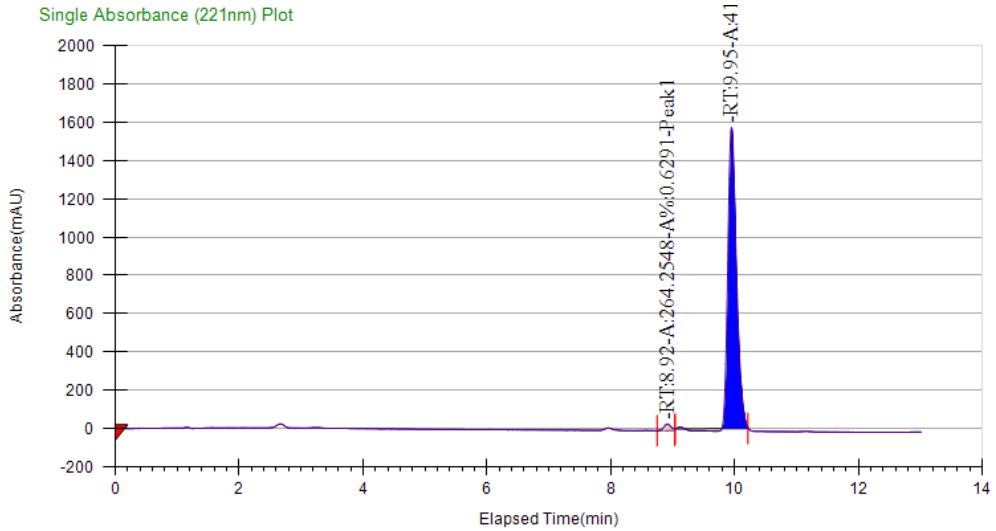

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 1.7516 | 539.7711 | 8.59 | 56.0896 |
| **2** | 98.2484 | 30276.6893 | 9.07 | 2201.2791 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent, 3mL/min, MeOH)



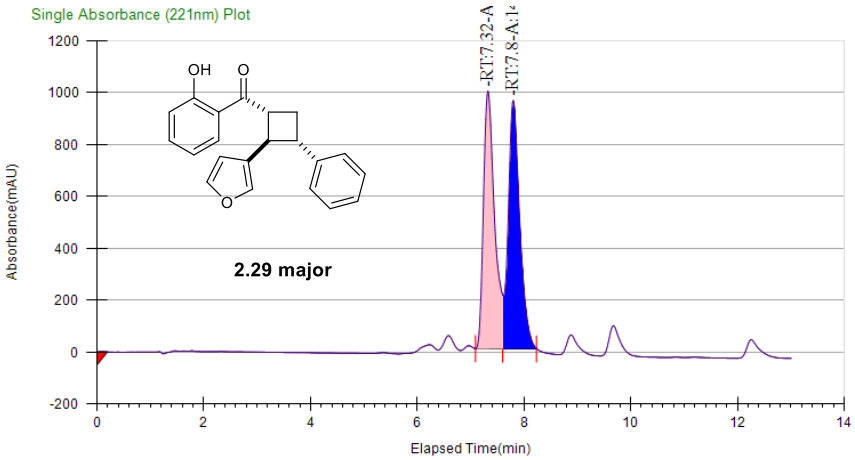

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 7.6205 | 2869.8504 | 8.84 | 354.1435 |
| **2** | 7.0705 | 2662.7284 | 9.9 | 281.4071 |
| **Total:** | 14.691 | | | |

Enantioenriched



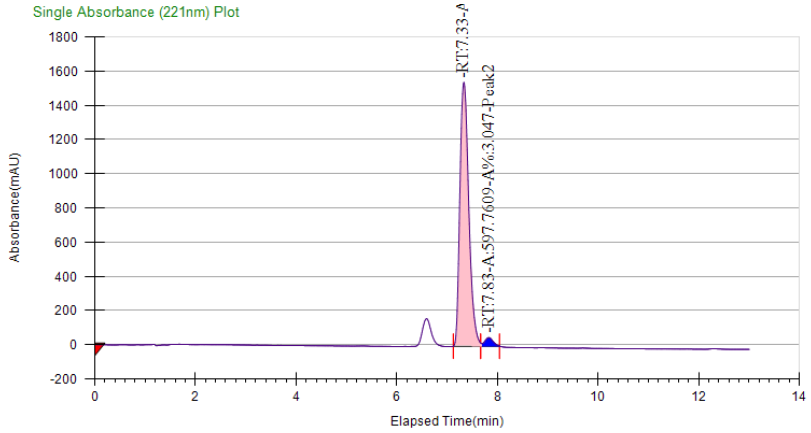

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 0.6291 | 264.2548 | 8.92 | 33.5107 |
| **2** | 99.3709 | 41741.5751 | 9.95 | 1573.825 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OJ-H, gradient 5% to 50% solvent, 3mL/min, MeOH)



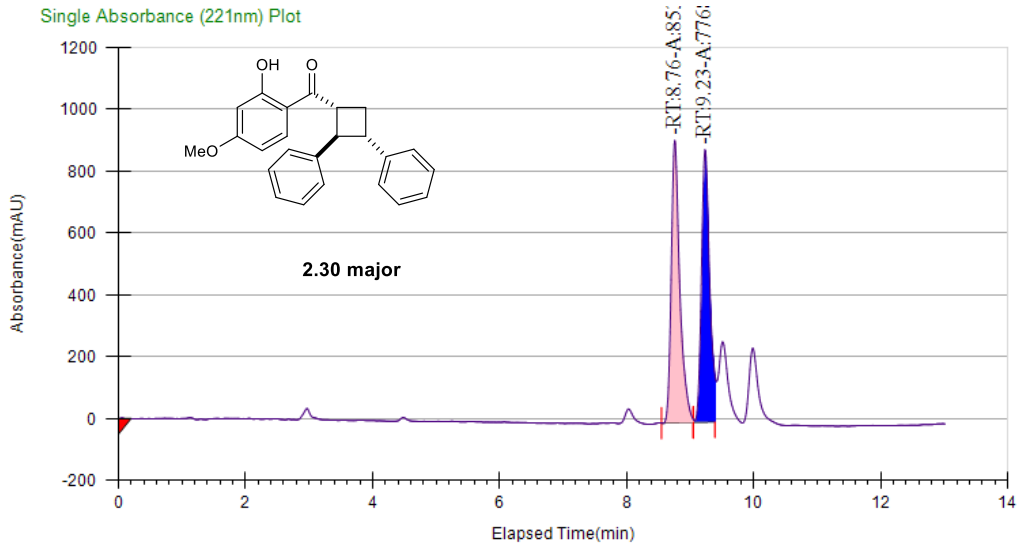

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 96.953 | 19020.1714 | 7.33 | 1543.0705 |
| **2** | 3.047 | 597.7609 | 7.83 | 50.5942 |
| **Total:** | 100 | | | |

Enantioenriched



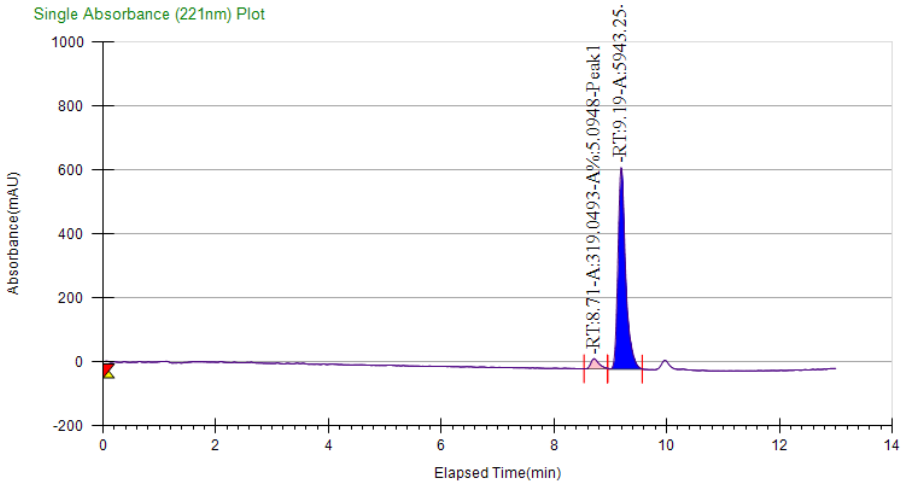

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 96.953 | 19020.1714 | 7.33 | 1543.0705 |
| **2** | 3.047 | 597.7609 | 7.83 | 50.5942 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent, 3mL/min, MeOH)



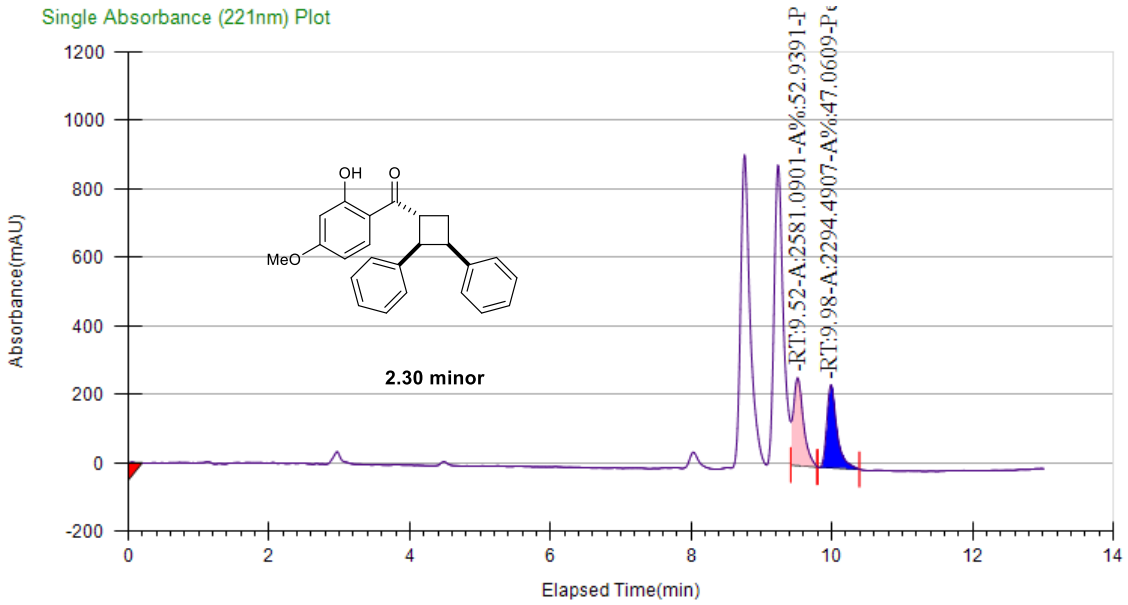

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 52.3642 | 8539.6696 | 8.76 | 913.9339 |
| **2** | 47.6358 | 7768.55 | 9.23 | 881.372 |
| **Total:** | 100 | | | |

Enantioenriched



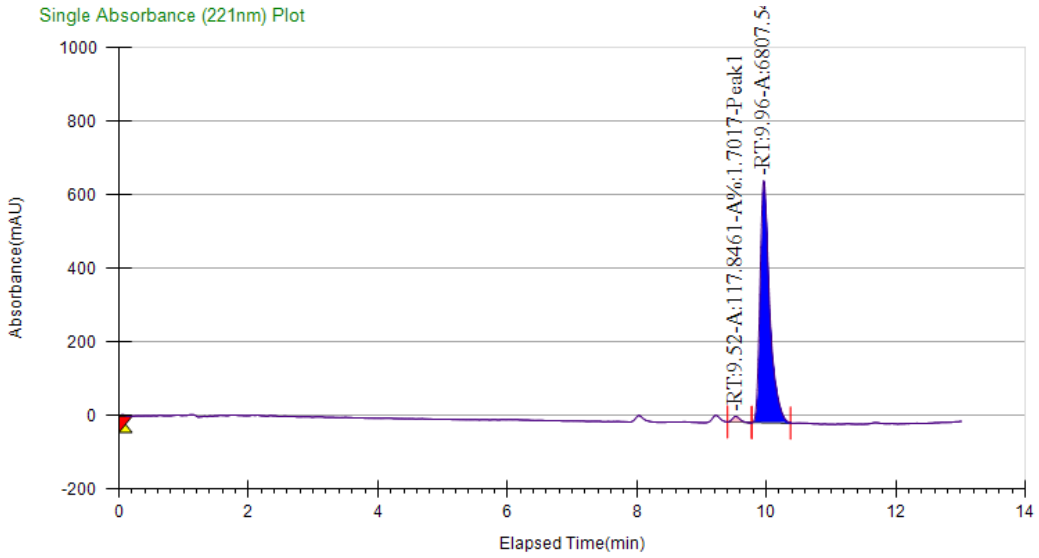

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 5.0948 | 319.0493 | 8.71 | 31.5135 |
| **2** | 94.9052 | 5943.25 | 9.19 | 629.3663 |
| **Total:** | 100 | | | |

Racemic minor (Daicel CHIRALPAK® OD-H, gradient 5% to 30% solvent, 3mL/min, MeOH)



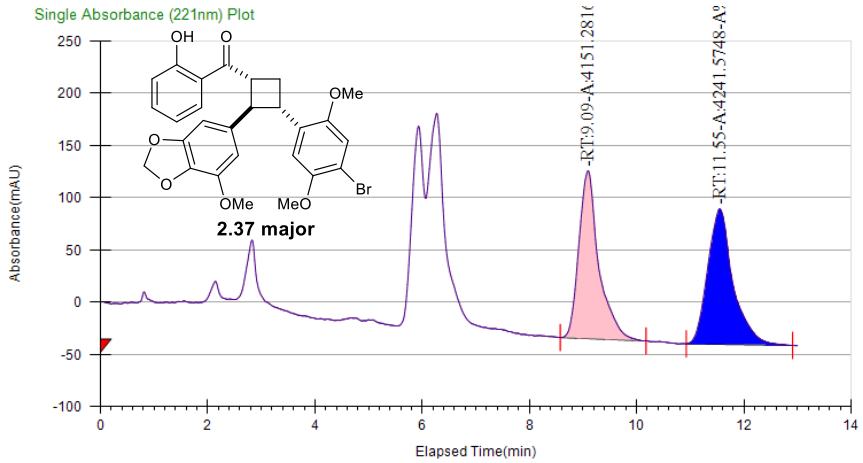

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 52.9391 | 2581.0901 | 9.52 | 255.3628 |
| **2** | 47.0609 | 2294.4907 | 9.98 | 241.6073 |
| **Total:** | 100 | | | |

Enantioenriched



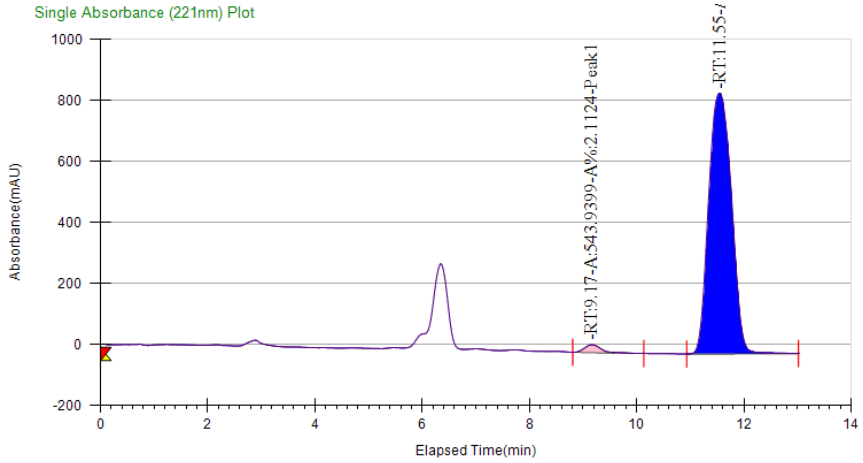

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 1.7017 | 117.8461 | 9.52 | 15.3401 |
| **2** | 98.2983 | 6807.5463 | 9.96 | 657.1825 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® AD-H, gradient 5 to 50% solvent, 5mL/min, MeOH)



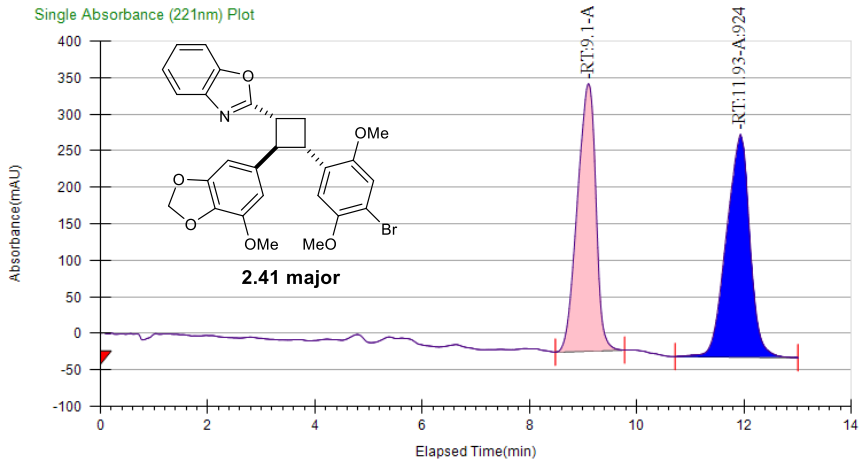

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.4621 | 4151.2816 | 9.09 | 160.7772 |
| **2** | 50.5379 | 4241.5748 | 11.55 | 129.7933 |
| **Total:** | 100 | | | |

Enantioenriched



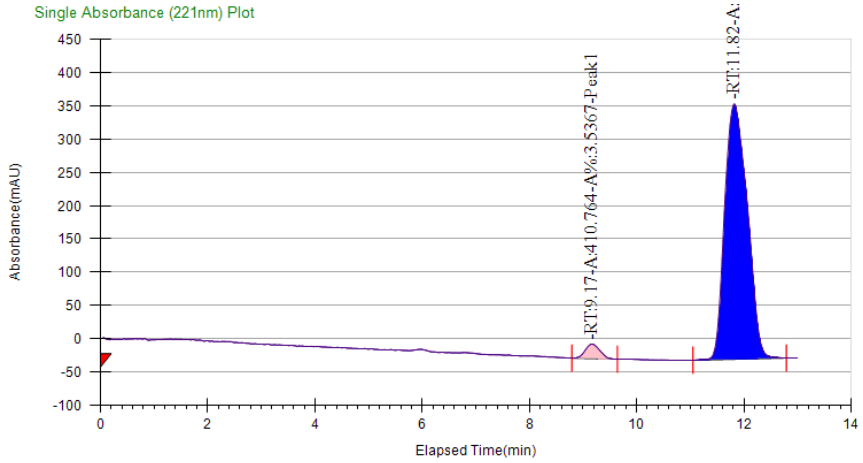

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 2.1124 | 543.9399 | 9.17 | 25.5009 |
| **2** | 97.8876 | 25206.3943 | 11.55 | 854.6219 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® AD-H, gradient 5 to 50% solvent, 5mL/min, MeOH)



