

DISSERTATION

OXIDATIVE QUENCHING ORGANIC PHOTOCATALYST DESIGN, SYNTHESIS AND
APPLICATION IN DUAL NICKEL/PHOTOREDOX-CATALYSIS

Submitted by

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In partial fulfillment of the requirements

For the Degree of Doctor of Philosophy

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Fall 2023

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ABSTRACT

OXIDATIVE QUENCHING ORGANIC PHOTOCATALYST DESIGN, SYNTHESIS AND APPLICATION IN DUAL NICKEL/PHOTOREDOX-CATALYSIS

The work described in this dissertation focuses on the development of a new class of organic photocatalysts and the application of oxidative quenching photocatalysts in dual nickel/photoredox-catalysis. The design of new organic photocatalysts is crucial for eliminating the need to use rare/expensive ruthenium and iridium that have dominated the field of photoredox catalysis. Additionally, the majority of the catalysts describe here-in operate through an oxidative quenching mechanism that remains underexplored in the field of dual nickel/photoredox catalysis. The first detailed mechanistic study on oxidative quenching in this field is reported and applied in a broad range of couplings.

DEDICATION

To my family, friends, and wonderful coworkers in the Miyake Group

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CHAPTER 1 – INTRODUCTION

DISSERTATION STRUCTURE

This dissertation consists of five chapters. Chapters 2-4 are adapted from previously published work and Chapter 5 is an early draft of unpublished work. Below is a list of the chapters including a summary of the content:

Chapter 2: Adapted from: Sartor, S. M.; Chrisman, C. H.; Pearson, R. M.; Miyake, G. M.; Damrauer, N. H., Designing High Triplet Yield Phenothiazine Donor-Acceptor Complexes for Photoredox Catalysis. *J. Phys. Chem. A*. **2020**, *124*, 817-823. This chapter focuses on optimizing and understanding photophysical properties of a new class of highly reducing phenothiazine catalysts.

Chapter 3: Adapted from: Chen, D.-F.; Chrisman, C. H.; Miyake, G. M., Bromine Radical Catalysis by Energy Transfer Photosensitization. *ACS Catal.* **2020**, *10*, 2609-2614. This chapter focuses on the use of organic photocatalysts to generate bromine radicals through energy transfer between a photocatalyst and an alkyl bromide. The bromine radical then catalyzes a [3 + 2] cycloaddition reaction.

Chapter 4: Adapted from: Chrisman, C. H.; Kudisch, M. K.; Puffer, K. O.; Stewart, T. K.; Lamb, Y. M. L.; Lim, C.-H.; Escobar, R.; Thordarson, P.; Johannes, J. W.; Miyake, G. M., Halide Noninnocence and Direct Photoreduction of Ni(II) Enables Coupling of Aryl Chlorides in Dual Catalytic, Carbon-Heteroatom Bond-Forming Reactions. *J. Am. Chem. Soc.* **2023**, *145*, 12293-12304. In this work, an oxidative quenching mechanism was spectroscopically elucidated for the first time in dual nickel/photoredox-catalysis. This enabled mechanistic guided optimization leading to a significant increase in reaction rate and substrate scope.

Chapter 5: Unpublished work from a manuscript draft tentatively titled “Substrate/Photocatalyst Reactivity Matching Enables Broad Aryl Halide Scope in Light Driven, Reductive Cross-Electrophile Coupling Utilizing ^{13}C NMR as a Predictor”. In this work, two sets of conditions were developed for a reductive cross-coupling using side reactivity identification and high-throughput experimentation. Substrate yield and reaction conditions were correlated with ^{13}C NMR shifts, enabling facile condition selection.

MOTIVATIONS

Over the past decade, photoredox catalysis has become a critical tool for small and macromolecule synthesis. Photoredox catalysis represents many ideals of green chemistry, including performing reactions under mild conditions fueled by solar energy. However, iridium (Ir) and ruthenium (Ru) complexes are the most commonly used photocatalysts (PCs) and there are concerns regarding their sustainability, including scarcity of the elements, greenhouse gas emissions from mining, and geopolitical tension in mining regions.^{1,2} Because of these issues, significant research has been dedicated to designing organic photocatalysts (OPCs) as more sustainable alternatives to Ir and Ru.

Our groups research focuses on the design, synthesis, and application of OPCs towards the goal of replacing Ru and Ir. In order to compete with Ru and Ir PCs, an OPC must have redox and photophysical properties rivaling the metals. One of the most challenging properties to access with OPCs is a high triplet quantum yield due to a lack of spin-orbit coupling arising from the heavy-atom effect in Ir/Ru PCs. To overcome this, our group has adopted an approach of designing OPCs with multiple charge-transfer excited states (Figure 1.1A).^{3,4} If these charge transfer states are orthogonal, spin-orbit coupling can be accessed, leading to a triplet quantum yield near unity. See Chapter 2 for an example of this in the design of a new class of phenothiazine catalysts.

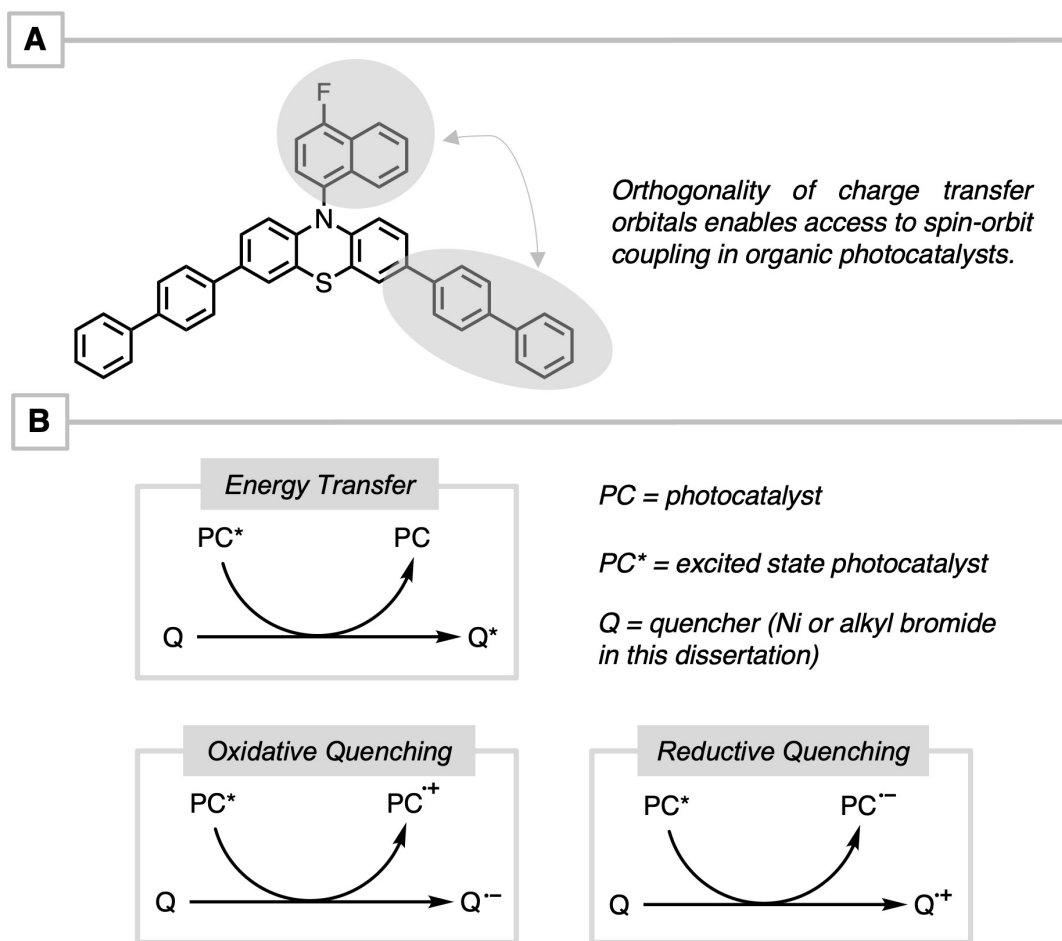


Figure 1.1. Overview of some concepts covered in this dissertation. (A) optimized phenothiazine photocatalyst as an example of introducing orbital orthogonality for spin orbit coupling (Chapter 2). (B) Schemes describing the different mechanisms through which PCs typically act (covered in Chapters 3-5).

While it is important to design new OPCs with properties rivaling metal PCs, they ultimately need to perform better than Ir/Ru in reactions to be truly viable replacements.⁵ Additionally, understanding the mechanism through which OPCs act is key in designing reaction systems for their application. Photocatalysts generally act through three different mechanisms: energy transfer, oxidative quenching, and reductive quenching.⁶ These modes of action are outlined in Figure 1.1B. Understanding how OPCs catalyze certain transformations is a sub-focus within our group and has been critical in guiding experiments for optimizing reactions. Chapters 3-5 focus on applying OPCs with properties rivaling metal PCs in small molecule transformations

with either an organic (Chapter 3) or nickel (Chapters 4 and 5) cocatalyst. Ultimately, the work described here-in tells the story of implementing OPCs from beginning (fundamental photophysics and property optimization) to end (applications and mechanistic understanding).

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- (3) For an example of PC structure-property relationships see: McCarthy, B. G.; Pearson, R. M.; Lim, C.-H.; Sartor, S. M.; Damrauer, N. H.; Miyake, G. M. *J. Am. Chem. Soc.* **2018**, *140*, 5088-5101.
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CHAPTER 2 – DESIGNING HIGH TRIPLET YIELD PHENOTHIAZINE DONOR-ACCEPTOR COMPLEXES FOR PHOTOREDOX CATALYSIS.

OVERVIEW

Phenothiazine, owing to its ease of oxidation and modularity with respect to facile functionalization, is an attractive central chemical unit from which to construct highly reducing organic photoredox catalysts. While design improvements have been made in the community, the yield of intersystem crossing (Φ_{ISC}), which determines access to the long-lived triplet excited state, has yet to be systematically optimized. Herein, we explore the impacts of *N*-aryl substituent variation on excited state dynamics using picosecond to millisecond transient absorption and emission spectroscopies. Design principles are uncovered that center on controlling the energy of an intermediate charge transfer (CT) state within the singlet excited state manifold, which, in turn, dictates the yield of CT-state formation and the rate constants for its depletion. Ultimately, we find Φ_{ISC} to be highly sensitive to the electron-withdrawing character of the *N*-aryl electron acceptor in the aforementioned CT state, with Φ_{ISC} ranging from ~0 to 0.96.

INTRODUCTION

Photoredox catalysis is an increasingly attractive method for achieving challenging chemical transformations under mild synthetic conditions.¹⁻⁷ Presently, however, rare-metal photocatalysts – primarily containing ruthenium or iridium – continue to dominate the field.^{1-5,8} Continued reliance on these rare metals limits the potential supply of photocatalysts, thus motivating the development of photocatalysts of comparable capability made from earth-abundant elements.^{6,9-11} There have been substantial research efforts to this end, which can be broadly classified into two categories possessing their own unique challenges and advantages: efforts to

replace rare metals with earth abundant metals^{9,12-14} and efforts to employ fully organic architectures.^{6,15-18} This contribution relates to the latter.

The development of organic photocatalysts is aided by the increased reaction scope that the diversity of organic systems provides.⁶ However, organic photocatalysts often suffer from inefficient intersystem crossing (ISC), thus limiting access to the long-lived triplet excited state.⁶ This is a significant drawback, as the long-lived triplet state (typically $\sim 10^3$ - 10^6 times longer-lived than the singlet) affords the photocatalyst sufficient time to efficiently engage in excited-state bimolecular electron transfer. We note that traditional methods of increasing the yield of ISC (Φ_{ISC}) (e.g., carbonyl or heavy atom functionalization) can be undesirable, as these can increase synthetic complexity, lessen reactive potency, reduce triplet lifetimes, and increase the likelihood of undesirable side reactions.¹⁹⁻²¹

An alternative to these traditional methods is SOCT-ISC (SOCT = spin-orbit charge transfer) involving a singlet charge transfer (CT) state with orthogonal (or nearly-orthogonal) donor and acceptor moieties.²⁰⁻²⁴ Such systems facilitate efficient ISC by slowing radiative decay and, because the recombination process (undoing the CT) requires a significant change in orbital angular momentum, providing the torque necessary for a change in spin angular momentum to the triplet manifold. Importantly, the SOCT-ISC mechanism does not suffer from the drawbacks stated above for traditional methods for increasing Φ_{ISC} .

In our labs, we have been interested in understanding and uncovering design principles behind highly reducing organic photocatalysts that have proven valuable for the synthesis of well-defined polymers and small molecules under visible-light excitation.^{25,26} To this end, a variety of organic architectures have been explored,²⁷ including those derived from a phenoxazine core.²⁸ Phenoxazine is an attractive central chemical unit as it is easily and reversibly oxidized while

possessing distinct core and *N*-substitutional positions that can be independently functionalized in order to imbue desired photochemical properties. For instance, aryl functionalization on the 3 and 7 carbons (so-called core substitution) results in increased π -conjugation, leading to increased molar absorptivity and red shifting absorption into the visible.^{28,29} In contrast, the *N*-position is sterically congested such that aryl substituents, such as naphthalene, are twisted and possess poor electronic coupling to the phenoxazine core. Formation of orthogonal CT states remains kinetically favored, and these states then facilitate efficient ISC to the long-lived triplet state on the extended core.³⁰

Encouraged by the function and facile tunability of these phenoxazine photocatalysts, we wished to investigate whether the design principles can be applied to related structures derived from phenothiazine. In such systems, replacement of the oxygen with a sulfur atom has little impact on the oxidation properties of the core, and the system, as a whole, offers comparable chemical modularity involving core and *N*-substitution. We also surmised at the outset that a heavier atom substitution might contribute to increased ISC rates. It is noted that a number of phenothiazine-based photocatalysts have been developed and employed for controlled radical polymerizations and small molecule transformations, some of which predate our labs' involvement with phenoxazine-based photocatalysts.^{19,31-36} However, the relationship between molecular design and photophysical properties relevant to photocatalysis remains underexplored for phenothiazine systems. In particular, while progress has been made in tuning the absorption of light and excited-state reduction potentials, relatively little emphasis has been placed on controlling Φ_{ISC} .

Interestingly, there have been recent investigations of phenothiazine-containing compounds designed to achieve high Φ_{ISC} in heavy-atom free organic systems, for a variety of

applications.^{20,21,37,38} In these compounds, phenothiazine is not the chromophore but rather serves as an intramolecular electron donor following optical excitation of an electronically distinct electron acceptor (e.g., anthracene, perylenemonoimide). The resulting CT state then facilitates ISC to a triplet state localized on the aforementioned electron acceptor via a SOCT-ISC mechanism.

Within the current work, we utilize molecular designs derived from our well-established phenoxazine analogues in order to develop compounds built upon on the phenothiazine core as potential photoredox catalysts.^{30,39} This approach is powerful inasmuch as it provides useful context for understanding photophysical behavior, and it allows for the isolation of the impact of the sulfur atom, which is unique to phenothiazine, on photophysical processes. To the latter point, for example, phenothiazine experiences geometric distortions resulting from the size of sulfur relative to oxygen.²⁸ Over the course of this investigation, we find it necessary to tune the electron-withdrawing character of the *N*-aryl electron acceptor in order to promote efficient ISC. Ultimately, we find that Φ_{ISC} varies considerably with this parameter, with Φ_{ISC} ranging from ~0 to 0.96.

RESULTS AND DISCUSSION

We begin with **Phen** and **Naph** (Figure 2.1), compounds that are direct sulfur-containing analogues to phenoxazine derivatives that have been previously developed and characterized by our groups. These and related molecules are synthesized via a bromination of the 3,7 positions of the phenothiazine followed by a Suzuki reaction for core substitution and a Buchwald-Hartwig reaction for *N*-aryl substitution (see S.I. for details). Figure 2 shows absorption spectra for **Phen** and **Naph** in DMAc. Both possess highly similar profiles with significant absorption in the visible region. The peak molar absorptivities (ϵ) of **Phen** and **Naph** were determined to be 15,400 M⁻¹cm⁻¹

¹ (at 363 nm) and 15,500 M⁻¹cm⁻¹ (at 376 nm), respectively. While reasonably absorptive, the comparable values in the respective phenoxazine analogues are 24,000 and 25,900 M⁻¹cm⁻¹ (both at 388 nm).²⁹ This variation with heteroatom may originate in core chromophore structural differences and their impact on transition dipole moments. The phenoxazine core is nearly planar while the phenothiazine core is significantly bent, driven by the size and hybridization of the sulfur atom.²⁸ Consistent with phenoxazine derivatives,³⁰ the spectral similarity shared by **Phen** and **Naph** indicates that the *N*-aryl substituent minimally impacts the absorption of light.

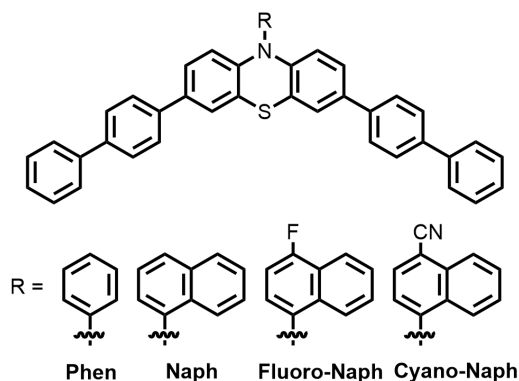


Figure 2.1. Compounds investigated in this study.

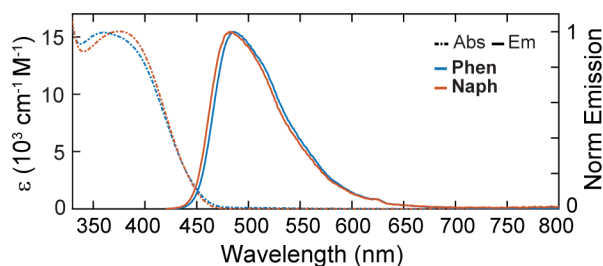


Figure 2.2. Steady-state absorption (dashed) and fluorescence (solid) of **Phen** and **Naph** in room-temperature (RT) dimethylacetamide (DMAC).

The fluorescence spectra of **Phen** and **Naph** in DMAC are also shown in Figure 2.2. Due to competing phosphorescence (see S.I.), fluorescence was isolated by collecting data in the presence of oxygen. As with absorption, the fluorescence profiles are highly similar, indicating emitting singlets of comparable electronic character, which therefore do not involve the *N*-aryl

substituent. Measurement of **Naph** fluorescence in multiple solvents reveals only modest solvatochromism (see Figure S2.23), highlighting a weakly polar emitting state. By the contrast of this emission behavior to that of well-characterized phenoxazine-containing analogues,^{30,39} we assign the state as being delocalized across the phenothiazine and both biphenyl substituents, which is accordingly denoted S_{deloc} (see SI for details). The formation of S_{deloc} in **Naph** is a departure from the behavior of its direct phenoxazine analogue, in which the S_1 involves a CT from the phenoxazine core to the *N*-aryl substituent.³⁰ Due to the similarity of the oxidation potential between phenoxazine and phenothiazine analogues (**Phen** and **Naph** oxidize at 0.61 and 0.64 V vs SCE in DMAc, respectively (see SI for details), which is highly comparable to the corresponding values of 0.62 and 0.65 V for their respective phenoxazine analogues), the failure to form a CT state in **Naph** (characterized by reduction of the *N*-aryl substituent) is not attributed to CT destabilization. Rather, it indicates that the phenothiazine complexes possess a lower-lying core-localized π^* , which is consistent with the lower energy fluorescence of non-core-substituted phenothiazines relative to their phenoxazine analogues.⁴⁰

However, despite the similarity of the **Phen** and **Naph** fluorescence profiles, their quantum yields of fluorescence (Φ_f) are substantially different at 0.41 and 0.17, respectively (Table 2.1). The lower Φ_f for **Naph** hints at the possible co-population of a weakly emissive state (e.g., an orthogonal CT state), which may be masked by the more emissive S_{deloc} . To interrogate this scenario, we turn to femtosecond transient absorption (FSTA) spectroscopy. Figure 3 shows spectra of **Phen** and **Naph**, in deaerated RT DMAc, following 400 nm excitation. Early dynamics for **Phen** (Figure 2.3A) include the rise and sharpening of the peaks at 460 and 630 nm and are thus understood as cooling from the Franck-Condon state, likely consisting of vibrational and solvent relaxation. These changes are complete by 10 ps. Afterwards, the spectra decay

monotonically with no shifting of features. Therefore, the spectrum at 10 ps is assigned to S_{deloc} .

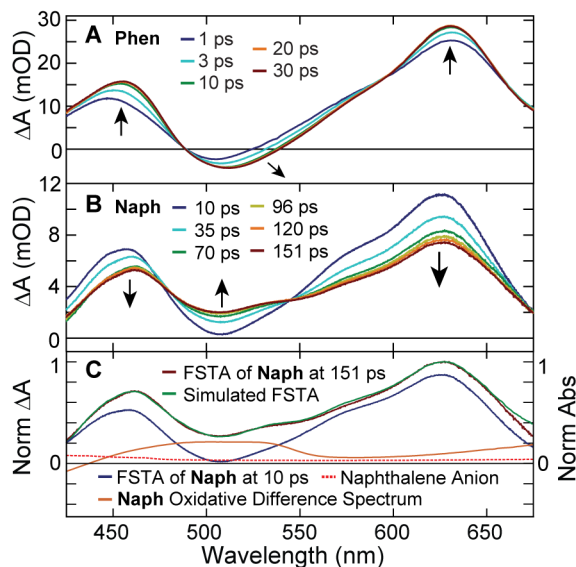


Figure 2.3. Selected FSTA spectra for Phen (A) and Naph (B) in deaerated RT DMAc, with arrows to indicate the direction of dynamics. (C) Observed and simulated late-time FSTA spectra of Naph, with the redox-derived data and early-time FSTA spectrum used for simulation. Solid and dashed lines refer to ΔA and absorbance spectra, respectively.

Naph initially looks similar, with early times revealing comparable cooling dynamics (see Figure S2.30). However, these are then followed by significant spectral changes occurring with a 34 ps time constant, comprising of the loss of the peaks at 460 and 630 nm and a rise in intensity at ~ 500 nm, with associated isosbestic points at 480 and 550 nm (Figure 2.3B). After these, spectral changes cease and all features decay monotonically on a timescale which cannot be resolved (> 2 ns). While these data strongly indicate a 34 ps electronic interconversion away from S_{deloc} , the remaining peaks at 460 and 630 nm suggest that this does not proceed to completion. Rather, an equilibrium of excited states is established at late times (e.g., ~ 100 ps), which is consistent with fluorescence data (vide supra) which hinted at the partial formation of a weakly emissive CT state. Such a state in **Naph** would most likely consist of CT from the phenothiazine to the naphthyl group (so-called $S_{\text{CT-Naph}}$).

In order to probe for the presence of $S_{\text{CT-Naph}}$, the late-time FSTA spectrum is simulated

using the absorption spectrum of anionic naphthalene, the oxidative difference spectrum of **Naph** generated by spectroelectrochemistry, and the early-time FSTA spectrum to account for the spectrum of the remaining S_{deloc} (Figure 2.3C; see SI for more details). The resemblance of the simulated FSTA spectrum to the late-time FSTA data is remarkable and provides compelling evidence that the late-time FSTA spectrum represents a combination of $S_{\text{CT-Naph}}$ and S_{deloc} and, further, that the phenothiazine donor and the naphthyl acceptor are electronically decoupled in the $S_{\text{CT-Naph}}$ state. Further, this modeling can be used to estimate the degree of interconversion from S_{deloc} to $S_{\text{CT-Naph}}$, at $\sim 50\%$ (see SI for details), thus indicating that the two states are nearly isoenergetic.

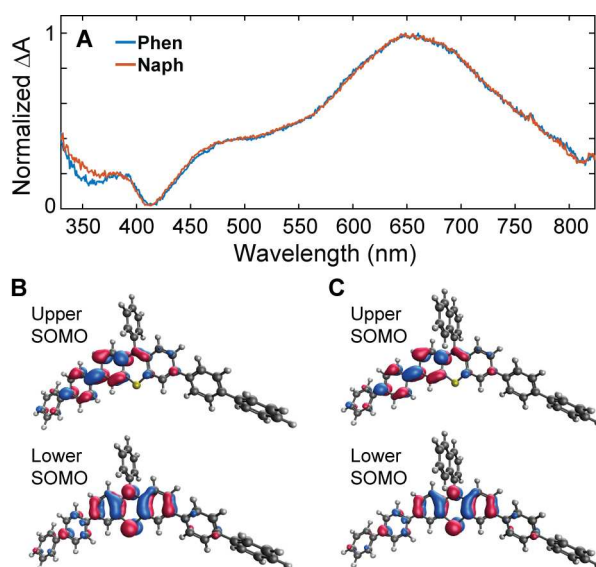


Figure 2.4. (A) Triplet NSTA spectra of Phen and Naph in deaerated RT DMAc, taken at a time delay of 10 microseconds. (B) & (C) Triplet SOMOS of Phen (B) and Naph (C) ($\mu\text{M06/6-31g(d,p)/CPCM-DMAc}$ level of theory).

We next turn to nanosecond TA (NSTA) to interrogate the long-lived lowest energy excited state. Figure 2.4A shows the spectrum of **Phen** and **Naph** observed in deaerated RT DMAc 10 μs after 355 nm excitation. Each of these spectra are understood to originate from the lowest energy triplet excited state (T_1) due to the long observed lifetimes (>15 ms, as measured via

phosphorescence experiments; see SI for more details) and high sensitivity of these lifetimes to oxygen. The similarity of the T_1 TA spectra of **Phen** and **Naph** indicates that both species possess a T_1 of comparable electronic character. DFT calculations reveal a T_1 characterized by a partial charge transfer from the phenothiazine core to a singlet core-biphenyl substituent (Figures 2.4B and 2.4C). We thus denote it in both compounds as $T_{CT-Biph}$. It is noted that the τ_{T_1} in both **Phen** and **Naph** is remarkably long for room-temperature solution phase compounds. These lifetimes are, in fact, more than 10 times longer than the phenoxazine analogues, which have electronically similar T_1 states ($T_{CT-Biph}$). The reason for triplet lifetime lengthening upon sulfur substitution for oxygen is not presently obvious⁴¹ and may be of interest for future studies. As a consequence of this extended lifetime, phosphorescence, albeit weak, can be observed in solution at room temperature, which conveniently allows for experimental determination of $T_{CT-Biph}$ energy, E_{00,T_1} , by vibronic analysis of the phosphorescence spectra (see SI for details), which yields $E_{00,T_1} = 2.27$ eV for both compounds. We note that E_{00,T_1} is close to the DFT calculated triplet energy of 2.34 eV for both **Phen** and **Naph**, which was computed at the uM06/6-31+g(d,p)/CPCM-n,n-dimethylacetamide level of theory.

As alluded to above, there are differences in the yield of T_1 formation for both compounds with $\Phi_{ISC} = 0.76$ and 0.41 for **Naph** and **Phen**, respectively. The higher triplet yield for the former is understood to be a result of occupation of the $S_{CT-Naph}$ state in the excited state equilibrium (vide supra): this CT state serves to both slow radiative decay and speed ISC.²⁰⁻²⁴ The latter effect is a consequence of the orthogonal π systems wherein the large change of angular momentum induced by the $S_{CT-Naph} \rightarrow T_{CT-Biph}$ transition facilitates spin-orbit coupling between the states. These results suggest a path forward for optimizing related phenothiazine compounds as potential photocatalysts with high triplet yields. Namely, we hypothesized that chemical modifications that selectively

lower the energy of the $S_{CT-Naph}$ state should, in turn, cause $S_{CT-Naph}$ to form with unity (or near-unity) yield, thus leading to the aforementioned benefits to Φ_{ISC} . With this hypothesis in mind, two new compounds were investigated that install electron withdrawing groups (EWGs) on the 4-position of the naphthyl moiety. These are referred to as **Fluoro-Naph** and **Cyano-Naph** (Figure 2.1). In the first case, the fluorine is a weak EWG due to competition between σ -withdrawing and π -donating character. In the second case, $S_{CT-Naph}$ is more significantly perturbed because the cyano substituent is both strongly σ - and π -withdrawing.⁴²

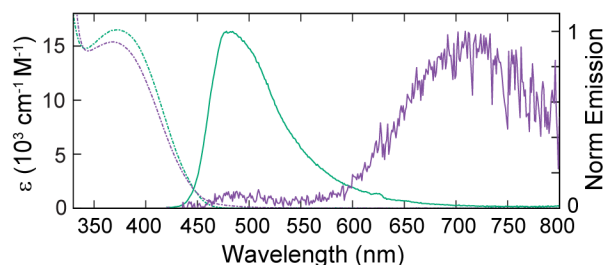


Figure 2.5. Steady-state absorption (dashed) and fluorescence (solid) of **Fluoro-Naph** and **Cyano-Naph** in RT DMAc. As with **Phen** and **Naph**, fluorescence spectra were collected under ambient air conditions to preclude emission from phosphorescence.

Figure 2.5 shows absorption spectra for **Fluoro-Naph** and **Cyano-Naph** in DMAc. As was also seen in the comparison between **Phen** and **Naph**, the *N*-aryl substituent does not meaningfully impact the Franck-Condon state. The fluorescence data, however, tell a different story about the impact of the EWG. In **Fluoro-Naph**, the spectrum, shown in Figure 2.5, is similar to that of **Phen** and **Naph**, although its Φ_{fl} of 0.034 is far weaker. The low Φ_{fl} suggests that fluorination has lowered the energy of the $S_{CT-Naph}$ state, thereby shifting the excited-state equilibrium away from the more highly emissive S_{deloc} to the relatively dark $S_{CT-Naph}$. In **Cyano-Naph**, both spectral and quantum yield perturbations are more striking. We observe significant broadening and red shifting relative to the other three compounds and Φ_{fl} is extremely low, at 0.0008. These data suggest that

Cyano-Naph has a substantially lowered $S_{CT-Naph}$ energy such that only emission from $S_{CT-Naph}$ is observed. In order to probe these assignments, we again turn to FSTA.

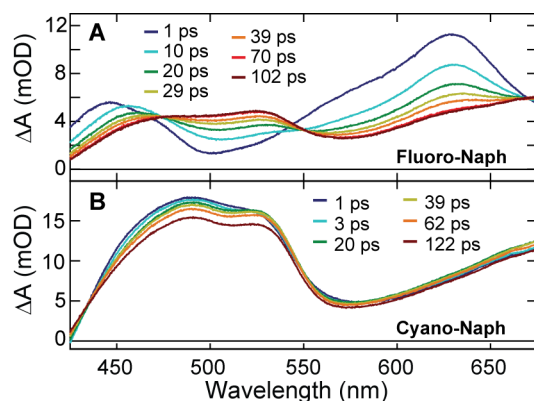


Figure 2.6. Selected FSTA spectra for Fluoro-Naph (A) and Cyano-Naph (B) in deaerated RT DMAc.

Figure 2.6A shows FSTA spectra collected for **Fluoro-Naph** in deaerated RT DMAc, following 400 nm excitation. At early times (e.g., 1 ps), the data resemble those of **Phen**, indicating occupation of S_{deloc} . However, dramatic spectral evolution is then observed on a 19 ps timescale, resulting in the formation of a new feature centered at 500 nm. This later feature strongly resembles the modeled $S_{CT-Naph}$ state of **Naph** (vide supra) and is assigned accordingly. The fluorescence of **Fluoro-Naph**, then, originates from a small population of thermally accessible S_{deloc} . For **Cyano-Naph** (Figure 2.6B), no significant spectral changes are observed, nor are any features present which resemble S_{deloc} . Rather, broad spectra centered around 500 nm are observed from the earliest time point, although subtle spectral changes consistent with cooling do occur. Given the similarity of the absorption profile of **Cyano-Naph** with the other compounds, and the assignment of the feature centered around 500 nm as originating from $S_{CT-Naph}$, it is inferred that S_{deloc} is initially populated but that $S_{CT-Naph}$ is formed on an ultrafast timescale not resolved by these measurements.

Figure 2.7A shows the NSTA spectrum of **Fluoro-Naph** collected 10 μs after 355 nm excitation in deaerated RT DMAc. As with **Phen** and **Naph**, this is understood to originate from a

triplet excited state due to the long lifetime (> 15 ms; see SI for details) and its high sensitivity to oxygen. Given the spectral similarity with data from **Phen** and **Naph** (Figure 2.4A), the T_1 of **Fluoro-Naph** is assigned as $T_{CT-Biph}$. Encouragingly, Φ_{ISC} of this species is measured to be near unity, at 0.96.

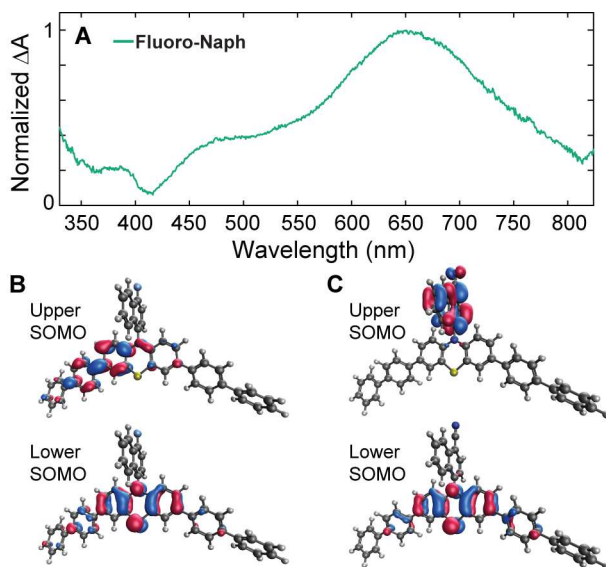


Figure 2.7. (A) Triplet NSTA spectrum of Fluoro-Naph in deaerated RT DMAc, taken at a time delay of 10 microseconds. (B) & (C) Triplet SOMOS of Fluoro-Naph (B) and Cyano-Naph (C) (*uM06/6-31g(d,p)/CPCM-DMAc level of theory*).

The compound **Cyano-Naph**, on the other hand, has a very low Φ_{ISC} , such that measurement of the T_1 spectrum proved challenging. Attempts were made to form this state using tris[2-phenylpyridinato- C^2,N]iridium(III) ($Ir(ppy)_3$) as a triplet-triplet energy transfer (TTET) sensitizer, and indeed triplet quenching of $Ir(ppy)_3$ is observed using NSTA ($Ir(ppy)_3$ is used as the TTET sensitizer in the measurement of Φ_{ISC} for the other three compounds in this study as well; see SI). However, despite $Ir(ppy)_3$ having a sufficient T_1 energy for TTET, no **Cyano-Naph** triplet is observed after quenching. This observation then suggests that the T_1 lifetime of **Cyano-Naph** is shorter than that of the sensitizer used (1.5 μs), thus preventing its accumulation. This observation is, in and of itself, important. The stark T_1 lifetime difference compared to what is seen in **Phen**,

Naph, and **Fluoro-Naph** tells us that the state in **Cyano-Naph** must be electronically very different. We again turn to DFT for insight. As expected, the **Cyano-Naph** T₁ SOMOs (Figure 2.7C) reveal substantive variations compared to what is seen for the other species (Figure 2.7B and Figures 2.4B and 2.4C). Now, rather than T_{CT-Biph}, the T₁ in **Cyano-Naph** is clearly T_{CT-Naph}.

Table 2.1. Key Photophysical Parameters of Compounds in this Study

	τ_{singlet}^a (ns)	Φ_{fl}	Φ_{ISC}	$E^{0*}_{\text{T1}}^b$ (V vs SCE)	$k_r^{c,d}$ (s ⁻¹)	k_{ISC}^c (s ⁻¹)	$k_{\text{nr}}^{c,d}$ (s ⁻¹)
Phen	4.03 ± 0.01	0.41 ± 0.04	0.41 ± 0.06	-1.66	1.0 x 10 ⁸ ± 1 x 10 ⁷	1.0 x 10 ⁸ ± 1 x 10 ⁷	5 x 10 ⁷ ± 2 x 10 ⁷
Naph	3.79 ± 0.03	0.17 ± 0.01	0.76 ± 0.10	-1.63	4.5 x 10 ⁷ ± 2 x 10 ⁶	2.0 x 10 ⁸ ± 3 x 10 ⁷	2 x 10 ⁷ ± 3 x 10 ⁷
Fluoro-Naph	5.41 ± 0.02	0.034 ± 0.003	0.96 ± 0.14	-1.61	6.3 x 10 ⁶ ± 5 x 10 ⁵	1.8 x 10 ⁸ ± 3 x 10 ⁷	8 x 10 ⁵ ± 3 x 10 ⁷
Cyano-Naph	1.33 ± 0.07	8 x 10 ⁻⁴ ± 1 x 10 ⁻⁴	--	--	6 x 10 ⁵ ± 1 x 10 ⁵	--	7.5 x 10 ⁸

^a τ_{singlet} is measured using time-correlated single photon counting, using 402 nm excitation in deaerated DMAc. ^bPotential of oxidation of the T₁, determined by the potential of oxidation of the ground-state compound (Table S2.3) minus $E_{00,T1}$ (Table S2.2). ^cRate constants are calculated using the following equations: $k_r = \Phi_{\text{fl}}/\tau_{\text{singlet}}$, $k_{\text{ISC}} = \Phi_{\text{ISC}}/\tau_{\text{singlet}}$ and $k_{\text{nr}} = \tau_{\text{singlet}}^{-1} - k_r - k_{\text{ISC}}$. ^dThese values refer exclusively to S₁ → ground-state pathways.

Both the change in the electronic character and the dramatic decrease in the yield of the T₁ arise due to the significant stabilization of the CT-Naph state in **Cyano-Naph**. The latter occurs by lowering the energy of T_{CT-Naph} below that of T_{CT-Biph}. To understand the former, it is useful to examine the rate constants for the different pathways of depletion from S_{CT-Naph} (radiative decay

(k_r), non-radiative ground-state recovery (k_{nr}), and ISC (k_{ISC})) shown in Table 1. Relative to the other compounds, **Cyano-Naph** has a significantly higher k_{nr} and, simultaneously, a much lower k_{ISC} , such that it could not be measured. These effects can be understood in the following way: First, k_{ISC} is slower because the nature of the T_1 is changed. **Cyano-Naph** undergoes a fundamentally different ISC process than the other compounds in this study, namely, $S_{CT-Naph} \rightarrow T_{CT-Naph}$ rather than the substantial electron density shifting $S_{CT-Naph} \rightarrow T_{CT-Biph}$. This new pathway has low driving force and no longer has the advantages of enhanced spin-orbit coupling afforded to the other pathway. Second, the substantial increase in k_{nr} is attributed to the Energy Gap Law. We can still presume that $S_{CT-Naph}$ lies in the Marcus Inverted region relative to the ground state, but it is now much less so compared to the other compounds in this study, thereby lowering the thermodynamic barrier for non-radiative decay.^{17,43} Combined, these effects on k_{nr} and k_{ISC} result in extremely low Φ_{ISC} for **Cyano-Naph**.

Lastly, considering the question kinetic differences in ISC between phenothiazine compounds and their phenoxazine analogues, we observe that **Phen**, **Naph**, and **Fluoro-Naph** have k_{ISC} values roughly comparable to phenoxazine analogues with S_1 states of similar electronic character (see SI for more details). Interestingly, this similarity in k_{ISC} is despite the lower driving force for the phenothiazine complexes that result from the lower-energy S_{deloc} and $S_{CT-Naph}$ states in these sulfur-containing species. These results may indicate that there is higher spin-orbit coupling for the phenothiazine complexes arising from the heavy atom effect but that competing effects obviate this spin-orbit coupling advantage.

CONCLUSION

Figure 2.8 shows a summarizing energy-level diagram of all four species studied here. We find that for **Phen**, the lowest energy singlet is S_{deloc} , a state whose high k_r competes effectively

against k_{ISC} , resulting in a relatively low Φ_{ISC} . **Naph** introduces a nearly isoenergetic singlet charge transfer state ($S_{CT-Naph}$) as an equilibrium partner. Within this state, the donor versus acceptor orthogonality lowers k_r while simultaneously increasing k_{ISC} towards a triplet characterized by charge transfer from the phenothiazine to a biphenyl arm ($T_{CT-Biph}$). **Fluoro-Naph**, by virtue of inclusion of an EWG, exhibits an excited-state equilibrium that is shifted significantly towards $S_{CT-Naph}$, ultimately resulting in a near-unity Φ_{ISC} . Interestingly, lowering the CT-Naph energy further in **Cyano-Naph** does not have the effect of increasing Φ_{ISC} that was desired at the outset but rather results in fast and efficient non-radiative ground-state recovery. In essence $S_{CT-Naph}$ has been lowered too much, speeding k_{nr} and taking away needed driving force for SOCT-ISC to the $T_{CT-Biph}$.

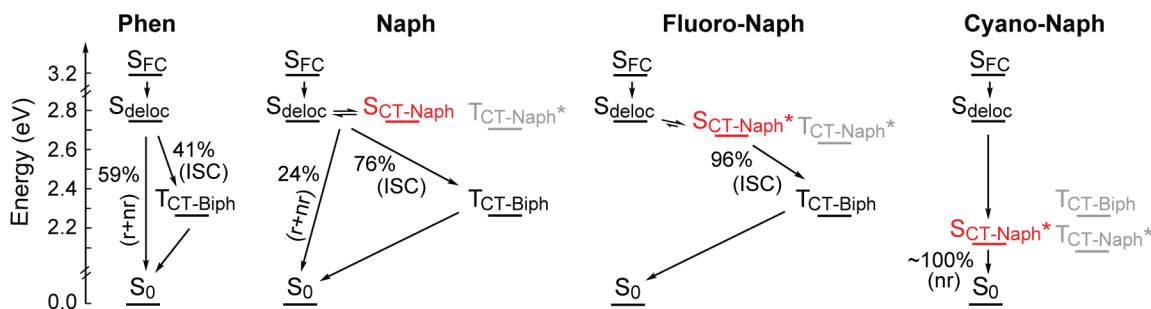


Figure 2.8. Energy-level diagrams of the compounds studied. The $S_{CT-Naph}$ state is highlighted in red, and the color grey indicates triplet states that are not populated. Only pathways that describe at least 10% of excited-state population decay are shown. * indicates that the energy of a given state is approximate and not intended to have quantitative accuracy. The energies of all other states originate from absorption or emission E_{00} energies.

More broadly, we have demonstrated that phenothiazine compounds, **Fluoro-Naph**, in particular, can be designed to have comparable properties as the leading phenoxazine photocatalysts. These properties include the absorption of visible light, highly negative excited state reduction potentials (see Table 2.1), and, in the case of **Fluoro-Naph**, a high Φ_{ISC} (with even longer triplet lifetimes). Importantly, many of the design principles established for phenoxazines translate well to phenothiazine systems. However, there are slight, yet impactful, differences in the

excited state behavior of phenothiazine complexes which must be accounted for in order to ensure a high Φ_{ISC} via a CT-mediated mechanism. The most critical difference is a lower-energy S_{deloc} state in the phenothiazine compounds, which necessitates a lowering of the CT state (relative to phenoxazine analogues) in order to ensure efficient CT formation. We have found that, while it is critical to stabilize the CT state below competing states, one should be cautious to not lower the CT energy by too much, as doing so can result in a lower k_{ISC} and a larger k_{nr} . For most efficient CT-mediated ISC, a general strategy would be to lower the energy of the CT state as little as possible while still achieving ~100% yield of CT formation in the singlet manifold. However, the effect of solvent polarity must also be taken into account, as low polarity solvents preferentially destabilize CT states relative to non-polar excited states and high polarity solvents can significantly lower the energy of CT states below what is optimal for ISC.

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(41) The longer triplet lifetime may arise from being more Marcus-inverted via a higher T1 energy and/or a lower reorganization energy for T1→S0. Alternatively, it may reflect a poorer coupling between T1 and S0.

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CHAPTER 3 – BROMINE RADICAL CATALYSIS BY ENERGY TRANSFER

PHOTOSENSITIZATION

OVERVIEW

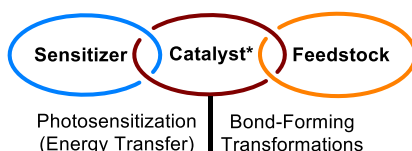
We report here a mild, safe, and user-friendly bromine radical catalysis system that enables efficient [3+2] cycloaddition of diversely substituted vinyl- and ethynylcyclopropanes with a broad range of alkenes, including drug-like molecules and pharmaceuticals. Key to the success is the use of photosensitizing triplet state β -fragmentation of a judiciously selected pre-catalyst, cinnamyl bromide, to generate bromine radicals in a controlled manner using ppm-level photocatalyst (i.e. 4CzIPN) loading.

INTRODUCTION

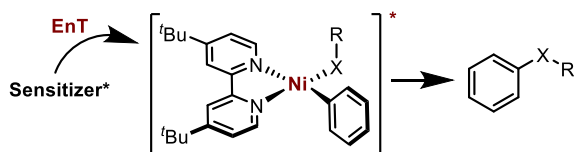
Excited-state molecules, compared to the ground state, possess distinct electronic configurations, which alter the spin-multiplicity and bond strength, thus exhibiting unique chemical properties and reactivity.¹ Although direct photoexcitation is straightforward to access excited-state reactivity, the majority of organic molecules require ultraviolet (UV) light irradiation and quartz reaction vessels that challenges practicality, selectivity, and functional group tolerance.² Recently, visible-light photocatalysis has emerged as a sustainable and powerful tool to access excited-state reactivity under mild conditions, enabling numerous bond-forming reactions.³ Most examples have utilized single electron-transfer (ET) mechanisms, i.e. photoredox catalysis,⁴ while transformations proceeding through energy transfer (EnT) catalysis, i.e. photosensitization,⁵ are relatively underdeveloped. EnT catalysis is unique in that it largely relies on the relative triplet energies of the photocatalyst (PC) and the substrates. Upon photosensitization, the partial diradical character of a substrate may significantly lower the kinetic barriers toward otherwise disfavored transformations, such as [2+2] photocycloadditions,⁶ photoisomerization of alkenes,⁷ and others.⁸

For billions of years nature has utilized EnT to convert solar energy into chemical energy (Figure 3.1a).⁹ This synergy has inspired synthetic chemists to develop excited-state organometallic catalysis via photosensitization as a novel activation pathway.¹⁰⁻¹¹ The paradigm of such catalysis is triplet excited-state Ni^{II} complex-catalyzed C-C and C-X (X = O, N) cross coupling reactions, (Figure 3.1b).¹¹ Another elegant example employed two-center photocatalysis for the generation and trapping of (hetero)aryl radicals.¹² Specifically, $\text{Ru}(\text{bpy})_2\text{Cl}_2$ was used to absorb visible light and transfer the energy to pyrene, enabling the efficient single-electron reduction of (hetero)aryl halides and triflates (Figure 3.1c). Although the concept of photosensitization-initiated catalysis has been established as a robust strategy with great synthetic potential, the excited-state activation mode and further application in discovering valuable and unique bond-forming reactions are still in their infancy.

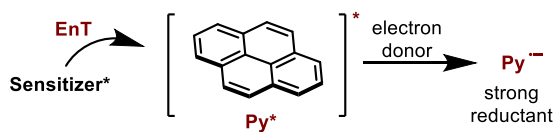
(a) Photosynthetic Process in Nature



(b) Excited-State Organometallics via EnT



(c) Photosensitization-Initiated Photoredox Catalysis



(d) This Work: Bromine Radical Catalysis by Photosensitization

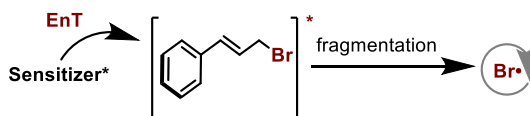


Figure 3.1. Photosensitization-Initiated Excited-State Catalysis

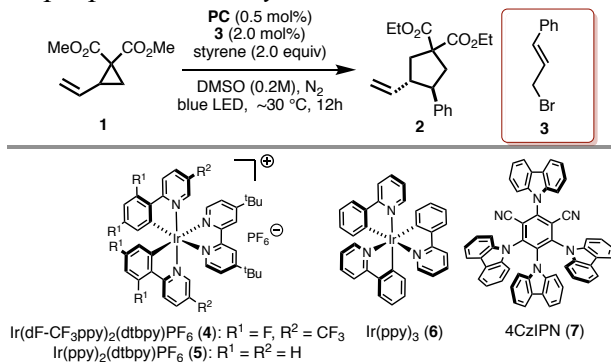
Heteroatom-centered radicals, e.g., bromine radicals, are vigorously involved in fundamental bromination reactions providing invaluable Br-containing compounds for further build-up of molecular complexity and diversity.¹³ One of the intriguing features of the bromine radical is that it can reversibly add to carbon-carbon π -bonds (via addition and elimination).¹⁴ Exploiting this reversibility, we envisioned a bromine radical catalysis system for the activation of alkenes or alkynes. To the best of our knowledge, such a catalysis still remains unknown. The immediate challenges to realize this bromine radical catalysis is the need for mild and controlled generation of bromine radicals. Two classical strategies to deliver a bromine radical includes (i) photolysis of molecular bromine (Br_2), a highly toxic, corrosive, and volatile liquid,¹⁵ and (ii) thermolysis of N-bromosuccinimide (NBS), meanwhile generating reactive succinimide radicals that can abstract hydrogen atoms from weak C-H bonds (e.g. allylic C-H bonds).¹⁶ The resulting carbon radical, after hydrogen atom abstraction (HAT), may terminate the bromine radical. In light of the [2+2] photocycloaddition of styrene derivatives,^{8a} we hypothesized that, upon photosensitization, the partial diradical character of an excited state styrene derivative, e.g., cinnamyl bromide, would allow β -fragmentation to liberate a bromine radical that may be intercepted for catalysis (Figure 3.1d).¹⁷

RESULTS AND DISCUSSION

[3+2] cycloaddition of vinyl cyclopropanes and alkenes is a typical reaction to evaluate the addition/elimination radical replay reactivity. It is important to note that such a cycloaddition has been well-established through classical thiyl¹⁸ and tin¹⁹ radical catalysis. However, several limitations still remain. First, commonly used precursors of tin or thiyl radicals are highly toxic and smelly tin hydride, thiols or disulfides. Second, harsh conditions for radical initiation, such as high temperature or UV light irradiation, which exhibits negative impact on practicality. Here, we

report a method for mildly controlling bromine radicals through parts-per-million (ppm) level EnT photocatalysis, which enables efficient cycloaddition of vinyl- and ethynylcyclopropane and alkenes with excellent functional group tolerance. Initial hypothesis validation began with investigation of the reaction between 1,1-dimethoxycarboxyl-2-vinylcyclopropane (**1**) and styrene as the substrates in DMSO, and 34 W blue LED as the light source (Table 3.1). Inspired by MacMillan's photoredox strategy to form bromine radicals,²⁰ catalyst combinations of **4** with various bromide salts in different solvents were evaluated (Table S3.1). Unfortunately, none of these experiments resulted in any conversion after 12 h. We then turned our attention to the strategy of photosensitization to generate bromine radicals. Due to the possibility of recombination of the bromine and carbon radicals, the use of substoichiometric quantities of **3** should favor high conversion. Gratifyingly, the [3+2] cycloaddition of **1** (1.0 equiv) and styrene (2.0 equiv) proceeded in the presence of **4** (0.5 mol%) and **3** (2.0 mmol%) to yield the cyclopentane product **2** in 95% NMR yield (Table 1, entry 1). The subsequent examination of popular photocatalysts (PCs) revealed a correlation between reaction efficiency and the PCs triplet energy (E_T). More specifically, reactions utilizing PCs with higher E_T resulted in higher yields, which is consistent with the photoinduced EnT mechanism (entries 1–2 and 4). The donor-acceptor fluorophore 4CzIPN (**7**)²¹ provides comparable yield to the precious iridium-based photocatalyst **4**. We chose **7** for further optimization. Importantly, no conversion was observed in the absence of light, PC or **3** (entries 6–8). Moreover, attempts on lower catalysts loading were successful that 0.005 mol% (50 ppm) of **7** and 1.0 mol% of **3** enabled the formation of **2**, as a 70:30 (trans/cis) mixture of diastereomers, in 88% isolated yield (entry 10), highlighting the robustness of this photocatalytic system.

Table 3.1. Optimization of Conditions for Visible Light-Gated Bromine Radical-Catalyzed [3+2] Cycloaddition of Vinylcyclopropane **1** and Styrene^a



Entry	PC	<i>E</i> _T (kcal/mol)	[Br]	Yield (%) ^b
1	4	61	3	95
2	5	49	3	11
3	6	55	3	0
4	7	58	3	93
5 ^c	7	58	3	0
6	-	-	3	0
7	7	58	-	0
8 ^{d,e}	7	58	3	93
9 ^{d,f}	7	58	3	92(88) ^g
10 ^{d,h}	7	58	3	30

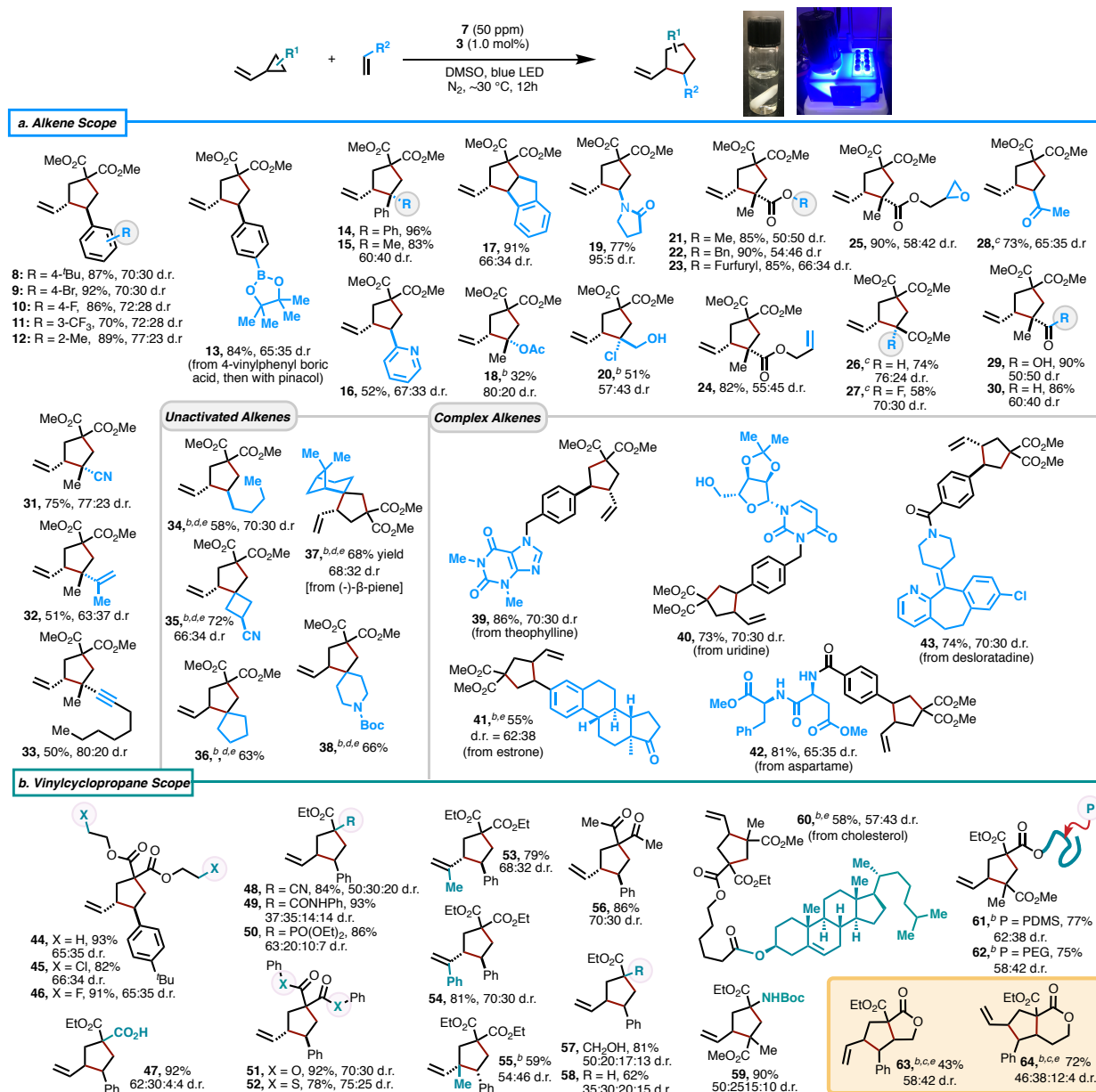
^aAll reactions were performed on 0.2 mmol scale. Regardless of reaction conditions, d.r. was 70:30. ^bDetermined by ¹H NMR using trimethoxybenzene as an internal standard. ^cNo light. ^d1.0 mol% **3** was used. ^e0.1 mol% 4CzIPN was used. ^f50 ppm 4CzIPN was used. ^gIsolated yield. ^h10 ppm 4CzIPN was used.

With optimal conditions in hand, we investigated the substrate scope (Table 3.2). Generally, a broad range of vinylcyclopropanes and alkenes is amenable to this protocol, affording vinylcyclopentane products in moderate to excellent yields and with distereomeric ratios (d.r.) ranging from 50:50 to 95:5. Reactions of **1** with styrenes bearing substituents on the phenyl ring or at α-position, including alkyl and aryl groups, proceed well to give products **8–15** in good to excellent yields (70–96% yield). Notably, boric acid is tolerated (**13**, 84% yield after a subsequent reaction with pinacol), providing opportunities for late-stage functionalization through cross-

coupling reactions. 2-vinyl pyridine and 1*H*-indene readily participate in this transformation (**16**, 48% yield; **17**, 91% yield). Electron-rich alkenes also engage in reactivity to afford products (**18–20**, 32–77% yield). It is noteworthy that the cycloaddition of **1** with N-vinylpyrrolidone exhibited excellent diastereoselectivity (d.r. = 95:5). With a diverse set of electron-deficient alkenes, we demonstrate excellent functional group tolerance of fluorine, epoxide, ketone, carboxylic acid, aldehyde and nitrile (**21–31**, 58–90% yield). Cycloadditions of diene and enyne substrates affords corresponding products in moderate yields (**32**, 51% yield; **33**, 50% yield). Although a higher loading of **7** (500 ppm) was used, good yields were maintained across a range of unactivated alkenes (**34–38**, 58–72% yield). In the reaction of (-)- β -piene, the bridged bicyclic motif is retained (**37**), suggesting that the ring-forming step in this cycloaddition is fast.

To demonstrate the utility of this new protocol, we selected several complex molecules of diverse biological activities for late-stage functionalization. 4-vinylbenzylated theophylline, a phosphodiesterase inhibitor,²² and uridine, one of the standard nucleosides, were efficient substrates (**39–43**, 73–86% yield). Due to solubility issue in DMSO, an estrone derivative affords product **41** in only moderate yield (55%). Aspartame, a dipeptide sweetener, is converted into **42** in 81% yield. Gratifyingly, this [3+2] cycloaddition is effective for 4-vinyl benzoylated desloratadine (**43**, 74% yield), a popular tricyclic antihistamine.

Table 3.2. Scope of Visible Light-Gated Bromine Radical-Catalyzed [3+2] Cycloaddition of Vinylcyclopropanes and Alkenes^a



^aConditions: vinylcyclopropane (0.20 mmol), alkene (0.40 mmol), **7** (50 ppm), **3** (1.0 mol%), DMSO (0.2 M), 30 °C, 34 W blue LED, 12h. ^b2.0 mol% **3** was used. ^c0.1 M in DMSO. ^d0.4 M in DMSO. ^e500 ppm of **7** was used.

We next explored the vinylcyclopropane scope (Table 3.2b). Diverse substituents on either the malonate motif (**44–46**, 82–93% yield), vinyl group (**53–54**, 79–81% yield), or cyclopropane scaffold (**55**, 59% yield) are tolerated. This cycloaddition is also amenable to a range of electron-

deficient patterns bearing various functionalities, such as carboxylic acid (**47**, 92% yield), amide (**49**, 93% yield), phosphonate (**50**, 86% yield), alcohol (**57**, 86% yield) and carbamate (**59**, 90% yield), delivering corresponding products in good to excellent yield (**47–52**, **56–59**, 62–93% yield). Reaction of a substrate containing hydrophobic cholesterol motif is challenging in DMSO and provides **60** in 58% yield. Vinylcyclopropanes bearing tethered polydimethylsiloxane (PDMS) or polyethylene glycol (PEG) efficiently react with methyl methacrylate (MMA) to afford products **61** and **62** in 77% and 75% yield, respectively. Moreover, well-designed substrates with pendant alkenyl functionality possibly engage in intramolecular reactivity to access advanced bicyclic scaffolds. This concept is demonstrated in the successful synthesis of γ - and δ -lactones **63** (43% yield) and **64** (72% yield).

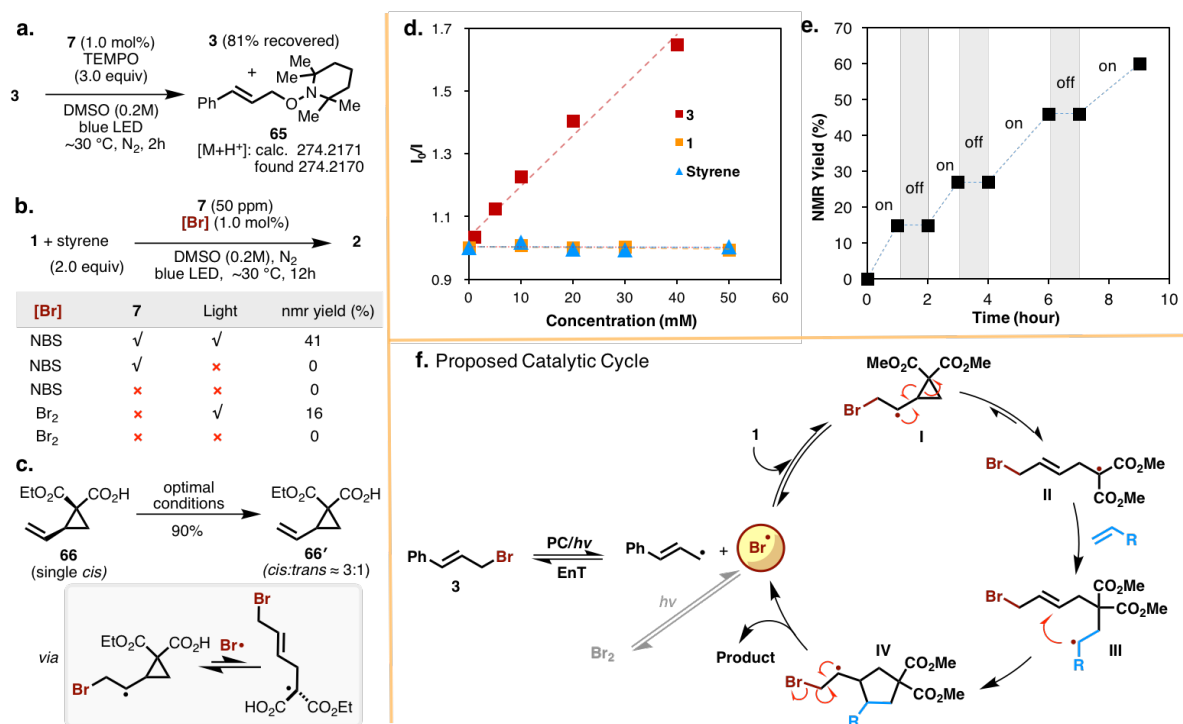


Figure 3.2. Mechanistic studies (a. TEMPO trapping experiment. b. Examination of alternative precatalysts. c. Radical epimerization experiment. d. Stern-Volmer quenching experiment. e. "On/off" experiment) and proposed catalytic cycle (f).

For the reaction mechanism, a Stern-Volmer quenching experiment reveals the feasible interaction between **7** and **3** (Figure 3.2d). However, the single-electron oxidation pathway to generate bromine radicals is thermodynamically unfavorable ($[E_{1/2}^{\text{red}}(\mathbf{7}^*/\mathbf{7}^{\cdot-})] = +1.37$ vs SCE, $[E_{1/2}^{\text{ox}}(\mathbf{3}/\mathbf{3}^{\cdot+})] = 2.01$ V vs SCE, see Figure S3.5), suggesting that previously proposed photosensitization via EnT is likely the dominant pathway. Several control experiments were performed to gain insight into this reaction mechanism. First, radical trapping using TEMPO supports the formation of cinnamyl carbon radical (Figure 3.2a). However, the bromine radical-TEMPO adduct was not detected, presumably due to stability issues. Second, reactivity of other precatalysts, such as NBS and Br₂, was investigated (Figure 3.2b). Photosensitization of NBS or direct photolysis of Br₂ provides similar catalytic reactivity, but in much lower yields (41% and 16% yield, respectively), evidencing the key role of bromine radical in this transformation. Third, epimerization of **66** under optimal conditions strongly supports the radical mechanism (Figure 3.2c). Furthermore, temporal “on/off” control on the reaction (Figure 3.2e) showcases the light-controlled feature of this bromine radical catalysis. Accordingly, we proposed a catalytic cycle as shown in Figure 3.2f. Upon visible light irradiation, PC **7** is capable of sensitizing triplet-state fragmentation of **3** to release a bromine radical. Addition of the bromine radical to the vinyl group of **1** gives a transient radical species **I**, which undergoes a fast but reversible ring-opening process to furnish intermediate **II**. A subsequent radical addition of **II** to alkenes, followed by a ring-closure reaction, affords intermediate **IV**. In this step, the spin center shifts to the position for β -elimination, giving the final product, meanwhile regenerating bromine radical to enter into next catalytic cycles. Efficient radical-radical coupling of bromine radical and cinnamyl carbon radical leads to the dormant precatalyst (**3**), which is evidenced by the high-yielding recovery of **3** in

TEMPO trapping experiment (81%, Figure 3.2b). Possibly, Br₂, formed through recombination of two bromine radicals, may be another dormant species within this photosystem.

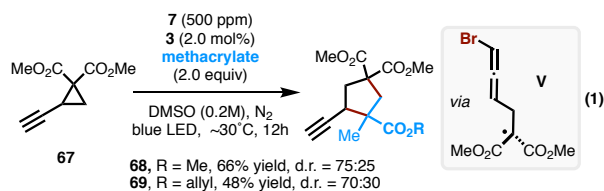


Figure 3.3. Alkyne functionalization via bromine radical catalysis.

Lastly, we examined the performance of bromine radicals in the activation of C-C triple bonds. Under optimal conditions, in situ generated bromine radicals add to alkyne group of ethynylcyclopropane **67**, followed by a similar ring-opening reaction, to give the key allenyl intermediate **V** (eq. 1). Trapping of **V** with methacrylates successfully afford ethynylcyclopentanes **68** and **69** in 66% and 48% yield, respectively. Continued efforts to functionalize more challenging molecules (such as alkanes via HAT) utilizing this mild bromine radical catalysis are underway.

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CHAPTER 4 – HALIDE NONINNOCENCE AND DIRECT PHOTOREDUCTION OF Ni(II) ENABLES COUPLING OF ARYL CHLORIDES IN DUAL CATALYTIC, CARBON- HETEROATOM BOND FORMING REACTIONS

OVERVIEW

Recent mechanistic studies of dual photoredox/Ni-catalyzed, light-driven cross-coupling reactions have found that the photocatalyst (PC) operates through either reductive quenching or energy transfer cycles. To date, reports invoking oxidative quenching cycles are comparatively rare and direct observation of such a quenching event has not been reported. However, when PCs with highly reducing excited states are used (e.g. Ir(ppy)₃), photo-reduction of Ni(II) to Ni(I) is thermodynamically feasible. Recently, a unified reaction system using Ir(ppy)₃ was developed for forming C–O, C–N, and C–S bonds under the same conditions, a prospect that is challenging with PCs that can photo-oxidize these nucleophiles. Herein, in a detailed mechanistic study of this system, we observe oxidative quenching of the PC (Ir(ppy)₃ or a phenoxazine) via nanosecond transient absorption spectroscopy. Speciation studies support that a mixture of Ni-bipyridine complexes form under the reaction conditions, and the rate constant for photoreduction increases when more than one ligand is bound. Oxidative addition of an aryl iodide was observed indirectly via oxidation of the resulting iodide by Ir(IV)(ppy)₃. Intriguingly, persistence of the Ir(IV)/Ni(I) ion pair formed in the oxidative quenching step was found to be necessary to simulate the observed kinetics. Both bromide and iodide anions were found to reduce the oxidized form of the PC back to its neutral state. These mechanistic insights inspired the addition of a chloride salt additive, which was found to alter Ni speciation, leading to a 36-fold increase in the initial turnover frequency, enabling the coupling of aryl chlorides.

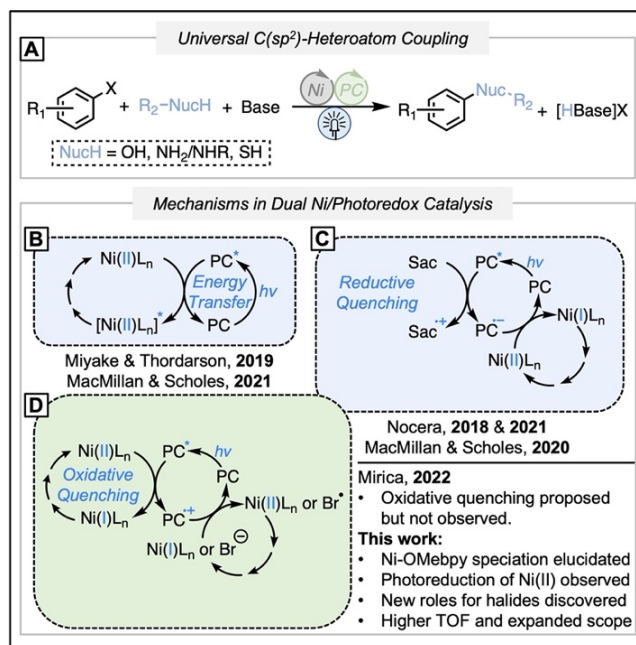


Figure 4.1. Schemes describing the net reaction for C(sp²)-heteroatom coupling (A), an energy transfer quenching (B),^{10,11} reductive quenching (C),^{13–15} or oxidative quenching (D)²⁶-initiated catalytic cycle with examples given that include detailed experimental support for the proposed quenching events. PC = photocatalyst; Sac = sacrificial reductant; TOF = turnover frequency.

INTRODUCTION

While light-driven, dual catalytic reaction systems involving a photocatalyst (PC) and a Ni catalyst have emerged as highly promising methods to form C(sp²)-heteroatom bonds under mild conditions with readily available coupling partners,^{1–4} the vast majority of these methods only demonstrate coupling of a single type of nucleophile.⁵ In contrast, one of our groups has recently reported a method in which coupling of aryl halides to O, N, or S nucleophiles occurs efficiently without changing the reaction conditions (Figure 4.1A).⁶ In addition, with a small change in reaction conditions, SCF₃ nucleophiles became effective, with 60 examples demonstrated.⁷ This universality of a single method is highly desirable for synthetic organic chemistry, especially in medicinal chemistry where these reactions are used at a high frequency.^{8,9} In the former system, we proposed a mechanistic hypothesis involving an energy transfer quenching event, supported by literature precedent and a stoichiometric nickel study demonstrating that no added sacrificial

oxidant/reductant is needed to promote reactivity—something necessary for photocatalytic cycle turnover in many reductive/oxidative quenching mechanisms.

Recent mechanistic studies¹⁰⁻¹² have disclosed spectroscopic evidence for energy transfer from highly reducing PCs (i.e., Ir(ppy)₃ and a phenoxazine (PhenO) PC; ppy = 2-phenylpyridine and PhenO = 3,7-di([1,1'-biphenyl]-4-yl)-10-(naphthalen-1-yl)-10*H*-phenoxazine) to a Ni complex to generate a Ni-centered excited state that was crucial for catalysis (Figure 4.1B). Based on these reports, we hypothesized that energy transfer would also be the mode of activation of Ni in our unified C—heteroatom coupling system as these same PCs are used. However, the reduction of Ni(II) to Ni(I) by the excited state PCs ($E[PC^*/PC^{**}]$ for ³Ir(ppy)₃ = −1.66 V; for ³PhenO = −1.69 V; for ¹PhenO = −2.16 V; all V vs SCE)¹³ is thermodynamically feasible based on reported cyclic voltammetry data of relevant nickel–bipyridine complexes ($E[Ni(II)/Ni(I)]$ = −1.0 to −1.3 V vs SCE).^{12,14} Furthermore, in our study with SCF₃ nucleophiles, product yield was found to increase as the excited state reduction potential of the PC became more negative, while the triplet energy of the PCs was found to have no correlation with yield. These considerations taken together suggest that the alternate hypothesis of an oxidative quenching cycle (Figure 4.1D) should be considered seriously in these systems, motivating a mechanistic study to distinguish between electron transfer and energy transfer as the mode of quenching of the Ir(ppy)₃ excited state.

Recently, a number of detailed mechanistic studies have been reported that use a wide range of techniques to elucidate catalytic cycles involving cationic iridium PCs which, as strong photooxidants, were reported to participate in reductive quenching cycles¹⁵⁻¹⁷ (Figure 4.1C) or energy transfer.¹⁸ Although these reports are highly useful, they provide only limited insight into systems in which highly reducing PCs such as Ir(ppy)₃ are used. In contrast, while oxidative quenching cycles (Figure 4.1D) have been proposed in the literature occasionally with regard to

Ni/PC dual catalytic C—C, C—O, C—N, or C—S bond-forming systems, sometimes with computational support,¹⁹⁻²³ experiments capable of distinguishing between oxidative quenching, reductive quenching, and energy transfer (see reviews for relevant spectroscopic and electrochemical methods)²⁴⁻²⁶ have not been performed in the study of these systems.

Furthermore, computational approaches must explicitly define the species involved, a requirement that can be challenging and even misleading when the precise speciation is unknown due to a lack of experimental studies. While the speciation of Ni(II) in the presence of bipyridine type ligands has been studied rigorously,²⁷ the results are fairly complicated (i.e., slow equilibrium formation of a mixture of species with 0, 1, 2, or 3 bipyridine ligand molecules bound to Ni), and the speciation is expected to vary depending on the particular reaction conditions (e.g., solvent, Ni/ligand molar ratio, ligand identity, and the presence of other reaction components that may ligate Ni). As a result, data concerning the reactivity of specific Ni–bipyridine complexes in dual Ni photocatalysis is severely limited.

More recently, a detailed mechanistic study of a Ni-catalyzed C—O bond formation between alcohols and aryl halides was carried out by Mirica and co-workers.²⁸ In this work, a tridentate pyridinophane ligand was developed to stabilize Ni(I/III) and utilized to obtain evidence in the form of EPR and stoichiometric studies that supports oxidative addition at Ni(I), binding of the alcohol substrate to Ni(III), deprotonation by the base, and finally reductive elimination to form the aryl ether product. In the case where they use Ir(ppy)₃ as a PC, oxidative quenching was proposed on the basis of a redox argument and the observation that product only formed with sufficiently reducing PCs. Although this work is a significant advance in terms of elucidating the reactivity of Ni(I) and Ni(III) intermediates, experimental evidence for the photoreduction of Ni(II) to Ni(I) remains elusive.

Therefore, we undertook a detailed mechanistic study of the system described in Figure 4.1A, finding that the photoreduction of Ni(II) to Ni(I) by the Ir(ppy)₃ excited state can be directly observed. Further, we have characterized the nickel–bipyridine complexes formed in this system, studied their reactivity with excited state Ir(ppy)₃, found evidence to support oxidative addition of aryl halides at Ni(I) as well as the existence of a “dark” Ni(I)/Ni(III) cycle, and discovered that bromide and iodide anions are oxidized by Ir(IV) to aid in photocatalyst turnover. Intriguingly, the observed kinetics following the photoreduction event were best fit with a model invoking a persistent heteronuclear Ni(I)/Ir(IV) ion pair. These findings have enabled us to advance this system and achieve improved reactivity and scope with aryl chloride coupling partners.

RESULTS AND DISCUSSION

Results reported in this section are presented in order of steps in the proposed catalytic cycle, starting with steps that occur prior to light exposure.

Speciation of the Ni Catalyst Prior to Irradiation. Upon mixing all of the reaction components, the Ni precatalyst (i.e., NiBr₂·glyme) reacts with *N,N'*-dimethylformamide (DMF) solvent and 4,4'-dimethoxy-2,2'-bipyridine (OMebpy) to form a mixture of Ni–OMebpy complexes (Figure 4.2). We elected to follow the series of dark speciation equilibria through UV–visible spectroscopy, as each complex possesses unique d–d absorption bands that can aid in deconvoluting the complex mixtures that result when one mixes NiBr₂·glyme with OMe bpy in DMF. As such, we conducted a UV–vis titration experiment (Figure 4.2A) in which the Ni/OMebpy molar ratio was changed systematically while the solution volume was kept constant (for further details, see Supporting Information Section 2.2).

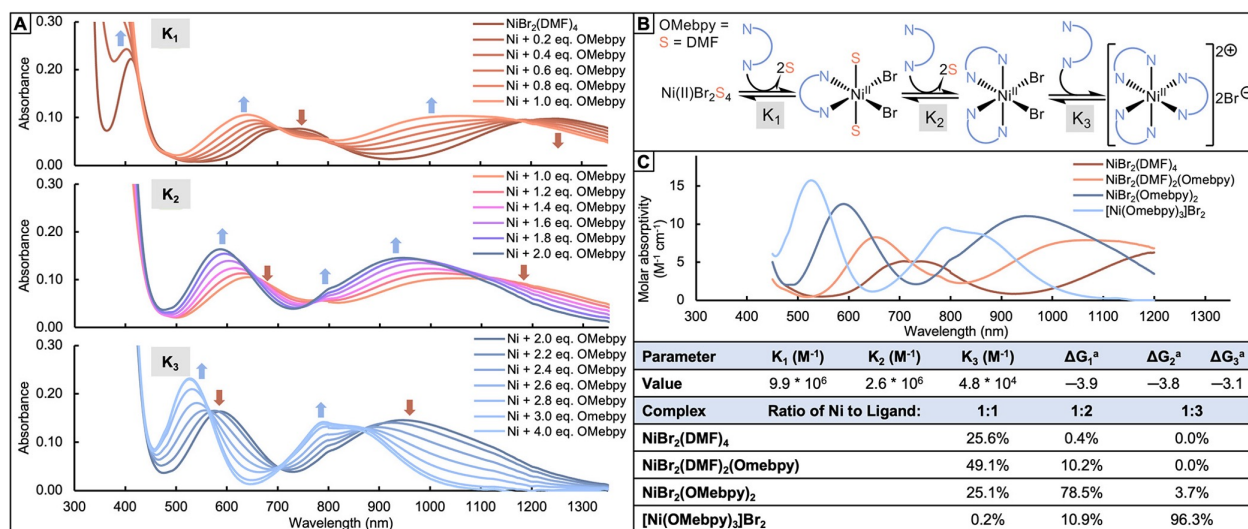


Figure 4.2. (A) UV–visible spectra of NiBr₂·glyme dissolved in DMac (15 mM) in the presence of increasing molar ratio of OMe bpy. (B) Scheme describing stepwise series of equilibria included in the model. (C) Calculated molar absorptivity of each complex as output from the 1:3 Ni/ligand binding model. Spectral region used for fitting = 450–1200 nm. Equilibrium constants, binding energies, and solution compositions are reported. OMe bpy = 4-4'-dimethoxy-2-2'-bipyridine. See the Supporting Information for details. ^aUnits of kcal mol⁻¹.

In DMF, the NiBr₂·glyme is proposed to form the octahedral NiBr₂(DMF)₄ as the dominant species in solution based on published spectra of related species (see Supporting Information Section 2.1).^{11,29} As a Ni/OMe bpy ratio of 1:1 is approached, the characteristic broad absorption bands of NiBr₂(DMF)₄ with maxima at ~420, ~710, ~760, and ~1250 nm weaken in intensity, while new signals appear with maxima at ~650, ~1020, and ~1120 nm. We assign this spectral change to the first addition of OMe bpy to the Ni center to form NiBr₂(DMF)₂(OMe bpy). Next, as the 1:1 ratio is exceeded and 1:2 is approached, these signals which just formed die away, concomitant with the rise of new signals at ~590, ~800, and ~950 nm that we assign to NiBr₂(OMe bpy)₂. Finally, signals corresponding to NiBr₂(OMe bpy)₂ disappear as the ratio of 1:3 is exceeded, and signals with maxima at ~530, ~780, and ~860 nm assigned to [Ni(OMe bpy)₃]Br₂ appear. Notably, these signals closely match those observed in the literature for [Ni(bpy)₃]BF₄ (bpy = 2,2'-bipyridine), supporting our assignment.²⁷

To precisely determine the ratio of each species in the Ni–OMebpy mixture, the titration data was fit to four variants (flavors)³⁰ of a 1:3 (metal/ligand or host/guest) binding model.¹¹ This fit was performed using a Matlab code based on the analytical solution to the system of equations for the 1:3 equilibria,¹¹ similar to that described in an NMR study on a 3:1 complexation of a bis-antimony receptor with halide anions.³¹ A global analysis³² using the UV–vis binding isotherms from $\lambda = 450\text{--}1200$ nm was performed (see the Supporting Information for details, Section 2.2). Comparing how the variants (flavors) of the 1:3 binding model fitted the data^{11,30,33} showed that the “full” 1:3 model which assumes both (i) cooperativity and (ii) that the 1:1, 1:2, and 1:3 stepwise complexes have distinct spectra, gave a significantly better fit to the data.

The full model allowed us not only to extract the stepwise equilibrium binding constants but also the molar absorptivity of each species (Figure 4.2C), giving $K_1 = 9.9 \times 10^6 \text{ M}^{-1}$, $K_2 = 2.6 \times 10^6 \text{ M}^{-1}$, and $K_3 = 4.8 \times 10^4 \text{ M}^{-1}$ with the corresponding free energies (after correcting for statistical factors) $\Delta G_1 = -3.9 \text{ kcal mol}^{-1}$, $\Delta G_2 = -3.8 \text{ kcal mol}^{-1}$, and $\Delta G_3 = -3.1 \text{ kcal mol}^{-1}$, respectively (Figure 4.2C). The increasing ΔG values indicate negative binding cooperativity, or less favorable addition of OMebpy to Ni(II) with each successive association, particularly with the addition of the third ligand (K_3), consistent with the increased steric demand posed by ligation of three OMebpy ligands.

While K_1 agrees well with literature values given for bpy in H₂O and mixed alcohol/aqueous solutions,²⁷ K_2 and K_3 are several orders of magnitude higher here than in those systems. This difference could be due to the electron-rich nature of OMebpy compared with bpy and/or the difference in binding strength of DMF compared with protic solvents in terms of coordination to Ni. Given that DMF and other polar, aprotic solvents are often used in dual Ni photocatalysis, we expect these results to be widely applicable.

In addition, the binding model allowed calculation of the exact concentrations of each species at relevant Ni/OMebpy ratios for catalysis (Figure 4.2C). Importantly, at the 1:2 ratio used in our system, the dominant species in the Ni–bipyridine mixture is $\text{NiBr}_2(\text{OMebpy})_2$ at 78.5%, with 10.9% $[\text{Ni}(\text{OMebpy})_3]\text{Br}_2$ and $\text{NiBr}_2(\text{DMF})_2(\text{OMebpy})$ (10.2%), while only 0.4% of the starting $\text{NiBr}_2(\text{DMF})_4$ remains. Control experiments confirm that the aryl halide, alcohol, and $\text{Ir}(\text{ppy})_3$ do not significantly affect the UV–vis signal (see Supporting Information Figures S4.9 and S4.10) and thus are unlikely to affect the speciation as determined above. Importantly, the alcohol does not bind to the Ni center at this stage, consistent with our hypothesis of transmetalation occurring at Ni(III) as detailed below.

However, K_2CO_3 causes a blue shift in the observed signal and increase in absorption at ~ 530 and ~ 780 nm (Fig. S4.10) that is consistent with a shift in the equilibria toward increased formation of $[\text{Ni}(\text{OMebpy})_3]\text{Br}_2$. This shift can potentially be explained by carbonate displacing bromide in the outer coordination sphere, inhibiting the dissociation step of K_3 . If carbonate were bound to Ni(II) in the inner sphere, a change in the UV–vis spectrum would be expected that departs significantly from the signals of the species identified herein. Ni(II) complexes with varying ligation exposed to a carbonate source tend to form multinuclear Ni complexes with bridging carbonate ligands and distinct d–d bands in absorption spectra that are not observed here.^{34–36}

Mechanistic Hypothesis. With the speciation of the Ni/ligand mixture known, we elected to study the C–O coupling reaction between alcohols and aryl halides as a model system for our mechanistic study (Figure 4.3A). We propose a general mechanism, similar to that reported by Mirica and co-workers,²⁸ that begins with the dark speciation equilibria described in the previous section (Figure 4.3E(a)). Next, the PC absorbs a photon of light (b) and is oxidatively quenched

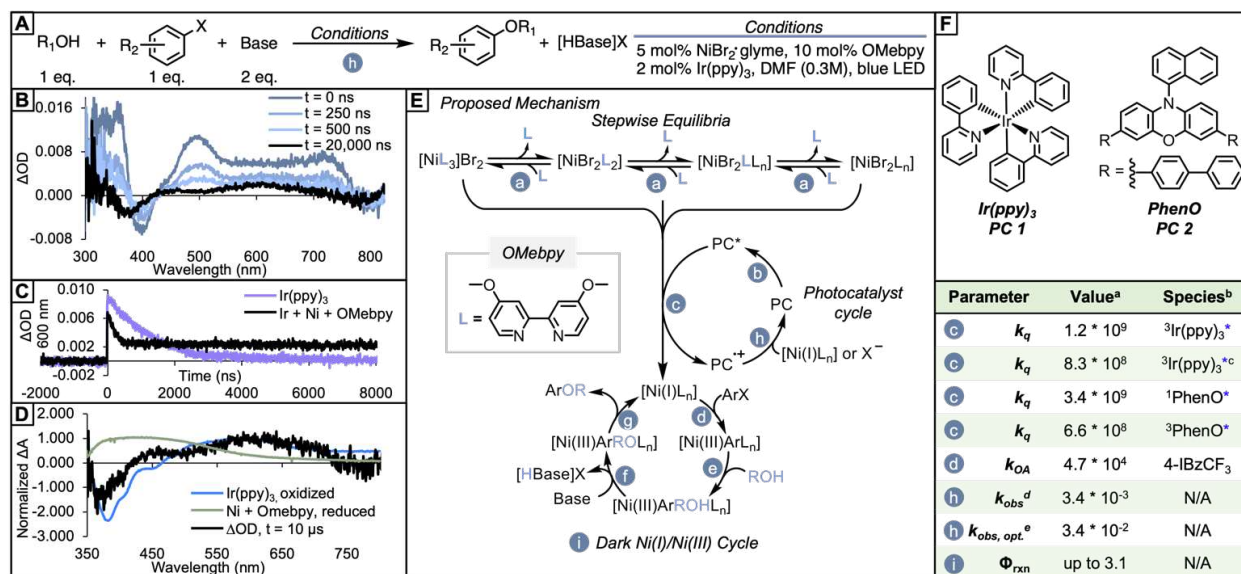


Figure 4.3. (A) Scheme describing net C–O coupling reaction. (B) ns-TA difference spectra at the indicated time delay following the pump pulse ($\lambda = 355\text{ nm}$, 2–5 mW, ~6 ns pulse width) for a mixture containing $\text{Ir}(\text{ppy})_3$ (31.4 μM), $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM), and OMeppy (3.0 mM, 2 equiv relative to Ni) dissolved in DMF. (C) Kinetic traces of $\text{Ir}(\text{ppy})_3$ alone and of the same mixture as in (B) at $\lambda_{\text{probe}} = 600\text{ nm}$. (D) Normalized (to highest peak) difference spectra from spectroelectrochemical experiments in which $\text{Ir}(\text{ppy})_3$ was oxidized to $\text{Ir}(\text{IV})$ or a mixture of $\text{NiBr}_2\cdot\text{glyme}$ and OMeppy (2 equiv relative to Ni) was reduced electrochemically, overlaid with the $t = 10\text{ }\mu\text{s}$ ns-TA spectrum from the same experiment in (B). (E) Generalized mechanism for C–O bond formation. We note that when $\text{PC} = \text{Ir}(\text{ppy})_3$ the observed kinetics are consistent with a persistent ion-pairing mechanism as described below (see Figures 4.4 and 4.5) that differs from this scheme. (F) PCs and structures used in this work. Rate constants measured in this work are reported with lowercase letters indicating the relevant mechanistic steps. Stern–Volmer quenching rate constants (k_q) were measured using ns-TA data, except for the singlet state quenching of PhenO, which used time-correlated single photon counting. See the Supporting Information for additional details. ^aBimolecular rate constants in $\text{M}^{-1}\text{s}^{-1}$, pseudo-first-order rate constants in s^{-1} . ^bSpecies being quenched in Stern–Volmer studies. The quencher was a mixture of $\text{NiBr}_2\cdot\text{glyme}$ and OMeppy (2 equiv relative to Ni) unless otherwise indicated. For k_{OA} , the aryl halide was 4-iodobenzotrifluoride. ^cThe quencher was a mixture of $\text{NiBr}_2\cdot\text{glyme}$ and OMeppy (1 equiv relative to Ni). ^dObserved pseudo-first-order rate constant from full reaction under standard conditions (see below, Figure 4.7). ^eReoptimized conditions, see Figure 4.7.

by one of the Ni species (c) to form a Ni(I) complex that undergoes oxidative addition of the aryl halide (d). Following oxidative addition, the alcohol substrate binds to the Ni center (e) and is deprotonated by the base (f). Finally, the Ni(III) aryl alkoxy complex undergoes reductive elimination to furnish the product (g), closing the Ni(I/III) cycle. The oxidized form of the PC is converted back to the neutral PC through single electron transfer (h) with either a halide anion or

the Ni(I) complex, closing both cycles. Steps (d–g) can repeat, constituting a dark Ni cycle (i) that turns over with a frequency distinct from that of the oxidative quenching cycle.

Initiation of Catalysis via Oxidative Quenching. With the possible Ni(II) complexes that may serve as quenchers of the Ir(ppy)₃ excited state known, we set out to determine the nature of the reaction between these species. Using nanosecond transient absorption spectroscopy (ns-TA) in combination with electrochemical methods, we engaged in a mechanistic exploration of the quenching step. In the absence of a quencher, the photophysical characteristics of Ir(ppy)₃ are well known; here, we measured the lifetime of the metal-to-ligand charge transfer triplet excited state (³MLCT) at $1.47 \pm 0.03 \mu\text{s}$ at $\lambda_{\text{probe}} = 365 \text{ nm}$ in degassed DMF under N₂, which agrees well with the reported value of $1.41 \pm 0.04 \mu\text{s}$.¹² In the presence of a Ni–OMebpy quenching mixture (1:2 OMebpy/Ni), a strong quenching effect is observed, shortening the lifetime to $0.37 \pm 0.01 \mu\text{s}$ at $\lambda_{\text{probe}} = 365 \text{ nm}$ (Figure 4.3C).

Following quenching, signals with maxima at $\lambda = 375$ (negative) and $\lambda = 600 \text{ nm}$ (positive) are observed to persist well beyond the period of excited state decay and the time window of the experiment (Figure 4.3B). To gain insight into the identity of the species produced from the quenching reaction, oxidative spectroelectrochemistry was performed on Ir(ppy)₃. The difference spectrum acquired by subtracting spectra before/after electrolysis corresponds to the presence of [Ir(IV)(ppy)₃]⁺ and matches that reported in the literature (Figure 4.3D).¹² Importantly, the signals in the spectroelectrochemistry difference spectrum match those in the ns-TA spectrum well, suggesting Ir(IV) is produced in the quenching reaction. The detection of Ir(IV) strongly suggests the production of Ni(I).

To confirm the formation of Ni(I), a second experiment was performed in which a Ni–OMebpy solution (1:2 Ni/OMebpy) was reduced electrochemically while monitoring its UV–vis

spectrum. The resulting difference spectrum (Figure 4.3D) shows a broad feature with a maximum spanning from ~380 to 460 nm as the only feature of significance, which is distinct from the spectrum obtained for a related Ni(I) complex produced via cathodic reduction of NiBr₂(dtbpy), where dtbpy = 4-4'-di-*tert*-butyl-2-2'-bipyridine (features at λ = ~430 and ~600 nm).³⁷ This variation is consistent with the fact that the Ni species present in greatest concentration would be distinct in the two cases due to differences in the conditions (mono vs bis bipyridine complexes, and *tert*-butyl vs methoxy substitution on the bipyridine).

Interestingly, the observed spectrum can reasonably account for some of the inconsistencies between the ns-TA spectrum and that of Ir(IV) in the spectroelectrochemistry difference spectrum, in particular in the spectral region at λ = ~430 nm where Ni(I) shows strongest absorbance. As such, the spectroelectrochemical data supports assignment of the species contributing to the ns-TA signal at t = 10 μ s as Ir(IV) and Ni(I). Control experiments support that no species aside from Ni (i.e., free ligand, K₂CO₃, aryl halide, or alcohol) quenches [Ir(ppy)₃]* significantly (see Supporting Information Section 3.4). In addition, this reduction is electrochemically feasible based on cyclic voltammetry data ($E[\text{Ir(III)*}/\text{Ir(IV)}] = -1.66$ V vs SCE; $E[\text{Ni(II)}/\text{Ni(I)}] = -1.23$ V vs SCE, see Supporting Information Table S4.5). The PhenO PC is also highly reducing ($E[{}^3\text{PhenO}^*/\text{PhenO}^+] = -1.69$ V vs SCE; $E[{}^1\text{PhenO}^*/\text{PhenO}^+] = -2.16$ V vs SCE),¹³ and ns-TA experiments conducted here support that it also engages with Ni-OMebpy complexes via an oxidative quenching pathway (see Supporting Information Section 3.5). This finding raises the broader possibility that any PC with a sufficiently reducing excited state might engage with Ni(II) via oxidative quenching.

We note that we cannot exclude the possibility that an energy transfer pathway contributes to the observed quenching, producing a Ni-centered excited state that is too short-lived to detect

with our ns-TA setup (see Supporting Information Figures S4.38–S4.42). Our lack of detection of Ni–OMebpy excited state complexes irradiated in the absence of a PC is consistent with the very short excited state lifetimes observed in the literature for other Ni(II) complexes.^{10,12,38–40} However, given the significant signal strength assigned to photoinduced electron transfer (PET) products, we assume that PET is the major pathway contributing to k_q in the following discussion.

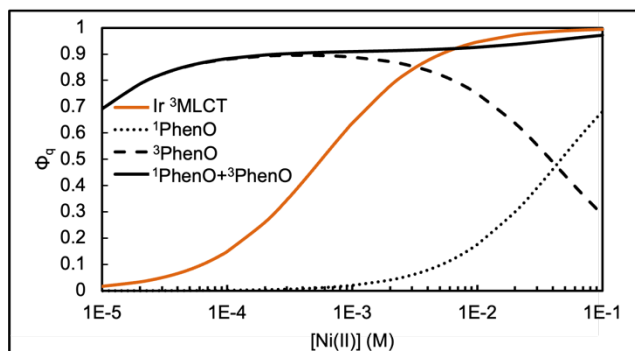


Figure 4.4. Quantum yield of quenching for each PC as a function of total Ni(II) complex concentration. Ir ³MLCT refers to the lowest energy triplet metal-to-ligand charge transfer state for Ir(ppy)₃. ¹PhenO and ³PhenO refer to the lowest-energy singlet and triplet excited states of PhenO, respectively.

Rate of Quenching of PC* by Ni-OMebpy Complexes. Bimolecular rate constants associated with quenching of the Ir(ppy)₃ and PhenO excited states were determined by conducting a Stern–Volmer²⁵ quenching study and monitoring lifetime shortening via ns-TA (Figure 4.3F). Rate constants of 1.2×10^9 and $6.6 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ were obtained for the triplet excited states of the Ir and PhenO PCs, respectively. Despite the relatively high triplet quantum yield of 0.91 for PhenO,⁴¹ significant quenching of the PhenO singlet excited state was detectable via time-correlated single photon counting (TCSPC) at total Ni concentrations relevant to catalysis (i.e., 0.2–14.5 mM), giving a rate constant of $3.4 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ (Figure 4.3F). Recent collaborative work by several of the authors suggests that the relatively short-lived singlet states are only expected to be significant contributors to catalysis when the quencher is present in sufficiently high concentration.¹³

We calculated (see Supporting Information Section 3.3) the quantum yield of quenching (Φ_q) of the singlet ($^1\text{PhenO}$) and triplet ($^3\text{PhenO}$) excited states and the $^3\text{MLCT}$ of $\text{Ir}(\text{ppy})_3$ (Figure 4.4). Per the discussion in the previous section, the following analysis assumes that most of the excited-state quenching is due to electron transfer. These quantities are calculated using Stern–Volmer quenching rate constants and are therefore not sensitive to mechanistic steps occurring after PET from PC^* to the $\text{Ni}(\text{II})$ complex. At high Ni loadings (e.g., 40 mM Ni), Φ_q calculated for $\text{Ir}(\text{ppy})_3$ is 0.99 (associated with the $^3\text{MLCT}$), while for PhenO $\Phi_q = 0.95$ (0.46 from $^1\text{PhenO}$ and 0.49 from $^3\text{PhenO}$). Thus, it is expected that $\text{Ir}(\text{ppy})_3$ may exhibit slightly better performance at high Ni loadings. The results are consistent with (but may not be the sole contributing factor to) the higher rate of product formation when $\text{Ir}(\text{ppy})_3$ is used as opposed to PhenO under the standard Ni loading of 20 mM (see Supporting Information for details, Section 6.2). Importantly, quenching of the $^1\text{PhenO}$ state as observed here, despite the relatively few studies elsewhere in dual Ni/photoredox catalysis,¹¹ should be considered more commonly as a relevant mechanistic pathway when experimental conditions permit (i.e., when organic PCs are used with high quencher concentrations).

In contrast, at low Ni loadings (e.g., 0.2 mM), the calculated quantum yield suggests that PhenO should exceed the performance of $\text{Ir}(\text{ppy})_3$ in the oxidative quenching step as Φ_q values for Ir $^3\text{MLCT}$ and $^3\text{PhenO}$ are 0.26 and 0.90, respectively. Indeed, we observed a modest increase in conversion when PhenO was used compared to $\text{Ir}(\text{ppy})_3$ at Ni concentrations of 2, 0.2, and 0.02 mM (see Supporting Information Section 6.2). Since the overall reaction performance at this Ni loading is poor, we suspect that another step is limiting reaction progress, most likely oxidative addition.

To gain insight into which Ni–OMebpy complex undergoes preferential reduction, dynamic ns-TA quenching experiments were carried out with 1:1, 1:2, or 1:3 ratios of Ni/OMebpy. Under these conditions, the complex present in the highest concentration is $\text{NiBr}_2(\text{DMF})_2(\text{OMebpy})$, $\text{NiBr}_2(\text{OMebpy})_2$, or $[\text{Ni}(\text{OMebpy})_3]\text{Br}_2$, respectively. Interestingly, the 1:1 mixture was revealed to have a significantly lower rate constant for oxidative quenching than the 1:2 mixture (8.3×10^8 vs $1.2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$), while the 1:3 mixture showed nonlinear behavior with a similar degree of quenching compared with the 1:2 mixture (see Supporting Information Figure S4.65), suggesting a more complicated mechanism. These results are consistent with the 1:2 Ni/ligand ratio offering the best reaction performance (see Supporting Information Figure S93).

Oxidative Addition at Ni(I). After the formation of Ni(I), it is proposed that oxidative addition (OA) of the aryl halide occurs. Oxidative addition at Ni(I) has been directly observed in recent reports with aryl iodides, with a reduced Ir complex, a radiolytic pulse, or photolysis of an organonickel(II) complex as the source of the Ni(II) to Ni(I) reduction.^{15,37,42} Furthermore, oxidative addition of aryl bromides has been followed via EPR in recent work²⁸ and also through stoichiometric studies of a dimeric Ni(I) complex,⁴³ both of which support oxidative addition occurring at a monomeric Ni(I) center. Although useful, none of these studies followed Ni(I) generated directly through photoinduced electron transfer (PET) as in our approach.

While the Ni(I) signal was too weak to follow via ns-TA here, presumably due to the low molar absorptivity of Ni–OMebpy complexes (~ 1 to $15 \text{ M}^{-1} \text{ cm}^{-1}$), we observed a slow exponential decay of the signal at $\lambda = 600 \text{ nm}$ that is predominately due to Ir(IV) on a timescale spanning several hundred μs . Since the signal returns to zero, this decay can be assigned to a back electron transfer reaction ($k_{\text{BET}} = 5.4 \times 10^3 \text{ s}^{-1}$) within the geminate ion pair where Ir(IV) oxidizes Ni(I) to

regenerate the neutral pair of species (Figure 4.5A). We propose that this [Ir(IV)][Ni(I)] complex remains as an ion pair during this step, resulting in the observed unimolecular decay kinetics. If a diffusional bimolecular BET step is considered instead, a rate constant with a value above the diffusion limit in DMF would be required (see Supporting Information Figure S4.28).

It is worth noting that the dominant Ni species here is [Ni(I)Br₂(OMebpy)₂]⁻ which is well suited to ion pair with [Ir(ppy)₃]⁺. These ion-pairing interactions facilitate back electron transfer and therefore may result in low cage escape yields. Low cage escape yields (e.g., <0.15) have been observed recently in DMF following photooxidation of arylamines by an iron(III) PC and in CH₃CN following photooxidation of electron-rich arenes by a chromium(III) PC.^{44,45}

However, in the presence of aryl iodide (i.e., 4-iodobenzotrifluoride, 4-IBzCF₃) the lifetime of the BET decay is shortened significantly (Figure 4.5A), indicating a faster recovery of Ir(III). This initially surprising result can be explained through a hypothesis in which Ir(IV) oxidizes OA-generated iodide to produce an iodine radical and recover Ir(III). By variation of the aryl iodide concentration in a Stern–Volmer approach, a rate constant is obtained for the reaction with 4-IBzCF₃ of $4.7 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$, in agreement with previously measured rate constants for oxidative addition with similar aryl iodides at related Ni(I)–bipyridine type complexes (Figure 4.5B).^{15,37}

In order to explain why the observed kinetics conform to the Stern–Volmer equation, justifying the plot in Figure 4.5B, we hypothesize a unimolecular BET event in competition with bimolecular oxidative addition, followed by a fast ($>6.0 \times 10^5 \text{ s}^{-1}$, see Supporting Information) unimolecular oxidation of OA-generated iodide by Ir(IV) (see scheme in Figure 4.5C). Ir(IV) is thermodynamically capable of oxidizing iodide based on cyclic voltammetry experiments (see Supporting Information Table S4.5), and we observe byproducts of iodide oxidation in TA experiments in the presence of added NaI (see Supporting Information Figures S4.50 and S4.51).

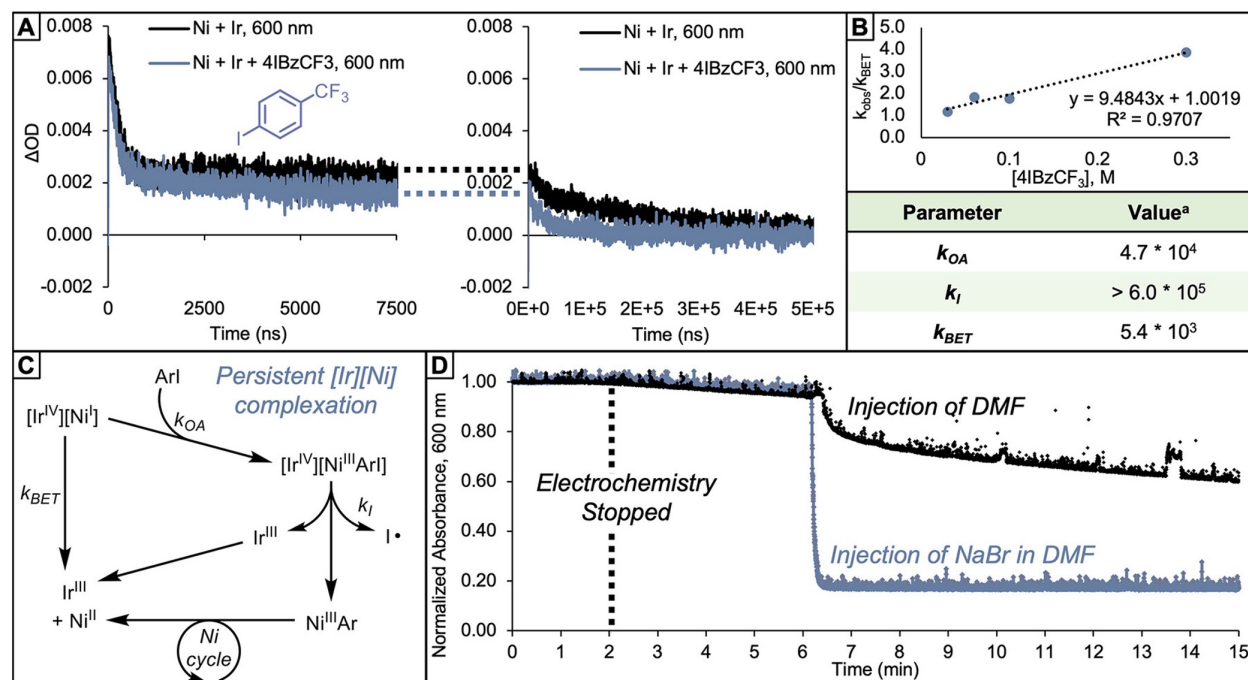


Figure 4.5. (A) ns-TA kinetic traces ($\lambda_{pump} = 355$ nm, 2-5 mW, $\lambda_{probe} = 600$ nm) comparing a mixture containing $Ir(ppy)_3$, $NiBr_2 \cdot glyme$ and $OMebpy$ (2 eq. relative to Ni) with a mixture containing the same components with added 4-iodobenzotrifluoride (0.3 M) over a 7.5 μs time window (left) and a 500 μs time window (right). (B) Plot of k_{obs}/k_{BET} vs. 4-iodobenzotrifluoride concentration (top left). Table of rate constants measured in this segment (bottom left). Scheme defining rate constant. (C) Kinetic spectroelectrochemistry experiment. $Ir(ppy)_3$ was oxidized to completion and the UV-vis signal at $\lambda_{probe} = 600$ nm was monitored over time. At $t = 2$ min, the potentiostat was turned off. At approx. $t = 6$ min, degassed solutions were injected.

In sum, our observations are consistent with the hypothesis that OA can be followed indirectly through monitoring the Ir(IV) to Ir(III) turnover kinetics. Furthermore, this observation implicates halide oxidation as a relevant mechanistic step in dual Ni/photoredox catalysis.

In addition, a CV experiment was carried out in which a Ni- $OMebpy$ mixture (1:2, Ni/ $OMebpy$) was reduced alone and in the presence of 4-bromobenzotrifluoride or 4-iodobenzotrifluoride (see Supporting Information Figure S77). In the presence of either aryl halide, the quasi-reversible reduction becomes irreversible with the disappearance of the oxidation waves, consistent with oxidative addition. A greater catalytic current is observed for the aryl iodide compared with the aryl bromide, suggesting that oxidative addition occurs at a faster rate with that type of substrate, consistent with known OA rates at Ni(I).³⁷

Photocatalyst Regeneration Through Bromide Oxidation. The reaction scheme described above in which iodide liberated through oxidative addition regenerates Ir(III) from Ir(IV) provokes the question as to whether the same chemistry might occur with bromide (either introduced with the NiBr₂ source or generated via oxidative addition of an aryl bromide). By CV, the reaction appears to be feasible (see Supporting Information Table S4.5), although the overpotential is significantly less compared with iodide. To investigate this potential pathway directly, an experiment was designed in which electrochemically generated Ir(IV) was exposed to bromide after the potentiostat was turned off and the kinetics were followed by UV-vis (Figure 4.5D). Importantly, bromide reacted with Ir(IV) as evidenced by a significantly faster decrease in the signal at $\lambda_{\text{probe}} = 600$ nm compared with a control run where DMF was injected, causing only a dilution effect. Thus, bromide might serve as a redox mediator to accelerate PC turnover, with the resulting bromine radical deactivating the active Ni(I) complex to form a Ni(II) bromide complex. Other deleterious termination pathways for the bromine radical are certainly possible, for example the radical addition of Br• to a Ni(II) or Ni(III) intermediate, the OMe₂bpy ligand, the substrate, or the nucleophile. We did not detect bromination of the aryl halide substrate or product via ¹⁹F NMR (see Supporting Information Figure S4.87) and the reaction proceeds to high yield, suggesting a low frequency of termination pathways that lead to Ni catalyst destruction or modification of the coupling partners.

Quantum Yield of Product Formation (Φ_{RXN}). Our proposed mechanism invokes the presence of a dark Ni(I)/Ni(III) cycle (Figure 4.3E(i)) in which light is only needed for initiation through Ni(II) reduction by the excited state PC to generate Ni(I). After initiation, this cycle can continuously generate product without further light input. One way to support this type of dark cycle is through Φ_{RXN} experiments since a $\Phi_{\text{RXN}} > 1$ can only be obtained if product formation

occurs independently of a light-promoted cycle. We utilized standard ferrioxalate actinometry to measure Φ_{RXN} (see Supporting Information Section 7.1 for further discussion) as a function of light intensity. At the lowest intensity of $I_0 = 5.7 \times 10^{-6} \text{ E L}^{-1} \text{ s}^{-1}$, we obtained $\Phi_{\text{RXN}} = 3.1$, further supporting our mechanistic hypothesis and ruling out any cycle in which each product formation requires the input of a photon. The fact that Φ_{RXN} is flux-dependent is consistent with a two-cycle mechanism as detailed above in which the PC cycle can operate with a turnover frequency distinct from that of the Ni cycle. Increasing the flux increases the turnover frequency of the PC cycle through increasing the concentration of PC^* . Since the total Ni concentration has a fixed maximum, there is a light intensity threshold at which Φ_q begins to decrease with a corresponding increase in Φ for other PC^* decay pathways (e.g., internal conversion and radiative decay). At high fluxes beyond this threshold value, Φ_{RXN} decreases below 1 due to the increased prevalence of these PC^* decay pathways which do not form product. Broadly, this mechanism has the consequence that the lowest flux at which the rate of product formation is practical for the process will lead to the highest quantum efficiency. Given the mechanistic findings here and in previous sections, we next sought to improve the photocatalytic coupling performance.

Effect of Halide Additives on Reaction Rate. First, we noted a shortcoming of the model system in the use of K_2CO_3 as a base in that the reaction is heterogeneous. In order to monitor reaction kinetics with all components present, we replaced K_2CO_3 with 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU) as the base to achieve homogeneous reaction conditions for improved reproducibility. Importantly, we also found that although yields are reproducible in the Hepatochem photoreactor used in our previous work, the kinetics vary drastically by position, likely due to the asymmetric irradiation imposed by the reactor geometry. As such, we conducted kinetic studies in a custom 96-well plate photoreactor (see Supporting Information Figure S4.90)

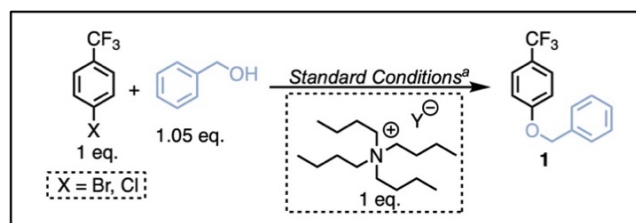
				
Entry	Time (hr)	X	Y	% Conversion ^b
1	3	Br	-	42
2	3	Br	Br	74
3	18	Cl	-	48
4	18	Cl	Br	58
5	18	Cl	I	23
6	18	Cl	Cl	96
7	3	Br	Cl	89

Figure 4.6. Effect of halide additive on the rate of coupling between 4-ClBzCF₃/4-BrBzCF₃ and benzyl alcohol. ^aStandard Conditions: DMF (0.4 M), Ir(ppy)₃ (1 mol%), NiBr₂·glyme (5 mol%), OMeppy (10 mol%), DBU (2 eq.), 35 °C, 445 nm HTE setup. Time and halide additive vary. When used, halide additives at 1 eq. ^bDetermined via ¹⁹F NMR (*n* = 3).

which showed much improved reproducibility (% conversion standard deviation = 2.1%, *n* = 16; see Supporting Information Section 6.1 for details) compared to the Hepatochem (standard deviation = 11%, *n* = 8).

With the new conditions in hand, we explored the hypothesis that an additional halide source might serve to improve photocatalyst recovery, thereby enabling the Ni(I)/Ni(III) cycle to turn over a greater number of times before deactivation. We screened bromide as an additive with the hypothesis that it would increase the reaction rate through faster catalyst turnover. Indeed, we found that in the coupling between model substrates 4-bromobenzotrifluoride (4-BrBzCF₃) and benzyl alcohol (BzOH), tetrabutylammonium bromide (TBABr) increased the conversion by 32% at the 3-h time point (Figure 4.6, entry 2), which is well outside of the well-to-well variability (std. dev. = 2.1%) of our setup. Next, since aryl chlorides are challenging substrates in dual Ni/photoredox methodologies,⁴⁶ we tested 4-chlorobenzotrifluoride (4-ClBzCF₃) as a substrate with the hypothesis that slower deactivation could improve the coupling with this substrate. As

with the aryl bromide, the coupling with 4-ClBzCF₃ had a higher conversion with bromide additive (entry 4) relative to no additive (entry 3).

Since iodide is easier to oxidize than bromide, we next explored increasing the overpotential for Ir(IV) reduction with tetrabutylammonium iodide (TBAI) additive to further increase the rate of catalyst recovery. However, the reaction with TBAI (entry 5) performed worse than no additive. This loss in performance could be due to the formation of I₂^{•-} and I₃⁻ when iodide is used as an additive. Oxidation of iodide by Ir(IV) is expected to be faster than bromide and the production of X₂^{•-} and X₃⁻ intermediates is also faster with iodide.⁴⁷ The reactivity of these intermediates or the ability of I₃⁻ and I₂^{•-} to absorb blue light could potentially explain the differences in reactivity between iodide and bromide additives.

While iodide and bromide are thermodynamically capable of reducing Ir(IV) to Ir(III), chloride is outside of the redox window for Ir(IV) reduction (0.98 V vs SCE; see Supporting Information Table S4.5). Because of this, we hypothesized that using tetrabutylammonium chloride (TBACl) as an additive would give no increase in conversion relative to the additive-free reaction. To our surprise, the coupling with TBACl as an additive significantly outperformed the other additive screens, reaching 96% conversion in 18 h (entry 6). The same increase in reactivity was observed when using TBACl with 4-BrBzCF₃ as the substrate (entry 7), giving 89% conversion in 3 h compared to 42% (entry 1) without additive. It is also worth noting that fluoride gave no conversion in a similar screen (see Supporting Information Section 6.4). To further understand the role of chloride we undertook additional reaction kinetics, UV-vis, and cyclic voltammetry experiments.

Kinetics and Nickel Speciation with Halide Additives. In Rovis and co-workers' recent deaminative cross-coupling, chloride significantly improved the system.⁴⁸ They hypothesized that

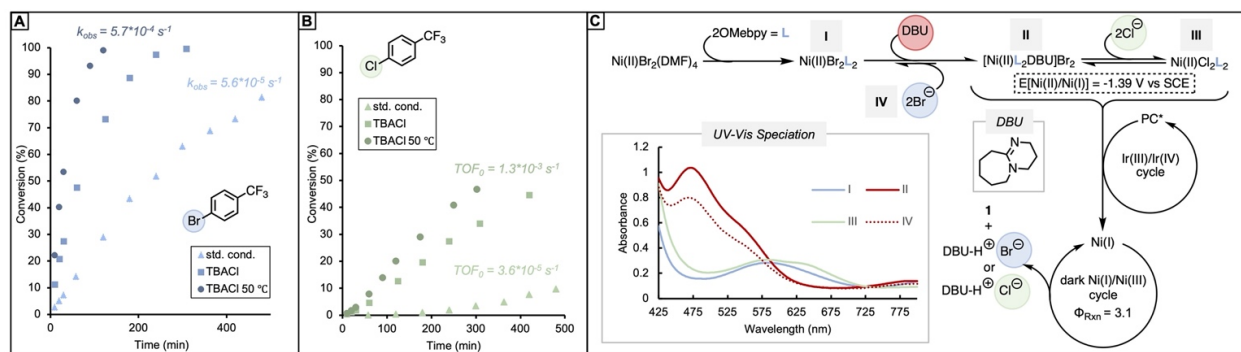


Figure 4.7. Standard conditions were used. All conversions determined via ^{19}F NMR ($n = 3$). (A) Kinetics for coupling between 4-BrBzCF₃ and benzyl alcohol under standard conditions, with TBACl additive (1 eq.), and at elevated temperatures. (B) Kinetics for coupling between 4-ClBzCF₃ and benzyl alcohol under standard conditions, with TBACl additive (1 eq.), and at elevated temperatures. (C) Proposed nickel speciation under standard conditions and modified conditions with halide additives, with UV-vis experiments supporting speciation.

one potential role of chloride additive was stopping catalyst death by preventing aggregation. This was supported by the reaction going to high conversion ($\sim 90\%$) with chloride while plateauing at low conversion ($\sim 50\%$) with no additive. However, we did not see this same trend in our kinetics studies. For 4-BrBzCF₃, the rate was pseudo-first order with no additive and reached high conversion (Figure 4.7A), suggesting that prevention of catalyst death is not the main role of chloride in our system. When running the reaction with 1 equiv TBACl, there was a 4.7-fold increase in k_{obs} and a further 2.2-fold increase at elevated temperature (35 vs 50 °C), likely due to faster thermal oxidative addition. Thus, further studies were performed to elucidate the role of the additive.

Running the same kinetics experiments on 4-ClBzCF₃ gave more insight into the role of the chloride additive. When the reaction was performed with no external chloride, there was a noticeable induction period (Figure 4.7B), suggesting that the byproducts of the aryl chloride coupling are noninnocent. The only byproduct of this coupling is the DBU–HCl salt, which we reasoned could be a source of chloride generated in situ when no exogenous chloride is present. By saturating the reaction with chloride in the form of TBACl, the coupling with 4-

ClBzCF₃ displays pseudo-first-order kinetics, suggesting that TBACl is involved in the formation of a more active catalyst species. By calculating the initial turnover frequency (TOF₀) for the two cases (added chloride/no added chloride) we found that the species formed with chloride is at least 36-fold more active than the species present with no chloride. Taken together, these results further support chloride as the main contributor to the rate increase and UV–vis studies confirmed a change in nickel speciation that we hypothesize is responsible.

Though nickel speciation was elucidated in the experiments above (Figure 4.2), these were under the conditions used in our previous methodology study.⁶ Since DBU is a known ligand that can change the speciation under our newly developed conditions, we hypothesized that the previously identified Ni(II) complexes may not be the species present in the highest concentration under our new conditions. Indeed, upon adding DBU to a mixture in which the bis-ligated nickel complex is the dominant species (Figure 4.7C(I,II)), there was a 112 nm hypsochromic shift and an increase in molar absorptivity. The increase in molar absorptivity likely arises from the formation of a five-coordinate complex from one DBU displacing both bromides to form the complex [Ni(II)L₂DBU]Br₂ (see the Supporting Information for additional discussion).

Next, upon addition of 20 equiv TBACl relative to nickel, we observed a 113 nm bathochromic shift and decrease in molar absorptivity, resembling the spectrum of the Ni(II)Br₂L₂ complex (Figure 4.7C(III)). This complex was confirmed to be Ni(II)Cl₂L₂ by comparing the diffuse reflectance spectrum of the isolated species to the complex formed directly from NiCl₂·glyme and 2 equiv OMe bpy (see Supporting Information Figure S4.13), with matching features and a reflectance maximum at ~630 nm. Additionally, the formation of Ni(II)Cl₂L₂ as a more active catalyst was further supported by an increase in conversion when NiCl₂·glyme was used in place of NiBr₂·glyme in the absence of additive (see Supporting Information Section 6.5),

though $\text{NiBr}_2\cdot\text{glyme}$ with TBACl still gave the best conversion. Lastly, upon addition of TBABr to $[\text{Ni(II)L}_2\text{DBU}]\text{Br}_2$ we observed only a very minor change in the spectral features (Figure 4.7C(IV)), and the formation of a small amount of $\text{Ni(II)Br}_2\text{L}_2$ was confirmed in the normalized difference spectrum (see Supporting Information Figure S4.12). To understand why $\text{Ni(II)Cl}_2\text{L}_2$ is responsible for the observed increase in reactivity, we next turned to studying the redox properties of the above species.

Recent work found a similar change in speciation upon addition of chloride and a concomitant decrease in the Ni(I)/Ni(II) redox couple of 0.15 V.⁴⁹ The authors hypothesized that lowering the reduction potential of Ni(II) increases the overall reaction rate. However, we found that the Ni(I)/Ni(II) couple was identical for $[\text{Ni(II)L}_2\text{DBU}]\text{Br}_2$ and $\text{Ni(II)Cl}_2\text{L}_2$ ($E[\text{Ni(II)/Ni(I)}] = -1.39$ V vs SCE), meaning a redox argument is not sufficient for explaining the difference in reactivity. Since the redox couples are identical, we are currently focusing our efforts on rates of other steps in the catalytic cycle (e.g., back electron transfer, oxidative addition, and transmetalation) to explain the increase in reactivity with chloride additive.

Expanded Reaction Scope. Based on the faster rate of product formation as quantified by an increase in k_{obs} and TOF_0 with DBU and added chloride, as well as the high conversion we observed with 4-ClBzCF₃, we explored the scope of the reaction with other challenging aryl halides and nucleophiles (Figure 4.8). First, under our newly developed conditions, we were able to obtain model compound 1 in 74% isolated yield. Though a similar coupling product was obtained in our previous work in 64% isolated yield, these conditions gave highly variable results in the formation of 1, with NMR yields ranging from 9 to 30% herein. We believe this variability could arise from differing amounts of chloride contamination in the batches of carbonate that were used (see Supporting Information Section 6.7 for further discussion). Next, we were able to couple electron-

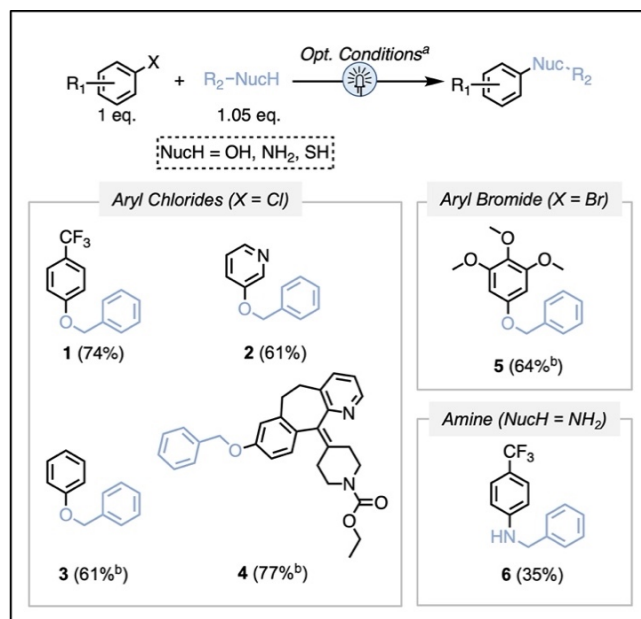


Figure 4.8. Aryl halide and nucleophile scope with optimized conditions. ^aOptimized conditions: aryl halide (1 mmol), nucleophile (1.05 mmol), Ir(ppy)_3 (0.01 mmol), DBU (2 mmol), $\text{NiBr}_2\cdot\text{glyme}$ (0.05 mmol), OMeppy (0.1 mmol), DMF (0.4 M), 440 nm Hepatochem setup, 50 °C, 18 hr. ^bRun at 70 °C.

deficient 3-chloropyridine and benzyl alcohol to give product 2 in 61% yield. We then investigated the ability of our system to enable coupling with electronically neutral aryl chlorides and successfully isolated the products from the coupling with chlorobenzene (3, 61%) and loratadine (4, 77%), albeit at elevated temperature (70 °C).

The coupling with loratadine demonstrates the applicability of our method in late-stage functionalization and it was particularly encouraging that we saw no transesterification due to the mild nature of our conditions. Though electron-rich aryl chlorides, such as *N*-Boc-5-chloroindole, were unsuccessful under our conditions (<10% crude yield), likely due to slow oxidative addition, we were able to couple the highly electron-rich 5-bromo-1,2,3-trimethoxybenzene to yield 5 in 64% yield. Lastly, the coupling with benzyl amine instead of benzyl alcohol to yield 6 (35%) demonstrates that our new conditions do not prevent reactivity with other nucleophiles. However, the coupling with benzyl mercaptan was unsuccessful, which we believe arises from thiol deprotonation by DBU and the resulting thiolate altering the Ni speciation. Though the new

conditions inhibited reactivity with thiols, the ability to turn on chloride reactivity and maintain amine reactivity demonstrates how utilizing mechanistic insights can improve reaction scope in dual photoredox/Ni-catalyzed couplings.

CONCLUSION

In summary, through spectroscopic and electrochemical studies, this work provides mechanistic insights into an oxidative quenching pathway in dual Ni/PC-catalyzed C–X bond-forming reactions. Specifically, oxidative quenching of the PC excited state to form a Ni(I) complex was observed spectroscopically, as well as the subsequent oxidative addition of an aryl iodide at Ni(I) and consequent oxidation of iodide by Ir(IV). Interestingly, persistent tight ion pairing in a series of [Ir][Ni] complexes was invoked to simulate the observed oxidative addition kinetics. Future studies ought to confirm or falsify this deduction by utilizing experimental methods capable of distinguishing tight and solvent-separated ion pairs formed as a result of PET, such as time-resolved dielectric loss spectroscopy.⁵⁰

Additionally, turnover of the Ir(IV) species to recover Ir(III) by halides (Br[–], I[–]) or Ni(I) was confirmed with spectroelectrochemistry and ns-TA experiments. A new role of chloride additive was discovered in binding to the Ni center to displace DBU, forming an octahedral Ni chloride species which led to a significant increase in reactivity to enable coupling of electron-deficient/neutral aryl chlorides and highly electron-rich aryl bromides. Notably, a novel loratadine derivative was synthesized with the reoptimized conditions, supporting the potential utility of the method discovered through the mechanistic studies herein for late-stage functionalization of medically relevant compounds.

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CHAPTER 5 – SUBSTRATE/PHOTOCATALYST REACTIVITY MATCHING ENABLES BROAD ARYL HALIDE SCOPE IN LIGHT DRIVEN, REDUCTIVE CROSS- ELECTROPHILE COUPLING UTILIZING ^{13}C NMR AS A PREDICTOR

OVERVIEW/INTRODUCTION

There has been much recent effort in the development of methods for the formation of $\text{C}(\text{sp}^2)\text{-C}(\text{sp}^3)$ bonds, concomitant with an increased desire to form such bonds in the pharmaceutical industry.¹ Pioneering work by Weix and coworkers introduced reductive nickel catalysis as a method to form $\text{C}(\text{sp}^2)\text{-C}(\text{sp}^3)$ bonds from readily available alkyl and aryl halides (Figure 5.1A).² While this work led to a plethora of strategies for halide-halide cross-electrophile couplings (HHCEC),³ there remain concerns about the practicality of scale due to the need to suspend the Zn/Mn reductant.⁴ An alternative approach was introduced by MacMillan and coworkers,^{5,6} utilizing a highly oxidizing iridium photocatalyst (PC) and silyl radical precursor to drive the reductive coupling between halides. Building off of this, Lei and Vannucci found that triethanolamine (TEOA) could be used as a terminal reductant in photocatalytic reductive halide-halide couplings, obfuscating the need for a costly silane while still requiring precious metal iridium PCs (Figure 5.1B).^{7,8} The authors hypothesized that the excited state iridium PC oxidizes TEOA, generating a ground state Ir(II) reductant capable of reducing Ni(II) to Ni(0) prior to oxidative addition. In these couplings, the ground state Ir(II) performs essentially the same role as Zn/Mn in the early HHCEC work. Along these lines, Weix and coworkers recently introduced quantum dots as a tool for activating nickel, again with TEOA as the terminal reductant.⁹ Utilizing a cheap, readily available amine as a terminal reductant marks a significant step forward in increasing the practicality of dual Ni/PC catalyzed HHCEC, but there remain issues with scope

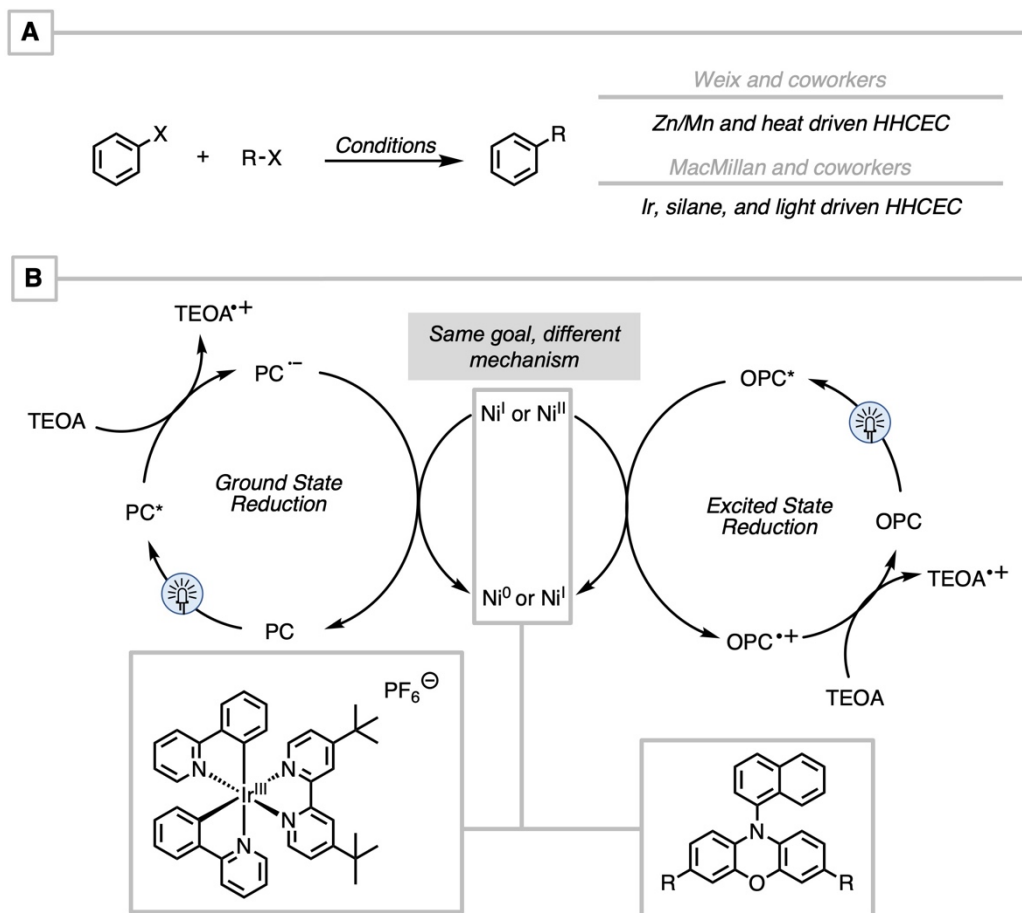


Figure 5.1. (A) Previous work on nickel catalyzed cross-electrophile couplings. (B) Recent work involving oxidative quenching PCs with TEOA as a terminal reductant (left) and hypothesized reactivity by oxidative quenching PCs developed in our group (right).

due to substrate/PC incompatibility. Additionally, oxidative quenching PCs have yet to be implemented in HHCEC despite recent reports on their ability to mediate dual nickel catalyzed transformations.¹⁰⁻¹²

Taking inspiration from our recent work on carbon-heteroatom bond formations,¹⁰ we hypothesized that highly reducing photocatalysts could act as a means to generate reactive Ni(0) or Ni(I) intermediates (Figure 5.1B, right). In our previous work, we found that excited state reductants were oxidatively quenched by Ni(II), forming a Ni(I) species primed for oxidative addition and further steps in a dark Ni(I)/Ni(III) cycle. In the work described here-in, we explore

using oxidative quenching PCs in HHCEC, identify side reactivity leading to substrate specific optimization, and introduce ^{13}C NMR as a method for matching substrate and catalyst electronics.

RESULTS AND DISCUSSION

To test the hypothesis that oxidative quenching PCs can perform HHCEC, we ran initial screening reactions between 4-bromobenzotrifluoride (**1**, 4-BrBzCF₃) and 4-bromotetrahydropyran (**2**, BrTHP), following conversion and selectivity (%DP) by ^{19}F NMR (Figure 5.2A). Excitingly, the cross coupling furnished the desired product (**3**) with a variety of oxidative quenching PCs (**4-7**) and 1,10-phenanthroline as the ligand (Figure 5.2B, see Supporting Information for full optimization details). While the iridium PC **4** gave the highest conversion and

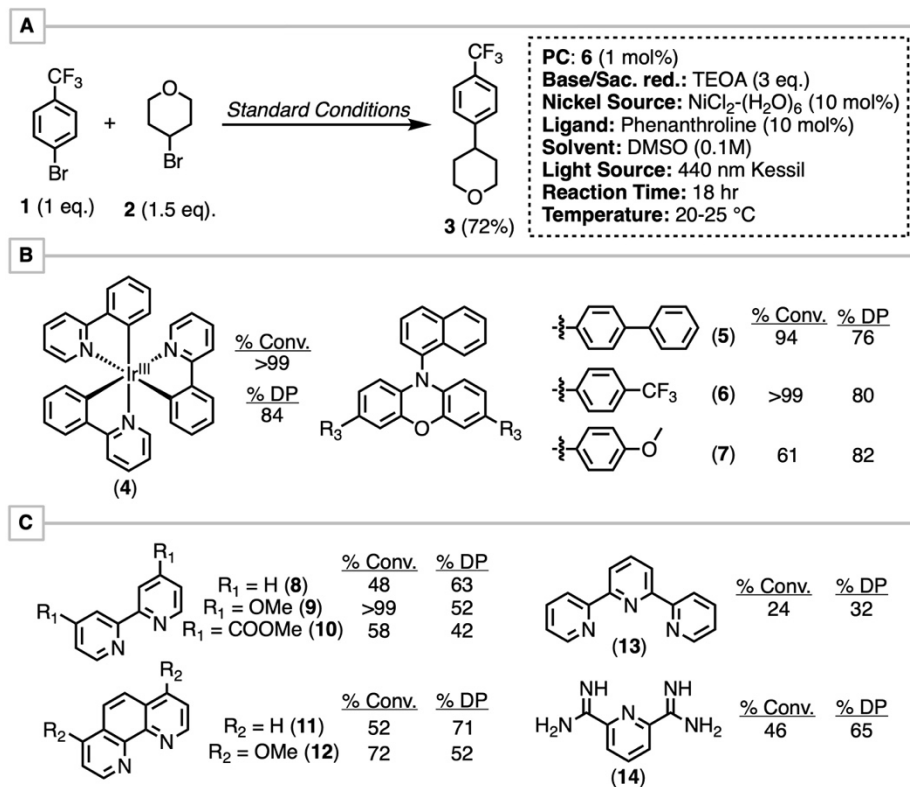


Figure 5.2. Initial optimization results for the coupling between **1** and **2** to give **3**. (A) general reaction scheme with final conditions listed (isolated yield with final conditions). (B) ^{19}F NMR conversion and selectivity (shown as % DP) for a variety of oxidative quenching PCs. Only deviation from standard conditions was the use of a blue Kessil LED. (C) ^{19}F NMR conversion and selectivity for a variety of ligands. Deviations from standard conditions: ligand and nickel ($\text{NiCl}_2\text{-glyme}$ in this case) used at 2 mol% loading. PC **5** used in place of **6**. Blue Kessil used in place of 440 nm Kessil.

selectivity, OPC **6** performed similarly, and we opted to use it for further studies. Ligand screens with a similar OPC (**5**) revealed bidentate ligands as the best performing with a notable trend between electronics and selectivity/conversion (Figure 5.2C). Electron rich ligands (**9**, **12**) led to an increase in rate relative to the deficient (**10**) and neutral (**8**, **11**) ligands, likely due to faster oxidative addition of 4-BrBzCF₃. However, both deficient and rich ligands gave a significant amount of homocoupled Ar-Ar product resulting in a lower selectivity. Tridentate ligands **13** and **14** also furnished the desired product with **13** performing worse than all bidentate ligands. While **14** gave the desired product with comparable rate and selectivity as the best performing bidentate ligand (**11**), the presence of homocoupled product with **14** led to our decision to use 1,10-phenanthroline as our ligand for further studies. After further optimization, we were able to obtain **3** in 72% isolated yield (Figure 5.2A) and began exploring other substrates.

Using our optimized conditions, we next tested 5-bromophthalide (**15**) as a substrate in the formation of **16** (Figure 5.3A). While we were initially discouraged by the low conversion (57%) and selectivity (30%) under our standard conditions (Figure 5.3B, entry 1), control studies revealed sources of side reactivity responsible for the poor performance. First, we opted to increase both the intensity and energy of our light source by switching to a 405 nm high flux reactor used in our previous work.¹³ Consistent with previous results,¹⁰ this led to an increase in the reaction rate but no increase in selectivity (entry 2). By removing the nickel catalyst and ligand, we found that **15** is still fully consumed giving a mixture of mostly **17** and **18** (entry 3). This is not surprising considering OPC **6**'s highly reducing excited state ($E^\circ(\text{PC}^{*+}/\text{PC}^*) = -1.87 \text{ V vs SCE}$)¹⁴ is within the range needed to reduce **15** ($E_{\text{on}} = -1.65 \text{ V vs SCE}$ for structurally similar methyl 4-bromobenzoate),¹⁵ resulting in formation of **15** radical anion, subsequent bromide elimination, and HAT (yielding **17**) or radical-radical coupling (yielding **18**). By further removing the PC, leaving

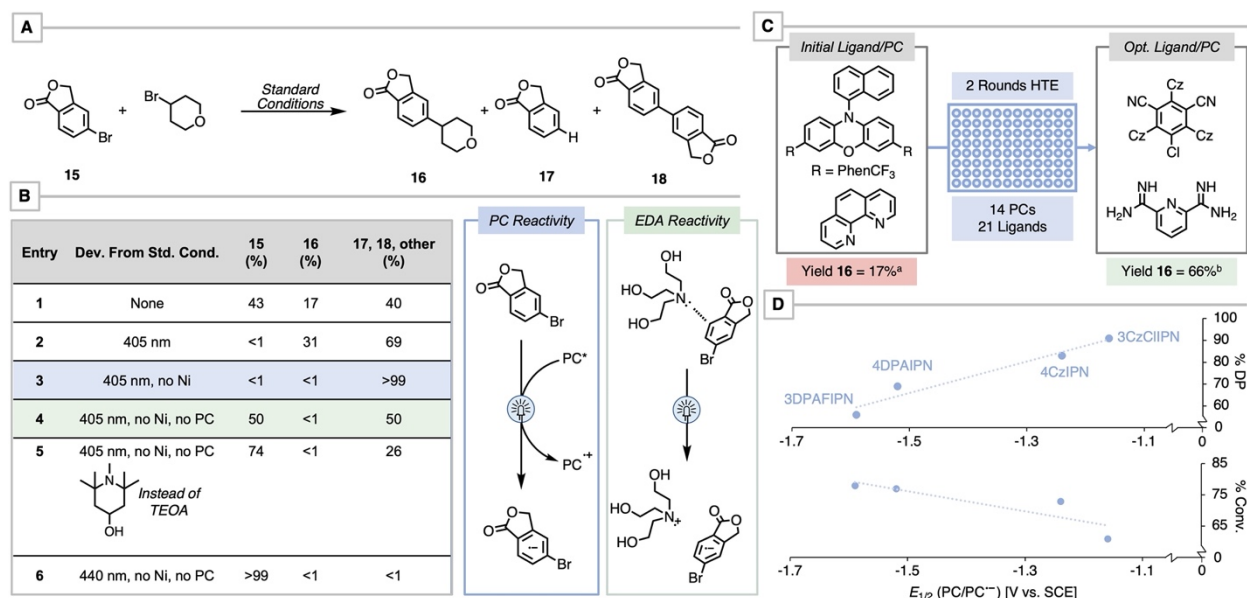


Figure 5.3. Side reactivity identification and reoptimization with 5-bromophthalide as the substrate. (A) General scheme for coupling with **15** as the substrate and most abundant products formed (**16**, **17**, **18**). (B) Table (left) summarizing side reactivity identification with hypothesized modes of reactivity shown (right). Deviations from standard conditions listed in table. Yields of products determined by HPLC using methyl benzoate as an internal standard (see SI for more details on method development). (C) Summary of HTE optimization. Only deviation from standard conditions was the use of NiCl_2 -glyme and PC/ligand identity. ^aHPLC yield. ^bisolated yield. (D) Correlation between ground state reduction potentials and selectivity (shown as % DP) and conversion. Internal standard degraded during storage of the HTE plate so these values are just based on relative areas and not HPLC yield.

only the coupling partners and TEOA, we were surprised to find that **17** and **18** were still forming in an appreciable amount (entry 4). We hypothesize that this reactivity arises from an electron donor acceptor (EDA) complex forming between **15** and TEOA that, upon irradiation, results in the formation of **15** radical anion and TEOA radical cation. Similar EDA reactivity between amines and deficient 5-membered heterocycles is known but, to the best of our knowledge, hasn't been identified as a source of side reactivity in dual Ni/PC catalyzed transformations.¹⁶

To further support reactivity arising from an EDA complex, we altered both the amine and light source. By changing the amine to the more sterically hindered 1,2,2,6,6-pentamethyl-4-piperidinol, we found a decrease in conversion of **15** (entry 5), likely arising from a weaker interaction between the amine and **15**. Lastly, no **17** or **18** were detected when a 440 nm light

source was used (entry 6). This is consistent with the fact that no color change was observed when **15** and TEOA were mixed, meaning the EDA complex either completely absorbs in the UV or has a very weak visible absorption. While we believe EDA reactivity should be more broadly considered as a possible source of side reactivity in similar reactions, the nearly identical selectivity between 405 nm (entry 2) and 440 nm (entry 1) in the coupling indicates that the EDA side reaction likely doesn't contribute to a loss of selectivity. Instead, we hypothesize that excited state reduction by OPC **6** leads to most of the observed side reactivity.

We next opted to utilize High-Throughput Experimentation (HTE) to optimize the coupling with **15** so that a more expansive group of PCs and ligands could be screened in a simplified manner. Two rounds of HTE resulted in significantly improved yield with pyridine-2,6-bis(carboximidamide) and 3-CzCIIPN as the optimal ligand and PC, respectively (Figure 5.3C). In light of the results identifying reduction by the excited state PC as a significant source of side reactivity, it is not surprising that 3-CzCIIPN gave the highest yield. PCs in this class tend to operate via a reductive quenching pathway and have less negative excited state ($E_{1/2}$ [3-CzCIIPN^{•+}/3-CzCIIPN*] = -0.93 V vs SCE) and ground state ($E_{1/2}$ [3-CzCIIPN/3-CzCIIPN^{•-}] = -1.16 V vs SCE)¹⁷ reduction potentials relative to OPC **6**, disfavoring substrate reduction. In fact, there was a trend between $E_{1/2}$ (PC/PC^{•-}) of structurally similar PCs and selectivity/conversion. The more reducing PCs within this class gave higher conversion but lower selectivity, and vice versa for less reducing PCs. This is consistent with an increased driving force at lower reduction potentials increasing rate but also a greater propensity to reduce **15**. In sum, we identified a new set of conditions (termed Deficient Conditions) for substrates prone to reduction and turned our attention to electron rich substrates.

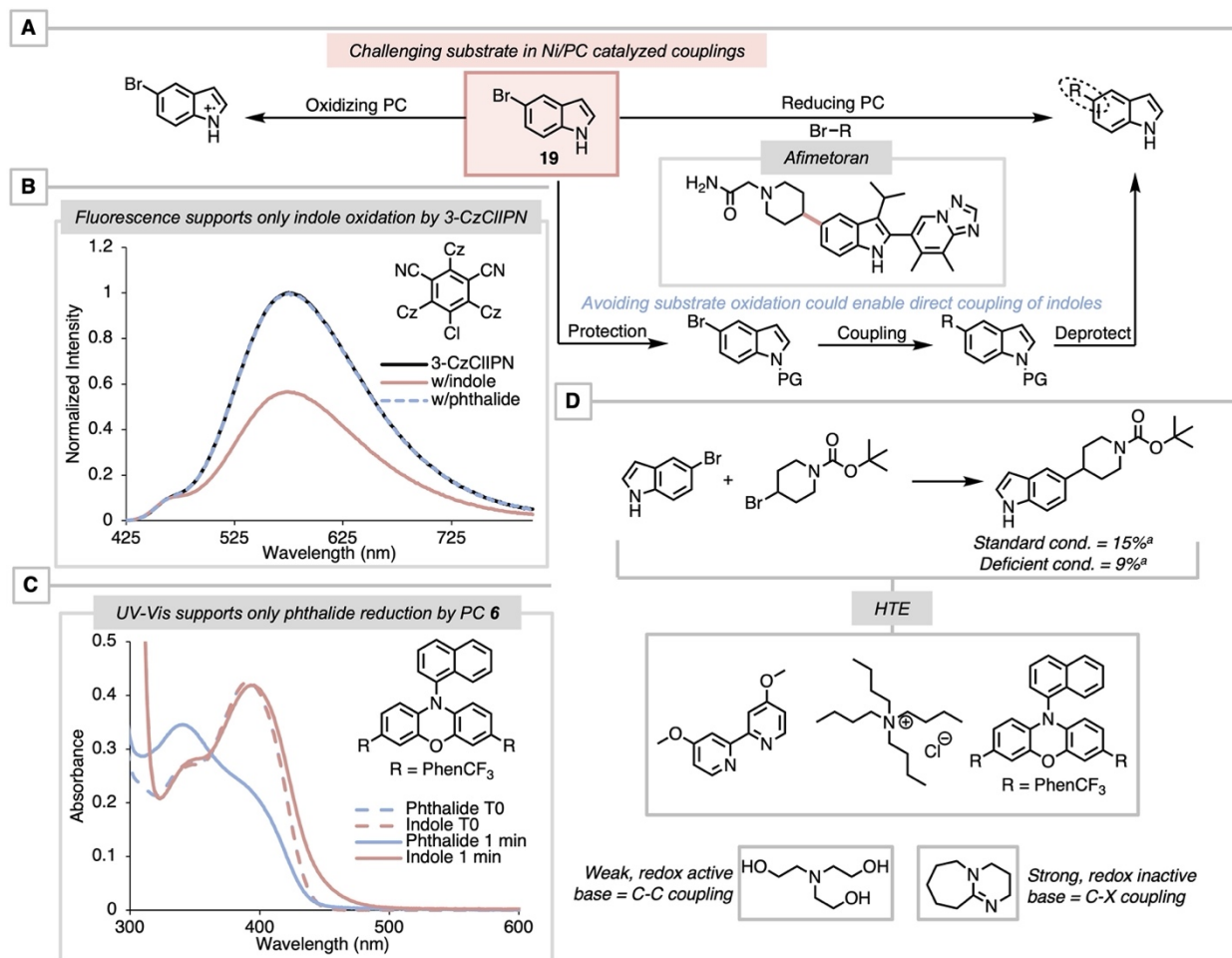


Figure 5.4. Optimization with 5-bromoindole (**19**). (A) Scheme demonstrating the utility of coupling to unprotected indoles. Hypothesized side reactivity with oxidizing PCs (left), hypothesized coupling with reducing PCs (top right), and route required when using oxidizing PCs (bottom right). (B) Fluorescence quenching with 3-CzClIPN. Excitation wavelength = 400 nm. 0.2 mM in 3-CzClIPN and 20 mM in either 5-bromophthalide or 5-bromoindole. (C) UV-vis of mixtures of PC **6** (0.02 mM) and 5-bromophthalide or 5-bromoindole (2 mM) before and after 1 minute irradiation with 445 nm HTE LEDs. (D) optimization of coupling between **19** and boc-br-pip. Results with previous conditions (top). New conditions developed (bottom). New condition deviations from Deficient Conditions: NiBr₂-glyme (5 mol%), OMe₂py (10 mol%), tetrabutylammonium chloride (1 eq.), alkyl halide (1.3 eq.), DMF (0.4 M). ^aNMR yield.

Unprotected bromoindoles have rarely been reported on as substrates in photoredox catalyzed cross-electrophile couplings and, to the best of our knowledge, only been successful in recent couplings between aryl halides and alkyl boronic esters.^{18,19} Enabling successful coupling of these substrates in HHCEC would allow for direct (i.e. without needing to protect/deprotect) formation of medically relevant compounds through a route complimentary to halide-boronic

ester methodologies (Figure 5.4A). We previously hypothesized that the highly oxidizing nature of PCs (typically > 1 V vs SCE)⁵ used in most HHCEC could inhibit successful coupling of bromoindoles like **19** (1.08 V vs SCE)²⁰ through side reactions involving substrate oxidation.²¹ To test this, we ran fluorescence quenching studies with the highly oxidizing 3-CzClIPN ($E_{1/2}$ [PC^{*}/PC^{•+}] = +1.56 V vs SCE) identified for our Deficient Conditions. Indeed, significant quenching of 3-CzClIPN fluorescence was observed at reaction relevant ratios of PC:bromoindole (1:100), supporting substrate oxidation as a possible side reaction in systems with such highly oxidizing PCs (Figure 5.4B). Furthermore, when 5-bromoindole was replaced with the standard substrate for the Deficient Conditions (5-bromophthalide), no quenching event was observed, likely giving rise to the high selectivity described in Figure 5.3. On the other hand, we hypothesized that the opposite trend in quenching would be observed with PC **6** as it is an excited state reductant.

No notable fluorescence quenching was observed for PC **6** with either substrate as a quencher. However, this might be an indication of reactivity occurring from the triplet and not a lack of reactivity. Instead, we opted to run a series of UV-vis experiments to identify side reactivity with PC **6** (Figure 5.4C). A mixture of PC **6** and either 5-bromoindole or 5-bromophthalide was irradiated for 1 minute and the UV-vis was compared to the same mixture prior to irradiation. After irradiation with 5-bromophthalide, a significant amount of PC **6** was consumed and a new peak that we tentatively assign as PC **6** radical cation appeared with a $\lambda_{\text{max}} = 345$ nm, indicating substrate reduction by PC **6**. When 5-bromoindole was used, almost no change in absorption was observed after irradiation, supporting the notion that PC **6** would have the opposite trend in substrate reactivity as 3-CzClIPN. Taken together, these data support the need to match PC redox properties with substrate electronics in dual Ni/PC catalyzed transformations.

As would be expected given the quenching data, the Deficient Conditions failed to give synthetically useful yields (6%) for the coupling between 5-bromoindole and 1-boc-4-bromopiperidine (boc-Br-pip, Figure 5.4D). While the PC **6** and phenanthroline gave higher yield (15%), we decided to run another series of HTE experiments to obtain a yield comparable to the halide-boronic ester methodologies. After screening solvents, PCs, and ligands, we found that PC **6** was still the best performing catalyst while 4,4'-bis(tert-butyl)-2,2'-bipyridine (dtbbpy) was the best ligand and DMF the best solvent, giving 32% yield. This system was reminiscent of our previously reported C-O/C-N coupling in the use of electron rich bipyridine ligands.¹⁰ Considering the similarity, we replaced dtbbpy with 4,4'-dimethoxy-2,2'-bipyridine (OMebpy), used NiBr₂-glyme instead of NiCl₂, and added tetrabutylammonium chloride (TBACl), further improving the yield to 51%. This result is noteworthy since the final conditions (termed Rich Conditions) only differ from our C-O/C-N coupling in the identity of the base and PC. Since the cross-electrophile coupling is also successful with the PC used in our C-O/C-N work (Ir(ppy)₃, Figure 5.2), only the base identity is critical for reaction success, with our C-O/C-N methodology requiring DBU. This ability to perform different classes of couplings under nearly identical conditions highlights the versatility of oxidative quenching PCs in a field where they have found comparatively little use to date.

With the three sets of conditions in hand, we began exploring the scope of our coupling with both electronically rich and deficient aryl bromides (Figure 5.5A). First, we eliminated the need for the conditions used to optimize the coupling with 4-BrBzCF₃ since both the Rich and Deficient Conditions successfully coupled 4-BrBzCF₃ to 1-boc-4-bromopiperidine (61% and 58% ¹⁹F NMR yield, respectively), albeit at slightly lower yields. We next began investigating the scope of electronically deficient substrates with the Deficient Conditions using either Boc-Br-pip or

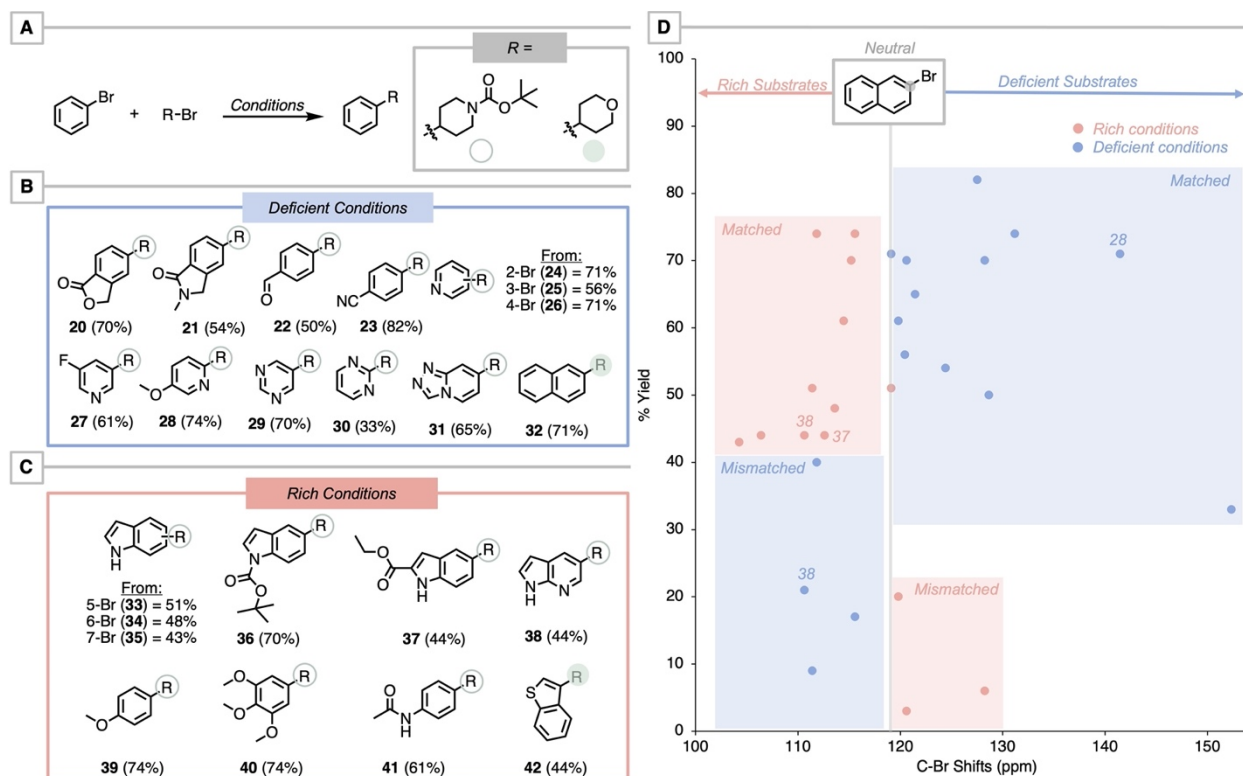


Figure 5.5. Substrate scope and NMR prediction. (A) General scheme for coupling. (B) Scope of electron deficient aryl bromides using Deficient Conditions (detailed in Figure 5.3). (C) Scope of electron rich aryl bromides using Rich Conditions (detailed in Figure 5.4). (D) ^{13}C NMR shifts for aryl bromide C-Br bond (measured in d-DMSO to replicate reaction conditions) plotted against yields for either Rich Conditions or Deficient Conditions.

BrTHP as the alkyl halide coupling partner (Figure 5.5B). Model 5-bromophthalide successfully coupled to generate **20** in 70% yield. Amide (**21**), aldehyde (**22**), and nitrile (**23**) functional groups were all well tolerated giving the desired coupling products in 50-82% yield. Pyridine with bromide at the 2-(**24**), 3-(**25**) and 4-(**26**) position successfully coupled in moderate to high yield (56-71%). Additionally, withdrawing (**27**, 61%) and donating (**28**, 74%) groups were tolerated on pyridine scaffolds. Increasing the nitrogen content of the substrate yielded pyrimidine products **29** (70%) and **30** (33%), with **30** being particularly noteworthy since, to the best of our knowledge, 2-bromopyrimidines have not been successfully coupled in HHCEC. Further increasing the complexity and heteroatom content was tolerated in yielding **31** (65%). Lastly, neutral 2-bromonaphthalene coupled under these conditions to give **32** (71%).

We next turned our attention to electron rich aryl bromides using the Rich Conditions (Figure 5.5C). Model 5-bromoindole coupled to give **33** in 51 % yield. Both 6- and 7-bromoindole coupled to give **34** and **35** (48% and 43%, respectively), with **35** demonstrating the ability of these conditions to couple ortho-substituted aryl bromides. N-Boc-5-bromoindole coupled to give **36** (70%) which is advantageous for situations where downstream reactions require the protecting group. Additional functionality and increased nitrogen content were also tolerated in the synthesis of **37** (44%) and pyrrolopyridine **38** (44%). Aryl bromides containing amide and ether function groups were also suitable substrates, yielding **39** (74%), **40** (74%), and **41** (61%). Lastly, sulfur containing **42** (44%) demonstrates the ability of our methodology to couple diverse heterocycles.

While condition selection for most substrates could be done intuitively, we sought to tie reactivity to a physical parameter. This would aid in selecting conditions for complex substrates or ones with both withdrawing and donating moieties. We hypothesized that carbon NMR shifts could provide insight into how electron rich or deficient a given substrate is (Figure 5.5D). Specifically, we thought that the C-Br shift for the aryl halide could be an indication of both its propensity to undergo side reactivity (higher shifts more likely to be reduced under Deficient Conditions and vice versa) and its relative rates in specific steps of a nickel cycle (e.g. lower shift = slower oxidative addition and may require rich OMe₂bpy ligands). We acquired ¹³C NMR of all substrates discussed above and, excitingly, noticed a trend supporting our hypothesis. Using the shift of 2-bromonaphthalene (119.1 ppm) as the “neutral substrate”, we classified every substrate with a C-Br shift >119.1 ppm as electron deficient and <119.1 ppm as electron rich. This led to four sets of yields (e.g. Rich Conditions with shift <119.1 ppm, etc.). Electron deficient substrates (>119.1 ppm) worked best under our Deficient Conditions (avg. yield = 63%, n = 12) while a subset of these substrates worked poorly under our Rich Conditions (avg. yield = 10%, n = 3). The

electron rich substrates (<119.1 ppm) followed the opposite trend, with Rich Conditions significantly outperforming Deficient Conditions, giving average yields of 55% (n = 11) and 22% (n = 5), respectively. Most notably, this method can accurately predict reactivity when both a donating and withdrawing moiety are present (substrates **28**, **37**, and **38**). We believe this offers chemists a simple method for condition selection based on data they likely already have or can easily acquire (^{13}C NMR of a substrate). We are working on expanding the data set of mismatched conditions/substrates since it is currently relatively small.

Other work to be completed on this project includes trying complex substrates from the Bristol Myers Squibb library, testing aryl chlorides and iodides, and exploring a small alkyl halide scope.

CONCLUSION

In sum, we have developed two sets of conditions for coupling a diverse range of aryl bromides in a reductive halide-halide cross electrophile coupling. Identification of side reactivity and HTE enabled photocatalyst selection based on a matching of photocatalyst redox properties and substrate electronics. Instead of solely relying on intuition, we introduced ^{13}C NMR as a tool for selecting conditions for a given substrate. Lastly, this work expands on the use of oxidative quenching catalysts in dual Ni/PC methodologies, further demonstrating their utility in a field where they have found little use.

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APPENDIX A: SUPPLEMENTARY INFORMATION FOR CHAPTER 2

1. Phenothiazine Compounds Synthesis

1.1. General Information

Purchased Chemicals

General:

All reagents were purchased from commercial suppliers and used without any further purification. Acetic acid (certified ACS), chloroform (ACS reagent), BHT stabilized tetrahydrofuran (ACS reagent), dichloromethane (ACS reagent), methanol (ACS reagent), hexanes (ACS reagent), and ethyl acetate (ACS reagent) were purchased from Fischer. Unstabilized tetrahydrofuran and toluene were purified using an mBraun MB-SPS-800 solvent purification system and kept under nitrogen atmosphere. Anhydrous MgSO_4 and Na_2SO_4 were purchased from Fischer.

Buchwald Coupling:

Phenothiazine, 4-bromo-1-naphthonitrile, 1-bromonaphthalene, sodium tert-butoxide (NaO^tBu), tri-tert-butylphosphine (P^tBu_3), and palladium dibenzylideneacetone ($\text{Pd}(\text{dba})_2$) were purchased from Sigma Aldrich. Bromobenzene and 1-bromo-4-fluoronaphthalene were purchased from TCI.

Bromination:

N-Bromosuccinamide (NBS) and phenothiazine were purchased from Sigma Aldrich.

Suzuki Coupling:

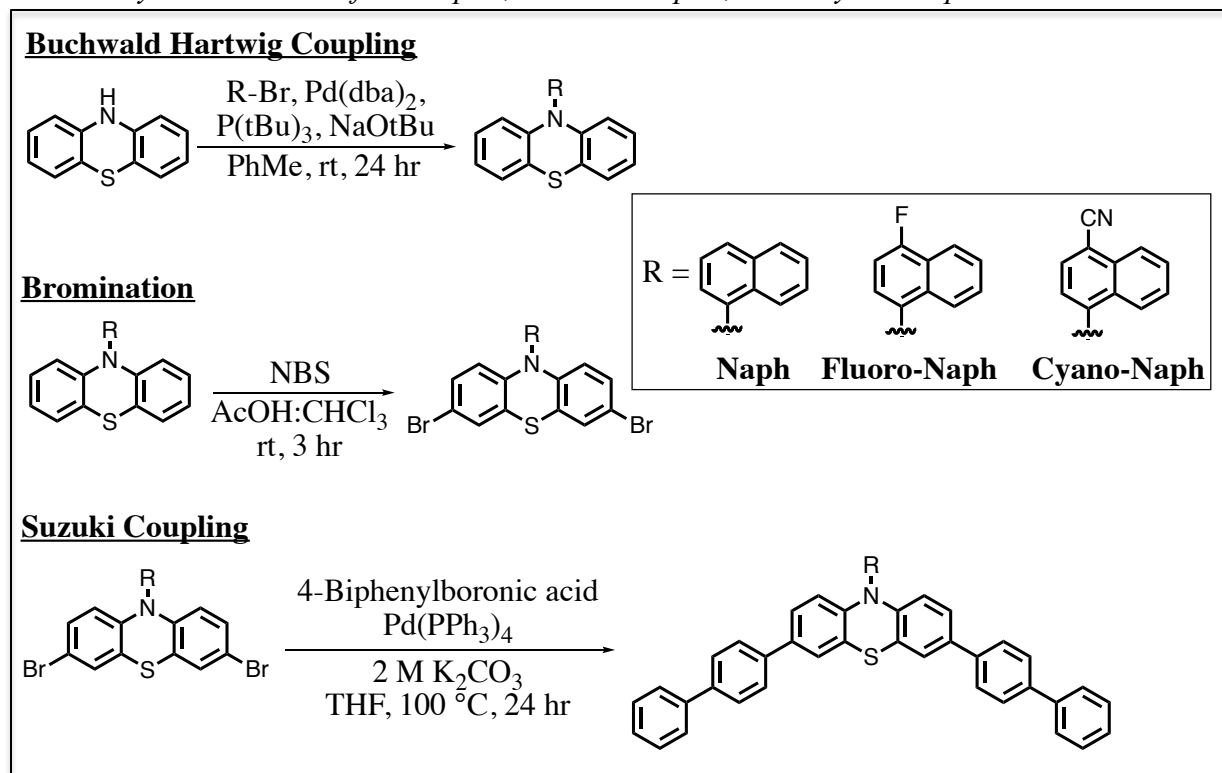
Potassium carbonate (K_2CO_3) was purchased from Fischer. Tetrakis(triphenylphosphine)palladium(0) ($\text{Pd}(\text{PPh}_3)_4$) was purchased from Sigma Aldrich. 4-Biphenylboronic acid was purchased from Oxchem.

Instruments for Compound Characterization:

Nuclear magnetic resonance spectra were recorded on a Bruker 400 MHz NMR Spectrometer. All ^1H NMR experiments are reported in δ units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) benzene (7.15 ppm) or dimethylsulfoxide (2.50 ppm) in deuterated solvent. All ^{13}C NMR spectra are reported in ppm relative to *d*-DMSO (39.52 ppm) or benzene-*d*₆ (128.62 ppm). Electrospray Ionization Mass Spectroscopy (ESI-MS) and Atmospheric Pressure Chemical Ionization Mass Spectroscopy (APCI-MS) were performed by the Colorado State University Central Instrumentation Facility.

1.2. Procedures and Characterization:

General Synthetic Scheme for “Naph”, “Fluoro-Naph”, and “Cyano-Naph”



Synthesis of Naph:

10-(Naphthalen-1-yl)-10*H*-Phenothiazine:

Phenothiazine (0.996 g, 5.00 mmol, 1.00 eq.) and NaO^tBu (0.720 g, 7.50 mmol, 1.50 eq.) were added to a flame-dried storage tube, cycled 3x with N₂ and vacuum, and brought into an N₂-filled glovebox. Pd(dba)₂ (28.8 mg, 50.0 μmol, 1.00 mol%), 1 M P(^tBu)₃ in toluene (40.0 μL, 40.0 μmol, 0.800 mol%) and 7.5 mL toluene were added and the storage tube was brought out of the glove box. Sparged 1-bromonaphthalene (0.770 mL, 5.50 mmol, 1.10 eq) was added and the reaction mixture was heated at 60 °C for 24 hours. The reaction mixture was diluted with EtOAc, transferred to a separatory funnel and washed with H₂O and brine. The organic layer was dried over Na₂SO₄, concentrated and sublimed at 150 °C yielding the desired product as an off white solid (1.03 g, 63% yield). The NMR matched that previously reported.¹

3,7-Dibromo-10-(Naphthalen-1-yl)-10*H*-Phenothiazine:

In a 250 mL round bottom flask, charged with a stir bar and wrapped in foil, 10-(naphthalen-1-yl)-10*H*-phenothiazine (0.651 g, 2.00 mmol, 1.00 eq.) was dissolved in 60 mL 1:1 AcOH:CHCl₃. *N*-Bromosuccinimide (0.748 g, 4.20 mmol, 2.10 eq.) was added portion wise over 10 minutes and the reaction was stirred for 2 hours. The reaction mixture was concentrated under vacuum, re-dissolved in DCM, washed with H₂O and brine and the organic layer was dried over Na₂SO₄. The crude mixture was concentrated until solid began precipitating and minimal DCM was added until the solution became homogeneous. MeOH was layered on top of this solution and the flask was put in a -25 °C freezer. The recrystallization was filtered, yielding the desired product as a slightly red solid (0.622 g, 64% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.15 (dd, *J* = 17.7, 7.9 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.81 – 7.74 (m, 2H), 7.64 – 7.55 (m, 2H), 7.32 (d, *J* = 2.4 Hz, 2H), 6.97 (dd, *J* = 8.9, 2.4 Hz, 2H), 5.83 (d, *J* = 8.8 Hz, 2H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 142.07, 135.25, 130.15, 129.86, 129.64, 129.56, 129.12, 128.42, 127.88, 127.09, 126.99, 122.20,

120.59, 117.11, 114.15. HRMS (ESI): calculated for M⁺ C₂₂H₁₃Br₂NS, 480.9135; observed 480.9111.

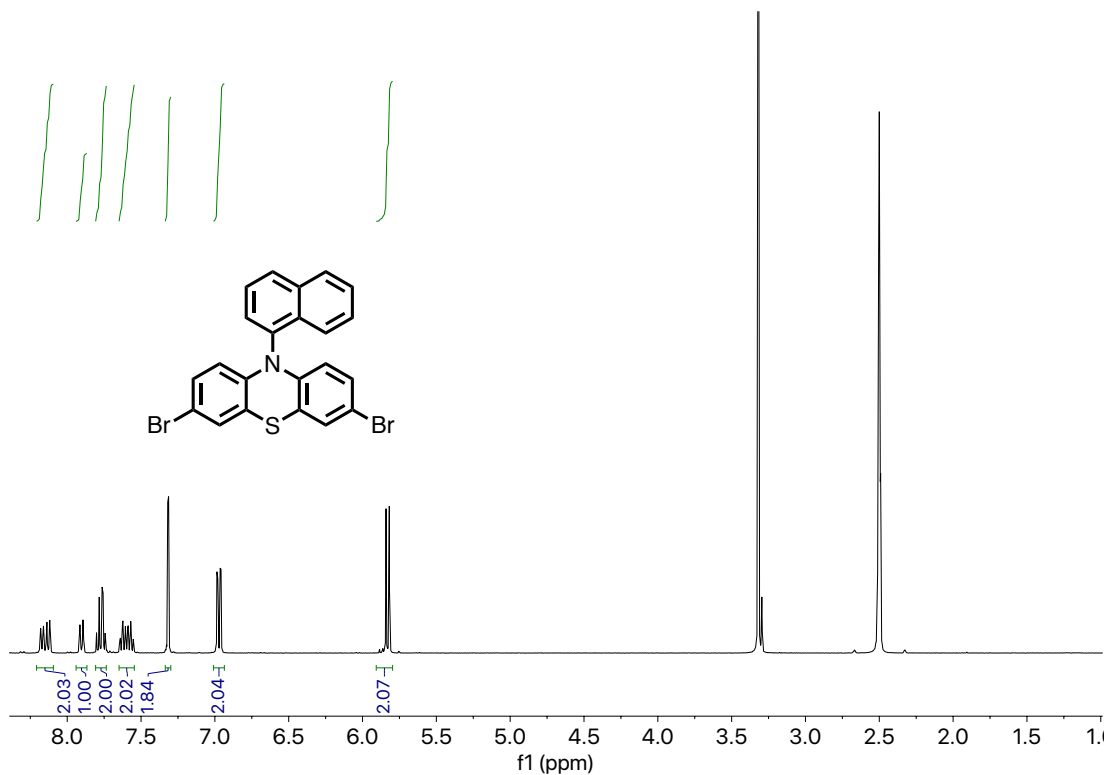


Figure S2.2. ¹H NMR of 3,7-Dibromo-10-(Naphthalen-1-yl)-10H-Phenothiazine in DMSO-*d*₆.

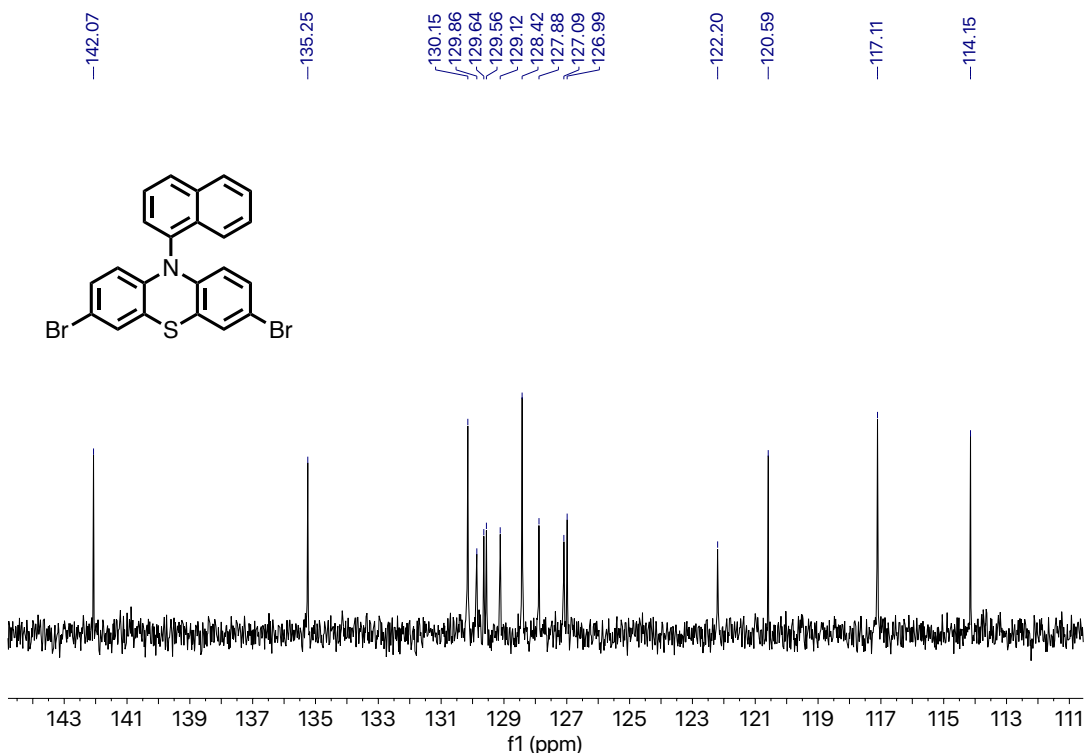


Figure S2.3. ^{13}C NMR of 3,7-Dibromo-10-(Naphthalen-1-yl)-10H-Phenothiazine in $\text{DMSO-}d_6$.

