UNIVERSITAT POLITÈCNICA DE VALÈNCIA

Departamento de Química

PRODUCTION OF NEW CARBON-HETEROATOM BONDS INDUCED BY VISIBLE LIGHT

Doctoral Thesis

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STYLE

This Doctoral Thesis is written in a journal article compilation style format constituted by eight chapters in which the main features of the developed work are described. In Chapter 1 is detailed a literature review of photophysical properties and organic photochemistry, related to the contents of the doctoral thesis. Chapter 2 collects the objectives of the work. Chapters 3, 4, 5 and 6 show the research results of this thesis. Chapter 7 exhibits the conclusions of the thesis. Annexes collect the publications and participation in conferences and the NMR spectra of the reported compounds.

"Life before Death.

Strength before Weakness.

Journey before Destination."

—Brandon Sanderson, The Way of Kings

ABBREVIATIONS AND ACRONYMS

1D: one dimension

3D: three dimensions

*****: excited state

μs: microseconds

π,π*: Pi-Pi antibonding molecular orbital

A: acceptor

ACN: acetonitrile

aq: aqueous

Aq-OH: 1,8-dihydroxyanthraquinone

Ar: Argon

Ar$_3$N: triaryl amine

B: boron atom

B$_2$hex$_2$: bishexamethylglycolato diboron

B$_2$neo$_2$: bisneopentylglycolato diboron

B$_2$oct$_2$: bisoctamethylglycolato diboron

B$_2$pin$_2$: bispinacolato diboron

BET: back electron transfer

BNAH: 1-benzyl-1,4-dihydronicotinamide

Br: bromo atom

BrCCl$_3$: bromotrichloromethane

C: carbon atom

CDCl$_3$: deuterated chloroform

Ce: cerium (III) atom

CeCl$_3$: cerium (III) chloride

Cl: chloro atom

CO: carbon monoxide

CO$_2$: carbon dioxide

ConPET: consecutive photoinduced electron transfer

Cu: copper atom

Cu(O$_2$CCF$_3$)$_2$: copper (II) trifluoromethylacetate

Cu(OAc)$_2$: copper (II) acetate

Cy$_2$NMe: dicyclohexyl methyl amine

D: donor

DABCO: 1,4-diazabicyclo[2.2.2]octane

DBK: dibenzyl ketone

DBU: 1,8-diazabicyclo(5.4.0)undec-7-ene

DCA: 9,10-dicyanoanthracene

DIPA: *N*,*N*-diisopropylamine

DIPEA: *N*,*N*-diisopropyl ethyl amine

DTBP: ditertbutyl peroxide

$\mathbf{e^-}$: electron

EA: electronic affinity

EDA: electron donor acceptor

EnT: energy transfer

ET: electron transfer

$\mathbf{Et_3N}$: triethyl amine

FRET: Förster resonance energy transfer

fs: femtoseconds

$\mathbf{H_2O}$: water

$\mathbf{H_2O_2}$: hydrogen peroxide

HOMO: highest occupied molecular orbital

HIV: human immunodeficiency virus

IC: internal conversion

IP: ionization potential

$\boldsymbol{i}\mathbf{Pr_2NEt}$: *N*,*N*-diisopropyl ethyl amine

$\boldsymbol{i}\mathbf{Pr_2NH}$: *N*,*N*-diisopropyl amine

***i*PrOH**: isopropanol

***i*PrSS*i*Pr**: diisopropyl disulfide

Ir: iridium atom

ISC: intern system crossing

LEDs: light-emitted diodes

LMW: low molecular-weight

LUMO: lowest unoccupied molecular orbital

MeCN: acetonitrile

MeSSMe: dimethyl disulfide

MOF: metal organic framework

ms: milliseconds

n,π^*: non-bonding-Pi antibonding molecular orbital

N: nitrogen atom

N_2: molecular nitrogen

$Na_2S_2O_8$: sodium persulfate

NADH: 1,4-dihydronicotinamide adenine dinucleotide

$(NH_4)_2S_2O_8$: ammonium persulfate

Ni: nickel atom

NDI: naphthalene diimide

nm: nanometer

NMR: nuclear magnetic resonance

O_2: molecular oxygen

P: phosphorus atom

PC: photocatalyst

Pd: palladium atom

PDI: perylene diimide

PET: photoinduced electron transfer

pH: potential of hydrogen

Ph_3N: triphenylamine

PhSSPh: diphenyl disulfide

$P(OEt)_3$: triethyl phosphite

$P(OMe)_3$: trimethyl phosphite

$P(OPh)_3$: triphenyl phosphite

PPh_3: triphenyl phosphine

QY: quantum yield

Rh-6G: rhodamine 6G

S: sulfur atom

Si: silicon atom

S_n: singlet state electronic level n

sp^2: hybrid orbital formed by one *s* orbital and two *p* orbitals

sp^3: hybrid orbital formed by one *s* orbital and three *p* orbitals

SET: single electron transfer

T_n: triplet state electronic level n

TTA: triplet-triplet annihilation

V: volts

Abstract

This thesis doctoral describes novel, simple, and rapid methodologies using visible light to produce compounds with new C–heteroatom bonds such as C–B, C–P and C–S that represent valuable scaffolds in modern organic synthesis. The employment of visible light as energy source highlights the concepts of green and sustainable chemistry considering its mild, safe, and eco-friendly advantages. On the other hand, spatially nanoreactors such as viscoelastic gel networks by 'bottom-up' approaches to improve different processes in comparison to solution, in terms of kinetics, selectivity or processability have been also developed.

Thus, Chapter 3 describes a novel, straightforward, and fast procedure to produce boron-containing thiophenes employing visible light in anaerobic solution. Interestingly, the process does not require the use of any external photocatalyst. This study has been extended to the borylation of commercially available heteroarene halides under aerobic conditions in an easy-to-use gel nanoreactor (Chapter 4). The gel network provides an adequate stabilizing microenvironment to support wide substrate scope, including furan, thiophene, selenophene, and pyrrole boronate esters.

Chapter 5 focus on a new strategy to achieve efficient aerobic phosphorylation of five-membered heteraroenes using dichromatic photoredox catalysis in a gel-based nanoreactor. The methodology, which operates by a consecutive photoinduced electron transfer (ConPET) mechanism, has been successfully applied to the straightforward and clean synthesis of a number of different heteroarene (furan, thiophene, selenophene, pyrrole, oxazole, or thioxazole) phosphonates, extending to the late-stage phosphonylation of the anticoagulant rivaroxaban.

Lastly, regarding the construction of new C–S bonds, Chapter 6 shows a simple and effective metal-free thiolation of commercial heteroarene halides using visible light. The experimental results are consistent with the reaction taking place from an electron donor–acceptor (EDA) complex between an alkylamine and the heteroarene halide. Mechanistic aspects of the whole process have been demonstrated by spectroscopic measurements whereas the strength of this novel method has been proven by gram-scale experiment and late-stage derivatization.

Resumen

En la presente tesis doctoral se describen metodologías novedosas, simples y rápidas con luz visible para producir compuestos con nuevos enlaces C-heteroátomo como C-B, C-P y C-S que representan estructuras valiosas en la síntesis orgánica moderna. La luz visible se emplea como fuente de energía más suave y sostenible que la tradicional (energía térmica). Por otro lado, también se han empleado nanorreactores espaciales como las redes de gel viscoelástico mediante enfoques 'ascendentes' para mejorar diferentes procesos en comparación con la disolución, en términos de cinética, selectividad o procesabilidad.

Por lo tanto, el Capítulo 3 describe un procedimiento novedoso, directo y rápido para producir tiofenos que contienen boro empleando luz visible en disolución anaeróbica sin el uso de ningún fotocatalizador externo. Este estudio se ha ampliado a la borilación de haluros de heteroareno comerciales en condiciones aeróbicas en un nanorreactor de gel fácil de usar (Capítulo 4). La red de gel proporciona un microambiente estabilizador adecuado para soportar una amplia gama de sustratos, incluidos los ésteres de boronato de furano, tiofeno, selenofeno y de pirrol.

El Capítulo 5 se centra en una nueva estrategia para lograr una fosforilación aeróbica eficiente de heteroarenos de cinco miembros mediante catálisis fotorredox dicromática en un nanorreactor basado en gel. La metodología, que opera mediante un mecanismo de transferencia de electrones fotoinducida consecutiva (ConPET), se ha aplicado con éxito a la síntesis sencilla y limpia de varios fosfonatos de heteroareno diferentes (furano, tiofeno, selenofeno, pirrol, oxazol o tioxazol), extendiéndose a la etapa tardía de la fosforilación del anticoagulante rivaroxabán. Por último, el Capítulo 6 muestra una tiolación (formación enlaces C-S) simple y efectiva, libre de metales, de haluros de heteroareno comerciales usando luz visible. Los resultados experimentales son consistentes con una reacción basada en un complejo aceptor-donador de electrones (EDA) entre una alquilamina y el haluro de heteroareno. El mecanismo del proceso se ha demostrado mediante estudios espectroscópicos, mientras que la robustez se ha demostrado mediante experimentos a escala de gramo y derivatización de última etapa.

Resum

En la present tesi doctoral es descriuen metodologies noves, simples i ràpides amb llum visible per a produir compostos amb nous enllaços C-heteroàtom com C-B, C-P i C-S que representen estructures valuoses en la síntesi orgànica moderna. La llum visible s’utilitza com a font d'energia mes suau i sostenible que la tradicional (energia tèrmica). D'altra banda, també s'han emprat nanorreactors espacials com les xarxes de gel viscoelàstic mitjançant enfocaments 'ascendents' per a millorar diferents processos en comparació amb la dissolució, en termes de cinètica, selectivitat o procesabilitat. Per tant, el Capítol 3 descriu un procediment nou, directe i ràpid per a produir tiofens que contenen bor emprant llum visible en dissolució anaeròbica sense l'ús de cap fotocatalitzador extern. Aquest estudi s'ha ampliat a la borilació d'halurs d’heteroaré comercials en condicions aeròbiques en un nanorreactor de gel fàcil d'usar (Capítol 4). La xarxa de gel proporciona un microambient estabilitzador adequat per a suportar una àmplia gamma de substrats, inclosos els èsters de boronat de furan, tiofé, selenofé i de pirrol. El Capítol 5 se centra en una nova estratègia per a aconseguir una fosforilació aeròbica eficient de heteroarens de cinc membres mitjançant catàlisis fotorredox dicromàtica en un nanorreactor basat en gel. La metodologia, que opera mitjançant un mecanisme de transferència d'electrons fotoinducida consecutiva (ConPET), s'ha aplicat amb èxit a la síntesi senzilla i neta de diversos fosfonats d’heteroaré diferents (furan, tiofé, selenofé, pirrol, oxazol o tioxazol), estenent-se a l'etapa tardana de la fosforilació de l'anticoagulant rivaroxabán. Finalment, el Capítol 6 mostra una tiolació (formació d’enllaços C-S) simple i efectiva, lliure de metalls, d'halurs d’heteroaré comercials usant llum visible. Els resultats experimentals són consistents amb una reacció basada en un complex acceptor-donador d'electrons (EDA) entre una alquilamina i l'halur d’heteroaré. El mecanisme del procés s'ha demostrat mitjançant estudis espectroscòpics, mentre que la robustesa s'ha demostrat mitjançant experiments a escala de gram i derivatització d'última etapa.

INDEX

"And so, does the destination matter? Or is it the path we take? I declare that no accomplishment has substance nearly as great as the road used to achieve it. We are not creatures of destinations. It is the journey that shapes us. Our callused feet, our backs strong from carrying the weight of our travels, our eyes open with the fresh delight of experiences lived."

—Brandon Sanderson, The Way of Kings

Chapter 1
Introduction

Introduction

1.1. Photochemistry evolution

Based on the compendium of chemical terminology by IUPAC, Photochemistry is defined as “the branch of chemistry concerned with the chemical effects of light (far UV to IR)”.[1] Chemical transformations induced by light could be considered older than life itself.[2] In nature, plants and microorganisms (algae) have harnessed the sunlight energy to produce organic matter by consuming water and carbon dioxide in the process of photosynthesis.[3] Even now, the solar radiation is the fundamental energy source in Earth evolution. It is interesting to highlight that the sunlight energy which strikes the planet *per* day, is greater than the energy the humanity consumes in a whole year.[4] Encourage by the actual social problems related to global warming or the scarceness of fossil resources, it is therefore reasonable to direct all the efforts to search novel procedures using the solar energy at the visible region (**Figure 1**) in order to achieve low energy demanding synthetic protocols to produce photochemical transformations.[5]

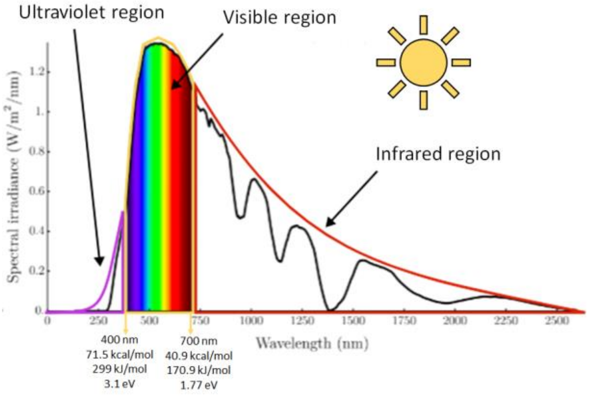

Figure 1. Relationship between wavelength and energy and the spectral ranges.

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[1] IUPAC. Compendium of Chemical Terminology, 2nd ed. (the "Gold Book"). Compiled by A. D. McNaught and A. Wilkinson. Blackwell Scientific Publications, Oxford (1997). Online version (2019-) created by S. J. Chalk. ISBN 0-9678550-9-8. https://doi.org/10.1351/goldbook

[2] Canuto, V. M.; et al. *Nature* **1983**, *305* (5932), 281-286.

[3] Nelson, N.; Ben-Shem, A. *Nat. Rev. Mol. Cel. Bio.* **2004**, *5*, 971.

[4] *Solar Photocatalysis for Enviromental Remediation*; Chakrabarti, S., Ed.; CRC Press Taylor & Francis Group, USA, 2019; pp 18-20.

[5] a) Scholes, G. D.; et al. *Nat. Chem.,* **2011**, 3. b) Scholes, G. D.; et al. *Energy Environ. Sci.*, **2012**, *5*, 9374.

From a chronological point of view, although the first hominids used sunlight for lighting and heating purposes, Conrad Gesned documented in 1599 the first experiments utilizing sunlight in the "*The maner of Distilling in the Sunne*".[6] In the 18th century, Priestly reported a photochemical transformation in which nitric acid solutions changed the color under sunlight exposure due to nitrogen dioxide formation.[7] Moreover, the basic principles of photosynthesis were also attributed to him. Later, Nicholas Theodore de Saussure demonstrated the production of oxygen by plants from water, carbon dioxide and light.[8]

Regarding organic synthetic applications, the irradiation of sunlight to santonin might be the first organic photoreaction discovered.[9] A color change from white to yellow was observed during the photoreaction, forming a crystal burst afterwards. In addition, the author studied the influence of a prism in the reaction and realized that formation of the yellow crystals only appeared by sunlight, blue and violet rays' exposure; whereas no formation was detected when yellow, green or red beams were employed.

During the 19th century photochemistry was practically a dormant field, and the number of examples was quite limited. However, at the beginning of the 20th century, the Italian chemist G. Ciamician published a *Science* paper[10] ("The Photochemistry of the Future") where he recognized that sunlight could be utilized as a promoter of organic reactions. Inspired by the ability of plants to make use of solar energy, he was the first scientist to investigate the photochemical reactions in a systematic way. His predictions on the advantages of utilizing solar energy to convert it into fuels has earned him to be considered a pioneer of modern photochemistry.[11]

1.2. Fundamentals on photochemistry

Photochemistry is the science derived from chemistry in which the interaction of light with atoms and/or small molecules is studied. For this purpose, these atoms or molecules must first absorb light, thanks to the chromophores that are the main

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[6] Gestner, C.; *The Practise of the New and Old Phisicke*. London, 1599; p 23-24.

[7] Priestly, J.; *Experiments and observations on different kinds of air.* J. Johnson: London, 1775.

[8] Ihde, A. J.; *The Development of Modern Chemistry*. Dover Publications: 1984.

[9] Trommsdorff, H.; Ueber Santonin. *Annalen der Pharmacie* **1834**, *11* (2), 190-207.

[10] Ciamician, G.; *Science*, **1912**, *36*, 385.

[11] In 1998, this report was cited for the first time in a JRC journal: see for instance Gust, D.; Moore, T. A.; Moore, A. L. Pure & Appl. Chem. 1998, 70, 2189. (Source: SciFinder).

functional groups responsible for photochemical activity.[12] Chromophores possess molecular orbitals, the result of overlapping s and p atomic orbitals. These orbitals are classified as bonding (σ or π), antibonding (σ* or π*), and nonbonding (n). In most organic molecules, the electronic shell is full and the highest energy occupied molecular orbital (HOMO) can be bonding or non-bonding type. After exciting the molecule, the transition from a HOMO orbital to a LUMO (lowest unoccupied energy molecular orbital) occurs, which is usually an antibonding orbital, resulting in an unstable species. The most frequent excitations are:

- π→π*, typical of alkenes, alkynes, and aromatic molecules.
- n→π*, typical of compounds with carbonyls, thiocarbonyls, nitro, azo and imino groups.
- n→σ*, typical of amines, alcohols and haloalkanes.

In the molecule, each electron in a molecule carries an angular spin momentum with a quantum spin of s = ½ that can have two orientations:

- Spin up ↑ or α (m_s = +½).
- Spin down ↓ or β (m_s = -½).

The total spin angular momentum of a molecule is represented by the total spin quantum number S, which is the vector sum of the electron spin quantum number. If the spins are opposite, the sum is 0, if they are parallel, it is 1. The spin multiplicity is given by 2S+1.

In the ground electronic state of most organic molecules the electrons are paired, so S = 0 and the multiplicity is 1. In the case that both electrons are in the same orientation, the multiplicity will be then 3 (S = 1) naming now the triplet excited state.

Therefore, a molecule in an upper excited state will tend to return to its ground state and the absorbed energy will be used to produce some change in its structure such as a photochemical change or, on the contrary, to look for another way to lose the energy and return to the ground state by a photophysical process. These photophysical processes are divided into three types:

- Radiative: To return to the ground state by emitting electromagnetic radiation.
- Non-radiative: when the return to the ground state is not associated with the emission of radiation.

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[12] *Photochemistry and Photophysics*; Balzani, V.; Ceroni, P.; Juris, A.; Ed. Wiley-VCH Verlag GmbH & Co. kGaA: Weinheim, Germany, 2014; p 32.

- Quenching (molecular deactivation): it is deactivated by the collision with another molecule.

Thus, photochemistry may be attributed to the excited state chemistry, in which light is used as the energy contribution to initiate chemical reactions.[13] This excited state is reached after a photon absorption by a chromophore (molecule, molecular complex, supramolecular structure…). Usually, the electrons of a chromophore are paired in the ground state. Then, the effect of the absorbed light provokes the promotion of an electron from the HOMO to the LUMO (**Figure 2**), changing the molecular structure and, consequently, generating the excited states that are generally singlets and triplets.

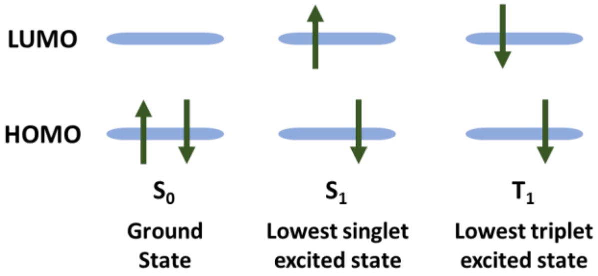

Figure 2. Molecule valence electrons configuration in the singlet ground state (Left), lowest singlet excited state (Middle) and lowest triplet excited state (Right).

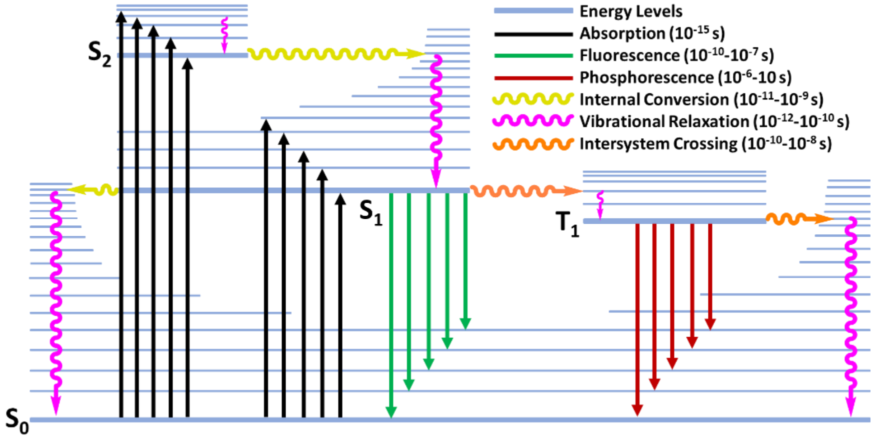

Figure 3. Jablonski diagram.

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[13] *Photochemistry Essentials*; Scaiano, T. American Chemical Society, 2022.

As depicted in **Figure 3**, the Jablonski diagram is a remarkable tool where the energetic, multiplicity, and dynamic connections between the electronic states of a molecule can be easily visualized. After absorption of one photon by a molecule at the ground state, this promotes from S_0 to an electronic excited state S_n, preserving the same multiplicity. Following the well-accepted *Kasha's rule,*[14], these upper excited states (higher than S_1, such as S_2, …, S_n) relax quickly to the lowest excited electronic state, S_1, from which most photochemistry and photophysics (such as fluorescence) take place, whereas other processes are frequently not competitive. This relaxation is produced by a two phenomenons called internal conversion (IC) and vibrational relaxation (VR) which are non-radiative. The IC is a transition-permitted process where the energy is released from an electronic level to a different electronic level but at the same level of vibrational energy (same multiplicity) and suddenly it is relaxed to the lowest vibrational level by VR. Once the electron reaches the S_1, this may relax to the S_0 by fluorescence emission (radiative) or by IC (non-radiative) to the S_0. Other possible path from the S_1 is the intersystem crossing (ISC) to a triplet state, T_1, with a multiplicity change, which could relax by phosphorescence emission (radiative) or by another ISC (non-radiative) to a high vibrational level of S_0. The ISC normally occurs at longer time scales due to the spin forbidden transition. Nevertheless, *El-Sayed's rule* asserts that the ratio of ISC, for instance from the lowest singlet state to the triplet ($S_1 \rightarrow T_1$), is relatively fast if the radiationless transition includes a change of orbital type (**Figure 4**).[15]

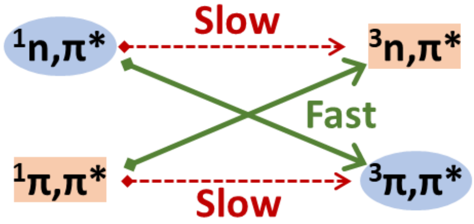

Figure 4. ISC ratio according on the orbital exchange rate.

Therefore, when a molecule absorbs a photon with equal or higher energy than the difference between the bonding and antibonding orbitals, this reaches its excited state. In this scenario the molecule now presents different energy content,

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[14] Kasha, M.; *Discuss. Faraday Soc.* **1950**, *9*, 14–19.

[15] El-Sayed, M. A.; *Acc. Chem. Res.* **1968**, *1*, 8–16.

electronic and geometric structure than in its ground state,[7] conferring it different properties (**Figure 5**).[16] For example, the electron affinity in the excited state (EA*) is found to be higher and, consequently, it could be reduced more efficiently than in the ground state, releasing more energy when the electron is added. Regarding the ionization potential in the excited state (IP*), to remove an electron from the excited state is found to be easier than in the ground state in terms of energetic costs and therefore the oxidation of the molecule is more effective.

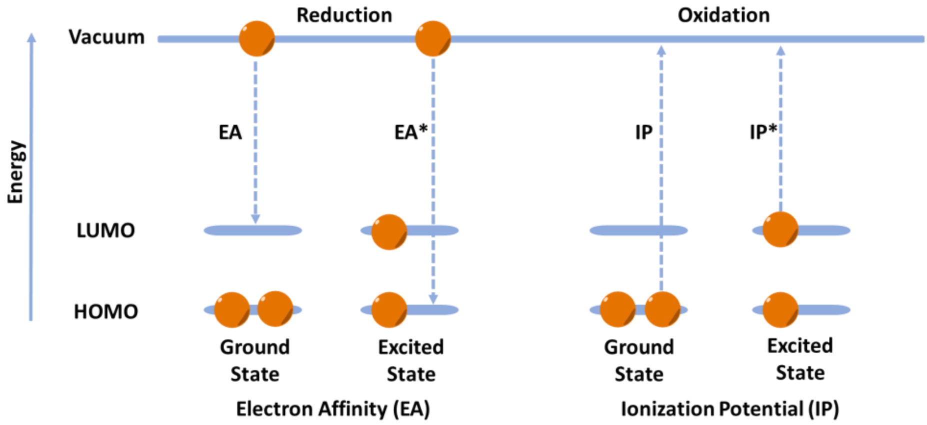

Figure 5. Difference between the ground and excited state of a molecule electron affinity and ionization potential.

Thereby, the redox properties of a molecule completely change when it is presented in its excited state, becoming better reductant or oxidizing species. As a matter of fact, this capability can be interestingly exploited in photochemistry or photocatalysis as a powerful tool to be applied in Organic Chemistry. The typical photochemical transformation implies a fast electron transfer (ET) process to an electron-deficient acceptor species (A) or from an electron-rich donor species (D). Other important pathway in photochemical reactions is the energy transfer (EnT) process that only requires the transmission of energy absorbed.[17] Currently, both processes are the most employed in photochemistry and photocatalysis and a vast number of applications can be found in literature (**Figure 6**). Although a photocatalyst can be employed in these two processes, different terminology is

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[16] *Handbook of Photochemistry*. Montalti, M.; Credi, A.; Prodi, L.; Gandolfi, M. T. Ed. CRC Press Taylor & Francis Group, USA, 2006.

[17] Arias-Rotondo, D. M.; McKuster, J.K. *Chem. Soc. Rev.* **2016**, *45*, 5803.

used depending on the process. Thus, in the case of ET one can refer to “photoredox catalyst” whereas in the case of EnT the appropriate name is “photosensitizer”. In addition, there are other methodologies involving these two mechanisms, such as triplet-triplet annihilation (TTA),[18] multiphoton excitation[19] or singlet fission.[20]

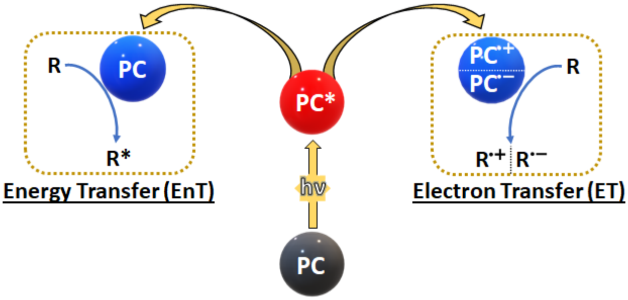

Figure 6. Energy transfer and Electron Transfer processes for an excited PC.

1.2.1. Energy transfer (EnT) processes

The simplest form of EnT is called trivial energy transfer, where an excited donor (D) releases radiation energy (fluorescence, phosphorescence) that is absorbed by an acceptor (A). In this mechanism, no electron exchange occurs, and the main requisite is the overlap between D emission and A absorbance. The efficiency depends on the distance between the two vessels and the irradiance of the D.

On the other hand, the most common EnT consist of non-radiative interactions via: Dexter and Föster energy transfer mechanism. Hence, Dexter or exchange energy transfer may occur in singlet or triplet states through an electron exchange between the D* to the ground state A and requires spatial proximity with spin conservation and lack of radiation release (**Figure 7**). The rates of the Dexter energy transfer are normally very fast in fluid solution, becoming very close to the diffusion-controlled rates. It is obvious that the efficiency of EnT decrease exponentially with the distance, so a “contact” or at least the presence of the D and A at the same solvent cage is warranted. The Förster resonance energy transfer (FRET) is produced by dipole–dipole interactions between the D and A where energy is transferred without electron exchange. The D* generates an electronic oscillation, inducing a dipole that may produce an electronic oscillation of the A

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[18] Majek, M.; et al. *Chem. Eur. J.* **2015**, *21*,15496-15501.

[19] Castellanos, J.; et al. *Org. Chem. Front.* **2020**, *7*, 1709-1716.

[20] Cerrato, E; Paganini, M. C.; Giamello, E. *J. Photochem. Photobiol. A.* **2020**, *397*, 112531.

ground state. This resonant interaction provokes that the electron at the LUMO of D drops to its ground state meanwhile one electron at the HOMO of the A promotes to the excited state (**Figure 8**). This FRET mechanism occurs normally from the singlet state (due to spin conservation rules this process is forbidden in the triplet state) and even at rather long distances (>10 nm) between the D and the A. The efficiency of the process requires an overlap between the fluorescence of D and the absorption spectrum of A. The fluorescence lifetime of D must be long enough to produce FRET and the transition dipole vectors of the D and A must be nearly parallel.

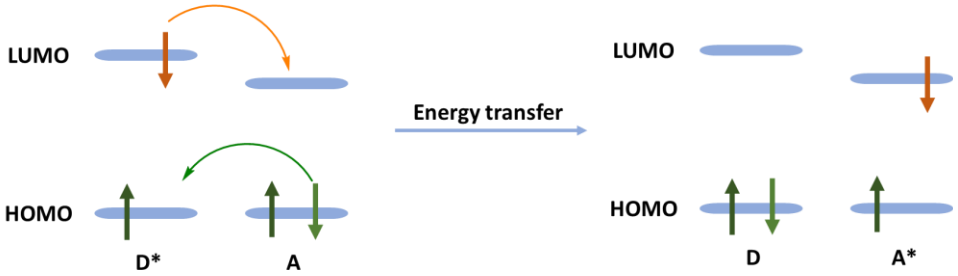

Figure 7. Dexter energy transfer by an electron exchange between an excited D and a ground state A.

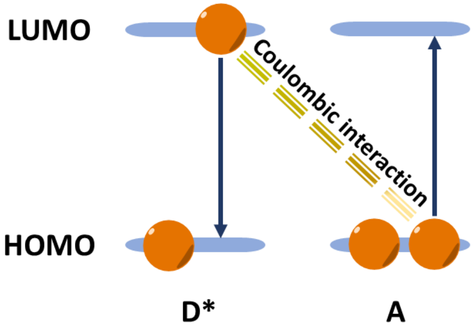

Figure 8. Förster resonance energy transfer (FRET).

1.2.2. Electron transfer (ET) process

Much of the recent renewal of interest in photochemical synthesis has been based upon the propensity of photoexcited molecules to participate in ET (or "photoredox") processes.[21] Thus, a single ET (SET) consists of transferring an

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[21] Kavarnos, G. J.; Turro, N. J. *Chem. Rev.* **1986**, *86*, 401−449.

electron from the excited state of one molecule to another molecule in its ground state. This radical ion pair generated by SET is stabilized in polar solvents. In this context, two possible scenarios are depicted relying on which excited state is involved (**Figure 9**). The reaction can take place from both singlet or triplet excited states and makes two radical ions when **D** and **A** are neutral molecules. The resulting organic radical ion species can directly react in a number of different bond-forming reactions. Alternatively, the radical ions can undergo mesolytic fragmentation to afford separate radical and ionic intermediates, either of which can be productively intercepted in synthetic transformations.

Donor Excited

$$\mathrm{D} \xrightarrow{h\nu} \mathrm{D^*}$$

$$\mathrm{D^*} + \mathrm{A} \longrightarrow \mathrm{D^{\bullet+}} + \mathrm{A^{\bullet-}}$$

Acceptor Excited

$$\mathrm{A} \xrightarrow{h\nu} \mathrm{A^*}$$

$$\mathrm{D} + \mathrm{A^*} \longrightarrow \mathrm{D^{\bullet+}} + \mathrm{A^{\bullet-}}$$

Back electron transfer (BET)

$$\mathrm{D^{\bullet+}} + \mathrm{A^{\bullet-}} \longrightarrow \mathrm{D} + \mathrm{A}$$

Figure 9. Electron transfer processes from an excited **D** (Left), an excited **A** (Middle) and the back electron transfer process (Right).

1.3. Photoredox catalysis

Many researchers have explored ways to efficiently harvest and use visible light energy for the activation of organic molecules. The main one has been the design, synthesis, and development of photocatalysts that are able to absorb visible light and mediate the desired chemical transformations by means of rapid ET processes. Activation of molecules with visible light offers the possibility of reaction pathways which are otherwise impossible to reach with classical nonphotochemical strategies. Another fascinating aspect of visible light promoted photochemistry is the use of photons as “traceless and green reagents”, rendering photochemical processes green and sustainable.

In this context, the last decade has witnessed the fantastic growing in the field of Organic Photocatalysis using visible light as energy source, emerging as a new and powerful tool for activating small molecules. This new field largely relies on the ability of metal complexes and organic dyes to harvest visible light photons and convert this energy to an electrochemical potential, engaging in SET processes with organic substrates upon photoexcitation with visible light. Taking into account the generally mild reaction conditions, the use of visible light as a perennial energy source and its broad applicability, ***visible light photoredox catalysis*** has gained tremendous momentum over the past years and has triggered a renewed interest toward photochemistry in general (**Figure 10**). One of the first synthetic applications of a photoredox catalyst (PC) was reported by Deronzier,[22] wherein a ruthenium photocatalyst was used in a Pschorr-type transformation via a single-electron reduction of an aryl diazonium moiety. In 2008, Yoon and MacMillan concurrently reported the utilization of $Ru(bpy)_3^{2+}$ as photoredox catalyst to perform [2+2] cycloadditions and α-alkylation of aldehydes, respectively,[23,24] whereas Stephenson,[25] one year later, employed the same photocatalyst for the dehalogenation of activated alkyl halides. These reports were the kick-off of what we currently known as *Photoredox Catalysis* and numerous groups have developed creative applications with a variety of photocatalysts.

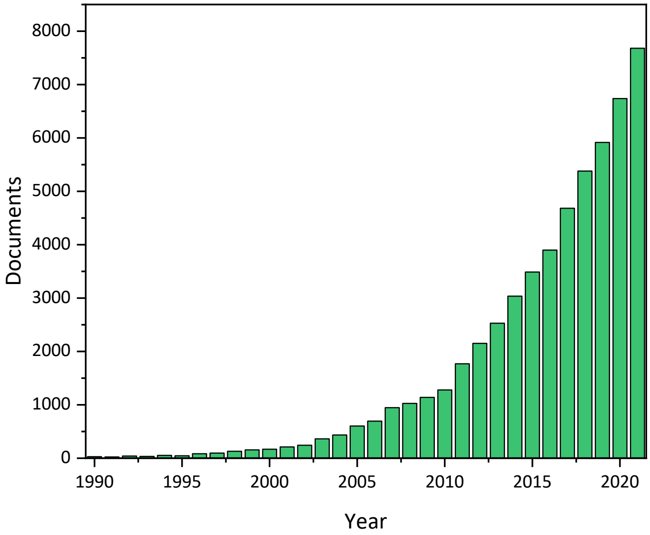

Figure 10. Number of publications that include photocatalysts in the last 30 years. Data from SCOPUS database searching photocatalyst.

Light-driven systems that have excited states and promote a chemical reaction can be generally classified as "excitonic chemical conversion systems" or more commonly named in the literature as "photocatalysts". The International Union of Pure and Applied Chemistry (IUPAC) defines a "photocatalyst" as a "catalyst able to

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[22] Cano-Yelo, H.; Deronzier, A. *Tetrahedron Lett.* **1984**, *25*, 5517–5520.

[23] Nicewicz, D.A.; MacMillan, D.W.C.; *Science*, **2008**, *322*, 77–80.

[24] Ischay, M.A.; Anzovino, M.E.; Du, J.; Yoon T.P.; *J Am Chem Soc*, **2008**, *130*, 12886–12887.

[25] Narayanam, J. M. R.; Tucker, J. W.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2009**, *131*, 8756.

produce, upon absorption of light, chemical transformations of the reaction partners. The excited state of the photocatalyst repeatedly interacts with the reaction partners forming reaction intermediates and regenerates itself after each cycle of such interactions." **Figure 11** outlines the generalized photoredox processes available to a photocatalyst. An electronically excited state is generated after a photon absorption; this can undergo relaxation back to the ground state via a number of unimolecular radiative and non-radiative pathways at relatively rapid rates. The redox properties of the excited state, however, can be exploited upon fast ET to an electron-deficient acceptor species (A) or from an electron-rich donor species (D). These species are referred to as oxidative and reductive quenchers, respectively, because they result in the formation of a different oxidation state of a photocatalyst in its electronic ground-state configuration. Regeneration of the photochemically active state requires a second ET process from a complementary D or A species. Thus, photoredox catalysis typically results in a formal transfer of an electron from one reagent to another, which produces a pair of reactive radical ions comprising the oxidized donor ($D^{\bullet+}$) and reduced acceptor ($A^{\bullet-}$).

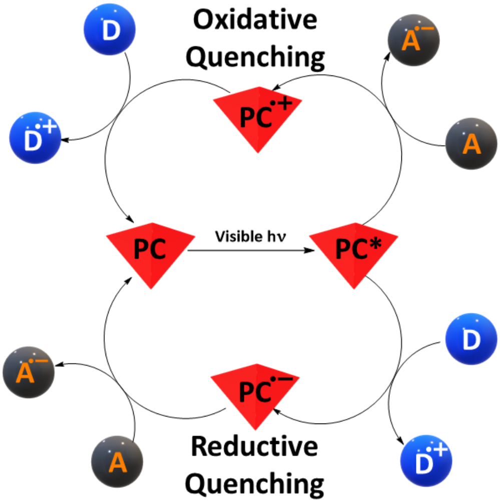

Figure 11. Oxidative and reductive quenching cycle of a PC.

Many of the common visible light photocatalysts are oligopyridyl complexes of ruthenium and iridium, typified by tris(2,2′-bipyridine) ruthenium(II), $Ru(bpy)_3^{2+}$. It is known that such complexes absorb light in the visible region of the

electromagnetic spectrum, leading to stable, long-lived excited states (1100 ns for $Ru(bpy)_3^{2+}$).[26,27,28]
On the other hand, several organic molecules can also act as visible light photocatalyst; metal-free alternatives are appreciated for their lower price, wider structural variation, and better environmental profile. Thus, organic dyes such as methylene blue,[29] rose Bengal,[30] Eosin Y,[31] triphenylpyrylium salts[32] or 9-mesityl-10-methylacridinium ion[33] readily absorb visible light to give excited states capable of SET.

1.3.1. Consecutive Photoinduced Electron Transfer (ConPET)

At the photosynthesis, plants manufacture autotrophically their energy source from water, carbon dioxide and visible light through a Z-scheme mechanism by two-step accumulative photon absorption. Surprisingly, this concept has been only recently applied as a powerful synthetic strategy wherein activation of chemical compounds with high-energetic demanding bonds has been successfully achieved. Thus, the adapted ConPET mechanism to organic transformations mimics the Z-scheme. Briefly, selective excitation of the photocatalyst (PC) led to its excited state which is quenched by an appropriate donor generating the PC radical anion. Then, excitation of the PC radical anion results in the formation of an excited PC radical anion (doublet excited state), a highly reducing agent (**Figure 12**).

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[22] Nicewicz, D.A.; MacMillan, D.W.C.; *Science*, **2008**, *322*, 77–80.
[23] Ischay, M.A.; Anzovino, M.E.; Du, J.; Yoon T.P.; *J Am Chem Soc*, **2008**, *130*, 12886–12887.
[26] Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322−5363.
[27] Xi, Y.; Yi, H.; Lei, A.; *Org. Biomol. Chem.* **2013**, *11*, 2387−2403.
[28] Xuan, J.; Xiao, W.-J.; *Angew. Chem., Int. Ed.* **2012**, *51*, 6828−6838.
[29] Pitre, S. P.; et al. *J. Am.Chem. Soc.* 2013, *135*, 13286–13289.
[30] Xiang, L.; *ACS Catal.*2014 ,*4*, 1897–1900.
[31] Hari, D.P.; König, B.; Chem. Commun. **2014**, *50*, 6688–6699.
[32] Alfonzo E.; et al. *Org. Lett.* **2017**, *19* (11), 2989–2992.
[33] Joshi-Pangu, A.; *J. Org. Chem.* **2016**, *81* (16), 7244–72499.

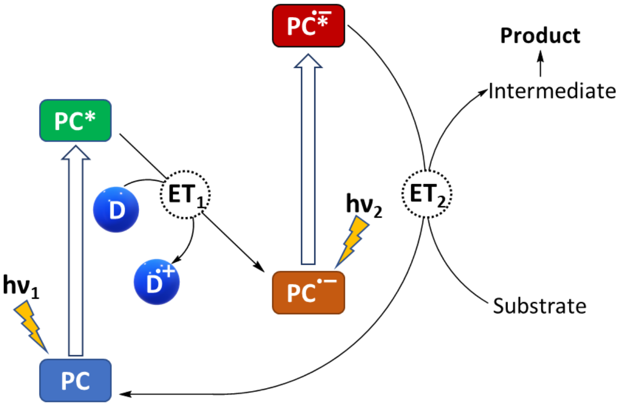

Figure 12. Photosynthesis Z-Scheme.

The first example concerning to this concept was reported by König and co-workers where they described the use of a perylene diimide (PDI) derivative as organic photocatalyst.[34] In this case, the PC was capable of activating aryl halides by collecting the energy of two visible light photons; the subsequent generated aryl radicals were trapped by hydrogen atom donors or by specific nucleophiles. Later, the same PDI-based photocatalyst was used at heterogeneous conditions facilitating the ConPET process for the visible light-driven dehalogenation of aryl halides reducing markedly the irradiation times.[35] Several drawbacks were found related to diimide-like photocatalysts such as tedious synthesis and low solubility in organic solvents. Hence, König and co-workers exploited this idea employing other organic, commercially available dyes such as 1,8- dihydroxyanthraquinone (Aq-OH)[36] or rhodamine 6G (Rh-6G)[37] which is currently the most widely use photocatalyst for organic synthesis.[26,27,38,39] In this context, Pérez-Ruiz and co-workers[40] recently contributed to this field using the commercial dye 9,10-

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[34] Ghosh, I.; et al. *Science*, **2014**, *346*, 725.

[35] a) Zeng, L. ; et al. J. Am. Chem. Soc. 2016, *138*, 3958. b) He, J.; et al. *ACS Appl. Mater. Interfaces*, **2020**, *12*, 2199.

[36] Bardagi, J. I.; et al. *Eur. J. Org. Chem*. **2018**, 34.

[37] Ghosh, I.; König, B.; *Angew. Chem., Int. Ed.* **2016**, *55*, 7676.