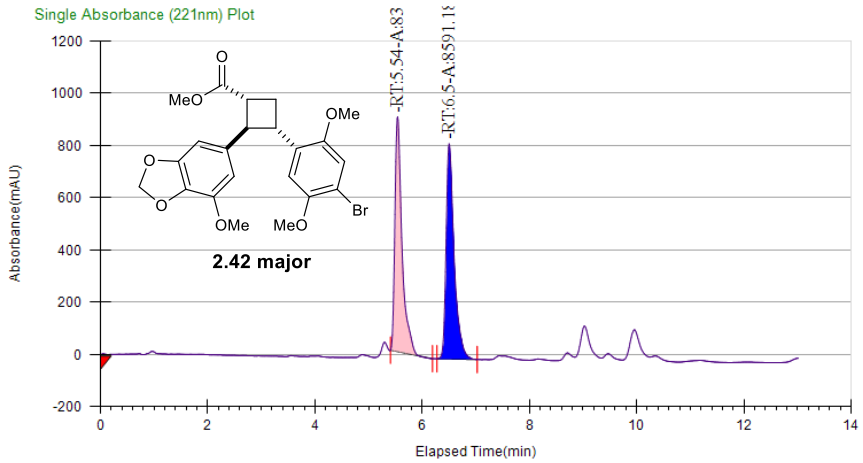

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 48.6781 | 8765.4519 | 9.10 | 366.0019 |
| **2** | 51.3219 | 9241.5201 | 11.93 | 304.7944 |
| **Total:** | 100 | | | |

Enantioenriched



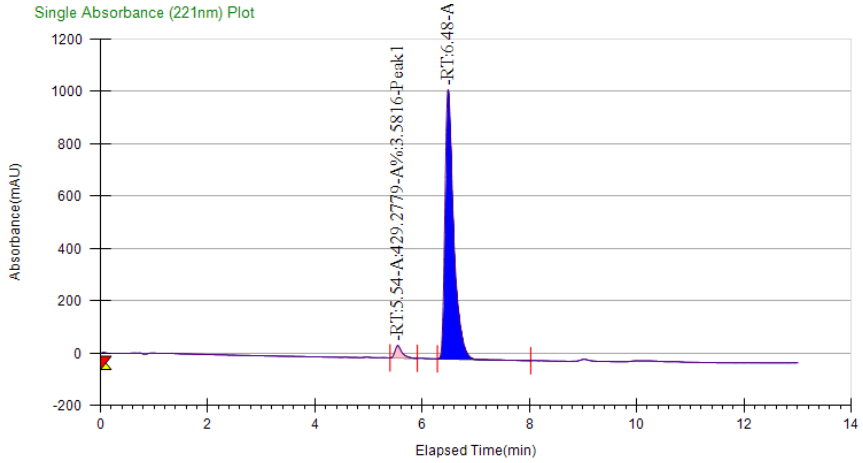

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 3.5367 | 410.764 | 9.17 | 21.6636 |
| **2** | 96.4633 | 11203.4688 | 11.82 | 383.3582 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OJ-H, gradient 5 to 50% solvent, 5mL/min, MeOH)



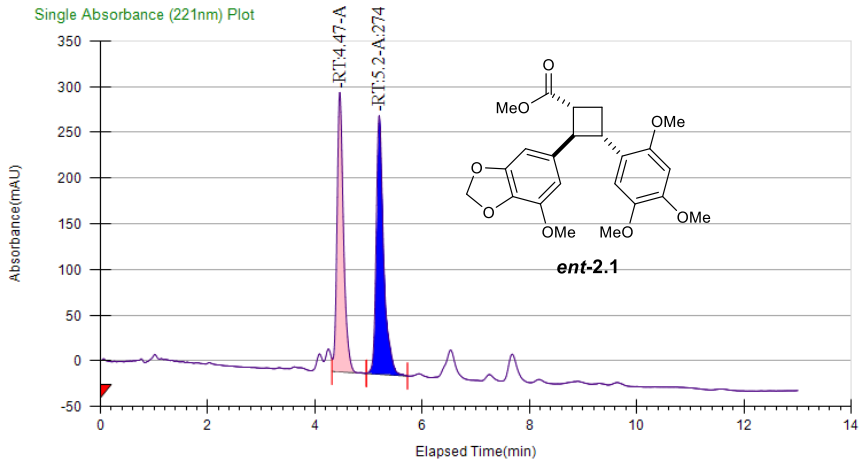

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 49.172 | 8311.2745 | 5.54 | 900.1531 |
| **2** | 50.828 | 8591.1842 | 6.50 | 824.9173 |
| **Total:** | 100 | | | |

Enantioenriched



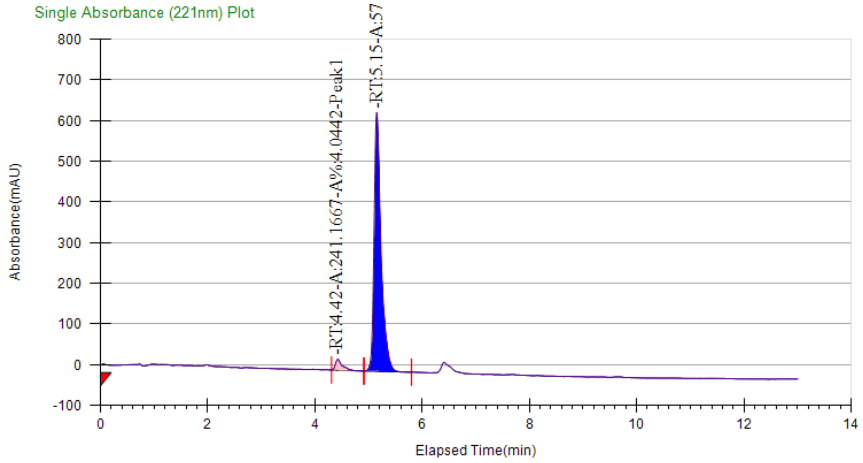

| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 3.5816 | 429.2779 | 5.54 | 47.54 |
| **2** | 96.4184 | 11556.2187 | 6.48 | 1030.8046 |
| **Total:** | 100 | | | |

Racemic major (Daicel CHIRALPAK® OJ-H, gradient 5 to 50% solvent, 5mL/min, MeOH)

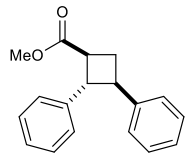



| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 48.5137 | 2582.2245 | 4.47 | 305.8375 |
| **2** | 51.4863 | 2740.4449 | 5.2 | 283.4192 |
| **Total:** | 100 | | | |

Enantioenriched

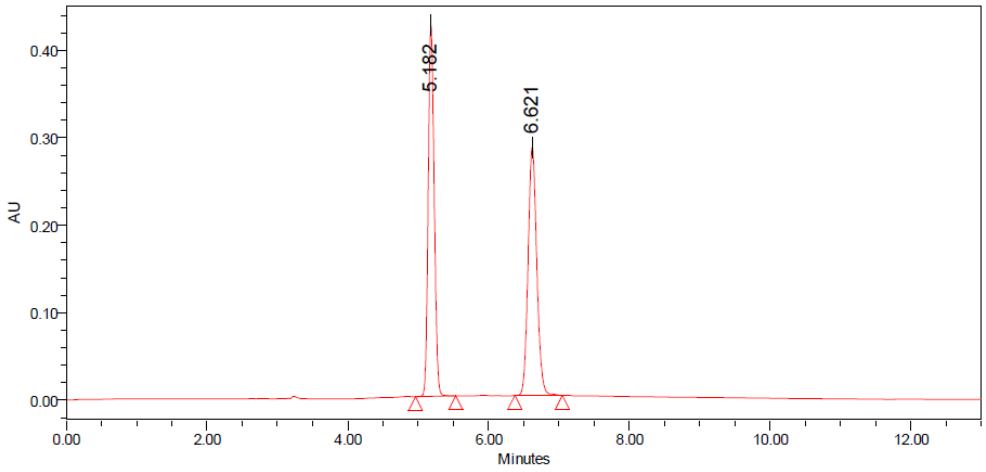



| Peak No | % Area | Area | RT (min) | Height (mV) |
|---|---|---|---|---|
| **1** | 4.0442 | 241.1667 | 4.42 | 27.0703 |
| **2** | 95.9558 | 5722.0333 | 5.15 | 636.4942 |
| **Total:** | 100 | | | |




**2.45**

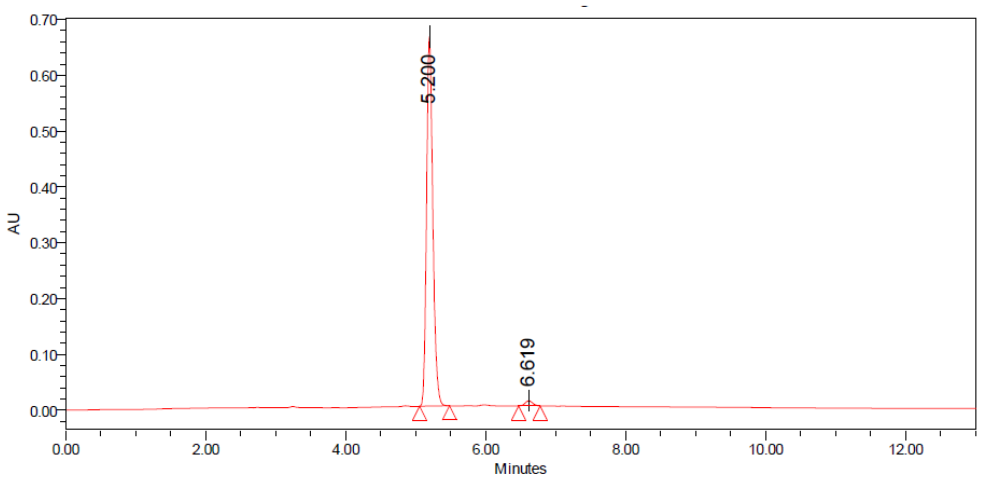
**Racemic** (Daicel CHIRALCEL® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

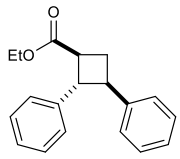
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.182 | 2505467 | 424874 | 50.64 |
| 2 | 6.621 | 2442238 | 283495 | 49.36 |

**Enantioenriched**



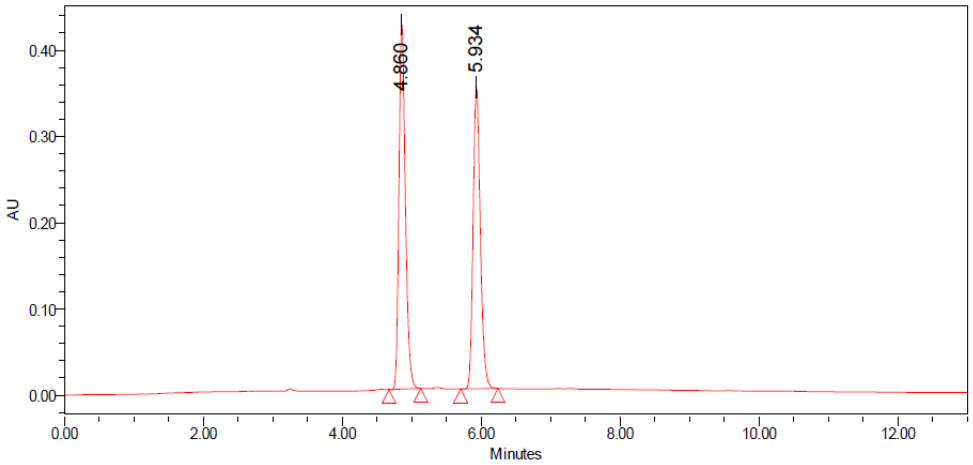

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.200 | 4135532 | 661989 | 98.38 |
| 2 | 6.619 | 68086 | 9061 | 1.62 |




**2.46**

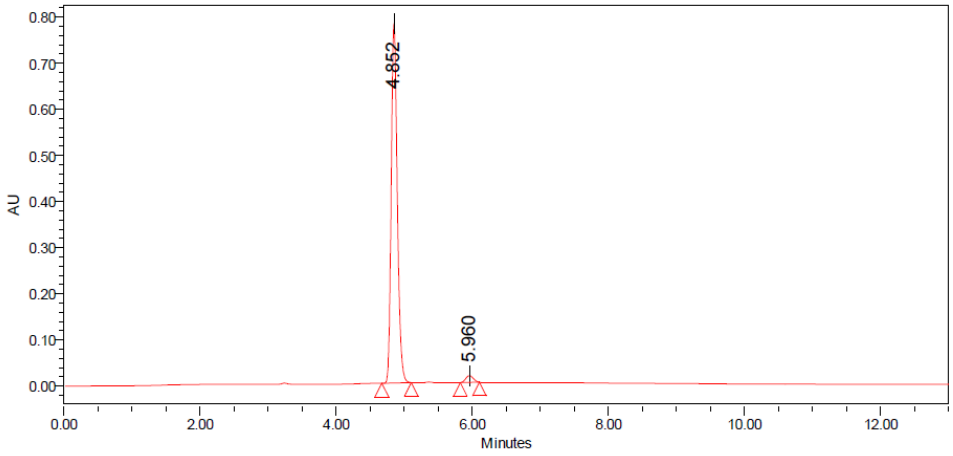
**Racemic** (Daicel CHIRALCEL® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

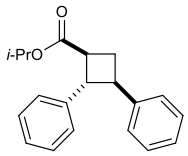
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 4.860 | 2741451 | 423072 | 52.09 |
| 2 | 5.934 | 2521587 | 349914 | 47.91 |

**Enantioenriched**



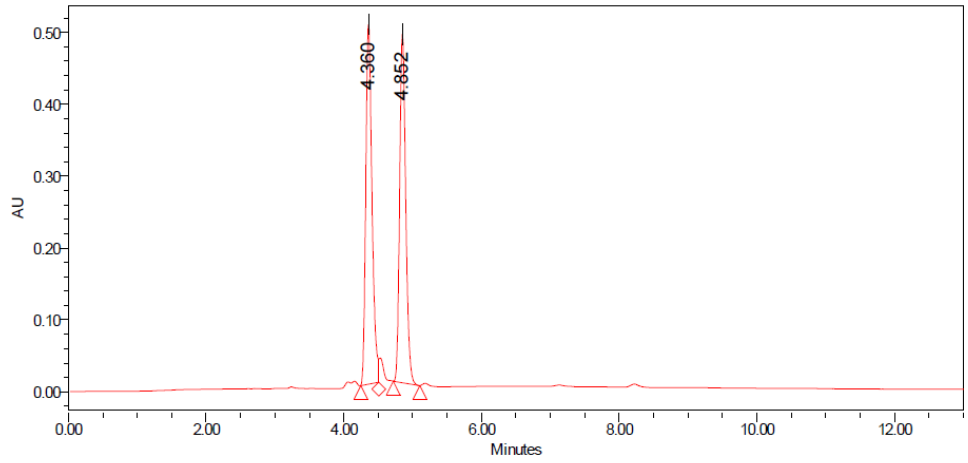

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 4.852 | 4829024 | 779656 | 97.67 |
| 2 | 5.960 | 115099 | 14688 | 2.33 |




**2.47**

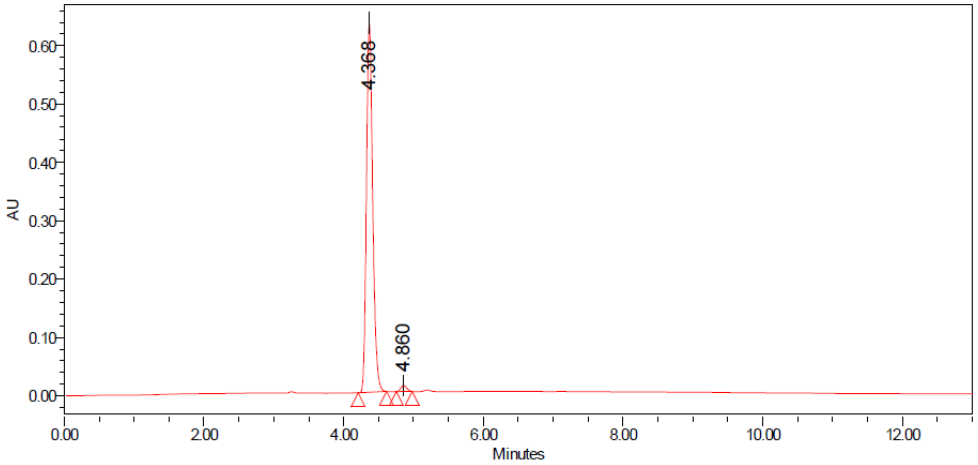
**Racemic** (Daicel CHIRALCEL® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

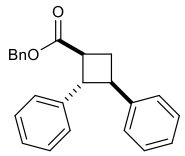
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 4.360 | 3143640 | 500909 | 51.36 |
| 2 | 4.852 | 2976642 | 485148 | 48.64 |

**Enantioenriched**



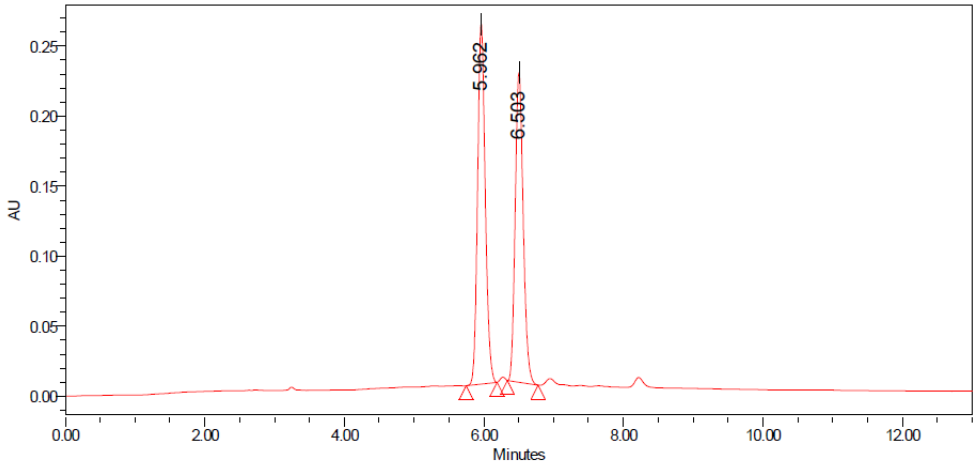

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 4.368 | 3943265 | 633231 | 98.45 |
| 2 | 4.860 | 61916 | 10305 | 1.55 |




