Controlling Stereoselectivity and Chemoselectivity of Cyclopropyl Ketyl Radical Anions with Visible Light Photocatalysis

by

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Controlling Stereoselectivity and Chemoselectivity of Cyclopropyl Ketyl Radical Anions with Visible Light Dual Catalysis

Adrian Gabriel Amador
Under the Supervision of Professor Tehshik P. Yoon
At the University of Wisconsin–Madison

A defining characteristic of research in the Yoon laboratory is a focus on the formation and utilization of high-energy reactive intermediates to accomplish difficult transformations. Recent efforts have been aimed at controlling the reactivity of open-shell radical intermediates; both in terms of chemoselectivity and stereoselectivity. Transition metal photocatalysis has proven to be a particularly successful strategy for accomplishing a wide variety of transformations ranging from net redox neutral as well as net reductive and oxidative transformations. This thesis describes one such approach where the combination of a photocatalyst and a Lewis acid can be used to achieve highly selective and high yielding [3 + 2] cycloadditions between aryl cyclopropyl ketones and a wide range of unsaturated (e.g. olefin and imine) coupling partners. Key to the success of these studies was understanding and carefully optimizing both photocatalyst and Lewis acid to achieve the desired reactivity. These studies have resulted in the development of a highly enantioselective [3 + 2] cycloaddition between cyclopropyl ketones and olefins for the synthesis of cyclopentanes as well as the development of a more general redox-auxiliary approach for the [3 + 2] cycloaddition of cyclopropyl ketones and simple olefins and imine derivatives.

Acknowledgments

One of the first things that Tehshik tells members of the Yoon group after joining is that "research doesn't occur in a vacuum." I believe that this is certainly true and would be remiss if I didn't acknowledge the many people that have helped me on my way to (1) get to the beginning of graduate school and (2) get to the end of graduate school. First, I must thank Tehshik. He gave me the wonderful opportunity to work in his group and then while a member tolerated me staying in his group. I have learned a lot from working under Tehshik despite how differently we tend to think about many things. I was taught to think more deeply about the science that I was working on and this has helped me to improve me ability to think about that grander themes in research than just solving small puzzles.

I must also thank my committee members for agreeing to serve on my behalf. From working around many of you over the years I realize how packed your schedules can be and how great the demands on your time are. I also appreciate the various bit of input I've received from some over you over my time at UW-Madison. It has been an honor to learn from some of the top experts in chemical research. I hope to be able to interact with all of you throughout my career.

I am very grateful to all of the members of the Yoon group. Working with the members of our group past and present has helped to alleviate much of the stress of graduate school. Special thanks go to the members of the "broffice." You all are a hilarious bunch of people to work around and I have enjoyed spending the last few years both in and outside of the lab alongside all of you. From playing "Farngo" to the office Olympics there have been too many great memories to count. I appreciate you all for knowing to not take me seriously most of the time. I can only hope that my future lab has people as awesome to be around as all of you.

Finally, I am most grateful to my family and friends from back home in Georgia. My parents have provided unquestioning support through my life and financially through my undergraduate education even though I didn't want to become and engineer. They have continued to provide the most generous support through graduate school even though they don't fully understand what it is that I am doing. They taught me to be strong and to take responsibility for and then solve my problems. Without their love and support graduate school would have been substantially more difficult if not impossible.

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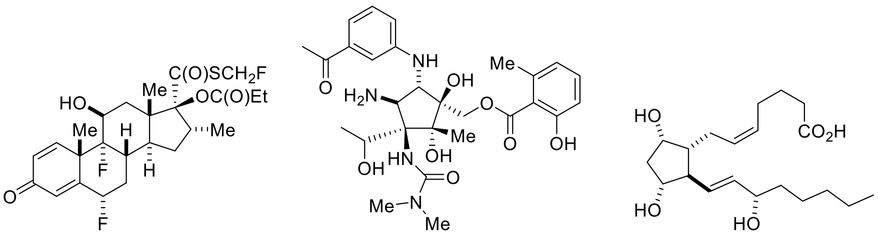
Chapter 1. Catalytic Asymmetric [3 + 2] Cycloadditions for Carbocycle Synthesis

1.1 Introduction

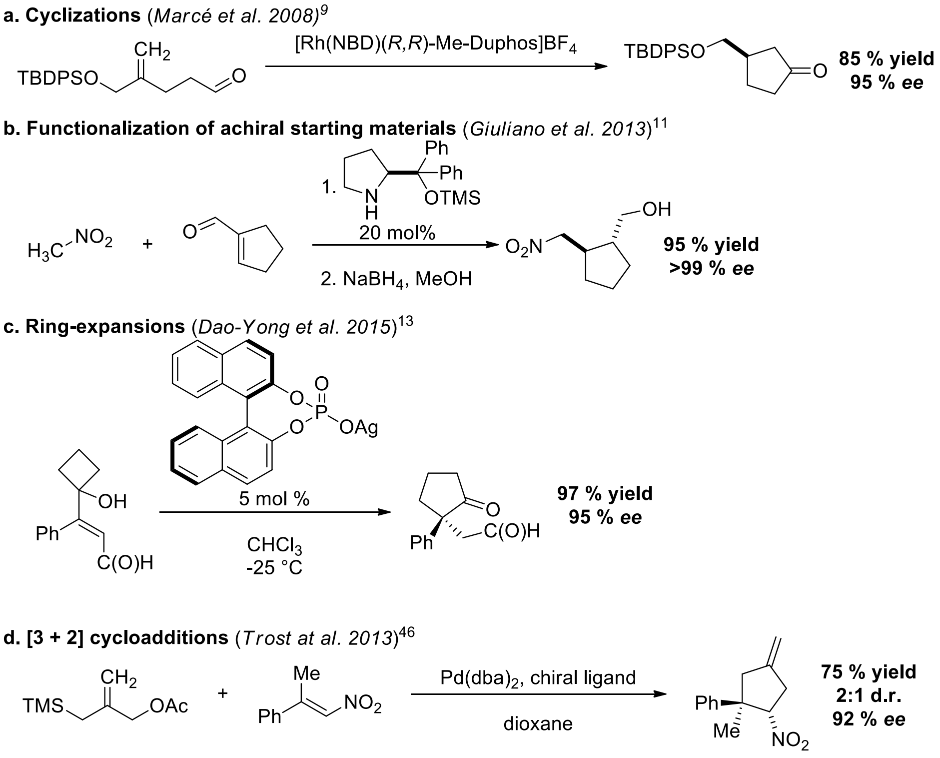
Five-membered rings are an important structural motif found in many natural products and biologically active compounds (figure 1-1). Due to their ubiquity, significant efforts have been dedicated to the development of efficient and stereoselective synthetic methodologies.[1–5] There exists many common strategies for accessing enantioenriched 5-membered carbocycles including: cyclizations[6–10], desymmetrizations of prochiral carbocycles[11,12], ring-expansions[13,14], and [3 + 2] cycloadditions of a 3-carbon and 2-carbon components (Scheme 1-1).

Figure 1-1. Biologically active molecules containing 5-membered carbocycles



Advair **Pactamycin** **Prostaglandin PGF$_{2a}$**

Scheme 1-1. Select examples of enantioselective 5-membered carbocycle synthesis

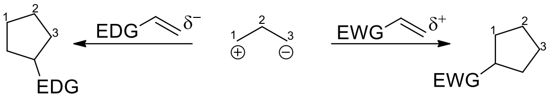

a. Cyclizations (*Marcé et al. 2008)*[9]

b. Functionalization of achiral starting materials (*Giuliano et al. 2013*)[11]

c. Ring-expansions (*Dao-Yong et al. 2015*)[13]

d. [3 + 2] cycloadditions (*Trost at al. 2013*)[46]

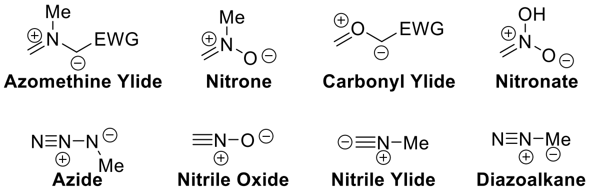
Scheme 1-2. Regioselectivity of 1,3-dipolar [3 + 2] cycloadditions



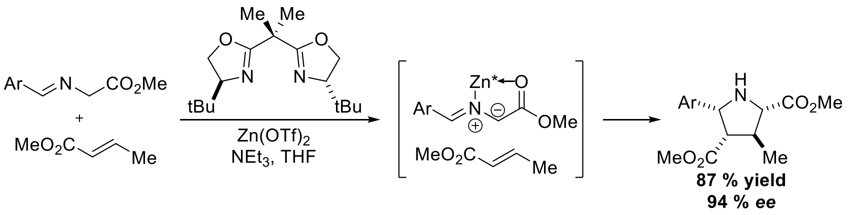
While each of these strategies have their own inherent advantages, [3 + 2] cycloadditions have shown great promise and have drawn significant attention from researchers due to the potential flexibility of efficient intermolecular reactions of diverse coupling partners as well as the potential for very atom-economic methodologies. This review will focus exclusively on catalytic asymmetric formal [3 + 2] cycloadditions that provide direct access to 5-membered carbocycles in a single step. For references pertaining to the other strategies for asymmetric cyclopentanoid synthesis, the reader is directed to the selected examples referenced above (refs. 6–14).

1,3-Dipoles react with many unsaturated 2-atom components in a [3 + 2] cycloaddition to yield a variety of five-membered cyclic molecules. Due to the dipolar nature of the 3-atom component, [3 + 2] cycloadditions are generally observed to occur with coupling partners of complementary polarities with the regioselectivity of the cycloaddition being driven by the nature of the coupling partner (Scheme 1-2). Most 1,3-dipoles will contain a heteroatom (e.g. nitrogen or oxygen) on the central atom to stabilize the positive charge of the 1,3-dipole (Scheme 1-3).

Scheme 1-3a. Examples of common 1,3-dipoles used for [3 + 2] cycloadditions

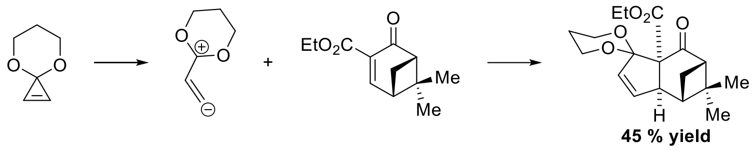


Scheme 1-3b. 1,3-Dipolar [3 + 2] cycloaddition with an azomethine ylide[203]

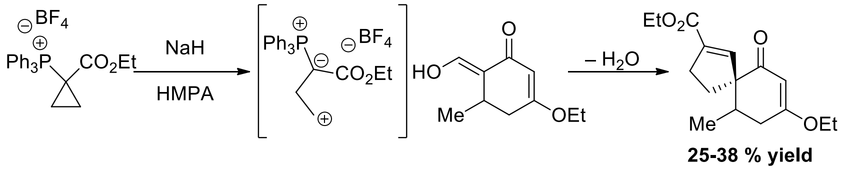


Several reviews have been published recently detailing approaches for the enantioselective synthesis of heterocycles with 1,3-dipolar cycloadditions.[1,15] While many methods for the synthesis of 5-membered heterocycles via [3 + 2] cycloadditions of 1,3-dipoles are well established, the synthesis of carbocycles via this strategy has enjoyed much more limited success. Early progress in this field utilized specialized precursors such as cyclopropenone ketals (Scheme 1-4a) or cyclopropylphosphonium salts (Scheme 1-4b).[3] Neither of these methods proved to be general, and stereoselective examples of these 1,3-dipolar cycloadditions have never been developed. However, the flexibility of 1,3-dipolar cycloadditions for heterocycle synthesis has inspired many approaches for cyclopentane synthesis, and numerous successful methodologies have been developed that make use of 1,3-dipole "surrogates" to mimic this mode of reactivity.

Scheme 1-4a. 1,3-Dipolar [3 + 2] cycloaddition with cyclopropenone ketals



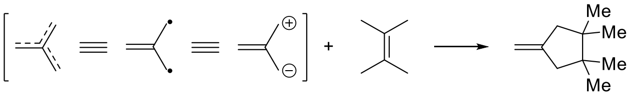
Scheme 1-4b. 1,3-Dipolar [3 + 2] cycloaddition with cyclopropylphosphonium salt



1.2 Transition metal catalyzed asymmetric [3 + 2] cycloadditions

Transition metal catalysis has led to some of the most important breakthroughs in modern organic chemistry for the development of novel synthetic methodologies. Over the last several decades, there has been substantial interest in developing transition metal catalyzed [3 + 2] cycloadditions for the efficient construction of 5-membered carbocycles. Even more so, the development of asymmetric catalytic [3 + 2] cycloadditions has been viewed as a potentially powerful approach to stereo defined five-membered rings. The different strategies and building blocks used in transition metal catalyzed formal [3 + 2] cycloadditions are highly variable. This section aims to provide a brief survey of the most successful and promising catalytic asymmetric methodologies that have emerged as well as the fundamental precedent that led to their development.

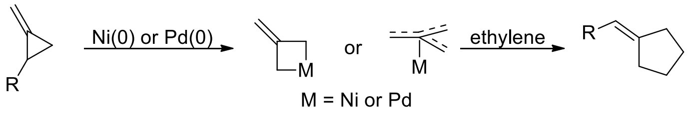
Scheme 1-5. The trimethylenemethane intermediate



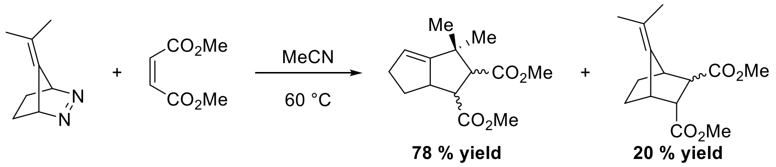
1.2.1 Trimethylenemethane [3 + 2] cycloadditions

One promising approach to develop all carbon 1,3-dipole equivalents came from an intermediate of theoretical interest known as the trimethylenemethane intermediate (Scheme 1-5).[16] Despite early theoretical and practical interest, accessing and controlling the reactivity of this intermediate was initially very challenging. Early work involved insertion of Ni(0) or Pd(0) into the carbon-carbon σ-bond of methylenecyclopropanes (Scheme 1-6).[17–20] The exact nature of the intermediate is unclear (TMM vs. metallocyclobutane) and appears to depend upon the conditions used.[21,22] While some strategies have been developed for enantioinduction using chiral auxiliaries in [3 + 2] cycloadditions of methylenecyclopropanes, a catalytic asymmetric strategy for cyclopentanoid synthesis has yet to be realized.[23–26] Other early work in forming this intermediate was through the formation of the biradical via nitrogen extrusion of diazo intermediates.[27] While the biradical was observed to undergo [3 + 2] cycloadditions with olefins, the reactions were very low yielding and difficult to control. Only constrained systems such as shown in Scheme 1-7

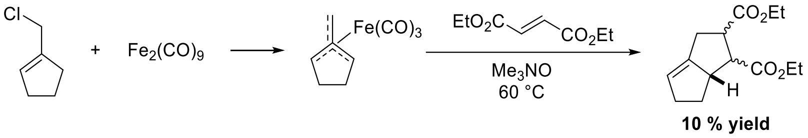
Scheme 1-6. [3 + 2] Cycloadditions with methylenecyclopropane



Scheme 1-7. Biradical trimethylenemethane cycloadditions with constrained ring systems.



Scheme 1-8. [3 + 2] cycloadditions of trimethylenemethaneiron species



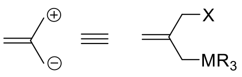
provided cycloadduct with activated alkenes in good yields. Again, catalytic asymmetric variants of these reactions have yet to be realized.

1.2.1.1 Zwitterionic trimethylenemethane [3 + 2] cycloadditions

The most successful approach towards stabilizing this intermediate is through the formation of π-adducts with transition metals. Initial work involved the formation of an iron-tricarbonyl TMM complex; however, this intermediate proved to be too stable, providing only low yields of cycloadduct with diethyl fumarate after heating for 12 h under oxidative conditions (Scheme 1-8).[28,29]

The zwitterionic equivalent of the TMM intermediate has by far been the most versatile approach for [3 + 2] cycloadditions. The precursor to this species has an anionic leaving group (e.g. carboxylate, halide, or triflate) in the 1-position and an electrofugal moiety such as a silyl or stannyl group in the 3-position (Scheme 1-9). In the presence of a transition metal, these precursors will lose both groups to generate the stabilized TMM zwitterionic intermediate (Scheme 1-10).[30]

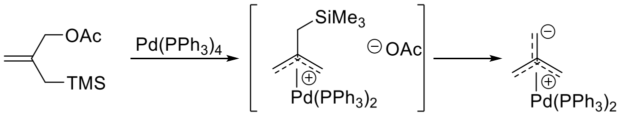
Scheme 1-9. Zwitterionic TMM equivalents



X = OAc, OCO_2R, OTf, or I

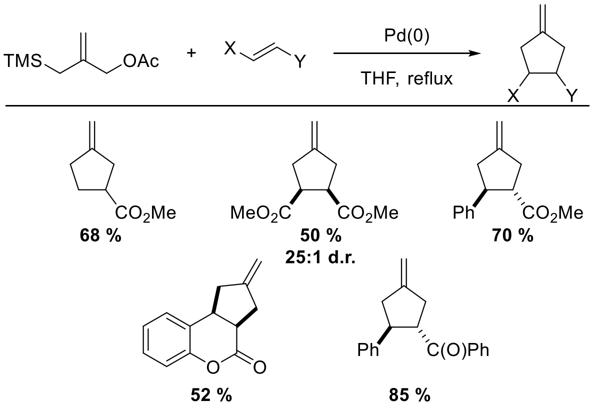
MR_3 = $Si(CH_3)_3$, $Sn(CH_3)_3$, or $SnBu_3$

Scheme 1-10. Formation of zwitterionic TMM intermediate with Pd(0)



Early pioneering work for racemic cycloadditions was reported by Trost and coworkers.[31–34] Their first seminal report showed a general and high yielding substrate scope wherein the TMM-palladium adduct was observed to react smoothly with electron deficient olefins (Figure 1-2). Mechanistic studies by Trost and coworkers provided substantial evidence for the TMM complex and revealed the nucleophilic nature of this intermediate.[22] Support for the stepwise nature of the formal [3 + 2] cycloaddition was also observed through the use of stereochemically defined olefins.[35]

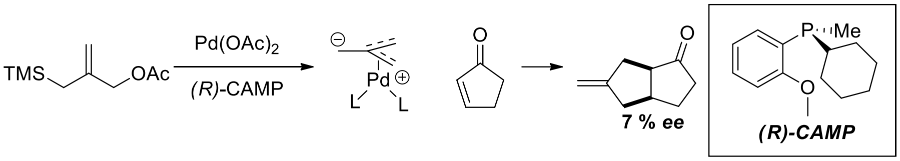
Figure 1-2. First reported palladium catalyzed TMM [3 + 2] cycloadditions



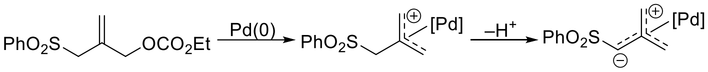
1.2.1.2 Asymmetric zwitterionic trimethylenemethane [3 + 2] cycloadditions

The first example of asymmetric induction in a [3 + 2] cycloaddition with the TMM intermediate was published by Trost and coworkers as part of a mechanistic study, although only poor enantioselectivities were observed (Scheme 1-11).[22] Though there were several subsequent reports by Trost and coworkers utilizing chiral auxiliaries for enantioinduction,[36–38] it wasn't until 1989 that an improved, highly enantioselective catalytic asymmetric variant of this reaction was published by Hayashi and coworkers.[39]

Scheme 1-11. Seminal example of enantioinduction in TMM [3 + 2] cycloaddition



Scheme 1-12. Sulfonyl carbonate TMM precursor utilized by Hayashi



Importantly, the strategy taken by Hayashi and coworkers was also markedly different from those reported previously. The TMM intermediate used in this study made use of a sulfonyl substituent which undergoes deprotonation in place of a silane to form the carbanion equivalent (Scheme 1-12). A series of chiral bisphosphine ligands were screened to optimize the stereoselectivity of the [3 + 2] cycloaddition with methyl acrylate and methyl vinyl ketone. The optimal conditions utilized $Pd_2(dba)_3$ and a ferrocenylphosphine ligand substituted with a *N*-methyl-*N*-bis(hydroxymethyl)methylamino group (Figure 1-3). The authors proposed the model shown in Figure 1-3. The difficulty in achieving good enantiocontrol is thought to be due to the approach of the coupling partner distal to the metal center leading to poor transfer of chirality.[40]

Figure 1-3. Asymmetric TMM [3 + 2] cycloaddition with methyl vinyl ketone

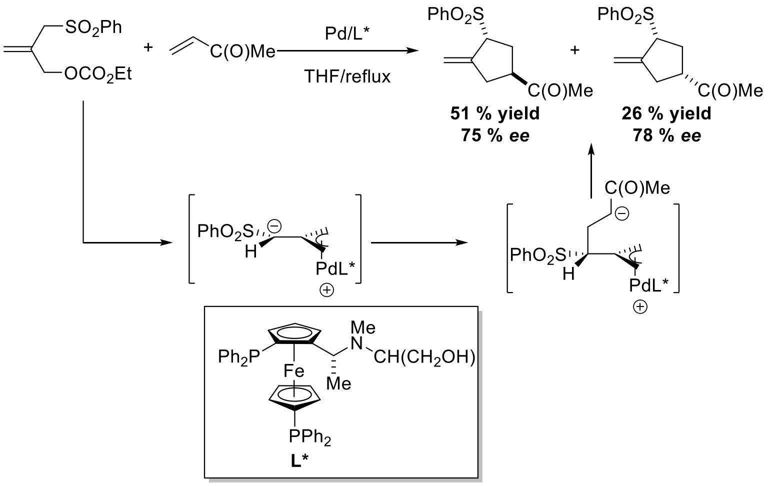
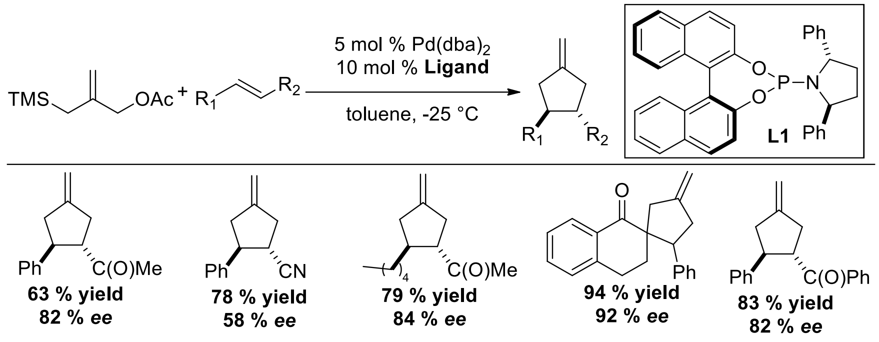


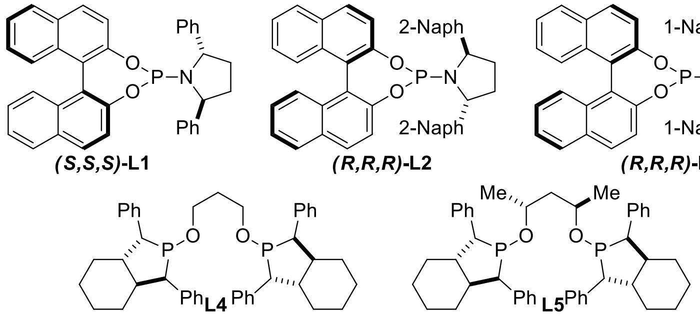
Figure 1-4. Select examples of enantioselective [3 + 2] cycloadditions by Trost and coworkers



In 2006 Trost and coworkers reported an improved palladium catalyzed enantioselective [3 + 2] cycloaddition between 3-acetoxy-2-trimethylsilyl-methyl-1-propene and a variety of electron-deficient coupling partners. These studies used key insights from previous work in developing chiral phosphoramidite ligands for asymmetric catalysis (Figure 1-4).[41,42] This system provided excellent yields and synthetically useful enantioselectivities for a range of electron-deficient coupling partners.

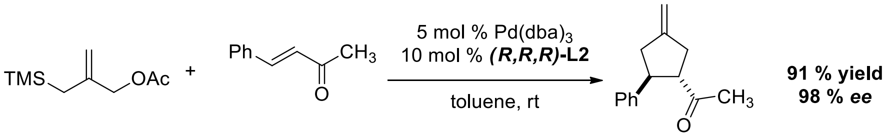
Trost and coworkers have been responsible for most of the progress in this field and have developed a suite of different chiral phophoramidite and diamidophosphite ligands to achieve high selectivities across a range of different substrate classes (Figure 1-5). A selected example for each class of substrates has been compiled in Scheme 1-13. Additionally Trost and coworkers have extended palladium-catalyzed asymmetric [3 + 2] cycloadditions with trimethylenemethane to accommodate both imines and carbonyls for the expedient synthesis of enantioenriched 5-membered heterocycles.[43,44]

Figure 1-5. Ligands developed for TMM [3 + 2] cycloadditions

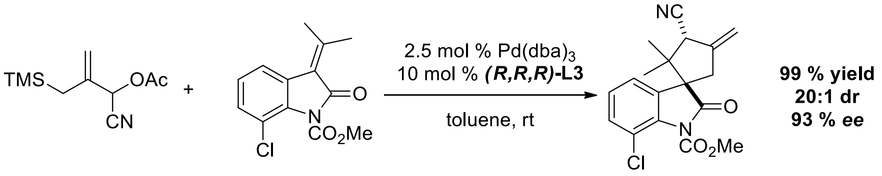


Scheme 1-13. Select examples of substrates for TMM asymmetric [3 + 2] cycloadditions

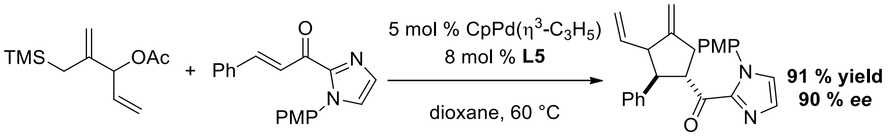
A. *Improved ligand set for simple enones*[204]



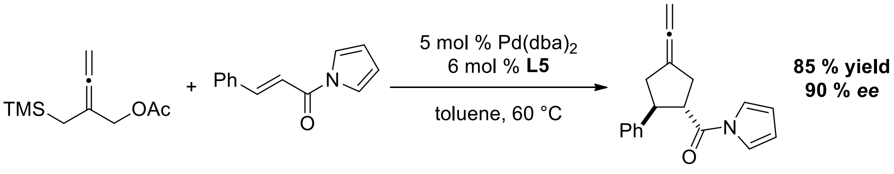
B. *3-alkylidene-oxindoline-2-ones*[205]



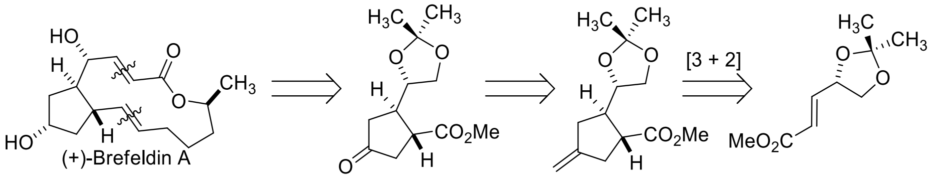
C. *Vinyl-substituted trimethylenemethanes*[206]



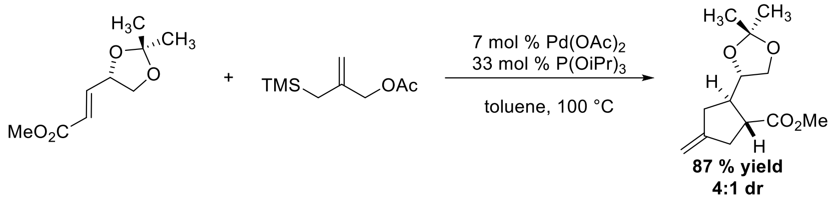
D. *Methylene-substitute trimethylenemethanes*[207]



Scheme 1-14. Retrosynthetic analysis for synthesis of (+)-brefeldin A



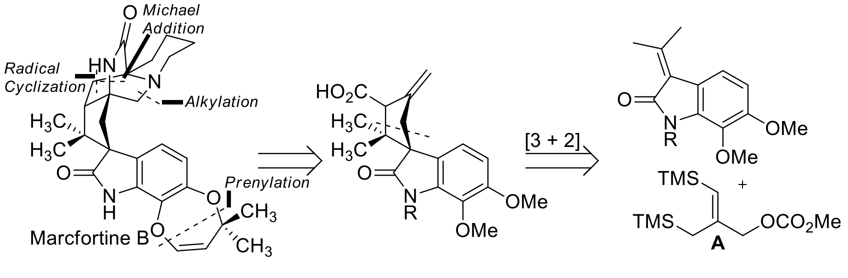
Scheme 1-15. Key cyclopentane construction in synthesis of (+)-brefeldin A



1.2.1.3 Applications of TMM [3 + 2] cycloadditions to complex molecule synthesis

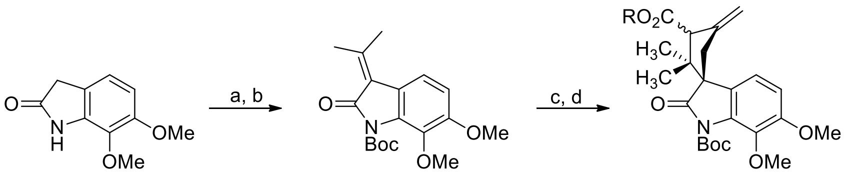
Palladium-catalyzed trimethylenemethane [3 + 2] cycloadditions were applied early on in the synthesis of cyclopentanoid natural products and other complex molecules. The earliest example was the use of a chiral auxiliary by Trost and coworkers in the synthesis of (+)-Brefeldin A (Scheme 1-14).[36] The key retrosynthetic disconnect in this synthesis was the Pd-catalyzed [3 + 2] cycloaddition with an enantiopure coupling partner. The [3 + 2] cycloaddition with 7 mol% of $Pd(OAc)_2$ proceeded in 87% yield with a modest 4:1 diastereoselectivity (Scheme 1-15). Following this key step, the synthesis was completed in a total of 10 steps in a 10% overall yield.

Scheme 1-16. Retrosynthetic analysis for total synthesis of marcfortine B



Outside of a few examples of chiral auxiliaries being used for stereocontrol in trimethylenemethane mediated [3 + 2] cycloadditions, the application of catalytic asymmetric variants to total synthesis has remained limited to one example.[25,36–38] Trost and coworkers illustrated the effectiveness of racemic Pd-catalyzed trimethylenemethane [3 + 2] cycloadditions in route to the natural product (±)-marcfortine B (Scheme 1-16).[45] Key to their retrosynthetic analysis was the construction of the 5-membered spirocyclic ring system in a [3 + 2] cycloaddition from an achiral precursor. They completed the first racemic total synthesis of (±)-marcfortine B in 22 steps in a 2% overall yield. The trimethylenemethane cycloaddition was utilized early on in the synthesis and efficiently provided the key spirocyclic framework in 93% yield as the first step in a two-step sequence (Scheme 1-17).

Scheme 1-17. Construction of 5-membered spirocyclic framework

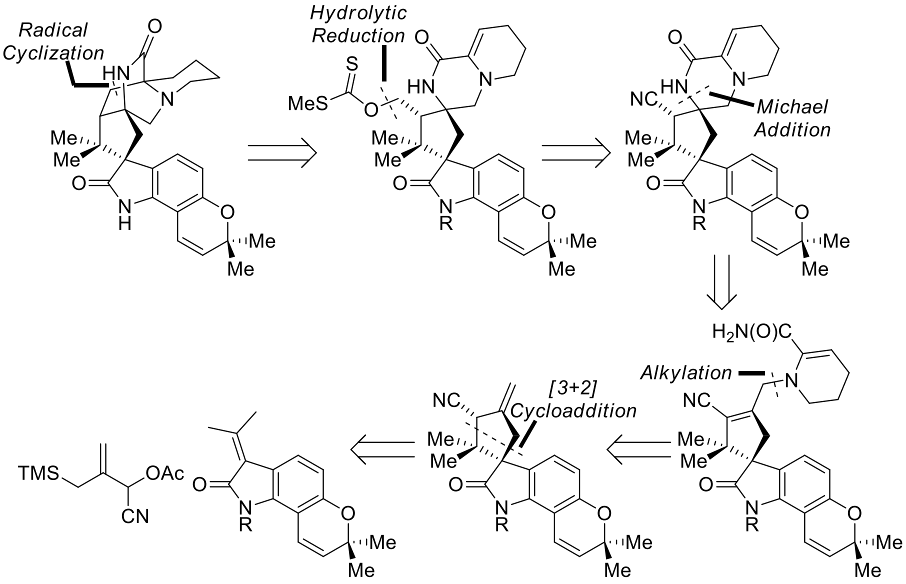


Conditions: (a) acetone, HCl, rt, 70 %; (b) Boc$_2$O, DMAP, NEt$_3$, CH$_2$Cl$_2$, 85 %; (c) **A**, 5 % PdOAc, 35 % P(OiPr)$_3$, toluene, reflux; (d) Me$_2$SO$_4$, K$_2$CO$_3$, acetone, reflux, 93 % over two steps

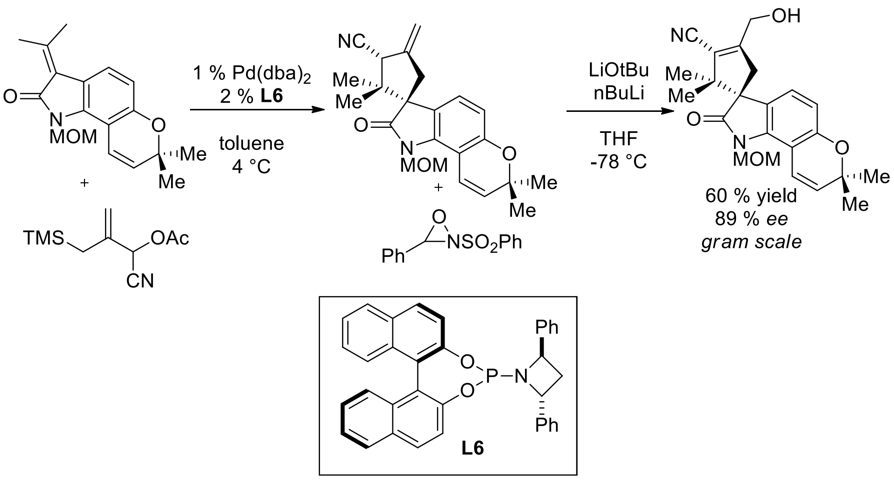
In 2013 Trost and coworkers completed an enantioselective total synthesis of (–)-marcfortine C in which they applied their retrosynthetic disconnect for marcfortine B with the asymmetric conditions that were developed in their labs (Scheme 1-18).[46] The researchers installed the spirocyclic framework early on in a catalytic asymmetric [3 + 2] cycloaddition using their enantioselective TMM methodology. After screening a wide range of phophoramidite ligands they were able to affect the key ring-construction and subsequent oxidation on gram scale in 60 % yield and 89% ee over two steps using the azetidine phosphoramidite **L6** (Scheme 1-19). The remainder of the synthesis was completed as planned to provide (–)-marcfortine C in a total of 19 steps and 2.6% overall yield.

While the catalytic asymmetric TMM [3 + 2] cycloaddition has only found application in one total synthesis to date, it has proven to be a powerful strategy for the stereoselective construction of densely functionalized five-membered rings. The methodology has also been showcased in the formal synthesis of (+)-cephalotoxine as well as in the multi-step construction of densely functionalized polycyclic hydrocarbons.[47,48] However, this powerful approach to the construction of five-membered carbocycles still has several limitations. Due to the inherent sensitivity of the nucleophilic TMM-Pd intermediate to the electronics and the steric environment of the coupling partner. This often requires lengthy multi-step syntheses of multiple phosphoramidite ligands to tune the system for desired reactivity.

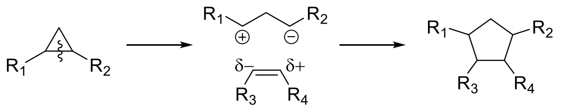
Scheme 1-18. Retrosynthetic analysis for total synthesis of (–)-Marcfortine C



Scheme 1-19. Asymmetric construction of spirocyclic framework in route to (–)-Marcfortine C



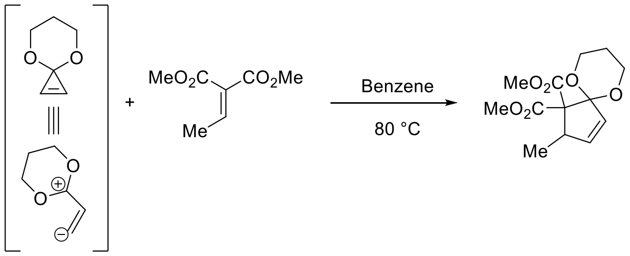
Scheme 1-20. Formal [3 + 2] cycloadditions with cyclopropanes as 1,3-dipole surrogates



1.2.2 Asymmetric [3 + 2] cycloadditions with cyclopropanes as 1,3-dipole surrogates

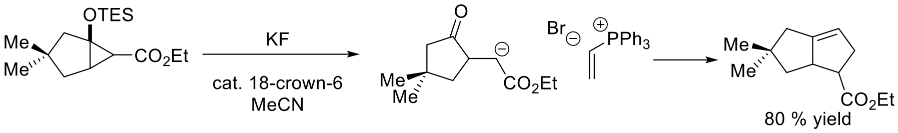
Cyclopropanes have attracted interest as ideal precursors for 1,3-dipole equivalents to accomplish [3 + 2] cycloadditions. The inherent ring strain of these systems offer the possibility for thermal or catalyzed ring opening to the active 3-carbon building block in the absence of any leaving group (Scheme 1-20). Several approaches have been used for ring-cleavage and subsequent cycloadditions, the most successful of which have involved donor-acceptor cyclopropanes in the presence of either a Lewis acid or transition metal catalyst.

Scheme 1-21. Thermal formal [3 + 2] cycloaddition with cyclopropenone ketals



An early racemic example comes from the work of Dale Boger and coworkers.[49] They reported that cyclopropenone ketals undergo thermal heterolytic ring cleavage and formal [3 + 2] cycloadditions with electron deficient alkenes to provide cyclopentenone ketals (Scheme 1-21). The earliest report of an annulation with a donor-acceptor cyclopropane was reported by Marino *et al.* in which 2-(silyloxy)cyclopropane carboxylate esters were shown to react efficiently with vinyl phosphonium salts for a tandem nucleophilic addition-Wittig olefination in the presence of fluoride salts (Scheme 1-22).[50] These initial reports set the stage for the development of catalytic activation of donor-acceptor cyclopropanes for the efficient synthesis of substituted cyclopentanes.

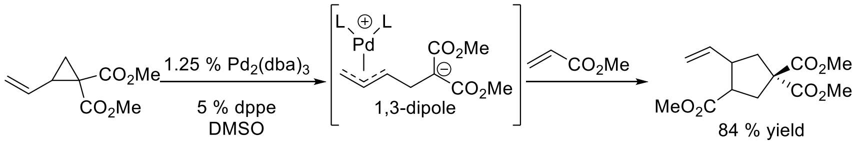
Scheme 1-22. Annulation of donor-acceptor cyclopropane to yield cyclopentenes



1.2.2.1 Palladium catalyzed asymmetric [3 + 2] cycloadditions with cyclopropanes as 1,3-dipole surrogates

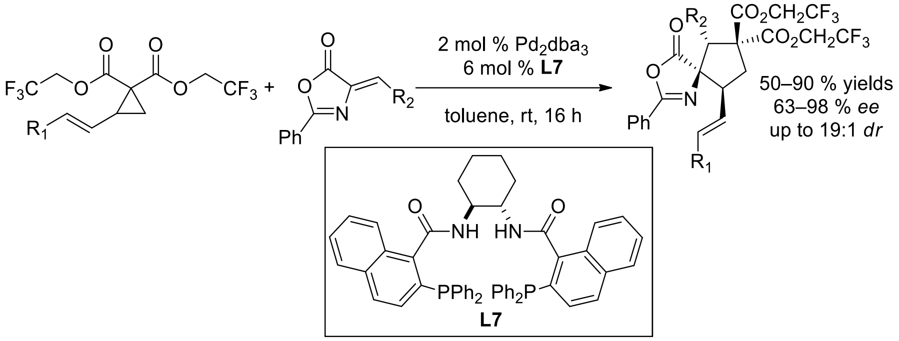
The first example of catalytic activation of a donor-acceptor cyclopropane was reported by Tsuji and coworkers in 1985.[51] The researchers observed that vinylcyclopropanes with two electron withdrawing substituents would undergo formal [3 + 2] cycloadditions with electron deficient alkenes in the presence of a palladium catalyst to provide efficient access to racemic vinyl cyclopentanes (Scheme 1-23). The proposed mechanism for the transformation was the formation of a zwitterionic π-allyl palladium complex that could serve as the 1,3-dipole equivalent.

Scheme 1-23. First example of catalytic activation of donor-acceptor cyclopropane by palladium for [3 + 2] cycloadditions.



The first example of an asymmetric variant of this reaction did not come until nearly three decades later when Trost and coworkers reported a highly enantioselective and diastereoselective formal [3 + 2] cycloaddition of vinyl cyclopropanes and alkylidene azalactones using a chiral palladium catalyst.[52] This initial study came as an extension to the considerable developments coming out of Trost's lab for the asymmetric alkylation of π-allylpalladium intermediates. Key to the success of this transformation was the use of highly electron-withdrawing bis-trifluoroester substituents on the cyclopropane ring to increase the stability of the π-allylpalladium intermediate involved in the cycloaddition (Scheme 1-24). This methodology provided access to a range of substituted enantioenriched spirocyclopentane products that can readily be converted to constrained amino acid derivatives.

Scheme 1-24. First example of an asymmetric [3 + 2] cycloaddition with vinyl cyclopropanes

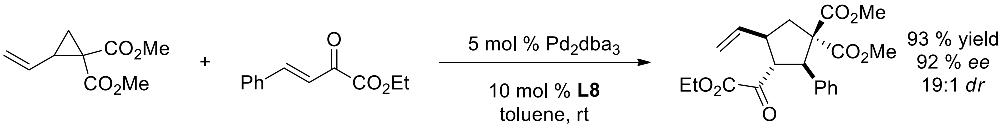


A variety of palladium-catalyzed asymmetric [3 + 2] cycloadditions have since been reported.[52–58] The majority of these transformations make use of a Pd(II) catalyst with C_2 symmetric phosphine and amine containing ligands (Figure 1-6). A selection of examples is shown in Scheme 1-25.

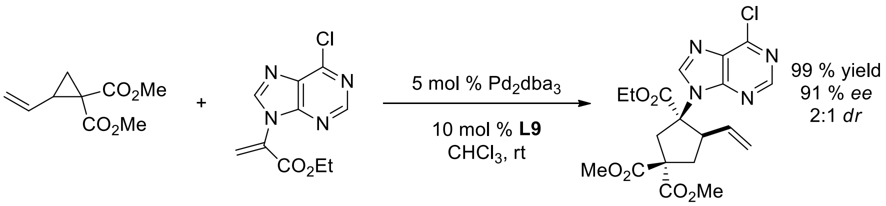
An alternative strategy for similar [3 + 2] cycloadditions is using dual catalysis with a chiral organocatalyst.[59–61] Condensation of a chiral secondary amine with an enal forms a activated iminium ion which undergoes a [3 + 2] cycloaddition with a π-allypalladium intermediate providing products with four contiguous stereocenters and several synthetic handles for derivatization (Scheme 1-26).

Scheme 1-25. Palladium catalyzed asymmetric [3 + 2] cycloadditions with vinyl cyclopropanes

[3 + 2] cycloadditions with α,ß-unsaturated α-Keto esters[55]



[3 + 2] cycloadditions with α-nucleobase substituted acrylates[56]



[3 + 2] cycloadditions with nitrostyrenes[58]

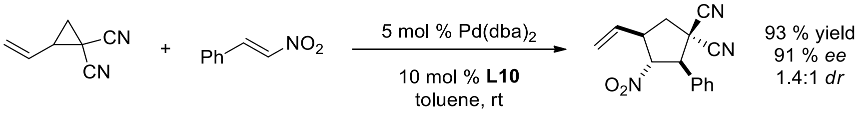
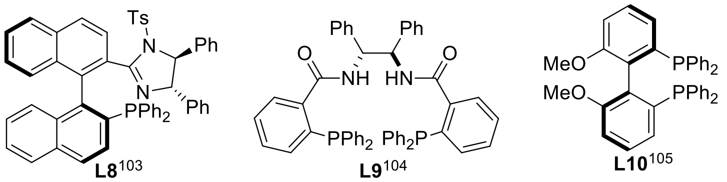


Figure 1-6. Selection of chiral ligands used in asymmetric [3 + 2] cycloadditions with vinyl cyclopropanes.



In addition to the many palladium-catalyzed asymmetric [3 + 2] cycloadditions with vinyl cyclopropanes, intramolecular enantioselective [3 + 2] cycloadditions have also been developed with rhodium catalysts. Zhi-Xiang Yu and coworkers were able to accomplish these transformations using a dimeric $[Rh(CO)_2Cl]_2$ catalyst with a BINAP derived chiral ligand to provide bicyclo[3.3.0] products in good enantioselectivities.[53]

Scheme 1-26. Asymmetric [3 + 2] cycloaddition with Palladium-iminium dual catalysis

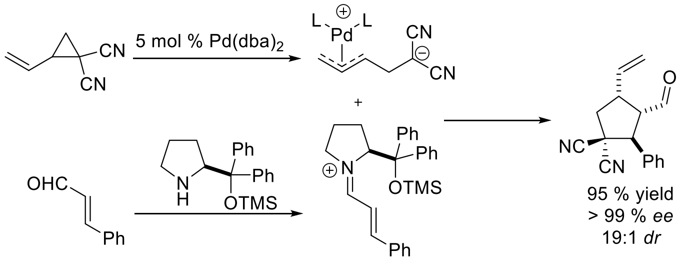
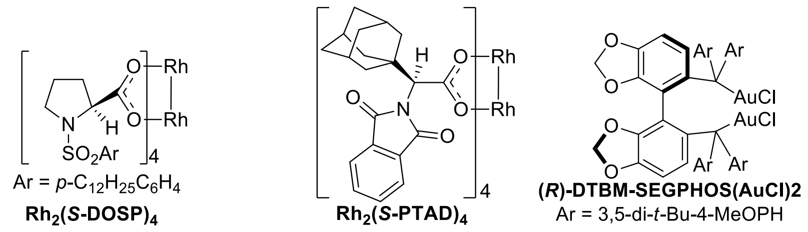


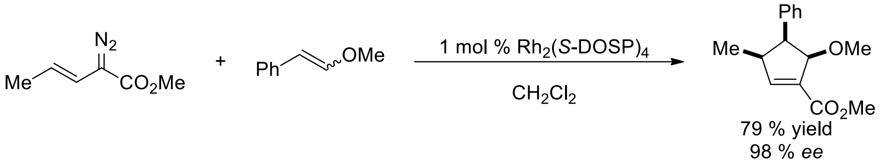
Figure 1-7. Dimeric rhodium and gold catalysts



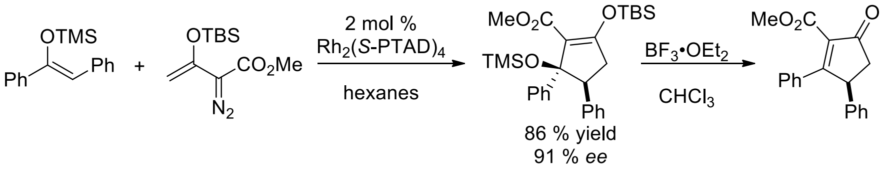
1.2.3 Asymmetric [3 + 2] cycloadditions of diazoacetates

Transition metal catalyzed transformations of diazoacetates have emerged as an extremely powerful strategy for a wide variety of transformations. The dimeric Rh_2(*S*-DOSP)$_4$ catalyst has proven to be a particularly effective catalyst for these transformation with high levels of

Scheme 1-27. Asymmetric formal [3 + 2] cycloadditions with vinyldiazoacetates



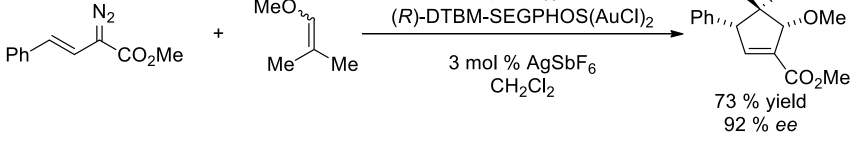
Scheme 1-28. Expanded scope for rhodium catalyzed formal [3 + 2] cycloadditions with vinyldiazoacetates



enantioselectivities (Figure 1-7). In 2001 Davies and coworkers reported a highly enantioselective formal [3 + 2] cycloaddition between vinyl diazoacetates and alkyl enol ethers to provide functionalized cyclopentenes with limited substrate scope (Scheme 1-27).[62] Later work by Davies and coworkers expanded upon this methodology by using the Rh_2(*S*-PTAD)$_4$ catalyst, which allowed for the asymmetric formal [3 + 2] cycloaddition between vinyldiazoacetates and silyl enol ethers with a much broader scope of functionalized cyclopentene products in high enantioselectivities and yields (Scheme 1-28).[63] Treatment of the resulting products with BF_3•OEt_2 cleanly provides enantioenriched cyclopentenones.

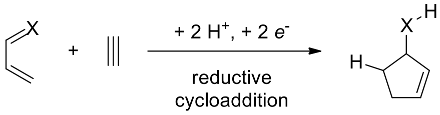
Further developments in catalytic asymmetric formal [3 + 2] cycloadditions with vinyldiazoacetates have resulted from the use of gold catalysts. In 2013 Davies and coworkers reported a gold catalyzed system for the highly enantioselective synthesis of a range of pentasubstituted cyclopentene products (Scheme 1-29).[64] This system makes use of a chiral dimeric gold catalyst (Figure 1-7) and $AgSbF_6$ for [3 + 2] cycloadditions between vinyl enol ethers

Scheme 1-29. Gold catalyzed formal [3 + 2] cycloaddition with vinyldiazoacetates



and vinyldiazoacetates. This methodology, much like the previously described methods with vinyldiazoacetates, is extremely sensitive to the electronic nature of the 2-carbon coupling partner and requires very electron rich olefins such as alkyl enol ethers to observe appreciable reactivity.

Scheme 1-30. General depiction of reductive [3 + 2] cycloadditions

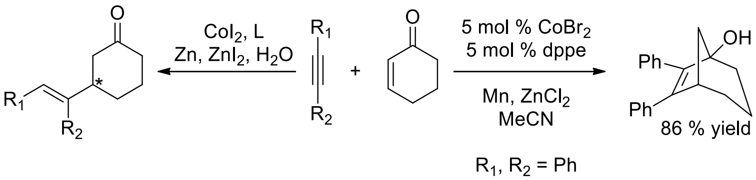


1.2.4 Transition metal catalyzed reductive [3 + 2] cycloadditions

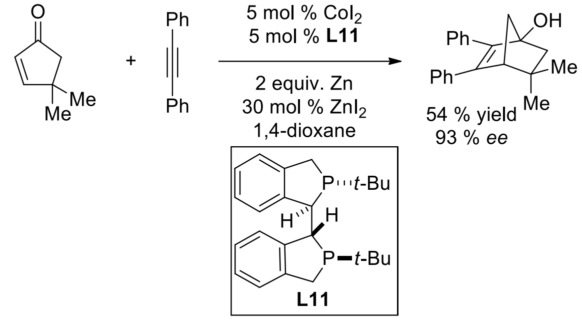
Most of the transformations discussed in previous sections of this review have been redox neutral overall; however, net reductive [3 + 2] cycloadditions using transition metal catalysts have also been an area of significant interest. There is substantial racemic precedent in transition metal catalyzed reductive [3 + 2] cycloadditions between α,ß-unsaturated carbonyl compounds and alkenes or alkynes (Scheme 1-30).[65–73] These early reports showed that a wide variety of transition metals (eg. Ti, Ni, Co) can be used with a variety of coupling partners for both intramolecular and intermolecular transformations. These varied reports have provided racemic though often highly diastereoselective methods for direct access to range of cyclopentenones and cyclopentenols.

The development of reductive catalytic asymmetric [3 + 2] cycloadditions has been rather limited. One of the earliest reports came from the work of Chien-Hong Cheng and coworkers in 2012.[74] Earlier work from this research group focused on the development of enantioselective reductive couplings between enones and alkynes (Scheme 1-31).[71] It was observed that

Scheme 1-31. Cobalt-catalyzed reductive couplings of alkynes and enones



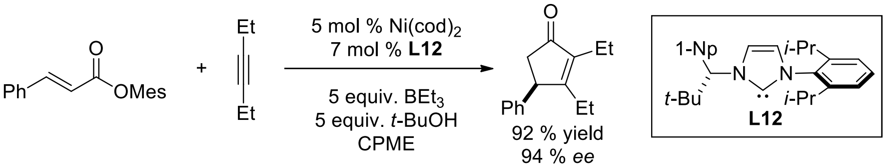
Scheme 1-32. Cobalt-catalyzed enantioselective reductive [3 + 2] cycloaddition



diphenylacetylene and cyclohexenone undergo formal [3 + 2] cycloadditions instead of the expected reductive coupling in the presence of $CoBr_2$ and Mn^0. These researchers were able to take this initial observation and optimize the reaction conditions to achieve enantioselective reductive [3 + 2] cycloadditions to provide a range of enantioenriched bicyclic cyclohexenols (Scheme 1-32).[74] The substrate scope for this transformation proved to be rather limited due to the sensitivity of this transformation to the sterics and electronics of each coupling partner with only small changes resulting in large drops in stereoselectivity.

Another example of a catalytic enantioselective reductive [3 + 2] cycloaddition was developed by Cramer and coworkers in 2014.[75] Much of the groundwork was developed by the groups of Ogoshi and Montgomery for the racemic [3 + 2] cycloaddition of enoates with alkynes to provide cyclopentenone products using nickel catalysts and triethylborane as a terminal reductant.[72,73] Cramer and coworkers found that the use of a chiral NHC ligand provided good yields and enantioselectivities of the desired cyclopentenone products (Scheme 1-33). The substrate scope for this transformation was rather broad, tolerating a large variety of substitutions on both the enoate and alkyne coupling partners.

Scheme 1-33. Nickel-catalyzed enantioselective reductive [3 + 2] cycloadditions



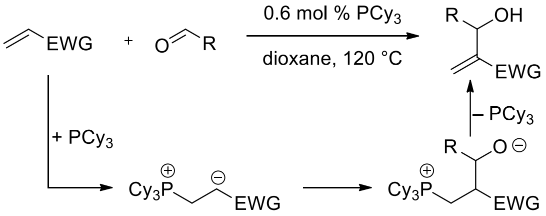
1.2.5 Summary

Asymmetric [3 + 2] cycloadditions via transition metal catalysis has thus far showed great promise as an extremely versatile and efficient strategy for the synthesis of a variety of cyclopentanoid products. To date, there have been only a handful of mechanistically distinct strategies for successful asymmetric [3 + 2] cycloadditions catalyzed by transition metals. Considering the large number of racemic methodologies that have been developed, the opportunities for future development and growth in this field are substantial.

1.3 Organocatalytic asymmetric [3 + 2] cycloadditions

Over the last several decades, organocatalysis has led to the development of many novel methodologies that allow for new modes of substrate activation and new strategies for forming carbon–carbon bonds. Due to the availability of a wide range of chiral organocatalysts, these reactions facilitate the rapid construction of complex products in a single sequence in high stereoselectivities. Several methodologies have been developed over the last decade making use of this strategy for the stereoselective construction of 5-membered carbocycles in a formal [3 + 2] cycloaddition between a 3-carbon and 2-carbon building block. This section of the review will be organized by the mode of activation of the catalyst and the types of reactions that are involved in the overall transformation. Due to the wide variety of reports this section will not be a comprehensive review of all that has been accomplished in the field. This section will cover only the early methodology developments and the applications of these methodologies to complex molecule synthesis.

Scheme 1-34. Morita-Baylis-Hillman reaction



1.3.1 Nucleophilic organocatalysis for asymmetric [3 + 2] cycloadditions

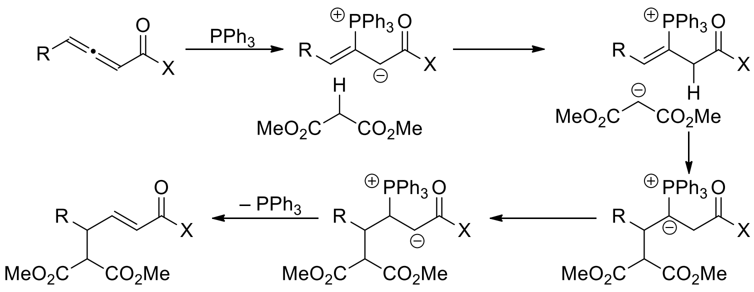
Organophosphorus compounds have been widely used in synthetic and organometallic chemistry for many decades.[76,77] In the late 20th and early 21st century an appreciation for these compounds as nucleophilic catalysts grew substantially. One early example of a 1,4-addition activation pathway is the Morita-Baylis-Hillman reaction, discovered in 1968 (Scheme 1-34).[78] This mode of activation has proven to be general across a wide range of synthetically useful transformations over the years as evidenced be their application in a number of natural product total syntheses.[79]

In addition to their activation of simple Michael acceptors and carbonyl-containing compounds, organophosphines have also been used successfully in the catalytic activation of alkynes and allenes to generate vinyl phosphonium intermediates. One of the earliest examples of organophosphorus activation of alkynes and allenes for the construction of C–C bonds was developed by Trost and coworkers in 1994 (Scheme 1-35).[80]

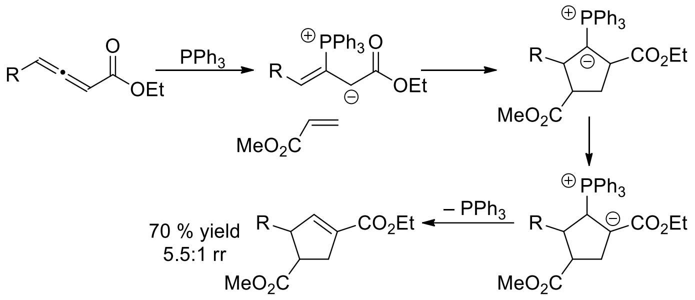
Soon after this initial report, Xiyan Lu reported a novel formal [3 + 2] cycloaddition via this same mode of activation for the construction of racemic cyclopentenes. It was found that electron-deficient alkenes could act as good coupling partners with the phosphonium intermediates derived from both allenes and alkynes to give cyclopentene products with reasonably good regioselectivities (Scheme 1-36).[81]

While this first example only accommodated the cycloaddition between simple mono-substituted allenoates and simple acrylates and acrylonitrile, there have since been numerous

Scheme 1-35. Umpolung γ-alkylation of allenes



Scheme 1-36. Seminal example of a phosphorus catalyzed [3 + 2] cycloaddition by Lu.

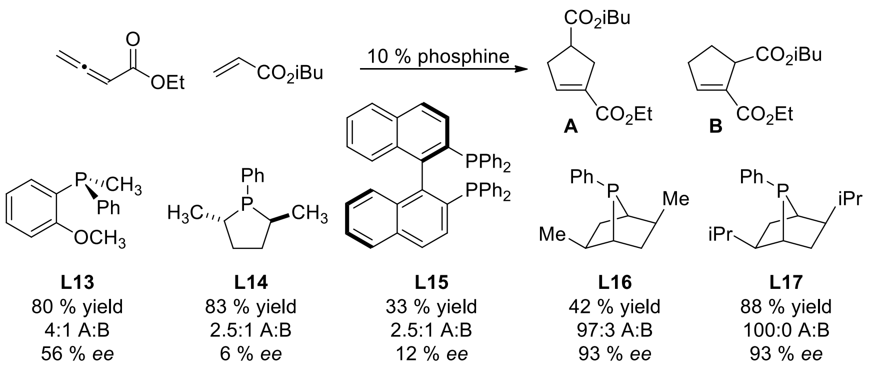


developments in the field to allow for the racemic construction of cyclopentenoates, cyclopentyl ketones, spirocyclic cyclepentanes, and other more densely substituted cyclopentenes from both allenyl and alkynyl precursors.[82–86]

1.3.1.1 Asymmetric [3 + 2] cycloadditions of allenes

Following the seminal results of Lu and coworkers for racemic [3 + 2] cycloadditions with organophosphorus catalysts an asymmetric [3 + 2] cycloaddition with chiral organophosphine catalysts was reported by Zhang and coworkers.[87] The researchers screened a small subset of these phosphines as well as a novel chiral phosphine containing a rigid phosphabicyclic structure which was first synthesized in their lab.[88] This initial report contained only a simple optimization between monosubstituted acrylates and ethyl 2,3-butadienoate. Over the course of their optimization, they showed that the rigid bicyclic phosphine synthesized in their lab was especially selective in the [3 + 2] cycloaddition, giving them complete regioselectivity and 93% ee (Figure 1-

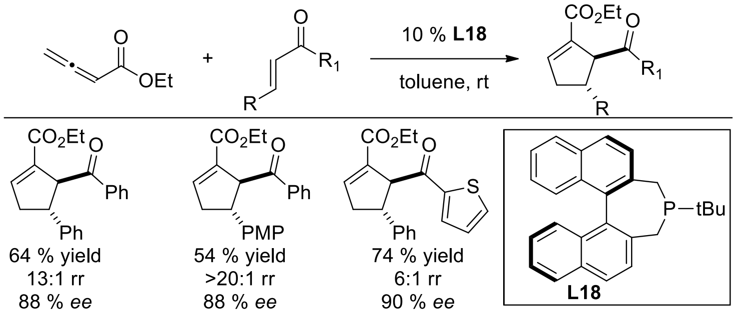
Figure 1-8. Optimization of [3 + 2] cycloaddition by Zhang and coworkers



8). The scope in this study was limited to just ethyl 2,3-butadiene as the allene and monosubstituted acrylates and diethylmalonate as the coupling partner.

The next major advance in this field was reported by Fu,[89] who had previously found that the phosphepine **L18** was an excellent nucleophilic catalyst for the enantioselective [4 + 2] cycloaddition of allenes with imines to provide piperidine derivatives.[90] They found that this catalyst worked well to provide a much expanded substrate scope for enantioselective [3 + 2] cycloadditions with allenoates. This catalyst provided good selectivities for cycloadditions with a range of chalcones and other extended π-systems (Figure 1-9).

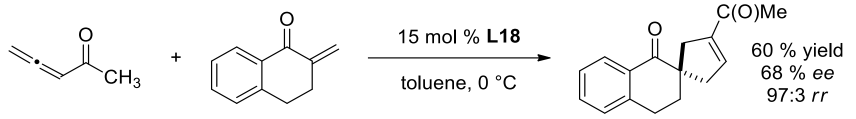
Figure 1-9. Select examples of asymmetric [3 + 2] cycloadditions reported by Fu *et al*



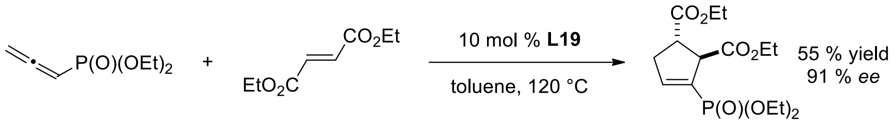
Following these initial reports on asymmetric phosphine catalyzed [3 + 2] cycloadditions of allenes, there has been a flurry of research from several different research groups contributing to this field. Notable developments have included the extension of this methodology to accommodate allenic ketones[91–94] and allenic phosphonates[93,95,96] as well as a large range of different coupling partners that can undergo a stereoselective [3 + 2] cycloadditions with allene derivatives.[92–109] A selection of these examples is depicted in Scheme 1-37. These methodologies allow for the expedient synthesis of heavily functionalized cyclopentanes from readily accessible starting materials in a single step. The intense activity in this field has resulted in the development of a large number of distinct chiral phosphine catalysts that are effective in controlling the stereoselectivity of these transformations (Figure 1-10) offering a large space for optimization of new transformations.

Scheme 1-37. Select examples of asymmetric [3 + 2] cycloadditions with allenes

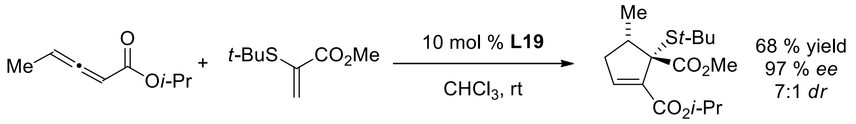
[3 + 2] cycloadditions with allenic ketones[91]



[3 + 2] cycloadditions with allenic phophonates[98]



[3 + 2] cycloadditions with γ-substitute allenoates[97,105]



[3 + 2] cycloadditions with maleimides[92]

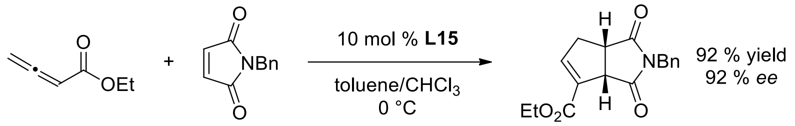
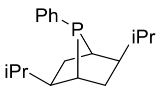
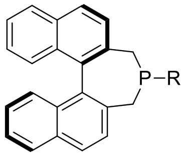


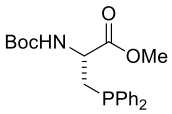
Figure 1-10. Examples of chiral phosphine ligands used in asymmetric [3 + 2] cycloadditions with allenes



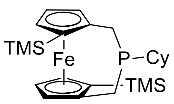
L17[88]



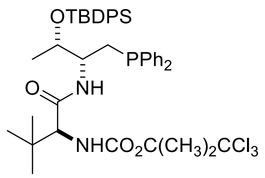
L18: R = *t*-Bu[89]
L19: R = Ph[98]



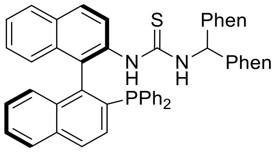
L20[97]



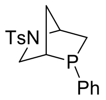
L21[99]



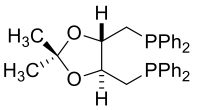
L22[104]



L23[94]



L24[208]

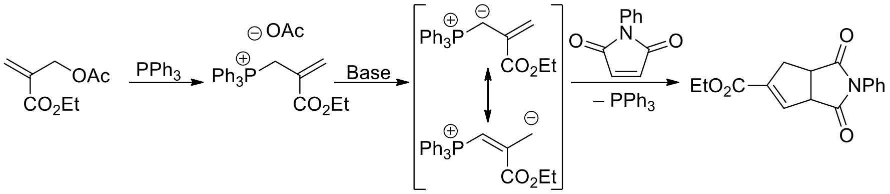


L25[91]

1.3.1.2 Asymmetric [3 + 2] cycloadditions of Morita-Baylis-Hillman adducts

A similar strategy to achieve asymmetric [3 + 2] cycloadditions with Morita-Baylis-Hillman adducts emerged not long after the development of enantioselective allene cycloadditions. Much of this work is rooted in the early racemic work of Lu and coworkers (Scheme 1-38).[110,111] It was hypothesized that analogous cycloadditions to those observed with allenoate and alkynoate precursors could be achieved with modified allylic phosphorus ylides wherein deprotonation of the ylide in situ would provide the active intermediate for a [3 + 2] cycloaddition with an electrophilic alkene coupling partner.

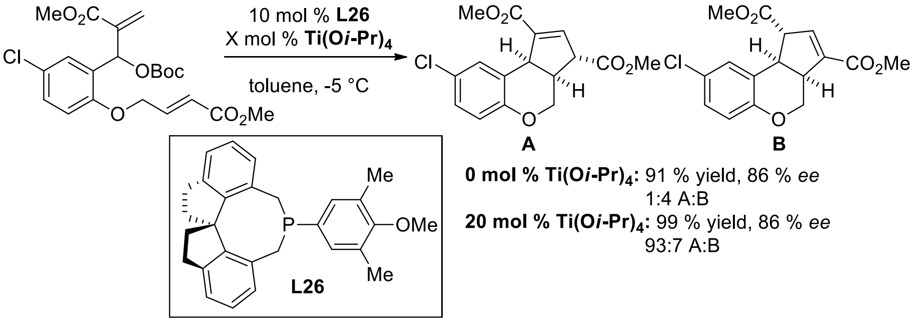
Scheme 1-38. Development of [3 + 2] cycloadditions with Morita-Baylis-Hillman adducts



This early report found both allylic bromide and allylic carbonates to be competent precursors to the zwitterionic intermediate. In the presence of 10 mol% of phosphine catalysts good yields of the cyclopentene product were obtained in excellent regioselectivities with electrophilic alkene coupling partners.

The first enantioselective example of [3 + 2] cycloadditions with Morita-Baylis-Hillman adducts were reported by Yong Tang, Qi-Lin Zhou, and coworkers.[112] In this report the researchers were

Scheme 1-39. First enantioselective [3 + 2] cycloaddition with Morita-Baylis Hillman adducts

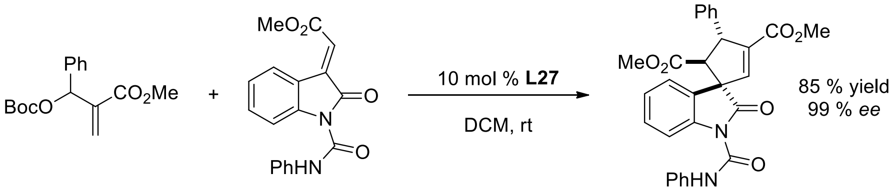


able to accomplish asymmetric intramolecular [3 + 2] cycloadditions in excellent enantioselectivities with a limited substrate scope using 10 mol% of chiral phosphine **L26** as catalyst (Scheme 1-39). In the presence of only the phosphine catalyst poor regioselectivities were observed for the location of the double bond due to isomerization of the product over the course of the reaction. It was shown that addition of 20 mol% Ti(O*i*-Pr)$_4$ could hinder this isomerization and provide the opposite major regioisomer.

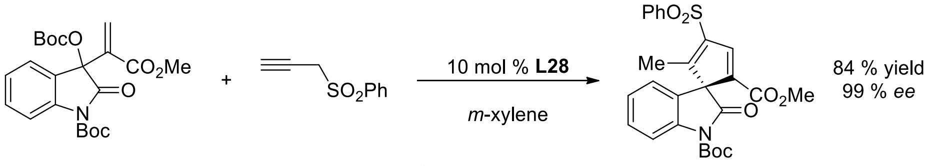
Like the [3 + 2] cycloadditions with allenes discussed in the previous section, after this initial publication a series of reports from multiple different groups were published in quick succession expanding this methodology to a larger range of substrates allowing for intermolecular asymmetric [3 + 2] cycloadditions with Morita-Baylis-Hillman adducts. Most these reports were for the synthesis of spirocyclic and bicyclic products, a small selection of examples are shown in Scheme 1-40.[113–121] Both chiral phosphines and chiral tertiary amines were found to be effective catalysts for this transformation (Figure 1-11).

Scheme 1-40. Examples of [3 + 2] cycloadditions with MBH adducts

[3 + 2] cycloaddition with methyleneindolinones[121]



[3 + 2] cycloadditions with propargyl sulfone[120]



[3 + 2] cycloadditions with maleimides[118]

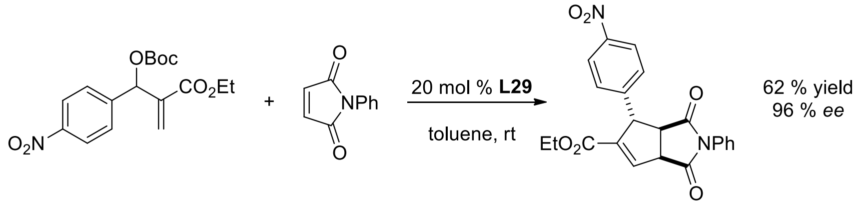
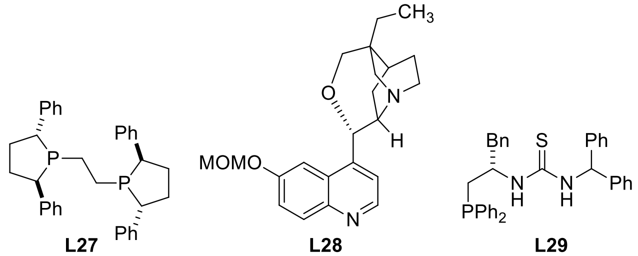


Figure 1-11. Selection of nucleophilic ligands used in [3 + 2] cycloadditions with MBH adducts



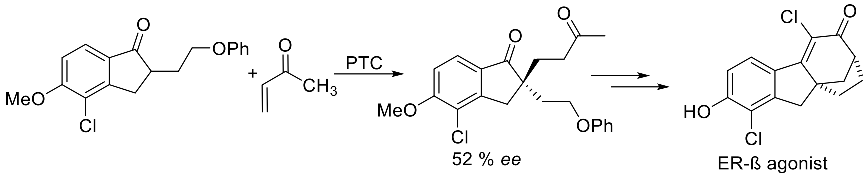
L27 **L28** **L29**

1.3.1.3 Applications of nucleophile catalyzed [3 + 2] cycloadditions to complex molecule synthesis

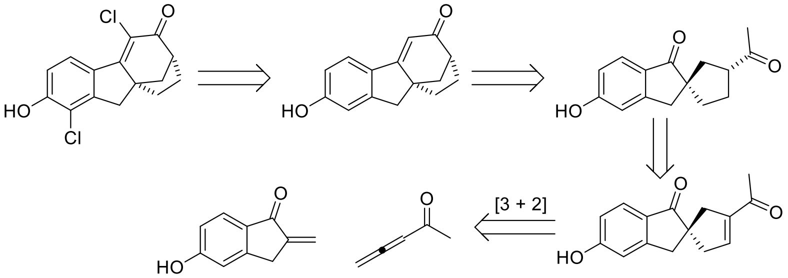
The applications of these strategies to natural product and complex molecule synthesis are still relatively limited. A good example of the application of this strategy was reported by Debra Wallace and the Department of Process Chemistry at Merck for an improved route to an estrogen receptor containing a spirocyclic quaternary stereocenter with two cyclopentane rings (Scheme 1-41).[122] The first generation route generated the spirocyclic stereocenter through a Michael addition under phase transfer conditions that provided only modest enantioselectivities.

The researchers wanted to develop an alternative route that avoided the use of the toxic reagents N,N-dimethylhydrazine and methyl vinyl ketone which were involved in some of the key steps. The researchers hypothesized that an asymmetric phosphine catalyzed [3 + 2] cycloaddition between an allenic ketone and an enone would provide a more efficient route to spirocyclic ring system (Scheme 1-42). Through a series of optimizations, the [3 + 2] cycloaddition step of the synthesis was accomplished in 73% ee in a 93:7 ratio of regioisomers (Scheme 1-43). Despite being able to construct the quaternary stereocenter in better selectivity through the new route, the original route remained more efficient for the synthesis of kilogram quantities of the ER-ß agonist due to low yields in the dichlorination step, high catalyst loadings for the [3 + 2] cycloaddition, and the requirement for chromatographic purification of several intermediates.

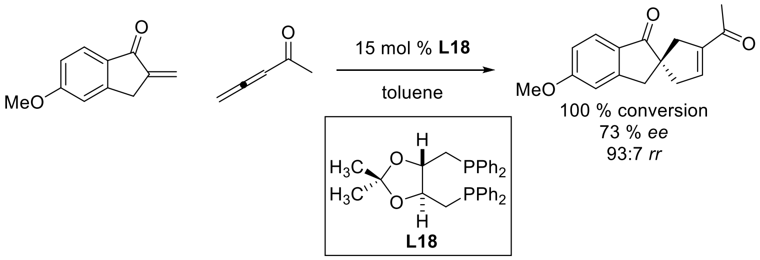
Scheme 1-41. First generation route to ER-ß agonist



Scheme 1-42. Retrosynthesis for second generation route



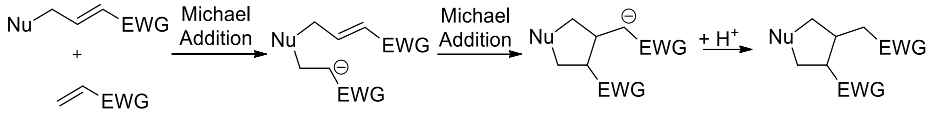
Scheme 1-43. Asymmetric [3 + 2] cycloaddition for second generation route



1.3.2 Organocatalytic double Michael additions

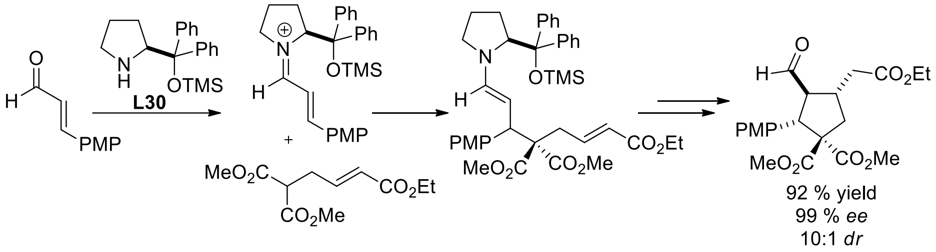
Double Michael additions have received substantial interest in the field of organocatalysis as a strategy for the rapid construction of multiple C–C bonds in a single step from accessible starting materials. This strategy relies on one coupling partner being functionalized with a nucleophilic substituent and a Michael acceptor and the other coupling partner being functionalized with only a Michael acceptor. A very general mechanism for the construction of 5-membered rings is shown in Scheme 1-44. The earliest examples for achieving stereocontrol in double Michael additions made use of chiral auxilaries[123] and chiral precursors.[124] Early work by researchers in the field of organocatalysis had shown that activation of enals with chiral secondary amines to form chiral

Scheme 1-44. General mechanism for double Michael addition



iminium species allowed for the highly enantioselective construction of six-membered heterocycles through a tandem Michael/aldol process.[125] The initial Michael addition in this cascade process involved the attack of a heteroatom nucleophile onto the activated chiral iminium species. Wang and coworkers hypothesized that an enolate could serve as the nucleophilic species and allow access to carbocylic products through the formation of two C–C bonds. The researchers reported their findings in 2007 for the highly enantioselective construction of cyclopentanes through a formal [3 + 2] double Michael addition process (Scheme 1-45).[126]

Scheme 1-45. First catalytic enantioselective double Michael addition for cyclopentane synthesis via iminium intermediates



Stereocontrol through formation of an iminium intermediate with prolinol derivatives has become a general strategy for the construction of a number of different five-membered rings including the construction of heterocyclic products.[127–130] In addition, several Michael–Henry tandem reactions have been developed for asymmetric cyclopentane synthesis that make use of the iminium intermediate for stereocontrol.

Hydrogen-bond donors have also been reported as effective catalysts in these cascade processes. One of the earliest examples of hydrogen-bonding catalysis for double Michael additions was reported by Zhong and coworkers in 2008.[131] They reported a highly enantioselective double Michael addition between ethyl 2-acetyl-5-oxohexanoate and nitroolefins using cinchona alkaloid derivatives (Scheme 1-46). The proposed action of the catalyst is shown in Figure 1-12. Several other reports have since been published utilizing hydrogen-bond donor catalysts for cyclopentane synthesis with double Michael additions allowing for the construction of a variety of densely functionalized cyclopentane rings.[132,133] These developments tolerate a range of different carbon-based nucleophiles including malonates and nitroalkanes as well as enone, enoates, and nitroolefins as Michael acceptors.

Scheme 1-46. Asymmetric double Michael additions via hydrogen-bond donor catalysis

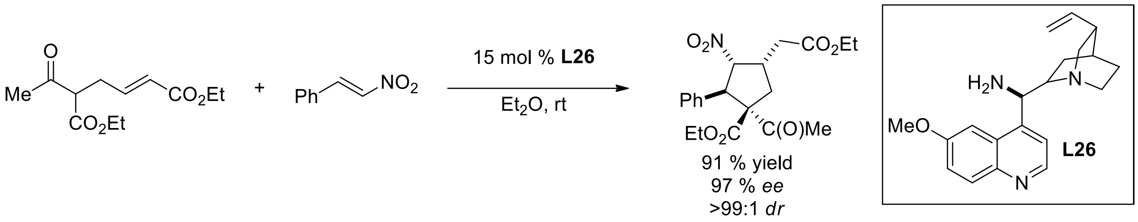
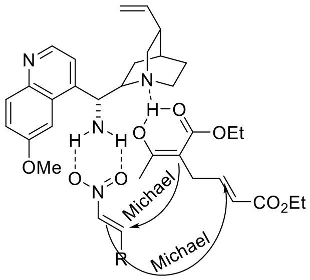


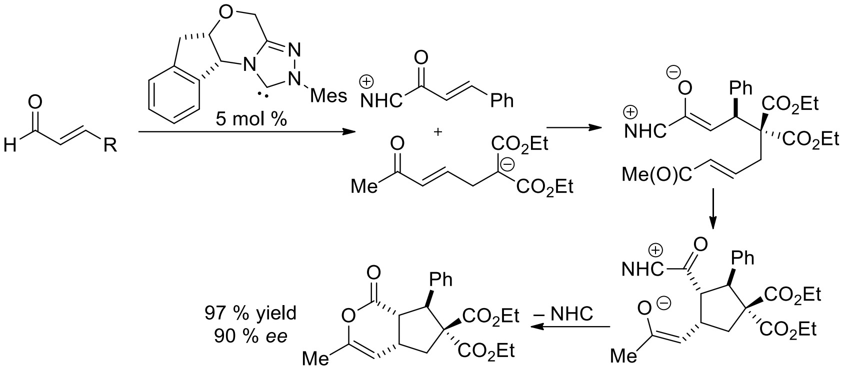
Figure 1-12. Proposed action of Cinchona alkaloid catalysts



N-Heterocyclic carbenes (NHCs) have been reported as effective catalysts for stereoselective formal [3 + 2] cycloadditions via double Michael additions. This mode of catalysis works via activation of aldehyde starting materials through either formation of a Breslow intermediate or through formation of a homologous enolate. The first report of an NHC-catalyzed [3 + 2] cycloaddition *via* tandem Michael additions was published in 2015 by Studer and coworkers.[134] In this report, the researchers developed a formal [3 + 2] cycloaddition for the synthesis of substituted δ-lcatones from enals and a 3-carbon coupling partner (Scheme 1-47).

The reaction proceeds through formation of a Breslow intermediate from the enal followed by tandem Michael addition reactions and regeneration of the NHC catalyst by formation of a lactone

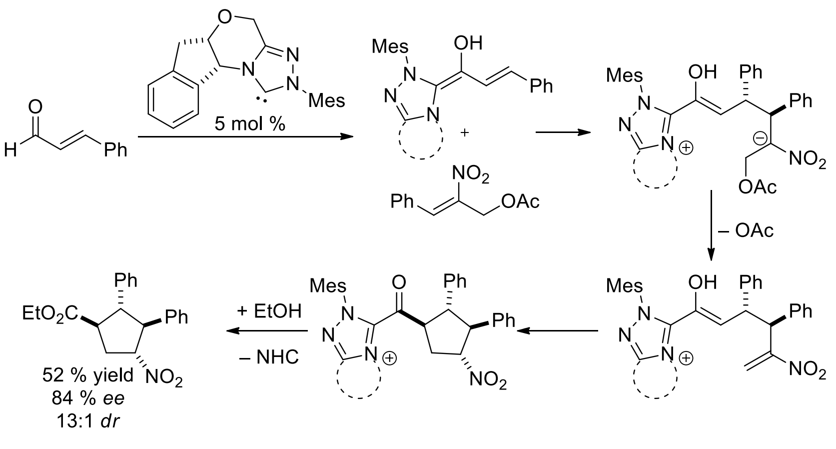
Scheme 1-47. Mechanism for NHC-catalyzed formal [3 + 2] cycloaddition for substituted lactone formation



through nucleophilic attack on the carbonyl. This method provides high yields and selectivities of the lactone for a range of enals and enones.

Dieter Enders and coworkers later reported a mechanistically distinct NHC-catalyzed formal [3 + 2] cycloaddition.[135] The active intermediate in this reaction is a homologous enolate formed between the enal and a chiral NHC catalyst (Scheme 1-48). The homologous enolate acts as a nucleophile and undergoes a Michael addition to a nitroolefin. After loss of a leaving group, a subsequent Michael addition and esterification to regenerate the NHC catalyst provides cyclopentane products with four contiguous stereocenters in high enantioselectivities. The substrate scope for this methodology was more limited than the previously reported method and required nitrostyrenes and a ß-arylenal coupling partners.

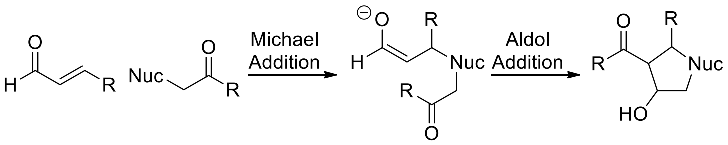
Scheme 1-48. Mechanism for NHC-catalyzed formal [3 + 2] cycloaddition via homoenolates



1.3.3 Organocatalytic Michael–aldol tandem reactions

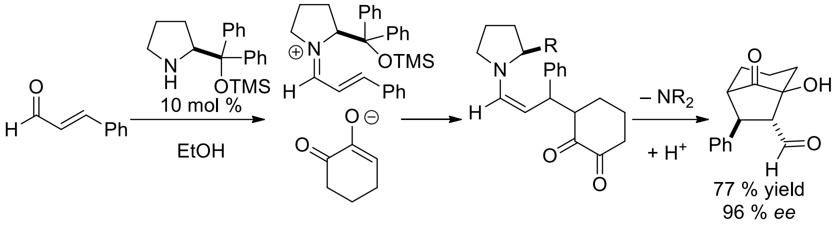
An alternative organocatalytic cascade process is the Michael–aldol tandem reaction. These reactions proceed in a similar manner mechanistically to those in the previous section, however a Michael acceptor substituent is present on only one of the coupling partners and the reaction proceeds via 1,4-addition followed by 1,2-addition. A general mechanistic scheme is shown in Scheme 1-49. In most scenarios, the 3-carbon component will have a nucleophilic substituent (e.g. enolate) and an electrophilic substituent (e.g. carbonyl) and the 2-carbon component will simply be a Michael acceptor (e.g. enal or nitroolefin). Catalytic enantioselective reactions have been developed with strategies very similar to those used for Michael–Michael tandem reactions. The most common strategy is through activation of one of the components with a chiral secondary amine to form an enamine or an iminium.

Scheme 1-49. General mechanism for Michael–aldol tandem reactions



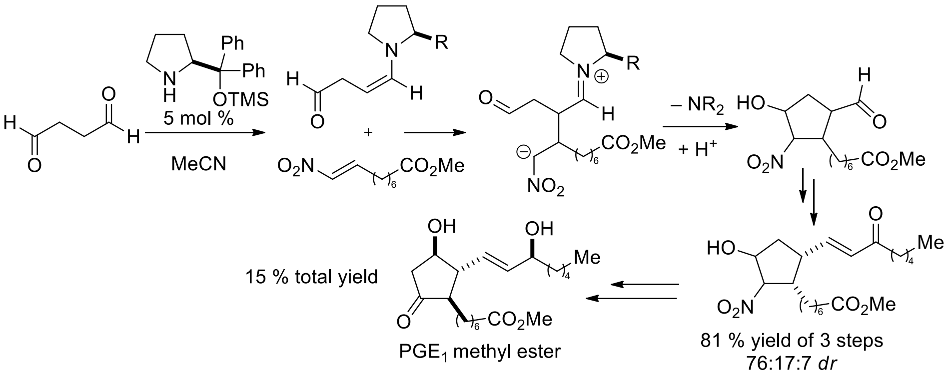
One of the earliest reports of a catalytic enantioselective Michael–aldol domino reaction was reported by Magnus Reuping and coworkers in 2009.[136] This report detailed the activation of cinnamaldehyde precursors with a prolinol organocatalyst to form a chiral activated iminium intermediate. The activated Michael acceptor undergoes nucleophilic attack by an enolate on the 3-carbon building block. The resulting enamine intermediate then acts as a nucleophile for a 1,2-addition on the 3-carbon component for a net formal [3 + 2] cycloaddition (Scheme 1-50). Due to the nature of the 3-carbon component in this reaction, the overall substrate scope proved to be relatively limited, offering variability only on the enal substituent.

Scheme 1-50. Organocatalytic formal [3 + 2] cycloaddition via Michael–aldol domino reaction with iminium catalysis



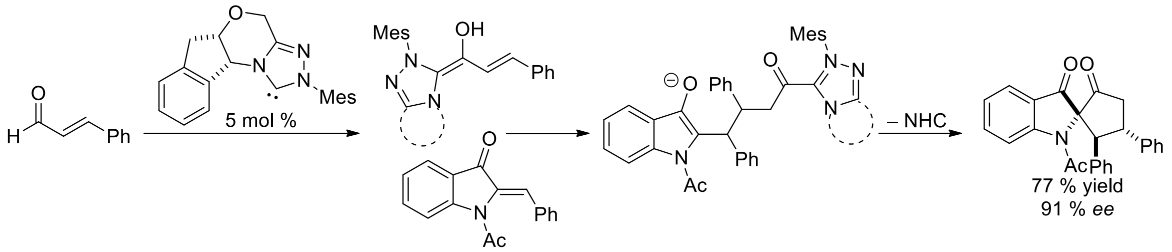
Formal [3 + 2] cycloadditions were later developed between 1,4-dialdehydes and nitroolefins. The secondary amine catalyst activates the 3-carbon component for the initial Michael addition through formation of an enamine intermediate (Scheme 1-51). The strategy was first reported by Hayashi and coworkers in 2013 in route to synthesize the methyl esters of prostaglandins A_1 and E_1.[137] The methodology was eventually extended to be more general and explore a broader substrate scope.[138]

Scheme 1-51. Organocatalytic formal [3 + 2] cycloaddition via Michael–aldol domino reaction with enamine catalysis.



N-Heterocyclic carbenes have also been reported to be effective organocatalysts for enantioselective Michael–aldol domino reactions to afford cyclopentanoid products in high enantioselectivities. One of the earliest reports came from the work of Frank Glorius and coworkers wherein the NHC-catalyst activates enal precursors to form a homologous enolate which can act as the nucleophile in a Michael addition with methylene indolinones. The intermediate enolate then engages the acylazolium intermediate in a 1,2-attack to generate the product and regenerate the NHC-catalyst (Scheme 1-52). This methodology provides facile access to a variety of substituted spirocycles in high enantioselectivities.

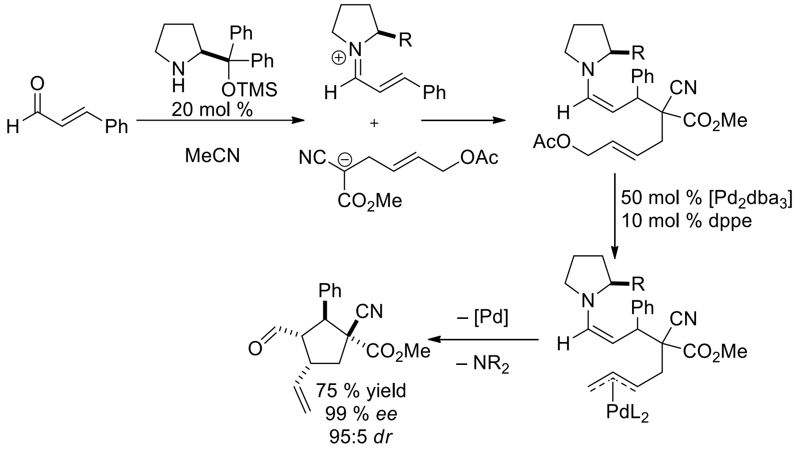
Scheme 1-52. NHC-catalyzed formal [3 + 2] cycloadditions via Michael–aldol domino reactions



1.3.4 Dual catalytic domino reactions

There have been recent efforts to synthesize other classes of enantioenriched cyclopentane products in formal [3 + 2] cycloaddition cascade processes. One such strategy is that of dual catalytic reactions with an organocatalyst and a transition metal catalyst such as palladium. One of the earliest reports came from the efforts of Córdova and coworkers in 2013.[139] Taking insight from the previously reported Michael–Michael and Michael–aldol cascade processes, the researchers replaced the Michael-acceptor or carbonyl electrophilic component with a π-allylpalladium intermediate (Scheme 1-53). An enolate served as the initial nucleophile for a Michael-addition onto the chiral iminium intermediate. The resulting enamine intermediate then attacks a π-allylpalladium species generated in situ to affect a stereocontrolled alkylation reaction. The methodology provides a relatively high scope of densely substituted vinylcyclopentanes with quaternary stereocenters. There have not been any notable extensions of this methodology to further increase the generality; however, there is ample opportunity for this mode of reactivity in cascade reactions to accomplish formal [3 + 2] cycloadditions.

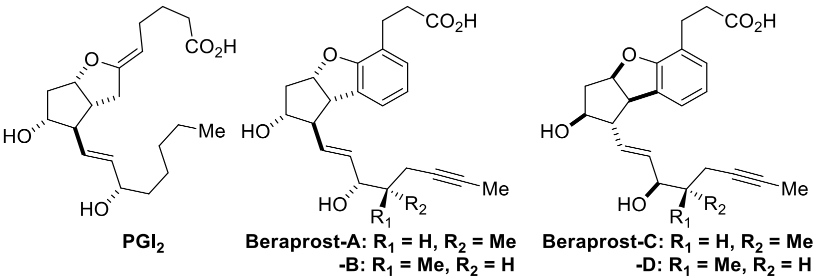
Scheme 1-53. Dual catalytic domino formal [3 + 2] cycloaddition with iminium/palladium catalysis



1.3.5 Application to complex molecule synthesis

Asymmetric domino reactions for formal [3 + 2] cycloadditions have proven themselves to be useful tools for the rapid construction of highly functionalized cyclopentane rings. As mentioned previously, these methodologies have been applied in the synthesis of several prostaglandin natural products. Another prostaglandin that has attracted interest is prostaglandin I_2 (PGI_2) (Figure 1-13) which has several bioactivities including vasodilation and inhibition of platelet aggregation. The PGI_2 derivatives collectively referred to as beraprost were developed as a more stable and less toxic analog of PGI_2. Due to the varying bioactivities of the different isomers of beraprost, an efficient and selective synthesis of the most active isomer is highly desirable. In 2017 Hayashi and coworkers extended the enantioselective Michael–aldol domino reaction to allow efficient synthesis of the beraprost-A core (Scheme 1-54).[130] In a 3-step 2-pot sequence the

Figure 1-13. Prostaglandin I_2 and stereoisomers of beraprost

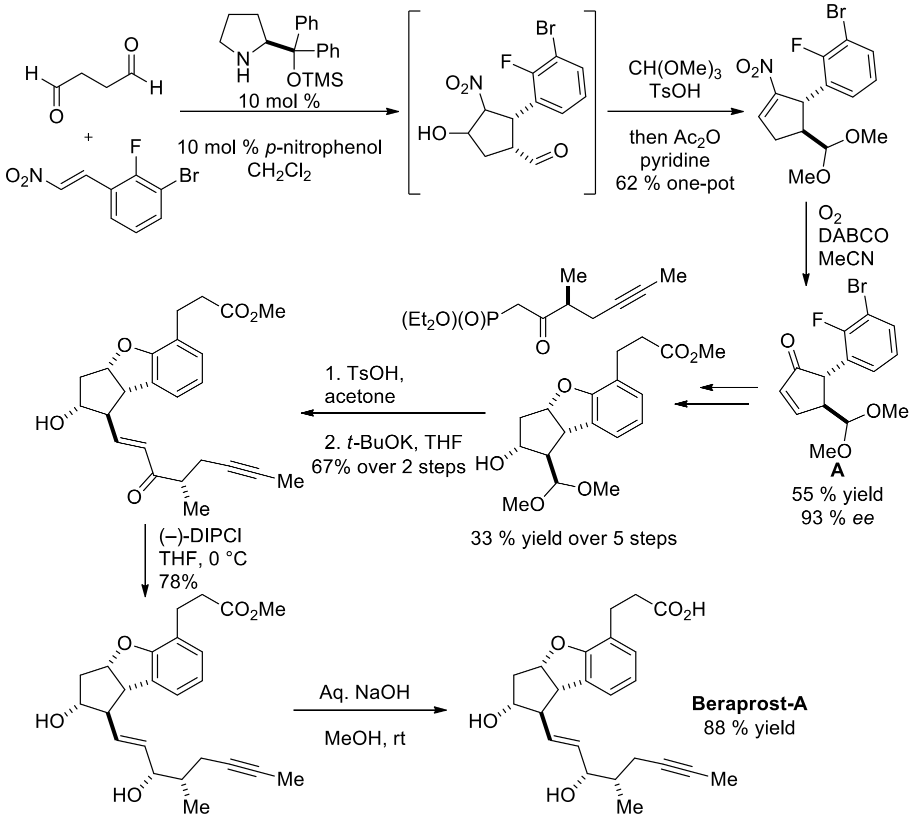


researchers were able to get to intermediate **A** in 34% yield and 93% ee. They were then able to complete the total synthesis of beraprost-A in a convergent synthesis of 17 total combined steps (12 steps for longest linear sequence).

1.3.6 Summary

Organocatalytic reactions for formal [3 + 2] cycloadditions have become an incredibly powerful approach for the synthesis of highly functionalized cyclopentanoid compounds. While these methodologies are very sensitive to the electronics of the coupling partners, the resulting cyclopentanoid products often have multiple functional groups available for further derivatization. The flexibility of the resulting products has been demonstrated through the efficient total synthesis of several different prostaglandin natural products and prostaglandin derivatives in high enantioselectivities.

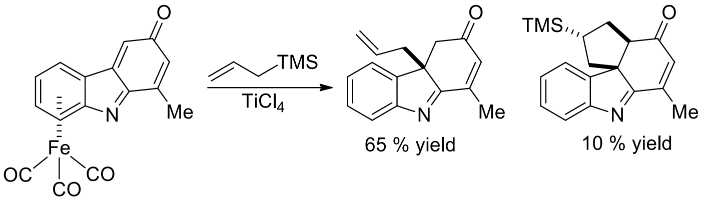
Scheme 1-54. Total synthesis of Beraprost-A by Hayashi and coworkers



1.4 Asymmetric [3 + 2] cycloadditions with Lewis and Brønsted acid catalysis

Many formal [3 + 2] cycloadditions involve the formation of ionic or zwitterionic intermediates as the active species for the desired stepwise cycloaddition reaction. The catalysts covered so far have been transition metals and nucleophilic catalysts. Other types of catalysts that provide access to these intermediates are Lewis/Brønsted acids and hydrogen bond donors. These catalysts can interact with substrates in a variety of different ways typically to generate cationic or zwitterionic intermediates. This section of the review will briefly discuss the successful acid catalyzed strategies that have been applied towards asymmetric [3 + 2] cycloadditions for the synthesis of carbocycles.

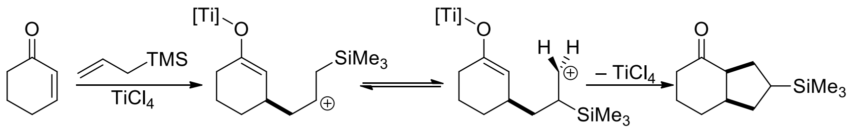
Scheme 1-55. Sakurai reaction of an irontricarbonyl complex with unexpected [3 + 2] cycloaddition byproduct.



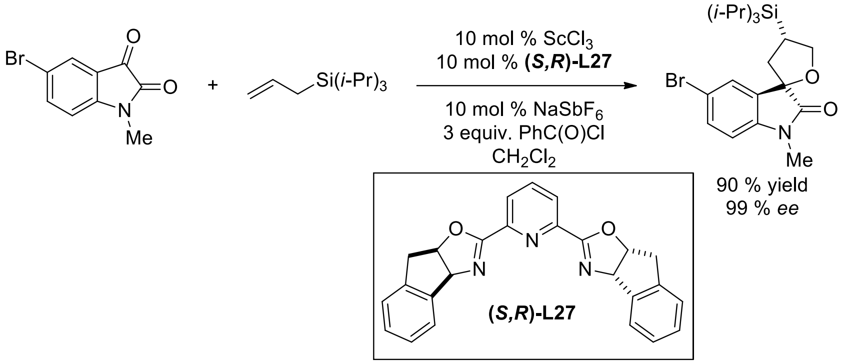
1.4.1 Asymmetric [3 + 2] cycloadditions of allylsilanes

Lewis acid catalyzed transformations of allylsilanes have significant historical precedent particularly for the alkylation of electrophilic reaction partners. One example of such a reaction is the Sakurai reaction. In 1990 Knolker and coworkers observed that the Sakurai reaction of the irontricarbonyl-complexed dihydrocarbzol-3-one provided the expected alkylation product along with a byproduct resulting from a formal [3 + 2] cycloaddition (Scheme 1-55).[140] The proposed mechanism for the formal [3 + 2] cycloaddition involved an initial conjugate addition of the allylsilane reagent followed by a cationic 1,2-silyl shift and cyclization (Scheme 1-56).

Scheme 1-56. Proposed mechanism for [3 + 2] cycloaddition of allylsilanes

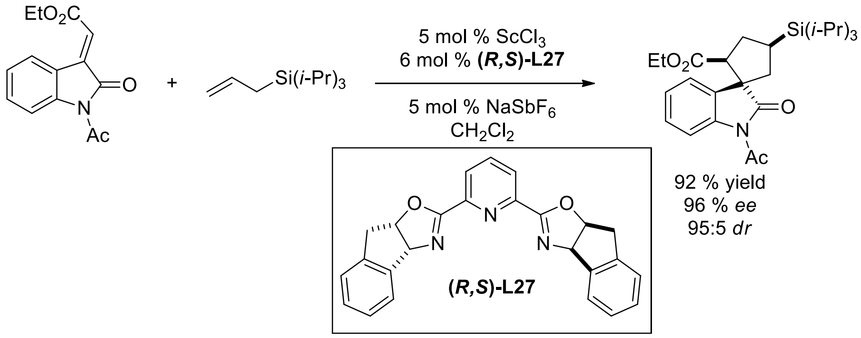


Scheme 1-57. [3 + 2] cycloaddition with allylsilane for spirooxindole synthesis

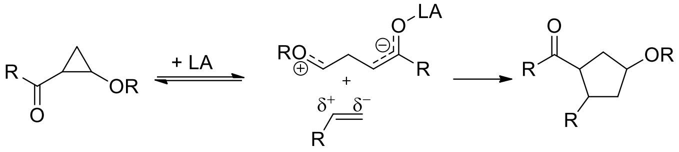


The overall transformation was intriguing as a new strategy for the synthesis of cyclopentane rings, and several reports were published over the years including the development of [3 + 2] cycloadditions with propargyl silanes[141] and chiral allylsilanes.[142,143] The first catalytic enantioselective method was not developed until 2012 when Franz and coworkers reported the enantioselective annulation of allylsilanes with isatins for the synthesis of spirooxindoles (Scheme 1-57).[144] Key to this development was the use of a bulky silane and a chiral [Sc(indanopybox)]Cl_3 Lewis acid. Franz and coworkers were able to extend this strategy for the catalytic enantioselective synthesis of spirocyclopentanes through the formal [3 + 2] cycloaddition between allylsilanes and alkylidene oxindoles (Scheme 1-58).[145] Further applications of this strategy have yet to be reported.

Scheme 1-58. [3 + 2] cycloaddition of allylsilanes for spirocyclopentane synthesis



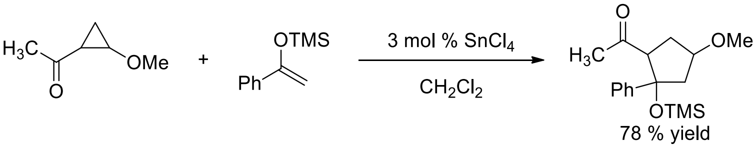
Scheme 1-59. Lewis acid activation of a donor–acceptor cyclopropane



1.4.2 Asymmetric [3 + 2] cycloadditions with cyclopropanes as 1,3-dipole surrogates under Lewis acid catalysis

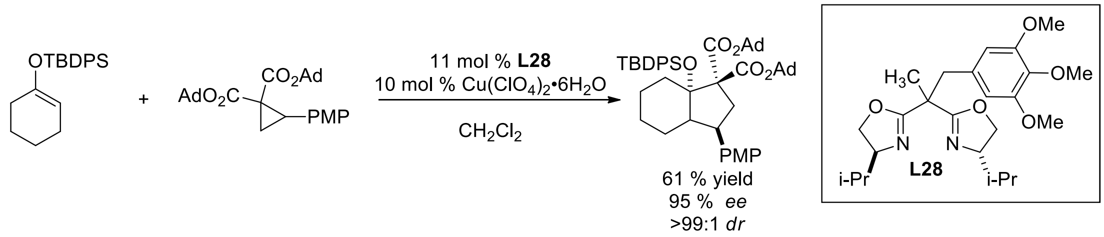
Donor-acceptor cyclopropanes are susceptible to activation and heterolytic cleavage by Lewis acid catalysis (Scheme 1-59). There are a large number of Brønsted and Lewis acid catalyzed transformations that have been reported with donor–acceptor cyclopropanes including formal [3 + 2] cycloadditions for the synthesis of both carbocycles and heterocycles.[1,146–149] Early reports for acid-catalyzed formal [3 + 2] cycloadditions of cyclopropanes for the synthesis of five-membered carbocycles utilized simples cyclopropanes substituted with only an electron withdrawing group.[150–154] One of the earliest examples of a racemic acid-catalyzed [3 + 2] cycloaddition with a donor–acceptor cyclopropane was reported by Kuwajima and coworkers (Scheme 1-60).[155] In this early report it was shown that $SnCl_4$ could efficiently catalyze the formal [3 + 2] cycloaddition between donor–acceptor cyclopropyl ketones and electron rich silyl enol ethers. Several racemic [3 + 2] cycloadditions have since be developed utilizing both Lewis acids and Brønsted acids for activation of the cyclopropane for reaction with electron-rich alkene and alkyne coupling partners.

Scheme 1-60. Early racemic example of a Lewis acid catalyzed [3 + 2] cycloaddition with a donor–acceptor cyclopropane.



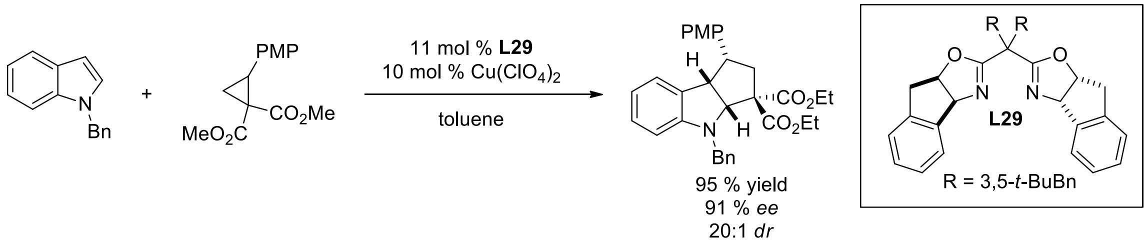
While asymmetric [3 + 2] cycloadditions of donor–acceptor cyclopropanes with aldehydes and imines were readily developed, developing the equivalent transformations for cyclopentane synthesis has proven difficult.[156–159] Tang and coworkers developed a number of highly diastereoselective copper-catalyzed formal [3 + 2] cycloadditions between donor–acceptor cyclopropanes and a variety of silyl enol ethers for the synthesis of racemic cyclopentanes.[160,161] The researchers were able to develop an asymmetric variant of the reaction using copper(II)/bisoxazoline (BOX) catalysts for highly enantioselective [3 + 2] cycloadditions between cyclic silyl enol ethers and a variety of donor–acceptor cyclopropanes (Scheme 1-61).[162] In order to achieve high enantioselectivities in this transformation the researchers had to use the bulky adamantyl ester of the cyclopropane as well as the very electron-donating *para*-methoxyphenyl (PMP) as the donor substituent. Less electron-rich cyclopropanes proceed as a kinetic resolution of the racemic cyclopropane starting material.

Scheme 1-61. First enantioselective Lewis acid catalyzed [3 + 2] cycloaddition with donor–acceptor cyclopropanes



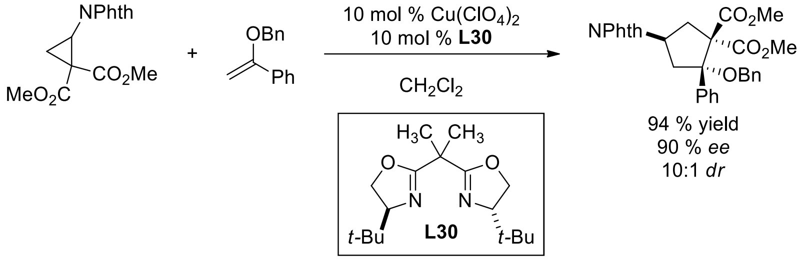
Tang and coworkers were able to extend this methodology to [3 + 2] cycloadditions with indoles as coupling partners through use of indano-BOX ligand **L29** (Scheme 1-62).[163] This modification provides an efficient route to a key bicyclic motif that is present in a number of indoline natural products. The scope for this methodology proved to be rather large with respect to the indole coupling partner, however only small modifications on the cyclopropane were tolerated without substantial losses in reaction efficiency and selectivity.

Scheme 1-62. Asymmetric [3 + 2] cycloadditions with indoles

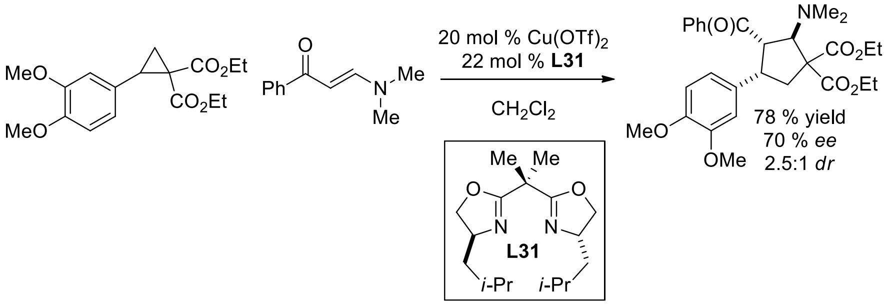


Waser and coworkers developed an asymmetric [3 + 2] cycloaddition between phthalimidocyclopropanes and alkylenol ethers using a chiral Cu(II)/BOX Lewis acid catalyst. These conditions were able to accommodate a much larger scope of coupling partners including electron rich olefins as well as a range of aldehydes (Scheme 1-63).[164]

Scheme 1-63. Asymmetric [3 + 2] cycloaddition between phthalimidocyclopropanes and alkylenol ethers



Scheme 1-64. Asymmetric [3 + 2] cycloadditions with enamine coupling partners.



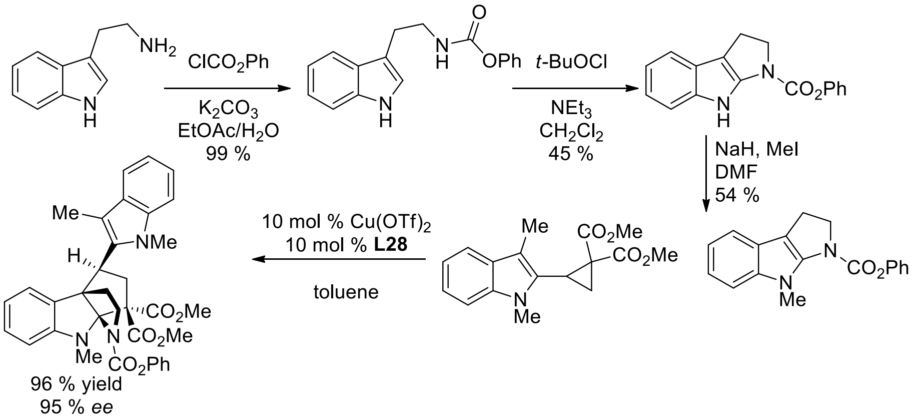
There has been a recent report extending this methodology for the copper-catalyzed asymmetric [3 + 2] cycloadditions of donor–acceptor cyclopropanes with enamines using BOX ligands (Scheme 1-64).[165] These conditions provide substituted cyclopentanes in modest enantioselectivities and poor diastereoselectivities across a relatively limited substrate scope.

1.4.2.3 Applications to complex molecule synthesis

Lewis acid catalyzed [3 + 2] cycloadditions of donor–acceptor cyclopropanes offer efficient access to densely substituted cyclopentane rings with predictable regioselectivites. These cycloadditions provide a strategic disconnect in route to several natural products and complex products with promising bioactivities. There are a few examples in the literature of racemic [3 +

2] cycloadditions with donor–acceptor cyclopropanes being used in the synthesis of natural products.[149] The application of asymmetric [3 + 2] cycloadditions with donor–acceptor cyclopropanes has remained more limited. One of the early reports by Tang and coworkers showed the use of an asymmetric [3 + 2] cycloaddition as a key step towards the synthesis of the tetracyclic core of borreverine (Scheme 1-65).[163] In this synthesis, the key cycloaddition was accomplished in good yields and high enantioselectivies, affording the cycloadduct as a single diastereomer.

Scheme 1-65. Synthesis of the core of Borreverine



1.4.3 1,3-Dipolar cycloadditions via excited state proton transfer (ESPT)

The photochemical and photophysical properties of 3-hydroxyflavones have attracted significant interest from physical chemists due to the unique spectroscopic properties inherent to these compounds. Specifically, these compounds absorb light at 350 nm and undergo efficient excited state intramolecular proton transfer (ESIPT) to generate the zwitterionic intermediate shown in Scheme 1-66 which can act as a 1,3-dipole.[166–169] This ESIPT is extremely sensitive to solvent polarity and the presence of hydrogen-bonding additives in solution.

Scheme 1-66. Excited state intramolecular proton transfer with 3-hydroxyflavones to generate a 1,3-dipole intermediate

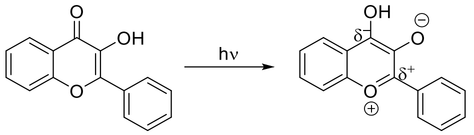
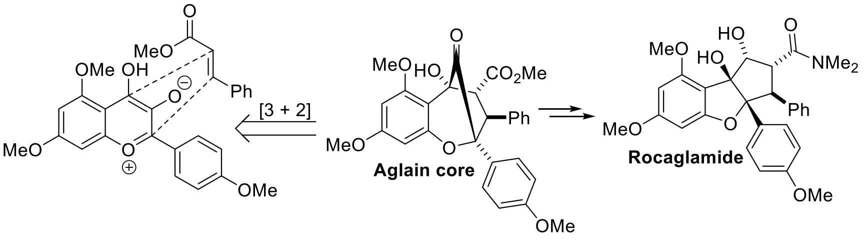
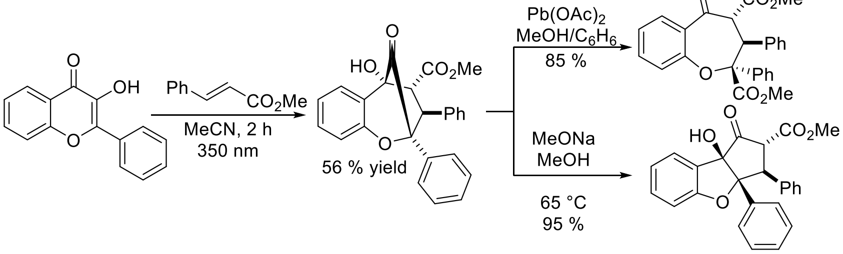


Figure 1-14. Proposed biomimetic route to rocaglamides

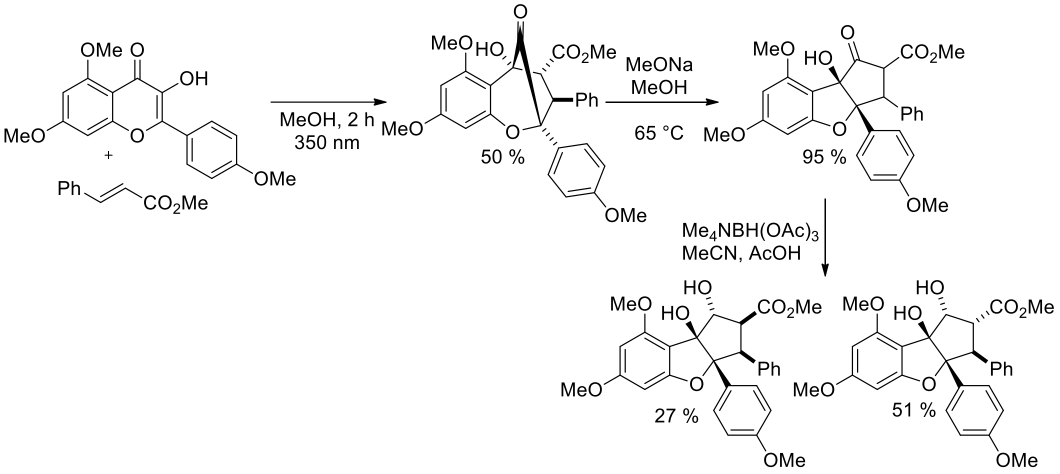


It has been proposed that rocaglamides and related natural products are likely biosynthesized from the reaction of 3-hydroxyflavones with cinnamides. Based on this proposal and the known photochemical properties of 3-hydroxyflavones, Porco and coworkers developed a biomimetic route to the aglain core via a 1,3-dipolar cycloaddition of the oxidopyrillium intermediate generated with ESIPT (Figure 1-14).[170] In the optimization of this racemic [3 + 2] cycloaddition, the researchers found that photoirradiation of the 3-hydroxyflavone precursor in the presence of methyl cinnamate using a filtered 450W medium-pressure mercury lamp generated the desired cycloadduct (Scheme 1-67). Further experiments lead to conditions to convert the aglain core to both forbaglin and rocaglamide ring systems through either an oxidative cleavage with Pb(OAc)$_2$ or an α-ketol shift. A total synthesis of (±)-methyl rocaglate was completed using this strategy in three steps starting from the substituted 3-hydroxyflavone precursor in 24% overall yield (Scheme 1-68).

Scheme 1-67. Synthesis of forbaglin and rocaglamide ring systems

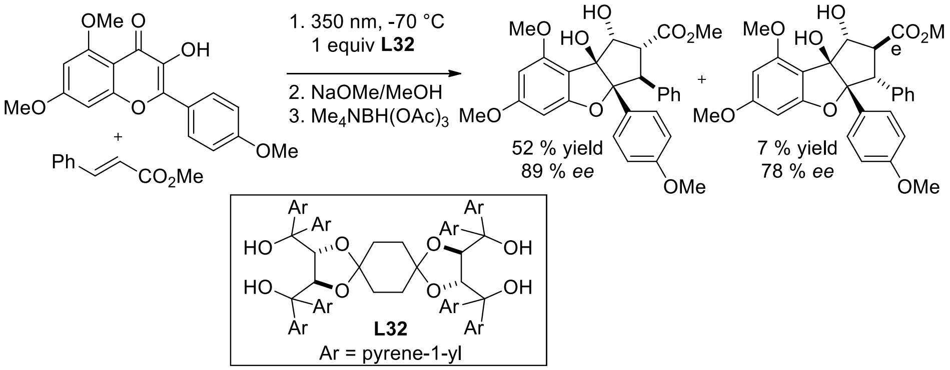


Scheme 1-68. Total synthesis of (±)-methyl rocaglate

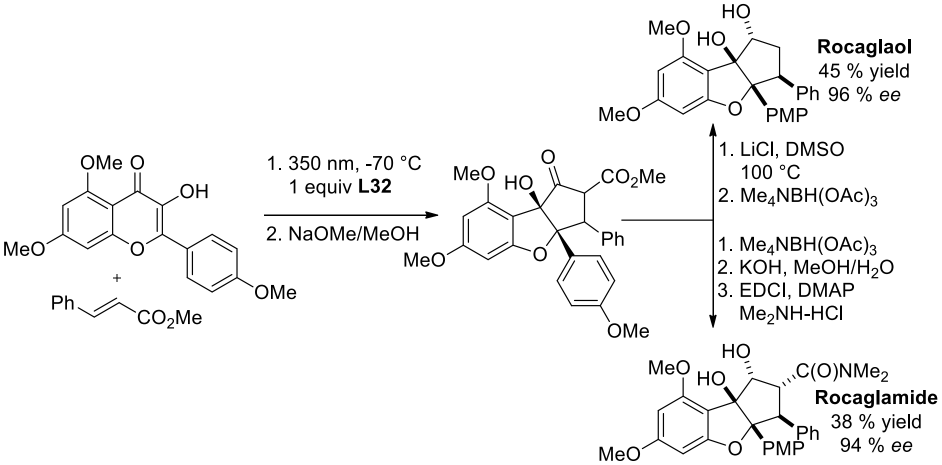


During the development of this racemic total synthesis, the researchers noted that the [3 + 2] photocycloaddition proceeded much more efficiently in the presence of polar protic solvents (e.g MeOH). Porco and coworkers hypothesized that a chiral hydrogen bond donor in an aprotic solvent could be used to control the stereoselectivity of the [3 + 2] photocycloaddition.[171] The researchers screened a range of chiral hydrogen-bonding additives and found that TADDOL reagents could efficiently mediate the photochemical cycloaddition and provide excellent enantioselectivities of the desired cycloadduct (Scheme 1-69). This strategy was then used for the asymmetric synthesis of rocaglaol and rocaglamide in 45 % yield and 38 % yield respectively (Scheme 1-70).

Scheme 1-69. Asymmetric [3 + 2] cycloaddition with TADDOL mediator



Scheme 1-70. Asymmetric total synthesis of Rocaglaol and Rocaglamide

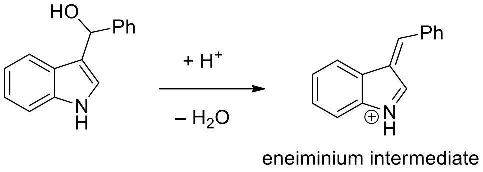


Since this initial report Porco and coworkers have published a series of papers synthesizing several natural products containing these forbaglin and rocaglamide ring systems.[172–176] The stereoselectivities of these photocycloadditions are all mediated by a TADDOL derivative to provide excellent enantioselectivities of the desired cycloadduct. Asymmetric [3 + 2] cycloadditions of 3-hydroxyflavones via ESIPT provides an efficient route to the core of this subset of natural products and allows for efficient syntheses of several derivatives. However, due to the mechanism through which the active intermediate is generated this strategy is not broadly applicable to other substrate classes. Other methodologies have yet to be developed which expand this mechanistic approach to other asymmetric 1,3-dipolar cycloadditions.

1.4.4 Asymmetric [3 + 2] cycloadditions with indolylmethanol derivatives

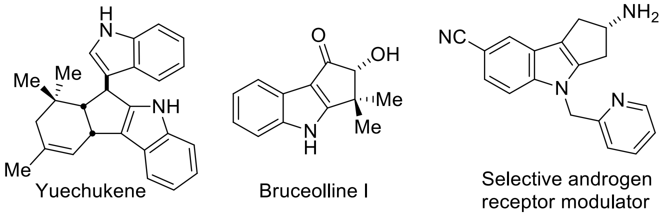
Iminium ions are well known as versatile intermediates for a range of synthetic transformations including stereoselective alkylations, cyclizations, and cycloadditions.[177,178] Due to the large number of natural products and bioactive compounds containing indole ring-systems there is significant interest in developing new methodologies for the functionalization and diversification of simple indole building blocks. Indolylmethanol derivatives have attracted recent interest as precursors to vinylogous iminium species for rapid and efficient diversification of simple indole starting materials (Scheme 1-71). While much of the early work in this field focused simply on

Scheme 1-71. Formation of electrophilic eneiminium intermediate under acidic conditions



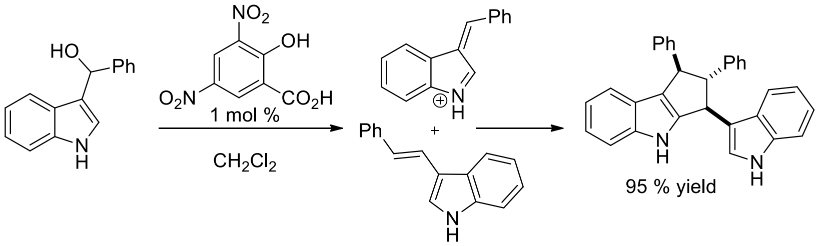
alkylation and cyclization reactions of these intermediates, [3 + 2] cycloadditions provide a route for rapid construction of (spiro)cyclopenta[b]indole scaffolds that are present in a significant number of natural products (Figure 1-15).[179]

Figure 1-15. Select examples of cyclopenta[b]indole containing natural products and bioactive compounds



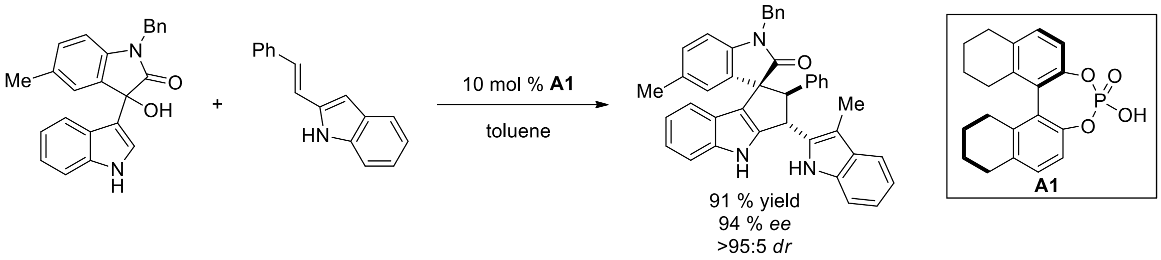
Early reports of [3 + 2] cycloadditions with indolylmethanol precursors came from the labs of Qi-Xiang Guo in 2014.[180] They envisioned that the activated iminium species could service as an excellent coupling partner with nucleophilic 3-vinylindoles to provide cyclopentane products in a formal [3 + 2] cycloaddition. They were able to develop a Brønsted acid catalyzed [3 + 2] cycloaddition for the efficient construction of racemic 2,3'-bisindoles containing the desired cyclopenta[b]indole ring system (Scheme 1-72).

Scheme 1-72. Racemic Brønsted acid catalyzed [3 + 2] cycloaddition with 3-indolylmethanols



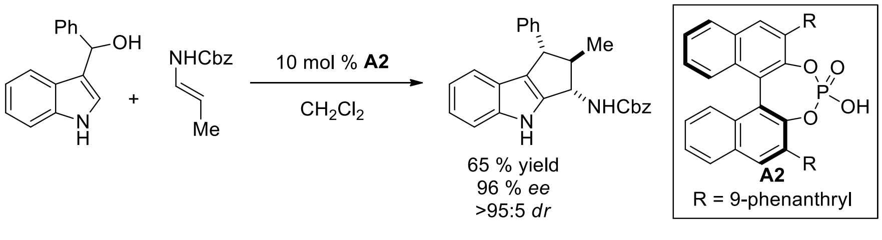
Shi and coworkers later reported an enantioselective formal [3 + 2] cycloaddition with isatin-derived 3-indolylmethanols and 2-vinylindoles by introduction of a chiral BINOL phosphoric acid catalyst (Scheme 1-73).[179] This development provides an efficient route to spirocyclopenta[*b*]indoles in high yields and high stereoselectivities albeit with a substrate scope limited to the substituents on the aryl rings. Soon after this intial report, Shi and coworkers were able to further extend this methodology to use 7-vinylindoles as coupling partners using similar Brønsted acid catalysts.[181]

Scheme 1-73. Asymmetric Brønsted acid catalyzed [3 + 2] cycloadditions with 3-indolylmethanols

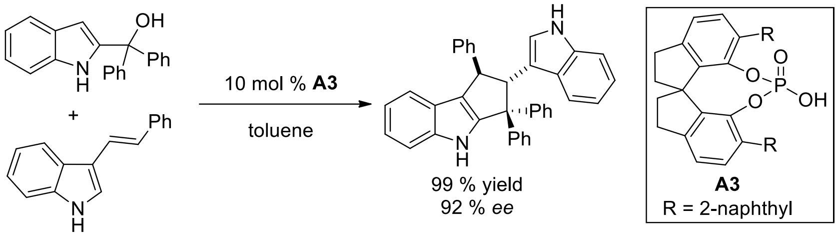


Multiple researchers in the field have developed much more general methodologies to access simple cyclopentane[b]indole scaffold in a single step via formal [3 + 2] cycloadditions with indolylmethanol species. Masson and coworkers reported in 2015 that highly enantioselective [3 + 2] cycloadditions can be accomplished under chiral Brønsted acid conditions with 3-indolylmethanols and simple enecarbamates to provide functionalized tricyclic rings systems with three contiguous stereocenters (Scheme 1-74).[182] Further extending this strategy, Shi and coworkers reported in 2016 that these transformations can also be accomplished with 2-indolylmethanols under very similar conditions (Scheme 1-75).[183]

Scheme 1-74. Asymmetric [3 + 2] cycloadditions with 3-indolylmethanols and enecarbamates



Scheme 1-75. Asymmetric [3 + 2] cycloadditions with 2-indolylmethanols and 2-vinyldindoles



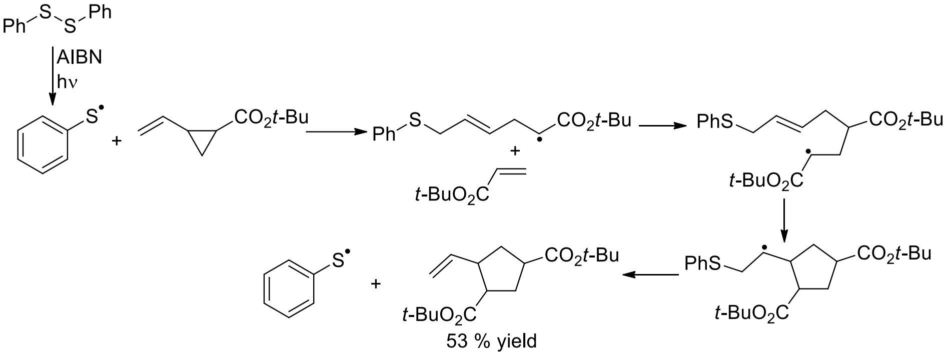
1.5 Asymmetric [3 + 2] cycloadditions via free radical intermediates

The previous sections of this review have covered a number of methodologies for catalytic enantioselective [3 + 2] cycloadditions that involve a wide range of mechanistically distinct transformations. One common aspect of all these transformations, however, is that they involve closed shell intermediates. Radical transformations allow for distinct and often complementary reaction pathways that are not possible for two-electron pathways involving closed shell species. One property of single electron pathways that are distinct from two-electron pathways is that the favorability of a given reaction is generally controlled by homolytic bond strength rather than heterolytic bond strength. This key difference often allows for radical reactions to occur with substrates that are generally considered “unactivated” and tolerates many polar functional groups that would generally be incompatible with two-electron transformations. There have been substantial developments in achieving stereocontrol using organocatalysts and Lewis acid catalysts to control enantioselectivity of radical transformations. While there has been numerous examples of enantioselective radical cyclizations and [2 + 2] cycloadditions, there are very few examples for catalytic enantioselective [3 + 2] cycloadditions which proceed through radical intermediates. This section of the review will briefly cover the developments that have been reported so far.

1.5.1 Asymmetric [3 + 2] cycloadditions with organic thiyl radical catalysts

Reactions of thiyl radicals have attracted significant interest as an efficient method to generate radical intermediates from many different organic compound (e.g. olefins) and thus promote

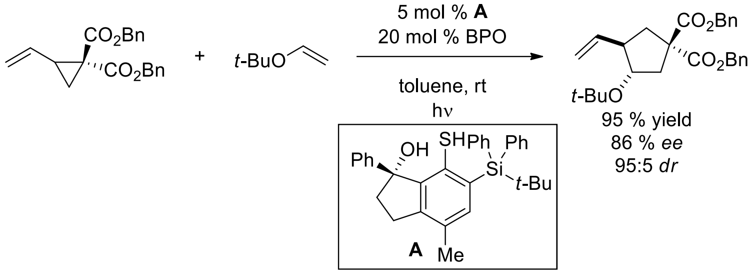
Scheme 1-76. Thiyl radical catalyzed [3 + 2] cycloaddition of vinylcyclopropanes



radical processes. Thiyl radicals are particularly promising for catalyzing radical reactions because they can easily be generated in situ by the homolysis of disulfides. In 1988, Feldman and coworkers reported a racemic [3 + 2] cycloaddition between vinylcyclopropanes and various electron-rich and electron-poor olefins catalyzed by phenylthiol radicals generated in situ from phenyldisulfide (Scheme 1-76).[184] The reaction proceeds through activation of the vinylcyclopropane through radical addition of the phenylthiol radical onto the olefin and subsequent homolytic ring cleavage to generate a homoallylic radical intermediate. The homoallylic radical can then add into the olefin coupling partner. Cyclization of this radical intermediate generates the cyclopentane ring and homolysis of the carbon–sulfur bond regenerates the thiyl radical catalyst and produced the vinylcyclopentane product. One notable feature of this transformation is that good yields were achieved for vinylcyclopropanes with both electron-donating and electron-withdrawing substituents as well as with both electron-rich and electron-poor olefin coupling partners. This insensitivity to the substrate polarity is a common feature of many radical transformations.

While there was some early precedent for asymmetric catalysis with thiyl radicals[185,186], an asymmetric version of the thiyl radical catalyzed [3 + 2] cycloaddition was not reported until 2014 by Maruoka and coworkers.[187] In this report the researchers developed an expedient route to a series of chiral thiols to optimize the thiyl radical catalyzed [3 + 2] cycloaddition of vinylcyclopropanes (Scheme 1-77). The optimized conditions provided modest to excellent

Scheme 1-77. Enantioselective thiyl catalyzed [3 + 2] cycloaddition



enantioselectivities and high yields for a relatively large substrate scope. Unfortunately, The asymmetric transformation seems to be far more sensitive to the electronics of the substrates than the original racemic transformation. Only dipolar cyclopropanes and electron-rich olefins appear to be tolerated in the optimized conditions.

While this initial asymmetric transformation appears to be relatively limited with regards to scope for the synthesis of enantioenriched cyclopentanes the authors have been able to extend this strategy for the synthesis of pyrrolidine rings through the ring opening of vinylaziridines with a chiral thiyl catalyst.[188]

1.5.2 Asymmetric [3 + 2] cycloadditions of cyclopropyl ketones via photoredox catalysis

Another approach for achieving asymmetric [3 + 2] cycloadditions through radical intermediates is based on the fundamental electrochemical investigations of Tanko and coworkers as well the work of several other groups for reductive ring cleavage of cyclopropyl ketones to affect cyclization reactions.[189–193] It has been established that one-electron reduction of cyclopropyl ketones results in a rapidly equilibrating mixture consisting of ring-closed cyclopropyl ketyl radical and ring-opened homoallylic distonic radical anion (Scheme 1-78). This behavior is responsible for the well-known cyclizations and dimerizations that can occur with

Scheme 1-78. Reversible ring-opening of cyclopropyl ketones

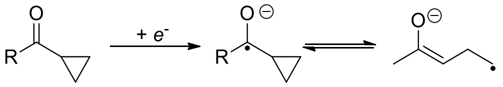
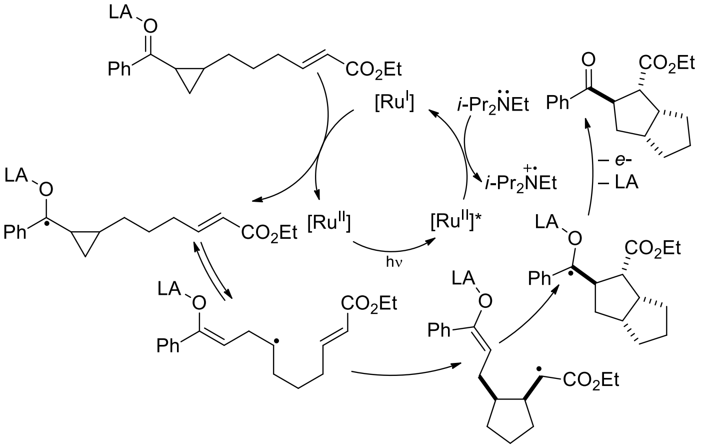


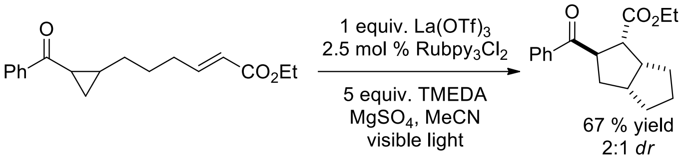
Figure 1-16. Proposed mechanism for intramolecular [3 + 2] cycloaddition of cyclopropyl ketones with visible light catalysis



cyclopropyl ketones through outer sphere one-electron reduction by photoelectron transfer (PET) and inner-sphere reduction by SmI_2.[194,195] Inspired by these early studies, Yoon and coworkers envisioned the possibility to achieve an intramolecular formal [3 + 2] cycloaddition between an aryl cyclopropyl ketone and a pendant olefin. It was predicted that 1-electron reduction of the cyclopropyl ketone could be accomplished using a photocatalyst such as $Ru(bpy)_3Cl_2$ in the presence of a tertiary amine.[196–199] The proposed mechanism for the transformation is shown in Figure 1-16.[200] It was predicted that Ru^{1+} (E_0 ($Ru^{2+/1+}$) = –1.31 V vs. SCE) formed by quenching of the excited state with a one-electron donor such as a tertiary amine would be able to reduce a cyclopropyl ketone in the presence of a Lewis acid. The resulting cyclopropyl ketyl radical would ring-open to the homoallylic distonic radical anion which could engage in a step-wise formal [3 + 2] cycloaddition with the pendant olefin. One electron oxidation would then provide the final cycloadduct in an overall redox-neutral process. A series of optimizations found the Lewis acid $La(OTf)_3$ to be effective in mediating the desired cycloaddition (Scheme 1-79). These conditions tolerate a broad substrate scope to provide bi- and tricyclic products in good yields and modest diastereoselectivities.

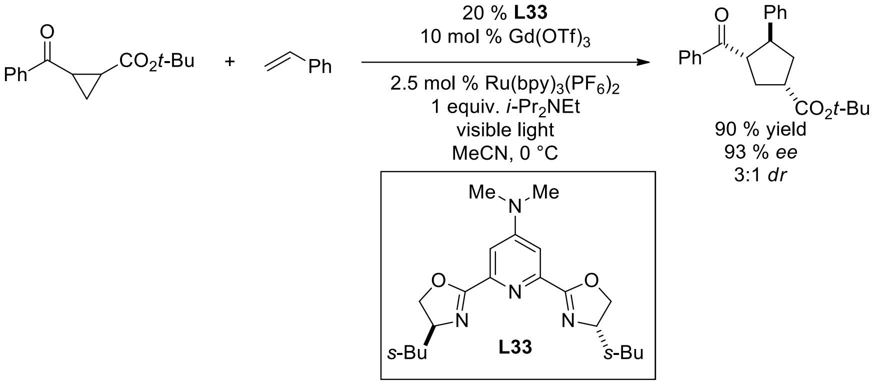
Yoon and coworkers developed an enantioselective intermolecular variant several years later through a slight modification of the reaction conditions. Improved intermolecular reactivity was

Scheme 1-79. Racemic intramolecular [3 + 2] cycloaddition with a cyclopropyl ketone



observed using Gd(OTf)$_3$ as a Lewis acid and incorporation of an electron-rich pybox ligand **L33** allowed for catalytic loadings of Lewis acid (Scheme 1-80). This transformation tolerates a very broad substrate scope of both electron-rich and electron-poor aryl cyclopropyl ketones as well and both electron-rich and electron-poor olefins. This transformation is described in significantly greater detail in later chapters of this thesis.

Scheme 1-80. Enantioselective intermolecular [3 + 2] cycloaddition of a cyclopropyl ketone via visible light photocatalysis



1.5.3 Summary

Radical transformations have the potential to offer divergent and complementary reactivity to what is typically observed for 2-electron transformations and nobel-metal transition metal catalysis. The impact that radical transformations have made to date on catalytic asymmetric [3 + 2] cycloadditions is still limited however there is likely still significantly more room for growth. There have been several additional reports for racemic [3 + 2] cycloadditions for cyclopentanoid synthesis in recent years.[201,202] Further developments in this field for asymmetric catalysis will likely continue in the future. Some of these efforts will be discussed in greater detail in the following chapters of this thesis.

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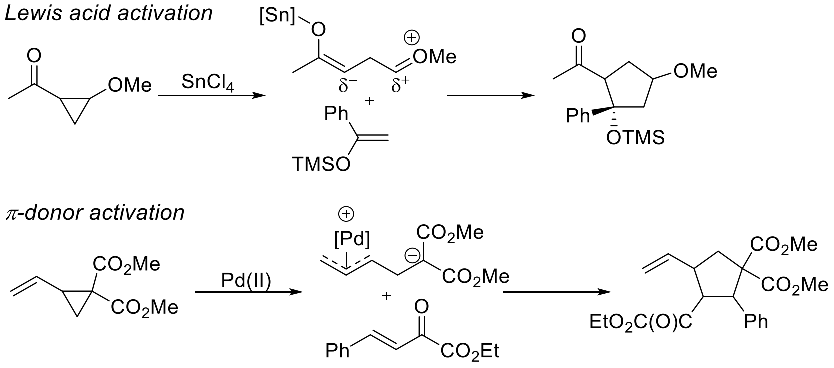
Chapter 2. The Development of [3 + 2] Cycloadditions Using Visible Light Dual Catalysis

2.1 Introduction

Cyclopentane rings are present in many natural products and other compounds of biological interest. As a result, there has been a great deal of research focused on developing selective and flexible methods to synthesize cyclopentanes.[1–5] While there are numerous strategies available (e.g. cyclizations, desymmetrizations, ring expansions, etc), the [3 + 2] cycloaddition is appealing as a very efficient route to access a diverse array of cyclopentanoid frameworks.[6–14] Common strategies for [3 + 2] cycloadditions make use of 1,3-dipole and zwitterionic reagents, vinyl carbenoids, reductive cycloadditions, metal insertions, and organocatalytic activations (see Chapter 1 for enantioselective variants of these methodologies). While these different methods offer flexibility in designing synthetic routes to complex cyclopentane containing products, they are generally sensitive to the polarity of the coupling partners and are often incompatible with polar functional groups.

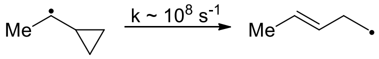
Due to their inherent ring strain, cyclopropanes can undergo ring-cleavage and subsequent rearrangements upon thermal or catalytic activation.[15–21] Due to the accessibility of these rearrangements, cyclopropanes have attracted interest as strategic 3-carbon building blocks for several transformations. Cyclopropanes have been used for a number of [3 + 2] cycloaddition methodologies, the most well-developed of which are [3 + 2] cycloadditions with donor–acceptor cyclopropanes.[22,23] Donor–acceptor cycloadditions rely on vicinal substitution of a donor

Scheme 2-1. [3 + 2] cycloadditions with donor acceptor cyclopropanes



substituent (e.g. heteroatom, aryl, vinyl, etc.) and an acceptor substituent (e.g. carbonyl, -NO_2, etc.). In the presence of a π-donor or Lewis acid catalyst, heterolytic cleavage of the cyclopropane can occur to provide a 1,3-dipole equivalent for subsequent [3 + 2] cycloadditions (Scheme 2-1). While donor–acceptor [3 + 2] cycloadditions have proven to be powerful for the construction of both carbocyclic and heterocyclic rings, they are similarly very sensitive to the identity of the unsaturated coupling partner due to the polar nature of the 1,3-dipolar intermediate, which requires electronically matched coupling partners.

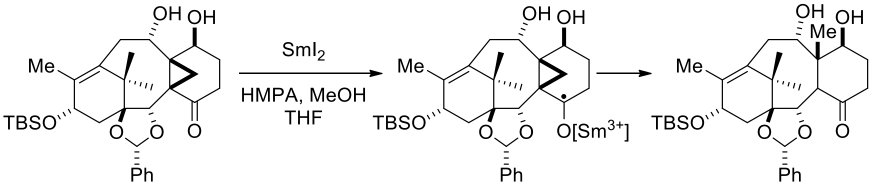
Scheme 2-2. Radical rearrangement of cyclopropane to homoallylic radical



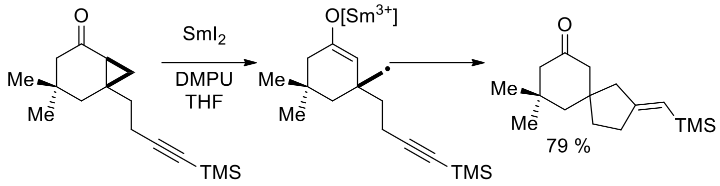
Organic radicals and other open-shell species often react in a manner complementary to closed shell intermediates because the kinetics of bond formation and breakage are determined by homolytic bond strength in radical reactions rather than heterolytic bond strength. This feature often allows for radical reactions to operate on substrates that are otherwise "unactivated" towards 2-electron transformations.[24] Radical rearrangements are a widely-used mechanism to achieve cyclopropane ring-cleavage. When a radical center is adjacent to a cyclopropane ring, rapid rearrangement occurs to generate a homoallylic radical (Scheme 2-2).[25] Among the most common applications of these rearrangements are radical clock experiments that take advantage of the fast rates of these ring-opening processes.

Radical rearrangements of cyclopropyl ketones have been used in complex molecule synthesis primarily for selective ring-cleavage in order to introduce alkyl groups (Scheme 2-3a) or to effect cyclizations (Scheme 2-3b). There are several methodologies reported in the literature for both inner-sphere and outer-sphere electron transfer that result in the reduction of a pendant ketone to provide a cyclopropyl ketyl radical which undergoes homolytic ring-cleavage. SmI_2 has become a very common reductant for these transformations, providing relatively selective and

Scheme 2-3a. SmI_2 mediated cyclopropane cleave for methyl group addition[27]

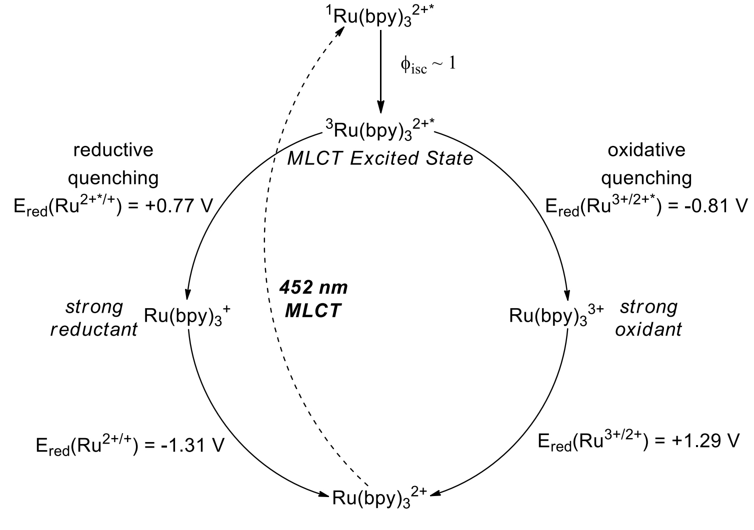


Scheme 2-3b. SmI_2 mediated cyclopropane cleavage for cyclizations[26]



efficient reactivity (Scheme 2-3).[26,27] A notable feature of many of these transformations is the high degree of functional group tolerance and the ability to react the intermediate radical species with otherwise unactivated olefins. While the reduction of cyclopropyl ketones has been applied towards cyclizations and other rearrangements, the application of the distonic radical anion intermediate to cycloaddition reactions has remained limited. A related strategy for radical cleavage and [3 + 2] cycloadditions of cyclopropanes using thiyl radical catalysts has been reported recently.[28,29] While the initial report of this mode of activation showed great promise, more recent reports have been limited to donor–acceptor cyclopropanes.

Figure 2-1. Spectroscopic and electrochemical properties of $Ru(bpy)_3^{2+}$



A major theme of research in our group has been the use of one-electron redox chemistry to activate substrates towards a wide variety of transformations. One strategy that has emerged has been the application of homogeneous transition metal complexes as photosensitizers to oxidize or reduce substrates in solution.[30,31] Substantial research over many decades has been dedicated to these transition metal complexes to characterize and understand their excited state properties.[32–35] Complexes such as the ruthenium(II) polypyridyl complex $Ru(bpy)_3Cl_2$ absorb light strongly in the visible region through a metal to ligand charge transfer (MLCT) transition. In the excited state, the complex is redox active with an oxidation potential of –0.81 V vs SCE and a reduction potential of +0.77 V vs SCE (Figure 2-1). Furthermore, through the interaction with a reductant or an oxidant the Ru(I) and Ru(III) oxidation states are readily accessible allowing for an even greater thermodynamic driving force for electron transfer. Due to their desirable spectroscopic and redox properties as well as their long-lived excited states (600 ns), these complexes have served as excellent photocatalysts for many applications including organic synthesis and solar energy conversion. Applications of these photocatalysts are the subject of

Scheme 2-4. Racemic intramolecular [3 + 2] cycloaddition with a cyclopropyl ketone

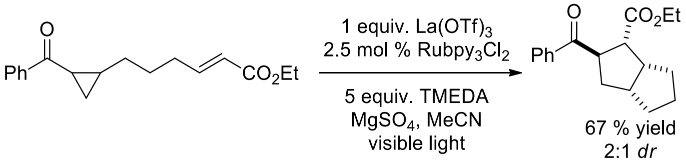
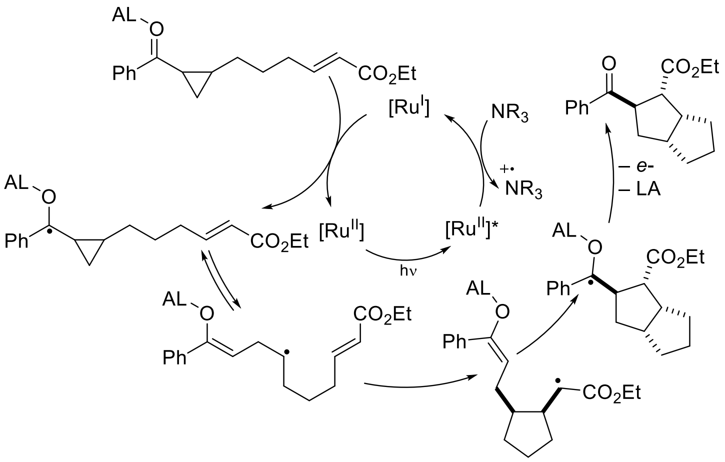


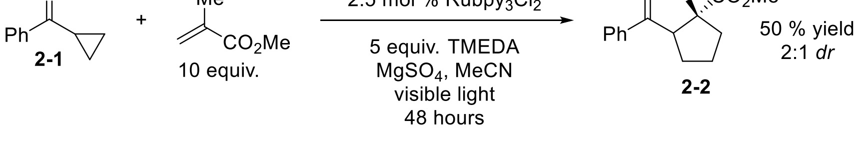
Figure 2-2. Proposed mechanism for intramolecular [3 + 2] cycloaddition



multiple recent reviews.[36–40]

We hypothesized that the redox properties of visible light photocatalysts would allow mild access to cyclopropyl ketyl radical anion intermediates which could engage olefin coupling partners in [3 + 2] cycloadditions. In 2011, our group published the successful realization of this goal for intramolecular [3 + 2] cycloadditions between aryl cyclopropyl ketones and acrylates (Scheme 2-4).[15] Key to the success of this transformation was the correct choice of Lewis acid. In the absence of a Lewis acid a cyclopropyl ketone has a reduction potential of ~-1.9 V vs. SCE, which is far outside of the range of most visible light photocatalysts (see experimental information of Chapter 4). Lanthanide Lewis acids proved to be particularly effective for lowering the reduction potential of aryl cyclopropyl ketones to allow for efficient [3 + 2] cycloadditions to be observed. The proposed mechanism is shown in Figure 2-2. Upon excitation with visible light the excited state of $Ru(bpy)_3^{2+*}$ is quenched by a tertiary amine to generate a Ru(I) species. Ru(I) is then able to reduce the Lewis acid–cyclopropane complex to generate the cyclopropyl ketyl radical anion, which is in equilibrium with the open-chain distonic radical anion. The distonic radical anion can engage the tethered olefin in a stepwise formal [3 + 2] cycloaddition to generate the radical anion of the cycloadduct. The radical anion is oxidized to generate the final product in an overall redox neutral process. This initial publication included some preliminary experiments showing the feasibility of intermolecular [3 + 2] cycloadditions though the reactivity was sluggish and poor conversions were observed (Scheme 2-5). This chapter will discuss the optimization of an intermolecular [3 + 2] cycloaddition between aryl cyclopropyl ketones and styrenes and detail a brief survey of the substrate scope.

Scheme 2-5. Preliminary results for intermolecular [3 + 2] cycloadditions



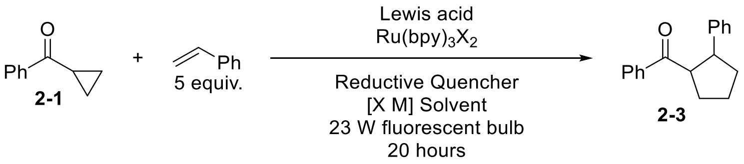
2.2 Results and Discussion

2.2.1 Optimization of the reaction conditions

Optimization of the reaction conditions began with the conditions used in the intramolecular reaction developed by our group employing 1 equiv. of the Lewis acid La(OTf)$_3$, 2.5 mol % of the photocatalyst Ru(bpy)$_3$Cl$_2$, and 5 equiv. of TMEDA as reductive quencher. Styrene was used as the coupling partner as it was believed that that this would provide more efficient reactivity do the stabilization of the intermediate radical during the cycloaddition. An initial experiment provided the desired cycloadduct in a promising 33% yield after 24 h (Table 2-1, entry 1).

Screening other solvents showed few improvements in the overall efficiency of the reaction though faster rates were observed under higher concentrations (Table 2-1, entry 2). The most significant improvements in the reaction efficiency were observed by varying the identity of the Lewis acid. A screen of Lewis acids revealed Gd(OTf)$_3$ to be superior for the desired [3 + 2]

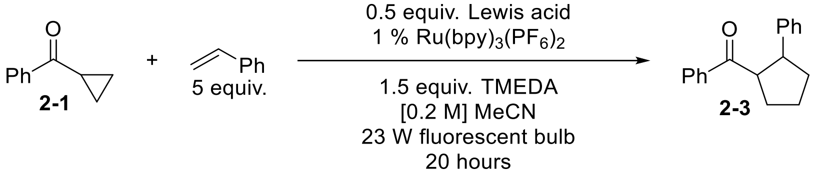
Table 2-1. Optimization of reaction conditions



Entry	Conditions[a]	yield[b]
1[c]	Ru(bpy)$_3$Cl$_2$, 5 equiv. TMEDA, MeCN, 1 equiv. La(OTf)$_3$	33 %
2	Ru(bpy)$_3$Cl$_2$, 5 equiv. TMEDA, MeCN, 1 equiv. La(OTf)$_3$	44 %
3	Ru(bpy)$_3$Cl$_2$, 5 equiv. TMEDA, DCM, 1 equiv. La(OTf)$_3$	0 %
4	Ru(bpy)$_3$Cl$_2$, 5 equiv. TMEDA, EtOAc, 1 equiv. La(OTf)$_3$	32 %
5	Ru(bpy)$_3$(PF$_6$)$_2$, 5 equiv. TMEDA, MeCN, 1 equiv. La(OTf)$_3$	56 %
6	Ru(bpy)$_3$(PF$_6$)$_2$, 5 equiv. TMEDA, MeCN, 1 equiv. LiBF$_4$	0 %
7	Ru(bpy)$_3$(PF$_6$)$_2$, 5 equiv. TMEDA, MeCN, 1 equiv. Mg(OTf)$_2$	0 %
8	Ru(bpy)$_3$(PF$_6$)$_2$, 5 equiv. TMEDA, MeCN, 1 equiv. Gd(OTf)$_3$	69 %
9	Ru(bpy)$_3$(PF$_6$)$_2$, 5 equiv. TMEDA, MeCN, 0.5 equiv. Gd(OTf)$_3$	49 %
10[d]	Ru(bpy)$_3$(PF$_6$)$_2$, 1.5 equiv. TMEDA, MeCN, 0.5 equiv. Gd(OTf)$_3$	71 %

[a] [0.2 M] in indicated solvent, 0.04 mmol cyclopropane, 2.5 % [Ru]. [b] Yields determined by ^{1}H NMR using phenanthrene as internal standard. [c] [0.1 M] in MeCN. [d] 1 % Ru(bpy)$_3$(PF$_6$)$_2$

Table 2-2. Variation of diastereoselectivity with ionic radius of Lewis acid



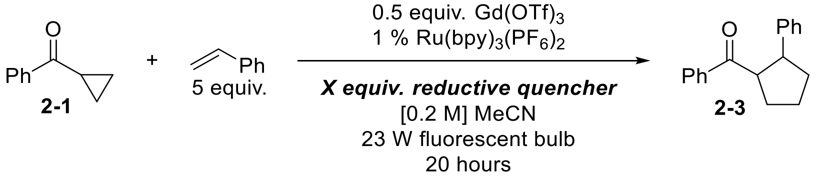
Entry	Lewis acid	% yield	d.r.	Ionic radius (Å)
1	La(OTf)$_3$	50 %	17:1	1.03
2	Gd(OTf)$_3$	71 %	8:1	0.94
3	Er(OTf)$_3$	55 %	4:1	0.89

0.04 mmol cyclopropane. Yields determined by ^{1}H NMR using phenanthrene as internal standard

cycloaddition (Table 2-1, entry 8). The loading of Gd(OTf)$_3$ could be decreased to 50 mol % by also decreasing the loading of TMEDA to 1.5 equiv. This is thought to be due to the dual role of TMEDA as both a reductive quencher for the photocatalyst and as a ligand for the Lewis acid.

The reaction efficiency showed a pronounced sensitivity to the steric environment of the Lewis acid (Table 2-3). The use of bulkier tertiary amines tended to hinder the reaction presumably due to blocking the approach of substrate. Additionally, there was observed a correlation between Lewis acid ionic radius and the diastereoselectivity of the cycloaddition (Table 2-2). Further details for the reaction optimization can be found in the experimental sections of this chapter. The optimal conditions provided the desired cycloadduct in 70 % yield after 20

Table 2-3. Variation of reaction rate with reductive quencher

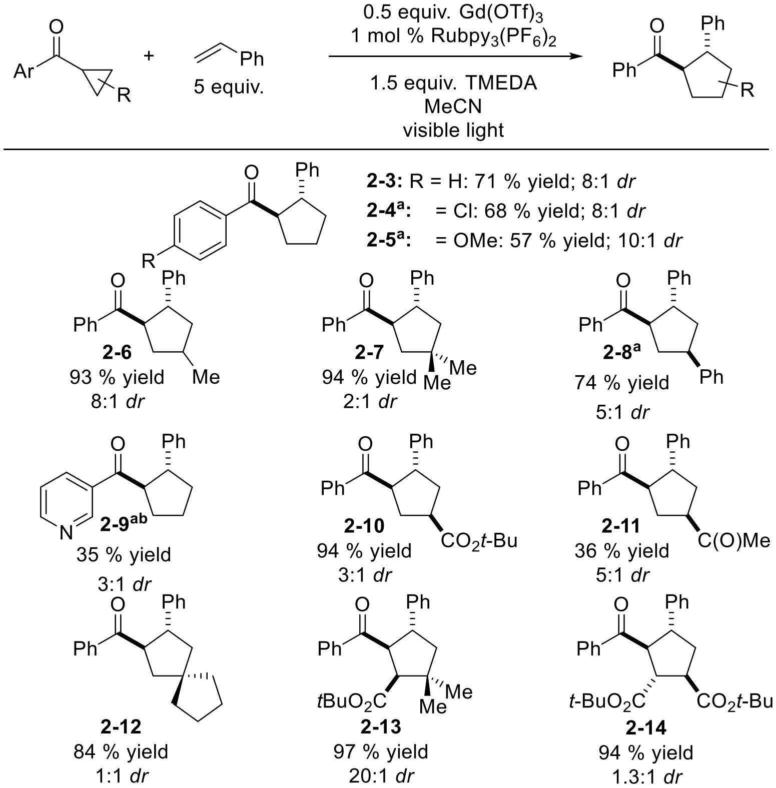


Entry	Reductive Quencher (Equiv.)	% yield
1	*i*-Pr$_2$NEt (3 equiv.)	9 %
2	1,2,2,6,6-pentamethylpiperidine (3 equiv.)	7 %
3	TMEDA (1 equiv.)	30 %
4	TMEDA (1.5 equiv.)	71
5	TMEDA (3 equiv.)	60

0.04 mmol cyclopropane. Yields determined by ^{1}H NMR using phenanthrene as internal standard hours (Table 2-1 entry 10). Control reactions showed the requirement of photocatalyst, Lewis acid, and TMEDA in order to observe any reactivity (see experimental information).

2.2.2 Substrate scope

Figure 2-3. Cyclopropane substrate scope for intermolecular [3 + 2] cycloadditions

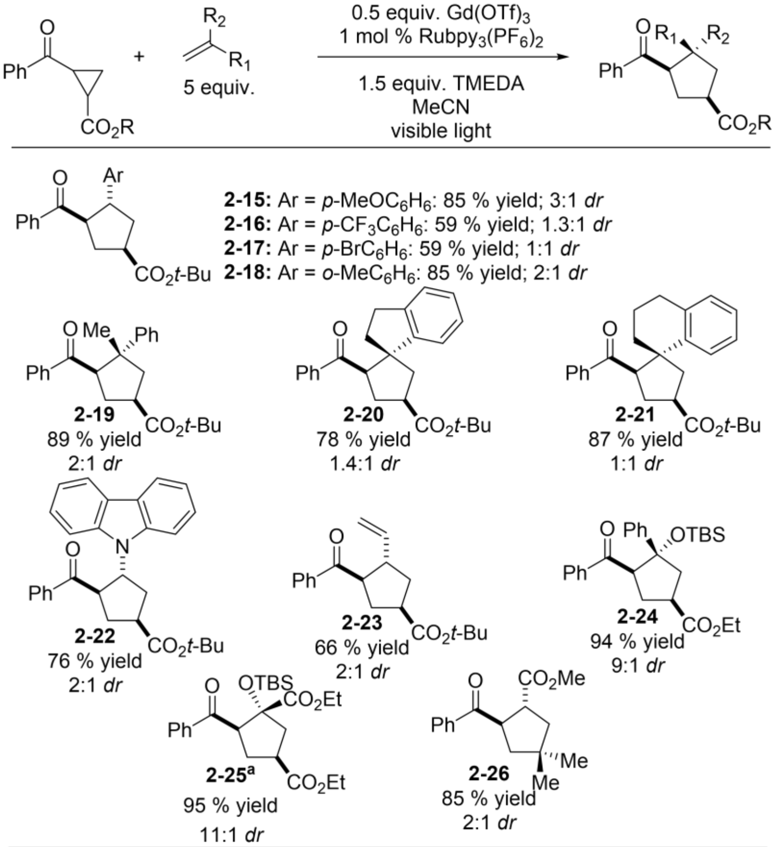


Reactions carried out with Ru(bpy)$_3$(PF$_6$)$_2$ (1 mol %), Gd(OTf)$_3$ (0.5 equiv.), and TMEDA (1.5 equiv.) in MeCN (0.2 M). Reactions were irradiated with a 23 W compact fluorescent bulb. All yields are isolated yields unless otherwise indicated. Diastereomeric ratios were determined by ^{1}H NMR analysis of crude product. [a] Yield determined by ^{1}H NMR spectroscopy using phenanthrene as internal standard [b] Using 2 equiv. Gd(OTf)$_3$ and 6 equiv. TMEDA.

With the optimal reaction conditions in hand, we next explored the generality of this transformation (Figure 2-3 and Figure 2-4). The scope with respect to the cyclopropane substrate proved to be relatively general, although most products were obtained in modest diastereoselectivities. Both electron-donating and electron-withdrawing substituents as well as heteroatoms were tolerated on the aryl ring of the ketone (**2-4, 2-5,** and **2-9**). Substitutions on the cyclopropane itself provided more efficient reactivity than unsubstituted cyclopropyl phenyl ketone, presumably due to stabilization of the radical after homolytic cleavage of the cyclopropane ring (**2-6**). Multiple alkyl substitutions were well tolerated, allowing for the construction of quaternary centers (**2-7** and **2-12**). High regioselectivities were observed for a cyclopropane with different substitutions on each carbon of the cyclopropane ring; the major product was consistent with reaction through the more stable radical intermediate (**2-13**). Interestingly this cycloaddition tolerated both electron-donating (e.g phenyl, **2-8**) and electron-withdrawing (e.g., ester and ketone, **2-10** and **2-11**) substituents on the cyclopropane ring all in high yields. This is in stark contrast to the large majority of methodologies available for [3 + 2] cycloadditions which tend to be very sensitive to the polarity of each coupling partner.

The scope with respect to the olefin substrate proved to be similarly broad so long as the olefin bears a substituent that can stabilize the radical intermediate after the first bond formation.

Figure 2-4. Olefin substrate scope for intermolecular [3 + 2] cycloadditions



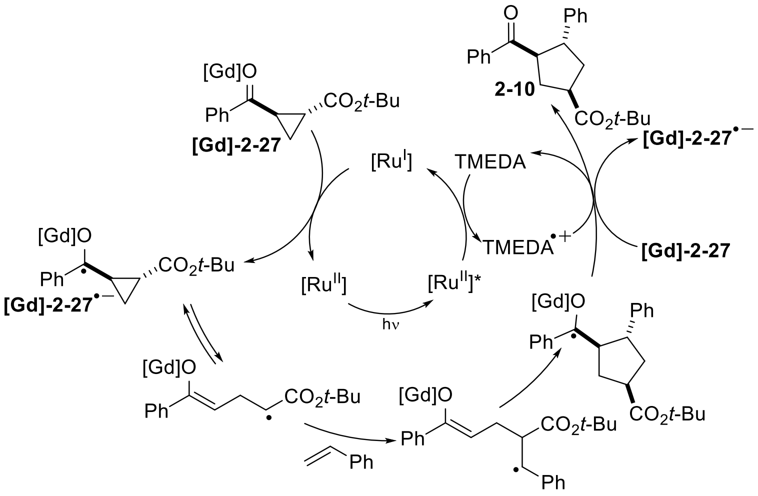
Reactions carried out with Ru(bpy)$_3$(PF$_6$)$_2$ (1 mol %), Gd(OTf)$_3$ (0.5 equiv.), and TMEDA (1.5 equiv.) in MeCN (0.2 M). Reactions were irradiated with a 23 W compact fluorescent bulb. All yields are isolated yields unless otherwise indicated. Diastereomeric ratios were determined by ^{1}H NMR analysis of crude product. [a] Yield determined by ^{1}H NMR spectroscopy using phenanthene as internal standard

Electron-poor and electron-rich styrenes were efficient coupling partners (**2-15–2-17**). Sterics on the α-position of the styrene were well tolerated (**2-19–2-21**). Very electron-deficient coupling partners such as acrylates (**2-26**) and very electron-rich coupling partners such as N-vinylcarbazole (**2-22**) and silyl enol ethers (**2-24** and **2-25)** worked well under these conditions. Interestingly dienes such 1,3-butadiene and isoprene were also very efficient coupling partners in the [3 + 2] cycloaddition (**2-23** and **2-40** in the experimental section). The insensitivity of this [3 + 2] cycloaddition to the polarity of the olefin coupling partner is again a complementary feature to many of the existing [3 + 2] cycloaddition methodologies.

2.2.3 Mechanism

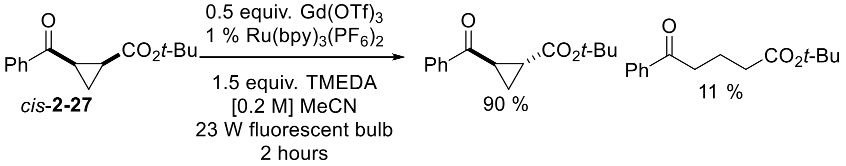
The proposed mechanism for the intermolecular [3 + 2] cycloaddition is believed to be analogous to the mechanism proposed for the intramolecular system (Figure 2-5). Visible light excitation of Ru(bpy)$_3$$^{2+}$ and subsequent quenching by TMEDA produces Ru(bpy)$_3$$^{1+}$, which can the reduce the [Gd]–cyclopropane complex ([Gd]-2-27). The ketyl radical anion then undergoes reversible ring opening to the distonic radical. The ring-opened distonic radical anion then undergoes stepwise [3 + 2] cycloaddition with the olefin to produce the radical anion of the product. Oxidation to produce the neutral product occurs through either reduction of the radical

Figure 2-5. Proposed mechanism for intermolecular [3 + 2] cycloaddition



cation of TMEDA or through a radical chain process to produce another equivalent of the radical anion of [Gd]–2-27. The rapid reversibility of the ring-opening of the ketyl radical anion has been studied extensively by Tanko and coworkers.[41–43] Additionally, diastereomerically pure *cis*-2-27 was observed to undergo isomerization to *trans*-2-27 under the reaction conditions (Figure 2-6). This isomerization only occurs in the presence of photocatalyst, Lewis acid, and TMEDA indicating that the isomerization is occurring through an electron-transfer process. Support for a radical chain process is based on work reported previously by our group.[44]

Scheme 2-6. Isomerization of *cis*-cyclopropane under photocatalytic conditions



2.3 Conclusion

In conclusion, we have developed conditions for an efficient intermolecular [3 + 2] cycloaddition between simple aryl cyclopropyl ketones and olefins. The choice of Lewis acid and reductive quencher proved critical in attaining efficient reactivity. This [3 + 2] cycloaddition provides an excellent complement to the existing methodologies in the literature for the construction of 5-membered carbocycles. A feature of this methodology is the relative insensitivity of this cycloaddition to the polarity of the substrates. The only constraints are that the cyclopropane has a substituent with an accessible reduction potential and the olefin coupling partners has a substituent capable of stabilizing the intermediate radical of the step-wise cycloaddition. Both electron-withdrawing and electron-donating substituents were tolerated on both the cyclopropane ring and the olefin. Additionally, the dual catalytic nature of this reaction and the effect that the identity of the Lewis acid has on the stereoselectivity of the transformation is promising for the development of catalytic enantioselective transformations. The following chapter in this thesis will show our progress in exploring these possibilities.

2.4 Experimental information

2.4.1 General Information

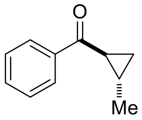
Acetonitrile, THF, and CH_2Cl_2 were purified by elution through alumina as described by Grubbs.[45] A 23W (1200 lumens) SLI Lighting Mini-Lynx compact fluorescent light bulb was used for all photochemical reactions. $Gd(OTf)_3$, $La(OTf)_3$, and other Lewis acids were purchased from Strem, stored in a glove box, and used without further purification. Flash column chromatography was performed with Silicycle 40-63Å silica (230-400 mesh). Styrene, diisopropylethylamine, *N,N,N',N'*-tetramethylethylenediamine, triethylamine, 1,2,2,6,6-pentamethylpiperidine, and DABCO were purchased from Sigma Aldrich and subsequently purified either by distillation or recrystallization. Cyclopropyl phenyl ketone, Cyclopropyl 4-chloro-phenyl ketone, and cyclopropyl 4-MeO-phenyl ketone was purchased from Sigma Aldrich and purified by short-path distillation prior to use. Sodium oxalate was purchased from Sigma Aldrich and used without further purification. All glassware was oven-dried at 130 °C overnight or flame-dried immediately prior to use.

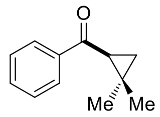
^1H and $^{13}C\{H\}$ NMR data for all previously uncharacterized compounds were obtained using a Bruker AVANCE-400 spectrometer and are referenced to TMS (0.0 ppm) and $CDCl_3$ (77.0 ppm), respectively. IR spectral data were obtained using a Bruker Vector 22 spectrometer. Melting points were obtained using a Mel-Temp II (Laboratory Devices, Inc., USA) melting point apparatus. Mass spectrometry was performed with a Micromass LCT (electrospray ionization, time-of-flight analyzer or electron impact). These facilities are funded by the NSF (CHE-9974839, CHE-9304546) and the University of Wisconsin.

2.4.2 Synthesis and Characterization of Starting Materials

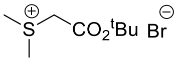
Trans tert-butyl 2-benzoylcyclopropanecarboxylate and 1-((2-benzoylcyclopropyl)ethanone were prepared according to procedures reported by Gaunt and coworkers.[46] 1-Methylene-1,2,3,4-tetrahydronaphthalene and 1-methylene-2,3-dihydro-1H-indene were prepared according to a procedure described by Liwosz and Chemler.[47] 4-Trifluoromethylstyrene was prepared according to a procedure described by Warren and coworkers.[48] Cyclopropyl(pyridine-3-yl)methanone was prepared according to a procedure described by William.[49] Phenyl(2-phenylcyclopropyl)methanone was synthesized as described by Eric and coworkers.[50] Ethyl 2-((tert-butyldimethylsilyl)oxy)acrylate was synthesized as described by Catteau and coworkers.[51] Tert-butyldimethyl((1-phenylvinyl)oxy)silane was synthesized as described by Schiesser and coworkers.[52] $Ru(bpy)_3(PF_6)_2$ was synthesized as described previously by Wrighton.[53]

***trans* 2-Methylcyclopropyl(phenyl)methanone (2-28):** A flame-dried 100 mL flask was charged with solid NaH (60% in mineral oil, 190.3 mg, 4.8 mmol) and trimethylsulfoxonium iodide (1.05 g, 4.80 mmol) and the flask was placed under a nitrogen atmosphere. DMSO (10 mL) was then added dropwise to the flask. After hydrogen evolution ceased, the reaction mixture was stirred for an additional 15 min, during which time the solution became clear. (E)-1-Phenylbut-2-en-1-one (585 mg, 4.0 mmol) was then added in one portion via syringe. The reaction mixture was allowed to stir for 24 h at room temperature. The reaction was then quenched by addition of water, and the mixture extracted three times with Et_2O. The combined organic layers were dried over Na_2SO_4, and volatiles were removed under reduced pressure to yield the crude product as a dark residue. The crude product was purified by bulb-to-bulb distillation (170 °C, 1 Torr) to give 0.506 g (79% yield, 3.16 mmol) as a clear oil. Spectral data were in agreement with those published previously in the literature.[54] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.1 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 2.40 (dt, *J* = 8.1, 4.3 Hz, 1H), 1.61 (dqd, *J* = 8.5, 6.1, 3.9 Hz, 1H), 1.49 (ddd, *J* = 8.4, 4.6, 3.5 Hz, 1H), 1.23 (d, *J* = 6.0 Hz, 3H), 0.90 (ddd, *J* = 7.8, 6.4, 3.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.15, 138.14, 132.59, 128.47, 127.97, 26.41, 21.35, 20.16, 18.33.



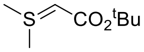


2,2-Dimethylcyclopropyl(phenyl)methanone (2-29): A flame-dried 100 mL flask was charged with solid NaH (60% in mineral oil, 193 mg, 4.8 mmol) and trimethylsulfoxonium iodide (1.06 g, 4.8 mmol) and the flask was placed under a nitrogen atmosphere. DMSO (10 mL) was then added dropwise to the flask. After hydrogen evolution ceased, the reaction mixture was stirred for an additional 15 min, during which the solution became clear. 3-Methyl-1-phenylbut-2-en-1-one (641 mg, 4.0 mmol) was then added in one portion via syringe. The reaction mixture was allowed to stir for 24 h at room temperature. The reaction was then quenched by addition of water and the mixture extracted three times with Et_2O. The combined organic layers were dried over Na_2SO_4, and volatiles were removed under reduced pressure to yield the crude product as a dark residue. The crude product was purified by bulb-to-bulb distillation (180 °C, 1 Torr) to give 0.432 g (62% yield, 2.48 mmol) as a clear oil. Spectral data were in agreement with those published previously in the literature.[55] ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.1 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.47 (t, J = 7.4 Hz, 2H), 2.48 (dd, J = 7.5, 5.6 Hz, 1H), 1.52 (dd, J = 5.6, 4.1 Hz, 1H), 1.36 (s, 2H), 1.09 (s, 2H), 0.96 (dd, J = 7.5, 4.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.60, 139.06, 132.41, 128.46, 127.99, 32.89, 27.07, 26.98, 22.00, 18.50.



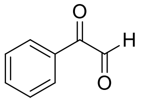
(2-(tert-Butoxy)-2-oxoethyl)dimethylsulfonium bromide (2-30): A 50 mL round-bottomed flask was charged with *tert*-butyl bromoacetate (5.00 g, 25.7 mmol), Acetone (15 mL), and dimethylsulfide (5.1 mL, 69 mmol). The reaction vessel was sealed and placed in the refridgerator overnight, during which the product precipitated. The solid product was then filtered and washed several times with cold acetone and dried under reduced presure to give the product as a white crystalline solid (6.62 g, 25.7 mmol, quant.). The product was used in the subsequent step without further purification or characterization.

(2-(tert-Butoxy)-2-oxoethyl)dimethylsulfonium ylide (2-31): A 25 mL round-bottomed flask



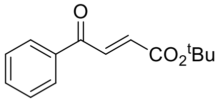
was charged with (2-(tert-butoxy)-2-oxoethyl)dimethylsulfonium bromide (1.82 g, 7.10 mmol) and $CHCl_3$ (8 mL). The reaction mixture was allowed to stir for 5 min until the reaction mixture had become homogeneous. The reaction mixture was cooled to 0 °C and saturated K_2CO_3 (4.6 mL) and aq. NaOH solution (1 mL, 12 M, 7.2 mmol) were added in quick succession with vigorous stirring. The reaction mixture immediately became heterogeneous and the reaction mixture was brought to r.t. and stirred. After 15 min the reaction mixture was filtered, and the top organic layer was separated from the aqueous layer. The aqueous layer was extracted once more with $CHCl_3$. The combined organics were dried over K_2CO_3 and concentrated under reduced pressure to provide the crude product as an off-white solid in quantitative yield (1.25 g, 7.09 mmol), which was used in the subsequent step without further purification. ^1H NMR (400 MHz, $CDCl_3$) δ 2.84 (br s, 1H), 2.73 (s, 6H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.63, 32.78, 30.79, 30.75, 29.27, 29.07.

Phenylglyoxal (2-32): A 500 mL round-bottomed flask was charged with selenium dioxide (18.0

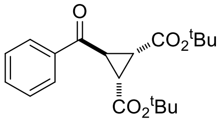


g, 162.2 mmol), EtOH (100 mL), and H_2O (4 mL). The reaction vessel was equipped with a reflux condenser and stirred at 50 °C until the reaction mixture became homogeneous. Acetophenone (18.9 mL, 162 mmol) was then added and the reaction mixture brought to reflux for 12 h. During this time the reaction mixture turned dark red and eventually became colorless again. The hot reaction mixture was then decanted away from precipitated selenium and filtered. The solvent was carefully removed under reduced pressure to give the crude product. Pure phenylglyoxal was obtained by distillation under reduced pressure, collecting the fractions distilling at 90-100 °C. Phenylglyoxal was obtained as a yellow oil which polymerized readily at room temperature (16.3 g, 121.7 mmol, 75% yield). The product was used in subsequent step without further characterization.

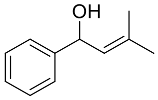
(E)-tert-Butyl 4-oxo-4-phenylbut-2-enoate (2-33): A flame-dried 25 mL round-bottomed flask was charged with phenylglyoxal (0.345 g, 2.57 mmol), *tert*-butoxycarbonylmethylenetriphenylphosphorane (0.968 g, 2.57 mmol), and CH_2Cl_2 (5 mL). The reaction mixture was stirred for 24 h at r.t. under an N_2 atmosphere. The solvent was then stripped under reduced pressure and crude product purified by column chromatography (Et_2O/pentanes) to provide the product as a colorless oil (0.457 g, 1.97 mmol, 77 % yield). Spectral data were in agreement with those reported previously in the literature.[56] ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.2 Hz, 2H), 7.81 (d, *J* = 15.6 Hz, 1H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 6.81 (d, *J* = 15.6 Hz, 1H), 1.54 (s, 9H).



(1R,2S,3S)-tert-Butyl 3-benzoylcyclopropane-1,2-dicarboxylate (2-34): A flame-dried 25 mL round-bottomed flask was charged with (E)-tert-butyl 4-oxo-4-phenylbut-2-enoate (0.464 g, 2.0 mmol), (2-(tert-butoxy)-2-oxoethyl)dimethylsulfonium ylide (0.514 g, 2.92 mmol), and acetone (10 mL). The reaction mixture was fit with a reflux condenser, purged several times with N_2, and stirred at reflux for 6 h. After this time the solvent was stripped under reduced pressure to give the crude product as a yellow oil. Crude product was purified by column chromatography (Et_2O/pentane) to give the pure product as a white crystalline solid (0.425 g, 1.23 mmol, 62% yield). ν_{max} (film) / cm^{-1} 2980, 1726, 1679, 1368, 1301, 1215, 1144. ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.2 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 3.67 (t, *J* = 5.6 Hz, 1H), 2.62 (d, *J* = 5.6 Hz, 2H), 1.48 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.67 , 167.13 , 136.68 , 133.63 , 128.73 , 128.56 , 81.88 , 31.47 , 29.11 , 28.06. HRMS (ESI) calculated for $[C_{20}H_{27}O_5]^+$ {M+H^+) requires 347.1853, found 347.1851. (mp = 100.3-103.3 °C)

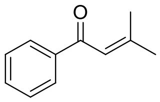


3-Methyl-1-phenylbut-2-en-1-ol (2-35): A flame-dried 250 mL round-bottomed flask was charged with crushed magnesium turnings (0.761 g, 31.4 mmol). The flask was placed under vacuum and magnesium was flame-dried. The flask was backfilled with N_2, THF (55 mL) was added, and the flask sealed with a rubber septum. 1-Bromo-2-methyl-

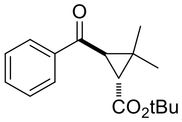


prop-1-ene (4.22 g, 31.2 mmol) was then added to the flask via syringe. Heat was soon evolved and the reaction mixture took on a dark brown color. After all of the magnesium turnings had been consumed (30 min), freshly distilled benzaldehyde (3.0 mL, 29 mmol) was added dropwise via syringe. Reaction was complete after 1 h and quenched by addition of saturated NH_4Cl and diluted with EtOAc. The reaction mixture was transferred to a separatory funnel and the organic layer was washed with saturated $NaHCO_3$ followed by brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to give the crude product as a pale green oil. Crude product was purified by bulb-to-bulb distillation (140 °C, 15 Torr) to give the product as a colorless oil (3.86 g, 23.8 mmol, 82% yield). Spectral data matched those reported previously in the literature.[57] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.32 (m, 4H), 7.29 – 7.23 (m, 1H), 5.47 (d, J = 9.8 Hz, 1H), 5.44 – 5.39 (m, 1H), 1.81 (d, J = 1.1 Hz, 3H), 1.75 (d, J = 1.0 Hz, 3H).

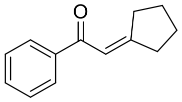
3-Methyl-1-phenylbut-2-en-1-one (2-36): A 250 mL round-bottomed flask was charged with 3-methyl-1-phenylbut-2-en-1-ol (3.86 g, 23.8 mmol), CH_2Cl_2 (150 mL), and activated MnO_2 (20.2 g, 232 mmol). The reaction was then allowed to stir at r.t. for 20 h under open air. The reaction mixture was then filtered through a pad of Celite and the filter cake was washed several times with CH_2Cl_2. The filtrate was then concentrated under reduced pressure to give the crude product as a thick oil. Spectral data matched those reported previously in the literature.[58] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.3 Hz, 2H), 7.45 (t, J = 7.4 Hz, 1H), 7.34 (t, J = 7.5 Hz, 2H), 6.75 (s, 1H), 2.21 (s, 3H), 2.02 (s, 3H).



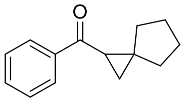
tert-Butyl 3-benzoyl-2,2-dimethylcyclopropanecarboxylate (2-37): A flame-dried 25 mL round-bottomed flask was charged with 3-methyl-1-phenylbut-2-en-1-one (0.34 g, 2.13 mmol), (2-(tert-butoxy)-2-oxoethyl)dimethylsulfonium ylide (0.564 g, 3.2 mmol), and acetone (12 mL). The reaction mixture was fit with a reflux condenser, purged several times with N_2(g), and stirred at reflux for 6 h. After this time the solvent was stripped under reduced pressure to give the crude product as a yellow oil. Crude product was purified by column



chromatography (Et_2O/pentane) to give the pure product as a clear oil (0.24 g, 0.87 mmol, 41% yield). ν_{max} (film) / cm^{-1} 1978, 1720, 1670, 1364, 1150, 1010. ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.1 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 2H), 3.00 (d, *J* = 5.7 Hz, 1H), 2.44 (d, *J* = 5.7 Hz, 1H), 1.39 (m, 12H), 1.08 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.27 , 169.94 , 138.07 , 132.98 , 128.59 , 128.16 , 80.94 , 38.53 , 34.26 , 32.77 , 28.19 , 20.18. HRMS (ESI) calculated for $[C_{17}H_{26}NO_3]^+$ ($M+NH_4^+$) requires 292.1907, found 292.1905.



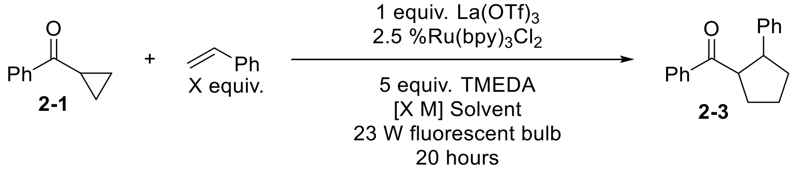
2-Cyclopentylidene-1-phenylethanone (2-38): A 50 mL flame-dried round-bottomed flask was charged with NaH (60 % dispersion in mineral oil, 0.147 g, 3.74 mmol) and dry tetrahydrofuran. The flask was sealed with a rubber septum and purged 3x with N_2(g). To the mixture diethyl (2-oxo-2-phenylethyl)phosphonate (0.898 g, 3.50 mmol) was added dropwise via syringe and the reaction mixture was allowed to stir for 15 min at room temperature. Cyclopentanone (0.282 g, 3.35 mmol) was added via syringe. The reaction flask was then equipped with a reflux condenser stirred at reflux overnight. After this time the reaction mixture was filtered and carefully diluted with Et_2O followed by brine. The aqueous layer was extracted twice more with Et_2O. The combined organics were dried over Na_2SO_4 and concentrated in vacuo to give the crude product as a dark yellow oil. The product was then purified by flash column chromatography (Et_2O/pentanes) to give the final product as a pale yellow oil (0.318 g, 1.71 mmol, 51% yield). The crude product was carried forward without additional purification or characterization. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 6.7 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.0 Hz, 2H), 7.00 (p, *J* = 2.2 Hz, 1H), 2.91 (t, *J* = 6.6 Hz, 2H), 2.56 (t, *J* = 7.0 Hz, 2H), 1.80 (p, *J* = 7.5 Hz, 2H), 1.71 (p, *J* = 6.1 Hz, 2H).