[26] Xi, Y.; Yi, H.; Lei, A.; *Org. Biomol. Chem.* **2013**, *11*, 2387−2403.

[27] Xuan, J.; Xiao, W.-J.; *Angew. Chem., Int. Ed.* **2012**, *51*, 6828−6838.

[38] Shaikh, R. S.; Düsel, S. J. S.; König, B.; *ACS Catal.,* **2016**, *6*, 8410.

[39] Brandl, F.; et al. *Chem. Eur. J*, **2020**, *26*, 7946.

[40] Neumeier, M.; et al. *Chem. Eur. J.* **2018**, *24*,105-108.

dicyanoanthracene (DCA) that enabled photocatalytic aromatic substitutions of non-activated aryl halides. This reaction was found to operate under VIS-irradiation via sequential photonic, electronic, and photonic activation of the simple organic dye. The resultant highly reducing excited photocatalyst anion readily effected C-H, C-C, C-P, C-S, and C-B bond formations. Detailed synthetic, spectroscopic, and theoretical studies supported a ConPET catalytic mechanism using *N*,*N*-diisopropylethylamine (DIPEA) as electron donor molecule (Figure 13).

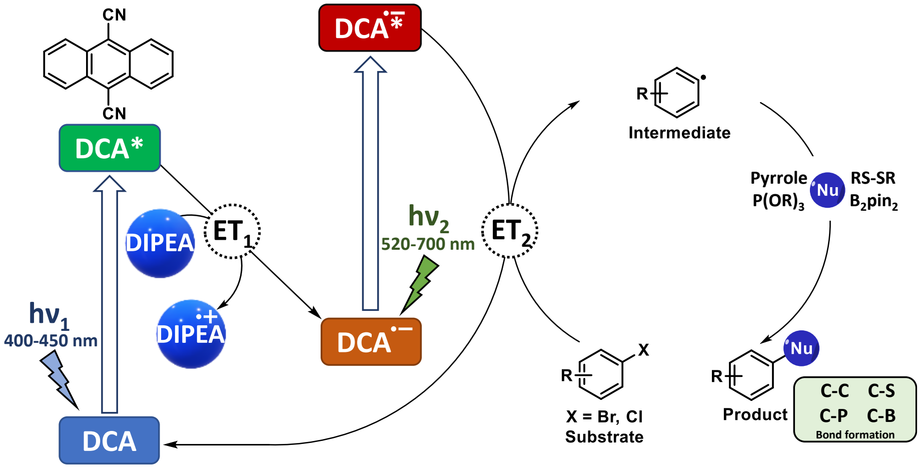

Figure 13. Z-Scheme of DCA as ConPET catalyst for the dehalogenation of aryl halides.

1.4. EDA Complexes

An interesting way to facilitate the generation of photoinduced electron transfer could be the formation of a new molecular aggregate named an electron donor−acceptor (EDA) complex[41] or charge transfer complex.[42] [43, 44] This complex consists of an association of an electron-rich substrate with an electron-poor molecule. The photochemical strategy based on the visible light-absorbing EDA complex is a cheap and environmentally friendly organic synthetical method. The photochemistry of the EDA complex has attracted considerable interest to a

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[41] Foster, R. J. Phys. Chem. **1980**, *84*, 2135−2141.

[42] Rosokha, S. V.; Kochi, J. K. *Acc. Chem. Res.* **2008**, *41*, 641−653.

[43] Arceo, E.; et al. *Chem. Sci.* **2014**, *5*, 2438−2442.

[44] Nappi, M.; et al. *Angew. Chem., Int. Ed.* **2014**, *53*, 4921−4925.

growing number of synthetic chemists[45] Thus, the methodology exploits the combination between A and D in order to produce a new molecular aggregate in the ground state (**Figure 14**). The resulting EDA complex can now absorb at the visible region. Then, visible light excitation powers an intramolecular SET, giving rise a radical ion pair ([$D^{+\bullet}$, $A^{-\bullet}$]). In the presence of appropriate leaving groups (LGs), irreversible fragmentation productively renders two reactive open-shell intermediates, which can engage in synthetically useful radical processes

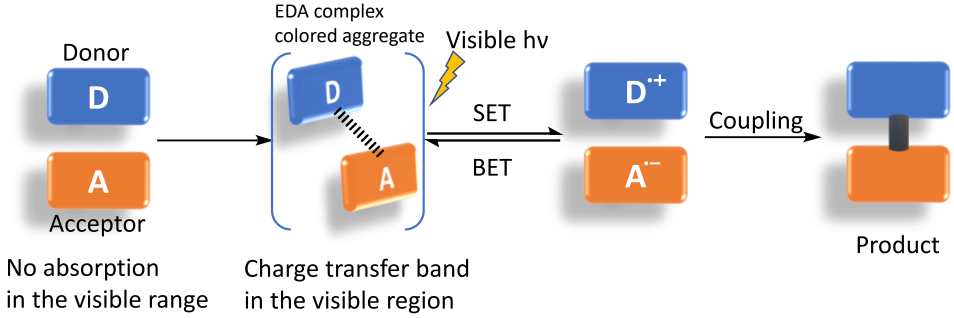

Figure 14. EDA complex excitation giving rise the corresponding ions and the coupling.

The application of the visible light EDA complex as a powerful tool for synthetic strategies is well-reflected by the vast number of publications found in literature.[46] Some representative examples are detailed as follows: i) the C2-arylation of pyrroles was successfully achieved by photoinduced SET initiation from the EDA complex between the pyrrole (donor) and the iodinium salt (acceptor), generating the aryl radical intermediate;[47] ii) Marzo and co-workers reported the blue light mediated (hetero)arylation of anilines formation by a π–π EDA complex between an electron-withdrawing (hetero)aryl halide (acceptor) and aniline (donor), giving rise *ortho* and *para* (hetero)arylated anilines in good yields;[48] iii) other π–π EDA complexes were defined by *N*-alkoxyl derivatives (*N*-phthalimide) and Hantzsch ester as donor agent in the visible light-induced allylation/alkenylation of primary, secondary, and tertiary alkoxyl radicals, that are essential reactive intermediate in

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[45] (a) Shaw, M. H.; Twilton, J.; MacMillan, D. W. C. *J. Org. Chem.* **2016**, *81*, 6898–6926. (b) Wei, Y.; et al. *Synthesis* **2019**, *51*, 3021–3054.

[46] Crisenza, G. E. M.; Mazzarella, D.; Melchiorre, P. *J. Am. Chem. Soc.* **2020**, *142* (12), 5461–5476; and the references therein.

[47] Tobisu, M.; Furukawa, T.; Chatani, N. *Chem. Lett.* **2013**, *42*, 1203–1205

[48] Marzo, L. ; Wang, S.; König, B. *Org. Lett.* **2017**, *19* (21), 5976–5979.

chemical and biological studies.[49] iv) electron-poor tetrachlorophthalimides were used as effective organocatalytic acceptors to achieve EDA complexes formation with a variety of radical precursors not amenable to previous catalytic methods;[50] v) direct benzylation of allylic C-H bonds was gained by a radical-based organocatalytic method. Interestingly, mechanistic details revealed that combination of EDA photochemistry and hydrogen atom transfer activation was possible. Thus, the organic catalyst was capable to form benzylic and allylic radicals, respectively, to then govern then their selective coupling.[51]
In view of this continuous growing, novel methodologies that imply the EDA complex photochemistry using visible light in the absence of both photoredox catalysts and transition metals typically required to effect cross coupling reactions are desired.

1.5. Supramolecular Gel-Based as Nanoreactor

The previously photoinduced processes described are highly depending on the environment. As a matter of fact, nature has normalized confined and compartmentalized environments such as cell organelles to perform sophisticated chemical reactions with an accurate control of kinetics and selectivity. Inspired by this fact, many research groups have developed artificial nanoreactors based on hierarchical self-assembly of low molecular-weight (LMW) molecules through noncovalent interactions (e.g., hydrogen-bonding, van der Waals, charge transfer, dipolar, $\pi-\pi$ stacking).[52] Within this respect, photochemistry has taken advantage of reactivity in confined spaces such as mesoporous inorganic materials,[53] microemulsions,[54] micelles,[55] vesicles,[56] and gels.[57] The reason is due to the enhancement of crucial properties of reactants in a confinement medium such as light absorption and lifetime of redox intermediates.[58] Supramolecular gels are

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[49] Zhang, J.; Li, Y.; Xu, R.; Chen, Y. *Angew. Chem., Int. Ed.* **2017**, *56*, 12619−12623.

[50] Zhou, W.; Wu, S.; Melchiorre, P. *J. Am. Chem. Soc.* **2022**, *144* (20), 8914–8919.

[51] Le Saux, E.; Zanini, M.; Melchiorre, P. *J. Am. Chem. Soc.* **2022**, *144* (3), 1113–1118.

[52] a) Otte, M. *ACS Catal.* **2016**, *6*, 6491−6510. b) Timmermans, S. B. P. E.; van Hest, J. C. M. *Curr. Opin. Colloid Interface Sci.* **2018**, *35*, 26−35.

[53] Nakamura, T.; et al. *Bioconjugate Chem.* **2016**, *27*, 1058−1066.

[54] Kagalwala, H. N.; et al. *Inorg. Chem.* **2017**, *56*, 10162−10171.

[55] Limones-Herrero, D.; et al. *Photochem. Photobiol.* **2014**, 90, 1012−1016.

[56] Wen, J.; *J. Environ. Sci.* **2017**, *60*, 98−107.

[57] Perez-Ruiz, R.; Díaz Díaz, D. *Soft Matter* **2015**, *11*, 5180−5187.

[58] a) Shchukin, D.; Sviridov, D.; *J. Photochem. Photobiol., C* **2006**, *7*, 23−39. b) Maldotti, A.; Molinari, A.; Amadelli, R.; *Chem. Rev.* **2002**, *102*, 3811−3836.

normally built with LMW molecules. The immobilization of the liquid (major component) into the interstices of a self-assembled solid matrix (minor component) due to surface tension and capillary forces make these materials to adopt a solid-like appearance with characteristic mechanical properties.[59] The viscosity of the medium then is increased by factors up to 10^{10}. Supramolecular gels usually show reversible gel-to-sol phase modulations that can be initiated by a variety of external stimulus (e.g., irradiation, temperature, pH…), constituting an important issue in terms of recycling.

At most of the scenarios in nature, the efficiency of biochemical reactions is even enhanced by aerobic environments where different reactive intermediates are involved. Potential deactivation routes could be therefore avoided by molecular compartmentalization while preserving the desired chemical pathways. In this sense, LMW gels, displaying high specific surface areas, stimuli-responsive reversibility, good diffusion properties, and functional tunability, have been recognized as a potential choice to mimic natural systems with the aim of achieving challenged photochemical reactions. Indeed, the viscoelastic nature of gel-based materials may also help to reduce overconcentration and overheating effects compared to more rigid systems. Thus, several transformations such as photodimerization,[60] triplet-triplet annihilation coupled to SET,[61] and trifluoromethylation[62] illustrate the main advantages associated with the emerging use of gel-based materials as nonconventional reaction media to facilitate and control photochemical reactions.

1.6. Carbon (sp^2)–Heteroatom Bonds using visible light

The selective formation of C-C bonds is at the heart of organic synthesis. However, the function is often derived from the presence of heteroatoms. Almost all fine chemical, bioactive, natural, and polymeric molecules contain C–heteroatom bonds that are often introduced by the synthetic chemists through nucleophilic substitutions and transition metal-catalyzed cross-coupling reactions. The past years have also witnessed the rediscovery of visible light as ubiquitous source of energy for C-heteroatom bond-forming reactions that are complementary to

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[59] Díaz Díaz, D.; et al. *Chem. Soc. Rev.* **2011**, *40*, 427−448.

[60] Dawn, A.; et al. *Chem. Commun.* **2009**, 2100−2102.

[61] Sripathy, K.; et al. *J. Mater. Chem. C* **2015**, *3*, 616−622.

[62] Haring, M.; et al. *J. Org. Chem.* **2018**, *83*, 7928−7938.

traditional transformations.[63] Thus, C–heteroatom cross-couplings reactions can be photocatalyzed by ET or EnT with an appropriate photocatalyst. Other photocatalyst-free methods are possible using photolabile substrates or by generating photoactive EDA complexes. In this thesis, we have focused our attention on the formation of new C-boron (C–B) bonds, C-phosphorous (C–P) bonds, and C-sulfur (C–S) bonds using visible light and following the abovementioned strategies.

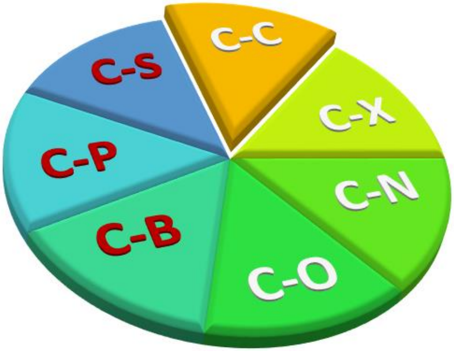

Figure 15. Carbon sp^2 heteroatom of interest in organic chemistry.

1.6.1. C–B Bond

Organoboron reagents are very important intermediates in a broad range of chemical transformations, since they can be converted into numerous functional groups. Therefore, the diverse type of organoboron substances may attract considerable attention in terms of their synthesis and applications.[64] In particular, the heteroaryl boronic acids and esters are found to be as the most important classes of organoboron reagents, participating in many organic reactions such as

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[63] a) Hartwig, J.; et al. *Nature* **2008**, *455*, 314–322. b) Cavedon, C.; Seeberger, P.H.; Pieber, B. *Eur. J. Org. Chem.* **2019**, 1379–1392.

[64] a) J. W. B. Fyfe, J. W. B.; Watson, A. J. B. *Chem.* **2017**, *3*, 31–55. b) Panda, S.; Coffin, A.; Nguyen, Q. N.; Tantillo,D. J.; Ready, J. M. *Angew.Chem.Int. Ed.***2016**, *55*, 2205–2209.

Suzuki-Miyaura cross-coupling,[65] Chan-Lam couplings[66] or borono-Mannich reaction.[67]

Formation of new C–B bonds are usually produced by the substitution of Grignard and lithium components with electrophilic boron molecule; however, the most important inconvenient from these methods is the incompatibility of the functional group due to the large amounts employed of organometallic compounds. More recently, the synthetic strategies of organoboron compounds have experienced an improvement in terms of milder conditions based on transition metal catalysts.[68,69,70]

Regarding light-induced protocols, fabrication of boronate derivatives has been normally performed by photoredox catalysis employing metal-based photocatalysts such as $CeCl_3$[71] or transition metal complexes such as iridium,[72] copper,[73] rhodium,[74] tungsten[75] or palladium.[76] The utilization of black light lamps (350 nm) or complex synthesis of the corresponding photocatalysts make necessary the development of new and "greener" strategies with milder conditions (**Figure 16**).

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[65] a) Hodgson, P. B. ; Salingue, F. H. *Tetrahedron Lett.* **2004**, *45*, 685–687. b) Billingsley, K.; Buchwald, S. L. *J. Am.Chem.Soc.* **2007**, *129*, 3358–3366. c) Laulhé, S.; Blackburn, J. M.; Roizen, J. L. *Org.Lett.* **2016**, *18*, 4440–4443. d)Kassel, V. M. et al. *J. Am. Chem.Soc.* **2021**, *143*, 13845–138.

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[67] a) Petasis, N. A.; Goodman, A.; Zavialov, I. A. *Tetrahedron* **1997**, *53*, 16463–16470. b) Candeias, N. R. et al. *Chem.Rev.* **2010**, *110*, 6169–6193.

[68] Hemming, D.; *Chem. Soc. Rev.* **2018**, *47*, 7477−7494.

[69] Xu, L.; et al. *Eur. J. Org. Chem.* **2018**, 3884−3890.

[70] He, Z.; et al. *Org. Biomol. Chem.* **2019**, *17*, 6099−6113.

[71] Qiao, Y.; Yang, Q.; Schelter, E. J.; *Angew. Chem., Int. Ed.* **2018**, *57*, 10999−11003.

[72] Jiang, M.; Yang, H. J.; Fu, H.; *Org. Lett.* **2016**, *18*, 5248−5251.

[73] Nitelet, A.; et al. *Chem. Eur. J.* **2019**, *25*, 3262−3266.

[74] Sieck, C.; et al. *Chem. Eur. J.* **2016**, *22*, 10523−10532.

[75] Yu, D.; et al. *Chem. Sci.* **2020**, *11*, 6370−6382.

[76] Zhao, J.-H.; *Org. Biomol. Chem.* **2020**, *18*, 4390−4394.

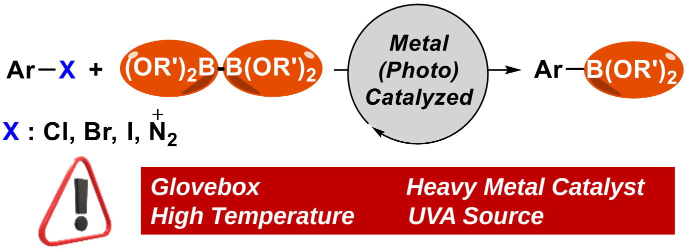

Figure 16. Schematic reaction for the aryl halides borylation and their disadvantages.

1.6.2. C–P Bond

The extensive application of phosphonates in different fields for instance: pharmaceutical molecules,[77] agrochemicals,[78] organic materials,[79] or in catalysis (as ligands)[80] convert them into very important scaffolds. Specially, new C(sp^2)–P bonds are mostly formed by coupling with palladium,[81] nickel,[82] or copper[83] catalysts.

A good alternative to prepare aryl phosphonates under milder conditions would be to introduce the light as energy source. In this context, the denitrogenative coupling of benzotriazoles with phosphite by means of visible light was found as an efficient protocol to create C(sp^2)–P bond.[84] In this case, an iridium (III) complex was used as photoredox catalyst. Other examples involving metal-based complexes (nickel or cobalt) as catalysts in dual catalysis were reported.[85, 86] Concerning to organic photocatalyst, Eosin B successfully photocatayzed the phosphorylation of arylhydrazines with trialkylphosphites.[87] Another metal-free strategy by the simple combination of diaryliodonium salts with phosphites in the presence of a base and under visible-light illumination gained a large variety of aryl phosphonates.[88]

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[77] Alexandre, F.-R.; *J. Med. Chem.* **2011**, *54*, 392–395.
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[79] Jeon, S. O.; Lee, J. Y. *J. Mater. Chem.* **2012**, *22*, 7239–7244.
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[81] Berger, O.; et al. *Adv. Synth. Catal*. **2013**, *355*, 1361–1373.
[82] Shen, C. R.; Yang, G. Q.; Zhang, W. B.; *Org. Biomol. Chem.* **2012**, *10*, 3500–3505.
[83] Huang, C.; Tang, X.; Fu, H.; Jiang, Y.; Zhao, Y. ; *J. Org. Chem.* **2006**, *71*, 5020–5022.
[84] Jian, Y.; et al. *Org. Lett.* **2018**, *20*, 5370–5374.
[85] Liao, L.; et al. *Org. Lett.* **2017**, *19*, 3735–3738.
[86] Niu, L.; et al. *ACS Catal.* **2017**, *7*, 7412–7416.
[87] Li, R.; et al. *Adv. Synth. Catal.* **2018**, *360*, 4807–4813.
[88] Lecroq, W.; et al. *Org. Lett.* **2018**, *20*, 14, 4164–4167.

(**Figure 17**). To highlight that little attention has been paid to the fabrication of a broad scope of five-membered heteroarene phosphonates directly between furan, thiophene, selenophene, or pyrrole halides (Cl, Br) with phosphites by visible-light photoredox catalysis.

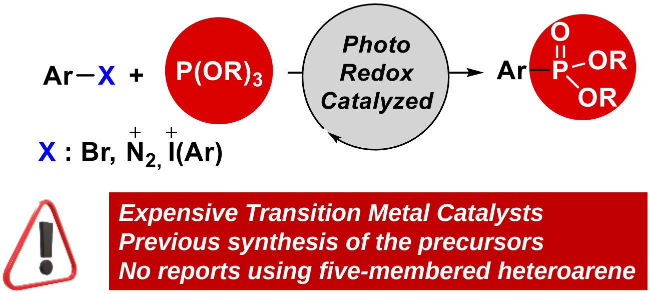

Figure 17. Schematic phosphorylation of aryl halides and their limitations.

1.6.3. C–S Bond

Organic compounds containing sulfur atoms are essential in nature[89] and, therefore, to develop novel strategies for producing new C–S bonds has become an important task. Within this respect, synthesis of sulfides plays a crucial role in medicinal drug innovation,[90] due to high presence of C–S bonds in pharmaceutical drugs for various diseases such as cancer, HIV, and Alzheimer's disease.[91]

Typically, thiolation of aryl halides is successfully achieved by cross-coupling reactions using transition metals (Pd, Cu or Ni) as catalysts;[92] however, one significant drawback is the deactivation of the corresponding catalysts by coordination of the formed thiol. Alternatively, formation of aryl sulfides induced by visible light can be a powerful complementary strategy for the current synthetic protocols. Thus, common photocatalysts such as Eosin Y,[93] Ir(III) complex,[94,95] rose

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[89] Jacob, C.; *Nat. Prod. Rep.* **2006**, *23*, 851–863.

[90] Cernak, T.; et al. *Chem. Soc. Rev.* **2016**, *45*, 546–576.

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[92] (a) Stadler, O.; *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 2075–2081. (b) Ziegler, J. H.; *Ber. Dtsch. Chem. Ges.* **1890**, *23*, 2469–2472; (c) Abeywickrema, A. N.; Beckwith, A. L. J.; *J. Am. Chem. Soc.* **1986**, *108*, 8227–8229.

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[95] Czyz, M. L.; et al. *Org. Biomol. Chem.*, **2018**, *16*, 1543-1551.

bengal,[96] or even Eosin B[97] have been already employed (**Figure 18**). In these cases, however, expensive transition–metal complexes or organic dyes that easily suffered degradation after prolonged light exposure can result in problematic scenarios.

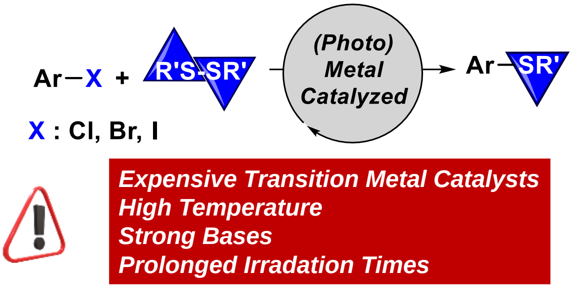

Figure 18. Schematic aryl sulfides synthesis from aryl halides and their drawbacks.

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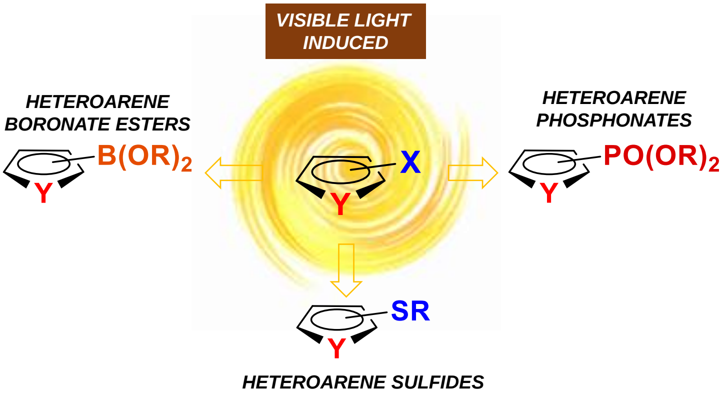
Chapter 2
Objectives

Visible light photoredox catalysis constitutes a novel emerging method to drive chemical reactions between organic molecules that exhibit two rather ubiquitous properties: colorlessness and redox activity.

Given the relevance of the use of visible light as energy source to drive new reactions such as forming C–heteroatom bonds and the role of supramolecular gels as nanoreactors, the present PhD aims to contribute to the field of ***organic (photo)chemistry*** by developing novel strategies to create new compounds at different media with broad applications, employing mild conditions (room temperature) and safety, green energy (visible light irradiation by 3W LEDs or sunlight).



The specific objectives referred to each chapter are:

- To explore a novel, straightforward, and fast procedure for the construction of new boron-containing thiophenes using visible light as energy source under very mild conditions in oxygen-free solutions.
- In connection with the previous objective, to further develop the proposed methodology which includes aerobic conditions and the utilization of supramolecular gels as reaction vessels. The study will be extended to the formation of furan, thiophene, selenophene, and pyrrole boronate esters.
- To develop a new strategy based on the ConPET photoredox catalysis using a small organic and stable dye to afford efficient aerobic phosphorylation of five-membered heteraroenes in a gel-based nanoreactor.
- To exploit the visible light-absorbing EDA complex in order to achieve for the first time the direct thiolation of five-membered heteroarenes.

Chapter 3

Rapid Access to Borylated Thiophenes Enabled by Visible Light

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Organic Letters **2020**, *22* (8), 3273-3278

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3.1 Abstract

Boron-containing thiophenes are important entities in organic/medicinal chemistry as well as in material science. In this Letter, a novel, straightforward, and fast procedure for their production employing visible light as an energy source at room temperature and ambient pressure is reported. All substrates are commercially available, and the process does not require the use of any external photocatalyst.

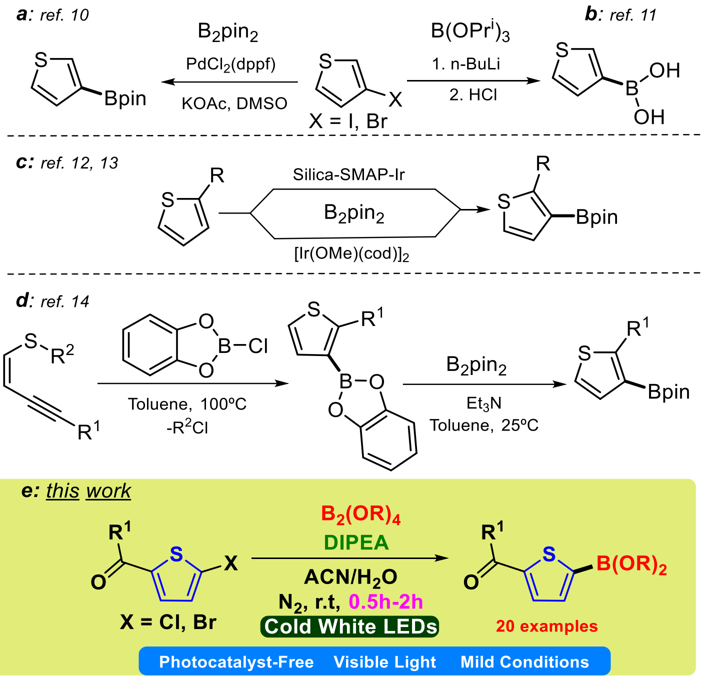
3.2 Introduction

Organoboron compounds play a key role as intermediate targets in organic/medicinal chemistry and material science[1] due to their versatility and environmentally benign and user-friendly characteristics. Sophisticated and elegant methods have been reported for the insertion of boryl groups into organic molecules, including recent advances in the transition-metal-catalyzed or UV-photoinduced borylation of alkanes, arenes, heteroarenes, fused arenes, olefins, and other substrates.[2]

Among these products, borylated heteroarene rings are considered important building blocks for subsequent derivatization.[3] Of particular interest is the fast production of C−C bonds for the preparation of bioactive molecules.[1b,4] In this context, boron-containing thiophenes are important scaffolds, for example, in conjugated materials[5] showing organic electronic applications[6] or the fabrication of lightemitting diodes[7] or even in antimicrobial activity.[8] Early reports on synthesizing 2-thiophenyl boronate esters used stoichiometric or catalytic metalation protocols.[9] In 1995, Miyaura et al. published the Pd-catalyzed reaction between tetraalkoxydiboron reagents with haloarenes to form arylboronates, including the 3-iodobenzothiophene (**Scheme 1a**).[10] Later, Li et al. reported an efficient alternative for producing some arylboronic acids using a lithium−halogen exchange with an in situ quench with borate (**Scheme 1b**).[11] Regarding iridium-catalyzed reactions, Sawamura et al. realized an estereodirected borylation on a silica-supported iridium complex (**Scheme 1c**, top reaction),[12] whereas Smith et al. showed an alternative strategy that included a sequential diborylation/monodeborylation pathway to obtain boron-containing thiophenes (**Scheme 1c**, bottom reaction).[13] Recently, Blum et al. discovered a simple and transition-metal-free protocol to exclusively produce 3-borylated thiophene derivatives (**Scheme 1d**).[14]

All these methodologies somehow require mostly complex conditions, such as the performance of the reaction in a glovebox, the employment of high temperatures or iridium precatalysts, the preliminary synthesis of the starting materials, or sometimes the need for prolonged reaction times. To reduce costs and unwarranted residues in the final products, the development of new and "greener" strategies with milder conditions is highly desired. Herein we report as a proof of concept a straightforward, rapid, and photocatalyst-free process to fabricate borylated thiophenes using visible light under mild conditions (**Scheme 1e**).

Scheme 1. Strategies related to the borylation of thiophenes.



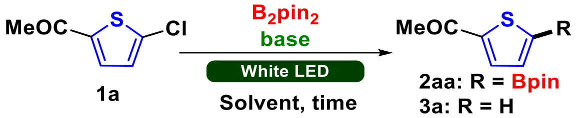
3.3 Results & Discussion

3.3.1 Optimization

This reaction implies the in-situ generation of a ground state complex that is capable of absorbing light in the visible region, initiating the process. In view of the successful merging of visible-light excitation for chemical transformations[15] and inspired by our previous experience,[16] we commenced with a reaction of 2-acetyl-5-chlorothiophene (**1a**) and bis(pinacolato)diboron (**B_2pin_2**) in the presence of Hünig's base (diisopropylethylamine, **DIPEA**) and catalytic amounts of 9,10-dicyanoanthracene (**DCA**) using cold-white LEDs (**Table 1**, entry 1). The expected product **2aa** was obtained in moderate yield after the incomplete conversion of **1a**. Surprisingly, a control experiment in the absence of **DCA** afforded the complete conversion of **1a** together with adduct **2aa** in good yield (**Table 1**, entry 2). No product formation was detected in the absence of base or after heating the reaction mixture to 50 °C overnight in the dark (**Table 1**, entries 3 and 4), demonstrating that both components (base and light) were essential for this photochemical protocol. Changes in solvent conditions did not improve the results (**Table 1**, entries 5 and 6).

On the basis of the literature data,[17] we performed the reaction using an acetonitrile (ACN)/water mixture as the solvent, anticipating that the process could be accelerated. Indeed, the complete conversion of 1a was observed after 30 min of irradiation, leading to product **2aa** in excellent yield and with high selectivity (**Table 1**, entry 7). Varying the amount of **DIPEA** or **B_2pin_2** did not gain better outputs of the reaction in terms of the conversion and yield (**Table 1**, entries 8−11). Changing the base under optimal conditions presented good results when triethylamine (**Et_3N**), diisopropylamine (**DIPA**), 1,8-diazabicyclo(5.4.0)undec-7-ene (**DBU**), or 1,4-diazabicyclo[2.2.2]octane (**DABCO**) was used (Table 1,entries 12−15), whereas the reaction did not occur withtriphenylamine (**Ph_3N**) or pyridine (**Table 1**, entries 16 and 17). Finally, the procedure was applied to the thioaryl bromide or iodide derivative, and excellent results were also obtained (**Table 1**, entries 18 and 19).

Table 1. Searching for the optimal conditions[a]



No.	Solvent	Base	Time(h)	Conv(%)[b]	**2aa/3a**	Yield(%)[b]
1[c]	ACN	DIPEA	6	27	75/25	22
2	ACN	DIPEA	6	100	85/15	53
3	ACN	-	6	0	-	0
4[d]	ACN	DIPEA	overnight	0	-	0
5	MeOH	DIPEA	6	52	44/56	8
6	DMF	DIPEA	6	9	-	0
7[e]	**ACN-H_2O**	**DIPEA**	**0.5**	**100**	**92/8**	**84**[f]
8	ACN-H_2O	DIPEA[g]	0.5	61	89/11	51
9	ACN-H_2O	DIPEA[h]	0.5	100	84/16	58
10[i]	ACN-H_2O	DIPEA	0.5	74	80/20	31
11[j]	ACN-H_2O	DIPEA	0.5	85	88/12	45
12	ACN-H_2O	Et$_3$N	0.5	68	87/13	56
13	ACN-H_2O	DIPA	0.5	71	92/8	63
14	ACN-H_2O	DBU	0.5	86	90/10	63
15	ACN-H_2O	DABCO	0.5	10	85/15	10
16	ACN-H_2O	Ph$_3$N	0.5	3	-	0
17	ACN-H_2O	Pyridine	0.5	0	-	0
18[k]	**ACN-H_2O**	**DIPEA**	**0.5**	**100**	**85/15**	**80**
19[l]	**ACN-H_2O**	**DIPEA**	**0.5**	**100**	**85/15**	**76**

[a] **1a** (0.08 mmol), **B_2pin_2** (1.6 mmol), base (0.12 mmol) in 3 mL N_2/solvent; irradiation (cold-white LED), 23 °C; [b] GC-FID yields of **2aa**; [c] with **DCA** (10 mol%); [d] heating (50 °C) in dark; [e] ACN-H2O (9:1 v:v); [f] isolated yield; [g] **DIPEA** (0.08 mmol); [h] **DIPEA** (0.16 mmol); [i] **B_2pin_2** (0.4 mmol); [j] **B_2pin_2** (0.8 mmol); [k] using 2-acetyl-5-bromothiophene (0.08 mmol); [l] using 2-acetyl-5-iodothiophene (0.08 mmol).

3.3.2 Mechanism

To better understand this methodology, absorptivity measurements of different mixtures under reaction conditions were carried out (**Figure 1**). Before irradiation, new bands at ca. 400 and 550 nm were clearly observed when the three ingredients (**1a** + **B_2pin_2** + **DIPEA**) were present, and, indeed, the solution turned red (**Figure 1**, inset). This fact, together with the colorless mixtures to the naked eye for the rest of combinations (**Figure 1**, inset), pointed to the formation of a complex in the ground state with remarkable absorbance in the visible region, which allowed the initiation of the investigated reaction.

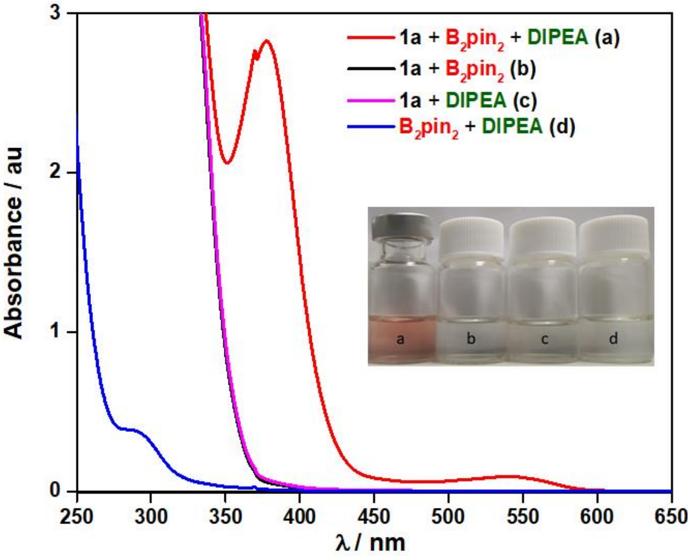


Figure 1. UV-vis absorption spectra. Inset: photographs of different solutions. Conditions: **1a** (0.08 mmol), B_2pin_2 (0.16 mmol) and DIPEA (0.12 mmol); solvent: ACN/H_2O (9/1 v/v) in a total volume of 3 mL under air atmosphere

To shed light on the nature of this complex, NMR experiments were conducted (**Figure 2**). First, the ^{11}B NMR spectrum of **B_2pin_2** showed its characteristic δ at 31 ppm. However, a new species was observed (δ 22.5 and 20) when **DIPEA** or **DIPEA/1a** was added, which was safely ascribed to the sp^3–sp^2 diboron **A** (**Figure 2a**).[2n,17,18] Thus the treatment of **B_2pin_2** in water with Hünig's base gave rise to **A** and the cationic protonated **DIPEA**.

Furthermore, the interaction between **B_2pin_2** and **1a** did not take place, and **2aa** was not detected in the three-component mixture (**Figure 2a**), supporting the notion that light was a crucial parameter for the reaction (see **Table 1**, entries 3 and 4). Besides, the ^{13}C NMR spectroscopic analysis of the starting material **1a** in the absence/presence of **B_2pin_2** + **DIPEA** was achieved (**Figure 2b**). Interestingly, in addition to the carbonyl signal (δ 192), a new weakly shifted peak appeared in the mixture, suggesting the possibility of a hydrogen-bonding equilibrium between **A** and the C=O group of **1a**.

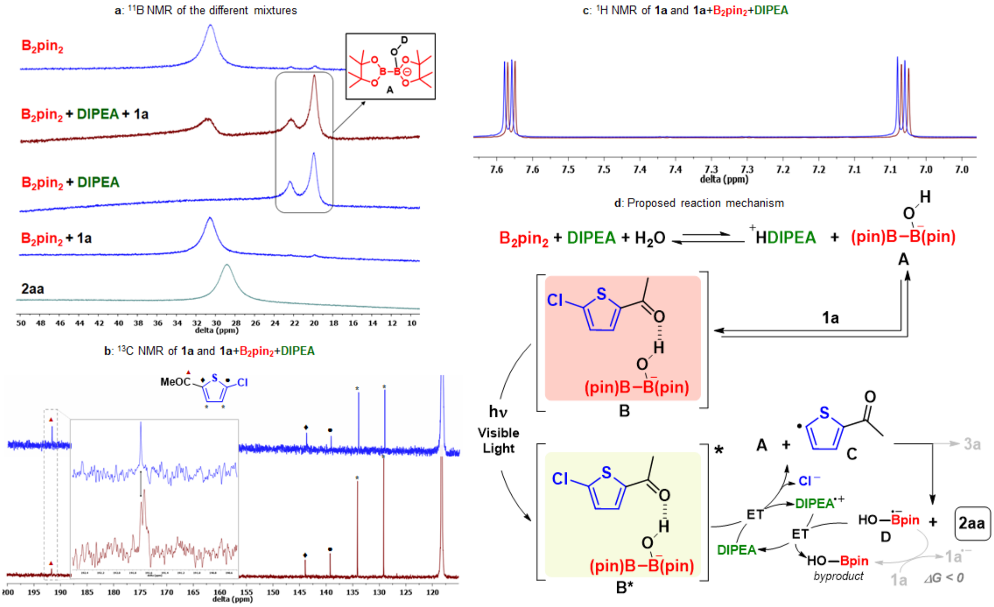
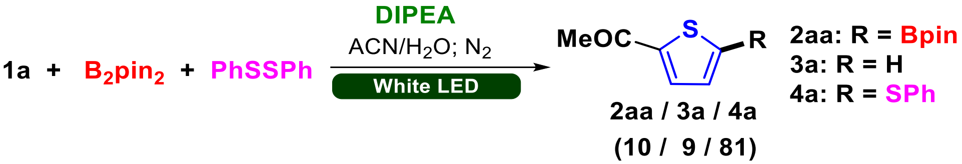


Figure 2. (a) ^{11}B-NMR spectra in CD$_3$CN/D$_2$O (9/1 v/v), (b) ^{13}C-NMR spectra of **1a** (top) and **1a+B$_2$pin$_2$+DIPEA** (bottom) in CD$_3$CN/D$_2$O (9/1 v/v), (c) ^{1}H-NMR spectra of **1a** (blue) and **1a+B$_2$pin$_2$+DIPEA** (red) in CD$_3$CN/D$_2$O (9/1 v/v) and (d) proposed reaction mechanism.

Moreover, the quaternary carbon in the α position and the CH in the β position related to the C=O group were somehow affected due to this presumably noncovalent interaction (**Figure 2b**). Assuming that this hydrogen-bonding interaction between **1a** and **A** could induce some effects on aromatic substituents, the most relevant part of the ^{1}H NMR spectra (**Figure 2c**) showed a weak shift of the CH resonances of the thiophene core. The foregoing experimental results pointed out the formation of a three-component complex in the ground state, where the carbonyl group played a pivotal role in this type of processes. To support this hypothesis, several carbonyl-free thiophenes were submitted to visible-light irradiation under the standard conditions. As expected, no conversion of the starting material was observed, even after 6 h of reaction. (**Figure E1**, Experimental section)

With these data in hand, we proposed the following reaction mechanism (**Figure 2d**). After the formation of intermediate **A**, a hydrogen-bonding interaction with **1a** occurs, affording a new complex **B** that might tentatively be responsible for the red color of the solution. Hence, under visible-light irradiation, complex **B** is promoted to its excited state (**B***). This species is now capable of oxidizing **DIPEA** (this pathway is feasible based on theoretical calculations; data not shown), and, after a fast splitting of the C−Cl bond, the thiophene radical intermediate C is generated, which was confirmed by **PhSSPh**[19] trapping (**Scheme 2**).

Scheme 2. Trapping of Thiophene Radical.



Now, **C** would react with **A** to lead to the desired **2aa** and the boryl radical anion **D**.[18b,20] Finally, one single electron transfer (**SET**) from **D** to the **DIPEA** radical cation would provide **OH-Bpin** as the byproduct,**2n** which hydrolyzes to volatile products upon workup.[21] Importantly, the role of **DIPEA** could be two-fold because it can act as (i) a base and (ii) a photoreductant in the electron transfer process. To further rationalize the proposed reaction mechanism, computational studies under the framework of the density functional of theory (DFT) were performed. Thus, different alternatives for complex **B** were first computed (**Figure E2**, experimental section). From this preliminary screening, the proposed structure of **B** including a hydrogen bond between **A** and **1a** was found to be the predominant one that was fully in agreement with the experimental data (NMR and UV−vis). Then, the electronic absorption spectrum of B was calculated using 6-31+G** as the basis set together with a variety of functionals. (**Figure E2**, Experimental section.) Although a similar qualitative trend was found, the B3LYP functional showed the best theoretical−experimental relationship. As depicted in **Figure 3a**, the absorption spectrum of **B** in acetonitrile was dominated by the thiophene-type transition at 292 nm that thoroughly matches with the computed value for **1a** (292 nm; experimental value: 289 nm). Interestingly, two additional small absorption bands at longer wavelengths appeared for **B** (**Figure 3b**) at 543 and 423 nm, with an oscillator strength of f = 0.00001 and 0.0005, respectively; this finding differed from the **1a** absorption spectrum where these two bands were not found.