**2.48**

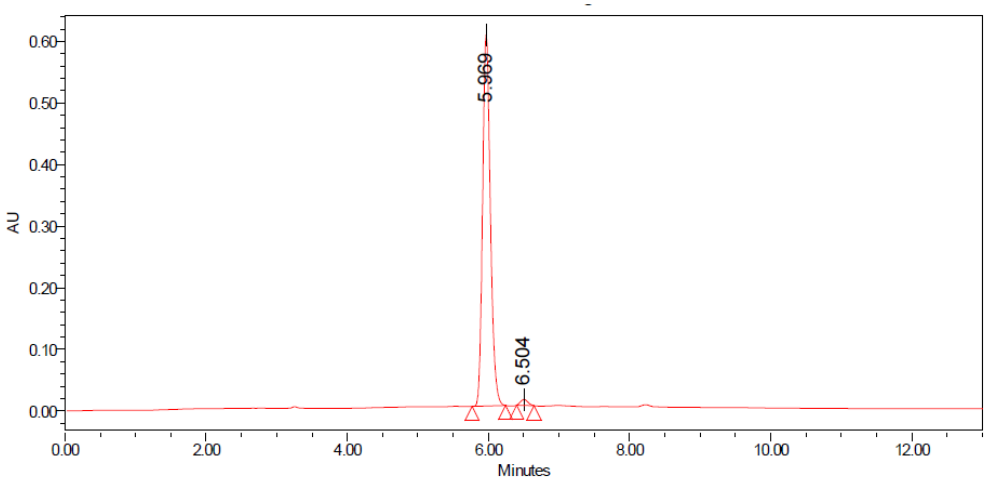
**Racemic** (Daicel CHIRALCEL® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

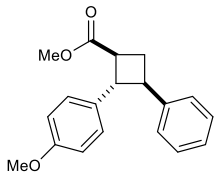
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.962 | 1968532 | 257137 | 52.65 |
| 2 | 6.503 | 1770448 | 221110 | 47.35 |

**Enantioenriched**



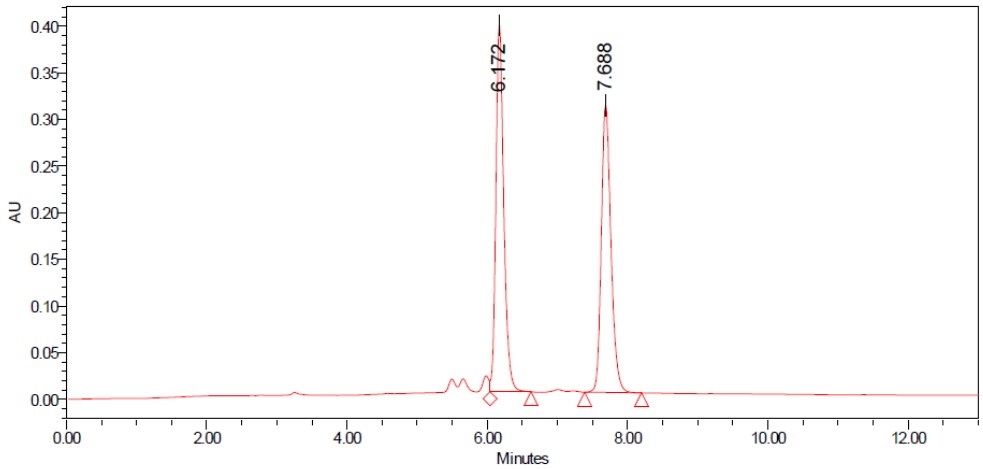

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.969 | 4628115 | 602809 | 98.52 |
| 2 | 6.504 | 69524 | 9568 | 1.48 |




**2.50**

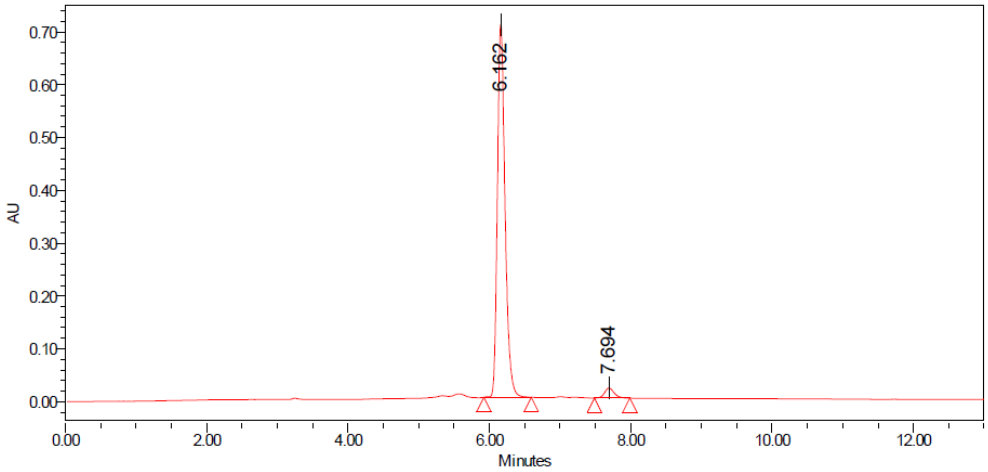
**Racemic** (Daicel CHIRALCEL® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

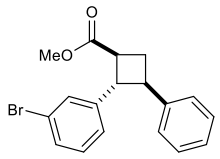
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 6.172 | 3064029 | 393182 | 51.03 |
| 2 | 7.688 | 2939879 | 308173 | 48.97 |

**Enantioenriched**



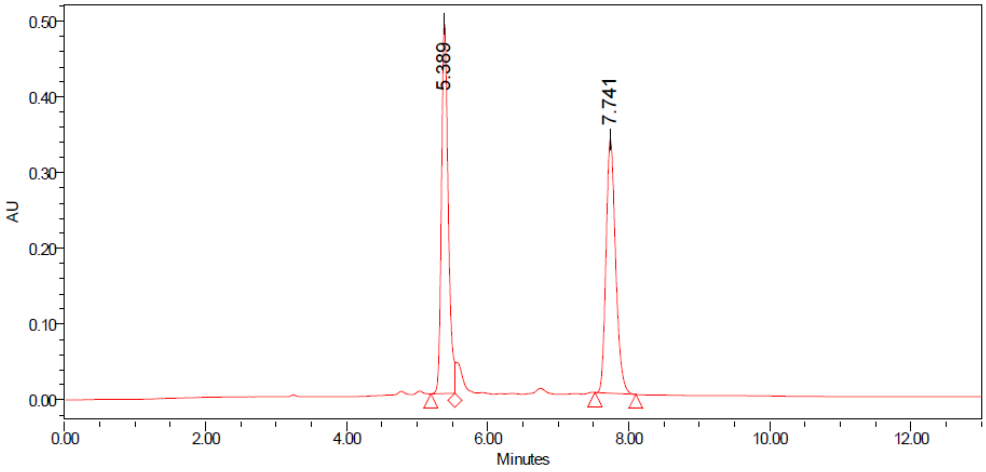

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 6.162 | 5299039 | 705817 | 96.80 |
| 2 | 7.694 | 174918 | 18695 | 3.20 |




**2.51**

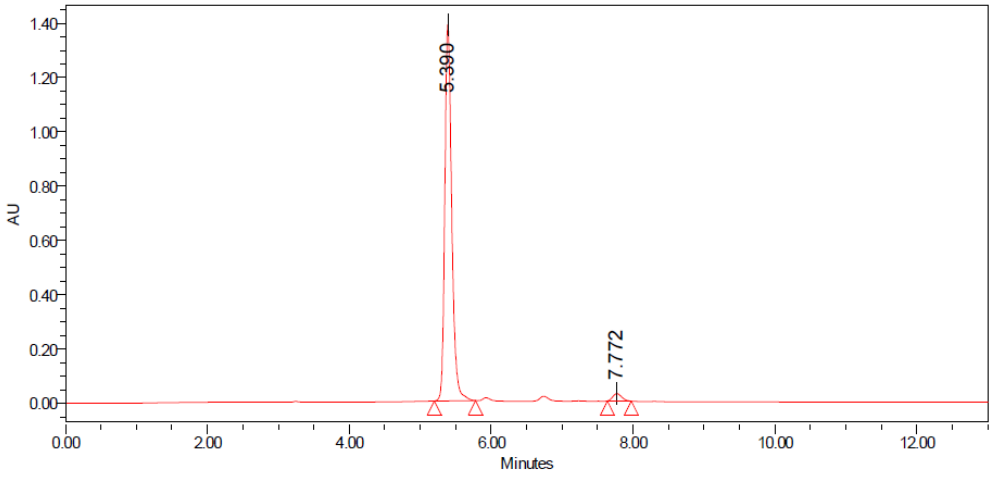
**Racemic** (Daicel CHIRALCEL® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

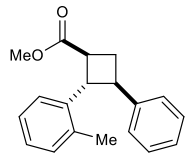
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.389 | 3238774 | 488643 | 50.50 |
| 2 | 7.741 | 3174993 | 335236 | 49.50 |

**Enantioenriched**



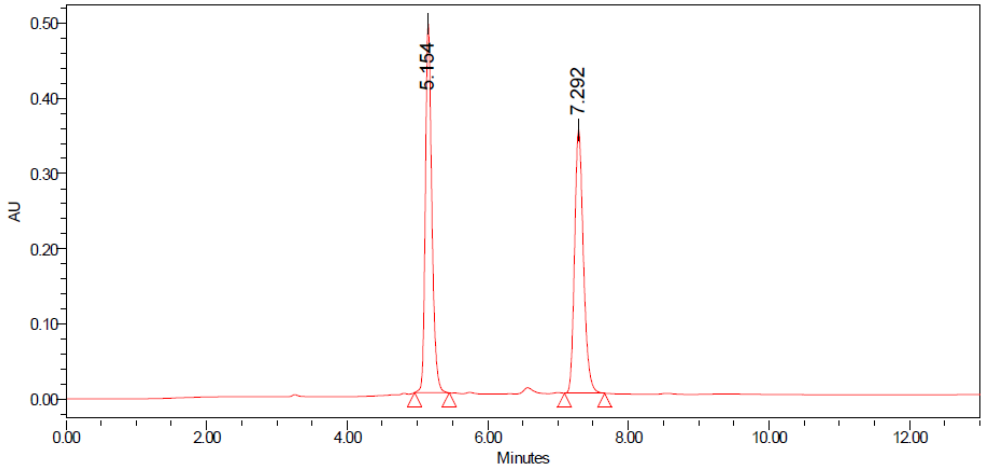

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.390 | 9362557 | 1385896 | 97.49 |
| 2 | 7.772 | 240671 | 27374 | 2.51 |




**2.52**

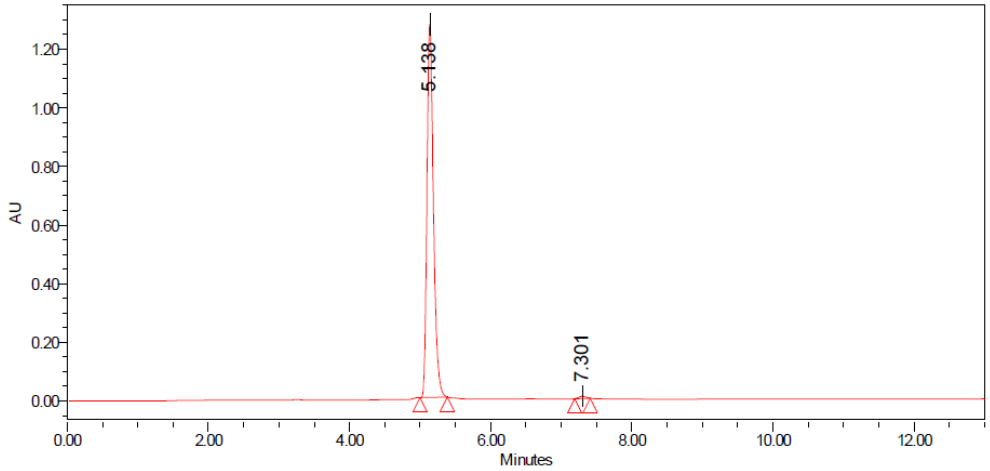
**Racemic** (Daicel CHIRALCEL® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

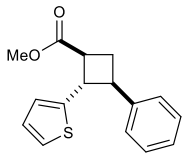
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.154 | 3135303 | 491017 | 50.68 |
| 2 | 7.292 | 3051152 | 350664 | 49.32 |

**Enantioenriched**



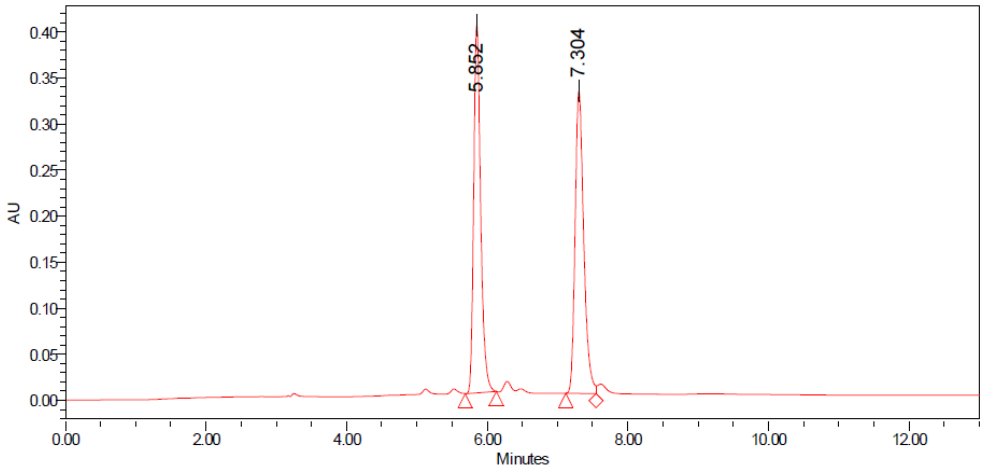

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.138 | 8121765 | 1274227 | 99.37 |
| 2 | 7.301 | 51870 | 7422 | 0.63 |




**2.53**

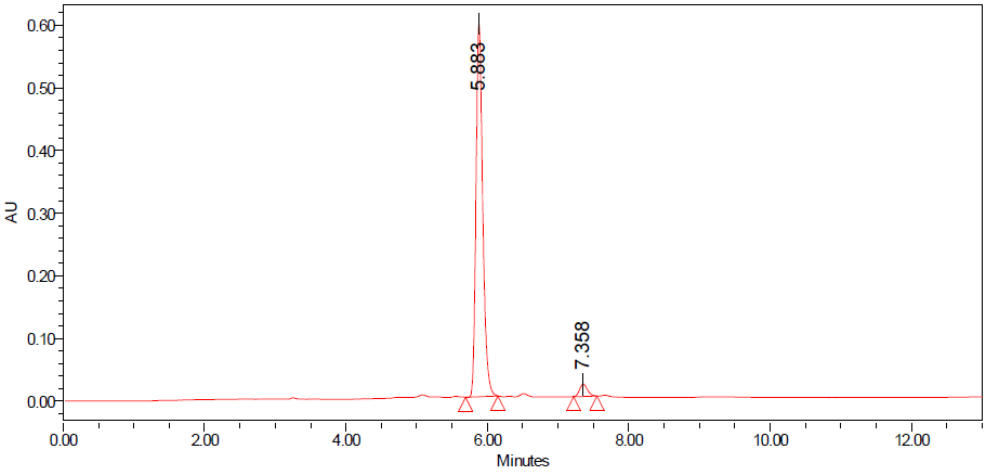
**Racemic** (Daicel CHIRALCEL® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

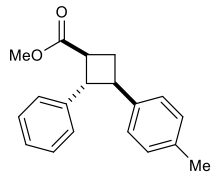
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.852 | 2739494 | 399438 | 49.42 |
| 2 | 7.304 | 2803356 | 328354 | 50.58 |

**Enantioenriched**



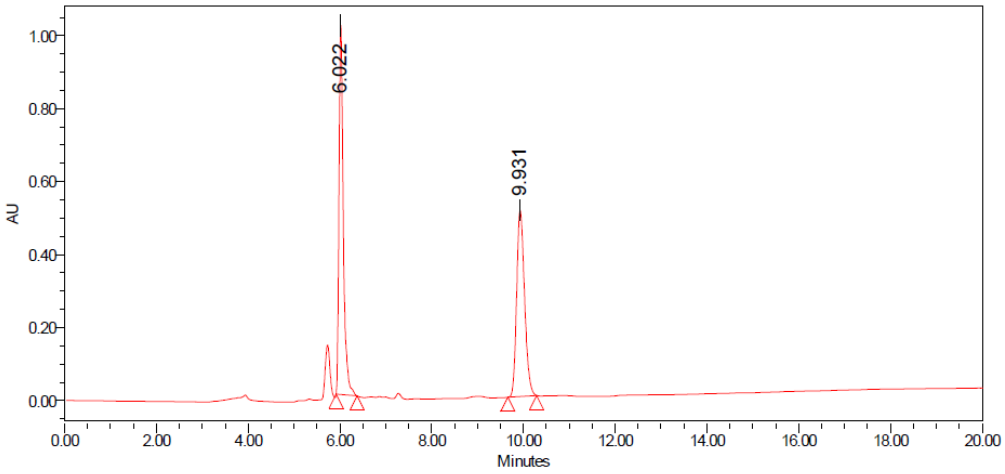

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.883 | 3948375 | 595783 | 96.25 |
| 2 | 7.358 | 153883 | 19668 | 3.75 |