Phenyl(spiro[2.4]heptan-1-yl)methanone (2-39): A flame-dried 100 mL flask was charged with solid NaH (60% in mineral oil, 82.5 mg, 2.05 mmol) and trimethylsulfoxonium iodide (0.451 g, 2.05 mmol) and the flask was placed under a nitrogen atmosphere. DMSO (5 mL) was then added dropwise to the flask. After hydrogen evolution ceased, the reaction mixture was stirred for an additional 15 min, during which the solution became clear. 3-Methyl-1-phenylbut-2-en-1-one (0.318 g, 1.71 mmol) was then added in one portion via syringe. The reaction mixture was allowed to stir for 24 h at room temperature. The reaction was then quenched by addition of water and the mixture extracted three times with Et_2O. The combined organic layers were dried over Na_2SO_4 and volatiles were removed under reduced pressure to yield the crude product as a dark residue. The crude product was purified by flash column chromatography (Et_2O/pentanes) to give the product as a clear oil (0.216 g, 1.08 mmol, 63% yield). v_{max} (film) / cm^{-1} 2942, 1667, 1431, 1390, 1208 ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.1 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 2H), 2.69 (dd, *J* = 7.6, 5.6 Hz, 1H), 2.03 – 1.35 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.95 , 138.98 , 132.42 , 128.47 , 127.86 , 38.64 , 37.35 , 32.45 , 29.82 , 26.09 , 26.03 , 21.89 . HRMS (ESI) calculated for $[C_{14}H_{20}NO]^+$ ($M+NH_4^+$) requires *m/z* 218.1122, found 218.1119.

2.4.3 Optimization data

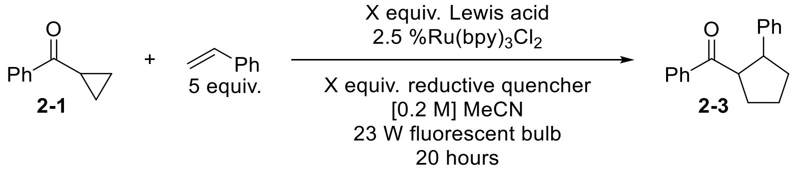
Table 2-4. Initial optimization of solvent and styrene equivalents



Entry	Conditions[a]	% yield[b]	% RSM	dr
1	0.05 M MeCN, 5 equiv. styrene	24 %	58 %	5:1
2	0.1 M MeCN, 5 equiv. styrene	33 %	26 %	7.5:1
3	0.2 M MeCN, 5 equiv. styrene	43.5 %	39 %	17:1
4	0.3 M MeCN, 5 equiv. styrene	38 %	36 %	12:1
5	0.4 M MeCN, 5 equiv styrene	20 %	42 %	12:1
6	0.2 M DMF, 5 equiv. styrene	0 %	99 %	---
7	0.2 M DCM, 5 equiv. styrene	0 %	98 %	---
8	0.2 M EtOAc, 5 equiv. styrene	32 %	61 %	3.5:1
9	0.2 M Acetone, 5 equiv. styrene	0 %	100 %	---
10	0.2 M MeCN, 2 equiv. styrene	35 %	60 %	10:1
11	0.2 M MeCN, 10 equiv. styrene	41 %	53 %	17:1

[a]0.04 mmol cyclopropane. [b]Yields determined by ^{1}H NMR using phenanthrene as internal standard

Table 2-5. Lewis acid and reductive quencher optimization

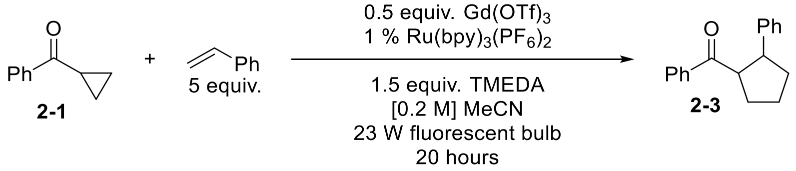


Entry	Conditions[a]	% yield[b]	% RSM	dr
1	1 equiv. La(OTf)$_3$, 5 equiv. TMEDA	56 %	22 %	17:1
2	2 equiv. La(OTf)$_3$, 5 equiv. TMEDA	58 %	21 %	ND
3	1 equiv. Gd(OTf)$_3$, 5 equiv. TMEDA	69 %	12 %	8:1
4	1 equiv. Mg(OTf)$_2$, 5 equiv. TMEDA	0 %	100 %	---
5	1 equiv. LiBF$_4$, 5 equiv. TMEDA	0 %	100 %	---
6	1 equiv. Zn(OTf)$_2$, 5 equiv. TMEDA	0 %	100 %	---
7	1 equiv. Er(OTf)$_3$, 5 equiv. TMEDA	55 %	40 %	4:1
8	1 equiv. GdCl$_3$, 5 equiv. TMEDA	Trace	>95 %	---

9	1 equiv. Gd(acac)$_3$, 5 equiv. TMEDA	Trace	94 %	---
10	2 equiv. Gd(OTf)$_3$, 5 equiv. TMEDA	65 %	7 %	ND
11	1 equiv. Gd(OTf)$_3$, 5 equiv. PMP	7 %	90 %	1:1
12	1 equiv. Gd(OTf)$_3$, 5 equiv. DIPEA	9 %	74 %	2.4:1
13	1 equiv. Gd(OTf)$_3$, 10 equiv. TMEDA	28 %	63 %	ND
14	1 equiv. Gd(OTf)$_3$, 3 equiv. TMEDA	47 %	40 %	ND
15	1 equiv. Gd(OTf)$_3$, 5 equiv. sodium oxalate	6 %	93 %	---
16	0.5 equiv. Gd(OTf)$_3$, 5 equiv. TMEDA	49 %	40 %	7:1
17	0.5 equiv. Gd(OTf)$_3$, 1.5 equiv. TMEDA	69 %	23 %	8:1
18[c]	0.5 equiv. Gd(OTf)$_3$, 1.5 equiv. TMEDA	70 %	20 %	ND
19[d]	0.5 equiv. Gd(OTf)$_3$, 1.5 equiv. TMEDA	71 %	22 %	8:1
20	0.2 equiv. Gd(OTf)$_3$, 1.5 equiv. TMEDA	19 %	75 %	ND
21	0.2 equiv. Gd(OTf)$_3$, 0.6 equiv. TMEDA	27 %	71 %	ND
22	0.5 equiv. Gd(OTf)$_3$, 3 equiv. DIPEA	9 %	88 %	ND
23	0.5 equiv. Gd(OTf)$_3$, 3 equiv. PMP	8 %	91 %	ND
24	0.5 equiv. Gd(OTf)$_3$, 3 equiv. TMEDA	60 %	30 %	5.3:1

[a]0.04 mmol cyclopropane. [b]Yields determined by ^{1}H NMR using phenanthrene as internal standard.
[c]with 100 wt% $MgSO_4$. [d] With 1% [Ru]

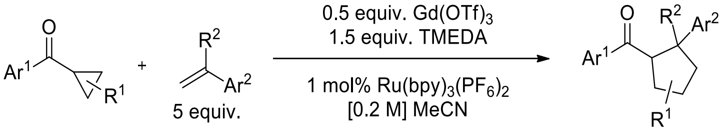
Table 2-6. Control Reactions



Entry	Change from conditions	% yield[a]
1	No photocatalyst	0 %
2	No Lewis acid	0 %
3	No TMEDA	0 %
4	No light	0 %

[a]Yields determined by ^{1}H NMR using phenanthrene as internal standard

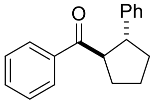
2.4.4 Experimental details for intermolecular [3 + 2] cycloadditions



General procedure:

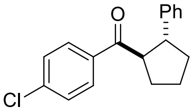
An oven-dried Schlenk tube equipped with a magnetic stir-bar was charged with $Gd(OTf)_3$ (0.5 equivalents). A 2 mL volumetric flask was charged with cyclopropane (1 equiv.), alkene (5 equiv.), $Ru(bpy)_3(PF_6)_2$ (1 mol %), TMEDA (1.5 equiv.) and MeCN (0.2 M concentration). The contents of the volumetric flask were then transferred to the Schlenk tube. The reaction mixture was then thoroughly degassed through three freeze-pump-thaw cycles, then backfilled with N_2. The reaction flask was then placed in front of a 23 W (1380 lumen) compact fluorescent lamp and stirred at room temperature. Upon consumption of starting material, the reaction was diluted with 1:1 Et_2O/pentanes and passed through a short plug of silica. The filtrate was concentrated and the residue purified by column chromatography.

Phenyl(*trans* 2-phenylcyclopentyl)methanone (2-3): Prepared according to general



procedure cyclopropyl phenyl ketone (20.9 mg, 0.143 mmol), styrene (71.2 mg, 0.680 mmol), $Ru(bpy)_3(PF_6)_2$ (2.98 mg, 0.004 mmol), TMEDA (31 μL, 0.21 mmol), $Gd(OTf)_3$ (46.7 mg, 0.135 mmol), and 0.7 mL MeCN. The reaction mixture was then irradiated for 48 hours where complete consumption of starting material was observed. Product was purified by column chromatography using 9:1 pentanes/Et_2O provide phenyl(*trans* 2-phenylcyclopentyl)methanone is a colorless oil (25.8 mg, 0.101 mmol, 71 % yield, 8:1 d.r.). Spectral data agreed with those published previously in the literature.[59]

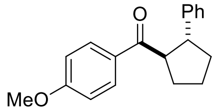
(4-chlorophenyl)(2-phenylcyclopentyl)methanone (2-4): Prepared according to general



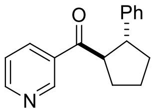
procedure with cyclopropyl(4-chlorophenyl)methanone (100.9 mg, 0.56 mmol), styrene (294.5 mg, 2.83 mmol), $Ru(bpy)_3(PF_6)_2$ (4.9 mg, 0.006 mmol), TMEDA

(194 mg, 1.7 mmol), Gd(OTf)$_3$ (334.9 mg, 0.55 mmol), and 2.2 mL MeCN. The reaction mixture was then irradiated for 48 hours where complete consumption of starting material was observed. Product was purified by column chromatography using 20:1 pentanes/Et$_2$O (4-chlorophenyl)(2-phenylcyclopentyl)methanone as a colorless oil (108.4 mg, 0.381 mmol, 68 % yield, 8:1 d.r.). *Major diastereomer:* ^{1}H-NMR (300 MHz, CDCl$_3$) δ 7.73 (d, 9 Hz, 2H), δ 7.33 (d, 9 Hz, 2H), δ 7.3-7.1 (m, 5H), δ 3.76 (q, 8.7 Hz, 1H), δ 3.6 (q, 8.7 Hz, 1H), δ 2.35-2.15 (m, 2H), 2.05-1.8 (m, 4H); HRMS (ESI) calculated for [$C_{18}H_{21}ClNO$]$^+$ (M+NH$_4^+$) requires *m/z* 302.1306, found 302.1305.

(4-methoxyphenyl)(2-phenylcyclopentyl)methanone (2-5): Prepared according to general procedure with cyclopropyl(4-methoxyphenyl)methanone (100.5 mg, 0.57 mmol), styrene (293.2 mg, 2.83 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.9 mg, 0.006 mmol), TMEDA (194 mg, 1.7 mmol), Gd(OTf)$_3$ (335.0 mg, 0.55 mmol), and 2.2 mL MeCN. The reaction mixture was then irradiated for 48 hours where complete consumption of starting material was observed. Product was purified by column chromatography using 20:1 pentanes/Et$_2$O (4-chlorophenyl)(2-phenylcyclopentyl)methanone as a colorless oil (91.1 mg, 0.32 mmol, 57 % yield, 10:1 d.r.). *Major diastereomer:* ^{1}H-NMR (300 MHz, CDCl$_3$) δ 7.81 (d, 9 Hz, 2H), δ 7.3-7.2 (m, 5H), δ 6.84 (d, 9 Hz, 2H), δ 3.82 (s, 3H), δ 3.77 (q, 7.7 Hz, 1H), δ 3.63 (q, 7.7 Hz, 1H), δ 2.3-2.15 (m, 2H), δ 2-1.8 (m, 4H). HRMS (ESI) calculated for [$C_{19}H_{24}NO_2$]$^+$ (M+NH$_4^+$) requires *m/z* 298.1802, found 298.1800.

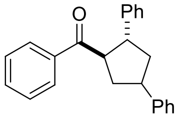


(2-phenylcyclopentyl)(pyridine-3-yl)methanone (2-9): Prepared according to general procedure with cyclopropyl(pyridine-3-yl)methanone (18.3 mg, 0.12 mmol), styrene (67.2 mg, 0.65 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (1.3 mg, 0.002 mmol), TMEDA (25.6 µL, 0.22 mmol), Gd(OTf)$_3$ (43.1 mg, 0.071 mmol), and 0.8 mL MeCN. The reaction mixture was then irradiated for 48 hours where complete consumption of starting material was observed. Product was purified by column chromatography using 4:1 pentanes/Et$_2$O to provide (2-

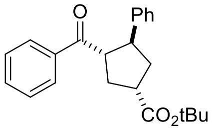


phenylcyclopentyl)(pyridine-3-yl)methanone as a colorless oil (10.0 mg, 0.04 mmol, 35 % yield, 3:1 d.r.). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 9 (d, 1.8 Hz, 1H), δ 8.7 (dd, 4.6, 1.6 Hz, 1H), δ 8 (dt, 8, 1.8 Hz, 1H), δ 7.43 (ddd, 8, 4.6, 0.9 Hz, 1H), δ 7.3-7.2 (m, 5H), δ 3.8 (q, 8.9 Hz, 1H), δ 3.6 (q, 8.9 Hz, 1H), δ 2.33-2.2 (m, 2H), δ 2.1-1.8 (m, 4H). HRMS (ESI) calculated for $[C_{17}H_{18}NO]^+$ $(M+H^+)$ requires *m/z* 252.1383, found 252.1382.

2,4-diphenylcyclopentyl(phenyl)methanone (2-8): *Experiment 1:* Prepared according to

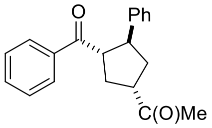


general procedure with phenyl (2-phenylcyclopropyl)methanone (40.1 mg, 0.18 mmol), styrene (92.6 mg, 0.890 mmol), $Ru(bpy)_3(PF_6)_2$ (1.6 mg, 0.002 mmol), TMEDA (35.6 µL, 0.31 mmol), $Gd(OTf)_3$ (54.0 mg, 0.09 mmol), and 0.8 mL MeCN. The reaction mixture was then irradiated for 36 hours where complete consumption of starting material was observed. Product was purified by column chromatography using 9:1 pentanes/Et_2O provide phenyl(*trans* 2-phenylcyclopentyl)methanone is a colorless oil (36.4 mg, 0.11 mmol, 62 % yield, 5:1 d.r.). *Experiment 2:* Prepared according to general procedure with phenyl (2-phenylcyclopropyl)methanone (101.3 mg, 0.46 mmol), styrene (239.3 mg, 2.3 mmol), $Ru(bpy)_3(PF_6)_2$ (3.9 mg, 0.005 mmol), TMEDA (76.5 µL, 0.66 mmol), $Gd(OTf)_3$ (138.7 mg, 0.23 mmol), and 2.0 mL MeCN. The reaction mixture was then irradiated for 36 hours where complete consumption of starting material was observed. Product was purified by column chromatography using 9:1 pentanes/Et_2O provide phenyl(*trans* 2-phenylcyclopentyl)methanone as a colorless oil (111.1 mg, 0.34 mmol, 74 % yield, 5:1 d.r.). *Major diastereomer:* ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.84 (d, 7.77 Hz, 2H), δ 7.49 (t, 7.8 Hz, 1H), δ 7.37 (t, 7.8 Hz, 2H), δ 7.4-7.15 (m, 10H), δ 4.06 (dt, 10.3, 7.4 Hz, 1H), δ 3.95 (q, 7.5, 1H), δ 3.58 (dq, 10.3, 7.4 Hz, 1H), δ 2.6 (dt, 12.3, 7.3, Hz, 1H), δ 2.45-2.5 (m, 2H), δ 2.17 (dt, 12.3, 10.5 Hz, 1H); HRMS (ESI) calculated for $[C_{24}H_{26}NO]^+$ $(M+NH_4^+)$ requires *m/z* 344.2009, found 344.2009.

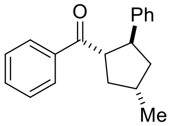


tert-Butyl 3-benzoyl-4-phenylcyclopentanecarboxylate (2-10): Prepared according to general procedure with *trans* tert-butyl 2-benzoylcyclopropanecarboxylate (49.3 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (34.9 mg, 0.300 mmol), $Ru(bpy)_3(PF_6)_2$ (4.3 mg, 0.005 mmol), $Gd(OTf)_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:9, Et_2O/pentanes) providing tert-butyl 3-benzoyl-4-phenylcyclopentanecarboxylate as a white solid (65.9 mg, 0.188 mmol, 94 % yield, 3:1 dr). Major diastereomer: ν_{max} (film) / cm^{-1} 2980, 1722, 1682, 1368, 1265, 1151. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.9 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.28-7.22 (m, 4H), 7.16 (dq, *J* = 9.1, 4.3 Hz, 1H), 3.94 – 3.73 (m, 2H), 3.17 – 3.00 (m, 1H), 2.58 – 2.44 (m, 2H), 2.22 (dt, *J* = 13.3, 9.0 Hz, 1H), 2.13 (dt, *J* = 13.1, 9.0 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.56 , 174.21 , 143.74 , 136.85 , 132.92 , 128.52 , 128.47 , 128.39 , 127.31 , 126.42 , 80.52 , 54.75 , 47.14 , 44.46 , 37.31 , 35.36 , 28.08. M.p. 97.1-98.5 ^{o}C. HRMS (ESI) calculated for $[C_{23}H_{27}O_3]^+$ $(M+H^+)$ requires *m/z* 351.1955, found 351.1955.

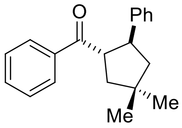
Minor Diastereomer: ν_{max} (film) / cm^{-1} 2981, 1719, 1684, 1365, 1262, 1150. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.28-7.22 (m, 4H), 7.15 (t, *J* = 6.8 Hz, 1H), 3.99 (q, *J* = 9.3 Hz, 1H), 3.68 (dt, *J* = 11.0, 8.4 Hz, 1H), 3.00 (ddd, *J* = 16.6, 9.2, 7.5 Hz, 1H), 2.62 – 2.43 (m, 2H), 2.14 (dt, *J* = 13.2, 8.9 Hz, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.32 , 174.92 , 142.96 , 136.62 , 133.04 , 128.51 , 128.50 , 127.42 , 126.53 , 80.49 , 53.70 , 48.34 , 44.20 , 38.84 , 34.83 , 28.13. M.p. 111.5-113.0^{o}C. HRMS (ESI) calculated for $[C_{23}H_{30}NO_3]^+$ $(M+NH_4^+)$ requires *m/z* 368.2220, found 368.2220.



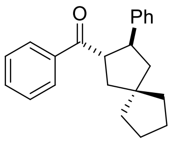
1-(3-Benzoyl-4-phenylcyclopentyl)ethanone (2-11): Reaction was carried out with *trans* 2-benzoylcyclopropylethanone (37.6 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), DIPEA (51.7 mg, 0.400 mmol), 2,6-bis(4,5-dihydrooxazol-2-yl)-N,N-dimethylpyridin-4-amine (78.1 mg, 0.300 mmol), $Ru(bpy)_3(PF_6)_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:15, acetone/pentanes) providing 1-(3-benzoyl-4-phenylcyclopentyl)ethanone as a white solid (21.1 mg, 0.072 mmol, 36% yield, 5:1 dr). ν_{max} (film) / cm^{-1} 2966, 1708, 1683, 1262, 1114. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.72 (d, *J* = 8.6 Hz, 2H), 7.45 – 7.38 (m, 1H), 7.30 (dd, *J* = 8.4, 7.1 Hz, 2H), 7.23 – 7.04 (m, 4H), 6.97 – 6.84 (m, 1H), 3.85 (q, *J* = 8.7 Hz, 1H), 3.60 (q, *J* = 8.7 Hz, 1H), 3.19 (qd, *J* = 8.5, 5.9 Hz, 1H), 2.55 – 2.32 (m, 2H), 2.23 – 2.18 (m, 1H), 2.15 (s, 3H), 2.04 (dt, *J* = 13.3, 9.4 Hz, 1H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 208.91 , 200.61 , 143.46 , 136.73 , 133.00 , 128.59 , 128.49 , 128.40 , 127.27 , 126.55 , 54.47 , 51.45 , 47.51 , 36.23 , 33.80 , 28.41. HRMS (ESI) calculated for $[C_{20}H_{21}O_2]^+$ (M+H$^+$) requires *m/z* 293.1536, found 293.1535.



(4-Methyl-2-phenylcyclopentyl)(phenyl)methanone (2-6): Reaction was carried out according to general procedure with *trans* 2-methylcyclopropyl)(phenyl)methanone (32.0 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (34.9 mg, 0.300 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 24 h. The crude product was purified by column chromatography (1:10, Et$_2$O/pentanes) providing (4-methyl-2-phenylcyclopentyl)(phenyl)methanone as a white solid (49.1 mg, .186 mmol, 93 % yield, 11:1 dr). White solid (mp = 44.9-51 ^{o}C). ν_{max} (film) / cm^{-1} 2957, 2868, 1681, 1602, 1451, 1266, 1012. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.74 (d, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.24 – 7.11 (m, 4H), 7.13 – 7.00 (m, 1H), 3.90 – 3.69 (m, 2H), 2.48 – 2.22 (m, 2H), 2.02 (dt, *J* = 15.2, 7.8 Hz, 1H), 1.82 (ddd, *J* = 13.0, 8.8, 7.2 Hz, 1H), 1.55 – 1.43 (m, 1H), 1.03 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 201.90 , 145.50 , 132.80 , 128.55 , 128.44 , 128.41 , 127.37 , 127.30 , 126.07 , 55.96 , 46.89 , 42.50 , 41.01 , 34.44 , 20.78. HRMS (ESi) calculated for $[C_{19}H_{24}O]^+$ (M+NH$_4^+$) requires *m/z* 282.1852, found 282.1853.

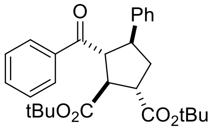


(4,4-Dimethyl-2-phenylcyclopentyl)(phenyl)methanone (2-7): Reaction was carried out according to general procedure with (2,2-dimethylcyclopropyl)(phenyl)methanone (34.8 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (34.9 mg, 0.300 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:10, Et$_2$O/pentanes) providing (4,4-dimethyl-2-phenylcyclopentyl)(phenyl)methanone as a white solid (52.3 mg, 0.188 mmol, 94% yield, 2:1 dr). Major diastereomer: White solid (mp = 105.3-107.8 ^{o}C). v_{max} (film) / cm^{-1} 2941, 2863, 1678, 1448, 1283, 1015. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.29 – 7.18 (m, 4H), 7.12 (t, *J* = 7.0 Hz, 1H), 4.04 – 3.84 (m, 2H), 2.12 (dd, *J* = 13.0, 9.2 Hz, 1H), 2.04 (dd, *J* = 12.7, 6.8 Hz, 1H), 1.86 (t, *J* = 11.9 Hz, 1H), 1.73 (dd, *J* = 13.1, 7.8 Hz, 1H), 1.21 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 201.72 , 144.08 , 137.00 , 132.80 , 128.43 , 128.38 , 127.39 , 126.15 , 54.88 , 49.42 , 46.79 , 46.76 , 39.02 , 30.59 , 29.55 . HRMS (ESI) calculated for [C$_{20}$H$_{23}$O]$^{+}$ (M+H^{+}) requires *m/z* 279.1743, found 279.1743. Minor Diastereomer: White solid (mp = 71.6-73.4 ^{o}C). v_{max} (film) / cm^{-1} 2953, 1927, 2866, 1679, 1463, 1448, 1367, 1221. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.33 – 7.06 (m, 5H), 3.98 (q, *J* = 9.3 Hz, 1H), 3.62 (ddd, *J* = 11.3, 9.4, 7.6 Hz, 1H), 3.02 (ddd, *J* = 16.5, 9.2, 7.3 Hz, 1H), 2.63 – 2.38 (m, 2H), 2.25 – 2.00 (m, 2H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 202.23 , 142.11 , 136.99 , 132.03 , 128.46 , 127.96 , 127.93 , 127.71 , 125.98 , 50.97 , 48.93 , 48.45 , 43.26 , 38.47 , 29.40 , 28.53. HRMS (ESI) calculated for [C$_{20}$H$_{23}$O]$^{+}$ (M+H^{+}) requires *m/z* 279.1743, found 279.1741.



Phenyl(3-phenylspiro[4.4]nonan-2-yl)methanone (2-12): Reaction was carried out according to general procedure with phenyl(spiro[2.4]heptan-1-yl)methanone (40.1 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (34.9 mg, 0.300 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (60.5 mg, 0.100 mmol), and

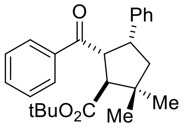
MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:30, Et_2O/pentanes) providing phenyl(3-phenylspiro[4.4]nonan-2-yl)methanone as a white solid (51.1 mg, 0.168 mmol, 84 % yield, 1:1 dr) Major Diastereomer: Colorless oil. ν_{max} (film) / cm^{-1} 2945, 2858, 1680, 1448, 1216. ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.1 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.32 – 7.18 (m, 4H), 7.13 (t, *J* = 6.9 Hz, 1H), 3.97 – 3.82 (m, 2H), 2.21 (dd, *J* = 12.9, 9.6 Hz, 1H), 2.12 (dd, *J* = 12.6, 6.5 Hz, 1H), 2.02 – 1.88 (m, 1H), 1.83 (dd, *J* = 12.9, 6.9 Hz, 1H), 1.77 – 1.49 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.76 , 144.22 , 136.98 , 132.77 , 128.44 , 128.42 , 128.36 , 127.38 , 126.13 , 54.64 , 50.57 , 47.52 , 46.91 , 44.98 , 40.28 , 39.78 , 24.40 , 24.34. HRMS (ESI) calculated for $[C_{22}H_{25}O]^+$ (M+H$^+$) requires *m/z* 305.1900, found 305.1899. Minor Diastereomer: Colorless oil. ν_{max} (film) / cm^{-1} 2950, 2863, 1679, 1448, 1220, 1023. ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.3 Hz, 1H), 7.29 – 7.18 (m, 2H), 6.97 (7.02 – 6.90 (m, 5H), 4.34 – 4.21 (m, 1H), 3.71 (td, *J* = 10.4, 7.6 Hz, 1H), 2.39 (dd, *J* = 13.0, 9.0 Hz, 1H), 2.16 – 1.97 (m, 2H), 1.90 – 1.47 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.33, 142.17, 138.18, 132.06, 128.39, 127.97, 127.96, 127.72, 125.97, 50.89, 49.81, 48.59, 46.82, 41.52, 39.26, 38.89, 24.81, 24.66. HRMS (ESI) calculated for $[C_{22}H_{25}O]^+$ (M+H$^+$) requires *m/z* 305.1900, found 305.1900.



Di-tert-butyl 3-benzoyl-4-phenylcyclopentane-1,2-dicarboxylate (2-14): Reaction was carried out according to general procedure with (1R,2S,3s)-di-tert-butyl 3-benzoylcyclopropane-1,2-dicarboxylate (69.3 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (34.9 mg, 0.300 mmol), $Ru(bpy)_3(PF_6)_2$ (4.3 mg, 0.005 mmol), $Gd(OTf)_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:5, Et_2O/pentanes) to give tert-butyl 5-benzoyl-2,2-dimethyl-4-phenylcyclopentanecarboxylate as a white solid (84.7 mg, 0.188 mmol, 94% yield, 1.3:1 dr). Major Diastereomer: White solid (mp = 96-97 ^oC). ν_{max} (film) / cm^{-1} 2977, 1724, 1681, 1393, 1368, 1257, 1158. ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J*

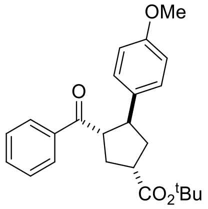
= 7.7 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.29 (t, *J* = 7.7 Hz, 2H), 7.24-7.2 (m, 4H), 7.14 (dq, *J* = 8.2, 5.5, 4.8 Hz, 1H), 4.17 (t, *J* = 9.5 Hz, 1H), 3.64 (dt, *J* = 25.1, 8.8 Hz, 2H), 3.36 (dq, *J* = 9.3, 5.5 Hz, 1H), 2.51 (ddd, *J* = 13.4, 8.1, 5.5 Hz, 1H), 2.27 (dt, *J* = 13.2, 9.8 Hz, 1H), 1.49 (s, 9H), 1.25 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.49 , 173.03 , 172.54 , 141.91 , 137.22 , 132.93 , 128.59 , 128.40 , 128.29 , 127.20 , 126.81 , 81.21 , 80.89 , 57.00 , 53.04 , 49.76 , 47.34 , 37.16 , 28.05 , 27.78. HRMS (ESI) calculated for [$C_{28}H_{35}O_5$] (M+H$^+$) requires 451.2479, found 451.2479. <u>Minor Diastereomer:</u> White solid (mp = 83.7-85.1 ^{o}C). v_{max} (film) / cm^{-1} 2978, 2936, 1725, 1680, 1367, 1257, 1154. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.0 Hz, 2H), 7.46 – 7.33 (m, 1H), 7.27 – 7.23 (m, 2H), 7.07 – 6.91 (m, 5H), 4.50 (dd, *J* = 10.0, 7.7 Hz, 1H), 3.93 (dd, *J* = 10.3, 7.7 Hz, 1H), 3.70 (td, *J* = 10.0, 7.3 Hz, 1H), 3.10 (td, *J* = 10.5, 7.9 Hz, 1H), 2.57 – 2.36 (m, 2H), 1.53 (s, 9H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.61, 132.42, 128.32, 128.07, 128.05, 127.94, 126.59, 53.83, 48.52, 48.27, 36.85, 28.15, 28.08. HRMS (ESI) calculated for [$C_{28}H_{35}O_5$] (M+H$^+$) requires 451.2479, found 451.2478.

tert-Butyl 5-benzoyl-2,2-dimethyl-4-phenylcyclopentanecarboxylate (2-13): Reaction was



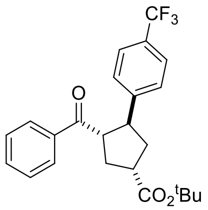
carried out according to general procedure with tert-butyl 3-benzoyl-2,2-dimethylcyclopropanecarboxylate (54.9 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (34.9 mg, 0.300 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. Product was purified by column chromatography (1:10, Et_2O/pentanes) to give tert-butyl 5-benzoyl-2,2-dimethyl-4-phenylcyclopentanecarboxylate as a white solid (74.2 mg, 0.196 mmol, 97% yield, 20:1 dr). White solid (mp = 134.7-138.5 ^{o}C). v_{max} (film) / cm^{-1} 2960, 1722, 1667, 1369, 1153. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.1 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.28 (t, *J* = 8.1 Hz, 4H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H), 4.37 (dd, *J* = 10.2, 8.1 Hz, 1H), 3.68 (td, *J* = 10.5, 8.4 Hz, 1H), 2.86 (d, *J* = 8.1 Hz, 1H), 2.15 – 1.94 (m, 2H), 1.40 (s, 9H), 1.28 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.86 , 173.23 , 142.94 , 137.18 , 132.79 , 128.47 (d, J = 6.8 Hz), 128.22 , 127.58 , 126.46 , 80.96 , 59.98 , 57.17 , 49.51 , 47.24 , 42.31 , 30.24 , 28.09 , 26.41 . HRMS (ESI) calculated for $[C_{25}H_{31}O_3]^+$ (M+H$^+$) requires *m/z* 379.2268, found 379.2268.

***tert*-Butyl 3-benzoyl-4-(4-methoxyphenyl)cyclopentanecarboxylate (2-15):** Reaction was

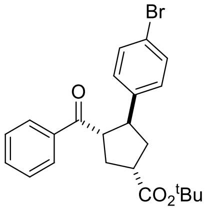


carried out according to general procedure with *trans* tert-butyl 2-benzoylcyclopropanecarboxylate (49.6 mg, 0.201 mmol), 4-methoxystyrene (139.0 mg, 1.04 mmol), TMEDA (34.9 mg, 0.300 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.2 mg, 0.005 mmol), Gd(OTf)$_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:29, acetone/pentanes) providing *tert*-butyl 3-benzoyl-4-(4-methoxyphenyl)cyclopentanecarboxylate as a white solid (65 mg, 0.170 mmol, 85 % yield, 3:1 dr). Major diastereomer: White solid (mp = 95.5 – 98.5 °C). ν_{max} (film) / cm^{-1} 2975, 1721, 1679, 1612, 1513, 1448, 1366, 1246, 1149, 1035, 1012, 829, 701. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.81 (d, J = 6.9 Hz, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.37 (t, J = 7.8 Hz, 2H), 7.15 (d, J = 8.7 Hz, 2H), 6.78 (d, J = 8.6 Hz, 2H), 3.82 (td, J = 9.5, 8.0 Hz, 1H), 3.77 – 3.71 (m, 1H), 3.75 (s, 3H), 3.07 (qd, J = 8.4, 5.7 Hz, 1H), 2.54 – 2.43 (m, 2H), 2.21 (ddd, J = 13.2, 9.8, 8.3 Hz, 1H), 2.08 (dt, J = 13.3, 9.1 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 200.72, 174.30, 158.12, 136.92, 135.69, 132.90, 128.47, 128.39, 128.23, 113.90, 80.46, 55.24, 54.88, 46.54, 44.30, 37.40, 35.27, 28.08. HRMS (ESI) calculated for $[C_{24}H_{29}O_4]^+$ (M+H$^+$) requires *m/z* 381.2060, found *m/z* 381.2053. Minor diastereomer: White solid (mp = 110.5 – 113.5 °C_. ν_{max} (film) / cm^{-1} 2975, 1723, 1680, 1514, 1448, 1367, 1249, 1220, 1152, 1036, 830, 701. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.82 (d, J = 7.2 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.37 (t, J = 7.7 Hz, 2H), 7.18 (d, J = 8.6 Hz, 2H), 6.78 (d, J = 8.7 Hz, 2H), 3.93 (q, J = 9.4 Hz, 1H), 3.74 (s, 3H), 3.69 – 3.54 (m, 1H), 2.99 (ddd, J = 16.6, 9.3, 7.3 Hz, 1H), 2.54 – 2.41 (m, 2H), 2.18 – 2.01 (m, 2H), 1.48 (s, 15H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 201.51, 175.01, 158.20, 136.69, 134.93, 133.01, 128.49, 128.49, 128.34, 113.89, 80.46, 55.24, 53.85, 47.74, 44.11, 38.92, 34.76, 28.14. HRMS (ESI) calculated for $[C_{24}H_{32}NO_4]^+$ $(M+NH_4^+)$ requires *m/z* 398.2326, found *m/z* 398.2322.

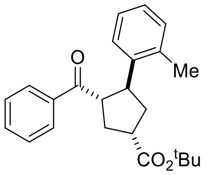
***tert*-Butyl 3-benzoyl-4-(4-trifluoromethylphenyl)cyclopentanecarboxylate (2-16):** Reaction was carried out according to general procedure with *trans* tert-butyl 2-benzoylcyclopropanecarboxylate (50.0 mg, 0.203 mmol), 4-trifluoromethylstyrene (172.5 mg, 1.000 mmol), TMEDA (34.9 mg, 0.300 mmol), $Ru(bpy)_3(PF_6)_2$ (4.8 mg, 0.006 mmol), $Gd(OTf)_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:49 acetone/pentanes) providing *tert*-butyl 3-benzoyl-4-(4-trifluoromethylphenyl)cyclopentanecarboxylate as a white solid (50 mg, 0.119 mmol, 59% yield, 1.3:1 dr). <u>Major diastereomer</u>: White solid. (mp = 106.9 – 108.4 °C). ν_{max} (film) / cm^{-1} 2978, 1724, 1682, 1619, 1449, 1368, 1326, 1258, 1156, 1124, 1069, 1017, 842, 701. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.1 Hz, 2H), 7.55 – 7.47 (m, 3H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 3.93 – 3.81 (m, 2H), 3.15 – 3.07 (m, 1H), 2.55 (qd, *J* = 8.2, 4.1 Hz, 2H), 2.19 (ddd, *J* = 13.1, 9.5, 8.0 Hz, 1H), 2.12 (dt, *J* = 13.5, 9.2 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.89, 173.95, 147.72, 136.59, 133.17, 128.75 (q, *J* = 32.5 Hz), 128.59, 128.35, 127.70, 125.45 (q, *J* = 3.9 Hz), 124.47 (q, *J* = 272.9 Hz), 80.73, 54.76, 46.57, 44.28, 37.02, 35.45, 28.05. ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.46. HRMS (ESI) calculated for $[C_{24}H_{26}F_3O_3]^+$$(M+H^+)$ requires *m/z* 419.1829, found *m/z* 419.1826. <u>Minor diastereomer</u>: White solid (mp = 122.8 – 125.9 °C). ν_{max} (film) / cm^{-1} 2974, 1722, 1677, 1369, 1327, 1281, 1247, 1225, 1164, 1138, 1170, 1018, 842, 699. ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.1 Hz, 2H), 7.57 – 7.46 (m, 3H), 7.40 (t, *J* = 7.5 Hz, 4H), 3.98 (q, *J* = 9.4 Hz, 1H), 3.83 – 3.71 (m, 1H), 3.01 (ddd, *J* = 16.4, 9.2, 7.3 Hz, 1H), 2.60 – 2.48 (m, 2H), 2.20 – 2.06 (m, 2H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.62, 174.73, 147.10, 136.36, 133.29, 128.80 (q, *J* = 31.1 Hz), 128.62, 128.45, 127.82, 125.44 (q, *J* = 3.7 Hz), 124.16 (q, *J* = 271.3), 80.72, 53.75, 47.67, 44.03, 38.34, 34.99, 28.11. ^{19}F NMR (377 MHz,



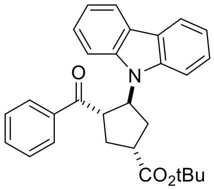
$CDCl_3$) δ –62.47. HRMS (ESI) calculated for $[C_{24}H_{29}F_3NO_3]^+$(M+NH_4^+) requires *m/z* 436.2095, found *m/z* 436.2093.



***tert*-Butyl 3-benzoyl-4-(4-bromophenyl)cyclopentanecarboxylate (2-17):** Reaction was carried out according to general procedure with *trans* tert-butyl 2-benzoylcyclopropanecarboxylate (49.6 mg, 0.201 mmol), 4-bromostyrene (181.5 mg, 0.991 mmol), TMEDA (34.9 mg, 0.300 mmol), $Ru(bpy)_3(PF_6)_2$ (4.3 mg, 0.005 mmol), $Gd(OTf)_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:29, acetone/pentanes) providing *tert*-butyl 3-benzoyl-4-(4-bromophenyl)cyclopentanecarboxylate as a white solid (51 mg, 0.118 mmol, 59% yield, 1:1 dr). Major Diastereomer: White solid (mp = 103.1 – 104.4 °C). ν_{max} (film) / cm^{-1} 2976, 1722, 1681, 1490, 1448, 1366, 1257, 1150, 1074, 1010, 848, 821, 701. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.3 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.42 – 7.34 (m, 4H), 7.12 (d, *J* = 8.4 Hz, 2H), 3.83 – 3.74 (m, 2H), 3.08 (qd, *J* = 8.2, 5.7 Hz, 1H), 2.57 – 2.45 (m, 2H), 2.23 – 2.13 (m, 1H), 2.07 (dt, *J* = 13.4, 9.2 Hz, 1H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.16, 174.05, 142.62, 136.69, 133.11, 131.56, 129.10, 128.57, 128.35, 120.13, 80.65, 54.77, 46.40, 44.26, 37.09, 35.41, 28.06. HRMS (ESI) calculated for $[C_{23}H_{26}BrO_3]^+$(M+H^+) requires *m/*z 429.1060, found *m/z* 429.1074. Minor Diastereomer: White solid (mp = 129.1 – 132.8 °C). ν_{max} (film) / cm^{-1} 2975, 1722, 1680, 1490, 1448, 1367, 1284, 1246, 1220, 1152, 1074, 1011, 823, 700. ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.3 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.44 – 7.32 (m, 4H), 7.15 (d, *J* = 8.4 Hz, 2H), 3.92 (q, *J* = 9.4 Hz, 1H), 3.65 (ddd, *J* = 11.3, 9.5, 7.6 Hz, 1H), 2.99 (ddd, *J* = 16.5, 9.3, 7.3 Hz, 1H), 2.50 (ddd, *J* = 13.3, 9.8, 6.8 Hz, 2H), 2.17 – 2.02 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.92, 174.82, 141.95, 136.47, 133.23, 131.56, 129.20, 128.60, 128.46, 120.25, 80.64, 53.74, 47.56, 44.03, 38.46, 34.93, 28.12. HRMS (ESI) calculated for $[C_{23}H_{29}BrNO_3]^+$(M+NH_4^+) requires *m/z* 446.1326, found *m/z* 446.1313.

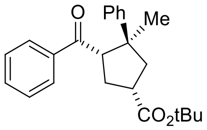


***tert*-Butyl 3-benzoyl-4-(2-methylphenyl)cyclopentanecarboxylate (2-18):** Reaction was carried out with according to general procedure *trans* tert-butyl 2-benzoylcyclopropanecarboxylate (49.2 mg, 0.200 mmol), 2-methylstyrene (118.2 mg, 1.000 mmol), TMEDA (34.9 mg, 0.300 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.4 mg, 0.005 mmol), Gd(OTf)$_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:49 Et$_2$O/pentanes) providing *tert*-butyl 3-benzoyl-4-(2-methylphenyl)cyclopentanecarboxylate as a colorless oil (62 mg, 0.170 mmol, 85% yield, 1.7:1 d.r). Major Diastereomer: White solid (mp = 70.7 – 74.1 °C). v$_{max}$ (film) / cm^{-1} 2975, 1723, 1681, 1448, 1367, 1218, 1149, 1101, 848, 753, 700. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.81 (d, *J* = 7.3 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.26 (d, *J* = 7.7 Hz, 1H), 7.16 (dt, *J* = 7.9, 4.3 Hz, 2H), 7.10 – 7.01 (m, 3H), 4.08 – 3.92 (m, 3H), 3.09 (td, *J* = 8.5, 6.5 Hz, 2H), 2.59 – 2.45 (m, 3H), 2.31 (s, 3H), 2.24 (dt, *J* = 13.1, 8.8 Hz, 1H), 1.96 (dt, *J* = 13.3, 8.5 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 200.83, 174.40, 142.30, 136.88, 136.65, 133.05, 130.57, 128.60, 128.49, 126.38, 126.28, 125.49, 80.60, 54.16, 44.80, 43.00, 37.70, 35.29, 28.21, 20.00. HRMS (ESI) calculated for $[C_{24}H_{29}O_3]^+$(M+H$^+$) requires *m/z* 365.2111, found *m/z* 365.2105. Minor Diastereomer: Colorless oil. v$_{max}$ (film) / cm^{-1} 2976, 1723, 1680, 1448, 1367, 1290, 1216, 1151, 848, 575, 700. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.81 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.41 – 7.31 (m, 3H), 7.23 – 7.12 (m, 1H), 7.10 – 7.01 (m, 2H), 4.09 (q, *J* = 9.0 Hz, 1H), 3.88 (dt, *J* = 11.0, 8.3 Hz, 1H), 3.01 (p, *J* = 8.9 Hz, 1H), 2.51 (dq, *J* = 13.5, 7.3 Hz, 2H), 2.28 (s, 3H), 2.23 – 2.12 (m, 1H), 2.05 – 1.91 (m, 1H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 201.48, 174.93, 141.45, 136.53, 136.33, 133.01, 130.31, 128.46, 128.46, 126.42, 126.20, 125.81, 80.45, 53.47, 44.43, 43.81, 39.39, 34.61, 28.13, 19.83.HRMS (ESI) calculated for $[C_{24}H_{32}NO_3]^+$(M+NH$_4^+$) requires *m/z* 382.2377, found *m/z* 382.2372.



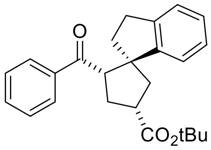
tert-Butyl 3-benzoyl-4-(9H-carbazol-9-yl)cyclopentanecarboxylate (2-22): Reaction was carried out according to general procedure with *trans* tert-butyl 2-benzoylcyclopropanecarboxylate (50.1 mg, 0.203 mmol), 9-vinylcarbazole (195.0 mg, 1.010 mmol), TMEDA (34.9 mg, 0.300 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.5 mg, 0.005 mmol), Gd(OTf)$_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:29, acetone/pentanes) providing tert-butyl 3-benzoyl-4-(9H-carbazol-9-yl)cyclopentanecarboxylate as a white foam (68 mg, 0.155 mmol, 76% yield, 1.6:1 dr). Major diastereomer: Colorless oil. v_{max} (film) / cm^{-1}2976, 1724, 1682, 1597, 1484, 1453, 1367, 1337, 1227, 1154, 847, 750, 724, 698. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (d, *J* = 7.7 Hz, 2H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.57 (d, *J* = 8.3 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.14 (m, 4H), 5.94 (q, *J* = 9.1 Hz, 1H), 4.66 (q, *J* = 9.1 Hz, 1H), 3.40 (p, *J* = 8.1 Hz, 1H), 2.85 – 2.57 (m, 3H), 2.38 (dt, *J* = 13.3, 9.1 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 199.53, 173.42, 139.31, 136.18, 133.14, 128.39, 128.26, 125.66, 123.41, 120.39, 119.08, 109.76, 81.12, 56.17, 49.49, 44.09, 34.36, 31.36, 28.10. HRMS (ESI) calculated for [C$_{29}$H$_{30}$NO$_3$]$^+$(M+H$^+$) requires *m/z* 440.2220, found *m/z* 440.2217. Minor diastereomer: Colorless oil. v_{max} (film) / cm^{-1} 2977, 1722, 1681, 1597, 1484, 1453, 1367, 1337, 1221, 1151, 750, 724, 699. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.05 (d, *J* = 7.7 Hz, 2H), 7.71 (d, *J* = 7.2 Hz, 2H), 7.49 – 7.35 (m, 3H), 7.41 (s, 0H), 7.28 – 7.17 (m, 5H), 5.81 (dt, *J* = 11.0, 8.5 Hz, 1H), 4.85 – 4.74 (m, 1H), 3.09 (dt, *J* = 15.9, 7.8 Hz, 1H), 2.97 – 2.84 (m, 1H), 2.76 (ddd, *J* = 13.5, 9.9, 7.7 Hz, 1H), 2.51 (dt, *J* = 13.3, 8.1 Hz, 1H), 2.30 (dt, *J* = 14.0, 7.6 Hz, 1H), 1.52 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 200.20, 174.24, 139.40, 135.75, 133.31, 128.49, 128.47, 125.71, 123.40, 120.34, 119.11, 109.90, 81.07, 56.75, 47.76, 42.78, 33.31, 32.53, 28.15. HRMS (ESI) calculated for [C$_{29}$H$_{30}$NO$_3$]$^+$(M+H$^+$) requires *m/z* 440.2220, found *m/z* 440.2217.

***tert*-Butyl 3-benzoyl-4-(4-methylphenyl)cyclopentanecarboxylate (2-19):** Reaction was carried out according to general procedure with *trans* tert-butyl 2-benzoylcyclopropanecarboxylate (50.3 mg, 0.204 mmol), α-methylstyrene (120.5 mg, 1.019 mmol), TMEDA (34.9 mg, 0.300 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.4 mg, 0.005 mmol), Gd(OTf)$_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (neat toluene to 1:9 acetone/toluene) providing *tert*-butyl 3-benzoyl-4-(4-methylphenyl)cyclopentanecarboxylate as a colorless oil (66 mg, 0.181 mmol, 89% yield, 2.0:1 d.r.). Major Diastereomer: White solid (mp = 74.2 – 79.5 °C). ν_{max} (film) / cm^{-1} 2977, 1675, 1597, 1447, 1367, 1285, 1253, 848, 732, 700. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.52 (d, *J* = 7.0 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.31 – 7.16 (m, 7H), 4.09 (dd, *J* = 9.8, 6.7 Hz, 1H), 3.08 (dt, *J* = 18.3, 9.3 Hz, 1H), 2.63 (dt, *J* = 13.3, 10.0 Hz, 1H), 2.53 (dd, *J* = 13.7, 9.2 Hz, 1H), 2.29 – 2.14 (m, 2H), 1.49 (s, 9H), 1.26 (s, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 201.35, 174.34, 148.87, 137.78, 132.57, 128.39, 128.38, 128.15, 126.15, 125.88, 80.38, 57.65, 49.53, 45.42, 43.63, 32.71, 28.14, 24.30. HRMS (ESI) calculated for $[C_{24}H_{29}O_3]^+$(M+H$^+$) requires *m/z* 365.2112, found *m/z* 365.2115. Minor Diastereomer: Colorless oil. ν_{max} (film) / cm^{-1} 2977, 1724, 1676, 1449, 1369, 1258, 1222, 1154, 1086, 1026, 803, 700. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.49 (d, *J* = 7.1 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.25 – 7.09 (m, 5H), 4.17 (t, *J* = 8.7 Hz, 1H), 3.17 (qd, *J* = 9.0, 5.6 Hz, 1H), 2.68 – 2.57 (m, 2H), 2.28 (ddd, *J* = 13.9, 8.6, 5.6 Hz, 1H), 2.17 (dd, *J* = 13.1, 8.2 Hz, 1H), 1.49 (s, 9H), 1.30 (s, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 201.56, 175.76, 147.07, 137.78, 132.47, 128.29, 128.23, 128.05, 126.21, 126.19, 80.42, 56.74, 50.65, 46.99, 42.29, 32.17, 28.15, 22.14. HRMS (ESI) calculated for $[C_{24}H_{32}NO_3]^+$(M+NH$_4^+$) requires *m/z* 382.2377, found *m/z* 382.2376.

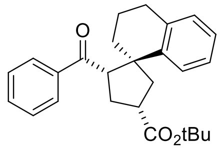


tert-Butyl 2-benzoyl-2',3'-dihydrospiro[cyclopentane-1,1'-indene]-4-carboxylate (2-20):

Reaction was carried out according to general procedure with *trans* tert-butyl 2-benzoylcyclopropanecarboxylate (48.8 mg, 0.198 mmol), 1-methylene-2,3-



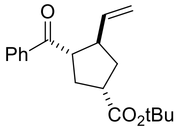
dihydro-1H-indene (130.2 mg, 1.000 mmol), TMEDA (34.9 mg, 0.300 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.2 mg, 0.005 mmol), Gd(OTf)$_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 24 h. The crude product was purified by column chromatography (1:49 acetone/pentanes) providing tert-butyl 2-benzoyl-2',3'-dihydrospiro[cyclopentane-1,1'-indene]-4-carboxylate as a colorless oil (58 mg, 0.154 mmol, 78% yield, 1.4:1 dr). <u>Major diastereomer</u>: Colorless oil. v_{max} (film) / cm^{-1} 2975, 2935, 1724, 1672, 1478, 1448, 1392, 1367, 1225, 1151, 1002, 849, 756, 732, 691. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.49 (d, *J* = 7.0 Hz, 2H), 7.40 – 7.32 (m, 2H), 7.26 (m, 3H), 7.17 (t, *J* = 7.8 Hz, 2H), 7.09 (t, *J* = 7.3 Hz, 1H), 6.93 (d, *J* = 6.9 Hz, 1H), 3.91 (dd, *J* = 10.4, 6.9 Hz, 1H), 3.06 (dt, *J* = 17.3, 8.3 Hz, 1H), 2.73 – 2.60 (m, 2H), 2.44 (dd, *J* = 13.3, 9.1 Hz, 1H), 2.38 – 2.22 (m, 4H), 1.93 – 1.83 (m, 1H), 1.48 (s, 9H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 201.23, 174.36, 149.28, 143.69, 137.38, 132.57, 128.16, 128.02, 127.08, 126.62, 124.69, 122.27, 80.35, 59.06, 56.04, 44.49, 43.23, 36.75, 33.47, 30.97, 28.12. HRMS (ESI) calculated for [C$_{25}$H$_{29}$O$_3$]$^+$(M+H$^+$) requires *m/z* 377.2111, found *m/z* 377.2107. <u>Minor diastereomer</u>: Colorless oil. v_{max} (film) / cm^{-1} 2976, 2932, 1720, 1671, 1448, 1367, 1220, 1150, 908, 846, 729, 690. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.49 – 7.41 (m, 3H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.26 – 7.18 (m, 1H), 7.11 (t, *J* = 7.8 Hz, 2H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.5 Hz, 1H), 4.05 (t, *J* = 8.7 Hz, 1H), 3.11 (tdd, *J* = 9.9, 7.6, 6.1 Hz, 1H), 2.71 (dt, *J* = 13.6, 9.7 Hz, 1H), 2.67 – 2.57 (m, 1H), 2.54 (dd, *J* = 12.8, 9.8 Hz, 1H), 2.47 – 2.25 (m, 2H), 2.27 – 2.09 (m, 2H), 1.76 (dt, *J* = 12.4, 8.9 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 201.42, 175.61, 147.06, 143.90, 137.16, 132.45, 128.14, 127.82, 127.19, 126.54, 124.57, 122.60, 80.39, 60.28, 55.35, 46.18, 42.58, 34.90, 31.96, 30.78, 28.17. HRMS (ESI) calculated for [C$_{25}$H$_{32}$NO$_3$]$^+$(M+NH$_4$$^+$) requires *m/z* 394.2377, found *m/z* 394.2374.



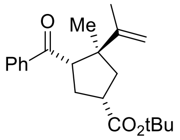
tert-Butyl 2-benzoyl-3',4'-dihydro-2'H-spiro[cyclopentane-1,1'-naphthalene]-4-carboxylate (2-21): Reaction was carried out according to general procedure with *trans* tert-butyl 2-benzoylcyclopropanecarboxylate (50.0 mg, 0.203

mmol), 1-methylene-1,2,3,4-tetrahydronaphthalene (145.0 mg, 1.005 mmol), TMEDA (34.9 mg, 0.300 mmol), $Ru(bpy)_3(PF_6)_2$ (4.4 mg, 0.005 mmol), $Gd(OTf)_3$ (60.5 mg, 0.100 mmol), and MeCN (2 mL total volume). The reaction was complete after 6 h. The crude product was purified by column chromatography (1:49 acetone/pentanes) providing tert-butyl 2-benzoyl-3',4'-dihydro-2'H-spiro[cyclopentane-1,1'-naphthalene]-4-carboxylate as a colorless oil (69 mg, 0.177 mmol, 87% yield, 1.1:1 dr). <u>Major Diastereomer</u>: White solid (mp = 104.0 – 106.8 °C). ν_{max} (film) / cm^{-1} 2974, 2936, 1724, 1673, 1447, 1366, 1254, 1230, 1152, 754, 720, 691. ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.9 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.27 (d, *J* = 6.2 Hz, 1H), 7.14 (t, *J* = 7.8 Hz, 2H), 7.10 (t, *J* = 7.7 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 4.16 (dd, *J* = 11.6, 6.4 Hz, 1H), 3.10 (dtd, *J* = 11.6, 9.3, 7.2 Hz, 1H), 2.72 (q, *J* = 11.8 Hz, 1H), 2.57 (dt, *J* = 16.5, 5.5 Hz, 1H), 2.36 (qd, *J* = 11.7, 10.4, 4.5 Hz, 2H), 2.23 (ddd, *J* = 13.5, 7.9, 5.5 Hz, 2H), 1.81 – 1.64 (m, 2H), 1.66 – 1.50 (m, 2H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.38, 174.27, 143.94, 137.78, 137.47, 132.45, 129.28, 128.34, 128.08, 126.70, 126.46, 125.88, 80.39, 58.96, 49.24, 48.71, 43.93, 34.36, 33.26, 29.98, 28.13, 20.23. HRMS (ESI) calculated for $[C_{26}H_{31}O_3]^+(M+H^+)$ requires *m/z* 391.2273, found *m/z* 391.2263. <u>Minor Diastereomer</u>: Colorless oil. ν_{max} (film) / cm^{-1} 2976, 2937, 1723, 1674, 1447, 1366, 1218, 1151, 733, 691. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.30 – 7.21 (m, 1H), 7.13 (t, *J* = 7.8 Hz, 2H), 7.04 (t, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 4.32 (t, *J* = 8.3 Hz, 1H), 3.17 – 3.04 (m, 1H), 2.73 (dt, *J* = 13.7, 8.7 Hz, 1H), 2.52 (dt, *J* = 16.1, 5.0 Hz, 1H), 2.40 – 2.22 (m, 4H), 1.73 (ddd, *J* = 13.1, 9.4, 3.4 Hz, 1H), 1.67 – 1.49 (m, 3H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.08, 175.59, 141.75, 138.18, 137.82, 132.34, 129.00, 128.31, 127.96, 127.36, 126.41, 125.88, 80.36, 58.12, 50.62, 49.53, 42.83, 32.01, 31.97, 30.32, 28.16, 20.50. HRMS (ESI) calculated for $[C_{26}H_{34}NO_3]^+(M+NH_4^+)$ requires *m/z* 408.2533, found *m/z* 408.2529.

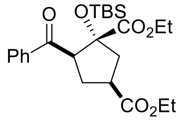
tert-Butyl 3-benzoyl-4-vinylcyclopentanecarboxylate (2-23): Reaction was carried out according to general procedure with *trans* tert-butyl 2-(4-methoxybenzoyl)cyclopropanecarboxylate (152.6 mg, 0.620 mmol), butadiene (1.36 mL, 3.098 mmol, 15 %wt solution in toluene), TMEDA (108.0 mg, .93 mmol), Ru(bpy)-$_3$(PF$_6$)$_2$ (5.2 mg, 0.006 mmol), Gd(OTf)$_3$ (368.1 mg, 0.620 mmol), and MeCN (6 mL total volume). The reaction was complete after 6 h. The crude product was purified by column chromatography (1:9 Et$_2$O/pentanes) providing tert-butyl 3-benzoyl-4-vinylcyclopentanecarboxylate as a colorless oil (122.8 mg, 0.409 mmol, 66% yield,1.5:1 dr). Major Diastereomer: Colorless oil. ν$_{max}$ (film) / cm^{-1} 2977, 2933, 1725, 1681, 1449, 1367, 1258, 1152. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.87 (d, *J* = 7.3 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 5.71 (ddd, *J* = 17.4, 10.2, 7.4 Hz, 1H), 4.95 (d, *J* = 17.1 Hz, 1H), 4.87 (d, *J* = 10.3 Hz, 1H), 3.49 (q, *J* = 8.3 Hz, 1H), 3.10 (p, *J* = 7.9 Hz, 1H), 2.95 – 2.73 (m, 1H), 2.28 (dt, *J* = 13.1, 8.2 Hz, 1H), 2.17 (ddd, *J* = 14.0, 8.0, 6.4 Hz, 1H), 2.07 (dt, *J* = 13.1, 9.1 Hz, 1H), 1.76 (dt, *J* = 13.1, 8.6 Hz, 1H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 200.70, 174.32, 140.11, 137.02, 132.99, 128.56, 128.46, 114.72, 80.39, 52.21, 45.98, 43.86, 35.09, 34.47, 28.06. HRMS (ESI) calculated for [C$_{19}$H$_{25}$O$_3$]$^+$ (M+H$^+$) requires *m/z* 301.1804, found *m/z* 301.1803. Minor Diastereomer: Colorless oil. ν$_{max}$ (film) / cm^{-1} 2981, 2934, 1719, 1678, 1368, 1155. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (d, *J* = 7.3 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 5.61 (dt, *J* = 16.9, 9.7 Hz, 1H), 4.81 – 4.71 (m, 2H), 3.92 (q, *J* = 9.0 Hz, 1H), 3.05 (p, *J* = 8.0 Hz, 1H), 2.83 (dt, *J* = 17.3, 8.7 Hz, 1H), 2.48 (dt, *J* = 13.2, 10.0 Hz, 1H), 2.22 (dt, *J* = 13.4, 8.0 Hz, 1H), 2.12 (dt, *J* = 13.9, 7.4 Hz, 1H), 1.99 (ddd, *J* = 13.3, 8.9, 7.4 Hz, 1H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 200.46, 174.29, 138.13, 137.62, 132.81, 128.48, 128.31, 115.40, 80.30, 50.58, 47.40, 44.08, 35.63, 31.60, 28.10. HRMS (ESI) calculated for [C$_{19}$H$_{18}$NO$_3$]$^+$ (M+NH$_4^+$) requires *m/z* 318.2069, found 318.2067.



tert-Butyl 4-benzoyl-3-methyl-3-(prop-1-en-2-yl)cyclopentanecarboxylate (2-40): Reaction was carried out according to general procedure with *trans* tert-butyl 2-(4-methoxybenzoyl)cyclopropanecarboxylate (103.2 mg, 0.419 mmol), 2,3-dimethyl-1,2-butadiene (166.8 mg, 2.031 mmol), TMEDA (70.8 mg, 0.609 mmol), $Ru(bpy)_3(PF_6)_2$ (8.7 mg, 0.01 mmol), $Gd(OTf)_3$ (245.0 mg, 0.405 mmol), and MeCN (4 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:9 Et_2O/pentanes) providing tert-butyl 4-benzoyl-3-methyl-3-(prop-1-en-2-yl)cyclopentanecarboxylate as a colorless oil (71.6 mg, 0.218 mmol, 52% yield, 1.44:1 dr). Major Diastereomer: Colorless oil. ν_{max} (film) / cm^{-1} 2978, 1719, 1674, 1368, 1265, 1154. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.3 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 4.78 (s, 1H), 4.73 (s, 1H), 3.94 (dd, *J* = 8.8, 7.2 Hz, 1H), 2.87 (p, *J* = 9.1 Hz, 1H), 2.51 (dt, *J* = 13.1, 9.4 Hz, 1H), 2.20-2.10 (m, 2H), 1.91 (dd, *J* = 13.5, 9.6 Hz, 1H), 1.85 (s, 3H), 1.48 (s, 9H), 1.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.02, 174.40, 149.71, 138.42, 132.75, 128.39, 128.33, 110.86, 80.24, 51.67, 50.85, 43.26, 41.92, 32.48, 28.13, 23.24, 20.05. HRMS (ESI) calculated for $[C_{21}H_{29}O_3]^+$ (M+H$^+$) requires *m/z* 329.2117, found *m/z* 329.2118. Minor Diastereomer: Colorless oil. ν_{max} (film) / cm^{-1} 2975, 1724, 1677, 1448, 1367, 1219, 1152. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.3 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 4.72 (s, 1H), 4.69 (s, 1H), 4.00 (t, *J* = 8.3 Hz, 1H), 3.08 (ddd, *J* = 17.8, 9.3, 6.4 Hz, 1H), 2.48 – 2.37 (m, 1H), 2.26 – 2.17 (m, 2H), 1.84 (dd, *J* = 12.9, 8.3 Hz, 1H), 1.80 (s, 3H), 1.47 (s, 9H), 1.09 (s, 3H). ^{13}C NMR (101 MHz, v) δ 202.29, 175.59, 149.19, 138.54, 132.75, 128.41, 128.15, 111.41, 80.27, 52.04, 51.55, 43.44, 42.28, 32.44, 28.12, 21.46, 20.15. HRMS (ESI) calculated for $[C_{21}H_{32}NO_3]^+$ (M+NH$_4^+$) requires *m/z* 346.2381, found 346.2382.

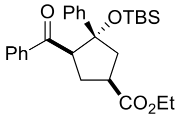


diethyl 5-benzoyl-1-((tert-butyldimethylsilyl)oxy)cyclopentane-1,3- dicarboxylate (2-25): Reaction was carried out according to general procedure with Ethyl benzoylcyclopropanecarboxylate (39.0 mg, 0.18 mmol), ethyl 2-((tert-

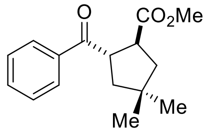


butyldimethylsilyl)oxy)acrylate (202.2 mg, 0.88 mmol), TMEDA (31.4 mg, 0.270 mmol), Ru(bpy)-$_3$(PF$_6$)$_2$ (3.4 mg, 0.004 mmol), Gd(OTf)$_3$ (54.4 mg, 0.09 mmol), and MeCN (0.9 mL). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:10 EtOAc/hexane) to provide the pure product as a clear oil (76.6 mg, 0.171 mmol, 95 % yield, 11:1 dr). ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.96 (d, 8.28 Hz, 2H), δ 7.55 (t, 8.3 Hz, 1H), δ 7.44 (t, 8.3 Hz, 2H), δ 4.15 (q, 7.15 Hz, 2H), δ 3.98 (t,8.27 Hz, 1H), δ 3.92 (dq, 10.72, 7.13 Hz, 1H), δ 3.82 (dq, 10.72, 7.13 Hz, 1H), δ 3.18 (dq, 10.6, 8.9Hz, 1H), δ 2.66 (dd, 13.5, 10.8 Hz, 1H), δ 2.42 (t, 8.54 Hz, 2H), δ 2.27 (dd, 13.5, 7.7 Hz, 1H), δ 1.26 (t, 7.13 Hz, 3H), δ 1.05 (t, 7.15 Hz, 3H), δ 0.93 (s, 9H), δ 0.12 (s, 3H), δ 0.11 (s, 3H). HRMS (ESI) calculated for [$C_{24}H_{37}O_6Si$]$^+$ (M+H$^+$) requires *m/z* 449.2354, found 449.2352.

ethyl 4-benzoyl-3-((tert-butyldimethylsilyl)oxy)-3-phenylcyclopentane carboxylate (2-24):



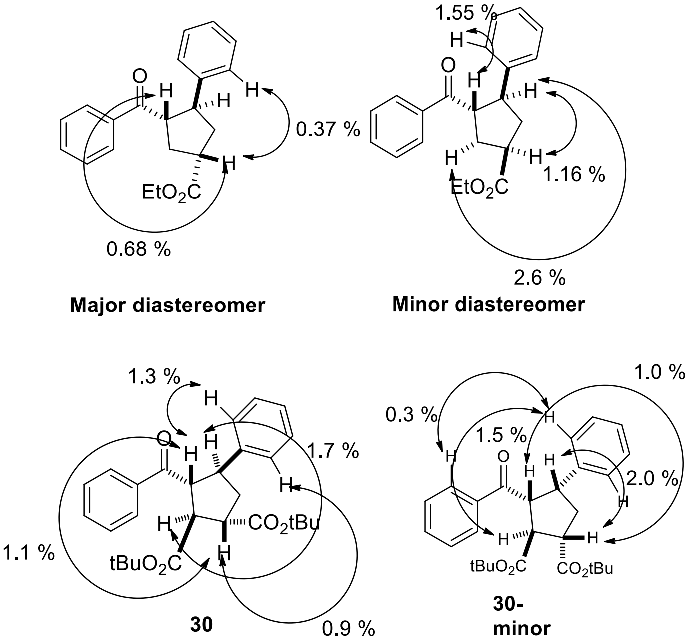
Prepared according to general procedure with *trans*-ethyl 2-benzoylcyclopropanecarboxylate (41.1 mg, 0.19 mmol), tert-butyldimethyl((1-phenylvinyl)oxy)silane (82.5 mg, 036 mmol), Ru(bpy)3(PF6)2 (4.0 mg, 0.005 mmol), TMEDA (33.1 mg, 0.285 mmol), Gd(OTf)3 (57.4 mg, 0.095 mmol), and MeCN (0.44 mL). The reaction was complete after 2 hours. The crude product was purified by column chromatography using 5:1 pentanes/Et$_2$O to provide the product as a clear oil (80.8 mg, 0.18 mmol, 94 % yield, 9:1 d.r.). ^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.76 (d, 7.76 Hz, 2H), δ 7.5 (t, 7.8 Hz, 1H), δ 7.4 (t, 7.8 Hz, 2H), δ 7.35-7.3 (m, 2H), δ 7.2-7.1 (m, 3H), δ 4.4 (ddd, 8.6, 3.6, 1.3 Hz, 1H), δ 4.25 (q, 7.1 Hz, 2H), δ 3.43 (tt, 10.8, 7.4 Hz, 1H), δ 3.15 (dd, 13.1, 10.9 Hz, 1H), δ 2.7 (dt, 13.1, 9.8 Hz, 1H), δ 2.57 (dd, 13.1, 7.4 Hz, 1H), δ 2.41 (ddd, 13.1, 6.7, 4.1 Hz, 1H), δ 1.34 (t, 7.1 H, 3H), δ 0.97 (s, 9H), δ -0.07 (s, 3H), δ -0.45 (s, 3H). HRMS (ESI) calculated for [$C_{27}H_{37}O_4Si$]$^+$ (M+H$^+$) requires *m/z* 453.2456, found 453.2456.



methyl 2-benzoyl-4,4-dimethylcyclopentanecarboxylate (2-26): Reaction was carried out according to general procedure with (2,2-dimethylcyclopropyl)(phenyl)methanone (34.8 mg, 0.200 mmol), Methyl acrylate (86.1 mg, 1.00 mmol), TMEDA (34.9 mg, 0.30 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (10.0 mg, 0.005 mmol), Gd(OTf)$_3$ (60.4 mg, 0.100 mmol), and MeCN (5.7 mL total volume). The reaction was complete after 3 h. The crude product was purified by column chromatography (1:19, Et$_2$O/pentanes) providing methyl 2-benzoyl-4,4-dimethylcyclopentanecarboxylate as a clear oil (44.3 mg, 0.17 mmol, 85% yield, 2:1 dr). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.98 (d, *J* = 7.1 Hz, 1H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 4.23 (q, *J* = 8.9 Hz, 1H), 3.55 (q, *J* = 8.8 Hz, 1H), 1.95 (ddd, *J* = 19.5, 12.8, 9.4 Hz, 2H), 1.78 (dd, *J* = 12.7, 8.9 Hz, 1H), 1.60 (dd, *J* = 12.8, 8.8 Hz, 1H), 1.37 (s, 9H), 1.10 (s, 3H), 1.03 (s, 3H). HRMS (ESI) calculated for $[C_{16}H_{21}O_3]^+$ (M+H$^+$) requires *m/z* 260.14, found 260.15

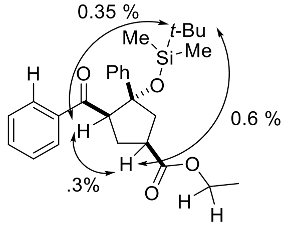
2.4.5 Determination of relative stereochemistry

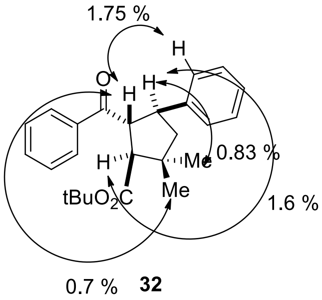
Figure 2-6. Observed nOe enhancements



Major diastereomer **Minor diastereomer**

30 **30-minor**


0.35 %
Me
t-Bu
Si
Me
O
Ph
H
O
H
H
O
O
H
H
0.6 %
.3%


1.75 %
H
O
H
H
H
Me
0.83 %
tBuO2C
Me
1.6 %
0.7 %

32

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Chapter 3. Development of Enantioselective [3 + 2] Cycloadditions via Visible Light Dual Catalysis

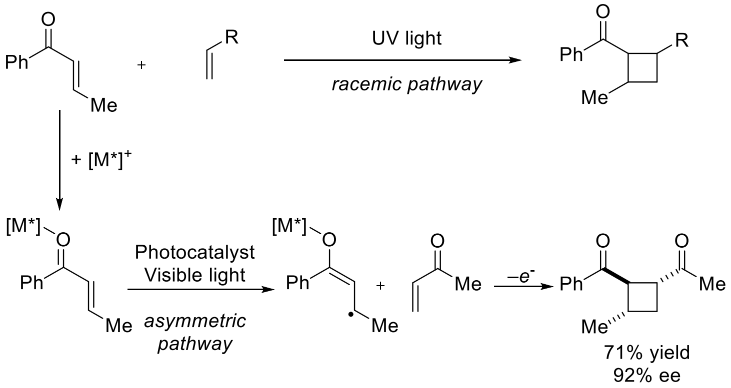
Portions of this work have previously been published:

Amador, A. G.; Sherbrook, E. M.; Yoon, T. P. Enantioselective Photocatalytic [3 + 2] Cycloadditions of Aryl Cyclopropyl Ketones. *J. Am. Chem. Soc.* **2016**, *138*, 4722–4725.

3.1 Introduction

Stereocontrolled cycloadditions are valued in synthetic chemistry both as methods to construct the ring systems that are ubiquitous in chiral bioactive compounds and as model reactions to evaluate new concepts in enantioselective synthesis.[1–3] Control over the absolute stereochemistry of photochemical cycloadditions, however, remains a substantial challenge without a general solution.[4–6] A relatively small number of highly enantioselective organocatalytic[7–12] and Lewis acid[13–16] catalyzed photocycloadditions have been described in the past several years, but these successful methods have been focused upon [2 + 2] cycloadditions of enones. No strategies for photocatalytic stereocontrol have emerged that appear to be broadly applicable to the asymmetric catalysis of other classes of photocycloaddition reactions.

Scheme 3-1. Dual-catalytic enantioselective [2 + 2] photocycloaddition

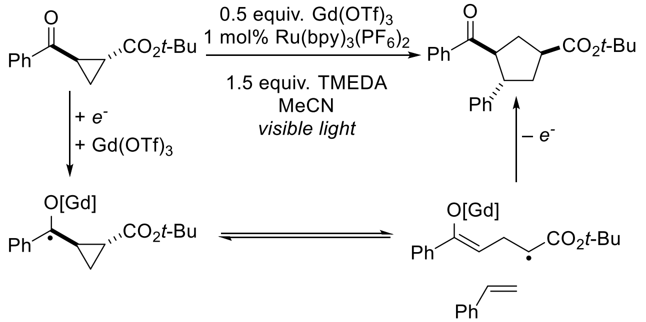


Our laboratory recently reported a dual catalyst system for enantioselective [2 + 2] photocycloaddition using a chiral Lewis acid in tandem with a transition metal photoredox catalyst (Scheme 3-1).[17] This transformation occurs through the photocatalytic reduction of the enone under visible light irradiation to generate an open-shell intermediate and provide the driving force for the overall redox neutral [2 + 2] cycloaddition. Due to the strongly negative reduction potential of the free enone, a Lewis acid is required in order for the photocatalyst to reduce the substrate. This requirement has the added benefit of eliminating background reactivity in the absence of a Lewis acid and provides the opportunity for highly enantioselective cycloadditions through incorporation of a chiral ligand. The success of this strategy relies upon the ability to tune the structure of the stereocontrolling chiral catalyst for optimal selectivity without adversely affecting the performance of the photocatalyst. We speculated, therefore, that this combination of catalytic strategies might successfully control the stereochemical behavior of many of the reactions now known to be amenable to photoredox catalysis.[18–20]

We became interested in designing an asymmetric version of the photocatalytic intermolecular [3 + 2] cycloaddition between aryl cyclopropyl ketones and alkenes that was described in the previous chapter (Scheme 3-2). Catalytic and highly enantioselective [3 + 2] cycloadditions are an area of interest for synthetic chemists due to the prevalence of 5-membered carbocycles in many natural products and bioactive compounds. While asymmetric [3 + 2] cycloadditions for the synthesis of five-membered heterocycles are relatively well-developed, the analogous transformations for carbocycle synthesis remain substantially more challenging. Cyclopropanes have attracted significant interest as an ideal three-carbon building block via C–C bond cleavage and subsequent cycloadditions driven by the inherent ring-strain of the three-membered ring. While enantioselective cycloadditions of highly activated "donor–acceptor" cyclopropanes are known,[21–26] no catalytic asymmetric [3 + 2] cycloadditions of less activated cyclopropyl ketones have been reported. Our photocatalytic process involves photoreduction of a Lewis acid activated

Scheme 3-2. Precedent and objectives

■ ***Prior work (chapter 2)***

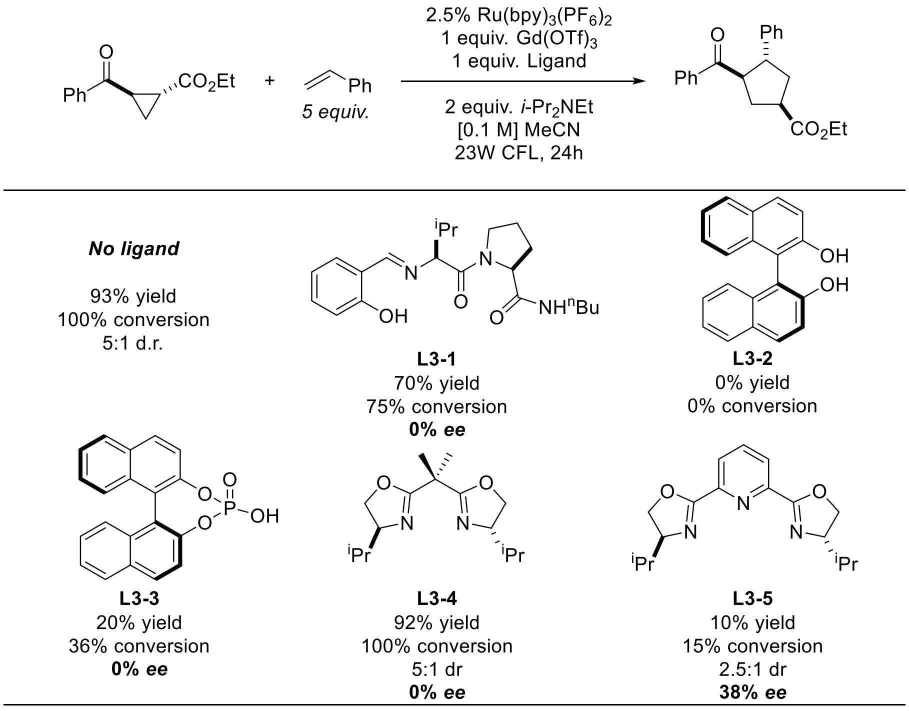


■ ***Challenges:***

- ***Reduce Lewis acid loading***
- ***Replace TMEDA with a chiral ligand + achiral amine quencher***
- ***Optimize for high enantioselectivities***

aryl cyclopropyl ketone to afford a ring-opened distonic radical anion that can react with olefin coupling partners (Scheme 3-2). While this methodology enables the facile synthesis of structurally diverse cyclopentane-containing products, the reaction requires near-stoichiometric $Gd(OTf)_3$ as a Lewis acid catalyst, and employs super-stoichiometric TMEDA as both a ligand for Gd^{3+} and a reductive quencher of $Ru^*(bpy)_3^{2+}$. At the outset of this project we foresaw three key challenges: reduction of the Lewis acid loading, identification of a compatible chiral ligand and replacement of TMEDA with a less coordinating reductive quencher, and optimization of the conditions for high enantioselectivities. This chapter will detail our efforts to address these challenges.

Figure 3-1. Preliminary screen of chiral ligands for asymmetric [3 + 2] cycloadditions



Yields determined by ^1H NMR spectroscopy using phenanthrene as internal standard.

3.2 Results and Discussion

3.2.1 Optimization of the reaction conditions

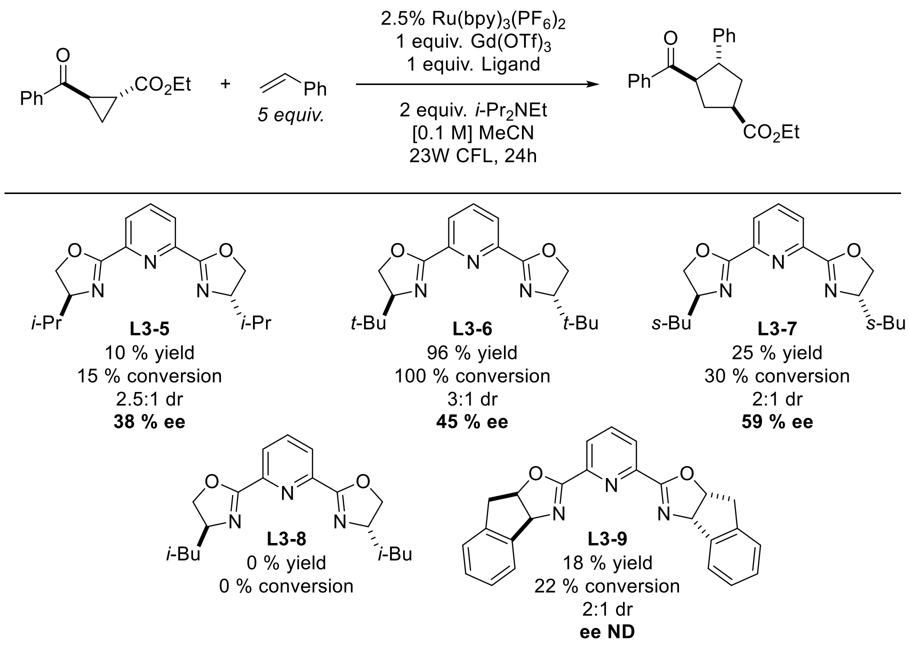
We began our investigation by screening a range of chiral ligands known to be effective in asymmetric catalysis with lanthanide Lewis acids using the less coordinating tertiary amine *i*-

Pr₂NEt as a reductive quencher (Figure 3-1). The incorporation of most chiral ligands either had no effect on the stereoselectivity or proved to be deleterious to the efficiency of the reaction. Surprisingly, the peptide Schiff base ligands that were very effective in enantioselective [2 + 2] cycloaddition provided reduced yields of racemic product (**L3-1**). Promisingly, we observed experimentally significant enantioselectivities with a Gd(III)–*i*-propylpybox complex, albeit in low yields (**L3-5**, 10% yield, 38% ee).[27–30]

With this promising result, we carried out a more thorough optimization of the pybox ligand scaffold (Figure 3-2). Despite the promising conversions observed with *t*-butylpybox, other pybox ligands provided overall poor conversions, though we saw a promising increase in enantioselectivities by using the *s*-butylpybox ligand (**L3-7**, 25% yield, 59% ee). An extensive screen of other Lewis acidic metal triflates failed to provide any improvements in the reaction efficiency (see experimental data Table 3-6).

Analysis of reaction progress revealed that the rate of product formation was decreasing within the first hour of the reaction time. We hypothesized that *i*-Pr₂NEt and Gd(OTf)₃ slowly formed an

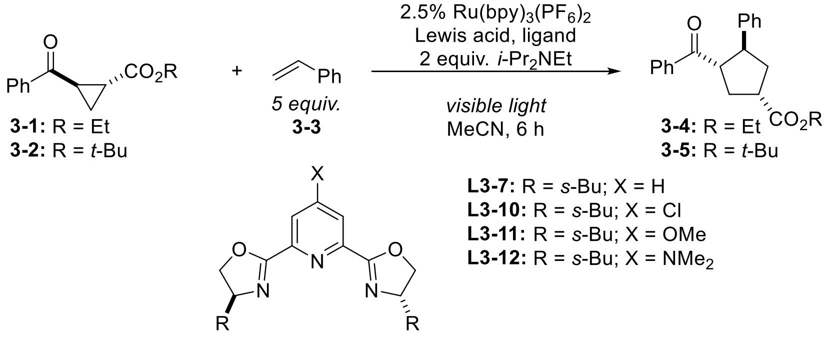
Figure 3-2. Screen of pybox ligand derivatives



Yields determined by ^{1}H NMR spectroscopy using phenanthrene as internal standard.

inactive Lewis acid-base complex over several hours. UV-Vis titrations of a solution of the Gd(III)–pybox complex with *i*-Pr_2NEt revealed the formation of a new complex which can be fit with a 1:1 binding model indicating a K_a of 6.26×10^4 M^{-1} (See experimental information). We increased the ligand-to-metal ratio in an attempt to slow formation of the deactivated complex, with little beneficial effect (Table 3-1, entry 2). An extensive screen of alternative reductive quenchers provided no improvements to the overall reaction efficiency (Table 3-7, experimental information). As an alternative strategy, we wondered if we might stabilize the active Gd-pybox complex by increasing the coordinating ability of the chiral ligand.[31–35] Indeed, while chloride-substituted ligand **L3-10** resulted in no product formation, electron-rich methoxy-substituted ligand **L3-11** provided **3-4** in excellent yield (entry 4). Dimethylamino-substituted ligand **L3-12** provided optimal rate and

Table 3-1. Final optimization studies

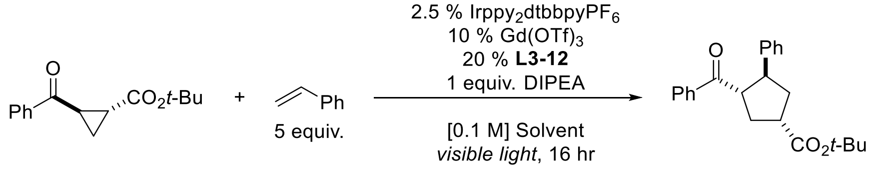


Entry	Conditions[a]	Yield[b]	% ee	dr
1	100% $Gd(OTf)_3$, 100% **L3-7**	25%	59%	2:1
2	100% $Gd(OTf)_3$, 200% **L3-7**	36%	63%	3:1
3	100% $Gd(OTf)_3$, 200% **L3-10**	0%	---	---
4	100% $Gd(OTf)_3$, 200% **L3-11**	90%	64%	2:1
5	100% $Gd(OTf)_3$, 200% **L3-12**	89%	85%	2:1
6	10% $Gd(OTf)_3$, 20% **L3-12**	96%	79%	2:1
7	10% $Gd(OTf)_3$, 20% **L3-12**, 0 °C	80%	85%	3:1
8	10% $Gd(OTf)_3$, 20% **L3-12**, –20 °C	41%	91%	3:1
9[c]	10% $Gd(OTf)_3$, 20% **L3-12**, 0 °C	86%	90%	3:1
10[cd]	10% $Gd(OTf)_3$, 20% **L3-12**, 0 °C	95%	93%	3:1

[a] Reactions carried out on 0.045 mmol scale, irradiating with a 23 W CFL for 6 h. [b] Yields determined by ^1H-NMR yield using phenanthrene as an internal standard. [c] Using **3-1** instead of **3-2**. [d] Using 1 equiv of *i*-Pr_2NEt.

stereoselectivity (entry 5), and with this ligand, the Lewis acid loading could be decreased to 10 mol% with little effect on ee (entry 6). Lowering the temperature to 0 °C resulted in an increase in the enantioselectivity to 85% ee (entry 7). The ee was further improved at –20 °C, but we observed an increased proportion of an undesired reductive ring-opening product (entry 8). Increasing the bulk of the ester substituent provided somewhat higher ee at 0 °C (entry 9), and the occurrence of the reductive ring-opening side-product could be minimized by lowering the concentration of *i*-Pr_2NEt (entry 10). Under these optimized conditions, cycloadduct **3-5** was obtained in 95% yield and 93% ee. In an attempt to improve the diastereoselectivity of the transformation we explored a range of other solvent conditions. Interestingly, while less polar solvents offered substantial improvements in the diastereoselectivity, the enantioselectivity exhibited the opposite trend (Table 3-2).

Table 3-2. Solvent optimization



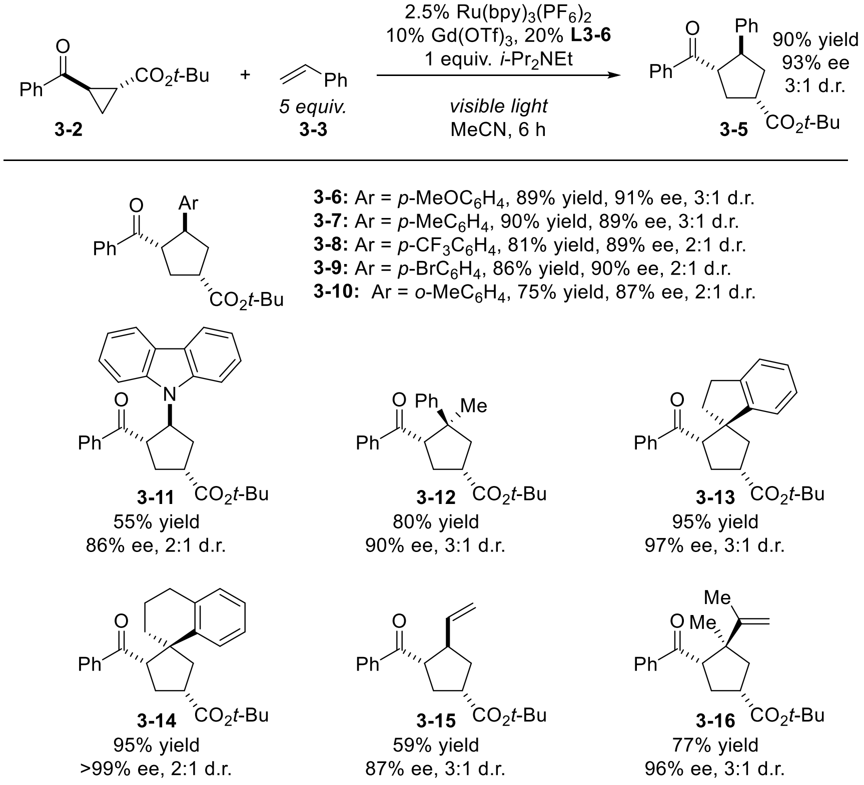
Entry	Solvent	% yield[a]	dr	% ee
1	Toluene	37%	15:1	3.5%
2	Et_2O	66%	3.9:1	39%
3	THF	50%	2.3:1	45%
4	CH_2Cl_2	95%	4.5:1	71%
5	MeCN	92%	2.3:1	85%

[a]Yields determined by 1H-NMR spectroscopy using phenanthrene as internal standard.

3.2.2 Exploration of the substrate scope

We next conducted an exploration of the scope of the enantioselective cycloaddition under these conditions. Figure 3-3 outlines the effect of varying the structure of the alkene reaction partner.[36] We have proposed a stepwise cycloaddition initiated by radical addition of a ring-opened distonic radical anion to an alkene. Consistent with this proposal, simple aliphatic alkenes are not

Figure 3-3. Alkene substrate scope^a



3-6: Ar = $p\text{-}MeOC_6H_4$, 89% yield, 91% ee, 3:1 d.r.
3-7: Ar = $p\text{-}MeC_6H_4$, 90% yield, 89% ee, 3:1 d.r.
3-8: Ar = $p\text{-}CF_3C_6H_4$, 81% yield, 89% ee, 2:1 d.r.
3-9: Ar = $p\text{-}BrC_6H_4$, 86% yield, 90% ee, 2:1 d.r.
3-10: Ar = $o\text{-}MeC_6H_4$, 75% yield, 87% ee, 2:1 d.r.

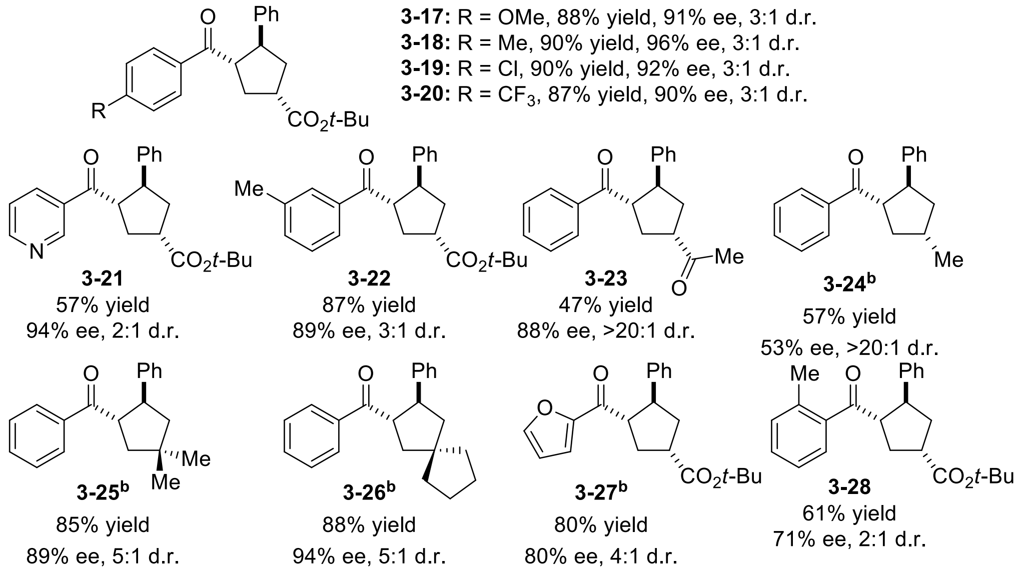
3-11 55% yield, 86% ee, 2:1 d.r.
3-12 80% yield, 90% ee, 3:1 d.r.
3-13 95% yield, 97% ee, 3:1 d.r.
3-14 95% yield, >99% ee, 2:1 d.r.
3-15 59% yield, 87% ee, 3:1 d.r.
3-16 77% yield, 96% ee, 3:1 d.r.

^{a} Reactions irradiated with a 23 W CFL for 6 h. Yields reported are the combined isolated yields of all diastereomers. Major diastereomer shown. Absolute stereochemistry of major diastereomer determined by X-ray crystallographic analysis of **3-9**, other structures assigned by analogy.

reactive. However, a variety of electronically modified styrenes react smoothly and with good ee (**3-6–3-8**). Potentially reactive aryl halides are well tolerated (**3-9**), providing a handle for derivatization of the enantioenriched cycloadducts. The enantioselectivity is relatively insensitive to the position of substituents on the aryl ring (**3-10**). While heterocycles containing Lewis basic heteroatoms resulted in a loss in stereoselectivity, alkenes bearing less basic heterocycles such as carbazoles react smoothly with good ee (**3-11**). Internal olefins, unfortunately, were unreactive under these reaction conditions; however, 1,1-disubstituted styrenes react smoothly and provide excellent ee (**3-12–3-14**). Finally, dienes are also competent reaction partners, affording vinyl cyclopentane products in good ee (**3-15**, **3-16**).

The scope of this reaction with respect to the aryl ketone component is summarized in Figure 3-4. The aryl moiety tolerates significant electronic perturbation: both electron-rich and electron-deficient substituents provided the corresponding cyclopentanes in good yield and excellent ee (**3-17**–**3-20**). Heteroaryl cyclopropyl ketones are also tolerated (**3-21**), although the ee suffers if the heterocycle is positioned to provide an alternate site for Lewis acid chelation (**3-27**). Arene substituents at the 3-position have minimal impact on the selectivity of the reaction (**3-22**). However, 2-substituents have a large deleterious effect, which would be expected if the ketone were coordinated to the chiral Lewis acid in the enantioselectivity-determining step (**3-28**). The ester moiety can be replaced by a ketone with minimal impact on the stereoselectivity (**3-23**), but a methyl-substituted cyclopropane provides poor ee (**3-24**). On the other hand, cyclopropyl ketones bearing geminal ß-dialkyl substituents afford excellent ee, although higher Lewis acid concentrations were required for optimal rate (**3-25**, **3-26**).

Figure 3-4. Cyclopropane substrate scope[a]



3-17: R = OMe, 88% yield, 91% ee, 3:1 d.r.
3-18: R = Me, 90% yield, 96% ee, 3:1 d.r.
3-19: R = Cl, 90% yield, 92% ee, 3:1 d.r.
3-20: R = CF_3, 87% yield, 90% ee, 3:1 d.r.

3-21
57% yield
94% ee, 2:1 d.r.

3-22
87% yield
89% ee, 3:1 d.r.

3-23
47% yield
88% ee, >20:1 d.r.

3-24[b]
57% yield
53% ee, >20:1 d.r.

3-25[b]
85% yield
89% ee, 5:1 d.r.

3-26[b]
88% yield
94% ee, 5:1 d.r.

3-27[b]
80% yield
80% ee, 4:1 d.r.

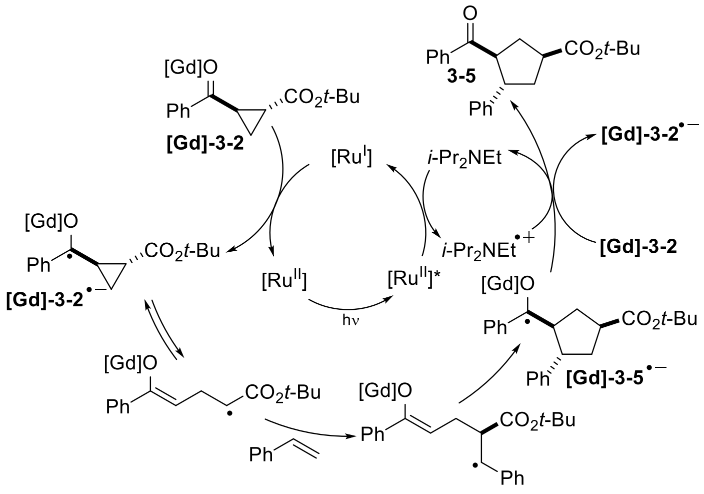
3-28
61% yield
71% ee, 2:1 d.r.

[a] Reactions irradiated with a 23 W CFL for 6 h. Combined isolated yields of all diastereomers. Absolute stereochemistry by X-ray crystallographic analysis. [b] Reaction conducted using 20 mol% $Gd(OTf)_3$ and 30 mol% L3-6 and 2 equiv. *i*-Pr_2NEt at –20 °C for 48 h.

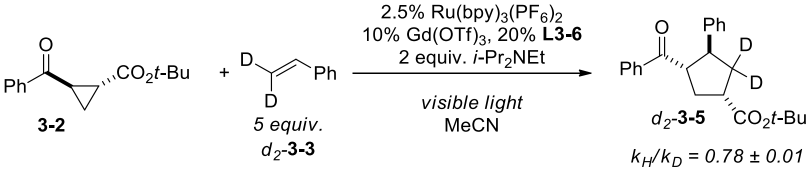
3.2.3 Mechanism

Figure 3-5 depicts our working model for the mechanism of this reaction. Photoexcitation of $Ru(bpy)_3^{2+}$ and reductive quenching by *i*-Pr_2NEt affords $Ru(bpy)_3^{+}$. Subsequent electron transfer to phenyl ketone 3-2 occurs only upon activation with the chiral Gd(III) Lewis acid; the resulting

Figure 3-5. Proposed mechanism for enantioselective [3 + 2] cycloaddition



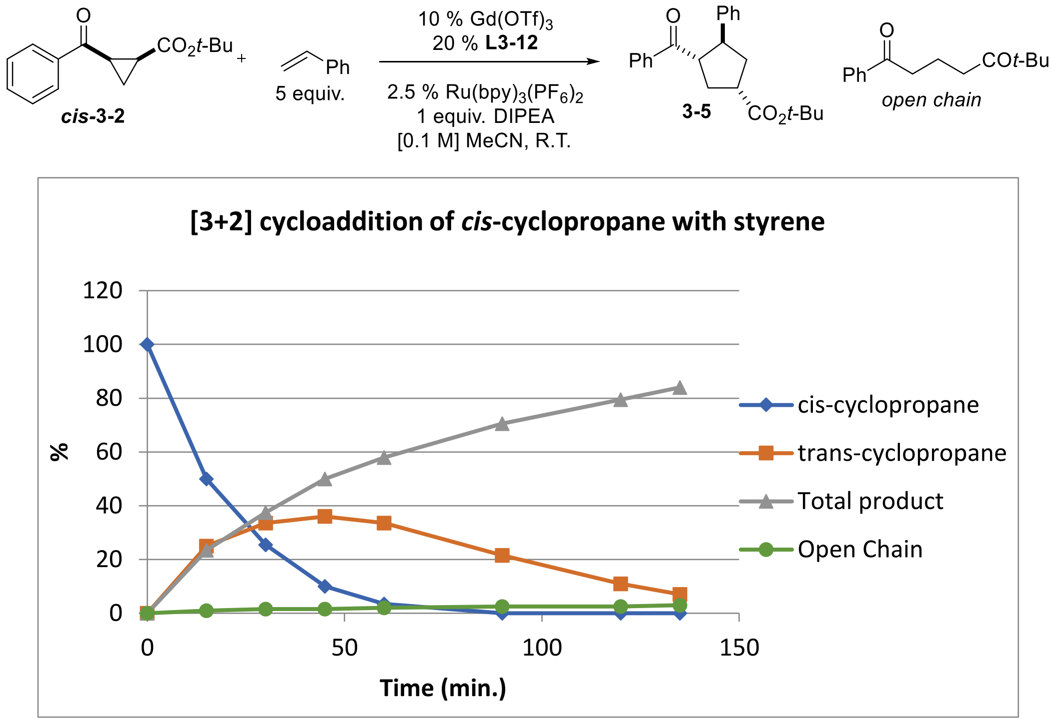
Scheme 3-3. Kinetic isotope effect study of relative initial rates



ketyl radical (**[Gd]-3-2$^{\bullet-}$**) undergoes reversible ring-opening followed by slow stepwise cycloaddition with styrene to afford product ketyl radical **[Gd]-3-5$^{\bullet-}$**. Formation of the neutral product **3-5** could occur either by chain-propagating electron transfer to another equivalent of substrate or by chain-terminating reduction of the photogenerated amine radical cation.

The mechanism proposed in Figure 3-4 is supported by several lines of evidence. First, a reaction with deuterium-labeled styrene ***d*₂-3-3** gives an inverse secondary kinetic isotope effect (k_H/k_D = 0.78) consistent with a rate-limiting intermolecular C–C bond-forming step (Scheme 3-3). This finding is consistent with the observation that internal olefins are not tolerated giving only trace desired cycloadduct. Second, Tanko has reported that the ring-opening of similar cyclopropyl ketyl radicals is reversible and endergonic.[37] To validate this expectation, we monitored a reaction starting with the *cis* isomer of **3-2** and found that the cyclopropane was completely isomerized to the *trans* isomer within 1 h, well before the reaction was complete (Figure 3-6). This reversible cleavage is consistent with the observation that racemic ß,ß'-

Figure 3-6. [3 + 2] cycloaddition with diastereomerically pure cis-cyclopropane



disubstituted cyclopropane **3-29** undergoes stereoconvergent cycloaddition to cyclopentyl ketone **3-30** in good diastereoselectivity and excellent ee (Scheme 3-4). The cycloaddition of unsymmetrically substituted cyclopropyl ketone **3-31** also provides excellent stereoselectivity as well as exclusive chemoselectivity for the formation of enantioenriched cyclopentane **3-32** and not its constitutional isomer (Figure 3-7). This result indicates an interesting kinetic scenario where C–C bond cleavage occurs at both possible positions providing a epimerization pathway of the starting material for a highly regio-, diastereo-, and enantioselective dynamic kinetic transformation.

Scheme 3-4. [3 + 2] cycloaddition with ß,ß'-disubstituted cyclopropylketone

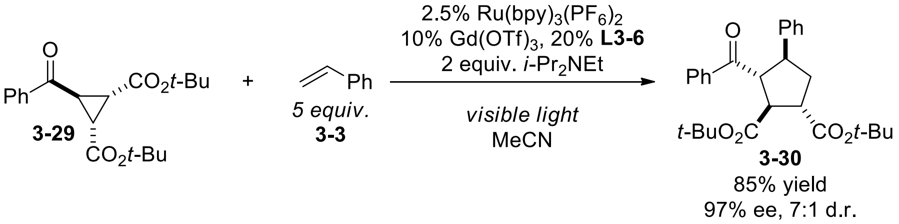
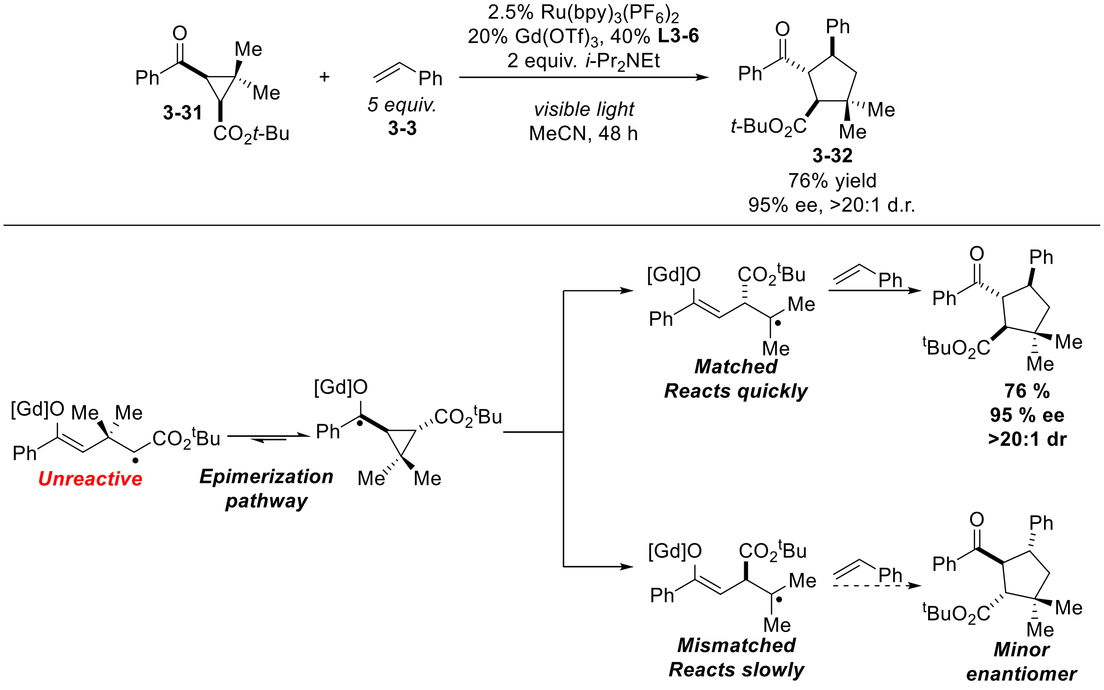


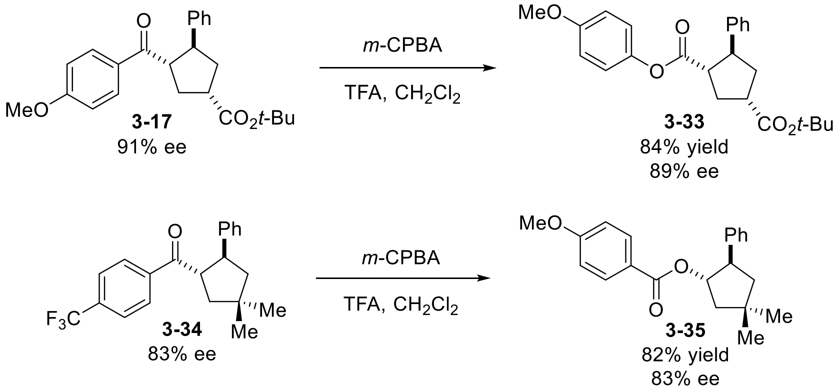
Figure 3-7. [3 + 2] cycloaddition of unsymmetrically substituted cyclopropylketone



3.2.4 Product derivatization

While the scope of this new asymmetric [3 + 2] cycloaddition is complementary to the established enantioselective reactions of donor-acceptor cyclopropanes, the aryl ketone moiety required for the initial one-electron reduction process imposes an undesirable limitation on scope. Thus, we wondered if the aryl ketone could be removed with retention of stereochemistry through a Baeyer–Villiger cleavage (Scheme 3-5). Indeed, the *p*-methoxyphenyl ketone cycloadduct **3-17** undergoes completely regioselective oxidation to afford **3-33** in good yield, the activated ester of which is poised for further manipulation into diverse carboxylic acid derivatives. Under identical conditions, *p*-trifluoromethylphenyl ketone **3-34** undergoes regiocomplementary oxidation to afford benzoate ester **3-35**. Thus, the applicability of this [3 + 2] photocycloaddition method to reactions of electronically varied aryl ketones provides a flexible strategy for the conversion of the enantioenriched products to a diverse array of five-membered carbocyclic derivatives.

Scheme 3-5. Cleavage of the aryl ketone moiety



3.3 Conclusions

These studies have several important implications. From a practical perspective, this method provides an asymmetric catalytic method to assemble structurally complex five-membered carbocycles, which are a class of compounds that remain challenging to prepare in enantioenriched form. This methodology provides a complementary approach to existing methodologies for the construction of enantioenriched cyclopentanes. The inherent advantage of exploiting radical intermediates is clear in looking at the substrate scope where both electron-donating and electron-withdrawing substituents are tolerated on the cyclopropane ring. This is in stark contrast to donor-acceptor cyclopropane methodologies where there are strict electronic requirements in order to stabilize the active zwitterionic intermediates. More broadly, these results demonstrate that the combination of chiral Lewis acid and photoredox catalysis offers a robust and potentially general approach to photochemical stereocontrol that is broadly applicable to the increasing number of powerful transformations achievable using photoredox catalysis.

3.4 Experimental information

3.4.1 General information

MeCN, THF, and CH_2Cl_2 were purified by elution through alumina as described by Grubbs.[1] A 23W (1200 lumens) SLI Lighting Mini-Lynx compact fluorescent light bulb was used for all photochemical reactions. $Gd(OTf)_3$, $La(OTf)_3$, and other Lewis acids were purchased from Strem, stored in a glove box, and used without further purification. Flash column chromatography was performed with Silicycle 40-63A silica (230-400 mesh). Styrene, diisopropylethylamine, *N,N,N',N'*-tetramethylethylenediamine, triethylamine, tributylamine, 1,4-dimethylpiperazine, N-methylpyrrolidine, *N,N,N',N'*-tetramethylpropylenediamine, *N,N,N',N'*-tetramethylbutanediamine, ethyldicyclohexylamine, N,N-dimethylbenzylamine, *N*-methylpiperidine, 4-methylmorpholine, *N,N,N',N'*-tetramethylphenylenediamine, *N,N,N',N'*-tetramethylbenzidine, *N,N,N',N",N"*-pentamethyldiethylenetriamine, 1,2,2,6,6-pentamethylpiperidine, 4-aminophenol, *p*-toluidine, 4-methoxy-*N,N*-diphenylaniline, 2,6-di-*tert*-butyl-4-methyl-phenol, 2,4,6-trimethylaniline, DABCO, 2,6-lutidine, and DBU were purchased from Sigma Aldrich and subsequently purified either by distillation or recrystallization. K_4FeCN_6 hexahydrate, cesium oxalate, and *(R,R)*-binaphthol were purchased from Sigma Aldrich and used without further purification. All glassware was oven-dried at 130 °C overnight or flame-dried immediately prior to use.

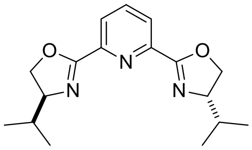
^1H and $^{13}C\{H\}$ NMR data for all previously uncharacterized compounds were obtained using a Bruker AVANCE-400 spectrometer and are referenced to TMS (0.0 ppm) and $CDCl_3$ (77.0 ppm), respectively. IR spectral data were obtained using a Bruker Vector 22 spectrometer. Melting points were obtained using a Mel-Temp II (Laboratory Devices, Inc., USA) melting point apparatus. Mass spectrometry was performed with a Micromass LCT (electrospray ionization, time-of-flight analyzer or electron impact). These facilities are funded by the NSF (CHE-9974839, CHE-9304546) and the University of Wisconsin. Enantiomeric excesses were determined by chiral SFC of isolated material using a Waters Investigator system with Daicel CHIRALPAK®

columns and Chromasolv®-grade *i*-PrOH, MeOH, and hexane. Optical rotations were measured using a Rudolph Research Autopol III polarimeter at room temperature in CH_2Cl_2.

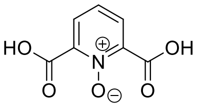
3.4.2 Ligand synthesis

Bis(oxazoline) ligands and pyridine bis(oxazoline) ligands were synthesized as described by Pires.[2] A representative procedure is shown below.

2,6-Bis(*(S)*-4-isopropyl-4,5-dihydrooxazol-2-yl)pyridine (L3-5). Prepared using a procedure described by Pires and coworkers.[2] A 250 mL round bottom flask was charged with pyridine-2,6-dicarbonitrile (2.1692 g, 16.8 mmol, 1 equiv.), zinc triflate (422 mg, 1.2 mmol, 0.07 equiv.) , and anhydrous toluene (100 mL). A solution of *(S)*-valinol (3.47 g, 33.6 mmol, 2 equiv.) in toluene (20 mL) was added. The flask was fit with a reflux condenser and purged several times with nitrogen. The solution was heated under reflux for 48 h. After cooling, the reaction mixture was diluted with EtOAc (200 mL). The solution was then washed with saturated NaCl (3x100 mL), saturated $NaHCO_3$ (3x100 mL), and water (100 mL). The organic layer was then dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the product as an off-white crystalline solid. The crude product was purified by recrystallization from hexanes and EtOAc to give the pure product as a white crystalline solid (4.31 g, 14.3 mmol, 85 % yield). Spectroscopic data match those reported previously in the literature.[2]

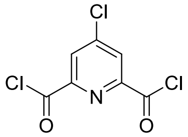


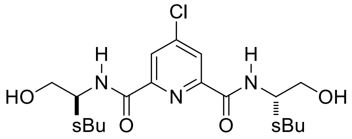
2,6-Dicarboxypyridine 1-oxide (3-36). Prepared using a procedure described by Mitsui and Parquette.[3] A 500 mL round-bottomed flask was charged with $Na_2WO_4{\cdot}2H_2O$ (1.91 g, 5.79 mmol), pyridine-2,6-dicarboxylic acid (30.0 g, 180 mmol), and 30 % aq. H_2O_2 (90 mL). The reaction flask was equipped with a reflux condenser and heated to 100 °C . After 2 h, an additional 210 mL of 30 % aq. H_2O_2 was added at r.t. The reaction mixture was stirred at 100 °C for an additional 14 h, after which the reaction mixture had become



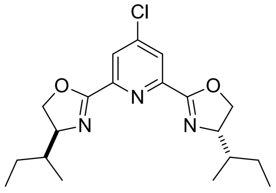
homogeneous. The reaction mixture was then cooled to 0 °C, and the resulting white precipitate was separated by filtration. The filter cake was washed several times with ice-cold H_2O. The filtrate was washed with $CHCl_3$ (3x200 mL) to afford additional product. The combined solid crude product was purified by recrystallization from boiling H_2O. The isolated crystalline product was dried over P_2O_5 under reduced pressure at 80 °C for 15 h to provide 2,6-dicarboxypyridine-N-oxide as a white crystalline solid (19.1 g, 104 mmol, 58 % yield). All spectroscopic data match those reported previously in the literature. ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.9 (br s, 2H), 8.23 (d, *J* = 8.0 Hz, 2H), 7.95 (t, *J* = 8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.3, 139.7, 132.7, 129.4. (mp = 157–159 °C).

4-Chloropyridine-2,6-dicarbonyl dichloride (3-37). Prepared using a procedure described by Mitsui *et al*.[3] A 250 mL flame-dried round-bottomed flask was charged with 2,6-dicarboxypyridine 1-oxide (5.30 g, 22.2 mmol) and anhydrous CH_2Cl_2 (50 mL). The reaction flask was sealed with a septum and purged several times with nitrogen. The reaction flask was then cooled to –10 °C and oxalyl chloride (25.0 mL, 291 mmol) was added slowly over 5 min. After stirring for 10 min, one drop of dry DMF was added to the suspension via syringe. The reaction mixture was allowed to warm very slowly to r.t. over a 12 h period and then stirred an additional 60 h. The excess oxalyl chloride and solvent were removed under aspirator pressure at r.t. to yield crude 4-chloropyridine-2,6-dicarbonyl dichloride as a pale yellow solid. The crude product was further purified by bulb-to-bulb distillation to afford the pure product as a white crystalline solid (4.24 g, 17.8 mmol, 80 % yield). All spectroscopic data match those reported previously in the literature. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 150.2, 147.9, 128.9. mp = 96–98 °C.



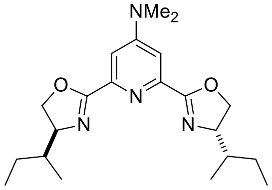


4-Chloro-*N2,N6*-bis((*2S,3S*)-1-hydroxy-3-methylpentan-2-yl)pyridine-2,6-dicarboxamide (3-38). A flame-dried 250 mL round-bottomed flask was charged with *(S)*-isoleucinol (1.78 g, 15.2 mmol), NEt_3 (3.0 mL, 21 mmol), and CH_2Cl_2 (45 mL). The reaction flask was sealed with a septum, purged several times with N_2 (g), and cooled to 0 °C. A solution of 4-chloropyridine-2,6-dicarbonyl dichloride (1.8120 g, 7.5988 mmol) in CH_2Cl_2 (10 mL) was then added via syringe over 5 min. The reaction mixture was then allowed to warm to r.t. and stirred overnight. After this time the reaction mixture was washed with saturated $NaHCO_3$ (3x 30 mL) and water (30 mL). The organic layer was then dried over Na_2SO_4, filtered, and concentrated under reduced pressure to yield the crude product as an off-white solid. The crude product was carried forward without further purification or characterization (2.69 g, 6.73 mmol, 89 % crude yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 2H), 7.98 (d, *J* = 8.4 Hz, 2H), 4.00 (tt, *J* = 8.6, 4.6 Hz, 2H), 3.89 – 3.80 (m, 4H), 1.91 – 1.75 (m, 2H), 1.67 – 1.48 (m, 2H), 1.24 (tt, *J* = 14.7, 7.4 Hz, 2H), 1.02 (d, *J* = 5.2 Hz, 6H), 0.95 (t, *J* = 7.4 Hz, 6H).



(S,4S,4'S)-2,2'-(4-Chloropyridine-2,6-diyl)bis(4-((S)-sec-butyl)-4,5-dihydrooxazole) (L3-10): A flame-dried 100 mL round-bottomed flask was charged with 4-chloro-*N2,N6*-bis((2*S*,3*S*)-1-hydroxy-3-methylpentan-2-yl)pyridine-2,6-dicarboxamide (2.69 g, 6.73 mmol) and CH_2Cl_2 (30 mL). The reaction vessel was sealed with a rubber septum, purged several times with N_2 (g), and cooled to –78 °C. Diethylaminosulfur trifluoride (DAST) (1.87 mL, 14.2 mmol) was then added slowly via syringe. The reaction mixture was stirred for 12 h at this temperature. After 12 h, solid K_2CO_3 (2.7 g) was added in one portion and the reaction mixture was allowed to warm to r.t. The reaction was then carefully quenched by slow addition of saturated $NaHCO_3$. The reaction mixture was diluted with additional CH_2Cl_2 (30 mL) and transferred to a separatory funnel. The organic layer was washed with H_2O and the aqueous layer was extracted with CH_2Cl_2 (3x30 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to provide the crude product as a yellow oil. The crude product was purified by column chromatography (1:3 to 1:2 EtOAc/hexanes) to provide the product as a colorless oil (1.49 g, 4.11 mmol, 61 % yield). All spectroscopic data matched those reported previously in the literature.[4] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 2H), 4.56-4.47 (m, 2H), 4.30-4.21 (m, 4H), 1.77-1.68 (m, 4H), 1.69-1.61 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 6H), 0.88 (d, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.3, 148.0, 145.3, 125.8, 71.5, 70.8, 39.0, 26.0, 14.5, 11.4. HRMS (ESI) calculated for $[C_{19}H_{26}ClN_3O_2]^+$ (M+H$^+$) requires *m/z* 363.1714, found 363.1711.

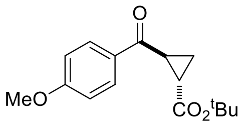
2,6-Bis((*S*)-4-((*S*)-sec-butyl)-4,5-dihydrooxazol-2-yl)-*N,N*-dimethylpyridin-4-amine (L3-12):



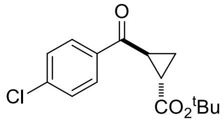
Prepared using a modified procedure provided by Tse *et al*.[5] A 100 mL round-bottomed flask was charged with **L4** (0.4601 g, 1.264 mmol), THF (15 mL), and 40 % aq. $HNMe_2$ (50 mL). The reaction mixture was then heated at 40 °C for 24 hours. The reaction mixture was then extracted with CH_2Cl_2 (3x 50 mL). The combined organics were then dried over Na_2SO_4 and concentrated under reduced pressure to provide the crude product as a yellow oil which slowly solidified. The product was purified by column chromatography (85 % hexane, 10 % NEt_3, 5 % EtOH) followed by recrystallization from EtOAc:hexane to give the product as a white crystalline solid (386.1 mg, 1.037 mmol, 82 % yield). $[\alpha]_D^{22}$ -47.6 (*c*1.76, CH_2Cl_2). ν_{max} (film) / cm^{-1} 2963, 2930, 2876, 1643, 1590, 1522, 1405, 1002, 983. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 2H), 4.60 – 4.33 (m, 4H), 4.34 – 4.11 (m, 4H), 3.10 (s, 6H), 1.8 – 1.7 (m, 2H), 1.67 – 1.59 (m, 2H), 1.30 – 1.19 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 6H), 0.87 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.16, 154.94, 146.99, 107.97, 71.23, 70.11, 39.51, 39.09, 26.24, 14.39, 11.60. HRMS (ESI) calculated for $[C_{21}H_{32}N_4O_2]^+$ (M+H$^+$) requires *m/z* 373.2598, found 373.2598. (mp = 115.8-120.0 ^{o}C.)

3.4.3 Synthesis of substrates

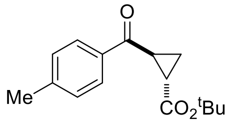
Trans Ethyl 2-benzoylcyclopropanecarboxylate (**3-1**) was prepared according to a procedure described previously by McAllister *et al*.[6] *Trans tert*-butyl 2-benzoylcyclopropanecarboxylate (**3-2**) and 1-((2-benzoylcyclopropyl)ethanone were prepared according to procedures reported by Gaunt and coworkers.[7] 1-Methylene-1,2,3,4-tetrahydronaphthalene and 1-methylene-2,3-dihydro-1H-indene were prepared according to a procedure described by Liwosz and Chemler.[8] 4-Trifluoromethylstyrene was prepared according to a procedure described by Warren and coworkers.[9]



***trans tert*-Butyl 2-(4-methoxybenzoyl)cyclopropanecarboxylate (3-39):** A 100 mL round-bottomed flask was charged with dry MeCN (17 mL), DABCO (0.449 g, 4.0 mmol), and 2-bromo-1-(4-methoxyphenyl)ethanone (0.916 g, 4.0 mmol). A thick white precipitate formed immediately, and the mixture was allowed to stir at room temperature under a nitrogen atmosphere for 30 min. After this time NaOH (0.241 g, 6.0 mmol) and tert-butyl acrylate (0.6 mL, 4 mmol) were added. The reaction flask was equipped with a reflux condenser and the reaction mixture brought to 80 °C until completion as indicated by TLC. The reaction was then quenched with saturated aqueous ammonium chloride and extracted three times with Et$_2$O. The combined organic layers were washed once with brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure to give the crude product as a dark red oil. The crude product was then purified by bulb-to-bulb distillation (190 °C, 1 Torr) to give 0.939 g (3.4 mmol, 85% yield) as a colorless oil. ν_{max} (film) / cm^{-1} 2978, 1720, 1663, 1599, 1335, 1213, 1148, 1016. ^{1}H-NMR: (400 MHz, CDCl$_3$) δ 8 (d, J = 9.5 Hz, 2H), δ 7 (d, J = 9.5 Hz, 2H), δ 3.9 (s, 3H), δ 3.1 (ddd, J = 9.3, 5.7, 3.9 Hz, 1H), δ 2.3 (ddd, J = 9.5, 6, 3.9 Hz, 1H), δ 1.57-1.48 (m, 2H), δ 1.47 (s, 9H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 195.65 , 171.63 , 163.70 , 130.56 , 130.21 , 113.80 , 81.17 , 55.50 , 28.09 , 25.45, 25.45, 17.53 . HRMS (ESI) calculated for [C$_{16}$H$_{21}$O$_4$]$^+$ (M+H$^+$) requires *m/z* 277.1434, found 277.1425.

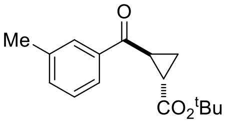


***trans* tert-Butyl 2-(4-chlorobenzoyl)cyclopropanecarboxylate (3-40):** A 100 mL round-bottomed flask was charged with dry MeCN (17 mL), DABCO (0.448 g, 4.0 mmol), and 2-bromo-1-(4-chlorophenyl)ethanone (0.934 g, 4.0 mmol). A thick white precipitate formed immediately and the mixture was allowed to stir at room temperature under a nitrogen atmosphere for 30 min. After this time NaOH (0.240 g, 6.0 mmol) and tert-butyl acrylate (0.6 mL, 4 mmol) were added. The reaction flask was equipped with a reflux condenser and the reaction mixture brought to 80 °C until completion as indicated by TLC. The reaction was then quenched with saturated aqueous ammonium chloride and extracted three times with Et_2O. The combined organic layers were washed once with brine, dried over Na_2SO_4, and concentrated under reduced pressure to give the crude product as a dark red oil. The crude product was then purified by bulb-to-bulb distillation (190 °C, 1 Torr) to give 0.910 g (3.2 mmol, 81% yield) as a white solid. v_{max} (film) / cm^{-1} 2978, 1721, 1672, 1589, 1334, 1216, 1150, 1092, 1009. ^1H-NMR: (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.7 Hz, 2H), δ 7.47 (d, J = 7.7 Hz, 2H), δ 3.1 (ddd, J = 9.4, 5.5, 3.9 Hz, 1H), δ 2.3 (ddd, J = 8.7, 6, 3.9 Hz, 1H), δ 1.6-1.52 (m, 2H), δ 1.47 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.17 , 171.26 , 139.80 , 135.45 , 129.68 , 128.98 , 81.43 , 28.10 , 25.92 , 25.69 , 18.01 . M.p. 62.6-63.6 °C. HRMS (ESI) calculated for $[C_{15}H_{21}NO_3Cl]^+$ ($M+NH_4^+$) requires *m/z* 298.1205, found 298.1204.

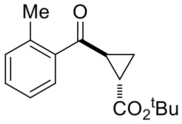


***trans* tert-Butyl 2-(4-methylbenzoyl)cyclopropanecarboxylate (3-41):** A 100 mL round-bottomed flask was charged with dry MeCN (17 mL), DABCO (0.449 g, 4.0 mmol), and 2-bromo-1-(4-methylphenyl)ethanone (0.852 g, 4.0 mmol). A thick white precipitate formed immediately and the mixture was allowed to stir at room temperature under a nitrogen atmosphere for 30 min. After this time NaOH (0.242 g, 6.0 mmol) and tert-butyl acrylate (0.60 mL, 4.0 mmol) were added. The reaction flask was equipped with a reflux condenser and the reaction mixture brought to 80 °C until completion as indicated by TLC. The reaction was then quenched with saturated aqueous ammonium chloride and extracted three times with Et_2O. The combined organic layers were washed once with brine, dried over Na_2SO_4, and concentrated under reduced pressure to give the crude product as a dark red oil. The crude product was then purified by bulb-to-bulb distillation (180 °C, 1 Torr) to give 0.906 g (3.5 mmol, 87% yield) as a white solid. ν_{max} (film) / cm^{-1} 2978, 1722, 1669, 1607, 1368, 1335, 1150, 1014. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 3.10 (ddd, *J* = 8.6, 5.7, 3.8 Hz, 1H), 2.43 (s, 3H), 2.28 (ddd, *J* = 8.6, 5.9, 3.8 Hz, 1H), 1.58 – 1.51 (m, 2H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.89 , 171.55 , 144.15 , 134.69 , 129.33 , 128.40 , 81.22 , 28.11 , 25.69 , 25.65 , 21.68 , 17.69 . M.p. 50-52 °C. HRMS (ESI) calculated for $[C_{16}H_{24}NO_3]^+$ $(M+NH_4^+)$ requires *m/z* 278.1751, found 278.1749.

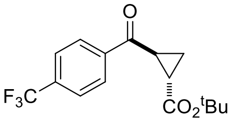
trans **tert-Butyl 2-(3-methylbenzoyl)cyclopropanecarboxylate (3-42):** A 100 mL round-bottomed flask was charged with dry MeCN (17 mL), DABCO (0.449 g, 4.0 mmol), and 2-bromo-1-(3-methylphenyl)ethanone (0.852 g, 4.0 mmol). A thick white precipitate formed immediately and the mixture was allowed to stir at room temperature under a nitrogen atmosphere for 30 min. After this time NaOH (0.243 g, 6.0 mmol) and tert-butyl acrylate (0.60 mL, 4 mmol) were added. The reaction flask was equipped with a reflux condenser and the reaction mixture brought to 80 °C until completion as indicated by TLC. The reaction was then quenched with saturated aqueous ammonium chloride and extracted three times with Et_2O. The combined organic layers were washed once with brine, dried over Na_2SO_4, and concentrated under reduced pressure to give the crude product as a dark red oil. The crude product was then purified by bulb-to-bulb distillation (180 °C, 1 Torr) to give 0.923 g (3.16 mmol, 79% yield) as a colorless oil. ν_{max} (film) / cm^{-1} 2978, 1721, 1671, 1368, 1333, 1214, 1149. ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.73 (m, 2H), 7.39 (m, 2H), 3.11 (ddd, *J* = 8.6, 5.7, 3.9 Hz, 1H), 2.43 (s, 2H), 2.30 (ddd, *J* = 8.6, 5.9, 3.9 Hz, 1H), 1.59 – 1.50 (m, 2H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.49 , 171.49 , 138.44 , 137.20 , 134.03 , 128.79 , 128.52 , 125.49 , 81.23 , 28.10 , 25.87 , 25.73 , 21.36 , 17.82 . HRMS (ESI) calculated for $[C_{16}H_{24}NO_3]^+$ $(M+NH_4^+)$ requires *m/z* 278.1751, found 278.1743.



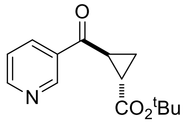
***trans* tert-Butyl 2-(2-methylbenzoyl)cyclopropanecarboxylate (3-43):** A 100 mL round-bottomed flask was charged with dry MeCN (17 mL), DABCO (0.450 g, 4.0 mmol), and 2-bromo-1-(2-methylphenyl)ethanone (0.850 g, 4.0 mmol). A thick white precipitate formed immediately and the mixture was allowed to stir at room temperature under a nitrogen atmosphere for 30 min. After this time NaOH (0.243 g, 6.0 mmol) and tert-butyl acrylate (0.60 mL, 4 mmol) were added. The reaction flask was equipped with a reflux condenser and the reaction mixture brought to 80 °C until completion as indicated by TLC. The reaction was then quenched with saturated aqueous ammonium chloride and extracted three times with Et_2O. The combined organic layers were washed once with brine, dried over Na_2SO_4, and concentrated under reduced pressure to give the crude product as a dark red oil. The crude product was then purified by bulb-to-bulb distillation (180 °C, 1 Torr) to give 0.854 g (3.28 mmol, 82% yield) as a colorless oil. ν_{max} (film) / cm^{-1} 2978, 1722, 1675, 1368, 1329, 1213, 1150, 1009. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.39 (td, *J* = 7.5, 1.5 Hz, 1H), 7.35 – 7.18 (m, 2H), 2.90 (ddd, *J* = 8.5, 5.7, 3.8 Hz, 1H), 2.50 (s, 3H), 2.29 (ddd, *J* = 8.7, 5.9, 3.8 Hz, 1H), 1.61 – 1.49 (m, 2H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.05 , 171.23 , 138.33 , 137.69 , 131.74 , 131.49 , 128.88 , 125.78 , 81.25 , 28.95 , 28.09 , 26.16 , 21.01 , 17.92 . HRMS (ESI) calculated for $[C_{16}H_{24}NO_3]^+$ ($M+NH_4^+$) requires *m/z* 278.1751, found 278.1743.



***trans* tert-Butyl 2-(4-(trifluoromethyl)benzoyl)cyclopropanecarboxylate (3-44):** A 100 mL round-bottomed flask was charged with dry MeCN (17 mL), DABCO (0.450 g, 4.0 mmol), and 2-bromo-1-(4-trifluoromethyl)phenyl)ethanone (1.07 g, 4.0 mmol). A thick white precipitate formed immediately and the mixture was allowed to stir at room temperature under a nitrogen atmosphere for 30 min. After this time NaOH (0.243 g, 6.0 mmol) and tert-butyl acrylate (0.60 mL, 4 mmol) were added. The reaction flask was equipped with a reflux condenser and the reaction mixture brought to 80 °C until completion as indicated by TLC. The reaction was then quenched with saturated aqueous ammonium chloride and extracted three times with Et_2O. The combined organic layers were washed once with brine, dried over Na_2SO_4,

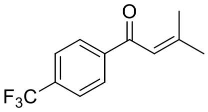


and concentrated under reduced pressure to give the crude product as a dark red oil. The crude product was then purified by bulb-to-bulb distillation (200 °C, 1 Torr) to give 0.893 g (2.84 mmol, 71% yield) as a white solid. ν_{max} (film) / cm^{-1} 2978, 1724, 1680, 1322, 1157, 1133, 1068, 1012. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.1 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 3.10 (ddd, *J* = 8.6, 5.7, 3.8 Hz, 1H), 2.34 (ddd, *J* = 8.6, 6.1, 3.8 Hz, 1H), 1.60 (dddd, *J* = 11.8, 8.3, 6.6, 3.6 Hz, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.57 , 171.07 , 139.78 , 134.6 (q, J = 32.7 Hz), 128.60 , 125.73 (q, *J* = 3.8 Hz), 123.57 (q, *J* = 272.7 Hz), 81.57 , 28.09 , 26.21 , 25.98 , 18.24 . ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.14. HRMS (ESI) calculated for $[C_{16}H_{21}NO_3F_3]^+$ ($M+NH_4^+$) requires *m/z* 332.1468, found 332.1467. (mp = 74.0-75.5 °C)

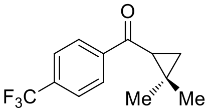


***trans* tert-Butyl 2-nicotinoylcyclopropanecarboxylate (3-45):** A 100 mL round-bottomed flask was charged with dry MeCN (17 mL), DABCO (0.890 g, 8.0 mmol), and 3-(2-bromoacetyl)pyridin-1-ium bromide (1.12 g, 4.0 mmol). A thick white precipitate formed immediately and the mixture was allowed to stir at room temperature under a nitrogen atmosphere for 30 min. After this time NaOH (0.324 g, 8.0 mmol) and tert-butyl acrylate (0.60 mL, 4 mmol) were added. The reaction flask was equipped with a reflux condenser and the reaction mixture brought to 80 °C until completion as indicated by TLC. The reaction was then quenched with saturated aqueous ammonium chloride and extracted three times with Et_2O. The combined organic layers were washed once with brine, dried over Na_2SO_4, and concentrated under reduced pressure to give the crude product as a dark red oil. The crude product was then purified by bulb-to-bulb distillation (190 °C, 1 Torr) to give 0.584 g (2.36 mmol, 59% yield) as a white solid. ν_{max} (film) / cm^{-1} 2980, 1722, 1675, 1586, 1341, 1216, 1153, 1010. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (d, *J* = 1.8 Hz, 6H), 8.81 (dd, *J* = 4.8, 1.6 Hz, 5H), 8.27 (dt, *J* = 8.0, 2.0 Hz, 4H), 7.45 (dd, *J* = 8.0, 4.8 Hz, 5H), 3.09 (ddd, *J* = 9.3, 5.7, 3.9 Hz, 5H), 2.35 (ddd, *J* = 8.7, 6.1, 3.8 Hz, 5H), 1.66 – 1.54 (m, 1H), 1.48 (s, 37H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.34 , 170.96 , 153.70 , 149.75 , 135.50 , 132.39 , 123.62 , 81.60 , 28.09 , 26.17 , 25.93 , 18.08. HRMS (ESI) calculated for $[C_{14}H_{18}NO_3]^+$ ($M+H^+$) requires *m/z* 248.1281, found 248.1274. (mp = 48.7-51.2 °C)

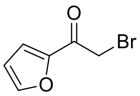
3-Methyl-1-(4-(trifluoromethyl)phenyl)but-2-en-1-one (3-46): Prepared as described previously by Okamoto *et al*.[12] ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.02 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 6.74 (s, 1H), 2.25 (s, 3H), 2.05 (s, 3H).



(2,2-Dimethylcyclopropyl)(4-(trifluoromethyl)phenyl)methanone (3-47): A flame-dried 50 mL flask was charged with solid NaH (60% in mineral oil, 80.5 mg, 2.0 mmol) and trimethylsulfoxonium iodide (0.440 g, 2.0 mmol) and the flask was placed under a nitrogen atmosphere. DMSO (5 mL) was then added dropwise to the flask. After hydrogen evolution ceased, the reaction mixture was stirred for an additional 15 min during which the solution became clear. 3-Methyl-1-(4-(trifluoromethyl)phenyl) but-2-en-1-one (0.380 g, 1.67 mmol) was then added in one portion via syringe. The reaction mixture was allowed to stir for 24 h at room temperature. The reaction was then quenched by addition of water, and the mixture extracted three times with Et$_2$O. The combined organic layers were dried over Na$_2$SO$_4$ and volatiles were removed under reduced pressure to yield the crude product as a dark residue. The crude product was purified by column chromatography (3.3% Et$_2$O in pentane) to give the product as a colorless oil. ν_{max} (film) / cm^{-1} 2978, 1688, 1432, 1318, 1159, 1010. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 2.48 (dd, *J* = 7.4, 5.7 Hz, 1H), 1.59 – 1.55 (m, 1H), 1.38 (s, 3H), 1.10 (s, 3H), 1.03 (dd, *J* = 7.4, 4.1 Hz, 1H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 197.60 , 141.69 , 133.76 (q, *J* = 32.6 Hz), 128.25 , 125.54 (q, *J* = 3.8 Hz), 123.71 (d, *J* = 272.6 Hz), 33.18 , 27.99 , 27.03 , 22.64 , 18.42. ^{19}F NMR (377 MHz, CDCl$_3$) δ –63.02. HRMS (ESI) calculated for $[C_{13}H_{17}F_3NO]^+$ (M+NH$_4^+$) requires *m/z* 260.1257, found 260.1257.

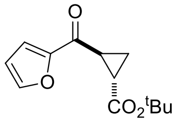


2-Bromo-1-(furan-2-yl)ethanone: A 100 mL round-bottomed flask was charged with 2-acetylfuran (2.20 g, 20.0 mmol) and anhydrous Et$_2$O (30 mL). The reaction vessel was sealed with a septum and purged several times with N$_2$ (g). The reaction vessel was cooled to 0 °C and Br$_2$ (1.03 mL, 20.0 mmol) was added dropwise via syringe. The reaction mixture was allowed to stir 20 min at 0 °C before slowly warming to r.t. After 12 h the reaction was

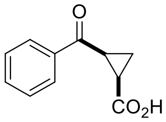


quenched by addition of H_2O (20 mL). The mixture was then extracted with Et_2O (2x 20 mL) and the combined organics were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (Et_2O/pentane) to provide the product as a clear oil (3.44 g, 18.2 mmol, 91% yield). Spectral data were in agreement with those published previously in the literature.[13] ^1H NMR (300 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.34 (dd, *J* = 3.6, 0.7 Hz, 1H), 6.60 (dd, *J* = 3.6, 1.7 Hz, 1H), 4.32 (s, 2H).

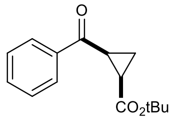
***trans*-tert-Butyl 2-(furan-2-carbonyl)cyclopropanecarboxylate (3-48):** A flame-dried 100 mL round-bottomed flask was charged with 2-bromo-1-(furan-2-yl)ethanone (3.44 g, 18.2 mmol), DABCO (2.04 g, 18.2 mmol) and anhydrous MeCN (45 mL). The reaction mixture was allowed to stir for 30 min. at r.t. under a N_2 atmosphere. After this time dry NaOH (1.13 g, 28.1 mmol) and *tert*-butyl acrylate (2.6 mL, 18.2 mmol) was added in quick succession. The reaction vessel was equipped with a reflux condenser and the reaction mixture was stirred at 85 °C for 16 h. After cooling to r.t the reaction was quenched by addition of saturated aq. NH_4Cl and extracted with Et_2O (3x 50 mL). The combined organic were dried over Na_2SO_4 and concentrated under reduced pressure to provide the crude product as a dark yellow oil. The crude product was purified by column chromatography (Et_2O/pentane) to provide **1j** as a white solid (3.48 g, 14.7 mmol, 81 % yield). ν_{max} (film) / cm^{-1} 2979, 1723, 1666, 1570, 1469, 1336, 1215, 1154. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.61 (m, 1H), 7.31 – 7.25 (m, 1H), 6.58 (dd, *J* = 3.6, 1.7 Hz, 1H), 3.01 (ddd, *J* = 9.4, 5.7, 3.9 Hz, 1H), 2.28 (ddd, *J* = 8.8, 6.0, 3.9 Hz, 1H), 1.58 – 1.49 (m, 2H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.88 , 171.25 , 152.75 , 146.86 , 117.64 , 112.44 , 81.31 , 28.09 , 25.85 , 25.45 , 17.29. HRMS (ESI) calculated for $[C_{13}H_{17}O_4^+]$ $(M+H^+)$ requires 237.1121, found 237.1119. (mp = 68.2-70.2 ^oC)



***cis* 2-Benzoylcyclopropanecarboxylic acid (3-49):** Prepared using a modification of the procedure by Augustine and coworkers.[17] A 50 mL flame-dried round bottom flask was charged with $AlCl_3$ (2.01 g, 15.1 mmol) and anhydrous benzene (8 mL). The



flask was sealed with a rubber septum and purged several times with N_2 (g). 3-Oxabicyclo[3.1.0]-hexane-2,4-dione (0.688 g, 6.14 mmol) was dissolved in anhydrous benzene (7 mL) and slowly added to the flask containing $AlCl_3$ via syringe. The reaction mixture was allowed to stir overnight. After this time the reaction mixture was refluxed for 3 h, cooled to room temperature and quenched by pouring into a beaker containing cold dilute HCl. The heterogeneous mixture was extracted by washing with EtOAc (4x). The combined organics were dried over Na_2SO_4 and concentrated under reduced pressure to provide the crude product as a yellow solid. The crude product was purified by recrystallization from hot CH_2Cl_2 to provide the pure product as a white crystalline solid (0.716 g, 3.76 mmol, 61% yield). All spectroscopic data were in agreement with those reported previously in the literature. ^{1}H NMR (400 MHz, CD_3OD) δ 8.07 (d, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 2.96 (ddd, *J* = 9.5, 8.2, 7.0 Hz, 1H), 2.36 (ddd, *J* = 9.3, 8.1, 6.3 Hz, 1H), 1.75 (td, *J* = 6.6, 4.4 Hz, 1H), 1.37 (td, *J* = 8.1, 4.4 Hz, 1H).

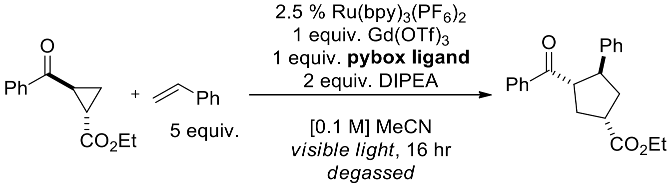


***cis* tert-Butyl 2-benzoylcyclopropanecarboxylate (*cis*-3-2):** A 100 mL round bottom flask was charged with cis 2-benzoylcyclopropanecarboxylic acid (0.716 g, 3.76 mmol), *t*-butanol (30 mL), Boc_2O (1.232 g, 5.65 mmol), and DMAP (3 mg, 24.6 μmol). The flask was then sealed with a rubber septum and purged with N_2(g). The reaction mixture was then stirred at 40 ^{o}C for 5 h. After cooling, the reaction mixture was quenched by the addition of saturated NH_4Cl solution and the mixture was extracted 3x with CH_2Cl_2. The combined organics were dried over Na_2SO_4 and concentrated under reduced pressure to provide the crude product as a yellow solid. The crude product was purified by column chromatography (25 % Et_2O/pentanes) to provide the pure product as a white solid (0.834 g, 3.39 mmol, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.6 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 2.78 – 2.62 (m, 1H), 2.22 (td, *J* = 8.7, 6.3 Hz, 1H), 1.92 – 1.77 (m, 1H), 1.33 – 1.23 (m, 3H), 1.18 (s, 8H).^{13}C NMR (101 MHz, $CDCl_3$) δ 194.31, 169.20, 137.20, 133.08, 128.50, 128.42, 81.12, 27.66, 26.51, 23.88, 10.87. v_{max} (film) / cm^{-1} 2977, 1713, 1675, 1391, 1450, 1369, 1233, 1153.

HRMS (ESI) calculated for $[C_{15}H_{19}O_3]^+$ (M+H$^+$) requires *m/z* 247.1334, found 247.1334. (mp = 146.5-149.4 ^{o}C)

3.4.4 Optimization data

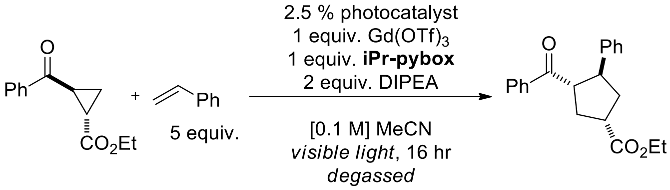
Table 3-3. Pybox ligand screen.



Entry	Ligand	% Yield[a] (time)	% conversion	% ee
1	iPr-pybox	10 % (16 h)	15 %	38 %
2	tBu-pybox	95 % (3 h)	100 %	40 %
3	sBu-pybox	32 % (16 h)	56 %	58 %
4	Bn-pybox	100 % (3 h)	100 %	<4 %
5	iBu-pybox	trace (16 h)	<5 %	N.D.
6	indano-pybox	6 % (16 h)	10 %	11 %
7	Ph-dbfox	85 % (16 h)	100 %	0 %

[a]Yield determined by 1H-NMR using phenanthrene as an internal standard.

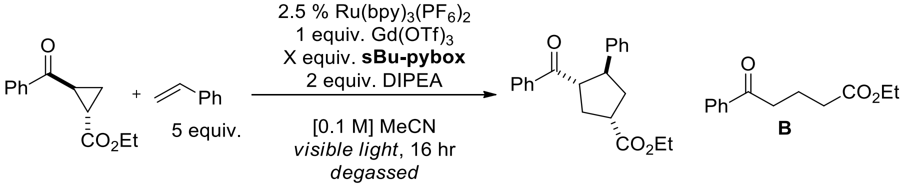
Table 3-4. Optimization of photocatalyst



Entry	Photocatalyst	% Yield[a]	% RSM
1	$Ru(bpy)_3(PF_6)_2$	21.2 %	78 %
2	$Ru(dtbbpy)_3(PF_6)_2$	12.5 %	85 %
3	$Ir(ppy)_3$	5.4 %	93 %
4	$Ir(ppy)_2dtbbpy(PF_6)$	23.2 %	70 %

[a]Yield determined by ^{1}H-NMR using phenanthrene as an internal standard.

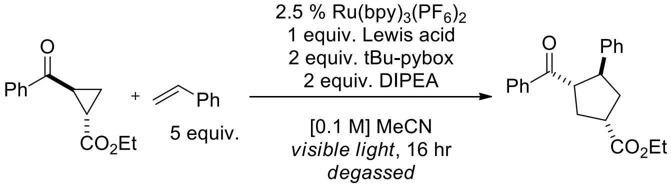
Table 3-5. Optimization of sBu-pybox equivalents.



Entry	Equiv. sBu-pybox	% yield[a]	% conversion	%B	d.r.	% ee
1	1 equiv.	32 %	56 %	23 %	2.3:1	58 %
2	2 equiv.	36 %	50 %	11 %	2.5:1	60 %
3	3 equiv.	13 %	15 %	3 %	2:1	N.D.

[a]Yields determined by 1H-NMR using phenanthrene as internal standard. [b]Compound **B** is a known compound[26]

Table 3-6. Lewis acid screen with tBu-pybox.

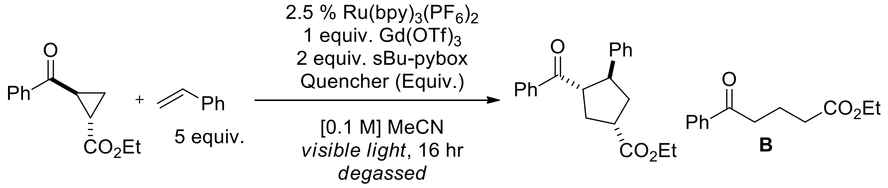


Entry	Lewis acid	% yield[a]	% RSM	% ee
1	$Gd(OTf)_3$	53 %	40 %	41 %
2	$La(OTf)_3$	5 %	94 %	---
3	$Y(OTf)_3$	27 %	71 %	38 %
4	$Fe(OTf)_2$	0 %	100 %	---
5	$Cu(OTf)_2$	0 %	100 %	---
6	$Ni(OTf)_2$	0 %	100 %	---
7	$In(OTf)_3$	trace	92 %	---
8	$Yb(OTf)_3$	11 %	71 %	---
9	$Zn (OTf)_2$	trace	>95 %	---
10	$Sc(OTf)_3$	26 %	60 %	0 %
11	$ZrCl_4$	0 %	93 %	---
12	$Mg(OTf)_2$	0 %	100 %	---
13	$Er(OTf)_3$	trace	>95 %	---
14	$Bi(OTf)_3$	0 %	100 %	---
15	$Sm(OTf)_3$	0 %	100 %	---

16	$Sn(OTf)_2$	trace	93 %	---
17	$Ce(OTf)_3$	0 %	100 %	---
18	$Mn(ClO_4)_2$	0 %	100 %	---
19	$Al(OTf)_3$	3 %	96 %	---
20	$Mg(ClO_4)_2$	0 %	100 %	---
21	$Cd(ClO_4)_2$	0 %	100 %	---
22	$Ba(ClO_4)_2$	21 %	73 %	4 %
23	$Eu(OTf)_3$	0 %	100 %	---
24	$Nd(OTf)_3$	3 %	>95 %	---
25	$Dy(OTf)_3$	10 %	89 %	0 %
26	$Pr(OTf)_3$	15 %	82 %	8 %

[a] Yield determined by 1H-NMR using phenanthrene as internal standard

Table 3-7. Reductive quencher screen.

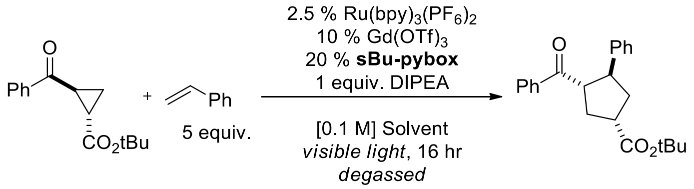


Entry	Quencher (Equiv.)	% yield[a]	% B	% RSM	% ee
1	DIPEA (1)	15 %	trace	80 %	N.D.
2	DIPEA (2)	24 %	6 %	32 %	63 %
3	DIPEA (5)	36 %	11 %	50 %	60 %
4	DIPEA (10)	trace	trace	>95 %	N.D.
5	TMEDA (1)	40 %	11.5 %	48 %	57 %
6	NEt_3 (2)	35 %	18 %	42 %	55 %
7	NBu_3 (2)	32 %	25 %	32 %	N.D.
8	1,4-dimethylpiperazine (2)	trace	trace	>95 %	N.D.
9	N-methyl-pyrrolidine (2)	37 %	25 %	26 %	N.D.
10	*N,N,N',N'*-tetramethylpropylenediamine (2)	41 %	30 %	20 %	58.5 %
11	*N,N,N',N'*-tetramethylbutanediamine (2)	17 %	13.5 %	65 %	N.D.
12	$NEtCy_2$ (2)	21 %	7 %	68 %	N.D.
13	*N,N*-dimethylbenzylamine (2)	20 %	13 %	68 %	N.D.
14	4-methylmorpholine (2)	trace	trace	>95 %	N.D.

15	N-methylpiperidine (2)	0 %	0 %	100 %	---
16	*N,N,N',N'*-tetramethyl-p-phenylene diamine (2)	0 %	0 %	100 %	---
17	*N,N,N',N'*- tetramethylbenzidine (2)	0 %	0 %	100 %	---
18	*N,N,N',N",N"*-pentamethyldiethylenetramine (2)	25 %	22 %	10 %	63 %
19	1,2,2,6,6-pentamethylpiperidine (2)	26 %	4.5 %	61 %	60 %
20	4-aminophenol (2)	0 %	0 %	100 %	---
21	p-toluidine (2)	0 %	0 %	100 %	---
22	4-MeO-*N,N*-diphenylaniline (2)	0 %	0 %	100 %	---
23	2,6-di-tert-butyl-4-methylphenol (2)	0 %	0 %	100 %	---
24	2,4,6-trimethylaniline (2)	0 %	0 %	100 %	---
25	DABCO (2)	0 %	0 %	100 %	---
26	2,6-lutidine (2)	0 %	0 %	100 %	---
27	DBU (2)	trace	trace	50 %	N.D.
28	K_4FeCN_6 hexahydrate (2)	0 %	0 %	100 %	---
29	cesium oxalate (2)	0 %	0 %	100 %	---

[a]Yields determined by 1H-NMR using phenanthrene as an internal standard

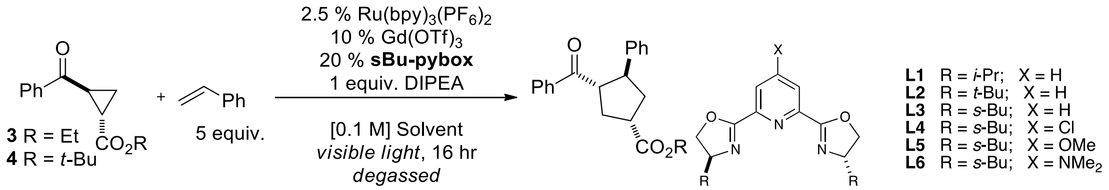
Table 3-8. Solvent optimization



Entry	Solvent	% yield[a]	dr	% ee
1[b]	Toluene	37 %	15:1	3.5 %
2[b]	Et_2O	66 %	3.9:1	39 %
3[b]	THF	50 %	2.3:1	45 %
4[b]	CH_2Cl_2	95%	4.5:1	71 %
5	Acetone	86 %	2.6:1	84 %
6	MeCN	93 %	2.3:1	85 %
7[b]	MeCN	92 %	2.3:1	85 %
8	DMF	52 %	2.6:1	15 %

[a]Yields determined by 1H-NMR spectroscopy using phenanthrene as internal standard. [b]Reaction carried out using $Ir(ppy)_2(dtbbpy)(PF_6)$ as photocatalyst.

Table 3-9. Final optimization of reaction conditions

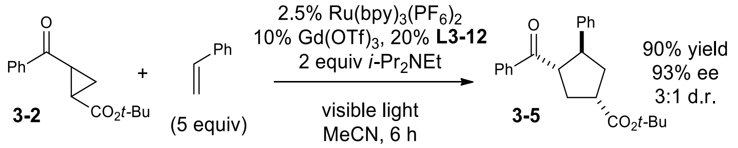


Entry	Conditions[a]	Yield[b]	dr; % ee
1	100 % La(OTf)$_3$	25 %	14:1; ---
2	100 % La(OTf)$_3$, 100% **L2**	5 %	--- ; ---
3	100 % Gd(OTf)$_3$, 100 % **L1**	15 %	3:1; 38 %
4	100 % Gd(OTf)$_3$, 100 % **L2**	96 %	3:1; 45 %
5	100 % Gd(OTf)$_3$, 100 % **L3**	25 %	2:1; 59 %
6	100 % Gd(OTf)$_3$, 200 % **L3**	36 %	3:1; 63 %
7	100 % Gd(OTf)$_3$, 200 % **L4**	0 %	---;---
8	100 % Gd(OTf)$_3$, 200 % **L5**	90 %	2:1; 64 %
9	100 % Gd(OTf)$_3$, 200 % **L6**	89 %	2:1; 85 %
10	10 % Gd(OTf)$_3$, 20% **L6**	96 %	2:1; 79 %
11	10 % Gd(OTf)$_3$, 20% **L6**, 0 °C	80%	3:1; 85 %
12	10 % Gd(OTf)$_3$, 20% **L6**, –20 °C	41 %	3:1; 91 %
13[c]	10 % Gd(OTf)$_3$, 20 % **L6**, 0 °C	86 %	3:1; 90 %
14[c,d]	10 % Gd(OTf)$_3$, 20 % **L6**, 0 °C	95 %	3:1; 93 %

[a] Reactions carried out on 0.045 mmol scale, irradiating with a 23 W CFL for 6 h. [b] Yields determined by ^{1}H-NMR yield using phenanthrene as an internal standard. [c] Using **4** instead of **3**. [d] Using 1 equiv of *i*-Pr$_2$NEt.

3.4.5 Control studies

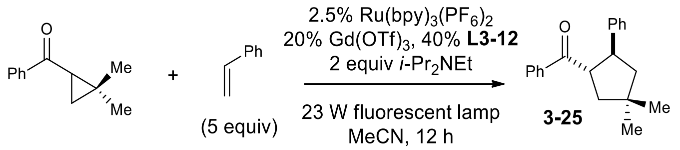
Table 3-10. Control studies with tert-butyl 2-benzoylcyclopropanecarboxylate (**4**).



Entry	Change from std. conditions	% yield[a]	dr
1	none	95 %	3:1
2	No photocatalyst	trace	N.D.
3	No light	0 %	---
4	No Gd(OTf)$_3$	0 %	---
5	No *i*-Pr$_2$NEt	0%	---

[a] Yields determined by ^{1}H-NMR using phenanthrene as an internal standard

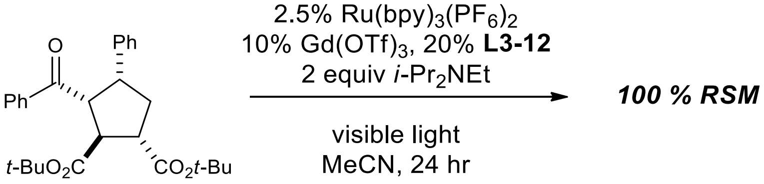
Table 3-11. Control studies with (2,2-dimethylcyclopropyl)(phenyl)methanone.



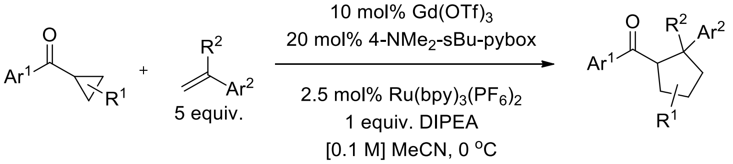
Entry	Change from std. conditions	% yield[a]	dr
1	none	55 %	5:1
2	No photocatalyst	36 %	5:1
3	No light	0 %	---
4	1 equiv. Gd(OTf)$_3$, 3 equiv. TMEDA, no ligand, no *i*-Pr$_2$NEt	0 %	---
5	No photocatalyst, no *i*-Pr$_2$NEt	0 %	---
6	No photocatalyst, blue LEDS instead of 23W fluorescent bulb	0 %	---

[a] Yields determined by ^{1}H-NMR using phenanthrene as an internal standard

Figure 3-8. Product isomerization control



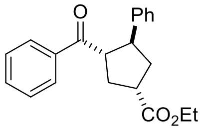
3.4.6 Asymmetric [3+2] cycloadditions



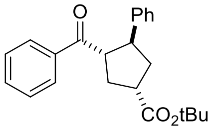
General asymmetric procedure:

An oven-dried 2 mL volumetric flask was charged with $Gd(OTf)_2$ (0.04 mmol) and 4-NMe_2-^{s}Bu-pybox (0.08 mmol). The solids were dissolved in MeCN (2 mL total volume). A separate 2 mL volumetric flask was charged with cyclopropane (0.4 mmol), alkene (2.0 mmol), $Ru(bpy)_3(PF_6)_2$ (0.01 mmol), diisopropylethylamine (0.4 mmol), and MeCN (4 mL total volume). The contents of both volumetric flasks were then transferred to a dry Schlenk tube equipped with a magnetic stir-bar. The reaction mixture was then thoroughly degassed through three freeze-pump-thaw cycles, then backfilled with N_2. The reaction flask was then transferred to a cooling bath of 0 °C in front of a 23 W (1380 lumen) compact fluorescent lamp. Upon consumption of starting material, the reaction was diluted with 1:1 Et_2O/pentanes and passed through a short plug of silica. The filtrate was concentrated and the residue purified by column chromatography. Diastereomeric ratios were determined by ^{1}H-NMR analysis of the crude reaction mixture. Only two diastereomers were observed in the crude reaction mixtures.

Ethyl 3-benzoyl-4-phenylcyclopentanecarboxylate (3-4): Prepared according to the general procedure using 24.5 mg (0.04 mmol) of Gd(OTf)$_3$, 30.1 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 87.3 mg (0.4 mmol) of *trans* ethyl 2-benzoylcyclopropanecarboxylate, 209.4 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, and 58.1 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M) in MeCN. The reaction was complete after 6 h. The crude product was purified by column chromatography (1:5, Et$_2$O/pentanes) to give 123.8 mg (0.384 mmol, 96 % yield) of cycloadduct as two separable diastereomers (3:1 d.r.). Major Diastereomer: 79.3% ee [Daicel Chiracel AD-H, 10 to 40 % iPrOH, 3 mL/min, 263 nm; t_1=4.71 min, t_2=6.04 min]. $[\alpha]_D^{22}$ 38.7 (*c*1.021, CH$_2$Cl$_2$) White solid (mp = 43.9-46.8 °C). ν_{max} (film) / cm^{-1} 2978, 1728, 1680, 1597, 1265, 1180 ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.73 (d, *J* = 7.3 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.29 (t, *J* = 7.7 Hz, 2H), 7.24 – 7.14 (m, 4H), 7.13 – 7.02 (m, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.82 (q, *J* = 8.9 Hz, 1H), 3.73 (q, *J* = 8.7 Hz, 1H), 3.11 (qd, *J* = 8.4, 6.2 Hz, 1H), 2.57 – 2.39 (m, 2H), 2.21 (dt, *J* = 13.2, 8.9 Hz, 1H), 2.10 (dt, *J* = 13.3, 8.9 Hz, 1H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 200.52 , 174.95 , 143.58 , 136.80 , 132.98 , 128.57 , 128.49 , 128.40 , 127.29 , 126.49 , 60.72 , 54.67 , 47.25 , 43.43 , 37.31 , 35.17 , 14.26. HRMS (ESI) calculated for $[C_{21}H_{23}O_3]^+$ (M+H$^+$) requires *m/z* 323.1642, found 323.1642.



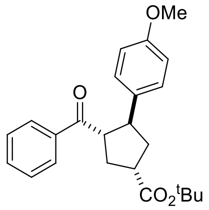
tert-Butyl 3-benzoyl-4-phenylcyclopentanecarboxylate (3-5): Prepared according to the general procedure using 24.6 mg (0.04 mmol) of Gd(OTf)$_3$, 30.0 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 98.5 mg (0.4 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 209.5 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, and 58.2 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M) in MeCN. The reaction was complete after 6 h. The crude product was purified by column chromatography (1:9, Et$_2$O/pentanes) to give 133.2 mg (0.384 mmol, 95 % yield) of cycloadduct as two separable diastereomers (2.7:1 d.r.). Major diastereomer: 93% ee [Daicel Chiracel AD-H,



5 to 50 % iPrOH, 3 mL/min, 263 nm; t_1=6.10 min, t_2=7.08 min]. $[\alpha]_D^{22}$ 40.6 (*c*0.990, CH_2Cl_2). v_{max} (film) / cm^{-1} 2980, 1722, 1682, 1368, 1265, 1151. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.9 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.28-7.22 (m, 4H), 7.16 (dq, *J* = 9.1, 4.3 Hz, 1H), 3.94 – 3.73 (m, 2H), 3.17 – 3.00 (m, 1H), 2.58 – 2.44 (m, 2H), 2.22 (dt, *J* = 13.3, 9.0 Hz, 1H), 2.13 (dt, *J* = 13.1, 9.0 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.56 , 174.21 , 143.74 , 136.85 , 132.92 , 128.52 , 128.47 , 128.39 , 127.31 , 126.42 , 80.52 , 54.75 , 47.14 , 44.46 , 37.31 , 35.36 , 28.08. M.p. 97.1-98.5 ^{o}C. HRMS (ESI) calculated for $[C_{23}H_{27}O_3]^+$ ($M+H^+$) requires *m/z* 351.1955, found 351.1955.

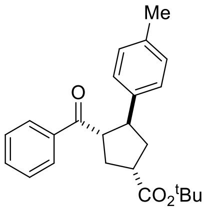
Minor Diastereomer: v_{max} (film) / cm^{-1} 2981, 1719, 1684, 1365, 1262, 1150. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.28-7.22 (m, 4H), 7.15 (t, *J* = 6.8 Hz, 1H), 3.99 (q, *J* = 9.3 Hz, 1H), 3.68 (dt, *J* = 11.0, 8.4 Hz, 1H), 3.00 (ddd, *J* = 16.6, 9.2, 7.5 Hz, 1H), 2.62 – 2.43 (m, 2H), 2.14 (dt, *J* = 13.2, 8.9 Hz, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.32 , 174.92 , 142.96 , 136.62 , 133.04 , 128.51 , 128.50 , 127.42 , 126.53 , 80.49 , 53.70 , 48.34 , 44.20 , 38.84 , 34.83 , 28.13. M.p. 111.5-113.0^{o}C. HRMS (ESI) calculated for $[C_{23}H_{30}NO_3]^+$ ($M+NH_4^+$) requires *m/z* 368.2220, found 368.2220.

***tert*-Butyl 3-benzoyl-4-(4-methoxyphenyl)cyclopentanecarboxylate (3-6):** Prepared according to the general procedure using 24.4 mg (0.04 mmol) of $Gd(OTf)_3$, 30.6 mg (0.08 mmol) of 4-NMe_2-^{s}Bu-pybox, 98.5 mg (0.4 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 241.2 mg (2.0 mmol) of 4-vinylanisole, 8.9 (0.01 mmol) mg of $Ru(bpy)_3(PF_6)_2$, 53.4 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M). The reaction was ended after 20 h. The crude product was purified by column chromatography (1:29, acetone/pentanes) to give 135 mg (0.36 mmol, 89% yield) of the cycloadduct as two separable diastereomers (2.8:1 d.r.). Major diastereomer: 90.7% ee [Daicel Chiracel AD-H, 10 to 20 % iPrOH, 3 mL/min, 240 nm; t_1=6.09 min, t_2=8.71 min]. $[\alpha]_D^{22}$ 65.9 (*c*1.080, CH_2Cl_2). White solid (mp = 95.5 – 98.5 °C). v_{max} (film) / cm^{-1} 2975, 1721, 1679, 1612,



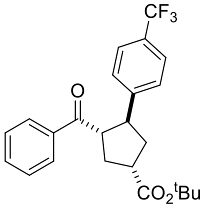
1513, 1448, 1366, 1246, 1149, 1035, 1012, 829, 701. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 6.9 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 8.7 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 3.82 (td, *J* = 9.5, 8.0 Hz, 1H), 3.77 – 3.71 (m, 1H), 3.75 (s, 3H), 3.07 (qd, *J* = 8.4, 5.7 Hz, 1H), 2.54 – 2.43 (m, 2H), 2.21 (ddd, *J* = 13.2, 9.8, 8.3 Hz, 1H), 2.08 (dt, *J* = 13.3, 9.1 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.72, 174.30, 158.12, 136.92, 135.69, 132.90, 128.47, 128.39, 128.23, 113.90, 80.46, 55.24, 54.88, 46.54, 44.30, 37.40, 35.27, 28.08. HRMS (ESI) calculated for $[C_{24}H_{29}O_4]^+$ $(M+H^+)$ requires *m/z* 381.2060, found *m/z* 381.2053. Minor diastereomer: White solid (mp = 110.5 – 113.5 °C_. v_{max} (film) / cm^{-1} 2975, 1723, 1680, 1514, 1448, 1367, 1249, 1220, 1152, 1036, 830, 701. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.18 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 3.93 (q, *J* = 9.4 Hz, 1H), 3.74 (s, 3H), 3.69 – 3.54 (m, 1H), 2.99 (ddd, *J* = 16.6, 9.3, 7.3 Hz, 1H), 2.54 – 2.41 (m, 2H), 2.18 – 2.01 (m, 2H), 1.48 (s, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.51, 175.01, 158.20, 136.69, 134.93, 133.01, 128.49, 128.49, 128.34, 113.89, 80.46, 55.24, 53.85, 47.74, 44.11, 38.92, 34.76, 28.14. HRMS (ESI) calculated for $[C_{24}H_{32}NO_4]^+$ $(M+NH_4^+)$ requires *m/z* 398.2326, found *m/z* 398.2322.

***tert*-Butyl 3-benzoyl-4-(4-methylphenyl)cyclopentanecarboxylate (3-7):** Prepared according to the general procedure using 24.6 mg (0.04 mmol) of $Gd(OTf)_3$, 30.1 mg (0.08 mmol) of 4-NMe_2-^{s}Bu-pybox, 98.9 mg (0.4 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 242.0 mg (2.0 mmol) of 4-methylstyrene, 9.0 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, 52.2 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M). The reaction was ended after 20 h. The crude product was purified by column chromatography (1:69 acetone/pentanes) to give 131 mg (0.36 mmol, 90% yield) of the cycloadduct as two separable diastereomers (2.8:1 d.r.). Major diastereomer: 88.7% ee [Daicel Chiracel AD-H, 10 to 40 % iPrOH, 3 mL/min, 241 nm; t_1=6.01 min, t_2=7.36 min]. $[\alpha]_D^{22}$ 60.7 (*c*1.060, CH_2Cl_2). White solid (mp = 84.2 – 85.9 °C). v_{max} (film) / cm^{-1} 2976, 1723, 1681, 1515,

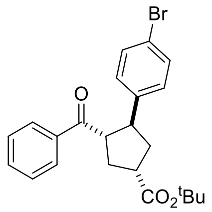


1448, 1367, 1249, 1150, 848, 815, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.3 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 3.85 (q, *J* = 9.0 Hz, 1H), 3.77 (q, *J* = 8.6 Hz, 1H), 3.08 (qd, *J* = 8.4, 6.2 Hz, 1H), 2.56 – 2.42 (m, 2H), 2.27 (s, 3H), 2.20 (dt, *J* = 13.1, 9.3 Hz, 1H), 2.10 (dt, *J* = 13.2, 8.9 Hz, 1H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.62, 174.26, 140.70, 136.89, 135.91, 132.88, 129.19, 128.46, 128.41, 127.17, 80.47, 54.71, 46.73, 44.43, 37.38, 35.33, 28.08, 20.97. HRMS (ESI) calculated for $[C_{24}H_{29}O_3]^+$(M+H$^+$) requires *m/z* 365.2111, found *m/z* 365.2105. Minor diastereomer: White solid (mp = 129.1 – 131.9 °C). ν_{max} (film) / cm^{-1} 2973, 2930, 1726, 1678, 1448, 1365, 1280, 1245, 1227, 1155, 818, 699. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.4 Hz, 2H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 7.9 Hz, 2H), 3.96 (q, *J* = 9.3 Hz, 1H), 3.69 – 3.60 (m, 1H), 2.99 (ddd, *J* = 16.7, 9.3, 7.5 Hz, 1H), 2.54 – 2.44 (m, 2H), 2.27 (s, 3H), 2.11 (tdd, *J* = 17.1, 9.8, 4.3 Hz, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.40, 174.96, 139.90, 136.66, 136.04, 133.00, 129.18, 128.52, 128.48, 127.28, 80.45, 53.71, 47.93, 44.19, 38.93, 34.83, 28.14, 20.98. HRMS (ESI) calculated for $[C_{24}H_{32}NO_3]^+$ (M+NH$_4^+$) requires *m/z* 382.2377, found *m/z* 382.2372.

***tert*-Butyl 3-benzoyl-4-(4-trifluoromethylphenyl)cyclopenanecarboxylate (3-8):** Prepared according to the general procedure using 24.2 mg (0.04 mmol) of Gd(OTf)$_3$, 28.8 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 98.0 mg (0.4 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 344.6 mg (2.0 mmol) of 4-trifluoromethylstyrene, 8.8 mg (0.01 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, 52.6 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M). The reaction was ended after 20 h. The crude product was purified by column chromatography (1:49 acetone/pentanes) to give 135 mg (0.34 mmol, 81% yield) of the cycloadduct as two separable diastereomers (2.4:1 d.r.). Major diastereomer: 89.4% ee [Daicel Chiracel AD-H, 10 to 20 % iPrOH, 3 mL/min, 240 nm; t$_1$=3.38 min, t$_2$=4.67 min]. $[\alpha]_D^{22}$ 52.1 (*c*1.000, CH_2Cl_2). White solid. (mp = 106.9 – 108.4 °C). ν_{max} (film) /



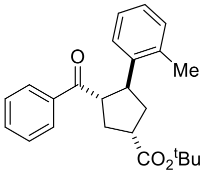
cm^{-1} 2978, 1724, 1682, 1619, 1449, 1368, 1326, 1258, 1156, 1124, 1069, 1017, 842, 701. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.1 Hz, 2H), 7.55 – 7.47 (m, 3H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 3.93 – 3.81 (m, 2H), 3.15 – 3.07 (m, 1H), 2.55 (qd, *J* = 8.2, 4.1 Hz, 2H), 2.19 (ddd, *J* = 13.1, 9.5, 8.0 Hz, 1H), 2.12 (dt, *J* = 13.5, 9.2 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.89, 173.95, 147.72, 136.59, 133.17, 128.75 (q, *J* = 32.5 Hz), 128.59, 128.35, 127.70, 125.45 (q, *J* = 3.9 Hz), 124.47 (q, *J* = 272.9 Hz), 80.73, 54.76, 46.57, 44.28, 37.02, 35.45, 28.05. **^{19}**F NMR (377 MHz, $CDCl_3$) δ -62.46. HRMS (ESI) calculated for $[C_{24}H_{26}F_3O_3]^+(M+H^+)$ requires *m/z* 419.1829, found *m/z* 419.1826. Minor diastereomer: White solid (mp = 122.8 – 125.9 °C). v_{max} (film) / cm^{-1} 2974, 1722, 1677, 1369, 1327, 1281, 1247, 1225, 1164, 1138, 1170, 1018, 842, 699. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.1 Hz, 2H), 7.57 – 7.46 (m, 3H), 7.40 (t, *J* = 7.5 Hz, 4H), 3.98 (q, *J* = 9.4 Hz, 1H), 3.83 – 3.71 (m, 1H), 3.01 (ddd, *J* = 16.4, 9.2, 7.3 Hz, 1H), 2.60 – 2.48 (m, 2H), 2.20 – 2.06 (m, 2H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.62, 174.73, 147.10, 136.36, 133.29, 128.80 (q, *J* = 31.1 Hz), 128.62, 128.45, 127.82, 125.44 (q, *J* = 3.7 Hz), 124.16 (q, *J* = 271.3), 80.72, 53.75, 47.67, 44.03, 38.34, 34.99, 28.11. **^{19}**F NMR (377 MHz, $CDCl_3$) δ –62.47. HRMS (ESI) calculated for $[C_{24}H_{29}F_3NO_3]^+(M+NH_4^+)$ requires *m/z* 436.2095, found *m/z* 436.2093.



***tert*-Butyl 3-benzoyl-4-(4-bromophenyl)cyclopentanecarboxylate (3-9):** Prepared according to the general procedure using 24.5 mg (0.04 mmol) of $Gd(OTf)_3$, 30.0 mg (0.08 mmol) of 4-NMe_2-^{s}Bu-pybox, 100.6 mg (0.4 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 367.0 mg (2.0 mmol) of 4-bromostyrene, 9.0 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, 52.6 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M). The reaction was ended after 20 h. The crude product was purified by column chromatography (1:29, acetone/pentanes) to give 148 mg (0.34 mmol, 84% yield) of the cycloadduct as two separable diastereomers (2.3:1 d.r.). Major Diastereomer: 89.7% ee [Daicel Chiracel AD-H, 10 to 40 % iPrOH, 3 mL/min, 239 nm; t_1 =7.91, t_2=10.09 min]. $[\alpha]_D^{22}$ 50.8 (*c*1.020,

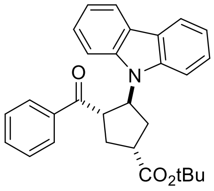
CH_2Cl_2). White solid (mp = 103.1 – 104.4 °C). ν_{max} (film) / cm^{-1} 2976, 1722, 1681, 1490, 1448, 1366, 1257, 1150, 1074, 1010, 848, 821, 701. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.3 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.42 – 7.34 (m, 4H), 7.12 (d, *J* = 8.4 Hz, 2H), 3.83 – 3.74 (m, 2H), 3.08 (qd, *J* = 8.2, 5.7 Hz, 1H), 2.57 – 2.45 (m, 2H), 2.23 – 2.13 (m, 1H), 2.07 (dt, *J* = 13.4, 9.2 Hz, 1H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.16, 174.05, 142.62, 136.69, 133.11, 131.56, 129.10, 128.57, 128.35, 120.13, 80.65, 54.77, 46.40, 44.26, 37.09, 35.41, 28.06. HRMS (ESI) calculated for $[C_{23}H_{26}BrO_3]^+(M+H^+)$ requires *m/z* 429.1060, found *m/z* 429.1074. Minor Diastereomer: White solid (mp = 129.1 – 132.8 °C). ν_{max} (film) / cm^{-1} 2975, 1722, 1680, 1490, 1448, 1367, 1284, 1246, 1220, 1152, 1074, 1011, 823, 700. ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.3 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.44 – 7.32 (m, 4H), 7.15 (d, *J* = 8.4 Hz, 2H), 3.92 (q, *J* = 9.4 Hz, 1H), 3.65 (ddd, *J* = 11.3, 9.5, 7.6 Hz, 1H), 2.99 (ddd, *J* = 16.5, 9.3, 7.3 Hz, 1H), 2.50 (ddd, *J* = 13.3, 9.8, 6.8 Hz, 2H), 2.17 – 2.02 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.92, 174.82, 141.95, 136.47, 133.23, 131.56, 129.20, 128.60, 128.46, 120.25, 80.64, 53.74, 47.56, 44.03, 38.46, 34.93, 28.12. HRMS (ESI) calculated for $[C_{23}H_{29}BrNO_3]^+(M+NH_4^+)$ requires *m/z* 446.1326, found *m/z* 446.1313.

***tert*-Butyl 3-benzoyl-4-(2-methylphenyl)cyclopentanecarboxylate (3-10):** Prepared according to the general procedure using 25.5 mg (0.04 mmol) of $Gd(OTf)_3$, 30.7 mg (0.08 mmol) of 4-NMe_2-^{s}Bu-pybox, 98.4 mg (0.4 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 236.3 mg (2.0 mmol) of 2-methylstyrene, 8.7 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, 56.7 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M). The reaction was ended after 20 h. The crude product was purified by column chromatography (1:49 Et_2O/pentanes) to give 110 mg (0.30 mmol, 75% yield) of cycloadduct as two separable diastereomers (2.0:1 d.r.). Major Diastereomer: 86.8% ee [Daicel Chiracel AD-H, 10 to 20 % iPrOH, 3 mL/min, 240 nm; t_1=4.20 min, t_2=5.47 min]. $[\alpha]_D^{22}$ 47.0 (*c*1.020, CH_2Cl_2). White solid (mp = 70.7 – 74.1 °C). ν_{max} (film) / cm^{-1} 2975, 1723, 1681, 1448,



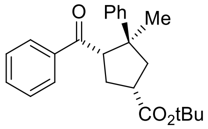
1367, 1218, 1149, 1101, 848, 753, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.3 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.26 (d, *J* = 7.7 Hz, 1H), 7.16 (dt, *J* = 7.9, 4.3 Hz, 2H), 7.10 – 7.01 (m, 3H), 4.08 – 3.92 (m, 3H), 3.09 (td, *J* = 8.5, 6.5 Hz, 2H), 2.59 – 2.45 (m, 3H), 2.31 (s, 3H), 2.24 (dt, *J* = 13.1, 8.8 Hz, 1H), 1.96 (dt, *J* = 13.3, 8.5 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.83, 174.40, 142.30, 136.88, 136.65, 133.05, 130.57, 128.60, 128.49, 126.38, 126.28, 125.49, 80.60, 54.16, 44.80, 43.00, 37.70, 35.29, 28.21, 20.00. HRMS (ESI) calculated for $[C_{24}H_{29}O_3]^+(M+H^+)$ requires *m/z* 365.2111, found *m/z* 365.2105. Minor Diastereomer: Colorless oil. v_{max} (film) / cm^{-1} 2976, 1723, 1680, 1448, 1367, 1290, 1216, 1151, 848, 575, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.41 – 7.31 (m, 3H), 7.23 – 7.12 (m, 1H), 7.10 – 7.01 (m, 2H), 4.09 (q, *J* = 9.0 Hz, 1H), 3.88 (dt, *J* = 11.0, 8.3 Hz, 1H), 3.01 (p, *J* = 8.9 Hz, 1H), 2.51 (dq, *J* = 13.5, 7.3 Hz, 2H), 2.28 (s, 3H), 2.23 – 2.12 (m, 1H), 2.05 – 1.91 (m, 1H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.48, 174.93, 141.45, 136.53, 136.33, 133.01, 130.31, 128.46, 128.46, 126.42, 126.20, 125.81, 80.45, 53.47, 44.43, 43.81, 39.39, 34.61, 28.13, 19.83.HRMS (ESI) calculated for $[C_{24}H_{32}NO_3]^+(M+NH_4^+)$ requires *m/z* 382.2377, found *m/z* 382.2372.

tert-Butyl 3-benzoyl-4-(9H-carbazol-9-yl)cyclopentanecarboxylate (3-11): Prepared according to the general procedure using 18.1 mg (0.03 mmol) of $Gd(OTf)_3$, 22.4 mg (0.06 mmol) of 4-NMe_2-^{s}Bu-pybox, 73.9 mg (0.3 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 289.8 mg (1.5 mmol) of 9-vinylcarbazole, 6.4 mg (0.0075 mmol) of $Ru(bpy)_3(PF_6)_2$, 38.8 mg (0.3 mmol) of diisopropylethylamine with a total volume of 3 mL (0.1 M). The reaction was ended after 20 h. The crude product was purified by column chromatography (1:29, acetone/pentanes) to give 74 mg (0.17 mmol, 57% yield) of the cycloadduct as two separable diastereomers (1.9:1 d.r.). Major diastereomer: 85.8% ee [Daicel Chiracel AD-H, 5% MeOH, 3 mL/min, 241 nm; t_1=5.76 min, t_2=9.18 min]. $[\alpha]_D^{22}$ 35.8 (*c*0.550, CH_2Cl_2). Colorless oil. v_{max} (film) / cm^{-1}2976, 1724, 1682, 1597,



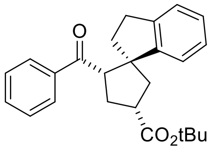
1484, 1453, 1367, 1337, 1227, 1154, 847, 750, 724, 698. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (d, *J* = 7.7 Hz, 2H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.57 (d, *J* = 8.3 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.14 (m, 4H), 5.94 (q, *J* = 9.1 Hz, 1H), 4.66 (q, *J* = 9.1 Hz, 1H), 3.40 (p, *J* = 8.1 Hz, 1H), 2.85 – 2.57 (m, 3H), 2.38 (dt, *J* = 13.3, 9.1 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 199.53, 173.42, 139.31, 136.18, 133.14, 128.39, 128.26, 125.66, 123.41, 120.39, 119.08, 109.76, 81.12, 56.17, 49.49, 44.09, 34.36, 31.36, 28.10. HRMS (ESI) calculated for $[C_{29}H_{30}NO_3]^+$(M+H$^+$) requires *m/z* 440.2220, found *m/z* 440.2217. <u>Minor diastereomer</u>: Colorless oil. ν_{max} (film) / cm^{-1} 2977, 1722, 1681, 1597, 1484, 1453, 1367, 1337, 1221, 1151, 750, 724, 699. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.05 (d, *J* = 7.7 Hz, 2H), 7.71 (d, *J* = 7.2 Hz, 2H), 7.49 – 7.35 (m, 3H), 7.41 (s, 0H), 7.28 – 7.17 (m, 5H), 5.81 (dt, *J* = 11.0, 8.5 Hz, 1H), 4.85 – 4.74 (m, 1H), 3.09 (dt, *J* = 15.9, 7.8 Hz, 1H), 2.97 – 2.84 (m, 1H), 2.76 (ddd, *J* = 13.5, 9.9, 7.7 Hz, 1H), 2.51 (dt, *J* = 13.3, 8.1 Hz, 1H), 2.30 (dt, *J* = 14.0, 7.6 Hz, 1H), 1.52 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 200.20, 174.24, 139.40, 135.75, 133.31, 128.49, 128.47, 125.71, 123.40, 120.34, 119.11, 109.90, 81.07, 56.75, 47.76, 42.78, 33.31, 32.53, 28.15. HRMS (ESI) calculated for $[C_{29}H_{30}NO_3]^+$(M+H$^+$) requires *m/z* 440.2220, found *m/z* 440.2217.