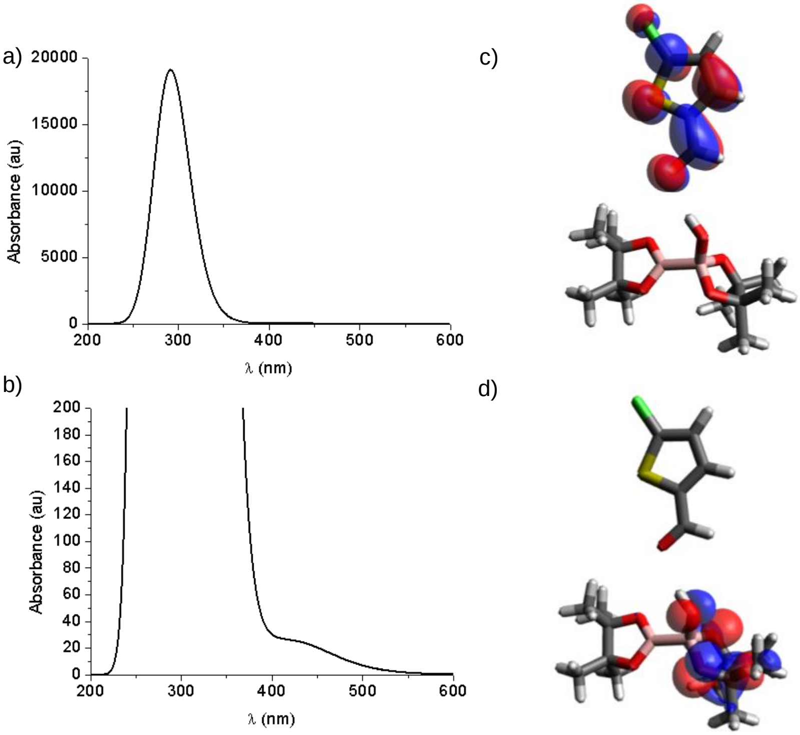
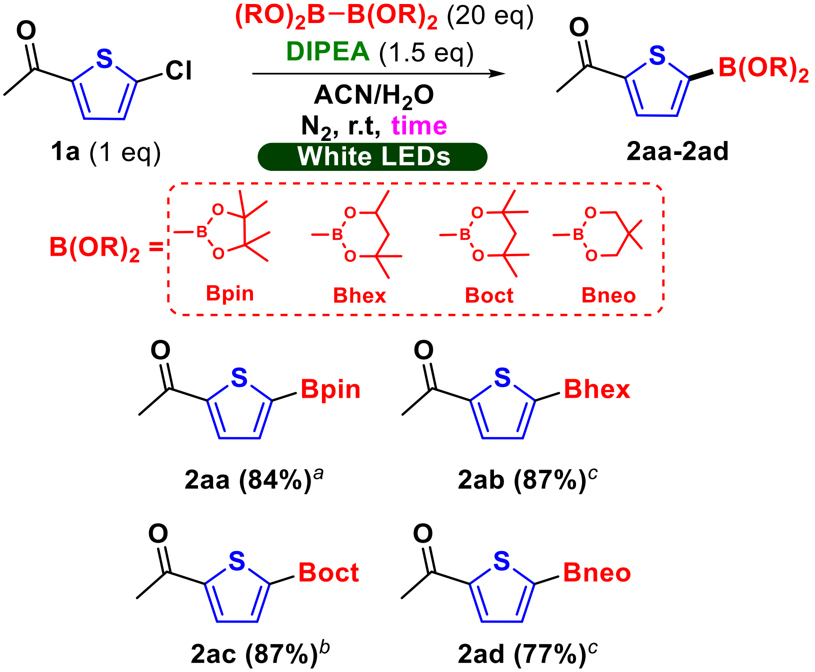


Figure 3. Absorption spectrum a) and detail b) for **B** computed using B3LYP/6-31+G** in acetonitrile. Orbitals involved in the transition at 423 nm c) LUMO d) HOMO-1.

Therefore, a good correlation could be established between the results from the UV−vis measurements and the computational data. In addition, the electronic transition at 423 nm might imply the movement of an electron from the **B_2pin_2** moiety to the thiophene unit (**Figure 3c,d**).

3.3.3 Scope

Scheme 3. Substrate Scope for Borylated Thiophenes.[a]

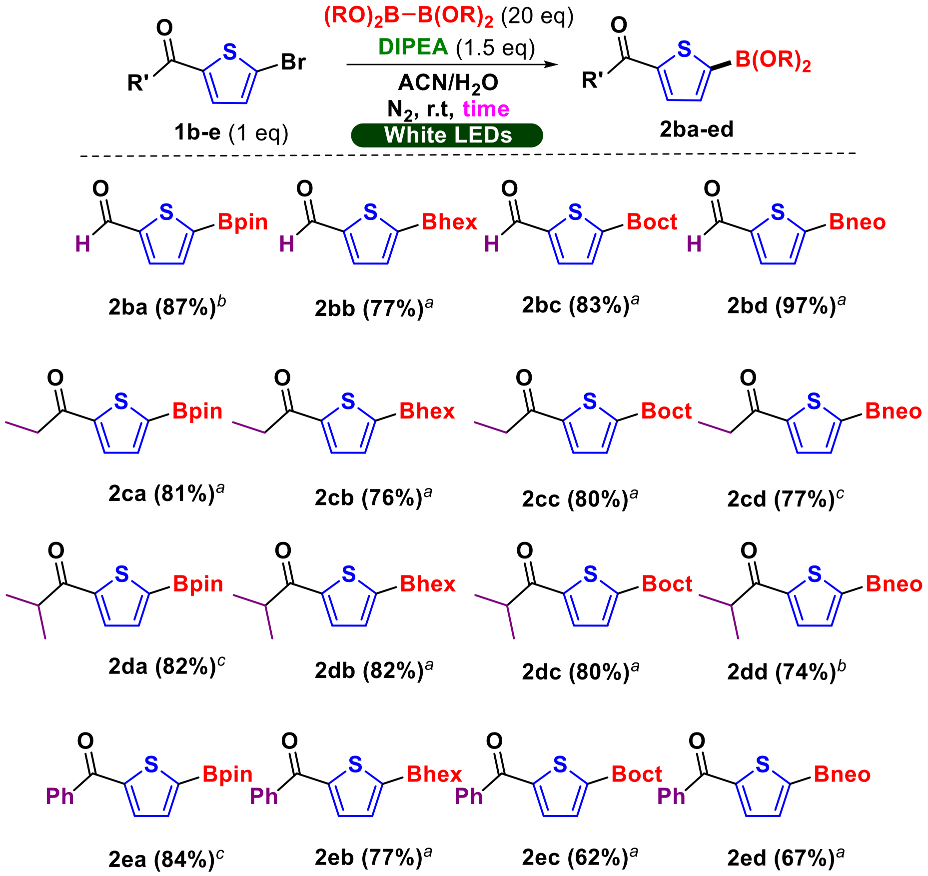


[a]**1a** (1 eq), **$(OR)_2B$-$B(OR)_2$** (20 eq) and **DIPEA** (1.5 eq). Full conversion of **1a** in all cases; GC-FID yields of products; [b]0.5h, [c]1h and [d]2h of irradiation time.

Having established the optimal conditions and understood the method, we next conducted the substrate scope using different diboron derivatives (**Scheme 3**). After cold-white LED irradiation, full conversion of the starting thiophene material **1a** was effectively observed in all cases, and high yields of products (**2aa–ad**) were obtained. It is noteworthy that the borylation reactions magnificently occurred using other diboron esters as counterparts such as 1,1,3-trimethylethylene glycol (**Bhex**), 1,1,4,4-tetramethylethylene glycol (**Boct**), and neopentyl glycol (**Bneo**), delivering the corresponding thiophene boronic esters in high yield under very mild conditions.

To strongly support this proof of concept and demonstrate the versatility of the protocol, we proceeded to investigate the reaction, combining several commercially available thiophene derivatives and the diboron compounds previously employed (**Scheme 4**).

Scheme 4. Versatility Screening for Photocatalyst-Free Visible Light Thiophene Borylations.[a]



[a]**1b-e** (1 eq), **$(OR)_2B$-$B(OR)_2$** (20 eq) and **DIPEA** (1.5 eq). Full conversion of **1** in all cases; GC-FID yields of products; [b]0.5h, [c]1h and [d]2h of irradiation time.

Gratifyingly, all tested reactions worked perfectly under the optimal conditions, and the desired products (**2ba–ed**) were obtained in high yield and with high selectivities. Therefore, these types of thiophene−boronates can be easily prepared at shorter irradiation times (ranging from 0.5 to 2 h), making this protocol feasible for a late-stage functionalization of boron-based compounds for the synthesis of more complex organic molecules.

3.4 Conclusion

In conclusion, fast access to borylated-like thiophenes by means of visible light (cold-white LEDs) as an energy source has been reported. This photocatalyst-free reaction is proposed to proceed via the in-situ formation of a ground-state complex that, after visible-light absorption, evolves to the formation of the corresponding borylation of the thiophene core. The mechanistic aspects have been demonstrated by spectroscopic measurements and theoretical calculations, and the scope and the versatility of the procedure have been successfully proven. This work constitutes a new, mild strategy for affording boroncontaining thiophenes that should be of potential application extending beyond borylation. Finally, this challenged coupling offers a novel route toward synthetic highly valuable heteroarene boronates with a new, likely exploitable mechanistic paradigm.[22]

3.5 References

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3.6 Experimental section

3.6.1 Materials and methods

All reagents (≥97% purity) and solvents (≥99% purity) were purchased from commercial suppliers (Merck, TCI, Apollo Scientific, Fluorochem, Scharlab) and used as received unless otherwise indicated. Reactions were carried out in Metria®-Crimp Headspace clear vial flat bottom (10 mL, Ø 20 mm) sealed with Metria®-aluminium crimp cap with moulded septum butyl/natural PTFE (Ø 20 mm). Irradiation was performed with a cool white LED (LED Cree MK-R, cold-white, 11.6 V, 700 mA, P = 8.5 W). TLC was performed on commercial SiO_2-coated aluminium and plastic sheets (DC60 F254, Merck).

The absorption spectra were recorded on a JASCO V-630 spectrophotometer Visualization was done by UV-light (254nm).

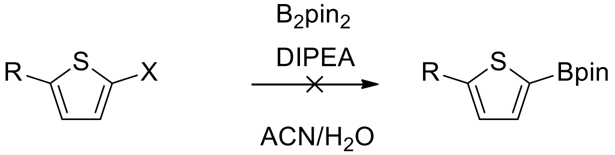
Product were isolated materials after TLC on silica gel (Merck, mesh 35-70, 60 Å pore size) and their corresponding yields were determined by quantitative GC-FID measurements on an Agilent 8860 GC-System with N_2 as carrier gas. Dodecanenitrile was used as an internal standard in the GC-FID quantitative measurements; yield products were estimated as: [conversion × selectivity]/mass balance. Determination of purity and structure confirmation of the literature known products was performed by ^{1}H NMR, ^{11}B NMR, ^{13}C NMR and low-resolution mass spectrometry (LRMS)–LRMS measurements were replaced by high-resolution mass spectrometry (HRMS) in case of unknown products. NMR spectral data were collected on a Bruker Advance 400 (400 MHz for ^{1}H; 101 MHz for ^{13}C, 128 MHz for ^{11}B) spectrometer at 20 °C. Chemical shifts are reported in δ/ppm, coupling constants J are given in Hertz. Solvent residual peaks were used as internal standard for all NMR measurements. The quantification of ^{1}H cores was obtained from integrations of appropriate resonance signals. Abbreviations used in NMR spectra: s – singlet, d – doublet, t – triplet, q – quartet, m – multiplet, bs – broad singlet, dd – doublet of doublet, ddd – doublet of doublet of doublet. HRMS was carried out was performed in the mass facility of SCSIE University of Valencia. LRMS was carried out on an HP 6890 Series GC System with Agilent 5973 Network Mass Selective Detector and H_2 as carrier gas. Abbreviations used in MS spectra: M–molar mass of target compound, EI – electron impact ionization, ESI – electrospray ionization.

3.6.2 General procedure

A vial (10 mL) was charged with a magnetic stirring bar, thiophene derivative (80 µmol, 1.0 equiv.), diborylates (1600 µmol, 20.0 equiv.). Acetonitrile/H_2O (9/1 v/v) mixture (4.0 mL) was poured, and it was stirred until complete solution. Then, DIPEA (120 µmol, 1.5 equiv.) and dodecanenitrile (80 µmol, 1.0 equiv.) were added with 25 µL Hamilton syringe. Quickly, the vial was sealed with a septum. It was purged with a nitrogen gas stream for 10 minutes. The reaction was irradiated with an external cold white LED through the plain bottom side of the vial at 23 °C during the corresponding time. The reaction progress was monitored by GC-FID analysis until 100% total conversion of the thiophene derivative. Then, brine (6 mL) was added, and the aqueous phase was extracted with ethyl acetate (4 mL). The organic phase was dried over anhydrous sodium sulfate, filtered from the drying agent, and concentrated in vacuo. After crystallization of the excess of starting diboron derivative, the crude was purified via TLC plastic sheet using a hexane/ethyl acetate mixture as the mobile phase.

3.6.3 Beyond carbonyl thiophenes

The reaction did not work once it was carried out with thiophenes containing another substituent or even with the carbonyl substituent in different positions.



R: -CN, X: -Cl

R: $-(CH_2)_{11}CH_3$, X: -Br

R: $-CH_3$, X: -Br

R: -Cl, X: -Cl

R: -MgBr, X: -Cl

R: -Pyrrol, X: -Cl

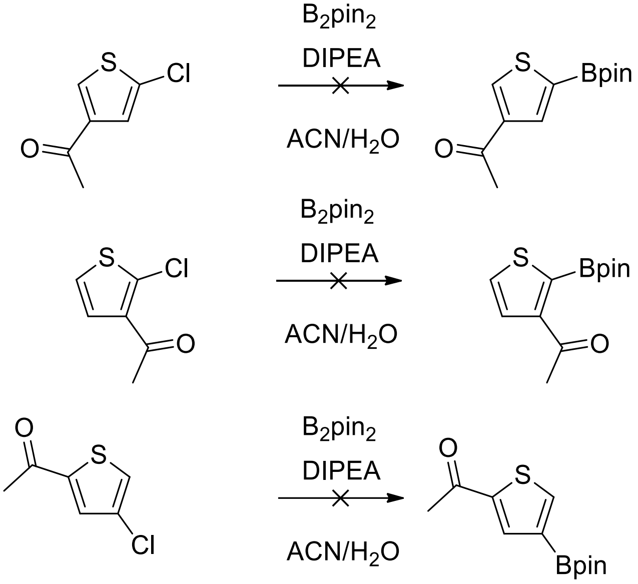


Figure E1. Exceptions to the general reactions

3.6.4 Computational details

Most of the calculations were performed under the Density Functional Theory (DFT) framework using the 6-31+G** basis set and different functionals: CAM-B3LYP,[1] mPW1PW91,[2] M062X[3] and B3LYP.[4] Geometry optimizations were performed without symmetry restrictions and in all cases the solvent (acetonitrile) effect was taken into account by means of the polarizable continuum model (PCM).[5] The vertical transitions (*i.e.* excitation energies) have been computed at the TD-DFT level of theory using ten roots. The electron transfer between **D** and **1a** was computed at the MP2 level. All calculations were carried out with the Gaussian 16 program package.

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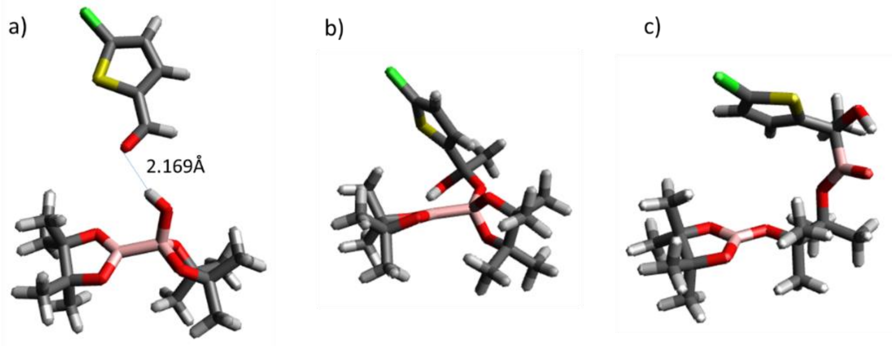
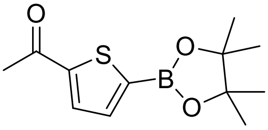


Figure E2. Computed alternative geometries for **B**. Experimental data agrees with structure a).

3.6.5 Characterization of compounds

1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)ethenone (2aa)



The compound was prepared according to the general procedure using 1-(5-chlorothiophen-2-yl)ethenone (12.8 mg, 80 µmol, 1.0 equiv.), bis(pinacolato)diboron (404.8 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 84% product yield of isolated product as white solid powder.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 3.7 Hz, 1H), 7.58 (d, *J* = 3.7 Hz, 1H), 2.57 (s, 3H), 1.35 (s, 12H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8 (C), 149.6 (C), 137.4 (CH), 132.8 (CH), 84.8 (C), 27.6 (CH_3), 24.9 (CH_3) ppm.

Spectral data were consistent with literature.[6]

For an up-scale reaction the corresponding product would be prepared following the general procedure taking into account these amounts: starting material 1-(5-chlorothiophen-2-yl)ethenone (160 mg, 1 mmol, 1.0 equiv.), bis(pinacolato)diboron (5 g, 20 mmol, 20.0 equiv.), dodecanenitrile (0.219 mL, 1 mmol, 1.0 equiv.) as internal standard and DIPEA (0.260 mL, 1.5 mmol, 1.5 equiv.) are dissolved in 50 mL acetonitrile/water (9/1 v/v) mixture in order to keep concentration conditions similar to the general procedure.

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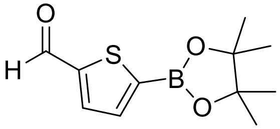
5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carbaldehyde (2ba)



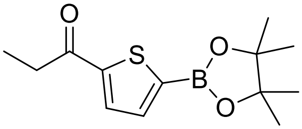
The compound was prepared according to the general procedure using 5-bromothiophene-2-carbaldehyde (10.0 µL, 80 µmol, 1.0 equiv.), bis(pinacolato)diboron (404.8 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 1 hour, obtaining 87% product yield according to GC-FID analysis (64% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.79 (d, *J* = 3.7 Hz, 1H), 7.65 (d, *J* = 3.7 Hz, 1H), 1.35 (s, 12H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 183.1 (C), 149.1 (C), 137.4 (CH), 136.2 (CH), 85.0 (C), 24.9 (CH_3) ppm.

Product commercially available.

1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)propan-1-one (2ca)



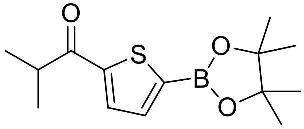
The compound was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)propan-1-one (17.5 mg, 80 µmol, 1.0 equiv.), bis(pinacolato)diboron (404.8 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 81% product yield according to GC-FID analysis (60% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 3.7 Hz, 1H), 7.55 (d, *J* = 3.7 Hz, 1H), 2.92 (q, *J* = 7.3 Hz, 2H), 1.32 (s, 12H), 1.21 – 1.17 (t, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9 (C), 149.2 (C), 137.3 (CH), 132.0 (CH), 84.7 (C), 33.2 (CH_2), 24.6 (CH_3), 8.5 (CH_3) ppm.

GC-MS (EI): *m/z* (relative intensity): 266 (20) [$M^{+\bullet}$], 237 (100), 167 (20), 155 (20), 137 (30).

2-methyl-1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)propan-1-one (2da)



The compound was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)-2-methylpropan-1-one (13.0 µL, 80 µmol, 1.0 equiv.), bis(pinacolato)diboron (404.8 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and

DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 2 hours, obtaining 82% product yield according to GC-FID analysis (59% isolated yield as white powder).

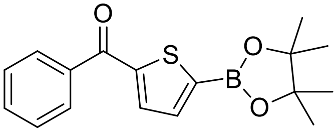
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 3.7 Hz, 1H), 7.58 (d, *J* = 3.7 Hz, 1H), 3.36 (dp, *J* = 13.7, 6.8 Hz, 1H), 1.34 (s, 12H), 1.23 (t, *J* = 4.4 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6 (C), 148.7 (C), 137.4 (CH), 132.2 (CH), 84.8 (C), 38.0 (CH), 24.9 (CH_3), 19.5 (CH_3) ppm.

GC-MS (EI): *m/z* (relative intensity): 280 (10) [$M^{+\bullet}$], 265 (5), 237 (100), 181 (5), 155 (20), 137 (20).

HRMS (EI): m/z (M+H)+ = calcd. for $C_{14}H_{21}BO_3S$: 281.1377, found: 281.1381.

Phenyl(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)methanone (2ea)



The compound was prepared according to the general procedure using (5-bromothiophen-2-yl)(phenyl)methanone (21.8 mg, 80 µmol, 1.0 equiv.), bis(pinacolato)diboron (404.8 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 2 hours, obtaining 84% product yield according to GC-FID analysis (66% isolated yield as yellow-pale powder).

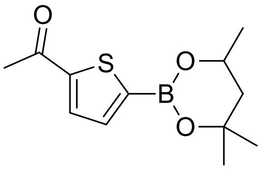
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 2H), 7.70 (d, *J* = 3.7 Hz, 1H), 7.61 (d, *J* = 3.7 Hz, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 1.35 (s, 12H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.8 (C), 148.6 (C), 138.4 (C), 137.1 (CH), 135.0 (CH), 132.5 (CH), 129.4 (2xCH), 128.5 (2xCH), 84.8 (C), 24.7 (CH_3) ppm.

GC-MS (EI): *m/z* (relative intensity): 314 (100) [$M^{+\bullet}$], 299 (50), 271 (30), 257 (10), 237 (20), 228 (60), 215 (70), 137 (50), 105 (70), 77 (50).

HRMS (EI): m/z (M+H)+ = calcd. for $C_{17}H_{19}BO_3S$: 315.1221, found: 315.1225.

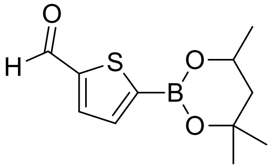
1-(5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)ethenone (2ab)



The compound was prepared according to the general procedure using 1-(5-chlorothiophen-2-yl)ethenone (12.8 mg, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (404.8 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 2 hours, obtaining 87% product yield according to GC-FID analysis (63% isolated yield as white powder).

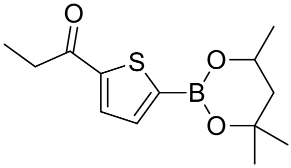
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 3.7 Hz, 1H), 7.43 (d, *J* = 3.7 Hz, 1H), 4.29 (ddd, *J* = 11.6, 6.1, 2.9 Hz, 1H), 2.50 (s, 3H), 1.82 (dd, *J* = 14.0, 2.9 Hz, 1H), 1.56 (dd, *J* = 13.9, 11.7 Hz, 1H), 1.31 (s, 6H), 1.28 (d, *J* = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8 (C), 148.2 (C), 135.5 (CH), 132.7 (CH), 72.1 (C), 65.8 (CH), 45.6 (CH_2), 31.1 (CH_3), 27.7 (CH_3), 23.0 (CH_3) ppm.
GC-MS (EI): *m/z* (relative intensity): 252 (30) [$M^{+•}$], 237 (100), 153 (15), 137 (40), 43 (20).
HRMS (EI): m/z (M+H)+ = calcd. for $C_{12}H_{17}BO_3S$: 253.1064, found: 253.1064.

5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophene-2-carbaldehyde (2bb)



The compound was prepared according to the general procedure using 5-bromothiophene-2-carbaldehyde (10.0 µL, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (404.8 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 77% product yield according to GC-FID analysis (55% isolated yield as white powder).
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 7.69 (d, *J* = 3.7 Hz, 1H), 7.49 (d, *J* = 3.7 Hz, 1H), 4.29 (ddd, *J* = 11.6, 6.1, 2.9 Hz, 1H), 1.82 (dd, *J* = 14.1, 2.9 Hz, 1H), 1.60 – 1.51 (m, 1H), 1.30 (s, 6H), 1.27 (d, *J* = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 183.1 (C), 147.8 (C), 136.2 (CH), 135.5 (CH), 71.9 (C), 65.7 (CH), 45.6 (CH_2), 31.0 (CH_3), 27.7 (CH_3), 22.9 (CH_3) ppm.
GC-MS (EI): *m/z* (relative intensity): 238 (80) [$M^{+•}$], 223 (100), 180 (30), 139 (50), 59 (50), 43 (60).
HRMS (EI): m/z (M+H)+ = calcd. for $C_{11}H_{15}BO_3S$: 239.0908, found: 239.0906.

1-(5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)propan-1-one (2cb)



The compound was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)propan-1-one (17.5 mg, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (404.8 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 76% product yield according to GC-FID analysis (58% isolated yield as white powder).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 3.7 Hz, 1H), 7.48 (d, *J* = 3.7 Hz, 1H), 4.33 (dqd, *J* = 12.4, 6.2, 2.9 Hz, 1H), 2.92 (q, *J* = 7.3 Hz, 2H), 1.86 (dd, *J* = 14.0, 2.9 Hz, 1H),

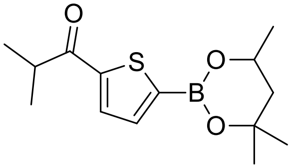
1.60 (dd, *J* = 13.9, 11.7 Hz, 1H), 1.35 (s, 6H), 1.32 (d, *J* = 6.2 Hz, 3H), 1.19 (t, *J* = 7.3 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1 (C), 148.0 (C), 135.5 (CH), 132.0 (CH), 72.0 (C), 65.7 (CH), 46.1 (CH_2), 33.1 (CH_2), 31.2 (CH_3), 28.1 (CH_3), 8.6 (CH_3) ppm.

GC-MS (EI): *m/z* (relative intensity): 266 (10) [$M^{+\bullet}$], 237 (100), 167 (5), 155 (10), 137 (20), 43 (10).

HRMS (EI): m/z (M+H)+ = calcd. for $C_{13}H_{19}BO_3S$: 267.1221, found: 267.1219.

2-methyl-1-(5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)propan-1-one (2db)



The compound was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)-2-methylpropan-1-one (13.0 µL, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (404.8 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 82% product yield according to GC-FID analysis (67% isolated yield as white powder).

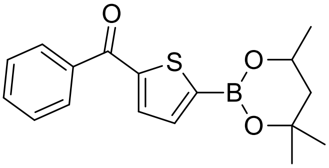
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 3.7 Hz, 1H), 7.46 (d, *J* = 3.7 Hz, 1H), 4.30 (ddd, *J* = 11.6, 6.1, 2.9 Hz, 1H), 3.33 (dt, *J* = 13.7, 6.8 Hz, 1H), 1.83 (dd, *J* = 14.0, 2.9 Hz, 1H), 1.57 (dd, *J* = 13.9, 11.7 Hz, 1H), 1.32 (s, 6H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.17 – 1.12 (m, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5 (C), 147.3 (C), 135.5 (CH), 132.0 (CH), 71.9 (C), 65.6 (CH), 46.0 (CH_2), 37.7 (CH), 31.1 (CH_3), 28.1 (CH_3), 23.0 (CH_3), 19.4 (CH_3) ppm.

GC-MS (EI): *m/z* (relative intensity): 280 (10) [$M^{+\bullet}$], 237 (100), 155 (10), 137 (20), 43 (10).

HRMS (EI): m/z (M+H)+ = calcd. for $C_{14}H_{21}BO_3S$: 281.1377, found: 281.1373

Phenyl(5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)methanone (2eb)



The compound was prepared according to the general procedure using (5-bromothiophen-2-yl)(phenyl)methanone (21.8 mg, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (404.8 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 77% product yield according to GC-FID analysis (61% isolated yield as yellow-pale powder).

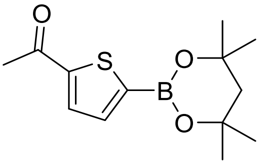
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.57 (d, *J* = 3.6 Hz, 1H), 7.49 (t, *J* = 7.1 Hz, 1H), 7.46 – 7.43 (m, 1H), 7.39 (t, *J* = 7.5 Hz, 2H), 4.35 – 4.21 (m, 1H), 1.81 (dd, *J* = 14.0, 2.7 Hz, 1H), 1.59 – 1.49 (m, 1H), 1.29 (s, 6H), 1.26 (d, *J* = 6.2 Hz, 3H) ppm.

^{13}C NMR (101 MHz, CDCl$_3$) δ 188.0 (C), 147.1 (C), 138.3 (CH), 135.2 (CH), 134.8 (CH), 132.1 (CH), 129.1 (2xCH), 128.2 (2xCH), 71.8 (C), 65.5 (CH), 45.6 (CH$_2$), 31.0 (CH$_3$), 27.6 (CH$_3$), 22.9 (CH$_3$) ppm.

GC-MS (EI): *m/z* (relative intensity): 314 (80) [M$^{+•}$], 299 (30), 237 (100), 215 (30), 137 (30), 105 (30), 77 (30),43 (20).

HRMS (EI): m/z (M+H)+ = calcd. for $C_{17}H_{19}BO_3S$: 315.1221, found: 315.1216.

1-(5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)ethenone (2ac)



The compound was prepared according to the general procedure using 1-(5-chlorothiophen-2-yl)ethenone (12.8 mg, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (451.2 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 1 hour, obtaining 87% product yield according to GC-FID analysis (73% isolated yield as white powder).

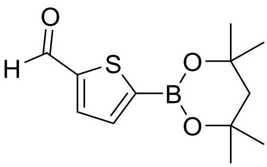
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.68 (d, *J* = 3.7 Hz, 1H), 7.50 (d, *J* = 3.7 Hz, 1H), 2.55 (s, 3H), 1.92 (s, 2H), 1.41 (s, 12H) ppm.

^{13}C NMR (101 MHz, CDCl$_3$) δ 191.0 (C), 148.3 (C), 135.5 (CH), 132.8 (CH), 71.9 (C), 49.1 (CH$_2$), 31.8 (CH$_3$), 27.5 (CH$_3$) ppm.

GC-MS (EI): *m/z* (relative intensity): 266 (50) [M$^{+•}$], 251 (100), 207 (20), 153 (40), 137 (35), 56 (35), 43 (50)

HRMS (EI): m/z (M+H)+ = calcd. for $C_{13}H_{19}BO_3S$: 267.1221, found: 267.1216.

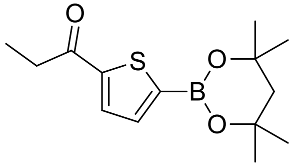
5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophene-2-carbaldehyde (2bc)



The compound was prepared according to the general procedure using 5-bromothiophene-2-carbaldehyde (10.0 µL, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (451.2 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 83% product yield according to GC-FID analysis (67% isolated yield as white powder).

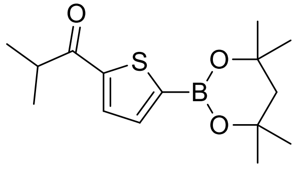
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 7.75 (d, *J* = 3.6 Hz, 1H), 7.57 (d, *J* = 3.6 Hz, 1H), 1.92 (s, 2H), 1.41 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3 (C), 147.9 (C), 136.3 (CH), 135.5 (CH), 72.0 (C), 49.1 (CH_2), 31.7 (CH_3) ppm.
GC-MS (EI): *m/z* (relative intensity): 252 (100) [$M^{+\bullet}$], 237 (90), 153 (20), 139 (30), 99 (30), 56 (50), 43 (50).
HRMS (EI): m/z (M+H)+ = calcd. for $C_{12}H_{17}BO_3S$: 253.1064, found: 253.1062.

1-(5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)propan-1-one (2cc)



The compound was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)propan-1-one (17.5 mg, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (451.2 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 80% product yield according to GC-FID analysis (62% isolated yield as white powder).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 3.7 Hz, 1H), 7.51 (d, *J* = 3.7 Hz, 1H), 2.94 (d, *J* = 7.3 Hz, 2H), 1.93 (s, 2H), 1.42 (s, 12H), 1.22 (t, *J* = 7.3 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2 (C), 147.9 (C), 135.5 (CH), 132.1 (CH), 71.9 (C), 49.2 (CH_2), 33.2 (CH_3), 8.7 (CH_3) ppm.
GC-MS (EI): *m/z* (relative intensity): 280 (20) [$M^{+\bullet}$], 251 (100), 207 (15), 155 (25), 137 (25), 43 (25)
HRMS (EI): m/z (M+H)+ = calcd. for $C_{14}H_{21}BO_3S$: 281.1377, found: 281.1375.

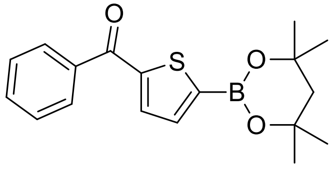
2-methyl-1-(5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)propan-1-one (2dc)



The compound was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)-2-methylpropan-1-one (13.0 µL, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (451.2 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 80% product yield according to GC-FID analysis (66% isolated yield as white powder).

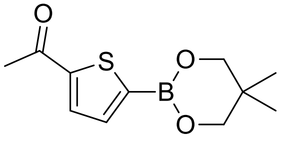
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 3.7 Hz, 1H), 7.52 (d, *J* = 3.7 Hz, 1H), 3.38 (dt, *J* = 13.7, 6.8 Hz, 1H), 1.93 (s, 2H), 1.42 (s, 12H), 1.23 (d, *J* = 6.8 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8 (C), 147.4 (C), 135.6 (CH), 132.2 (CH), 71.9 (C), 49.2 (CH_2), 37.8 (CH), 31.8 (CH_3), 19.6 (CH_3) ppm.
GC-MS (EI): *m/z* (relative intensity): 294 (10) [$M^{+\bullet}$], 251 (100), 207 (5), 155 (20), 137 (20), 43 (20).
HRMS (EI): m/z (M+H)+ = calcd. for $C_{15}H_{23}BO_3S$: 295.1534, found: 295.1534.

Phenyl(5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)methanone (2ec)



The compound was prepared according to the general procedure using (5-bromothiophen-2-yl)(phenyl)methanone (21.8 mg, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (451.2 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 62% product yield according to GC-FID analysis (51% isolated yield as yellow-pale powder).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 2H), 7.67 (d, *J* = 3.7 Hz, 1H), 7.57 (dd, *J* = 12.3, 5.5 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 1.94 (s, 2H), 1.43 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.5 (C), 147.3 (C), 138.7 (C), 135.3 (CH), 132.3 (CH), 129.4 (2xCH), 128.5 (2xCH), 71.9 (C), 49.2 (CH_2), 31.8 (CH_3) ppm.
GC-MS (EI): *m/z* (relative intensity): 328 (80) [$M^{+\bullet}$], 313 (50), 251 (50), 229 (30), 215 (100), 137 (50), 105 (50), 77 (50), 56 (40), 43 (50).
HRMS (EI): m/z (M+H)+ = calcd. for $C_{18}H_{21}BO_3S$: 329.1377, found: 329.1379.

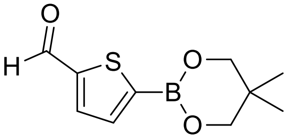
1-(5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)ethenone (2ad)



The compound was prepared according to the general procedure using 1-(5-chlorothiophen-2-yl)ethenone (12.8 mg, 80 µmol, 1.0 equiv.), bis(neopentylglycolato)diboron (361.4 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 2 hours, obtaining 77% product yield according to GC-FID analysis (61% isolated yield as white powder).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 3.7 Hz, 1H), 7.50 (d, *J* = 3.7 Hz, 1H), 3.75 (s, 4H), 2.55 (s, 3H), 1.01 (s, 6H) ppm.

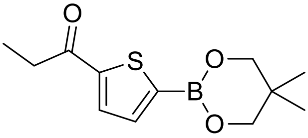
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.9 (C), 148.7 (C), 135.9 (CH), 132.9 (CH), 73.1 (CH_2), 32.1 (C), 27.5 (CH_3), 21.9 (CH_3) ppm.
GC-MS (EI): *m/z* (relative intensity): 238 (20) [$M^{+•}$], 223 (100), 153 (5), 137 (30).
HRMS (EI): m/z (M+H)+ = calcd. for $C_{11}H_{15}BO_3S$: 239.0908, found: 239.0903.

5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophene-2-carbaldehyde (2bd)



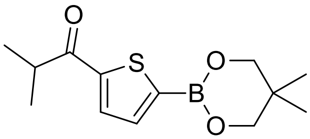
The compound was prepared according to the general procedure using 5-bromothiophene-2-carbaldehyde (10.0 µL, 80 µmol, 1.0 equiv.), bis(neopentylglycolato)diboron (361.4 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 97% product yield according to GC-FID analysis (85% isolated yield as white powder).
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.78 (d, *J* = 3.7 Hz, 1H), 7.59 (d, *J* = 3.7 Hz, 1H), 3.78 (s, 4H), 1.03 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3 (C), 148.3 (C), 136.4 (CH), 136.0 (CH), 72.7 (CH_2), 32.2 (C), 22.0 (CH_3) ppm.
GC-MS (EI): *m/z* (relative intensity): 224 (80) [$M^{+•}$], 223 (100), 181 (20), 137 (25), 56 (50), 41 (20).
HRMS (EI): m/z (M+H)+ = calcd. for $C_{10}H_{13}BO_3S$: 225.0751, found: 225.0747.

1-(5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)propan-1-one (2cd)



The compound was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)propan-1-one (17.5 mg, 80 µmol, 1.0 equiv.), bis(neopentylglycolato)diboron (361.4 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 2 hours, obtaining 77% product yield according to GC-FID analysis (62% isolated yield as white powder).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 3.7 Hz, 1H), 7.51 (d, *J* = 3.7 Hz, 1H), 3.76 (s, 4H), 2.94 (q, *J* = 7.3 Hz, 2H), 1.22 (t, *J* = 7.3 Hz, 3H), 1.03 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1 (C), 148.4 (C), 135.9 (CH), 132.1 (CH), 72.6 (CH_2), 33.2 (CH_2), 32.2 (C), 22.0 (CH_3), 8.6 (CH_3) ppm.
GC-MS (EI): *m/z* (relative intensity): 252 (10) [$M^{+•}$], 223 (100), 183 (10), 137 (20).
HRMS (EI): m/z (M+H)+ = calcd. for $C_{12}H_{17}BO_3S$: 253.1064, found: 253.1063.

1-(5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)-2-methylpropan-1-one (2dd)



The compound was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)-2-methylpropan-1-one (13.0 µL, 80 µmol, 1.0 equiv.), bis(neopentylglycolato)diboron (361.4 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 1 hour, obtaining 74% product yield according to GC-FID analysis (59% isolated yield as white powder).

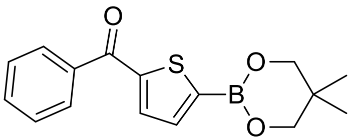
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 3.7 Hz, 1H), 7.52 (d, *J* = 3.7 Hz, 1H), 3.77 (s, 4H), 3.43 – 3.25 (m, 1H), 1.23 (d, *J* = 6.8 Hz, 6H), 1.03 (s, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7 (C), 147.8 (C), 136.0 (CH), 132.3 (C), 72.6 (CH_2), 37.9 (CH), 32.2 (C), 22.0 (CH_3), 19.5 (CH_3) ppm.

GC-MS (EI): *m/z* (relative intensity): 266 (10) [$M^{+\bullet}$], 223 (100), 183 (10), 137 (20).

HRMS (EI): m/z (M+H)+ = calcd. for $C_{13}H_{19}BO_3S$: 267.1221, found: 267.1222.

(5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)(phenyl)methanone (2ed)



The compound was prepared according to the general procedure using (5-bromothiophen-2-yl)(phenyl)methanone (21.8 mg, 80 µmol, 1.0 equiv.), bis(neopentylglycoltao)diboron (361.4 mg, 1600 µmol, 20.0 equiv.), dodecanenitrile (17.5 µL, 80 µmol, 1.0 equiv.) as internal standard and DIPEA (21 µL, 120 µmol, 1.5 equiv.). The reaction mixture was irradiated for 30 minutes, obtaining 67% product yield according to GC-FID analysis (54% isolated yield as yellow-pale powder).

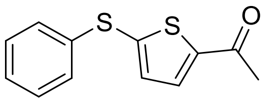
^{1}H NMR (400 MHz, CDCl3) δ 7.88 (d, J = 7.4 Hz, 2H), 7.69 (d, J = 3.7 Hz, 1H), 7.57 (dd, J = 12.0, 5.5 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 3.78 (s, 4H), 1.04 (s, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.4 (C), 147.7 (C), 138.5 (C), 135.7 (CH), 135.2 (CH), 132.4 (CH), 129.4 (CH), 128.5 (CH), 72.7 (CH_2), 32.2 (C), 22.0 (CH_3) ppm.

GC-MS (EI): *m/z* (relative intensity): 300 (50) [$M^{+\bullet}$], 223 (100), 137 (20), 105 (20), 77 (20).

HRMS (EI): m/z (M+H)+ = calcd. for $C_{16}H_{17}BO_3S$: 301.1064, found: 301.1063.

1-(5-(phenylthio)thiophen-2-yl)ethanone



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 3.9 Hz, 1H), 7.43 – 7.38 (m, 2H), 7.36 – 7.28 (m, 3H), 7.10 (d, *J* = 3.9 Hz, 1H), 2.50 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.0 (C), 146.3 (C), 145.7 (C), 135.2 (C), 132.8 (CH), 132.1 (CH), 130.9 (CH), 129.6 (CH), 128.2 (CH), 26.6 (CH_3) ppm.

This compound was synthesized as previously described for comparison purpose.[7]

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Chapter 4

Aerobic Visible-Light-Driven Borylation of Heteroarenes in a Gel Nanoreactor

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4.1 Abstract

Heteroarene boronate esters constitute valuable intermediates in modern organic synthesis. As building blocks, they can be further applied to the synthesis of new materials, since they can be easily transformed into any other functional group. Efforts toward novel and efficient strategies for their preparation are clearly desirable.

Here, we have achieved the borylation of commercially available heteroarene halides under very mild conditions in an easy-to-use gel nanoreactor. Its use of visible light as the energy source at room temperature in photocatalyst-free and aerobic conditions makes this protocol very attractive. The gel network provides an adequate stabilizing microenvironment to support wide substrate scope, including furan, thiophene, selenophene, and pyrrole boronate esters.

4.2 Introduction

Organoboron-containing molecules continue to attract considerable interest from scientists that seek new synthetic approaches since the reactivity of these entities is broad.[1] Their incorporation in appropriate cores by combination of a multitude of methods and their ability to continually expand by converting carbon−boron bonds into nearly any other functional group makes organoboronates a key functional group in modern organic synthesis, material science, and drug discovery.[2] The importance of these molecules is further enhanced by their capacity to undergo stereospecific transformations, generating an extensive range of enantioenriched building blocks for synthesis.[3] In this decade, we have witnessed notable developments in numerous strategies using either transition metal catalysis[4] or noncatalytic methods[5] for the synthesis of organoboron derivatives and their subsequent assemblage. Aryl halides are frequently employed as precursors of aryl boronate esters due to their widespread and cheap availability in the market.