**2.54**

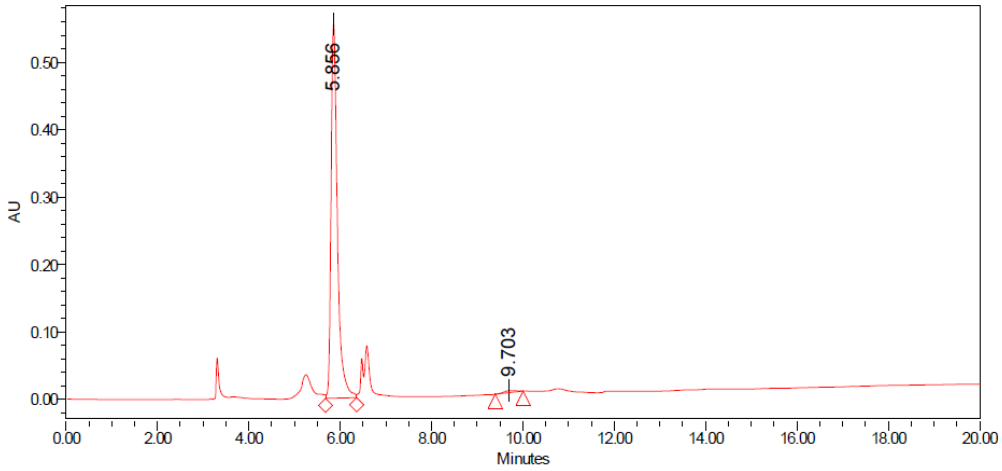
**Racemic** (Daicel CHIRALCEL® OD-H, 1–40% IPA:hexanes over 20 min, 1 mL/min, 222.0 nm)




**Peak Results**

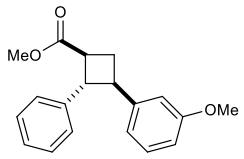
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 6.022 | 6617919 | 1012168 | 51.94 |
| 2 | 9.931 | 6123303 | 510341 | 48.06 |

**Enantioenriched**



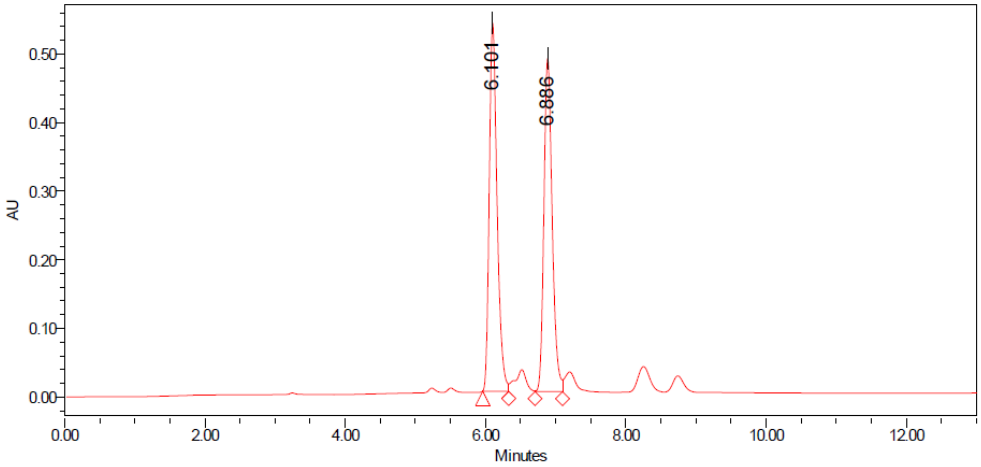

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.856 | 5334179 | 555139 | 98.98 |
| 2 | 9.703 | 54952 | 3014 | 1.02 |




**2.55**

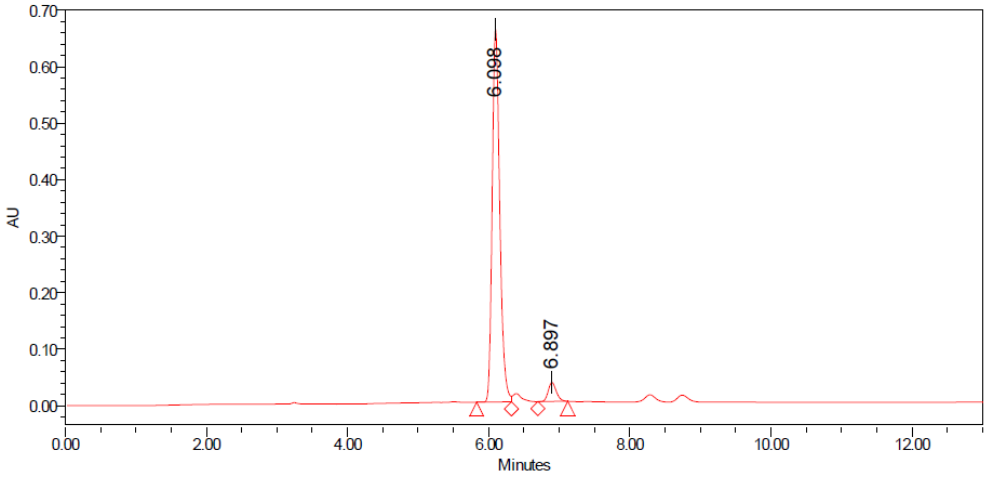
**Racemic** (Daicel CHIRALCEL® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

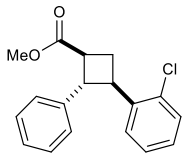
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 6.101 | 4167690 | 537195 | 51.07 |
| 2 | 6.886 | 3993218 | 485683 | 48.93 |

**Enantioenriched**



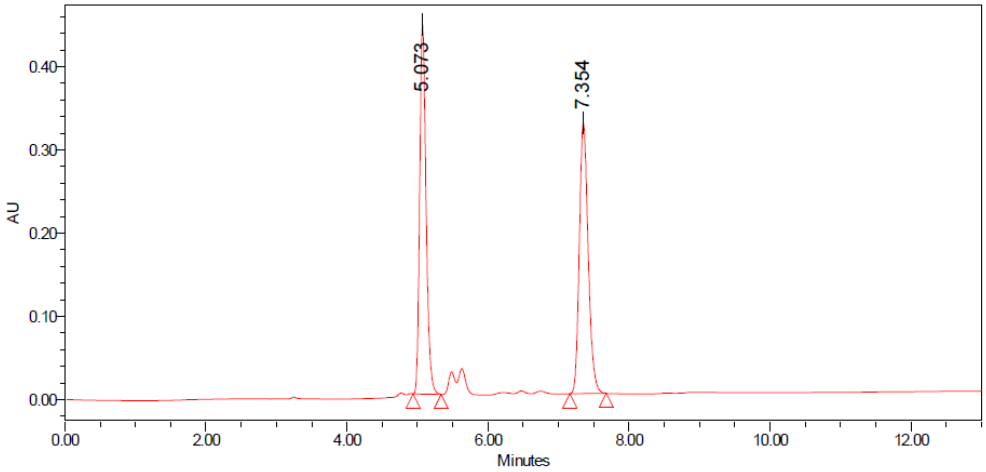

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 6.098 | 4895403 | 659959 | 94.82 |
| 2 | 6.897 | 267668 | 33513 | 5.18 |




**2.56**

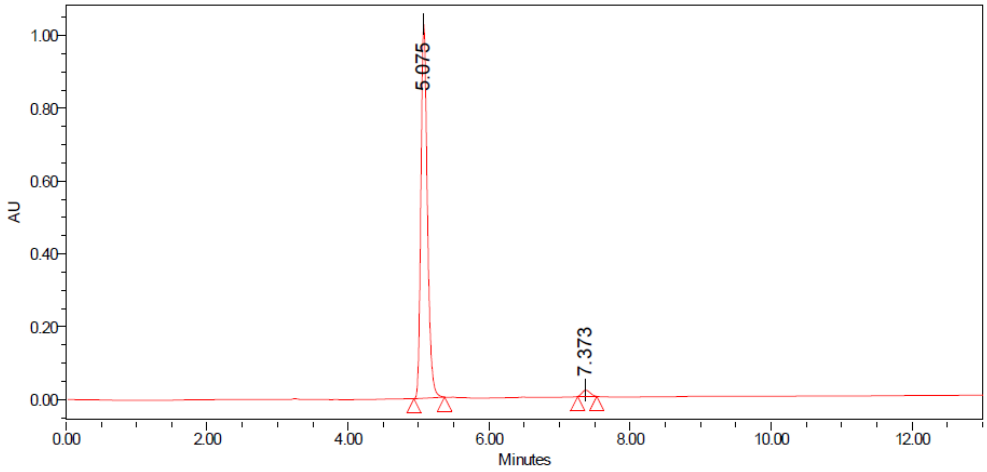
**Racemic** (Daicel CHIRALCEL® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

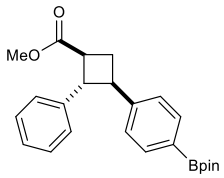
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.073 | 2788651 | 444284 | 49.60 |
| 2 | 7.354 | 2834015 | 325080 | 50.40 |

**Enantioenriched**



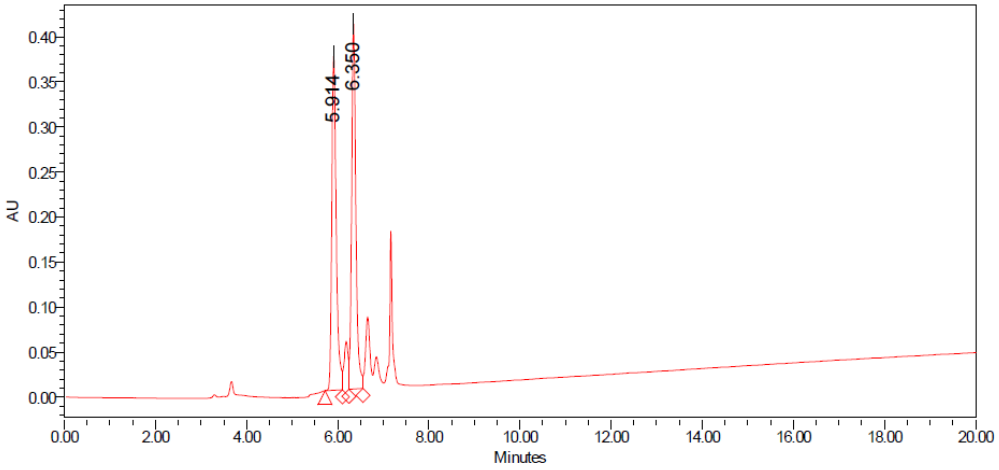

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.075 | 6538986 | 1027820 | 97.97 |
| 2 | 7.373 | 135710 | 17242 | 2.03 |




**2.57**

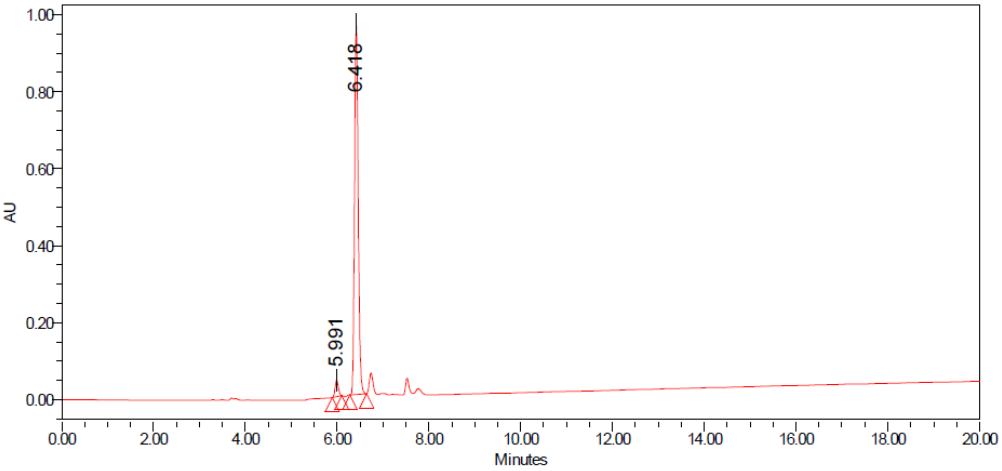
**Racemic** (Daicel CHIRALCEL® IC, 1–40% IPA:hexanes over 20 min, 1 mL/min, 222.0 nm)




**Peak Results**

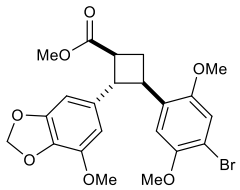
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.914 | 2519166 | 370995 | 48.94 |
| 2 | 6.350 | 2628640 | 405362 | 51.06 |

**Enantioenriched**



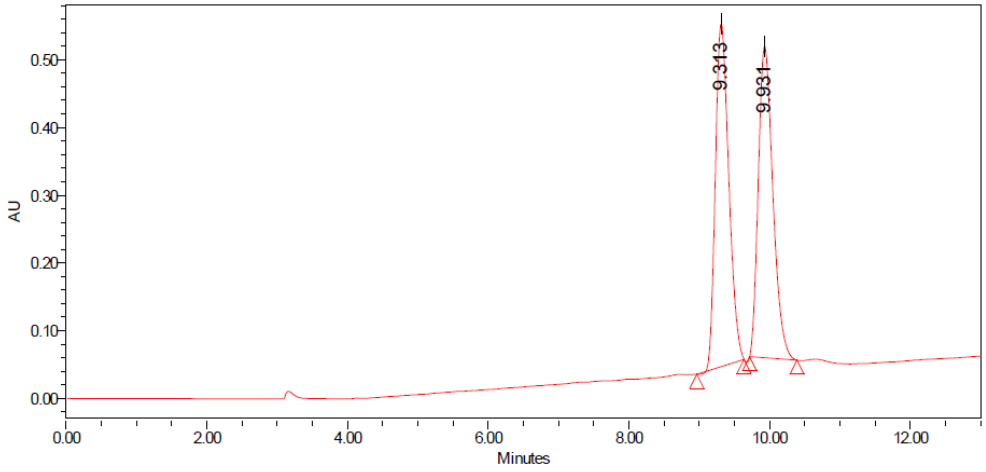

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 5.991 | 212213 | 42518 | 3.81 |
| 2 | 6.418 | 5351911 | 962642 | 96.19 |




***ent*-2.42**

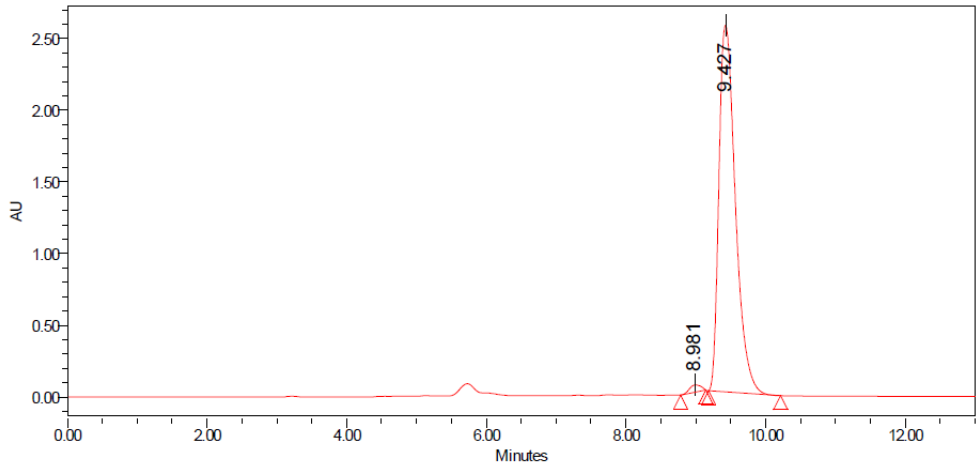
**Racemic** (Daicel CHIRALPAK® OD-H, 5–50% IPA:hexanes over 13 min, 1 mL/min, 222.0 nm)




**Peak Results**

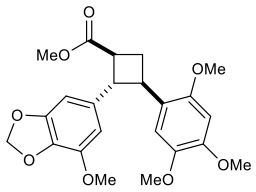
| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 9.313 | 6713611 | 506088 | 50.36 |
| 2 | 9.931 | 6617844 | 459606 | 49.64 |

**Enantioenriched**



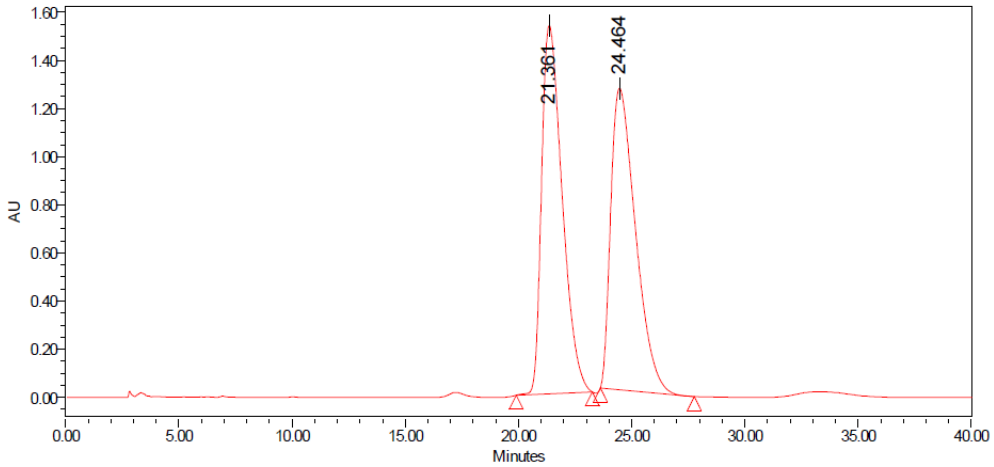

**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 8.981 | 556397 | 50487 | 1.31 |
| 2 | 9.427 | 41866658 | 2558349 | 98.69 |




**2.1**

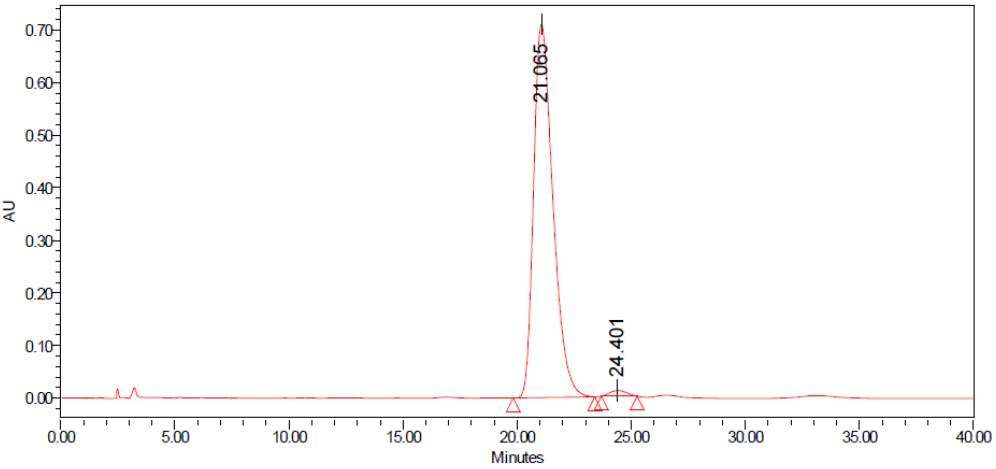
**Racemic** (Daicel CHIRALPAK® OJ-H, 40% EtOH:hexanes over 40 min, 4 mL/min, 222.0 nm)




**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 21.361 | 96695479 | 1531585 | 50.39 |
| 2 | 24.464 | 95206991 | 1253920 | 49.61 |

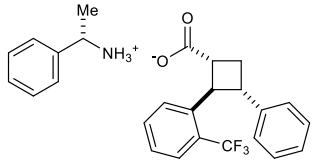
**Enantioenriched**




**Peak Results**

| | RT | Area | Height | % Area |
|---|---|---|---|---|
| 1 | 21.065 | 41785892 | 709963 | 98.69 |
| 2 | 24.401 | 553368 | 10701 | 1.31 |

# Appendix C. X-ray Crystallographic Data




**C1**

**Data Collection.** A colorless crystal with approximate dimensions 0.40×0.04×0.04 $mm^3$ was selected under oil under ambient conditions and attached to the tip of a MiTeGen MicroMount©. The crystal was mounted in a stream of cold nitrogen at 100(1) K and centered in the X-ray beam by using a video camera. The crystal evaluation and data collection were performed on a Bruker Quazar SMART APEXII diffractometer with Mo $K_\alpha$ ($\lambda$ = 0.71073 Å) radiation and the diffractometer to crystal distance of 4.96 cm.[i] The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 12 frames collected at intervals of 0.5º in a 6º range about ω with the exposure time of 30 seconds per frame. The reflections were successfully indexed by an automated indexing routine built in the APEXII program suite. The final cell constants were calculated from a set of 9795 strong reflections from the actual data collection.