***Tert*-butyl 3-benzoyl-4-methyl-4-phenylcyclopenanecarboxylate (3-12):** Prepared according to the general procedure using 24.4 mg (0.04 mmol) of Gd(OTf)$_3$, 28.7 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 98.2 mg (0.4 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 236.0 mg (2.0 mmol) of α-methylstyrene, 8.8 mg (0.01 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, 53.6 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M) in MeCN. The reaction was ended after 20 h. The crude product was purified by column chromatography (neat toluene to 1:9 acetone/toluene) to give 118 mg (0.32 mmol, 81% yield) of the cycloadduct as two separable diastereomers (2.9:1 d.r.). <u>Major Diastereomer</u>: 89.5% ee [Daicel Chiracel AD-H, 10 to 20 % iPrOH, 3 mL/min, 240 nm; t_1=4.16 min, t_2=4.78 min]. $[\alpha]_D^{22}$ 117.5 (*c*=0.930, CH$_2$Cl$_2$). White solid (mp = 74.2 – 79.5 °C). ν_{max} (film) / cm^{-1} 2977, 1675, 1597,



1447, 1367, 1285, 1253, 848, 732, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.0 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.31 – 7.16 (m, 7H), 4.09 (dd, *J* = 9.8, 6.7 Hz, 1H), 3.08 (dt, *J* = 18.3, 9.3 Hz, 1H), 2.63 (dt, *J* = 13.3, 10.0 Hz, 1H), 2.53 (dd, *J* = 13.7, 9.2 Hz, 1H), 2.29 – 2.14 (m, 2H), 1.49 (s, 9H), 1.26 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.35, 174.34, 148.87, 137.78, 132.57, 128.39, 128.38, 128.15, 126.15, 125.88, 80.38, 57.65, 49.53, 45.42, 43.63, 32.71, 28.14, 24.30. HRMS (ESI) calculated for $[C_{24}H_{29}O_3]^+$(M+H$^+$) requires *m/z* 365.2112, found *m/z* 365.2115. <u>Minor Diastereomer</u>: Colorless oil. v_{max} (film) / cm^{-1} 2977, 1724, 1676, 1449, 1369, 1258, 1222, 1154, 1086, 1026, 803, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.1 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.25 – 7.09 (m, 5H), 4.17 (t, *J* = 8.7 Hz, 1H), 3.17 (qd, *J* = 9.0, 5.6 Hz, 1H), 2.68 – 2.57 (m, 2H), 2.28 (ddd, *J* = 13.9, 8.6, 5.6 Hz, 1H), 2.17 (dd, *J* = 13.1, 8.2 Hz, 1H), 1.49 (s, 9H), 1.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.56, 175.76, 147.07, 137.78, 132.47, 128.29, 128.23, 128.05, 126.21, 126.19, 80.42, 56.74, 50.65, 46.99, 42.29, 32.17, 28.15, 22.14. HRMS (ESI) calculated for $[C_{24}H_{32}NO_3]^+$(M+NH$_4^+$) requires *m/z* 382.2377, found *m/z* 382.2376.

tert-Butyl 2-benzoyl-2',3'-dihydrospiro[cyclopentane-1,1'-indene]-4-carboxylate (3-13):

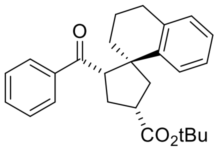


Prepared according to the general procedure using 24.3 (0.04 mmol) of Gd(OTf)$_3$, 30.3 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 100.0 mg (0.4 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 260.9 mg (1.5 mmol) of 1-methylene-2,3-dihydro-1H-indene, 8.3 mg (0.01 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, 57.8 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M). The reaction was ended after 20 h. The crude product was purified by column chromatography (1:49 acetone/pentanes) to give 144 mg (0.38 mmol, 95% yield) of cycloadduct as two separable diastereomers (2.7:1 d.r.). <u>Major diastereomer</u>: 97.2% ee [Daicel Chiracel AD-H, 5% iPrOH, 8 mL/min, 240 nm; t_1=3.57 min, t_2=5.09 min]. $[\alpha]_D^{22}$ 102.3 (*c*1.580, CH_2Cl_2). Colorless oil. v_{max} (film) / cm^{-1} 2975, 2935, 1724, 1672, 1478, 1448, 1392, 1367, 1225, 1151, 1002, 849, 756, 732, 691. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J*

= 7.0 Hz, 2H), 7.40 – 7.32 (m, 2H), 7.26 (m, 3H), 7.17 (t, *J* = 7.8 Hz, 2H), 7.09 (t, *J* = 7.3 Hz, 1H), 6.93 (d, *J* = 6.9 Hz, 1H), 3.91 (dd, *J* = 10.4, 6.9 Hz, 1H), 3.06 (dt, *J* = 17.3, 8.3 Hz, 1H), 2.73 – 2.60 (m, 2H), 2.44 (dd, *J* = 13.3, 9.1 Hz, 1H), 2.38 – 2.22 (m, 4H), 1.93 – 1.83 (m, 1H), 1.48 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.23, 174.36, 149.28, 143.69, 137.38, 132.57, 128.16, 128.02, 127.08, 126.62, 124.69, 122.27, 80.35, 59.06, 56.04, 44.49, 43.23, 36.75, 33.47, 30.97, 28.12. HRMS (ESI) calculated for $[C_{25}H_{29}O_3]^+(M+H^+)$ requires *m/z* 377.2111, found *m/z* 377.2107.

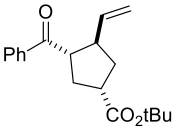
<u>Minor diastereomer</u>: Colorless oil. ν_{max} (film) / cm^{-1} 2976, 2932, 1720, 1671, 1448, 1367, 1220, 1150, 908, 846, 729, 690. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.41 (m, 3H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.26 – 7.18 (m, 1H), 7.11 (t, *J* = 7.8 Hz, 2H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.5 Hz, 1H), 4.05 (t, *J* = 8.7 Hz, 1H), 3.11 (tdd, *J* = 9.9, 7.6, 6.1 Hz, 1H), 2.71 (dt, *J* = 13.6, 9.7 Hz, 1H), 2.67 – 2.57 (m, 1H), 2.54 (dd, *J* = 12.8, 9.8 Hz, 1H), 2.47 – 2.25 (m, 2H), 2.27 – 2.09 (m, 2H), 1.76 (dt, *J* = 12.4, 8.9 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.42, 175.61, 147.06, 143.90, 137.16, 132.45, 128.14, 127.82, 127.19, 126.54, 124.57, 122.60, 80.39, 60.28, 55.35, 46.18, 42.58, 34.90, 31.96, 30.78, 28.17. HRMS (ESI) calculated for $[C_{25}H_{32}NO_3]^+(M+NH_4^+)$ requires *m/z* 394.2377, found *m/z* 394.2374.

tert-Butyl 2-benzoyl-3',4'-dihydro-2'H-spiro[cyclopentane-1,1'-naphthalene]-4-carboxylate



(3-14): Prepared according to the general procedure using 18.1 mg (0.03 mmol) of $Gd(OTf)_3$, 22.4 mg (0.06 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 78.9 mg (0.3 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 216.3 mg (1.5 mmol) of 1-methylene-1,2,3,4-tetrahydronaphthalene, 6.4 mg (0.0075 mmol) of $Ru(bpy)_3(PF_6)_2$, 38.8 mg (0.3 mmol) of diisopropylethylamine with a total volume of 3 mL (0.1 M). The reaction was ended after 20 h. The crude product was purified by column chromatography (1:49 acetone/pentanes) to give 95 mg (0.33 mmol, 83% yield) of the cycloadduct as two separable diastereomers (2.7:1 d.r.). <u>Major Diastereomer</u>: 99.5% ee [Daicel Chiracel AD-H, 5 % iPrOH, 8 mL/min, 241 nm; t_1=4.14 min, t_2=5.94 min]. $[\alpha]_D^{22}$ 169.0 (*c*0.720, CH_2Cl_2). White solid (mp = 104.0 – 106.8 °C). ν_{max} (film) / cm^{-1}

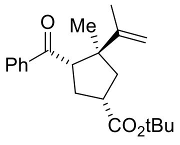
2974, 2936, 1724, 1673, 1447, 1366, 1254, 1230, 1152, 754, 720, 691. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.9 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.27 (d, *J* = 6.2 Hz, 1H), 7.14 (t, *J* = 7.8 Hz, 2H), 7.10 (t, *J* = 7.7 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 4.16 (dd, *J* = 11.6, 6.4 Hz, 1H), 3.10 (dtd, *J* = 11.6, 9.3, 7.2 Hz, 1H), 2.72 (q, *J* = 11.8 Hz, 1H), 2.57 (dt, *J* = 16.5, 5.5 Hz, 1H), 2.36 (qd, *J* = 11.7, 10.4, 4.5 Hz, 2H), 2.23 (ddd, *J* = 13.5, 7.9, 5.5 Hz, 2H), 1.81 – 1.64 (m, 2H), 1.66 – 1.50 (m, 2H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.38, 174.27, 143.94, 137.78, 137.47, 132.45, 129.28, 128.34, 128.08, 126.70, 126.46, 125.88, 80.39, 58.96, 49.24, 48.71, 43.93, 34.36, 33.26, 29.98, 28.13, 20.23. HRMS (ESI) calculated for $[C_{26}H_{31}O_3]^+(M+H^+)$ requires *m/z* 391.2273, found *m/z* 391.2263. Minor Diastereomer: Colorless oil. ν_{max} (film) / cm^{-1} 2976, 2937, 1723, 1674, 1447, 1366, 1218, 1151, 733, 691. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.30 – 7.21 (m, 1H), 7.13 (t, *J* = 7.8 Hz, 2H), 7.04 (t, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 4.32 (t, *J* = 8.3 Hz, 1H), 3.17 – 3.04 (m, 1H), 2.73 (dt, *J* = 13.7, 8.7 Hz, 1H), 2.52 (dt, *J* = 16.1, 5.0 Hz, 1H), 2.40 – 2.22 (m, 4H), 1.73 (ddd, *J* = 13.1, 9.4, 3.4 Hz, 1H), 1.67 – 1.49 (m, 3H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.08, 175.59, 141.75, 138.18, 137.82, 132.34, 129.00, 128.31, 127.96, 127.36, 126.41, 125.88, 80.36, 58.12, 50.62, 49.53, 42.83, 32.01, 31.97, 30.32, 28.16, 20.50. HRMS (ESI) calculated for $[C_{26}H_{34}NO_3]^+(M+NH_4^+)$ requires *m/z* 408.2533, found *m/z* 408.2529.



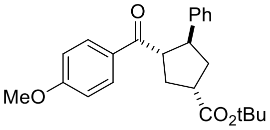
tert-Butyl 3-benzoyl-4-vinylcyclopentanecarboxylate (3-15): Prepared according to general procedure using 24.6 mg (0.04 mmol) of $Gd(OTf)_3$, 30.0 mg (0.08 mmol) of 4-NMe_2-^{s}Bu-pybox, 98.4 mg (0.4 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 140 μL (2.0 mmol) of butadiene (15 wt% in toluene), 8.7 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, 53.5 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M) in MeCN. The reaction was complete after 6 h. The crude product was purified by column chromatography (1:9 Et_2O/pentanes) to give 70.8 mg (0.2357 mmol, 59 % yield) of cycloadduct as two separable diastereomers (3:1 dr). Major Diastereomer: 87.2% ee [Daicel

Chiracel AD-H, 5 to 50 % MeOH, 3 mL/min, 240 nm; t_1=3.63 min, t_2=4.68 min]. $[\alpha]_D^{22}$ 58.1 (*c*0.410, CH_2Cl_2). Colorless oil. ν_{max} (film) / cm^{-1} 2977, 2933, 1725, 1681, 1449, 1367, 1258, 1152. ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.3 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 5.71 (ddd, *J* = 17.4, 10.2, 7.4 Hz, 1H), 4.95 (d, *J* = 17.1 Hz, 1H), 4.87 (d, *J* = 10.3 Hz, 1H), 3.49 (q, *J* = 8.3 Hz, 1H), 3.10 (p, *J* = 7.9 Hz, 1H), 2.95 – 2.73 (m, 1H), 2.28 (dt, *J* = 13.1, 8.2 Hz, 1H), 2.17 (ddd, *J* = 14.0, 8.0, 6.4 Hz, 1H), 2.07 (dt, *J* = 13.1, 9.1 Hz, 1H), 1.76 (dt, *J* = 13.1, 8.6 Hz, 1H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.70, 174.32, 140.11, 137.02, 132.99, 128.56, 128.46, 114.72, 80.39, 52.21, 45.98, 43.86, 35.09, 34.47, 28.06. HRMS (ESI) calculated for $[C_{19}H_{25}O_3]^+$ ($M+H^+$) requires *m/z* 301.1804, found *m/z* 301.1803. Minor Diastereomer: Colorless oil. ν_{max} (film) / cm^{-1} 2981, 2934, 1719, 1678, 1368, 1155. ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.3 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 5.61 (dt, *J* = 16.9, 9.7 Hz, 1H), 4.81 – 4.71 (m, 2H), 3.92 (q, *J* = 9.0 Hz, 1H), 3.05 (p, *J* = 8.0 Hz, 1H), 2.83 (dt, *J* = 17.3, 8.7 Hz, 1H), 2.48 (dt, *J* = 13.2, 10.0 Hz, 1H), 2.22 (dt, *J* = 13.4, 8.0 Hz, 1H), 2.12 (dt, *J* = 13.9, 7.4 Hz, 1H), 1.99 (ddd, *J* = 13.3, 8.9, 7.4 Hz, 1H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.46, 174.29, 138.13, 137.62, 132.81, 128.48, 128.31, 115.40, 80.30, 50.58, 47.40, 44.08, 35.63, 31.60, 28.10. HRMS (ESI) calculated for $[C_{19}H_{18}NO_3]^+$ ($M+NH_4^+$) requires *m/z* 318.2069, found 318.2067.

tert-Butyl 4-benzoyl-3-methyl-3-(prop-1-en-2-yl)cyclopentanecarboxylate (3-16): Prepared according to general procedure using 24.6 mg (0.04 mmol) of $Gd(OTf)_3$, 30.0 mg (0.08 mmol) of 4-NMe_2-^{s}Bu-pybox, 98.4 mg (0.4 mmol) of *trans* tert-butyl 2-benzoylcyclopropanecarboxylate, 166.7 mg (2.0 mmol) of 2,3-dimethyl-1,3-butadiene, 8.7 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, 53.5 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M) in MeCN. The reaction was complete after 6 h. The crude product was purified by column chromatography (1:9 Et_2O/pentanes) to give 101.0 mg (0.3076 mmol, 77 % yield) of cycloadduct as two separable diastereomers (3:1 dr). Major Diastereomer: 95.6% ee [Daicel Chiracel AD-H, 5 % MeOH, 3 mL/min, 239 nm; t_1=3.44 min, t_2=5.45 min]. $[\alpha]_D^{22}$

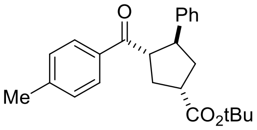


47.0 (*c*0.540, CH_2Cl_2). Colorless oil. v_{max} (film) / cm^{-1} 2978, 1719, 1674, 1368, 1265, 1154. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.3 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 4.78 (s, 1H), 4.73 (s, 1H), 3.94 (dd, *J* = 8.8, 7.2 Hz, 1H), 2.87 (p, *J* = 9.1 Hz, 1H), 2.51 (dt, *J* = 13.1, 9.4 Hz, 1H), 2.20-2.10 (m, 2H), 1.91 (dd, *J* = 13.5, 9.6 Hz, 1H), 1.85 (s, 3H), 1.48 (s, 9H), 1.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.02, 174.40, 149.71, 138.42, 132.75, 128.39, 128.33, 110.86, 80.24, 51.67, 50.85, 43.26, 41.92, 32.48, 28.13, 23.24, 20.05. HRMS (ESI) calculated for $[C_{21}H_{29}O_3]^+$ ($M+H^+$) requires *m/z* 329.2117, found *m/z* 329.2118. Minor Diastereomer: Colorless oil. v_{max} (film) / cm^{-1} 2975, 1724, 1677, 1448, 1367, 1219, 1152. ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.3 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 4.72 (s, 1H), 4.69 (s, 1H), 4.00 (t, *J* = 8.3 Hz, 1H), 3.08 (ddd, *J* = 17.8, 9.3, 6.4 Hz, 1H), 2.48 – 2.37 (m, 1H), 2.26 – 2.17 (m, 2H), 1.84 (dd, *J* = 12.9, 8.3 Hz, 1H), 1.80 (s, 3H), 1.47 (s, 9H), 1.09 (s, 3H). ^{13}C NMR (101 MHz, v) δ 202.29, 175.59, 149.19, 138.54, 132.75, 128.41, 128.15, 111.41, 80.27, 52.04, 51.55, 43.44, 42.28, 32.44, 28.12, 21.46, 20.15. HRMS (ESI) calculated for $[C_{21}H_{32}NO_3]^+$ ($M+NH_4^+$) requires *m/z* 346.2381, found 346.2382.



tert-Butyl 3-(4-methoxybenzoyl)-4-phenylcyclopentanecarboxylate (3-17): Prepared according to the general procedure using 24.6 mg (0.04 mmol) of $Gd(OTf)_3$, 30.0 mg (0.08 mmol) of 4-NMe_2-^{s}Bu-pybox, 109.9 mg (0.4 mmol) of *trans* tert-butyl 2-(4-methoxybenzoyl)cyclopropanecarboxylate, 209.6 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) or $Ru(bpy)_3(PF_6)_2$, and 58.2 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M). The reaction was complete after 6 h. The crude product was purified by column chromatography (1:9, Et_2O/pentanes) to give 142.2 mg (0.37 mmol, 94 % yield) of cycloadduct as two separable diastereomers (3:1 dr). Major diastereomer: 91.1% ee [Daicel Chiracel AD-H, 5 to 50 % iPrOH, 3 mL/min, 238 nm; t_1=7.65 min, t_2=8.98 min]. $[\alpha]_D^{22}$ 45.0 (*c*0.667, CH_2Cl_2). White solid (mp = 97.5-98.2 °C). v_{max} (film) / cm^{-1} 2795, 1725, 1672, 1600, 1259, 1152. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 7.25 (m, 5H), 7.15 (dq, *J* = 5.8, 3.0 Hz, 1H), 6.84 (d, *J* = 8.9 Hz, 2H), 3.83 (s, 3H), 3.88 – 3.72 (m, 2H), 3.08 (qd, *J* = 8.7, 6.3 Hz, 1H), 2.60 – 2.39 (m, 2H), 2.31 – 2.01 (m, 2H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 199.02 , 174.26 , 163.36 , 143.92 , 130.67 , 129.92 , 128.50 , 127.31 , 126.35 , 113.61 , 80.45 , 55.44 , 54.40 , 47.25 , 44.49 , 37.25 , 35.54 , 28.08. HRMS (ESI) calculated for $[C_{24}H_{29}O_4]^+$ (M+H$^+$) requires *m/z* 381.2060, found 381.2060. Minor diastereomer: White solid (mp = 86.6-89.1 ^{o}C). ν$_{max}$ (film) / cm^{-1} 2792, 1726, 1671, 1606, 1301, 1150. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.80 (d, *J* = 8.9 Hz, 2H), 7.27-7.10 (m, 5H), 6.84 (d, *J* = 8.9 Hz, 2H), 3.98 – 3.89 (m, 1H), 3.83 (s, 3H), 3.71 – 3.60 (m, 1H), 3.05 – 2.94 (m, 1H), 2.55-2.4 (m, 2H), 2.2-2.0 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 199.84 , 175.04 , 163.45 , 143.11 , 130.80 , 129.73 , 128.49 , 127.43 , 126.47 , 113.64 , 80.43 , 55.45 , 53.32 , 48.43 , 44.22 , 38.86 , 34.94 , 28.14. HRMS (ESI) calculated for $[C_{24}H_{32}NO_4]^+$ (M+NH$_4^+$) requires *m/z* 398.2326, found 398.2325.

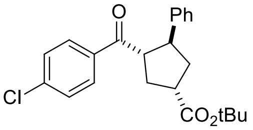
tert-Butyl 3-(4-methylbenzoyl)-4-phenylcyclopentanecarboxylate (3-18): Prepared according



to the general procedure using 24.3 mg (0.04 mmol) of Gd(OTf)$_3$, 29.7 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 105.0 mg (0.4 mmol) of *trans* tert-butyl 2-(4-methylbenzoyl)cyclopropanecarboxylate, 208.9 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, and 52.3 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 6 h. The crude product was purified by column chromatography (1:10, Et$_2$O/pentanes) to give 137.0 mg (0.38 mmol, 94% yield) of cycloadduct as two separable diastereomers (3:1 dr). Major diastereomer: 96.8% ee [Daicel Chiracel AD-H, 10 to 40 % iPrOH, 3 mL/min, 238 nm; t$_1$=5.91 min, t$_2$=8.09 min]. [α]$_D^{22}$ 30.2 (*c*0.940, CH$_2$Cl$_2$). White solid (mp = 103-105 ^{o}C). ν$_{max}$ (film) / cm^{-1} 2977, 1725, 1675, 1607, 1366, 1261, 1150. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.28-7.17 (m, 5H), 7.17 (d, *J* = 8.2Hz, 2H), 4.02 – 3.69 (m, 2H), 3.16 – 3.03 (m, 1H), 2.58 – 2.42 (m, 2H), 2.36 (s, 3H), 2.26 – 2.05 (m, 2H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 200.13 , 174.24 , 143.86 , 143.73 , 134.37 , 129.16 , 128.53 , 128.50 , 127.31 , 126.36 , 80.47 , 54.58 , 47.09 , 44.48 , 37.27 , 35.51

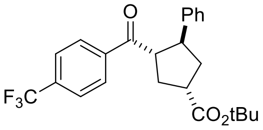
, 28.08 , 21.60. HRMS (ESI) calculated for $[C_{24}H_{29}O_3]^+$ (M+H$^+$) requires *m/z* 365.2111, found 365.2111. Minor diastereomer: White solid (mp = 86.4-88.0 ^oC). v_{max} (film) / cm^{-1} 2975, 1724, 1675, 1604, 1370, 1256, 1152. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.34 – 7.15 (m, 5H), 7.17 (d, *J* = 8.2 Hz, 2H), 4.05 – 3.85 (m, 1H), 3.74 – 3.55 (m, 1H), 2.61 – 2.40 (m, 2H), 2.36 (s, 3H), 2.20 – 1.99 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.93 , 174.97 , 143.87 , 143.06 , 134.15 , 129.19 , 128.63 , 128.49 , 127.43 , 126.48 , 80.45 , 53.52 , 48.28 , 44.22 , 38.84 , 34.92 , 28.13 , 21.61 . HRMS (ESI) calculated for $[C_{24}H_{32}NO_3]^+$ (M+NH$_4^+$) requires *m/z* 382.2377, found 382.2377.

tert-Butyl 3-(4-chlorobenzoyl)-4-phenylcyclopentanecarboxylate (3-19): Prepared according to the general procedure using 24.9 mg (0.04 mmol) of $Gd(OTf)_3$, 30.7 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 112.3 mg (0.4 mmol) of *trans* tert-butyl 2-(4-chlorobenzoyl)cyclopropanecarboxylate, 210.1 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) or $Ru(bpy)_3(PF_6)_2$, and 54.2 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M). The reaction was complete after 6 h. The crude product was purified by column chromatography (1:9, Et_2O/pentanes) to give 138.6 mg (0.36 mmol, 90 % yield) of cycloadduct as two separable diastereomers (4:1 dr). Major diastereomer: 92.4% ee [Daicel Chiracel AD-H, 5 to 50 % iPrOH, 3 mL/min, 263 nm; t_1=6.34 min, t_2=7.00 min]. $[\alpha]_D^{22}$ 51.0 (*c*0.980, CH_2Cl_2). White solid (mp = 109-111 ^oC). v_{max} (film) / cm^{-1} 3056, 2987, 1725, 1684, 1591, 1372, 1265, 1156. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.28 – 7.10 (m, 2H), 3.97 – 3.54 (m, 2H), 3.09 (qd, *J* = 8.2, 6.0 Hz, 1H), 2.49 (ddt, *J* = 21.0, 15.9, 6.9 Hz, 3H), 2.19 (ddt, *J* = 44.0, 13.3, 8.8 Hz, 2H), 1.46 (s, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.44 , 174.13 , 143.52 , 139.36 , 135.16 , 129.80 , 128.76 , 128.60 , 127.26 , 126.56 , 80.58 , 54.80 , 47.42 , 44.42 , 37.37 , 35.08 , 28.08 . HRMS (ESI) calculated for $[C_{23}H_{26}ClO_3]^+$ (M+H$^+$) requires *m/z* 385.1565, found 385.1565. Minor diastereomer: White solid (mp = 82.9-88.3 ^oC). v_{max} (film) / cm^{-1} 3057, 2984, 1727, 1681, 1590, 1367, 1260, 1164. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.5



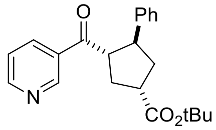
Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.29 – 7.21 (m, 4H), 7.17 (h, *J* = 4.3 Hz, 1H), 3.92 (q, *J* = 9.3 Hz, 1H), 3.61 (ddd, *J* = 11.3, 9.4, 7.5 Hz, 1H), 3.05 – 2.95 (m, 1H), 2.58 – 2.40 (m, 2H), 2.20 – 2.06 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.21 , 174.87 , 142.73 , 139.51 , 134.95 , 129.90 , 128.79 , 128.59 , 127.38 , 126.68 , 80.57 , 53.77 , 48.70 , 44.16 , 38.88 , 34.65 , 28.13 . HRMS (ESI) calculated for $[C_{23}H_{29}NClO_3]^+$ ($M+NH_4^+$) requires *m/z* 402.1830, found 402.1830.

tert-Butyl 3-phenyl-4-(4-(trifluoromethyl)benzoyl)cyclopentane carboxylate (3-20):



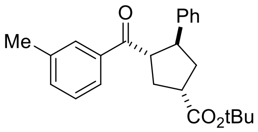
Prepared according to the general procedure using 24.3 mg (0.04 mmol) of $Gd(OTf)_3$, 29.7 mg (0.08 mmol) of 4-NMe_2-^{s}Bu-pybox, 126.1 mg (0.4 mmol) of *tert*-butyl 2-(4-(trifluoromethyl)benzoyl)cyclopropanecarboxylate, 209.2 mg (2.0 mmol) of styrene, 8.6 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, and 51.3 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 6 h. The crude product was purified by column chromatography (1:10, Et_2O/pentanes) to give 144.8 mg (0.35 mmol, 87 % yield) of cycloadduct as two separable diastereomers (2.8:1 dr). <u>Major diastereomer:</u> 89.5% ee [Daicel Chiracel OD-H, 1 to 20 % iPrOH, 3 mL/min, 263 nm; t_1=5.97 min, t_2=6.28 min]. $[\alpha]_D^{22}$ 54.6 (*c*0.780, CH_2Cl_2). White solid (mp = 83-87 °C). ν_{max} (film) / cm^{-1} 2980, 1729, 1691, 1328, 1160, 1136, 1070. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.32 – 7.10 (m, 5H), 3.84 (q, *J* = 8.9 Hz, 1H), 3.75 (q, *J* = 8.7 Hz, 1H), 3.11 (qd, *J* = 8.2, 5.6 Hz, 1H), 2.60 – 2.41 (m, 2H), 2.27 (ddd, *J* = 13.3, 9.3, 7.9 Hz, 1H), 2.15 (dt, *J* = 13.3, 9.0 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.83 , 174.08 , 143.34 , 139.57 , 134.14 (q, *J* = 32.5 Hz), 128.67 , 128.65 , 127.25 , 126.66 , 125.50 (q, *J* = 3.7 Hz), 123.6 (q, J = 271.2), 80.66 , 55.19 , 47.47 , 44.39 , 37.43 , 34.84 , 28.07 . ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.14. HRMS (ESI) calculated for $[C_{24}H_{26}F_3O_3]^+$ ($M+H^+$) requires *m/z* 419.1829, found 419.1829. Minor diastereomer: White solid (mp = 58.9-61.7 °C). ν_{max} (film) / cm^{-1} 2983, 1730, 1692, 1330, 1160, 1135, 1073. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.27

– 7.22 (m, 4H), 7.20 – 7.14 (m, 2H), 3.98 (q, *J* = 9.3 Hz, 1H), 3.62 (ddd, *J* = 11.3, 9.4, 7.6 Hz, 1H), 3.02 (ddd, *J* = 16.5, 9.2, 7.3 Hz, 1H), 2.67 – 2.33 (m, 2H), 2.33 – 2.02 (m, 2H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.55 , 174.79 , 142.55 , 139.32 , 134.26 (q, *J* = 32.8 Hz), 128.77 , 128.64 , 127.35 , 126.77 , 125.53 (q, *J* = 3.6 Hz), 123.54 (q, *J* = 272.8 Hz), 80.64 , 54.20 , 48.80 , 44.13 , 38.86 , 34.54 , 28.12. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.16 . HRMS (ESI) calculated for $[C_{24}H_{29}NF_3O_3]^+$ ($M+NH_4^+$) requires *m/z* 436.2094, found 436.2094.



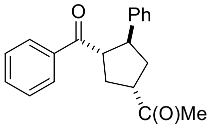
tert-Butyl 3-nicotinoyl-4-phenylcyclopentanecarboxylate (3-21): Prepared according to the general procedure using 24.3 mg (0.04 mmol) of $Gd(OTf)_3$, 30.0 mg (0.08 mmol) of 4-NMe_2-^{s}Bu-pybox, 99.2 mg (0.4 mmol) of *trans* tert-butyl 2-nicotinoylcyclopropanecarboxylate, 210.1 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, and 51.7 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 8 h. The crude product was purified by column chromatography (2:1, Et_2O/pentanes) to give 80.4 mg (0.23 mmol, 57 % yield) of cycloadduct as two separable diastereomers (2:1 dr). <u>Major diastereomer:</u> 88.5% ee [Daicel Chiracel AD-H, 5 to 50 % iPrOH, 3 mL/min, 238 nm; t_1=6.45 min, t_2=6.92 min]. $[\alpha]_D^{22}$ 65.7 (*c*0.420, CH_2Cl_2). White solid (mp = 86.1-88.5 ^{o}C). ν_{max} (film) / cm^{-1} 2982, 1722, 1687, 1586, 1368, 1265, 1151. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, *J* = 1.8 Hz, 1H), 8.69 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.05 (dt, *J* = 8.0, 1.9 Hz, 1H), 7.31 (dd, *J* = 8.1, 5.0 Hz, 1H), 7.30 – 7.11 (m, 5H), 3.82 (q, *J* = 9.0 Hz, 1H), 3.75 (q, *J* = 8.7 Hz, 1H), 3.11 (qd, *J* = 8.2, 5.8 Hz, 1H), 2.59 – 2.40 (m, 2H), 2.29 (dt, *J* = 13.3, 8.6 Hz, 1H), 2.23 – 2.09 (m, 1H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.62 , 174.10 , 153.30 , 149.83 , 143.16 , 135.69 , 132.05 , 128.68 , 127.25 , 126.71 , 123.48 , 80.66 , 55.25 , 47.46 , 44.33 , 37.45 , 34.69 , 28.08. HRMS (ESI) calculated for $[C_{22}H_{26}NO_3]^+$ ($M+H^+$) requires *m/z* 352.1907, found 352.1907. Minor Diastereomer: White solid (mp = 88.0-89.6 ^{o}C). ν_{max} (film) / cm^{-1} 2980, 1724, 1682, 1583, 1370, 1265, 1145. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, *J* = 1.8 Hz, 1H), 8.69 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.04 (dt, *J* = 8.0, 1.9 Hz, 1H), 7.30 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.2 (s, 4H), 7.22 – 7.12 (m, 1H), 3.96 (q, *J* = 9.4 Hz, 1H), 3.61 (ddd, *J* = 11.4, 9.5, 7.5 Hz, 1H), 3.09 – 2.90 (m, 1H), 2.59 – 2.40 (m, 2H), 2.26 – 2.09 (m, 2H), 1.49 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.46 , 174.71 , 153.39 , 149.97 , 142.42 , 135.72 , 131.82 , 128.68 , 127.35 , 126.83 , 123.43 , 80.66 , 54.25 , 48.87 , 44.16 , 38.82 , 34.37 , 28.13. HRMS (ESI) calculated for $[C_{22}H_{26}NO_3]^+$ ($M+H^+$) requires *m/z* 352.1907, found 352.1907.

tert-Butyl 3-(3-methylbenzoyl)-4-phenylcyclopentanecarboxylate (3-22): Prepared according

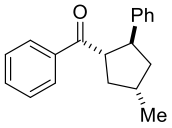


to the general procedure using 24.2 mg (0.04 mmol) of $Gd(OTf)_3$, 29.8 mg (0.08 mmol) of 4-NMe_2-^{s}Bu-pybox, 106.8 mg (0.4 mmol) of *trans* tert-butyl 2-(3-methylbenzoyl)cyclopropanecarboxylate, 208.3 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, and 51.7 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 6 h. The crude product was purified by column chromatography (1:10, Et_2O/pentanes) to give 130.0 mg (0.36 mmol, 89 % yield) of cycloadduct as a white solid as two separable diastereomers (3:1 d.r.). Major diastereomer: 89.3% ee [Daicel Chiracel AD-H, 5 to 50 % iPrOH, 3 mL/min, 238 nm; t_1=5.37 min, t_2=6.00 min]. $[\alpha]_D^{22}$ 55.2 (*c*1.000, CH_2Cl_2). White solid (mp = 87-89 ^{o}C). ν_{max} (film) / cm^{-1} 2978, 1721, 1671, 1368, 1333, 1214, 1149. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.29 – 7.20 (m, 5H), 7.20 – 7.11 (m, 1H), 3.91 – 3.79 (m, 1H), 3.78 (q, *J* = 8.6 Hz, 1H), 3.09 (qd, *J* = 8.4, 6.1 Hz, 1H), 2.59 – 2.42 (m, 2H), 2.32 (s, 3H), 2.17 (ddt, *J* = 33.6, 13.2, 9.0 Hz, 2H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.74 , 174.24 , 143.86 , 138.22 , 136.89 , 133.68 , 129.01 , 128.51 , 128.32 , 127.34 , 126.39 , 125.58 , 80.49 , 54.88 , 47.21 , 44.50 , 37.28 , 35.43 , 28.09 , 21.31. HRMS (ESI) calculated for $[C_{24}H_{29}O_3]^+$ ($M+H^+$) requires *m/z* 365.2111, found 365.2110. Minor Diastereomer: Colorless oil. ν_{max} (film) / cm^{-1} 2986, 1932, 1720, 1677, 1367, 1265, 1151. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.56 (m, 2H), 7.34 – 7.20 (m, 6H), 7.20 – 7.10 (m, 1H), 3.96 (td, *J* = 9.4, 7.8 Hz, 1H), 3.65 (ddd, *J* = 11.4, 9.3, 7.4 Hz, 1H), 2.99 (ddd, *J* = 16.8, 9.4, 7.3 Hz, 1H), 2.62 – 2.41 (m, 2H), 2.32 (s, 3H), 2.22 – 2.06 (m, 2H), 1.48 (s, 9H). ^{13}C

NMR (101 MHz, CDCl$_3$) δ 201.50 , 174.93 , 143.05 , 138.25 , 136.64 , 133.79 , 129.10 , 128.50 , 128.37 , 127.46 , 126.52 , 125.72 , 80.46 , 53.77 , 48.46 , 44.27 , 38.85 , 34.80 , 28.14 , 21.30. M.p. 72.5-76 ^{o}C. HRMS (ESI) calculated for $[C_{24}H_{32}NO_3]^+$ ($M+NH_4^+$) requires *m/z* 382.2377, found 382.2377.

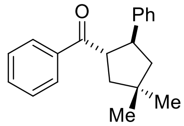


1-(3-Benzoyl-4-phenylcyclopentyl)ethanone (3-23): Prepared according to the general procedure using 24.2 mg (0.04 mmol) of Gd(OTf)$_3$, 29.8 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 77.3 mg (0.4 mmol) of 1-((2-benzoylcyclopropyl)ethanone), 416.4 mg (4.0 mmol) of styrene, 8.7 mg (0.01 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, and 51.9 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 6 h. The crude product was purified by column chromatography (1:15, acetone/pentanes) to give 56.4 mg (0.19 mmol, 48 % yield) of cycloadduct as a clear oil (single diastereomer). 88.2% ee [Daicel Chiracel AD-H, 5 % iPrOH, 6 mL/min, 238 nm; t_1=3.02 min, t_2=3.78 min]. $[\alpha]_D^{22}$ 47.8 (*c*1.213, CH$_2$Cl$_2$). ν_{max} (film) / cm^{-1} 2966, 1708, 1683, 1262, 1114. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.72 (d, *J* = 8.6 Hz, 2H), 7.45 – 7.38 (m, 1H), 7.30 (dd, *J* = 8.4, 7.1 Hz, 2H), 7.23 – 7.04 (m, 4H), 6.97 – 6.84 (m, 1H), 3.85 (q, *J* = 8.7 Hz, 1H), 3.60 (q, *J* = 8.7 Hz, 1H), 3.19 (qd, *J* = 8.5, 5.9 Hz, 1H), 2.55 – 2.32 (m, 2H), 2.23 – 2.18 (m, 1H), 2.15 (s, 3H), 2.04 (dt, *J* = 13.3, 9.4 Hz, 1H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 208.91 , 200.61 , 143.46 , 136.73 , 133.00 , 128.59 , 128.49 , 128.40 , 127.27 , 126.55 , 54.47 , 51.45 , 47.51 , 36.23 , 33.80 , 28.41. HRMS (ESI) calculated for $[C_{20}H_{21}O_2]^+$ ($M+H^+$) requires *m/z* 293.1536, found 293.1535.



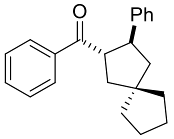
(4-Methyl-2-phenylcyclopentyl)(phenyl)methanone (3-24): Prepared according to the general procedure at -20 °C using 60.4 mg (0.1 mmol) of Gd(OTf)$_3$, 74.5 mg (0.2 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 32.3 mg (0.2 mmol) of *trans* 2-methylcyclopropyl(phenyl)methanone, 104.2 mg (1.0 mmol) of styrene, 4.2 mg (0.005 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, and 51.7 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 48 h. The crude product was purified by column chromatography (1:10, Et_2O/pentanes) to give 21.3 mg (0.08 mmol, 40 % yield) of cycloadduct as a white solid as a single diastereomer. 49.5% ee [Daicel Chiracel AD-H, 5 % iPrOH, 3 mL/min, 263 nm; t_1=3.78 min, t_2=6.26 min]. $[\alpha]_D^{22}$ 38.2 (*c*1.011, CH_2Cl_2). White solid (mp = 44.9-51 ^{o}C). ν_{max} (film) / cm^{-1} 2957, 2868, 1681, 1602, 1451, 1266, 1012. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.24 – 7.11 (m, 4H), 7.13 – 7.00 (m, 1H), 3.90 – 3.69 (m, 2H), 2.48 – 2.22 (m, 2H), 2.02 (dt, *J* = 15.2, 7.8 Hz, 1H), 1.82 (ddd, *J* = 13.0, 8.8, 7.2 Hz, 1H), 1.55 – 1.43 (m, 1H), 1.03 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.90 , 145.50 , 132.80 , 128.55 , 128.44 , 128.41 , 127.37 , 127.30 , 126.07 , 55.96 , 46.89 , 42.50 , 41.01 , 34.44 , 20.78. HRMS (ESi) calculated for $[C_{19}H_{24}O]^+$ ($M+NH_4^+$) requires *m/z* 282.1852, found 282.1853.

(4,4-Dimethyl-2-phenylcyclopentyl)(phenyl)methanone (3-25): Prepared according to the general procedure at –20 ^{o}C using 48.6 mg (0.04 mmol) of $Gd(OTf)_3$, 59.4 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 69.7 mg (0.4 mmol) of *tert*-butyl (2,2-dimethylcyclopropyl)(phenyl)methanone, 209.2 mg (2.0 mmol) of styrene, 8.6 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, and 51.3 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 6 h. The crude product was purified by column chromatography (1:10, Et_2O/pentanes) to give 96.8 mg (0.35 mmol, 87 % yield) of cycloadduct as two separable diastereomers (2.8:1 dr). Major diastereomer: 88.6% ee [Daicel Chiracel AD-H, 5 to 50 % iPrOH, 3 mL/min, 238 nm; t_1=5.19 min, t_2=6.70 min]. $[\alpha]_D^{22}$ 68.7 (*c*0.591, CH_2Cl_2). White solid (mp = 105.3-107.8 ^{o}C). ν_{max} (film) / cm^{-1} 2941, 2863, 1678, 1448, 1283, 1015. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.29 – 7.18 (m, 4H), 7.12 (t, *J* = 7.0 Hz, 1H), 4.04 – 3.84 (m, 2H), 2.12 (dd, *J* = 13.0, 9.2 Hz, 1H), 2.04 (dd, *J* = 12.7, 6.8 Hz, 1H), 1.86 (t, *J* = 11.9 Hz, 1H), 1.73 (dd, *J* = 13.1, 7.8 Hz, 1H), 1.21 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.72 , 144.08 , 137.00 , 132.80 , 128.43 , 128.38 , 127.39 , 126.15 , 54.88 , 49.42 , 46.79 , 46.76 , 39.02 , 30.59 , 29.55 . HRMS (ESI) calculated



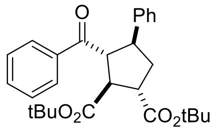
for $[C_{20}H_{23}O]^+$ (M+H$^+$) requires *m/z* 279.1743, found 279.1743. Minor Diastereomer: White solid (mp = 71.6-73.4 ºC). ν_{max} (film) / cm^{-1} 2953, 1927, 2866, 1679, 1463, 1448, 1367, 1221. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.33 – 7.06 (m, 5H), 3.98 (q, *J* = 9.3 Hz, 1H), 3.62 (ddd, *J* = 11.3, 9.4, 7.6 Hz, 1H), 3.02 (ddd, *J* = 16.5, 9.2, 7.3 Hz, 1H), 2.63 – 2.38 (m, 2H), 2.25 – 2.00 (m, 2H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.23 , 142.11 , 136.99 , 132.03 , 128.46 , 127.96 , 127.93 , 127.71 , 125.98 , 50.97 , 48.93 , 48.45 , 43.26 , 38.47 , 29.40 , 28.53. HRMS (ESI) calculated for $[C_{20}H_{23}O]^+$ (M+H$^+$) requires *m/z* 279.1743, found 279.1741.

Phenyl(3-phenylspiro[4.4]nonan-2-yl)methanone (3-26): Prepared according to the general procedure at –20 ºC using 24.4 mg (0.04 mmol) of $Gd(OTf)_3$, 29.9 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 80.1 mg (0.4 mmol) of phenyl(spiro[2.4]heptan-1-yl)methanone, 209.8 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, and 51.5 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 48 h. The crude product was purified by column chromatography (1:30, Et_2O/pentanes) to give 107.2 mg (0.352 mmol, 88% yield) of cycloadduct as two separable diastereomers (5.3:1 d.r.). Major Diastereomer: 94.1% ee [Daicel Chiracel AD-H, 10 to 50 % iPrOH, 3 mL/min, 263 nm; t_1=5.49 min, t_2=6.60 min]. $[\alpha]_D^{22}$ 96.7 (*c*0.999, CH_2Cl_2). Colorless oil. ν_{max} (film) / cm^{-1} 2945, 2858, 1680, 1448, 1216. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.1 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.32 – 7.18 (m, 4H), 7.13 (t, *J* = 6.9 Hz, 1H), 3.97 – 3.82 (m, 2H), 2.21 (dd, *J* = 12.9, 9.6 Hz, 1H), 2.12 (dd, *J* = 12.6, 6.5 Hz, 1H), 2.02 – 1.88 (m, 1H), 1.83 (dd, *J* = 12.9, 6.9 Hz, 1H), 1.77 – 1.49 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.76 , 144.22 , 136.98 , 132.77 , 128.44 , 128.42 , 128.36 , 127.38 , 126.13 , 54.64 , 50.57 , 47.52 , 46.91 , 44.98 , 40.28 , 39.78 , 24.40 , 24.34. HRMS (ESI) calculated for $[C_{22}H_{25}O]^+$ (M+H$^+$) requires *m/z* 305.1900, found 305.1899. Minor Diastereomer: Colorless oil. ν_{max} (film) / cm^{-1} 2950, 2863, 1679, 1448, 1220, 1023. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.3

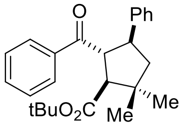


Hz, 1H), 7.29 – 7.18 (m, 2H), 6.97 (7.02 – 6.90 (m, 5H), 4.34 – 4.21 (m, 1H), 3.71 (td, *J* = 10.4, 7.6 Hz, 1H), 2.39 (dd, *J* = 13.0, 9.0 Hz, 1H), 2.16 – 1.97 (m, 2H), 1.90 – 1.47 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.33, 142.17, 138.18, 132.06, 128.39, 127.97, 127.96, 127.72, 125.97, 50.89, 49.81, 48.59, 46.82, 41.52, 39.26, 38.89, 24.81, 24.66. HRMS (ESI) calculated for $[C_{22}H_{25}O]^+$ ($M+H^+$) requires *m/z* 305.1900, found 305.1900.

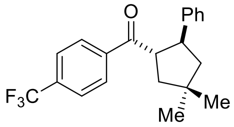
Di-tert-butyl 3-benzoyl-4-phenylcyclopentane-1,2-dicarboxylate (3-30): Prepared according



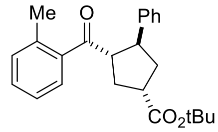
to the general procedure using 24.3 mg (0.04 mmol) of $Gd(OTf)_3$, 29.9 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 138.6 mg (0.4 mmol) of (1R,2S,3s)-di-tert-butyl 3-benzoylcyclopropane-1,2-dicarboxylate, 209.6 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, and 51.2 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 6 h. The crude product was purified by column chromatography (1:5, Et_2O/pentanes) to give 153.2 mg (0.340 mmol, 85 % yield) of cycloadduct as two separable diastereomers (7:1 dr) <u>Major Diastereomer:</u> 98.7% ee [Daicel Chiracel OD-H, 5 to 30 % iPrOH, 3 mL/min, 238 nm; t_1=4.26 min, t_2=4.67 min]. $[\alpha]_D^{22}$ 56.4 (*c*1.010, CH_2Cl_2). White solid (mp = 96-97 ^{o}C). v_{max} (film) / cm^{-1} 2977, 1724, 1681, 1393, 1368, 1257, 1158. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.7 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.29 (t, *J* = 7.7 Hz, 2H), 7.24-7.2 (m, 4H), 7.14 (dq, *J* = 8.2, 5.5, 4.8 Hz, 1H), 4.17 (t, *J* = 9.5 Hz, 1H), 3.64 (dt, *J* = 25.1, 8.8 Hz, 2H), 3.36 (dq, *J* = 9.3, 5.5 Hz, 1H), 2.51 (ddd, *J* = 13.4, 8.1, 5.5 Hz, 1H), 2.27 (dt, *J* = 13.2, 9.8 Hz, 1H), 1.49 (s, 9H), 1.25 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.49 , 173.03 , 172.54 , 141.91 , 137.22 , 132.93 , 128.59 , 128.40 , 128.29 , 127.20 , 126.81 , 81.21 , 80.89 , 57.00 , 53.04 , 49.76 , 47.34 , 37.16 , 28.05 , 27.78. HRMS (ESI) calculated for $[C_{28}H_{35}O_5]$ ($M+H^+$) requires 451.2479, found 451.2479. <u>Minor Diastereomer:</u> White solid (mp = 83.7-85.1 ^{o}C). v_{max} (film) / cm^{-1} 2978, 2936, 1725, 1680, 1367, 1257, 1154. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.0 Hz, 2H), 7.46 – 7.33 (m, 1H), 7.27 – 7.23 (m, 2H), 7.07 – 6.91 (m, 5H), 4.50 (dd, *J* = 10.0, 7.7 Hz, 1H), 3.93 (dd, *J* = 10.3, 7.7 Hz, 1H), 3.70 (td, *J* = 10.0, 7.3 Hz, 1H), 3.10 (td, *J* = 10.5, 7.9 Hz, 1H), 2.57 – 2.36 (m, 2H), 1.53 (s, 9H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.61, 132.42, 128.32, 128.07, 128.05, 127.94, 126.59, 53.83, 48.52, 48.27, 36.85, 28.15, 28.08. HRMS (ESI) calculated for [$C_{28}H_{35}O_5$] (M+H$^+$) requires 451.2479, found 451.2478.



tert-Butyl 5-benzoyl-2,2-dimethyl-4-phenylcyclopentanecarboxylate (3-32): Prepared according to the general procedure at –20 °C using 48.6 mg (0.04 mmol) of Gd(OTf)$_3$, 59.4 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 109.7 mg (0.4 mmol) of tert-butyl 3-benzoyl-2,2-dimethylcyclopropanecarboxylate, 209.2 mg (2.0 mmol) of styrene, 8.6 mg (0.01 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, and 103.4 mg (0.8 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 48 h. The crude product was purified by column chromatography (1:10, Et_2O/pentanes) to give 132.5 mg (0.35 mmol, 87% yield) of cycloadduct as a single diastereomer. 96.5% ee [Daicel Chiracel OD-H, 5 to 30 % iPrOH, 3 mL/min, 238 nm; t_1=3.64 min, t_2=4.69 min]. $[\alpha]_D^{22}$ 76.4 (*c*1.110, CH_2Cl_2). White solid (mp = 134.7-138.5 °C). ν_{max} (film) / cm^{-1} 2960, 1722, 1667, 1369, 1153. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.1 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.28 (t, *J* = 8.1 Hz, 4H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H), 4.37 (dd, *J* = 10.2, 8.1 Hz, 1H), 3.68 (td, *J* = 10.5, 8.4 Hz, 1H), 2.86 (d, *J* = 8.1 Hz, 1H), 2.15 – 1.94 (m, 2H), 1.40 (s, 9H), 1.28 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.86 , 173.23 , 142.94 , 137.18 , 132.79 , 128.47 (d, *J* = 6.8 Hz), 128.22 , 127.58 , 126.46 , 80.96 , 59.98 , 57.17 , 49.51 , 47.24 , 42.31 , 30.24 , 28.09 , 26.41 . HRMS (ESI) calculated for [$C_{25}H_{31}O_3$]$^+$ (M+H$^+$) requires *m/z* 379.2268, found 379.2268.



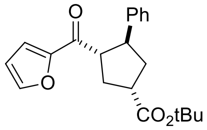
(4,4-Dimethyl-2-phenylcyclopentyl)(4-(trifluoromethyl)phenyl)methanone (3-34): Prepared according to the general procedure at –20 °C using 24.2 mg (0.04 mmol) of Gd(OTf)$_3$, 29.8 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 96.9 mg (0.4 mmol) of (2,2-dimethylcyclopropyl)(4-(trifluoromethyl)phenyl)methanone, 209.2 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, and 51.3 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 48 h. The crude product was purified by column chromatography (1:30, Et$_2$O/pentanes) to give 103.9 mg (0.300 mmol, 75 % yield) of cycloadduct (>10:1 dr). Major Diastereomer: 82.9% ee [Daicel Chiracel OD-H, 5 to 50 % (1:4 iPrOH/hexane), 3 mL/min, 235 nm; t$_1$=2.68 min, t$_2$=3.66 min]. $[\alpha]_D^{22}$ 62.6 (*c*0.991, CH$_2$Cl$_2$). White solid (mp = 63.9-65.7 ^{o}C). ν_{max} (film) / cm^{-1} 2942, 2866, 1690, 1445, 1281, 1015. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.88 (d, *J* = 8.1 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.29 – 7.19 (m, 4H), 7.18 – 7.08 (m, 1H), 3.90 (tt, *J* = 9.8, 5.0 Hz, 2H), 2.08 (ddd, *J* = 20.9, 13.0, 8.0 Hz, 2H), 1.93 – 1.83 (m, 1H), 1.82 – 1.71 (m, 1H), 1.22 (s, 3H), 1.14 (s, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 200.99, 143.67, 139.72, 134.03 (q, *J* = 32.7 Hz), 128.68, 128.49, 127.32, 126.38, 125.46 (q, *J* = 3.8 Hz), 123.59 (q, *J* = 272.7 Hz), 55.35, 49.43, 47.22, 46.33, 39.12, 30.52, 29.47. ^{19}F NMR (377 MHz, CDCl$_3$) δ -63.13 . HRMS (ESI) calculated for [C$_{20}$H$_{23}$O]$^+$ (M+H$^+$) requires *m/z* 347.1617, found 347.1617.



tert-butyl 3-(2-methylbenzoyl)-4-phenylcyclopentanecarboxylate (3-28): Prepared according to the general procedure using 24.3 mg (0.04 mmol) of Gd(OTf)$_3$, 29.7 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 105.3 mg (0.4 mmol) of *Trans* tert-butyl 2-(2-methylbenzoyl)cyclopropanecarboxylate, 209.3 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) of Ru(bpy)$_3$(PF$_6$)$_2$, and 52.6 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 6 hours. The crude product was purified by column chromatography (1:20, Et$_2$O/pentanes) to give 88.0 mg (0.244 mmol, 61 % yield) of cycloadduct as two separable diastereomers (2:1 dr). Major diastereomer: 71.3% ee [Daicel Chiracel AD-H, 7 % iPrOH, 6 mL/min, 263 nm; t$_1$=2.47 min, t$_2$=4.65 min]. $[\alpha]_D^{22}$ 52.9 (*c*0.982, CH$_2$Cl$_2$). White solid M.p. 66-68 ^{o}C. ν_{max} (film) / cm^{-1} 2983, 1714, 1694, 1422, 1265, 1154. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.33 – 7.06 (m, 9H), 3.76-3.68 (m, 2H), 3.04 (qd, *J* = 8.4, 5.7 Hz, 1H), 2.55 – 2.45 (m, 1H), 2.45 – 2.36 (m, 1H), 2.35 (s, 3H), 2.26 – 2.15 (m, 1H), 2.14 – 2.03 (m, 1H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 205.05 , 174.35 , 143.62 , 138.66 , 137.73 , 131.59 , 130.81 , 128.50 , 127.84 , 127.26 , 126.42 , 125.39 , 80.49 , 58.03 , 47.57 , 44.25 , 37.39 , 34.98 , 28.10

, 20.81. HRMS (ESI) calculated for $[C_{24}H_{29}O_3]^+$ ($M+H^+$) requires *m/z* 365.2111, found 365.2111. Minor diastereomer: White solid M.p. 93-94.8 °C. ν_{max} (film) / cm^{-1} 2975, 2931, 1724, 1684, 1455, 1367, 1249, 1151. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.20 (m, 6H), 7.19 – 7.05 (m, 3H), 3.86 (q, *J* = 9.3 Hz, 1H), 3.59 (ddd, *J* = 11.5, 9.7, 7.4 Hz, 1H), 3.00 (ddd, *J* = 16.6, 9.4, 7.2 Hz, 1H), 2.55 – 2.45 (m, 1H), 2.45 – 2.33 (m, 4H), 2.22 – 2.03 (m, 2H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.80 , 174.93 , 142.71 , 138.24 , 137.96 , 133.58 , 131.64 , 131.05 , 128.49 , 128.35 , 127.34 , 126.56 , 125.53 , 80.47 , 56.70 , 49.17 , 44.02 , 38.78 , 34.48 , 28.12 , 21.05. HRMS (ESI) calculated for $[C_{24}H_{32}NO_3]^+$ ($M+NH_4^+$) requires *m/z* 382.2377, found 382.2375.

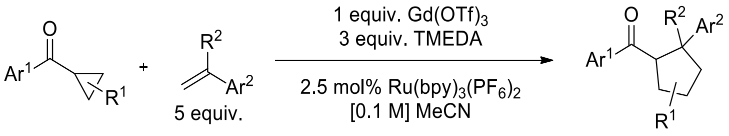
tert-Butyl 3-(furan-2-carbonyl)-4-phenylcyclopentanecarboxylate (3-27): Prepared



according to the general procedure at –30 °C using 24.2 mg (0.04 mmol) of $Gd(OTf)_3$, 30.1 mg (0.08 mmol) of 4-NMe$_2$-^{s}Bu-pybox, 94.5 mg (0.4 mmol) of *trans* tert-butyl 2-(furan-2-carbonyl)cyclopropanecarboxylate, 210.0 mg (2.0 mmol) of styrene, 8.7 mg (0.01 mmol) of $Ru(bpy)_3(PF_6)_2$, and 51.4 mg (0.4 mmol) of diisopropylethylamine with a total volume of 4 mL (0.1 M, MeCN). The reaction was complete after 6 h. The crude product was purified by column chromatography (4:1, Et_2O/pentanes) to give 108.9 mg (0.320 mmol, 80 % yield) of cycloadduct as two separable diastereomers (4:1 dr). Major diastereomer: 78.8% ee [Daicel Chiracel AD-H, 10 % iPrOH, 6 mL/min, 263 nm; t_1=1.89 min, t_2=2.74 min]. $[\alpha]_D^{22}$ 49.6 (*c*1.130, CH_2Cl_2). White solid (mp = 100.2-103.6 °C). ν_{max} (film) / cm^{-1} 2977, 1722, 1670, 1466, 1367, 1151. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.47 (m, 1H), 7.32 – 7.19 (m, 5H), 7.20 – 7.11 (m, 1H), 6.97 (d, *J* = 3.5 Hz, 1H), 3.79 – 3.59 (m, 2H), 3.08 (qd, *J* = 8.5, 6.0 Hz, 1H), 2.50 (ddt, *J* = 15.4, 13.0, 6.8 Hz, 2H), 2.25 (dt, *J* = 13.0, 9.2 Hz, 1H), 2.11 (dt, *J* = 13.3, 9.1 Hz, 1H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.52 , 174.24 , 152.74 , 146.41 , 143.47 , 128.48 , 127.30 , 126.45 , 117.51 , 112.13 , 80.52 , 55.34 , 47.29 , 44.36 , 37.33 , 34.90 , 28.09. HRMS (ESI) calculated for $[C_{21}H_{25}O_4]^+$ ($M+H^+$) requires 341.1747, found 341.1747. Minor Diastereomer: White solid (mp = 94.9-98 °C). ν_{max} (film) / cm^{-1} 2976, 1724, 1673, 1464, 1365, 1150. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.52 – 7.47 (m, 1H), 7.29 – 7.20 (m, 5H), 7.21 – 7.11 (m, 1H), 6.96 (d, *J* = 3.5 Hz, 1H), 6.41 (dd, *J* = 3.6, 1.7 Hz, 1H), 3.77 (q, *J* = 9.4 Hz, 1H), 3.57 (ddd, *J* = 11.4, 9.7, 7.3 Hz, 1H), 3.02 (ddd, *J* = 16.7, 9.5, 7.3 Hz, 1H), 2.55 – 2.38 (m, 2H), 2.29 – 2.03 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.26 , 174.92 , 148.16 , 146.73 , 142.62 , 128.48 , 127.39 , 126.60 , 118.01 , 112.11 , 80.47 , 54.14 , 48.84 , 44.10 , 38.87 , 34.23 , 28.13. HRMS (ESI) calculated for $[C_{21}H_{25}O_4]^+$ (M+H$^+$) requires 341.1747, found 341.1748.

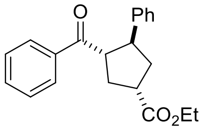
3.4.7 Racemic [3+2] cycloadditions



General racemic procedure:

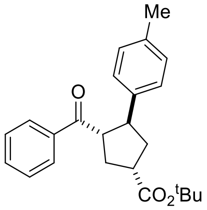
A flame-dried Schlenk tube equipped with a magnetic stir-bar was charged with $Gd(OTf)_3$ (0.2 mmol). A 2 mL volumetric flask was charged with cyclopropane (0.2 mmol), alkene (1.0 mmol), $Ru(bpy)_3(PF_6)_2$ (0.005 mmol), TMEDA (0.6 mmol) and MeCN (2 mL total volume). The contents of the volumetric flask were then transferred to the Schlenk tube. The reaction mixture was then thoroughly degassed through three freeze-pump-thaw cycles, then backfilled with N_2. The reaction flask was then placed in front of a 23 W (1380 lumen) compact fluorescent lamp and stirred at room temperature. Upon consumption of starting material, the reaction was diluted with 1:1 Et_2O/pentanes and passed through a short plug of silica. The filtrate was concentrated and the residue purified by column chromatography.

Ethyl 3-benzoyl-4-phenylcyclopentanecarboxylate (3-4): Reaction was carried out with *trans* ethyl 2-benzoylcyclopropanecarboxylate (43.6 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (69.8 mg, 0.601 mmol), $Ru(bpy)_3(PF_6)_2$ (4.3 mg,

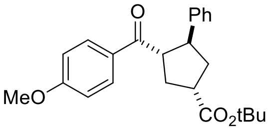


0.005 mmol), Gd(OTf)$_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h providing **ethyl 3-benzoyl-4-phenylcyclopentanecarboxylate** as a white solid (60.0 mg, 0.186 mmol, 93 % yield, 4:1 dr). All spectroscopic data match those reported above.

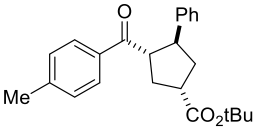
***tert*-butyl 3-benzoyl-4-(4-methylphenyl)cyclopentanecarboxylate (3-7):** Reaction was carried out with *trans* tert-butyl 2-benzoylcyclopropanecarboxylate (49.5 mg, 0.201 mmol), 4-methylstyrene (120.5 mg, 1.02 mmol), TMEDA (69.5 mg, 0.598 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.4 mg, 0.005 mmol), Gd(OTf)$_3$ (122.8 mg, 0.203 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h providing ***tert*-butyl 3-benzoyl-4-(4-methylphenyl)cyclopentanecarboxylate** as a white solid (43 mg, 0.118 mmol, 59 % yield, 1.7:1 dr). All spectroscopic data match those reported above.



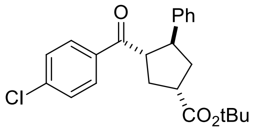
tert-Butyl 3-(4-methoxybenzoyl)-4-phenylcyclopentanecarboxylate (3-17): Reaction was carried out with *trans* tert-butyl 2-(4-methoxybenzoyl)cyclopropanecarboxylate (55.3 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (69.8 mg, 0.601 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h providing **tert-butyl 3-(4-methoxybenzoyl)-4-phenylcyclopentanecarboxylate** as a white solid (61.0 mg, 0.174 mmol, 87% yield, 2.7:1 dr). All spectroscopic data match those reported above.



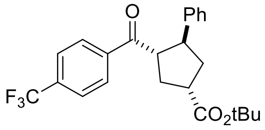
tert-Butyl 3-(4-methylbenzoyl)-4-phenylcyclopentanecarboxylate (3-18): Reaction was carried out with *trans* tert-butyl 2-(4-methylbenzoyl)cyclopropanecarboxylate (52.1 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (69.8 mg, 0.601 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete



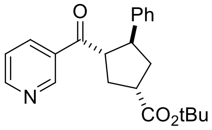
after 3 h providing **tert-butyl 3-(4-methylbenzoyl)-4-phenylcyclopentanecarboxylate** as a white solid (63.4 mg, 0.174 mmol, 87% yield, 3:1 dr). All spectroscopic data match those reported above.



tert-Butyl 3-(4-chlorobenzoyl)-4-phenylcyclopentanecarboxylate (3-19): Reaction was carried out with *trans* tert-butyl 2-(4-chlorobenzoyl)cyclopropanecarboxylate (56.1 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (69.8 mg, 0.601 mmol), $Ru(bpy)_3(PF_6)_2$ (4.3 mg, 0.005 mmol), $Gd(OTf)_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h providing **tert-butyl 3-(4-chlorobenzoyl)-4-phenylcyclopentanecarboxylate** as a white solid (71.6 mg, 0.186 mmol, 93% yield, 1:1 dr). All spectroscopic data match those reported above.

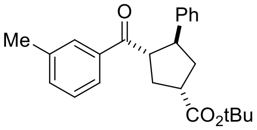


tert-Butyl 3-phenyl-4-(4-(trifluoromethyl)benzoyl)cyclopentane carboxylate (3-20): Reaction was carried out with *trans* tert-butyl 2-(4-(trifluoromethyl)benzoyl)cyclopropanecarboxylate (62.9 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (69.8 mg, 0.601 mmol), $Ru(bpy)_3(PF_6)_2$ (4.3 mg, 0.005 mmol), $Gd(OTf)_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 hours providing **tert-butyl 3-phenyl-4-(4-(trifluoromethyl)benzoyl)cyclopentanecarboxylate** as a white solid (80.3 mg, 0.192 mmol , 96 % yield, 1.6:1 dr). All spectroscopic data match those reported above.

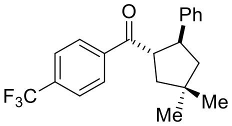


tert-Butyl 3-nicotinoyl-4-phenylcyclopentanecarboxylate (3-21): Reaction was carried out with *trans* tert-butyl 2-nicotinoylcyclopropanecarboxylate (49.5 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (69.8 mg, 0.601 mmol), $Ru(bpy)_3(PF_6)_2$ (4.3 mg, 0.005 mmol), $Gd(OTf)_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h providing **tert-butyl 3-nicotinoyl-4-phenylcyclopentanecarboxylate** as a white solid (35.8 mg, 0.102 mmol, 51% yield, 1.6:1 dr). All spectroscopic data match those reported above.

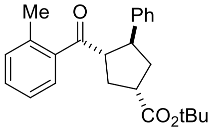
tert-Butyl 3-(3-methylbenzoyl)-4-phenylcyclopentanecarboxylate (3-22): Reaction was carried out with *trans* tert-butyl 2-(3-methylbenzoyl)cyclopropanecarboxylate (52.1 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (69.8 mg, 0.601 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h providing **tert-butyl 3-(3-methylbenzoyl)-4-phenylcyclopentanecarboxylate** as a white solid (59.8 mg, 0.164 mmol, 82% yield, 2.4:1 dr). All spectroscopic data match those reported above.



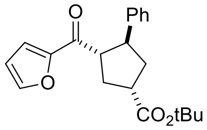
(4,4-Dimethyl-2-phenylcyclopentyl)(4-(trifluoromethyl)phenyl)methanone (3-34): Reaction was carried out with (2,2-dimethylcyclopropyl)(4-(trifluoromethyl)phenyl)methanone (48.4 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (69.8 mg, 0.601 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h providing **(4,4-dimethyl-2-phenylcyclopentyl)(4-(trifluoromethyl)phenyl)methanone** as a white solid (41.6 mg, 0.120 mmol, 60% yield, 0.8:1 dr). All spectroscopic data match those reported above.



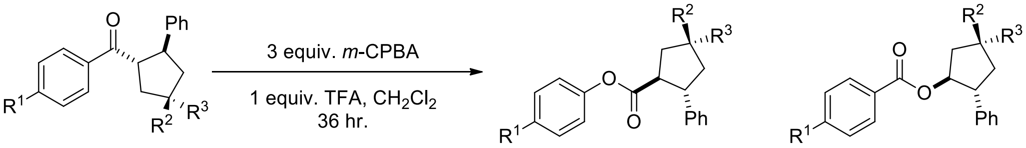
tert-Butyl 3-(2-methylbenzoyl)-4-phenylcyclopentanecarboxylate (3-28): Reaction was carried out with *trans* tert-butyl 2-(2-methylbenzoyl)cyclopropanecarboxylate (52.1 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (69.8 mg, 0.601 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h providing **tert-butyl 3-(2-methylbenzoyl)-4-phenylcyclopentanecarboxylate** as a white solid (37.9 mg, 0.104 mmol, 52% yield, 1.5:1 dr). All spectroscopic data match those reported above.



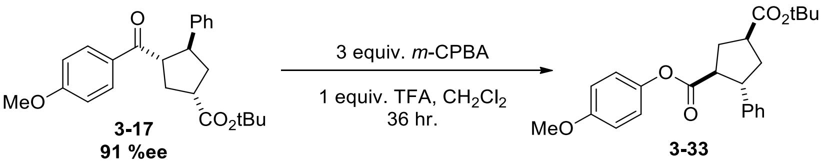
tert-Butyl 3-(furan-2-carbonyl)-4-phenylcyclopentanecarboxylate (3-27): Reaction was carried out with *trans* tert-butyl 2-(furan-2-carbonyl)cyclopropanecarboxylate (47.3 mg, 0.200 mmol), styrene (104.3 mg, 1.001 mmol), TMEDA (69.8 mg, 0.601 mmol), Ru(bpy)$_3$(PF$_6$)$_2$ (4.3 mg, 0.005 mmol), Gd(OTf)$_3$ (120.9 mg, 0.200 mmol), and MeCN (2 mL total volume). The reaction was complete after 3 h providing **tert-butyl 3-(furan-2-carbonyl)-4-phenylcyclopentanecarboxylate** as a white solid (60.6 mg, 0.178 mmol, 89% yield, 1.6:1 dr). All spectroscopic data match those reported above.



3.4.8 Baeyer-Villiger product derivatization



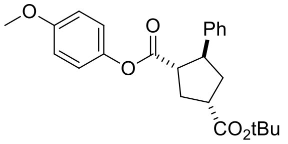
General procedure: A small flame-dried vial with magnetic stir bar was charged with cyclopentyl ketone (0.05 mmol), *m*-CPBA (≤77%, 26.0 mg, 0.15 mmol), and CH$_2$Cl$_2$ (1.0 mL). The vial was sealed with a rubber septum, purged three times with N$_2$(g) and cooled to 0 ^{o}C with an ice bath. Trifluoroacetic acid (9.1 µL, 0.05 mmol) was then added via syringe. The vial was then sealed with a Teflon cap, covered in aluminum foil, and stirred for 36 h at room temperature. After this time the reaction was quenched by washing with saturated aqueous Na$_2$SO$_3$. The aqueous layer was washed twice more with CH$_2$Cl$_2$. The combined organics were washed with brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure to give the crude product as a yellow oil. Products were purified by flash column chromatography (Et$_2$O/pentane).

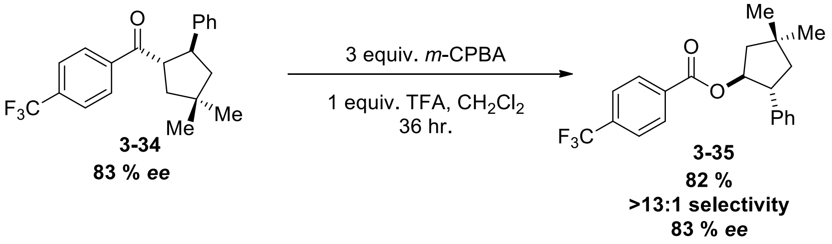


3-17
91 %ee

3-33
84 % yield
>20:1 selectivity
89 %ee

1-tert-Butyl 3-(4-methoxyphenyl) 4-phenylcyclopentane-1,3-dicarboxylate (3-33): Reaction was carried out according to the general procedure with cyclopentane **3-17** (19.1 mg, 0.05 mmol), *m*-CPBA (28.3 mg, 0.15 mmol), CH_2Cl_2 (1.0 mL) and trifluoroacetic acid (9.1 µL, 0.05 mmol) to give rearrangement product **3-33** as a clear oil as the sole product. Product was purified by column chromatography (20% Et_2O/pentanes) to give the pure product (16.7 mg, 0.042 mmol, 84% yield). 88.7% ee [Daicel Chiracel AD-H, 15 % iPrOH, 3 mL/min, 263 nm; t_1=4.08 min, t_2=5.70 min]. $[\alpha]_D^{22}$ 45.1 (*c*0.901, CH_2Cl_2). ν_{max} (film) / cm^{-1} 2974, 1752, 1723, 1506, 1455, 1367, 1248, 1195, 1134, 1033. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 4H), 7.25-7.21 (m, 1H), 6.82 (m, 4H), 3.76 (s, 3H), 3.61 (q, *J* = 9.9 Hz, 1H), 3.14 – 2.97 (m, 2H), 2.61 – 2.44 (m, 2H), 2.38 (ddd, *J* = 13.1, 10.4, 8.4 Hz, 1H), 2.08 (dt, *J* = 13.4, 9.8 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.57 , 173.33 , 157.28 , 144.27 , 142.63 , 128.75 , 127.40 , 126.92 , 122.33 , 114.46 , 80.75 , 55.70 , 52.49 , 48.99 , 43.78 , 37.63 , 34.35 , 28.23. HRMS (ESI) calculated for $[C_{24}H_{29}O_5]^+$ (M+H$^+$) requires *m/z* 397.2010, found 397.2010.

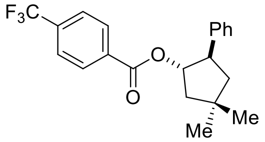




3-34
83 % *ee*

3-35
82 %
>13:1 selectivity
83 % *ee*

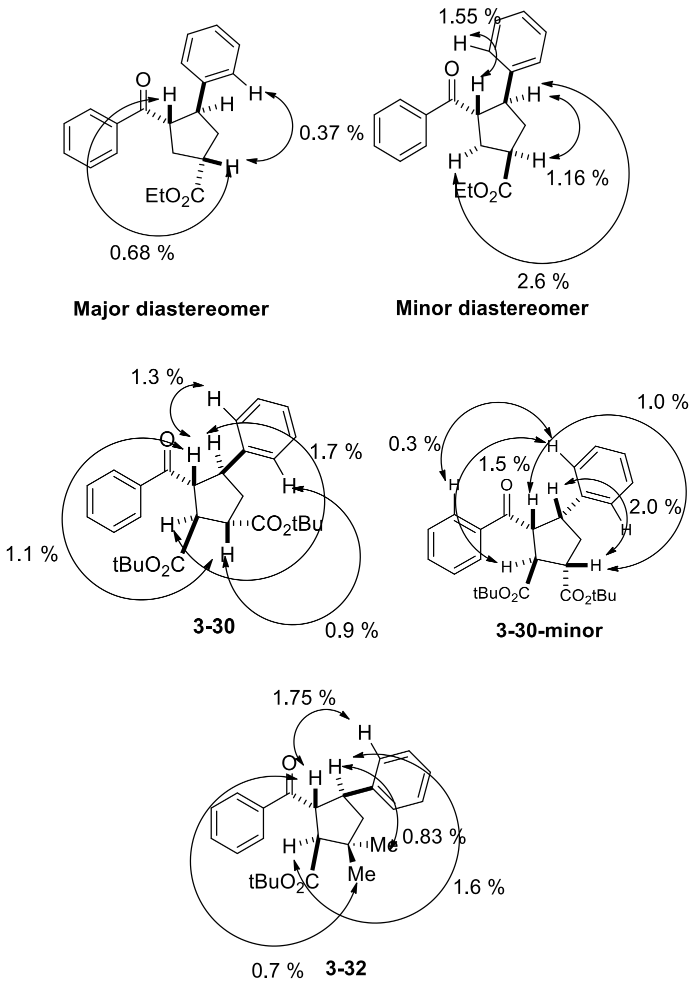
4,4-Dimethyl-2-phenylcyclopentyl 4-(trifluoromethyl)benzoate (3-35): Reaction was carried out according to the general procedure with cyclopentane **3-34** (50.1 mg, 0.144 mmol), *m*-CPBA (74.6 mg, 0.432 mmol), CH_2Cl_2 (2.9 mL), and trifluoroacetic acid (26.2 µL, 0.144 mmol) to give the rearranged product **3-35** as a clear oil. Product was purified by column chromatography (5% Et_2O/pentanes) (42.8 mg, 0.118 mmol, 82% isolated yield). 83.1% ee [Daicel Chiracel OD-H, 5 to 30 % iPrOH, 3 mL/min, 235 nm; t_1=4.71 min, t_2=6.04 min]. $[\alpha]_D^{22}$ 63.3 (*c*0.900, CH_2Cl_2). ν_{max} (film) / cm^{-1} 2956, 1723, 1412, 1325, 1275, 1131, 1067, 1018. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.1 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.35



– 7.25 (m, 4H), 7.24 – 7.16 (m, 1H), 5.44 (td, *J* = 8.0, 5.8 Hz, 1H), 3.57 (dt, *J* = 11.9, 7.9 Hz, 1H), 2.28 (dd, *J* = 13.8, 8.1 Hz, 1H), 2.05 (dd, *J* = 13.0, 7.9 Hz, 1H), 1.78 – 1.66 (m, 2H), 1.24 (s, 3H), 1.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.97 , 142.27 , 134.30 (q, *J* = 32.7 Hz), 133.69 , 129.92 , 128.55 , 127.20 , 126.59 , 125.35 (q, *J* = 3.7 Hz), 123.64 (q, *J* = 273.6 Hz) , 82.63 , 50.52 , 47.33 , 47.08 , 37.07 , 30.71 , 30.18. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.10. HRMS (ESI) calculated for $[C_{21}H_{24}NF_3O_2]^+$ (M+NH_4^+) requires *m/z* 380.1832, found 380.1832.

3.4.9 NOe assignment of relative stereochemistry

Figure 3-9. Observed nOe enhancements



Major diastereomer **Minor diastereomer**

3-30 **3-30-minor**

3-32

3.4.10 Isomerization of cis-cyclopropanes under photocatalytic conditions

Figure 3-10. Control reaction in the absence of photocatalyst.

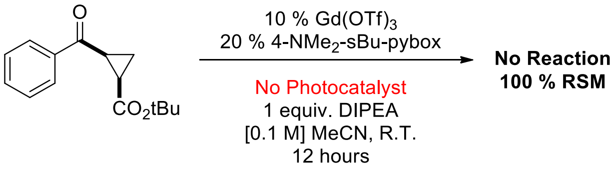
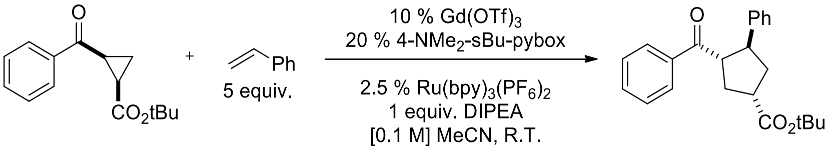
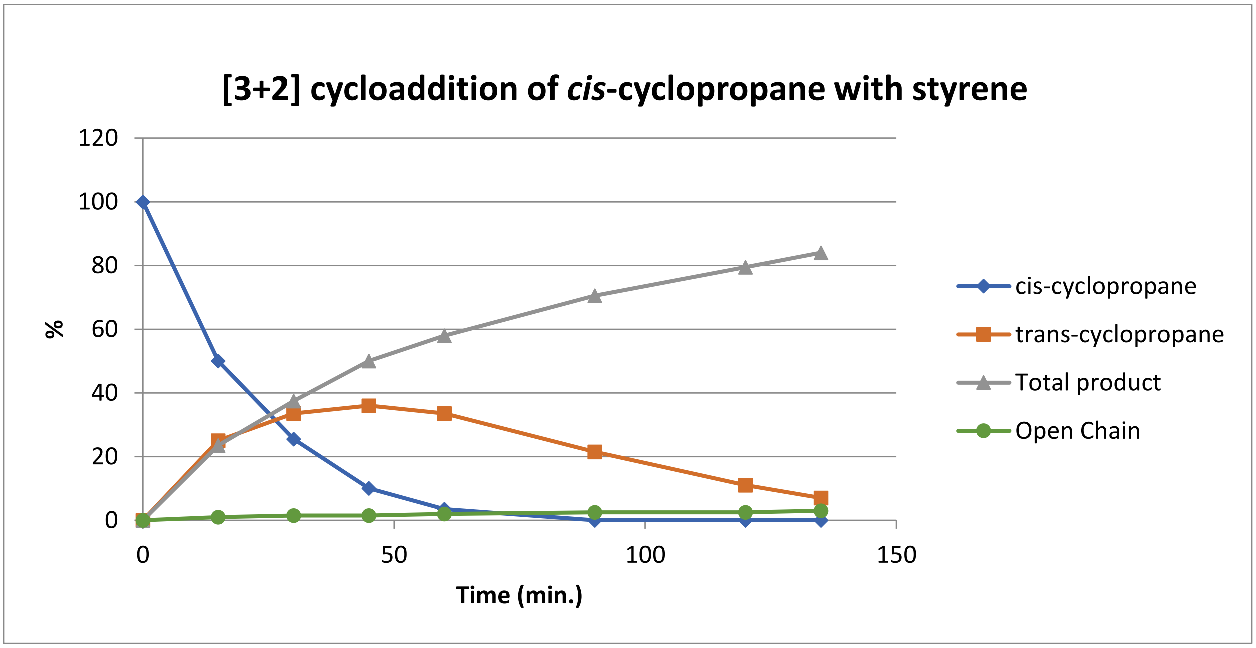
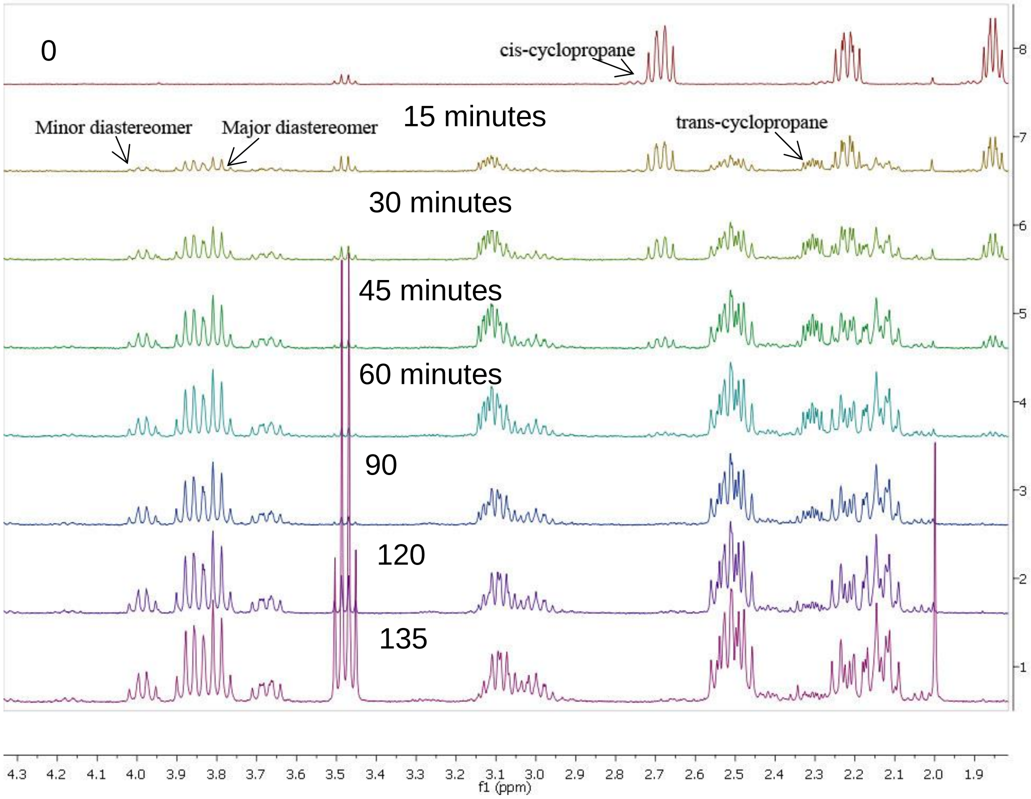


Figure 3-11. Time course of photocatalytic [3+2] cycloaddition of cis-cyclopropane with styrene







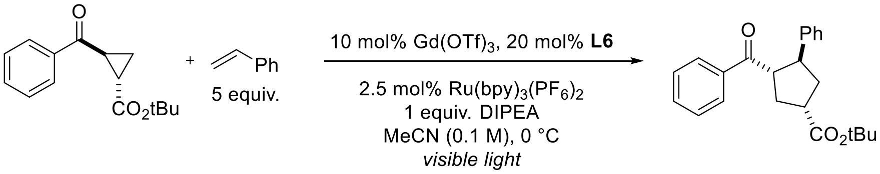
3.4.11 Kinetic Isotope Effect Measurements

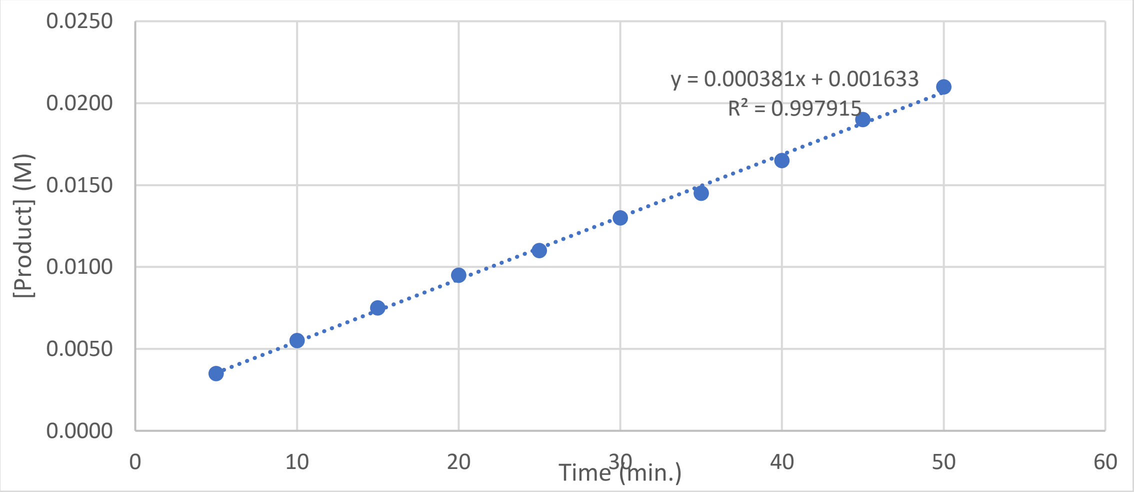
The intermolecular kinetic isotope effect of the [3+2] photocycloaddition was determined by studying the initial rates of reactions with (a) tert-butyl 2-benzoylcyclopropanecarboxylate **3-2** and styrene and (b) tert-butyl 2-benzoylcyclopropanecarboxylate **3-2** and β,β-dideuterostyrene.

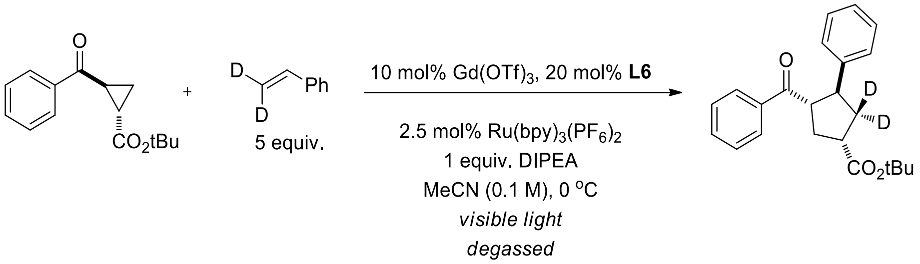
General procedure for kinetic experiments (initial rates measurements). The experiments were conducted in dry 15 mL Schlenk tubes under degassed conditions 15 cm from a 26 W fluorescent lamp. Reaction were run to about 20% conversion and the data ([product] versus time) was analyzed by the initial rates method. Reported values for initial rates are the average of the experiments all conducted under identical conditions using the same stock solutions. The reported error is the standard deviation of this three experiments. Representative kinetics experiments are shown in Figure **3-11.**

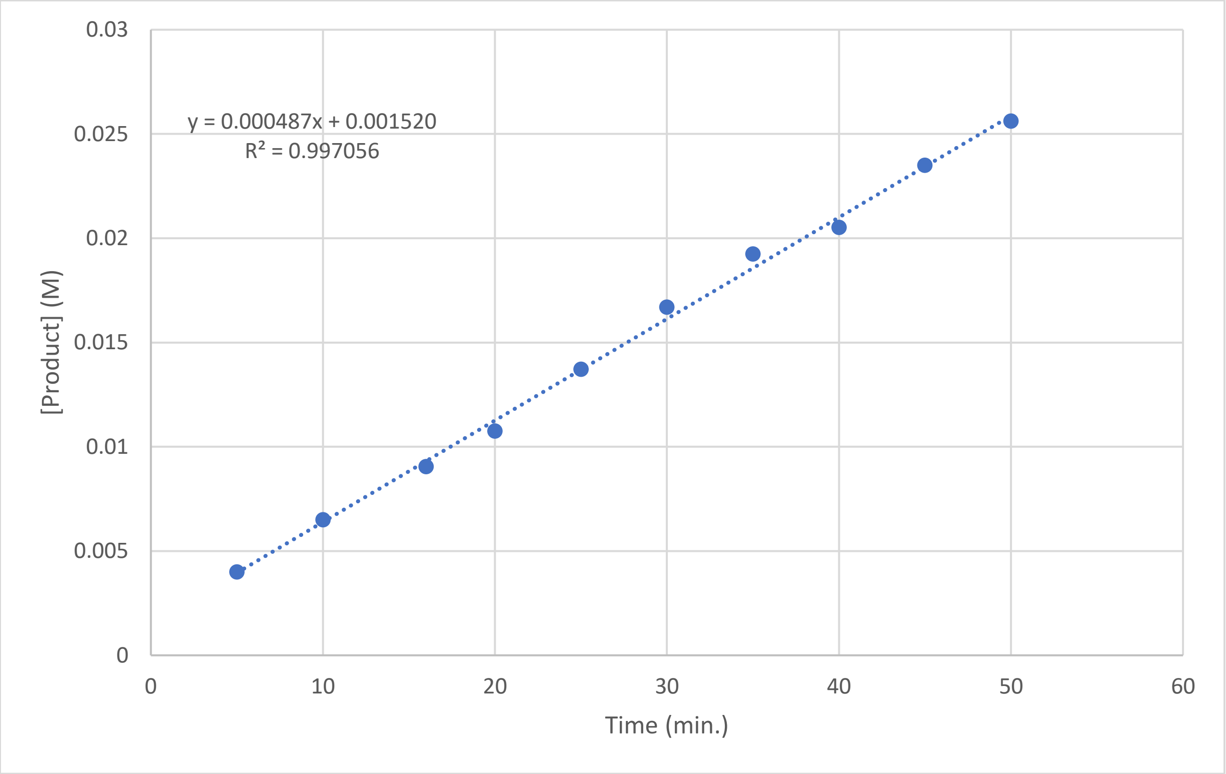
Reaction procedure. For each set of three experiments a 10 mL stock solution was generated containing substrate (123.15 mg, 0.5 mmol), styrene (260.4 mg, 2.5 mmol), $Ru(bpy)_3(PF_6)_2$ (10.7 mg, 0.125 mmol), $Gd(OTf)_3$ (30.2 mg, 0.05 mmol), ligand **L3-12** (37.3 mg, 0.1 mmol), phenanthrene (internal standard), and MeCN (10 mL total volume in a volumetric flask). Stock solution (2 mL) was transferred to a flame-dried 15 mL Schlenk tube and degassed by three freeze/pump/thaw cycles under nitrogen in the dark. After backfilling with nitrogen the reaction was allowed to stir at 0 °C while being irradiated by a 23 watt fluorescent bulb at a distance of 15 cm. For each time point, the Schlenk tube's side arm was purged several times by vacuum/nitrogen cycles, opened under a positive pressure of nitrogen, and a small aliquot was taken with a nitrogen purged needles. The aliquot was diluted in 1:1 Et_2O/pentanes, flashed through a short pipette silica plug and concentrated under reduced pressure for analysis by ^{1}H-NMR spectroscopy. The yield of product was determined versus phenanthrene as the internal standard.

Figure 3-12. Representative kinetics experiments.



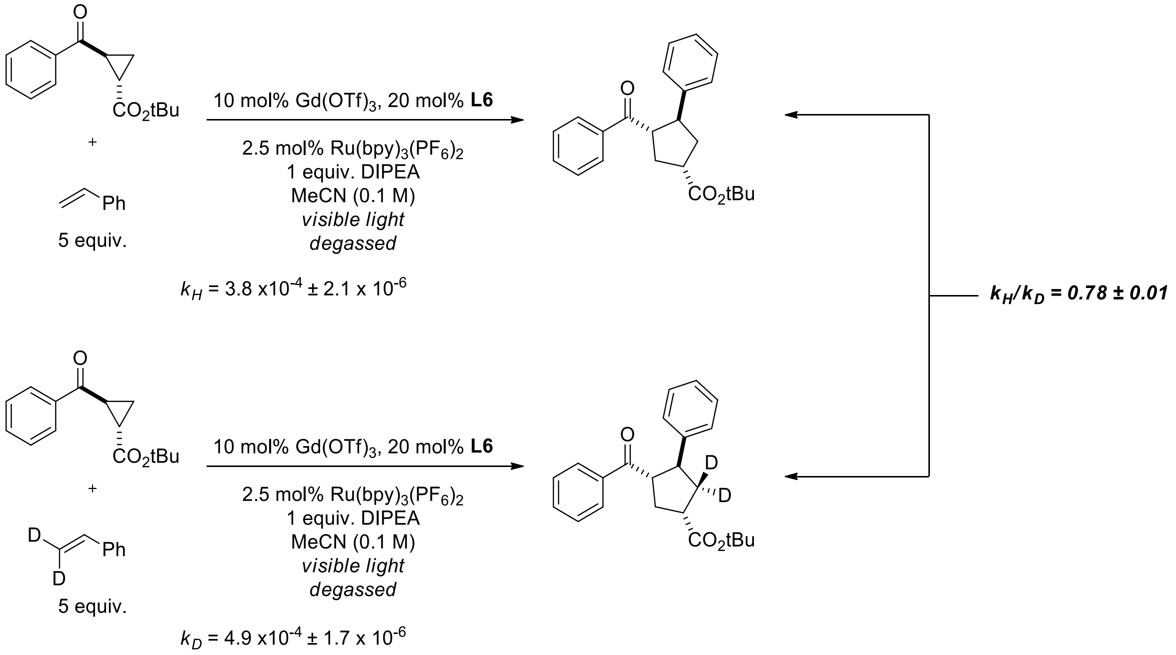



O
+
D
Ph
D
CO$_2$tBu
5 equiv.
10 mol% Gd(OTf)$_3$, 20 mol% **L6**
2.5 mol% Ru(bpy)$_3$(PF$_6$)$_2$
1 equiv. DIPEA
MeCN (0.1 M), 0 °C
visible light
degassed
O
D
D
CO$_2$tBu


0.03
0.025
0.02
0.015
0.01
0.005
0
y = 0.000487x + 0.001520
R² = 0.997056
[Product] (M)
0
10
20
30
40
50
60
Time (min.)

Kinetic isotope effects. Obtained values for rate constants and its use in the calculation of kinetic isotope effects are displayed below.

Figure 3-13. Computed kinetic isotope effect.



3.4.12 UV-vis titration of Gd(III)–pybox complex with *i*-Pr$_2$NEt

General procedure for titration: An acetonitrile solution of (*n*-Bu)$_4$NPF$_6$ (0.1 M), *s*-Bupybox (5x10^{-5} M) and Gd(OTf)$_3$ (2.5x10^{-5} M) was titrated across 27 data points with an acetonitrile solution of *i*-Pr$_2$NEt (1x10^{-9} M) and (*n*-Bu)$_4$NPF$_6$. After each addition of *i*-Pr$_2$NEt the solution was allowed 5 minutes to equilibrate. A UV-vis spectrum was obtained for each data point. A local absorption maximum at 285 nm was used for analysis. Data was analyzed in Microsoft Excel for equivalents of *i*-Pr$_2$NEt added vs. ΔAbs^{285}. Data was fit to a 1:1 binding model using the quadratic equation shown below using the Solver function in Excel with the GRG nonlinear solving method (equation 3-1). The data was fit with K$_{eq}$ and $\Delta\varepsilon$(285 nm) set as objectives. The accuracy of the fit was analyzed using the SolvStat addin for excel. The binding isotherm obtained is shown in Figure 3-13. The statistical analysis of the fit is shown in Table 3-12.

Equation 3-1. 1:1 binding model

$$\Delta \mathrm{Abs285} = \Delta\varepsilon(285\ \mathrm{nm}) * 0.5 * \left([DIPEA]_0 + [Gd\text{–}pybox]_0 + \frac{1}{K_{eq}}\right) - \sqrt{0.25 * \left([DIPEA]_0 + [Gd\text{–}pybox]_0 + \frac{1}{K_{eq}}\right)^2 - [Gd\text{–}pybox]_0 * [DIPEA]_0}$$

Figure 3-14. Binding isotherm for titration of Gd(III)–pybox complex with *i*-Pr_2NEt

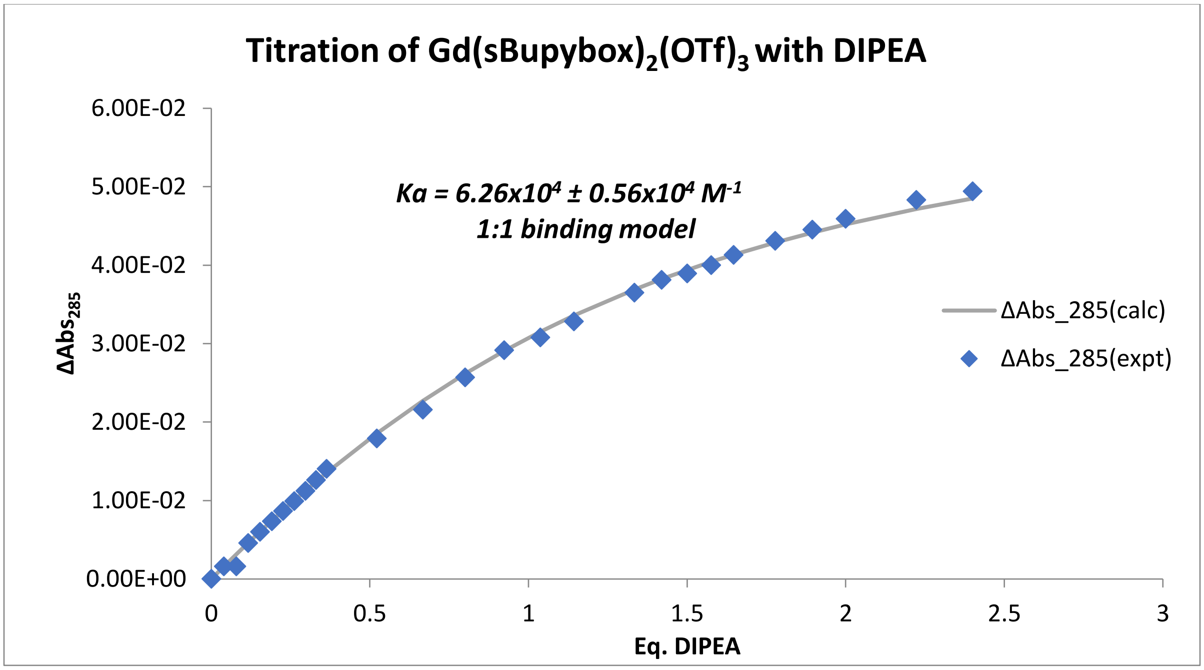


Table 3-12. Statistical analysis of titration using SolvStat

	K_{eq}	Δε(285 nm)
Value	62637.33763	2679.712755
Standard deviation	5551.738283	75.30502295
R^2, SE(y)	0.998714015	0.000602467

3.4.13 X-ray crystallographic information

Data Collection

A colorless crystal with approximate dimensions 0.184 × 0.037 × 0.026 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_α (λ = 0.71073 Å) radiation and the diffractometer to crystal distance of 4.96 cm.[18]

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 0.5° in a 6° range about ω with the exposure time of 10 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 8678 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 0.70 Å. A total of 30318 data were harvested by collecting 4 sets of frames with 0.5° scans in ω and φ with exposure times of 120 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.[19]

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.[20-25]

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 were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients.

The only crystal large enough for the single-crystal X-ray diffraction experiment proved to be a crystal with at least two smaller crystals attached to it in a random manner. These smaller crystals were not visible under the microscope and their presence was inferred from the diffraction pattern. The data collection was treated as if the major crystal were single.

The final least-squares refinement of 247 parameters against 4215 data resulted in residuals R (based on F^2 for $I \geq 2\sigma$) and wR (based on F^2 for all data) of 0.0365 and 0.0885, respectively.

Summary

Crystal Data for $C_{23}H_{25}BrO_3$ (M =429.34 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 5.633(2) Å, b = 16.777(7) Å, c = 21.917(8) Å, V = 2071.4(14) Å^3, Z = 4, T = 100.0 K, μ(MoKα) = 2.004 mm^{-1}, $Dcalc$ = 1.377 g/cm^3, 30318 reflections measured (3.058° ≤ 2Θ ≤ 52.822°), 4215 unique (R_{int} = 0.0568, R_{sigma} = 0.0382) which were used in all calculations. The final R_1 was 0.0365 (I > 2σ(I)) and wR_2 was 0.0885 (all data).

Figure 3-15. A molecular drawing of 3-9 shown with 50% probability ellipsoids. All H atoms are omitted unless they are on anomeric carbon atoms.

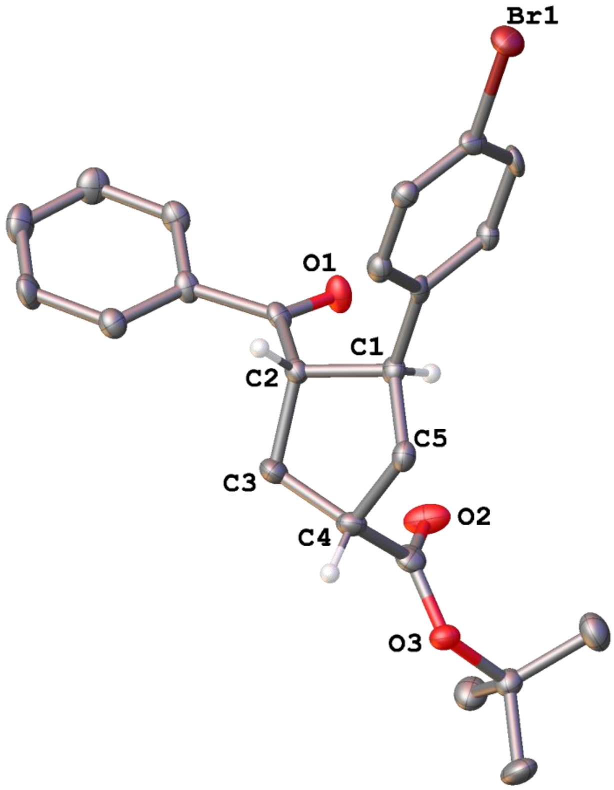


Table 3-13 Crystal data and structure refinement for 3-9.

Identification code	yoon42
Empirical formula	$C_{23}H_{25}BrO_3$
Formula weight	429.34
Temperature/K	100.0
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	5.633(2)
b/Å	16.777(7)

c/Å	21.917(8)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2071.4(14)
Z	4
ρ_{calc}g/cm^3	1.377
μ/mm^{-1}	2.004
F(000)	888.0
Crystal size/mm^3	0.184 × 0.037 × 0.026
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.058 to 52.822
Index ranges	$-7 \le h \le 7$, $-20 \le k \le 20$, $-25 \le l \le 27$
Reflections collected	30318
Independent reflections	4215 [R_{int} = 0.0568, R_{sigma} = 0.0382]
Data/restraints/parameters	4215/0/247
Goodness-of-fit on F^2	1.068
Final R indexes [I>=2σ (I)]	R_1 = 0.0365, wR_2 = 0.0858
Final R indexes [all data]	R_1 = 0.0449, wR_2 = 0.0885
Largest diff. peak/hole / e Å^{-3}	0.51/-0.28
Flack parameter	0.002(5)

Table 3-14 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 11. U$_{eq}$ is defined as 1/3 of of the trace of the orthogonalised U$_{IJ}$ tensor.

Atom	***x***	***y***	***z***	**U(eq)**
Br1	9807.7(8)	1810.9(3)	3546.2(2)	28.62(14)
O1	4364(5)	5424.9(19)	4753.8(15)	25.1(7)
O2	5841(5)	5574(2)	6384.9(16)	32.8(8)
O3	8823(5)	5545.7(19)	7076.8(14)	21.2(7)
C1	8355(7)	4702(3)	5269(2)	17.0(9)
C2	8501(7)	5523(3)	4958(2)	16.1(9)
C3	9177(9)	6118(3)	5484(2)	24.6(10)
C4	9889(9)	5604(2)	6039.3(18)	21.0(9)
C5	10216(8)	4754(2)	5775.7(18)	19.7(9)
C6	8708(7)	4006(3)	4843(2)	16.3(9)
C7	6958(7)	3427(3)	4784(2)	17.8(9)
C8	7252(8)	2766(3)	4398(2)	21.5(10)
C9	9342(8)	2698(2)	4079(2)	20.7(10)
C10	11129(7)	3266(3)	4124.4(19)	18.5(9)
C11	10784(7)	3914(3)	4507(2)	20(1)
C12	6225(7)	5755(3)	4636(2)	16.7(9)
C13	6283(7)	6393(3)	4158(2)	18.2(9)
C14	8185(7)	6917(3)	4082(2)	21.2(10)
C15	8153(9)	7483(3)	3616(2)	27.1(11)
C16	6223(9)	7522(3)	3233(2)	29.9(11)

C17	4350(8)	6997(3)	3293(2)	27.3(11)
C18	4365(8)	6442(3)	3754(2)	22(1)
C19	7922(8)	5584(3)	6509(2)	23(1)
C20	7238(8)	5477(3)	7615(2)	21.6(10)
C21	5439(10)	6146(3)	7621(2)	30.7(11)
C22	6068(9)	4663(3)	7617(3)	34.4(12)
C23	8976(9)	5565(3)	8143(2)	32.1(12)

Table 3-15 Anisotropic Displacement Parameters ($Å^2×10^3$) for 11. The Anisotropic displacement factor exponent takes the form: $-2π^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+…]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br1	38.9(3)	18.0(2)	28.9(2)	-5.8(2)	-0.2(2)	1.1(2)
O1	16.9(16)	23.2(17)	35.1(19)	8.4(14)	-1.1(13)	-3.2(13)
O2	21.1(17)	52(2)	25.7(19)	-10.3(17)	-1.9(14)	7.7(14)
O3	24.0(16)	22.4(17)	17.2(16)	-2.2(13)	-2.0(13)	0.9(13)
C1	17(2)	17(2)	17(2)	1.5(18)	3.5(17)	-0.3(17)
C2	17(2)	14(2)	17(2)	-0.8(18)	1.5(17)	-1.8(17)
C3	35(3)	17(2)	22(2)	-2.9(19)	-3.6(19)	-5.8(19)
C4	23(2)	21(2)	19(2)	-3.5(16)	-5(2)	-1(2)
C5	21(2)	17(2)	20(2)	4.1(16)	2(2)	0(2)
C6	20(2)	11(2)	18(2)	5.9(18)	-0.9(17)	1.4(17)
C7	17(2)	16(2)	20(2)	3.5(18)	2.2(17)	-0.7(16)
C8	23(2)	13(2)	28(3)	5(2)	-2(2)	-8.9(18)
C9	32(3)	12(2)	19(2)	-0.8(17)	-4.8(19)	4.2(18)

C10	17.8(19)	20(2)	18(2)	1.5(19)	-0.8(16)	1.1(19)
C11	18(2)	20(2)	22(2)	3.6(19)	-0.6(17)	-2.9(17)
C12	17(2)	10(2)	23(2)	-2.0(18)	1.9(17)	1.1(16)
C13	15(2)	14(2)	27(3)	2.1(19)	1.6(18)	3.2(17)
C14	21(2)	17(2)	25(2)	0(2)	0.3(17)	0.5(18)
C15	33(2)	12(2)	36(3)	5(2)	-4(2)	-2.2(18)
C16	35(3)	19(2)	36(3)	9(2)	4(2)	6(2)
C17	24(2)	25(3)	32(3)	4(2)	-2.6(19)	7.4(18)
C18	17(2)	18(2)	30(3)	1.3(19)	-0.5(17)	0.6(17)
C19	30(2)	15(2)	24(2)	-6(2)	1(2)	2.2(17)
C20	26(2)	20(2)	18(2)	-1(2)	2.8(19)	-0.5(19)
C21	42(3)	24(2)	26(2)	-3(2)	6(2)	3(2)
C22	41(3)	22(3)	41(3)	0(2)	2(2)	-6(2)
C23	38(3)	43(3)	15(2)	0(2)	-4(2)	-7(2)

Table 3-16 Bond Lengths for 11.

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
Br1	C9	1.909(4)	C7	C8	1.404(6)
O1	C12	1.213(5)	C8	C9	1.375(6)
O2	C19	1.204(6)	C9	C10	1.389(6)
O3	C19	1.346(6)	C10	C11	1.387(6)
O3	C20	1.483(5)	C12	C13	1.498(6)
C1	C2	1.539(6)	C13	C14	1.396(6)
C1	C5	1.530(6)	C13	C18	1.400(6)

C1	C6	1.509(6)	C14	C15	1.395(6)
C2	C3	1.571(6)	C15	C16	1.375(7)
C2	C12	1.515(6)	C16	C17	1.380(7)
C3	C4	1.545(6)	C17	C18	1.375(6)
C4	C5	1.549(6)	C20	C21	1.512(7)
C4	C19	1.512(6)	C20	C22	1.517(7)
C6	C7	1.390(6)	C20	C23	1.523(7)
C6	C11	1.390(6)			

Table 3-17 Bond Angles for 11.

Atom	**Atom**	**Atom**	**Angle/˚**	**Atom**	**Atom**	**Atom**	**Angle/˚**
C19	O3	C20	120.8(3)	C10	C11	C6	121.7(4)
C5	C1	C2	103.5(3)	O1	C12	C2	121.0(4)
C6	C1	C2	114.4(4)	O1	C12	C13	119.6(4)
C6	C1	C5	113.8(4)	C13	C12	C2	119.4(4)
C1	C2	C3	104.9(3)	C14	C13	C12	123.4(4)
C12	C2	C1	113.0(3)	C14	C13	C18	118.6(4)
C12	C2	C3	112.6(4)	C18	C13	C12	117.9(4)
C4	C3	C2	106.6(3)	C15	C14	C13	120.4(4)
C3	C4	C5	104.6(3)	C16	C15	C14	119.3(4)
C19	C4	C3	111.0(4)	C15	C16	C17	121.1(5)
C19	C4	C5	108.8(4)	C18	C17	C16	119.9(4)
C1	C5	C4	104.0(3)	C17	C18	C13	120.6(4)
C7	C6	C1	120.4(4)	O2	C19	O3	125.1(4)

C7	C6	C11	118.0(4)	O2	C19	C4	124.1(5)
C11	C6	C1	121.6(4)	O3	C19	C4	110.7(4)
C6	C7	C8	121.6(4)	O3	C20	C21	110.7(4)
C9	C8	C7	118.2(4)	O3	C20	C22	109.5(4)
C8	C9	Br1	119.6(3)	O3	C20	C23	102.1(4)
C8	C9	C10	121.8(4)	C21	C20	C22	112.1(4)
C10	C9	Br1	118.6(3)	C21	C20	C23	110.6(4)
C11	C10	C9	118.7(4)	C22	C20	C23	111.3(4)

Table 3-18 Torsion Angles for 11.

A	**B**	**C**	**D**	**Angle/˚**	**A**	**B**	**C**	**D**	**Angle/˚**
Br1	C9	C10	C11	179.5(3)	C6	C1	C2	C3	-156.6(4)
O1	C12	C13	C14	166.0(4)	C6	C1	C2	C12	80.4(5)
O1	C12	C13	C18	-16.6(6)	C6	C1	C5	C4	166.0(4)
C1	C2	C3	C4	11.3(5)	C6	C7	C8	C9	0.4(6)
C1	C2	C12	O1	18.0(6)	C7	C6	C11	C10	-0.3(6)
C1	C2	C12	C13	-161.0(4)	C7	C8	C9	Br1	-179.7(3)
C1	C6	C7	C8	-179.0(4)	C7	C8	C9	C10	-0.6(6)
C1	C6	C11	C10	178.7(4)	C8	C9	C10	C11	0.4(6)
C2	C1	C5	C4	41.3(4)	C9	C10	C11	C6	0.0(6)
C2	C1	C6	C7	-121.7(4)	C11	C6	C7	C8	0.1(6)
C2	C1	C6	C11	59.3(5)	C12	C2	C3	C4	134.6(4)
C2	C3	C4	C5	13.8(5)	C12	C13	C14	C15	178.2(4)
C2	C3	C4	C19	-103.3(4)	C12	C13	C18	C17	-177.9(4)

C2	C12	C13	C14	-15.0(6)	C13	C14	C15	C16	0.2(7)
C2	C12	C13	C18	162.4(4)	C14	C13	C18	C17	-0.4(7)
C3	C2	C12	O1	-100.6(5)	C14	C15	C16	C17	-1.7(7)
C3	C2	C12	C13	80.3(5)	C15	C16	C17	C18	2.2(7)
C3	C4	C5	C1	-34.0(5)	C16	C17	C18	C13	-1.1(7)
C3	C4	C19	O2	36.4(6)	C18	C13	C14	C15	0.8(7)
C3	C4	C19	O3	-146.3(4)	C19	O3	C20	C21	-55.0(5)
C5	C1	C2	C3	-32.2(4)	C19	O3	C20	C22	69.1(5)
C5	C1	C2	C12	-155.2(3)	C19	O3	C20	C23	-172.8(4)
C5	C1	C6	C7	119.6(4)	C19	C4	C5	C1	84.6(4)
C5	C1	C6	C11	-59.4(5)	C20	O3	C19	O2	0.6(7)
C5	C4	C19	O2	-78.1(5)	C20	O3	C19	C4	-176.7(3)
C5	C4	C19	O3	99.2(4)					

Table 3-19 Hydrogen Atom Coordinates (Å×10^{4}) and Isotropic Displacement Parameters (Å^{2}×10^{3}) for 11.

Atom	***x***	***y***	***z***	**U(eq)**
H1	6756	4650	5463	20
H2	9820	5513	4653	19
H3A	10518	6462	5357	29
H3B	7807	6463	5587	29
H4	11400	5801	6224	25
H5A	11837	4684	5609	24
H5B	9930	4345	6092	24
H7	5526	3480	5009	21

H8	6039	2375	4360	26
H10	12558	3211	3898	22
H11	11996	4305	4541	24
H14	9510	6887	4349	25
H15	9451	7837	3563	33
H16	6178	7917	2922	36
H17	3054	7020	3016	33
H18	3061	6087	3798	26
H21A	6253	6656	7562	46
H21B	4608	6150	8014	46
H21C	4289	6065	7291	46
H22A	5276	4577	8009	52
H22B	7277	4250	7555	52
H22C	4896	4635	7287	52
H23A	8112	5529	8530	48
H23B	9771	6083	8116	48
H23C	10162	5138	8123	48

3.5 References

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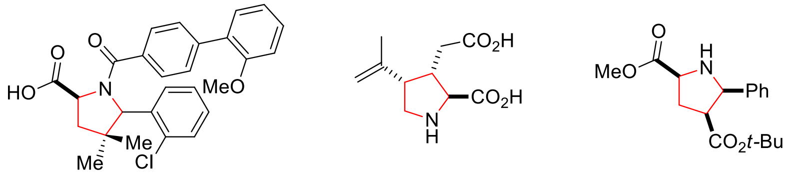
Chapter 4. Development of a Redox Auxiliary Strategy for [3 + 2] Cycloadditions with Visible Light Photocatalysis

4.1 Introduction

Figure 4-1. Bioactive pyrrolidine containing compounds



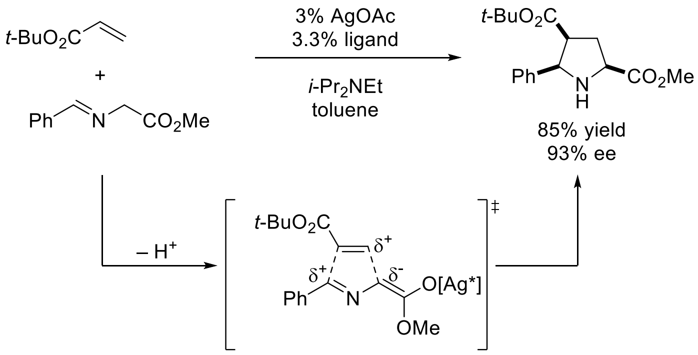
GPR43 agonist
Treatment of inflammatory diseases

(-)-kainic acid
Potent neuroexcitatory aminoacid

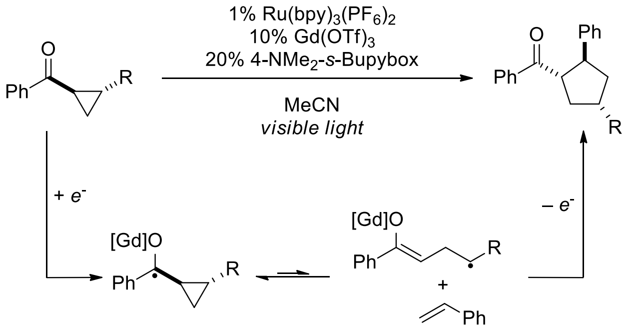
Antiproliferative effect against HRPC PC-3 cell line

Saturated five-membered rings such as pyrrolidines, tetrahydrofurans, and cyclopentanes are structural motifs found in a significant number of natural products and compounds of biological interest.[1–3] In pursuit of efficient synthetic routes to these motifs, [3 + 2] cycloadditions have proven to be an invaluable strategy. In particular, 1,3-dipolar cycloadditions have seen considerable development over the last several decades, including several stereoselective methodologies (Scheme 4-1).[4–11] While 1,3-dipoles and 1,3-dipole surrogates have provided a diverse set of building blocks for the rapid construction of five-membered rings, these strategies have some inherent disadvantages due to the polar nature of the intermediates. Foremost among these limitations are strict electronic requirements to access the zwitterionic dipolar intermediate. Furthermore, the coupling partner must be electronically matched to achieve appreciable reactivity.

Scheme 4-1. 1,3-Dipolar cycloaddition with azomethine ylides



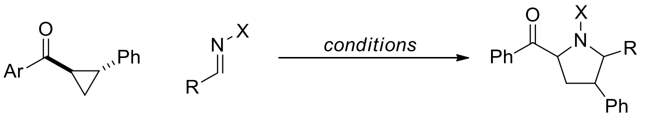
Scheme 4-2. Photocatalytic intermolecular [3 + 2] cycloadditions with olefins



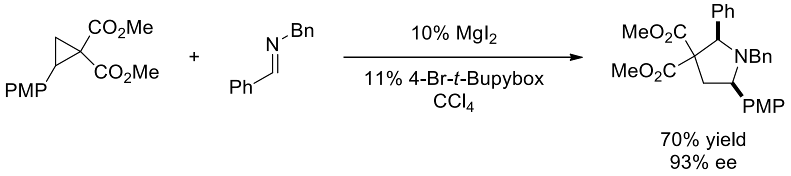
Our laboratory recently reported dual catalytic racemic and enantioselective intermolecular [3 + 2] cycloadditions between aryl cyclopropyl ketones and olefins (Scheme 4-2).[12] These cycloadditions proceed through photocatalytic one-electron reduction of a Lewis acid activated cyclopropyl ketone under visible light irradiation. The active intermediate is formed upon rearrangement of the ketyl radical anion to a distonic radical anion. This [3 + 2] cycloaddition provides a complementary approach towards the synthesis of five-membered carbocycles and is characterized by a large scope of both electron-deficient and electron-rich reaction partners.

We became interested in extending this methodology for [3 + 2] cycloadditions with imine derivatives to access pyrrolidine products (Scheme 4-3). We hypothesized that this approach would provide a novel and complementary approach to existing strategies for pyrrolidine synthesis. While strategies exist for the synthesis of pyrrolidines using donor-acceptor cyclopropanes, a radical pathway is expected to give complementary regiochemistry and a more general substrate scope (Scheme 4-4).[13]

Scheme 4-3. Proposed photocatalytic [3 + 2] cycloaddition for pyrrolidine synthesis



Scheme 4-4. [3 + 2] cycloadditions of donor-acceptor cyclopropanes with imines[9]

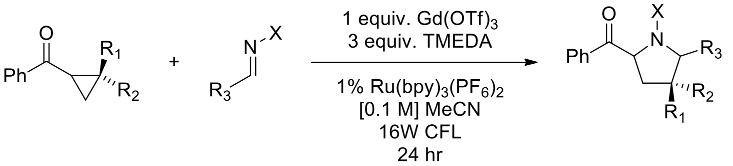


4.2 Results and Discussion

4.2.1 Preliminary results for [3 + 2] cycloadditions with imine derivatives

Our investigations began with the racemic conditions described in Chapter 2 (Table 4-1). These conditions include a full equivalent of $Gd(OTf)_3$ as Lewis acid, 3 equiv. of TMEDA as reductive quencher, and $Ru(bpy)_3(PF_6)_2$ as photocatalyst. Disappointingly, a preliminary screen with these conditions between a range of different cyclopropanes and imine derivatives provided no productive reactivity (see Experimental section, Table 4-9 for further information).

Table 4-1. Preliminary screen under racemic conditions

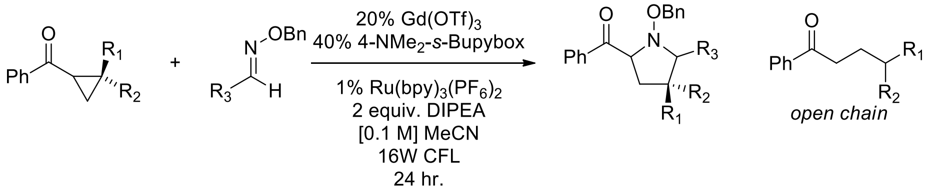


Entry	$-R_1, R_2$	$-R_3$	−X	% yield[a]	% RSM
1	−Me, Me (**4-1**)	−Ph	−OMe	0%	80%
2	−Me, Me (**4-1**)	−Ph	−Ts	0%	100%
3	$-CO_2Et$, H (**4-2**)	−Ph	−OMe	0%	100%
4	−Me, Me (**4-1**)	−H	−OBn	0%	100%
5	$-CO_2Et$, H (**4-2**)	−H	−OBn	0%	100%
6	−Ph, H (**4-3**)	−H	−OBn	0%	100%

[a] Yields determined by ^1H NMR using phenanthrene as internal standard

A second screen using our asymmetric photocatalytic [3 + 2] cycloaddition conditions provided more promising results (Table 4-2). These conditions used a 20% loading of $Gd(OTf)_3$, 40% 4-NMe_2-*s*-Bupybox, 2 equiv. *i*-Pr_2NEt, and 1% $Ru(bpy)_3(PF_6)_2$. To our delight, a geminally

Table 4-2. Preliminary screen under asymmetric conditions



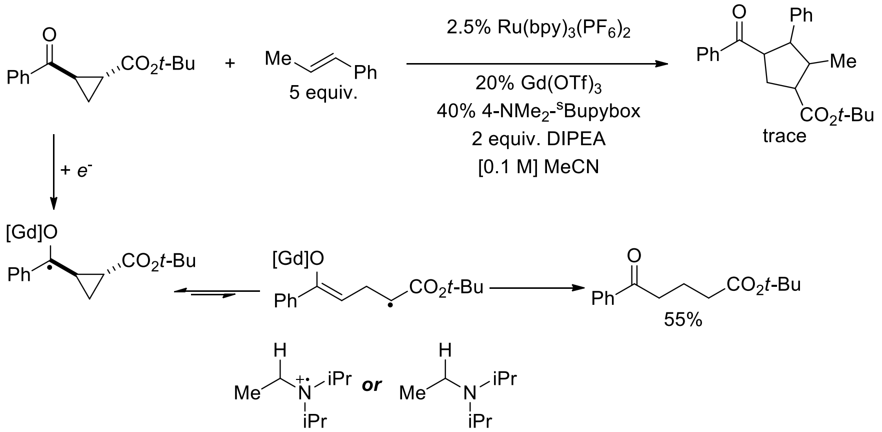
Entry	$–R_1, R_2$	$–R_3$	% yield[a]	% RSM	%open chain
1	–Me, Me (**4-1**)	–H	53%	21%	0%
2	$–CO_2Et$, H (**4-2**)	–H	25%	35%	20%
3	–Me, Me (**4-1**)	–Ph	0%	82%	0%
4	–Ph, H (**4-3**)	–H, H,	0%	90%	0%

[a] Yields determined by ^1H NMR using phenanthrene as internal standard

dimethyl-substituted cyclopropane underwent the desired [3 + 2] cycloaddition with a formaldehyde-derived oxime ether in 53% yield (Table 4-2, entry 1). A quick survey of other cyclopropanes and imine derivatives, however, revealed significant limitations in the scope of this reaction.

We propose that one critical obstacle towards expanding the scope of the photocatalytic [3 + 2] cycloaddition reaction is the propensity of the key electrophilic distonic radical anion intermediate to undergo competitive hydrogen-atom abstraction from the tertiary amine quencher present in solution. Indeed, this competitive reaction pathway was one of the major factors limiting the substrate scope described in the previous two chapters; for less activated

Figure 4-2. Competitive reaction pathways for electrophilic cyclopropylketones

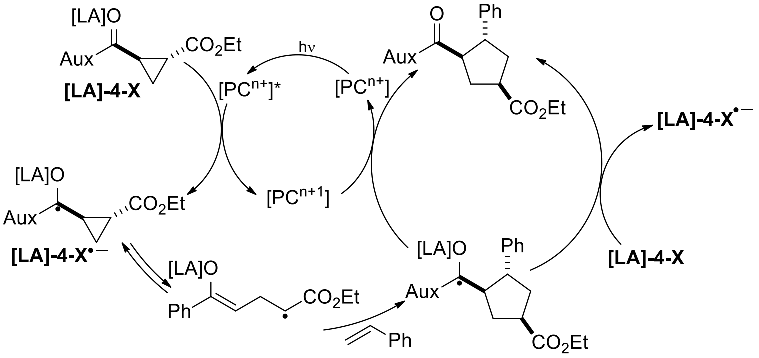


coupling partners (e.g. internal olefins and simple non-conjugated olefins), this undesired reductive ring-opening process becomes the predominant reaction pathway and only trace amounts of desired [3 + 2] cycloadduct are formed (Figure 4-2). Additionally, tertiary amines can also act as ligands to Lewis acids, including the lanthanoid Lewis acids that have been optimal in our studies. This acid-base interaction can decrease the Lewis acidity of the co-catalyst and thus inhibit productive reactivity.

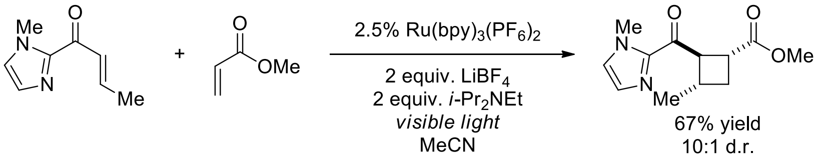
For these reasons, we hypothesized that a more general system might be possible by designing a reaction that proceeds in the absence of an exogenous amine as a reductive quencher. The addition of the amine in the photoreductive methods that we have developed to date is a strict requirement because reductive quenching provides access to a sufficiently reducing oxidation state of the catalyst for reduction of the aryl cyclopropyl ketone. We reasoned that the need for the amine might be circumvented by (1) utilizing a substrate with a more positive reduction potential than phenyl cyclopropyl ketones, and by (2) employing a photocatalyst with an intrinsically more negative excited state reduction potential than $Ru(bpy)_3^{2+}$.

The mechanism that we envisioned is shown in Figure 4-3. Absorption of visible light by the photocatalyst (**PC^{n+}**) would provide the excited state of the photocatalyst (**PC^{n+}***) which would reduce the cyclopropane–Lewis acid complex (**[LA]-4-X**) to give the ketyl radical anion. The ketyl radical anion can then rearrange to the distonic radical anion which will undergo a

Figure 4-3. Proposed mechanism for [3 + 2] cycloaddition in absence of reductive quencher



Scheme 4-5. Photocatalytic [2 + 2] cycloaddition using a cleavable redox auxiliary

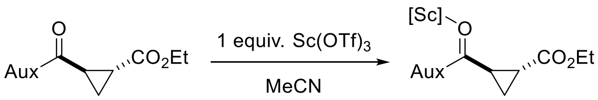


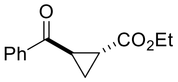
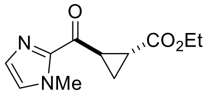
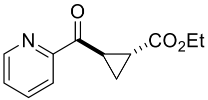
stepwise [3 + 2] cycloaddition with an unsaturated coupling partner (e.g. styrene) to give the radical anion of the product. The neutral product would be formed either through oxidation by **PC^{n+1}** to regenerate the photocatalyst or through radical chain propagation.[14] The results of our successful investigations are described in the following sections.

4.2.2 Design of a redox auxiliary strategy

Our laboratory recently proposed the concept of a "redox auxiliary," which we defined as a cleavable moiety that is temporarily installed onto a substrate to facilitate one-electron redox activation. The initial demonstration of the utility of this concept was in the design of a photocatalytic [2 + 2] enone cycloaddition (Scheme 4-5), and we hypothesized that this strategy might also prove to be enabling in the context of a [3 + 2] cycloaddition as well.[15] In particular,

Table 4-3. Electrochemical studies of redox auxiliaries



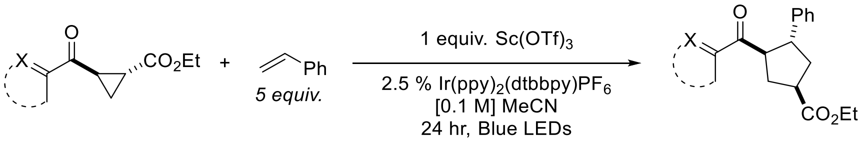
Auxiliary	$E_{p/2}$ (V) (w/o Sc(OTf)$_3$)[a]	$E_{p/2}$ (V) (w/ 1 equiv. Sc(OTf)$_3$)[a]	$\Delta E_{p/2}$ (V)
 Phenyl **4-2**	-1.88 V	-1.02 V	0.86 V
 2-imidazolyl **4-4**	-1.95 V	-0.85 V	1.1 V
 2-pyridyl **4-5**	-1.7 V	-0.50 V	1.2 V

[a] 1 mM concentration of substrate in MeCN, versus SCE, referenced against ferrocene.

we hypothesized that cyclopropyl heteroaryl ketones with additional coordination sites might exhibit a much more pronounced modulation in reductive potential when bound to a Lewis acid.

To test this hypothesis, we performed a series of electrochemical studies in the presence and absence of an added Lewis acid for three (hetero)arylcyclopropanes (Table 4-3). In all cases, an irreversible reduction was observed in the absence of Lewis acid. An approximate $E_{p/2}$ was determined using the method described by Nicewicz and coworkers.[16] The reduction potentials of the substrates in the absence of Lewis acid trend as expected: the most electron-rich auxiliary (2-imidazolyl) is the hardest to reduce, and the most electron-deficient (2-pyridyl) is the easiest to reduce. After addition of 1 equiv of $Sc(OTf)_3$, new features were observed in each voltammogram. As predicted, the apparent reduction potentials of the heteroaromatic auxiliaries were increased to significantly more positive reduction potentials than the phenyl auxiliary (See experimental information for voltammograms). Encouragingly, these potentials were within the range of the excited state reduction potential of many heteroleptic and homoleptic iridium photocatalysts.[17]

Table 4-4. [3 + 2] cycloadditions of cyclopropane derivatives in absence of quencher

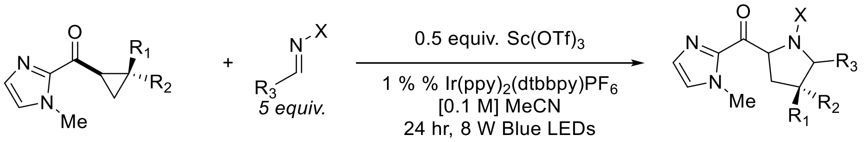


Auxiliary	$E_{p/2}$[a]	% yield[b]	d.r.	% RSM
Phenyl (**4-2**)	-1.02 V	0 %	---	100 %
2-imidazolyl (**4-4**)	-0.85 V	88 %	2:1	0 %
2-pyridyl (**4-5**)	-0.50 V	70 %	1:1	13 %

[a] Versus SCE. [b] ^{1}H NMR yield using phenanthrene as internal standard.

As a probe of the efficacy of these heteroaryl ketones in photoreductive applications, we first tested each cyclopropane in a model [3 + 2] cycloaddition with styrene using $Ir(ppy)_2(dtbbpy)PF_6$ ($E_0(PC^+/PC^*) = -1.00$ V vs. SCE) as photocatalyst and 1 equivalent of $Sc(OTf)_3$ as Lewis acid (Table 4-4). Consistent with our electrochemical studies only the 2-imidazolyl and 2-pyridyl cyclopropyl ketones gave appreciable reactivity in the absence of reductive quencher.

Table 4-5. [3 + 2] cycloadditions of imidazolylcyclopropyl ketones with oxime ethers



Entry	$-R_1$, R_2	$-R_3$	$-X$	% yield[a]	% RSM
1	$-CO_2Et$, H (**4-4**)	–H	–OBn	75 %	23 %
2	$-CO_2Et$, H (**4-4**)	$-CO_2Et$	–OBn	45 %	50 %
3	–Ph, H (**4-6**)	–H	–OBn	22 %	15 %
4[b]	–Ph, H (**4-6**)	$-CO_2Et$	–OMe	28 %	65 %

[a] Yields determined by ^1H NMR spectroscopy using phenanthrene as internal standard. [b] Reaction carried out for 20 hours.

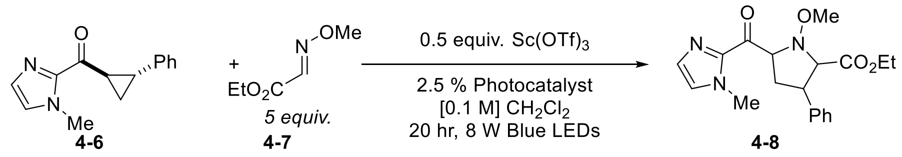
Encouragingly, the most successful substrate proved to be the 2-imidazolyl ketone, which also provides access to products bearing an excellent synthetic handle for further derivatization.[18,19]

With these results in hand, we returned to the original goal of developing a method for [3 + 2] cycloadditions with imine coupling partners (Table 4-5). A series of 2-imidazolyl cyclopropyl ketones were tested across a selection of oxime ethers. We observed that both electron-withdrawing (e.g. ester) and electron-donating (e.g. phenyl) substituents on the cyclopropane provided promising reactivity with formaldehyde and glyoxylate derived oxime ethers. We were particularly encouraged by the promising reactivity using phenyl-substituted cyclopropanes (Table 4-5, Entries 3 and 4) because these substrates had not proven to be successful under our previous conditions (Table 4-2, Entry 4). These results suggested, therefore, that the amine-free conditions might indeed offer the opportunity of a much wider substrate scope. As expected, reductive ring-opening by-products were not observed in any of these experiments.

4.2.3 Optimization of the reaction conditions

Having identified an optimal redox auxiliary structure, we turned our attention to optimization of the remaining variables. Because the substrate is interacting directly with the relatively short-lived excited state of the photocatalyst in the proposed mechanism, we predicted that the identity of the photocatalyst should have a significant effect on the rate of substrate

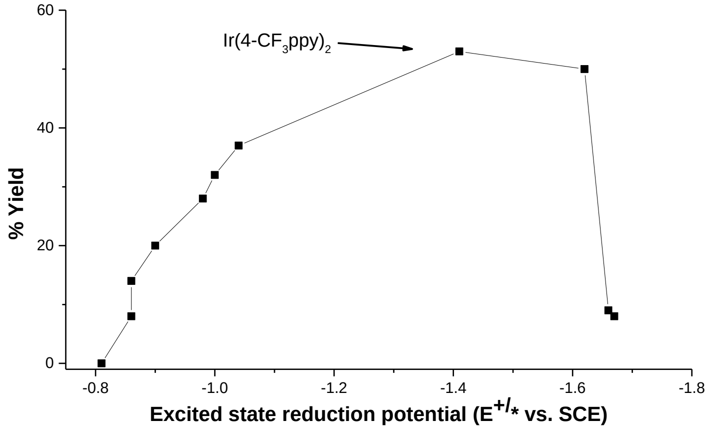
Table 4-6. Photocatalyst optimization



Entry	Photocatalyst	E_0 (PC^{n+1}/PC^{n*})[a]	E_0 (PC^{n+1}/PC^{n})	% yield[b]	% RSM
1	$Ru(bpy)_3(PF_6)_2$	-0.81 V	1.29 V	0%	100%
2	$Ir(dF(CF_3)ppy)_2dtbbpyPF_6$	-0.86 V	1.72 V	8%	90%
3	Ir(dF(*t*-Bu)ppy)$_2$(dtbbpy)PF$_6$	-0.86 V	1.54 V	14%	85%
4	$Ir(Fppy)_2(dtbbpy)PF_6$	-0.90 V	1.40 V	20%	75%
5	$Ir(ppy)_2(dtbbpy)PF_6$	-0.98 V	1.23 V	28%	56%
6	$Ir(ppy)_2(dMeObpy)PF_6$	-1.00 V	1.21 V	32%	54%
8	$Ir(dtbppy)_2(dtbbpy)PF_6$	-1.04 V	1.13 V	37%	65%
9	$Ir(4\text{-}CF_3ppy)_3$	-1.41 V	1.04 V	53%	39%
10	$Ir(dFppy)_3$	-1.62 V	0.98 V	50%	44%
11	Ir(3-*t*-Buppy)$_3$	-1.66 V	0.70 V	9%	88%
12	$Ir(ppy)_3$	-1.67 V	0.72 V	8%	98%

[a] Versus SCE reference electrode. [b] Yields determined by ^1H NMR using phenanthrene as internal standard.

Figure 4-4. Plot of excited state reduction potential vs. % yield of cycloadduct

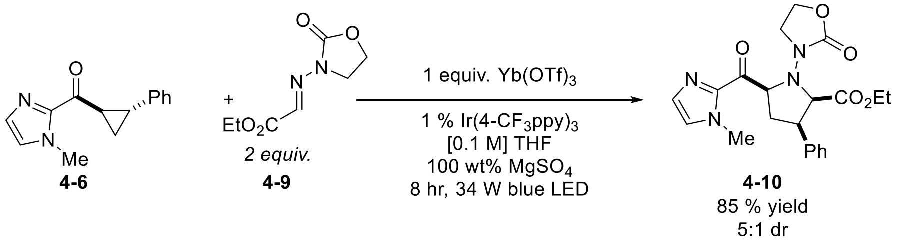


reduction relative to back electron transfer to the photocatalyst and thus the overall reaction rate. A series of twelve photocatalyst derivatives were prepared and tested in the [3 + 2] cycloaddition between cyclopropane **4-6** and oxime either **4-7** (Table 4-6). As expected, we observed a clear relationship between reaction rate and excited state reduction potential of the photocatalyst (Figure 4-4).

Interestingly, the reaction rate is much slower for the most reducing homoleptic iridium photocatalysts (Entries 11 and 12). A plausible explanation for this dropoff in reaction rate is that these two photocatalysts have a much-decreased reduction potential (**PC^{n+1}/PC^{n}**). For less oxidizing photocatalysts the rate limiting step of the catalytic cycle may in fact be regeneration of the photocatalyst due to increased stabilization of the Ir(IV) oxidation state. However, we can't rule out that these photocatalysts simply have less favorable photophysical properties. Stern-Volmer and excited state lifetime measurements would be required for a more detailed understanding of this trend.

Finally, the results of optimization studies using the Ir(4-CF_3ppy)$_3$ catalyst identified in Table 4-6 are shown in Table 4-7. The identity of the N-protecting group and Lewis acid were found to have a substantial effect on the efficiency and diastereoselectivity of the transformation. Hydrazone **4-9** was a more efficient coupling partner than the analogous oxime ether, though a decrease in diastereoselectivity was observed. Using Yb(OTf)$_3$ as a Lewis acid instead of Sc(OTf)$_3$ provided an increase in diastereoselectivity (Entry 6). Further improvements in

Table 4-7. Final optimization of the reaction conditions

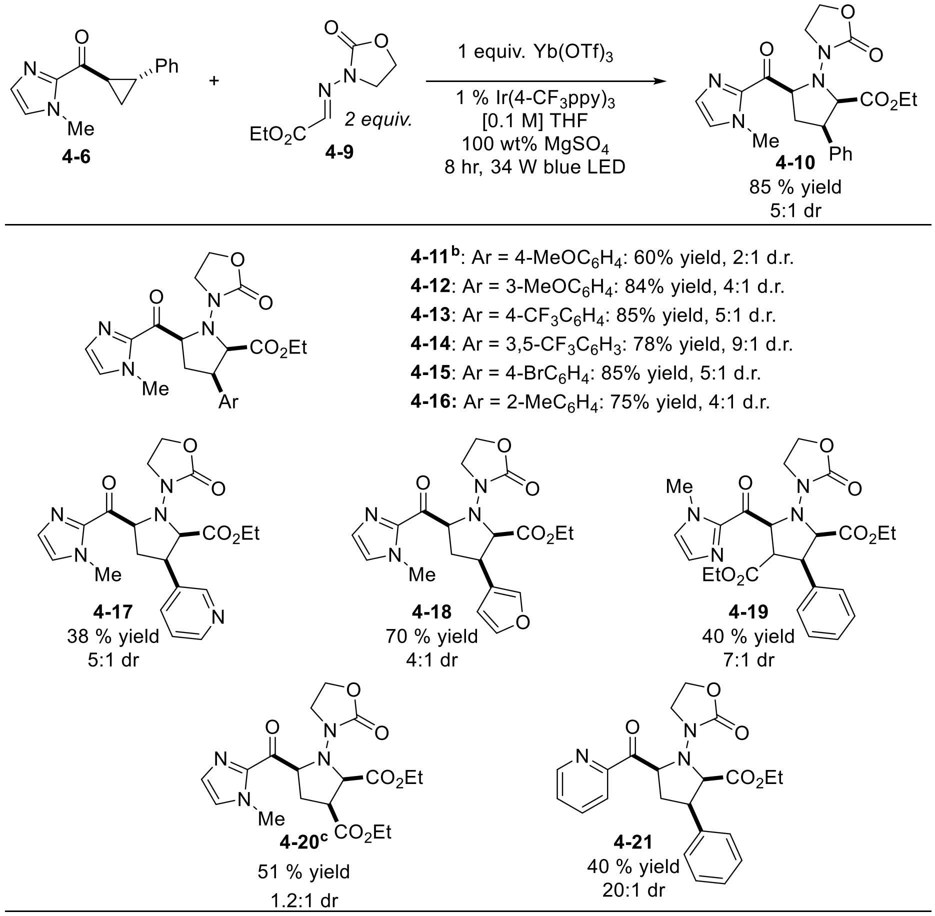


Entry	Change from standard conditions	% yield[a]	d.r.	% RSM
1[b]	none	85%	5:1	0%
2[c]	1.1 equiv. **4-9**	75%	3.4:1	10%
3[d]	1.1 equiv. **4-9**	51%	3.4:1	47%
4[d]	1.1 equiv. **4-9**, no $MgSO_4$	46%	3:1	54%
5[d]	1.1 equiv. **4-9**, 0.5 equiv. Yb(OTf)$_3$, no $MgSO_4$	47%	2.5:1	50%
6[d]	1.1 equiv. **4-9**, 0.5 equiv Yb(OTf)$_3$, CH_2Cl_2, no $MgSO_4$	56%	2:1	40%
7[d]	1.1 equiv. **4-9**, 0.5 equiv. Sc(OTf)$_3$, CH_2Cl_2, no $MgSO_4$	62%	1:1	36%
8[d]	1.1 equiv. **4-9**, 0.1 equiv Yb(OTf)$_3$	45%	2.5:1	30%

[a] Yields determined by ^1H NMR using phenanthrene an internal standard. [b] Isolated yield on 0.4 mmol scale of **4-6**. [c] 0.04 mmol scale, 3 hours reaction time. [d] Using an 18W white LED, 0.04 mmol scale, 5 hr reaction time.

diastereoselectivity were seen by performing the reaction in THF instead of CH_2Cl_2 and with a higher loading of $Yb(OTf)_3$ (Entries 5 and 4 respectively). Further improvements in rate and selectivity were observed upon the addition of a desiccant ($MgSO_4$) and using a more intense light source (Entries 3 and 2 respectively). Finally, there was an unexpected increase in d.r. at higher loadings of hydrazone to provide cycloadduct **4-10** in 85% yield and 5:1 d.r. after 8 hours (Entry 1). A series of control studies showed the requirement of all reaction components for productive reactivity (Table 4-18, experimental information). See the experimental information for more detailed data on the reaction optimization.

Figure 4-5. Cyclopropane substrate scope



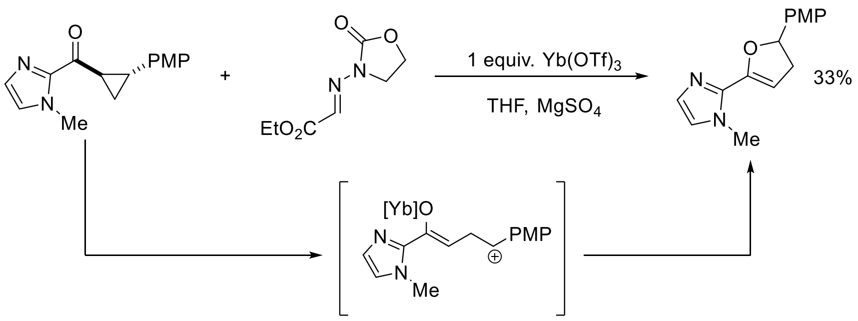
4-11[b]: Ar = 4-$MeOC_6H_4$: 60% yield, 2:1 d.r.
4-12: Ar = 3-$MeOC_6H_4$: 84% yield, 4:1 d.r.
4-13: Ar = 4-$CF_3C_6H_4$: 85% yield, 5:1 d.r.
4-14: Ar = 3,5-$CF_3C_6H_3$: 78% yield, 9:1 d.r.
4-15: Ar = 4-BrC_6H_4: 85% yield, 5:1 d.r.
4-16: Ar = 2-MeC_6H_4: 75% yield, 4:1 d.r.

[a] Isolated yields on 0.4 mmol scale of cyclopropane. Diastereomeric ratio determined by ^1H NMR analysis of crude product. Relative stereochemistry of **4-10** determined by X-ray crystallographic analysis. Stereochemistry of other products assigned by analogy. [b] Reaction carried out with 0.3 equiv. $Yb(OTf)_3$. [c] Reaction carried out with 0.5 equiv. of $Sc(OTf)_3$ instead of $Yb(OTf)_3$.

4.2.4 Exploration of the substrate scope

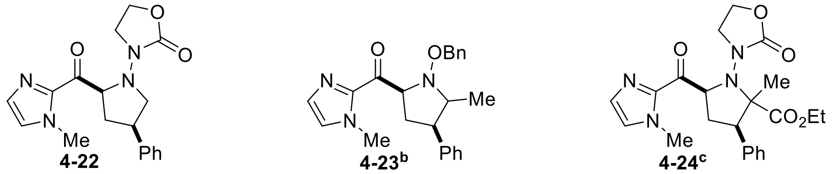
With the optimal conditions in hand, we turned our attention to an exploration of the substrate scope (Figure 4-5). The scope with respect to the ß-aryl substituent was relatively general. Electron rich aryl rings were well tolerated in good yields and modest diastereoselectivities (**4-11** and **4-12**). However, the Yb(OTf)$_3$ loading was decreased for the *p*-methoxy-aryl cyclopropane to slow down competitive heterolytic cleavage of the cyclopropane ring (Scheme 4-6). Very electron-deficient aryl rings were also well tolerated in good yields and good to excellent diastereoselectivities (**4-13** and **4-14**). A potentially reactive aryl bromide was an excellent substrate under these conditions, and placing steric bulk in the ortho-position of the aromatic ring was also well tolerated (**4-15** and **4-16** respectively). Both electron-deficient and electron-rich heteroaryl-substituted cyclopropanes were viable substrates, though Lewis basic substitutions such as pyridine rings provide reduced yields (**4-17** and **4-18**). Trisubstituted cyclopropanes exhibited excellent regioselectivity and good diastereoselectivities under these conditions, although the reactivity was relatively sluggish (**4-19**). A more electron-deficient cyclopropane derivative with an ester substituent was also a viable substrate in this transformation (**4-20**). This result highlights the generality that can be accessed by exploiting radical intermediates: both electron-withdrawing and electron-donating substituents are well tolerated. As suggested by our earlier experiments while exploring redox auxiliaries, a 2-pyridyl cyclopropyl ketone also shows productive reactivity in this transformation (**4-21**).

Scheme 4-6. Heterolytic of electron-rich cyclopropane with full equivalent of Yb(OTf)$_3$



The substrate scope for imine derivatives proved to be significantly more limited (Figure 4-6). A formaldehyde derived hydrazone was an excellent substrate under these conditions (**4-22**). Acetaldehyde-derived hydrazones produced intractable mixtures of products; however, the benzyl oxime ether derived from acetaldehyde was an excellent coupling partner in this transformation and afforded modest yields and high diastereoselectivities (**4-23**). A ketimine derived from ethyl pyruvate showed productive reactivity to generate a quaternary stereocenter, although the rate of this reaction was significantly diminished (**4-24**).

Figure 4-6. Imine derivative substrate scope



4-22
70 % yield
5:1 dr

4-23[b]
60 % yield
10:1 dr

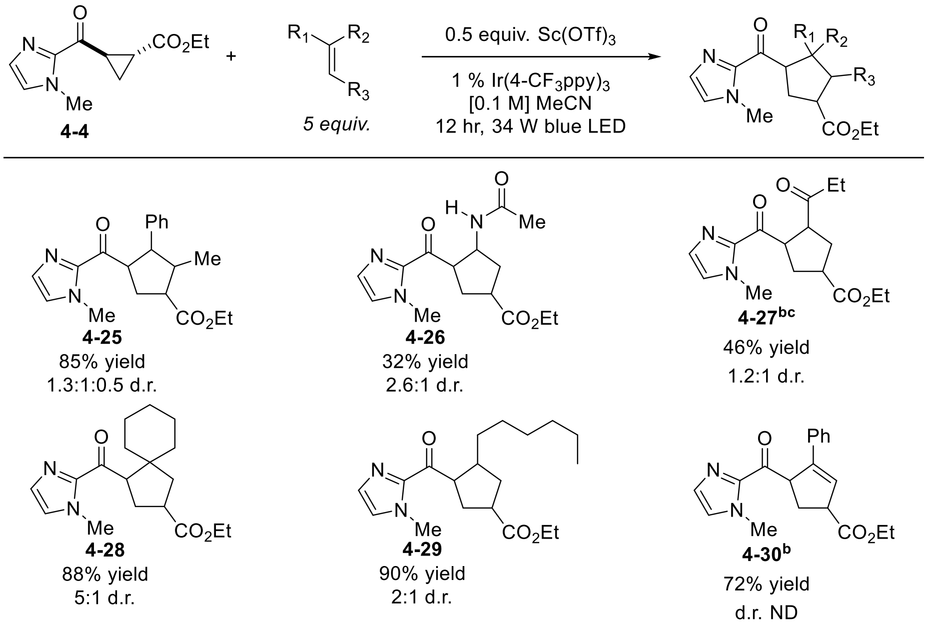
4-24[c]
31 % yield
>10:1 dr

[a] Isolated yields on 0.4 mmol scale of cyclopropane. Diastereomeric ratio determined by ^{1}H NMR analysis of crude product. Relative stereochemistry of **4-10** determined by X-ray crystallographic analysis. Stereochemistry of other products assigned by analogy. [b] Reaction carried out with 0.5 equiv. Sc(OTf)$_3$. [c] Reaction carried out for 72 hours, 65 % RSM.

4.2.5 Preliminary exploration of simple and unactivated olefins

Encouraged by the increased generality observed in the absence of reductive quencher, we have begun to explore the scope using less activated olefins that were unsuccessful under our original conditions (Figure 4-7). We were delighted to observe that the redox auxiliary strategy provides excellent yields of cycloadduct between cyclopropane **4-4** and ß-methylstyrene, a coupling partner that gave only trace product under our previous conditions (**4-25**). Productive reactivity was also observed with the electron-rich *N*-vinylacetamide as well as electron-deficient ethylvinylketone (**4-26** and **4-27** respectively). Simple olefins such as methylenecyclohexane and 1-octene were also excellent coupling partners in the [3 + 2] cycloaddition despite the absence of strongly radical-stabilizing substituents (**4-28** and **4-29** respectively). Phenylacetylene was also an excellent coupling partner in this transformation providing the cyclopentene cycloadduct **4-30** in 72% yield.

Figure 4-7. Preliminary substrate scope with simple and unactivated coupling partners



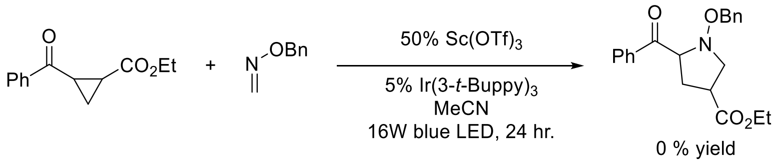
[a] ^{1}H NMR yields unless otherwise indicated. Diastereomeric ratio determined by ^{1}H NMR analysis of crude product. [b] With Niecia Flikweert
[c] Isolated yield on 0.4 mmol scale.

4.2.6 Future work

There remains several aspects of this chemistry to be explored. Regarding the mechanism of this transformation: more detailed investigations will be required to gain deeper insights into the success of heteroaryl redox auxiliaries. These auxiliaries are substantially easier to reduce in the presence of a Lewis acid. However, more reducing photocatalysts do not allow for productive reactivity for phenyl cyclopropyl ketones despite a thermodynamically favorable electron-transfer (Scheme 4-7). This indicates that reduction potential may not be the only important factor for consideration.

Additional synthetic work involves the development of a stereoselective variant of this reaction. The identity of the nitrogen-protecting group raises the possibility for the incorporation of a chiral auxiliary for a stereocontrolled [3 + 2] cycloaddition to provided enantioenriched pyrrolidine products. The presence of a Lewis acid in the reaction conditions also raises the question of stereocontrol through incorporation of a chiral ligand. Other future synthetic work involves the elaboration of cycloadducts through the cleavage of the redox auxiliary and the nitrogen protecting group.

Scheme 4-7. Phenylcyclopropylketone with more reducing photocatalyst



4.3 Conclusions

This investigation has led to the development of a significantly more general radical [3 + 2] cycloaddition than what has been reported previously in the literature. Key to its success was the design of redox auxiliary system which obviates the need for a reductive quencher and allows for favorable direct reduction of substrates from the excited state of the photocatalyst. While [3 + 2] cycloadditions with activated conjugated terminal olefins are high yielding in the presence of reductive quenchers such as tertiary amines, undesirable side-reactions such as hydrogen atom transfer (HAT) begin to dominate with less reactive coupling partners. It was found that the reduction potentials of ketones substituted with chelating heteroaromatic moieties are modulated by over a volt in the presence of strong Lewis acids such as $Sc(OTf)_3$. By tuning the excited state properties of the transition metal photocatalyst a novel and very efficient [3 + 2] cycloaddition between arylcyclopropylketones and imine derivatives has been developed. This methodology is complementary to existing methods in the literature and has a very broad scope with respect to the electronics of each of the coupling partners. Additionally, this redox auxiliary strategy has allowed for [3 + 2] cycloadditions with less activated olefins in good yields. Investigations into the substrate scope for this transformation continue.

4.4 Experimental Information

4.4.1 General information

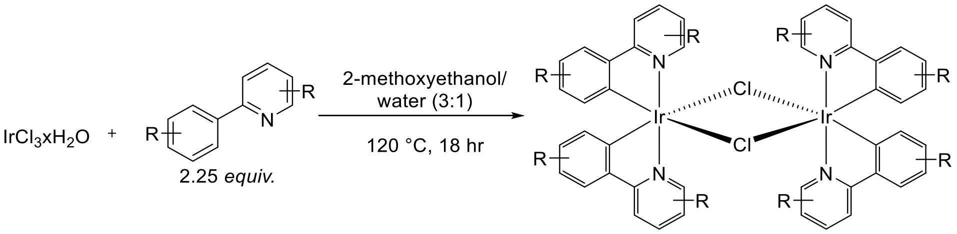
MeCN, THF, and CH_2Cl_2 were purified by elution through alumina as described by Grubbs.[1] A 34W blue LED lamp (H-150 blue) manufactured by Kessil was used for all isolation scale experiments. Lewis acids were purchased from Strem, stored in a glove box, and used without further purification. Flash column chromatography was performed with Silicycle 40-63A silica (230-400 mesh). Styrene, diisopropylethylamine, *N,N,N',N'*-tetramethylethylenediamine, and DABCO were purchased from Sigma Aldrich and subsequently purified either by distillation or recrystallization. All glassware was oven-dried at 130 °C overnight or flame-dried immediately prior to use.

^1H and $^{13}C\{H\}$ NMR data for all previously uncharacterized compounds were obtained using a Bruker 500 MHz spectrometer and are referenced to TMS (0.0 ppm) and $CDCl_3$ (77.0 ppm), respectively. IR spectral data were obtained using a Bruker Vector 22 spectrometer. Melting points were obtained using a Mel-Temp II (Laboratory Devices, Inc., USA) melting point apparatus. Mass spectrometry was performed with a Micromass LCT (electrospray ionization, time-of-flight analyzer or electron impact). These facilities are funded by the NSF (CHE-9974839, CHE-9304546) and the University of Wisconsin.

4.4.2 Photocatalyst synthesis and characterization

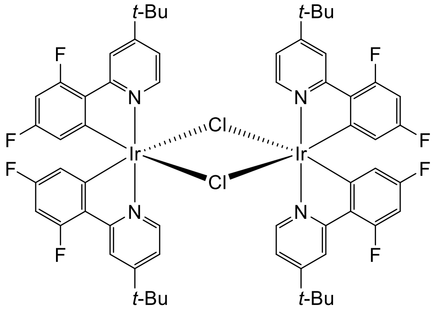
$Ru(bpy)_3(PF_6)_2$ was prepared as described previously by Wrighton, all spectral data match those reported previously.[20] $Ir(dF(CF_3)ppy)_2dtbbpyPF_6$, $Ir(Fppy)_2(dtbbpy)PF_6$, $Ir(ppy)_2(dtbbpy)PF_6$, Ir(3-*t*-Buppy)$_3$, and $Ir(ppy)_3$ were all prepared as described previously by Weaver and coworkers, all spectral data match those reported previously.[17] $Ir(4\text{-}CF_3ppy)_3$ and $Ir(dFppy)_3$, were prepared as described below, spectral data match those reported previously in the literature.

General procedure for synthesis of chloro-bridged iridium dimers:



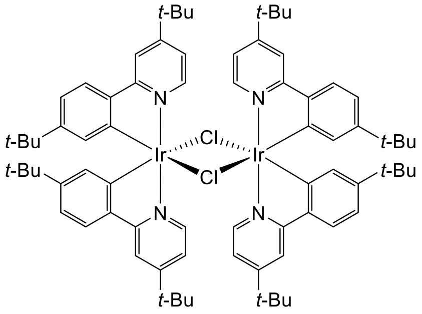
Complexes were synthesized using the general procedure described by Weaver and coworkers.[17] A three-necked round bottom flask equipped with a reflux condenser was charged with iridium(III) chloride (1 equiv.), phenylpyridine ligand (2.25 equiv.) and a 2:1 mixture of 2-methoxyethanol/water (0.02 M). The flask was sparged for 15 minutes under a flow of N_2(g) and then heated at 120 °C for 18 hours. After this time the reaction mixture was cooled to room temperature where precipitation of the iridium dimer was observed. If precipitation does not occur additional water can be added. The mixture as then filtered and the precipitate washed with water and dried and air. Dimers were carried on without additional purification.

tetrakis-(3,5-difluoro-2-(5-*t*-butyl-pyridin-2-yl)phenyl)diiridium(III) dichloride (4-31):

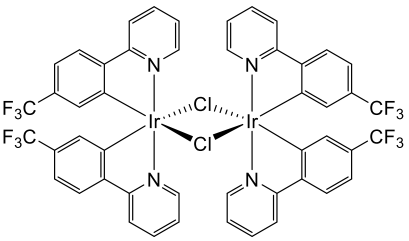


Prepared using the general procedure with $IrCl_3$ (208.6 mg, 0.7 mmol), 2-(2,4-difluorophenyl)-5-*t*-butylpyridine (364 mg, 1.47 mmol), 2-ethoxyethanol (9 mL), and H_2O (3 mL). Provided product as a yellow powder of sufficient purity for the next step (343 mg, 68 % yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.07 (d, *J* = 6.2 Hz, 1H), 8.35 (t, *J* = 2.7 Hz, 1H), 6.89 (dd, *J* = 6.2, 2.2 Hz, 1H), 6.46 – 6.21 (m, 1H), 5.18 (dd, *J* = 9.2, 2.4 Hz, 1H), 1.53 (s, 9H).

Tetrakis-(2-(4-*t*-butyl-pyridin-2-yl)-5-*t*-butylphenyl)diiridium(III) dichloride (4-32):

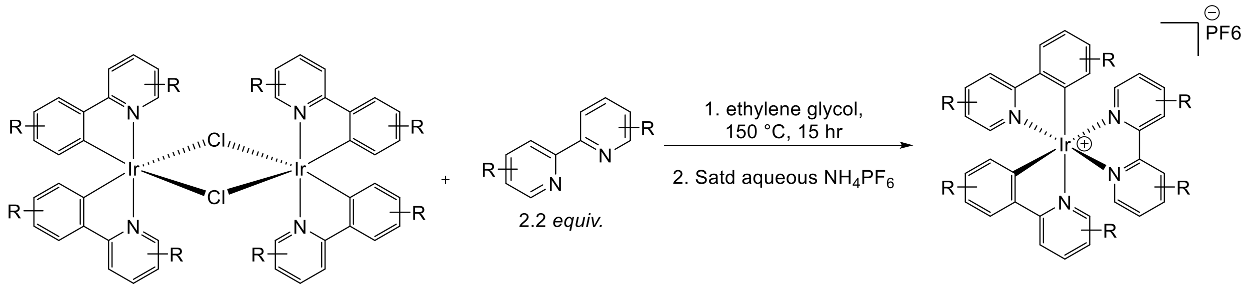


Prepared using the general procedure with $IrCl_3$ (0.28 g, 0.938 mmol), 4-(*t*-butyl)-2-(4-*t*-butyl)phenyl)pyridine (0.564 g, 2.11 mmol), 2-methoxyethanol (35.2 mL), and H_2O (12 mL). Provided product as a bright orange solid in sufficient purity for the subsequent step without further characterization.

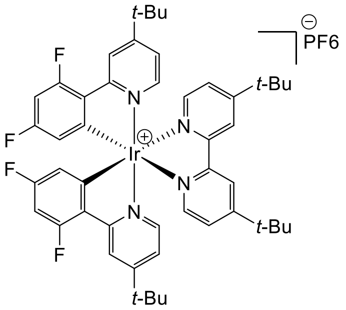


Tetrakis-((4-trifluoromethyl-2-pyridin-2-yl)phenyl)diiridium dichloride (4-33): Prepared using the general procedure with irdium chloride hydrate (0.1 g, 0.335 mmol), 2-(4-trifluoromethyl)phenyl)pyridine (0.168 g, 0.754 mmol), 1-methoxyethanol (13 mL), and H_2O (4 mL). Provided a bright yellow solid of sufficient purity for the subsequent step without further purification or characterization.

General procedure for synthesis of heteroleptic iridium complexes from chloro-bridged dimers:

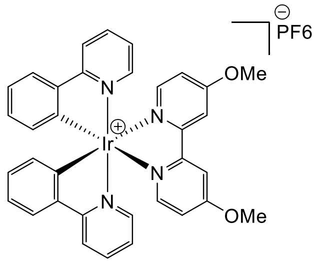


Complexes were prepared using the general procedure described by Weaver and coworkers. Chloro-bridging dimer (1 equiv.), bipyridyl ligand (2.2 equiv.), and ethylene glycol (0.02 M) were placed in a round-bottom flask equipped with a reflux condenser. The flask was purged several times with N_2(g) and heated at 150 °C for 18 hours. After cooling to room temperature the homogeneous mixture was washed three times with hexanes and then heated to 85 °C to remove residual hexane. A saturated aqueous solution of ammonium hexafluorophosphate was then added resulting in precipitation of the iridium PF_6 salt. The precipitate was collected by filtration and purified by either column chromatography (MeOH/DCM) or by liquid/liquid diffusion (DCM/pentanes) to give the photocatalyst as a yellow or orange solid.



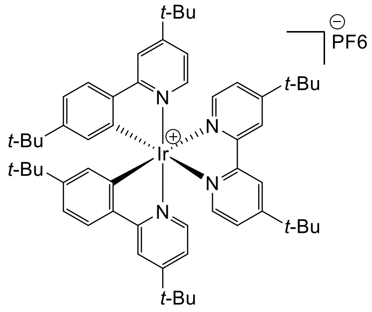
bis-(3,5-difluoro-2-(5-*t*-butyl-pyridin-2-yl)phenyl)-4,4'-di-*t*-butyl-2,2'-bipyridyliridium(III) hexafluorophosphate (Ir(dF(tBu)ppy)$_2$dtbbpyPF$_6$) (4-34): Synthesized using a modified version of the general procedure with tetrakis-(3,5-difluoro-2-(5-t-butyl-pyridin-2-yl)phenyl)diiridium(III) dichloride (343 mg, 0.238 mmol), 4,4'-di-*t*-butyl-2,2'-bipyridine (281 mg, 1.05 mmol), ethylene glycol (30 mL), and ammonium hexafluorophosphate (2.0 g, in 20 mL H_2O). The resulting precipitate was purified by recrystallization (DCM/Et_2O) so give to product as a pale yellow solid (345 mg, 66 % yield). the identity of the nitrogen-protecting group raises the possibility for the incorporation of a chiral auxiliary for a stereocontrolled [3 + 2] cycloaddition to provided enantioenriched pyrrolidine products. The presence of a Lewis acid in the reaction conditions also raises the question of stereocontrol through incorporation of a chiral ligand. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.79 (d, *J* = 2.0 Hz, 1H), 8.34 – 8.21 (m, 1H), 7.82 (d, *J* = 5.8 Hz, 1H), 7.43 (dd, *J* = 5.8, 1.9 Hz, 1H), 7.38 (d, *J* = 6.2 Hz, 1H), 7.12 (dd, *J* = 6.3, 2.2 Hz, 1H), 6.54 (ddd, *J* = 12.5, 9.0, 2.3 Hz, 1H), 5.67 (dd, *J* = 8.4, 2.3 Hz, 1H), 1.48 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 164.94, 163.60 (d, *J* = 7.2 Hz), 163.47, 162.39 (d, *J* = 12.6 Hz), 162.16 (d, *J* = 12.6 Hz), 155.71, 154.83 (d, *J* = 6.4 Hz), 149.36, 148.22, 127.89, 125.21, 123.18, 121.35, 120.52 (d, *J* = 20.4 Hz), 113.93 (d, *J* = 18.0 Hz), 98.72 (t, *J* = 26.8 Hz), 35.98, 35.32, 30.36, 30.32. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -72.68 (d, *J* = 713.3 Hz), -106.77 (d, *J* = 10.6 Hz), -109.40 (d, *J* = 10.7 Hz). HRMS (ESI) calculated for $[C_{48}H_{52}F_4IrN_4]^+$ {M^+} requires 951.3729, found 951.3728.

bis-(2-(pyridin-2-yl)phenyl)-4,4’-di-MeO-2,2’-bipyridyliridium(III) hexafluorophosphate (Irppy$_2$dMeObpyPF$_6$) (4-35):



Prepared using the general procedure with tetrakis-(2-(pyridin-2-yl)phenyl)diiridium(III) dichloride (200.0 mg, 0.187 mmol), 4,4’-dimethoxy-2,2’-bipyridine (89.0 mg, 0.410 mmol), ethylene glycol (12 mL), and ammonium hexafluorophosphate. Provided a yellow solid as crude product which was purified by recrystallization (DCM/pentanes) to provide the pure product as a bright yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.99 (d, *J* = 2.6 Hz, 2H), 7.89 (dt, *J* = 8.2, 1.2 Hz, 2H), 7.77 – 7.71 (m, 2H), 7.68 – 7.64 (m, 4H), 7.62 – 7.57 (m, 2H), 7.08 – 6.97 (m, 4H), 6.89 (td, *J* = 7.4, 1.3 Hz, 2H), 6.85 (dd, *J* = 6.3, 2.5 Hz, 2H), 6.30 (dd, *J* = 7.7, 1.2 Hz, 2H), 4.12 (s, 6H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.99, 167.92, 157.71, 150.89, 150.49, 148.64, 143.57, 137.77, 131.82, 130.68, 124.67, 123.19, 122.31, 119.36, 115.64, 109.83, 56.99. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -72.85 (d, *J* = 712.7 Hz). HRMS (ESI) calculated for $[C_{34}H_{28}IrN_4O_2]^+$ {M$^+$} requires 715.1813, found 715.1812.

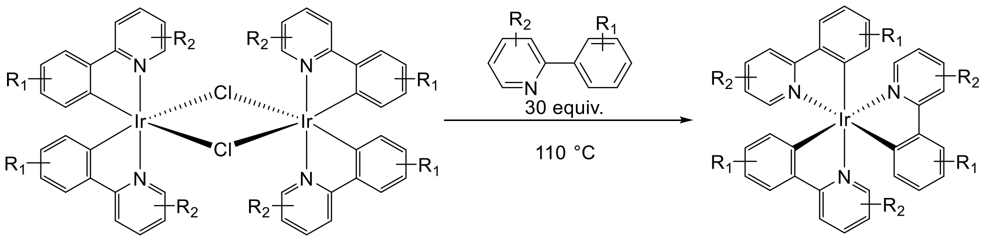
Bis-(2-(4-*t*-butyl-pyridin-2-yl)-5-*t*-butylphenyl-4,4’-di-*t*-butyl-2,2’-bipyridyliridium(III) hexafluorophosphate (Ir(dtbppy)$_2$dtbbpyPF$_6$) (4-36):



Prepared using the general procedure with Tetrakis-(2-(4-t-butyl-pyridin-2-yl)-5-t-butylphenyl)diiridium(III) dichloride (0.1932 g, 0.127 mmol), 4,4’-di-*t*-butyl-2,2’-bipyridine (0.075 g, 0.279 mmol), ethylene glycol (5 mL), and saturated ammonium hexafluorophosphate. Provided a yellow solid as crude product which was purified by recrystallization (aceton/pentanes). Pure product was obtained as a bright yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 2.0 Hz, 1H), 7.82 (d, *J* = 5.8 Hz, 1H), 7.77 (d, *J* = 2.1 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 6.2 Hz, 1H), 7.37 (dd, *J* = 5.9, 1.9 Hz, 1H), 7.09 (dd, *J* = 6.3, 2.2 Hz, 1H), 7.01 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.18 (d, *J* = 1.9 Hz, 1H), 1.44 (s, 10H), 1.35 (s, 9H), 1.08

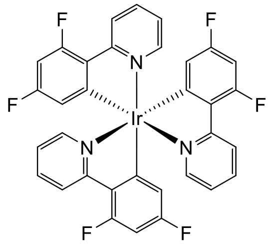
(s, 9H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.56, 163.46, 162.16, 155.95, 153.15, 150.90, 149.75, 148.45, 141.44, 127.77, 125.05, 123.63, 121.55, 120.36, 119.31, 115.56, 35.68, 35.14, 34.52, 31.11, 30.45, 30.27. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -72.97 (d, *J* = 713.2 Hz). HRMS (ESI) calculated for $[C_{56}H_{72}IrN_4]^+$ $\{M^+\}$ requires 991.5357, found 991.5357.

General procedure for synthesis of homoleptic iridium complexes from chloro-bridged dimers:

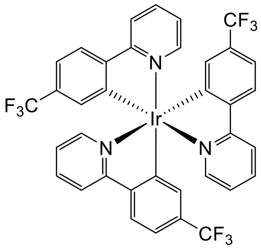


A small vial was charged with chloro-bridging dimer (1 equiv.), phenylpyridyl ligand (30 equiv.), and silver trifluoromethanesulfonate (2 equiv.). The vial was purged several times with N_2(g) and sealed with a Teflon cap and heated at 110 °C for 24 hours. The phenylpyridyl ligand will often start as a solid and melt above 70 °C. The reaction mixture was then cooled to room temperature and the crude product purified by flash column chromatography (acetone/pentanes, dry-loaded).

***fac*-Tris-(3,5-difluoro-2-pyridin-2-yl)phenyliridium(III) (IrdFppy$_3$) (4-37):** Prepared using the general procedure with tetrakis-((3,5-difluoro-2-pyridin-2-yl)phenyl)diiridium(III) dichloride (0.1805 g, 0.148 mmol), 2-(2,4-difluorophenyl)pyridine (0.851 g, 4.45 mmol), and silver trifluoromethanesulfonate (0.076 g, 0.297 mmol). Provided a brown-yellow solid as crude product. Product was purified by column chromatography (acetone/pentanes dry loaded) to provide the pure complex as a bright fluorescent yellow powder (0.093 g, 0.122 mmol, 41 % yield). Spectral data match those reported previously in the literature.



***fac*-Tris-(3-trifluoromethyl-2-pyridin-2-yl)phenyliridium(III) (Ir4-CF$_3$ppy$_3$) (4-38):** Prepared using the general procedure with tetrakis-((4-trifluoromethyl-2-pyridin-2-yl)phenyl)diiridium(III) dichloride (0.1574 g, 0.117 mmol), 2-(4-trifluoromethyl)phenyl)pyridine (0.784 g, 3.51 mmol), and silver trifluoromethanesulfonate (0.060 g, 0.234 mmol). Provided a brown-yellow solid as crude product. Product was purified by column chromatography (acetone/pentanes dry loaded) to provide the pure product as a yellow power which can be further purified by recrystallization (acetone/pentanes) to give a crystalline golden yellow solid (0.121 g, 0.141 mmol, 60 % yield). Spectral data match those reported previously in the literature.



Electrochemical characterization

Electrochemical data for photocatalysts were obtained by cyclic voltammetry. Cyclic voltammetry experiments were carried out in dry acetonitrile with 0.1 M tetrabutylammonium hexafluorophosphate as supporting electrolyte and 0.001 M of photocatalyst. A glassy carbon electrode was used as working electrode, platinum wire as counter electrode, and Ag/AgNO$_3$ (0.01M in MeCN) as reference electrode. All potentials were referenced against the Fc$^+$/Fc redox couple in a second experiment. For each experiment, the acetonitrile solutions were degassed by sparging with N$_2$(g) prior to measurements. An initial set of scans were taken at 50 mV/sec. Ferrocene was then added for referencing. Emission data for previously unreported were obtained on a Hitachi F-4500 fluorescence spectrophotometer with an excitation wavelength of 370nm. Excited state potentials of all the listed photocatalysts were determined using the Rehm-Weller equation (equation 1).[21] Spectroscopic data reported by Weaver and coworkers was used for entries 2, 4, and 9–12 in Table 4-8.[17]

$$E^*_{1/2}(red) = E^{red}_{1/2} + E_{0,0} + w_r \quad (1)$$

Table 4-8. Spectroscopic and electrochemical data of photocatalysts used in optimization

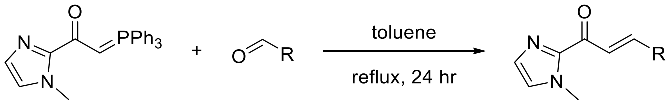
Entry	Photocatalyst	$E_0(PC^{n+1}/PC^{n}*)^a$	$E_0(PC^{n+1}/PC^{n})$	λ_{max}^{em}	E_{00}
1	$Ru(bpy)_3(PF_6)_2$	-0.81 V	1.29 V	588 nm	2.1 eV
2	$Ir(dF(CF_3)ppy)_2dtbbpyPF_6$	-0.86 V	1.72 V	480 nm[17]	2.58 eV
3	$Ir(dF(t\text{-}Bu)ppy)_2(dtbbpy)PF_6$	-0.86 V	1.54 V	524 nm	2.40 eV
4	$Ir(Fppy)_2(dtbbpy)PF_6$	-0.90 V	1.40 V	540 nm[17]	2.30 eV
5	$Ir(ppy)_2(dtbbpy)PF_6$	-0.98 V	1.23 V	561 nm	2.21 eV
6	$Ir(ppy)_2(dMeObpy)PF_6$	-1.00 V	1.21 V	562 nm	2.21 eV
8	$Ir(dtbppy)_2(dtbbpy)PF_6$	-1.04 V	1.13 V	571 nm	2.17 eV
9	$Ir(4\text{-}CF_3ppy)_3$	-1.41 V	1.04 V	507 nm[17]	2.45 eV
10	$Ir(dFppy)_3$	-1.62 V	0.98 V[17]	476 nm[17]	2.60 eV
11	$Ir(3\text{-}t\text{-}Buppy)_3$	-1.66 V	0.70 V	525 nm[17]	2.36 eV
12	$Ir(ppy)_3$	-1.67 V	0.72 V	518 nm[17]	2.39 eV

[a] Versus SCE reference electrode. [b] Yields determined by ^1H NMR using phenanthrene as internal standard.

4.4.3 Substrate synthesis

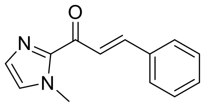
1-methyl-1H-imidazol-2-yl)prop-2-en-1-ones were prepared using methods described previously by Evans and coworkers using the following general procedure.[22] Synthesis of the phosphonium ylide is described in the previous reference.

<u>General procedure for enone preparation:</u>



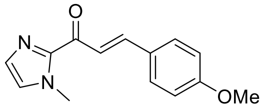
A flame-dried round bottom flask was charged with phosphonium ylide (1 equiv.), aldehyde (2 equiv.), and toluene (0.1 M). The flask was equipped with a reflux condenser and the reaction mixture held at reflux under and inert atmosphere for 24 hours. After this time, the reaction mixture was cooled to room temperature and flashed through a plug of silica with 150 mL EtOAc. The eluent was concentrated to give the crude product as an oil. Product was then purified by column chromatography (acetone/hexanes).

(E)-1-(1-methyl-1H-imidazol-2-yl)-3-phenylprop-2-en-1-one (4-39): Prepared using the



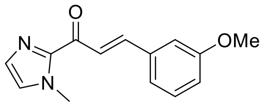
general procedure with 1-(1-methyl-1H-imidazol-2-yl)-2-(triphenylphosphoranylidene)ethanone (4.0 g, 10.41 mmol), benzaldehyde (2.2 g, 20.8 mmol), and toluene (50 mL). Product was purified by column chromatography (25 % acetone/hexanes) to give the product as an off-white solid (1.436 g, 6.76 mmol, 65 % yield). Spectroscopic data match those described previously by Evans and coworkers.[22] ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.08 (d, *J* = 16.0, 1H), 7.83 (d, *J* = 15.5 Hz, 1H), 7.70 (m, 2H), 7.39 (m, 3H), 7.22 (s, 1H), 7.07 (s, 1H), 4.09 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 180.4, 144.0, 143.3, 134.8, 130.4, 129.3, 128.8, 128.7, 127.2, 122.7, 36.3.

(E)-3-(4-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (4-40): Prepared



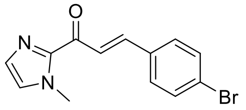
using the general procedure with 1-(1-methyl-1H-imidazol-2-yl)-2-(triphenylphosphoranylidene)ethanone (4.0 g, 10.41 mmol), 4-MeO-benzaldehyde (2.2 g, 20.8 mmol), and toluene (50 mL). Product was purified by column chromatography (25 % acetone/hexanes) to give the product as an off-white solid (1.436 g, 6.76 mmol, 65 % yield). Spectroscopic data match those described previously by Evans and coworkers.[22] ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.95 (d, *J* = 15.5 Hz, 1H), 7.80 (d, *J* = 16.0 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.21 (s, 1H), 7.06 (s, 1H), 6.92 (d, *J* = 8.5 Hz, 2H), 4.09 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 180.5, 161.6, 144.1, 143.2, 130.5, 129.1, 127.6, 127.0, 120.4, 114.2, 55.3, 36.3.

(E)-3-(3-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (4-41): Prepared



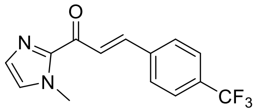
using the general procedure with 1-(1-methyl-1H-imidazol-2-yl)-2-(triphenylphosphoranylidene)ethanone (4.0 g, 10.41 mmol), 3-MeO-benzaldehyde (2.2 g, 20.8 mmol), and toluene (50 mL). Product was purified by column chromatography (25 % acetone/hexanes) to give the product as an off-white solid (1.436 g, 6.76 mmol, 65 % yield). Product was carried on without further characterization.

(E)-3-(4-bromophenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (4-42): Prepared using



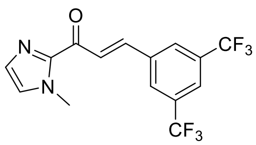
the general procedure with 1-(1-methyl-1H-imidazol-2-yl)-2-(triphenylphosphoranylidene)ethanone (4.0 g, 10.41 mmol), 4-bromo-benzaldehyde (2.2 g, 20.8 mmol), and toluene (50 mL). Product was purified by column chromatography (25 % acetone/hexanes) to give the product as an off-white solid (1.436 g, 6.76 mmol, 65 % yield). Spectroscopic data match those described previously by Scheidt and coworkers.[23] ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.05 (d, *J* = 16.0, 1H), 7.58 (d, *J* = 15.5 Hz, 1H), 7.53 (m, 4H), 7.21 (s, 1H), 7.08 (s, 1H), 4.08 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 180.0, 143.8, 141.7, 133.7, 132.0, 130.0, 129.3, 127.3, 124.6, 123.3, 36.3.

(E)-1-(1-methyl-1H-imidazol-2-yl)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (4-43):



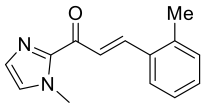
Prepared using the general procedure with 1-(1-methyl-1H-imidazol-2-yl)-2-(triphenylphosphoranylidene)ethanone (4.0 g, 10.41 mmol), 4-CF3-benzaldehyde (2.2 g, 20.8 mmol), and toluene (50 mL). Product was purified by column chromatography (25 % acetone/hexanes) to give the product as an off-white solid (1.436 g, 6.76 mmol, 65 % yield). Spectroscopic data match those described previously by Gonzalez-Soria and coworkers.[24] ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.14 (d, *J* = 16.0 Hz, 1H), 7.63–7.85 (m, 5H), 7.24 (d, *J* = 0.9, 1H), 7.07–7.16 (m, 1H), 4.10 (s, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 180.1, 144.0, 138.4, 131.8 (q, *J* = 32.6 Hz), 125.9 (q, *J* = 3.7 Hz), 141.3, 129.7, 128.8, 127.7, 125.2, 124.0 (q, *J* = 273.4 Hz), 36.5.

(E)-3-(3,5-bis(trifluoromethyl)phenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (4-44):



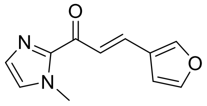
Prepared using the general procedure with 1-(1-methyl-1H-imidazol-2-yl)-2-(triphenylphosphoranylidene)ethanone (4.0 g, 10.41 mmol), 3,4-bis(CF$_3$-)-benzaldehyde (2.2 g, 20.8 mmol), and toluene (50 mL). Product was purified by column chromatography (25 % acetone/hexanes) to give the product as an off-white solid (1.436 g, 6.76 mmol, 65 % yield). Product was carried on without further characterization.

(E)-1-(1-methyl-1H-imidazol-2-yl)-3-(o-tolyl)prop-2-en-1-one (4-45): Prepared using the



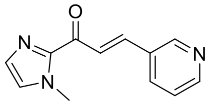
general procedure with 1-(1-methyl-1H-imidazol-2-yl)-2-(triphenylphosphoranylidene)ethanone (4.0 g, 10.41 mmol), 2-methyl-benzaldehyde (2.2 g, 20.8 mmol), and toluene (50 mL). Product was purified by column chromatography (25 % acetone/hexanes) to give the product as an off-white solid (1.436 g, 6.76 mmol, 65 % yield). Spectroscopic data match those described previously by Qiang Kang and coworkers.[25] ^{1}H NMR (400 MHz, $CDCl_3$): 8.15 (d, *J* = 15.8 Hz, 1 H), 8.01 (d, *J* = 15.8 Hz, 1 H), 7.81 (d, *J* = 7.8 Hz, 1 H), 7.29 (t, *J* = 7.2 Hz, 1 H), 7.24-7.20 (m, 3 H), 7.08 (s, 1 H), 4.10 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 180.6, 144.1, 140.9, 138.4, 133.8, 130.8, 130.2, 129.4, 127.3, 126.8, 126.3, 123.6, 36.4, 19.8.

(E)-3-(furan-3-yl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (4-46): Prepared using the

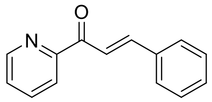


general procedure with 1-(1-methyl-1H-imidazol-2-yl)-2-(triphenylphosphoranylidene)ethanone (4.0 g, 10.41 mmol), 3-furaldehyde (2.2 g, 20.8 mmol), and toluene (50 mL). Product was purified by column chromatography (25 % acetone/hexanes) to give the product as an off-white solid (1.436 g, 6.76 mmol, 65 % yield). Spectroscopic data match those described previously by Inokuma *et al*.[26] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 16.0 Hz, 1H), 7.75 (d, *J* = 2.3 Hz, 1H), 7.73 (d, *J* = 16.0 Hz, 1H), 7.45 (s, 1H), 7.21 (s, 1H), 7.07 (s, 1H), 6.77 (d, *J* = 1.6 Hz, 1H), 4.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.4, 145.5, 144.4, 143.9, 133.4, 129.2, 127.1, 123.4, 122.7, 107.8, 36.3.

(E)-1-(1-methyl-1H-imidazol-2-yl)-3-(pyridin-3-yl)prop-2-en-1-one (4-47): Prepared using the

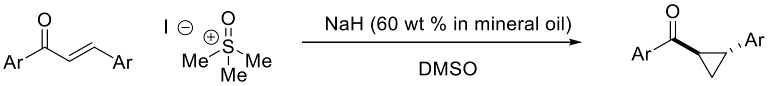


general procedure with 1-(1-methyl-1H-imidazol-2-yl)-2-(triphenylphosphoranylidene)ethanone (4.0 g, 10.41 mmol), 3-nicotinaldehyde (2.2 g, 20.8 mmol), and toluene (50 mL). Product was purified by column chromatography (25 % acetone/hexanes) to give the product as an off-white solid (1.436 g, 6.76 mmol, 65 % yield). Product was carried on without further purification. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.86 (m, 1H), 8.61 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.15 (d, *J* = 16.2 Hz, 1H), 8.03 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.80 (d, *J* = 16.1 Hz, 1H), 7.34 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.25 (s, 1H), 7.11 (s, 1H), 4.10 (s, 3H).

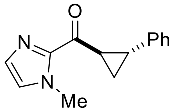


(*E*)-3-phenyl-1-(pyridin-2-yl)prop-2-en-1-one (4-48): Prepared as described previously by Baoan Song and coworkers.[27] ^{1}H NMR (300 MHz, DMSO) δ 7.43– 7.51 (m, 3H), 7.69 (ddd, *J* = 7.6, 4.7, 1.5, 1H), 7.78–7.83 (m, 2H), 7.93 (d, *J* = 16.2, 1H), 8.05 (td, *J* = 7.6, 1.5, 1H), 8.11 (ddd, *J* = 7.6, 1.5, 1.0, 1H), 8.27 (d, *J* = 16.2, 1H), 8.80 (ddd, *J* = 4.7, 1.5, 1.0 Hz, 1H); ^{13}C NMR (75 MHz, DMSO) δ 120.8, 122.5, 127.6, 128.7, 129.1, 130.8, 137.7, 149.1, 134.6, 144.0, 153.4, 188.7.