3,7-Di([1,1'-Biphenyl]-4-yl)-10-(Naphthalen-1-yl)-10H-Phenothiazine (Naph):

3,7-Dibromo-10-(naphthalen-1-yl)-10H-phenothiazine (0.232 g, 0.480 mmol, 1.00 eq.) and 4-biphenylboronic acid (0.382 g, 1.90 mmol, 4.00 eq.) were added to a flame dried 200 mL schlenk flask equipped with a reflux condenser. 20 mL THF and 6 mL sparged 2 M K_2CO_3 were added, followed by $\text{Pd}(\text{PPh}_3)_4$ (93.0 mg, 72.0 μmol , 15.0 mol%). The reaction was heated to 100 $^\circ\text{C}$ for 24 hours, concentrated under vacuum, dissolved in DCM, and washed with H_2O and brine. The organics were dried with MgSO_4 , concentrated under reduced pressure and purified by flash chromatography (1:4 DCM:Hexanes, $R_f = 0.15$) followed by a recrystallization from DCM/MeOH yielding the product as a bright yellow solid (0.230 mg, 76% yield). ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 8.22 (dd, $J = 6.5, 2.8$ Hz, 1H), 8.17 (d, $J = 7.4$ Hz, 1H), 8.03 (d, $J = 8.0$ Hz, 1H), 7.89 – 7.80 (m, 2H), 7.74 – 7.56 (m, 14H), 7.52 – 7.42 (m, 6H), 7.41 – 7.32 (m, 2H), 7.19 (dd, $J = 8.7, 2.2$ Hz, 2H), 6.02 (d, $J = 8.6$ Hz, 2H). ^{13}C NMR (101 MHz, $\text{Benzene-}d_6$) δ 143.36, 141.31, 140.24, 139.04,

137.75, 135.92, 135.65, 132.05, 129.58, 129.34, 129.11, 129.08, 127.50, 127.36, 127.20, 127.01, 125.94, 125.38, 124.25, 120.43, 116.68 (Note that signal to noise was low due to poor solubility).

HRMS (APCI): calculated for M+H C₄₆H₃₁NS, 630.2255; observed 630.2266.

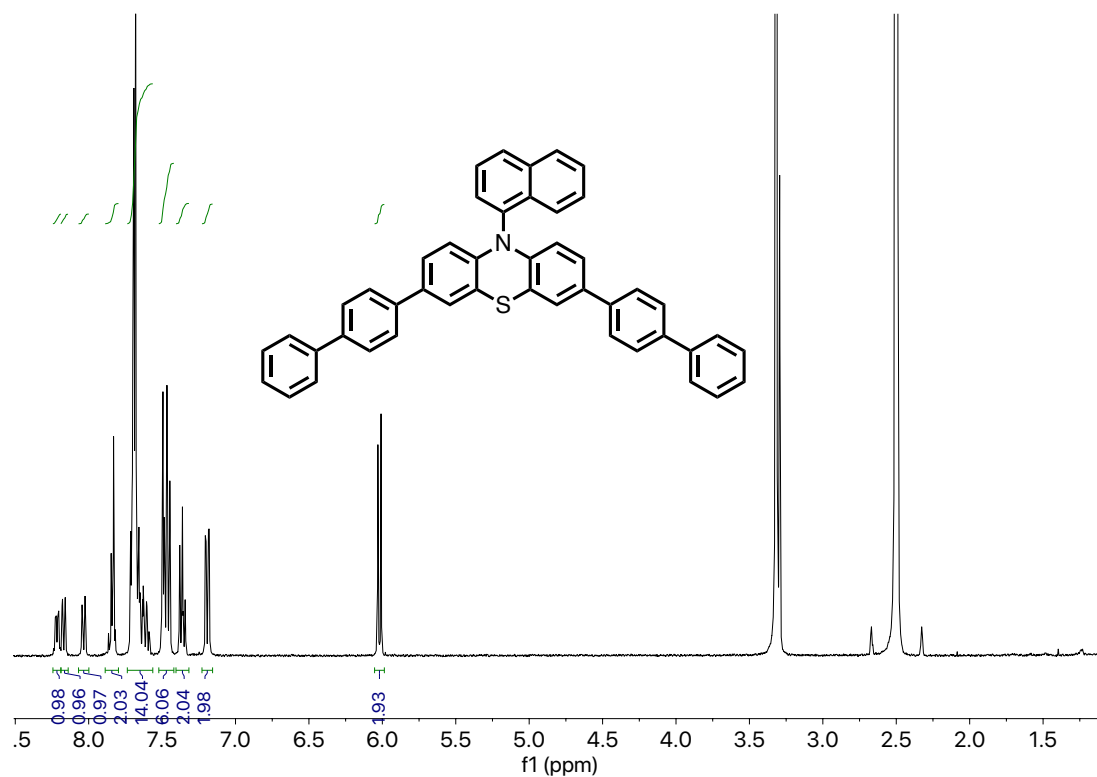


Figure S2.4. ¹H NMR of Naph in DMSO-d₆.

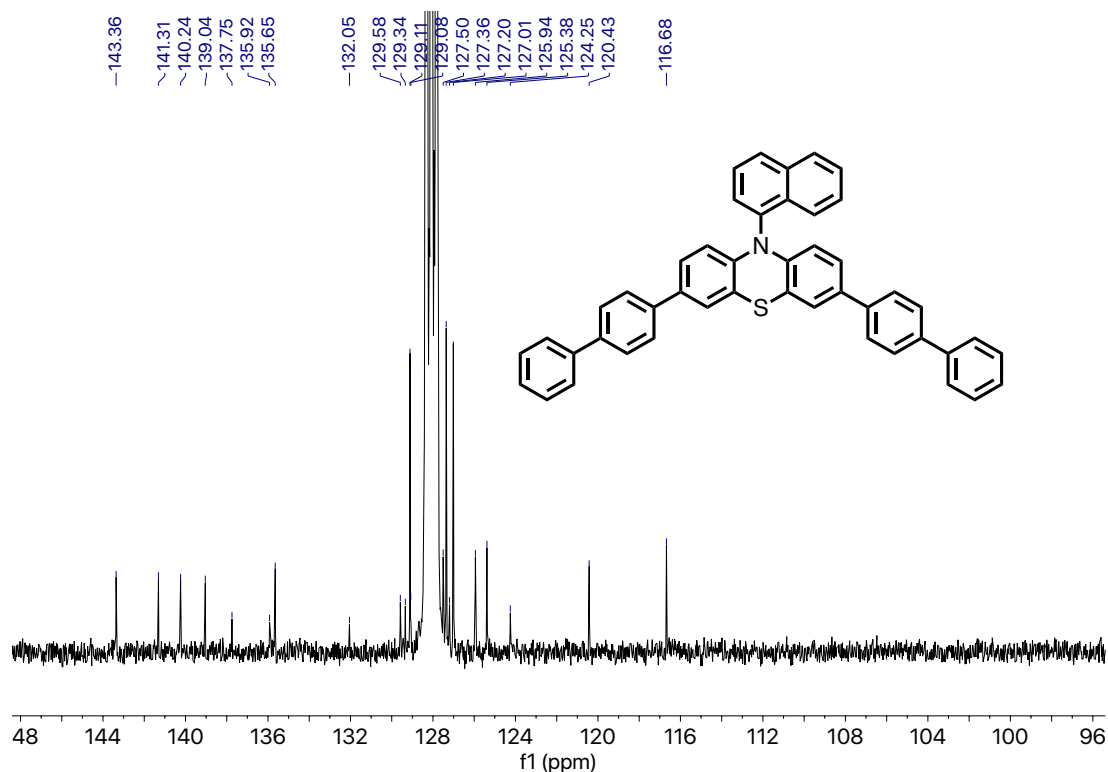


Figure S2.5. ^{13}C NMR of Naph in $\text{benzene-}d_6$.

Synthesis of Fluoro-Naph:

10-(4-Fluoronaphthalen-1-yl)-10H-Phenothiazine:

1-Bromo-4-fluoronaphthalene (2.50 g, 11.1 mmol, 2.00 eq.), phenothiazine (1.11 g, 5.55 mmol, 1.00 eq.) and NaO^tBu (1.07 g, 11.1 mmol, 2.00 eq.) were weighed into 20 mL scintillation vials, brought into an N_2 filled glovebox and added to a flame-dried storage tube. $\text{Pd}(\text{dba})_2$ (63.8 mg, 0.111 mmol, 2.00 mol%), 1 M P^tBu_3 in toluene (0.160 mL, 0.167 mmol, 3.00 mol%) and 15 mL toluene were added to the storage tube. The reaction was brought out of the glovebox, heated to 60 °C for 24 hours, exposed to air, and concentrated to dryness. The crude reaction mixture was re-dissolved in DCM and washed with H_2O and brine. The organics were dried over MgSO_4 , concentrated to minimal solvent and passed through a silica plug (washing with 8:1 hexanes:EtOAc). This was concentrated and cold MeOH was added. The crashed out solid was collected by filtration yielding the target compound as a slightly yellow solid (0.975 g, 51% yield).

^1H NMR (400 MHz, Benzene- d_6) δ 8.06 (d, $J = 8.4$ Hz, 1H), 7.96 (d, $J = 8.5$ Hz, 1H), 7.09 (t, $J = 7.6$ Hz, 1H), 7.02 – 6.88 (m, 4H), 6.77 (dd, $J = 10.1, 8.1$ Hz, 1H), 6.55 (td, $J = 7.4, 1.3$ Hz, 2H), 6.47 (td, $J = 7.8, 7.4, 1.6$ Hz, 2H), 5.96 (dd, $J = 8.2, 1.2$ Hz, 2H). ^{13}C NMR (101 MHz, Benzene- d_6) δ 160.01, 157.48, 144.33, 133.56, 133.52, 133.23, 133.17, 129.84, 129.75, 128.54, 127.37, 127.35, 127.26, 127.05, 127.05, 125.74, 125.56, 124.27, 124.25, 122.99, 121.58, 121.53, 120.39, 116.18, 110.57, 110.36. ^{19}F NMR (376 MHz, Benzene- d_6) δ -120.77. HRMS (ESI): calculated for M^+ $\text{C}_{22}\text{H}_{14}\text{FNS}$, 343.0831; observed 343.0832.

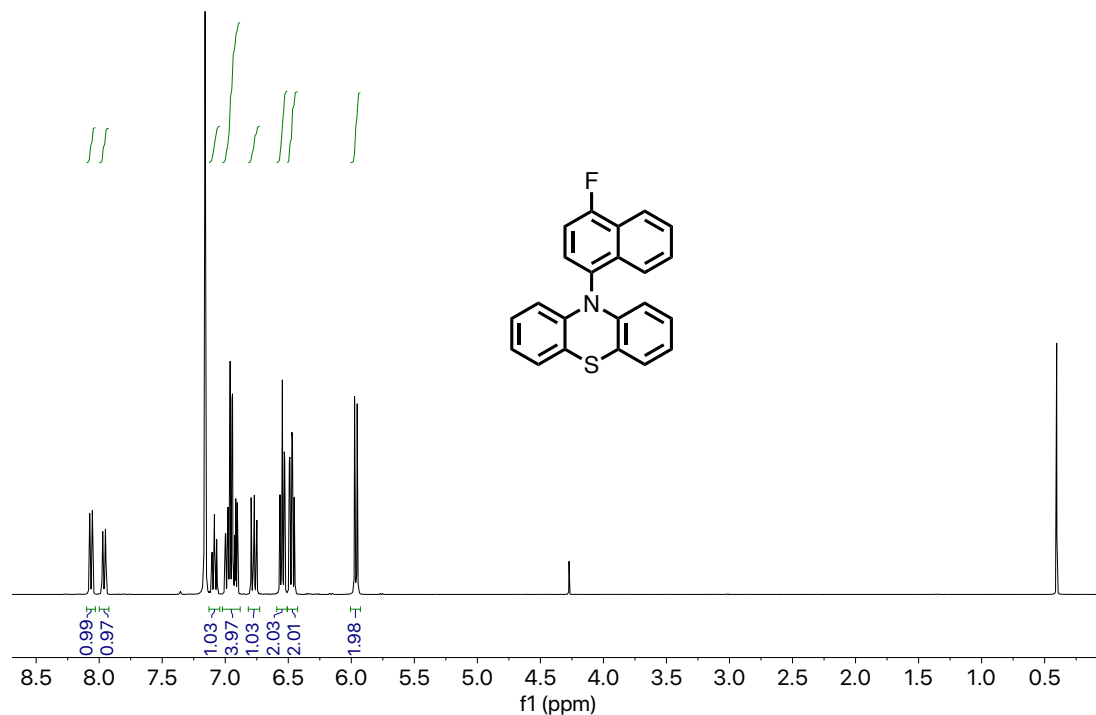


Figure S2.6. ^1H NMR of 10-(4-Fluoronaphthalen-1-yl)-10H-Phenothiazine in benzene- d_6 .

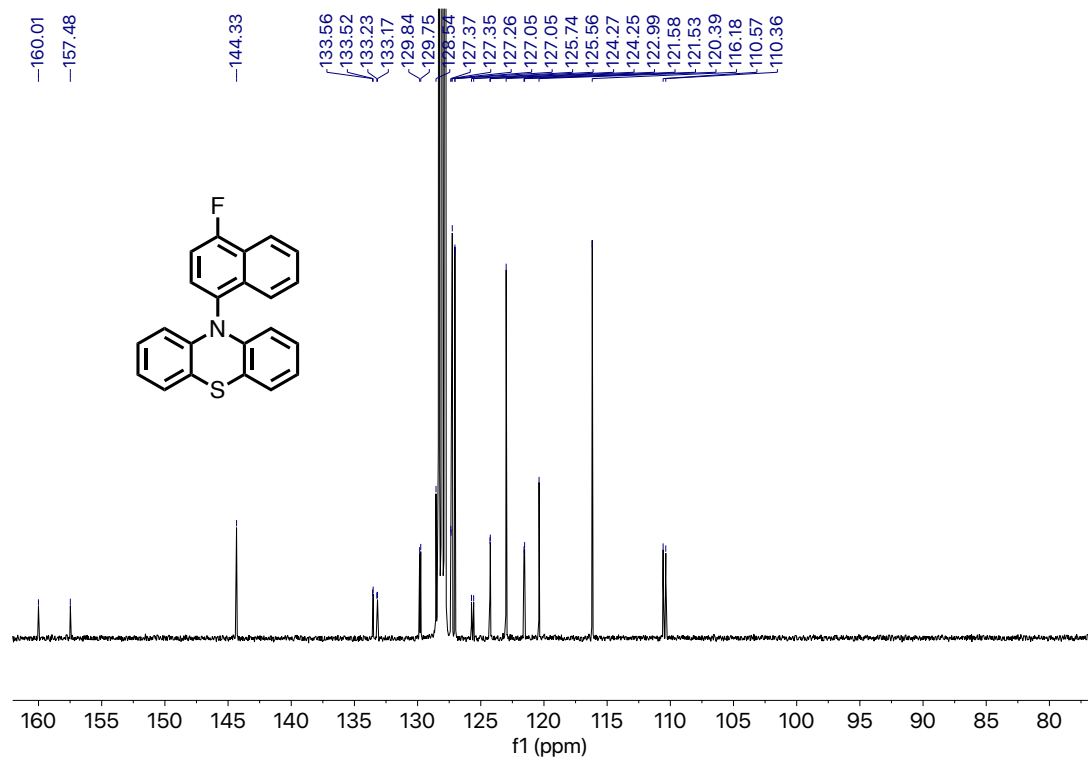


Figure S2.7. ¹³C NMR of 10-(4-Fluoronaphthalen-1-yl)-10H-Phenothiazine in benzene-d₆.

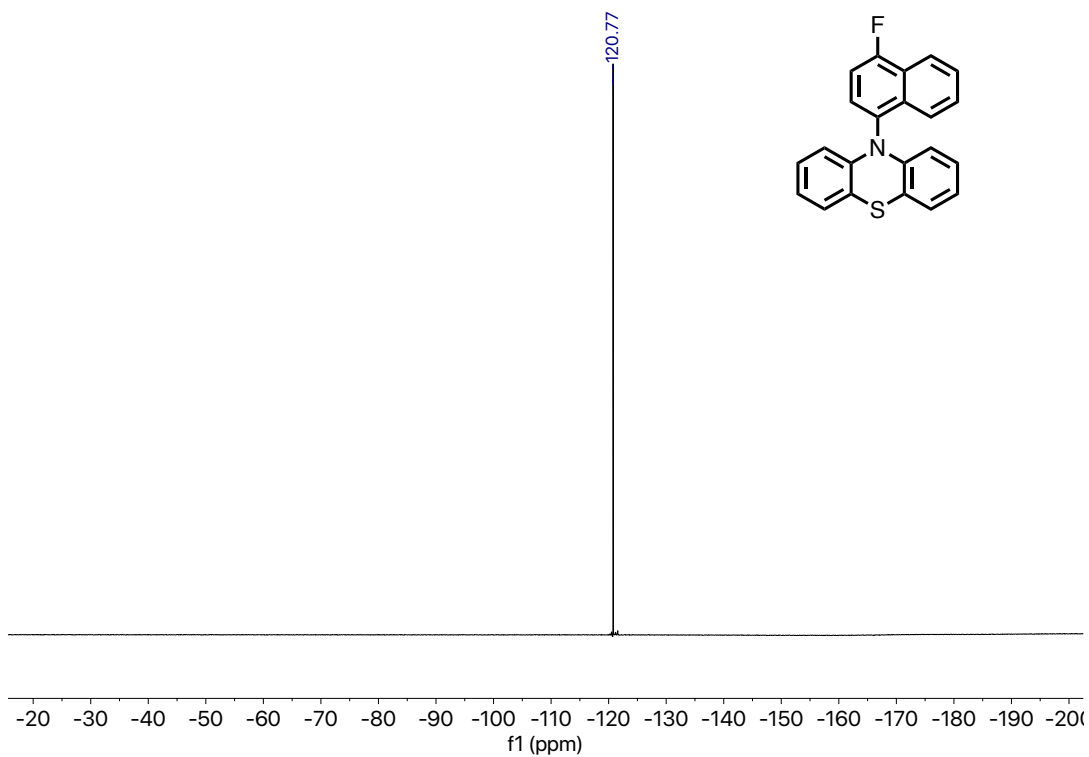


Figure S2.8. ¹⁹F NMR of 10-(4-Fluoronaphthalen-1-yl)-10H-Phenothiazine in benzene-d₆.

3,7- Dibromo-10-(4-Fluoronaphthalen-1-yl)-10*H*-Phenothiazine:

In a 250 mL round bottom flask wrapped in foil, 10-(4-Fluoronaphthalen-1-yl)-10*H*-Phenothiazine (0.687 g, 2.00 mmol, 1.00 eq.) was dissolved in 60.0 mL 1:1 AcOH:CHCl₃. NBS (0.748 g, 4.20 mmol, 2.10 eq.) was added portion-wise over the course of 20 minutes. The reaction was stirred for 3 hours, quenched with saturated NaHCO₃, and the aqueous layer was extracted with DCM. The combined organics were washed with H₂O and brine, dried over Na₂SO₄, and concentrated under reduced pressure. Recrystallization from DCM:MeOH at -25 °C yielded the target compound as a white solid (0.711 g, 71% yield). ¹H NMR (400 MHz, Benzene-*d*₆) δ 8.04 (d, *J* = 8.2 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.13 – 7.01 (m, 2H), 6.96 (d, *J* = 2.3 Hz, 2H), 6.73 (d, *J* = 7.4 Hz, 2H), 6.53 (dd, *J* = 8.8, 2.3 Hz, 2H), 5.55 (d, *J* = 8.8 Hz, 2H). ¹³C NMR (101 MHz, Benzene-*d*₆) δ 160.16, 157.62, 132.53, 132.47, 132.47 130.13, 129.50, 129.41, 129.24, 128.76, 127.61, 127.59, 125.78, 125.61 123.64, 123.61, 121.87, 121.79, 121.74, 117.24, 115.39, 110.58, 110.37. ¹⁹F NMR (376 MHz, C₆D₆) δ -119.74. HRMS (ESI): calculated for M+2 (most abundant isotope) C₂₂H₁₂Br₂FNS, 500.9021; observed 500.9008.

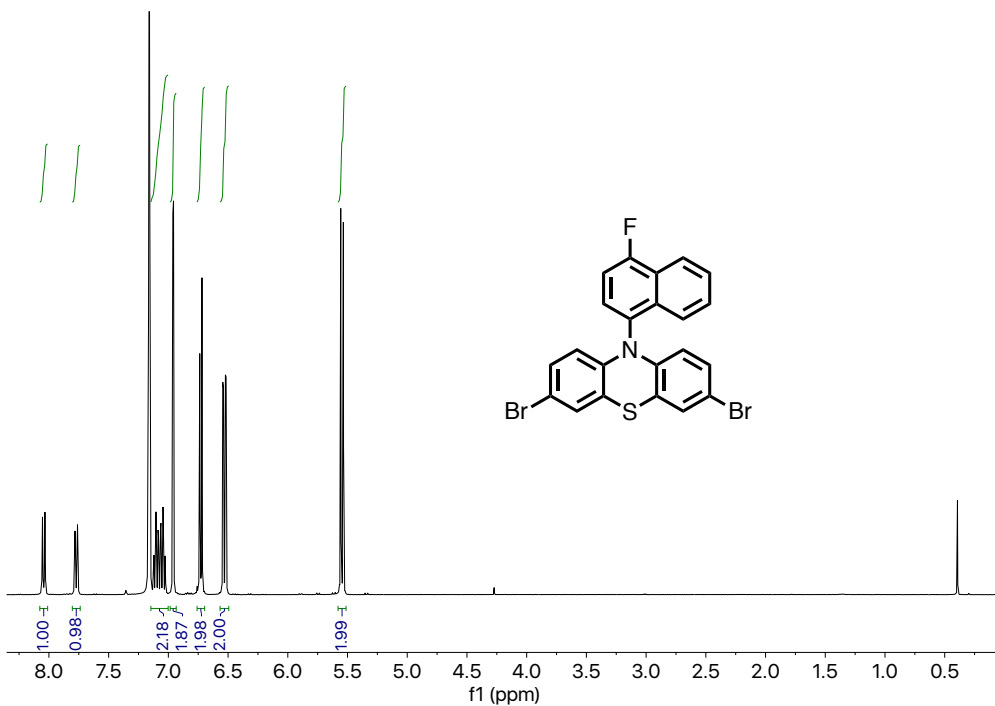


Figure S2.8. ¹H NMR of 3,7-Dibromo-10-(4-Fluoronaphthalen-1-yl)-10H-Phenothiazine in benzene-d₆.

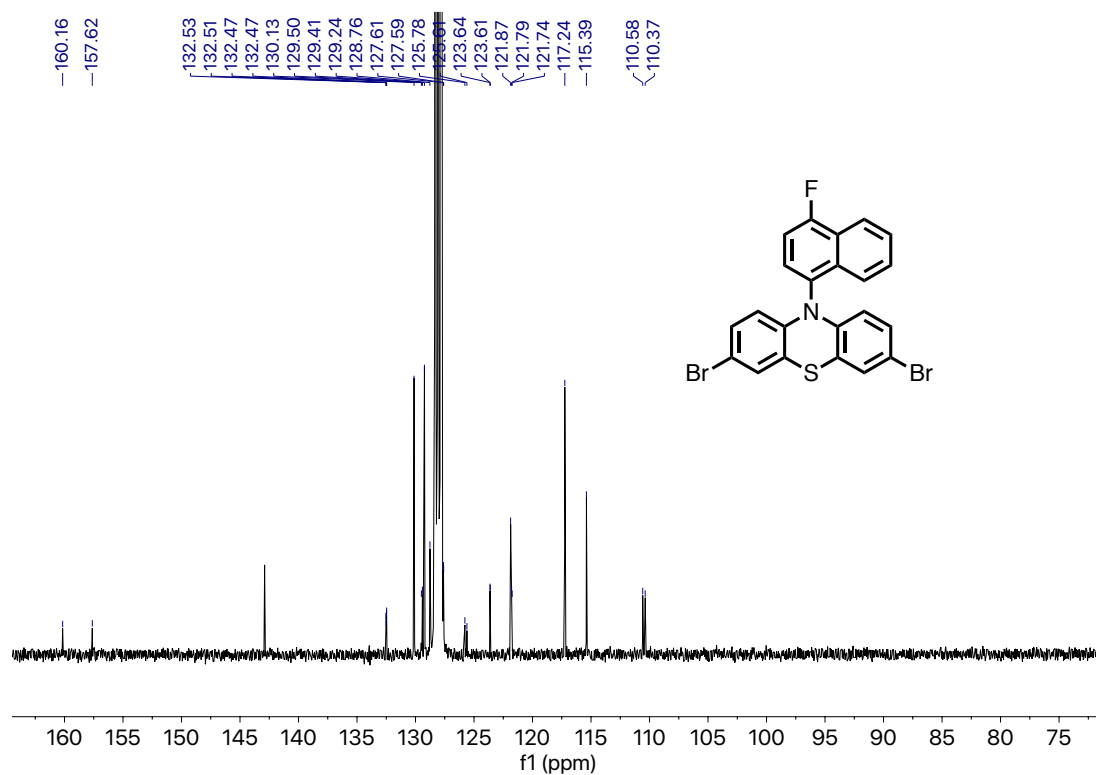


Figure S2.9. ¹³C NMR of 3,7-Dibromo-10-(4-Fluoronaphthalen-1-yl)-10H-Phenothiazine in benzene-d₆.

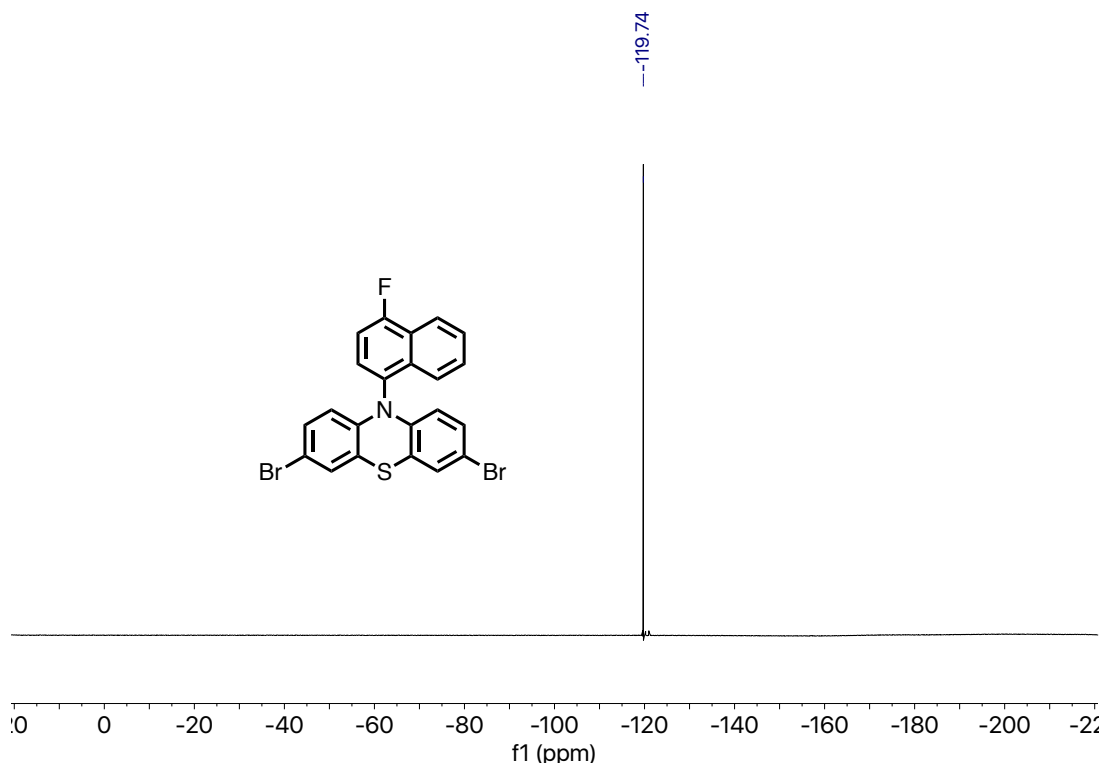


Figure S2.10. ^{19}F NMR of 3,7-Dibromo-10-(4-Fluoronaphthalen-1-yl)-10H-Phenothiazine in benzene- d_6 .

3,7-Di([1,1'-Biphenyl]-4-yl)-10-(4-Fluoronaphthalen-1-yl)-10H-Phenothiazine (Fluoro-Naph):

3,7-Dibromo-10-(4-fluoronaphthalen-1-yl)-10H-phenothiazine (0.501 g, 1.00 mmol, 1.00 eq.) and 4-biphenylboronic acid (0.792 g, 4.00 mmol, 4.00 eq) were added to a 250 mL storage tube. After cycling the tube with N_2 and vacuum three times, the storage tube was taken into a nitrogen filled glove box. $\text{Pd}(\text{PPh}_3)_4$ (58.0 mg, 50.0 μmol , 5.00 mol%) was added to the storage tube and the mixture was dissolved in 20 mL THF. The storage tube was removed from the glove box and 10 mL of sparged 2 M K_2CO_3 was added. The resultant heterogeneous mixture was heated for 24 hours at 100 $^\circ\text{C}$. After the reaction was complete, the mixture was cooled to room temperature, exposed to oxygen, concentrated under reduced pressure and transferred to a separatory funnel, rinsing with DCM. The aqueous layer was extracted twice with DCM. The

combined organics were washed with H₂O, brine, dried with Na₂SO₄ and concentrated under reduced pressure. The resultant solid was dissolved in toluene, passed through a silica plug and again concentrated under reduced pressure. Recrystallization from DCM:MeOH at -25 °C yielded the desired product as a yellow solid (0.550 g, 85% yield). ¹H NMR (400 MHz, Benzene-*d*₆) δ 8.12 (dd, *J* = 14.0, 8.3 Hz, 2H), 7.62 – 7.43 (m, 10H), 7.37 (d, *J* = 8.3 Hz, 4H), 7.25 (t, *J* = 7.6 Hz, 4H), 7.18 (s, 2H), 7.15 – 7.05 (m, 3H), 6.92 – 6.83 (m, 3H), 6.06 (d, *J* = 8.5 Hz, 2H). ¹³C NMR (101 MHz, Benzene-*d*₆) δ 143.31, 141.26, 140.36, 138.95, 135.86, 133.48, 133.44, 129.79, 129.70, 129.14, 128.75, 128.70, 127.92, 127.55, 127.36, 127.04, 125.95, 125.47, 124.27, 124.24, 121.78, 121.74, 120.61, 116.57, 110.77, 110.55 (Note that signal to noise was low due to poor solubility). ¹⁹F NMR (376 MHz, C₆D₆) δ -120.27. HRMS (ESI): calculated for M+K C₄₆H₃₀FNS, 686.1715; observed 686.1878.

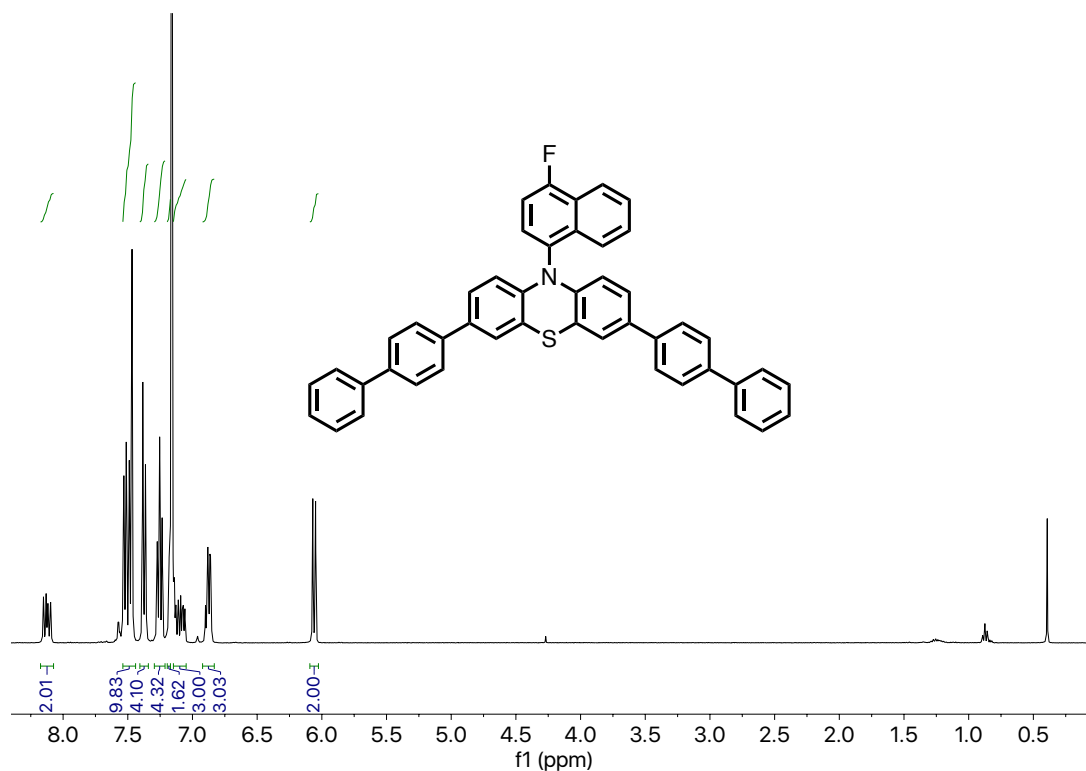


Figure S2.11. ¹H NMR of Fluoro-Naph in benzene-*d*₆.

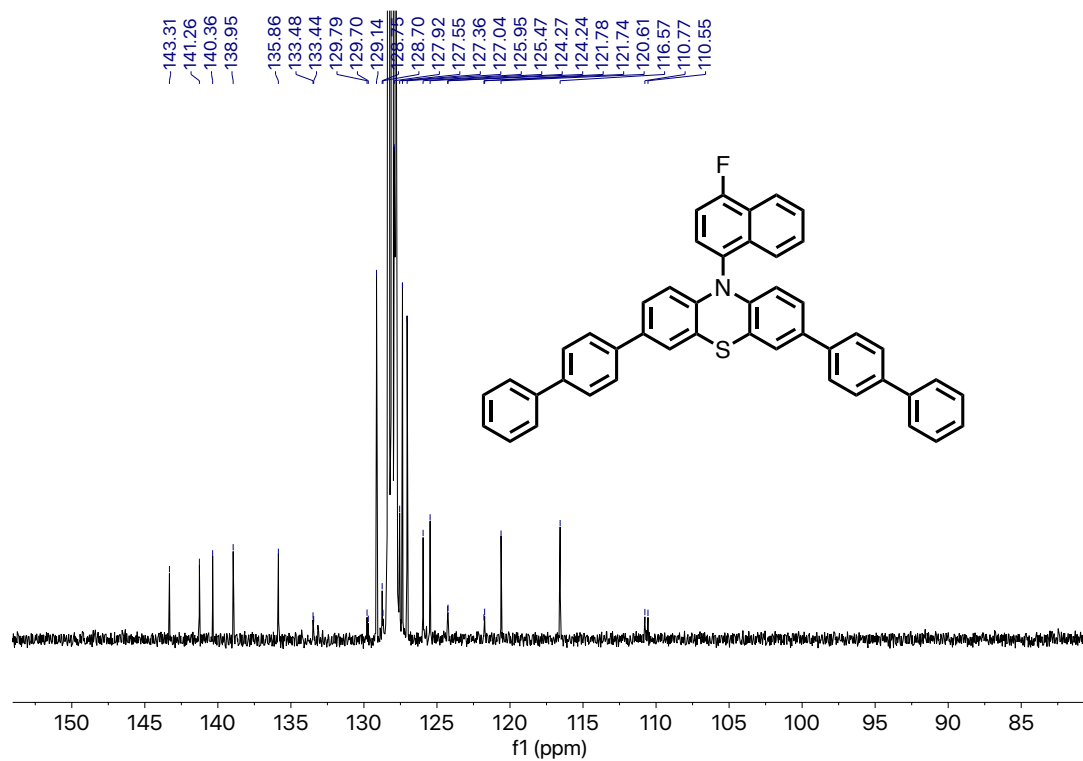


Figure S2.12. ¹³C NMR of Fluoro-Naph in benzene-d₆.

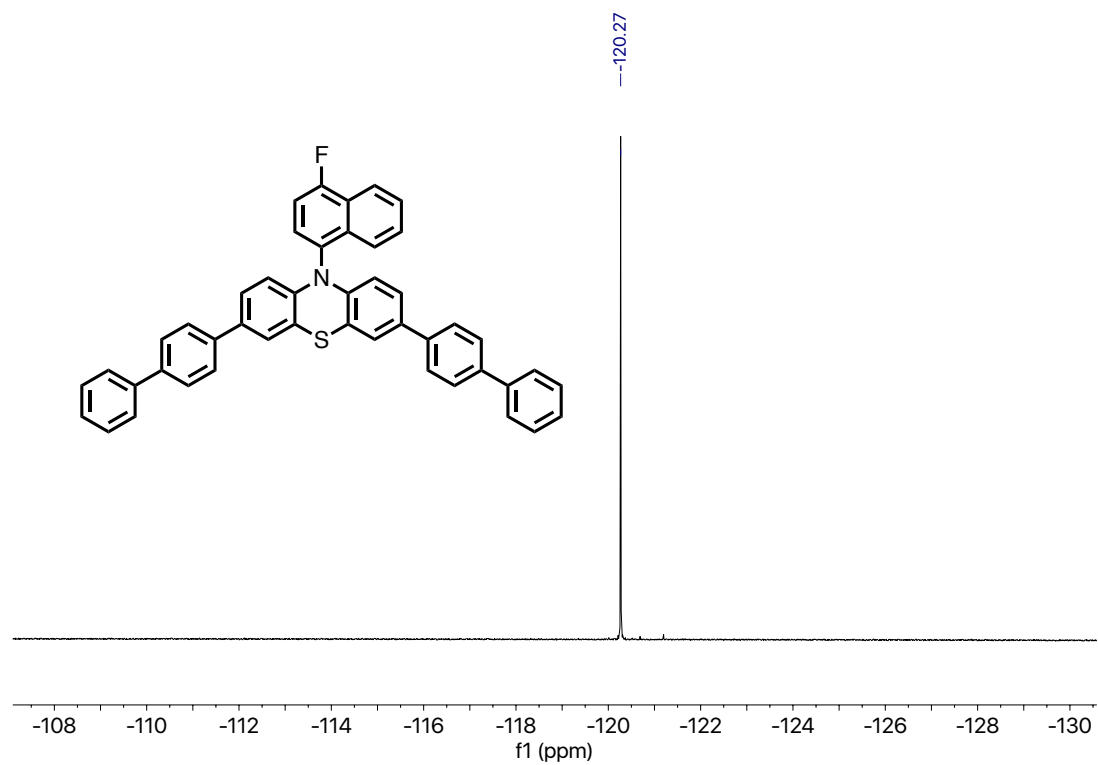


Figure S2.13. ¹⁹F NMR of Fluoro-Naph in benzene-d₆.

Synthesis of Cyano-Naph:

4-(10*H*-Phenothiazin-10-yl)-1-Naphthonitrile

4-Bromo-1-naphthonitrile (1.28 g, 5.50 mmol, 1.10 eq.), phenothiazine (0.996 g, 5.00 mmol, 1.00 eq.) and NaO^tBu (0.720 g, 7.50 mmol, 1.50 eq.) were added to a flame-dried 100 mL storage tube and brought into an N₂ filled glovebox. Pd(dba)₂ (29.0 mg, 50.0 μmol, 2.00 mol%), 1 M P(^tBu)₃ in toluene (40.0 μL, 40.0 μmol, 0.800 mol%) and 15 mL toluene were added to the storage tube. The reaction was brought out of the glovebox, heated to 50 °C for 24 hours, exposed to air, and concentrated to dryness. The crude reaction mixture was re-dissolved in DCM and washed with H₂O then brine and the organics were dried over Na₂SO₄. This was concentrated to minimal solvent layered with MeOH and put in a -25 °C freezer to recrystallize. The crystals that formed were collected by filtration, yielding the target compound as an orange solid (1.41 g, 81% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.46 (d, *J* = 7.6 Hz, 1H), 8.29 (d, *J* = 8.3 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.89 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.75 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.13 (dd, *J* = 7.4, 1.8 Hz, 2H), 6.91 – 6.78 (m, 4H), 6.03 (dd, *J* = 7.9, 1.4 Hz, 2H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 142.59, 141.19, 134.36, 133.96, 130.55, 130.31, 129.33, 127.51, 126.78, 123.62, 123.20, 119.13, 117.16, 115.70, 110.04. HRMS (ESI): calculated for M⁺ C₂₃H₁₄N₂S, 350.0878; observed 350.0883.

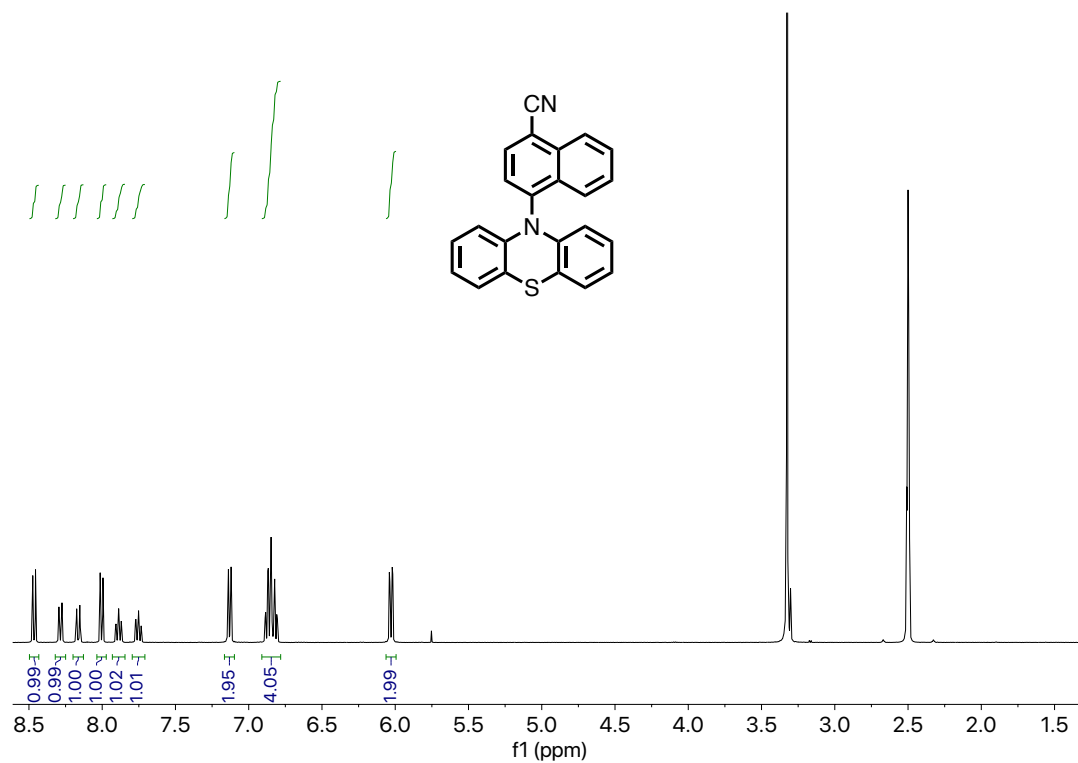


Figure S2.14. ^1H NMR of 4-(10H-Phenothiazin-10-yl)-1-Naphthonitrile in $\text{DMSO}-d_6$.

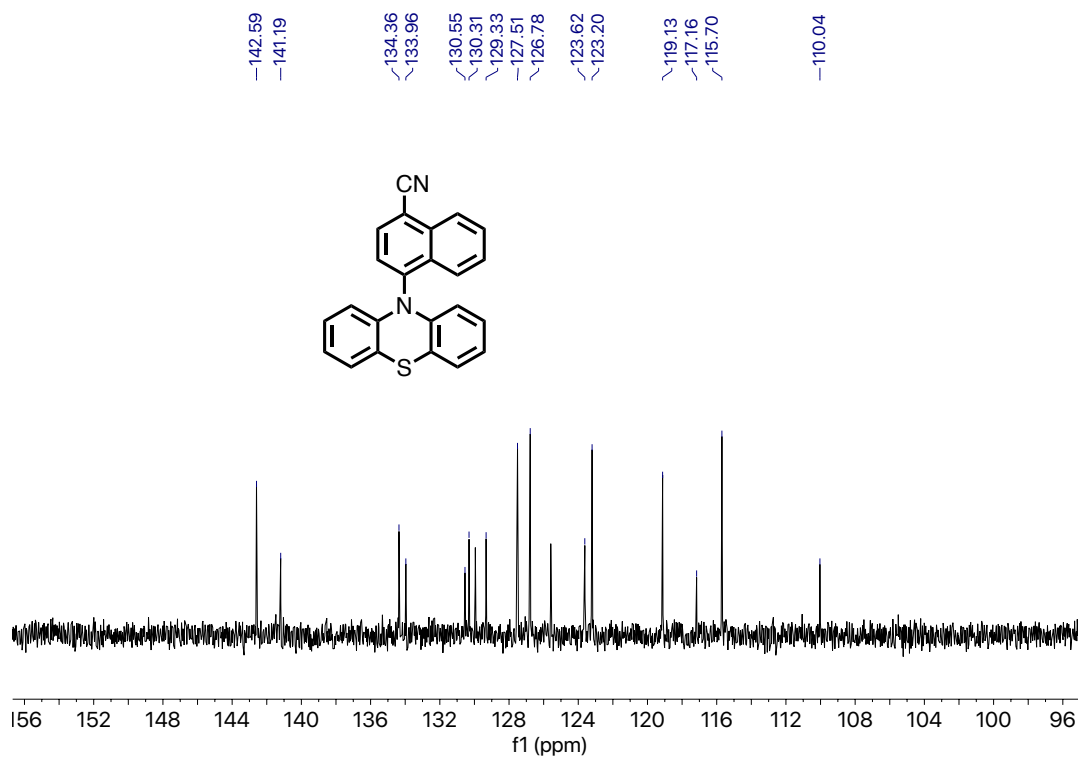


Figure S2.15. ^{13}C NMR of 4-(10H-Phenothiazin-10-yl)-1-Naphthonitrile in $\text{DMSO}-d_6$.

4-(3,7-Dibromo-10*H*-Phenothiazin-10-yl)-1-Naphthonitrile

To a 250 mL round bottom flask wrapped in foil, 4-(10*H*-phenothiazin-10-yl)-1-naphthonitrile (0.700 g, 2.00 mmol, 1.00 eq.) was dissolved in 60 mL 1:1 AcOH:CHCl₃. NBS (0.743 g, 4.20 mmol, 2.10 eq.) was added portion-wise over the course of 20 minutes. The reaction was stirred for 3 hours and the reaction mixture was concentrated to dryness. The crude mixture was re-dissolved in DCM and washed with H₂O and brine. The organics were dried over Na₂SO₄ and concentrated under reduced pressure. Recrystallization twice from DCM:MeOH at -25 °C yielded the target compound as a green solid (0.593 g, 58% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.47 (d, *J* = 7.6 Hz, 1H), 8.29 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.91 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.78 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.37 (d, *J* = 2.3 Hz, 2H), 6.98 (dd, *J* = 8.8, 2.4 Hz, 2H), 5.88 (d, *J* = 8.8 Hz, 2H). ¹³C NMR (101 MHz, Benzene-*d*₆) δ 142.28, 140.84, 134.62, 133.14, 131.11, 130.13, 129.68, 129.44, 129.14, 128.69, 126.48, 123.98, 122.07, 117.10, 117.06, 115.84, 112.02. HRMS (ESI): calculated for M⁺ C₂₃H₁₂Br₂N₂S, 505.9088; observed 505.9082.

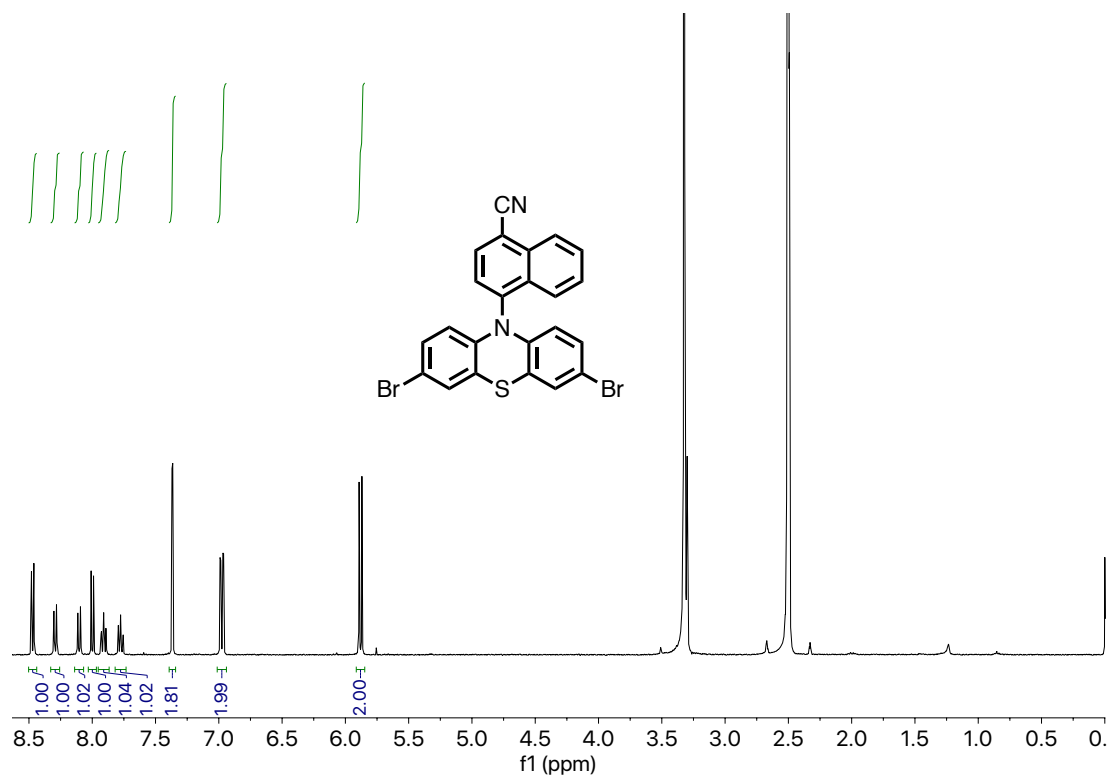


Figure S2.16. ^1H NMR of 4-(3,7-Dibromo-10H-Phenothiazin-10-yl)-1-Naphthonitrile in $\text{DMSO}-d_6$.

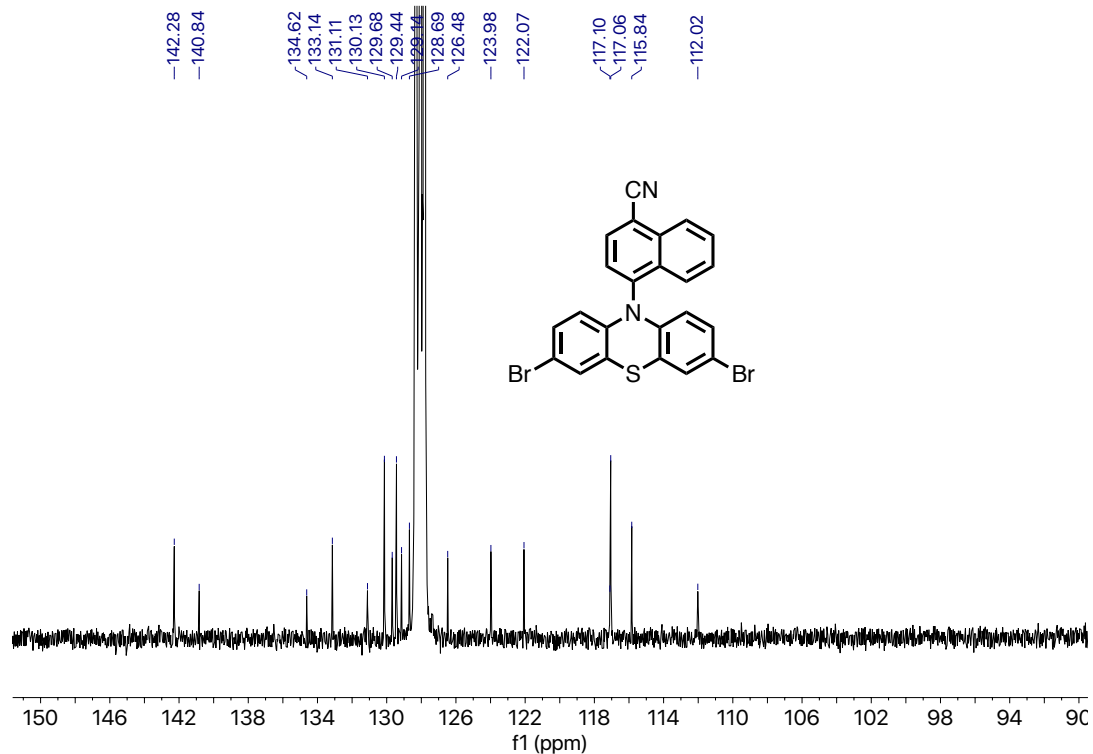


Figure S2.17. ^{13}C NMR of 4-(3,7-Dibromo-10H-Phenothiazin-10-yl)-1-Naphthonitrile in $\text{benzene}-d_6$.

4-(3,7-Di([1,1'-Biphenyl]-4-yl)-10*H*-Phenothiazin-10-yl)-1-Naphthonitrile:

4-(3,7-Dibromo-10*H*-phenothiazin-10-yl)-1-naphthonitrile (0.381 g, 0.750 mmol, 1.00 eq.) and 4-biphenylboronic acid (0.594 g, 3.00 mmol, 4.00 eq) were added to a 100 mL storage tube. After cycling the tube with N₂ and vacuum three times, the storage tube was taken into a nitrogen filled glove box. Pd(PPh₃)₄ (58.0 mg, 50.0 μmol, 5.00 mol%) was added to the storage tube and the mixture was dissolved in 20 mL THF. The storage tube was removed from the glove box and 10 mL of sparged 2 M K₂CO₃ was added. The resultant heterogeneous mixture was heated for 24 hours at 100 °C. After the reaction was complete, the mixture was cooled to room temperature, exposed to oxygen, concentrated under reduced pressure and transferred to a separatory funnel, rinsing with DCM. The aqueous layer was extracted with DCM. The combined organics were washed with H₂O, brine, dried with Na₂SO₄ and concentrated under reduced pressure. The resultant solid was dissolved in toluene, passed through a silica plug and again concentrated under reduced pressure. Recrystallization from DCM:MeOH at -25 °C yielded the desired product as an orange solid (0.384 g, 78% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.53 (d, *J* = 7.6 Hz, 1H), 8.34 (dt, *J* = 8.4, 1.0 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.94 (ddd, *J* = 8.4, 7.0, 1.2 Hz, 1H), 7.82 (ddd, *J* = 8.3, 6.9, 1.1 Hz, 1H), 7.75 – 7.64 (m, 12H), 7.54 (d, *J* = 2.2 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 4H), 7.41 – 7.32 (m, 2H), 7.20 (dd, *J* = 8.6, 2.2 Hz, 2H), 6.06 (d, *J* = 8.6 Hz, 2H). ¹³C NMR (101 MHz, Benzene-*d*₆) δ 142.69, 141.92, 141.17, 140.59, 138.72, 136.31, 134.76, 133.44, 131.78, 129.65, 129.17, 129.13, 129.08, 127.98, 127.65, 127.37, 127.08, 126.47, 125.93, 125.63, 124.63, 120.82, 117.33, 116.42, 111.84. HRMS (APCI): calculated for M+H C₄₇H₃₀N₂S, 655.2208; observed 655.2209.

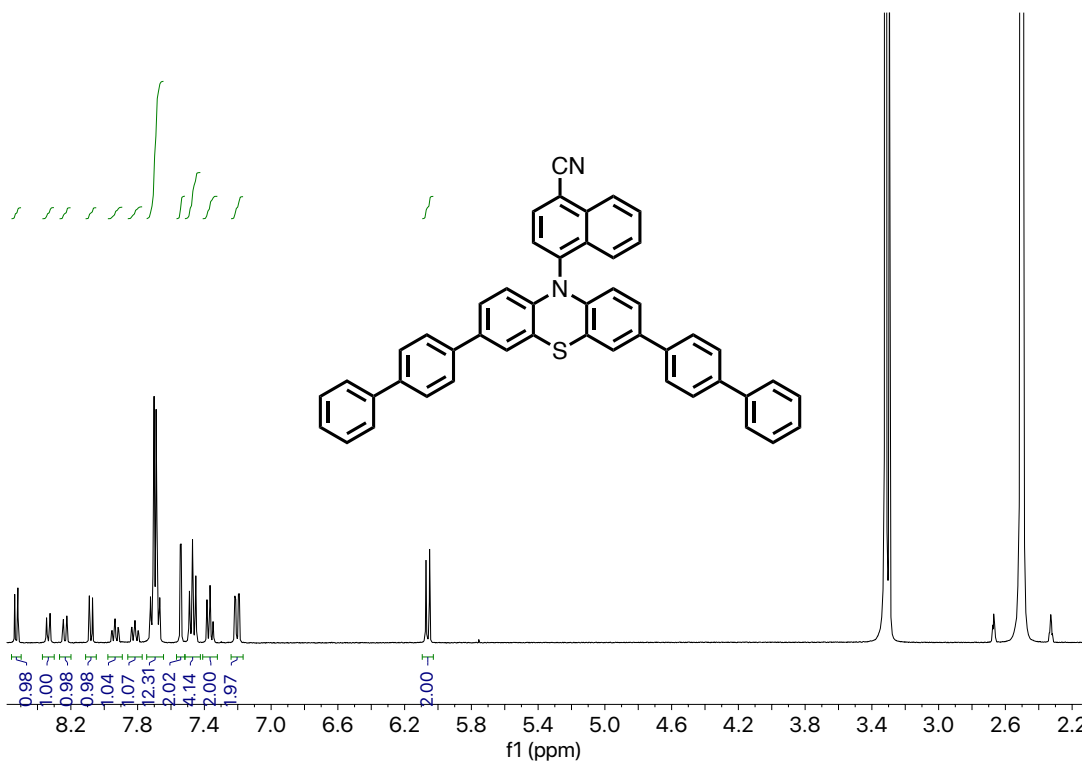


Figure S2.19. ¹H NMR of Cyano-Naph in DMSO-d₆.

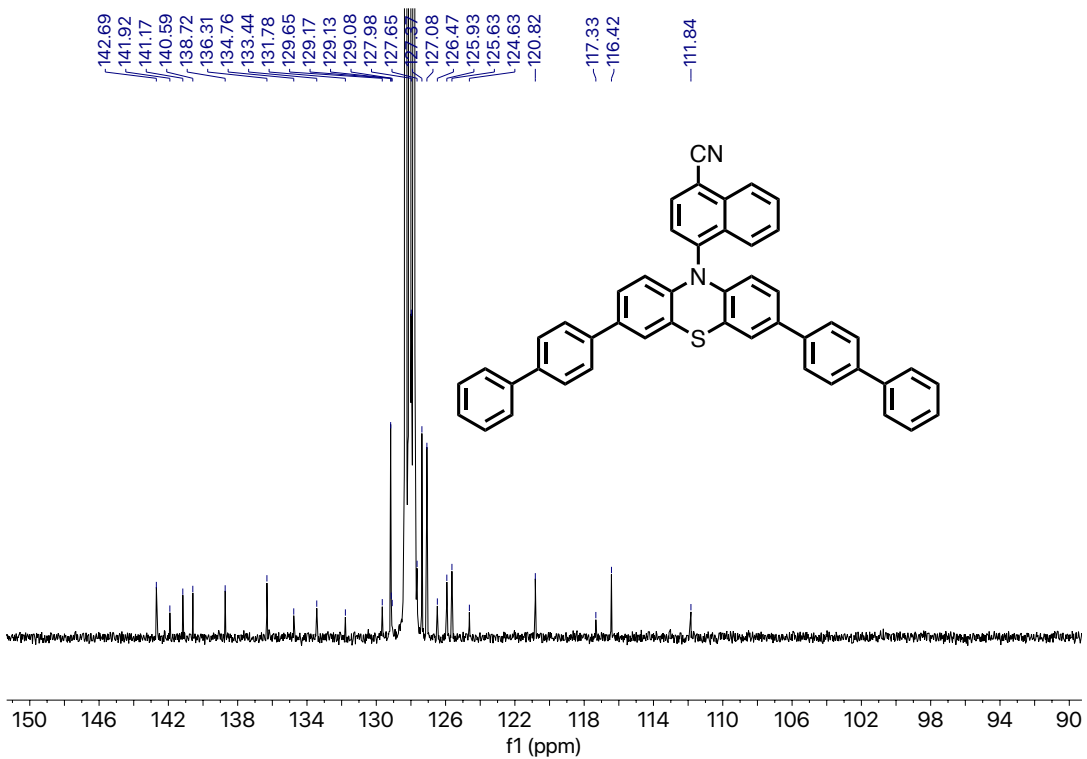
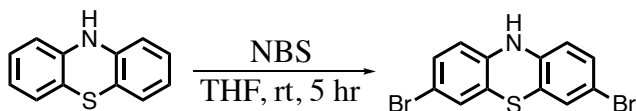


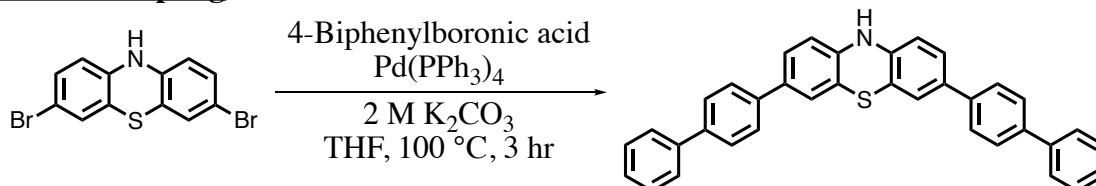
Figure S2.110. ¹³C NMR of Cyano-Naph in benzene-d₆.

Synthesis of Phen

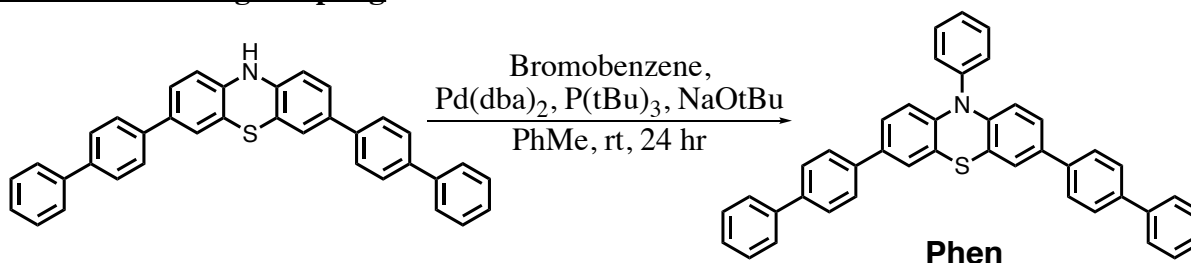
Bromination



Suzuki Coupling



Buchwald Hartwig Coupling



3,7-Dibromo-10*H*-Phenothiazine:

Phenothiazine (1.99 g, 10.0 mmol, 1.00 eq.) was added to a 200 mL schlenk flask equipped with an addition funnel and cycled with N₂ and vacuum 3x. THF (20 mL) was added and the flask was cooled to 0 °C. NBS (3.93 g, 22.0 mmol, 2.20 eq.) was dissolved in 45 mL sparge and stabilized THF and added to the addition funnel. The entire apparatus was covered in foil and the NBS was added at ~1 drop/sec. After addition, the reaction was stirred for 4 hours. The crude reaction mixture was concentrated, re-dissolved in 1:1 EtOAc:hexanes and passed through a silica plug. The solvent was removed under reduced pressure and the solid was re-dissolved in toluene at ~50 °C, cooled and the solid was collected by filtration, yielding the desired compound as a white powder (0.652 g, 18% yield). NMR matched previously reported.²

3,7-Di([1,1'-Biphenyl]-4-yl)-10*H*-Phenothiazine:

3,7-dibromo-10*H*-phenothiazine (0.250 g, 0.700 mmol, 1.00 eq.) and 4-biphenylboronic acid (0.554 g, 2.80 mmol, 4.00 eq) were added to a 100 mL storage tube. After cycling the tube with nitrogen and vacuum three times, the storage tube was taken into a nitrogen filled glove box. Pd(PPh₃)₄ (41.0 mg, 35.0 μmol, 5.00 mol%) was added to the storage tube and the mixture was dissolved in 14 mL THF. The storage tube was removed from the glove box and 7 mL of sparged 2 M K₂CO₃ was added. The resultant heterogeneous mixture was heated for 3 hours at 100 °C. After the reaction was complete, the mixture was cooled to room temperature, exposed to oxygen, and filtered. The solid was washed with H₂O, MeOH, acetone and DCM yielding the desired product as a yellow solid (0.234 g, 66% yield). Due to very poor solubility, carbon NMR was unable to be obtained. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.69 – 7.61 (m, 9H), 7.57 (d, *J* = 8.5 Hz, 4H), 7.46 (t, *J* = 7.6 Hz, 4H), 7.40 (d, *J* = 1.9 Hz, 2H), 7.39 – 7.34 (m, 2H), 7.23 (s, 2H), 7.19 (d, *J* = 1.7 Hz, 2H). Not detected by mass spectrometry.

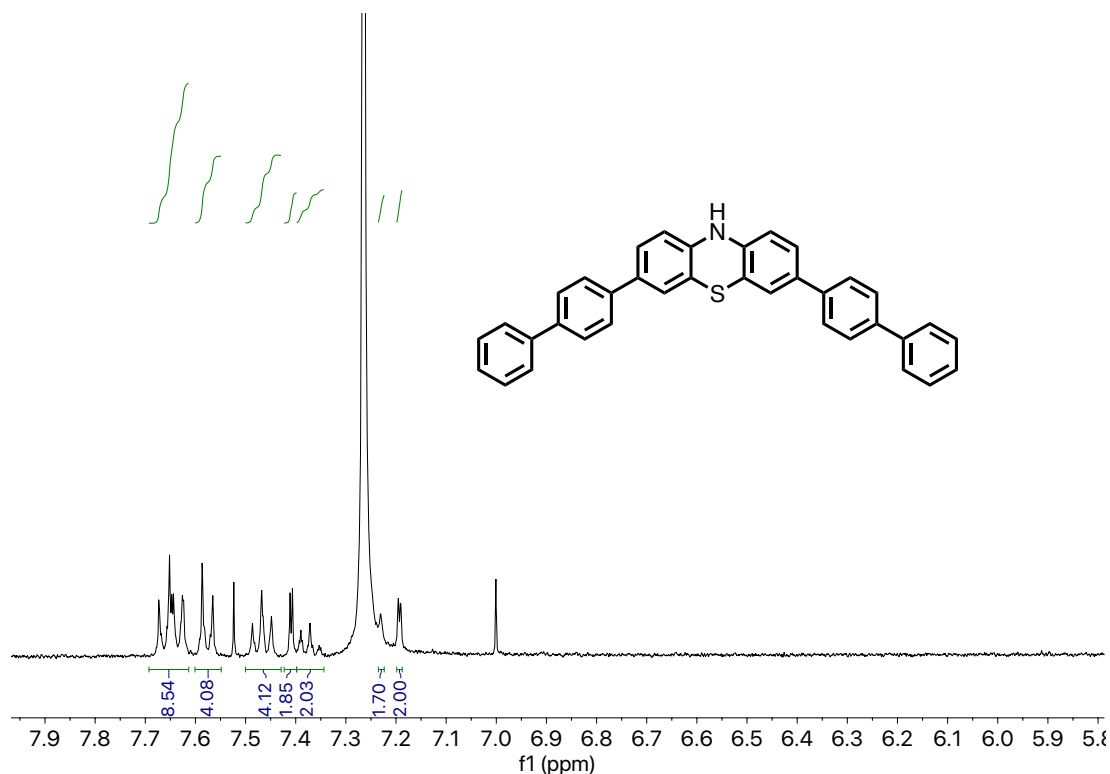


Figure S2.20. ¹H NMR of 3,7-Di([1,1'-Biphenyl]-4-yl)-10H-Phenothiazine in CDCl₃.

3,7-Di([1,1'-Biphenyl]-4-yl)-10-Phenyl-10H-Phenothiazine:

3,7-di([1,1'-biphenyl]-4-yl)-10H-phenothiazine (0.151 g, 0.300 mmol, 1.00 eq.) and NaO^tBu (43.3 mg, 0.450 mmol, 1.50 eq.) were added to a flame-dried 50 mL storage tube, cycled 3x through N₂ and vacuum, and brought into an N₂ filled glovebox. Pd(dba)₂ (8.6 mg, 15.0 μmol, 5.00 mol%), 1 M P(^tBu)₃ in toluene (12.0 μL, 12.0 μmol, 4.00 mol%) and 5 mL toluene were added and the storage tube was brought out of the glove box. Sparged bromobenzene (34.5 μL, 0.330 mmol, 1.10 eq) was added and the reaction mixture was heated at 50 °C for 24 hours. The reaction mixture was diluted with 50 mL toluene and passed through a silica plug. Solvent was removed under reduced pressure and the resulting solid was recrystallized from DCM:MeOH, yielding the desired product as a bright yellow solid (0.109 g, 63% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.78 – 7.66 (m, 14H), 7.63 (d, *J* = 7.4 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.51 – 7.43 (m, 6H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.32 (dd, *J* = 8.4, 2.2 Hz, 2H), 6.19 (d, *J* = 8.5 Hz, 2H). Due to

very poor solubility, carbon NMR was unable to be obtained. HRMS (ESI): calculated for M⁺ C₄₂H₂₉NS, 579.2021; observed 579.2019.

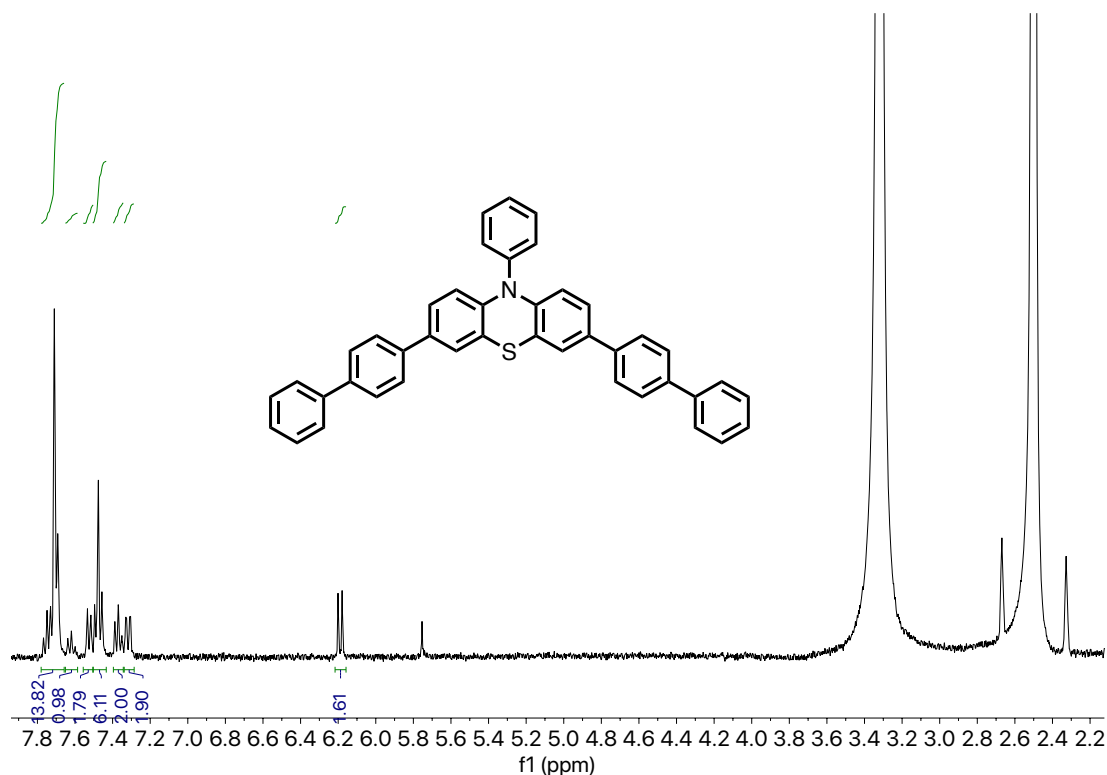


Figure S2.21. ¹H NMR of Phen in DMSO-*d*₆.

2. Photophysical Characterization

2.1. General Information

For steady state experiments, Time Correlated Single Photon Counting (TCSPC) fluorescence lifetime experiments, Nanosecond Transient Absorption (NSTA) experiments, and triplet-triplet energy transfer (TTET) intersystem crossing yield (Φ_{ISC}) experiments, samples were prepared in 1 cm x 1 cm quartz cuvettes with optical densities near or below 0.1 at the excitation wavelength.

All samples used anhydrous *N,N*-dimethylacetamide (DMAc) and were degassed prior to experiments by bubbling with argon for at least 15 minutes, except where otherwise stated. The

anhydrous DMAc was purchased from Sigma Aldrich. Experiments with tetrahydrofuran (THF) and toluene used anhydrous solvent purchased from Sigma Aldrich.

All reported lifetimes and quantum yields with error bounds are the average of at least three independent measurements, and the reported error bounds are 2 times the standard deviation of a set of measurements.

Absorption and Emission Spectra and Emission Quantum Yield

Absorption spectra were measured using an Agilent Cary 60 UV-Vis Spectrophotometer. Emission spectra were measured using an SLM 8000C Spectrofluorometer with the appropriate wavelength-dependent correction applied to the raw data. The quantum yield of emission (Φ_{em}) was determined by the comparative method, using Coumarin 500 in methanol as the standard. In order to isolate the quantum yield of fluorescence (Φ_{fl}) from Φ_{em} , Φ_{em} was measured in the presence of oxygen (ambient air). In order to account for oxygen quenching of the singlet state, the singlet lifetime of the ambient air sample was measured. Then, Φ_{fl} of deaerated samples can be calculated in the following way: $\Phi_{fl} = (\Phi_{em, ambient\ air} * \tau_{singlet, ambient\ air}^{-1}) / \tau_{singlet, deaerated}^{-1}$.

Molar Absorptivity

Molar absorptivities (ϵ) were determined by first preparing 5 solutions of known concentration for each compound in the range of 5 – 50 μ M. This was done by dissolving a known mass (> 5 mg) of compound to a known volume of DMAc (HPLC grade, Sigma Aldrich) and performing subsequent dilutions. Then, the absorbance spectra of these solutions were measured using an Agilent Cary 60 UV-Vis, and the absorbance at the wavelength of maximum absorbance (λ_{max}) was plotted as a function of concentration. For all compounds, these data fit to a linear function ($R^2 \geq 0.9998$), indicating linear Beer-Lambert behavior. Thus, the slopes of these fits were taken as the $\epsilon(\lambda_{max})$ for each compound.

Cyclic Voltammetry (CV)

CV measurements were performed using a 3-electrode technique, which employed a 0.01 M Ag/AgNO₃ reference electrode and a CH Instruments 601C electrochemical analyzer. For both the reference and sample electrodes (platinum working and counter electrodes were used), anhydrous DMAc was used for the solvent and 0.1 M tetrabutylammonium hexafluorophosphate (purchased from Sigma Aldrich) was used as the electrolyte. Potentials versus the standard calomel electrode (SCE) were determined by employing the oxidation of ferrocene as an internal standard and then adding 380 mV.³

Spectroelectrochemical Measurements

Spectroelectrochemistry experiments were conducted using a home-built glass optically transparent thin layer electrode cell with a 0.2 cm path length and a Pt mesh working electrode, a Pt wire counter electrode, and a freshly prepared 0.01 M Ag/AgNO₃ reference electrode which used anhydrous DMAc for the solvent. 0.1 M tetrabutylammonium hexafluorophosphate (TBAPF₆) was used as the electrolyte. The sample was dissolved in anhydrous DMAc, degassed with Ar, then blanketed with Ar for the duration of the experiment. Bulk electrolysis of the sample was performed using an electrochemical analyzer (CH Instruments 601C), and electronic absorption spectra were acquired using a Hewlett Packard diode array UV-vis spectrophotometer (HP8452A).

Time-Correlated Single Photon Counting (TCSPC) and Time-resolved Emission

Time-resolved emission measurements were made using a DeltaFlex Modular Fluorescence Lifetime System from Horiba Scientific. For TCSPC measurements, a Horiba NanoLED-405L was used as the excitation source (402 nm, < 200 ps pulse duration) and emission was detected at magic angle. TCSPC traces were fit to a model of exponentials convoluted with a

Gaussian fit of the instrument response function (FWHM of ~230 ps), with the lowest number of exponentials used that would give a reasonable fit. This always resulted in a fit which required only a single exponential, although an offset was often required to account for phosphorescence when fitting singlet lifetimes.

For longer timescale time-resolved emission measurements ($> \mu\text{s}$), a Horiba SpectraLED ($417 \pm 18 \text{ nm}$) was used as the excitation source. Here, emission traces were fit to a simple single-exponential model.

Nanosecond Transient Absorption (NSTA)

NSTA spectra were acquired using a Edinburgh Instruments LP980KS spectrometer equipped with a Continuum Minilite Nd:YAG Q-switched laser (355 nm) and an Andor iStar ICCD camera.

NSTA lifetime and TTET measurements were made using a previously described home-built setup.⁴ Φ_{ISC} was measured using a TETT method described previously,⁴ with *fac*-Ir(ppy)₃ (purchased from Sigma Aldrich) as the sensitizer.

Femtosecond Transient Absorption (FSTA)

FSTA data were collected using a previously described home-built setup.⁵ Samples were prepared and sealed in a quartz cuvette with a path length of 0.2 cm. Samples were excited at 400 nm and were prepared such that the percent of molecules excited per pulse was kept near or under 5%. FSTA data were fit to an exponential model using an in-house global fitting procedure.

2.2. Oxygen Sensitivity of Steady-state Emission

In order to assess the O₂ sensitivity of the steady-state of **Phen**, **Naph**, **Fluoro-Naph**, and **Cyano-Naph** in DMAc, emission spectra of each species were measured after purging with argon for at least 20 minutes, and, following this, the emission of each sample was measured after being exposed to ambient air. The results, shown in the following figure, demonstrate that **Naph**, and **Fluoro-Naph** (and to some extent, **Phen**) possess different emission profiles under these different conditions, indicating the presence of at least two emitting states with different timescales for emission (i.e., fluorescence and phosphorescence).

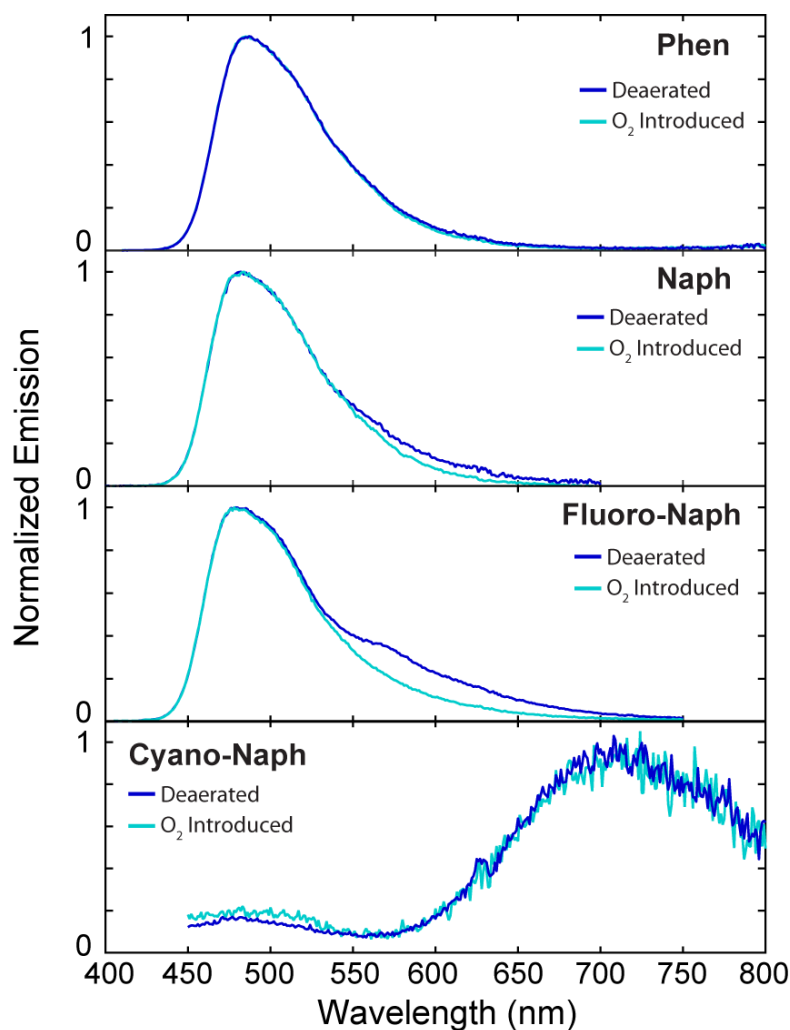


Figure S2.22: Normalized emission spectra of Phen, Naph, Fluoro-Naph, and Cyano-Naph taken in the absence of oxygen and, subsequently, in the presence of oxygen.

2.3. Fluorescence of Naph in Multiple Solvents

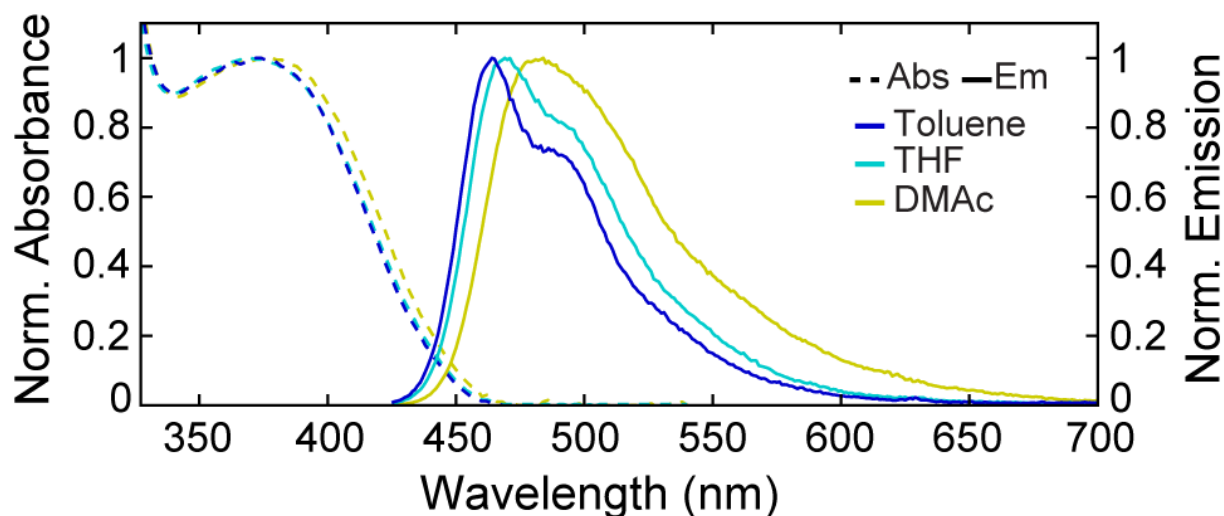


Figure S2.23: Absorbance and fluorescence spectra of Naph in DMAc, THF, and toluene at 20 °C.

2.4. Fitting the Fluorescence Spectra of Phen and Naph

To determine the energy of S_{deloc} , the fluorescence spectra of **Phen** and **Naph** were each fit to a vibronic progression to extract E_0 ,⁶ which is then converted to E_{00} by consideration of the spectral linewidth.⁷ The number of Gaussians used for the fit was determined as the number after which an additional Gaussian would not improve the fit. The fluorescence spectra of **Fluoro-Naph** and **Cyano-Naph** could not be fit to vibronic progressions. For **Fluoro-Naph**, this is presumably due to the presence of two distinct emitting state resulting from the more significant contribution of $S_{\text{CT-Naph}}$ emission. For **Cyano-Naph**, this is due to the fact that emission from $S_{\text{CT-Naph}}$ is so broad that vibronic peaks cannot be distinguished.

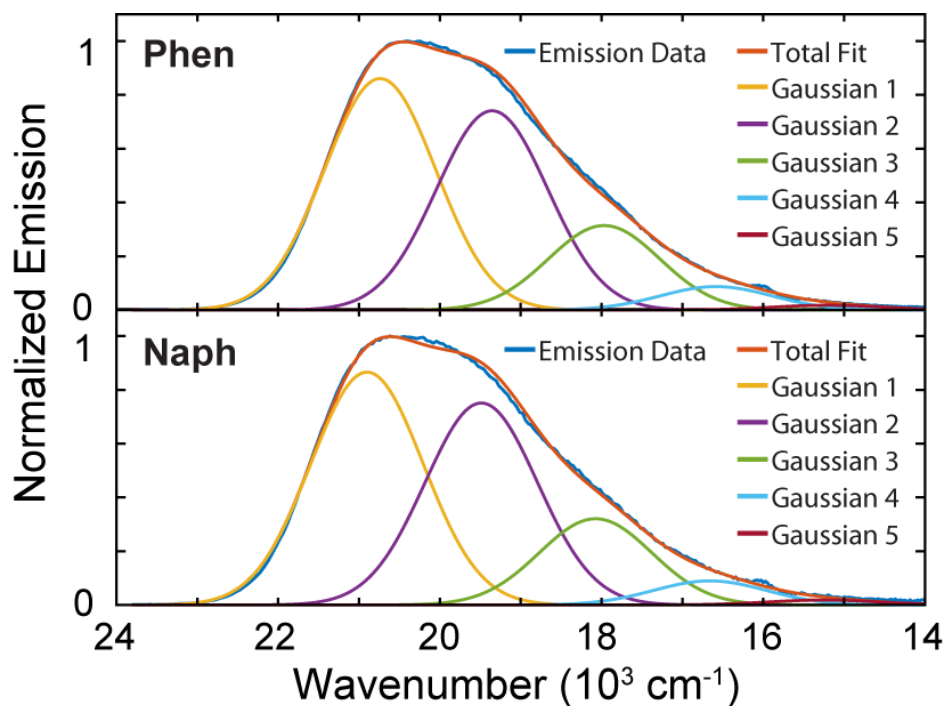


Figure S2.24: Fluorescence spectra and fits of Phen and Naph in DMAc at 20 °C.

Table S2.1. Fit parameters to the fluorescence spectra of Phen and Naph in DMAc at 20 °C.

	Phen	Naph
E_{00} (eV)	2.713	2.736
E_0 (eV)	2.571	2.591
ω (cm ⁻¹)	1385	1413
FWHM (cm ⁻¹)	1622	1637
S	1.059	1.070

2.5. Assignment of S_{deloc}

The assignment of the fluorescent state of **Phen** and **Naph** is aided by the context of the phenoxazine analogues to **Phen**, which have been characterized in previous works.^{8,9} The chemical analogues discussed in this section are shown and labeled in Figure S2.25.

The direct phenoxazine analogue to **Phen** (called **1**) possesses distinct fluorescence behavior from **Phen** and **Naph**. **1** has a higher degree of solvatochromism and a broader

fluorescence profile—both of which indicate a more polar S_1 . The assignment of the S_1 of **1** was additionally aided by comparison its fluorescence behavior to that of a chemical analogue, **1a**, which possesses only a single biphenyl substituent. Along with the broad, solvatochromic fluorescence of **1**, the similarity of the fluorescence behavior of **1** and **1a** led to the assignment of the S_1 of **1** as $S_{CT-Biph}$, in which charge is transferred from the phenoxazine moiety to a single biphenyl substituent.

In contrast to **1**, a separate phenoxazine compound analogue to **Phen** (called **1'**) exhibits similar emission behavior to that of **Phen** and **Naph**. **1'** possesses a more structured fluorescence profile than **1** and is only weakly solvatochromic. As with **1**, the fluorescence of **1'** was characterized by comparison to a chemical analogue, **1a'**, in which one of the phenyl substituents is absent. The fluorescence behavior of **1a'** was found to be distinct from **1'**, being broader and more highly solvatochromic. This difference between **1'** and **1a'** indicates that while the S_1 of **1a'** is a CT state (from the phenoxazine to a single phenyl substituent), **1'** possesses a less polar S_1 state which involves both phenyl substituents. Consequently, the S_1 of **1'** has been assigned as S_{deloc} . The similarity of the fluorescence behavior of **Phen** and **Naph** to **1'**, and the contrast of **Phen** and **Naph**'s fluorescence behavior with **1**, leads to the assignment of the S_1 of **Phen** and **Naph** as S_{deloc} .

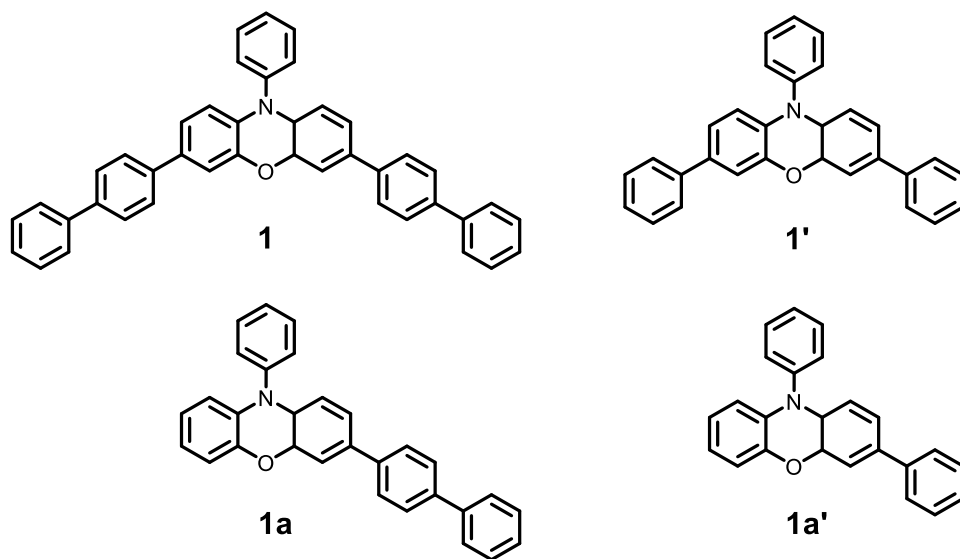


Figure S2.25. The phenoxazine analogues discussed in this section and their labels.

2.6. TCSPC Kinetic Traces

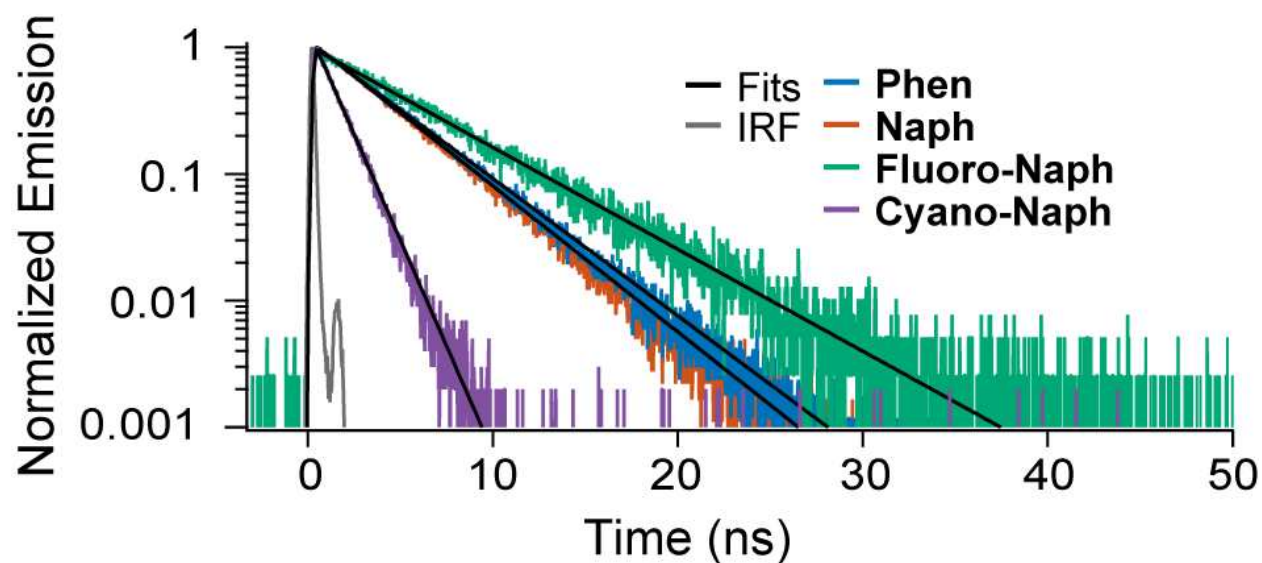


Figure S2.26: TCSPC traces of all four molecules in this study and their respective single-exponential fits convolved with Gaussian fit of IRF. These traces were collected at the wavelength of maximum fluorescence for all compounds but Fluoro-Naph. Fluoro-Naph data was collected at 650 nm due to an ultrafast component observed at lower wavelengths (see next figure).

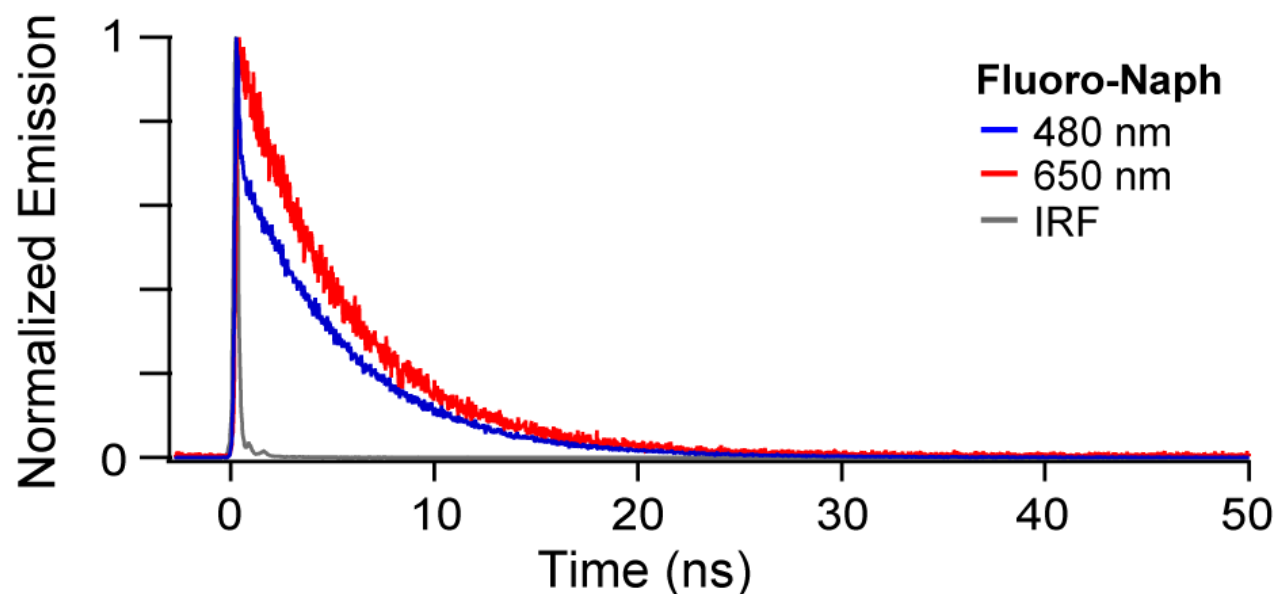


Figure S2.27: TCSPC traces of Fluoro-Naph at 480 and 650 nm. The early emission component (IRF limited) at lower wavelengths indicates emission from a transiently occupied higher-lying excited state than the S_1 . While FSTA data suggests that similar relaxation dynamics should be present for Phen and Naph as well, the greater emissivity of the S_1 states of those compounds likely masks the observation of such dynamics via TCSPC.

2.7. Phosphorescence Lifetimes

Time-resolved emission traces of the phosphorescence of **Phen**, **Naph**, and **Fluoro-Naph** in RT anhydrous DMAc were measured. However, the lifetimes of each compound were not found to be reproducible between measurements of independently prepared samples. This may be due to variable concentrations of oxygen, to which the triplet lifetimes of the compounds are extremely sensitive, owing to their long lifetimes. While preparation of samples in a glovebox utilizing ultra-high-purity nitrogen resulted in relatively consistent lifetime measurements among the compounds (~ 15 ms), sample preparation which employed purging with argon resulted in longer lifetimes than 15 ms in multiple instances. However, these lifetimes were not readily reproducible. Therefore, the triplet lifetimes of **Phen**, **Naph**, and **Fluoro-Naph** are uncertain and are reported as greater than 15 ms.

2.8. Phosphorescence Spectra and Spectral Fitting

The phosphorescence spectra of **Phen**, **Naph**, and **Fluoro-Naph** were measured by collecting time-resolved emission traces at multiple wavelengths for a fixed time duration at each wavelength. The individual traces were integrated starting at a sufficient delay (on the order of milliseconds) in order to generate phosphorescence spectra. We note that a slight amount of fluorescence remains, due to triplet-triplet annihilation (TTA), which results in emission features which extend to ~ 525 nm. These spectra were then corrected to account for variable PMT response at different wavelengths. The corrected phosphorescence spectra were trimmed slightly to exclude fluorescence resulting from TTA and then fit to a vibronic progression in a manner similar to the fitting of fluorescence spectra described earlier.

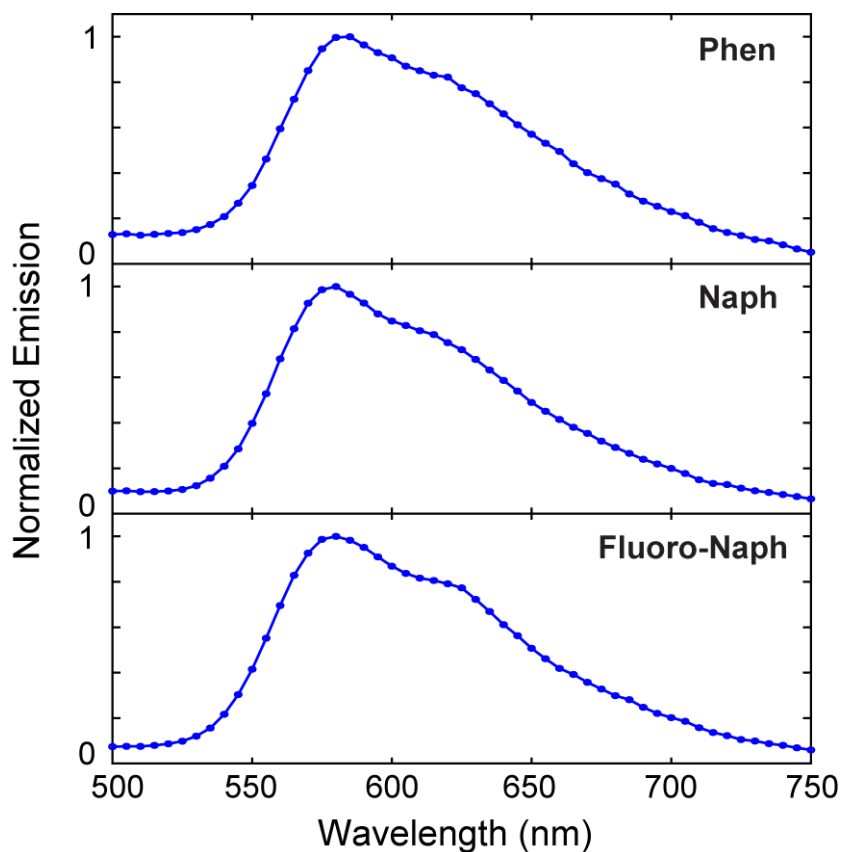


Figure S2.28: Phosphorescence spectra of Phen, Naph and Fluoro-Naph in RT DMAc.

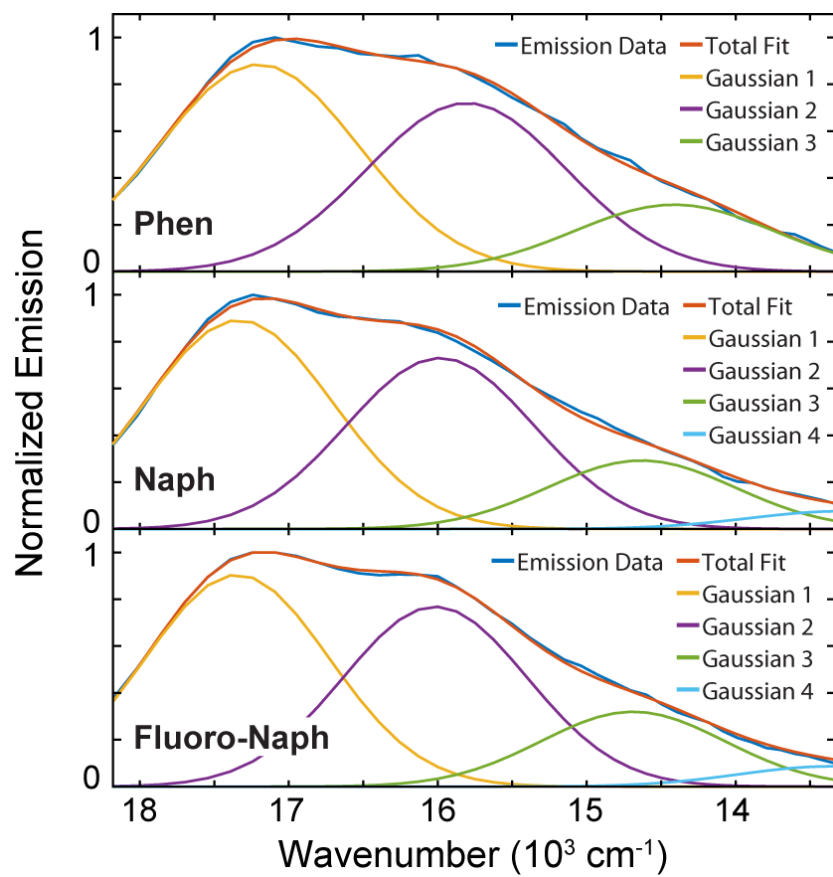


Figure S2.29: Phosphorescence spectra and fits of Phen, Naph and Fluoro-Naph in RT DMAc.

Table S2.2. Fit parameters to the phosphorescence spectra of Phen, Naph, and Fluoro-Naph in RT DMAc.

	Phen	Naph	Fluoro-Naph
E_{00} (eV)	2.267	2.268	2.264
E_0 (eV)	2.133	2.149	2.151
ω (cm ⁻¹)	1394	1351	1329
FWHM (cm ⁻¹)	1580	1482	1453
S	1.048	1.044	1.079

2.9. Early FSTA Dynamics in Naph

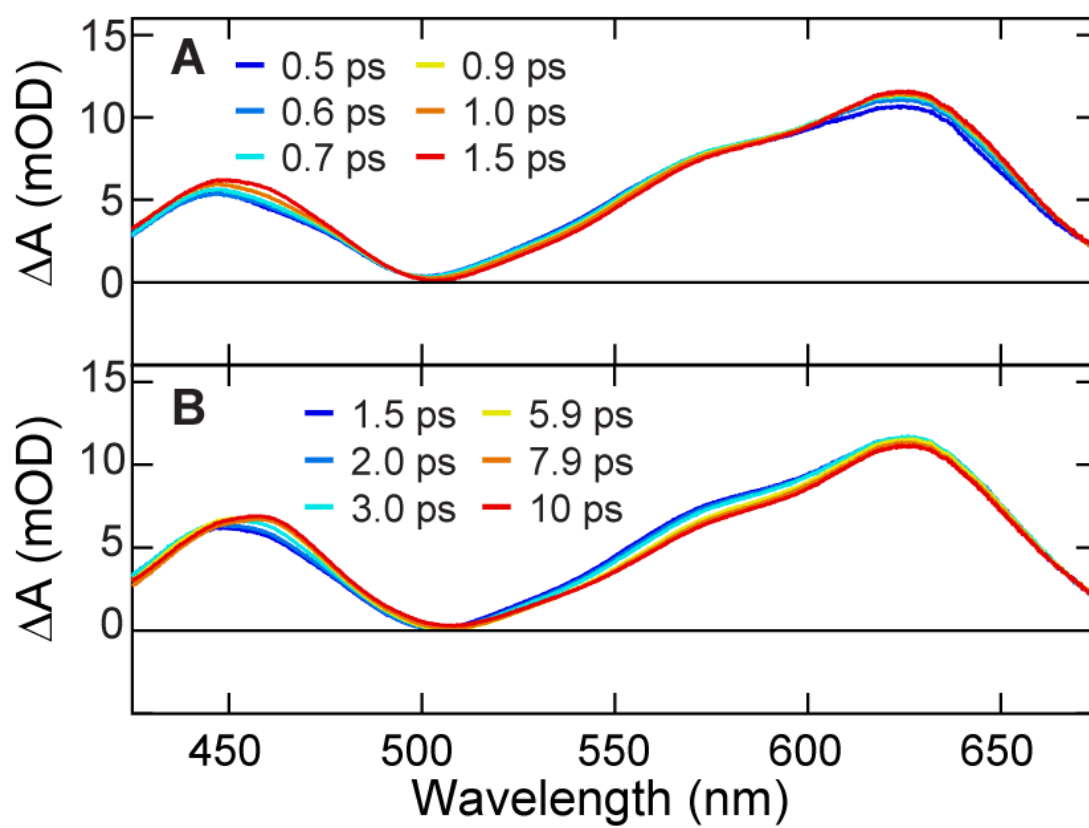


Figure S2.30: Early FSTA dynamics of Naph in RT DMAc.

2.10. Cyclic Voltammetry

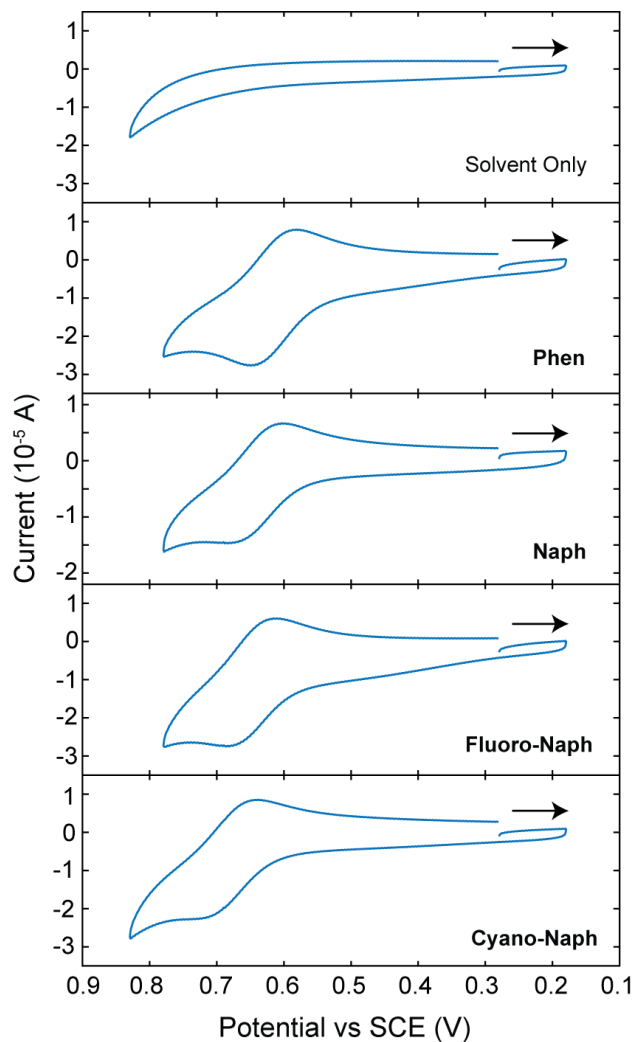


Figure S2.31. Cyclic voltammograms of Phen, Naph, Fluoro-Naph, and Cyano-Naph, taken at a scan rate of 50 mV/s. Arrows indicate the initial scan direction.

Table S2.3. Electrochemical data for compounds (C), values in Volts vs SCE.

	$E_{1/2}(C^{•+}/C)$	$\Delta E_p(C^{•+}/C)$
Phen	0.61	0.073
Naph	0.64	0.074
Fluoro-Naph	0.65	0.076
Cyano-Naph	0.68	0.085

2.11. Spectroelectrochemistry of Naph

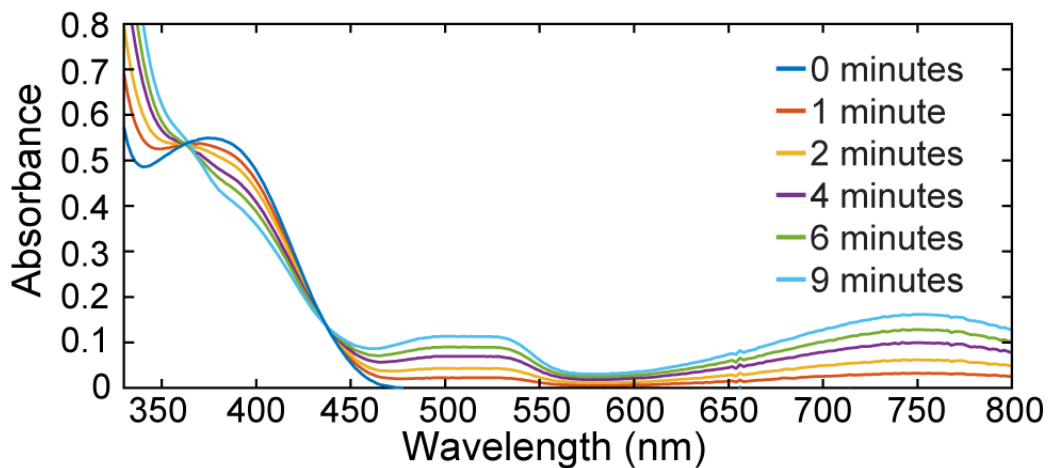


Figure S2.32. Spectroelectrochemical data of Naph at various time delays following the onset of bulk electrolysis at a potential of 0.75 V vs SCE, in RT DMAc.

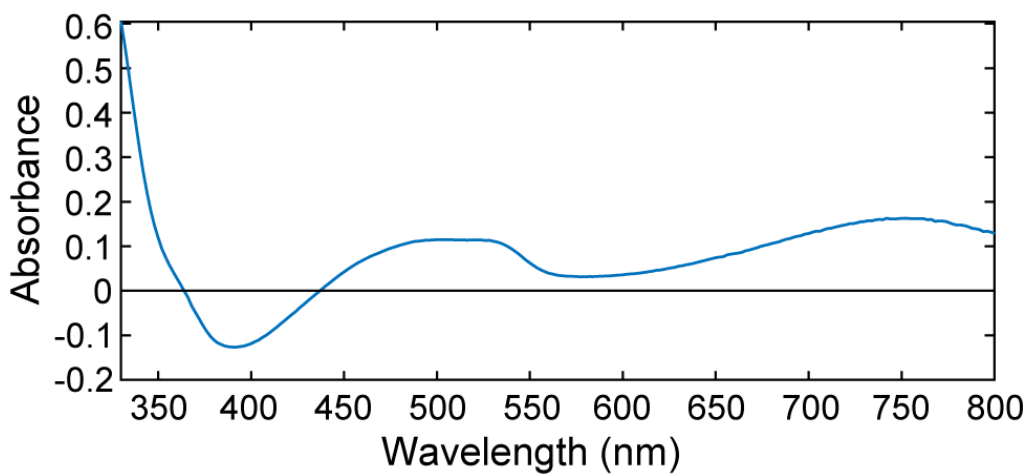


Figure S2.33: Oxidative difference spectrum of Naph, generated by subtracting the ground state spectrum from the spectrum acquired at the latest time delay (9 minutes).

2.12. Simulation of Late-time FSTA Spectrum of Naph

The late-time FSTA spectrum of **Naph** was simulated using the following: an early-time FSTA spectrum of **Naph** (10 ps), the oxidative difference spectrum of **Naph**, and the absorption spectrum of a naphthyl radical anion⁸ (Figure S2.34). The former spectrum is used to account for the remaining S_{deloc} at late times, and the latter two spectra are used to simulate $S_{\text{CT-Naph}}$. The 10 ps spectrum, in particular, is chosen to reflect the relaxed S_{deloc} but is sufficiently early such that no significant $S_{\text{CT-Naph}}$ formation has taken place (see Figure S2.30). The ability to model the late-time spectrum with these three basis spectra is strong evidence that the S_1 of **Naph** consists of an equilibrium between S_{deloc} and $S_{\text{CT-Naph}}$. Furthermore, this modelling can be used to estimate the relative concentrations of each species in equilibrium and therefore the equilibrium constant. This is done in the following way:

Since the 10 ps spectrum follows the cooling of S_{deloc} but precedes significant $S_{\text{CT-Naph}}$ formation, ΔA at 10 ps may be taken as corresponding to the initial concentration of S_{deloc} . Between 10 ps and 151 ps, the ΔA at the λ_{max} of S_{deloc} (625 nm) falls from 11.1 mOD to 7.4 mOD. If no other features grew in during this time, this would indicate a ~67% decrease in S_{deloc} concentration. However, $S_{\text{CT-Naph}}$ is formed during this time, and this new state possesses ΔA features at 625 nm. To quantify how significant this contribution from $S_{\text{CT-Naph}}$ is, we can monitor the growth of $S_{\text{CT-Naph}}$ features in a region in which S_{deloc} has a very low ΔA (e.g., 505 nm). Between 10 ps and 151 ps, the ΔA at 505 nm grows by 1.76 mOD. Due to the goodness fit of the modeled FSTA with the 151 ps spectrum, the spectrum of $S_{\text{CT-Naph}}$ is considered to be well defined. Using the spectrum of $S_{\text{CT-Naph}}$, it is determined that a 1.76 mOD increase at 505 nm corresponds to a 0.91 mOD increase at 625 nm. With this taken into account, we see that the ΔA signal, which consists of a contribution from S_{deloc} drops, from 11.1 mOD to 6.5 mOD between 10 ps to 151 ps. This corresponds to a drop

in S_{deloc} concentration to $\sim 59\%$ of the initial concentration. As there is no significant ground-state recovery on this timescale, it therefore is inferred that $S_{\text{CT-Naph}}$ constitutes 41% of the excited state population. This corresponds to an equilibrium constant of 0.695, which in turn, at RT (22.2 °C, in this instance) corresponds to an energy difference of ~ 9 meV.

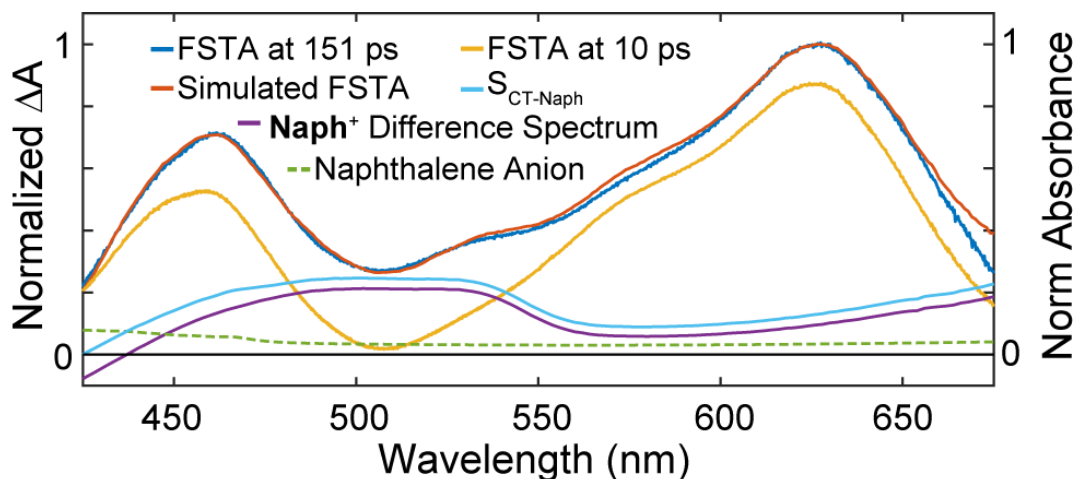


Figure S2.34: Observed and simulated late-time FSTA spectra of Naph, with the redox-derived data and early-time FSTA spectrum used for simulation. $S_{\text{CT-Naph}}$ consists of ‘Naph⁺ Difference spectrum’ + ‘Naphthalene Anion’. Solid and dashed lines refer to ΔA and absorbance spectra, respectively.

2.13. Comparing k_{ISC} of Phenothiazine and Phenoxazine Analogues

The direct phenoxazine analogue to **Phen** (**1**, in Figure S2.25) has a k_{ISC} value of 3.8×10^7 s⁻¹,⁸ which is less than half that of **Phen** despite its greater driving force for ISC (~ 0.7 eV⁹ for **1** versus 0.45 eV for **Phen**). However, ISC for the phenoxazine analogue to **Phen** represents a different electronic transition than for **Phen**, as the two compounds have S_1 states of different electronic character. A more suitable comparison for **Phen** may be the phenoxazine analogue to **Phen** in which the biphenyl substituents have been replaced with phenyl substituents (**1'**, in Figure S2.25). For this second analogue, as with **Phen**, ISC consists of a transition from S_{deloc} to a T_1 which consists of a core-localized (i.e., involving the 3- or 7-substituent) CT state. This second analogue has a k_{ISC} value of 9.3×10^7 ,⁹ which is comparable to **Phen**. However, the driving force for ISC is higher for the phenoxazine analogue (0.74 eV⁹) relative to **Phen** (0.45 eV). These results

indicate that there may be higher spin-orbit coupling for **Phen**, arising from the heavy atom effect, but that competing effects which lower the driving force for ISC cancel out this spin-orbit coupling advantage.

The direct phenoxazine analogue to **Naph** (not shown in Figure S25) has a k_{ISC} value of $1.8 \times 10^8 \text{ s}^{-1}$.⁸ ISC for this analogue consists of a comparable electronic transition to that of **Fluoro-Naph** (i.e., $S_{\text{CT-Naph}} \rightarrow T_{\text{CT-Biph}}$), and both compounds possess highly similar k_{ISC} values. However, the driving force for ISC is higher for the phenoxazine analogue ($\sim 0.6 \text{ eV}$)⁹ than for **Fluoro-Naph** (0.47 eV). Similar to **Phen**, these results suggest the possibility of a higher spin-orbit coupling for **Fluoro-Naph** but that a lower driving force for ISC cancels out this advantage.

2.14. Computed Nuclear Geometries

All calculations utilized the GAUSSIAN 16 Revision A.03 computational chemistry package.¹⁰ All coordinates in Tables S2.5 – S2.12 are reported in Angstrom in the XYZ format. Lowest energy singlet state and triplet state geometries, as well as triplet energies (E_{T1}), of all compounds were computed at the uM06/6-31+g(d,p)/CPCM-n,n-dimethylacetamide level of theory. E_{T1} was calculated as the difference in energy (not zero-point energy or thermally corrected) between the lowest energy singlet and lowest energy triplet states.

Table S2.4. Computed Triplet Energies

	E_{T1} (eV)
Phen	2.34
Naph	2.34
Fluoro-Naph	2.40
Cyano-Naph	2.03

Table S2.5. Computed lowest energy singlet state of Phen

C	3.7090950	0.4719000	0.1281340
C	2.5526770	-0.1479640	0.6167860
C	1.3498420	0.5393640	0.7226140
C	1.2357900	1.8707760	0.2887140
C	2.3919910	2.4908000	-0.2004200
C	3.6005650	1.8088070	-0.2658290
C	-1.2257960	1.8693180	0.2749820
C	-1.3469790	0.5433180	0.7218800
C	-2.5493870	-0.1439380	0.6072610
H	-2.5849140	-1.1839500	0.9290960
C	-3.6982290	0.4710410	0.0953570
C	-3.5818800	1.8021000	-0.3158910
C	-2.3735600	2.4836470	-0.2406770
H	2.5950640	-1.1773220	0.9709470
H	2.3534560	3.5224770	-0.5365330
H	4.4681070	2.3284290	-0.6671330
H	-4.4546340	2.3323960	-0.6910780
H	-2.3334500	3.5173660	-0.5704330
C	0.0049180	3.9619190	0.0766530
C	-0.0064440	4.8644460	1.1349400
C	0.0150120	4.4173630	-1.2417190
C	-0.0072880	6.2339660	0.8740290
H	-0.0145430	4.4851630	2.1546110
C	0.0141950	5.7843900	-1.4990620
H	0.0235610	3.6942100	-2.0561270
C	0.0029720	6.6933350	-0.4407730
H	-0.0160610	6.9410520	1.6996720
H	0.0220950	6.1411900	-2.5258830
H	0.0022490	7.7614550	-0.6431420
C	-4.9798820	-0.2546730	0.0072450
C	-5.3383470	-1.2151600	0.9628030
C	-5.8838890	-0.0030980	-1.0338160
C	-6.5483970	-1.8918350	0.8826790
H	-4.6762000	-1.4132890	1.8036910
C	-7.0945790	-0.6781750	-1.1121860
H	-5.6235910	0.7110990	-1.8128120
C	-7.4541990	-1.6363910	-0.1551520
H	-6.8084630	-2.6074390	1.6605590
H	-7.7593750	-0.4789480	-1.9507360
C	4.9878190	-0.2581690	0.0374480
C	5.0238300	-1.6272350	-0.2594400
C	6.2102940	0.3963740	0.2407240
C	6.2292820	-2.3105920	-0.3530570
H	4.0957330	-2.1613310	-0.4548540
C	7.4151300	-0.2868620	0.1453360

H	6.2193190	1.4512740	0.5084430
C	7.4516260	-1.6549330	-0.1552740
H	6.2206660	-3.3661480	-0.6184890
H	8.3436490	0.2469190	0.3391150
C	-8.7460300	-2.3487640	-0.2378310
C	-9.8951760	-1.6973740	-0.7070140
C	-8.8559330	-3.6912790	0.1502020
C	-11.1129150	-2.3654170	-0.7872100
H	-9.8398270	-0.6479670	-0.9909370
C	-10.0736600	-4.3599920	0.0715550
H	-7.9723200	-4.2248780	0.4959590
C	-11.2078830	-3.7003060	-0.3980510
H	-11.9933530	-1.8379500	-1.1470460
H	-10.1342440	-5.4039970	0.3702950
H	-12.1593830	-4.2228670	-0.4601100
C	8.7356930	-2.3780930	-0.2629520
C	9.8732980	-1.7454950	-0.7833470
C	8.8496980	-3.7127150	0.1505630
C	11.0841290	-2.4229350	-0.8857180
H	9.8035060	-0.7172400	-1.1336850
C	10.0597610	-4.3917810	0.0468500
H	7.9864600	-4.2183490	0.5796880
C	11.1830110	-3.7498990	-0.4713000
H	11.9518900	-1.9143480	-1.2994670
H	10.1271940	-5.4245890	0.3809680
H	12.1288600	-4.2801710	-0.5516600
N	0.0045730	2.5552690	0.3649190
S	-0.0002810	-0.2448670	1.5676530

Table S2.6. Computed lowest energy triplet state of Phen

C	-3.8187060	0.3706400	-0.0546250
C	-2.6025490	-0.3670890	-0.0738520
C	-1.3654910	0.2311660	-0.0900400
C	-1.2272560	1.6703590	-0.0878700
C	-2.4367580	2.4188190	-0.0866850
C	-3.6618800	1.8188670	-0.0722480
C	1.2440900	1.6703110	-0.0751250
C	1.3727490	0.2602480	-0.0980390
C	2.6346510	-0.3371670	-0.0872500
H	2.6864300	-1.4252630	-0.0737010
C	3.8076240	0.4118450	-0.0555670
C	3.6737400	1.8181130	-0.0365430
C	2.4388620	2.4255290	-0.0468030
H	-2.6292680	-1.4546870	-0.0714620
H	-2.3904260	3.5040250	-0.0985030
H	-4.5370350	2.4603640	-0.0795600
H	4.5604940	2.4472190	-0.0399400
H	2.3882820	3.5097970	-0.0429070
C	0.0048710	3.7429220	-0.0306710
C	0.0189710	4.4636560	-1.2189350
C	-0.0164710	4.3784830	1.2052700
C	0.0142360	5.8552830	-1.1653030
H	0.0338680	3.9328880	-2.1688160
C	-0.0209600	5.7698480	1.2507120
H	-0.0289850	3.7815780	2.1151080
C	-0.0056230	6.5063910	0.0670330
H	0.0255070	6.4303510	-2.0873740
H	-0.0368350	6.2783360	2.2110400
H	-0.0093140	7.5926520	0.1051970
C	5.1295080	-0.2336300	-0.0370250
C	5.3465900	-1.4725260	-0.6587890
C	6.2200250	0.3692150	0.6077170
C	6.5933020	-2.0808620	-0.6323380
H	4.5323260	-1.9629780	-1.1886270
C	7.4665810	-0.2403790	0.6330730
H	6.0897940	1.3229970	1.1150640
C	7.6818410	-1.4792710	0.0143610
H	6.7197380	-3.0492660	-1.1127330
H	8.2923310	0.2640830	1.1313200
C	-5.0968920	-0.2559100	-0.0218540
C	-5.2598300	-1.6759770	-0.0370490
C	-6.3104800	0.4973970	0.0301350
C	-6.4995210	-2.2706920	-0.0024060
H	-4.3893520	-2.3246340	-0.0933660
C	-7.5472830	-0.1092240	0.0603460

H	-6.2781460	1.5829140	0.0650420
C	-7.6963650	-1.5142250	0.0460120
H	-6.5521300	-3.3571930	-0.0446570
H	-8.4300650	0.5242080	0.1282920
C	9.0084510	-2.1280310	0.0406360
C	9.8438970	-2.0146770	1.1608800
C	9.4650730	-2.8748450	-1.0544780
C	11.0926530	-2.6277120	1.1855400
H	9.5020020	-1.4601560	2.0329500
C	10.7133120	-3.4886590	-1.0303410
H	8.8451790	-2.9568050	-1.9454350
C	11.5333270	-3.3680560	0.0900950
H	11.7205940	-2.5336660	2.0685420
H	11.0502790	-4.0565280	-1.8945340
H	12.5089570	-3.8476340	0.1095260
C	-9.0137220	-2.1525200	0.0789840
C	-10.1644640	-1.4800580	-0.3767320
C	-9.1820820	-3.4630180	0.5671160
C	-11.4152730	-2.0843800	-0.3434950
H	-10.0745440	-0.4769220	-0.7885950
C	-10.4332370	-4.0674760	0.5969060
H	-8.3238540	-4.0085470	0.9543150
C	-11.5612720	-3.3838350	0.1428780
H	-12.2825580	-1.5397410	-0.7108700
H	-10.5297880	-5.0781040	0.9881730
H	-12.5399010	-3.8569630	0.1674500
N	0.0090860	2.3008420	-0.0764920
S	0.0127110	-0.8375920	-0.1273300

Table S2.7. Computed lowest energy singlet state of Naph

C	3.7216890	0.0261150	-0.3431200
C	2.5617230	-0.6677070	-0.7070940
C	1.3469820	-0.0145900	-0.8812480
C	1.2281640	1.3641440	-0.6445030
C	2.3880240	2.0585480	-0.2793180
C	3.6061190	1.4053300	-0.1442170
C	-1.2405710	1.3626930	-0.6274660
C	-1.3586390	-0.0183070	-0.8531050
C	-2.5708120	-0.6719010	-0.6671410
H	-2.6177650	-1.7419310	-0.8661370
C	-3.7296080	0.0223460	-0.2996210
C	-3.6146200	1.4025540	-0.1078310
C	-2.3984420	2.0569200	-0.2554970
H	2.5974520	-1.7451040	-0.8635220
H	2.3458050	3.1314580	-0.1148570
H	4.4858300	1.9933160	0.1084040
H	-4.4828940	1.9832690	0.1961820
H	-2.3525440	3.1274820	-0.0773430
C	-5.0170390	-0.6786080	-0.1327180
C	-5.0712240	-1.9922220	0.3523160
C	-6.2289530	-0.0540570	-0.4572160
C	-6.2832170	-2.6529250	0.5032030
H	-4.1514300	-2.5034580	0.6304990
C	-7.4408540	-0.7142530	-0.3035500
H	-6.2246860	0.9602660	-0.8519110
C	-7.4947000	-2.0286620	0.1784060
H	-6.2859210	-3.6787650	0.8669990
H	-8.3635830	-0.1928900	-0.5514590
C	5.0124260	-0.6710650	-0.1836040
C	5.3485500	-1.7746600	-0.9792560
C	5.9464750	-0.2491790	0.7723490
C	6.5646790	-2.4270360	-0.8251470
H	4.6554030	-2.1213380	-1.7435350
C	7.1631820	-0.9005060	0.9246120
H	5.7127660	0.5945190	1.4190190
C	7.4989320	-2.0040040	0.1292990
H	6.7862040	-3.2901970	-1.4501790
H	7.8709890	-0.5356100	1.6666400
C	-8.7841250	-2.7327750	0.3373840
C	-9.8349560	-2.5230560	-0.5663960
C	-8.9884190	-3.6291450	1.3956170
C	-11.0488390	-3.1866710	-0.4172630
H	-9.6924980	-1.8498460	-1.4098600
C	-10.2015330	-4.2940370	1.5449570
H	-8.1955650	-3.7905840	2.1237930

C	-11.2378280	-4.0757790	0.6391130
H	-11.8475640	-3.0146250	-1.1351260
H	-10.3404140	-4.9792800	2.3780330
H	-12.1861250	-4.5948560	0.7555250
C	8.7932170	-2.6984420	0.2908710
C	9.3774330	-2.8458000	1.5564870
C	9.4686810	-3.2278980	-0.8174990
C	10.5957570	-3.5004540	1.7091270
H	8.8602420	-2.4641070	2.4349840
C	10.6866470	-3.8833940	-0.6657310
H	9.0465520	-3.1048520	-1.8133220
C	11.2560540	-4.0227190	0.5985780
H	11.0266200	-3.6105850	2.7016430
H	11.1971490	-4.2792610	-1.5406980
H	12.2079170	-4.5346700	0.7174640
N	-0.0080070	2.0275730	-0.7841510
S	-0.0113010	-0.9411730	-1.5492430
C	-0.0086540	3.4627500	-0.7857960
C	0.0003300	4.1923730	0.4373570
C	-0.0170780	4.1123510	-1.9960930
C	0.0089570	3.5646690	1.7082310
C	0.0010400	5.6176270	0.3700520
C	-0.0168310	5.5228650	-2.0548680
H	-0.0236380	3.5197370	-2.9084410
C	0.0180600	4.3155590	2.8589810
H	0.0085200	2.4775810	1.7635750
C	0.0106200	6.3620780	1.5770900
C	-0.0077570	6.2573690	-0.8950140
H	-0.0235850	6.0196170	-3.0213410
C	0.0190260	5.7278730	2.7949010
H	0.0246830	3.8211590	3.8272740
H	0.0112940	7.4492220	1.5176360
H	-0.0071780	7.3455000	-0.9284960
H	0.0264120	6.3087070	3.7137810

Table S2.8. Computed lowest energy triplet state of Naph

C	3.8114290	-0.0014310	-0.3477790
C	2.6456300	-0.7597200	-0.4151800
C	1.3848920	-0.1719470	-0.5332080
C	1.2508750	1.2355520	-0.5907190
C	2.4375240	1.9998370	-0.5277950
C	3.6721150	1.4022620	-0.4093050
C	-1.2188130	1.2208980	-0.6690830
C	-1.3475530	-0.2140420	-0.5437500
C	-2.5777490	-0.8116700	-0.4237740
H	-2.5984270	-1.8959890	-0.3392960
C	-3.7974560	-0.0764080	-0.4209900
C	-3.6523910	1.3612410	-0.6150510
C	-2.4323640	1.9607870	-0.7252740
H	2.7004990	-1.8453660	-0.3442900
H	2.3813030	3.0827260	-0.5831200
H	4.5551640	2.0362370	-0.3868920
H	-4.5322190	1.9937260	-0.6723440
H	-2.3918440	3.0388540	-0.8551770
C	-5.0660990	-0.6965310	-0.2485760
C	-5.2136620	-2.1031360	-0.0369530
C	-6.2860110	0.0490000	-0.2729360
C	-6.4447160	-2.6921180	0.1309700
H	-4.3375850	-2.7460170	-0.0102640
C	-7.5143340	-0.5531330	-0.1098860
H	-6.2645940	1.1264450	-0.4111540
C	-7.6476150	-1.9442120	0.1002220
H	-6.4867950	-3.7716420	0.2644260
H	-8.4020780	0.0770490	-0.1138730
C	5.1313920	-0.6369210	-0.2084730
C	5.3946550	-1.9005490	-0.7577220
C	6.1715350	0.0002700	0.4841340
C	6.6370720	-2.5019830	-0.6138720
H	4.6209400	-2.4172300	-1.3222970
C	7.4134470	-0.6024650	0.6274500
H	6.0033620	0.9756780	0.9362030
C	7.6739130	-1.8676970	0.0842430
H	6.7996670	-3.4901450	-1.0402310
H	8.2003140	-0.0726640	1.1610160
C	-8.9550200	-2.5777880	0.2824130
C	-10.1293160	-1.9978860	-0.2358190
C	-9.0886150	-3.7912070	0.9848040
C	-11.3700400	-2.5982610	-0.0584620
H	-10.0669050	-1.0753030	-0.8093860
C	-10.3297160	-4.3917750	1.1593820
H	-8.2101930	-4.2587820	1.4249760

C	-11.4816210	-3.8006210	0.6401600
H	-12.2567910	-2.1282560	-0.4785720
H	-10.3992300	-5.3246860	1.7148680
H	-12.4524890	-4.2703510	0.7776850
C	8.9949050	-2.5089020	0.2446660
C	9.7373080	-2.3360720	1.4212180
C	9.5395570	-3.3050450	-0.7726010
C	10.9824700	-2.9372730	1.5755300
H	9.3244700	-1.7429220	2.2351710
C	10.7846030	-3.9072510	-0.6187520
H	8.9926860	-3.4352050	-1.7047590
C	11.5121970	-3.7258650	0.5558780
H	11.5372540	-2.7957760	2.5002150
H	11.1917810	-4.5138890	-1.4243940
H	12.4852560	-4.1959550	0.6758250
N	0.0145510	1.8584700	-0.6988710
S	0.0332110	-1.2767960	-0.6532020
C	0.0036070	3.2981970	-0.7793460
C	-0.0632840	4.0522430	0.4217470
C	0.0537060	3.8980610	-2.0114810
C	-0.1146460	3.4566300	1.7065060
C	-0.0773020	5.4742650	0.3108790
C	0.0397250	5.3060780	-2.1098720
H	0.1030590	3.2773640	-2.9038330
C	-0.1780400	4.2405320	2.8331300
H	-0.1040960	2.3716900	1.7939670
C	-0.1437680	6.2517300	1.4946270
C	-0.0248840	6.0737980	-0.9727210
H	0.0795920	5.7743620	-3.0893570
C	-0.1929990	5.6502500	2.7281430
H	-0.2173330	3.7744190	3.8144040
H	-0.1548070	7.3365470	1.4047340
H	-0.0366090	7.1601220	-1.0404630
H	-0.2438480	6.2560870	3.6292070

Table S2.9. Computed lowest energy singlet state of Fluoro-Naph

C	3.7255220	-0.1587590	-0.3008230
C	2.5628070	-0.8517220	-0.6576300
C	1.3462050	-0.1987920	-0.8193490
C	1.2290510	1.1788330	-0.5762740
C	2.3909160	1.8720710	-0.2160500
C	3.6106160	1.2192810	-0.0938830
C	-1.2414260	1.1779610	-0.5507050
C	-1.3610400	-0.2014390	-0.7839780
C	-2.5753670	-0.8534490	-0.6057120
H	-2.6243980	-1.9218420	-0.8128800
C	-3.7337900	-0.1590550	-0.2374920
C	-3.6158140	1.2190760	-0.0332860
C	-2.3978630	1.8716020	-0.1739270
H	2.5978700	-1.9283400	-0.8194000
H	2.3501290	2.9443290	-0.0471190
H	4.4918690	1.8070440	0.1536530
H	-4.4833570	1.7996810	0.2728770
H	-2.3508080	2.9409080	0.0112100
C	-5.0253420	-0.8565870	-0.0886650
C	-5.0905730	-2.1758910	0.3792650
C	-6.2308110	-0.2227430	-0.4190090
C	-6.3069050	-2.8341390	0.5053000
H	-4.1762780	-2.6944220	0.6620830
C	-7.4467940	-0.8803450	-0.2901240
H	-6.2180540	0.7965280	-0.8004400
C	-7.5116020	-2.2015760	0.1715310
H	-6.3180740	-3.8648460	0.8549510
H	-8.3641780	-0.3521420	-0.5432010
C	5.0190650	-0.8548200	-0.1601780
C	5.3456620	-1.9552400	-0.9641800
C	5.9664450	-0.4339390	0.7830220
C	6.5656540	-2.6048270	-0.8310070
H	4.6419850	-2.3012630	-1.7190590
C	7.1872430	-1.0822630	0.9140620
H	5.7407640	0.4069910	1.4361110
C	7.5138500	-2.1819310	0.1096640
H	6.7795700	-3.4654570	-1.4621200
H	7.9055070	-0.7176270	1.6461070
C	-8.8057130	-2.9040490	0.2961420
C	-9.8379190	-2.6747330	-0.6243670
C	-9.0337810	-3.8178400	1.3343030
C	-11.0569680	-3.3356300	-0.5107160
H	-9.6762670	-1.9880260	-1.4533160
C	-10.2522520	-4.4801820	1.4481230
H	-8.2558970	-3.9954010	2.0747890

C	-11.2699000	-4.2419380	0.5261890
H	-11.8407440	-3.1480430	-1.2410340
H	-10.4100250	-5.1793340	2.2661510
H	-12.2221630	-4.7591790	0.6151540
C	8.8129190	-2.8725380	0.2471870
C	9.4196850	-3.0213930	1.5019860
C	9.4704950	-3.3970860	-0.8742430
C	10.6421900	-3.6732110	1.6315450
H	8.9169670	-2.6432570	2.3903700
C	10.6925800	-4.0497640	-0.7455390
H	9.0309350	-3.2724710	-1.8622950
C	11.2843010	-4.1909690	0.5082740
H	11.0906510	-3.7846890	2.6160800
H	11.1887760	-4.4418880	-1.6303610
H	12.2394020	-4.7007460	0.6091710
N	-0.0082220	1.8434300	-0.7059250
S	-0.0150500	-1.1245170	-1.4822160
C	-0.0086480	3.2765760	-0.7074080
C	0.0051960	4.0077400	0.5159070
C	-0.0218530	3.9280430	-1.9163810
C	0.0188030	3.3800280	1.7858130
C	0.0057610	5.4331850	0.4639490
C	-0.0219520	5.3367510	-1.9819020
H	-0.0320950	3.3405900	-2.8313080
C	0.0323440	4.1286080	2.9379130
H	0.0186190	2.2930820	1.8376570
C	0.0199110	6.1830070	1.6650410
C	-0.0082690	6.0406240	-0.8121860
H	-0.0323140	5.8601880	-2.9328650
C	0.0330220	5.5402040	2.8785680
H	0.0427310	3.6315690	3.9045730
H	0.0202700	7.2680870	1.6122070
H	0.0439160	6.1179070	3.7990320
F	-0.0078790	7.3866560	-0.8580510

Table S2.10. Computed lowest energy triplet state of Fluoro-Naph

C	3.7802480	-0.2216650	-0.1854630
C	2.6083980	-0.9249920	0.0809060
C	1.3520370	-0.3195730	0.0260460
C	1.2279120	1.0486720	-0.3134980
C	2.4207390	1.7601080	-0.5720820
C	3.6518160	1.1470980	-0.5073730
C	-1.2423310	1.0779160	-0.2156800
C	-1.3793360	-0.3337200	0.0719020
C	-2.6141540	-0.9301410	0.1383130
H	-2.6432710	-1.9927580	0.3701130
C	-3.8290320	-0.2123400	-0.0502440
C	-3.6752020	1.2242080	-0.2485500
C	-2.4507800	1.8191440	-0.3308720
H	2.6599440	-1.9749170	0.3670540
H	2.3714120	2.8103790	-0.8427370
H	4.5363170	1.7339520	-0.7429830
H	-4.5515240	1.8565600	-0.3464010
H	-2.4034790	2.8915690	-0.4991300
C	-5.1036290	-0.8448310	-0.0318830
C	-5.2579380	-2.2607700	0.0894720
C	-6.3208230	-0.1028290	-0.1338550
C	-6.4948930	-2.8615950	0.1149720
H	-4.3815980	-2.9020000	0.1398270
C	-7.5543870	-0.7161030	-0.1110500
H	-6.2949540	0.9805170	-0.2122410
C	-7.6950590	-2.1160990	0.0152630
H	-6.5410380	-3.9473100	0.1790600
H	-8.4429220	-0.0893020	-0.1627340
C	5.0955280	-0.8792190	-0.1363150
C	5.2446140	-2.2347570	-0.4652380
C	6.2465210	-0.1712160	0.2401380
C	6.4859270	-2.8529810	-0.4179440
H	4.3791880	-2.8130950	-0.7828630
C	7.4874640	-0.7911630	0.2874200
H	6.1702740	0.8782080	0.5177990
C	7.6357770	-2.1452900	-0.0416900
H	6.5608600	-3.9097580	-0.6672650
H	8.3609450	-0.2066400	0.5702760
C	-9.0095740	-2.7616130	0.0374220
C	-10.1315370	-2.1567440	-0.5613180
C	-9.2018550	-4.0111980	0.6576120
C	-11.3793810	-2.7677160	-0.5384060
H	-10.0199490	-1.2047840	-1.0764260
C	-10.4498200	-4.6226590	0.6773100
H	-8.3669200	-4.4999570	1.1556950

C	-11.5496820	-4.0062880	0.0805480
H	-12.2241690	-2.2773940	-1.0175670
H	-10.5666510	-5.5845250	1.1721330
H	-12.5258640	-4.4847800	0.0971300
C	8.9578290	-2.8025920	0.0000970
C	9.9076490	-2.4513630	0.9695260
C	9.2965220	-3.7937580	-0.9318770
C	11.1536550	-3.0695460	1.0055400
H	9.6596730	-1.7016200	1.7187260
C	10.5420060	-4.4127070	-0.8962080
H	8.5850240	-4.0663540	-1.7092760
C	11.4769210	-4.0532730	0.0727010
H	11.8720880	-2.7870640	1.7716680
H	10.7861140	-5.1730500	-1.6345430
H	12.4506080	-4.5363700	0.1008570
N	-0.0049850	1.6847890	-0.3869790
S	-0.0043080	-1.3243810	0.4897800
C	-0.0024580	3.0997120	-0.6520950
C	0.0766930	3.9998220	0.4436080
C	-0.0796180	3.5420700	-1.9476780
C	0.1470910	3.5692040	1.7910490
C	0.0822710	5.3994740	0.1701780
C	-0.0753470	4.9234210	-2.2284510
H	-0.1418650	2.8186060	-2.7574800
C	0.2210990	4.4862530	2.8115680
H	0.1401530	2.5029700	2.0101390
C	0.1604630	6.3233350	1.2398430
C	0.0051800	5.7999780	-1.1832100
H	-0.1333750	5.2939310	-3.2469980
C	0.2288570	5.8718250	2.5352120
H	0.2737400	4.1441310	3.8418280
H	0.1647680	7.3875520	1.0223500
H	0.2883420	6.5831250	3.3546420
F	0.0115190	7.1206410	-1.4391430

Table S2.11. Computed lowest energy singlet state of Cyano-Naph

C	3.6875450	-0.2426850	-0.1303900
C	2.5424440	-0.7397560	0.5037520
C	1.3474920	-0.0313300	0.4984500
C	1.2335310	1.1844350	-0.1931750
C	2.3767400	1.6859170	-0.8237920
C	3.5797010	0.9910670	-0.7797630
C	-1.2321130	1.1818430	-0.1975840
C	-1.3458940	-0.0340170	0.4939450
C	-2.5398230	-0.7441110	0.4963880
H	-2.5860770	-1.6817410	1.0486480
C	-3.6840860	-0.2486950	-0.1405350
C	-3.5763140	0.9844920	-0.7908890
C	-2.3742380	1.6810830	-0.8320620
H	2.5881740	-1.6777830	1.0553450
H	2.3302610	2.6273900	-1.3634570
H	4.4397540	1.4070930	-1.3000670
H	-4.4359070	1.3990460	-1.3131840
H	-2.3275560	2.6223920	-1.3720040
C	-4.9485200	-1.0091710	-0.1258980
C	-4.9470690	-2.4104080	-0.1469290
C	-6.1892750	-0.3588000	-0.0949050
C	-6.1342910	-3.1300730	-0.1343430
H	-4.0027510	-2.9482730	-0.2074950
C	-7.3766490	-1.0792370	-0.0843690
H	-6.2278570	0.7278410	-0.0453650
C	-7.3750660	-2.4802880	-0.1026520
H	-6.0962190	-4.2167340	-0.1828770
H	-8.3219480	-0.5425910	-0.0279540
C	4.9521410	-1.0031490	-0.1181990
C	4.9505930	-2.4041770	-0.1465380
C	6.1930080	-0.3531680	-0.0867820
C	6.1378350	-3.1238720	-0.1447740
H	4.0055720	-2.9425520	-0.1885120
C	7.3804050	-1.0736560	-0.0872480
H	6.2323520	0.7338980	-0.0481920
C	7.3788040	-2.4744340	-0.1169720
H	6.0984620	-4.2115330	-0.1531890
H	8.3267430	-0.5360040	-0.0794730
C	-8.6380440	-3.2471750	-0.0872500
C	-9.7761000	-2.7746230	-0.7552580
C	-8.7285520	-4.4670760	0.5969950
C	-10.9651650	-3.4973170	-0.7390330
H	-9.7230760	-1.8413330	-1.3130970
C	-9.9166670	-5.1911060	0.6127590
H	-7.8647750	-4.8423680	1.1428630

C	-11.0408290	-4.7092170	-0.0551830
H	-11.8338600	-3.1158200	-1.2707190
H	-9.9664580	-6.1315820	1.1566810
H	-11.9696820	-5.2742870	-0.0428670
C	8.6419780	-3.2413340	-0.1232740
C	9.7608190	-2.7940170	0.5928850
C	8.7521790	-4.4360030	-0.8480740
C	10.9499690	-3.5167200	0.5841870
H	9.6922870	-1.8812880	1.1821620
C	9.9404690	-5.1598140	-0.8566150
H	7.9044540	-4.7908790	-1.4314280
C	11.0452830	-4.7033050	-0.1403740
H	11.8032780	-3.1551400	1.1534050
H	10.0057390	-6.0799830	-1.4327020
H	11.9743030	-5.2681870	-0.1470060
N	0.0000220	1.8686380	-0.2350330
S	-0.0002840	-0.6153840	1.4973900
C	-0.0009760	3.2641030	-0.5330200
C	-0.0046940	4.1789290	0.5575010
C	0.0014640	3.7070570	-1.8354680
C	-0.0073010	3.7418550	1.9053400
C	-0.0058750	5.5779220	0.2823580
C	0.0004510	5.0831010	-2.1168750
H	0.0041600	2.9826960	-2.6470060
C	-0.0110140	4.6530560	2.9329620
H	-0.0063220	2.6731240	2.1108630
C	-0.0097020	6.4918340	1.3620140
C	-0.0031230	5.9991740	-1.0824340
H	0.0024460	5.4284780	-3.1467160
C	-0.0122390	6.0381480	2.6589570
H	-0.0130220	4.3084900	3.9636630
H	-0.0106500	7.5603070	1.1559160
H	-0.0152020	6.7497360	3.4803590
C	-0.0040330	7.3945180	-1.3912480
N	-0.0047750	8.5320630	-1.6384480

Table S2.12. Computed lowest energy triplet state of Cyano-Naph

C	3.7808190	-0.3212860	-0.2831440
C	2.6153680	-1.0795940	-0.2391110
C	1.3545580	-0.4874750	-0.3223320
C	1.2226610	0.9161420	-0.4524970
C	2.4104040	1.6778550	-0.5018630
C	3.6440790	1.0779820	-0.4188460
C	-1.2309340	0.9143060	-0.4405360
C	-1.3592070	-0.4897800	-0.3122070
C	-2.6183150	-1.0843260	-0.2218840
H	-2.6727140	-2.1637030	-0.0929030
C	-3.7854040	-0.3280420	-0.2560330
C	-3.6523060	1.0720160	-0.3855900
C	-2.4202460	1.6743590	-0.4761240
H	2.6724290	-2.1584300	-0.1068100
H	2.3383830	2.7544850	-0.6163120
H	4.5309110	1.7027360	-0.4840980
H	-4.5409100	1.6952960	-0.4406870
H	-2.3508170	2.7515640	-0.5866790
C	-5.1078170	-0.9630570	-0.1582840
C	-5.3298050	-2.2537010	-0.6595170
C	-6.1838030	-0.2981800	0.4470070
C	-6.5751780	-2.8550500	-0.5561040
H	-4.5287840	-2.7826300	-1.1717310
C	-7.4268820	-0.9043570	0.5552240
H	-6.0399730	0.6912510	0.8757890
C	-7.6497810	-2.1950250	0.0563690
H	-6.7238810	-3.8433860	-0.9859980
H	-8.2307710	-0.3768970	1.0643850
C	5.1053660	-0.9520990	-0.1865440
C	5.3316430	-2.2438770	-0.6827460
C	6.1793390	-0.2810890	0.4153940
C	6.5789180	-2.8412280	-0.5762110
H	4.5273550	-2.7849520	-1.1768440
C	7.4242720	-0.8826440	0.5257470
H	6.0374340	0.7168620	0.8245250
C	7.6510050	-2.1753550	0.0340750
H	6.7176540	-3.8502350	-0.9590020
H	8.2394600	-0.3311460	0.9893860
C	-8.9737100	-2.8389090	0.1721790
C	-10.1507780	-2.0836910	0.0784770
C	-9.0836400	-4.2207230	0.3803360
C	-11.3976710	-2.6905750	0.1890340
H	-10.0903320	-1.0128990	-0.1070720
C	-10.3302650	-4.8279530	0.4919700
H	-8.1829050	-4.8234340	0.4807540

C	-11.4927980	-4.0654070	0.3965900
H	-12.2988240	-2.0877690	0.1046620
H	-10.3932670	-5.9001060	0.6625380
H	-12.4672990	-4.5396540	0.4836330
C	8.9769170	-2.8137530	0.1579050
C	9.7794830	-2.5832430	1.2838890
C	9.4643800	-3.6636130	-0.8445130
C	11.0291900	-3.1822690	1.4037970
H	9.4113270	-1.9470610	2.0865610
C	10.7148070	-4.2620310	-0.7254550
H	8.8693300	-3.8388760	-1.7388840
C	11.5026490	-4.0239420	0.3991370
H	11.6319320	-2.9968340	2.2897550
H	11.0783530	-4.9108020	-1.5188810
H	12.4797020	-4.4917660	0.4920830
N	-0.0049660	1.5577170	-0.5237370
S	-0.0011170	-1.5778410	-0.2484760
C	-0.0065230	2.9972940	-0.6470740
C	0.0019820	3.7834610	0.5415000
C	-0.0153340	3.5651380	-1.9328920
C	0.0103870	3.2244490	1.8365260
C	0.0020280	5.2111000	0.4033360
C	-0.0155050	4.9350200	-2.0760250
H	-0.0218260	2.9115680	-2.8039070
C	0.0189720	4.0308670	2.9708540
H	0.0102970	2.1406230	1.9496600
C	0.0107540	5.9951030	1.5681640
C	-0.0067920	5.7803160	-0.9290160
H	-0.0223000	5.3830710	-3.0668660
C	0.0191440	5.4189860	2.8377350
H	0.0255030	3.5733530	3.9577290
H	0.0109280	7.0802190	1.4694680
H	0.0258930	6.0553910	3.7197970
C	-0.0068770	7.1729790	-1.0930580
N	-0.0067100	8.3421440	-1.2225850

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APPENDIX B: SUPPLEMENTARY INFORMATION FOR CHAPTER 3

1. General Considerations

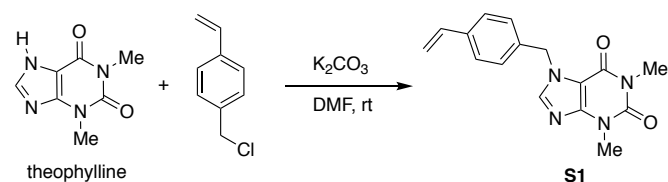
Commercial reagents and anhydrous solvents were purchased from *Millipore-Sigma*, *Alfa* and *TCI*, and were used as received unless otherwise indicated. All catalytic reactions were carried out under N₂ with oven-dried vials. Thin layer chromatography was performed on SiliCycle® 250 μ m, 60A plates. Column chromatography was performed on *SiliCycle®SilicaFlash®* P60, 40-63 μ m, 60A. Visualization was accomplished with I₂-silica.

¹H, ¹³C, and ¹⁹F NMR spectra were recorded on a Bruker 400 Hz (101 Hz, 162 Hz and 376 Hz for ¹³C, ³¹P and ¹⁹F, respectively) spectrometer at ambient temperature. All NMR spectra are referenced to the residual solvent (CHCl₃) signal. Data for ¹H, ¹⁹F and ³¹P NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration. Data for ¹³C NMR are reported as follows: chemical shift (δ ppm).

Mass spectra (MS) were obtained from Colorado State University Central Instrument Facility on an Agilent 6224 Time of flight (TOF) LC-MS spectrometer using ESI+/DART+ ionization model.

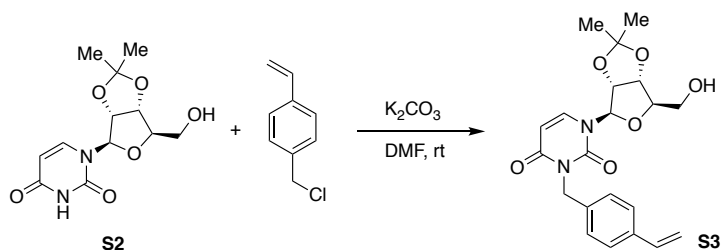
2. Substrate Synthesis and Characterization

2.1 Alkene Synthesis



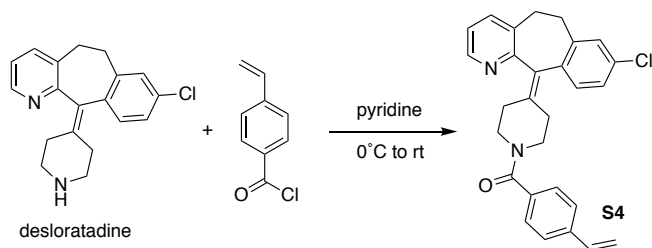
To a solution of theophylline (0.90 g, 5.0 mmol, 1.0 equiv) in 15.0 mL of anhydrous DMF, 4-vinylbenzyl chloride (1.15 g, 7.5 mmol, 1.5 equiv) and K₂CO₃ (1.38g, 10.0 mmol, 2.0 equiv)

were added sequentially. The slurry was vigorously stirred at room temperature for 12h. The white solid was filtered off, and the filtrate was diluted with EtOAc (100 mL), washed with H₂O (50 mL × 3), brine (50 mL), dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. The residue was subjected to silica gel chromatography using hexane/acetone (10:1 to 5:1) as the eluent, giving **S1** as a white solid (1.31g, 89% yield). **¹H NMR** (400 MHz, CDCl₃) δ 7.56 (s, 1H), 7.46 – 7.35 (m, 2H), 7.30 – 7.26 (m, 2H), 6.68 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.74 (dd, *J* = 17.6, 0.8 Hz, 1H), 5.48 (s, 2H), 5.27 (dd, *J* = 10.9, 0.8 Hz, 1H), 3.58 (s, 3H), 3.40 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 155.3, 151.7, 148.9, 140.8, 138.0, 136.0, 134.7, 128.2, 126.9, 114.8, 107.0, 50.1, 29.8, 28.0. **DART-TOF-LC/MS** *m/z* calcd. for C₁₆H₁₇N₄O₂ [M+H⁺] 297.1352, found 297.1351.

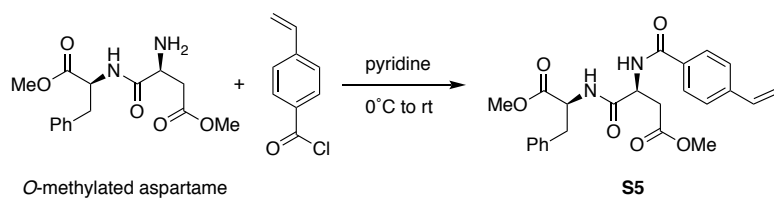


To a solution of protected uridine **S2**¹ (1.42 g, 5.0 mmol, 1.0 equiv) in 15.0 mL of anhydrous DMF, 4-vinylbenzyl chloride (1.15g, 7.5 mmol, 1.5 equiv) and K₂CO₃ (1.38g, 10.0 mmol, 2.0 equiv) were added sequentially. The slurry was vigorously stirred at room temperature. After 12 h, the solid was filtered off. The filtrate was diluted with EtOAc (100 mL), washed with H₂O (50 mL × 3), brine (50 mL), dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. The residue was subjected to silica gel chromatography using hexane/acetone (10:1 to 5:1) as the eluent, giving **S3** as a colorless oil (1.41g, 78% yield). **¹H NMR** (400 MHz, CDCl₃) δ 7.37 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 13.3 Hz, 1H), 6.63 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.73 (d, *J* = 8.0 Hz, 1H), 5.66 (dd, *J* = 17.6, 1.0 Hz, 1H), 5.48 (d, *J* = 2.9 Hz, 1H), 5.17 (dd, *J* = 10.9, 0.9 Hz, 1H), 5.08 – 4.88 (m, 4H), 4.23 (q, *J* = 3.1 Hz, 1H), 3.89 – 3.81 (m, 1H), 3.74 (ddd, *J* = 12.0, 7.5, 3.3 Hz, 1H), 2.70 (dd, *J* = 7.5, 3.3 Hz, 1H), 1.52 (s, 3H), 1.30 (s, 3H). **¹³C NMR** (101

MHz, CDCl₃) δ 162.4, 151.0, 140.7, 137.1, 136.4, 135.9, 129.5, 126.2, 114.3, 114.0, 102.2, 97.0, 86.9, 83.8, 80.3, 62.7, 43.9, 27.3, 25.3. **ESI-TOF-LC/MS** m/z calcd. for C₂₁H₂₅N₂O₆ [M+H⁺] 401.1713, found 401.1710.

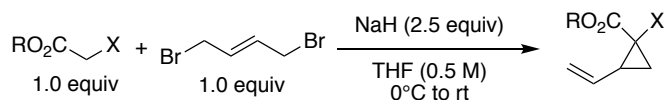


To a solution of desloratadine (1.0 g, 3.2 mmol, 1.0 equiv) in 5.0 mL of anhydrous pyridine at 0 °C, 4-vinylbenzoyl chloride (0.54g, 3.2 mmol, 1.0 equiv) was added dropwise. The mixture was stirred at 0 °C for 30 min, then was warmed up to room temperature and stirred for 12h. The reaction was quenched by addition of sat. NH₄Cl (20 mL), then diluted with CH₂Cl₂ (100 mL). The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (10 mL $\times$ 2). The combined organic phase was washed with H₂O (50 mL $\times$ 3), brine (50 mL), dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. The residue was subjected to silica gel chromatography using hexane/acetone (5:1 to 3:1) as the eluent, giving the final product as a white solid (1.12g, 79% yield). **¹H NMR** (400 MHz, CDCl₃) δ 8.38 (brs, 1H), 7.48 – 7.33 (m, 5H), 7.22 – 7.01 (m, 4H), 6.70 (dd, J = 17.6, 10.9 Hz, 1H), 5.77 (dd, J = 17.6, 0.8 Hz, 1H), 5.29 (J = 10.9, 0.8 Hz, 1H), 4.18 (brs, 1H), 3.64 (brs, 1H), 3.45 – 3.13 (m, 4H), 2.92 – 2.73 (m, 4H), 2.70 – 2.15 (m, 4H). **¹³C NMR** (101 MHz, CDCl₃) δ 170.2, 156.8, 146.7, 139.6, 138.9, 137.6, 136.9, 136.1, 135.2, 134.7, 133.4, 133.0, 130.5, 129.0, 127.3, 126.2, 122.4, 115.2, 31.7, 31.5. **ESI-TOF-LC/MS** m/z calcd. for C₂₈H₂₆ClN₂O [M+H⁺] 441.1734, found 441.1735.



To a solution of O-methylated aspartame² (0.72 g, 2.0 mmol, 1.0 equiv) in 4.0 mL of anhydrous pyridine at 0 °C, 4-vinylbenzoyl chloride (0.33g, 2.0 mmol, 1.0 equiv) was added dropwise. The mixture was stirred at 0 °C for 30 min, then was warmed up to room temperature and stirred for 12h. The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (10 mL × 2). The combined organic phase was washed with H₂O (50 mL×3), brine (50 mL), dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. The residue was subjected to silica gel chromatography using CH₂Cl₂/MeOH (20:1 to 1:1) as the eluent, giving the final product as a colorless oil (0.73g, 83% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.18 – 7.02 (m, 6H), 6.76 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.87 (d, *J* = 17.5 Hz, 1H), 5.39 (d, *J* = 10.9 Hz, 1H), 5.00 (ddd, *J* = 7.9, 6.4, 3.8 Hz, 1H), 4.80 (td, *J* = 7.3, 5.3 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.22 – 2.98 (m, 3H), 2.67 (dd, *J* = 17.0, 6.4 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 173.1, 171.4, 170.1, 166.7, 141.2, 135.9, 135.6, 132.2, 129.2, 128.5, 127.5, 127.1, 126.4, 116.3, 53.5, 52.4, 52.2, 49.3, 37.7, 34.9. **DART-TOF-LC/MS** *m/z* calcd. for C₂₄H₃₀N₃O₆ [M+NH₄⁺] 456.2135, found 456.2133.

2.2 Vinylcyclopropane Synthesis



Procedure A: To a suspension of 60% NaH (1.0 g, 25.0 mmol, 2.5 equiv) in 25.0 mL of anhydrous THF at 0 °C, *trans*-1,4-dibromo-2-butene (2.1 g, 10.0 mmol, 1.0 equiv) was added in one portion. Appropriate activated methylene compounds (10.0 mmol, 1.0 equiv) was added dropwise over 10 min. The reaction was then vigorously stirred at room temperature. Conversion was assessed by

TLC (10% EtOAc in hexanes). Upon completion, the reaction was cooled to 0 °C with an ice bath and carefully quenched by slow addition of sat. NH_4Cl (10 mL). The mixture was then diluted with H_2O (30 mL) and ether (100 mL). The layers were separated, and the aqueous phase was extracted with ether (30 mL $\times$ 3). The combined organic phase was washed with H_2O (50 mL $\times$ 2), brine (50 mL), dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. The residue was purified by silica gel chromatography using hexane/EtOAc as the eluent.

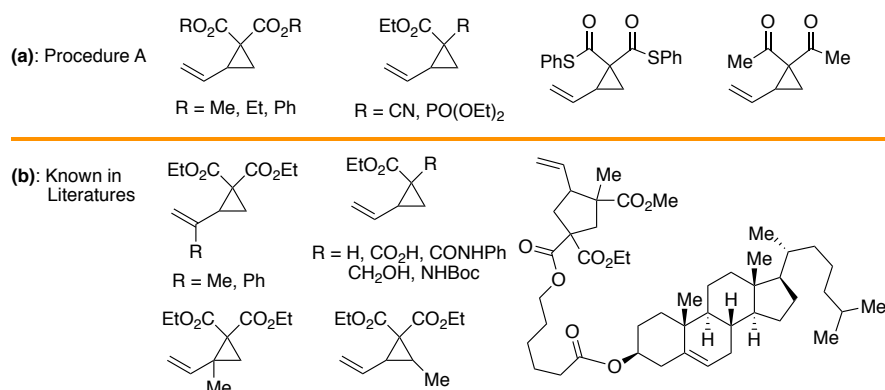
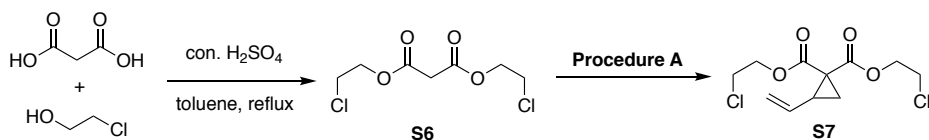
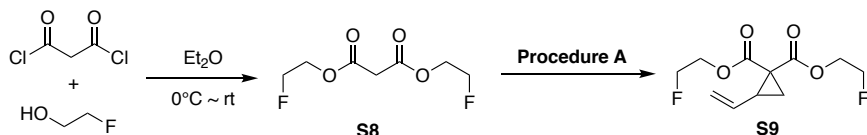


Figure S3.1. Known vinylcyclopropanes synthesized according to Procedure A or methods in literature.³

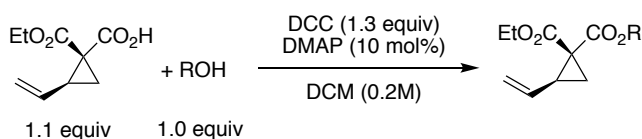


A solution of malonic acid (4.0 g, 38.5 mmol), 2-chloroethanol (13.0 mL, 206 mmol) and concentrated H_2SO_4 (0.5 mL) in anhydrous toluene (20.0 mL) was heated to reflux for 3 h. After cooling to room temperature, the reaction was carefully quenched by slow addition of 10% NaHCO_3 . The layers were separated, and the aqueous phase was extracted with ether (50 mL $\times$ 3). The combined organic phase was washed with 5% NaHCO_3 (50 mL $\times$ 2), H_2O (50 mL $\times$ 2) and brine (50 mL), dried over anhydrous Na_2SO_4 , concentrated *in vacuo* to give crude **S6** as a colorless oil (5.2 g), which was used without further purification. **S7** was then synthesized according to **Procedure A**. Colorless oil, 4.34 g, 40% yield for two steps. ^1H NMR (400 MHz, CDCl_3) δ 5.48

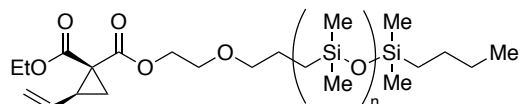
(ddd, $J = 17.0, 10.2, 8.1$ Hz, 1H), 5.32 (dd, $J = 17.0, 1.5$ Hz, 1H), 5.17 (dd, $J = 10.2, 1.5$ Hz, 1H), 4.50 – 4.28 (m, 4H), 3.90 – 3.40 (m, 4H), 2.65 (dd, $J = 9.0, 7.7$ Hz, 1H), 1.79 (dd, $J = 7.7, 5.0$ Hz, 1H), 1.64 (dd, $J = 9.0, 5.0$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 169.0, 166.7, 132.4, 119.2, 65.1, 65.0, 41.3, 41.2, 35.6, 31.8, 20.8. **DART-TOF-LC/MS** m/z calcd. for $\text{C}_{11}\text{H}_{18}\text{Cl}_2\text{NO}_4$ $[\text{M}+\text{NH}_4^+]$ 298.0613, found 298.0611.



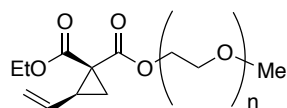
To a solution of 2-fluoroethanol (1.41 mL, 24.0 mmol) in anhydrous Et_2O (100 mL) at 0 °C, malonyl chloride (2.82 g, 38.5 mmol) was added dropwise. The reaction was vigorously stirred at room temperature. After 12h, the reaction was carefully quenched by slow addition of 10% NaHCO_3 . The layers were separated, and the aqueous phase was extracted with ether (50 mL $\times$ 2). The combined organic layer was washed with 5% NaHCO_3 (100 mL), H_2O (100 mL) and brine (100 mL), dried over anhydrous Na_2SO_4 , concentrated *in vacuo* to give crude **S8** as a colorless oil, which was used without further purification. **S9** was then synthesized according to **Procedure A**. Colorless oil, 2.89 g, 57% yield for two steps. ^1H NMR (400 MHz, CDCl_3) δ 5.47 (ddd, $J = 17.0, 10.1, 8.1$ Hz, 1H), 5.36 – 5.28 (m, 1H), 5.19 – 5.15 (m, 1H), 4.68 – 4.62 (m, 2H), 4.56 – 4.52 (m, 2H), 4.51 – 4.26 (m, 4H), 2.65 (dd, $J = 9.0, 7.9$ Hz, 1H), 1.79 (dd, $J = 7.7, 5.0$ Hz, 1H), 1.64 (dd, $J = 9.0, 5.0$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 169.2, 166.9, 132.4, 119.2, 81.9 (d, $J = 12.2$ Hz), 80.2 (d, $J = 12.2$ Hz), 64.5 (d, $J = 14.7$ Hz), 64.2 (d, $J = 14.7$ Hz), 35.6, 31.8, 20.8. ^{19}F NMR (376 MHz, CDCl_3) δ -224.7, -224.9. **DART-TOF-LC/MS** m/z calcd. for $\text{C}_{11}\text{H}_{18}\text{F}_2\text{NO}_4$ $[\text{M}+\text{NH}_4^+]$ 266.1204, found 266.1207.



Procedure B: To a solution of 1-(ethoxycarbonyl)-2-vinylcyclopropane-1-carboxylic acid^{3b} (1.1 equiv.) in anhydrous DCM (0.2 M) at 0 °C, appropriate alcohol (1.0 equiv), DMAP (0.10 equiv.), and DCC (1.3 equiv.) was sequentially added. The mixture was then vigorously stirred at room temperature for 12h. The white precipitate was filtered off and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel chromatography using hexane/EtOAc as the eluent.

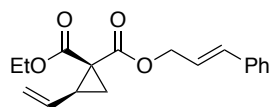


Synthesized from 1-(ethoxycarbonyl)-2-vinylcyclopropane-1-carboxylic acid and 1 kDa monocarbinol terminated polydimethylsiloxane (5.0 mmol scale). Colorless oil, 5.23g, 88% yield. ¹H NMR (400 MHz, CDCl₃) δ 5.44 (ddd, *J* = 17.0, 10.2, 8.3 Hz, 1H), 5.29 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.13 (dd, *J* = 10.1, 1.7 Hz, 1H), 4.35 – 4.07 (m, 4H), 3.62 (t, *J* = 5.0 Hz, 2H), 3.41 (t, *J* = 7.0 Hz, 2H), 2.60 (q, *J* = 8.3 Hz, 1H), 1.71 (dd, *J* = 7.6, 4.9 Hz, 1H), 1.64 – 1.50 (m, 3H), 1.36 – 1.16 (m, 7H), 0.92 – 0.78 (m, 3H), 0.59 – 0.46 (m, 4H), 0.09 – 0.03 (m, 89H). ¹³C NMR (101 MHz, CDCl₃) δ 168.6, 166.2, 132.0, 117.5, 73.1, 67.2, 63.7, 60.4, 34.8, 30.3, 25.3, 24.4, 22.4, 19.5, 16.9, 13.1, 13.0, 12.8, 0.4, 0.1, 0.0, -0.4, -0.9, -1.0. *M_n* (NMR) = 1.4 kDa.

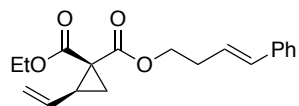


Synthesized from 1-(ethoxycarbonyl)-2-vinylcyclopropane-1-carboxylic acid and PEG 550 (5.0 mmol scale). Colorless oil, 5.23g, 88% yield. ¹H NMR (400 MHz, CDCl₃) δ ¹H NMR (400 MHz, Chloroform-*d*) δ 5.43 (ddd, *J* = 17.0, 10.1, 8.2 Hz, 1H), 5.28 (dd, *J* = 17.1, 1.6 Hz, 1H), 5.13 (dd, *J* = 10.0, 1.7 Hz, 1H), 4.33 – 4.13 (m, 4H), 3.68 (t, *J* = 4.9 Hz, 2H), 3.65 – 3.61 (m, 34H), 3.55 – 3.52 (m, 2H), 3.37 (s, 3H), 2.58 (q, *J* = 8.3 Hz, 1H), 1.70 (dd, *J* = 7.6, 4.9 Hz, 1H), 1.56 (dd, *J* = 9.0, 4.9 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 1169.6, 167.2,

133.0, 118.6, 71.9, 70.63, 70.60, 70.57, 70.51, 68.8, 64.6, 61.5, 59.0, 35.8, 31.3, 20.5, 14.2. M_n (NMR) = 625.



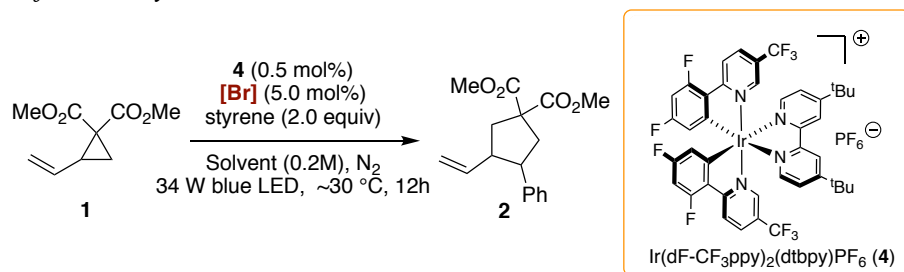
Synthesized from 1-(ethoxycarbonyl)-2-vinylcyclopropane-1-carboxylic acid and cinnamyl alcohol (2.0 mmol scale). Colorless oil, 0.49 g, 82% yield. ^1H NMR (400 MHz, CDCl_3) δ 7.35 – 7.14 (m, 5H), 6.59 (d, J = 15.8 Hz, 1H), 6.24 – 6.13 (m, 1H), 5.36 (dd, J = 10.0, 8.1 Hz, 1H), 5.23 (dd, J = 17.0, 1.6 Hz, 1H), 5.07 (dd, J = 10.0, 1.6 Hz, 1H), 4.80 – 4.65 (m, 2H), 4.24 – 4.05 (m, 2H), 2.54 (dd, J = 9.0, 7.6 Hz, 1H), 1.66 (dd, J = 7.6, 4.9 Hz, 1H), 1.52 (dd, J = 9.0, 4.9 Hz, 1H), 1.18 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 169.5, 167.3, 136.1, 134.3, 133.0, 128.6, 128.1, 126.6, 122.7, 118.6, 66.1, 61.5, 35.9, 31.3, 20.5, 14.2. **DART-TOF-LC/MS** m/z calcd. for $\text{C}_{18}\text{H}_{24}\text{NO}_4$ [$\text{M}+\text{NH}_4^+$] 318.1705, found 318.1705.



Synthesized from 1-(ethoxycarbonyl)-2-vinylcyclopropane-1-carboxylic acid and *trans*-4-phenylbut-3-en-1-ol (2.0 mmol scale). Colorless oil, 0.44 g, 70% yield. ^1H NMR (400 MHz, CDCl_3) δ 7.30 – 7.09 (m, 5H), 6.39 (d, J = 15.9 Hz, 1H), 6.07 (dt, J = 15.7, 7.0 Hz, 1H), 5.35 (ddd, J = 16.6, 10.1, 8.3 Hz, 1H), 5.19 (dd, J = 17.0, 1.6 Hz, 1H), 5.04 (dd, J = 10.0, 1.6 Hz, 1H), 4.31 – 4.02 (m, 4H), 2.56 – 2.40 (m, 3H), 1.61 (dd, J = 7.5, 4.9 Hz, 1H), 1.47 (dd, J = 9.0, 4.9 Hz, 1H), 1.14 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 169.6, 167.3, 137.2, 133.1, 132.6, 128.5, 127.3, 126.1, 125.3, 118.5, 64.7, 61.5, 35.9, 32.3, 31.2, 20.5, 14.2. **DART-TOF-LC/MS** m/z calcd. for $\text{C}_{19}\text{H}_{26}\text{NO}_4$ [$\text{M}+\text{NH}_4^+$] 332.1862, found 332.1860.