The data were collected by using the full sphere data collection routine to survey the reciprocal space to the extent of a full sphere to a resolution of 0.82 Å. A total of 114577 data were harvested by collecting 5 sets of frames with 0.5º scans in ω and φ with exposure times of 200 sec per frame. These highly redundant datasets were corrected for Lorentz and polarization effects. The absorption correction was based on fitting a function to the empirical transmission surface as sampled by multiple equivalent measurements.[ii]

**Structure Solution and Refinement:** The systematic absences in the diffraction data were uniquely consistent for the space group $P2_12_12_1$ that yielded chemically reasonable and computationally stable results of refinement.[iii,iv,v,vi,vii,viii] A successful solution by the direct methods provided most non-hydrogen atoms from the *E*-map. The remaining non-hydrogen atoms were located in an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined with anisotropic displacement coefficients. All hydrogen atoms were included in the structure factor calculation at idealized positions and allowed to ride on the neighboring atoms with relative isotropic displacement coefficients.

There are three symmetry-independent ion pairs in the unit cell and two partially occupied molecules of solvent dichloromethane. The absolute configuration of all ions has been unambiguously established by resonant scattering effects as follows: C1, C1a, C1b, C4, C4a, C4b – *R*; C2, C2a, C2b, C25, C25a, C25b –

*S*. The ions are labeled identically, except for the “a” and “b” suffixes. Whereas the composition of the ions is identical, conformational differences are observed (Figures 2, 4). The Cl1 dichloromethane molecule is occupied 90.3(4)% of the time whereas the Cl3 dichloromethane molecule is present 66.8(4)% of the time. Distance restraints were applied to the latter molecule.

Thus, the overall composition is $[C_8H_{12}N][C_{18}H_{14}F_3O_2]\cdot 0.52CH_2Cl_2$. The final least-squares refinement of 927 parameters against 14512 data resulted in residuals *R* (based on $F^2$ for $I \geq 2\sigma$) and *wR* (based on $F^2$ for all data) of 0.0520 and 0.1494, respectively. The final difference Fourier map was featureless.

**Summary:** Crystal Data for $C_{22.73}H_{23.18}Cl_{0.89}F_{2.57}N_{0.85}O_{1.71}$ (*M* =416.53 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 17.965(7) Å, *b* = 19.203(7) Å, *c* = 21.951(7) Å, *V* = 7573(5) $Å^3$, *Z* = 14, *T* = 100.0 K, μ(MoKα) = 0.201 $mm^{-1}$, *Dcalc* = 1.279 $g/cm^3$, 114577 reflections measured ($2.818° \leq 2\Theta \leq 51.63°$), 14512 unique ($R_{int}$ = 0.0738, $R_{sigma}$ = 0.0444) which were used in all calculations. The final $R_1$ was 0.0520 ($I > 2\sigma(I)$) and $wR_2$ was 0.1494 (all data).

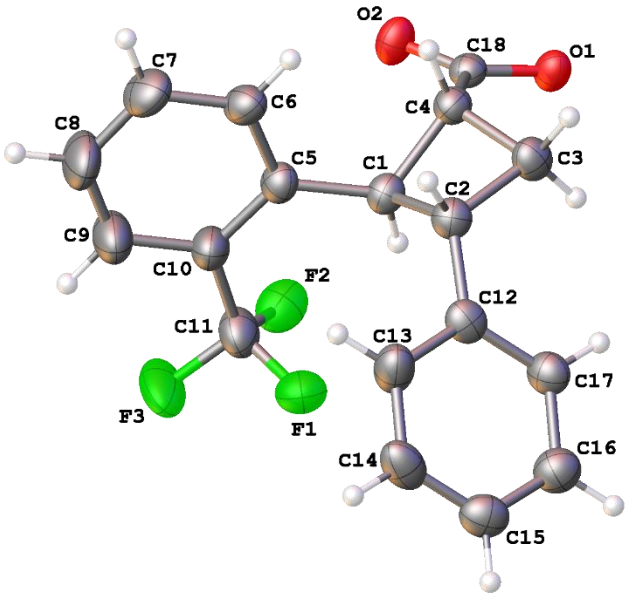



**Figure C.1.** A molecular drawing of the F1 anion in **C1** shown with 50% probability ellipsoids.

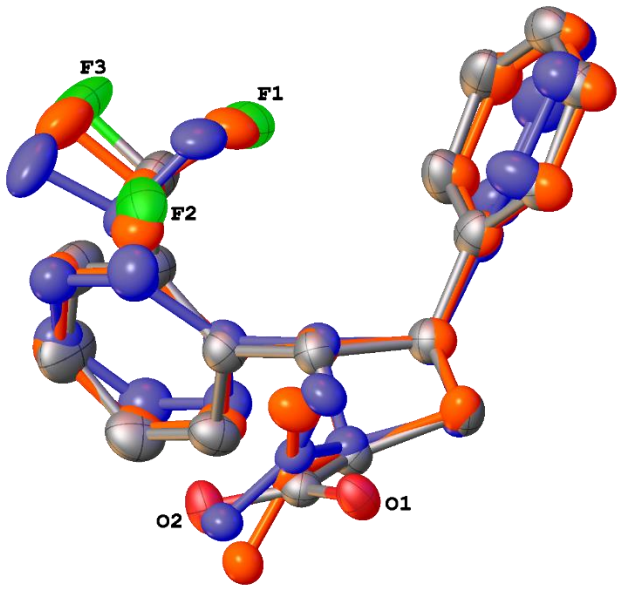



**Figure C.2** A superposition of the three anions in **C1** shown with 50% probability ellipsoids. All H atoms are omitted.

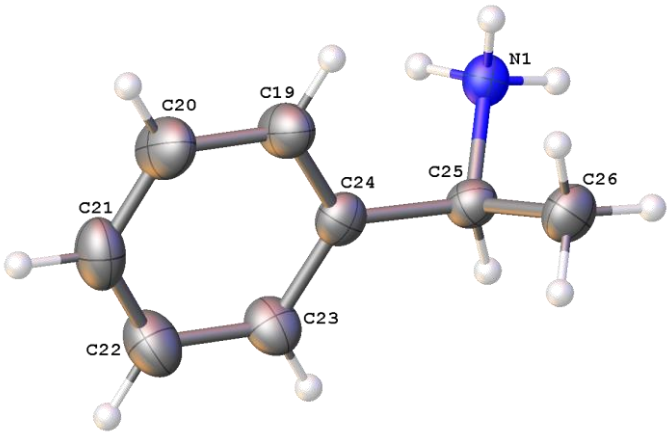



**Figure C.3.** A molecular drawing of the N1 cation in **C1** shown with 50% probability ellipsoids.

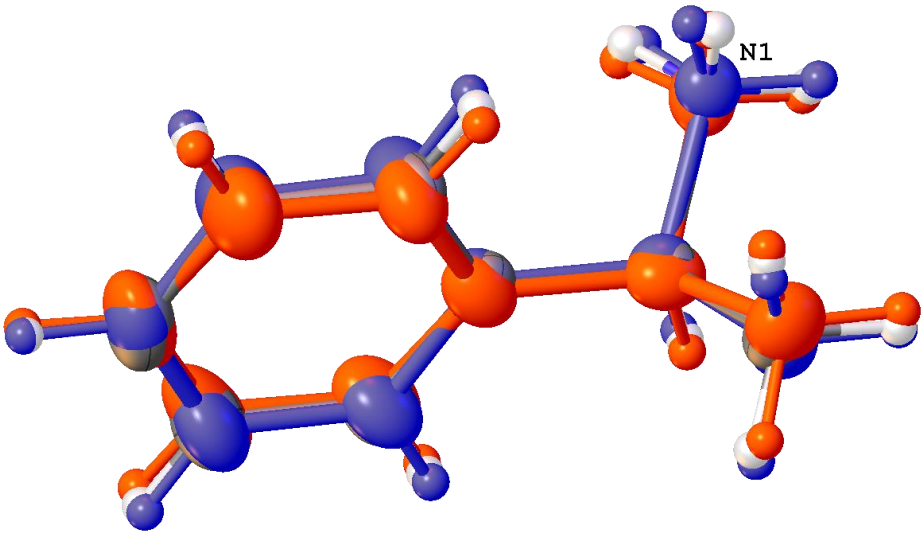



**Figure C.4.** A superposition of the three cations in **C1** shown with 50% probability ellipsoids. All H atoms are omitted.

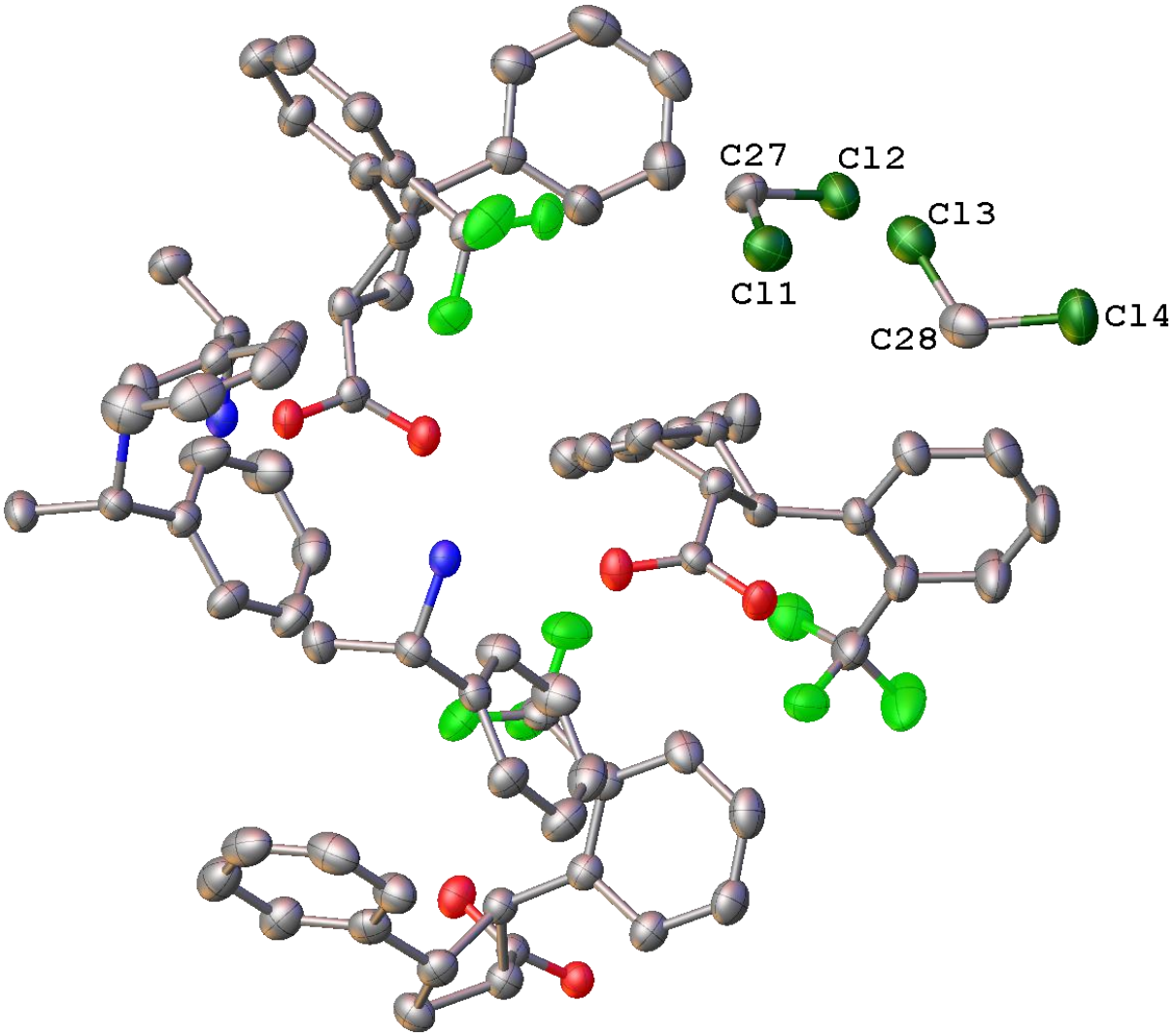



**Figure C.5**. Three symmetry-independent ion pairs and two $CH_2Cl_2$ molecules of **C1** shown with 50% probability ellipsoids. All H atoms are omitted. The Cl1 dichloromethane molecule is occupied 90.3(4) % of the time whereas the Cl3 dichloromethane molecule is present 66.8(4) % of the time.

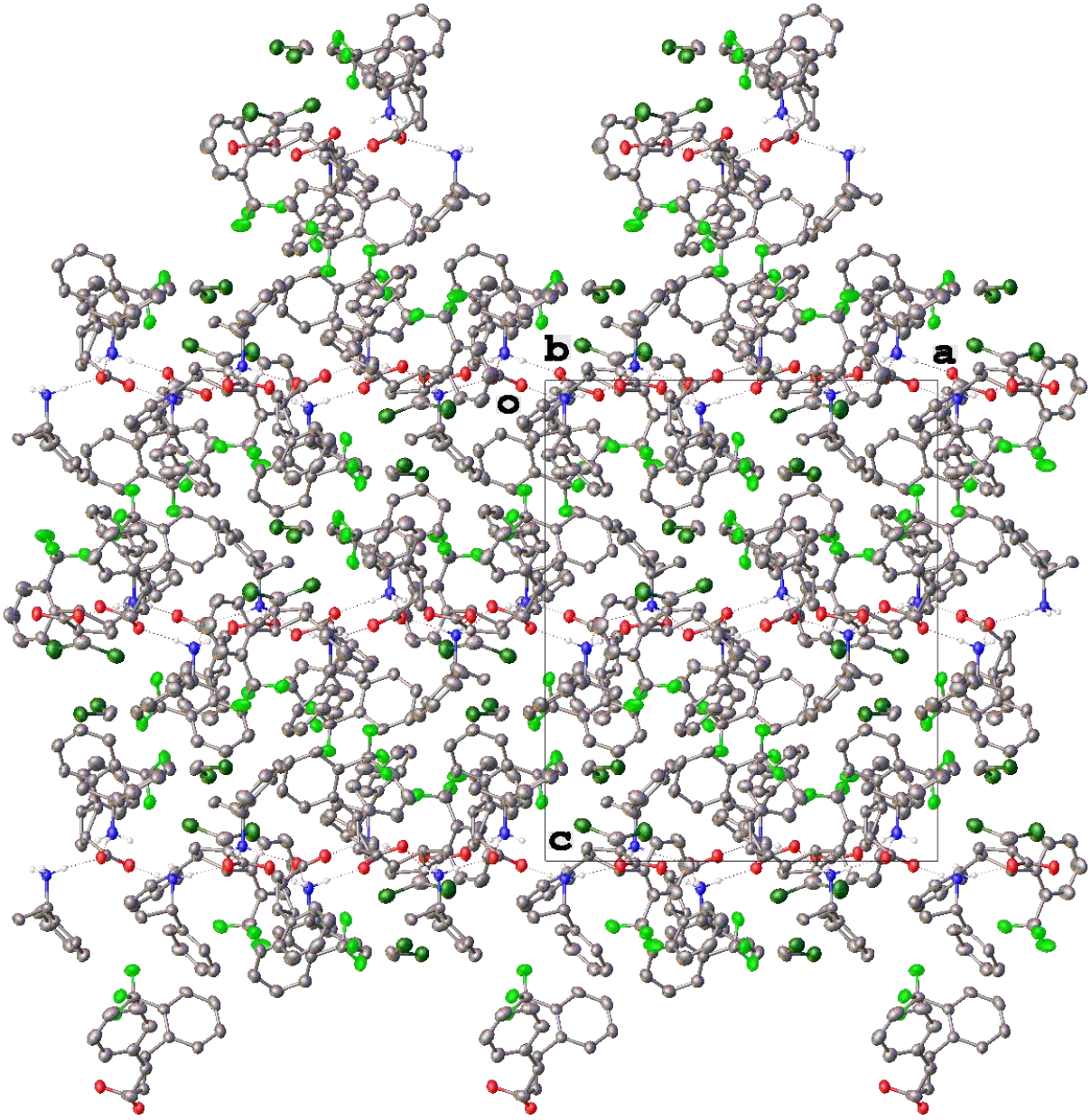



**Figure C.6.** A packing diagram of **C1** shown along the *b* axis. Only H atoms on the N atoms are shown. The dash lines denote hydrogen-bonding interactions that form one-dimensional chains in the crystallographic *a* direction.