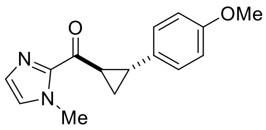
General cyclopropanation procedure:



A flame-dried round-bottom flask is charged with trimethylsulfoxonium iodide (1.2 equiv.) and NaH (60 % dispersion in mineral oil, 1.2 equiv.). The flask is sealed with a rubber septum and a nitrogen inlet is inserted. DMSO (0.3 M) is then added dropwise keeping the evolution of gas controlled. After addition, the mixture is allowed to stir vigorously until homogenous. A solution of aryl enone in DMSO (1 M, 1 equiv.) is then added via syringe. The reaction mixture is then stirred overnight at room temperature. After this time the reaction mixture is diluted with Et_2O and quenched by very careful addition of H_2O. The mixture is diluted further with Et_2O and H_2O. The organic phase is isolated and the aqueous phase is extracted twice more with Et_2O. The combined organic layers are washed with brine and dried over Na_2SO_4 before concentrating under reduced pressure to provide the crude product. Products are then purified by column chromatography using acetone/hexanes.

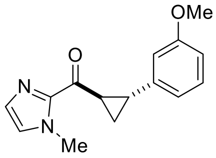


(1-methyl-1H-imidazol-2-yl)(2-phenylcyclopropyl)methanone (4-6): Prepared using the general procedure with (E)-1-(1-methyl-1H-imidazol-2-yl)-3-phenylprop-2-en-1-one (1.0 g, 4.71 mmol), trimethylsulfoxonium iodide (1.244 g, 5.65 mmol), NaH (0.226 g, 5.65 mmol), and DMSO (15 mL). The crude product was purified by column chromatography (20 % Acetone in hexanes) to give the product as a white solid (0.8 g, 3.53 mmol, 75 % yield). v_{max} (film) / cm^{-1} 1666, 1412, 1030, 995. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.31 – 7.24 (m, 2H), 7.21 – 7.15 (m, 4H), 7.04 (d, *J* = 0.9 Hz, 1H), 4.02 (s, 3H), 3.61 (ddd, *J* = 8.3, 5.3, 4.1 Hz, 1H), 2.69 (ddd, *J* = 9.0, 6.6, 4.1 Hz, 1H), 1.80 (ddd, *J* = 9.2, 5.4, 4.0 Hz, 1H), 1.53 (ddd, *J* = 8.3, 6.6, 4.0 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 190.37, 143.58, 140.42, 129.39, 128.40, 126.99, 126.40, 126.25, 36.17, 29.65, 29.23, 20.18. M.p. 77–79 °C. HRMS (ESI) calculated for $[C_{14}H_{15}N_{2}O]^{+}$ {M+H^{+}} requires 227.1179, found 227.1176.

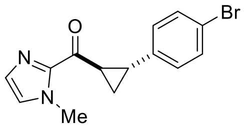


(2-(4-methoxyphenyl)cyclopropyl)(1-methyl-1H-imidazol-2-yl)methanone (4-38): Prepared using the general procedure with (E)-3-(4-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (0.462 g, 1.91 mmol), trimethylsulfoxonium iodide (0.504 g, 2.29 mmol), NaH (0.092 g, 2.29 mmol), and DMSO (6 mL). The crude product was purified by column chromatography (20 % Acetone in hexanes) to give the product as a white solid (0.406 g, 1.58 mmol, 83 % yield). v_{max} (film) / cm^{-1} 1665, 1411, 1030, 998. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.15 (d, *J* = 0.9 Hz, 1H), 7.10 (d, *J* = 8.7 Hz, 2H), 7.04 (d, *J* = 0.9 Hz, 1H), 6.81 (d, *J* = 8.7 Hz, 2H), 4.02 (s, 3H), 3.78 (s, 3H), 3.53 (ddd, *J* = 8.2, 5.3, 4.1 Hz, 1H), 2.65 (ddd, *J* = 9.1, 6.7, 4.1 Hz, 1H), 1.76 (ddd, *J* = 9.2, 5.3, 4.0 Hz, 1H), 1.47 (ddd, *J* = 8.3, 6.7, 4.0 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 190.66, 158.47, 143.77, 132.60, 129.49, 127.56, 127.07, 114.03, 55.48, 36.32, 29.43, 29.24, 20.10. M.p. 55.6–56.7 °C. HRMS (ESI) calculated for $[C_{15}H_{17}N_{2}O_{3}]^{+}$ {M+H^{+}} requires 257.1285, found 257.1283.

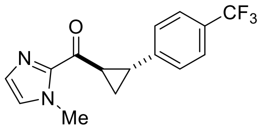
(2-(3-methoxyphenyl)cyclopropyl)(1-methyl-1H-imidazol-2-yl)methanone (4-39): Prepared using the general procedure with (E)-3-(3-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (0.5204 g, 2.15 mmol), trimethylsulfoxonium iodide (0.567 g, 2.58 mmol), NaH (0.103 g, 2.58 mmol), and DMSO (7 mL). The crude product was purified by column chromatography (20 % Acetone in hexanes) to give the product as a white solid (0.468 g, 1.83 mmol, 85 % yield). v_{max} (film) / cm^{-1} 1669, 1410, 1032, 990. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.18 (t, *J* = 7.9 Hz, 1H), 7.16 (d, *J* = 0.9 Hz, 1H), 7.04 (d, *J* = 0.9 Hz, 1H), 6.78 – 6.69 (m, 3H), 4.02 (s, 3H), 3.79 (s, 3H), 3.60 (ddd, *J* = 8.3, 5.4, 4.1 Hz, 1H), 2.66 (ddd, *J* = 9.0, 6.5, 4.1 Hz, 1H), 1.78 (ddd, *J* = 9.2, 5.4, 4.0 Hz, 1H), 1.52 (ddd, *J* = 8.3, 6.6, 4.1 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 190.44, 159.87, 143.70, 142.24, 129.55, 127.14, 118.75, 112.16, 112.07, 55.35, 36.32, 29.79, 29.44, 20.29. M.p. 50–52 °C. HRMS (ESI) calculated for $[C_{15}H_{17}N_2O_2]^+$ {M+H$^+$} requires 257.1285, found 257.1283.



(2-(4-bromophenyl)cyclopropyl)(1-methyl-1H-imidazol-2-yl)methanone (4-40): Prepared using the general procedure with (E)-3-(4-bromophenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (0.6185 g, 2.12 mmol), trimethylsulfoxonium iodide (0.561 g, 2.55 mmol), NaH (0.102 g, 2.55 mmol), and DMSO (7 mL). The crude product was purified by column chromatography (20 % Acetone in hexanes) to give the product as a white solid (0.571 g, 1.87 mmol, 88 % yield). v_{max} (film) / cm^{-1} 1660, 1410, 1032, 995. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 8.5 Hz, 1H), 7.16 (d, *J* = 1.0 Hz, 1H), 7.07 – 7.02 (m, 2H), 4.02 (s, 2H), 3.57 (ddd, *J* = 8.3, 5.4, 4.1 Hz, 1H), 2.63 (ddd, *J* = 9.1, 6.6, 4.2 Hz, 1H), 1.79 (ddd, *J* = 9.3, 5.4, 4.1 Hz, 1H), 1.47 (ddd, *J* = 8.4, 6.6, 4.1 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 190.11, 143.63, 139.69, 131.60, 129.63, 128.17, 127.26, 120.23, 36.32, 29.25, 29.00, 20.10. M.p. 91–93 °C. HRMS (ESI) calculated for $[C_{14}H_{14}BrN_2O]^+$ {M+H$^+$} requires 305.0284, found 305.0282.

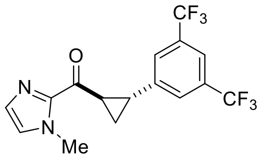


(1-methyl-1H-imidazol-2-yl)(2-(4-(trifluoromethyl)phenyl)cyclopropyl)methanone (4-41):



Prepared using the general procedure with (E)-1-(1-methyl-1H-imidazol-2-yl)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (0.56494 g, 2.02 mmol), trimethylsulfoxonium iodide (0.532 g, 2.42 mmol), NaH (0.097 g, 2.42 mmol), and DMSO (7 mL). The crude product was purified by column chromatography (20 % Acetone in hexanes) to give the product as a white solid (0.534 g, 1.81 mmol, 90 % yield). v_{max} (film) / cm^{-1} 1664, 1417, 1325, 1164, 1121, 1069. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 3H), 7.17 (d, *J* = 0.9 Hz, 1H), 7.06 (d, *J* = 0.9 Hz, 1H), 4.03 (s, 3H), 3.65 (ddd, *J* = 8.4, 5.5, 4.1 Hz, 1H), 2.71 (ddd, *J* = 9.1, 6.5, 4.1 Hz, 1H), 1.84 (ddd, *J* = 9.4, 5.5, 4.2 Hz, 1H), 1.54 (ddd, *J* = 8.4, 6.5, 4.2 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 189.69, 144.71, 143.41, 129.55, 128.66 (q, *J* = 32.7 Hz), 127.21, 126.49, 125.36 (q, *J* = 3.8 Hz), 1234.22 (q, *J* = 272.03 Hz), 36.18, 29.35, 28.86, 20.12. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -62.42. M.p. 91.4–92 °C. HRMS (ESI) calculated for $[C_{15}H_{14}F_3N_2O]^+$ $\{M+H^+\}$ requires 295.1053, found 295.1051.

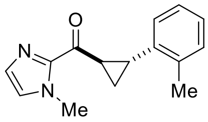
(2-(3,5-bis(trifluoromethyl)phenyl)cyclopropyl)(1-methyl-1H-imidazol-2-yl)methanone (4-42):



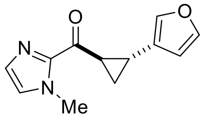
Prepared using the general procedure with (E)-3-(3,5-bis(trifluoromethyl)phenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (1.655 g, 4.75 mmol), trimethylsulfoxonium iodide (1.255 g, 5.70 mmol), NaH (0.228 g, 5.70 mmol), and DMSO (16 mL). The crude product was purified by column chromatography (20 % Acetone in hexanes) to give the product as a white solid (1.067 g, 2.95 mmol, 62 % yield). v_{max} (film) / cm^{-1} 1666, 1420, 1398, 1278, 1359, 1130, 1170. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 (br s, 1H), 7.59 (br s, 1H), 7.18 (d, *J* = 0.9 Hz, 1H), 7.09 (d, *J* = 0.9 Hz, 1H), 4.03 (s, 3H), 3.66 (ddd, *J* = 8.5, 5.5, 4.2 Hz, 1H), 2.79 (ddd, *J* = 9.0, 6.5, 4.1 Hz, 1H), 1.88 (ddd, *J* = 9.0, 5.5, 4.5 Hz, 1H), 1.59 (ddd, *J* = 8.6, 6.5, 4.5 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 188.99, 143.26, 143.20, 131.78 (q, *J* = 33.3 Hz), 129.67, 127.42, 126.44 (q, *J* =

3.7 Hz), 123.27 (q, *J* = 272.9 Hz), 120.36 (hept, *J* = 3.8 Hz), 36.20, 29.41, 28.07, 19.73. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -62.89. M.p. 128.5–131 °C. HRMS (ESI) calculated for $[C_{16}H_{13}F_6N_2O]^+$ {M+H$^+$} requires 363.0927, found 363.0925.

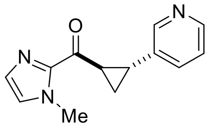
(1-methyl-1H-imidazol-2-yl)(2-(o-tolyl)cyclopropyl)methanone (4-43): Prepared using the general procedure with (E)-1-(1-methyl-1H-imidazol-2-yl)-3-(o-tolyl)prop-2-en-1-one (0.4572 g, 2.02 mmol), trimethylsulfoxonium iodide (0.534 g, 2.43 mmol), NaH (0.097 g, 2.43 mmol), and DMSO (7 mL). The crude product was purified by column chromatography (20 % Acetone in hexanes) to give the product as a white solid (0.413 g, 1.72 mmol, 85 % yield). Colorless oil. v$_{max}$ (film) / cm^{-1} 1660, 1415, 1031, 996. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.17 (d, *J* = 1.0 Hz, 1H), 7.16 – 7.08 (m, 4H), 7.06 (d, *J* = 0.9 Hz, 1H), 4.04 (s, 3H), 3.50 (ddd, *J* = 8.2, 5.1, 4.4 Hz, 1H), 2.70 (ddd, *J* = 9.0, 6.9, 4.4 Hz, 1H), 2.34 (s, 3H), 1.76 (ddd, *J* = 8.9, 5.1, 3.8 Hz, 1H), 1.52 (ddd, *J* = 8.3, 6.9, 3.8 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 190.91, 143.55, 138.22, 137.90, 129.75, 129.38, 126.98, 126.62, 125.89, 36.19, 27.96, 27.30, 19.68, 18.57. HRMS (ESI) calculated for $[C_{15}H_{17}N_2O]^+$ {M+H$^+$} requires 241.1335, found 241.1334.



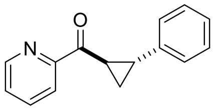
(2-(furan-3-yl)cyclopropyl)(1-methyl-1H-imidazol-2-yl)methanone (4-44): Prepared using the general procedure with (E)-3-(furan-3-yl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (0.3709 g, 1.83 mmol), trimethylsulfoxonium iodide (0.484 g, 2.20 mmol), NaH (0.088 g, 2.20 mmol), and DMSO (6 mL). The crude product was purified by column chromatography (20 % Acetone in hexanes) to give the product as a white solid (0.361 g, 1.67 mmol, 85 % yield). v$_{max}$ (film) / cm^{-1} 1660, 1416, 1034, 1007, 915, 779. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.35 – 7.30 (m, 0H), 7.17 (d, *J* = 0.9 Hz, 0H), 7.05 (d, *J* = 0.9 Hz, 1H), 6.22 (t, *J* = 1.4 Hz, 0H), 4.01 (s, 2H), 3.46 (ddd, *J* = 8.2, 5.2, 4.1 Hz, 1H), 2.51 (ddd, *J* = 8.9, 6.6, 4.1 Hz, 1H), 1.70 (ddd, *J* = 9.0, 5.2, 3.8 Hz, 1H), 1.34 (ddd, *J* = 8.3, 6.6, 3.9 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 190.44, 143.57, 143.06, 139.24, 129.40, 126.99, 125.08,



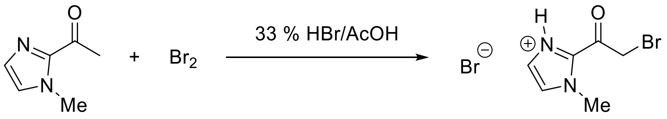
109.00, 36.17, 27.72, 20.62, 19.30. M.p. 65.8–69.6 °C. HRMS (ESI) calculated for $[C_{12}H_{13}N_2O_2]^+$ {M+H$^+$} requires 217.0972, found 217.0973.

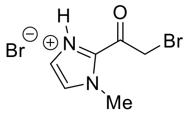


(1-methyl-1H-imidazol-2-yl)(2-(pyridin-3-yl)cyclopropyl)methanone (4-45): Prepared using the general procedure with (E)-1-(1-methyl-1H-imidazol-2-yl)-3-(pyridin-3-yl)prop-2-en-1-one (0.4033 g, 1.89 mmol), trimethylsulfoxonium iodide (0.499 g, 2.27 mmol), NaH (0.091 g, 2.27 mmol), and DMSO (6.3 mL). The crude product was purified by column chromatography (50 % Acetone in hexanes) to give the product as a white solid (0.335 g, 1.48 mmol, 78 % yield). ν_{max} (film) / cm^{-1} 1661, 1415, 991. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.51 (d, *J* = 2.3 Hz, 1H), 8.45 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.42 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.20 (ddd, *J* = 7.9, 4.9, 0.8 Hz, 1H), 7.17 (d, *J* = 0.9 Hz, 1H), 7.07 (d, *J* = 0.9 Hz, 1H), 4.03 (s, 3H), 3.62 (ddd, *J* = 8.4, 5.4, 4.1 Hz, 1H), 2.68 (ddd, *J* = 9.1, 6.6, 4.2 Hz, 1H), 1.83 (ddd, *J* = 9.4, 5.4, 4.2 Hz, 1H), 1.53 (ddd, *J* = 8.4, 6.6, 4.2 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 189.71, 148.81, 147.86, 143.42, 136.01, 132.98, 129.54, 127.23, 123.29, 36.19, 28.70, 26.58, 19.45. M.p. 112–115 °C. HRMS (ESI) calculated for $[C_{13}H_{14}N_3O]^+$ {M+H$^+$} requires 228.1131, found 228.1131.

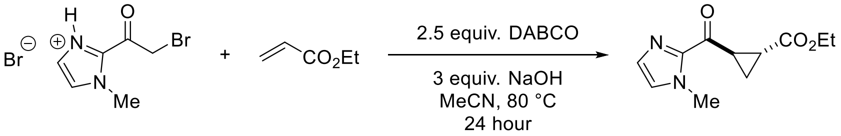


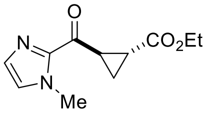
(2-phenylcyclopropyl)(pyridin-2-yl)methanone (4-46): Prepared using the general procedure with (E)-3-phenyl-1-(pyridin-2-yl)prop-2-en-1-one (1.00 g, 4.78 mmol), trimethylsulfoxonium iodide (1.262 g, 5.73 mmol), NaH (0.229 g, 5.73 mmol), and DMSO (16 mL). The crude product was purified by column chromatography (20 % Acetone in hexanes) to give the product as a white solid (0.726 g, 3.25 mmol, 68 % yield). ν_{max} (film) / cm^{-1} 3057, 1678, 1438, 1396, 1341, 1220, 1030, 995, 749, 696. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.70 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.06 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.47 (ddd, *J* = 7.6, 4.7, 1.2 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.23 – 7.17 (m, 3H), 3.85 (ddd, *J* = 8.3, 5.4, 4.1 Hz, 1H), 2.75 (ddd, *J* = 8.9, 6.6, 4.1 Hz, 1H), 1.88 (ddd, *J* = 9.1, 5.3, 3.9 Hz, 1H), 1.60 (ddd, *J* = 8.3, 6.6, 3.9 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 199.52, 153.49, 149.03, 140.65, 136.86, 128.43, 126.99, 126.43, 126.28, 121.85, 30.72, 27.50, 21.00. M.p. 82–84.5 °C. HRMS (ESI) calculated for $[C_{15}H_{14}NO]^+$ $\{M+H^+\}$ requires 224.1070, found 224.1068.



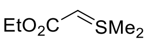


2-(2-bromoacetyl)-1-methyl-1H-imidazol-3-ium bromide (4-47): Prepared as described previously by Nakao and coworkers.[28] A 100 mL round bottom flask was charged with 2-acyl-1-methylimidazole (4.9 g, 39.47 mmol) followed by careful addition of HBr (33 % in AcOH, 30 mL). The flask was cooled to 0 °C and Br_2 (2.46 mL, 7.68 g, 48.06 mmol) was added slowly by syringe. The cooling bath was removed and the reaction mixture was allowed to stir at room temperature for 2 hours. The flask was then cooled to 0 °C and Et_2O (30 mL) was added very carefully. The mixture was filtered and the isolated solid was washed with copious amounts of additional Et_2O. The off-white solid was allowed to air-dry and then dried under vacuum at 40 °C to give the product in sufficient purity for subsequent steps (8.97 g, 31.58 mmol, 80 % yield). Spectroscopic data agreed with those reported previously.

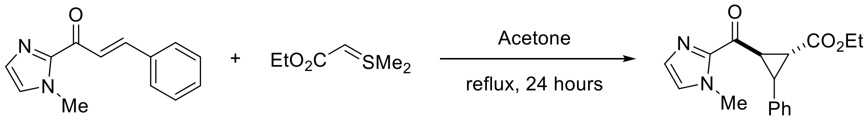




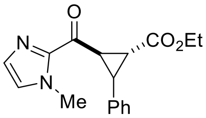
Ethyl 2-(1-methyl-1H-imidazole-2-carbonyl)cyclopropanecarboxylate (4-4): Prepared using a modified procedure first reported by Gaunt and coworkers.[29] A 100 mL flame-dried round-bottom flask was charged with 2-(2-bromoacetyl)-1-methyl-1H-imidazol-3-ium bromide (2.2752 g, 8 mmol, 1 equiv.), DABCO (2.24 g, 20 mmol, 2.5 equiv.) and MeCN (50 mL). The flask was sealed with a rubber septum and stirred at 50 °C for 1 hours. After this time NaOH (0.96 g, 24 mmol, 3 equiv.) and ethyl acrylate (1.2 mL, 10 mmol, 1.25 equiv.) were added. The flask was equipped with a reflux condenser and heated at 80 °C for 24 hours. After this time the reaction mixture was cooled to room temperature and quenched by addition of saturated aq. NH_4Cl. The reaction mixture was transferred to a separatory funnel and extracted 3x with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the crude product as a dark red oil. The crude product was purified by column chromatography (20 % acetone/pentanes) to give the pure product as a white solid (1.0 g, 4.5 mmol, 56 % yield). ν_{max} (film) / cm^{-1} 2983, 1726, 1666, 1414, 1398, 1318, 1184, 1005, 910, 730. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.20 (d, *J* = 0.9 Hz, 1H), 7.08 (d, *J* = 0.9 Hz, 1H), 4.15 (qd, *J* = 7.1, 3.1 Hz, 2H), 3.99 (s, 3H), 3.80 (ddd, *J* = 8.6, 5.8, 3.9 Hz, 1H), 2.31 (ddd, *J* = 8.5, 5.9, 3.9 Hz, 1H), 1.62 (ddd, *J* = 9.1, 6.0, 3.4 Hz, 1H), 1.54 (ddd, *J* = 9.0, 5.8, 3.4 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 188.73, 171.72, 143.20, 129.73, 127.38, 60.93, 36.14, 26.39, 24.83, 17.56, 14.18. HRMS (ESI) calculated for $[C_{11}H_{15}N_2O_3]^+$ {M+H$^+$} requires 223.1077, found 223.1074.



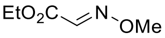
Ethyl (Dimethylsulfuranylidene)acetate (4-47): Prepared as described previously by Payne.[30]



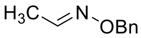
Ethyl 2-(1-methyl-1H-imidazole-2-carbonyl)-3-phenylcyclopropanecarboxylate (4-48):



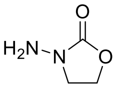
Prepared using a modified procedure originally reported by Payne.[30] A flame-dried round-bottom flask was charged with (E)-1-(1-methyl-1H-imidazol-2-yl)-3-phenylprop-2-en-1-one (0.4 g, 1.89 mmol), ethyl (dimethylsulfuranylidene)acetate (0.335 g, 2.26 mmol), and CH_2Cl_2 (10 mL). The flask was equipped with a reflux condenser and refluxed under an inert atmosphere for 24 hours. After cooling to room temperature the reaction mixture was concentrated under reduced pressure to give the crude product as a yellow oil in 3:1 d.r. Product was purified by column chromatography (2:3 EtOAc/hexanes) to give the pure product as a white solid (0.534 g, 1.79 mmol, 95 % yield). ν_{max} (film) / cm^{-1} 2983, 1728, 1667, 1436, 1406, 1186, 1031. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.33 – 7.27 (m, 2H), 7.25 – 7.21 (m, 3H), 7.17 (d, *J* = 0.9 Hz, 1H), 7.04 (d, *J* = 0.9 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 3H), 3.76 (dd, *J* = 9.6, 6.3 Hz, 1H), 3.33 (t, *J* = 6.3 Hz, 1H), 2.65 (dd, *J* = 9.7, 6.4 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 185.88, 169.07, 143.46, 138.20, 129.47, 128.58, 127.04, 126.98, 126.63, 60.97, 36.14, 34.54, 33.08, 30.35, 14.15. M.p. 76.5–82.6 °C. HRMS (ESI) calculated for $[C_{17}H_{19}N_2O_3]^+$ $\{M+H^+\}$ requires 299.1390, found 229.1384.



(E)-ethyl 2-(methoxyimino)acetate (4-49): Synthesized using a procedure described by Baker and coworkers.[31]

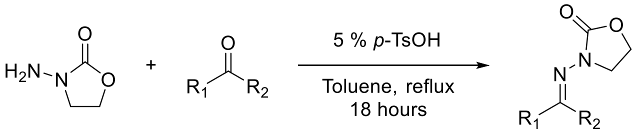


(E)-acetaldehyde O-benzyl oxime (4-50): Synthesized using a procedure described by Christensen and coworkers.[32]

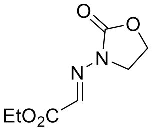


3-aminooxazolidin-2-one (4-51): Synthesized using a procedure described by Sentim and coworkers.[33]

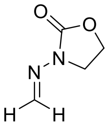
General procedure for the synthesis of hydrazone derivatives



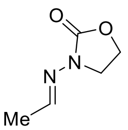
A round bottom flask was charged with 3-aminooxazolidin-2-one (1 equiv.), aldehyde (1 equiv.), *p*-TsOH (5 mol %), and toluene (0.2 M). The flask was fit with a reflux condenser and purged several times with N_2. The reaction flask was then held at reflux for 18 hours. After cooling to room temperature the reaction mixture was concentrated under reduced pressure to give the crude product as a dark oil. Product was then purified by column chromatography (acetone/pentanes).



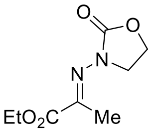
(E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (4-9): Synthesized according to general procedure with 3-aminooxazolidin-2-one (5.0 g, 49 mmol), ethyl glyoxylate (50 % in toluene, 10 mL, 49 mmol), *p*-TsOH (0.435 g, 4.57 mmol), and toluene (250 mL). Product was purified by column chromatography (gradient 1:2 to 1:1 acetone/pentanes) followed by recrystallization from acetone/hexanes to give the pure product as a white crystalline solid (8.02 g, 43.1 mmol, 88 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.19 (s, 1H), 4.65 – 4.53 (m, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.92 – 3.87 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.82, 152.85, 134.61, 61.87, 61.51, 42.71, 14.19. M.p. 96.0–97.4 °C. HRMS (ESI) calculated for $[NaC_7H_{10}N_2O_4]^+$ {M+Na$^+$} requires 209.0533, found 209.0530.



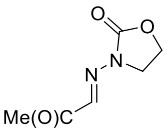
3-(methyleneamino)oxazolidin-2-one (4-52): Synthesized according to general procedure with 3-aminooxazolidin-2-one (0.500 g, 4.9 mmol), paraformaldehyde (0.221 g mL, 7.35 mmol), *p*-TsOH (0.050 g, 0.5 mmol), and toluene (25 mL). Product was purified by column chromatography (gradient 1:2 to 1:1 acetone/pentanes) followed by recrystallization from acetone/hexanes to give the pure product as a white crystalline solid (0.324 g, 2.84 mmol, 58 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.66 (d, *J* = 10.7 Hz, 2H), 6.62 (d, *J* = 10.7 Hz, 2H), 4.60 – 4.44 (m, 2H), 3.85 – 3.71 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 154.26, 133.21, 61.39, 41.21. M.p. 84.4–87.2 °C. HRMS (ESI) calculated for $[C_5H_7N_2O_2]^+$ {M+H$^+$} requires 115.0502, found 115.0500.



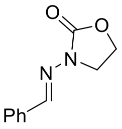
(E)-3-(ethylideneamino)oxazolidin-2-one (4-53): Synthesized according to general procedure with 3-aminooxazolidin-2-one (1.0 g, 9.8 mmol), acetaldehyde (0.83 mL, 14.69 mmol), *p*-TsOH (0.109 g, 1.14 mmol), and toluene (50 mL). Product was purified by column chromatography (gradient 1:2 to 1:1 acetone/pentanes) followed by recrystallization from acetone/hexanes to give the pure product as a white crystalline solid (2.279 g, 7.64 mmol, 78 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.10 (q, *J* = 5.3 Hz, 1H), 4.54 – 4.42 (m, 2H), 3.85 – 3.75 (m, 2H), 2.09 (d, *J* = 5.3 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 154.62, 144.51, 61.33, 42.33, 18.76. M.p. 84.7–88.6 °C. HRMS (ESI) calculated for $[C_5H_9N_2O_2]^+$ {$M+H^+$} requires 129.0659, found 129.0656.



ethyl 2-((2-oxooxazolidin-3-yl)imino)propanoate (4-54): Synthesized according to general procedure with 3-aminooxazolidin-2-one (1.0 g, 9.8 mmol), ethyl 2-oxopropanoate (1.6 mL, 14.69 mmol), *p*-TsOH (0.109 g, 1.14 mmol), and toluene (50 mL). Product was purified by column chromatography (gradient 1:2 to 1:1 acetone/pentanes) followed by recrystallization from acetone/hexanes to give the pure product as a white crystalline solid (2.396 g, 8.03 mmol, 82 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.48 (dd, *J* = 8.1, 6.9 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.04 (dd, *J* = 8.0, 6.9 Hz, 2H), 2.25 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.81, 161.22, 153.31, 62.43, 62.07, 49.31, 17.67, 14.13. M.p. 61.5–63.2 °C. HRMS (ESI) calculated for $[NaC_8H_{12}N_2O_4]^+$ {$M+Na^+$} requires 223.0689, found 223.0687.



(E)-3-((2-oxopropylidene)amino)oxazolidin-2-one (4-55): Synthesized according to general procedure with 3-aminooxazolidin-2-one (.500 g, 4.9 mmol), 2-oxopropanal (40 % aq., 1.17 mL, 7.35 mmol), *p*-TsOH (0.0435 g, .457 mmol), and toluene (25 mL). Product was purified by column chromatography (gradient 1:2 to 1:1 acetone/pentanes) followed by recrystallization from acetone/hexanes to give the pure product as a white crystalline solid (0.543 g, 3.48 mmol, 71 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.00 (s, 1H), 4.76 – 4.48 (m, 2H), 3.95 – 3.76 (m, 2H), 2.49 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 197.57, 152.93, 141.06, 61.51, 42.00, 24.98. M.p. 134.2–135.8 °C. HRMS (ESI) calculated for $[NaC_6H_8N_2O_3]^+$ {$M+Na^+$} requires 179.0427, found 179.0426.

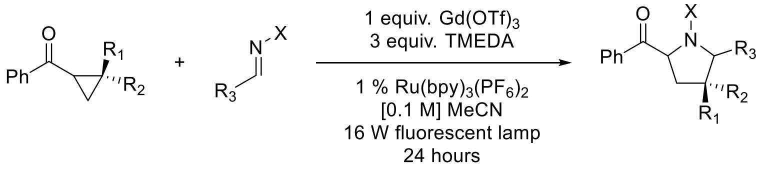


(E)-3-(benzylideneamino)oxazolidin-2-one (4-56): Synthesized according to general procedure with 3-aminooxazolidin-2-one (0.500 g, 4.9 mmol), benzaldehyde

(0.62 g, 5.88 mmol), *p*-TsOH (0.0543 g, 0.57 mmol), and toluene (25 mL). Product was purified by column chromatography (gradient 1:2 to 1:1 acetone/pentanes) followed by recrystallization from acetone/hexanes to give the pure product as a white crystalline solid (1.286 g, 4.31 mmol, 88 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.78 – 7.71 (m, 3H), 7.43 – 7.38 (m, 3H), 4.58 – 4.53 (m, 2H), 3.99 – 3.94 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 154.25, 144.49, 133.74, 130.32, 128.71, 127.51, 61.30, 42.68. M.p. 137–140.1 °C. HRMS (ESI) calculated for $[C_{10}H_{11}N_2O_2]^+$ $\{M+H^+\}$ requires 191.0815, found 191.0813.

4.4.4 Optimization data

Table 4-9. Initial screen for [3 + 2] cycloadditions of phenylcyclopropyl ketones with imine derivatives



Entry	–R$_1$,R$_2$	–R$_3$	–X	% yield[a]	% RSM	% Other
1	–Me,Me	–Ph	–OMe	0 %	80 %	8.5 %
2	–Me,Me	–Ph	–Ts	0 %	100 %	---
3	–CO$_2$*t*-Bu,H	–Ph	–OMe	0 %	100 %	---
4	–Me,Me	–Ph	–C(O)O*t*-Bu	0 %	93 %	---
5	–Me,Me	–H,H	–Ph	0 %	90 %	---
6	–Me,Me	–H,H	–OBn	0 %	90 %	---
7	–Me,Me	–Ph	–N(Me)C(O)Ph	0 %	82 %	---
8	–Me,Me	–H,H	N(Me)C(O)Ph	0 %	97 %	---
9	–Me,Me	–CO$_2$Me	N(Me)C(O)Ph	0 %	100 %	---
10	–CO$_2$*t*-Bu,H	–H,H	–OBn	0 %	97 %	---
11	–Ph,H	–H,H	–OBn	0 %	75 %	---
12[b]	–Me,Me	–H,H	–OBn	53 %	21 %	---
13[b]	–Me,Me	–H,H	–N(Me)C(O)Ph	0 %	53 %	---
14[c]	–Me,Me	–H,H	–OBn	4 %	83 %	---
15[b]	–CO$_2$*t*-Bu,H	–H,H	–OBn	25 %	35 %	20 %
16[b]	–Me,Me	–Ph,H	–OMe	0 %	82 %	---

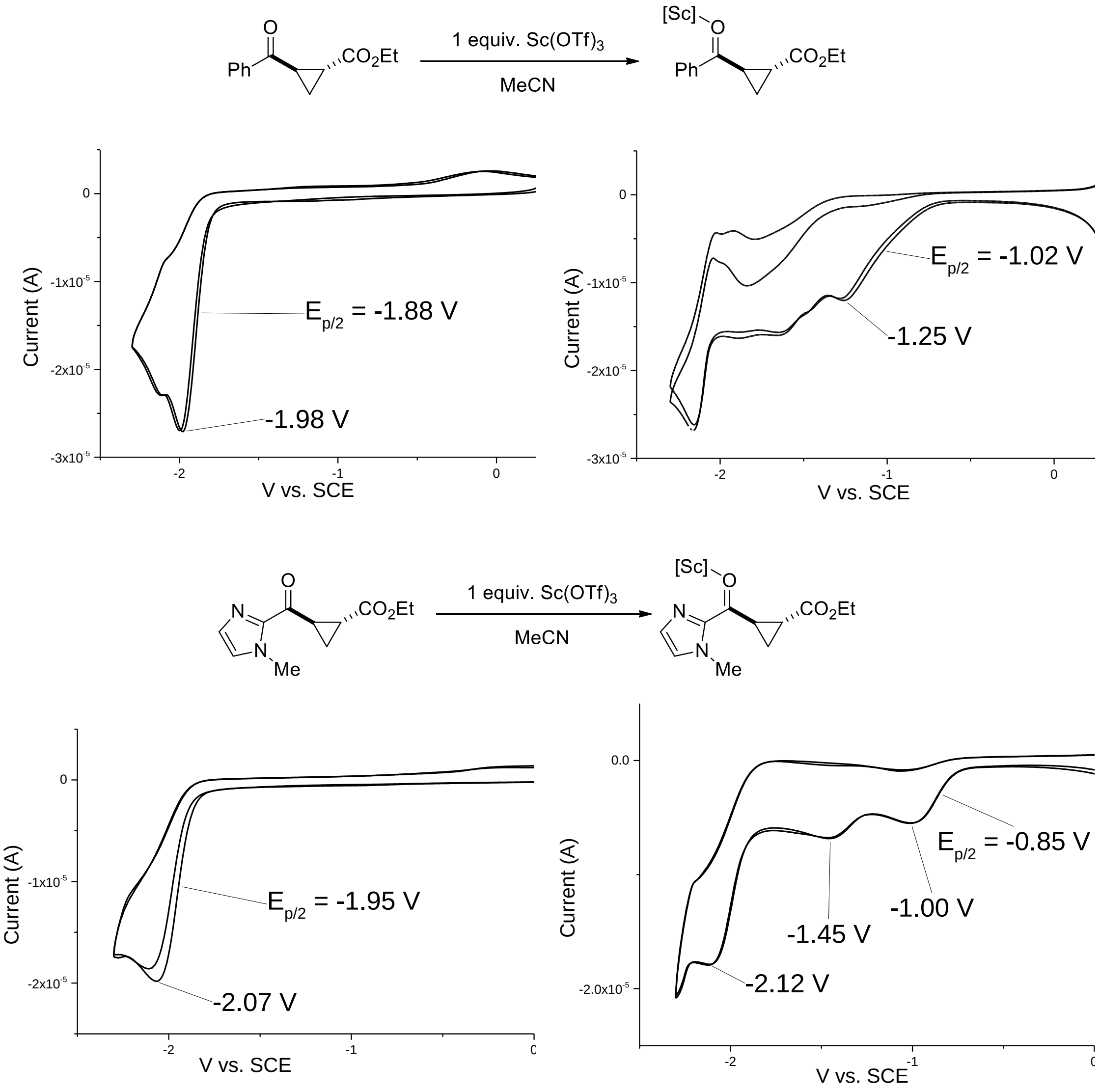
[a] Yields determined by ^{1}H NMR using phenanthrene as internal standard. [b] Reaction carried out with 20 mol % Gd(OTf)$_3$, 40 mol % 4-NMe$_2$-*s*-Bu-pybox, and 2 equiv. DIPEA.

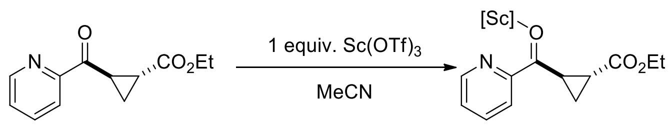
Design of a redox auxiliary system

CV experiments:

Cyclic voltammetry experiments were carried out in dry acetonitrile with 0.1 M tetrabutylammonium hexafluorophosphate as supporting electrolyte and 0.001 M of cyclopropane. A glassy carbon electrode was used as working electrode, platinum wire as counter electrode, and Ag/AgNO$_3$ (0.01M in MeCN) as reference electrode. All potentials were referenced against the Fc$^+$/Fc redox couple in a second experiment. For each experiment the acetonitrile solutions were degasses by sparging with N_2(g) prior to measurements. An initial set of scans were taken at 50 mV/sec. Following initial scans, 1 equiv. $Sc(OTf)_3$ (relative to cyclopropane) was added, the sample was sparged again for 15 min. and another set of scans at 50 mV/sec were taken. Ferrocene was then added for referencing. Half-wave potentials for non-reversible redox waves were determined by the potential at half the peak current relative to the baseline current as recently described by Nicewicz and coworkers.[16]

Figure 4-8. Electrochemical characterization of cyclopropane starting materials





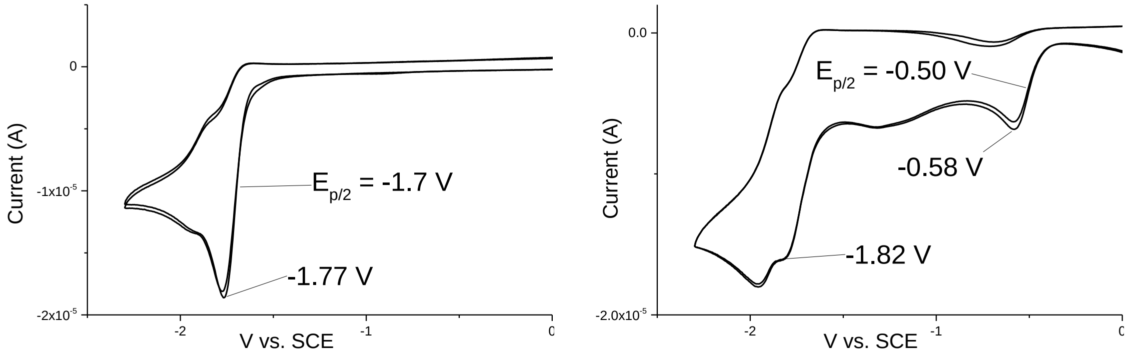
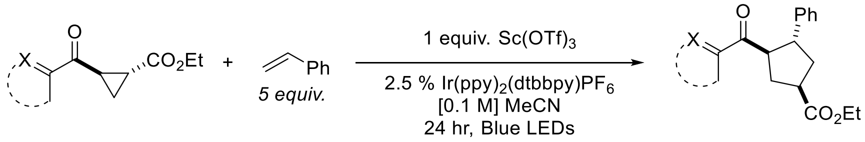


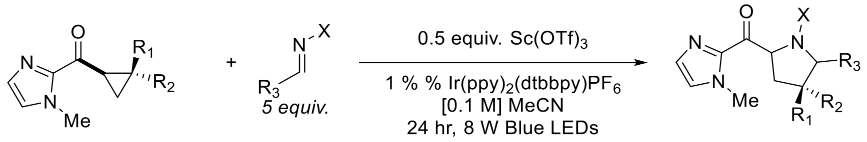
Table 4-10. Screen of redox auxiliaries under photocatalytic conditions



Auxiliary	$E_{p/2}$[a]	% Yield[b]	d.r	% RSM
Phenyl	-1.03 V	0 %	---	100 %
Imidazolyl	*-0.85 V*	*88 %*	*2:1*	*0 %*
Pyridyl	-0.50 V	70 %	1:1	13 %

[a]Versus SCE. b 1H-NMR yield based on phenanthrene.

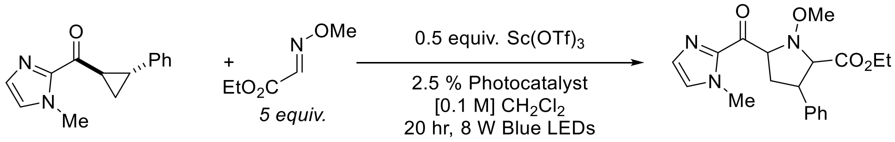
Table 4-11. Initial screen for [3 + 2] cycloadditions of imidazolylcyclopropyl ketones with imine derivatives



Entry	$–R_1$, R_2	$–R_3$	–X	% yield[a]	% RSM
1	$–CO_2$*t*-Bu, H	–H, H	–OBn	75 %	23 %
2	$–CO_2$*t*-Bu, H	$–CO_2Et$, H	–OBn	45 %	50 %
3	–Me, Me	$–CO_2Et$, H	–OBn	trace	40 %
4	$–CO_2$*t*-Bu, H	–Ph, H	–OBn	10 %	27 %
5	–Ph, H	–H, H	–OBn	22 %	15 %
6[b]	–Ph, H	$–CO_2Et$	–OMe	28 %	65 %

[a] Yields determined by ^{1}H NMR using phenanthrene as internal standard. [b] Reaction carried out for 20 hours.

Table 4-12. Photocatalyst optimization



Entry	Photocatalyst	$E_0(PC^+/PC^*)$[a]	$E_0(PC^+/PC)$	% yield[b]	% RSM
1	$Ru(bpy)_3(PF_6)_2$	-0.81 V	1.29 V	0%	100 %
2	$Ir(dF(CF_3)ppy)_2dtbbpyPF_6$	-0.86 V	1.72 V	8%	90 %
3	Ir(dF(*t*-Bu)ppy)$_2$(dtbbpy)PF$_6$	-0.86 V	1.54 V	14%	85 %
4	$Ir(Fppy)_2(dtbbpy)PF_6$	-0.90 V	1.40 V	20%	75 %
5	$Ir(ppy)_2(dtbbpy)PF_6$	-0.98 V	1.23 V	28%	56 %
6	$Ir(ppy)_2(dMeObpy)PF_6$	-1.00 V	1.21 V	32%	54 %
8	$Ir(dtbppy)_2(dtbbpy)PF_6$	-1.04 V	1.13 V	37%	65 %
9	$Ir(4\text{-}CF_3ppy)_3$	-1.41 V	1.04 V	53%	39 %
10	$Ir(dFppy)_3$	-1.62 V	0.98 V	50%	44 %
11	Ir(3-*t*-Buppy)$_3$	-1.66 V	0.70 V	9%	88 %
12	$Ir(ppy)_3$	-1.67 V	0.72 V	8%	98 %

[a] Versus SCE reference electrode. [b] Yields determined by ^{1}H NMR using phenanthrene as internal standard.

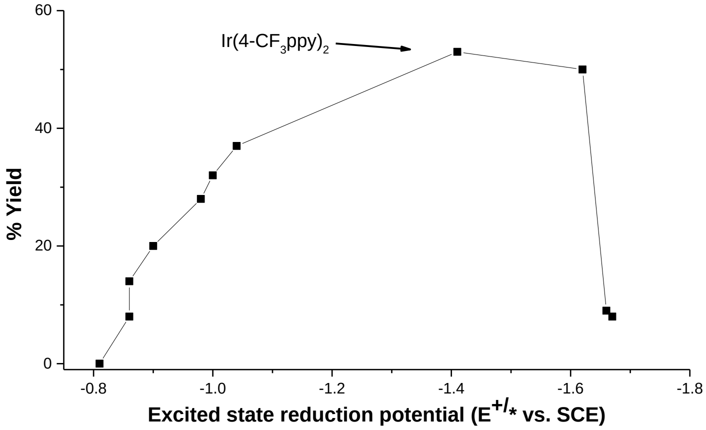
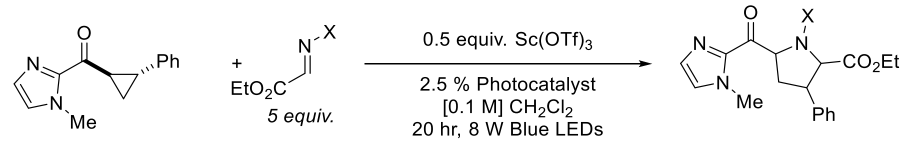
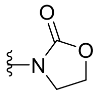
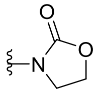


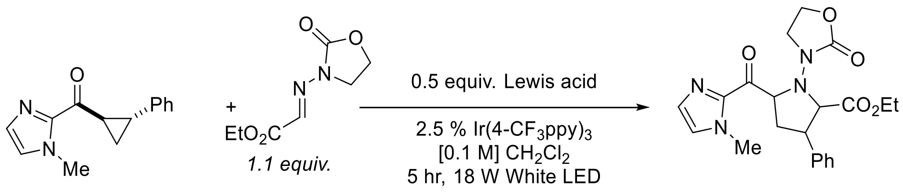
Table 4-13. Optimization of N-protecting group



Entry	–X	% yield[a]	dr	% RSM
1	–OMe	53 %	2:1	34 %
2	–OBn	51 %	2:1	43 %
3	–OH	trace	---	65 %
4	–N(Me)C(O)Me	0 %	---	20 %
5	–N(Me)Ts	12 %	ND	0 %
6		62 %	1:1	36 %
7	–S(O)*t*-Bu	trace	---	97 %
8[b]		70 %	1:1	0 %
9[c]	–OMe	51 %	2.5:1.6:1	16 %

[a] Yields determined by ^{1}H NMR using phenanthrene as internal standard. [b]Reaction carried out with 1.1 equiv. coupling partner and 18W white LED lamp for 24 hours. [c] Reaction carried out with 18W white LED for 24 hours.

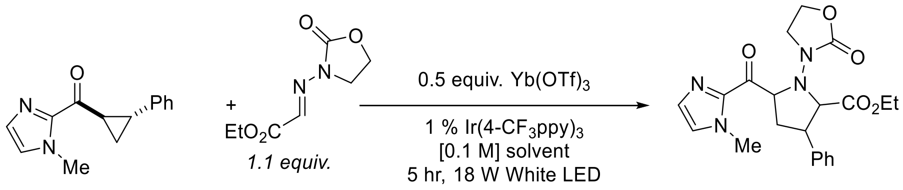
Table 4-14. Lewis acid optimization



Entry	Lewis acid	% yield[a]	dr	% RSM
1	$Sc(OTf)_3$	25 %	1:1	72 %
2	$Al(OTf)_3$	27 %	1.4:1	67 %
3	$La(OTf)_3$	19 %	1.7:1	72 %
4	$Gd(OTf)_3$	35 %	2:1	56 %
5	$Eu(OTf)_3$	0 %	---	95 %
6	$Yb(OTf)_3$	56 %	2:1	40 %
7	*p*-TsOH	17 %	ND	82 %

a Yields determined by ^{1}H NMR using phenanthrene as internal standard

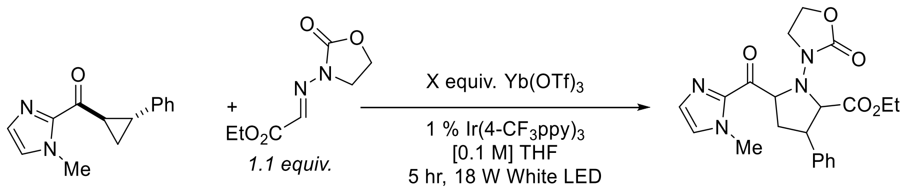
Table 4-15. Solvent Optimization



Entry	Solvent	% yield[a]	dr	% RSM
1	CH_2Cl_2	56 %	2:1	40 %
2	1,2-DCE	37 %	2:1	52 %
3	MeCN	50 %	2.7:1:0.5	23 %
4	EtOAc	trace	---	71 %
5	THF	47 %	3.4:1:0.5	50 %
6	Toluene	3 %	ND	81 %
7	DMSO	0 %	---	85 %
8	Dioxane	27 %	3.2:1	3.2:1

[a] Yields determined by ^{1}H NMR with phenanthrene as internal standard.

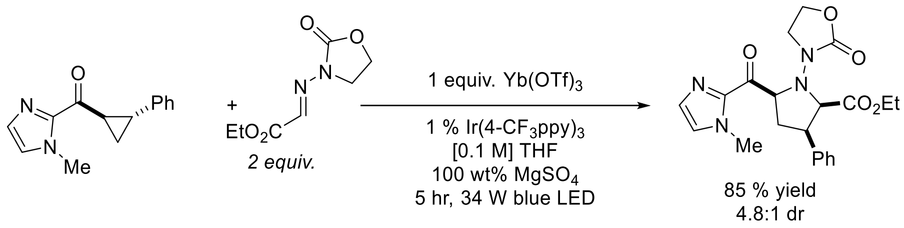
Table 4-16. Equivalents of $Yb(OTf)_3$



Entry	Equiv. [Yb]	% yield	dr	% RSM
1	0.1 equiv.	29 %	1.4:1:0.7	60 %
2	0.3 equiv.	46 %	2:1:0.5	51 %
3	0.5 equiv.	47 %	3.4:1:0.5	50 %
4	1 equiv.	46 %	3.7:1:0.3	54 %

[a] Yields determined by ^1H NMR with phenanthrene as internal standard.

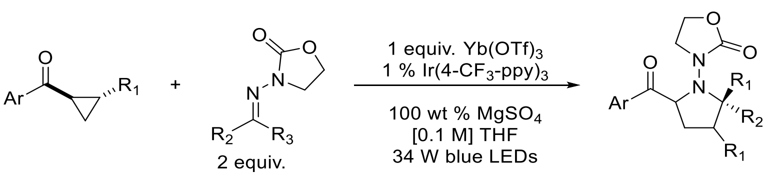
Table 4-17. Final optimization and control studies



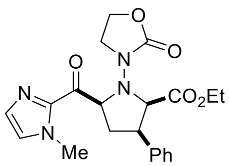
Entry	Change from standard conditions	% yield	dr	% RSM
1	None	85	4.8:1	0
2	1.1 equiv hydrazone	75	3.4:1	10
3	18 W white LED, 1.1 equiv hydrazone	51	3.4:1	47
4	18 W white LED, 1.1 equiv hydrazone, no $MgSO_4$	30	3.4:1	70
5	18 W white LED, 1.1 equiv X, no $MgSO_4$, $Yb(OTf)_3$ hydrate	20	3.4:1	80
6	18 W white LED, 1.1 equiv X, no $MgSO_4$, [0.2 M] in THF	28	5.5:1	66
7	10 % $Yb(OTf)_3$	45	2.5:1	30
8	No photocatalyst	0%	---	80%
9	No light	0%	---	100%
10	No Lewis acid	0%	---	100%

[a] Yields determined by ^1H NMR with phenanthrene as internal standard.

4.4.5 General experimental procedure for [3 + 2] cycloadditions with hydrazones

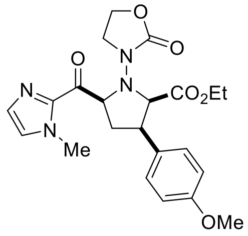


A 25 mL Schlenk tube was charged with $MgSO_4$ and flame dried under vacuum. A flame dried vial was charged with cyclopropane (1 equiv.), hydrazone (2 equiv.), $Yb(OTf)_3$ (1 equiv.), Ir(4-CF_3-ppy)$_3$ (0.01 equiv.) and THF (0.1 M). The vial was briefly sonicated until homogenous and the contents were then transferred to the cooled Schlenk tube and the Schlenk tube was sealed. The reaction mixture was then degassed by three cycles of freeze-pump-thaw and then backfilled with nitrogen. The reaction vessel was then placed 15 cm away from a 34 W blue LED (Kessil) and irradiated for the indicated time. After this time, the reaction mixture was diluted with EtOAc and extracted with H_2O. The aqueous phase was extracted once with H_2O and the combined organic were washed with 10 % aq. K_2CO_3 and brine. The organic layer was then dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was then purified by column chromatography.

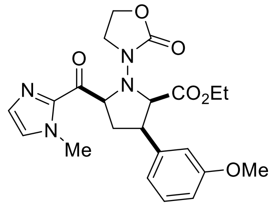


ethyl 5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)-3-phenylpyrrolidine-2-carboxylate (4-10): Reaction was carried out according to the general procedure with (1-methyl-1H-imidazol-2-yl)(2-phenylcyclopropyl)methanone (91.0 mg, 0.4 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (149.0 mg, 0.8 mmol), $Yb(OTf)_3$ (248.0 mg, 0.4 mmol), Ir(4-CF_3-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 8 hours giving the crude product as a yellow oil (5:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt_3 then 2:3 acetone/pentanes) to give the pure product as a white solid (140 mg, 0.34 mmol, 85 % yield). Relative stereochemistry determined by single crystal X-ray crystallography (see below). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.14 (m, 5H), 7.14 (s, 1H), 7.04 (s, 1H), 5.69 (dd, *J* =

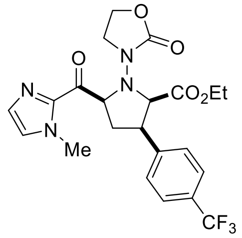
9.5, 8.4 Hz, 1H), 4.89 (d, *J* = 9.2 Hz, 1H), 4.25 (dtd, *J* = 21.1, 8.6, 7.0 Hz, 2H), 4.13 – 3.97 (m, 2H), 4.05 (s, 3H), 3.91 (td, *J* = 8.9, 7.5 Hz, 1H), 3.74 (dq, *J* = 9.3, 6.4, 5.7 Hz, 1H), 3.66 (dq, *J* = 10.7, 7.1, 6.4 Hz, 1H), 3.10 (dt, *J* = 13.0, 8.5 Hz, 1H), 2.20 (ddd, *J* = 13.0, 9.6, 7.3 Hz, 1H), 0.79 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 189.19, 170.68, 155.50, 141.97, 140.90, 129.63, 128.37, 128.12, 127.02, 126.89, 67.68, 66.43, 62.32, 60.31, 46.42, 44.59, 36.08, 35.84, 13.59. M.p. 151–154.5 °C. HRMS (ESI) calculated for $[C_{21}H_{25}N_4O_5]^+$ {M+H$^+$} requires 413.1820, found 413.1820.



ethyl 3-(4-methoxyphenyl)-5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)pyrrolidine-2-carboxylate (4-11): Reaction was carried out with a modified version of the general procedure with (2-(4-methoxyphenyl)cyclopropyl)(1-methyl-1H-imidazol-2-yl)methanone (104.8 mg, 0.41 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (149.0 mg, 0.8 mmol), Yb(OTf)$_3$ (76.0 mg, 0.123 mmol, 0.3 equiv.), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 8 hours giving the crude product as a yellow oil (2:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt$_3$ then 2:3 acetone/pentanes) to give the pure product as a white solid (109 mg, 0.25 mmol, 60 % yield). Major Diastereomer: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.18 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 0.9 Hz, 1H), 7.07 (d, *J* = 0.8 Hz, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.58 (dd, *J* = 9.1, 1.7 Hz, 1H), 4.50 (d, *J* = 8.0 Hz, 1H), 4.28 – 4.14 (m, 4H), 4.08 (dt, *J* = 11.6, 7.8 Hz, 1H), 4.01 (s, 3H), 3.85 – 3.76 (m, 4H), 3.70 (dq, *J* = 10.7, 7.2 Hz, 1H), 3.65 – 3.59 (m, 1H), 2.67 (td, *J* = 12.1, 9.1 Hz, 1H), 2.54 (ddd, *J* = 12.5, 7.6, 1.8 Hz, 1H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 188.89, 172.26, 158.76, 157.70, 143.64, 129.84, 129.16, 129.01, 127.66, 113.64, 68.99, 61.72, 60.50, 59.65, 55.29, 43.80, 40.96, 35.99, 29.50, 13.70. M.p. 186.1–184.3 °C. HRMS (ESI) calculated for $[C_{22}H_{27}N_4O_6]^+$ {M+H$^+$} requires 443.1925, found 443.1925.

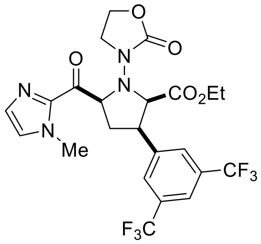


ethyl 3-(3-methoxyphenyl)-5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)pyrrolidine-2-carboxylate (4-12): Reaction was carried out with the general procedure with (2-(3-methoxyphenyl)cyclopropyl)(1-methyl-1H-imidazol-2-yl)methanone (103.2 mg, 0.40 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (149.0 mg, 0.8 mmol), Yb(OTf)$_3$ (248.0 mg, 0.40 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 8 hours giving the crude product as a yellow oil (3.5:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt$_3$ then 2:3 acetone/pentanes) to give the pure product as a colorless oil (150.2 mg, 0.34 mmol, 84 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.16 – 7.10 (m, 2H), 7.03 (d, *J* = 0.9 Hz, 1H), 6.93 (dd, *J* = 2.5, 1.7 Hz, 1H), 6.85 (dt, *J* = 7.6, 1.3 Hz, 1H), 6.72 (ddd, *J* = 8.2, 2.6, 1.0 Hz, 1H), 5.66 (t, *J* = 8.9 Hz, 1H), 4.89 (d, *J* = 8.9 Hz, 1H), 4.32 – 4.18 (m, 2H), 4.10 (ddd, *J* = 9.4, 8.3, 7.2 Hz, 1H), 4.06 – 3.98 (m, 4H), 3.87 (td, *J* = 8.9, 7.0 Hz, 1H), 3.81 – 3.69 (m, 5H), 3.11 (dt, *J* = 13.1, 8.7 Hz, 1H), 2.18 (ddd, *J* = 13.1, 9.1, 6.9 Hz, 1H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 189.26, 170.64, 159.41, 155.51, 142.56, 141.96, 129.63, 129.01, 126.95, 120.68, 113.54, 112.92, 67.58, 66.41, 62.32, 60.32, 55.21, 46.43, 44.68, 36.04, 35.77, 13.65. HRMS (ESI) calculated for $[C_{22}H_{27}N_4O_6]^+$ {M+H$^+$} requires 443.1925, found 443.1925.

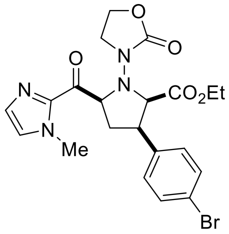


ethyl 5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)-3-(4-(trifluoromethyl)phenyl)pyrrolidine-2-carboxylate (4-13): Reaction was carried out with the general procedure with (1-methyl-1H-imidazol-2-yl)(2-(4-(trifluoromethyl)phenyl)cyclopropyl)methanone (121.3 mg, 0.41 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (149.0 mg, 0.8 mmol), Yb(OTf)$_3$ (248.0 mg, 0.40 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 12 hours giving the crude product as a yellow oil (5:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt$_3$ then 2:3

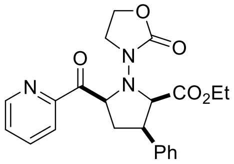
acetone/pentanes) to give the pure product as a white solid (168.1 mg, 0.35 mmol, 85 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 0.9 Hz, 1H), 7.05 (d, *J* = 0.8 Hz, 1H), 5.70 (t, *J* = 9.0 Hz, 1H), 4.96 (d, *J* = 8.9 Hz, 1H), 4.32 – 4.19 (m, 2H), 4.11 (ddd, *J* = 9.5, 8.3, 7.1 Hz, 1H), 4.05 (s, 3H), 4.06 – 3.96 (m, 1H), 3.94 (td, *J* = 8.9, 6.5 Hz, 1H), 3.81 – 3.67 (m, 2H), 3.15 (dt, *J* = 13.2, 8.9 Hz, 1H), 2.16 (ddd, *J* = 13.2, 9.0, 6.6 Hz, 1H), 0.80 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 188.93, 170.20, 155.49, 145.35, 141.87, 129.75, 129.18 (q, *J* = 32.3 Hz), 128.77, 127.17, 125.07 (q, *J* = 3.7 Hz), 124.15 (q, *J* = 272.03), 67.37, 66.10, 62.37, 60.49, 46.42, 44.21, 36.08, 35.53, 13.55. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -62.56. M.p. 175.1–177.6 °C. HRMS (ESI) calculated for $[C_{22}H_{24}F_3N_4O_5]^+$ {M+H$^+$} requires 481.1693, found 481.1694.



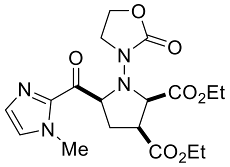
ethyl 3-(3,5-bis(trifluoromethyl)phenyl)-5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)pyrrolidine-2-carboxylate (4-14): Reaction was carried out with the general procedure with (2-(3,5-bis(trifluoromethyl)phenyl)cyclopropyl)(1-methyl-1H-imidazol-2-yl)methanone (147.1 mg, 0.41 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (149.0 mg, 0.8 mmol), Yb(OTf)$_3$ (248.0 mg, 0.40 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 14 hours giving the crude product as a yellow oil (9:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt$_3$ then 2:3 acetone/pentanes) to give the pure product as a white solid (174.0 mg, 0.32 mmol, 78 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.85 (d, *J* = 1.5 Hz, 2H), 7.74 – 7.69 (m, 1H), 7.15 (d, *J* = 0.9 Hz, 1H), 7.05 (d, *J* = 0.9 Hz, 1H), 5.68 (dd, *J* = 9.5, 8.1 Hz, 1H), 5.00 (d, *J* = 8.3 Hz, 1H), 4.33 – 4.19 (m, 2H), 4.09 (ddd, *J* = 9.4, 8.4, 7.1 Hz, 1H), 4.04 (s, 3H), 4.02 – 3.92 (m, 2H), 3.84 – 3.70 (m, 2H), 3.21 (ddd, *J* = 13.4, 9.5, 8.7 Hz, 1H), 2.17 (ddd, *J* = 13.8, 8.2, 5.7 Hz, 1H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 188.63, 169.69, 155.59, 143.67, 141.82, 131.36 (q, *J* = 33.2 Hz), 129.81, 128.89 (q, *J* = 3.8 Hz), 127.22, 123.28 (q, J = 272.8 Hz), 120.85 (sept, J = 7.6 Hz), 67.26, 65.82, 62.44, 60.69, 46.45, 44.25, 36.04, 34.97, 13.52. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -62.92. M.p. 159.8–161.4 °C. HRMS (ESI) calculated for $[C_{23}H_{23}F_6N_4O_5]^+$ {M+H$^+$} requires 549.1567, found 549.1570.



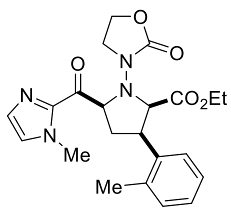
ethyl 3-(4-bromophenyl)-5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)pyrrolidine-2-carboxylate (4-15): Reaction was carried out with the general procedure with (2-(4-bromophenyl)cyclopropyl)(1-methyl-1H-imidazol-2-yl)methanone (123.4 mg, 0.40 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (149.0 mg, 0.8 mmol), Yb(OTf)$_3$ (248.0 mg, 0.40 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 8 hours giving the crude product as a yellow oil (5:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt$_3$ then 2:3 acetone/pentanes) to give the pure product as a white solid (159 mg, 0.32 mmol, 85 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 (d, J = 8.5 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 0.9 Hz, 1H), 7.04 (d, J = 0.9 Hz, 1H), 5.67 (t, J = 9.0 Hz, 1H), 4.91 (d, J = 8.9 Hz, 1H), 4.31 – 4.19 (m, 2H), 4.09 (ddd, J = 9.4, 8.3, 7.1 Hz, 1H), 4.04 (s, 3H), 4.00 (ddd, J = 9.3, 8.3, 6.8 Hz, 1H), 3.84 (td, J = 9.0, 6.8 Hz, 1H), 3.81 – 3.69 (m, 2H), 3.11 (dt, J = 13.2, 8.8 Hz, 1H), 2.12 (ddd, J = 13.2, 9.1, 6.7 Hz, 1H), 0.87 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 189.04, 170.32, 155.47, 141.88, 140.19, 131.20, 130.16, 129.71, 127.11, 120.83, 67.39, 66.14, 62.34, 60.47, 46.41, 43.93, 36.07, 35.67, 13.70. M.p. 169.0–172.3 °C. HRSM (ESI) calculated for $[C_{21}H_{24}BrN_4O_5]^+$ {M+H$^+$} requires 491.0925, found 491.0925.



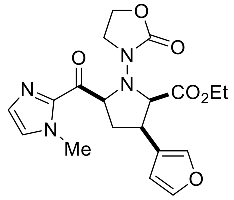
ethyl 1-(2-oxooxazolidin-3-yl)-3-phenyl-5-picolinoylpyrrolidine-2-carboxylate (4-21): Reaction was carried out with a modified version of the general procedure with (2-phenylcyclopropyl)(pyridin-2-yl)methanone (89.4 mg, 0.40 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (224.0 mg, 1.20 mmol), Sc(OTf)$_3$ (99.0 mg, 0.20 mmol, 0.5 equiv.), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 8 hours giving the crude product as a yellow oil (20:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt_3 then 1:3 acetone/pentanes) to give the pure product as a colorless oil in a 20:1 mixture of two inseparable diastereomers (65.6 mg, 0.16 mmol, 40 % yield). Product decomposes slowly at room temperature. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.65 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.08 (d, *J* = 7.9 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.46 (ddd, *J* = 7.5, 4.7, 1.2 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.20 – 7.12 (m, 1H), 5.89 (t, *J* = 9.1 Hz, 1H), 4.96 (d, *J* = 9.1 Hz, 1H), 4.32 – 4.20 (m, 2H), 4.19 – 4.11 (m, 2H), 3.89 (td, *J* = 9.0, 6.7 Hz, 1H), 3.79 – 3.65 (m, 2H), 3.18 (dt, *J* = 13.1, 8.9 Hz, 1H), 2.06 (ddd, *J* = 13.1, 9.5, 6.8 Hz, 1H), 0.81 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 198.20, 170.51, 155.56, 152.48, 149.05, 141.20, 136.80, 128.37, 128.11, 127.36, 126.88, 122.31, 67.42, 66.02, 62.45, 60.30, 46.54, 44.54, 35.51, 13.60. HRMS (ESI) calculated for $[C_{22}H_{24}N_3O_5]^+$ {M+H$^+$} requires 410.1711, found 410.1707.



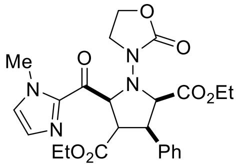
diethyl 5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)pyrrolidine-2,3-dicarboxylate (4-20): Reaction was carried out with a modified version of the general procedure with ethyl 2-(1-methyl-1H-imidazole-2-carbonyl)cyclopropanecarboxylate (89.0 mg, 0.40 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (372.0 mg, 2.0 mmol), $Sc(OTf)_3$ (98.0 mg, 0.20 mmol), Ir(4-CF_3-ppy)$_3$ (3.4 mg, 0.004 mmol), and MeCN (4 mL). The reaction was complete after 20 hours giving the crude product as a yellow oil (1.2:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt_3 then 2:3 acetone/pentanes) to give the pure product in a 1.2:1 ratio of separable diastereomers (83.0 mg, 0.20 mmol, 51 % yield). Major diastereomer: Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.12 (d, *J* = 0.9 Hz, 1H), 7.06 (d, *J* = 0.9 Hz, 1H), 5.53 (dd, *J* = 9.3, 2.3 Hz, 1H), 4.46 (d, *J* = 7.8 Hz, 1H), 4.23 – 4.09 (m, 7H), 3.98 (s, 3H), 3.67 – 3.59 (m, 2H), 2.69 (ddd, *J* = 12.8, 11.0, 9.3 Hz, 1H), 2.48 (ddd, *J* = 12.8, 8.4, 2.3 Hz, 1H), 1.33 – 1.19 (m, 6H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 188.70, 171.14, 171.05, 157.14, 143.14, 129.37, 127.69, 64.24, 61.70, 61.24, 61.02, 60.00, 43.86, 41.93, 35.99, 27.87, 14.10, 14.05. HRMS (ESI) calculated for $[C_{18}H_{25}N_4O_7]^+$ {M+H$^+$} requires 409.1718, found 409.1719. Minor diastereomer: Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.14 (d, *J* = 0.9 Hz, 1H), 7.04 (d, *J* = 0.9 Hz, 1H), 5.44 (dd, *J* = 8.7, 7.9 Hz, 1H), 4.55 (d, *J* = 8.3 Hz, 1H), 4.28 (ddd, *J* = 9.4, 8.6, 6.1 Hz, 1H), 4.25 – 4.15 (m, 3H), 4.15 – 4.08 (m, 2H), 4.02 – 3.94 (m, 4H), 3.79 (ddd, *J* = 9.2, 8.3, 6.1 Hz, 1H), 3.64 (q, *J* = 8.2 Hz, 1H), 2.93 (dt, *J* = 12.8, 7.8 Hz, 1H), 2.42 (dt, *J* = 12.8, 8.6 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 188.57, 170.96, 170.77, 155.74, 141.95, 129.56, 127.02, 67.24, 65.41, 62.23, 60.9, 60.9, 46.54, 44.45, 35.97, 31.21, 14.09, 14.05. HRMS (ESI) calculated for $[C_{18}H_{25}N_4O_7]^+$ {M+H$^+$} requires 409.1718, 409.1718.



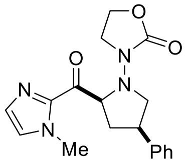
ethyl 5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)-3-(o-tolyl)pyrrolidine-2-carboxylate (4-16): Reaction was carried out with the general procedure with (1-methyl-1H-imidazol-2-yl)(2-(o-tolyl)cyclopropyl)methanone (96.0 mg, 0.40 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (149.0 mg, 0.8 mmol), Yb(OTf)$_3$ (248.0 mg, 0.40 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 12 hours giving the crude product as a yellow oil (4:1 d.r.). Product was purified by column chromatography (3:1:1 hexanes/EtOH/NEt$_3$) and recrystallization (acetone/pentanes liquid/liquid diffusion) to give the pure product as a white crystalline solid (128.0 mg, 0.30 mmol, 75 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.33 – 7.30 (m, 1H), 7.14 (d, *J* = 0.9 Hz, 1H), 7.12 – 7.05 (m, 3H), 7.04 (d, *J* = 0.9 Hz, 1H), 5.69 (dd, *J* = 10.2, 7.4 Hz, 1H), 4.82 (d, *J* = 9.7 Hz, 1H), 4.35 – 4.18 (m, 3H), 4.09 – 3.95 (m, 5H), 3.69 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.58 (dq, *J* = 10.7, 7.1 Hz, 1H), 2.98 (dt, *J* = 12.5, 7.6 Hz, 1H), 2.38 (s, 3H), 2.32 (dt, *J* = 12.6, 9.8 Hz, 1H), 0.74 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 189.21, 171.04, 155.66, 142.06, 138.27, 136.72, 129.78, 129.60, 127.04, 126.99, 126.74, 126.01, 67.00, 66.94, 62.24, 60.26, 46.47, 40.52, 36.07, 35.19, 19.91, 13.47. M.p. 156.9–158.6 °C. HRMS (ESI) calculated for $[C_{22}H_{27}N_4O_5]^+$ {M+H$^+$} requires 427.1976, found 427.1978.



ethyl 3-(furan-3-yl)-5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)pyrrolidine-2-carboxylate (4-18): Reaction was carried out with the general procedure with (2-(furan-3-yl)cyclopropyl)(1-methyl-1H-imidazol-2-yl)methanone (86.0 mg, 0.40 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (149.0 mg, 0.8 mmol), Yb(OTf)$_3$ (248.0 mg, 0.40 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 8 hours giving the crude product as a yellow oil (4:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt$_3$ then 2:3 acetone/pentanes) to give the product as a clear oil in a 4:1 mixture of two inseparable diastereomers (113.0 mg, 0.28 mmol, 70 % yield). Product decomposes at room temperature. Major Diastereomer: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 2H), 7.13 (d, *J* = 0.9 Hz, 1H), 7.05 (d, *J* = 0.9 Hz, 1H), 6.39 (dd, *J* = 2.0, 0.9 Hz, 1H), 5.58 (t, *J* = 8.8 Hz, 1H), 4.76 (d, *J* = 8.3 Hz, 1H), 4.31 – 4.13 (m, 3H), 4.04 (s, 3H), 3.93 (q, *J* = 7.4 Hz, 2H), 3.81 (td, *J* = 8.2, 6.5 Hz, 1H), 3.04 (ddd, *J* = 13.0, 9.2, 8.1 Hz, 1H), 2.11 (ddd, *J* = 13.0, 8.4, 6.6 Hz, 1H), 1.03 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 189.20, 170.71, 155.60, 143.10, 142.52, 140.00, 129.59, 127.02, 124.19, 110.76, 67.35, 66.26, 62.26, 60.46, 46.38, 36.06, 35.72, 35.34, 13.82. HRMS (ESI) calculated for $[C_{19}H_{23}N_4O_6]^+$ {M+H$^+$} requires 403.1612, found 403.1609. Minor diastereomer: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.40 (m, 1H), 7.37 – 7.35 (m, 1H), 7.14 (d, *J* = 0.9 Hz, 1H), 7.07 (d, *J* = 0.9 Hz, 1H), 6.58 (dd, *J* = 2.0, 0.9 Hz, 1H), 5.65 (dd, *J* = 8.5, 5.8 Hz, 1H), 4.35 (d, *J* = 7.0 Hz, 1H), 4.24 – 4.10 (m, 3H), 4.09 – 4.00 (m, 1H), 4.00 (s, 3H), 3.98 – 3.93 (m, 1H), 3.81 – 3.74 (m, 1H), 3.57 (dt, *J* = 9.2, 7.1 Hz, 1H), 2.77 (dt, *J* = 12.9, 8.8 Hz, 1H), 2.23 (ddd, *J* = 13.0, 7.2, 5.8 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 189.36, 171.23, 156.85, 142.91, 141.93, 139.37, 129.33, 127.50, 125.78, 109.95, 68.21, 64.88, 61.72, 61.27, 43.76, 36.38, 36.13, 33.26, 14.08.



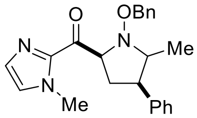
diethyl 5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)-3-phenylpyrrolidine-2,4-dicarboxylate (4-19): Reaction was carried out with the general procedure with ethyl 2-(1-methyl-1H-imidazole-2-carbonyl)-3-phenylcyclopropanecarboxylate (119.0 mg, 0.40 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (149.0 mg, 0.8 mmol), Yb(OTf)$_3$ (248.0 mg, 0.40 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was stopped after 24 hours giving the crude product as a yellow oil (7:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt$_3$ then 2:3 acetone/pentanes) to give the product as colorless oil (73.6 mg, 0.15 mmol, 38 % yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.36 (m, 2H), 7.30 – 7.25 (m, 3H), 7.23 – 7.18 (m, 1H), 7.17 (s, 1H), 7.08 (s, 1H), 5.96 (d, *J* = 8.7 Hz, 1H), 5.05 (d, *J* = 9.2 Hz, 1H), 4.25 – 4.17 (m, 1H), 4.14 – 4.00 (m, 8H), 3.78 – 3.63 (m, 2H), 3.63 – 3.53 (m, 2H), 1.09 (t, *J* = 7.1 Hz, 3H), 0.79 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 187.52, 171.47, 169.64, 155.38, 142.73, 140.04, 129.99, 128.68, 128.28, 127.63, 127.29, 67.48, 66.20, 62.04, 61.23, 60.49, 51.96, 47.32, 36.03, 29.71, 13.90, 13.55. HRMS (ESI) calculated for $[C_{24}H_{29}N_4O_7]^+$ {M+H$^+$} requires 485.2031, found 485.2032.



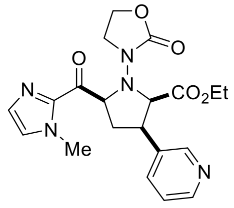
3-(2-(1-methyl-1H-imidazole-2-carbonyl)-4-phenylpyrrolidin-1-yl)oxazolidin-2-one (4-22): Reaction was carried out with the general procedure with (1-methyl-1H-imidazol-2-yl)(2-phenylcyclopropyl)methanone (91.0 mg, 0.40 mmol), 3-(methyleneamino)oxazolidin-2-one (91.0 mg, 0.8 mmol), Yb(OTf)$_3$ (248.0 mg, 0.40 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 12 hours giving the crude product as a yellow oil (5:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt$_3$ and 9:1 EtOAc/pentanes) and to give the product in a 13:1 mixture of diastereomers as a white solid (95.0 mg, 0.28 mmol, 70 % yield). ^{1}H

NMR (500 MHz, Chloroform-*d*) δ 7.33 – 7.27 (m, 4H), 7.23 – 7.17 (m, 1H), 7.14 (d, *J* = 0.9 Hz, 1H), 7.04 (d, *J* = 0.9 Hz, 1H), 5.59 (dd, *J* = 10.6, 6.7 Hz, 1H), 4.33 – 4.20 (m, 2H), 4.03 (s, 3H), 3.89 – 3.72 (m, 4H), 3.48 (dd, *J* = 9.0, 7.4 Hz, 1H), 2.92 (dt, *J* = 12.0, 6.8 Hz, 1H), 2.08 (dt, *J* = 12.6, 10.3 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 190.06, 155.94, 142.80, 142.36, 129.52, 128.54, 127.28, 127.12, 126.55, 67.63, 61.60, 58.34, 44.66, 42.54, 38.18, 36.08. HRMS (ESI) calculated for $[C_{18}H_{21}N_4O_3]^+$ {M+H$^+$} requires 341.1608, found 341.1606.

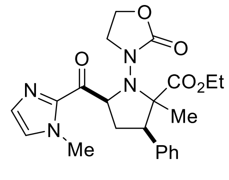
3-(2-(1-methyl-1H-imidazole-2-carbonyl)-4-phenylpyrrolidin-1-yl)oxazolidin-2-one (4-23):



Reaction was carried out with a modified version of the general procedure with (1-methyl-1H-imidazol-2-yl)(2-phenylcyclopropyl)methanone (91.0 mg, 0.40 mmol), (E)-acetaldehyde O-benzyl oxime (298.0 mg, 2.0 mmol), Sc(OTf)$_3$ (98.0 mg, 0.20 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and CH$_2$Cl$_2$ (4 mL). The reaction of irradiated with a 8 W blue LED strip. The reaction was stopped after 72 hours giving the crude product as a yellow oil (10:1 d.r.). Product was purified by column chromatography (1:4 acetone/pentanes) to give the product as a colorless oil as an inseparable mixture of two diastereomers (90.2 mg, 0.24 mmol, 60 % yield, 10:1 dr). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 7.0 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.33 – 7.19 (m, 4H), 7.06 – 7.00 (m, 3H), 4.51 (d, *J* = 10.2 Hz, 1H), 4.25 (d, *J* = 10.2 Hz, 1H), 4.16 – 4.04 (m, 2H), 4.01 (s, 3H), 3.42 (dq, *J* = 9.3, 6.1 Hz, 1H), 2.33 – 2.20 (m, 2H), 1.33 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 192.95, 142.94, 141.84, 137.22, 129.36, 128.78, 128.36, 128.21, 128.10, 127.69, 127.49, 127.40, 77.27, 70.99, 65.34, 48.21, 36.26, 34.33, 18.33. HRMS (ESI) calculated for $[C_{23}H_{26}N_3O_2]^+$ {M+H$^+$} requires 376.2020, found 376.2016.



ethyl 5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)-3-(pyridin-3-yl)pyrrolidine-2-carboxylate (4-17): Reaction was carried out with a modified version of the general procedure with (1-methyl-1H-imidazol-2-yl)(2-(pyridin-3-yl)cyclopropyl)methanone (91.0 mg, 0.40 mmol), (E)-ethyl 2-((2-oxooxazolidin-3-yl)imino)acetate (149.0 mg, 0.8 mmol), Yb(OTf)$_3$ (149.0 mg, 0.20 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was complete after 8 hours giving the crude product as a yellow oil (5:1 d.r.). Product was purified twice by column chromatography (3:1:1 hexanes/EtOH/NEt$_3$ then 3:1 acetone/pentanes) to give the pure product as a colorless oil in a mixture of inseparable diastereomers (62.8 mg, 0.15 mmol, 38 % yield, 6.5:1:0.5 dr). Product decomposes at room temperature. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.47 (dd, *J* = 2.4, 0.8 Hz, 1H), 8.44 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.79 (dt, *J* = 8.0, 1.9 Hz, 1H), 7.21 (ddd, *J* = 8.0, 4.7, 0.8 Hz, 1H), 7.15 (d, *J* = 0.9 Hz, 1H), 7.05 (d, *J* = 0.9 Hz, 1H), 5.70 (t, *J* = 9.0 Hz, 1H), 4.98 (d, *J* = 8.6 Hz, 1H), 4.31 – 4.19 (m, 2H), 4.15 – 4.08 (m, 1H), 4.05 (s, 3H), 3.99 (ddd, *J* = 9.2, 8.3, 6.9 Hz, 1H), 3.86 (td, *J* = 8.8, 6.0 Hz, 1H), 3.82 – 3.70 (m, 2H), 3.17 (dt, *J* = 13.4, 9.1 Hz, 1H), 2.13 (ddd, *J* = 13.3, 8.7, 6.0 Hz, 1H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 188.94, 170.02, 155.48, 149.91, 148.45, 141.87, 136.84, 135.77, 129.80, 127.18, 123.29, 67.26, 65.83, 62.38, 60.59, 46.40, 41.74, 36.07, 35.33, 13.71. HRMS (ESI) calculated for [C$_{20}$H$_{24}$N$_5$O$_5$]$^+$ {M+H$^+$} requires 414.1772, found 414.1772.



ethyl 2-methyl-5-(1-methyl-1H-imidazole-2-carbonyl)-1-(2-oxooxazolidin-3-yl)-3-phenylpyrrolidine-2-carboxylate (4-24): Reaction was carried out with the general procedure with (1-methyl-1H-imidazol-2-yl)(2-(pyridin-3-yl)cyclopropyl)methanone (91.0 mg, 0.40 mmol), ethyl 2-((2-oxooxazolidin-3-yl)imino)propanoate (160.0 mg, 0.8 mmol), Yb(OTf)$_3$ (248.0 mg, 0.40 mmol), Ir(4-CF$_3$-ppy)$_3$ (3.4 mg, 0.004 mmol), and THF (4 mL). The reaction was quenched after 72 hours giving the crude product as a yellow oil (>10:1 d.r.). Product was purified twice by column chromatography (8:1:1

hexanes/EtOH/NEt$_3$ then 2:1 acetone/pentanes) to give the product as a colorless oil with minor impurities (52.9 mg, 0.12 mmol, 31 % yield, >10:1 dr; 65 % RSM). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.26 – 7.17 (m, 5H), 7.13 (d, *J* = 0.9 Hz, 1H), 7.02 (d, *J* = 0.9 Hz, 1H), 6.00 (dd, *J* = 9.7, 7.6 Hz, 1H), 4.30 – 4.24 (m, 2H), 4.10 (q, *J* = 8.9 Hz, 1H), 4.05 (s, 3H), 3.89 – 3.82 (m, 1H), 3.80 – 3.73 (m, 1H), 3.72 – 3.64 (m, 1H), 3.52 (dd, *J* = 10.5, 7.3 Hz, 1H), 2.96 (dt, *J* = 12.4, 7.4 Hz, 1H), 2.48 (q, *J* = 10.4 Hz, 1H), 1.64 (s, 3H), 0.88 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 189.89, 173.17, 157.03, 142.03, 138.96, 129.46, 128.33, 128.11, 127.18, 126.78, 73.73, 64.41, 62.01, 60.49, 54.00, 47.29, 36.07, 33.42, 20.20, 13.64. HRMS (ESI) calculated for $[C_{22}H_{26}N_4O_5]^+$ {M+H$^+$} requires 427.1976, found 427.1976.

4.4.6 Crystallographic Experimental Section

Data Collection

A colorless crystal with approximate dimensions 0.116 x 0.079 x 0.030 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 SMART APEXII diffractometer with Cu K$_\alpha$ (λ = 1.54178 Å) radiation and the diffractometer to crystal distance of 4.03 cm [1].

The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 41 frames collected at intervals of 0.6º in a 25º range about ω with the exposure time of 20 seconds per frame. The reflections were successfully indexed by an automated indexing routine built in the APEX3 program. The final cell constants were calculated from a set of 4336 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 0.80 Å. A total of 30871 data were harvested by collecting 20 sets of frames with 0.7º scans in ω and φ with an exposure time 20-50 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. [2]

Structure Solution and Refinement

The systematic absences in the diffraction data were uniquely consistent for the space group *P*2$_1$/*n* that yielded chemically reasonable and computationally stable results of refinement [3-8].

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 were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients.

The relative configuration is 4C-*S*, 5C-*S* and 7C-*R*. The two stereoisomers present in the crystal structure are *SSR* and *RRS*.

The final least-squares refinement of 273 parameters against 3870 data resulted in residuals R (based on F^2 for $I \geq 2\sigma$) and wR (based on F^2 for all data) of 0.0394 and 0.0990, respectively. The final difference Fourier map was featureless.

Summary

Crystal Data for $C_{21}H_{24}N_4O_5$ (M =412.44 g/mol): monoclinic, space group $P2_1/n$ (no. 14), a = 11.6421(10) Å, b = 8.1352(9) Å, c = 20.7146(14) Å, β = 99.782(7)°, V = 1933.4(3) Å^3, Z = 4, T = 100.03 K, μ(CuKα) = 0.851 mm^{-1}, *Dcalc* = 1.417 g/cm^3, 30871 reflections measured (8.174° ≤ 2Θ ≤ 147.3°), 3870 unique (R_{int} = 0.0574, R_{sigma} = 0.0353) which were used in all calculations. The final R_1 was 0.0394 (I > 2σ(I)) and wR_2 was 0.0990 (all data).

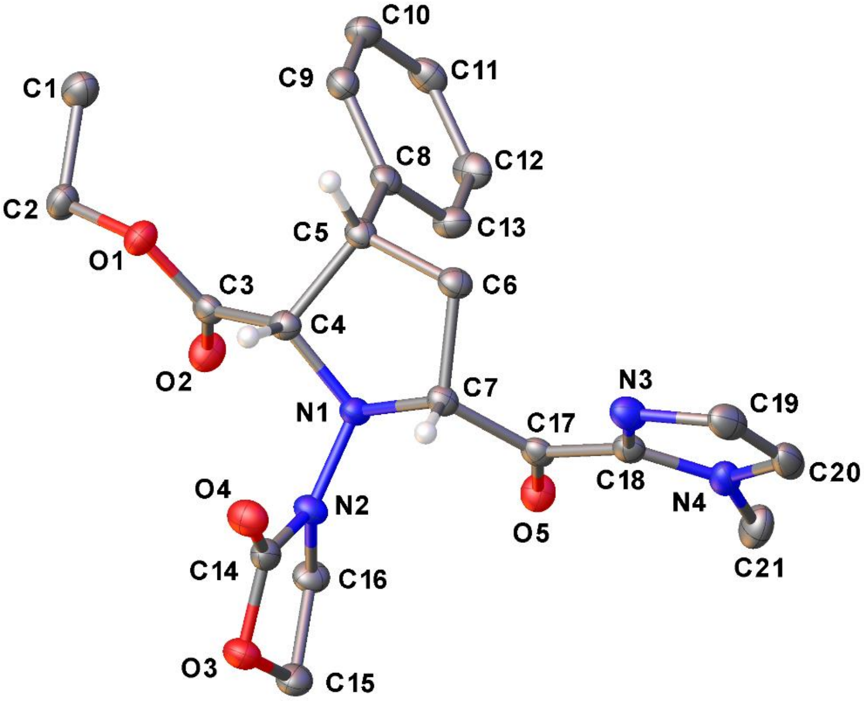


Figure 4-9. A molecular drawing of 4-10 shown with 50% probability ellipsoids. All H atoms, except for H atoms bonded to the chiral centers, are omitted.

Table 4-18. Crystal data and structure refinement for 4-10

Identification code	Yoon48
Empirical formula	$C_{21}H_{24}N_4O_5$
Formula weight	412.44
Temperature/K	100.03
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	11.6421(10)
b/Å	8.1352(9)
c/Å	20.7146(14)
α/°	90
β/°	99.782(7)
γ/°	90
Volume/Å^3	1933.4(3)
Z	4
ρ_{calc}g/cm^3	1.417
μ/mm^{-1}	0.851

F(000)	872.0
Crystal size/mm^3	0.116 × 0.079 × 0.03
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	8.174 to 147.3
Index ranges	$-14 \le h \le 14$, $-10 \le k \le 9$, $-25 \le l \le 25$
Reflections collected	30871
Independent reflections	3870 [R_{int} = 0.0574, R_{sigma} = 0.0353]
Data/restraints/parameters	3870/0/273
Goodness-of-fit on F^2	1.011
Final R indexes [I>=2σ (I)]	R_1 = 0.0394, wR_2 = 0.0923
Final R indexes [all data]	R_1 = 0.0513, wR_2 = 0.0990
Largest diff. peak/hole / e Å^{-3}	0.34/-0.17

Table 4-19. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 4-10. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
O1	6167.8(9)	6914.2(14)	1307.2(5)	22.1(2)

O2	4278.7(9)	6615.2(15)	1420.1(5)	25.2(3)
O3	4055.6(10)	10083.3(14)	3263.6(6)	25.4(3)
O4	5933.4(10)	9285.8(14)	3353.0(6)	26.5(3)
O5	3625.6(9)	4437.9(14)	3493.5(5)	22.6(2)
N1	4979.7(11)	6154.0(15)	2783.4(6)	17.6(3)
N2	4402.4(11)	7617.5(16)	2892.0(6)	19.0(3)
N3	6237.4(12)	3860.4(17)	4648.6(7)	23.4(3)
N4	4523.0(12)	2679.7(16)	4692.6(7)	22.8(3)
C1	6415.7(16)	5777(2)	265.3(9)	28.7(4)
C2	5889.0(15)	7149(2)	602.1(8)	24.3(3)
C3	5299.2(13)	6620.0(18)	1642.6(8)	18.3(3)
C4	5844.6(12)	6280.2(18)	2347.3(7)	17.5(3)
C5	6454.6(12)	4572.0(18)	2436.3(7)	18.4(3)
C6	6450.5(13)	4179.9(19)	3168.6(8)	20.3(3)
C7	5553.3(12)	5362.0(18)	3392.6(7)	17.3(3)
C8	5874.6(13)	3259.8(18)	1971.2(7)	18.7(3)
C9	6405.1(13)	2770.0(19)	1446.7(8)	21.0(3)

C10	5899.5(14)	1584(2)	1005.8(8)	24.4(3)
C11	4855.8(14)	858(2)	1082.7(8)	25.0(3)
C12	4325.0(14)	1314(2)	1606.6(9)	26.1(4)
C13	4827.5(14)	2506(2)	2048.1(8)	23.7(3)
C14	4908.3(13)	8991.2(19)	3179.1(8)	21.0(3)
C15	2940.6(14)	9217(2)	3145.2(8)	25.1(4)
C16	3143.4(13)	7785(2)	2709.4(8)	22.6(3)
C17	4657.6(13)	4487.9(18)	3726.3(7)	18.2(3)
C18	5137.1(13)	3694.1(18)	4351.7(8)	19.6(3)
C19	6322.2(15)	2921(2)	5198.7(8)	27.6(4)
C20	5278.3(16)	2180(2)	5230.4(8)	27.9(4)
C21	3281.8(16)	2271(2)	4552.1(9)	30.5(4)

Table 4-20. Anisotropic Displacement Parameters (Å^2×10^3) for 4-10. 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}**
O1	22.9(5)	25.6(6)	18.6(5)	0.7(5)	5.8(4)	-1.0(4)
O2	20.4(6)	32.8(6)	21.2(6)	3.4(5)	0.5(4)	0.0(5)
O3	27.1(6)	20.6(6)	29.5(6)	-	7.7(5)	5.2(5)

				1.3(5)		
O4	24.1(6)	22.8(6)	32.1(6)	-4.5(5)	3.3(5)	-1.6(4)
O5	20.2(5)	25.7(6)	20.9(5)	1.2(5)	0.2(4)	-1.8(4)
N1	19.2(6)	17.3(6)	16.5(6)	0.5(5)	3.3(5)	4.2(5)
N2	18.2(6)	17.7(6)	20.4(6)	-0.6(5)	1.4(5)	4.3(5)
N3	26.0(7)	24.2(7)	18.9(7)	0.1(5)	0.4(5)	6.2(5)
N4	32.2(7)	18.5(6)	18.3(6)	-0.2(5)	6.4(5)	0.3(5)
C1	35.7(9)	26.1(9)	26.1(9)	-1.9(7)	10.5(7)	-0.9(7)
C2	32.3(8)	23.5(8)	18.4(8)	0.5(6)	7.9(6)	-0.5(6)
C3	20.9(7)	12.8(7)	21.8(8)	-1.0(6)	4.8(6)	0.1(5)
C4	16.4(7)	16.9(7)	19.1(7)	-1.7(6)	2.9(6)	-0.3(5)
C5	16.0(6)	18.5(7)	20.6(7)	0.9(6)	2.5(6)	1.7(5)
C6	19.2(7)	20.4(8)	20.6(8)	-	1.5(6)	3.8(6)

				0.1(6)		
C7	17.7(7)	17.0(7)	16.2(7)	-0.5(6)	0.0(5)	1.8(6)
C8	18.9(7)	16.7(7)	19.7(7)	1.5(6)	1.2(6)	4.1(6)
C9	20.6(7)	19.6(8)	23.1(8)	1.2(6)	4.5(6)	1.0(6)
C10	29.5(8)	22.1(8)	22.5(8)	-2.5(7)	7.0(6)	3.5(6)
C11	28.0(8)	18.4(7)	26.9(9)	-4.8(7)	-0.1(7)	0.5(6)
C12	22.7(8)	22.3(8)	33.9(9)	-3.1(7)	6.4(7)	-3.7(6)
C13	22.6(7)	23.9(8)	25.5(8)	-3.9(7)	6.7(6)	0.6(6)
C14	25.3(8)	20.3(7)	18.2(7)	2.9(6)	5.5(6)	3.7(6)
C15	23.1(8)	25.7(8)	27.2(9)	3.0(7)	6.2(6)	7.0(6)
C16	18.5(7)	26.7(8)	22.0(8)	1.9(7)	1.4(6)	6.5(6)
C17	22.1(7)	14.4(7)	17.8(7)	-3.8(6)	2.1(6)	1.3(6)
C18	24.3(7)	16.6(7)	18.3(7)	-	4.8(6)	2.1(6)

				2.3(6)		
C19	34.5(9)	28.9(9)	17.7(8)	0.7(7)	-0.6(7)	10.7(7)
C20	45.1(10)	21.0(8)	18.0(8)	2.6(6)	6.4(7)	7.6(7)
C21	34.4(9)	28.9(9)	29.9(9)	1.6(7)	10.1(7)	-8.7(7)

Table 4-21. Bond Lengths for 4-10.

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
O1	C2	1.4541(19)	C1	C2	1.502(2)
O1	C3	1.3421(18)	C3	C4	1.515(2)
O2	C3	1.1991(19)	C4	C5	1.557(2)
O3	C14	1.3654(19)	C5	C6	1.551(2)
O3	C15	1.461(2)	C5	C8	1.517(2)
O4	C14	1.211(2)	C6	C7	1.548(2)
O5	C17	1.2168(18)	C7	C17	1.522(2)
N1	N2	1.4040(17)	C8	C9	1.396(2)
N1	C4	1.4661(18)	C8	C13	1.398(2)
N1	C7	1.4721(19)	C9	C10	1.389(2)

N2	C14	1.353(2)	C10	C11	1.384(2)
N2	C16	1.4566(19)	C11	C12	1.388(2)
N3	C18	1.330(2)	C12	C13	1.392(2)
N3	C19	1.362(2)	C15	C16	1.517(2)
N4	C18	1.365(2)	C17	C18	1.470(2)
N4	C20	1.359(2)	C19	C20	1.368(3)
N4	C21	1.463(2)			

Table 4-22. Bond Angles for 4-10

Atom	**Atom**	**Atom**	**Angle/˚**	**Atom**	**Atom**	**Atom**	**Angle/˚**
C3	O1	C2	118.96(12)	N1	C7	C17	110.35(12)
C14	O3	C15	108.02(12)	C17	C7	C6	113.28(12)
N2	N1	C4	115.91(12)	C9	C8	C5	119.14(14)
N2	N1	C7	113.17(11)	C9	C8	C13	118.25(15)
C4	N1	C7	107.44(11)	C13	C8	C5	122.60(14)
N1	N2	C16	121.72(12)	C10	C9	C8	121.06(15)
C14	N2	N1	125.90(12)	C11	C10	C9	120.20(15)

C14	N2	C16	112.37(12)	C10	C11	C12	119.47(15)
C18	N3	C19	104.89(14)	C11	C12	C13	120.47(15)
C18	N4	C21	128.41(14)	C12	C13	C8	120.54(15)
C20	N4	C18	106.40(14)	O4	C14	O3	122.31(15)
C20	N4	C21	125.07(14)	O4	C14	N2	128.90(14)
O1	C2	C1	109.26(13)	N2	C14	O3	108.79(13)
O1	C3	C4	107.58(12)	O3	C15	C16	104.28(12)
O2	C3	O1	125.88(14)	N2	C16	C15	99.72(12)
O2	C3	C4	126.54(14)	O5	C17	C7	122.83(14)
N1	C4	C3	112.78(12)	O5	C17	C18	122.42(14)
N1	C4	C5	102.22(12)	C18	C17	C7	114.74(13)
C3	C4	C5	112.64(12)	N3	C18	N4	111.73(14)
C6	C5	C4	102.84(12)	N3	C18	C17	123.67(14)
C8	C5	C4	114.07(12)	N4	C18	C17	124.59(14)
C8	C5	C6	113.66(13)	N3	C19	C20	110.42(15)
C7	C6	C5	106.25(12)	N4	C20	C19	106.56(15)
N1	C7	C6	104.24(12)				

Table 4-23. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 4-10

Atom	*x*	*y*	*z*	U(eq)
H1A	6287.1	5981.12	-207.74	43
H1B	6049.19	4733.96	352.29	43
H1C	7254.65	5719.53	431.59	43
H2A	6201.61	8217.35	481.95	29
H2B	5032.77	7159.28	461.08	29
H4	6419.45	7164.2	2507.83	21
H5	7280.47	4700.59	2369.3	22
H6A	6221.8	3022.06	3221.68	24
H6B	7234.24	4359.78	3430.51	24
H7	5970.36	6210.22	3694.58	21
H9	7123.52	3255.9	1390.35	25
H10	6271.06	1269.23	650.5	29
H11	4505.73	53.34	779.19	30
H12	3613.47	809.94	1664.3	31
H13	4455.78	2810.05	2404.66	28

H15A	2312.15	9940.84	2922.38	30
H15B	2727.95	8822.8	3561.4	30
H16A	2729.36	6782.52	2813.93	27
H16B	2910.24	8053.58	2239.19	27
H19	7009.23	2797.48	5515.66	33
H20	5113.66	1457.07	5563.23	34
H21A	2821.57	3242.3	4623.22	46
H21B	3118.58	1383.45	4843.57	46
H21C	3073.83	1912.07	4095.57	46

4.5 References

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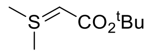
Appendix A. ^{1}H and ^{13}C Spectra for New Compounds

A-1. List of New Compounds for Chapter 2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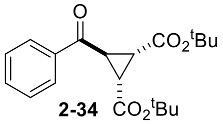
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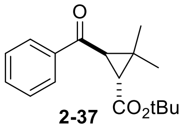
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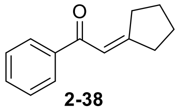
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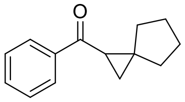
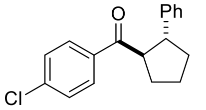
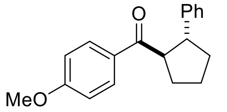
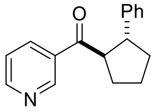

2-39


2-4


2-5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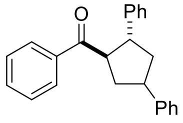
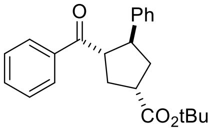
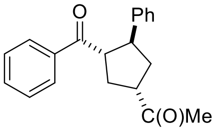
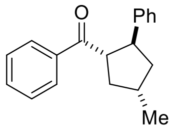
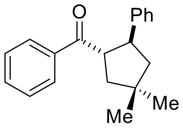
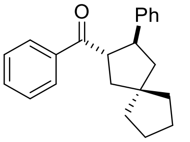

2-8

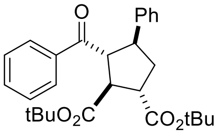

2-10

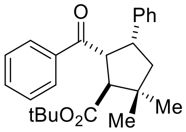

2-11


2-6


2-7


2-12


2-14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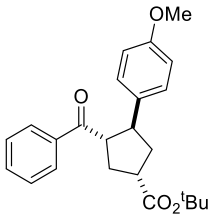
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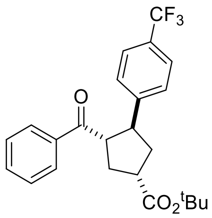
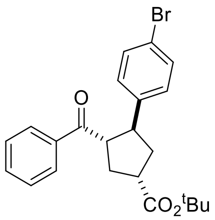

2-16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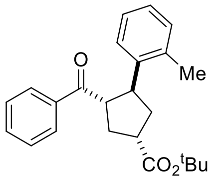
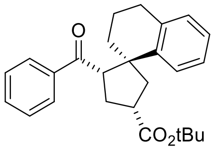
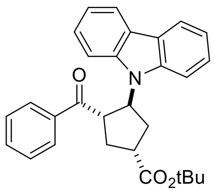
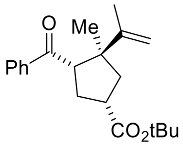

2-18


2-21


2-22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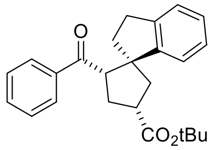
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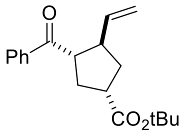
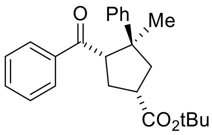
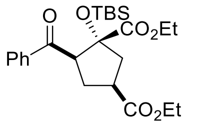
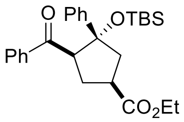
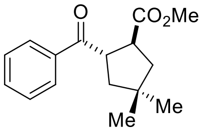
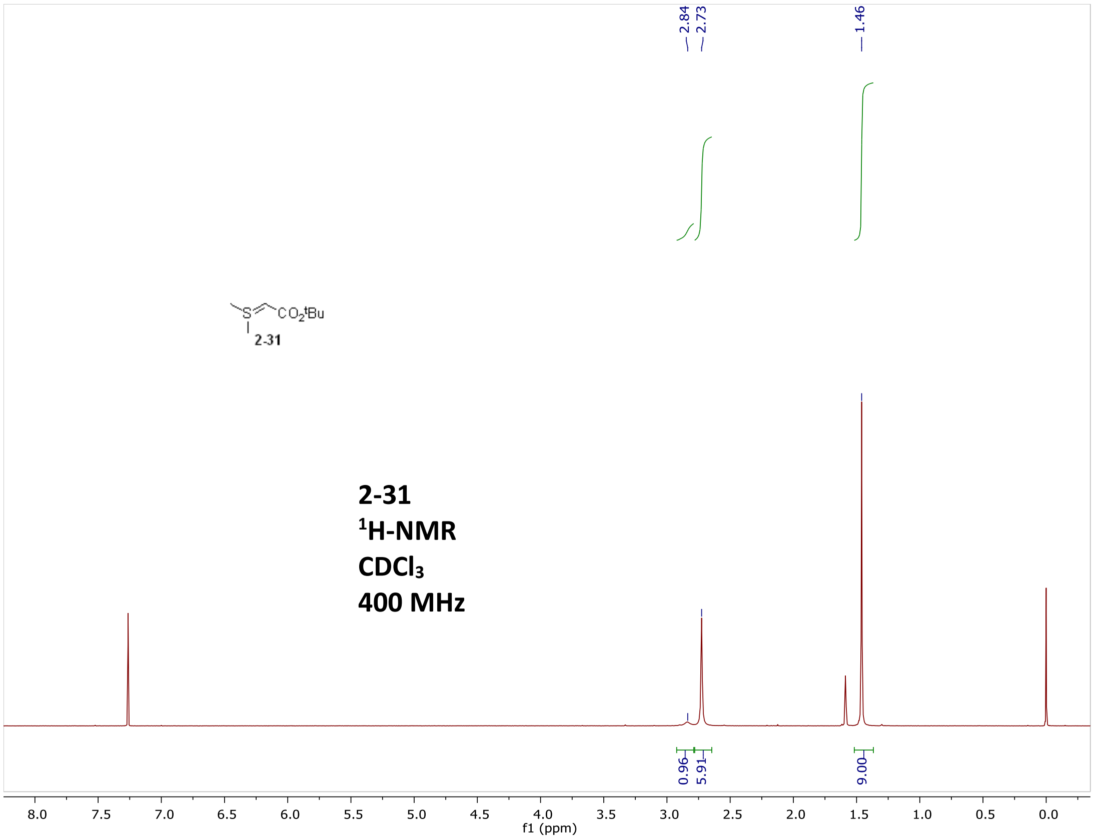

2-23


2-19

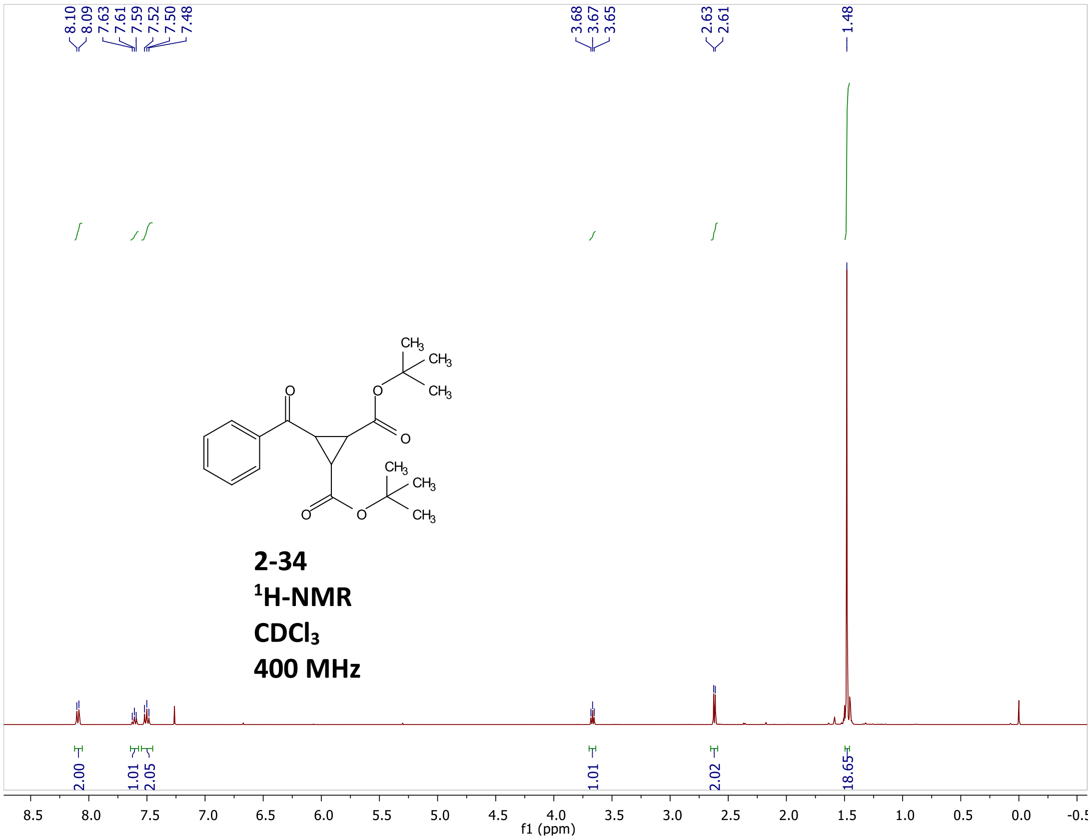

2-25


2-24


2-26

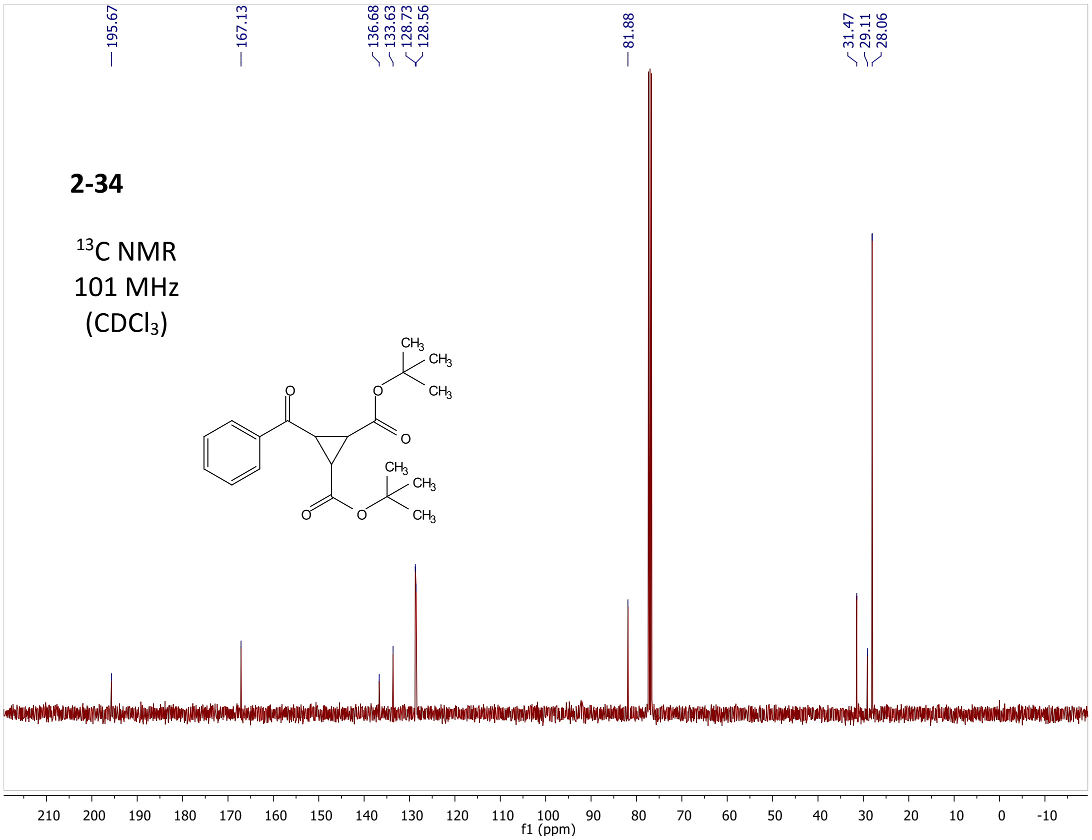


2-31
^{1}H-NMR
$CDCl_3$
400 MHz

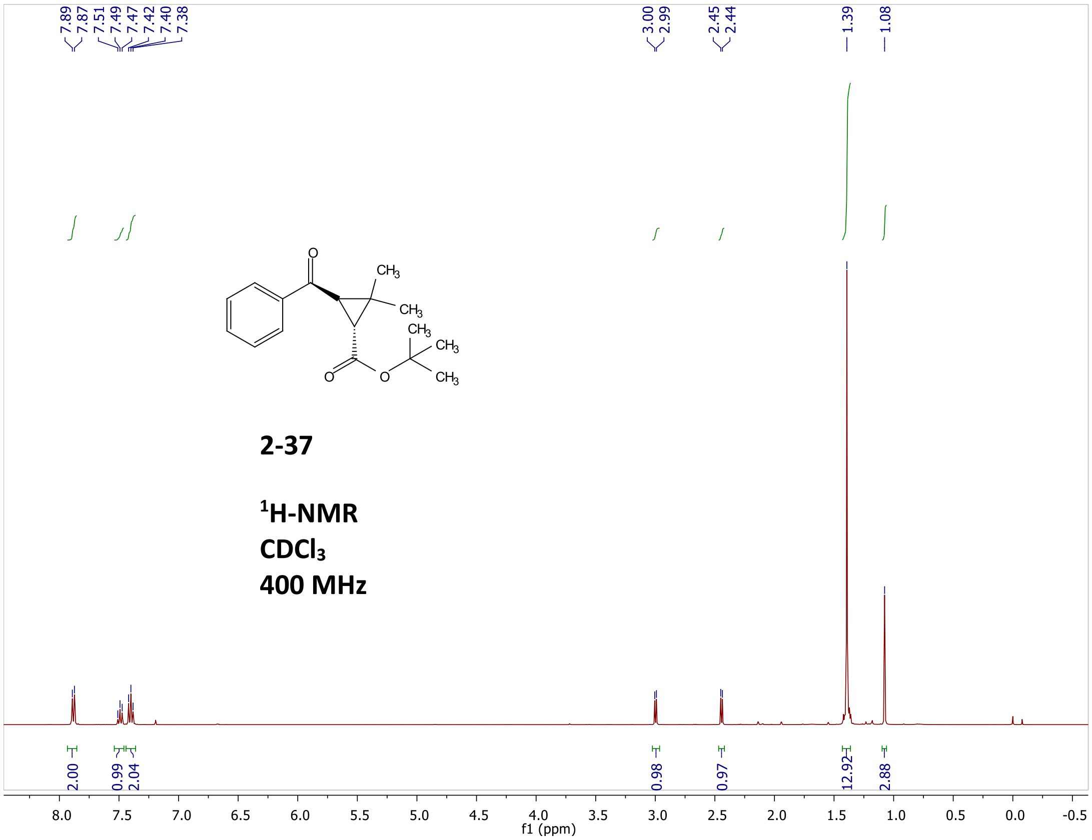


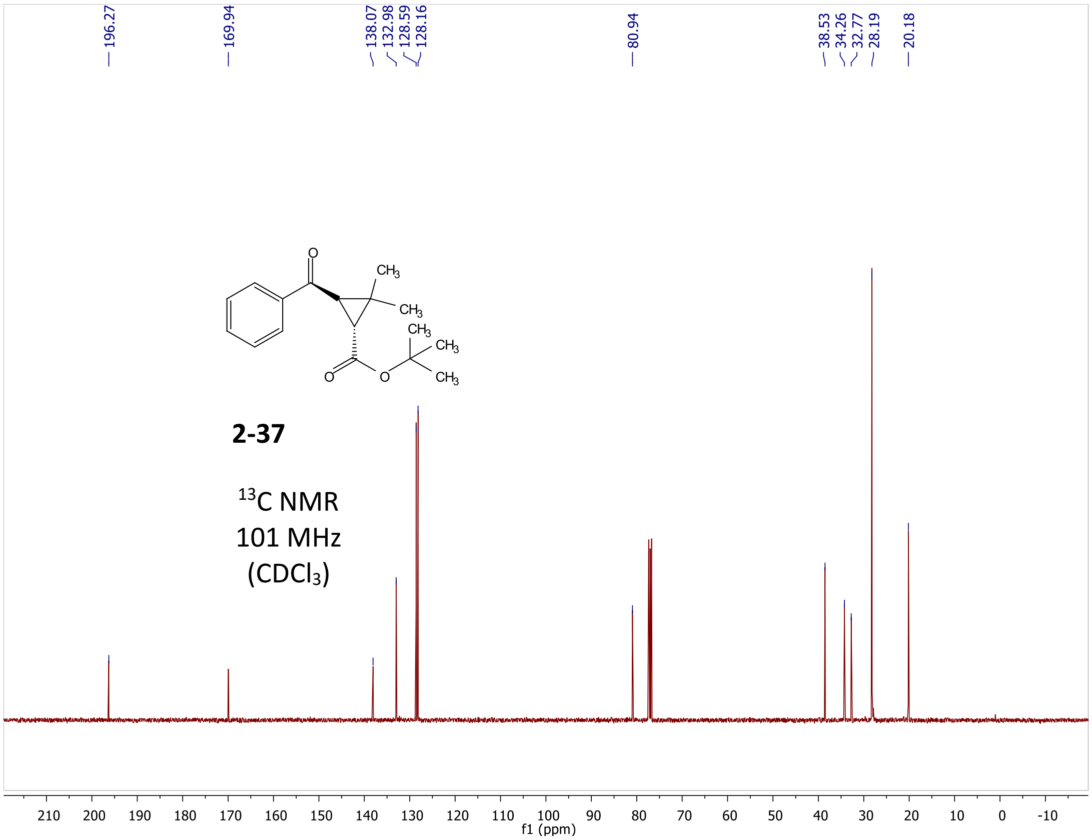
2-34
^{1}H-NMR
$CDCl_3$
400 MHz

2-34


195.67
167.13
136.68
133.63
128.73
128.56
81.88
31.47
29.11
28.06
^{13}C NMR
101 MHz
(CDCl$_3$)
O
O
O
CH$_3$
CH$_3$
CH$_3$
CH$_3$
CH$_3$
CH$_3$
O
O
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)

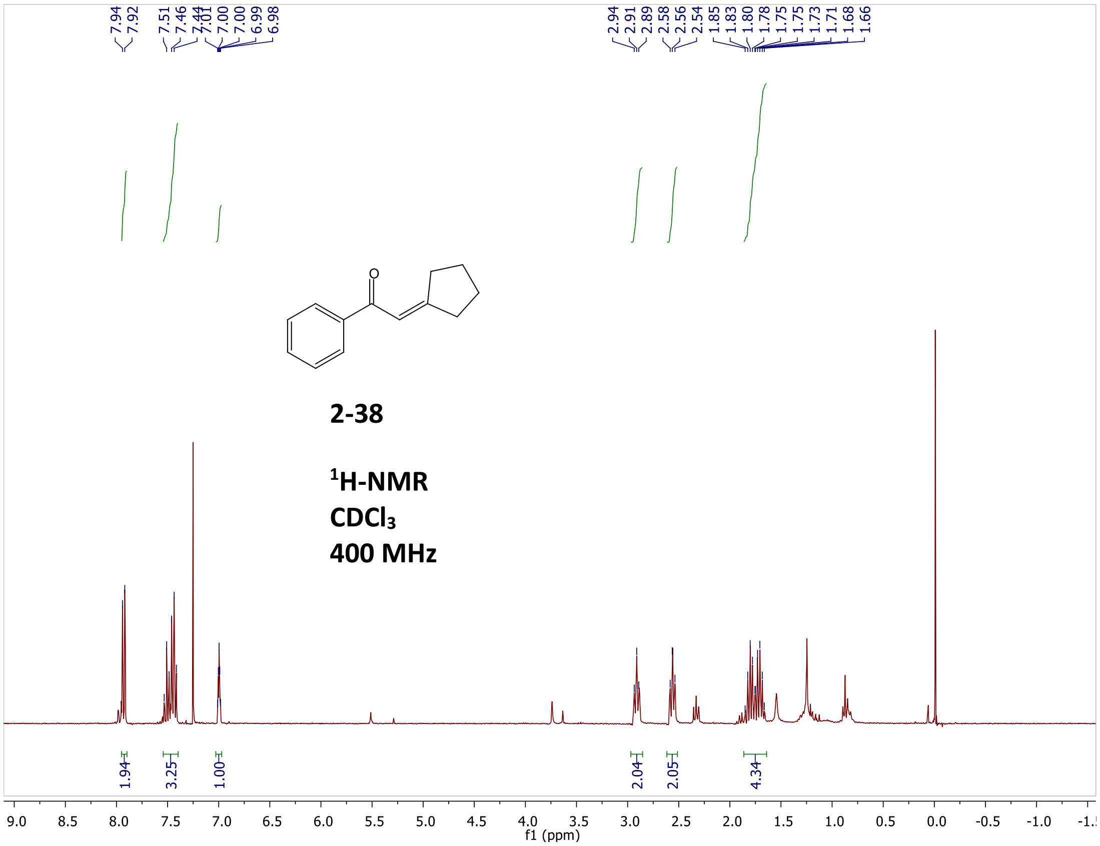
2-37


7.89
7.87
7.51
7.49
7.47
7.42
7.40
7.38
3.00
2.99
2.45
2.44
1.39
1.08
O
CH$_3$
CH$_3$
CH$_3$
CH$_3$
CH$_3$
O
O
^{1}H-NMR
CDCl$_3$
400 MHz
2.00
0.99
2.04
0.98
0.97
12.92
2.88
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)



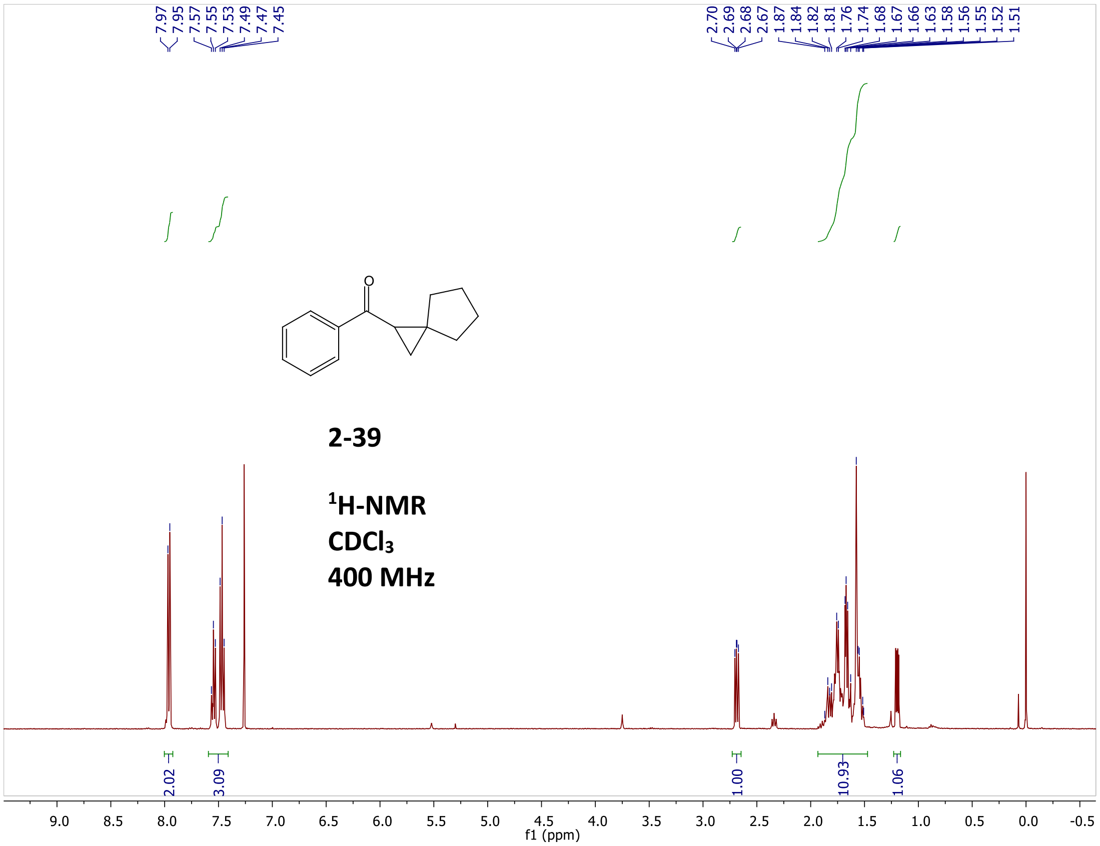
2-37

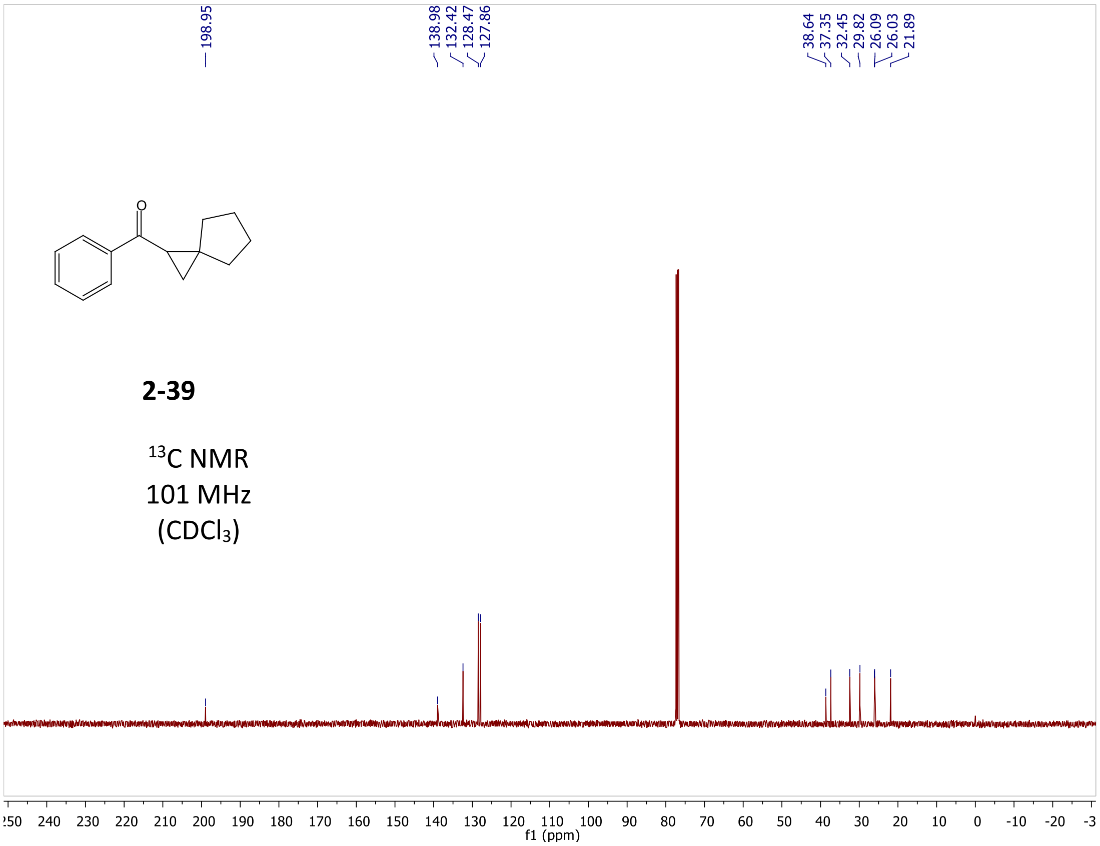
^{13}C NMR
101 MHz
(CDCl$_3$)

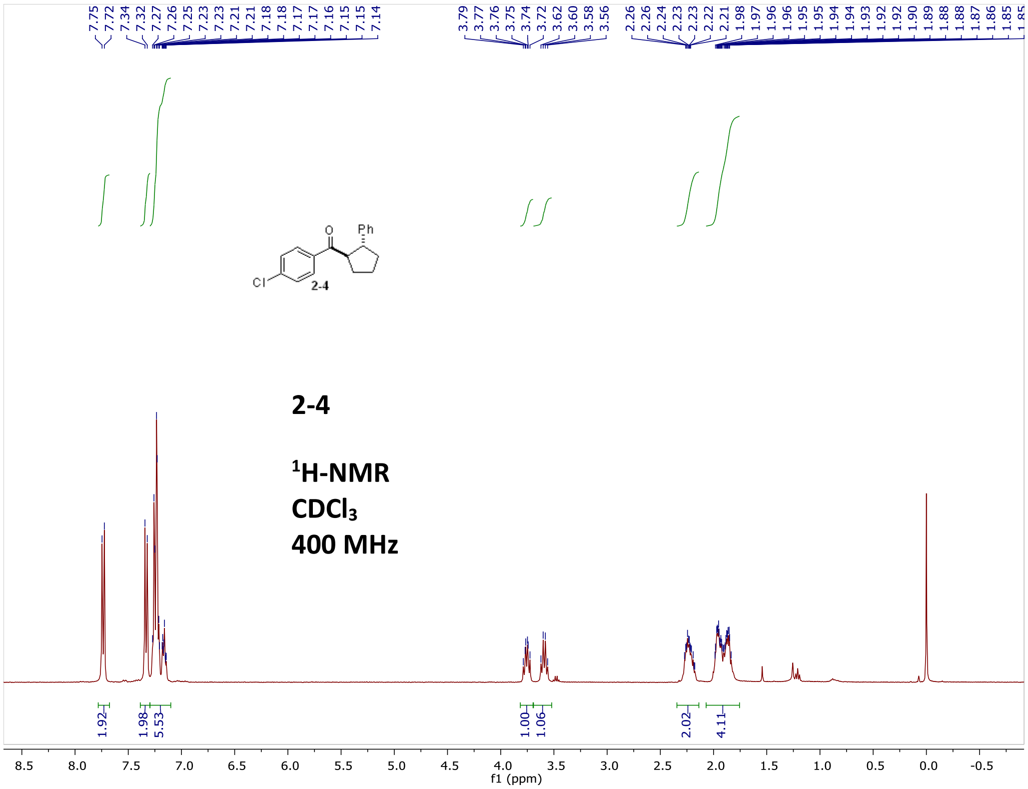


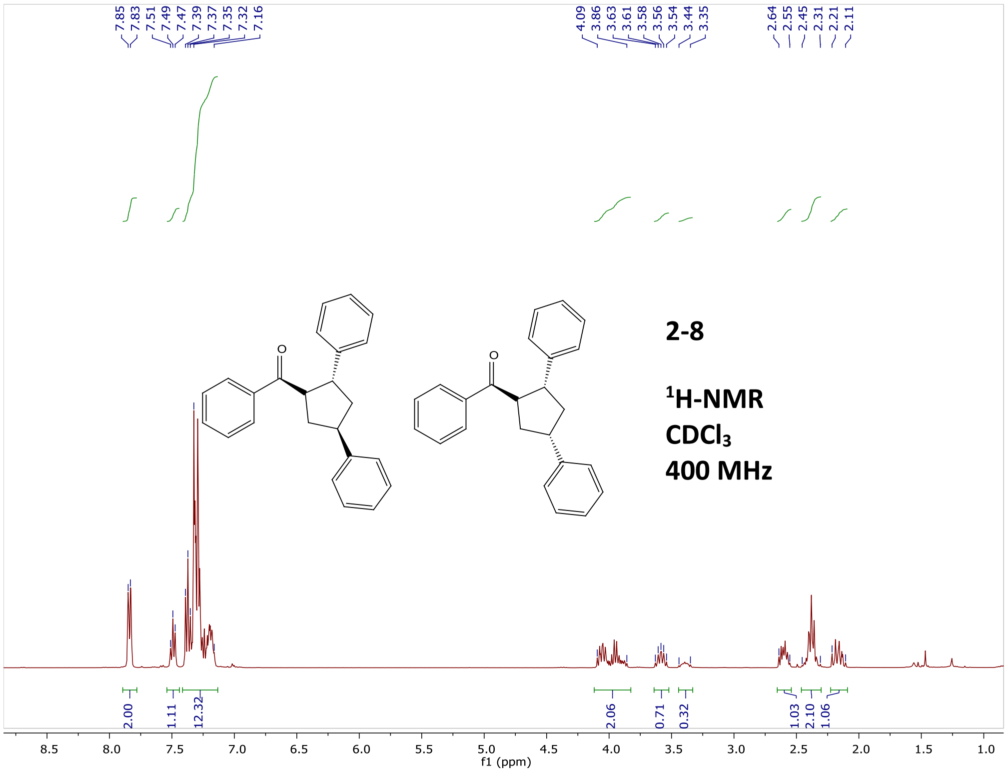
2-38

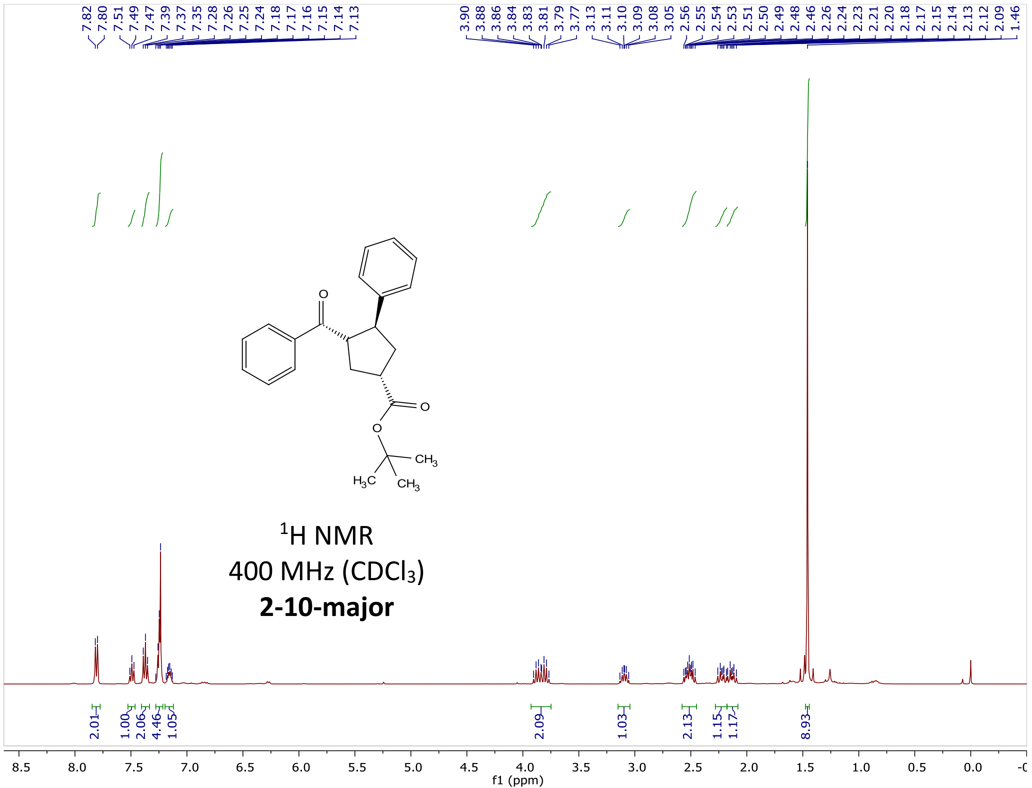
^{1}H-NMR
CDCl$_3$
400 MHz


7.97
7.95
7.57
7.55
7.53
7.49
7.47
7.45
2.70
2.69
2.68
2.67
1.87
1.84
1.82
1.81
1.76
1.74
1.68
1.67
1.66
1.63
1.58
1.56
1.55
1.52
1.51
O
2-39
^{1}H-NMR
CDCl$_3$
400 MHz
2.02
3.09
1.00
10.93
1.06
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
f1 (ppm)

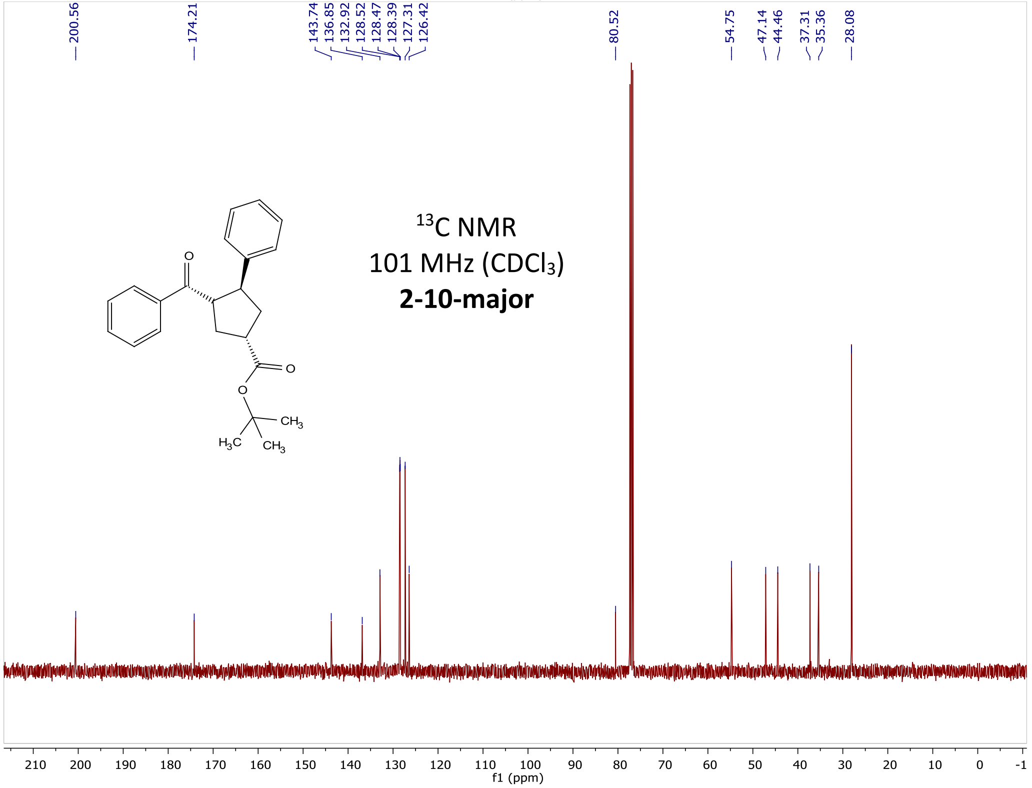

198.95
138.98
132.42
128.47
127.86
38.64
37.35
32.45
29.82
26.09
26.03
21.89
O
2-39
^{13}C NMR
101 MHz
(CDCl$_3$)
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
f1 (ppm)


7.75
7.72
7.34
7.32
7.27
7.26
7.25
7.23
7.23
7.21
7.21
7.18
7.18
7.17
7.17
7.16
7.15
7.14
3.79
3.77
3.76
3.75
3.74
3.72
3.62
3.60
3.58
3.56
2.26
2.26
2.24
2.23
2.23
2.22
2.21
1.98
1.97
1.96
1.96
1.95
1.95
1.94
1.94
1.93
1.92
1.92
1.90
1.89
1.88
1.87
1.86
1.85
O
Ph
Cl
2-4
2-4
¹H-NMR
CDCl₃
400 MHz
1.92
1.98
5.53
1.00
1.06
2.02
4.11
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)

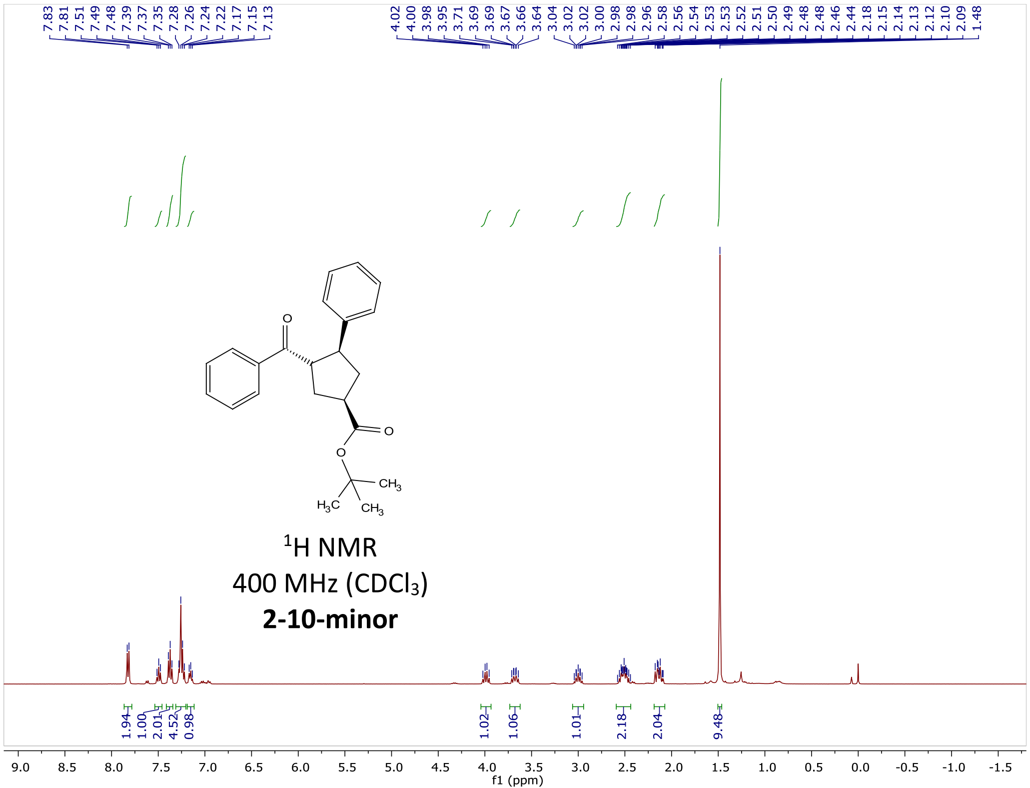

7.85
7.83
7.51
7.49
7.47
7.39
7.37
7.35
7.32
7.16
4.09
3.86
3.63
3.61
3.58
3.56
3.54
3.44
3.35
2.64
2.55
2.45
2.31
2.21
2.11
O
O
2-8
¹H-NMR
CDCl₃
400 MHz
2.00
1.11
12.32
2.06
0.71
0.32
1.03
2.10
1.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

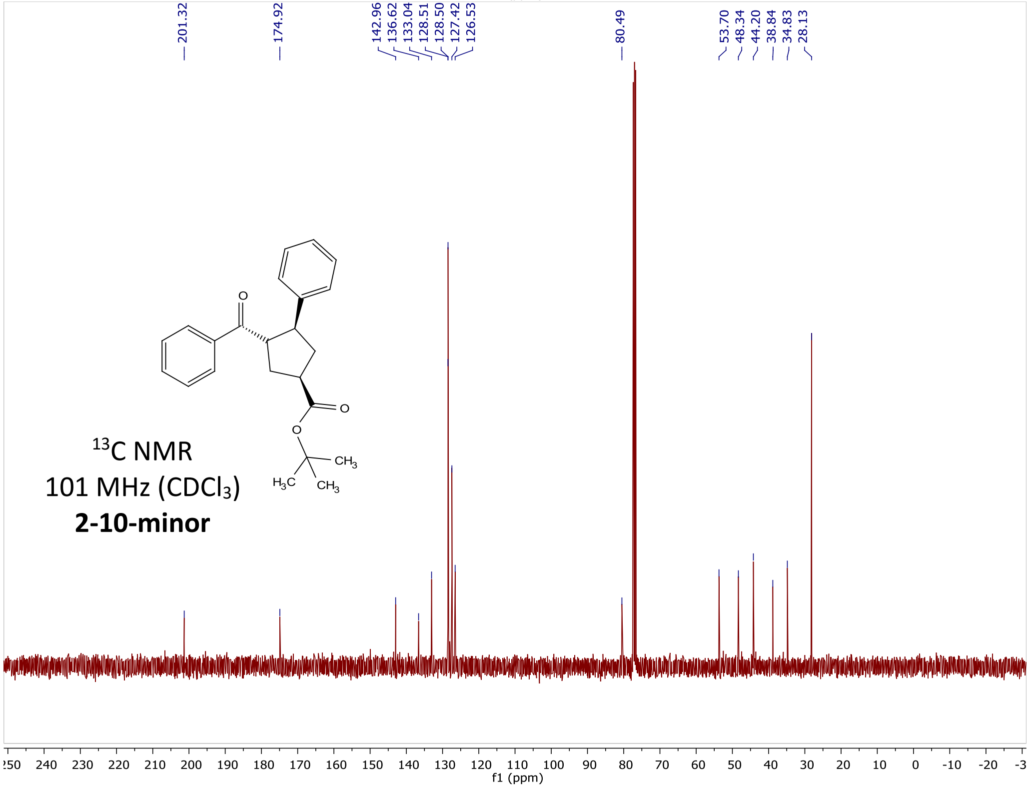


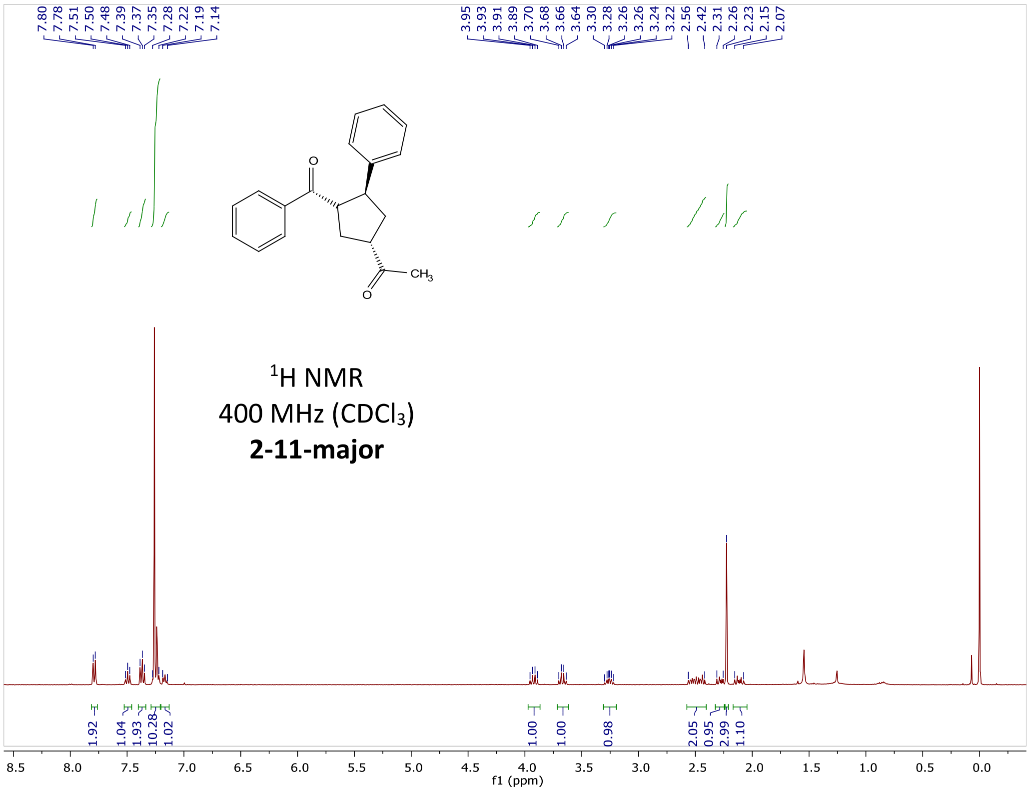
^{1}H NMR
400 MHz (CDCl$_3$)
2-10-major

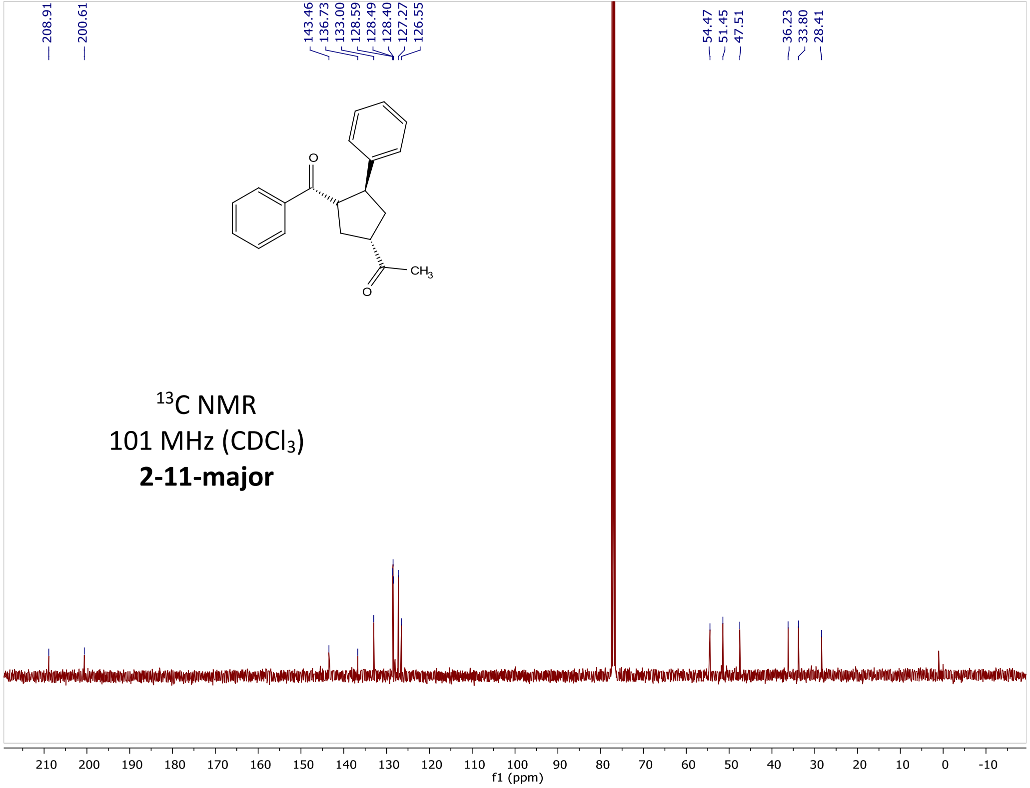


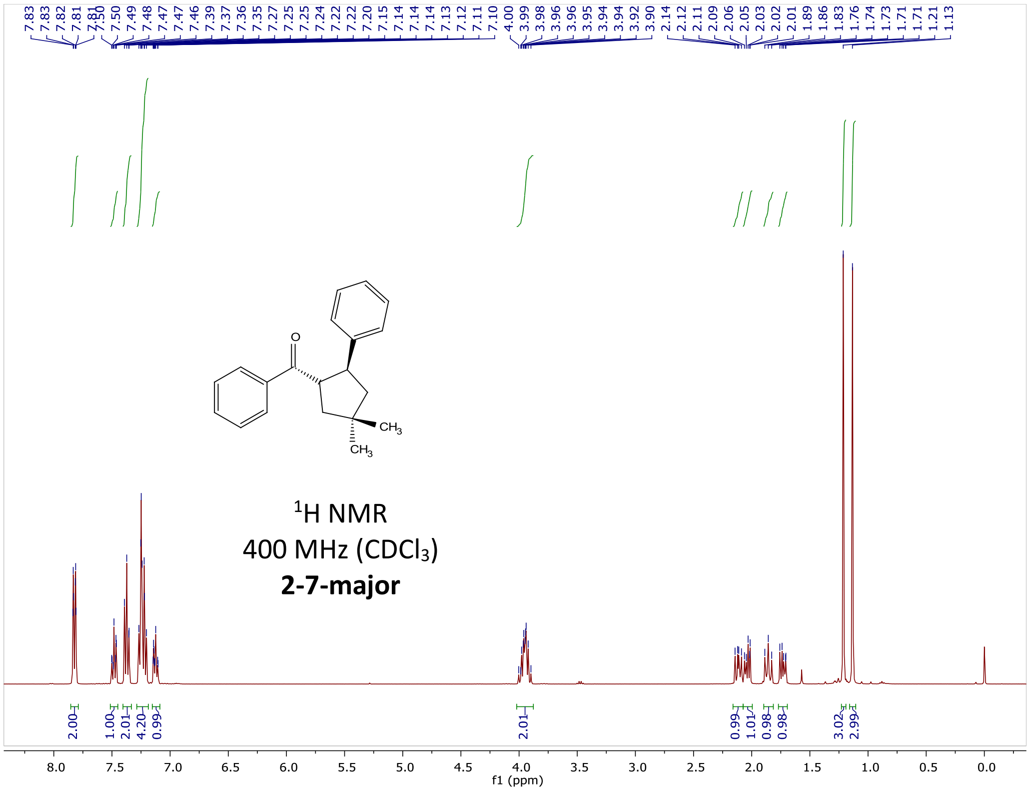
^{13}C NMR
101 MHz (CDCl$_3$)
2-10-major

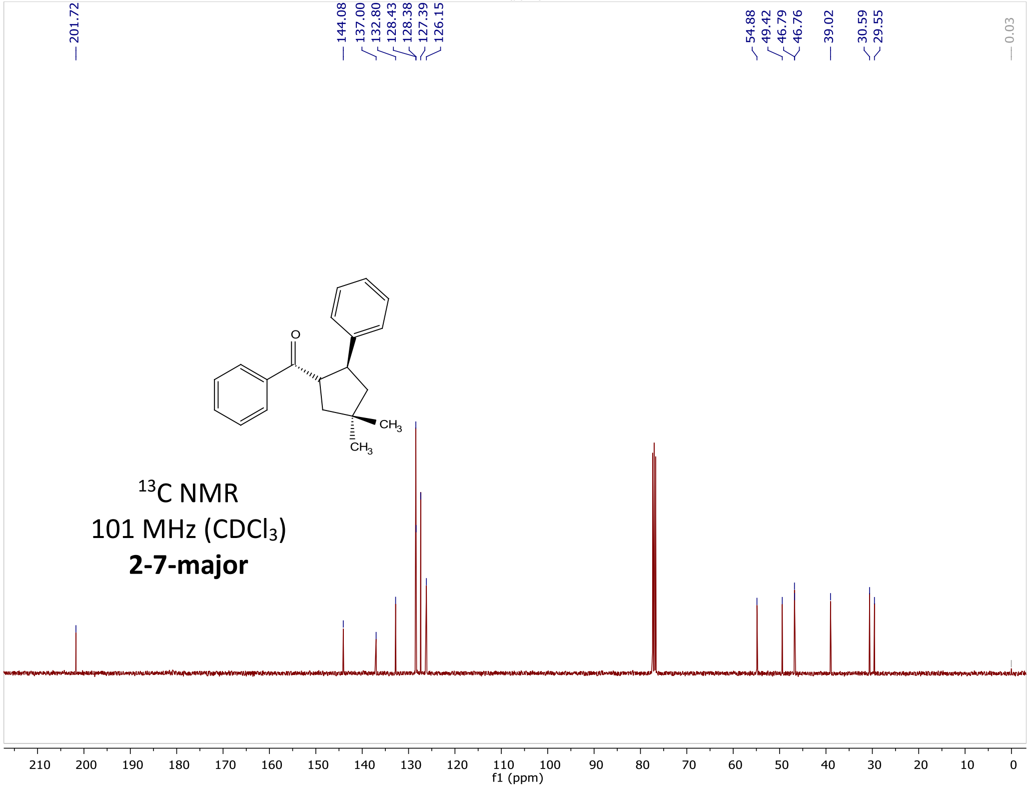

7.83
7.81
7.51
7.49
7.48
7.39
7.37
7.35
7.28
7.26
7.24
7.22
7.17
7.15
7.13
4.02
4.00
3.98
3.95
3.71
3.69
3.69
3.67
3.66
3.64
3.04
3.02
3.02
3.00
2.98
2.98
2.96
2.58
2.56
2.54
2.53
2.53
2.52
2.51
2.50
2.49
2.48
2.46
2.44
2.18
2.15
2.14
2.13
2.12
2.10
2.09
1.48
O
O
O
CH3
H3C
CH3
1H NMR
400 MHz (CDCl3)
2-10-minor
1.94
1.00
2.01
4.52
0.98
1.02
1.06
1.01
2.18
2.04
9.48
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 -1.5
f1 (ppm)

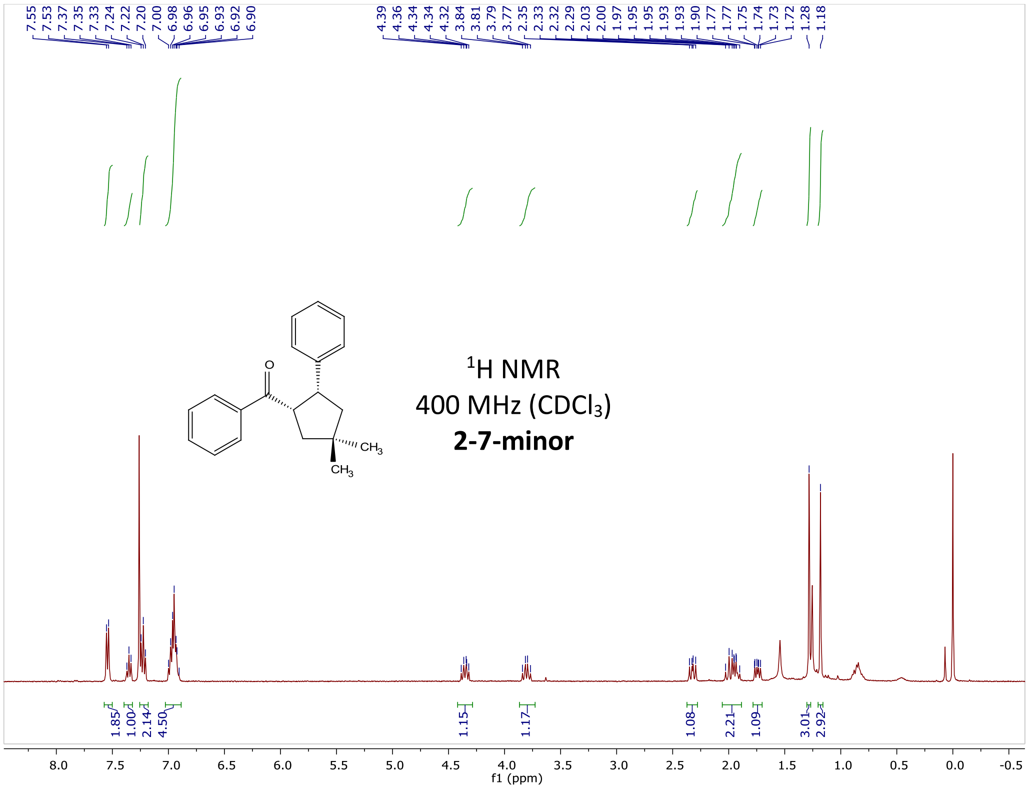

201.32
174.92
142.96
136.62
133.04
128.51
128.50
127.42
126.53
80.49
53.70
48.34
44.20
38.84
34.83
28.13
O
O
O
CH3
H3C
CH3
13C NMR
101 MHz (CDCl3)
2-10-minor
250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -3
f1 (ppm)

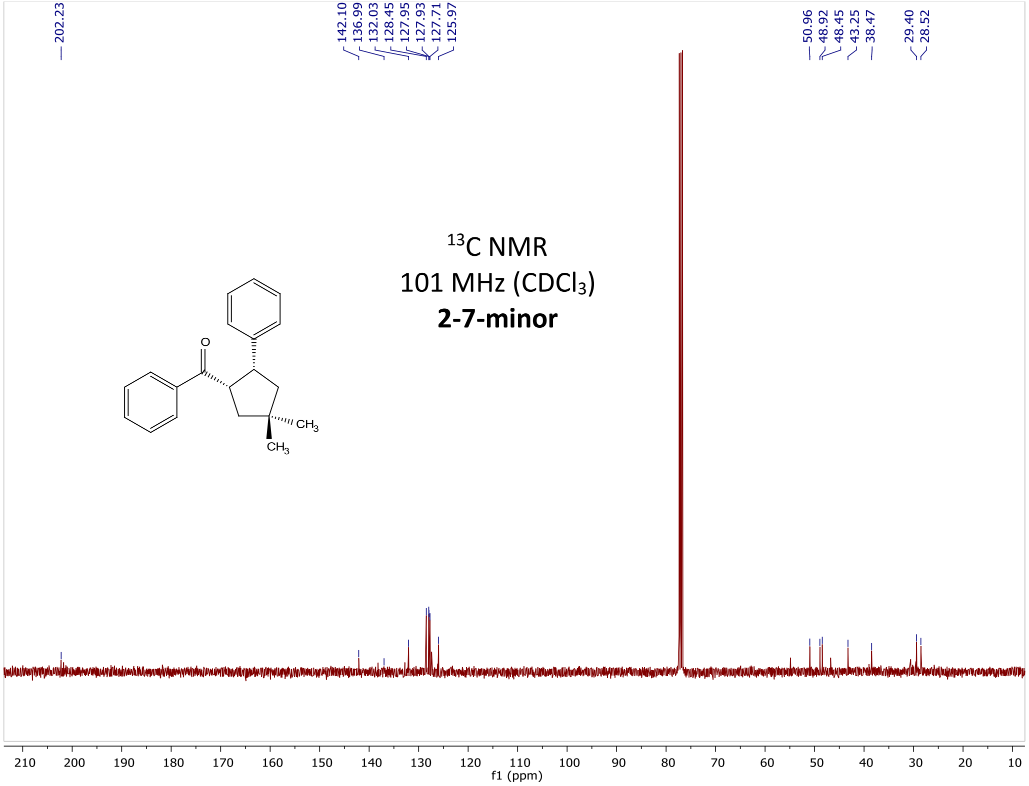

7.80
7.78
7.51
7.50
7.48
7.39
7.37
7.35
7.28
7.22
7.19
7.14
3.95
3.93
3.91
3.89
3.70
3.68
3.66
3.64
3.30
3.28
3.26
3.24
3.22
2.56
2.42
2.31
2.26
2.23
2.15
2.07
O
O
CH3
^{1}H NMR
400 MHz (CDCl$_3$)
2-11-major
1.92
1.04
1.93
10.28
1.02
1.00
1.00
0.98
2.05
0.95
2.99
1.10
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

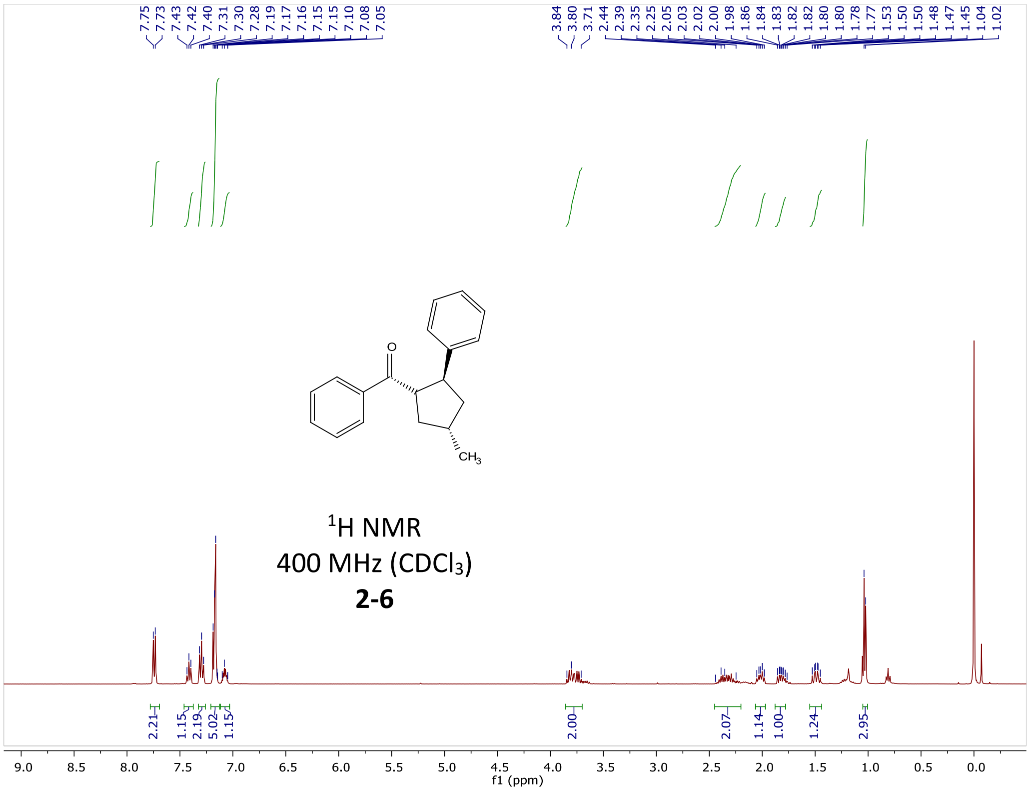

208.91
200.61
143.46
136.73
133.00
128.59
128.49
128.40
127.27
126.55
54.47
51.45
47.51
36.23
33.80
28.41
O
O
CH3
^{13}C NMR
101 MHz (CDCl$_3$)
2-11-major
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

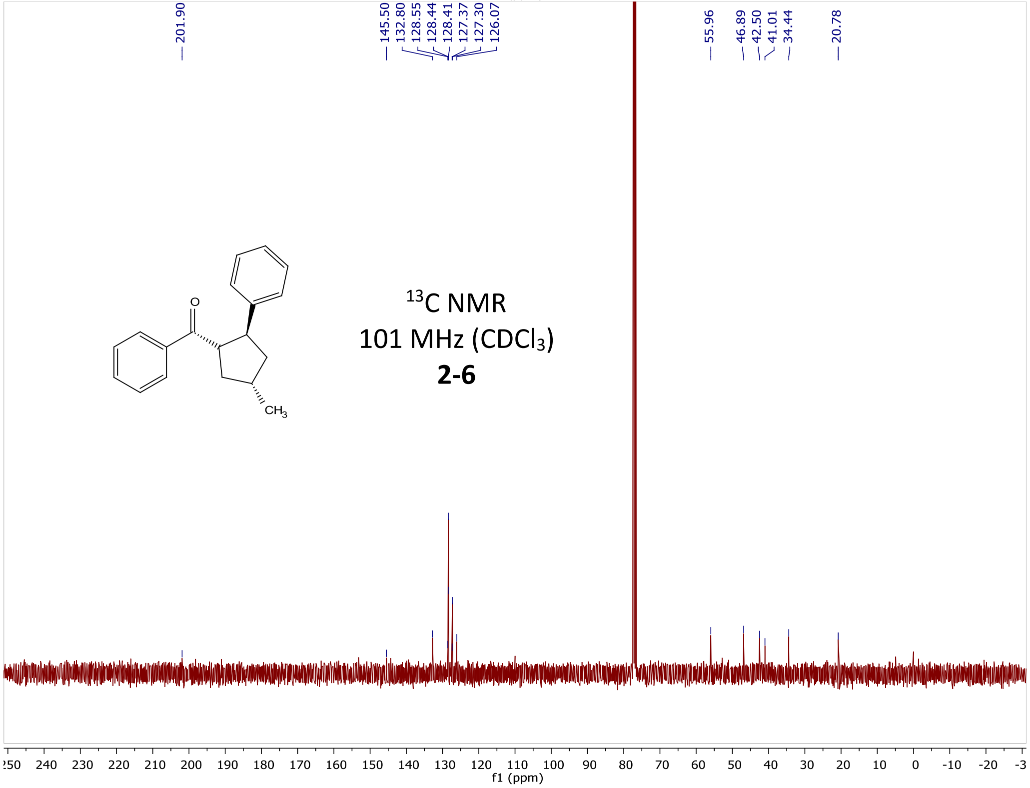

7.83 7.83 7.82 7.81 7.81 7.50 7.49 7.48 7.47 7.47 7.46 7.39 7.37 7.36 7.35 7.27 7.25 7.25 7.24 7.22 7.22 7.20 7.15 7.14 7.14 7.14 7.13 7.12 7.11 7.10 4.00 3.99 3.98 3.96 3.96 3.95 3.94 3.94 3.92 3.90 2.14 2.12 2.11 2.09 2.06 2.05 2.03 2.02 2.01 1.89 1.86 1.83 1.76 1.74 1.73 1.71 1.71 1.21 1.13
O
CH3
CH3
1H NMR
400 MHz (CDCl3)
2-7-major
2.00 1.00 2.01 4.20 0.99 2.01 0.99 1.01 0.98 0.98 3.02 2.99
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
f1 (ppm)

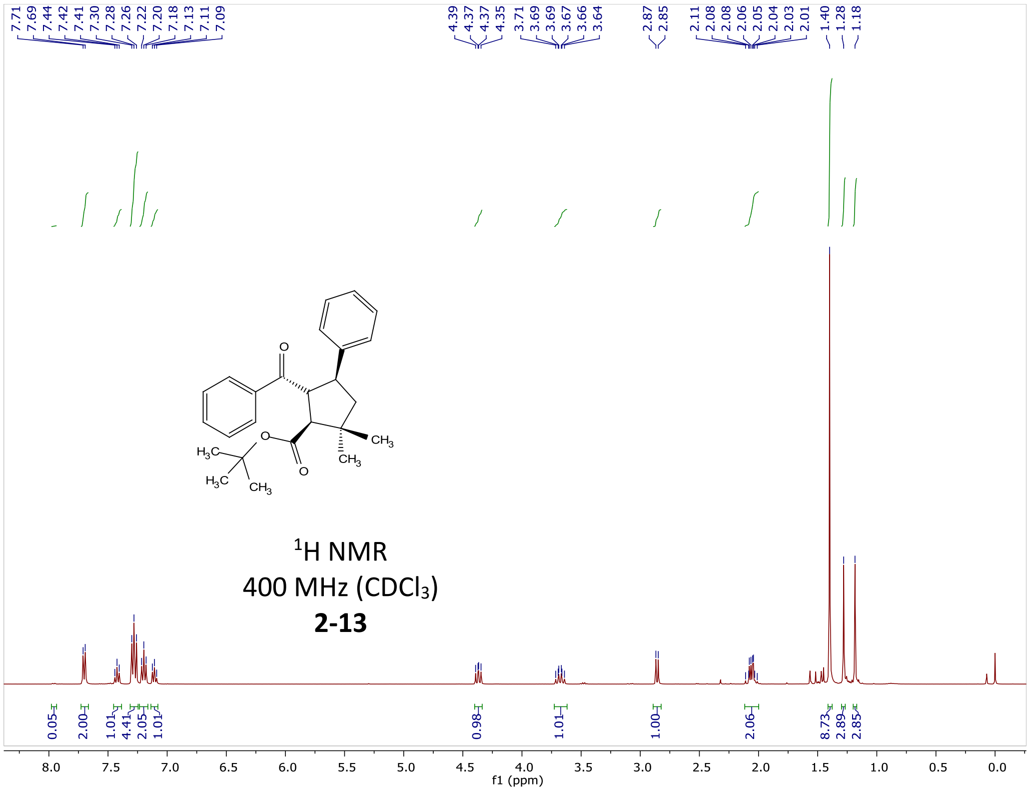

201.72
144.08 137.00 132.80 128.43 128.38 127.39 126.15
54.88 49.42 46.79 46.76 39.02 30.59 29.55
0.03
O
CH3
CH3
13C NMR
101 MHz (CDCl3)
2-7-major
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

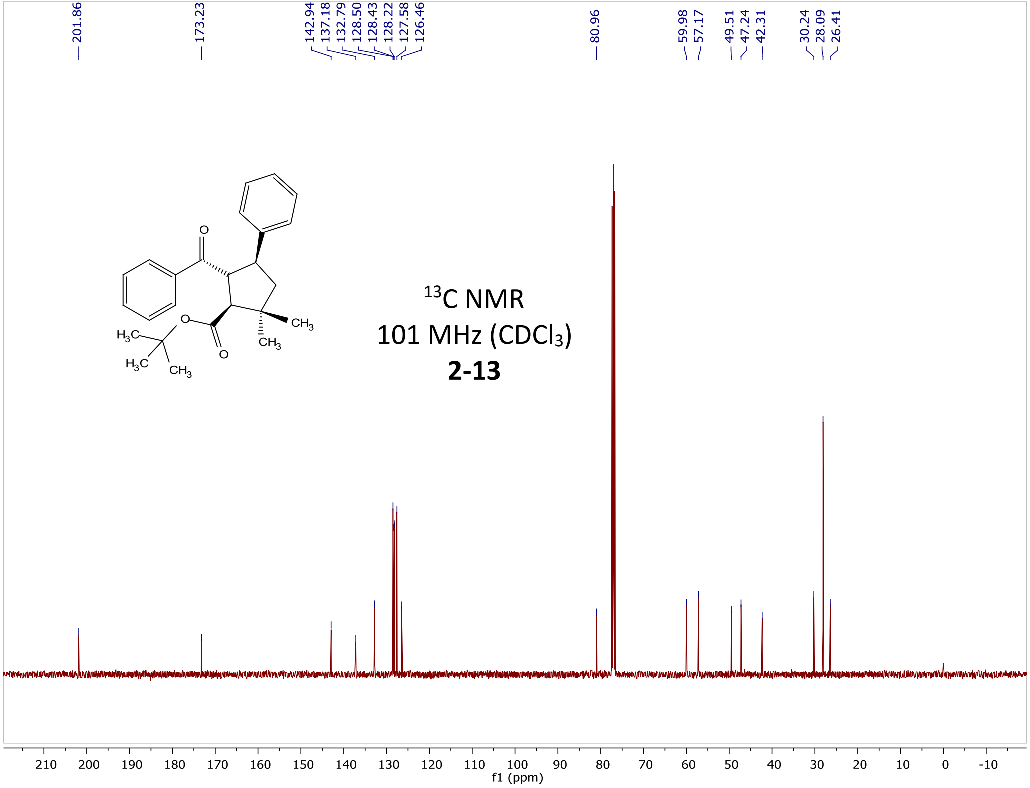

7.55
7.53
7.37
7.35
7.33
7.24
7.22
7.20
7.00
6.98
6.96
6.95
6.93
6.92
6.90
4.39
4.36
4.34
4.34
4.32
3.84
3.81
3.79
3.77
2.35
2.33
2.32
2.29
2.03
2.00
1.97
1.95
1.95
1.93
1.93
1.90
1.77
1.77
1.75
1.74
1.73
1.72
1.28
1.18
O
CH3
CH3
^{1}H NMR
400 MHz (CDCl$_3$)
2-7-minor
1.85
1.00
2.14
4.50
1.15
1.17
1.08
2.21
1.09
3.01
2.92
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)

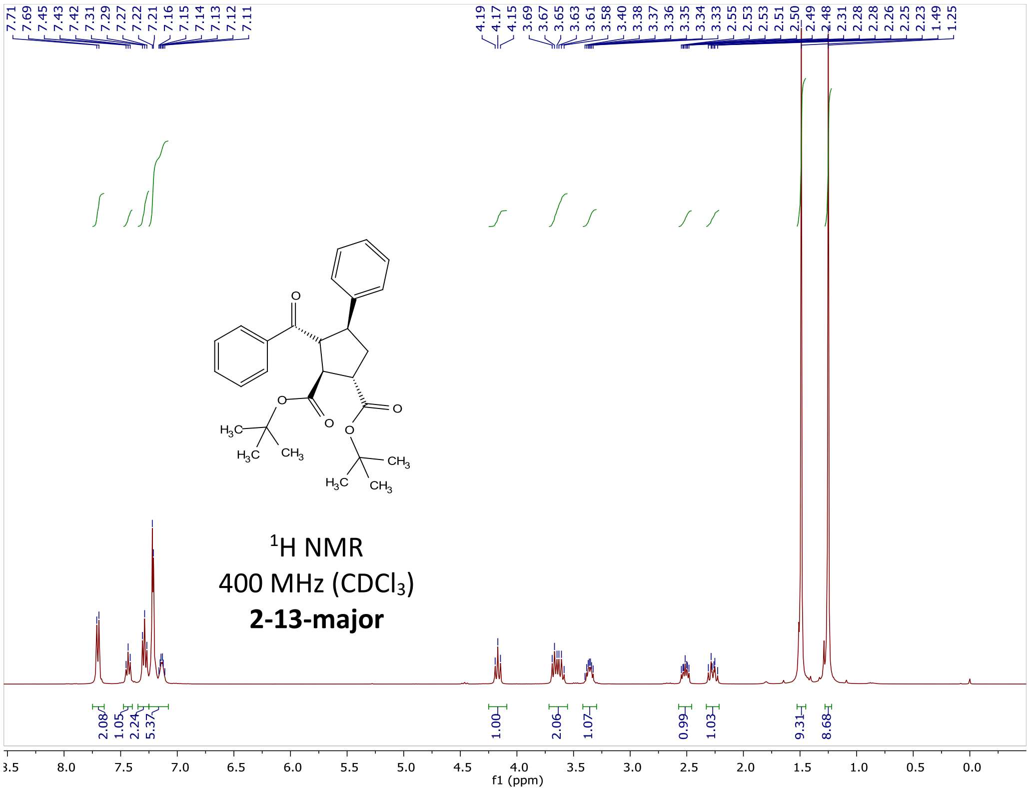

202.23
142.10
136.99
132.03
128.45
127.95
127.93
127.71
125.97
50.96
48.92
48.45
43.25
38.47
29.40
28.52
^{13}C NMR
101 MHz (CDCl$_3$)
2-7-minor
O
CH3
CH3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.75
7.73
7.43
7.42
7.40
7.31
7.30
7.28
7.19
7.17
7.16
7.15
7.15
7.10
7.08
7.05
3.84
3.80
3.71
2.44
2.39
2.35
2.25
2.05
2.03
2.02
2.00
1.98
1.86
1.84
1.83
1.82
1.82
1.80
1.80
1.78
1.77
1.53
1.50
1.50
1.48
1.47
1.45
1.04
1.02
O
CH3
^{1}H NMR
400 MHz (CDCl$_3$)
2-6
2.21
1.15
2.19
5.02
1.15
2.00
2.07
1.14
1.00
1.24
2.95
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
f1 (ppm)

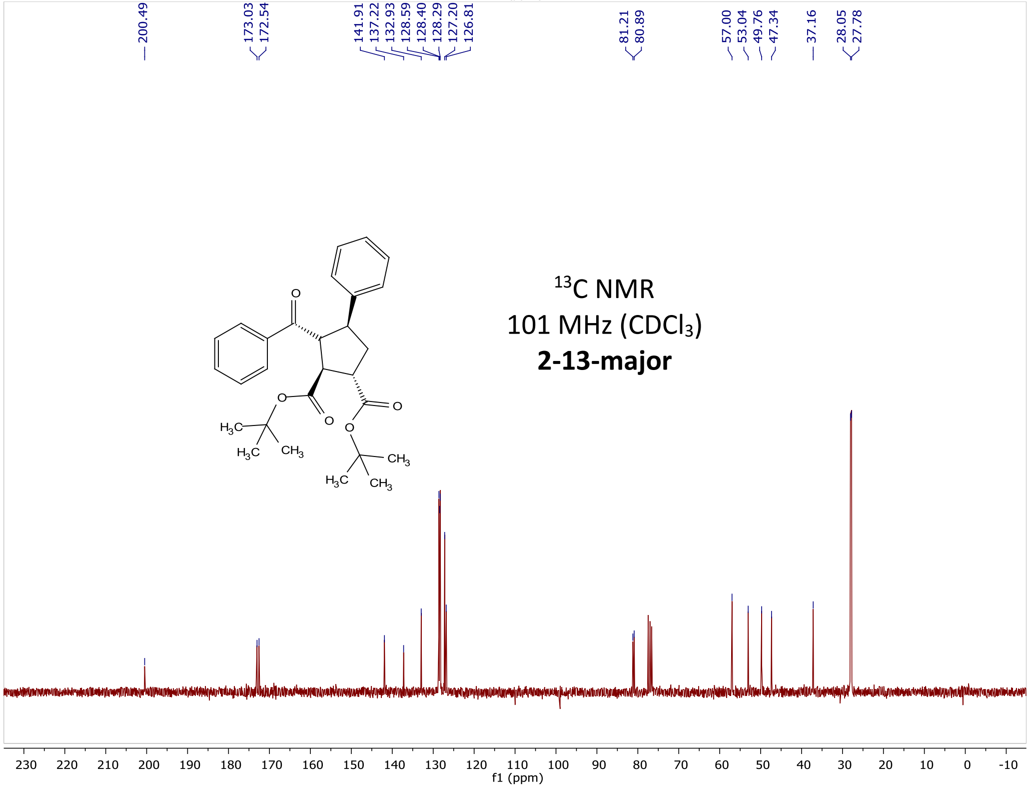

201.90
145.50
132.80
128.55
128.44
128.41
127.37
127.30
126.07
55.96
46.89
42.50
41.01
34.44
20.78
O
CH3
^{13}C NMR
101 MHz (CDCl$_3$)
2-6
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-3
f1 (ppm)


^{1}H NMR
400 MHz (CDCl$_3$)
2-13

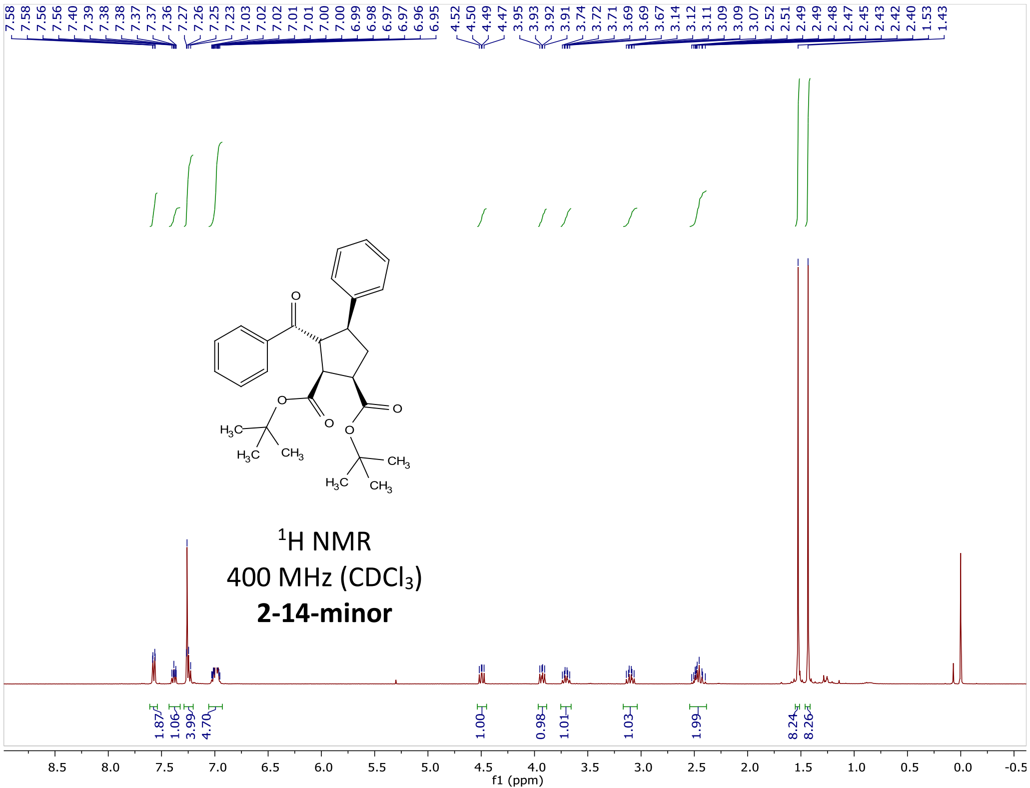

^{13}C NMR
101 MHz (CDCl$_3$)
2-13



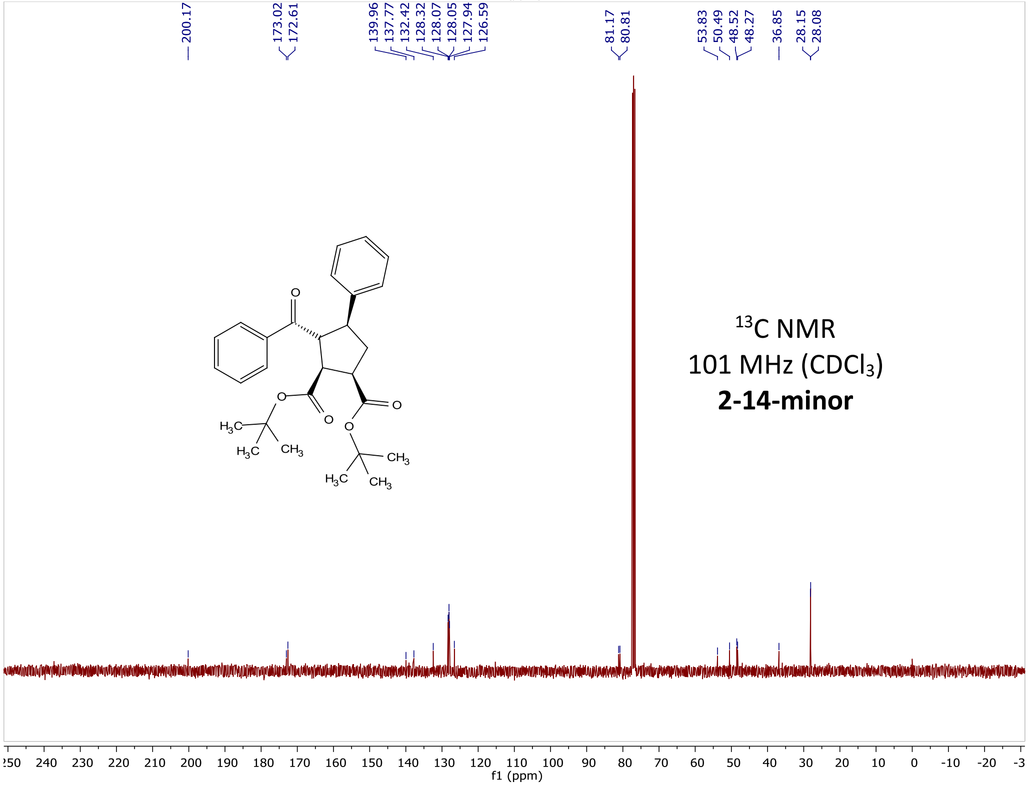
^{1}H NMR
400 MHz ($CDCl_3$)
2-13-major



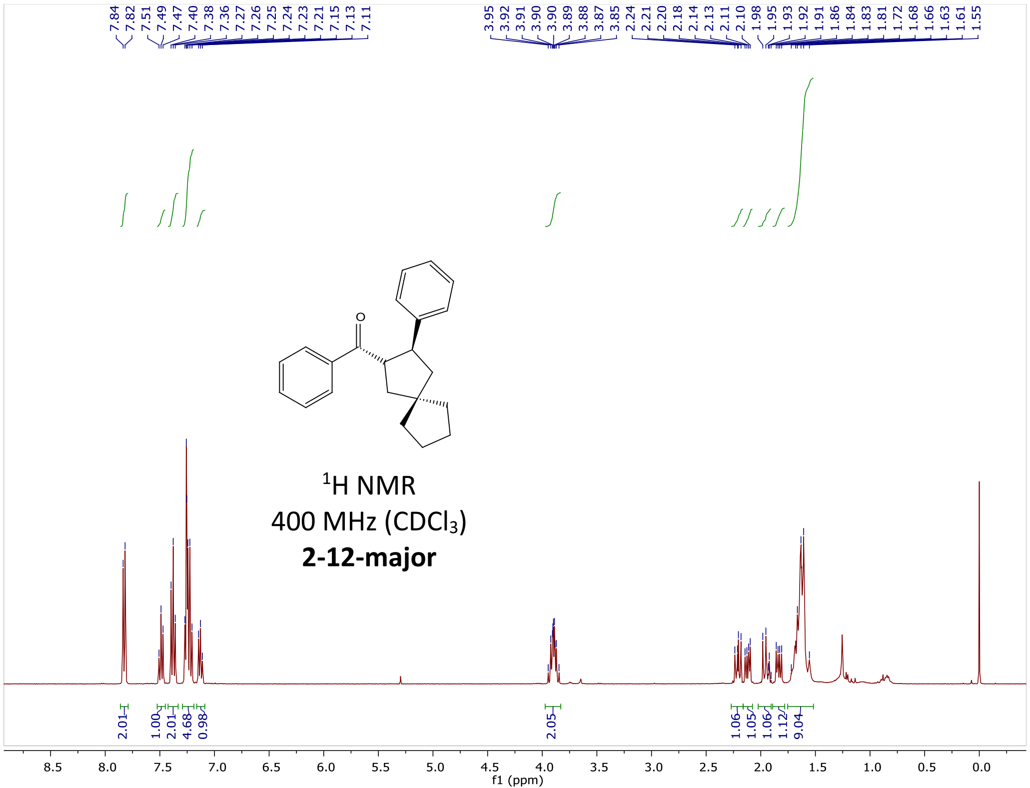
^{13}C NMR
101 MHz ($CDCl_3$)
2-13-major