3. Complementary Optimization of Conditions

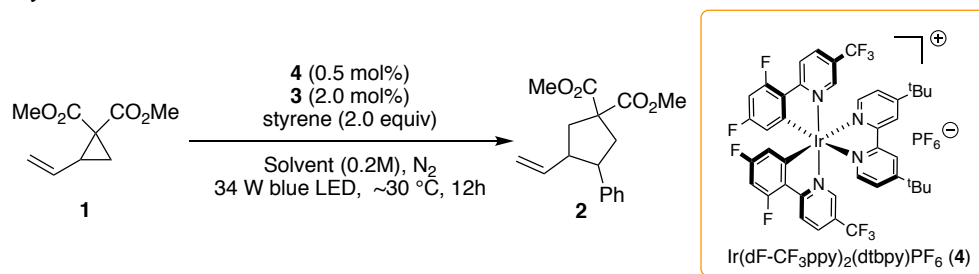
Table S3.1. Single-electron oxidation of bromide salts to generate bromine radicals for the [3+2] cycloaddition of **1** and styrene. ^a



Entry	[Br]	Solvent	NMR Yield (%) ^b
1	NaBr	MeCN	0
2	KBr	MeCN	0
3	LiBr	MeCN	0
4	TBAB	MeCN	0
5	NaBr	DMSO	0
6	KBr	DMSO	0
7	LiBr	DMSO	0
8	TBAB	DMSO	0
9	NaBr	DMF	0
10	KBr	DMF	0
11	LiBr	DMF	0
12	TBAB	DMF	0
13	LiBr	acetone	0
14	TBAB	acetone	0
15	LiBr	THF	0
16	TBAB	THF	0
17	LiBr	MeOH	0
18	TBAB	MeOH	0

^aGeneral reaction conditions: **1** (0.2 mmol), styrene (0.4 mmol), **4** (0.5%), bromide salt (5.0 %), anhydrous solvent (1.0 mL), 34 W Kessil blue LED. ^bTrimethoxybenzene was used as an internal standard. TBAB = tetrabutylammonium bromide

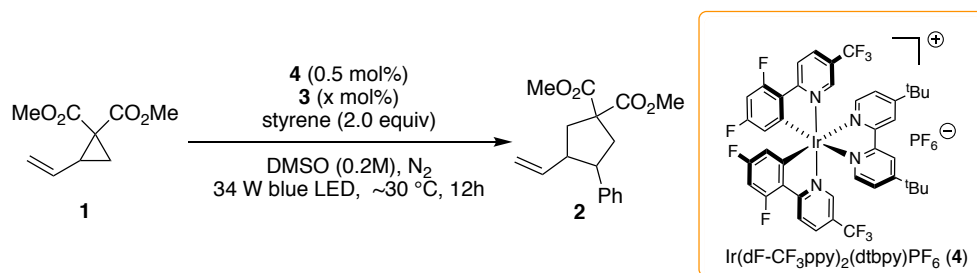
Table S3.2. Solvent effect in the [3+2] cycloaddition of **1** and styrene using cinnamyl bromide as the precatalyst.^a



Entry	Solvent	NMR Yield (%) ^b
1	MeCN	< 5
2	acetone	< 5
3	DMF	11
4	THF	0
5	MeOH	0
6	benzene	0
7	DMSO	95
8	NMP	22
9	DCM	0
10	DCE	0
11	PhCl	< 5

^aReaction conditions: **1** (0.2 mmol), styrene (0.4 mmol), **4** (0.5%), cinnamyl bromide **3** (2.0 %), anhydrous solvent (1.0 mL), 34 W Kessil blue LED. ^bTrimethoxylbenzene was used as an internal standard.

Table S3.3. Examination of precatalyst (**3**) loading in the [3+2] cycloaddition of **1** and styrene.^a



Entry	x	NMR Yield % ^b
1	2.0	95
2	5.0	95
3	1.0	94
4	0.5	77
5	0.1	41
11	0.01	< 5

^aReaction conditions: **1** (0.2 mmol), styrene (0.4 mmol), **4** (0.5%), **3** (x mol%), anhydrous DMSO (1.0 mL), 34 W Kessil blue LED. ^bTrimethoxybenzene was used as an internal standard.

4. General Reaction Setup and Experimental Procedures

Procedure C: In a N₂-filled glovebox, an oven-dried vial (0.5 dram) equipped with a magnet stir bar was charged with vinyl- or ethynylcyclopropane (0.2 mmol, 1.0 equiv.), appropriate alkene (2.0 equiv.), 50 μ L stock solution of cinnamyl bromide **3** in DMSO (40 mM for 1.0 mol%; 80 mM for 2.0 mol%), anhydrous DMSO (1.90 mL for 0.1 M; 0.90 mL for 0.2 M; 0.40 mL for 0.4 M), and 50 μ L stock solution of 4CzIPN **7** in DMSO (0.2 mM for 50 ppm; 2.0 mM for 500 ppm). The vial was then tightly capped and removed out of glovebox. The reaction was placed into a photoreactor (HeptatoChem HCK 1006-01-004) equipped with a blue LED (Kessil, 34 W). The reactor was cooling by air flow that the temperature was ~ 30 °C). After 12 h, the reaction mixture was diluted with water (10 mL) and extracted with ether (20 mL $\times$ 3). The combined organic phase was washed with H₂O (20 mL $\times$ 3), brine (30 mL), dried over anhydrous Na₂SO₄, concentrated *in vacuo*. The residue was then subjected to silica gel chromatography for purification.

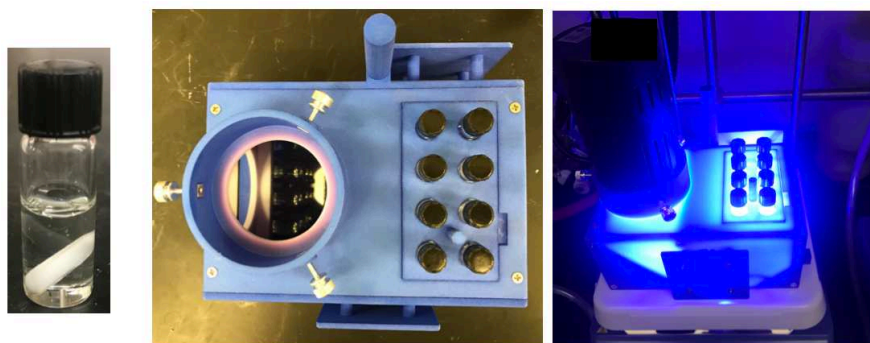


Figure S3.2. Reaction setup (HeptatoChem HCK 1006-01-004 with Kessil 34 W H-150 blue LED).

5. Mechanistic Study

5.1 TEMPO-trapping experiment

In a N₂-filled glovebox, an oven-dried vial (0.5 dram) equipped with a magnet stir bar was charged with cinnamyl bromide **3** (39.4 mg, 0.2 mmol), TEMPO (93.8 mg, 0.6 mmol), anhydrous DMSO (1.0 mL) and 4CzIPN **7** (1.6 mg, 0.002 mmol). The vial was then tightly capped and removed out of glovebox. The reaction was placed into a photoreactor (HeptatoChem HCK 1006-01-004) equipped with a blue LED (Kessil, 34 W). The reactor was cooling by air flow that the temperature was ~30 °C). After 2 h, an aliquot of 10 uL was taken for ESI-TOF LC/MS analysis. The reaction mixture was diluted with water (10 mL) and extracted with ether (20 mL × 3). The combined organic phase was washed with H₂O (20.0 mL × 2), brine (30 mL), dried over anhydrous Na₂SO₄, concentrated *in vacuo*. 32.0 mg (81% yield) cinnamyl bromide was recovered through silica gel chromatography.

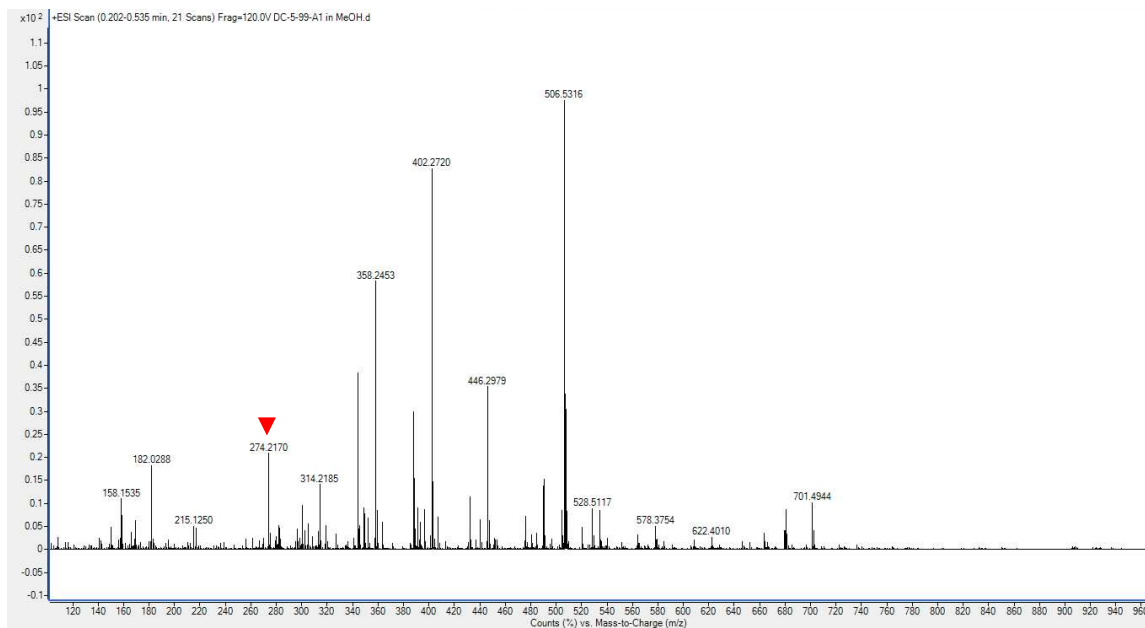


Figure S3.3. ESI-TOF LC/MS spectrum of aliquot taken from TEMPO-trapping experiment

5.2 Investigation of alternative precatalysts

in a N₂-filled glovebox, an oven-dried vial (0.5 dram) equipped with a magnet stir bar was charged with vinylcyclopropane **1** (0.2 mmol, 1.0 equiv.), styrene (46.0 uL, 0.4 mmol), 50 uL stock solution of **7** in DMSO (0.2 mM), anhydrous DMSO (0.90 mL), and 50 uL stock solution of precatalyst in DMSO (40 mM). The vial was then tightly capped and removed out of glovebox. The reaction was placed into a photoreactor (HeptatoChem HCK 1006-01-004) equipped with a blue LED (Kessil, 34 W). The reactor was cooling by air flow that the temperature was ~30 °C). After 12 h, the vial was opened to the air and 1,3,5-trimethoxylbenzene (16.8 mg, 0.1 mmol) was added as an internal standard. An aliquot of 0.10 mL was taken for direct ¹H NMR analysis to determine the yield.

Table S4. Results of [3+2] cycloaddition of **1** and styrene using alternative precatalyst.^a

Entry	precatalyst	7	light	NMR (%) ^b	Yield
1	allyl bromide	√	√	0	
2	cinnamyl chloride	√	√	0	
3	NBS	√	√	41	
4	NBS	√	×	0	
5	NBS	×	√	0	
6	NBS	×	×	0	
7	Br ₂	√	√	26	
8	Br ₂	√	×	0	
9	Br ₂	×	√	16	
10	Br ₂	×	×	0	

^aReaction conditions: **1** (0.2 mmol), styrene (0.4 mmol), **7** (50 ppm), precatalyst (1.0 %), anhydrous DMSO (1.0 mL), 34 W Kessil blue LED, 12h. ^bTrimethoxylbenzene was used as an internal standard.

5.3 Radical epimerization experiment

In a N₂-filled glovebox, an oven-dried vial (0.5 dram) equipped with a magnet stir bar was charged with *cis*-1-(ethoxycarbonyl)-2-vinylcyclopropane-1-carboxylic acid (36.8 mg, 0.2 mmol), 50 uL stock solution of cinnamyl bromide **3** in DMSO (40 mM), anhydrous DMSO (0.90 mL), and 50 uL stock solution of 4CzIPN **7** in DMSO (0.2 mM). The vial was then tightly capped and removed out of glovebox. The reaction was placed into a photoreactor (HeptatoChem HCK 1006-01-004) equipped with a blue LED (Kessil, 34W). The reactor was cooling by air flow that the temperature was ~30 °C). After 12 h, the reaction mixture was diluted with water (10 mL) and extracted with CH₂Cl₂ (20 mL × 3). The combined organic phase was washed with brine (30.0 mL), dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Crude ¹H NMR was taken to determine the *cis*/*trans* ratio.

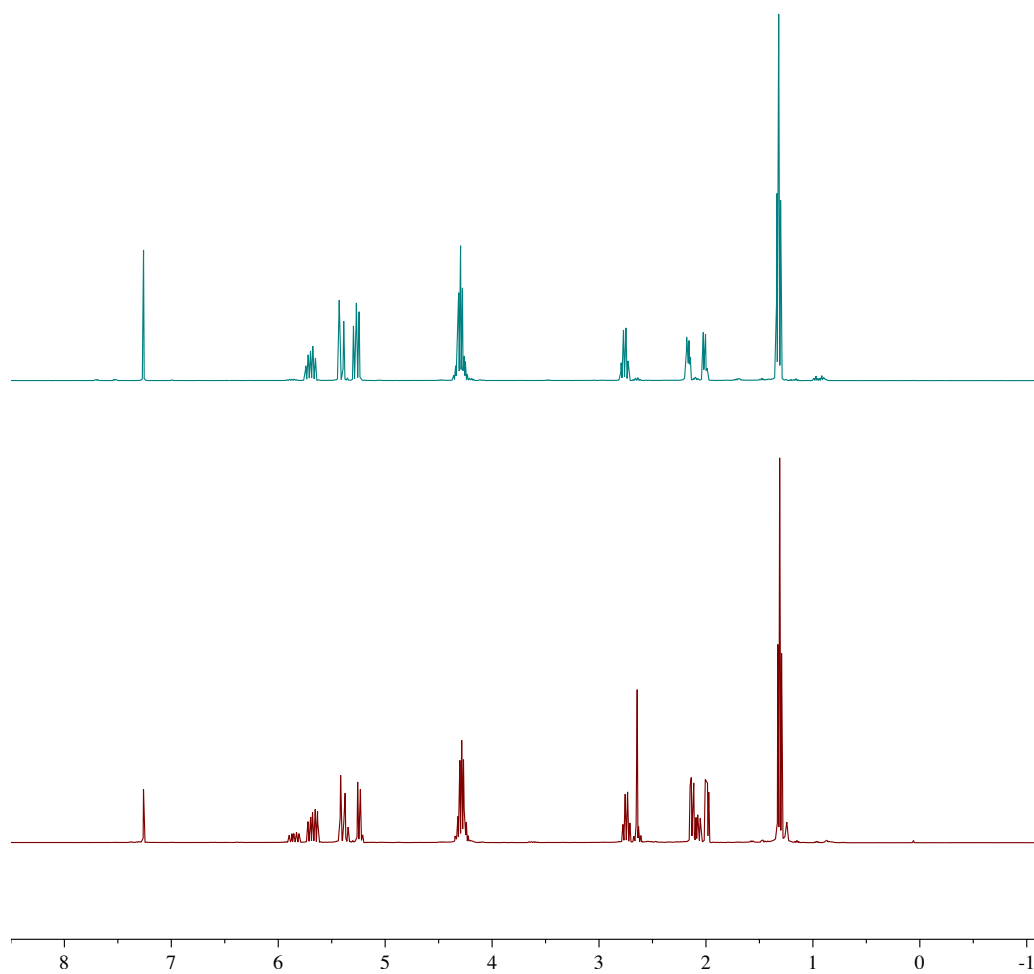


Figure S3.4. Comparison of ^1H NMR spectra before (teal, top) and after (bottom) radical epimerization

5.4 Cyclic voltammetry

Cyclic voltammetry (CV) was performed on an Interface 1010B Potentiostat (*Gamry Instruments*) with a scan rate of 0.10 V/s. A solution of Ag/AgNO₃ (0.01M) and 0.1 M Bu₄NPF₆ in MeCN was used as the reference electrode (*Gamry Instruments*, part no. 930-00059). A 0.1 M Bu₄NPF₆ in MeCN was used as the electrolyte for cinnamyl bromide solution (0.05M). A platinum disk was used for the working electrode (*Gamry Instruments*, part no. 932-00024) and a platinum wire was used as the counter electrode (*Gamry Instruments*, part no. 990-00193).

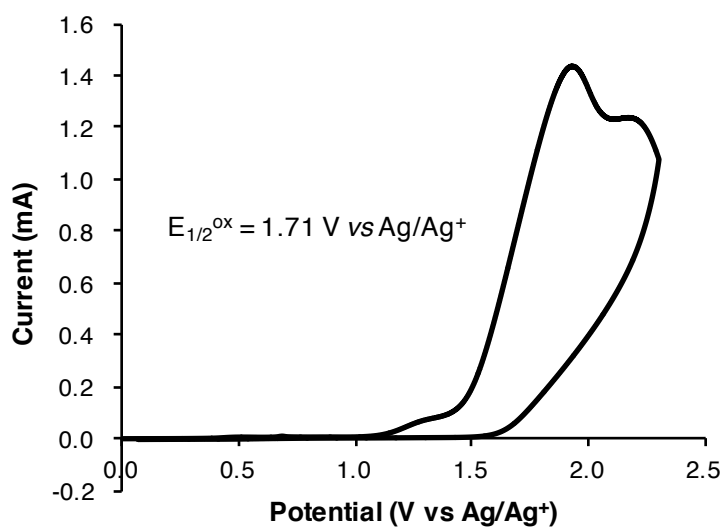


Figure S3.5. CV spectrum of cinnamyl bromide ($E_{1/2}^{ox} = 1.71 \text{ vs Ag/Ag}^+ = 2.01 \text{ V vs SCE}$)

5.5 Stern-Volmer quenching experiment

Stern-Volmer experiments were operated on spectrofluorometer FS5 (*Edinburgh Instruments*) and with different solutions containing 10.0 μM 4CzIPN **7** in DMSO and x mM **3** ($x = 1, 5, 10, 20, 40$), or vinylcyclopropane **1** ($x = 10, 20, 30, 50$), or styrene ($x = 10, 20, 30, 50$) in DMSO under irradiation at 380 nm. The luminescence was measured at 560 nm. Averaged data from three different runs were used for graphical representation.

Table S3.5. Luminescence quenching of 4CzIPN **7** at variable concentration of **3**

3a (mM)	0	1	5	10	20	40
I_0/I	1.0000	1.0344	1.1250	1.2273	1.4040	1.6488

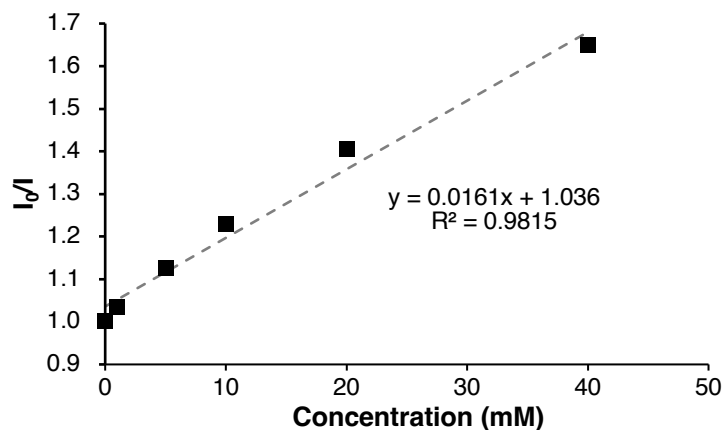


Figure S3.6. Stern-Volmer plots of 4CzIPN **7** at variable concentration of **3**.

Table S3.6. Luminescence quenching of 4CzIPN 7 at variable concentration of vinylcyclopropane 1.

1 (mM)	0	10	20	30	50
I₀/I	1.0000	1.0076	1.0013	1.0036	0.9949

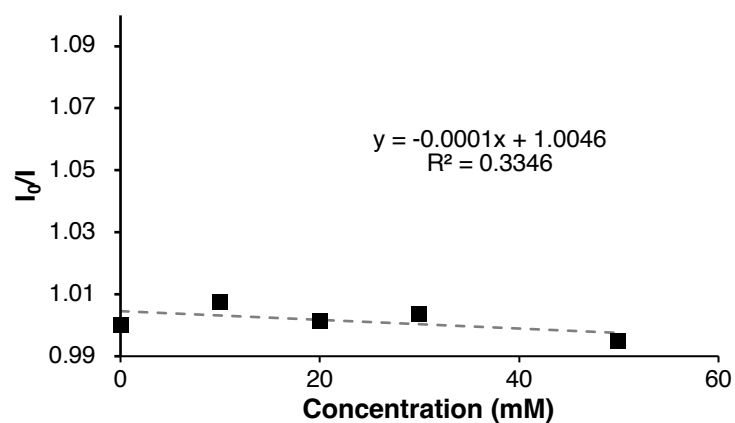


Figure S3.7. Stern-Volmer plots of 4CzIPN 7 at variable concentration of vinylcyclopropane 1.

Table S3.7. Luminescence quenching of 4CzIPN 7 at variable concentration of styrene

styrene (mM)	0	10	20	30	50
I_0/I	1.0000	1.0076	1.0013	1.0036	0.9949

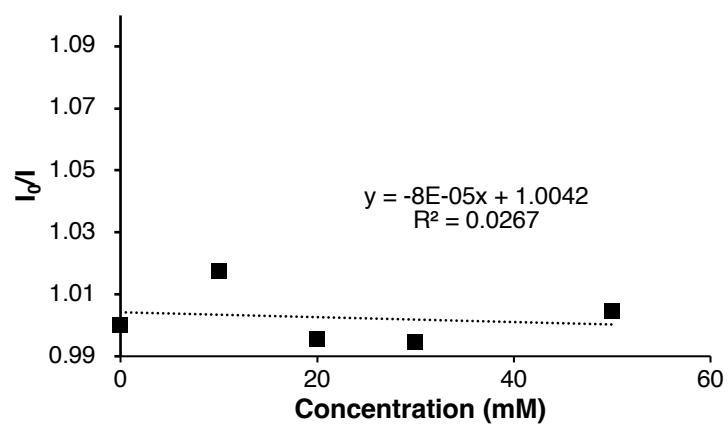


Figure S3.8. Stern-Volmer plots of 4CzIPN 7 at variable concentration of styrene.

5.6 “On/off” experiment

The reaction was set up in a N₂-filled glovebox according to the **Procedure C**. The reaction mixture was irradiated for an hour. An aliquot of 0.10 mL was taken from the reaction mixture and injected into a vial containing 0.50 mL of CDCl₃ containing trimethoxylbenzene (4.2 mg) as the internal standard. The yield of product was determined by crude ¹H NMR analysis. The reaction mixture was then wrapped by aluminum foil and re-subject to 34 W Kessil Blue LED. The yields later on were determined in the same way after some time light on or off.

Table S3.8. Results of “on/off” experiment

Entry	Time (h)	NMR Yield (%) ^a
1	0	0
2	1	15
3	2 (off)	15
4	3	27
5	4 (off)	27
6	6	46
7	7 (off)	46
8	9	60

^aTrimethoxybenzene was used as an internal standard.

5.7 Determination of quantum yield (Φ)

In a N₂-filled glovebox, an oven-dried J-Young NMR tube equipped with a micro stir bar was charged with vinylcyclopropane **1** (18.4 mg, 0.10 mmol), styrene (23.0 uL, 0.20 mmol), 25 uL stock solution of cinnamyl bromide **3** in DMSO (40 mM), anhydrous DMSO (0.45 mL), and 25 uL stock solution of 4CzIPN **7** in DMSO (0.2 mM). The sealed NMR tube was removed out of the glovebox and irradiated at 419 nm. After 8 h ($t = 28800$ s), 8.0 mg trimethoxylbenzene was added to the NMR tube. An aliquot (0.050 mL) was then taken and injected into a HPLC vial containing 0.55 mL of CDCl₃ for direct ¹H-NMR analysis. The NMR yield was determined to be 5.2% (Fig. S8).

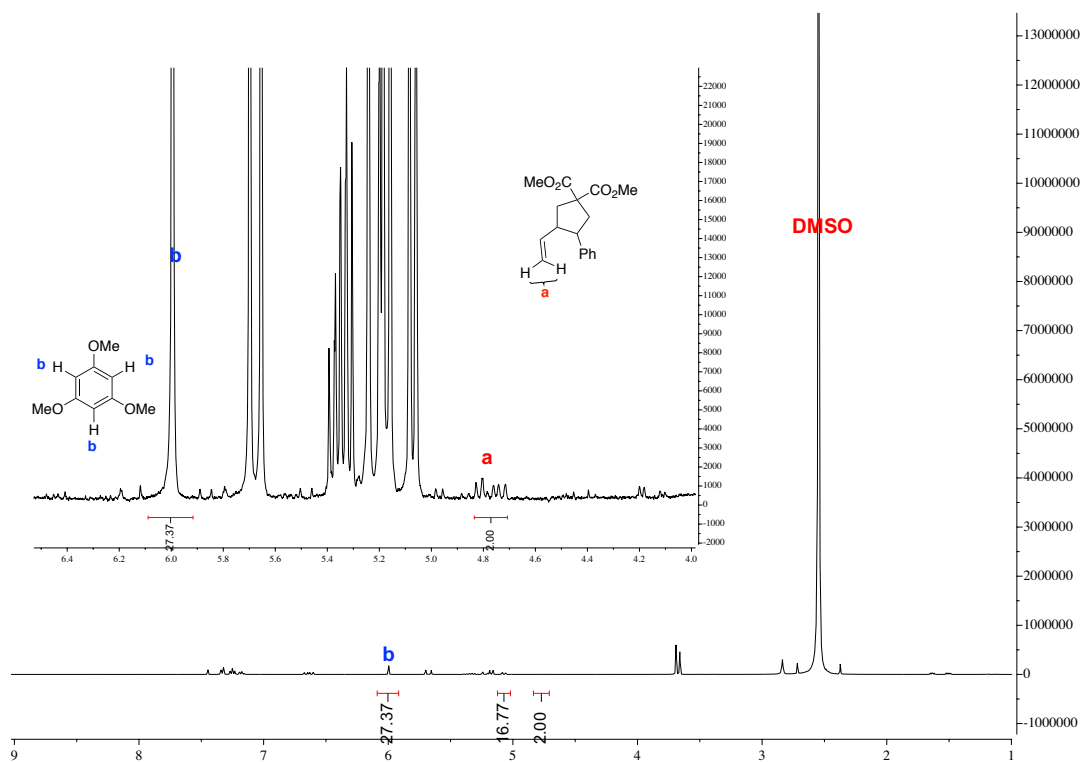


Figure S3.9. Crude ¹H NMR analysis.

The quantum yield (Φ) can be calculated by using the equation as shown below:

$$\Phi = \frac{\text{mol product}}{\text{photon flux} \cdot f \cdot t}$$

The photon flux at 419 nm for the aforementioned setup was previously determined to be 5.2×10^{-9} einstein/s.

Fraction of light absorbed (f) was calculated by $f = 1 - 10^{-A}$. A is the absorbance of PC in a specific solvent and concentration. In this experiment, the concentration of 4CzIPN was 10 μ M. A was determined to be 0.09146 at 419 nm for a 10 μ M solution of 4CzIPN in DMSO (Fig. S10), therefore, $f = 0.1899$.

The quantum yield was calculated by:

$$\Phi = \frac{\text{mol product}}{\text{photon flux} \cdot f \cdot t}$$

$$= \frac{5.2\% \times 0.1/1000}{5.2 \times 10^{-9} \times 0.1899 \times 28800} = 18.3\%$$

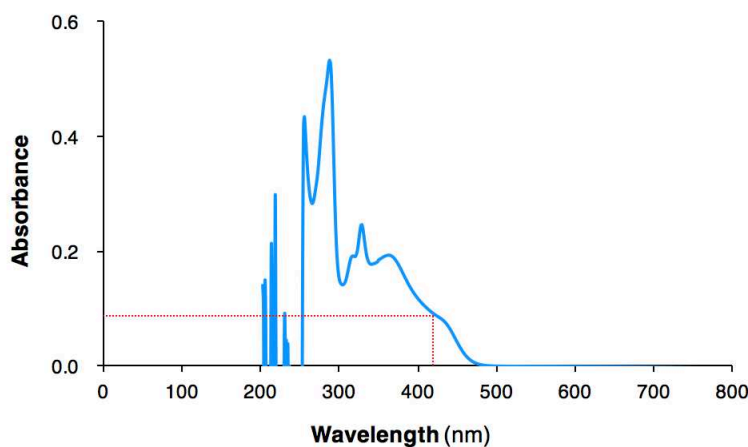
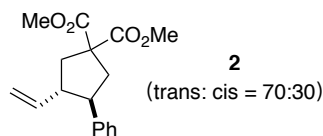


Figure S3.10. UV-Vis Spectrum of 4CZIPN in DMSO (10 μ M)

6. Characterization of Products

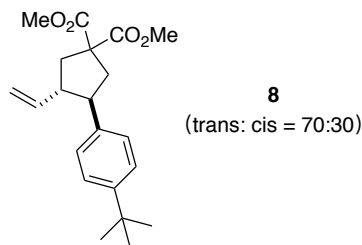


Prepared according to **Procedure C**. Colorless oil (50.4 mg, 88% yield) as a mixture of diastereomers (trans : cis = 70:30). R_f = 0.35 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.27 – 6.95 (m, 5H), 5.57 (ddd, J = 16.8, 10.8, 7.0 Hz, 0.30H), 5.29 (ddd, J = 17.1, 10.3, 8.0 Hz, 0.70H), 4.90 – 4.58 (m, 2.0H), 3.80 – 3.55 (m, 6.0H), 3.37 (dt, J = 10.7, 7.5 Hz, 0.70H), 2.94 (p, J = 7.3 Hz, 0.70H), 2.84 – 2.43 (m, 3.30H), 2.38 – 2.21 (m, 1.0H), 2.15 – 2.03 (m, 0.30H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.1, 173.0, 172.9, 172.7, 141.5, 140.8, 138.7, 138.2, 128.4, 128.3, 128.1, 127.6, 126.6, 126.3, 115.6, 115.4, 59.0, 58.1, 52.9, 52.8, 51.5, 50.9, 48.0, 47.3, 42.5, 40.3, 39.0, 38.1.

DART-TOF LC/MS m/z calcd. for $\text{C}_{17}\text{H}_{21}\text{O}_4$ $[\text{M}+\text{H}^+]$ 289.1440, found 289.1442.

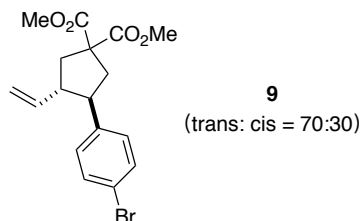


Prepared according to **Procedure C**. Colorless oil (60.1 mg, 87% yield) as a mixture of diastereomers (trans : cis = 70:30). R_f = 0.45 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.34 – 7.25 (m, 2.0H), 7.15 (d, J = 8.3 Hz, 0.60H), 7.08 (d, J = 8.3 Hz, 1.40H), 5.73 – 5.60 (m, 0.30H), 5.39 (ddd, J = 17.1, 10.3, 7.9 Hz, 0.70H), 4.99 – 4.80 (m, 2.0H), 3.82 – 3.70 (m, 6.0H), 3.41 (dt, J = 10.5, 7.4 Hz, 0.70H), 3.05 – 2.96 (m, 0.70H), 2.92 – 2.52 (m, 3.30H), 2.46 – 2.27 (m, 1.0H), 2.21 – 2.11 (m, 0.30H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.2, 173.0, 173.0, 172.7, 149.3, 149.0, 139.0, 138.4, 138.3, 137.6, 128.0, 127.2, 125.3, 124.9, 115.5, 115.3, 59.0, 58.1, 52.9, 52.8, 50.8, 50.4, 47.6, 47.2, 42.6, 40.3, 38.9, 38.2, 34.4, 34.4, 31.4.

DART-TOF LC/MS m/z calcd. for $\text{C}_{21}\text{H}_{29}\text{O}_4$ $[\text{M}+\text{H}^+]$ 345.2066, found 345.2067.

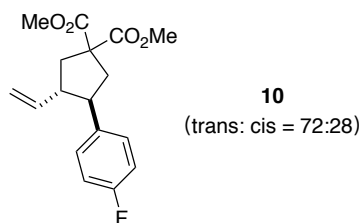


Prepared according to **Procedure C**. Colorless oil (67.3 mg, 92% yield) as a mixture of diastereomers (trans : cis = 70:30). R_f = 0.40 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.39 (dd, J = 8.4, 6.5 Hz, 2.0H), 7.09 (d, J = 8.5 Hz, 0.60H), 7.04 – 6.98 (m, 1.40H), 5.60 (ddd, J = 17.3, 10.3, 7.1 Hz, 0.30H), 5.33 (ddd, J = 17.1, 10.3, 8.1 Hz, 0.70H), 4.94 – 4.79 (m, 2.0H), 3.90 – 3.70 (m, 6.0H), 3.39 (dt, J = 10.7, 7.5 Hz, 0.70H), 3.04 – 2.93 (m, 0.70H), 2.87 – 2.47 (m, 3.30H), 2.40 – 2.26 (m, 1.0H), 2.22 – 2.09 (m, 0.30H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.0, 172.9, 172.8, 172.6, 140.6, 139.8, 138.3, 137.8, 131.5, 131.1, 130.1, 129.4, 120.3, 120.1, 116.0, 115.8, 58.9, 58.1, 53.0, 52.9, 52.9, 52.8, 51.0, 50.9, 47.5, 47.3, 42.2, 40.3, 39.0, 38.1.

DART-TOF LC/MS m/z calcd. for $\text{C}_{17}\text{H}_{19}\text{BrO}_4$ $[\text{M}+\text{H}^+]$ 367.0545, found 367.0541.



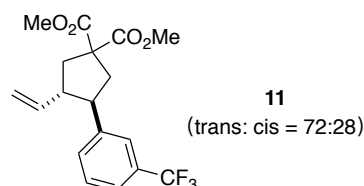
Prepared according to **Procedure C**. Colorless oil (52.7 mg, 86% yield) as a mixture of diastereomers (trans : cis = 72:28). R_f = 0.35 (10% EtOAc in hexane).

¹H NMR (400 MHz, CDCl₃) δ 7.21 – 6.90 (m, 4.0H), 5.59 (d, *J* = 17.3 Hz, 0.28H), 5.34 (ddd, *J* = 17.1, 10.3, 8.1 Hz, 0.72H), 4.94 – 4.77 (m, 2.0H), 3.90 – 3.65 (m, 6.0H), 3.41 (dt, *J* = 10.8, 7.5 Hz, 0.72H), 3.05 – 2.93 (m, 0.72H), 2.89 – 2.47 (m, 2.28H), 2.40 – 2.26 (m, 1.0H), 2.22 – 2.10 (m, 0.28H).

¹³C NMR (101 MHz, CDCl₃) δ 173.0, 172.9, 172.8, 172.6, 162.8, 162.6, 160.4, 160.2, 138.5, 138.0, 137.2, 137.1, 136.4, 136.4, 129.7, 129.6, 129.0, 128.9, 115.8, 115.6, 115.3, 115.1, 114.9, 114.7, 58.9, 58.0, 52.9, 52.8, 52.8, 51.1, 50.7, 47.4, 47.3, 42.4, 40.2, 38.9, 38.3.

¹⁹F NMR (376 MHz, CDCl₃) δ -116.6, -117.0.

DART-TOF LC/MS *m/z* calcd. for C₁₇H₁₉FO₄ [M+H⁺] 307.1346, found 307.1349.



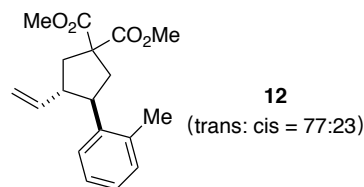
Prepared according to **Procedure C**. Colorless oil (49.6 mg, 70% yield) as a mixture of diastereomers (trans : cis = 72:28). *R*_f = 0.40 (10% EtOAc in hexane).

¹H NMR (400 MHz, CDCl₃) δ 7.49 – 7.30 (m, 4H), 5.62 (ddd, *J* = 17.4, 10.4, 7.2 Hz, 0.28H), 5.32 (ddd, *J* = 17.1, 10.3, 8.2 Hz, 0.72H), 4.96 – 4.76 (m, 2.0H), 3.90 – 3.65 (m, 6.0H), 3.55 – 3.42 (m, 0.72H), 3.17 – 3.00 (m, 0.72H), 2.98 – 2.86 (m, 0.28H), 2.85 – 2.52 (m, 3.0H), 2.45 – 2.30 (m, 1.0H), 2.25 – 2.12 (m, 0.28H).

¹³C NMR (101 MHz, CDCl₃) δ 172.9, 172.8, 172.7, 172.5, 142.6, 141.7, 138.2, 137.5, 131.7, 131.7, 131.7, 131.0, 130.9, 130.8, 130.5, 130.5, 130.2, 129.9, 128.8, 128.5, 125.6, 125.1, 125.1, 125.0, 125.0, 124.4, 124.4, 124.3, 123.5, 123.4, 123.4, 123.2, 123.2, 123.1, 123.1, 122.9, 116.2, 116.1, 58.9, 58.1, 53.0, 52.9, 52.8, 51.1, 51.0, 47.9, 47.3, 42.2, 40.3, 38.9, 37.9.

¹⁹F NMR (376 MHz, CDCl₃) δ -62.60, -62.61.

DART-TOF LC/MS m/z calcd. for C₁₈H₁₉F₃O₄ [M+H⁺] 357.1314, found 357.1314.

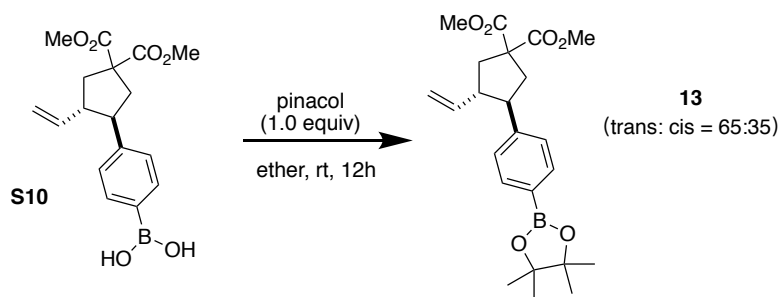


Prepared according to **Procedure C**. Colorless oil (53.9 mg, 89% yield) as a mixture of diastereomers (trans : cis = 72:28). R_f = 0.40 (10% EtOAc in hexane).

¹H NMR (400 MHz, CDCl₃) δ 7.24 – 7.06 (m, 4.0H), 5.63 (ddd, *J* = 17.4, 10.4, 7.2 Hz, 0.23H), 5.31 (ddd, *J* = 17.0, 10.3, 8.3 Hz, 0.77H), 4.97 – 4.70 (m, 2.0H), 3.83 – 3.72 (m, 6.0H), 3.58 (ddd, *J* = 11.0, 8.3, 7.1 Hz, 0.77H), 3.23 – 3.03 (m, 1.0H), 2.95 – 2.55 (m, 3.0H), 2.39 – 2.27 (m, 3.77H), 2.13 (ddd, *J* = 13.8, 11.3, 2.4 Hz, 0.46H).

¹³C NMR (101 MHz, CDCl₃) δ 173.1, 173.0, 173.0, 172.7, 139.6, 138.6, 138.5, 138.3, 136.5, 136.4, 130.2, 130.1, 126.7, 126.3, 126.2, 126.1, 125.7, 125.6, 115.6, 114.9, 58.8, 58.0, 52.9, 52.8, 50.0, 46.6, 45.0, 43.9, 42.1, 40.0, 39.1, 38.1, 20.1, 19.8.

DART-TOF LC/MS m/z calcd. for C₁₈H₂₃O₄ [M+H⁺] 303.1596, found 303.1595.

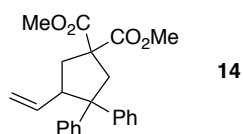


The boric acid product **S10** was prepared according to **Procedure C**. To a solution of crude **S10** in anhydrous ether (10.0 mL), pinacol (23.6 mg, 0.2 mmol, 1.0 equiv) was added. The reaction was stirred at room temperature for 12h. The solvent was then removed under vacuum, and the residue was purified by silica gel chromatography to give **13** as a colorless oil (69.7 mg, 84% yield, trans : cis = 65:35). R_f = 0.45 (10% EtOAc in hexane).

¹H NMR (400 MHz, CDCl₃) δ 7.78 – 7.66 (m, 2.0H), 7.24 – 7.20 (m, 0.70H), 7.17 – 7.12 (m, 1.30H), 5.62 (ddd, *J* = 16.7, 10.7, 7.1 Hz, 0.35H), 5.34 (ddd, *J* = 17.1, 10.3, 8.0 Hz, 0.65H), 4.92 – 4.74 (m, 2.0H), 3.95 – 3.65 (m, 6.0H), 3.50 – 3.40 (m, 0.65H), 3.10 – 2.98 (m, 0.65H), 2.88 (td, *J* = 11.1, 7.6 Hz, 0.35H), 2.81 – 2.53 (m, 3.0H), 2.44 – 2.30 (m, 1.0H), 2.22 – 2.12 (m, 0.35H), 1.32 (s, 12.0H).

¹³C NMR (101 MHz, CDCl₃) δ 173.1, 172.9, 172.8, 172.6, 144.8, 144.0, 138.6, 138.0, 134.9, 134.6, 127.8, 127.1, 115.7, 115.5, 83.7, 59.0, 58.1, 52.9, 52.8, 52.8, 51.7, 50.9, 48.2, 47.3, 42.3, 40.3, 39.0, 37.9, 24.9, 24.9, 24.8.

DART-TOF LC/MS *m/z* calcd. for C₂₃H₃₂BO₆ [M+H]⁺ 415.2292, found 415.2292.

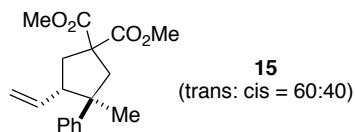


Prepared according to **Procedure C**. Colorless oil (70.1 mg, 96% yield). *R*_f = 0.40 (10% EtOAc in hexane).

¹H NMR (400 MHz, CDCl₃) δ 7.36 – 6.75 (m, 10H), 5.37 (ddd, *J* = 17.1, 10.3, 8.1 Hz, 1H), 5.03 (dd, *J* = 17.2, 1.4 Hz, 1H), 4.92 – 4.81 (m, 1H), 3.69 (s, 3H), 3.56 (dd, *J* = 8.6, 6.4 Hz, 1H), 3.47 (s, 3H), 3.44 (d, *J* = 14.7 Hz, 1H), 2.89 (d, *J* = 14.7 Hz, 1H), 2.59 (dd, *J* = 13.8, 6.4 Hz, 1H), 2.14 (dd, *J* = 13.8, 9.2 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ 172.7, 172.6, 148.2, 144.9, 138.5, 129.0, 128.1, 127.6, 127.4, 126.1, 126.0, 116.1, 58.1, 57.8, 53.0, 52.8, 50.2, 46.5, 38.7.

DART-TOF LC/MS *m/z* calcd. for C₂₃H₂₅O₄ [M+H]⁺ 365.1753, found 365.1758.

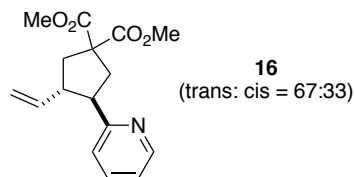


Prepared according to **Procedure C**. Colorless oil (50.0 mg, 83% yield) as a mixture of diastereomers (trans : cis = 60:40). R_f = 0.40 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.39 – 7.01 (m, 5.0H), 5.64 (ddd, J = 17.4, 10.5, 7.0 Hz, 0.60H), 5.11 (ddd, J = 17.1, 10.1, 8.5 Hz, 0.40H), 4.99 – 4.72 (m, 2.0H), 3.75 – 3.61 (m, 6.0H), 3.04 – 2.89 (m, 1.0H), 2.72 – 2.58 (m, 1.0H), 2.58 – 2.33 (m, 2.60H), 2.22 (dd, J = 13.8, 8.6 Hz, 0.40H), 1.33 (s, 1.20H), 1.14 (d, J = 0.8 Hz, 1.80H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.4, 173.4, 173.0, 172.8, 147.7, 146.0, 138.6, 136.6, 128.2, 127.8, 127.3, 126.1, 126.0, 125.8, 116.5, 115.6, 58.7, 57.5, 55.0, 53.0, 53.0, 52.9, 52.9, 52.8, 49.9, 49.5, 48.8, 45.8, 39.2, 38.3, 29.4, 21.8.

DART-TOF LC/MS m/z calcd. for $\text{C}_{18}\text{H}_{23}\text{O}_4$ $[\text{M}+\text{H}^+]$ 303.1596, found 303.1602.

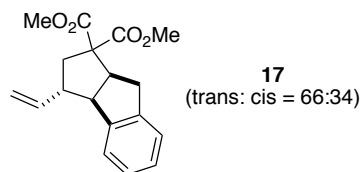


Prepared according to **Procedure C**. Colorless oil (30.2 mg, 52% yield) as a mixture of diastereomers (trans : cis = 67:33). R_f = 0.25 (30% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 8.58 – 8.44 (m, 1.0H), 7.63 – 7.48 (m, 1.0H), 7.17 – 7.01 (m, 2.0H), 5.67 (ddd, J = 17.1, 10.4, 7.5 Hz, 0.33H), 5.33 (ddd, J = 17.1, 10.2, 8.3 Hz, 0.67H), 4.94 – 4.69 (m, 2.0H), 3.85 – 3.69 (m, 6.0H), 3.56 (dd, J = 8.0, 7.9 Hz, 0.67H), 3.18 – 2.68 (m, 3.33H), 2.62 – 2.43 (m, 1.67H), 2.13 (dd, J = 13.7, 10.7 Hz, 0.33H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.5, 173.1, 172.6, 172.6, 160.8, 160.8, 149.4, 148.9, 138.9, 138.1, 136.2, 135.7, 123.3, 123.0, 121.7, 121.3, 115.5, 115.4, 59.6, 58.4, 53.3, 52.9, 52.8, 52.8, 52.7, 50.3, 50.2, 47.7, 40.9, 40.1, 39.1, 37.8.

DART-TOF LC/MS m/z calcd. for $\text{C}_{16}\text{H}_{20}\text{NO}_4$ $[\text{M}+\text{H}^+]$ 290.1392, found 290.1393.

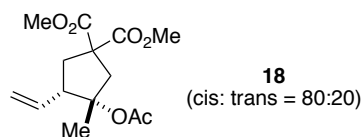


Prepared according to **Procedure C**. Colorless oil (54.8 mg, 91% yield) as a mixture of diastereomers (trans : cis = 66:34). $R_f = 0.40$ (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.20 – 7.05 (m, 4.0H), 5.95 – 5.79 (m, 0.34H), 5.35 (ddd, $J = 17.1$, 10.1, 8.6 Hz, 0.66H), 5.12 – 4.88 (m, 2.0H), 4.01 – 3.71 (m, 6.68H), 3.66 (s, 1.0H), 3.49 (dd, $J = 8.5$, 7.1 Hz, 0.34H), 3.08 (ddd, $J = 16.7$, 9.7, 7.9 Hz, 1.0H), 2.91 – 2.72 (m, 1.66H), 2.67 – 2.55 (m, 0.66H), 2.28 – 1.94 (m, 1.66H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.8, 172.3, 171.2, 170.8, 145.2, 142.7, 142.0, 141.7, 140.6, 138.9, 126.9, 126.9, 126.8, 126.7, 125.9, 124.4, 124.1, 123.8, 115.2, 114.7, 64.1, 62.9, 56.5, 52.9, 52.9, 52.7, 52.5, 52.3, 50.2, 50.0, 47.8, 45.5, 41.8, 37.9, 35.9, 34.9.

DART-TOF LC/MS m/z calcd. for $\text{C}_{18}\text{H}_{21}\text{O}_4$ $[\text{M}+\text{H}^+]$ 301.1440, found 301.1442.

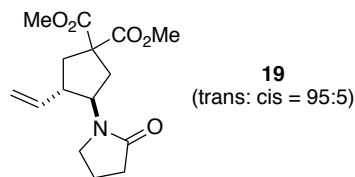


Prepared according to **Procedure C**. Colorless oil (19.0 mg, 32% yield) as a mixture of diastereomers (cis : trans = 80:20). $R_f = 0.35$ (30% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.87 – 5.60 (m, 1.0H), 5.17 – 5.05 (m, 2.0H), 3.93 – 3.52 (m, 6.0H), 3.40 (d, $J = 15.4$ Hz, 0.20H), 2.99 – 2.87 (m, 0.80H), 2.83 – 2.57 (m, 2.40H), 2.52 – 2.18 (m, 0.80H), 2.04 (dd, $J = 14.0$, 9.4 Hz, 0.80H), 1.95 (s, 2.40H), 1.92 (s, 0.60H), 1.52 (s, 0.60H), 1.37 (s, 2.40H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.0, 172.4, 172.4, 172.3, 170.5, 170.3, 136.0, 134.9, 118.1, 117.1, 89.2, 88.6, 57.3, 57.1, 55.5, 52.9, 52.8, 52.7, 51.9, 45.1, 43.5, 38.2, 36.0, 22.0, 22.0, 21.2, 20.0.

DART-TOF LC/MS m/z calcd. for $\text{C}_{14}\text{H}_{24}\text{NO}_6$ $[\text{M}+\text{NH}_4^+]$ 302.1604, found 302.1604.

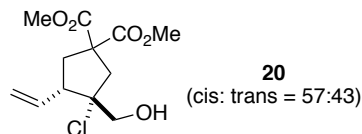


Prepared according to **Procedure C**. Colorless oil (45.4 mg, 77% yield) as a mixture of diastereomers (trans : cis = 95:5). R_f = 0.30 (50% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.77 – 5.62 (m, 1H), 5.07 – 4.91 (m, 2H), 4.59 (q, J = 8.0 Hz, 1H), 3.68 (d, J = 6.3 Hz, 6H), 3.32 (dt, J = 9.3, 7.0 Hz, 1H), 3.24 (dt, J = 9.3, 6.8 Hz, 1H), 2.90 (dddd, J = 9.7, 6.9, 2.8, 1.5 Hz, 1H), 2.60 (ddd, J = 14.4, 8.1, 1.0 Hz, 1H), 2.49 (ddd, J = 13.8, 7.1, 0.9 Hz, 1H), 2.36 – 2.23 (m, 3H), 2.16 (dd, J = 13.7, 9.6 Hz, 1H), 1.93 – 1.78 (m, 2H).

^{13}C NMR (101 MHz, CDCl_3) δ 175.2, 172.1, 172.0, 136.0, 116.5, 58.2, 53.7, 53.0, 52.9, 45.7, 45.3, 37.7, 35.5, 31.1, 18.3.

DART-TOF LC/MS m/z calcd. for $\text{C}_{15}\text{H}_{23}\text{NO}_5$ $[\text{M}+\text{H}]^+$ 296.1498, found 296.1495.

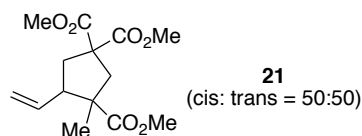


Prepared according to **Procedure C**. Colorless oil (28.3 mg, 51% yield) as a mixture of diastereomers (cis : trans = 57:43). R_f = 0.35 (50% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.82 – 5.66 (m, 1.0H), 5.23 – 5.00 (m, 2.0H), 3.79 – 3.48 (m, 8.0H), 3.14 – 2.53 (m, 4.0H), 2.38 (dd, J = 13.5, 7.0 Hz, 0.43H), 2.22 – 2.06 (m, 1.57H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.7, 172.5, 171.9, 171.6, 135.4, 134.2, 118.6, 118.2, 77.4, 77.0, 76.7, 67.8, 67.0, 57.4, 57.0, 54.9, 53.2, 53.2, 53.1, 53.0, 50.6, 46.5, 44.9, 38.2, 37.6.

DART-TOF LC/MS m/z calcd. for $\text{C}_{12}\text{H}_{18}\text{ClO}_5$ $[\text{M}+\text{H}^+]$ 277.0843, found 277.0846.

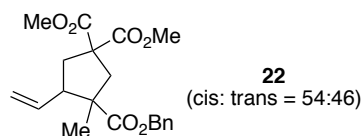


Prepared according to **Procedure C**. Colorless oil (48.6 mg, 85% yield) as a mixture of diastereomers (cis : trans = 50:50). R_f = 0.40 (20% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.85 – 5.66 (m, 0.50H), 5.66 – 5.55 (m, 0.50H), 5.12 – 4.94 (m, 2H), 3.82 – 3.48 (m, 9.0H), 3.12 – 2.98 (m, 0.50H), 2.91 (d, J = 14.4 Hz, 0.50H), 2.82 (d, J = 14.3 Hz, 0.50H), 2.57 – 2.44 (m, 1.50H), 2.40 – 2.29 (m, 1.0H), 2.28 – 2.11 (m, 1.0H), 1.26 (s, 1.50H), 1.07 (s, 1.50H).

^{13}C NMR (101 MHz, CDCl_3) δ 176.5, 175.6, 173.5, 172.5, 172.1, 136.0, 135.7, 117.1, 116.8, 58.7, 57.8, 54.6, 53.0, 53.0, 52.9, 52.9, 52.7, 52.1, 51.9, 51.5, 49.7, 44.8, 44.7, 38.9, 37.5, 22.7, 18.9.

DART-TOF LC/MS m/z calcd. for $\text{C}_{14}\text{H}_{21}\text{O}_6$ $[\text{M}+\text{H}^+]$ 285.1338, found 285.1334.

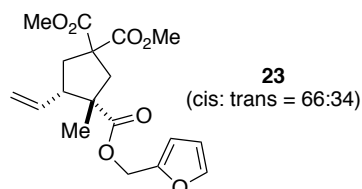


Prepared according to **Procedure C**. Colorless oil (64.7 mg, 90% yield) as a mixture of diastereomers (cis : trans = 54:46). R_f = 0.40 (50% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.39 – 7.28 (m, 5H), 5.74 (ddd, J = 17.4, 10.5, 7.2 Hz, 0.46H), 5.65 – 5.53 (m, 0.54H), 5.16 – 4.94 (m, 4.0H), 3.81 – 3.55 (m, 6.0H), 3.15 – 3.04 (m, 0.46H), 2.94 (dd, J = 32.8, 14.4 Hz, 1.0H), 2.62 – 2.48 (m, 1.54H), 2.44 – 2.14 (m, 2.0H), 1.32 (s, 1.62H), 1.13 (s, 1.38H).

^{13}C NMR (101 MHz, CDCl_3) δ 175.9, 175.1, 173.5, 172.5, 172.4, 171.9, 135.9, 135.8, 135.6, 128.5, 128.5, 128.4, 128.2, 128.1, 127.9, 117.2, 117.0, 66.6, 66.4, 58.7, 57.9, 54.7, 53.0, 53.0, 52.9, 52.9, 52.7, 51.9, 49.8, 44.8, 44.7, 38.9, 37.6, 22.9, 19.1.

DART-TOF LC/MS m/z calcd. for $\text{C}_{20}\text{H}_{25}\text{O}_6$ $[\text{M}+\text{H}^+]$ 361.1651, found 361.1652.

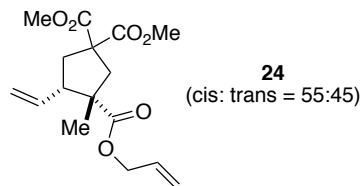


Prepared according to **Procedure C**. Colorless oil (59.6 mg, 85% yield) as a mixture of diastereomers (cis : trans = 66:34). R_f = 0.40 (20% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.39 (dd, J = 1.9, 0.8 Hz, 1.0H), 6.39 – 6.29 (m, 2.0H), 5.70 (ddd, J = 17.4, 10.5, 7.2 Hz, 0.34H), 5.60 – 5.48 (m, 0.66H), 5.10 – 4.91 (m, 4.0H), 3.70 (dd, J = 8.2, 1.9 Hz, 6.0H), 3.10 – 3.00 (m, 0.34H), 2.95 (d, J = 14.4 Hz, 0.66H), 2.84 (d, J = 14.3 Hz, 0.34H), 2.60 – 2.44 (m, 1.66H), 2.39 – 2.30 (m, 1.0H), 2.27 – 2.12 (m, 1.0H), 1.27 (s, 1.98H), 1.08 (s, 1.02H).

^{13}C NMR (101 MHz, CDCl_3) δ 175.7, 174.8, 173.5, 172.4, 172.4, 171.9, 149.5, 149.4, 143.1, 143.0, 135.8, 135.5, 117.1, 117.0, 110.6, 110.5, 110.4, 58.7, 58.4, 58.0, 57.9, 54.7, 53.0, 53.0, 52.9, 52.7, 52.0, 49.8, 44.7, 44.6, 38.9, 37.5, 22.8, 18.9.

DART-TOF LC/MS m/z calcd. for $\text{C}_{18}\text{H}_{23}\text{O}_7$ $[\text{M}+\text{H}^+]$ 351.1444, found 351.1449.

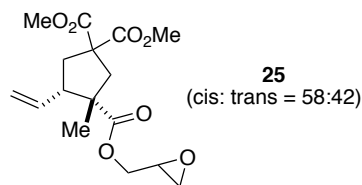


Prepared according to **Procedure C**. Colorless oil (50.7 mg, 82% yield) as a mixture of diastereomers (cis : trans = 55:45). R_f = 0.45 (20% EtOAc in hexane).

¹H NMR (400 MHz, CDCl₃) δ 6.12 – 5.48 (m, 1.0H), 5.40 – 4.94 (m, 4.0H), 4.59 – 4.45 (m, 2.0H), 3.78 – 3.63 (m, 6.0H), 3.14 – 3.02 (m, 0.45H), 2.94 (d, *J* = 14.4 Hz, 0.55H), 2.86 (d, *J* = 14.3 Hz, 0.45H), 2.61 – 2.46 (m, 1.55H), 2.42 – 2.30 (m, 1.0H), 2.29 – 2.11 (m, 1.0H), 1.29 (s, 1.65H), 1.10 (s, 1.35H).

¹³C NMR (101 MHz, CDCl₃) δ 175.7, 174.8, 173.5, 172.4, 172.4, 172.0, 136.0, 135.7, 132.1, 118.2, 118.0, 117.2, 116.9, 65.4, 65.2, 58.7, 57.9, 54.6, 53.0, 52.9, 52.9, 52.7, 51.9, 49.7, 44.8, 44.7, 39.0, 37.5, 22.8, 19.0.

DART-TOF LC/MS *m/z* calcd. for C₁₆H₂₃O₆ [M+H⁺] 311.1495, found 311.1491.

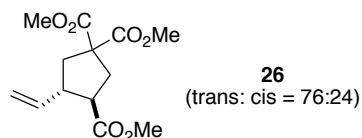


Prepared according to **Procedure C**. Colorless oil (58.6 mg, 90% yield) as a mixture of diastereomers (cis : trans = 58:42). *R_f* = 0.30 (20% EtOAc in hexane).

¹H NMR (400 MHz, CDCl₃) δ 5.81 – 5.55 (m, 1.0H), 5.13 – 4.99 (m, 2.0H), 4.39 (ddd, *J* = 12.3, 4.6, 3.0 Hz, 0.42H), 4.31 (dd, *J* = 12.2, 3.1 Hz, 0.58H), 3.90 (ddd, *J* = 12.3, 6.1, 1.5 Hz, 0.42H), 3.81 (ddd, *J* = 12.3, 6.4, 0.9 Hz, 0.58H), 3.74 – 3.67 (m, 6.0H), 3.21 – 2.73 (m, 3.40H), 2.67 – 2.46 (m, 2.60H), 2.42 – 2.13 (m, 2.0H), 1.28 (s, 1.74H), 1.09 (s, 1.26H).

¹³C NMR (101 MHz, CDCl₃) δ 175.8, 175.7, 174.9, 174.8, 173.4, 172.4, 172.0, 171.9, 135.8, 135.6, 117.3, 117.1, 117.0, 65.3, 65.2, 65.1, 65.1, 58.6, 57.9, 54.5, 54.5, 53.1, 53.0, 52.9, 52.9, 52.8, 52.7, 52.0, 52.0, 49.7, 49.2, 49.1, 49.1, 44.8, 44.7, 44.6, 44.6, 44.4, 44.4, 38.8, 38.8, 37.5, 22.8, 22.8, 19.1, 19.0.

DART-TOF LC/MS *m/z* calcd. for C₁₆H₂₆NO₇ [M+NH₄⁺] 344.1709, found 344.1705.

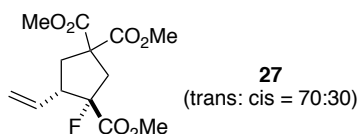


Prepared according to **Procedure C**. Colorless oil (39.8 mg, 74% yield) as a mixture of diastereomers (trans : cis = 76:24). R_f = 0.30 (30% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.82 – 5.56 (m, 1.0H), 5.16 – 4.90 (m, 2.0H), 3.89 – 3.52 (m, 9.0H), 3.17 – 2.79 (m, 1.76H), 2.74 – 2.31 (m, 4.0H), 1.97 (dd, J = 13.6, 10.8 Hz, 0.24H).

^{13}C NMR (101 MHz, CDCl_3) δ 174.0, 173.6, 172.9, 172.3, 172.0, 171.8, 138.3, 136.6, 116.5, 115.9, 59.3, 58.7, 52.9, 52.9, 52.8, 51.8, 51.5, 49.5, 48.0, 47.5, 45.8, 39.9, 38.6, 37.4, 35.9.

DART-TOF LC/MS m/z calcd. for $\text{C}_{13}\text{H}_{19}\text{O}_6$ $[\text{M}+\text{H}^+]$ 271.1182, found 271.1180.



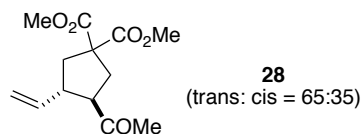
Prepared according to **Procedure C**. Colorless oil (33.3 mg, 58% yield) as a mixture of diastereomers (trans : cis = 70:30). R_f = 0.35 (30% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.84 – 5.49 (m, 1.0H), 5.24 – 4.96 (m, 2.0H), 4.01 – 3.55 (m, 9.0H), 3.28 – 2.69 (m, 3.70H), 2.57 (dd, J = 13.6, 7.7 Hz, 0.30H), 2.51 – 2.42 (m, 0.30H), 2.24 (dd, J = 13.7, 10.0 Hz, 0.70H).

^{13}C NMR (101 MHz, CDCl_3) δ 171.9, 171.5, 171.1, 171.0, 169.9, 169.8, 169.6, 169.6, 133.8, 133.7, 132.2, 132.1, 119.1, 118.6, 103.7, 103.1, 101.8, 101.1, 57.9, 57.9, 57.8, 53.2, 53.2, 53.1, 53.0, 52.8, 52.7, 52.4, 52.2, 52.0, 44.1, 43.9, 42.8, 42.6, 37.6, 37.6, 37.5.

^{19}F NMR (376 MHz, CDCl_3) δ -149.0, -170.0.

DART-TOF LC/MS m/z calcd. for $\text{C}_{13}\text{H}_{18}\text{FO}_6$ $[\text{M}+\text{H}^+]$ 289.1087, found 289.1086.

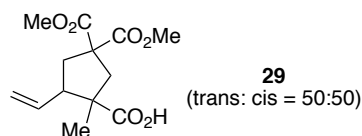


Prepared according to **Procedure C**. Colorless oil (37.0 mg, 73% yield) as a mixture of diastereomers (trans : cis = 65:35). R_f = 0.30 (30% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.71 (ddd, J = 17.0, 10.2, 7.6 Hz, 0.35H), 5.59 (ddd, J = 17.0, 10.1, 9.2 Hz, 0.65H), 5.15 – 4.96 (m, 2.0H), 3.94 – 3.50 (m, 6.0H), 3.22 (td, J = 8.6, 7.1 Hz, 0.65H), 3.08 – 2.96 (m, 0.65H), 2.86 – 2.72 (m, 0.65H), 2.67 – 2.50 (m, 1.35H), 2.48 – 2.22 (m, 2.35H), 2.12 (s, 1.05H), 2.08 (s, 1.95H), 2.02 – 1.89 (m, 0.35H).

^{13}C NMR (101 MHz, CDCl_3) δ 208.3, 208.2, 172.9, 172.4, 172.0, 171.9, 139.1, 137.0, 116.6, 116.1, 59.0, 58.7, 57.2, 55.4, 52.9, 52.9, 52.8, 47.0, 45.8, 40.3, 39.4, 36.4, 34.8, 31.0, 30.0.

DART-TOF LC/MS m/z calcd. for $\text{C}_{34}\text{H}_{19}\text{O}_5$ $[\text{M}+\text{H}^+]$ 255.1232, found 255.1233.

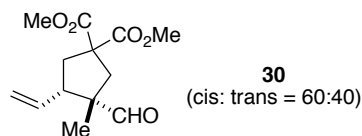


Prepared according to **Procedure C**. Colorless oil (48.7 mg, 90% yield) as a mixture of diastereomers (trans : cis = 50:50). R_f = 0.40 (10% MeOH in DCM).

^1H NMR (400 MHz, CDCl_3) δ 11.63 (brs, 1.0H), 5.93 – 5.54 (m, 1.0H), 5.19 – 4.98 (m, 2.0H), 3.88 – 3.60 (m, 6.0H), 3.13 – 3.03 (m, 0.50H), 2.95 (d, J = 14.4 Hz, 0.50H), 2.88 (d, J = 14.4 Hz, 0.50H), 2.55 (ddd, J = 12.4, 9.2, 4.8 Hz, 1.50H), 2.44 – 2.33 (m, 1.0H), 2.31 – 2.13 (m, 1.0H), 1.28 (s, 1.50H), 1.10 (s, 1.50H).

^{13}C NMR (101 MHz, CDCl_3) δ 182.7, 181.9, 173.4, 172.4, 172.4, 171.9, 135.6, 135.4, 117.7, 117.2, 58.8, 57.9, 54.7, 53.0, 53.0, 53.0, 52.8, 52.8, 51.7, 49.6, 44.8, 44.6, 39.0, 37.6, 22.6, 18.8.

DART-TOF LC/MS m/z calcd. for $\text{C}_{13}\text{H}_{20}\text{O}_6$ $[\text{M}+\text{H}^+]$ 271.1182, found 271.1185.

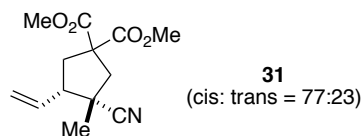


Prepared according to **Procedure C**. Colorless oil (43.8 mg, 86% yield) as a mixture of diastereomers (cis : trans = 60:40). $R_f = 0.40$ (20% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 9.48 (s, 0.40H), 9.43 (s, 0.60H), 5.76 (ddd, $J = 17.1, 10.3, 8.0$ Hz, 0.40H), 5.60 (ddd, $J = 17.1, 10.5, 7.5$ Hz, 0.60H), 5.22 – 4.97 (m, 2.0H), 3.93 – 3.55 (m, 6.0H), 2.89 (dd, $J = 11.7, 0.9$ Hz, 0.60H), 2.78 (dd, $J = 25.8, 14.5$ Hz, 1.0H), 2.52 (dd, $J = 13.6, 6.9$ Hz, 1.0H), 2.45 – 2.37 (m, 0.40H), 2.36 – 2.10 (m, 2.0H), 1.24 (s, 1.20H), 1.00 (s, 1.80H).

^{13}C NMR (101 MHz, CDCl_3) δ 204.7, 203.1, 172.9, 172.4, 172.1, 171.9, 135.0, 134.4, 118.0, 117.6, 58.4, 58.1, 56.2, 56.1, 53.8, 53.1, 53.0, 53.0, 52.9, 47.5, 41.8, 40.5, 38.9, 38.0, 19.8, 15.8.

DART-TOF LC/MS m/z calcd. for $\text{C}_{13}\text{H}_{19}\text{O}_5$ $[\text{M}+\text{H}^+]$ 255.1232, found 255.1231.

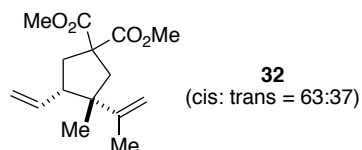


Prepared according to **Procedure C**. Colorless oil (37.8 mg, 75% yield) as a mixture of diastereomers (trans : cis = 77:23). $R_f = 0.30$ (30% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.90 – 5.62 (m, 1.0H), 5.31 – 5.14 (m, 2.0H), 3.96 – 3.53 (m, 6.0H), 3.05 – 2.90 (m, 1.0H), 2.83 (d, $J = 14.4$ Hz, 0.77H), 2.62 – 2.48 (m, 1.77H), 2.48 – 2.31 (m, 0.46H), 2.30 – 2.14 (m, 1.0H), 1.38 (s, 0.69H), 1.20 (s, 2.31H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.2, 171.7, 171.6, 171.0, 134.4, 133.3, 123.8, 122.0, 119.7, 119.2, 57.7, 57.5, 53.9, 53.3, 53.2, 53.2, 53.2, 51.5, 45.7, 45.2, 43.4, 40.3, 39.2, 36.6, 22.8, 19.7.

DART-TOF LC/MS m/z calcd. for $\text{C}_{13}\text{H}_{18}\text{NO}_4$ $[\text{M}+\text{H}^+]$ 252.1236, found 252.1232.

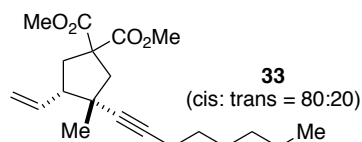


Prepared according to **Procedure C**. Colorless oil (27.1 mg, 51% yield) as a mixture of diastereomers (cis : trans = 63:37). R_f = 0.40 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.78 – 5.57 (m, 1.0H), 5.08 – 4.89 (m, 2.0H), 4.85 – 4.69 (m, 2.0H), 4.02 – 3.52 (m, 6.0H), 2.88 – 2.76 (m, 1.0H), 2.71 (dd, J = 14.1, 6.8 Hz, 0.37H), 2.51 – 2.20 (m, 3.63H), 1.77 (d, J = 1.0 Hz, 1.89H), 1.69 (d, J = 1.4 Hz, 1.11H), 1.11 (s, 1.11H), 0.96 (s, 1.89H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.5, 173.4, 173.1, 173.0, 149.7, 149.6, 139.0, 137.0, 116.0, 114.7, 111.0, 110.5, 58.5, 57.4, 53.3, 52.9, 52.9, 52.8, 51.3, 49.9, 49.0, 46.2, 44.0, 38.9, 38.0, 26.2, 21.0, 20.1, 20.0.

DART-TOF LC/MS m/z calcd. for $\text{C}_{15}\text{H}_{26}\text{NO}_4$ $[\text{M}+\text{NH}_4^+]$ 284.1862, found 284.1868.

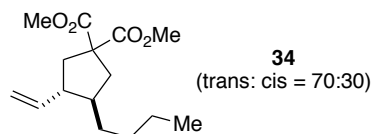


Prepared according to **Procedure C**. Colorless oil (33.6 mg, 50% yield) as a mixture of diastereomers (cis : trans = 80:20). R_f = 0.45 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.88 – 2.42 (m, 1.0H), 5.24 – 4.88 (m, 2.0H), 3.93 – 3.43 (m, 6.0H), 2.81 – 2.63 (m, 1.0H), 2.60 – 2.42 (m, 2.60H), 2.33 – 2.02 (m, 3.40H), 1.50 – 1.21 (m, 8.0H), 1.19 (s, 0.60H), 0.99 (s, 2.40H), 0.90 – 0.84 (m, 3.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.5, 172.8, 172.8, 172.2, 137.6, 136.2, 116.8, 116.4, 85.8, 83.9, 82.5, 80.9, 57.8, 57.7, 55.0, 53.4, 52.9, 52.8, 52.8, 52.6, 48.9, 48.0, 42.5, 40.8, 39.4, 36.8, 31.3, 31.3, 29.0, 28.9, 28.4, 28.4, 25.3, 22.5, 22.0, 18.6, 14.0, 14.0.

DART-TOF LC/MS m/z calcd. for $\text{C}_{20}\text{H}_{31}\text{O}_4$ $[\text{M}+\text{H}^+]$ 335.2222, found 335.2226.

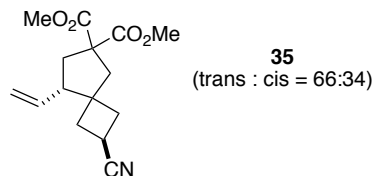


Prepared according to **Procedure C**. Colorless oil (31.2 mg, 58% yield) as a mixture of diastereomers (trans : cis = 70:30). R_f = 0.45 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.80 – 5.50 (m, 1H), 5.06 – 4.91 (m, 2.0H), 3.76 – 3.66 (m, 6.0H), 2.76 – 2.62 (m, 0.70H), 2.59 – 2.51 (m, 0.30H), 2.47 (dd, J = 13.9, 7.1 Hz, 1.0H), 2.40 – 2.31 (m, 0.70H), 2.23 – 1.89 (m, 3.0H), 1.78 (dd, J = 13.4, 10.8 Hz, 0.30H), 1.67 – 1.05 (m, 6.0H), 0.90 – 0.82 (m, 3.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 168.6, 168.5, 168.4, 168.4, 135.6, 133.6, 110.5, 110.4, 72.6, 72.3, 72.0, 54.2, 53.6, 48.0, 48.0, 45.7, 41.6, 40.5, 38.3, 35.9, 35.6, 34.5, 28.1, 25.6, 25.6, 25.3, 18.1, 18.1, 9.3, 9.2.

DART-TOF LC/MS m/z calcd. for $\text{C}_{15}\text{H}_{25}\text{O}_4$ $[\text{M}+\text{H}^+]$ 269.1753, found 269.1757.

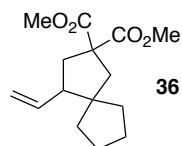


Prepared according to **Procedure C**. Colorless oil (39.8 mg, 72% yield) as a mixture of diastereomers (trans : cis = 66:34). R_f = 0.30 (20% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.84 – 5.64 (m, 1.0H), 5.31 – 4.96 (m, 2.0H), 3.90 – 3.45 (m, 6.0H), 3.07 – 2.92 (m, 0.34H), 2.88 – 2.73 (m, 0.66H), 2.61 (dd, J = 27.5, 14.0 Hz, 1.0H), 2.52 – 1.88 (m, 8.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.5, 172.5, 172.5, 136.0, 135.7, 122.4, 122.0, 118.4, 118.3, 57.4, 57.3, 52.3, 52.9, 51.5, 51.4, 47.5, 47.3, 47.2, 45.3, 37.9, 37.7, 34.4, 34.4, 33.3, 32.4, 16.9, 16.4.

DART-TOF LC/MS m/z calcd. for $\text{C}_{15}\text{H}_{23}\text{N}_2\text{O}_4$ $[\text{M}+\text{NH}_4^+]$ 295.1658, found 295.1656.

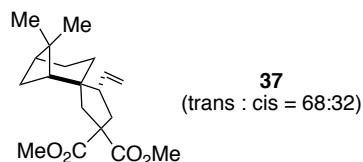


Prepared according to **Procedure C** (0.4 mmol). Colorless oil (67.2 mg, 63% yield). $R_f = 0.45$ (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.78 – 5.60 (m, 1H), 5.08 – 4.91 (m, 2H), 3.70 (s, 3H), 3.69 (s, 3H), 2.57 – 2.31 (m, 3H), 2.19 – 2.01 (m, 2H), 1.65 – 1.13 (m, 8H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.4, 173.2, 137.6, 116.2, 57.8, 53.7, 52.7, 52.7, 51.8, 47.4, 39.2, 37.2, 32.1, 24.7, 24.4.

DART-TOF LC/MS m/z calcd. for $\text{C}_{15}\text{H}_{23}\text{O}_4$ $[\text{M}+\text{H}^+]$ 267.1596, found 267.1600.

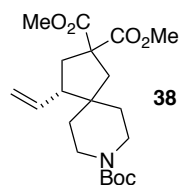


Prepared according to **Procedure C**. Colorless oil (43.5 mg, 68% yield) as a mixture of diastereomers (trans : cis = 68:32). $R_f = 0.40$ (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.97 – 5.82 (m, 0.68H), 5.72 – 5.52 (m, 0.32H), 5.09 – 4.81 (m, 2.0H), 3.75 – 3.65 (m, 6.0H), 2.60 (d, $J = 14.1$ Hz, 0.68H), 2.50 – 2.24 (m, 2.64H), 2.18 (d, $J = 14.1$ Hz, 0.68H), 2.12 – 1.97 (m, 2.0H), 1.94 – 1.59 (m, 5.32H), 1.45 – 1.22 (m, 1.68H), 1.17 (s, 3.0H), 0.99 (s, 2.04H), 0.97 (s, 0.96H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.5, 173.4, 173.3, 173.3, 139.1, 138.9, 115.9, 114.8, 59.4, 57.8, 55.9, 53.5, 52.8, 52.7, 52.7, 50.6, 50.2, 49.3, 48.4, 47.2, 40.2, 39.8, 39.2, 38.9, 38.3, 37.8, 29.6, 28.1, 27.8, 27.8, 27.6, 25.6, 25.4, 23.9, 23.8, 22.6.

DART-TOF LC/MS m/z calcd. for $\text{C}_{19}\text{H}_{32}\text{NO}_4$ $[\text{M}+\text{NH}_4^+]$ 338.2331, found 338.2326.

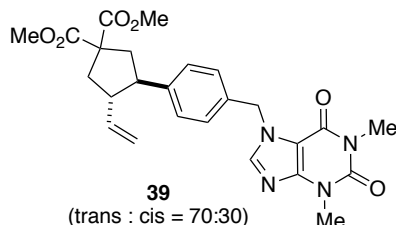


Prepared according to **Procedure C**. Colorless oil (50.3 mg, 66% yield). $R_f = 0.30$ (30% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.63 (ddd, $J = 17.0, 10.3, 7.7$ Hz, 1H), 5.11 – 4.92 (m, 2H), 3.89 (brs, 2H), 3.70 (s, 3H), 3.70 (s, 3H), 2.93 – 2.67 (m, 2H), 2.57 (d, $J = 14.2$ Hz, 1H), 2.48 (dd, $J = 12.9, 6.0$ Hz, 1H), 2.35 – 2.11 (m, 2H), 2.01 (dd, $J = 14.1, 1.5$ Hz, 1H), 1.64 – 1.50 (m, 1H), 1.41 (s, 9H), 1.34 – 1.13 (m, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.1, 173.0, 154.8, 136.3, 117.1, 79.3, 57.8, 53.6, 52.9, 52.8, 44.3, 41.7, 37.5, 36.1, 29.7, 28.4.

DART-TOF LC/MS m/z calcd. for $\text{C}_{20}\text{H}_{32}\text{NO}_6$ $[\text{M}+\text{H}^+]$ 382.2230, found 382.2232.

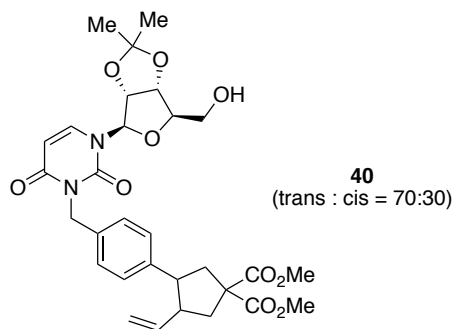


Prepared according to **Procedure C**. Colorless oil (82.5 mg, 86% yield) as a mixture of diastereomers (trans : cis = 70:30). $R_f = 0.30$ (30% acetone in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.52 (s, 0.30H), 7.51 (s, 0.70H), 7.23 – 7.04 (m, 4.0H), 5.54 (ddd, $J = 17.2, 10.5, 7.0$ Hz, 0.30H), 5.40 (s, 2.0H), 5.25 (ddd, $J = 17.1, 10.3, 8.0$ Hz, 0.70H), 4.86 – 4.68 (m, 2.0H), 3.90 – 3.58 (m, 6.0H), 3.49 (s, 3H), 3.42 – 3.26 (m, 3.70H), 3.00 – 2.88 (m, 0.70H), 2.86 – 2.74 (m, 0.30H), 2.72 – 2.41 (m, 3.0H), 2.33 – 2.16 (m, 1.0H), 2.14 – 2.03 (m, 0.30H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.9, 172.8, 172.7, 172.5, 155.2, 151.6, 148.8, 142.1, 141.4, 140.9, 138.5, 137.8, 133.7, 133.3, 129.0, 128.3, 128.1, 127.8, 115.8, 115.6, 106.9, 106.9, 58.8, 58.0, 52.9, 52.8, 52.8, 50.9, 50.7, 49.9, 49.9, 47.7, 47.3, 42.2, 40.2, 38.9, 38.0, 29.7, 27.9.

DART-TOF LC/MS m/z calcd. for $\text{C}_{25}\text{H}_{29}\text{N}_4\text{O}_6$ $[\text{M}+\text{H}^+]$ 481.2087, found 481.2089.

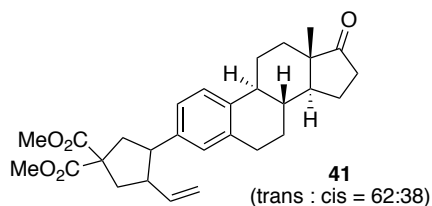


Prepared according to **Procedure C**. Colorless oil (85.2 mg, 73% yield) as a mixture of diastereomers (trans : cis = 70:30). R_f = 0.30 (30% acetone in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.40 – 7.31 (m, 3.0H), 7.17 – 7.00 (m, 2.0H), 5.73 (dd, J = 8.0, 1.1 Hz, 1.0H), 5.66 – 5.54 (m, 1.30H), 5.33 (ddd, J = 17.1, 10.3, 7.9 Hz, 0.70H), 5.12 – 4.76 (m, 6.0H), 4.28 (q, J = 2.9 Hz, 1.0H), 3.94 – 3.82 (m, 1.0H), 3.81 – 3.69 (m, 7.0H), 3.43 – 3.30 (m, 0.70H), 3.10 – 2.92 (m, 1.70H), 2.88 – 2.77 (m, 0.30H), 2.76 – 2.46 (m, 3.0H), 2.36 (dd, J = 14.0, 6.0 Hz, 0.70H), 2.32 – 2.22 (m, 0.30H), 2.19 – 2.07 (m, 0.30H), 1.55 (s, 3.0H), 1.34 (s, 3.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.1, 172.9, 172.9, 172.6, 162.6, 151.0, 141.1, 140.5, 140.3, 138.6, 138.1, 134.6, 134.3, 129.3, 128.9, 128.4, 127.6, 115.7, 115.5, 114.2, 102.0, 96.4, 96.4, 86.9, 84.0, 80.4, 62.6, 58.9, 58.1, 52.9, 52.9, 52.8, 51.0, 50.6, 50.5, 47.7, 47.2, 43.9, 42.5, 40.2, 38.9, 38.1, 27.3, 25.3.

ESI-TOF LC/MS m/z calcd. for $\text{C}_{30}\text{H}_{37}\text{N}_2\text{O}_{10}$ $[\text{M}+\text{H}^+]$ 585.2448, found 585.2453.

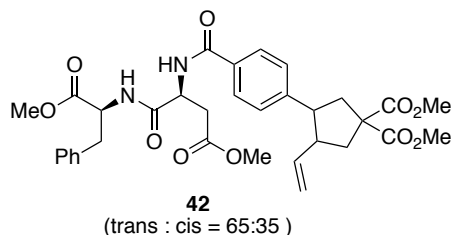


Prepared according to **Procedure C**. Colorless oil (50.8 mg, 55% yield) as a mixture of diastereomers (trans : cis = 62:38). R_f = 0.35 (20% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.24 – 7.15 (m, 1.0H), 7.05 – 6.82 (m, 2.0H), 5.73 – 5.58 (m, 0.38H), 5.49 – 5.32 (m, 0.62H), 5.01 – 4.76 (m, 2.0H), 4.00 – 3.55 (m, 6.0H), 3.44 – 3.27 (m, 0.62H), 3.06 – 2.95 (m, 0.62H), 2.92 – 1.91 (m, 13.76H), 1.74 – 1.37 (m, 6.0H), 0.90 (s, 3.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.1, 173.0, 173.0, 172.9, 172.7, 138.9, 138.9, 138.4, 138.1, 138.1, 138.0, 138.0, 137.6, 136.4, 136.4, 136.0, 129.2, 128.8, 128.4, 128.0, 126.0, 125.7, 125.4, 125.4, 125.1, 125.0, 124.8, 115.5, 115.3, 58.9, 58.0, 52.9, 52.8, 50.9, 50.9, 50.5, 50.3, 50.3, 48.0, 47.5, 47.5, 47.1, 47.1, 44.3, 44.3, 42.7, 42.6, 40.2, 39.0, 38.3, 38.2, 38.2, 38.1, 35.9, 31.6, 29.7, 29.5, 29.4, 26.6, 25.7, 21.6, 13.9.

DART-TOF LC/MS m/z calcd. for $\text{C}_{29}\text{H}_{37}\text{O}_5$ $[\text{M}+\text{H}^+]$ 465.2641, found 465.2642.



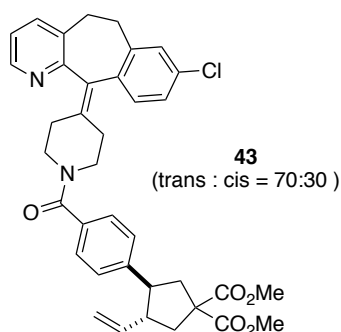
Prepared according to **Procedure C**. Colorless oil (100.4 mg, 81% yield) as a mixture of diastereomers (trans : cis = 65:35). R_f = 0.30 (30% acetone in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.72 – 7.54 (m, 3.0H), 7.35 – 6.98 (m, 8.0H), 5.69 – 5.56 (m, 0.35H), 5.34 (ddd, J = 17.1, 10.3, 8.2 Hz, 0.65H), 5.07 – 4.70 (m, 4.0H), 3.83 – 3.76 (m, 6.0H),

3.71 (s, 6.0H), 3.55 – 3.44 (m, 0.65H), 3.19 – 2.53 (m, 8.0H), 2.44 – 2.32 (m, 1.0H), 2.26 – 2.13 (m, 0.35H).

¹³C NMR (101 MHz, CDCl₃) δ 173.1, 173.1, 173.0, 172.9, 172.8, 172.5, 171.4, 170.2, 167.0, 146.2, 145.4, 138.3, 137.7, 135.6, 135.6, 131.5, 131.1, 129.1, 128.6, 128.5, 128.5, 127.9, 127.4, 127.0, 127.0, 116.1, 115.9, 59.0, 58.2, 53.5, 53.0, 53.0, 52.9, 52.9, 52.4, 52.2, 51.3, 49.3, 47.9, 47.5, 42.1, 40.4, 39.0, 38.0, 37.9, 37.7, 34.8.

ESI-TOF LC/MS m/z calcd. for C₃₃H₄₂N₃O₁₀ [M+NH₄⁺] 640.2870, found 640.2872.

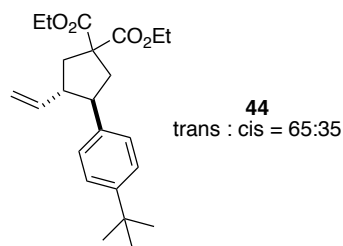


Prepared according to **Procedure C**. Colorless oil (92.7 mg, 74% yield) as a mixture of diastereomers (trans : cis = 70:30). R_f = 0.35 (30% acetone in hexane).

¹H NMR (400 MHz, CDCl₃) δ 8.37 (brs, 1.0H), 7.50 – 6.95 (m, 9.0H), 5.59 (ddd, *J* = 17.2, 10.5, 6.9 Hz, 0.30H), 5.29 (ddd, *J* = 17.0, 10.3, 8.0 Hz, 0.70H), 4.89 – 4.74 (m, 2.0H), 4.17 (brs, 1.0H), 3.86 – 3.70 (m, 6.0H), 3.68 – 3.54 (m, 1H), 3.50 – 3.13 (m, 4.30H), 3.05 – 2.94 (m, 0.70H), 2.91 – 2.08 (m, 11.0H).

¹³C NMR (101 MHz, CDCl₃) δ 173.0, 172.9, 172.8, 172.5, 170.4, 170.4, 146.7, 143.4, 142.7, 139.6, 138.3, 137.8, 137.6, 136.9, 134.7, 134.3, 133.9, 133.4, 133.0, 130.5, 129.0, 128.4, 127.7, 127.1, 126.8, 126.2, 122.3, 115.9, 115.8, 58.9, 58.1, 53.0, 52.9, 52.9, 52.9, 51.2, 50.9, 47.9, 47.3, 42.3, 40.3, 38.9, 38.1, 31.7, 31.6, 31.5.

ESI-TOF LC/MS m/z calcd. for C₃₇H₃₈ClN₂O₅ [M+H]⁺ 625.2469, found 625.2473.

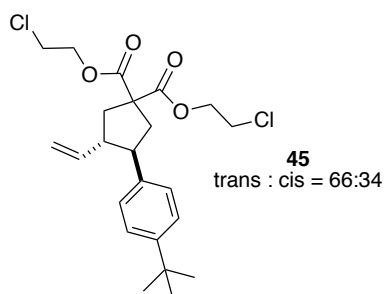


Prepared according to **Procedure C**. Colorless oil (69.1 mg, 93% yield) as a mixture of diastereomers (trans : cis = 65:35). R_f = 0.45 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.34 – 7.25 (m, 2.0H), 7.20 – 7.02 (m, 2.0H), 5.68 (ddd, J = 17.3, 10.5, 6.9 Hz, 0.35H), 5.40 (ddd, J = 17.0, 10.3, 7.8 Hz, 0.65H), 4.98 – 4.78 (m, 2.0H), 4.44 – 4.00 (m, 4.0H), 3.45 – 3.33 (m, 0.65H), 3.07 – 2.95 (m, 0.65H), 2.91 – 2.51 (m, 3.35H), 2.44 – 2.25 (m, 1.0H), 2.15 (dd, J = 13.2, 10.5 Hz, 0.35H), 1.39 – 1.16 (m, 15.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.8, 172.6, 172.6, 172.3, 149.2, 148.9, 139.1, 138.5, 138.5, 137.8, 128.0, 127.2, 125.2, 124.9, 115.4, 115.2, 61.6, 61.5, 61.5, 59.1, 58.2, 50.9, 50.4, 47.6, 47.3, 42.5, 40.1, 38.8, 38.1, 34.4, 34.4, 31.4, 14.1, 14.0.

DART-TOF LC/MS m/z calcd. for $\text{C}_{23}\text{H}_{33}\text{O}_4$ $[\text{M}+\text{H}^+]$ 373.2379, found 373.2381.



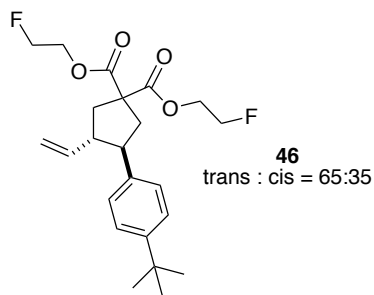
Prepared according to **Procedure C**. Colorless oil (72.5 mg, 82% yield) as a mixture of diastereomers (trans : cis = 66:34). R_f = 0.45 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.34 – 7.28 (m, 2.0H), 7.19 – 7.05 (m, 2.0H), 5.68 (ddd, J = 16.6, 11.0, 6.9 Hz, 0.34H), 5.41 (ddd, J = 17.1, 10.3, 7.8 Hz, 0.66H), 5.01 – 4.78 (m, 2.0H), 4.68 – 4.20

(m, 4.0H), 3.78 – 3.66 (m, 4.0H), 3.45 (dt, $J = 10.5, 7.4$ Hz, 0.66H), 3.11 – 2.98 (m, 0.66H), 2.94 – 2.58 (m, 3.34H), 2.51 – 2.32 (m, 1.0H), 2.26 – 2.17 (m, 0.34H), 1.31 (s, 9.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.1, 171.9, 171.9, 171.7, 149.4, 149.2, 138.8, 138.2, 138.1, 137.4, 128.0, 127.2, 125.3, 125.0, 115.6, 115.5, 65.1, 65.1, 65.0, 59.0, 58.1, 50.9, 50.4, 47.6, 47.3, 42.5, 41.4, 41.4, 40.1, 38.9, 38.2, 34.4, 34.4, 31.4.

DART-TOF LC/MS m/z calcd. for $\text{C}_{23}\text{H}_{31}\text{Cl}_2\text{O}_4$ $[\text{M}+\text{H}^+]$ 441.1599, found 441.1602.



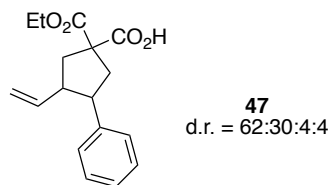
Prepared according to **Procedure C**. Colorless oil (74.5 mg, 91% yield) as a mixture of diastereomers (trans : cis = 65:35). $R_f = 0.33$ (30% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.37 – 7.28 (m, 2.0H), 7.20 – 7.04 (m, 2.0H), 5.78 – 5.61 (m, 0.35H), 5.41 (ddd, $J = 17.1, 10.3, 7.8$ Hz, 0.65H), 4.99 – 4.81 (m, 2.0H), 4.70 – 4.62 (m, 2.0H), 4.58 – 4.52 (m, 2.0H), 4.46 – 4.43 (m, 2.0H), 4.42 – 4.34 (m, 2.0H), 3.45 (dt, $J = 10.6, 7.4$ Hz, 0.65H), 3.11 – 2.98 (m, 0.65H), 2.95 – 2.57 (m, 3.35H), 2.51 – 2.32 (m, 1.0H), 2.27 – 2.15 (m, 0.35H), 1.31 (s, 9.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 172.2, 172.1, 171.9, 149.4, 149.1, 138.8, 138.2, 138.1, 137.4, 128.0, 127.2, 125.3, 125.0, 115.6, 115.4, 81.8, 80.2, 80.1, 64.6, 64.5, 64.5, 64.4, 64.3, 64.3, 58.9, 58.1, 50.8, 50.4, 47.6, 47.3, 42.5, 40.1, 38.8, 38.1, 34.4, 34.4, 31.4.

^{19}F NMR (376 MHz, CDCl_3) δ -225.09, -225.10, -225.12, -225.12, -225.16, -225.16.

DART-TOF LC/MS m/z calcd. for $\text{C}_{23}\text{H}_{34}\text{F}_2\text{NO}_4$ $[\text{M}+\text{NH}_4^+]$ 426.2456, found 426.2452.

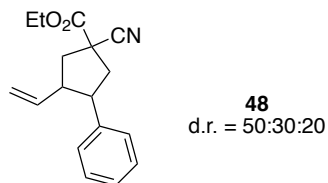


Prepared according to **Procedure C**. Colorless oil (53.0 mg, 92% yield) as a mixture of diastereomers (d.r. = 62:30:4:4). R_f = 0.35 (10% MeOH in DCM).

^1H NMR (400 MHz, CDCl_3) δ 11.14 (brs, 1.0H), 7.43 – 6.79 (m, 5.0H), 5.73 – 5.57 (m, 0.30H), 5.46 – 5.32 (m, 0.66H), 5.28 – 5.22 (m, 0.04H), 4.97 – 4.76 (m, 2.0H), 4.37 – 4.12 (m, 2.0H), 3.58 – 3.40 (m, 0.66H), 3.14 – 2.98 (m, 0.66H), 2.97 – 1.93 (m, 4.68H), 1.45 – 1.20 (m, 3.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 178.6, 178.3, 178.1, 172.1, 171.8, 141.3, 140.7, 140.6, 138.6, 138.1, 138.0, 128.4, 128.3, 128.1, 127.6, 126.7, 126.3, 115.8, 115.8, 115.5, 115.5, 62.1, 62.0, 59.1, 59.1, 58.1, 51.6, 50.9, 50.9, 48.1, 48.0, 47.4, 42.6, 42.5, 40.4, 40.3, 39.0, 39.0, 38.1, 38.1, 14.0.

DART-TOF LC/MS m/z calcd. for $\text{C}_{17}\text{H}_{21}\text{O}_4$ $[\text{M}+\text{H}^+]$ 289.1440, found 289.1441.



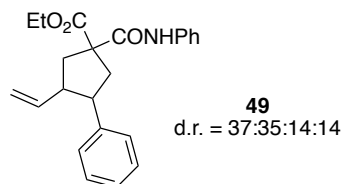
Prepared according to **Procedure C**. Colorless oil (45.1 mg, 84% yield) as a mixture of diastereomers (d.r. = 50:30:20). R_f = 0.35 (30% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.32 – 6.99 (m, 5.0H), 5.67 – 5.50 (m, 0.30H), 5.42 – 5.31 (m, 0.20H), 5.25 (ddd, J = 17.1, 10.2, 8.1 Hz, 0.50H), 4.99 – 4.68 (m, 2.0H), 4.40 – 4.10 (m, 2.0H), 3.68 – 3.56 (m, 0.50H), 3.52 – 3.41 (m, 0.20H), 3.20 – 3.12 (m, 0.50H), 3.09 – 2.31 (m, 4.50H), 2.27 – 2.15 (m, 0.30H), 1.36 – 1.21 (m, 3.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 169.9, 169.7, 169.6, 169.1, 140.5, 139.9, 139.7, 139.1, 137.7, 137.2, 137.1, 136.5, 128.7, 128.6, 128.4, 128.3, 128.3, 128.2, 127.6, 127.5, 127.1, 127.0, 126.7,

121.3, 121.2, 121.1, 116.7, 116.7, 116.6, 116.1, 63.1, 51.7, 51.6, 51.2, 50.5, 48.5, 47.8, 47.8, 47.3, 47.0, 45.2, 45.1, 43.3, 43.1, 42.0, 41.6, 41.6, 40.8, 14.0, 14.0.

DART-TOF LC/MS m/z calcd. for $C_{17}H_{23}N_2O_2$ $[M+NH_4^+]$ 287.1760, found 287.1758.

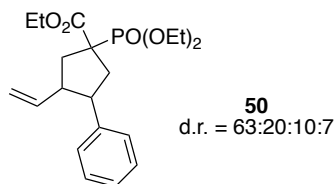


Prepared according to **Procedure C**. Colorless oil (67.6 mg, 93% yield) as a mixture of diastereomers (d.r. = 37:35:14:14). R_f = 0.45 (30% EtOAc in hexane).

1H NMR (400 MHz, $CDCl_3$) δ 8.33 (brs, 0.28H), 8.07 (brs, 0.37H), 7.99 (brs, 0.35H), 7.52 – 7.39 (m, 2.0H), 7.32 – 6.96 (m, 8.0H), 5.70 – 5.49 (m, 0.30H), 5.32 (dddd, J = 17.1, 10.4, 7.9, 1.7 Hz, 0.70H), 4.92 – 4.66 (m, 2.0H), 4.37 – 4.08 (m, 2.0H), 3.46 (dt, J = 10.8, 7.4 Hz, 0.37H), 3.36 (dt, J = 10.6, 7.7 Hz, 0.35H), 3.09 – 2.40 (m, 4.86H), 2.39 – 2.29 (m, 0.28H), 2.22 – 2.12 (m, 0.14H), 1.36 – 1.19 (m, 3.0H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 174.8, 174.7, 169.1, 168.7, 168.1, 141.6, 141.0, 140.9, 138.9, 138.8, 138.5, 138.2, 137.9, 137.8, 129.1, 129.0, 128.5, 128.4, 128.3, 128.1, 128.0, 127.7, 127.6, 126.6, 126.6, 126.3, 126.2, 124.5, 124.5, 120.0, 120.0, 119.9, 119.9, 115.6, 115.6, 115.4, 115.3, 62.5, 62.4, 62.3, 61.1, 60.5, 59.3, 52.0, 51.5, 51.3, 51.0, 48.1, 48.0, 47.4, 47.3, 43.1, 42.9, 41.1, 39.5, 39.4, 38.2, 37.7, 14.1, 14.0.

DART-TOF LC/MS m/z calcd. for $C_{23}H_{29}N_2O_3$ $[M+NH_4^+]$ 381.2178, found 381.2173.



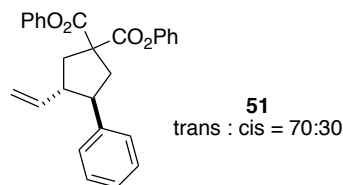
Prepared according to **Procedure C**. Colorless oil (65.7 mg, 86% yield) as a mixture of diastereomers (d.r. = 37:35:14:14). $R_f = 0.35$ (30% acetone in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.26 – 7.05 (m, 5.0H), 5.56 (ddd, $J = 17.2, 9.9, 7.2$ Hz, 0.32H), 5.28 (ddd, $J = 17.1, 10.2, 8.4$ Hz, 0.68H), 4.91 – 4.57 (m, 2.0H), 4.35 – 3.92 (m, 6.0H), 3.52 – 3.15 (m, 0.73H), 3.04 – 2.03 (m, 5.27H), 1.54 – 1.02 (m, 9.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.3, 171.8, 171.7, 141.9, 141.4, 141.3, 139.2, 138.9, 138.5, 137.4, 128.6, 128.4, 128.2, 128.0, 128.0, 127.7, 127.6, 126.6, 126.5, 126.2, 126.1, 115.8, 115.7, 115.4, 114.9, 63.1, 63.0, 62.9, 62.9, 62.9, 62.8, 62.8, 62.7, 61.8, 61.8, 55.0, 53.6, 51.6, 51.6, 51.5, 51.1, 51.0, 50.8, 50.8, 47.8, 47.7, 47.6, 47.4, 47.2, 41.1, 41.1, 40.2, 38.0, 38.0, 37.6, 37.6, 37.3, 37.3, 16.5, 16.5, 16.4, 16.4, 14.1.

^{31}P NMR (162 MHz, CDCl_3) δ 27.3, 26.6, 26.1.

DART-TOF LC/MS m/z calcd. for $\text{C}_{20}\text{H}_{33}\text{NPO}_5$ $[\text{M}+\text{NH}_4^+]$ 398.2096, found 398.2100.

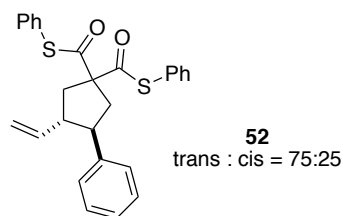


Prepared according to **Procedure C**. Colorless oil (75.9 mg, 92% yield) as a mixture of diastereomers (trans : cis = 70:30). $R_f = 0.35$ (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.43 – 6.94 (m, 15.0H), 5.64 (ddd, $J = 17.3, 9.9, 7.0$ Hz, 0.30H), 5.39 (ddd, $J = 17.1, 10.3, 7.9$ Hz, 0.70H), 4.95 – 4.76 (m, 2.0H), 3.54 (dt, $J = 10.6, 7.4$ Hz, 0.70H), 3.17 – 3.04 (m, 0.70H), 3.02 – 2.74 (m, 3.30H), 2.65 – 2.50 (m, 1.0H), 2.45 – 2.31 (m, 0.30H).

^{13}C NMR (101 MHz, CDCl_3) δ 171.1, 170.6, 150.7, 150.7, 141.2, 140.4, 138.4, 137.8, 129.6, 128.6, 128.4, 128.2, 127.7, 126.8, 126.5, 126.3, 121.2, 121.2, 116.0, 115.9, 59.3, 58.4, 51.6, 50.9, 48.2, 47.6, 42.6, 40.4, 39.1, 38.2.

DART-TOF LC/MS m/z calcd. for C₂₇H₂₈NO₄ [M+NH₄⁺] 430.2018, found 430.2015.

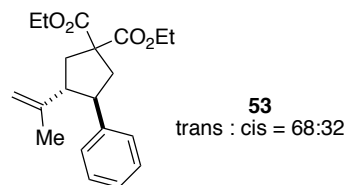


Prepared according to **Procedure C**. Colorless oil (69.4 mg, 78% yield) as a mixture of diastereomers (trans : cis = 75:25). R_f = 0.40 (30% EtOAc in hexane).

¹H NMR (400 MHz, CDCl₃) δ 7.53 – 6.96 (m, 15.0H), 5.68 – 5.48 (m, 0.25H), 5.27 (ddd, *J* = 17.6, 10.3, 7.8 Hz, 0.75H), 4.94 – 4.65 (m, 2.0H), 3.46 – 3.31 (m, 0.75H), 3.07 – 2.41 (m, 5.0H), 2.30 (dd, *J* = 13.8, 10.8 Hz, 0.25H).

¹³C NMR (101 MHz, CDCl₃) δ 196.8, 196.6, 196.5, 196.0, 141.1, 140.4, 138.4, 137.8, 134.8, 134.8, 134.7, 129.8, 129.4, 129.4, 128.5, 128.4, 128.2, 127.6, 127.0, 127.0, 126.8, 126.5, 116.1, 115.8, 74.8, 73.8, 51.3, 50.6, 47.6, 46.9, 42.3, 40.1, 38.8, 38.0.

DART-TOF LC/MS m/z calcd. for C₂₇H₂₈NO₂S₂ [M+NH₄⁺] 462.1561, found 462.1560.

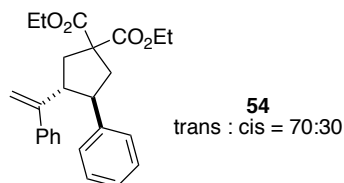


Prepared according to **Procedure C**. Colorless oil (52.0 mg, 79% yield) as a mixture of diastereomers (trans : cis = 68:32). R_f = 0.35 (4:1 hex:EtOAc).

¹H NMR (400 MHz, CDCl₃) δ 7.27 – 6.99 (m, 5.0H), 4.64 – 4.50 (m, 2.0H), 4.26 – 4.09 (m, 4.0H), 3.49 – 3.36 (m, 0.68H), 3.06 – 2.64 (m, 2.32H), 2.56 (dd, *J* = 13.6, 7.4 Hz, 0.32H), 2.49 – 2.34 (m, 2.0H), 2.18 (ddd, *J* = 25.3, 13.7, 11.6 Hz, 0.68H), 1.56 (s, 0.96H), 1.24 – 1.10 (m, 8.04H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.7, 172.6, 172.6, 172.1, 145.0, 144.1, 142.4, 142.1, 128.4, 127.8, 127.4, 126.5, 126.1, 112.1, 111.7, 61.6, 61.5, 59.3, 57.9, 53.5, 49.9, 49.1, 46.8, 42.8, 40.1, 39.5, 37.8, 22.7, 19.8, 14.1.

DART-TOF LC/MS m/z calcd. for $\text{C}_{20}\text{H}_{30}\text{NO}_4$ $[\text{M}+\text{NH}_4^+]$ 348.2175, found 348.2171.

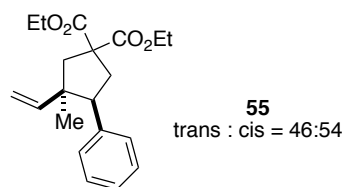


Prepared according to **Procedure C**. Colorless oil (63.2 mg, 81% yield) as a mixture of diastereomers (trans : cis = 70:30). R_f = 0.35 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.25 – 6.58 (m, 10.0H), 5.10 (d, J = 0.9 Hz, 0.30H), 5.02 (d, J = 0.8 Hz, 0.30H), 4.95 (d, J = 0.9 Hz, 0.70H), 4.75 (d, J = 0.8 Hz, 0.70H), 4.31 – 4.04 (m, 4.0H), 3.64 – 3.51 (m, 0.70H), 3.42 (td, J = 8.7, 5.9 Hz, 0.70H), 3.32 – 3.11 (m, 0.60H), 2.95 (ddd, J = 14.5, 8.6, 1.2 Hz, 0.70H), 2.84 (dd, J = 13.8, 7.5 Hz, 0.30H), 2.75 (dd, J = 13.6, 6.9 Hz, 0.30H), 2.64 (dd, J = 13.2, 12.1 Hz, 0.70H), 2.52 (ddd, J = 13.2, 6.1, 1.2 Hz, 0.70H), 2.38 (dd, J = 14.5, 5.9 Hz, 0.70H), 2.21 (dd, J = 13.8, 10.9 Hz, 0.30H), 2.01 (dd, J = 13.6, 11.2 Hz, 0.30H), 1.34 – 1.08 (m, 6.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.6, 172.6, 172.3, 172.1, 148.9, 148.0, 142.7, 142.0, 142.0, 141.9, 128.7, 128.4, 128.1, 127.9, 127.5, 127.4, 127.2, 127.1, 126.5, 126.5, 126.3, 125.9, 113.2, 113.2, 61.7, 61.6, 61.6, 61.5, 59.2, 57.7, 50.3, 49.7, 47.0, 46.3, 42.8, 41.7, 40.8, 38.1, 14.1, 14.1, 14.0.

DART-TOF LC/MS m/z calcd. for $\text{C}_{25}\text{H}_{32}\text{NO}_4$ $[\text{M}+\text{NH}_4^+]$ 410.2331, found 410.2330.

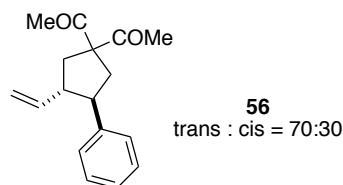


Prepared according to **Procedure C**. Colorless oil (38.8 mg, 59% yield) as a mixture of diastereomers (trans : cis = 46:54). R_f = 0.40 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.26 – 7.05 (m, 5.0H), 5.83 (dd, J = 17.4, 10.7 Hz, 0.46H), 5.46 (dd, J = 17.4, 10.9 Hz, 0.54H), 4.97 – 4.64 (m, 2.0H), 4.26 – 4.05 (m, 4.0H), 3.02 (dd, J = 13.4, 6.6 Hz, 0.46H), 2.92 (dd, J = 13.7, 6.0 Hz, 0.54H), 2.82 (t, J = 13.5 Hz, 0.46H), 2.74 – 2.58 (m, 1.08H), 2.55 – 2.46 (m, 0.92H), 2.41 – 2.28 (m, 1.08H), 2.22 (d, J = 14.1 Hz, 0.46H), 1.24 – 1.14 (m, 6.0H), 1.07 (s, 1.62H), 0.70 (s, 1.38H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.2, 172.9, 172.6, 172.4, 146.4, 141.9, 138.4, 138.3, 128.9, 128.5, 127.7, 127.7, 126.7, 126.6, 113.1, 112.4, 61.6, 61.6, 61.5, 57.4, 57.1, 55.4, 53.8, 48.4, 48.3, 47.0, 44.4, 38.0, 37.1, 25.7, 19.0, 14.1, 14.0.

DART-TOF LC/MS m/z calcd. for $\text{C}_{20}\text{H}_{30}\text{NO}_4$ [$\text{M}+\text{NH}_4^+$] 348.2175, found 348.2172.



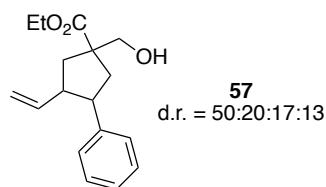
Prepared according to **Procedure C**. Colorless oil (44.1 mg, 86% yield) as a mixture of diastereomers (trans : cis = 70:30). R_f = 0.35 (20% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.28 – 6.97 (m, 5.0H), 5.61 – 5.44 (m, 0.30H), 5.22 (ddd, J = 17.1, 10.3, 7.9 Hz, 0.70H), 4.90 – 4.66 (m, 2.0H), 3.18 (dt, J = 10.6, 7.2 Hz, 0.70H), 2.90 – 2.80 (m, 0.70H), 2.75 (dd, J = 13.2, 7.4 Hz, 0.30H), 2.68 – 2.57 (m, 1.40H), 2.56 – 2.47 (m, 0.30H), 2.45 –

2.22 (m, 2.0H), 2.13 – 2.01 (m, 6.0H), 2.00 (dd, J = 13.3, 11.2 Hz, 0.30H), 1.84 (dd, J = 13.3, 10.8 Hz, 0.30H).

^{13}C NMR (101 MHz, CDCl_3) δ 204.9, 204.6, 204.5, 204.5, 141.4, 140.6, 138.7, 138.0, 128.5, 128.2, 128.1, 127.5, 126.7, 126.3, 115.7, 115.6, 74.4, 73.2, 51.2, 50.3, 47.8, 47.3, 39.3, 36.9, 35.5, 34.3, 27.0, 26.4, 26.3, 26.0.

DART-TOF LC/MS m/z calcd. for $\text{C}_{14}\text{H}_{24}\text{NO}_2$ [$\text{M}+\text{NH}_4^+$] 274.1807, found 274.1804.

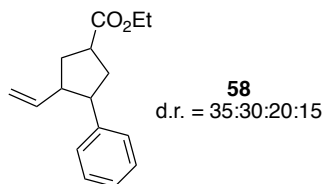


Prepared according to **Procedure C**. Colorless oil (44.3 mg, 81% yield) as a mixture of diastereomers (d.r. = 50:20:17:13). R_f = 0.30 (30% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.33 – 6.96 (m, 5.0H), 5.71 – 5.27 (m, 1.0H), 4.87 – 4.68 (m, 2.0H), 4.24 – 4.09 (m, 2.0H), 3.79 – 3.60 (m, 2.0H), 3.52 (dt, J = 11.8, 7.2 Hz, 0.50H), 3.31 (dt, J = 10.5, 7.4 Hz, 0.17H), 3.12 – 1.45 (m, 6.0H), 1.32 – 1.11 (m, 3.0H), 0.95 – 0.80 (m, 0.33H).

^{13}C NMR (101 MHz, CDCl_3) δ 177.7, 177.6, 177.6, 177.4, 142.0, 142.0, 141.3, 141.3, 139.4, 139.3, 139.0, 138.8, 128.4, 128.4, 128.3, 128.1, 128.0, 127.6, 127.5, 126.4, 126.1, 126.1, 115.3, 115.2, 115.2, 115.0, 69.2, 68.1, 68.0, 67.5, 61.2, 61.1, 61.1, 61.1, 54.3, 53.8, 52.8, 52.8, 51.8, 51.3, 51.1, 50.4, 48.2, 48.0, 47.4, 42.5, 41.6, 40.2, 39.1, 38.5, 38.2, 37.6, 36.2, 14.2, 14.2, 14.1.

DART-TOF LC/MS m/z calcd. for $\text{C}_{17}\text{H}_{26}\text{NO}_3$ [$\text{M}+\text{NH}_4^+$] 292.1907, found 292.1905.

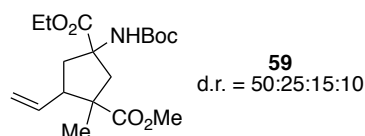


Prepared according to **Procedure C** (0.4 mmol). Colorless oil (60.9 mg, 62% yield) as a mixture of diastereomers (trans : cis = 35:30:20:15). $R_f = 0.45$ (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 7.30 – 7.01 (m, 5.0H), 5.72 – 5.50 (m, 0.55H), 5.42 – 5.22 (m, 0.45H), 4.91 – 4.57 (m, 2.0H), 4.24 – 3.91 (m, 2.0H), 3.45 – 1.74 (m, 7.0H), 1.32 – 1.04 (m, 3.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 176.9, 176.4, 176.3, 175.9, 143.2, 142.6, 141.8, 141.5, 140.0, 139.8, 139.3, 138.6, 128.5, 128.4, 128.3, 128.3, 128.0, 128.0, 127.6, 127.5, 126.4, 126.3, 126.1, 114.9, 114.8, 114.6, 60.5, 60.5, 52.6, 52.3, 51.2, 50.8, 49.0, 48.8, 48.1, 48.1, 42.9, 42.0, 41.8, 41.5, 38.7, 38.1, 36.6, 35.7, 34.9, 34.7, 34.2, 33.4, 14.3, 14.3.

DART-TOF LC/MS m/z calcd. for $\text{C}_{14}\text{H}_{24}\text{NO}_2$ $[\text{M}+\text{NH}_4^+]$ 262.1807, found 262.1805.

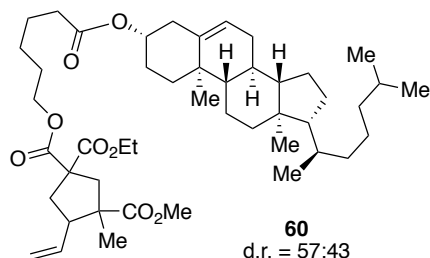


Prepared according to **Procedure C**. Colorless oil (63.7 mg, 90% yield) as a mixture of diastereomers (trans : cis = 50:25:15:10). $R_f = 0.35$ (20% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.90 – 5.57 (m, 1.0H), 5.44 – 4.80 (m, 3.0H), 4.28 – 4.04 (m, 2.0H), 3.75 – 3.40 (m, 3.0H), 3.36 – 1.72 (m, 5.0H), 1.58 – 0.92 (m, 15.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 177.9, 176.6, 175.9, 174.4, 173.4, 173.2, 155.2, 136.3, 136.2, 136.0, 135.9, 116.9, 116.7, 116.6, 65.2, 61.5, 61.4, 61.4, 61.4, 54.2, 54.0, 53.1, 52.5, 52.3, 52.0, 51.8, 51.7, 51.6, 51.0, 49.2, 48.8, 48.0, 42.1, 28.3, 24.9, 22.9, 20.7, 14.1, 14.1, 14.1.

ESI-TOF LC/MS m/z calcd. for $\text{C}_{18}\text{H}_{30}\text{NO}_6$ $[\text{M}+\text{H}^+]$ 356.2073, found 356.2075.

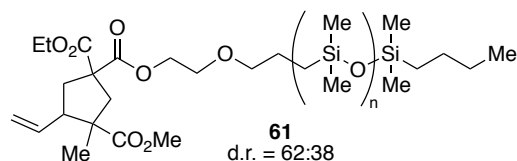


Prepared according to **Procedure C**. Colorless oil (89.2 mg, 58% yield) as a mixture of diastereomers (d.r. = 57:43). R_f = 0.50 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.81 – 5.55 (m, 1.0H), 5.36 (brs, 1.0H), 5.16 – 4.98 (m, 2.0H), 4.72 – 4.51 (m, 1.0H), 4.29 – 3.97 (m, 4.0H), 3.67 (s, 1.29H), 3.60 (s, 1.71H), 3.12 – 3.01 (m, 0.43H), 2.91 (dd, J = 14.4, 4.7 Hz, 0.57H), 2.83 (dd, J = 14.3, 3.2 Hz, 0.43H), 2.58 – 2.44 (m, 1.57H), 2.41 – 2.14 (m, 6.0H), 2.05 – 0.59 (m, 53.0H).

^{13}C NMR (101 MHz, CDCl_3) δ 176.6, 175.7, 173.1, 173.0, 172.8, 172.8, 172.8, 172.1, 172.0, 171.6, 171.5, 139.6, 136.1, 135.9, 122.6, 117.0, 116.8, 73.8, 73.8, 65.5, 65.5, 65.3, 61.7, 61.7, 61.7, 61.4, 58.9, 58.0, 56.7, 56.1, 54.6, 54.6, 53.0, 52.1, 52.0, 51.5, 51.5, 50.0, 49.8, 49.7, 44.8, 44.7, 44.6, 42.3, 39.7, 39.5, 38.9, 38.8, 38.1, 37.4, 37.0, 36.6, 36.2, 35.8, 34.5, 34.4, 31.9, 31.8, 28.2, 28.2, 28.0, 27.8, 25.4, 25.3, 24.6, 24.6, 24.5, 24.3, 23.8, 22.9, 22.9, 22.8, 22.6, 21.0, 19.3, 19.0, 18.9, 18.7, 14.1, 14.0, 11.8.

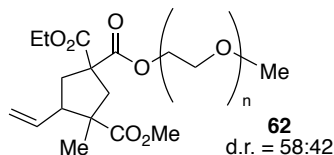
ESI-TOF LC/MS m/z calcd. for $\text{C}_{47}\text{H}_{75}\text{O}_8$ $[\text{M}+\text{H}^+]$ 767.5462, found 767.5466.



Prepared according to **Procedure C**. Colorless oil (229.7 mg, 77% yield) as a mixture of diastereomers (d.r. = 62:38). R_f = 0.50 (10% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.86 – 5.50 (m, 1.0H), 5.15 – 4.91 (m, 2.0H), 4.37 – 4.05 (m, 4.0H), 3.77 – 3.54 (m, 5.0H), 3.46 – 3.32 (m, 2.0H), 3.16 – 3.02 (m, 0.38H), 2.94 (d, J = 14.4 Hz, 0.62H), 2.86 (dd, J = 14.3, 10.6 Hz, 0.38H), 2.61 – 2.47 (m, 1.62H), 2.44 – 2.16 (m, 2.0H), 1.66 – 1.50 (m, 2.0H), 1.38 – 1.19 (m, 9.0H), 1.10 (d, J = 1.4 Hz, 1.0H), 0.92 – 0.82 (m, 3.0H), 0.61 – 0.45 (m, 4.0H), 0.28 – -0.17 (m, 74.0H).

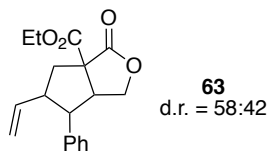
^{13}C NMR (101 MHz, CDCl_3) δ 175.5, 174.7, 174.6, 172.0, 171.9, 171.1, 170.8, 170.6, 170.3, 135.1, 134.9, 134.8, 116.0, 116.0, 115.8, 73.1, 73.0, 67.2, 67.2, 63.8, 63.7, 63.6, 60.7, 60.7, 60.6, 60.4, 57.9, 57.8, 57.0, 53.6, 53.5, 52.0, 52.0, 51.0, 50.9, 50.4, 48.7, 48.7, 43.7, 43.6, 43.6, 37.8, 36.4, 25.3, 24.4, 22.4, 21.9, 21.8, 17.9, 17.8, 16.9, 13.1, 13.1, 13.0, 12.9, 12.8, 0.4, 0.1, 0.00, -0.4, -0.9, -1.0.



Prepared according to **Procedure C**. Colorless oil (108.3 mg, 75% yield) as a mixture of diastereomers (d.r. = 58:42). R_f = 0.30 (30% acetone in hexane).

^1H NMR (400 MHz, CDCl_3) δ 5.82 – 5.54 (m, 1.0H), 5.15 – 4.90 (m, 2.0H), 4.36 – 4.09 (m, 4.0H), 3.81 – 3.48 (m, 44.0H), 3.35 (s, 3.0H), 3.11 – 2.99 (m, 0.42H), 2.90 (d, J = 14.4 Hz, 0.58H), 2.83 (dd, J = 14.3, 5.6 Hz, 0.42H), 2.60 – 2.43 (m, 1.58H), 2.41 – 2.14 (m, 2.0H), 1.35 – 1.17 (m, 4.74H), 1.08 (d, J = 1.8 Hz, 1.26H).

^{13}C NMR (101 MHz, CDCl_3) δ 176.5, 175.6, 175.6, 172.9, 172.8, 172.0, 171.8, 171.8, 171.5, 171.3, 136.0, 135.9, 135.8, 117.0, 117.0, 116.8, 71.9, 70.6, 70.6, 70.5, 70.5, 68.8, 68.8, 68.8, 64.7, 64.7, 64.6, 64.5, 61.7, 61.7, 61.7, 61.4, 59.0, 58.8, 58.8, 57.9, 57.9, 54.6, 53.0, 53.0, 52.0, 52.0, 51.9, 51.5, 49.7, 49.7, 44.7, 44.6, 44.6, 38.8, 37.3, 37.3, 22.9, 22.77, 18.9, 18.8, 14.0, 14.0.

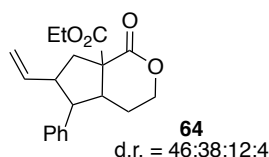


Prepared according to **Procedure C**. Colorless oil (25.7 mg, 43% yield) as a mixture of diastereomers (d.r. = 58:42). R_f = 0.30 (10% EtOAc in hexane).

¹H NMR (400 MHz, CDCl₃) δ 7.33 – 6.91 (m, 5.0H), 5.56 – 5.43 (m, 0.42H), 5.32 – 5.15 (m, 0.58H), 4.93 – 4.63 (m, 2.0H), 4.58 – 4.07 (m, 4.0H), 3.77 – 1.69 (m, 5.0H), 1.35 – 1.05 (m, 3.0H).

¹³C NMR (101 MHz, CDCl₃) δ 176.5, 176.4, 171.3, 169.7, 169.4, 169.0, 138.9, 138.9, 138.6, 137.7, 137.1, 136.5, 128.9, 128.5, 128.4, 128.1, 127.8, 127.5, 127.0, 126.8, 116.5, 116.4, 115.1, 72.0, 69.8, 69.4, 62.5, 62.5, 62.4, 61.6, 60.7, 59.3, 57.7, 56.6, 55.9, 55.1, 52.5, 51.8, 50.4, 48.7, 43.4, 38.1, 37.5, 33.6, 14.2, 14.1.

DART-TOF LC/MS m/z calcd. for C₁₈H₂₄NO₄ [M+NH₄⁺] 318.1705, found 318.1703.

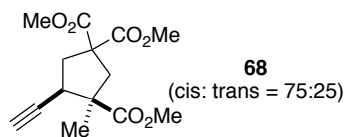


Prepared according to **Procedure C**. Colorless oil (45.1 mg, 72% yield) as a mixture of diastereomers (d.r. = 46:38:12:4). R_f = 0.30 (10% EtOAc in hexane).

¹H NMR (400 MHz, CDCl₃) δ 7.35 – 6.96 (m, 5.0H), 5.82 (ddd, *J* = 17.5, 10.2, 7.8 Hz, 0.04H), 5.51 (ddd, *J* = 17.4, 10.5, 7.1 Hz, 0.46H), 5.40 (ddd, *J* = 17.0, 10.4, 8.0 Hz, 0.38H), 5.23 (ddd, *J* = 17.2, 10.2, 8.1 Hz, 0.12H), 4.490 – 4.23 (m, 2.0H), 4.48 – 4.07 (m, 4.0H), 3.77 – 2.71 (m, 3.0H), 2.69 – 1.70 (m, 3.0H), 1.63 – 1.42 (m, 1.0H), 1.32 – 1.20 (m, 3.0H).

¹³C NMR (101 MHz, CDCl₃) δ 172.1, 171.7, 171.5, 171.4, 171.2, 170.1, 139.9, 139.5, 138.9, 138.9, 137.8, 137.6, 128.7, 128.7, 128.6, 128.3, 128.3, 127.7, 127.5, 127.2, 126.8, 126.6, 116.0, 115.9, 114.6, 67.9, 67.2, 67.0, 62.6, 62.4, 62.1, 59.5, 59.1, 59.0, 57.6, 56.9, 50.0, 50.0, 49.5, 47.9, 46.5, 45.2, 44.2, 40.7, 39.7, 37.0, 28.0, 27.9, 22.8, 14.1, 14.0, 14.0.

DART-TOF LC/MS m/z calcd. for C₁₉H₂₆NO₄ [M+NH₄⁺] 332.1862, found 332.1858.

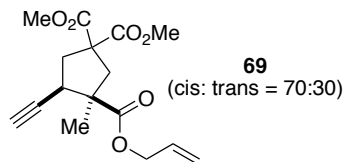


Prepared according to **Procedure C**. Colorless oil (37.3 mg, 66% yield) as a mixture of inseparable diastereomers (cis : trans = 75:25). $R_f = 0.30$ (20% EtOAc in hexane).

^1H NMR (400 MHz, CDCl_3) δ 3.74 (s, 2.25H), 3.72 (s, 3.00H), 3.71 (s, 0.75H), 3.70 (s, 0.75H), 3.67 (s, 2.25H), 3.34 (ddd, $J = 10.0, 7.2, 2.5$ Hz, 0.25 H), 2.99 (d, $J = 14.5$ Hz, 0.75H), 2.81 – 2.66 (m, 2H), 2.60 (dd, $J = 13.0, 6.9$ Hz, 0.75H), 2.45 (d, $J = 14.3$ Hz, 0.25H), 2.33 (dd, $J = 13.8, 10.2$ Hz, 0.25H), 2.20 – 2.10 (m, 1.75H), 1.36 (s, 2.25H), 1.33 (s, 0.75H).

^{13}C NMR (101 MHz, CDCl_3) δ 175.8, 175.0, 173.0, 172.0, 171.7, 171.4, 82.1, 81.7, 72.1, 71.5, 58.9, 58.1, 53.7, 53.1, 53.0, 53.0, 52.9, 52.4, 51.8, 43.8, 43.7, 41.4, 39.7, 39.2, 37.9, 29.7, 23.0, 20.5.

DART-TOF LC/MS m/z calcd. for $\text{C}_{14}\text{H}_{22}\text{NO}_6$ $[\text{M}+\text{NH}_4^+]$ 300.1447, found 300.1446.



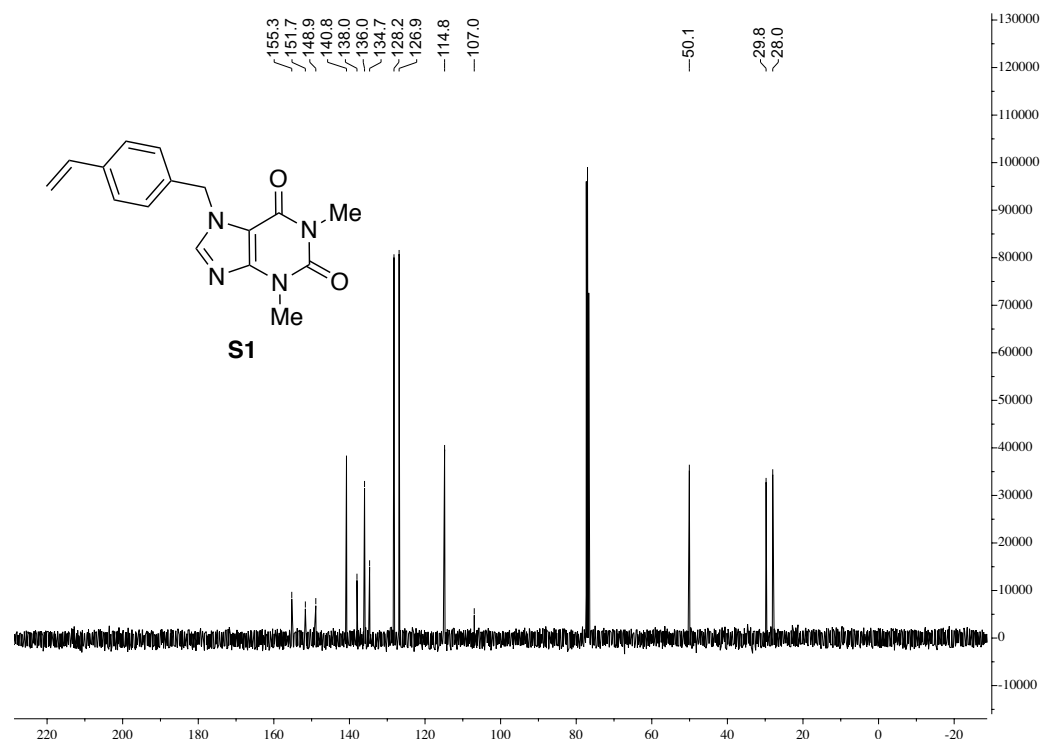
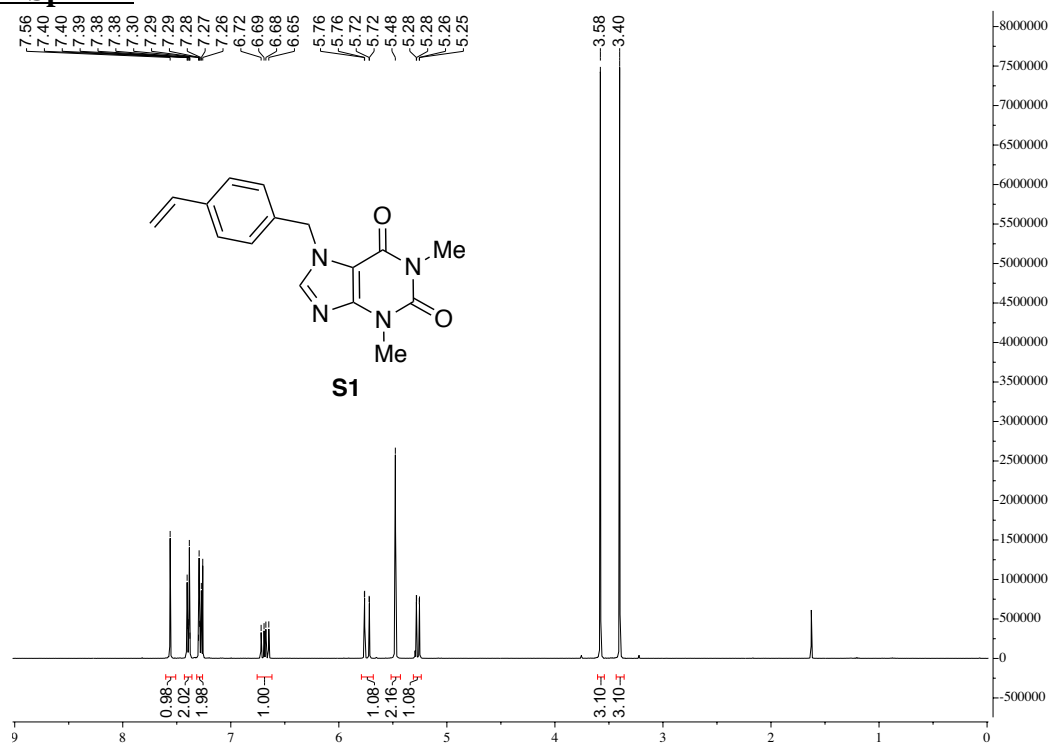
Prepared according to **Procedure C**. Colorless oil (29.8 mg, 48% yield) as a mixture of inseparable diastereomers (cis : trans = 70:30). $R_f = 0.35$ (20% EtOAc in hexane).

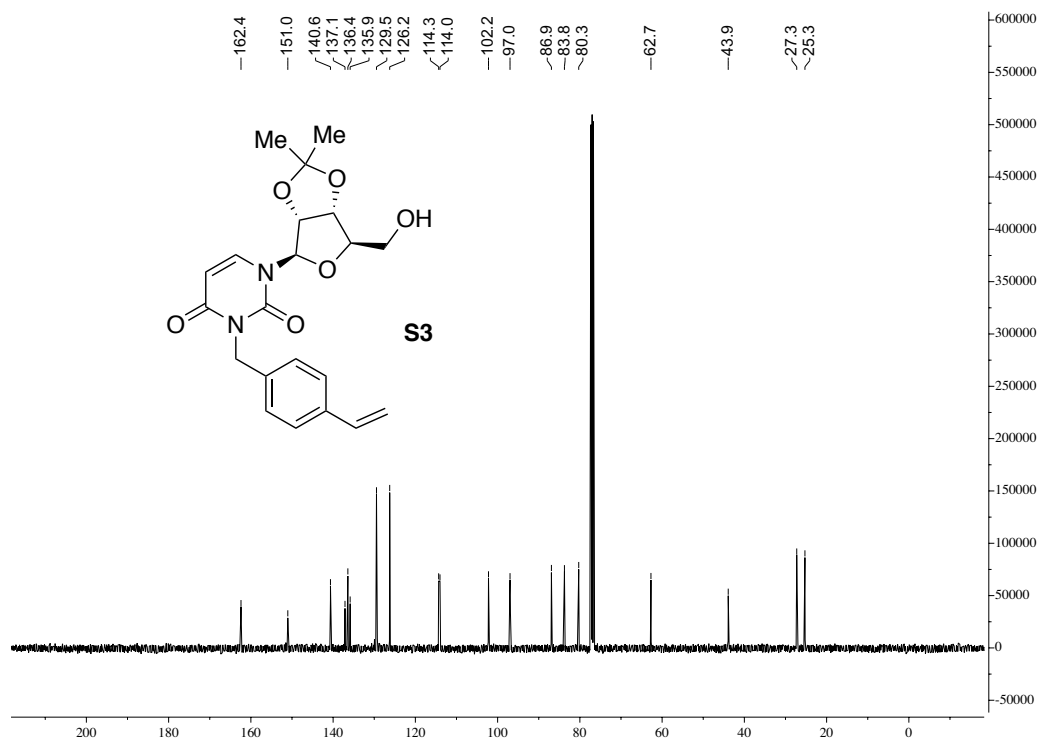
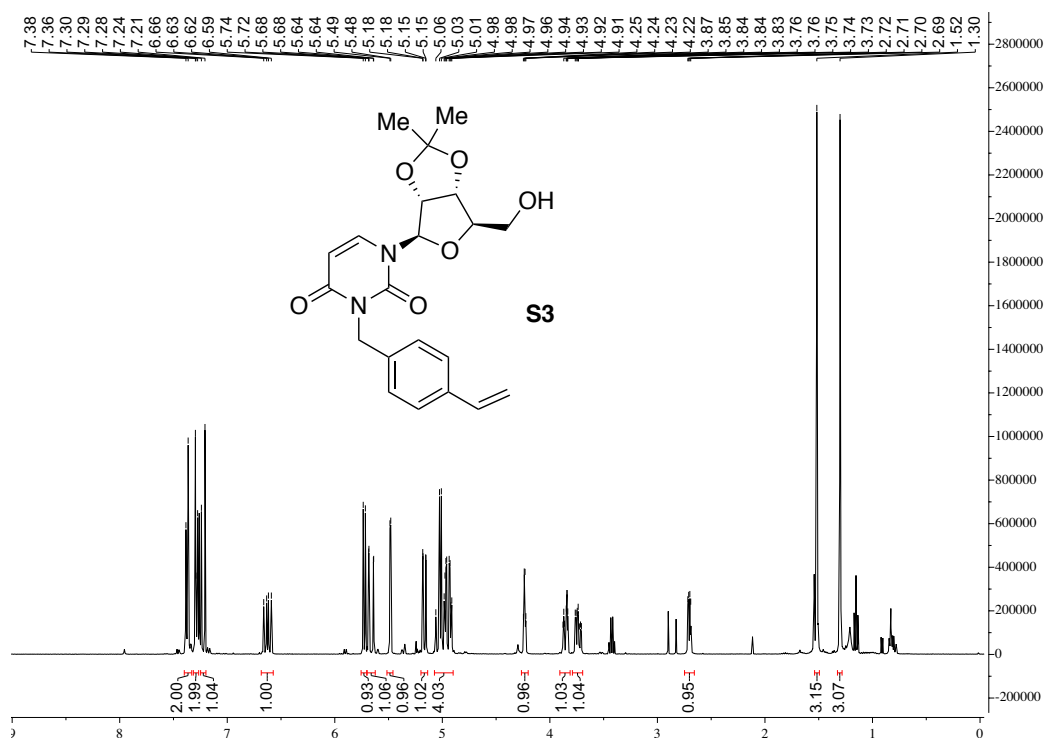
^1H NMR (400 MHz, CDCl_3) δ 5.93 – 5.76 (m, 1.0H), 5.26 (d, $J = 17.2$, 1.0H), 5.20 – 5.10 (m, 1.0H), 4.59 – 4.44 (m, 2.0H), 3.75 – 3.58 (m, 6.0H), 3.30 (ddd, $J = 10.0, 7.2, 2.5$ Hz, 0.30H), 2.96 (d, $J = 14.5$ Hz, 0.70H), 2.77 – 2.62 (m, 2.0H), 2.55 (dd, $J = 13.0, 6.8$ Hz, 0.70H), 2.41 (d, $J = 14.4$ Hz, 0.30H), 2.28 (dd, $J = 13.7, 10.3$ Hz, 0.30H), 2.18 – 2.02 (m, 1.70H), 1.33 (s, 2.10H), 1.30 (s, 0.90H).

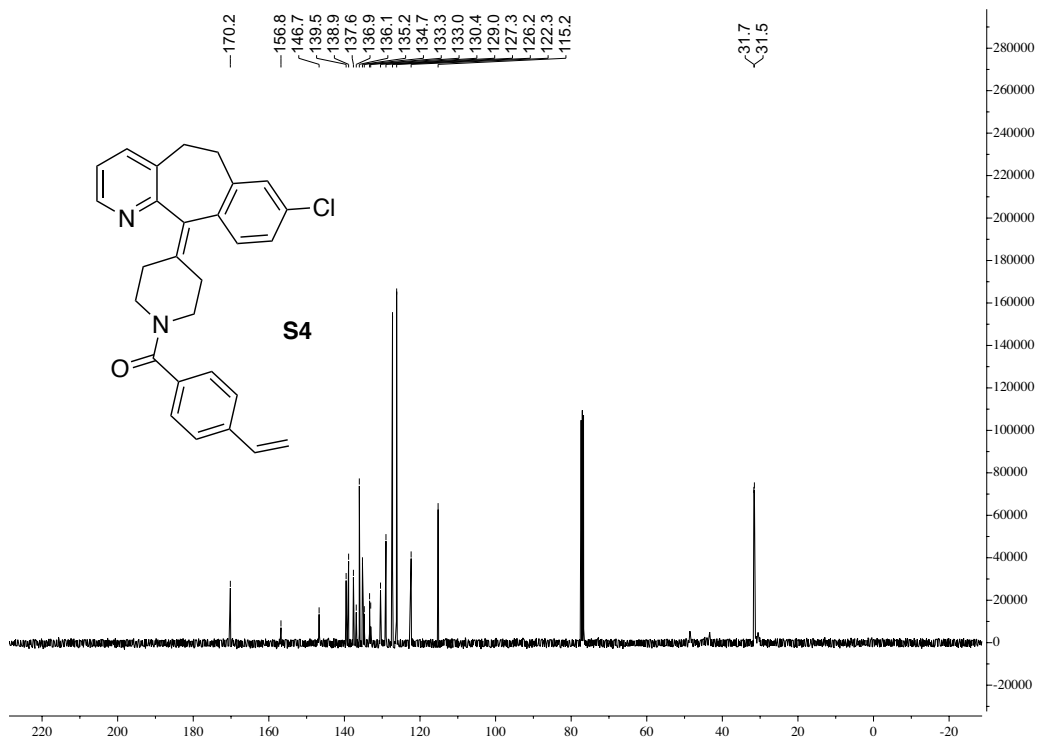
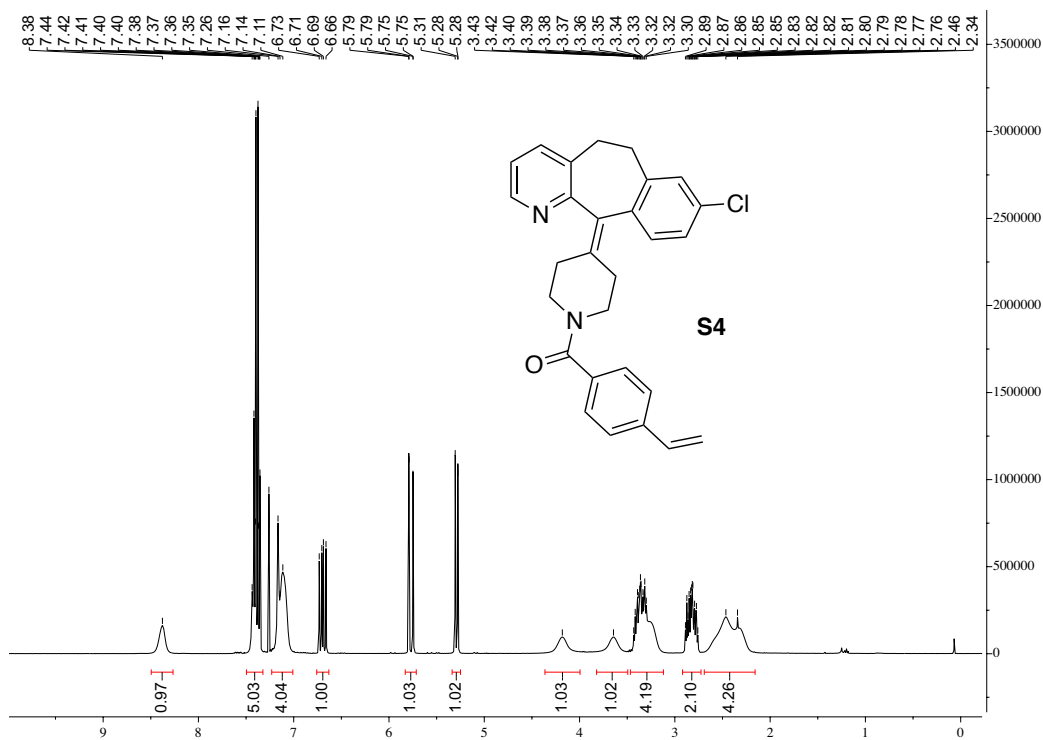
^{13}C NMR (101 MHz, CDCl_3) δ 174.9, 174.2, 173.1, 171.9, 171.7, 171.4, 132.1, 131.9, 118.2, 118.0, 82.1, 81.7, 72.1, 71.7, 65.7, 65.6, 58.9, 58.1, 53.7, 53.1, 53.1, 53.0, 52.9, 51.9, 43.8, 43.7, 41.4, 39.8, 39.3, 37.9, 29.7, 23.1, 20.5.

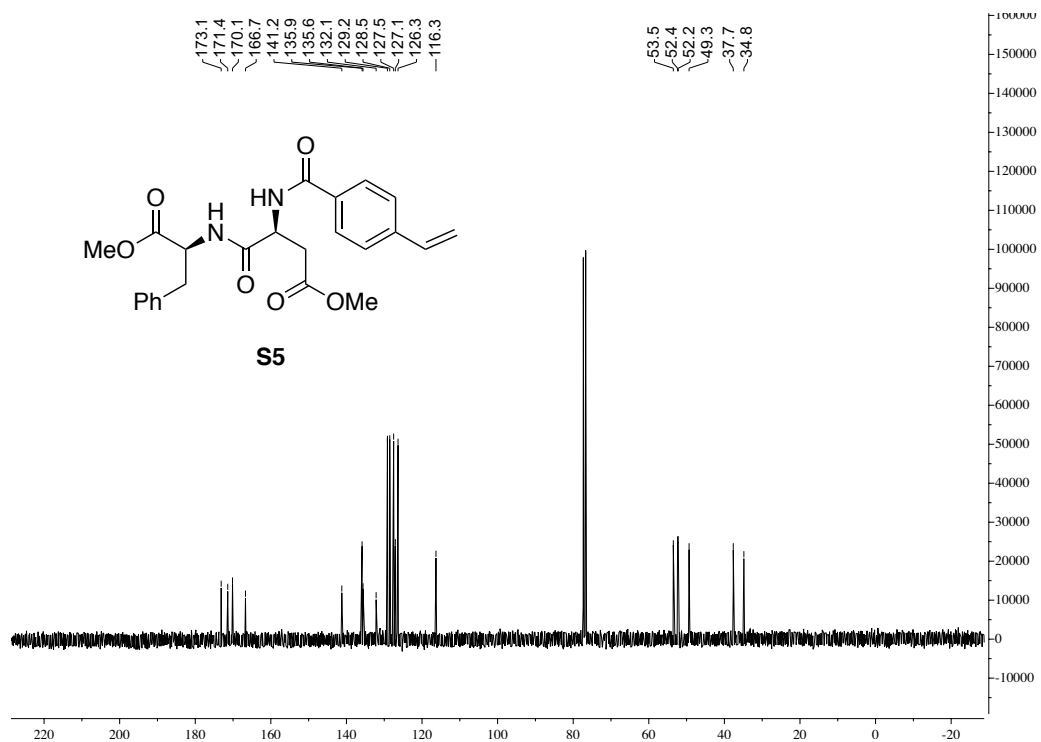
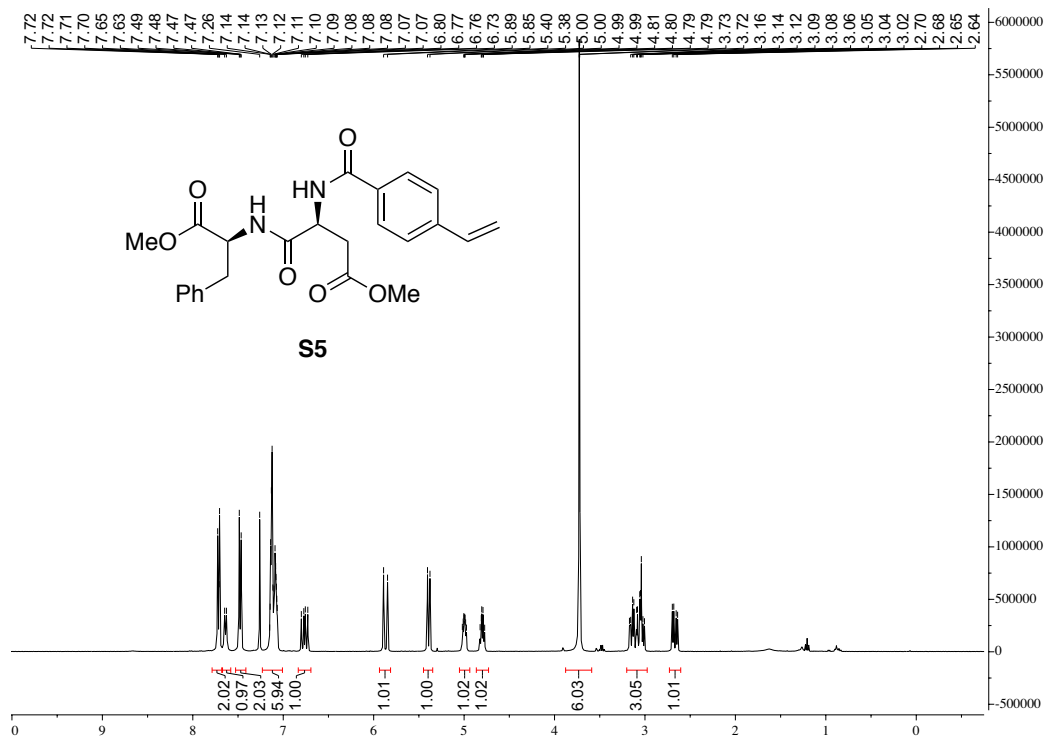
DART-TOF LC/MS m/z calcd. for $\text{C}_{16}\text{H}_{24}\text{NO}_6$ $[\text{M}+\text{NH}_4^+]$ 326.1604, found 326.1602.