Among methods for thermally induced borylation of aryl halides by transition metals,[6–11] photocatalysis has emerged as a powerful tool for the construction of aryl boronate esters.[12] For instance, procedures using UV-light have allowed the borylation of aryl halides, mesitylates, and ammonium salts;[13] however, the use of high-intensity UV photolysis could form undesired products, limiting the technique’s applicability. In terms of selectivity, visible-lightdriven processes are considered a superior strategy to generate aryl boronates from aryl halides, and many examples using metal or metal-free photocatalyst systems have been reported.[14]

In this vein, we have recently contributed to this field reporting a novel, straightforward, and rapid protocol to produce boron-containing thiophenes from thiophene halides, employing visible light under mild conditions.[15] The merits of this methodology mainly reside in the absence of any external photocatalyst system together with a drastic shortening in irradiation times (0.5−2 h). However, an anaerobic atmosphere is crucial since there is no such reaction in the presence of oxygen.

To circumvent this drawback, we envision employing viscoelastic supramolecular gels, often made of low-molecular-weight (LMW) compounds self-assembled through noncovalent interactions as compartmentalized reaction media.[16] Although many studies utilizing viscoelastic gels as reaction vessels and/or nanoreactors for other type of processes have been reported,[16] some examples of photochemical reactions in gel media can be found in literature.[17] Indeed, the reactivity to air-sensitive photochemical transformations has demonstrated that such gel networks provide a suitable stabilizing microenvironment under aerobic conditions.[17b−d]

Accomplishing the borylation of heteroarene halides under milder conditions, including photocatalyst-free, visible-light irradiation at room temperature under an aerobic atmosphere, appears challenging. Here, we have explored this option using physical gels as confined reaction media. Our results show the feasibility of the procedure, expanding the scope of the borylated reactions not only to thiophene halides but also to furan, pyrrole, and selenophene halides. Thus, application of this method may be extended beyond borylations to prepare bioactive molecules (**Figure 1A,B**).

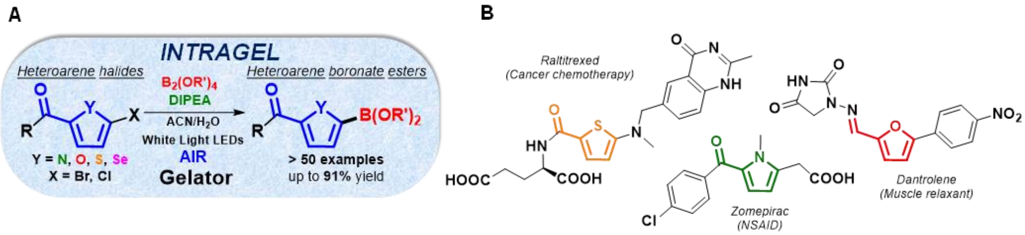


Figure 1. (A) Visible light-driven borylation of heteroarenes in gel media under air conditions. (B) Examples of pharmaceutical agents containing thiophene, furan, and pyrrole moieties.

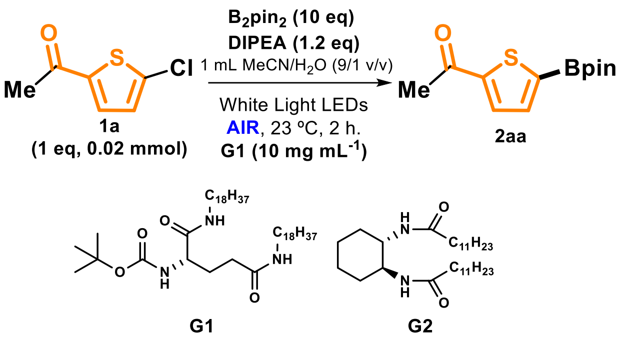
4.3 Results & Discussion

4.3.1 Optimization

Based on our previous work,[15] we first screened the photolysis of 2-acetyl-5-chlorothiophene (**1a**) with bis-(pinacolato)diboron (B_2pin_2) and *N*,*N*-diisopropylethylamine (DIPEA, Hünig's base) in aerated MeCN/H_2O (9/1 v/v) solution. The expected borylated thiophene **2aa** was not observed (**Table 1**, entry 1), confirming that the reaction was completely blocked by the dissolved molecular oxygen, presumably shifting the reaction mechanism to other unwanted pathways (vide infra). Conversely, the desired product **2aa** was formed in high yields when the physical gel formed by **G1** (*N,N'*-bis(octadecyl)-*L*-boc-glutamic diamide, molecular structure in **Table 1**)[18] was used as a confined medium under otherwise identical conditions (**Table 1**, entry 3; the balance of conversion was the dehalogenated product).

Optimal conditions involved lower reagent loading than reported elsewhere[15] (10 equiv of B_2pin_2 and 1.2 equiv of DIPEA), with irradiation in the visible range at 410−700 nm with cold-white LEDs in **G1** medium for 2 h under aerobic conditions. The result within the aerobic gel phase was gratifyingly comparable to that obtained in solution in a strict inert atmosphere (**Table 1**, entry 2).

Table 1. Optimization of Reaction Conditions[a]



Entry	Deviations for the conditions shown	Yield/%[a]
1	without **G1**	0
2	purged N_2 /without **G1**	56 (75)[b]
3	-	**72 (100)**
4	purged N_2	60 (73)
5	0.04 mmol of **1a**	64 (100)
6	5 eq of B_2pin_2	57 (92)
7	1 eq DIPEA	35 (46)
8	no DIPEA, or dark reaction	0 each
9	**G1**[c] (8 mg mL^{-1})	43 (70)
10	**G1**[c] (15 mg mL^{-1})	37 (59)
11	**G2**[c] (10 mg mL^{-1})	56 (86)

[a] GC yields of **2aa** (**1a** conversion in parentheses) were determined by quantitative GC-FID vs. internal 1-dodecanonitrile. [b] 3 h irradiation. [c] The self-assembly process of the gelator in organic solvents is driven by hydrogen bonds and van der Waals forces, leading to tangled fibrillar nanostructures over a wide concentration range (2–21 g L^{-1} and 2–44 g L^{-1} for **G1** and **G2**, respectively).[18,19]

The model reaction was also carried out under an oxygen-free atmosphere instead of aerobic conditions (**Table 1**, entries 4 versus 3), yielding a similar amount of **2aa**. This outcome reveals that the gel network offers an efficient confinement effect for visible-light-induced radical reactions in air. Varying the amount of each reactant did result in lower yields of **2aa**, although full conversion of **1a** was observed in some cases (**Table 1**, entries 5–7). The absence of DIPEA or light in control experiments confirmed the key role of these elements in the chemical transformation (**Table 1**, entry 8). Additionally, employment of other bases did not offer better yields (see **Table E1**, entries 26-30, Experimental section).

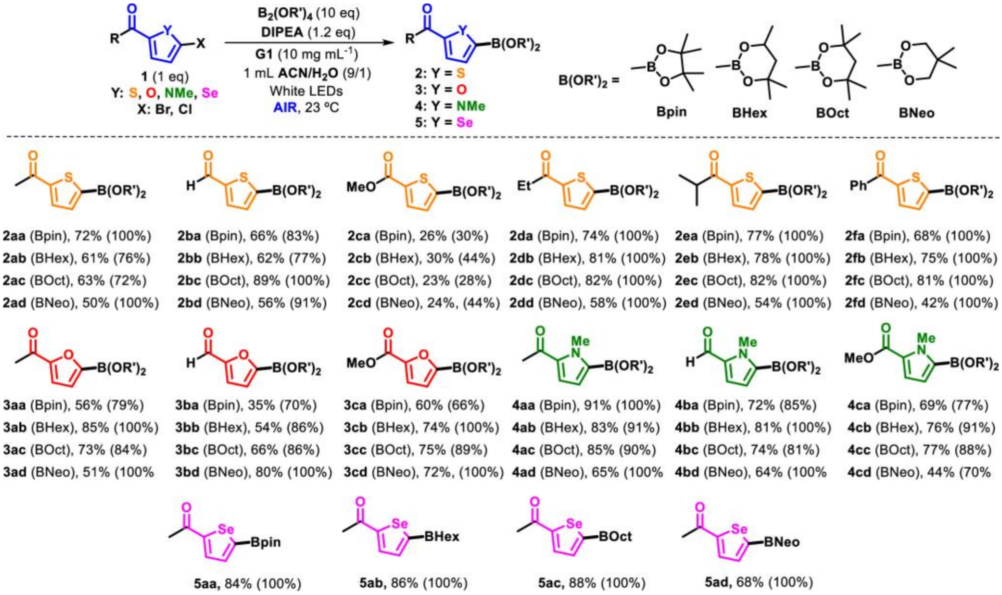
This visible-light-driven thiophene borylation thus improved considerably due to the gel network, which permitted the process to occur in air. Full conversion of **1a** and maximized **2aa** yield were obtained with an optimal concentration of **G1** (10 mg mL^{-1}); reductions in yield were observed at **G1** concentrations below 10 mg mL^{-1} (**Table 1**, entry 9). Perhaps the oxygen diffusion rate through the gel phase is faster, leading to the process being partially blocked. The diffusion of reactants might decrease inside the solvent pools above the optimal **G1** concentration, also reducing yield (**Table 1**, entry 10). Moreover, the effect of light scattering could be minimized by adjusting the solvent volume (see **Table E1**, entries 11,13 and 14, Experimental section). Thus, the lower the volume the higher the process efficiency, i.e., 72% yield (1 mL), 64% yield (2 mL), and 53% yield (4 mL).

To check whether this reaction may be associated specifically with gelator **G1**, the model reaction was performed in the gel of **G2** (*N*,*N*′-((1*S*,2*S*)-cyclohexane-1,2-diyl)-didodecanamide,[19] molecular structure in **Table 1**), which assembles with a different matrix. A 56% yield of **2aa** was produced under optimal conditions (**Table 1**, entry 11); therefore, **G2** also offered a suitable microenvironment for the investigated reaction. Note that the gelator can be easily separated by filtration and reused in subsequent experiments without detriment to its gelation properties.

4.3.2 Scope

The standardized conditions (**Table 1**, entry 3) were next applied to a diverse set of heteroarene halides and various diboron derivatives (**Scheme 1**). First, upon variation of both starting materials, thiophene boronate esters (**2aa—2fd**) were obtained in moderate-to-high yields (23−89%); these are important scaffolds in pharmaceuticals[20] and conjugated materials,[21] alongside other applications.

Scheme 1. Coupling of Heteroarene Halides with Diboron Derivatives (Conversion of **1** in Parentheses)



The reactivity was generally similar in all cases, except for thiophene halides bearing the −COOMe group, which presented lower conversions and yields (**2ca—cd**). To rule out that this reaction was specifically for thiophenes and the involvement of the sulfur atom in the radical process, the generality and the versatility of this protocol were explored using different haloheterocycles such as furan, pyrrole, and selenophene halides. All were submitted to visible light irradiation in the presence of DIPEA and various diboron derivatives, employing **G1** under air.

After an easy procedure for recovering the products (see General procedure, Experimental section), the results indicated that borylation of the corresponding heteroarenes succeeded, with gratifyingly high yields in some cases (for instance, 85% for **3ab** or 91% for **4aa** or 88% for **5ac**). To highlight that this photochemical reaction represents a useful method for organic synthesis, the model reaction was carried out as follows: (i) in a higher scale moving from 0.02 to 1 mmol, obtaining a 63% yield of **2aa** (see *1 mmol scale-up*, Experimental section) and (ii) under outdoor sunlight after 4 h, leading to the formation of the desired product in 66% yield (see **Figure E1**, Experimental section) Further, it provides access to a vast number of new borylated derivatives (more than 50 examples) with low toxicity, and presumably suitable reactivity to be employed as versatile precursors in organic reactions such as Suzuki−Miyaura[22] and Chan−Lam[23] coupling reactions.

4.3.3 Mechanism

The role of the viscoelastic gel network as an effective nanoreactor was supported by a combination of experimental measurements. First, kinetic studies of the model reaction revealed that conversion of starting material **1a** was faster in aerated gel medium than in inert solution for the same irradiation time (**Figure E2**, Experimental section). This was well-correlated with the formation of **2aa**, where yields were found to be higher in gel (**Figure E3**, Experimental section).

Interestingly, production of **2aa** was negligible from a frozen (193 K) aerated MeCN/H_2O solution of the model reaction due to, as expected, restricted molecular diffusion; conversely, a 30% yield of **2aa** was obtained under the same conditions in the presence of **G1** (see *Frozen model reaction*, Experimental section). This could be interpreted as meaning reactants are not only localized in the solvent pools between fibers, but may also spread through fibers, permitting photochemical reaction in a confined by dynamic space.

In addition, field-emission scanning electron microscopy (FESEM) images were used to show that inclusion of the reactants within the supramolecular gel provoked a slight densification of the network, while its morphological features were preserved after irradiation (**Figure 2** and **Figure E4**, Experimental section). Such densification could be interpretated by partial incorporation of reactants into the fibers that, gratifyingly, did not affect the thermal stability of the gel network, as supported by the same gel-to-sol transition temperature (T_{gel}) observed for both the undoped gel made of **G1** and the doped gel (i.e., as described in **Figure 2**) even after irradiation (T_{gel} = 50 ± 2 °C).[24] Visual inspection of the materials after the irradiation experiments suggested no change in the viscoelastic properties of the gels (i.e., no gravitational flow; see **Figure 2D**).

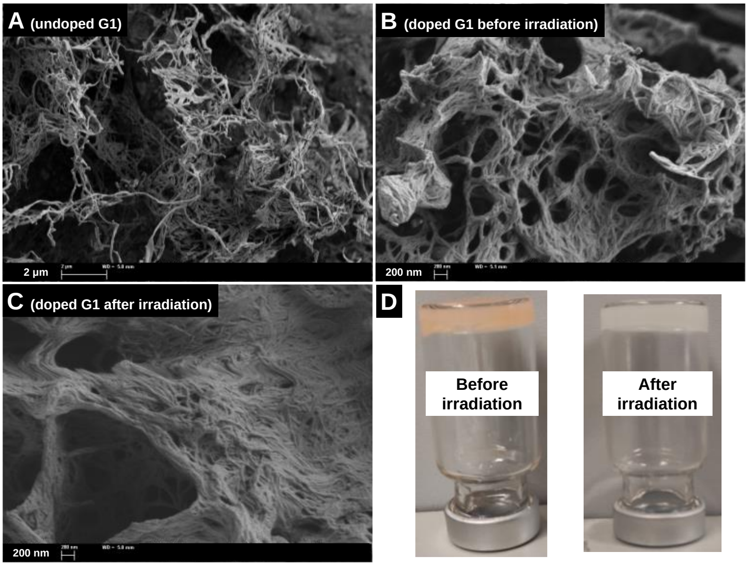
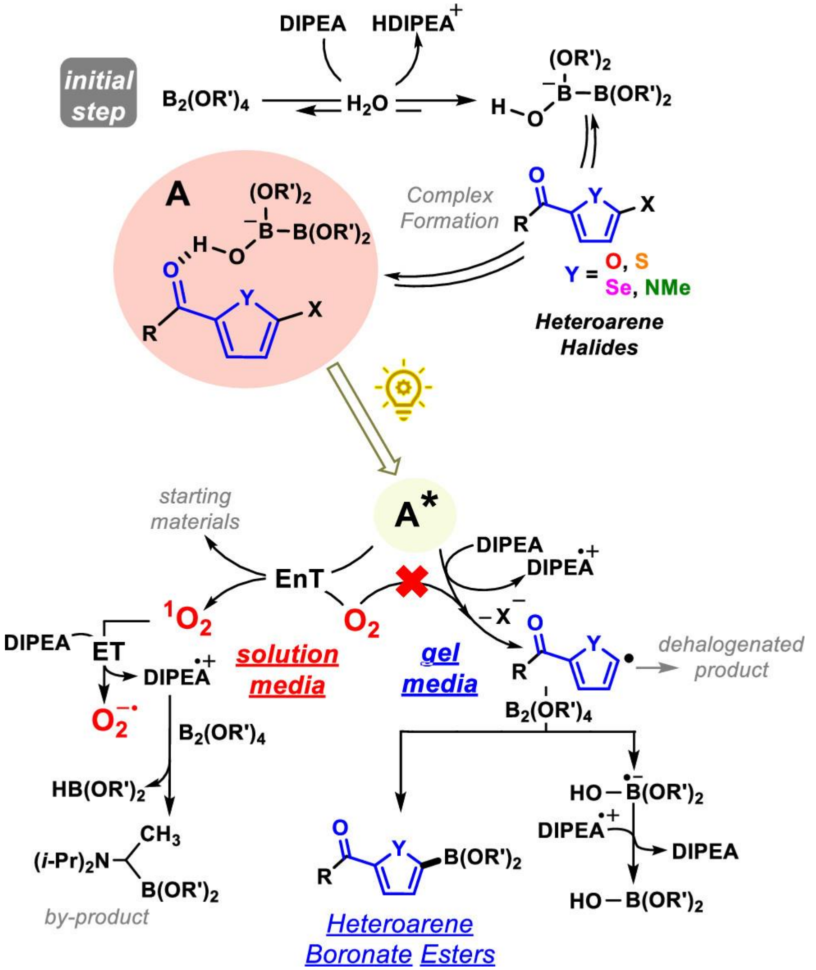


Figure 2. Representative field-emission scanning electron microscopy (FESEM) images: A: undoped gel of G1 (10 mg mL^{-1}) in 1 mL MeCN/H_2O (9/1 v/v); B, C: gel of **G1** (10 mg mL^{-1}) doped with **1a** (3.2 mg), B_2pin_2 (50 mg) and DIPEA (3.1 mg) in 1 mL MeCN/H_2O (9/1 v/v); D: Photograph of the doped gel with 5-bromo-2-furaldehyde+B_2pin_2+DIPEA at standard conditions before/after irradiation.

Based on literature,[15] the proposed reaction mechanism is outlined in **Scheme 2**. Complex **A** was formed at the ground state in all cases as confirmed by UV−vis spectrophotometry (**Figure E5**, Experimental section); a marked absorbance in the visible region was observed, permitting initiation of the photoreaction and generation of the corresponding excited states (**A***). Under aerobic conditions in solution, this species could be efficiently quenched by molecular oxygen through energy transfer (EnT), giving rise to the starting materials and singlet oxygen ($^1O_2$). Electron transfer (ET) from $^1O_2$ to DIPEA would occur,[25] and the resulting oxygen radical anion ($O_2^{\bullet-}$) might abstract a H from the DIPEA radical cation (DIPEA$^{\bullet+}$), forming an aminoalkyl radical which would react with the diboron derivative to produce the corresponding byproduct.

Scheme 2. Proposed Reaction Mechanism



Not even traces of the desired heteroarene boronate ester were detected in the crude, supporting an oxygen-locked process. Besides, spectroscopic measurements provided evidence of $^1O_2$ reactivity, with its lifetime dramatically decreased under the ideal reaction conditions (**Figure E6**, Experimental section). The scenario differed when supramolecular gels were used as confined media. The oxygen diffusion was negligible in this case, and the reaction proceeded following the mechanism we previously published.[15] Indeed, trapping experiments using diphenyldisulfide (PhSSPh) confirmed the involvement of the heteroarene radical as an intermediate (**Figure E7**, Experimental section).

4.4 Conclusion

In conclusion, we report an attractive and efficient methodology for building heteroarene boronate esters under very mild conditions. A simple operation that requires only commercially available reagents, visible light, room temperature, and ambient pressure and proceeds photocatalyst-free and under an aerobic atmosphere has been effectively employed in an LMW gel nanoreactor. A wide variety of products have been obtained that may act as versatile precursors for further synthetic work. The use of supramolecular viscoelastic gels has allowed us not only to protect against oxygen poisoning but also to accelerate the reaction relative to standard conditions.

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(24) In principle, changes in gel morphology might not be so obvious based only on SEM images, and careful analysis should be performed because possible artifacts created during sample preparation and/or measurements cannot be completely ruled out.

(25) Davidson, R. S.; Trethewey, K. R.; *J. Chem. Soc., Perkin Trans. 2* **1977**, *2*, 173−178.

4.6 Experimental section

4.6.1 Materials and methods

All reagents (≥97% purity) and solvents (≥99% purity) were purchased from commercial suppliers (Merck, TCI, Apollo Scientific, Fluorochem, Scharlab) and used as received unless otherwise indicated. Reactions were carried out in Metria®-Crimp Headspace clear vial flat bottom (10 mL, Ø 20 mm) sealed with Metria®-aluminium crimp cap with moulded septum butyl/natural PTFE (Ø 20 mm). Irradiation was performed with a cold white LED (LED Cree MK-R, cold-white, 11.6 V, 700 mA, P = 8.5 W).

TLC was performed on commercial SiO_2-coated aluminium and plastic sheets (DC60 F254, Merck). Visualization was done by UV-light (254nm). Product were isolated materials after TLC on silica gel (Merck, mesh 35-70, 60 Å pore size) and their corresponding yields were determined by quantitative GC-FID measurements on an Agilent 8860 GC-System with N_2 as carrier gas. Dodecanenitrile was used as an internal standard in the GC-FID quantitative measurements; yield products were estimated as: [conversion × selectivity]/mass balance. Determination of purity and structure confirmation of the literature known products was performed by ^{1}H NMR, ^{13}C NMR and high-resolution mass spectrometry (HRMS) in case of unknown products. NMR spectral data were collected on a Bruker Advance 400 (400 MHz for ^{1}H and 101 MHz for ^{13}C) spectrometer at 20 °C. Chemical shifts are reported in δ/ppm, coupling constants J are given in Hertz. Solvent residual peaks were used as internal standard for all NMR measurements. The quantification of ^1H cores was obtained from integrations of appropriate resonance signals. Abbreviations used in NMR spectra: s – singlet, d – doublet, t – triplet, q – quartet, m – multiplet, bs – broad singlet, dd – doublet of doublet, ddd – doublet of doublet of doublet. HRMS was carried out was performed in the mass facility of SCSIE University of Valencia. LRMS was carried out on an HP 6890 Series GC System with Agilent 5973 Network Mass Selective Detector and H_2 as carrier gas.

4.6.2 General procedure

A vial (10 mL) was charged with the hetereoarene derivative (20 µmol, 1.0 eq.), diborylate (200 µmol, 10.0 eq.) and the correspondent gelator (**G1**, 10 mg/mL). Acetonitrile/H_2O (9/1 v/v) mixture (1.0 mL) was poured. Then, DIPEA (24 µmol, 1.2 eq.) and dodecanenitrile (20 µmol, 1.0 eq.) were added with 10 µL Hamilton syringe. Quickly, the vial was sealed with a septum. It was heated to 150 °C for 1.5 minutes with manual stirring until complete clear solution. The vial cooled to room temperature until gel formation was observed. The reaction was irradiated with an external LED through the plain bottom side of the vial at 23 °C during the corresponding time.

Then, brine (2 mL) was added, and the aqueous phase was extracted with dichloromethane (1 mL). The reaction was monitored by GC-FID analysis. The organic phase was dried over anhydrous sodium sulfate, filtered from the drying agent, and concentrated in vacuo. After recrystallization of the excess of starting diboron derivative, which is recovered, the crude was purified via TLC plastic sheet using a hexane/ethyl acetate mixture as the mobile phase. Note: The gelator can be easily separated by filtration and reused in subsequent experiments without any detriment of its gelation properties.

4.6.3 Synthesis of Low Molecular Weight Gelators (LMW Gelators)

N,N'-Bis(octadecyl)-*L*-Boc-glutamic Diamide (**G1**)

Boc-glutamic acid (0.01 mol, 1.0 equiv) and octadecylamine (0.02 mol, 2.0 equiv) in dichloromethane (200 mL) were mixed. Then, 1-ethyl-3-(3-(dimethylamino)propyl)carbodiimide hydrochloride (EDC·HCl) (0.022 mol, 2.2 equiv) was added to the mixture and stirred at RT for 72 h. The obtained white solid was isolated by filtration and washed three times with dichloromethane. The crude product was dissolved in THF and precipitated by water. A fine white solid was

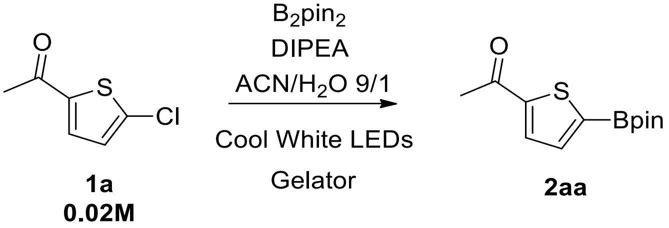
obtained (80%). Following the procedure reported previously *Soft Matter* **2007**, *3*, 1312−1317.
^{1}H NMR (300 MHz CDCl$_3$) δ 6.69 (br, 1H), 6.32 (br, 1H), 5.77 (br, 1H), 4.08 (br, 1H), 3.26−3.22 (m, 4H), 2.41−2.27 (m, 2H), 2.06−1.93 (m, 2H), 1.58−1.46 (m, 4H), 1.43 (s, 9H), 1.25 (s, 60H), 0.87 (t, 6H) ppm.

(*S,S*)-Dodecyl-3-[2(3-dodecyl-ureido)cyclohexyl]urea (**G2**).

A solution of dodecylisocyanate (15 mmol, 2.0 equiv) in toluene (20 mL) was slowly added to a solution of (*S,S*)-1,2-cyclohexyldiamine (7 mmol, 1.0 equiv) in toluene (100 mL). The reaction mixture was stirred for 16 h at RT and 2 h at 100 °C. After cooling to RT, the gel-like reaction mixture was filtered to give a white waxy solid. The waxy solid was further stirred for 16 h with dichloromethane (50 mL) and collected by filtration. This procedure was repeated with diethyl ether. After drying, a white solid was obtained (70%). Following the procedure reported previously *Chem. Eur. J.* **1999**, *5*, 937−950.
^{1}H NMR (300 MHz, CDCl$_3$) δ 5.18 (br, 2H), 4.67 (br, 2H), 3.42 (m, 2H), 3.08 (m, 4H), 2.03 (d, 2H), 1.72 (m, 6H), 1.45 (m, 4H), 1.25 (s, 36H), 0.87 (t, 6H) ppm.

4.6.4 Optimization

Table E1. Searching for the optimal conditions.



Entry	*B$_2$pin$_2$ (eq)*	*DIPEA (eq)*	*G1/solvent*	*Conv (%)*	*Yield of **2aa** (%)*
1	3	1.5	21 mg/2mL	**100**	**16**
2	5	1.2	10 mg/1mL	**92**	**57**
3	5	1.5	21 mg/2mL	**100**	**28**
4	15	1.2	10 mg/1mL	**26**	**18**
5	10	1.5	21 mg/2mL	**100**	**60**
6	20	1.5	21 mg/2mL	**92**	**69**
7	10	1	21 mg/2mL	**94**	**62**

8	10	1	10 mg/1mL	**46**	**35**
9	10	3	21 mg/2mL	**100**	**38**
10	10	3	10 mg/1mL	**100**	**58**
11	10	1.2	21 mg/2mL	**100**	**64**
12	10	1.5	42 mg/4mL	**92**	**40**
13	10	1.2	42 mg/4mL	**100**	**53**
14	10	1.2	10 mg/1mL	**100**	**72**
15	10	1.2	8 mg/1mL	**70**	**43**
16	10	1.2	15 mg/1mL	**59**	**37**
17	10	1.2	[a]8.5 mg/1mL	**59**	**38**
18	10	1.2	[a]10 mg/1mL	**86**	**56**
19	10	1.2	[a]5 mg/1mL	**55**	**44**
20	10	1.2	Air[b]	**-**	**-**
21	10	1.2	N_2[b]	**75**	**56**
22	10	1.2	G1/N_2[b]	**46**	**34**
23	10	-	10 mg/1mL	-	-
24	-	1.2	10 mg/1mL	-	-
25[c]	10	1.2	10 mg/1mL	-	-
26	10	Et_3N 1.2	10 mg/1mL	**19**	**11**
27	10	DIPA 1.2	10 mg/1mL	**29**	**29**
28	10	DBU 1.2	10 mg/1mL	**66**	**45**
29	10	DABCO 1.2	10 mg/1mL	**15**	**7.8**
30	10	Ph_3N 1.2	10 mg/1mL	-	-
31	10	1.2	Frozen No G1	-	-
32	10	1.2	Frozen; 10 mg/1mL	**35**	**30**
33	10	1.2	[d]N_2 and 10 mg/1mL	**73**	**60**

[a]**G2** as gelator was used. [b]Solution reaction without gel. [c]Without **1a**. [d]Purged with N_2 before gel formation.

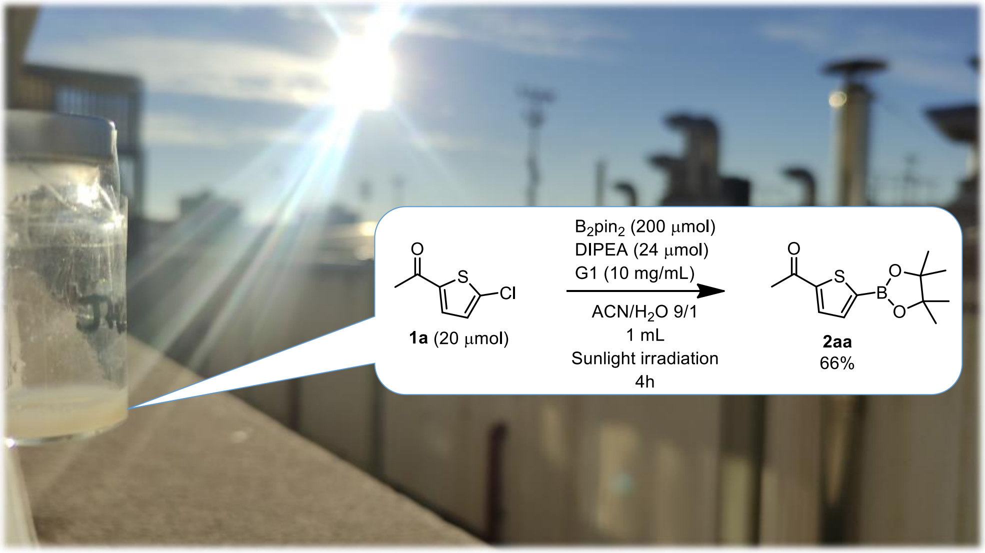
4.6.5 Sunlight irradiation procedure

The compound **2aa** (CAS 942070-32-8) was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (3.2 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.)

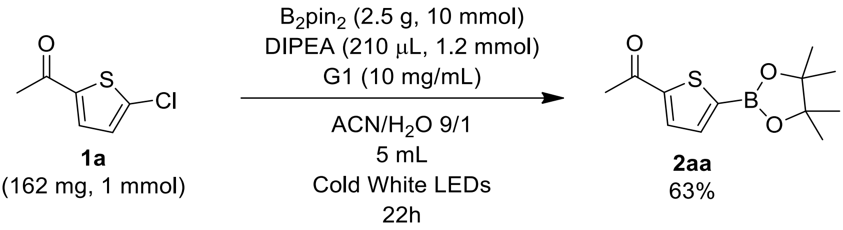
and **G1** (10 g/L). The reaction mixture was irradiated with sunlight for 4 hours, obtaining 66% product yield according to GC-FID analysis.

Location: Camí de Vera S/N, Chemistry Department, Universitat Politècnica de València (UPV), Valencia, Spain (coordinate: 39.482917, -0.341642), temperature: 12-16 °C, from 9:00 to 13:00. Date: 23/12/2020.

Figure E1. Sunlight irradiation reaction.

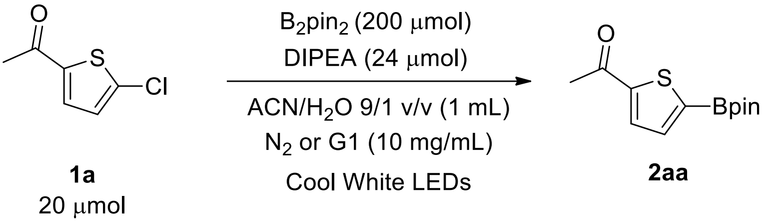


4.6.6 1 mmol scale procedure



The compound **2aa** (CAS 942070-32-8) was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (162 mg, 1 mmol, 1.0 eq.), bis(pinacolato)diboron (2.5 g, 10 mmol, 10.0 eq.), dodecanenitrile (220 µL, 1 mmol, 1.0 equiv.) as internal standard and DIPEA (210 µL, 1.2 mmol, 1.2 eq.) and **G1** (10 mg/mL) in 5 mL. The reaction mixture was irradiated for 22 hours, obtaining 63% product yield according to GC-FID analysis.

4.6.7 Kinetic studies



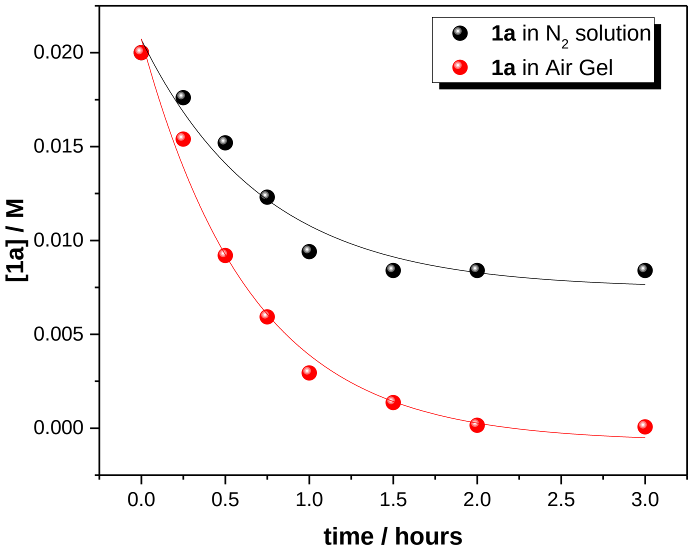


Figure E2. Variation of **1a** concentration upon irradiation time in different conditions.

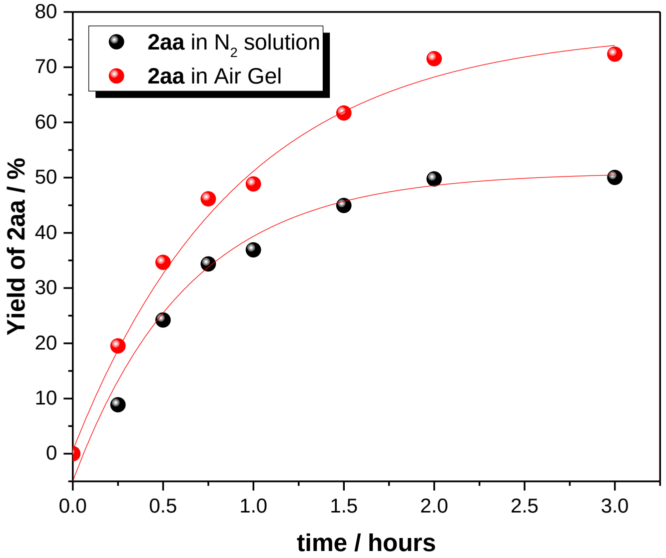
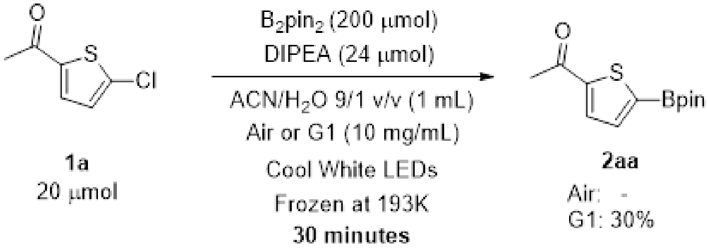


Figure E3. Formation of **2aa** upon irradiation time in different conditions.

4.6.8 Frozen model reaction



A vial (10 mL) was charged with 1-(5-chlorothiophen-2-yl)ethenone (3.2 mg, 20 μmol, 1.0 equiv.), bispinacolato diboron (50 mg, 200 μmol, 10.0 equiv.) and the correspondent gelator (**G1**, 10 mg/mL). Acetonitrile/H_2O (9/1 v/v) mixture (1.0 mL) was poured, and it was stirred until almost complete solution. Then, DIPEA (4.2 μL, 24 μmol, 1.2 equiv.) and dodecanenitrile (4.4 μL, 20 μmol, 1.0 equiv.) were added with 10 μL Hamilton syringe. Quickly, the vial was sealed with a septum. It was heated to 150 °C with heatgun for 1.5 minutes with manual stirring until complete clear solution.

The vial cooled to room temperature until gel formation was observed. The vial was frozen at 193K for 2 hours. Then, the reaction was irradiated with an external LED through the plain bottom side of the vial at 23 °C for 30 minutes. The reaction was monitored by GC-FID analysis. The gel was broken with dichloromethane (2 mL) and it was clean with brine (6 mL). The organic phase was dried over anhydrous sodium sulfate, filtered from the drying agent, and concentrated in vacuo.

4.6.9 Spectroscopic Measurements

The absorption spectra were recorded on a JASCO V-630 spectrophotometer.

Field-emission scanning electron microscopy (FESEM)

The equipment in operation in the UPV Microscopy Service is the ZEISS ULTRA 55 model, incorporating the following detectors:

- A Secondary Electron Detector (SE2), which provides an SEM topography image of the sample surface with a large depth of field.
- A Secondary Electron In-Lens Detector located inside the electron column, which works with low energy secondary electrons and provides images with a higher resolution.
- A Backscattered Electron Detector (AsB) which is sensitive to the variation of atomic number in the elements present in the sample; therefore, it is used to observe changes in the chemical composition of the specimen.
- A Backscattered Electron In-lens Detector (EsB), independent of the secondary In-lens detector, which provides a pure backscattered signal with no secondary electron contamination and very low acceleration potential.
- An X-Ray Dispersive Energy Detector, EDS, (Oxford Instruments) which receives x-rays from each surface point the electron beam passes over.

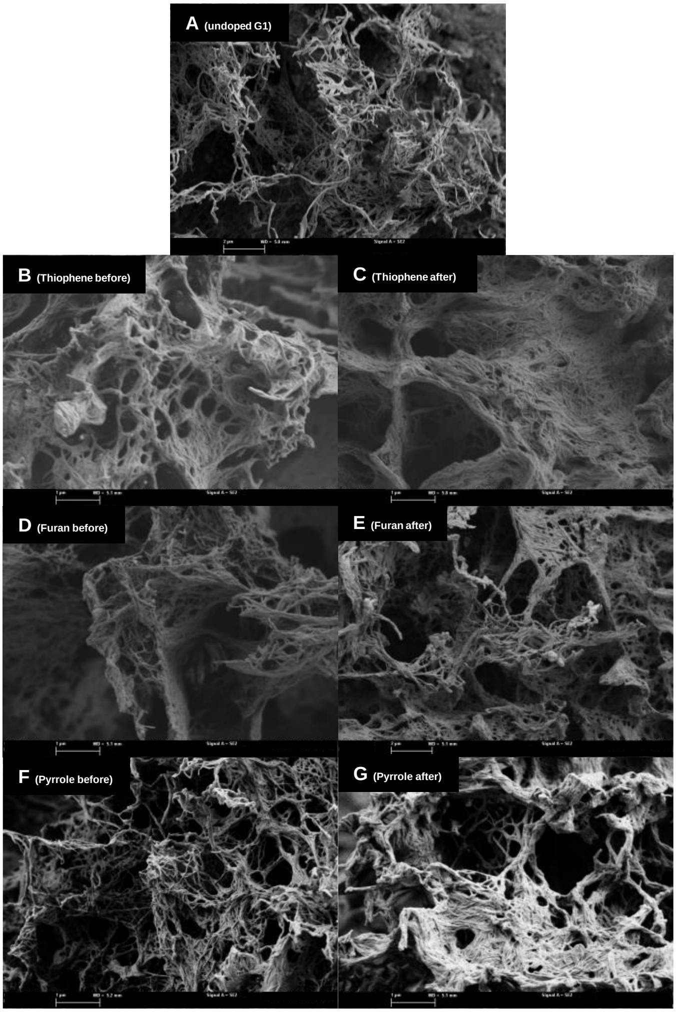


Figure E4. Representative field-emission scanning electron microscopy (FESEM) images. **A**: undoped gel of **G1** (10 mg/mL). **B, C**: gel of **G1** (10 mg/mL) doped with 2-acetyl-5-chlorothiophene (3.2 mg), B_2pin_2 (50 mg) and DIPEA (3.1 mg). **D, E**: gel of **G1** (10 mg/mL) doped with 2-acetyl-5-bromofuran (3.8 mg), B_2pin_2 (50 mg) and DIPEA (3.1 mg). **F, G**: gel of **G1** (10 mg/mL) doped with 2-acetyl-5-bromo-1H-methylpyrrole (4.0 mg), B_2pin_2 (50 mg) and DIPEA (3.1 mg).

4.6.10 Determination of gel-to-sol transition temperature (T_{gel})

T_{gel} values were determined using a custom-made set-up where a sealed vial was placed into a mold of an alumina block and heated up at 1 °C/5 min using an electric heating plate equipped with a temperature control couple as previously described (see for instance, *Chem. Commun.* **2015**, *51*, 16848-16851). The temperature at which the gel started to break was defined as T_{gel} with an estimated error of ± 2 ºC after several heating-cooling cycles.

UV-vis absorption spectra

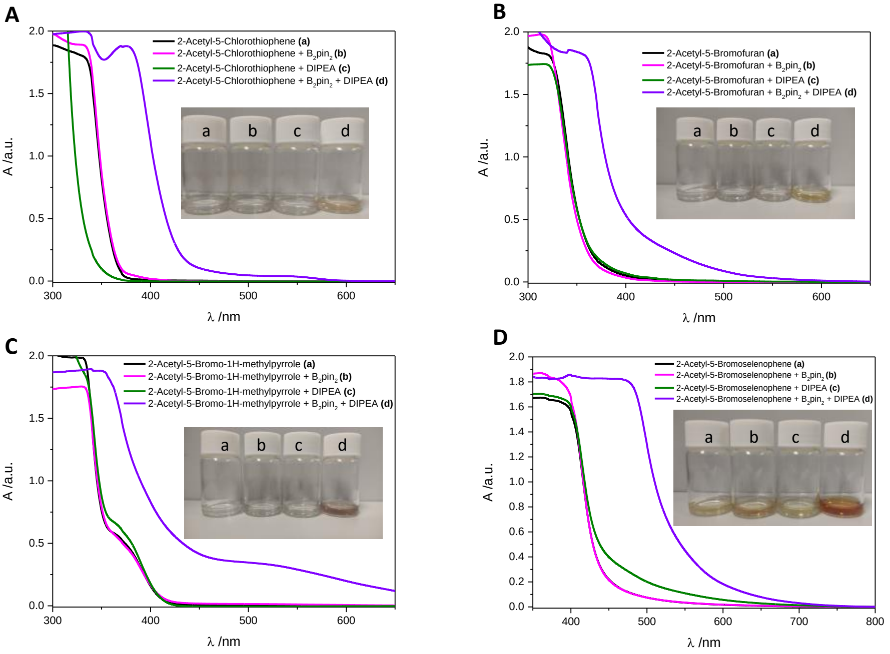


Figure E5. UV-vis absorption spectra. Inset: photographs of different solutions. **A**: 2-Acetyl-5-chlorothiophene (0.02 mmol), B_2pin_2 (0.2 mmol) and DIPEA (0.024 mmol) in ACN/H_2O 9/1 v/v 1 mL. **B**: 2-Acetyl-5-bromofuran (0.02 mmol), B_2pin_2 (0.2 mmol) and DIPEA (0.024 mmol) in ACN/H_2O 9/1 v/v 1 mL. **C**: 2-Acetyl-5-bromo-1*H*-methylpyrrole (0.02 mmol), B_2pin_2 (0.2 mmol) and DIPEA (0.024 mmol) in ACN/H_2O 9/1 v/v 1 mL. **D**: 2-Acetyl-5-bromoselenophene (0.02 mmol), B_2pin_2 (0.2 mmol) and DIPEA (0.024 mmol) in ACN/H_2O 9/1 v/v 1 mL.