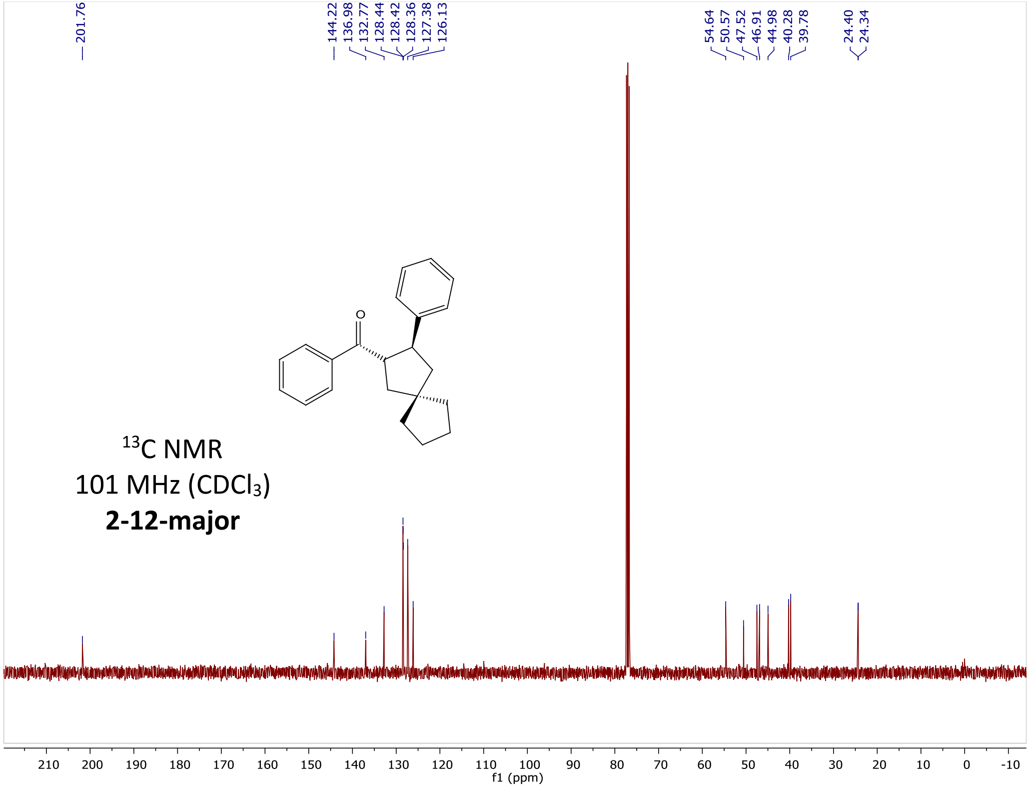


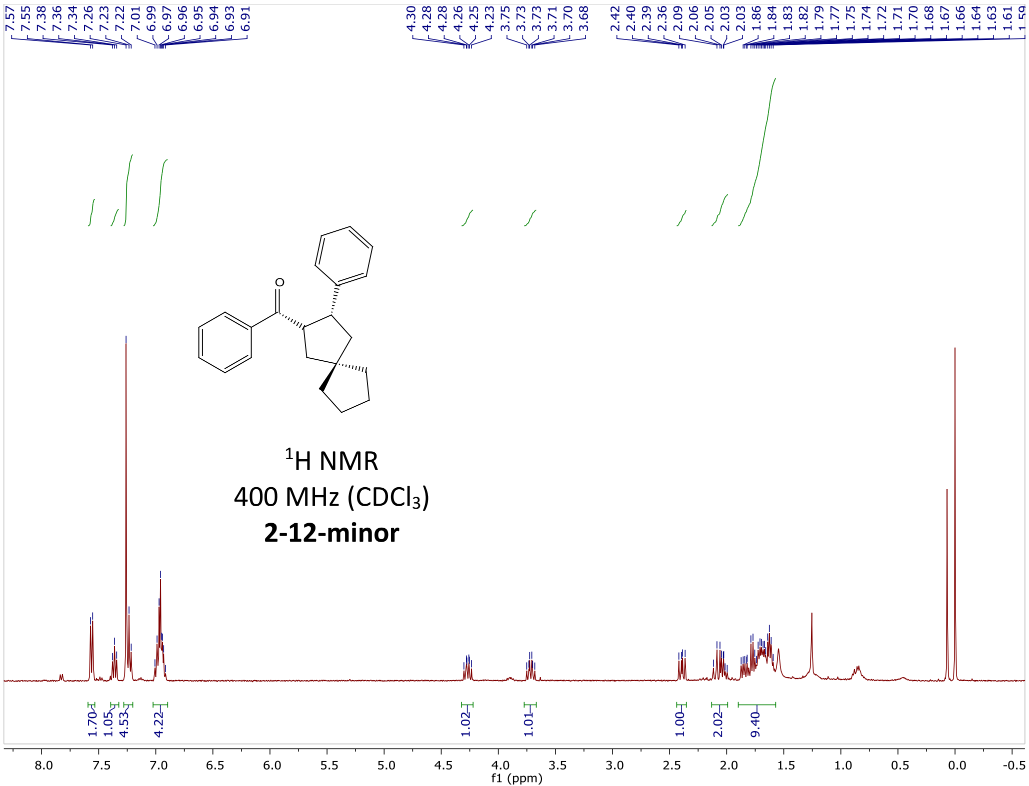
^{1}H NMR
400 MHz ($CDCl_3$)
2-14-minor



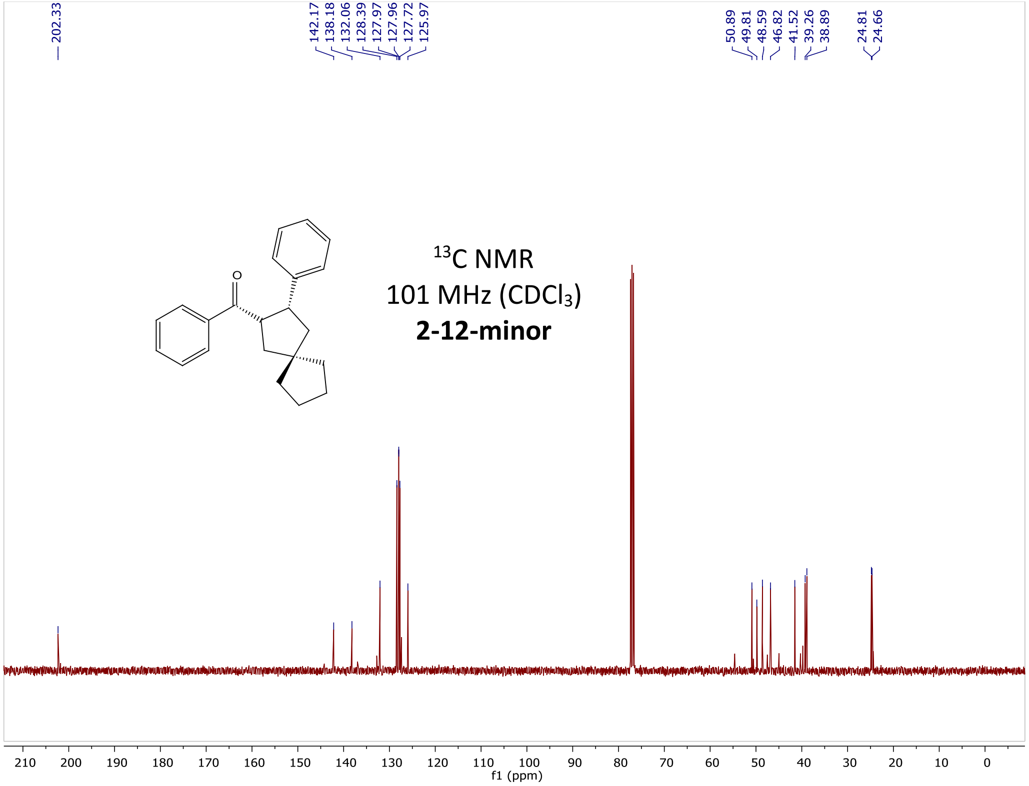
^{13}C NMR
101 MHz ($CDCl_3$)
2-14-minor


7.84
7.82
7.51
7.49
7.47
7.40
7.38
7.36
7.27
7.26
7.25
7.24
7.23
7.21
7.15
7.13
7.11
3.95
3.92
3.91
3.90
3.90
3.89
3.88
3.87
3.85
2.24
2.21
2.20
2.18
2.14
2.13
2.11
2.10
1.98
1.95
1.93
1.92
1.91
1.86
1.84
1.83
1.81
1.72
1.68
1.66
1.63
1.61
1.55
O
^{1}H NMR
400 MHz (CDCl$_3$)
2-12-major
2.01
1.00
2.01
4.68
0.98
2.05
1.06
1.05
1.06
1.12
9.04
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
f1 (ppm)

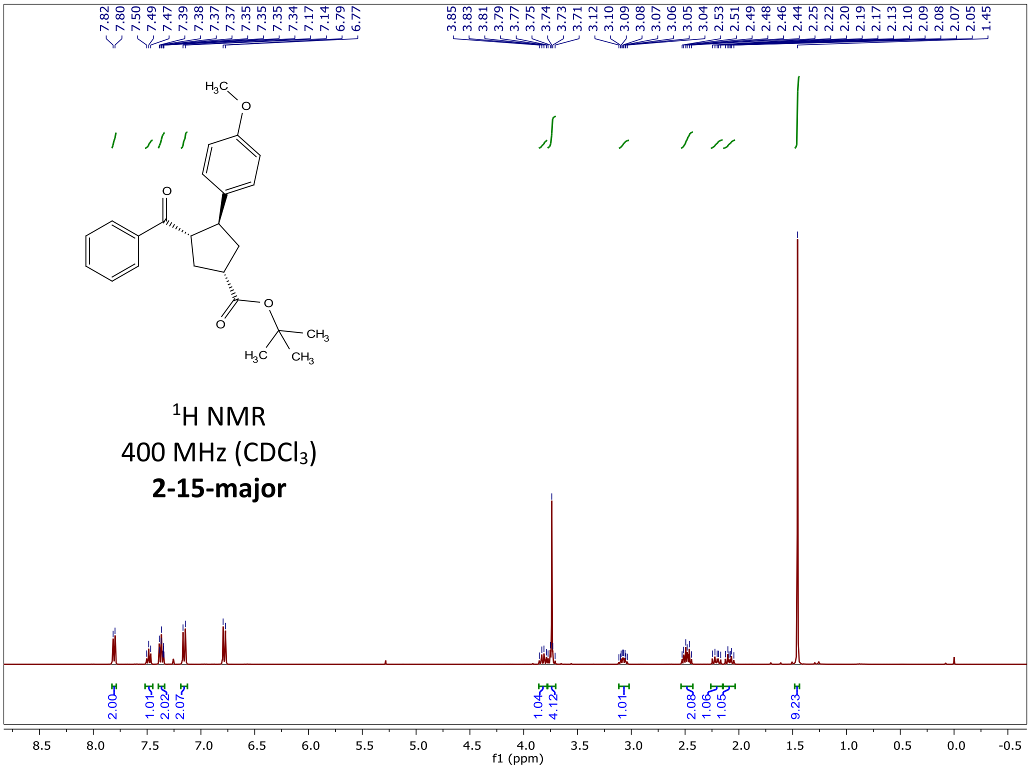

201.76
144.22
136.98
132.77
128.44
128.42
128.36
127.38
126.13
54.64
50.57
47.52
46.91
44.98
40.28
39.78
24.40
24.34
O
^{13}C NMR
101 MHz (CDCl$_3$)
2-12-major
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

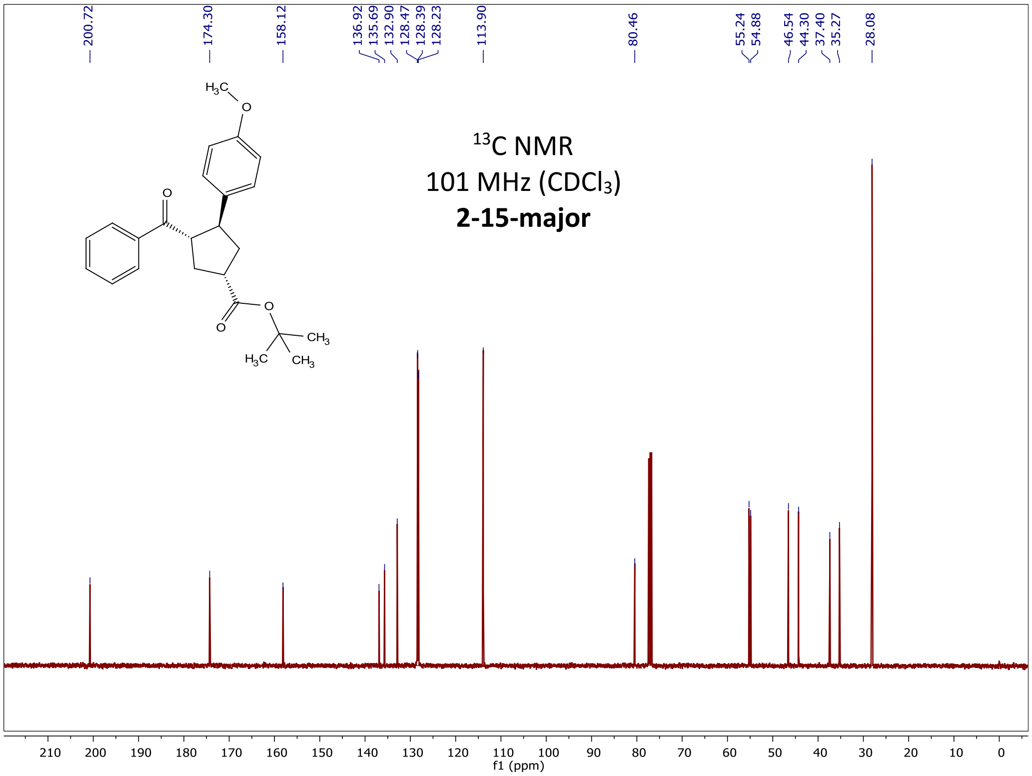


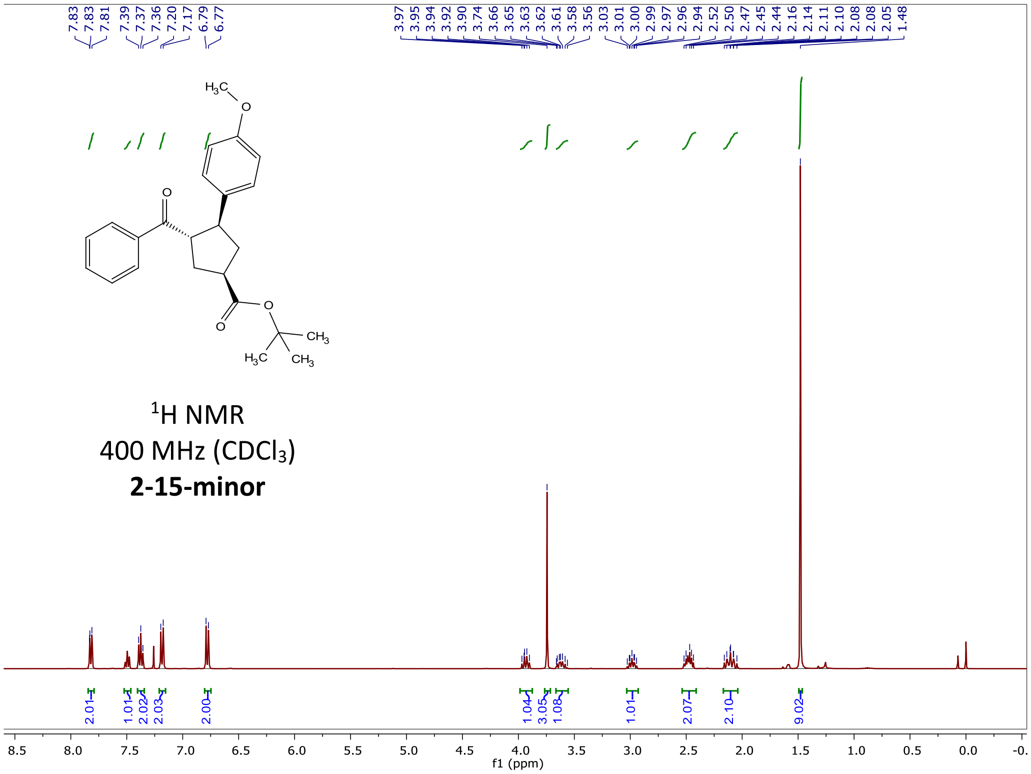
^{1}H NMR
400 MHz ($CDCl_3$)
2-12-minor

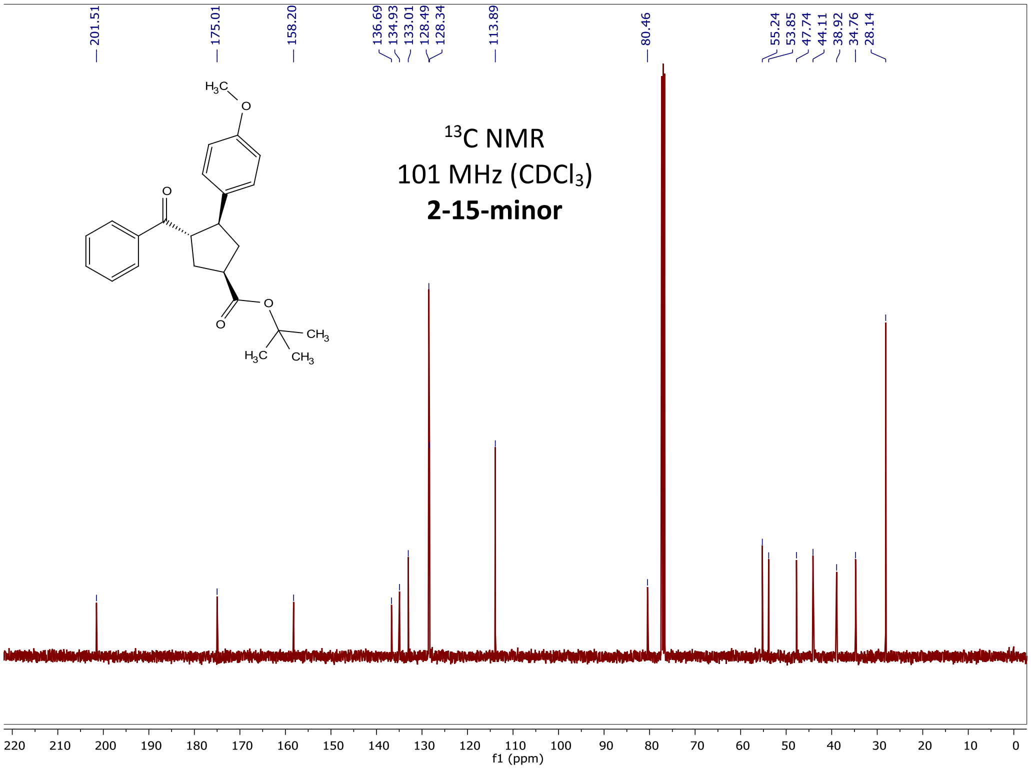


^{13}C NMR
101 MHz ($CDCl_3$)
2-12-minor


7.82
7.80
7.50
7.49
7.47
7.39
7.38
7.37
7.37
7.35
7.35
7.35
7.34
7.17
7.14
6.79
6.77
3.85
3.83
3.81
3.79
3.77
3.75
3.74
3.73
3.71
3.12
3.10
3.09
3.08
3.07
3.06
3.05
3.04
2.53
2.51
2.49
2.48
2.46
2.44
2.25
2.22
2.20
2.19
2.17
2.13
2.10
2.09
2.08
2.07
2.05
1.45
H$_3$C
O
O
O
O
CH$_3$
H$_3$C
CH$_3$
^{1}H NMR
400 MHz (CDCl$_3$)
2-15-major
2.00
1.01
2.02
2.07
1.04
4.12
1.01
2.08
1.06
1.05
9.23
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)


200.72
174.30
158.12
136.92
135.69
132.90
128.47
128.39
128.23
113.90
80.46
55.24
54.88
46.54
44.30
37.40
35.27
28.08
H$_3$C
O
O
O
O
CH$_3$
H$_3$C
CH$_3$
^{13}C NMR
101 MHz (CDCl$_3$)
2-15-major
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.83
7.83
7.81
7.39
7.37
7.36
7.20
7.17
6.79
6.77
3.97
3.95
3.94
3.92
3.90
3.74
3.66
3.65
3.63
3.62
3.61
3.58
3.56
3.03
3.01
3.00
2.99
2.97
2.96
2.94
2.52
2.50
2.47
2.45
2.44
2.16
2.14
2.11
2.10
2.08
2.08
2.05
1.48
H_3C
O
O
O
O
CH_3
H_3C
CH_3
^{1}H NMR
400 MHz ($CDCl_3$)
2-15-minor
2.01
1.01
2.02
2.03
2.00
1.04
3.05
1.08
1.01
2.07
2.10
9.02
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.
f1 (ppm)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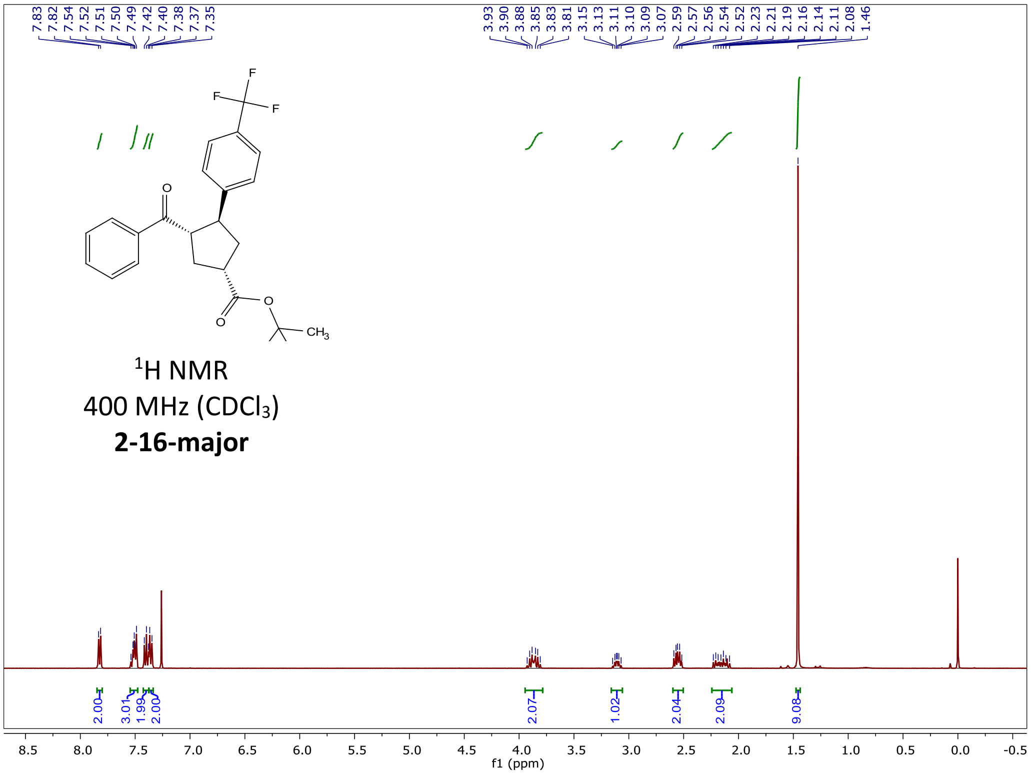
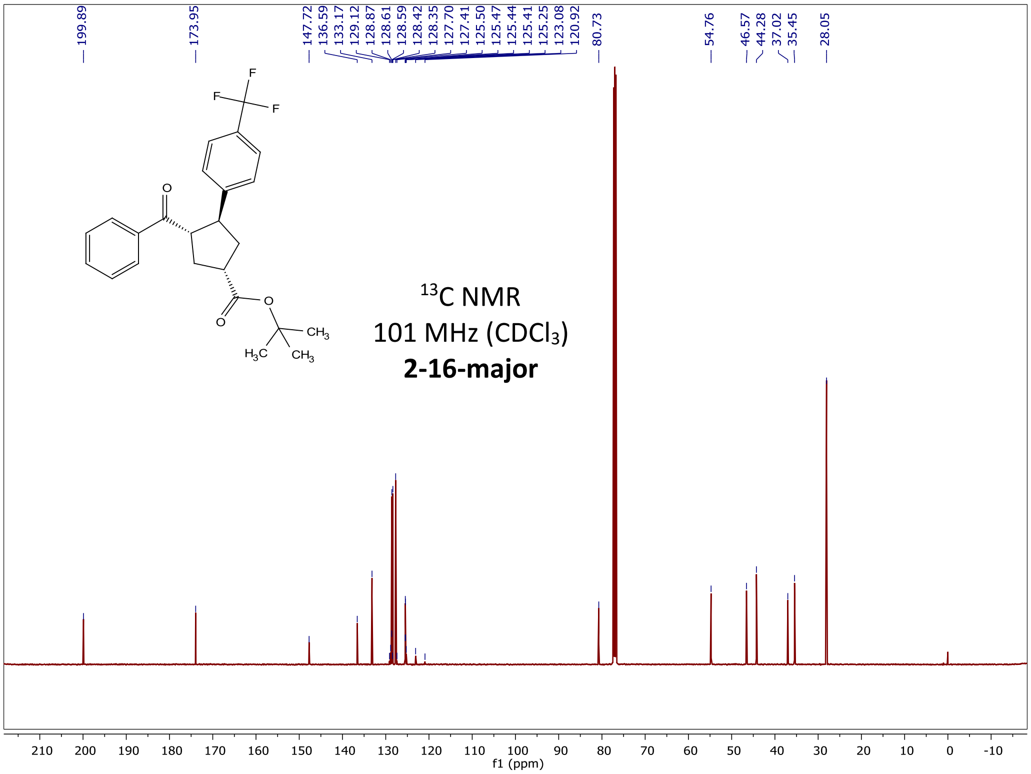
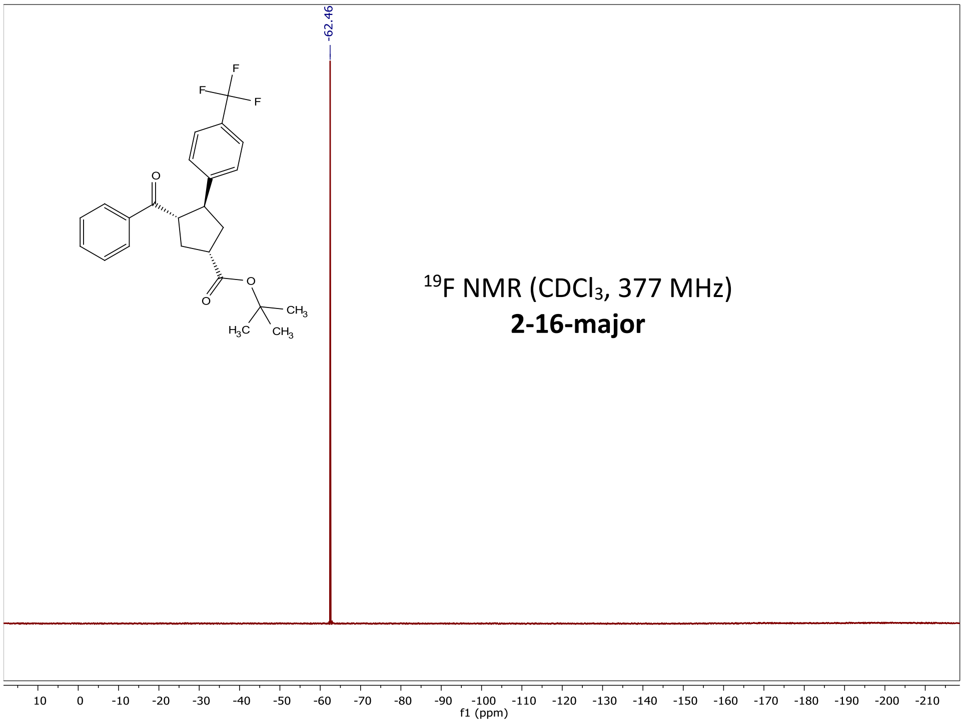
175.01
158.20
136.69
134.93
133.01
128.49
128.34
113.89
80.46
55.24
53.85
47.74
44.11
38.92
34.76
28.14
H_3C
O
O
O
O
CH_3
H_3C
CH_3
^{13}C NMR
101 MHz ($CDCl_3$)
2-15-minor
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



^{1}H NMR
400 MHz (CDCl$_3$)
2-16-major

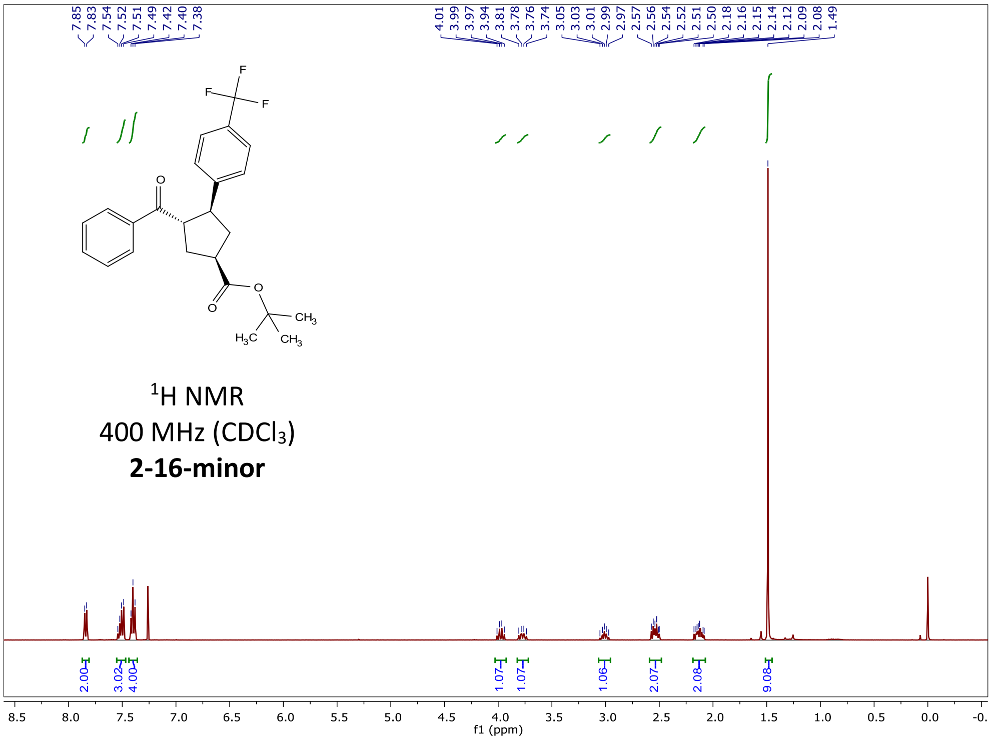


^{13}C NMR
101 MHz (CDCl$_3$)
2-16-major



^{19}F NMR (CDCl$_3$, 377 MHz)

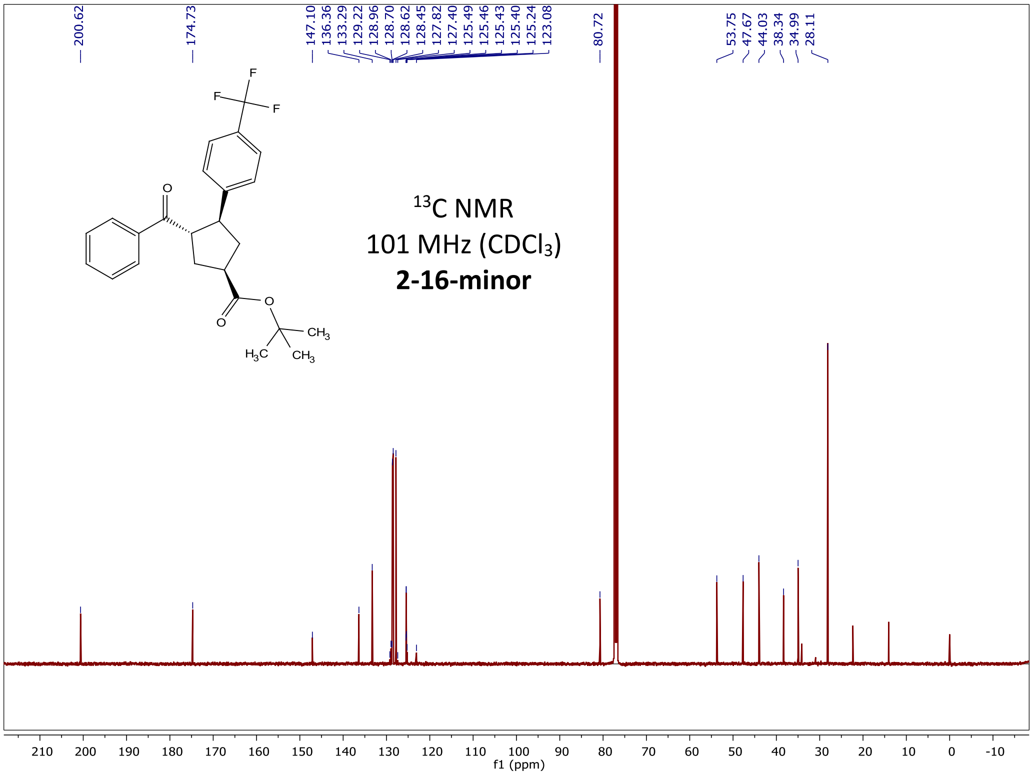
2-16-major



^{1}H NMR

400 MHz (CDCl$_3$)

2-16-minor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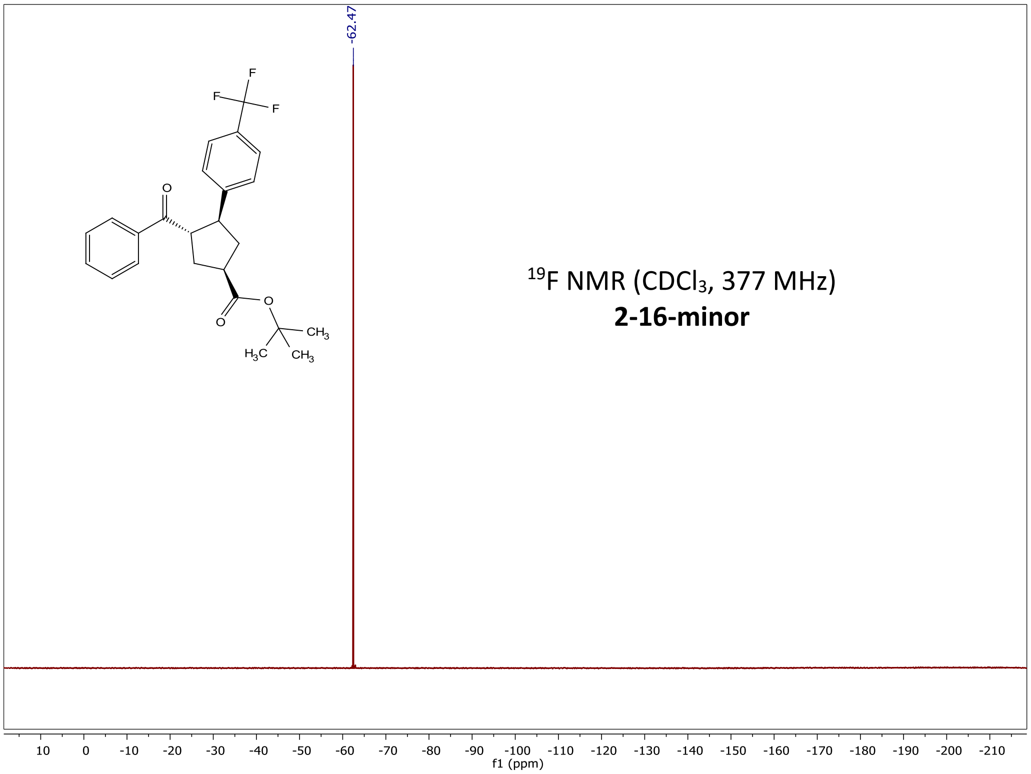
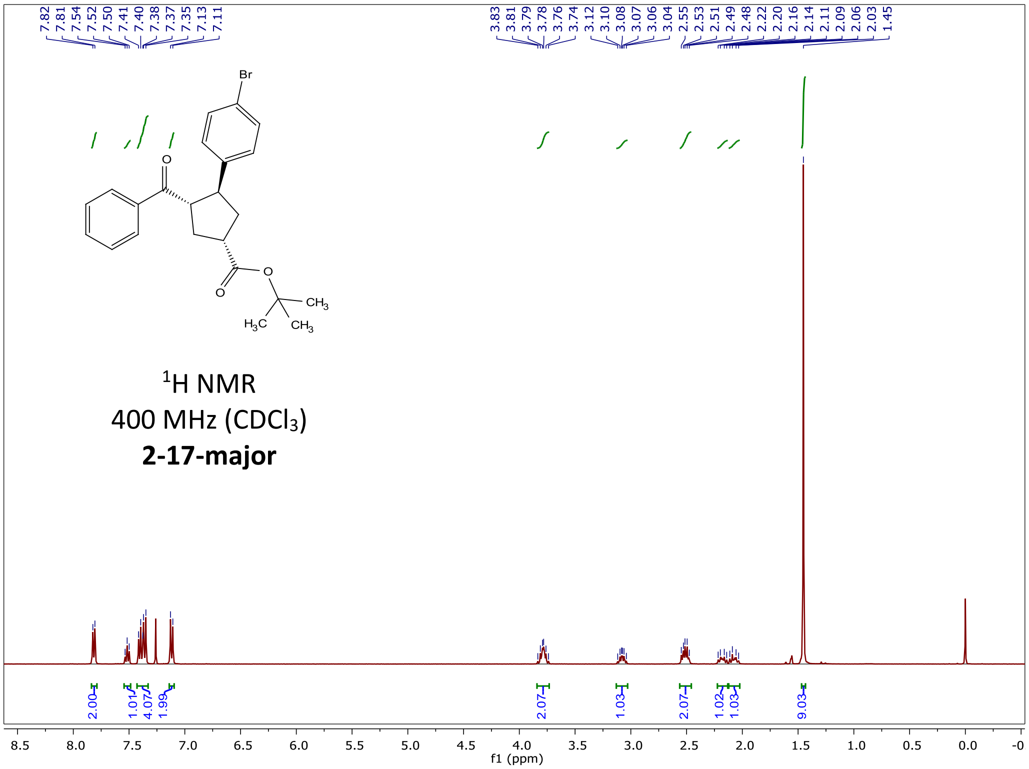
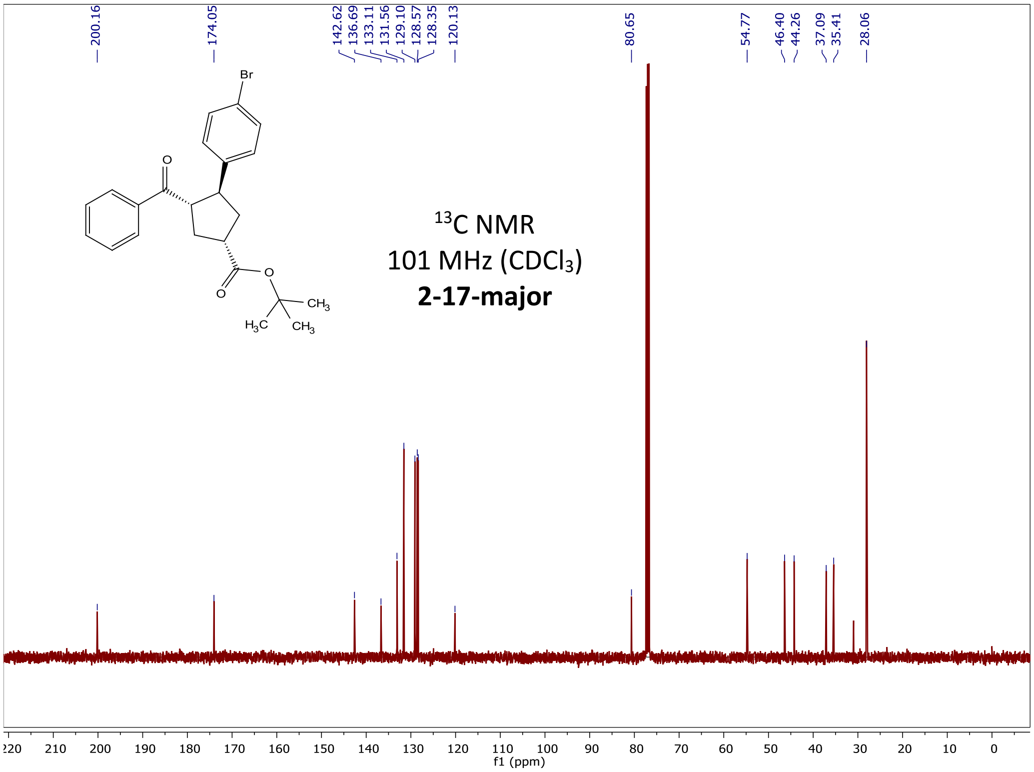
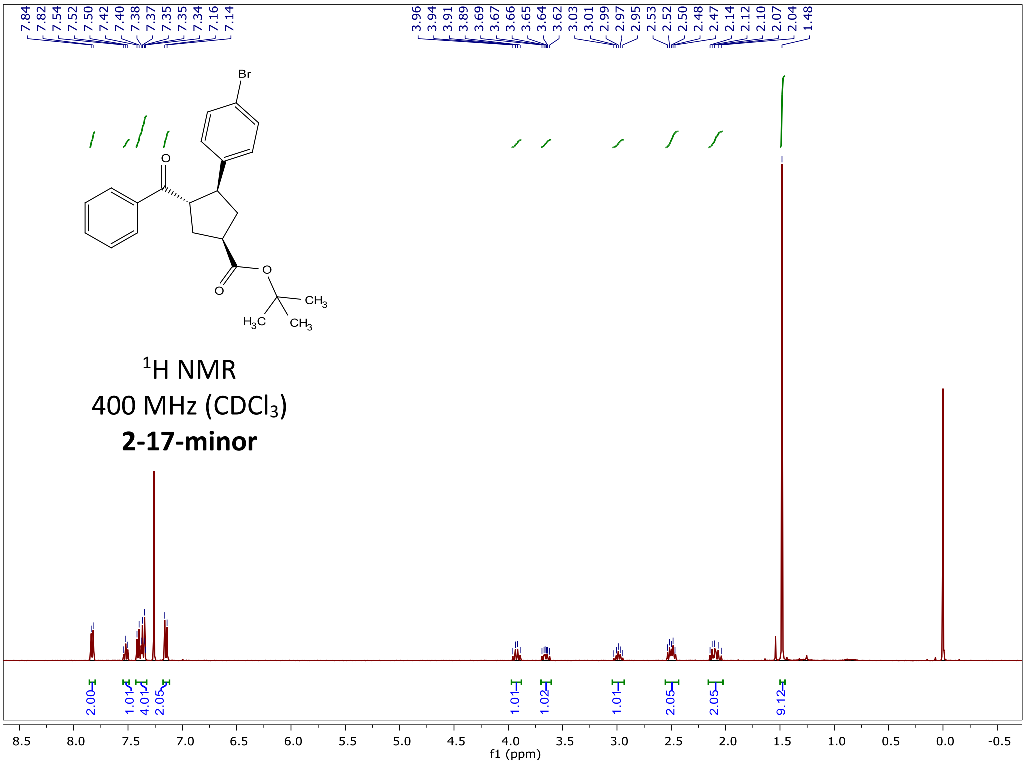
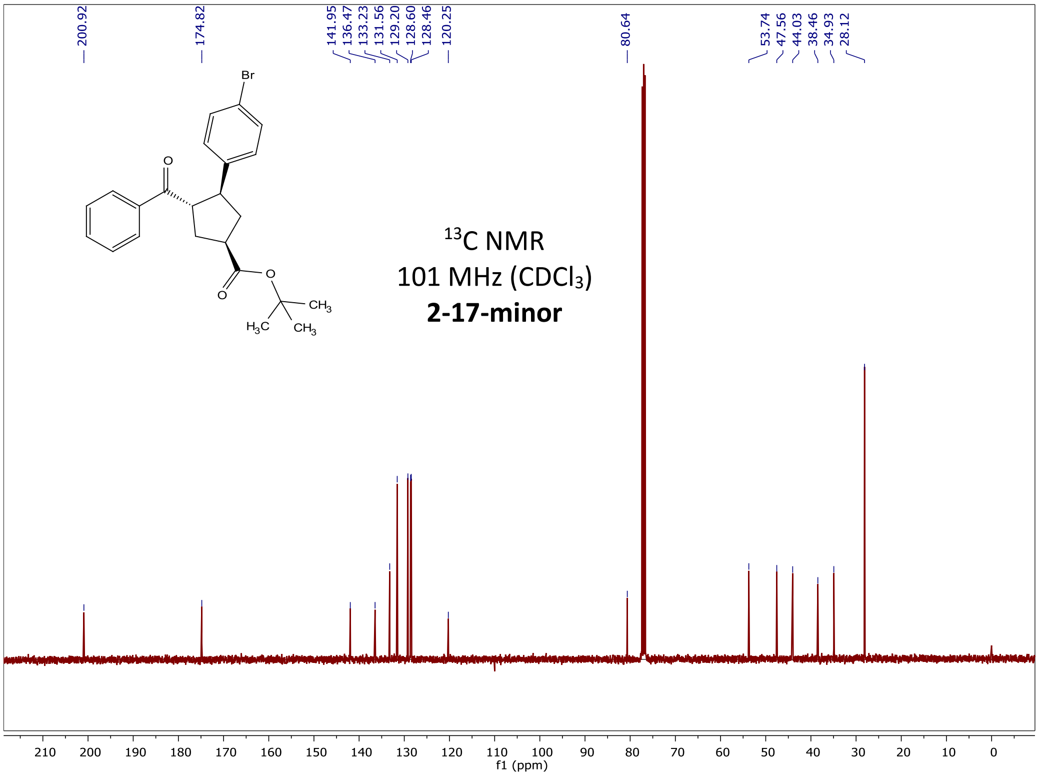
174.73
147.10
136.36
133.29
129.22
128.96
128.70
128.62
128.45
127.82
127.40
125.49
125.46
125.43
125.40
125.24
123.08
80.72
53.75
47.67
44.03
38.34
34.99
28.11
F
F
F
O
O
O
CH3
H3C
CH3
13C NMR
101 MHz (CDCl3)
2-16-minor
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

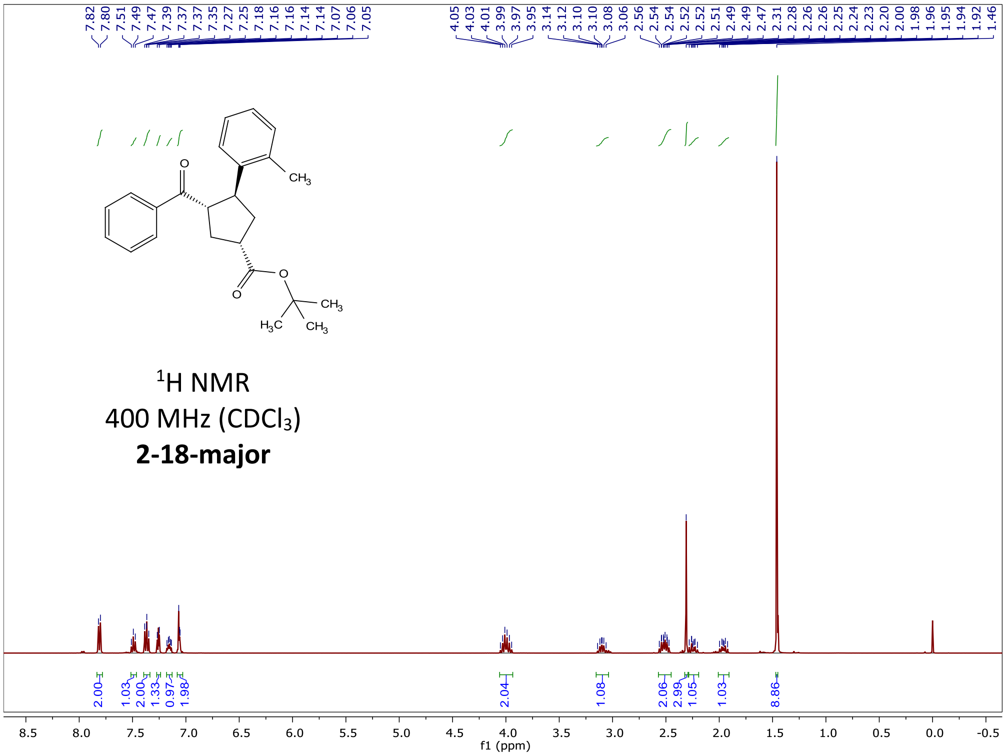

-62.47
F
F
F
O
O
O
CH3
H3C
CH3
19F NMR (CDCl3, 377 MHz)
2-16-minor
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

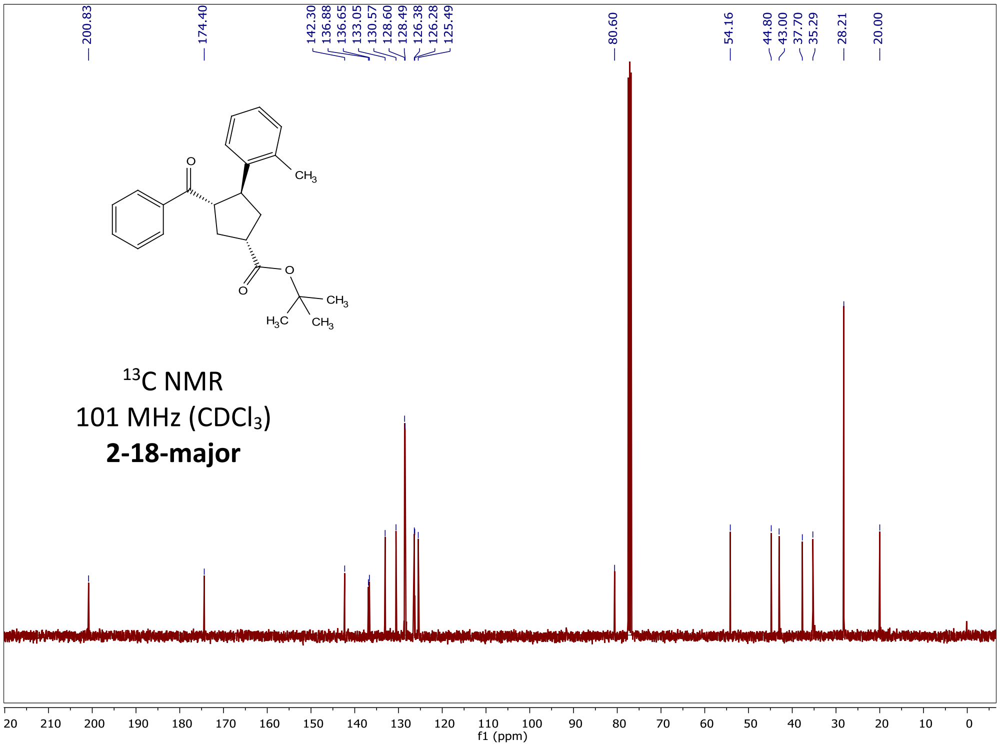

7.82
7.81
7.54
7.52
7.50
7.41
7.40
7.38
7.37
7.35
7.13
7.11
3.83
3.81
3.79
3.78
3.76
3.74
3.12
3.10
3.08
3.07
3.06
3.04
2.55
2.53
2.51
2.49
2.48
2.22
2.20
2.16
2.14
2.11
2.09
2.06
2.03
1.45
Br
O
O
O
CH3
H3C
CH3
1H NMR
400 MHz (CDCl3)
2-17-major
2.00
1.01
4.07
1.99
2.07
1.03
2.07
1.02
1.03
9.03
8.5
8.0
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
f1 (ppm)

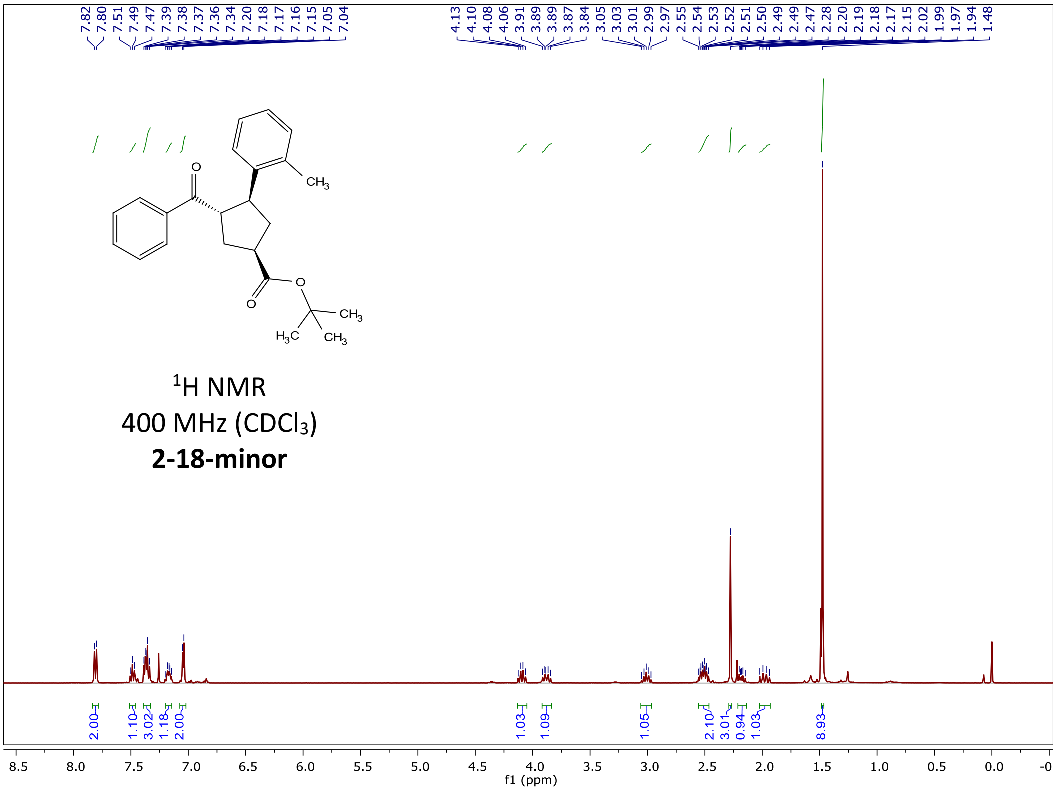

200.16
174.05
142.62
136.69
133.11
131.56
129.10
128.57
128.35
120.13
80.65
54.77
46.40
44.26
37.09
35.41
28.06
Br
O
O
O
CH3
H3C
CH3
13C NMR
101 MHz (CDCl3)
2-17-major
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.84
7.82
7.54
7.52
7.50
7.42
7.40
7.38
7.37
7.35
7.35
7.34
7.16
7.14
3.96
3.94
3.91
3.89
3.69
3.67
3.66
3.65
3.64
3.62
3.03
3.01
2.99
2.97
2.95
2.53
2.52
2.50
2.48
2.47
2.14
2.12
2.10
2.07
2.04
1.48
Br
O
O
O
CH3
H3C
CH3
1H NMR
400 MHz (CDCl3)
2-17-minor
2.00
1.01
4.01
2.05
1.01
1.02
1.01
2.05
2.05
9.12
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)

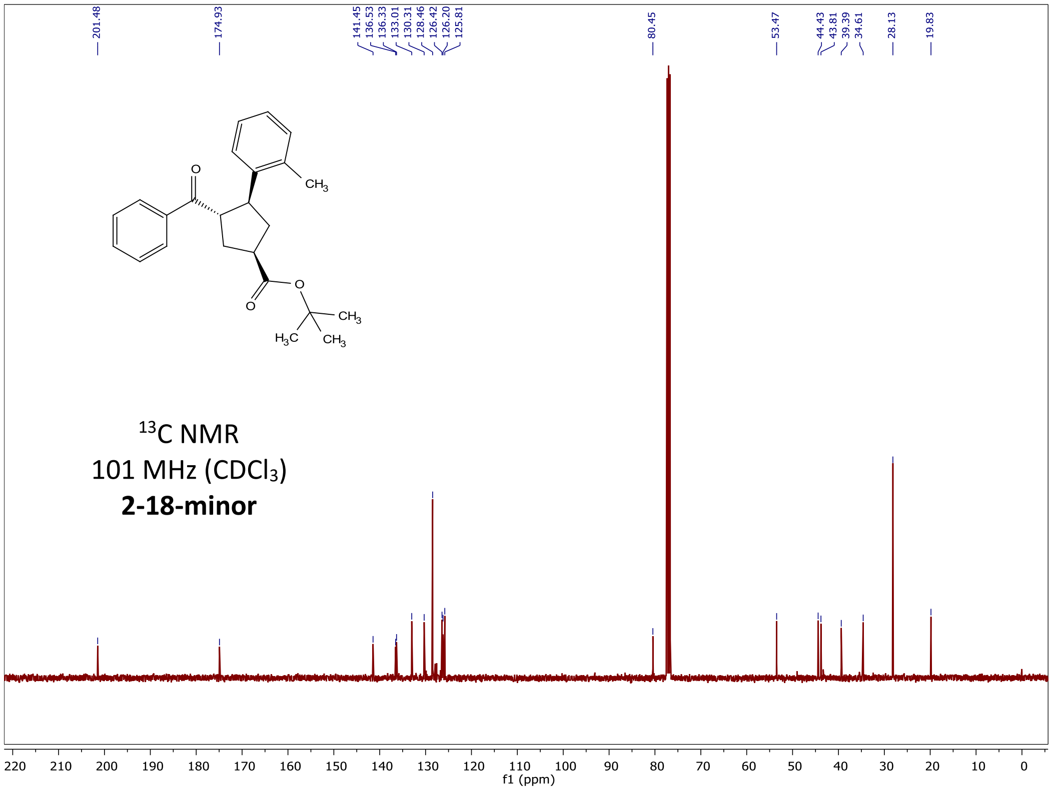

200.92
174.82
141.95
136.47
133.23
131.56
129.20
128.60
128.46
120.25
80.64
53.74
47.56
44.03
38.46
34.93
28.12
Br
O
O
O
CH3
H3C
CH3
13C NMR
101 MHz (CDCl3)
2-17-minor
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.82
7.80
7.51
7.49
7.47
7.39
7.37
7.37
7.35
7.27
7.25
7.18
7.16
7.16
7.14
7.14
7.07
7.06
7.05
4.05
4.03
4.01
3.99
3.97
3.95
3.14
3.12
3.10
3.10
3.08
3.06
2.56
2.54
2.54
2.52
2.52
2.51
2.49
2.49
2.47
2.31
2.28
2.26
2.26
2.25
2.24
2.23
2.20
2.00
1.98
1.96
1.95
1.94
1.92
1.46
O
CH3
O
O
CH3
H3C
CH3
^{1}H NMR
400 MHz (CDCl$_3$)
2-18-major
2.00
1.03
2.00
1.33
0.97
1.98
2.04
1.08
2.06
2.99
1.05
1.03
8.86
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)

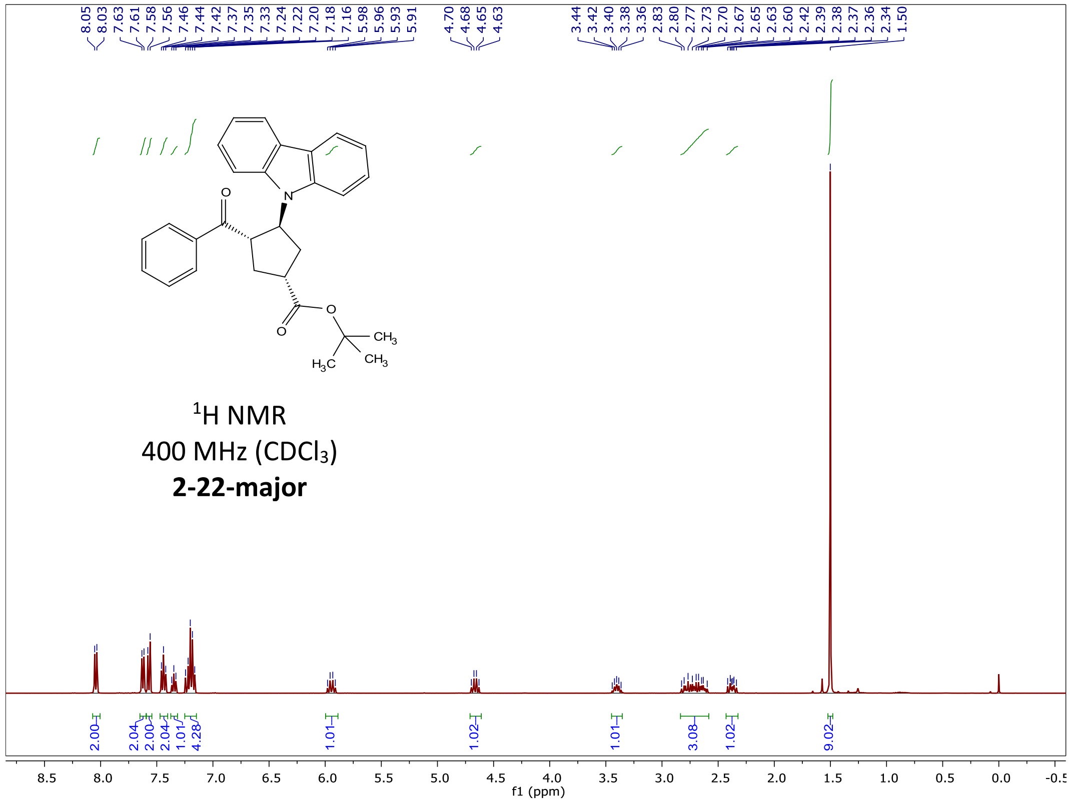

200.83
174.40
142.30
136.88
136.65
133.05
130.57
128.60
128.49
126.38
126.28
125.49
80.60
54.16
44.80
43.00
37.70
35.29
28.21
20.00
O
CH3
O
O
CH3
H3C
CH3
^{13}C NMR
101 MHz (CDCl$_3$)
2-18-major
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

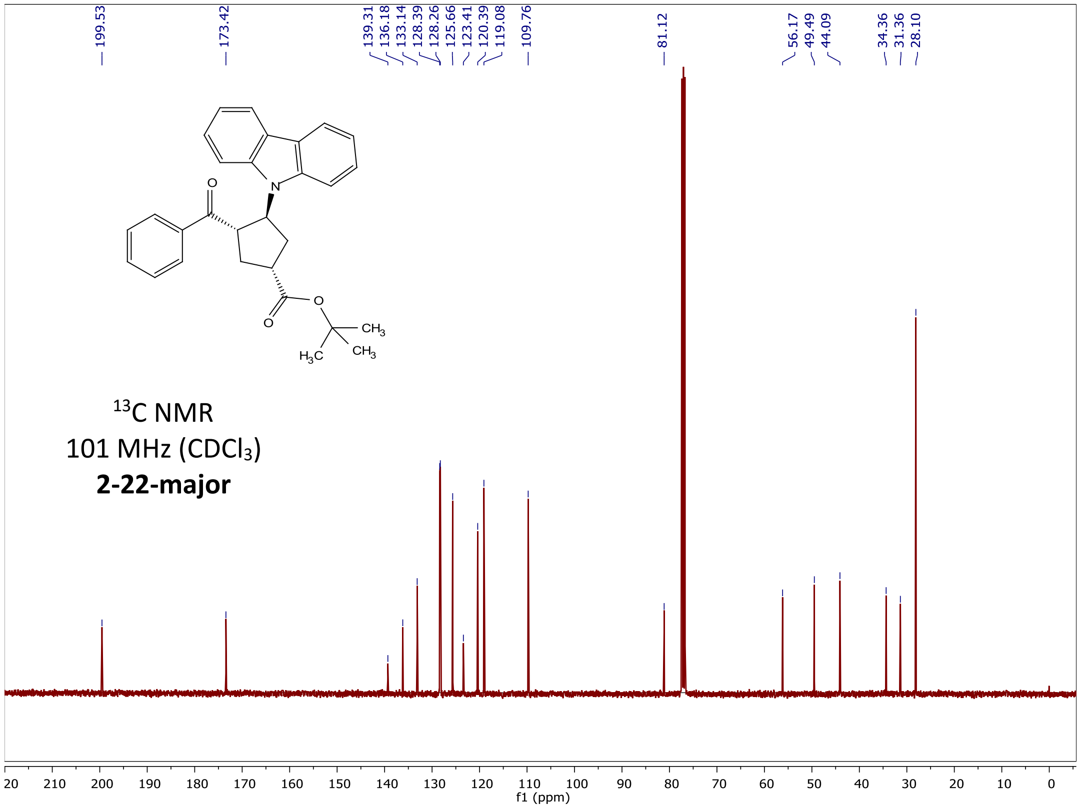


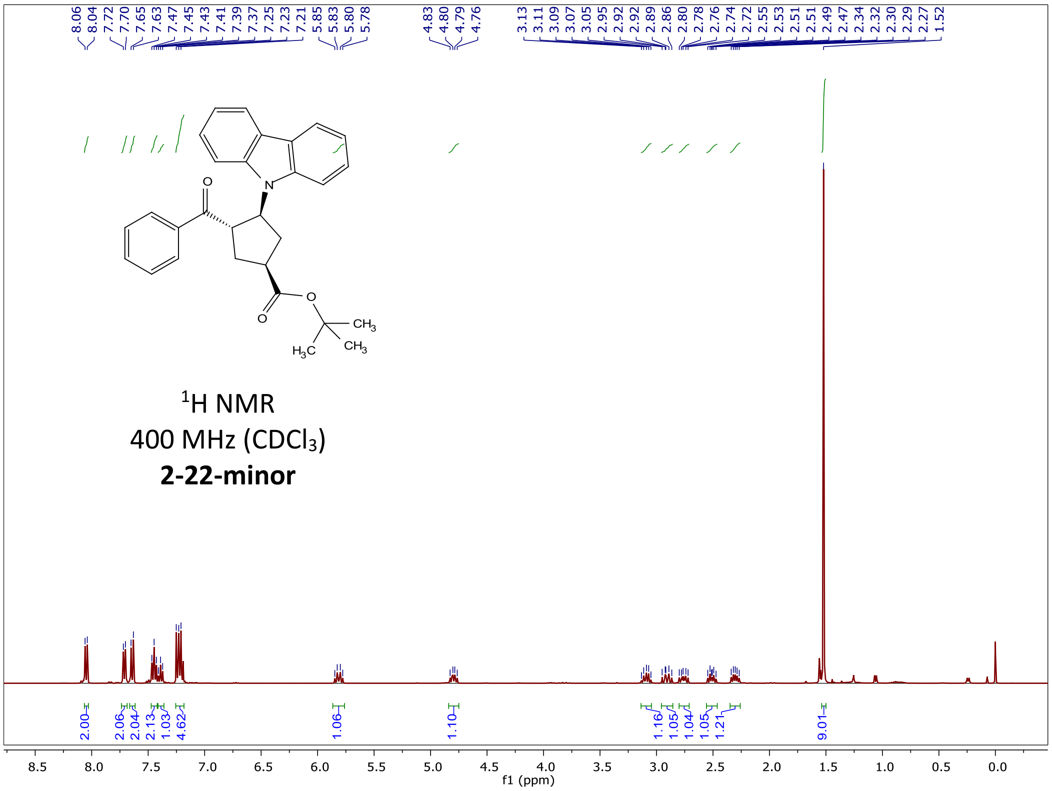
^{1}H NMR
400 MHz (CDCl$_3$)
2-18-minor



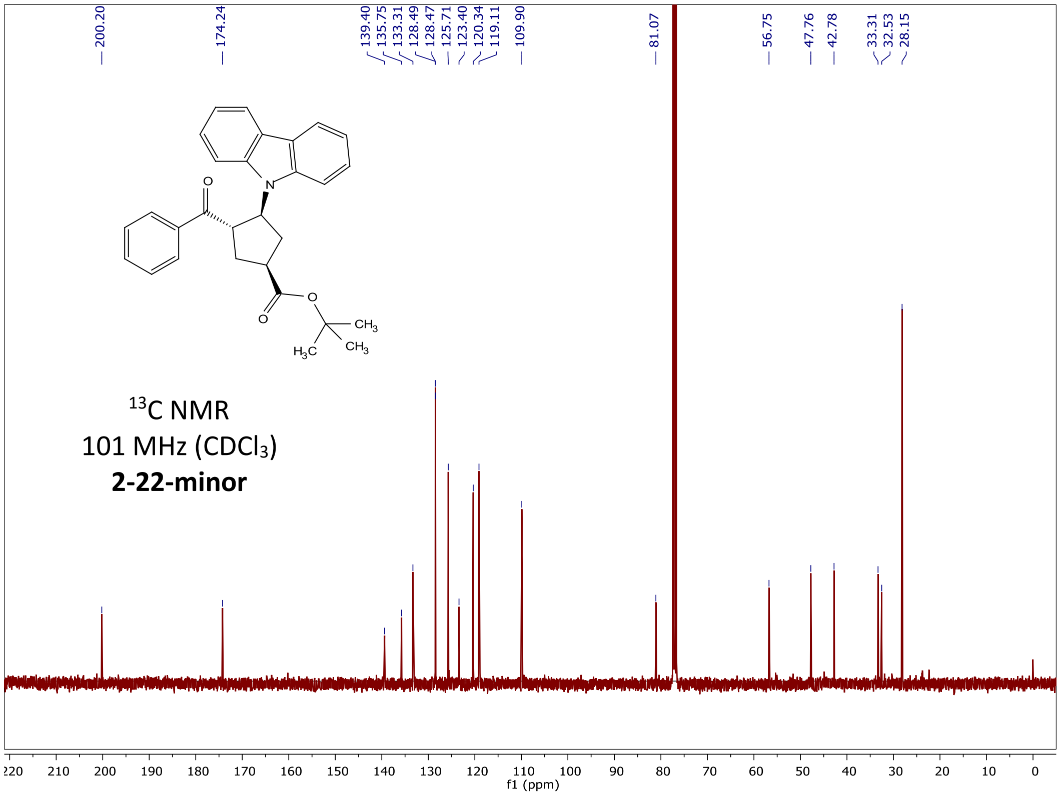
^{13}C NMR
101 MHz (CDCl$_3$)
2-18-minor


8.05
8.03
7.63
7.61
7.58
7.56
7.46
7.44
7.42
7.37
7.35
7.33
7.24
7.22
7.20
7.18
7.16
5.98
5.96
5.93
5.91
4.70
4.68
4.65
4.63
3.44
3.42
3.40
3.38
3.36
2.83
2.80
2.77
2.73
2.70
2.67
2.65
2.63
2.60
2.42
2.39
2.38
2.37
2.36
2.34
1.50
O
N
O
O
CH3
H3C
CH3
1H NMR
400 MHz (CDCl3)
2-22-major
2.00
2.04
2.00
2.04
1.01
4.28
1.01
1.02
1.01
3.08
1.02
9.02
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)

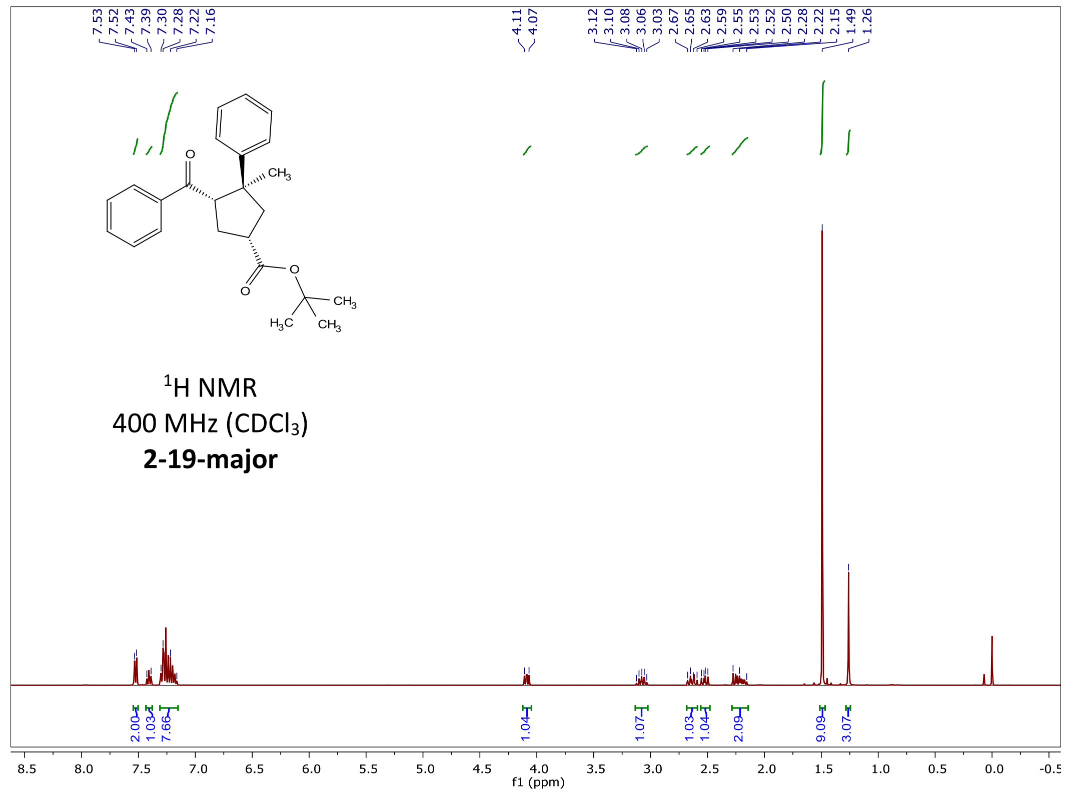

199.53
173.42
139.31
136.18
133.14
128.39
128.26
125.66
123.41
120.39
119.08
109.76
81.12
56.17
49.49
44.09
34.36
31.36
28.10
O
N
O
O
CH3
H3C
CH3
13C NMR
101 MHz (CDCl3)
2-22-major
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



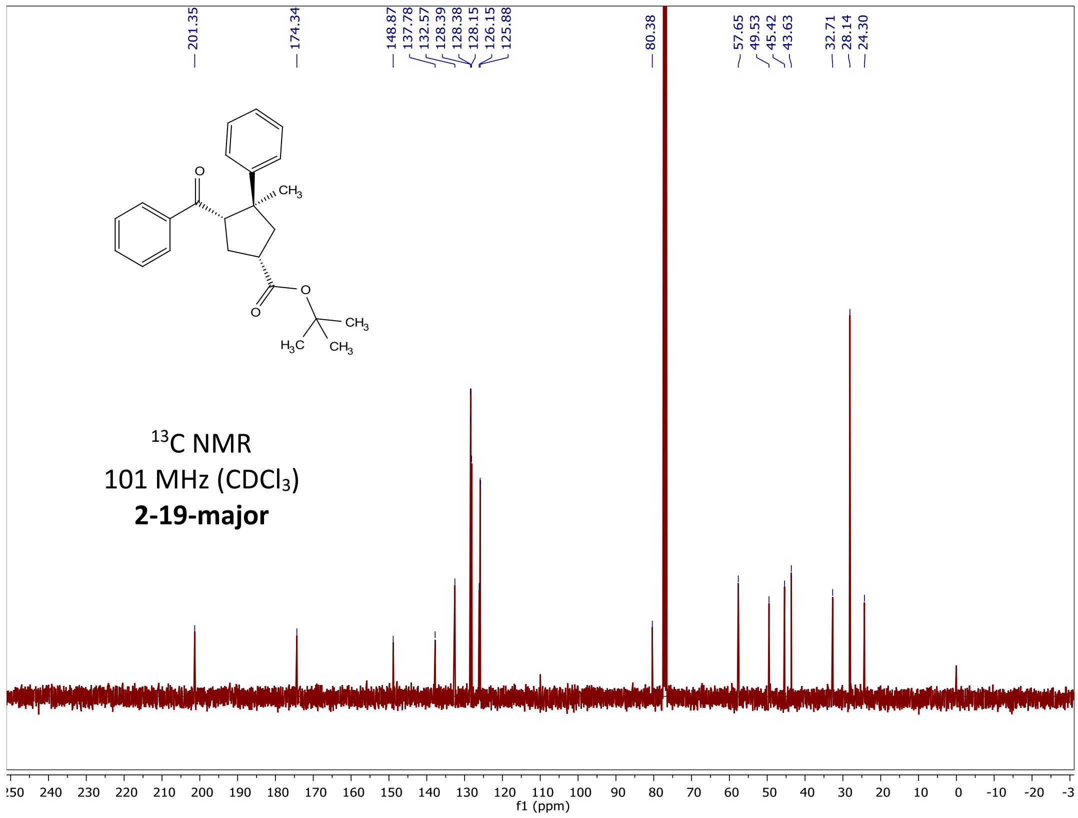
^{1}H NMR
400 MHz ($CDCl_3$)
2-22-minor



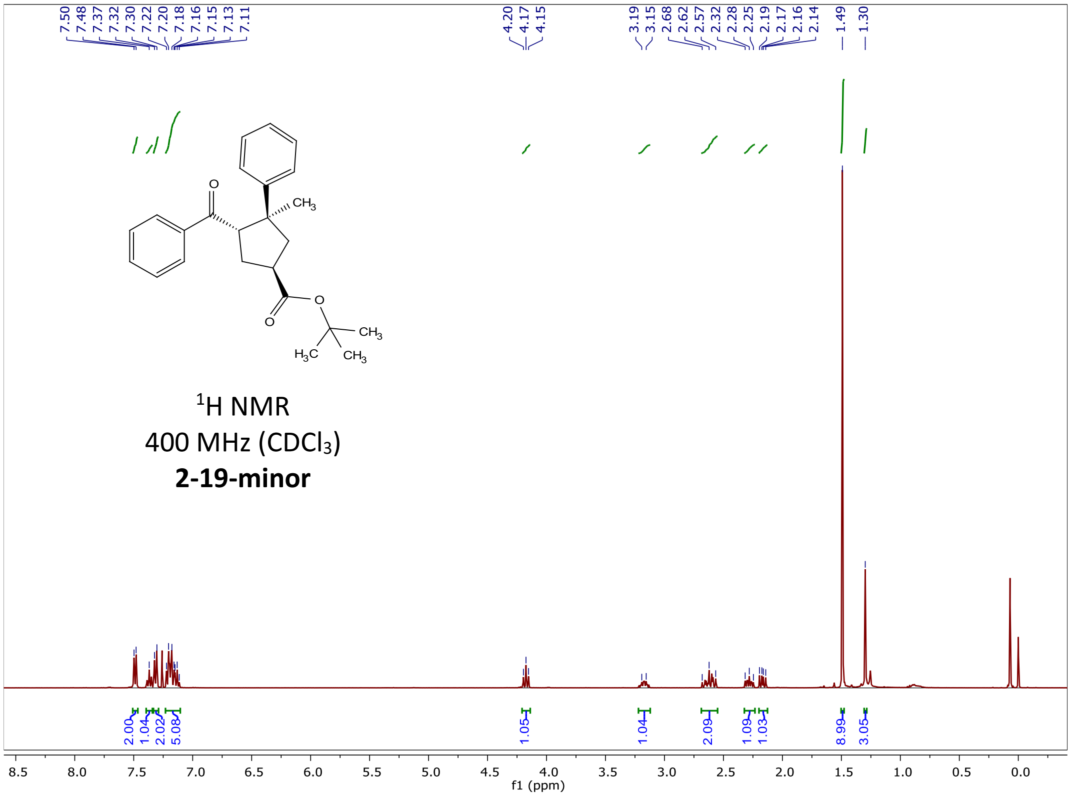
^{13}C NMR
101 MHz ($CDCl_3$)
2-22-minor

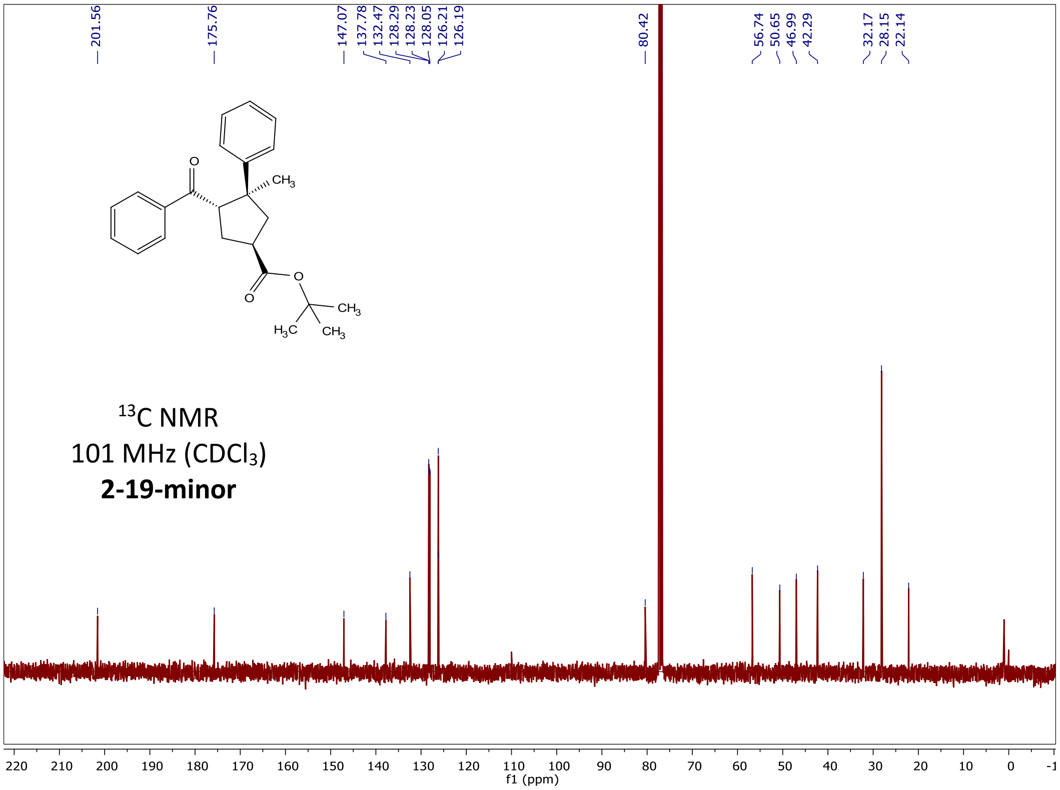


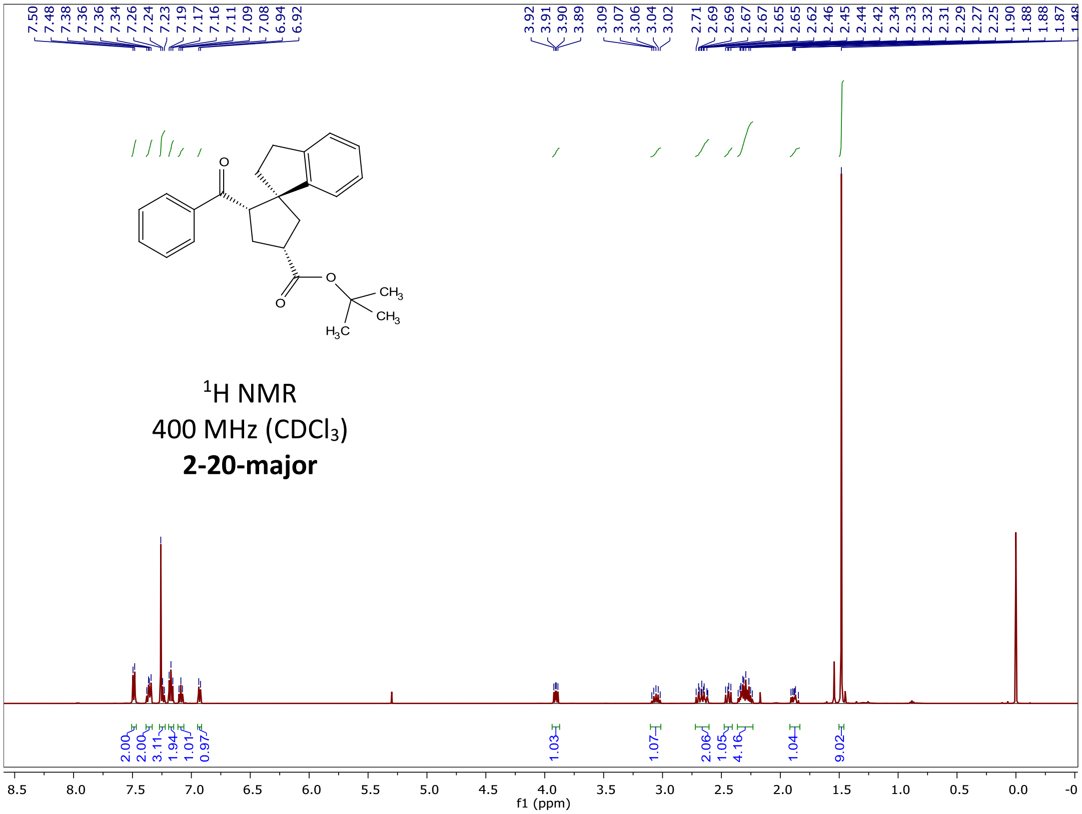
^{1}H NMR
400 MHz (CDCl$_3$)
2-19-major

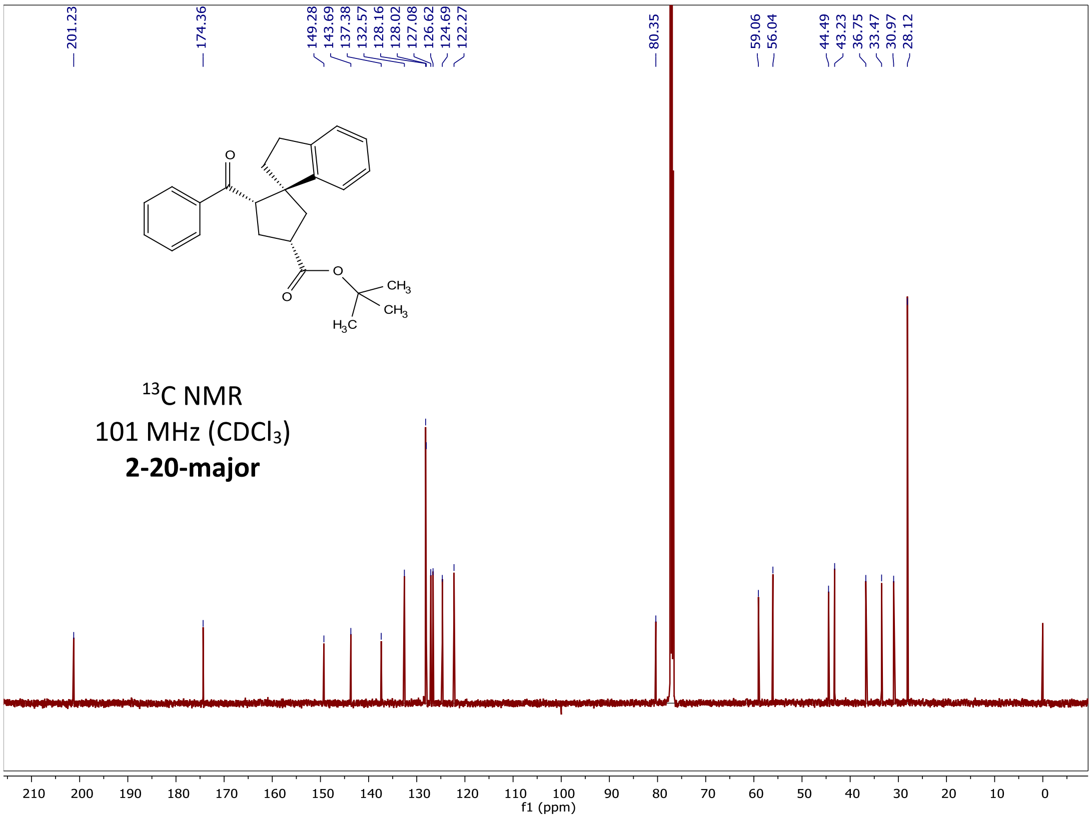


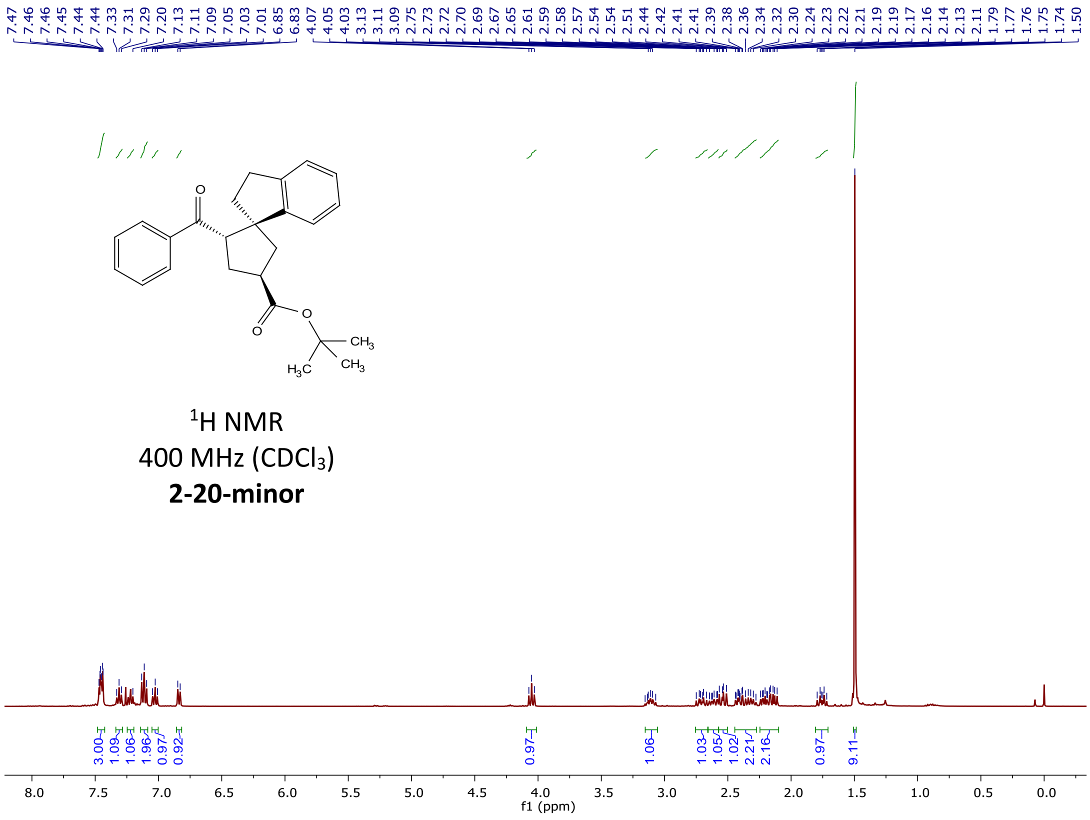
^{13}C NMR
101 MHz (CDCl$_3$)
2-19-major


7.50
7.48
7.37
7.32
7.30
7.22
7.20
7.18
7.16
7.15
7.13
7.11
4.20
4.17
4.15
3.19
3.15
2.68
2.62
2.57
2.32
2.28
2.25
2.19
2.17
2.16
2.14
1.49
1.30
O
CH3
O
O
CH3
H3C
CH3
1H NMR
400 MHz (CDCl3)
2-19-minor
2.00
1.04
2.02
5.08
1.05
1.04
2.09
1.09
1.03
8.99
3.05
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
f1 (ppm)

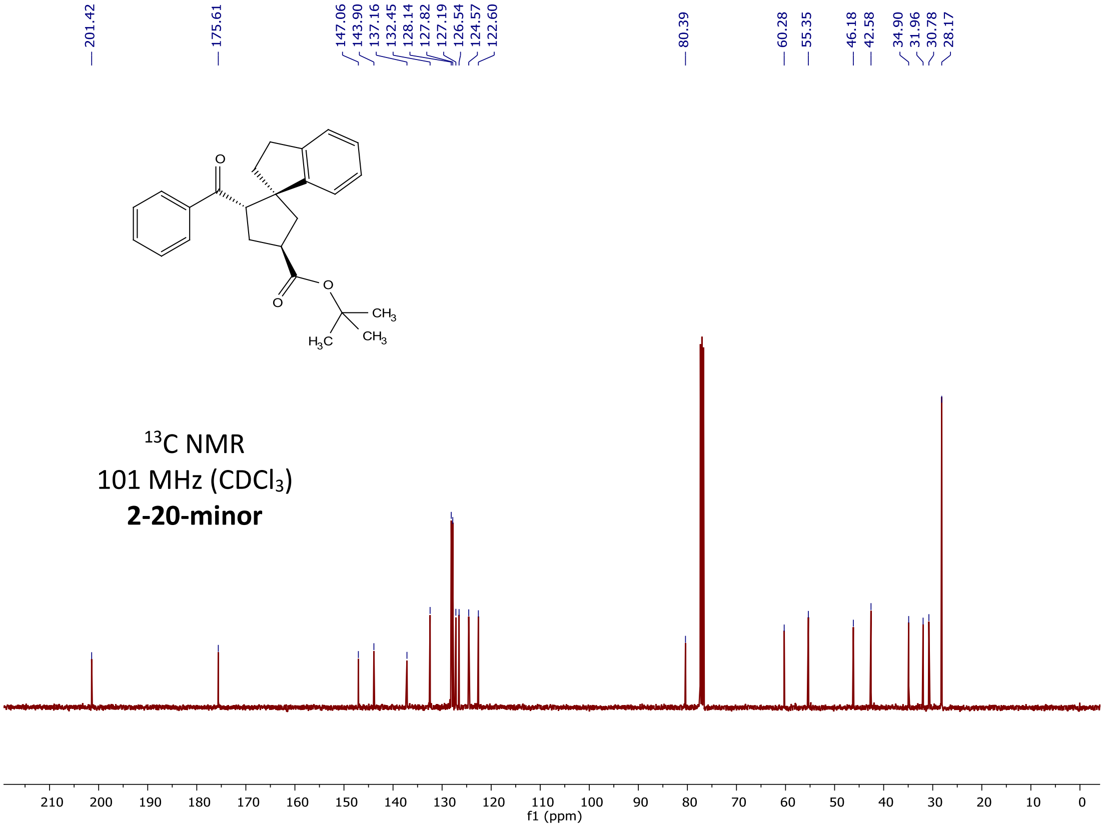

201.56
175.76
147.07
137.78
132.47
128.29
128.23
128.05
126.21
126.19
80.42
56.74
50.65
46.99
42.29
32.17
28.15
22.14
O
CH3
O
O
CH3
H3C
CH3
13C NMR
101 MHz (CDCl3)
2-19-minor
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


7.50
7.48
7.38
7.36
7.36
7.34
7.26
7.24
7.23
7.19
7.17
7.16
7.11
7.09
7.08
6.94
6.92
3.92
3.91
3.90
3.89
3.09
3.07
3.06
3.04
3.02
2.71
2.69
2.69
2.67
2.67
2.65
2.65
2.62
2.46
2.45
2.44
2.42
2.34
2.33
2.32
2.31
2.29
2.27
2.25
1.90
1.88
1.88
1.87
1.48
O
O
O
CH3
CH3
H3C
1H NMR
400 MHz (CDCl3)
2-20-major
2.00
2.00
3.11
1.94
1.01
0.97
1.03
1.07
2.06
1.05
4.16
1.04
9.02
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
f1 (ppm)

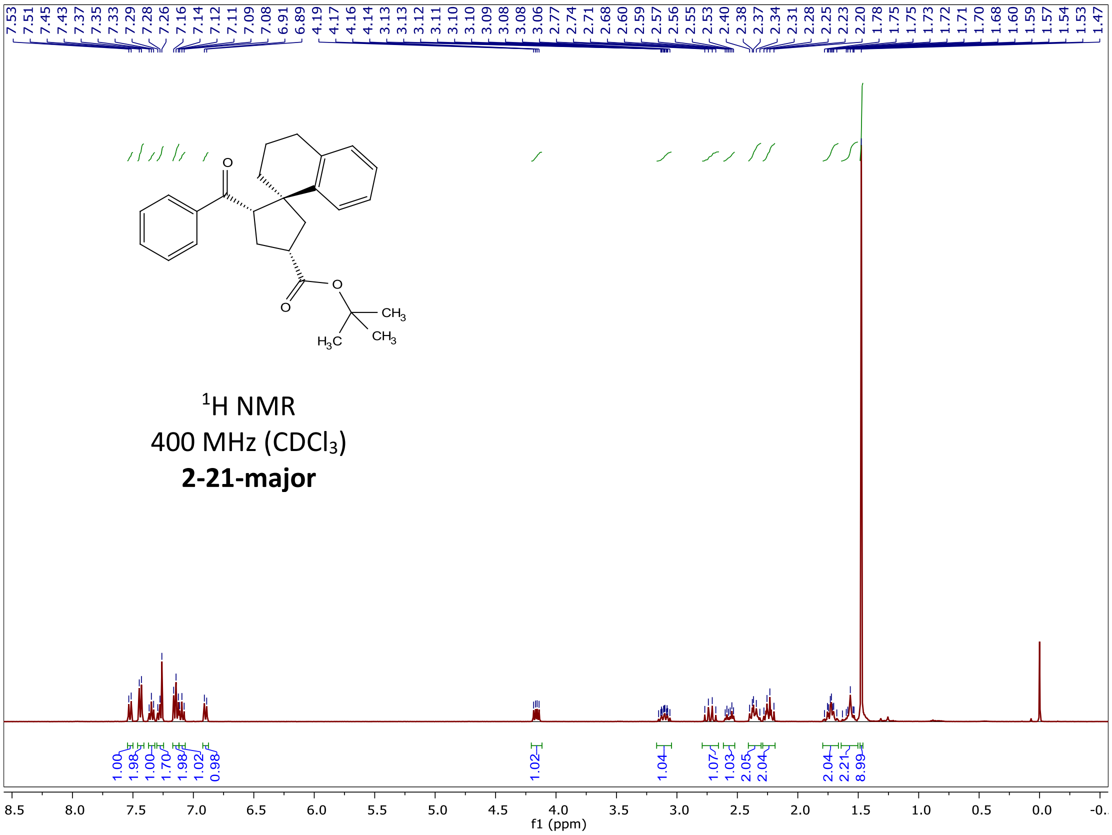

201.23
174.36
149.28
143.69
137.38
132.57
128.16
128.02
127.08
126.62
124.69
122.27
80.35
59.06
56.04
44.49
43.23
36.75
33.47
30.97
28.12
O
O
O
CH3
CH3
H3C
13C NMR
101 MHz (CDCl3)
2-20-major
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

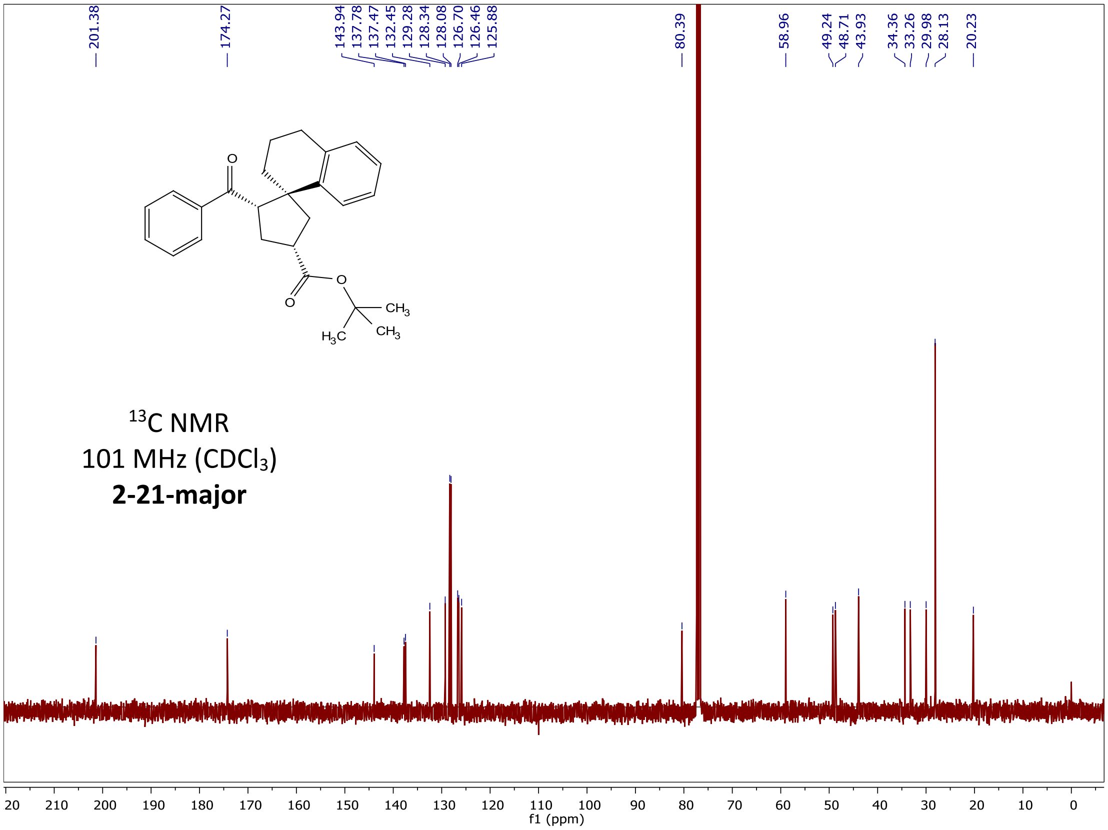


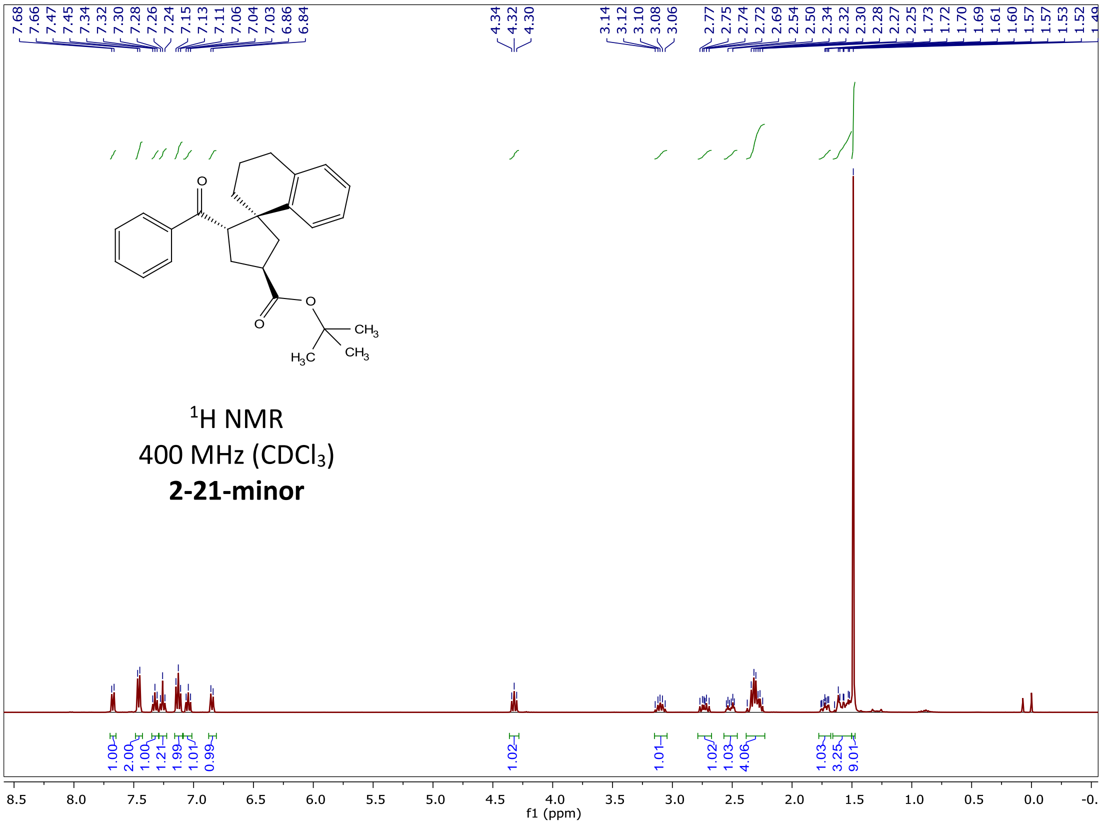
^{1}H NMR
400 MHz (CDCl$_3$)
2-20-minor

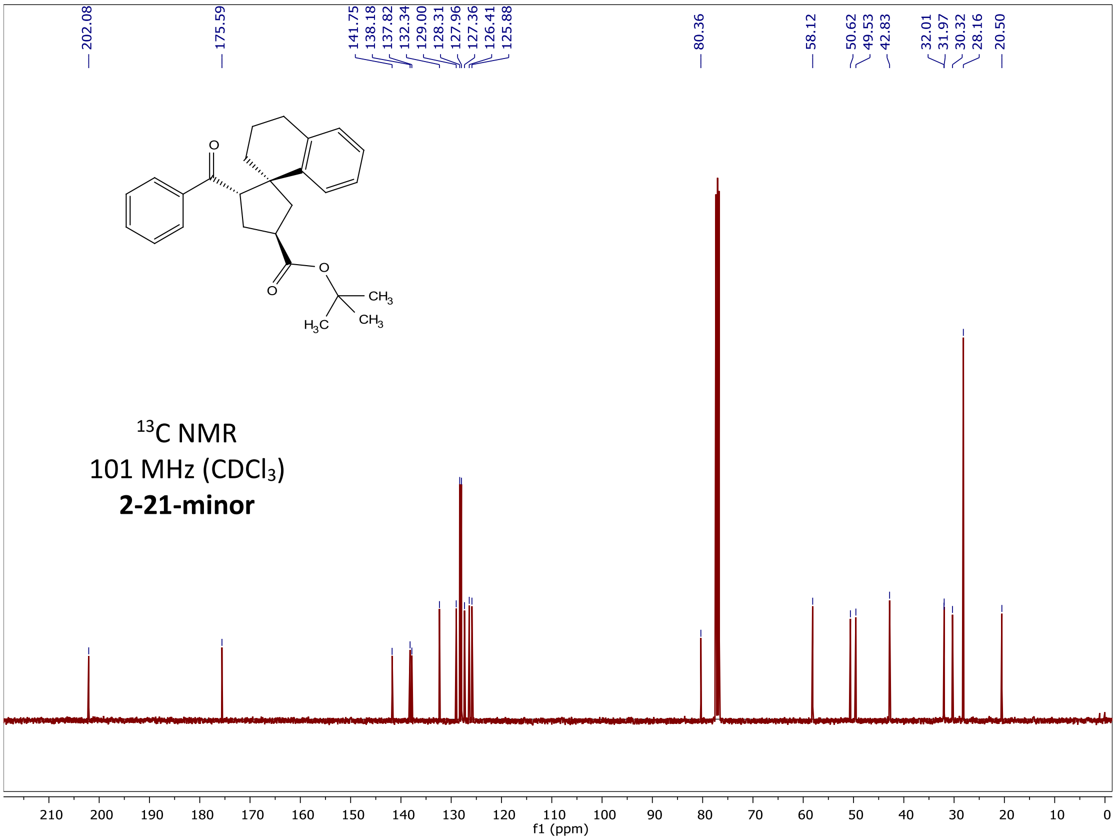


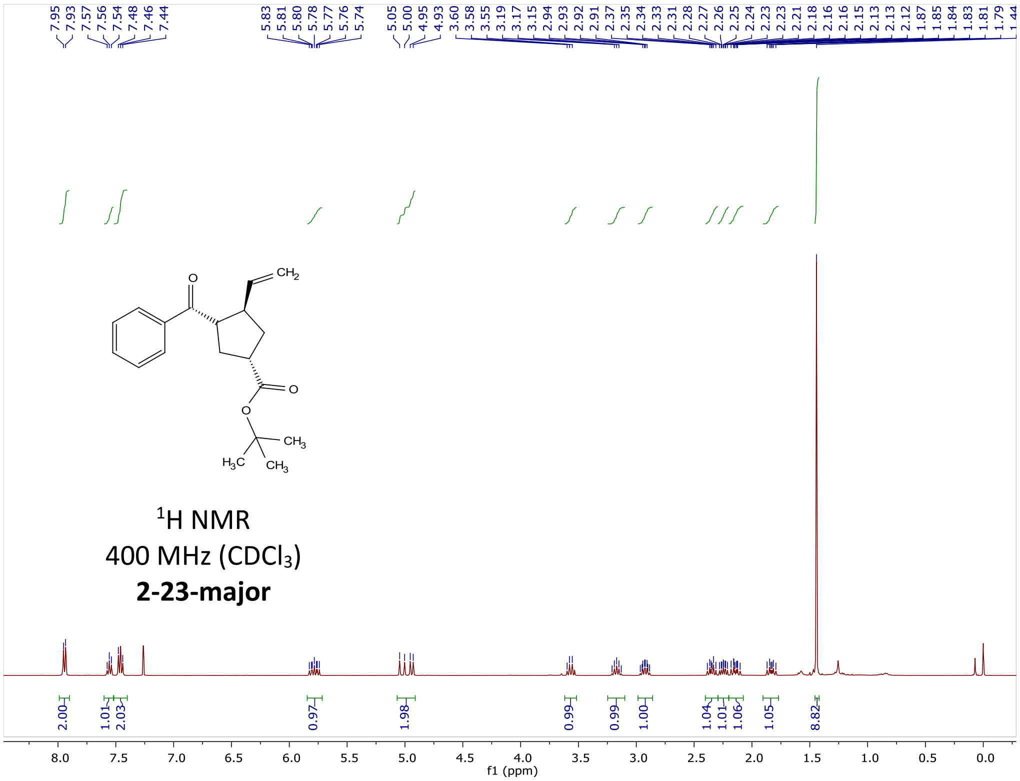
^{13}C NMR
101 MHz (CDCl$_3$)
2-20-minor


7.53 7.51 7.45 7.43 7.37 7.35 7.33 7.29 7.28 7.26 7.16 7.14 7.12 7.11 7.09 7.08 6.91 6.89 4.19 4.17 4.16 4.14 3.13 3.13 3.12 3.11 3.10 3.10 3.09 3.08 3.08 3.06 2.77 2.74 2.71 2.68 2.60 2.59 2.57 2.56 2.55 2.53 2.40 2.38 2.37 2.34 2.31 2.28 2.25 2.23 2.20 1.78 1.75 1.75 1.73 1.72 1.71 1.70 1.68 1.60 1.59 1.57 1.54 1.53 1.47
O
CH3
H3C
CH3
^{1}H NMR
400 MHz (CDCl$_3$)
2-21-major
1.00 1.98 1.00 1.70 1.98 1.02 0.98
1.02
1.04
1.07 1.03 2.05 2.04
2.04 2.21 8.99
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.
f1 (ppm)

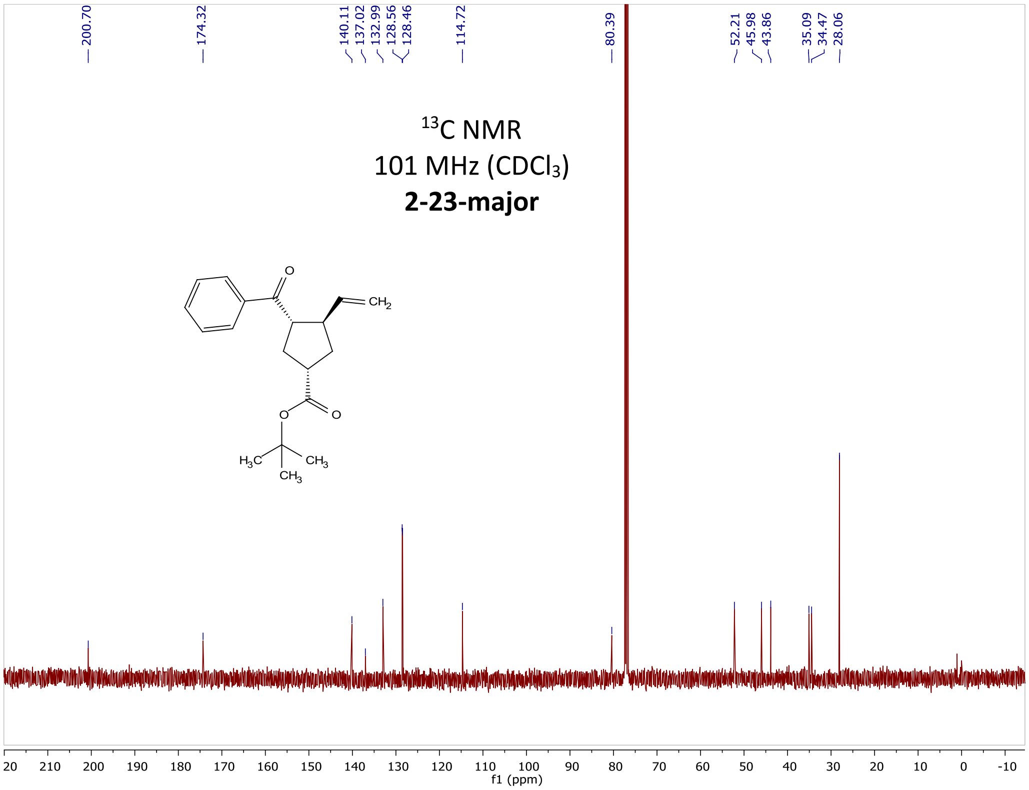

201.38
174.27
143.94 137.78 137.47 132.45 129.28 128.34 128.08 126.70 126.46 125.88
80.39
58.96
49.24 48.71 43.93
34.36 33.26 29.98 28.13
20.23
O
CH3
H3C
CH3
^{13}C NMR
101 MHz (CDCl$_3$)
2-21-major
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.68
7.66
7.47
7.45
7.34
7.32
7.30
7.28
7.26
7.24
7.15
7.13
7.11
7.06
7.04
7.03
6.86
6.84
4.34
4.32
4.30
3.14
3.12
3.10
3.08
3.06
2.77
2.75
2.74
2.72
2.69
2.54
2.50
2.34
2.32
2.30
2.28
2.27
2.25
1.73
1.72
1.70
1.69
1.61
1.60
1.57
1.53
1.52
1.49
O
O
O
CH3
CH3
H3C
1H NMR
400 MHz (CDCl3)
2-21-minor
1.00
2.00
1.00
1.21
1.99
1.01
0.99
1.02
1.01
1.02
1.03
4.06
1.03
3.25
9.01
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.
f1 (ppm)

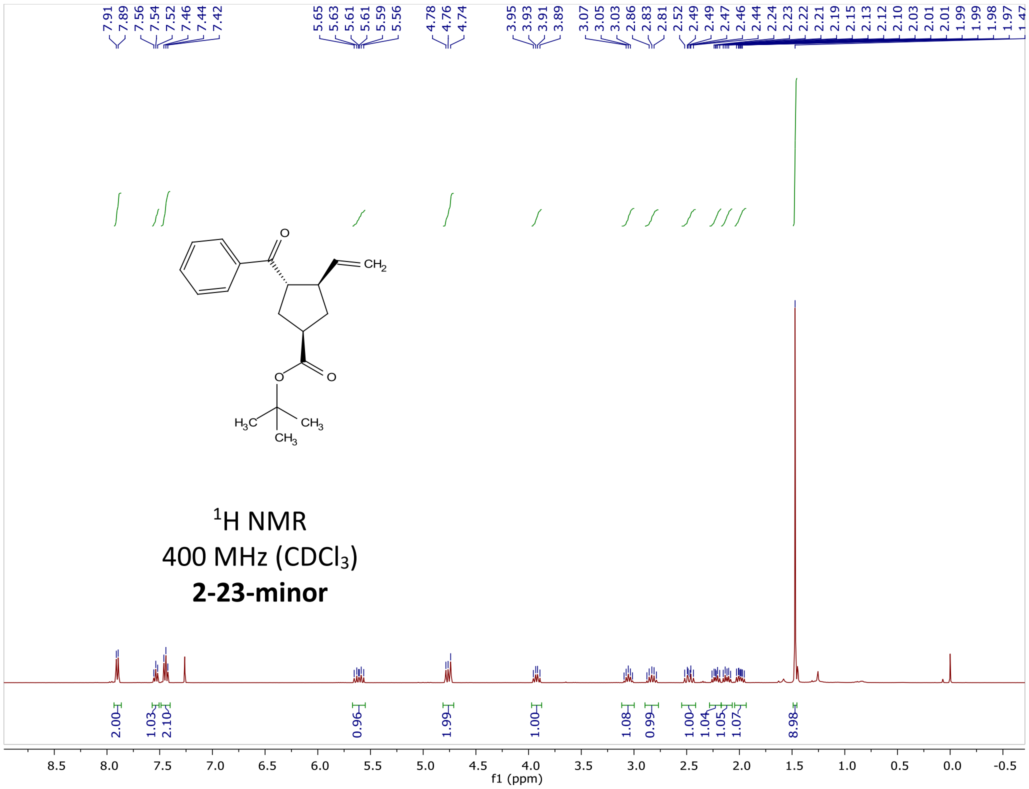

202.08
175.59
141.75
138.18
137.82
132.34
129.00
128.31
127.96
127.36
126.41
125.88
80.36
58.12
50.62
49.53
42.83
32.01
31.97
30.32
28.16
20.50
O
O
O
CH3
CH3
H3C
13C NMR
101 MHz (CDCl3)
2-21-minor
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



^{1}H NMR
400 MHz ($CDCl_3$)
2-23-major



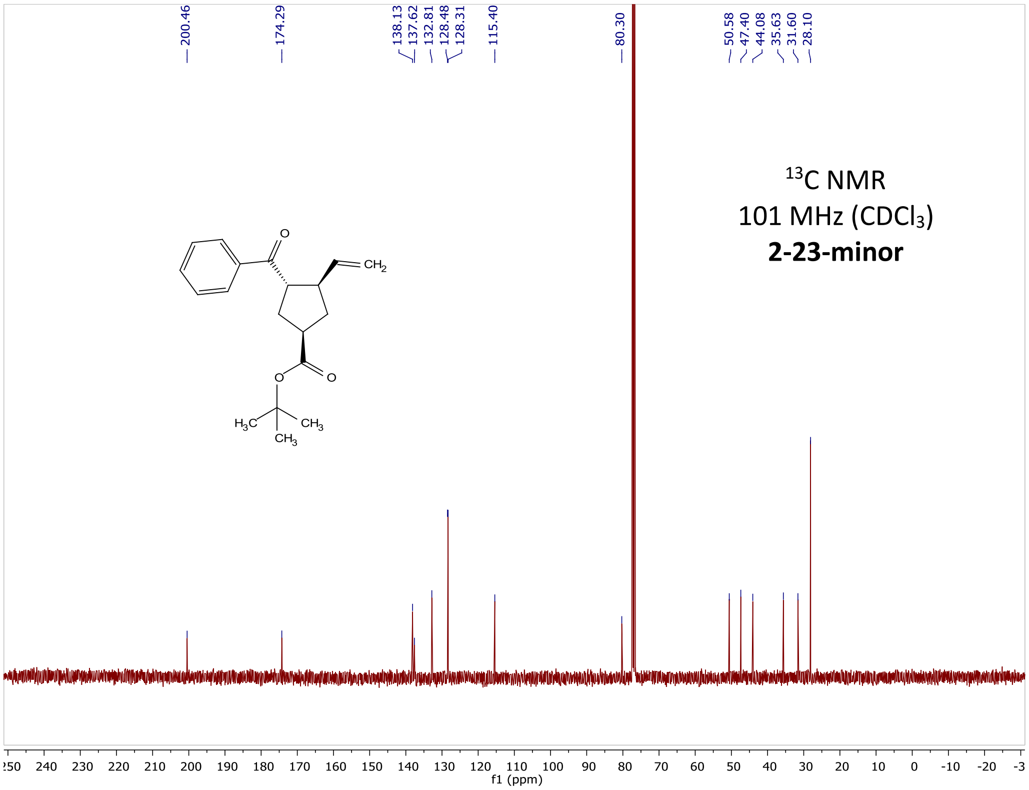
^{13}C NMR
101 MHz ($CDCl_3$)
2-23-major



^{1}H NMR

400 MHz ($CDCl_3$)

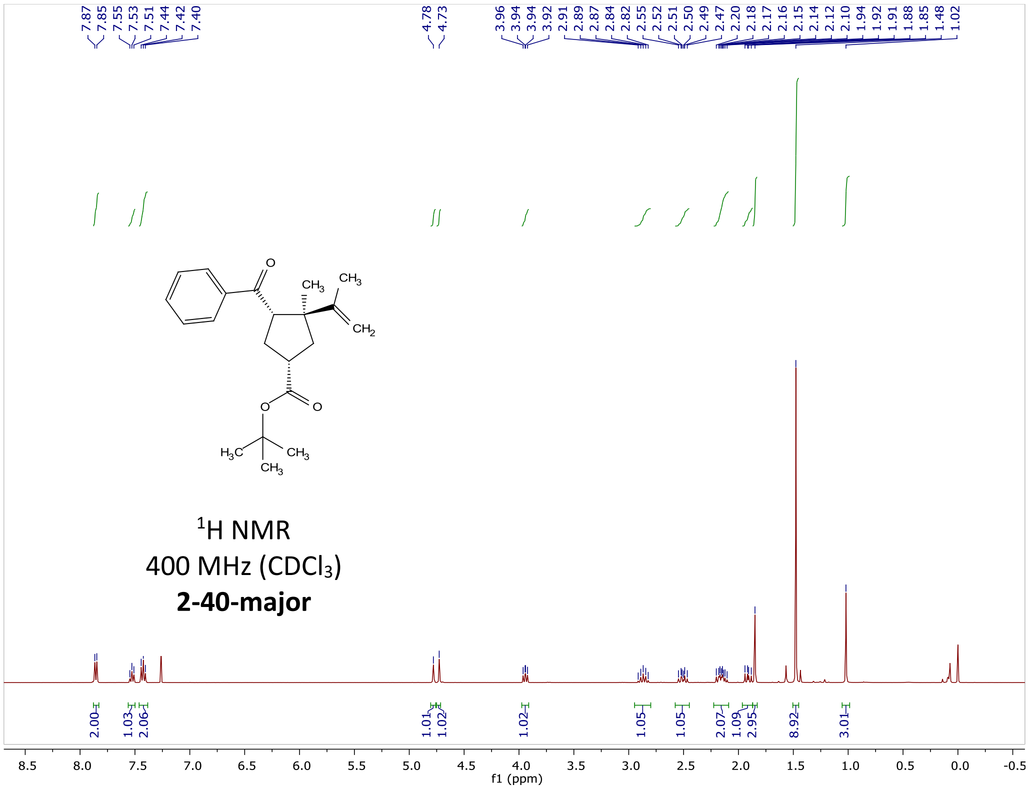
2-23-minor

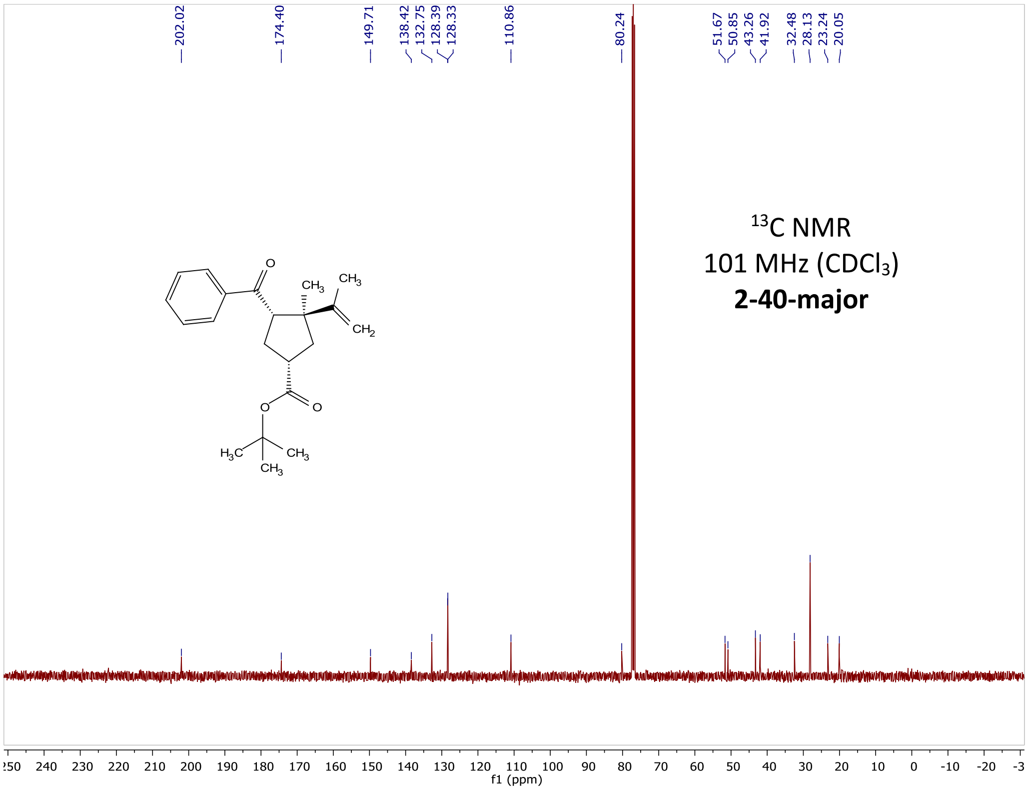


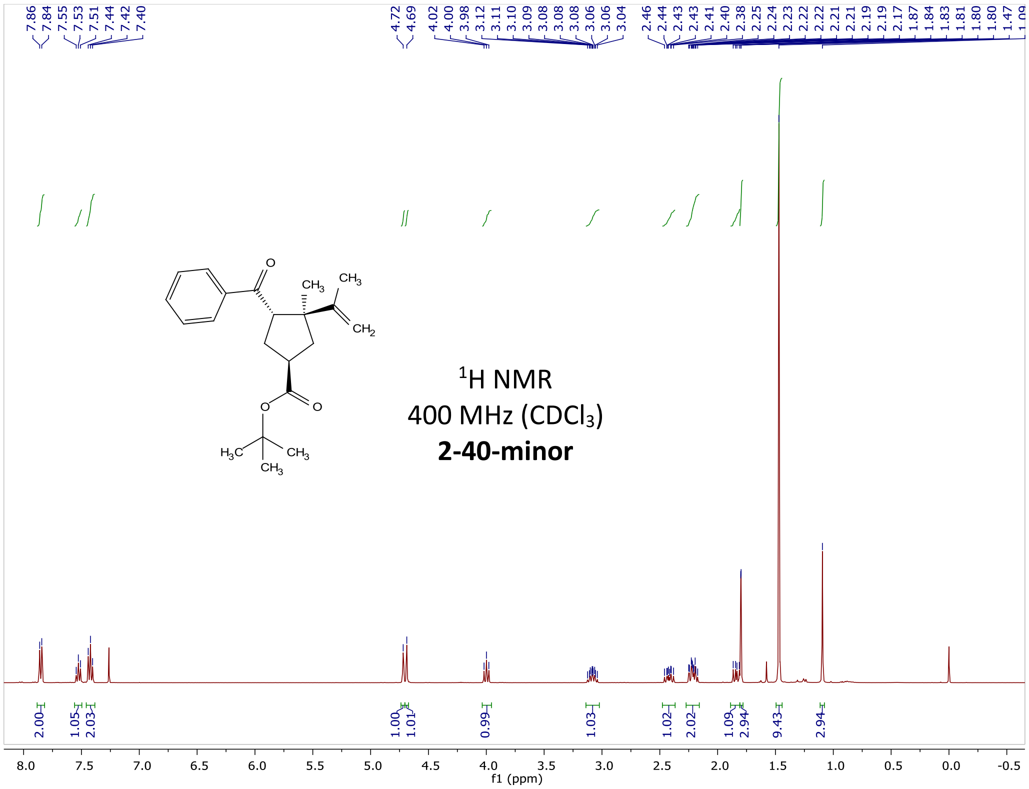
^{13}C NMR

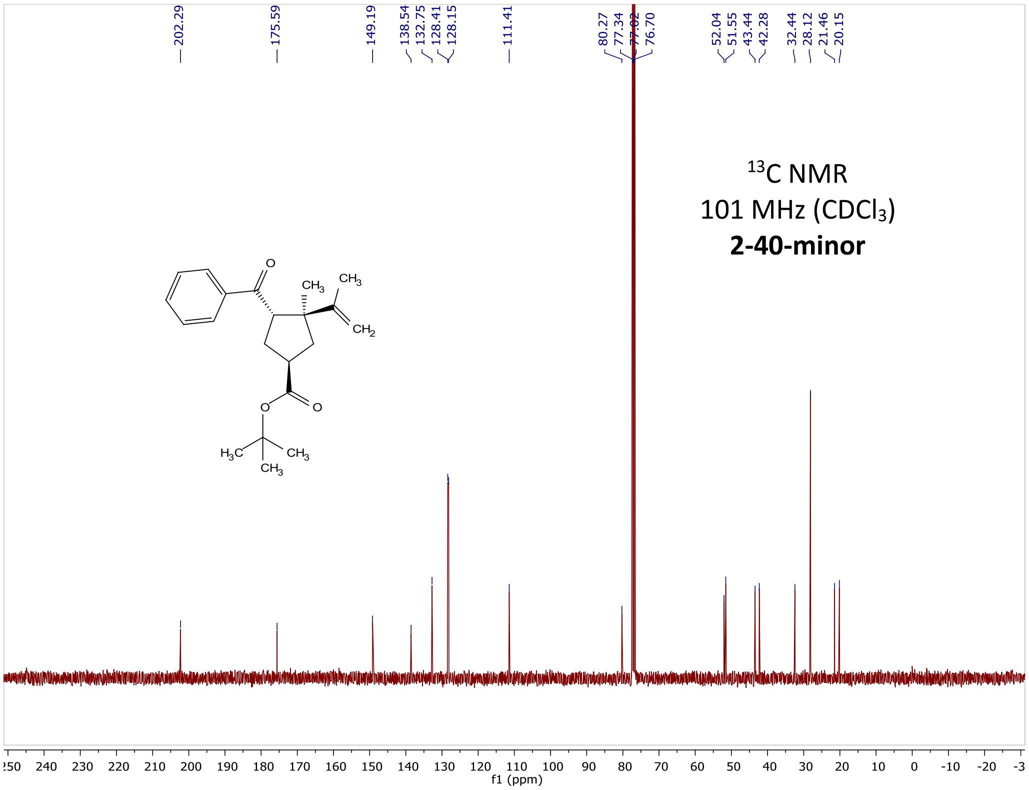
101 MHz ($CDCl_3$)

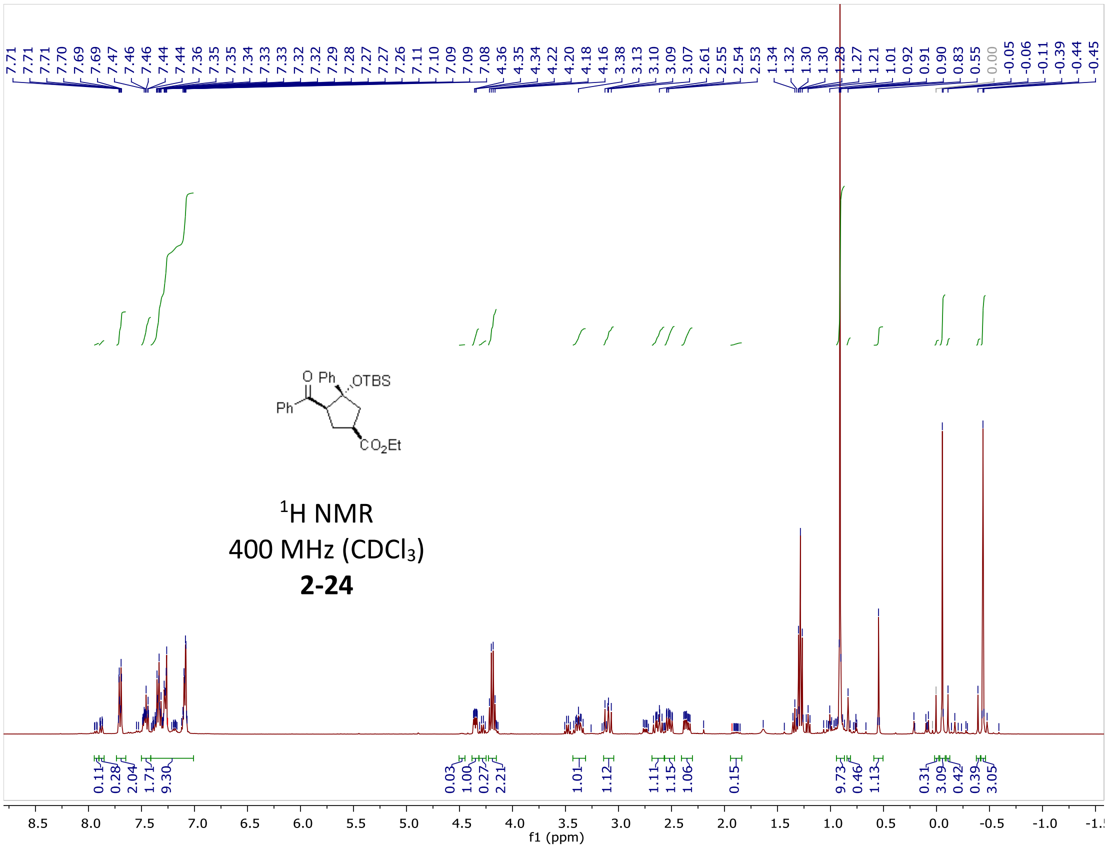
2-23-minor


7.87
7.85
7.55
7.53
7.51
7.44
7.42
7.40
4.78
4.73
3.96
3.94
3.94
3.92
2.91
2.89
2.87
2.84
2.82
2.55
2.52
2.51
2.50
2.49
2.47
2.20
2.18
2.17
2.16
2.15
2.14
2.12
2.10
1.94
1.92
1.91
1.88
1.85
1.48
1.02
O
CH3
CH3
CH2
O
O
H3C
CH3
CH3
^{1}H NMR
400 MHz (CDCl$_3$)
2-40-major
2.00
1.03
2.06
1.01
1.02
1.02
1.05
1.05
2.07
1.09
2.95
8.92
3.01
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)

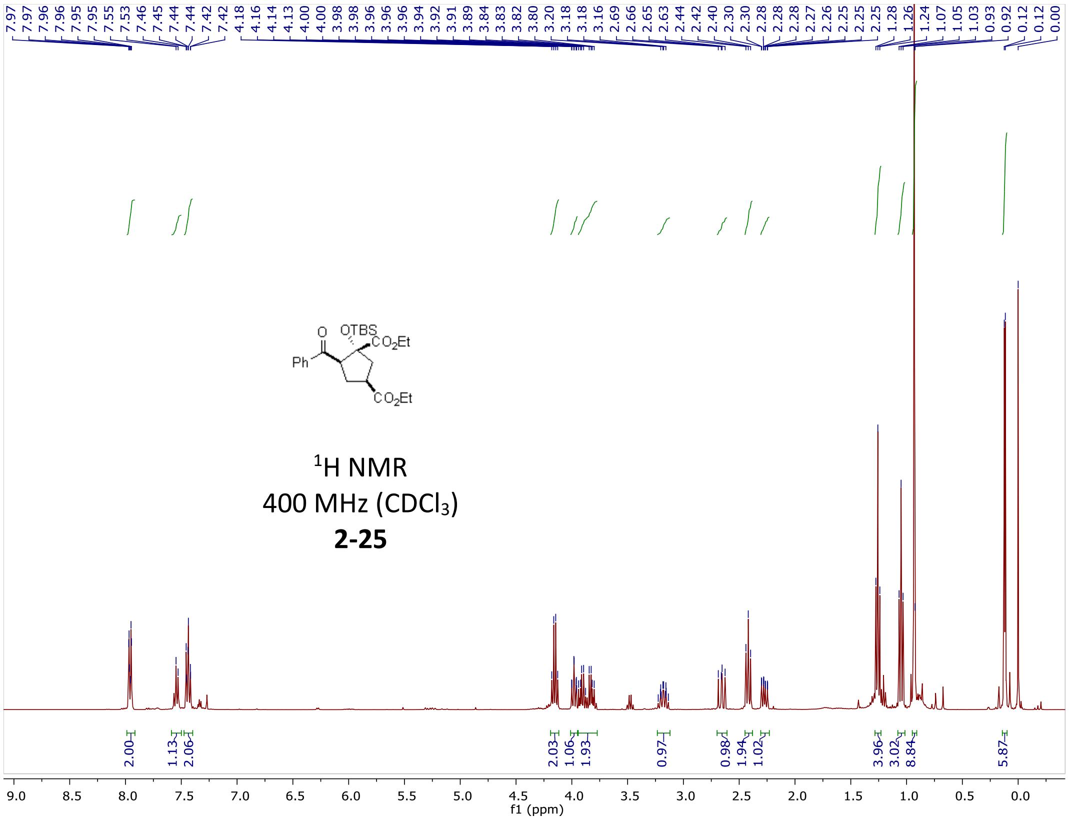

202.02
174.40
149.71
138.42
132.75
128.39
128.33
110.86
80.24
51.67
50.85
43.26
41.92
32.48
28.13
23.24
20.05
^{13}C NMR
101 MHz (CDCl$_3$)
2-40-major
O
CH3
CH3
CH2
O
O
H3C
CH3
CH3
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-3
f1 (ppm)


7.86
7.84
7.55
7.53
7.51
7.44
7.42
7.40
4.72
4.69
4.02
4.00
3.98
3.12
3.11
3.10
3.09
3.08
3.08
3.06
3.06
3.04
2.46
2.44
2.43
2.43
2.41
2.40
2.38
2.25
2.24
2.23
2.22
2.22
2.21
2.21
2.19
2.17
1.87
1.84
1.83
1.81
1.80
1.47
1.09
O
CH$_3$
CH$_3$
CH$_2$
O
O
H$_3$C
CH$_3$
CH$_3$
^{1}H NMR
400 MHz (CDCl$_3$)
2-40-minor
2.00
1.05
2.03
1.00
1.01
0.99
1.03
1.02
2.02
1.09
2.94
9.43
2.94
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)


202.29
175.59
149.19
138.54
132.75
128.41
128.15
111.41
80.27
77.34
77.02
76.70
52.04
51.55
43.44
42.28
32.44
28.12
21.46
20.15
^{13}C NMR
101 MHz (CDCl$_3$)
2-40-minor
O
CH$_3$
CH$_3$
CH$_2$
O
O
H$_3$C
CH$_3$
CH$_3$
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-3
f1 (ppm)

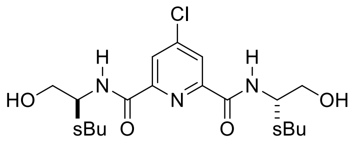


^{1}H NMR
400 MHz ($CDCl_3$)
2-24

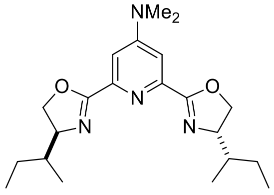


^{1}H NMR
400 MHz ($CDCl_3$)
2-25

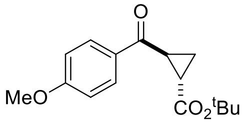
A-2. List of New Compounds for Chapter 3



3-38



L3-12



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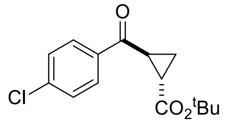

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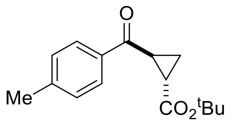

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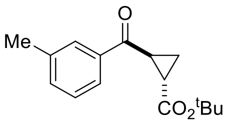

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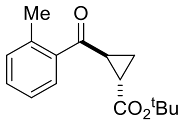

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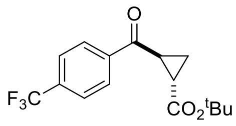

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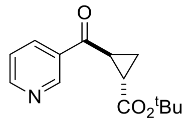
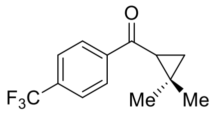


3-45



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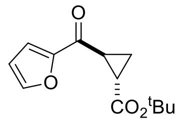

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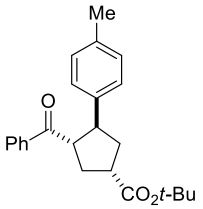

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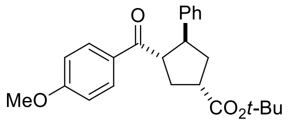

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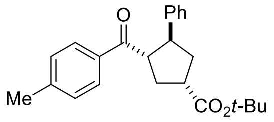

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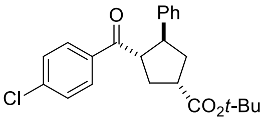

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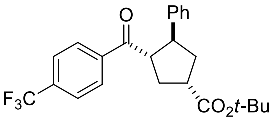

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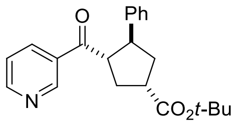

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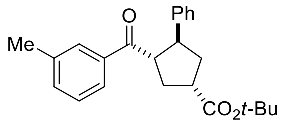
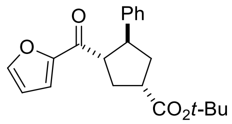


3-22



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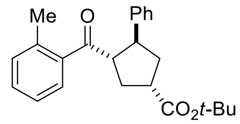

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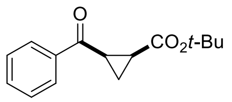
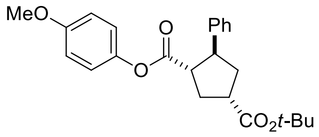


***cis*-3-2**



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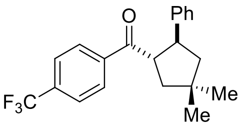

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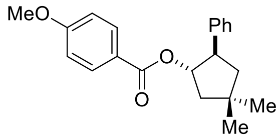
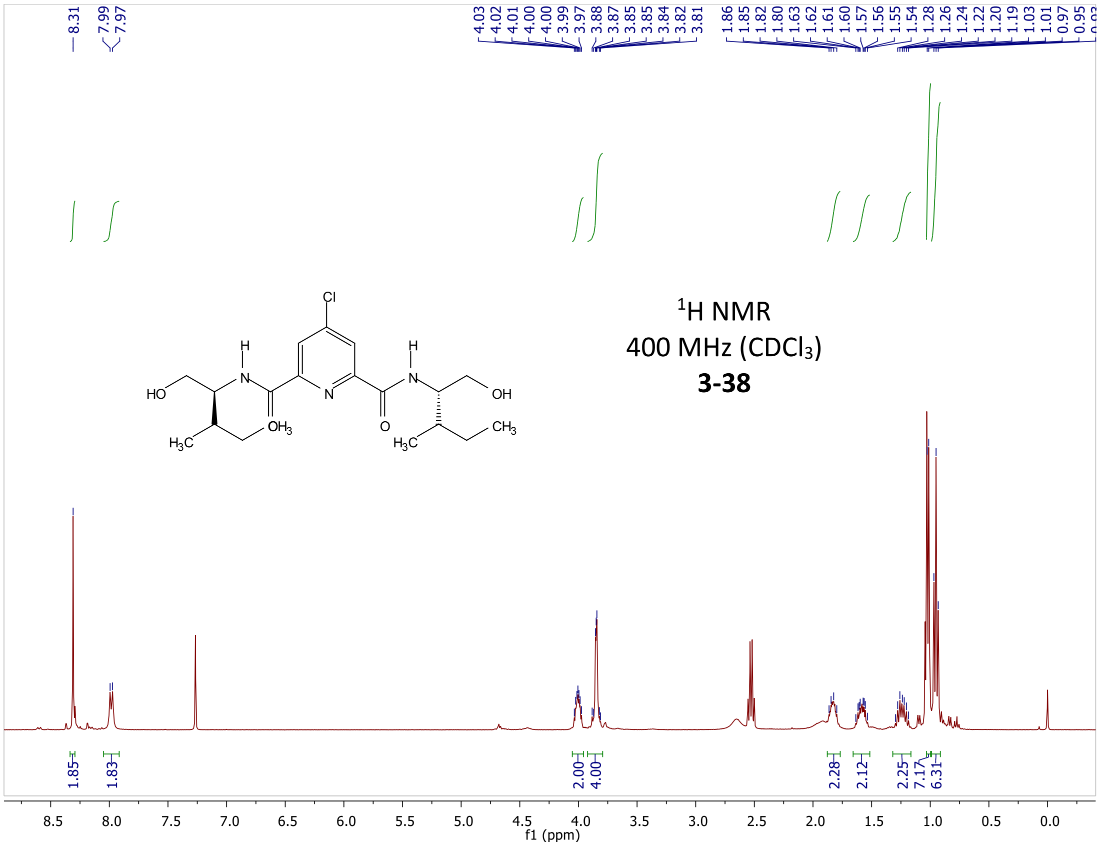
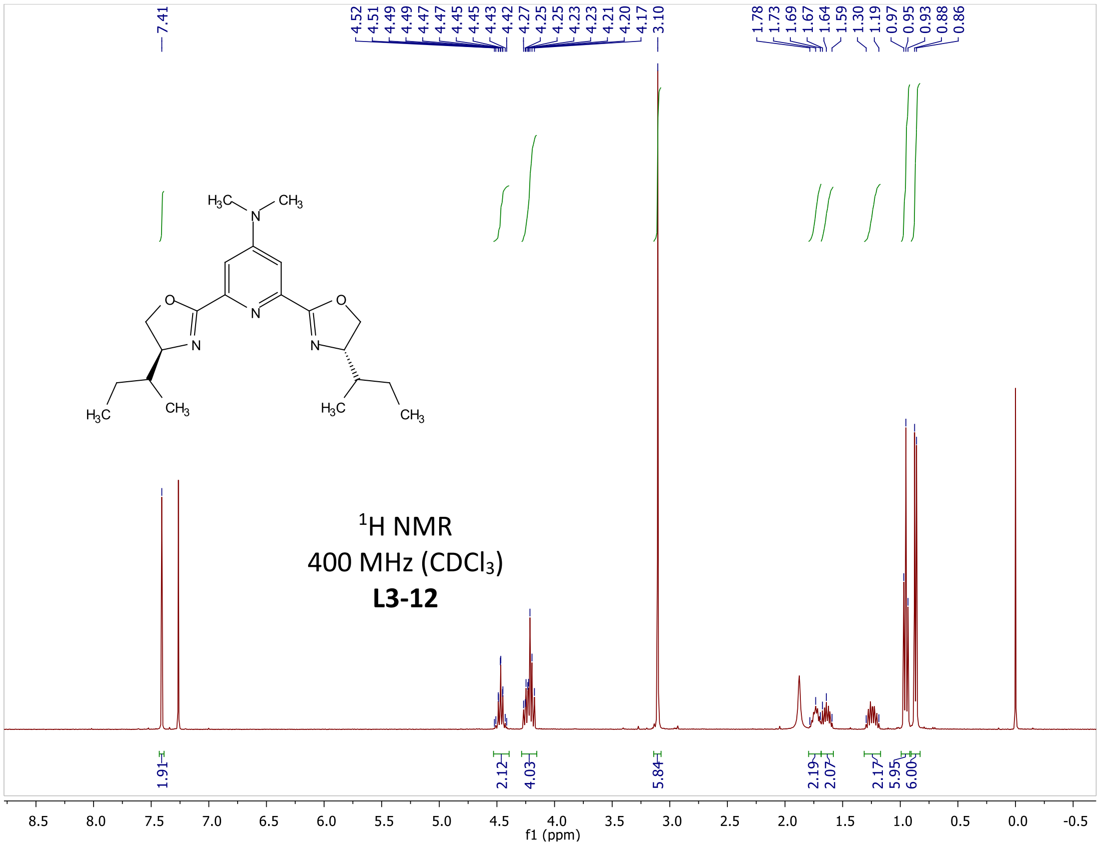
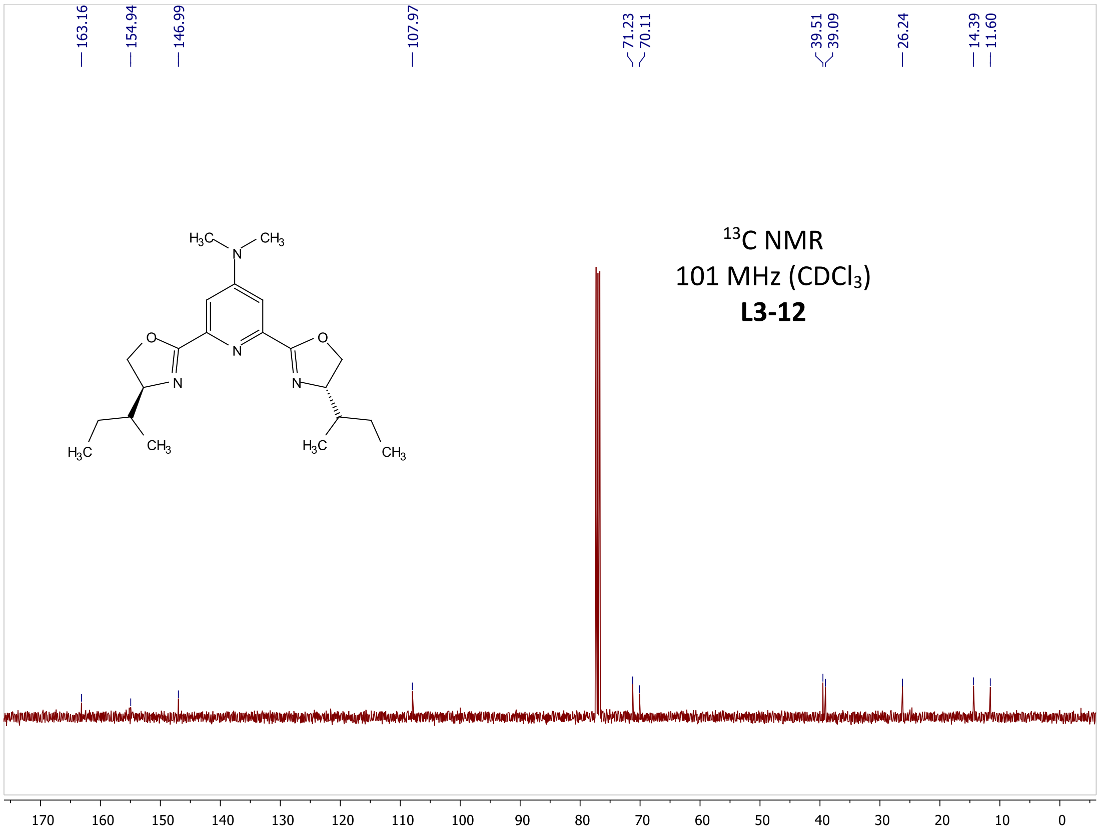


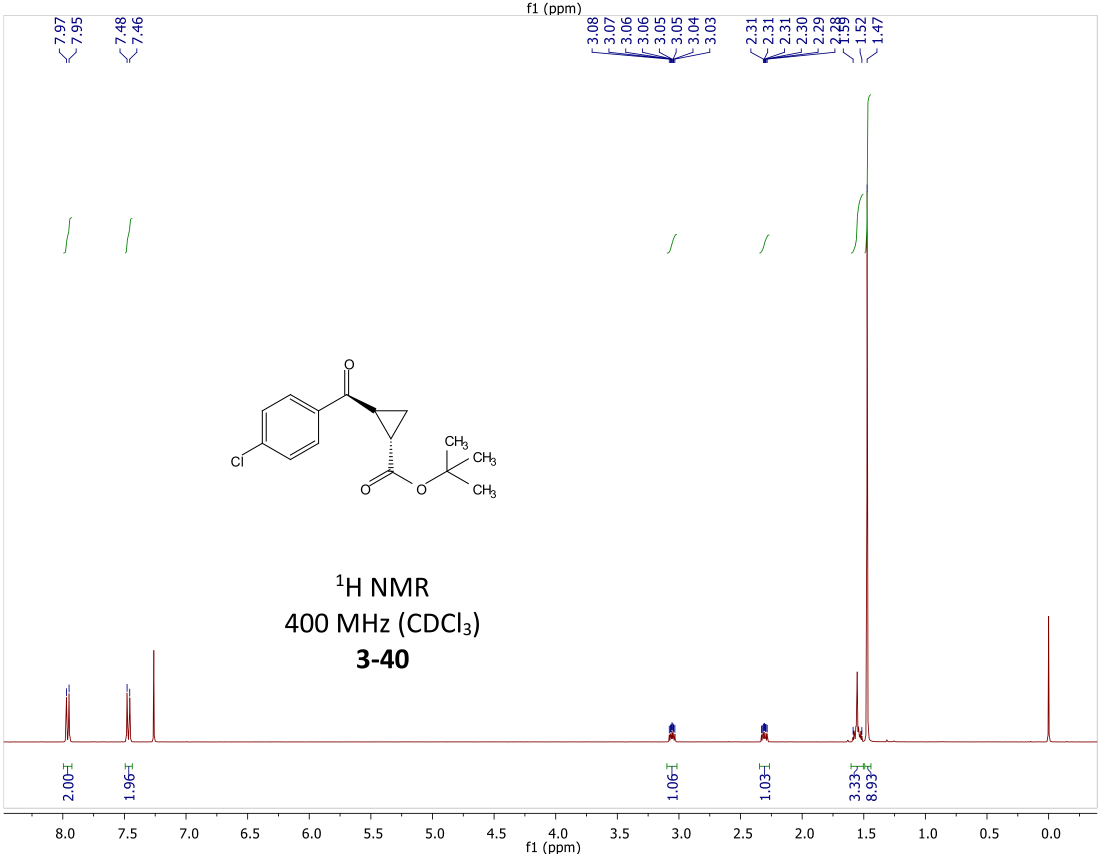
3-35


8.31
7.99
7.97
4.03
4.02
4.01
4.00
4.00
3.99
3.97
3.88
3.87
3.85
3.85
3.84
3.82
3.81
1.86
1.85
1.82
1.80
1.63
1.62
1.61
1.60
1.57
1.56
1.55
1.54
1.28
1.26
1.24
1.22
1.20
1.19
1.03
1.01
0.97
0.95
Cl
H
N
HO
N
O
OH
H
N
O
OH
H_3C
CH_3
H_3C
CH_3
^{1}H NMR
400 MHz ($CDCl_3$)
3-38
1.85
1.83
2.00
4.00
2.28
2.12
2.25
7.17
6.31
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
f1 (ppm)

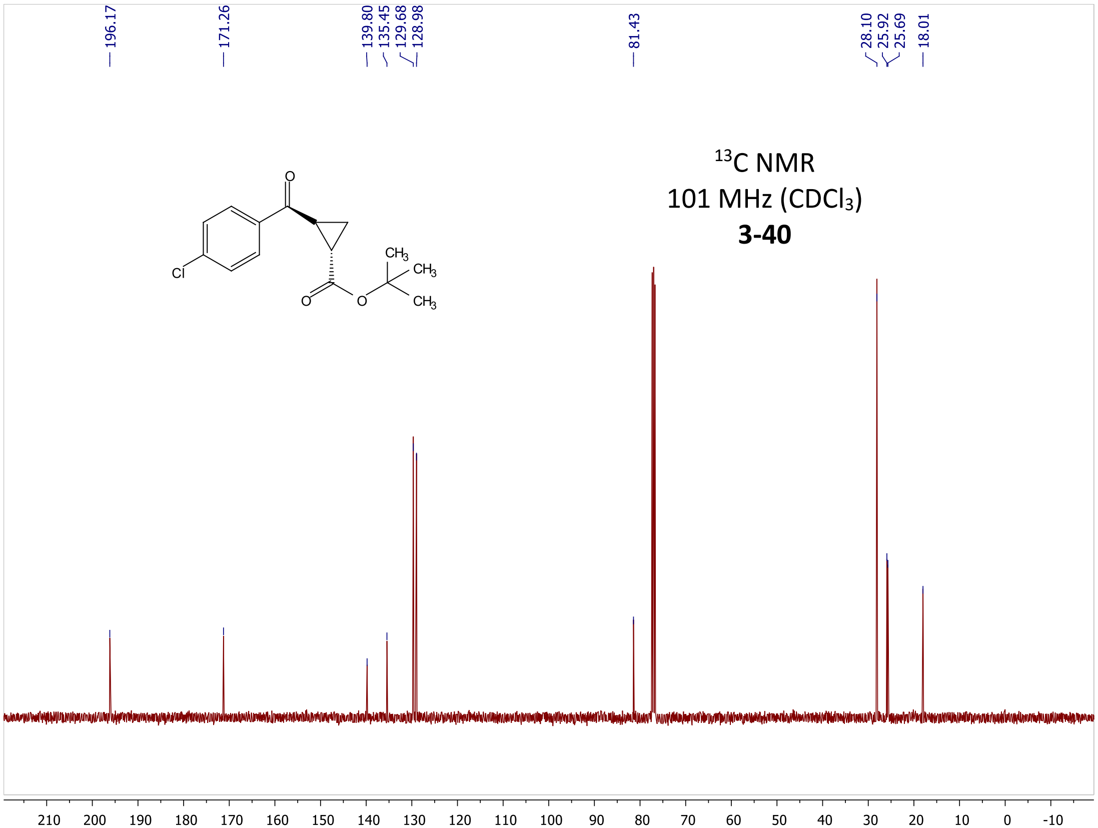

7.41
4.52
4.51
4.49
4.49
4.47
4.47
4.45
4.45
4.43
4.42
4.27
4.25
4.25
4.23
4.23
4.21
4.20
4.17
3.10
1.78
1.73
1.69
1.67
1.64
1.59
1.30
1.19
0.97
0.95
0.93
0.88
0.86
H_3C
CH_3
N
O
N
N
N
O
H_3C
CH_3
H_3C
CH_3
^{1}H NMR
400 MHz ($CDCl_3$)
L3-12
1.91
2.12
4.03
5.84
2.19
2.07
2.17
5.95
6.00
8.5
8.0
7.5
7.0
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)



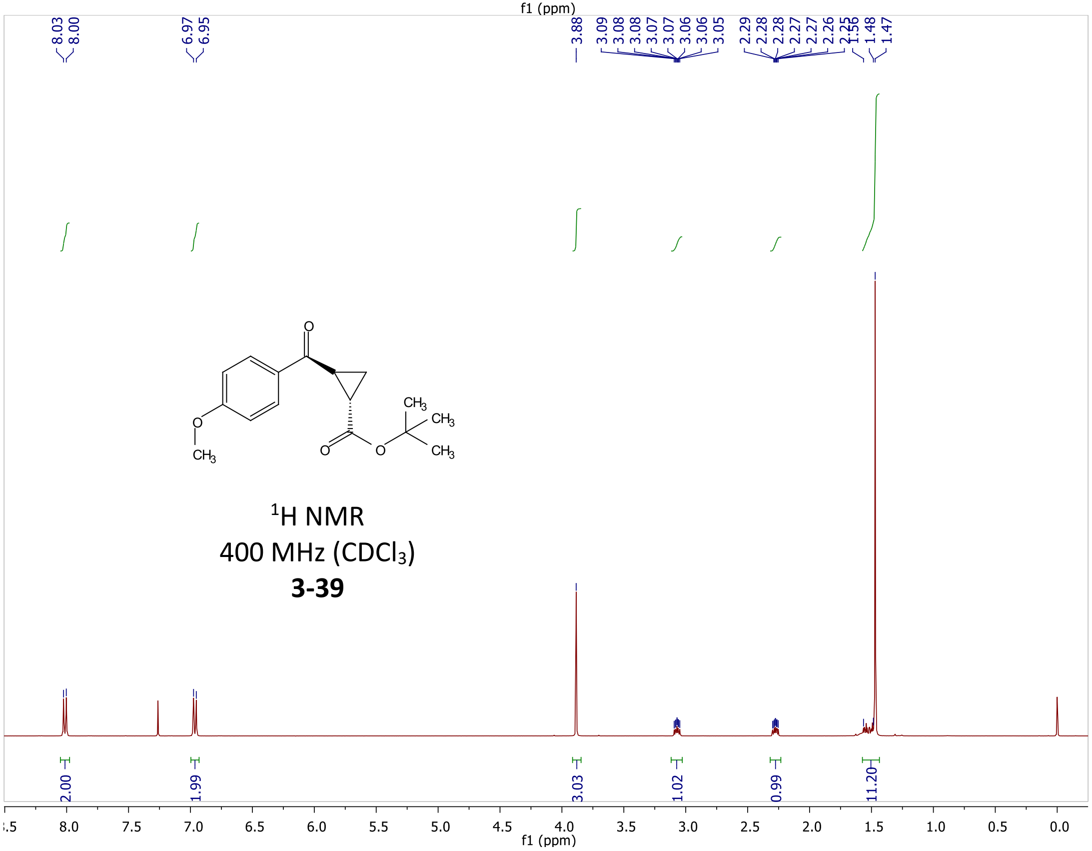
^{13}C NMR
101 MHz (CDCl$_3$)
L3-12



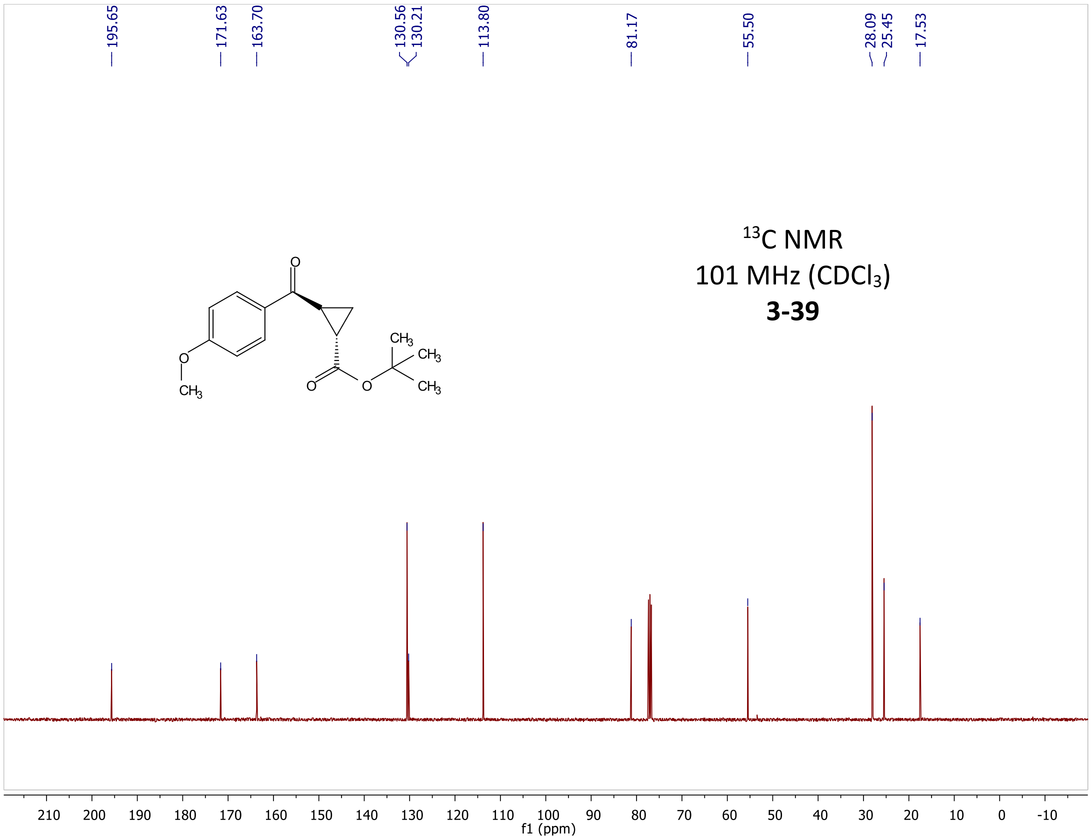
^{1}H NMR
400 MHz (CDCl$_3$)
3-40



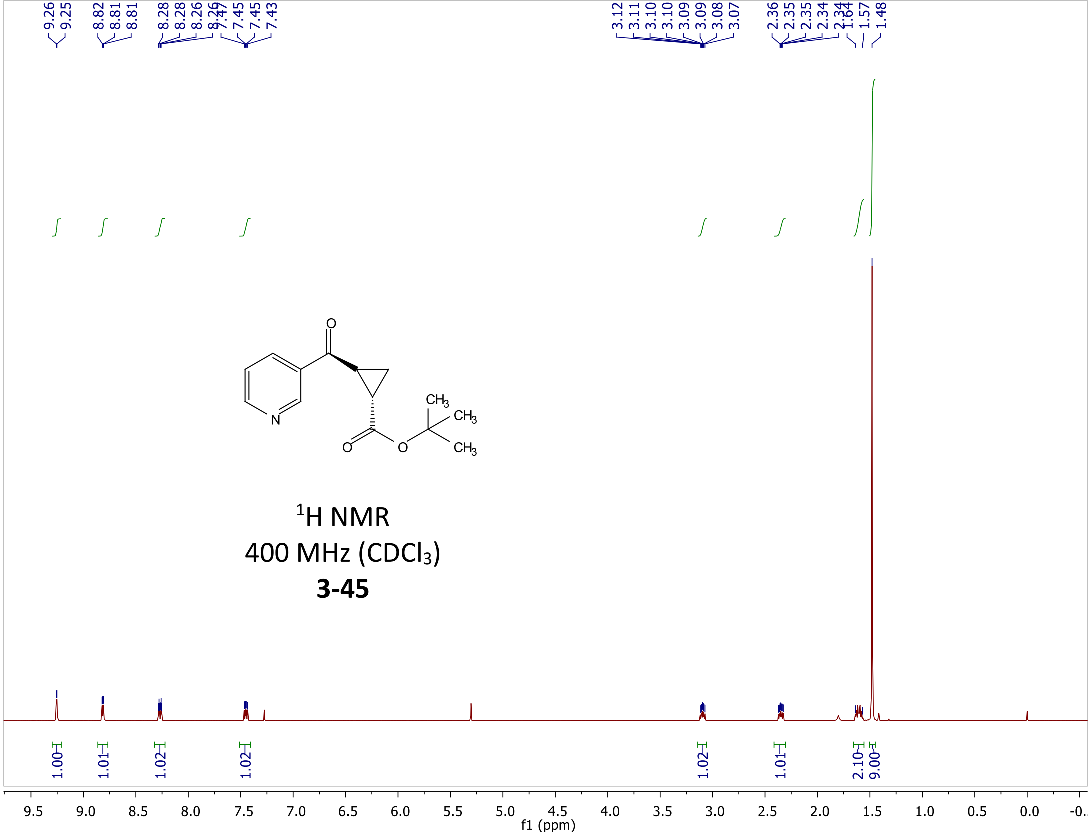
^{13}C NMR
101 MHz ($CDCl_3$)
3-40



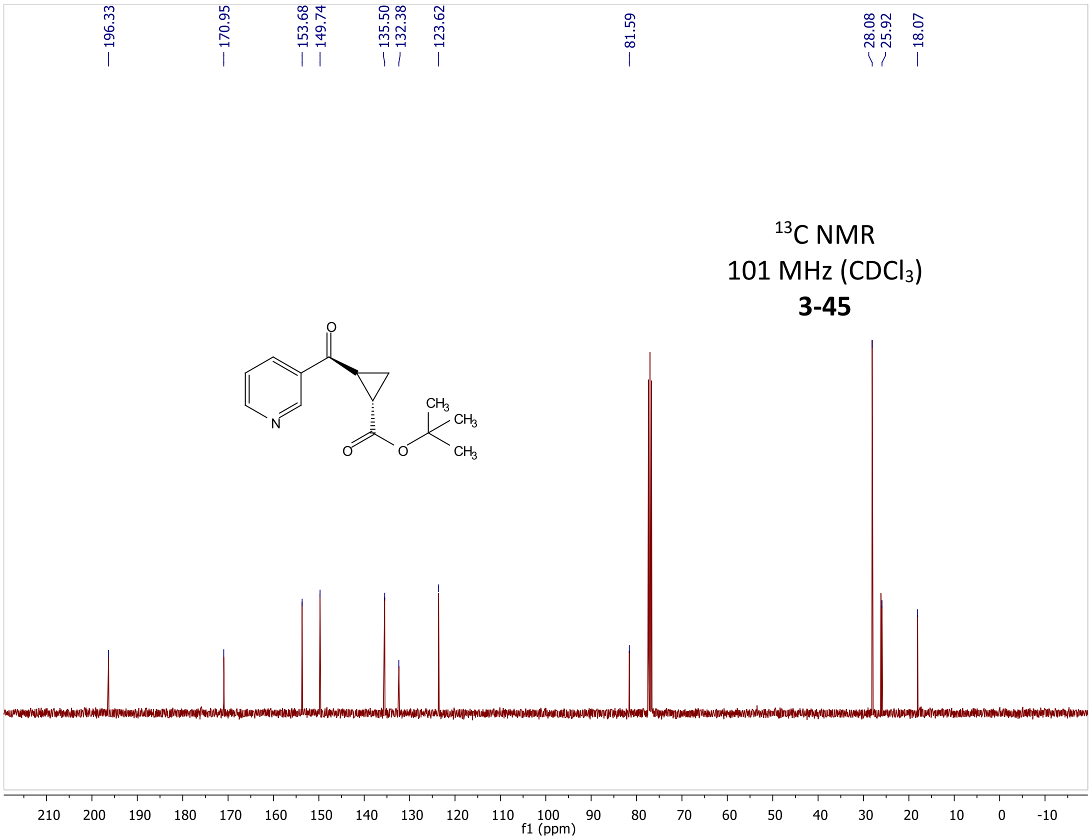
^{1}H NMR
400 MHz ($CDCl_3$)
3-39

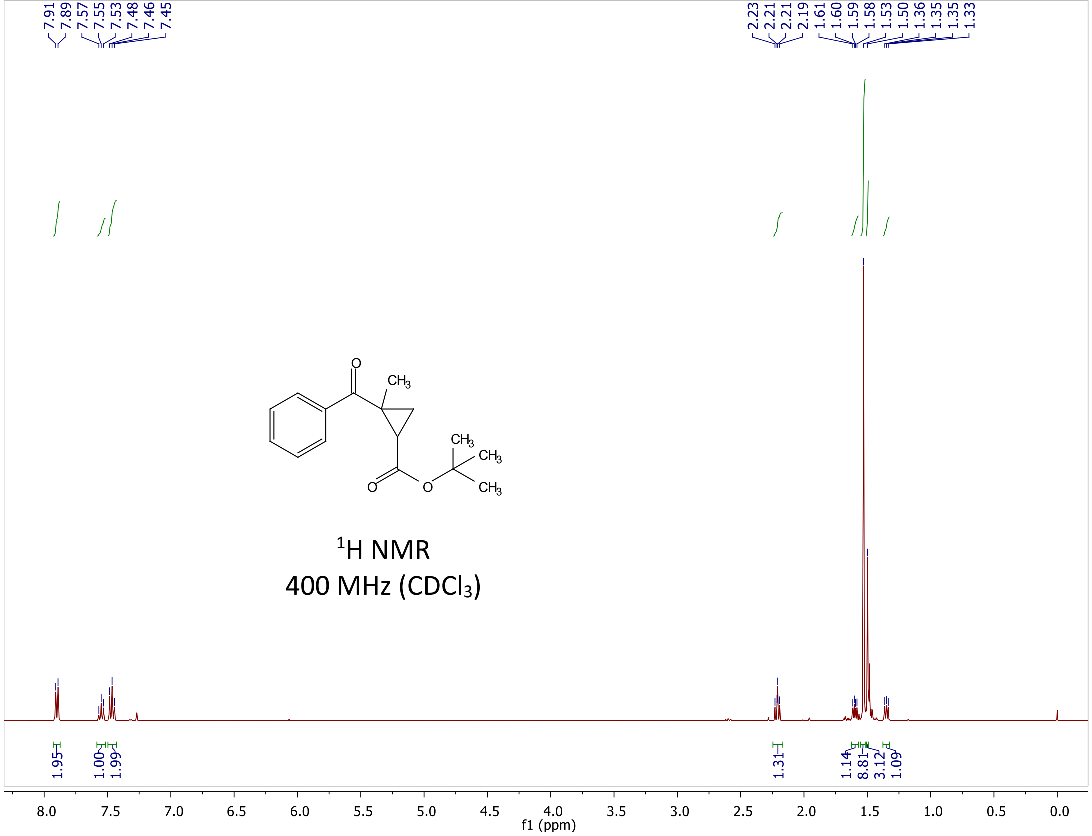


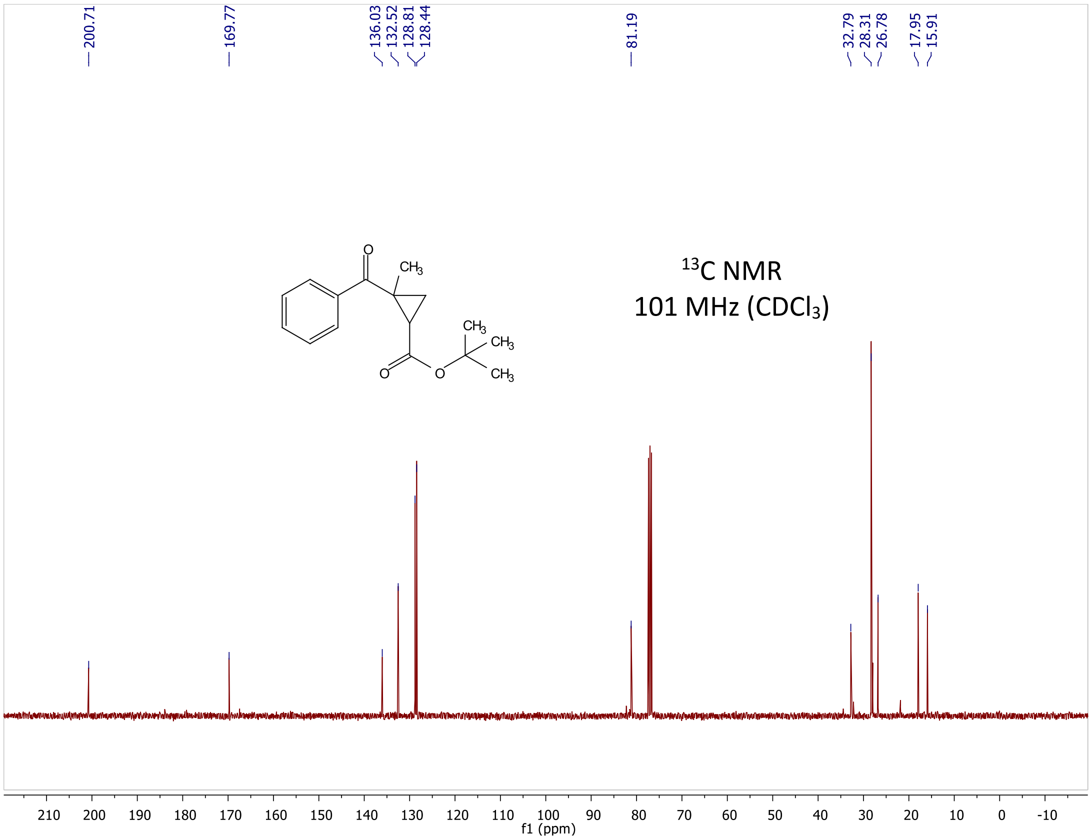
^{13}C NMR
101 MHz ($CDCl_3$)
3-39

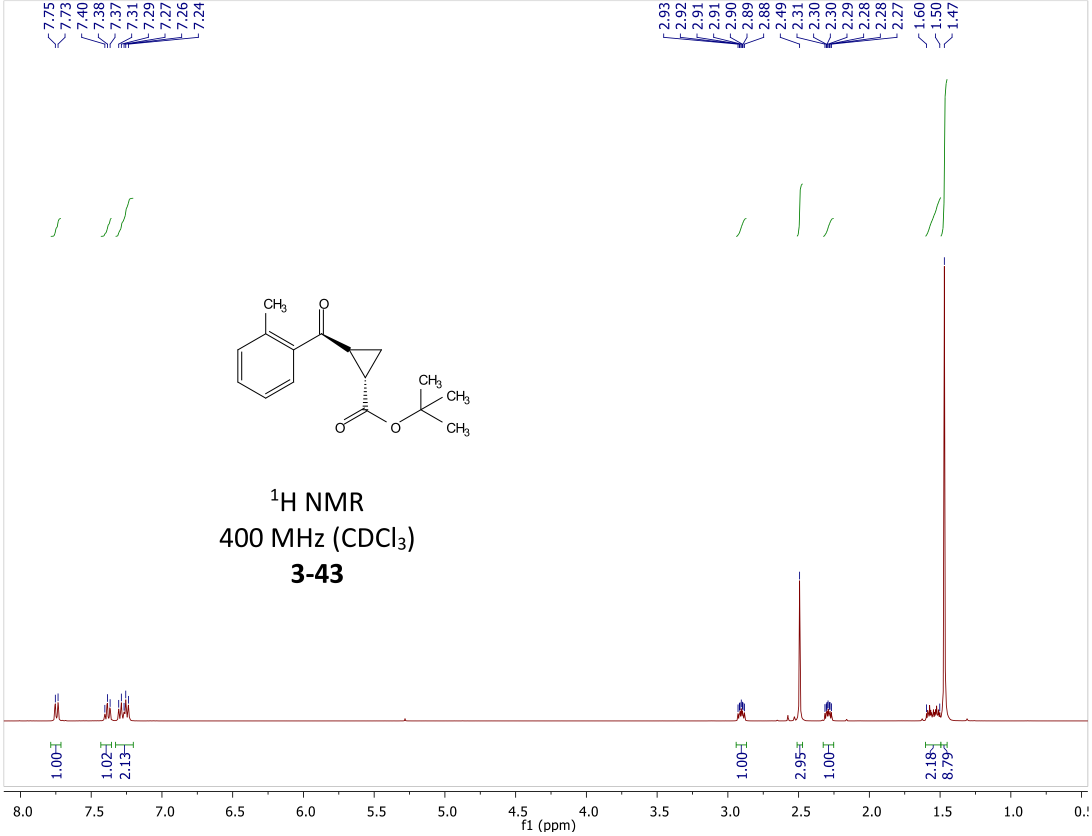


^{1}H NMR
400 MHz ($CDCl_3$)
3-45

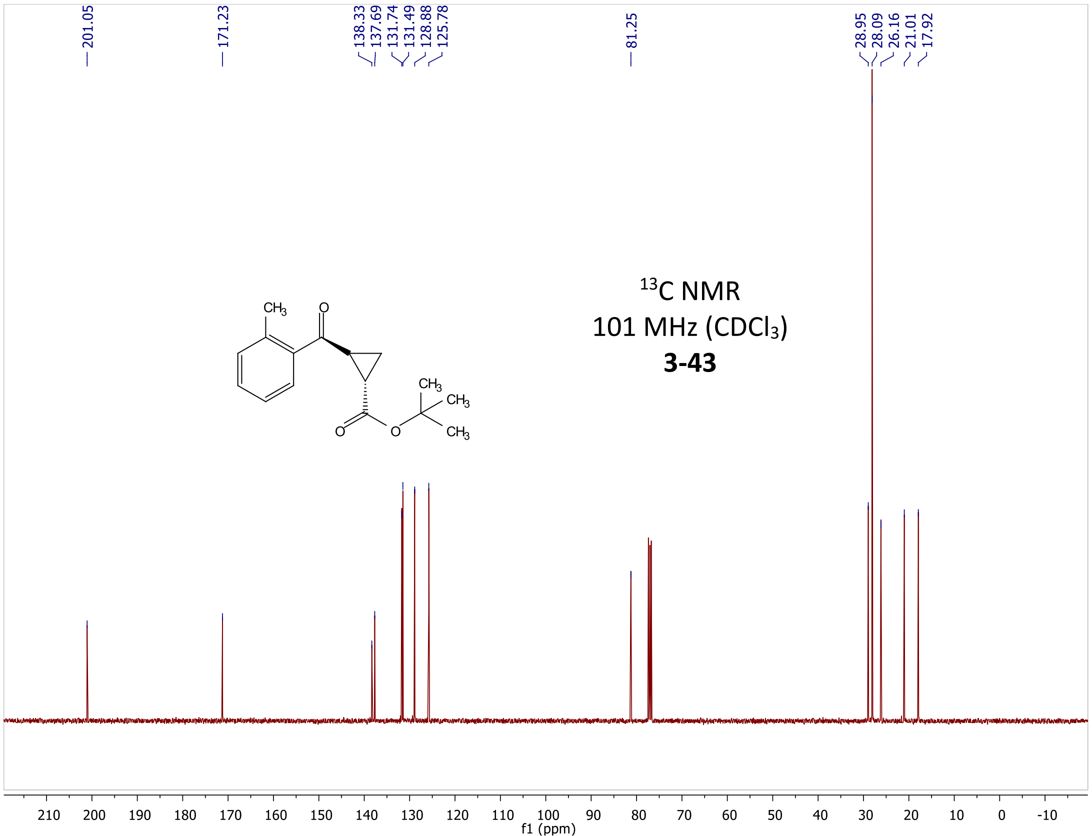

196.33
170.95
153.68
149.74
135.50
132.38
123.62
81.59
28.08
25.92
18.07
^{13}C NMR
101 MHz (CDCl$_3$)
3-45
O
N
CH$_3$
CH$_3$
CH$_3$
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.91
7.89
7.57
7.55
7.53
7.48
7.46
7.45
2.23
2.21
2.21
2.19
1.61
1.60
1.59
1.58
1.53
1.50
1.36
1.35
1.35
1.33
O
CH$_3$
CH$_3$
CH$_3$
CH$_3$
O
O
^{1}H NMR
400 MHz (CDCl$_3$)
1.95
1.00
1.99
1.31
1.14
8.81
3.12
1.09
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
f1 (ppm)