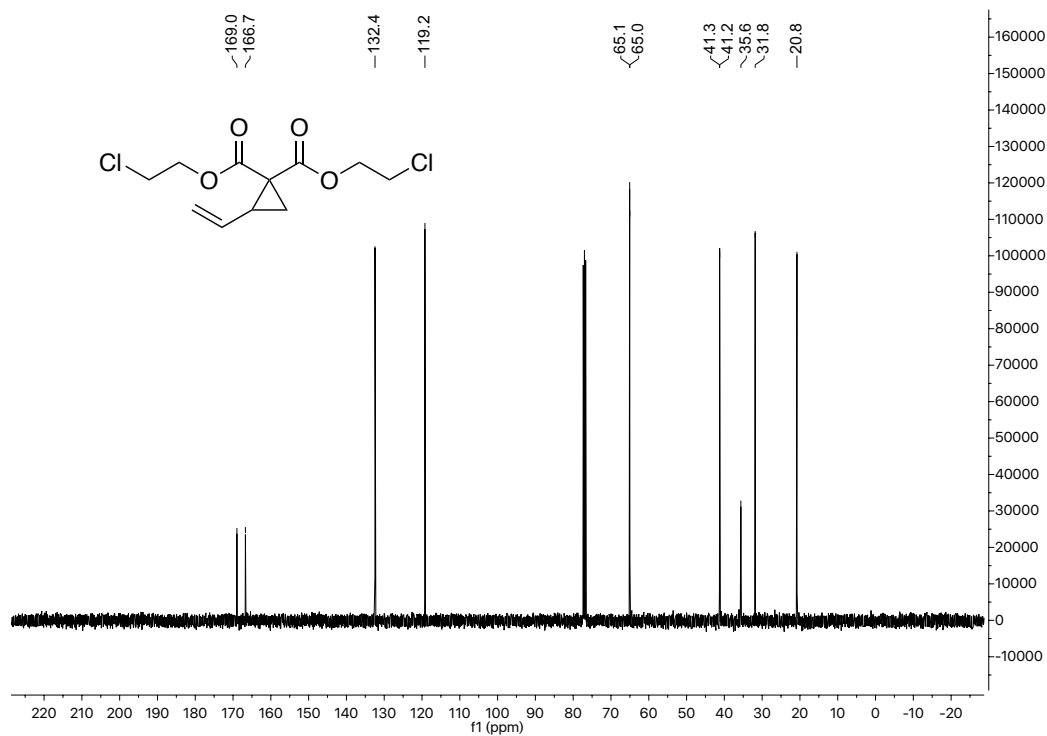
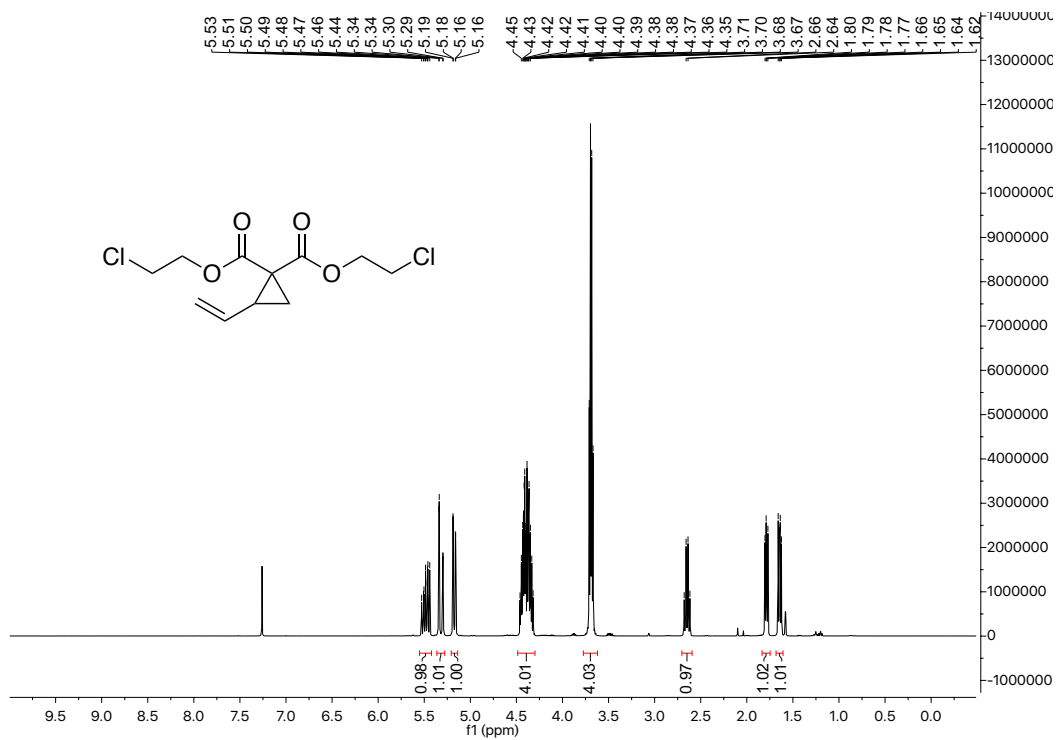
7. NMR Spectra

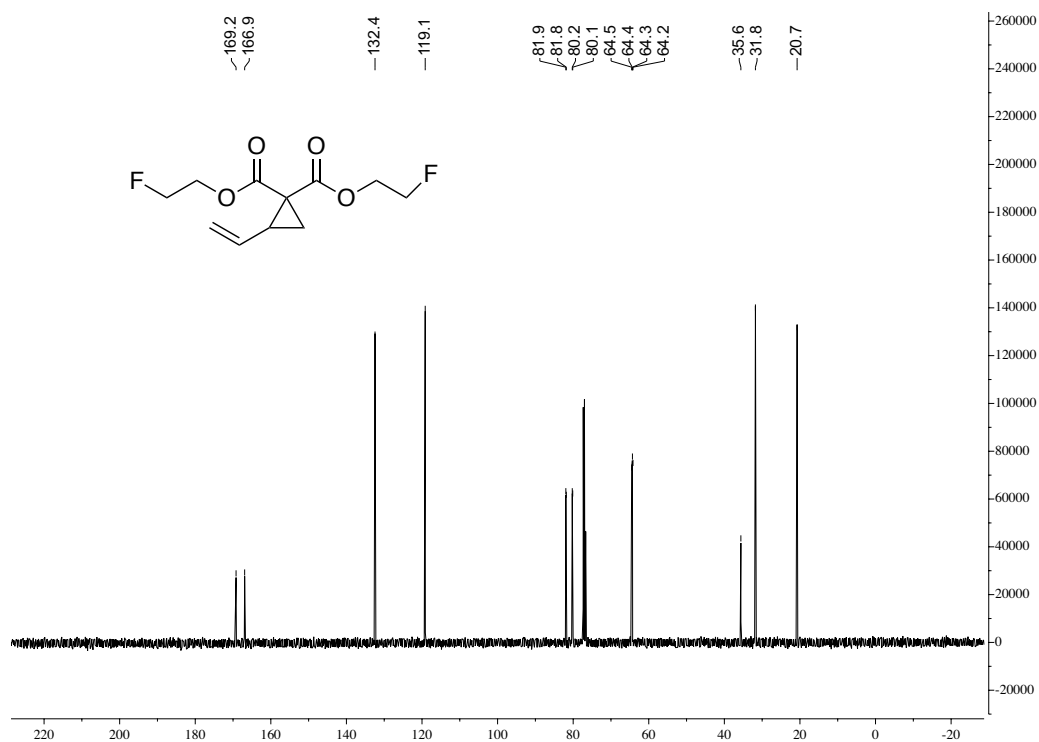
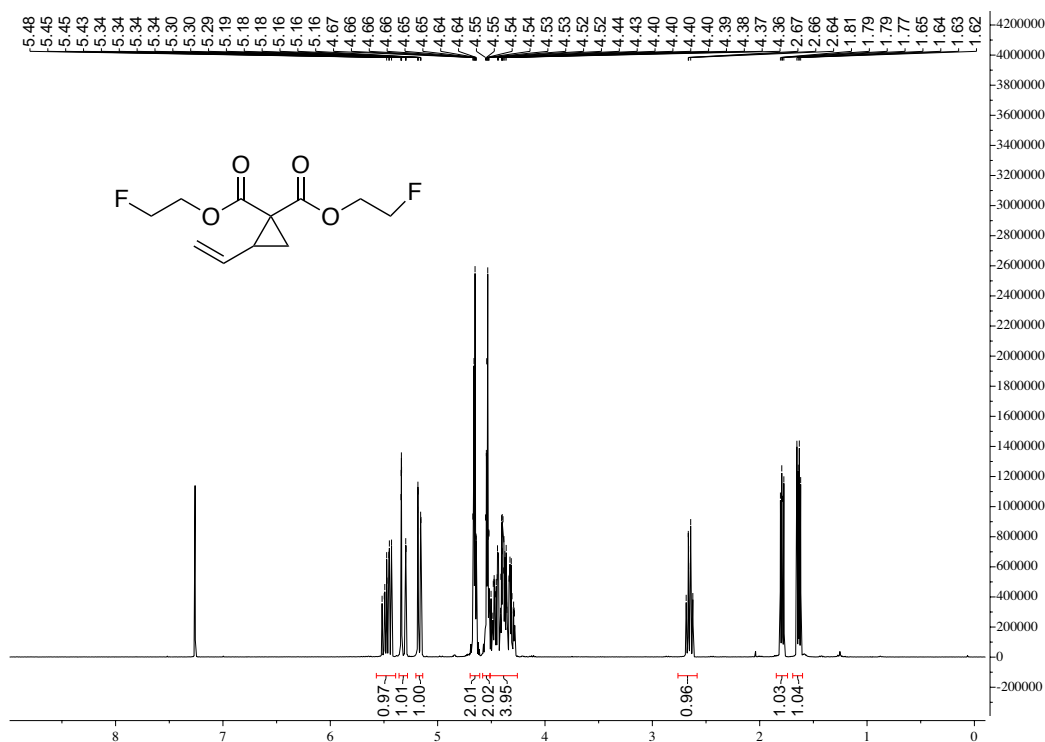


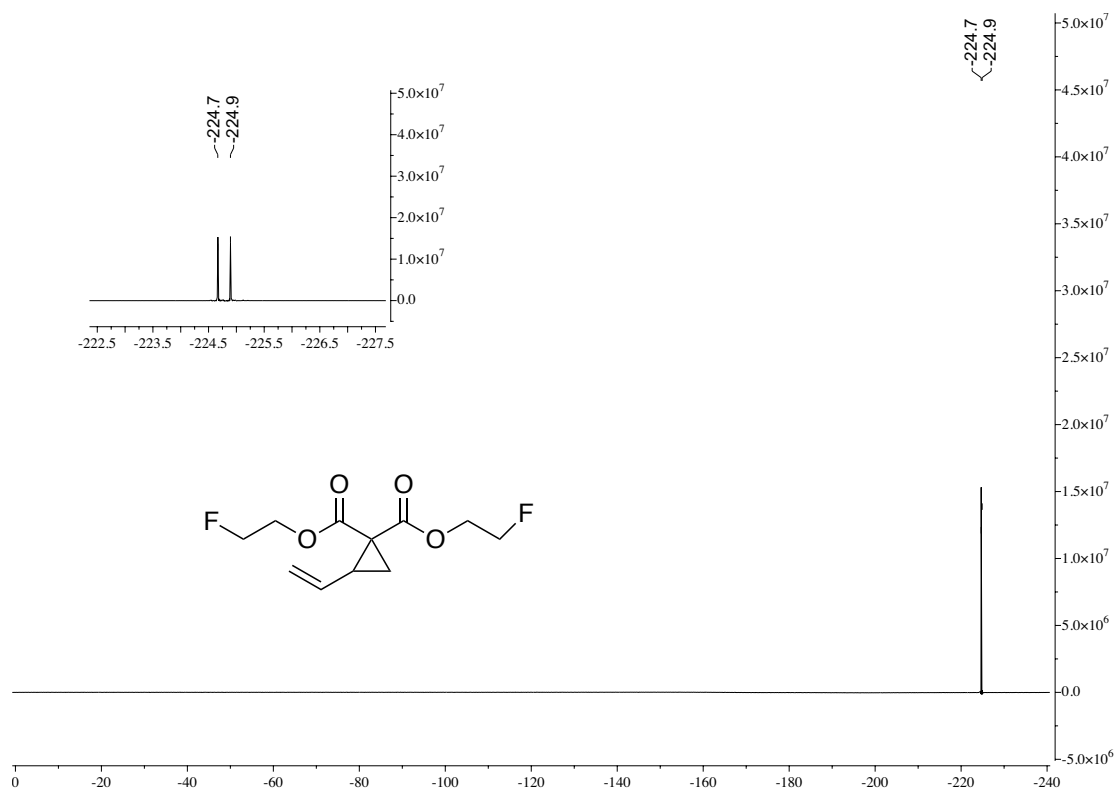


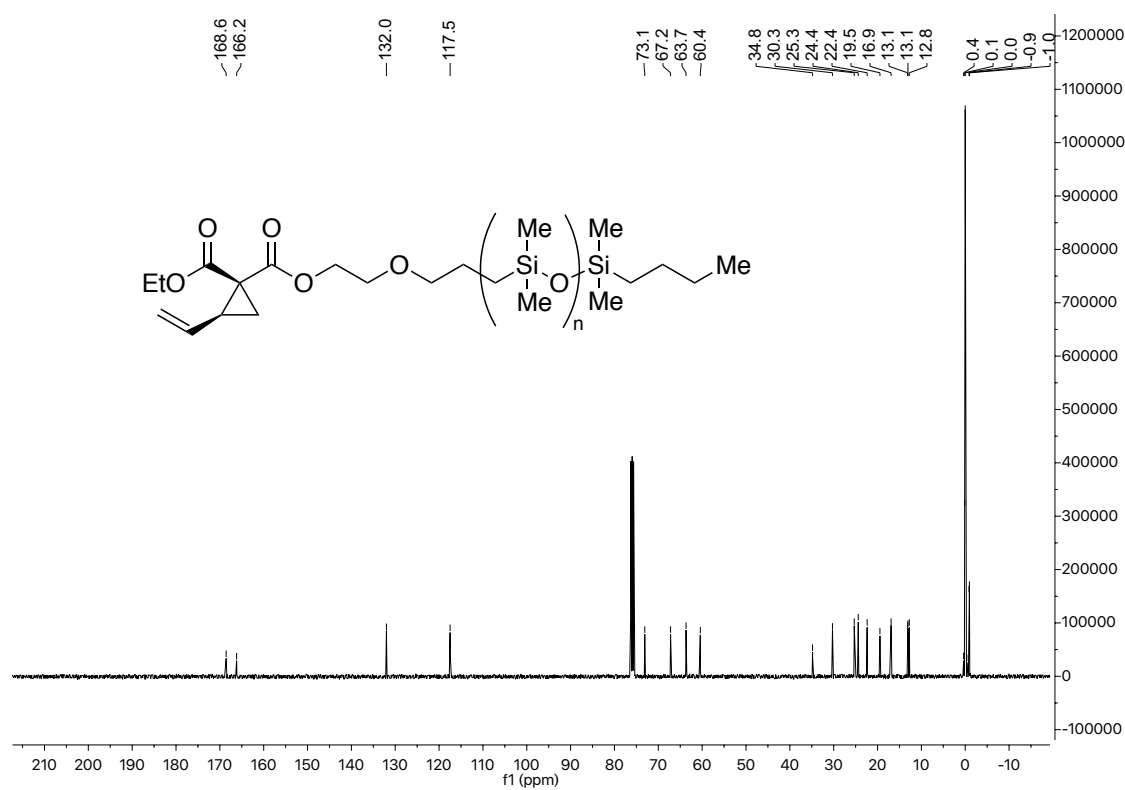
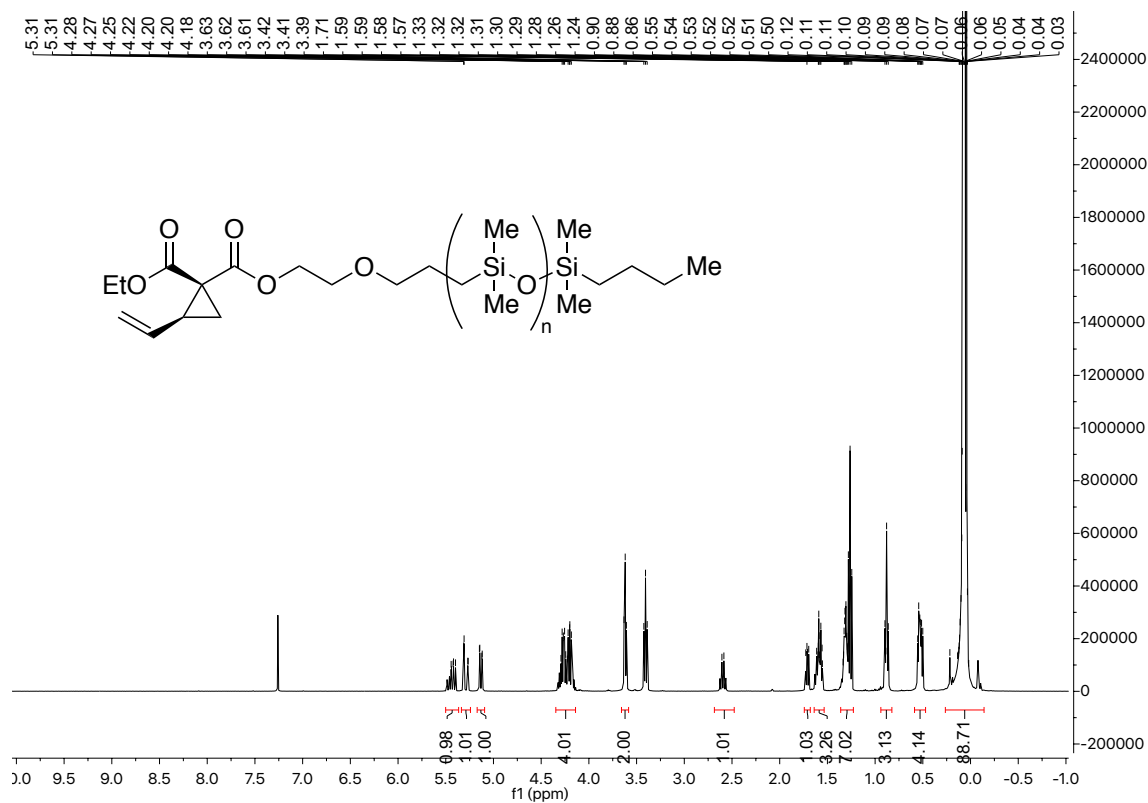


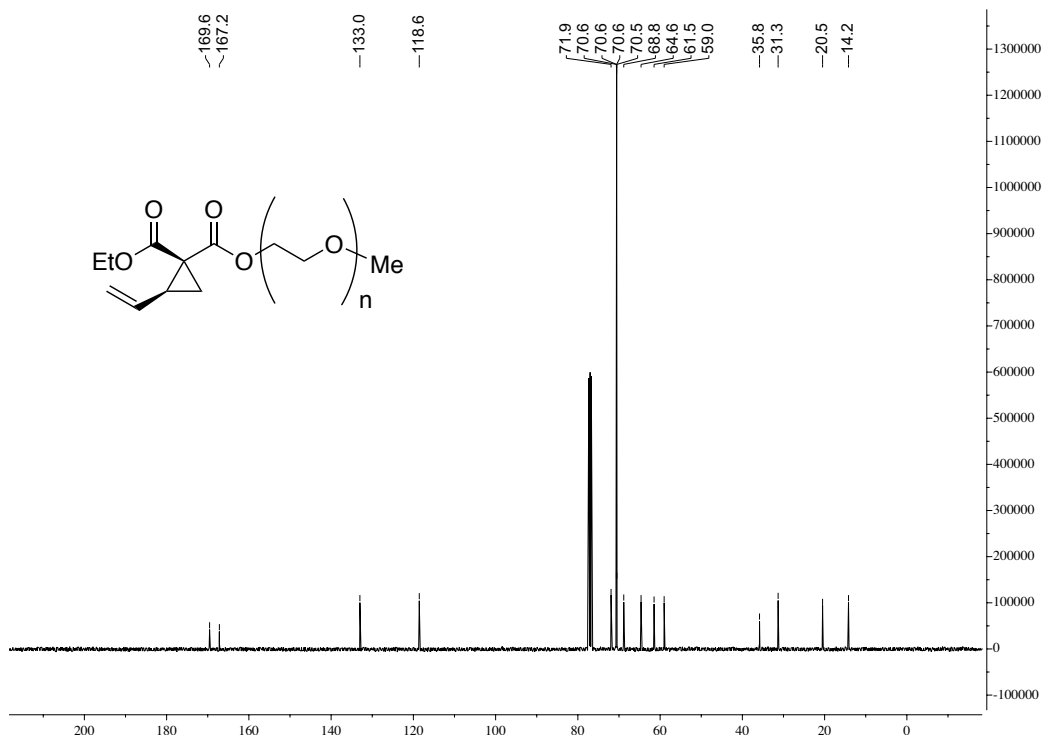
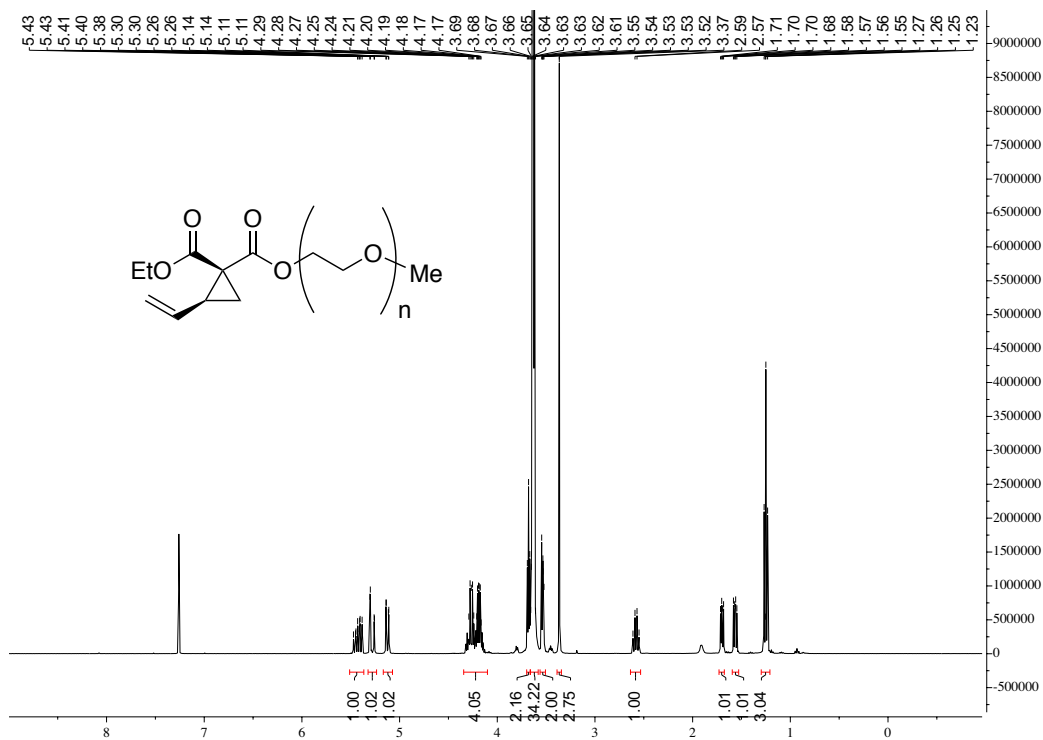


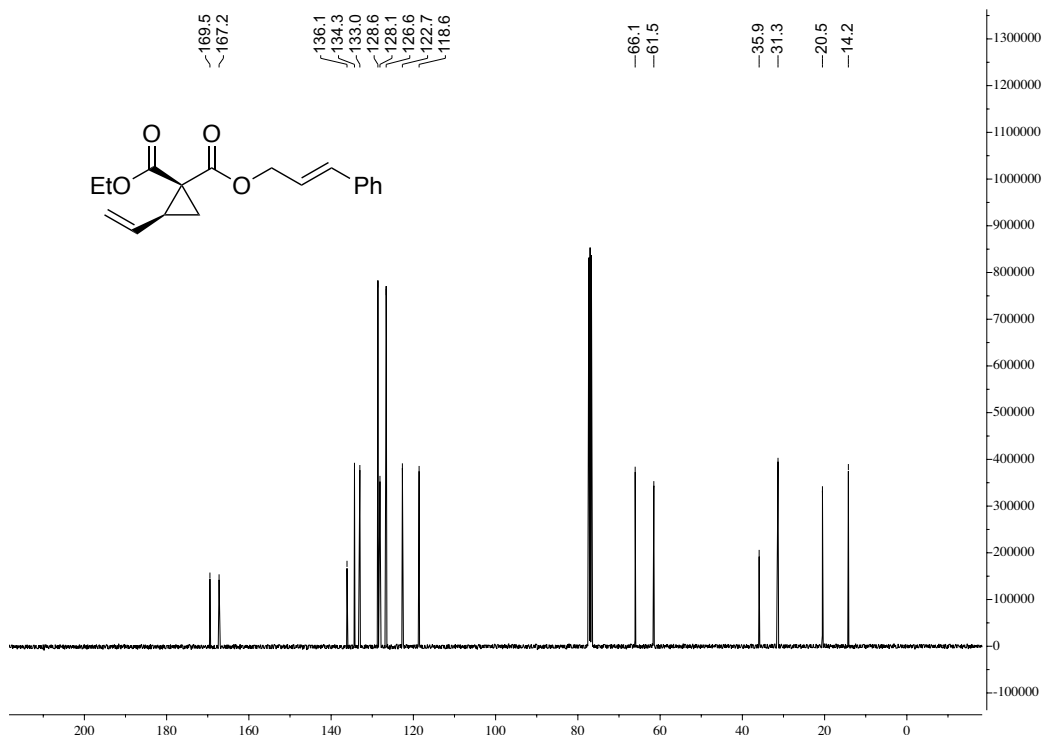
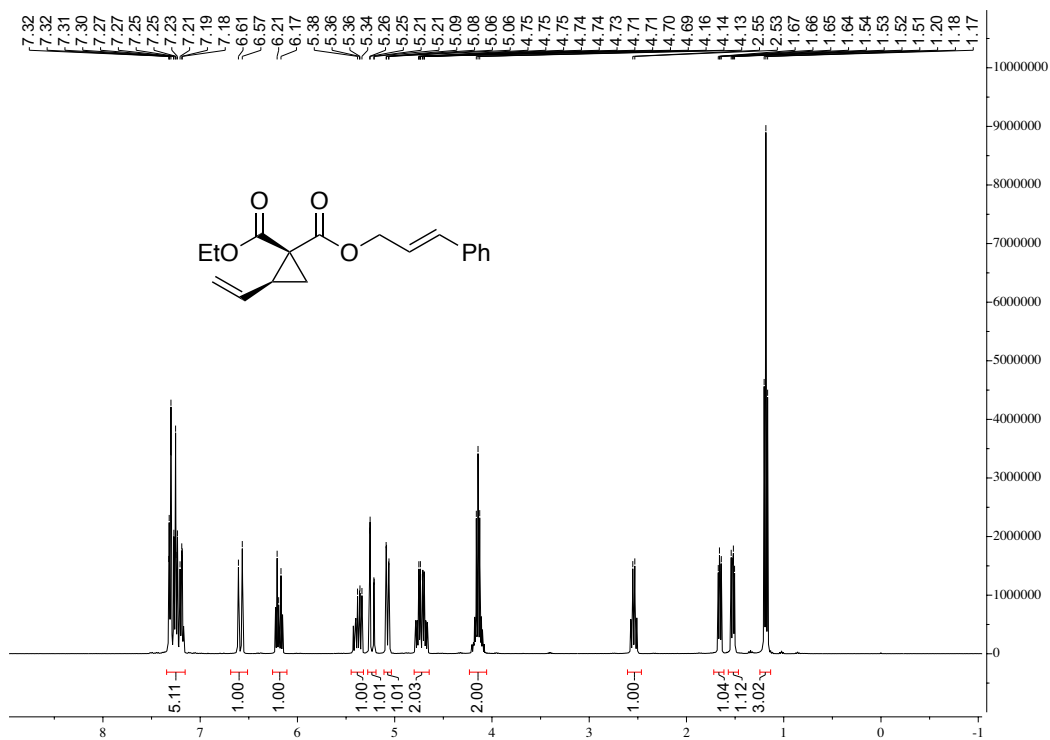


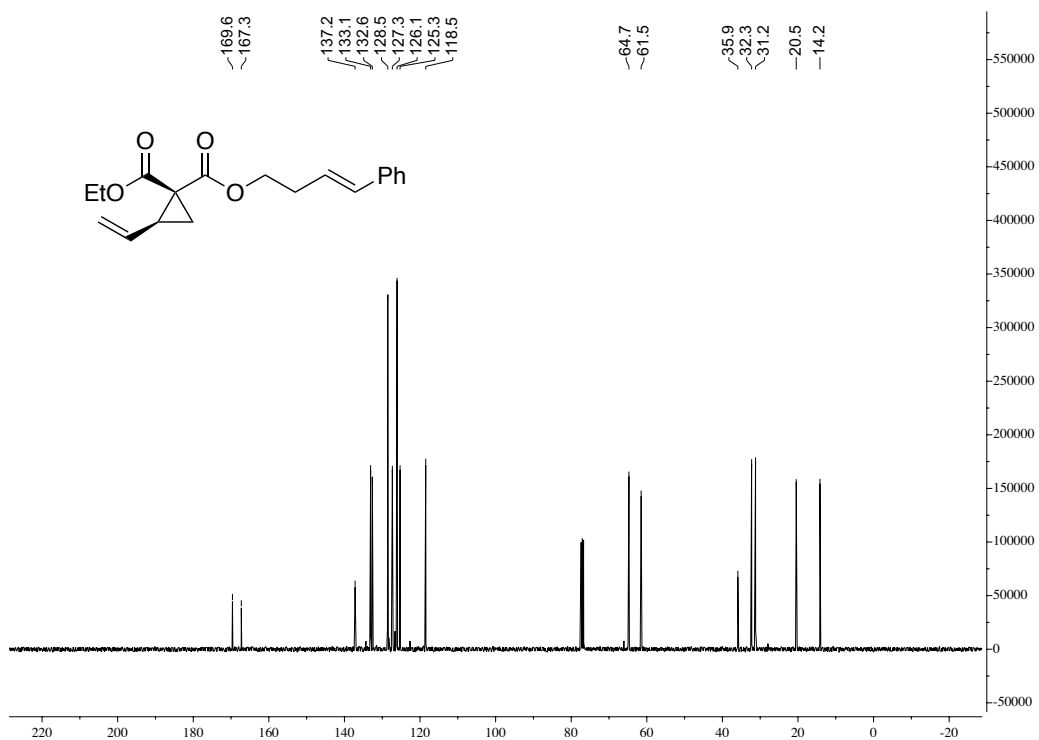
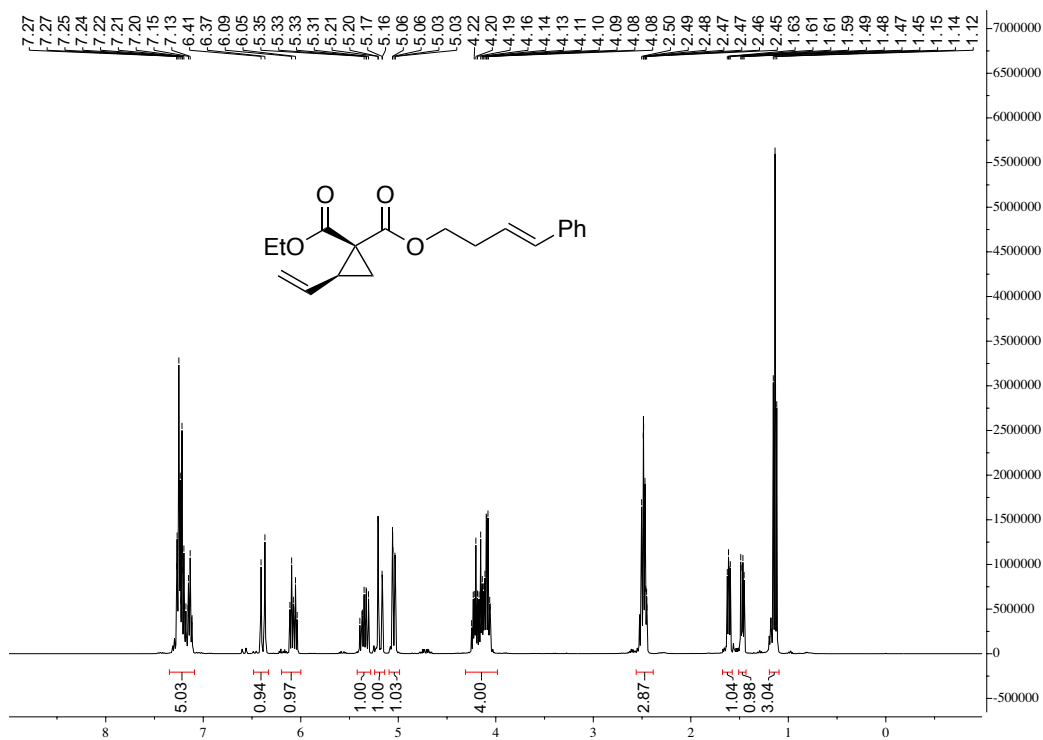


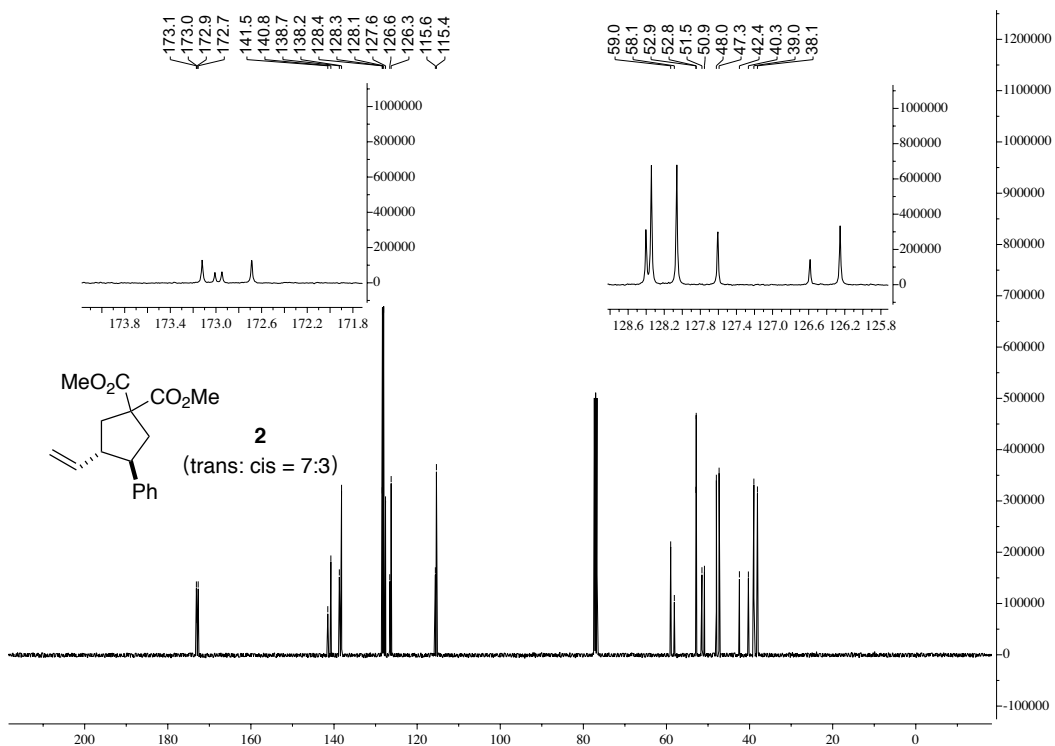
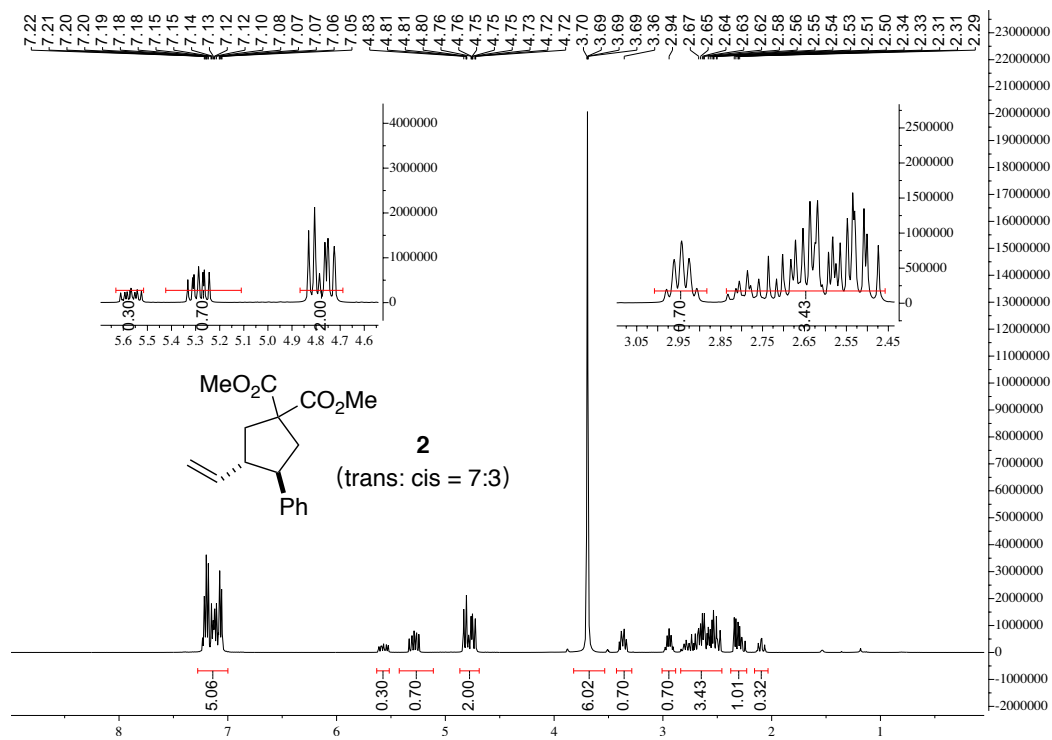


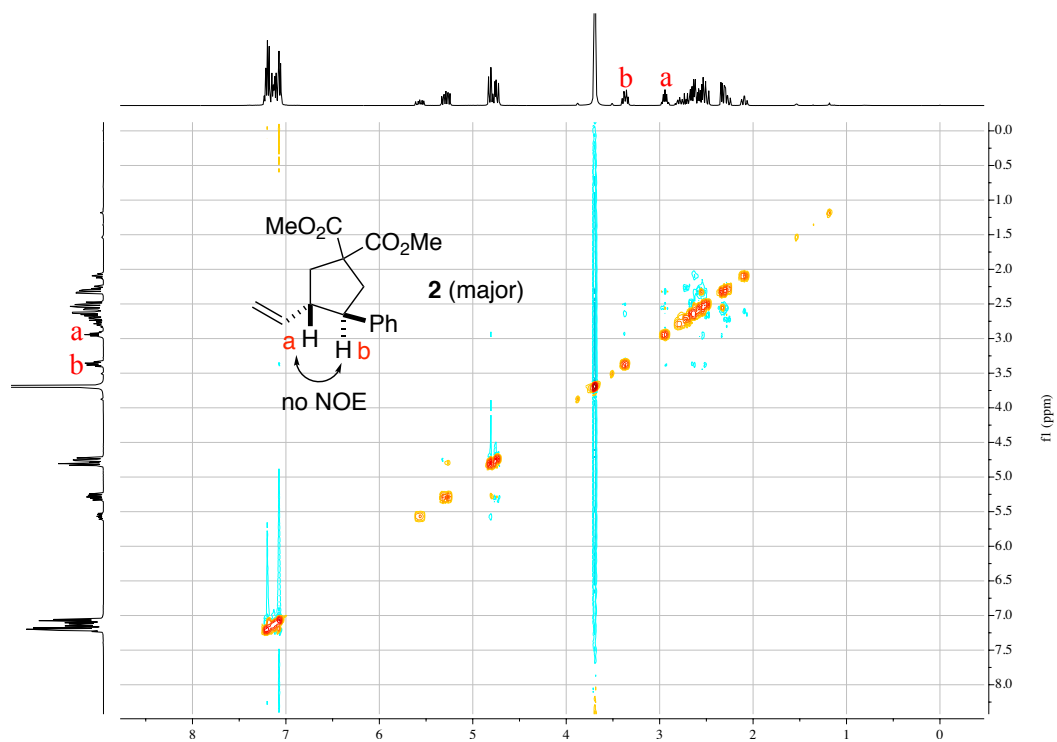
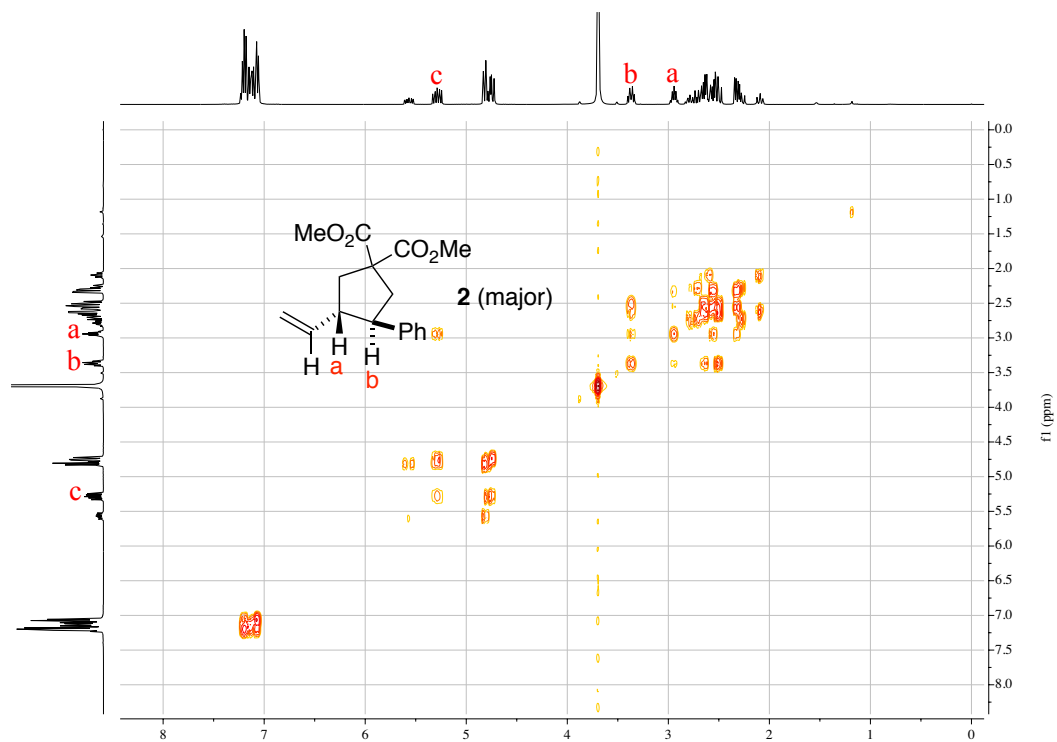


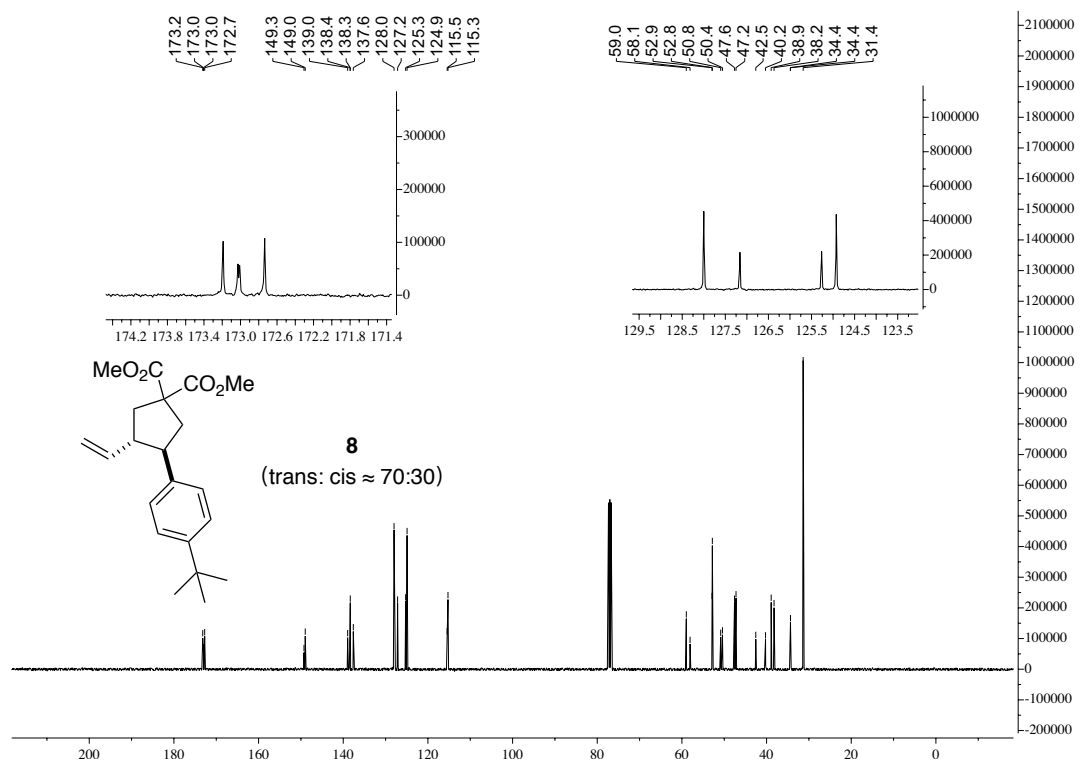
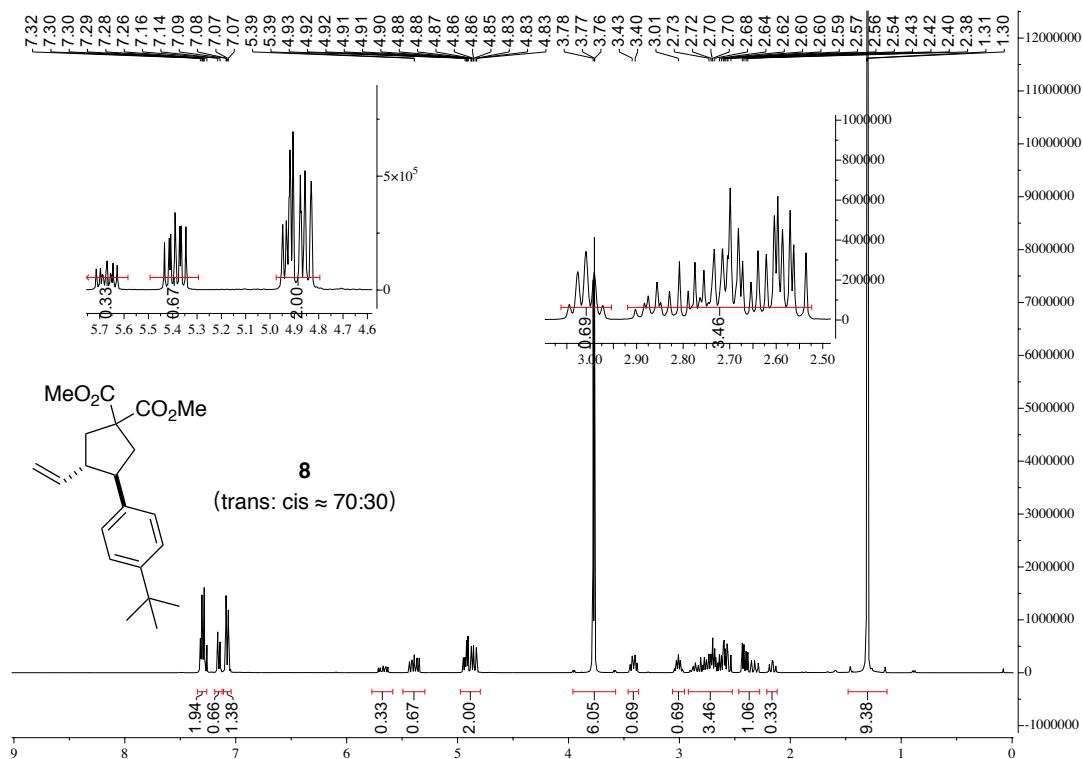


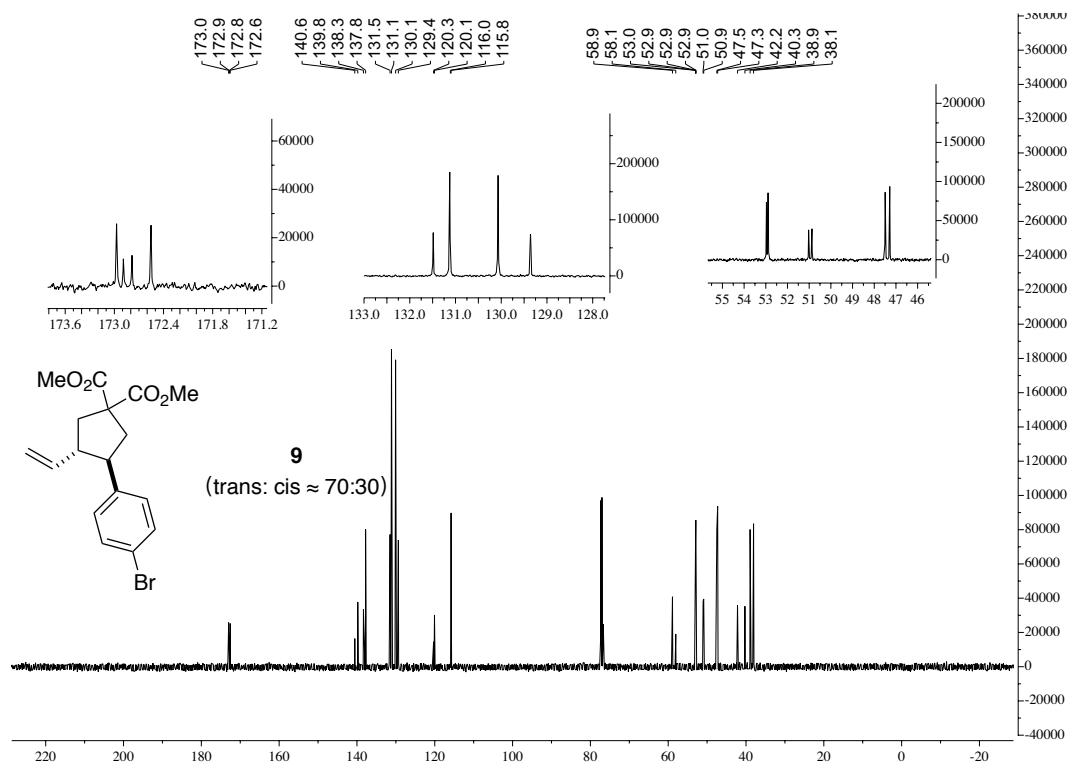
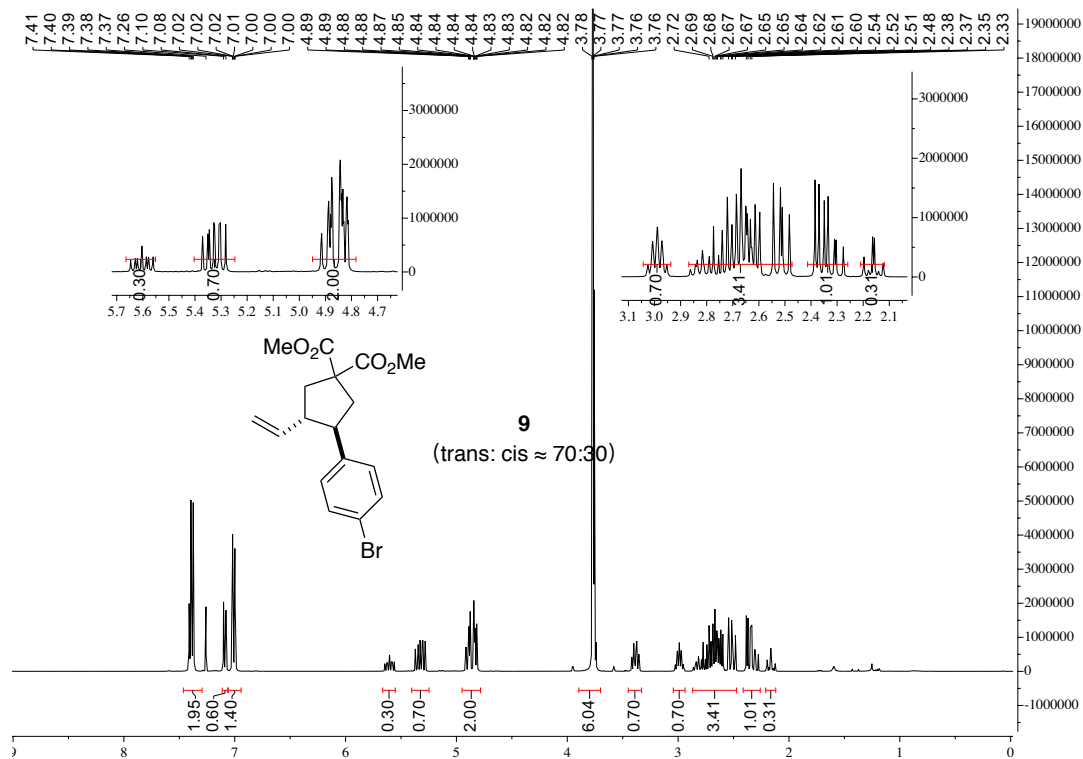


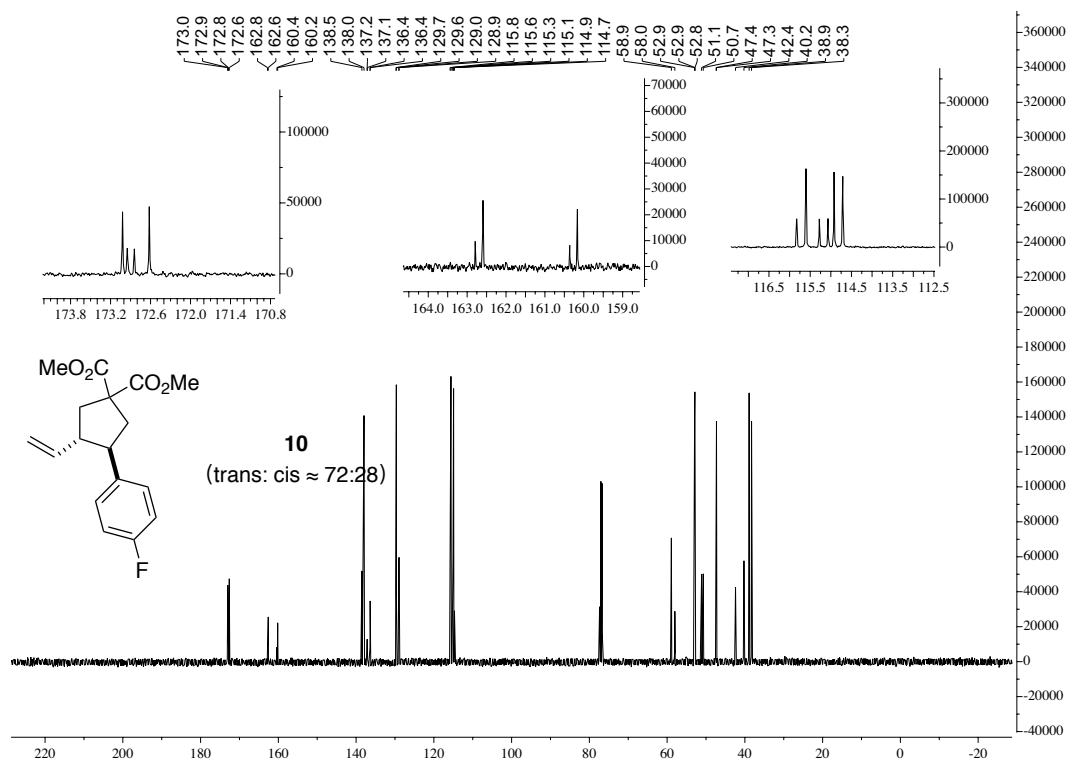
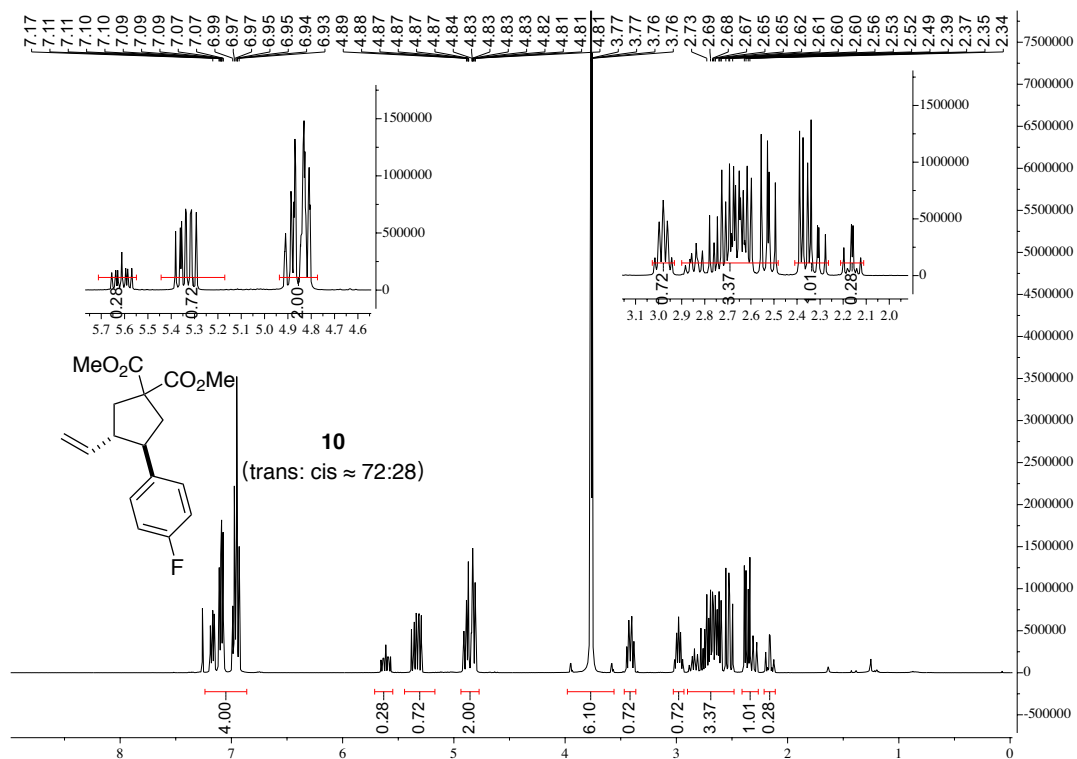


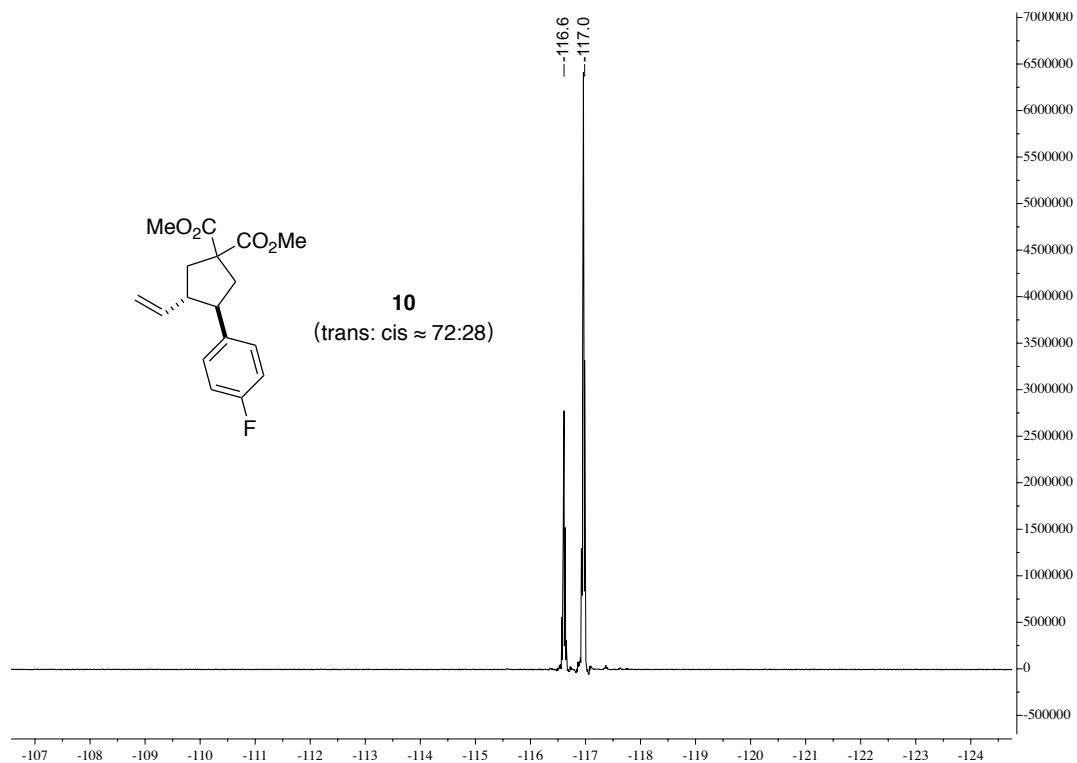


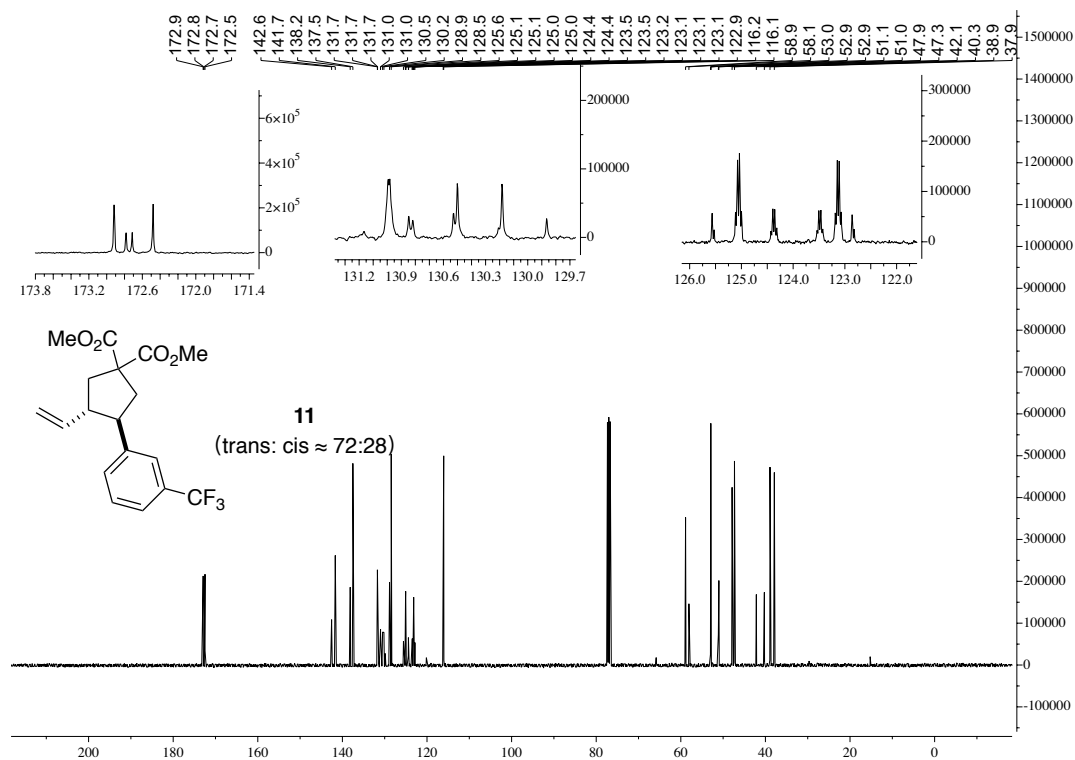
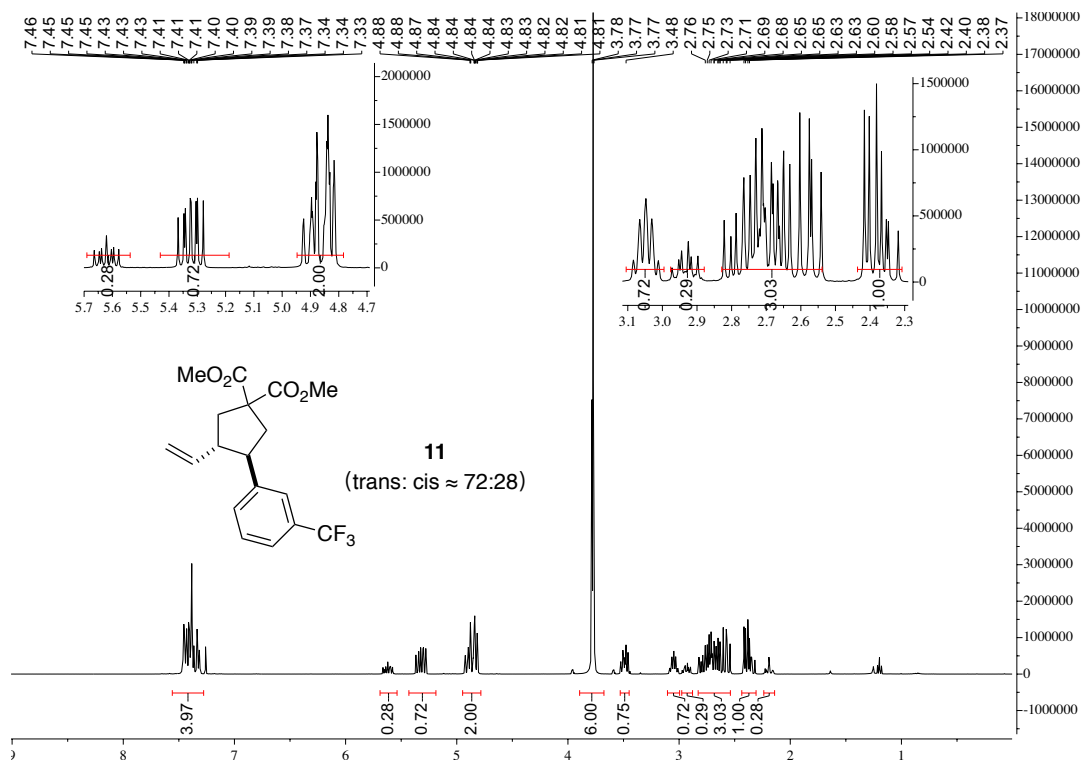


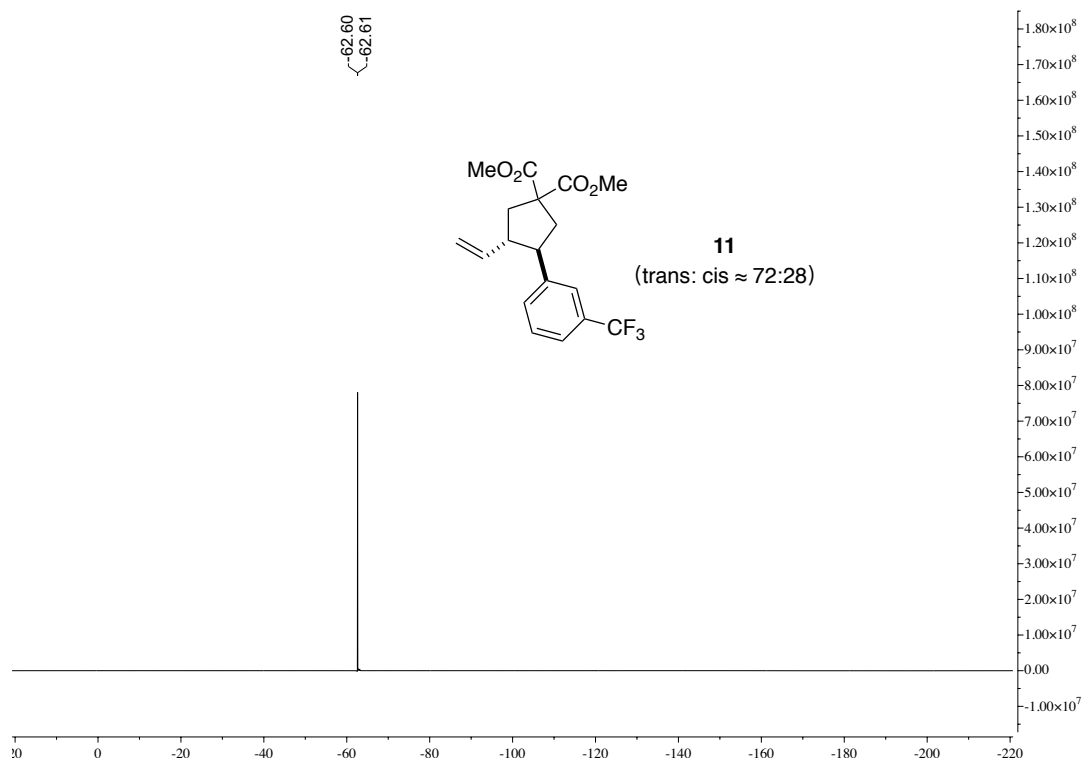


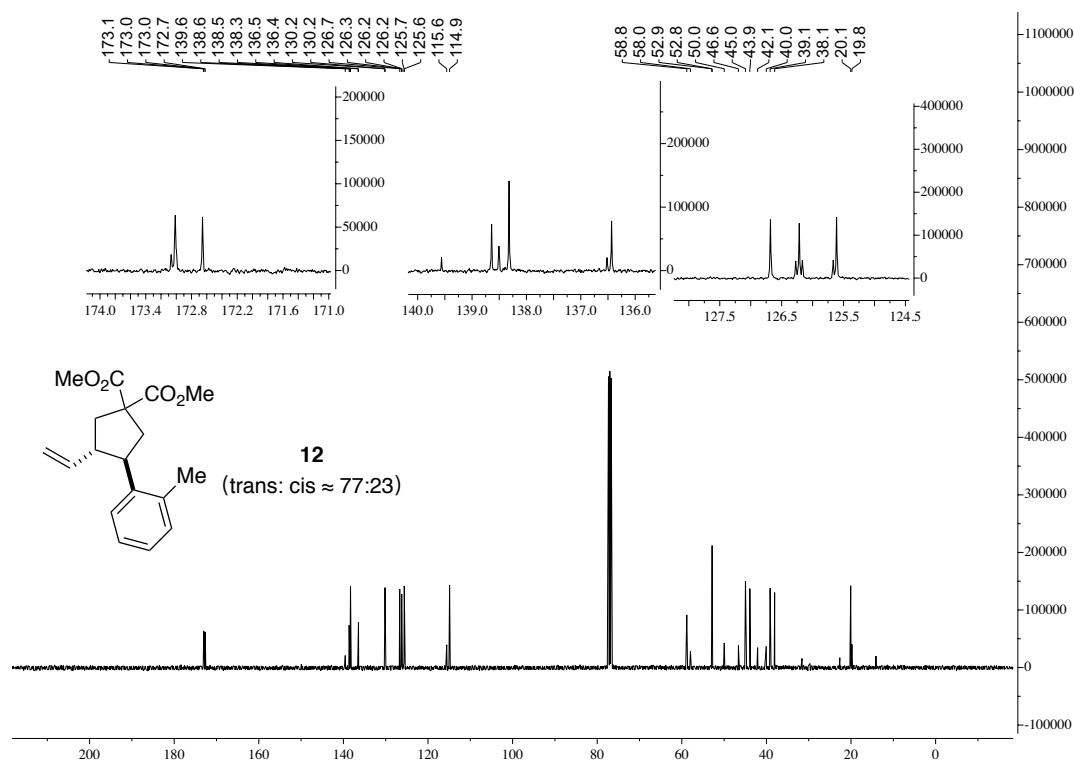
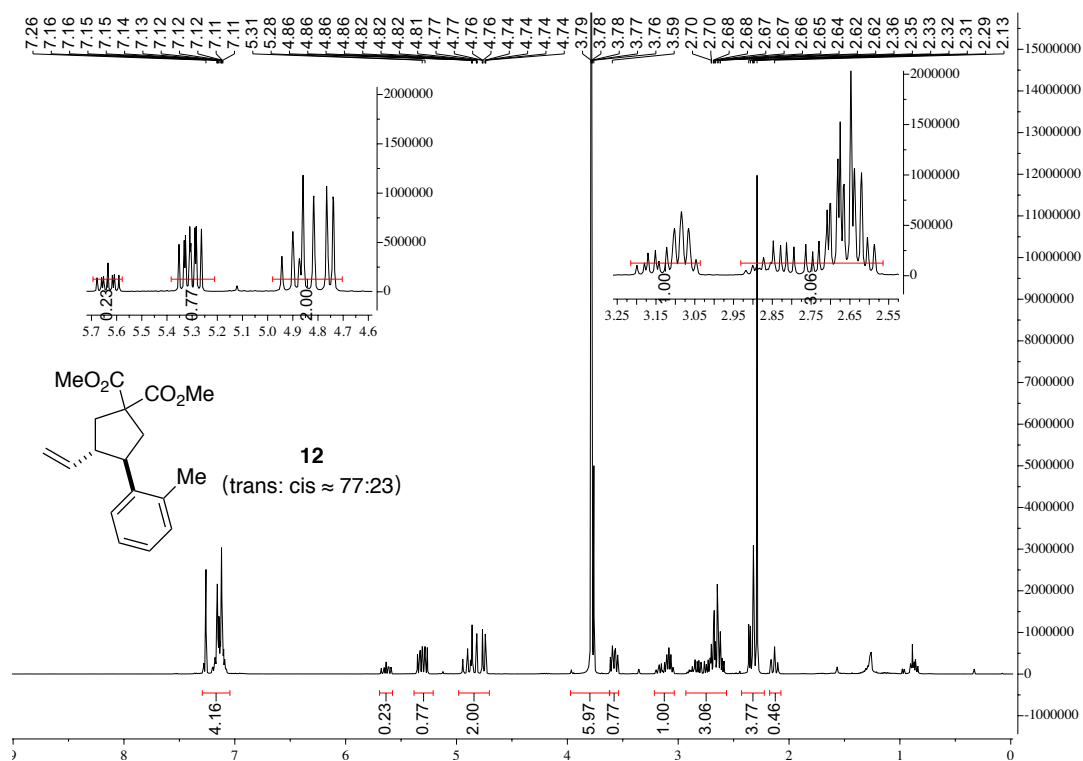


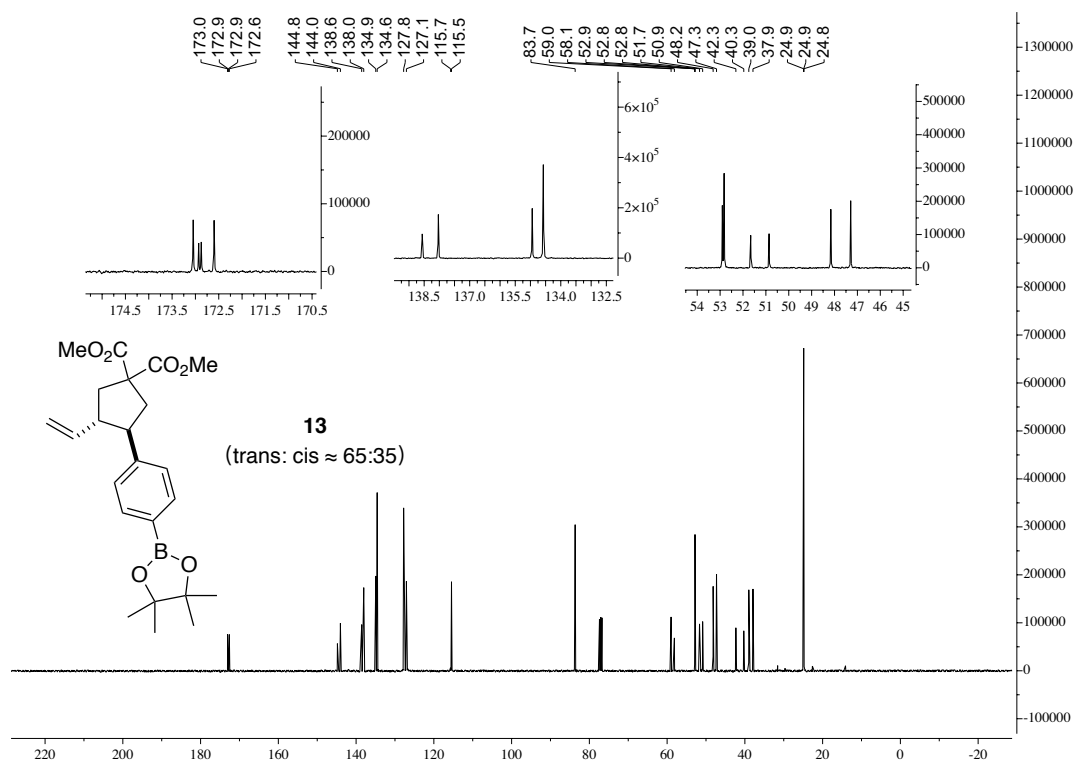
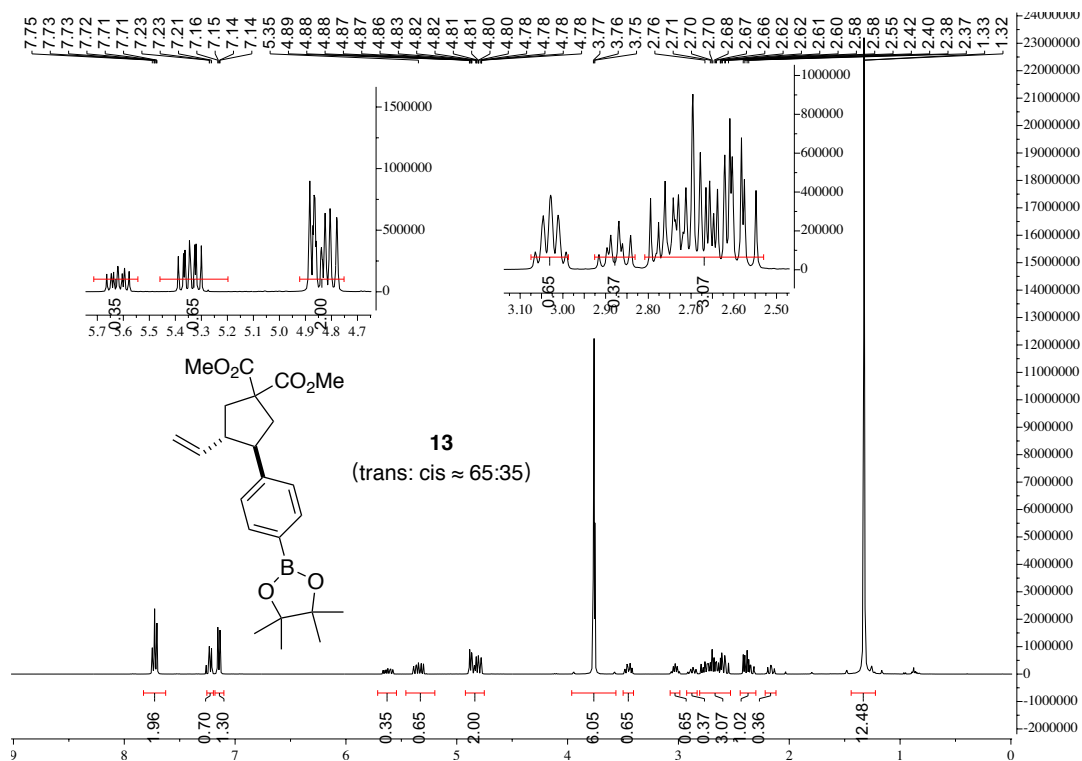


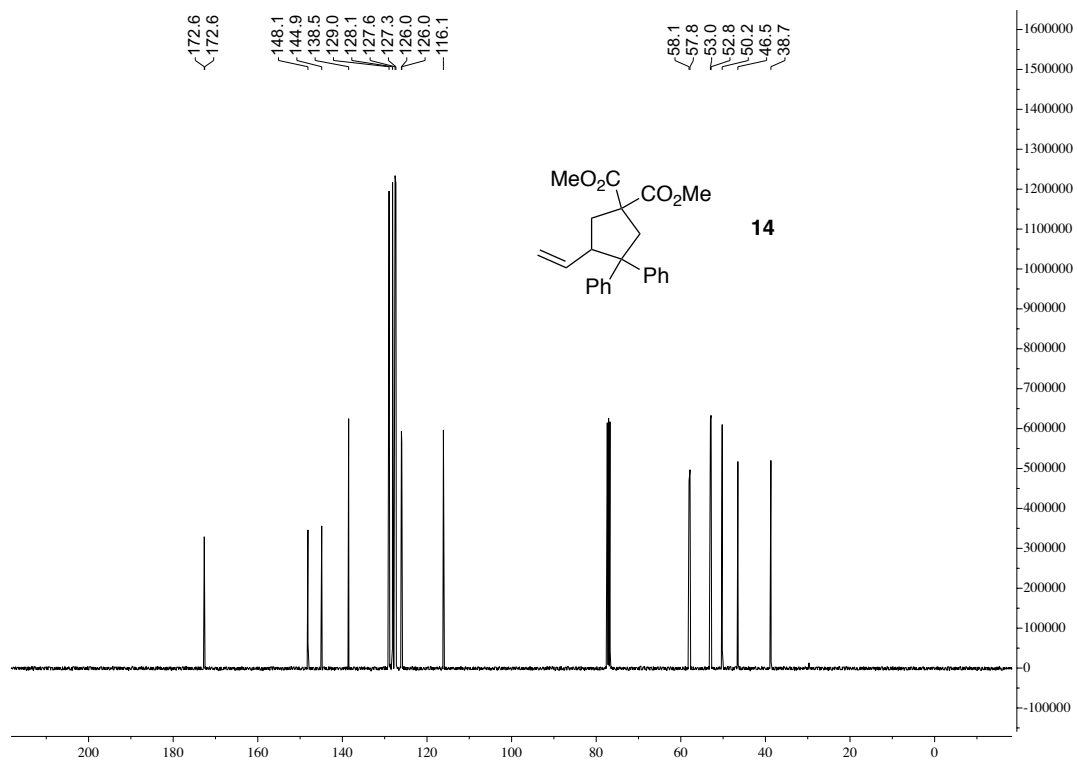
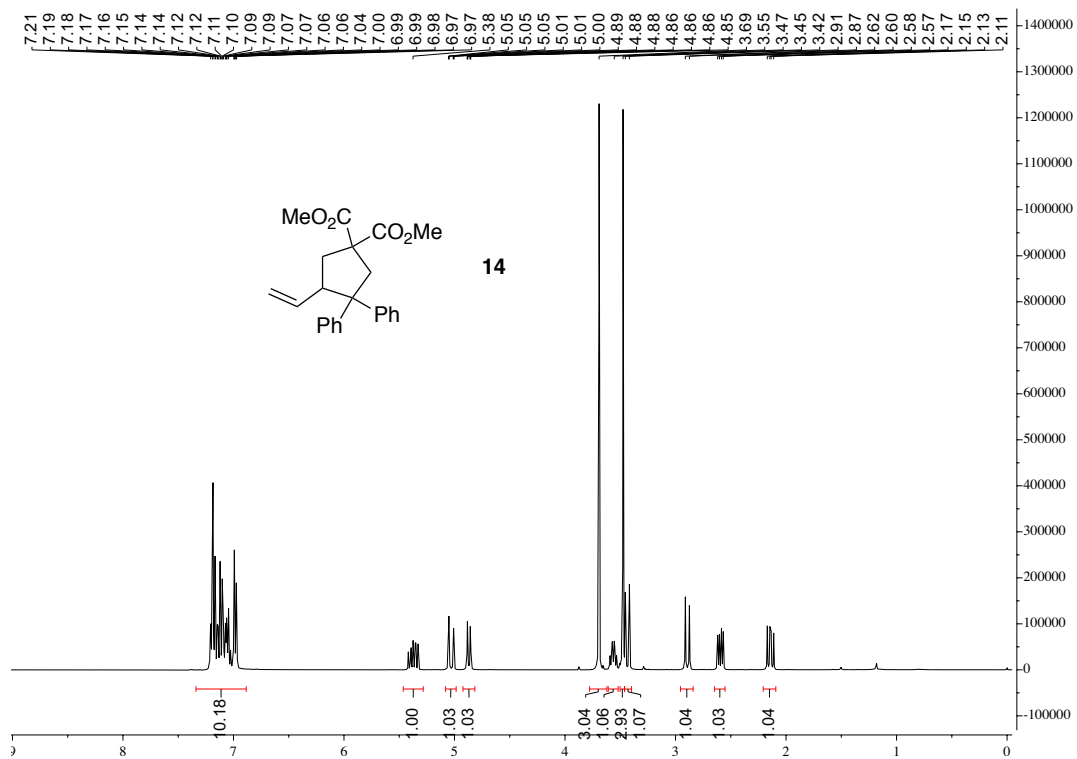


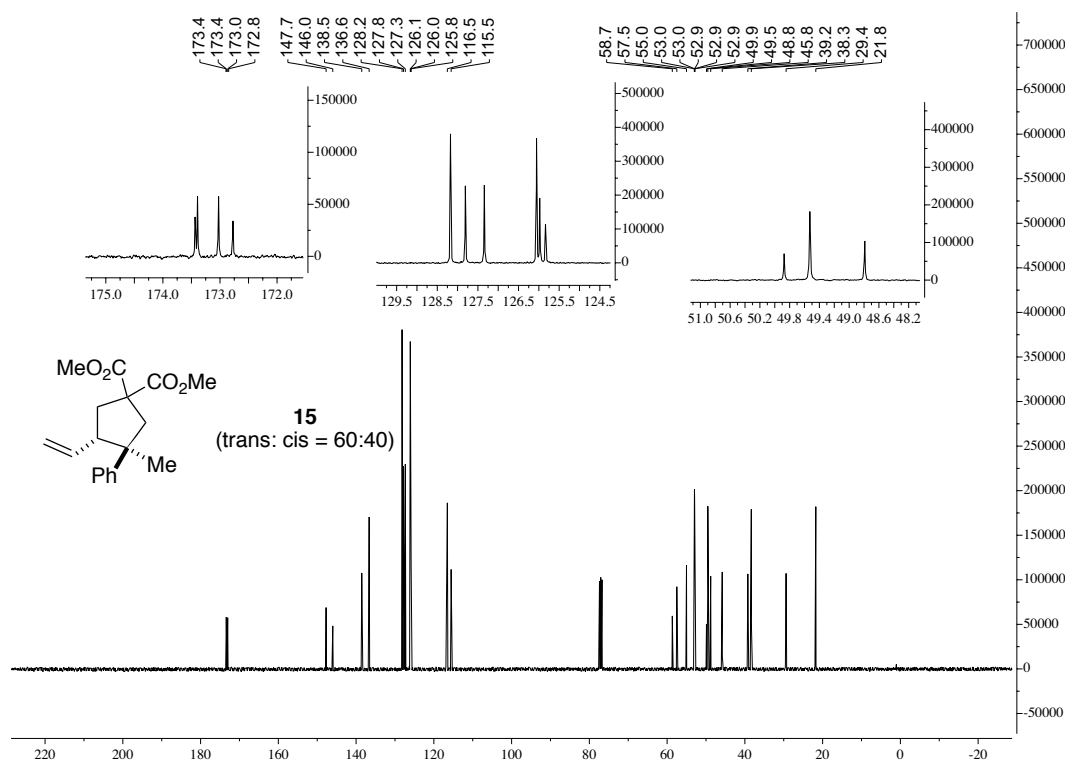
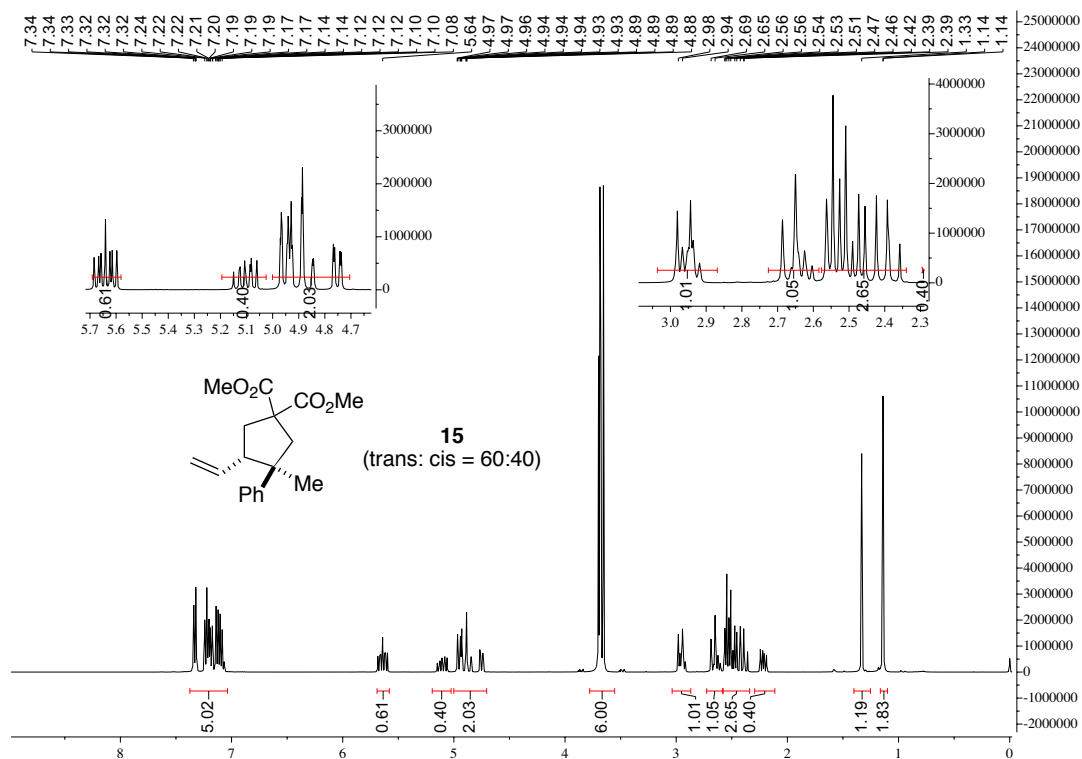


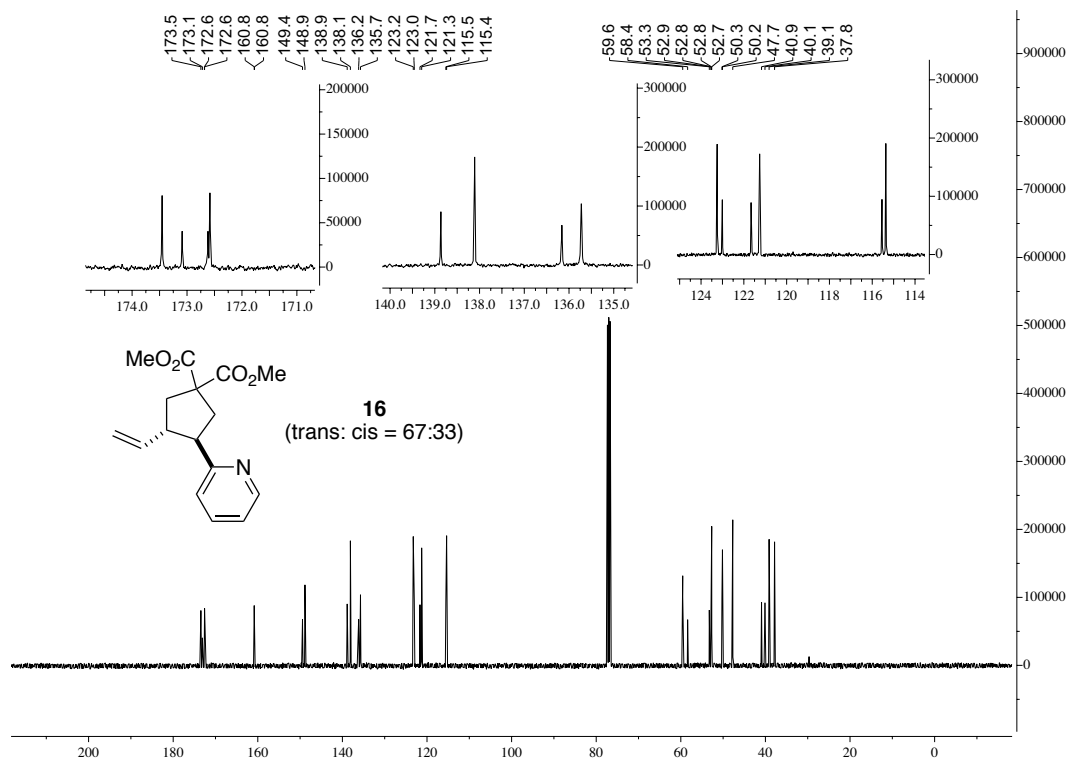
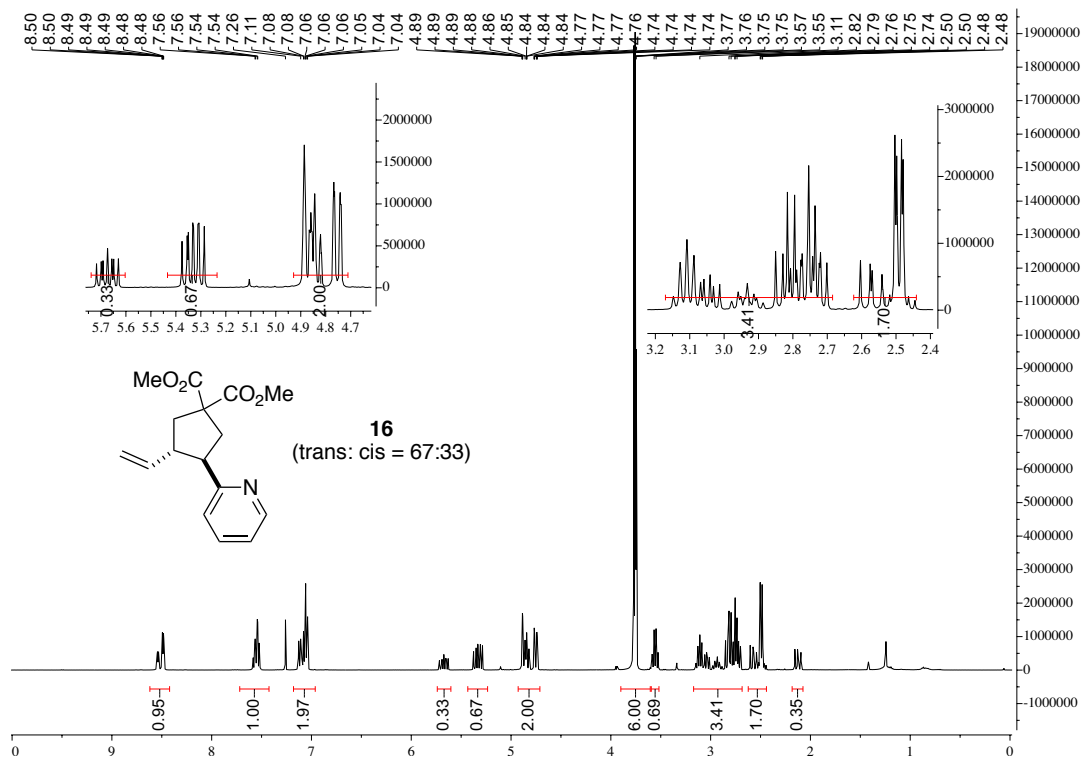


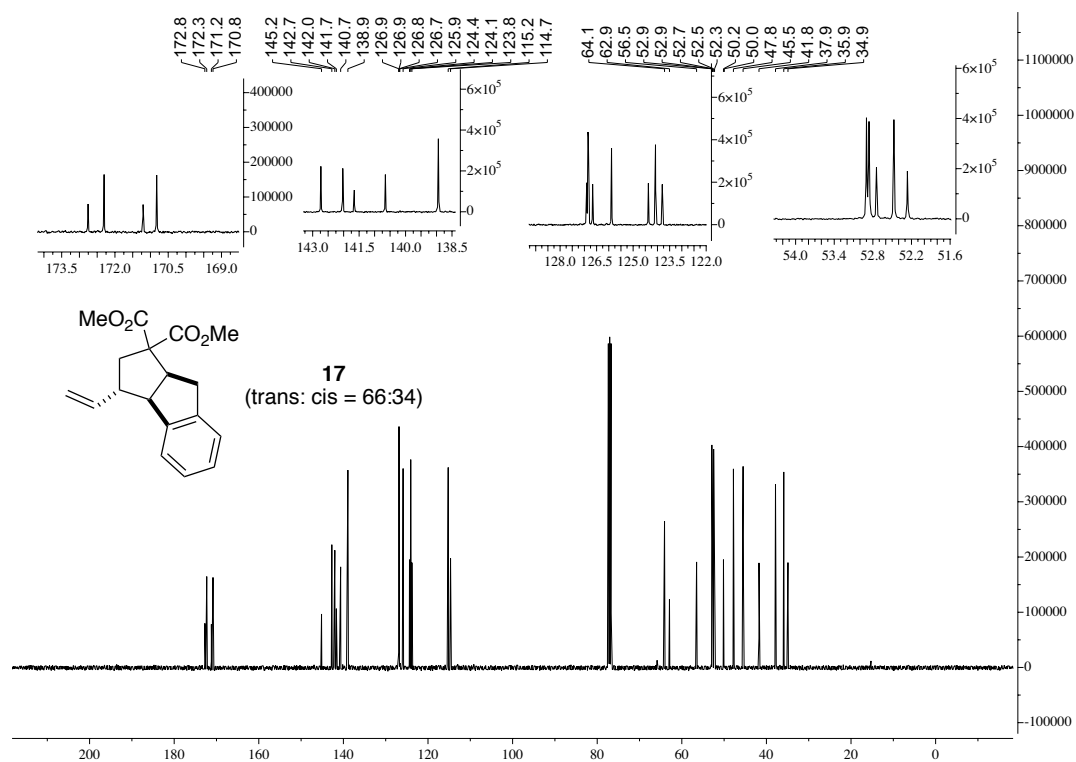
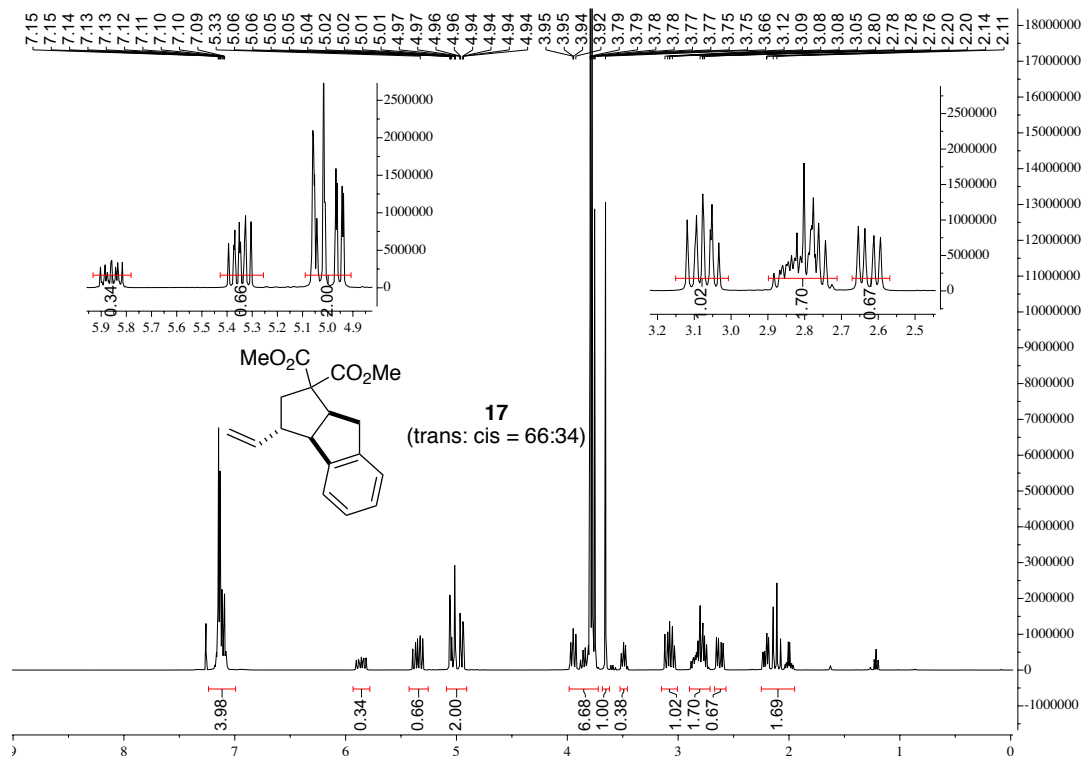


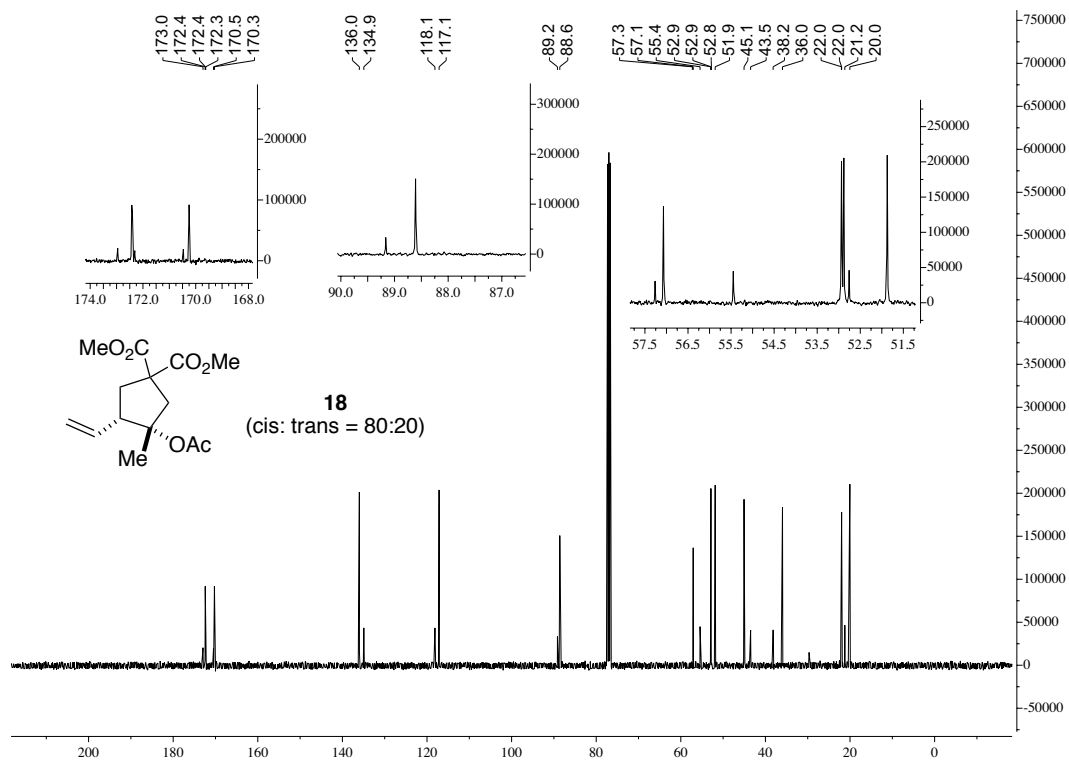
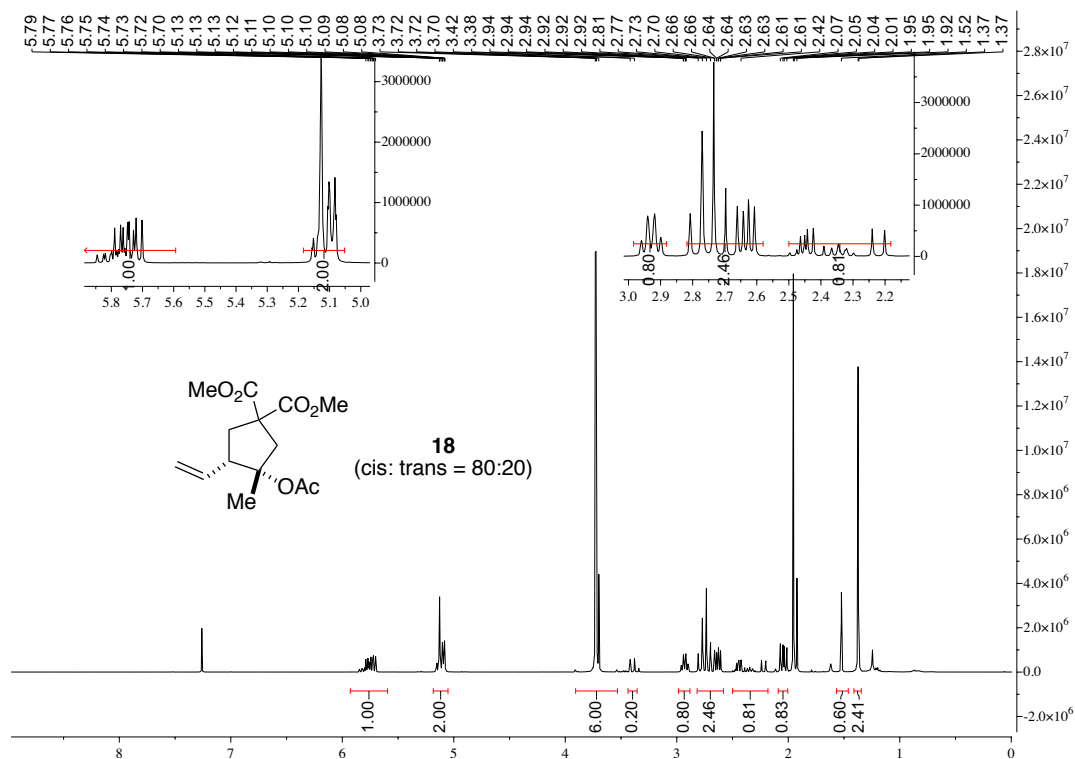


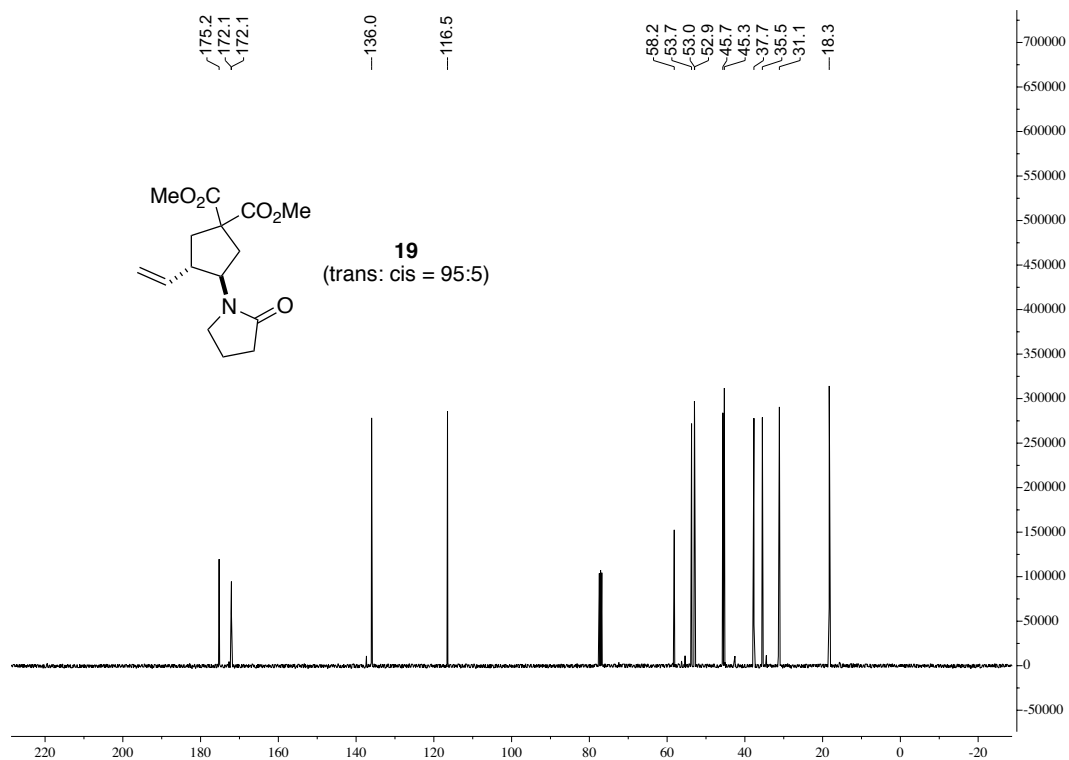
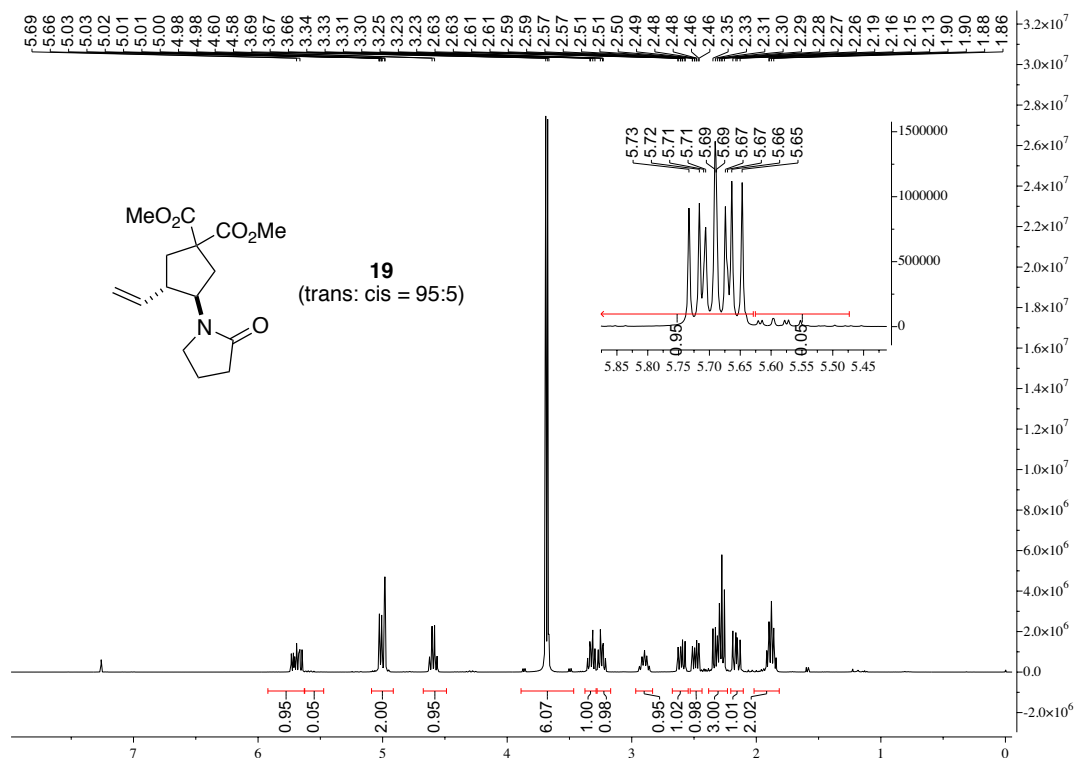


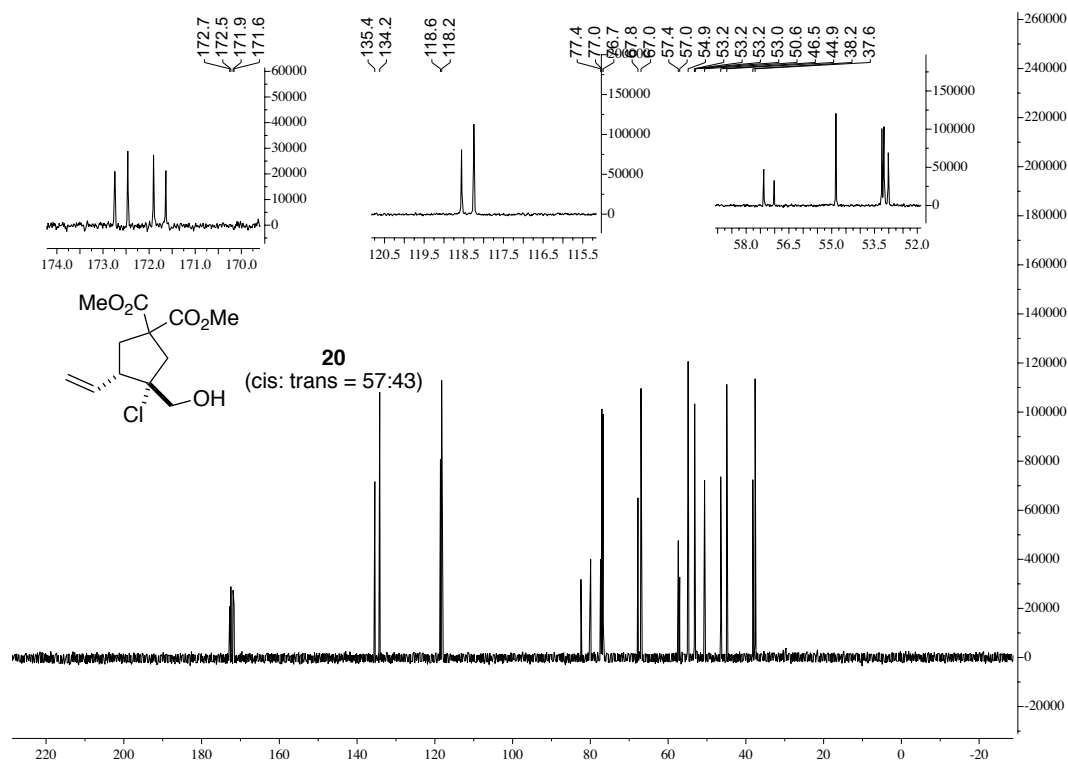
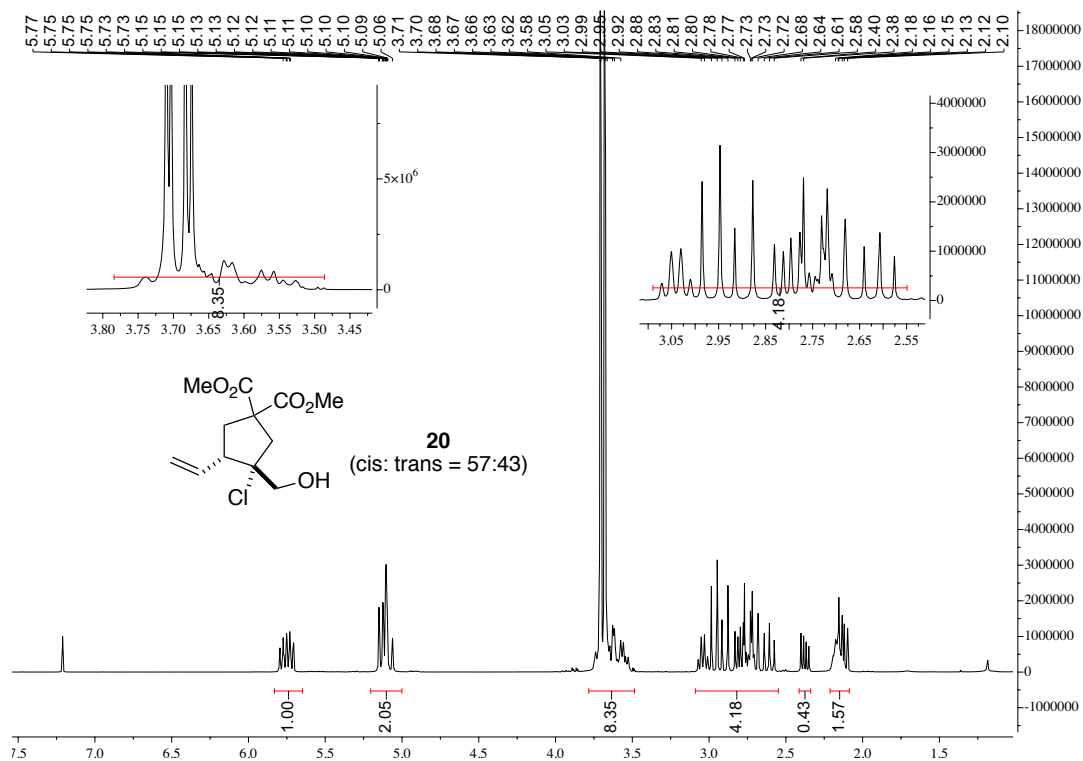


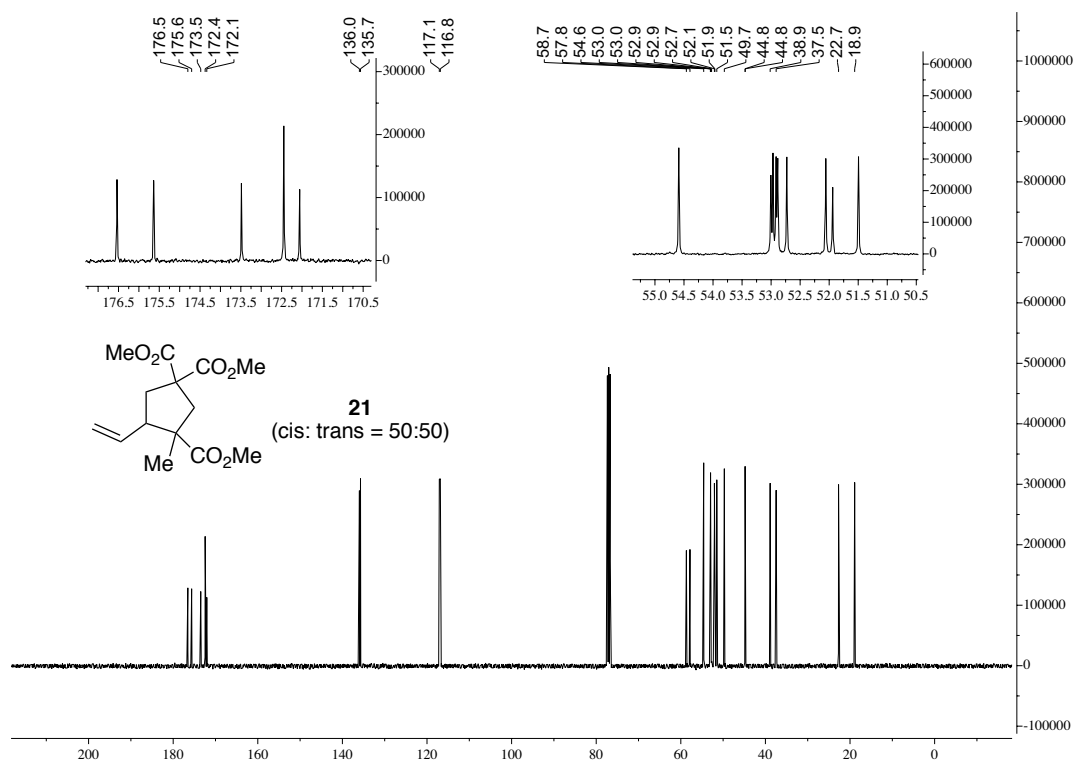
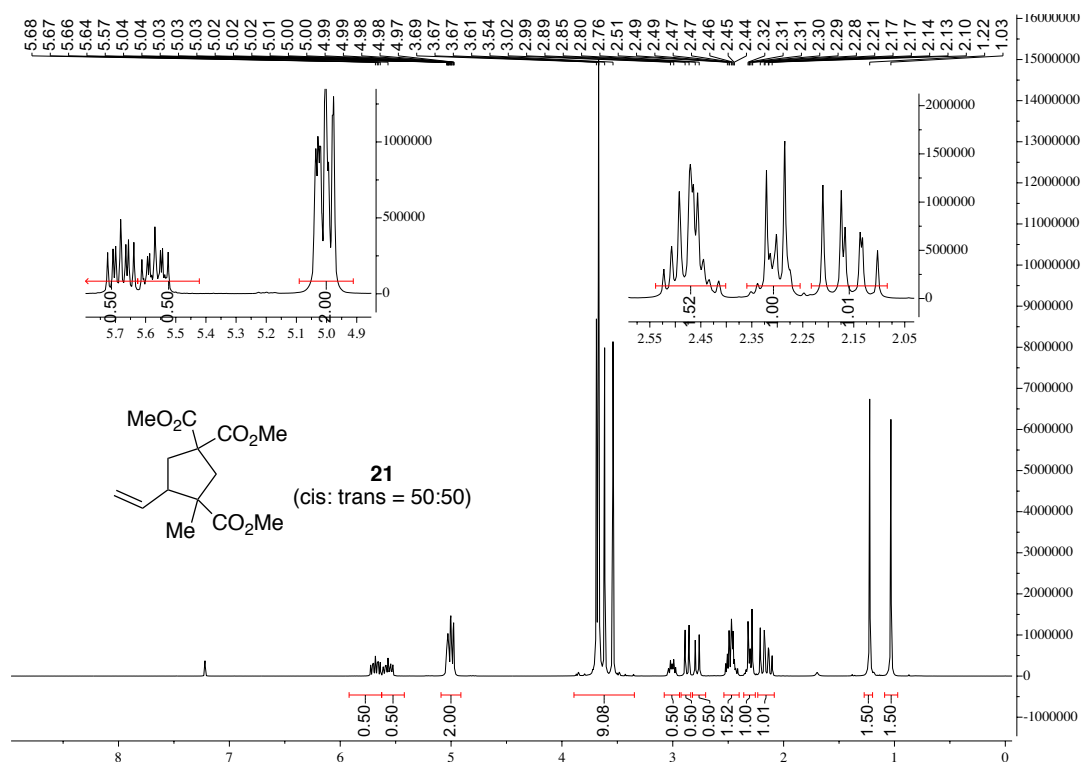


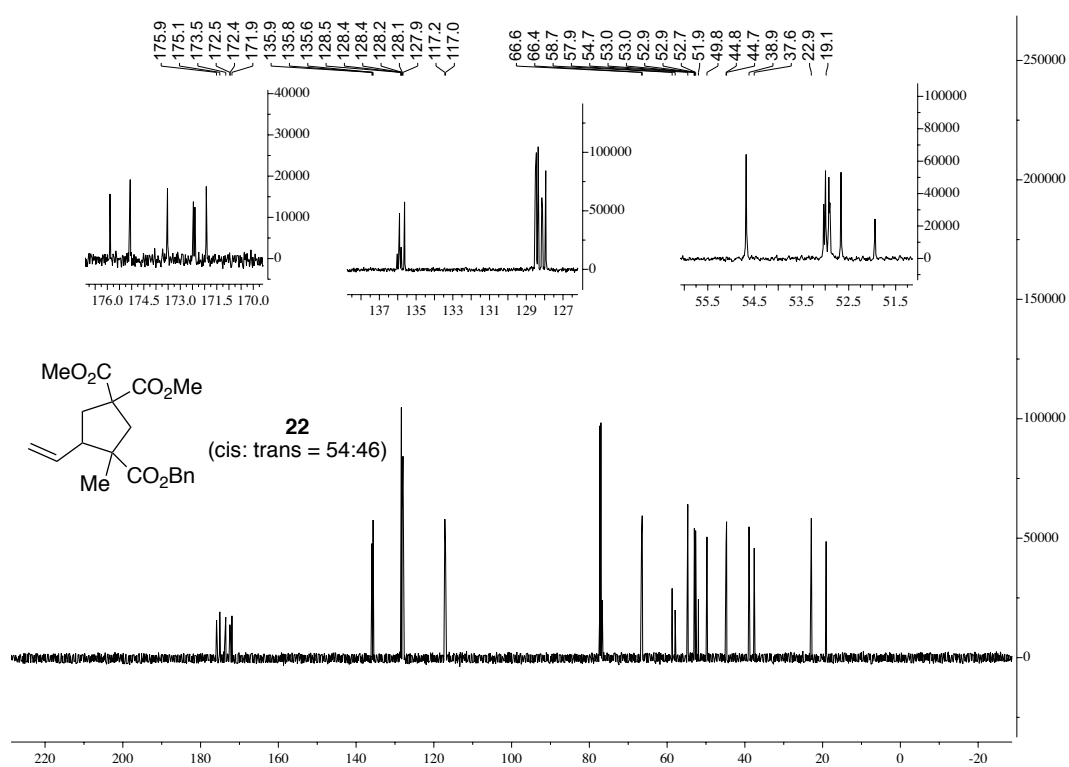
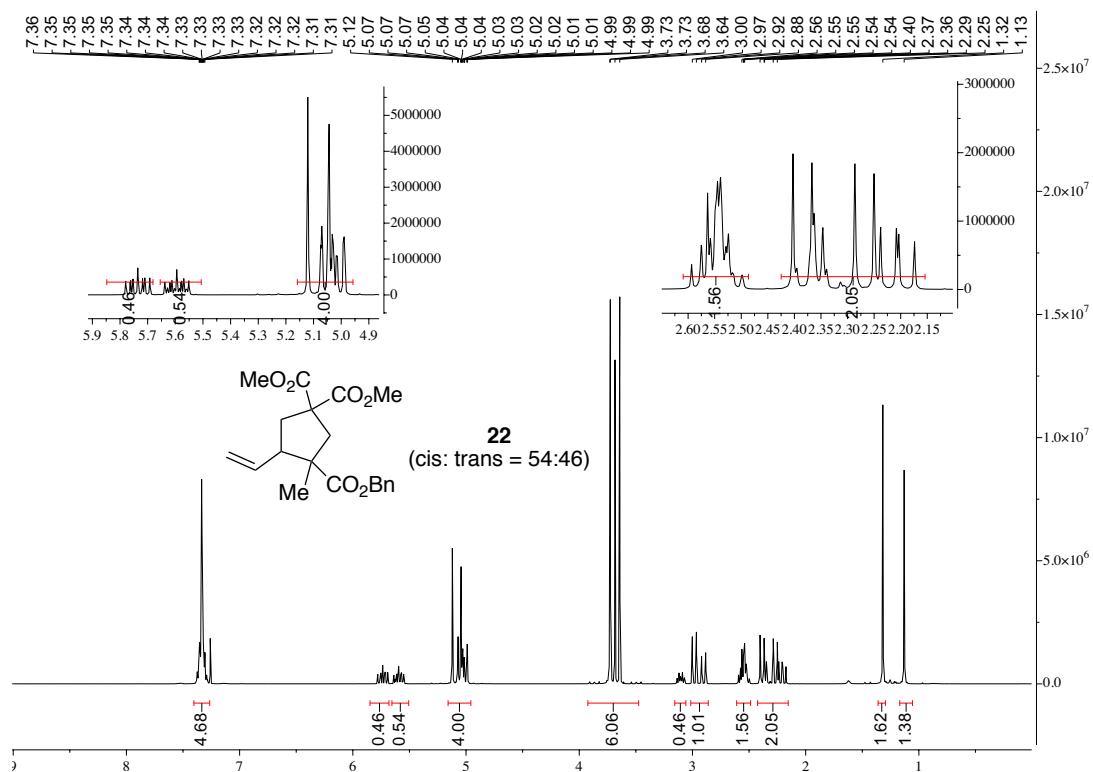


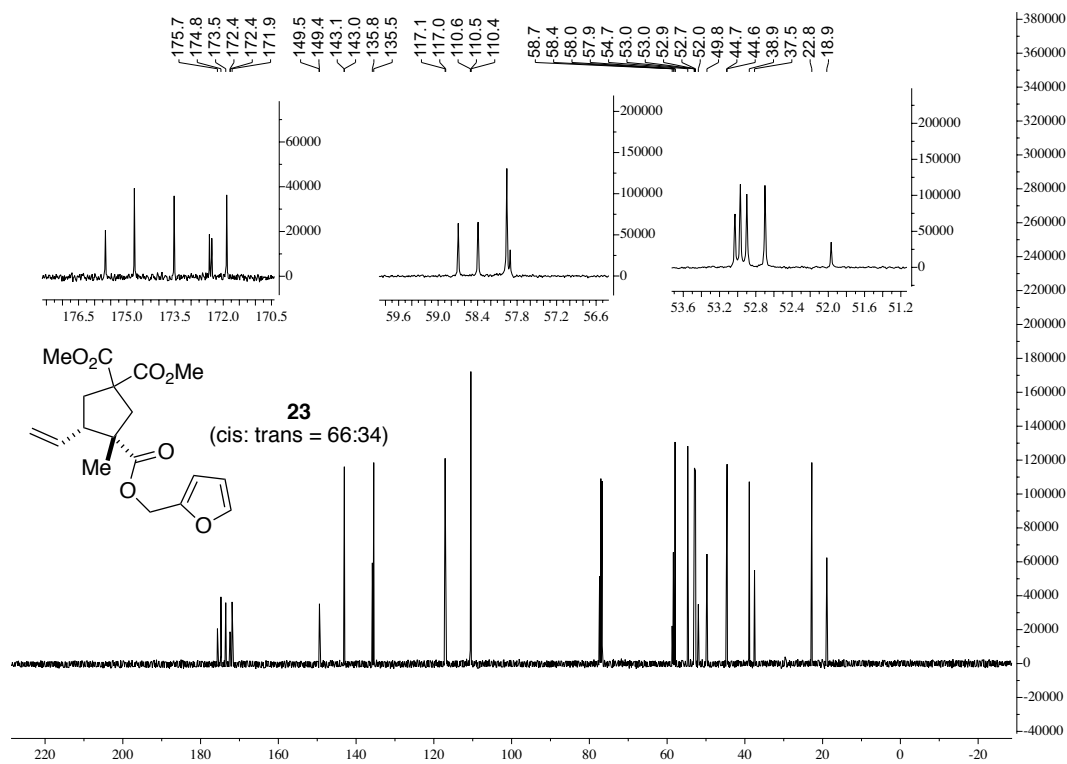
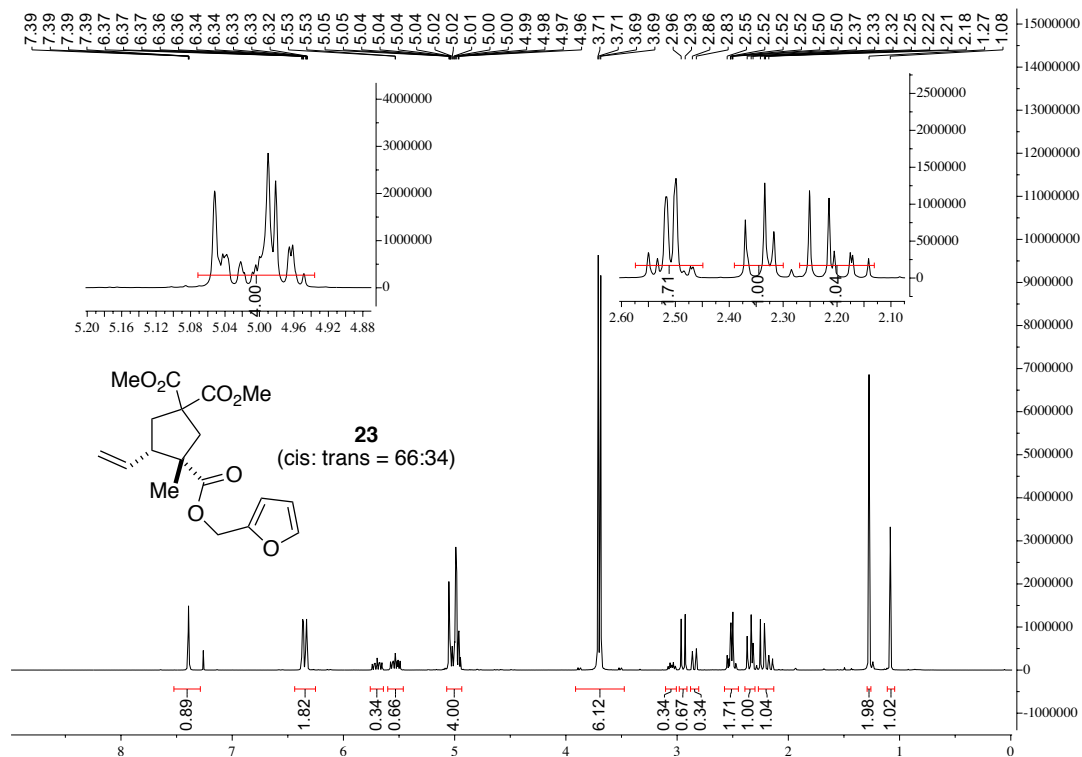


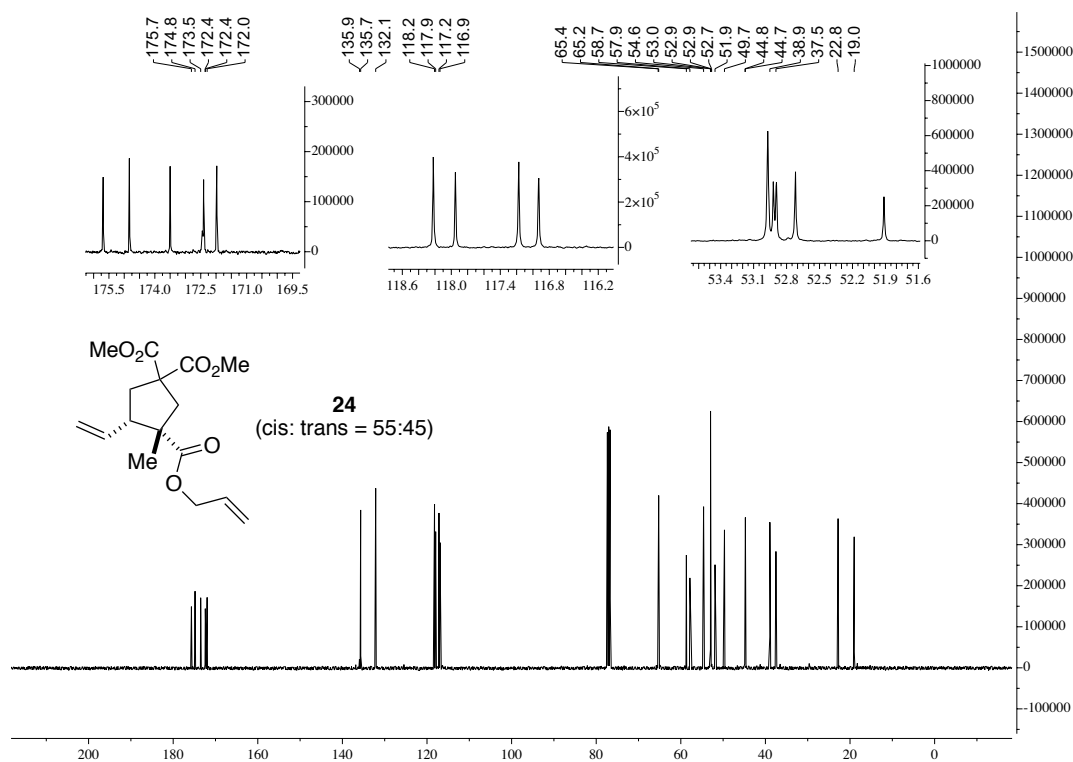
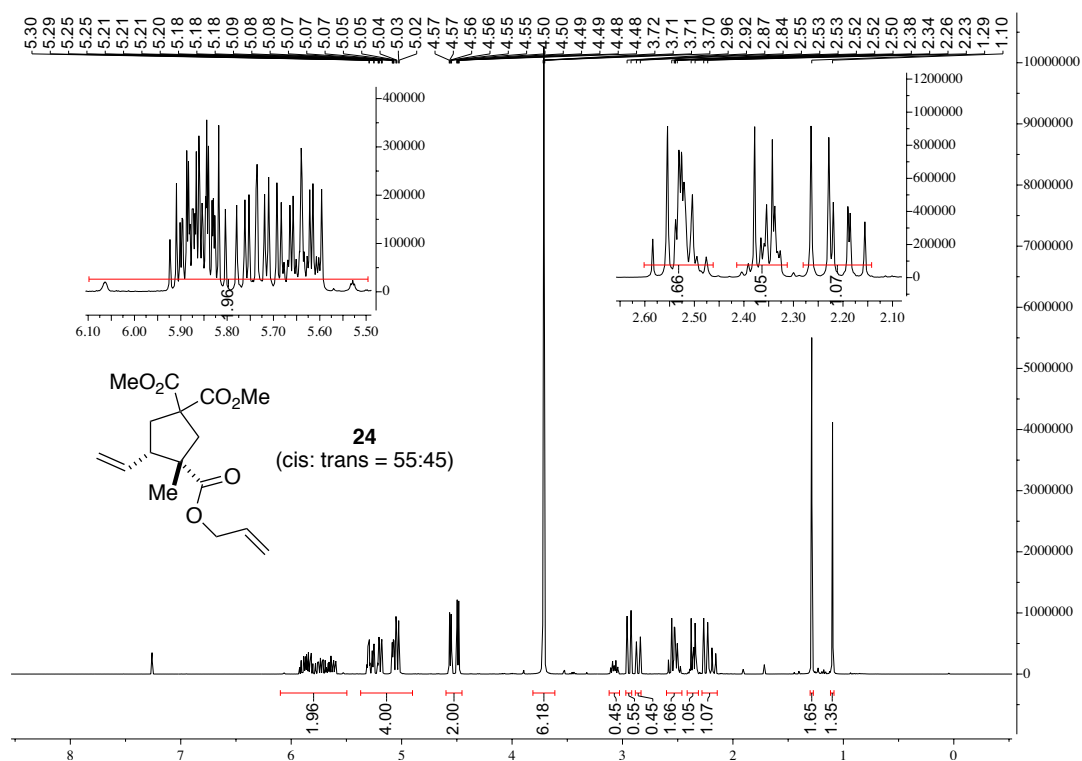


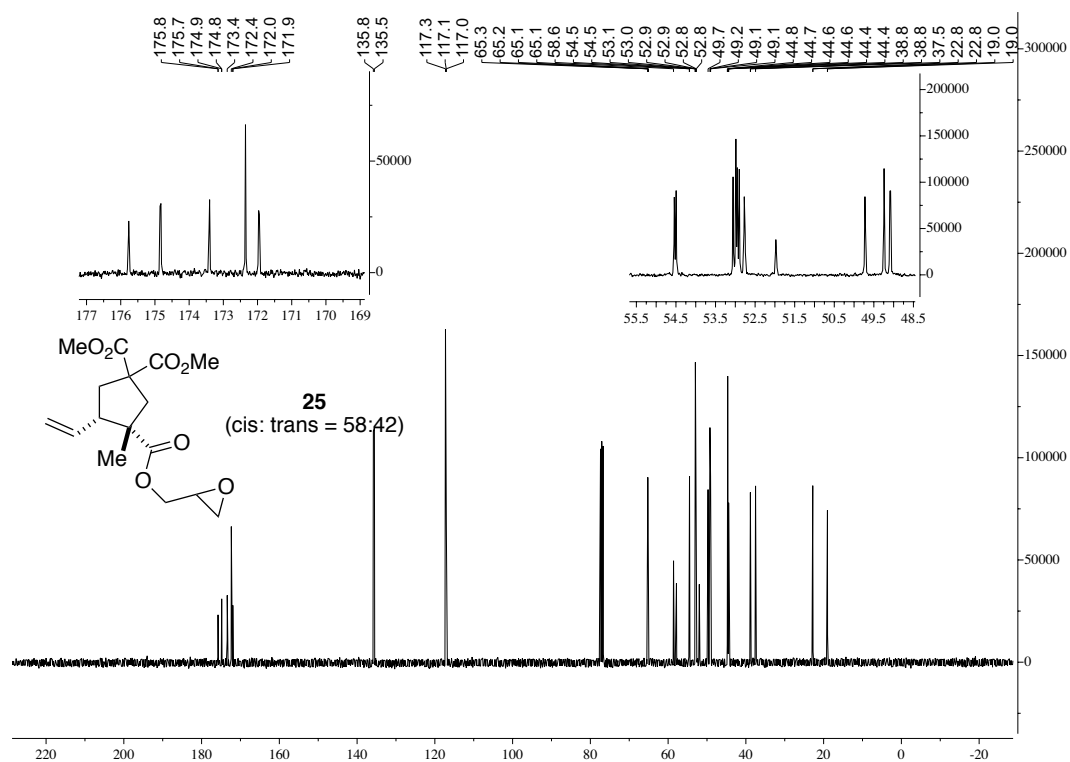
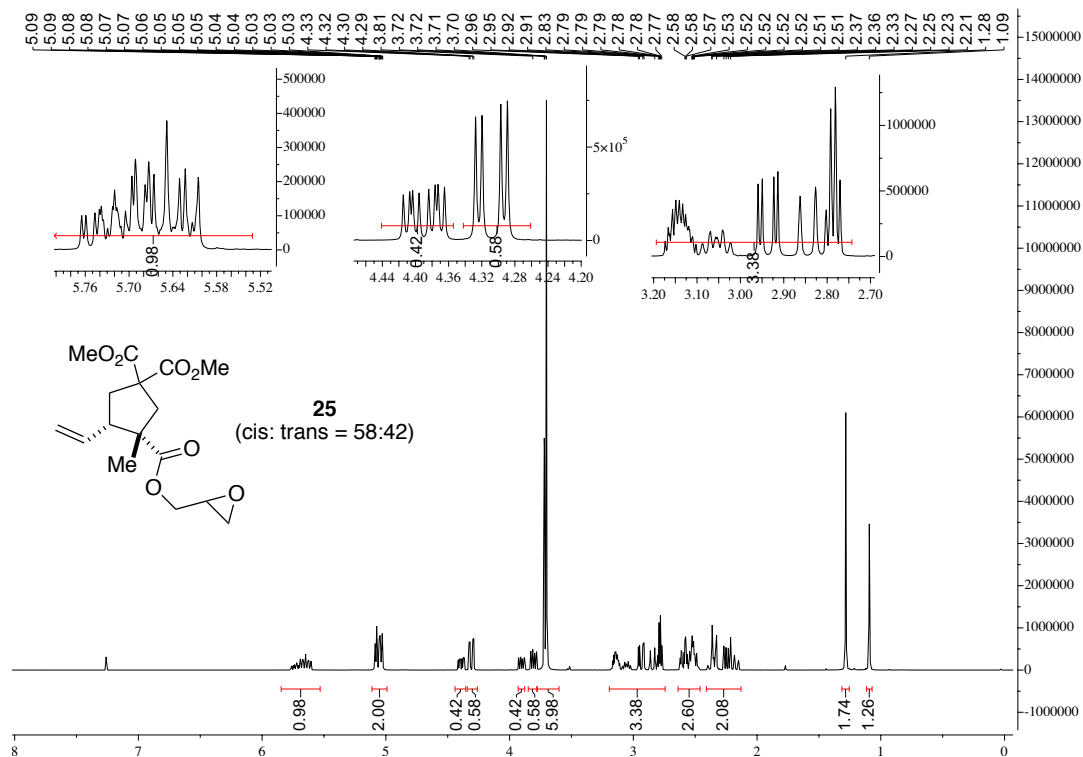


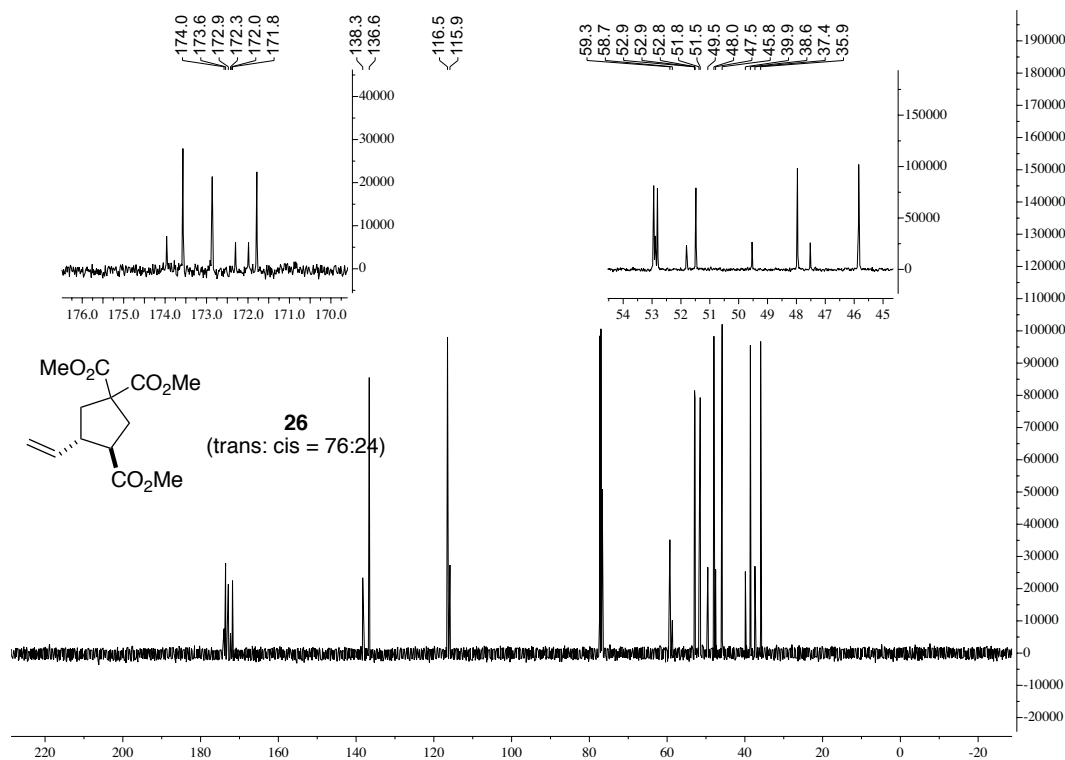
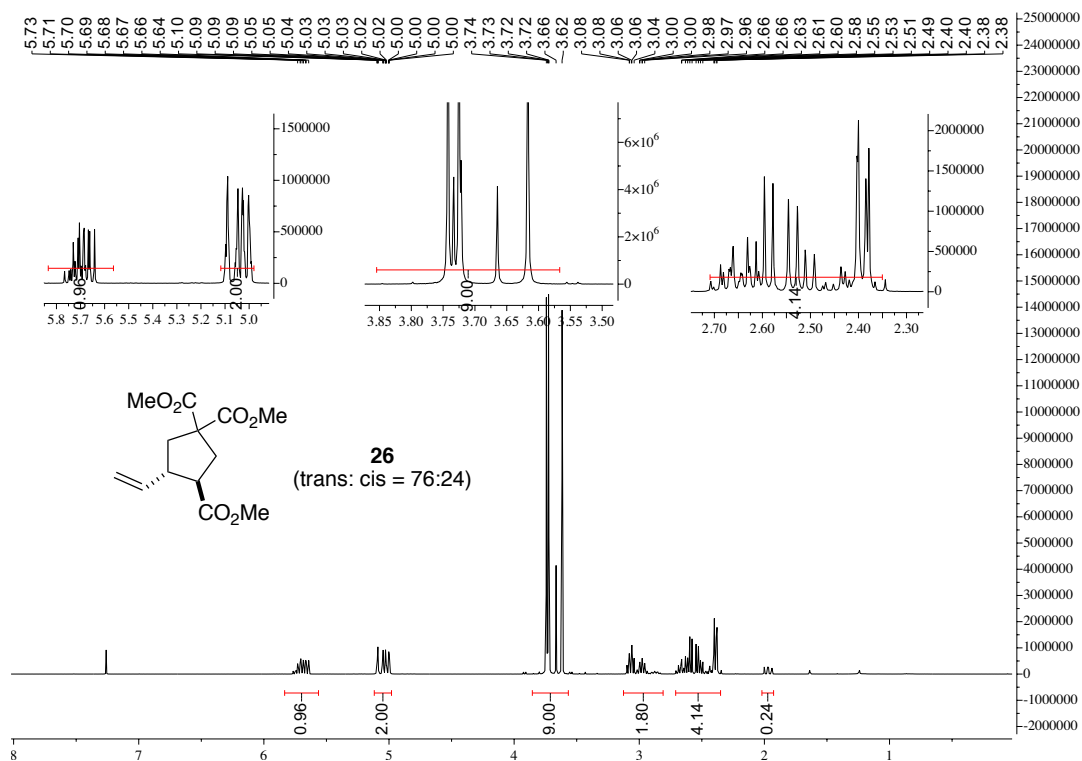


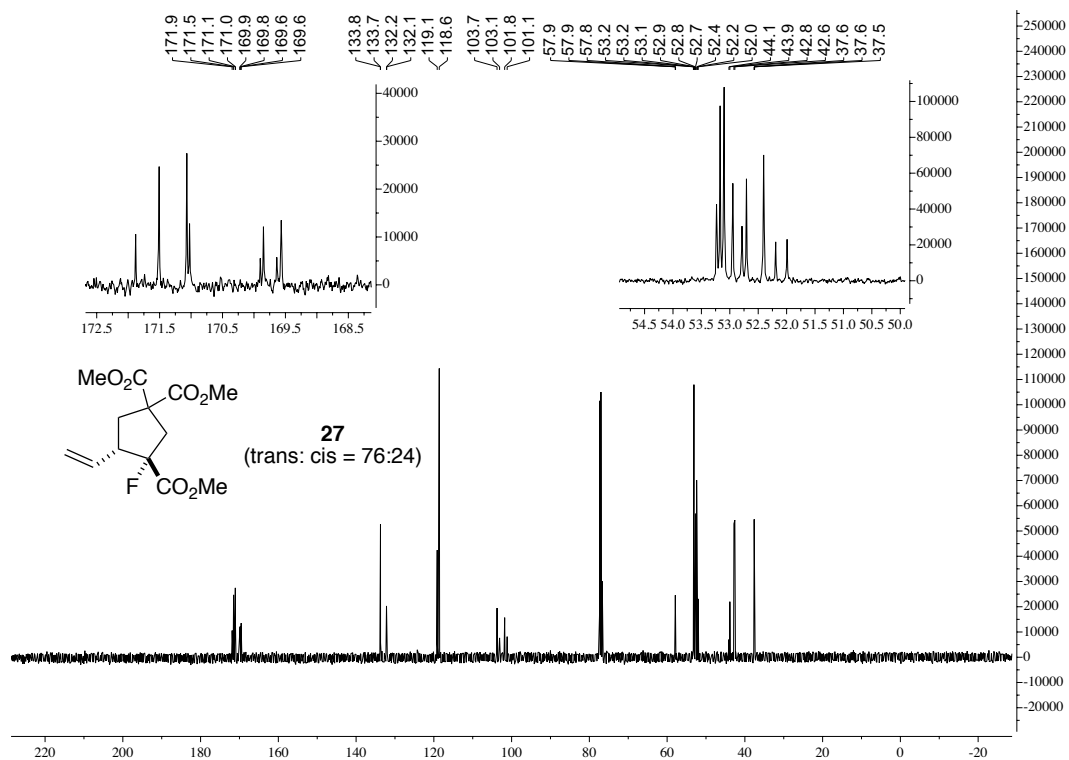
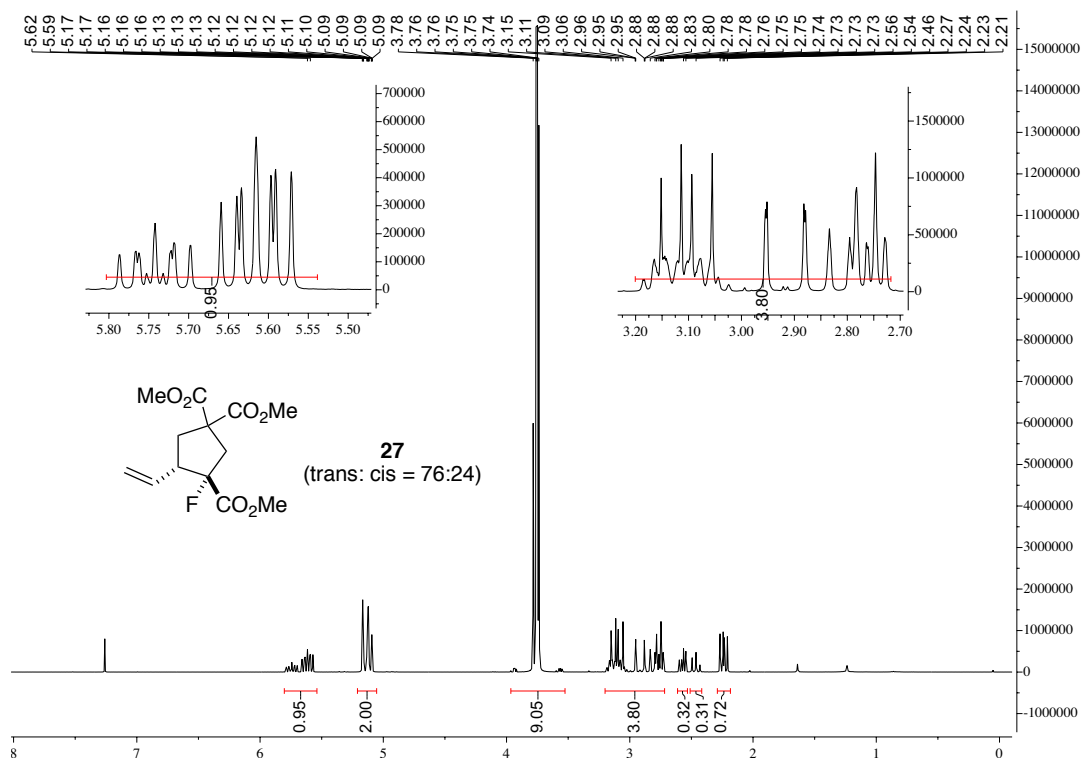


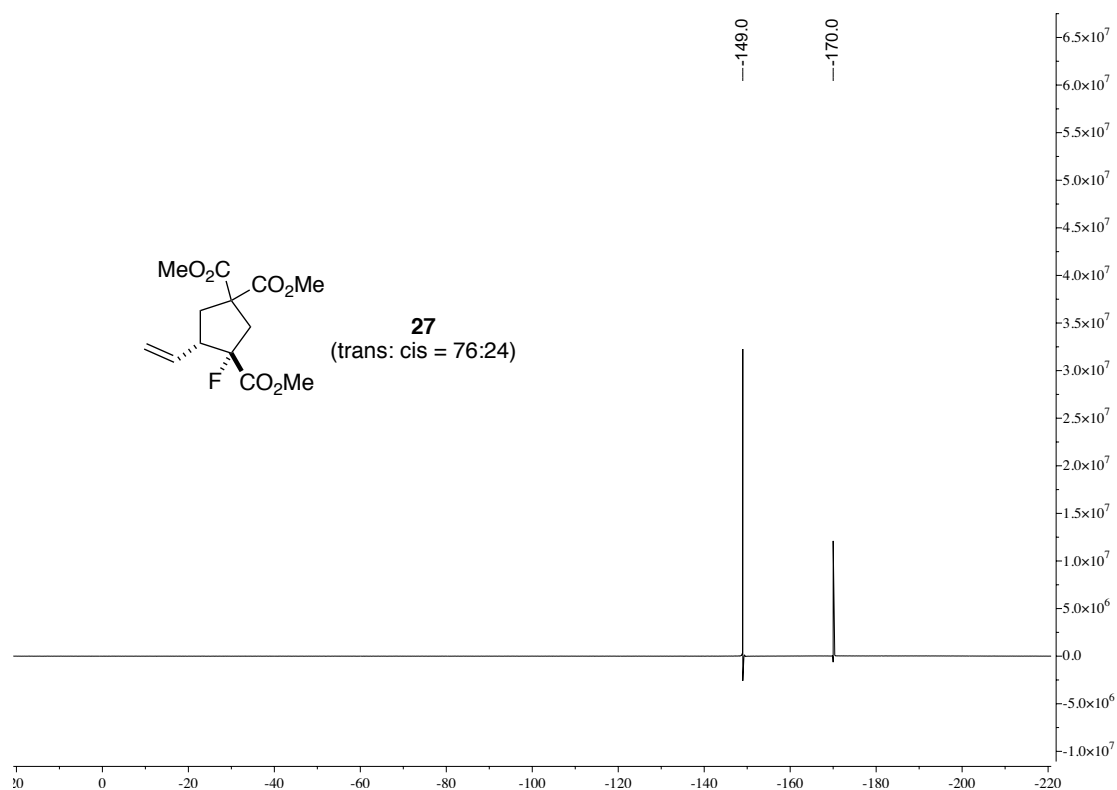


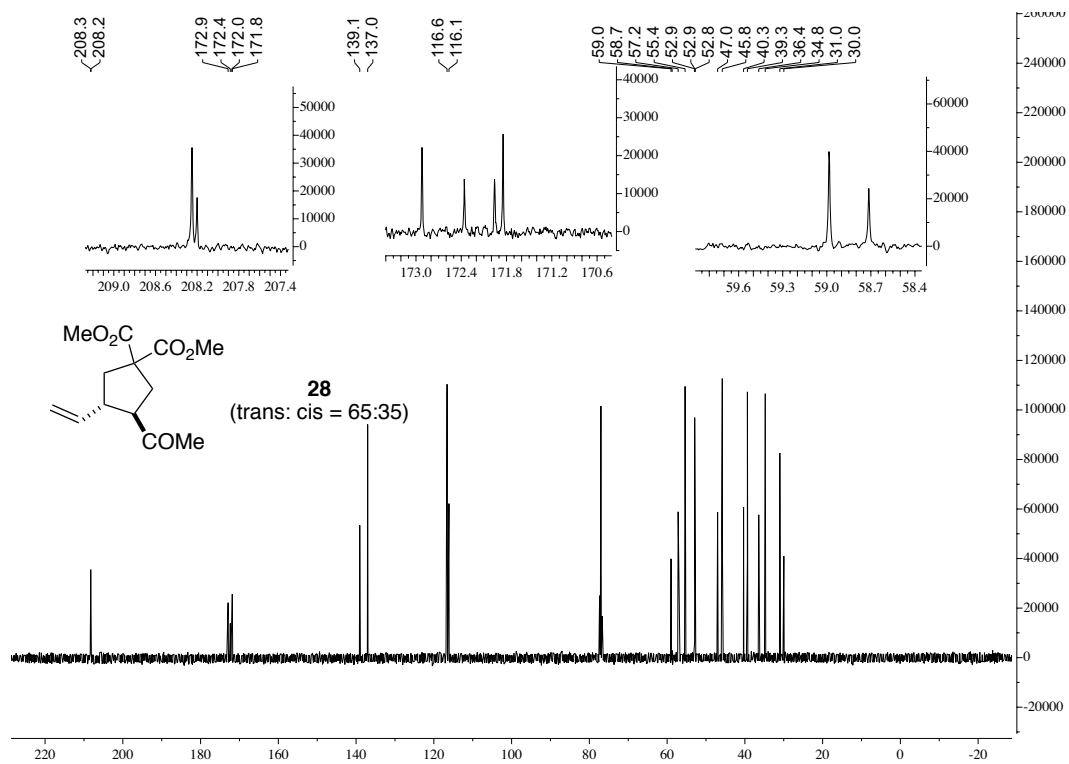
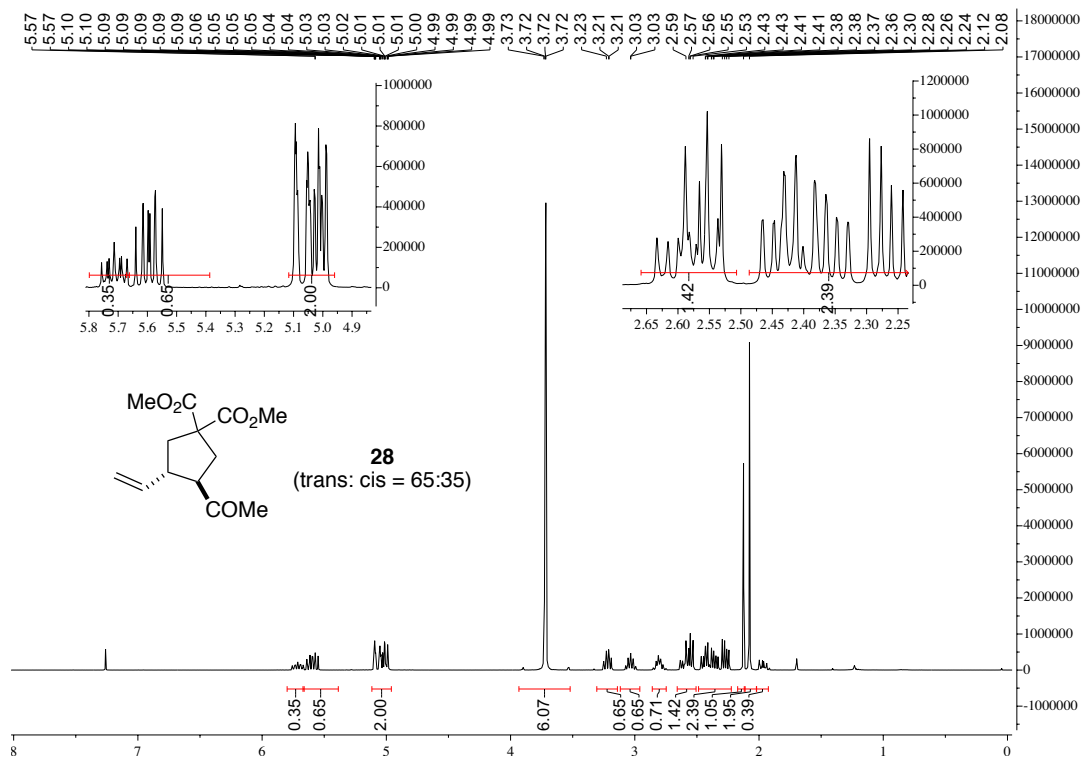


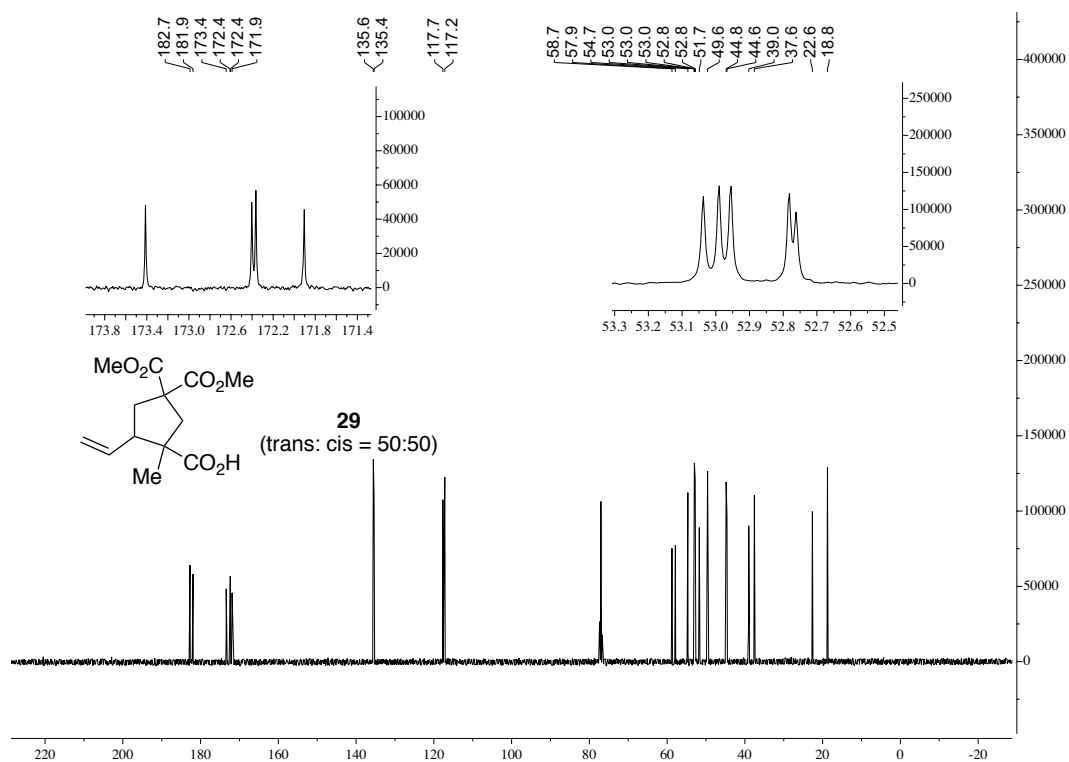
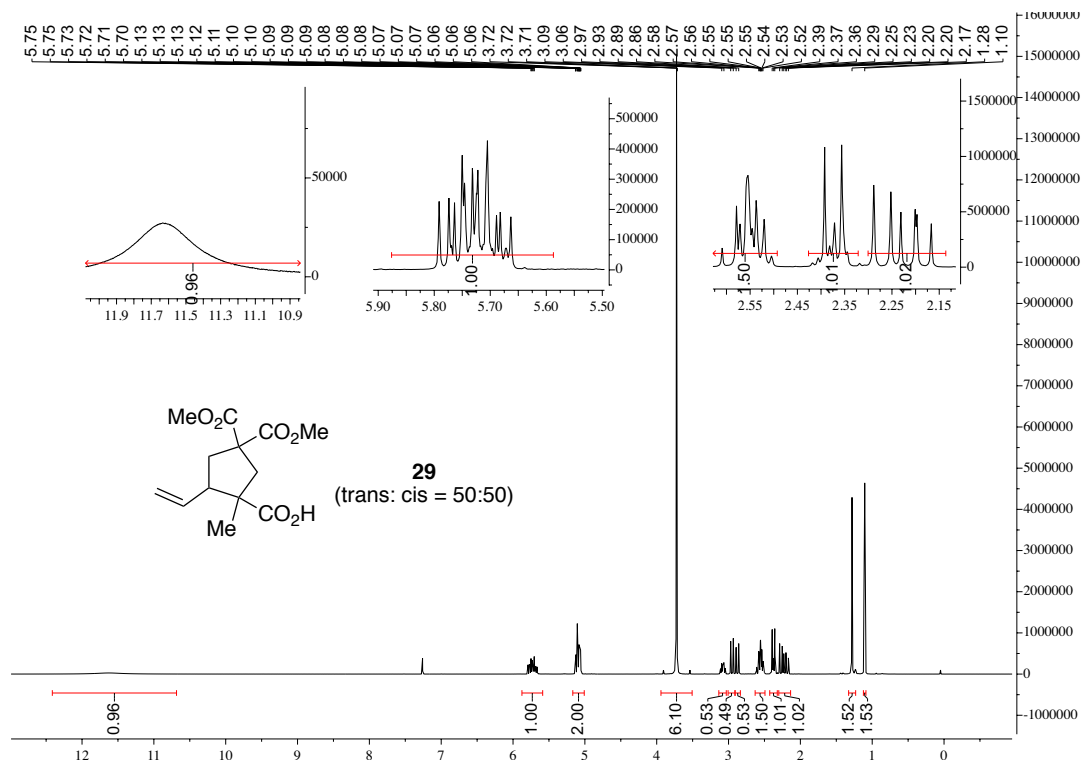


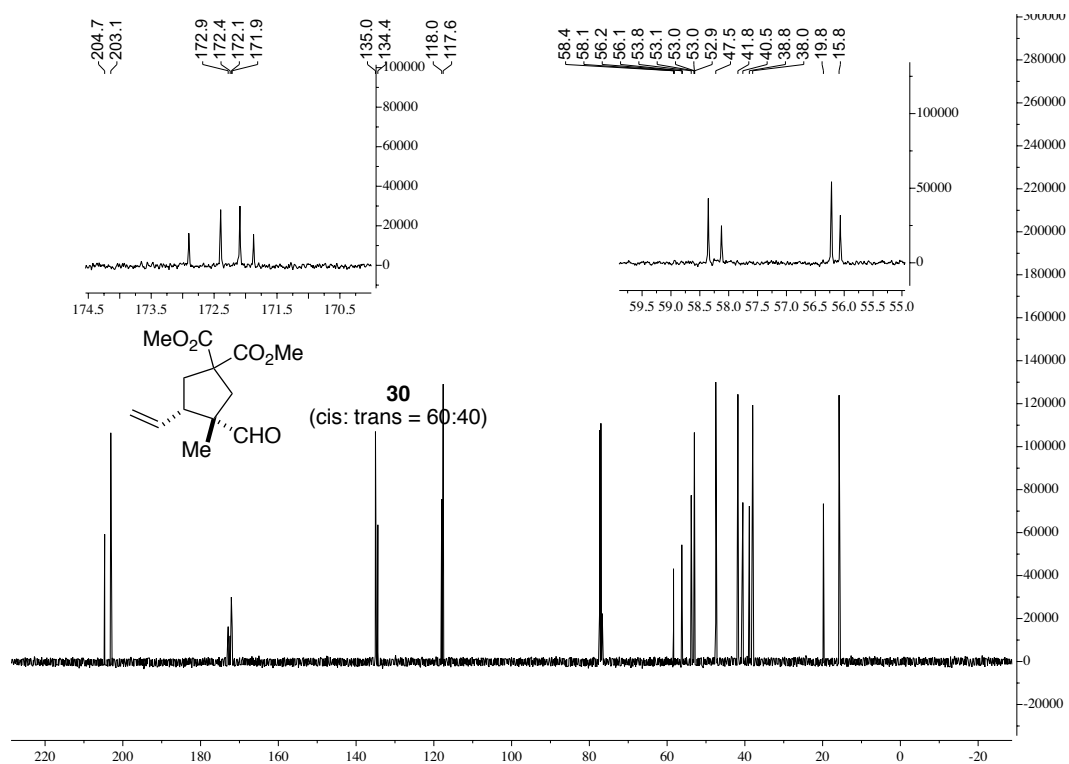
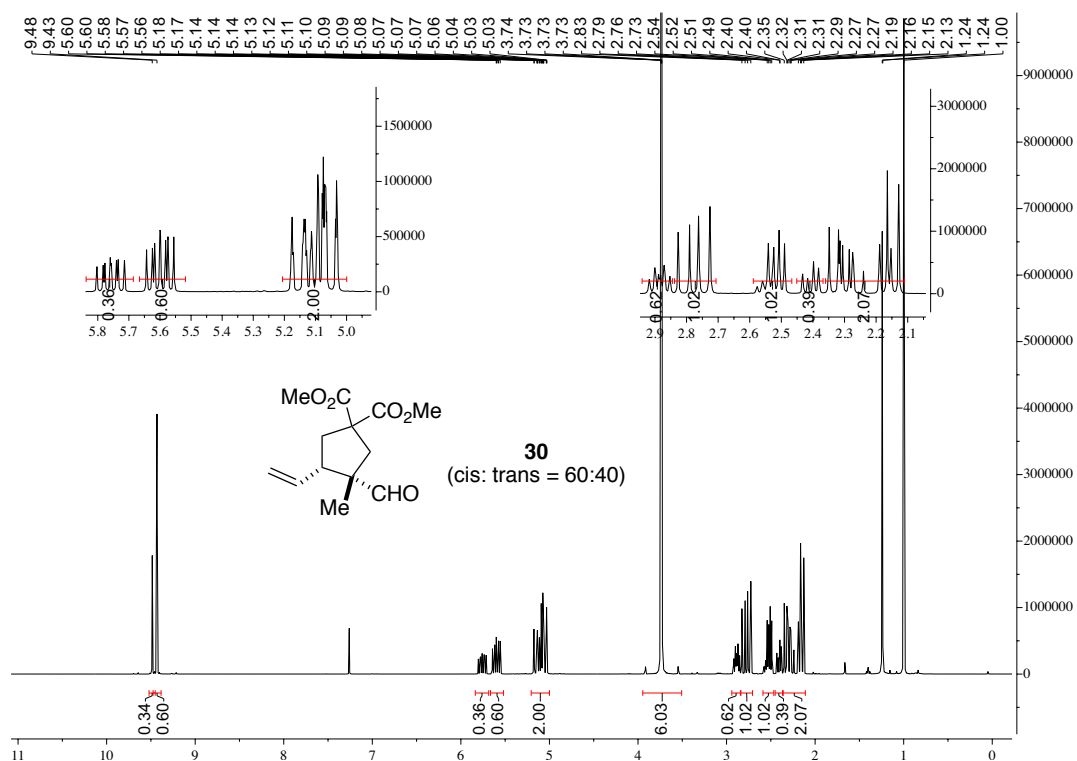


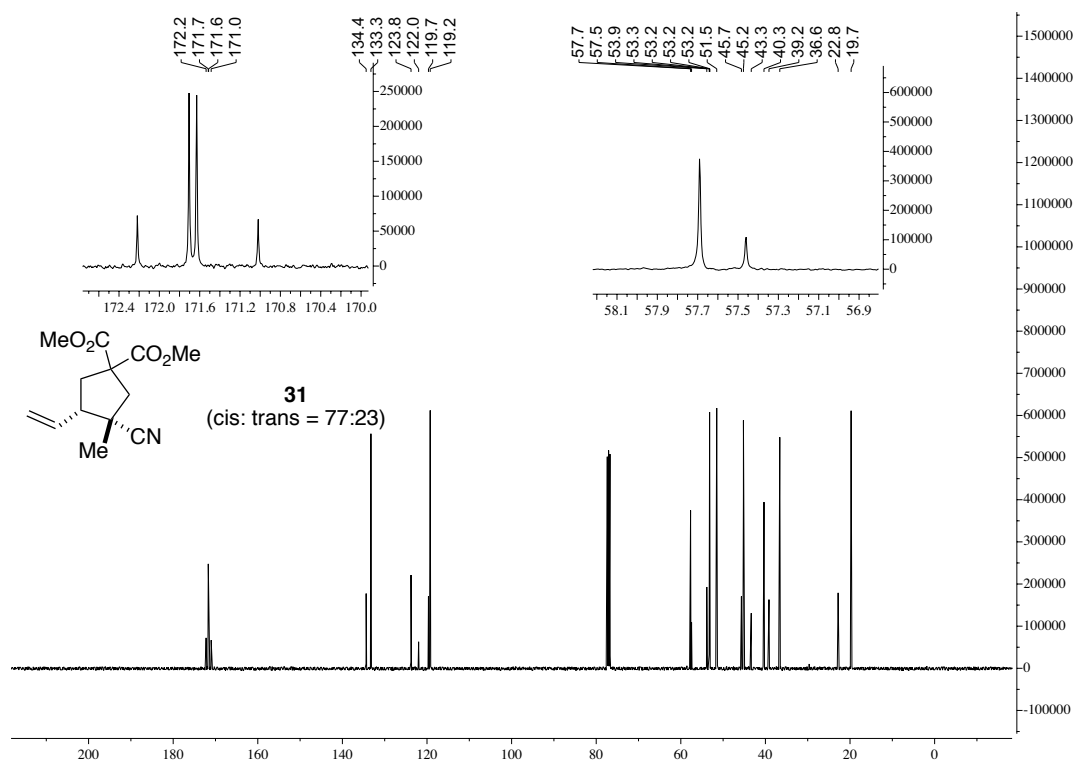
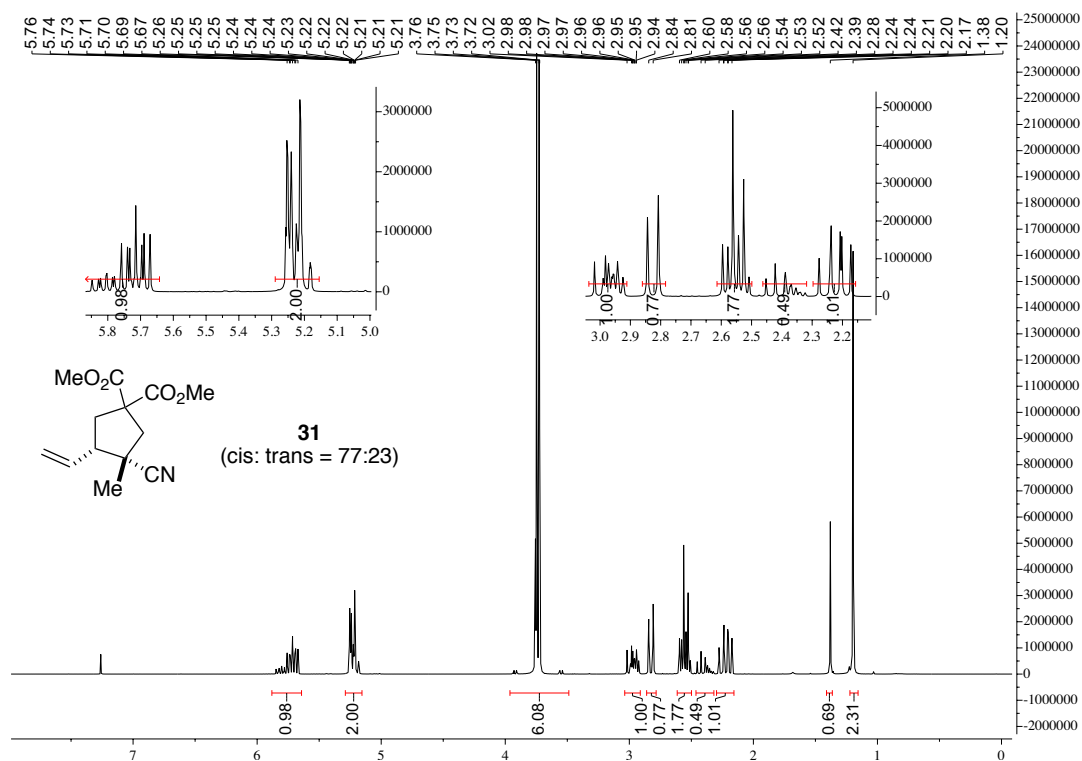


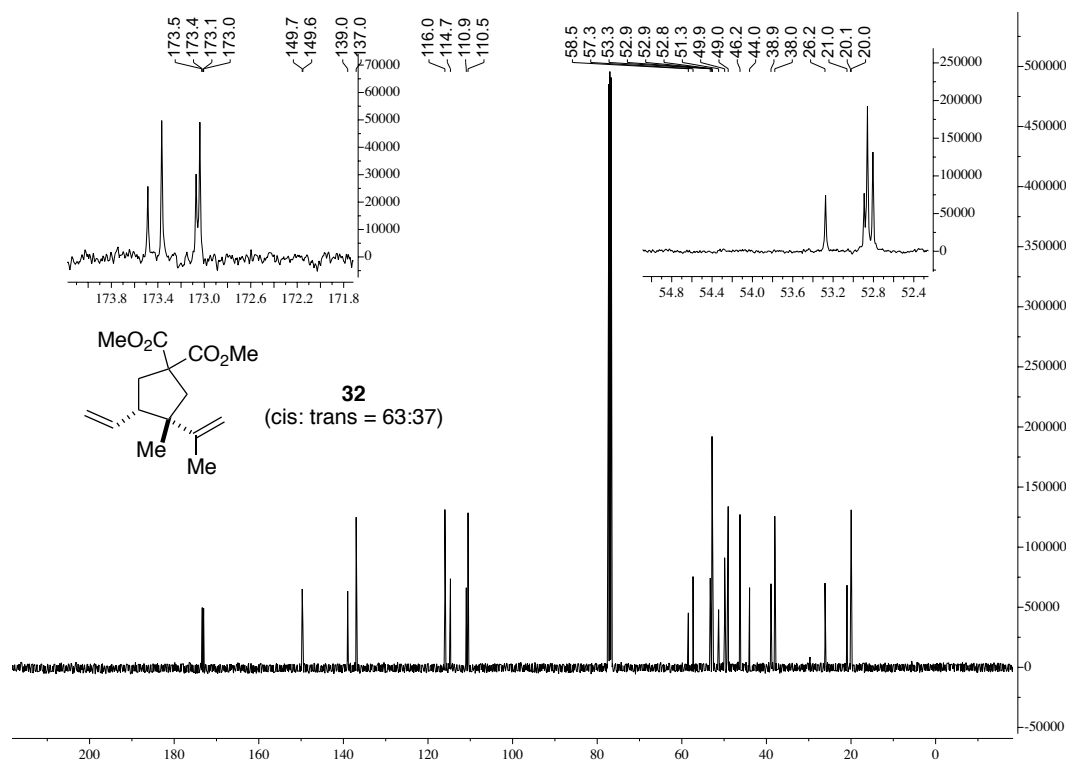
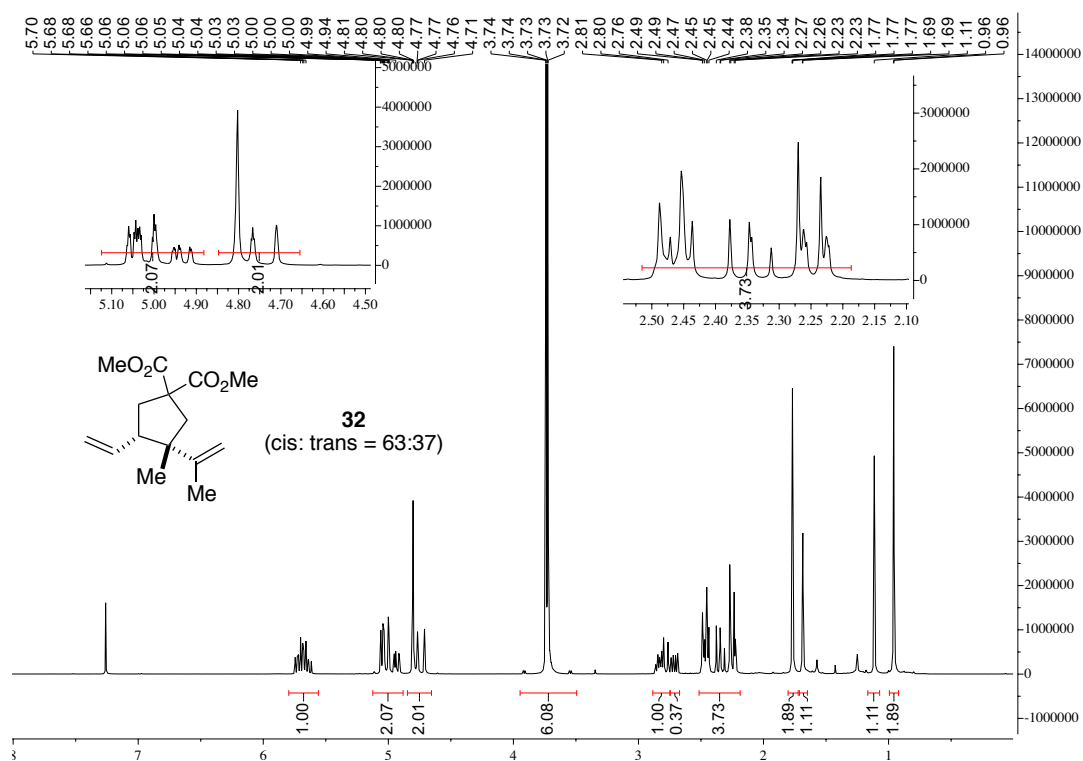


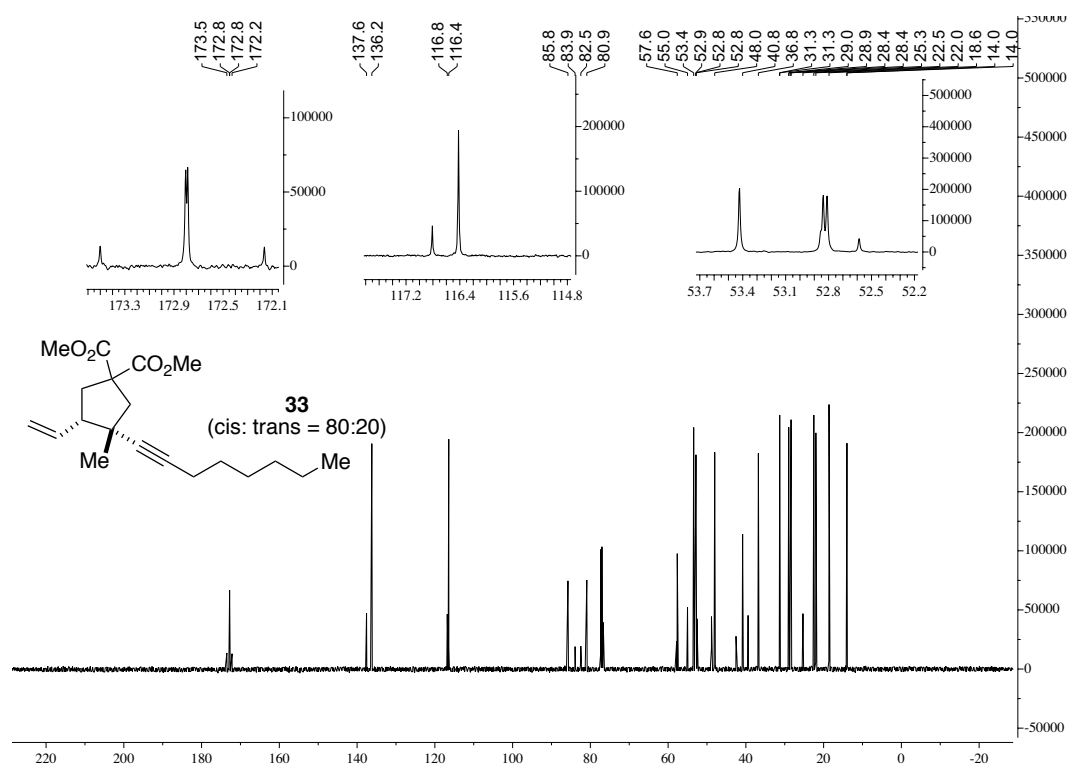
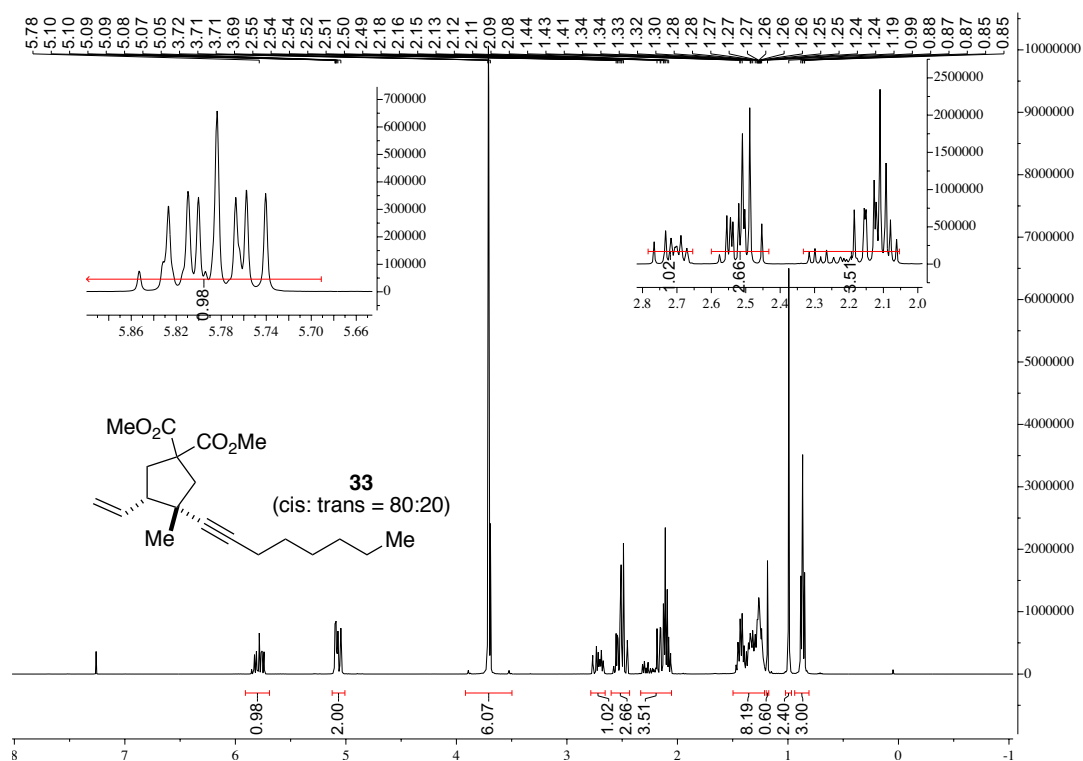


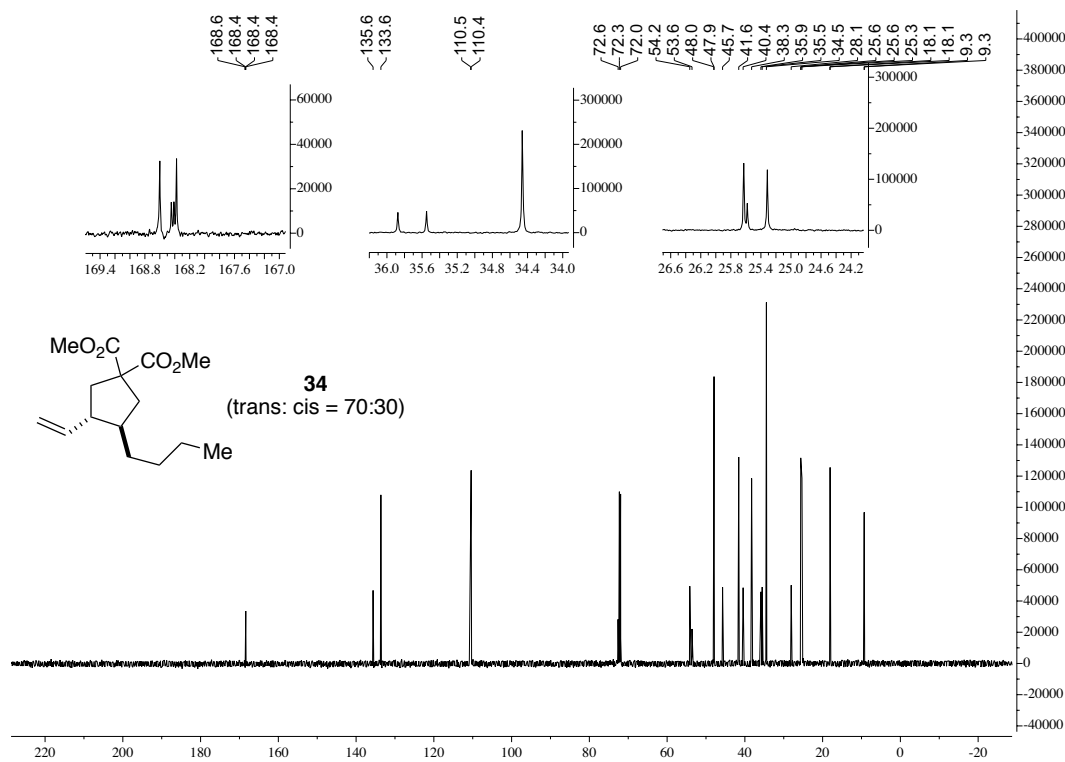
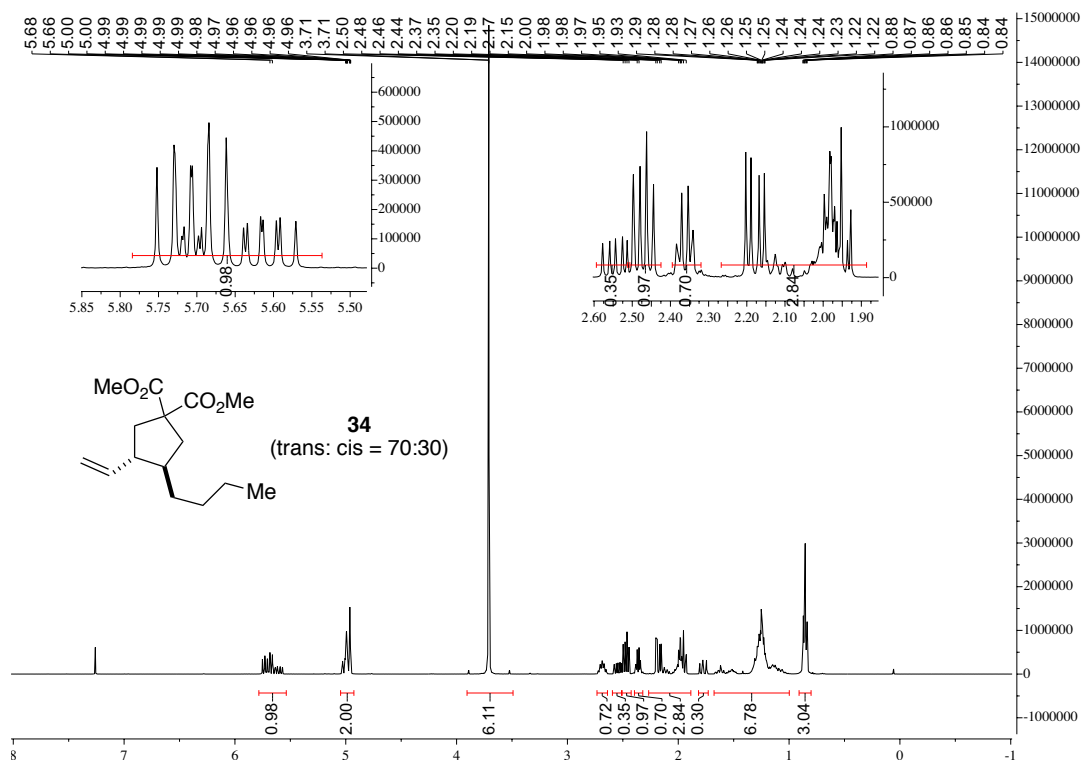


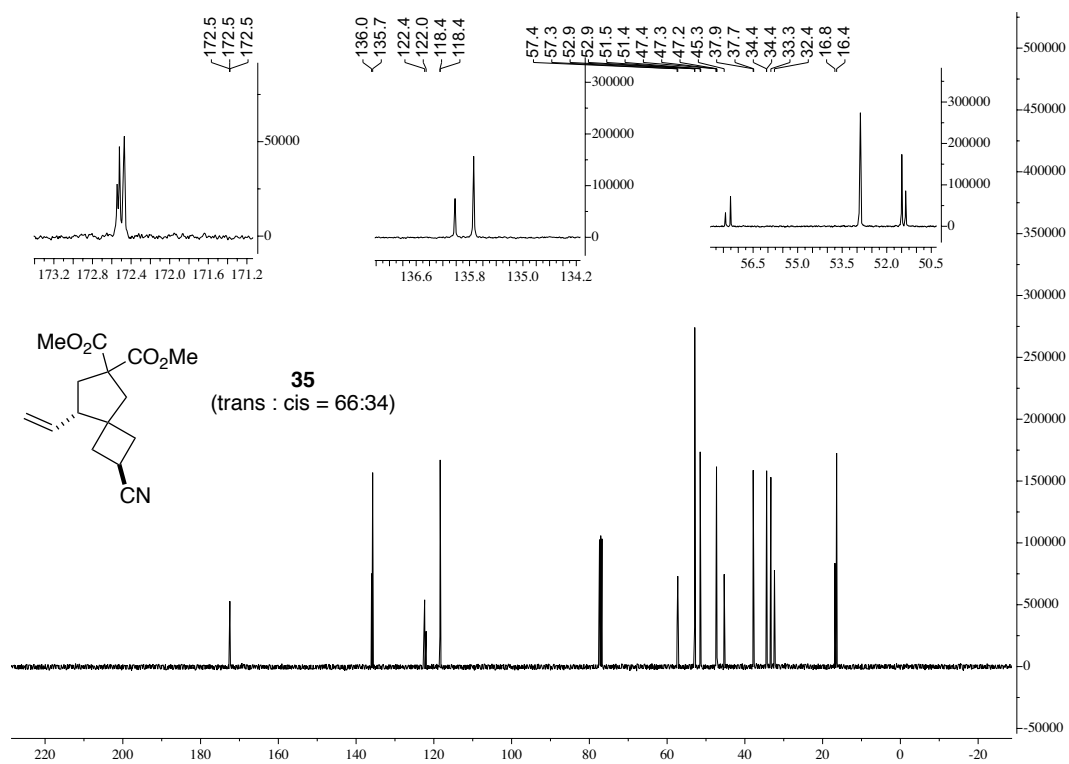
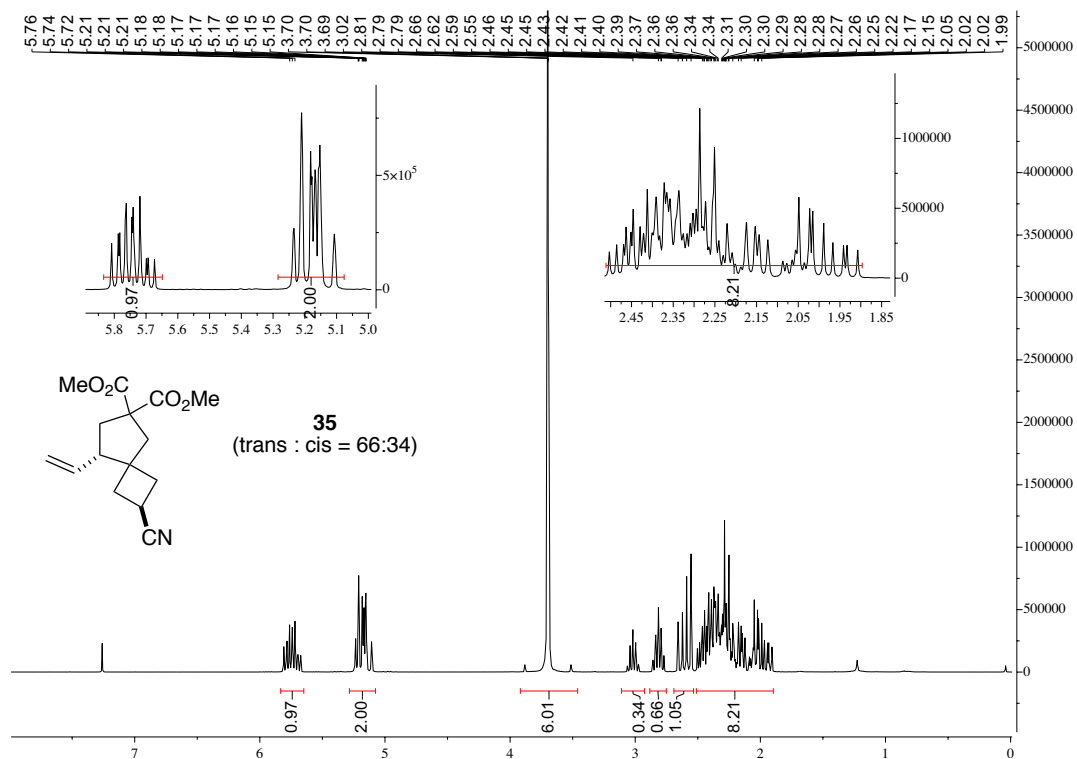