**Table C.1. Crystal data and structure refinement for C1.**

| | |
|---|---|
| Identification code | yoon49 |
| Empirical formula | $[C_8H_{12}N][C_{18}H_{14}F_3O_2]\cdot 0.52(CH_2Cl_2)$ |
| Formula weight | 416.53 |
| Temperature/K | 100.0 |
| Crystal system | orthorhombic |
| Space group | $P2_12_12_1$ |
| a/Å | 17.965(7) |
| b/Å | 19.203(7) |
| c/Å | 21.951(7) |
| α/° | 90 |
| β/° | 90 |
| γ/° | 90 |
| Volume/Å$^3$ | 7573(5) |
| Z | 12 |
| $\rho_{calc}$g/cm$^3$ | 1.279 |
| μ/mm$^{-1}$ | 0.201 |
| F(000) | 3048.0 |
| Crystal size/mm$^3$ | 0.4 × 0.04 × 0.04 |
| Radiation | MoKα (λ = 0.71073) |
| 2Θ range for data collection/° | 2.818 to 51.63 |
| Index ranges | $-21 \leq h \leq 21$, $-23 \leq k \leq 23$, $-26 \leq l \leq 26$ |

| | |
|---|---|
| Reflections collected | 114577 |
| Independent reflections | 14512 [$R_{int}$ = 0.0738, $R_{sigma}$ = 0.0444] |
| Data/restraints/parameters | 14512/1/927 |
| Goodness-of-fit on $F^2$ | 1.000 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0520, $wR_2$ = 0.1360 |
| Final R indexes [all data] | $R_1$ = 0.0738, $wR_2$ = 0.1494 |
| Largest diff. peak/hole / e $Å^{-3}$ | 0.57/-0.25 |
| Flack parameter | -0.03(2) |

**Table C.2. Fractional Atomic Coordinates (×$10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2$×$10^3$) for S55. $U_{eq}$ is defined as 1/3 of of the trace of the orthogonalised $U_{IJ}$ tensor.**

| Atom | *x* | *y* | *z* | U(eq) |
|---|---|---|---|---|
| Cl1 | 3151.3(9) | 5076.4(9) | 3052.3(7) | 56.1(5) |
| Cl2 | 3592.8(9) | 6515.0(8) | 3238.7(7) | 55.9(5) |
| C27 | 3897(3) | 5669(3) | 3062(3) | 50.1(15) |
| Cl3 | 4048.6(13) | 8178.9(11) | 4265.8(10) | 55.6(7) |
| Cl4 | 2477.5(13) | 8497.7(12) | 4403.6(12) | 66.4(8) |
| C28 | 3181(4) | 7905(4) | 4546(4) | 54(2) |
| F1 | 3285.9(17) | 6234.3(16) | 6370.7(13) | 52.3(8) |
| F2 | 2424.6(16) | 5474.6(17) | 6504.4(13) | 53.8(8) |
| F3 | 2245(2) | 6546(2) | 6764.8(15) | 81.6(12) |
| O1 | 3095.6(16) | 3547.3(15) | 5097.3(15) | 35.1(7) |

| | | | | |
|---|---|---|---|---|
| O2 | 2036.2(16) | 4140.0(16) | 5144.9(16) | 38.3(7) |
| C1 | 3110(2) | 5402(2) | 5205(2) | 31.4(9) |
| C2 | 3874(2) | 5581(2) | 4895(2) | 33.7(10) |
| C3 | 3945(2) | 4799(2) | 4742(2) | 36.5(10) |
| C4 | 3092(2) | 4744(2) | 4797(2) | 31.8(9) |
| C5 | 2497(2) | 5927(2) | 5196(2) | 33.1(10) |
| C6 | 2171(3) | 6103(2) | 4634(2) | 40.7(11) |
| C7 | 1621(3) | 6610(3) | 4589(3) | 52.4(14) |
| C8 | 1399(4) | 6966(3) | 5106(3) | 66.3(17) |
| C9 | 1710(3) | 6813(3) | 5658(3) | 61.1(16) |
| C10 | 2248(3) | 6291(3) | 5709(2) | 45.0(12) |
| C11 | 2551(3) | 6137(3) | 6327(2) | 48.9(13) |
| C12 | 4455(2) | 5960(2) | 5251(2) | 34.4(10) |
| C13 | 4390(3) | 6672(3) | 5331(3) | 46.5(12) |
| C14 | 4906(3) | 7045(3) | 5672(3) | 46.1(13) |
| C15 | 5494(3) | 6710(3) | 5939(2) | 42.6(11) |
| C16 | 5574(3) | 5999(3) | 5864(2) | 44.4(12) |
| C17 | 5057(3) | 5624(2) | 5520(2) | 37.8(11) |
| C18 | 2713(2) | 4093(2) | 5038.5(18) | 27.9(9) |
| F1A | 5845.1(16) | 5333.6(15) | 7822.8(13) | 46.8(7) |
| F2A | 5947.6(14) | 6370.6(14) | 8188.6(13) | 42.1(6) |
| F3A | 5537.1(18) | 6214.3(19) | 7283.3(13) | 59.4(8) |

| | | | | |
|---|---|---|---|---|
| O1A | 6354.9(17) | 6292.0(16) | 9706.0(14) | 37.1(7) |
| O2A | 5371.8(16) | 6771.3(14) | 10155.6(14) | 31.7(7) |
| C1A | 5203(2) | 5376(2) | 9083(2) | 30.9(9) |
| C2A | 5182(3) | 4618(2) | 9331(2) | 36.4(10) |
| C3A | 5570(3) | 4895(2) | 9905(2) | 38.7(11) |
| C4A | 5244(3) | 5622(2) | 9756(2) | 33.7(10) |
| C5A | 4595(2) | 5656(2) | 8677(2) | 31.6(9) |
| C6A | 3863(2) | 5666(2) | 8889(2) | 35.9(10) |
| C7A | 3293(3) | 5954(3) | 8541(2) | 42.1(12) |
| C8A | 3439(3) | 6211(3) | 7970(2) | 44.0(12) |
| C9A | 4156(3) | 6194(2) | 7740(2) | 39.7(11) |
| C10A | 4728(2) | 5929(2) | 8093(2) | 32.2(9) |
| C11A | 5499(3) | 5954(2) | 7843(2) | 37.4(10) |
| C12A | 5503(3) | 4050(2) | 8943(2) | 37.3(10) |
| C13A | 5097(3) | 3790(3) | 8453(2) | 45.2(12) |
| C14A | 5388(4) | 3268(3) | 8083(2) | 52.5(14) |
| C15A | 6076(3) | 3000(3) | 8196(3) | 51.2(14) |
| C16A | 6497(3) | 3240(3) | 8674(3) | 52.6(14) |
| C17A | 6212(3) | 3775(3) | 9050(2) | 44.7(12) |
| C18A | 5688(2) | 6269(2) | 9884.2(19) | 29.0(9) |
| F1B | 4912.5(14) | 4359.6(15) | 3213.5(13) | 45.5(7) |
| F2B | 5088.0(15) | 3464.6(15) | 3783.7(13) | 44.0(7) |

| | | | | |
|---|---|---|---|---|
| F3B | 4714.3(16) | 3327.4(18) | 2863.9(15) | 59.0(9) |
| O1B | 5614.3(16) | 4025.8(15) | 5097.1(14) | 35.7(7) |
| O2B | 6330.4(15) | 3102.5(14) | 4936.9(14) | 31.4(7) |
| C1B | 6413(2) | 4426(2) | 3889(2) | 33.3(10) |
| C2B | 6835(2) | 5130(2) | 3985(2) | 34.4(10) |
| C3B | 6836(3) | 4960(2) | 4674(2) | 36.7(10) |
| C4B | 6720(2) | 4186(2) | 4521(2) | 33.8(10) |
| C5B | 6544(2) | 3990(2) | 3332(2) | 34.1(10) |
| C6B | 7266(3) | 3901(2) | 3120(2) | 39.9(11) |
| C7B | 7425(3) | 3513(3) | 2602(2) | 45.3(12) |
| C8B | 6852(3) | 3208(3) | 2279(2) | 44.8(12) |
| C9B | 6125(3) | 3273(3) | 2488(2) | 40.3(11) |
| C10B | 5973(2) | 3657(2) | 3004(2) | 36(1) |
| C11B | 5182(3) | 3704(3) | 3216(2) | 39.1(11) |
| C12B | 6492(3) | 5780(2) | 3734(2) | 33.9(10) |
| C13B | 6778(3) | 6086(3) | 3219(2) | 45.5(12) |
| C14B | 6448(4) | 6678(3) | 2973(3) | 58.0(15) |
| C15B | 5823(3) | 6957(3) | 3227(3) | 52.5(14) |
| C16B | 5529(3) | 6667(3) | 3745(3) | 53.7(14) |
| C17B | 5862(3) | 6075(3) | 3992(3) | 48.6(13) |
| C18B | 6184(2) | 3746(2) | 4886(2) | 29.5(9) |
| N1 | 4509.1(19) | 3077.1(18) | 5377.1(16) | 28.3(8) |

| | | | | |
|---|---|---|---|---|
| C19 | 4573(3) | 4057(2) | 6445(2) | 40.3(11) |
| C20 | 4313(3) | 4565(3) | 6843(2) | 48.8(13) |
| C21 | 3761(3) | 4418(3) | 7255(2) | 47.4(12) |
| C22 | 3448(3) | 3767(3) | 7274(2) | 47.2(13) |
| C23 | 3692(2) | 3256(3) | 6868(2) | 38.4(11) |
| C24 | 4255(2) | 3395(2) | 6446(2) | 32.1(10) |
| C25 | 4523(2) | 2831(2) | 6024.5(19) | 31.4(9) |
| C26 | 5304(3) | 2587(3) | 6174(2) | 38.7(11) |
| N1A | 6041(2) | 1826.3(19) | 4422.8(17) | 32.9(8) |
| C19A | 5895(3) | 458(3) | 3726(3) | 46.6(12) |
| C20A | 5524(4) | -143(3) | 3567(3) | 57.7(15) |
| C21A | 4861(3) | -99(3) | 3248(3) | 55.9(14) |
| C22A | 4588(3) | 530(4) | 3079(3) | 57.9(15) |
| C23A | 4955(3) | 1137(3) | 3239(2) | 46.9(12) |
| C24A | 5614(2) | 1100(2) | 3565(2) | 36(1) |
| C25A | 6010(2) | 1770(3) | 3744(2) | 38.3(11) |
| C26A | 6789(3) | 1835(3) | 3495(2) | 45.0(12) |
| N1B | 7721.0(19) | 2764.8(18) | 5303.1(16) | 29.2(8) |
| C19B | 7844(3) | 4043(3) | 6057(3) | 53.4(14) |
| C20B | 7662(4) | 4681(3) | 6317(3) | 56.5(15) |
| C21B | 7128(3) | 4714(3) | 6767(2) | 45.7(12) |
| C22B | 6781(3) | 4115(3) | 6964(2) | 47.8(13) |

| | | | | |
|---|---|---|---|---|
| C23B | 6974(2) | 3474(3) | 6709(2) | 40.6(11) |
| C24B | 7504(2) | 3433(2) | 6251(2) | 31.7(9) |
| C25B | 7700(2) | 2737(2) | 5983.8(19) | 31.4(10) |
| C26B | 8430(3) | 2446(3) | 6221(2) | 39.0(11) |

**Table C.3. Anisotropic Displacement Parameters ($Å^2×10^3$) for S55. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.**

| Atom | $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{23}$ | $U_{13}$ | $U_{12}$ |
|---|---|---|---|---|---|---|
| Cl1 | 48.7(9) | 63.6(10) | 56.1(10) | 5.6(7) | -3.6(7) | -7.0(7) |
| Cl2 | 62.1(10) | 51.4(9) | 54.0(9) | 5.7(7) | -1.4(7) | 11.7(7) |
| C27 | 47(3) | 46(3) | 57(4) | 9(3) | 17(3) | 3(3) |
| Cl3 | 67.6(14) | 47.4(12) | 51.8(13) | -1.4(9) | -7(1) | -0.3(10) |
| Cl4 | 60.4(14) | 54.3(13) | 84.6(17) | 8.9(11) | -1.5(12) | 16(1) |
| C28 | 74(6) | 36(4) | 50(5) | 0(4) | 3(4) | -1(4) |
| F1 | 53.3(18) | 58.6(18) | 45.1(17) | -5.5(14) | -9.8(13) | 1.1(15) |
| F2 | 48.4(17) | 73(2) | 40.5(16) | 11.6(15) | 3.3(13) | 3.1(16) |
| F3 | 96(3) | 106(3) | 42.6(18) | -24.7(19) | -4.8(18) | 53(2) |
| O1 | 29.3(16) | 27.8(15) | 48.2(19) | -0.8(14) | -4.7(14) | 1.0(13) |
| O2 | 26.8(16) | 37.3(16) | 51(2) | 6.9(15) | 2.8(14) | 0.4(13) |
| C1 | 30(2) | 32(2) | 33(2) | 4.7(19) | 1.2(18) | 0.3(18) |
| C2 | 34(2) | 33(2) | 34(2) | 2.9(19) | 2.0(19) | -0.7(19) |
| C3 | 32(2) | 38(2) | 40(3) | -2(2) | 6(2) | -1.7(19) |
| C4 | 30(2) | 34(2) | 31(2) | -0.4(19) | -0.7(18) | 1.1(18) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C5 | 34(2) | 29(2) | 37(2) | 2.5(19) | -2(2) | 3.3(19) |
| C6 | 43(3) | 36(2) | 42(3) | -1(2) | -10(2) | 3(2) |
| C7 | 55(3) | 50(3) | 52(3) | 8(3) | -16(3) | 10(3) |
| C8 | 65(4) | 67(4) | 67(4) | -3(3) | -9(3) | 37(3) |
| C9 | 65(4) | 65(4) | 54(4) | -10(3) | -7(3) | 31(3) |
| C10 | 40(3) | 51(3) | 44(3) | -8(2) | -5(2) | 14(2) |
| C11 | 50(3) | 55(3) | 41(3) | -4(2) | 5(2) | 17(3) |
| C12 | 34(2) | 34(2) | 35(2) | 2.0(19) | 9(2) | -4.7(19) |
| C13 | 37(3) | 37(3) | 65(3) | -3(2) | -1(2) | 3(2) |
| C14 | 44(3) | 36(3) | 59(3) | -10(2) | 13(2) | -9(2) |
| C15 | 42(3) | 43(3) | 42(3) | -1(2) | 3(2) | -10(2) |
| C16 | 43(3) | 45(3) | 45(3) | 2(2) | -1(2) | -3(2) |
| C17 | 43(3) | 31(2) | 40(3) | 2(2) | 0(2) | -1(2) |
| C18 | 29(2) | 29(2) | 25(2) | 0.9(17) | -2.8(17) | 0.0(18) |
| F1A | 43.2(16) | 49.3(16) | 47.8(17) | -11.2(13) | 10.2(13) | 5.5(13) |
| F2A | 35.9(14) | 46.0(15) | 44.5(16) | -0.7(13) | 5.0(12) | -4.7(12) |
| F3A | 58.4(19) | 84(2) | 35.6(16) | 12.0(15) | 3.0(14) | 2.3(17) |
| O1A | 29.1(17) | 39.8(17) | 42.4(18) | -8.8(15) | -3.0(14) | -1.7(13) |
| O2A | 31.5(16) | 28.3(15) | 35.3(17) | 0.4(13) | 0.7(13) | 1.6(12) |
| C1A | 28(2) | 32(2) | 32(2) | -2.6(19) | -1.5(18) | -0.7(18) |
| C2A | 36(2) | 33(2) | 40(3) | -2(2) | 3(2) | -7(2) |
| C3A | 49(3) | 31(2) | 36(3) | 0.9(19) | -4(2) | -2(2) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C4A | 32(2) | 33(2) | 36(2) | -3(2) | -1.5(19) | -2.9(19) |
| C5A | 31(2) | 32(2) | 32(2) | -5.9(19) | -1.0(18) | -1.4(18) |
| C6A | 32(2) | 37(2) | 39(3) | -7(2) | 0(2) | -2.9(19) |
| C7A | 30(2) | 48(3) | 49(3) | -8(2) | -4(2) | 1(2) |
| C8A | 38(3) | 41(3) | 53(3) | -11(2) | -14(2) | 6(2) |
| C9A | 48(3) | 39(2) | 32(2) | -7(2) | -11(2) | 5(2) |
| C10A | 35(2) | 31(2) | 31(2) | -7.1(19) | -3.3(19) | -2.2(19) |
| C11A | 44(3) | 42(3) | 26(2) | 1(2) | 0(2) | 4(2) |
| C12A | 43(3) | 29(2) | 39(3) | 1(2) | 6(2) | -9(2) |
| C13A | 59(3) | 37(3) | 39(3) | -1(2) | 1(2) | 3(2) |
| C14A | 83(4) | 36(3) | 39(3) | -2(2) | -1(3) | -5(3) |
| C15A | 69(4) | 35(3) | 50(3) | -5(2) | 20(3) | -4(3) |
| C16A | 52(3) | 42(3) | 64(4) | -3(3) | 16(3) | 1(2) |
| C17A | 45(3) | 38(3) | 52(3) | -6(2) | 6(2) | -5(2) |
| C18A | 28(2) | 33(2) | 26(2) | -0.7(18) | -2.7(17) | 2.0(18) |
| F1B | 30.0(14) | 53.8(17) | 52.7(17) | 0.0(14) | -4.3(12) | 11.5(12) |
| F2B | 37.1(15) | 46.5(16) | 48.5(17) | 1.9(13) | 7.4(12) | -7.6(12) |
| F3B | 35.5(15) | 80(2) | 61(2) | -28.0(17) | -3.0(14) | -11.5(15) |
| O1B | 32.2(16) | 30.3(15) | 44.5(18) | 0.9(14) | 2.5(14) | 4.8(13) |
| O2B | 25.9(15) | 29.1(15) | 39.2(17) | -0.1(13) | -2.3(13) | 2.9(12) |
| C1B | 26(2) | 33(2) | 40(3) | 2(2) | -0.6(19) | -1.6(18) |
| C2B | 27(2) | 35(2) | 40(3) | 4(2) | -0.2(19) | -5.2(18) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C3B | 34(2) | 37(2) | 39(3) | -1(2) | -4(2) | -5(2) |
| C4B | 27(2) | 35(2) | 39(3) | 1.2(19) | -4.0(18) | -0.6(18) |
| C5B | 30(2) | 31(2) | 42(3) | 3(2) | 3.8(19) | 0.3(18) |
| C6B | 30(2) | 41(3) | 48(3) | -2(2) | 4(2) | 0.3(19) |
| C7B | 38(3) | 52(3) | 46(3) | 1(2) | 8(2) | 0(2) |
| C8B | 48(3) | 48(3) | 38(3) | -4(2) | 4(2) | 3(2) |
| C9B | 41(3) | 41(3) | 39(3) | 0(2) | -1(2) | 1(2) |
| C10B | 33(2) | 38(2) | 37(3) | 2(2) | -3.4(19) | 1(2) |
| C11B | 33(2) | 45(3) | 39(3) | -5(2) | -6(2) | -7(2) |
| C12B | 35(2) | 33(2) | 34(2) | -2.9(19) | -3.9(19) | -8.1(19) |
| C13B | 46(3) | 48(3) | 43(3) | 4(2) | 0(2) | -3(2) |
| C14B | 68(4) | 54(3) | 53(3) | 18(3) | -1(3) | -12(3) |
| C15B | 61(3) | 40(3) | 56(4) | 7(3) | -20(3) | -1(3) |
| C16B | 52(3) | 49(3) | 60(4) | 1(3) | -4(3) | 6(3) |
| C17B | 45(3) | 47(3) | 55(3) | 14(3) | 6(2) | 5(2) |
| C18B | 22(2) | 32(2) | 34(2) | -0.6(19) | -3.5(17) | -2.9(17) |
| N1 | 24.6(18) | 28.4(18) | 31.7(19) | -2.7(15) | -3.9(15) | 0.5(14) |
| C19 | 52(3) | 35(2) | 33(2) | -5(2) | 2(2) | -5(2) |
| C20 | 68(4) | 36(3) | 42(3) | -10(2) | 0(3) | -5(2) |
| C21 | 47(3) | 50(3) | 46(3) | -15(2) | -3(2) | 10(2) |
| C22 | 39(3) | 55(3) | 47(3) | -12(3) | 6(2) | -4(2) |
| C23 | 31(2) | 42(2) | 42(3) | -6(2) | 0(2) | -7(2) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C24 | 31(2) | 32(2) | 33(2) | 0.1(19) | -6.6(18) | 2.3(18) |
| C25 | 35(2) | 29(2) | 30(2) | 0.1(18) | -2.3(19) | -1.5(18) |
| C26 | 36(3) | 36(2) | 43(3) | 2(2) | -6(2) | 4(2) |
| N1A | 26.5(18) | 30.8(19) | 41(2) | -1.1(16) | -1.5(16) | 2.0(15) |
| C19A | 41(3) | 42(3) | 57(3) | -6(2) | -13(2) | -1(2) |
| C20A | 69(4) | 47(3) | 57(4) | -10(3) | -4(3) | -9(3) |
| C21A | 53(3) | 64(4) | 51(3) | -21(3) | -1(3) | -19(3) |
| C22A | 39(3) | 85(4) | 50(3) | -22(3) | -7(2) | -5(3) |
| C23A | 31(3) | 64(3) | 45(3) | -9(3) | -1(2) | 5(2) |
| C24A | 30(2) | 46(3) | 32(2) | -6(2) | 1.3(18) | 1(2) |
| C25A | 33(2) | 45(3) | 37(3) | 6(2) | -2(2) | 5(2) |
| C26A | 40(3) | 49(3) | 46(3) | 4(2) | 6(2) | -3(2) |
| N1B | 23.0(18) | 32.7(18) | 32(2) | -0.4(15) | -0.3(15) | 0.8(14) |
| C19B | 68(4) | 39(3) | 53(3) | -2(2) | 26(3) | -6(3) |
| C20B | 77(4) | 39(3) | 53(3) | -4(2) | 12(3) | 0(3) |
| C21B | 49(3) | 44(3) | 44(3) | -11(2) | -4(2) | 11(2) |
| C22B | 43(3) | 55(3) | 46(3) | -12(3) | 7(2) | 6(2) |
| C23B | 30(2) | 53(3) | 38(3) | -7(2) | 5(2) | -3(2) |
| C24B | 26(2) | 37(2) | 32(2) | -3.5(19) | -1.8(18) | 0.8(19) |
| C25B | 31(2) | 32(2) | 31(2) | 2.2(18) | -0.1(18) | 0.7(18) |
| C26B | 38(3) | 44(3) | 35(3) | -2(2) | -7(2) | 10(2) |