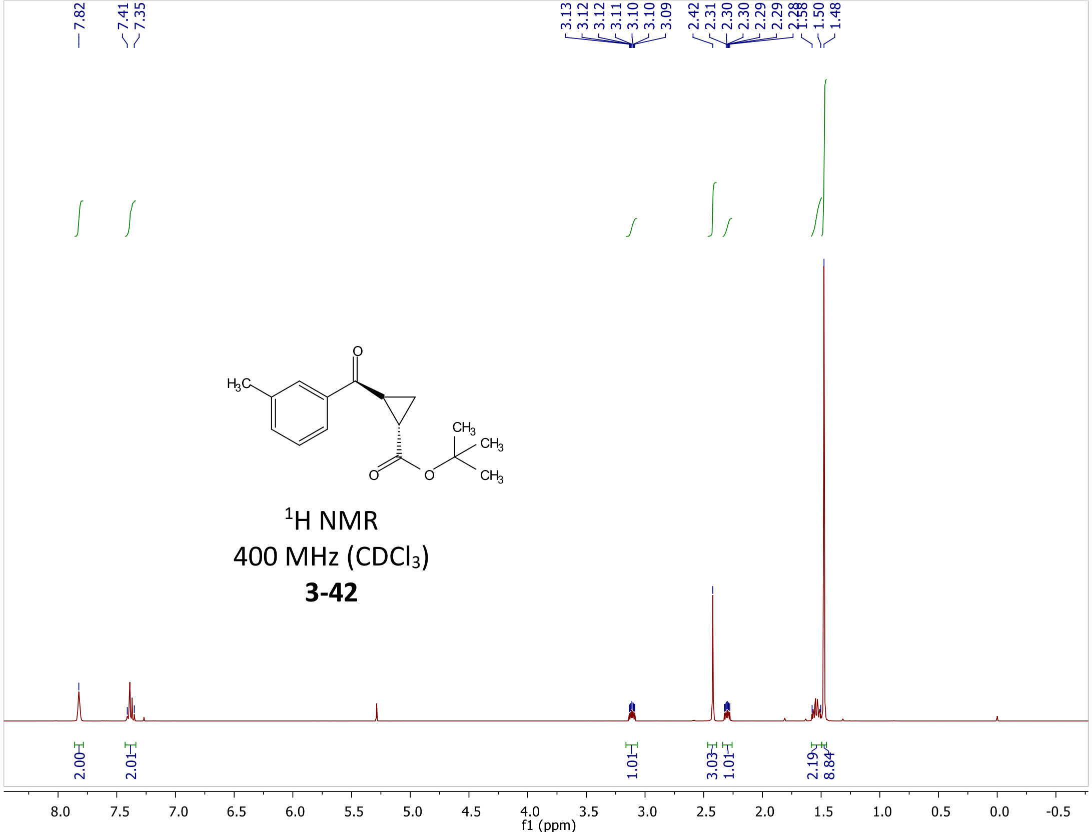




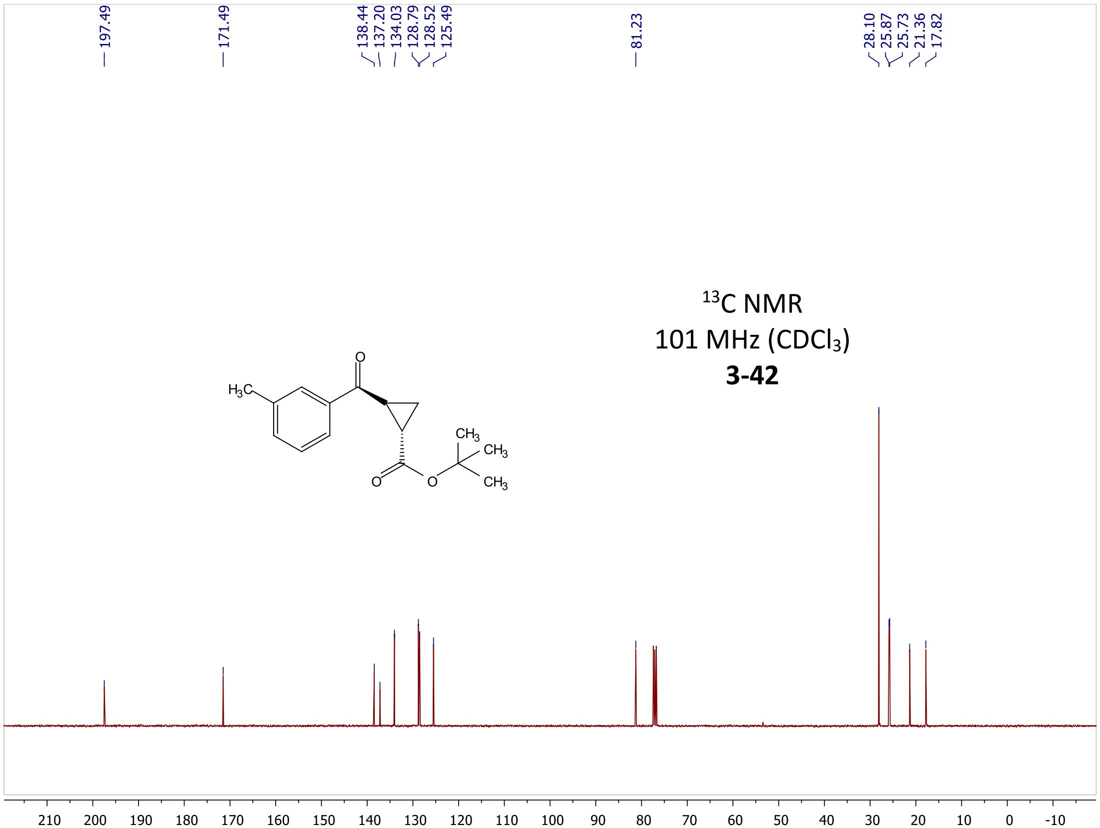
^{1}H NMR
400 MHz (CDCl$_3$)
3-43



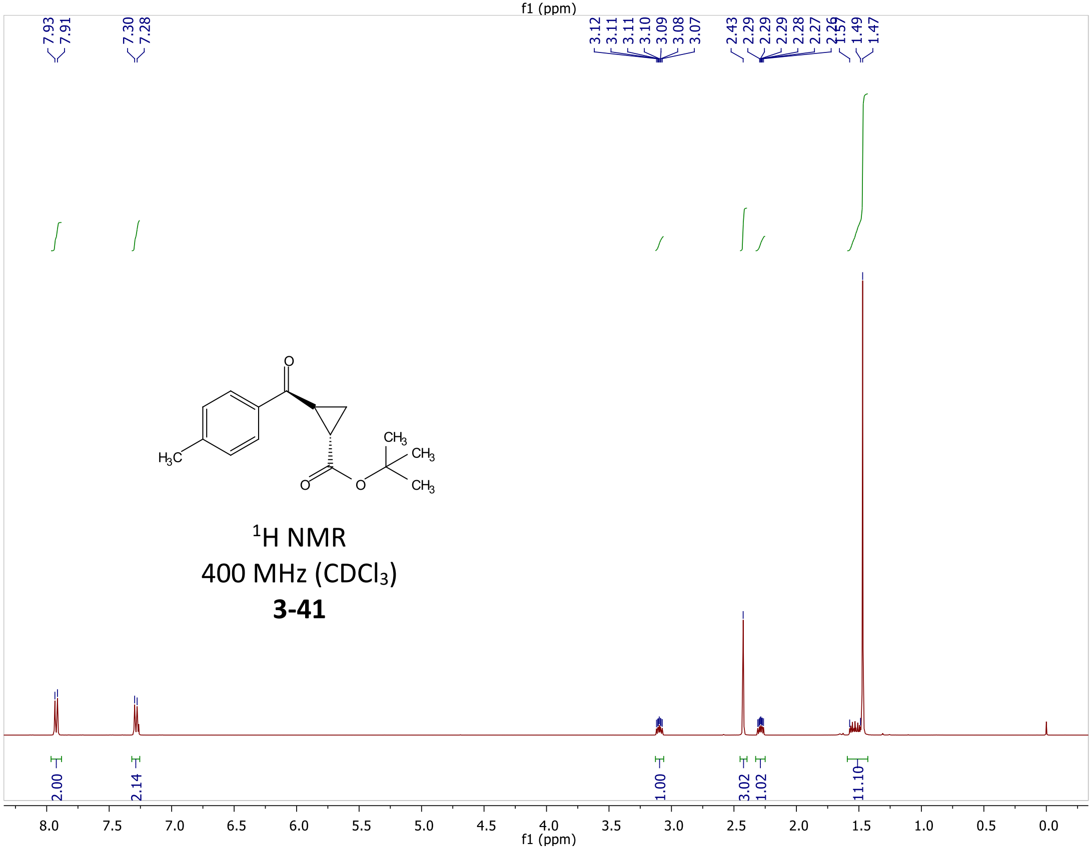
^{13}C NMR
101 MHz ($CDCl_3$)
3-43



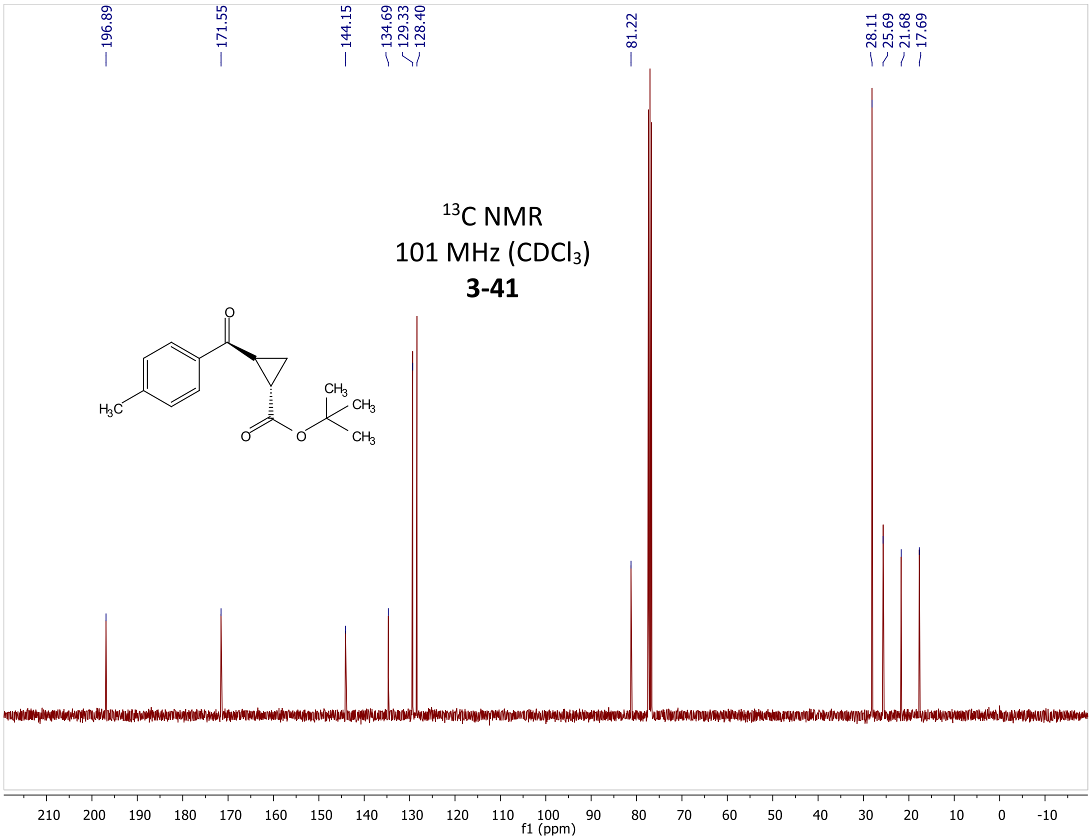
^{1}H NMR
400 MHz ($CDCl_3$)
3-42



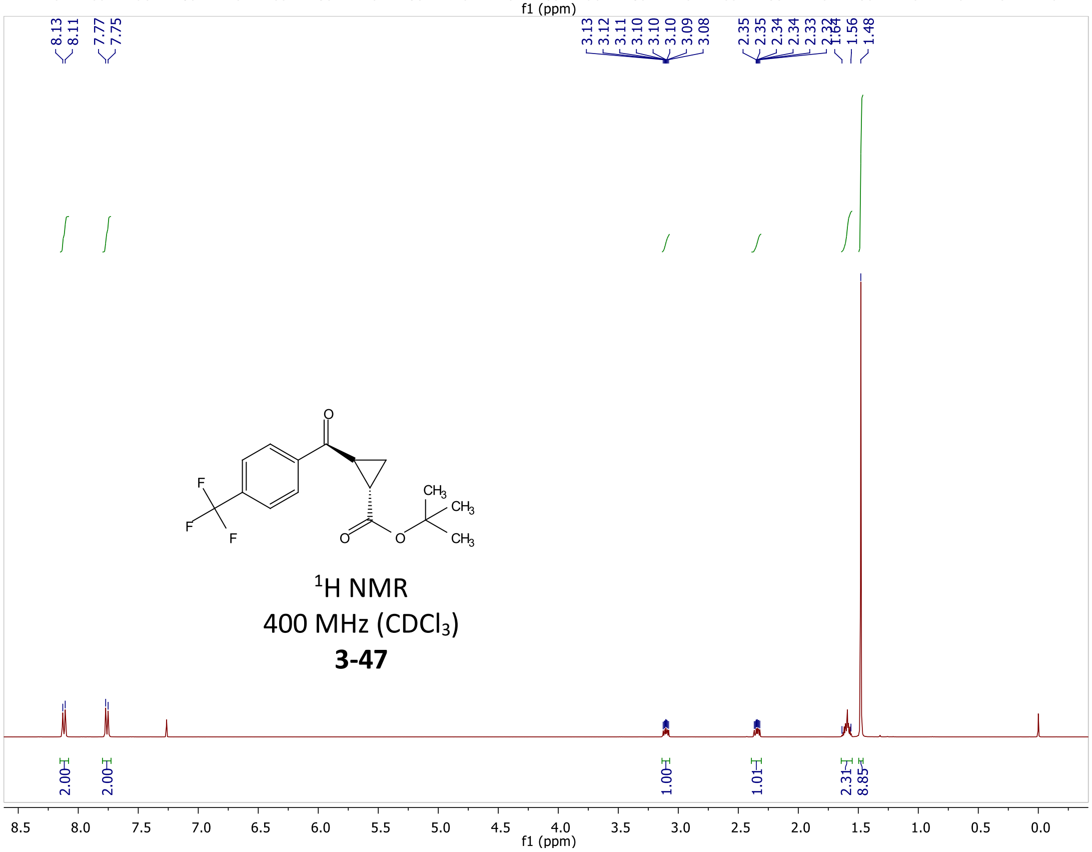
^{13}C NMR
101 MHz ($CDCl_3$)
3-42



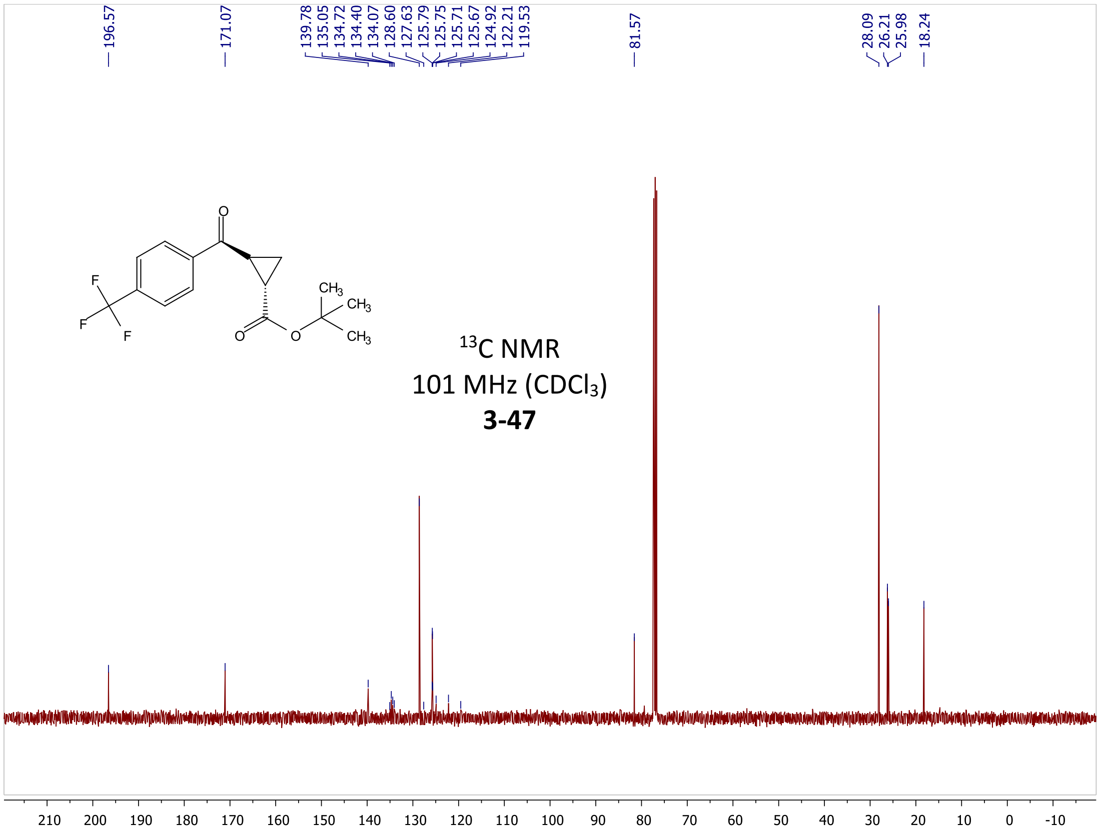
^{1}H NMR
400 MHz ($CDCl_3$)
3-41

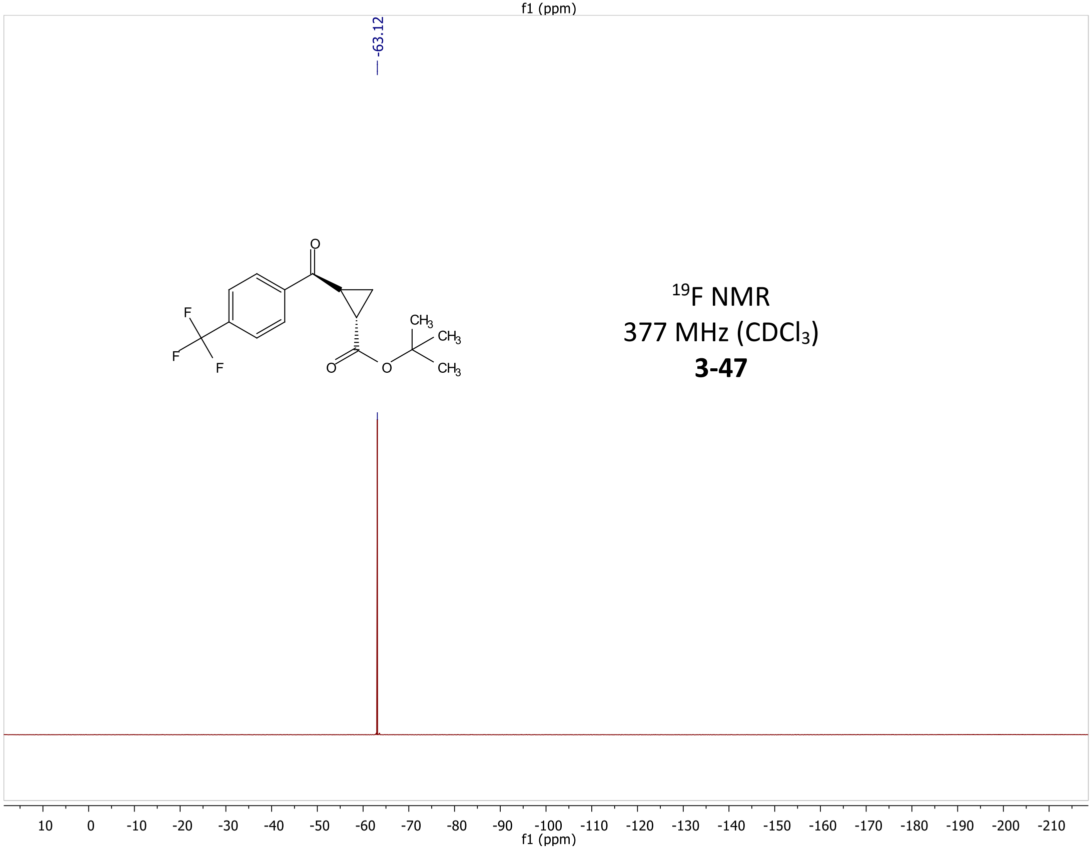


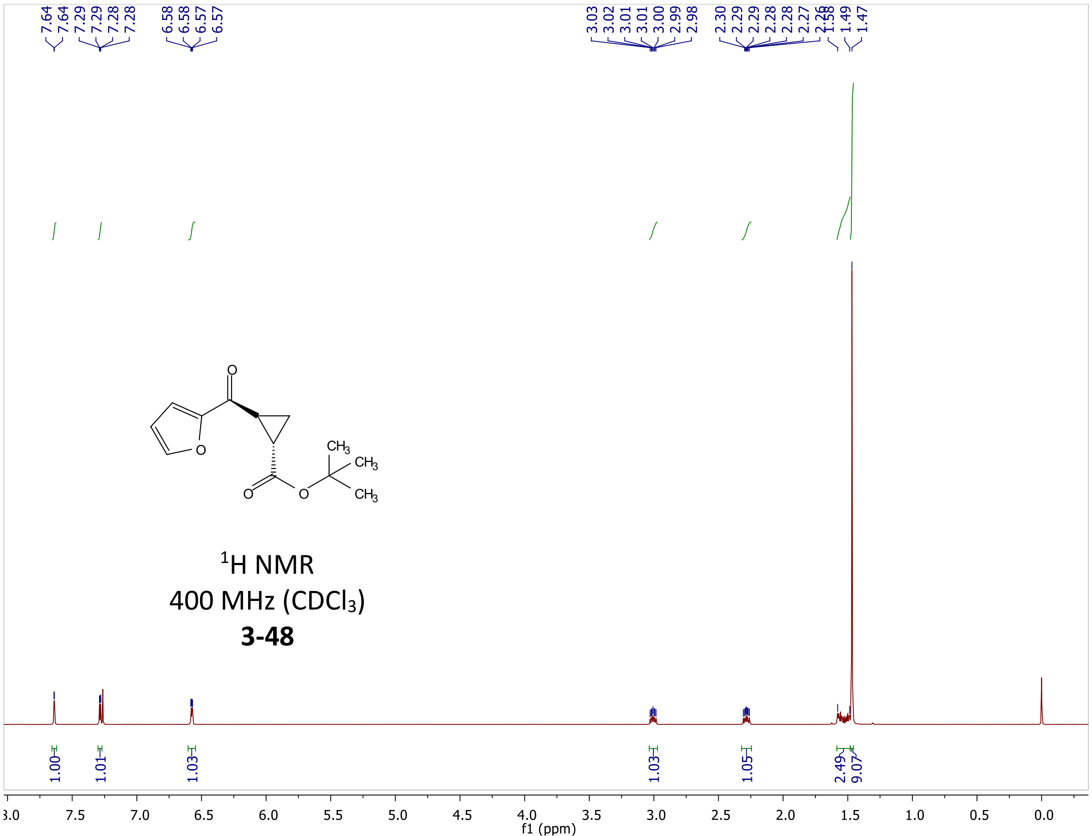
^{13}C NMR
101 MHz (CDCl$_3$)
3-41



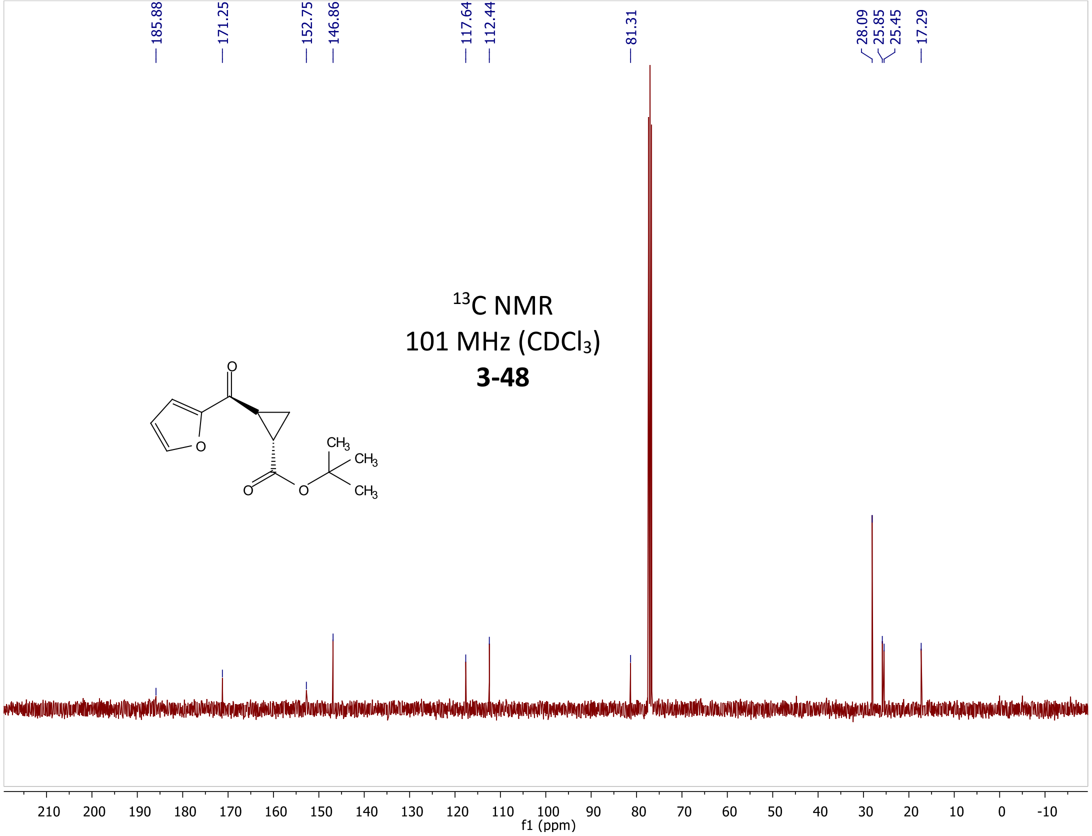
^{1}H NMR
400 MHz (CDCl$_3$)
3-47


196.57
171.07
139.78
135.05
134.72
134.40
134.07
128.60
127.63
125.79
125.75
125.71
125.67
124.92
122.21
119.53
81.57
28.09
26.21
25.98
18.24
O
F
F
F
CH3
CH3
CH3
O
O
^{13}C NMR
101 MHz (CDCl$_3$)
3-47
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)

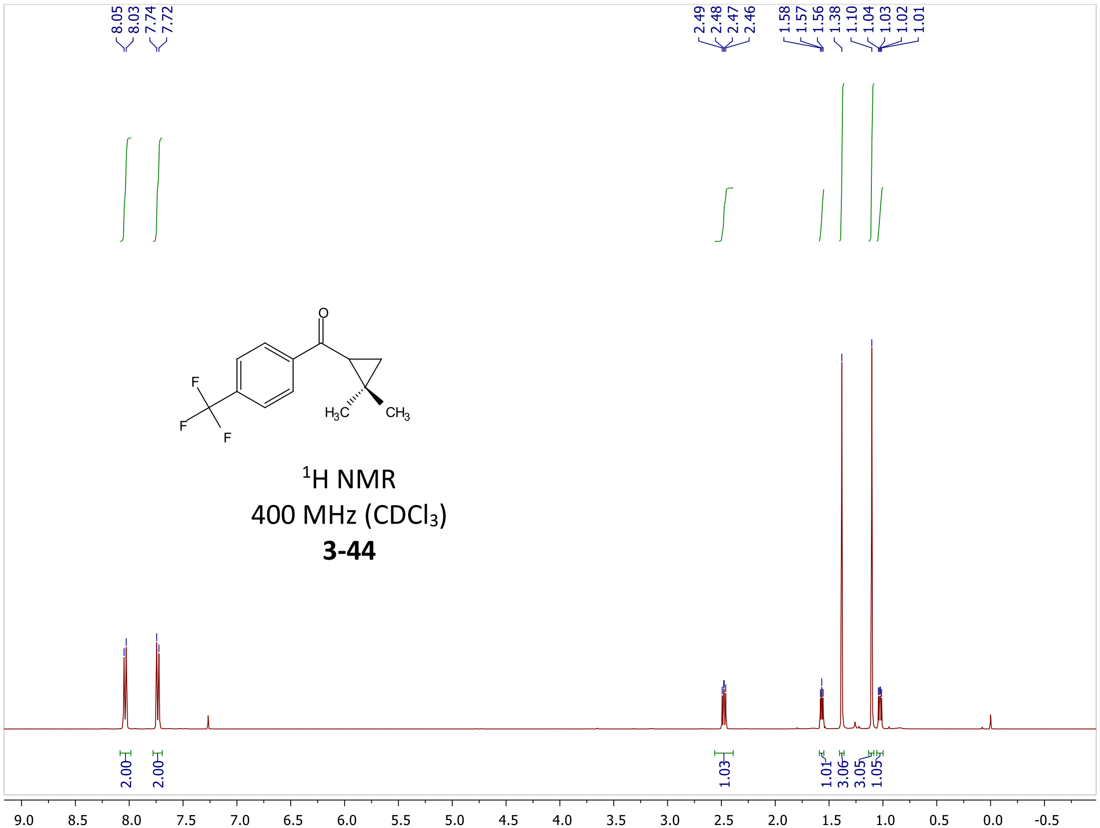

-63.12
O
F
F
F
CH3
CH3
CH3
O
O
^{19}F NMR
377 MHz (CDCl$_3$)
3-47
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)



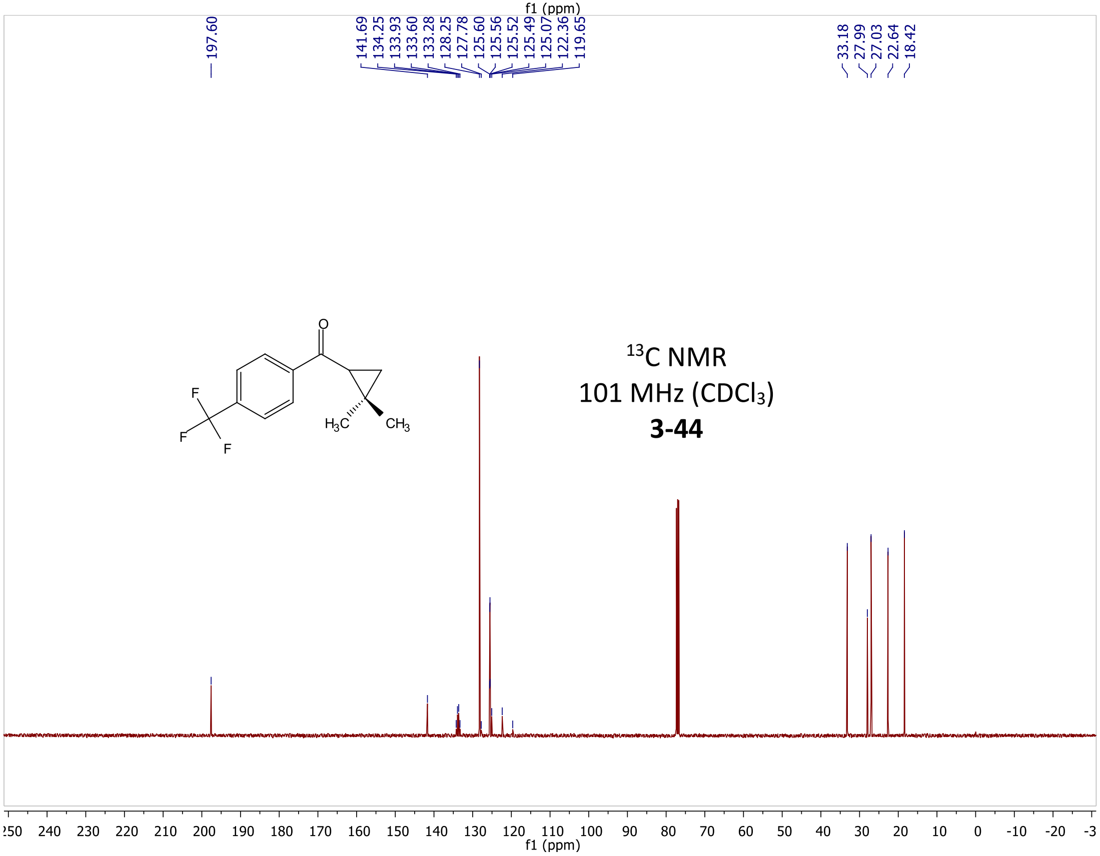
^{1}H NMR
400 MHz (CDCl$_3$)
3-48



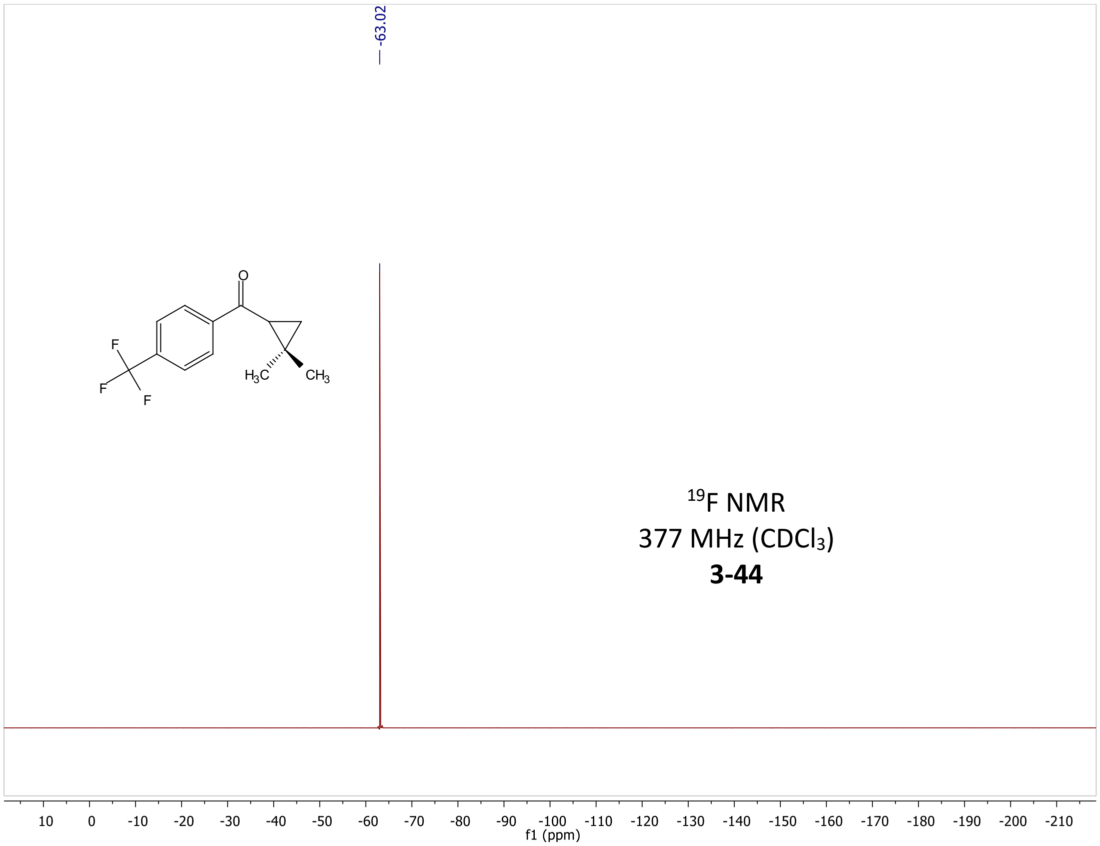
^{13}C NMR
101 MHz (CDCl$_3$)
3-48

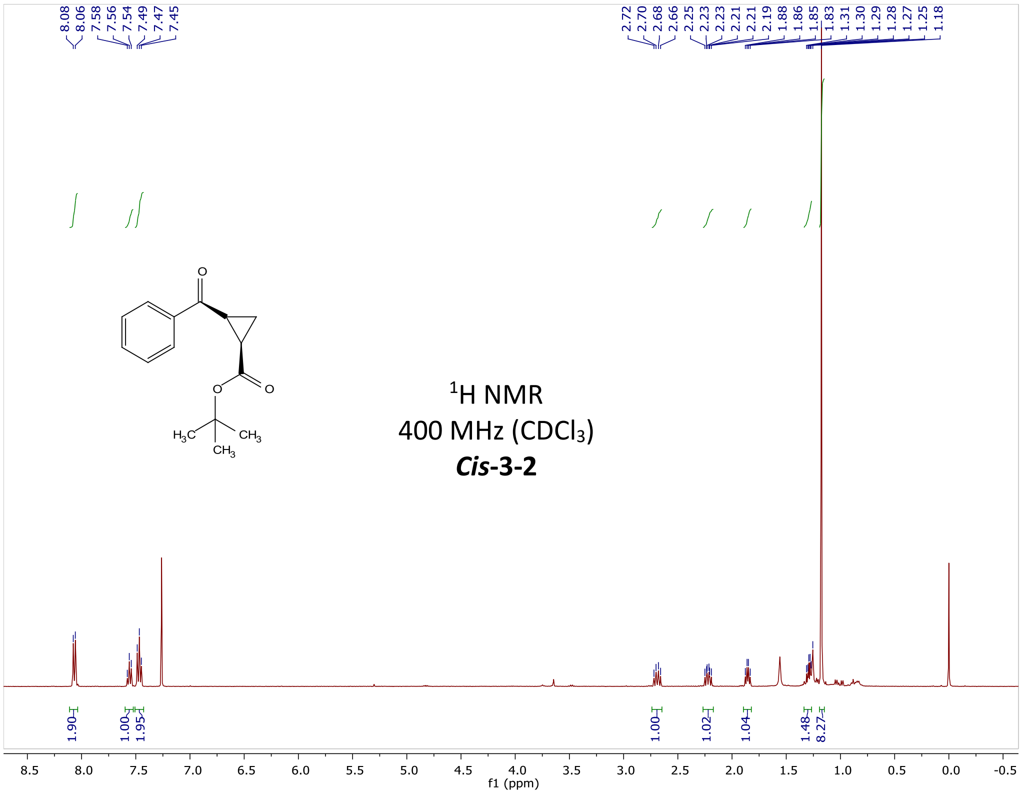


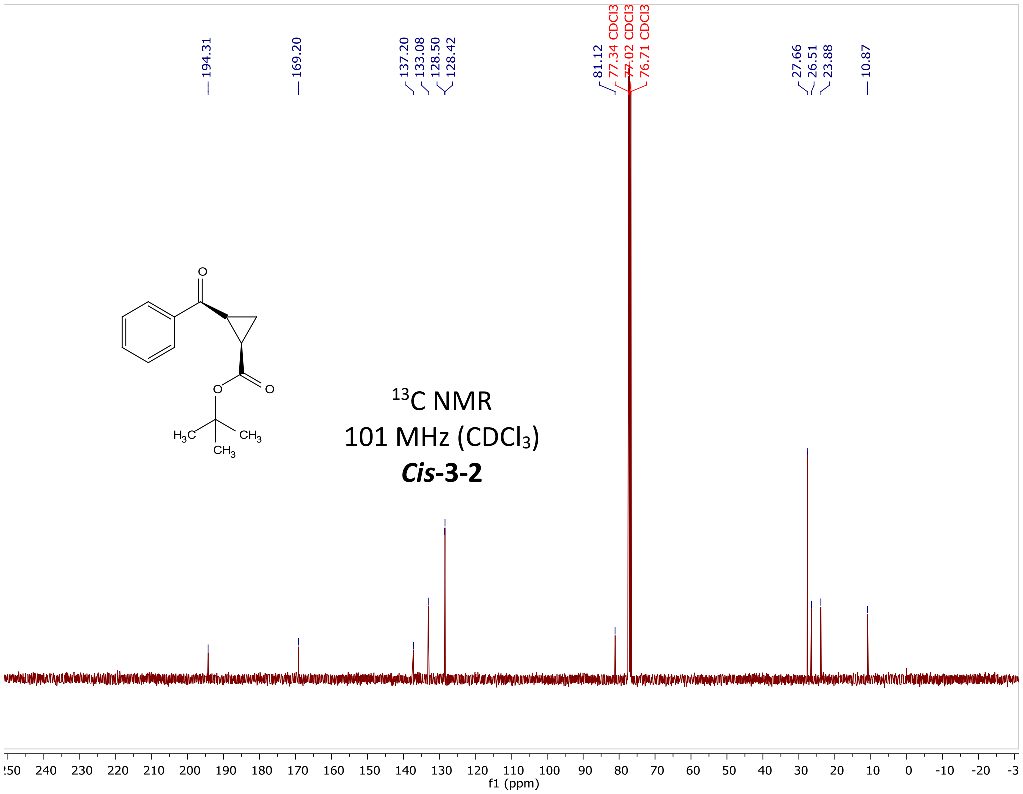
^{1}H NMR
400 MHz (CDCl$_3$)
3-44

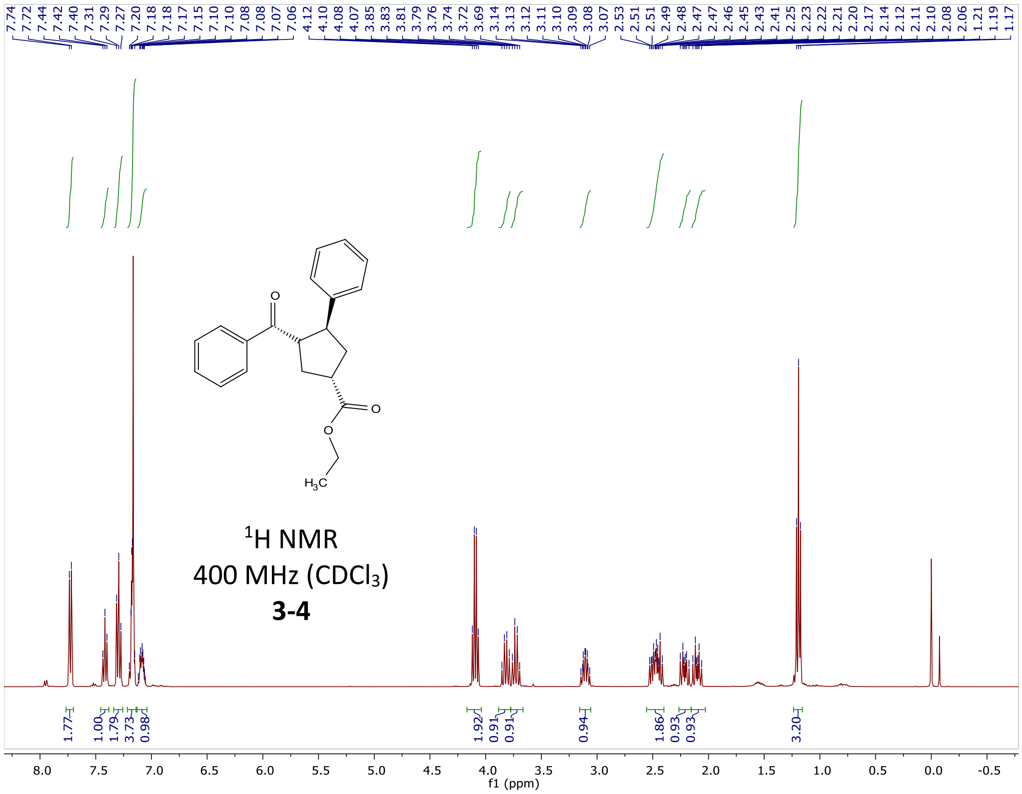


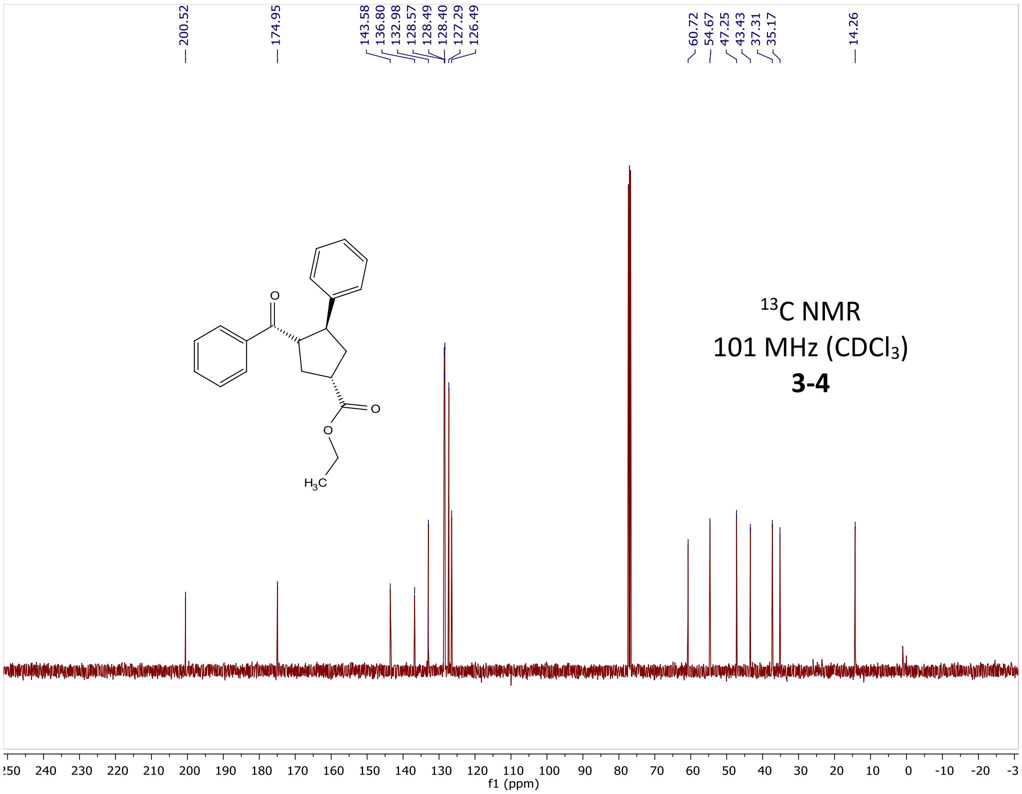
^{13}C NMR
101 MHz (CDCl$_3$)
3-44

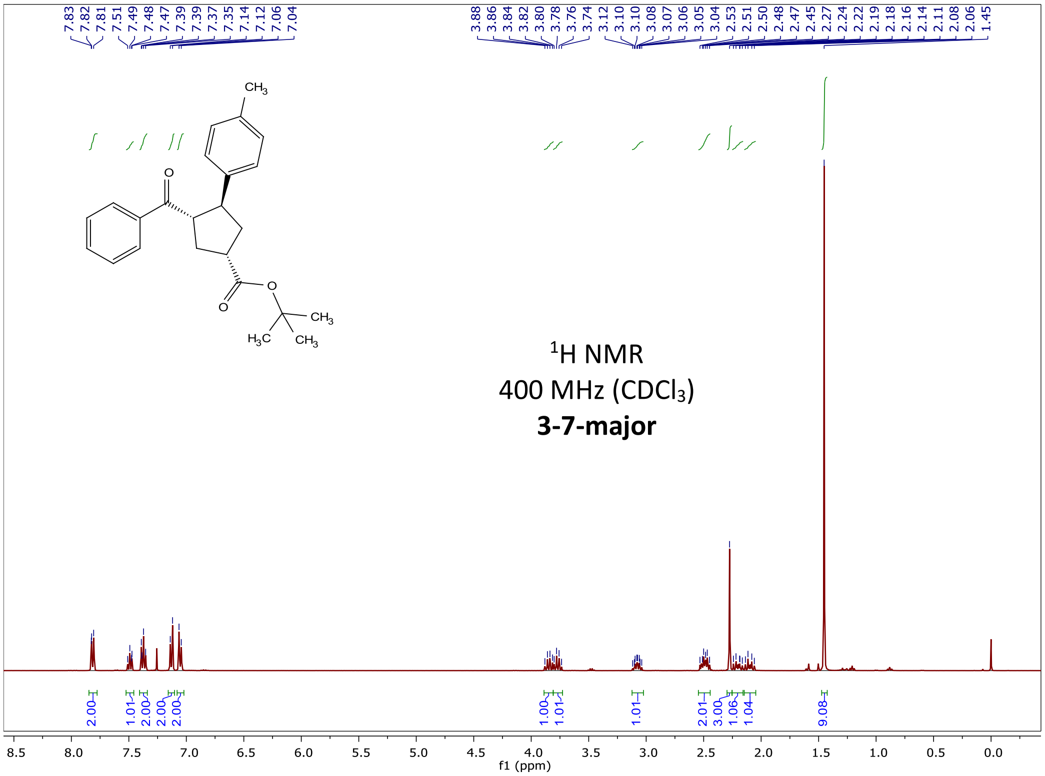

-63.02
O
F
F
F
H3C
CH3
19F NMR
377 MHz (CDCl3)
3-44
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

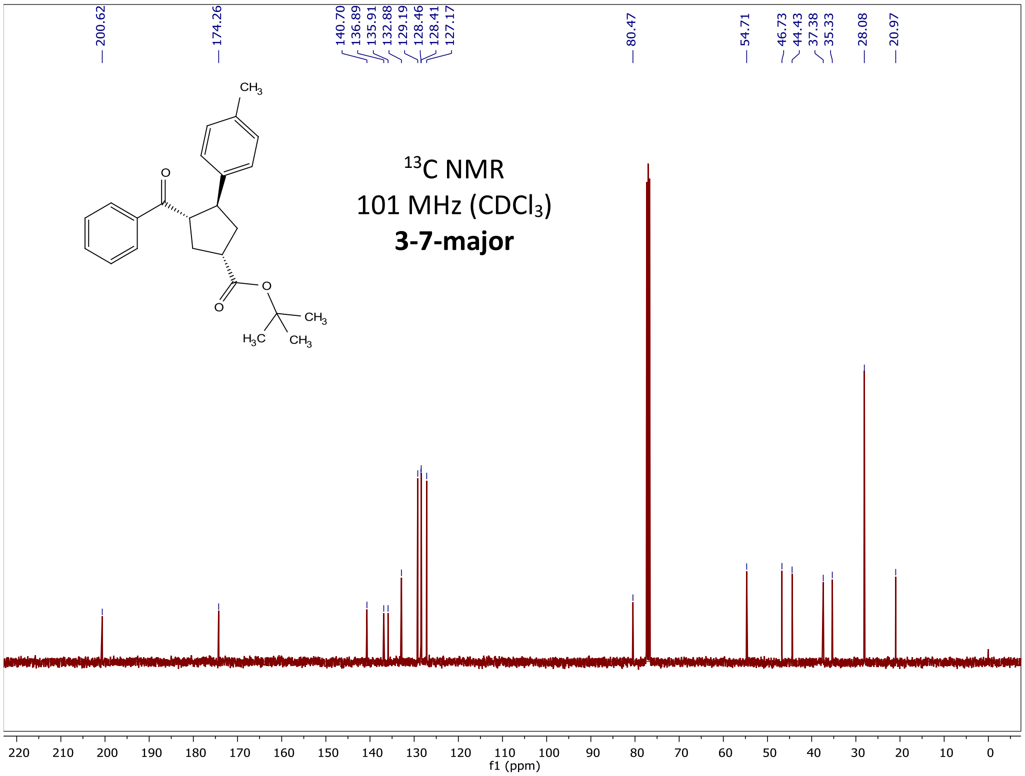

8.08
8.06
7.58
7.56
7.54
7.49
7.47
7.45
2.72
2.70
2.68
2.66
2.25
2.23
2.23
2.21
2.21
2.19
1.88
1.86
1.85
1.83
1.31
1.30
1.29
1.28
1.27
1.25
1.18
O
O
O
H3C
CH3
CH3
1H NMR
400 MHz (CDCl3)
Cis-3-2
1.90
1.00
1.95
1.00
1.02
1.04
1.48
8.27
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

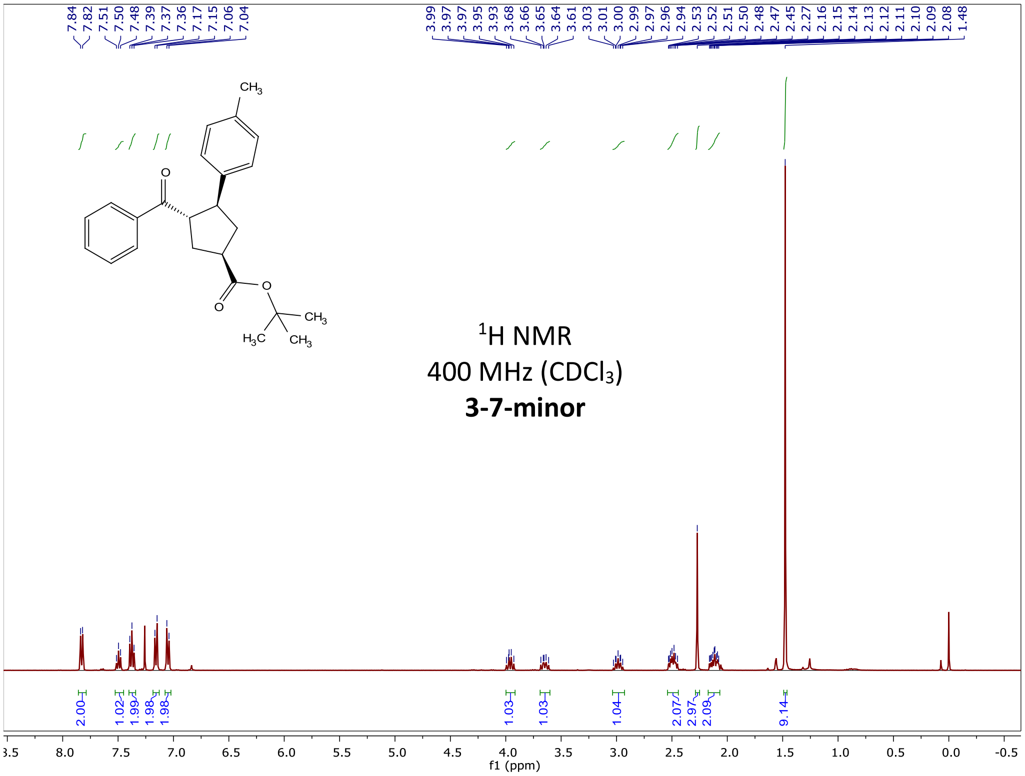

194.31
169.20
137.20
133.08
128.50
128.42
81.12
77.34 CDCl3
77.02 CDCl3
76.71 CDCl3
27.66
26.51
23.88
10.87
O
O
O
H3C
CH3
CH3
13C NMR
101 MHz (CDCl3)
Cis-3-2
250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -3
f1 (ppm)

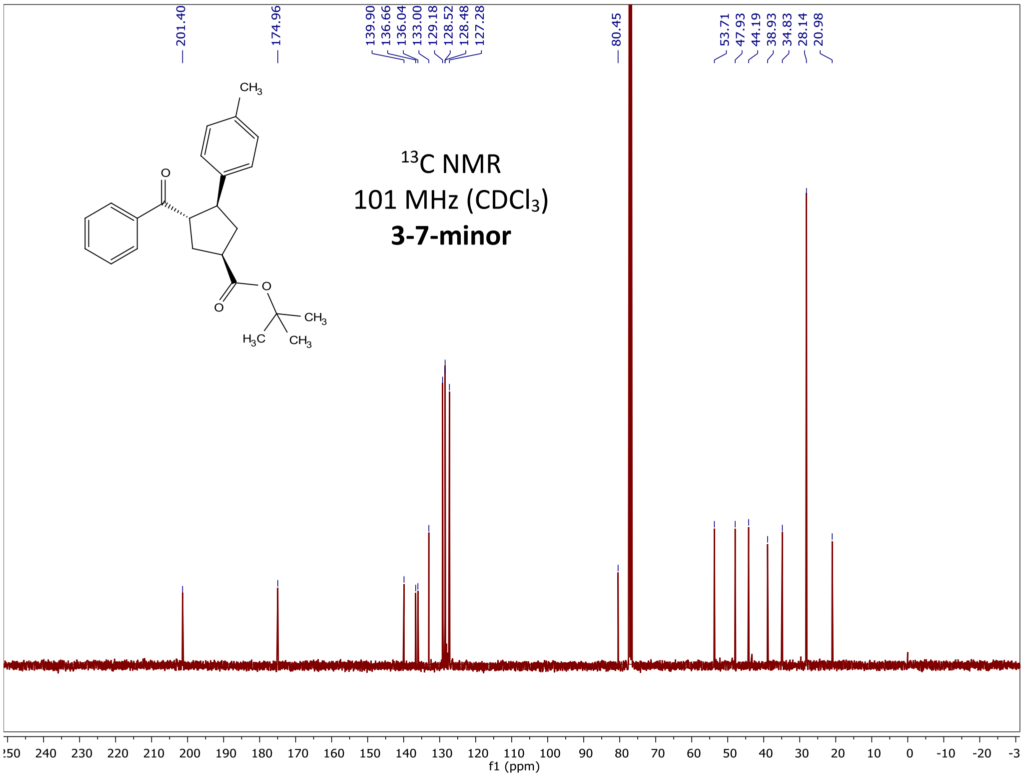

7.74
7.72
7.44
7.42
7.40
7.31
7.29
7.27
7.20
7.18
7.18
7.17
7.15
7.10
7.10
7.08
7.07
7.06
4.12
4.10
4.08
4.07
3.85
3.83
3.81
3.79
3.76
3.74
3.72
3.69
3.14
3.13
3.12
3.11
3.10
3.09
3.08
3.07
2.53
2.51
2.51
2.49
2.48
2.47
2.47
2.46
2.45
2.43
2.41
2.25
2.23
2.22
2.21
2.20
2.17
2.14
2.12
2.11
2.10
2.08
2.06
1.21
1.19
1.17
O
O
O
H3C
1H NMR
400 MHz (CDCl3)
3-4
1.77
1.00
1.79
3.73
0.98
1.92
0.91
0.91
0.94
1.86
0.93
0.93
3.20
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)


200.52
174.95
143.58
136.80
132.98
128.57
128.49
128.40
127.29
126.49
60.72
54.67
47.25
43.43
37.31
35.17
14.26
O
O
O
H_3C
^{13}C NMR
101 MHz ($CDCl_3$)
3-4
50 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -3
f1 (ppm)


7.83
7.82
7.81
7.51
7.49
7.48
7.47
7.39
7.39
7.37
7.35
7.14
7.12
7.06
7.04
3.88
3.86
3.84
3.82
3.80
3.78
3.76
3.74
3.12
3.10
3.10
3.08
3.07
3.06
3.05
3.04
2.53
2.51
2.50
2.48
2.47
2.45
2.27
2.24
2.22
2.19
2.18
2.16
2.14
2.11
2.08
2.06
1.45
CH3
O
O
O
CH3
H3C
CH3
^{1}H NMR
400 MHz (CDCl$_3$)
3-7-major
2.00
1.01
2.00
2.00
2.00
1.00
1.01
1.01
2.01
3.00
1.06
1.04
9.08
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
f1 (ppm)


200.62
174.26
140.70
136.89
135.91
132.88
129.19
128.46
128.41
127.17
80.47
54.71
46.73
44.43
37.38
35.33
28.08
20.97
CH3
O
O
O
CH3
H3C
CH3
^{13}C NMR
101 MHz (CDCl$_3$)
3-7-major
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)


7.84
7.82
7.51
7.50
7.48
7.39
7.37
7.36
7.17
7.15
7.06
7.04
3.99
3.97
3.97
3.95
3.93
3.68
3.66
3.65
3.64
3.61
3.03
3.01
3.00
2.99
2.97
2.96
2.94
2.53
2.52
2.51
2.50
2.48
2.47
2.45
2.27
2.16
2.15
2.14
2.13
2.12
2.11
2.10
2.09
2.08
1.48
CH3
O
O
O
CH3
H3C
CH3
1H NMR
400 MHz (CDCl3)
3-7-minor
2.00
1.02
1.99
1.98
1.98
1.03
1.03
1.04
2.07
2.97
2.09
9.14
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)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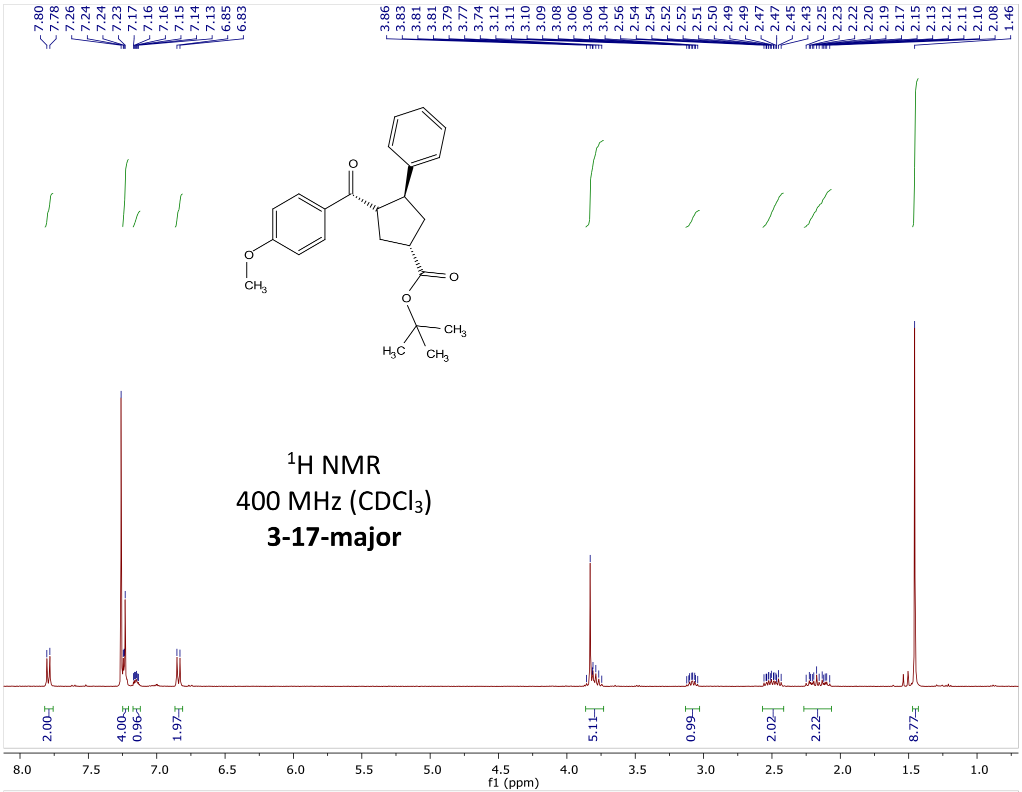
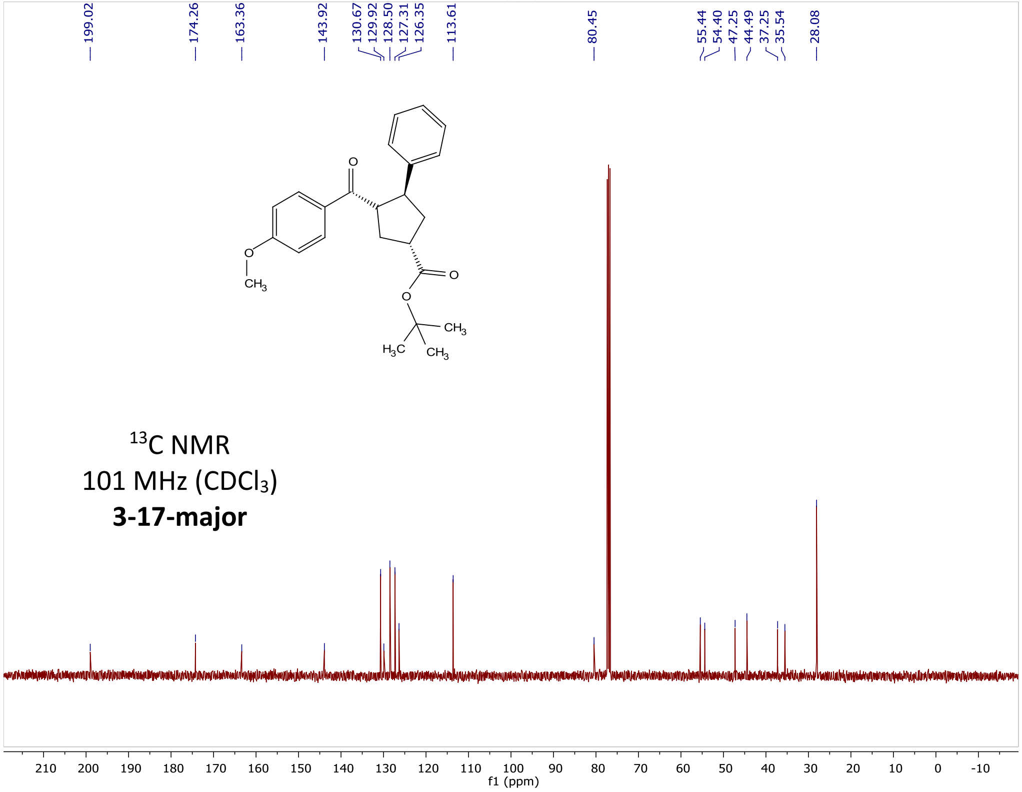
174.96
139.90
136.66
136.04
133.00
129.18
128.52
128.48
127.28
80.45
53.71
47.93
44.19
38.93
34.83
28.14
20.98
CH3
O
O
O
CH3
H3C
CH3
13C NMR
101 MHz (CDCl3)
3-7-minor
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-3
f1 (ppm)



^{1}H NMR

400 MHz (CDCl$_3$)

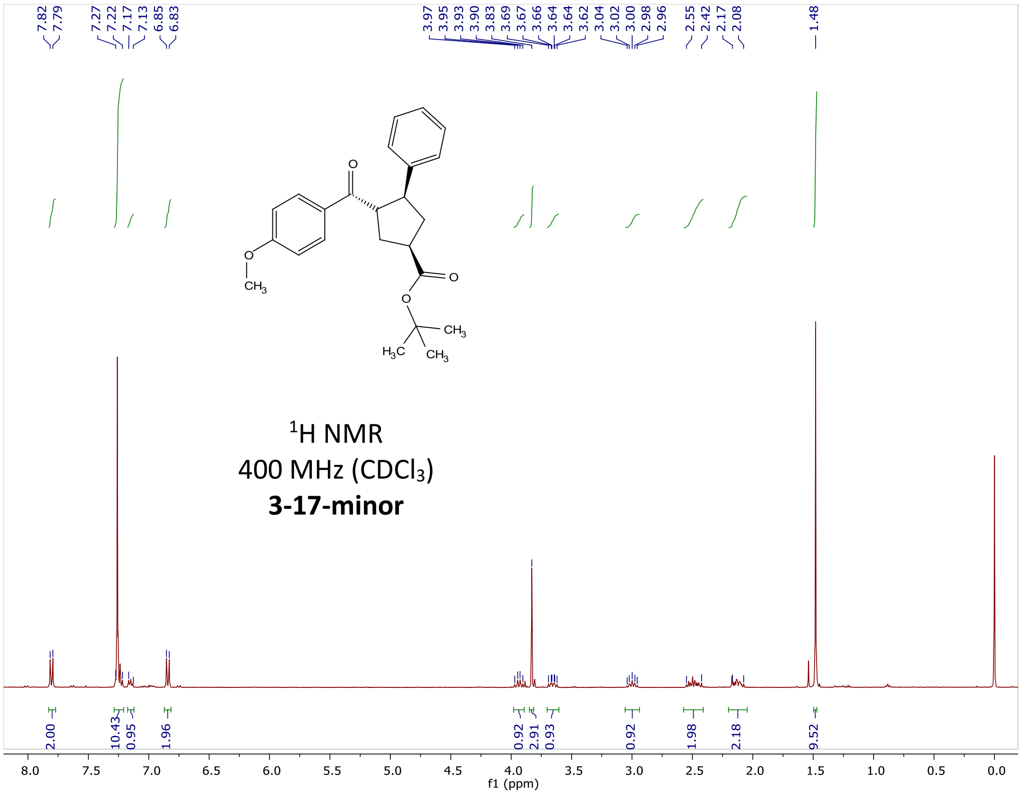
3-17-major

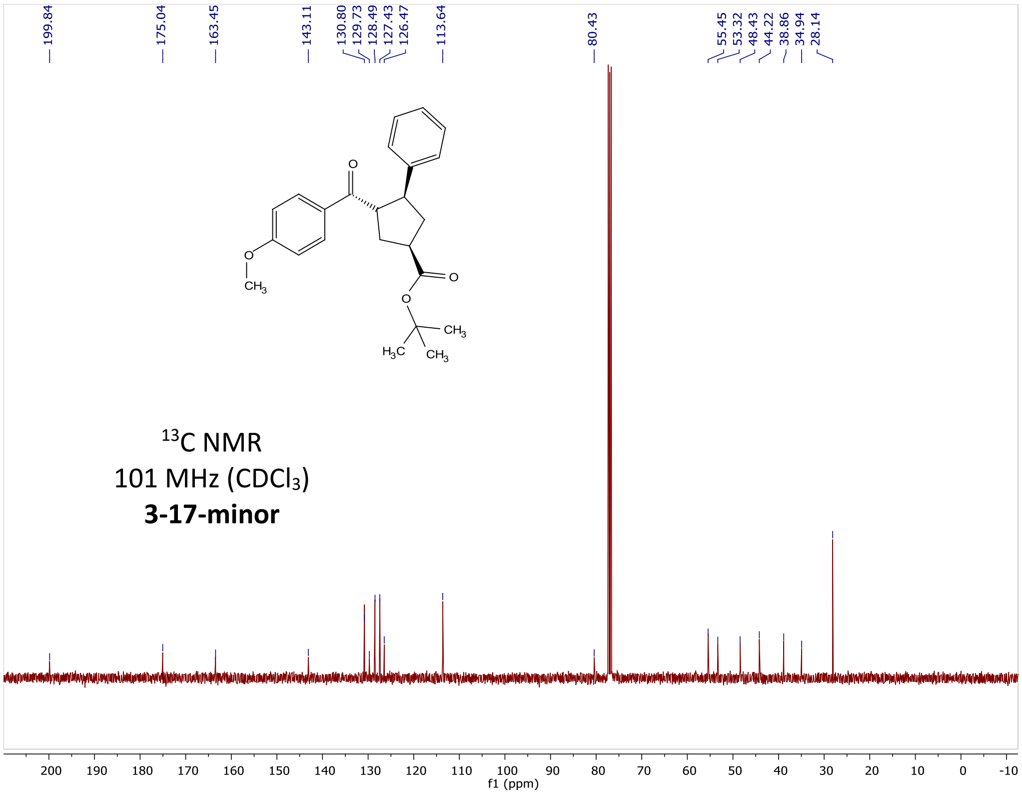


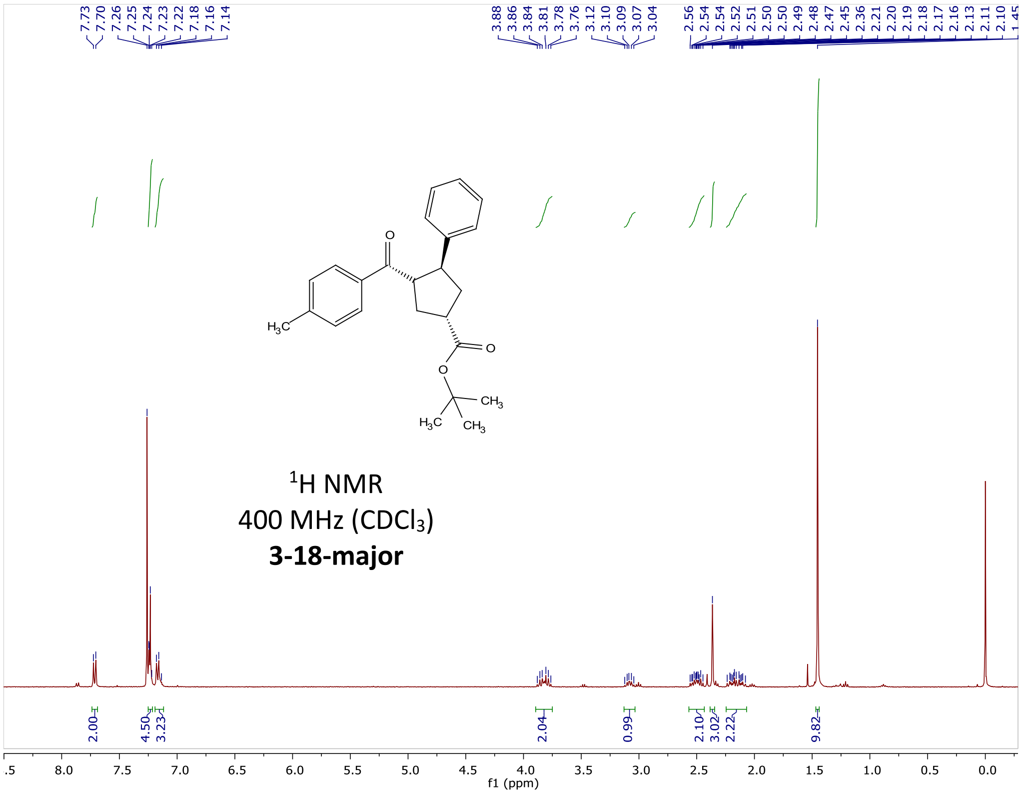
^{13}C NMR

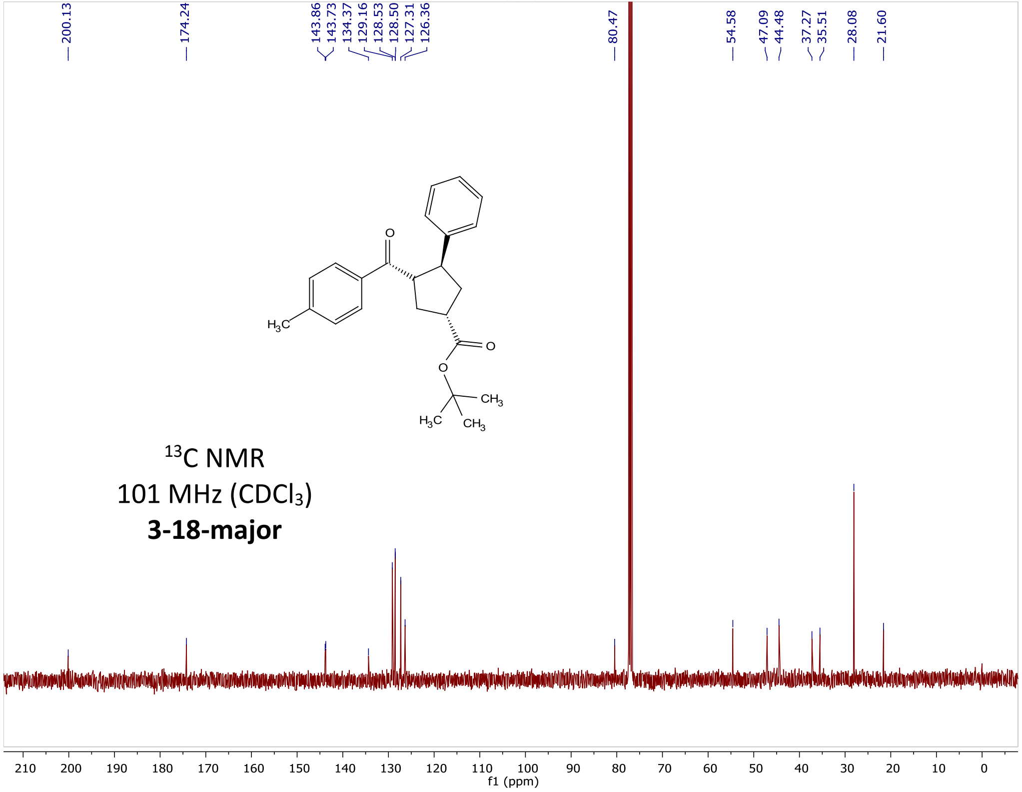
101 MHz (CDCl$_3$)

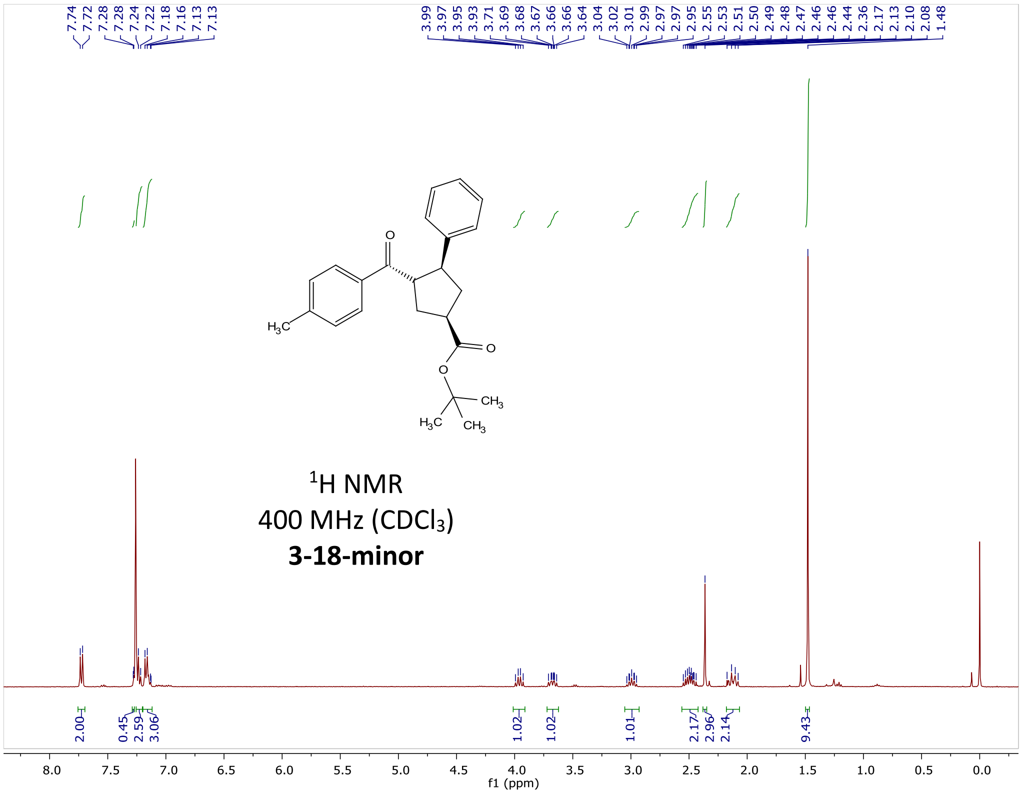
3-17-major


7.82
7.79
7.27
7.22
7.17
7.13
6.85
6.83
3.97
3.95
3.93
3.90
3.83
3.69
3.67
3.66
3.64
3.64
3.62
3.04
3.02
3.00
2.98
2.96
2.55
2.42
2.17
2.08
1.48
O
O
CH3
O
O
CH3
H3C
CH3
^{1}H NMR
400 MHz (CDCl$_3$)
3-17-minor
2.00
10.43
0.95
1.96
0.92
2.91
0.93
0.92
1.98
2.18
9.52
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
f1 (ppm)

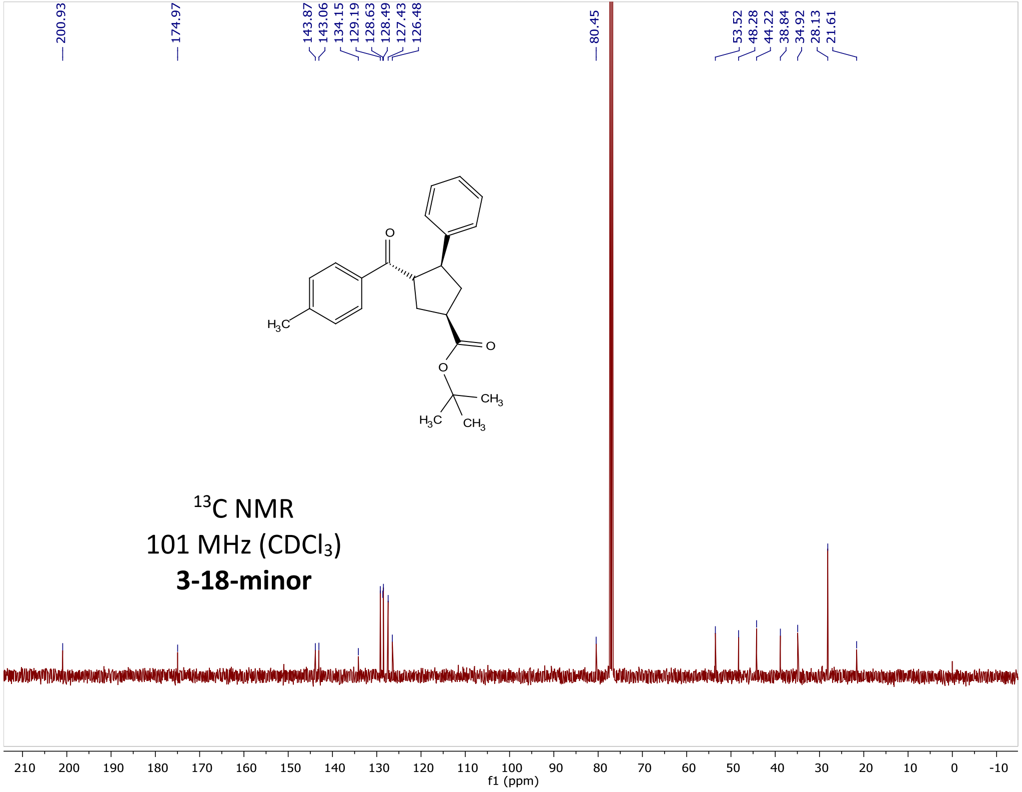

199.84
175.04
163.45
143.11
130.80
129.73
128.49
127.43
126.47
113.64
80.43
55.45
53.32
48.43
44.22
38.86
34.94
28.14
O
O
CH3
O
O
CH3
H3C
CH3
^{13}C NMR
101 MHz (CDCl$_3$)
3-17-minor
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.73
7.70
7.26
7.25
7.24
7.23
7.22
7.18
7.16
7.14
3.88
3.86
3.84
3.81
3.78
3.76
3.12
3.10
3.09
3.07
3.04
2.56
2.54
2.54
2.52
2.51
2.50
2.50
2.49
2.48
2.47
2.45
2.36
2.21
2.20
2.19
2.18
2.17
2.16
2.13
2.11
2.10
1.45
O
H3C
O
O
CH3
H3C
CH3
¹H NMR
400 MHz (CDCl₃)
3-18-major
2.00
4.50
3.23
2.04
0.99
2.10
3.02
2.22
9.82
.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
f1 (ppm)

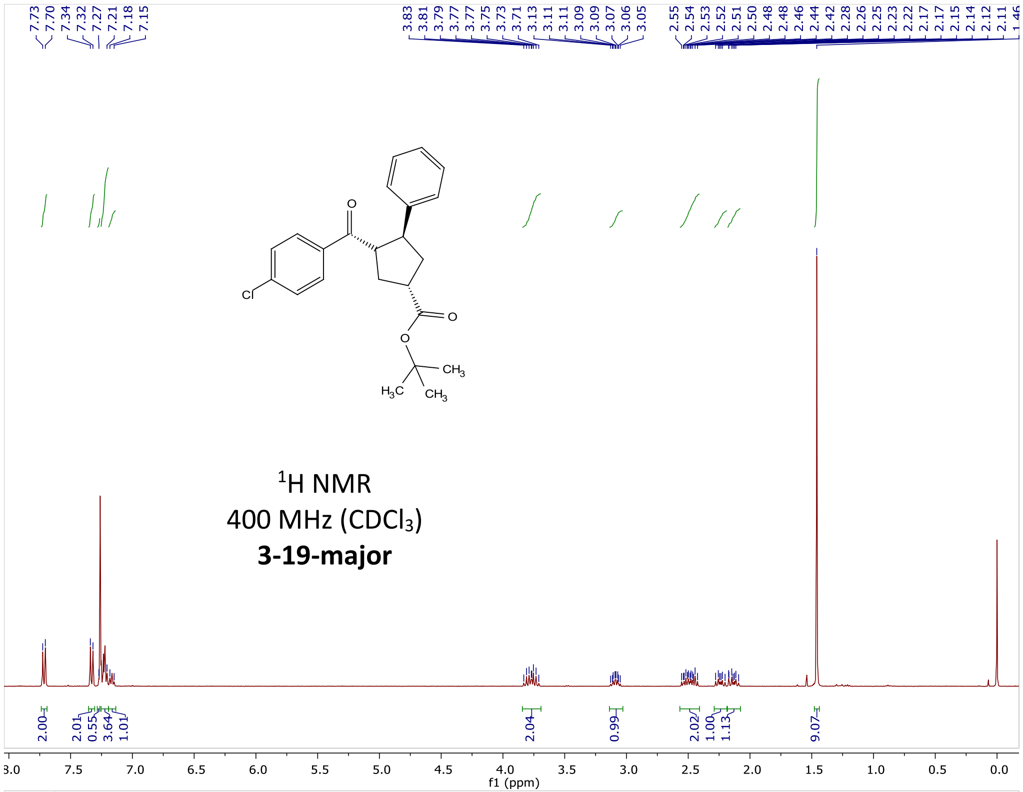

200.13
174.24
143.86
143.73
134.37
129.16
128.53
128.50
127.31
126.36
80.47
54.58
47.09
44.48
37.27
35.51
28.08
21.60
O
H3C
O
O
CH3
H3C
CH3
¹³C NMR
101 MHz (CDCl₃)
3-18-major
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

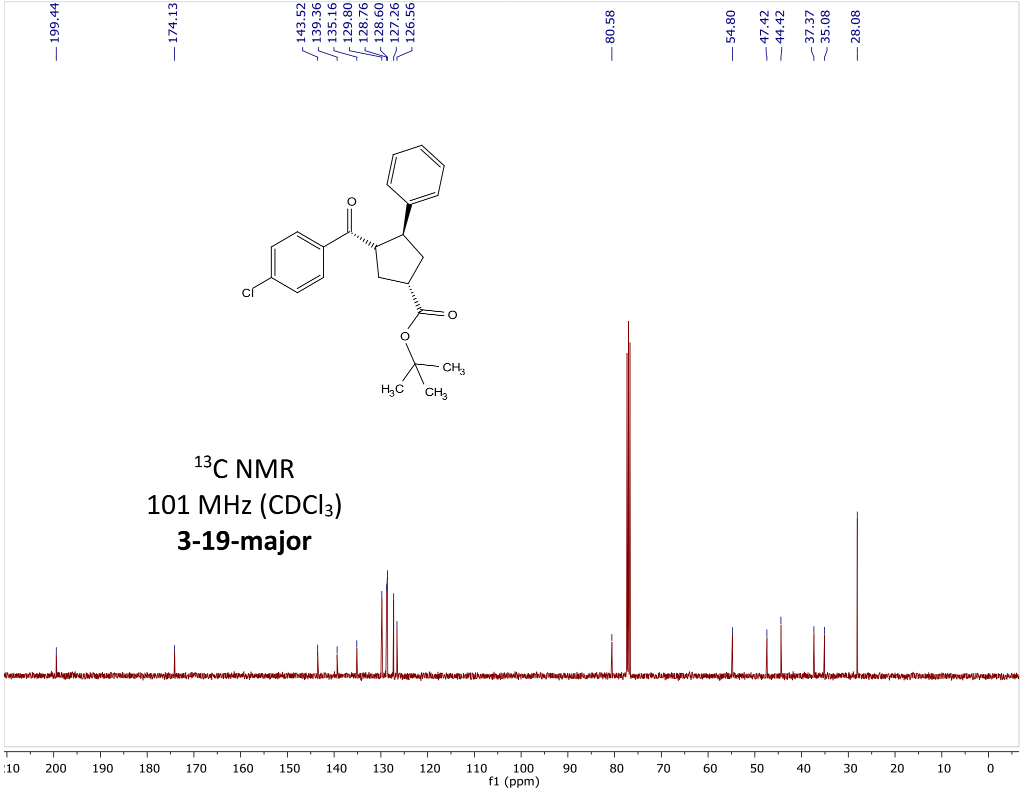


^{1}H NMR
400 MHz (CDCl$_3$)
3-18-minor



^{13}C NMR
101 MHz (CDCl$_3$)
3-18-minor


7.73
7.70
7.34
7.32
7.27
7.21
7.18
7.15
3.83
3.81
3.79
3.77
3.77
3.75
3.73
3.71
3.13
3.11
3.11
3.09
3.07
3.06
3.05
2.55
2.54
2.53
2.52
2.51
2.50
2.48
2.48
2.46
2.44
2.42
2.28
2.26
2.25
2.23
2.22
2.17
2.17
2.15
2.14
2.12
2.11
1.46
O
Cl
O
O
CH3
H3C
CH3
^{1}H NMR
400 MHz (CDCl$_3$)
3-19-major
2.00
2.01
0.55
3.64
1.01
2.04
0.99
2.02
1.00
1.13
9.07
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
f1 (ppm)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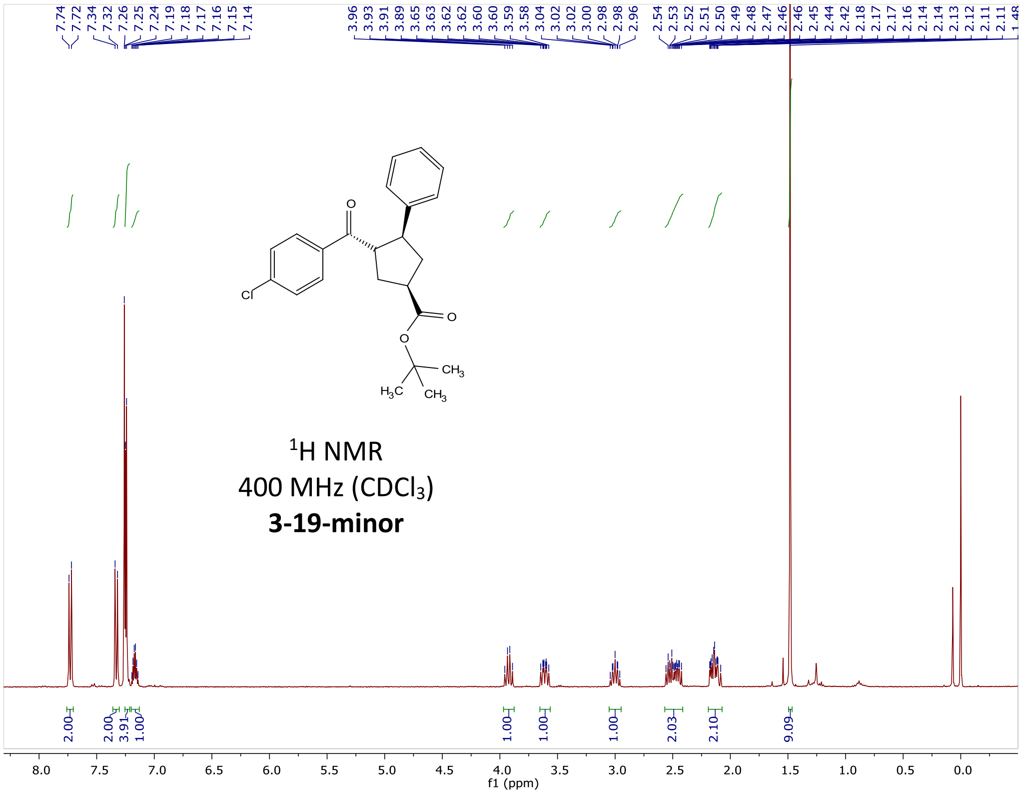
174.13
143.52
139.36
135.16
129.80
128.76
128.60
127.26
126.56
80.58
54.80
47.42
44.42
37.37
35.08
28.08
O
Cl
O
O
CH3
H3C
CH3
^{13}C NMR
101 MHz (CDCl$_3$)
3-19-major
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.74
7.72
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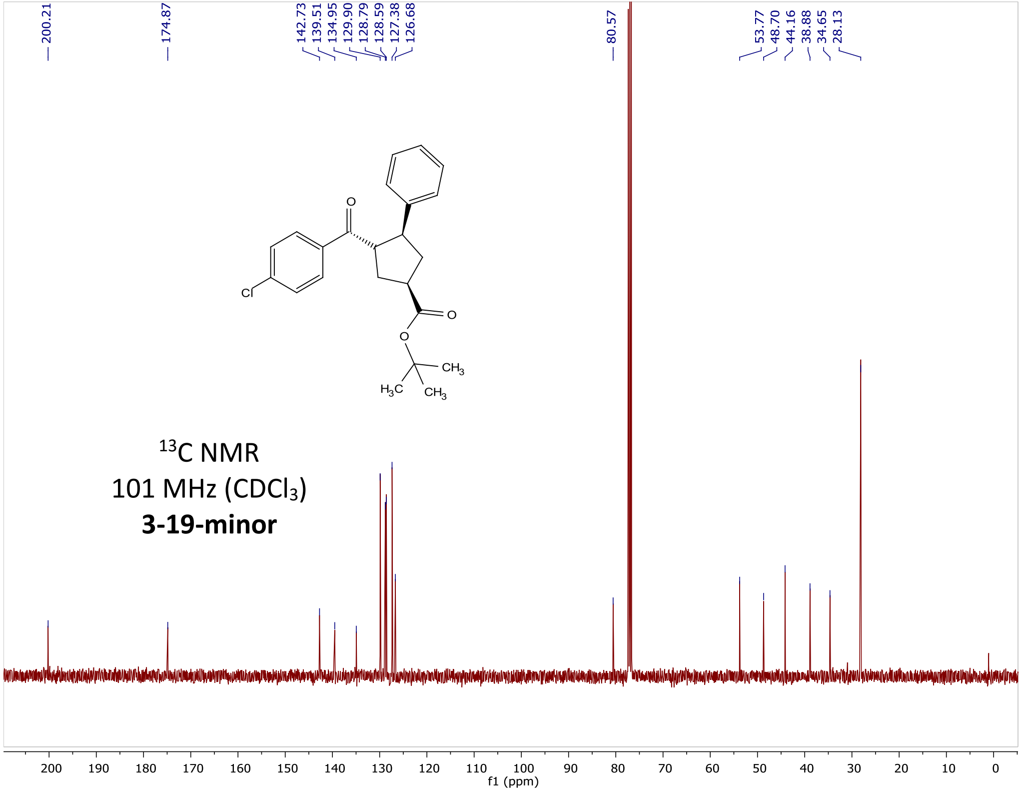
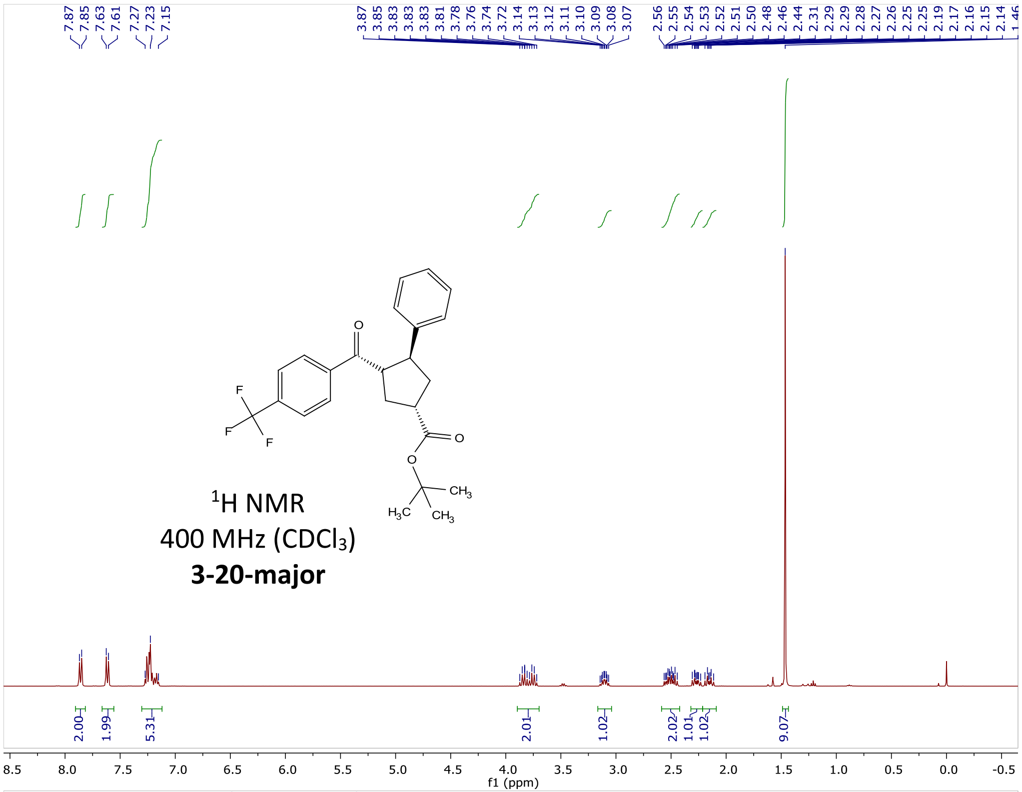
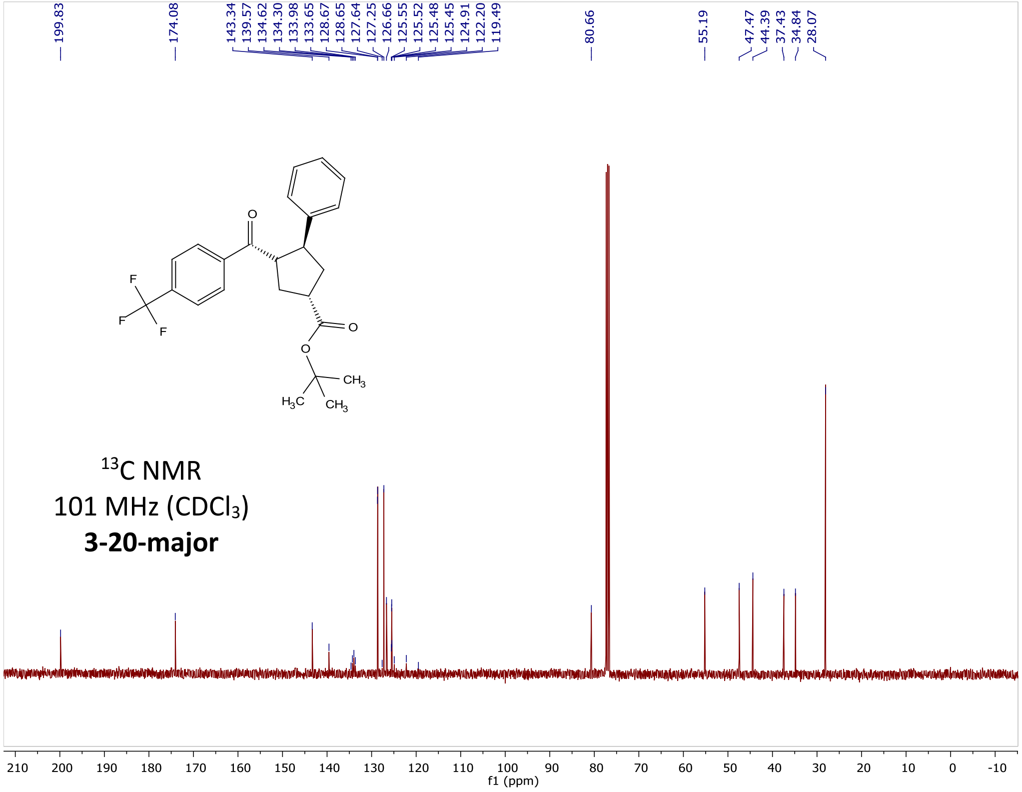
7.32
7.26
7.25
7.24
7.19
7.18
7.17
7.16
7.15
7.14
3.96
3.93
3.91
3.89
3.65
3.63
3.62
3.60
3.60
3.59
3.58
3.04
3.02
3.00
2.98
2.98
2.96
2.54
2.53
2.52
2.51
2.50
2.49
2.48
2.47
2.46
2.46
2.45
2.44
2.42
2.18
2.17
2.17
2.16
2.14
2.13
2.12
2.11
1.48
O
Cl
O
O
CH3
H3C
CH3
1H NMR
400 MHz (CDCl3)
3-19-minor
2.00
2.00
3.91
1.00
1.00
1.00
1.00
2.03
2.10
9.09
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
f1 (ppm)

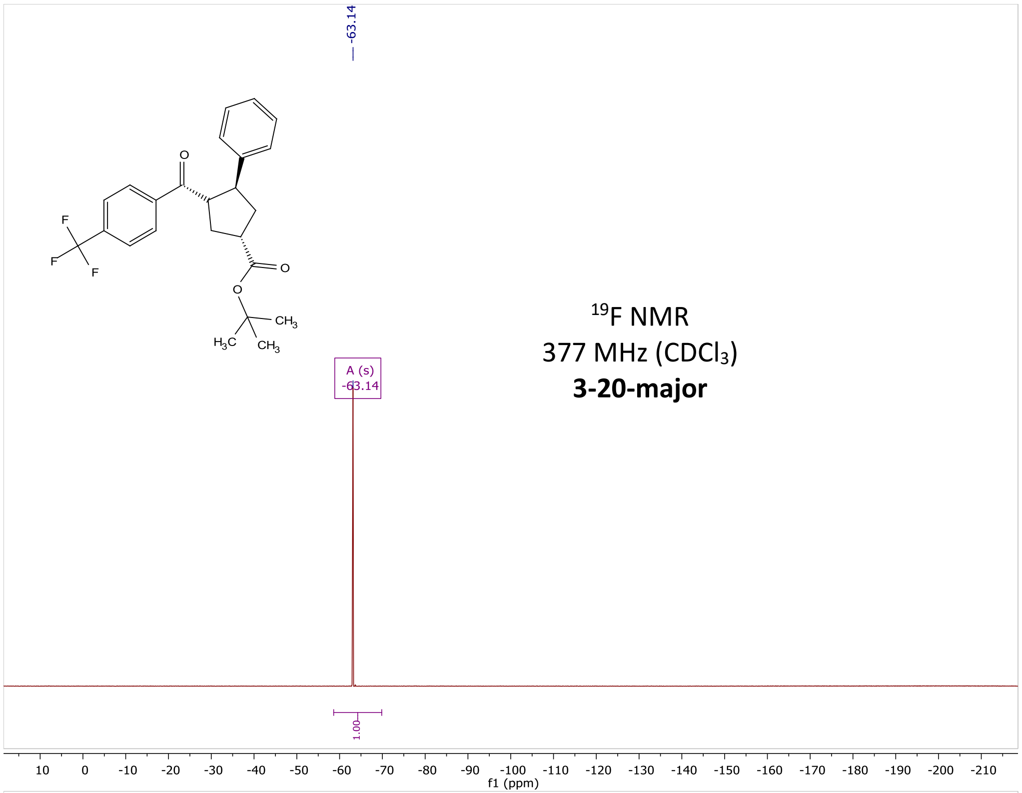

200.21
174.87
142.73
139.51
134.95
129.90
128.79
128.59
127.38
126.68
80.57
53.77
48.70
44.16
38.88
34.65
28.13
O
Cl
O
O
CH3
H3C
CH3
13C NMR
101 MHz (CDCl3)
3-19-minor
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

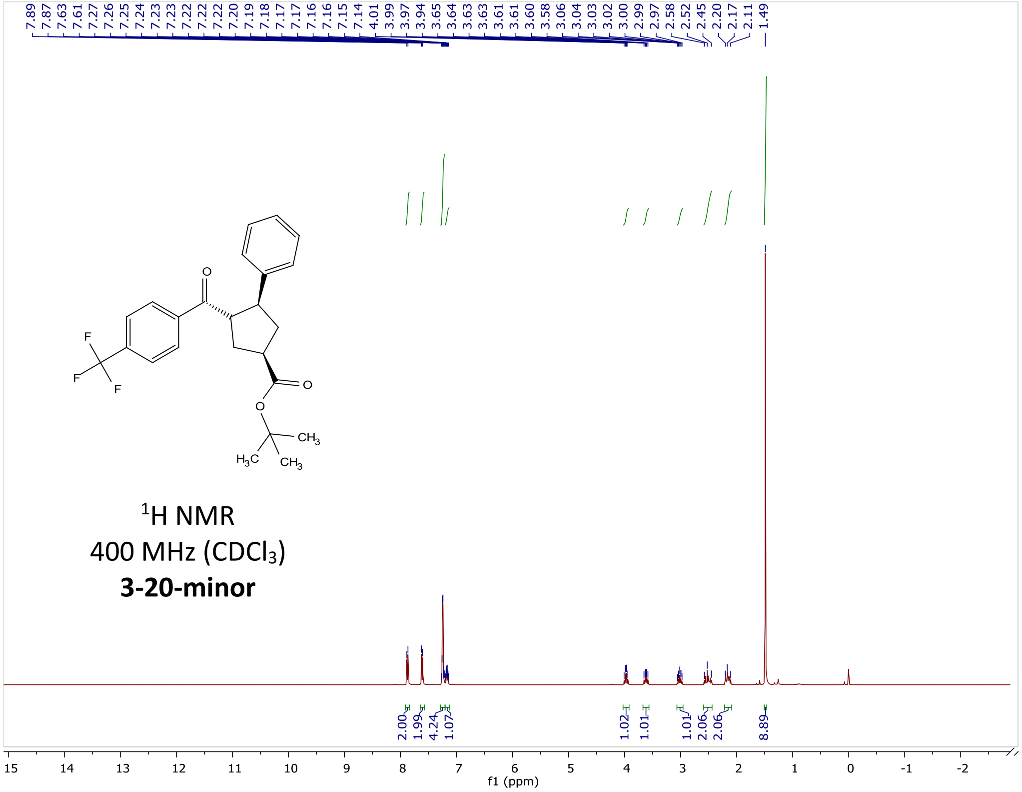


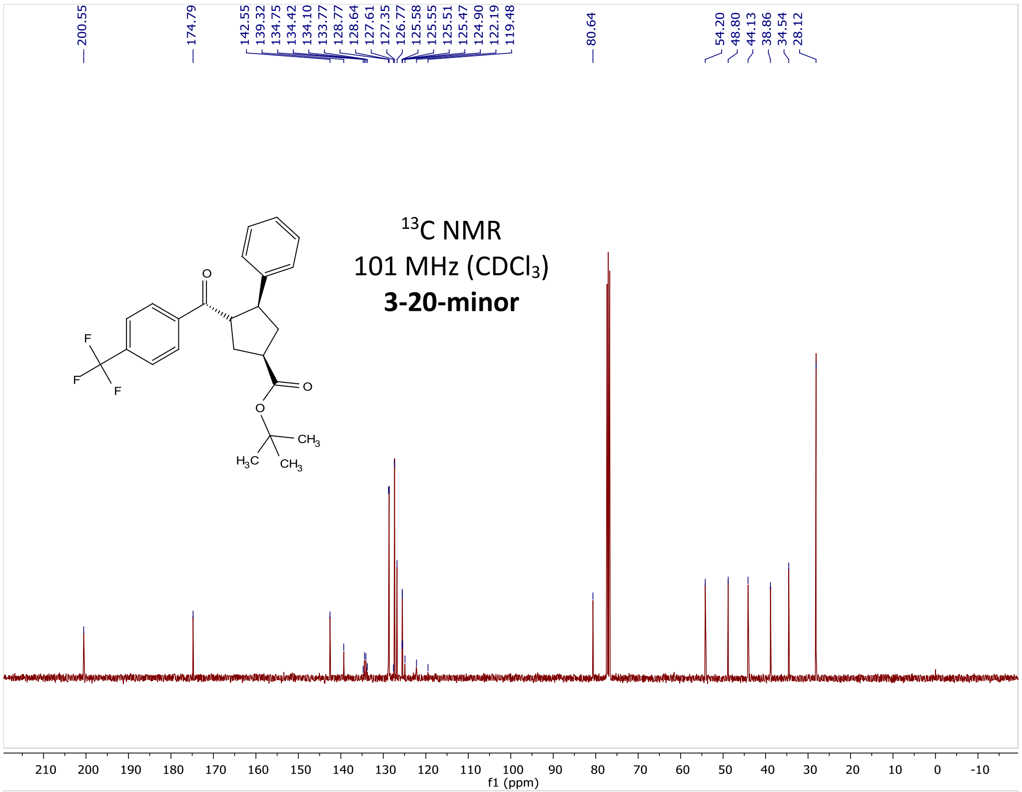
^{1}H NMR
400 MHz (CDCl$_3$)
3-20-major



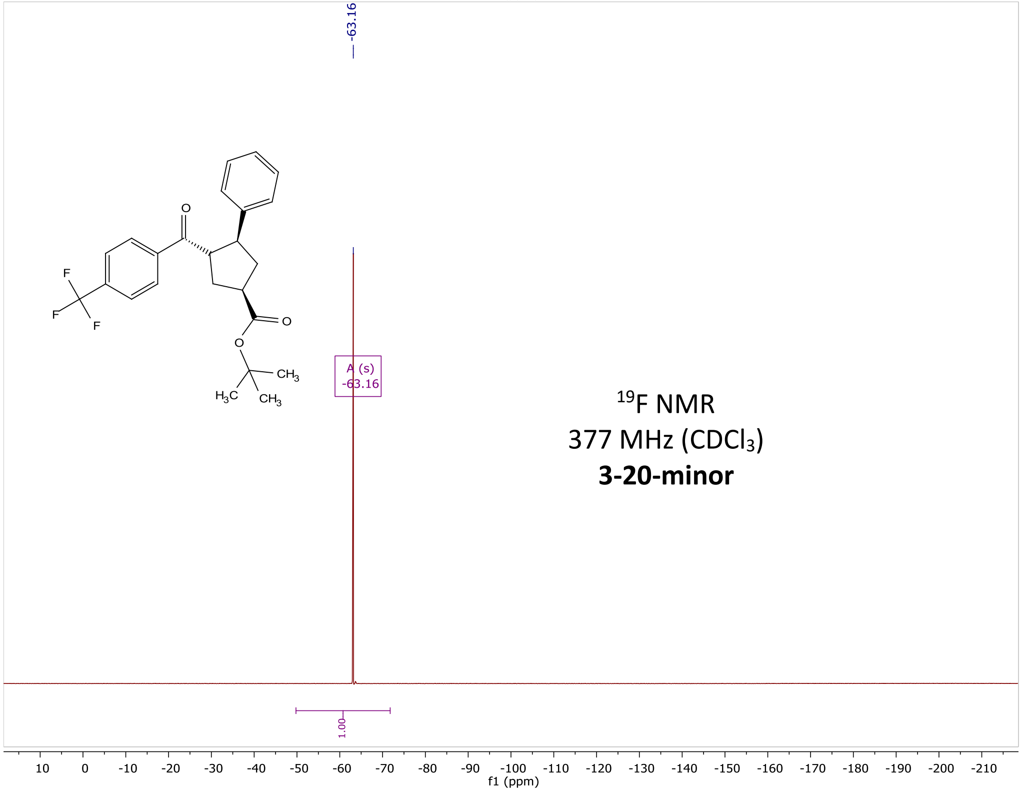
^{13}C NMR
101 MHz (CDCl$_3$)
3-20-major


-63.14
F
F
F
O
O
O
CH3
H3C
CH3
19F NMR
377 MHz (CDCl3)
3-20-major
A (s)
-63.14
1.00
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

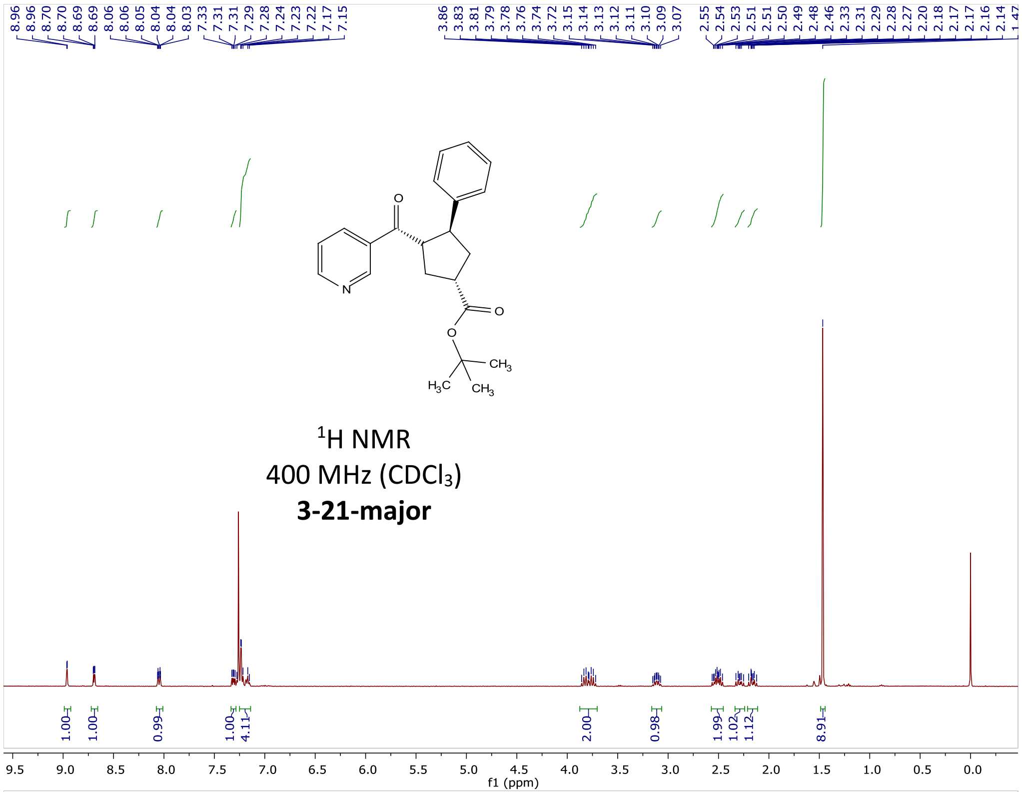

7.89 7.87 7.63 7.61 7.27 7.26 7.25 7.24 7.23 7.23 7.22 7.22 7.22 7.20 7.19 7.18 7.17 7.17 7.16 7.15 7.14 4.01 3.99 3.97 3.94 3.65 3.64 3.63 3.63 3.61 3.61 3.60 3.58 3.06 3.04 3.03 3.02 3.00 2.99 2.97 2.58 2.52 2.45 2.20 2.17 2.11 1.49
O
F
F
F
O
O
CH3
H3C
CH3
1H NMR
400 MHz (CDCl3)
3-20-minor
2.00 1.99 4.24 1.07 1.02 1.01 1.01 2.06 2.06 8.89
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)



^{13}C NMR
101 MHz (CDCl$_3$)
3-20-minor



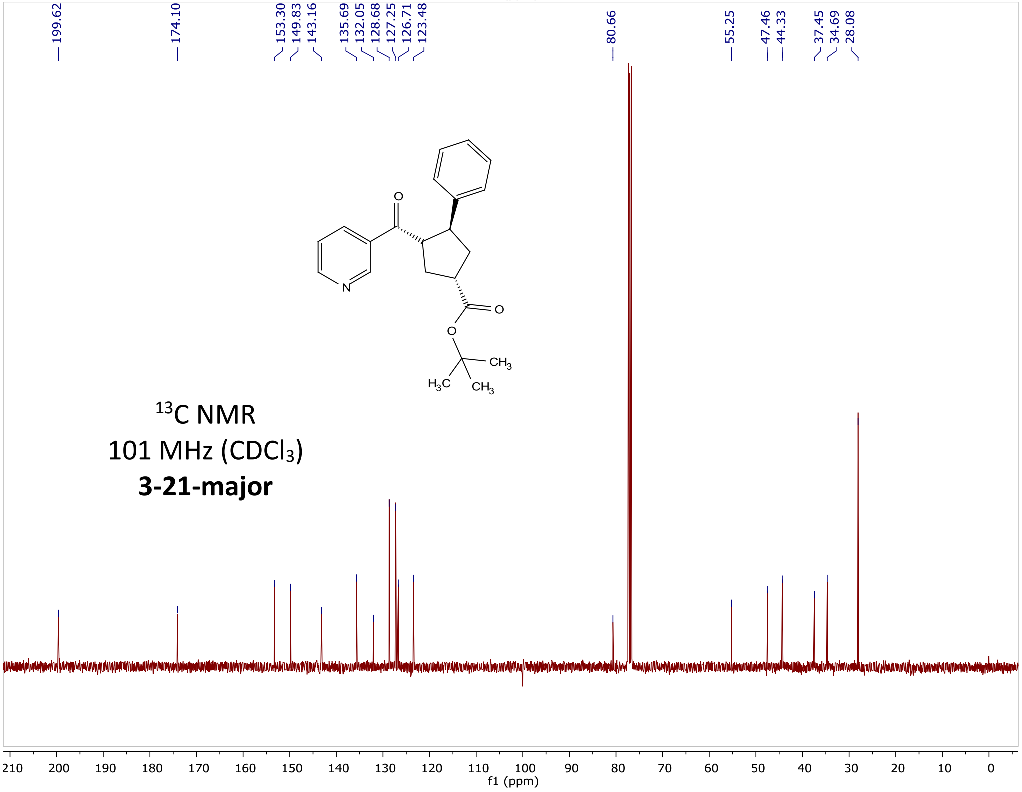
^{19}F NMR
377 MHz (CDCl$_3$)
3-20-minor



^{1}H NMR

400 MHz (CDCl$_3$)

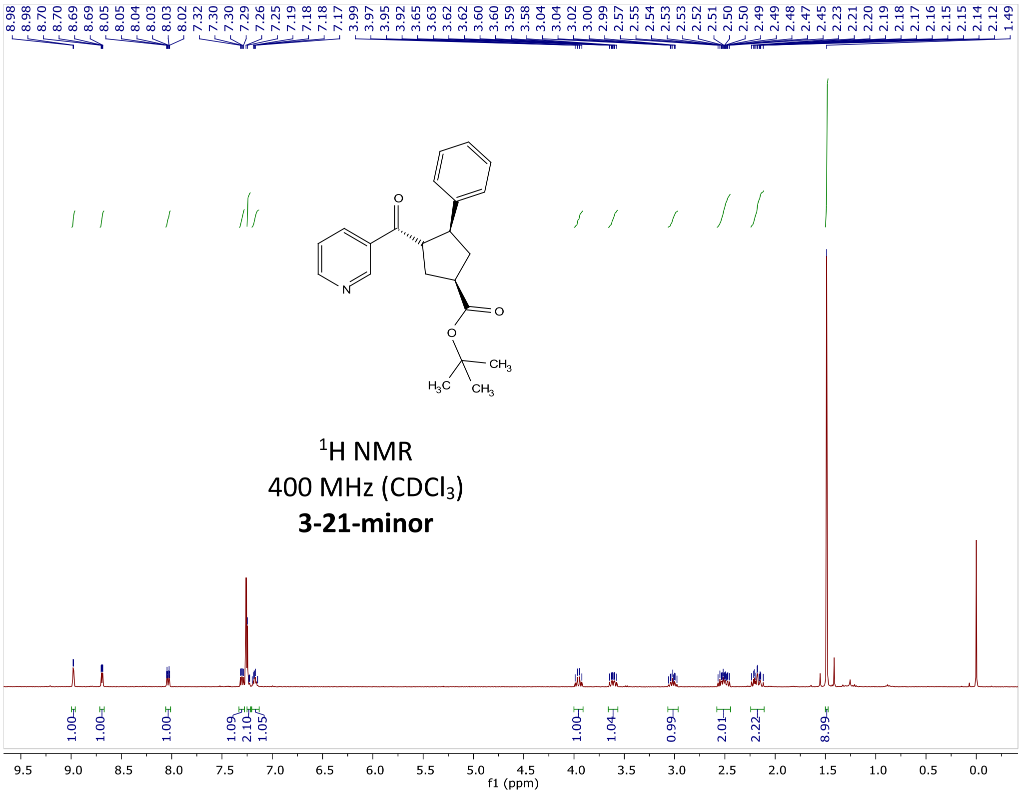
3-21-major



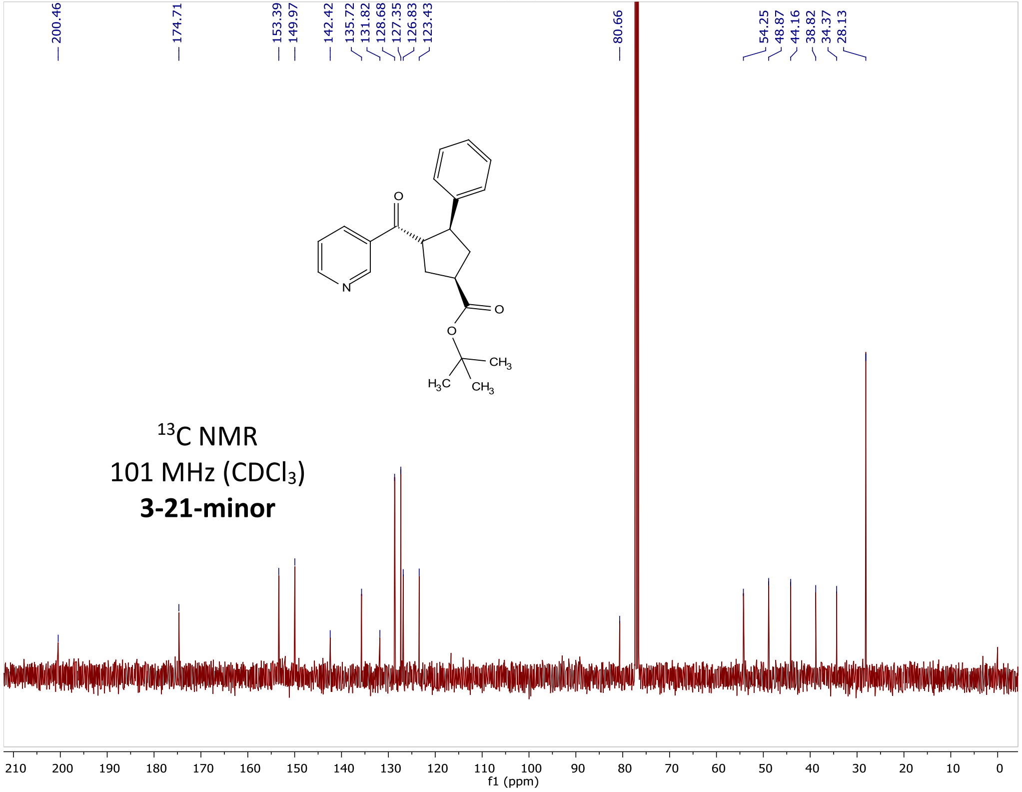
^{13}C NMR

101 MHz (CDCl$_3$)

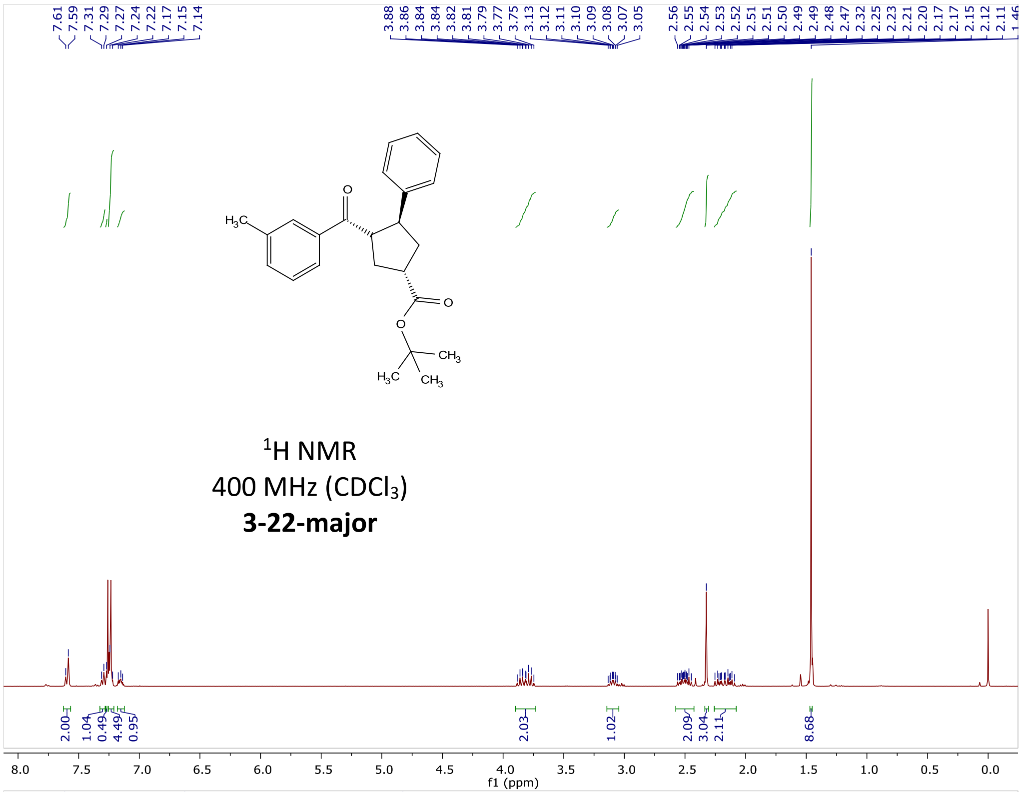
3-21-major



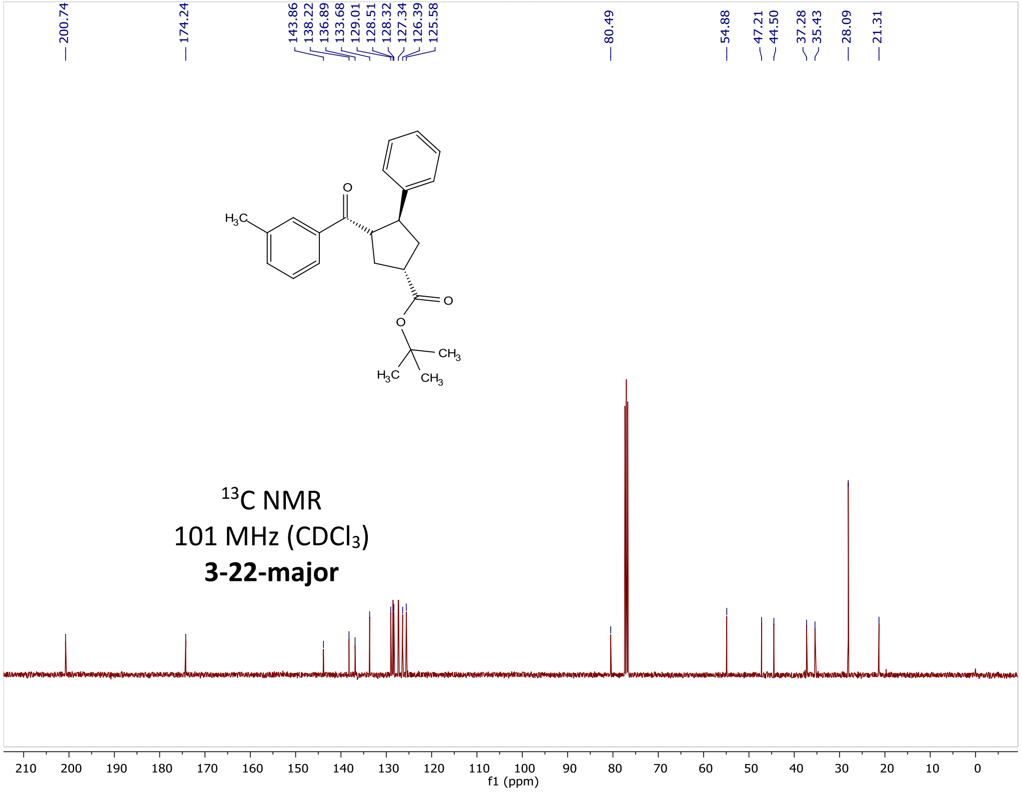
^{1}H NMR
400 MHz ($CDCl_3$)
3-21-minor



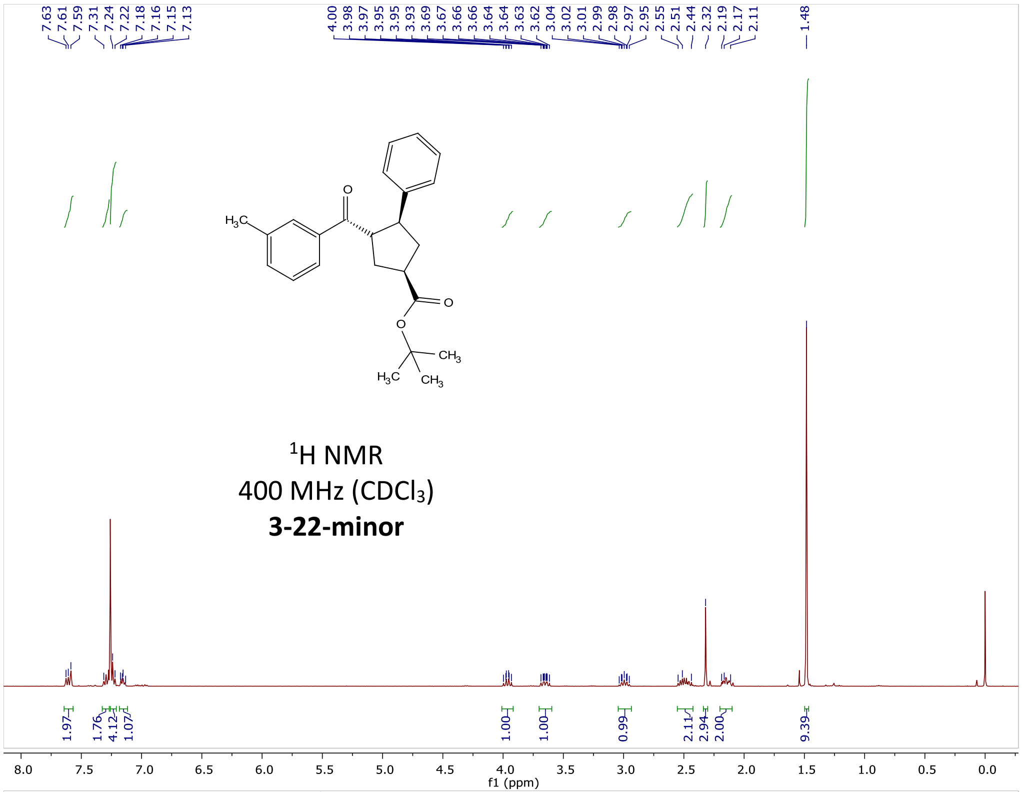
^{13}C NMR
101 MHz ($CDCl_3$)
3-21-minor



^{1}H NMR
400 MHz (CDCl$_3$)
3-22-major



^{13}C NMR
101 MHz (CDCl$_3$)
3-22-major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7.59
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7.24
7.22
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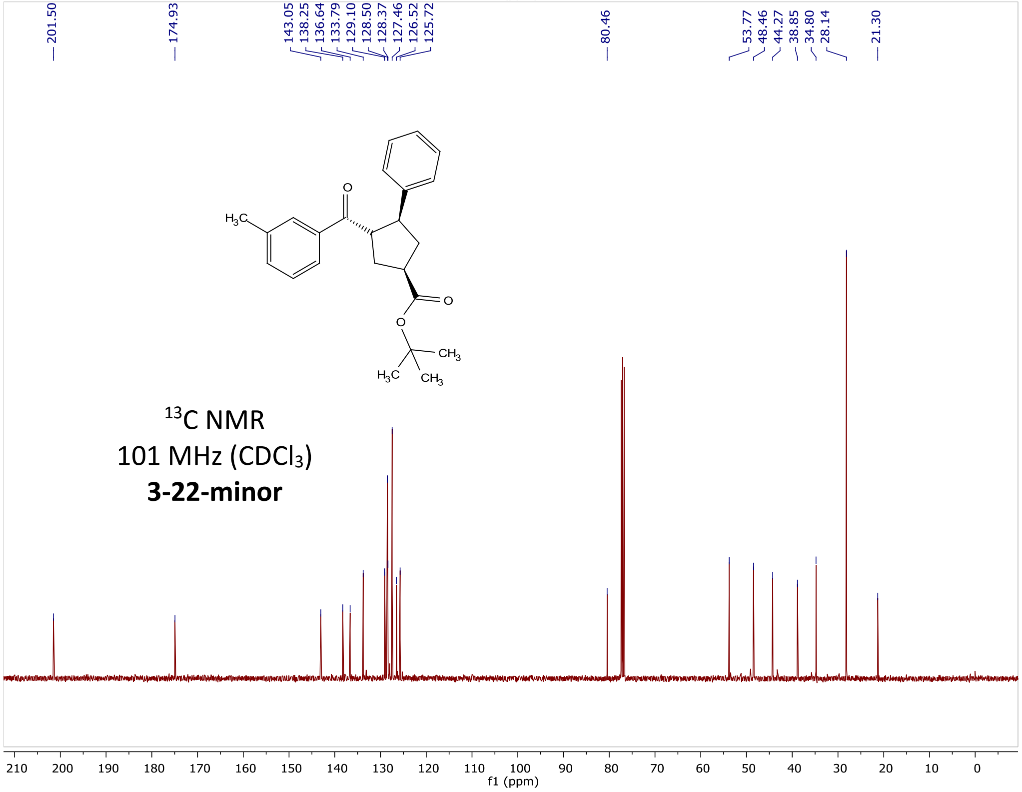
7.16
7.15
7.13
4.00
3.98
3.97
3.95
3.95
3.93
3.69
3.67
3.66
3.66
3.64
3.64
3.63
3.62
3.04
3.02
3.01
2.99
2.98
2.97
2.95
2.55
2.51
2.44
2.32
2.19
2.17
2.11
1.48
H3C
O
O
O
CH3
H3C
CH3
1H NMR
400 MHz (CDCl3)
3-22-minor
1.97
1.76
4.12
1.07
1.00
1.00
0.99
2.11
2.94
2.00
9.39
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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138.25
136.64
133.79
129.10
128.50
128.37
127.46
126.52
125.72
80.46
53.77
48.46
44.27
38.85
34.80
28.14
21.30
H3C
O
O
O
CH3
H3C
CH3
13C NMR
101 MHz (CDCl3)
3-22-minor
210
200
190
180
170
160
150
140
130
120
110
100
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80
70
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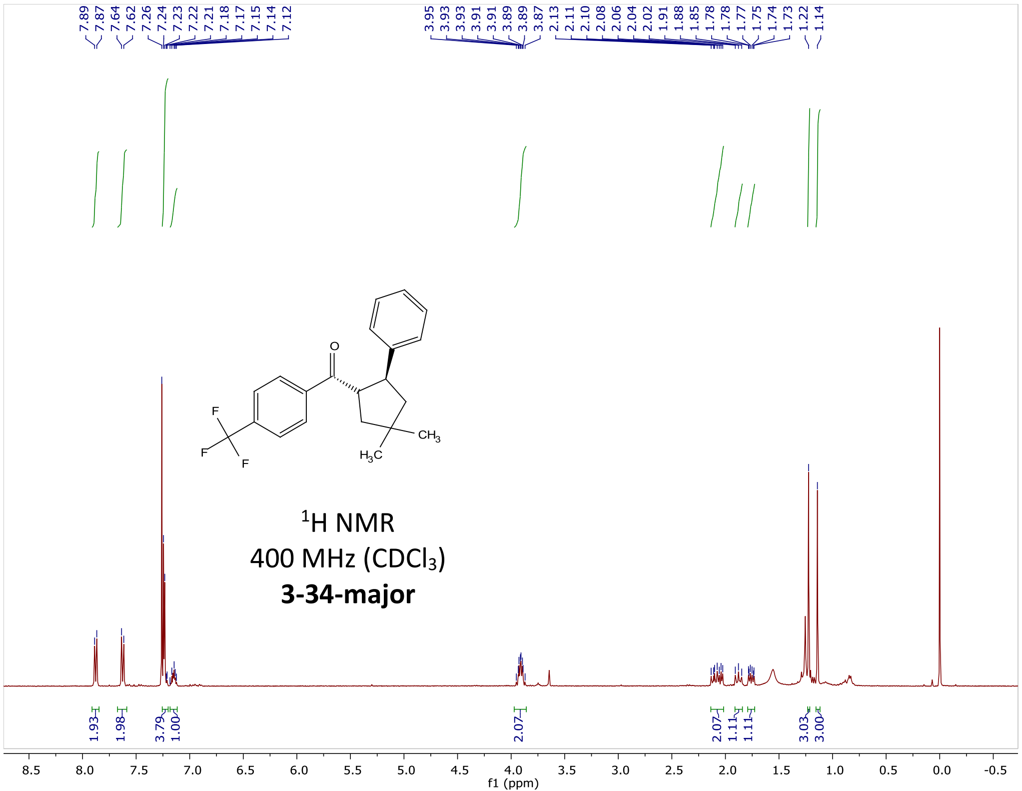
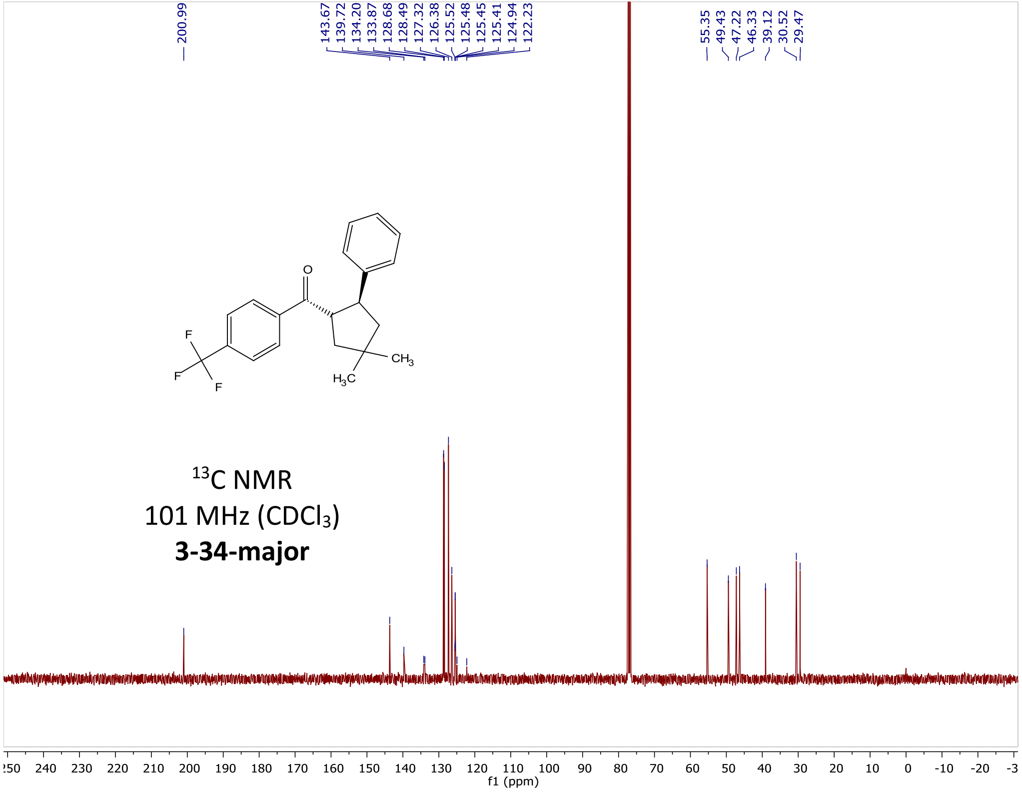
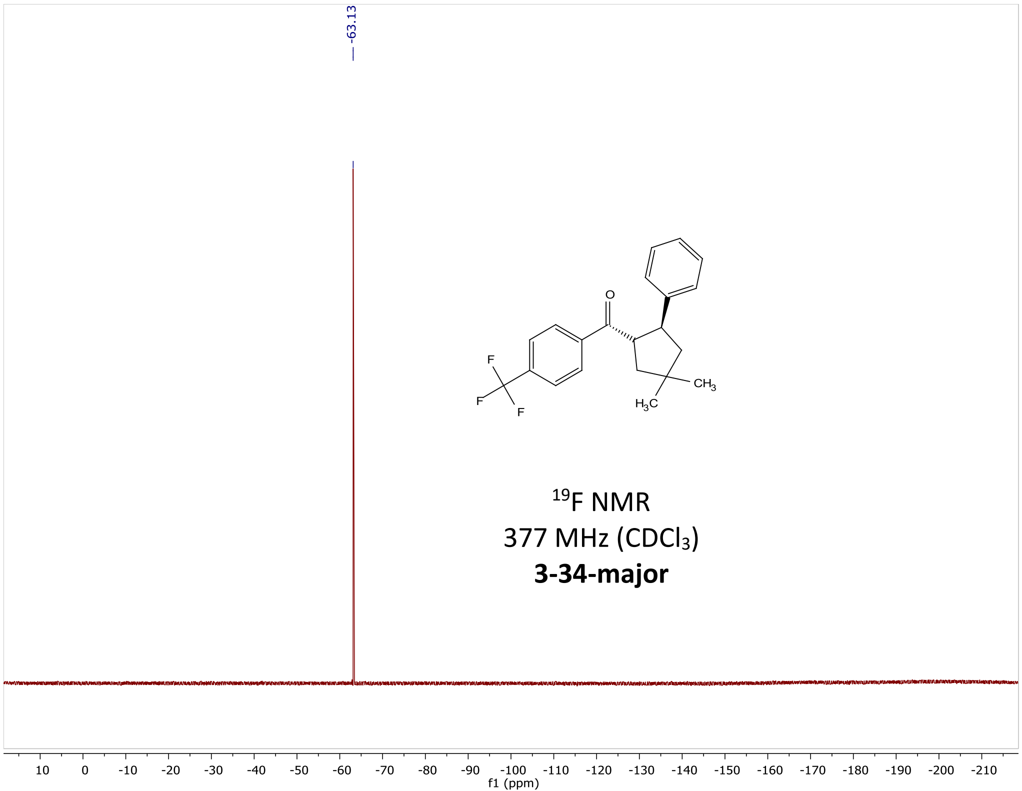
30
20
10
0
f1 (ppm)



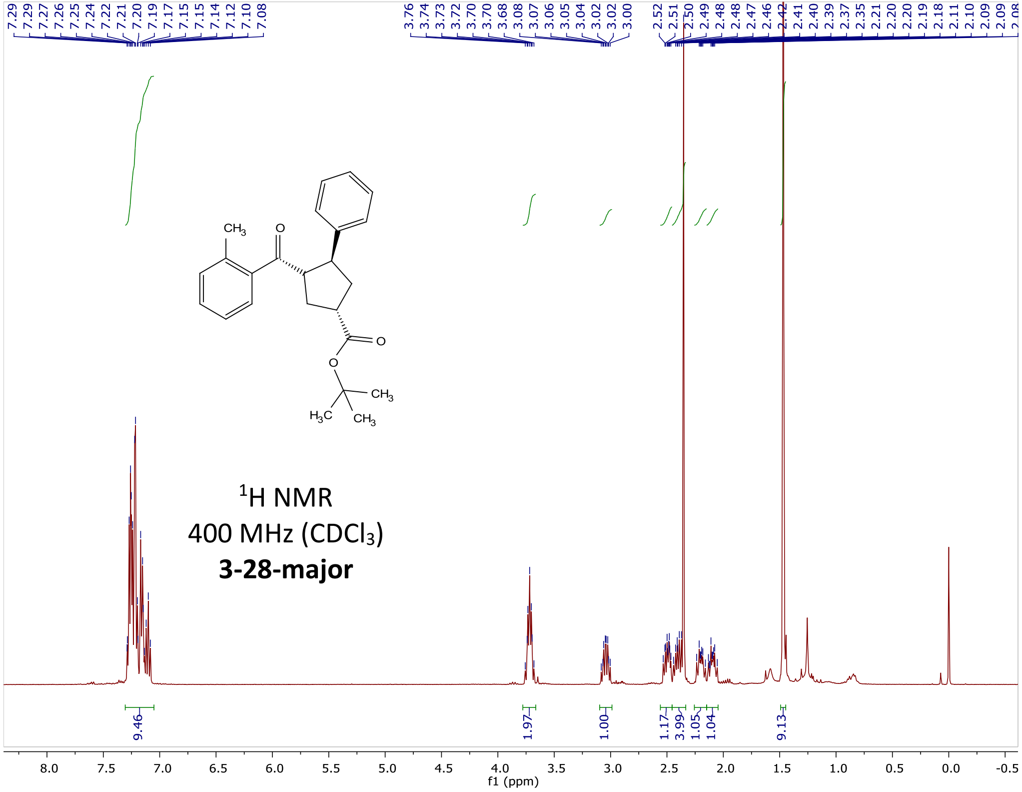
^{1}H NMR
400 MHz (CDCl$_3$)
3-34-major



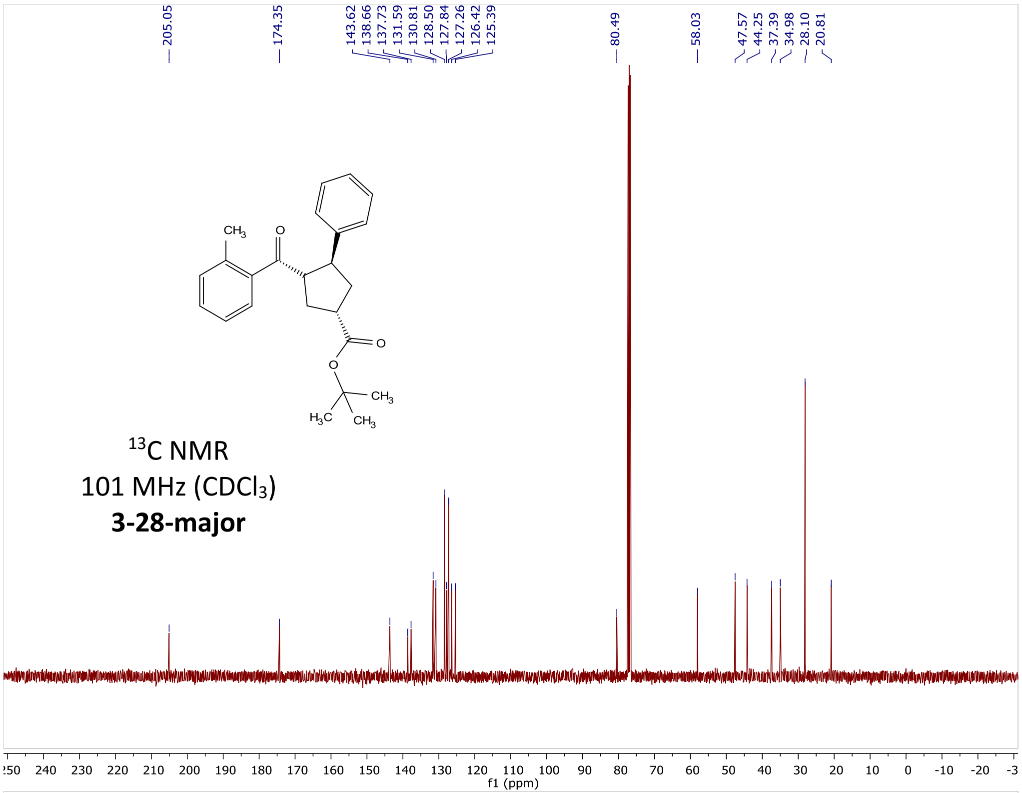
^{13}C NMR
101 MHz (CDCl$_3$)
3-34-major



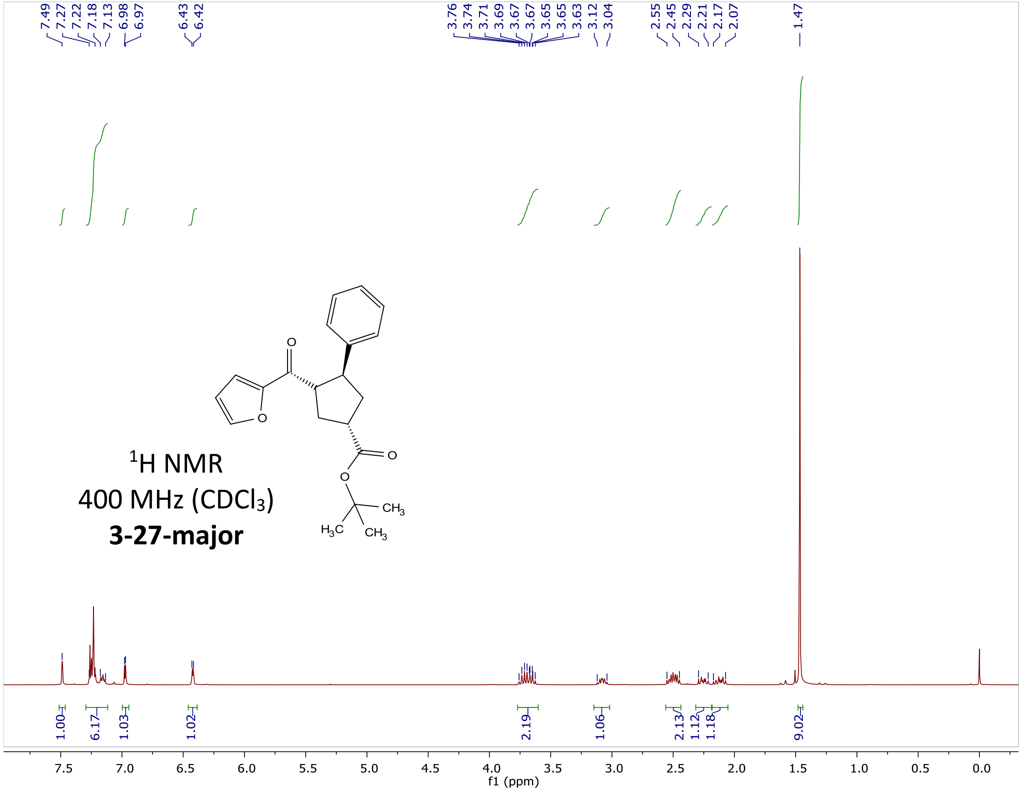
^{19}F NMR
377 MHz (CDCl$_3$)
3-34-major



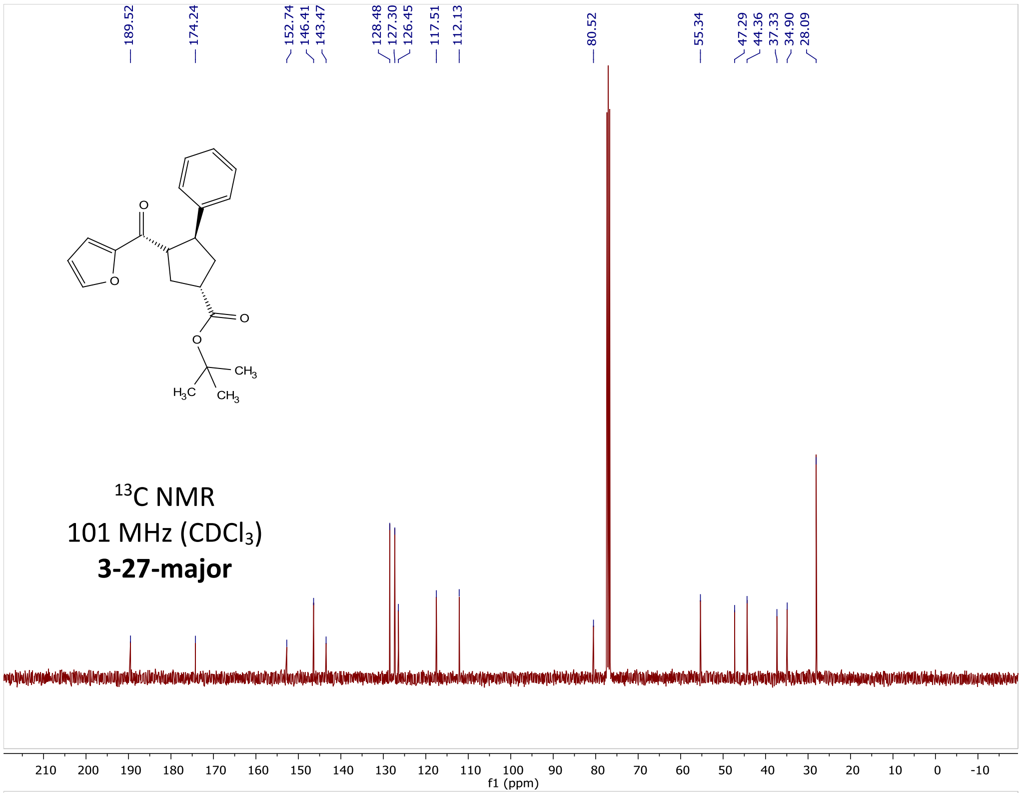
^{1}H NMR
400 MHz (CDCl$_3$)
3-28-major



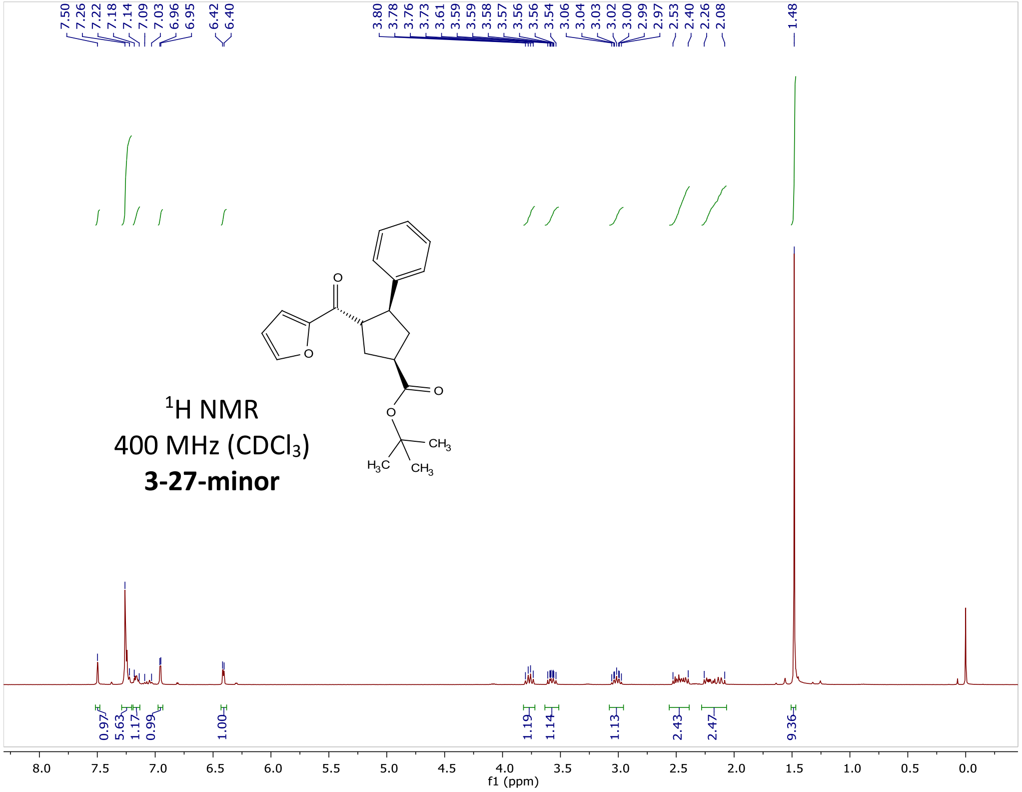
^{13}C NMR
101 MHz (CDCl$_3$)
3-28-major



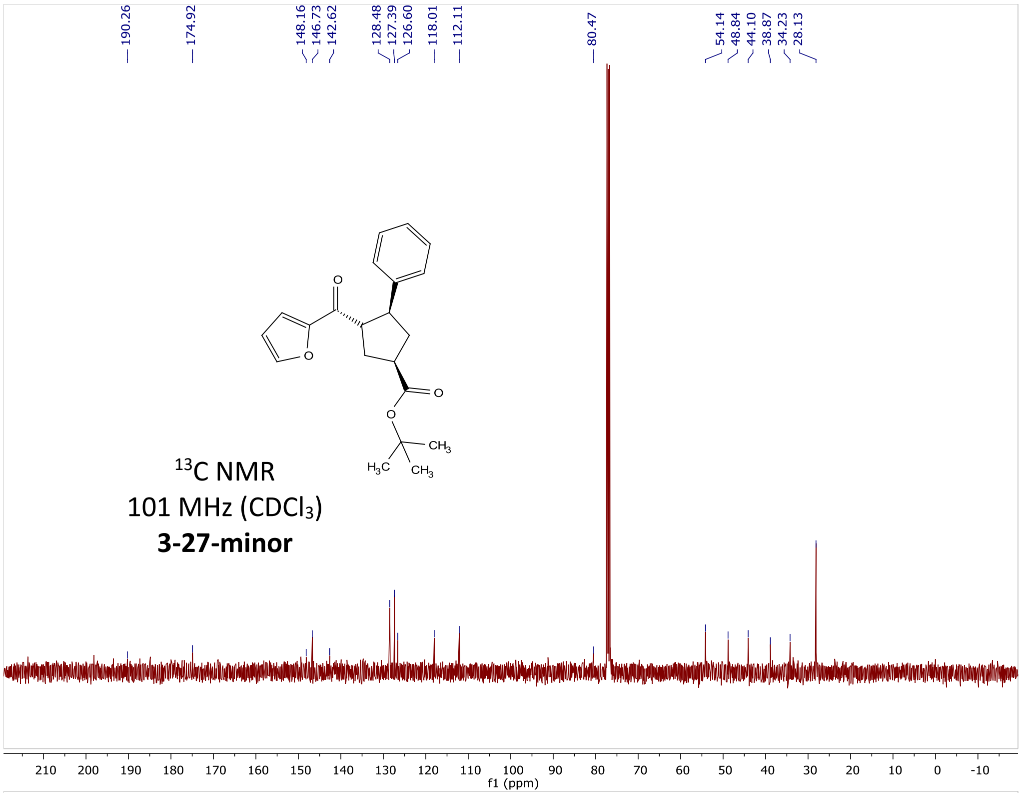
^{1}H NMR
400 MHz (CDCl$_3$)
3-27-major



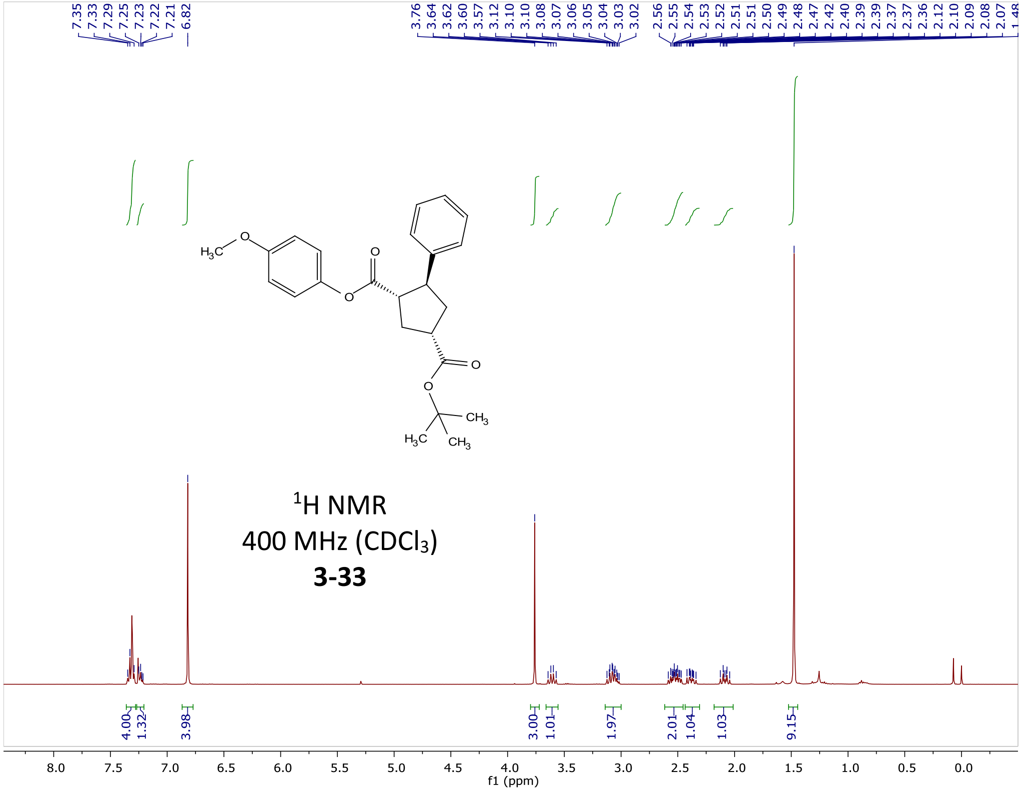
^{13}C NMR
101 MHz ($CDCl_3$)
3-27-major



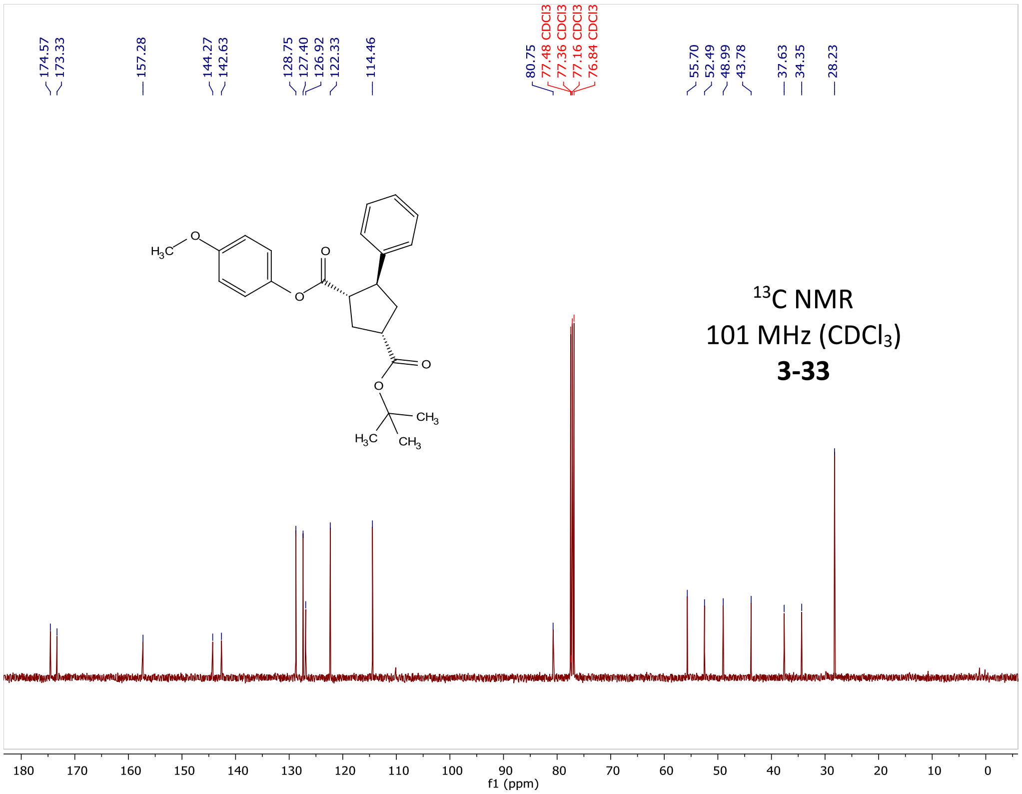
^{1}H NMR
400 MHz ($CDCl_3$)
3-27-minor



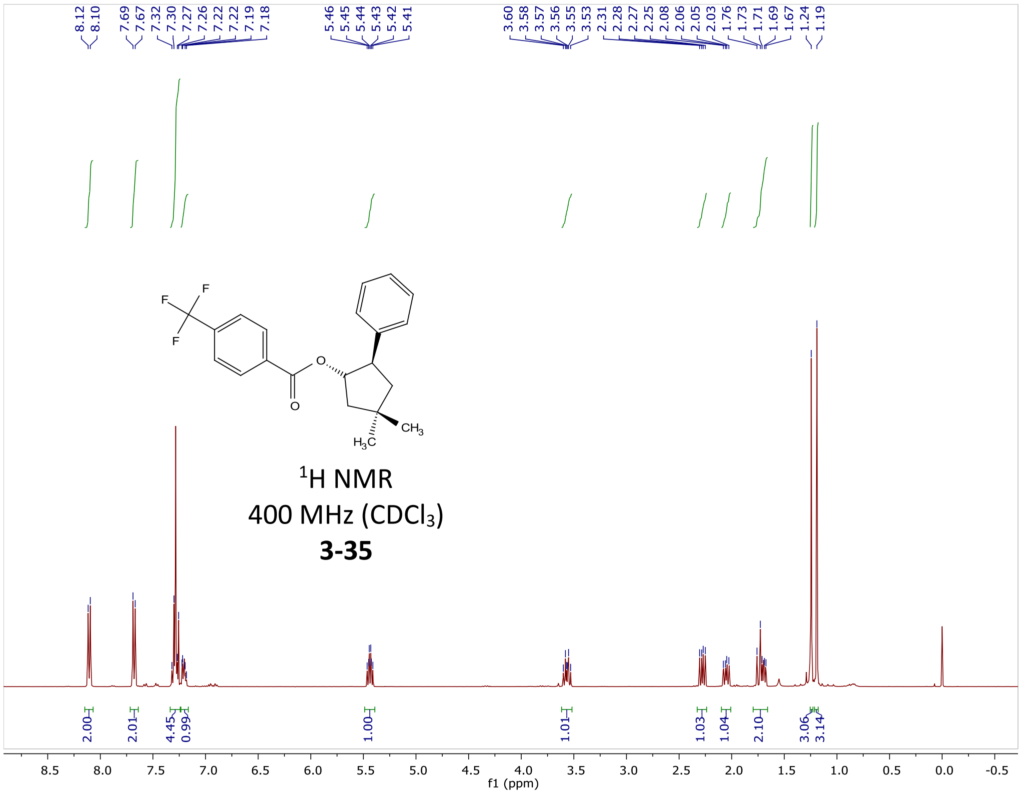
^{13}C NMR
101 MHz ($CDCl_3$)
3-27-minor



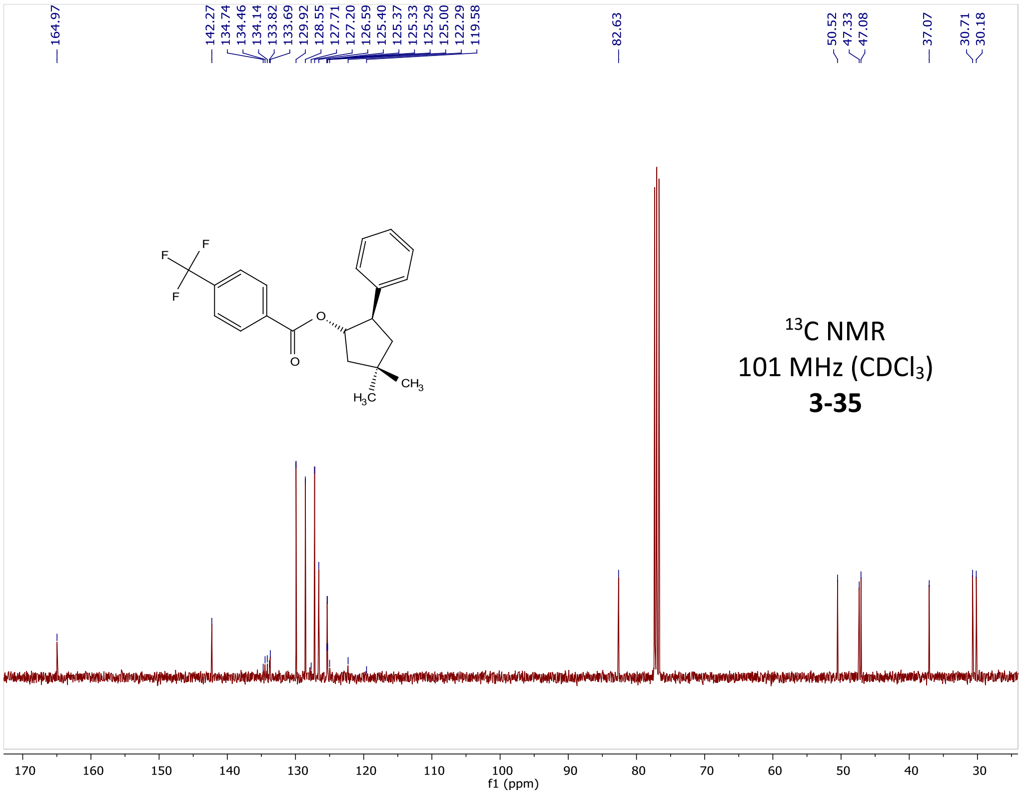
^{1}H NMR
400 MHz ($CDCl_3$)
3-33



^{13}C NMR
101 MHz (CDCl$_3$)
3-33



^{1}H NMR
400 MHz (CDCl$_3$)
3-35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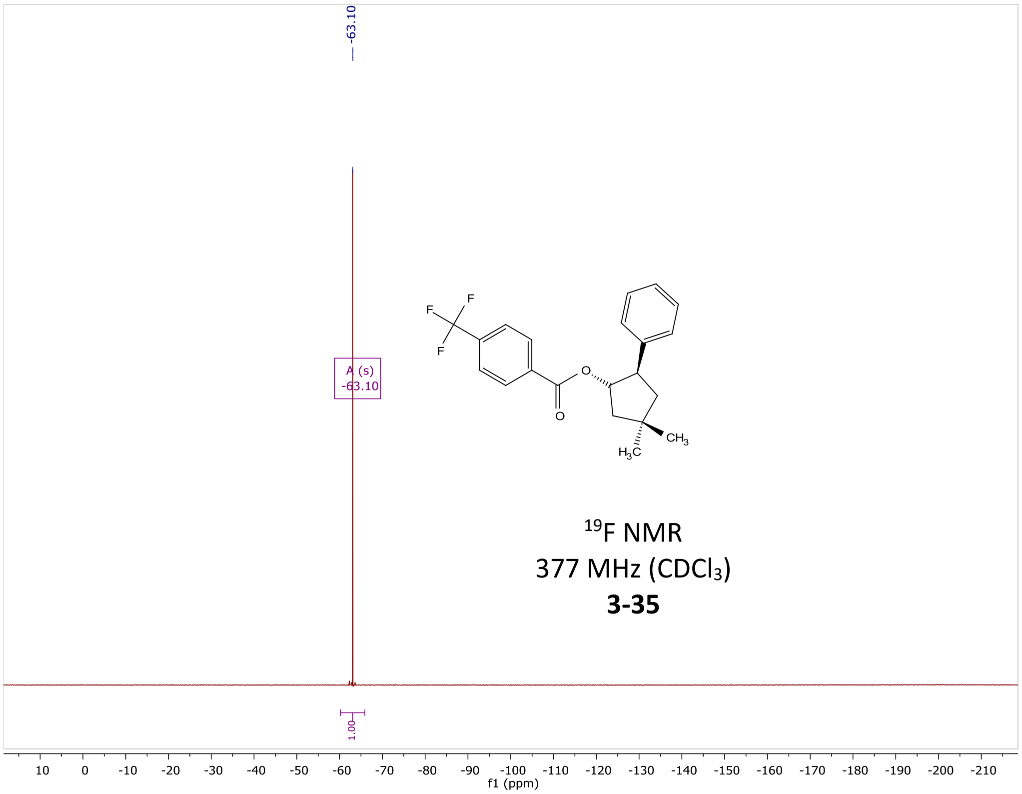
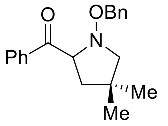
142.27
134.74
134.46
134.14
133.82
133.69
129.92
128.55
127.71
127.20
126.59
125.40
125.37
125.33
125.29
125.00
122.29
119.58
82.63
50.52
47.33
47.08
37.07
30.71
30.18
F
F
F
O
O
CH3
H3C
13C NMR
101 MHz (CDCl3)
3-35
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)


-63.10
A (s)
-63.10
1.00
F
F
F
O
O
CH3
H3C
19F NMR
377 MHz (CDCl3)
3-35
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

A-3. List of New Compounds from Chapter 4



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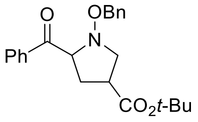

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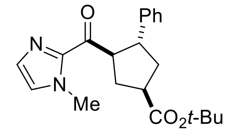

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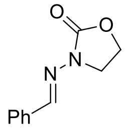

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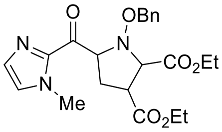

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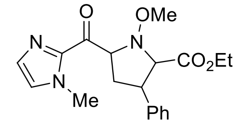

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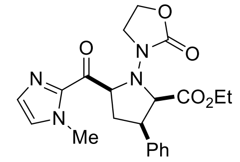

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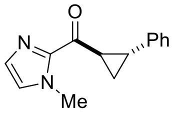

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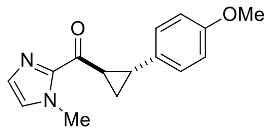

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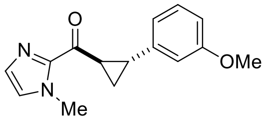

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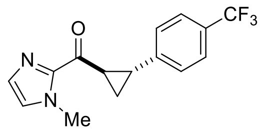

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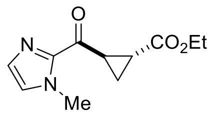

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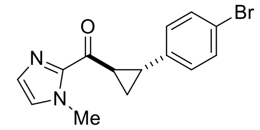

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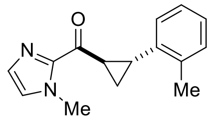

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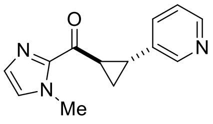

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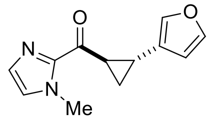

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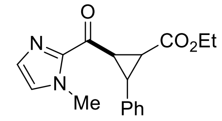

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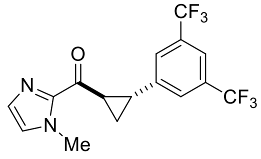

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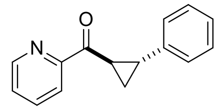

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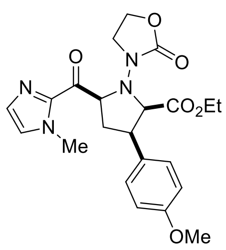

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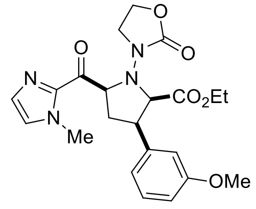

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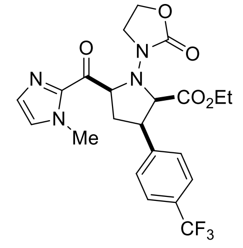

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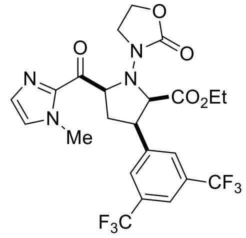

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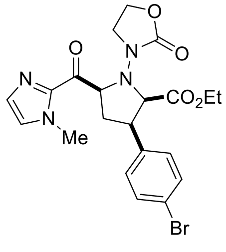

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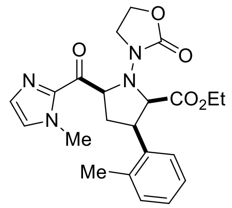

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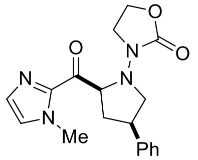

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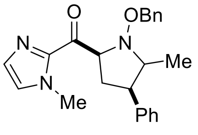

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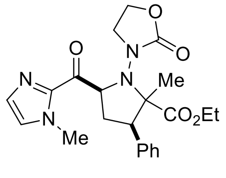

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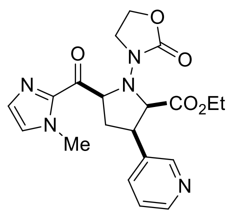

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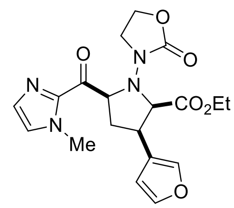

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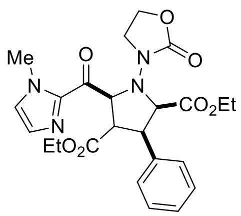

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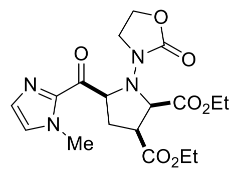

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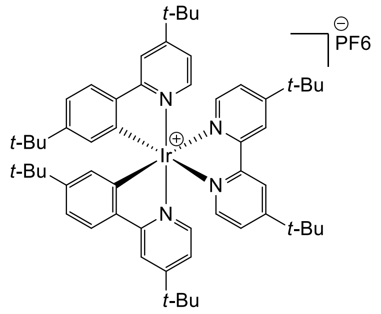

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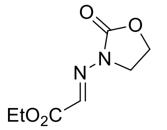

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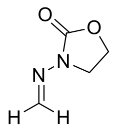

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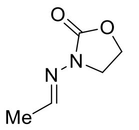

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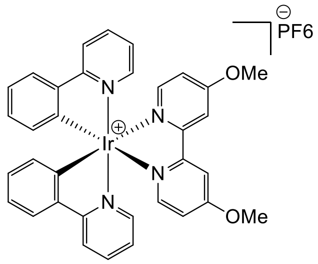

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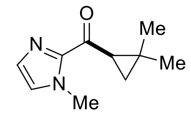

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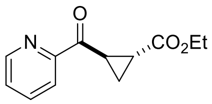

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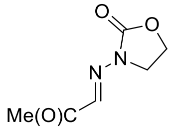

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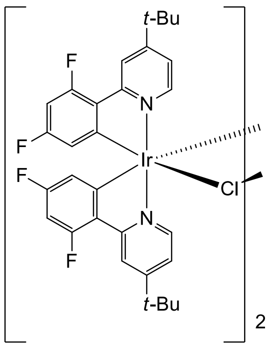

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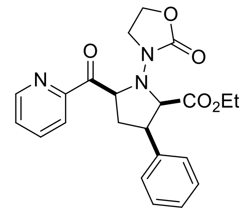

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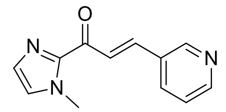

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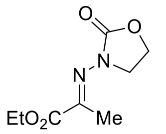

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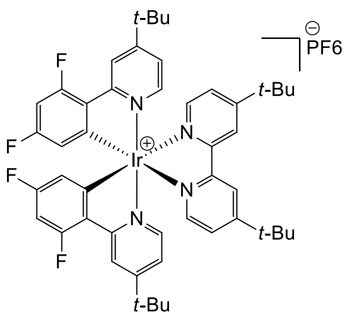
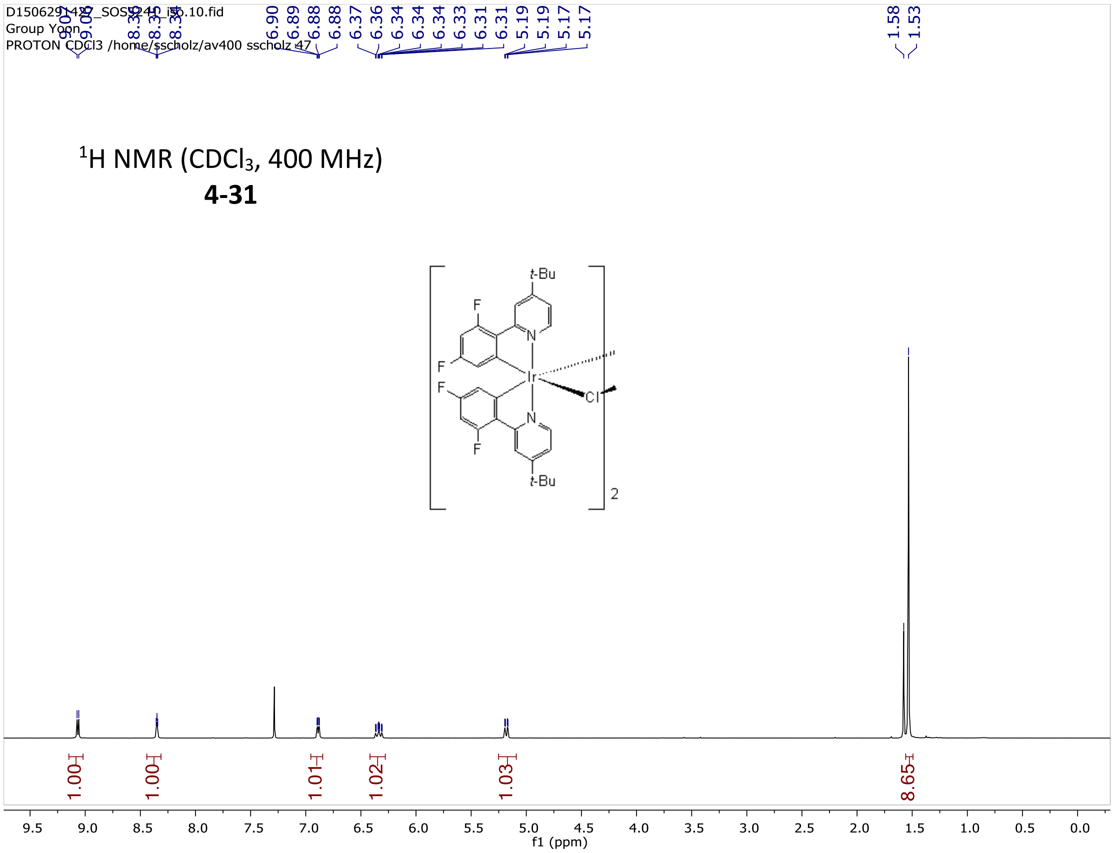
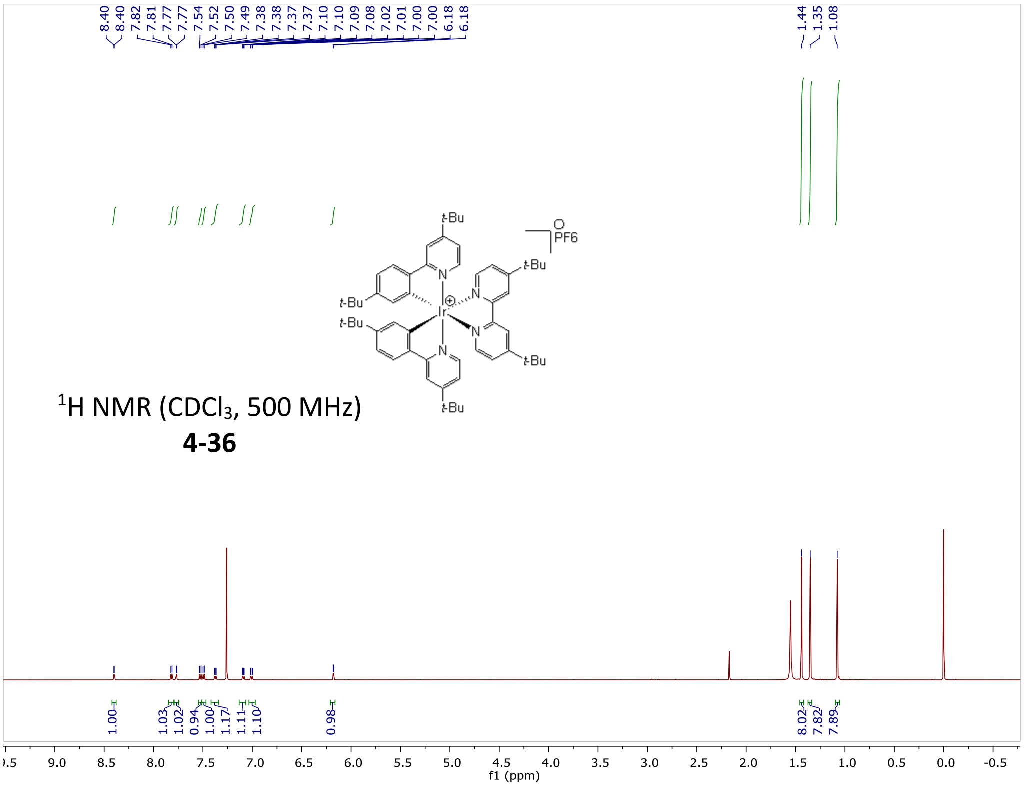


4-34



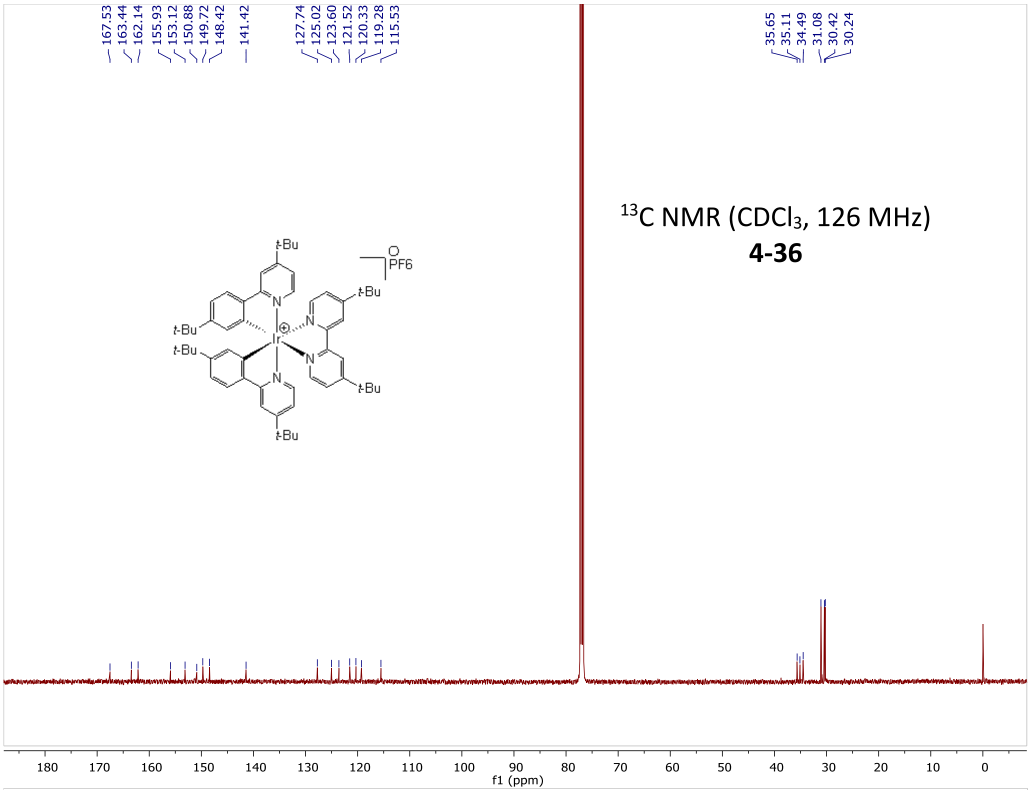
^{1}H NMR (CDCl$_3$, 400 MHz)

4-31



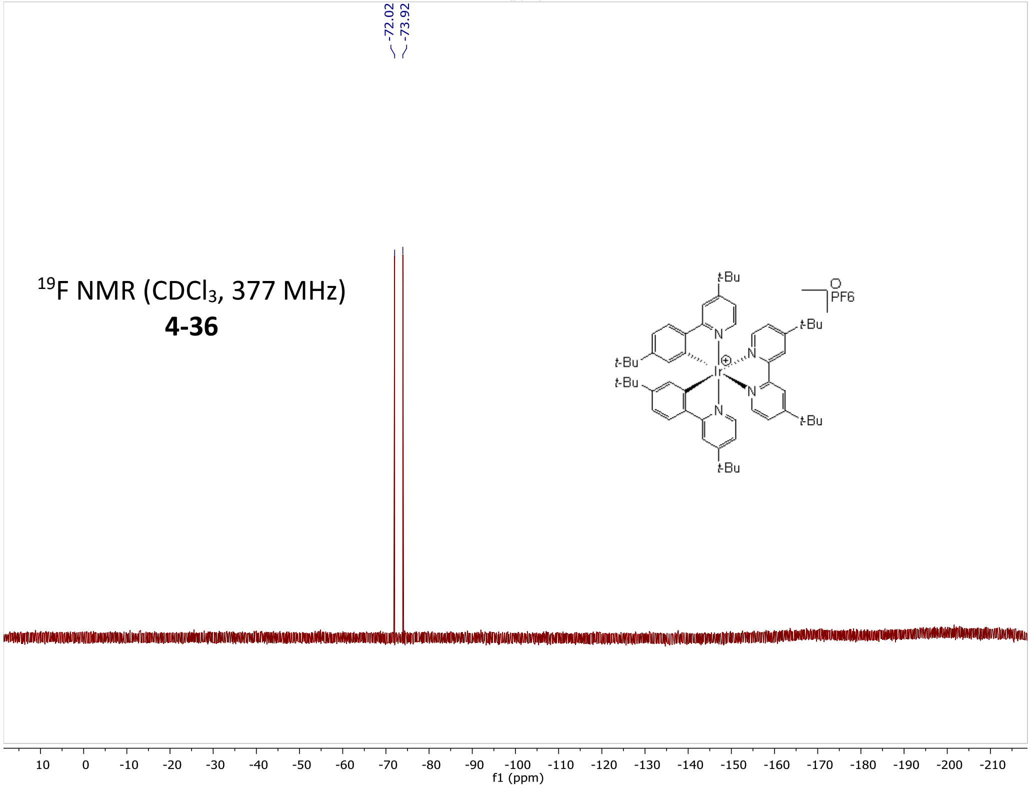
^{1}H NMR (CDCl$_3$, 500 MHz)