4.6.11 Singlet Oxygen

Time-resolved measurements of $^1O_2$ luminiscence were performed in a front face setup in FLS 1000 (Edinburgh Instruments) spectrophotometer by making use of a 450W Xe lamp and a NIR sensitive PMT 1700 detector (H10330C-75, Hamamatsu) in Peltier Cooled Housing.

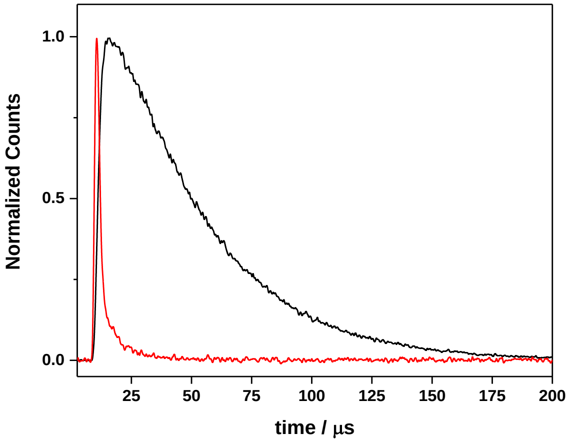


Figure E6. Decay traces of the $^1O_2$ emission (1275 nm) generated by an aerobic ACN/H_2O (9/1 v/v) solution of; **black**: Rose Bengal (0.1 mM, λ_{exc} = 532 nm); **red**: 1a+B_2pin_2+DIPEA (20 mM, 200 mM and 24 mM, respectively, λ_{exc} = 400 nm).

4.6.12 Trapping reaction

A vial (10 mL) was charged with heteroarene derivative (20 µmol, 1.0 equiv.), diborylates (200 µmol, 10.0 equiv.), diphenyl disulfide (20 µmol, 1.0 equiv.) and the correspondent gelator (**G1**, 10 mg/mL). Acetonitrile/H_2O (9/1 v/v) mixture (1.0 mL) was poured, and it was stirred until almost complete solution. Then, DIPEA (24 µmol, 1.2 equiv.) and dodecanenitrile (20 µmol, 1.0 equiv.) were added with 10 µL Hamilton syringe. Quickly, the vial was sealed with a septum. It was heated to 150 °C for 1.5 minutes with manual stirring until complete clear solution. The vial cooled to room temperature until gel formation was observed. The reaction was irradiated with an external LED through the plain bottom side of the vial at 23 °C for 3 hours.

Then, brine (6 mL) was added, and the aqueous phase was extracted with dichloromethane (2 mL). The reaction was monitored by GC-FID analysis. The organic phase was dried over anhydrous sodium sulfate, filtered from the drying agent, and concentrated in vacuo. After crystallization of the excess of starting diboron derivative, the crude was purified via TLC plastic sheet using a hexane/ethyl acetate mixture as the mobile phase.

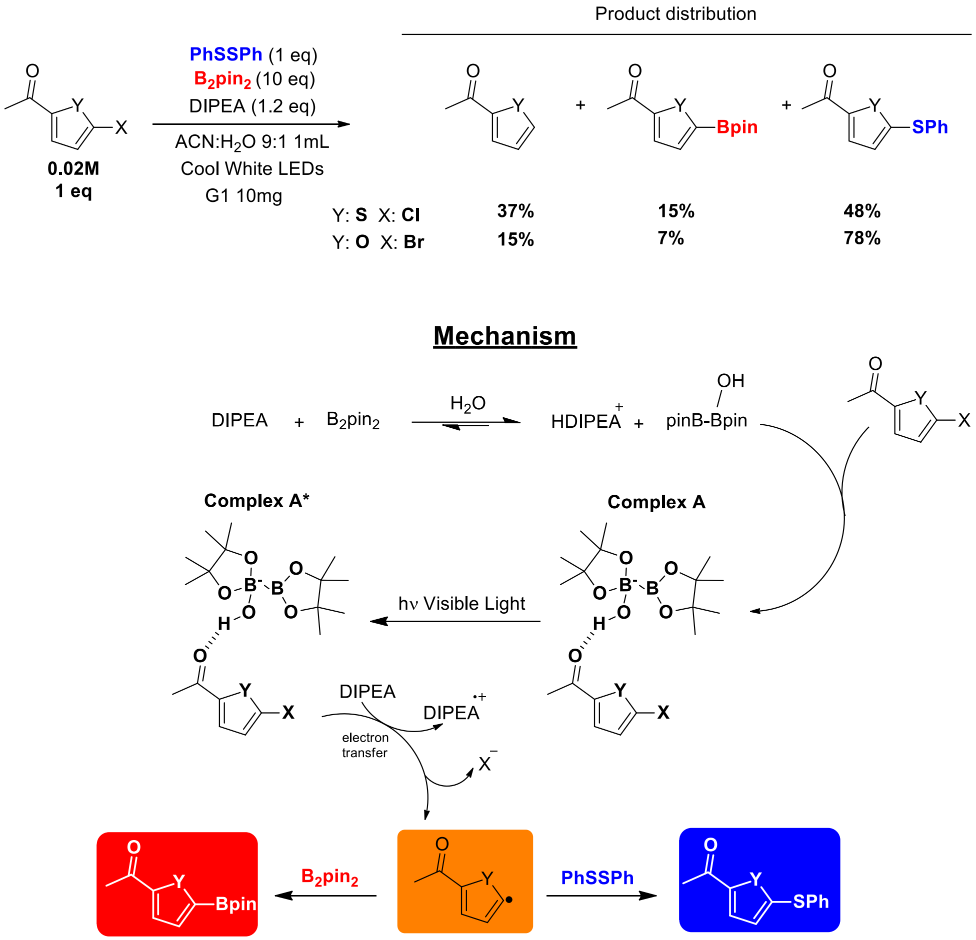
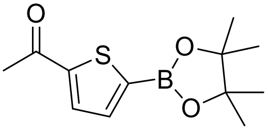


Figure E7. Trapping reaction and mechanism of 2-acetyl-5-chlorothiophene and 2-acetyl-5-bromofuran with diphenyl disulfide.

4.6.13 Characterization of compounds

THIOPHENES

2aa. 1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)ethenone

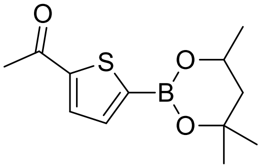


The compound (CAS 942070-32-8) was prepared according to the general procedure using 1-(5-chlorothiophen-2-yl)ethenone (3.2 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA

(4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 2 hours, obtaining 72% product yield according to GC-FID analysis (63% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 3.7 Hz, 1H), 7.58 (d, *J* = 3.7 Hz, 1H), 2.57 (s, 3H), 1.35 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8 (C), 149.6 (C), 137.4 (CH), 132.8 (CH), 84.8 (C), 27.6 (CH_3), 24.9 (CH_3).
Spectral data were consistent with literature.[1]

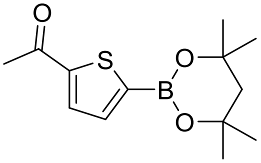
2ab. 1-(5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)ethenone



The compound (CAS 2414250-10-3) was prepared according to the general procedure using 1-(5-chlorothiophen-2-yl)ethenone (3.2 mg, 20 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 4 hours, obtaining 61% product yield according to GC-FID analysis (50% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 3.7 Hz, 1H), 7.43 (d, *J* = 3.7 Hz, 1H), 4.29 (ddd, *J* = 11.6, 6.1, 2.9 Hz, 1H), 2.50 (s, 3H), 1.82 (dd, *J* = 14.0, 2.9 Hz, 1H), 1.56 (dd, *J* = 13.9, 11.7 Hz, 1H), 1.31 (s, 6H), 1.28 (d, *J* = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8 (C), 148.2 (C), 135.5 (CH), 132.7 (CH), 72.1 (C), 65.8 (CH), 45.6 (CH_2), 31.1 (CH_3), 28.0 (CH_3), 27.7 (CH_3), 23.0 (CH_3) ppm.
Spectral data were consistent with literature.[1]

2ac. 1-(5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)ethenone



The compound (CAS 2414250-15-8) was prepared according to the general procedure using 1-(5-chlorothiophen-2-yl)ethenone (3.2 mg, 20 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL,

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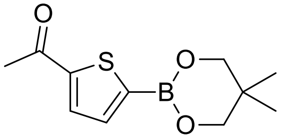
[1] J. C. Herrera-Luna, D. Sampedro, M. C. Jiménez and R. Pérez-Ruiz, *Organic Letters*, 2020, **22**, 3273-3278.

24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 63% product yield according to GC-FID analysis (50% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 3.7 Hz, 1H), 7.50 (d, *J* = 3.7 Hz, 1H), 2.55 (s, 3H), 1.92 (s, 2H), 1.41 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0 (C), 148.3 (C), 135.5 (CH), 132.8 (CH), 71.9 (C), 49.1 (CH_2), 31.8 (CH_3), 27.5 (CH_3) ppm.
Spectral data were consistent with literature.[1]

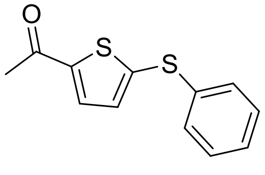
2ad. 1-(5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)ethenone



The compound (CAS 2414250-20-5) was prepared according to the general procedure using 1-(5-chlorothiophen-2-yl)ethenone (3.2 mg, 20 µmol, 1.0 equiv.), bis(neopentylglycolato)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 50% product yield according to GC-FID analysis (45% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 3.7 Hz, 1H), 7.50 (d, *J* = 3.7 Hz, 1H), 3.75 (s, 4H), 2.55 (s, 3H), 1.01 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.9 (C), 148.7 (C), 135.9 (CH), 132.9 (CH), 73.1 (CH_2), 32.1 (C), 27.5 (CH_3), 21.9 (CH_3) ppm.
Spectral data were consistent with literature.[1]

1-(5-(phenylthio)thiophen-2-yl)ethenone

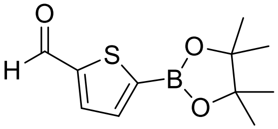


The compound (CAS: 90680-26-5) was prepared according to the general procedure using 1-(5-chlorothiophen-2-yl)ethenone (3.2 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), diphenyldisulfide (4.4 mg, 80 µmol, 1.0 equiv.) dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 3 hours, obtaining 78% product yield according to GC-FID analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 3.9 Hz, 1H), 7.43 – 7.38 (m, 2H), 7.36 – 7.28 (m, 3H), 7.10 (d, *J* = 3.9 Hz, 1H), 2.50 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.0 (C), 146.3 (C), 145.7 (C), 135.2 (C), 132.8 (CH), 132.1 (CH), 130.9 (CH), 129.6 (CH), 128.2 (CH), 26.6 (CH_3) ppm.
Spectral data were consistent with literature.[1]

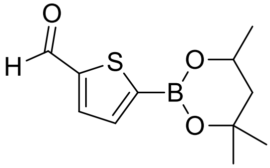
2ba. 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carbaldehyde



The compound (CAS 1040281-83-1) was prepared according to the general procedure using 5-bromothiophene-2-carbaldehyde (2.5 µL, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 66% product yield according to GC-FID analysis (52% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.79 (d, *J* = 3.7 Hz, 1H), 7.65 (d, *J* = 3.7 Hz, 1H), 1.35 (s, 12H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 183.1 (C), 149.1 (C), 137.4 (CH), 136.2 (CH), 85.0 (C), 24.9 (CH_3) ppm.
Spectral data were consistent with literature.[1]

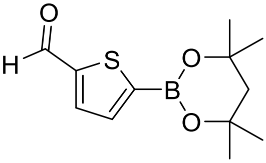
2bb. 5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophene-2-carbaldehyde



The compound (CAS 2414250-11-4) was prepared according to the general procedure using 5-bromothiophene-2-carbaldehyde (2.5 µL, 20 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 62% product yield according to GC-FID analysis (49% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 7.69 (d, *J* = 3.7 Hz, 1H), 7.49 (d, *J* = 3.7 Hz, 1H), 4.29 (ddd, *J* = 11.6, 6.1, 2.9 Hz, 1H), 1.82 (dd, *J* = 14.1, 2.9 Hz, 1H), 1.60 – 1.51 (m, 1H), 1.30 (s, 6H), 1.27 (d, *J* = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 183.1 (C), 147.8 (C), 136.2 (CH), 135.5 (CH), 71.9 (C), 65.7 (CH), 45.6 (CH_2), 31.0 (CH_3), 27.7 (CH_3), 22.9 (CH_3) ppm.
Spectral data were consistent with literature.[1]

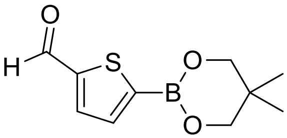
2bc. 5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophene-2-carbaldehyde



The compound (CAS 2414250-16-9) was prepared according to the general procedure using 5-bromothiophene-2-carbaldehyde (2.5 µL, 20 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 5 hours, obtaining 89% product yield according to GC-FID analysis (73% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 7.75 (d, *J* = 3.6 Hz, 1H), 7.57 (d, *J* = 3.6 Hz, 1H), 1.92 (s, 2H), 1.41 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3 (C), 147.9 (C), 136.3 (CH), 135.5 (CH), 72.0 (C), 49.1 (CH_2), 31.7 (CH_3) ppm.
Spectral data were consistent with literature.[1]

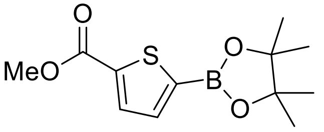
2bd. 5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophene-2-carbaldehyde



The compound (CAS 2414250-21-6) was prepared according to the general procedure using 5-bromothiophene-2-carbaldehyde (2.5 µL, 20 µmol, 1.0 equiv.), bis(neopentylglycolato)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 2 hours, obtaining 56% product yield according to GC-FID analysis (41% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.78 (d, *J* = 3.7 Hz, 1H), 7.59 (d, *J* = 3.7 Hz, 1H), 3.78 (s, 4H), 1.03 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3 (C), 148.3 (C), 136.4 (CH), 136.0 (CH), 72.7 (CH_2), 32.2 (C), 22.0 (CH_3) ppm.
Spectral data were consistent with literature.[1]

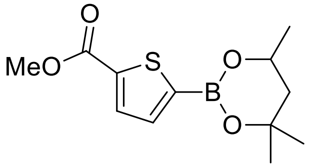
2ca. Methyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carboxylate



The compound (CAS 916138-13-1) was prepared according to the general procedure using methyl 5-bromothiophene-2-carboxylate (2.6 µL, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 20 hours, obtaining 26% product yield according to GC-FID analysis (19% isolated yield as white powder).

Spectral data were consistent with literature.[2]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 3.7 Hz, 1H), 7.54 (d, J = 3.6 Hz, 1H), 3.88 (s, 3H), 1.34 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8 (C), 139.5 (C), 137.0 (CH), 134.1 (CH), 84.7 (C), 52.4 (O-CH_3), 24.9 (CH_3) ppm.

2cb. Methyl 5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophene-2-carboxylate



The compound was prepared according to the general procedure using methyl 5-bromothiophene-2-carboxylate (2.6 µL, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 19 hours, obtaining 30% product yield according to GC-FID analysis (25% isolated yield as white powder).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 3.6 Hz, 1H), 7.47 (d, J = 3.6 Hz, 1H), 4.35 (ddd, J = 11.6, 6.0, 2.9 Hz, 1H), 3.87 (s, 3H), 1.87 (dd, J = 14.0, 2.9 Hz, 1H), 1.56 – 1.44 (m, 1H), 1.36 (s, 6H), 1.33 (d, J = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1 (C), 138.0 (C), 135.2 (CH), 134.0 (CH), 72.0 (C), 65.7 (CH), 52.2 (O-CH_3), 46.1 (CH_2) 31.05 (CH_3), 28.2 (CH_3), 21.18 (CH_3) ppm.
GC-MS (EI): m/z (relative intensity): 268.1 (40) [$M^{+\bullet}$], 253.1 (35), 237.1 (20), 169.0 (20), 137.0 (20), 43.1 (100).

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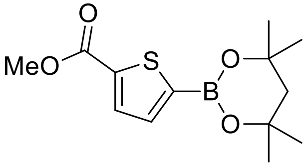
[2] Ghayoor A. Chotana, Venkata A. Kallepalli, Robert E. Maleczka Jr., Milton R. Smith III. *Tetrahedron* **2008**, *64*, 6103–6114.

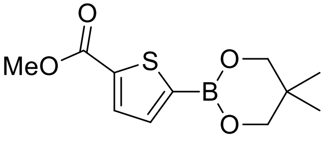
2cc. Methyl 5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophene-2-carboxylate



The compound was prepared according to the general procedure using methyl 5-bromothiophene-2-carboxylate (2.6 µL, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 5 hours, obtaining 23% product yield according to GC-FID analysis (15% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 3.6 Hz, 1H), 7.48 (d, J = 3.6 Hz, 1H), 3.87 (s, 3H), 1.92 (s, 2H), 1.41 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.03 (C), 137.96 (C), 135.18 (CH), 134.00 (CH), 119.97 (C), 71.81 (C), 52.17 ($O-CH_3$), 49.14 (CH_2), 31.76 (CH_3) ppm.
GC-MS (EI): m/z (relative intensity): 282.1 (100) [$M^{+\bullet}$], 267.1 (100), 251.1 (30), 183.0 (50), 169.0 (50), 137.0 (60), 99.1 (40), 56.1 (80), 43.1 (80).

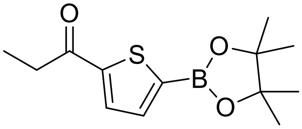
2cd. Methyl 5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophene-2-carboxylatecarboxylate



The compound was prepared according to the general procedure using methyl 5-bromothiophene-2-carboxylate (2.6 µL, 80 µmol, 1.0 equiv.), bis(neopentylglycoltao)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 5 hours, obtaining 24% product yield according to GC-FID analysis (16% isolated yield as rose-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 3.6 Hz, 1H), 7.49 (d, J = 3.6 Hz, 1H), 3.88 (s, 3H), 3.76 (s, 4H), 1.03 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3 (C), 135.7 (C), 134.1 (CH), 129.2 (CH), 72.6 (CH_2), 52.3 ($O-CH_3$), 32.2 (C), 22.0 (CH_3) ppm.
GC-MS (EI): m/z (relative intensity): 254.1 (40) [$M^{+\bullet}$], 223.1 (100), 136.9 (25), 111.0 (20), 70.1 (20), 61.0 (20), 43.1 (100).

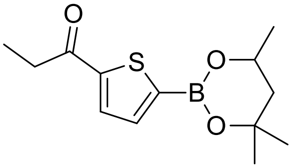
2da. 1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)propan-1-one



The compound (CAS 2414250-08-9) was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)propan-1-one (4.4 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 74% product yield according to GC-FID analysis (62% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 3.7 Hz, 1H), 7.55 (d, *J* = 3.7 Hz, 1H), 2.92 (q, *J* = 7.3 Hz, 2H), 1.32 (s, 12H), 1.21 – 1.17 (t, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9 (C), 149.2 (C), 137.3 (CH), 132.0 (CH), 84.7 (C), 33.2 (CH_2), 24.6 (CH_3), 8.5 (CH_3) ppm.
Spectral data were consistent with literature.[1]

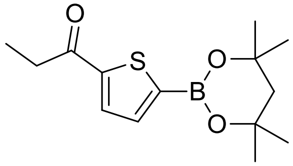
2db. 1-(5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)propan-1-one



The compound (CAS 2414250-12-5) was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)propan-1-one (4.4 mg, 20 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 81% product yield according to GC-FID analysis (69% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 3.7 Hz, 1H), 7.48 (d, *J* = 3.7 Hz, 1H), 4.33 (dqd, *J* = 12.4, 6.2, 2.9 Hz, 1H), 2.92 (q, *J* = 7.3 Hz, 2H), 1.86 (dd, *J* = 14.0, 2.9 Hz, 1H), 1.60 (dd, *J* = 13.9, 11.7 Hz, 1H), 1.35 (s, 6H), 1.32 (d, *J* = 6.2 Hz, 3H), 1.19 (t, *J* = 7.3 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1 (C), 148.0 (C), 135.5 (CH), 132.0 (CH), 72.0 (C), 65.7 (CH), 46.1 (CH_2), 33.1 (CH_2), 31.2 (CH_3), 28.1 (CH_3), 8.6 (CH_3) ppm.
Spectral data were consistent with literature.[1]

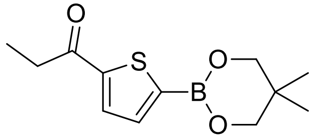
2dc. 1-(5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)propan-1-one



The compound (CAS 2414250-17-0) was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)propan-1-one (4.4 mg, 20 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 82% product yield according to GC-FID analysis (67% isolated yield as white powder).

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 3.7 Hz, 1H), 7.51 (d, *J* = 3.7 Hz, 1H), 2.94 (d, *J* = 7.3 Hz, 2H), 1.93 (s, 2H), 1.42 (s, 12H), 1.22 (t, *J* = 7.3 Hz, 3H) ppm.
^{13}**C NMR** (101 MHz, $CDCl_3$) δ 194.2 (C), 147.9 (C), 135.5 (CH), 132.1 (CH), 71.9 (C), 49.2 (CH_2), 33.2 (CH_3), 8.7 (CH_3) ppm.
Spectral data were consistent with literature.[1]

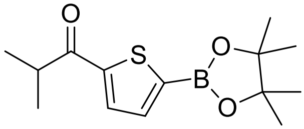
2dd. 1-(5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)propan-1-one



The compound (CAS 2414250-22-7) was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)propan-1-one (4.4 mg, 20 µmol, 1.0 equiv.), bis(neopentylglycolato)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 4 hours, obtaining 58% product yield according to GC-FID analysis (43% isolated yield as white powder).

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 3.7 Hz, 1H), 7.51 (d, *J* = 3.7 Hz, 1H), 3.76 (s, 4H), 2.94 (q, *J* = 7.3 Hz, 2H), 1.22 (t, *J* = 7.3 Hz, 3H), 1.03 (s, 6H) ppm.
^{13}**C NMR** (101 MHz, $CDCl_3$) δ 194.1 (C), 148.4 (C), 135.9 (CH), 132.1 (CH), 72.6 (CH_2), 33.2 (CH_2), 32.2 (C), 22.0 (CH_3), 8.6 (CH_3) ppm.
Spectral data were consistent with literature.[1]

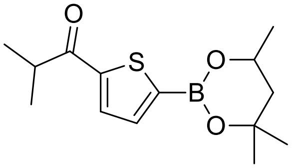
2ea. 2-methyl-1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)propan-1-one



The compound (CAS 2414250-09-0) was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)-2-methylpropan-1-one (3.2 µL, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 77% product yield according to GC-FID analysis (61% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 3.7 Hz, 1H), 7.58 (d, *J* = 3.7 Hz, 1H), 3.36 (dp, *J* = 13.7, 6.8 Hz, 1H), 1.34 (s, 12H), 1.23 (t, *J* = 4.4 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6 (C), 148.7 (C), 137.4 (CH), 132.2 (CH), 84.8 (C), 38.0 (CH), 24.9 (CH_3), 19.5 (CH_3) ppm.
Spectral data were consistent with literature.[1]

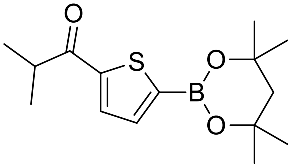
2eb. 2-methyl-1-(5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)propan-1-one



The compound (CAS 2414250-13-6) was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)-2-methylpropan-1-one (3.2 µL, 20 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 78% product yield according to GC-FID analysis (66% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 3.7 Hz, 1H), 7.46 (d, *J* = 3.7 Hz, 1H), 4.30 (ddd, *J* = 11.6, 6.1, 2.9 Hz, 1H), 3.33 (dt, *J* = 13.7, 6.8 Hz, 1H), 1.83 (dd, *J* = 14.0, 2.9 Hz, 1H), 1.57 (dd, *J* = 13.9, 11.7 Hz, 1H), 1.32 (s, 6H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.17 – 1.12 (m, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5 (C), 147.3 (C), 135.5 (CH), 132.0 (CH), 71.9 (C), 65.6 (CH), 46.0 (CH_2), 37.7 (CH), 31.1 (CH_3), 28.1 (CH_3), 23.0 (CH_3), 19.4 (CH_3) ppm.
Spectral data were consistent with literature.[1]

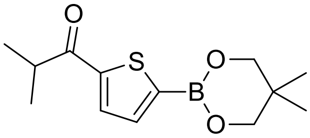
2ec. 2-methyl-1-(5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)propan-1-one



The compound (CAS 2414250-18-1) was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)-2-methylpropan-1-one (3.2 µL, 20 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 82% product yield according to GC-FID analysis (66% isolated yield as white powder).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.72 (d, *J* = 3.7 Hz, 1H), 7.52 (d, *J* = 3.7 Hz, 1H), 3.38 (dt, *J* = 13.7, 6.8 Hz, 1H), 1.93 (s, 2H), 1.42 (s, 12H), 1.23 (d, *J* = 6.8 Hz, 6H) ppm.
^{13}C NMR (101 MHz, CDCl$_3$) δ 197.8 (C), 147.4 (C), 135.6 (CH), 132.2 (CH), 71.9 (C), 49.2 (CH$_2$), 37.8 (CH), 31.8 (CH$_3$), 19.6 (CH$_3$) ppm.
Spectral data were consistent with literature.[1]

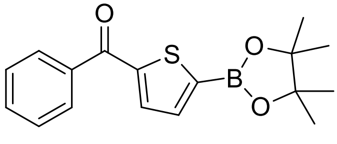
2ed. 1-(5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)-2-methylpropan-1-one



The compound (CAS 2414250-23-8) was prepared according to the general procedure using 1-(5-bromothiophen-2-yl)-2-methylpropan-1-one (3.2 µL, 20 µmol, 1.0 equiv.), bis(neopentylglycolato)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 2 hours, obtaining 54% product yield according to GC-FID analysis (40% isolated yield as white powder).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.74 (d, *J* = 3.7 Hz, 1H), 7.52 (d, *J* = 3.7 Hz, 1H), 3.77 (s, 4H), 3.43 – 3.25 (m, 1H), 1.23 (d, *J* = 6.8 Hz, 6H), 1.03 (s, 6H) ppm.
^{13}C NMR (101 MHz, CDCl$_3$) δ 197.7 (C), 147.8 (C), 136.0 (CH), 132.3 (C), 72.6 (CH$_2$), 37.9 (CH), 32.2 (C), 22.0 (CH$_3$), 19.5 (CH$_3$) ppm.
Spectral data were consistent with literature.[1]

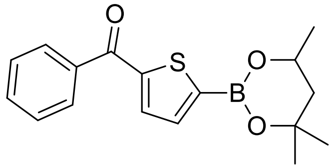
2fa. Phenyl(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)methanone



The compound (CAS 1220107-42-5) was prepared according to the general procedure using (5-bromothiophen-2-yl)(phenyl)methanone (5.5 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 68% product yield according to GC-FID analysis (51% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 2H), 7.70 (d, *J* = 3.7 Hz, 1H), 7.61 (d, *J* = 3.7 Hz, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 1.35 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.8 (C), 148.6 (C), 138.4 (C), 137.1 (CH), 135.0 (CH), 132.5 (CH), 129.4 (2xCH), 128.5 (2xCH), 84.8 (C), 24.7 (CH_3) ppm.
Spectral data were consistent with literature.[1]

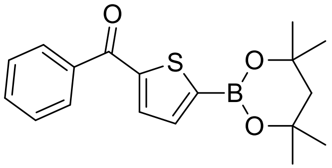
2fb. Phenyl(5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)methanone



The compound (CAS 2414250-14-7) was prepared according to the general procedure using (5-bromothiophen-2-yl)(phenyl)methanone (5.5 mg, 20 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 75% product yield according to GC-FID analysis (61% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.57 (d, *J* = 3.6 Hz, 1H), 7.49 (t, *J* = 7.1 Hz, 1H), 7.46 – 7.43 (m, 1H), 7.39 (t, *J* = 7.5 Hz, 2H), 4.35 – 4.21 (m, 1H), 1.81 (dd, *J* = 14.0, 2.7 Hz, 1H), 1.59 – 1.49 (m, 1H), 1.29 (s, 6H), 1.26 (d, *J* = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.0 (C), 147.1 (C), 138.3 (CH), 135.2 (CH), 134.8 (CH), 132.1 (CH), 129.1 (2xCH), 128.2 (2xCH), 71.8 (C), 65.5 (CH), 45.6 (CH_2), 31.0 (CH_3), 27.6 (CH_3), 22.9 (CH_3) ppm.
Spectral data were consistent with literature.[1]

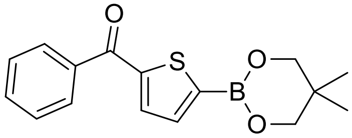
2fc. Phenyl(5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)methanone



The compound (CAS 2414250-19-2) was prepared according to the general procedure using (5-bromothiophen-2-yl)(phenyl)methanone (5.5 mg, 20 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 81% product yield according to GC-FID analysis (70% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 2H), 7.67 (d, *J* = 3.7 Hz, 1H), 7.57 (dd, *J* = 12.3, 5.5 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 1.94 (s, 2H), 1.43 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.5 (C), 147.3 (C), 138.7 (C), 135.3 (CH), 132.3 (CH), 129.4 (2xCH), 128.5 (2xCH), 71.9 (C), 49.2 (CH_2), 31.8 (CH_3) ppm.
Spectral data were consistent with literature.[1]

2fd. (5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophen-2-yl)(phenyl)methanone

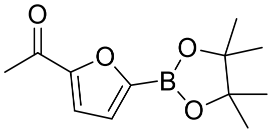


The compound (CAS 2414250-24-9) was prepared according to the general procedure using (5-bromothiophen-2-yl)(phenyl)methanone (5.5 mg, 20 µmol, 1.0 equiv.), bis(neopentylglycoltao)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 2 hours, obtaining 42% product yield according to GC-FID analysis (35% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, CDCl3) δ 7.88 (d, J = 7.4 Hz, 2H), 7.69 (d, J = 3.7 Hz, 1H), 7.57 (dd, J = 12.0, 5.5 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 3.78 (s, 4H), 1.04 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.4 (C), 147.7 (C), 138.5 (C), 135.7 (CH), 135.2 (CH), 132.4 (CH), 129.4 (CH), 128.5 (CH), 72.7 (CH_2), 32.2 (C), 22.0 (CH_3) ppm.
Spectral data were consistent with literature.[1]

FURANS

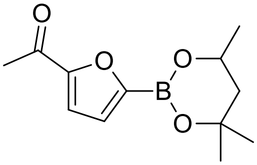
3aa. 1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)furan-2-yl)ethanone



The compound was prepared according to the general procedure using 1-(5-bromofuran-2-yl)ethanone (3.8 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 22 hours, obtaining 56% product yield according to GC-FID analysis (45% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 3.5 Hz, 1H), 7.09 (d, J = 3.5 Hz, 1H), 2.54 (s, 3H), 1.36 (s, J = 5.3 Hz, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.6 (C), 163.2 (C), 124.5 (CH), 116.5 (CH), 84.9 (C), 26.6 (CH_3), 24.8 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{18}BO_4$: 237.1293, found: 237.1297.

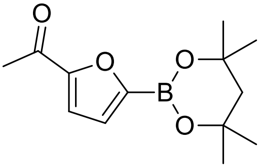
3ab. 1-(5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)furan-2-yl)ethanone



The compound was prepared according to the general procedure using 1-(5-bromofuran-2-yl)ethenone (3.8 mg, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 6 hours, obtaining 85% product yield according to GC-FID analysis (63% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, J = 3.5 Hz, 1H), 6.97 (d, J = 3.5 Hz, 1H), 4.36 (ddd, J = 11.6, 6.1, 2.9 Hz, 1H), 2.52 (s, 3H), 1.88 (dd, J = 14.1, 2.9 Hz, 1H), 1.65-1.59 (m, 1H), 1.37 (d, J = 2.4 Hz, 6H), 1.35 (d, J = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 187.8 (C), 155.8 (C), 122.6 (CH), 117.0 (CH), 72.2 (C), 65.8 (CH), 46.2 (CH_2), 31.2 (CH_3), 28.2 (CH_3), 23.1 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{17}BO_4$: 236.0706, found: 236.0711.

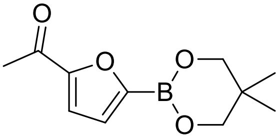
3ac. 1-(5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)furan-2-yl)ethanone



The compound was prepared according to the general procedure using 1-(5-bromofuran-2-yl)ethanone (3.8 mg, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 6 hours, obtaining 73% product yield according to GC-FID analysis (60% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, J = 3.5 Hz, 1H), 6.93 (d, J = 3.5 Hz, 1H), 2.46 (s, 3H), 1.88 (s, 2H), 1.37 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 187.7 (C), 155.6 (C), 122.4 (CH), 117.0 (CH), 71.8 (C), 49.2 (CH_2), 31.6 (CH_3), 26.3 (CH_3) ppm.
GC-MS (EI): m/z (relative intensity): 250.1 (20) [$M^{+•}$], 235.1 (30), 251.1 (30), 151.1 (20), 137.0 (20), 70.1 (20), 61.1 (20), 56.1 (10), 43.1 (100).

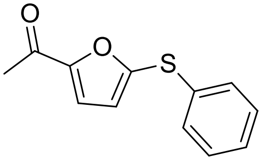
3ad. 1-(5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)furan-2-yl)ethanone



The compound was prepared according to the general procedure using 1-(5-bromofuran-2-yl)ethanone (3.8 mg, 80 µmol, 1.0 equiv.), bis(neopentylglycoltao)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 20 hours, obtaining 51% product yield according to GC-FID analysis (39% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 3.5 Hz, 1H), 7.00 (d, J = 3.5 Hz, 1H), 3.77 (s, 4H), 2.53 (s, 3H), 1.03 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 187.7 (C), 156.0 (C), 123.0 (CH), 116.8 (CH), 72.5 (C), 32.1 (CH_2), 26.5 (CH_3), 21.4 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{11}H_{15}BO_4$: 223.1117, found: 223.1125.

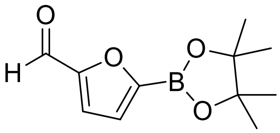
1-(5-(phenylthio)furan-2-yl)ethanone



The compound (CAS: 28569-36-0) was prepared according to the general procedure using 1-(5-bromofuran-2-yl)ethanone (3.8 mg, 80 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), diphenyldisulfide (4.4 mg, 80 µmol, 1.0 equiv.) dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 3 hours, obtaining 78% product yield according to GC-FID analysis (54% isolated yield as brown-yellow powder).

This compound is commercially available.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 5H), 7.17 (d, J = 3.5 Hz, 1H), 6.63 (d, J = 3.5 Hz, 1H), 2.45 (s, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 186.5 (C), 155.1 (C), 150.6 (C), 133.2 (C), 130.3 (CH), 129.6 (CH), 127.9 (CH), 118.6 (CH), 118.3 (CH), 26.1 (CH_3) ppm.

3ba. 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)furan-2-carbaldehyde



The compound (CAS 273731-82-1) was prepared according to the general procedure using 5-bromofuran-2-carbaldehyde (3.6 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 5 hours, obtaining 35% product yield according to GC-FID analysis (23% isolated yield as yellow-pale powder).

Spectral data were consistent with literature.[3]
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.23 (d, J = 3.6 Hz, 1H), 7.13 (d, J = 3.6 Hz, 1H), 1.35 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 179.4 (C), 156.4 (C), 124.5 (CH), 118.5 (CH), 85.1 (C), 24.9 (CH_3) ppm.

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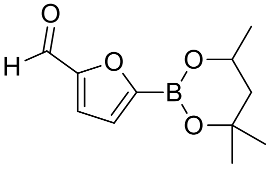
[3] Akitake Yamaguchi, Sherif J. Kaldas, Solomon D. Appavoo, Diego B. Diaz and Andrei K. Yudi. *Chem. Commun.,* **2019**, *55*, 10567-10570.

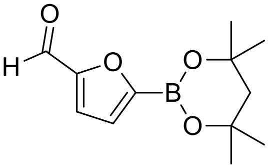
3bb. 5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)furan-2-carbaldehyde



The compound (CAS 1603976-11-9) was prepared according to the general procedure using methyl 5-bromo-2-furaldehyde (3.6 mg, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 20 hours, obtaining 54% product yield according to GC-FID analysis (45% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.21 (d, J = 3.6 Hz, 1H), 7.03 (d, J = 3.5 Hz, 1H), 4.37 (m, J = 12.3, 6.2, 2.8 Hz, 1H), 1.90 (dd, J = 14.1, 2.9 Hz, 1H), 1.65 (d, J = 12.0 Hz, 1H), 1.39 (d, J = 2.9 Hz, 6H), 1.36 (d, J = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 179.4 (C), 155.8 (C), 122.6.1 (CH), 119.5 (CH), 72.4 (C), 65.9 (CH), 46.3 (CH_2), 31.2 (CH_3), 28.2 (CH_3), 23.1 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{11}H_{16}BO_4$: 223.1136, found: 223.1139.

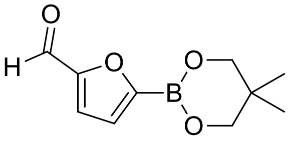
3bc. 5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)furan-2-carbaldehyde



The compound was prepared according to the general procedure using methyl 5-bromo-2-furaldehyde (3.6 mg, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 20 hours, obtaining 66% product yield according to GC-FID analysis (58% isolated yield yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.22 (d, J = 3.5 Hz, 1H), 7.04 (d, J = 3.5 Hz, 1H), 1.95 (s, 2H), 1.44 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 179.4 (C), 155.8 (C), 126.7 (CH), 119.6 (CH), 72.1 (C), 49.3 (CH_2), 31.8 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{17}BO_4$: 237.1293, found: 237.1299.

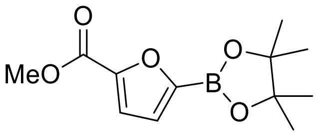
3bd. 5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)furan-2-carbaldehyde



The compound (CAS 1218791-07-1) was prepared according to the general procedure using 5-bromofuran-2-carbaldehyde (3.6 mg, 80 µmol, 1.0 equiv.), bis(neopentylglycoltao)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 20 hours, obtaining 80% product yield according to GC-FID analysis (62% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.22 (d, J = 3.6 Hz, 1H), 7.05 (d, J = 3.6 Hz, 1H), 3.78 (s, 4H), 1.03 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 179.2 (C), 156.0 (C), 123.0 (CH), 119.0 (CH), 72.6 (C), 32.3 (CH_2), 22.0 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{10}H_{14}BO_4$: 209.0985, found: 209.0982.

3ca. Methyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)furan-2-carboxylate



The compound (CAS 676501-87-4) was prepared according to the general procedure using methyl 5-bromofuran-2-carboxylate (4.1 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 22 hours, obtaining 60% product yield according to GC-FID analysis (51% isolated yield as yellow-pale powder).

Spectral data were consistent with literature.[4]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, J = 13.5, 3.5 Hz, 1H), 7.07 (d, J = 3.5 Hz, 1H), 3.88 (s, 3H), 1.33 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3 (C), 148.5 (C), 124.3 (C), 118.1 (C), 84.9 (C), 52.1 (O-CH_3), 24.2 (CH_3) ppm.

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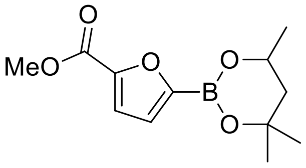
[4] Neely, Jamie M.; Bezdek, Mate J.; Chirik, Paul J. *ACS Central Science* **2016**, *2*, (12), 935-942.

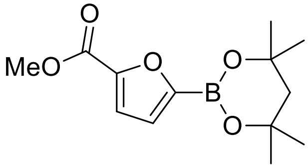
3cb. Methyl 5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)furan-2-carboxylate



The compound (CAS 1451144-93-6) was prepared according to the general procedure using methyl 5-bromofuran-2-carboxylate (4.1 mg, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 20 hours, obtaining 74% product yield according to GC-FID analysis (61% isolated yield as white powder).

Spectral data were consistent with literature.[5]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, J = 3.4 Hz, 1H), 6.92 (d, J = 3.4 Hz, 1H), 4.31 (dtd, J = 12.4, 6.2, 2.9 Hz, 1H), 3.85 (s, 3H), 1.84 (dd, J = 14.0, 2.9 Hz, 1H), 1.63 – 1.52 (m, 1H), 1.33 (d, J = 3.8 Hz, 6H), 1.31 (d, J = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4 (C), 147.5 (C), 122.0 (C), 118.0 (CH), 116.4 (CH), 72.0 (C), 65.7 (CH), 51.9 (O-CH_3), 46.2 (CH_2), 31.0 (CH_3), 28.1 (CH_3), 23.0 (CH_3) ppm.

3cc. Methyl 5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)furan-2-carboxylate



The compound was prepared according to the general procedure using methyl 5-bromofuran-2-carboxylate (4.1 mg, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 20 hours, obtaining 75% product yield according to GC-FID analysis (64% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, J = 3.4 Hz, 1H), 6.93 (d, J = 3.4 Hz, 1H), 3.85 (s, 3H), 1.88 (s, 2H), 1.39 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5 (C), 147.4 (C), 122.1 (CH), 118.1 (CH), 71.8 (C), 51.9 (O-CH_3), 49.3 (CH_2), 31.7 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{13}H_{20}BO_5$: 267.1188, found: 267.1183.

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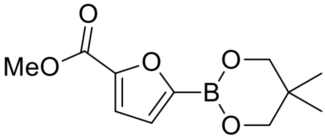
[5] Liskey, Carl W.; Hartwig, John F. *Synthesis* **2013**, *45*(13), 1837-1842.