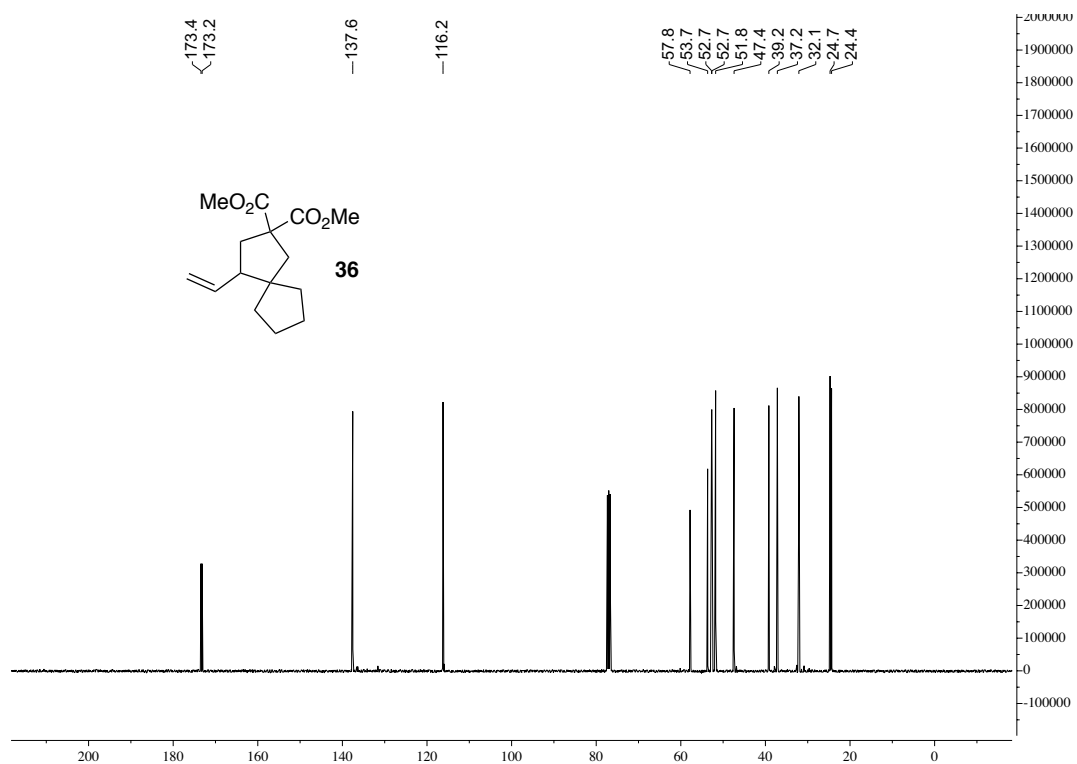
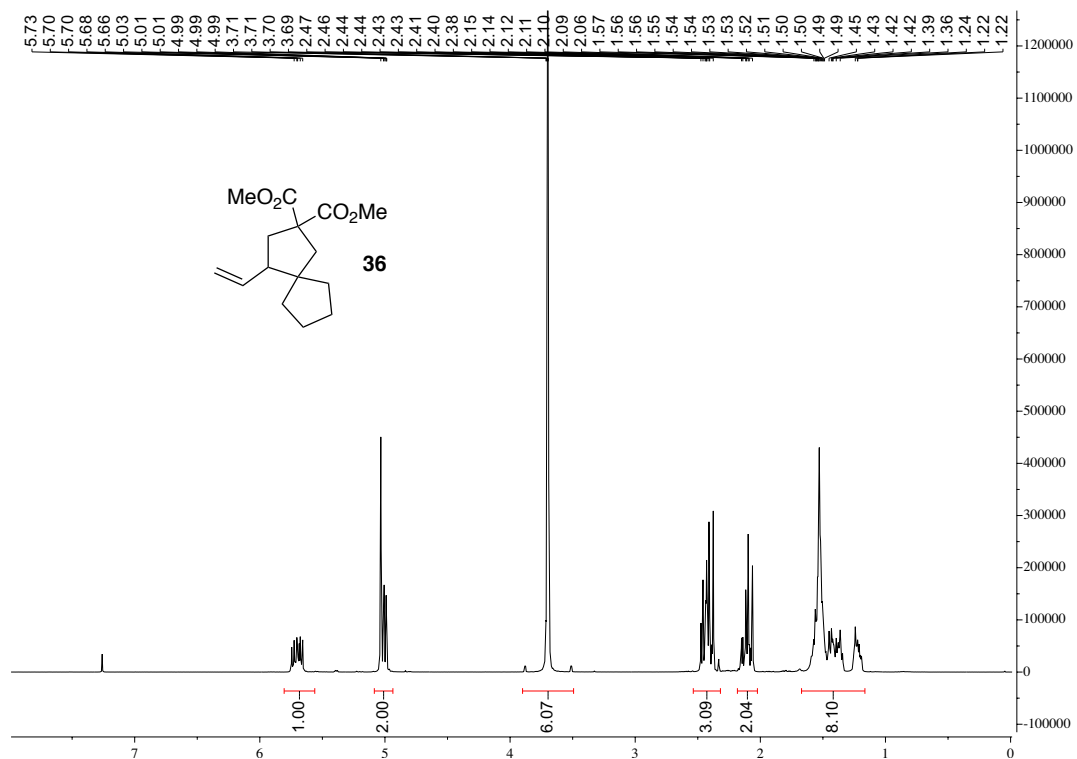


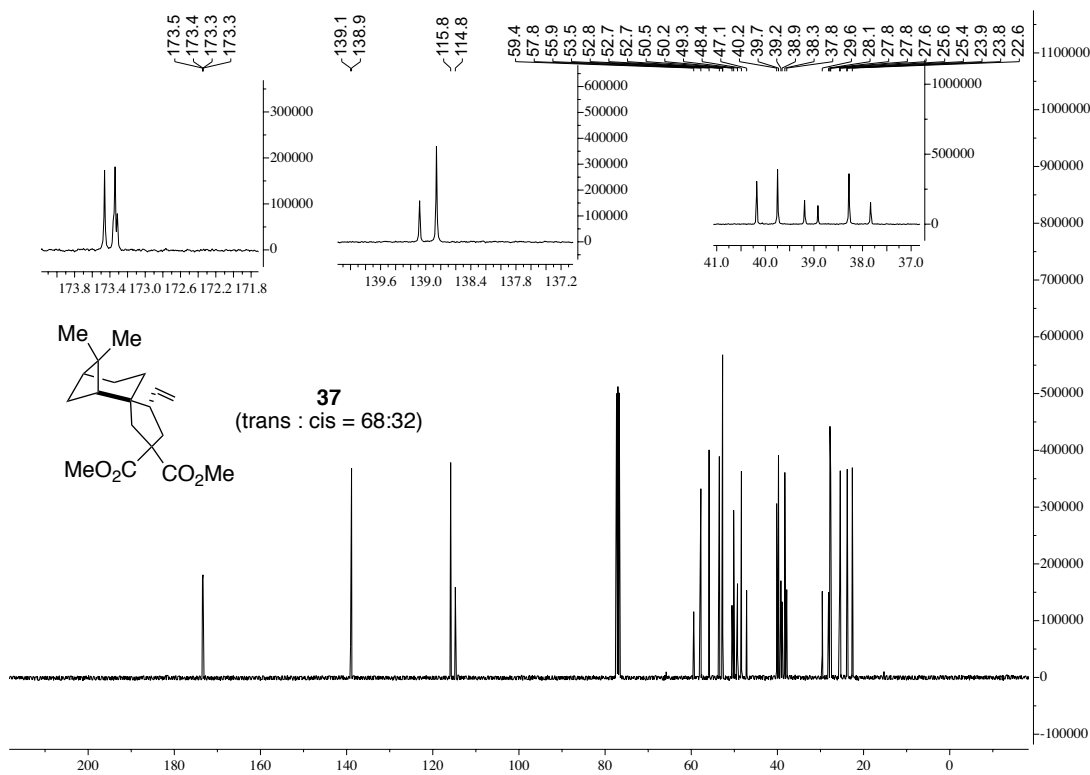
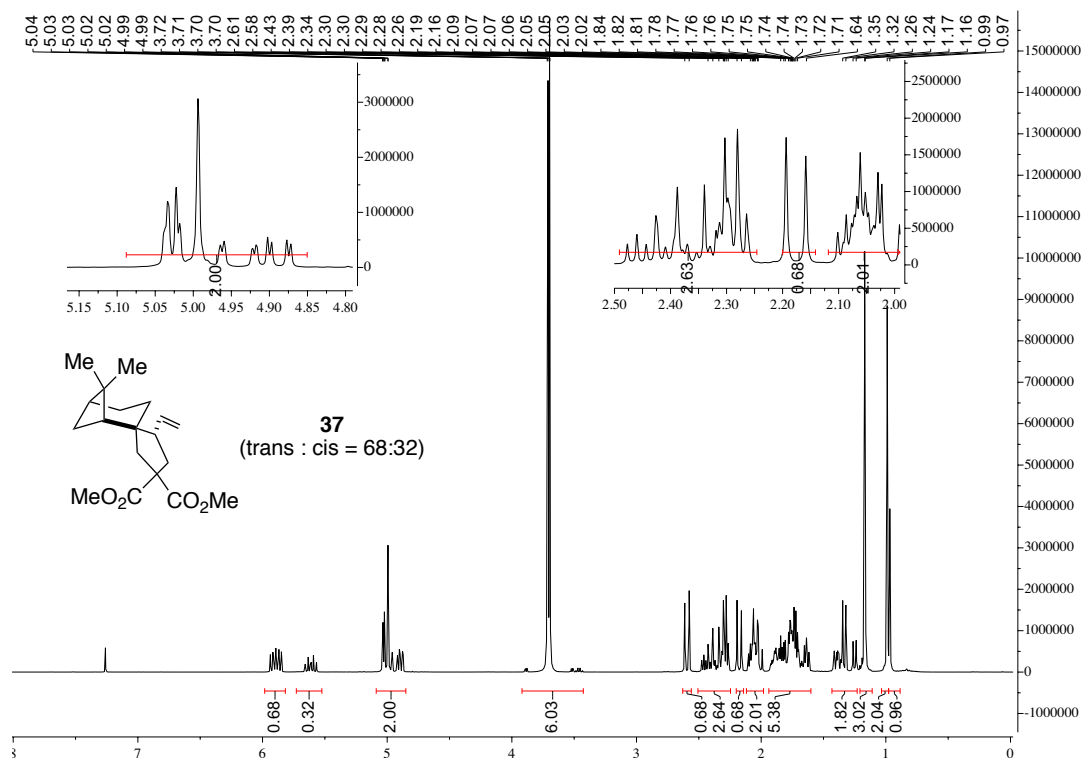


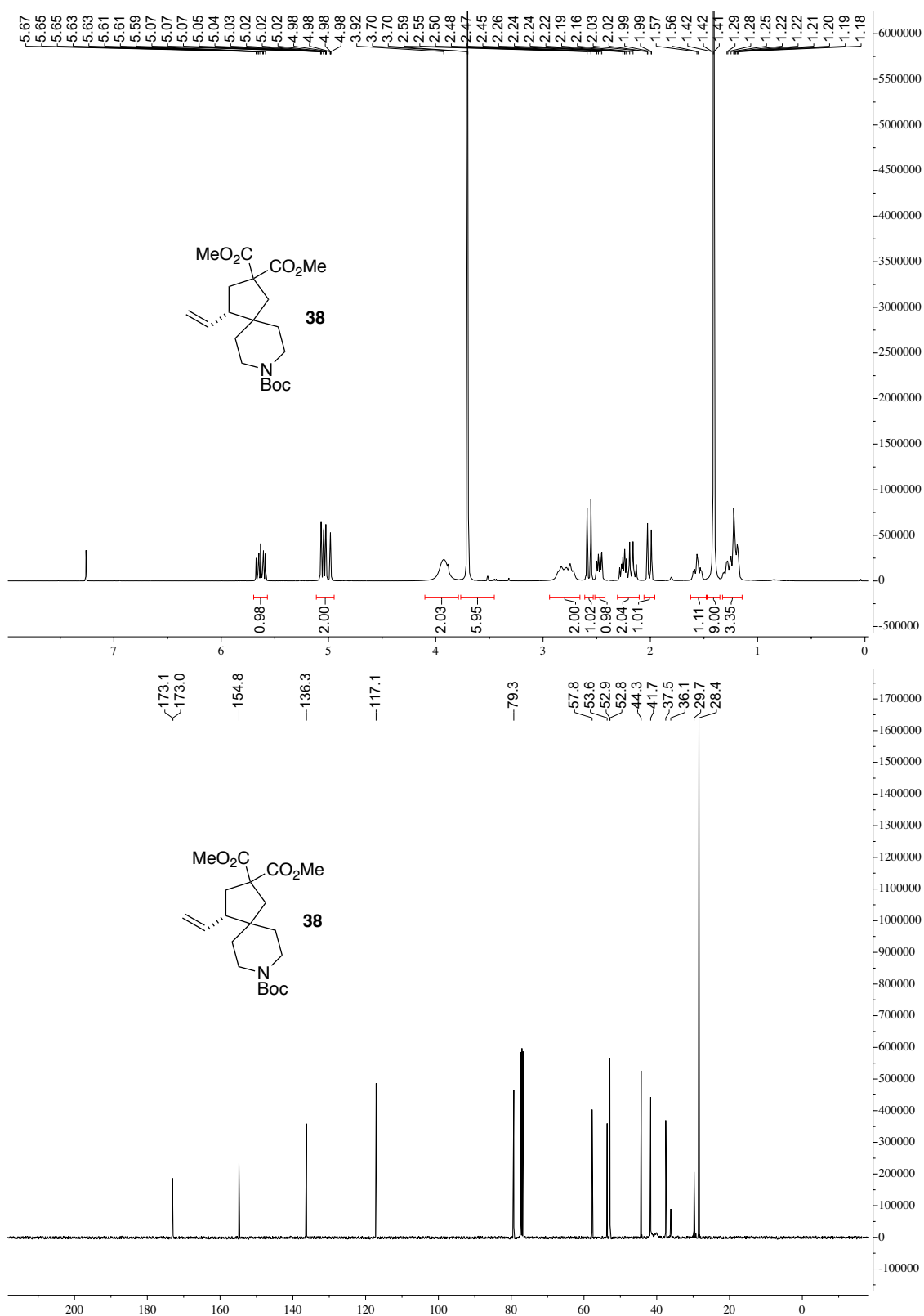


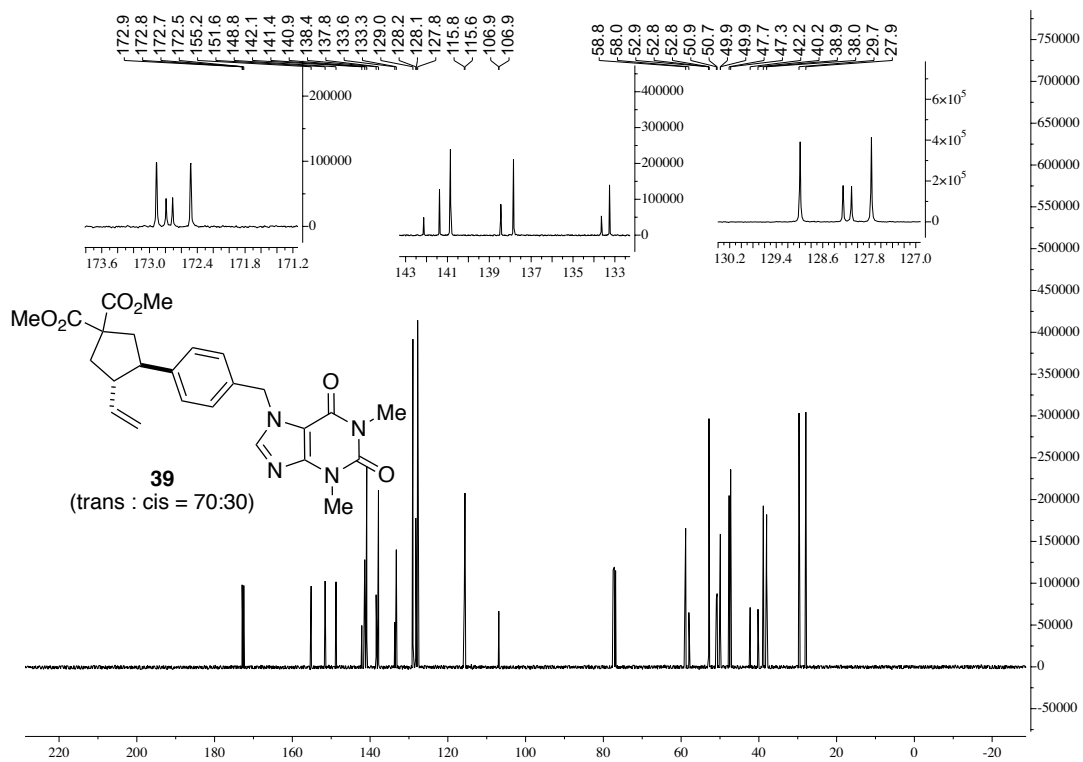
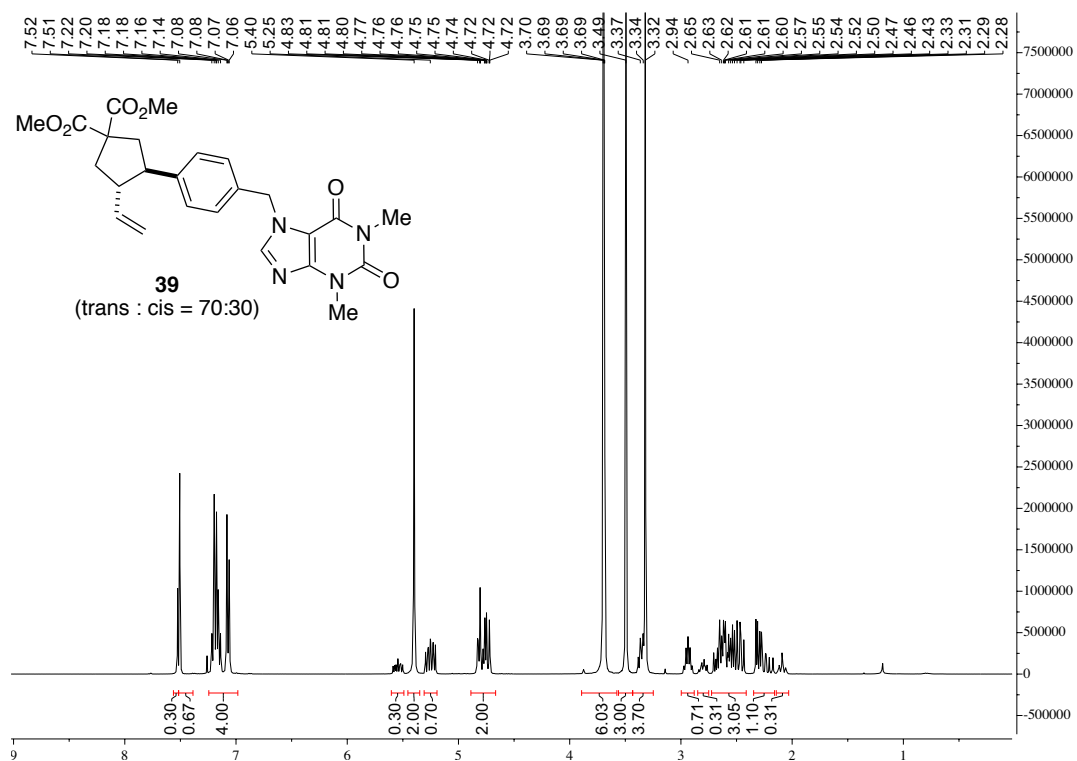


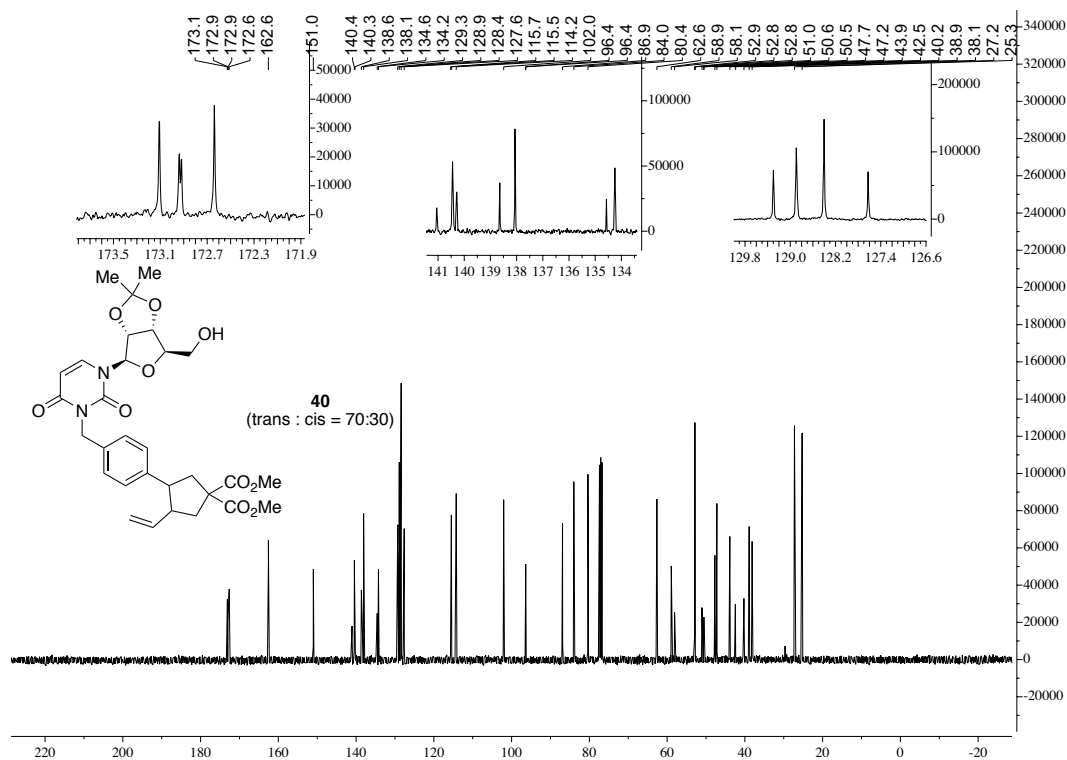
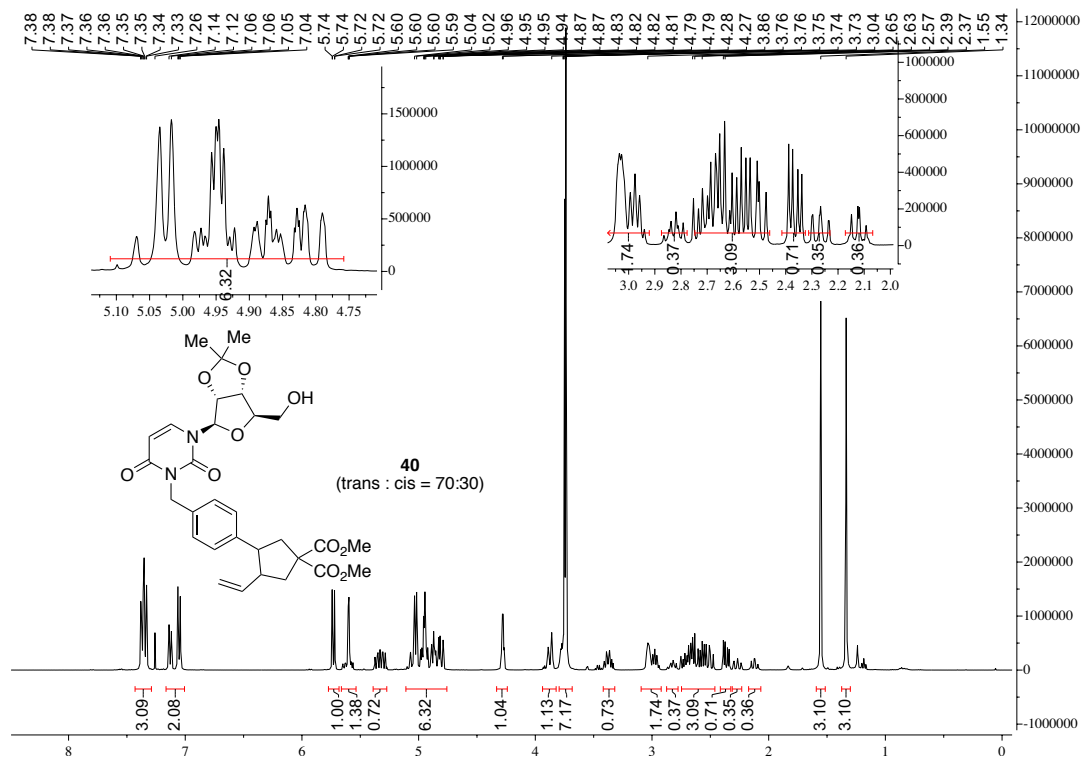


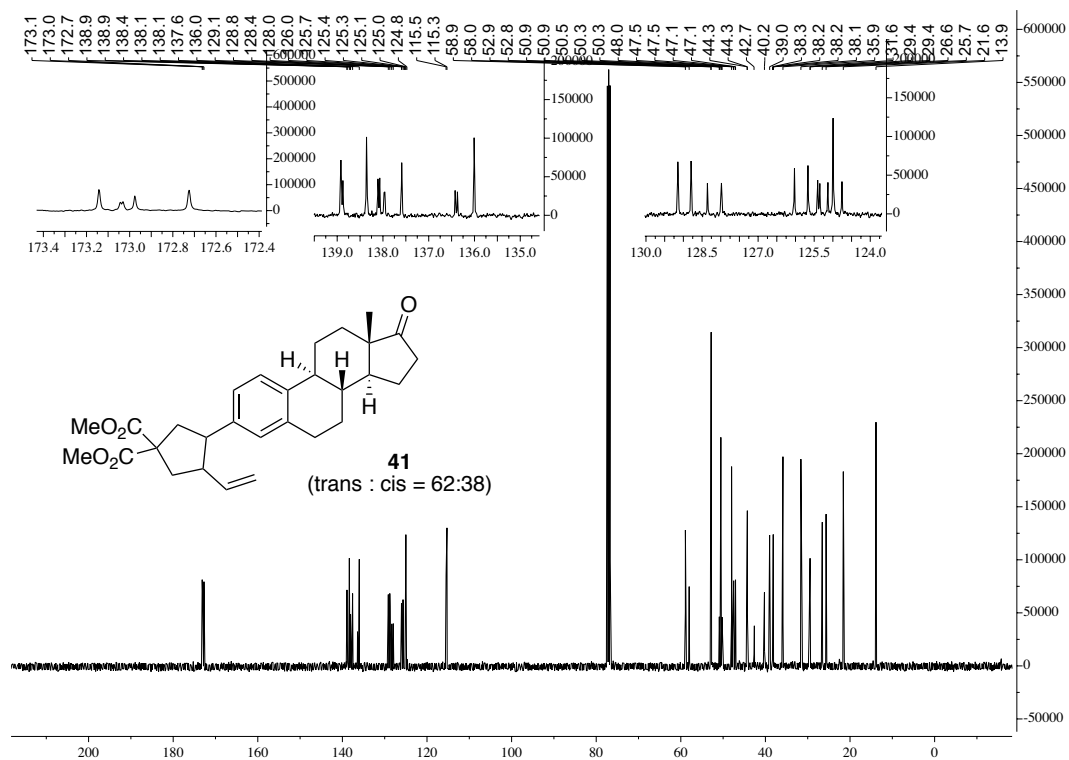
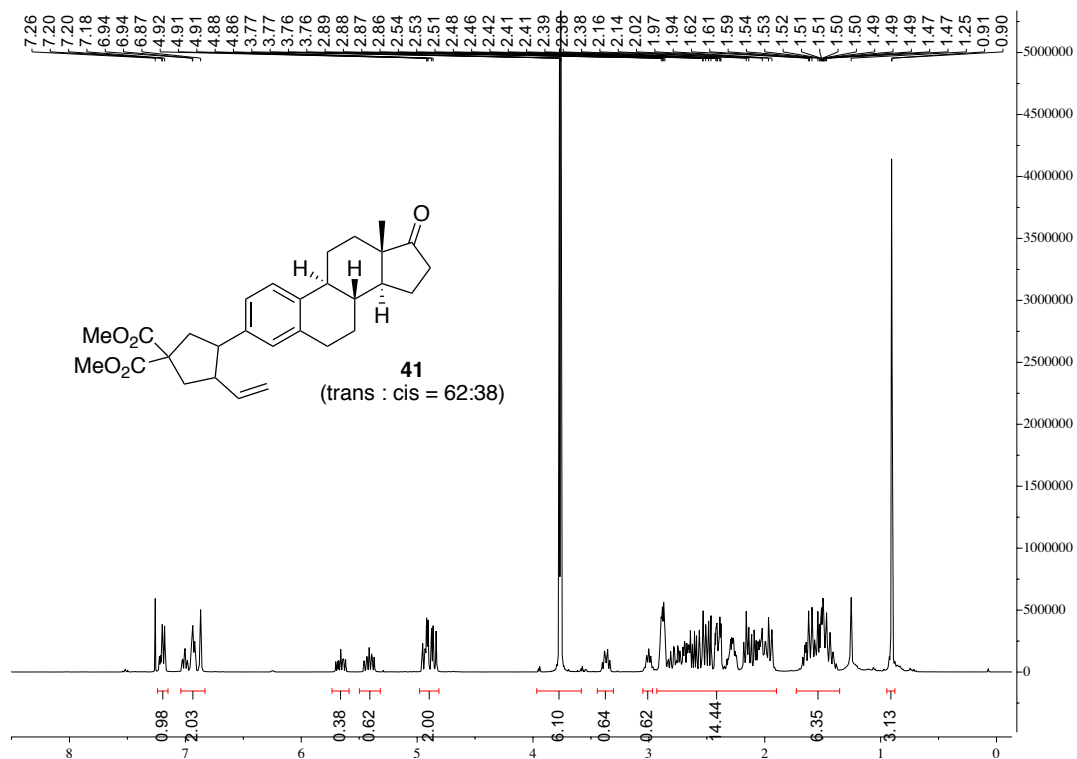


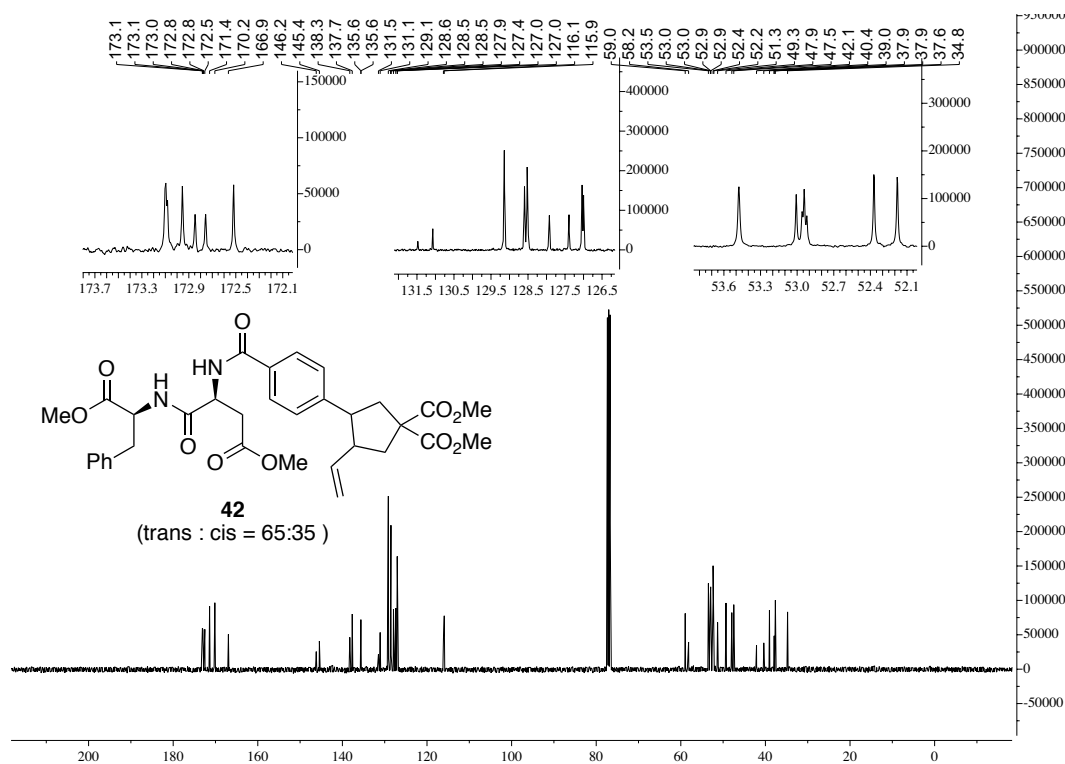
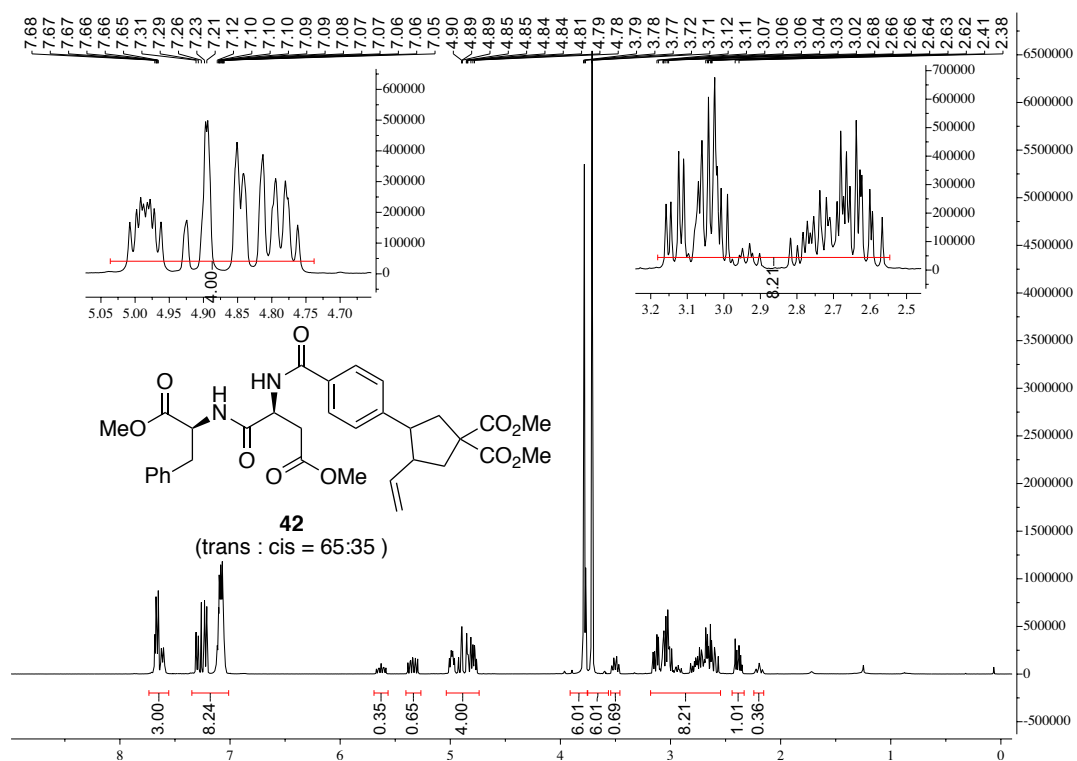


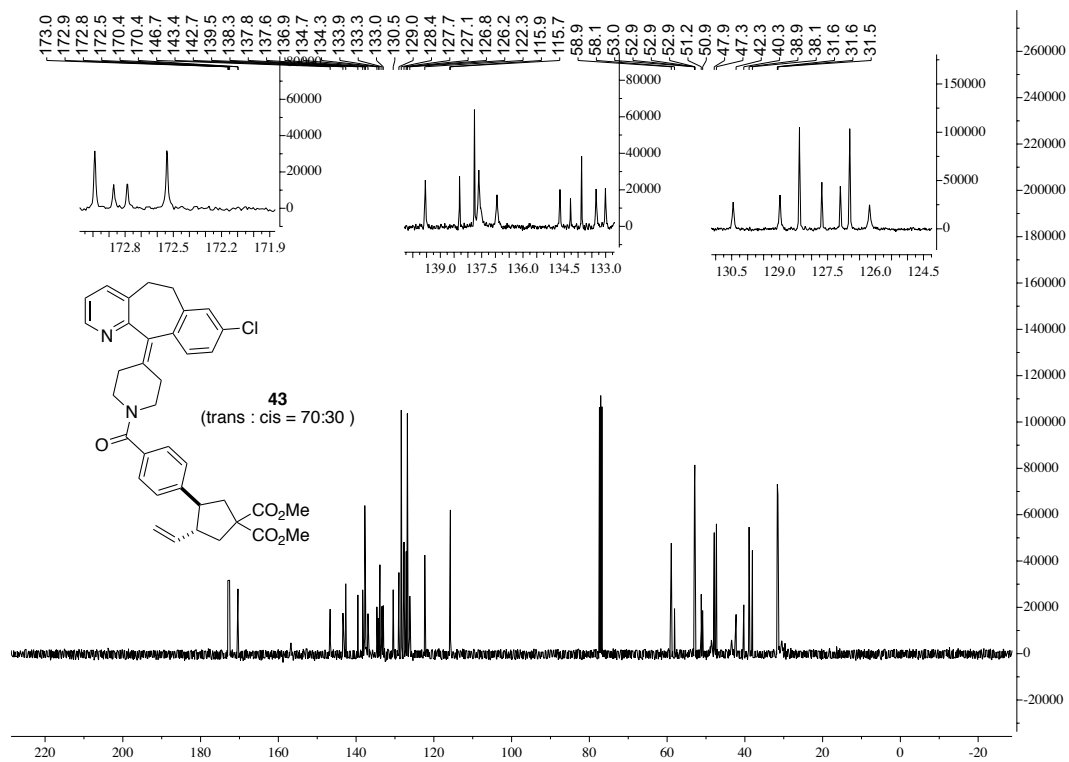
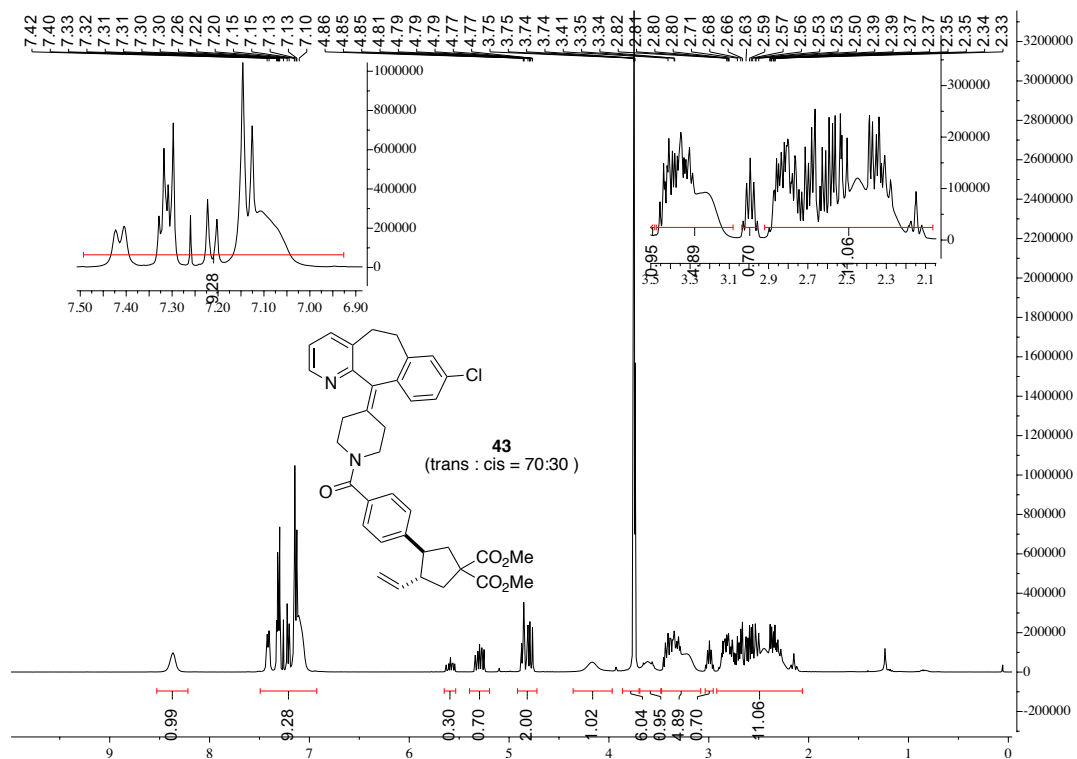


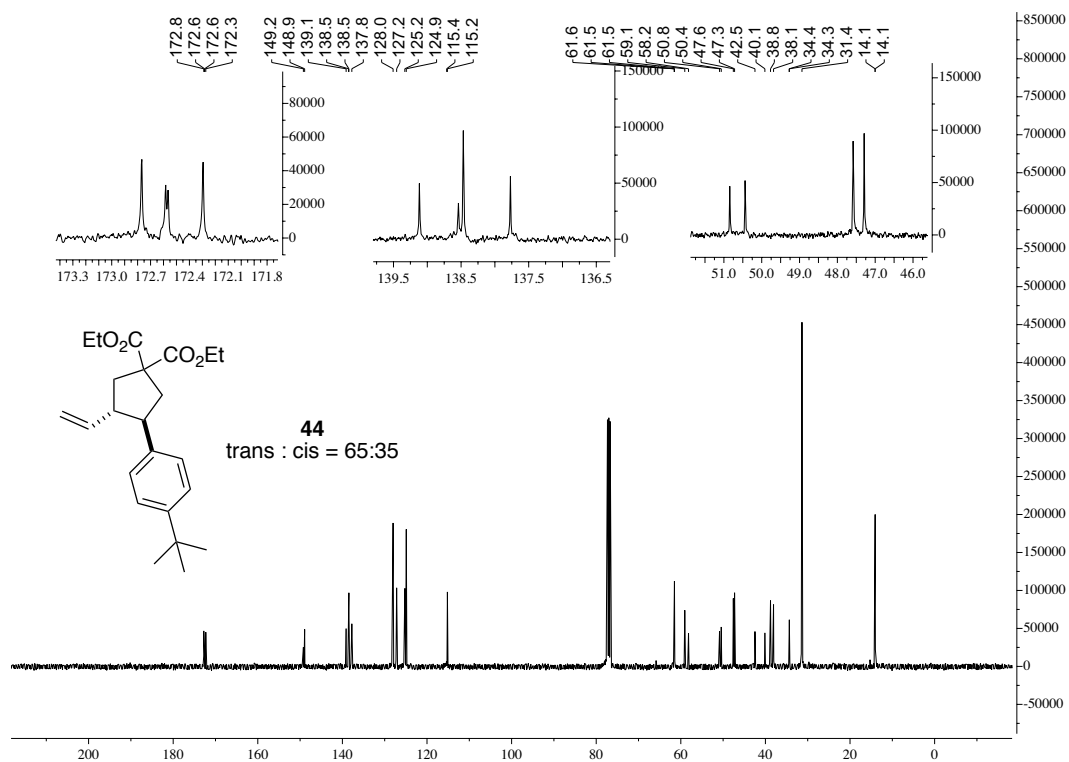
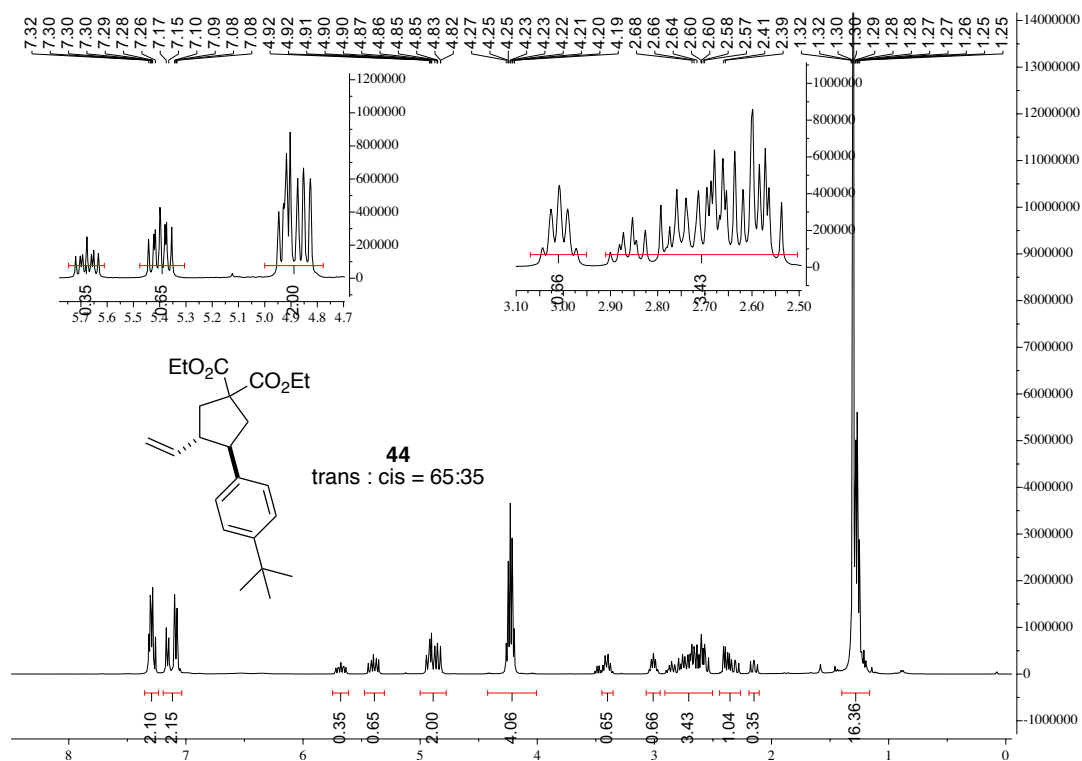


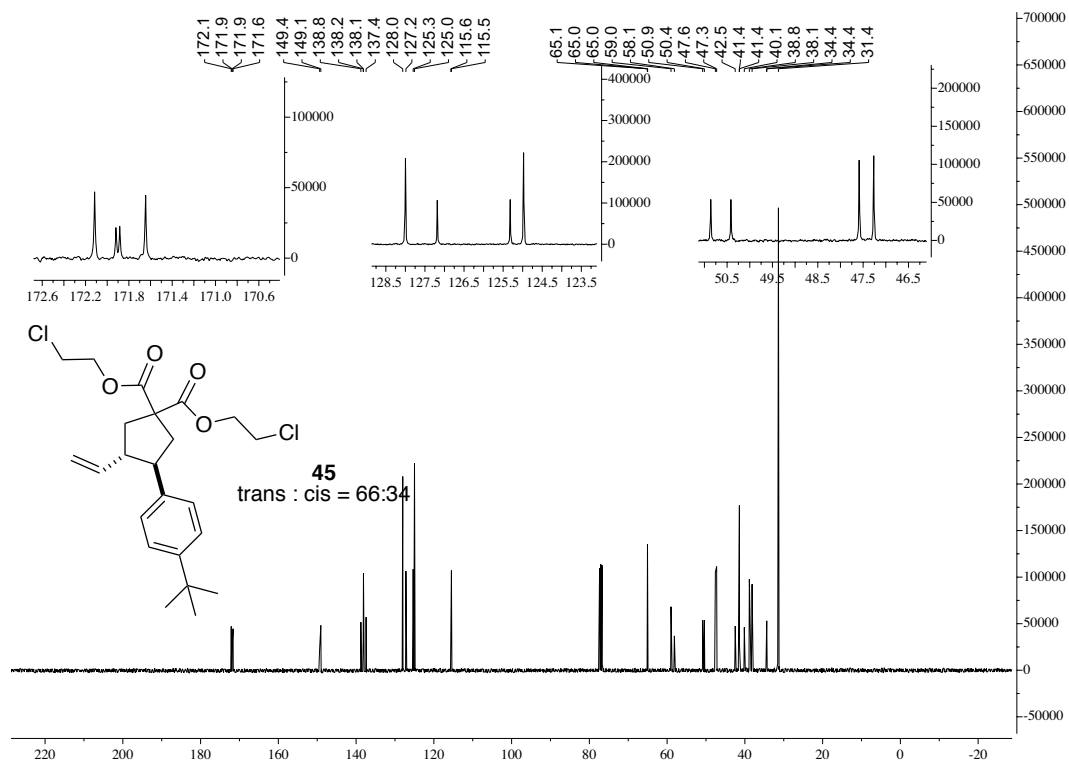
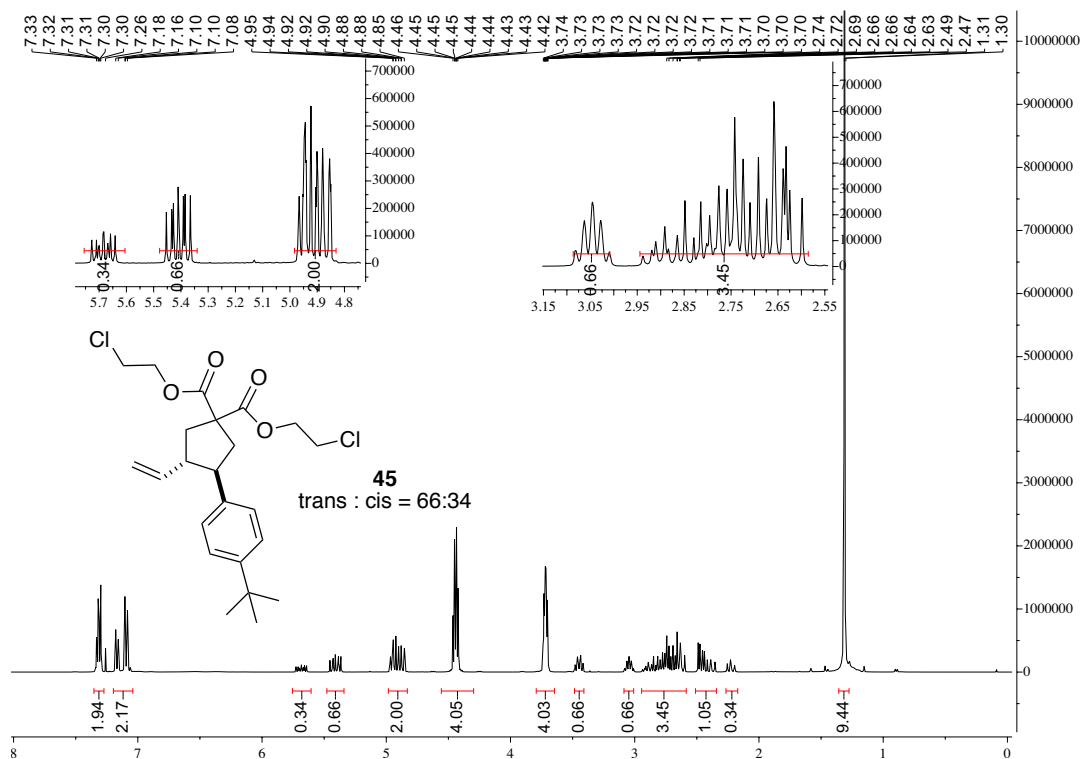


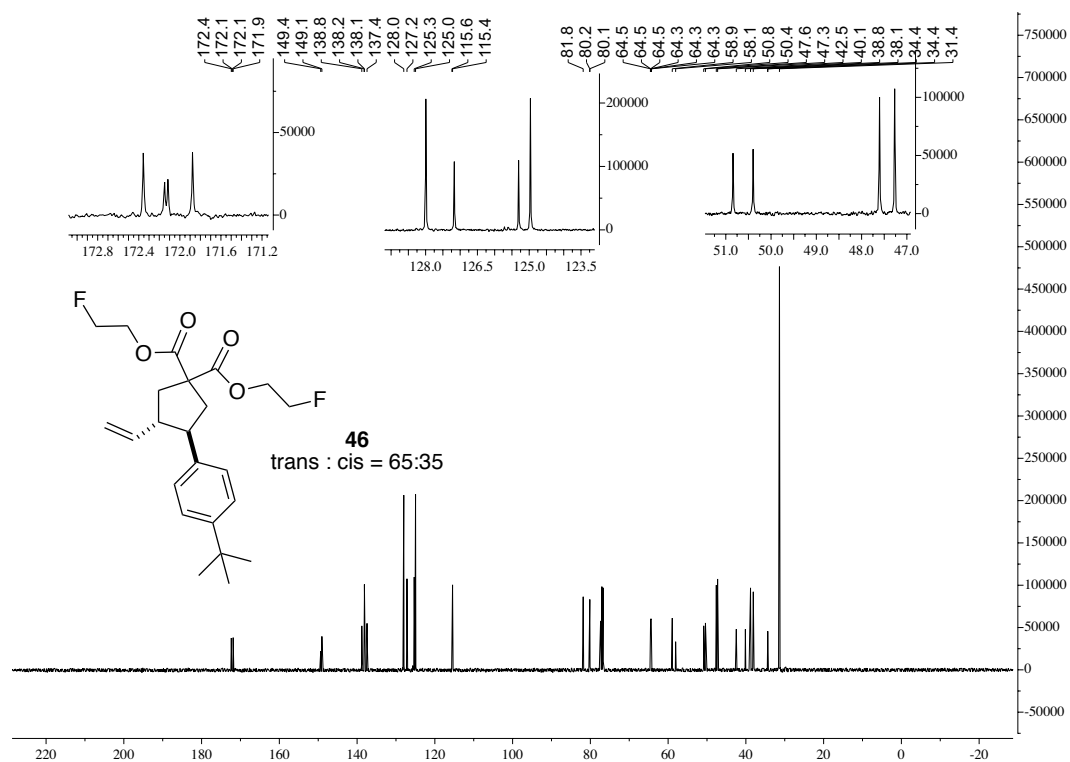
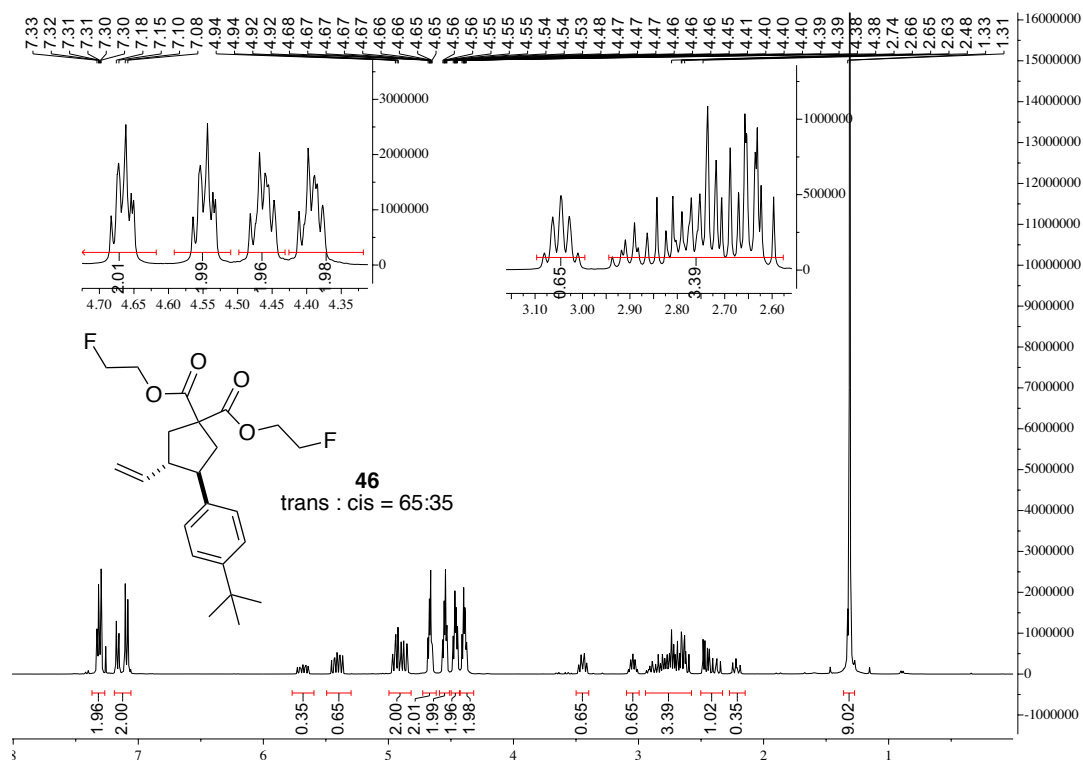


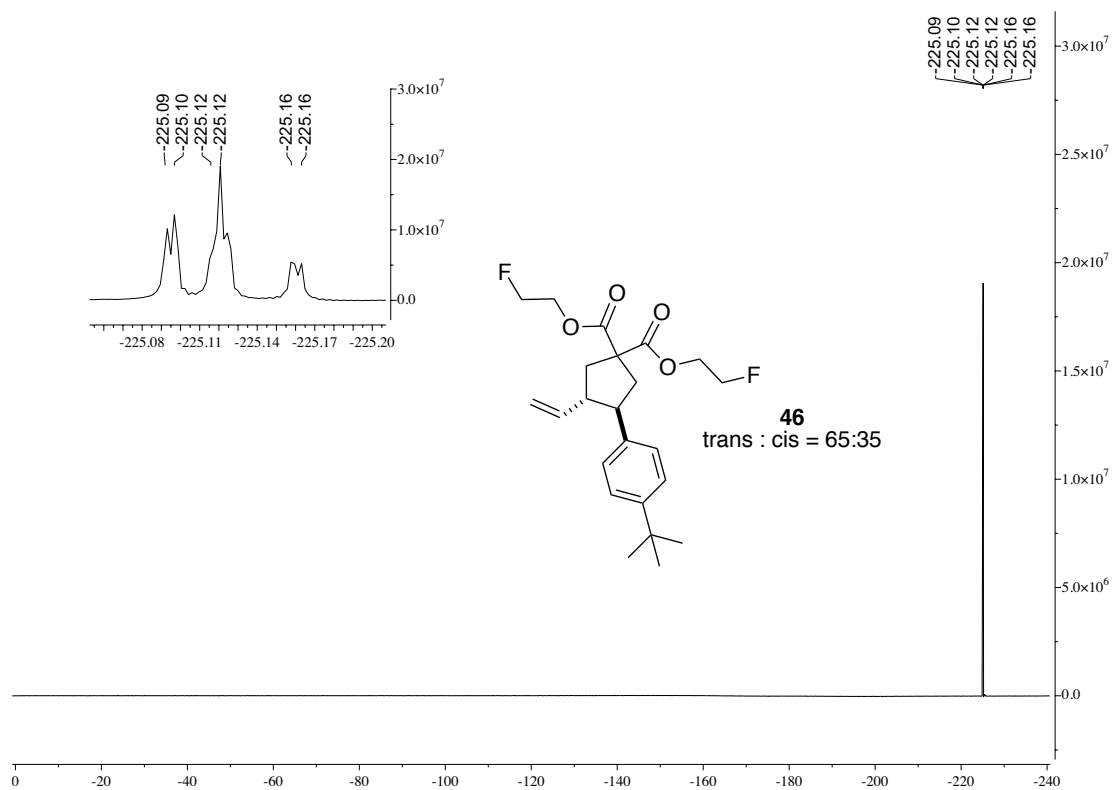


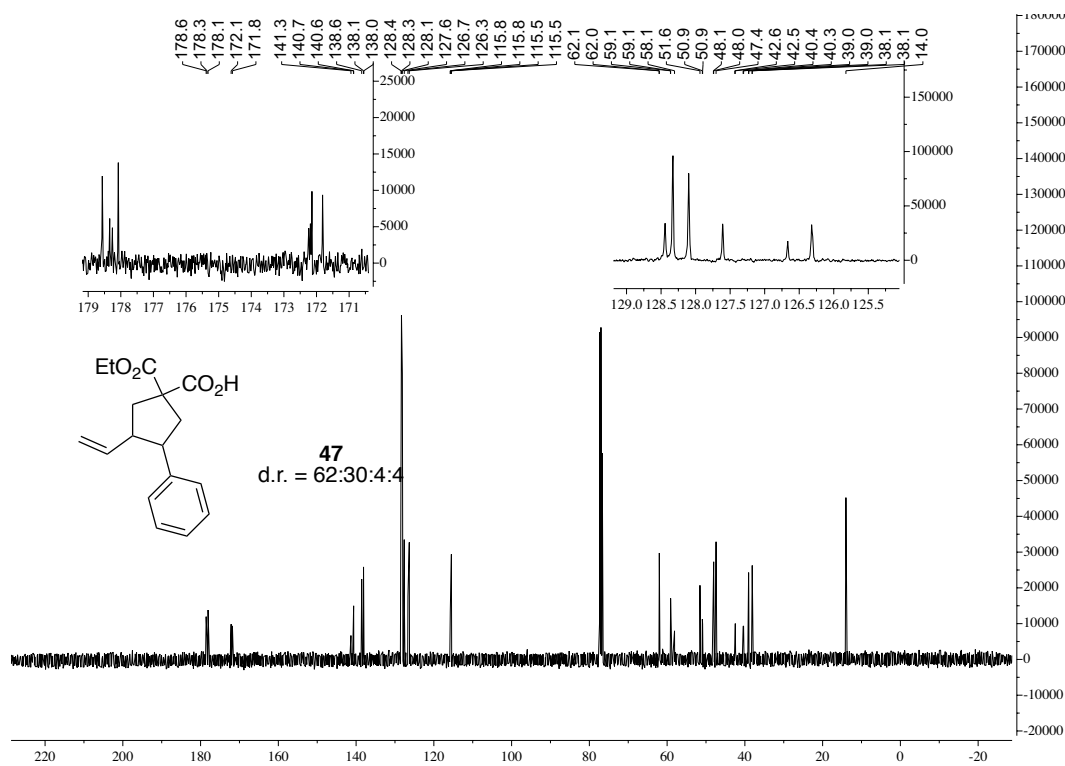
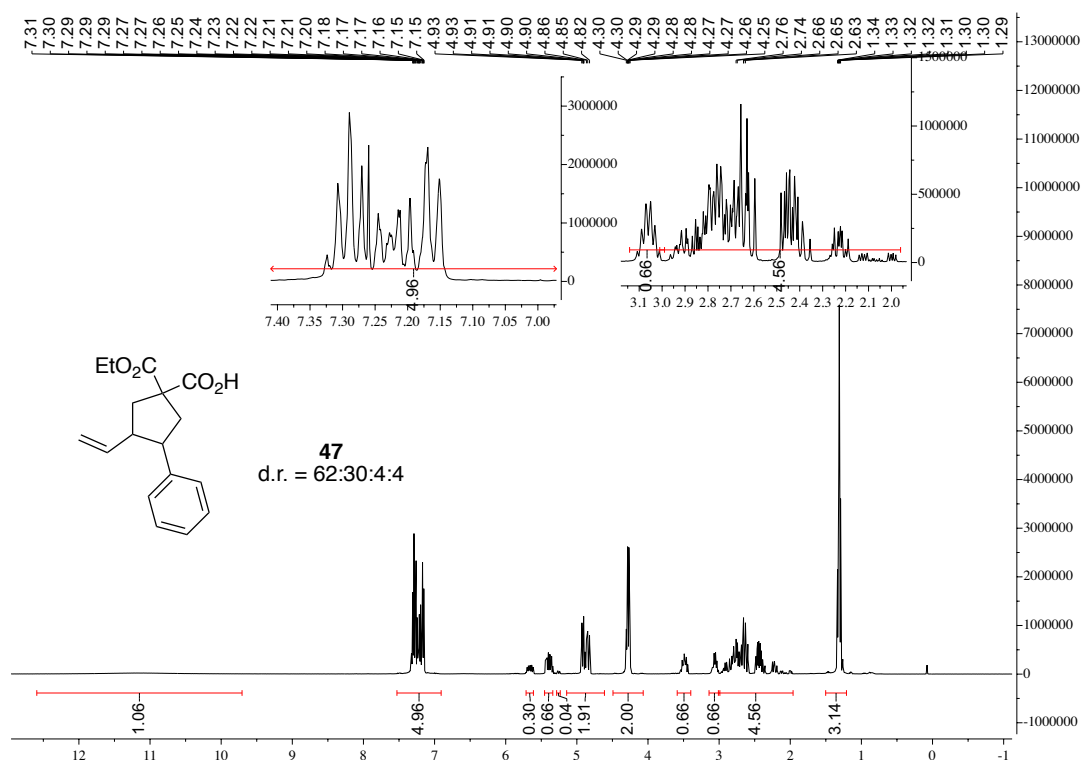


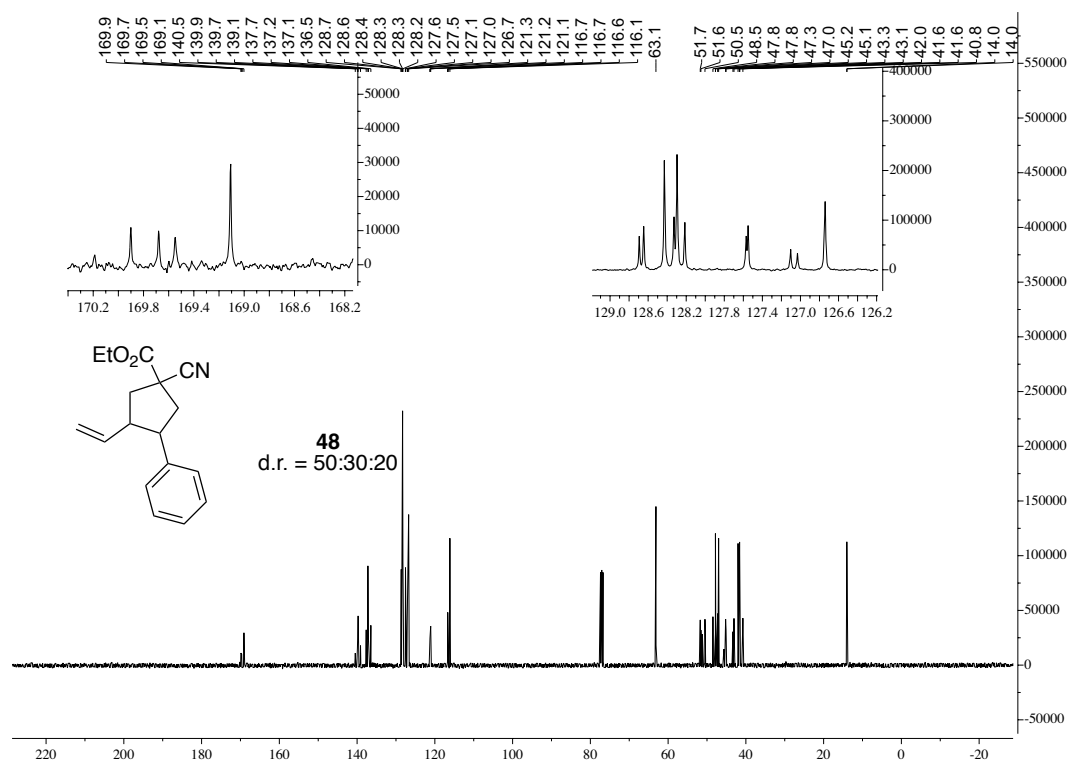
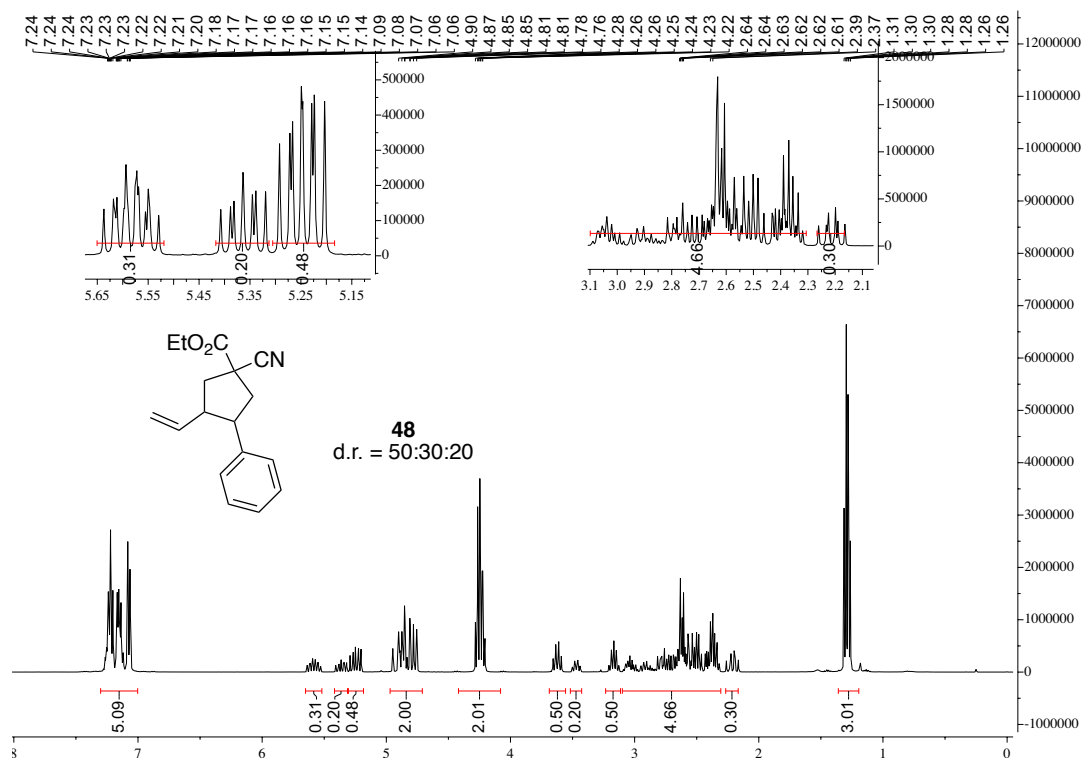


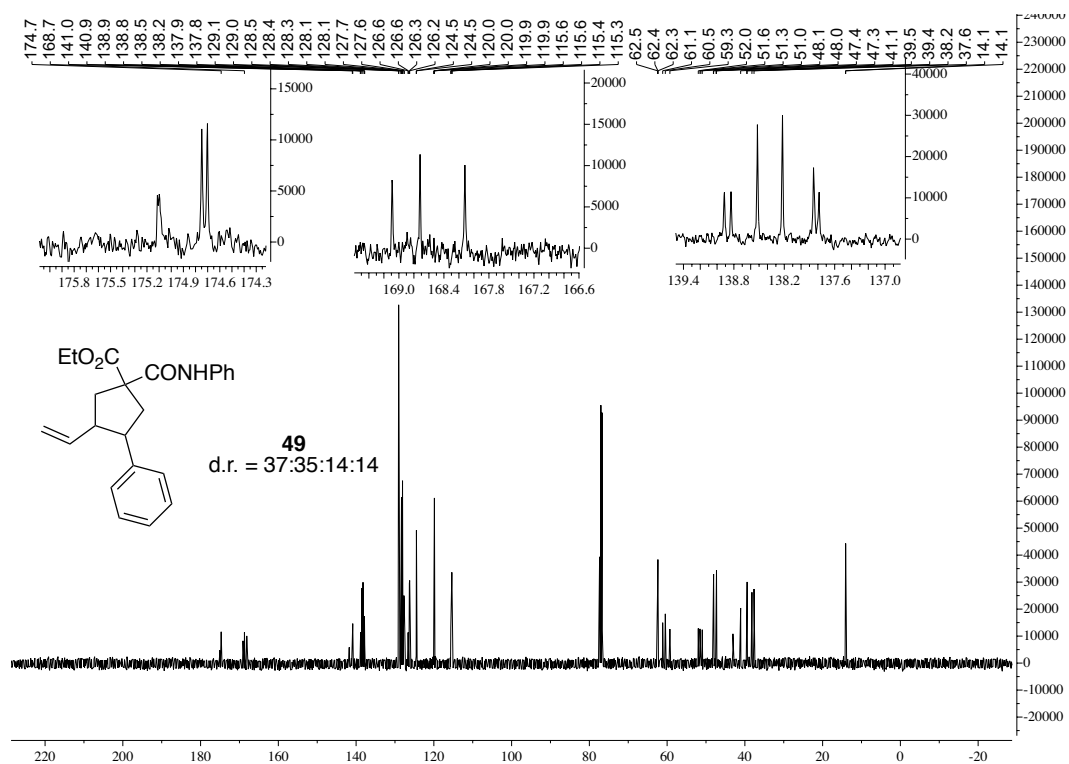
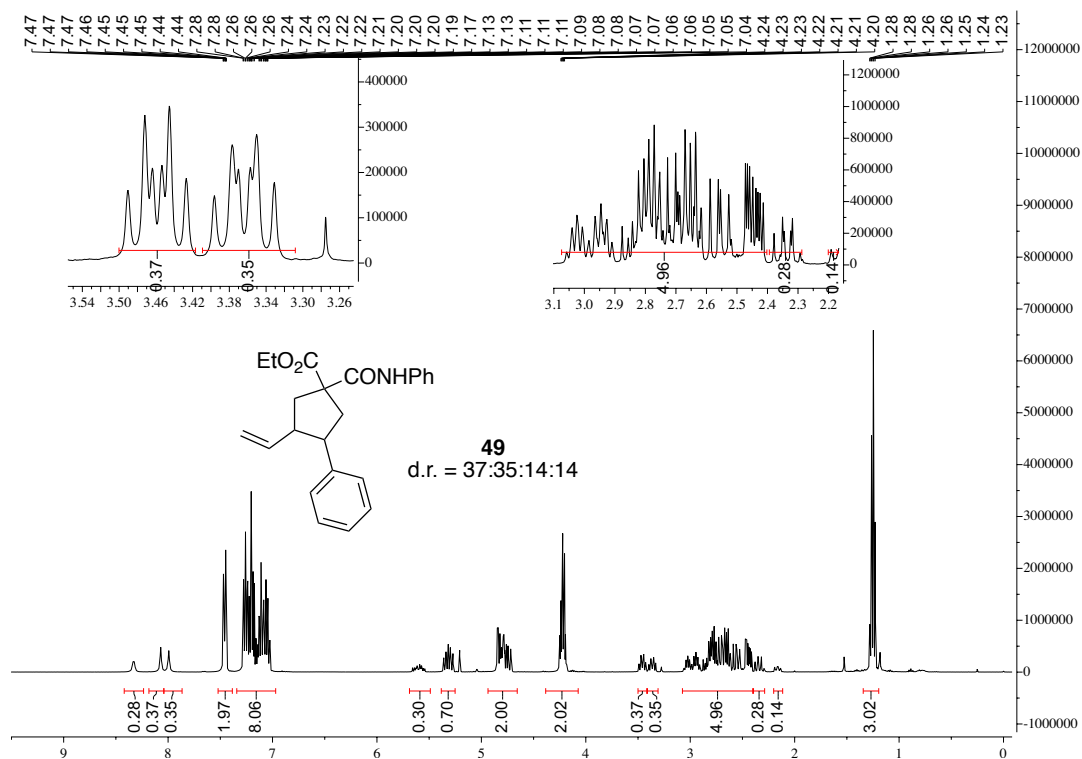


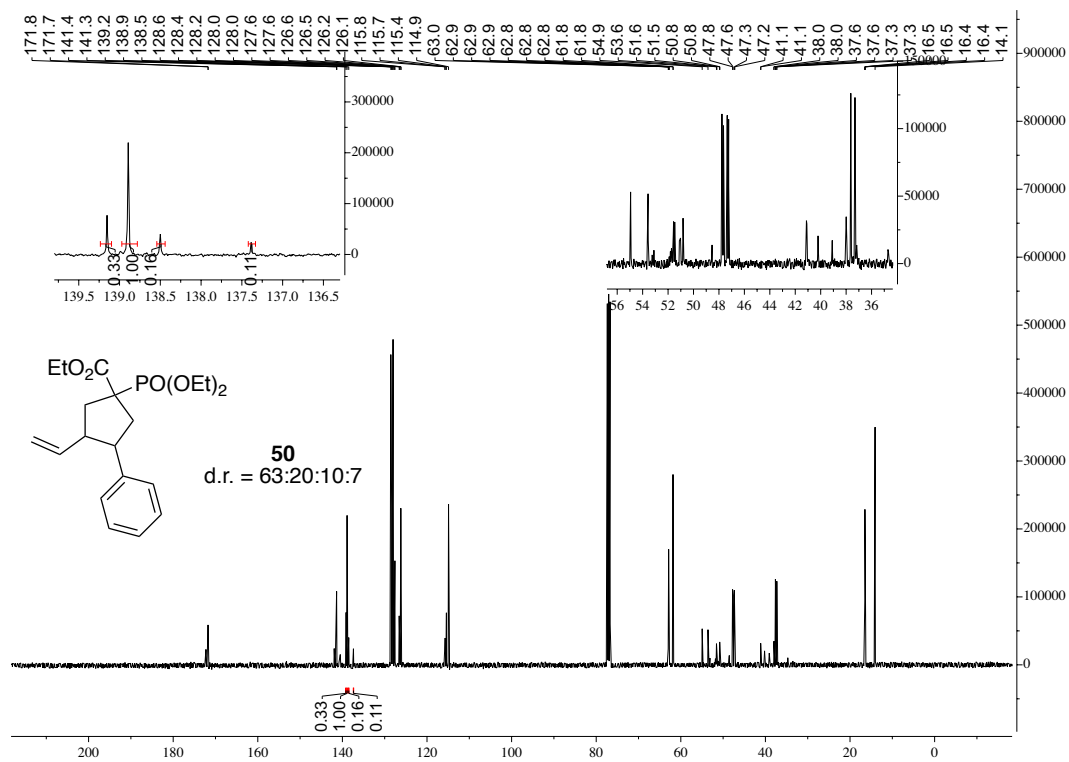
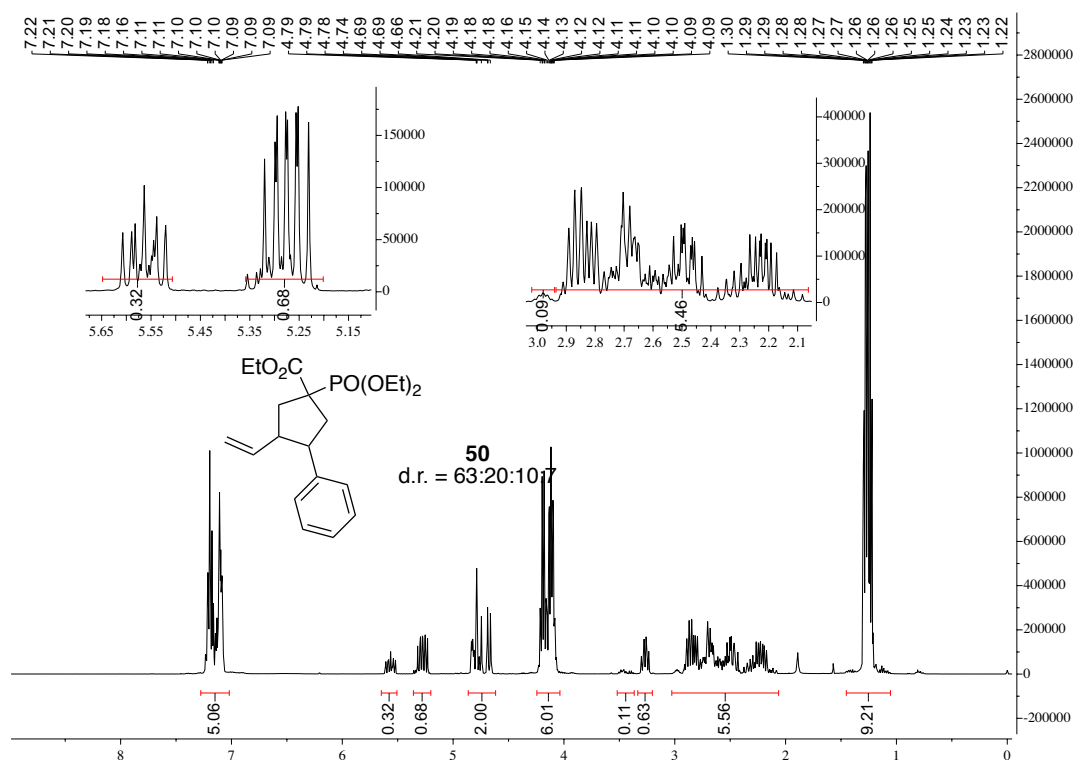


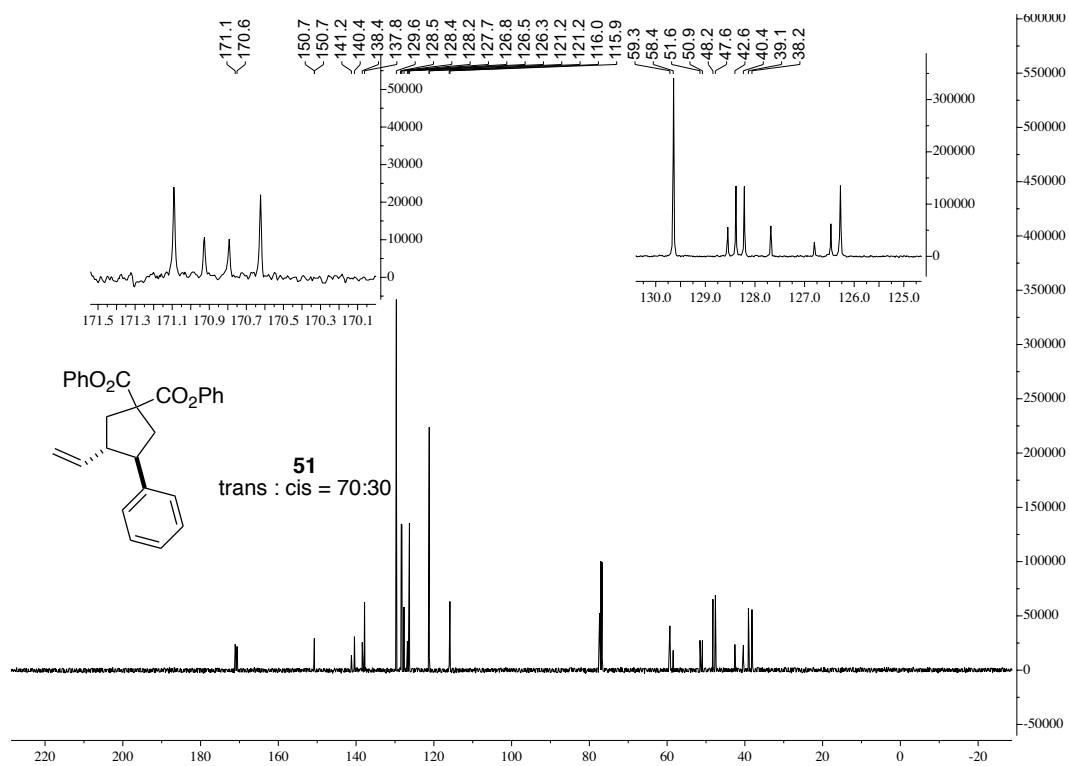
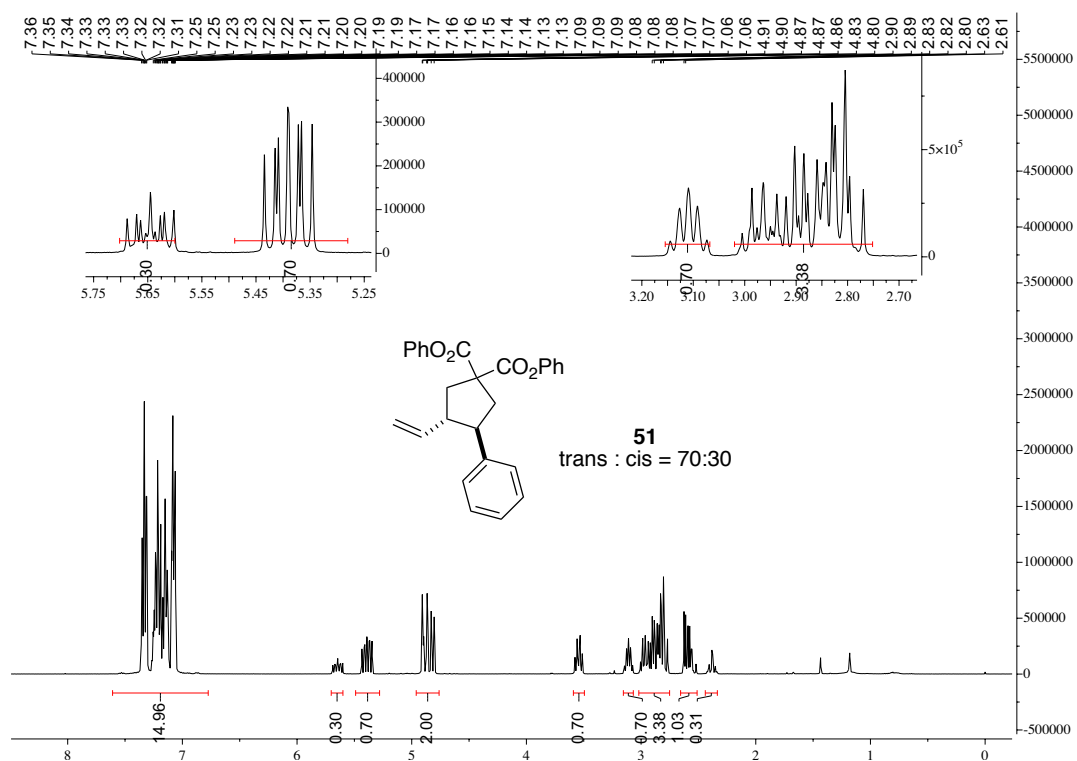


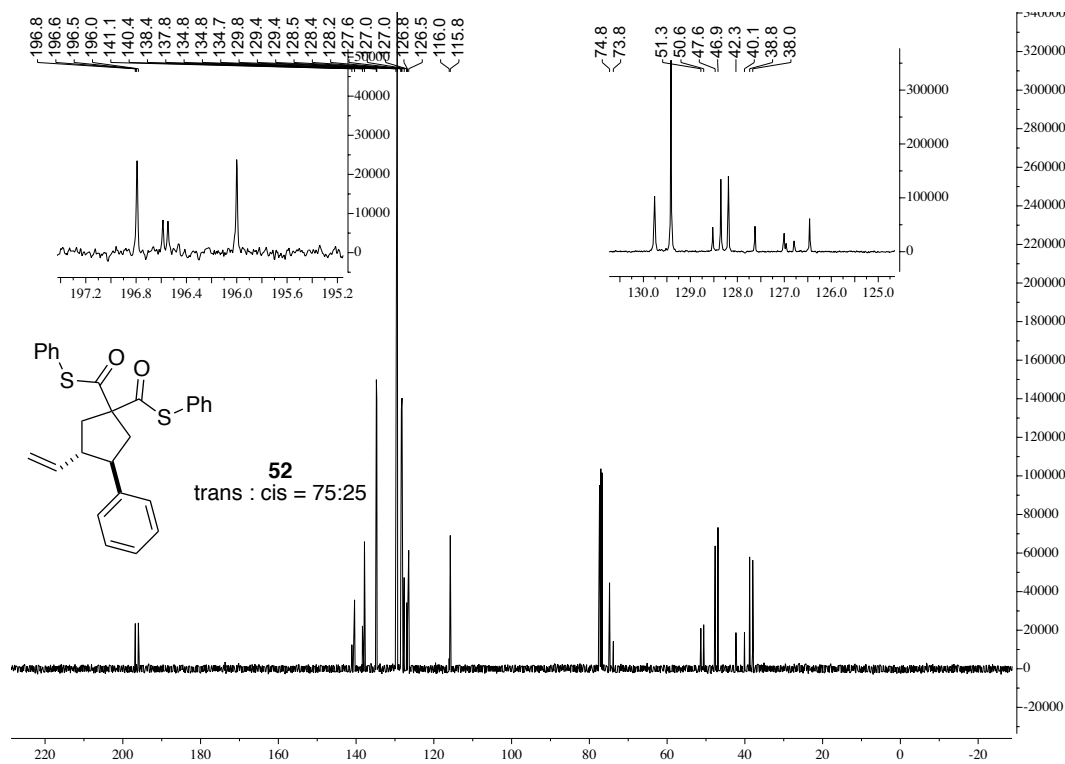
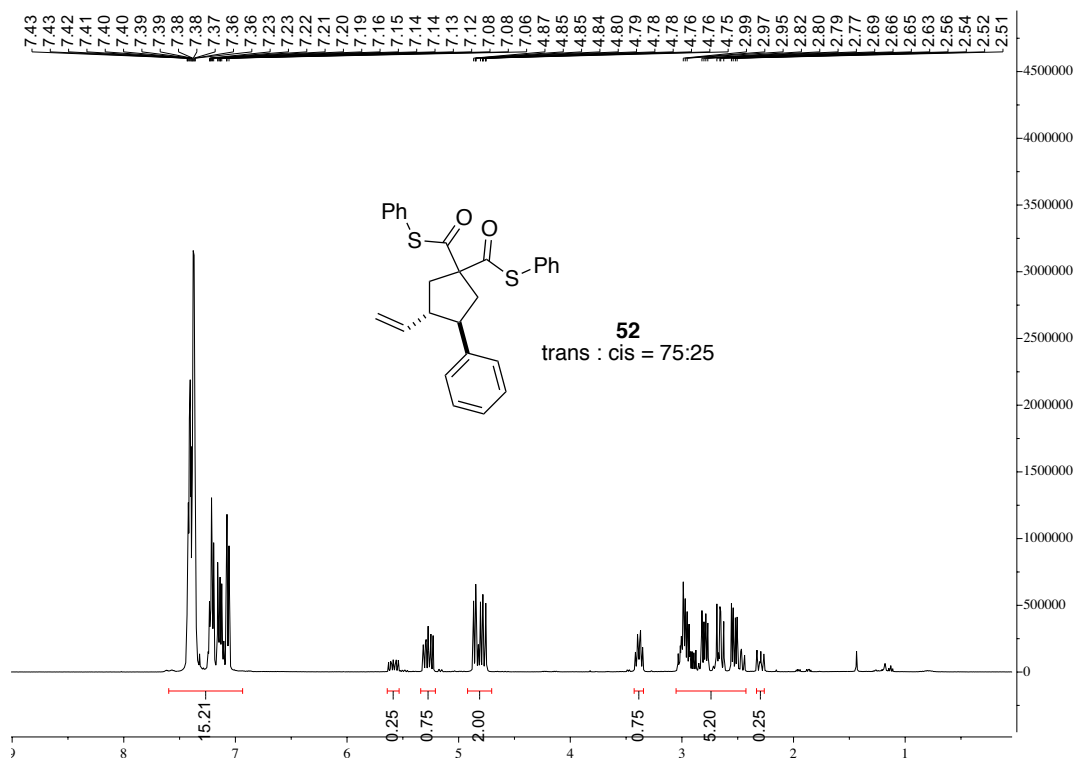


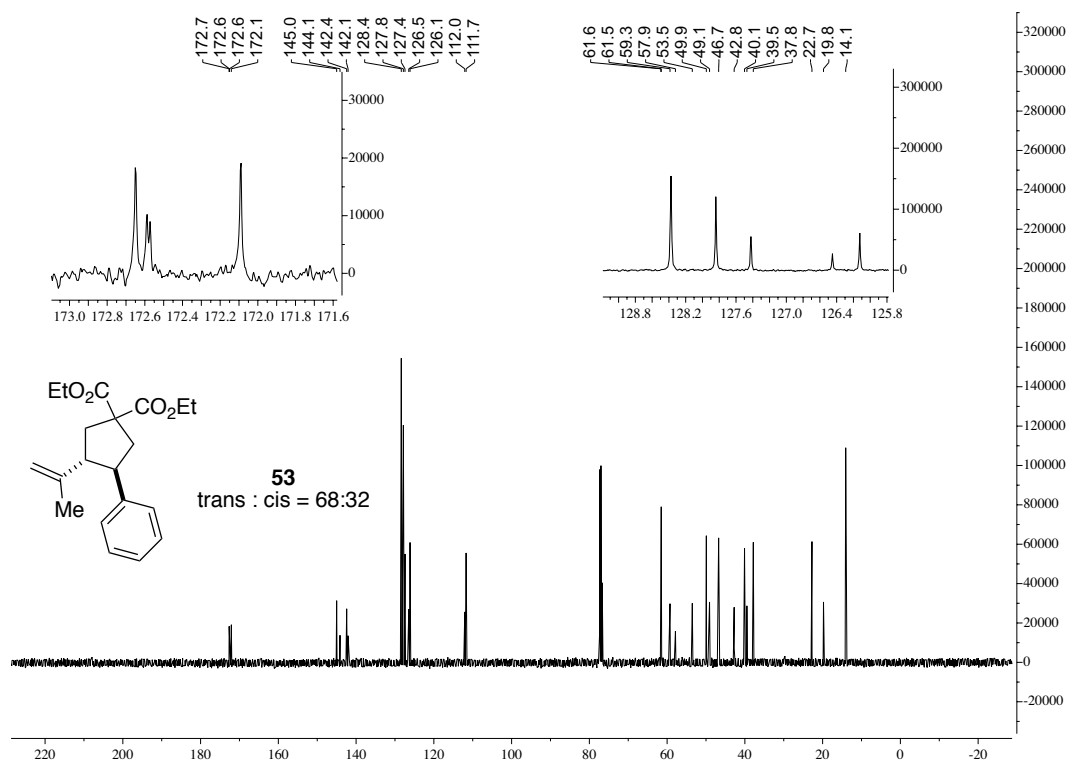
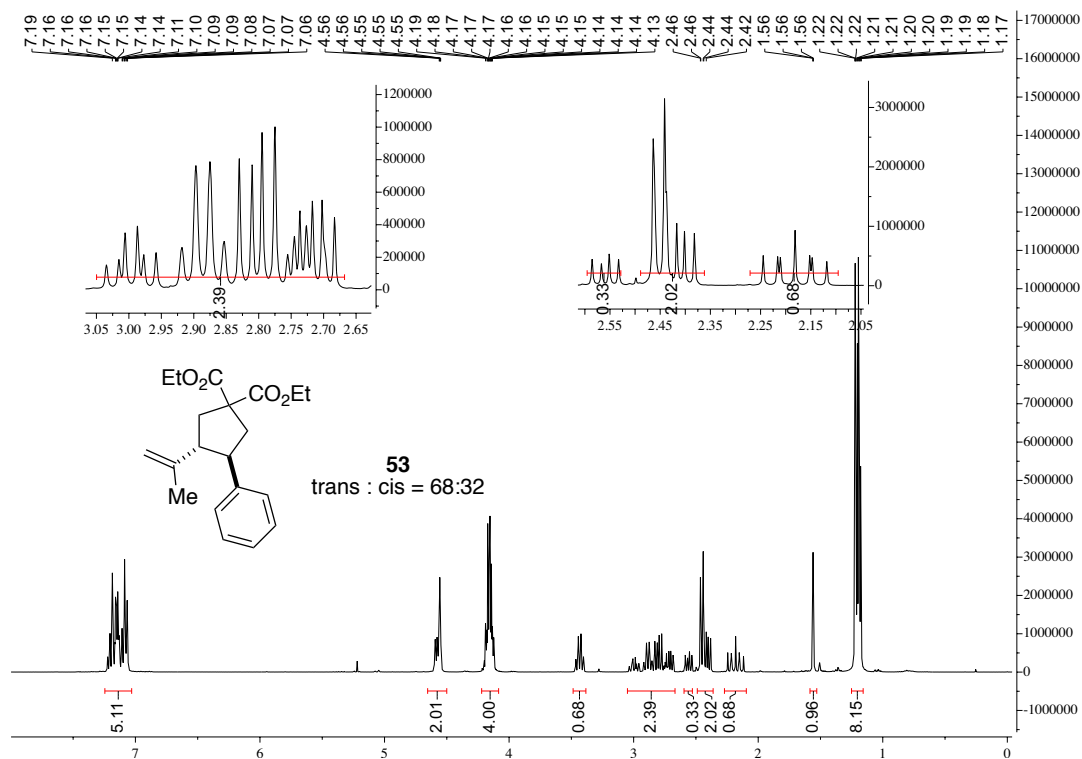


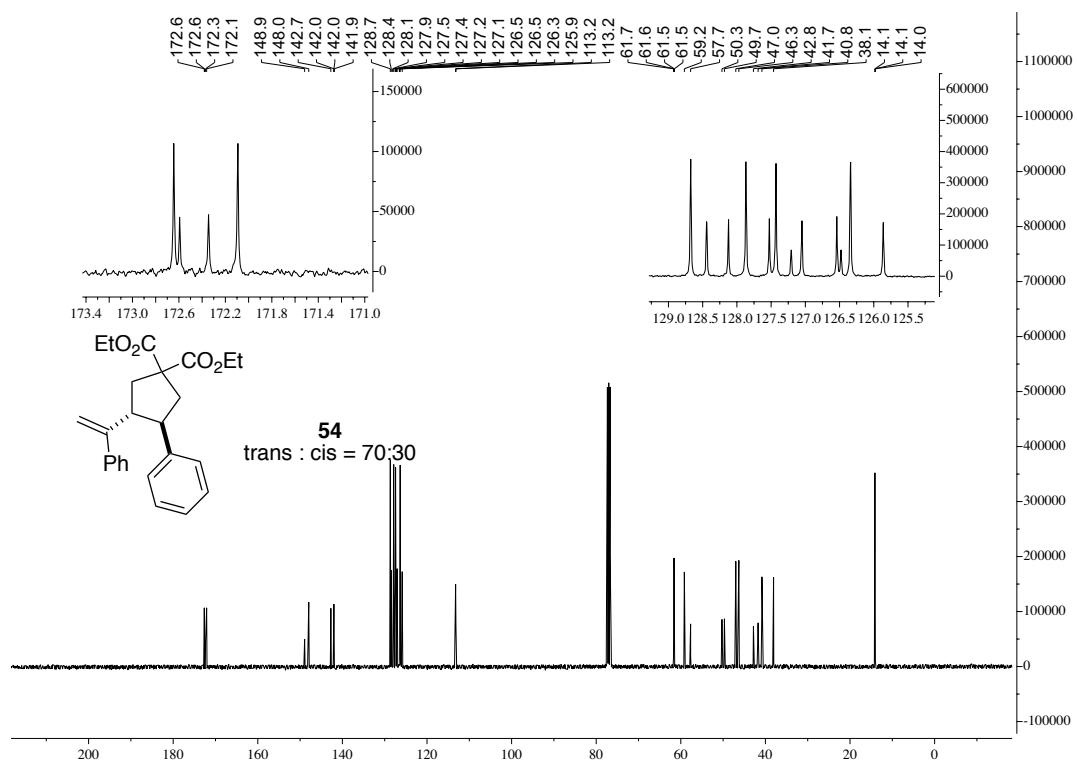
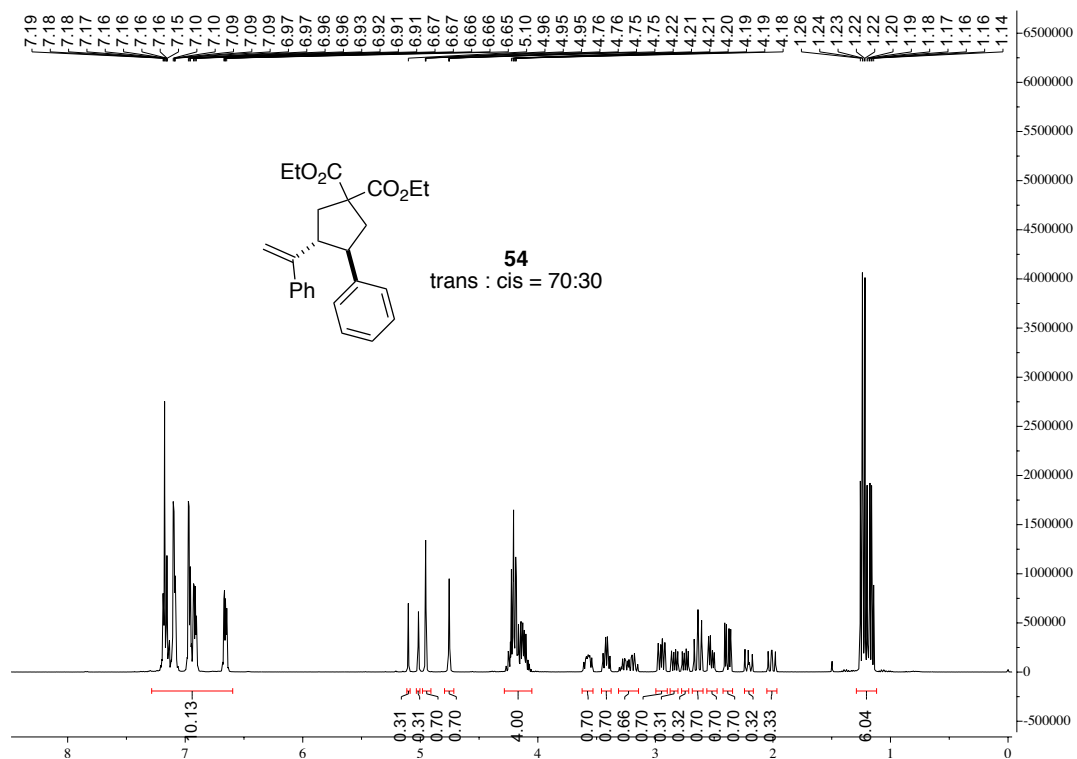


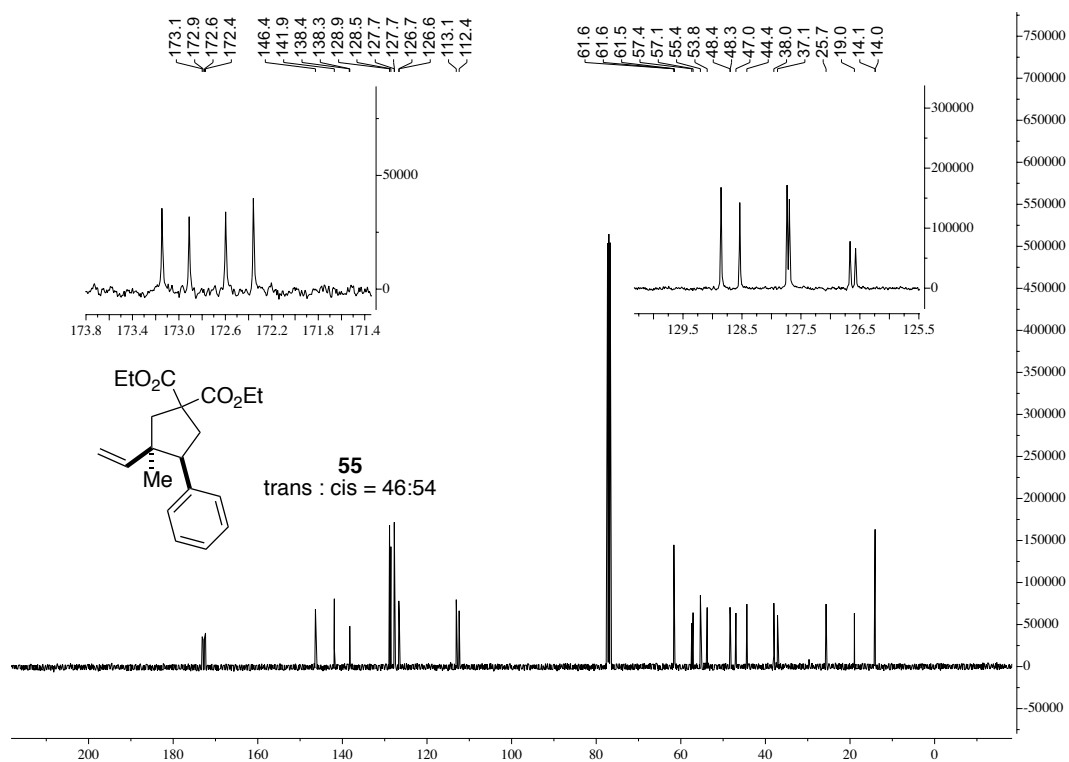
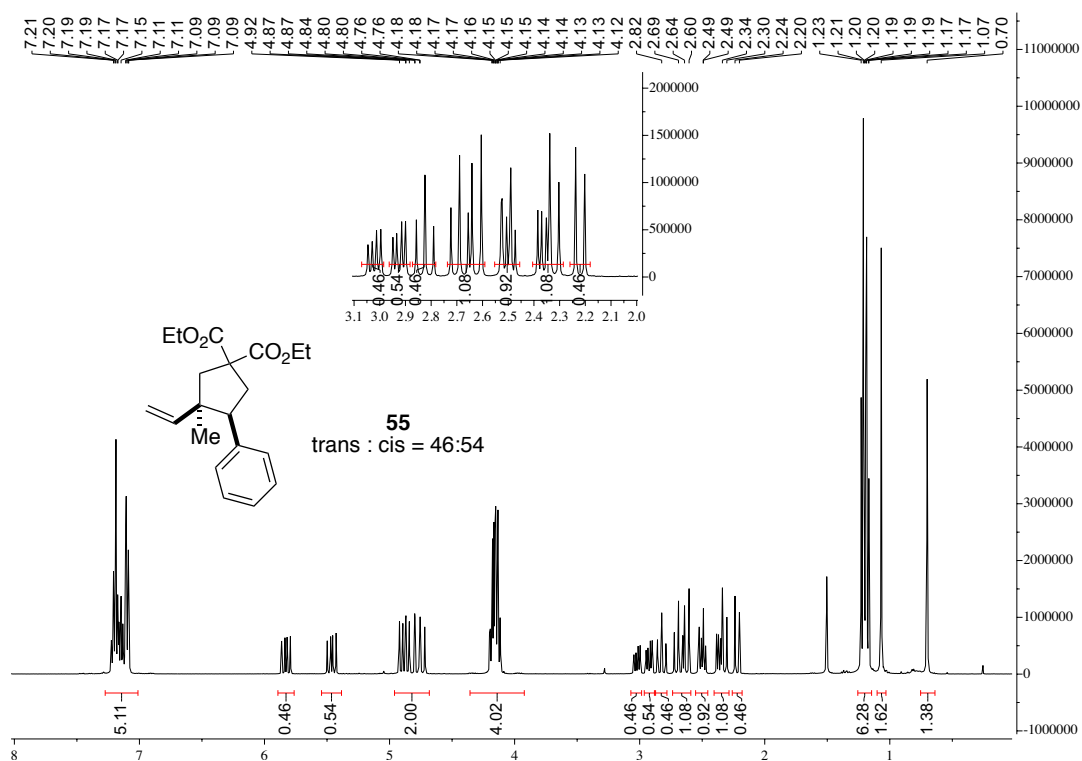


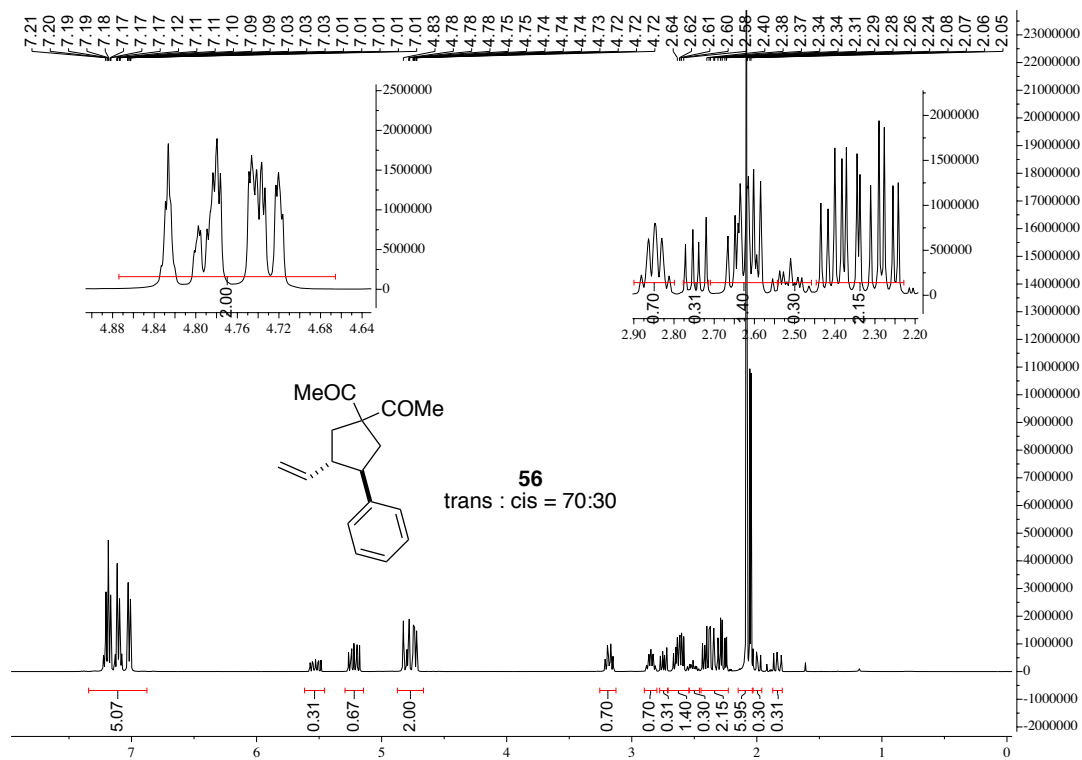
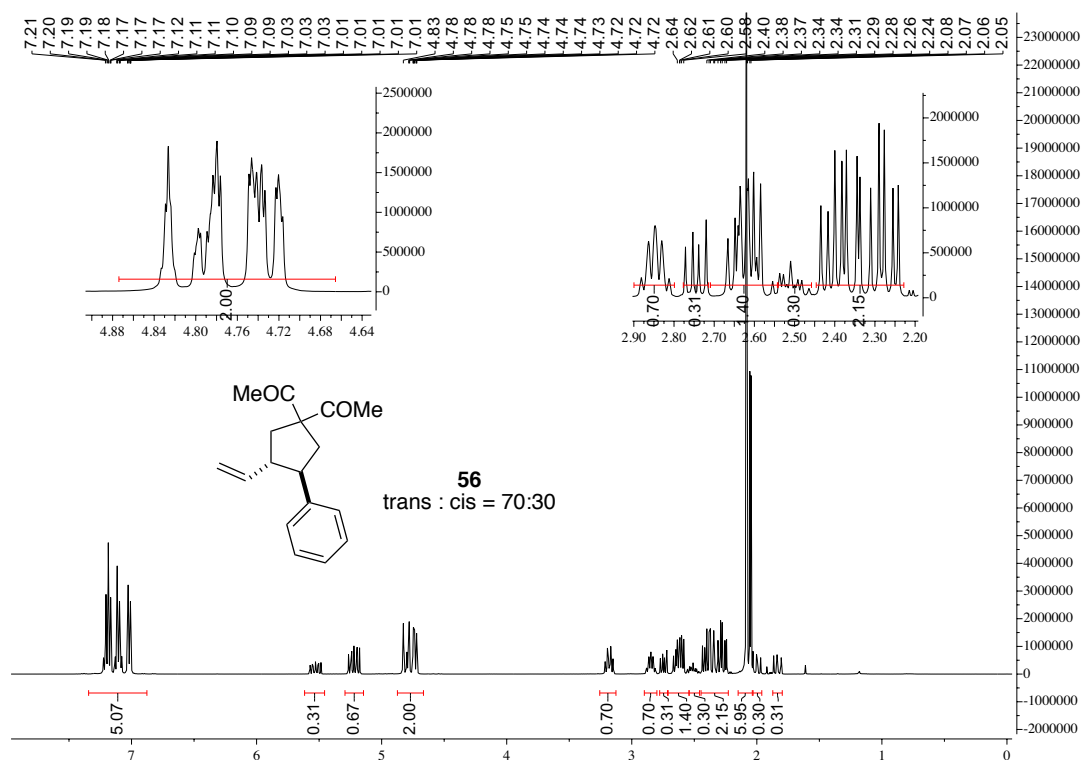


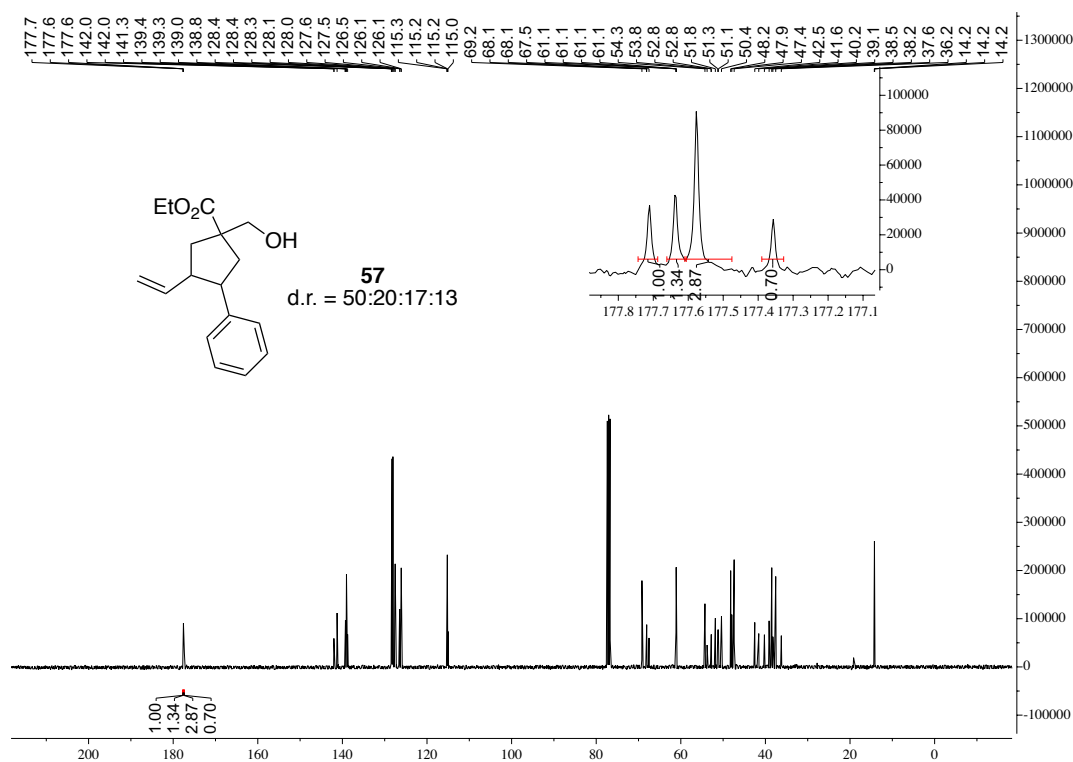
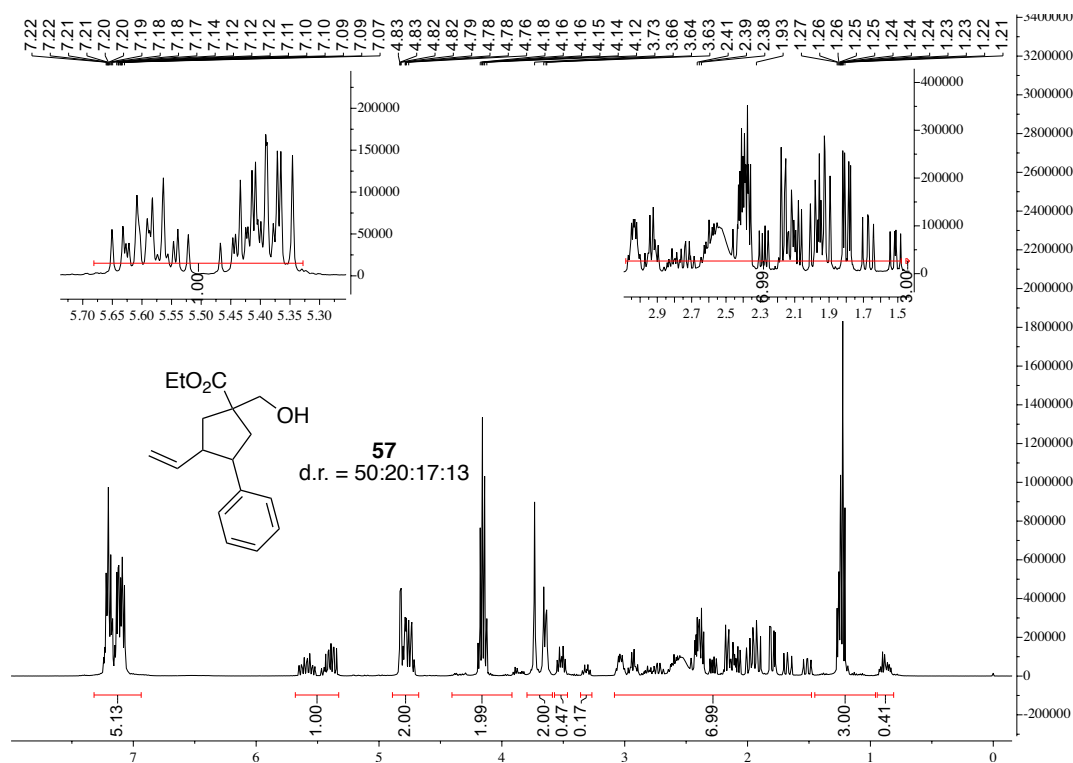


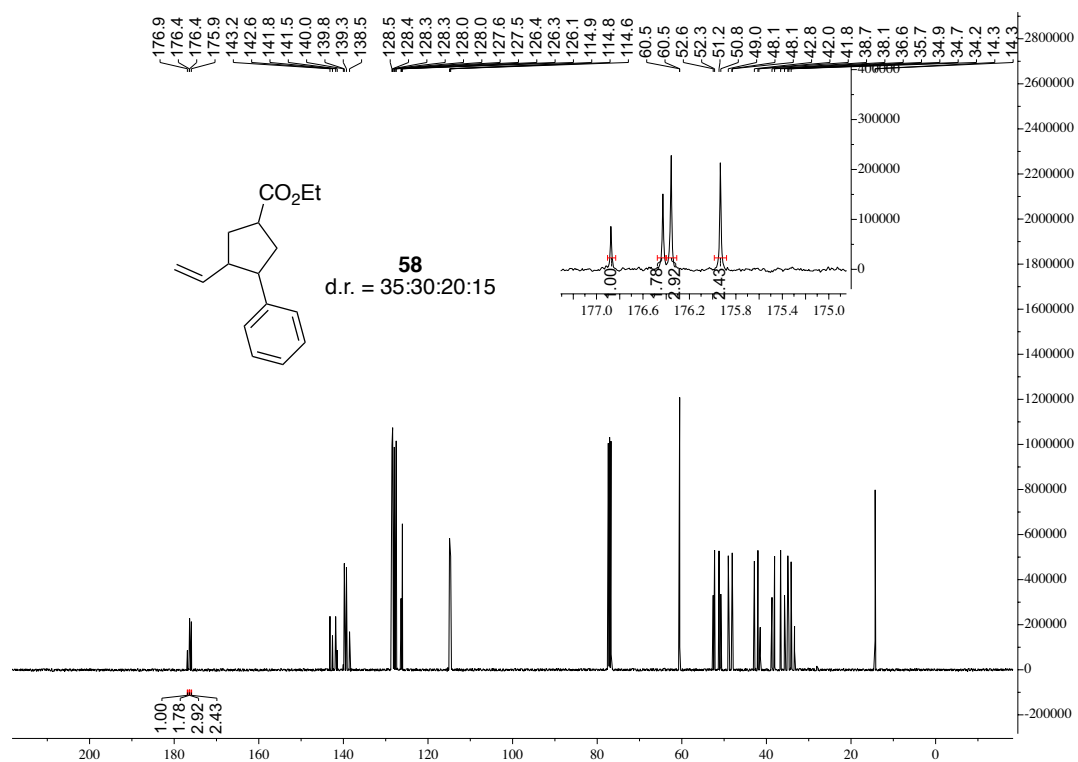
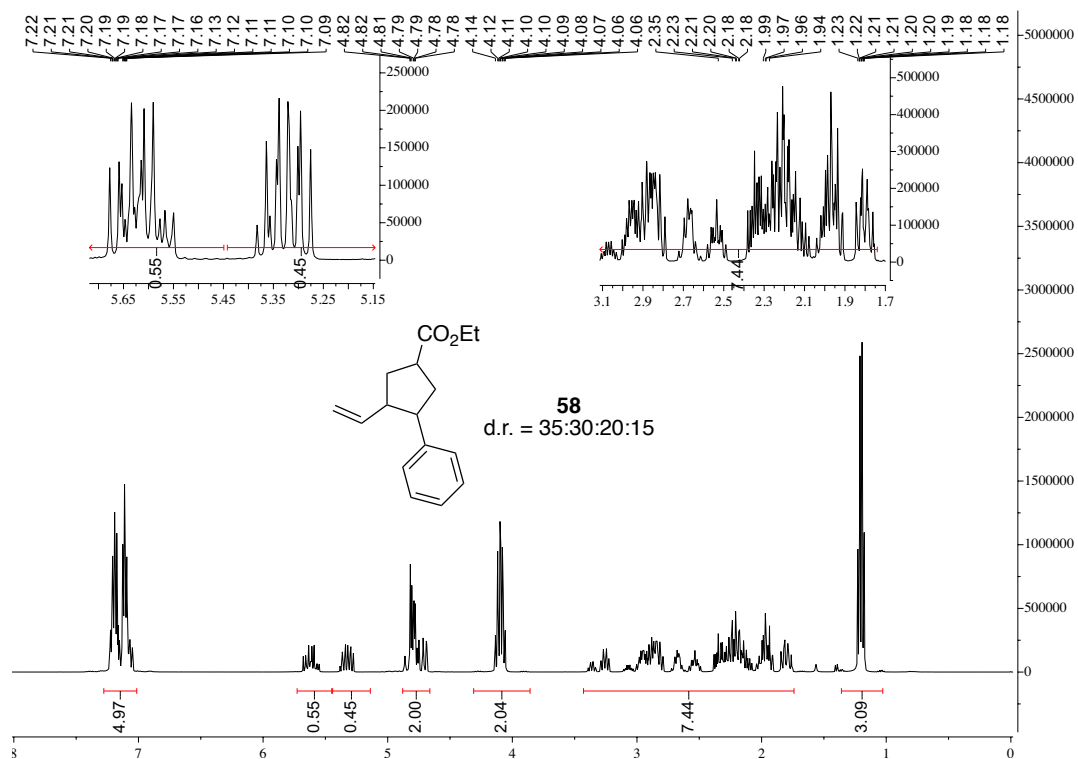


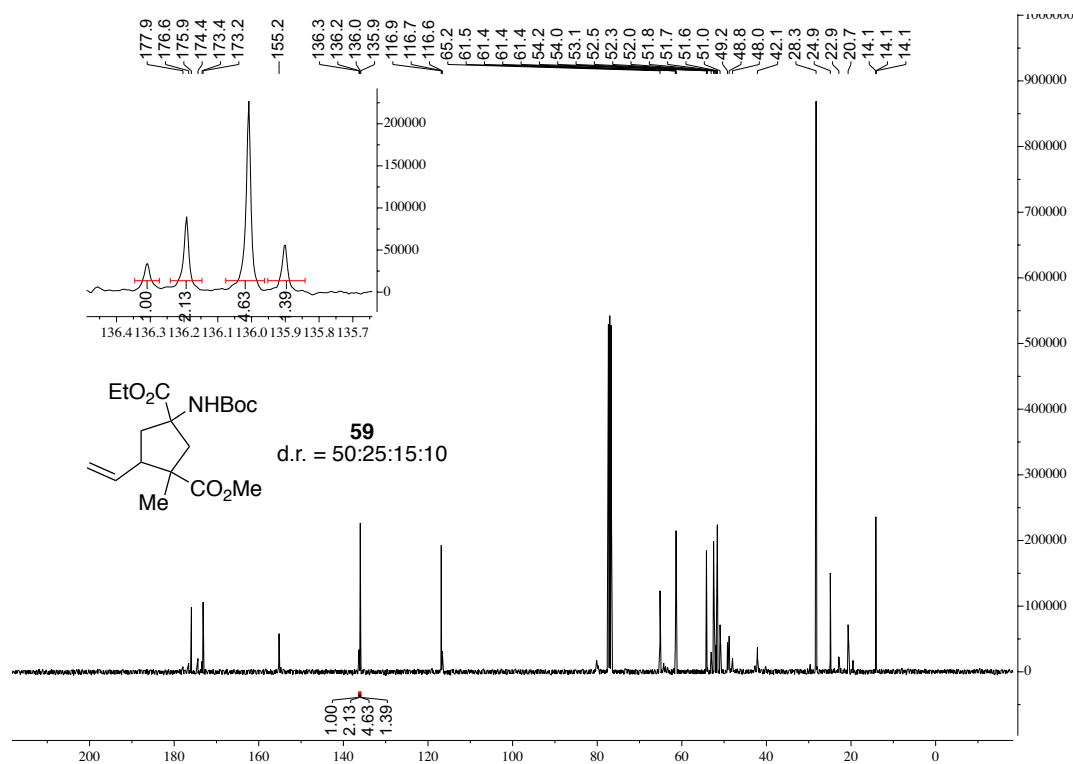
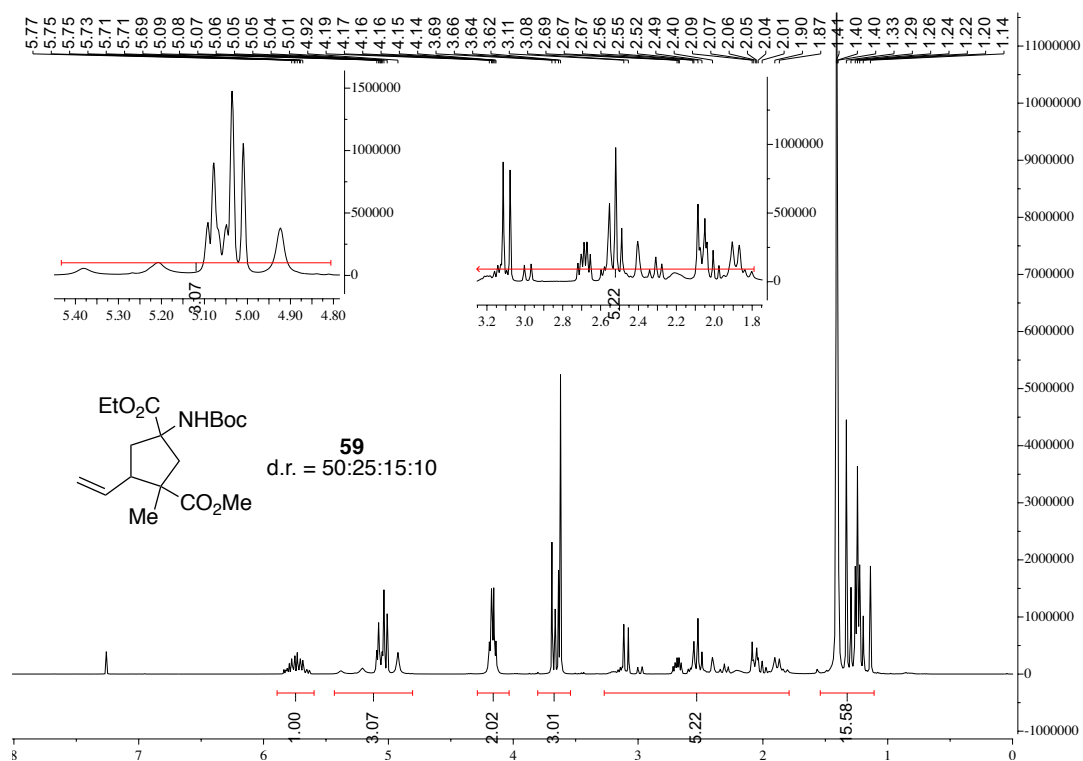


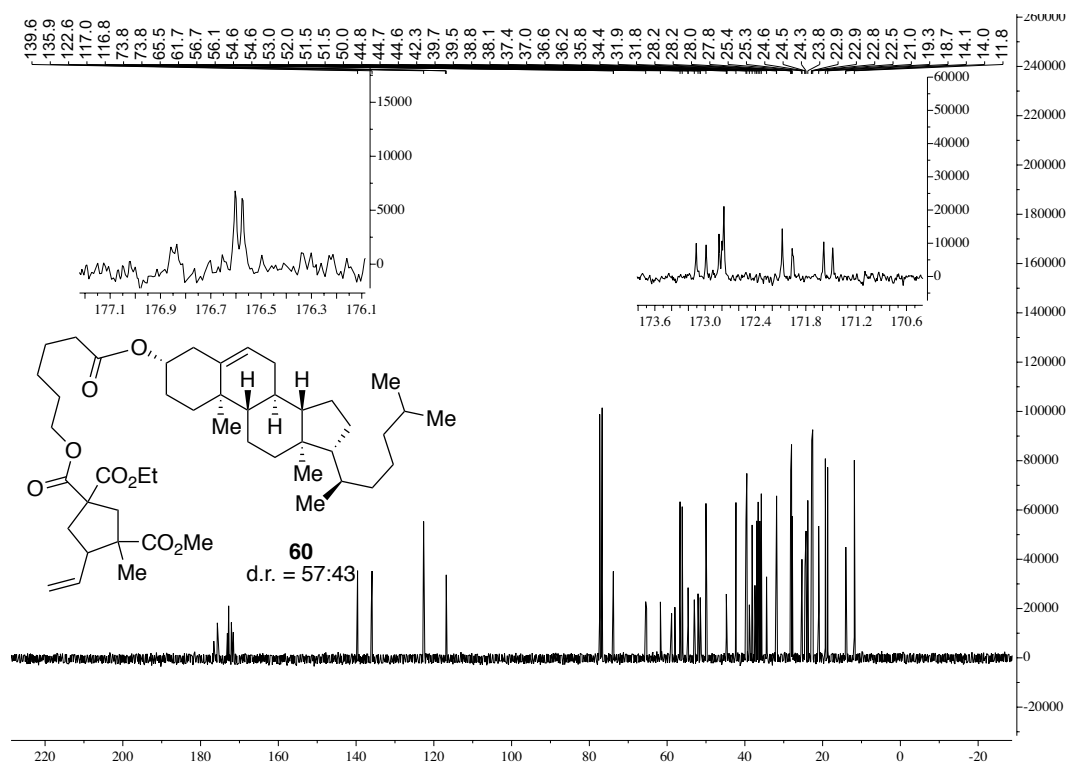
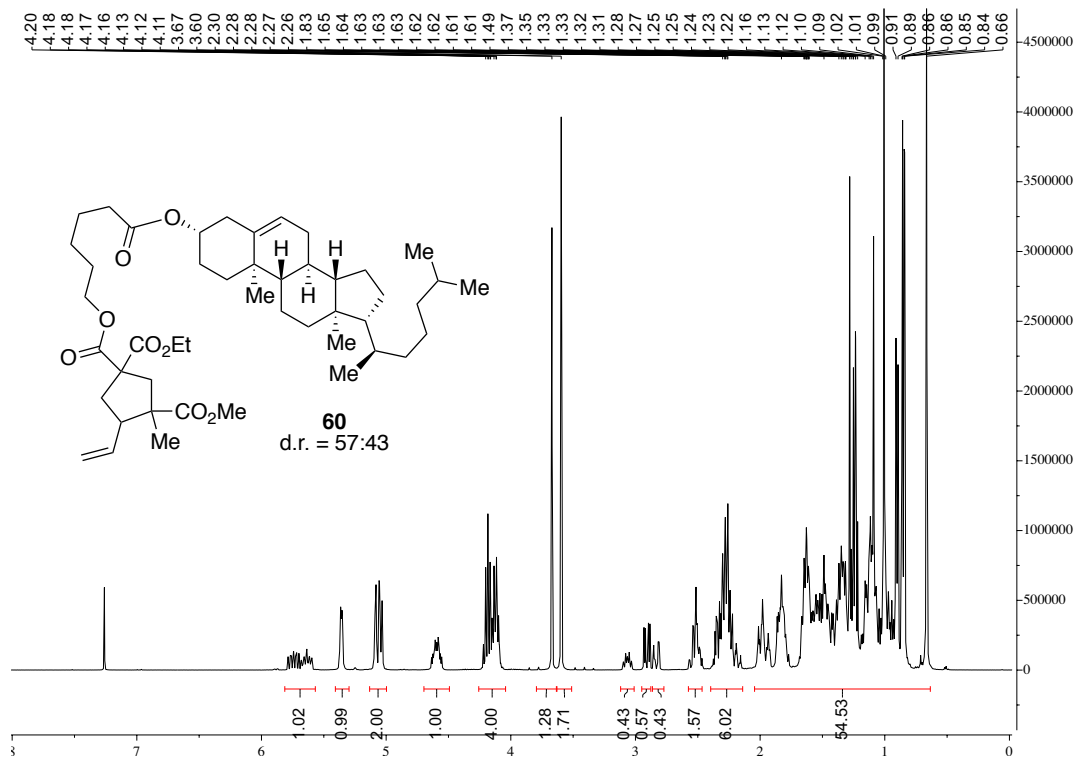


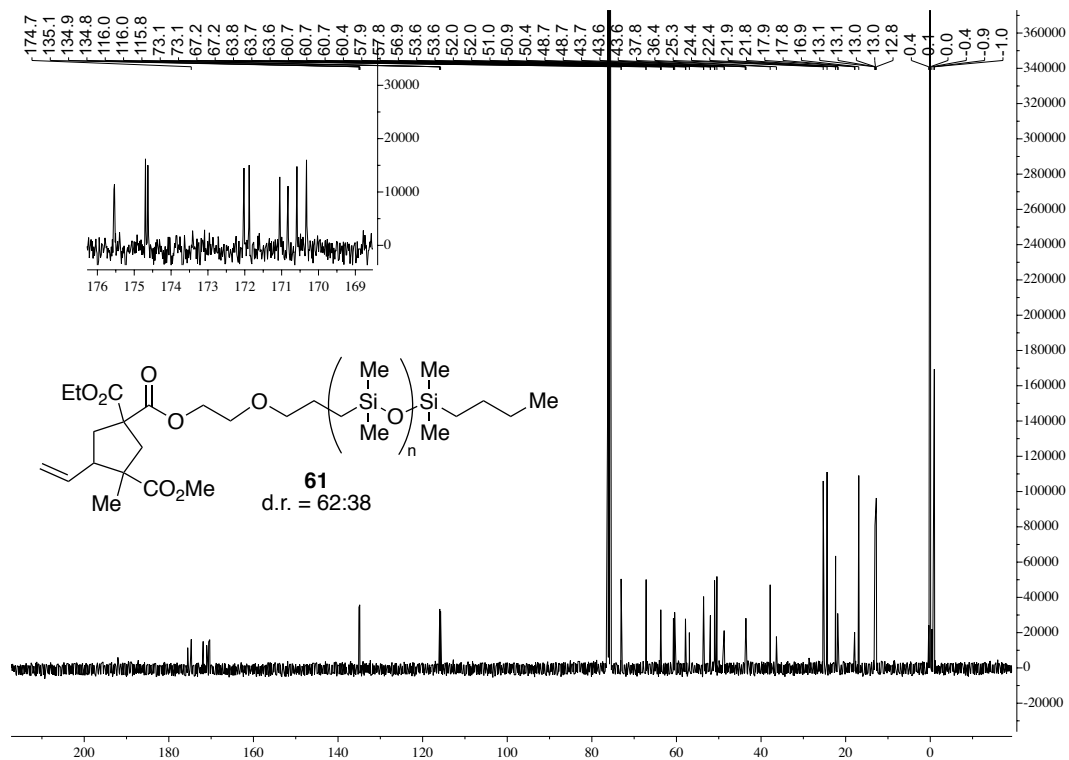
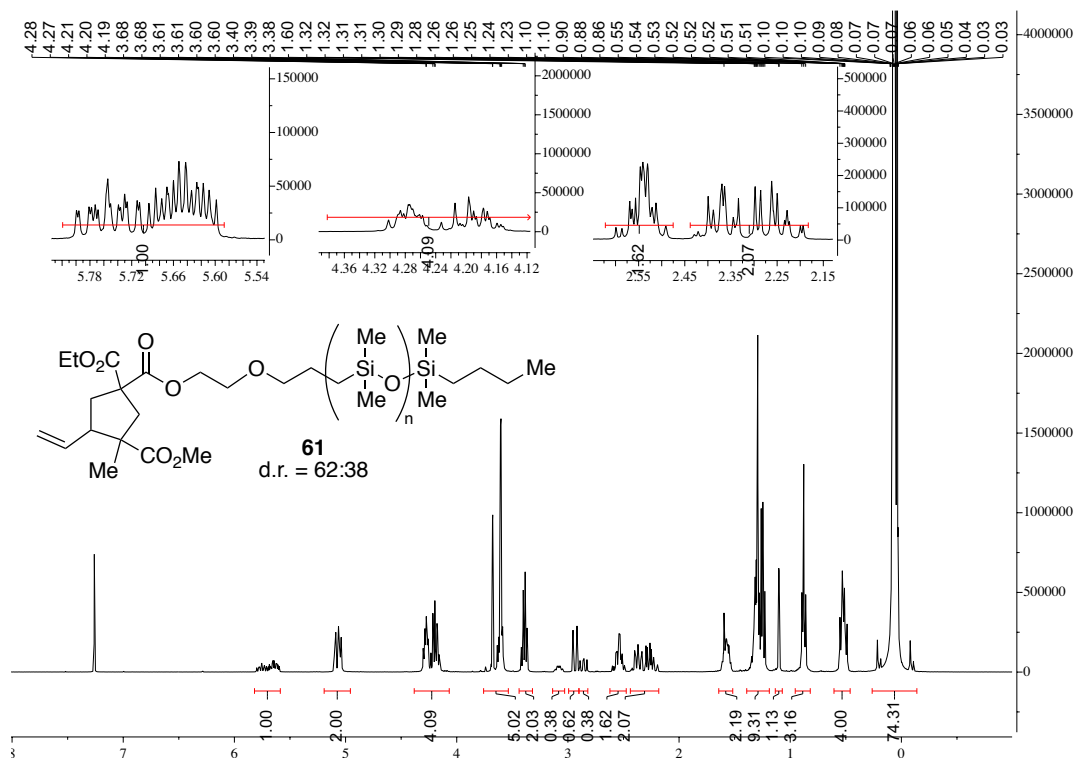


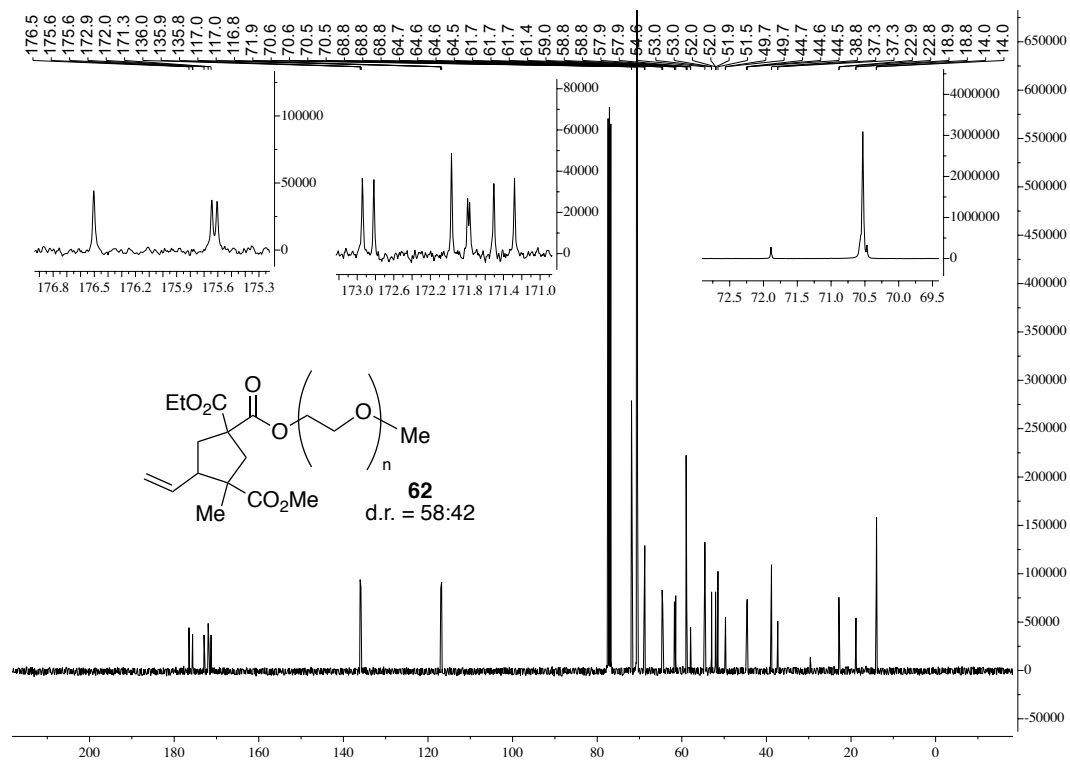
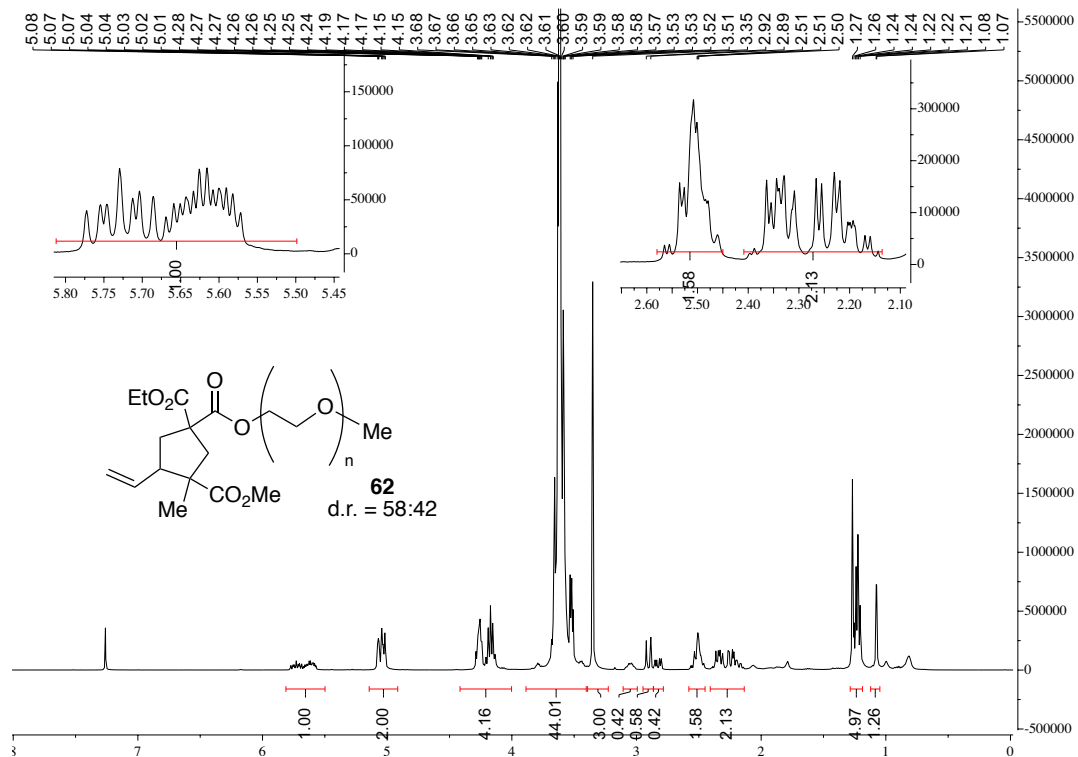


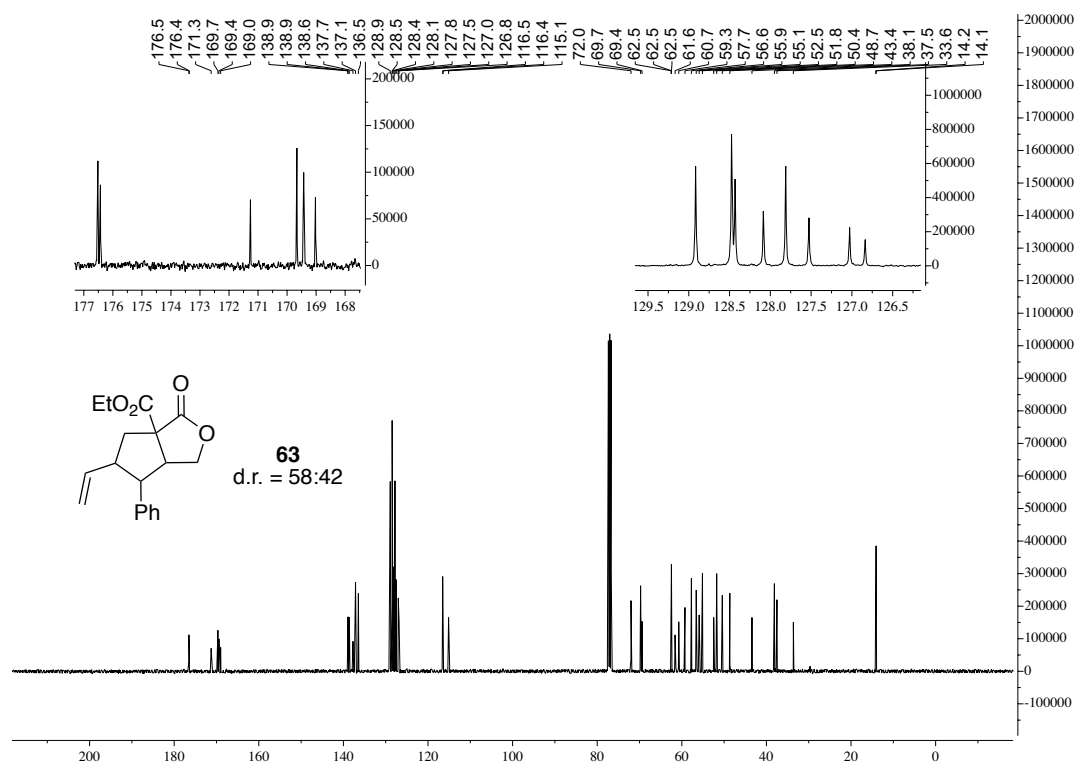
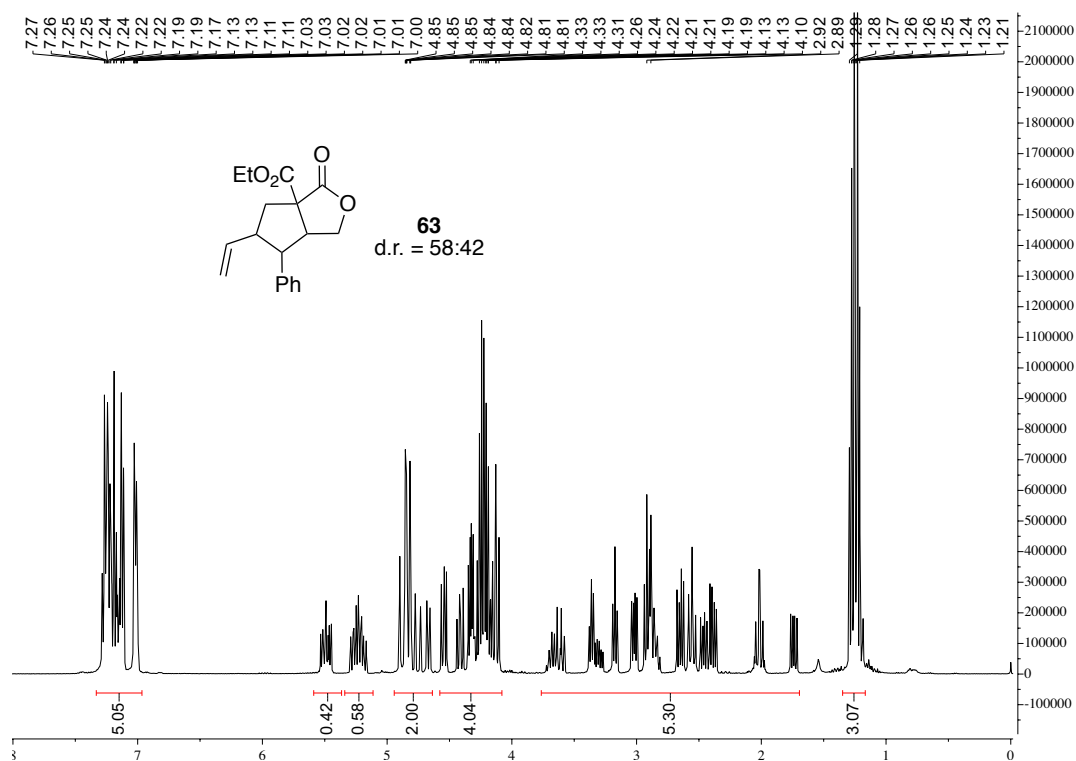


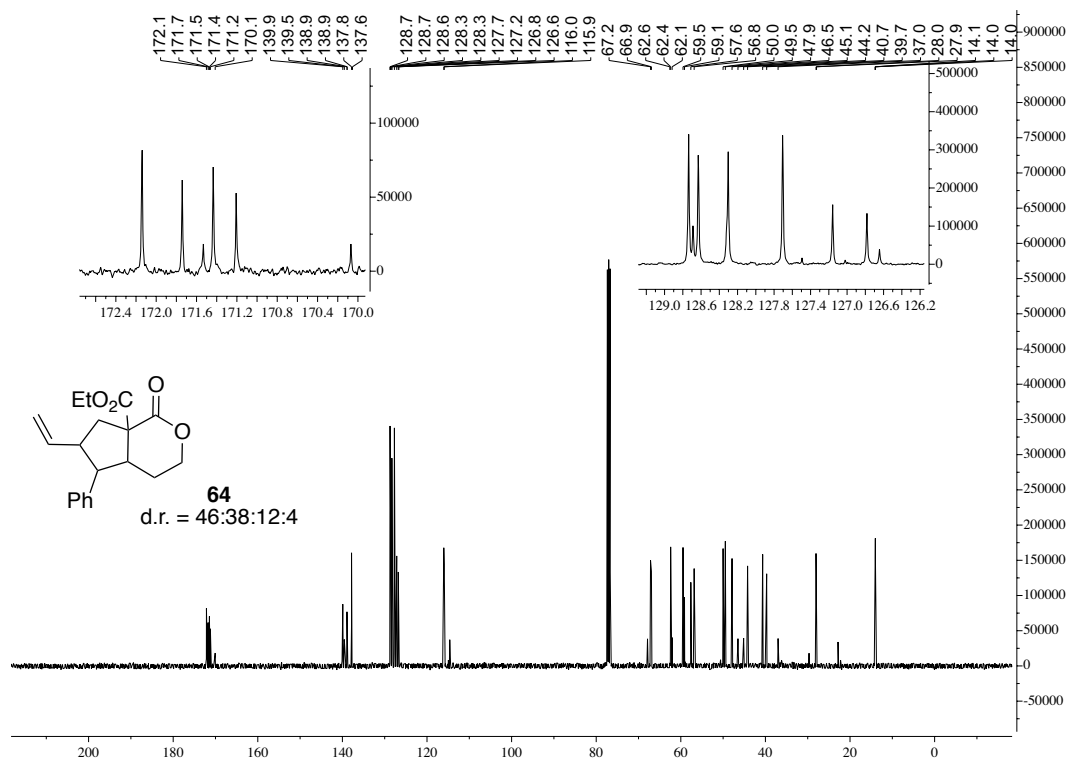
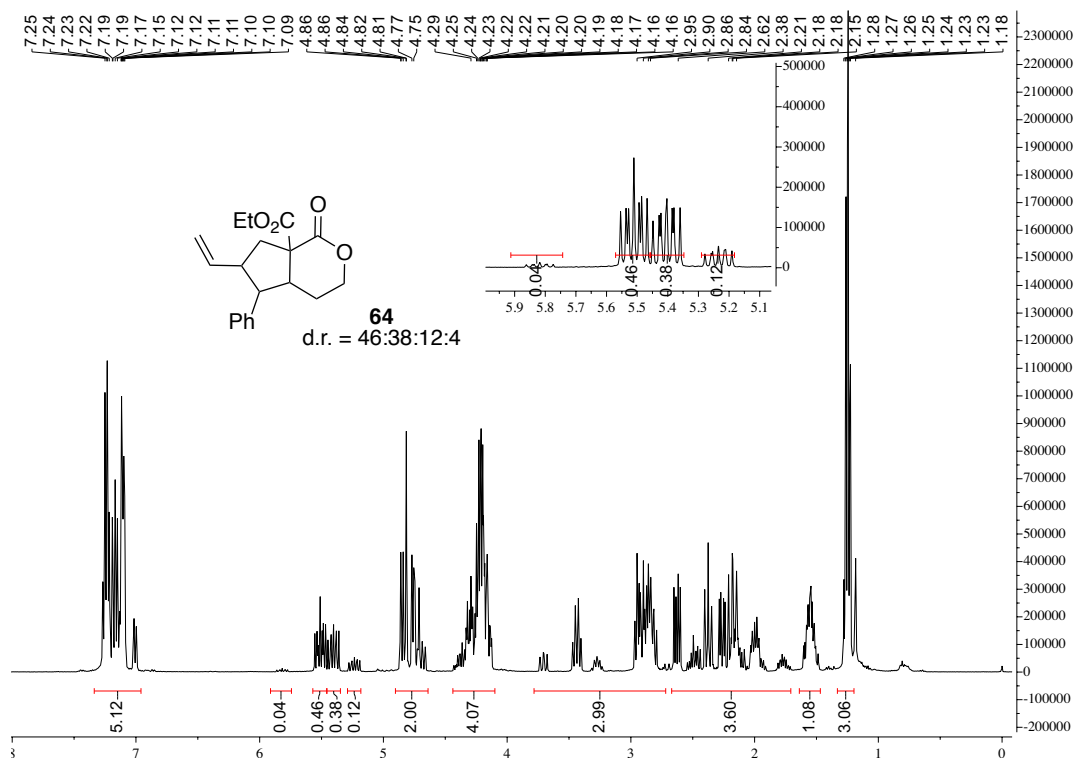


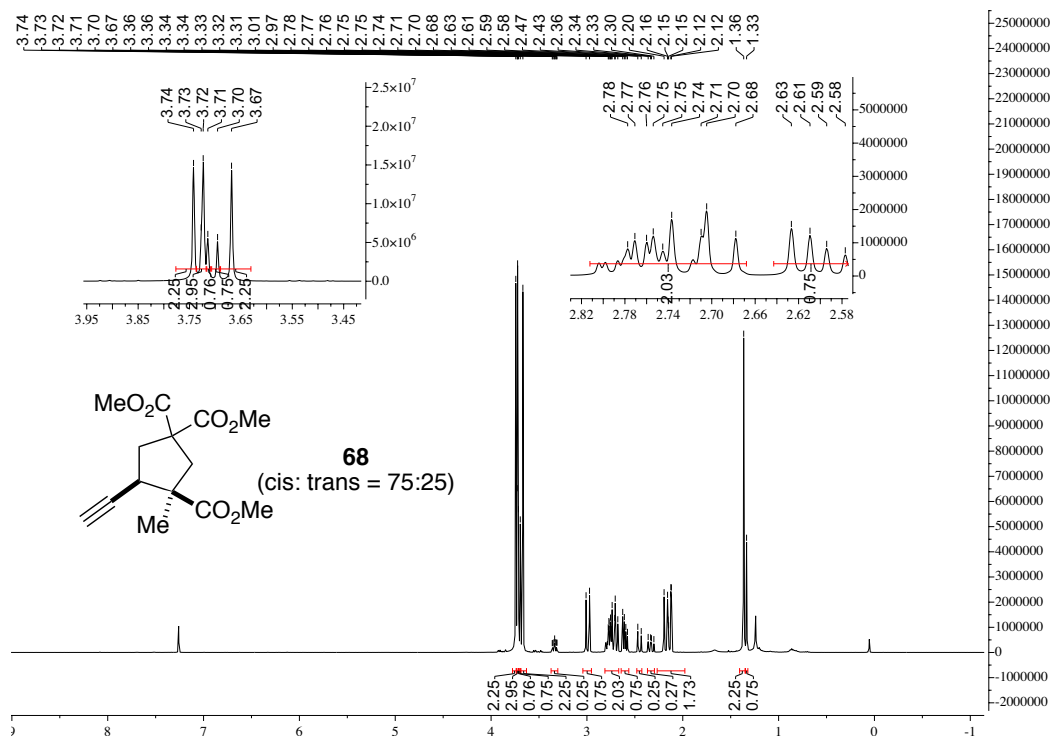


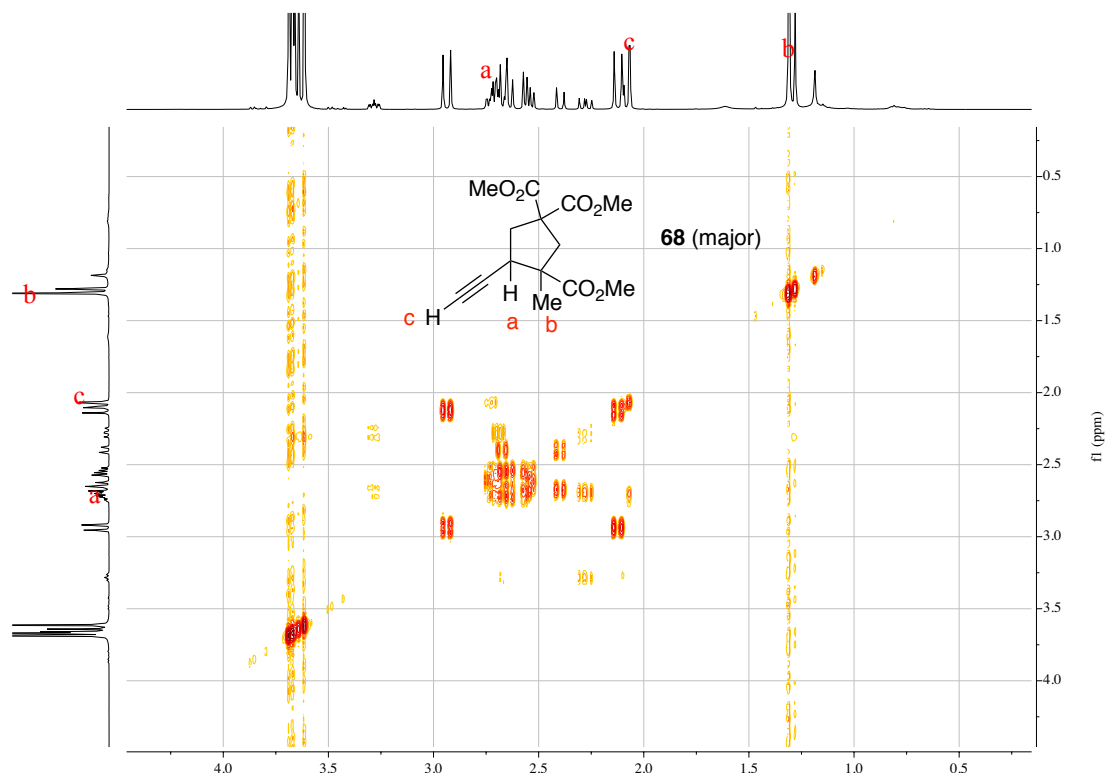


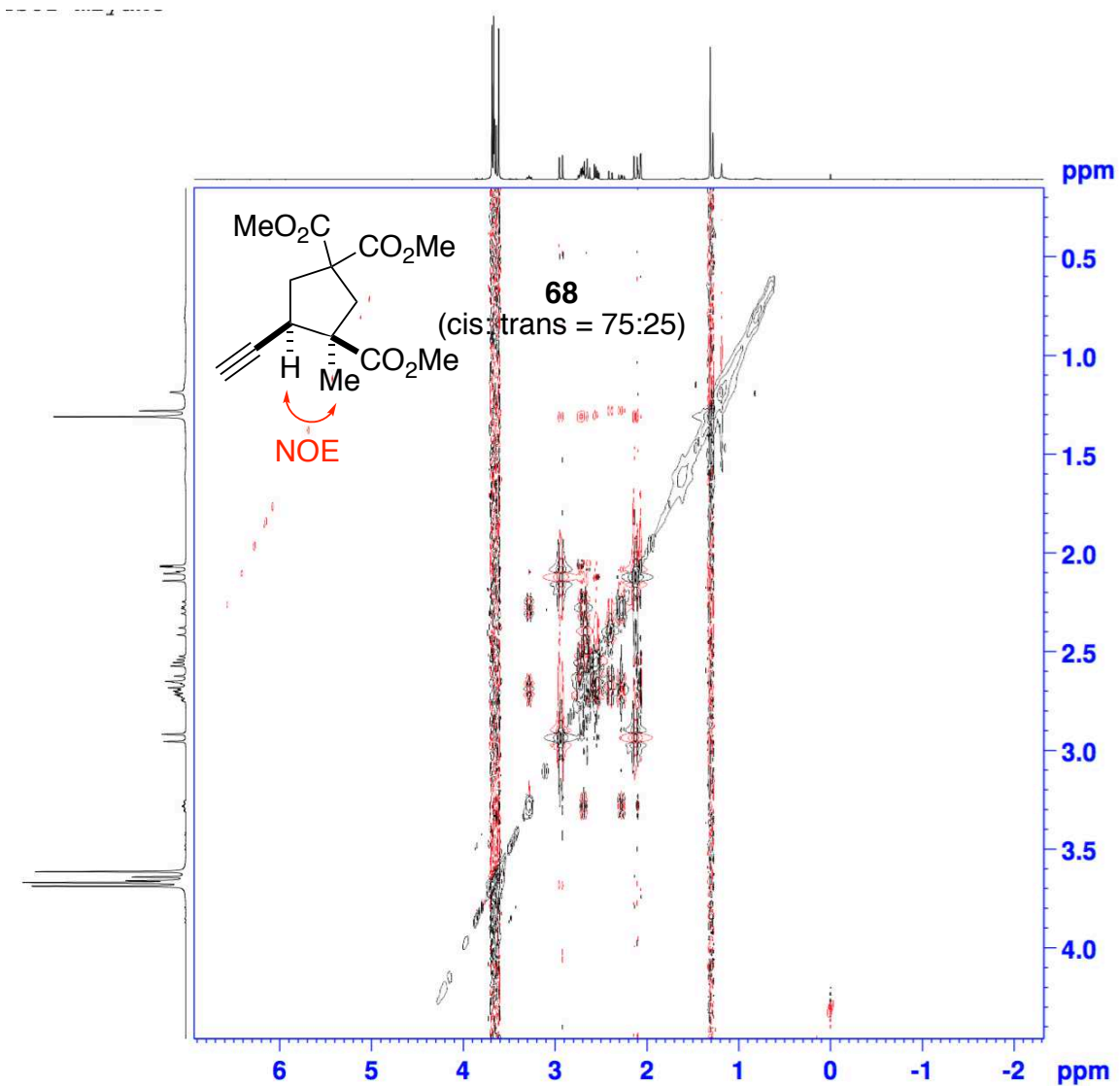


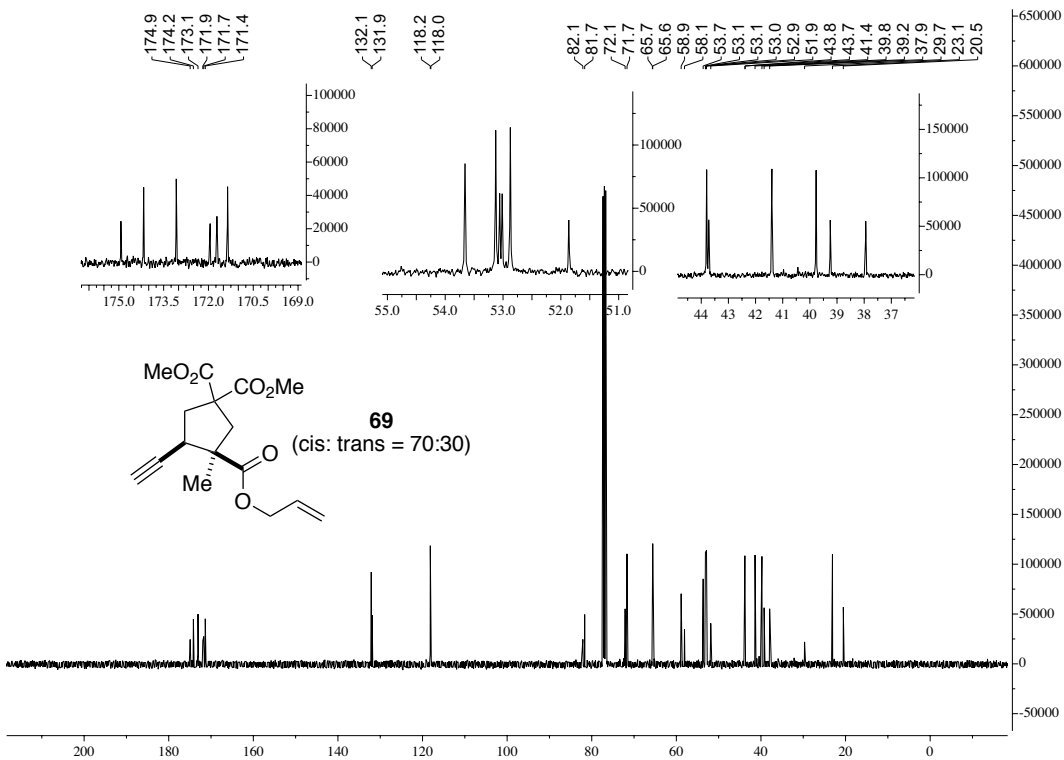
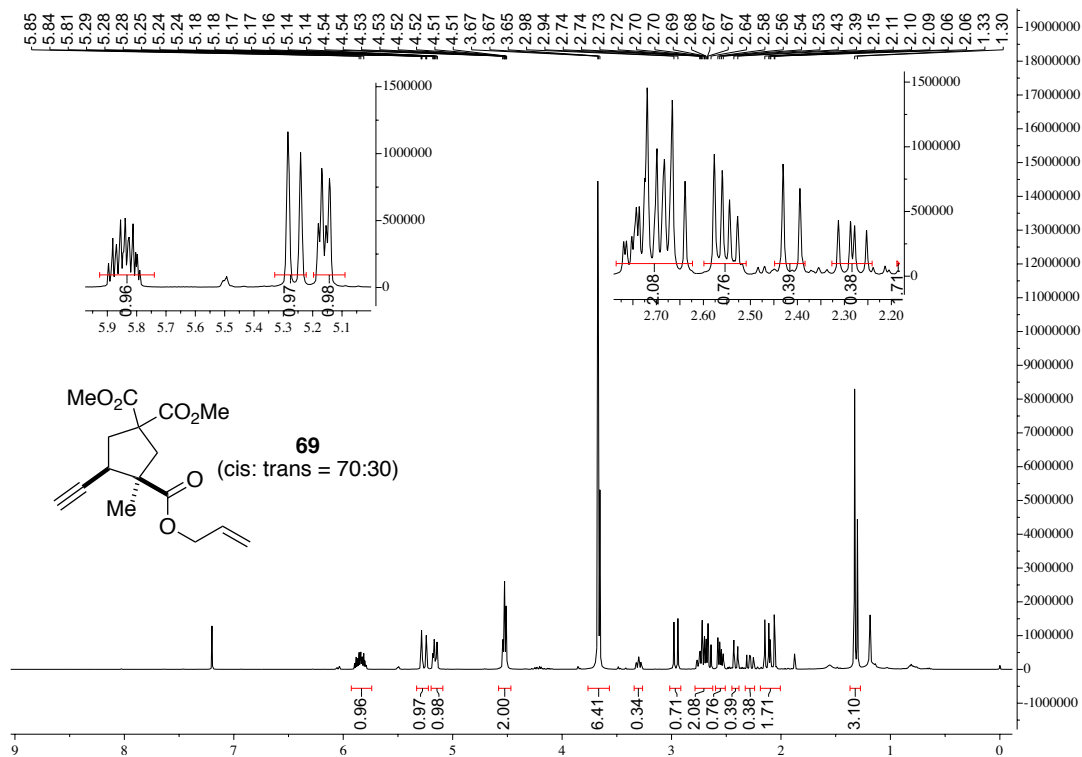












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APPENDIX C: SUPPLEMENTARY INFORMATION FOR CHAPTER 4

1. General Information

Unless noted below, all reagents and solvents were used as purchased without further purification. All liquid aryl halides were sparged with nitrogen and used in a nitrogen filled glovebox. PC2-PC5 were synthesized according to literature procedures.¹⁻³ 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) was dried over calcium hydride, vacuum distilled and used in a nitrogen filled glovebox. Benzyl alcohol was vacuum distilled and stored over 3 Å molecular sieves in a nitrogen filled glovebox. Tetrabutylammonium chloride (TBACl) was dried under highvac for 2 days and stored in a nitrogen filled glovebox. NiBr₂·glyme and NiCl₂·glyme were stored in a nitrogen filled glovebox.

NMR spectra were recorded on a Varian 400 MHz NMR Spectrometer and all ¹H and ¹³C shifts were measured relative to the residual solvent peaks for either chloroform or DMSO. Mass spectrometry was performed by the staff in the Analytical Resources Core at Colorado State University.

2. UV-Visible Spectroscopy

UV-visible spectroscopy was performed on a Cary 5000 instrument (Agilent) with the standard liquid cell holder and a 1 cm path length quartz cuvette. In all cases, the ultraviolet, visible, and near infrared lamps were allowed to warm up for 30 minutes before recording data. Background correction was performed for all runs utilizing a solvent blank (> 99.5 % purity DMF).

2.1 Speciation of NiBr₂·glyme in DMF.

We propose that dissolution of NiBr₂·glyme in DMF forms [NiBr₂(DMF)₄] as the dominant species based on several lines of evidence. The low molar absorptivity observed for this mixture (See section 2.2) suggests that the tetrabromonickelate anion, [NiBr₄]²⁻, is not present in significant

amounts as this tetrahedral species is known to possess a molar absorptivity of 100-200 M⁻¹cm⁻¹, more than tenfold higher than that observed here. In our previous work on NiBr₂ speciation in N,N-dimethylacetamide (DMAc), we identified and characterized [Ni(DMAc)₆][NiBr₄], while Cotton and Goodgame have also reported spectra of [(C₅H₅)₄P]₂[NiBr₄].⁴⁻⁵ In both cases, molar absorptivity in the above range was observed in conjunction with a strong teal color, while here in contrast we observe a more green color with broad visible bands with maxima at ~410, ~710 and ~760 nm and a NIR band at ~1200 nm with molar absorptivity 0-10 M⁻¹cm⁻¹. These weak bands are similar in energy and absorptivity, but not identical, to those of octahedral Ni(II) complexes with monodentate ligands binding through O, [NiL₆]²⁺, where L = DMF or dimethylsulfoxide (DMSO).⁶ Therefore, an equilibrium mixture of octahedral complexes is expected, consisting of [Ni(DMF)₆]Br₂, [NiBr(DMF)₅]Br, and [NiBr₂(DMF)₄].

2.2 Speciation of Ni.

Procedure and raw data for OMebpy binding study:

OMebpy (32.4 mg, 1:1 stock; 324.4 mg, 1:4 stock) was added to a 10 mL (1:1 stock) or 25 mL (1:4 stock) volumetric flask and brought into a N₂ filled glovebox. Inside the glovebox, NiBr₂•glyme (46.3 mg, 1:1 stock; 115.7 mg, 4:1 stock; 115.7 mg, 0:1 stock) was added to 3 scintillation vials (20 mL) containing stir bars. DMF was added to each vial (5 mL for 1:1 stock and 10 mL for 4:1 and 0:1) and the vials were allowed to stir at room temperature for 1 hour at which point the Ni was fully dissolved in DMF. Ni solutions were transferred to the appropriate volumetric flask and the scintillation vials were rinsed with DMF (1-2 mL, 3 times) to transfer any remaining Ni to the volumetric flasks. The volumetric flasks were then filled to the marking with DMF. After filling, a stir bar was added to each volumetric flask and the completed stock solutions (1:1, 15 mM NiBr₂•glyme and 15 mM OMebpy; 4:1, 15 mM NiBr₂•glyme and 60 mM OMebpy;

0:1, 15 mM NiBr₂•glyme) were allowed to stir for 1 hour at room temperature. Each of the 18 mixtures were then prepared in a 1-dram vial by mixing the stock solutions according to **Table S4.1**. Each mixture was inverted to mix and was allowed to equilibrate for 72 hours in the glovebox prior to UV-vis measurement. Mixtures were then transferred to quartz cuvettes with a 1 cm path length equipped with a sidearm and Kontes type screw cap valve, sealed, and removed from the glovebox. Outside the glovebox, cuvettes were allowed to equilibrate in a temperature-controlled water bath set to 25.0 °C for 15 minutes immediately prior to placement in the spectrometer and UV-vis measurement.

Table S4.1. Composition of mixtures used for titration experiment.