4-36



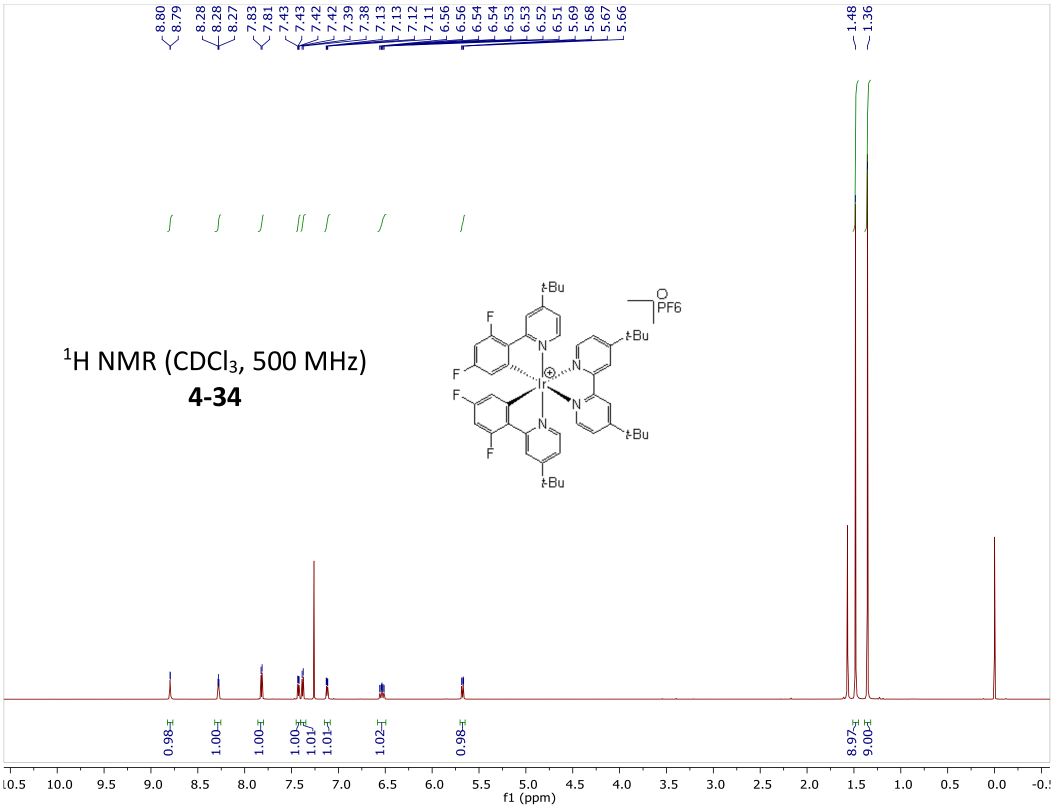
^{13}C NMR (CDCl$_3$, 126 MHz)

4-36



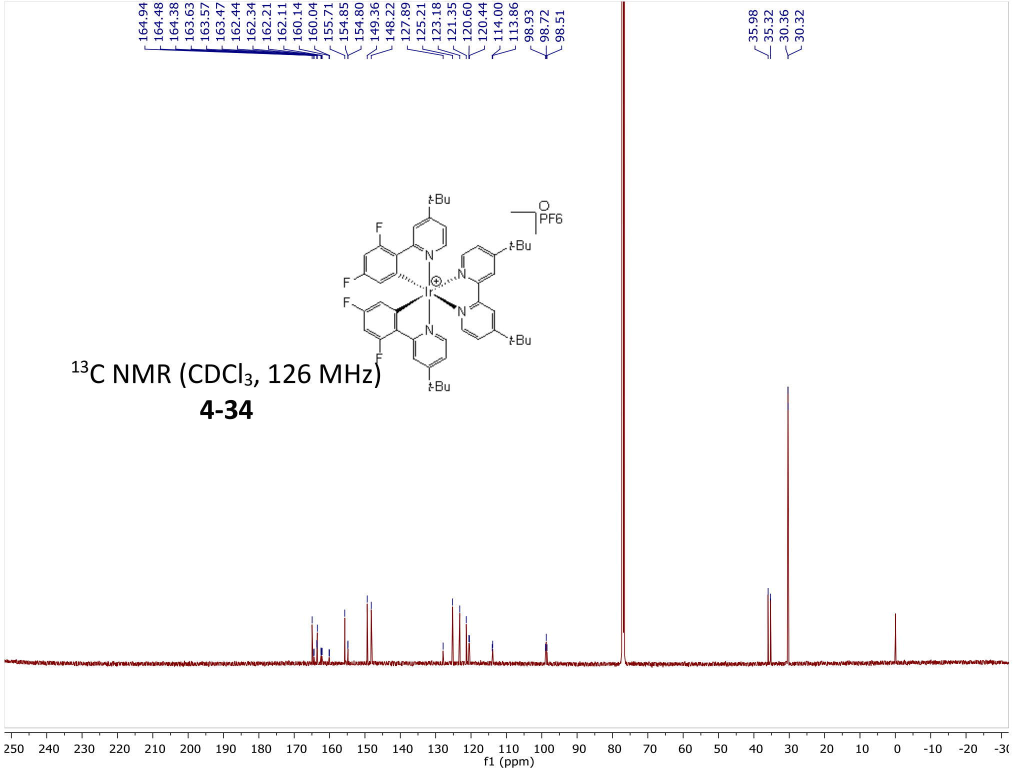
^{19}F NMR (CDCl$_3$, 377 MHz)

4-36



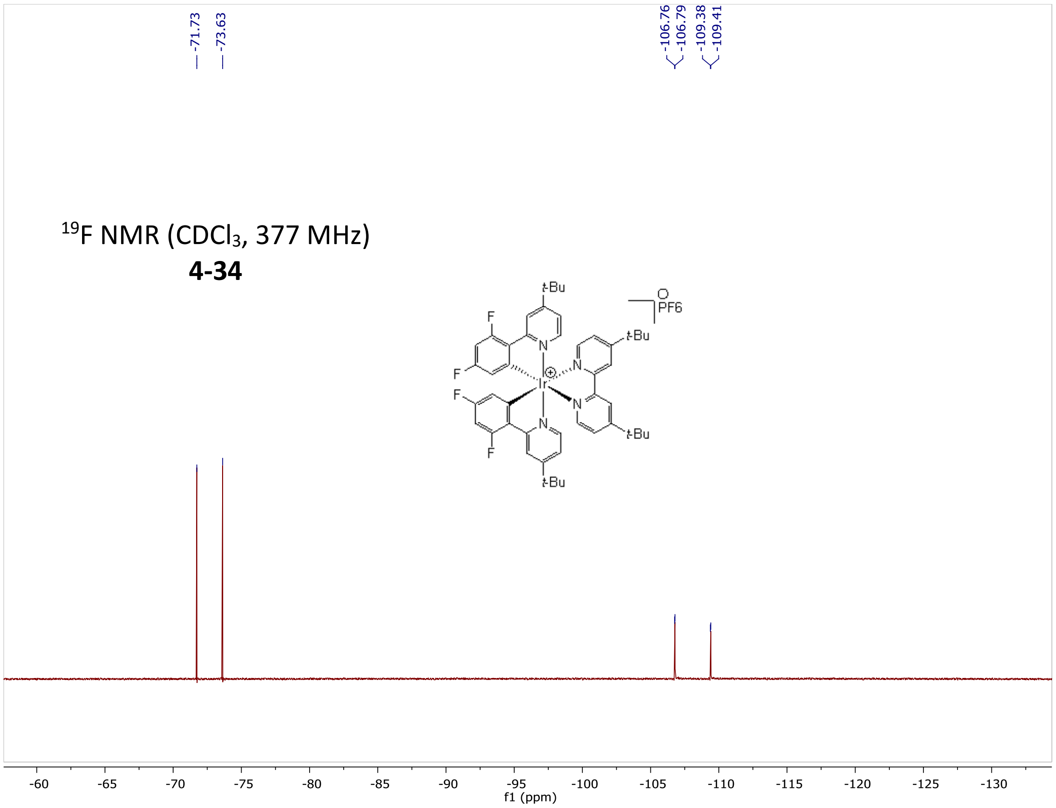
^{1}H NMR (CDCl$_3$, 500 MHz)

4-34



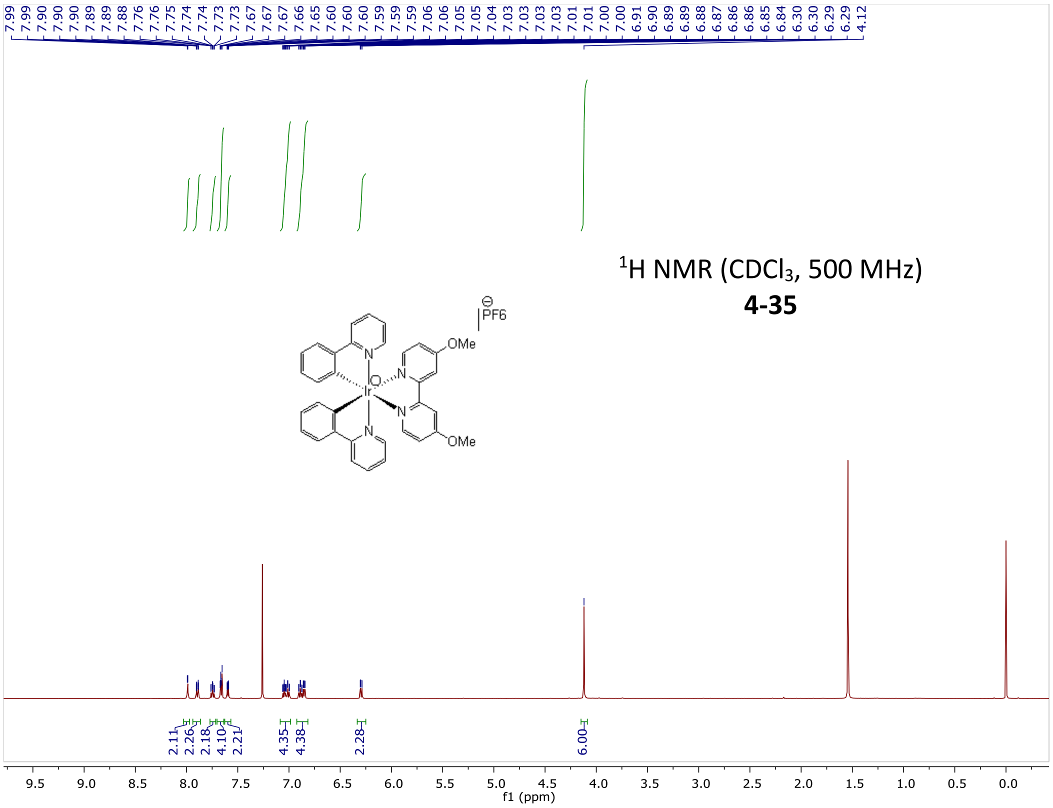
^{13}C NMR (CDCl$_3$, 126 MHz)

4-34



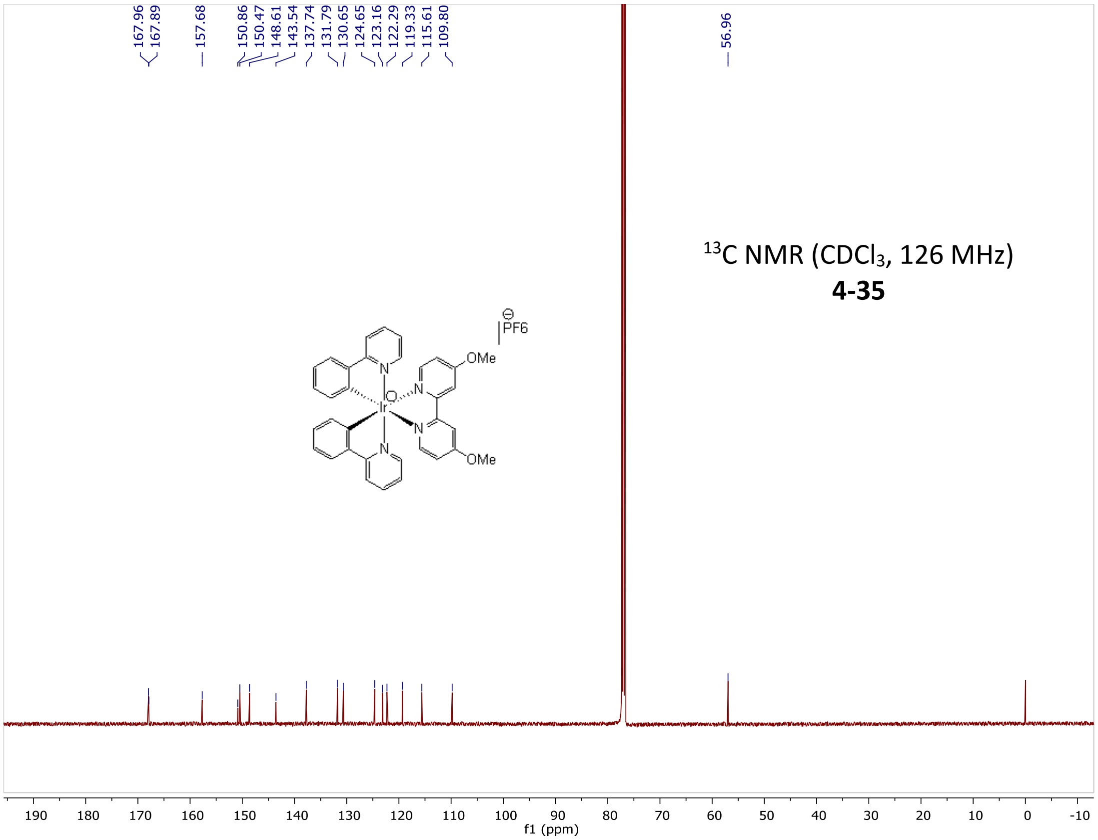
^{19}F NMR (CDCl$_3$, 377 MHz)

4-34



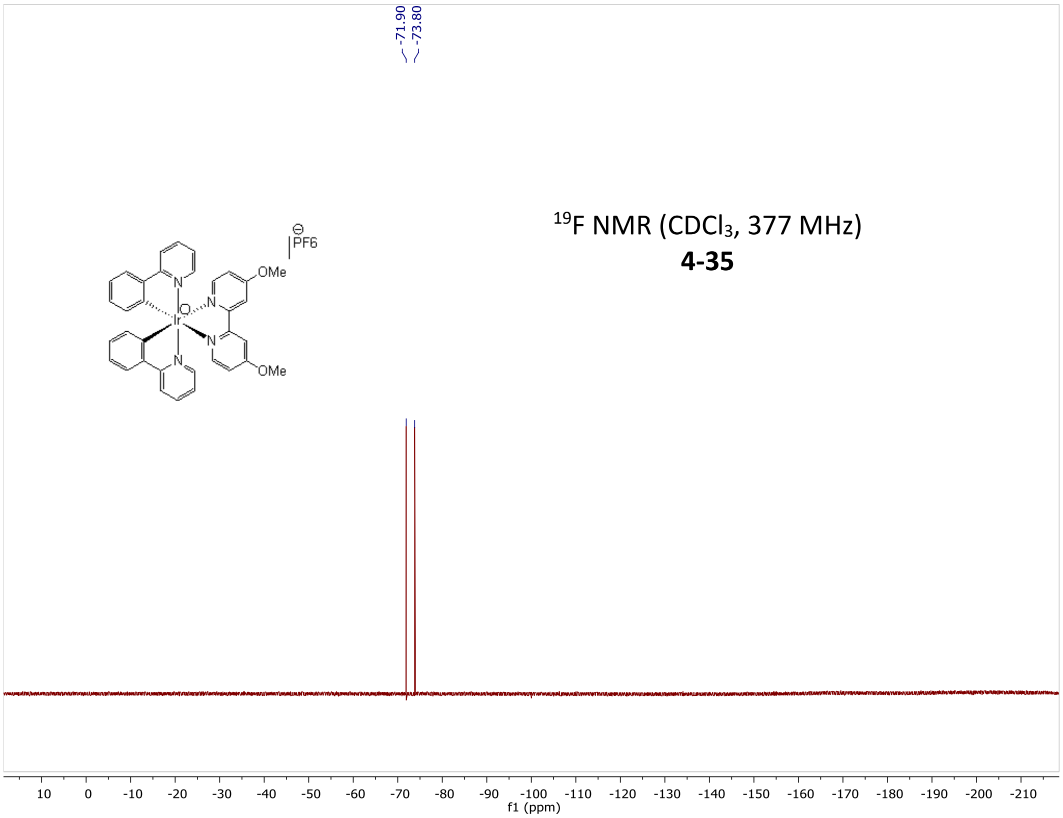
^{1}H NMR (CDCl$_3$, 500 MHz)

4-35



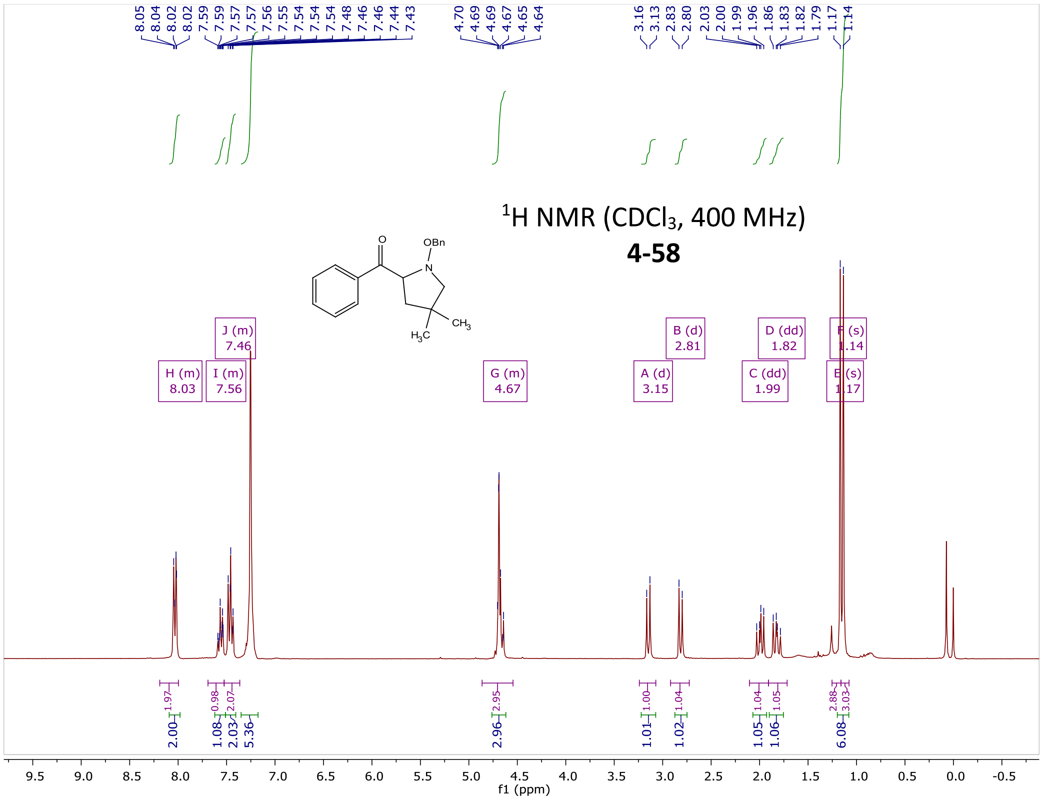
^{13}C NMR (CDCl$_3$, 126 MHz)

4-35



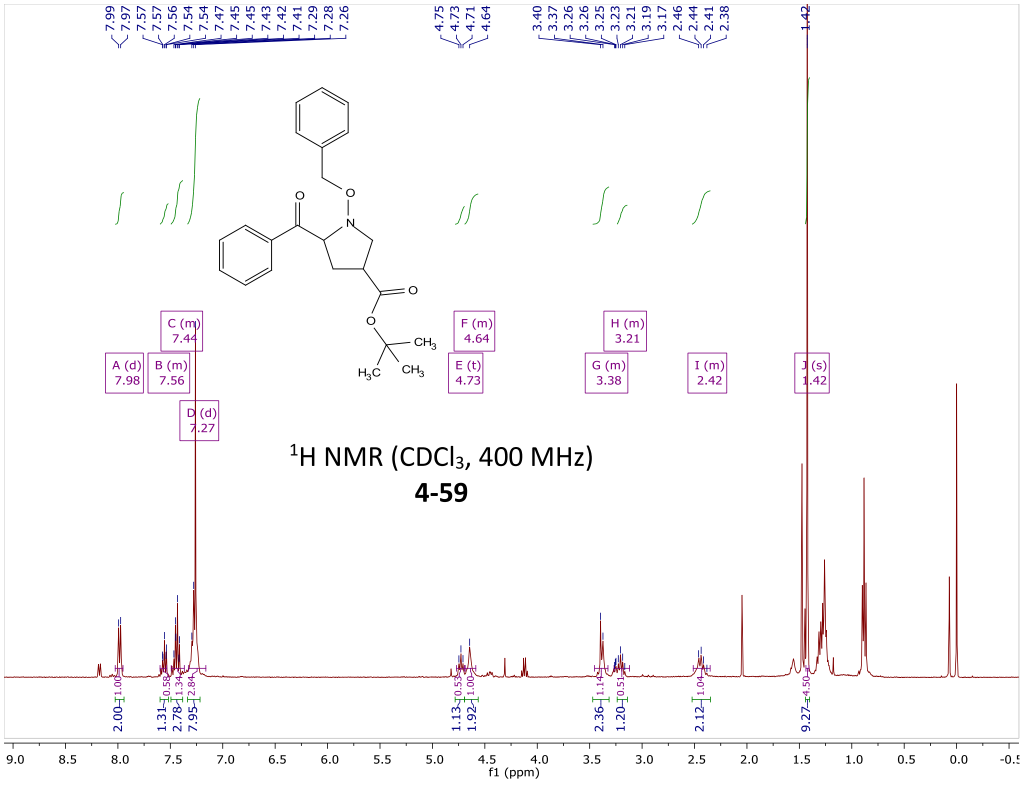
^{19}F NMR (CDCl$_3$, 377 MHz)

4-35



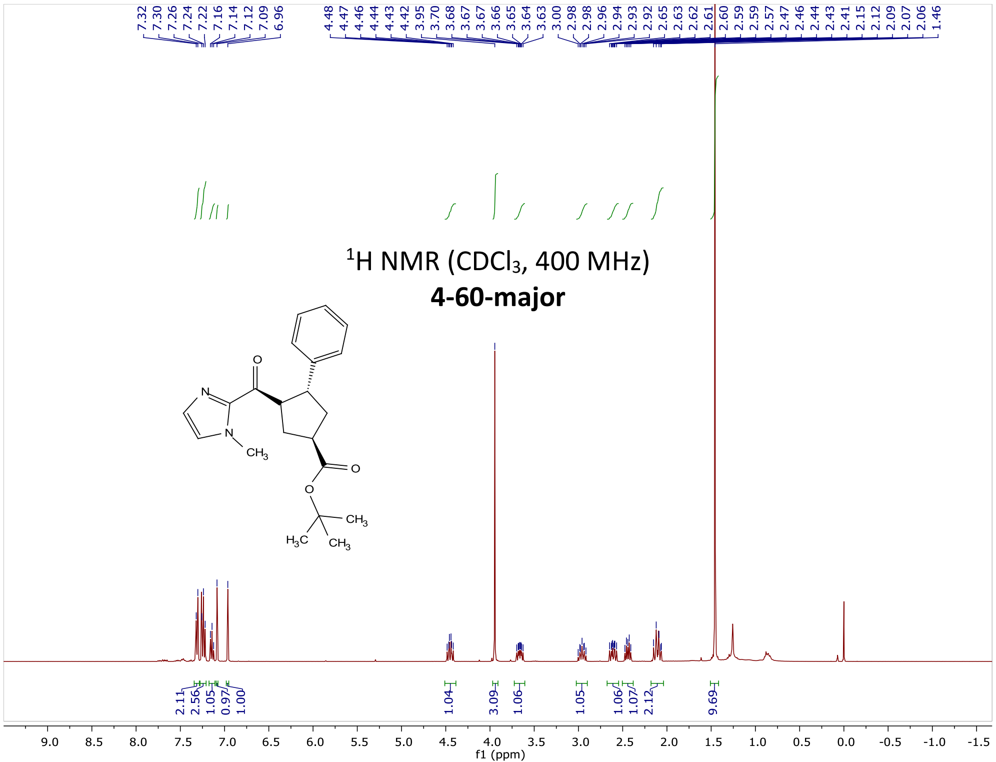
^{1}H NMR (CDCl$_3$, 400 MHz)

4-58



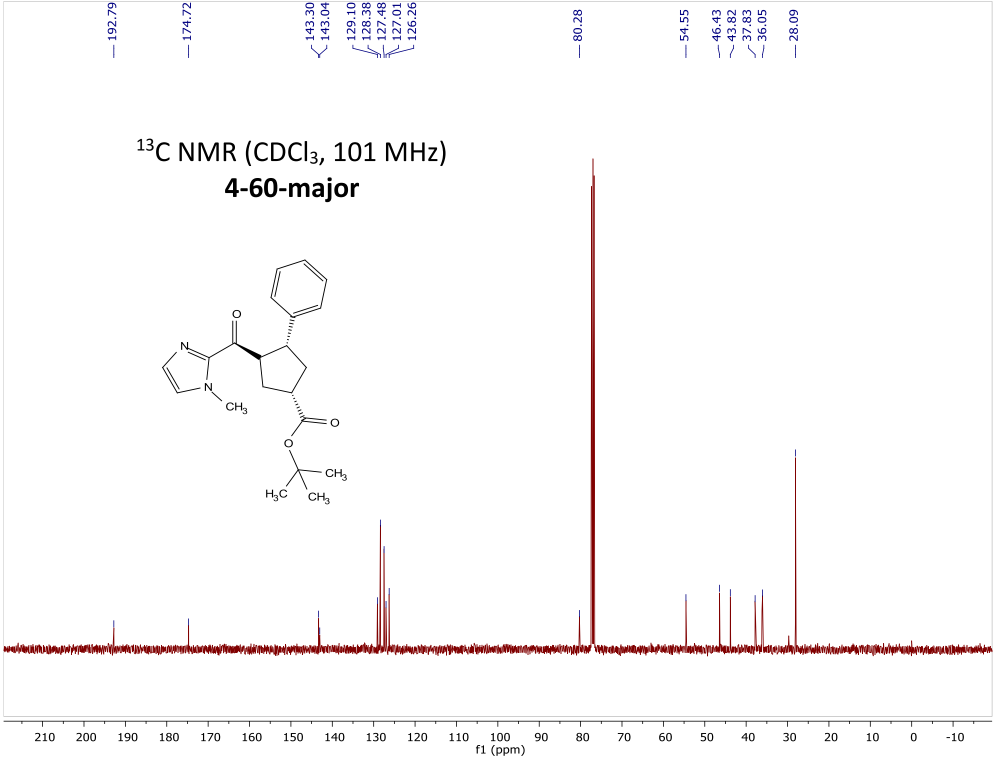
^{1}H NMR (CDCl$_3$, 400 MHz)

4-59



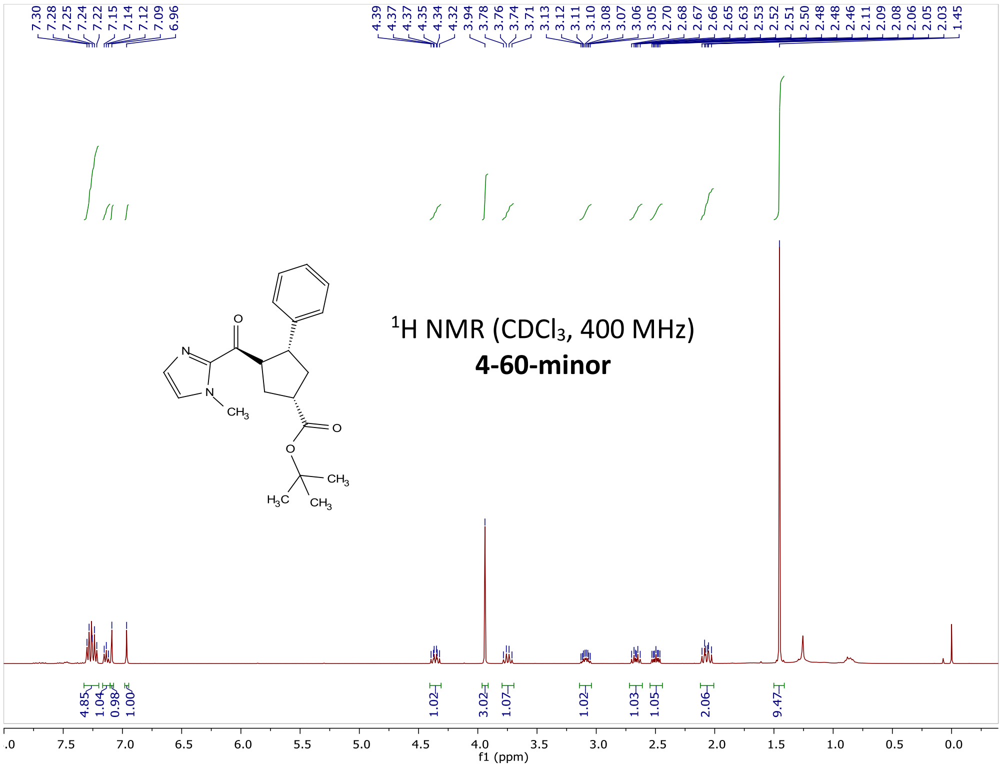
^{1}H NMR (CDCl$_3$, 400 MHz)

4-60-major



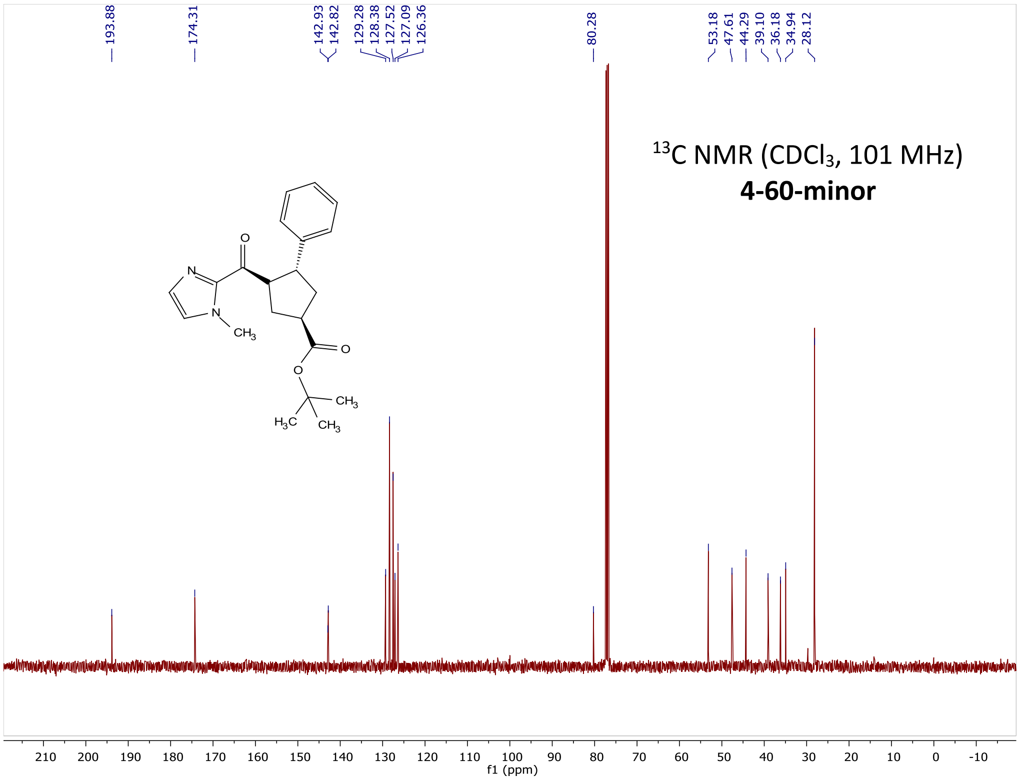
^{13}C NMR (CDCl$_3$, 101 MHz)

4-60-major



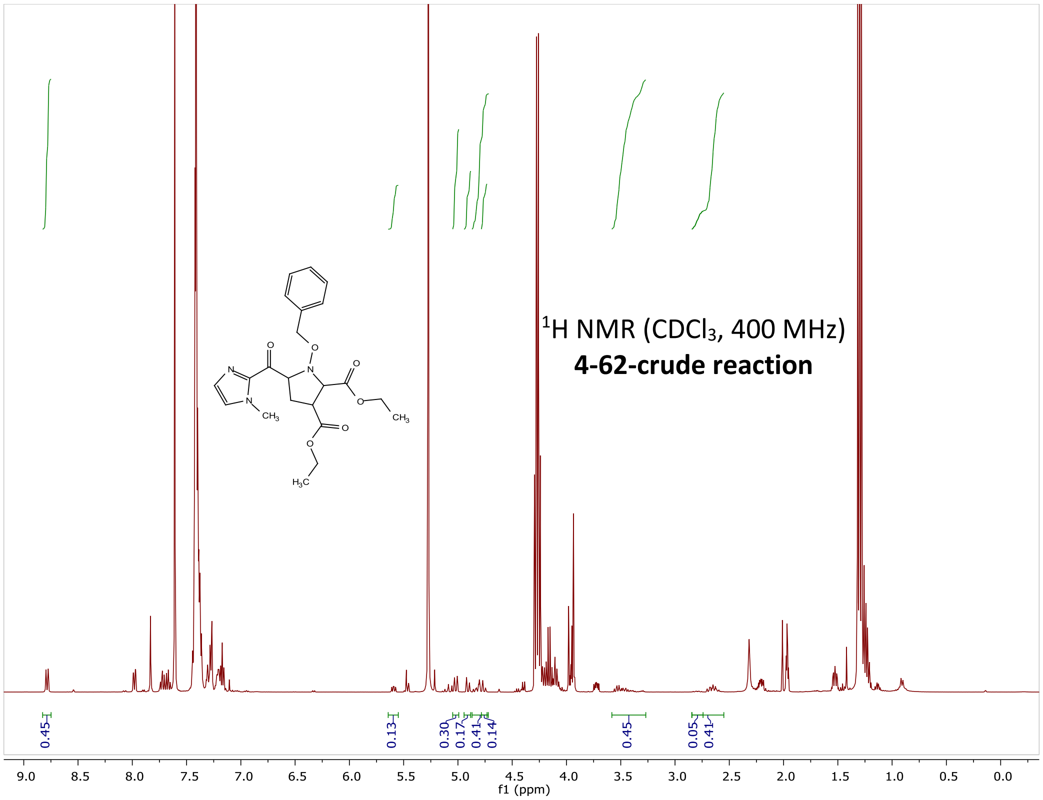
^{1}H NMR (CDCl$_3$, 400 MHz)

4-60-minor

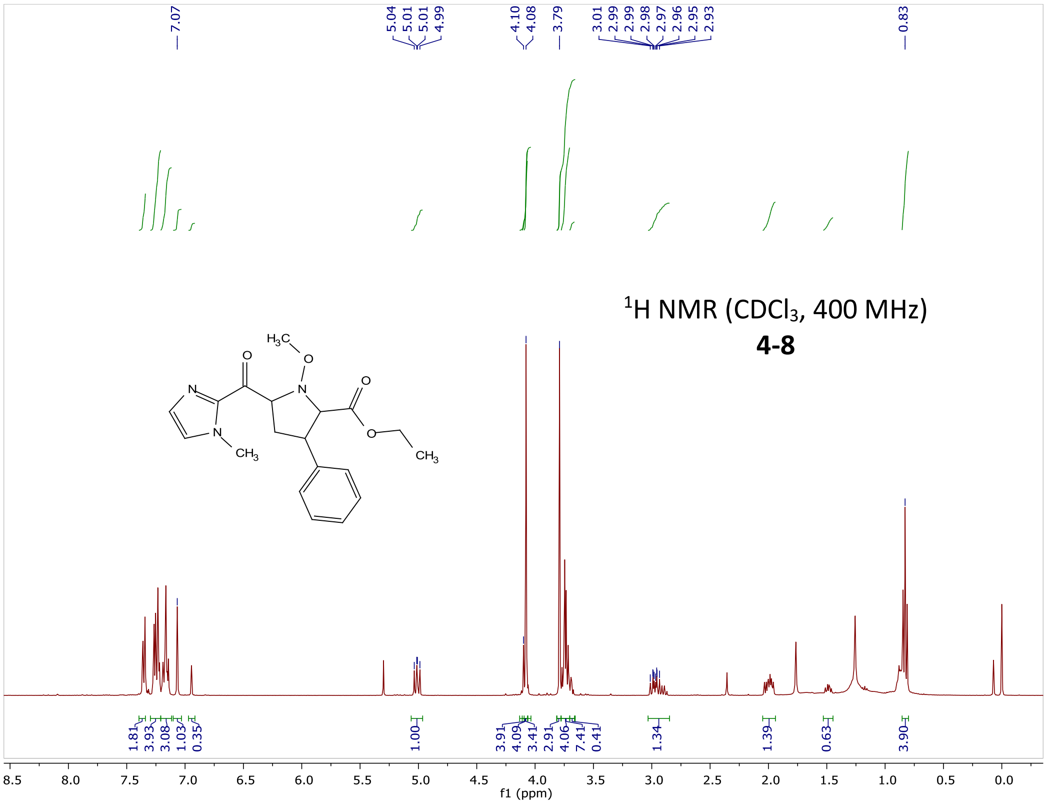


^{13}C NMR (CDCl$_3$, 101 MHz)

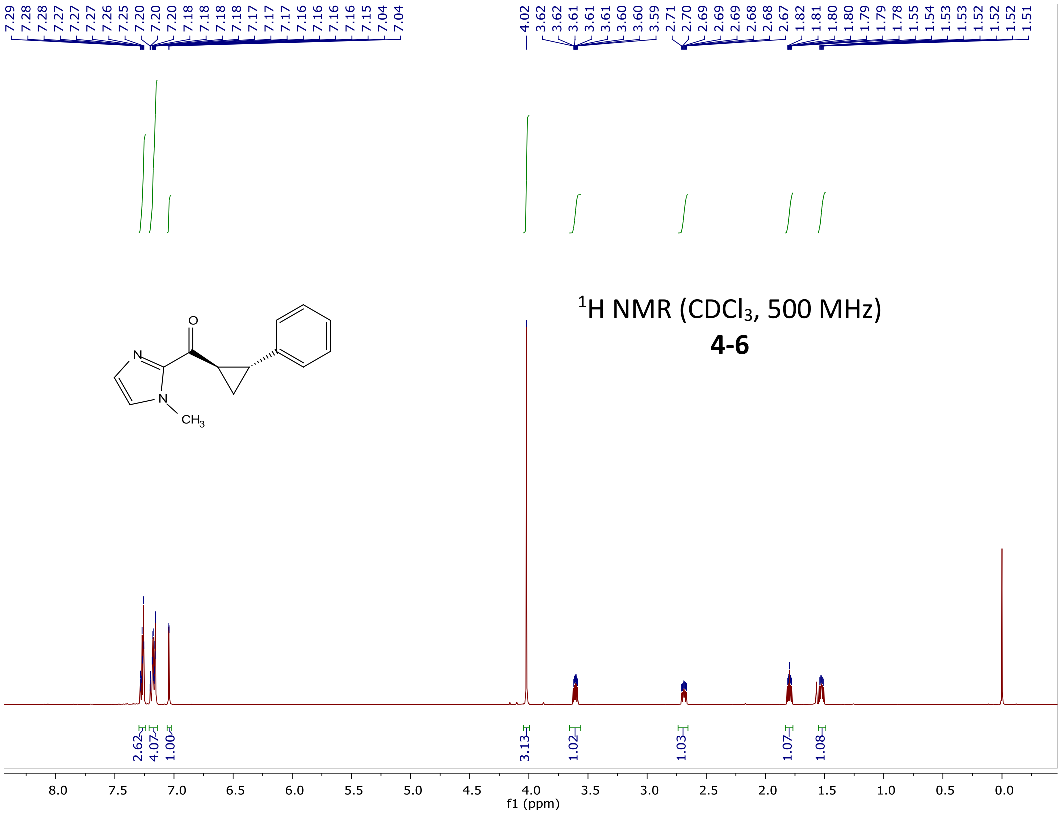
4-60-minor

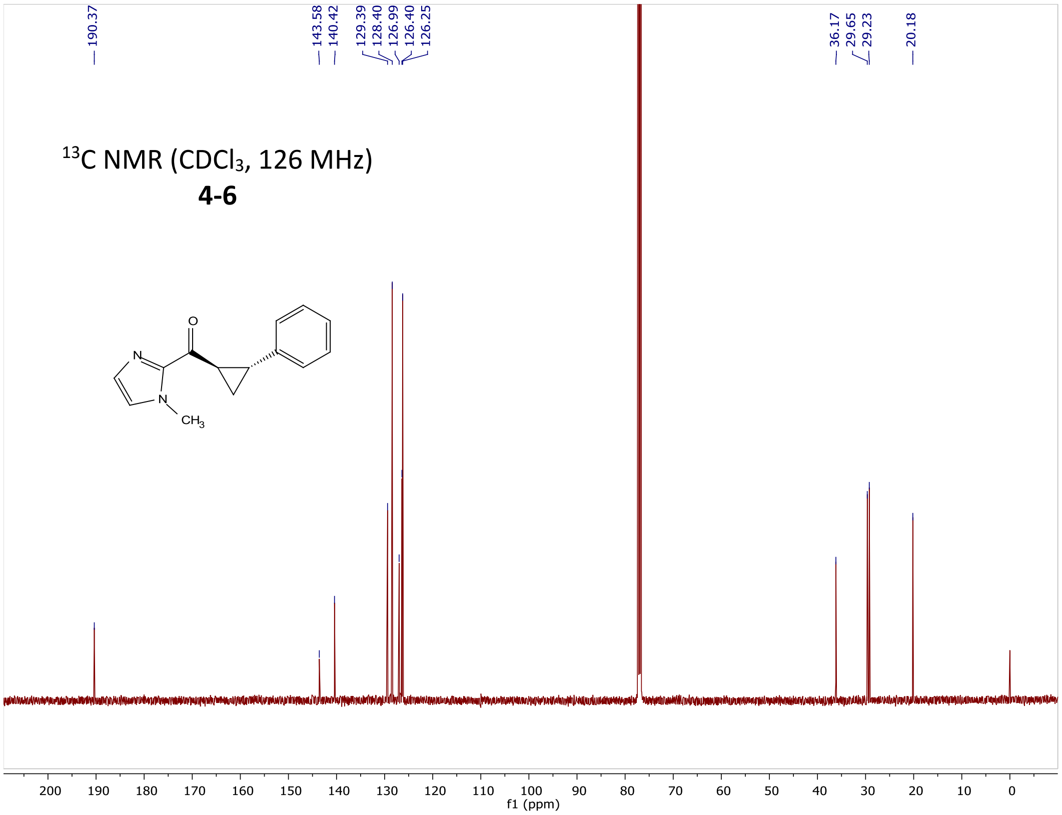


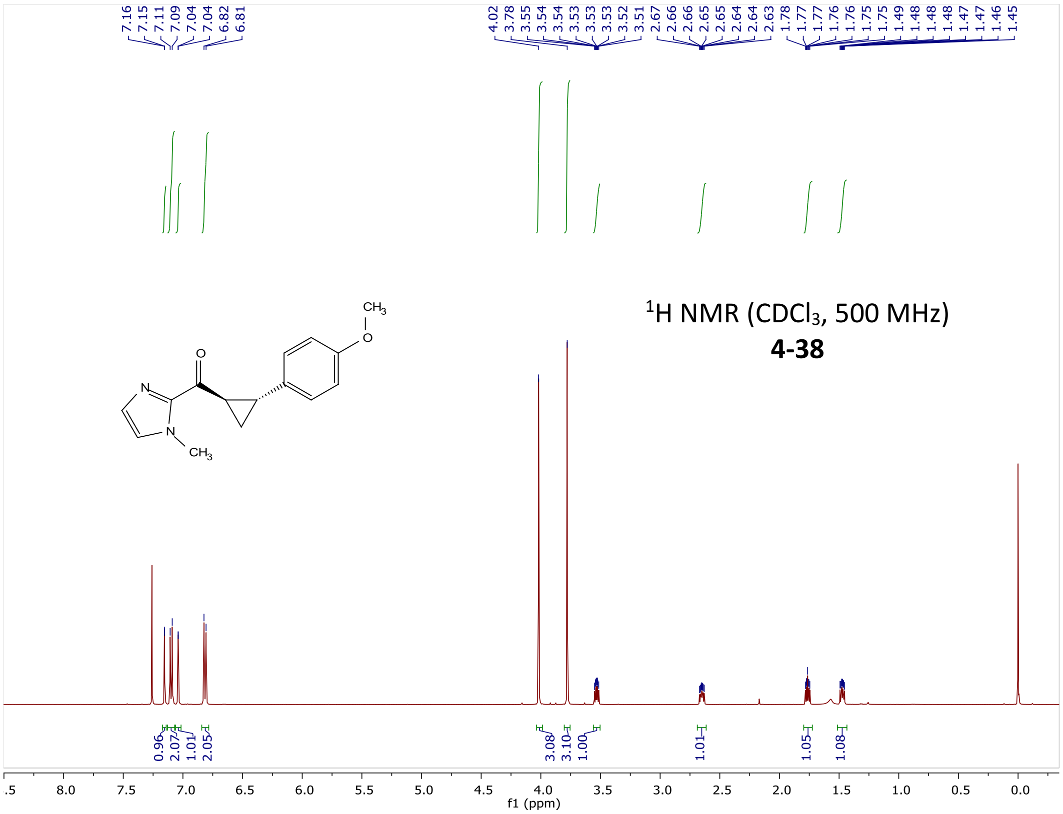
¹H NMR (CDCl₃, 400 MHz)
4-62-crude reaction
N
N
CH₃
O
N
O
O
O
CH₃
O
O
H₃C
0.45
0.13
0.30
0.17
0.41
0.14
0.45
0.05
0.41
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

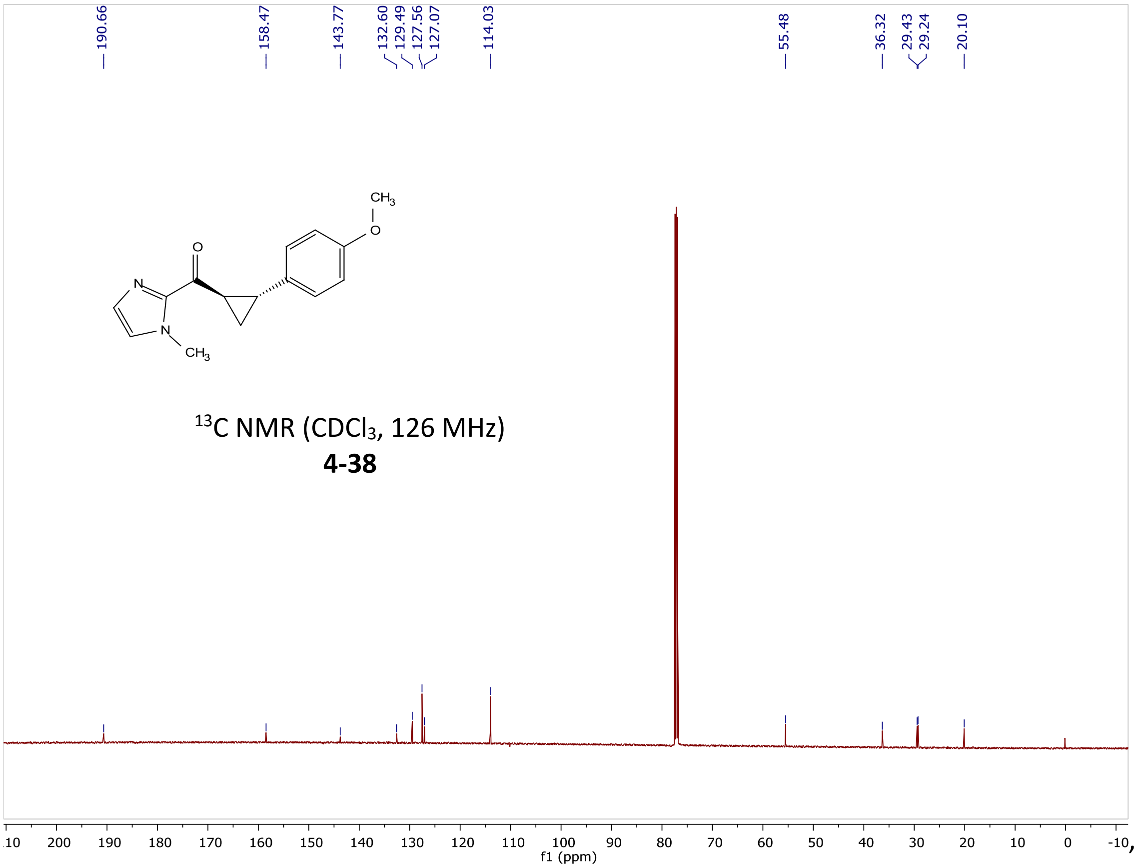


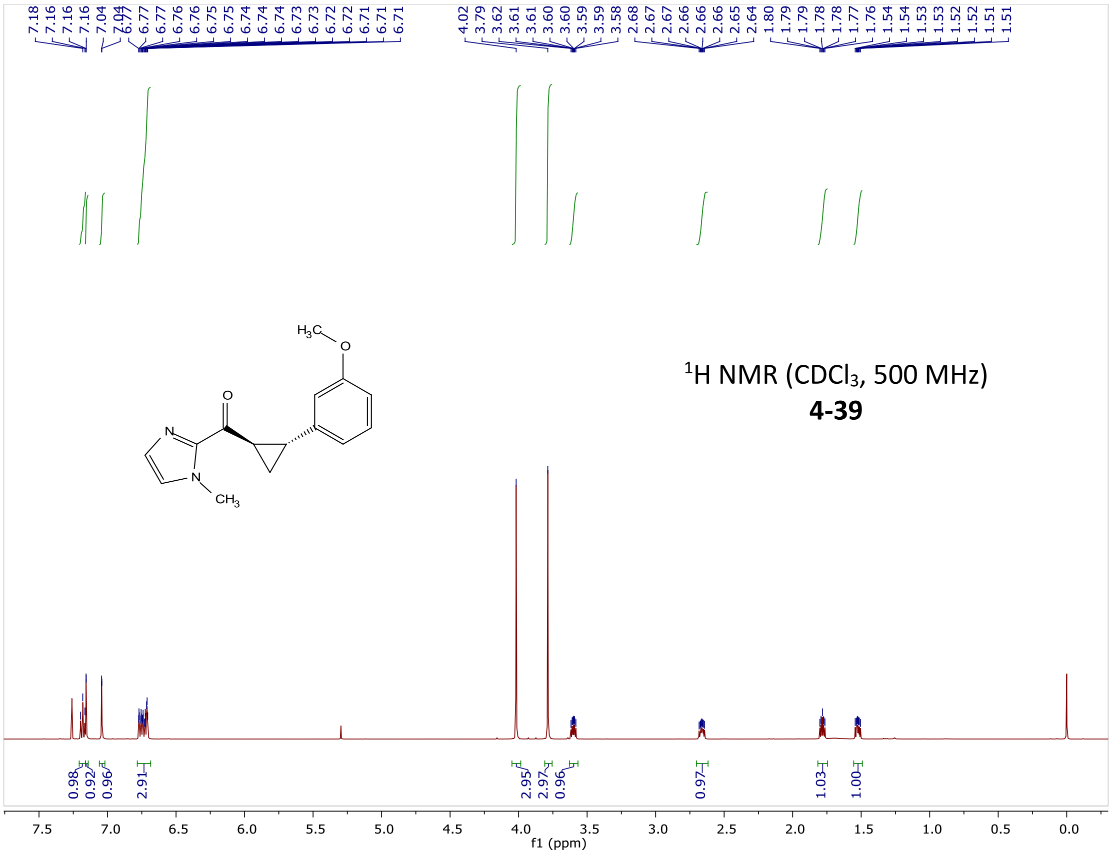
7.07
5.04
5.01
5.01
4.99
4.10
4.08
3.79
3.01
2.99
2.99
2.98
2.97
2.96
2.95
2.93
0.83
¹H NMR (CDCl₃, 400 MHz)
4-8
H₃C
O
O
N
N
N
CH₃
O
O
CH₃
1.81
3.93
3.08
1.03
0.35
1.00
3.91
4.09
3.41
2.91
4.06
7.41
0.41
1.34
1.39
0.63
3.90
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


7.29
7.28
7.28
7.27
7.27
7.26
7.25
7.20
7.20
7.20
7.18
7.18
7.18
7.17
7.17
7.17
7.16
7.16
7.16
7.15
7.04
7.04
4.02
3.62
3.62
3.61
3.61
3.61
3.60
3.60
3.59
2.71
2.70
2.69
2.69
2.69
2.68
2.68
2.67
1.82
1.81
1.80
1.80
1.79
1.79
1.78
1.55
1.54
1.53
1.53
1.52
1.52
1.51
O
N
N
CH3
^{1}H NMR (CDCl$_3$, 500 MHz)
4-6
2.62
4.07
1.00
3.13
1.02
1.03
1.07
1.08
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
f1 (ppm)


190.37
143.58
140.42
129.39
128.40
126.99
126.40
126.25
36.17
29.65
29.23
20.18
^{13}C NMR (CDCl$_3$, 126 MHz)
4-6
O
N
N
CH3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

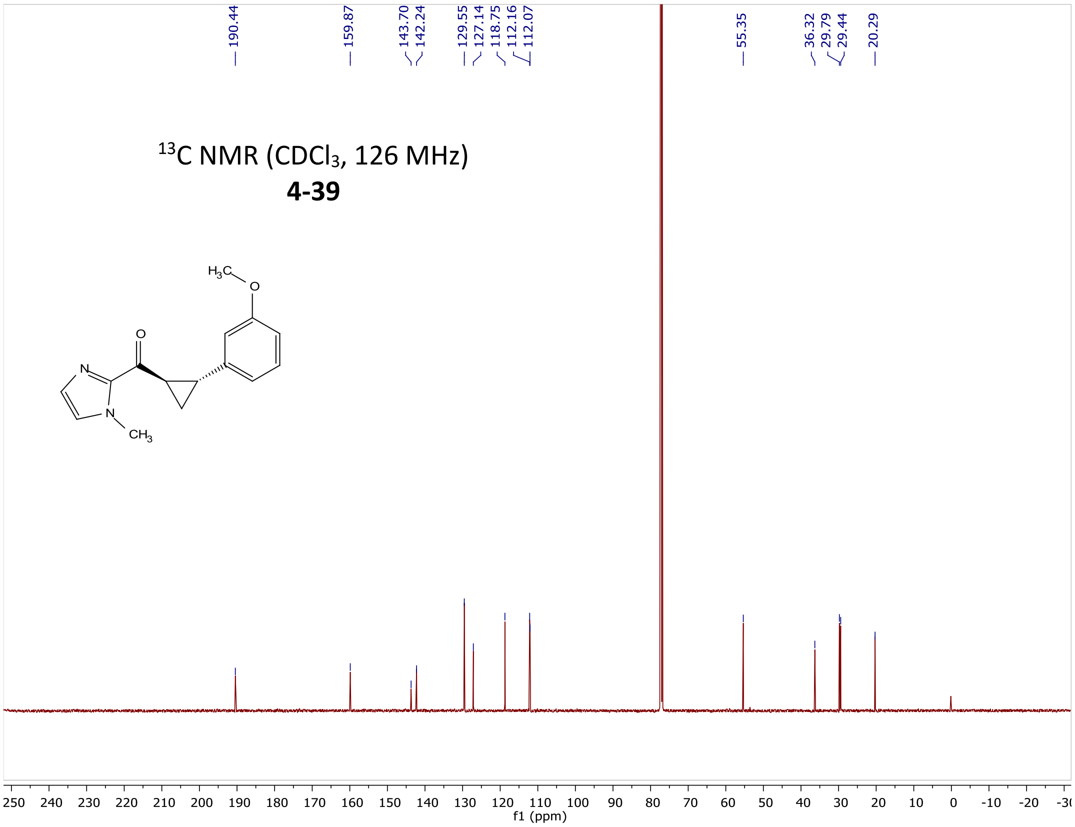

7.16
7.15
7.11
7.09
7.04
7.04
6.82
6.81
4.02
3.78
3.55
3.54
3.54
3.53
3.53
3.53
3.52
3.51
2.67
2.66
2.66
2.65
2.65
2.64
2.64
2.63
1.78
1.77
1.77
1.76
1.76
1.75
1.49
1.48
1.48
1.48
1.47
1.47
1.46
1.45
^{1}H NMR (CDCl$_3$, 500 MHz)
4-38
0.96
2.07
1.01
2.05
3.08
3.10
1.00
1.01
1.05
1.08
.5
8.0
7.5
7.0
6.5
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
f1 (ppm)


190.66
158.47
143.77
132.60
129.49
127.56
127.07
114.03
55.48
36.32
29.43
29.24
20.10
^{13}C NMR (CDCl$_3$, 126 MHz)
4-38
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



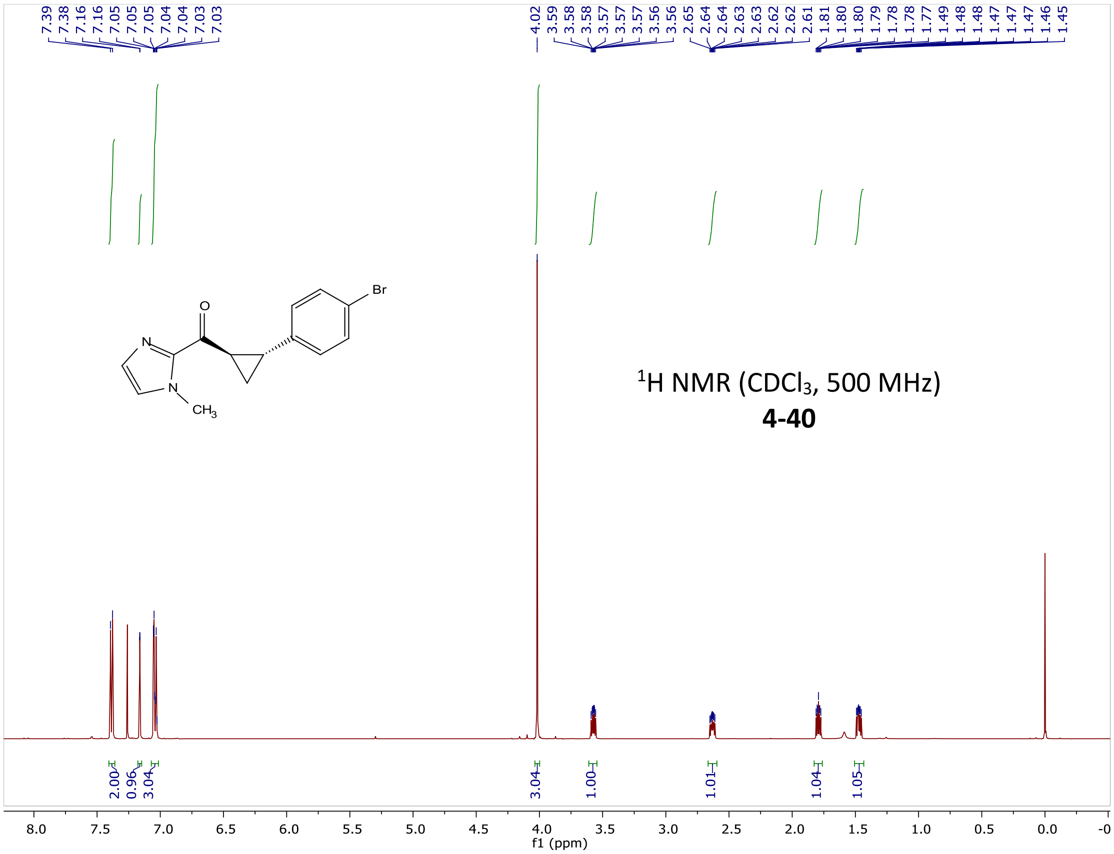
^{1}H NMR (CDCl$_3$, 500 MHz)

4-39



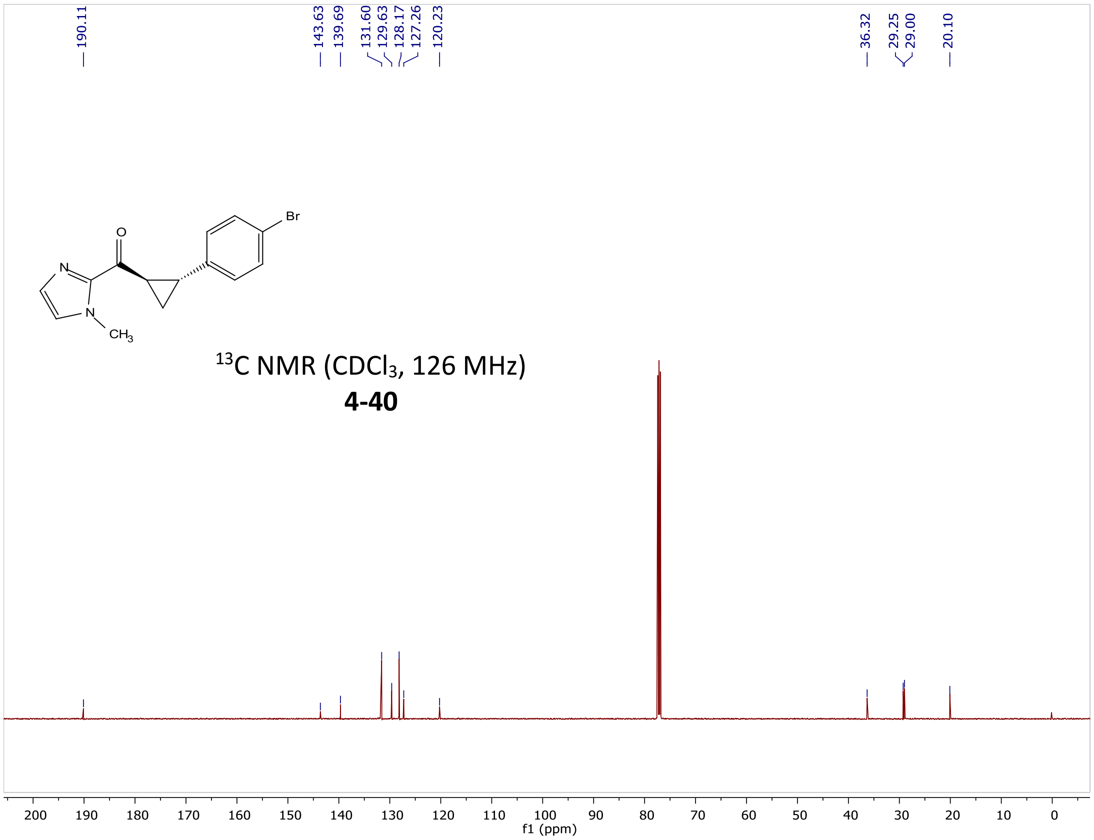
^{13}C NMR (CDCl$_3$, 126 MHz)

4-39



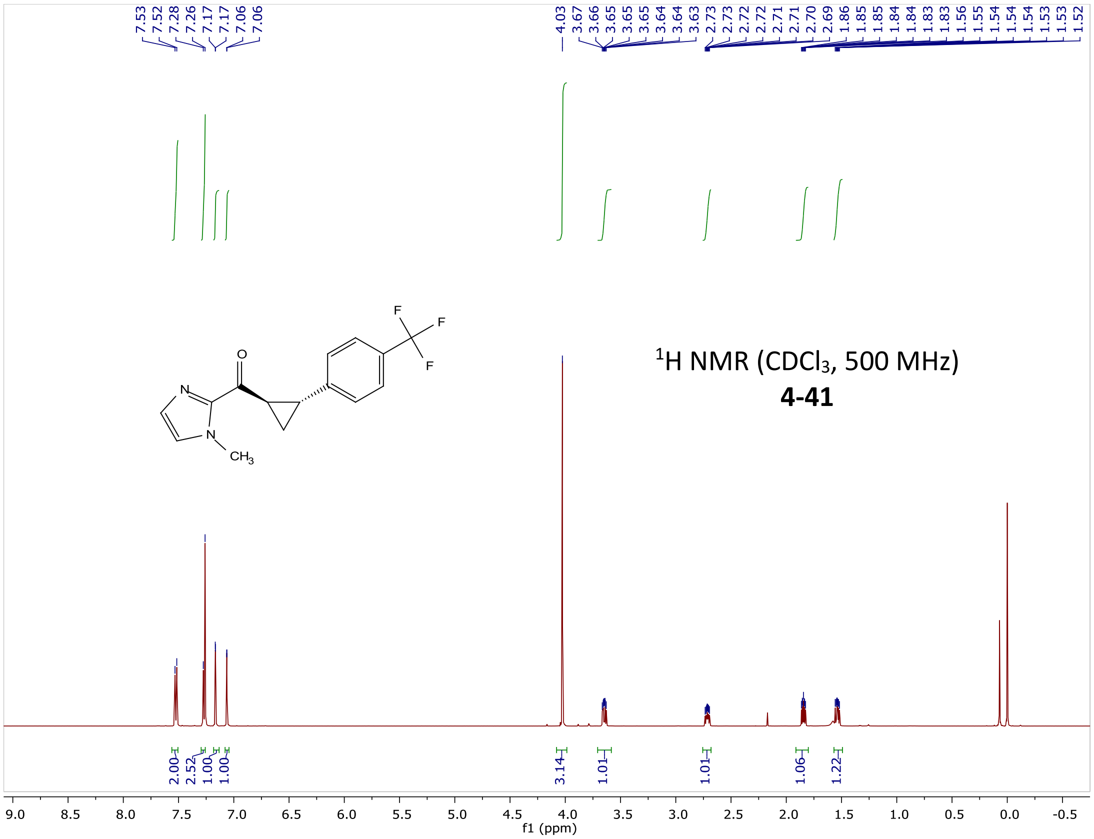
^{1}H NMR (CDCl$_3$, 500 MHz)

4-40



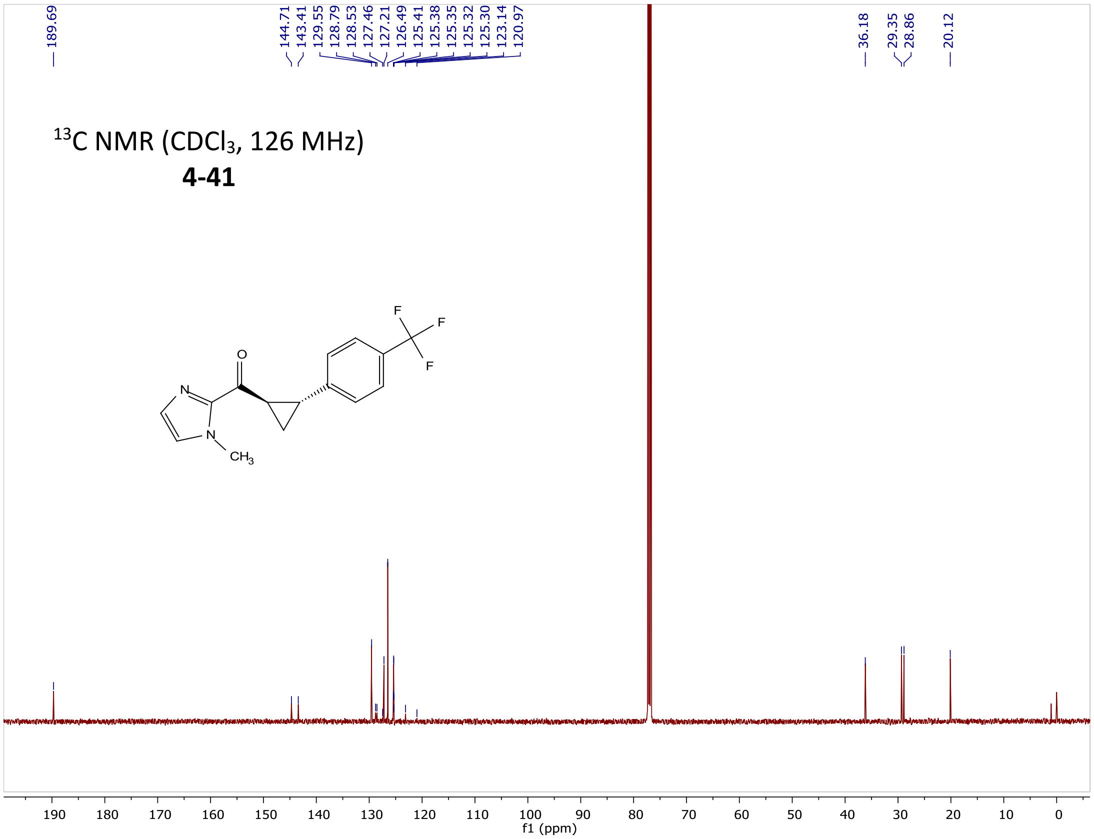
^{13}C NMR (CDCl$_3$, 126 MHz)

4-40



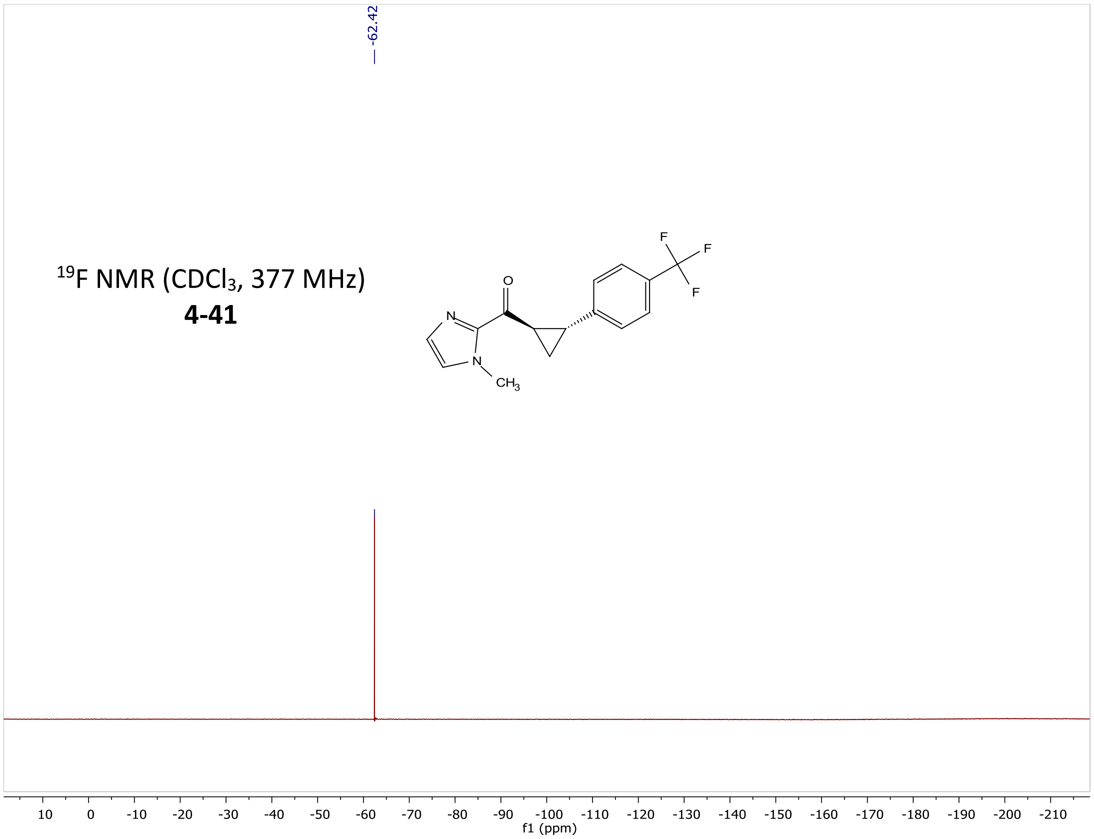
^{1}H NMR (CDCl$_3$, 500 MHz)

4-41



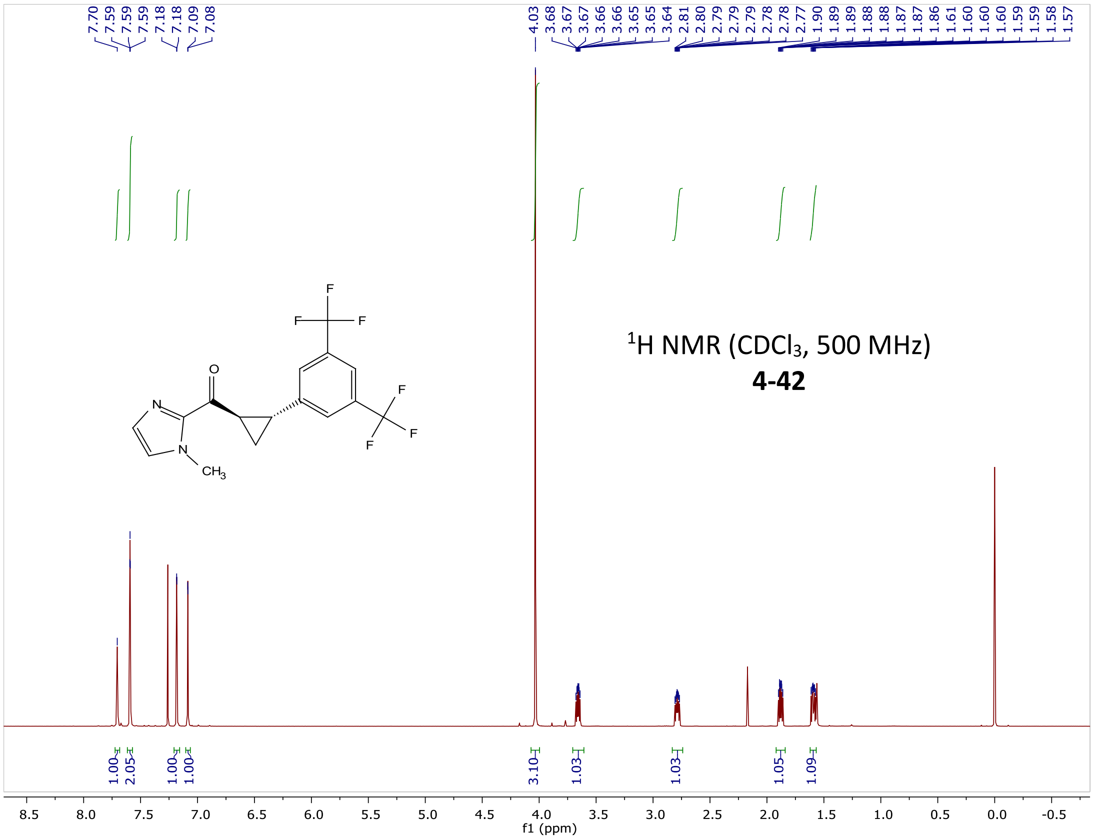
^{13}C NMR (CDCl$_3$, 126 MHz)

4-41



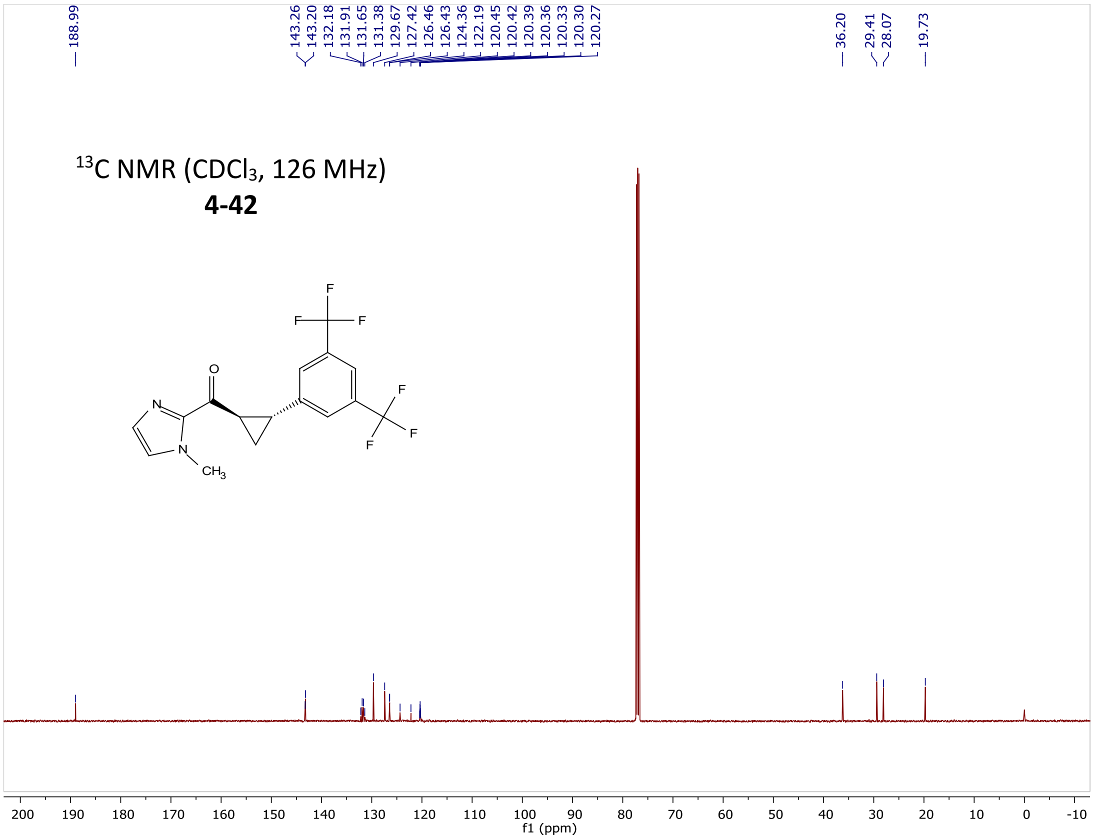
^{19}F NMR (CDCl$_3$, 377 MHz)

4-41



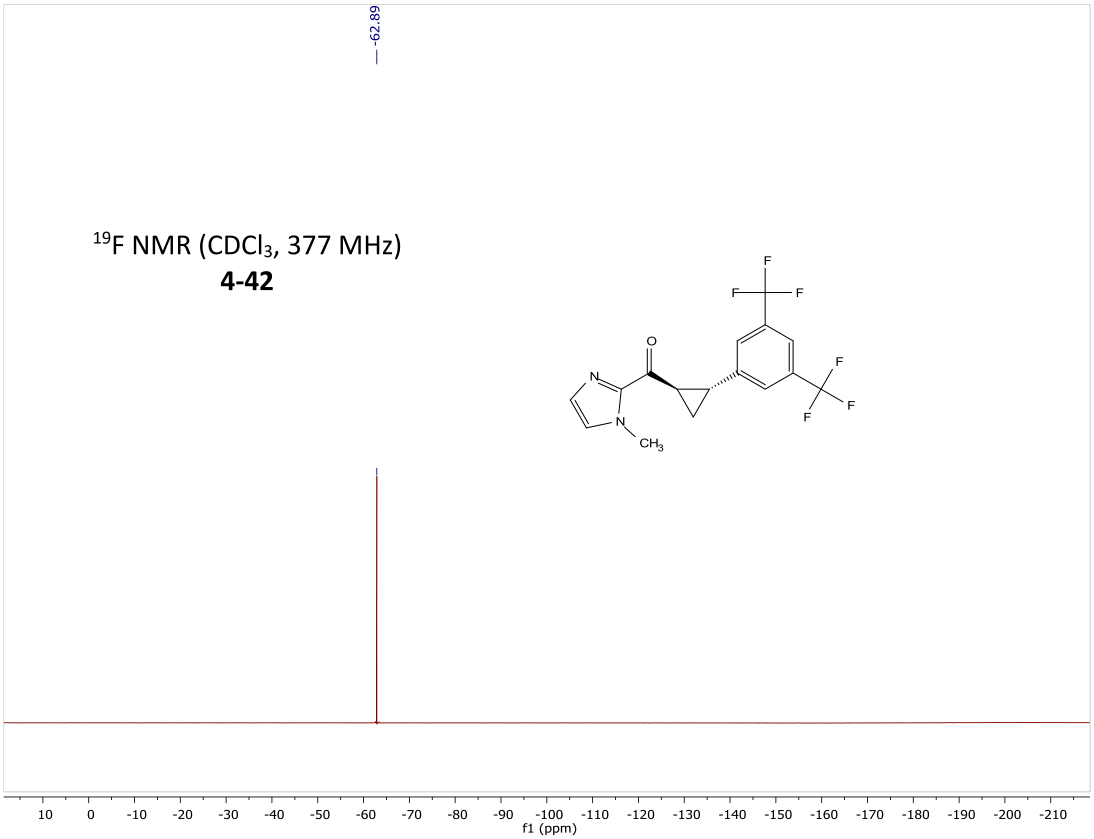
^{1}H NMR (CDCl$_3$, 500 MHz)

4-42



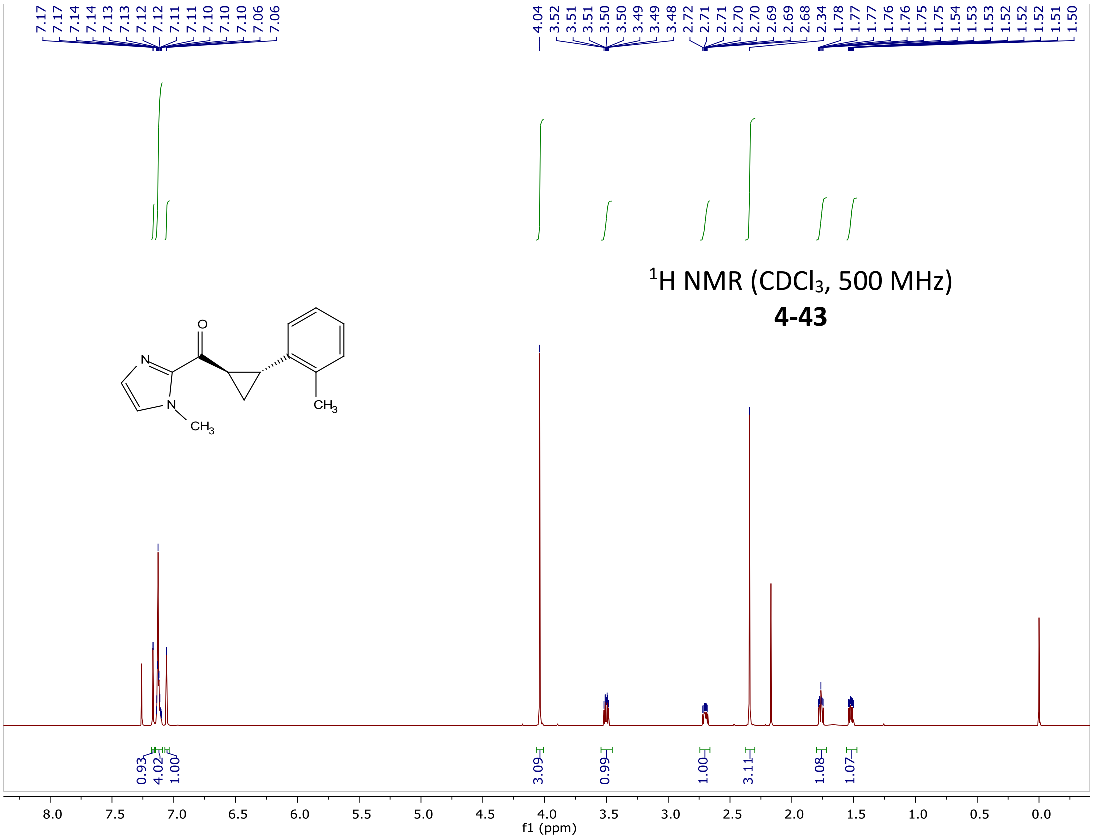
^{13}C NMR (CDCl$_3$, 126 MHz)

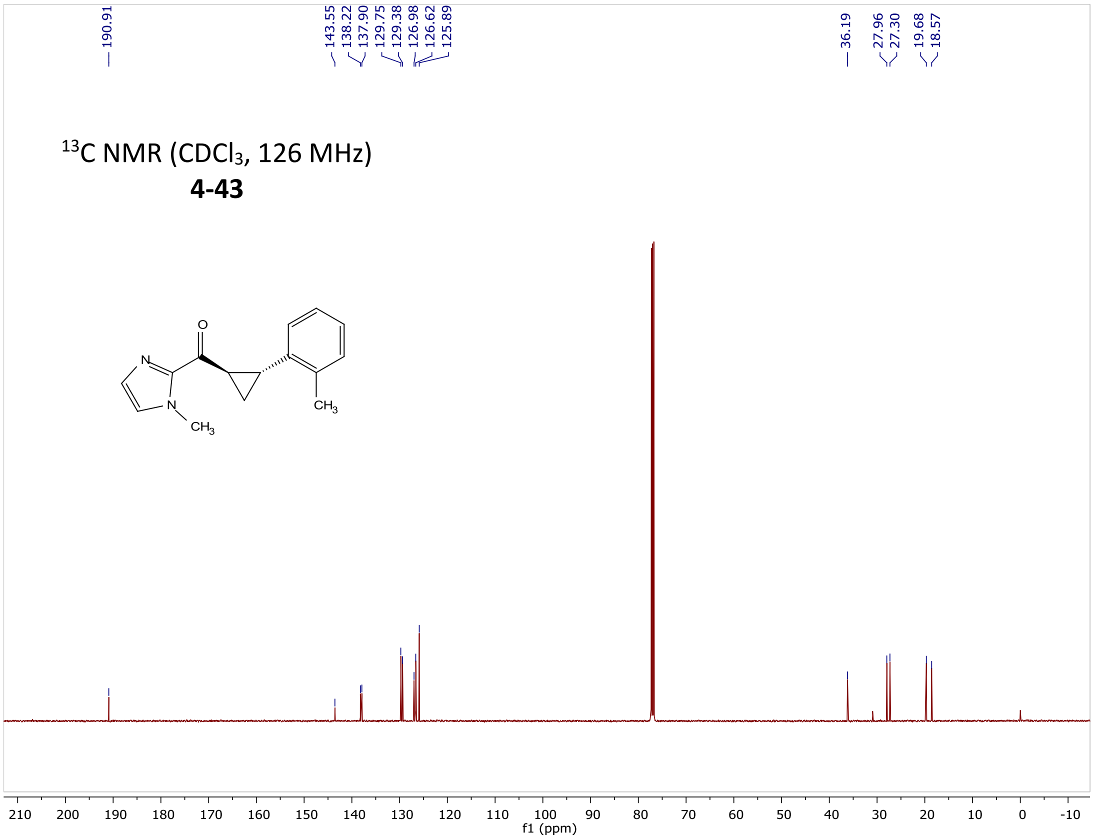
4-42

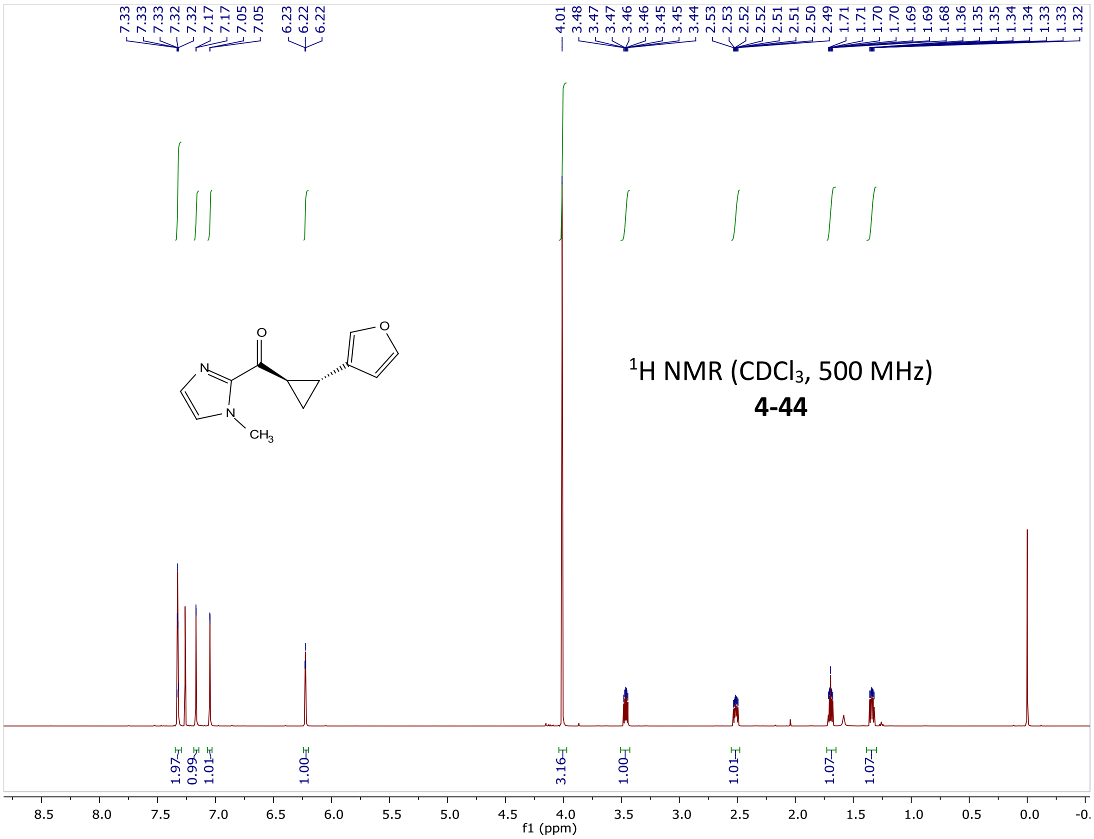


^{19}F NMR (CDCl$_3$, 377 MHz)

4-42

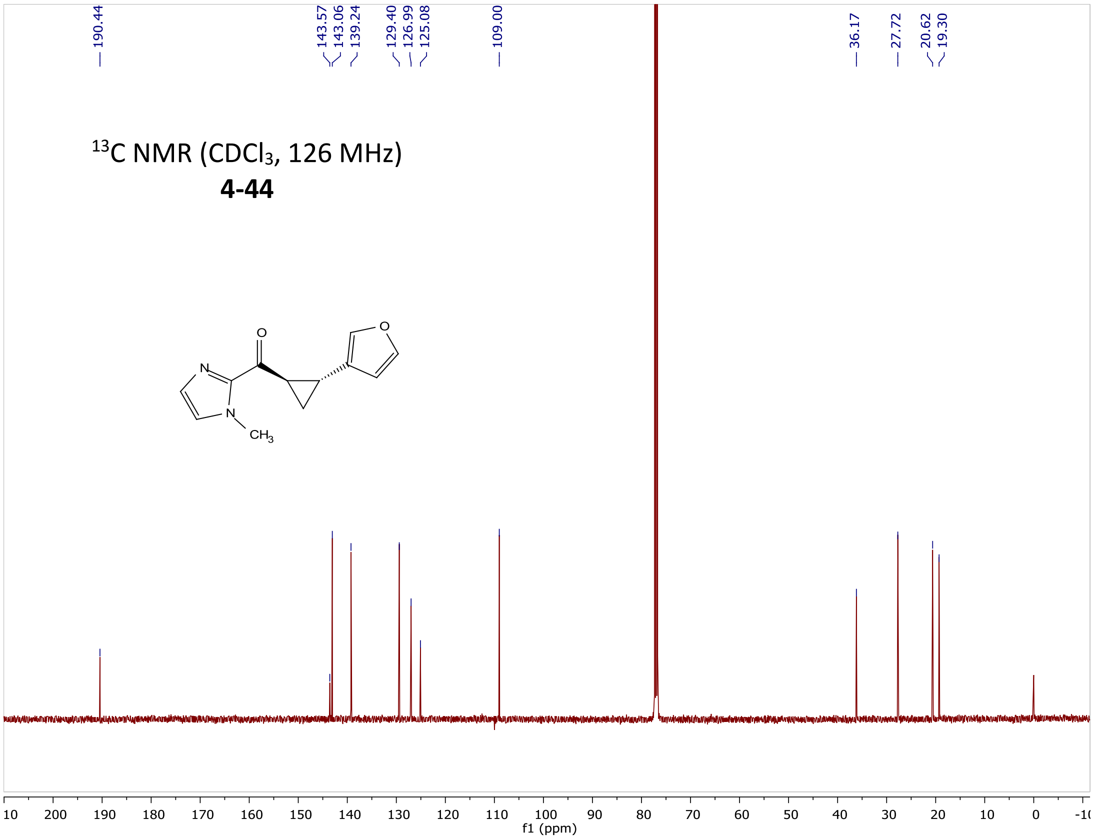

7.17
7.17
7.14
7.14
7.13
7.13
7.12
7.12
7.11
7.11
7.10
7.10
7.06
7.06
4.04
3.52
3.51
3.51
3.50
3.50
3.49
3.49
3.48
2.72
2.71
2.71
2.70
2.70
2.69
2.69
2.68
2.34
1.78
1.77
1.77
1.76
1.76
1.75
1.75
1.54
1.53
1.53
1.52
1.52
1.52
1.51
1.50
^{1}H NMR (CDCl$_3$, 500 MHz)
4-43
O
N
N
CH3
CH3
0.93
4.02
1.00
3.09
0.99
1.00
3.11
1.08
1.07
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
f1 (ppm)


190.91
143.55
138.22
137.90
129.75
129.38
126.98
126.62
125.89
36.19
27.96
27.30
19.68
18.57
^{13}C NMR (CDCl$_3$, 126 MHz)
4-43
O
N
N
CH3
CH3
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)



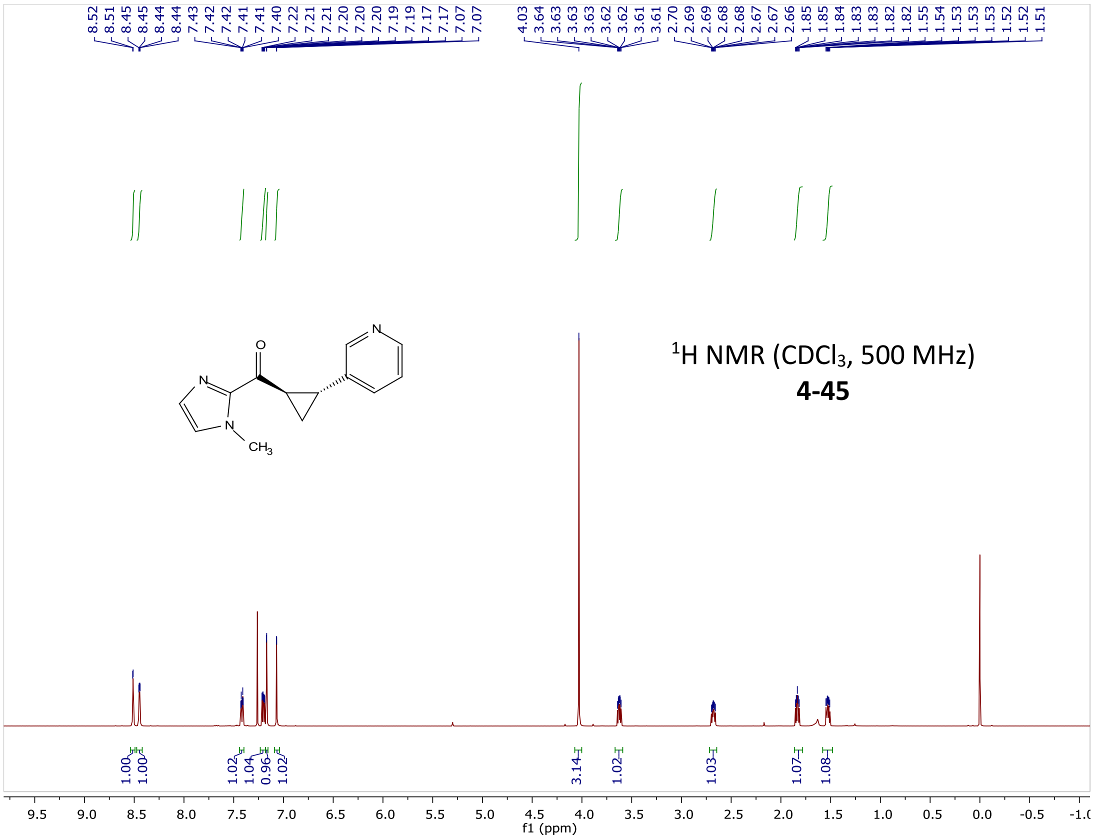
^{1}H NMR (CDCl$_3$, 500 MHz)

4-44



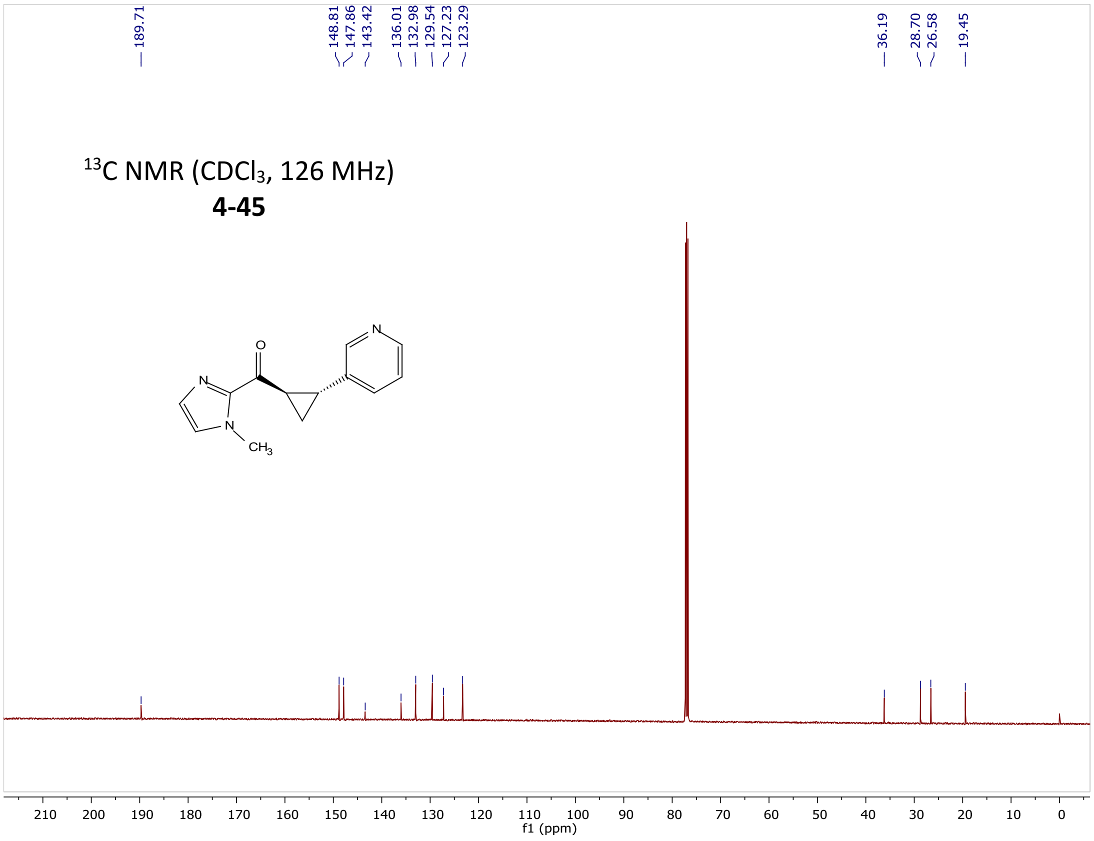
^{13}C NMR (CDCl$_3$, 126 MHz)

4-44



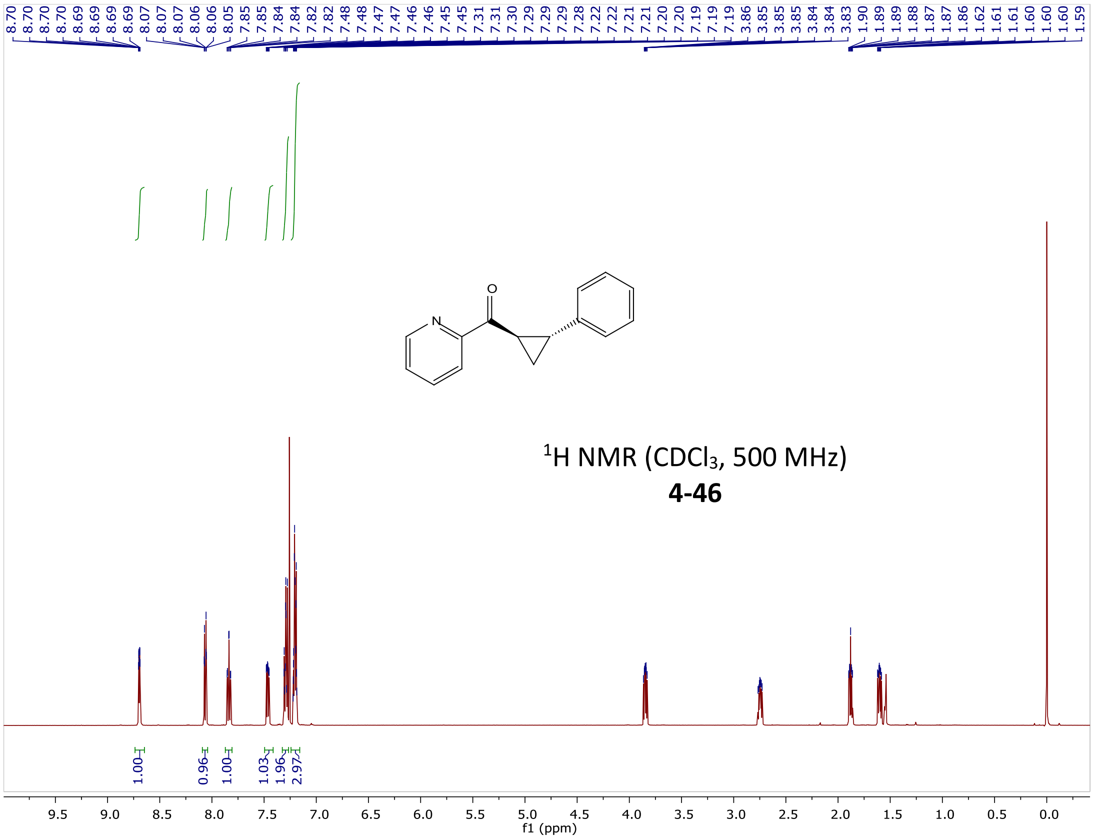
^{1}H NMR (CDCl$_3$, 500 MHz)

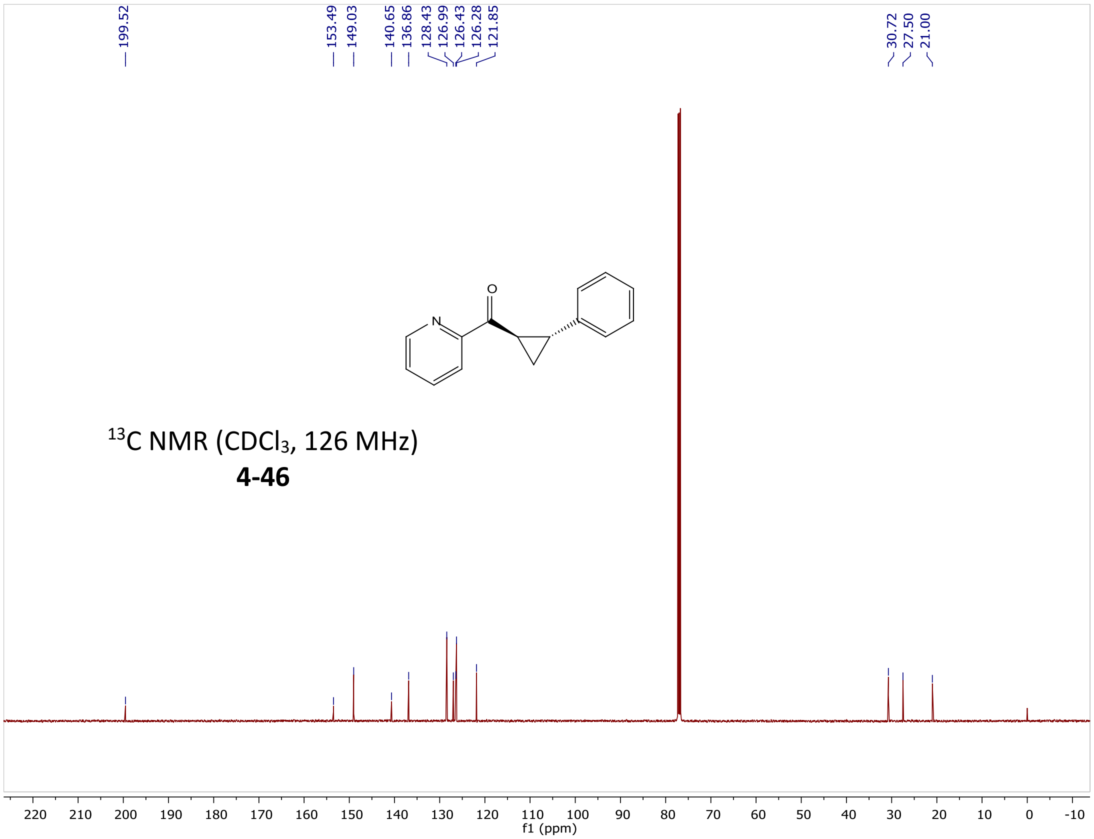
4-45

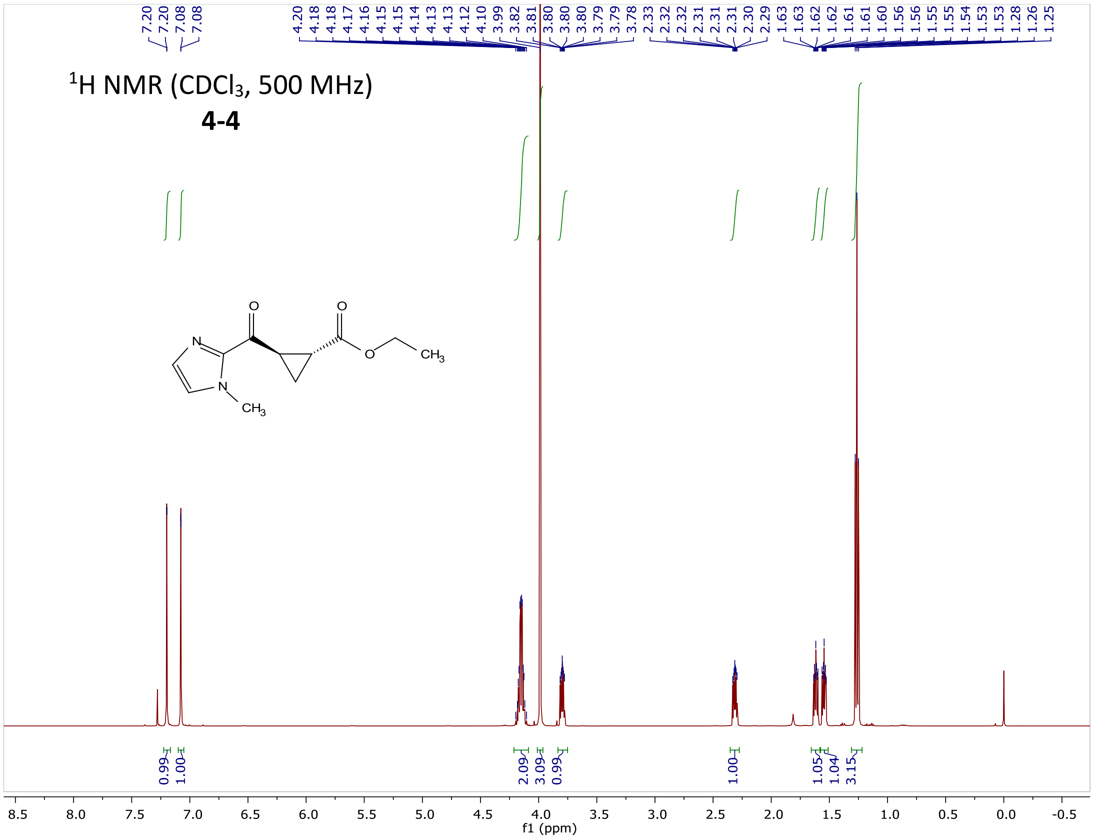


^{13}C NMR (CDCl$_3$, 126 MHz)

4-45

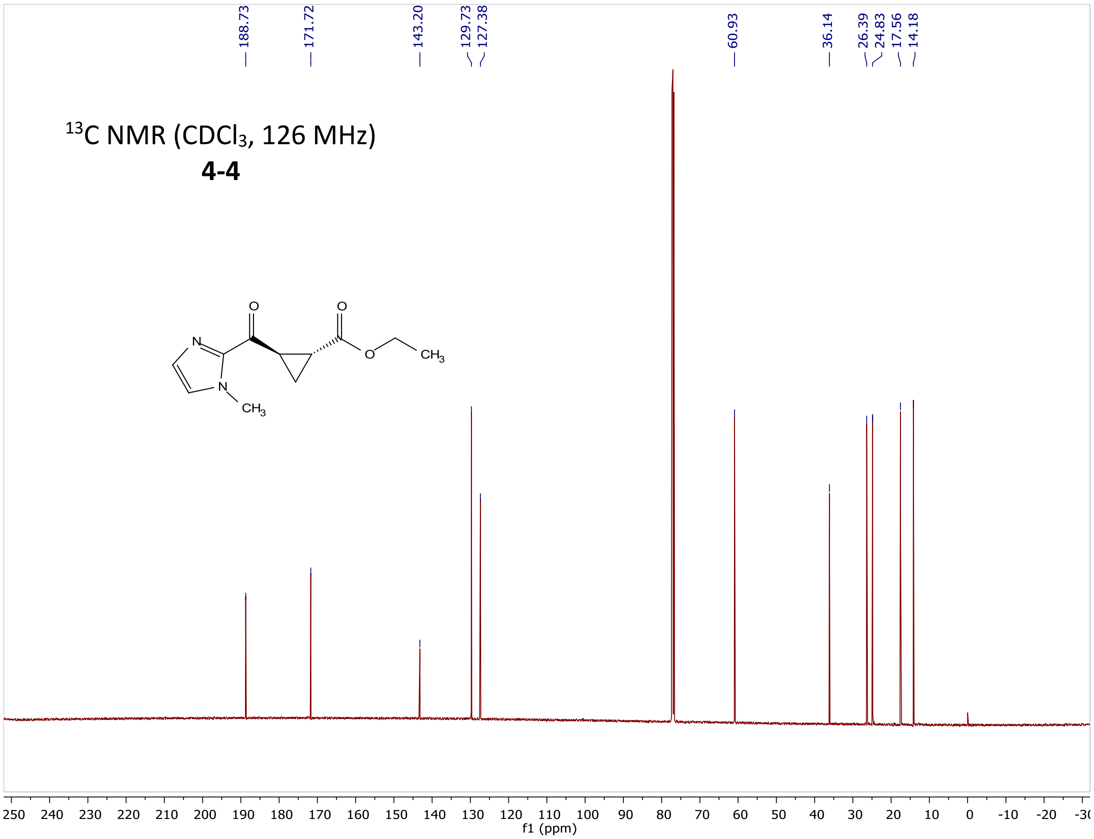

8.70
8.70
8.70
8.69
8.69
8.69
8.69
8.07
8.07
8.07
8.06
8.06
8.05
7.85
7.84
7.84
7.82
7.82
7.48
7.48
7.47
7.47
7.46
7.46
7.45
7.45
7.31
7.31
7.30
7.29
7.29
7.29
7.28
7.22
7.22
7.21
7.21
7.20
7.20
7.19
7.19
7.19
3.86
3.85
3.85
3.85
3.84
3.84
3.83
1.90
1.89
1.89
1.88
1.87
1.87
1.86
1.62
1.61
1.61
1.60
1.60
1.60
1.59
O
N
^{1}H NMR (CDCl$_3$, 500 MHz)
4-46
1.00
0.96
1.00
1.03
1.96
2.97
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
f1 (ppm)


199.52
153.49
149.03
140.65
136.86
128.43
126.99
126.43
126.28
121.85
30.72
27.50
21.00
O
N
^{13}C NMR (CDCl$_3$, 126 MHz)
4-46
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)



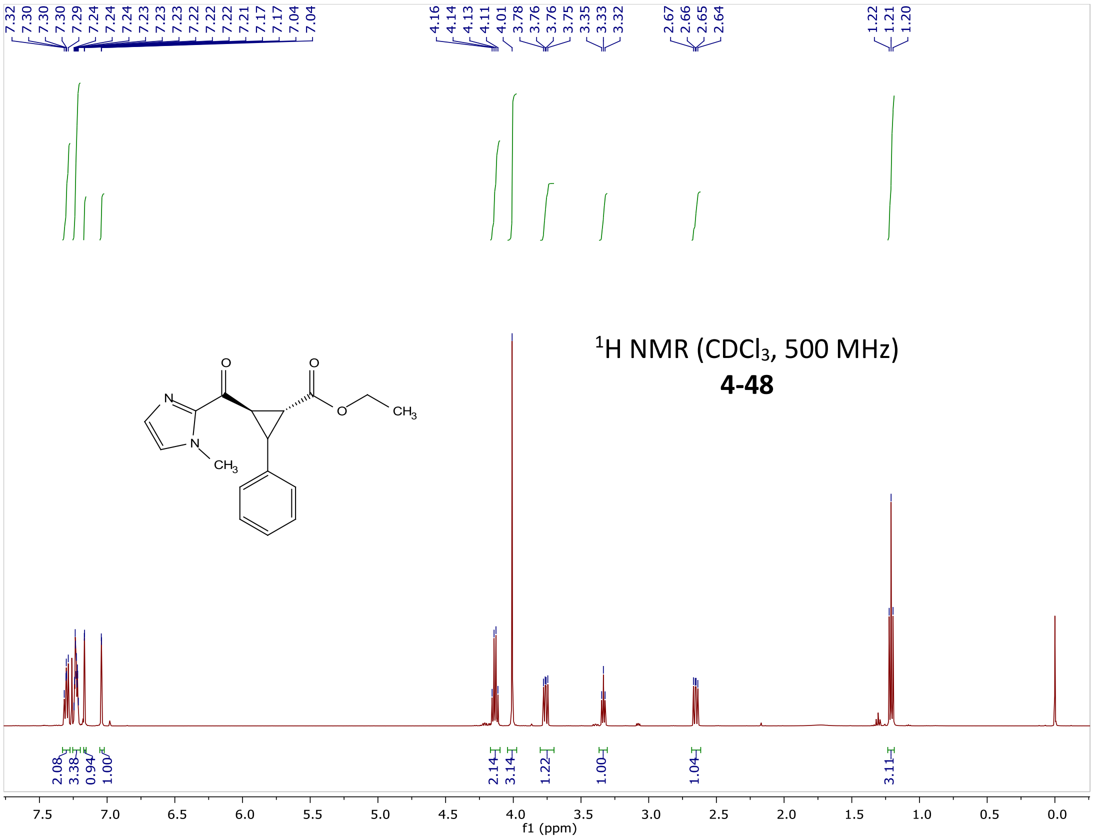
^{1}H NMR (CDCl$_3$, 500 MHz)

4-4



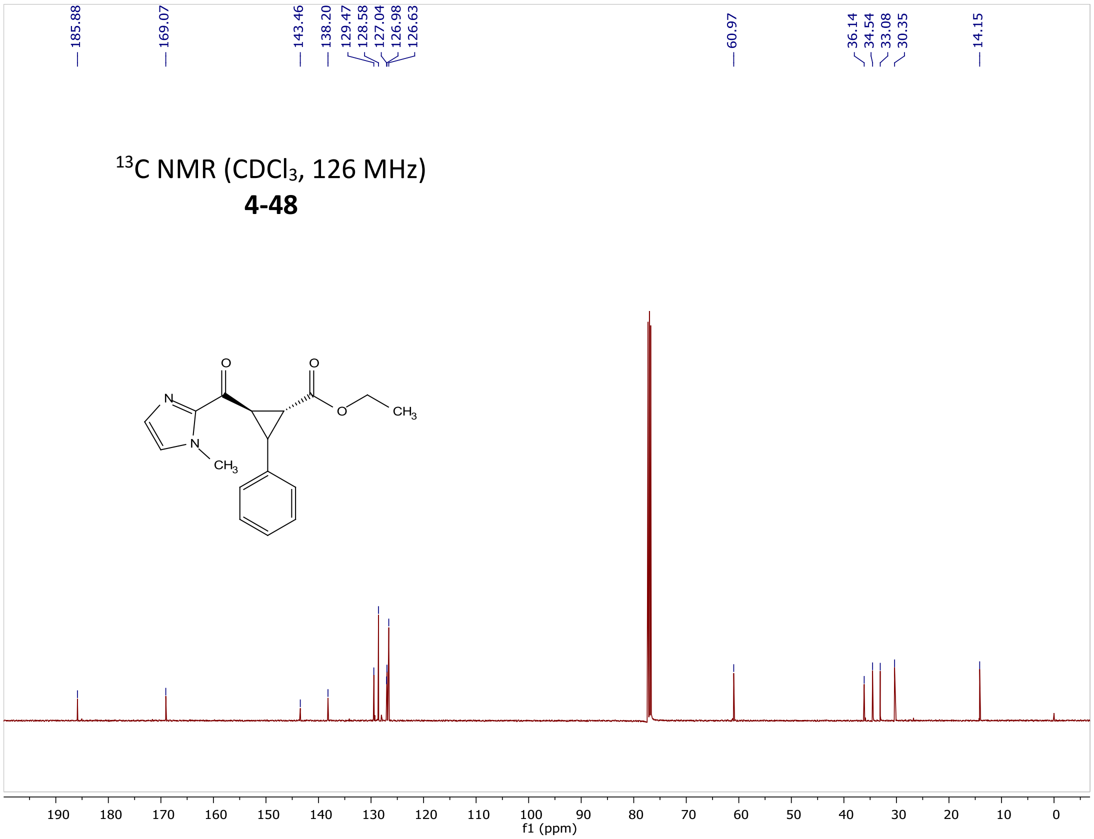
^{13}C NMR (CDCl$_3$, 126 MHz)

4-4



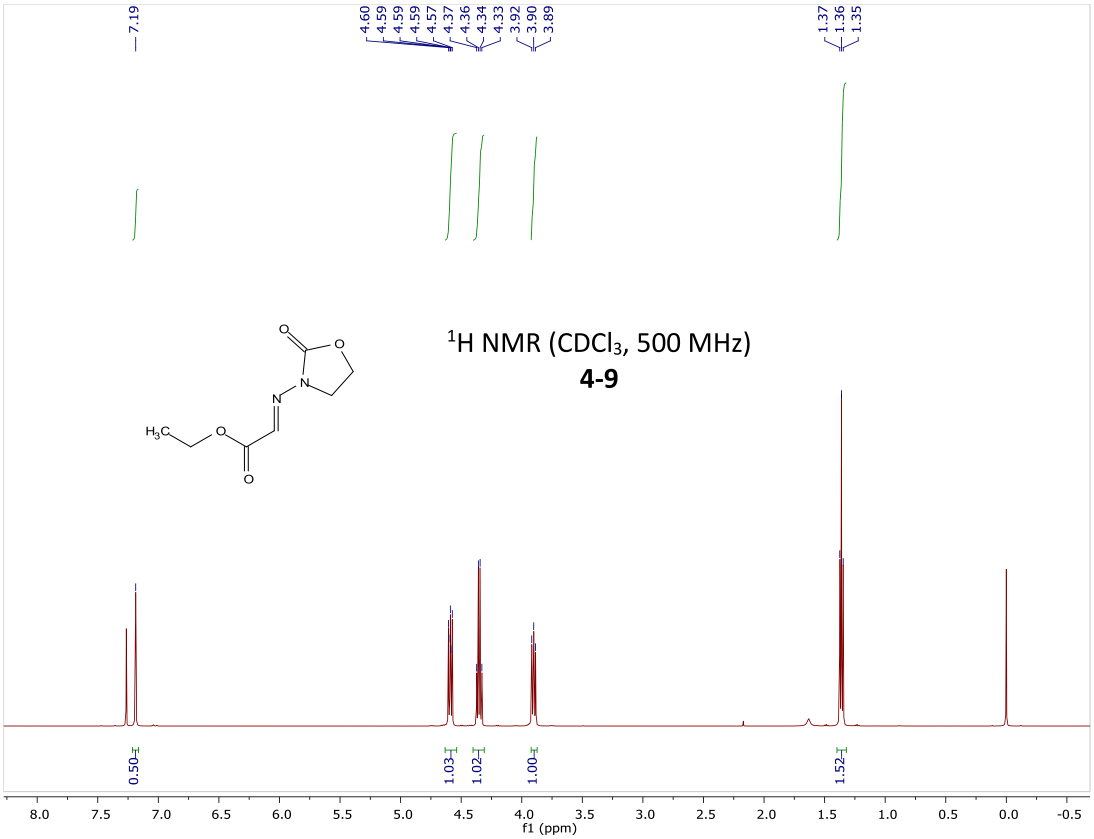
^{1}H NMR (CDCl$_3$, 500 MHz)

4-48



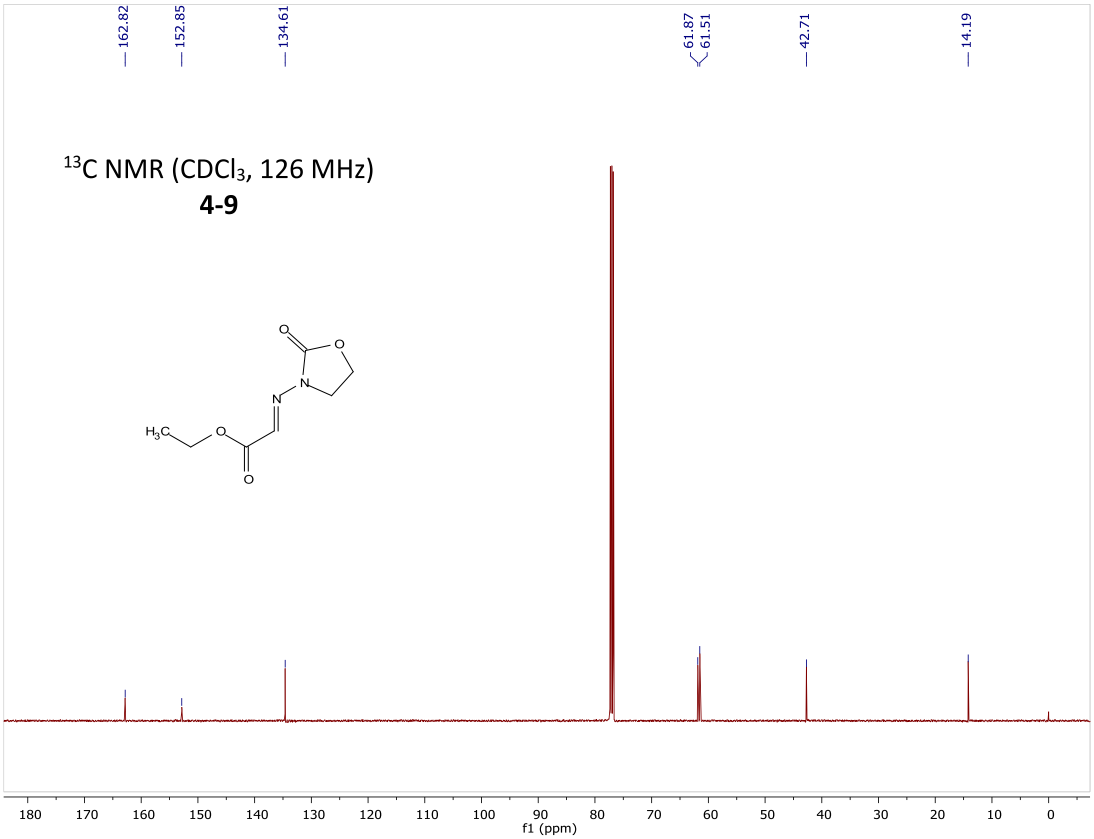
^{13}C NMR (CDCl$_3$, 126 MHz)

4-48



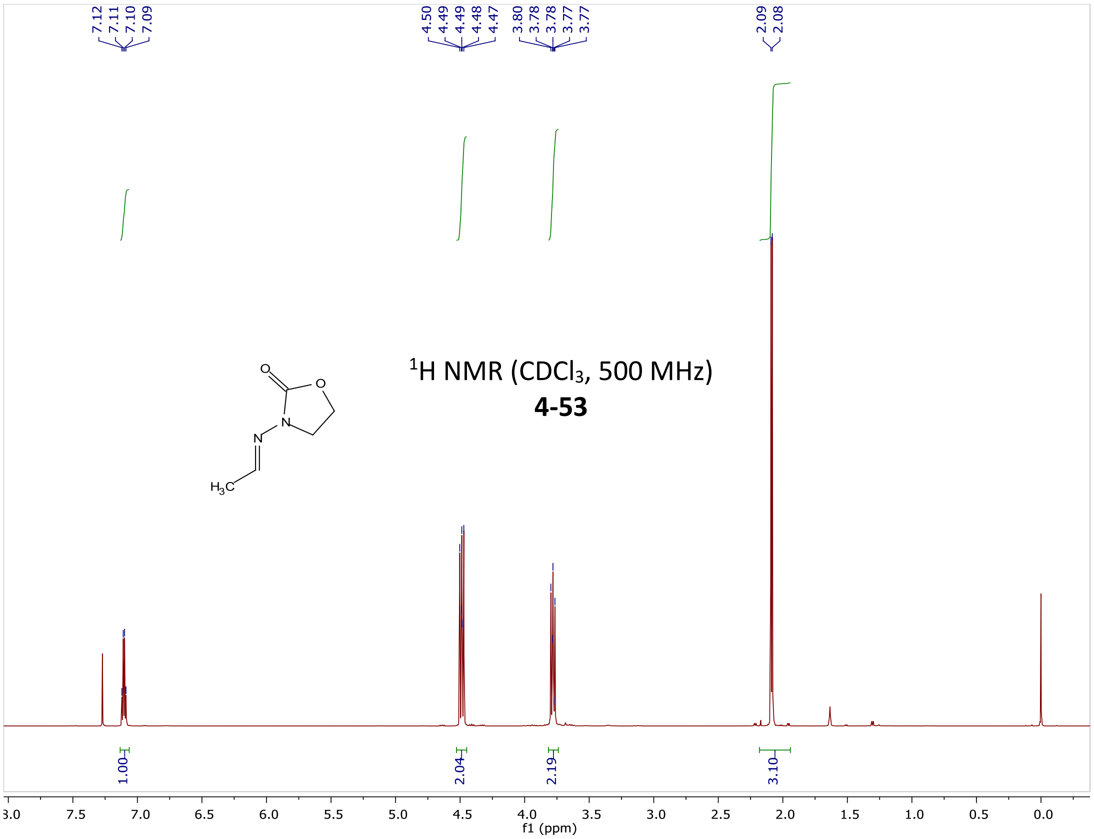
^{1}H NMR (CDCl$_3$, 500 MHz)

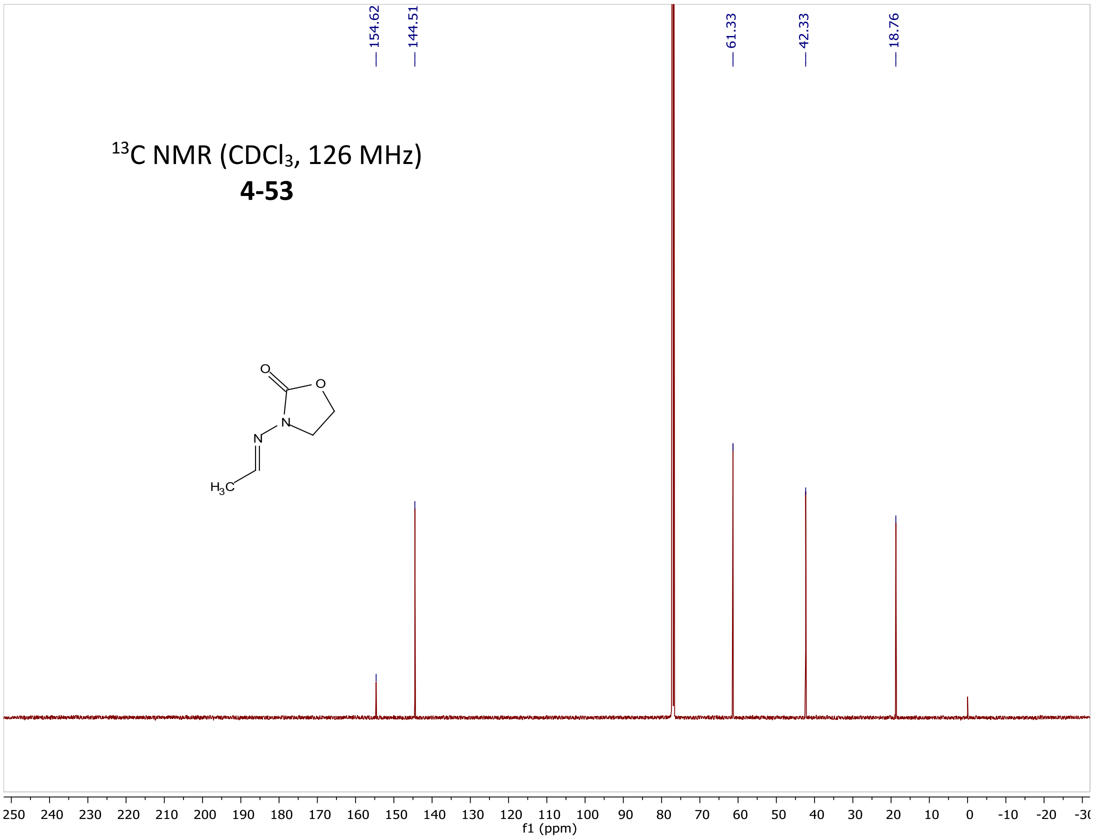
4-9

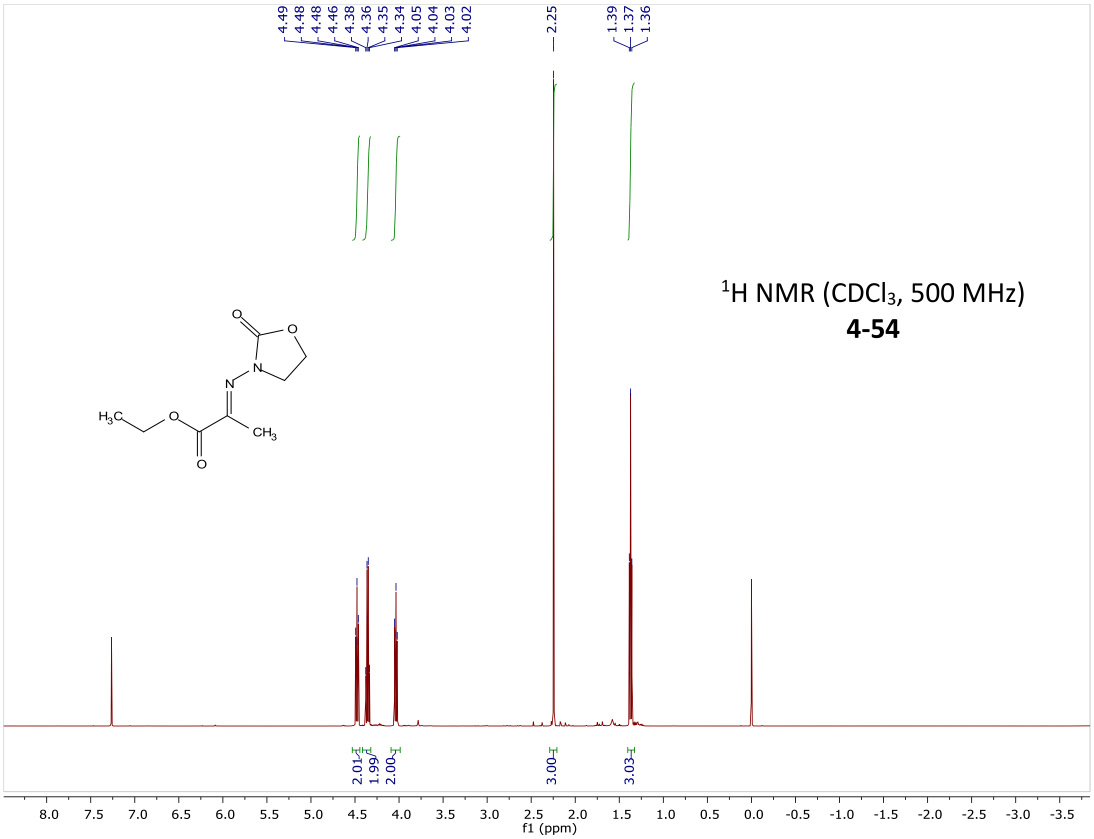


^{13}C NMR (CDCl$_3$, 126 MHz)

4-9

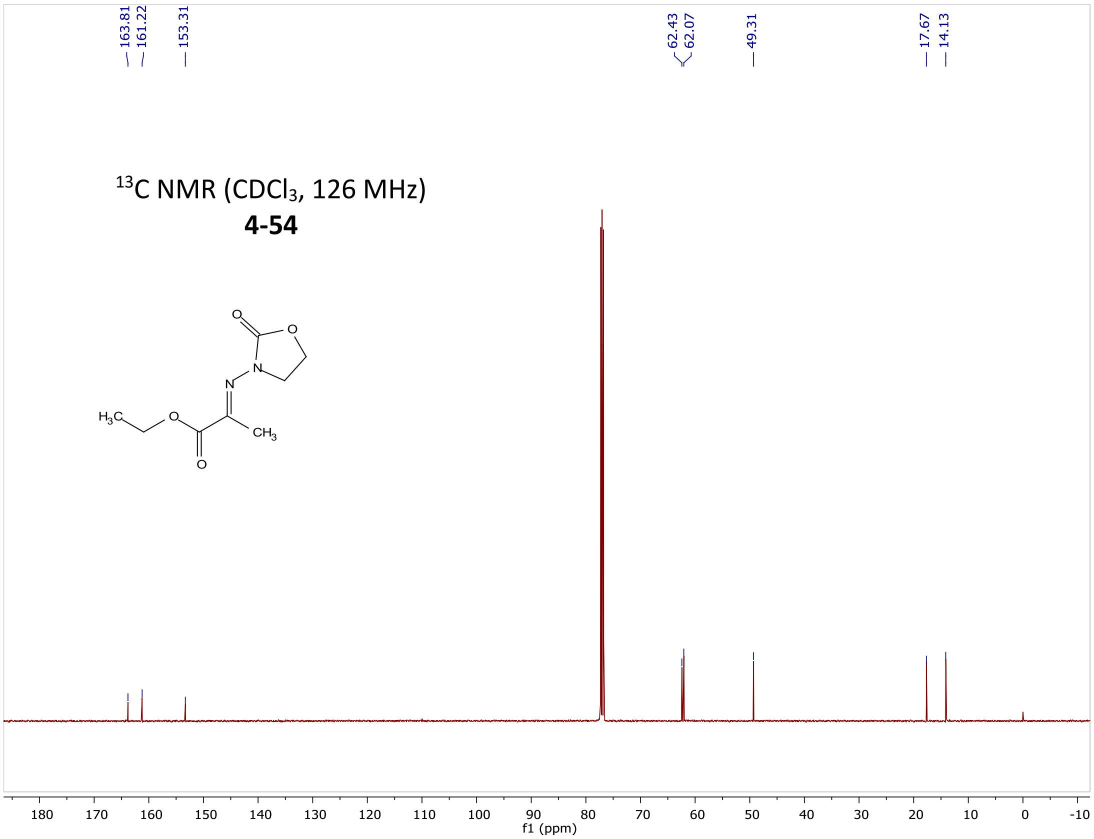

^{1}H NMR (CDCl$_3$, 500 MHz)
4-53


^{13}C NMR (CDCl$_3$, 126 MHz)
4-53



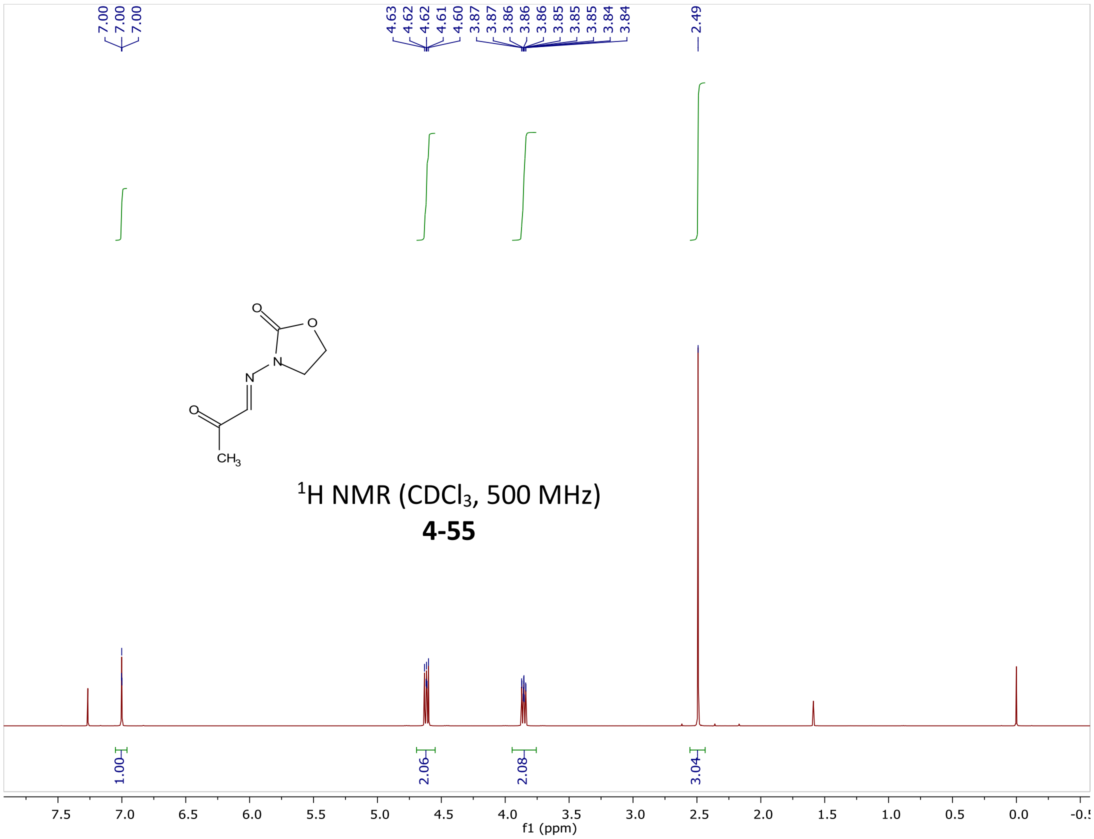
^{1}H NMR ($CDCl_3$, 500 MHz)

4-54



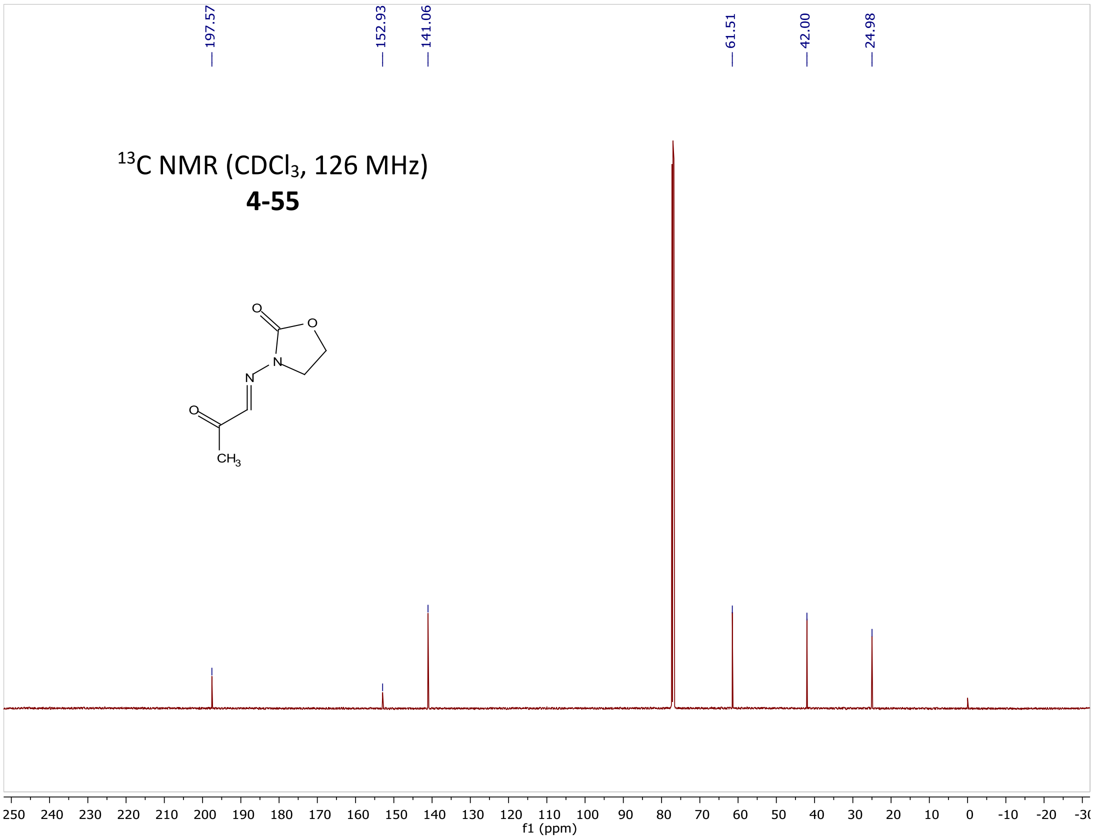
^{13}C NMR ($CDCl_3$, 126 MHz)

4-54



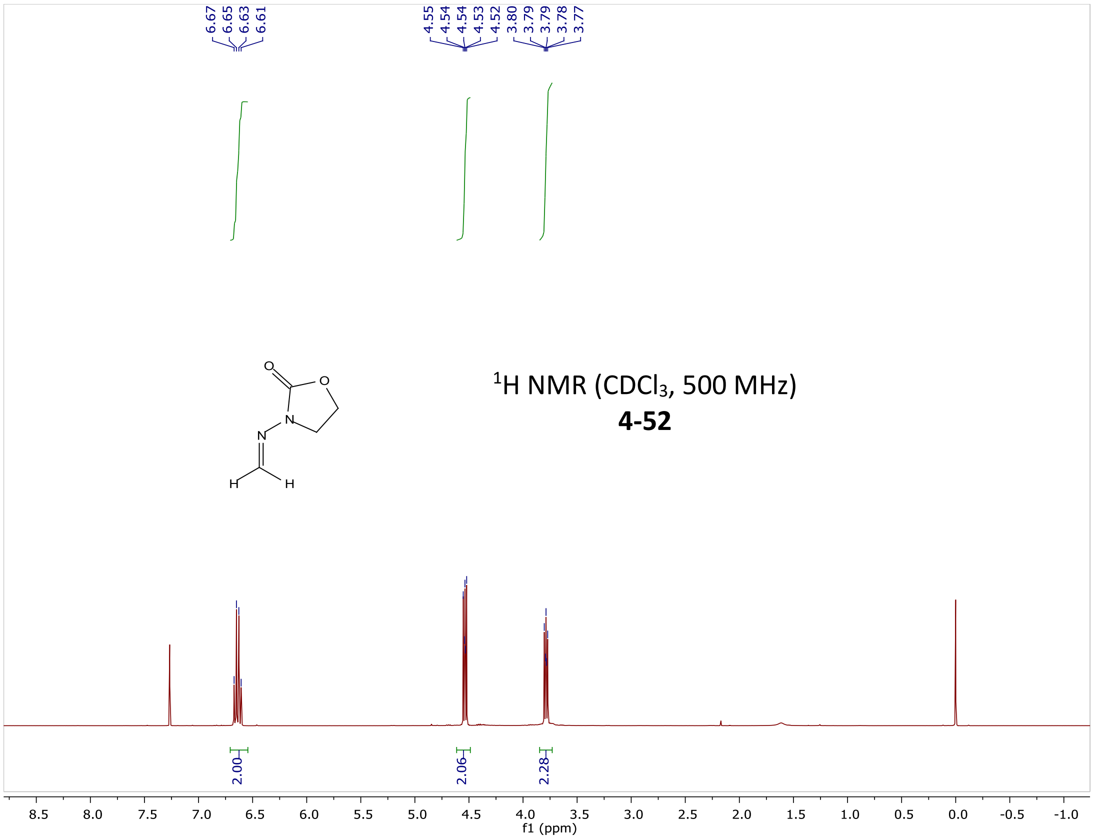
^{1}H NMR (CDCl$_3$, 500 MHz)

4-55



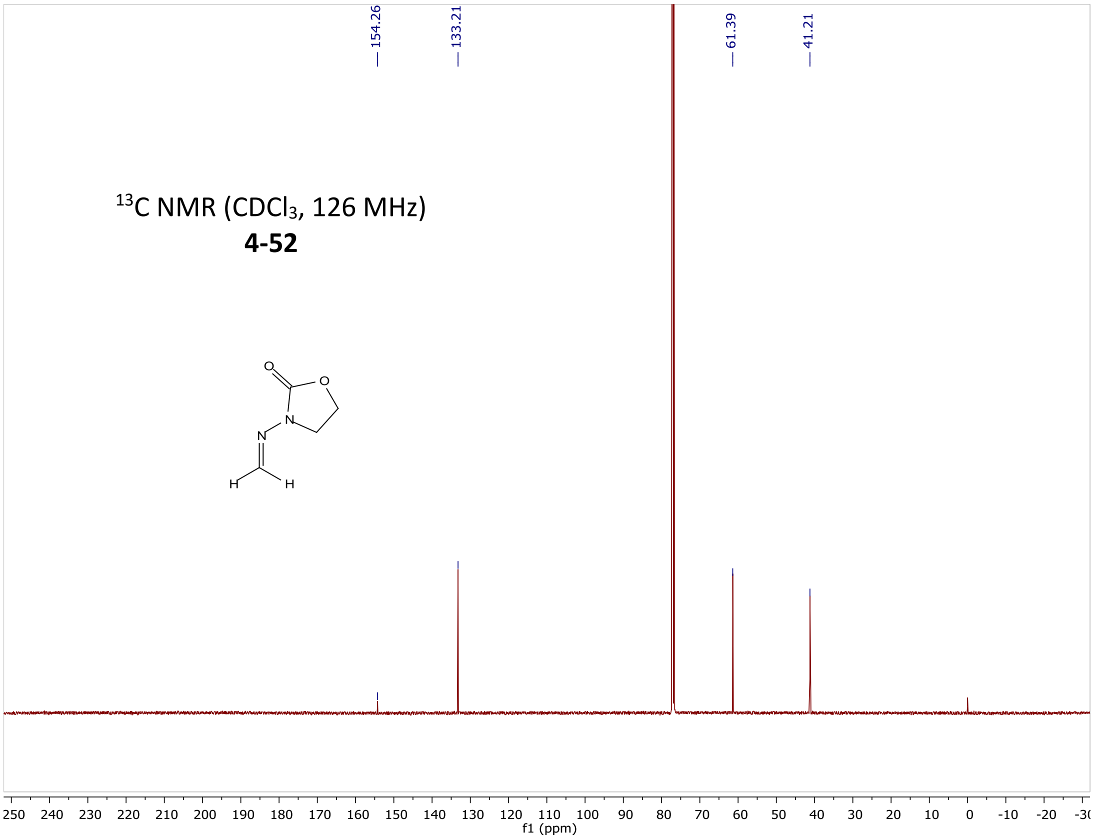
^{13}C NMR (CDCl$_3$, 126 MHz)

4-55



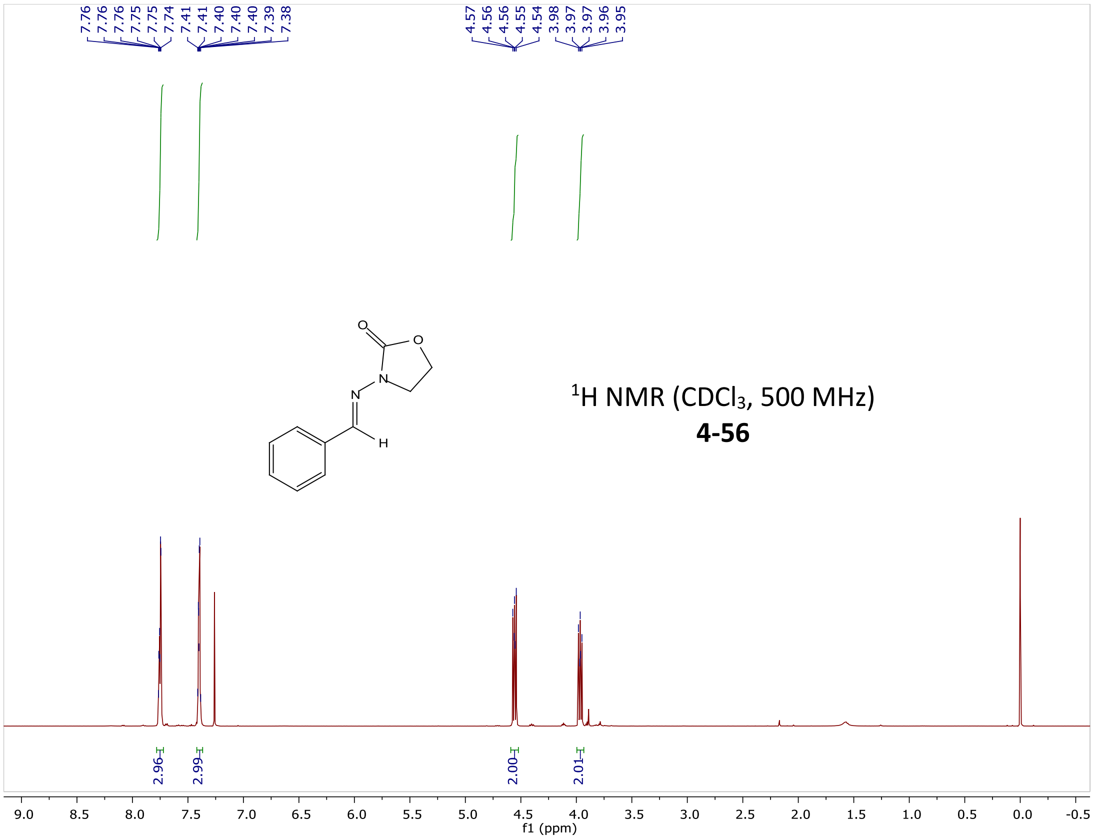
^{1}H NMR (CDCl$_3$, 500 MHz)

4-52



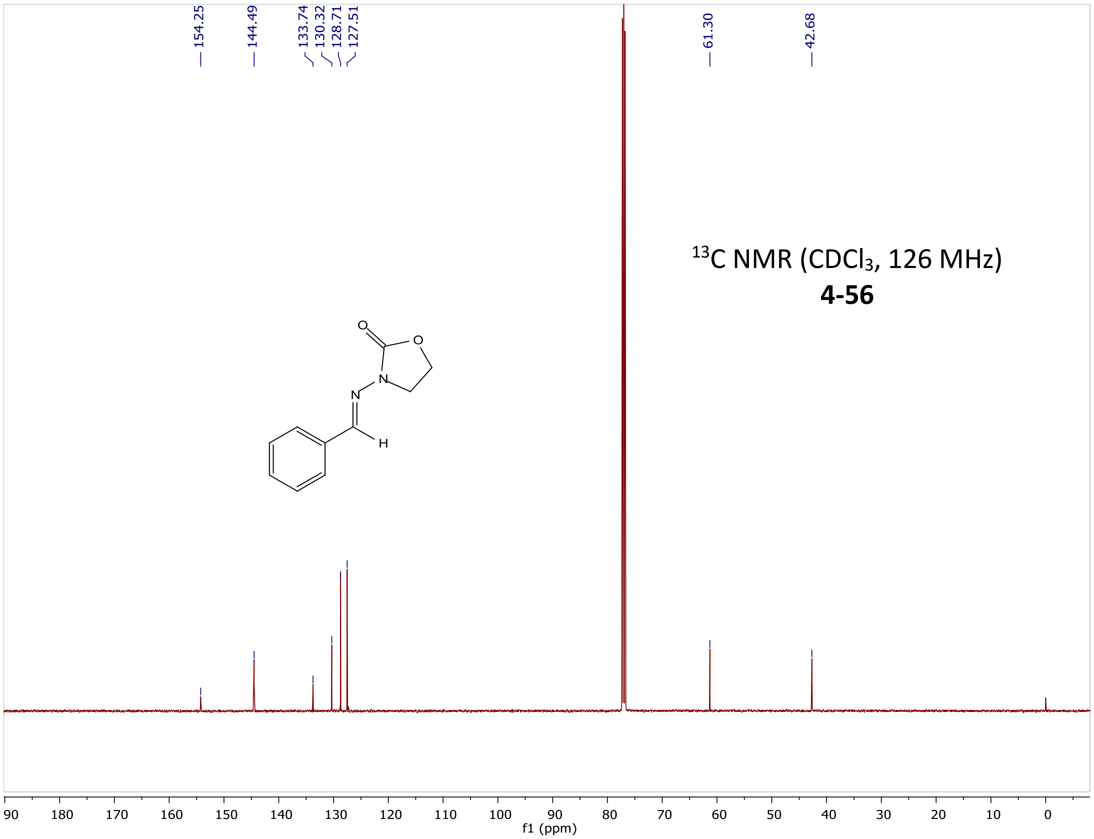
^{13}C NMR (CDCl$_3$, 126 MHz)

4-52



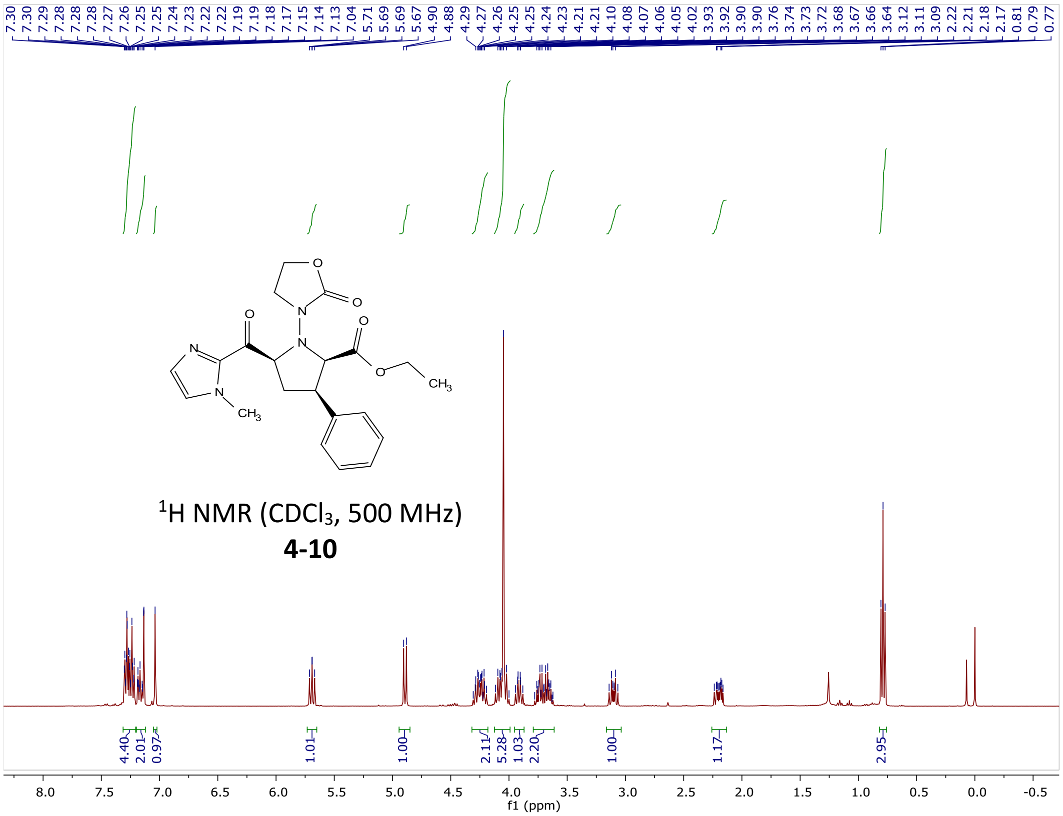
^{1}H NMR (CDCl$_3$, 500 MHz)

4-56



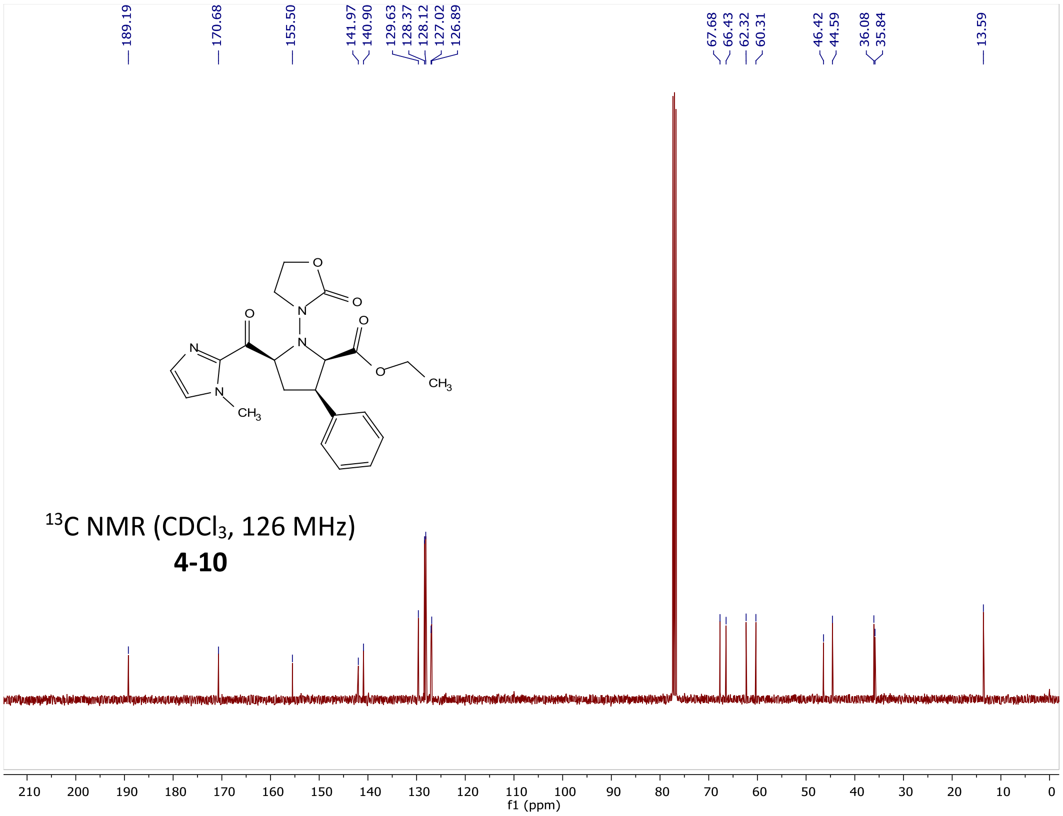
^{13}C NMR (CDCl$_3$, 126 MHz)

4-56



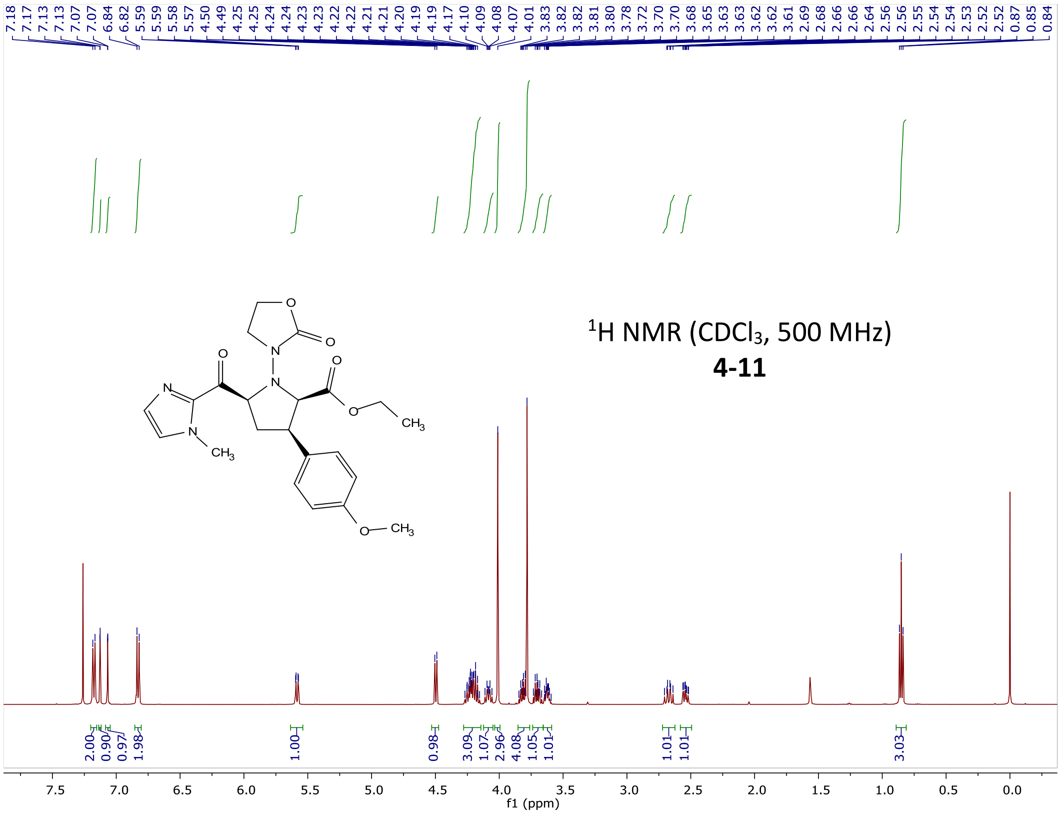
^{1}H NMR (CDCl$_3$, 500 MHz)

4-10



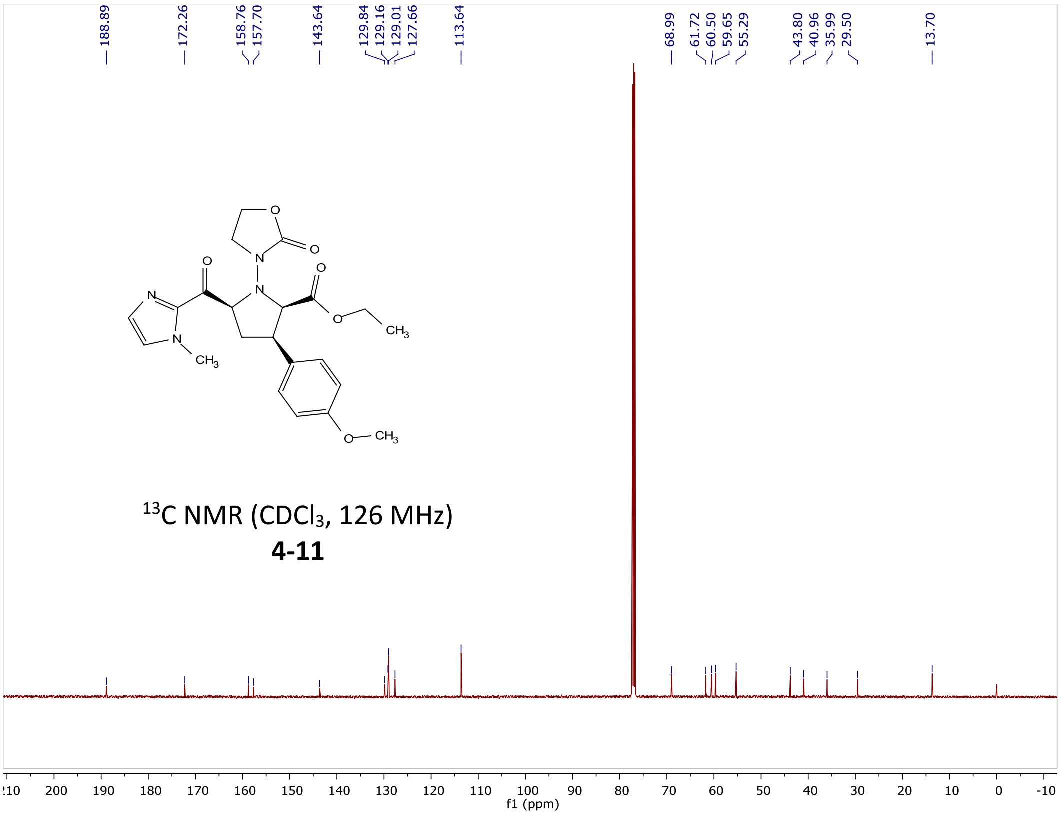
^{13}C NMR (CDCl$_3$, 126 MHz)

4-10



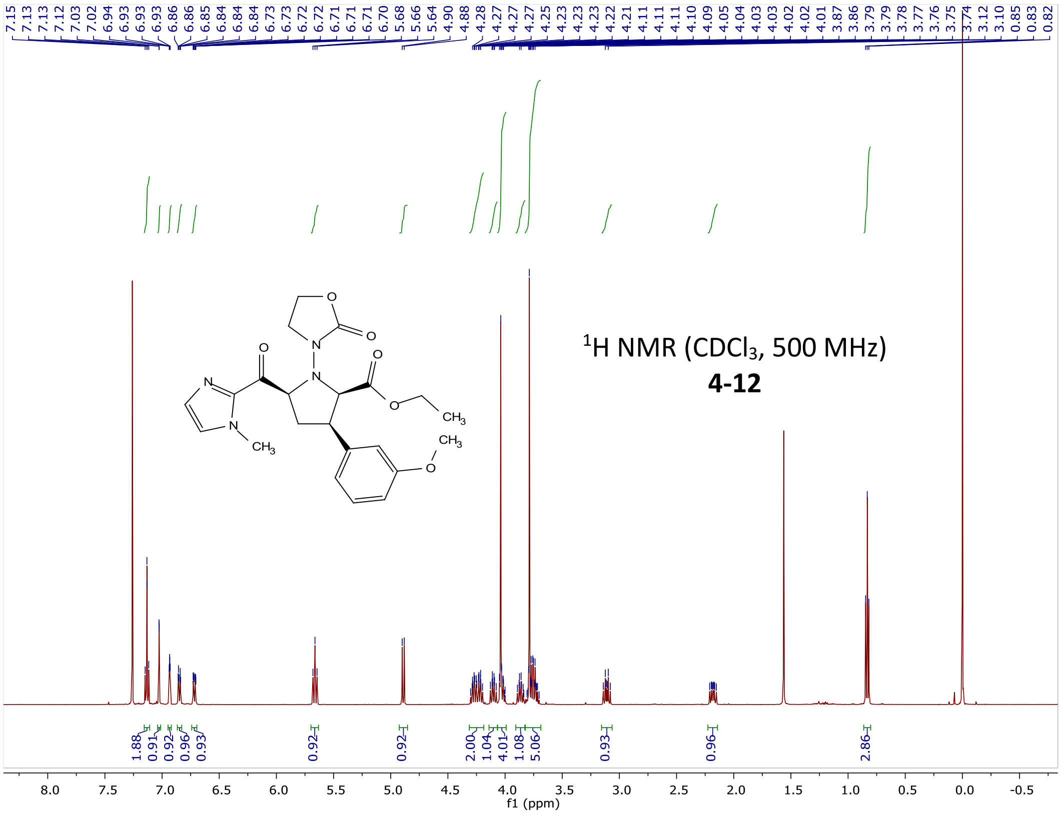
^{1}H NMR (CDCl$_3$, 500 MHz)

4-11



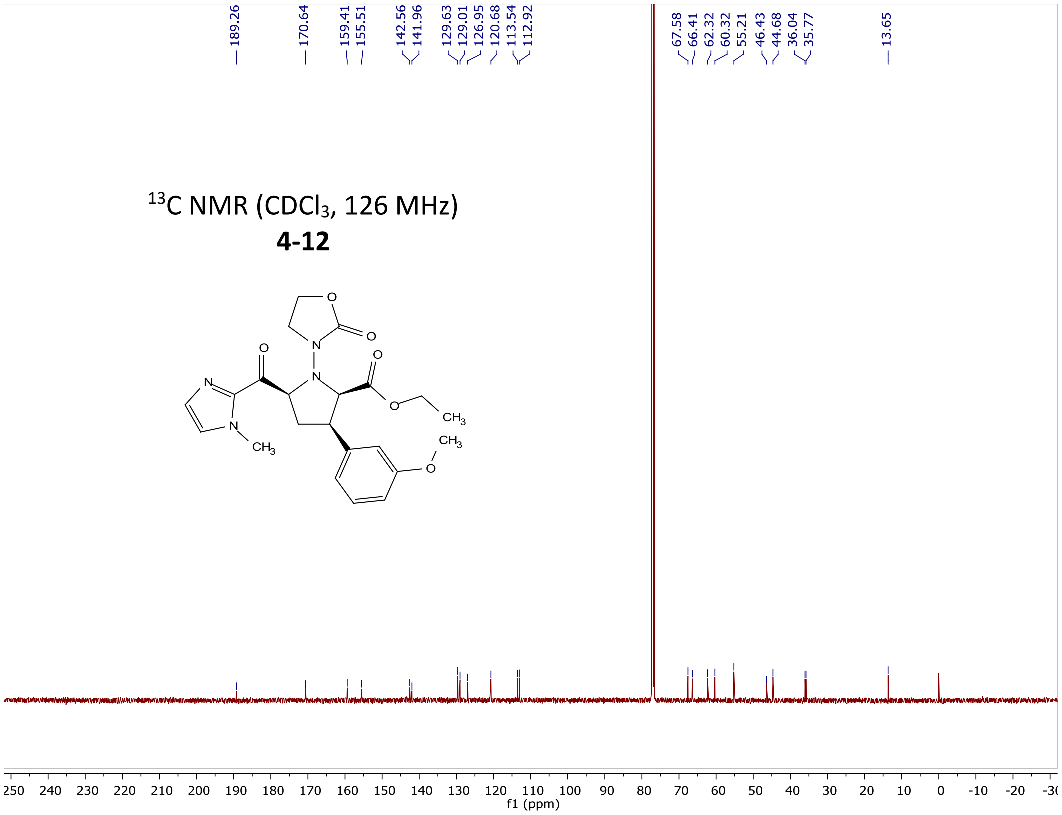
^{13}C NMR (CDCl$_3$, 126 MHz)

4-11



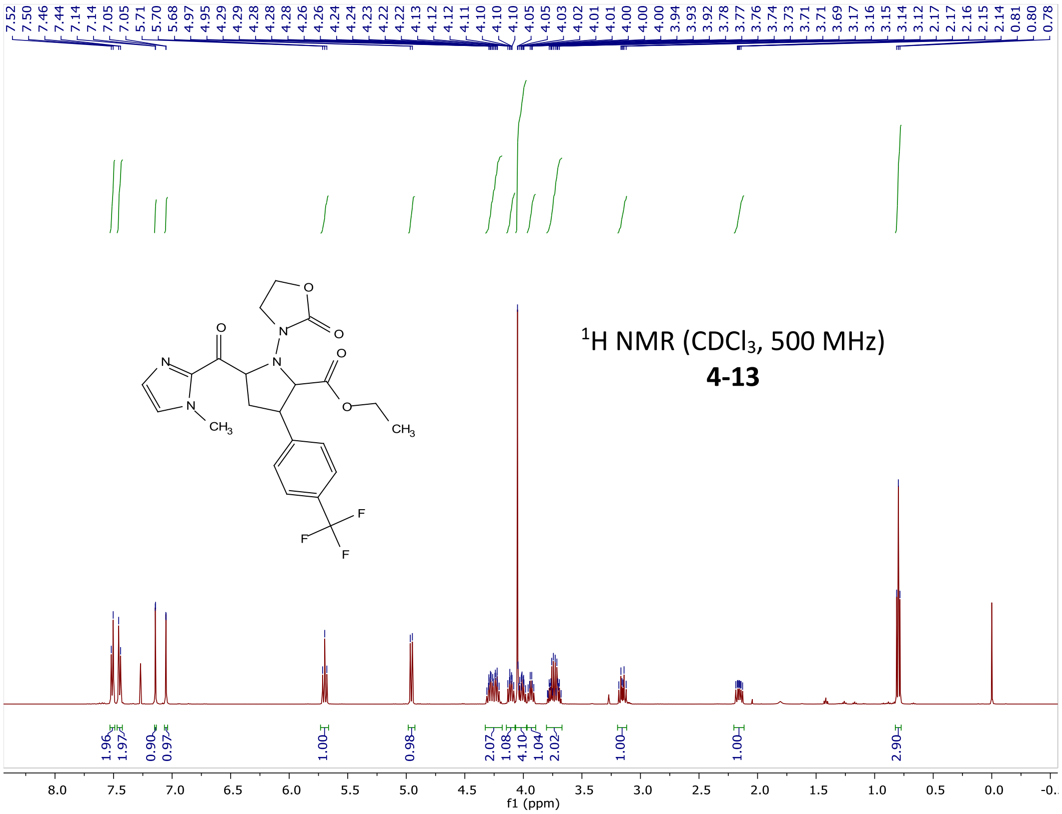
^{1}H NMR (CDCl$_3$, 500 MHz)

4-12



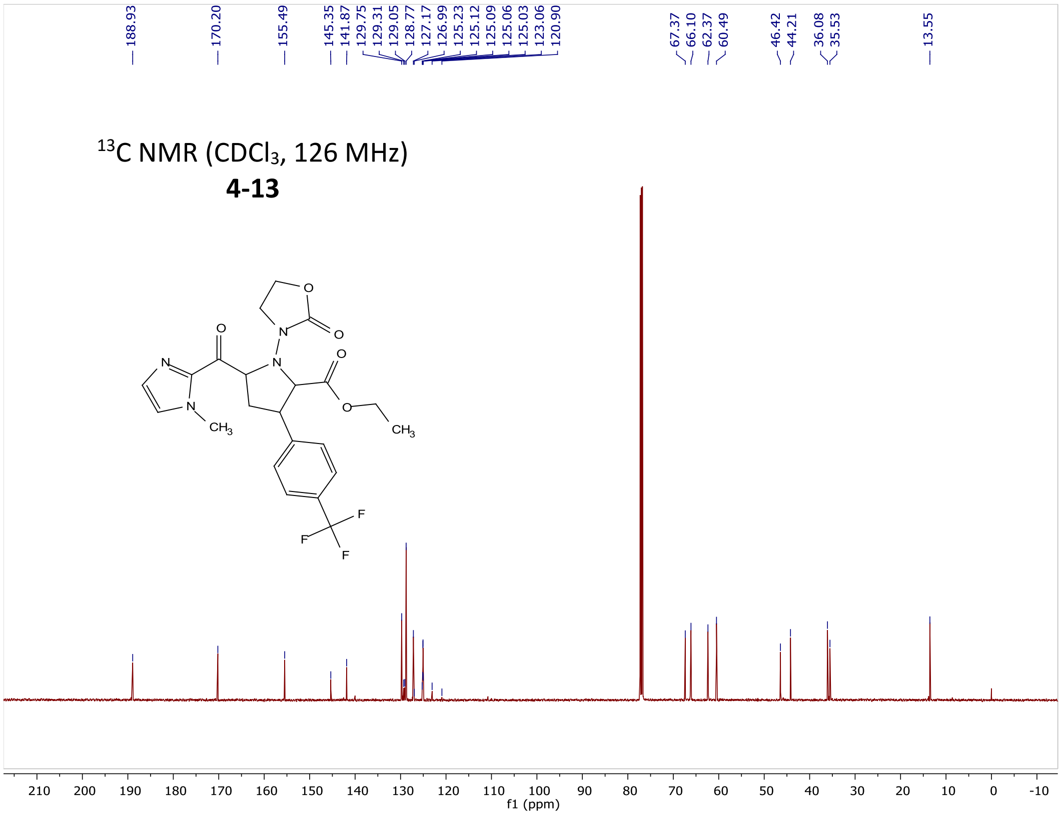
^{13}C NMR (CDCl$_3$, 126 MHz)

4-12



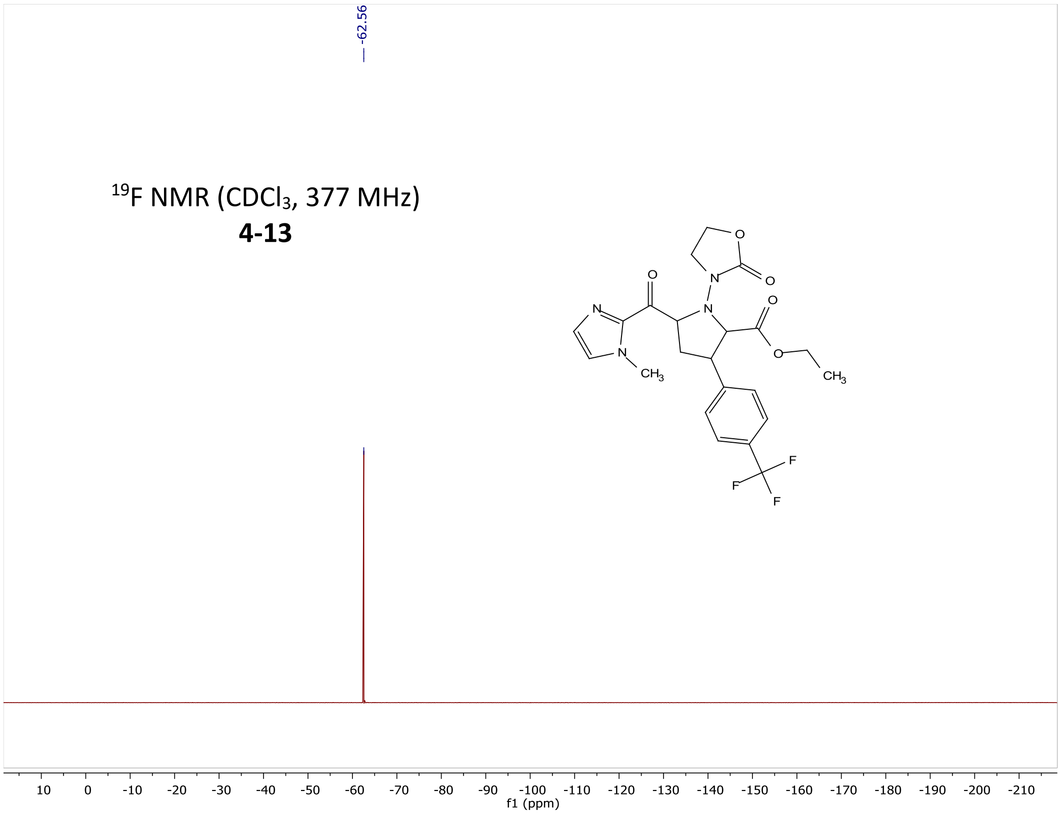
^{1}H NMR (CDCl$_3$, 500 MHz)

4-13



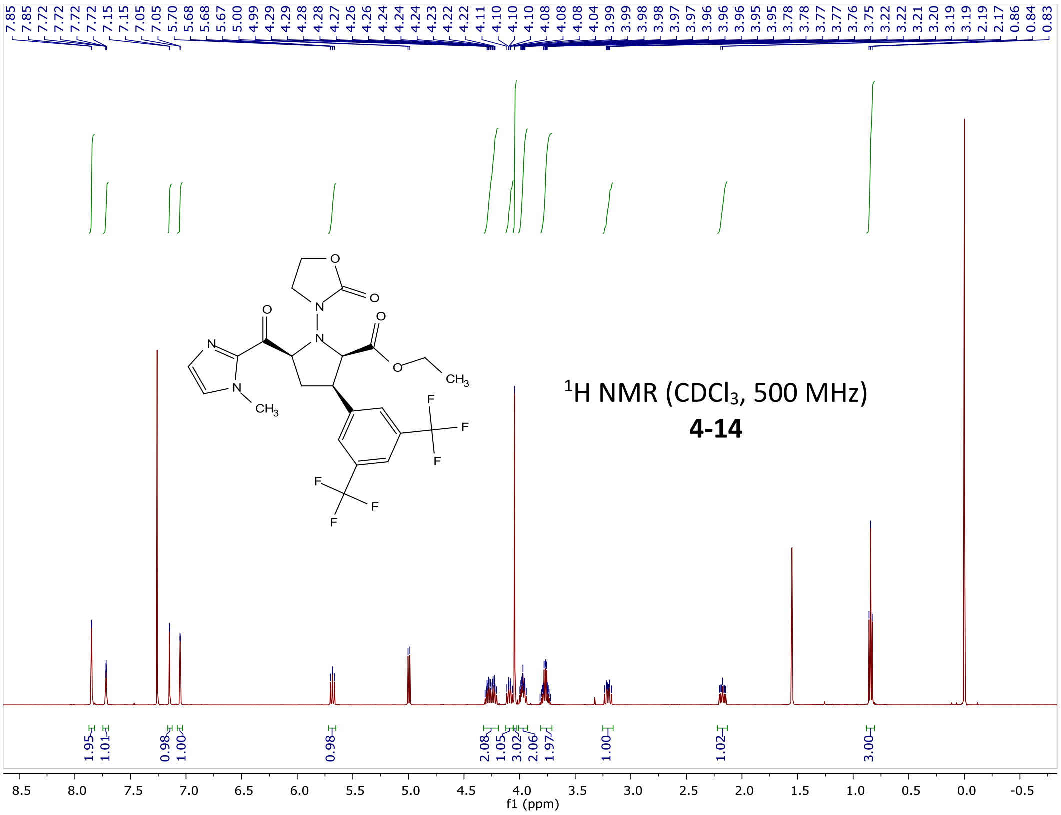
^{13}C NMR (CDCl$_3$, 126 MHz)

4-13



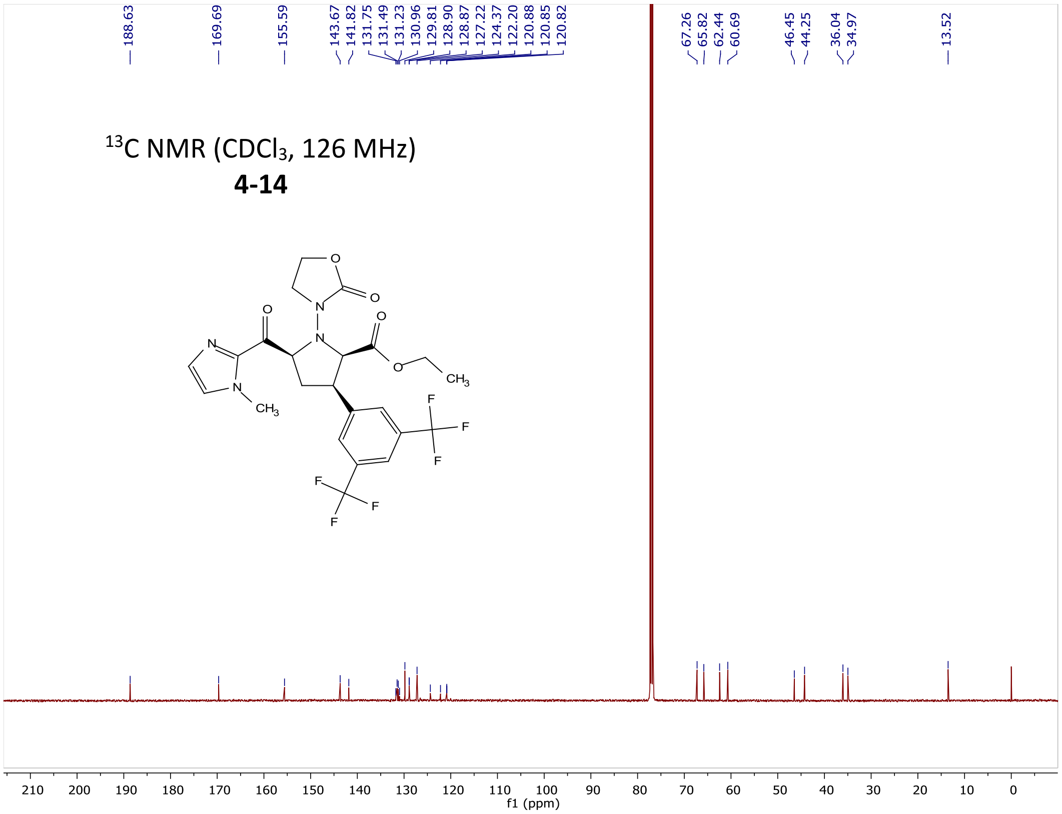
^{19}F NMR (CDCl$_3$, 377 MHz)

4-13



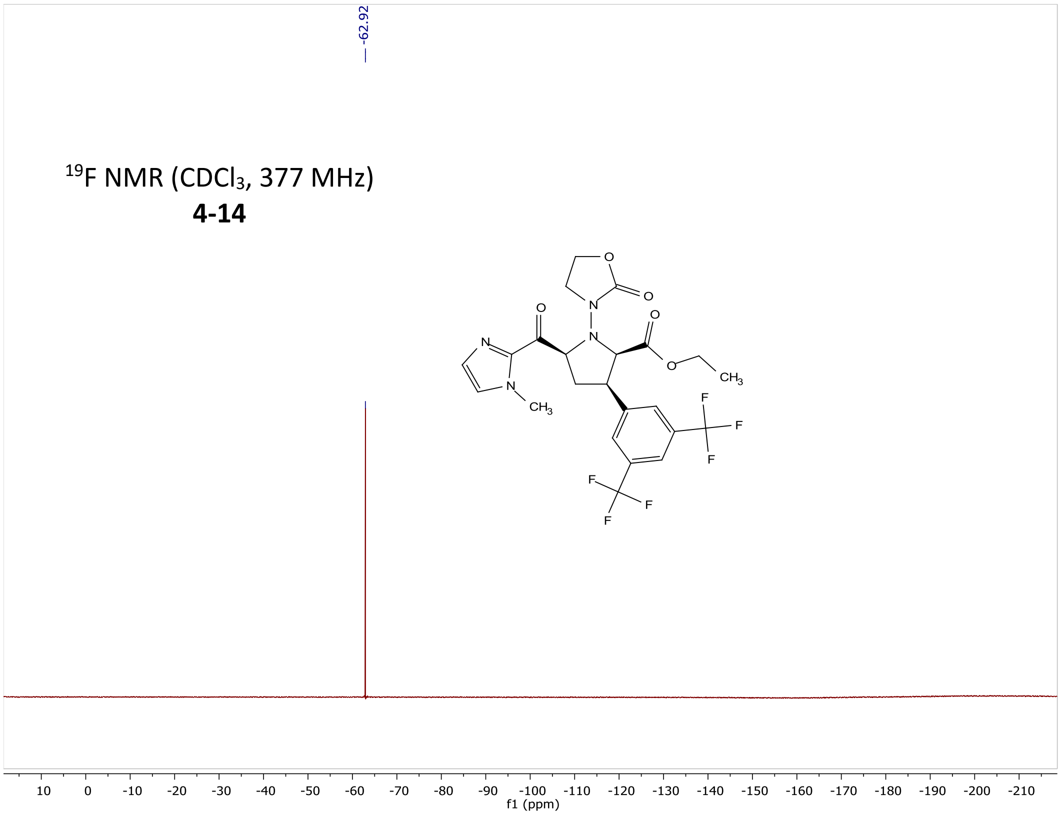
^{1}H NMR (CDCl$_3$, 500 MHz)

4-14



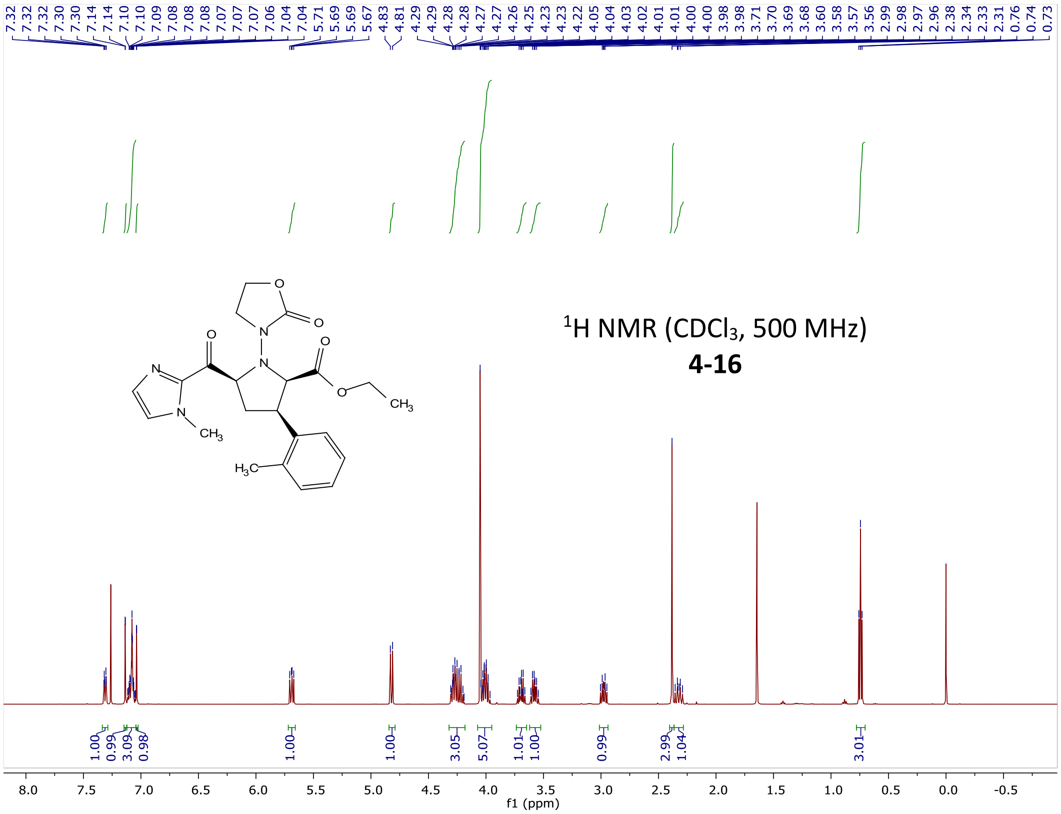
^{13}C NMR (CDCl$_3$, 126 MHz)

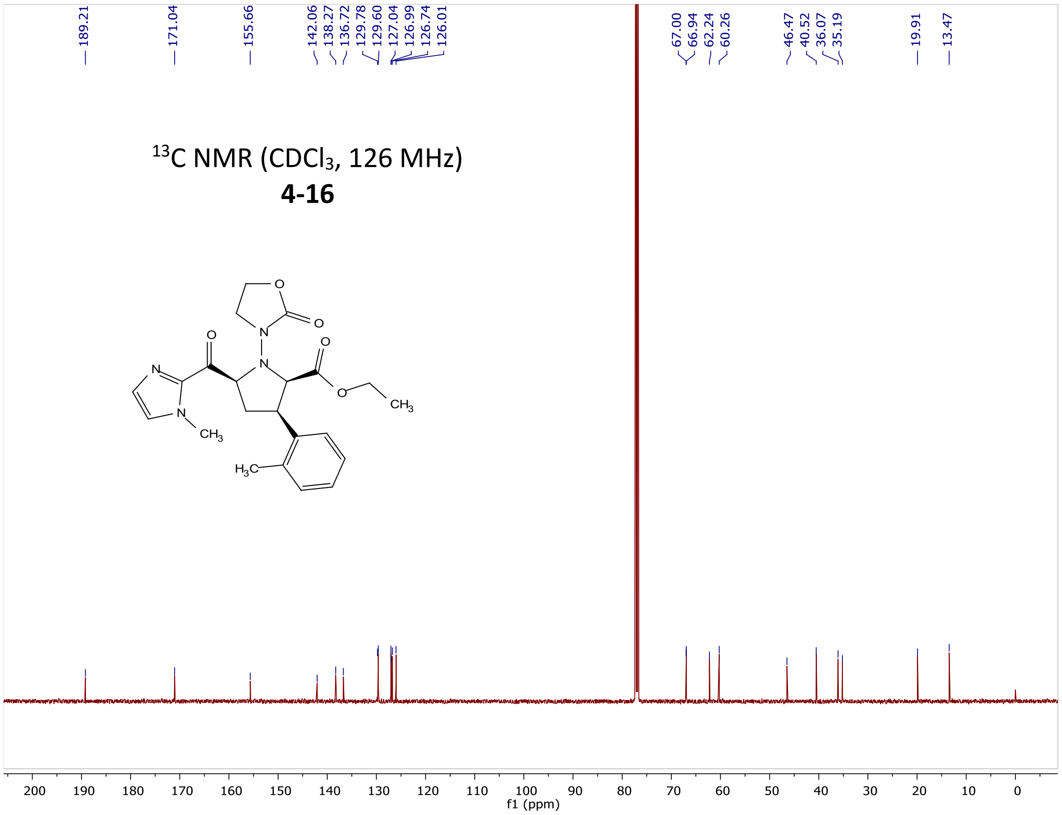
4-14

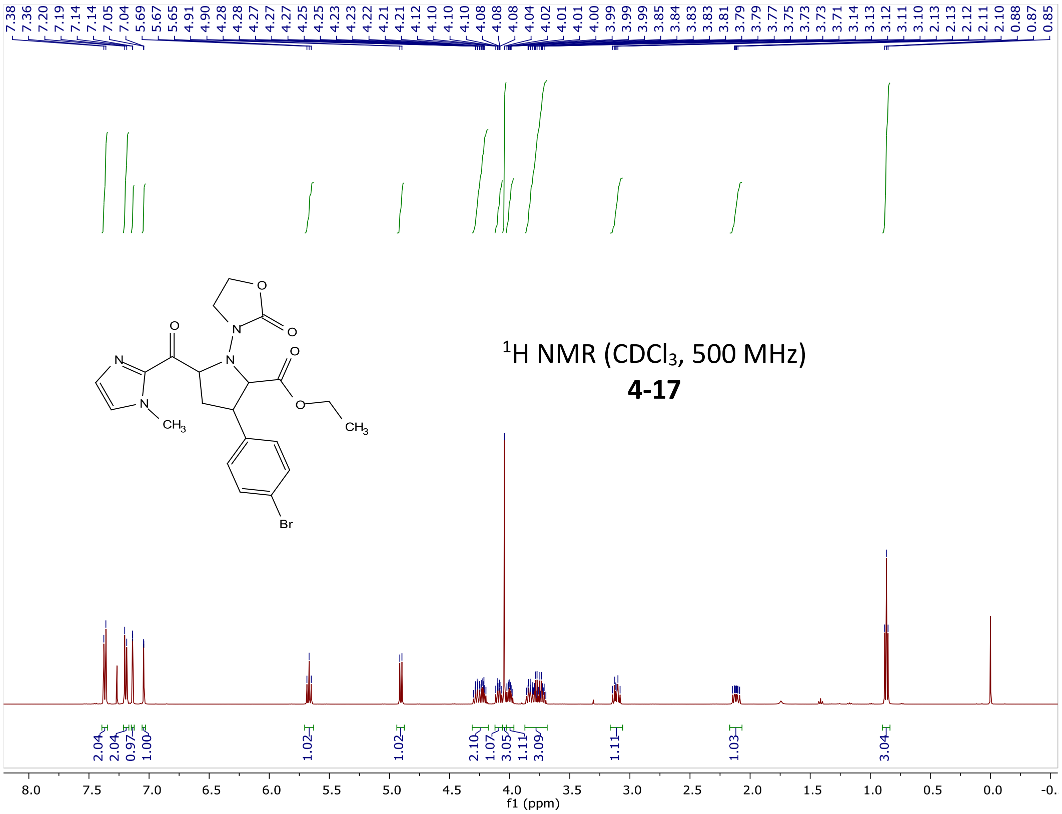


^{19}F NMR (CDCl$_3$, 377 MHz)

4-14

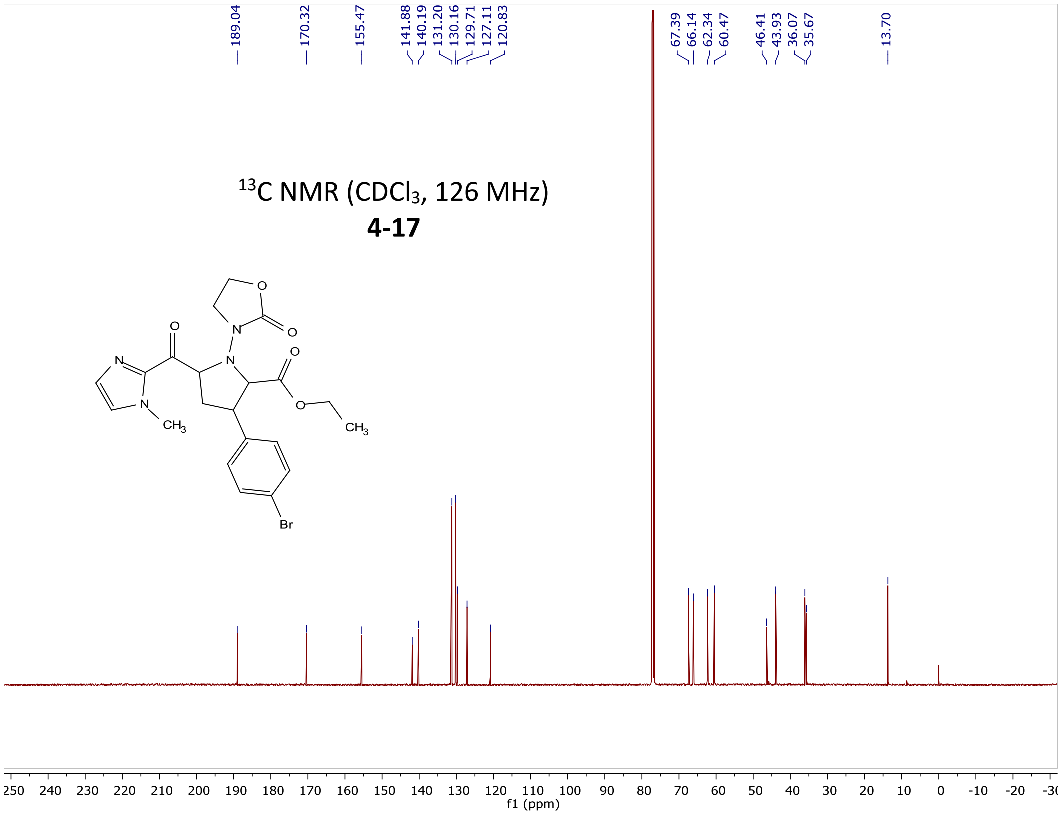

7.32
7.32
7.32
7.30
7.30
7.14
7.14
7.10
7.10
7.09
7.08
7.08
7.08
7.07
7.07
7.07
7.06
7.04
7.04
5.71
5.69
5.69
5.67
4.83
4.81
4.29
4.29
4.28
4.28
4.27
4.27
4.26
4.25
4.23
4.23
4.22
4.05
4.04
4.03
4.02
4.01
4.01
4.00
3.98
3.98
3.71
3.70
3.69
3.68
3.60
3.58
3.57
3.56
2.99
2.98
2.97
2.96
2.38
2.34
2.33
2.31
0.76
0.74
0.73
^{1}H NMR (CDCl$_3$, 500 MHz)
4-16
O
O
N
O
N
O
N
N
O
CH$_3$
CH$_3$
H$_3$C
1.00
0.99
3.09
0.98
1.00
1.00
3.05
5.07
1.01
1.00
0.99
2.99
1.04
3.01
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)


189.21
171.04
155.66
142.06
138.27
136.72
129.78
129.60
127.04
126.99
126.74
126.01
67.00
66.94
62.24
60.26
46.47
40.52
36.07
35.19
19.91
13.47
^{13}C NMR (CDCl$_3$, 126 MHz)
4-16
O
O
N
O
N
O
N
N
O
CH$_3$
CH$_3$
H$_3$C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



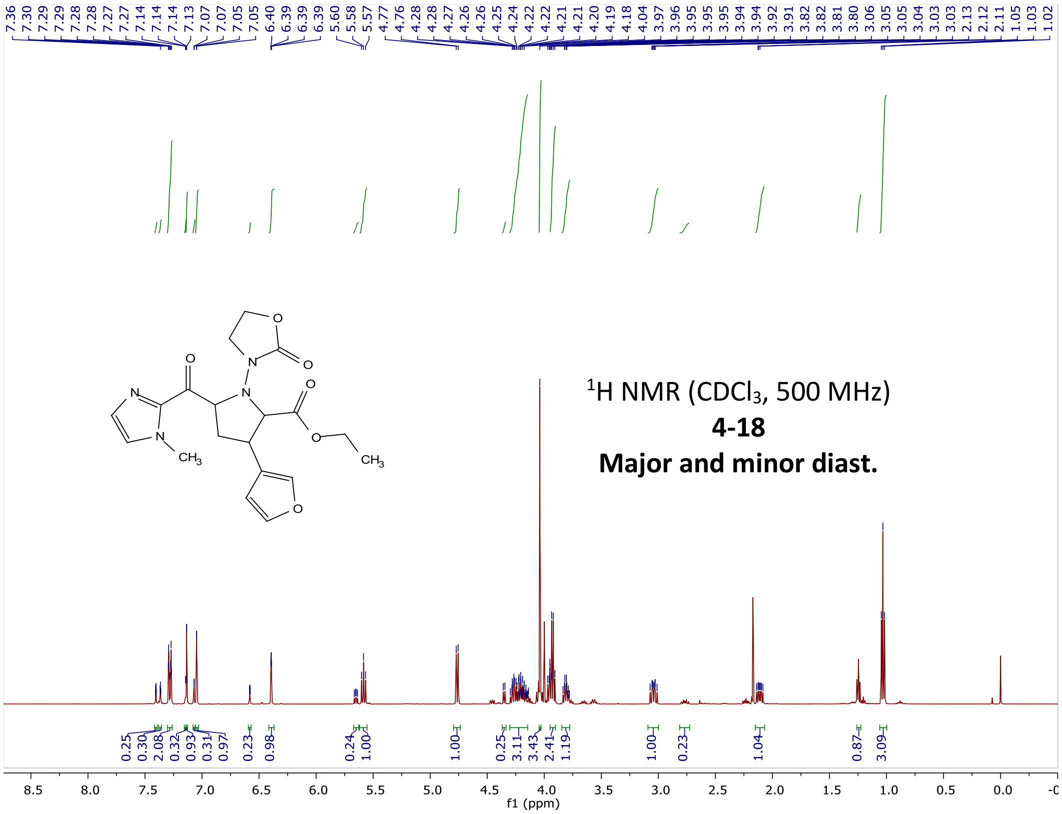
^{1}H NMR (CDCl$_3$, 500 MHz)

4-17



^{13}C NMR (CDCl$_3$, 126 MHz)

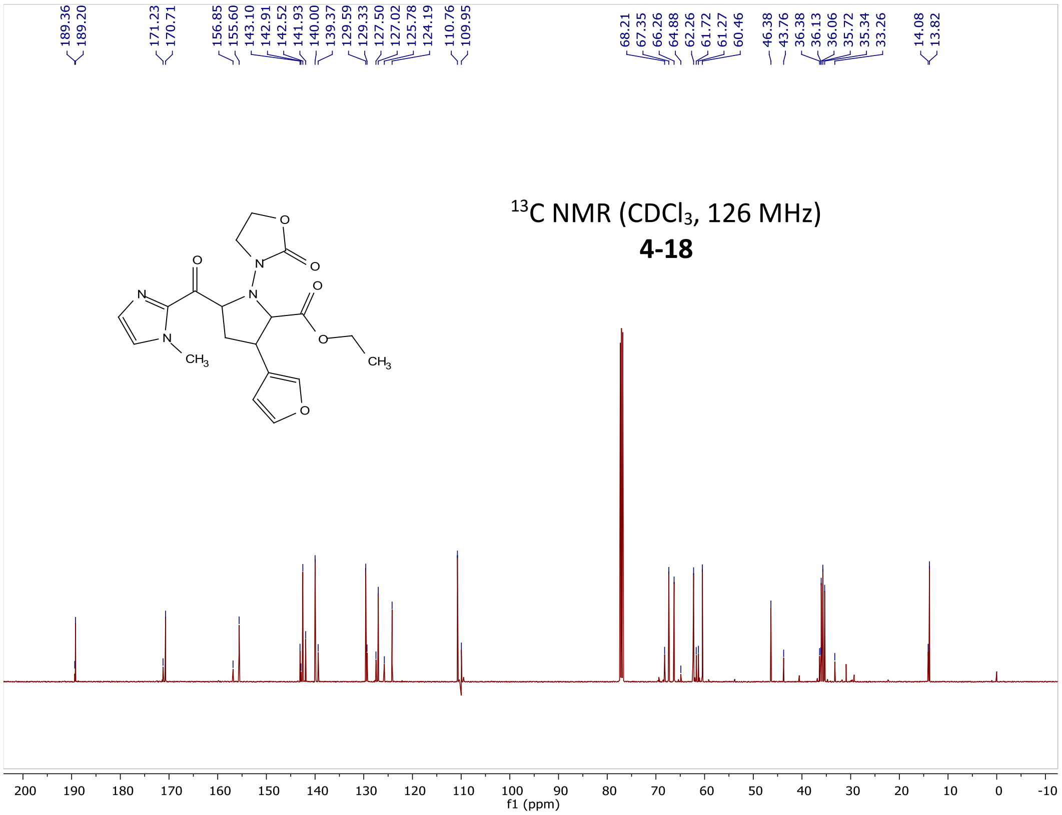
4-17



^{1}H NMR (CDCl$_3$, 500 MHz)

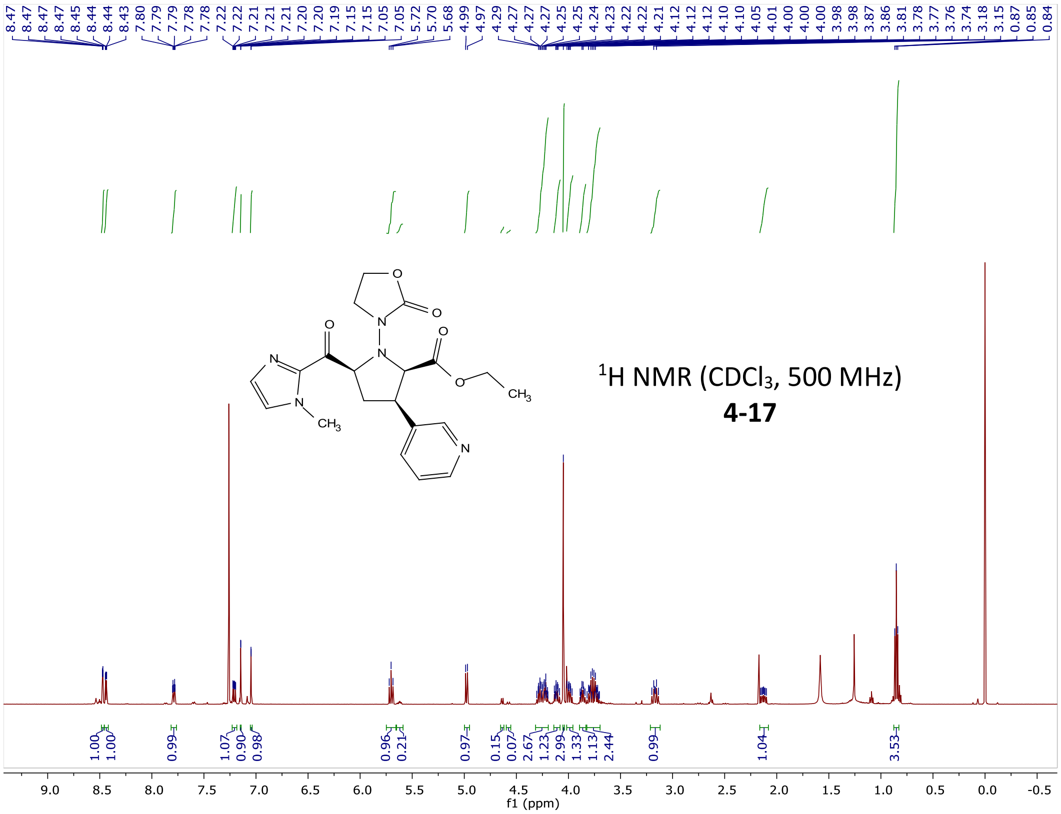
4-18

Major and minor diast.