3cd. Methyl 5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)furan-2-carboxylate

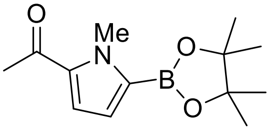


The compound was prepared according to the general procedure using methyl 5-bromofuran-2-carboxylate (4.1 mg, 80 µmol, 1.0 equiv.), bis(neopentylglycoltao)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 20 hours, obtaining 72% product yield according to GC-FID analysis (60% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 3.5 Hz, 1H), 6.98 (d, J = 3.5 Hz, 1H), 3.89 (s, 3H), 3.76 (s, 4H), 1.02 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4 (C), 147.9 (C), 122.5 (CH), 118.2 (CH), 73.1 (C), 52.1 (O-CH_3), 32.2 (CH_2), 21.7 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{11}H_{15}BO_5$: 239.1085, found: 239.1078.

PYRROLES

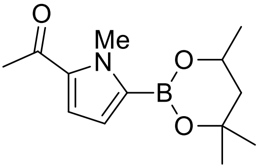
4aa. 1-(1-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrol-2-yl)ethanone



The compound was prepared according to the general procedure using 5-bromo-1-methyl-1H-pyrrole-2-carbaldehyde (4.0 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 22 hours, obtaining 91% product yield according to GC-FID analysis (72% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (d, J = 4.1 Hz, 1H), 6.70 (d, J = 4.0 Hz, 1H), 4.12 (s, 3H), 2.46 (s, 3H), 1.33 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 189.6 (C), 168.7 (C), 120.3 (CH), 119.0 (CH), 84.0 (C), 36.7 (CH_3), 28.2 (CH_3), 24.9 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{13}H_{20}BNO_3$: 250.1609, found: 250.1604.

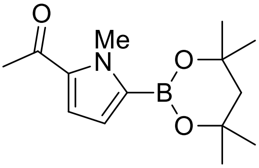
4ab. 1-(1-Methyl-5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)-1H-pyrrol-2-yl)ethanone



The compound was prepared according to the general procedure using 5-bromo-1-methyl-1H-pyrrole-2-carbaldehyde (4.0 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 20 hours, obtaining 83% product yield according to GC-FID analysis (61% isolated yield as yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (d, J = 4.0 Hz, 1H), 6.63 (d, J = 4.0 Hz, 1H), 4.33 (m, 1H), 4.12 (s, 3H), 2.43 (s, 3H), 1.86 (dd, J = 14.0, 2.9 Hz, 1H), 1.57 (t, J = 13.9 Hz, 1H), 1.35 (s, 6H), 1.32 (d, J = 6.1 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 189.4 (C), 165.7 (C), 119.1 (CH), 119.0 (CH), 71.8 (C), 65.5 (CH), 46.2 (CH_2), 36.4 (CH_3), 31.5 (CH_3), 28.3 (CH_3), 28.2 (CH_3), 23.3 (CH_3) ppm.
GC-MS (EI): m/z (relative intensity): 249.2 (30) [$M^{+\bullet}$], 234.1 (50), 134.1 (30), 70.1 (15), 61.0 (20), 56.1 (5), 43.1 (100).

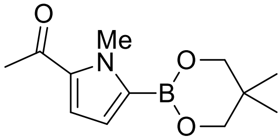
4ac. 1-(1-Methyl-5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)-1H-pyrrol-2-yl)ethanone



The compound was prepared according to the general procedure using 5-bromo-1-methyl-1H-pyrrole-2-carbaldehyde (4.0 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 20 hours, obtaining 85% product yield according to GC-FID analysis (63% isolated yield as yellow-pale powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (d, J = 4.0 Hz, 1H), 6.64 (d, J = 4.0 Hz, 1H), 4.14 (s, 3H), 2.44 (s, 3H), 1.91 (s, 2H), 1.41 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 189.4 (C), 134.8 (C), 119.1 (CH), 119.0 (CH), 71.5 (C), 49.0 (CH_2), 36.3 (CH_3), 31.9 (CH_3), 28.2 (CH_3) ppm.
GC-MS (EI): m/z (relative intensity): 263.1 (5) [$M^{+\bullet}$], 248.1 (5), 149.0 (5), 88.1 (10), 70.1 (20), 61.1 (30), 43.0 (100).

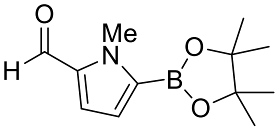
4ad. 1-(5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-methyl-1H-pyrrol-2-yl)ethanone



The compound was prepared according to the general procedure using 5-bromo-1-methyl-1H-pyrrole-2-carbaldehyde (4.0 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 20 hours, obtaining 65% product yield according to GC-FID analysis (44% isolated yield as yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (d, J = 3.7 Hz, 1H), 6.64 (d, J = 3.8 Hz, 1H), 4.11 (s, 3H), 3.74 (s, 4H), 2.44 (s, 3H), 1.01 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 189.5 (C), 135.0 (C), 119.3 (CH), 119.1 (CH), 73.1 (C), 36.4 (CH_3), 32.0 (CH_2), 28.2 (CH_3), 21.7 (CH_3) ppm.
GC-MS (EI): m/z (relative intensity): 235.1 (15) [$M^{+\bullet}$], 220.1 (40), 192.0 (5), 148.9 (5), 134.0 (10), 105.9 (5), 88.0 (10), 70.0 (20), 61.0 (20), 52.9 (5), 43.1 (100).

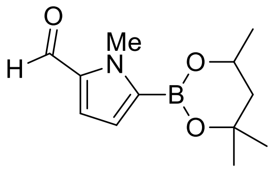
4ba. 1-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrole-2-carbaldehyde



The compound was prepared according to the general procedure using 5-bromo-1-methyl-1H-pyrrole-2-carbaldehyde (3.8 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 20 hours, obtaining 72% product yield according to GC-FID analysis (56% isolated yield as reddish to black powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 6.81 (d, J = 4.0 Hz, 1H), 6.67 (d, J = 4.0 Hz, 1H), 4.05 (s, 3H), 1.25 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 178.3 (C), 136.0 (C), 123.1 (CH), 112.6 (CH), 84.0 (C), 36.5 (CH_3), 24.0 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{18}BNO_3$: 236.0725, found: 236.0713.

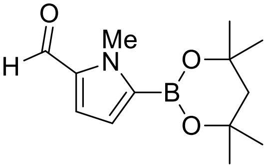
4bb. 1-Methyl-5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)-1H-pyrrole-2-carbaldehyde



The compound was prepared according to the general procedure using 5-bromo-1-methyl-1H-pyrrole-2-carbaldehyde (3.8 mg, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 14 hours, obtaining 81% product yield according to GC-FID analysis (65% isolated yield as reddish to black powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (s, 1H), 6.86 (d, J = 4.0 Hz, 1H), 6.69 (d, J = 4.0 Hz, 1H), 4.34 (ddd, J = 11.6, 6.1, 2.9 Hz, 1H), 4.13 (s, 3H), 1.88 (dd, J = 14.0, 2.9 Hz, 1H), 1.60 (t, J = 12.7 Hz, 1H), 1.37 (s, 6H), 1.33 (d, J = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 180.3 (C), 135.9 (C), 123.5 (CH), 120.0 (CH), 109.7 (CH), 71.9 (C), 65.6 (CH), 46.1 (CH_2), 35.5 (CH_3), 31.3 (CH_3), 28.3 (CH_3), 23.2 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{18}BNO_3$: 236.1453, found: 236.1445.

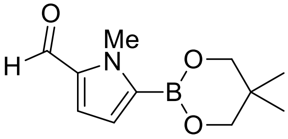
4bc. 1-Methyl-5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)-1H-pyrrole-2-carbaldehyde



The compound was prepared according to the general procedure using 5-bromo-1-methyl-1H-pyrrole-2-carbaldehyde (3.8 mg, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 20 hours, obtaining 74% product yield according to GC-FID analysis (59% isolated yield as reddish to black powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 6.85 (d, J = 4.0 Hz, 1H), 6.68 (d, J = 4.0 Hz, 1H), 4.13 (s, 3H), 1.91 (s, 2H), 1.40 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 179.7 (C), 135.8 (C), 123.4 (CH), 109.6 (CH), 71.6 (C), 49.0 (CH_2), 35.5 (CH_3), 31.8 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{13}H_{20}BNO_3$: 250.1609, found: 250.1604.

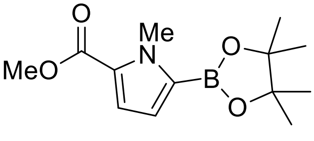
4bd. 5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-methyl-1H-pyrrole-2-carbaldehyde



The compound was prepared according to the general procedure using 5-bromo-1-methyl-1H-pyrrole-2-carbaldehyde (3.8 mg, 80 µmol, 1.0 equiv.), bis(neopentylglycoltao)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10 g/L). The reaction mixture was irradiated for 14 hours, obtaining 64% product yield according to GC-FID analysis (51% isolated yield reddish to black powder).

^{1}H NMR (400 MHz, $CDCl_3$) 9.59 (s, 1H), 6.85 (d, J = 4.0 Hz, 1H), 6.68 (d, J = 4.0 Hz, 1H), 4.11 (s, 3H), 3.73 (s, 4H), 1.00 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 179.7 (C), 132.2 (C), 124.3 (CH), 109.6 (CH), 73.0 (C), 36.4 (CH_3), 32.1 (CH_2), 21.7 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{11}H_{16}BNO_3$: 223.0944, found: 223.0956.

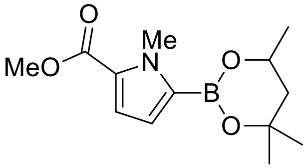
4ca. Methyl 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrole-2-carboxylate



The compound (CAS 2377607-43-5) was prepared according to the general procedure using methyl 5-bromo-1-methyl-1H-pyrrole-2-carboxylate (4.4 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 18 hours, obtaining 69% product yield according to GC-FID analysis (55% isolated yield as yellow-pale oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (d, J = 4.0 Hz, 1H), 6.70 (d, J = 4.0 Hz, 1H), 4.13 (s, 3H), 3.81 (s, 3H), 1.32 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.91 (C), 127.49 (C), 120.41 (CH), 117.29 (CH), 83.85 (C), 51.27 (O-CH_3), 35.92 (CH_3), 24.92 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{13}H_{21}BNO_4$: 266.1559, found: 266.1564.

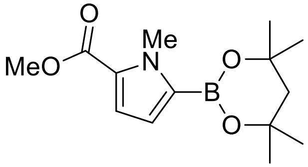
4cb. Methyl 1-methyl-5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)-1H-pyrrole-2-carboxylate



The compound was prepared according to the general procedure using methyl 5-bromo-1-methyl-1H-pyrrole-2-carboxylate (4.4 mg, 80 µmol, 1.0 equiv.), bis(hexyleneglycolato)diboron (53.0 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 19 hours, obtaining 76% product yield according to GC-FID analysis (62% isolated yield as yellow-pale oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (d, J = 3.9 Hz, 1H), 6.64 (d, J = 3.9 Hz, 1H), 4.32 (ddd, J = 11.7, 6.0, 3.0 Hz, 1H), 4.12 (s, 3H), 3.80 (s, 3H), 1.85 (dd, J = 13.9, 2.9 Hz, 1H), 1.63 – 1.52 (m, 1H), 1.36 (s, 6H), 1.32 (d, J = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1 (C), 126.7 (C), 119.1 (CH), 117.1 (CH), 71.6 (C), 65.4 (CH), 51.1 (O-CH_3), 46.1 (CH_2), 35.5 (CH_3), 31.4 (CH_3), 28.3 (CH_3), 23.3 (CH_3) ppm.
GC-MS (EI): m/z (relative intensity): 265.1 (60) [$M^{+\bullet}$], 233.9 (30), 206.8 (20), 166.0 (50), 152.0 (20), 134.1 (40), 108.0 (30), 72.1 (20), 43.1 (100).

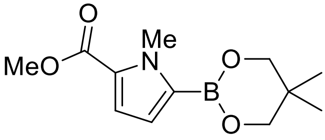
4cc. Methyl 1-methyl-5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)-1H-pyrrole-2-carboxylate



The compound was prepared according to the general procedure using methyl 5-bromo-1-methyl-1H-pyrrole-2-carboxylate (4.4 mg, 80 µmol, 1.0 equiv.), 4,4,4',4',6,6,6',6'-octamethyl-2,2'-bi(1,3,2-dioxaborinane) (56.4 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 15 hours, obtaining 77% product yield according to GC-FID analysis (63% isolated yield as yellow-pale oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (d, J = 3.9 Hz, 1H), 6.65 (d, J = 3.9 Hz, 1H), 4.14 (s, 3H), 3.80 (s, 3H), 1.91 (s, 2H), 1.41 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2 (C), 120.0 (C), 119.1 (CH), 117.1 (CH), 71.4 (C), 51.1 (O-CH_3), 49.1 (CH_2), 35.6 (CH_3), 31.9 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{14}H_{22}BNO_4$: 280.1715, found: 280.1710.

4cd. Methyl 5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-methyl-1H-pyrrole-2-carboxylate

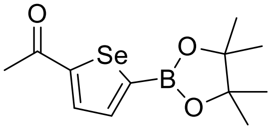


The compound was prepared according to the general procedure using methyl 5-bromo-1-methyl-1H-pyrrole-2-carboxylate (4.4 mg, 80 µmol, 1.0 equiv.), bis(neopentylglycoltao)diboron (45.2 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 19 hours, obtaining 44% product yield according to GC-FID analysis (36% isolated yield as yellow-pale oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (d, J = 3.9 Hz, 1H), 6.65 (d, J = 3.9 Hz, 1H), 4.12 (s, 3H), 3.80 (s, 3H), 3.74 (s, 4H), 1.02 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1 (C), 119.4 (C), 117.2 (CH), 111.8 (CH), 73.1 (CH_2), 51.2 (O-CH_3), 35.8 (CH_3), 32.1 (CH_3), 21.6 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{19}BNO_4$: 252.1402, found: 252.1406.

SELENOPHENES

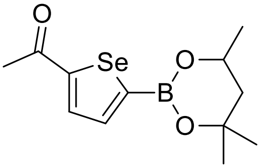
5aa. 1-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)selenophen-2-yl)ethenone



The compound was prepared according to the general procedure using 1-(5-bromoselenophen-2-yl)ethanone (5.0 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 16 hours, obtaining 84% product yield according to GC-FID analysis (70% isolated yield as yellow-brown powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 3.9 Hz, 1H), 7.90 (d, J = 3.9 Hz, 1H), 2.58 (s, 3H), 1.34 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2 (C), 156.8 (C), 140.0 (CH), 135.6 (CH), 84.8 (C), 26.9 (CH_3), 24.9 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{17}BO_3Se$: 301.0509, found: 301.0515.

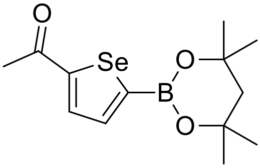
5ab. 1-(5-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)selenophen-2-yl)ethanone



The compound was prepared according to the general procedure using 1-(5-bromoselenophen-2-yl)ethanone (5.0 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 16 hours, obtaining 86% product yield according to GC-FID analysis (73% isolated yield as yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 3.8 Hz, 1H), 7.81 (d, J = 3.9 Hz, 1H), 4.34 (dtt, J = 12.2, 6.1, 3.1 Hz, 1H), 2.56 (s, 3H), 1.87 (dd, J = 14.0, 2.9 Hz, 1H), 1.67 – 1.56 (m, 1H), 1.36 (s, 6H), 1.33 (d, J = 6.2 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.3 (C), 155.1 (C), 137.9 (CH), 135.7 (CH), 72.1 (C), 65.8 (CH), 46.1 (CH_2), 31.2 (CH_3), 28.2 (CH_3), 26.8 (CH_3), 23.2 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{17}BO_3Se$: 301.0509, found: 301.0502.

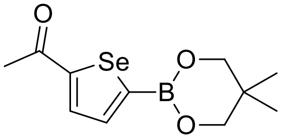
5ac. 1-(5-(4,4,6,6-tetramethyl-1,3,2-dioxaborinan-2-yl)selenophen-2-yl)ethanone



The compound was prepared according to the general procedure using 1-(5-bromoselenophen-2-yl)ethanone (5.0 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 16 hours, obtaining 88% product yield according to GC-FID analysis (69% isolated yield as yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 3.9 Hz, 1H), 7.83 (d, J = 3.9 Hz, 1H), 2.57 (s, 3H), 1.92 (s, 2H), 1.42 (s, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.3 (C), 155.0 (C), 137.8 (CH), 135.7 (CH), 71.9 (C), 49.1 (CH_2), 31.8 (CH_3), 26.8 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{13}H_{19}BO_3Se$: 315.0665, found: 315.0658.

5ad. 1-(5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)selenophen-2-yl)ethanone



The compound was prepared according to the general procedure using 1-(5-bromoselenophen-2-yl)ethanone (5.0 mg, 20 µmol, 1.0 equiv.), bis(pinacolato)diboron (50.6 mg, 200 µmol, 10.0 equiv.), dodecanenitrile (4.4 µL, 20 µmol, 1.0 equiv.) as internal standard and DIPEA (4.2 µL, 24 µmol, 1.2 equiv.) and G1 (10g/L). The reaction mixture was irradiated for 22 hours, obtaining 68% product yield according to GC-FID analysis (51% isolated yield as yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 3.9 Hz, 1H), 7.84 (d, J = 3.9 Hz, 1H), 3.76 (s, 4H), 2.58 (s, 3H), 1.03 (s, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 207.1 (C), 155.1 (C), 138.4 (CH), 135.8 (CH), 72.7 (C), 31.1 (CH_2), 26.8 (CH_3), 22.0 (CH_3) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{11}H_{15}BO_3Se$: 285.0060, found: 285.2277.

Chapter 5

Highly Efficient Production of Heteroarene Phosphonates by Dichromatic Photoredox Catalysis

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Highly Efficient Production of Heteroarene Phosphonates by Dichromatic Photoredox Catalysis

5.1 Abstract

A new strategy to achieve efficient aerobic phosphorylation of five-membered heteraroenes with excellent yields using dichromatic photoredox catalysis in a gel-based nanoreactor is described here. The procedure involves visible aerobic irradiation (cold white LEDs) of a mixture containing the heteroarene halide, trisubstituted phospite, *N*,*N*-diisopropylethylamine (DIPEA) as sacrificial agent, and catalytic amounts of 9,10-dicyanoanthracene (DCA) in the presence of an adequate gelator, which permits a faster process than at the homogeneous phase. The methodology, which operates by a consecutive photoinduced electron transfer (ConPET) mechanism, has been successfully applied to the straightforward and clean synthesis of a number of different heteroarene (furan, thiophene, selenophene, pyrrole, oxazole, or thioxazole) phosphonates, extending to the late-stage phosphonylation of the anticoagulant Rivaroxaban.

Strategically, employment of cold white light is critical since it provides both selective wavelengths for exciting first DCA (blue region) and subsequently its corresponding radical anion $DCA^{\bullet-}$ (green region). The resultant strongly reducing excited agent $DCA^{\bullet-}*$ is capable of even activate five-membered heteroarene halides (Br, Cl) with high reduction potentials (~-2.7 V) to effect the C(sp2)−P bond formation. Spectroscopic and thermodynamic studies have supported the proposed reaction mechanism. Interestingly, the rate of product formation has been clearly enhanced in gel media because reactants can be presumably localized not only in the solvent pools but also through to the fibers of the viscoelastic gel network. This has been confirmed by field-emission scanning electron microscopy images where a marked densification of the network has been observed, modifying its fibrillary morphology.

Finally, rheological measurements have shown the resistance of the gel network to the incorporation of the reactants and the formation of the desired products.

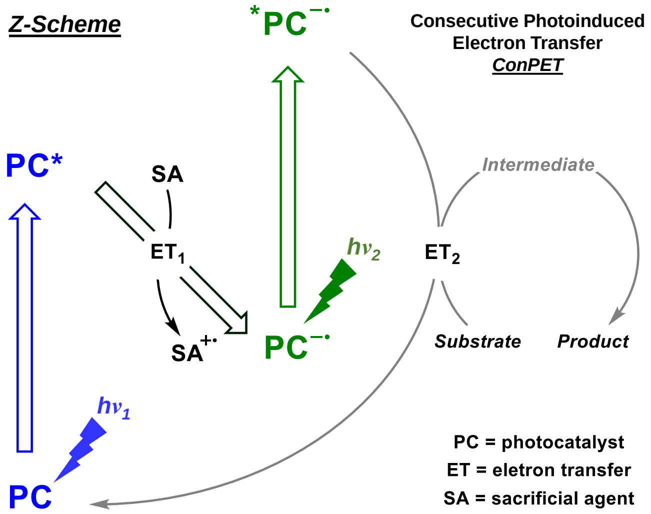
5.2 Introduction

Aryl phosphonates and their derivatives are very important entities which exhibit a widespread applicability in diverse scientific fields such as life science,[1−3] materials,[4−9] or even acting as ligands in catalysis.[10−15] In general, C(sp2)−P bonds are traditionally accessible by transition-metal-catalyzed coupling processes, and well-established methods using palladium,[16−19] nickel,[20,21] or copper[22,23] catalysts have been reported. However, required functionalized reactants that consequently reduce the substrate scope, expensive metal complexes, or harsh conditions have limited the development of novel synthetic metal-catalyzed protocols.

Visible-light photoredox catalysis has been postulated as an alternative and powerful strategy to forge new C(sp^2)−P bonds under milder conditions.[24−33] Generation of highly reactive aryl radical intermediates by direct single-electron transfer (SET) from the excited photocatalyst to the organic substrate has permitted the phosphorylation of aryl moieties with phosphorus-based nucleophiles to lead to the desired aryl phosphonates. For instance, six-membered (hetero)arene halides (Br, I) have been typically employed as precursors for the investigations of these cross-coupling reactions. Despite the fact that recent metal-catalyzed methods have been published,[34,35] little attention has been paid to the fabrication of a broad scope of five-membered heteroarene phosphonates directly between furan, thiophene, selenophene, or pyrrole halides (Cl, Br) with phosphites by visible-light photoredox catalysis.

Biphotonic technology has emerged as a valuable tool for organic synthesis, and a recent revision of this research field can be found in literature.[36,37] This accumulative two-photon approach allows us to tackle not only important bond activations but also SET processes under mild conditions and using lower energy visible light. Among others,[38,39] the consecutive photoinduced electron transfer (ConPET) mechanism is of great interest and mirrors the Z-scheme in biological photosynthesis,[40] and several organic dyes have been utilized as photocatalysts (**Scheme 1**).[41−46]

Scheme 1. Z-Scheme Adaptation to Organic Transformations through the ConPET Concept

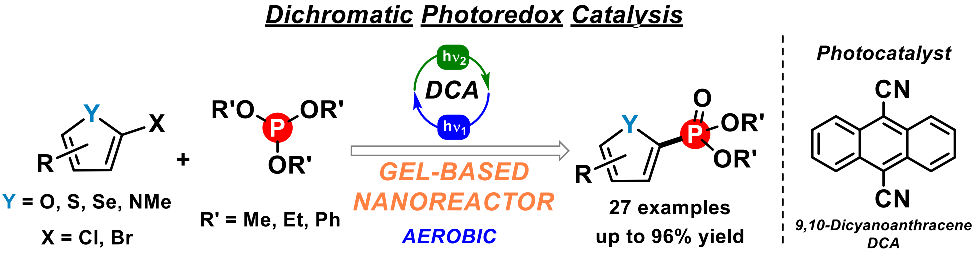


Briefly, upon selective excitation ($h\nu_1$) of the photocatalyst (PC), the resulting excited PC (PC*) is quenched by a sacrificial agent (SA) through single-electron transfer, giving rise to the radical ion pair (the PC anion radical, $PC^{\bullet-}$ and the SA cation radical, $SA^{\bullet+}$). Then the $PC^{\bullet-}$ can absorb another photon ($h\nu_2$) to yield its electronically excited anion radical ($^*PC^{\bullet-}$) which is found to be sufficiently reactive for high energy demanding bond activation. As a simple, low-weight molecule, soluble, photostable, and commercially available dye, the 9,10-dicyanoanthracene (DCA) has been recently found to be an ideal reducing photocatalyst for operating via a ConPET mechanism.[47] Interestingly, the management of a simpler setup with low power cold white LEDs is crucial since this energy source provides the simultaneous dichromatic light for exciting both the DCA ground state (near-UV-to-blue region) and the DCA radical anion (green region). From a mechanistic perspective, inert atmosphere conditions are mandatory to avoid quenching of DCA radical anion by oxygen. This differs from nature where visible light and oxygen are both abundant, playing a key role in aerobic photochemical reactions.

Smartly, nature has normalized confined and compartmentalized environments for addressing efficiently photochemical transformations under air conditions. In this sense, research groups have been devoted to developing artificial photonanoreactors based on low-molecular-weight (LMW) molecules self-assembled by noncovalent interactions (e.g., hydrogen bonding, van de Waals, charge transfer, dipolar, π–π stacking)[48,49] in order to access otherwise slow or forbidden pathways and achieve high selectivity under mild conditions. Supramolecular viscoelastic gels[50] fulfill properly the requirements to act as a photonanoreactor-like system, and investigations of air-sensitive photochemical reactions have been successfully achieved in such microenvironments.[51,52]

With this background, we describe herein our endeavors toward the aerobic visible-light-mediated phosphorylation of five-membered heteroarenes in gel-based nanoreactor that, as far as we are aware, remains unexplored (**Scheme 2**).

Scheme 2. Formation of Five-Membered Heteroarene Phosphonates via Dichromatic Photoredox Catalysis in Gel Nanoreactor



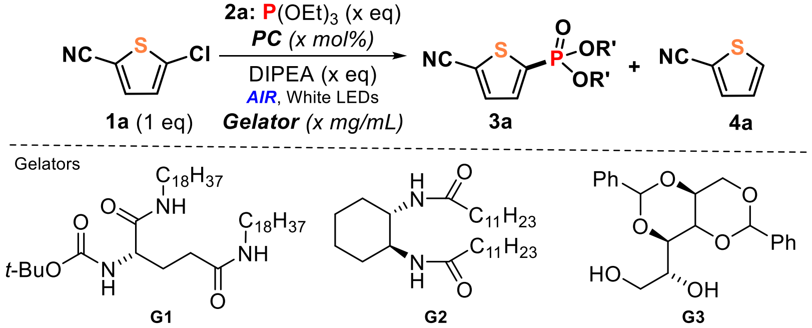
Thus, we propose a catalytic strategy for the activation of unreactive heteroarene halides via dichromatic photoredox catalysis, leading to heteroarene radical intermediates which further react with the corresponding phosphorus-type nucleophiles. The employed conditions which include visible light, room temperature, aerobic atmosphere, and supramolecular gels as confined media would reflect a similar scenario than in nature, becoming an efficient and attractive strategy for organic synthesis. Moreover, utilization of DCA as a ConPET photocatalyst has satisfactorily extended the scope of starting materials to heteroarene bromides or heteroarene chlorides, whereas the LMW gel nanoreactor has provided an adequate environment for substantially accelerating the reactivity in comparison with solution phase.

5.3 Results & Discussion

5.3.1 Optimization

We first tested the irradiation between 5-chloro-2-thiophenecarbonitrile (1a) and triethyl phosphite (2a) as model reactants in anhydrous acetonitrile (ACN) with cold white light LEDs in the presence of *N*,*N*-diisopropylethylamine (DIPEA), as sacrificial electron donor agent, and catalytic amounts of DCA under aerobic atmosphere. The desired heteroarene phosphonate (**3a**) was obtained in poor yields together with a low conversion of the starting material (**Table 1**, entry 1). This fact was, as expected, due to poisoning by oxygen exposure that dropped drastically down the effectiveness of the photoreaction. In sharp contrast, employment of the aerated physical gel built from **G1** (*N,N'*- bis(octadecyl)-L-boc-glutamic diamide, see the molecular structure in Table 1) as confined medium at same reaction conditions resulted not only in excellent conversion and yield but also in higher selectivity toward the coupled product **3a** (**Table 1**, entry 2), confirming the efficient compartmentalization provoked by the gel network for this visible-light-induced synthetic procedure.

Table 1. Optimization of the Reaction Conditions[a]



Entry	**2a** (eq)	DIPEA (eq)	**PC**[b] (mol%)	**G**[c] (mg/mL)	Conversion[d] (%)	Yield[d] (%)	**3a/4a**[d] ratio
1	5	1.2	10	-	14	10	71/29
2	**5**	**1.2**	**10**	**10**	**100**	**90**	**90/10**
3	5	1.2	10	15	85	74	87/13
4	5	1.2	10	5	87	75	86/14
5	20[e]	1.2	10	10	100	92	92/8
6	5	1.5	10	10	92	80	87/13
7	5	1	10	10	77	66	85/15

8	5	1.2	20	10	100	84	84/16
9	5	1.2	5	10	57	50	87/13
10	5	1.2	10[e]	10	40	32	80/20
11	5	1.2	10[f]	10	50	42	84/16
12	5	1.2	10[g]	10	55	48	87/13
13	5	1.2	10	10[h]	81	70	86/14
14	5	1.2	10	40[i]	73	56	76/24
15	5	-	10	10	0	0	0
16[j]	5	1.2	10	10	0	0	0

[a] **1a** (7.2 mg, 0.05 mmol) with **G1** in 1 mL of anhydrous ACN; irradiation with cold white-light (410-700 nm) LEDs at 23 °C for 4 hours unless otherwise indicated. [b] **DCA** as photocatalyst unless otherwise indicated. [c] **G**: gelator. H-bonding and van der Waals forces trigger the self-assembly process of gelators in organic solvent, affording tangled fibrillar nanostructures over a wide concentration range.[17] [d] Conversions, yields and ratios were calculated from quantitative GC analysis *vs.* internal standard 1-dodecanenitrile. [e] 2 hours of irradiation. [f] *N*,*N*-bis(2,6-diisopropylphenyl)perylene-3,4,9,10-bis(dicarboximide) (PDI). [f] Rhodamine 6G (Rh6G). [g] Sulforhodamine B (SRhB). [h] **G2**. [i] **G3**. [j] Using Blue (420 nm) lamps or Green (520 nm) LEDs.

In an attempt to turn the reaction into quantitative conditions, incremental changes in the amount of **2a** did show a slight improvement in the results (**Table 1**, entry 5), whereas variation at the DIPEA equivalents or different loading of the photocatalyst DCA gave lower yields of **3a** (**Table 1**, entries 6−9). Employment of other bases and solvents (see **Table S1**, entries 19−37) as well as other ConPET photocatalysts (**Table 1**, entries 10−12) showed less efficient reactions. Control experiments clearly demonstrated that the presence of DIPEA was essential for this photochemical protocol (**Table 1**, entry 15) and the negligible reactivity by photolysis with either blue (420 nm) lamps or green (520 nm) LEDs (**Table 1**, entry 16) reinforced the concept of a dichromatic excitation source for activating first the DCA and then its radical anion.

The question then arose whether the versatility of this photoredox catalytic process was only associated to the self-assembled matrix of **G1** or if other gel-based materials containing different assembly patterns could also act as photonanoreactors. Thus, the model reaction was carried out in gels **G2** (*N*,*N'*-

((1*S*,2*S*)-cyclohexane-1,2-diyl)- didodecanamide; see the molecular structure in **Table 1**) and **G3** (1,3:2,4-dibenzylidene-*D*-sorbitol; see the molecular structure in **Table 1**) as confined media. The desired **3a** was successfully obtained in 70% and 56% yield, respectively (**Table 1**, entries 13 and 14), indicating that supramolecular viscoelastic gels proposed a suitable microenvironment for this type of photoinduced process. It is worth mentioning that gelators could be easily separated by filtration and reused in subsequent procedures without detriment to its gelation properties. Therefore, the optimal conditions implied acceptable reagent loadings (5 equiv of **2a**, 1.2 equiv of DIPEA and 10 mol% of DCA), visible-light irradiation using cold white LEDs (410−700 nm) as the energy source in **G1** confined medium for 4 h under air atmosphere.

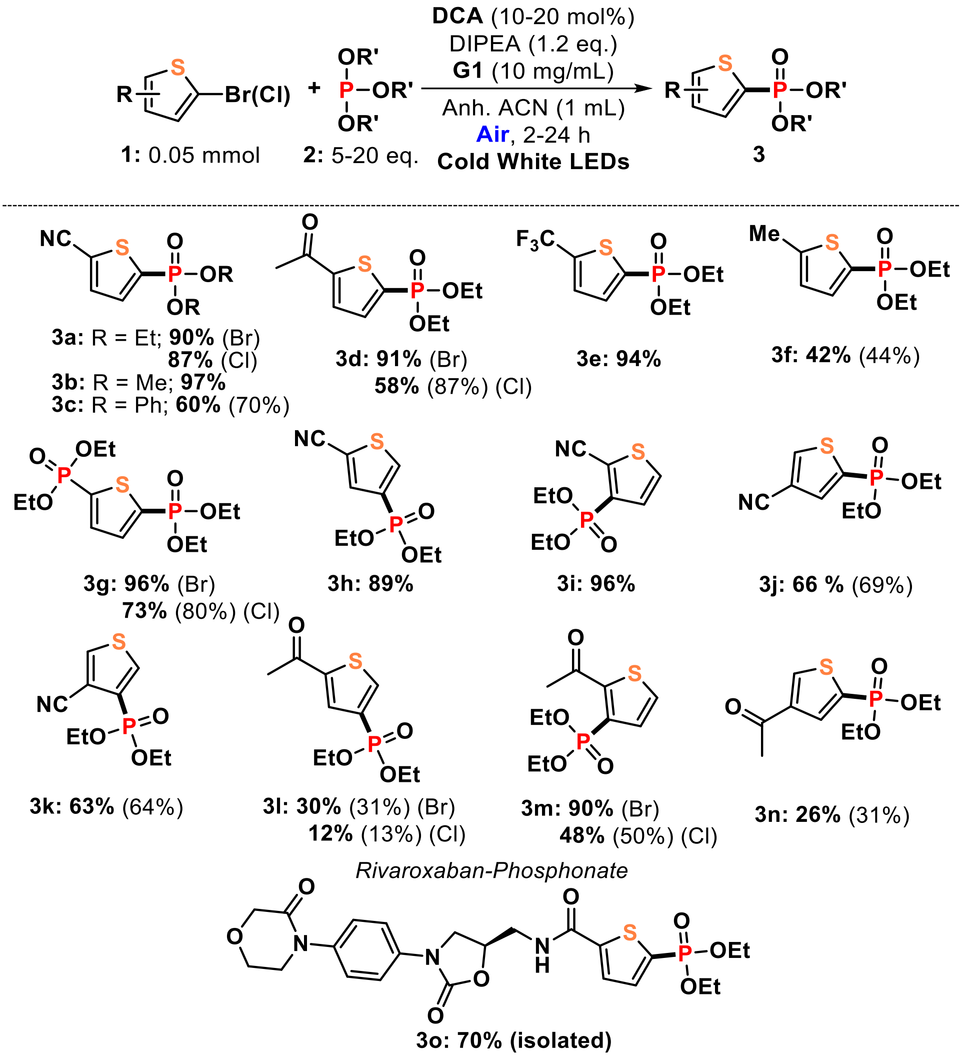
5.3.2 Scope

With the standardized conditions, we sought to examine the scope of this dichromatic photocatalyzed phoshorylation of thiophenes further (**Table 2**). In general, 10−20 mol % of DCA was necessary to observe a complete conversion of the starting materials. Although phosphite derivative **2a** was used as a representative coupling partner, other phosphites such as $P(OMe)_3$ or $P(OPh)_3$ were successfully coupled with **1a** (**Table 2**, entries **3b–c**) with special attention in product **3b** that was obtained almost in quantitative amount (97% yield).

Commercially available thiophene chloride (or bromide) precursors containing acetyl, trifluoromethyl, or methyl group afforded the corresponding phosphonylated product from moderate-to-excellent yields (**Table 2**, entries **3d−3f**), signaling that the reaction proceeded with an acceptable functional group tolerance and was clearly favored to thiophene halides bearing electron-acceptor groups. Interestingly, a diphoshonate thiophene (**Table 2**, entry **3g**) was quantitatively obtained after a one-pot full conversion of the 2,5-dibromothiophene, and the reaction was found to be tolerant in terms of regioselectivity. For instance, phosphorylation of 2-thiophenecarbonitrile halides containing the halogen atom in position 3 or 4 provided the desired products in excellent yields (**Table 2**, entries **3h,i**); however, the observed lower production when the nitrile group was in position 3 (**Table 2**, entries **3j,k**) could be correlated with the high reduction potentials of the precursors (vide infra).

Other regioisomers employing acetylthiophene-type halides were also obtained from moderate to excellent yields (**Table 2**, entries **3l–n**). To demonstrate the synthetic potential of the developed dichromatic photocatalyzed transformation, this method was applied to the late-stage phosphonylation of Rivaroxaban, an oral anticoagulant agent for the prevention and treatment of thromboembolic disorders.[56] Thus, the subsequent phosphonylated product (**Table 2**, entry **3o**) was obtained in very good, isolated yields (70%).

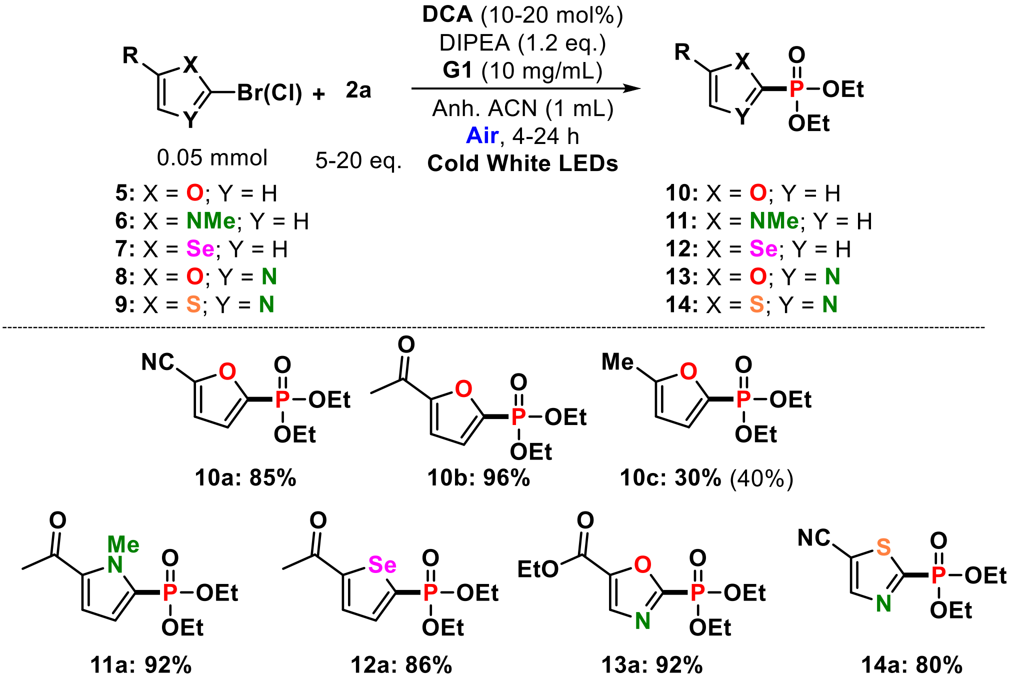
Table 2. Substrate scope of thiophenes[a]



[a]For detailed information on the reaction conditions, see the Supporting Information. Full conversion of compound **1** in all cases unless otherwise indicated in brackets.

In addition, the model reaction was submitted at higher scales (from 0.05 to 1 mmol), producing a 66% isolated yield of **3a** (86% GC yield) (**Figure E1**, Experimental section) and under outdoor sunlight generating **3a** after 8 h in an excellent 94% yield (**Figure E2**, Experimental section). Next, we explored the feasibility of this procedure using other five-membered haloheterocycles such as furan, pyrrole, selenophene, oxazole, or thioxazole halides (**Table 3**, entries **10a–c**, **11a**, **12a**, **13a**, and **14a**). The results indicated that the coupling reaction of **2a** with the corresponding heteroarenes brilliantly succeeded, with almost quantitative yields in some cases (for instance, 96% for **10b**).

Table 3. Phosphonylation of other five-membered heteroarene halides[a]



10a: 85% **10b: 96%** **10c: 30%** (40%)

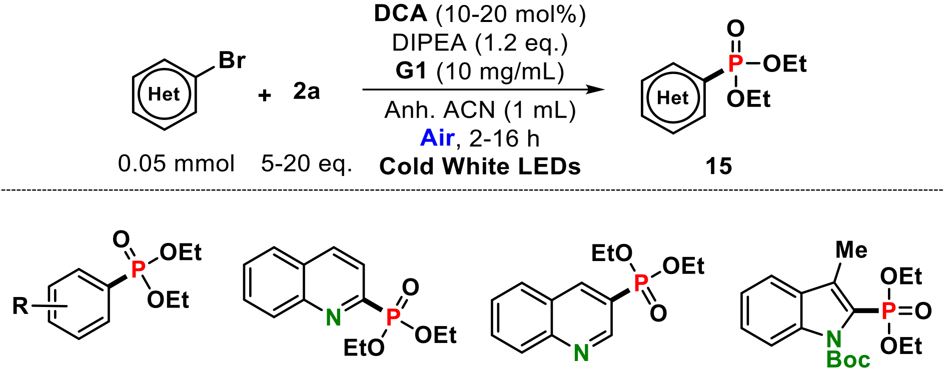
11a: 92% **12a: 86%** **13a: 92%** **14a: 80%**

[a]For detailed information on the reaction conditions, see the Supporting Information. Full conversion of starting materials in all cases unless otherwise indicated in brackets.

Finally, we expanded the investigations to the phosphorylation of (hetero)aryl halides and **2a** to check the generality of our procedure where the corresponding products were obtained in high-to-excellent yields (**Table 4**, entries **15a–e**).

Moreover, some of these findings were found to be comparable with that from example of rhodamine 6G as ConPET photocatalyst (i.e., 93%, 79% and 70% yields for **15a**, **15b** and **15e**, respectively),[46] despite the lower addition of **2a** or DIPEA, aerobic gel media, or shortener irradiation times.

Table 4. Coupling reaction of (hetero)aryl halides with triethyl phosphite **2a**[a]



15a: 98% (R = 4-CN)
15b: 92% (R = 2-CN)

15c: 90%

15d: 83% (84%)

15e: 81% (83%)

[a]For detailed information on the reaction conditions, see the Supporting Information. Full conversion of starting materials in all cases unless otherwise indicated in brackets.

5.3.3 Mechanism

Once product studies were established, we proposed the reaction mechanism for the dichromatic photoredox catalysis phosphonylation of five-membered heteroarene halides which is outlined in **Figure 1A**. To check whether the DCA properties may or may not be similar in gel medium to those for the homogeneous phase, excitation and emission measurements were carried out employing an integrating sphere spectrofluorometer. As depicted in **Figure E3** (Experimental section), the results revealed no medium dependent. Hence, the singlet excited state of the ConPET photocatalyst DCA (^{1}DCA*), generated upon blue-region light irradiation, oxidized DIPEA affording the corresponding radical ion pairs.