**Table C.4. Bond Lengths for C1.**

| Atom | Atom | Length/Å | Atom | Atom | Length/Å |
|---|---|---|---|---|---|
| Cl1 | C27 | 1.758(6) | C16A | C17A | 1.414(7) |
| Cl2 | C27 | 1.757(6) | F1B | C11B | 1.349(6) |
| Cl3 | C28 | 1.756(7) | F2B | C11B | 1.338(6) |
| Cl4 | C28 | 1.729(7) | F3B | C11B | 1.352(5) |
| F1 | C11 | 1.336(6) | O1B | C18B | 1.245(5) |
| F2 | C11 | 1.349(6) | O2B | C18B | 1.268(5) |
| F3 | C11 | 1.357(6) | C1B | C2B | 1.565(6) |
| O1 | C18 | 1.260(5) | C1B | C4B | 1.561(6) |
| O2 | C18 | 1.242(5) | C1B | C5B | 1.502(6) |
| C1 | C2 | 1.569(6) | C2B | C3B | 1.549(7) |
| C1 | C4 | 1.550(6) | C2B | C12B | 1.498(6) |
| C1 | C5 | 1.494(6) | C3B | C4B | 1.539(6) |
| C2 | C3 | 1.545(6) | C4B | C18B | 1.511(6) |
| C2 | C12 | 1.494(6) | C5B | C6B | 1.388(6) |
| C3 | C4 | 1.541(6) | C5B | C10B | 1.408(6) |
| C4 | C18 | 1.519(6) | C6B | C7B | 1.389(7) |
| C5 | C6 | 1.406(7) | C7B | C8B | 1.381(7) |
| C5 | C10 | 1.399(7) | C8B | C9B | 1.389(7) |
| C6 | C7 | 1.392(7) | C9B | C10B | 1.379(7) |
| C7 | C8 | 1.383(8) | C10B | C11B | 1.498(7) |

| | | | | | |
|---|---|---|---|---|---|
| C8 | C9 | 1.367(8) | C12B | C13B | 1.375(7) |
| C9 | C10 | 1.396(7) | C12B | C17B | 1.387(7) |
| C10 | C11 | 1.493(7) | C13B | C14B | 1.391(8) |
| C12 | C13 | 1.384(7) | C14B | C15B | 1.364(9) |
| C12 | C17 | 1.392(7) | C15B | C16B | 1.371(8) |
| C13 | C14 | 1.389(7) | C16B | C17B | 1.394(7) |
| C14 | C15 | 1.369(7) | N1 | C25 | 1.498(6) |
| C15 | C16 | 1.381(7) | C19 | C20 | 1.391(7) |
| C16 | C17 | 1.398(7) | C19 | C24 | 1.393(7) |
| F1A | C11A | 1.345(5) | C20 | C21 | 1.371(8) |
| F2A | C11A | 1.366(5) | C21 | C22 | 1.372(8) |
| F3A | C11A | 1.328(5) | C22 | C23 | 1.396(7) |
| O1A | C18A | 1.262(5) | C23 | C24 | 1.396(6) |
| O2A | C18A | 1.267(5) | C24 | C25 | 1.504(6) |
| C1A | C2A | 1.555(6) | C25 | C26 | 1.516(6) |
| C1A | C4A | 1.553(6) | N1A | C25A | 1.494(6) |
| C1A | C5A | 1.508(6) | C19A | C20A | 1.378(7) |
| C2A | C3A | 1.536(7) | C19A | C24A | 1.377(7) |
| C2A | C12A | 1.500(7) | C20A | C21A | 1.385(8) |
| C3A | C4A | 1.548(6) | C21A | C22A | 1.355(9) |
| C4A | C18A | 1.504(6) | C22A | C23A | 1.384(8) |
| C5A | C6A | 1.393(6) | C23A | C24A | 1.386(7) |

| | | | | | |
|---|---|---|---|---|---|
| C5A | C10A | 1.407(6) | C24A | C25A | 1.522(7) |
| C6A | C7A | 1.392(7) | C25A | C26A | 1.509(7) |
| C7A | C8A | 1.373(8) | N1B | C25B | 1.496(6) |
| C8A | C9A | 1.384(7) | C19B | C20B | 1.392(8) |
| C9A | C10A | 1.384(6) | C19B | C24B | 1.388(7) |
| C10A | C11A | 1.490(6) | C20B | C21B | 1.379(8) |
| C12A | C13A | 1.391(7) | C21B | C22B | 1.378(8) |
| C12A | C17A | 1.399(7) | C22B | C23B | 1.394(7) |
| C13A | C14A | 1.392(7) | C23B | C24B | 1.387(6) |
| C14A | C15A | 1.362(8) | C24B | C25B | 1.501(6) |
| C15A | C16A | 1.374(8) | C25B | C26B | 1.518(6) |

**Table C.5. Bond Angles for C1.**

| Atom | Atom | Atom | Angle/° | Atom | Atom | Atom | Angle/° |
|---|---|---|---|---|---|---|---|
| Cl2 | C27 | Cl1 | 111.3(3) | O1A | C18A | O2A | 123.0(4) |
| Cl4 | C28 | Cl3 | 112.9(5) | O1A | C18A | C4A | 118.3(4) |
| C4 | C1 | C2 | 86.9(3) | O2A | C18A | C4A | 118.6(4) |
| C5 | C1 | C2 | 119.4(4) | C4B | C1B | C2B | 88.0(3) |
| C5 | C1 | C4 | 121.8(4) | C5B | C1B | C2B | 120.9(4) |
| C3 | C2 | C1 | 87.4(3) | C5B | C1B | C4B | 120.2(4) |
| C12 | C2 | C1 | 119.4(4) | C3B | C2B | C1B | 87.1(3) |
| C12 | C2 | C3 | 121.9(4) | C12B | C2B | C1B | 118.1(4) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C4 | C3 | C2 | 88.1(3) | C12B | C2B | C3B | 122.4(4) |
| C3 | C4 | C1 | 88.2(3) | C4B | C3B | C2B | 89.4(3) |
| C18 | C4 | C1 | 118.5(4) | C3B | C4B | C1B | 87.6(3) |
| C18 | C4 | C3 | 121.9(4) | C18B | C4B | C1B | 114.3(3) |
| C6 | C5 | C1 | 118.8(4) | C18B | C4B | C3B | 120.7(4) |
| C10 | C5 | C1 | 124.2(4) | C6B | C5B | C1B | 119.2(4) |
| C10 | C5 | C6 | 117.0(4) | C6B | C5B | C10B | 117.0(4) |
| C7 | C6 | C5 | 121.7(5) | C10B | C5B | C1B | 123.7(4) |
| C8 | C7 | C6 | 119.5(5) | C5B | C6B | C7B | 122.1(5) |
| C9 | C8 | C7 | 120.2(5) | C8B | C7B | C6B | 119.6(5) |
| C8 | C9 | C10 | 120.5(5) | C7B | C8B | C9B | 119.6(5) |
| C5 | C10 | C11 | 121.1(4) | C10B | C9B | C8B | 120.3(5) |
| C9 | C10 | C5 | 121.0(5) | C5B | C10B | C11B | 120.4(4) |
| C9 | C10 | C11 | 117.9(5) | C9B | C10B | C5B | 121.2(4) |
| F1 | C11 | F2 | 106.2(4) | C9B | C10B | C11B | 118.4(4) |
| F1 | C11 | F3 | 105.6(4) | F1B | C11B | F3B | 105.9(4) |
| F1 | C11 | C10 | 113.5(4) | F1B | C11B | C10B | 113.2(4) |
| F2 | C11 | F3 | 105.9(4) | F2B | C11B | F1B | 106.3(4) |
| F2 | C11 | C10 | 112.8(5) | F2B | C11B | F3B | 105.7(4) |
| F3 | C11 | C10 | 112.3(4) | F2B | C11B | C10B | 112.9(4) |
| C13 | C12 | C2 | 119.3(4) | F3B | C11B | C10B | 112.2(4) |
| C13 | C12 | C17 | 118.1(4) | C13B | C12B | C2B | 120.3(4) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C17 | C12 | C2 | 122.6(4) | C13B | C12B | C17B | 117.8(5) |
| C12 | C13 | C14 | 121.4(5) | C17B | C12B | C2B | 121.8(4) |
| C15 | C14 | C13 | 120.2(5) | C12B | C13B | C14B | 120.6(5) |
| C14 | C15 | C16 | 119.6(5) | C15B | C14B | C13B | 120.9(5) |
| C15 | C16 | C17 | 120.3(5) | C14B | C15B | C16B | 119.7(5) |
| C12 | C17 | C16 | 120.4(4) | C15B | C16B | C17B | 119.2(6) |
| O1 | C18 | C4 | 118.4(4) | C12B | C17B | C16B | 121.6(5) |
| O2 | C18 | O1 | 125.1(4) | O1B | C18B | O2B | 124.0(4) |
| O2 | C18 | C4 | 116.4(4) | O1B | C18B | C4B | 118.7(4) |
| C4A | C1A | C2A | 87.3(3) | O2B | C18B | C4B | 117.3(4) |
| C5A | C1A | C2A | 121.5(4) | C20 | C19 | C24 | 120.1(5) |
| C5A | C1A | C4A | 119.2(4) | C21 | C20 | C19 | 120.8(5) |
| C3A | C2A | C1A | 87.3(3) | C20 | C21 | C22 | 120.3(5) |
| C12A | C2A | C1A | 118.2(4) | C21 | C22 | C23 | 119.5(5) |
| C12A | C2A | C3A | 123.0(4) | C22 | C23 | C24 | 121.0(4) |
| C2A | C3A | C4A | 88.1(3) | C19 | C24 | C23 | 118.2(4) |
| C3A | C4A | C1A | 86.9(3) | C19 | C24 | C25 | 121.6(4) |
| C18A | C4A | C1A | 117.0(4) | C23 | C24 | C25 | 120.1(4) |
| C18A | C4A | C3A | 120.3(4) | N1 | C25 | C24 | 110.6(3) |
| C6A | C5A | C1A | 119.4(4) | N1 | C25 | C26 | 108.6(4) |
| C6A | C5A | C10A | 117.4(4) | C24 | C25 | C26 | 112.7(4) |
| C10A | C5A | C1A | 123.2(4) | C24A | C19A | C20A | 120.5(5) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C7A | C6A | C5A | 121.1(5) | C19A | C20A | C21A | 119.5(6) |
| C8A | C7A | C6A | 120.2(5) | C22A | C21A | C20A | 120.3(5) |
| C7A | C8A | C9A | 120.2(5) | C21A | C22A | C23A | 120.6(5) |
| C8A | C9A | C10A | 119.7(5) | C22A | C23A | C24A | 119.6(5) |
| C5A | C10A | C11A | 120.4(4) | C19A | C24A | C23A | 119.5(5) |
| C9A | C10A | C5A | 121.4(4) | C19A | C24A | C25A | 121.3(4) |
| C9A | C10A | C11A | 118.2(4) | C23A | C24A | C25A | 119.3(4) |
| F1A | C11A | F2A | 105.3(4) | N1A | C25A | C24A | 109.7(4) |
| F1A | C11A | C10A | 114.4(4) | N1A | C25A | C26A | 108.7(4) |
| F2A | C11A | C10A | 111.3(4) | C26A | C25A | C24A | 114.2(4) |
| F3A | C11A | F1A | 106.2(4) | C24B | C19B | C20B | 120.9(5) |
| F3A | C11A | F2A | 105.2(4) | C21B | C20B | C19B | 119.9(5) |
| F3A | C11A | C10A | 113.6(4) | C22B | C21B | C20B | 120.0(5) |
| C13A | C12A | C2A | 119.9(4) | C21B | C22B | C23B | 119.9(5) |
| C13A | C12A | C17A | 118.2(5) | C24B | C23B | C22B | 120.7(5) |
| C17A | C12A | C2A | 121.9(4) | C19B | C24B | C25B | 121.8(4) |
| C12A | C13A | C14A | 120.9(5) | C23B | C24B | C19B | 118.5(4) |
| C15A | C14A | C13A | 120.4(5) | C23B | C24B | C25B | 119.6(4) |
| C14A | C15A | C16A | 120.8(5) | N1B | C25B | C24B | 111.4(3) |
| C15A | C16A | C17A | 119.4(5) | N1B | C25B | C26B | 109.5(4) |
| C12A | C17A | C16A | 120.3(5) | C24B | C25B | C26B | 113.4(4) |

**Table C.6. Hydrogen Bonds for C1.**

| D | H | A | d(D-H)/Å | d(H-A)/Å | d(D-A)/Å | D-H-A/° |
|---|---|---|---|---|---|---|
| N1 | H1C | O2A[1] | 0.91 | 1.90 | 2.775(4) | 160.9 |
| N1 | H1D | O1B | 0.91 | 1.86 | 2.764(5) | 172.1 |
| N1 | H1E | O1 | 0.91 | 1.88 | 2.764(4) | 164.9 |
| N1A | H1AA | O2A[1] | 0.91 | 1.83 | 2.704(5) | 160.4 |
| N1A | H1AB | O2B | 0.91 | 1.86 | 2.748(5) | 166.1 |
| N1A | H1AC | O2[2] | 0.91 | 1.84 | 2.746(5) | 172.7 |
| N1B | H1BA | O1A[3] | 0.91 | 1.90 | 2.785(5) | 162.7 |
| N1B | H1BB | O2B | 0.91 | 1.80 | 2.703(4) | 173.6 |
| N1B | H1BC | O1[2] | 0.91 | 1.84 | 2.752(5) | 175.9 |