#	1:1 stock	4:1 stock	0:1 stock	OMebpy (Eq.)	OMebpy (M)	Ni (M)
1	0	0	3	0	0	0.015
2	0.6	0	2.4	0.2	0.003	0.015
3	1.2	0	1.8	0.4	0.006	0.015
4	1.8	0	1.2	0.6	0.009	0.015
5	2.4	0	0.6	0.8	0.012	0.015
6	3	0	0	1	0.015	0.015
7	0	0.9	2.1	1.2	0.018	0.015
8	0	1.05	1.95	1.4	0.021	0.015
9	0	1.2	1.8	1.6	0.024	0.015
10	0	1.35	1.65	1.8	0.027	0.015
11	0	1.5	1.5	2	0.03	0.015
12	0	1.65	1.35	2.2	0.033	0.015
13	0	1.8	1.2	2.4	0.036	0.015
14	0	1.95	1.05	2.6	0.039	0.015
15	0	2.1	0.9	2.8	0.042	0.015
16	0	2.25	0.75	3	0.045	0.015
17	0	2.55	0.45	3.4	0.051	0.015
18	0	3	0	4	0.06	0.015

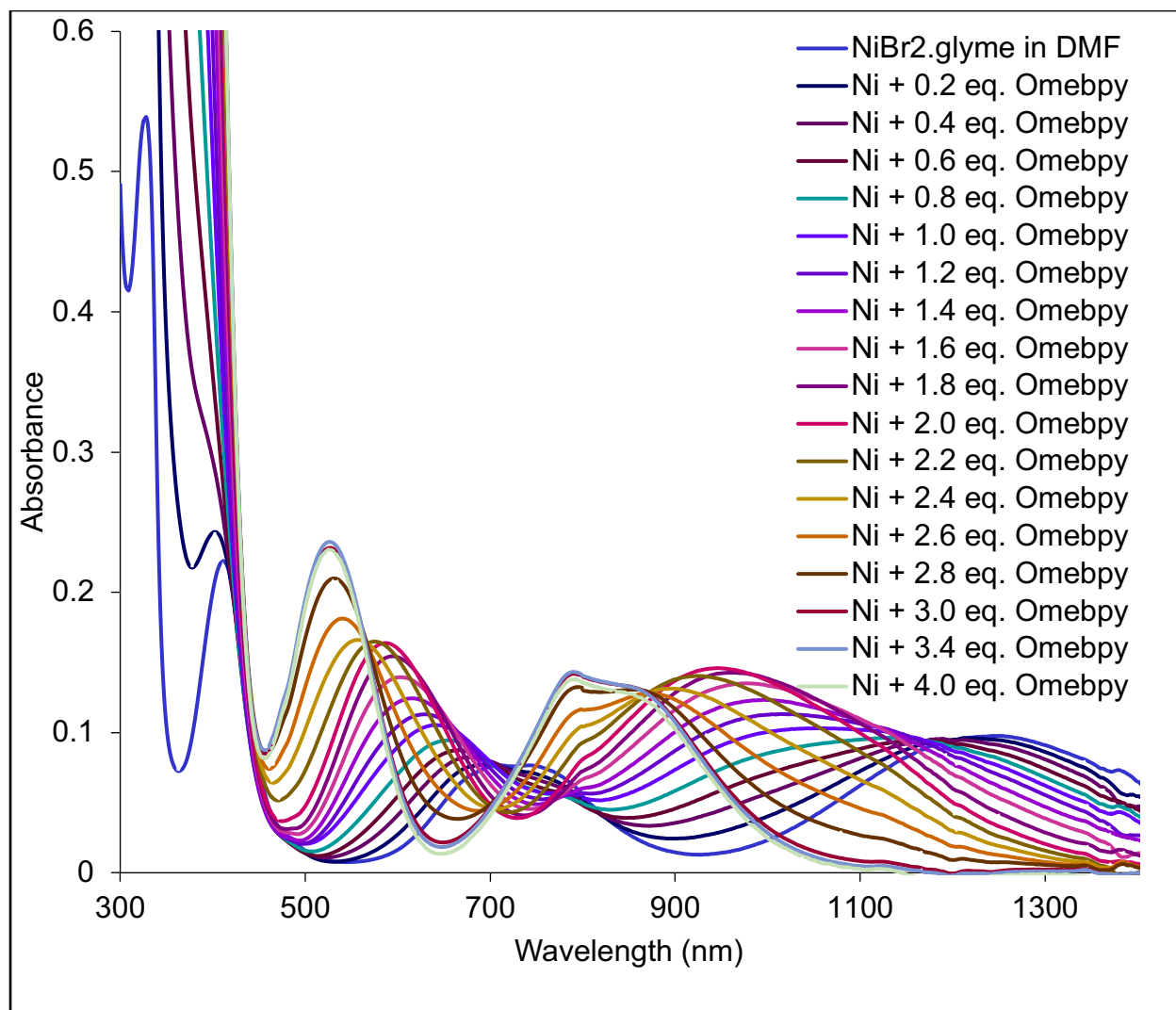


Figure S4.1. Raw UV-vis titration data of the mixtures described above (Table S1).

Development of the 1:3 Ni:OMebpy binding model:

Using an approach similar to our earlier work, we wrote a code in the Matlab program as described in our earlier work,⁵ with the only differences being that the spectra of free host was not subtracted from the dataset but rather, the spectra of host was one of the parameters fitted. After fitting the data to these models, a matlab data file (.mat) with all the inputs was generated.

Comparing the models:

To analyze and compare the model we used the same approach as in our previous work:⁵

We used two indicators for the quality of the fit; the covariance of the fit (cov_{fit}),⁷⁻⁸ and the Bayesian Information Criteria (BIC)⁹ as another robust method for model comparison. The challenge is that the more complicated the model (= higher number of parameters), the better the fit is likely to be. However, generally speaking, we should only pick a more complicated model if the fit is significantly better, when compared to a simpler model. As discussed previously, the cov_{fit} is relatively insensitive to the number of parameters used and if there is a more than 2-3 fold reduction in cov_{fit} then the more complicated model (flavor) is a reasonable one. The BIC is a different type of measure of fit and is based on both the calculated log-likelihood, the number of parameters and the number of data, whereby an increase in the number of parameters leads to a penalty (increase) in the BIC value. A low BIC is generally better and when comparing two models, a difference of more than 6-10 is usually considered as strong evidence that there is a significant difference between the two models being compared.

In this study, the “full” 1:3 model (flavor) always appeared to fit the experimental considerably better than any of the other models (flavors).

With this in mind, we can look at the comparison of the four models (flavors):

Table S4.2. Four models (flavors) used to fit UV-vis data above compared with two fit quality statistics, cov_{fit} and BIC.

Model (flavor) for the 1:3 complexation	cov_{fit}	Ratio compared to full model^a	BIC^b	□ BIC compared to full model^c
Full	0.028	n/a	-109776	n/a
Additive ^d	13.3	467	-40952	68824
Non-cooperative	0.14	5	-87977	21799
Statistical	16.5	583	11062	120839

^aThis is the cov_{fit} (for X model) / cov_{fit} (for full model). ^bThe lower, the better. BIC can be negative and if so, the more negative the better. ^cDefined here as $\text{BIC}(\text{X model}) - \text{BIC}(\text{full model})$. A $\Delta\text{BIC} > 6-10$ is usually considered as a strong evidence in favor of the model with a lower (more negative) BIC. Because this is a global fit with 751 dataset (corresponding to 450 to 1200 nm), it might be argued that a ΔBIC of $6-10 \times 751 = 4506-7510$ should be required as a strong evidence in favor of

a particular model. ^dThe fit here resulted in physically meaningless binding constants with values ranging from 1×10^{-19} to $1 \times 10^{17} \text{ M}^{-1}$.

The full 1:3 model fits better to the experimental data than any of the other models (flavors), however, the difference between that and the non-cooperative model is not very wide.

Overall results for the full 1:3 binding model:

After fitting the experimental data to the full 1:3 model, we then obtained the following binding constants.

$$K_1 = 9.9 \times 10^6 \text{ M}^{-1}$$

$$\Delta G_1 = -3.9 \text{ kcal mol}^{-1}$$

$$K_2 = 2.6 \times 10^6 \text{ M}^{-1}$$

$$\Delta G_2 = -3.8 \text{ kcal mol}^{-1}$$

$$K_3 = 4.8 \times 10^4 \text{ M}^{-1}$$

$$\Delta G_3 = -3.1 \text{ kcal mol}^{-1}$$

(note that the free energies, DG's, have all been corrected for statistical factors).⁵

We can also calculate the overall binding constant $\beta_{13} = K_1 K_2 K_3$ as:

$$\text{Overall binding constant } \beta_{13} = 1.3 \times 10^{18} \text{ M}^{-3}$$

$$\Delta G = -10.7 \text{ kcal mol}^{-1}$$

Calculating the spectra for the complexes formed:

The raw titration data was fit in the region from 450–1200 nm utilizing a MATLAB code as discussed above. At each wavelength point, the program therefore obtains an estimate of the differences between the free host spectra and that of the three complexes. A non-negative constraint was employed during the optimization process.

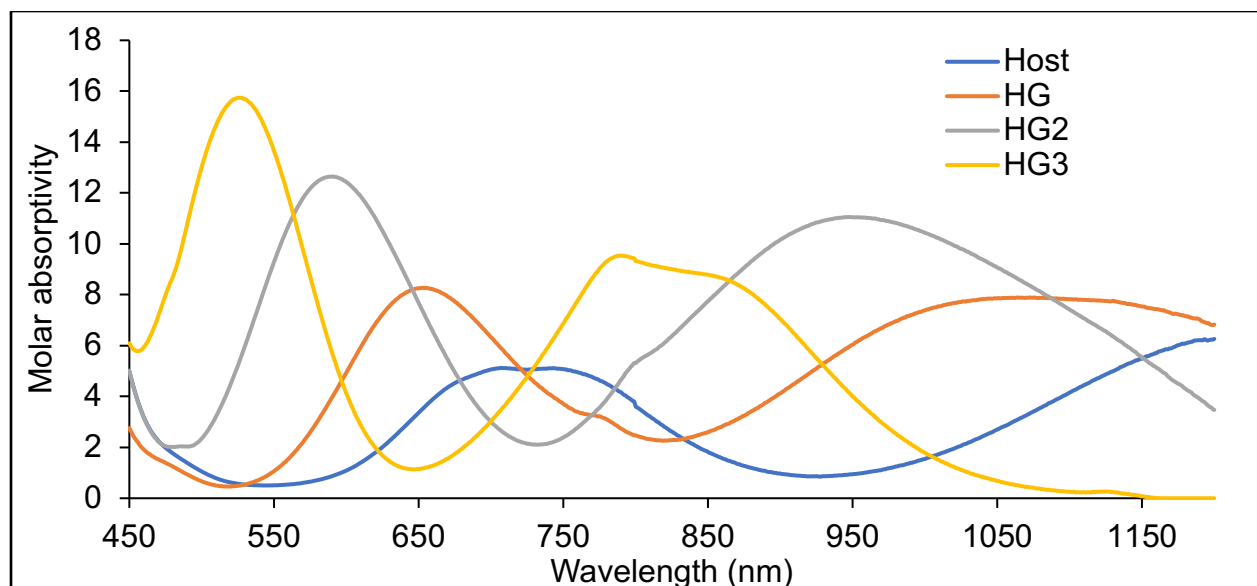


Figure S4.2. Calculated molar absorptivity for each species output from global analysis of titration data for the Ni:OMebpy mixture. Here, the host is the Ni species without any ligand present, HG is the 1:1 complex, HG2 is the 1:2 complex, and HG3 is the 1:3 complex.

The matlab program also yields an estimate of the changes in concentration of the free host and the three complexes (1:1, 1:2 and 1:3) as the titration experiments proceed:

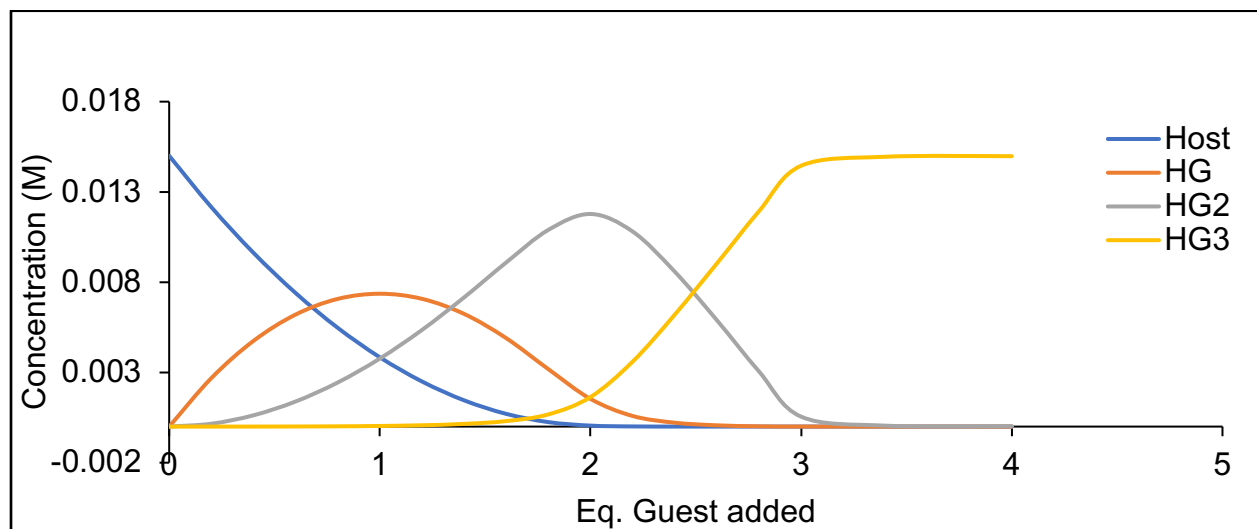


Figure S4.3. Calculated concentration of each species as a function of equivalents of added OMebpy output from global analysis of titration data for the Ni:OMebpy mixtures.

We can also analyze the residuals from the fits, i.e., the calculated overall spectra – the experimental spectra. For a model that gives a good fit to experimental data, the residuals should be relatively small and randomly distributed.

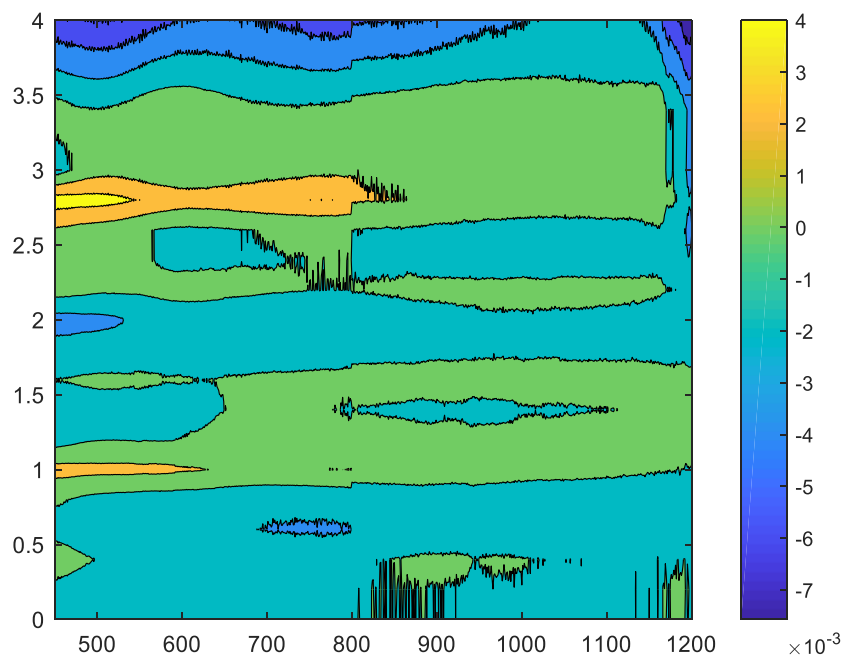


Figure S4.4. Fit residuals (absorbance units) plotted as a function of OMeby:Ni molar ratio (left axis) and wavelength (nm, x-axis). Notably, residuals are $< \pm 0.007$ absorbance across all ratios and wavelengths.

2.3 UV-vis of Mixtures Used in TA Experiments and Controls.

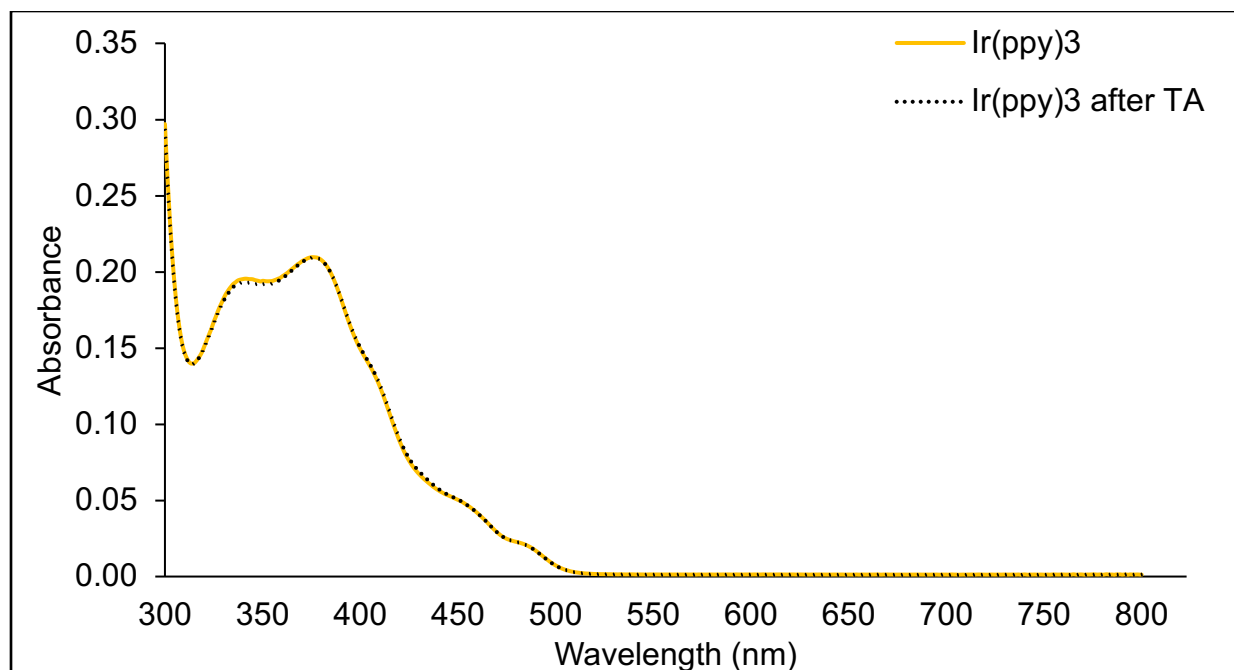


Figure S4.5. UV-vis traces of Ir(ppy)_3 ($15.7 \mu\text{M}$ in DMF) before and after TA experiments (see section 3) without any quencher.

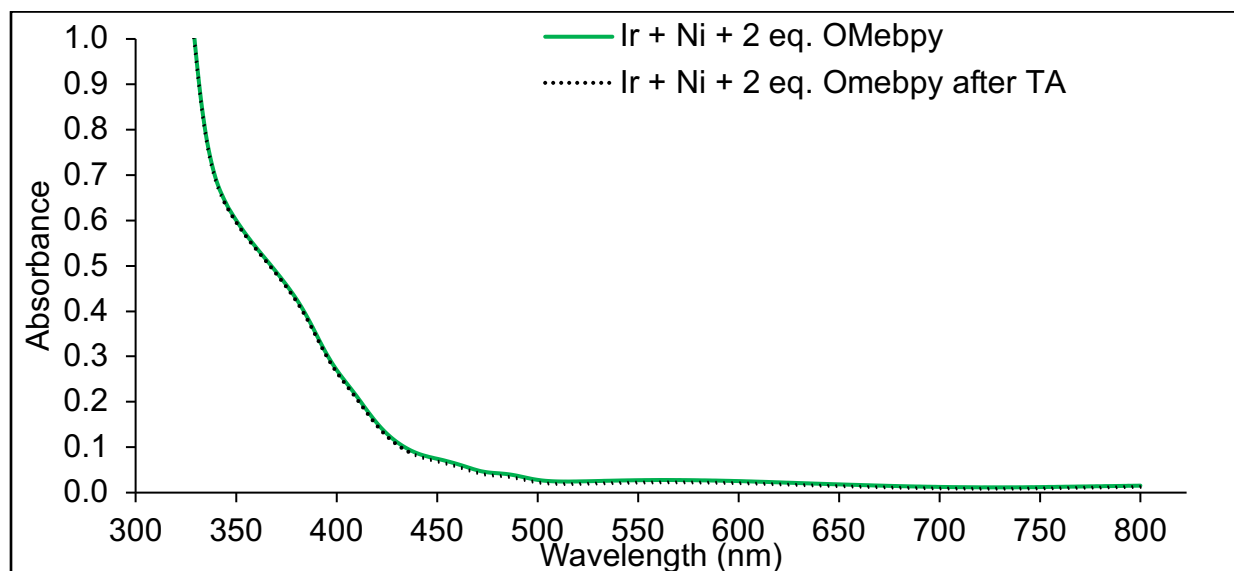


Figure S4.6. Representative UV-vis traces of a mixture containing Ir(ppy)_3 ($15.7 \mu\text{M}$), $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM), and OMeppy (3.0 mM , 2.0 eq. relative to Ni) in DMF before and after TA experiments.

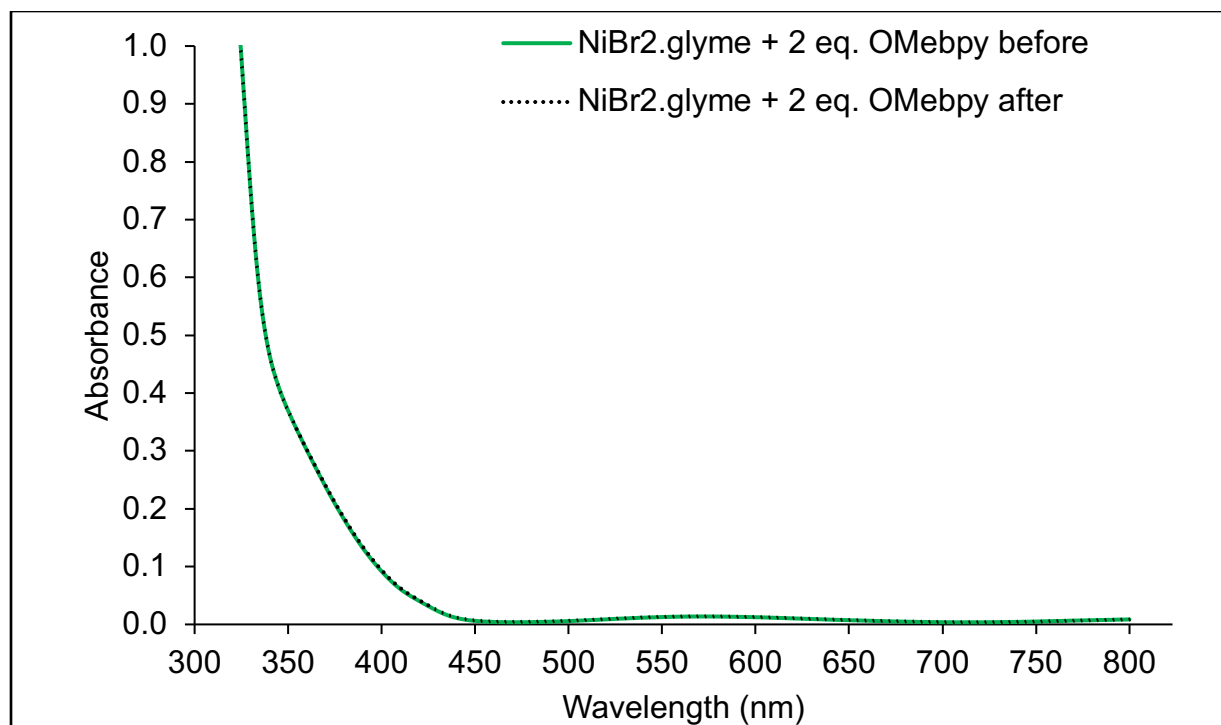


Figure S4.7. UV-vis traces of a mixture containing $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM), and OMeppy (3.0 mM, 2.0 eq. relative to Ni) in DMF before and after TA experiments.

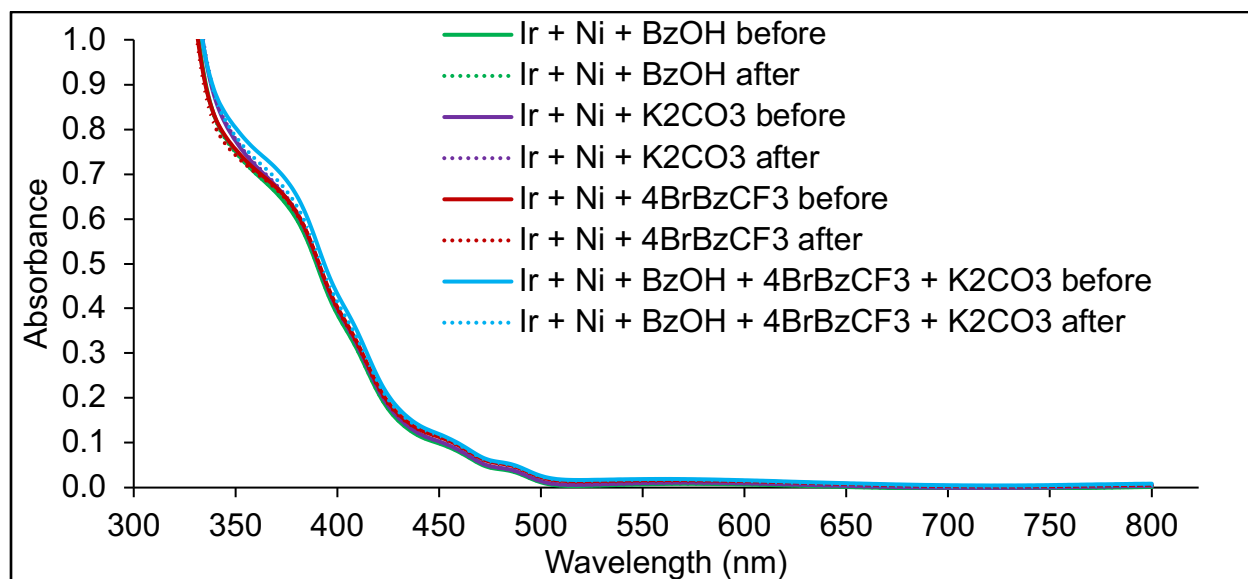


Figure S4.8. UV-vis traces of mixtures containing $\text{Ir}(\text{ppy})_3$ (31.4 μM in DMF) + $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM) + OMeppy (3.0 mM) + either 4-bromobenzotrifluoride (4-BrBzCF₃, 30 mM), benzyl alcohol (BzOH, 30 mM), or all reaction components (previously listed + K_2CO_3 , 60 mM) taken before and after TA experiments. We note that K_2CO_3 was not fully dissolved but allowed to settle prior to measurement.

The small increases in absorption as one approaches the UV region may be attributed to light scattering due to suspended K_2CO_3 . Small differences in the before/after spectra here could indicate small amounts of degradation in the samples (likely due to reaction progression) or changes in light scattering due to K_2CO_3 . Such differences are deemed too small to compromise TA experiment interpretation.

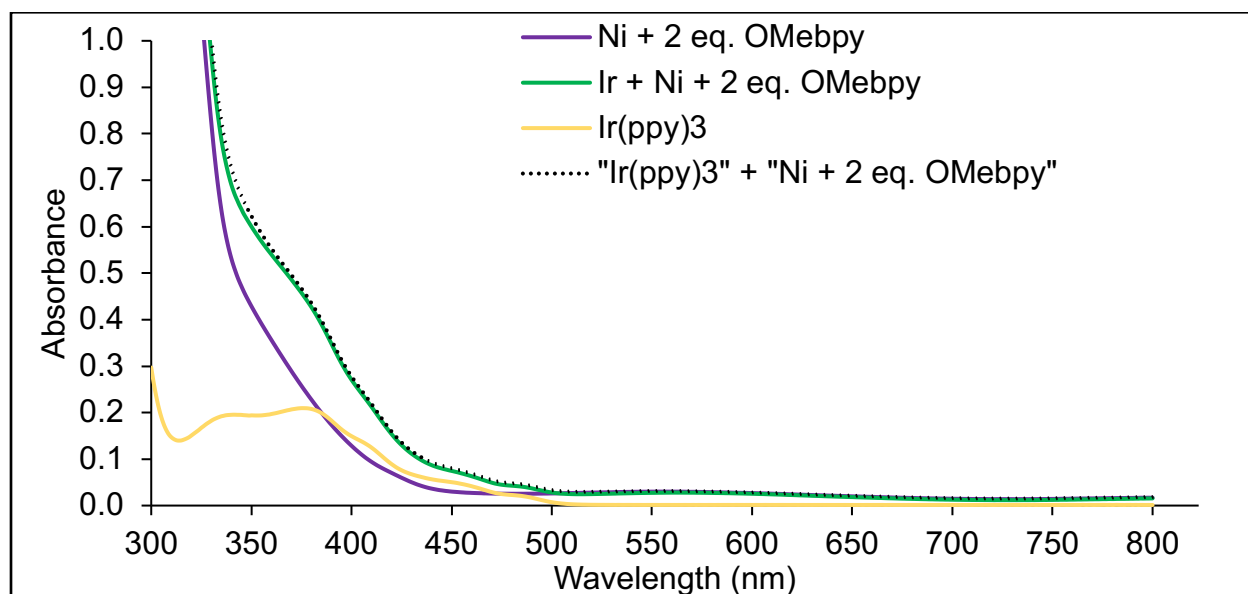


Figure S4.9. UV-vis traces of Ir(ppy)_3 ($15.7 \mu\text{M}$ in DMF) alone, a mixture of $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMebpy (3.0 mM , 2.0 eq. relative to Ni), and a mixture containing all 3 components at the same concentrations.

In the above plot, the spectra appear to be additive. The Ir(ppy)_3 trace added to the $\text{NiBr}_2 \cdot \text{glyme}$ + OMebpy trace (dotted line) overlays well with the experimental mixture containing all components, suggesting these components do not react in a manner that affects their UV-vis spectra in the absence of light (e.g. aggregation).

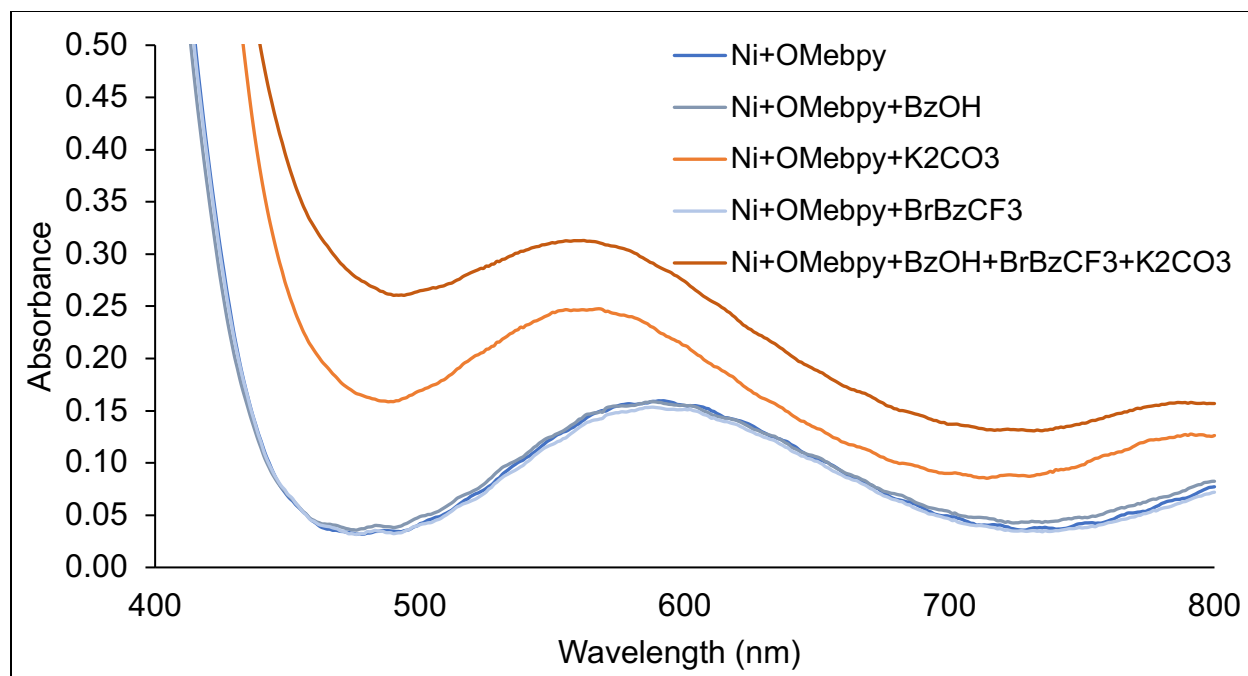


Figure S4.10. UV-vis traces of $\text{NiBr}_2 \cdot \text{glyme}$ (Ni , 1.5 mM) + OMebpy (3.0 mM, 2 eq. relative to Ni) and with relevant reagents (BzOH, 20 eq. relative to Ni, K_2CO_3 , 20 eq. relative to Ni, and BrBzCF₃, 40 eq. relative to Ni) in DMF. Absorbance was observed to increase for solutions containing K_2CO_3 ; solutions without K_2CO_3 were blue and solutions with K_2CO_3 were brown.

Some light scattering is expected to contribute to the spectra with K_2CO_3 , resulting in a rise in the baseline trending towards higher values near 400 nm, consistent with the fact that K_2CO_3 remains mostly undissolved in the mixture. The small blue-shift in features observed at ~590 nm and ~800 nm could also be due in part to a shift in the series of binding equilibria towards favoring $[\text{Ni}(\text{OMebpy})_3]\text{Br}_2$, as the presence of the carbonate anion could displace bromide from the outer coordination sphere of Ni, facilitating the binding of a 3rd OMebpy ligand. A larger shift in features would be expected if carbonate were bound in the inner coordination sphere of Ni. Ni(II) complexes with varying ligation exposed to a carbonate source tend to form multinuclear Ni complexes with bridging carbonate ligands and distinct d-d bands in absorption spectra that are not observed here.²⁹⁻³¹

2.4 UV-vis of Nickel Species Formed Under New Reaction Conditions.

To investigate the species formed under our newly developed reaction conditions (with

DBU and TBACl) we ran a series of UV-vis and diffuse reflectance experiments. UV-vis was run on the same instrument described above. Diffuse reflectance was also measured on this instrument fit with an Agilent Internal DRA 2500 attachment.

UV-vis spectra with DBU, TBACl and TBABr:

Four solutions relevant to the newly developed conditions were made in a nitrogen filled glovebox. $\text{NiBr}_2 \cdot \text{glyme}$ (20 mM) and OMe bpy (40 mM) were dissolved in anhydrous DMF and a sample was set aside for UV-vis. DBU (0.8 M) was added and a sample was set aside. TBACl (0.4 M) or tetrabutylammonium bromide (TBABr, 0.4 M) were added and samples were set aside for UV-vis. Then, the UV-vis for all four of these solutions were measured and are shown in Figure S4.11.

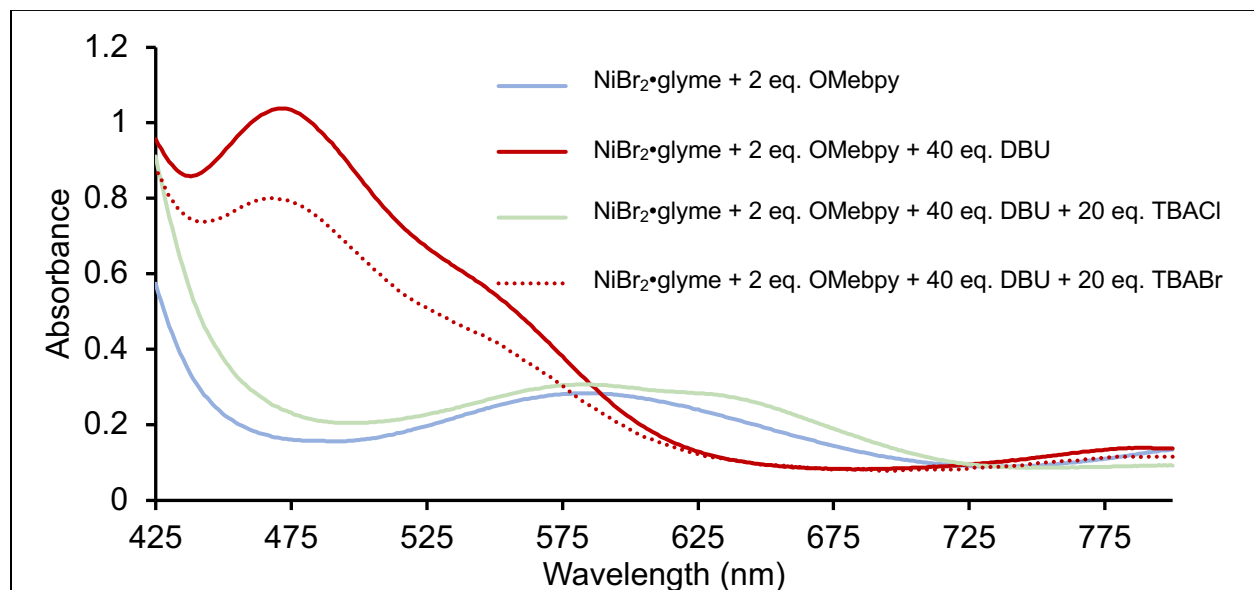


Figure S4.11. UV-vis traces of complexes relevant to the newly developed conditions. Blue trace = $\text{NiBr}_2 \cdot \text{glyme}$ (20 mM) + OMe bpy (40 mM, 2.0 eq. relative to Ni). Red trace = $\text{NiBr}_2 \cdot \text{glyme}$ (20 mM) + OMe bpy (40 mM, 2.0 eq. relative to Ni) + DBU (0.8 M, 40 eq. relative to Ni). Green trace = $\text{NiBr}_2 \cdot \text{glyme}$ (20 mM) + OMe bpy (40 mM, 2.0 eq. relative to Ni) + DBU (0.8 M, 40 eq. relative to Ni) + TBACl (0.4 M, 20 eq. relative to Ni). Dotted red trace = $\text{NiBr}_2 \cdot \text{glyme}$ (20 mM) + OMe bpy (40 mM, 2.0 eq. relative to Ni) + DBU (0.8 M, 40 eq. relative to Ni) + TBABr (0.4 M, 20 eq. relative to Ni).

Though chloride completely displaced the DBU bound to nickel upon addition of TBACl (Fig. S11, red trace to green trace), the addition of TBABr only diluted the sample (Fig. S11, solid

red trace to dotted red trace) and no DBU displacement was observed at first glance. However, a small amount of a species with a $\lambda_{\text{max}} \sim 625$ nm was observed in the normalized difference spectrum (Fig. S12), confirming bromide can also displace DBU bound to nickel to a lesser extent than chloride.

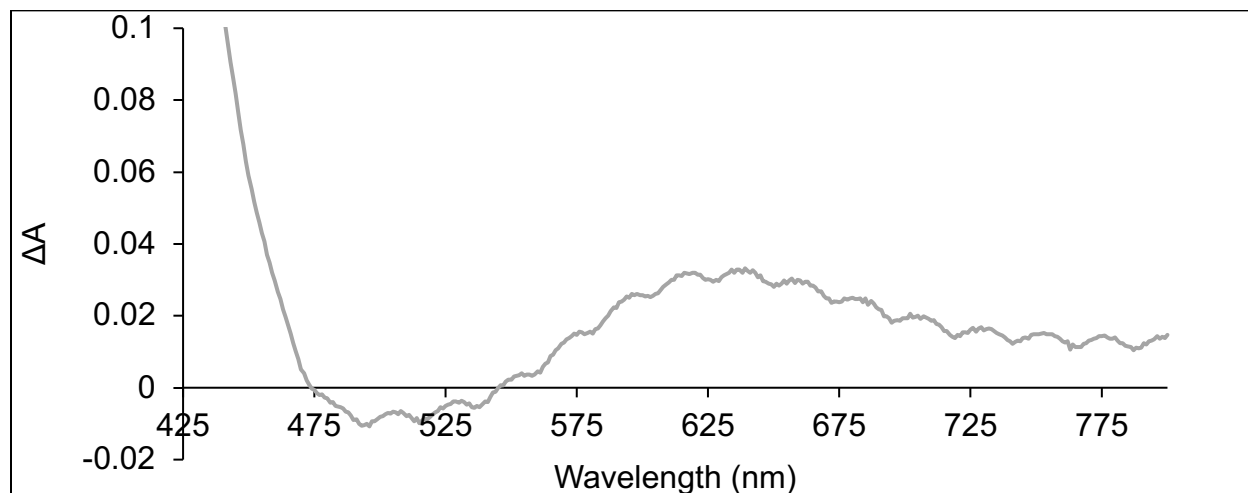


Figure S4.12. Difference spectrum of the solid red trace and dotted red trace from Fig. S4.11. Spectrum generated by normalizing the two UV-vis traces at the λ_{max} and subtracting.

2.5 DRA Spectra of Nickel Chloride Complexes.

To confirm that $\text{NiCl}_2(\text{OMebpy})_2$ forms upon addition of TBACl to $[\text{Ni}(\text{OMebpy})_2\text{DBU}]\text{Br}_2$, we sought to compare the UV-vis of this solution to that of $\text{NiCl}_2(\text{OMebpy})_2$ synthesized directly from $\text{NiCl}_2 \cdot \text{glyme}$ and 2 eq. OMebpy. However, when the complex is directly synthesized, a precipitate rapidly forms and prevents UV-vis measurements. Thus, we decided to compare the diffuse reflectance spectra of the complex made directly from $\text{NiCl}_2 \cdot \text{glyme}$ to that made from sequential addition of DBU and TBACl to $\text{NiBr}_2 \cdot \text{glyme}$. A precipitate also forms from sequential addition, just at a slower rate, which was why it could initially be characterized by UV-vis. Below is the procedure used to compare the DRA spectra of the two complexes.

Directly from $\text{NiCl}_2 \cdot \text{glyme}$:

In a 2-dram vial in a nitrogen filled glovebox, a 2.5 mL solution of $\text{NiCl}_2\cdot\text{glyme}$ (40 mM) and OMeppy (80 mM) in DMF was made. The solution was stirred for ~ 10 minutes and set aside for 18 hours to allow precipitate to form. Then, the vial was taken out of the glovebox and the solution was transferred to a 100 mL Eppendorf tube, diluted with 40 mL DMF and vortexed until all the solid was suspended. The solution was centrifuged, and the supernatant was discarded. The DMF wash was repeated followed by two toluene washes and one hexane wash. This yielded a light blue solid that was spread on a glass microscope slide so that a circle ~ 1 inch in diameter was fully covered with the sample. The residual hexane was allowed to evaporate, and a second glass slide was placed on top, secured by taping the edges of the two slides together. The sample was then run on the DRA described above and the data is summarized in Figure S4.13.

From $\text{NiBr}_2\cdot\text{glyme}$, DBU and TBACl:

In a 2-dram vial in a nitrogen filled glovebox, a 2.5 mL solution of $\text{NiBr}_2\cdot\text{glyme}$ (40 mM) and OMeppy (80 mM) in DMF was made. The solution was stirred for ~ 10 minutes and DBU (1.6 M) and TBACl (0.8 M) were added. After dissolution of TBACl, the solution was set aside for 18 hours to allow precipitate to form. The final washing and sample preparation steps were identical to the $\text{NiCl}_2\cdot\text{glyme}$ procedure described above.

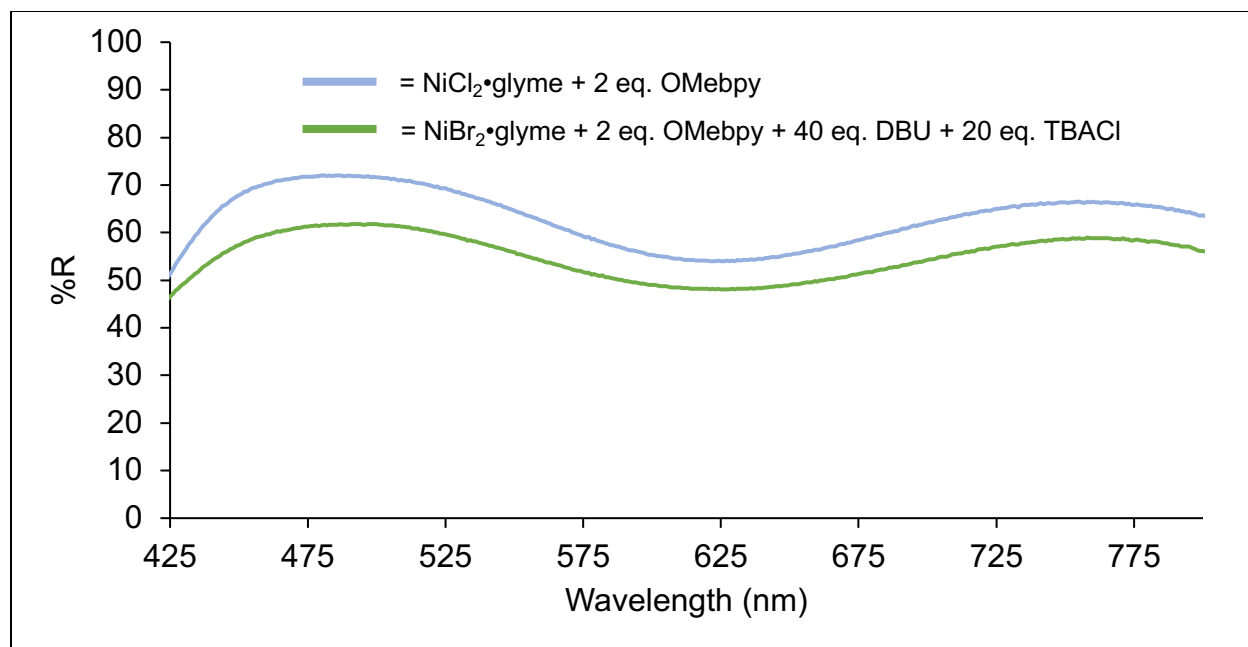


Figure S4.13. Diffuse reflectance spectra of NiCl_2 complexes made directly from $\text{NiCl}_2\cdot\text{glyme}$ and from sequential addition of DBU and TBACl to $\text{NiBr}_2\cdot\text{glyme}$. Nearly identical features support formation of $\text{NiCl}_2(\text{OMebpy})_2$ under reaction conditions.

3. Transient Absorption Spectroscopy

Nanosecond transient absorption spectra were acquired with an LP980KS spectrometer (Edinburgh Instruments) with a Minilite Nd:YAG Q-switched laser (Continuum Lasers) configured to deliver a 355 nm excitation pulse. Spectral data (absorption or emission) was acquired from 300-800 nm at the indicated time delay through use of an iStar ICCD camera (Andor) as the detector. Kinetic data was recorded on the same instrument utilizing a photomultiplier tube (included in the LP980) interfaced with an MD03022 mixed domain oscilloscope (Tektronix) as the detector. Time zero was set on the instrument using the emission of $[\text{Ru}(\text{bpy})_3]\text{Cl}_2$ to locate the pump pulse with 1 ns resolution.

General details:

Experiments were performed with spectroscopic grade DMF in airtight cuvettes equipped with a sidearm and Kontes screw cap valve. Solutions were prepared with 3 mL total volume in a N_2 filled glovebox and sealed prior to removal from the glovebox for measurement. Solutions were

not stirred, and the pump pulse was set to a repetition rate of 1 Hz with power of 2-5 mW and a pulse width of ~6 ns. Pre- t_0 data was collected in kinetic experiments and confirmed to show zero signal (i.e. lack of photoproduct buildup in bulk solution). UV-vis data was collected before/after experiments and solutions did not show significant spectral changes, indicative that the species probed did not permanently decompose (See UV-vis section).

3.1 Ir(ppy)₃ Characterization in DMF.

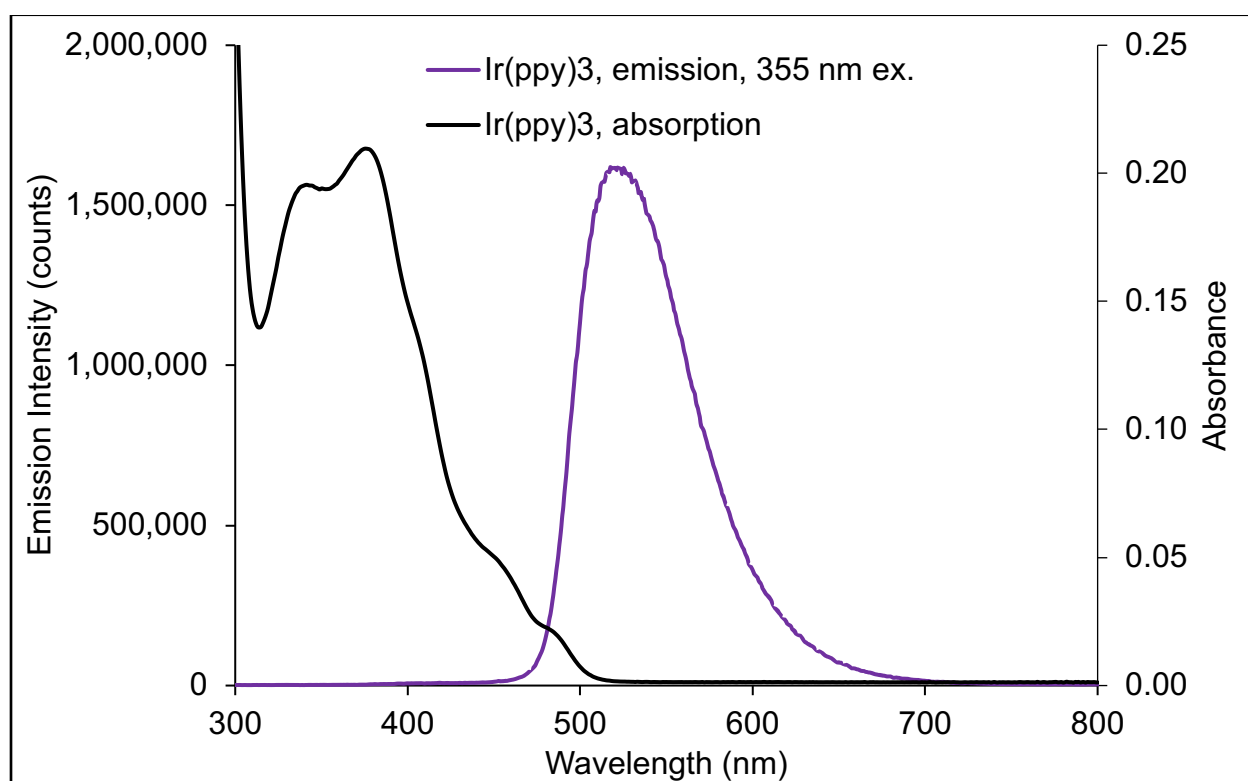


Figure S4.14. Absorption and time resolved emission ($t = 0$ ns) spectra of Ir(ppy)₃ (15.7 μ M in DMF).

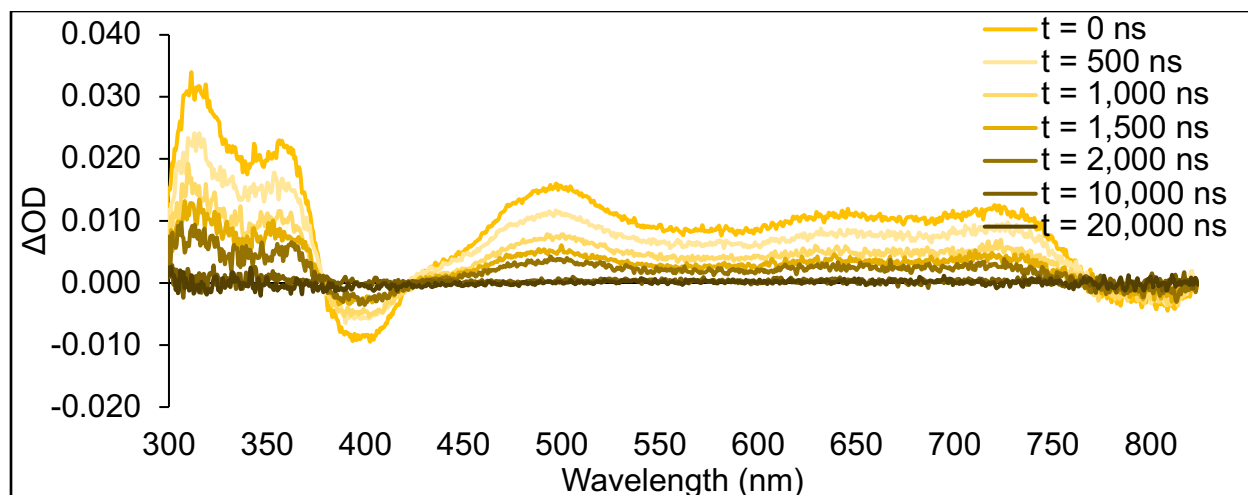


Figure S4.15. Spectral traces of Ir(ppy)_3 (31.4 μM in DMF) at indicated time delays. Data was offset corrected utilizing kinetic data acquired at $\lambda_{\text{probe}} = 600$ nm.

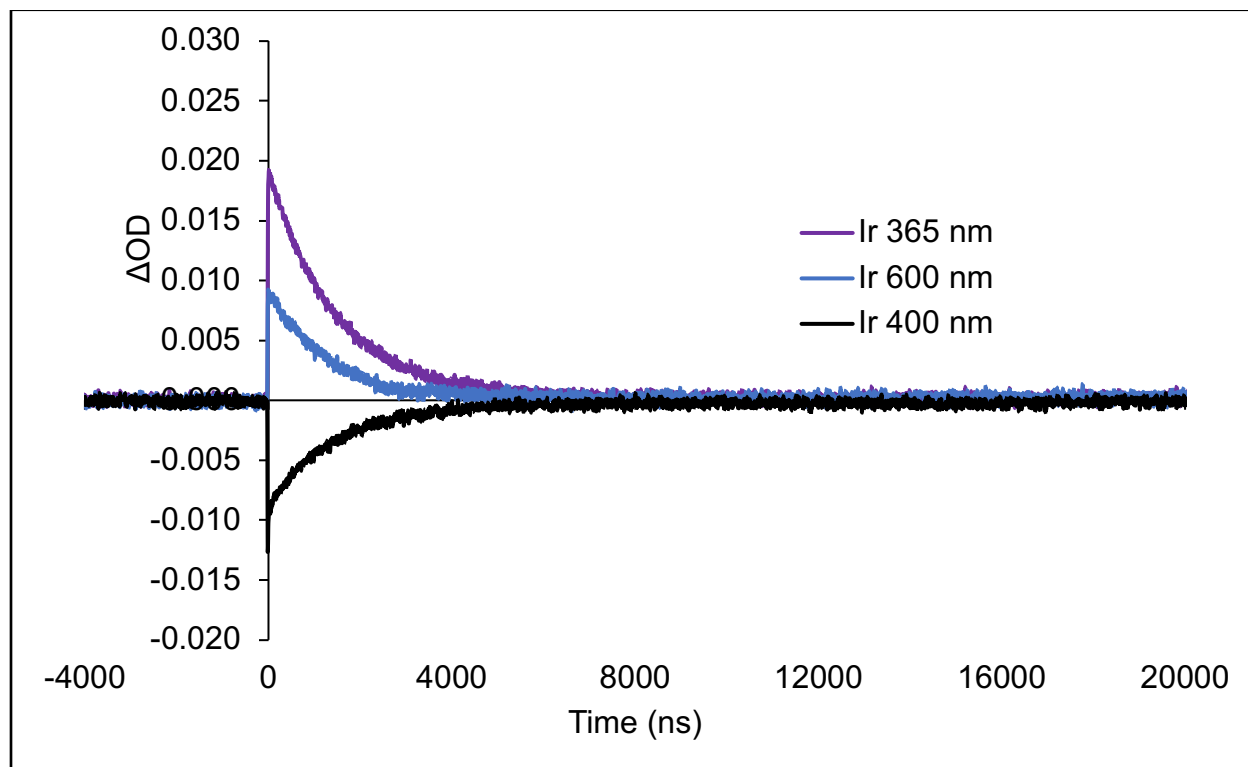


Figure S4.16. Kinetic traces of Ir(ppy)_3 (31.4 μM in DMF) at indicated probe wavelength in absence of quencher.

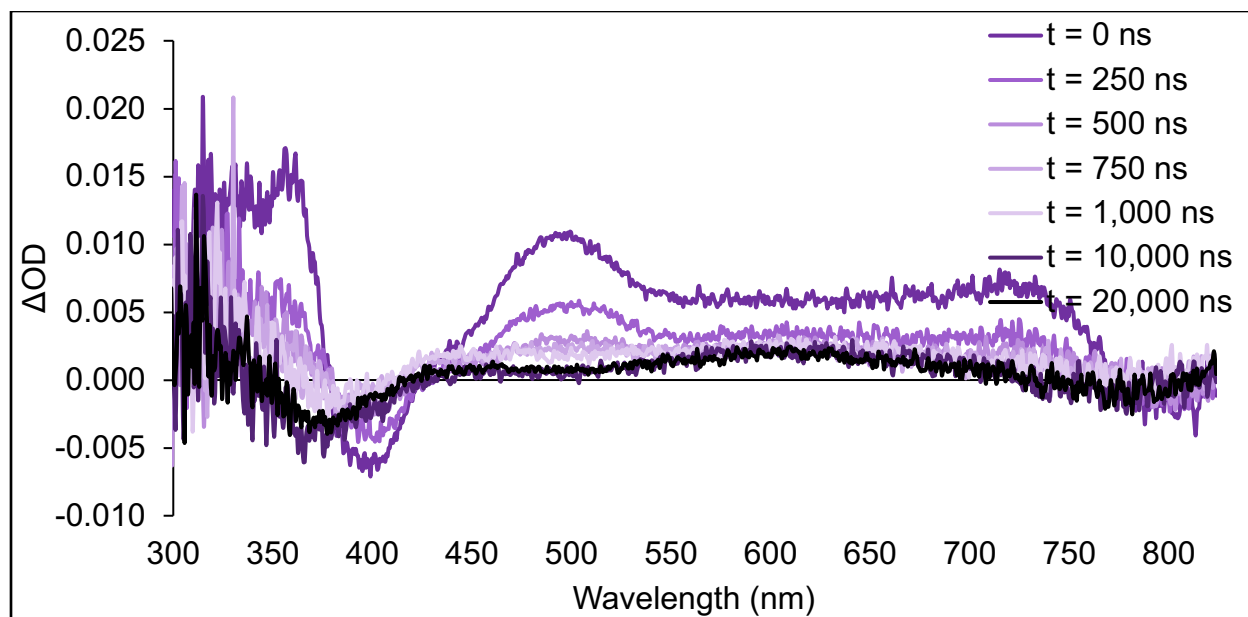


Figure S4.17. Spectral traces of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM) + OMeppy (3.0 mM) at indicated time delays. Data was offset corrected utilizing kinetic data acquired at $\lambda_{\text{probe}} = 600 \text{ nm}$.

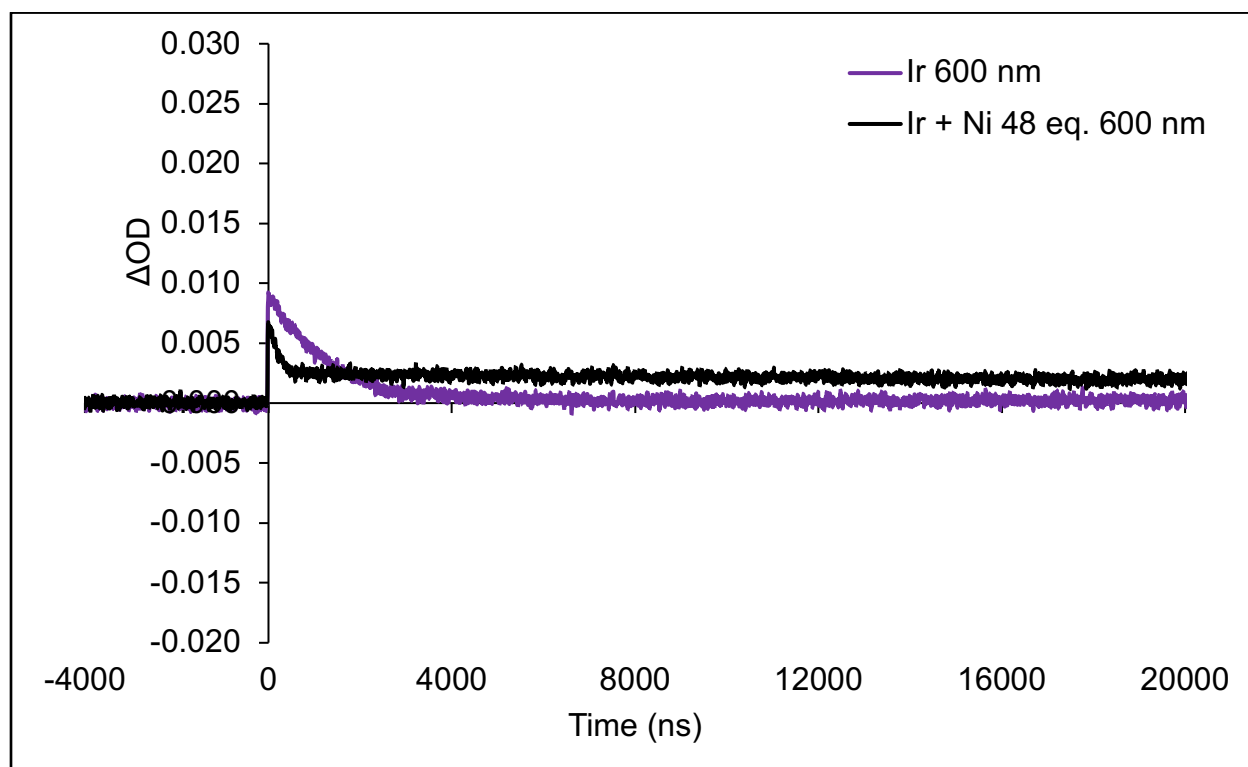


Figure S4.18. Kinetic traces of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) alone and with $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM) + OMeppy (3.0 mM) at $\lambda_{\text{probe}} = 600 \text{ nm}$.

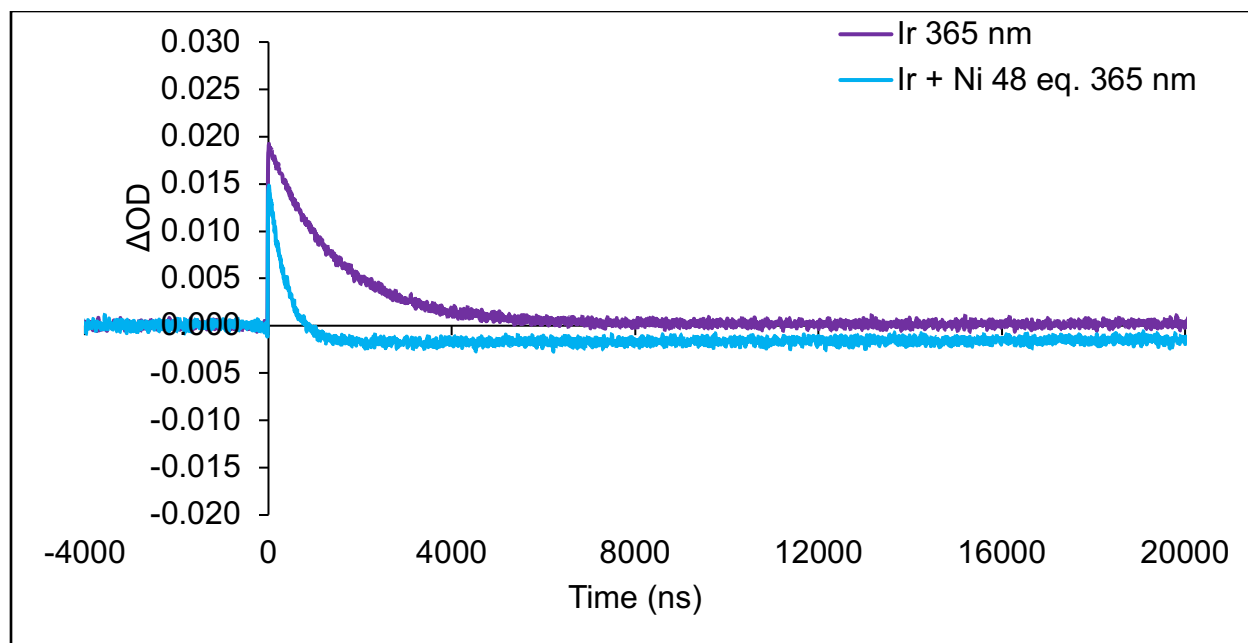


Figure S4.19. Kinetic traces of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) alone and with $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) at $\lambda_{\text{probe}} = 365 \text{ nm}$.

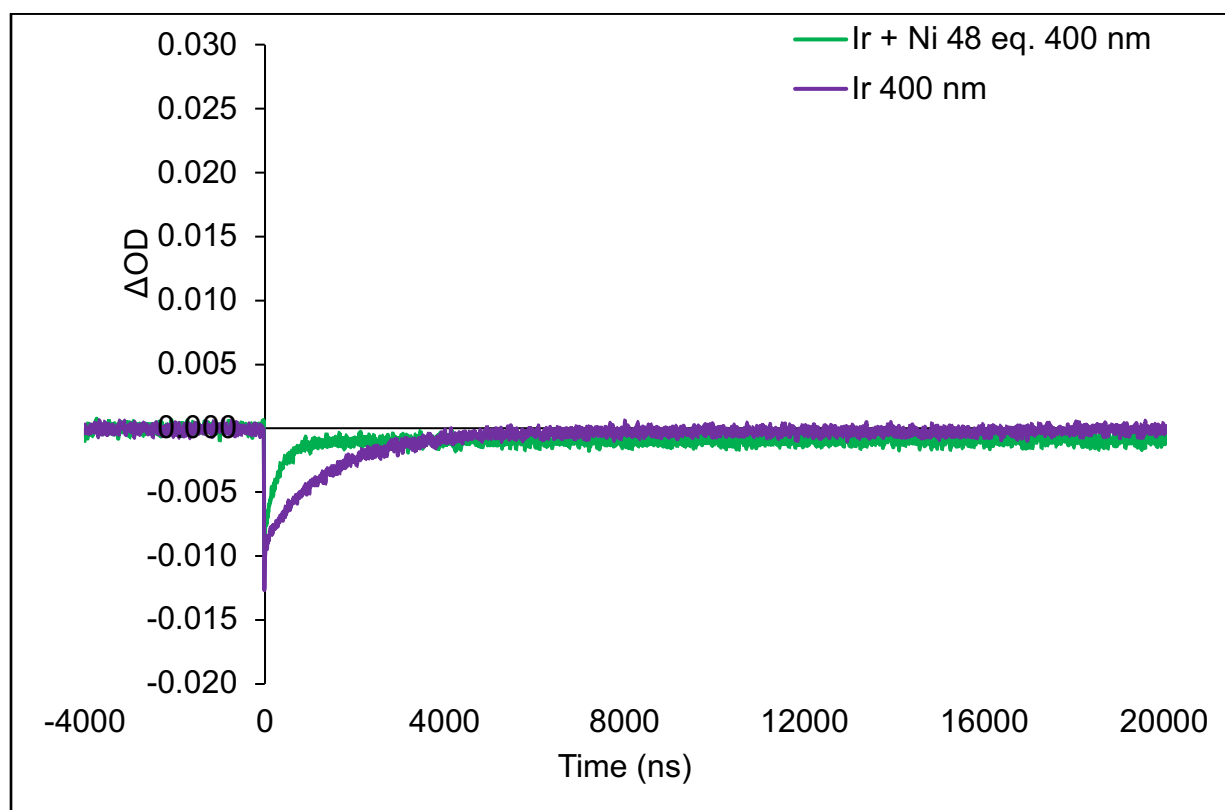


Figure S4.20. Kinetic traces of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) alone and with $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) at $\lambda_{\text{probe}} = 400 \text{ nm}$.

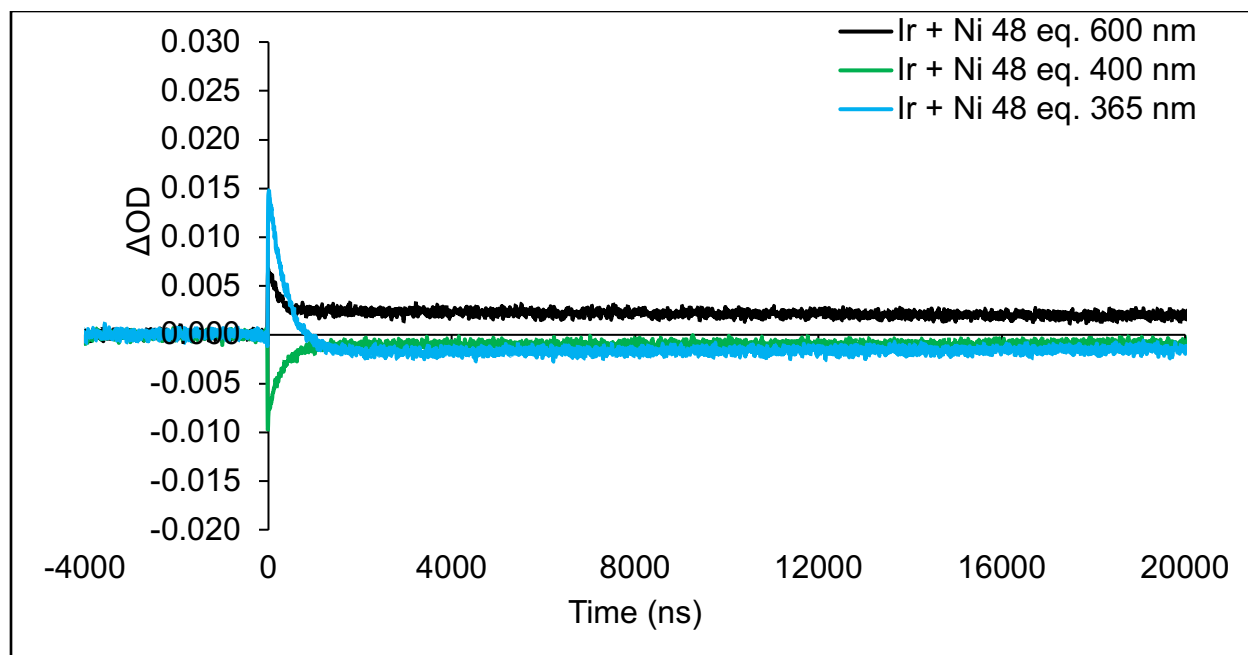


Figure S4.21. Kinetic traces of Ir(ppy)_3 (31.4 μM in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) at $\lambda_{\text{probe}} = 600, 400, \text{ and } 365 \text{ nm}$.

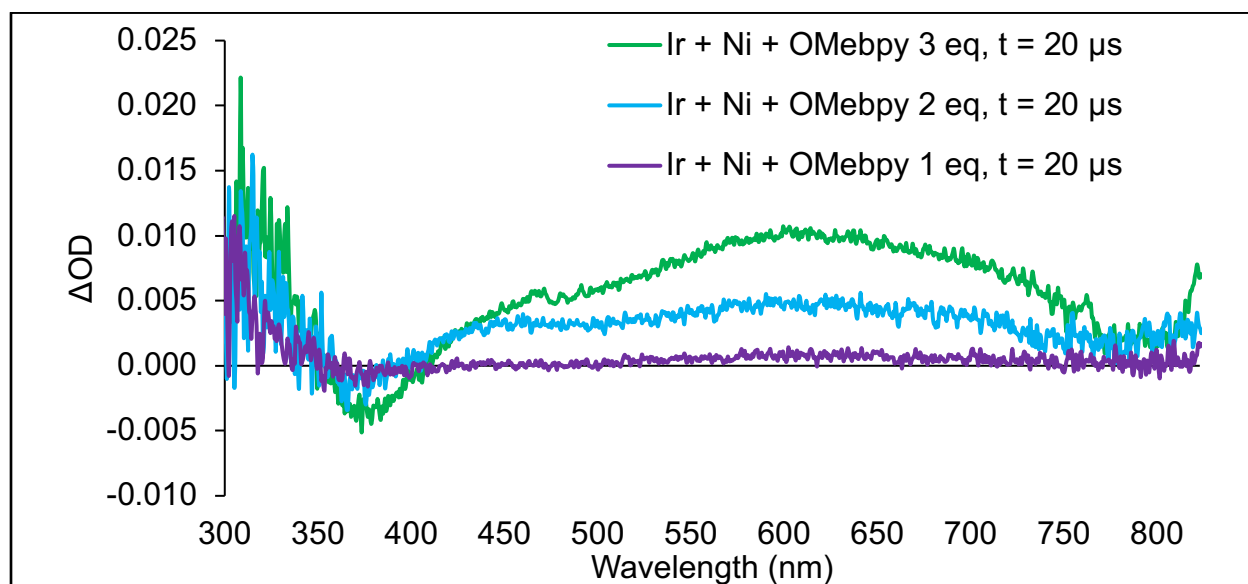


Figure S4.22. Spectral traces of Ir(ppy)_3 (31.4 μM in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMebpy (1.5, 3.0, or 4.5 mM) at indicated time delays. Data was offset corrected utilizing kinetic data acquired at $\lambda_{\text{probe}} = 355 \text{ nm}$.

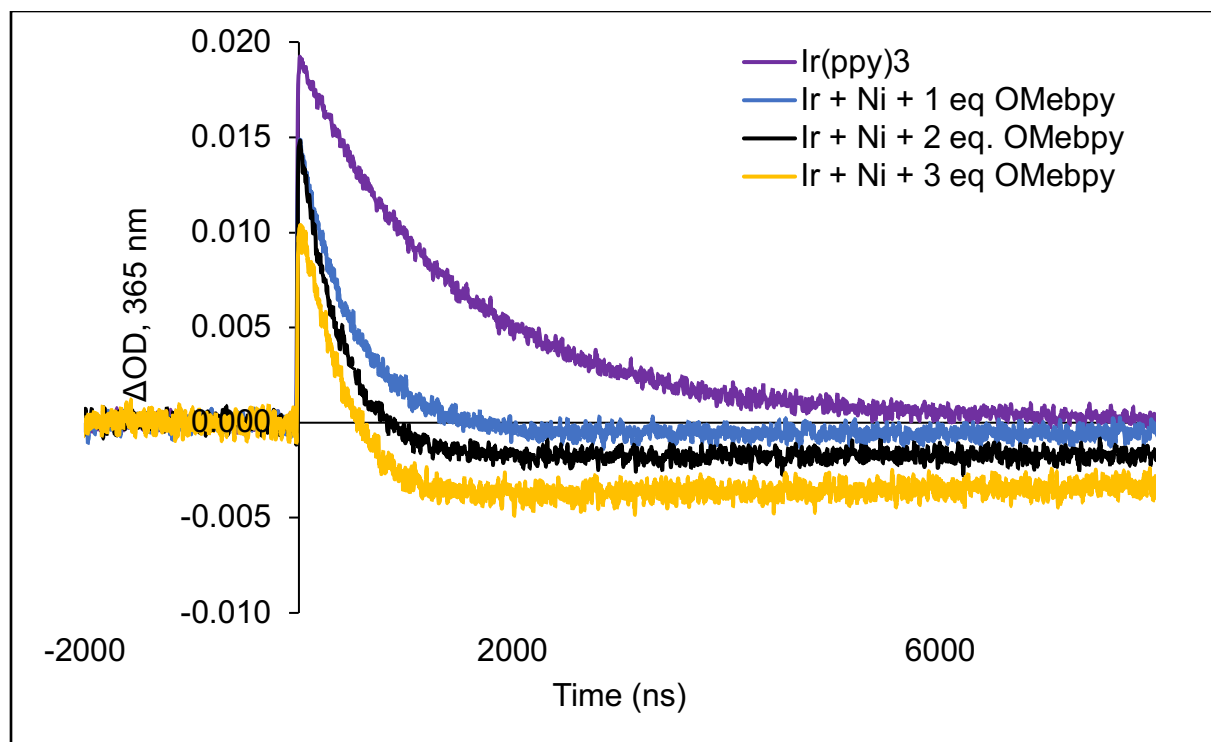


Figure S4.23. Kinetic traces of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMebpy ($1.5, 3.0$, or 4.5 mM) at $\lambda_{\text{probe}} = 365 \text{ nm}$.

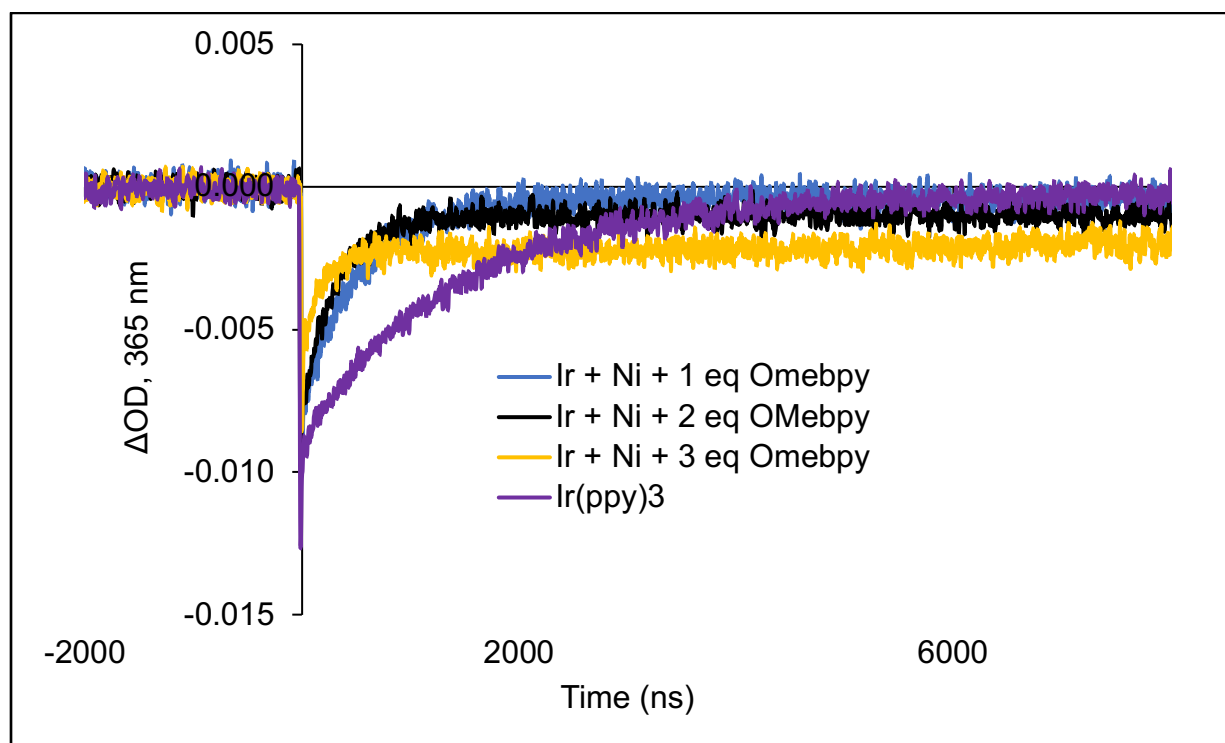


Figure S4.24. Kinetic traces of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMebpy ($1.5, 3.0$, or 4.5 mM) at $\lambda_{\text{probe}} = 400 \text{ nm}$.

Interestingly, at $t = 20 \mu\text{s}$, the magnitude of Ir(IV) signals varies significantly, increasing with OMeppy concentration. This difference is also observed in the kinetic data in the magnitude of persistent signal beyond the PET event. Mixtures with 2 or 3 eq. of OMeppy relative to Ni seem to lead to formation of a significantly larger amount of Ir(IV) as compared with 1 eq. of OMeppy. These differences could be due to varying reactivity in PET among the dominant Ni species in each case (i.e. a mono, bis, or tris OMeppy-ligated Ni complex; See UV-vis section speciation studies). Alternatively, these differences could result from variation in the rate of back electron transfer between Ni(I) and Ir(IV). Further studies will shed light on whether the latter is true. Regarding the former hypothesis, we observe that the 2 eq. mixture shows a higher quenching rate constant as compared to 1 eq., while 3 eq. also showed increased reactivity complicated by nonlinear behavior in the dynamic Stern-Volmer plot (See Stern-Volmer data below).

3.2 Quenching Experiments in the Presence of Aryl Iodide.

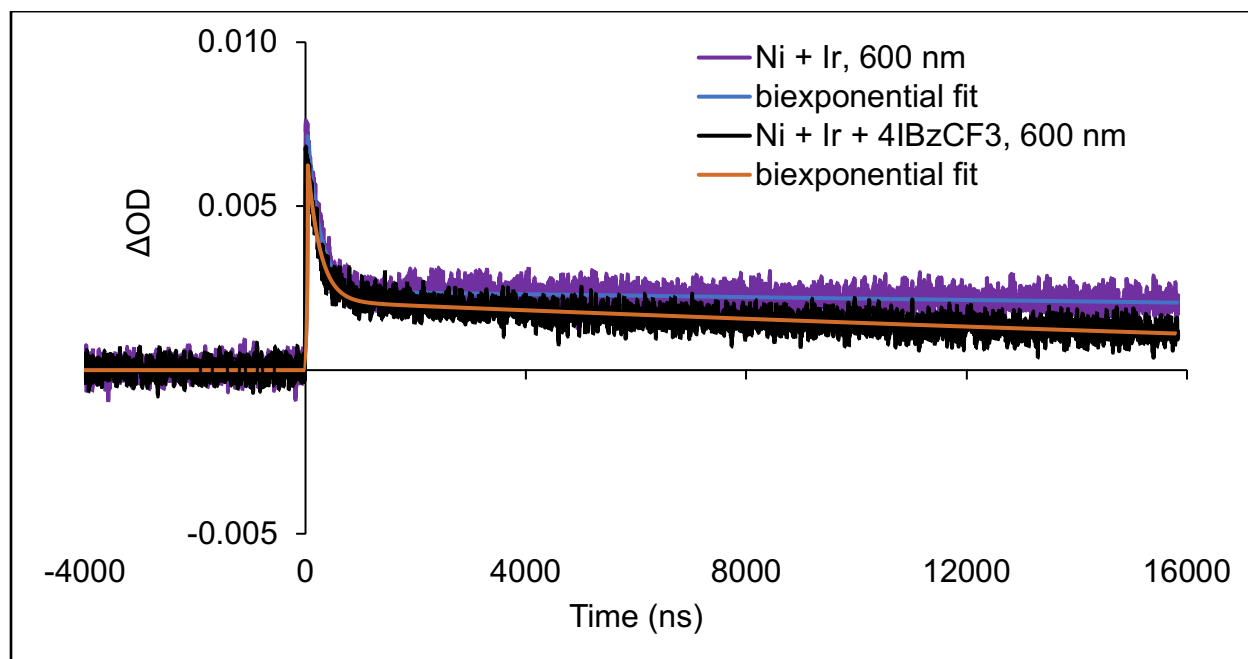


Figure S4.25. Kinetic traces of Ir(ppy)₃ (31.4 μM in DMF) + NiBr₂•glyme (1.5 mM) + OMeppy (3.0 mM) either with or without 4-iodobenzotrifluoride (300 mM) at $\lambda_{\text{probe}} = 600 \text{ nm}$. Biexponential fits utilizing a fixed value for the long 2nd component are shown. The fixed value was obtained by single exponential fitting of the long time window data shown in the plot below.

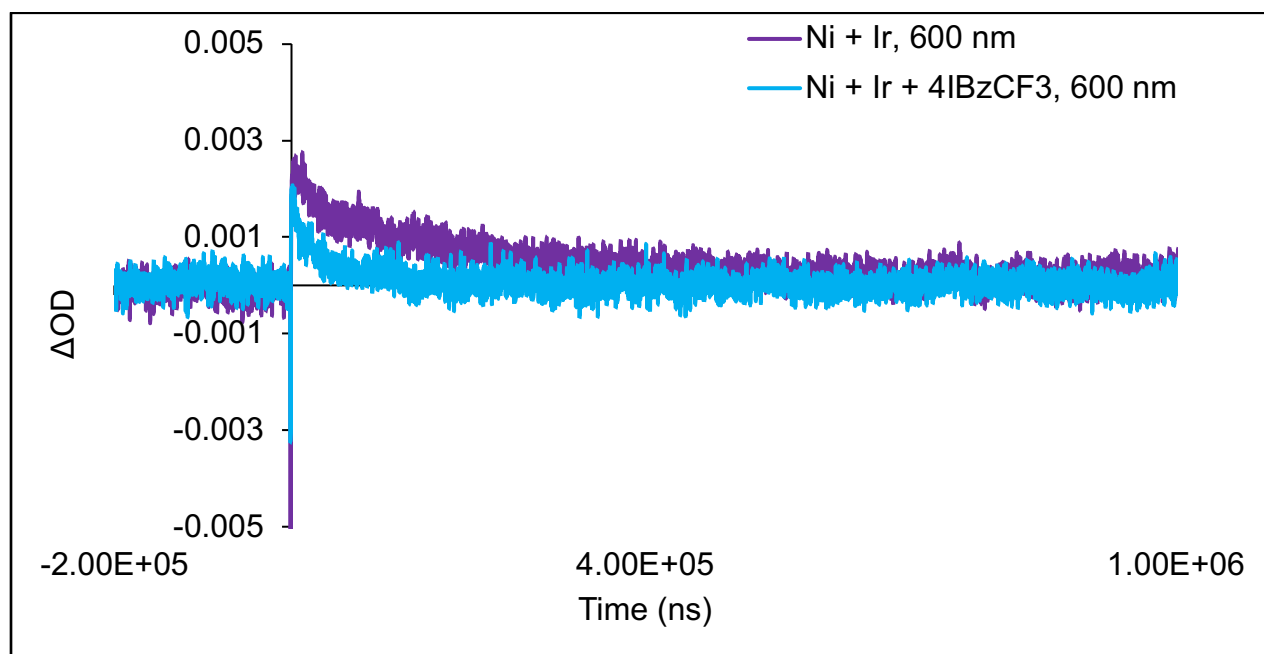


Figure S4.26. Kinetic traces of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) either with or without 4-iodobenzotrifluoride (300 mM) at $\lambda_{\text{probe}} = 600 \text{ nm}$.

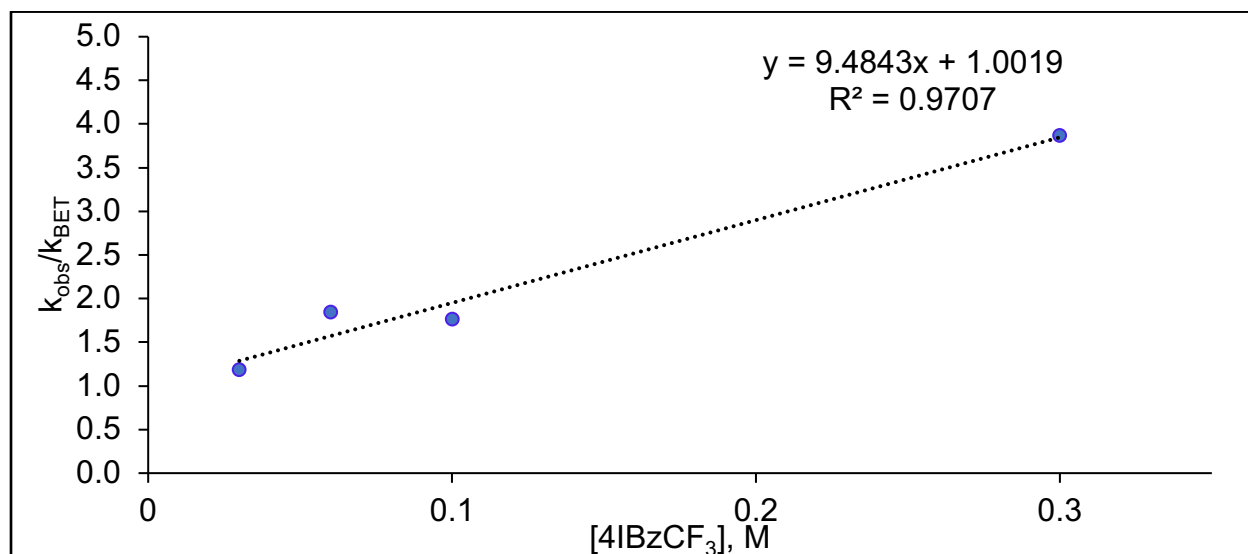


Figure S4.27. Plot of the ratio of $k_{\text{obs}}:k_{\text{BET}}$ vs. 4-iodobenzotrifluoride concentration for kinetics acquired with mixtures containing Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) with increasing 4-iodobenzotrifluoride (300 mM) at $\lambda_{\text{probe}} = 600 \text{ nm}$.

From the above Stern-Volmer plots, $k_{\text{OA}} = b/\tau_{\text{BET}}$, where b is the slope of the linear regression line and τ_{BET} is the lifetime of the unimolecular back electron transfer without the aryl iodide present, obtained from single exponential fitting of the long time window data above (i.e.

201 μs in this case). Applying this equation gives an oxidative addition rate constant of $4.7 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$.

3.3 Kinetic Analysis and Simulations.

Proposed mechanism for loss of Ir(IV):

In the absence of aryl iodide the positive TA signal at 600 nm ascribed to Ir(IV) returns to baseline in a mono-exponential fashion (Fig. S4.28) with a lifetime of $\tau_{\text{BET}} = 185 \mu\text{s}$. This kinetic behavior is typical of first-order and pseudo-first-order processes. The simplest mechanism by which these criteria would be met under the reaction conditions would be back-electron transfer (with rate coefficient $k_{\text{BET}} = \tau_{\text{BET}}^{-1} = 5.4 \times 10^3 \text{ s}^{-1}$) from Ni(I) to Ir(IV) within the geminate ion-pair. Pseudo-first-order kinetics would not be expected under these conditions because the two reactants in question are generated in stoichiometric amounts. For a bimolecular process to result in a decay this rapid, the rate coefficient would need to be greater than the diffusion limit in DMF (simulated kinetics for the system are plotted in Fig. S4.28). In the presence of a high concentration of aryl iodide the lifetime of the species is reduced. A quenching study was conducted by varying the concentration of aryl iodide between 0.03 M and 0.3 M, which resulted in lifetime reduction in accordance with the Stern-Volmer equation (Fig. S4.27). The dynamic quenching rate coefficient (k_q) extracted from this process is equal to $4.7 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$, which is comparable to rate coefficients recently measured for oxidative addition to Nickel complexes.¹⁰ However, oxidative addition involving the Ni(I) species should not accelerate the loss of Ir(IV) signal, unless a species is generated that capable of reducing Ir(IV). To explain this, the following mechanism (Fig. S4.29) is proposed. First, oxidative addition of the aryl iodide to Ni(I) results in the formation of a ion-paired species analogous to a donor-bridge-acceptor¹⁵ model: the iodide ligand takes on the role of the donor, the Ni(III) center as the bridge, and the Ir(IV) complex as the acceptor. Then,

intramolecular electron transfer occurs in which iodide is oxidized by Ir(IV), resulting in Ir(III) and I $\cdot$.

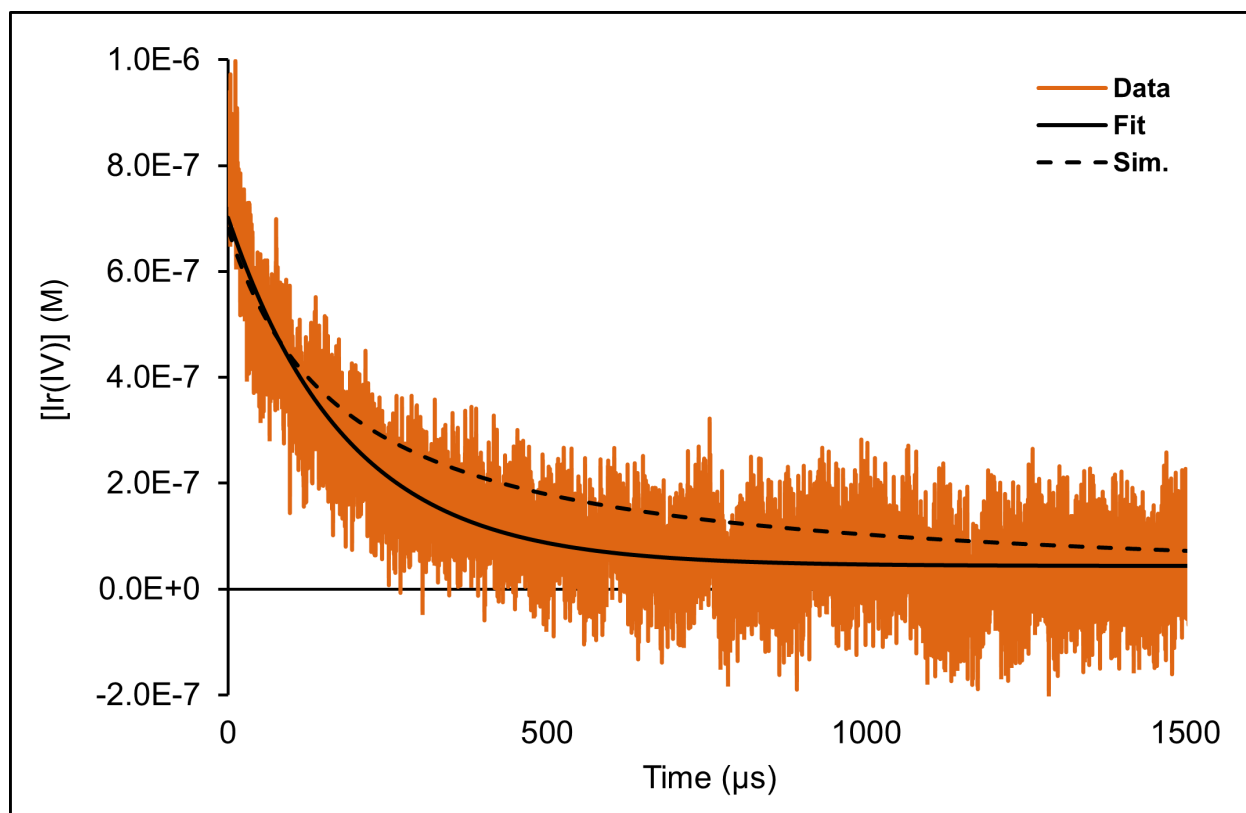


Figure S4.28: Loss of transient absorption signal of Ir(IV) which has been converted to $[Ir(IV)]$, along with a fit (solid line) of the data to a single exponential with rate coefficient $k_{BET} = 5.4 \times 10^3 \text{ s}^{-1}$, and a simulation of the decay (details below) in the case of a bimolecular, diffusion-limited ($k_{diff} = 8.24 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$) reaction. Here $k_{diff} = \frac{8RT}{3\eta}$ was estimated at 25 °C using the viscosity (η) of DMF.

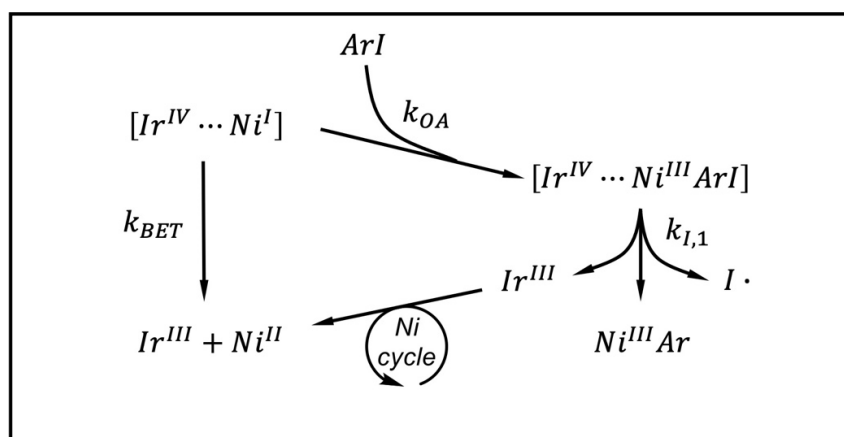


Figure S4.29. Mechanistic scheme describing loss pathways of Ir(IV).

Kinetic simulations were conducted to probe the feasibility of this mechanism resulting in the observed behavior for the sample with the greatest aryl-iodide concentration (0.3 M). The following full set of rate equations can be written from inspection of Figure S4.29:

$$\frac{d[Ir^{IV} \dots Ni^I]}{dt} = -k_{BET}[Ir^{IV} \dots Ni^I] - k_{OA}[Ir^{IV} \dots Ni^I][ArI] \quad \text{Eq. S4.1}$$

$$\frac{d[Ir^{IV} \dots Ni^{III}ArI]}{dt} = -k_I[Ir^{IV} \dots Ni^{III}ArI] + k_{OA}[Ir^{IV} \dots Ni^I][ArI] \quad \text{Eq. S4.2}$$

$$\frac{d[ArI]}{dt} = -k_{OA}[Ir^{IV} \dots Ni^I][ArI] \quad \text{Eq. S4.3}$$

The first two coupled differential equations were numerically integrated to generate the time dependent populations of the Ir(IV)Ni(I) ion pair and the same species after oxidative addition. To accomplish this, the `solve_ivp` functionality of the SciPy library in Python was used with the LSODA method,³² which was selected for its ability to handle stiff differential equations (such as these in which processes may be happening on massively different time scales). Eq. S4.3 was not included in this process because [ArI] is relatively large and invariant over the simulation timescale.

The y-axis of the TA data was converted from ΔA_{600} to [Ir(IV)] using Beer's law and the molar attenuation coefficient of the Ir(IV) species, $\Delta \epsilon_{600} = 2400 \text{ cm}^{-1}\text{M}^{-1}$, which was determined spectroelectrochemically. The initial conditions were set so that the concentrations of the relevant species at $t = 0$ were: $[IrNi]_0 = 5 \times 10^{-7} \text{ M}$, $[IrNiArI]_0 = 0 \text{ M}$, and $[ArI] = 0.3 \text{ M}$. The experimentally determined values of $k_{BET} = 5.4 \times 10^3 \text{ s}^{-1}$ and $k_{OA} = 4.7 \times 10^4 \text{ M}^{-1}\text{s}^{-1}$ were used, while the value of k_I was systematically altered to explore its effect on the simulated populations, as well as the total Ir(IV) population; this is the sum of the two and directly proportional to the observed ΔA_{600} signal.

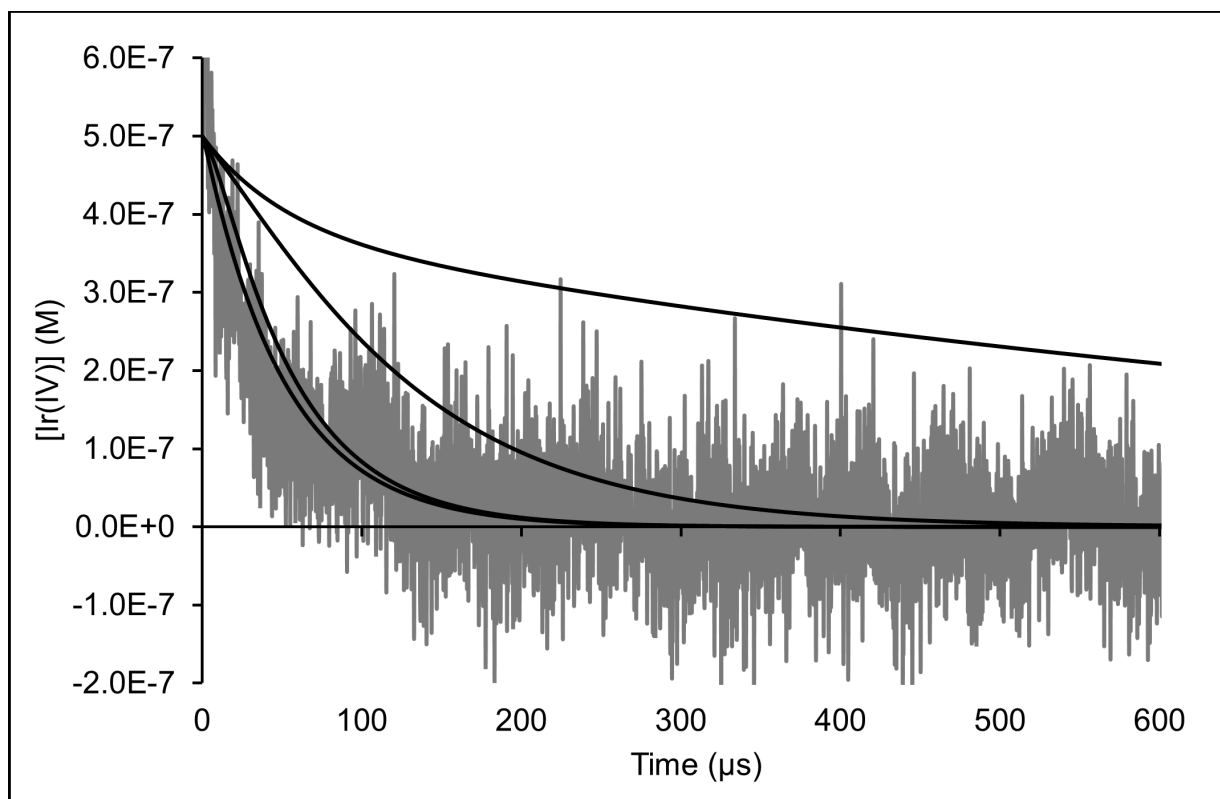


Figure S4.30. Experimental data (grey) from the observed Stern-Volmer quenching of Ir(IV) by intramolecular iodide oxidation following oxidative addition to the Ir(IV)Ni(I) complex, with $[ArI] = 0.3$ M. Total Ir(IV) concentrations (a–d) were simulated by numerical integration of the rate equations (Eqs. S4.1-S4.2) with the initial conditions: $[Ir]_0 = 0.5 \mu\text{M}$ and $[ArI] = 0.3$ M. Experimental rate coefficients were used for oxidative addition ($k_{OA} = 4.7 \times 10^4 \text{ M}^{-1}\text{s}^{-1}$) and back electron transfer ($k_{BET} = 5.4 \times 10^3 \text{ s}^{-1}$), and the k_I values used were (a) 10^3 s^{-1} , (b) 10^4 s^{-1} , (c) 10^5 s^{-1} , and (d) 10^6 s^{-1} .

Oxidative addition acts as a rate-limiting step in this kinetic scheme—total [Ir(IV)] loss cannot proceed more rapidly than loss of [Ir(IV)Ni(I)]. This is illustrated by varying k_I over several orders of magnitude from 10^3 s^{-1} to 10^6 s^{-1} . In the limit of fast iodide oxidation ($k_I \geq 10^6 \text{ s}^{-1}$), the total Ir(IV) loss kinetics align well with the experimental data. If the oxidation was to proceed with a rate coefficient much slower than 10^5 s^{-1} , the Ir(IV) signal would be expected to persist longer, and would not display the pseudo-first-order behavior that was observed in the Stern-Volmer quenching study. Therefore, we prescribe a lower limit of k_I of 10^6 s^{-1} for this process. Recently, rate coefficients for the oxidation of iodide by ruthenium polypyridyl complexes via an inner

sphere mechanism have been measured.¹⁶ For those systems, even slightly endergonic ($\Delta G^\circ = 0.04$ eV) electron transfers occur with rapid, near-diffusion-limited rate coefficients ($k_{\text{obs}} = 5.7 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$). In a later review by the authors,¹⁷ they plot these rate coefficients as a function of ΔG° and show a fit of Marcus theory to the data. Using that Marcus curve to its intersection with our system of study (at ΔG° roughly 0.3 eV greater than their weakest oxidant) would still result in a rate coefficient greater than $10^6 \text{ M}^{-1} \text{ s}^{-1}$ (this far from the diffusion limit $k_{\text{ET}} \sim k_{\text{obs}}$).¹⁸ An alternative bimolecular Ir(IV) quenching pathway in which I^- liberated by oxidative addition encounters Ir(IV) in Ir(IV)Ni(I) or Ir(IV)Ni(III)Ar by diffusion was also explored via simulation, however even with a diffusion-limited k_{obs} the low concentration of I^- generated was insufficient to accelerate the Ir(IV) decay to match the observed kinetics.

Quantum yields of Quenching of Ir(ppy)₃ and PhenO S₁, T₁ states:

The quantum yields for quenching of Ni(II) were calculated for the ³MLCT state of Ir(ppy)₃ and both the S₁ and T₁ states of PhenO using the following quantum-yield expressions (Eqs. S4.4-S4.6), each of which expresses the likelihood of an excited state of interest decaying as a result of quenching by Ni(II).

$$\Phi_{\text{Ir}} = \frac{k_{q,\text{Ir}}[\text{Ni(II)}]}{k_{q,\text{Ir}}[\text{Ni(II)}] + k_{0,\text{Ir}}} \quad \text{Eq. S4}$$

$$\Phi_{\text{S}_1} = \frac{k_{q,\text{S}_1}[\text{Ni(II)}]}{k_{q,\text{S}_1}[\text{Ni(II)}] + k_{0,\text{S}_1}} \quad \text{Eq. S5}$$

$$\Phi_{\text{T}_1} = \left(\frac{k_{\text{ISC}}}{k_{q,\text{S}_1}[\text{Ni(II)}] + k_{0,\text{S}_1}} \right) \left(\frac{k_{q,\text{T}_1}[\text{Ni(II)}]}{k_{q,\text{T}_1}[\text{Ni(II)}] + k_{0,\text{T}_1}} \right) \quad \text{Eq. S6}$$

The relevant quenching rate coefficients and excited state lifetimes used for the generation of Fig. S4.31 are listed in Table S4.3. For Ir(ppy)₃ this quantity is the most straightforward to analyze and predicts (the orange line in Fig. S4.31) inefficient quenching below mM concentrations of Ni(II). This concentration effect makes it so the more-energetic but short-lived

S_1 state of Pheno (dotted line) would not be expected to contribute in a meaningful manner until even higher $[\text{Ni(II)}]$. Conversely, the long-lived T_1 state of Pheno would be expected to be quenched with near-unity efficiency even at sub-mM $[\text{Ni(II)}]$, which is represented in both the dashed (T_1) and solid (collective S_1 and T_1 contribution) lines in Fig. S4.31. The second yield quantity in Eq. S4.6 is a necessary, $[\text{Ni(II)}]$ -dependent correction factor—formally the yield of intersystem crossing under these conditions—for expressing the total quantum yield of quenching from the phenoxazine's T_1 state. This is because at high $[\text{Ni(II)}]$ the S_1 state is quenched, reducing the number of T_1 states generated in the first place, as observed in Fig. S4.31. Thus, this organic PC with a high triplet yield and relatively long-lived S_1 state may act as a switchable photoredox partner under these conditions.

Table S4.3. Experimental quantities needed for calculating the quantum yields of quenching displayed in Fig. S4.31.

PC	τ_{S_1} (ns)	$k_{q,S_1} (\times 10^9 \text{ M}^{-1} \text{ s}^{-1})$	Φ_{ISC}	$k_{ISC} (\times 10^9 \text{ s}^{-1})$	$\tau_{T_1} (\mu\text{s})$	$k_{q,T_1} (\times 10^9 \text{ M}^{-1} \text{ s}^{-1})$
Ir(ppy)_3	-	-	1.0 ^c	-	1.47	1.2
Pheno	6.32 ^a	3.4	0.91 ^b	0.144 ^d	480 ^a	0.66

^aRef.¹⁹. ^bRef.¹³. ^cRef.²⁰. ^dCalculated as $k_{ISC} = \Phi_{ISC} / \tau_{S_1}$.

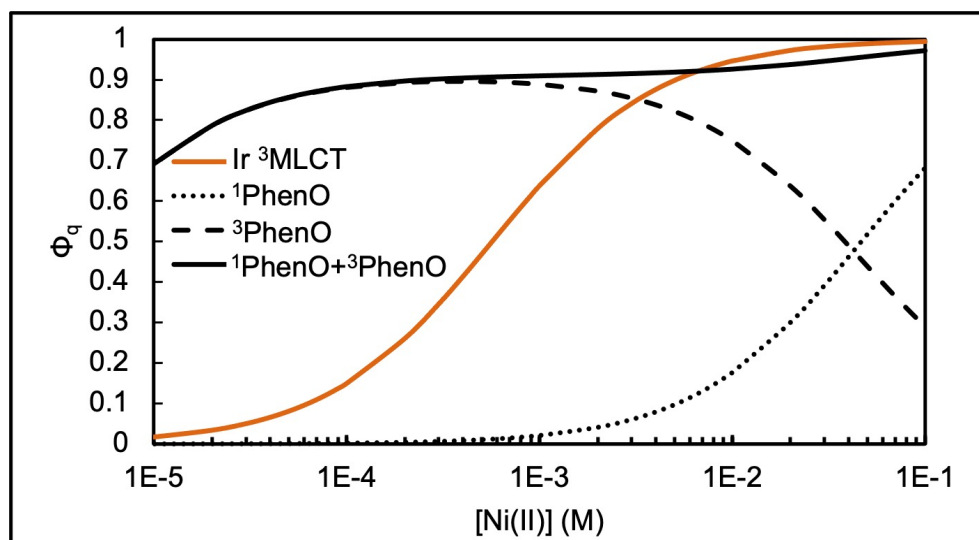


Figure S4.31. Quantum yields of quenching of the $^3\text{MLCT}$ state of Ir(ppy)_3 and the S_1 and T_1 states of Pheno (and their collective yield) calculated as a function of $[\text{Ni(II)}]$ over a concentration range of 10 μM to 100 mM (0.00025% to 25% loading respectively).

A selection of Φ_q values at different Ni(II) loading may serve to illustrate the expected behavioral differences from these two PCs with respect to producing the geminate ion complex. At 10% Ni(II) loading (40 mM Ni(II)) Ir(ppy)₃ is expected to outperform, with a yield of 0.99 to a collective 0.95 (0.46 from S₁ and 0.49 from T₁) for PhenO. On the other hand, at 0.05% loading (0.2 mM Ni(II)), Ir(ppy)₃ is 0.26 and PhenO is 0.9 (all T₁) . This is even more exaggerated at 0.005% loading (0.02 mM Ni(II)) where Ir(ppy)₃ is 0.03 and the T₁ of PhenO still has a predicted yield of 0.79 due to its near 500-fold longer-lived excited state with respect to the ³MLCT of Ir(ppy)₃. The predicted performance of Ir(ppy)₃ and PhenO matched experimental results in a screen of relevant nickel concentrations (See section 6.2).

3.4 Control Experiments.

In this section, mixtures containing various combinations of reaction components are probed, showing that introduction of base, alcohol, aryl halide, or ligand do not change the observed spectral signals or the kinetics of those signals at selected wavelengths.

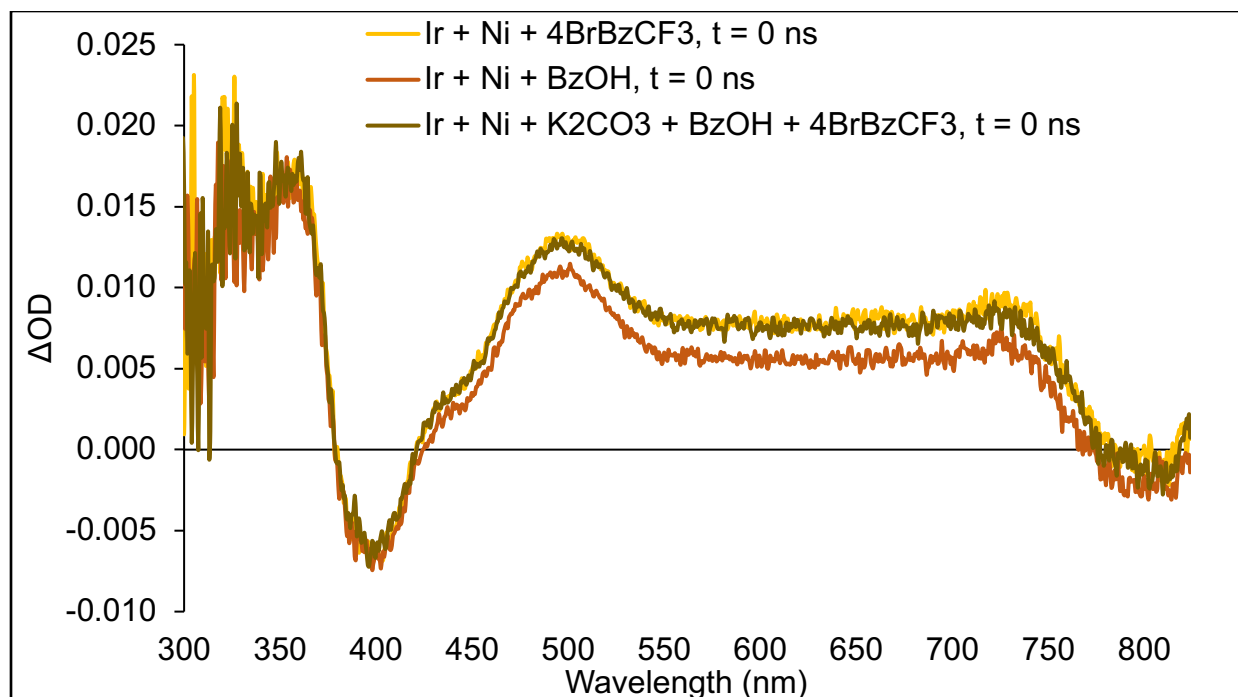


Figure S4.32. Spectral traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of $\text{Ir}(\text{ppy})_3$ ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) + either 4-bromobenzotrifluoride (4-BrBzCF₃, 30 mM), benzyl alcohol (BzOH, 30 mM), or all reaction components (previously listed + K_2CO_3 , 60 mM) at indicated time delay. Data was offset corrected utilizing kinetic data acquired at $\lambda_{\text{probe}} = 365 \text{ nm}$. We note that K_2CO_3 was not fully dissolved but allowed to settle prior to measurement.

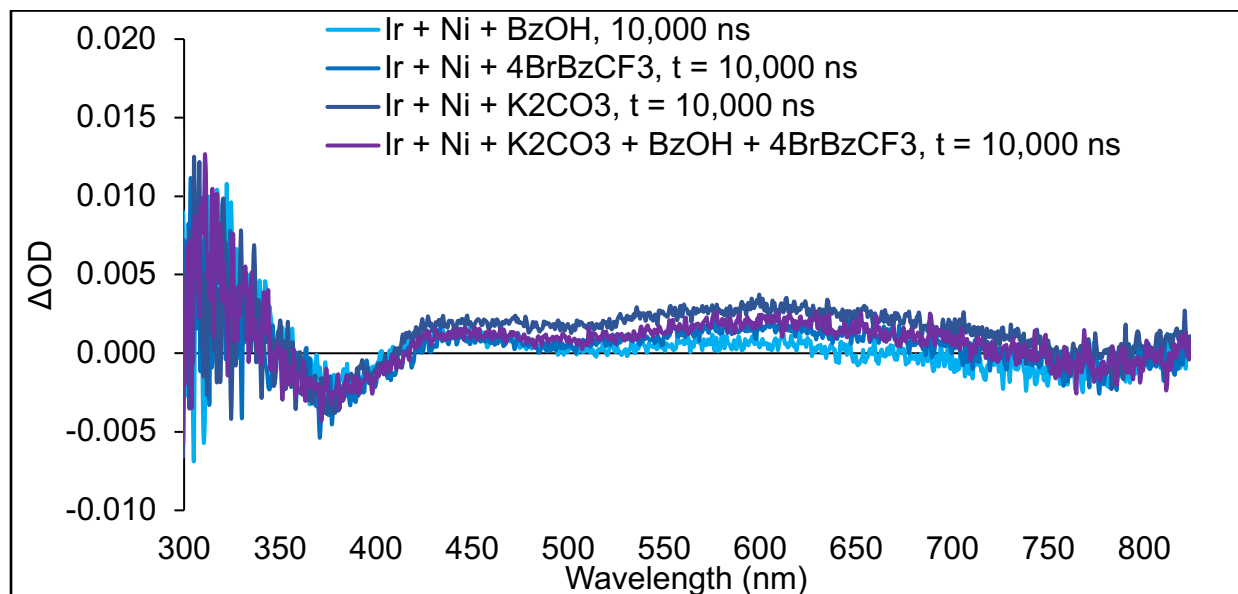


Figure S4.33. Spectral traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of $\text{Ir}(\text{ppy})_3$ ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) + either 4-bromobenzotrifluoride (4-BrBzCF₃, 30 mM), benzyl alcohol (BzOH, 30 mM), or all reaction components (previously listed + K_2CO_3 , 60 mM) at indicated time delay. Data was offset corrected utilizing kinetic data acquired at $\lambda_{\text{probe}} = 365 \text{ nm}$. We note that K_2CO_3 was not fully dissolved but allowed to settle prior to measurement.

In the later time point traces with additional components present ($t = 10 \mu\text{s}$), we see the same persistent signals as in the $\text{Ir(ppy)}_3 + \text{NiBr}_2\cdot\text{glyme} + \text{OMebpy}$ mixture. As such, we can conclude that in the full reaction mixture relevant to catalysis, the excited state Ir(ppy)_3 reduces Ni(II) to Ni(I) .

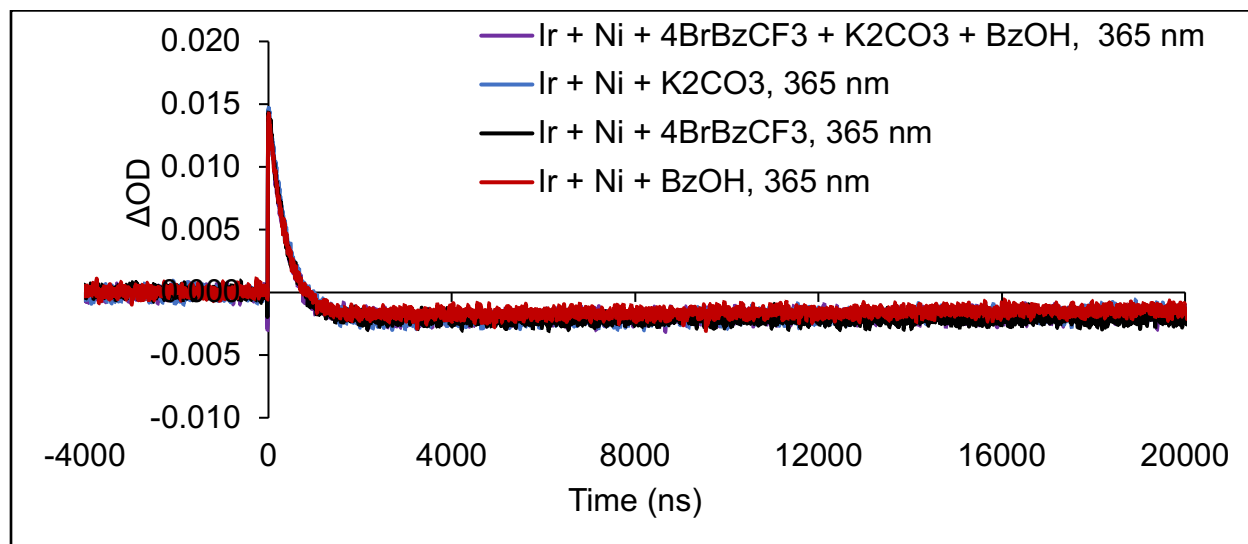


Figure S4.34. Kinetic traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) + either 4-bromobenzotrifluoride (4-BrBzCF₃, 30 mM), benzyl alcohol (BzOH, 30 mM), K_2CO_3 (60 mM), or all components at $\lambda_{\text{probe}} = 365 \text{ nm}$. We note that K_2CO_3 was not fully dissolved but allowed to settle prior to measurement.

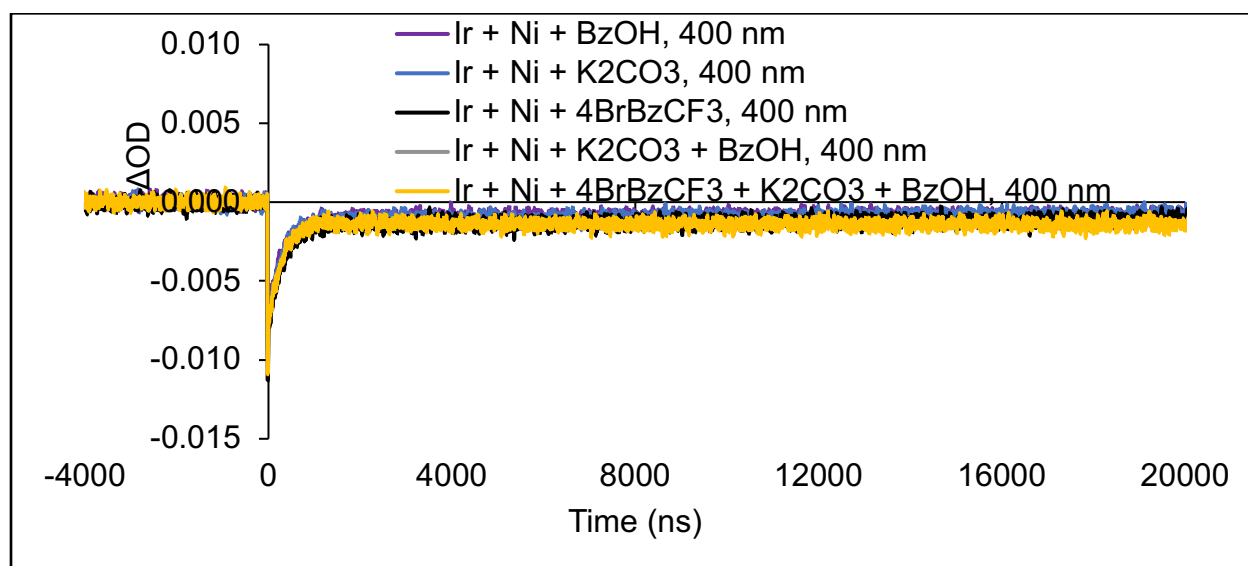


Figure S4.35. Kinetic traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2\cdot\text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) + either 4-bromobenzotrifluoride (4-BrBzCF₃, 30 mM), benzyl alcohol (BzOH, 30 mM), K_2CO_3 (60 mM), K_2CO_3 and benzyl alcohol, or all components at $\lambda_{\text{probe}} = 400 \text{ nm}$. We note that K_2CO_3 was not fully dissolved but allowed to settle prior to measurement.

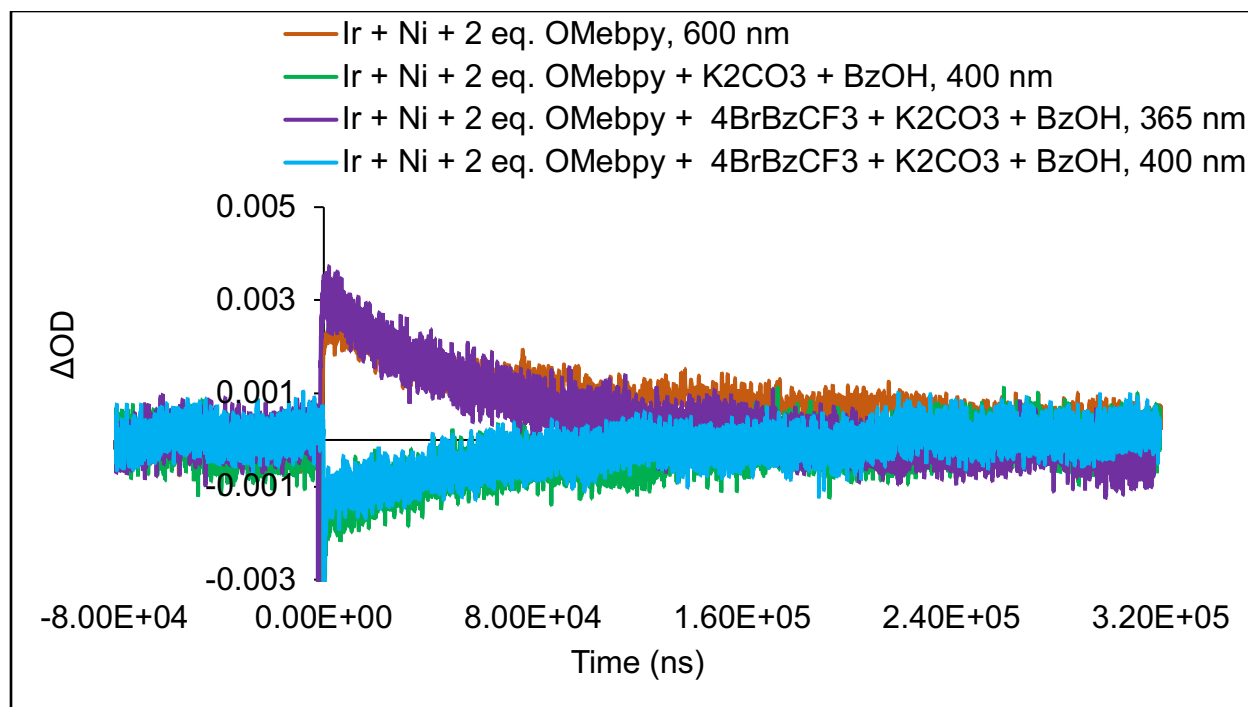


Figure S4.36. Kinetic traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of Ir(ppy)₃ (31.4 μM in DMF) + NiBr₂·glyme (1.5 mM) + OMeppy (3.0 mM) + either 4-bromobenzotrifluoride (4-BrBzCF₃, 30 mM), benzyl alcohol (BzOH, 30 mM), K₂CO₃ (60 mM), K₂CO₃ and benzyl alcohol, or all components at $\lambda_{\text{probe}} = 365$, 400, or 600 nm. We note that K₂CO₃ was not fully dissolved but allowed to settle prior to measurement.

In these kinetic experiments, at both $\lambda_{\text{probe}} = 365 \text{ nm}$ and $\lambda_{\text{probe}} = 400 \text{ nm}$, we observe indistinguishable kinetics over a 20 μs timescale, supporting the claim that reduction of Ni-OMeppy complexes is the only significant quenching pathway for the Ir(ppy)₃ excited state in these mixtures. Since all components are present at the same molar ratios as used in the catalytic reaction mixture, we can deduce that the observed oxidative quenching pathway is catalytically relevant. Furthermore, at longer timescales (i.e. 400 μs), the decay to the baseline is indistinguishable between these mixtures. Thus, the back electron transfer between Ir(IV) and Ni(I) proceeds at the same rate regardless of whether K₂CO₃, BzOH, or 4-BrBzCF₃ is present. Of these, only 4-BrBzCF₃ is expected to react with Ni(I), albeit at a rate too slow to affect the kinetics observed here. Indeed, the rate of oxidative addition has been studied with 4-BrBzCF₃ at Ni(I) and found to be $<10^4 \text{ M}^{-1} \text{ s}^{-1}$.¹⁰ Overall, these control experiments support that the conclusions drawn

from simpler analyte mixtures (eg. only Ir + Ni + OMeppy) can be extended to the full catalytic reaction mixture.

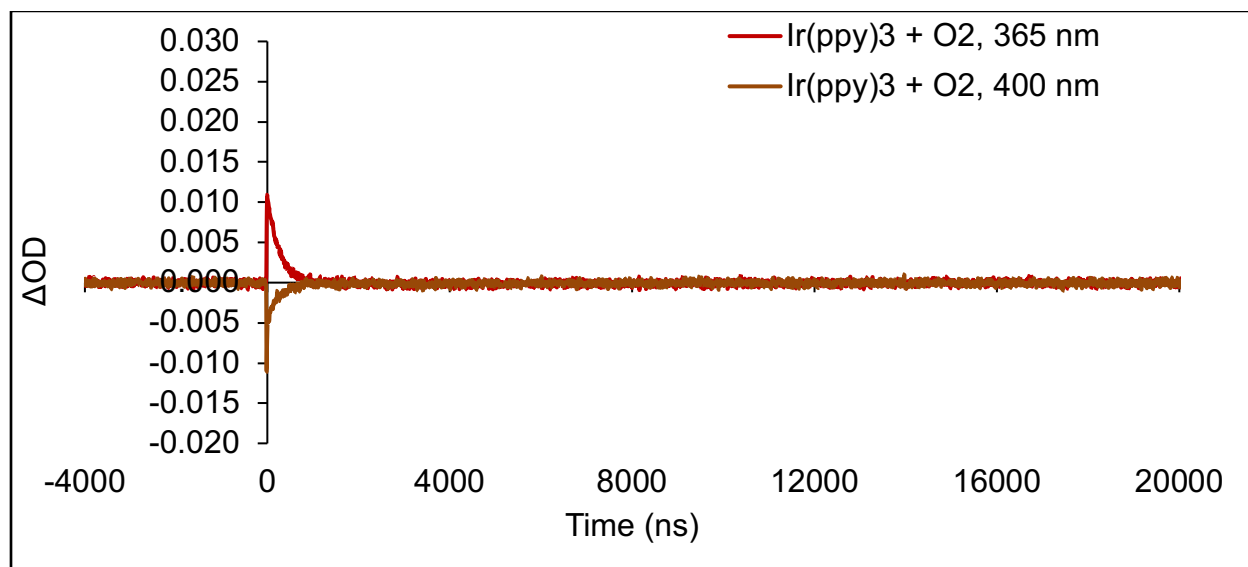


Figure S4.37. Kinetic traces of Ir(ppy)₃ (31.4 μM in DMF) exposed to air prior to measurement.

This control experiment suggests that the signals observed for Ir(ppy)₃ in the presence of Ni and OMeppy cannot be accounted for by accidental air exposure. Here, we see significant quenching but a full return to the baseline signal, consistent with energy transfer type quenching of [Ir(ppy)₃]* by O₂. Signals that would indicate presence of Ir(IV) in the event of O₂ reduction are not observed.

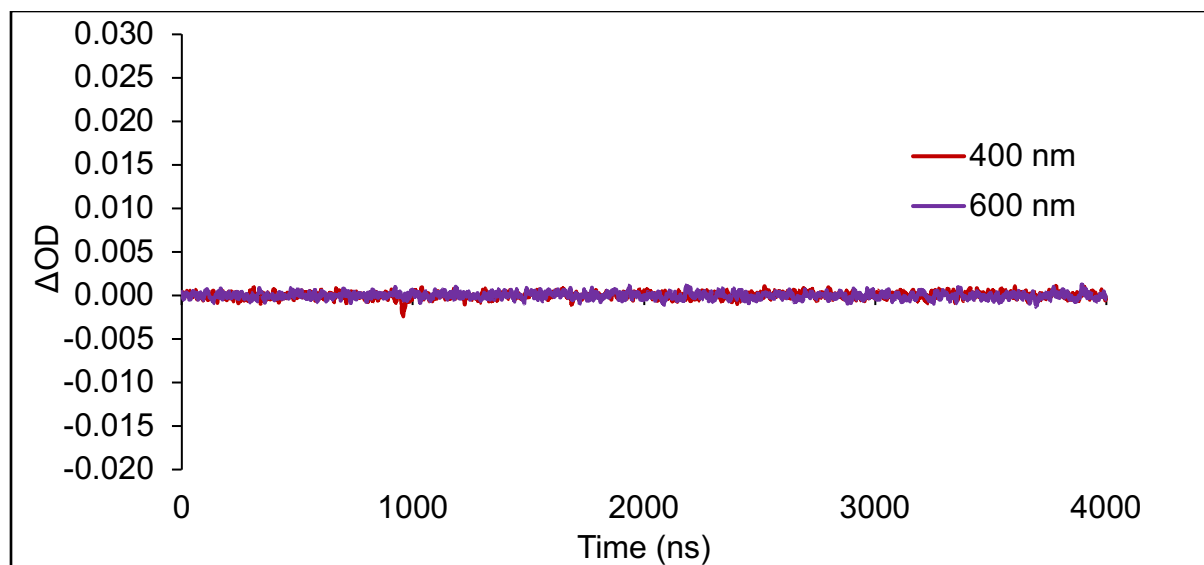


Figure S4.38. Kinetic traces ($\lambda_{pump} = 355$ nm) of $NiBr_2 \cdot glyme$ (1.5 mM) + $OMebpy$ (3.0 mM) at $\lambda_{probe} = 400$ nm or 600 nm.

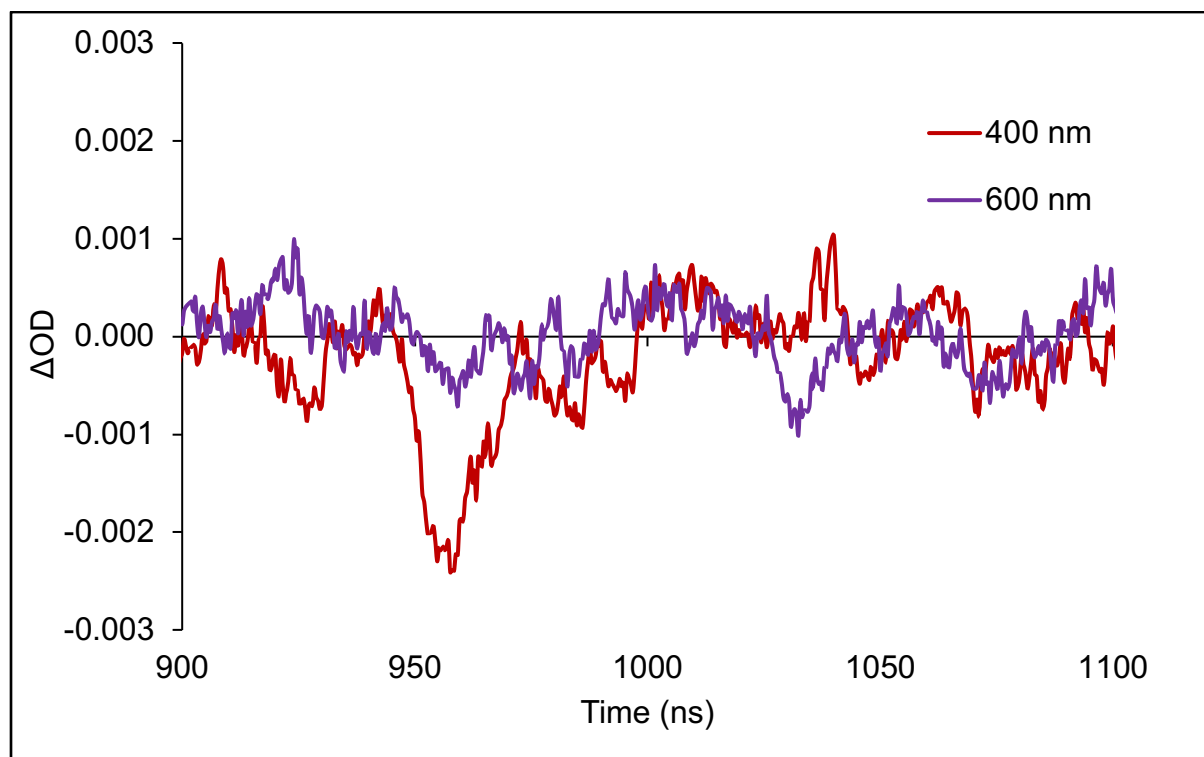


Figure S4.39. Narrow time window view of kinetic traces ($\lambda_{pump} = 355$ nm) of $NiBr_2 \cdot glyme$ (1.5 mM) + $OMebpy$ (3.0 mM) at $\lambda_{probe} = 400$ nm or 600 nm.

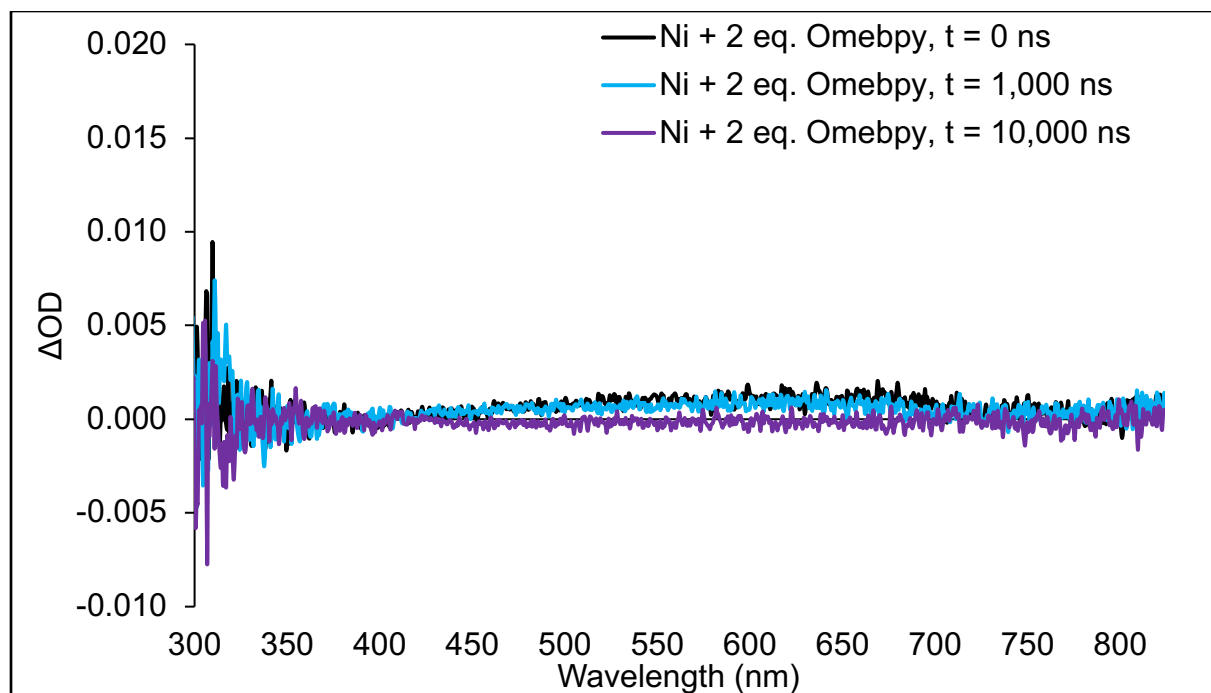


Figure S4.40. Spectral traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMeppy (3.0 mM) at the indicated time delays.

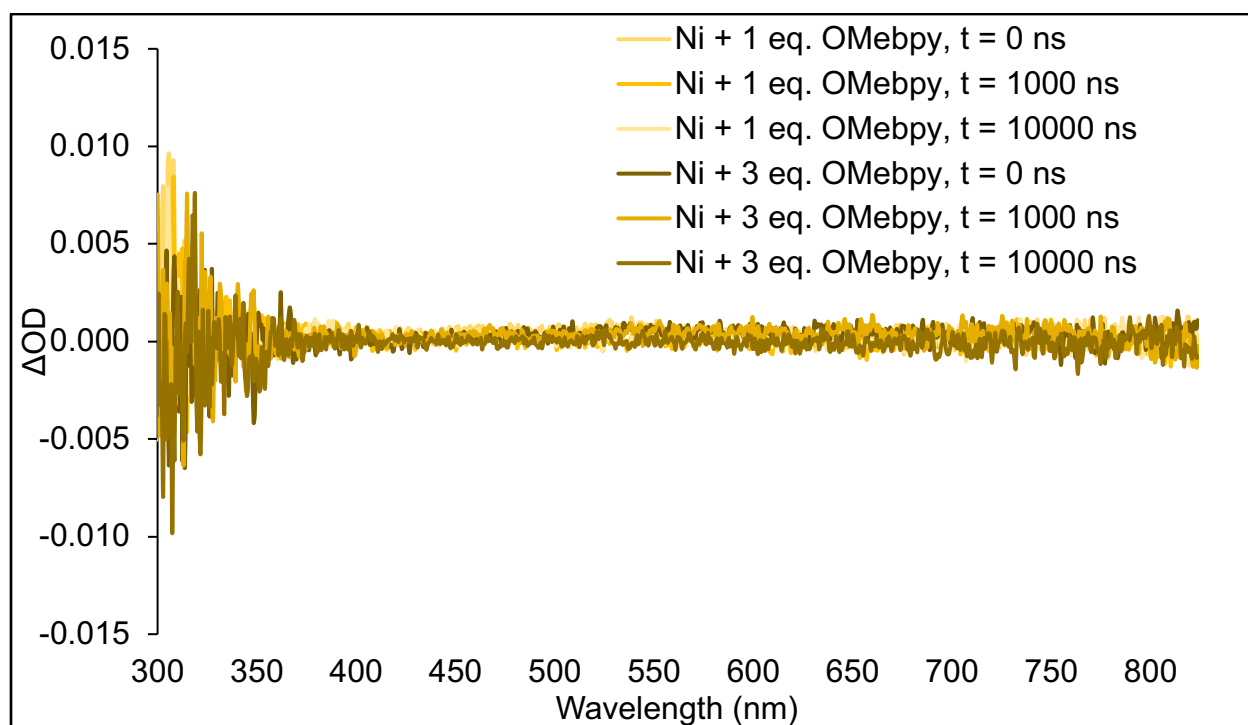


Figure S4.41. Spectral traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMeppy (1.5 or 4.5 mM) at the indicated time delays.

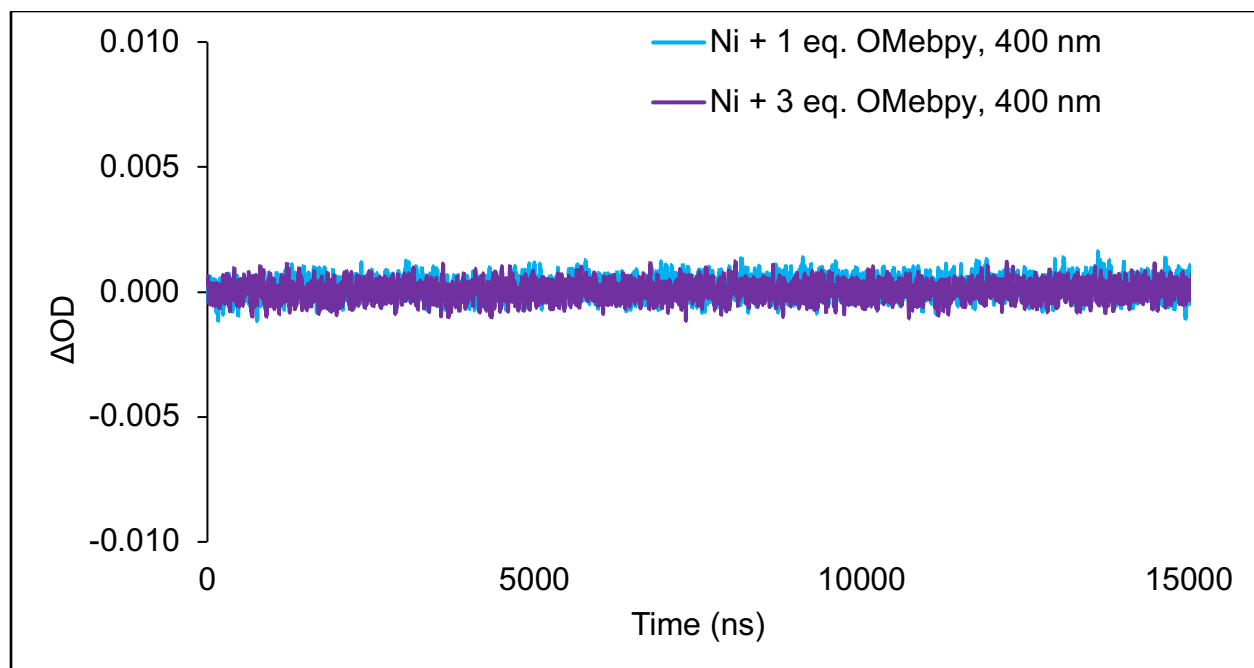


Figure S4.42. Kinetic traces ($\lambda_{pump} = 355$ nm) of $NiBr_2 \cdot glyme$ (1.5 mM) + OMebpy (1.5 or 4.5 mM) at $\lambda_{probe} = 400$ nm.

The spectral traces of the Ni-OMebpy 2:1 mixture alone do not indicate any significant signal. Apparent weak features at ~ 600 nm are revealed by the kinetic trace to be indistinguishable from noise. A very weak negative feature in the kinetic trace acquired at 400 nm could correspond to the ground state bleach signal of a Ni-centered excited state with a lifetime shorter than the instrumental limits of the TA setup used here. Thus, signals observed in spectral experiments above in the presence of $Ir(ppy)_3$ and other reaction components cannot be attributed to contributions from directly excited Ni complexes. In kinetic data, the weak signal observed at 400 nm could constitute a minor contribution to the signal within the first 50 ns in experiments above, with inconsequential effect on the interpretation of those experiments.

For the Ni-OMebpy 1:1 and 3:1 mixtures there are no measurable signals either in the kinetic or spectral experiments, suggesting that direct Ni excitation is a negligible contributor to signals in experiments containing $Ir(ppy)_3$ with these mixtures.

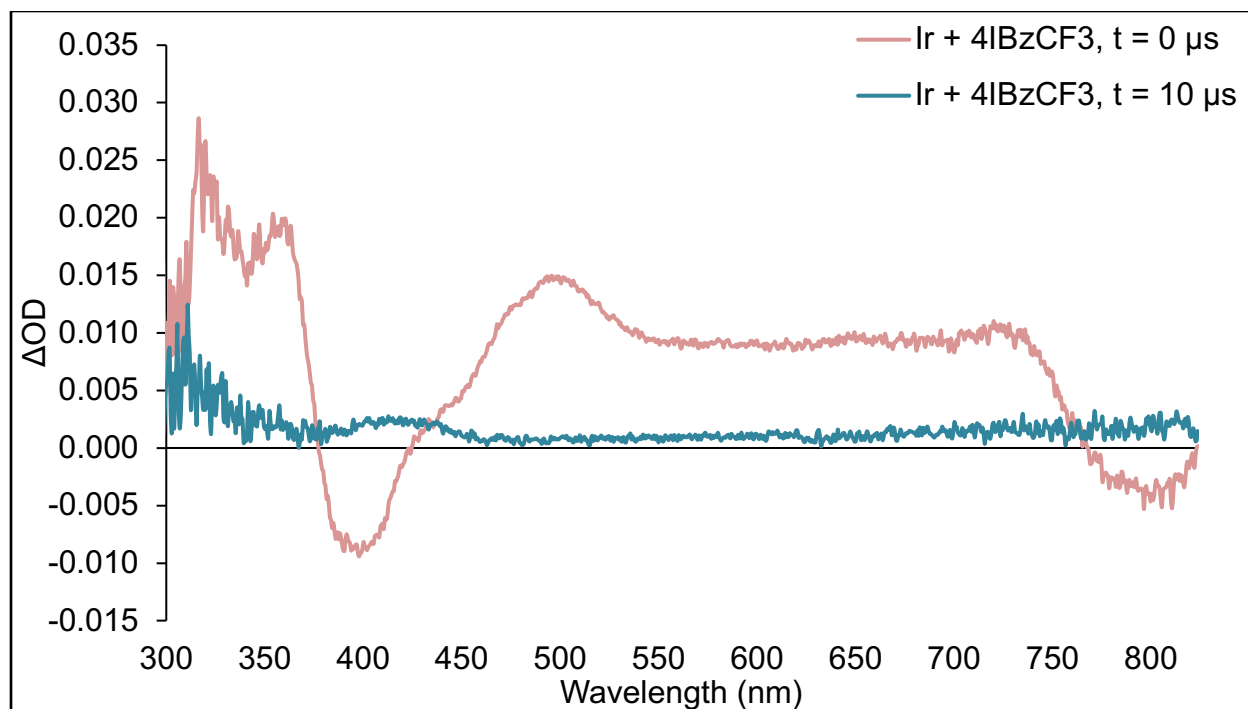


Figure S4.43. Spectral traces ($\lambda_{\text{pump}} = 355$ nm) of Ir(ppy)_3 (31.4 μM in DMF) alone or with 4-iodobenzotrifluoride (4-IBzCF₃, 300 mM) at the indicated time delays.

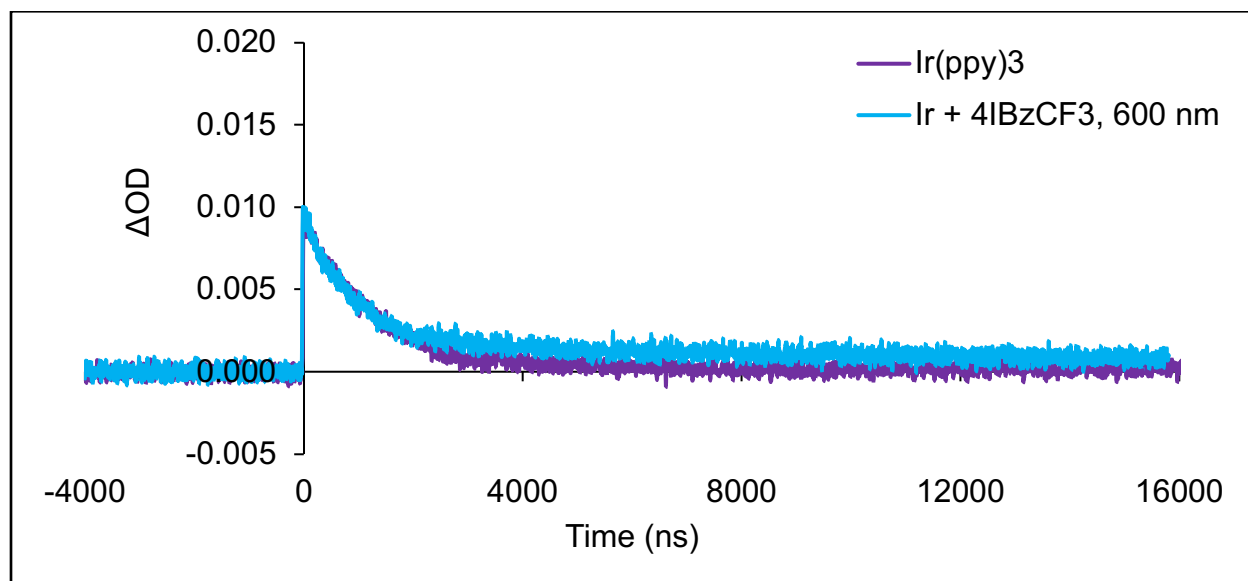


Figure S4.44. Kinetic traces ($\lambda_{\text{pump}} = 355$ nm) of Ir(ppy)_3 (31.4 μM in DMF) alone or with 4-iodobenzotrifluoride (4-IBzCF₃, 300 mM) at $\lambda_{\text{probe}} = 600$ nm.

The slightly raised baseline in kinetic data and small degree of quenching indicates a minor side reduction of 4-iodobenzotrifluoride by excited state Ir(ppy)_3 . In the spectral data, persistent signals due to Ir(IV) are extremely weak or absent, while an unknown species with broad peak ~ 400 –440 nm persists. One possibility is that this signal could be due to the aryl radical produced

when Ir(III)* reduces 4-IBzCF₃. The resulting Ir(IV) would likely oxidize photoproduct iodide to iodine radical, I[•]. I₂^{•-} derived from the diffusion-limited reaction of I[•] with iodide could also contribute to this signal.¹¹ Fast loss of Ir(IV) due to iodide oxidation, as well as the low degree of quenching, can explain why Ir(IV) signals are insignificant in the 10 μs trace. In sum, direct photo-reduction of 4-IBzCF₃ is a minor side quenching pathway which cannot provide an iodide concentration sufficient to account for the reduction of Ir(IV) to Ir(III) observed when Ni-bipyridine complexes are present (see kinetic modeling section).

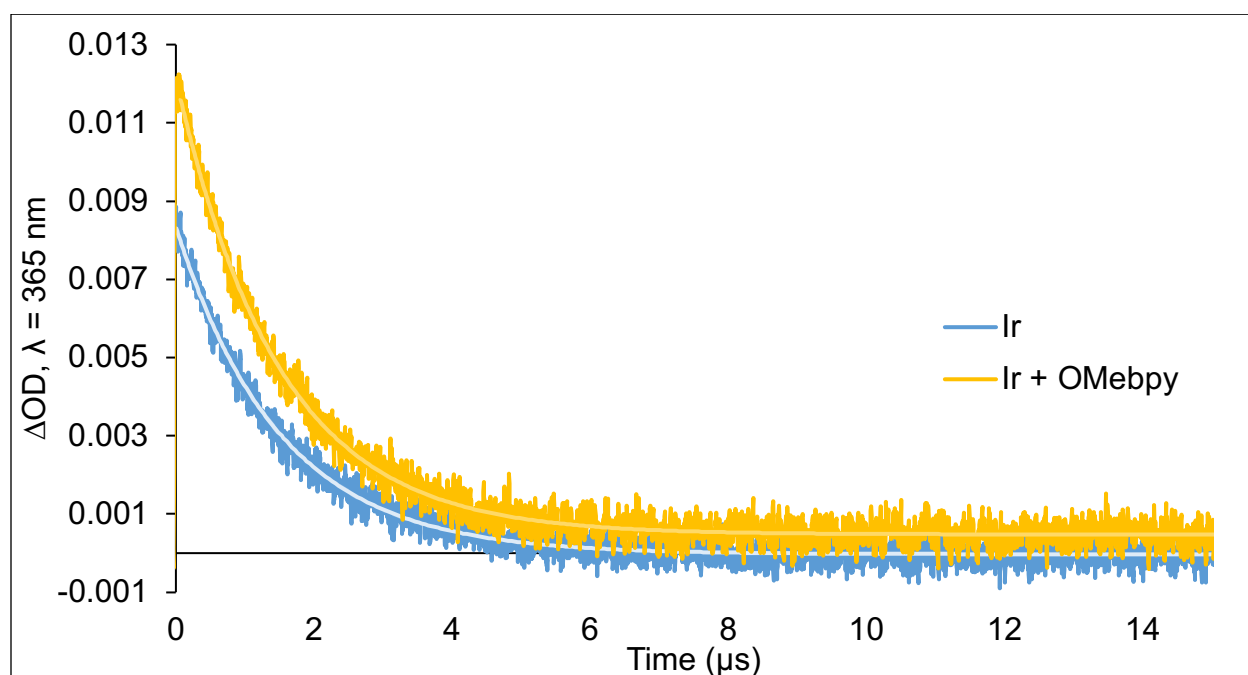


Figure S4.45. Kinetic traces for Ir(ppy)₃ (15.7 μM) in DMF and for Ir(ppy)₃ with 2 eq. OMeppy ligand (3.0 mM) in DMF at λ_{probe} = 365 nm.

In this control experiment, negligible difference between the lifetime of Ir(ppy)₃ in the solution with (1.49 μs) and without free OMeppy ligand (1.47 μs) indicates that excited state Ir(ppy)₃ is not reducing the free ligand. This observation supports that the Ni/OMeppy complex is the electron acceptor.

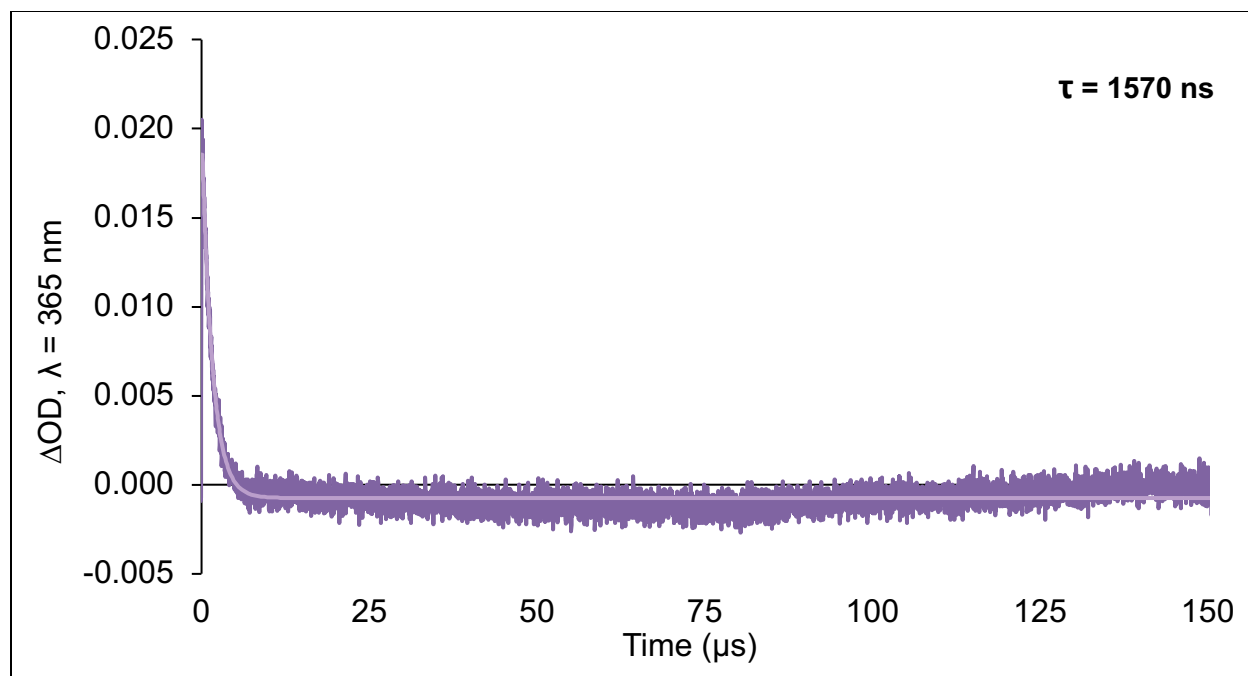


Figure S4.46. Kinetic traces for Ir(ppy)_3 ($31.4 \mu\text{M}$) with DBU (60 mM) in DMF (no nickel complex) at $\lambda_{\text{probe}} = 365 \text{ nm}$.

In this control experiment, negligible difference between the lifetime of Ir(ppy)_3 in the solution with DBU ($1.57 \mu\text{s}$) and without DBU ($1.47 \mu\text{s}$) indicates that excited state Ir(ppy)_3 is not reducing DBU. This control further supports that the Ni-ligand complex is the electron acceptor.

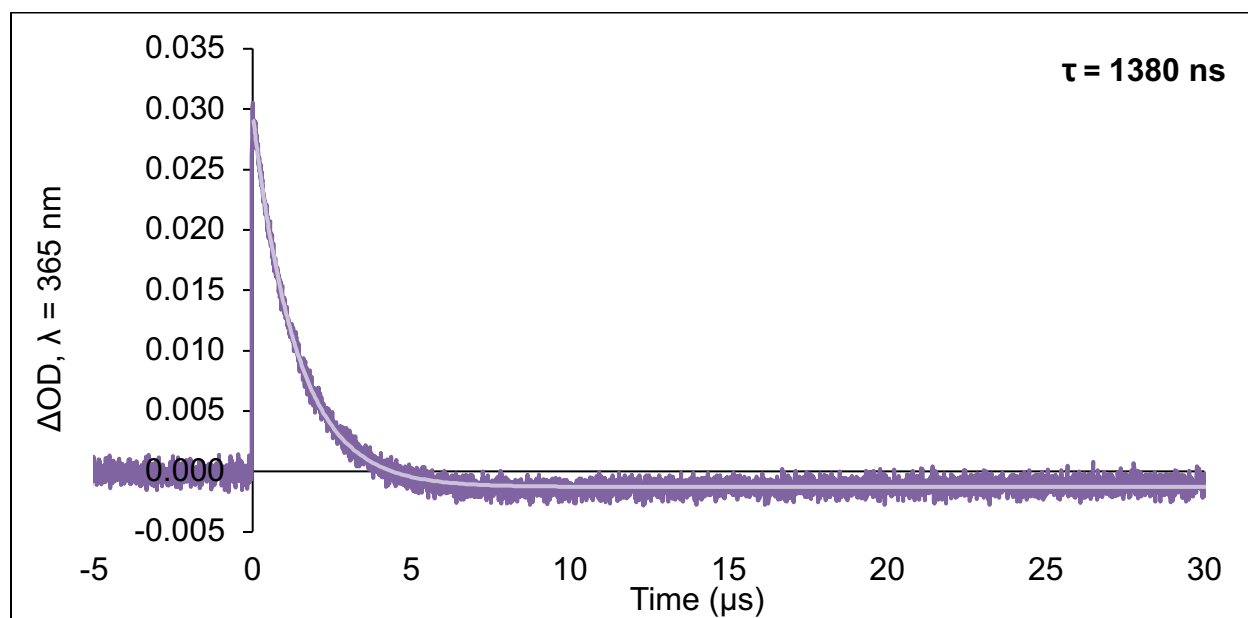


Figure S4.47. Kinetic trace for Ir(ppy)_3 ($15.7 \mu\text{M}$) with 4-BzBrCF_3 (400 mM) in DMF at $\lambda_{\text{probe}} = 365 \text{ nm}$.

To evaluate if the excited state of Ir(ppy)_3 , $[\text{Ir(ppy)}_3]^*$, can directly reduce an aryl bromide substrate, a control experiment was carried out with Ir(ppy)_3 and 4-bromobenzotrifluoride (4-BzBrCF₃) in DMF. It was hypothesized that little to no direct reduction of ArBr would occur. It is possible that the weakly negative signal observed in the decays corresponds to Ir(IV) at 365 nm, which would be formed by reduction of aryl bromide by $[\text{Ir(ppy)}_3]^*$. However, in our previous measurement of $[\text{Ir(ppy)}_3]^*$ decay the lifetime was found to be 1.47 μs , so there is negligible reduction in lifetime observed.

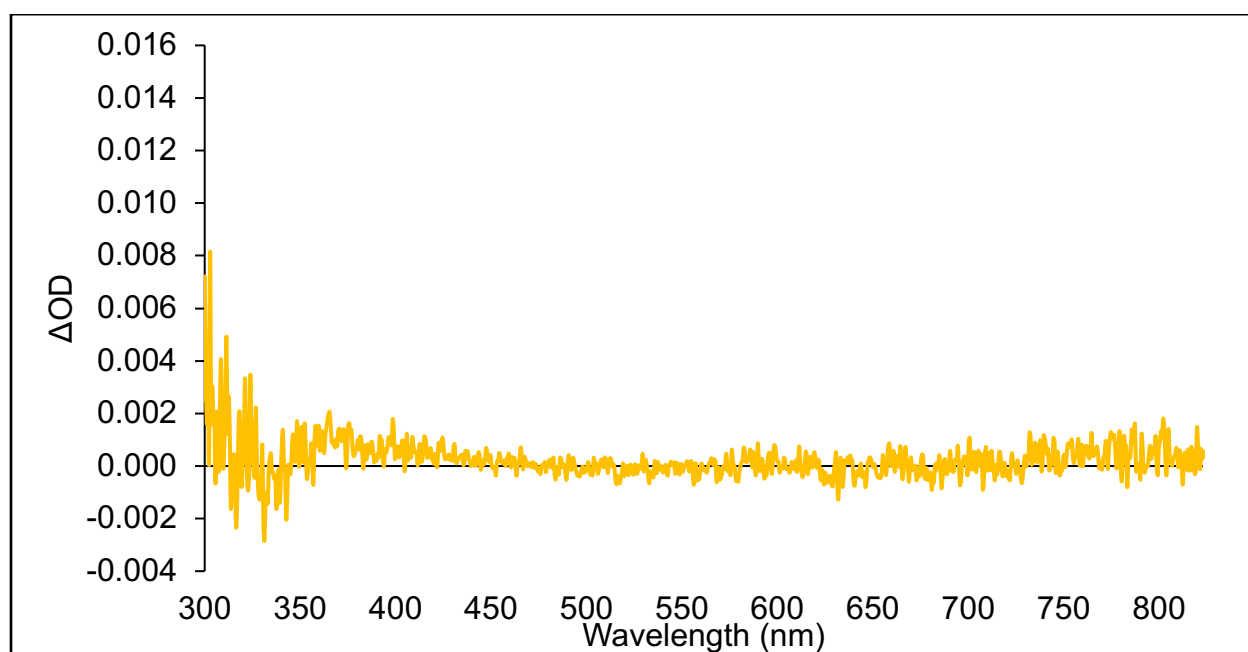


Figure S4.48. Spectral traces ($\lambda_{\text{pump}} = 355$ nm) of 4-IBzCF₃ (300 mM) at $t = 0$ ns. We observe a very weak, noisy signal at ~ 360 nm due to direct excitation of 4-IBzCF₃.

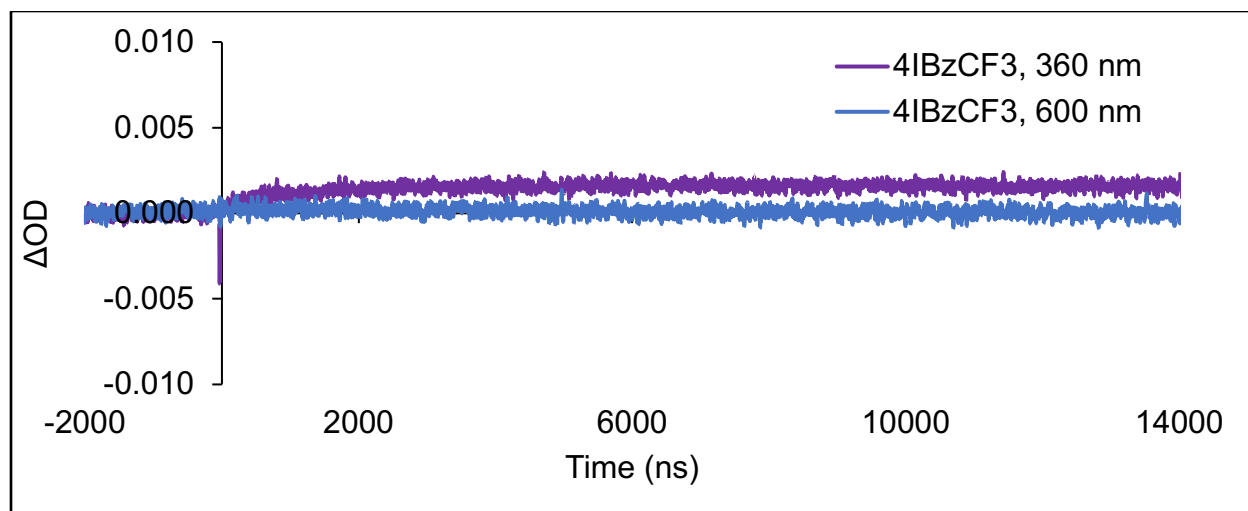


Figure S4.49. Kinetic traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of 4-iodobenzotrifluoride (4-IBzCF₃, 300 mM) at $\lambda_{\text{probe}} = 360 \text{ nm}$ or 600 nm.

We note there is no discernible signal at 600 nm due to direct excitation of 4-IBzCF₃. However, at 360 nm there is a positive signal that appears with a slow rise that we can attribute to a photolysis product produced via decomposition of 4-IBzCF₃. The photolysis of 4-IBzCF₃ results in I[•] and an aryl radical. I[•] is known to absorb in the UVC region in water ($\lambda_{\text{max}} = 255 \text{ nm}$; molar absorptivity = $1040 \text{ M}^{-1} \text{ cm}^{-1}$)¹¹, and so we conclude the observed signal may be due to a combination of I[•], an aryl radical, or a biaryl recombination product. In any case, the signal is extremely weak and this reaction cannot produce iodide. We expect this reaction to be negligible when Ir(ppy)₃ and N-bipyridine complexes are present, as they have much higher absorbance at 355 nm at the concentrations used in comparison to 4-IBzCF₃. Further, under catalysis conditions, the absorption of 4-IBzCF₃ is negligible as it does not absorb blue light significantly.

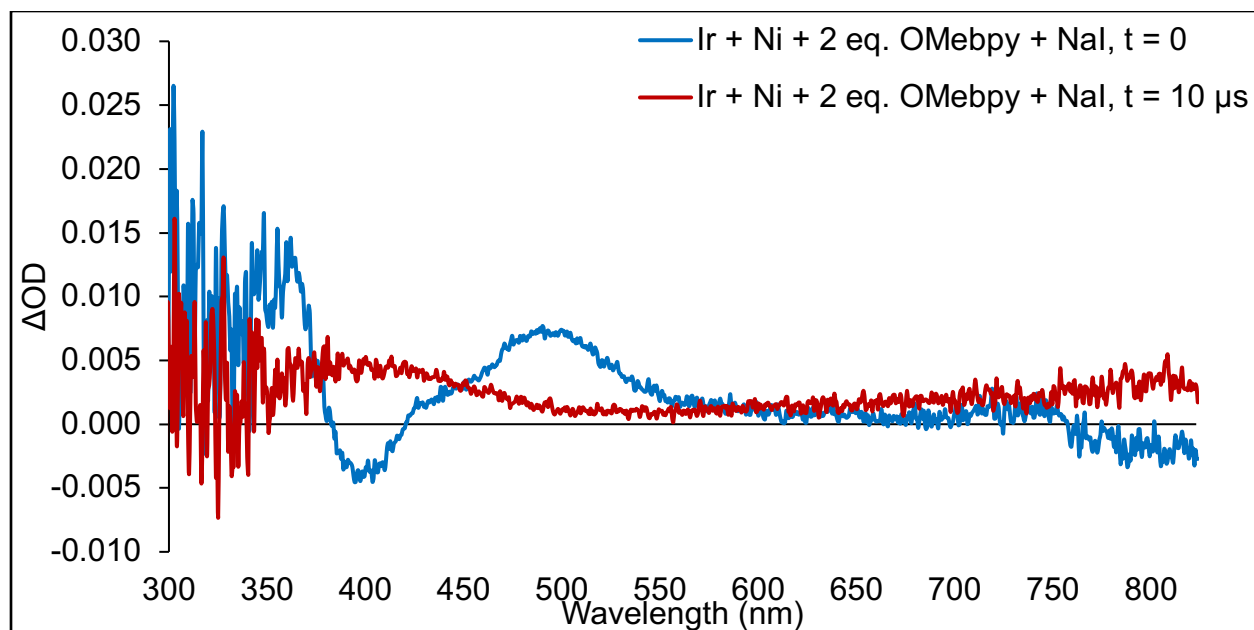


Figure S4.50. Spectral traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) + NaI (300 mM) at the indicated time delays.

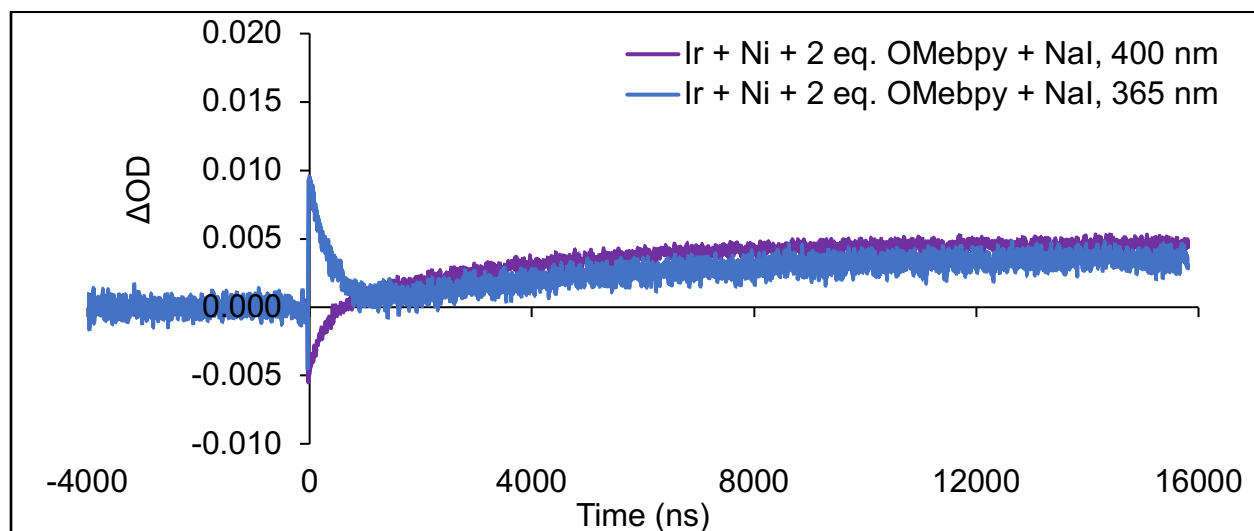


Figure S4.51. Kinetic traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of Ir(ppy)_3 ($31.4 \mu\text{M}$ in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) + NaI (300 mM) at $\lambda_{\text{probe}} = 365 \text{ nm}$ or 400 nm .

In the presence of large quantities of iodide in solution (without aryl iodide), the spectral traces show a rapidly quenched Ir(ppy)_3 excited state which presumably is oxidized to Ir(IV) , producing Ni(I) . Ir(IV) signals are not observed at $t = 10 \mu\text{s}$, consistent with a fast oxidation of iodide by Ir(IV) . A persistent broad signal centered at approximately 400 nm forms within $20 \mu\text{s}$

and is likely due to the production of $I_2^{\cdot-}$ ($\lambda_{\text{max}} = 385 \text{ nm}$, molar absorptivity $8,600 \text{ M}^{-1} \text{ cm}^{-1}$ in water)¹¹ derived from the diffusion-limited reaction of $I^{\cdot}$ with iodide, as well as the possible presence of Ni(I) (see Spectroelectrochemistry section). Ni(I) is likely also consumed by reaction with $I^{\cdot}$ to form a Ni(II) iodide species.

Ir(ppy)₃ with Tetrabutylammonium Iodide (TBAI):

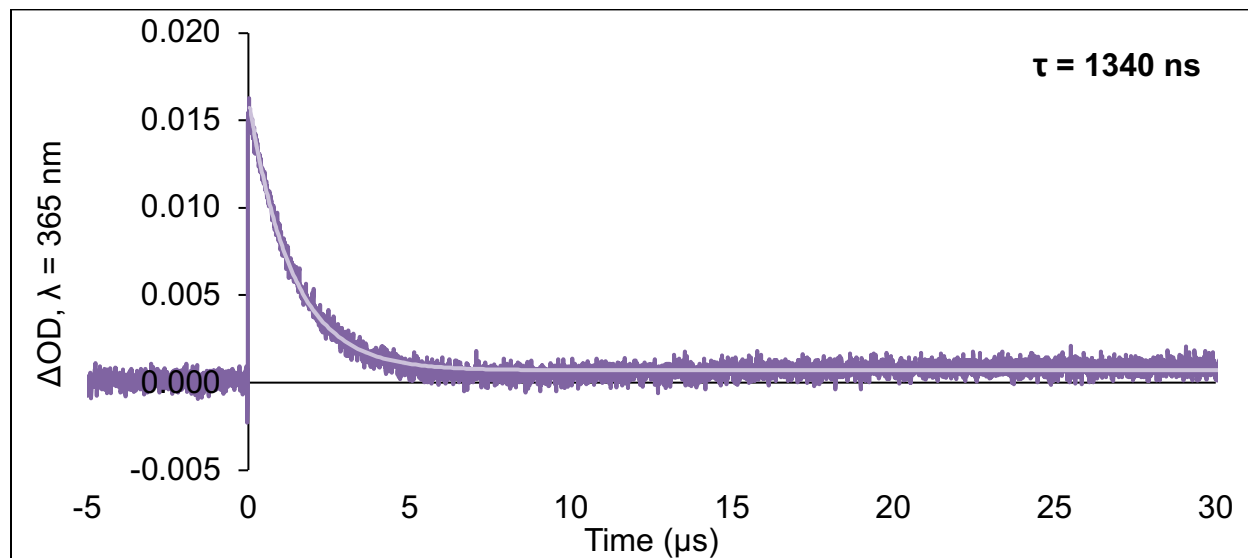


Figure S4.52. Kinetic trace for Ir(ppy)₃ (15.7 μM) with TBAI (0.10 M) in DMF at $\lambda_{\text{probe}} = 365 \text{ nm}$.

To evaluate if Ir(III)* can be quenched by direct oxidation of iodide, a control experiment was carried out with Ir(ppy)₃ and TBAI in DMF. We hypothesized that direct oxidation iodide by Ir(III)* would not occur. This data indicates Ir(III)* is not quenched by direct oxidation of iodide as the lifetime of this solution decreased negligibly (1.34 μs) .

3.5 Oxidative Quenching of Phenoxazine PC 2 by Ni(II).

In this section we observe reduction of a Ni-OMebpy mixture by the PhenO excited state.