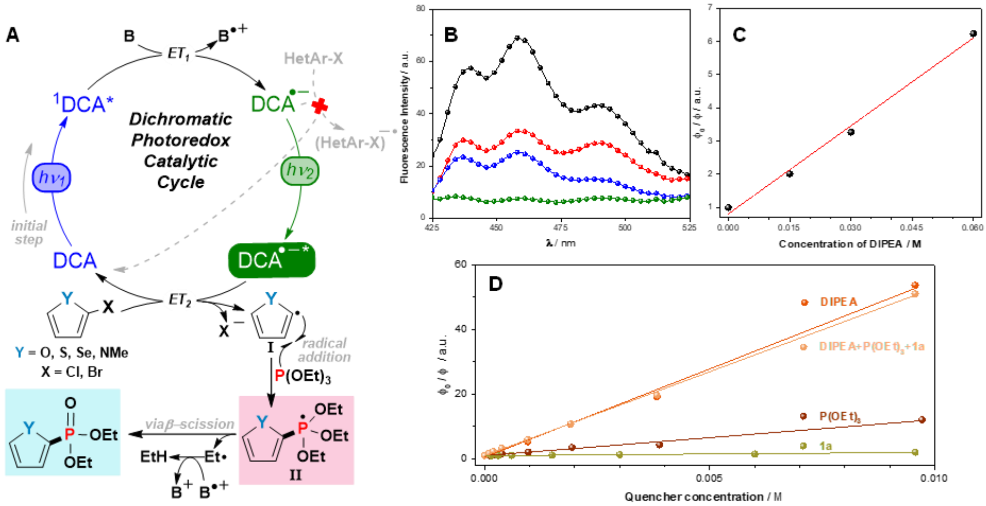


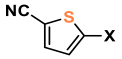
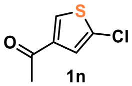
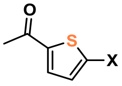
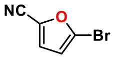
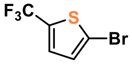
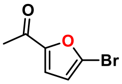
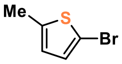
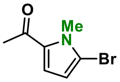
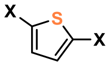
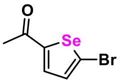
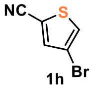
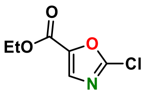
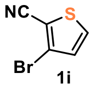
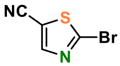
Figure 1. (A) Proposed reaction mechanism for the phosphonylation of five-membered heteroarenes dichromatic photoredox catalysis in gel nanoreactor. (B) Quenching of DCA fluorescence in the presence of increasing amounts of DIPEA in **G1** medium. [DCA] = 5 mM; [DIPEA] = 0 mM (black), 15 mM (red), 30 mM (blue) and 60 mM (green). (C) Stern−Volmer plot. (D) Stern−Volmer plots of **1a**, DIPEA, and $P(OEt)_3$ quench of DCA

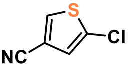
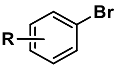
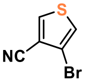
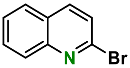
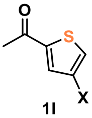
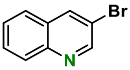
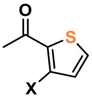
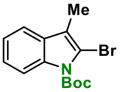
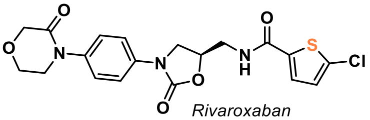
This was confirmed by emission measurements in gel medium where fluorescence intensity of DCA gradually decreased in the presence of increasing amounts of DIPEA, indicating completely quenching at reaction conditions (**Figure 1B**). From the ^{1}DCA* lifetime (15.9 ns in ACN)[57] and the obtained Stern−Volmer constant (88.3 M^{-1}, **Figure 1C**), the rate constant kq (S$_1$) for this pathway was found to be 5.5 × 109 M^{-1} s^{-1}.

Additionally, quenching experiments showed that neither the heteroarene halide nor the phosphite-like derivative interacted individually with the ^{1}DCA* and did not influence the deactivation by DIPEA (**Figure 1D**).

Table 5. Thermodynamic data of the SET processes from DCA$^{\bullet-*}$ and DCA$^{\bullet-}$ to HetArX

$$(\Delta G_1)\ \text{HetArX}^{\bullet-} \xleftarrow[\times]{\text{HetArX}} \text{DCA}^{\bullet-} \xrightarrow{h\nu_2} \text{DCA}^{\bullet-*} \xrightarrow{\text{HetArX}} \text{HetArX}^{\bullet-}\ (\Delta G_2)$$

HetArX	E$_{red}$ *vs* SCE[a] (V)	ΔG_1[b]/ΔG_2[c] (eV)	HetArX	E$_{red}$ *vs* SCE[a] (V)	ΔG_1[b]/ΔG_2[c] (eV)
 **1a**	−1.88 (X=Br) −1.97 (X=Cl)	+1.0 / −1.1 +1.1 / −1.0	 **1n**	−2.15	+1.2 / −0.8
 **1d**	−1.68 (X=Br) −1.66 (X=Cl)	+0.8 / −1.3 +0.8 / −1.3	 **5a**	−2.28	+1.4 / −0.7
 **1e**	−2.31	+1.4 / −0.6	 **5b**	−2.15	+1.2 / −0.5
 **1f**	−2.72	+1.8 / −0.2	 **6a**	−2.12	+1.2 / −0.8
 **1g**	−2.32 (X=Br) −2.64 (X=Cl)	+1.4 / −0.6 +1.7 / −0.3	 **7a**	−1.66	+0.7 / −1.3
 **1h**	−2.01	+1.1 / −0.9	 **8a**	−2.10	+1.2 / −0.9
 **1i**	−2.05	+1.1 / −0.9	 **9a**	−1.67	+0.8 / −1.3

 **1j**	−2.21	+1.3 / −0.7		−2.08 (R=4-CN) −2.11 (R=2-CN)	+1.2 / −0.9 +1.2 / −0.9
 **1k**	−2.44	+1.5 / −0.5		−1.95	+1.0 / −1.0
 **1l**	−1.85 (X=Br) −2.65 (X=Cl)	+0.9 / −1.1 +1.7 / −0.3		−1.96	+1.0 / −1.0
 **1m**	−1.74 (X=Br) −1.89 (X=Cl)	+0.8 / −1.2 +1.0 / −1.0		−2.48	+1.6 / −0.5
			 *Rivaroxaban*	−1.89	+1.0 / −1.1

[a] $E_{1/2}^{red}$ (vs SCE) in ACN was calculated from $E_{1/2}^{red}$ (vs SCE) = $E_{1/2}^{red}$ (vs ferrocene) + 0.38 V (see ESI for details). [b] Free energy changes were estimated as follows: $\Delta G_1 = E_{1/2}^{red}$ (**DCA**) – $E_{1/2}^{red}$ (HetArX); $\Delta G_2 = E_{1/2}^{red}$ (**DCA**) – $E_{1/2}^{red}$ (HetArX) – E_{ex}, where E_{ex} is the photoelectron ejection energy estimated as 2.08 V.[25]

Although the DCA radical anion ($DCA^{\bullet -}$) was efficiently generated, it possessed insufficient reducing power (−0.6 to −0.89 V vs SCE)[13] to reductively activate the heteroarene halides. The reduction potentials of the heteroarene halides were measured by cyclic voltammetry in ACN under argon, ranging from −1.66 to −2.72 V (**Table 5**). Thus, these processes did not appear to be thermodynamically feasible where the free energy changes (ΔG_1) associated with the electron transfer were estimated to be above zero (**Table 5**). This issue was fully supported by negligible formation of product in the photoreaction when using only blue lamps (**Table 1**, entry 16).

In addition, the α-aminoalkyl radical could be generated from DIPEA radical cation, and it may react with the heteroarene halides through the halogen atom transfer mechanism;[58,59] however, this mechanistic scenario appeared to be unlikely at these conditions due to lack of product formation. Then $DCA^{\bullet-}$ was excited by the green-light region, giving rise to its excited state, $DCA^{\bullet-*}$, a highly reactive species with an estimated reducing potential of −3.2 V (vs SCE)[60] and a lifetime of 13.5 ns[61] that allowed it to engage in reductive activation of heteroarene halides. In fact, the electron transfer from $DCA^{\bullet-*}$ would be an exergonic process in all cases, and the trend of substrate reactivity was very accurately mirrored by these thermodynamic data (**Table 5**). The radical anion of the heteroarene halide then suffered rapid mesolytic scission of the C−X bond, leading to the corresponding halide anion (X−) and the heteroarene radical I which could be added to the phosphite-like derivative via radical addition to afford the phosphoranyl radical intermediate II.[62,63]

The involvement of intermediate I was confirmed by a trapping experiment employing diphenyl disulfide where efficient formation of 2- carbonitrile-5-phenylthiothiophene was detected (**Figure E9**, Experimental section). Intermediate II could then undergo a β-scission fragmentation, giving rise to the desired heteroarene phosphonate and the ethyl radical which evolved to ethane by hydrogen-atom transfer.[25,26,64–69]

5.3.4 Gel-Based Nanoreactor

As stated above, the potential advantage of carrying out the dichromatic photocatalyzed phosphorylation of heteroarenes in gels as confined media has been well-established by steady-state irradiations. To further support the role of viscoelastic gel networks as successful nanoreactors, combination of several experimental investigations which comprises kinetic studies, field-scanning electron microscopy (FESEM), and oscillatory rheological measurements were performed. First, the kinetic of 1a conversion was investigated under both solution and gel media (**Figure 2A**). The result clearly revealed that **1a** converted remarkably faster in gel medium than in inert solution for the same irradiation time;[71] likewise, a similar trend was observed with the formation of product **3a** (**Figure E10**, Experimental section).

Along this vein, the model reaction was submitted to 30 min irradiation under frozen (193 K) aerated anhydrous ACN solution, affording negligible production of

3a that would indicate a molecular diffusion restriction. On the contrary, product **3a** was successfully obtained in 41% yield at identical conditions in the presence of **G1** (**Figure E11**, Experimental section). This might be hypothesized as the reactants may be not only localized in the solvent pools between the fibers but also widespread through the fibers, allowing the photochemical process in a confined but dynamic space. In addition, the aspect of the material to the naked eyes showed that the viscoelastic properties of the gels after irradiation did not vary in a critical manner; in other words, there was no gravitational flow (inset of **Figure 2A**).

To endorse these findings, field-emission scanning electron microscopy (FESEM) images of the unloaded **G1** and **G1** loaded with the photocatalyst, and substrates were recorded (**Figure 2D−G**). A marked densification of the network was clearly observed at the loaded gel, which could be attributed to the inclusion of the reactants within the supramolecular gel and therefore apparently triggering an impact on the fibrillar morphology of the gel network.

Interestingly, the gel phase did not appear to suffer dramatic morphological changes after the irradiation period, as can be seen from the FESEM images, indicating that the gel matrix only played the role of nanoreactor and did not interfere in the dichromatic photocatalyzed reaction.

When using a gel system as compartmented medium is important to ensure that, at least, its viscoelastic nature remains through the entire experiment. This was demonstrated by rheological experiments before and after irradiation (**Figure 2B,C**). These measurements indicated that the storage modulus G′ was always 1 order of magnitude higher than the loss modulus G″ during both dynamic frequency and strain sweeps (DFS and DSS, respectively). Analyzing in detail the plots, DFS (**Figure 2B**) data suggested that the gel strength decreased during the experiment as shown by the corresponding dissipation factor (i.e., tan δ (G″/G′) = 0.1158 (before irradiation) vs 0.2402 (after irradiation).

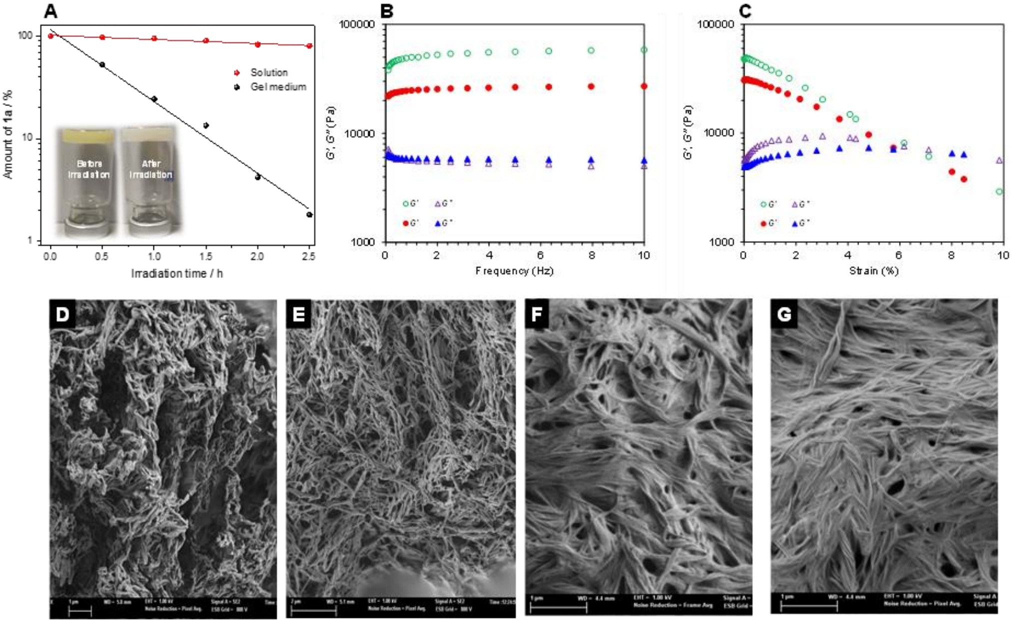


Figure 2. (A) Conversion of **1a** vs irradiation time at optimal reaction conditions in solution or gel medium. Inset: photograph of the loaded **G1** before/after irradiation. (B) Dynamic frequency sweep (DFS) plots: variation of G′ and G″ with frequency (from 0.1 to 10 Hz at 0.1% strain), loaded **G1** before (unfilled) and after (filled) irradiation. (C) Dynamic strain sweep (DSS) plots: variation of G′ and G″ with strain (from 0.01 to 100%), loaded **G1** before (unfilled) and after (filled) irradiation. Representative field-emission scanning electron microscopy (FESEM) images of **G1** prepared by freeze-drying the gel: (D) unloaded **G1** before irradiation; (E) unloaded **G1** after irradiation; (F) loaded **G1** before irradiation; (G) loaded **G1** after irradiation.

This was not totally unexpected as new species were formed during the irradiation, which could also destabilize the supramolecular network. Moreover, DSS (**Figure 2C**) measurements showed that the gel phase turned into liquid at 9.8% strain before irradiation, while this transition took place at 8% strain after the experiment, which was also in agreement with the DFS profiles. Despite the observed weakening, the gel network resisted during the entire experiment providing the unique environment to facilitate the discussed chemical transformations.

5.4 Conclusion

In conclusion, supramolecular gels made in acetonitrile can be used as reaction media to carry out aerobic visible-light mediated phosphorylation of five-membered heteroarenes affording the corresponding aryl phosphonates.

Optimized conditions include the use of white light LEDs (410−700 nm), DIPEA as sacrificial electron donor agent, catalytic amounts of DCA (10 mol %), and *N,N′*-bis(octadecyl)-*L*-Boc-glutamic diamide as gelator whose noncovalent nature of the supramolecular network enables its easy separation and reutilization. Interestingly, the gel media significantly enhanced the reaction rate in some cases compared to those in homogeneous solution. In terms of scope, commercially available fivemembered heteroarene chloride (or bromide) precursors containing an acetyl, ester, cyano, trifluoromethyl, or methyl group afforded the corresponding phosphonylated products in moderate to excellent yields within 4 h.

The synthetic potential of this dichromatic photocatalyzed transformation was demonstrated by its application in the late-stage phosphonylation of the anticoagulant rivaroxaban. Spectroscopic and thermodynamic studies supported the involvement of the strongly reducing excited radical anion $DCA^{\bullet-*}$ in the proposed reaction mechanism. This species was found to be capable to activate heteroarene halides with high reduction potentials.

Finally, FESEM and rheological measurements suggested that the gel network resisted the incorporation of the reactants and the formation of the desired products. Although certain detriment in the mechanical properties of the gels was observed during the reactions, it apparently did not harm their efficiency as confined reaction media. We believe this methodology could become a general approach to facilitate photoredox catalysis under aerobic conditions.

5.5 References

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5.6 Experimental section

5.6.1 Materials and Methods

All reagents (≥97% purity) and solvents (≥99% purity) were purchased from commercial suppliers (Merck, TCI, Apollo Scientific, Fluorochem, Scharlab) and used as received unless otherwise indicated. Reactions were carried out in a Metria-Crimp Headspace clear vial flat bottom (10 mL, Ø 20 mm) sealed with a Metria-aluminum crimp cap with molded septum butyl/ natural PTFE (Ø 20 mm). Irradiation was performed with a cool white LED (LED Cree MK-R, cold-white, 11.6 V, 700 mA, P = 8.5 W). TLC was performed on commercial SiO_2-coated aluminum and plastic sheets (DC60 F254, Merck). Visualization was done by UV light (254 nm).

Products were isolated materials after column flash chromatography or TLC on silica gel (Merck, mesh 35−70, 60 Å pore size), and their corresponding yields were determined by quantitative GC-FID measurements on an Agilent 8860 GC-System with N_2 as carrier gas. Dodecanenitrile was used as an internal standard in the GC-FID quantitative measurements; yield products were estimated as [conversion × selectivity]/mass balance. Determination of purity and structure confirmation of the literature known products was performed by ^1H, ^{13}C, ^{19}F, and ^{31}P NMR and high-resolution mass spectrometry (HRMS) in the case of unknown products. NMR spectral data were collected on a Bruker Advance 400 (400 MHz for ^1H, 101 MHz for ^{13}C, 376 MHz for ^{19}F, and 162 MHz for ^{31}P) spectrometer at 20 °C. Chemical shifts are reported in δ/ppm and coupling constants J are given in hertz. Solvent residual peaks were used as internal standard for all NMR measurements. The quantification of ^1H cores was obtained from integrations of appropriate resonance signals. Abbreviations used in NMR spectra: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublet; ddd, doublet of doublet of doublet; td, triplet of doublet; and dq, doublet of quartet. HRMS was performed in the mass facility of SCSIE University of Valencia.

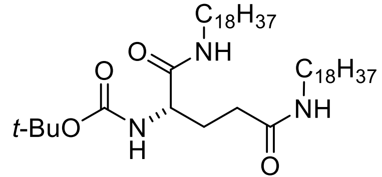
5.6.2 General Procedure for the Phosphorylation of Heteroarenes Halides

A vial (10 mL) was charged with 9,10-anthracenedicarbonitrile (1.2 mg, 5 µmol, 10 mol% and the correspondent gelator (**G1**, 10 mg/mL). Anhydrous acetonitrile (1.0 mL) was poured into the vial, and 5-chloro-2-thiophenecarbonitrile (5.4 µL, 50 µmol, 1.0 equiv) and triethyl phosphite (45 µL, 250 µmol, 5.0 equiv) were added. Then DIPEA (10.5 µL, 60 µmol, 1.2 equiv) and dodecanenitrile (12.0 µL, 50 µmol, 1.0 equiv) were added with a 25 µL Hamilton syringe. The vial was sealed with a septum. It was heated to 150 °C with a heatgun for 1.5 min with manual stirring until a clear solution was obtained. The vial was cooled to room temperature until gel formation was observed. The reaction was irradiated with an external LED through the plain bottom side of the vial at 23 °C during the corresponding time.

Then brine (2 mL) was added, and the aqueous phase was extracted with ethyl acetate (1 mL). The reaction was monitored by GC-FID analysis. The organic phase was dried over anhydrous sodium sulfate, filtered from the drying agent, and concentrated in vacuo. The crude was purified via a TLC plastic sheet or flash column chromatography using a hexane/ethyl acetate mixture as the mobile phase.

5.6.3 Synthesis of Low Molecular Weight Gelators (LMW Gelators)

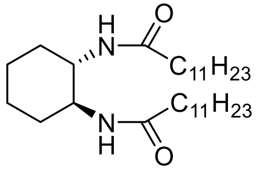
N,N'-Bis(octadecyl)-*L*-Boc-glutamic Diamide *(***G1***).*



G1

Boc-glutamic acid (0.01 mol, 1.0 equiv) and octadecylamine (0.02 mol, 2.0 equiv) in dichloromethane (200 mL) were mixed. Then, 1-ethyl-3-(3-(dimethylamino)propyl)carbodiimide hydrochloride (EDC·HCl) (0.022 mol, 2.2 equiv) was added to the mixture and stirred at RT for 72 h. The obtained white solid was isolated by filtration and washed three times with dichloromethane. The crude product was dissolved in THF and precipitated by water. A fine white solid was obtained (80%). Following the procedure reported previously *Soft Matter* ***2007****, 3,* 1312−1317*.*

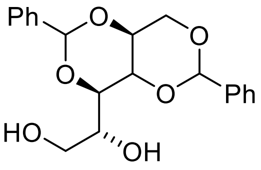
(*S,S*)-Dodecyl-3-[2(3-dodecyl-ureido)cyclohexyl]urea (**G2**).



G2

A solution of dodecylisocyanate (15 mmol, 2.0 equiv) in toluene (20 mL) was slowly added to a solution of (S,S)-1,2-cyclohexyldiamine (7 mmol, 1.0 equiv) in toluene (100 mL). The reaction mixture was stirred for 16 h at RT and 2 h at 100 °C. After cooling to RT, the gel-like reaction mixture was filtered to give a white waxy solid. The waxy solid was further stirred for 16 h with dichloromethane (50 mL) and collected by filtration. This procedure was repeated with diethyl ether. After drying, a white solid was obtained (70%). Following the procedure reported previously *Chem. - Eur. J.* ***1999****, 5,* 937–950.

*1,3,2,4-Dibenzylidene-D-sorbitol (***G3***).*

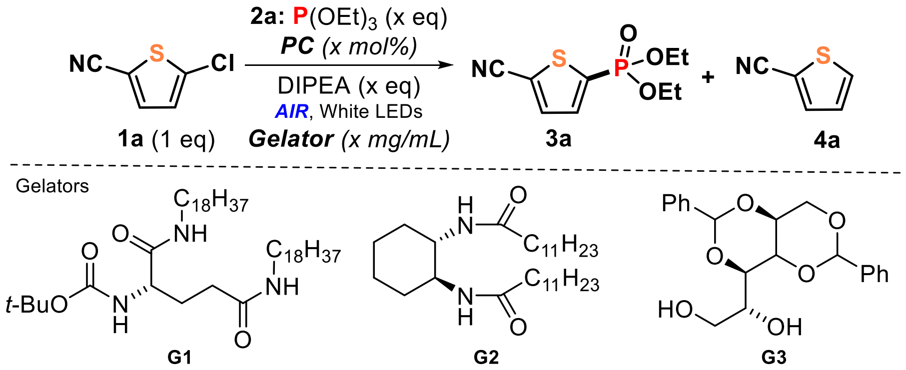


G3

Commercially available.

5.6.4 Searching for the optimal conditions

Table E1. Optimizing the reaction conditions[a]



Entry	2a (eq)	DIPEA (eq)	PC[b] (mol%)	G[c] (mg/mL)	Conversion[d] (%)	Yield[d] (%)	3a/4a[d] ratio
1	5	1.2	10	-	14	10	71/29
2	**5**	**1.2**	**10**	**10**	**100**	**90**	**90/10**
3	5	1.2	10	15	85	74	87/13
4	5	1.2	10	5	87	75	86/14
5	20[e]	1.2	10	10	100	92	92/8
6	5	1.5	10	10	92	80	87/13
7	5	1	10	10	77	66	85/15
8	5	1.2	20	10	100	84	84/16
9	5	1.2	5	10	57	50	87/13

10	5	1.2	10[e]	10	40	32	80/20
11	5	1.2	10[f]	10	50	42	84/16
12	5	1.2	10[g]	10	55	48	87/13
13	5	1.2	10	10[h]	81	70	86/14
14	5	1.2	10	40[i]	73	56	76/24
15	5	-	10	10	0	0	0
16[j]	5	1.2	10	10	0	0	0
17	5	1.2	10	22 in 2mL	55	51	93/7
18	5	1.2	10	45 in 4mL	24	22	92/8
19[k]	5	1.2	10	10	73	23	32/68
20[l]	5	1.2	10	10	63	17	27/73
21[m]	5	1.2	10	10	10	6	73/27
22[n]	5	1.2	10	10	46	12	27/73
23[o]	5	1.2	10	10	18	6	35/65
24[p]	5	1.2	10	10	12	0	0
25[q]	5	1.2	10	10	34	20	61/39
26[r]	5	1.2	10	10	94	80	86/14
27[s]	5	1.2	10	10	11	7	64/36
28[t]	5	1.2	10	10	8	3	42/58
29[u]	5	1.2	10	10	57	15	27/63
30[v]	5	1.2	10	10	90	79	88/12
31[w]	5	1.2	10	10	67	60	89/11
32	5	Et$_3$N 1.2	10	10	63	57	91/9
33	5	DIPA 1.2	10	10	35	31	89/11
34	5	DBU 1.2	10	10	93	74	80/20
35	5	DABCO 1.2	10	10	7	5	73/27
36	5	K$_2$CO$_3$ 1.2	10	10	26	20	79/21
37	5	Et$_3$N 1.2	10	10	63	57	91/9
38[x]	5	1.2	10	-	37	33	90/10

[a] **1a** (7.2 mg, 0.05 mmol) with **G1** in 1 mL of anhydrous ACN; irradiation with cold white-light (410-700 nm) LEDs at 23 ºC for 4 hours unless otherwise indicated. [b] **DCA** as photocatalyst unless otherwise indicated. [c] **G**: gelator. H-bonding and van der Waals forces trigger the self-assembly process of gelators in organic solvent, affording tangled fibrillar nanostructures over a wide concentration range.[1] [d] Conversions, yields and ratios were calculated from quantitative GC analysis vs. internal 1-dodecanonitrile. [e] 2 hours of irradiation. [f] *N,N*-bis(2,6-diisopropylphenyl)perylene-3,4,9,10-

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[1] (a) Li, Y.; Wang, T.; Liu, M. *Soft Matter* **2007**, *3*, 1312–1317. (b) Hanabusa, K.; Yamada, M.; Kimura, M.; Shirai, H. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1949–1951. (c) Watase, M.; Nakatani, Y.; Itagaki, H. *J. Phys. Chem. B* **1999**, *103*, 13, 2366–2373.

bis(dicarboximide) (PDI). [f] Rhodamine 6G (Rh6G). [g] Sulforhodamine B (SRhB). [h] **G2**. [i] **G3**. [j] Using Blue (420 nm) lamps or Green (520 nm) LEDs. [k]DMF, [l]DMA, [m]AcOEt, [n]EtOH, [o]Dioxane, [p]Toluene, [k]DCM, [r]Acetone, [s]Ether, [t]Hexane, [u]DMSO, [v]ACN, [w]ACN/H_2O (9/1, v/v), [x]under anaerobic conditions.

5.6.5 1 mmol scale procedure

To scale-up the procedure (from 0.05 mmol to 1 mmol), we performed the reaction following the general procedure inside a covered petri dish using 9-10-dicyanoanthracene (24 mg, 0.1 mmol, 10 mol%) as photocatalyst, 5-bromo-2-thiophenecarbonitrile (114 µL, 1 mmol, 1.0 equiv.), triethyl phosphite (900 µL, 5 mmol, 5.0 equiv.), dodecanenitrile (240 µL, 1 mmol, 1.0 equiv.) as internal standard and DIPEA (209 µL, 1.2 mmol, 1.2 equiv.) and G1 (200 mg/mL) in 20 mL of anhydrous acetonitrile. The reaction mixture was irradiated for 36 hours with cold white LEDs. Then, brine (30 mL) was added, and the aqueous phase was extracted with ethyl acetate (3 x 30 mL). The reaction was monitored by GC-FID analysis obtaining 86% product yield.

The organic phase was dried over anhydrous sodium sulfate, filtered from the drying agent, and concentrated in vacuo. The crude was purified via flash column chromatography using a hexane/ethyl acetate mixture as the mobile phase obtaining 161.7 mg, 66% isolated yield.

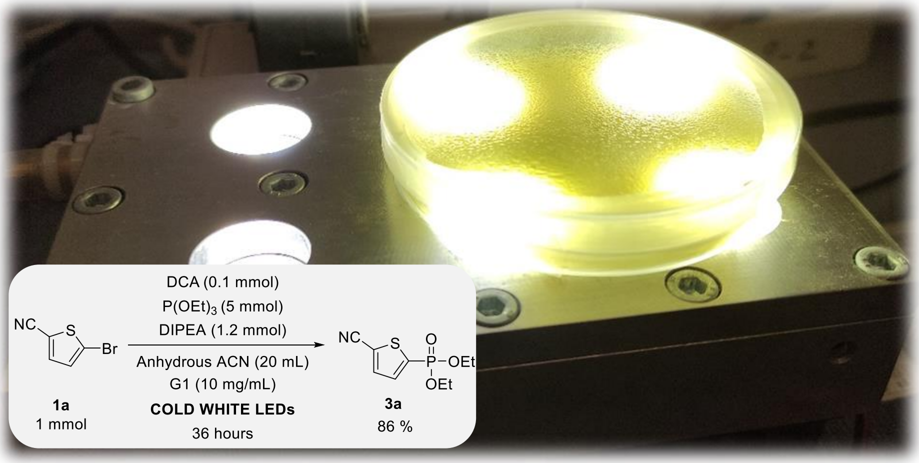


Figure E3. 1 mmol scale-up reaction.

5.6.6 Sunlight irradiation procedure

The compound **3a** was prepared according to the general procedure using 9-10-dicyanoanthracene (2.4 mg, 10 µmol, 20 mol%) as photocatalyst, 5-bromo-2-thiophenecarbonitrile (5.7 µL, 50 µmol, 1.0 equiv.), triethyl phosphite (180 µL, 1000 µmol, 20.0 equiv.), dodecanenitrile (12.0 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and **G1** (10 mg/mL). The gel mixture was irradiated with sunlight for 8 hours, obtaining 94% product yield according to GC-FID analysis. Location: Camí de Vera S/N, Chemistry Department, Universitat Politècnica de València (UPV), Valencia, Spain (coordinate: 39.482917, -0.341642), temperature: 16-23 °C, from 9:00 to 17:00. Date: 24/05/2021

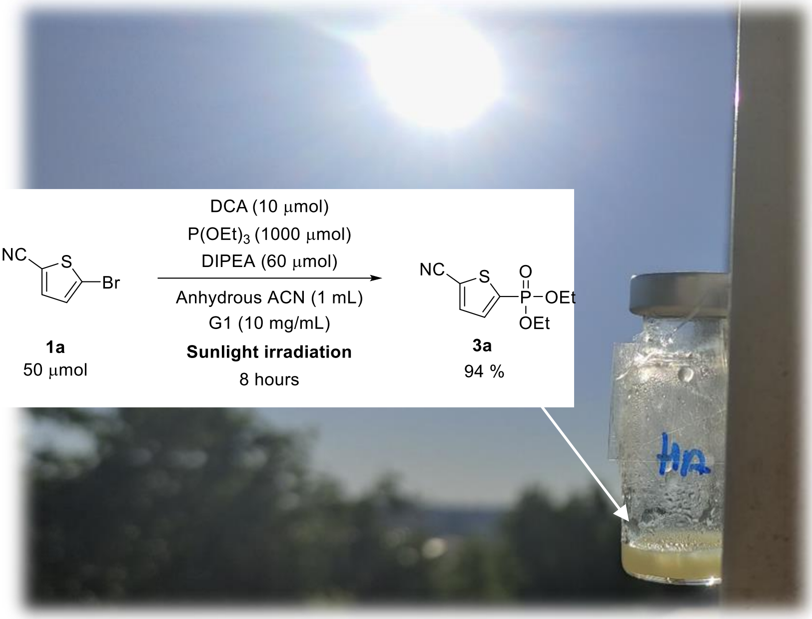


Figure E2. Sunlight irradiation reaction.

5.6.7 UV absorption and fluorescence quenching

The absorption spectra were recorded on a JASCO V-630 spectrophotometer. The fluorescence spectra were recorded on an FS5 Edinburgh instrument spectrofluorometer with a SC-05 standard cuvette holder module and an SC-30 integrating sphere module.

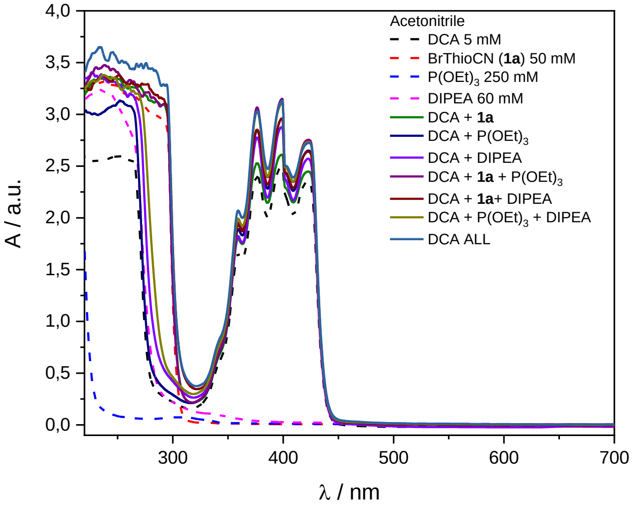


Figure E3. Absorption spectra of the corresponding photocatalyst and substrates in acetonitrile.

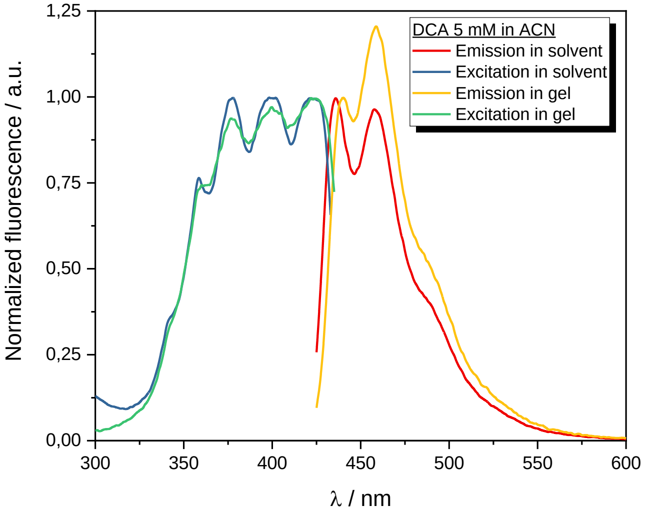


Figure E4. Emission and excitation spectra of DCA.

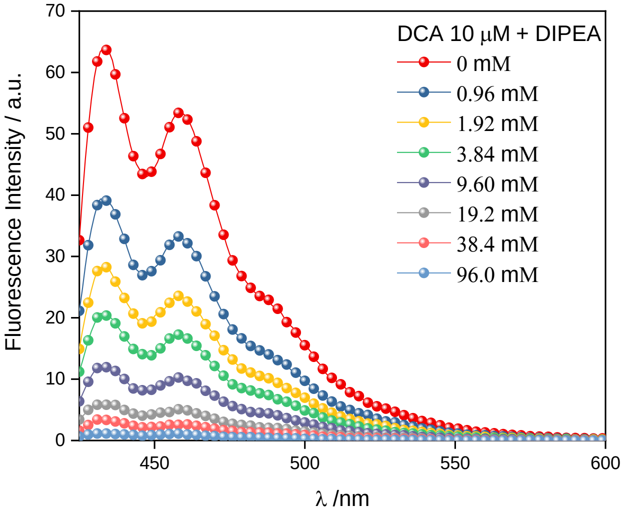


Figure E5. Emission spectra of DCA (10 μM) in the presence of increasing amounts of DIPEA in acetonitrile under aerobic conditions.

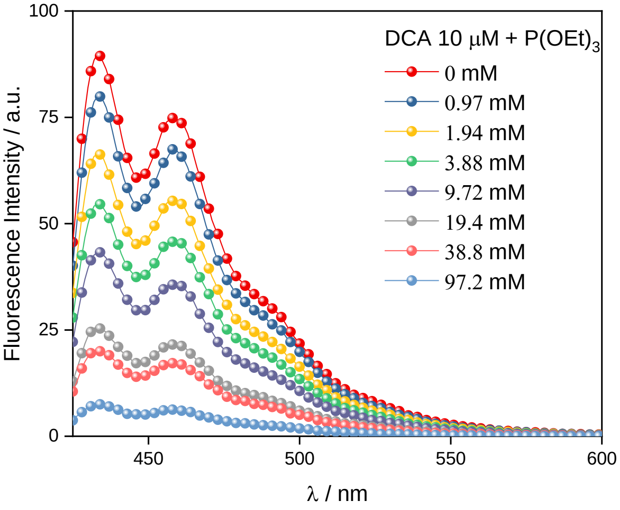


Figure E6. Emission spectra of DCA (10 μM) in the presence of increasing amounts of triethyl phosphite in acetonitrile under aerobic conditions.

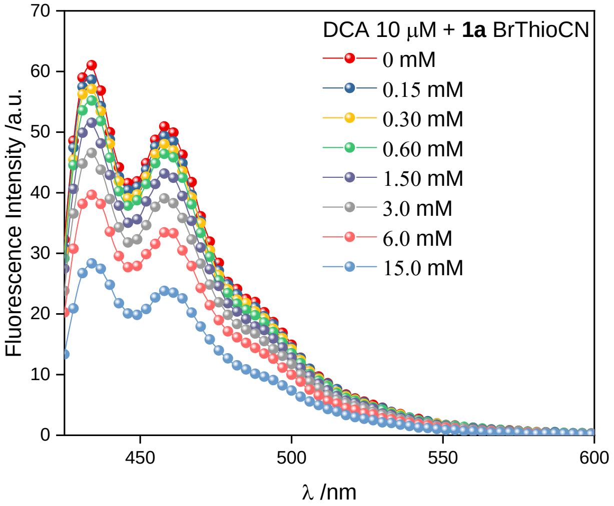


Figure E7. Emission spectra of DCA (10 µM) in the presence of increasing amounts of 2-bromo-5-thiophenecarbonitrile in acetonitrile under aerobic conditions.

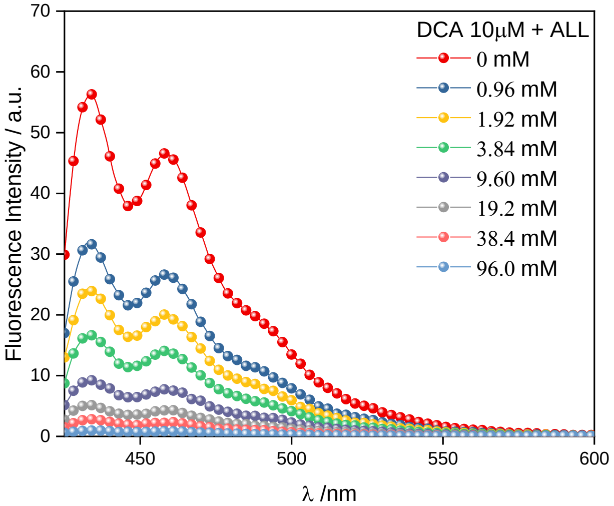


Figure E8. Emission spectra of DCA (10 µM) in the presence of increasing amounts of DIPEA + triethyl phosphite + 2-bromo-5-thiophenecarbonitrile in acetonitrile under aerobic conditions.

5.6.8 Trapping reaction

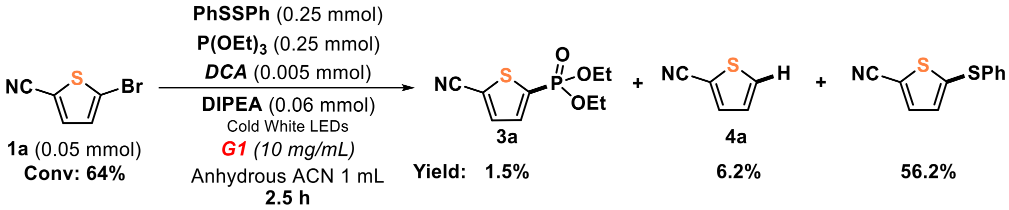
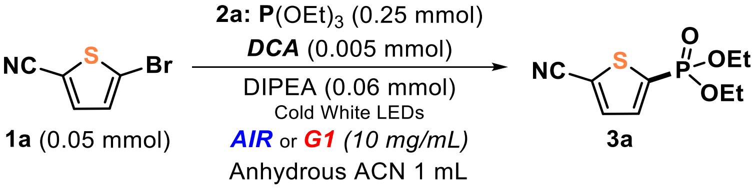


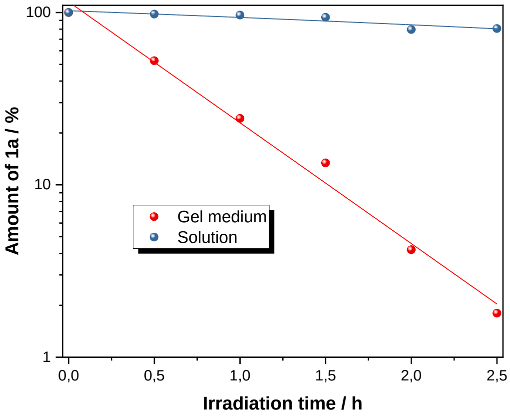
Figure E9. Trapping reaction of 1a with diphenyl disulfide.

A vial (10 mL) was charged with 9,10-anthracenedicarbonitrile (1.2 mg, 5 µmol, 10 mol%), diphenyl disulfide (47.5 mg, 250 µmol, 5.0 equiv.) and the correspondent gelator (**G1**, 10 mg). Anhydrous acetonitrile (1.0 mL) was poured and 5-bromo-2-thiophenecarbonitrile (5.7 µL, 50 µmol, 1.0 equiv.) and triethyl phosphite (45 µL, 250 µmol, 5.0 equiv.) were added. Then, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and dodecanenitrile (12.0 µL, 50 µmol, 1.0 equiv.) were added with 25 µL Hamilton syringe. Quickly, the vial was sealed with a septum. It was heated to 150 °C with heatgun for 1.5 minutes with manual stirring until complete clear solution. The vial cooled to room temperature until gel formation was observed. The reaction was irradiated with an external LED through the plain bottom side of the vial at 23 °C for 2.5 hours.

Then, brine (2 mL) was added, and the aqueous phase was extracted with ethyl acetate (1 mL). The reaction was monitored by GC-FID analysis obtaining. The organic phase was dried over anhydrous sodium sulfate, filtered from the drying agent, and concentrated in vacuo. The crude was purified via flash column chromatography using a hexane/ethyl acetate mixture as the mobile phase.