[1]1-X,-1/2+Y,3/2-Z; [2]1/2+X,1/2-Y,1-Z; [3]3/2-X,1-Y,-1/2+Z

**Table C.7. Torsion Angles for C1.**

| A | B | C | D | Angle/° | A | B | C | D | Angle/° |
|---|---|---|---|---|---|---|---|---|---|
| C1 | C2 | C3 | C4 | 23.0(3) | C12A | C13A | C14A | C15A | 0.3(8) |
| C1 | C2 | C12 | C13 | -78.4(6) | C13A | C12A | C17A | C16A | -1.1(7) |
| C1 | C2 | C12 | C17 | 100.0(5) | C13A | C14A | C15A | C16A | -0.3(8) |
| C1 | C4 | C18 | O1 | -119.5(4) | C14A | C15A | C16A | C17A | -0.4(8) |
| C1 | C4 | C18 | O2 | 62.8(5) | C15A | C16A | C17A | C12A | 1.1(8) |
| C1 | C5 | C6 | C7 | -177.1(5) | C17A | C12A | C13A | C14A | 0.4(7) |
| C1 | C5 | C10 | C9 | 175.0(5) | C1B | C2B | C3B | C4B | 21.3(3) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| C1 | C5 | C10 | C11 | -4.6(8) | C1B | C2B | C12B | C13B | -105.5(5) |
| C2 | C1 | C4 | C3 | 22.9(3) | C1B | C2B | C12B | C17B | 71.5(6) |
| C2 | C1 | C4 | C18 | 148.7(4) | C1B | C4B | C18B | O1B | -69.1(5) |
| C2 | C1 | C5 | C6 | 66.4(6) | C1B | C4B | C18B | O2B | 108.0(4) |
| C2 | C1 | C5 | C10 | -109.8(5) | C1B | C5B | C6B | C7B | -179.1(4) |
| C2 | C3 | C4 | C1 | -23.2(3) | C1B | C5B | C10B | C9B | 178.9(4) |
| C2 | C3 | C4 | C18 | -146.2(4) | C1B | C5B | C10B | C11B | -2.1(7) |
| C2 | C12 | C13 | C14 | 178.3(5) | C2B | C1B | C4B | C3B | 21.1(3) |
| C2 | C12 | C17 | C16 | -178.0(4) | C2B | C1B | C4B | C18B | 143.8(4) |
| C3 | C2 | C12 | C13 | 174.8(4) | C2B | C1B | C5B | C6B | 42.3(6) |
| C3 | C2 | C12 | C17 | -6.8(7) | C2B | C1B | C5B | C10B | -138.0(4) |
| C3 | C4 | C18 | O1 | -12.2(6) | C2B | C3B | C4B | C1B | -21.3(3) |
| C3 | C4 | C18 | O2 | 170.0(4) | C2B | C3B | C4B | C18B | -138.2(4) |
| C4 | C1 | C2 | C3 | -22.8(3) | C2B | C12B | C13B | C14B | 178.0(5) |
| C4 | C1 | C2 | C12 | -148.4(4) | C2B | C12B | C17B | C16B | -177.8(5) |
| C4 | C1 | C5 | C6 | -39.6(6) | C3B | C2B | C12B | C13B | 148.8(4) |
| C4 | C1 | C5 | C10 | 144.2(5) | C3B | C2B | C12B | C17B | -34.2(6) |
| C5 | C1 | C2 | C3 | -147.9(4) | C3B | C4B | C18B | O1B | 33.1(6) |
| C5 | C1 | C2 | C12 | 86.5(5) | C3B | C4B | C18B | O2B | -149.7(4) |
| C5 | C1 | C4 | C3 | 145.9(4) | C4B | C1B | C2B | C3B | -21.0(3) |
| C5 | C1 | C4 | C18 | -88.3(5) | C4B | C1B | C2B | C12B | -146.4(4) |
| C5 | C6 | C7 | C8 | 1.8(8) | C4B | C1B | C5B | C6B | -65.2(6) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| C5 | C10 | C11 | F1 | 59.9(7) | C4B | C1B | C5B | C10B | 114.5(5) |
| C5 | C10 | C11 | F2 | -60.9(7) | C5B | C1B | C2B | C3B | -145.5(4) |
| C5 | C10 | C11 | F3 | 179.6(5) | C5B | C1B | C2B | C12B | 89.1(5) |
| C6 | C5 | C10 | C9 | -1.2(8) | C5B | C1B | C4B | C3B | 146.2(4) |
| C6 | C5 | C10 | C11 | 179.2(5) | C5B | C1B | C4B | C18B | -91.1(5) |
| C6 | C7 | C8 | C9 | -1.1(10) | C5B | C6B | C7B | C8B | 0.6(8) |
| C7 | C8 | C9 | C10 | -0.7(10) | C5B | C10B | C11B | F1B | 63.0(6) |
| C8 | C9 | C10 | C5 | 1.9(9) | C5B | C10B | C11B | F2B | -57.8(6) |
| C8 | C9 | C10 | C11 | -178.5(6) | C5B | C10B | C11B | F3B | -177.1(4) |
| C9 | C10 | C11 | F1 | -119.7(6) | C6B | C5B | C10B | C9B | -1.4(7) |
| C9 | C10 | C11 | F2 | 119.5(6) | C6B | C5B | C10B | C11B | 177.6(4) |
| C9 | C10 | C11 | F3 | -0.1(8) | C6B | C7B | C8B | C9B | -2.3(8) |
| C10 | C5 | C6 | C7 | -0.6(7) | C7B | C8B | C9B | C10B | 2.1(8) |
| C12 | C2 | C3 | C4 | 146.4(4) | C8B | C9B | C10B | C5B | -0.2(7) |
| C12 | C13 | C14 | C15 | -0.2(8) | C8B | C9B | C10B | C11B | -179.2(5) |
| C13 | C12 | C17 | C16 | 0.5(7) | C9B | C10B | C11B | F1B | -118.0(5) |
| C13 | C14 | C15 | C16 | 0.3(8) | C9B | C10B | C11B | F2B | 121.2(5) |
| C14 | C15 | C16 | C17 | -0.1(8) | C9B | C10B | C11B | F3B | 1.9(6) |
| C15 | C16 | C17 | C12 | -0.3(7) | C10B | C5B | C6B | C7B | 1.2(7) |
| C17 | C12 | C13 | C14 | -0.2(8) | C12B | C2B | C3B | C4B | 143.0(4) |
| C1A | C2A | C3A | C4A | 24.2(3) | C12B | C13B | C14B | C15B | -1.7(8) |
| C1A | C2A | C12A | C13A | -78.0(6) | C13B | C12B | C17B | C16B | -0.8(8) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| C1A | C2A | C12A | C17A | 100.8(5) | C13B | C14B | C15B | C16B | 2.4(9) |
| C1A | C4A | C18A | O1A | -54.5(5) | C14B | C15B | C16B | C17B | -2.2(8) |
| C1A | C4A | C18A | O2A | 124.2(4) | C15B | C16B | C17B | C12B | 1.4(8) |
| C1A | C5A | C6A | C7A | 176.5(4) | C17B | C12B | C13B | C14B | 0.9(7) |
| C1A | C5A | C10A | C9A | -178.6(4) | C19 | C20 | C21 | C22 | -1.1(8) |
| C1A | C5A | C10A | C11A | -0.1(6) | C19 | C24 | C25 | N1 | -54.2(5) |
| C2A | C1A | C4A | C3A | 23.9(3) | C19 | C24 | C25 | C26 | 67.6(6) |
| C2A | C1A | C4A | C18A | 146.6(4) | C20 | C19 | C24 | C23 | -2.1(7) |
| C2A | C1A | C5A | C6A | 59.0(6) | C20 | C19 | C24 | C25 | -179.8(4) |
| C2A | C1A | C5A | C10A | -122.7(5) | C20 | C21 | C22 | C23 | -0.3(8) |
| C2A | C3A | C4A | C1A | -24.2(3) | C21 | C22 | C23 | C24 | 0.5(8) |
| C2A | C3A | C4A | C18A | -144.0(4) | C22 | C23 | C24 | C19 | 0.7(7) |
| C2A | C12A | C13A | C14A | 179.3(4) | C22 | C23 | C24 | C25 | 178.4(4) |
| C2A | C12A | C17A | C16A | -180.0(4) | C23 | C24 | C25 | N1 | 128.2(4) |
| C3A | C2A | C12A | C13A | 175.5(4) | C23 | C24 | C25 | C26 | -110.0(5) |
| C3A | C2A | C12A | C17A | -5.7(7) | C24 | C19 | C20 | C21 | 2.3(8) |
| C3A | C4A | C18A | O1A | 48.7(6) | C19A | C20A | C21A | C22A | 1.6(9) |
| C3A | C4A | C18A | O2A | -132.6(4) | C19A | C24A | C25A | N1A | -62.0(6) |
| C4A | C1A | C2A | C3A | -24.1(3) | C19A | C24A | C25A | C26A | 60.3(6) |
| C4A | C1A | C2A | C12A | -150.5(4) | C20A | C19A | C24A | C23A | -0.4(8) |
| C4A | C1A | C5A | C6A | -47.2(6) | C20A | C19A | C24A | C25A | 179.1(5) |
| C4A | C1A | C5A | C10A | 131.1(4) | C20A | C21A | C22A | C23A | -1.9(9) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| C5A | C1A | C2A | C3A | -147.1(4) | C21A | C22A | C23A | C24A | 1.1(8) |
| C5A | C1A | C2A | C12A | 86.6(5) | C22A | C23A | C24A | C19A | 0.1(8) |
| C5A | C1A | C4A | C3A | 148.9(4) | C22A | C23A | C24A | C25A | -179.4(5) |
| C5A | C1A | C4A | C18A | -88.4(5) | C23A | C24A | C25A | N1A | 117.5(5) |
| C5A | C6A | C7A | C8A | 2.4(7) | C23A | C24A | C25A | C26A | -120.2(5) |
| C5A | C10A | C11A | F1A | 56.8(5) | C24A | C19A | C20A | C21A | -0.4(9) |
| C5A | C10A | C11A | F2A | -62.4(5) | C19B | C20B | C21B | C22B | 0.8(9) |
| C5A | C10A | C11A | F3A | 179.0(4) | C19B | C24B | C25B | N1B | -46.9(6) |
| C6A | C5A | C10A | C9A | -0.2(6) | C19B | C24B | C25B | C26B | 77.2(6) |
| C6A | C5A | C10A | C11A | 178.2(4) | C20B | C19B | C24B | C23B | 0.5(8) |
| C6A | C7A | C8A | C9A | -0.8(7) | C20B | C19B | C24B | C25B | -179.0(5) |
| C7A | C8A | C9A | C10A | -1.3(7) | C20B | C21B | C22B | C23B | 0.3(8) |
| C8A | C9A | C10A | C5A | 1.8(7) | C21B | C22B | C23B | C24B | -1.0(8) |
| C8A | C9A | C10A | C11A | -176.7(4) | C22B | C23B | C24B | C19B | 0.6(7) |
| C9A | C10A | C11A | F1A | -124.7(4) | C22B | C23B | C24B | C25B | -179.9(4) |
| C9A | C10A | C11A | F2A | 116.1(4) | C23B | C24B | C25B | N1B | 133.7(4) |
| C9A | C10A | C11A | F3A | -2.5(6) | C23B | C24B | C25B | C26B | -102.3(5) |
| C10A | C5A | C6A | C7A | -1.9(6) | C24B | C19B | C20B | C21B | -1.2(9) |
| C12A | C2A | C3A | C4A | 146.5(4) | | | | | |

**Table C.8. Hydrogen Atom Coordinates (Å×10$^4$) and Isotropic Displacement Parameters (Å$^2$×10$^3$) for C1.**

| Atom | *x* | *y* | *z* | U(eq) |
|---|---|---|---|---|
| H27A | 4268.74 | 5517.64 | 3367.26 | 60 |
| H27B | 4142.1 | 5671.83 | 2657.65 | 60 |
| H28A | 3049.8 | 7454.2 | 4356.01 | 64 |
| H28B | 3220.29 | 7830.68 | 4990.97 | 64 |
| H1 | 3203.88 | 5257.62 | 5636.22 | 38 |
| H2 | 3774.11 | 5843.5 | 4509.85 | 40 |
| H3A | 4137.85 | 4704.53 | 4327.52 | 44 |
| H3B | 4219.97 | 4526.2 | 5052.02 | 44 |
| H4 | 2864.41 | 4869.21 | 4395.5 | 38 |
| H6 | 2330.9 | 5868.91 | 4275.87 | 49 |
| H7 | 1398.78 | 6710.88 | 4206.16 | 63 |
| H8 | 1029.83 | 7318.83 | 5076.52 | 80 |
| H9 | 1558.99 | 7063.56 | 6010.35 | 73 |
| H13 | 3983.5 | 6911.6 | 5149.58 | 56 |
| H14 | 4850.29 | 7534.05 | 5719.76 | 55 |
| H15 | 5844.99 | 6964.02 | 6173.37 | 51 |
| H16 | 5981.41 | 5765.1 | 6048.52 | 53 |
| H17 | 5117.09 | 5135.41 | 5469.39 | 45 |
| H1A | 5695.07 | 5460.35 | 8883.34 | 37 |
| H2A | 4656.16 | 4495.93 | 9434.8 | 44 |

| | | | | |
|---|---|---|---|---|
| H3AA | 6119.84 | 4874.42 | 9887.55 | 46 |
| H3AB | 5379.91 | 4691.83 | 10289.37 | 46 |
| H4A | 4731.27 | 5667.01 | 9929.39 | 40 |
| H6A | 3752.22 | 5473.54 | 9276.85 | 43 |
| H7A | 2801.59 | 5972.6 | 8699.56 | 51 |
| H8A | 3047.29 | 6402.03 | 7732.33 | 53 |
| H9A | 4255.03 | 6363.78 | 7341.29 | 48 |
| H13A | 4615.97 | 3971.68 | 8370.23 | 54 |
| H14A | 5104.12 | 3098.08 | 7749.08 | 63 |
| H15A | 6267.07 | 2642.3 | 7940.45 | 61 |
| H16A | 6975.13 | 3047.98 | 8751.6 | 63 |
| H17A | 6504.34 | 3949.7 | 9377.15 | 54 |
| H1B | 5866.07 | 4513.41 | 3929.08 | 40 |
| H2B | 7353.49 | 5083.28 | 3823.1 | 41 |
| H3BA | 7316.32 | 5058.59 | 4878.5 | 44 |
| H3BB | 6416.54 | 5171.42 | 4900.52 | 44 |
| H4B | 7208.52 | 3942.4 | 4472.75 | 41 |
| H6B | 7664.41 | 4112.56 | 3336.49 | 48 |
| H7B | 7925.27 | 3457.96 | 2470.68 | 54 |
| H8B | 6953.33 | 2956.22 | 1915.98 | 54 |
| H9B | 5730.71 | 3051.02 | 2274.35 | 48 |
| H13B | 7205.82 | 5892.06 | 3028.92 | 55 |

| | | | | |
|---|---|---|---|---|
| H14B | 6660.96 | 6891.1 | 2623.53 | 70 |
| H15B | 5591.41 | 7351.32 | 3046.41 | 63 |
| H16B | 5104.06 | 6867.71 | 3933.79 | 64 |
| H17B | 5650.92 | 5868.23 | 4345.18 | 58 |
| H1C | 4543.69 | 2704.4 | 5122.62 | 34 |
| H1D | 4899.77 | 3369 | 5310.62 | 34 |
| H1E | 4075.27 | 3307.35 | 5304.56 | 34 |
| H19 | 4967.99 | 4160.72 | 6172.55 | 48 |
| H20 | 4520.51 | 5020.25 | 6829.4 | 59 |
| H21 | 3595.51 | 4768.61 | 7528.6 | 57 |
| H22 | 3067.35 | 3664.69 | 7560.41 | 57 |
| H23 | 3471.94 | 2805.98 | 6878.83 | 46 |
| H25 | 4178.3 | 2424.59 | 6061.84 | 38 |
| H26A | 5439.83 | 2200.9 | 5904.2 | 58 |
| H26B | 5322.54 | 2429.22 | 6598.77 | 58 |
| H26C | 5654.69 | 2972.2 | 6117.11 | 58 |
| H1AA | 5592.26 | 1704.45 | 4583.08 | 39 |
| H1AB | 6149.99 | 2272.66 | 4529.63 | 39 |
| H1AC | 6399.45 | 1536.2 | 4568.84 | 39 |
| H19A | 6348.22 | 430.24 | 3947.17 | 56 |
| H20A | 5721.87 | -584.86 | 3676.48 | 69 |
| H21A | 4596.46 | -511.66 | 3146.81 | 67 |

| | | | | |
|---|---|---|---|---|
| H22A | 4140.63 | 554.24 | 2849.56 | 70 |
| H23A | 4756.02 | 1576.76 | 3124.63 | 56 |
| H25A | 5710.38 | 2170.25 | 3586.67 | 46 |
| H26D | 7004.5 | 2280.11 | 3625.44 | 67 |
| H26E | 6774.29 | 1816.98 | 3049.35 | 67 |
| H26F | 7095.53 | 1451.55 | 3649.52 | 67 |
| H1BA | 8073.94 | 3075.05 | 5181.61 | 35 |
| H1BB | 7268.48 | 2900.74 | 5159.6 | 35 |
| H1BC | 7833.22 | 2335.36 | 5153.83 | 35 |
| H19B | 8206.02 | 4024.68 | 5741.54 | 64 |
| H20B | 7905.22 | 5093.99 | 6185.51 | 68 |
| H21B | 6998.27 | 5150.23 | 6942.06 | 55 |
| H22B | 6411.74 | 4137.48 | 7272.89 | 57 |
| H23B | 6738.81 | 3061.42 | 6850.57 | 49 |
| H25B | 7297.77 | 2403.67 | 6101.9 | 38 |
| H26G | 8518.41 | 1986.59 | 6040.54 | 59 |
| H26H | 8406.02 | 2403.53 | 6665.06 | 59 |
| H26I | 8837.79 | 2760.61 | 6109.12 | 59 |

**Table C.9. Atomic Occupancy for C1.**

| Atom | *Occupancy* | Atom | *Occupancy* | Atom | *Occupancy* |
|---|---|---|---|---|---|
| Cl1 | 0.903(4) | Cl2 | 0.903(4) | C27 | 0.903(4) |
| H27A | 0.903(4) | H27B | 0.903(4) | Cl3 | 0.668(4) |
| Cl4 | 0.668(4) | C28 | 0.668(4) | H28A | 0.668(4) |
| H28B | 0.668(4) | | | | |

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