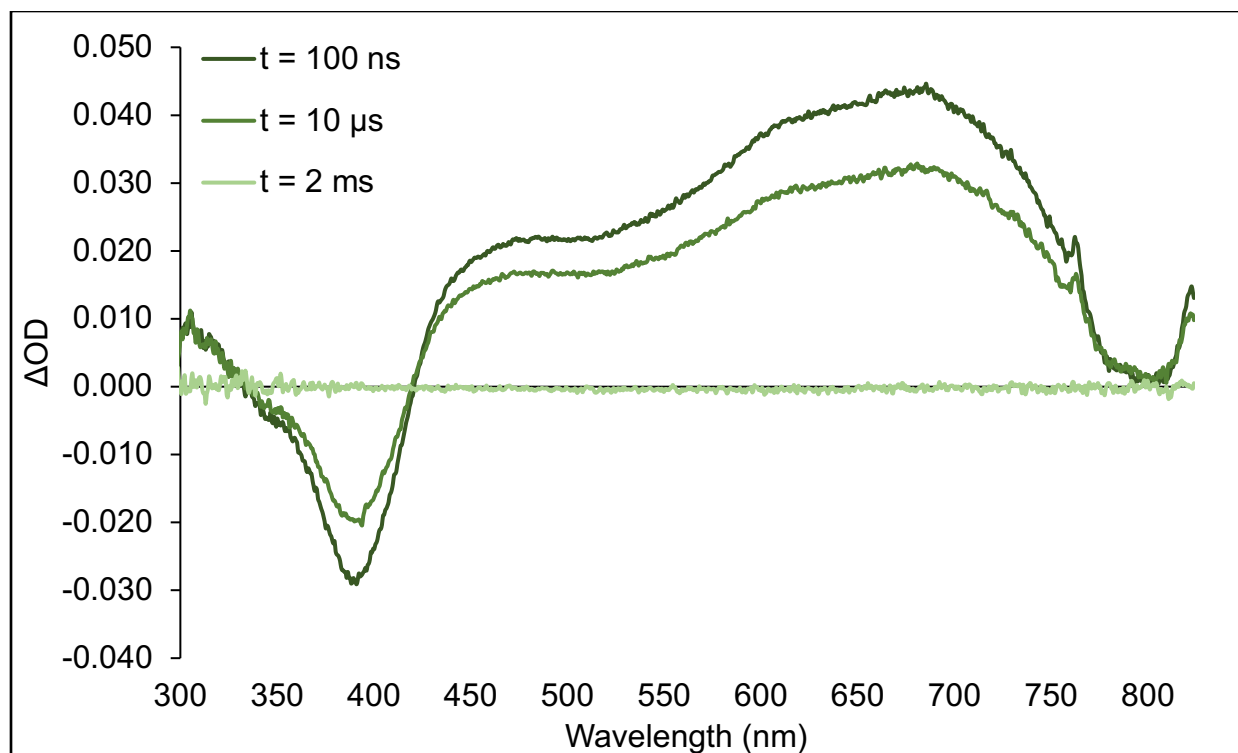


Figure S4.53. Spectral traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of PhenO ($10 \mu\text{M}$ in DMF) at the indicated time delays.

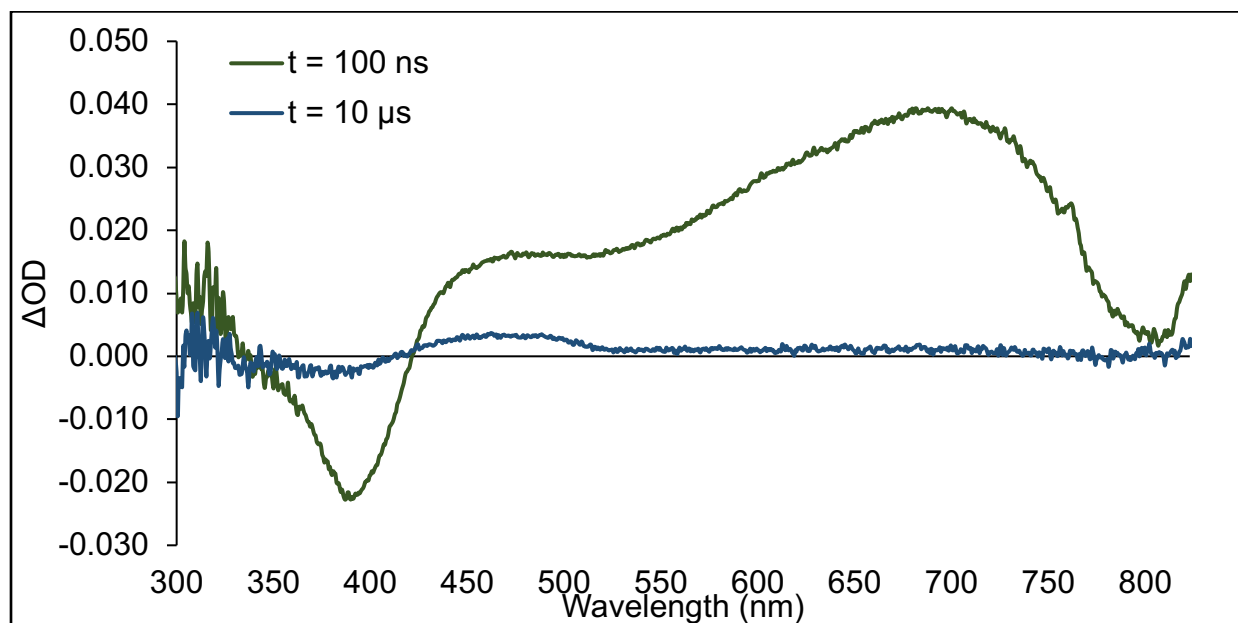


Figure S4.54. Spectral traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of PhenO ($10 \mu\text{M}$ in DMF) + NiBr₂•glyme (1.5 mM) + OMeppy (3.0 mM) at the indicated time delays.

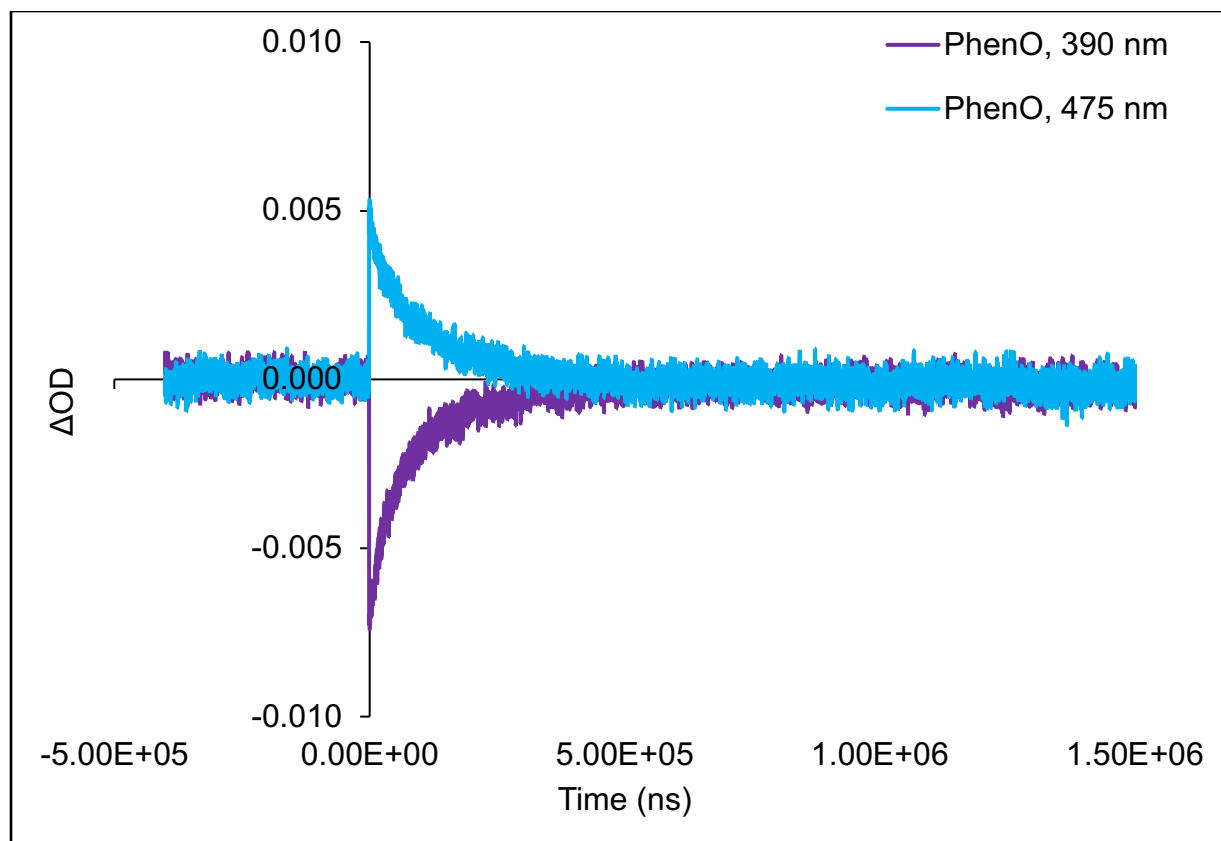


Figure S4.55. Kinetic traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of of PhenO (10 μM) at $\lambda_{\text{probe}} = 390 \text{ nm}$ or 475 nm.

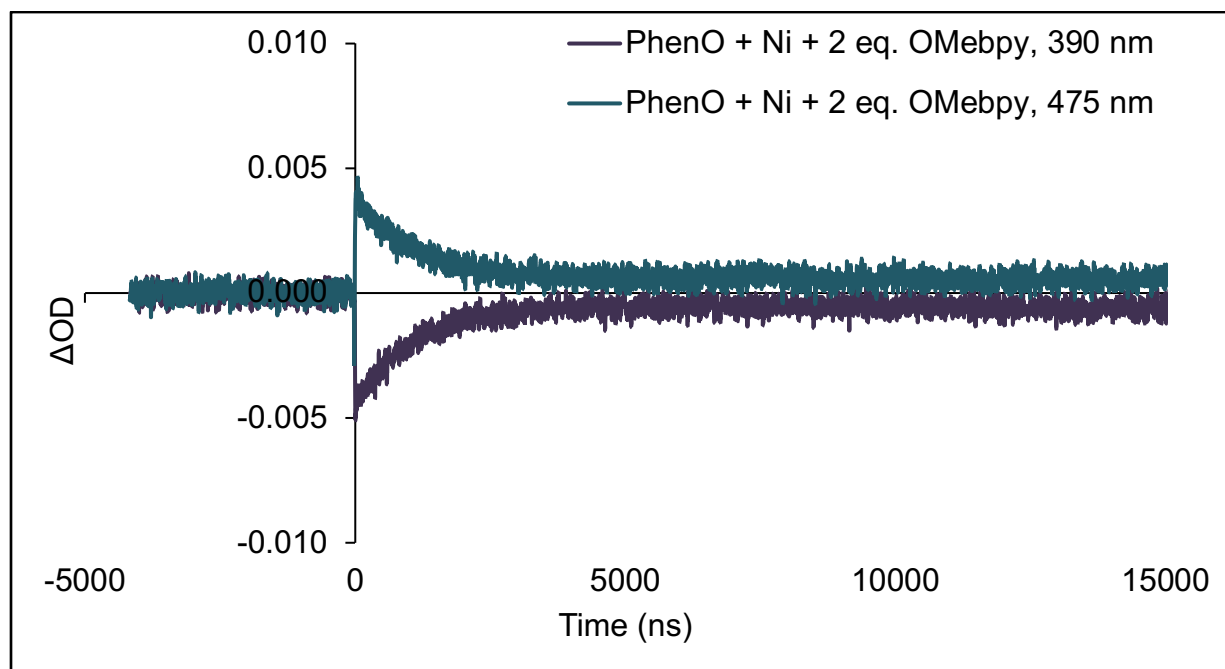


Figure S4.56. Kinetic traces ($\lambda_{\text{pump}} = 355 \text{ nm}$) of PhenO (10 μM) + NiBr₂•glyme (1.5 mM) + OMeby (3.0 mM) at $\lambda_{\text{probe}} = 390 \text{ nm}$ or 475 nm.

We note that a significantly lower laser power (0.4 mW) was used for kinetic experiments with the PhenO PC due to its extremely long-lived triplet state to avoid triplet-triplet annihilation as a competing pathway. In the presence of the Ni-OMebpy mixture, the prominent excited state absorption feature of the PhenO excited state at ~ 700 nm is completely quenched by 10 μ s, while persistent signals at ~ 390 nm and ~ 480 nm remain. Following the kinetics at 390 nm and 475 nm reveals that these signals do not return to baseline on the timescale of the excited state quenching event. Further, the PhenO excited state lifetime is quenched more than 100-fold. The major species contributing to the persistent signals can be assigned to the PhenO radical cation on the basis of reported spectroelectrochemistry data.¹²⁻¹³ The reduced Ni species also contributes to these spectra (see Spectroelectrochemistry section) in the region between 350-520 nm but is expected to have significantly lower molar absorptivity than the PhenO radical cation.

3.6 Stern-Volmer Quenching Experiments.

Kinetic traces were collected as described above with varying loading of a NiBr₂•glyme + N eq. OMebpy mixture, where N = 1, 2, or 3. A stock solution was made containing NiBr₂•glyme (15 mM in DMF) + N eq. OMebpy (15*N mM in DMF). A second stock solution was made containing Ir(ppy)₃ (1.57 mM in DMF) from which 30 μ L was added to each mixture (final conc. 15.7 μ M). The Ir(ppy)₃ concentration used here was half that in the above section to increase the maximum Ir:Ni ratio without increasing the Ni concentration beyond a practical level. The two stock solutions were mixed as appropriate and DMF was added to complete a 3 mL mixture ready for analysis. All solutions were made in a N₂ filled glovebox in Kontes valve screw cap quartz cuvettes. The information for a typical experiment is reported in the following table.

Table S4.4. Concentrations and molar ratios for Stern-Volmer quenching experiments.

mL Ni Stock	Ni:Ir Molar Ratio	DMF volume (mL)	Ni conc. (mM)
0.300	96	2.670	1.5
0.240	76	2.730	1.2
0.180	57	2.790	0.9
0.120	38	2.850	0.6
0.080	25	2.890	0.4
0.040	13	2.930	0.2

Stern Volmer quenching varying ratio of Ni:Ligand:

The lifetimes obtained from fitting the long time component data for each solution (1, 2, and 3 eq. OMeppy relative to Ni, shown below) were set as fixed in the biexponential fit to obtain a more accurate lifetime for the short component. Those short component lifetimes are used in the Stern Volmer plots.

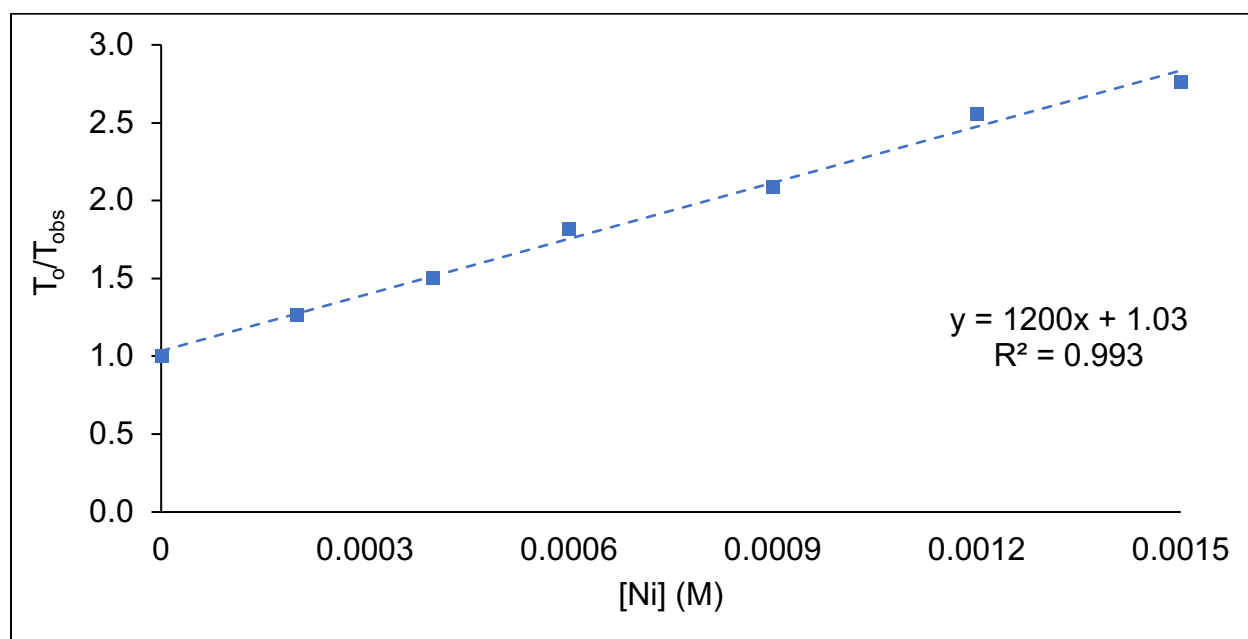


Figure S4.57. Stern-Volmer plots for mixtures containing $Ir(ppy)_3$ and Ni + OMeppy (1 eq. relative to Ni) as a function of total Ni concentration at $\lambda_{pump} = 355 \text{ nm}$, $\lambda_{probe} = 365 \text{ nm}$. τ_0 and τ_{obs} are the excited state lifetimes of $Ir(ppy)_3$ without and with the Ni-OMeppy mixture present, respectively. Here a monoexponential fit was applied – comparison to Figure S4.59 below demonstrates that a better fit, as indicated by a higher R^2 value, is obtained with when a biexponential fit is used.

1 eq. OMebpy:

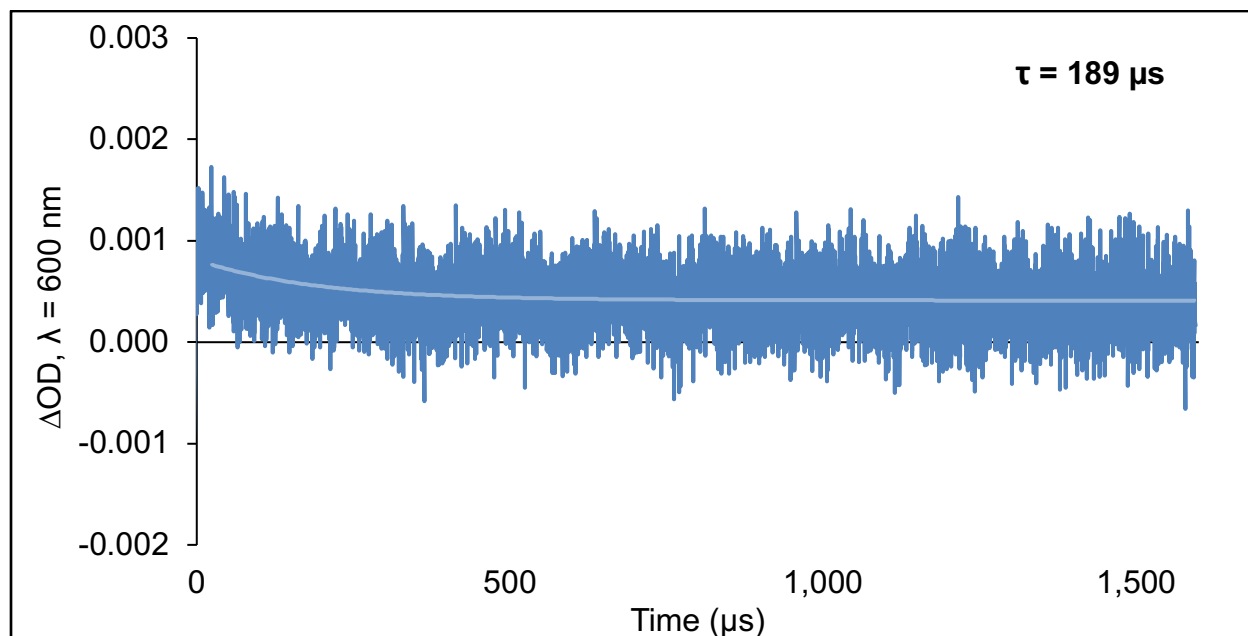


Figure S4.58. Long time component (2000 μs) kinetic trace for $\text{Ir}(\text{ppy})_3$ (15.7 μM) and $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) with OMebpy ligand (1.5 mM, 1 eq. relative to Ni) at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 600 \text{ nm}$.

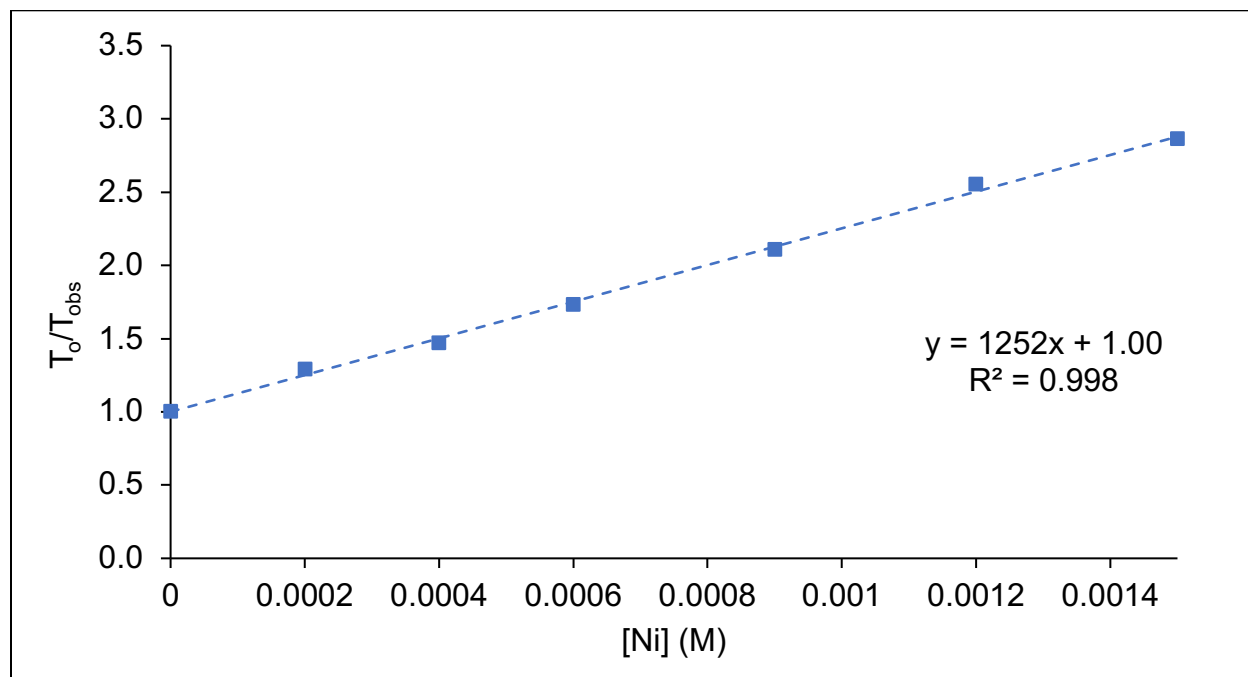


Figure S4.59. Stern-Volmer plots for mixtures containing $\text{Ir}(\text{ppy})_3$ and Ni + OMebpy (1 eq. relative to Ni) as a function of total Ni concentration at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 365 \text{ nm}$. A biexponential fit with a fixed long time component was applied. τ_0 and τ_{obs} are the excited state lifetimes of $\text{Ir}(\text{ppy})_3$ without and with the Ni-OMebpy mixture present, respectively.

From the above Stern-Volmer plots, $k_q = b/\tau_0$, (see literature for kinetic derivation of the Stern-Volmer relationship)¹⁴ where b is the slope of the linear regression line. Analysis of the Stern-Volmer plots gives a quenching rate constant of $8.3 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ (365 nm).

2 eq. OMeppy:

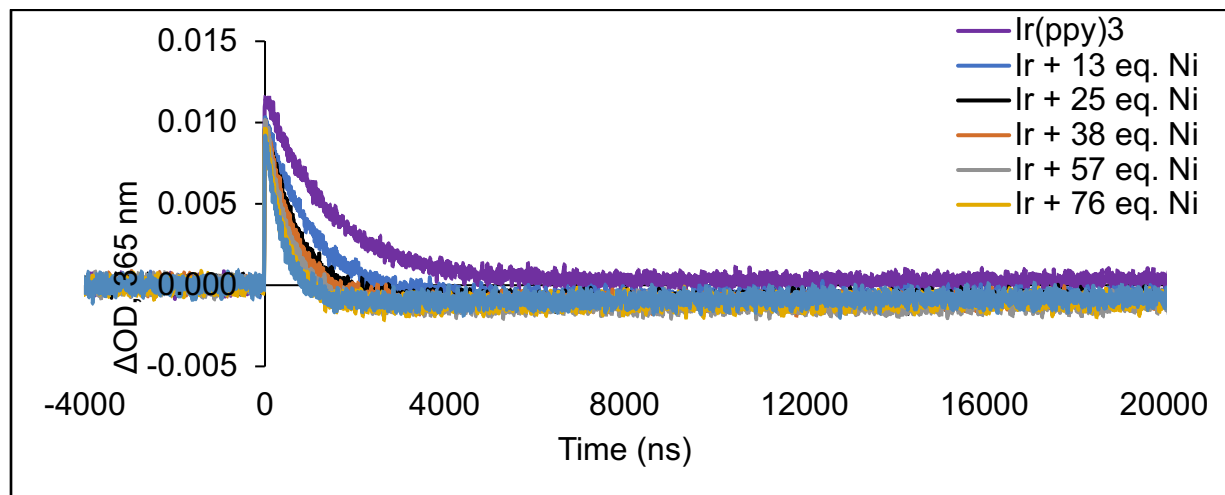


Figure S4.60. Raw kinetic traces of $[\text{Ir}(\text{ppy})_3]$ ($15.7 \mu\text{M}$ in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ ($0.2\text{-}1.5 \text{ mM}$) + OMeppy ($N = 2$, 2 eq. relative to Ni, $0.4\text{-}3.0 \text{ mM}$) at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 365 \text{ nm}$.

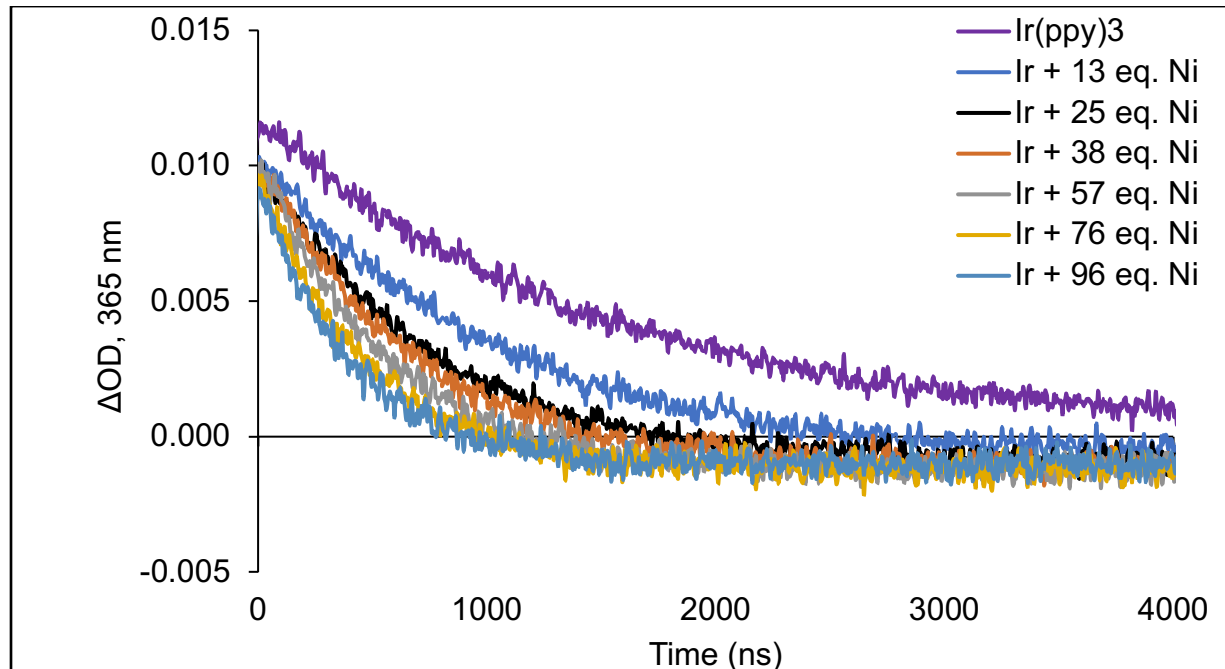


Figure S4.61. Raw kinetic traces of $\text{Ir}(\text{ppy})_3$ ($15.7 \mu\text{M}$ in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ ($0.2\text{-}1.5 \text{ mM}$) + OMeppy ($N = 2$, 2 eq. relative to Ni, $0.4\text{-}3.0 \text{ mM}$) at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 365 \text{ nm}$. Zoomed in on the initial 4000 ns of signal.

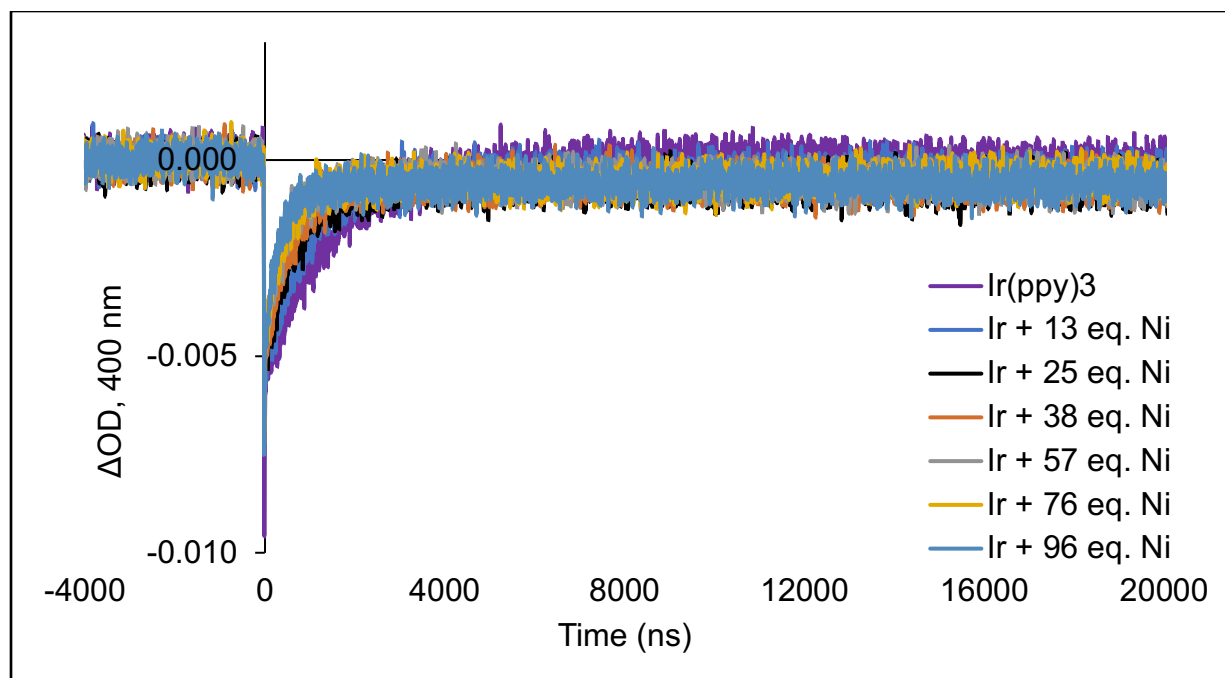


Figure S4.62. Raw kinetic traces of Ir(ppy)_3 ($15.7 \mu\text{M}$ in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ ($0.2\text{--}1.5 \text{ mM}$) + OMebpy ($N = 2$, 2 eq. relative to Ni, $0.4\text{--}3.0 \text{ mM}$) at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 400 \text{ nm}$.

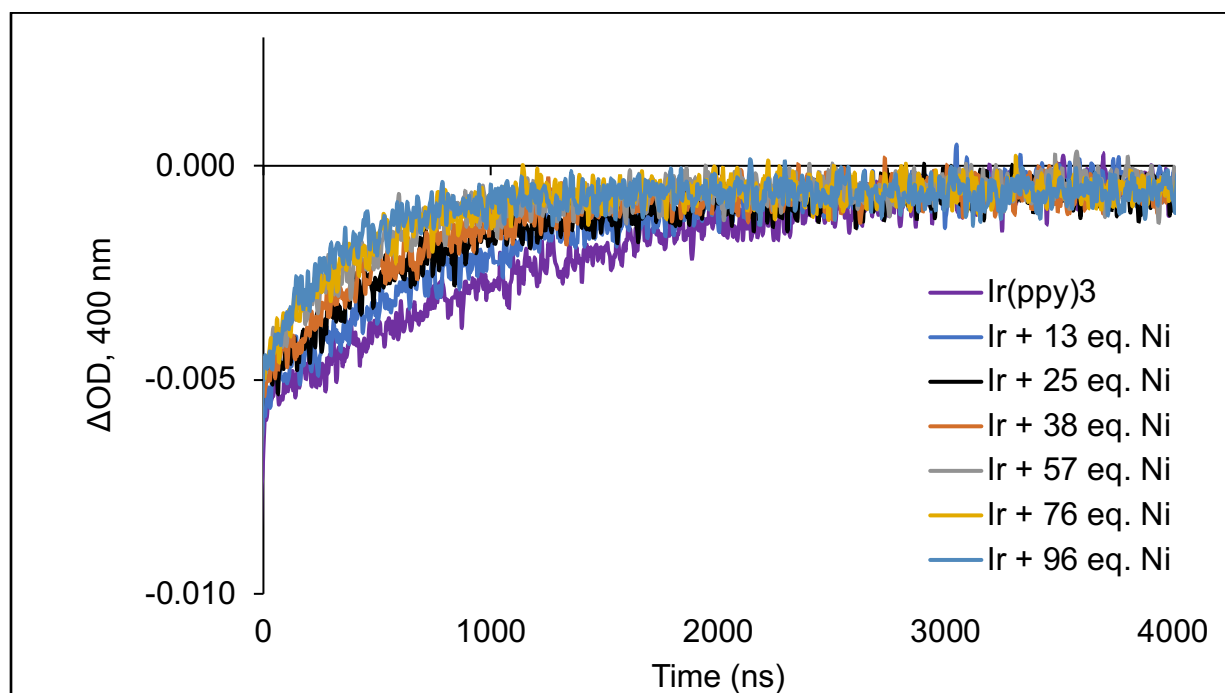


Figure S4.63. Raw kinetic traces of Ir(ppy)_3 ($15.7 \mu\text{M}$ in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ ($0.2\text{--}1.5 \text{ mM}$) + OMebpy ($N = 2$, 2 eq. relative to Ni, $0.4\text{--}3.0 \text{ mM}$) at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 400 \text{ nm}$. Zoomed in on the initial 4000 ns of signal.

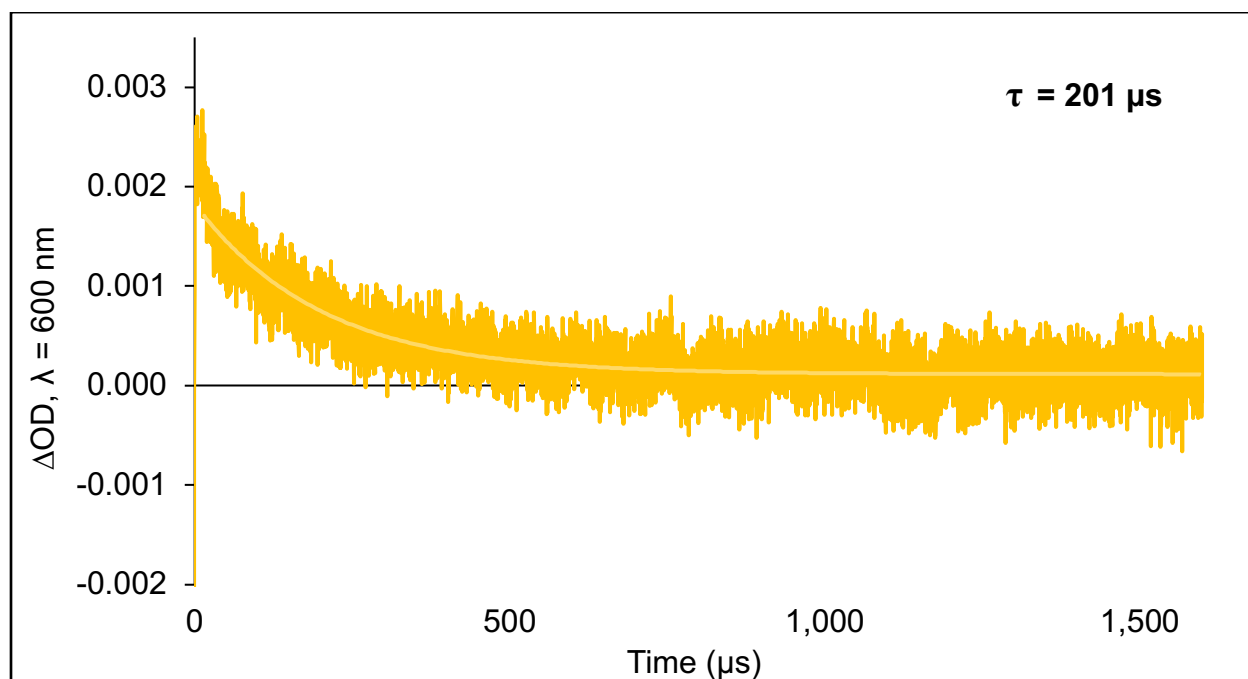


Figure S4.64. Long time component (2000 μs) kinetic trace for $\text{Ir}(\text{ppy})_3$ (15.7 μM) and $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) with OMeppy ligand (3.0 mM, 2 eq. relative to Ni) at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 600 \text{ nm}$.

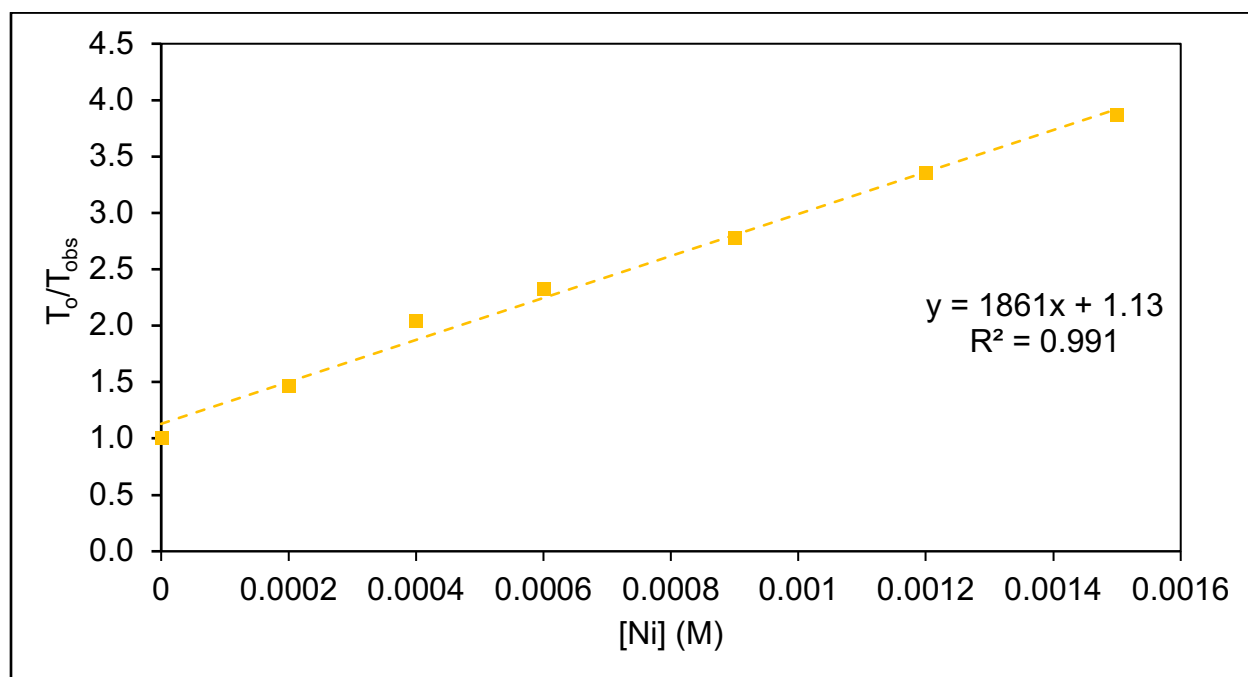


Figure S4.65. Stern-Volmer plots for mixtures containing $\text{Ir}(\text{ppy})_3$ and Ni + OMeppy (2 eq. relative to Ni) as a function of total Ni concentration at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 365 \text{ nm}$. A biexponential fit with a fixed long time component was applied. τ_0 and τ_{obs} are the excited state lifetimes of $\text{Ir}(\text{ppy})_3$ without and with the Ni-OMeppy mixture present, respectively.

From the above Stern-Volmer plots, $k_q = b/\tau_0$, (see literature for kinetic derivation of the Stern-Volmer relationship)¹⁴ where b is the slope of the linear regression line. Analysis of the Stern-Volmer plots gives a quenching rate constant of $1.2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ (365 nm).

3 eq. OMebpy:

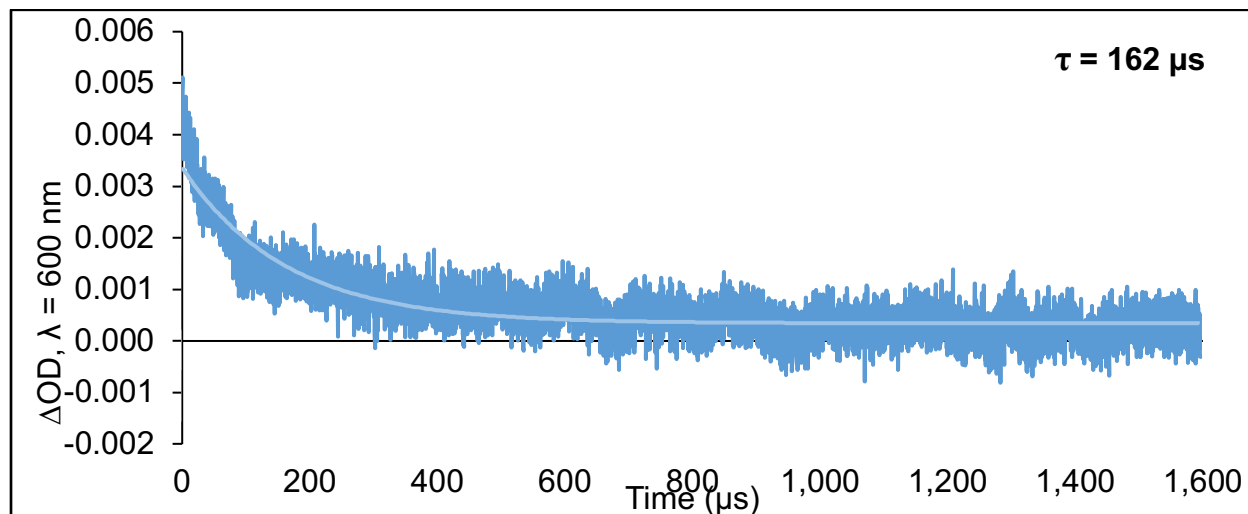


Figure S4.66. Long time component (2000 μs) kinetic trace for $\text{Ir}(\text{ppy})_3$ (15.7 μM) and $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) with OMebpy ligand (4.5 mM, 3 eq. relative to Ni) in DMF at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 600 \text{ nm}$.

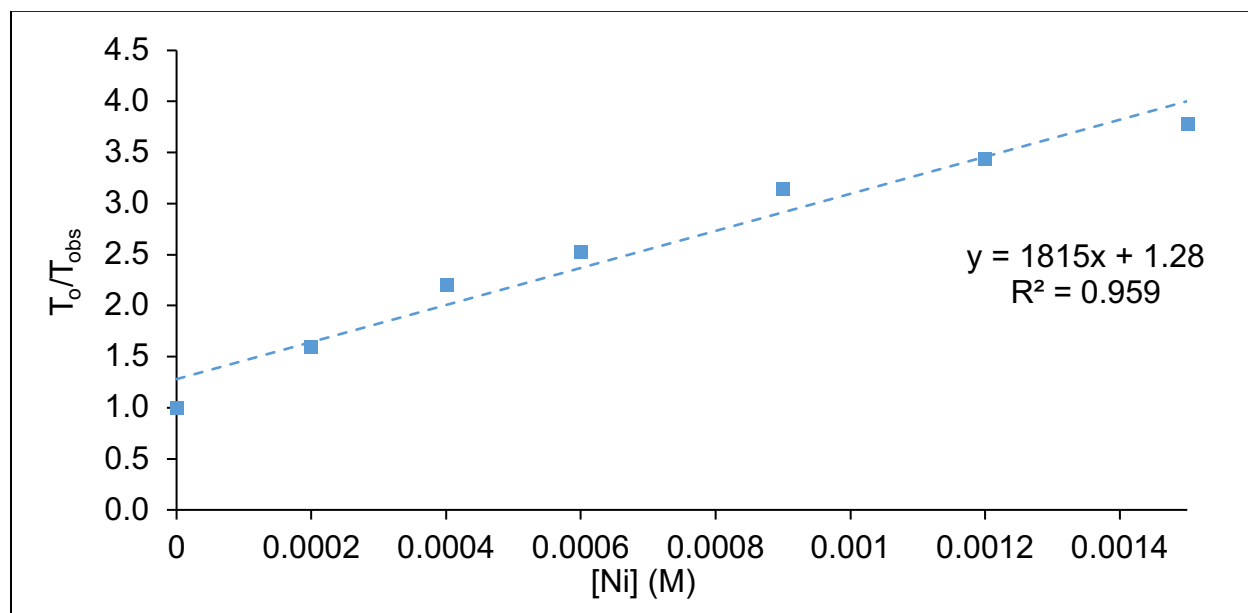


Figure S4.67. Stern-Volmer plots for mixtures containing $\text{Ir}(\text{ppy})_3$ and Ni + OMebpy (3 eq. relative to Ni) as a function of total Ni concentration at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 365 \text{ nm}$. A biexponential fit with a fixed long time component was applied. τ_0 and τ_{obs} are the excited state lifetimes of $\text{Ir}(\text{ppy})_3$ without and with the Ni-OMebpy mixture present, respectively. First of two repeats.

From the above Stern-Volmer plots, $k_q = b/\tau_0$, (see literature for kinetic derivation of the Stern-Volmer relationship)¹⁴ where b is the slope of the linear regression line. Analysis of the Stern-Volmer plots gives a quenching rate constant of $1.2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ (365 nm).

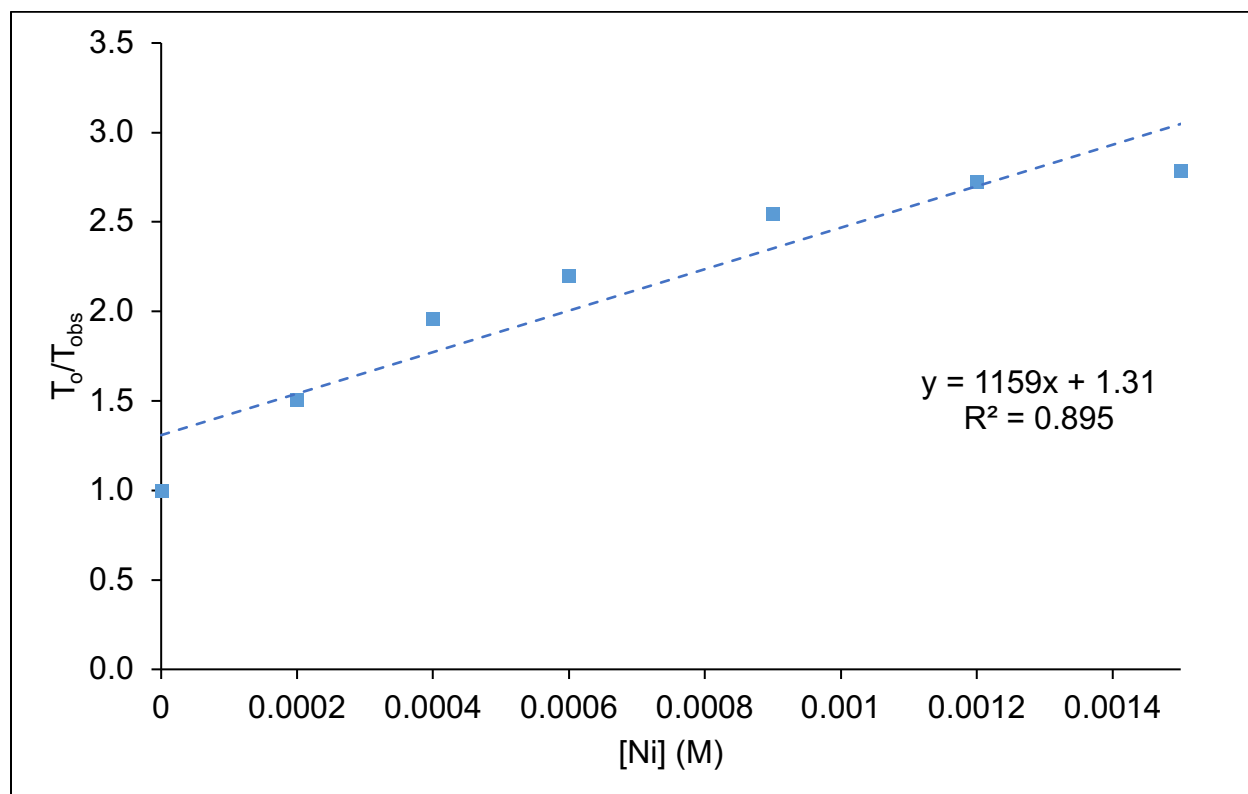


Figure S4.68. Stern-Volmer plots for mixtures containing Ir(ppy)_3 and $\text{Ni} + \text{OMebpy}$ (1 eq. relative to Ni) as a function of total Ni concentration at $\lambda_{\text{pump}} = 355 \text{ nm}$, $\lambda_{\text{probe}} = 365 \text{ nm}$. A biexponential fit with a fixed long time component was applied. τ_0 and τ_{obs} are the excited state lifetimes of Ir(ppy)_3 without and with the Ni-OMebpy mixture present, respectively. Second of two repeats.

From the above Stern-Volmer plots, $k_q = b/\tau_0$, (see literature for kinetic derivation of the Stern-Volmer relationship)¹⁴ where b is the slope of the linear regression line. Analysis of the Stern-Volmer plots gives a quenching rate constant of $7.7 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ (365 nm).

The lack of linearity in quenching plots for mixtures with 3 eq. OMebpy ligand present suggests a mechanism more complicated than that assumed in derivation of the Stern-Volmer equation. We hypothesize that $[\text{Ni(OMebpy)}_3]\text{Br}_2$, which is the main quencher present here, may undergo dissociation of an OMebpy ligand following reduction. Reassociation could involve a

second Ni complex and thus would depend on total Ni concentration. Further investigation of this unusual behavior is in progress.

PhenO PC Stern-Volmer:

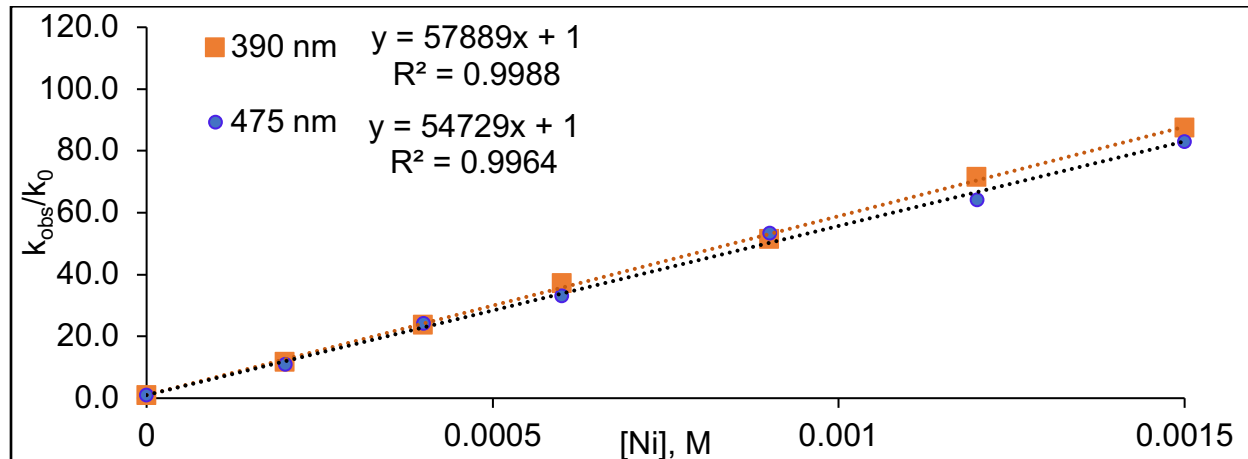


Figure S4.69. Stern-Volmer plots for mixtures containing PhenO + Ni + OMebpy (2 eq. relative to Ni) as a function of total Ni concentration. k_{obs} is the observed rate constant ($1/\tau_{obs}$) in the presence of quencher and k_0 is the excited state decay rate constant ($1/\tau_0$) of PhenO in absence of quencher. τ_0 and τ_{obs} are the excited state lifetimes of PhenO without and with the Ni-OMebpy mixture present, respectively.

From the above Stern-Volmer plots, $k_q = b/\tau_0$, (see literature for kinetic derivation of the Stern-Volmer relationship)¹⁴ where b is the slope of the linear regression line. Analysis of the Stern-Volmer plots gives a quenching rate constant of $6.6 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ (390 nm) or $6.3 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ (475 nm).

4. Time-Correlated Single Photon Counting

General procedure:

A commercial spectrometer (Edinburgh Instruments FS5) was equipped with a pulsed light emitting diode (Edinburgh Instruments EPLED 365 nm) and utilized for time-correlated single photon counting according to the manufacturer's instructions. Samples were prepared in airtight quartz cuvettes with Kontes screw capped valves in a N_2 -filled glovebox as described in section 3. Data was acquired over a 200 ns time window with a step size of 0.195 ns and a stop condition of

2000 counts. The repetition rate of the EPLED was 0.5 MHz. The instrumental response function (IRF) was measured utilizing a scattering suspension (chalk in H₂O). Data was fit taking into account the IRF using a reconvolution fit as defined in the instrument software.

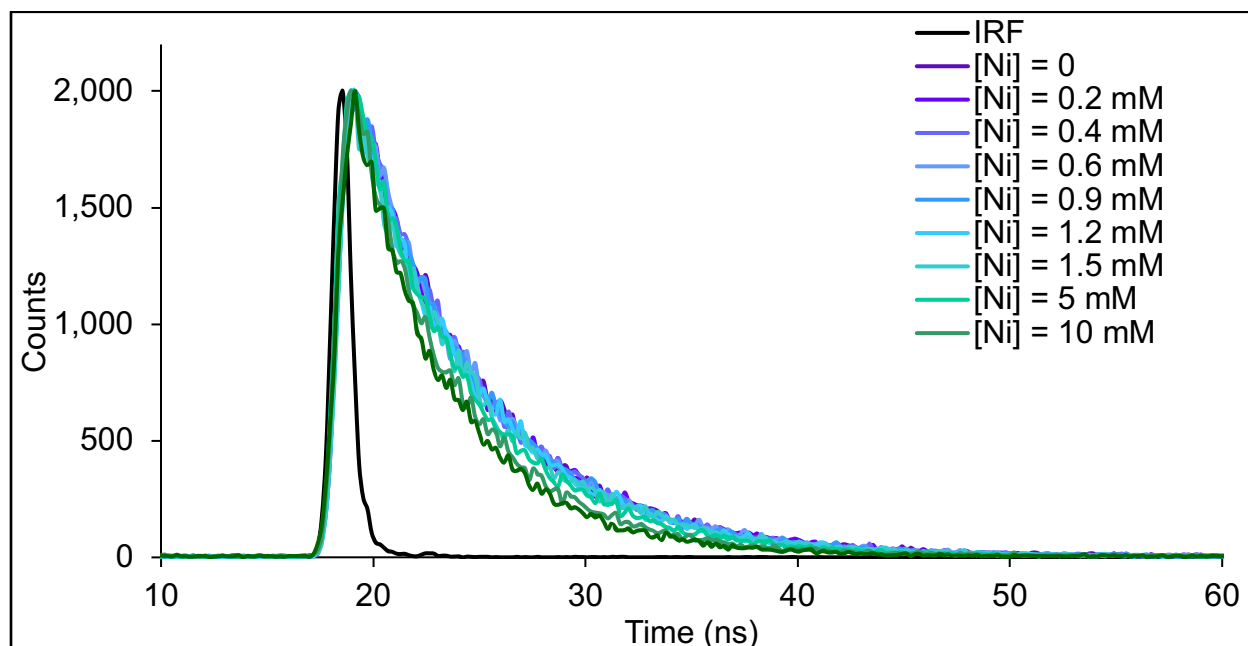


Figure S4.70. Raw kinetic traces ($\lambda_{exc} = 365 \text{ nm}$, $\lambda_{probe} = 510 \text{ nm}$) of PhenO ($10 \mu\text{M}$ in DMF) either with or without NiBr₂•glyme (0.2-14.5 mM) + OMeppy ($N = 2$, 2 eq. relative to Ni, 0.4-29.0 mM).

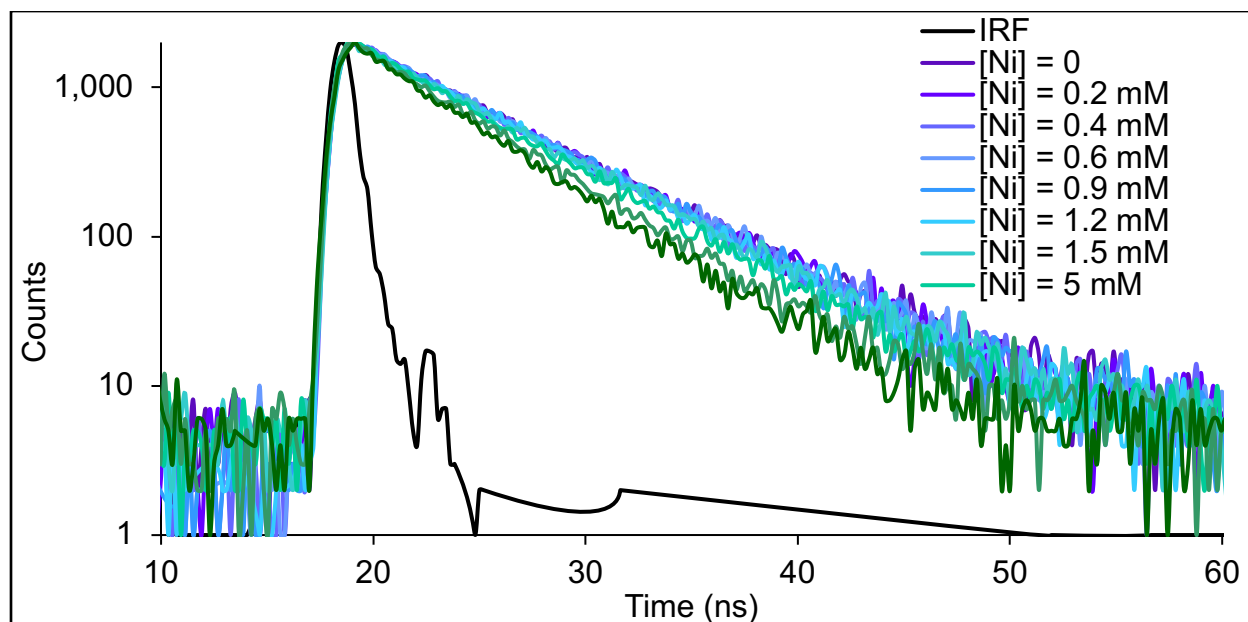


Figure S4.71. Raw kinetic traces ($\lambda_{exc} = 365 \text{ nm}$, $\lambda_{probe} = 510 \text{ nm}$) of PhenO ($10 \mu\text{M}$ in DMF) either with or without NiBr₂•glyme (0.2-14.5 mM) + OMeppy ($N = 2$, 2 eq. relative to Ni, 0.4-29.0 mM).

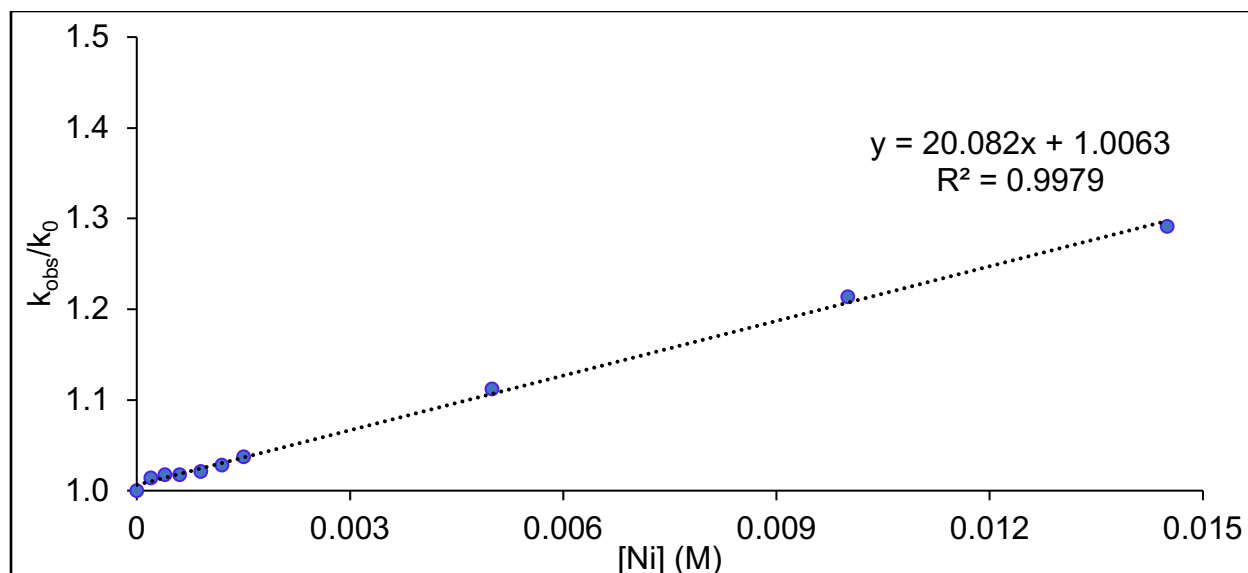


Figure S4.72. Stern-Volmer plot for mixtures containing PhenO + Ni + OMeppy (2 eq. relative to Ni) as a function of total Ni concentration. k_{obs} is the observed rate constant ($1/\tau_{obs}$) in the presence of quencher and k_0 is the excited state decay rate constant ($1/\tau_0$) of PhenO in absence of quencher. τ_0 and τ_{obs} are the excited state lifetimes of PhenO without and with the Ni-OMeppy mixture present, respectively.

From the above Stern-Volmer plot, $k_q = b/\tau_0$, (see literature for kinetic derivation of the Stern-Volmer relationship)¹⁴ where b is the slope of the linear regression line. Analysis of the Stern-Volmer plot gives a quenching rate constant of $3.4 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$.

5. Cyclic Voltammetry and Spectroelectrochemistry

5.1 Cyclic Voltammetry.

General procedure:

In an electrochemical cell consisting of a 5-necked flask containing a glassy carbon working electrode (IKA), a Pt wire counter electrode (Pt wire, 0.100 M Bu_4NPF_6 in DMF, separated from analyte by Vycor frit), and an Ag/AgNO₃ reference electrode (silver wire, Vycor frit, 0.01 M AgNO₃ in acetonitrile with 0.100 M Bu_4NPF_6 electrolyte), an analyte solution in DMF containing dissolved Bu_4NPF_6 (0.100 M) electrolyte was probed utilizing a potentiostat (Gamry Instruments) to perform cyclic voltammetry. All reported experiments were performed at a 100 mV/s scan rate. Prior to measurement, the cell was sealed with Parafilm and degassed by bubbling

with Ar for 10 minutes. Ferrocene (Fc) oxidation to ferrocenium (Fc^+) was evaluated separately prior to analyte runs. Between analyte solutions, the working electrode was rinsed with DMF and then polished with an electrode polishing pad and cleaning slurry, followed by sonication in H_2O for 5 min and then MeOH for 5 min.

Potentials in figures below are vs. Ag/AgNO_3 pseudoreference electrode and can be accordingly converted to vs. ferrocene/ferrocenium by subtracting 0.067 V (measured $E_{1/2}$ of Fc/Fc^+). Potentials were further converted to the saturated calomel electrode (SCE) using a reported measurement for the Fc/Fc^+ couple in DMF ($E_{1/2} = 0.40$ V vs. SCE).²¹

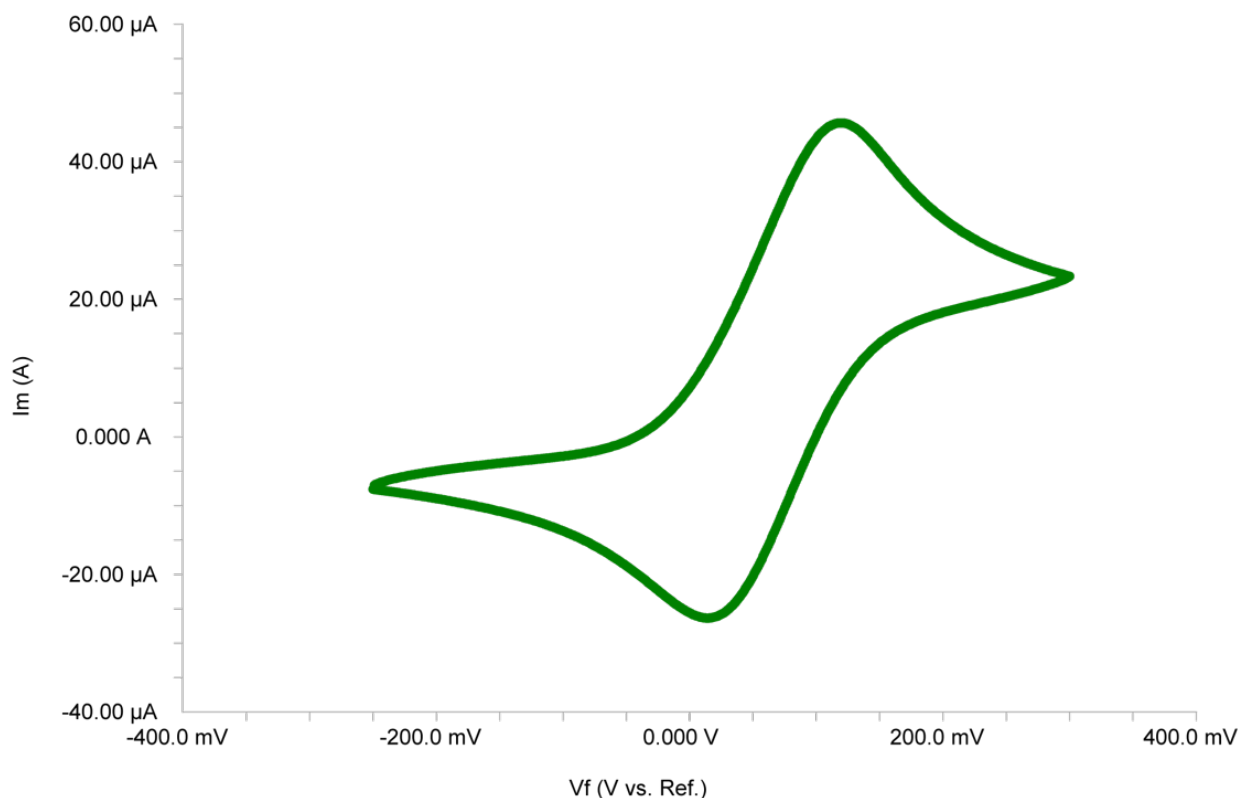


Figure S4.73. Cyclic voltammetry of ferrocene (2 mM in DMF). Scan rate = 100 mV/s. Potentials vs. Ag/AgNO_3 . For peak values, see table below.

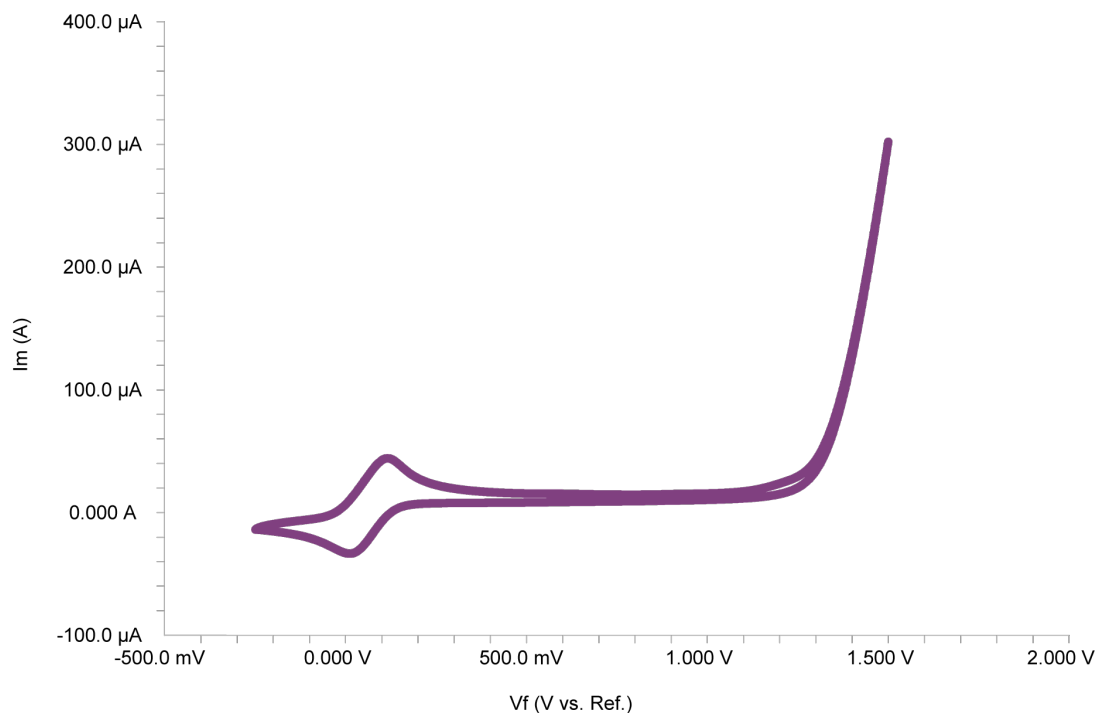


Figure S4.74. Cyclic voltammetry of ferrocene (2 mM in DMF) showing the potential window of DMF for oxidation. Scan rate = 100 mV/s. Potentials vs. Ag/AgNO₃.

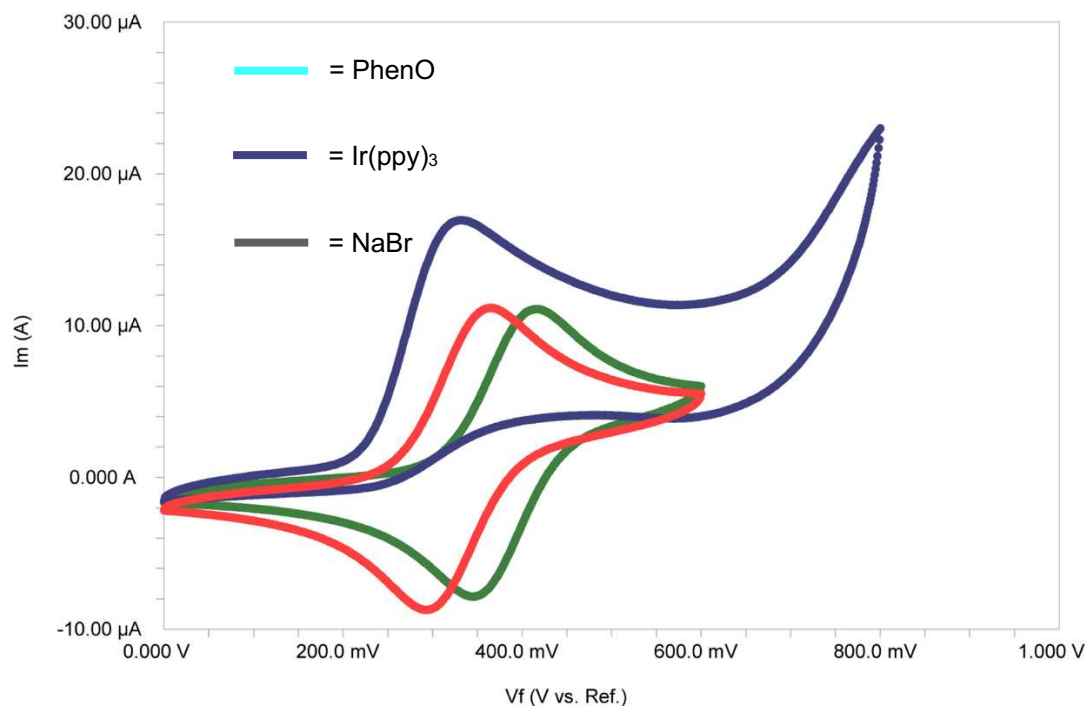


Figure S4.75. Cyclic voltammetry of PhenO (0.85 mM in DMF), Ir(ppy)₃ (0.79 mM in DMF), and NaBr (2.00 mM in DMF). Scan rate = 100 mV/s. Potentials vs. Ag/AgNO₃. For peak values, see table below.

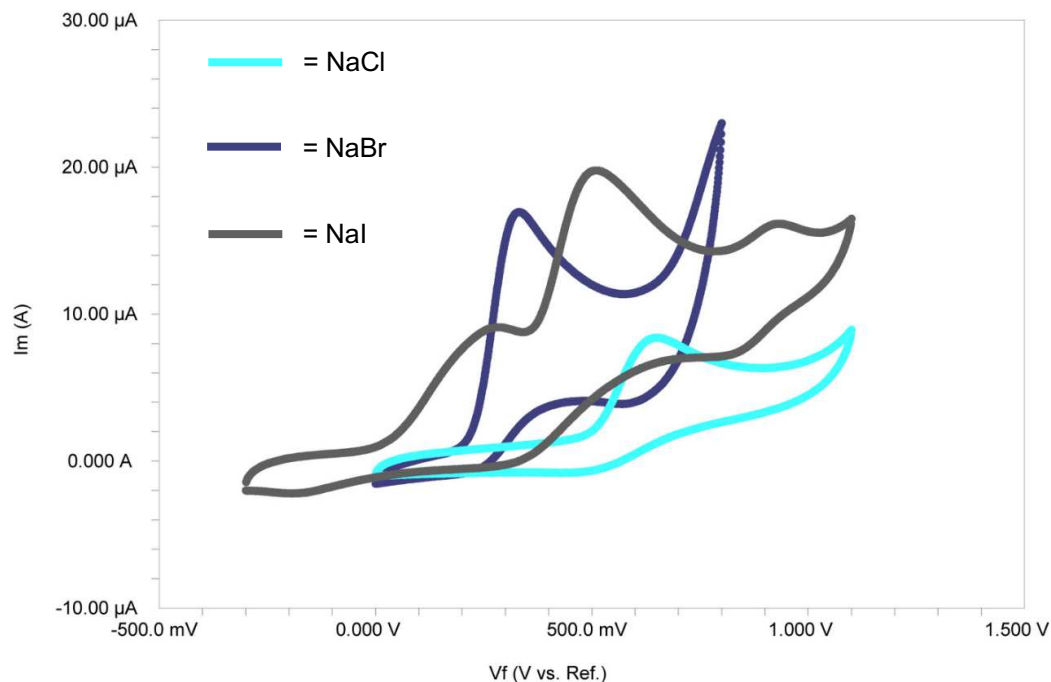


Figure S4.76. Cyclic voltammetry of NaCl (2.00 mM in DMF), NaBr (2.00 mM in DMF), and NaI (2.00 mM in DMF). Scan rate = 100 mV/s. Potentials vs. Ag/AgNO₃. For peak values, see table below.

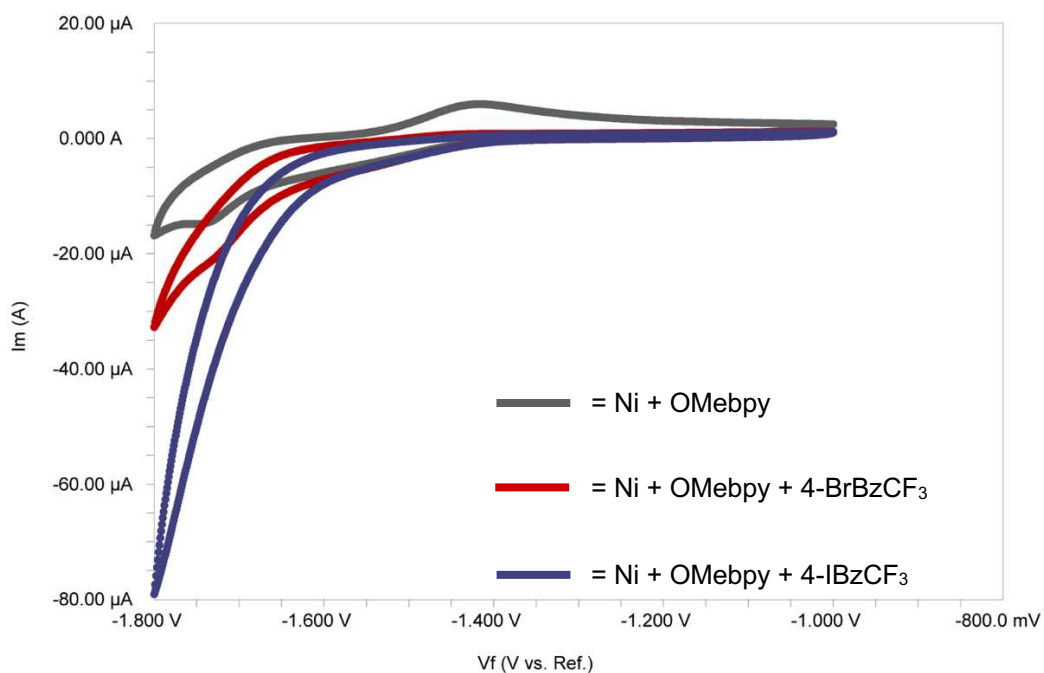


Figure S4.77. Cyclic voltammetry of a mixture containing NiBr₂•glyme (1.50 mM) + OMe bpy (2 eq. relative to Ni, 3.00 mM) either alone or with aryl halide (4-bromobenzotrifluoride or 4-iodobenzotrifluoride, 30 mM). Scan rate = 100 mV/s. Potentials vs. Ag/AgNO₃. For peak values, see table below.

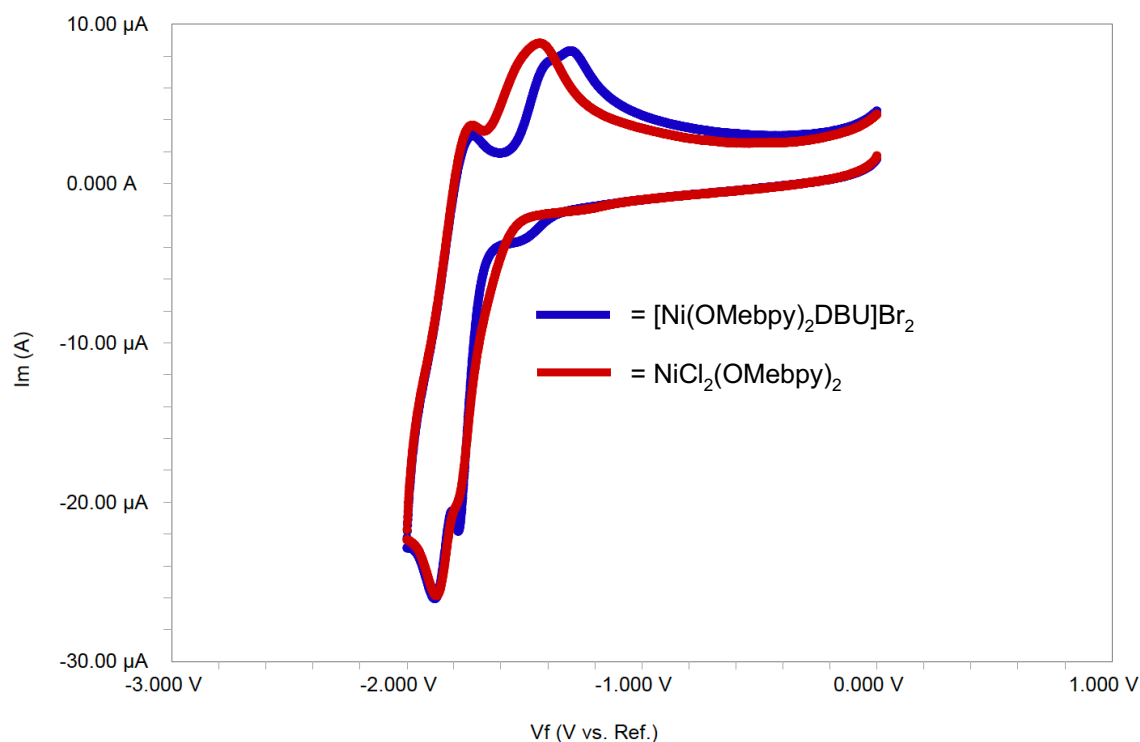


Figure S4.78. Cyclic voltammetry of a mixture containing $\text{NiBr}_2 \cdot \text{glyme}$ (2.0 mM) + OMebpy (2 eq. relative to Ni, 4.0 mM) with either DBU (40 eq. relative to Ni, 80 mM) alone or DBU and TBACl (20 eq. relative to Ni, 40 mM). Complex identities are hypothesized based on UV-vis and DRA experiments. Scan rate = 100 mV/s. Potentials vs. Ag/AgNO_3 . For peak values, see table below.

It is worth noting the presence of a very low intensity peak that is only present for the DBU complex. We believe this is a different species present in low concentrations and the rest of the two traces are nearly identical. Though the first peak is reported in the below table, the second peak is assigned as the $\text{Ni(II)}/\text{Ni(I)}$ couple for the complex of interest.

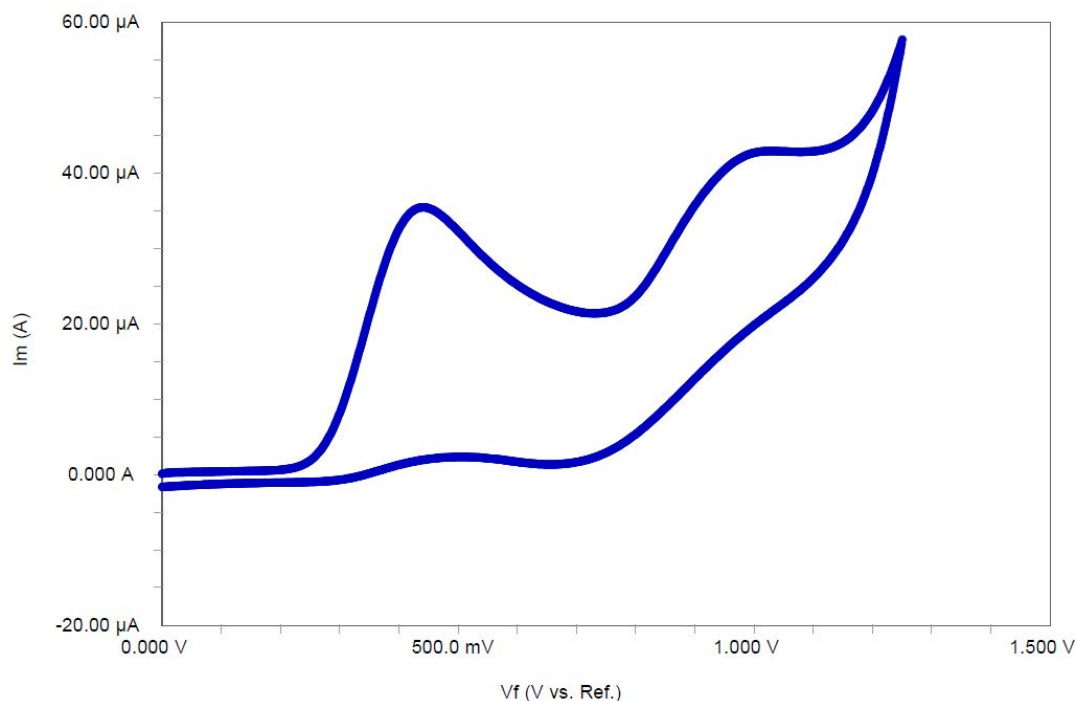


Figure S4.79. Oxidation of $\text{NiBr}_2\cdot\text{glyme}$ (2.0 mM) + OMebpy (4.0 mM, 2 eq. relative to Ni) solution in DMF with 0.1 M Bu_4NPF_6 .

Table S4.5. Measured potentials of various species in DMF. E_p is the peak value of the 1st irreversible peak unless otherwise indicated.

Redox Couple	Potential (V vs. Fc/Fc^+)	Potential (V vs. SCE) ^a
$\text{Cl}^-/\text{Cl}^\bullet$	$E_p = 0.58$	$E_p = 0.98$
$\text{Br}^-/\text{Br}^\bullet$	$E_p = 0.27$	$E_p = 0.67$
$\text{I}^-/\text{I}^\bullet$	$E_p = 0.21$	$E_p = 0.61$
$\text{Ir(III)(ppy)}_3/[\text{Ir(IV)(ppy)}_3]^+$	$E_{1/2} = 0.31$	$E_{1/2} = 0.71$
$\text{PhenO}/\text{PhenO}^{+\bullet}$	$E_{1/2} = 0.26$	$E_{1/2} = 0.66$
$^1\text{PhenO}^*/\text{PhenO}^{+\bullet}$	$E_{\text{red}}^* = -2.18^b$	$E_{\text{red}}^* = -1.73^b$
$^3\text{Ir(ppy)}_3/[\text{Ir(IV)(ppy)}_3]^+$	$E_{\text{red}}^* = -2.06^c$	$E_{\text{red}}^* = -1.66^c$
$\text{Ni(II)}/[\text{Ni(I)}]^-$, $\text{NiBr}_2\cdot\text{glyme}$ + 2 eq. OMebpy	$E_p = -1.63$	$E_p = -1.23$
$\text{Ni(II)}/[\text{Ni(I)}]^-$, $\text{NiBr}_2\cdot\text{glyme}$ + 2 eq. OMebpy	$E_p = -1.81^d$	$E_p = -1.41^d$
$\text{Br}^-/\text{Br}^\bullet$, $\text{NiBr}_2\cdot\text{glyme}$ + 2 eq. OMebpy	$E_p = 0.38^e$	$E_p = 0.78^e$
$\text{Br}^-/\text{Br}^\bullet$, $\text{NiBr}_2\cdot\text{glyme}$ + 2 eq. OMebpy	$E_p = 0.96^f$	$E_p = 1.36^f$
$\text{Ni(II)}/[\text{Ni(I)}]^-$, $[\text{Ni(OMebpy)}_2\text{DBU}]\text{Br}_2$	$E_p = -1.54$	$E_p = -1.14$
$\text{Ni(II)}/[\text{Ni(I)}]^-$, $[\text{Ni(OMebpy)}_2\text{DBU}]\text{Br}_2$	$E_p = -1.79^d$	$E_p = -1.39^d$
$\text{Ni(II)}/[\text{Ni(I)}]^-$, $\text{NiCl}_2(\text{OMebpy})_2$	$E_p = -1.79$	$E_p = -1.39$
Fc/Fc^+	$E_{1/2} = 0.00$	$E_{1/2} = 0.40$

^aliterature conversion value²¹ used for Fc/Fc^+ vs. SCE in DMF. ^bEstimated using the emission maximum, from reference²² Du et al. ^cEstimated using the emission maximum, 523 nm (2.37 eV). ^d2nd irreversible peak. ^eFirst oxidation peak for $\text{NiBr}_2\cdot\text{glyme}$ + 2 eq. OMebpy assigned to bromide bound to nickel. ^fSecond oxidation peak $\text{NiBr}_2\cdot\text{glyme}$ + 2 eq. OMebpy .

5.2 Spectroelectrochemistry.

The same setup was used as for CV except for several modifications. First, a fiber optic coupler and probe (1 cm path length, Harrick Scientific FiberMate) connected to the Agilent Cary 5000 UV-vis spectrometer was inserted into the 5-necked flask through the central neck. Second, a glassy carbon plate (1 cm x 5 cm, IKA) was used as the working electrode to increase the electrode surface area as compared with the electrode used for CV. Third, N₂ was used as the sparging gas and the solution was sparged continuously during the experiments. The cell was placed on a stir plate and stirred continuously throughout, and the assembly was placed within a light-tight box.

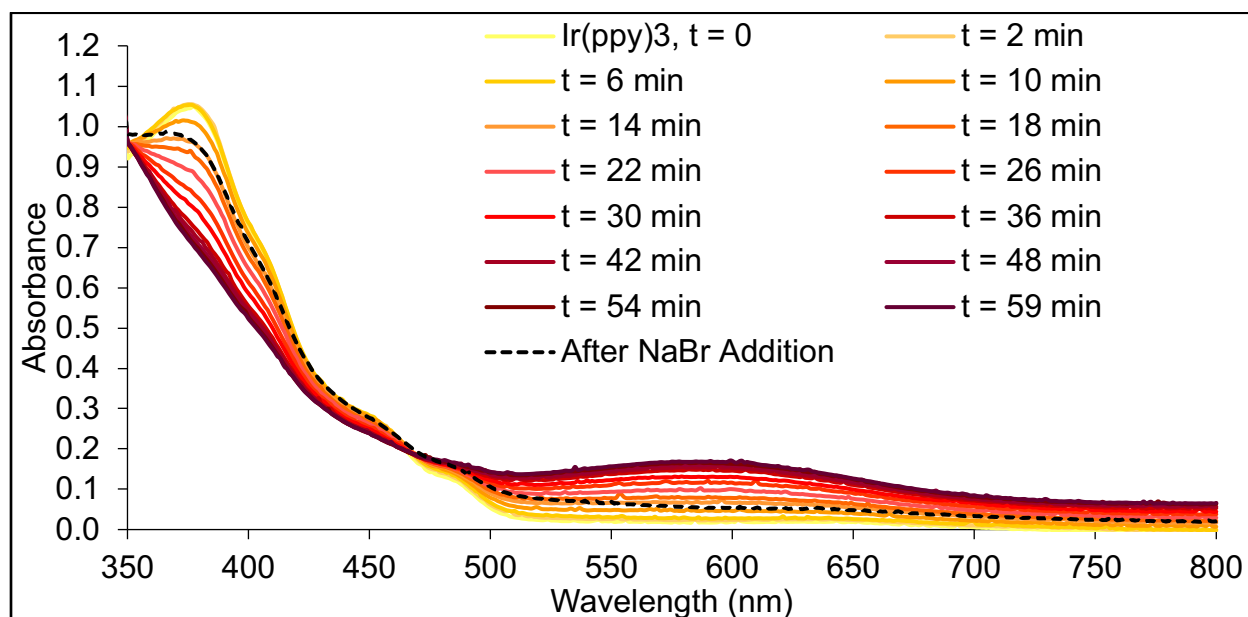


Figure S4.80. Spectroelectrochemistry of Ir(ppy)₃ (0.79 mM in DMF) oxidized at an applied potential of 1.00 V vs. Ag/AgNO₃. After applying the potential for 1 h, the potentiostat was turned off, and after 5 minutes, a solution containing NaBr (1.9 mg in 500 μ L DMF) was injected via airtight syringe.

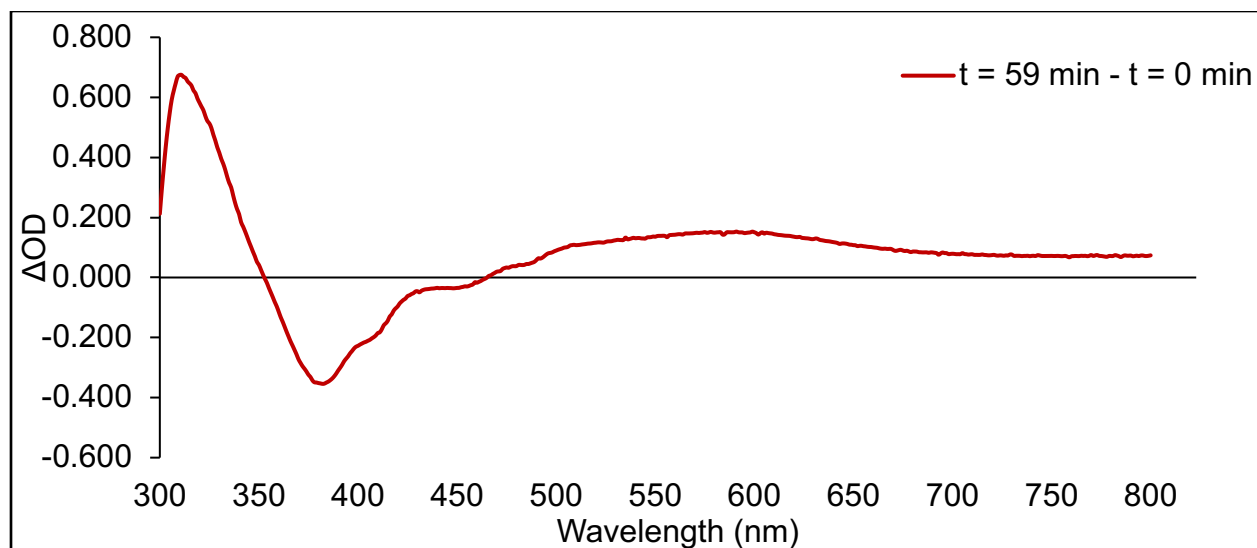


Figure S4.81. Difference spectrum from spectroelectrochemistry of Ir(ppy)_3 (0.79 mM in DMF) oxidized at an applied potential of 1.00 V vs. Ag/AgNO_3 .

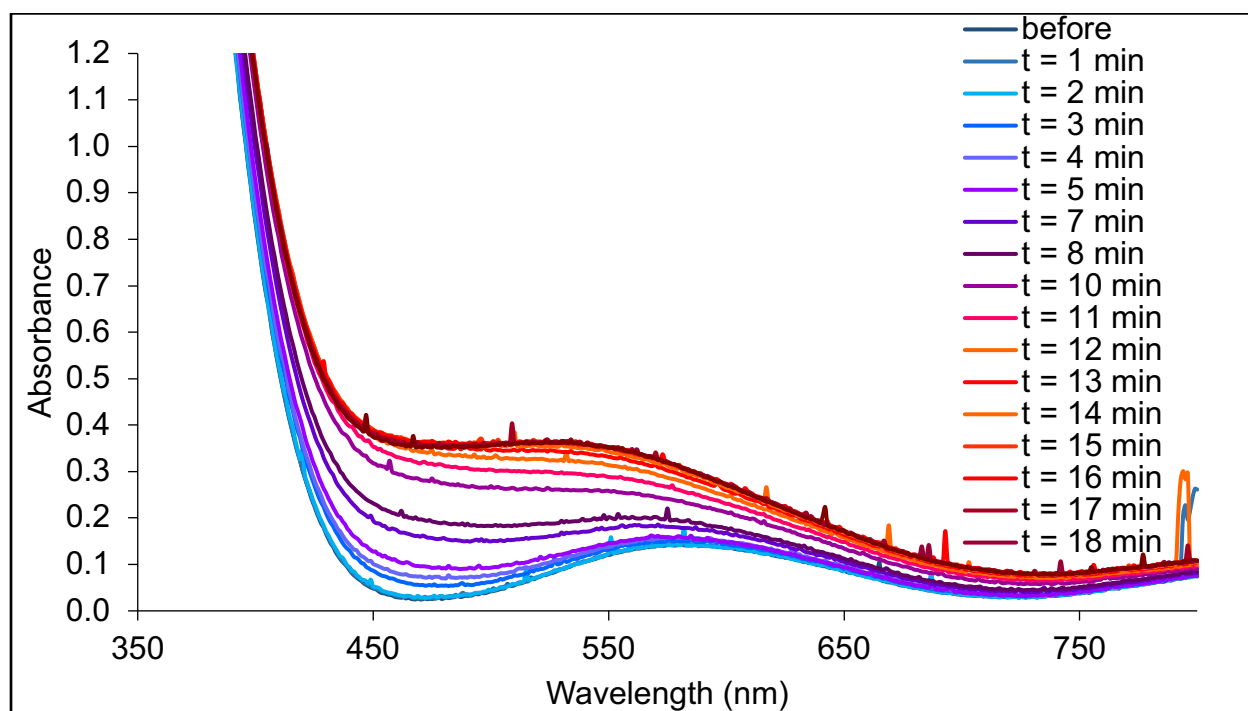


Figure S4.82. Spectroelectrochemistry of $\text{NiBr}_2 \cdot \text{glyme}$ (15.0 mM) + OMeppy (2 eq. relative to Ni, 30.0 mM) reduced at an applied potential of -2.00 V vs. Ag/AgNO_3 . Small spikes in signal were due to N_2 bubbles scattering light.

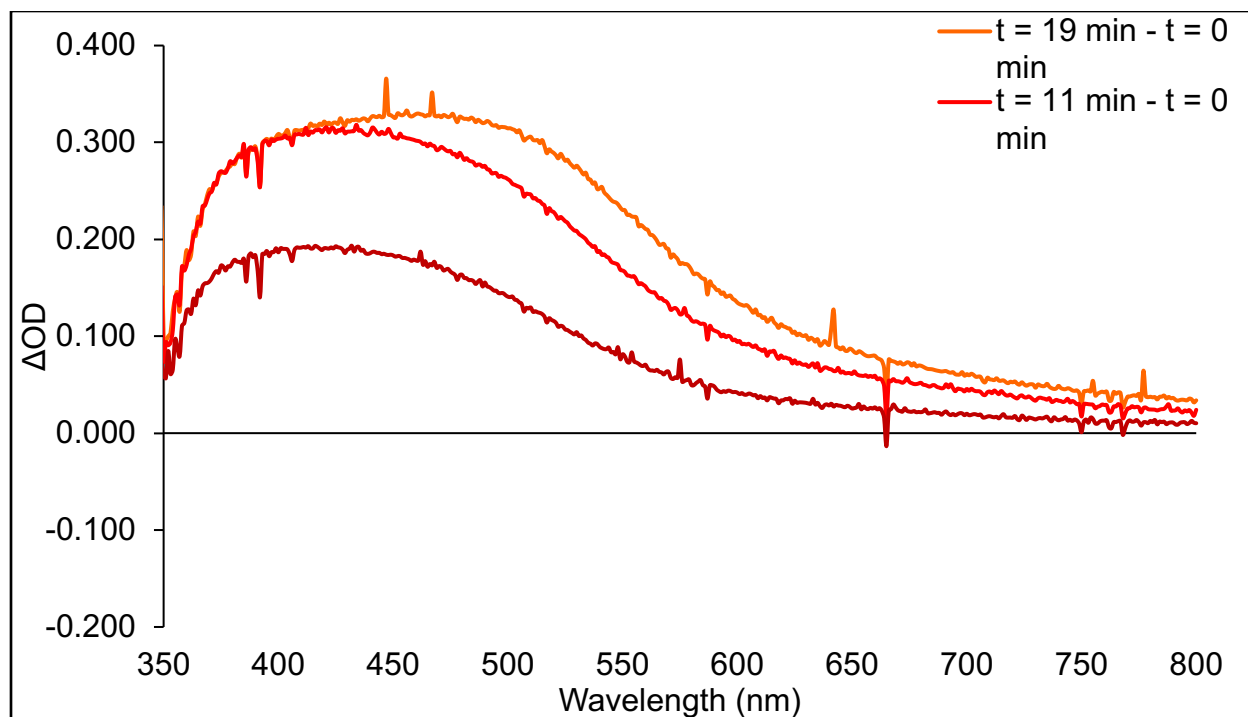


Figure S4.83. Difference spectra from spectroelectrochemistry of $\text{NiBr}_2 \cdot \text{glyme}$ (15.0 mM) + OMebpy (2 eq. relative to Ni, 30.0 mM) reduced at an applied potential of -2.00 V vs. Ag/AgNO_3 . Small spikes in signal were due to N_2 bubbles scattering light.

We assign the new species which forms with absorption centered around 420 nm to a Ni(I) intermediate. Previous work has found that reduction of $[\text{Ni(II)(Mebpy)}_3]^{2+}$ to Ni(I) is followed by the subsequent reduction of Ni(I) to Ni(0) at the electrode.²³ However, in the bulk solution, the major species observed was Ni(I) due to comproportionation of Ni(0) with Ni(II). As such, we expect the species observed in this experiment at earlier times to be the Ni(I) intermediate. The final difference spectrum ($t = 19\text{ min} - t = 0\text{ min}$) appears to have a slightly red-shifted spectrum compared to the others at earlier times. This shift could be due to instability of Ni(I) in the absence of other components of the reaction mixture.

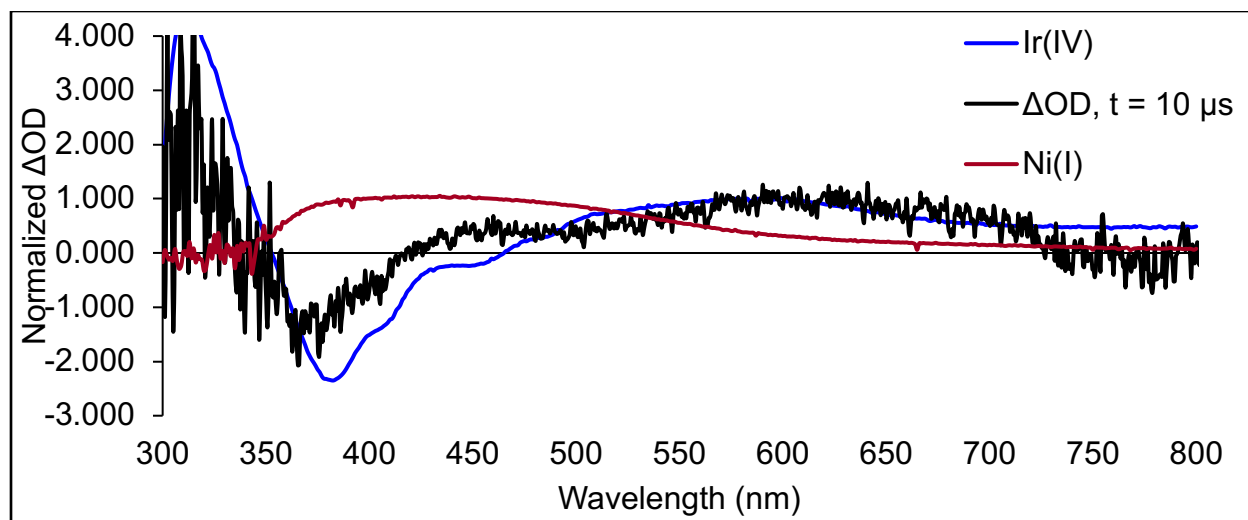


Figure S4.84. Difference spectra from spectroelectrochemistry of $\text{NiBr}_2 \cdot \text{glyme}$ (15.0 mM) + OMebpy (2 eq. relative to Ni, 30.0 mM) reduced at an applied potential of -2.00 V vs. Ag/AgNO_3 (red trace) and $\text{Ir}(\text{ppy})_3$ (0.79 mM in DMF) oxidized at an applied potential of 1.00 V vs. Ag/AgNO_3 (blue trace) overlaid with the nsTA difference spectrum (355 nm pump, $t = 10\mu\text{s}$) of a mixture containing $\text{Ir}(\text{ppy})_3$ (31.4 μM in DMF) + $\text{NiBr}_2 \cdot \text{glyme}$ (1.5 mM) + OMebpy (3.0 mM) (black trace) offset corrected utilizing kinetic data acquired at $\lambda_{\text{probe}} = 600\text{ nm}$. All traces were normalized to the highest peak.

The spectroelectrochemical data supports the hypothesis that the nsTA spectrum consists of an additive contribution from Ir(IV) and Ni(I).

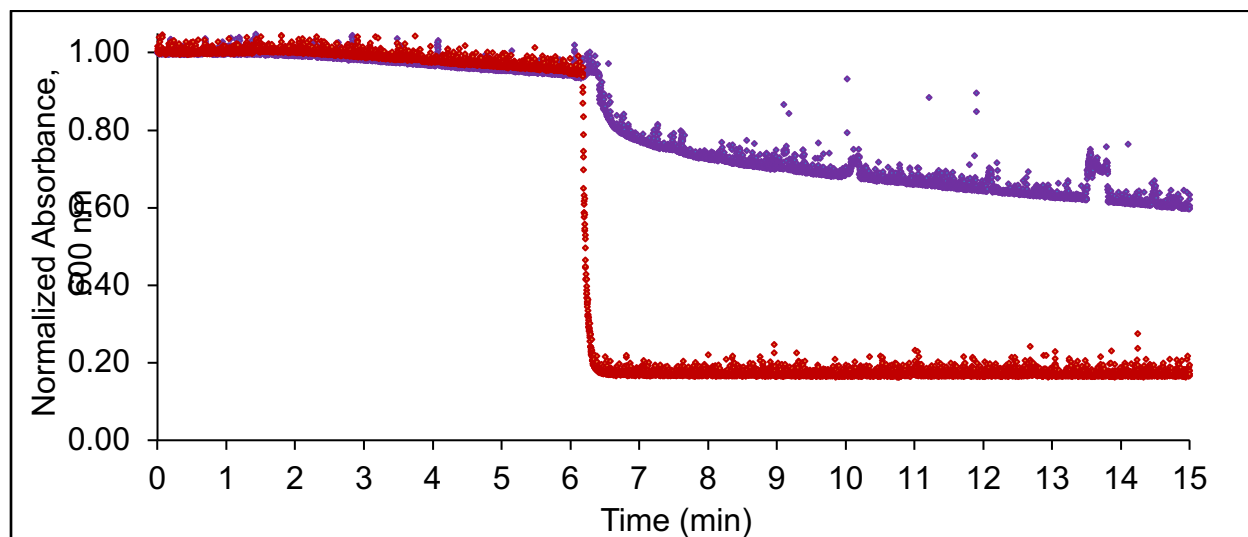


Figure S4.85. Spectroelectrochemistry kinetics monitored at 600 nm. $\text{Ir}(\text{ppy})_3$ (0.79 mM in DMF) oxidized at an applied potential of 1.00 V vs. Ag/AgNO_3 . After applying the potential for 1 h, the potentiostat was turned off ($t \sim 1\text{ min}$), and 5 minutes later ($t \sim 6\text{ min}$), a solution containing NaBr (1.9 mg in 500 μL DMF) was injected via airtight syringe. As a control, a blank solution containing only DMF was also injected (purple trace).

Observation of a much more significant loss in signal corresponding to Ir(IV) when bromide is injected suggests that Ir(IV) oxidizes bromide to bromine radical to recover Ir(III). Further, recovery of most of the Ir(III) starting signal in the full UV-vis spectrum post injection supports this interpretation.

Spectroelectrochemistry control with Ir(ppy)₃ and TBACl:

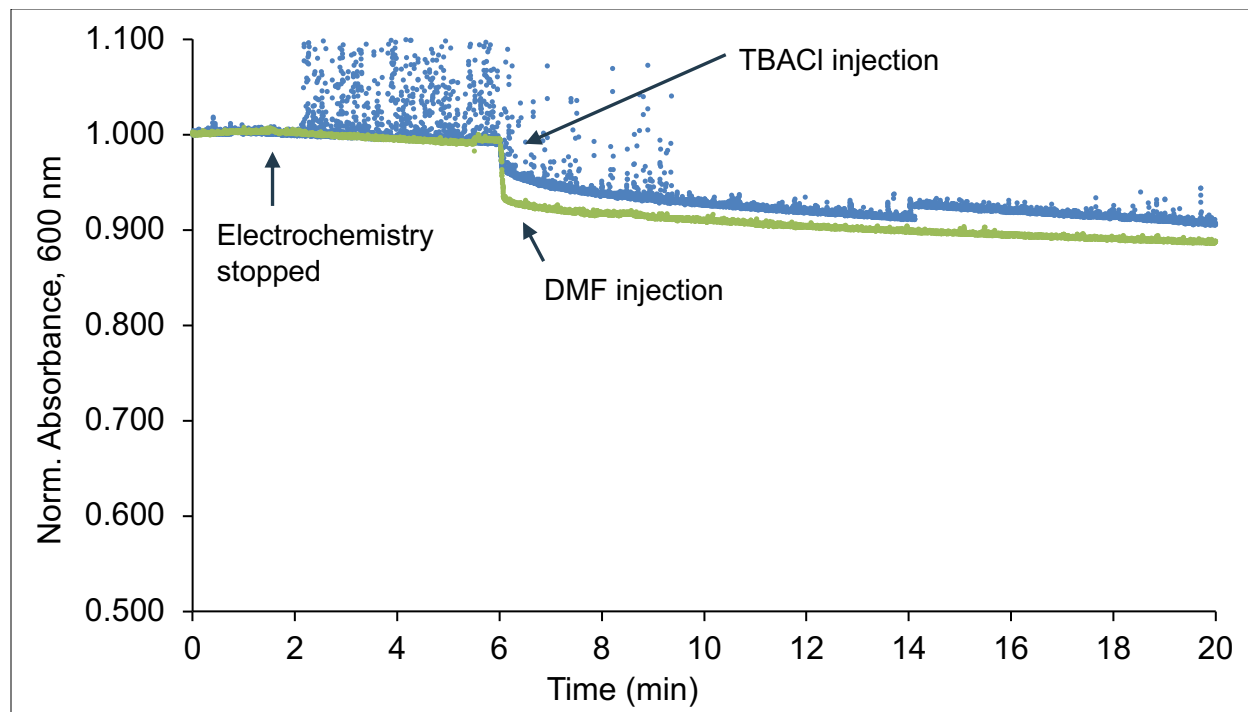


Figure S4.86. UV-vis spectra monitoring the absorbance of the Ir(IV) solution (15.7 μM) at 600 nm before and after injection of TBACl (3.3 mM, 46 eq. relative to Ir(ppy)₃) (shown in blue) or DMF (shown in green, control).

In this control experiment, the decay of the Ir(IV) signal after injection of TBACl matches the decay of the signal after injection of DMF, with the observed decrease in absorbance resulting from dilution. This suggests that chloride from TBACl is not oxidized by Ir(IV). Occasional points appearing as outliers in the data in the TBACl case are due to bubbles passing in front of the fiber optic probe.

6. Reaction Reoptimization and Kinetics.

General information:

All reaction optimizations and kinetics were run according to the general coupling shown in Fig. S4.87A. Conversion and selectivity were monitored by ^{19}F NMR. A representative ^{19}F NMR is shown in Fig. S4.87B, demonstrating that the main products were the desired product (DP) and debrominated (De-Br) product.

Preliminary kinetics screens with the photoreactor used in our previous work²⁴ (reactor 1, described below) yielded highly variable conversion from well-to-well. Because of this, we screened other photoreactors prior to running full kinetics experiments. Additionally, one of the reactors (reactor 3) lacked the ability to stir so we ran initial consistency screens with DBU to ensure homogeneity.

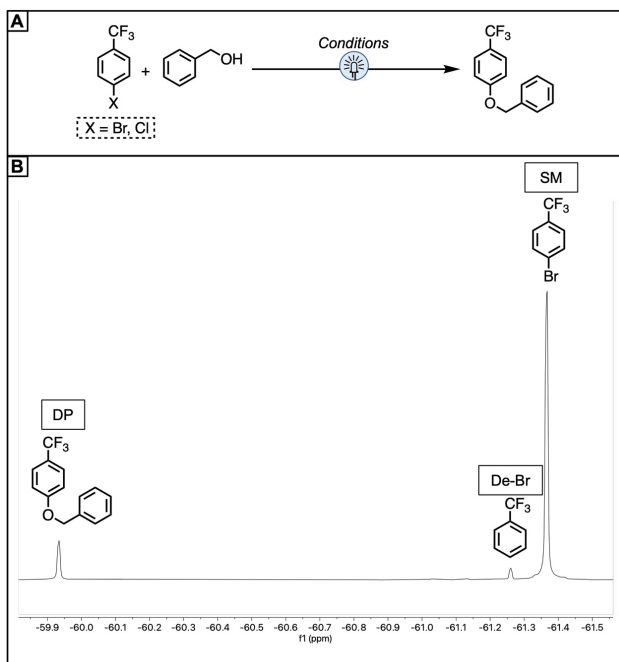


Figure S4.87. General scheme for coupling between aryl halides and benzyl alcohol (A). Representative ^{19}F NMR for coupling between 4-BrBzCF₃ and benzyl alcohol (B), showing starting material (SM), debromination (De-Br) and desired product (DP) as main components.

6.1 Reaction Reoptimization.

The following procedure was used for determining reactor consistency between positions. A 2-dram vial was charged with a stir bar. 4-4'-Dimethoxy-2-2'-bipyridine (10 mol%) and Ir(ppy)₃ (1.0 mol%) were added and the vial was taken into a nitrogen filled glovebox. NiBr₂-glyme (5.0 mol%) was added and the mixture was dissolved in anhydrous DMF (0.4 M with respect to 4-BrBzCF₃). Following ~5 minutes of stirring, 4-BrBzCF₃ (1.00 eq.), benzyl alcohol (1.05 mmol) and base (2.00 eq.) were added. Then, 0.50 mL of this solution was transferred to 6x0.5-dram vials (for reactors 1 and 2) or 70 μ L into 16xmicro-scale vials (for reactor 3. SKU: 96342 through Analytical Sales and Services). The next steps depended on the reactor used.

Reactor 1:

Only K₂CO₃ was tested as a base since the reactions could be stirred. After preparing the reaction according to the above procedure, the vials were capped, taken out of the glovebox, and placed in the Hepatochem PhotoRedOx Box TCTM. The temperature was set to 35 °C with a recirculator containing water/ethylene glycol. The reaction was illuminated with a Kessil PR160L-440nm light and allowed to react for two hours. After completion, 50 μ L of each reaction was transferred to NMR tubes containing 450 μ L d-DMSO and analyzed using ¹⁹F NMR. The % conversion was determined as: 100*(area of all products formed)/(area of starting material and products).

This reactor gave highly variable results depending on the position of the vials relative to the light (Figure S4.88A). Though the two vials closest to the light gave nearly identical conversion, we wanted to run a variety of conditions in triplicate, so this setup was not sufficient for kinetics. However, this setup was used for the reaction scope (See section 8).

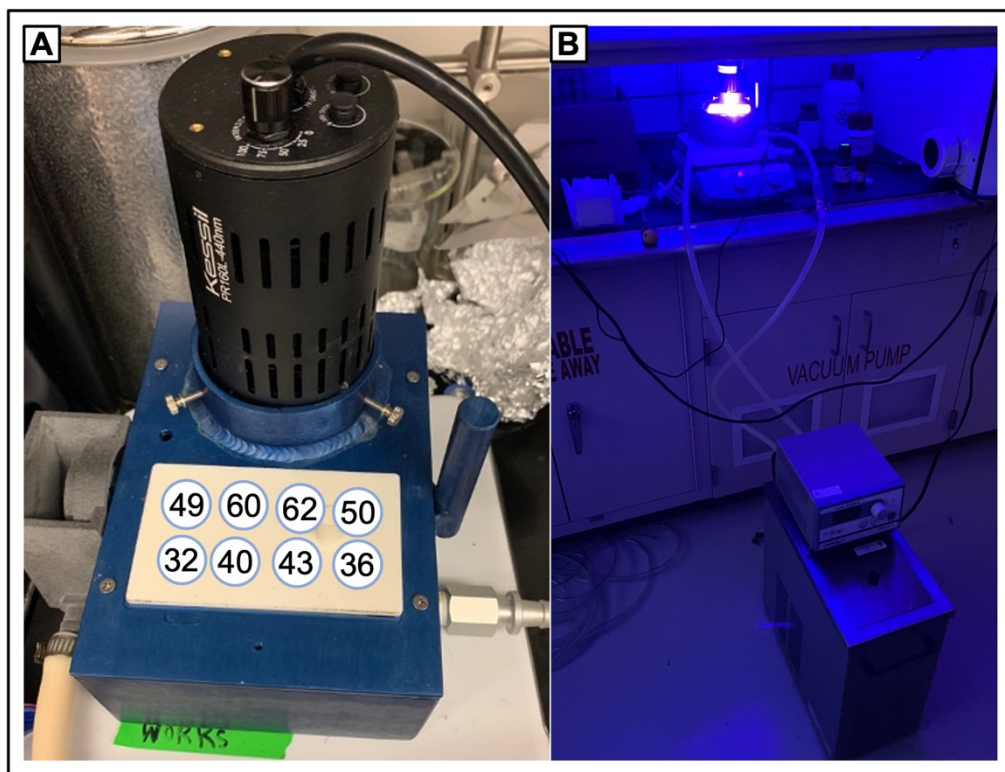


Figure S4.88. Conversion values for given wells in the Hepatochem reactor (A). Full reactor 1 setup (B).

Reactor 2:

Both K_2CO_3 and DBU were tested in this reactor because we noticed some difficulty stirring with K_2CO_3 in the setup. After preparing the reaction according to the above procedure, the vials were capped, taken out of the glovebox, and placed in custom built 405 nm photoreactors described in previous work,⁵ cooled with built in fans (Fig. S4.89A). The reactions were irradiated for 2 hours and 50 μ L of each reaction was transferred to NMR tubes containing 450 μ L d-DMSO and analyzed using ^{19}F NMR. The % conversion was determined as: $100 \times (\text{area of all products formed}) / (\text{area of starting material and products})$.

The conversion in this reactor was highly variable as well (Fig. S4.89B). When K_2CO_3 was used as the base, the conversion range was 18-57% with a standard deviation of 13%. The use of

DBU gave higher conversion but still lacked consistency with a range of 47-99% conversion and a standard deviation of 17%.

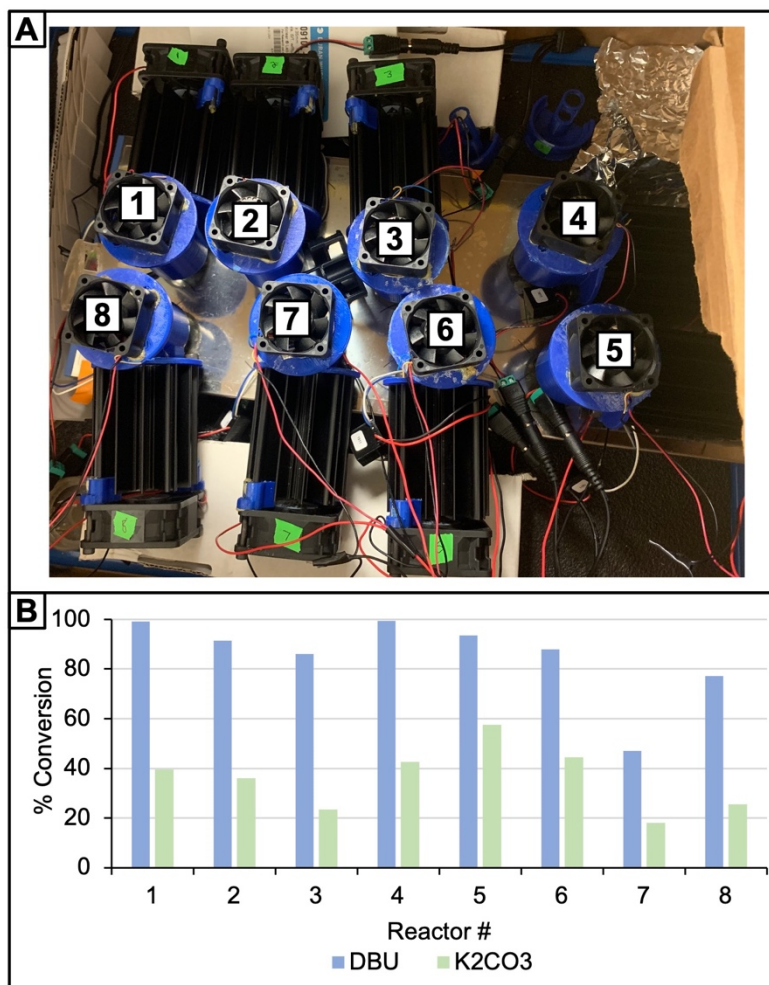


Figure S4.89. Reactor 2 setup (A). Conversion based on reactor number with either DBU or K₂CO₃ as the base (B).

Reactor 3:

Only DBU was tested as a base due to the inability to stir with this setup. After preparing the reaction, the micro-scale vials were placed in a custom photoreactor designed by New Iridium (prototype for now commercially available reactor. SKU: 489900 from Analytical Sales and Services). The top was fastened with an electric screwdriver to ensure no exposure to atmosphere and the plate was taken out of the glovebox. The plate was placed on a 445 nm Lumidox Gen II,

96-well LED Array (SKU: LUM296LS445) mounted on a thermal transfer deck (SKU: 266540) inside a nitrogen filled purgebox affixed with tubing for two circulating baths. The lights were cooled with one circulating bath and maintained at 20 °C. The reaction plate was heated to 35 °C with a separate circulator. The reactor was set to 270 mW/well and the reaction was run for 2 hours. After completion, 50 μ L was taken from each well, transferred to an NMR tube containing 450 μ L d-DMSO, and analyzed by ^{19}F NMR.

This reactor gave the lowest well-to-well variability (std. dev. = 2.1%) and a heat map for the conversion in the different wells is shown in Figure S4.90B. Because of the low variability and ability to run up to 96 reactions at once, we chose this reactor for kinetics studies.

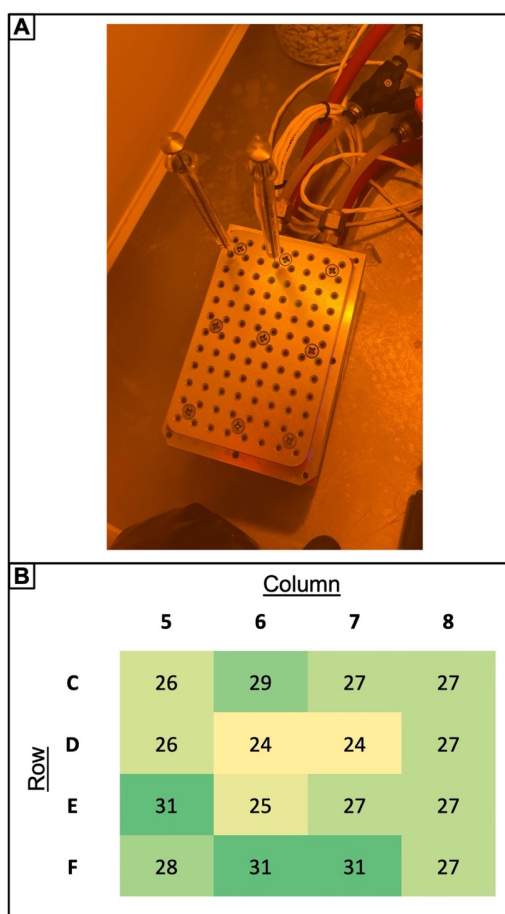


Figure S4.90. Reactor 3 setup (A). Heat map of conversion values for 16 wells (B).

6.2 Photocatalyst Screen.

Using the procedure from section 6.1 with reactor 3, photocatalysts with various photophysical properties were tested to assess the impact of quantum yield of intersystem crossing (Φ_{ISC}) and triplet lifetime (τ_{T1}) on reaction efficiency. We selected organic photocatalysts with similar redox properties as Ir(ppy)₃ (Fig. S4.91A) so that only photophysical properties were being varied. The organic photocatalysts selected had lifetimes ranging from 1.47 μ s to >15 ms and Φ_{ISC} of 0.11-1.0.^{1,13} We initially screened the photocatalysts at 5 mol% nickel loading and noticed a trend between Φ_{ISC} and conversion (Fig. S4.91B), with higher triplet yield PCs giving higher conversion compared to similar PCs with lower triplet yield. This aligns with the calculations in section 3.3, which predict higher reactivity for PC1 relative to organic PCs at nickel loadings of 5 mol%.

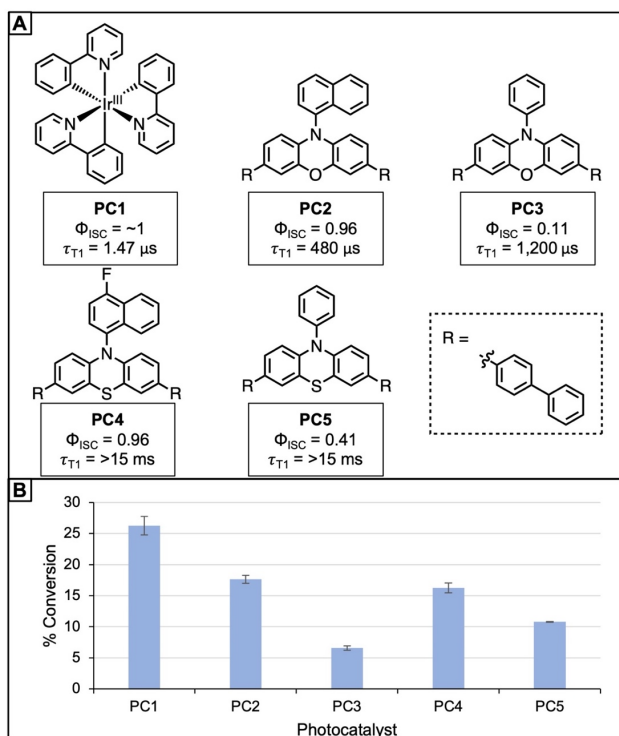


Figure S4.91. Photocatalysts selected for study on the impact of photophysical properties on reactivity (A). Conversion values for selected photocatalysts (B). All reactions run in triplicate.

While the calculations in section 3.3 predicted the higher reactivity for PC1 at 5 mol% nickel loading, PC2 was predicted to begin outperforming PC1 at loadings of ~ 0.5 mol% and below. To synthetically probe this, we ran a similar experiment to the one in Figure S4.90 but did 10-fold serial dilutions of the nickel catalyst to span nickel loadings ranging from 5 mol% down to 0.005 mol%, and ran the reaction for 3 hours at 510 mW/well to increase overall conversion. Again, PC1 outperformed the two OPCs at 5 mol% nickel loading but at loadings of 0.5 mol% and below the two OPCs outperform PC1 (Fig. S4.92), further synthetically supporting the calculations in section 3.3. However, since PC1 outperformed the OPCs at reaction relevant nickel loading, we ran the remaining experiments with this photocatalyst.

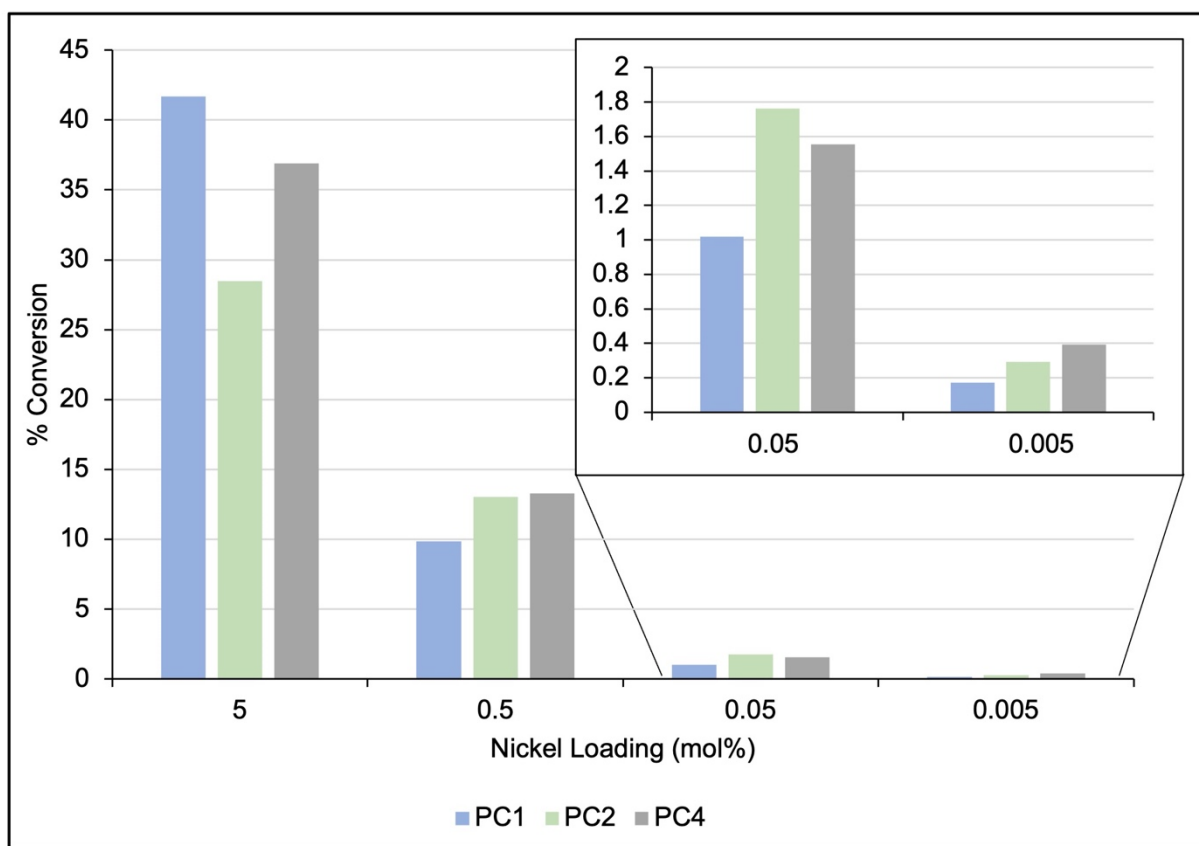


Figure S4.92. Conversion as a function of nickel loading with PC1, PC2 and PC4. All reactions run in triplicate and 15 μ L of the three reactions were combined into a single NMR tube to account for well-to-well variability.

6.3 Effect of Ni:Ligand Ratio on Rate and Selectivity.

Using the procedure from section 6.1 with reactor 3, the ratio of ligand to nickel was varied and conversion/selectivity were monitored by ^{19}F NMR (Fig. S4.93). Though conversion was high with 0.6 eq. ligand, the selectivity was poor, giving a significant amount of debrominated product. The conversion increased as equivalents of ligand was increased from 1 to 2 and then stayed roughly the same with further increases in ligand equivalents. However, even though conversion remained constant with >2 eq., selectivity decreased. Because of this, 2 eq. ligand was determined to give the best performance in terms of rate and selectivity.

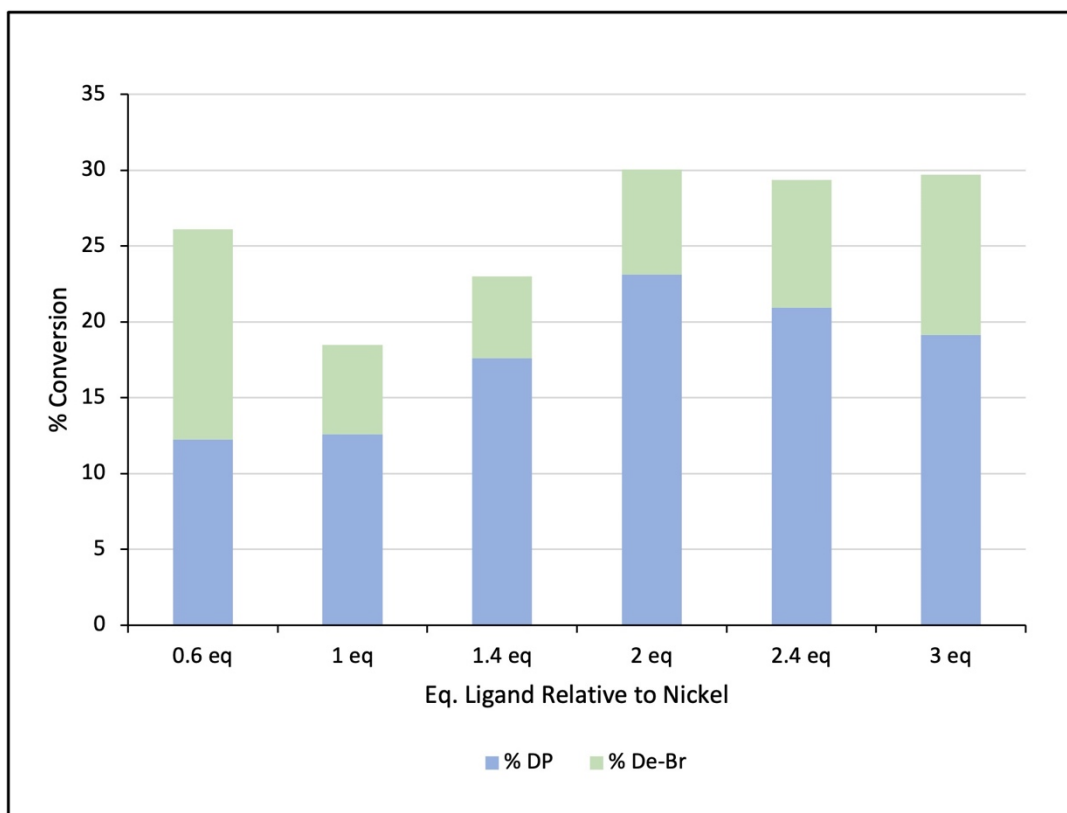


Figure S4.93. Conversion and selectivity as a function of nickel:ligand ratio. All reactions run in triplicate and 15 μL of the three reactions were combined into a single NMR tube to account for well-to-well variability.

6.4 Additive Screen.

Using the procedure from section 6.1 with reactor 3 for 3 hours at 510 mW/well, halide additives were screened, and conversion was monitored by ^{19}F NMR. First, tetrabutylammonium

bromide (TBABr) was screen as an additive at 0 eq., 0.1 eq., 1 eq. and 2 eq. with both 4-BrBzCF₃ and 4-ClBzCF₃ as substrates. For both substrates, the conversion increased with increasing amounts of TBABr (Fig. S4.94) but the overall conversion was low for 4-ClBzCF₃.

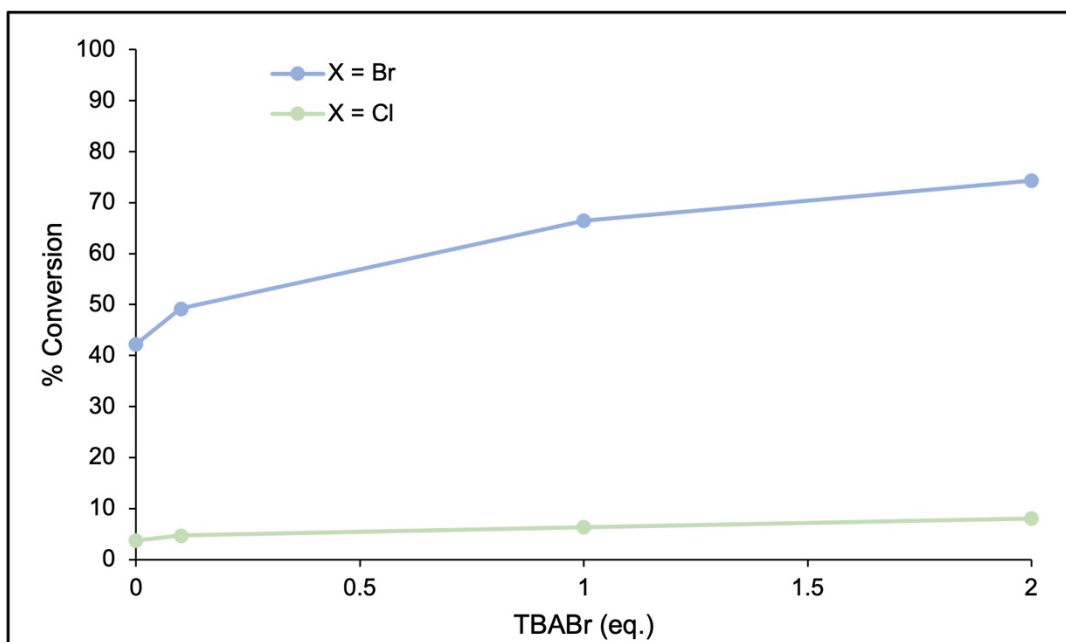


Figure S4.94. Conversion as a function of eq. TBABr additive with 4-BrBzCF₃ (X = Br) and 4-ClBzCF₃ (X = Cl). All reactions run in triplicate and 15 μ L of the three reactions were combined into a single NMR tube to account for well-to-well variability.

Coupling of 4-ClBzCF₃ with additives at 18 hours:

In order to follow the reaction with 4-ClBzCF₃ to higher conversion, we ran the same additive screen but for 18 hours. Additionally, we tested other halide additives (I⁻, Cl⁻). The results from this study are summarized in Figure S4.95. It is worth noting that the upward trend in conversion with increasing amounts of TBABr we observed in the 3-hour experiment was not observed in this experiment. We believe this may be due to slight variations in the microscale vials leading to varying rates of evaporation over the course of 18 hours.

Fluoride was also tested as an additive. However, no conversion was observed at a 4-hour timepoint with 1 eq. tetrabutylammonium fluoride so further screens were not run.

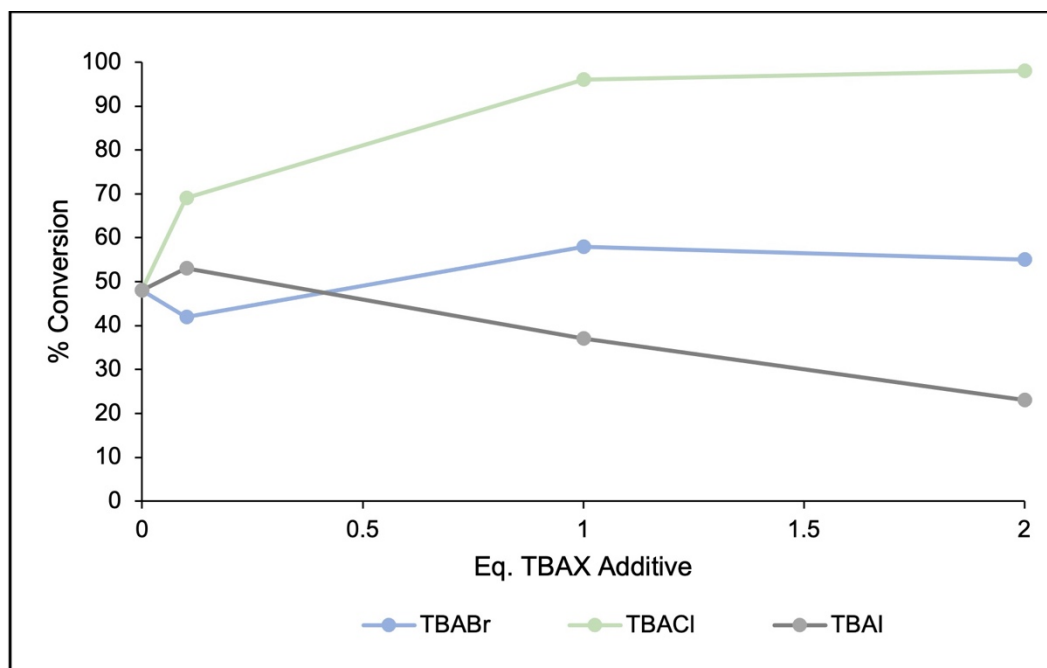


Figure S4.95. Conversion as a function of halide (Cl^- , Br^- , I^-) equivalents for the coupling with 4- ClBzCF_3 at 18 hours. All reactions run in triplicate and 15 μL of the three reactions were combined into a single NMR tube to account for well-to-well variability.

6.5 Reaction with $\text{NiCl}_2\cdot\text{glyme}$.

We reasoned that $\text{NiCl}_2\cdot\text{glyme}$ would lead to the direct formation of the more active catalyst $\text{NiCl}_2(\text{OMebpy})_2$ and should outperform the reaction starting from $\text{NiBr}_2\cdot\text{glyme}$ in the absence of additive. In order to test this hypothesis, we ran the coupling between 4- ClBzCF_3 and benzyl alcohol according to the procedure described in section 6.1 with reactor 3 using $\text{NiCl}_2\cdot\text{glyme}$ or $\text{NiBr}_2\cdot\text{glyme}$. The results of this are summarized in the below table. Though $\text{NiCl}_2\cdot\text{glyme}$ outperformed $\text{NiBr}_2\cdot\text{glyme}$ with no additive, both precatalysts still benefited from chloride additive. Additionally, $\text{NiBr}_2\cdot\text{glyme}$ outperformed $\text{NiCl}_2\cdot\text{glyme}$ with TBACl as an additive. We believe this is due to the rate at which $\text{NiCl}_2(\text{OMebpy})_2$ crashes out of solution depending on the method used to make it (Section 2.5). Since $\text{NiCl}_2(\text{OMebpy})_2$ precipitates more rapidly when made from $\text{NiCl}_2\cdot\text{glyme}$, $\text{NiBr}_2\cdot\text{glyme}$ is still a better precatalyst with TBACl since precipitation is not an issue on the timescale of the reaction.

Table S4.6. Screen of different precatalysts with and without additive

Entry	Nickel Source	Additive	% Conversion
1	NiBr ₂ •glyme	none	3
2	NiCl ₂ •glyme	none	10
3	NiBr ₂ •glyme	TBACl (1 eq.)	33
4	NiCl ₂ •glyme	TBACl (1 eq.)	25

6.6 Reaction Kinetics.

The same general procedure described in 6.1 with reactor 3 was followed with some deviations. The light intensity was set to 510 mW/Well. For each experiment, 36 microscale vials were filled with the reaction to be tested (12 timepoints in triplicate). At each timepoint, the lights were turned off and a Hamilton syringe was used to sample 15 μ L from three wells that were then combined into a single NMR tube containing 450 μ L d-DMSO. Conversion was analyzed by ¹⁹F NMR. With the exception of the reaction with 4-ClBzCF₃ and no additive (Fig. S4.96B) all reactions followed pseudo-first order kinetics. All pseudo-first order plots are shown in Figure S4.96 (4-BrBzCF₃) and Figure S4.97 (4-ClBzCF₃).

It is also worth noting the slight curvature in the pseudo-first order plots of the coupling with 4-BrBzCF₃ in the presence of chloride additive. One possible explanation for this is the formation of a new nickel complex as bromide is generated in the form of DBU-HBr. This bromide could lead to the formation of a mixed nickel halide complex (e.g. NiBrCl(OMebpy)₂) that is more active than the NiCl₂(OMebpy)₂ complex.

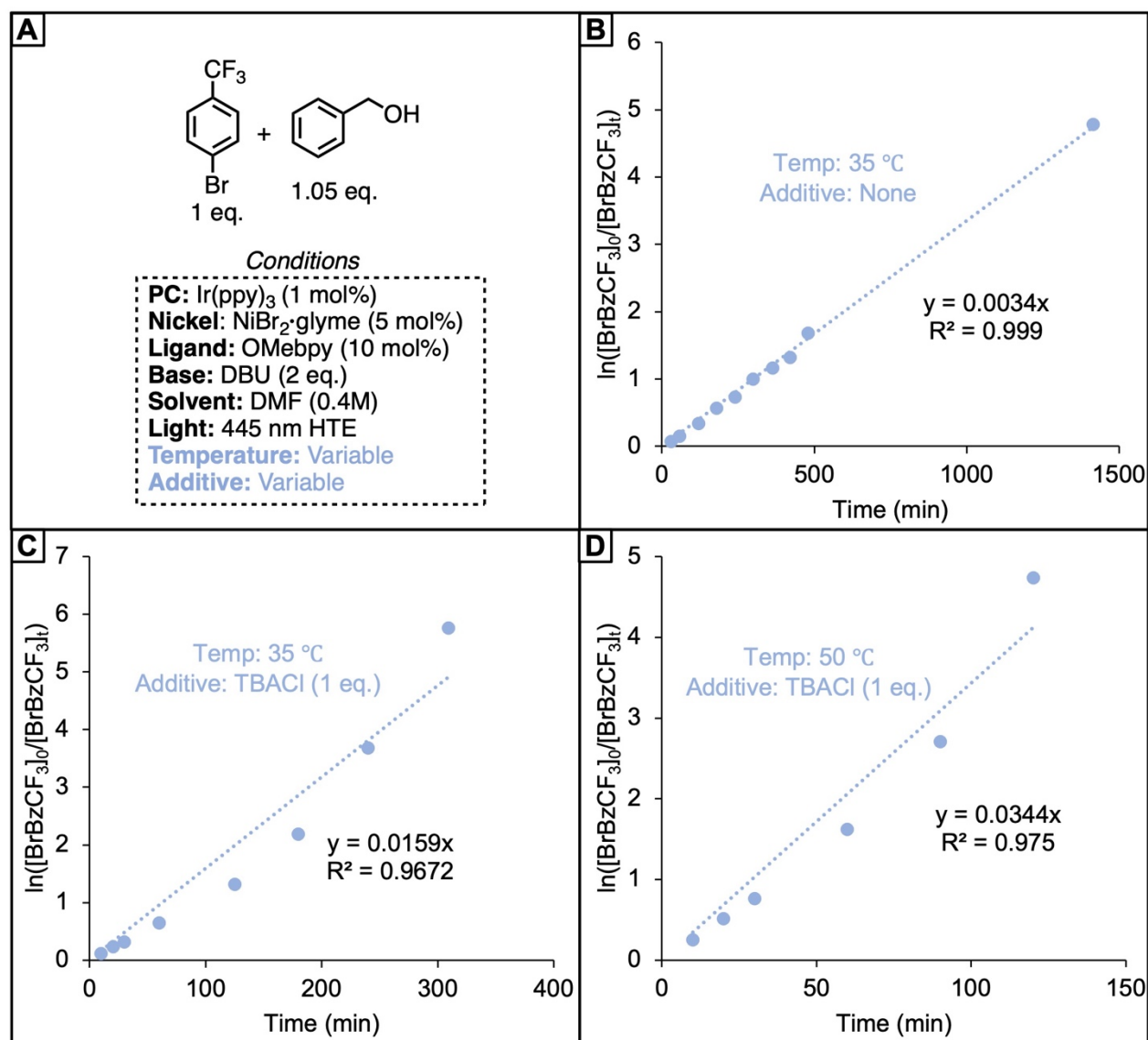


Figure S4.96. Pseudo-first order kinetics plots for the coupling between 4-BrBzCF₃ and benzyl alcohol without additive (A), with 1 eq. TBACl (B), and with 1 eq. TBACl at elevated temperatures (C). All reactions run in triplicate and 15 μ L of the three reactions were combined into a single NMR tube to account for well-to-well variability.

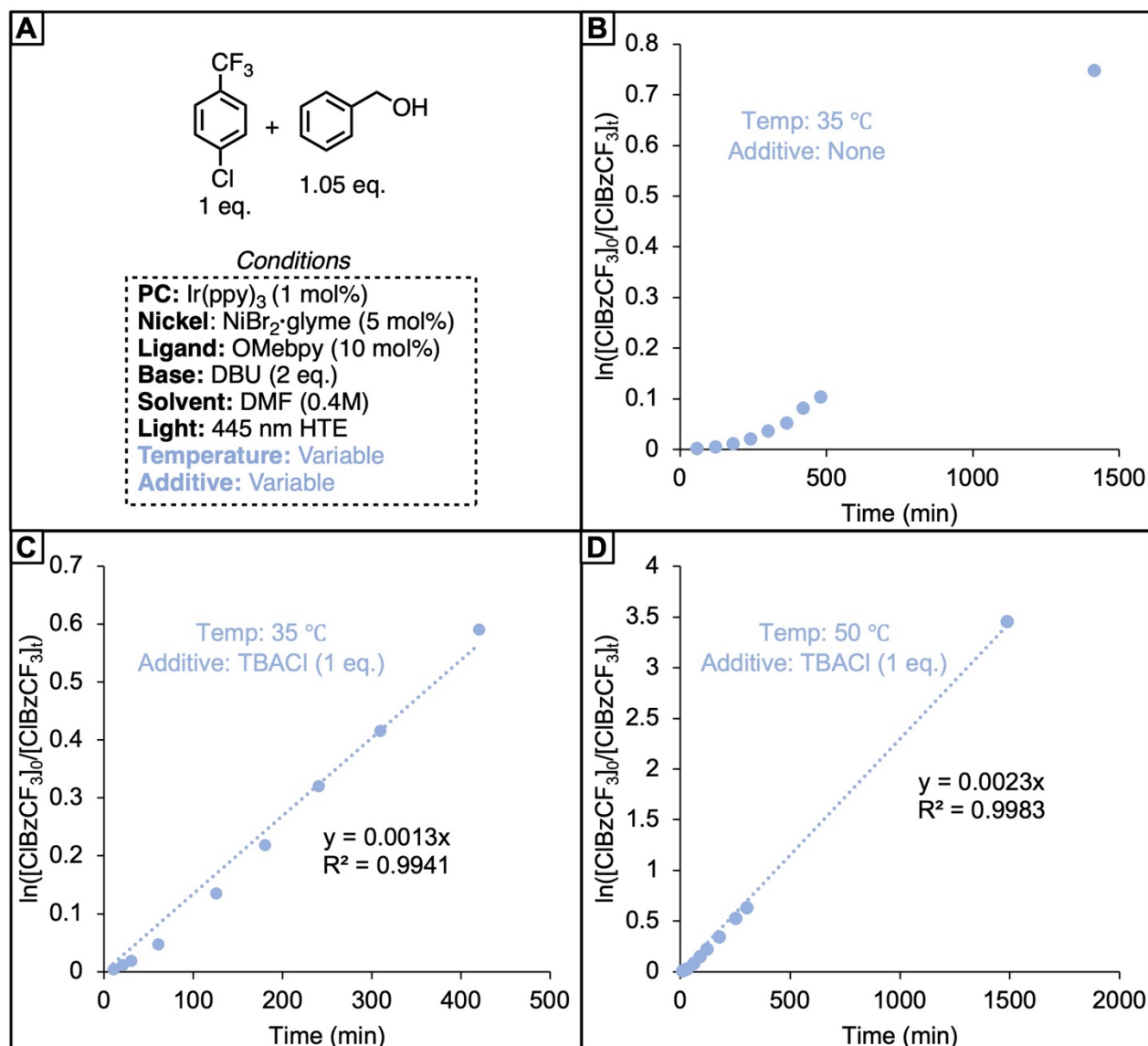


Figure S4.97. Pseudo-first order kinetics plots for the coupling between 4-ClBzCF₃ and benzyl alcohol without additive (A), with 1 eq. TBACl (B), and with 1 eq. TBACl at elevated temperatures (C). All reactions run in triplicate and 15 μ L of the three reactions were combined into a single NMR tube to account for well-to-well variability.

Since the reaction without additive for 4-ClBzCF₃ did not follow pseudo-first order kinetics, we opted to use initial turnover frequency (TOF₀) to compare relative reactivity with and without additive. This was calculated as the slope of the % conversion vs time plot for the first timepoint at which product was detected.²⁶ Since this value is limited by the detection limit of the

NMR, we can only generate a minimum increase in reactivity (TOF₀) based on when product begins to be detected.

6.7 Carbonate Base Variability

To compare our new conditions to our previous work, we ran the coupling between 4-ClBzCF₃ and benzyl alcohol with our previously reported conditions.²⁴ Surprisingly, the ¹⁹F NMR conversion was very low, even though we were able to couple a similar alcohol (4-methoxybenzyl alcohol) to 4-ClBzCF₃ in high yield (61%) previously. Based on the significant improvements we observed with added chloride in section 6.4, we wondered if there was potential for chloride contamination causing batch to batch variability with the carbonate base we used. First, when we ran the reaction with a different batch of Na₂CO₃ we found a significant increase in conversion, suggesting some variability in the carbonate batches. At this point, this variability can't conclusively be determined to arise from contamination and could potentially arise from particle size. However, when adding 5% TBACl to the reaction (equivalent to a 2.5% chloride contamination in the carbonate) the conversion further increased by 4%, supporting the hypothesis that chloride contamination in Na₂CO₃ could lead to the variability we observed.

Table S4.7. Batch variability of carbonate base and impact of chloride additive.

Entry	Base	Additive	% Conversion
1	Na ₂ CO ₃ Batch 1	N/A	9
2	Na ₂ CO ₃ Batch 2	N/A	26
3	Na ₂ CO ₃ Batch 2	TBACl (5 mol%)	30

7. Quantum Yield

7.1 Ferrioxalate Actinometry.

Reactors:

Reactor 3 was used for initial quantum yield measurements. Recent work on a similar Ni/PC catalyzed transformation found a significant increase in quantum yield with low power light.²⁵ In order to measure quantum yield at lower flux with our system, we also utilized a custom-made cooling block (Reactor 4a, Figure S4.98A), designed by New Iridium, made for 10 mL pressure tubes (Kemtech Part P160710) that fits on top of the same 445 nm LED array used for Reactor 3. The flux was further reduced by inserting black NMR tube caps drilled with 2 mm holes (Reactor 4b, Figure S4.98B).

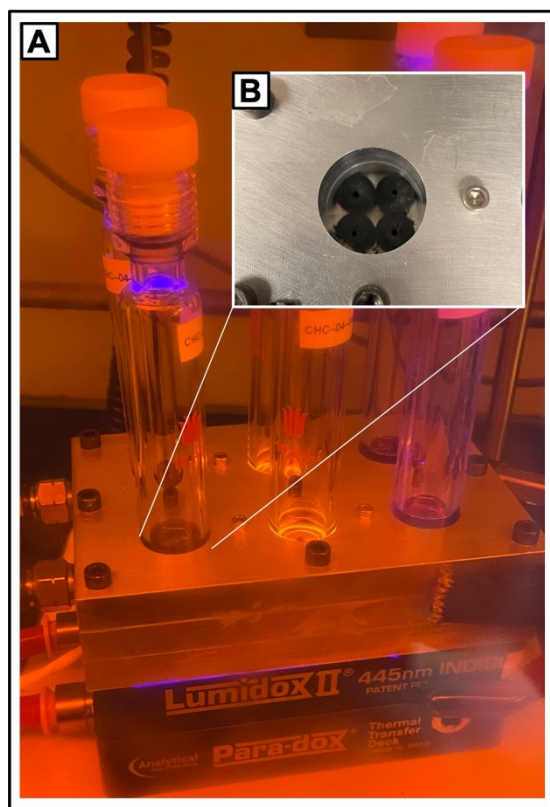


Figure S4.98. Reactor 4a and 4B used in quantum yield experiments to lower flux.

Procedure:

A modified literature procedure²⁷ was used to determine the output of our reactors. Solids were weighed without metal scoopulas to avoid Iron contamination. For reactor 4b, all solution preparation was done in a dark room illuminated with red LEDs since incident light gave issues

with initial actinometry measurements with this setup. Incident light was still minimized for reactor 3 and 4a by turning all lights off in the lab and blocking windows. Developer solution was prepared by dissolving 1,10-phenanthroline (1 g, 5.5 mmol) in 100 mL of a sodium acetate (13.6 g, 170 mmol) sulfuric acid (0.5 M) solution. In a 25 mL volumetric flask, $K_3[Fe(C_2O_4)_3] \cdot 3H_2O$ (1.84 g, 3.75 mmol) was dissolved in 25 mL 0.05M H_2SO_4 . This solution was added to the reaction vessels (Reactor 3 = 70 μ L/well, Reactor 4 = 2 mL/tube) and was irradiated at 445 nm with the recirculator set to 20 °C (510 mW/well for reactor 3, 90 mW/well for reactors 4a and 4b). At each timepoint, the lights were turned off and 10 μ L was transferred to a 2-dram vial wrapped in electrical tape containing 5 mL developer solution. Each timepoint was run in triplicate. After allowing the solution to develop for 1 hour, UV-vis was run on each sample along with a three T_0 samples (prepared the same way as the timepoints but prior to any irradiation).

Calculating [Fe(II)] and Intensity (I_0):

$$Moles\ Fe(II) = \frac{V_1 V_3 \Delta A(510\ nm)}{10^3 * V_2 l \epsilon(510\ nm)} \quad \text{Eq. S4.7}$$

V_1 = irradiated volume (0.07 mL or 2 mL)

V_2 = aliquot volume (0.01 mL)

V_3 = Final volume of V_2 in developer solution (5 mL)

$\Delta A(510\ nm)$ = difference in absorbance between timepoint and T_0 sample

l = pathlength of irradiation cell (Reactor 3 = 0.7 cm, Reactor 4 = 1.9 cm)

$\epsilon(510\ nm)$ = extinction coefficient for $Fe(phen)_3$ complex at 510 nm ($11,100\ M^{-1}\ cm^{-1}$)

The moles of Fe(II) formed in the reaction can be calculated from the above equation. A linear fit of [Fe(II)] vs time gives the rate of photodecomposition (k_{fer}) of the ferrioxalate actinometer (Figure S99). From this, the intensity (I_0) is calculated as $(k_{fer})/(\Phi_{445})$, where Φ_{445} is the quantum yield of ferrioxalate decomposition at 445 nm (extrapolated from literature values as 1.01^{28}).

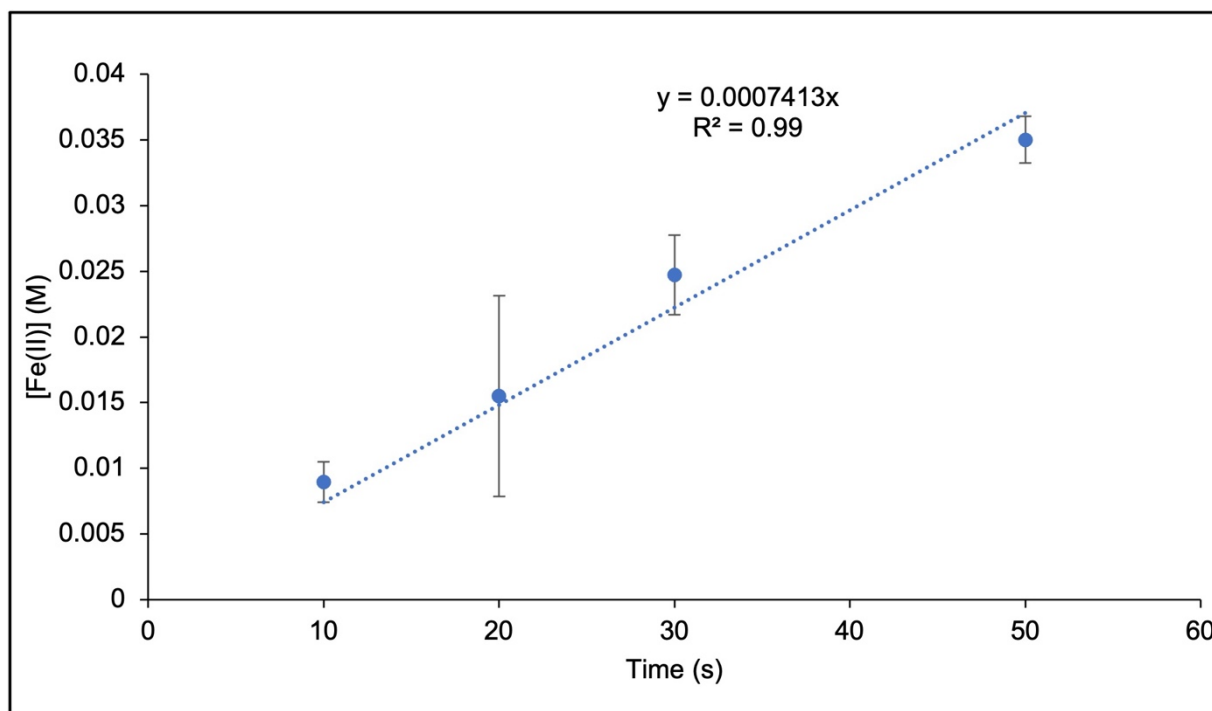


Figure S4.99. Representative plot of $[Fe(II)]$ vs time for ferrioxalate actinometry.

7.2 Determining Φ_{RXN}

After obtaining light intensity (I_0) for a setup, the reaction quantum yield is calculated as $\Phi_{RXN} = (k_{obs})/(I_0)$ where k_{obs} is the initial rate of product formation for the reaction of interest in the same reactor used for actinometry. For reactor 3, the kinetics for 4-BrBzCF₃ were used at 50 °C with TBACl (1 eq.). For reactors 4a and 4b, a single-point kinetics experiment was run to obtain k_{obs} according to a modified procedure from section 6.1. The same general solution preparation described in section 6.1 with TBACl (1 eq.) was followed and three pressure tubes were filled with 2 mL of reaction solution in a glovebox. The tubes were placed in reactor 4a or 4b with the recirculating bath set to 50 °C and allowed to heat up for 10 minutes. Then, the lights were set to 90 mW/well and the reaction was irradiated for 30 minutes. Following this, 50 μ L of each reaction was transferred to an NMR tube containing 450 μ L d-DMSO and analyzed by ¹⁹F NMR.

The resulting Φ_{RXN} data is summarized in Table S4.8. As has been observed in previous work⁵, Φ_{RXN} increased as I_0 was lowered. At high intensity, Φ_{RXN} is below 1.0. However, at the lowest intensity tested, $\Phi_{\text{RXN}} = 3.1$ suggesting the presence of a dark nickel cycle, a scheme in which product can be formed without input photons.

Table S4.8. Summary of reaction quantum yield experiments.

Entry	Reactor	I_0 (E L ⁻¹ s ⁻¹)	Φ_{RXN}
1	3	7.9×10^{-4}	0.14
2	4a	7.5×10^{-5}	0.49
3	4b	5.7×10^{-6}	3.1

This dependence of quantum yield on intensity is consistent with separate photoredox catalyst and Ni cycles as in our proposed mechanism. Specifically, the PC cycle and Ni cycle can have distinct turnover frequencies, and the PC cycle turnover frequency is expected to be flux dependent. Since only one quenching pathway of the excited state PC (photoinduced electron transfer) results in product formation but multiple pathways are possible (e.g. nonradiative decay, emission), increasing the population of the photoexcited PC as in the high light intensity regime will increase the propensity of unproductive pathways since the total Ni concentration is not increased accordingly.

8. Expanded Scope.

8.1 General Procedure A.

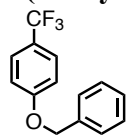
A 2-dram vial was charged with a stir bar. 4-4'-Dimethoxy-2-2'-bipyridine (0.10 mmol) and Ir(ppy)₃ (0.010 mmol) were added and the vial was taken into a nitrogen filled glovebox. NiBr₂-glyme (0.050 mmol) was added and the mixture was dissolved in 2.5 mL anhydrous DMF. Following ~5 minutes of stirring, aryl halide (1.00 mmol), alcohol/amine (1.05 mmol) and DBU (2.00 mmol) were added and a notable color change to red was observed. TBACl (1.00 mmol) was

added and a notable color change to green was observed. The reaction was capped, and the top was wrapped in electrical tape to prevent oxygen exposure. The reaction vial was taken out of the glovebox and allowed to react at 50 °C (general procedure A1) or 70 °C (general procedure A2) in a Hepatochem PhotoRedOx Box TCTM reactor (reactor 1) under 440 nm irradiation (Kessil PR160L-440nm) for 18 hours. The reaction was opened to air, transferred to a separatory funnel, diluted with ~50 mL EtOAc and washed with water/brine. The organic layer was dried over Na₂SO₄, filtered through cotton and dry loaded onto silica gel. The eluents for chromatographic separation are listed for each substrate.

Note on procedure: The reaction is highly moisture sensitive. No issues from the ligand, photocatalyst and aryl halide being used without drying were noted. However, TBACl, DBU and the nucleophiles all needed to be dried prior to use to avoid phenol formation. DBU was dried over calcium hydride and vacuum distilled. Benzyl alcohol and benzyl amine were vacuum distilled, taken into a nitrogen filled glovebox and stored over molecular sieves. Most of the water could be removed from commercial TBACl (determined by <10% phenol formation) by drying it under high vacuum for 2 days followed by storage in a glovebox (vacuum oven not recommended due to decomposition observed). If desired, the remaining trace amounts of water in the TBACl can be reduced by making a stock solution 2x the concentration needed for the reaction and storing it over sieves at least overnight. Then, this solution can be added to the reaction in place of solid TBACl. This method was not used in the substrate scope, but it led to a complete lack of phenol observed in some kinetics experiments.

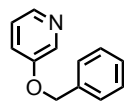
8.2 Product Characterization.

1-(benzyloxy)-4-(trifluoromethyl)benzene (1)



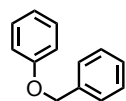
General procedure A1 was used with 4-chlorobenzotrifluoride (1.00 mmol) and benzyl alcohol (1.05 mmol). The product was purified by flash column chromatography (0-5% EtOAc in hexanes) and concentrated under vacuum to afford the title compound as a white solid (186 mg, 74%) ^1H NMR (400 MHz, DMSO- d_6) δ 7.66 (d, J = 8.6 Hz, 2H), 7.49 – 7.32 (m, 5H), 7.20 (d, J = 8.6 Hz, 2H), 5.20 (s, 2H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 161.17, 136.40, 128.50, 128.03, 127.78, 126.95 (q, J = 3.0 Hz), 124.55 (q, J = 272.7 Hz), 121.27 (q, J = 32.2 Hz), 115.30, 69.53. ^{19}F NMR (376 MHz, DMSO- d_6) -59.81. Several techniques were attempted for HRMS with no ionization observed.

3-(benzyloxy)pyridine (2)



General procedure A1 was used with 3-chloropyridine (1.00 mmol) and benzyl alcohol (1.05 mmol). The product was purified by flash column chromatography (20-40% EtOAc in hexanes) and concentrated under vacuum to afford the title compound as a pale-yellow oil (112 mg, 61%) ^1H NMR (400 MHz, DMSO- d_6) δ 8.36 (d, J = 2.6 Hz, 1H), 8.17 (d, J = 4.0 Hz, 1H), 7.54 – 7.29 (m, 7H), 5.18 (s, 2H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 154.54, 141.88, 138.09, 136.50, 128.49, 128.03, 127.84, 124.12, 121.38, 69.46. HRMS (MALDI-TOF): calculated for $[\text{M}+\text{H}]$ $\text{C}_{12}\text{H}_{12}\text{NO}$, 186.091; observed 186.084.

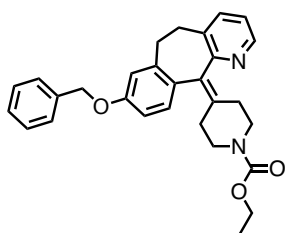
(benzyloxy)benzene (3)



General procedure A2 was used with chlorobenzene (1.00 mmol) and benzyl alcohol (1.05 mmol). The product was purified by flash column chromatography (0-5% EtOAc in hexanes) and concentrated under vacuum to afford the title compound as a white solid

(112 mg, 61%) ^1H NMR (400 MHz, DMSO-*d*6) δ 7.49 – 7.25 (m, 7H), 7.04 – 6.98 (m, 2H), 6.94 (t, J = 7.3 Hz, 1H), 5.09 (s, 2H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 158.32, 137.13, 129.49, 128.41, 127.78, 127.66, 120.70, 114.76, 69.05. Several techniques were attempted for HRMS with no ionization observed.

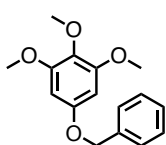
ethyl 4-(8-(benzyloxy)-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (4)



General procedure A2 was used with loratadine (1.00 mmol) and benzyl alcohol (1.05 mmol). The product was purified by flash column chromatography (67.5% hexanes, 30% acetone, 2.5% triethylamine) and concentrated under vacuum to afford the title compound as a white solid

(350 mg, 77%) ^1H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, J = 4.8, 1.5 Hz, 1H), 7.49 – 7.27 (m, 6H), 7.15–7.06 (m, 2H), 6.82–6.77 (m, 2H), 5.02 (s, 2H), 4.13 (q, J = 7.1 Hz, 2H), 3.82 (s, 2H), 3.45 – 3.29 (m, 2H), 3.19 – 3.06 (m, 2H), 2.90 – 2.74 (m, 2H), 2.48 (ddd, J = 14.1, 9.6, 4.6 Hz, 1H), 2.39 (t, J = 5.6 Hz, 2H), 2.29 (dt, J = 14.0, 4.2 Hz, 1H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.28, 157.98, 155.66, 146.30, 139.04, 137.67, 137.12, 136.91, 134.53, 133.93, 131.82, 130.68, 128.71, 128.09, 127.60, 122.22, 115.68, 112.22, 70.10, 61.41, 45.00, 44.93, 32.30, 31.69, 30.83, 30.71, 14.82. HRMS (ESI-TOF): calculated for $[\text{M}+\text{H}]$ $\text{C}_{29}\text{H}_{31}\text{N}_2\text{O}_3$, 455.2335; observed 455.2327.

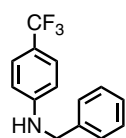
5-(benzyloxy)-1,2,3-trimethoxybenzene (5)



General procedure A2 was used with 5-bromo-1,2,3-trimethoxybenzene (1.00 mmol) and benzyl alcohol (1.05 mmol). The product was purified by flash column

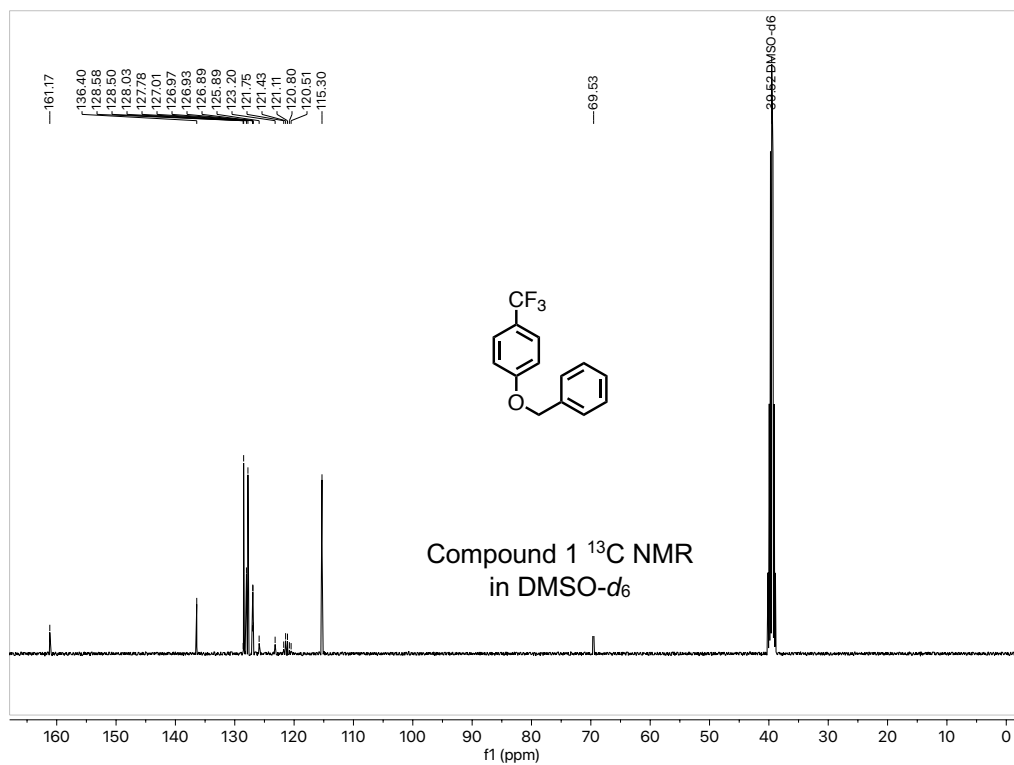
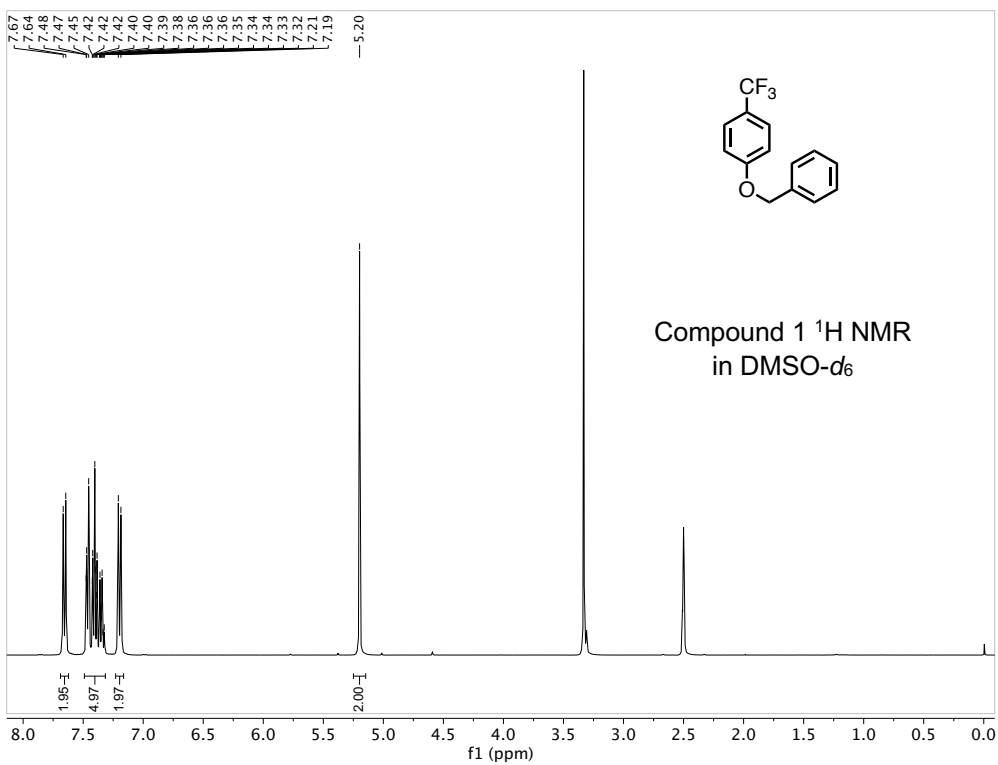
chromatography (5-10% EtOAc in hexanes) and concentrated under vacuum to afford the title compound as a white solid (176 mg, 64%). ^1H NMR (400 MHz, DMSO- d_6) δ 7.49-7.30 (m, 5H), 6.34 (s, 2H), 5.07 (s, 2H), 3.75 (s, 6H), 3.58 (s, 3H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 154.92, 153.33, 137.11, 131.74, 128.40, 127.83, 127.80, 92.82, 69.59, 60.11, 55.83. HRMS (MALDI-TOF): calculated for $[\text{M}^+]$ $\text{C}_{16}\text{H}_{18}\text{O}_4$, 274.121; observed 274.122.