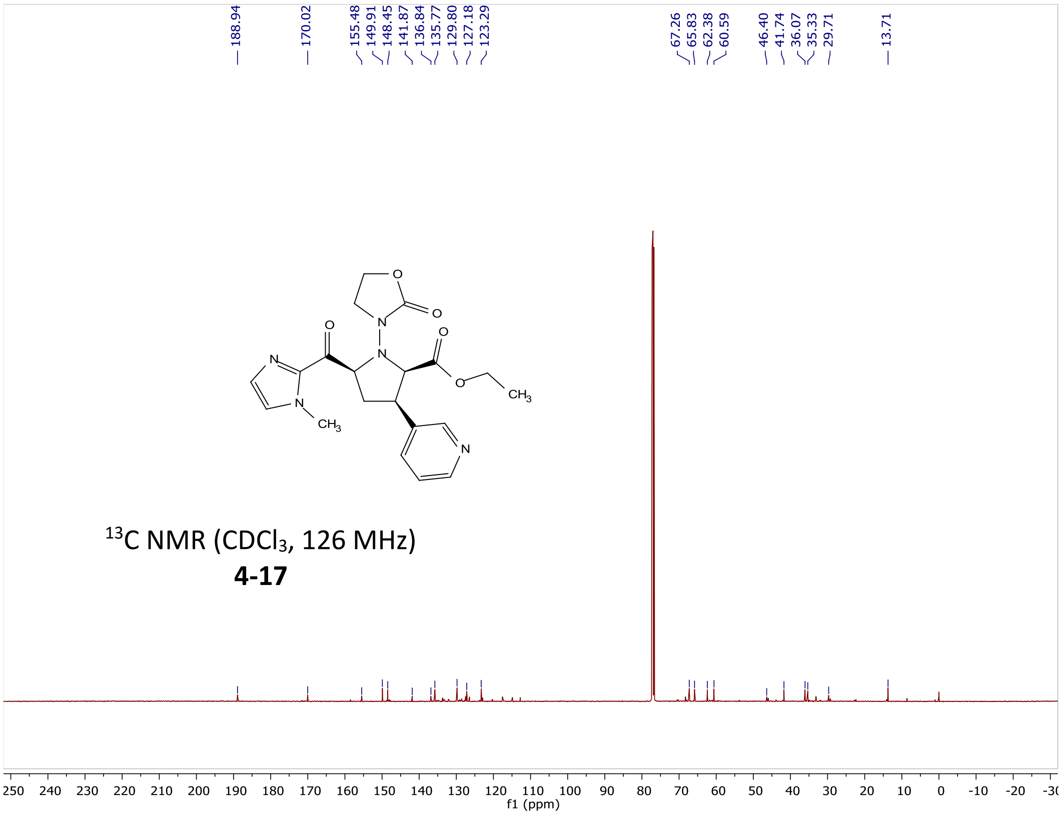
^{13}C NMR (CDCl$_3$, 126 MHz)

4-18



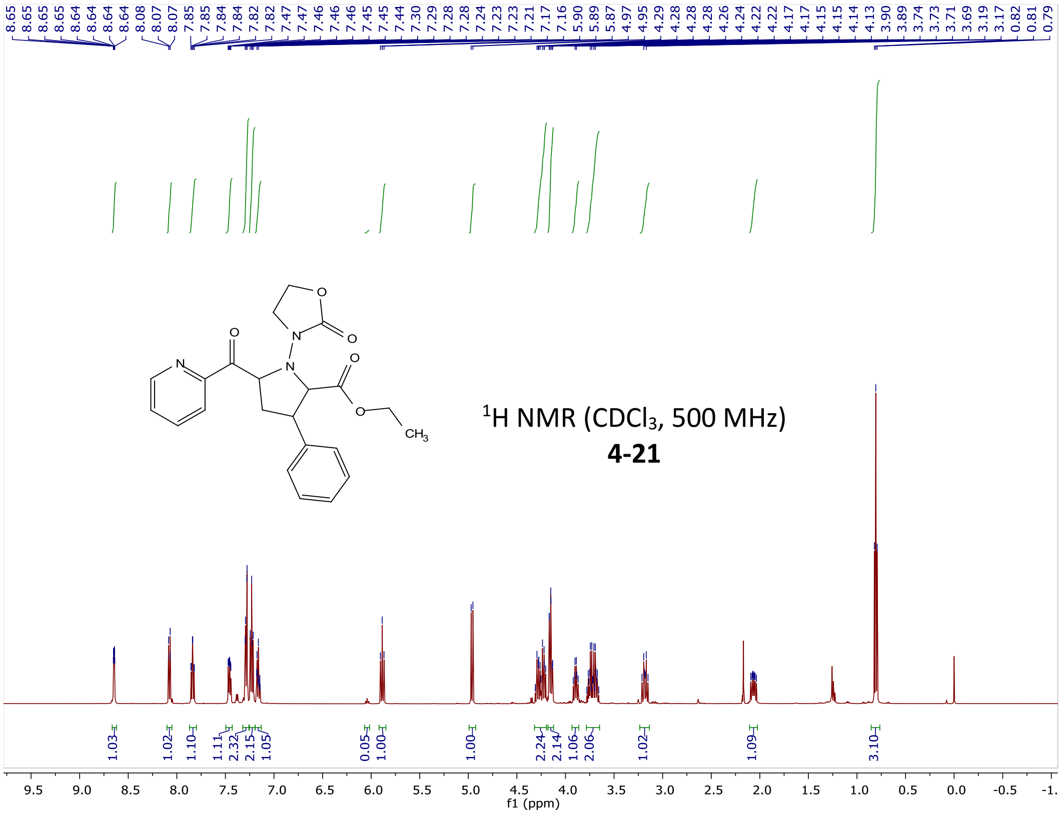
^{1}H NMR (CDCl$_3$, 500 MHz)

4-17



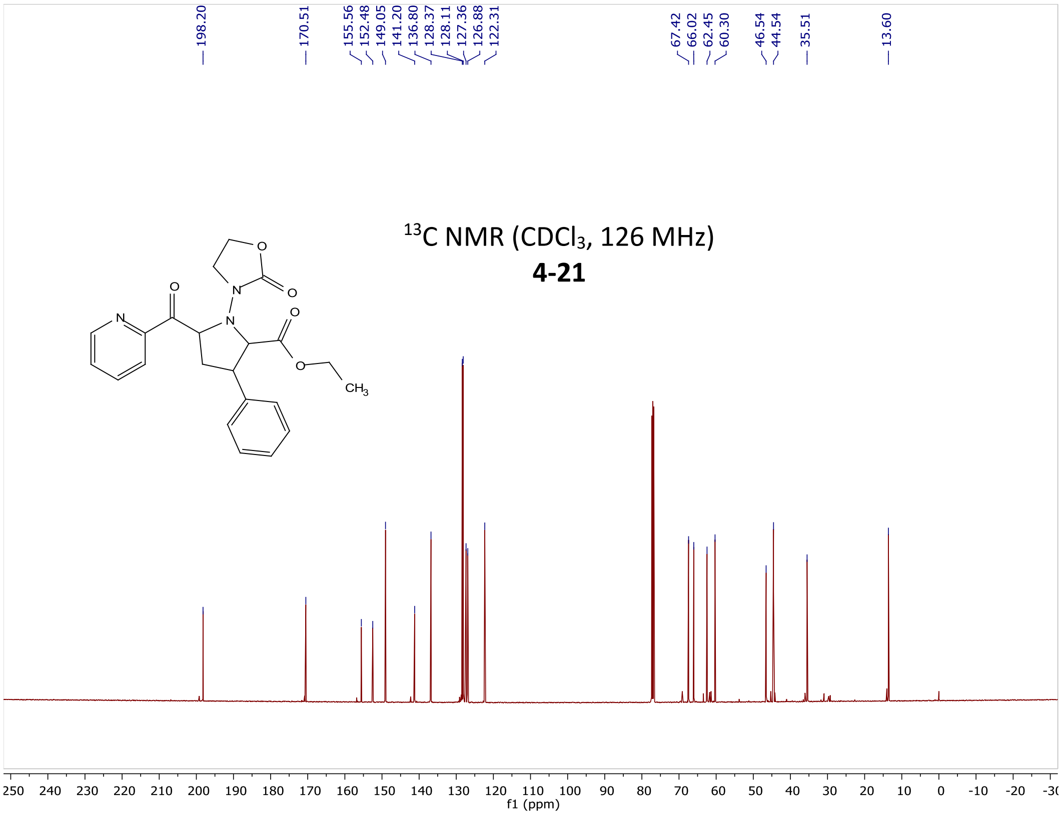
^{13}C NMR (CDCl$_3$, 126 MHz)

4-17



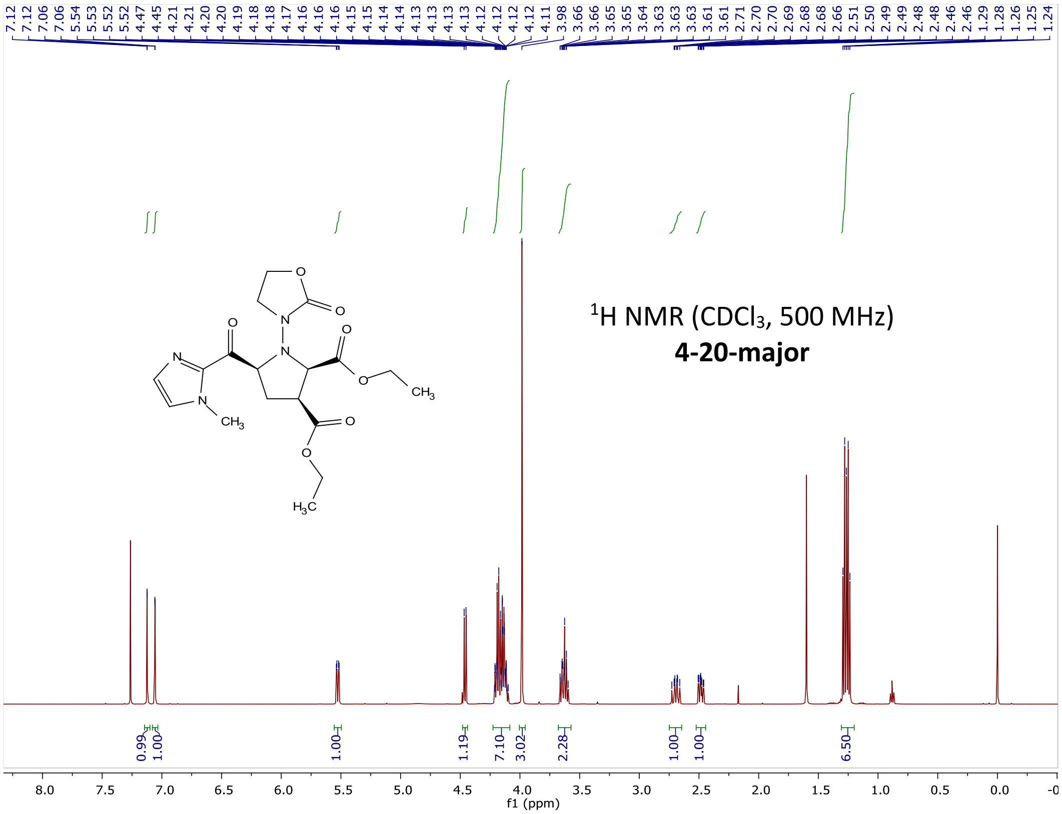
^{1}H NMR (CDCl$_3$, 500 MHz)

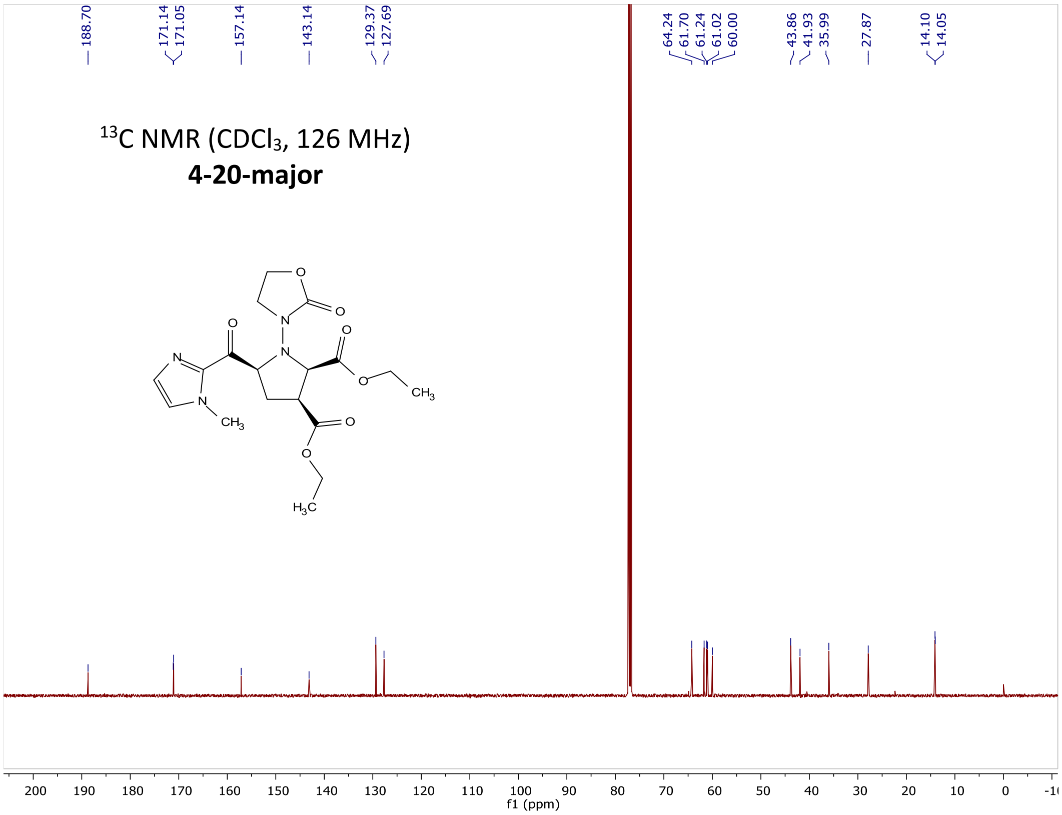
4-21

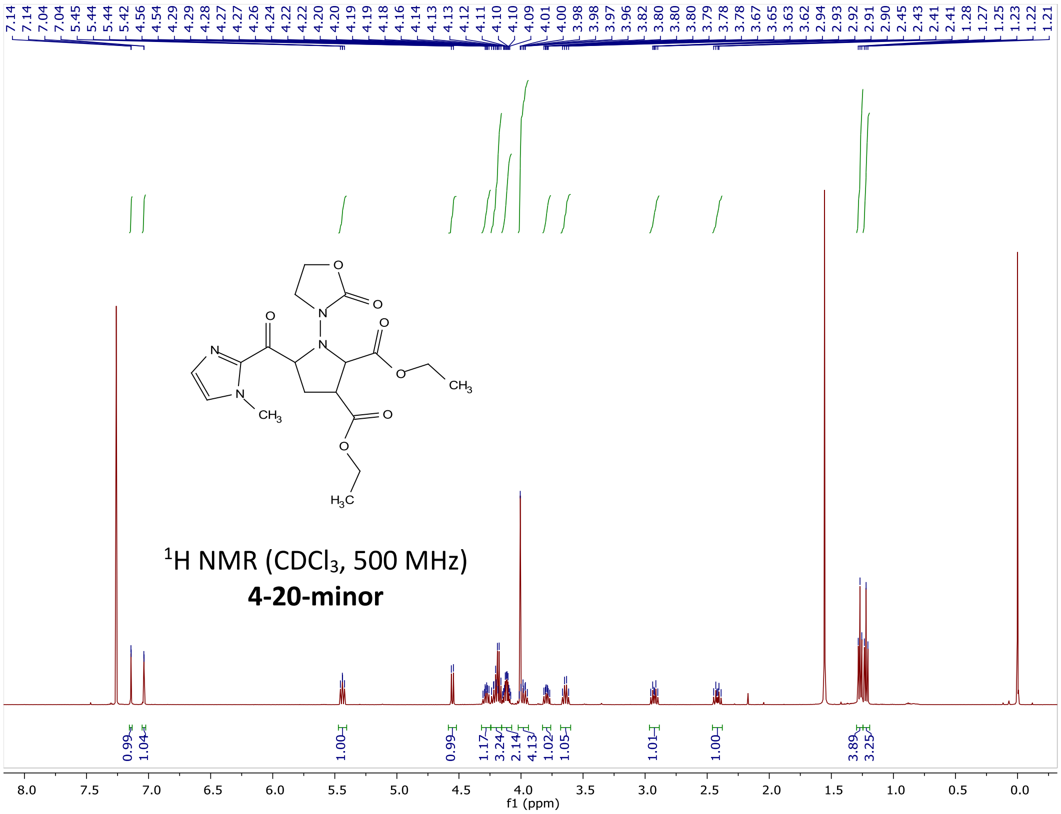


^{13}C NMR (CDCl$_3$, 126 MHz)

4-21

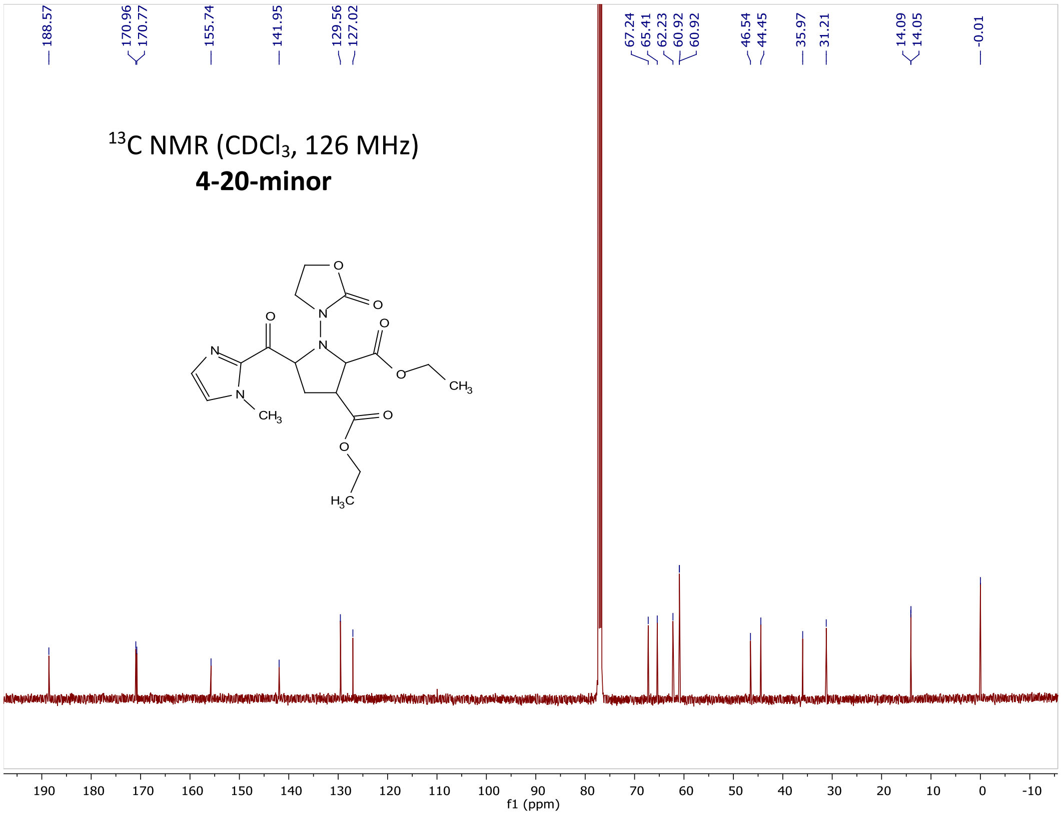

7.12
7.12
7.06
5.54
5.53
5.52
5.52
4.47
4.45
4.21
4.21
4.20
4.20
4.19
4.18
4.18
4.17
4.16
4.16
4.16
4.15
4.15
4.14
4.14
4.13
4.13
4.13
4.13
4.12
4.12
4.12
4.12
4.11
3.98
3.66
3.65
3.65
3.64
3.63
3.63
3.63
3.61
3.61
3.61
2.71
2.70
2.70
2.69
2.68
2.68
2.66
2.51
2.50
2.49
2.49
2.48
2.48
2.46
2.46
1.29
1.28
1.26
1.25
1.24
^{1}H NMR (CDCl$_3$, 500 MHz)
4-20-major
0.99
1.00
1.00
1.19
7.10
3.02
2.28
1.00
1.00
6.50
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
f1 (ppm)


188.70
171.14
171.05
157.14
143.14
129.37
127.69
64.24
61.70
61.24
61.02
60.00
43.86
41.93
35.99
27.87
14.10
14.05
^{13}C NMR (CDCl$_3$, 126 MHz)
4-20-major
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)



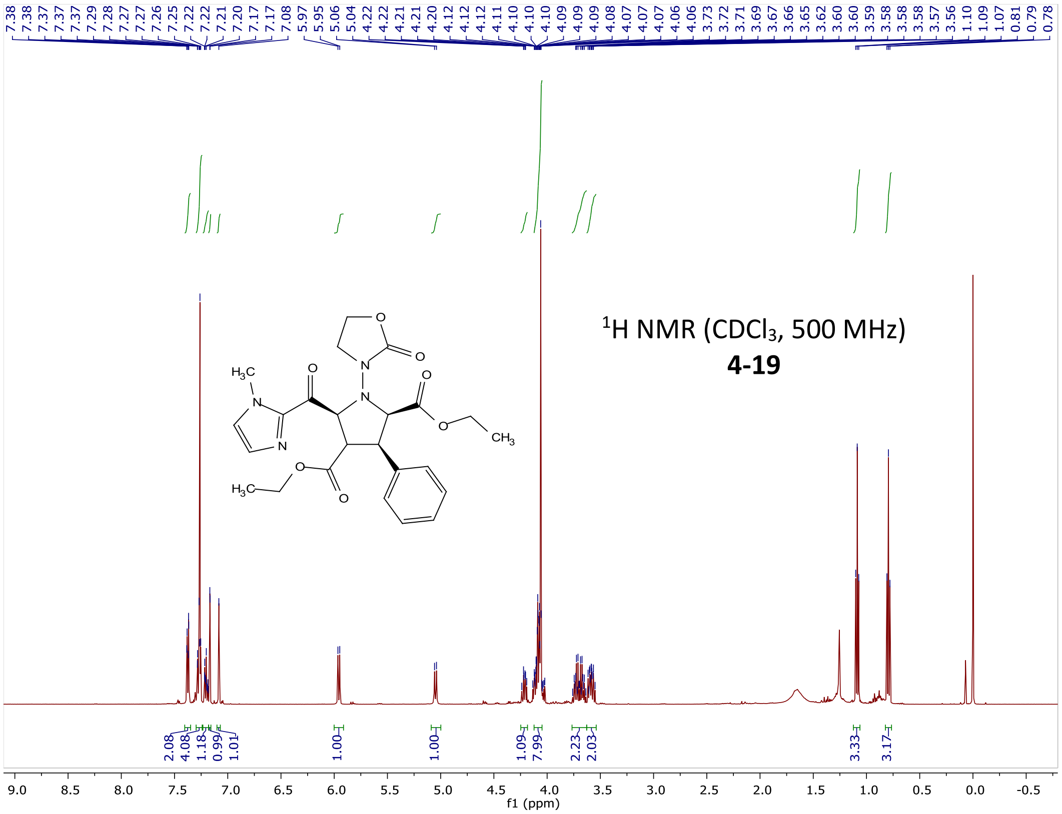
^{1}H NMR (CDCl$_3$, 500 MHz)

4-20-minor



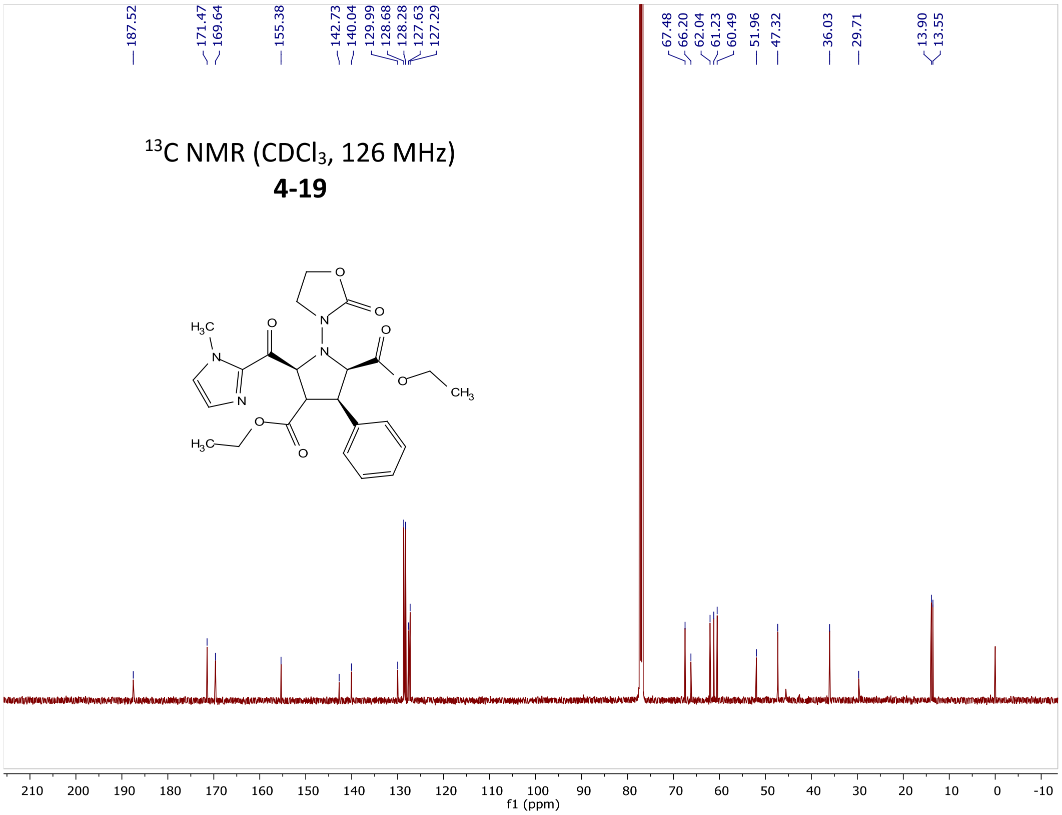
^{13}C NMR (CDCl$_3$, 126 MHz)

4-20-minor



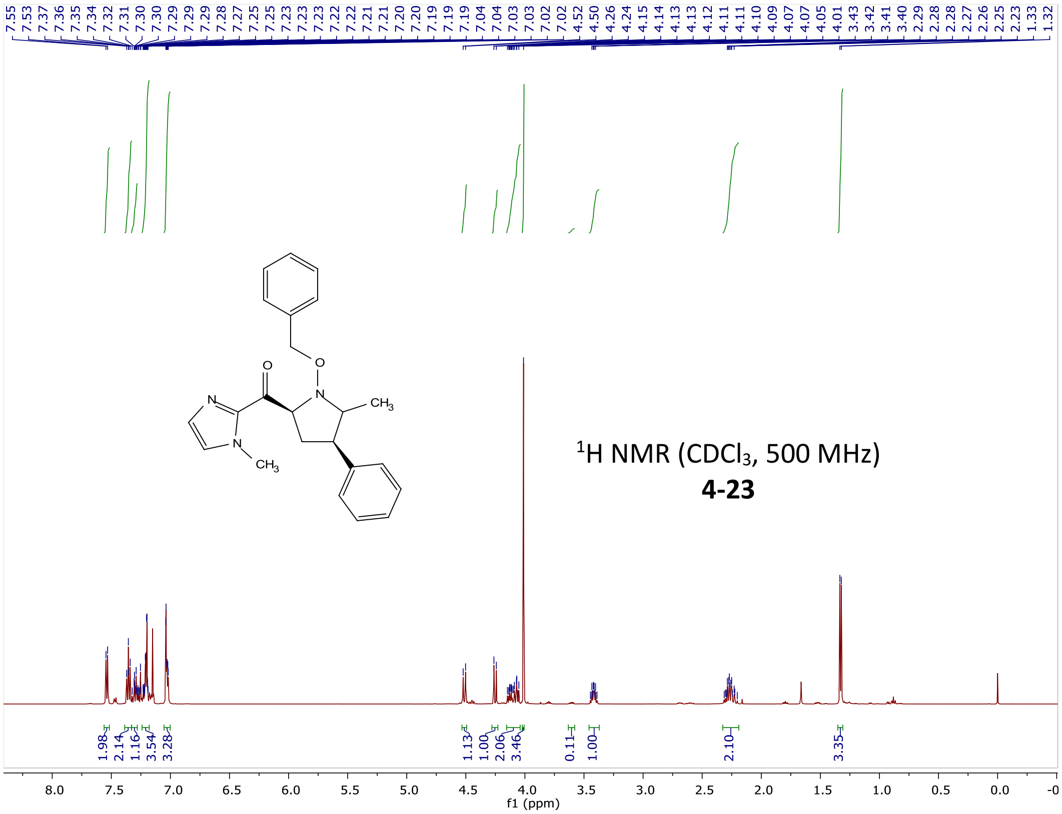
^{1}H NMR (CDCl$_3$, 500 MHz)

4-19



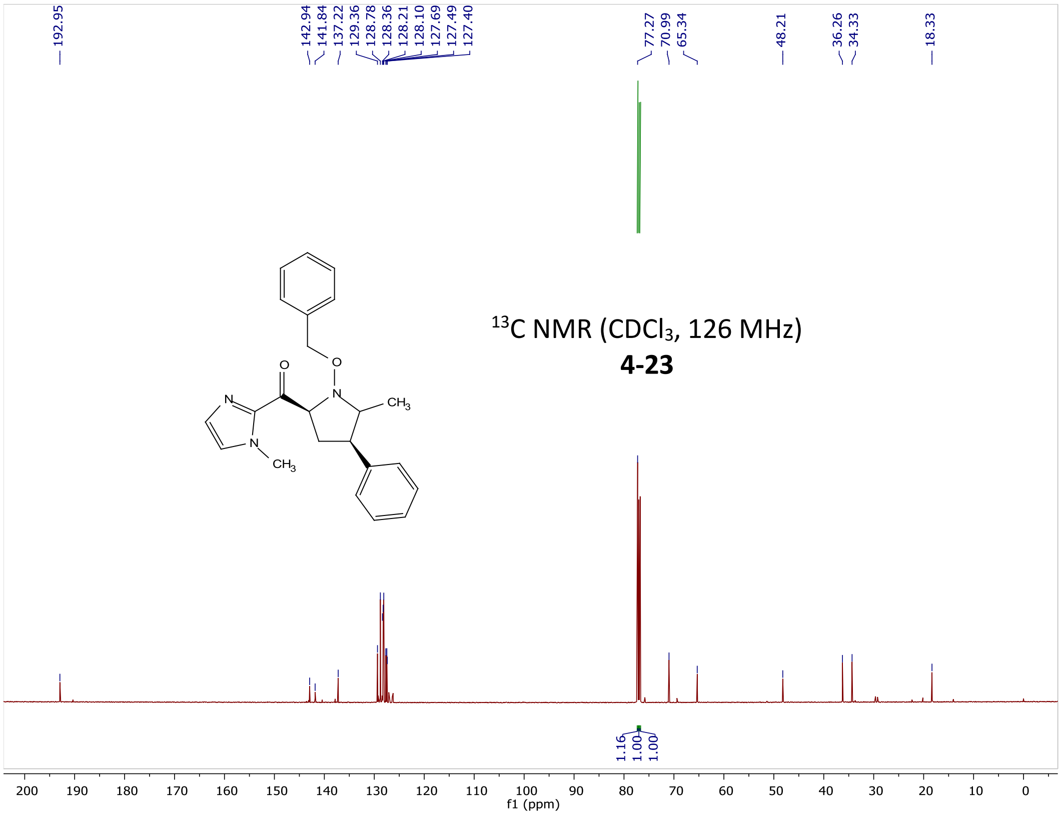
^{13}C NMR (CDCl$_3$, 126 MHz)

4-19



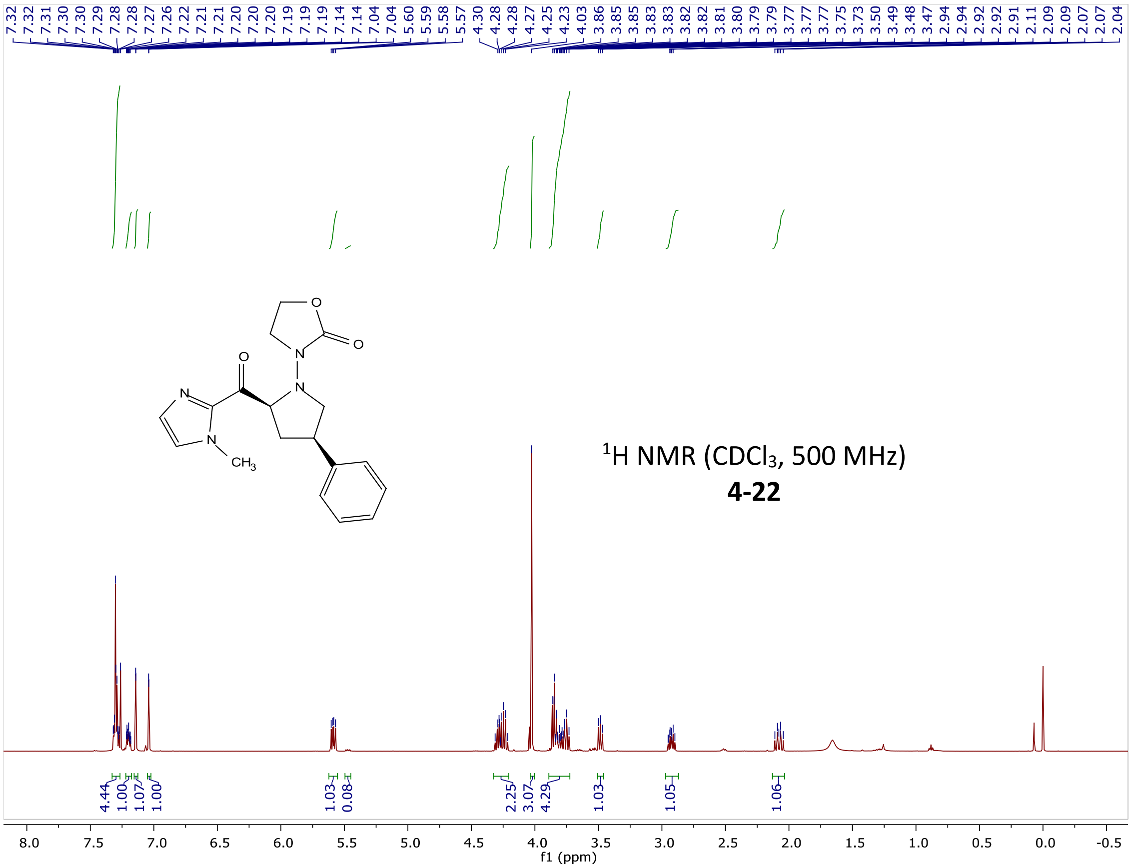
^{1}H NMR (CDCl$_3$, 500 MHz)

4-23



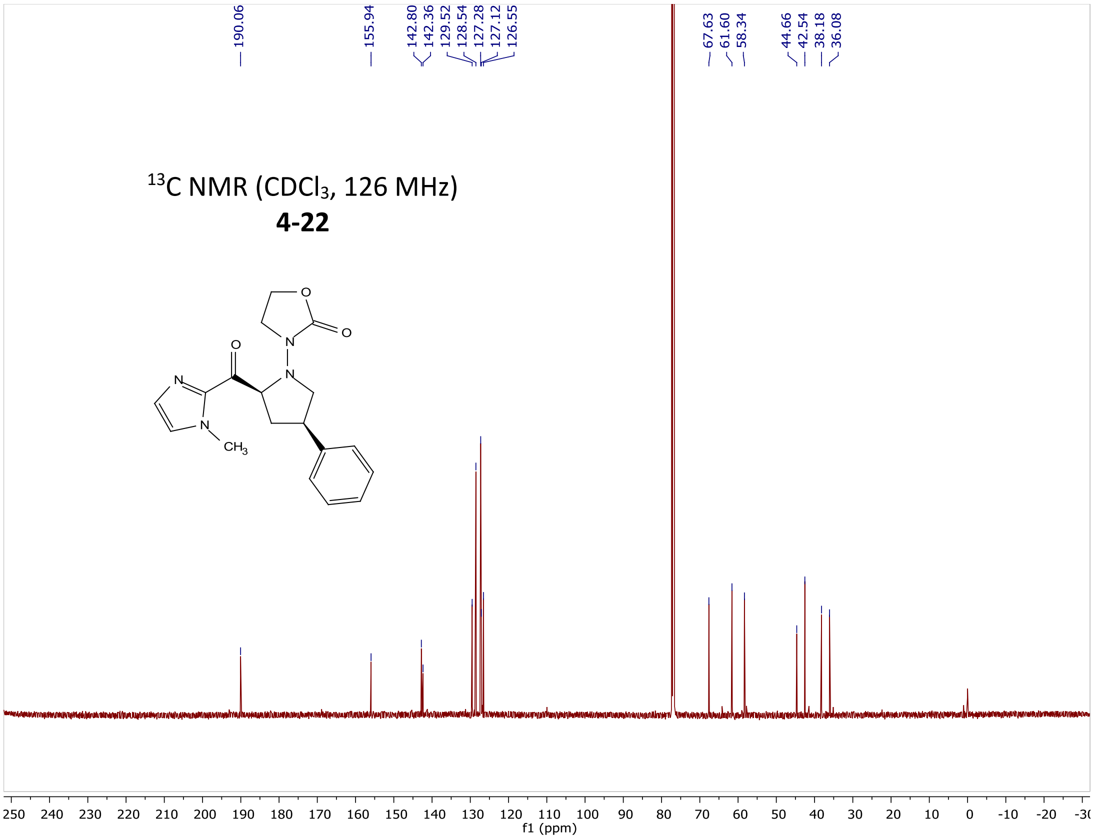
^{13}C NMR (CDCl$_3$, 126 MHz)

4-23



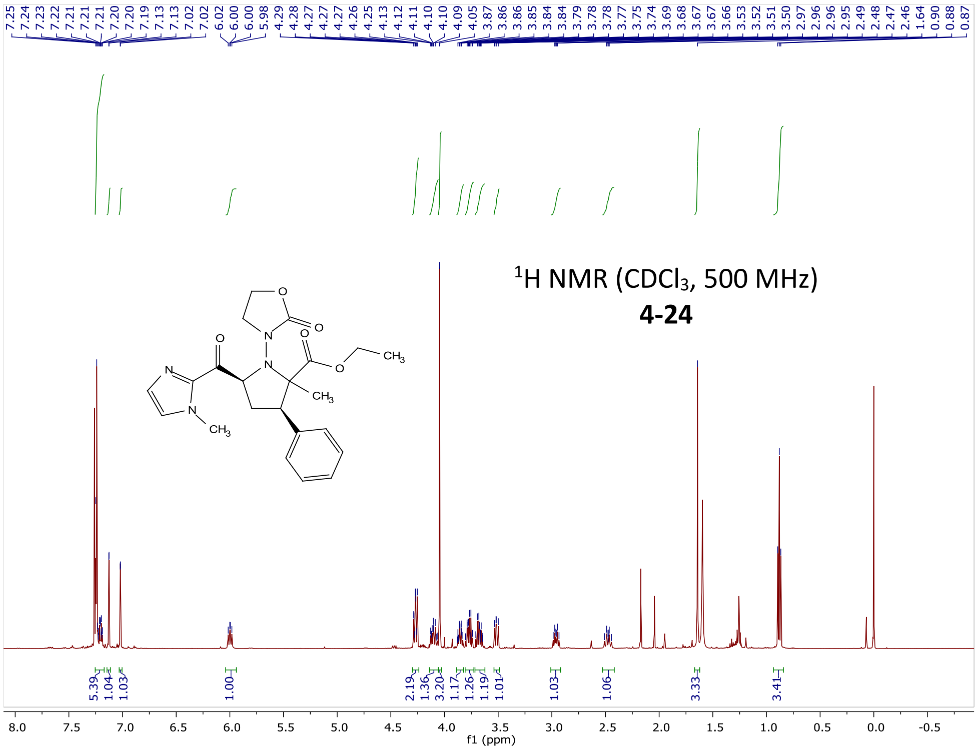
^{1}H NMR (CDCl$_3$, 500 MHz)

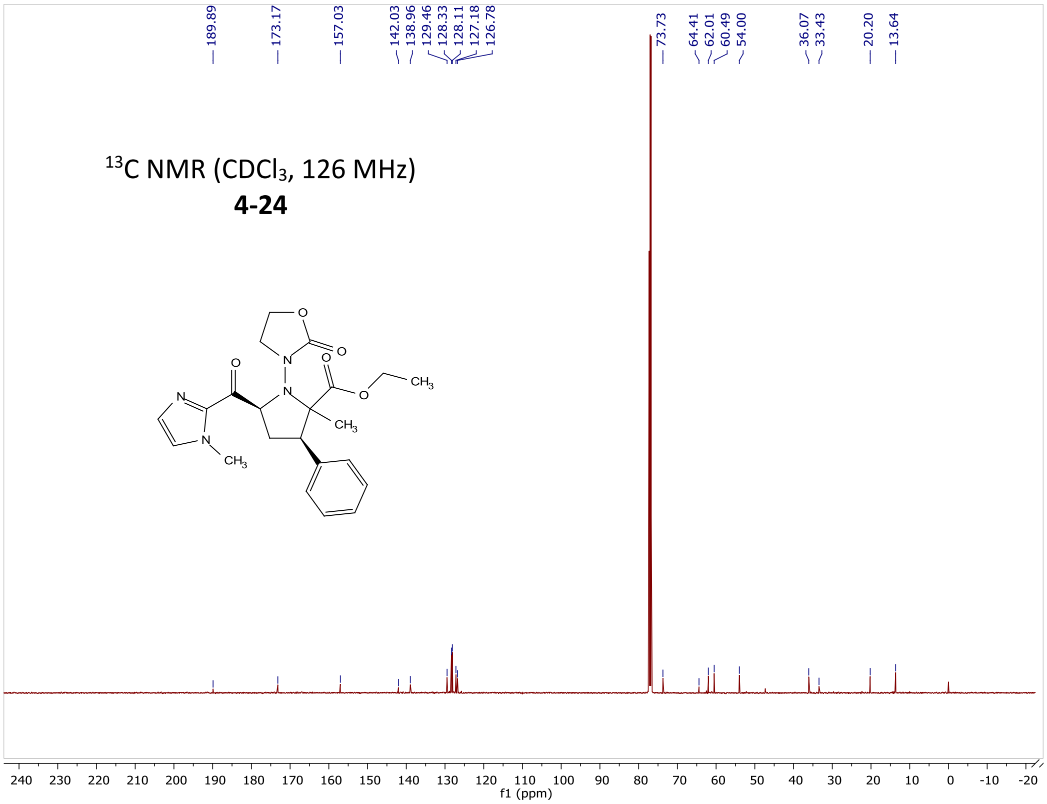
4-22



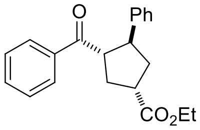
^{13}C NMR (CDCl$_3$, 126 MHz)

4-22


7.25
7.24
7.23
7.22
7.21
7.21
7.21
7.20
7.20
7.19
7.13
7.13
7.02
7.02
6.02
6.00
6.00
5.98
4.29
4.28
4.27
4.27
4.27
4.26
4.25
4.13
4.12
4.11
4.10
4.10
4.09
4.05
3.87
3.86
3.86
3.85
3.84
3.84
3.79
3.78
3.78
3.77
3.75
3.74
3.69
3.68
3.67
3.67
3.66
3.53
3.52
3.51
3.50
2.97
2.96
2.96
2.95
2.49
2.48
2.47
2.46
1.64
0.90
0.88
0.87
^{1}H NMR (CDCl$_3$, 500 MHz)
4-24
O
N
O
O
N
N
O
N
CH$_3$
CH$_3$
CH$_3$
O
5.39
1.04
1.03
1.00
2.19
1.36
3.20
1.17
1.26
1.19
1.01
1.03
1.06
3.33
3.41
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)


189.89
173.17
157.03
142.03
138.96
129.46
128.33
128.11
127.18
126.78
73.73
64.41
62.01
60.49
54.00
36.07
33.43
20.20
13.64
^{13}C NMR (CDCl$_3$, 126 MHz)
4-24
O
N
O
O
N
N
O
N
CH$_3$
CH$_3$
CH$_3$
O
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

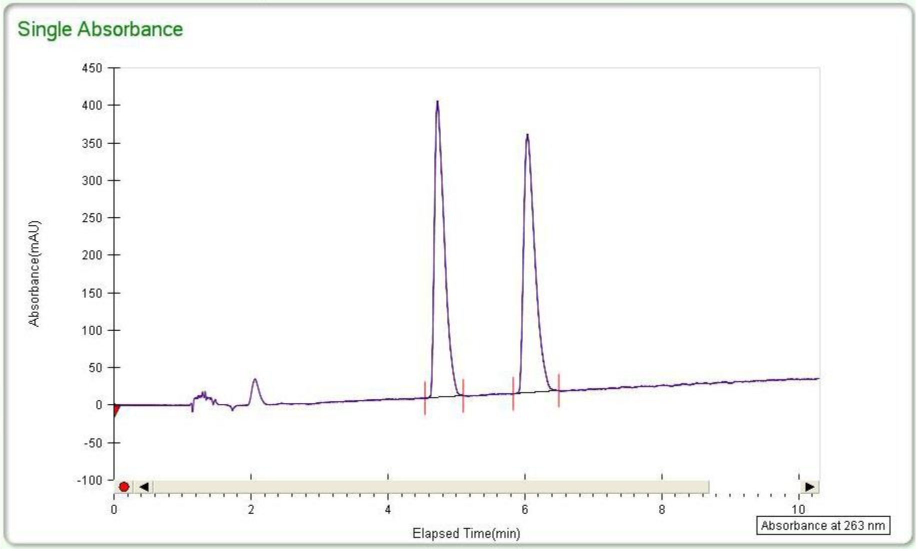
Appendix B. SFC Traces of New Compounds



(1S,3S,4S)-ethyl 3-benzoyl-4-phenylcyclopentanecarboxylate (3-4)

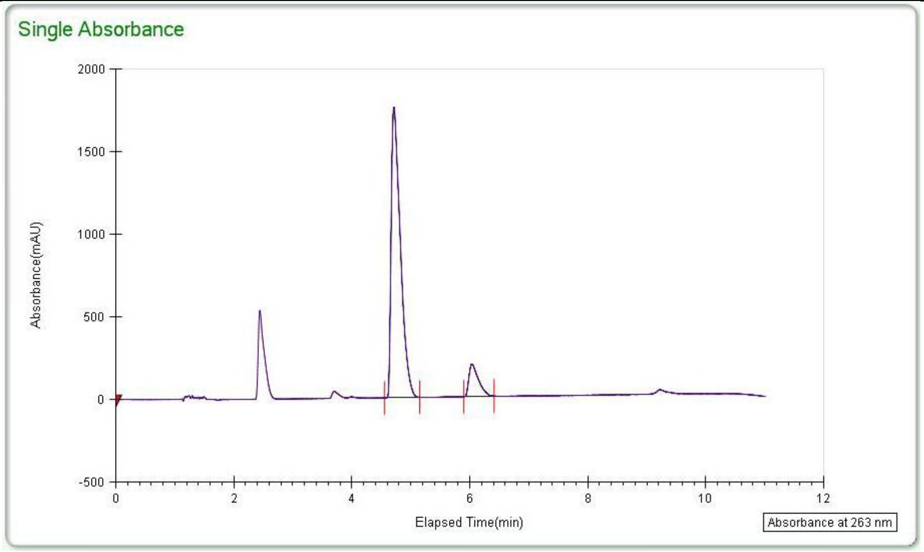
Racemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 40% iPrOH/CO_2, 3 mL/min, 263 nm

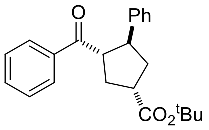
Peak	% area	area	RT(min)	height (mV)
1	50.0154	3947.7773	4.72	395.6174
2	49.9846	3945.353	6.04	344.3234
Total	100	7893.1302		



Scalemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 40% iPrOH/CO_2, 3 mL/min, 263 nm

Peak	% area	area	RT(min)	height (mV)
1	89.634	18949.1538	4.71	1759.1921
2	10.366	2191.4435	6.04	197.1945
Total	100	21140.5973		

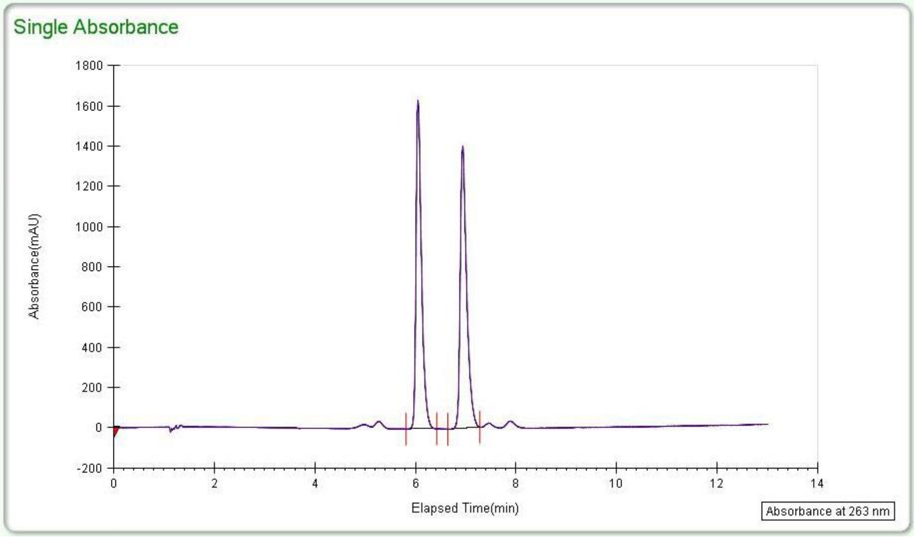




(1S,3S,4S)-tert-butyl 3-benzoyl-4-phenylcyclopentanecarboxylate (3-5)

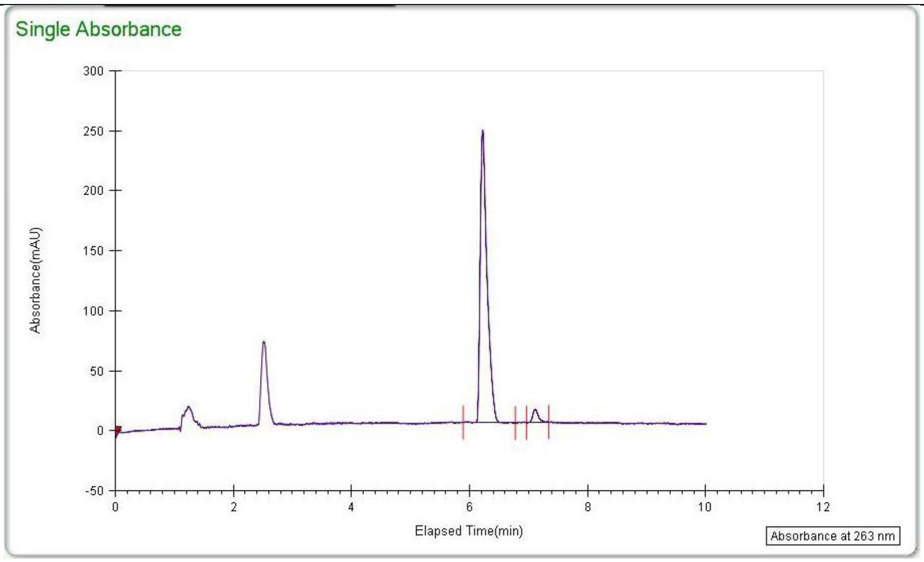
Racemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 263 nm

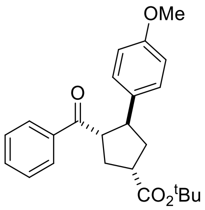
Peak	% area	area	RT(min)	height (mV)
1	49.8493	12332.9287	6.05	1634.0623
2	50.1507	12407.5172	6.94	1402.5703
Total	100	24740.4459		



Scalemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 263 nm

Peak	% area	area	RT(min)	height (mV)
1	96.5603	1974.8991	6.10	244.1414
2	3.4397	70.3497	7.08	10.9968
Total	100	2045.2488		

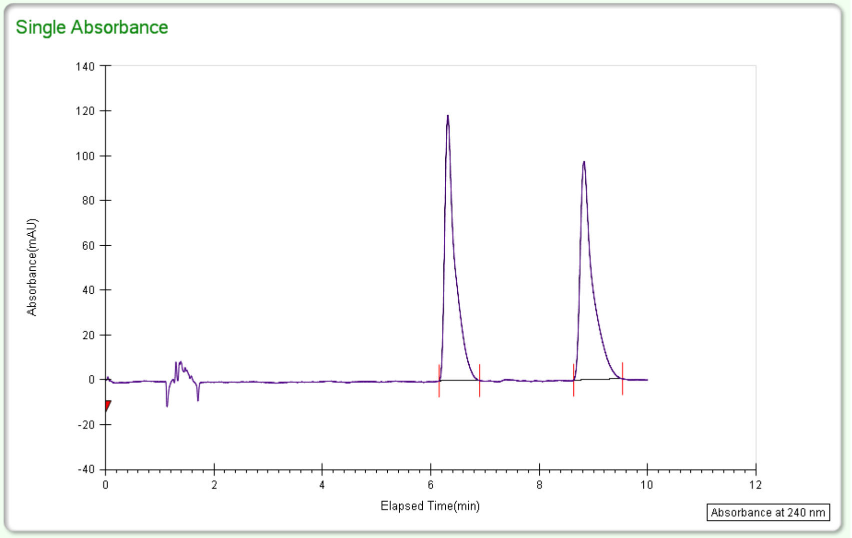




(1S,3S,4S)-tert-butyl 3-benzoyl-4-(4-methoxyphenyl)cyclopentanecarboxylate (3-6)

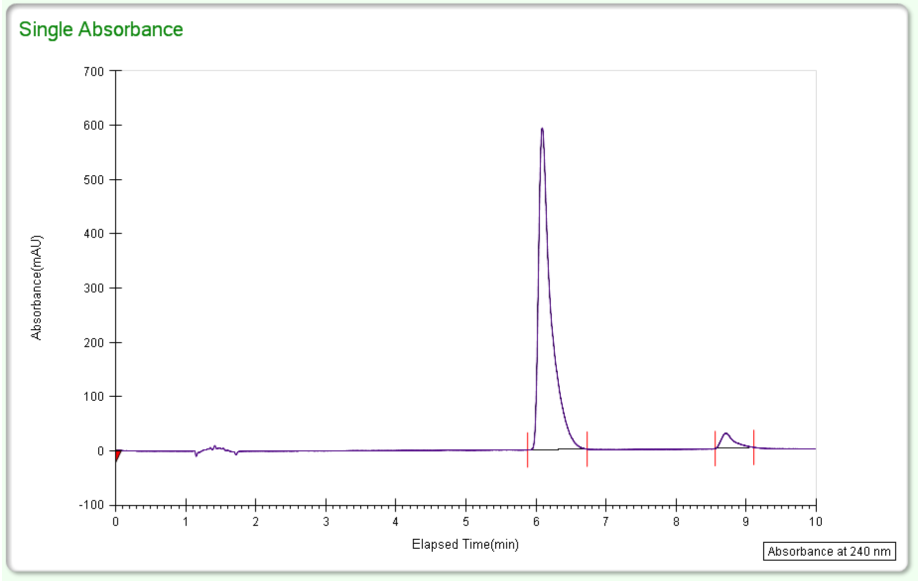
Racemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 20% iPrOH/CO_2, 3 mL/min, 240 nm

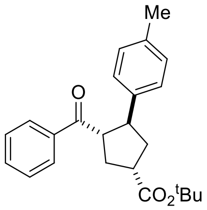
Peak	% area	area	RT(min)	height (mV)
1	49.8613	1535.3365	6.31	118.4
2	50.1387	1543.8767	8.83	97.473
Total	100	3079.2132		



Scalemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 20% iPrOH/CO_2, 3 mL/min, 240 nm

Peak	% area	area	RT(min)	height (mV)
1	95.3797	7181.3047	6.09	593.3232
2	4.6203	347.8706	8.71	27.2572
Total	100	7529.1753		

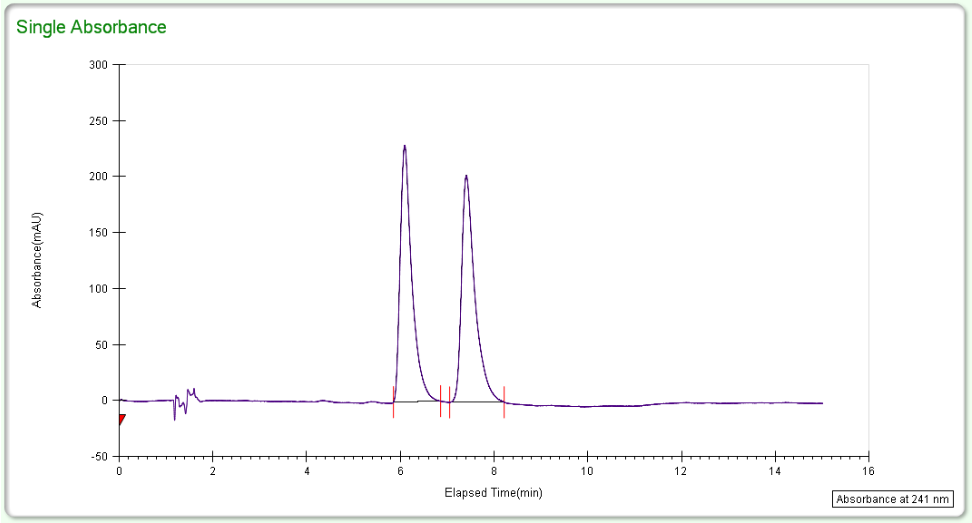




(1S,3S,4S)-tert-butyl 3-benzoyl-4-(4-methylphenyl)cyclopentanecarboxylate (3-7)

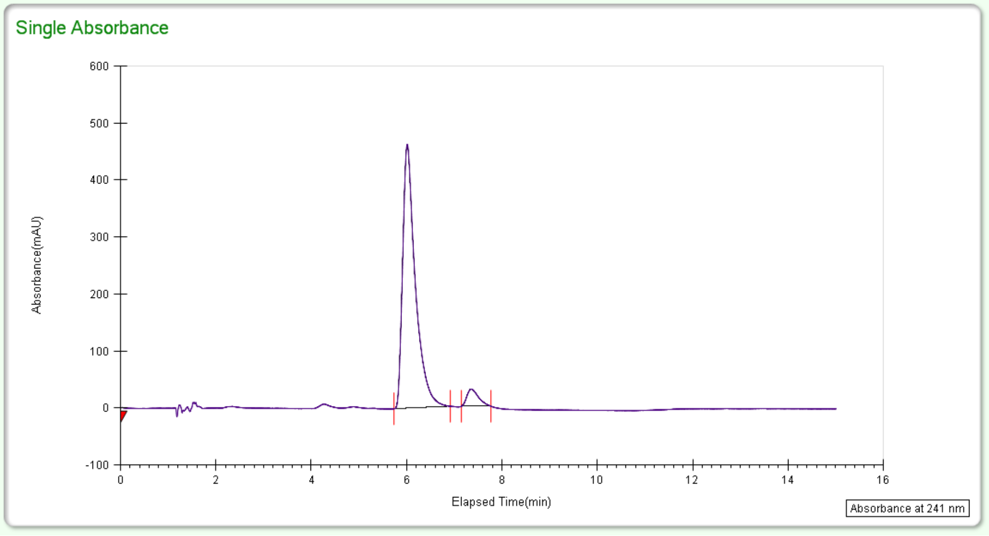
Racemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 20% iPrOH/CO_2, 3 mL/min, 241 nm

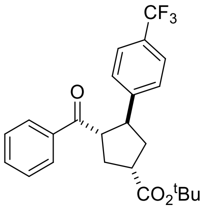
Peak	% area	area	RT(min)	height (mV)
1	49.7681	3969.6702	6.06	229.3664
2	50.2319	4006.6698	7.41	202.5068
Total	100	7976.3400		



Scalemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 20% iPrOH/CO_2, 3 mL/min, 241 nm

Peak	% area	area	RT(min)	height (mV)
1	94.3743	8492.9612	6.01	463.1925
2	5.6257	506.269	7.36	30.1824
Total	100	8999.2302		

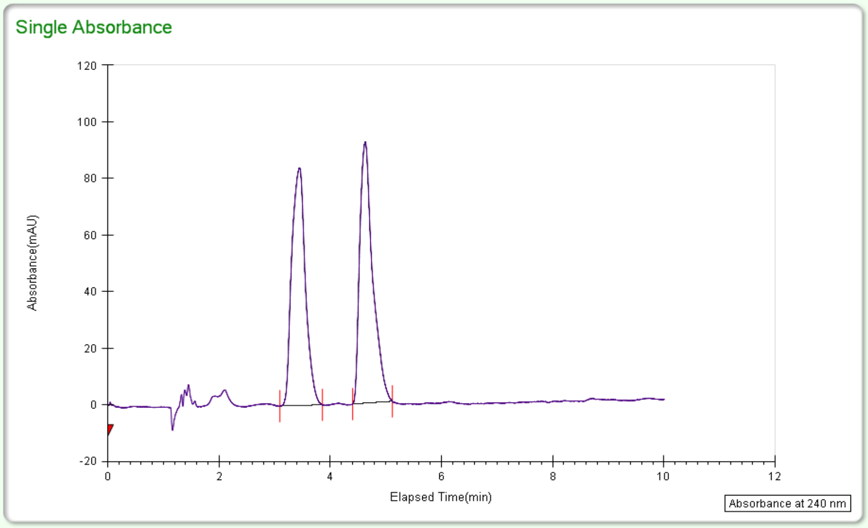




(1S,3S,4S)-tert-butyl 3-benzoyl-4-(4-(trifluoromethyl)phenyl)cyclopentanecarboxylate (3-8)

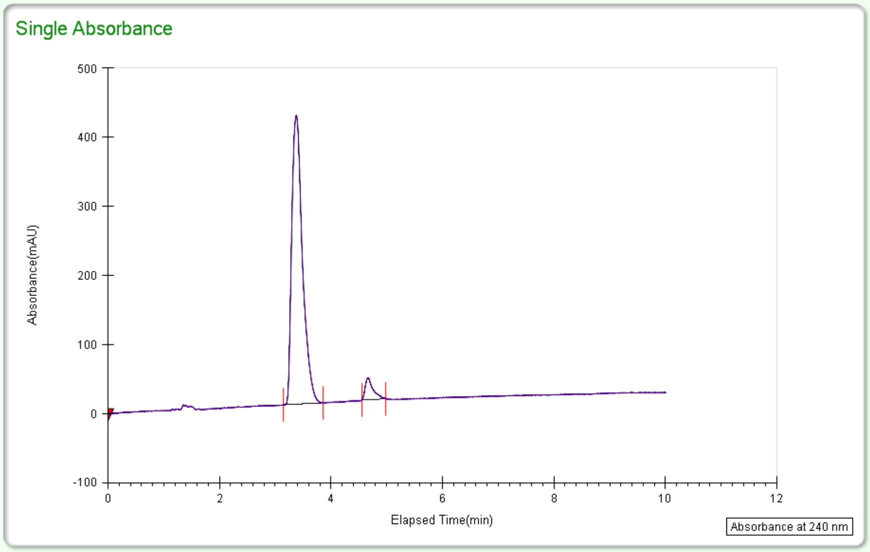
Racemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO$_2$ to 20% iPrOH/CO$_2$, 3 mL/min, 240 nm

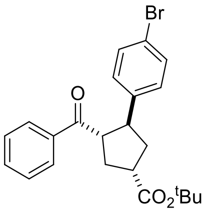
Peak	% area	area	RT(min)	height (mV)
1	48.965	1431.0998	3.45	82.0461
2	51.035	1491.5985	4.63	92.2654
Total	100	2922.6983		



Scalemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO$_2$ to 20% iPrOH/CO$_2$, 3 mL/min, 240 nm

Peak	% area	area	RT(min)	height (mV)
1	94.7142	5582.4521	3.38	418.3291
2	5.2858	311.5478	4.67	31.4191
Total	100	5894.9999		

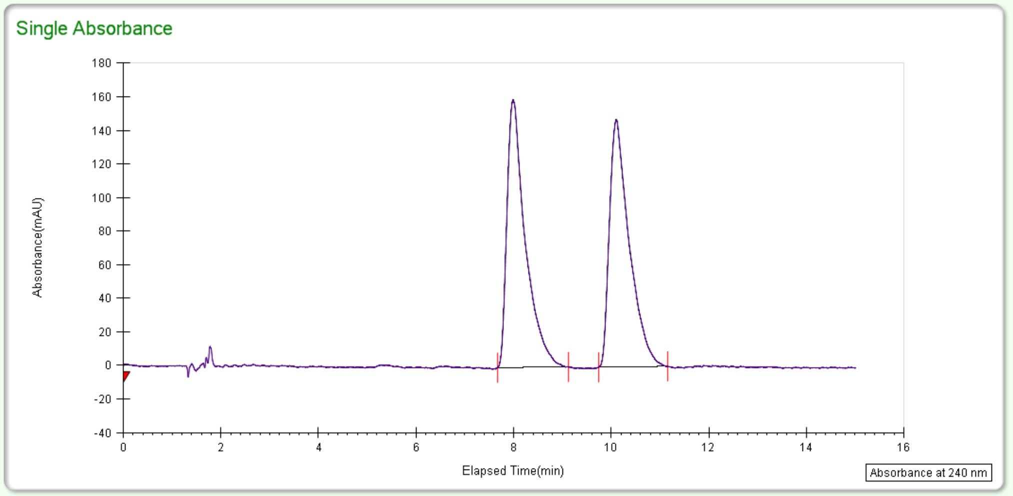




(1S,3S,4S)-tert-butyl 3-benzoyl-4-(4-bromophenyl)cyclopentanecarboxylate (3-9)

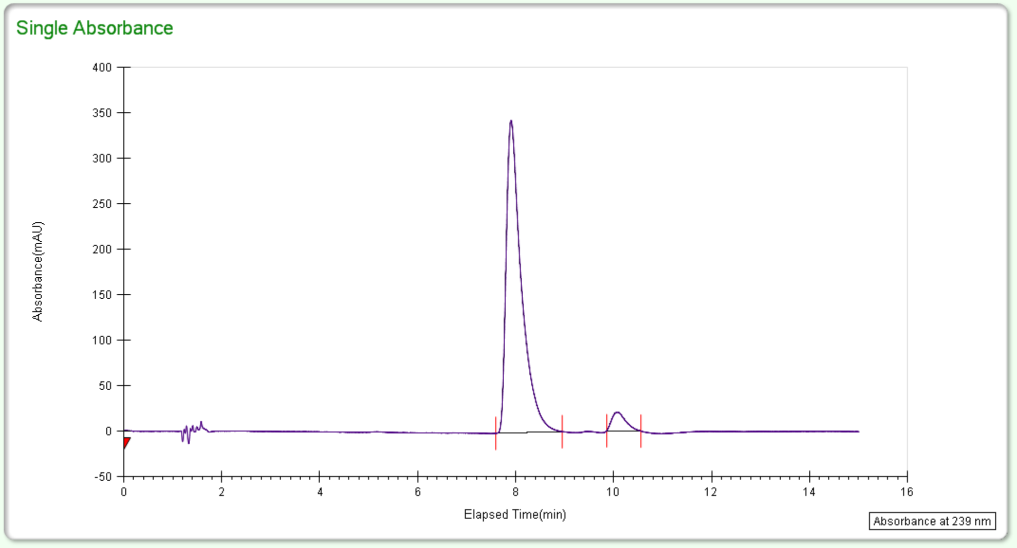
Racemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 20% iPrOH/CO_2, 3 mL/min, 239 nm

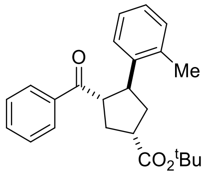
Peak	% area	area	RT(min)	height (mV)
1	50.0808	4152.8595	7.99	159.582
2	49.9192	4139.4583	10.11	147.4783
Total	100	8292.3178		



Scalemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 20% iPrOH/CO_2, 3 mL/min, 239 nm

Peak	% area	area	RT(min)	height (mV)
1	94.8503	7412.6292	7.91	343.5924
2	5.1497	402.4546	10.09	20.5212
Total	100	7815.0838		

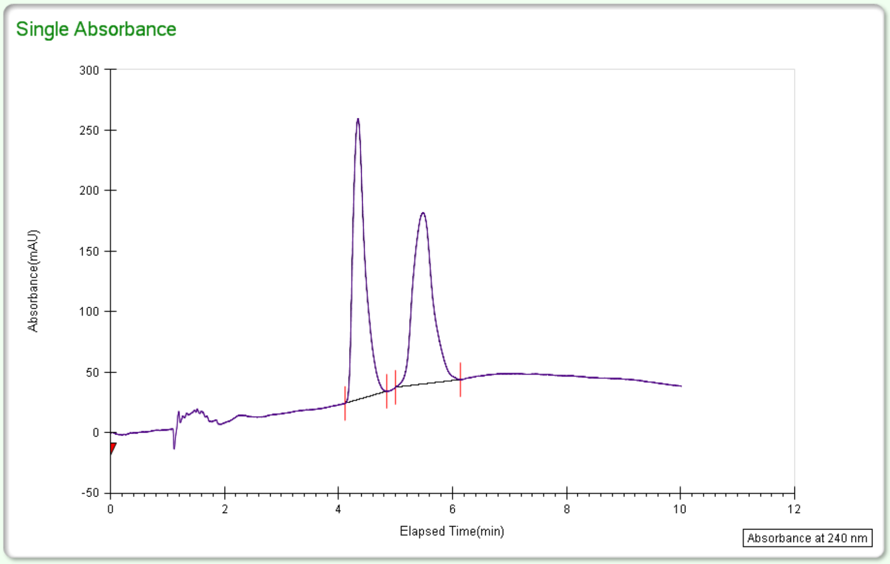




(1S,3S,4S)-tert-butyl 3-benzoyl-4-(o-tolyl)cyclopentanecarboxylate (3-10)

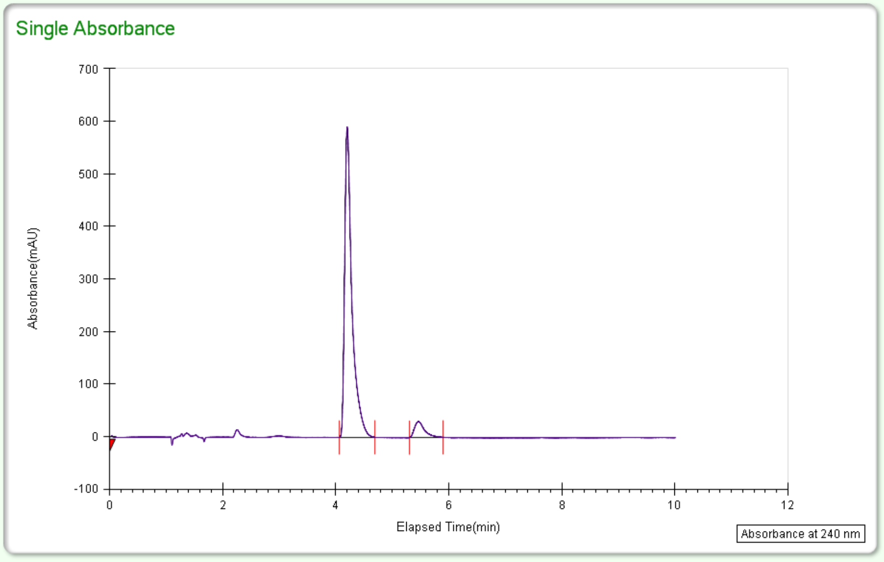
Racemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO$_2$ to 20% iPrOH/CO$_2$, 3 mL/min, 240 nm

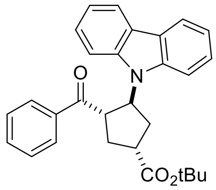
Peak	% area	area	RT(min)	height (mV)
1	50.2217	3440.3314	4.34	232.2605
2	49.7783	3409.9550	5.49	141.8507
Total	100	6850.2864		



Scalemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO$_2$ to 20% iPrOH/CO$_2$, 3 mL/min, 240 nm

Peak	% area	area	RT(min)	height (mV)
1	93.4141	5276.7255	4.20	591.2448
2	6.5859	372.0188	5.47	30.3867
Total	100	5648.7443		

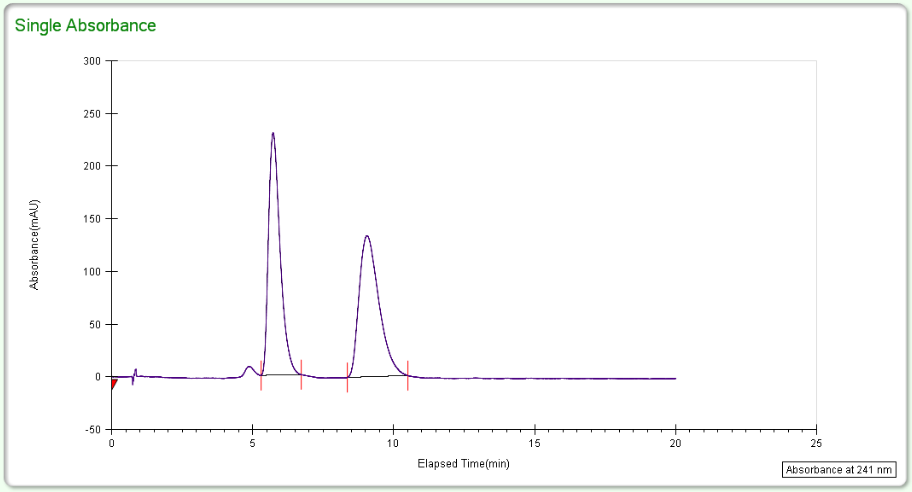




(1R,3S,4S)-tert-butyl 3-benzoyl-4-(9H-carbazol-9-yl)cyclopentanecarboxylate (3-11)

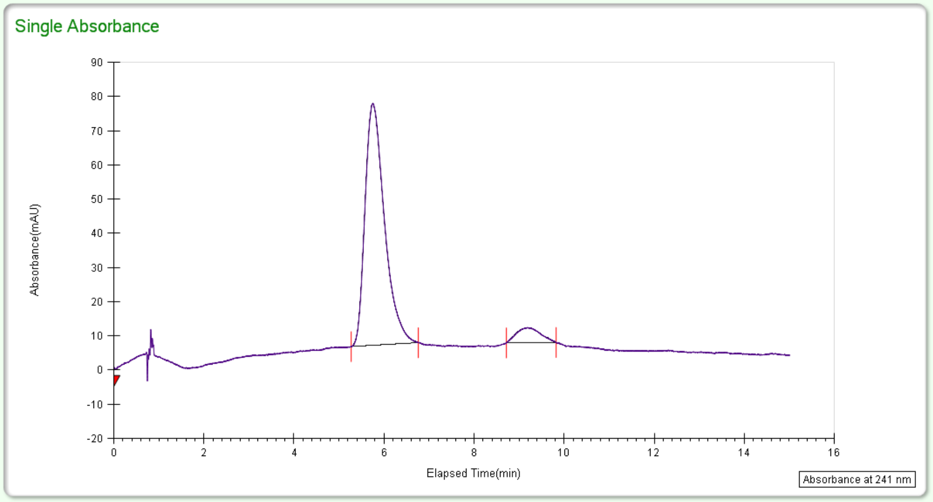
Racemic: SFC, Chiracel AD-H, 5% MeOH/CO_2, 5 mL/min, 241 nm

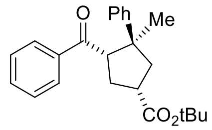
Peak	% area	area	RT(min)	height (mV)
1	50.0503	6587.3018	5.72	230.4808
2	49.9497	6574.0494	9.05	134.0597
Total	100	13161.3512		



Scalemic: SFC, Chiracel AD-H, 5% MeOH/CO_2, 5 mL/min, 241 nm

Peak	% area	area	RT(min)	height (mV)
1	92.8928	2123.9728	5.76	70.7194
2	7.1072	162.5037	9.18	4.4185
Total	100	2286.4765		

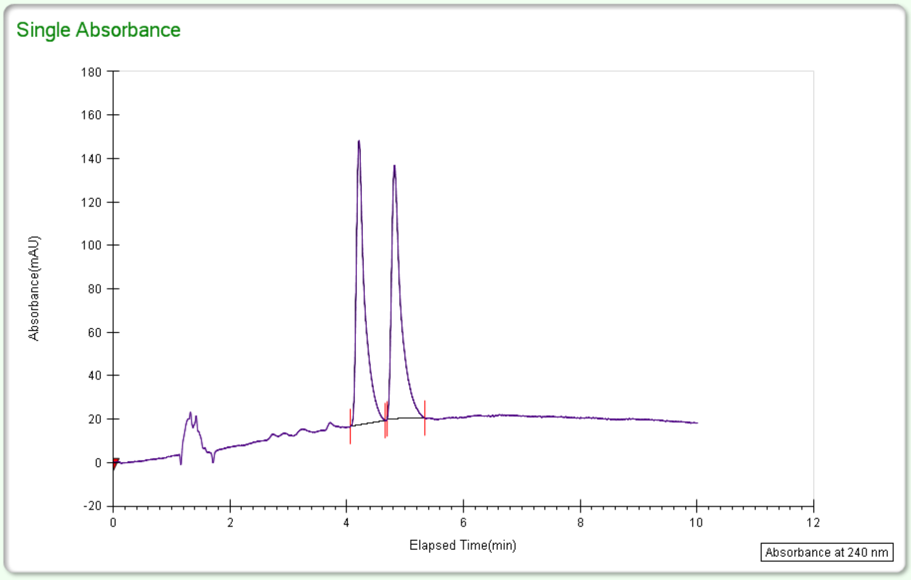




(1R,3S,4S)-tert-butyl 4-benzoyl-3-methyl-3-phenylcyclopentanecarboxylate (3-12)

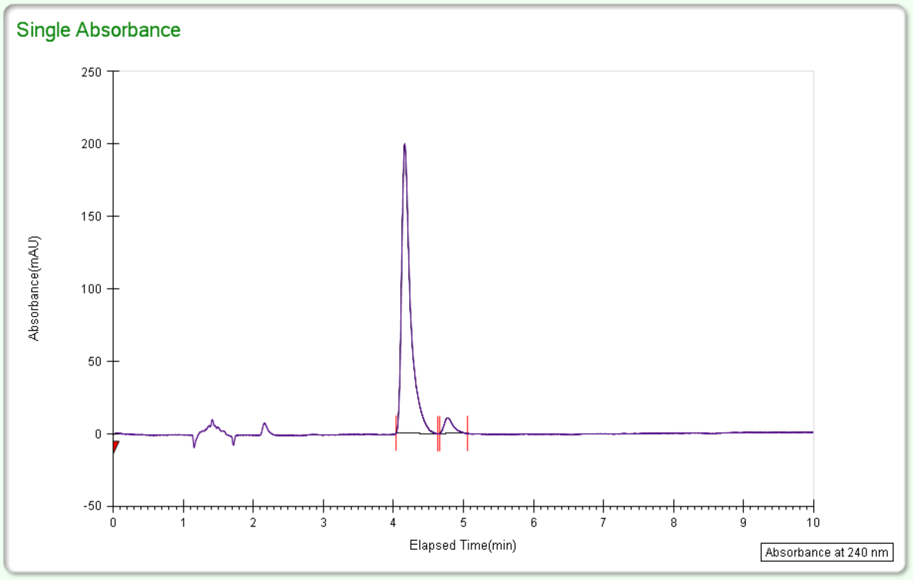
Racemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 20% iPrOH/CO_2, 3 mL/min, 240 nm

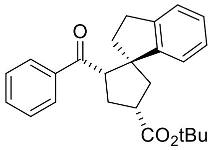
Peak	% area	area	RT(min)	height (mV)
1	50.1983	1300.4797	4.21	131.0374
2	49.8017	1290.2063	4.82	116.6899
Total	100	2560.6860		



Scalemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 20% iPrOH/CO_2, 3 mL/min, 240 nm

Peak	% area	area	RT(min)	height (mV)
1	94.7394	1739.5284	4.16	199.9115
2	5.2606	96.5903	4.78	10.8253
Total	100	1836.1187		

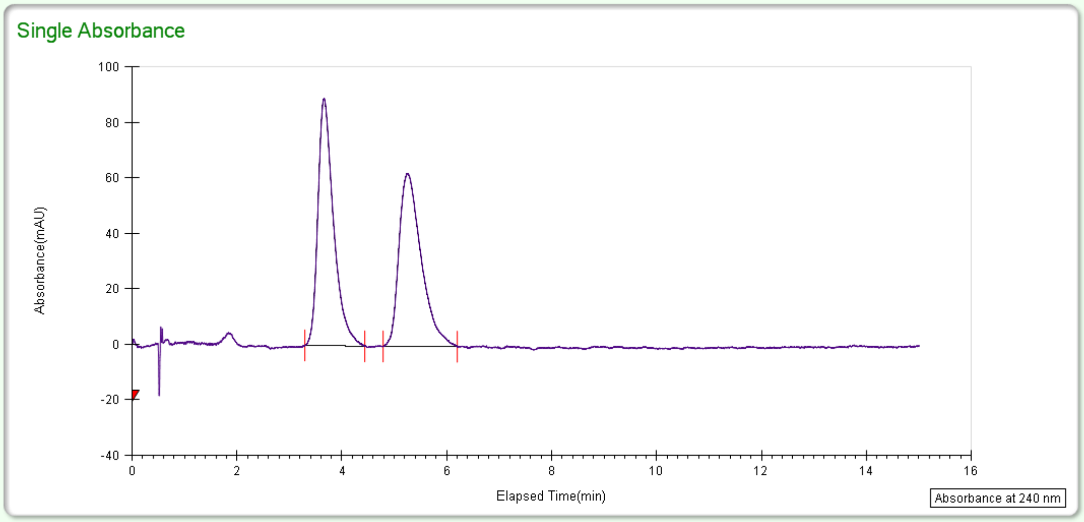




(1R,3S,4S)-tert-butyl 2-benzoyl-2',3'-dihydrospiro[cyclopentane-1,1'-indene]-4-carboxylate (3-13)

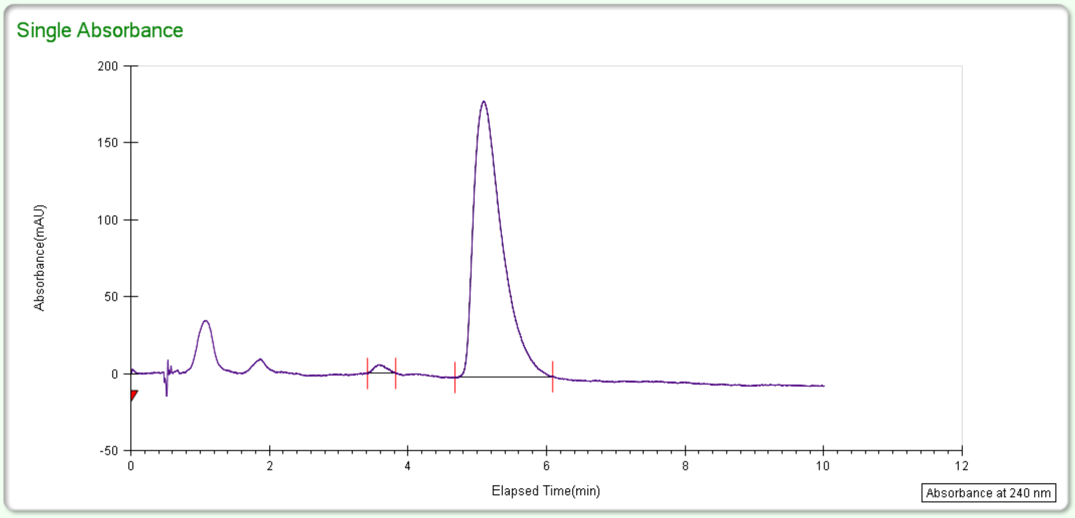
Racemic: SFC, Chiracel AD-H, 5% iPrOH/CO_2, 8 mL/min, 240 nm

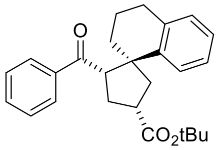
Peak	% area	area	RT(min)	height (mV)
1	50.2199	1850.3655	3.66	89.066
2	49.7801	1834.1622	5.24	62.3639
Total	100	3684.5277		



Scalemic: SFC, Chiracel AD-H, 5% iPrOH/CO_2, 8 mL/min, 240 nm

Peak	% area	area	RT(min)	height (mV)
1	1.4056	72.4063	3.57	5.6782
2	98.5944	5078.7299	5.09	1796159
Total	100	5151.1362		

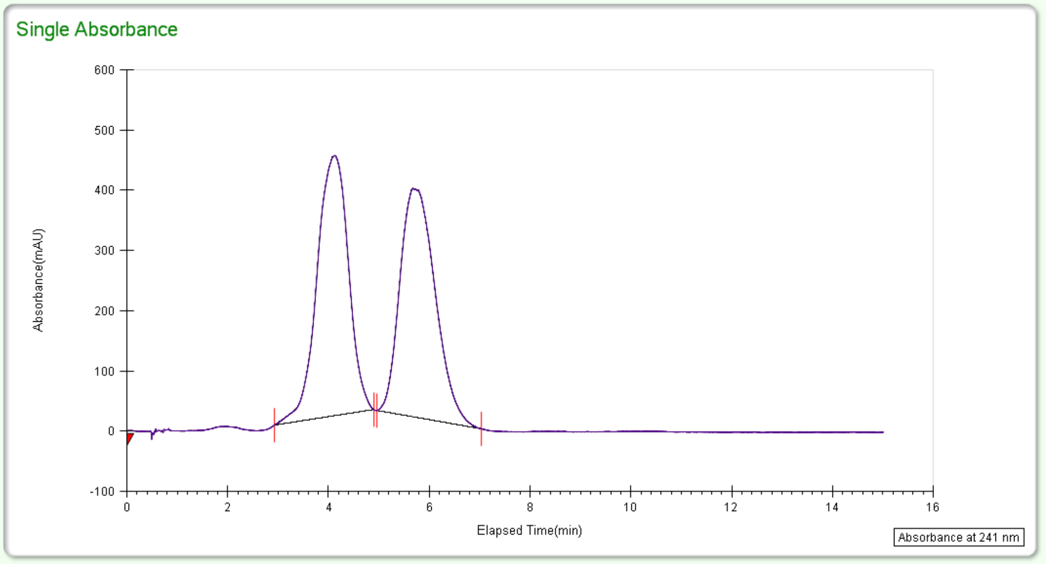




(1R,3S,4S)-tert-butyl 2-benzoyl-3',4'-dihydro-2'H-spiro[cyclopentane-1,1'-naphthalene]-4-carboxylate (3-14):

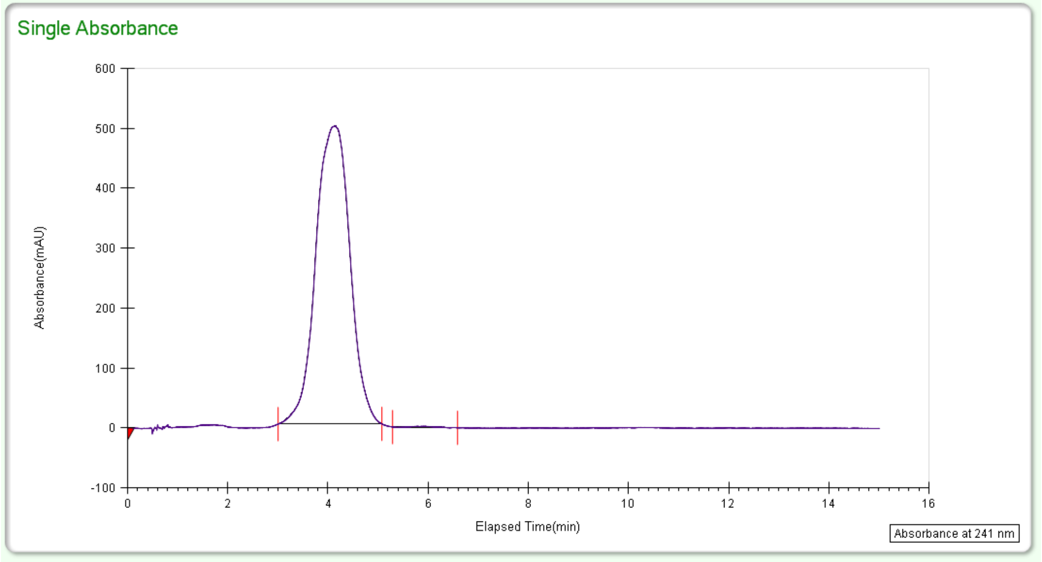
Racemic: SFC, Chiracel AD-H, 5% iPrOH/CO_2, 8 mL/min, 241 nm

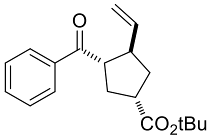
Peak	% area	area	RT(min)	height (mV)
1	50.2772	18731.3836	4.12	432.3556
2	49.7228	18524.834	5.68	379.5763
Total	100	37256.2176		



Scalemic: SFC, Chiracel AD-H, 5% iPrOH/CO_2, 8 mL/min, 241 nm

Peak	% area	area	RT(min)	height (mV)
1	99.7553	23569.4045	4.14	497.5829
2	0.2447	57.8048	5.94	379.5763
Total	100	37256.2176		

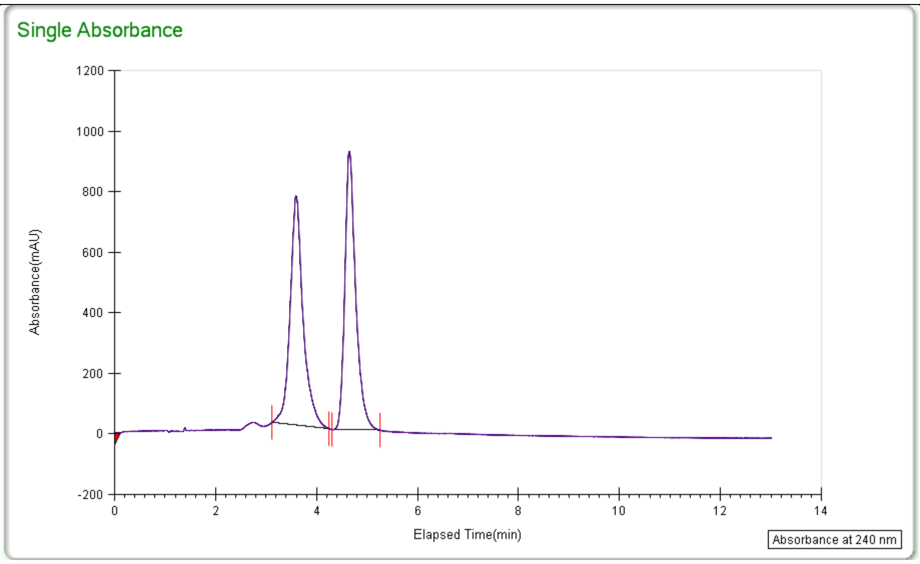




(1S,3S,4R)-tert-butyl 3-benzoyl-4-vinylcyclopentanecarboxylate (3-15)

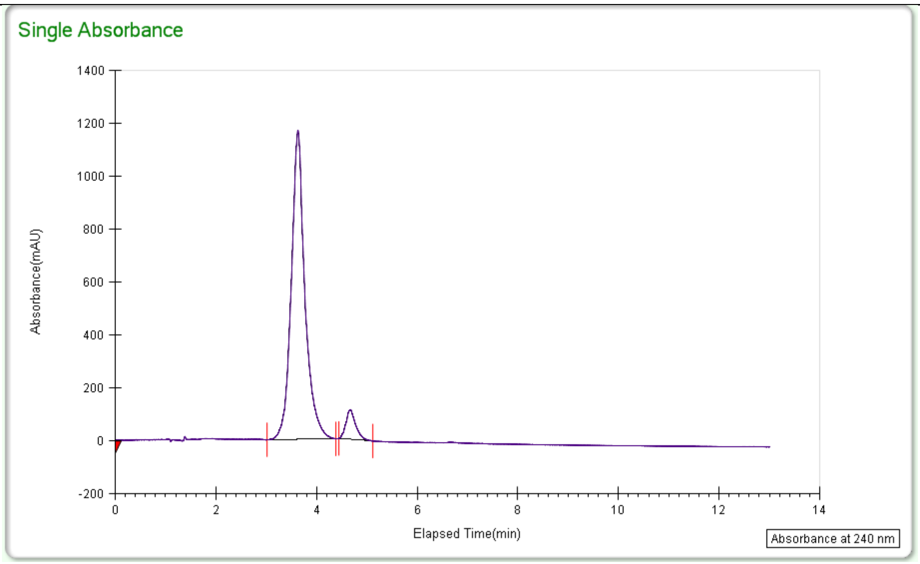
Racemic: SFC, Chiracel AD-H, gradient 5% MeOH/CO_2 to 50% MeOH/CO_2, 3 mL/min, 240 nm

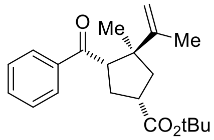
Peak	% area	area	RT(min)	height (mV)
1	49.6736	13545.4106	3.59	757.8009
2	50.3264	13723.4429	4.65	921.5475
Total	100	27268.8535		



Scalemic: SFC, Chiracel AD-H, gradient 5% MeOH/CO_2 to 50% MeOH/CO_2, 3 mL/min, 240 nm

Peak	% area	area	RT(min)	height (mV)
1	93.5841	21958.5768	3.63	1171.4658
2	6.4159	1505.4166	4.68	112.4463
Total	100	23463.9934		

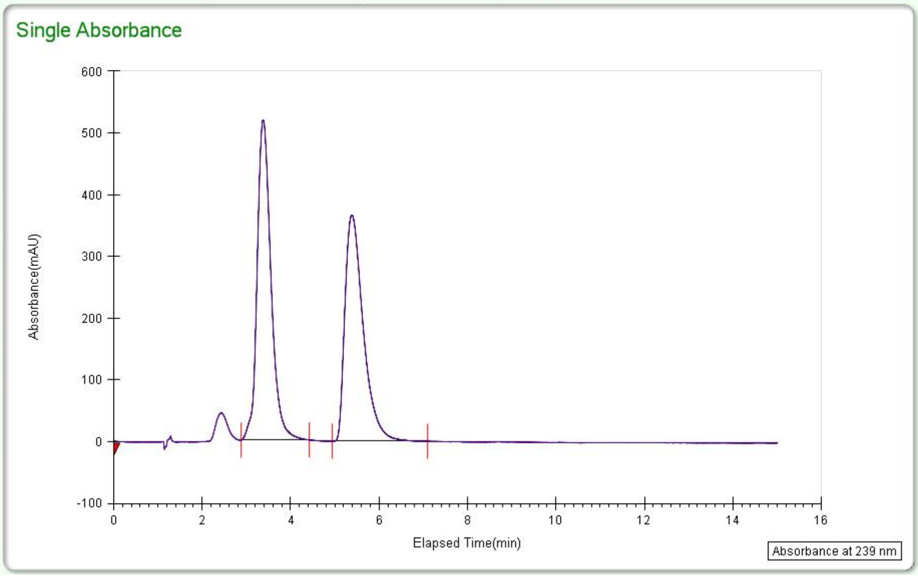




(1R,3S,4S)-tert-butyl 4-benzoyl-3-methyl-3-(prop-1-en-2-yl)cyclopentanecarboxylate (3-16)

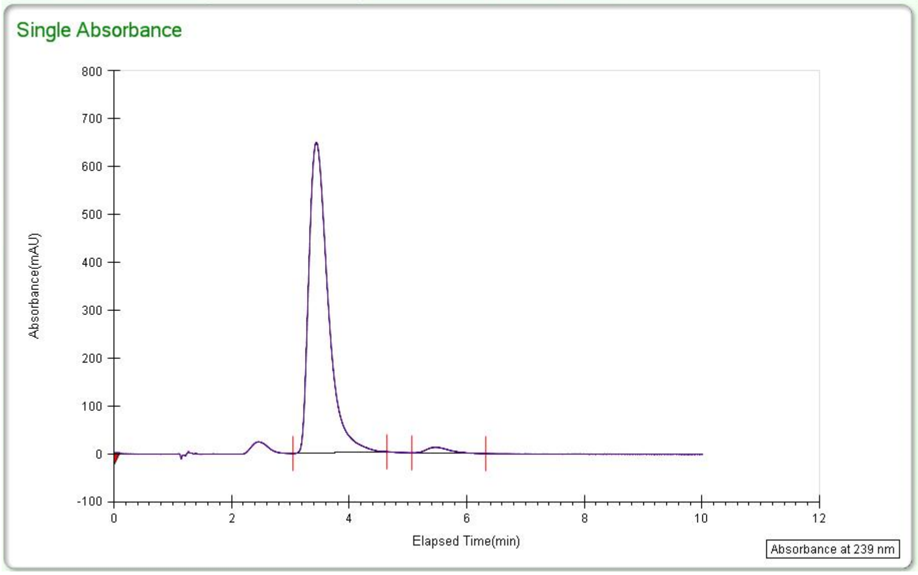
Racemic: SFC, Chiracel AD-H, 5% MeOH/CO_2, 3 mL/min, 239 nm

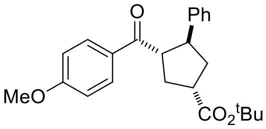
Peak	% area	area	RT(min)	height (mV)
1	50.4774	10975.9081	3.38	518.6331
2	49.5226	10768.2770	5.39	366.5323
Total	100	21744.1851		



Scalemic: SFC, Chiracel AD-H, 5% MeOH/CO_2, 3 mL/min, 239 nm

Peak	% area	area	RT(min)	height (mV)
1	97.801	14687.9628	3.44	649.8146
2	2.199	330.2534	5.45	12.2647
Total	100	15018.2161		

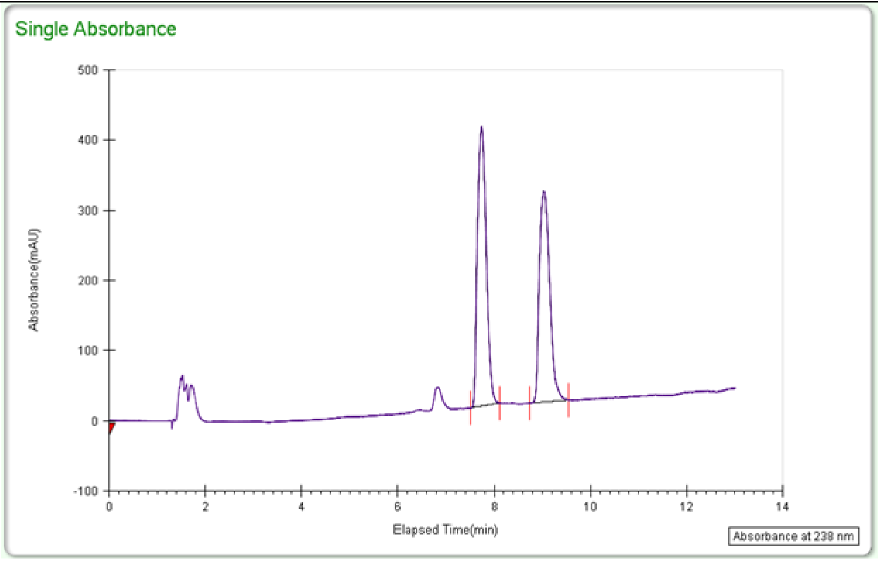




(1S,3S,4S)-tert-butyl 3-(4-methoxybenzoyl)-4-phenylcyclopentanecarboxylate (3-17)

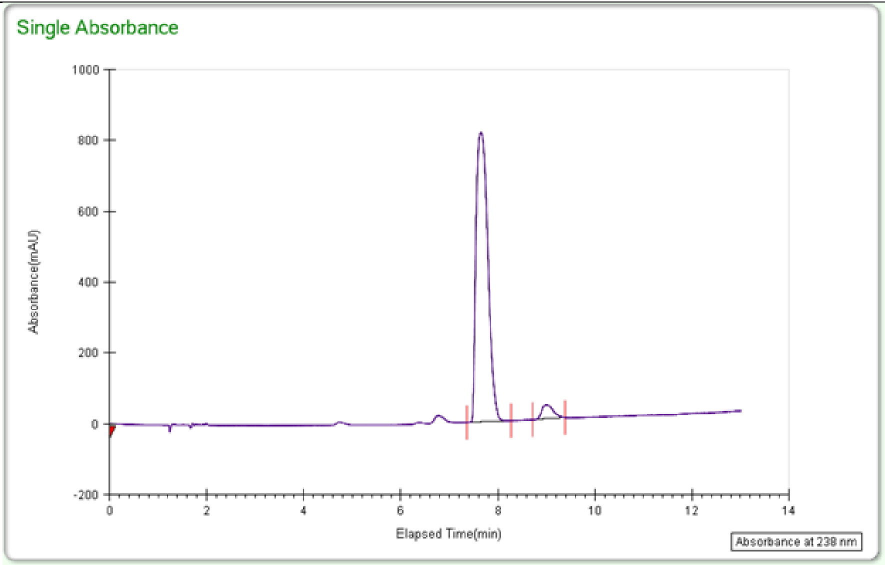
Racemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 238 nm

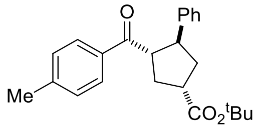
Peak	% area	area	RT(min)	height (mV)
1	50.9761	4885.3902	7.74	443.0142
2	49.0239	4669.4463	9.04	348.4219
Total	100	9524.8365		



Scalemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 238 nm

Peak	% area	area	RT(min)	height (mV)
1	95.5694	13807.2815	7.65	810.3921
2	4.4306	640.1019	8.98	20.1321
Total	100	14447.3834		

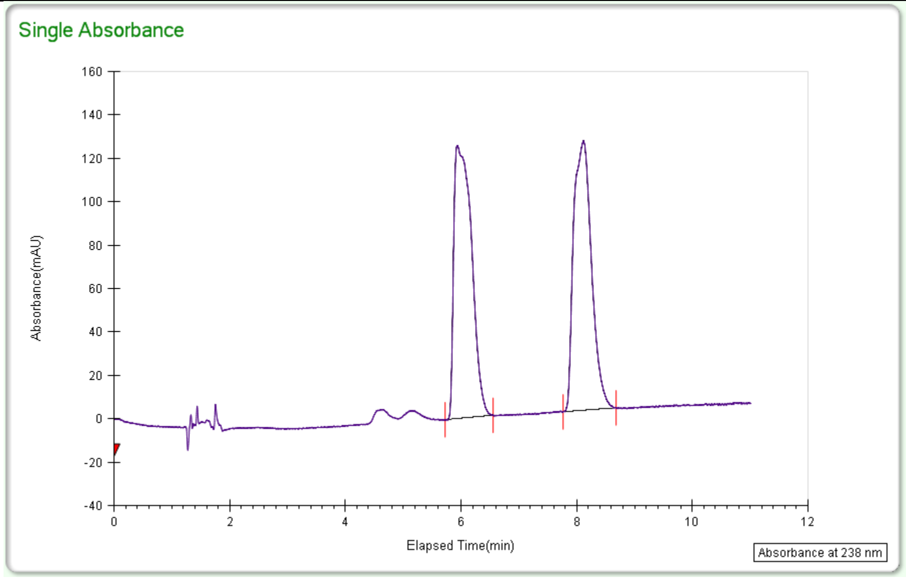




(1S,3S,4S)-tert-butyl 3-(4-methylbenzoyl)-4-phenylcyclopentanecarboxylate (3-18)

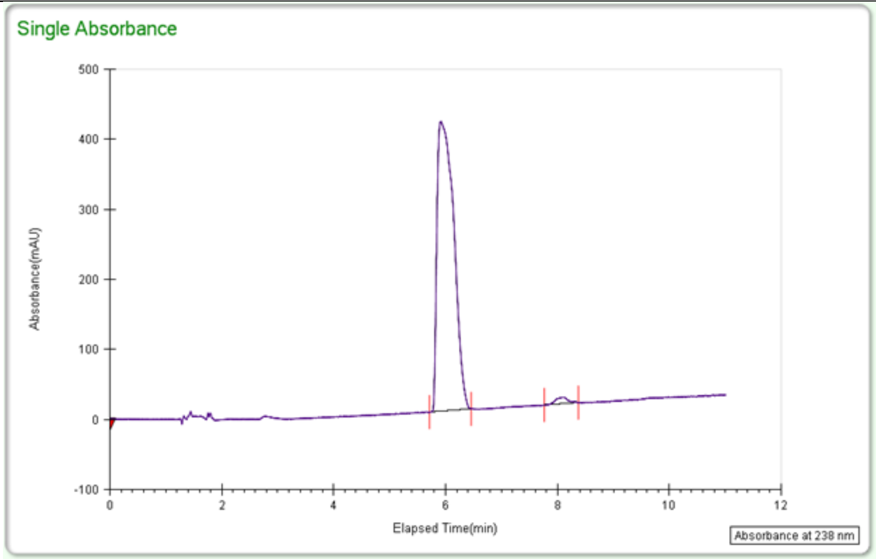
Racemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 40% iPrOH/CO_2, 3 mL/min, 238 nm

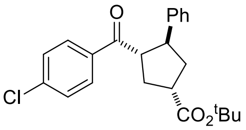
Peak	% area	area	RT(min)	height (mV)
1	50.165	2676.8148	5.94	
2	49.835	2659.2028	8.12	
Total	100	5336.0176		



Scalemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 40% iPrOH/CO_2, 3 mL/min, 238 nm

Peak	% area	area	RT(min)	height (mV)
1	98.4051	8582.6297	5.91	
2	1.5949	139.1014	8.09	
Total	100	8721.7311		

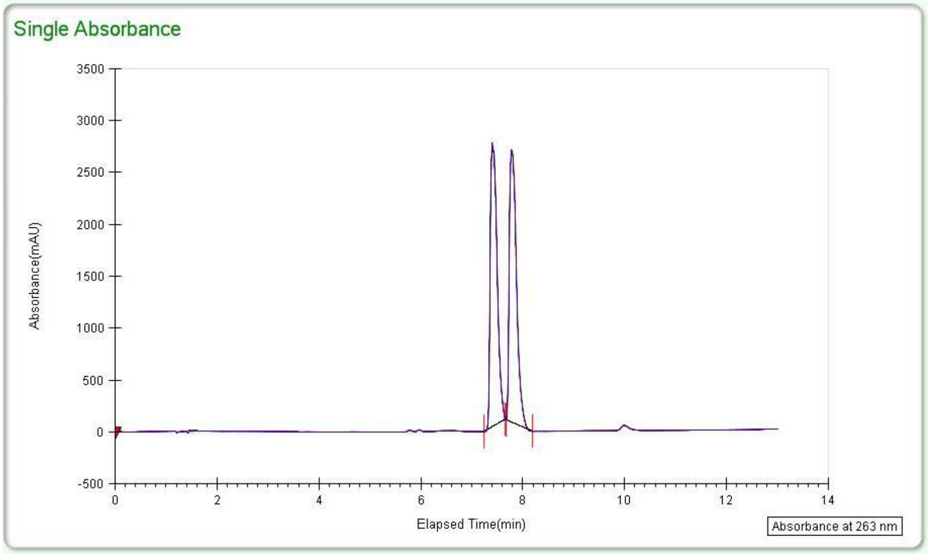




(1S,3S,4S)-tert-butyl 3-(4-chlorobenzoyl)-4-phenylcyclopentanecarboxylate (3-19)

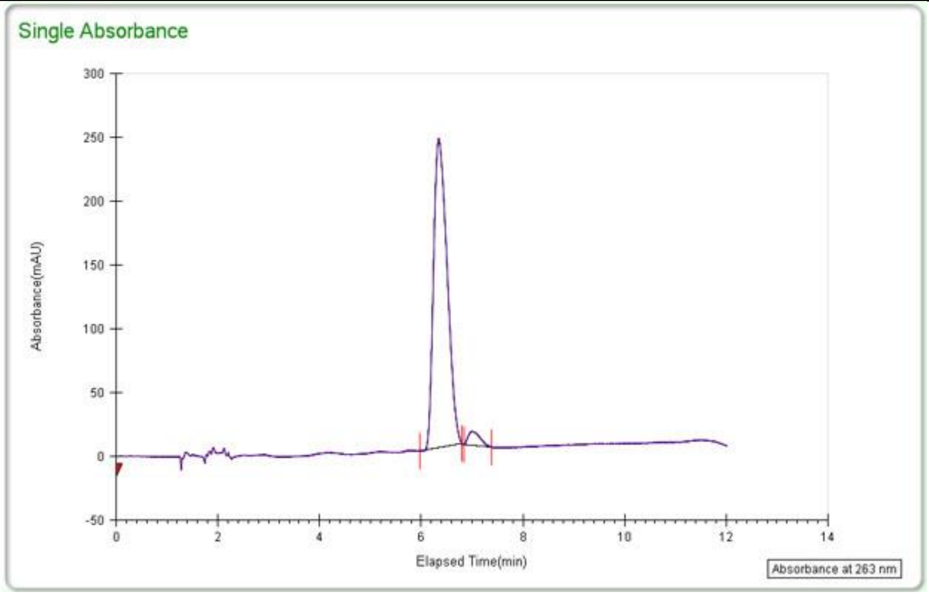
Racemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 263 nm

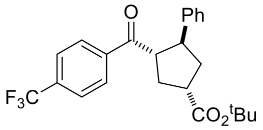
Peak	% area	area	RT(min)	height (mV)
1	49.8029	25505.2367	7.4	2737.1797
2	50.1971	25707.1071	7.78	2623.8135
Total	100	51212.3438		



Scalemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 263 nm

Peak	% area	area	RT(min)	height (mV)
1	96.1766	4487.9187	6.34	
2	3.8234	178.411	7.00	
Total	100	4666.3297		

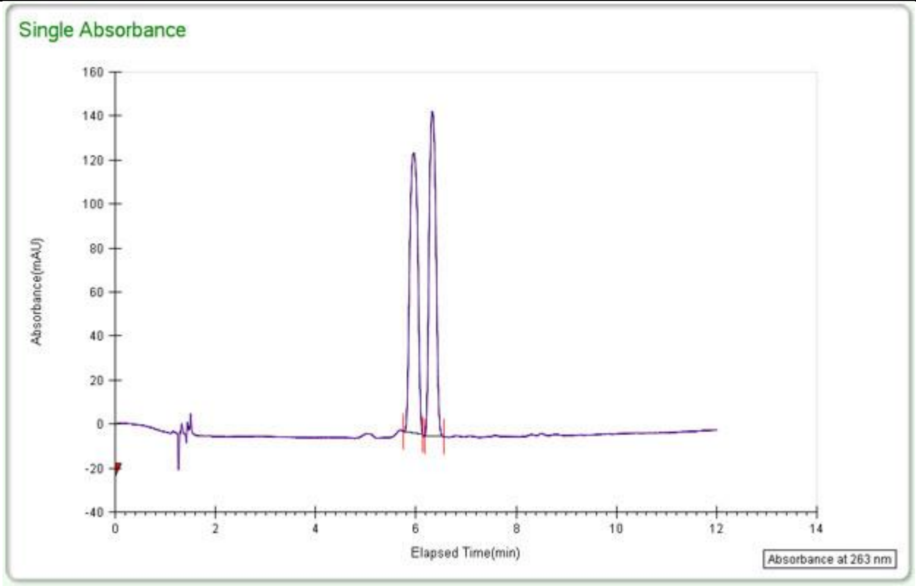




(1S,3S,4S)-tert-butyl 3-phenyl-4-(4-(trifluoromethyl)benzoyl)cyclopentanecarboxylate (3-20)

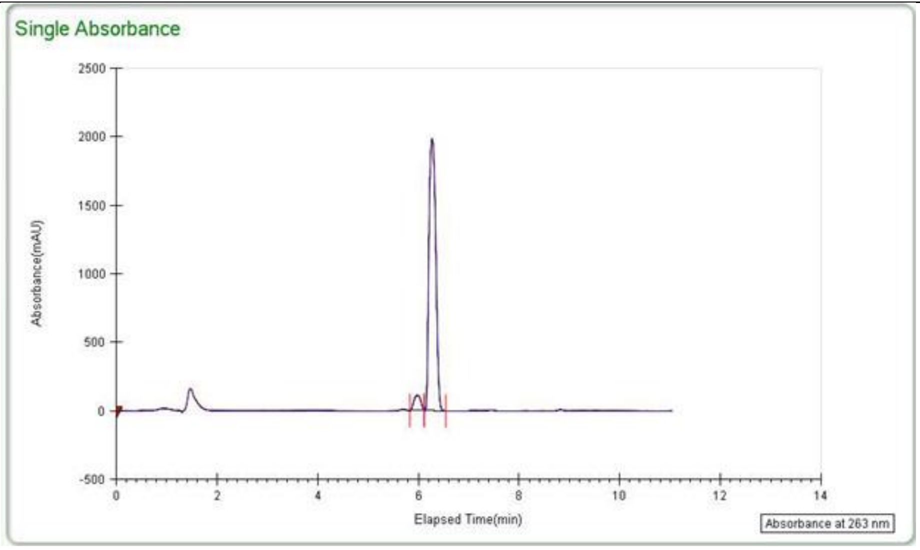
Racemic: SFC, Chiracel OD-H, gradient 1% iPrOH/CO_2 to 20% iPrOH/CO_2, 3 mL/min, 263 nm

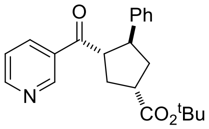
Peak	% area	area	RT(min)	height (mV)
1	50.4908	1403.9646	5.95	
2	49.5092	1376.6717	6.33	
Total	100	2780.6363		



Scalemic: SFC, Chiracel OD-H, gradient 1% iPrOH/CO_2 to 20% iPrOH/CO_2, 3 mL/min, 263 nm

Peak	% area	area	RT(min)	height (mV)
1	5.2538	1025.1958	5.97	
2	94.7462	18488.2842	6.28	
Total	100	19513.48		

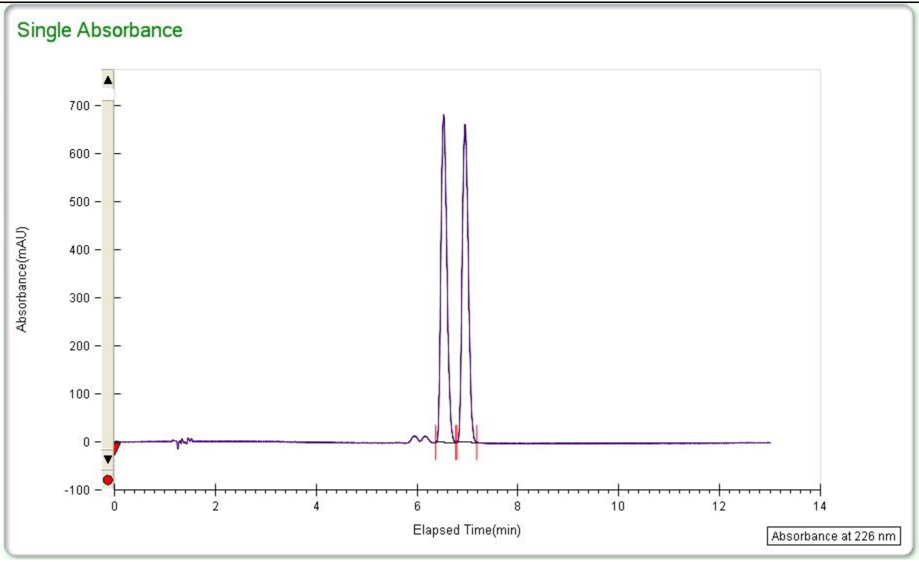




(1S,3S,4S)-tert-butyl 3-nicotinoyl-4-phenylcyclopentanecarboxylate (3-21)

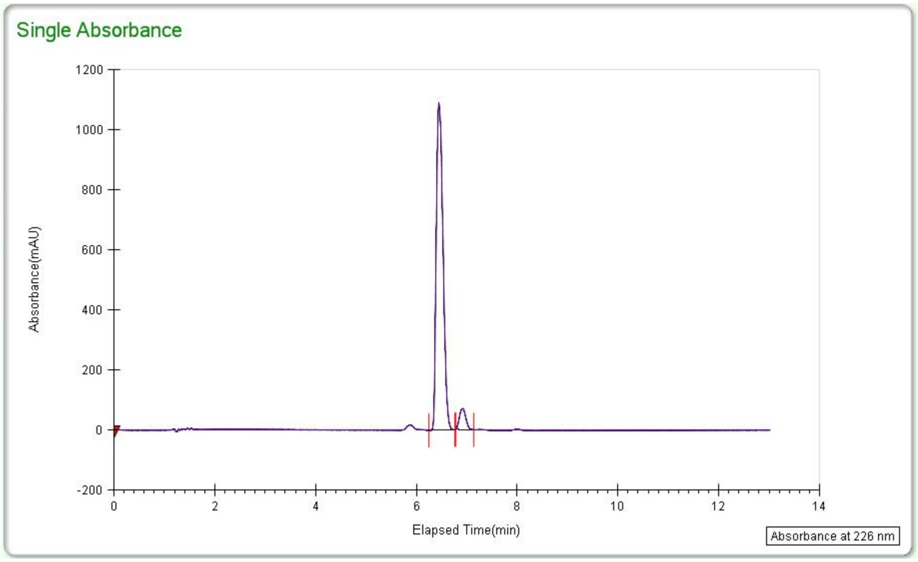
Racemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 238 nm

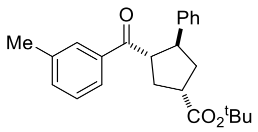
Peak	% area	area	RT(min)	height (mV)
1	50.0521	5567.4095	6.53	680.9274
2	49.9479	5555.829	6.95	660.2215
Total		11123.2385		



Scalemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 238 nm

Peak	% area	area	RT(min)	height (mV)
1	94.2451	10092.6171	6.45	1089.0392
2	5.7549	616.2901	6.92	70.1372
Total	100	10708.9071		

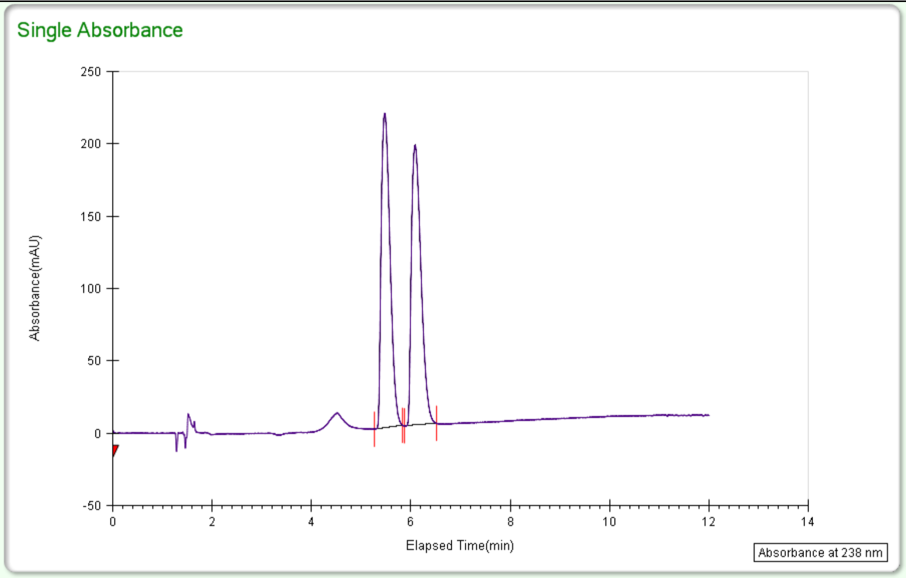




(1S,3S,4S)-tert-butyl 3-(3-methylbenzoyl)-4-phenylcyclopentanecarboxylate (3-22)

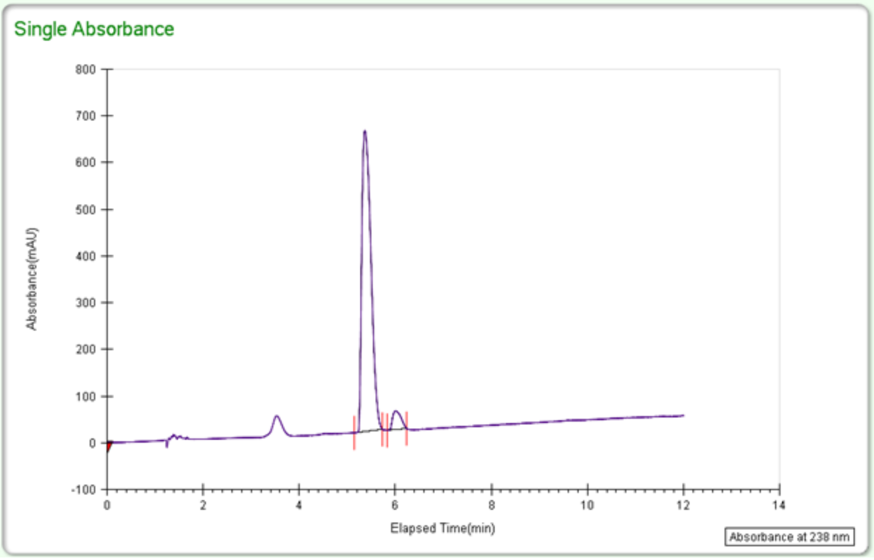
Racemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 238 nm

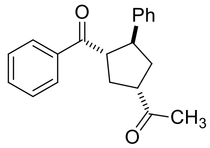
Peak	% area	area	RT(min)	height (mV)
1	50.8315	2675.353	5.47	
2	49.1685	2587.8288	6.09	
Total	100	5263.1818		



Scalemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 238 nm

Peak	% area	area	RT(min)	height (mV)
1	94.6587	8541.643	5.37	
2	5.3413	481.9796	6.00	
Total	100	9023.6226		

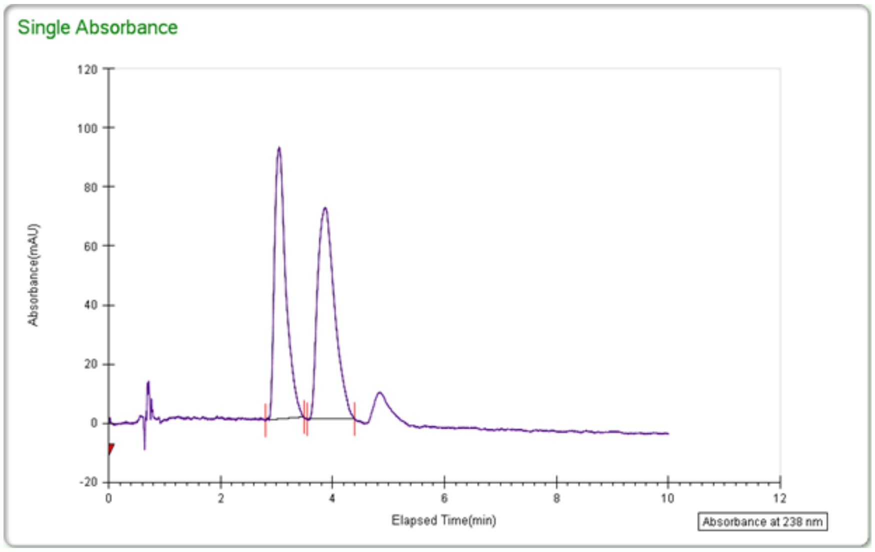




1-((1S,3S,4S)-3-benzoyl-4-phenylcyclopentyl)ethanone (3-23)

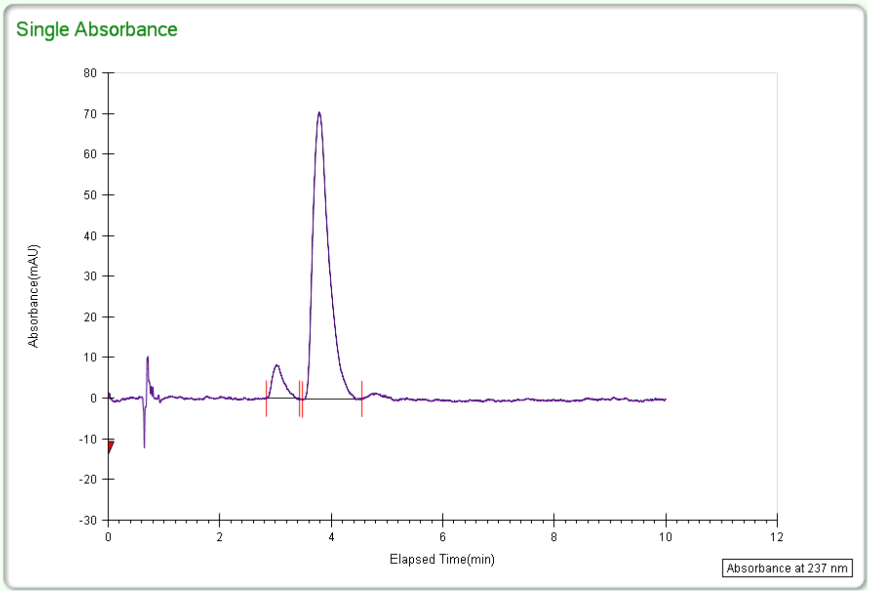
Racemic: SFC, Chiracel AD-H, 5% iPrOH/CO_2, 6 mL/min, 238 nm

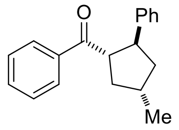
Peak	% area	area	RT(min)	height (mV)
1	46.3168	1306.1541	3.05	92.1535
2	53.6832	1513.8883	3.87	71.7254
Total	100	2820.0424		



Scalemic: SFC, Chiracel AD-H, 5% iPrOH/CO_2, 6 mL/min, 238 nm

Peak	% area	area	RT(min)	height (mV)
1	6.0123	90.6390	3.02	8.1857
2	93.9877	1416.9201	3.78	70.6342
Total	100	1507.5591		

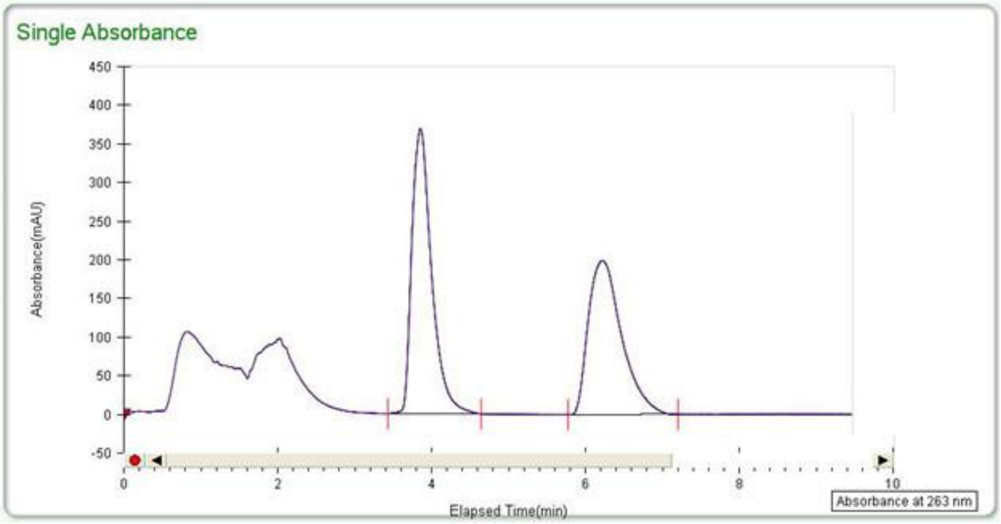




((1S,2S,4S)-4-methyl-2-phenylcyclopentyl)(phenyl)methanone (3-24)

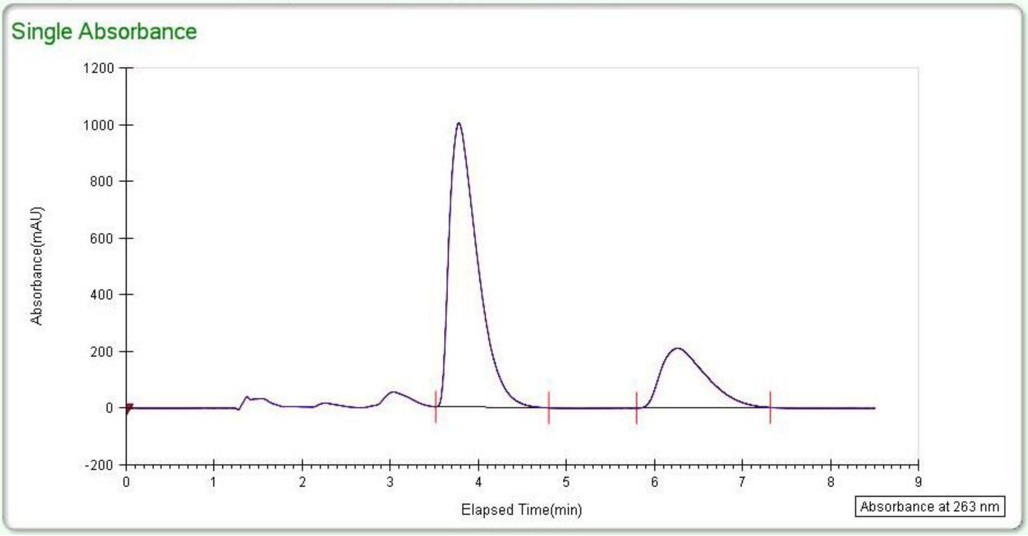
Racemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2, 3 mL/min, 263 nm

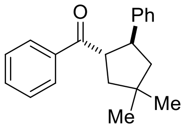
Peak	% area	area	RT(min)	height (mV)
1	52.4608	6592.7457	3.85	368.6752
2	47.5392	5974.2576	6.23	199.1554
Total	100	12567.0034		



Scalemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2, 3 mL/min, 263 nm

Peak	% area	area	RT(min)	height (mV)
1	74.7414	22252.5356	3.78	1001.6165
2	25.2586	7520.1736	6.26	210.3868
Total	100	29772.7091		

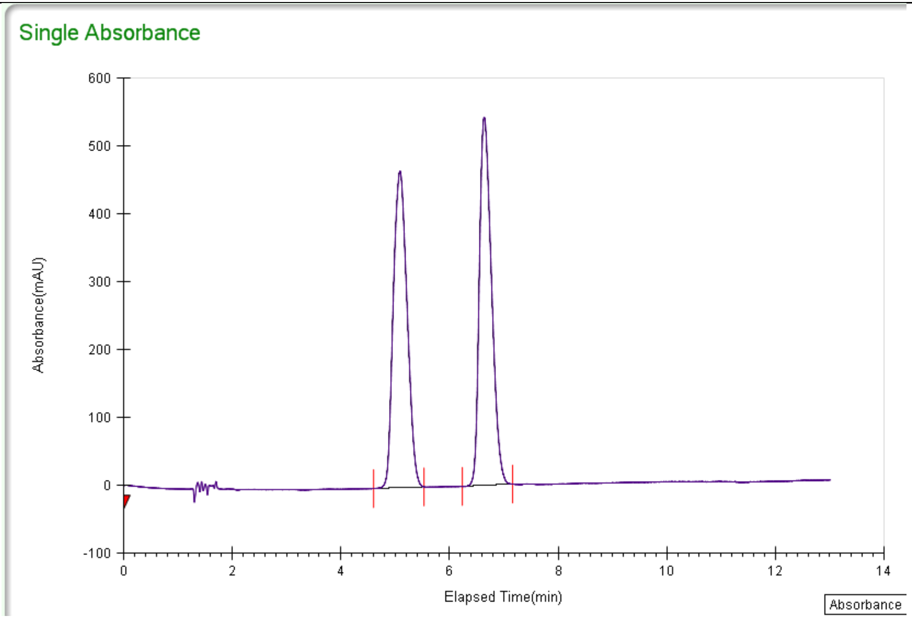




((1S,2S)-4,4-dimethyl-2-phenylcyclopentyl)(phenyl)methanone (3-25)

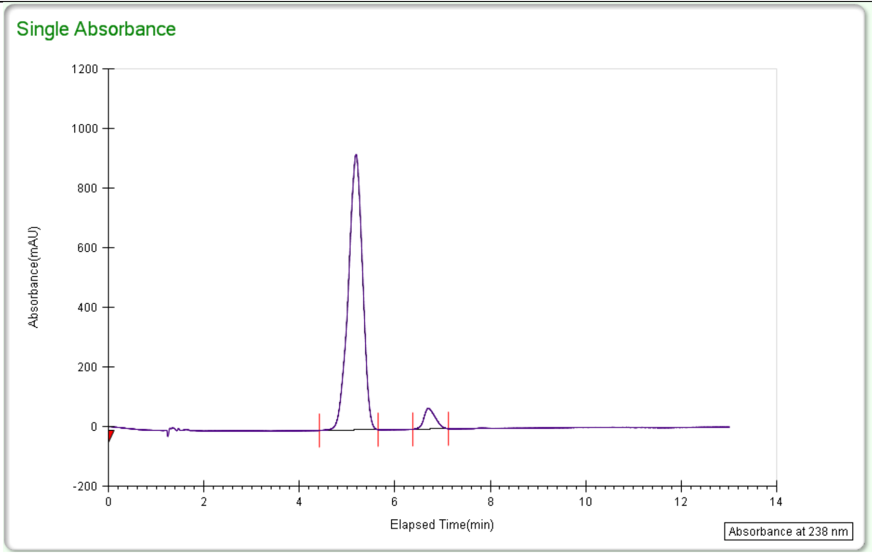
Racemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 238 nm

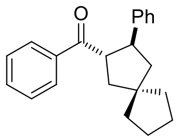
Peak	% area	area	RT(min)	height (mV)
1	49.3999	8225.7657	5.18	472.1342
2	50.6001	8425.6056	6.7	548.1129
Total	100	16651.3712		



Scalemic: SFC, Chiracel AD-H, gradient 5% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 238 nm

Peak	% area	area	RT(min)	height (mV)
1	94.3179	19058.3452	5.19	952.1298
2	5.6821	1148.1496	6.7	58.4213
Total	100	20206.4948		

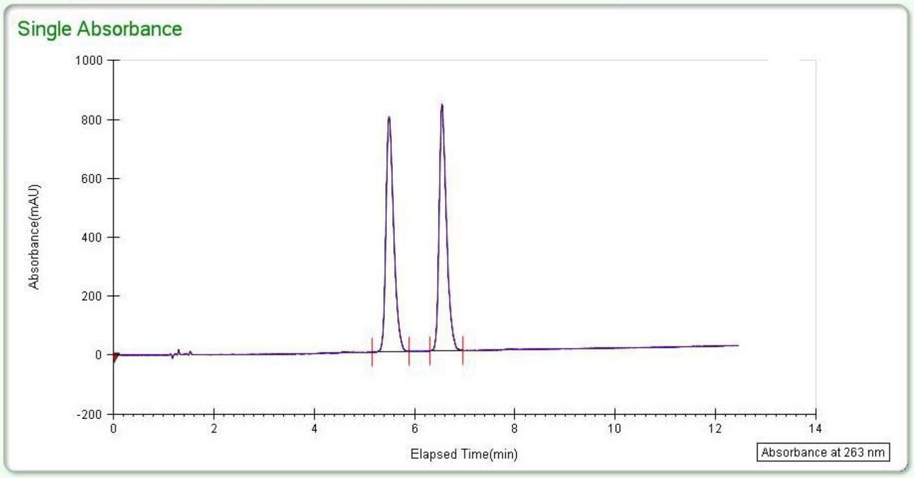




phenyl((2S,3S)-3-phenylspiro[4.4]nonan-2-yl)methanone (3-26)

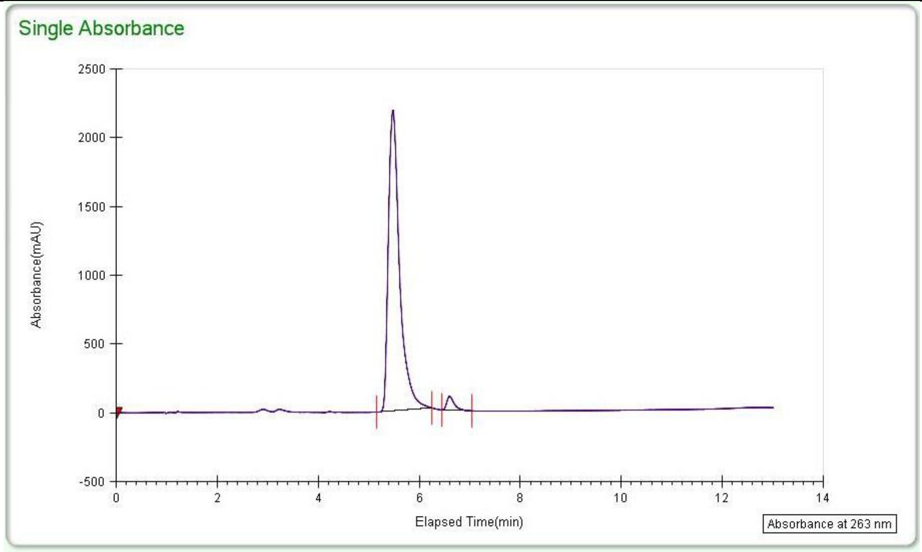
Racemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 263 nm

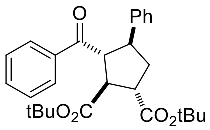
Peak	% area	area	RT(min)	height (mV)
1	50.2528	8530.2528	5.50	799.0081
2	49.7472	8444.3162	6.56	836.9197
Total	100	16974.4424		



Scalemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2 to 50% iPrOH/CO_2, 3 mL/min, 263 nm

Peak	% area	area	RT(min)	height (mV)
1	97.0312	33733.6188	5.49	2186.4065
2	2.9688	1032.1149	6.60	99.95
Total	100	34765.7317		

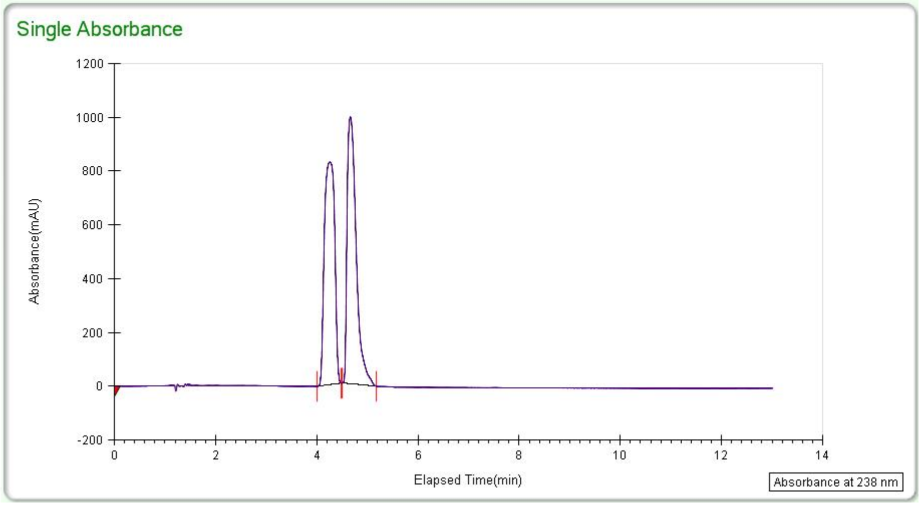




(1S,2S,3R,4S)-di-tert-butyl 3-benzoyl-4-phenylcyclopentane-1,2-dicarboxylate (3-30)

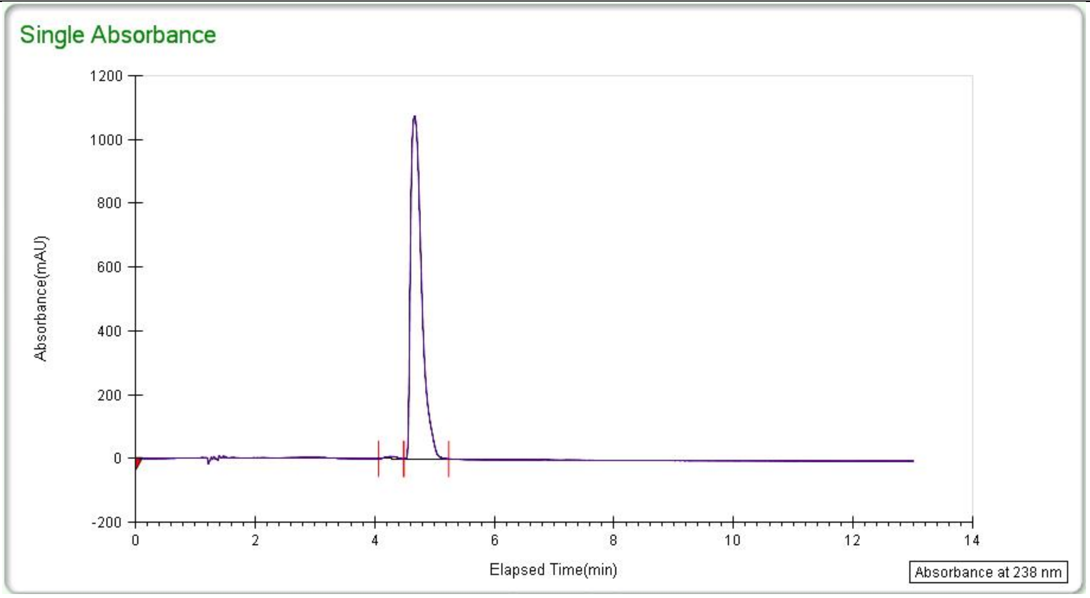
Racemic: SFC, Chiracel OD-H, gradient 5% iPrOH/CO_2 to 30% iPrOH/CO_2, 3 mL/min, 238 nm

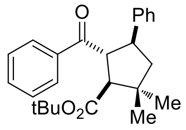
Peak	% area	area	RT(min)	height (mV)
1	48.589	11704.4724	4.27	827.3701
2	51.411	12384.259	4.66	991.9261
Total	100	24088.259		



Scalemic: SFC, Chiracel OD-H, gradient 5% iPrOH/CO_2 to 30% iPrOH/CO_2, 3 mL/min, 238 nm

Peak	% area	area	RT(min)	height (mV)
1	0.6737	93.2733	4.26	6.8032
2	99.3263	13750.9824	4.67	1073.6484
Total	100	13844.2557		

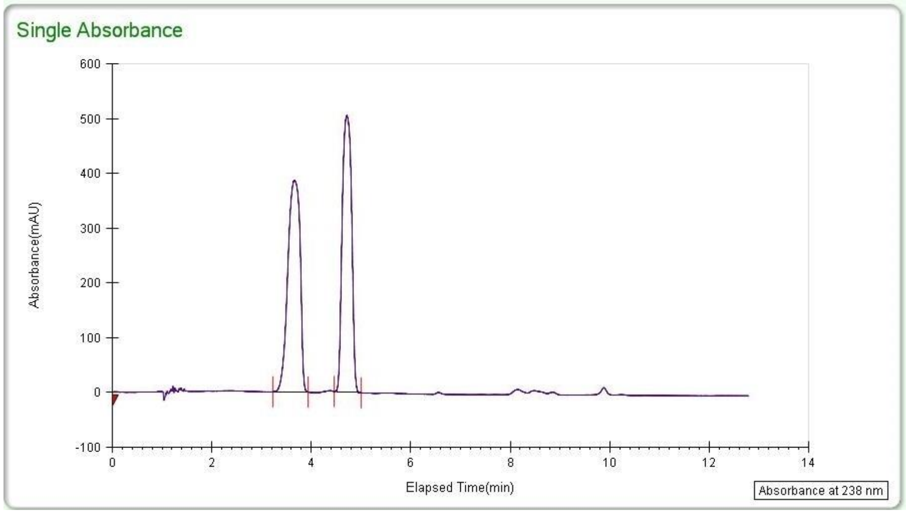




(1S,4S,5R)-tert-butyl 5-benzoyl-2,2-dimethyl-4-phenylcyclopentanecarboxylate (3-32)

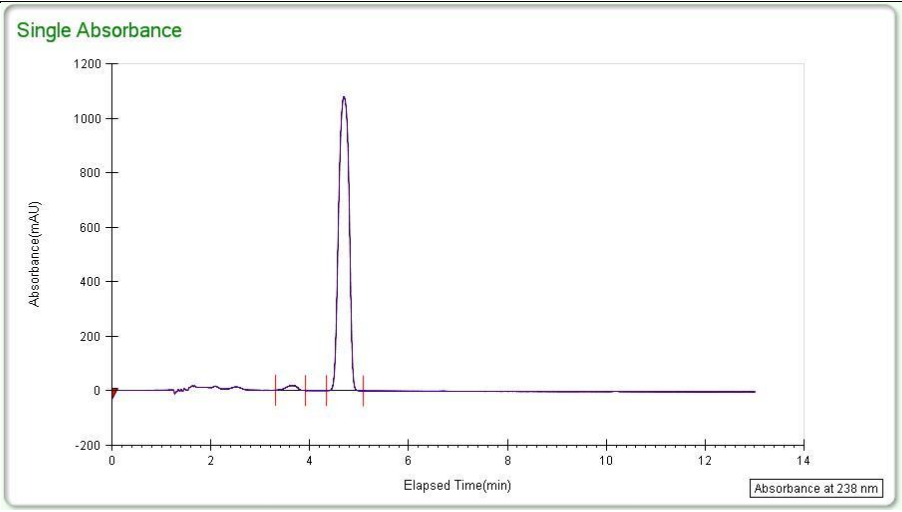
Racemic: SFC, Chiracel OD-H, gradient 5% iPrOH/CO_2 to 30% iPrOH/CO_2, 3 mL/min, 238 nm

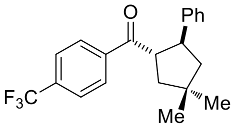
Peak	% area	area	RT(min)	height (mV)
1	50.0018	6620.3362	3.65	386.714
2	49.9982	6619.8586	4.66	506.2026
Total	100	13240.1948		



Scalemic: SFC, Chiracel OD-H, gradient 5% iPrOH/CO_2 to 30% iPrOH/CO_2, 3 mL/min, 238 nm

Peak	% area	area	RT(min)	height (mV)
1	1.7468	277.4604	3.64	17.5799
2	98.2532	15606.8709	4.69	1080.9641
Total	100	15884.3313		

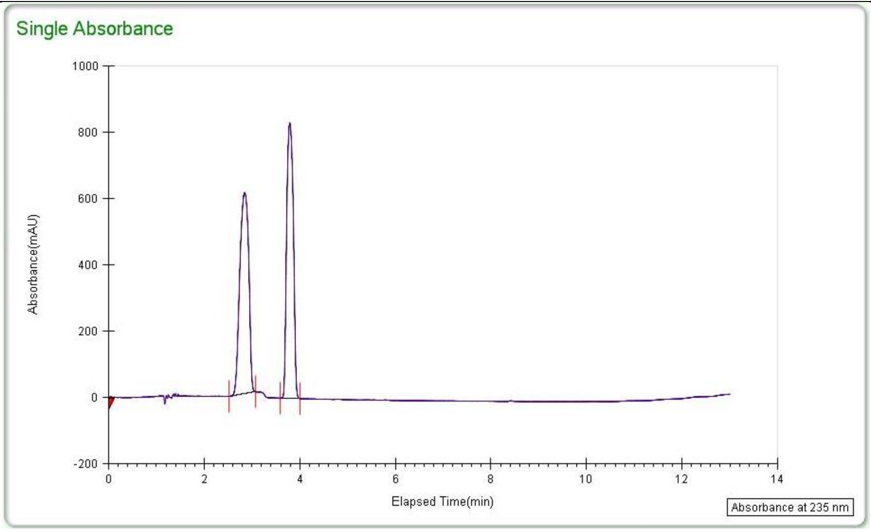




((1S,2S)-4,4-dimethyl-2-phenylcyclopentyl)(4-(trifluoromethyl)phenyl)methanone (3-34)

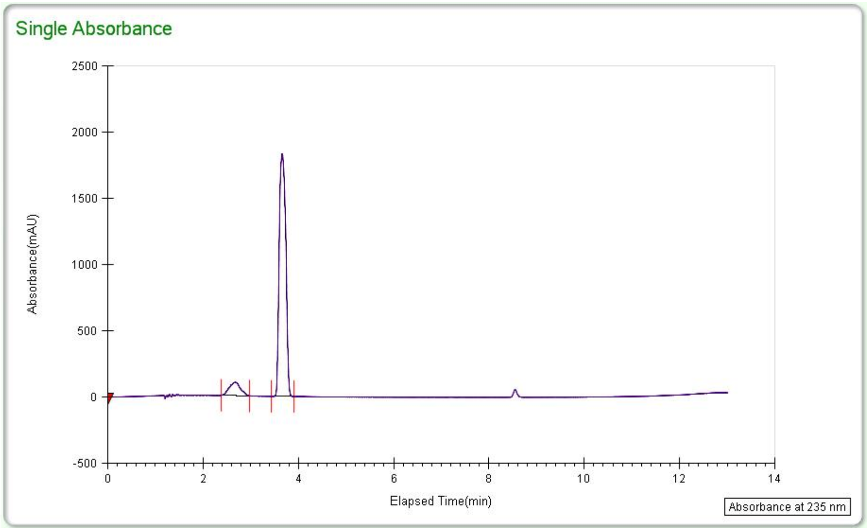
Racemic: SFC, Chiracel OD-H, gradient 5% (1:4 iPrOH/hexane)/CO_2 to 50% (1:4 iPrOH/hexane)/CO_2, 3 mL/min, 235 nm

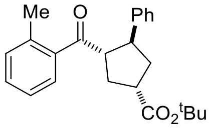
Peak	% area	area	RT(min)	height (mV)
1	49.5291	7852.5027	2.85	606.6880
2	50.4709	8001.8218	3.79	830.5841
Total	100	15854.3245		



Scalemic: SFC, Chiracel OD-H, gradient 5% (1:4 iPrOH/hexane)/CO_2 to 50% (1:4 iPrOH/hexane)/CO_2, 3 mL/min, 235 nm

Peak	% area	area	RT(min)	height (mV)
1	8.5386	1631.0355	2.68	99.9694
2	91.4614	17470.7852	3.66	1833.1693
Total	100	19101.8206		

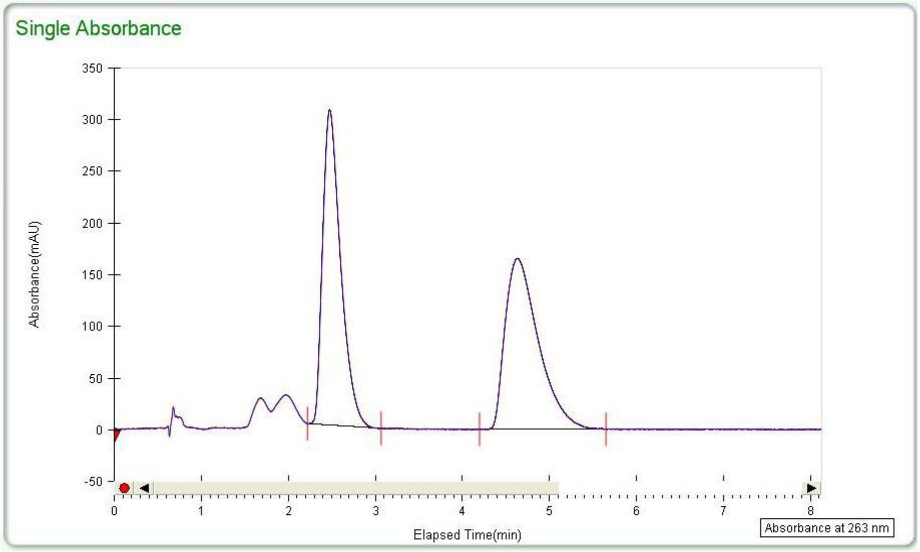




(1S,3S,4S)-tert-butyl 3-(2-methylbenzoyl)-4-phenylcyclopentanecarboxylate (3-28)

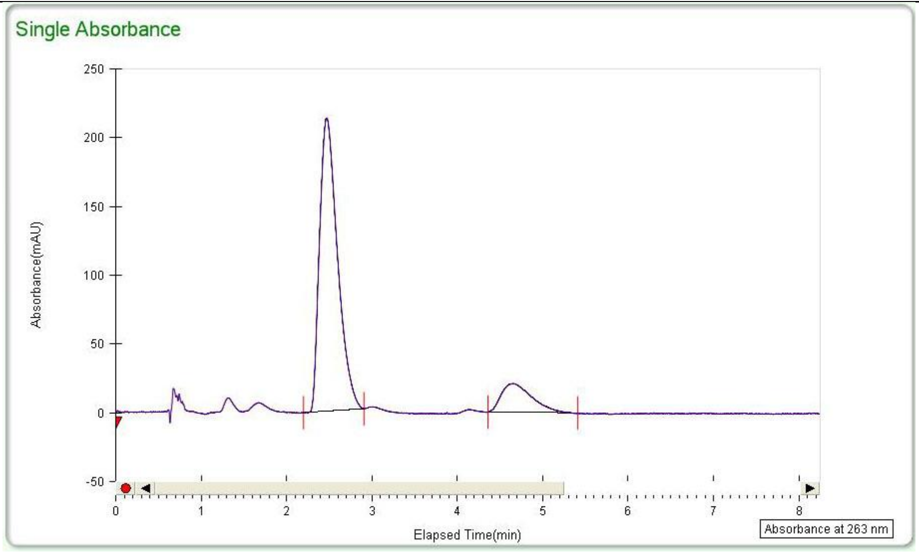
Racemic: SFC, Chiracel AD-H, 7% iPrOH/CO_2 iPrOH/CO_2, 6 mL/min, 263 nm

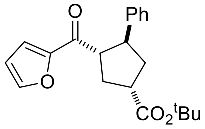
Peak	% area	area	RT(min)	height (mV)
1	50.0604	4391.855	2.47	305.0626
2	49.9396	4381.2509	4.63	165.3425
Total	100	8773.1059		



Scalemic: SFC, Chiracel AD-H, gradient 7% iPrOH/CO_2 iPrOH/CO_2, 6 mL/min, 263 nm

Peak	% area	area	RT(min)	height (mV)
1	85.6284	3103.9517	2.47	213.1387
2	14.3716	520.9562	4.65	20.933
Total	100	3624.9078		

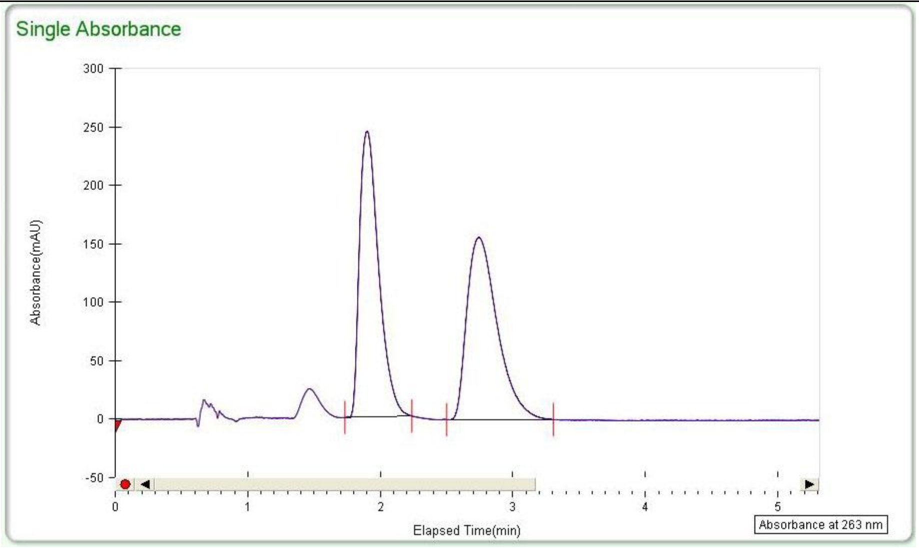




(1S,3S,4S)-tert-butyl 3-(furan-2-carbonyl)-4-phenylcyclopentanecarboxylate (3-27)

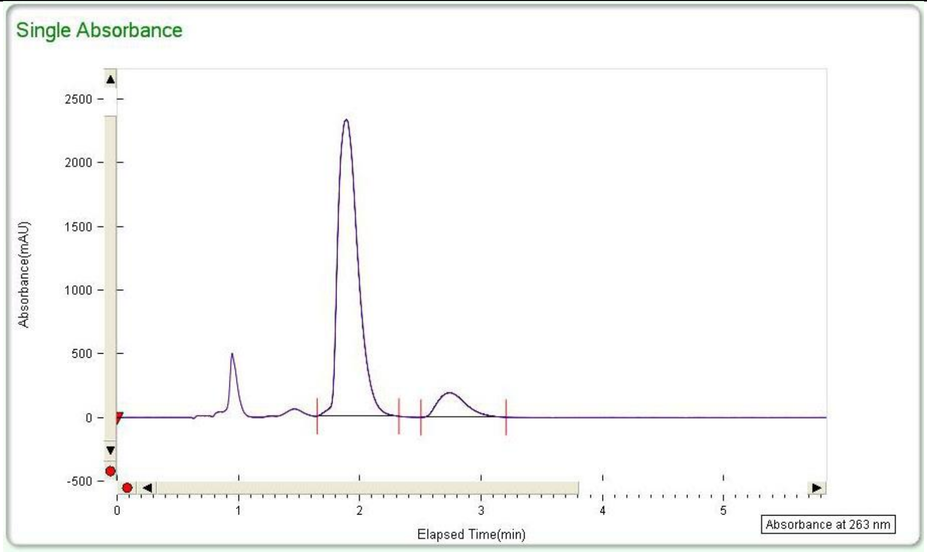
Racemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2, 6 mL/min, 263 nm

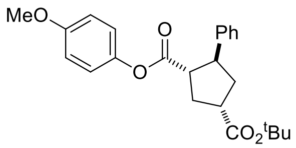
Peak	% area	area	RT(min)	height (mV)
1	49.83	2455.0862	1.9	244.5986
2	50.17	2471.8394	2.74	155.6862
Total	100	4926.9256		



Scalemic: SFC, Chiracel AD-H, gradient 10% iPrOH/CO_2, 6 mL/min, 263 nm

Peak	% area	area	RT(min)	height (mV)
1	89.4167	26631.9992	1.89	2327.4631
2	10.5833	3152.1447	2.74	192.9336
Total	100	39784.144		

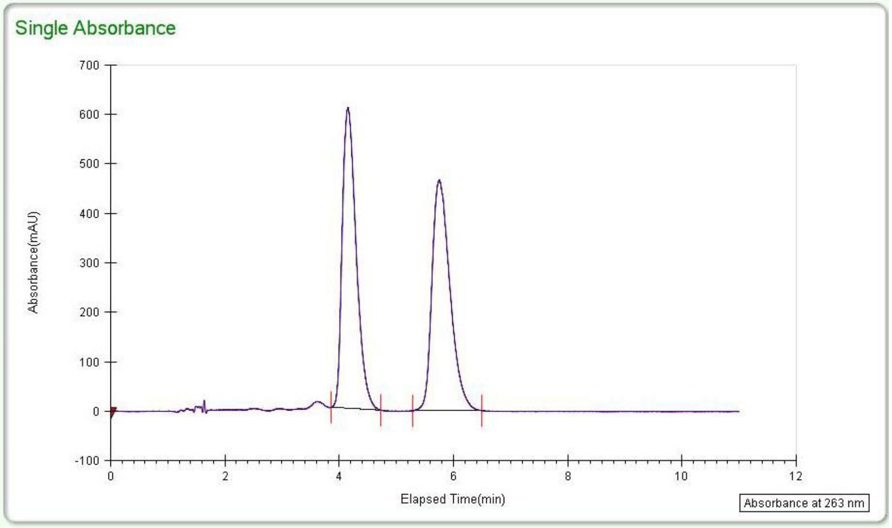




(1S,3S,4S)-1-tert-butyl 3-(4-methoxyphenyl) 4-phenylcyclopentane-1,3-dicarboxylate (3-33)

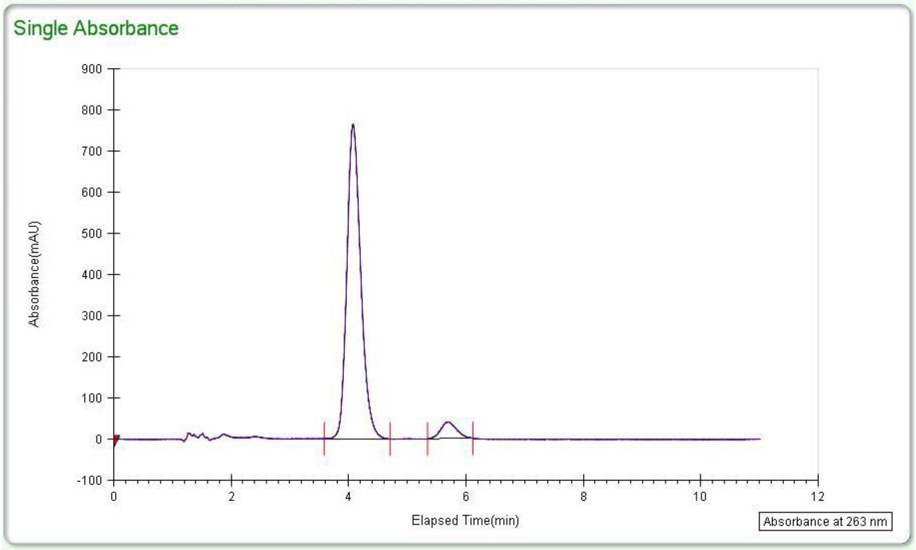
Racemic: SFC, Chiracel AD-H, gradient 15% iPrOH/CO$_2$, 3 mL/min, 263 nm

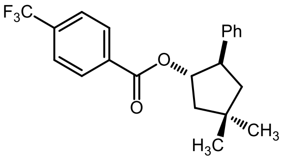
Peak	% area	area	RT(min)	height (mV)
1	50.2109	10299.0288	4.15	
2	49.7891	10212.4956	5.75	
Total	100	20511.5245		



Scalemic: SFC, Chiracel AD-H, gradient 15% iPrOH/CO$_2$, 3 mL/min, 263 nm

Peak	% area	area	RT(min)	height (mV)
1	94.3301	12566.3858	4.08	
2	5.6699	755.324	5.7	
Total	100	13321.7098		

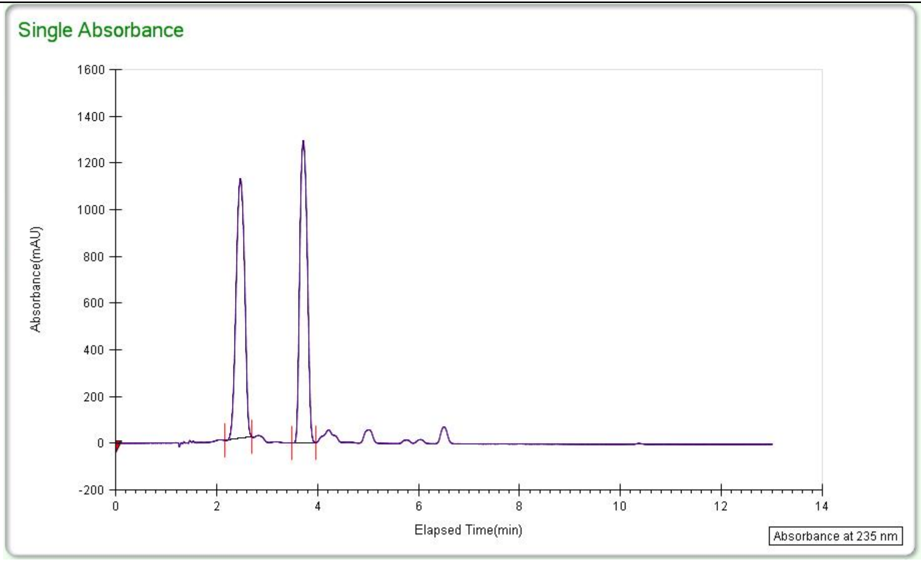




(1S,2R)-4,4-dimethyl-2-phenylcyclopentyl 4-(trifluoromethyl)benzoate (3-35)

Racemic: SFC, Chiracel OD-H, gradient 5% iPrOH/CO_2 to 30% iPrOH/CO_2, 3 mL/min, 235 nm

Peak	% area	area	RT(min)	height (mV)
1	49.4434	12968.7309	2.47	1112.3162
2	50.5566	13260.7238	3.72	1292.3761
Total	100	26229.4547		



Scalemic: SFC, Chiracel OD-H, gradient 5% iPrOH/CO_2 to 30% iPrOH/CO_2, 3 mL/min, 235 nm

Peak	% area	area	RT(min)	height (mV)
1	8.4522	1809.6007	2.51	128.8436
2	91.5478	19600.2886	3.73	1833.1819
Total	100	21409.8893