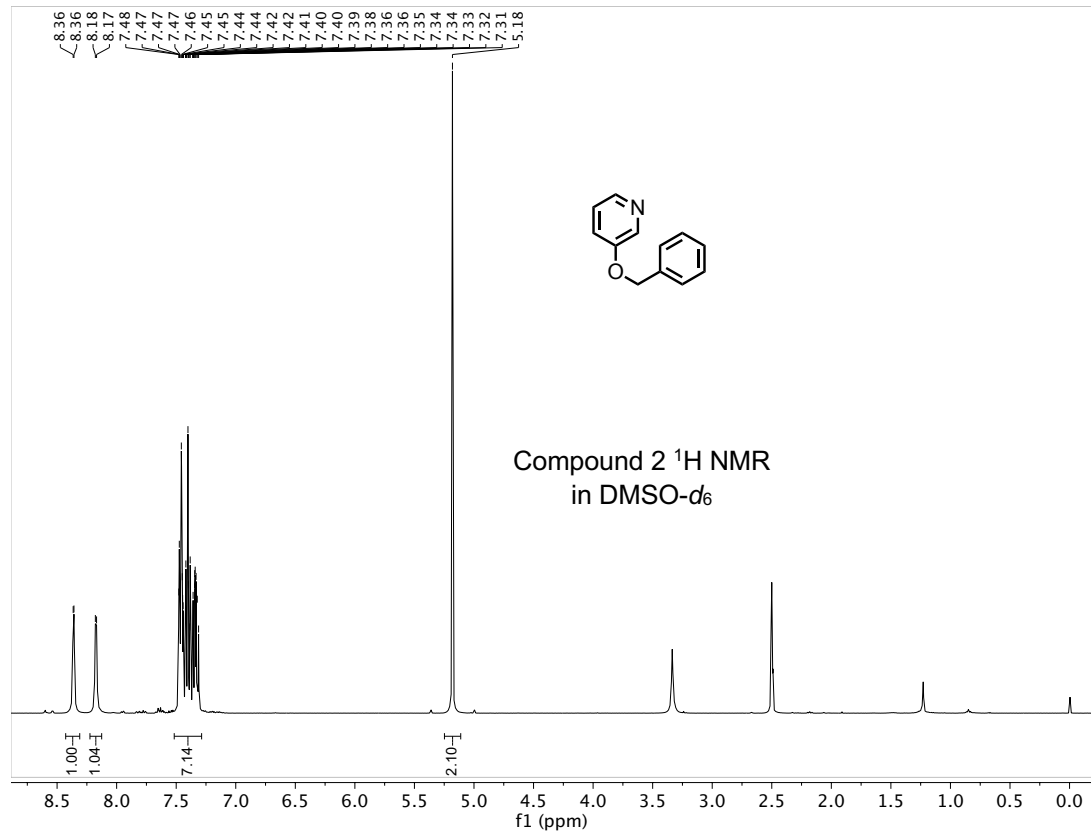
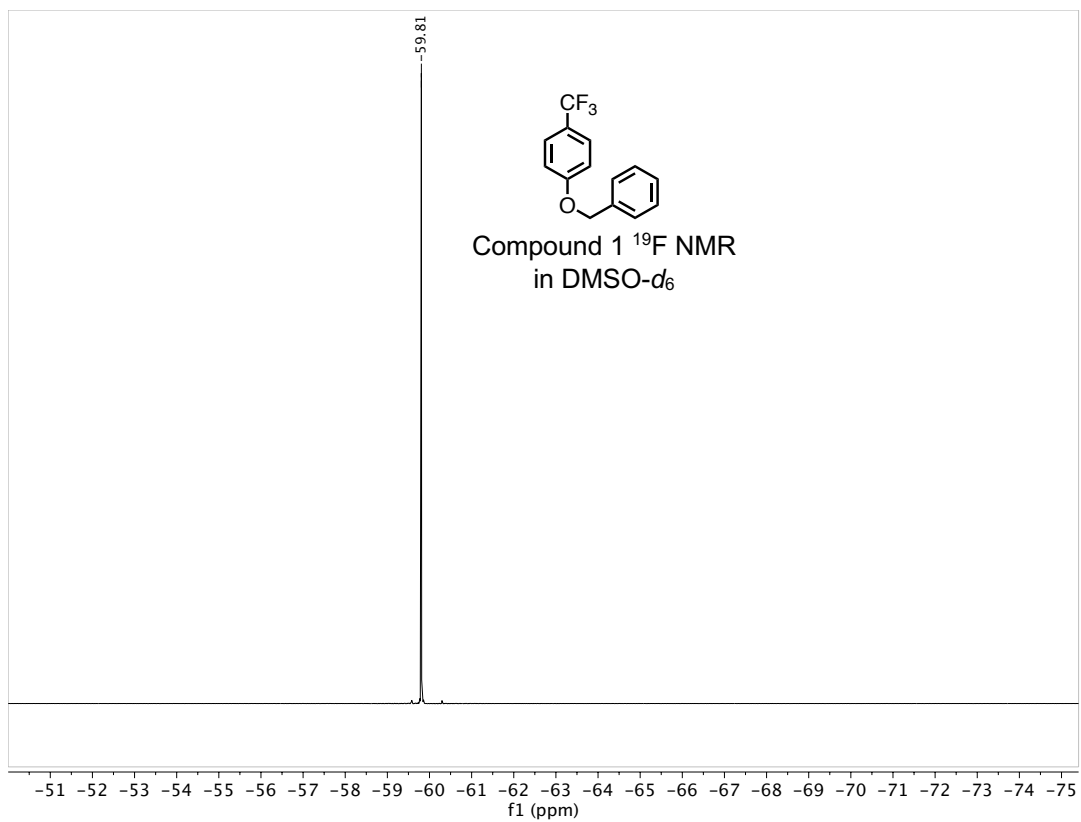
***N*-benzyl-4-(trifluoromethyl)aniline (6)**

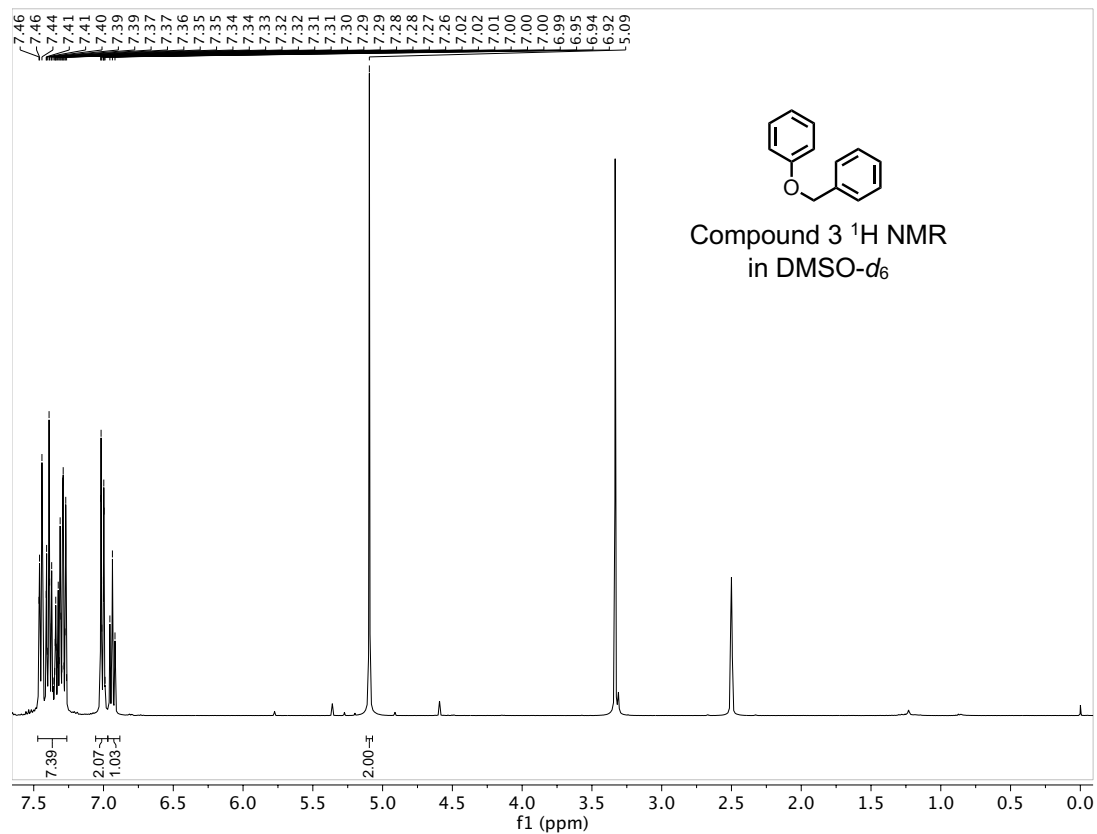
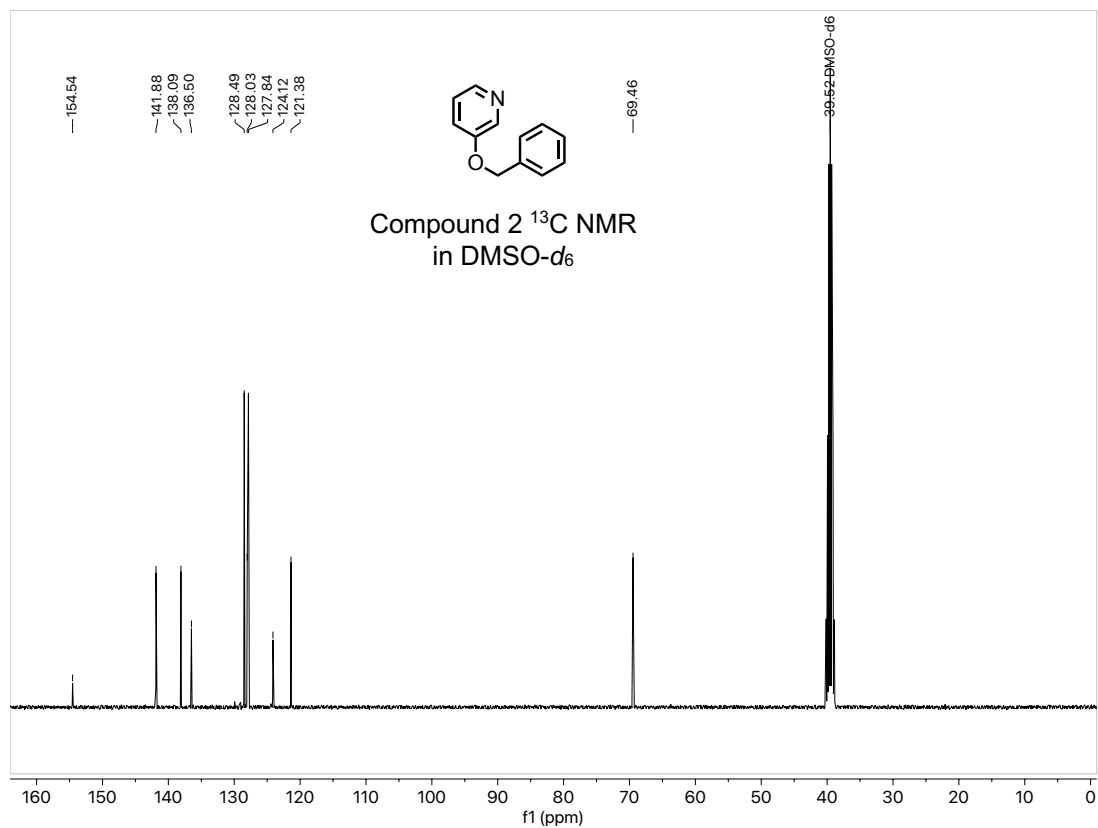


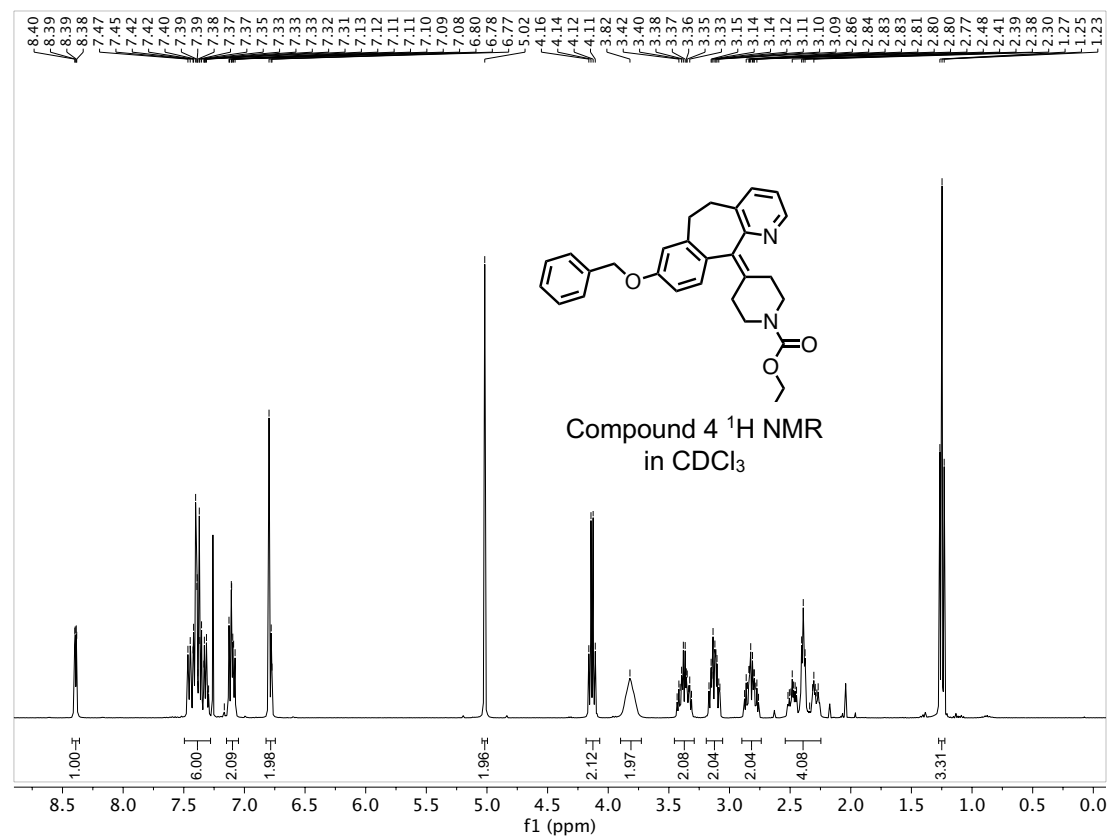
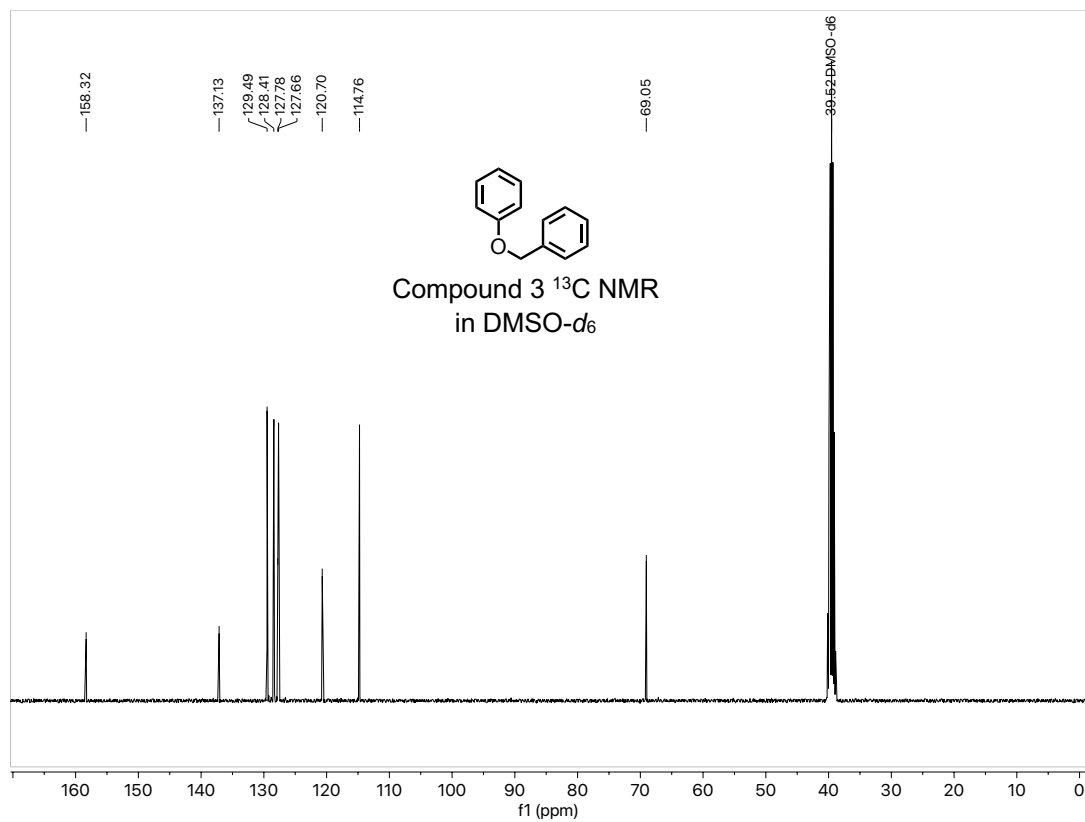
General procedure A1 was used with 4-chlorobenzotrifluoride (1.00 mmol) and benzyl amine (1.05 mmol). The product was purified by flash column chromatography (5-10% EtOAc in hexanes) and concentrated under vacuum to afford the title compound as a light-yellow solid (88 mg, 35%). ^1H NMR (400 MHz, Chloroform- d) δ 7.40 (d, J = 8.5 Hz, 2H), 7.38-7.33 (m, 4H), 7.33-7.27 (m, 1H), 6.64 (d, J = 8.5 Hz, 2H), 4.40 (br s, 1H), 4.38 (s, 2H). ^{13}C NMR (101 MHz, Chloroform- d) δ 150.60, 138.59, 128.94, 127.67, 127.51, 126.77 (q, J = 30.3 Hz), 125.10 (q, J = 271.7 Hz), 119.24 (q, J = 33.3 Hz), 112.12, 47.95. ^{19}F NMR (376 MHz, Chloroform- d) δ -61.02. HRMS (ESI-TOF): calculated for $[\text{M}-\text{H}]$ $\text{C}_{14}\text{H}_{11}\text{F}_3\text{N}$, 250.0844; observed 250.0867.

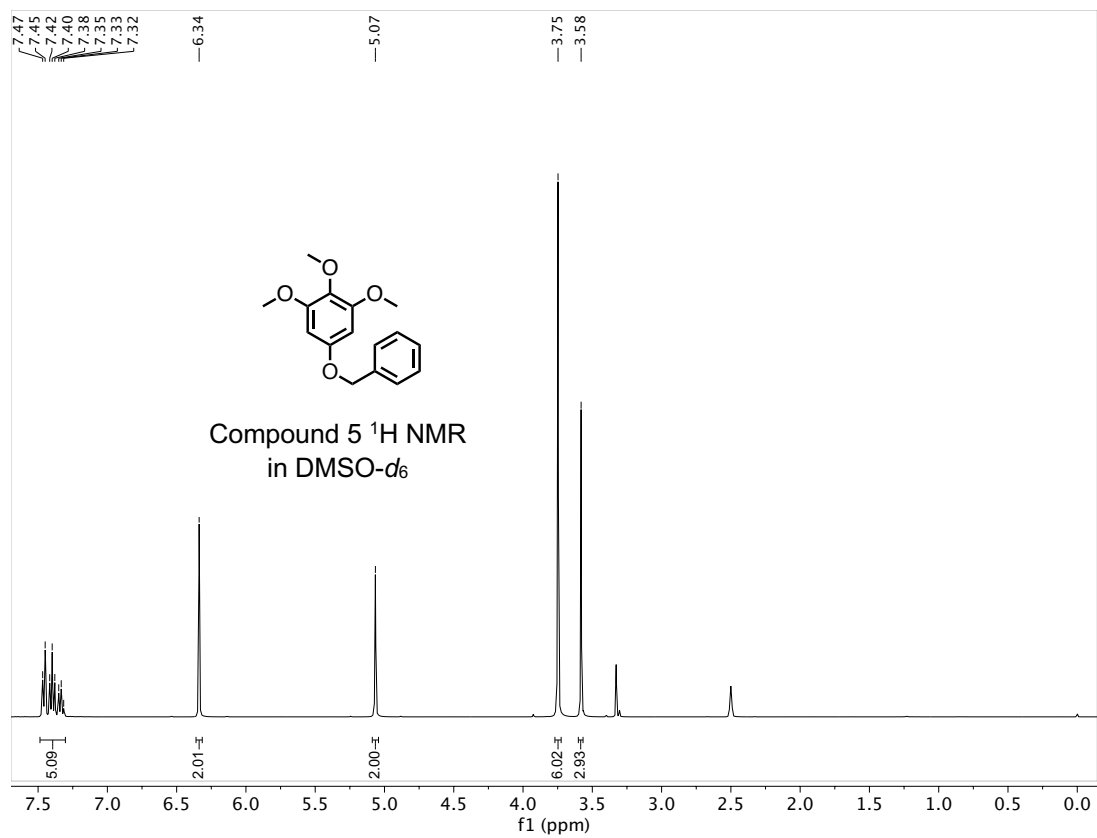
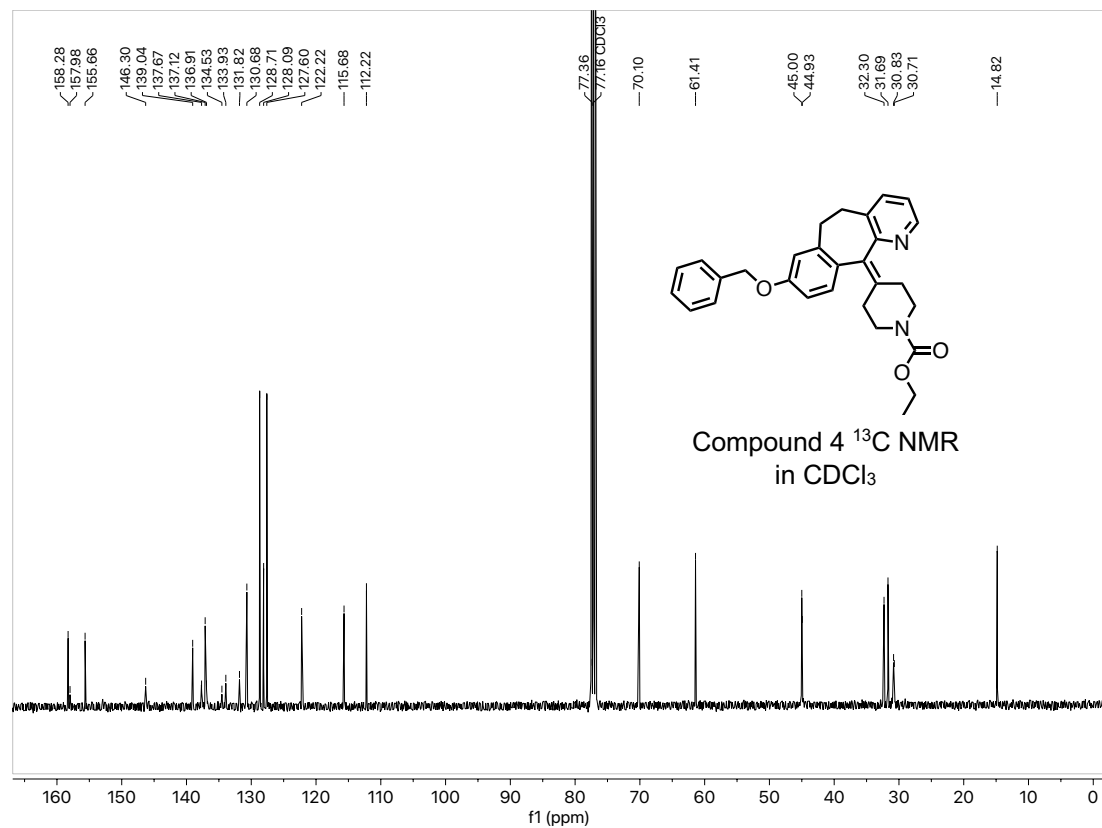
9. NMR Spectra

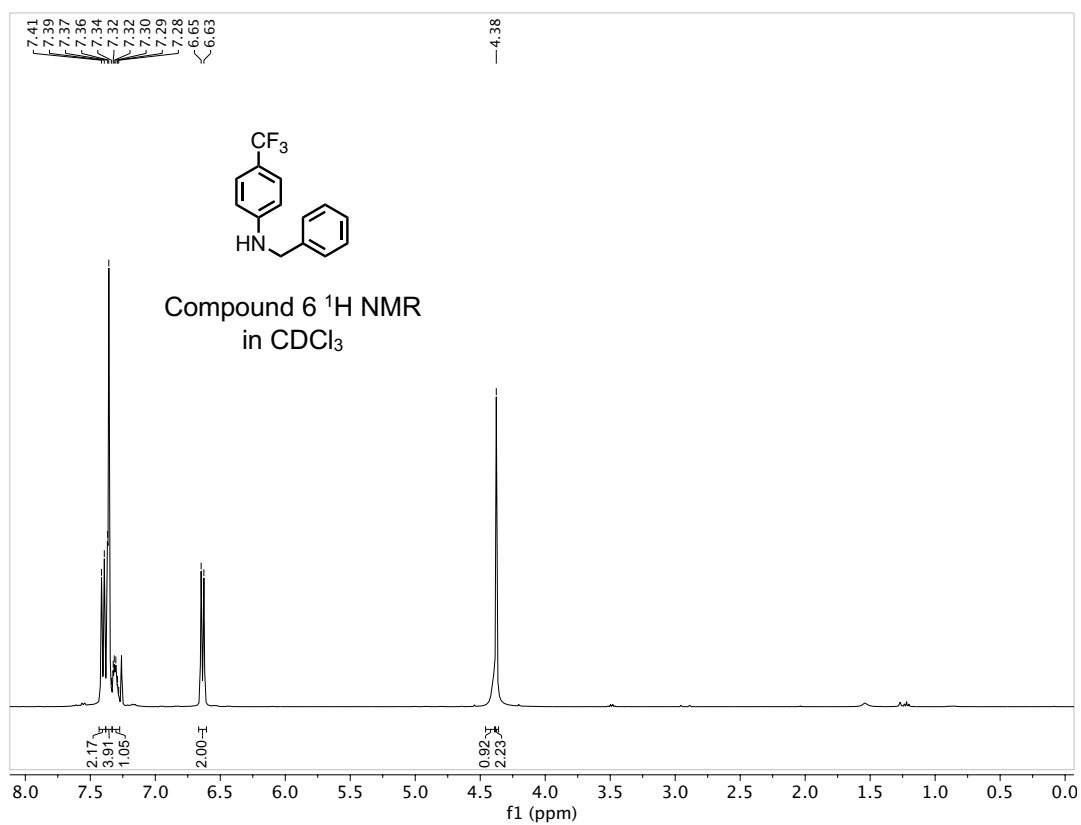
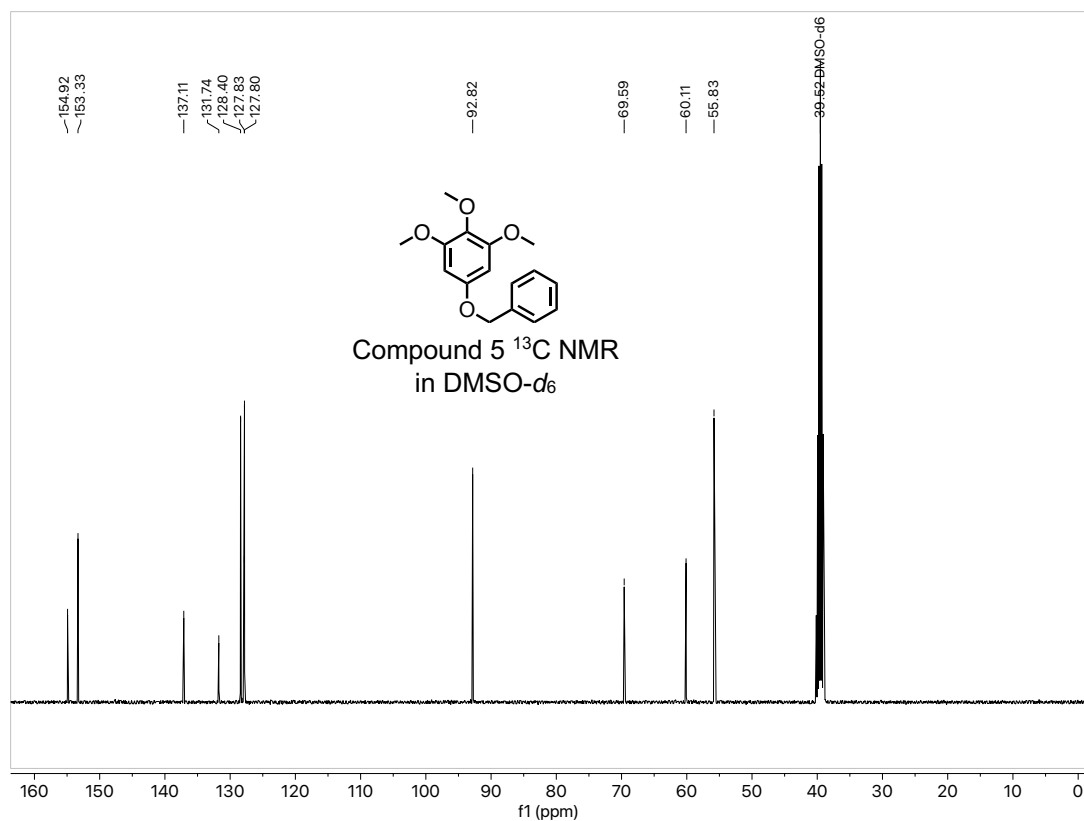


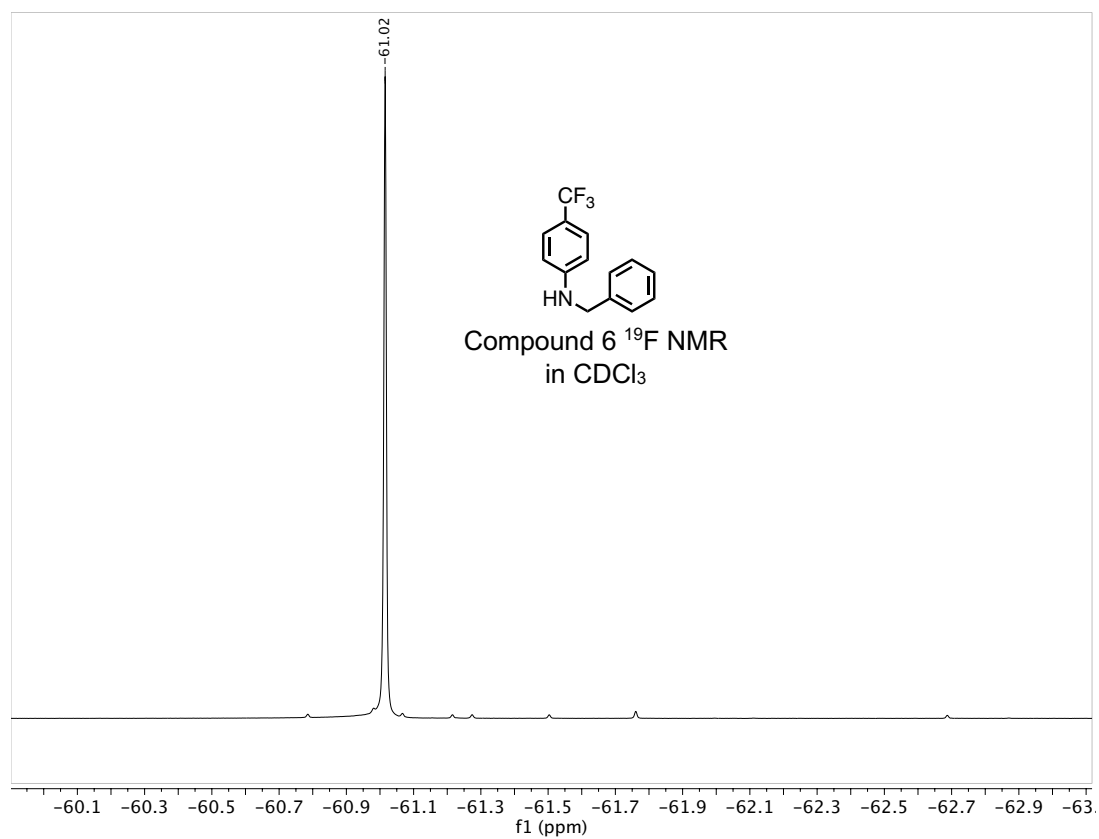
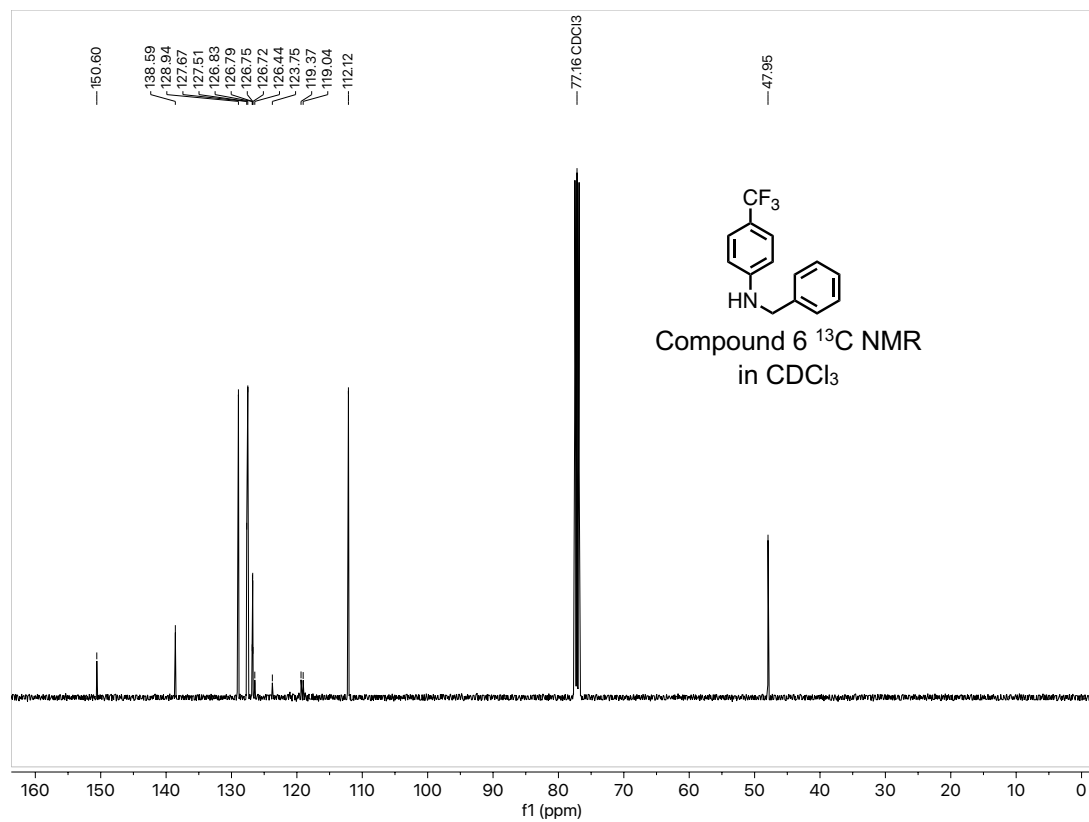












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APPENDIX D: SUPPLEMENTARY INFORMATION FOR CHAPTER 5

1. General Information

This supplementary information includes all data that has been acquired and processed. It is a rough draft as there are more experiments and further data to be included from collaborators. This data will be included in the final publication.

Unless noted below, all reagents and solvents were used as purchased without further purification. All liquid aryl and alkyl halides were sparged with nitrogen and used in a nitrogen filled glovebox. PCs in Figure S5.7 and Figure S5.8 were synthesized according to literature procedures or used from the New Iridium library.¹⁻⁴ Tetrabutylammonium chloride (TBACl) was dried under highvac for 2 days and stored in a nitrogen filled glovebox. NiBr₂·glyme and NiCl₂·glyme were stored in a nitrogen filled glovebox.

NMR spectra were recorded on a Varian 400 MHz NMR Spectrometer and all ¹H and ¹³C shifts were measured relative to the residual solvent peaks for either chloroform or DMSO. Mass spectrometry was performed by the staff in the Analytical Resources Core at Colorado State University.

2. Fluorescence Quenching and UV-Vis Experiments

UV-visible spectroscopy was performed on a Cary 5000 instrument (Agilent) with the standard liquid cell holder and a 1 cm path length quartz cuvette. In all cases, the ultraviolet, visible, and near infrared lamps were allowed to warm up for 30 minutes before recording data. Background correction was performed for all runs utilizing a solvent blank.

Fluorescence spectroscopy was performed on an Edinburgh Instruments FS5 spectrofluorimeter using DMSO as the solvent. All experiments were run with a 400 nm excitation and intensity was measure between 425 nm and 800 nm.

3. Optimization of 4-BrBzCF₃ Coupling.

General Optimization Procedure:

Constants:

- 4-bromobenzotrifluoride (4-BrBzCF₃, 14.0 uL, 0.100 mmol, 1.00 eq.)
- 4-bromotetrahydropyran (4-BrTHP, 16.9 uL, 0.150 mmol, 1.50 eq.)
- Concentration = 0.1 M

To a 0.5-dram vial charged with a stir bar, all solid reagents (i.e. base, ligand, PC) aside from nickel precatalyst were added. The vial was taken into a nitrogen filled glovebox and nickel precatalyst was added. Any liquid reagents, 4-BrBzCF₃ and 4-BrTHP were added (all sparged under nitrogen for 10 minutes prior to brining into glovebox). The mixture was dissolved in solvent (1.00 mL), capped, sealed with electrical tape, and taken out of the glovebox. The reaction was placed in either Reactor 1 (See Chapter 4, Figure S4.88) or Reactor 2 (See Chapter 4, Figure S4.89) and allowed to react for the specified times. After completion, the reaction was exposed to oxygen and 50 uL was added to an NMR tube containing 500 uL CDCl₃. Reaction performance was determined by ¹⁹F NMR, with the two important metrics being selectivity/composition and % conversion. Selectivity (reported as % DP) was calculated as 100*(area of the desired product)/(area of all products). Normalized composition of products was determined for each known/unknown product as (area of specific product)/(area of all products). Conversion (%) was calculated as 100*(area of all products)/(area of all products + starting material).

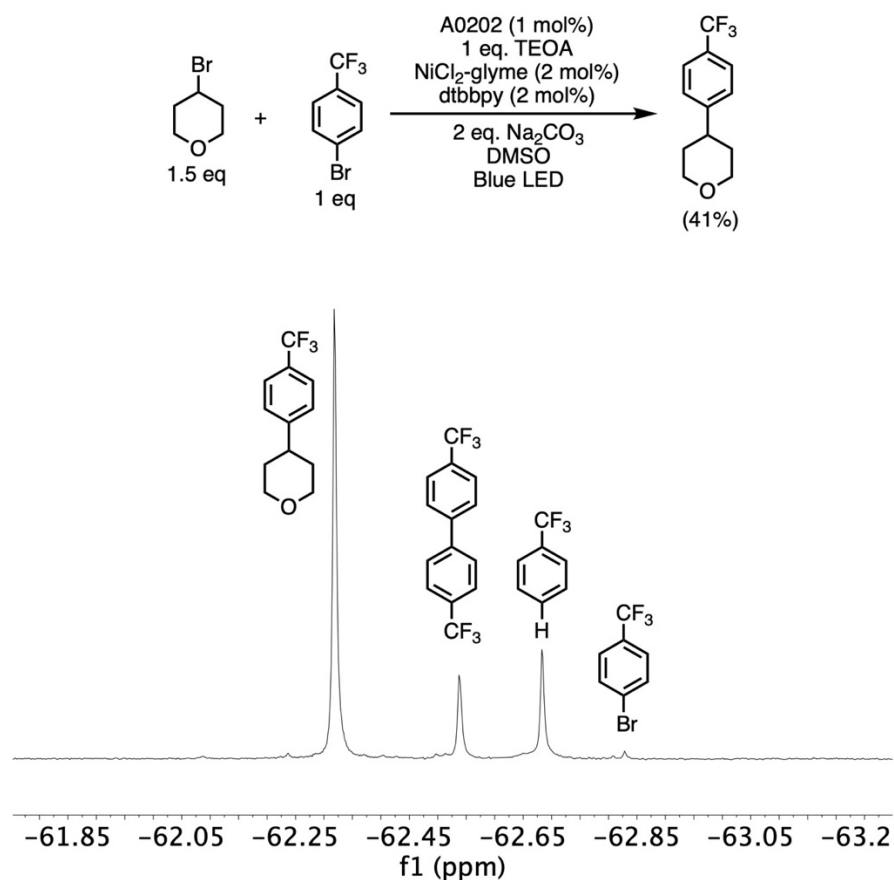


Figure S5.1. General reaction scheme for coupling between 4-BrBzCF₃ and BrTHP with conditions and yield for initial proof of concept reaction (top). Example ¹⁹F NMR showing main reaction components.

Table S5.1. Results for base/reductant screen validating TEOA as a suitable base.

Standard Conditions

PC: A0202 (1 mol%)
 Sacrificial reductant: 1 eq. TEOA
 Nickel Source: NiCl₂-glyme (2 mol%)
 Ligand: dtbbpy (2 mol%)
 Base: *Variable*
 Solvent: DMSO
 Light Source: Blue LED
 Reaction Time: 18 hr

Reaction	Conversion (%)	DP (%)	De-Br (%)	Homocouple (%)	Other (%)
Standard	>99	67	19	14	-
3 eq. TEOA 18 hr	93	55	19	19	7
3 eq. TEOA 36 hr	>99	60	16	14	8

Table S5.2. Results for solvent screen. Concentration = 0.1 M in every solvent.

Standard Conditions

PC: A0202 (1 mol%)
Sacrificial reductant: 1 eq. TEOA
Nickel Source: NiCl₂-glyme (2 mol%)
Ligand: dtbbpy (2 mol%)
Base: 2 eq. TEOA
Solvent: *Variable*
Light Source: Blue LED
Reaction Time: 18 hr

Solvent	% Conversion	% DP
DMSO	89	52
Propylene Carbonate	66	13
DMF	84	31
DMAc	84	25
Acetonitrile	14	6
THF	34	7
Dimethoxy Ethane	5	1
diglyme	37	8
Dimethoxy propane	0	0
Toluene	4	1
Methanol	7	0
Butanol	8	1

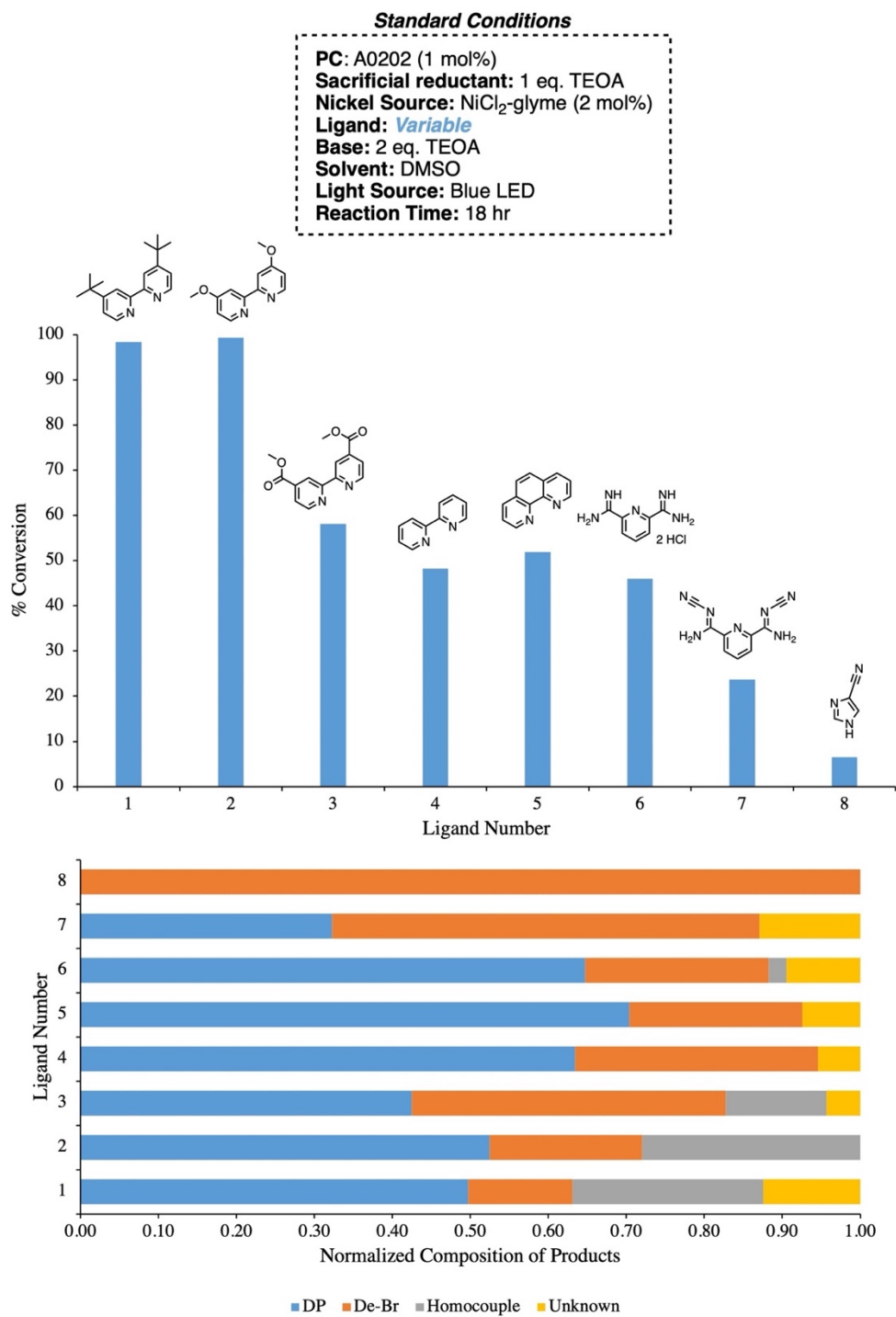


Figure S5.2. Conversion and selectivity data for first set of ligands.

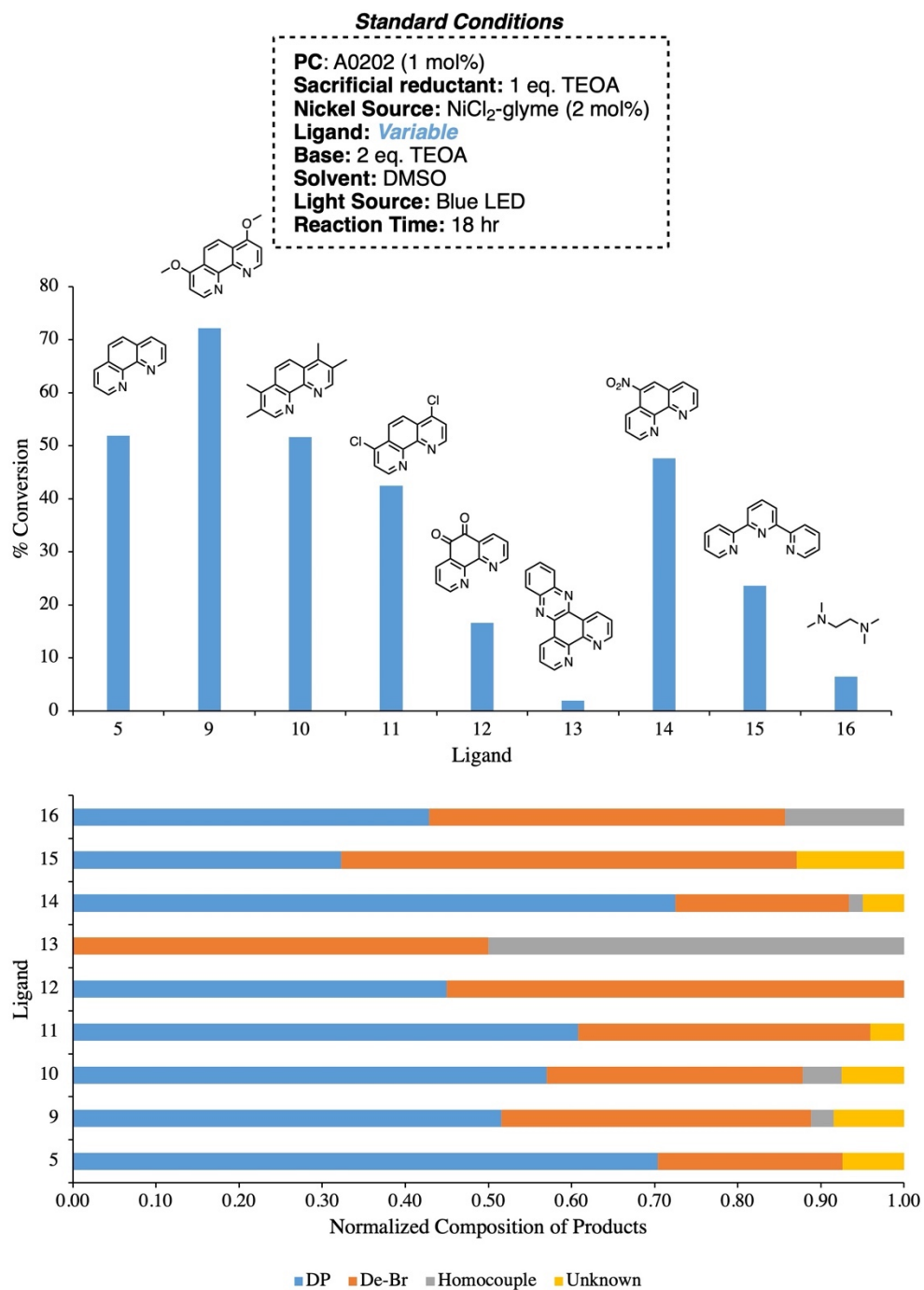


Figure S5.3. Conversion and selectivity data for second set of ligands.

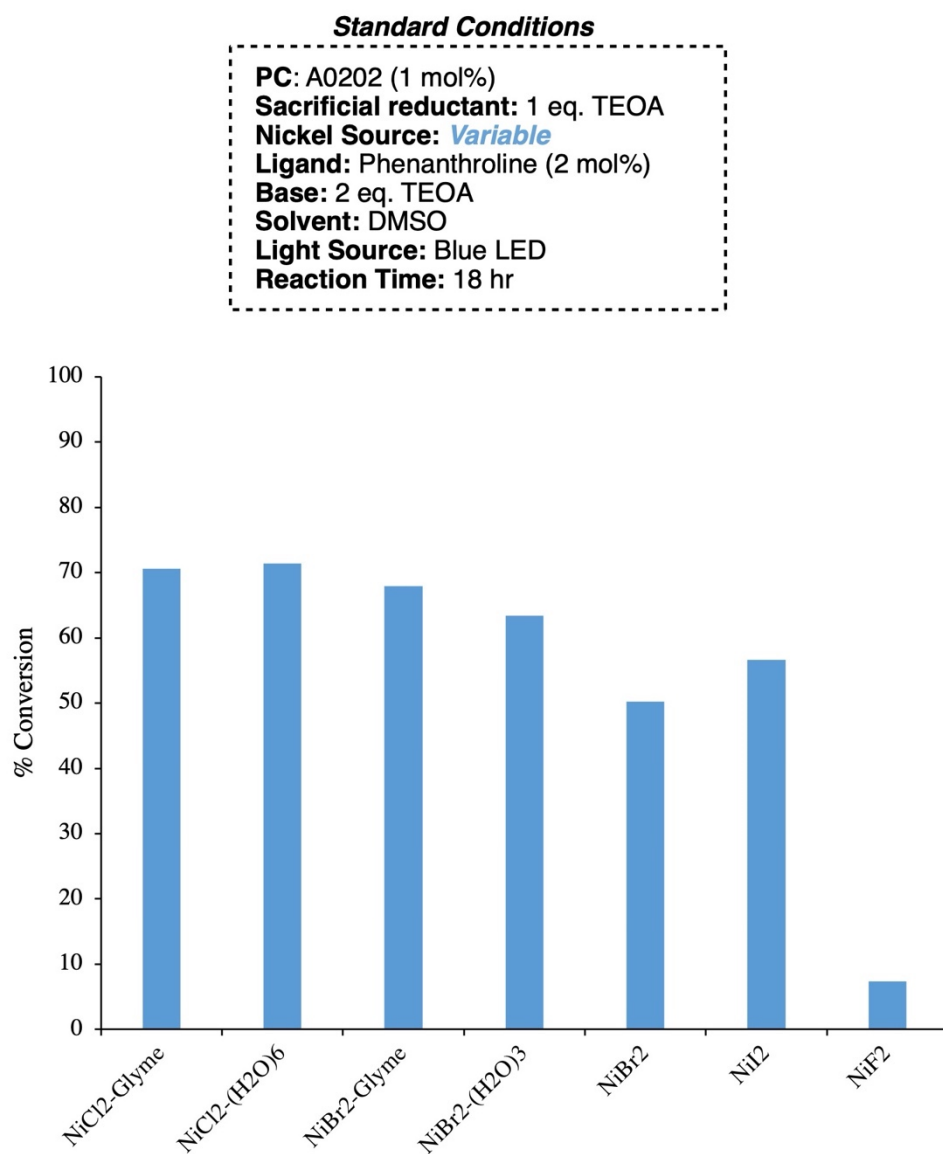


Figure S5.4. Conversion data for different nickel precatalysts. Selectivity was identical for all NiBr and NiCl precatalysts.

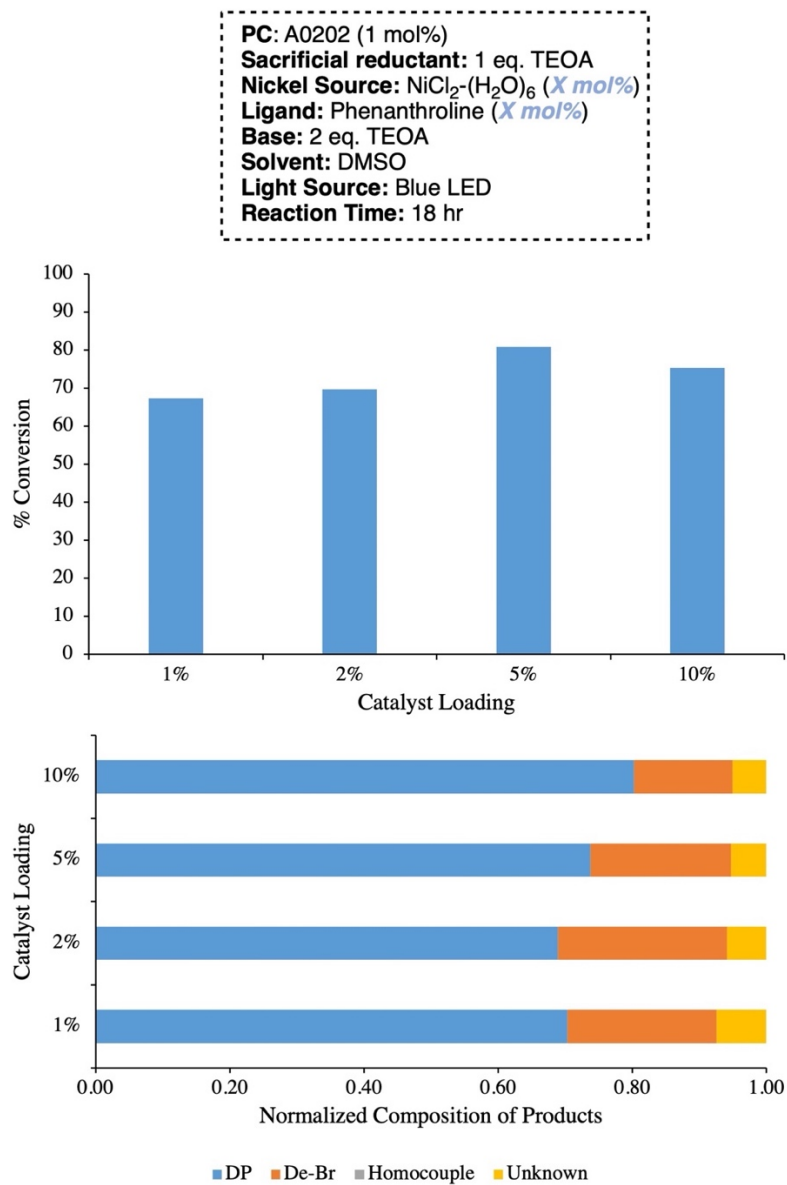


Figure S5.5. Conversion and selectivity data different ligand/Ni loadings.

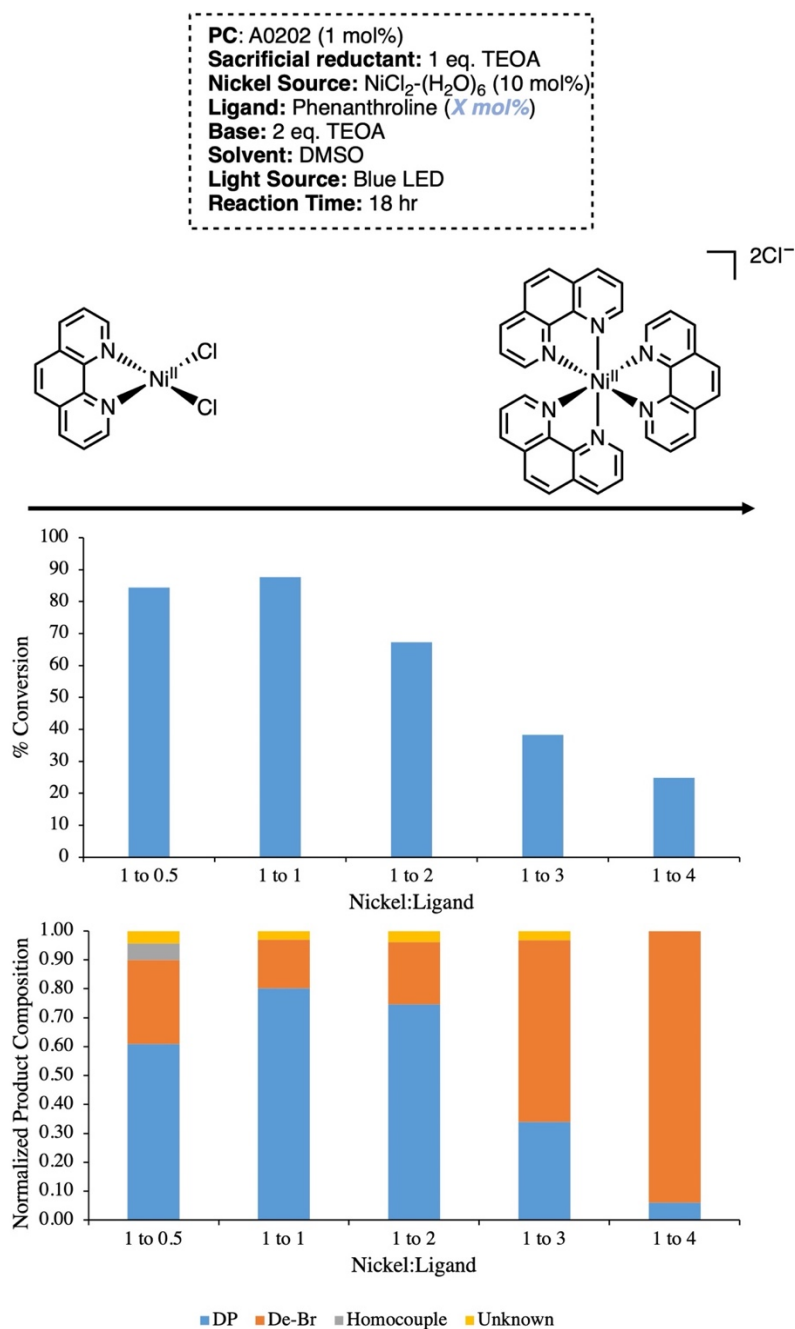


Figure S5.6. Conversion and selectivity data for different ratios of Ni:Ligand.

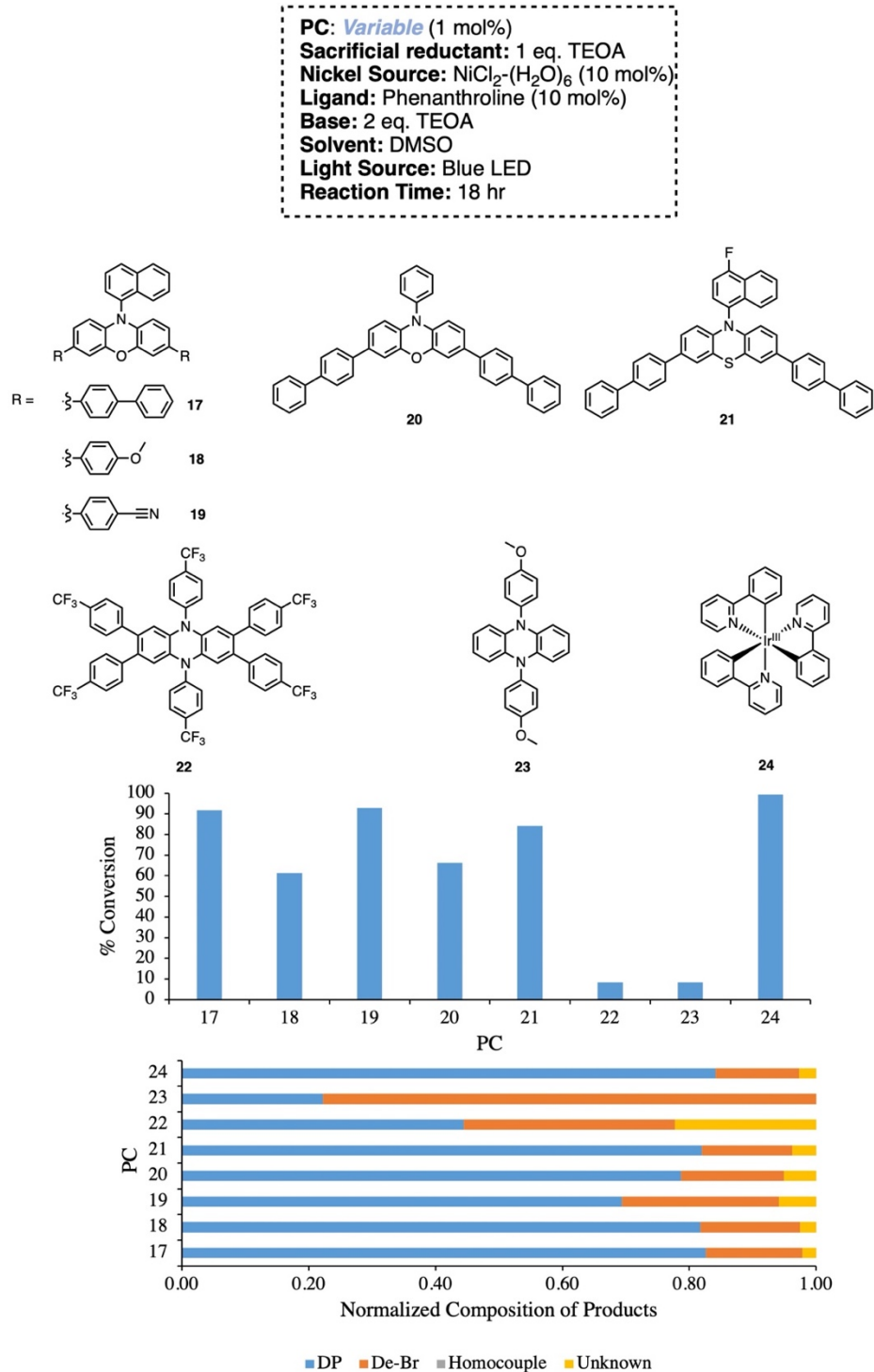


Figure S5.7. Conversion and selectivity data for first set of photocatalysts.

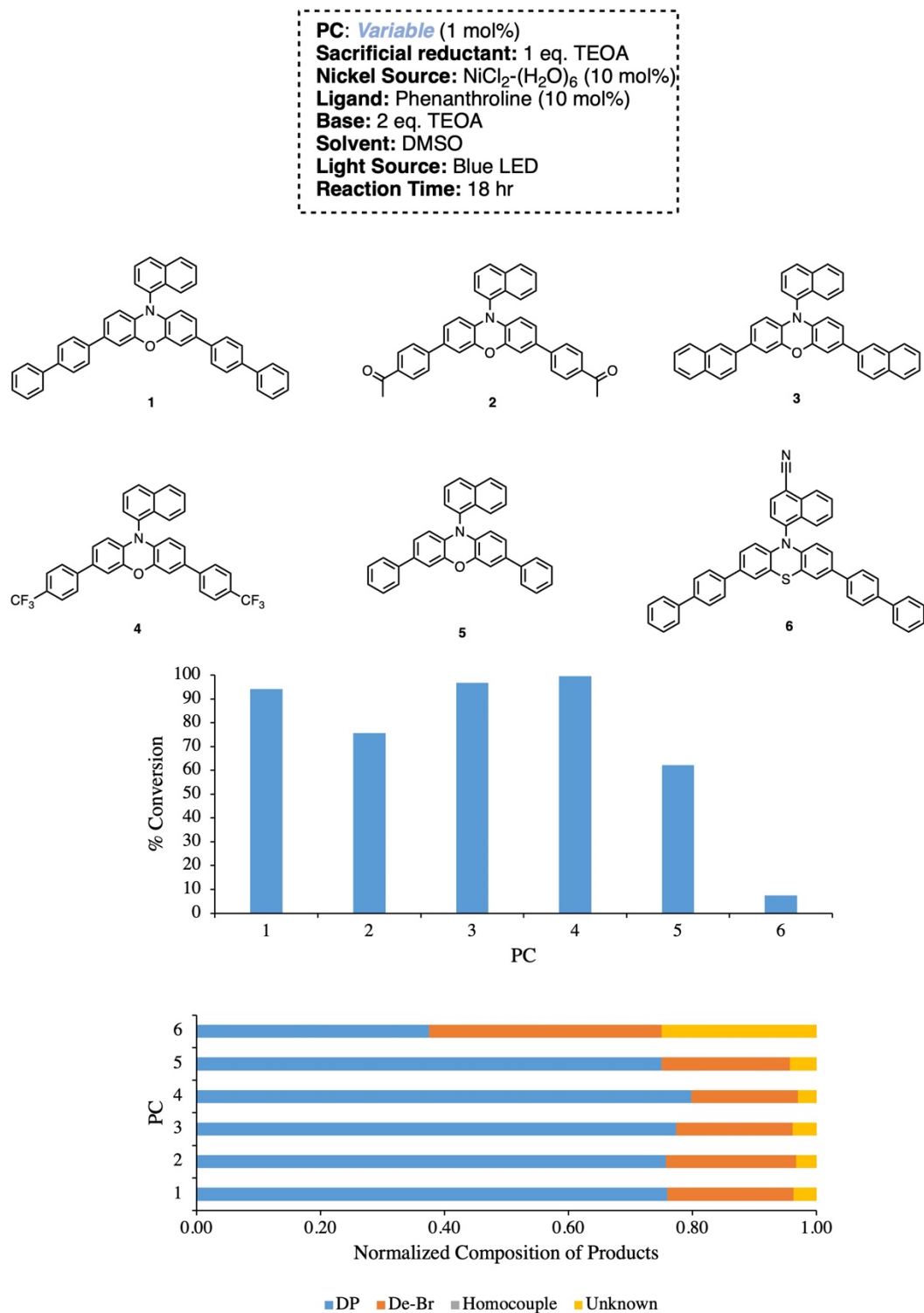


Figure S5.8. Conversion and selectivity data for second set of photocatalysts.

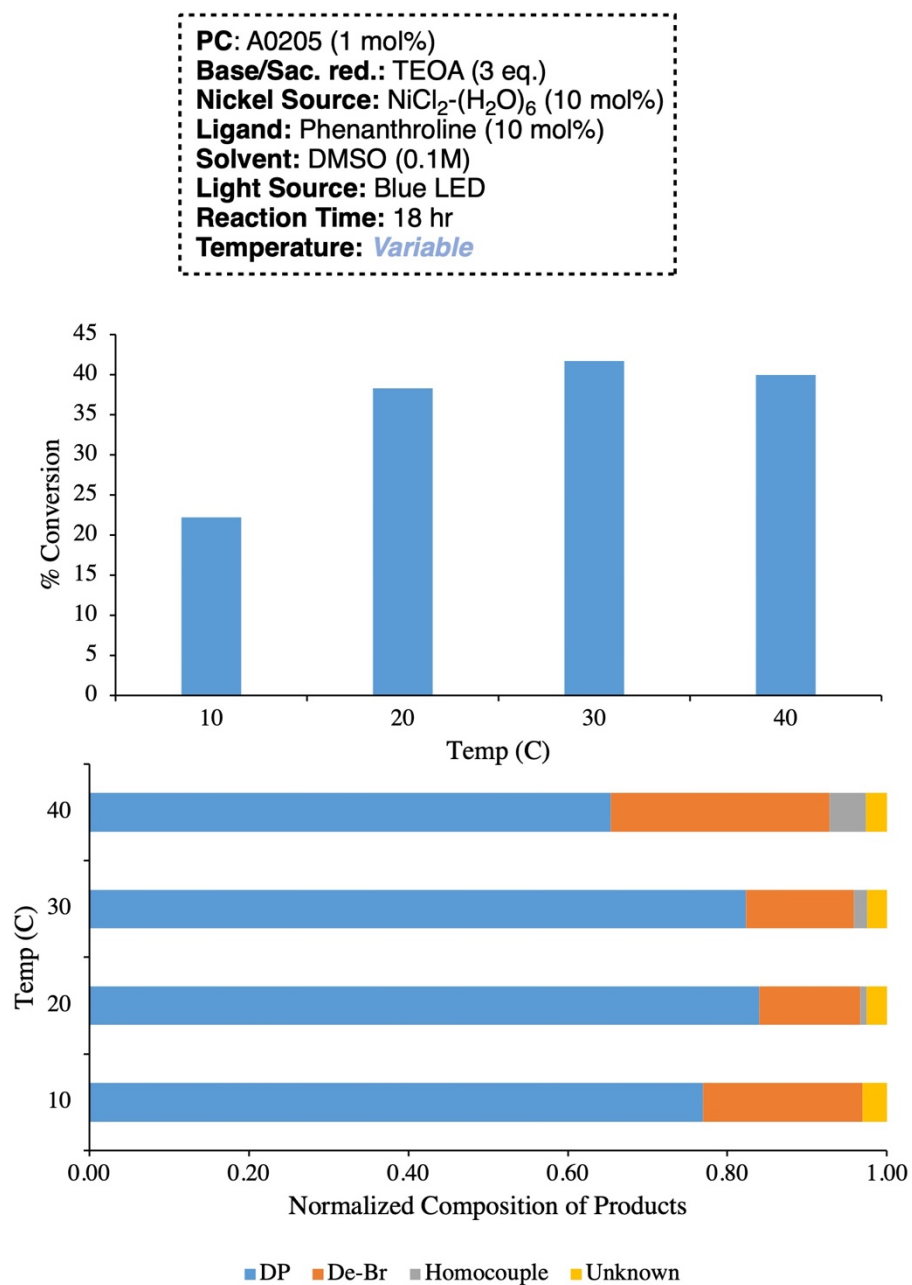


Figure S5.9. Conversion and selectivity data for temperature screen.

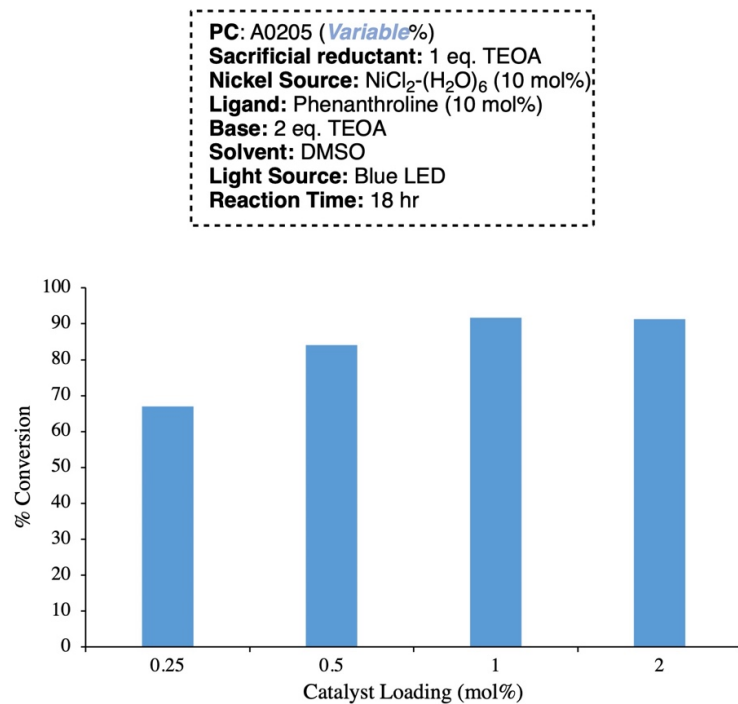


Figure S5.10. Conversion and selectivity data for PC loading experiment.

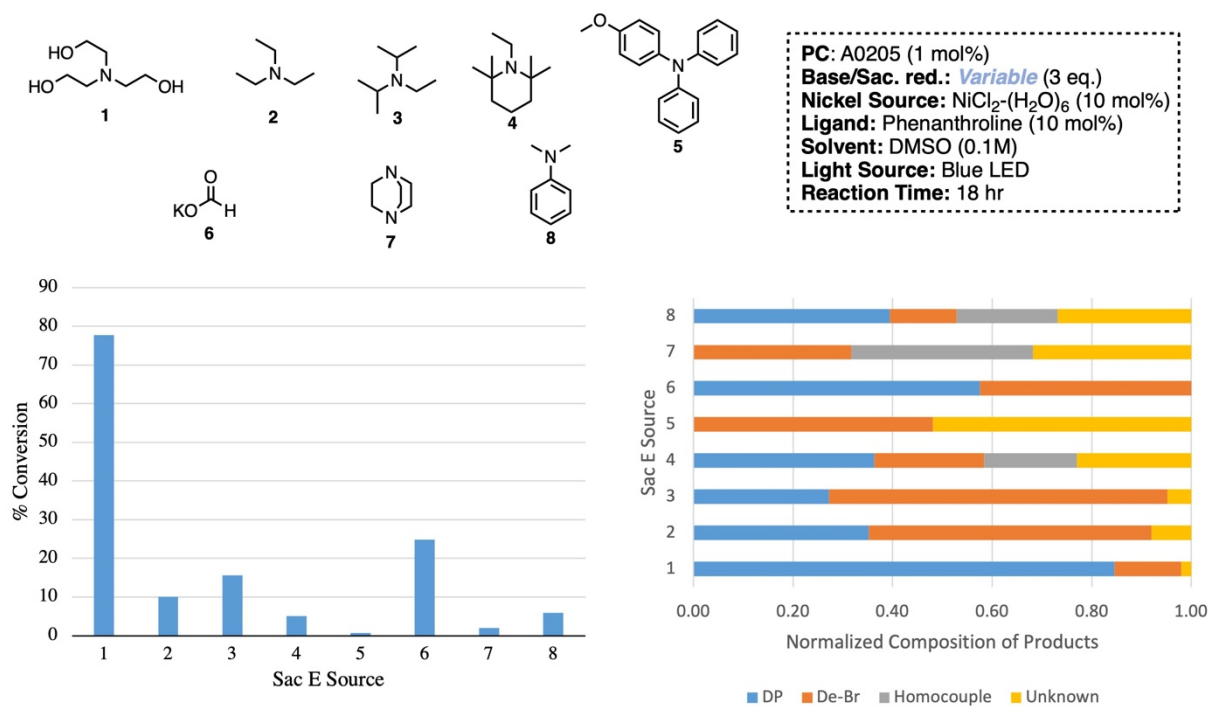


Figure S5.11. Conversion and selectivity data for sacrificial electron donors/bases.

Table S5.3. Conversion and selectivity data for different light sources.

PC: A0205 (1 mol%)
Sacrificial reductant: 1 eq. TEOA
Nickel Source: $\text{NiCl}_2 \cdot (\text{H}_2\text{O})_6$ (10 mol%)
Ligand: Phenanthroline (10 mol%)
Base: 2 eq. TEOA
Solvent: DMSO
Light Source: *Variable*
Reaction Time: 2 hr

Entry	Light	% conversion (2hr)	% DP (2hr)
1	blue kessil	30	82
2	400 nm kessil	64	81
3	405 nm high power	99	65
4	440 nm kessil	70	79
5	457 nm kessil	72	65
6	467 nm kessil	10	73

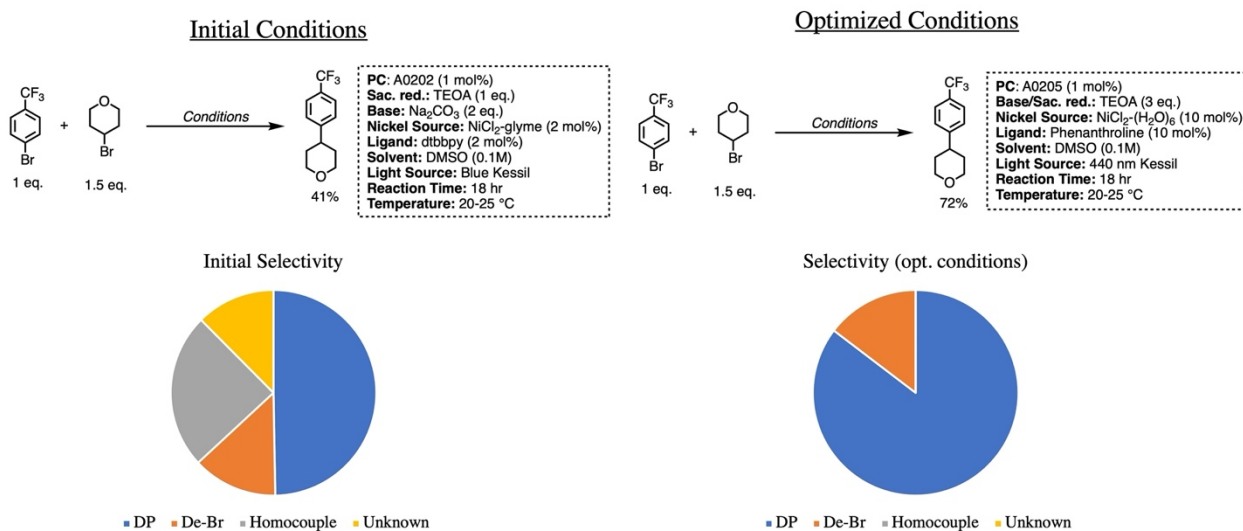


Figure S5.12. Summary of optimization results. Initial and optimized selectivity shown.

4. Phthalide Optimization.

General procedure for High-Throughput Experimentation (HTE):

See Chapter 4, Figure S4.90 and the corresponding discussion for details on the reactor setup.

PCs and ligands were loaded into the plate according to the following procedure. All PCs and ligands were initially screened for solubility in volatile solvents at 0.001 M and 0.01 M respectively. Once a suitable solvent was selected for each compound, a stock solution of each PC/ligand was made at the listed concentrations. 70 μ L of each ligand was added to all 12 wells in the corresponding column. The HTE plate was loosely covered with a ChemWipe and placed in a vacuum oven set to 40 $^{\circ}$ C. After allowing the plate to warm for approximately 10 minutes, the oven was slowly placed under vacuum and the solvent was allowed to evaporate overnight. The plate was then removed from the oven and the same procedure was followed for each PC.

A stock solution of all constants was made according to the following procedure. A 20 mL vial was charge with a stirbar, TEOA (448 mg, 3 mmol) and 5-bromophthalide (213 mg, 1 mmol) were added, and the vial was taken into a nitrogen filled glovebox. NiCl_2 -glyme (22.0 mg, 0.1 mmol), methyl benzoate (92.6 μ L, 10 mg/mL) and BrTHP (169 μ L, 1.5 mmol) were added and the mixture was dissolved in 10 mL DMSO. After dissolution, 70 μ L of the mixture was added to every well in the plate mentioned above, pipetting up and down several times to ensure dissolution of the ligand/PC. The plate was sealed and run for either 4 hours or 18 hours at 445 nm, 25 $^{\circ}$ C and 510 mW/well (see Chapter 4 supplementary info for more details on setup). After completion, the plate was removed from the purge box and unsealed. All reactions were transferred to a second 96 well plate containing 1 mL of 50:50 ACN:H₂O (0.1% formic acid) and cooled to $\sim$ 5 $^{\circ}$ C overnight. The plate was removed from the fridge and all wells were transferred to a filter plate containing

celite and filtered into a 96 well plate for HPLC. HPLC was run and the yield was determined based on a standard curve generated for the reaction components (SM, DP etc.).

Notes on procedure:

- We ran into issues with Eosin Y bumping in the vacuum oven. We believe this is due to this PC being acidic and, when mixed with the basic ligands, resulted in an exothermic acid-base reaction. This can be avoided by allowing the plate to sit for ~30 minutes prior to placing it in the vacuum oven. However, if no incompatibilities between ligands and PCs exist, this step can be avoided.
- Methyl benzoate was selected for several reasons. First, it fully separated from all of the reaction components by HPLC. It was also able to be added to the stock solution prior to the reaction because the same yield was achieved with it present in the reaction. This is advantageous because each reaction gets exactly the same amount of the internal standard and there is no error associated with adding it to the individual wells after reaction completion.
- Methyl benzoate was a suitable internal standard for our first HTE plate but appeared to have decomposed in our second plate. This may be due to HPLC issues leading to the plate being stored at room temperature for an extended period of time, resulting potential hydrolysis of the ester. This is not an issue when the plate is run immediately after reaction completion, but a different internal standard may be advantageous because of this issue.
- NiCl_2 -glyme was used in place of $\text{NiCl}_2 \cdot (\text{H}_2\text{O})_6$. This was due to the fact that $\text{NiCl}_2 \cdot (\text{H}_2\text{O})_6$ was not soluble when making the stock solution described above, likely because no ligands were present to aid in dissolution.

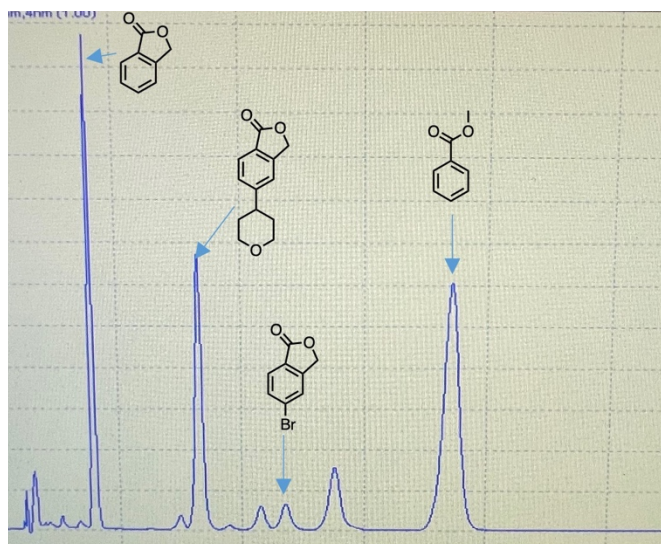


Figure S5.13. Example chromatogram for reaction with 5-bromophthalide.

	1	2	3	4	5	6	7	8	9	10	11	12
A	15.9	0.2	0.0	17.3	10.3	10.2	11.6	9.3	20.9	22.7	9.8	8.2
B	24.1	0.0	4.1	56.6	27.6	29.6	17.7	5.7	24.6	28.8	5.4	4.1
C	1.8	0.0	0.0	7.8	0.7	6.6	5.7	17.5	1.2	2.9	0.1	0.2
D	0.6	1.0	0.0	0.2	0.0	0.0	1.5	1.7	0.1	1.1	0.0	0.0
E	10.4	0.0	0.0	14.5	4.6	4.8	6.0	16.3	7.4	6.8	16.0	13.1
F	30.6	53.7	55.4	56.7	38.7	75.9	34.5	44.9	28.1	33.8	1.2	1.2
G	5.3	2.1	0.0	20.8	3.4	12.5	9.3	17.0	5.5	8.8	0.6	0.5
H	34.5	53.9	0.0	47.4	37.8	88.2	34.1	27.7	44.2	32.7	12.5	0.0

Figure S5.14. HPLC yield of desired product for first set of PCs/ligands. Best performing ligand and PCs highlighted.

c1ccc2c(c1)OCO2Br + C1COCCO1
 $\xrightarrow[\text{DMSO (0.1M), 445 nm HTE (485 mW/well), r.t. 4 hr}]{\text{NiCl}_2\text{-glyme (10 mol\%), TEOA (3 eq.)}}$
c1ccc2c(c1)OCO2C1COCCO1

1 eq. 1.5 eq.

	1	2	3	4	5	6	7	8	9	10	11	12
 A	17	69	74	72	67	61	79	84	76	61	63	72
 B	7	69	72	71	41	52	74	83	76	67	0	61
 C	4	71	73	69	58	46	56	69	78	80	0	48
 D	3	58	35	38	27	21	75	91	74	79	0	0
 E	8	71	70	67	67	62	54	56	72	42	22	43
 F	0	46	24	43	29	22	66	85	82	63	0	9
 G	0	0	0	0	0	0	29	39	24	40	0	0
 H	0	0	0	22	0	0	0	0	8	0	0	0

Figure S5.15. HPLC selectivity for second round of HTE. Actual yields of product/reaction components could not be determined due to internal standard degradation. However, we view the selectivity determined in this experiment as suitable for comparing relative selectivity between wells. Selectivity = $100 \times (\text{Area of DP}) / (\text{Area of DP} + \text{Area of De-Br})$.

	1	2	3	4	5	6	7	8	9	10	11	12
	85	100	67	100	97	92	88	91	31	35	9	46
	58	99	50	86	51	84	55	73	26	29	2	25
	22	92	40	97	75	61	79	77	28	48	2	12
	50	79	13	23	18	21	33	61	25	27	2	0
	42	87	73	98	98	100	71	78	45	40	9	37
	19	7	6	13	9	7	21	22	13	29	2	24
	9	0	0	5	6	6	7	7	6	8	2	4
	12	1	0	9	10	10	10	10	9	10	8	8

Figure S5.16. HPLC conversion for second round of HTE. Actual yields of product/reaction components could not be determined due to internal standard degradation. However, we view the conversion determined in this experiment as suitable for comparing relative conversion between wells. Conversion = $100 \times (\text{Area of DP} + \text{Area of De-Br}) / (\text{Area of DP} + \text{Area of De-Br} + \text{Area of SM})$.

5. Indole Optimization.

HTE optimization of the indole substrate was performed at Bristol Meyers Squibb and the results will be reported in due time.

6. Substrate Scope.

6.1 Deficient Conditions:

Stock solution of constants (Typically made for 3 reactions but written for 1):

To a 20 mL vial charged with a stir bar, triethanolamine (179 mg, 1.20 mmol, 3.00 eq.), 3CzCIIPN (2.6 mg, 0.0040 mmol, 1.0 mol%), and pyridine-2,6-bis(carboximidamide) dihydrochloride (9.4 mg, 0.040 mmol, 10.0 mol%) were added and the vial was taken into a nitrogen filled glovebox. NiCl₂-glyme (8.9 mg, 0.040 mmol, 10 mol%) was added and 4 mL

anhydrous DMSO was added. The mixture was allowed to stir for ~ 10 minutes. Once the mixture was dissolved, it was added to the vials containing the variable reagents (see below).

Aryl halide (0.400 mmol, 1.00 eq.) and alkyl bromide (0.600 mmol, 1.50 eq.) were added to a 2-dram vial charged with a stir bar, taken into a nitrogen filled glovebox, and stock solution was added. The reactions were capped, wrapped in electrical tape, and removed from the glovebox. The reactions were run in Reactor 4a (See SI for Chapter 4) at 25 °C for 16-18 hours (485 mW/well). The reaction was exposed to oxygen, transferred to a separatory funnel, ~ 100 mL EtOAc was added, and the organics were washed with water. The aqueous layer was extracted once with EtOAc and the combined organics were washed once with brine. The combined organics were dried over Na₂SO₄, concentrated, and purified by column chromatography.

6.2 Rich Conditions:

Stock solution of constants (Typically made for 3 reactions but written for 1):

To a 20 mL vial charged with a stir bar, triethanolamine (358 mg, 2.40 mmol, 3.00 eq.), A0205 (4.8 mg, 0.0080 mmol, 1.0 mol%), and 4-4'-dimethoxy-2-2'-bipyridine (17.3 mg, 0.0800 mmol, 10.0 mol%) were added and the vial was taken into a nitrogen filled glovebox. NiBr₂-glyme (12.3 mg, 0.0400 mmol, 5 mol%) was added and 2 mL anhydrous DMF was added. The mixture was allowed to stir for ~ 10 minutes and tetrabutylammonium chloride (222 mg, 0.800 mmol, 1.00 eq.) was added. Once the mixture was dissolved, it was added to the vials containing the variable reagents (see below).

Aryl halide (0.800 mmol, 1.00 eq.) and alkyl bromide (1.04 mmol, 1.30 eq.) were added to a 2-dram vial charged with a stir bar, taken into a nitrogen filled glovebox, and stock solution was added. The reactions were capped, wrapped in electrical tape, and removed from the glovebox. The reactions were run in Reactor 4a (See SI for Chapter 4) at 25 °C for 16-18 hours (485

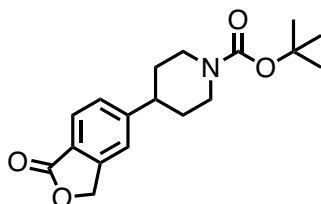
mW/well). The reaction was exposed to oxygen, transferred to a separatory funnel, ~ 100 mL EtOAc was added, and the organics were washed with water. The aqueous layer was extracted once with EtOAc and the combined organics were washed once with brine. The combined organics were dried over Na₂SO₄, concentrated, and purified by column chromatography.

Notes:

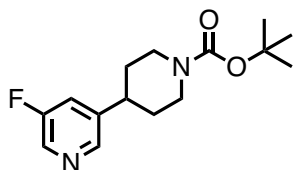
- Liquid aryl/alkyl halides were sparged with nitrogen for 10 minutes prior to being brought into the glove box to add to reaction vials.
- NiBr₂-glyme has a tendency to form clumps that take a long time to fully dissolve. After adding it to the stock solution, breaking the clumps up with a spatula speeds up dissolution.
- After completion, there is a significant amount of a precipitate mostly consisting of TEOA-HBr. This is insoluble in ethyl acetate and is transferred to the separatory funnel with water to ensure any trapped product is not lost.

6.3 Substrate Characterization

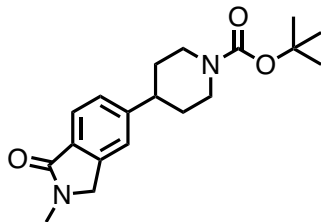
Some analytical data is currently being acquired. This includes ^{13}C NMR for some substrates and mass spec for all new substrates. This will all be included in the final draft of the dissertation.



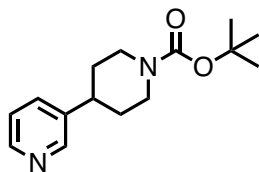
Synthesized according to **Deficient Conditions** with 5-bromophthalide and 1-boc-4-bromopiperidine. White solid (89 mg, 70% yield). The ^1H NMR was in agreement with the literature.⁵ ^1H NMR (400 MHz, CDCl_3) δ 7.83 (d, $J = 7.9$ Hz, 1H), 7.36 (d, $J = 8.0$ Hz, 1H), 7.30 (s, 1H), 5.27 (s, 2H), 4.26 (d, $J = 13.1$ Hz, 2H), 2.86 – 2.72 (m, 3H), 1.83 (d, $J = 13.0$ Hz, 2H), 1.63 (qd, $J = 12.6, 4.4$ Hz, 2H), 1.47 (s, 9H).



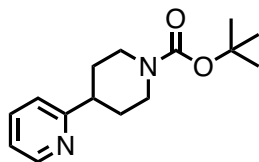
Synthesized according to **Deficient Conditions** with 3-bromo-5-fluoropyridine and 1-boc-4-bromopiperidine. White solid (68 mg, 61% yield). The ^1H NMR was in agreement with the literature.⁶ ^1H NMR (400 MHz, CDCl_3) δ 8.32 (d, $J = 5.3$ Hz, 2H), 7.22 (d, $J = 9.5$ Hz, 1H), 4.26 (s, 2H), 2.89 – 2.66 (m, 3H), 1.83 (d, $J = 12.5$ Hz, 2H), 1.60 (qd, $J = 12.6, 4.1$ Hz, 2H), 1.47 (s, 9H).



Synthesized according to **Deficient Conditions** with 5-bromo-2-methylisoindolin-1-one and 1-boc-4-bromopiperidine. White solid (71 mg, 54% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.72 (d, $J = 7.8$ Hz, 1H), 7.23 (d, $J = 5.2$ Hz, 2H), 4.30 (s, 2H), 3.14 (s, 3H), 2.86 – 2.62 (m, 3H), 1.80 (d, $J = 12.4$ Hz, 2H), 1.61 (qd, $J = 12.5, 4.0$ Hz, 2H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.65, 154.92, 149.64, 141.64, 131.44, 127.15, 123.78, 120.91, 79.69, 52.08, 44.44, 43.23, 33.34, 29.58, 28.61.

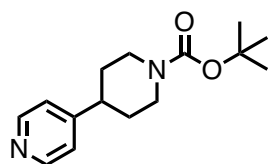


Synthesized according to **Deficient Conditions** with 3-bromopyridine and 1-boc-4-bromopiperidine. Clear oil (59 mg, 56% yield). The ^1H NMR was in agreement with the literature.⁵ ^1H NMR (400 MHz, CDCl_3) δ 8.44 – 8.36 (m, 2H), 7.44 (d, $J = 7.8$ Hz, 1H), 7.17 (dd, $J = 7.5, 5.1$ Hz, 1H), 4.19 (s, 2H), 2.74 (t, $J = 12.0$ Hz, 2H), 2.61 (t, $J = 12.2$ Hz, 1H), 1.76 (d, $J = 12.5$ Hz, 2H), 1.55 (qd, $J = 12.8, 4.0$ Hz, 2H), 1.41 (s, 9H).

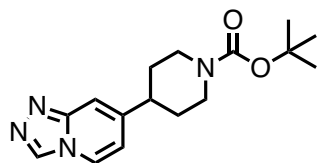


Synthesized according to **Deficient Conditions** with 2-bromopyridine and 1-boc-4-bromopiperidine. Clear oil (75 mg, 71% yield). The ^1H NMR was in agreement with the literature.⁷ ^1H NMR (400 MHz, CDCl_3) δ 8.53 (d, $J = 4.3$ Hz, 1H), 7.63 (t, $J = 7.7$ Hz, 1H), 7.13 (dd, $J =$

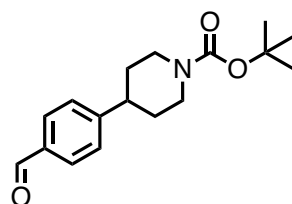
11.2, 7.5 Hz, 2H), 2.85 (ddd, $J = 11.8, 8.2, 3.7$ Hz, 3H), 1.91 (d, $J = 12.9$ Hz, 2H), 1.71 (qd, $J = 12.6, 4.3$ Hz, 2H), 1.47 (s, 9H).



Synthesized according to **Deficient Conditions** with 4-bromopyridine and 1-boc-4-bromopiperidine. Clear oil (75 mg, 71% yield). The ^1H NMR was in agreement with the literature.⁵ ^1H NMR (400 MHz, CDCl_3) δ 8.52 (d, $J = 4.9$ Hz, 2H), 7.14 (d, $J = 5.4$ Hz, 2H), 2.80 (t, $J = 12.1$ Hz, 2H), 2.65 (ddd, $J = 12.2, 8.7, 3.5$ Hz, 1H), 1.83 (d, $J = 12.8$ Hz, 2H), 1.61 (qd, $J = 12.7, 4.2$ Hz, 2H), 1.48 (s, 9H).

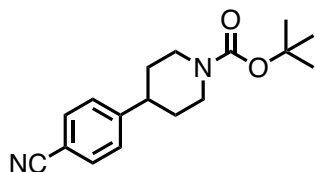


Synthesized according to **Deficient Conditions** with 7-bromo-[1,2,4]triazolo[4,3-a]pyridine and 1-boc-4-bromopiperidine. Clear oil (79 mg, 65% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.76 (s, 1H), 8.08 (d, $J = 7.1$ Hz, 1H), 7.53 (s, 1H), 6.74 (d, $J = 7.1$ Hz, 1H), 4.35 – 4.19 (m, 2H), 2.81 (t, $J = 12.0$ Hz, 2H), 2.70 (tt, $J = 12.5, 3.6$ Hz, 1H), 1.87 (d, $J = 13.0$ Hz, 2H), 1.60 (qd, $J = 12.7, 4.3$ Hz, 2H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 154.82, 149.92, 146.21, 135.18, 123.14, 114.88, 112.20, 79.89, 44.00, 42.19, 32.05, 28.55. NEED MASS



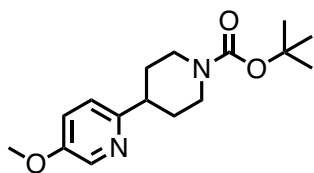
Synthesized according to **Deficient Conditions** with 4-bromobenzaldehyde and 1-boc-4-bromopiperidine. Clear oil (58 mg, 50% yield). The ^1H NMR was in agreement with the literature.⁸

^1H NMR (400 MHz, CDCl_3) δ 9.97 (s, 1H), 7.82 (d, $J = 7.9$ Hz, 2H), 7.36 (d, $J = 7.9$ Hz, 2H), 4.27 (d, $J = 12.6$ Hz, 2H), 2.86 – 2.68 (m, 3H), 1.83 (d, $J = 12.8$ Hz, 2H), 1.64 (qd, $J = 12.6$, 4.1 Hz, 2H), 1.48 (s, 9H).

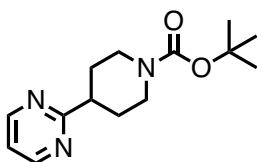


Synthesized according to **Deficient Conditions** with 4-bromobenzonitrile and 1-boc-4-bromopiperidine. Clear oil (94 mg, 82% yield). The ^1H NMR was in agreement with the literature.⁸

^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, $J = 8.0$ Hz, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 4.24 (d, $J = 10.0$ Hz, 2H), 2.84 – 2.64 (m, 3H), 1.80 (d, $J = 12.8$ Hz, 2H), 1.58 (qd, $J = 12.6$, 4.2 Hz, 2H), 1.46 (s, 9H).

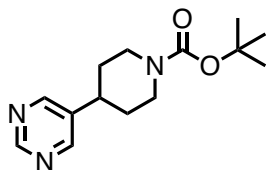


Synthesized according to **Deficient Conditions** with 2-bromo-5-methoxypyridine and 1-boc-4-bromopiperidine. Clear oil (86 mg, 74% yield). The ^1H NMR was in agreement with the literature.⁹ ^1H NMR (400 MHz, CDCl_3) δ 8.21 (d, $J = 3.0$ Hz, 1H), 7.13 (dd, $J = 8.7$, 3.0 Hz, 1H), 7.05 (d, $J = 8.6$ Hz, 1H), 4.21 (s, 2H), 3.81 (s, 3H), 2.85 – 2.71 (m, 3H), 1.91 – 1.82 (m, 2H), 1.64 (qd, $J = 12.6$, 4.3 Hz, 2H), 1.45 (s, 9H).

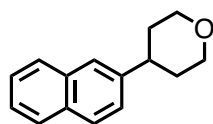


Synthesized according to **Deficient Conditions** with 2-bromopyrimidine and 1-boc-4-bromopiperidine. Clear oil (35 mg, 33% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.67 (d, $J = 4.8$ Hz,

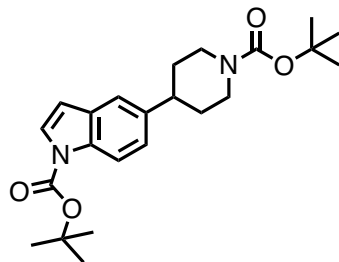
2H), 7.13 (t, $J = 4.8$ Hz, 1H), 3.02 (ddd, $J = 11.7, 8.2, 3.6$ Hz, 1H), 2.86 (t, $J = 13.4$ Hz, 2H), 1.98 (d, $J = 12.6$ Hz, 2H), 1.81 (qd, $J = 12.4, 4.2$ Hz, 2H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 173.02, 157.20, 154.92, 118.95, 79.48, 45.51, 43.77, 30.84, 28.62.



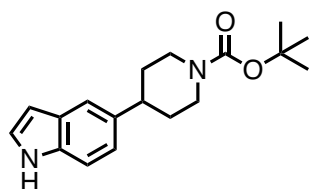
Synthesized according to **Deficient Conditions** with 5-bromopyrimidine and 1-boc-4-bromopiperidine. Clear oil (74 mg, 70% yield). The ^1H NMR was in agreement with the literature.⁵ ^1H NMR (400 MHz, CDCl_3) δ 9.10 (s, 1H), 8.60 (s, 2H), 4.28 (s, 2H), 2.82 (t, $J = 12.4$ Hz, 2H), 2.69 (tt, $J = 12.3, 3.5$ Hz, 1H), 1.86 (d, $J = 13.3$ Hz, 2H), 1.65 (qd, $J = 12.7, 4.3$ Hz, 2H), 1.48 (s, 9H).



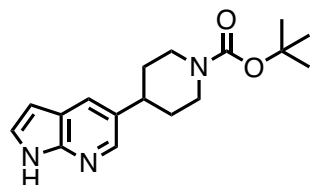
Synthesized according to **Deficient Conditions** with 2-bromonaphthalene and 4-bromotetrahydropyran. Clear oil (60 mg, 71% yield). The ^1H NMR was in agreement with the literature.⁹ ^1H NMR (400 MHz, CDCl_3) δ 7.81 (d, $J = 8.5$ Hz, 3H), 7.66 (s, 1H), 7.53 – 7.36 (m, 3H), 4.13 (dd, $J = 10.7, 3.7$ Hz, 2H), 3.59 (td, $J = 11.6, 2.4$ Hz, 2H), 2.93 (tt, $J = 11.7, 4.2$ Hz, 1H), 2.03 – 1.79 (m, 4H).



Synthesized according to **Rich Conditions** with N-boc-5-bromoindole and 1-boc-4-bromopiperidine. White solid (224 mg, 70% yield). The ^1H NMR was in agreement with the literature.⁵ ^1H NMR (400 MHz, CDCl_3) δ 8.05 (d, $J = 8.6$ Hz, 1H), 7.57 (d, $J = 3.7$ Hz, 1H), 7.38 (s, 1H), 7.16 (d, $J = 8.6$ Hz, 1H), 6.52 (d, $J = 3.7$ Hz, 1H), 4.26 (s, 2H), 2.88 – 2.78 (m, 2H), 2.73 (tt, $J = 12.2, 3.6$ Hz, 1H), 1.86 (d, $J = 13.1$ Hz, 2H), 1.66 (s, 11H), 1.49 (s, 9H).

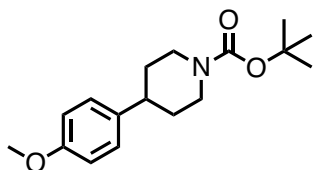


Synthesized according to **Rich Conditions** with 5-bromoindole and 1-boc-4-bromopiperidine. Brown solid (122 mg, 51% yield). The ^1H NMR was in agreement with the literature.⁵ ^1H NMR (400 MHz, CDCl_3) δ 8.29 (s, 1H), 7.47 (s, 1H), 7.33 (d, $J = 8.4$ Hz, 1H), 7.19 (t, $J = 2.9$ Hz, 1H), 7.05 (d, $J = 8.5$ Hz, 1H), 6.51 (t, $J = 2.6$ Hz, 1H), 4.26 (d, $J = 13.2$ Hz, 2H), 2.84 (t, $J = 12.8$ Hz, 2H), 2.74 (tt, $J = 12.2, 3.7$ Hz, 1H), 1.87 (d, $J = 12.9$ Hz, 2H), 1.69 (qd, $J = 12.7, 4.3$ Hz, 2H), 1.50 (s, 9H).

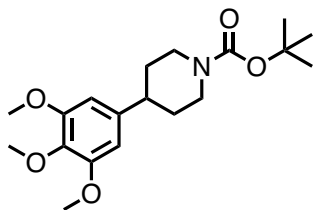


Synthesized according to **Rich Conditions** with 5-bromo-1H-pyrrolo[2,3-b]pyridine and 1-boc-4-bromopiperidine. White solid (107 mg, 44% yield). ^1H NMR (400 MHz, CDCl_3) δ 10.21

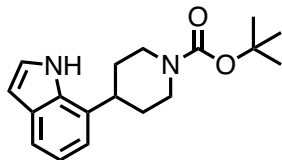
(s, 1H), 8.21 (s, 1H), 7.79 (s, 1H), 7.35 (d, $J = 3.6$ Hz, 1H), 6.47 (d, $J = 3.6$ Hz, 1H), 4.29 (s, 2H), 2.90 – 2.74 (m, 3H), 1.88 (d, $J = 14.3$ Hz, 2H), 1.71 (qd, $J = 12.6, 4.4$ Hz, 2H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.02, 147.76, 142.37, 133.43, 126.90, 125.62, 120.46, 100.77, 79.65, 44.58, 40.62, 33.91, 28.64.



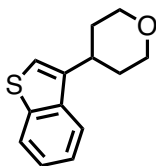
Synthesized according to **Rich Conditions** with 4-bromoanisole and 1-boc-4-bromopiperidine. Clear oil (172 mg, 74% yield). The ^1H NMR was in agreement with the literature.⁷ ^1H NMR (400 MHz, CDCl_3) δ 7.12 (d, $J = 8.5$ Hz, 2H), 6.85 (d, $J = 8.6$ Hz, 2H), 4.23 (d, $J = 13.2$ Hz, 2H), 3.79 (s, 3H), 2.79 (t, $J = 12.8$ Hz, 2H), 2.59 (tt, $J = 12.1, 3.7$ Hz, 1H), 1.79 (d, $J = 13.4$ Hz, 2H), 1.58 (qd, $J = 12.7, 4.3$ Hz, 2H), 1.48 (s, 9H).



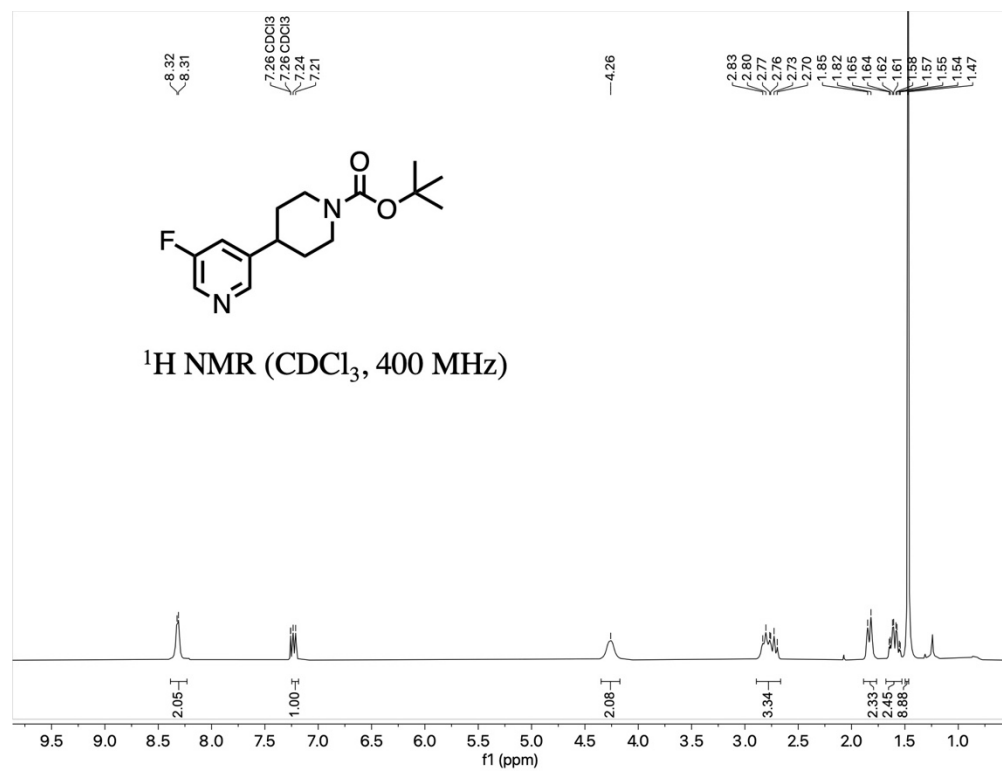
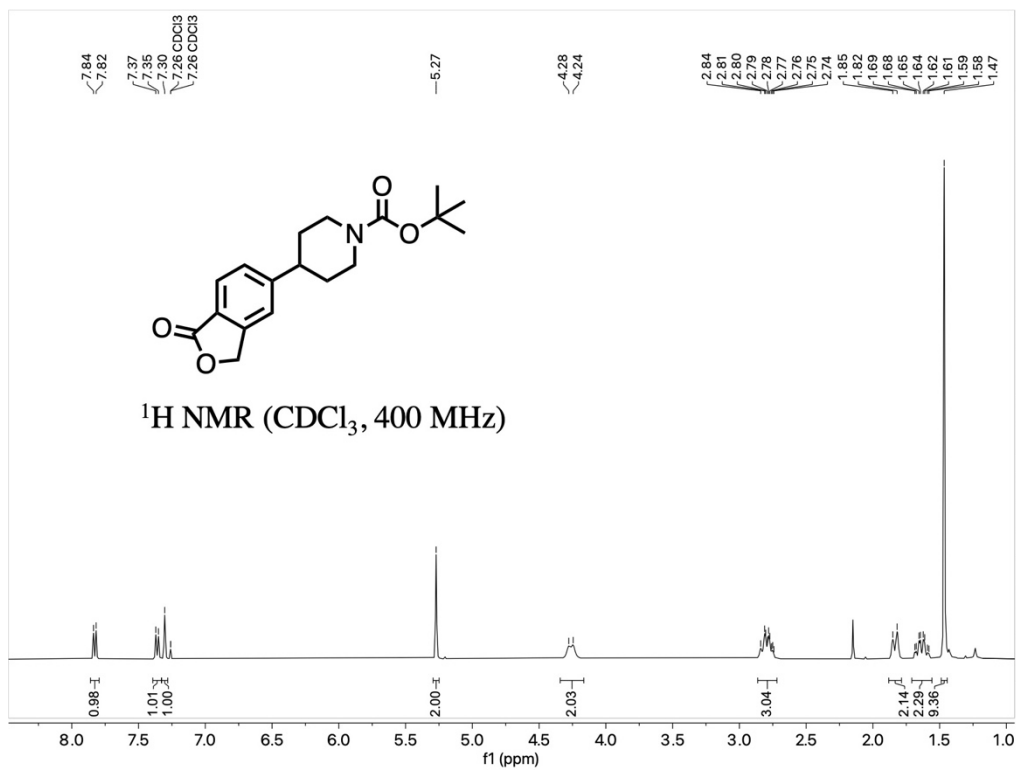
Synthesized according to **Rich Conditions** with 5-bromo-1,2,3-trimethoxybenzene and 1-boc-4-bromopiperidine. Clear oil (208 mg, 74% yield). ^1H NMR (400 MHz, CDCl_3) δ 6.41 (s, 2H), 4.25 (d, $J = 13.3$ Hz, 2H), 3.85 (s, 6H), 3.83 (s, 3H), 2.79 (t, $J = 12.8$ Hz, 2H), 2.58 (tt, $J = 12.2, 3.7$ Hz, 1H), 1.82 (d, $J = 13.0$ Hz, 2H), 1.63 (dd, $J = 12.3, 4.7$ Hz, 2H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.01, 153.35, 141.84, 136.56, 103.84, 79.65, 60.98, 56.23, 44.43, 43.33, 33.50, 28.64.

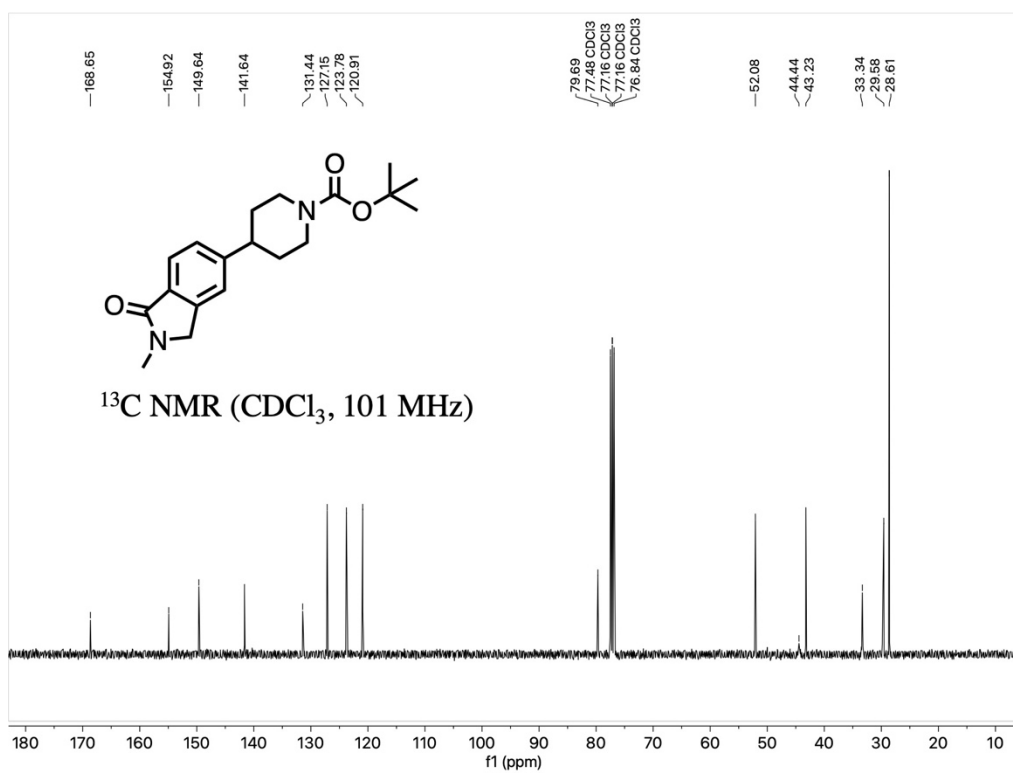
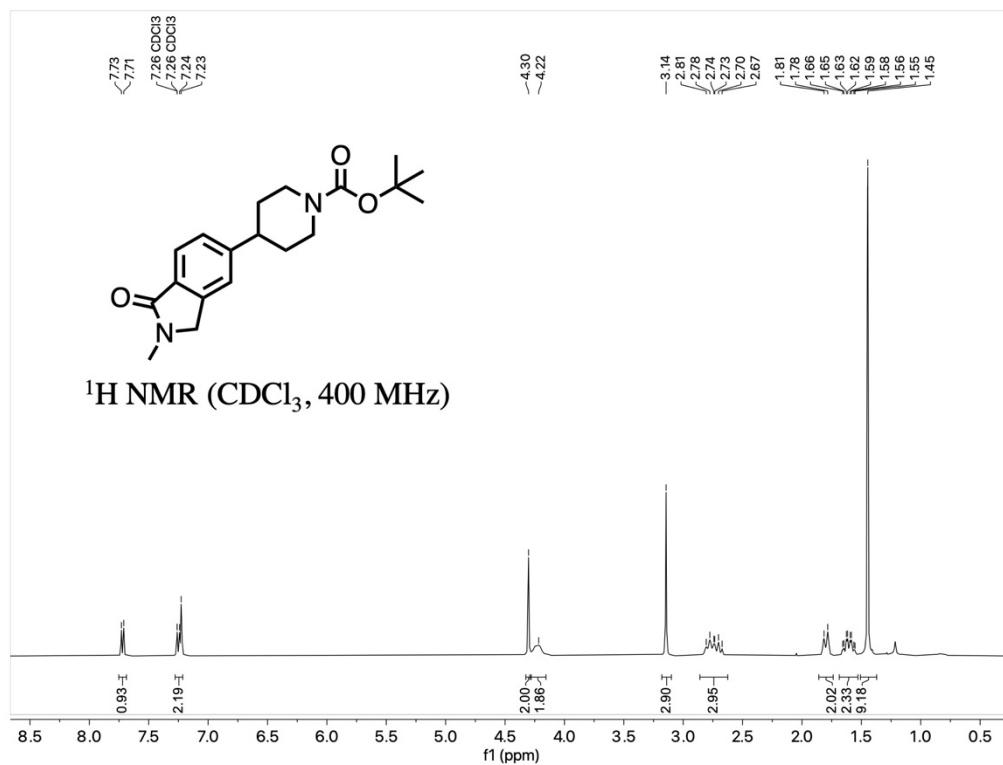


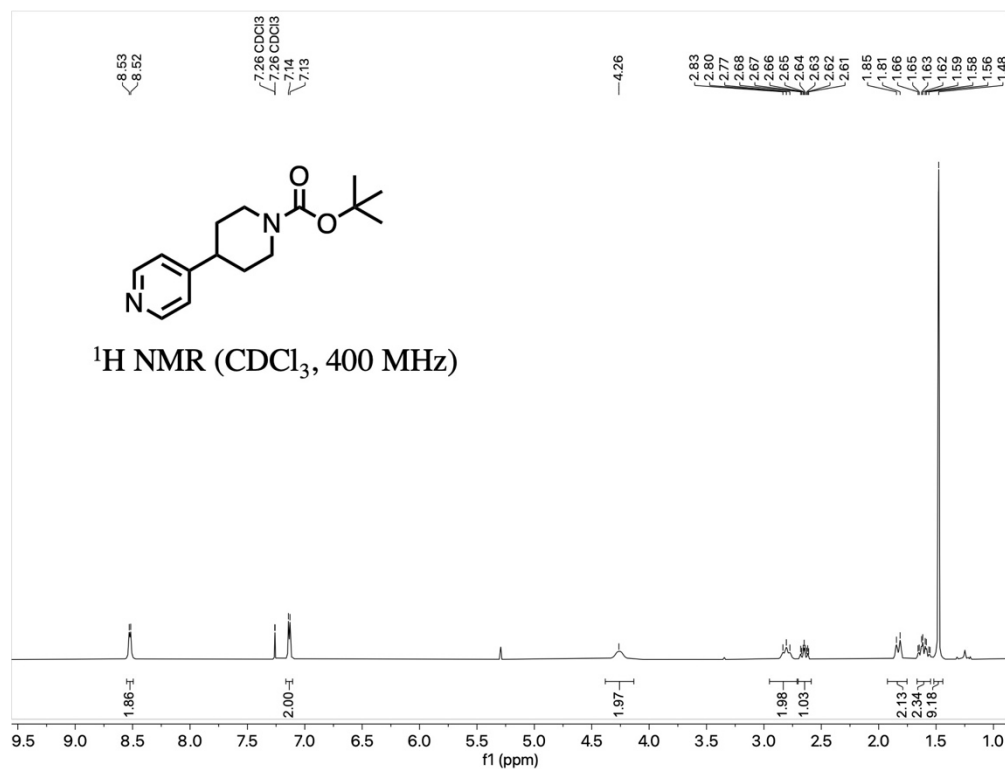
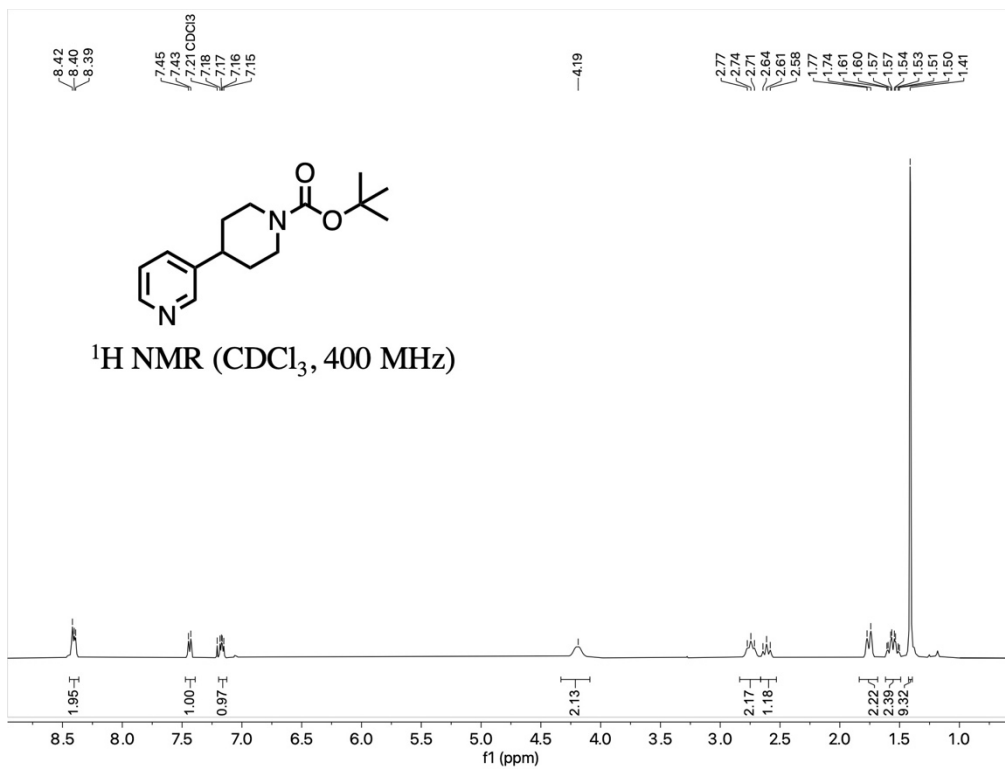
Synthesized according to **Rich Conditions** with 7-bromoindole and 1-boc-4-bromopiperidine. White solid (103 mg, 43% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.18 (s, 1H), 7.45 (d, $J = 7.8$ Hz, 1H), 7.14 (s, 1H), 7.03 (t, $J = 7.6$ Hz, 1H), 6.96 (d, $J = 7.3$ Hz, 1H), 6.51 (s, 1H), 4.24 (d, $J = 13.4$ Hz, 2H), 2.94 – 2.77 (m, 3H), 1.88 (d, $J = 14.0$ Hz, 2H), 1.74 (qd, $J = 12.6$, 4.4 Hz, 2H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.05, 134.11, 128.26, 128.15, 123.96, 120.33, 119.07, 118.79, 103.40, 79.76, 44.69, 38.54, 32.17, 28.65.

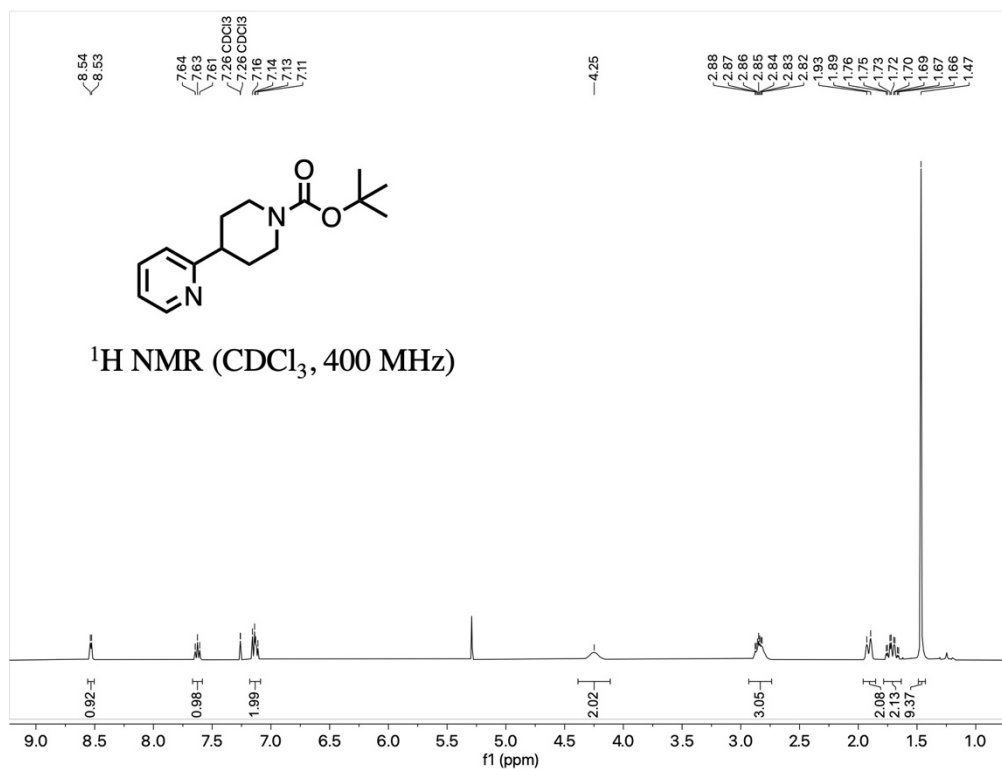
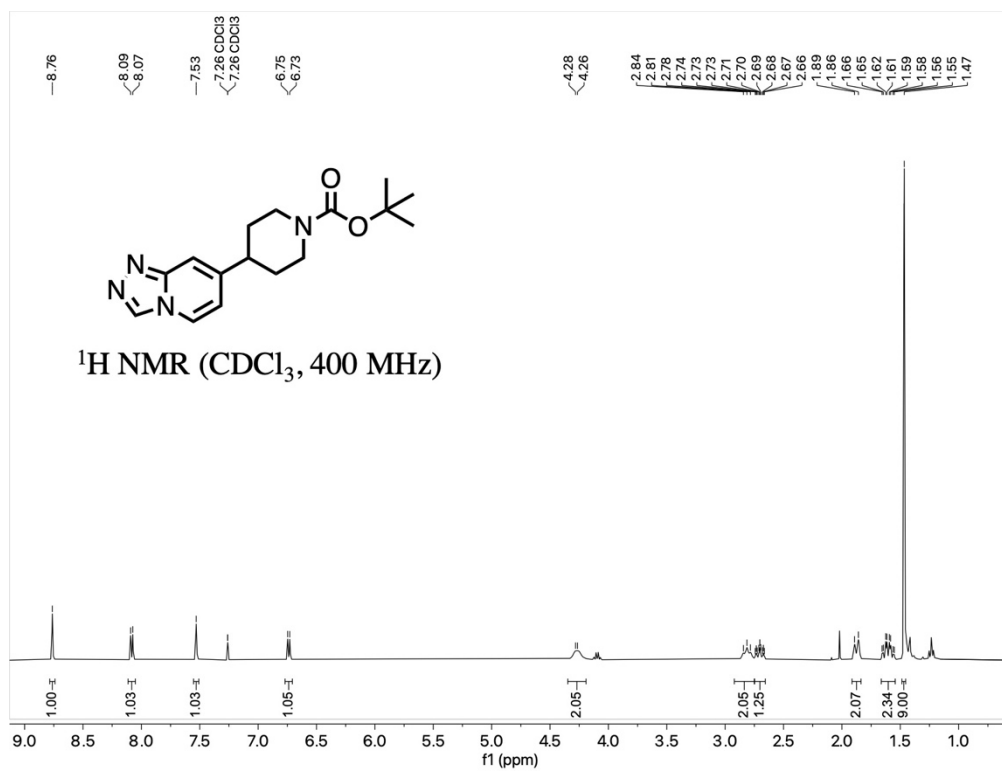


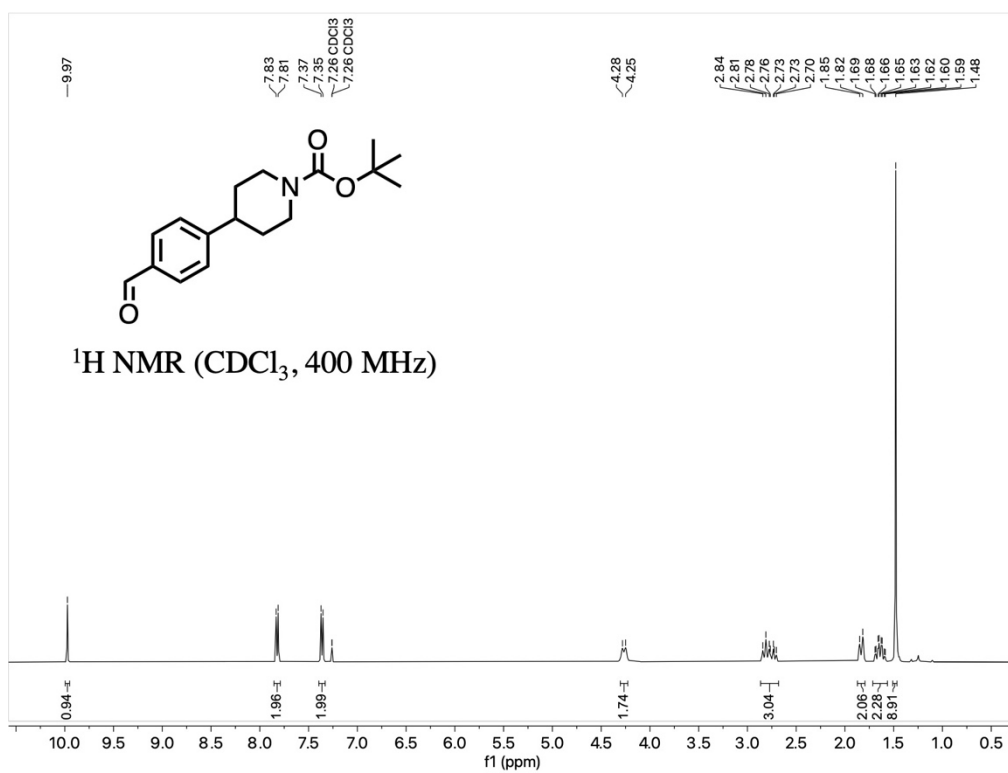
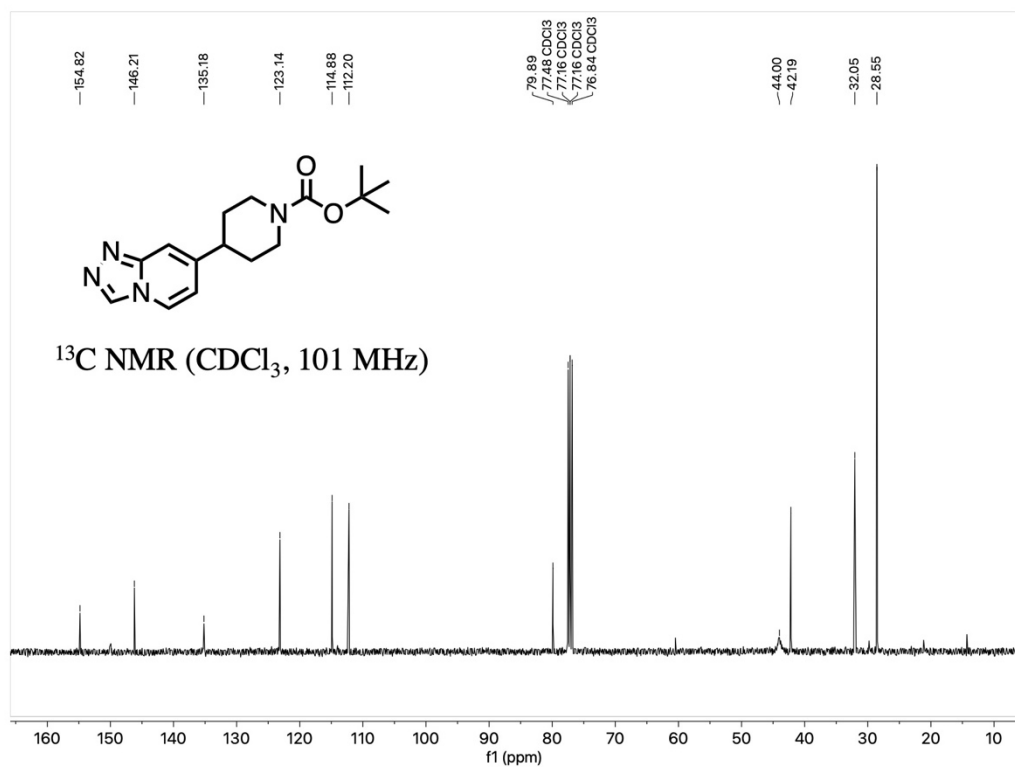
Synthesized according to **Rich Conditions** with 3-bromobenzo[b]thiophene and 4-bromotetrahydropyran. Clear oil (77 mg, 44% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.90 (d, $J = 8.1$ Hz, 1H), 7.82 (d, $J = 8.0$ Hz, 1H), 7.45 – 7.34 (m, 2H), 7.15 (s, 1H), 4.15 (dd, $J = 11.0$, 5.1 Hz, 2H), 3.66 (t, $J = 11.7$ Hz, 2H), 3.22 (tt, $J = 11.8$, 3.8 Hz, 1H), 2.03 – 1.86 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 140.83, 138.28, 124.43, 123.96, 123.80, 123.22, 121.65, 120.17, 68.49, 35.34, 33.28.

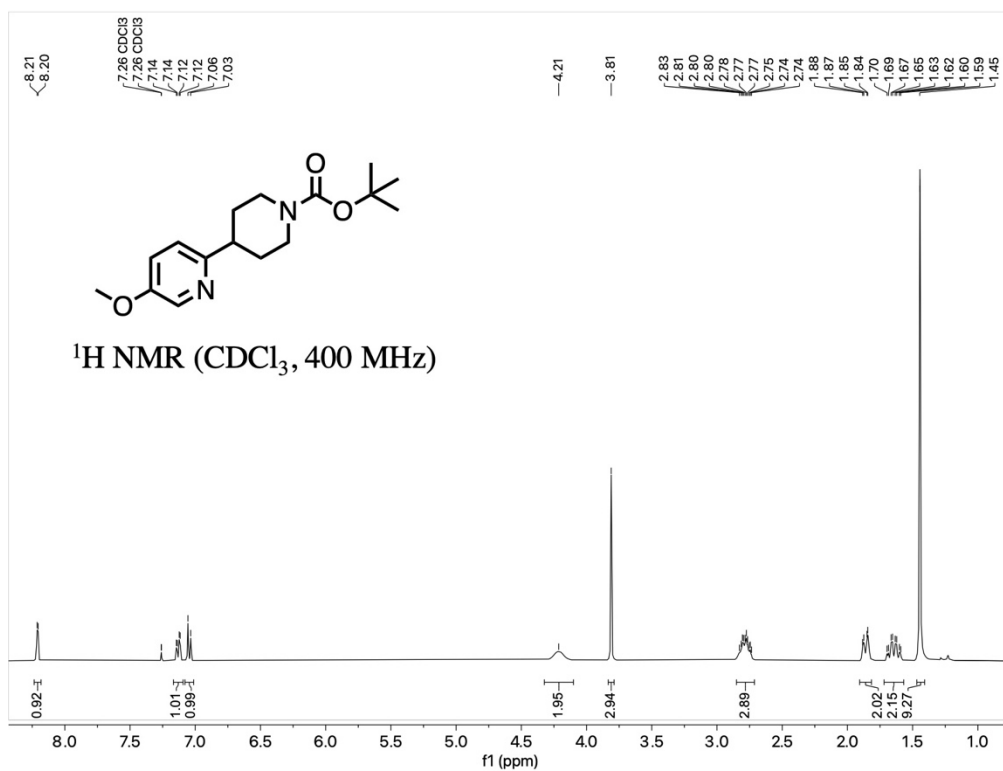
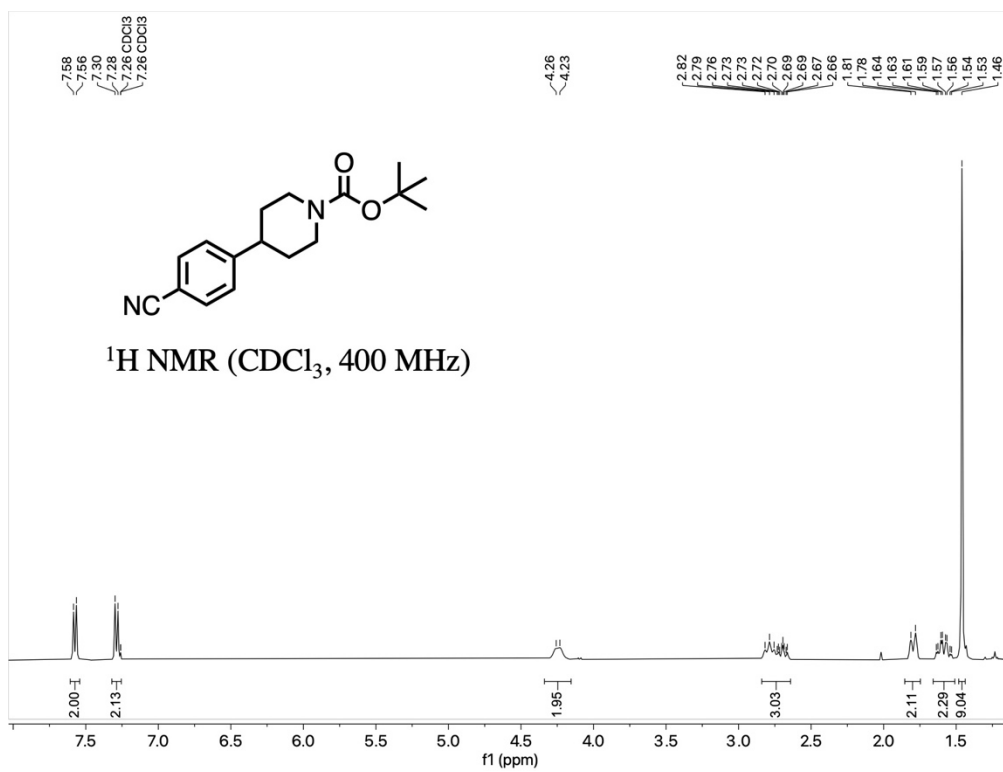


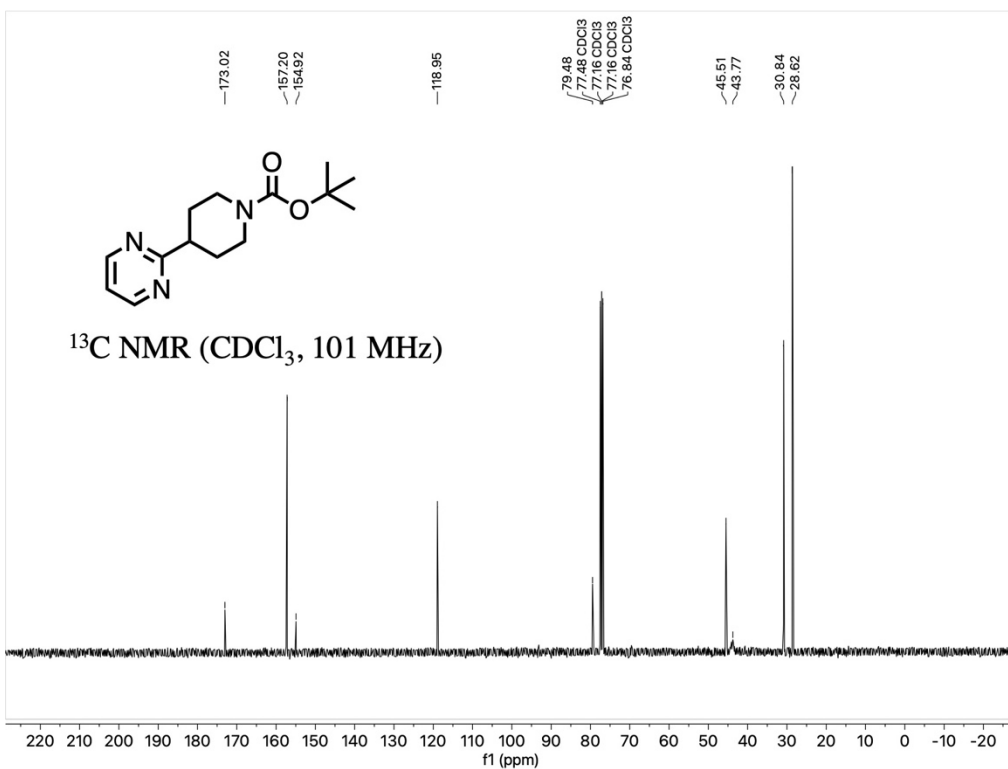
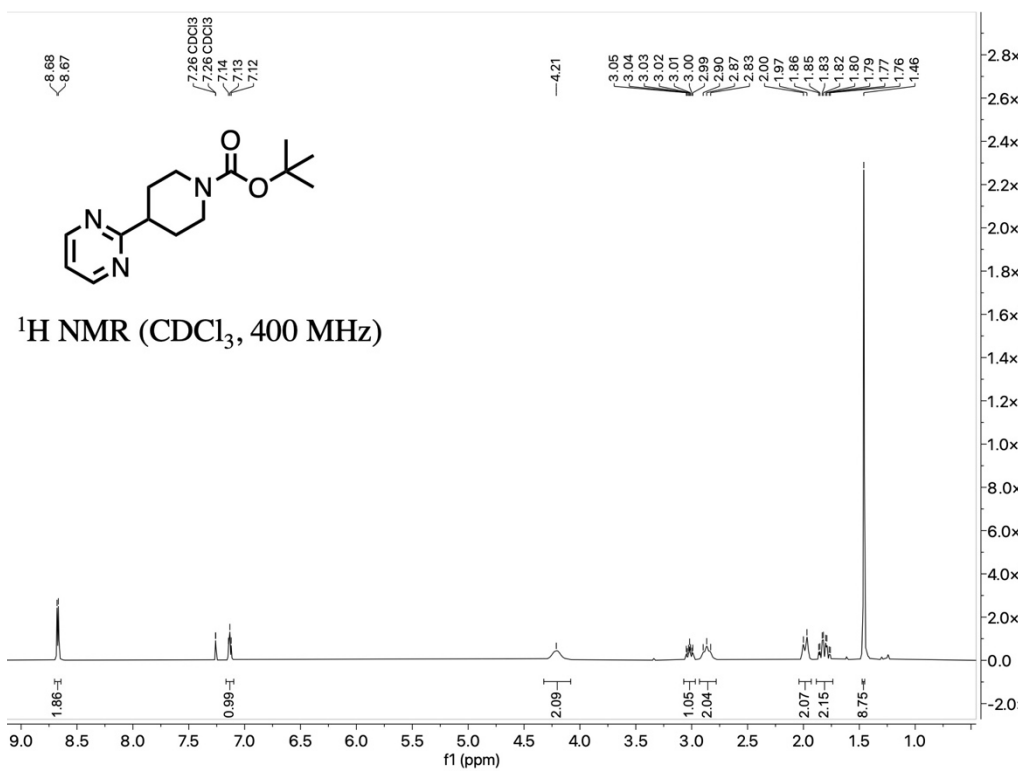


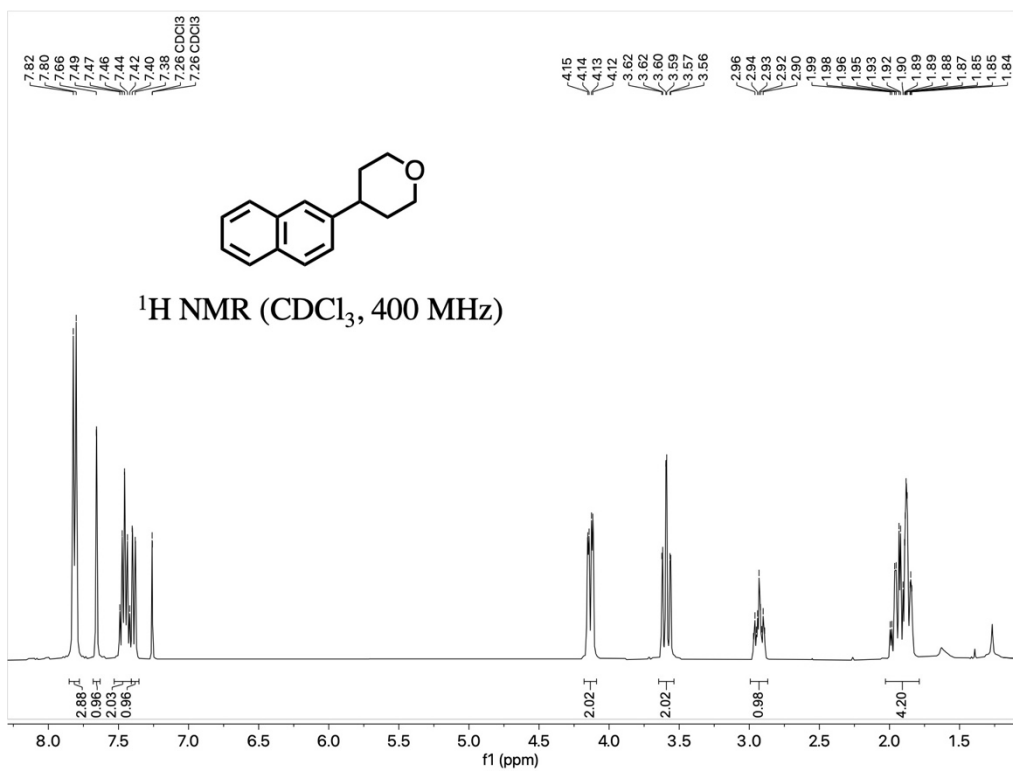
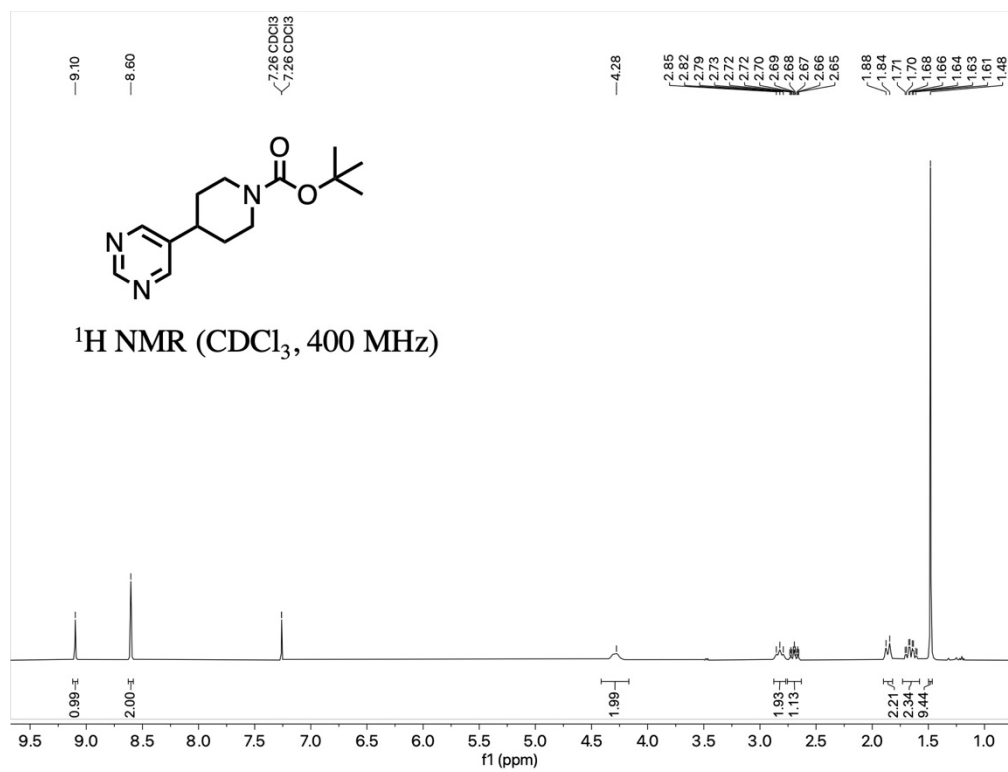


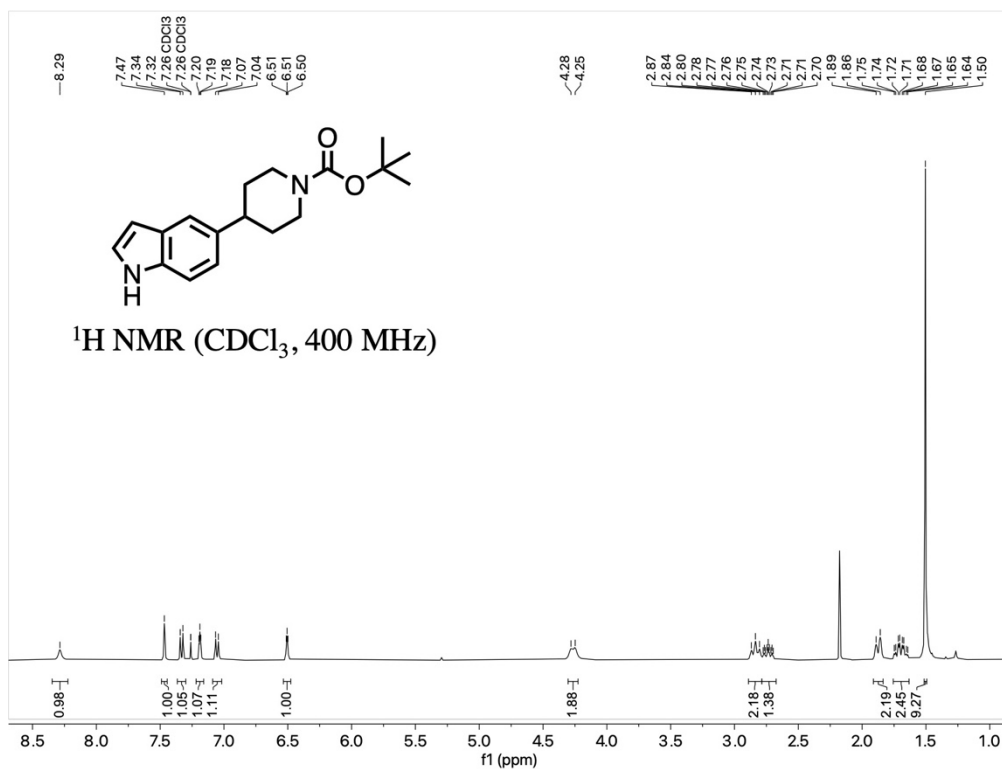
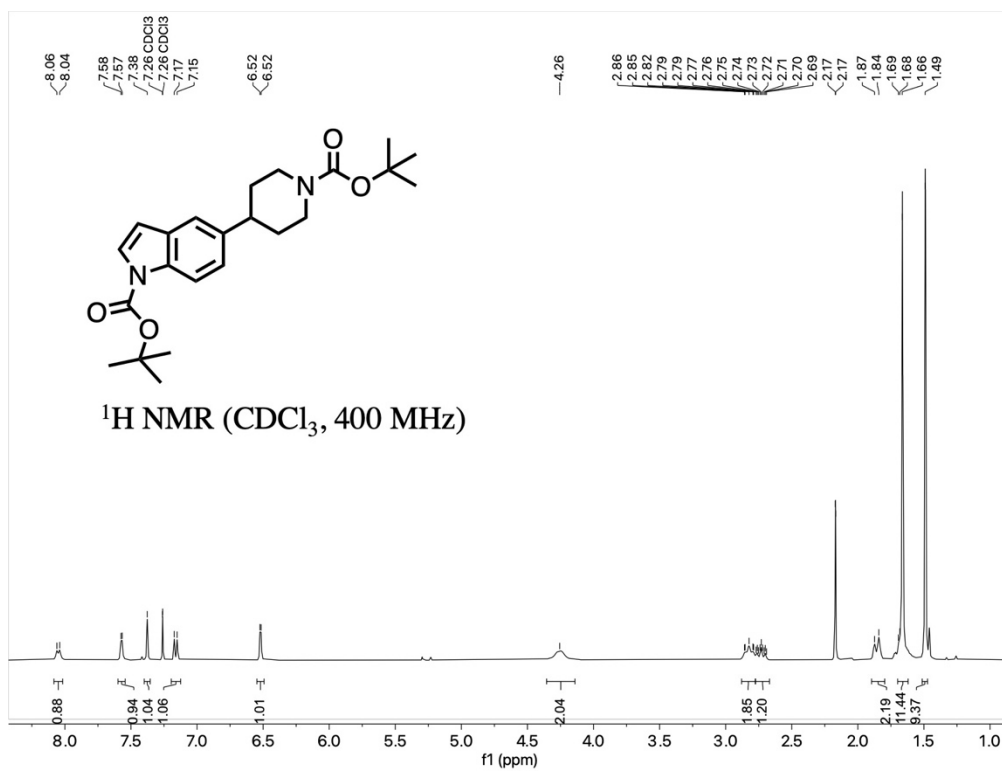


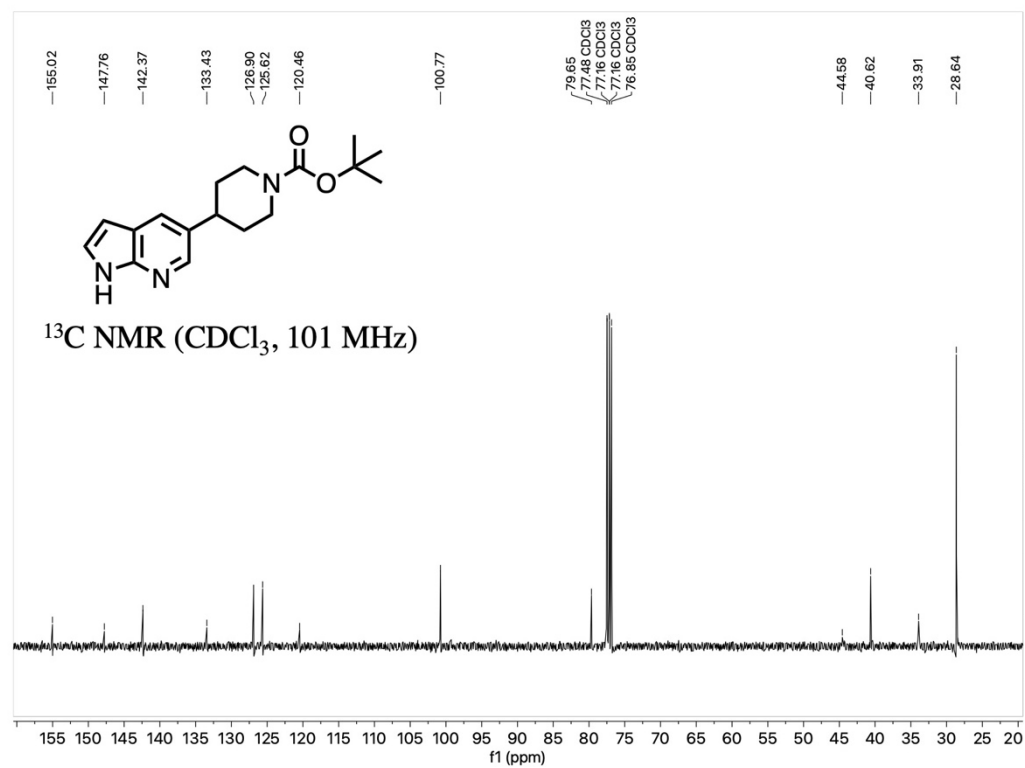
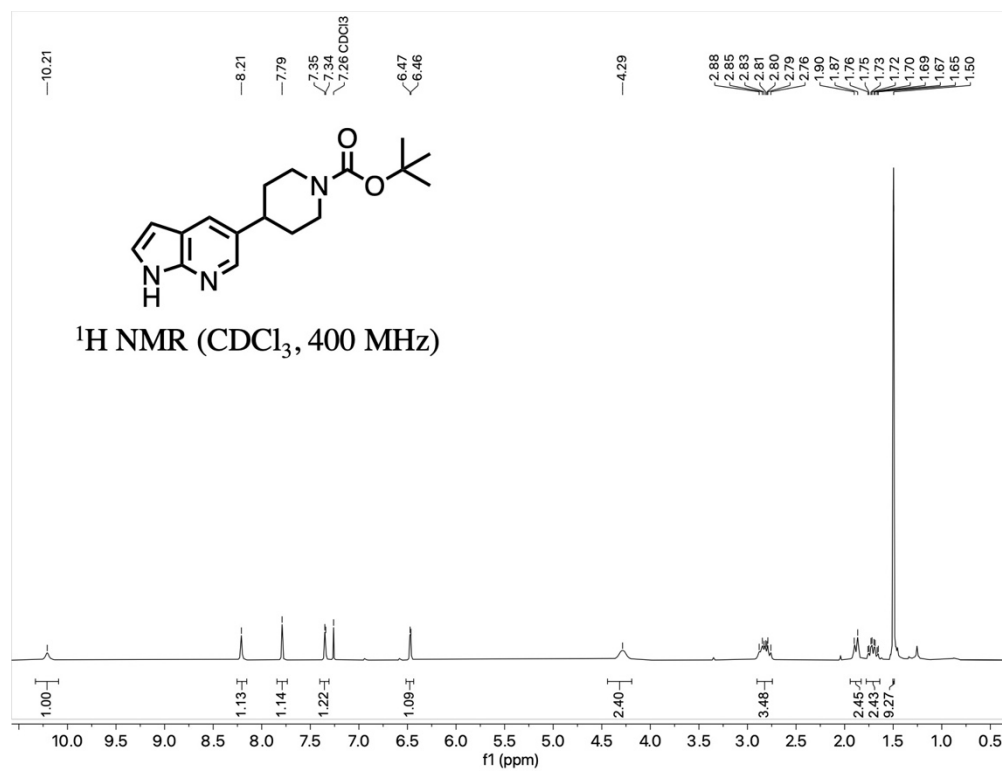


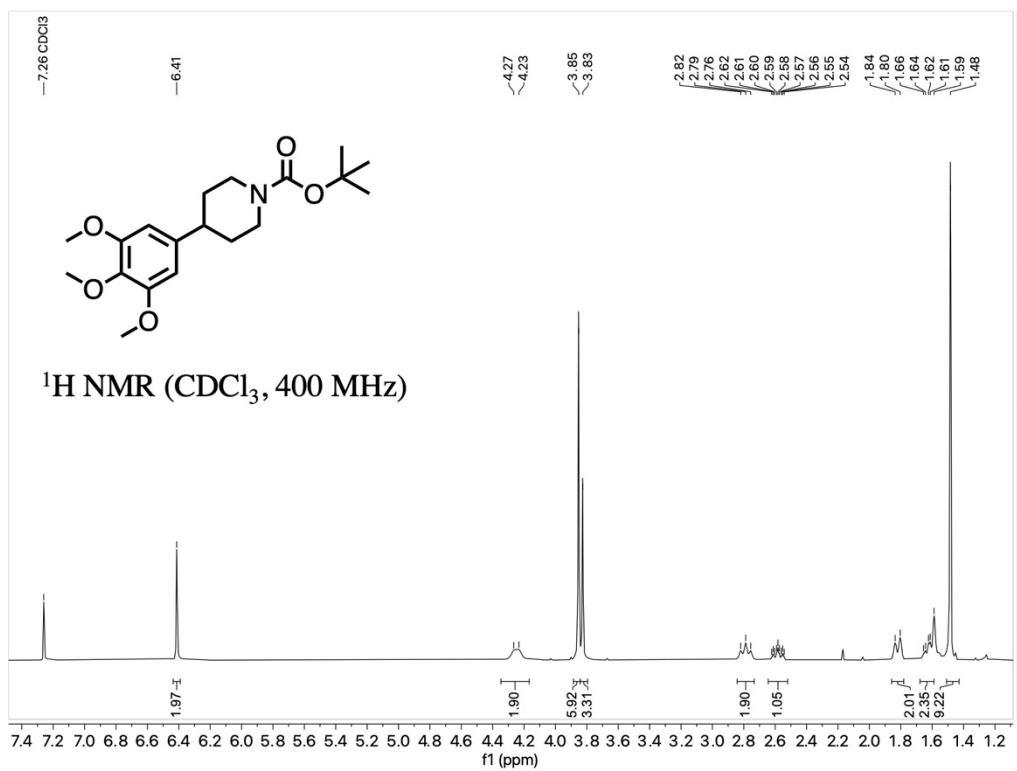
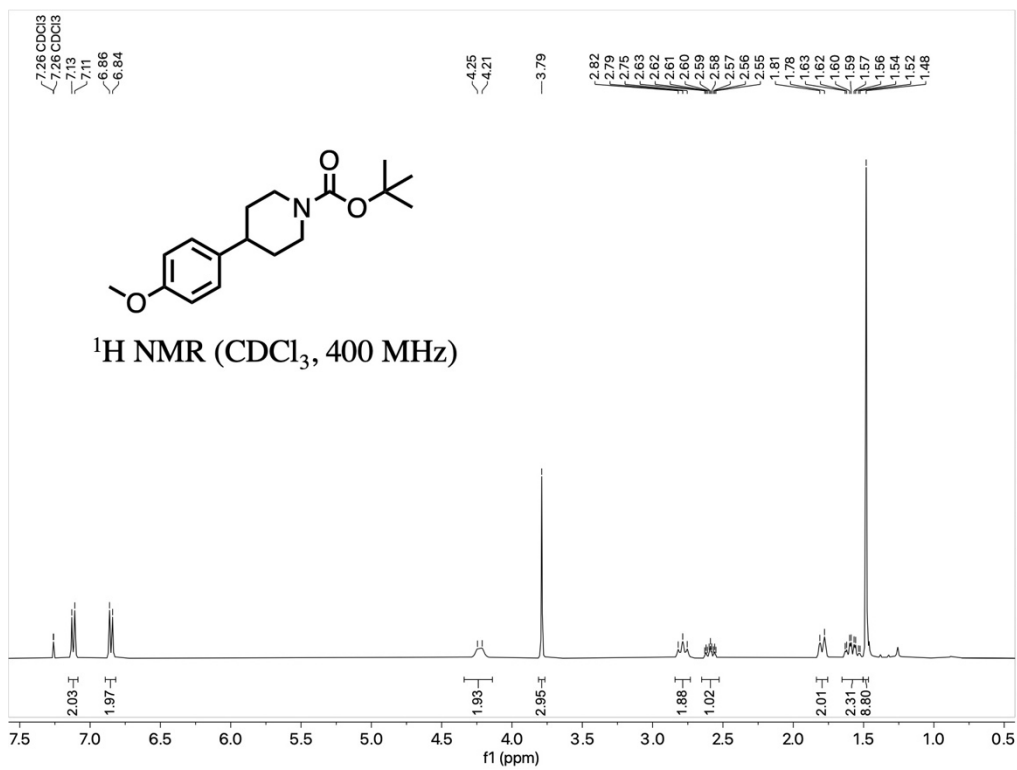


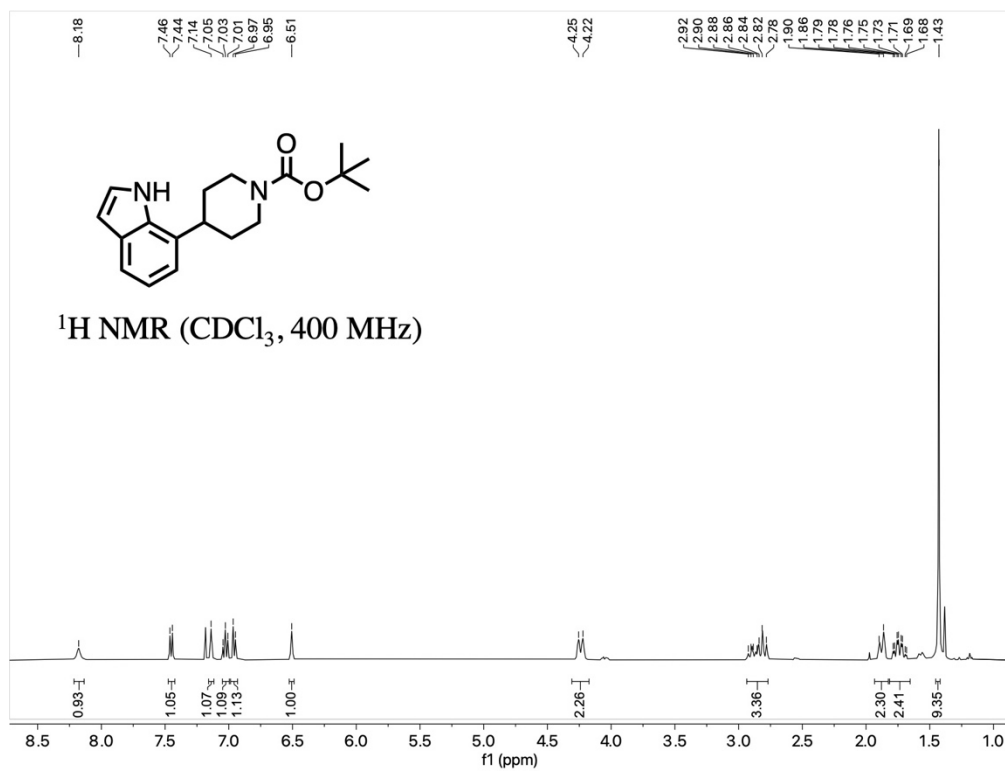
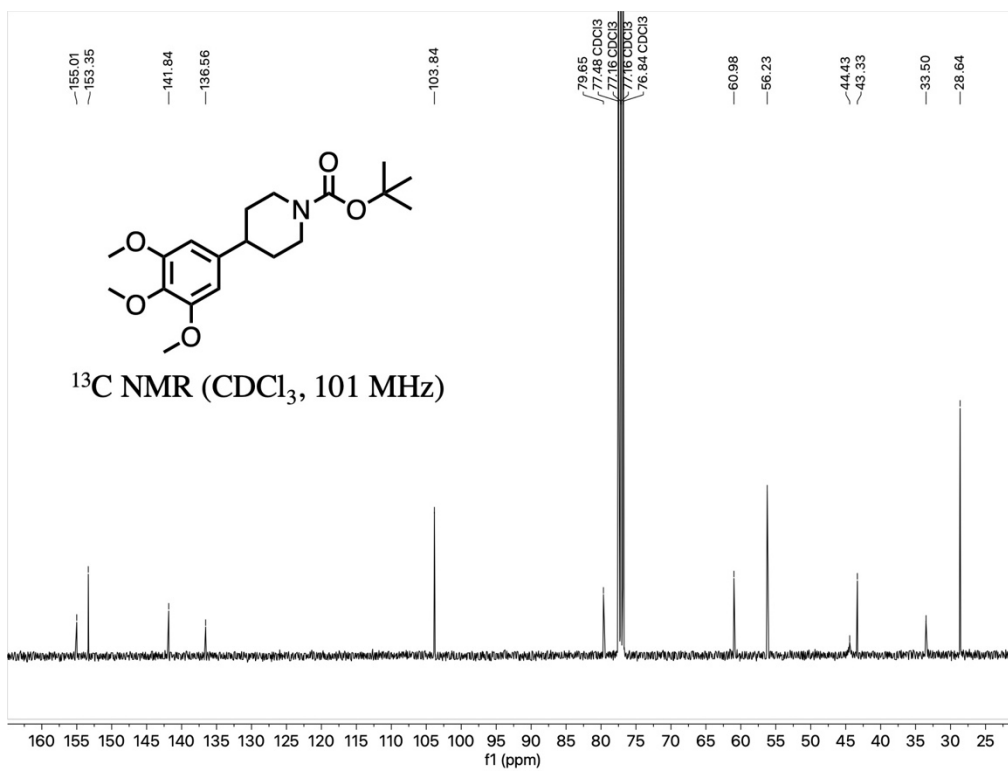


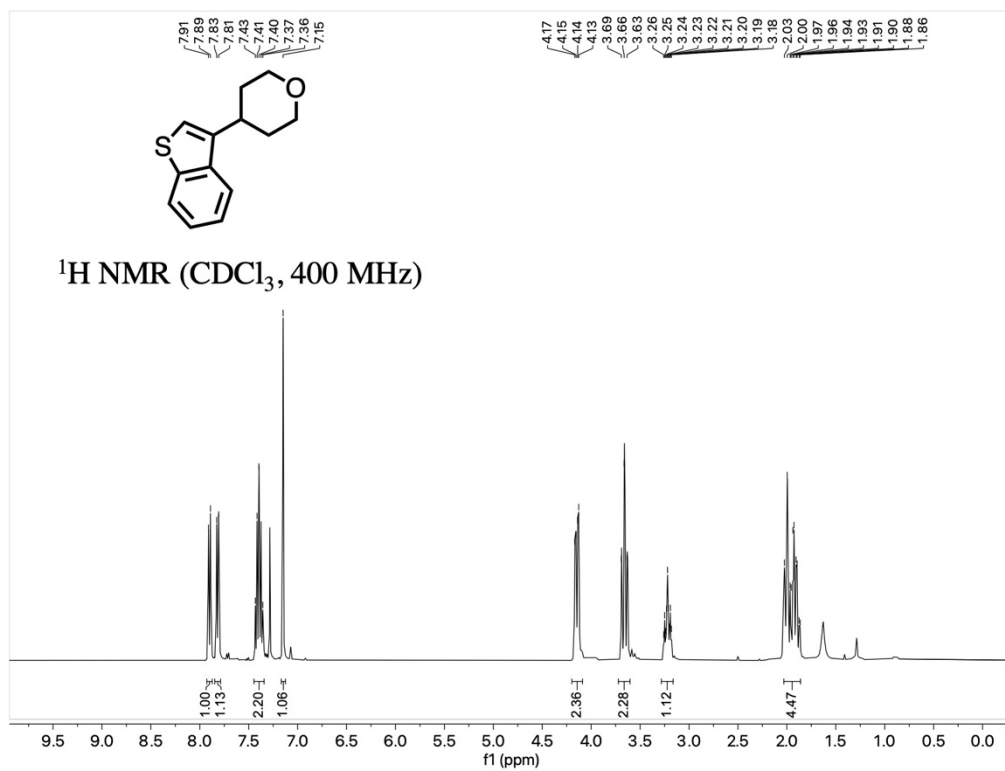
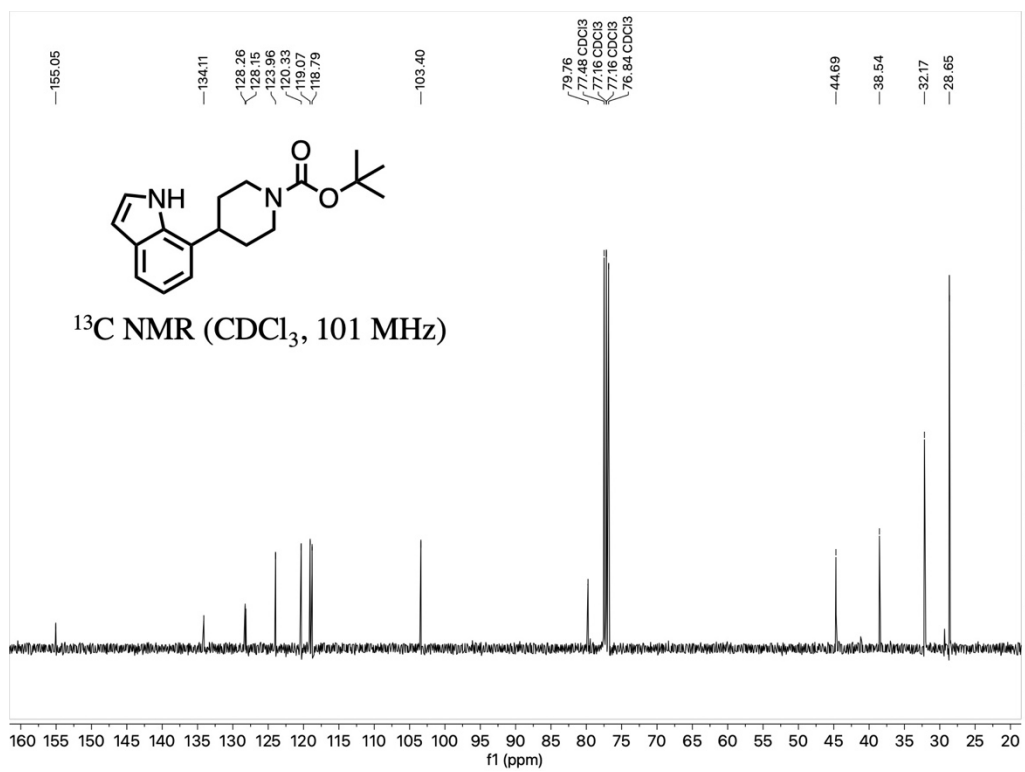


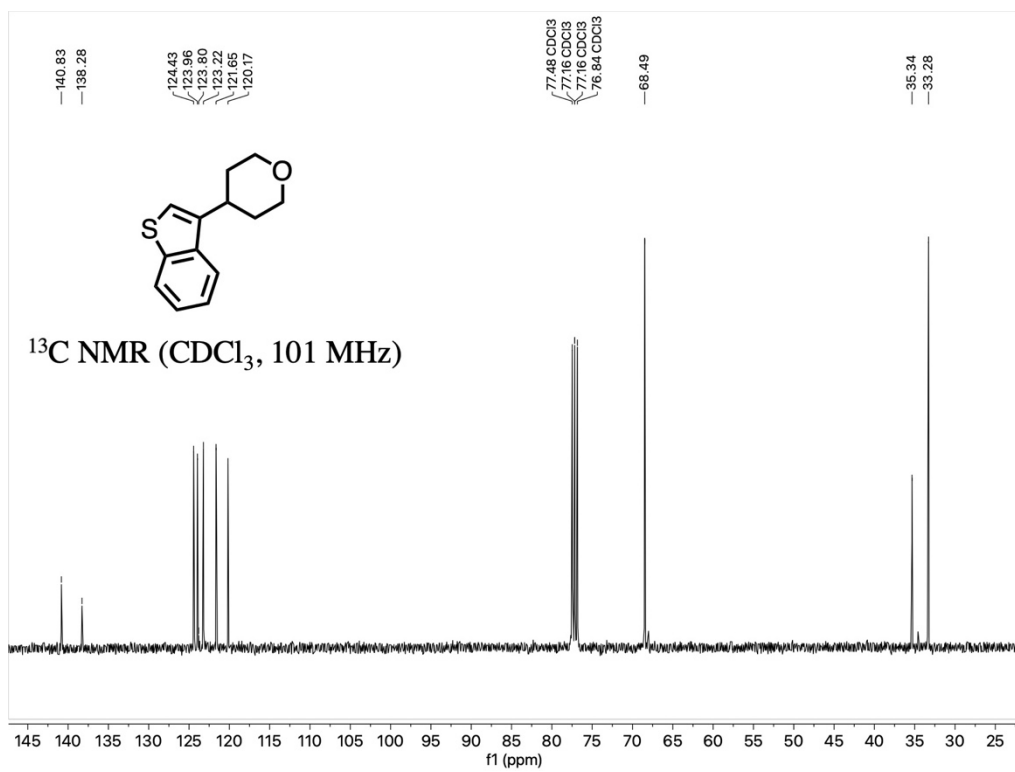












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