5.6.9 Kinetic studies





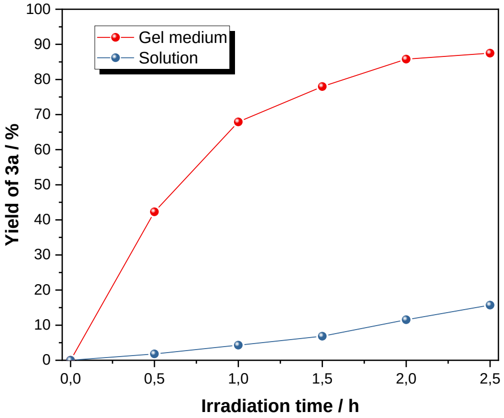


Figure E10. Top: Relationship between conversion of **1a** versus irradiation time. Bottom: Relationship between production of **3a** versus irradiation time.

5.6.10 Frozen model reaction procedure

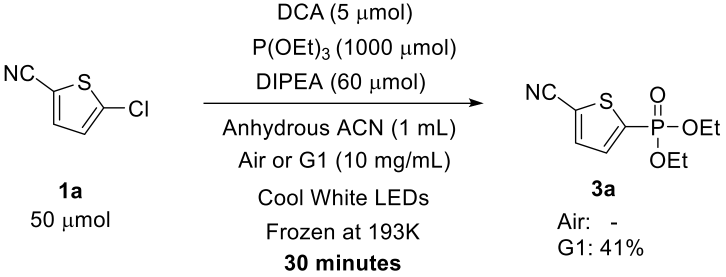


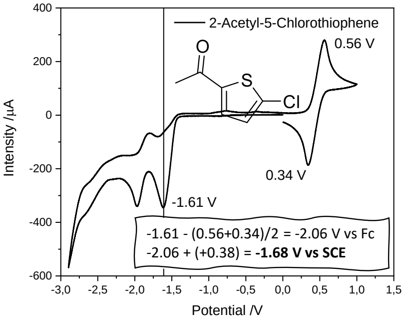
Figure E11. Frozen reaction in aerated frozen solution and aerated frozen gel.

A vial (10 mL) was charged with 9,10-anthracenedicarbonitrile (1.2 mg, 5 µmol, 10 mol% and the correspondent gelator (**G1**, 10 mg). Anhydrous acetonitrile (1.0 mL) was poured and 5-chloro-2-thiophenecarbonitrile (5.4 µL, 50 µmol, 1.0 equiv.) and triethyl phosphite (180 µL, 1000 µmol, 20.0 equiv.) were added. Then, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and dodecanenitrile (12.0 µL, 50 µmol, 1.0 equiv.) were added with 25 µL Hamilton syringe. Quickly, the vial was sealed with a septum. It was heated to 150 °C with heatgun for 1.5 minutes with manual stirring until complete clear solution. The vial cooled to room temperature until gel formation was observed. The vial was frozen at 193K for 2 hours. Later, the frozen vials were irradiated with an external LED through the plain bottom side of the vial at 23 °C for 30 minutes. The reactions were monitored by GC-FID analysis.

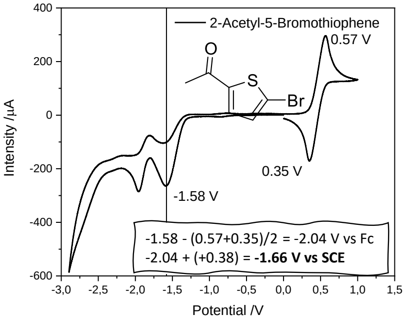
Finally, the gel was broken with ethyl acetate (1 mL), and it was clean with brine (2 mL). The organic phase was dried over anhydrous sodium sulfate, filtered from the drying agent, and concentrated in vacuo.

5.6.11 Cyclic Voltammetry

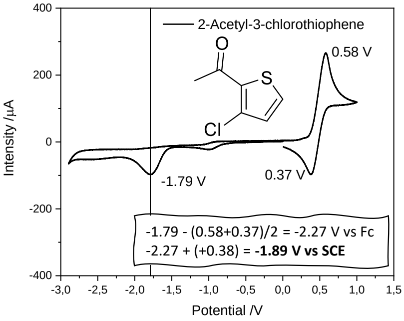
The redox potentials were measured by cyclic voltammetry with an Solartron 1284 potentiostat. All measurements were made in deaerated acetonitrile containing tetrabutylammonium tetrafluoroborate (0.1 M) as supporting electrolyte, a glassy carbon as working electrode, a platinum wire as counter electrode, a silver wire as pseudoreference, and ferrocene (0.01 M) as internal standard. The scan rate was 100 mV·s−1. Potentials are reported with respect to the saturated calomel electrode (SCE) as reference.



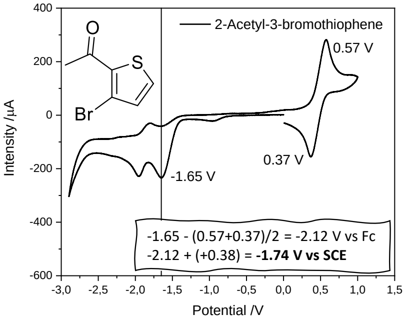
-1.61 - (0.56+0.34)/2 = -2.06 V vs Fc
-2.06 + (+0.38) = **-1.68 V vs SCE**



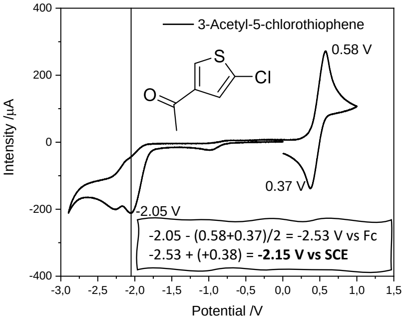
-1.58 - (0.57+0.35)/2 = -2.04 V vs Fc
-2.04 + (+0.38) = **-1.66 V vs SCE**



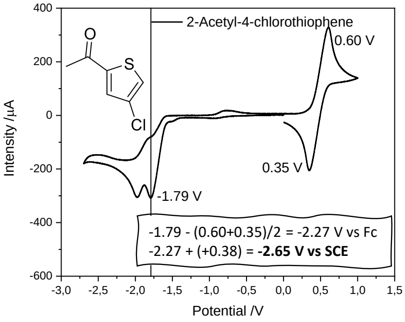
-1.79 - (0.58+0.37)/2 = -2.27 V vs Fc
-2.27 + (+0.38) = **-1.89 V vs SCE**



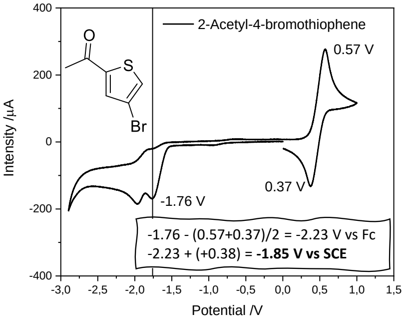
-1.65 - (0.57+0.37)/2 = -2.12 V vs Fc
-2.12 + (+0.38) = **-1.74 V vs SCE**



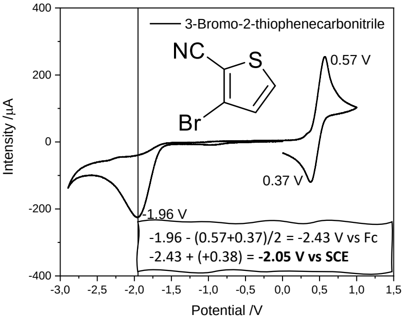
-2.05 - (0.58+0.37)/2 = -2.53 V vs Fc
-2.53 + (+0.38) = **-2.15 V vs SCE**



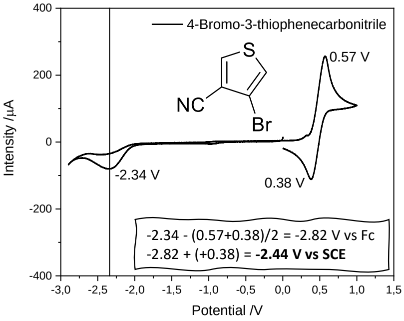
-1.79 - (0.60+0.35)/2 = -2.27 V vs Fc
-2.27 + (+0.38) = **-2.65 V vs SCE**



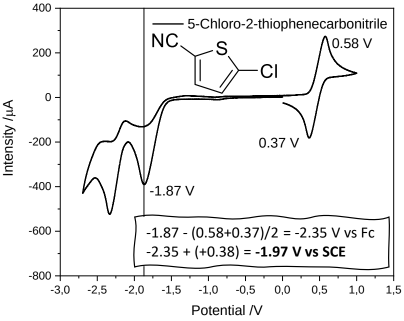
-1.76 - (0.57+0.37)/2 = -2.23 V vs Fc
-2.23 + (+0.38) = **-1.85 V vs SCE**



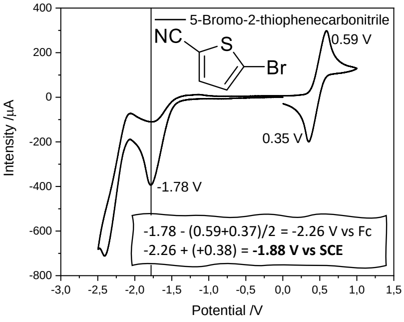
-1.96 - (0.57+0.37)/2 = -2.43 V vs Fc
-2.43 + (+0.38) = **-2.05 V vs SCE**



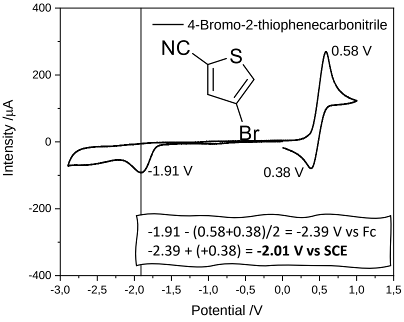
-2.34 - (0.57+0.38)/2 = -2.82 V vs Fc
-2.82 + (+0.38) = **-2.44 V vs SCE**



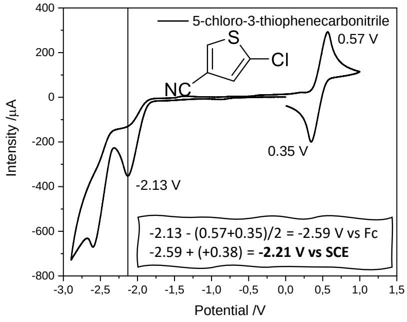
-1.87 - (0.58+0.37)/2 = -2.35 V vs Fc
-2.35 + (+0.38) = **-1.97 V vs SCE**



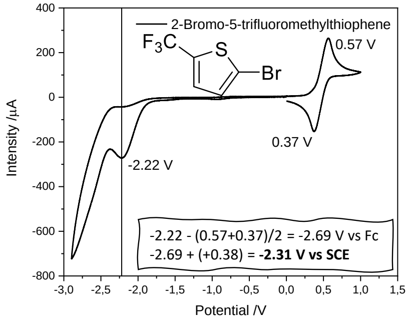
-1.78 - (0.59+0.37)/2 = -2.26 V vs Fc
-2.26 + (+0.38) = **-1.88 V vs SCE**



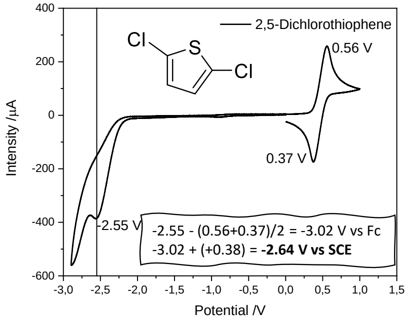
-1.91 - (0.58+0.38)/2 = -2.39 V vs Fc
-2.39 + (+0.38) = **-2.01 V vs SCE**



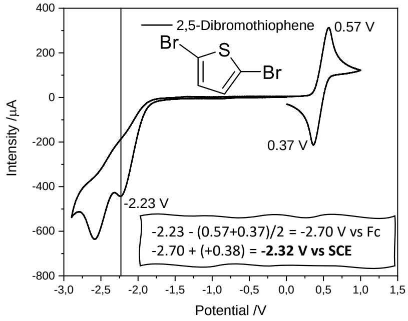
-2.13 - (0.57+0.35)/2 = -2.59 V vs Fc
-2.59 + (+0.38) = **-2.21 V vs SCE**



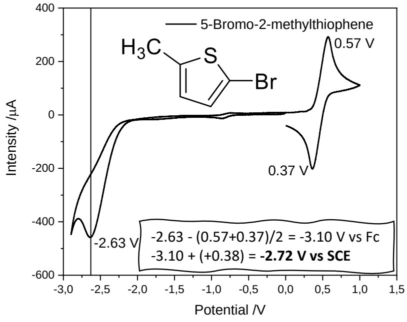
-2.22 - (0.57+0.37)/2 = -2.69 V vs Fc
-2.69 + (+0.38) = **-2.31 V vs SCE**



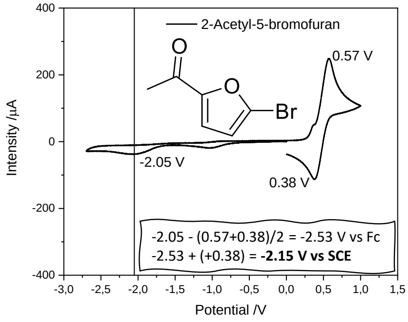
-2.55 - (0.56+0.37)/2 = -3.02 V vs Fc
-3.02 + (+0.38) = **-2.64 V vs SCE**



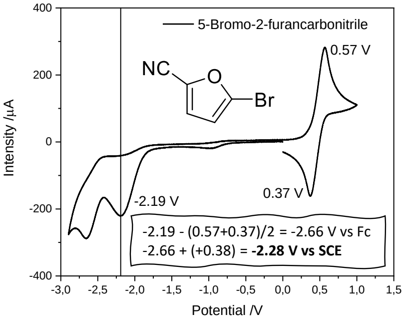
-2.23 - (0.57+0.37)/2 = -2.70 V vs Fc
-2.70 + (+0.38) = **-2.32 V vs SCE**

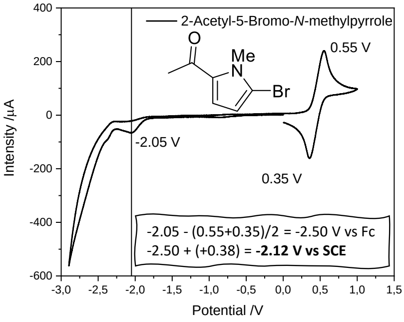


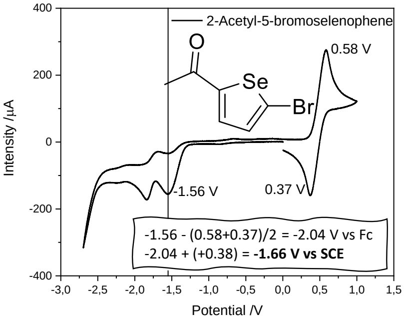
-2.63 - (0.57+0.37)/2 = -3.10 V vs Fc
-3.10 + (+0.38) = **-2.72 V vs SCE**

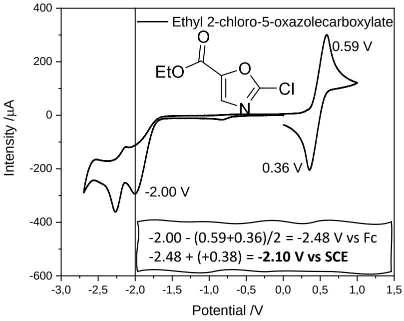


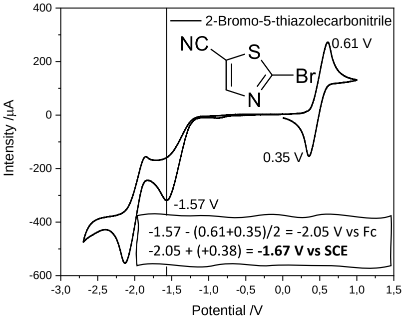
-2.05 - (0.57+0.38)/2 = -2.53 V vs Fc
-2.53 + (+0.38) = **-2.15 V vs SCE**

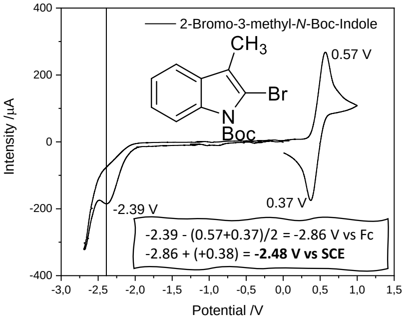

5-Bromo-2-furancarbonitrile
NC
O
Br
0.57 V
0.37 V
-2.19 V
-2.19 - (0.57+0.37)/2 = -2.66 V vs Fc
-2.66 + (+0.38) = **-2.28 V vs SCE**
Intensity /µA
Potential /V
400
200
0
-200
-400
-3,0
-2,5
-2,0
-1,5
-1,0
-0,5
0,0
0,5
1,0
1,5

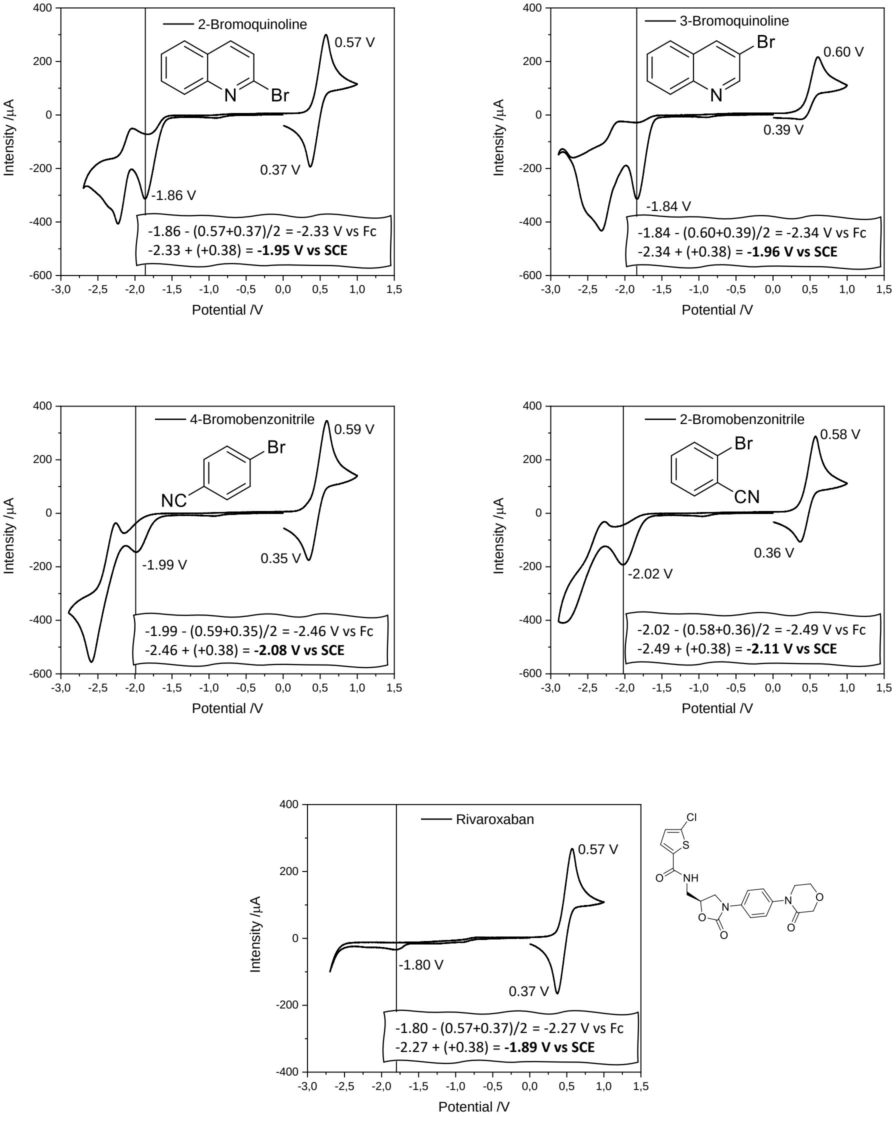

2-Acetyl-5-Bromo-*N*-methylpyrrole
O
Me
N
Br
0.55 V
0.35 V
-2.05 V
-2.05 - (0.55+0.35)/2 = -2.50 V vs Fc
-2.50 + (+0.38) = **-2.12 V vs SCE**
Intensity /µA
Potential /V
400
200
0
-200
-400
-600
-3,0
-2,5
-2,0
-1,5
-1,0
-0,5
0,0
0,5
1,0
1,5


2-Acetyl-5-bromoselenophene
O
Se
Br
0.58 V
0.37 V
-1.56 V
-1.56 - (0.58+0.37)/2 = -2.04 V vs Fc
-2.04 + (+0.38) = **-1.66 V vs SCE**
Intensity /µA
Potential /V
400
200
0
-200
-400
-3,0
-2,5
-2,0
-1,5
-1,0
-0,5
0,0
0,5
1,0
1,5


Ethyl 2-chloro-5-oxazolecarboxylate
O
EtO
O
Cl
N
0.59 V
0.36 V
-2.00 V
-2.00 - (0.59+0.36)/2 = -2.48 V vs Fc
-2.48 + (+0.38) = **-2.10 V vs SCE**
Intensity /µA
Potential /V
400
200
0
-200
-400
-600
-3,0
-2,5
-2,0
-1,5
-1,0
-0,5
0,0
0,5
1,0
1,5


2-Bromo-5-thiazolecarbonitrile
NC
S
Br
N
0.61 V
0.35 V
-1.57 V
-1.57 - (0.61+0.35)/2 = -2.05 V vs Fc
-2.05 + (+0.38) = **-1.67 V vs SCE**
Intensity /µA
Potential /V
400
200
0
-200
-400
-600
-3,0
-2,5
-2,0
-1,5
-1,0
-0,5
0,0
0,5
1,0
1,5


2-Bromo-3-methyl-*N*-Boc-Indole
CH3
Br
N
Boc
0.57 V
0.37 V
-2.39 V
-2.39 - (0.57+0.37)/2 = -2.86 V vs Fc
-2.86 + (+0.38) = **-2.48 V vs SCE**
Intensity /µA
Potential /V
400
200
0
-200
-400
-3,0
-2,5
-2,0
-1,5
-1,0
-0,5
0,0
0,5
1,0
1,5



-1.86 - (0.57+0.37)/2 = -2.33 V vs Fc
-2.33 + (+0.38) = **-1.95 V vs SCE**

-1.84 - (0.60+0.39)/2 = -2.34 V vs Fc
-2.34 + (+0.38) = **-1.96 V vs SCE**

-1.99 - (0.59+0.35)/2 = -2.46 V vs Fc
-2.46 + (+0.38) = **-2.08 V vs SCE**

-2.02 - (0.58+0.36)/2 = -2.49 V vs Fc
-2.49 + (+0.38) = **-2.11 V vs SCE**

-1.80 - (0.57+0.37)/2 = -2.27 V vs Fc
-2.27 + (+0.38) = **-1.89 V vs SCE**

Figure E12. Cyclic voltammetry spectra of the corresponding (hetero)arene halides.

5.6.12 Oscillatory Rheology

Oscillatory rheology was performed with an AR 2000 Advanced rheometer (TA Instruments) equipped with a Julabo C cooling system. A 1000 µm gap setting, and a torque setting of 40000 dyn cm−2 at 25 °C were used for the measurements in a plain-plate (40 mm, stainless steel). The following experiments were performed using 2 mL total gel volume: (a) dynamic strain sweep (DSS), variation of G′ and G′′ with strain (from 0.01 to 100%); (b) dynamic frequency sweep (DFS), variation of G′ and G′′ with frequency (from 0.1 to 10 Hz ar 0.1% strain).

5.6.13 Field-Emission Scanning Electron Microscopy

The equipment in operation in the UPV Microscopy Service is the ZEISS ULTRA 55 model, incorporating the following detectors:

- A secondary electron detector (SE2), which provides an SEM topography image of the sample surface with a large depth of field.
- A secondary electron in-lens detector located inside the electron column, which works with low energy secondary electrons and provides images with a higher resolution.
- A backscattered electron detector (AsB), which is sensitive to the variation of atomic number in the elements present in the sample; therefore, it is used to observe changes in the chemical composition of the specimen.
- A backscattered electron In-lens detector (EsB), independent of the secondary In-lens detector, which provides a pure backscattered signal with no secondary electron contamination and very low acceleration potential.
- An X-ray dispersive energy detector (EDS, Oxford Instruments), which receives X-rays from each surface point the electron beam passes over.

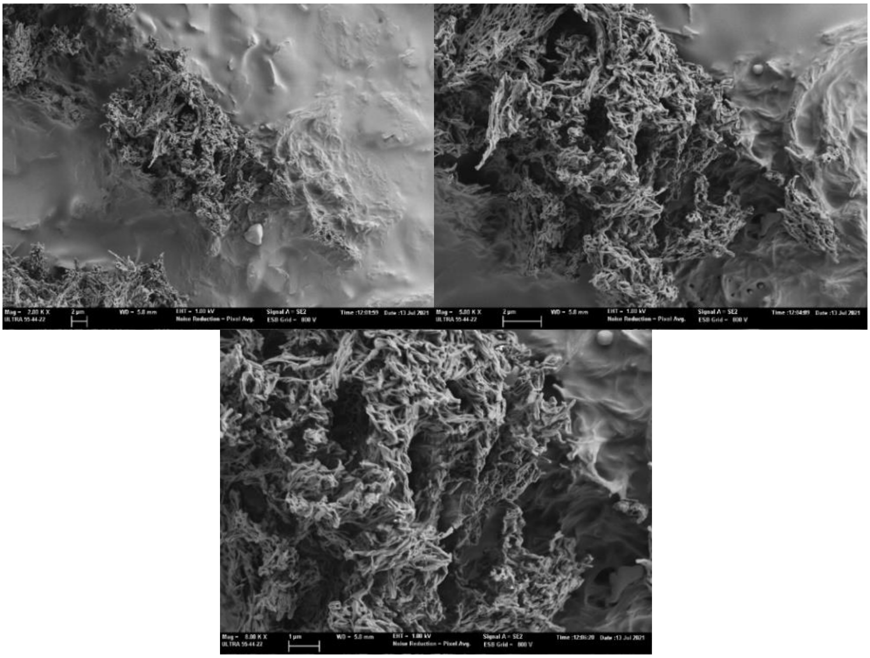


Figure E13. Representative images of FESEM of the unloaded **G1** before irradiation.

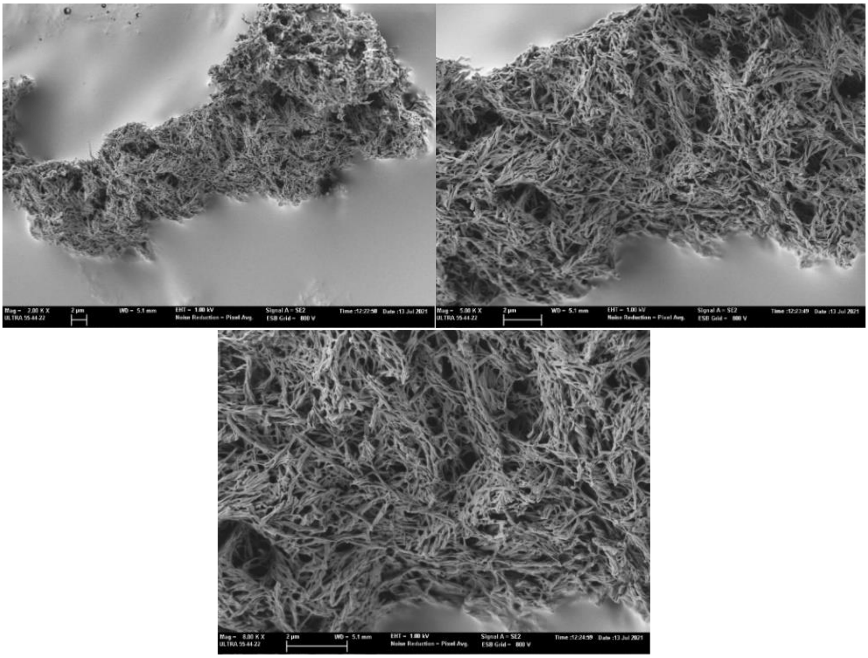


Figure E14. Representative images of FESEM of the unloaded **G1** after 2.5 hours of irradiation.

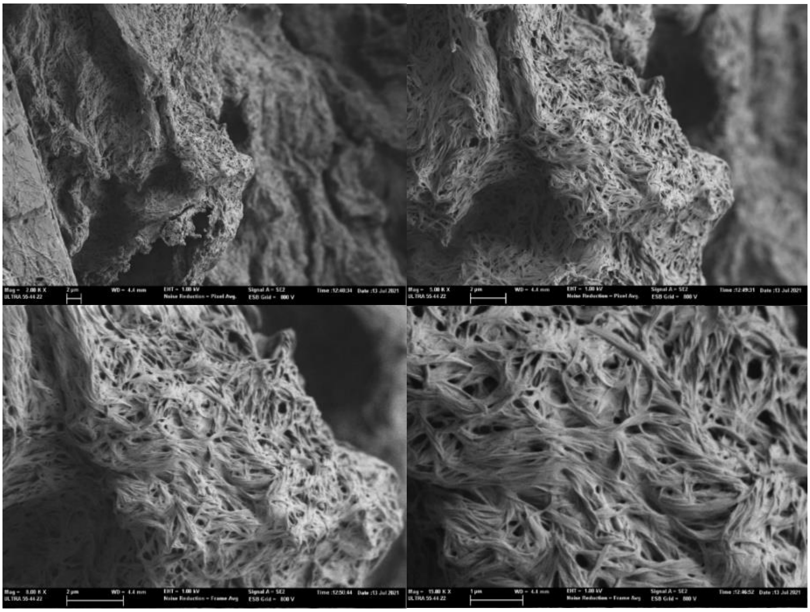


Figure E15. Representative images of FESEM of the loaded **G1** before irradiation.

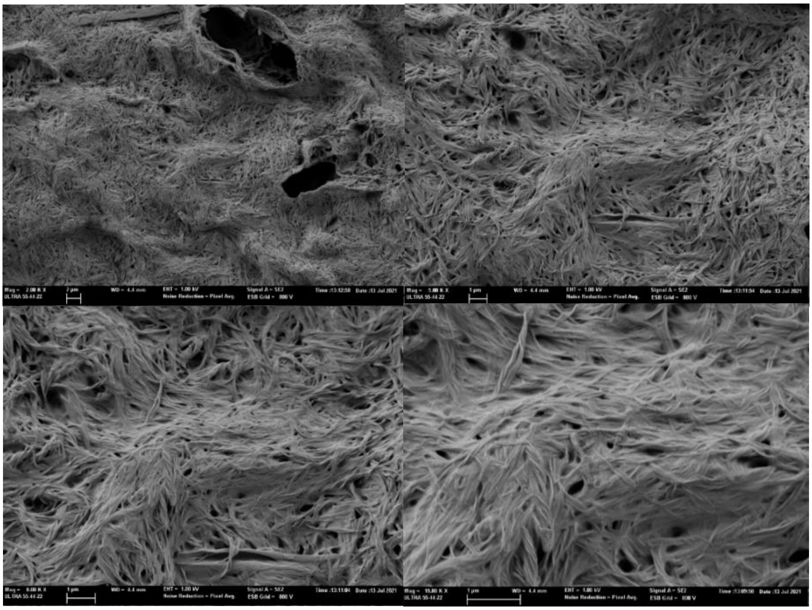
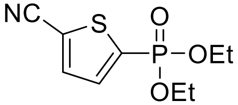


Figure E16. Representative images of FESEM of the loaded **G1** after 2.5 hours of irradiation.

5.6.14 Characterization of compounds

THIOPHENES

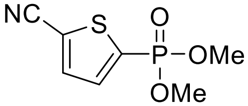
3a. Diethyl (5-cyanothiophen-2-yl)phosphonate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 5-bromo-2-thiophenecarbonitrile (5.7 µL, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 2.5 hours, obtaining **90%** product yield according to GC-FID analysis (75% isolated yield as yellow oil). Using 5-chloro-2-thiophenecarbonitrile, the gel mixture was irradiated for 4 hours, obtaining 87% product yield according to GC-FID analysis.

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.64 (t, *J* = 3.5 Hz, 1H), 7.59 (dd, *J* = 8.1, 3.8 Hz, 1H), 4.26 – 4.07 (m, 4H), 1.35 (t, *J* = 7.1 Hz, 6H) ppm.
^{13}**C NMR** (101 MHz, $CDCl_3$) δ 137.6 (CH, d, *J* = 16.8 Hz), 136.8 (C, d, *J* = 204.5 Hz), 135.7 (CH, d, *J* = 10.7 Hz), 116.8 (C, d, *J* = 10.0 Hz), 113.1 (C, d, *J* = 3.0 Hz), 63.6 (CH_2, d, *J* = 5.6 Hz), 16.4 (CH_3, d, *J* = 6.5 Hz) ppm.
^{31}**P NMR** (162 MHz, $CDCl_3$) δ 7.48 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_9H_{12}NO_3PS$: 246.0348, found: 246.0347.

3b. Dimethyl (5-cyanothiophen-2-yl)phosphonate

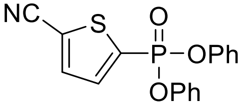


The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 5-bromo-2-thiophenecarbonitrile (5.7 µL, 50 µmol, 1.0 equiv.), trimethylphosphite (30.4 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 2 hours, obtaining **97**% product yield according to GC-FID analysis (80% isolated yield as yellow oil).

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.68 – 7.64 (m, 1H), 7.61 (dd, *J* = 8.1, 3.8 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H) ppm.
^{13}**C NMR** (101 MHz, $CDCl_3$) δ 137.7 (CH, d, *J* = 17.0 Hz), 136.2 (CH, d, *J* = 10.8 Hz), 135.0 (C, d, *J* = 206.0 Hz), 53.7 (CH_3, dd, *J* = 5.5, 2.2 Hz) ppm.

^{31}P NMR (162 MHz, $CDCl_3$) δ 10.47 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_7H_8NO_3PS$: 218.0035, found: 218.0036.

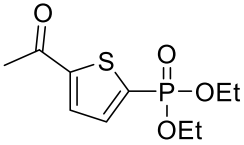
3c. Diphenyl (5-cyanothiophen-2-yl)phosphonate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 5-bromo-2-thiophenecarbonitrile (5.7 µL, 50 µmol, 1.0 equiv.), triphenylphosphite (67.5 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 10 hours, obtaining **60%** product yield according to GC-FID analysis (45% isolated yield as yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.4, 3.8 Hz, 1H), 7.64 (t, *J* = 3.7 Hz, 1H), 7.35 (dd, *J* = 11.1, 4.7 Hz, 4H), 7.21 (dd, *J* = 11.4, 4.0 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 149.9 (C, d, *J* = 9.7 Hz), 137.6 (CH, d, *J* = 15.6 Hz), 137.3 (CH, d, *J* = 11.3 Hz), 134.2 (C, d, *J* = 212.8 Hz), 130.2 (CH, s), 126.1 (CH, d, *J* = 1.2 Hz), 120.57 (CH, d, *J* = 4.7 Hz), 118.2 (C, d, *J* = 10.7 Hz), 112 (C, d, *J* = 3.0 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ -0.18 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{17}H_{12}NO_3PS$: 342.0348, found: 342.0344.

3d. Diphenyl (5-acetylthiophen-2-yl)phosphonate

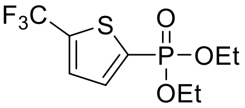


The compound (CAS: 1119779-20-2) was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 2-acetyl-5-bromothiophene (4 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 4 hours, obtaining **91%** product yield according to GC-FID analysis (78% isolated yield as yellow oil). Using 2-acetyl-5-chlorothiophene and 20 equivalents of triethylphosphite, the gel mixture was irradiated for 24 hours, obtaining 58% product yield according to GC-FID analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (t, *J* = 3.3 Hz, 1H), 7.63 (dd, *J* = 7.9, 3.7 Hz, 1H), 4.27 – 4.06 (m, 4H), 2.59 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.6 (C, d, *J* = 1.6 Hz), 150.6 (C, d, *J* = 7.2 Hz), 136.7 (CH, d, *J* = 11.5 Hz), 136.4 (C, d, *J* = 203.1 Hz), 132.1 (CH, d, *J* = 17.0 Hz), 63.2 (CH_2, d, *J* = 5.5 Hz), 27.3 (CH_3, s), 16.4 (CH_3, d, *J* = 6.6 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 9.61 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{10}H_{15}O_4PS$: 263.0501, found: 263.0505.

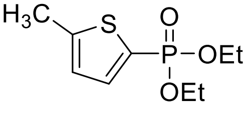
3e. Diethyl (5-(trifluoromethyl)thiophen-2-yl)phosphonate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 2-bromo-5-(trifluoromethyl)thiophene (7.2 µL, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 4 hours, obtaining **94%** product yield according to GC-FID analysis (71% isolated yield as yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (ddd, *J* = 8.1, 3.7, 1.2 Hz, 1H), 7.48 (td, *J* = 3.6, 1.0 Hz, 1H), 4.26 – 4.07 (m, 4H), 1.35 (td, *J* = 7.1, 0.4 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 138.6 (C, dq, *J* = 38.6, 8.5 Hz), 135.9 (CH, d, *J* = 11.3 Hz), 132.9 (C, dd, *J* = 206.1, 1.0 Hz), 129.7 – 128.9 (CH, m), 122.0 (CF_3, dq, *J* = 269.8, 2.9 Hz), 63.3 (d, *J* = 5.5 Hz), 16.4 (d, *J* = 6.6 Hz) ppm.
^{19}F NMR (376 MHz, $CDCl_3$) δ -55.65 (s) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 8.98 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_9H_{12}F_3O_3PS$: 289.0270, found: 289.0271.

3f. Diethyl (5-methylthiophen-2-yl)phosphonate

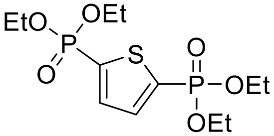


The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (2.4 mg, 10 µmol, 0.2 equiv.), 2-bromo-5-methylthiophene (6.0 µL, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 1000 µmol, 20 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 24 hours, obtaining **42%** product yield according to GC-FID analysis (25% isolated yield as yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 8.5, 3.5 Hz, 1H), 6.83 (td, *J* = 3.5, 1.0 Hz, 1H), 4.21 – 4.03 (m, 4H), 2.54 (d, *J* = 0.8 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 149.1 (C, d, *J* = 7.1 Hz), 137.5 (CH, d, *J* = 11.6 Hz), 126.8 (CH, d, *J* = 17.1 Hz), 124.1 (C, d, *J* = 213.1 Hz), 62.6 (CH_2, d, *J* = 5.3 Hz), 16.4 (CH_3, d, *J* = 6.7 Hz), 15.5 (CH_3, s) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 12.09 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_9H_{15}O_3PS$: 235.0552, found: 235.0554.

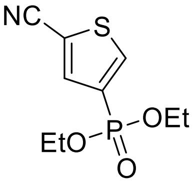
3g. Tetraethyl thiophene-2,5-diylbis(phosphonate)



The compound (CAS: 100651-98-7) was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 2,5-dibromothiophene (5.9 µL, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 1000 µmol, 20 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 10 hours, obtaining 96% product yield according to GC-FID analysis (81% isolated yield as colorless oil). Using 2,5-dichlorothiophene (5.4 µL, 50 µmol, 1.0 equiv.) and 9-10-dicyanoanthracene (2.4 mg, 10 µmol, 0.2 equiv.), the gel mixture was irradiated for 10 hours, obtaining **73%** product yield according to GC-FID analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 4.8 Hz, 1H), 7.64 (d, *J* = 4.8 Hz, 1H), 4.27 – 4.06 (m, 8H), 1.35 (t, *J* = 7.1 Hz, 12H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 136.8 – 136.4 (CH, m), 136.5 (C, dd, *J* = 203.2, 6.2 Hz), 63.3 (CH_2, dd, *J* = 4.1, 1.0 Hz), 16.4 (CH_3, dd, *J* = 4.8, 1.7 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 9.55 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{22}O_6P_2S$: 357.0685, found: 357.0683.

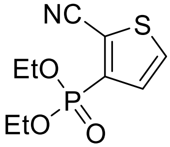
3h. Diethyl (5-cyanothiophen-3-yl)phosphonate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (2.4 mg, 10 µmol, 0.2 equiv.), 4-bromo-2-thiophenecarbonitrile (9.4 mg, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 1000 µmol, 20 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 21 hours, obtaining **89%** product yield according to GC-FID analysis (72% isolated yield as colorless oil).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.16 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.81 (dd, *J* = 4.5, 1.3 Hz, 1H), 4.25 – 4.04 (m, 4H), 1.39 – 1.29 (m, 6H) ppm.
^{13}C NMR (101 MHz, CDCl$_3$) δ 140.7 (CH, d, *J* = 16.7 Hz), 139.2 (CH, d, *J* = 16.3 Hz), 132.0 (C, d, *J* = 199.5 Hz), 113.1 (C, s), 112.3 (C, d, *J* = 21.9 Hz), 63.0 (CH$_2$, d, *J* = 5.6 Hz), 16.5 (CH$_3$, d, *J* = 6.4 Hz) ppm.
^{31}P NMR (162 MHz, CDCl$_3$) δ 9.25 (s) ppm.
HRMS (EI): m/z (M+H)$^+$ = calcd. for $C_9H_{12}NO_3PS$: 246.0348, found: 246.0344.

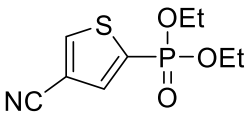
3i. Diethyl (5-cyanothiophen-3-yl)phosphonate



The compound (CAS: 1605306-51-1) was prepared according to the general procedure using 9-10-dicyanoanthracene (2.4 mg, 10 µmol, 0.2 equiv.), 3-bromo-2-thiophenecarbonitrile (5.7 µL, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 1000 µmol, 20 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 2.5 hours, obtaining **96%** product yield according to GC-FID analysis (81% isolated yield as pale-yellow oil).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.64 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.48 (t, *J* = 5.0 Hz, 1H), 4.31 – 4.08 (m, 4H), 1.38 (td, *J* = 7.1, 0.5 Hz, 6H) ppm.
^{13}C NMR (101 MHz, CDCl$_3$) δ 139.7 (C, d, *J* = 193.4 Hz), 132.4 (CH, d, *J* = 19.3 Hz), 132.0 (C, d, *J* = 14.6 Hz), 116.1 (C, d, *J* = 11.3 Hz), 112.6 (C, d, *J* = 3.8 Hz), 63.4 (CH$_2$, d, *J* = 5.9 Hz), 16.4 (CH$_3$, d, *J* = 6.4 Hz) ppm.
^{31}P NMR (162 MHz, CDCl$_3$) δ 7.14 (s) ppm.
HRMS (EI): m/z (M+H)$^+$ = calcd. for $C_9H_{12}NO_3PS$: 246.0348, found: 246.0344.

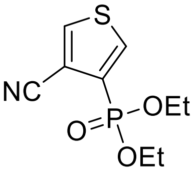
3j. Diethyl (4-cyanothiophen-2-yl)phosphonate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 5-chloro-3-thiophenecarbonitrile (7.6 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 24 hours, obtaining **66%** product yield according to GC-FID analysis (47% isolated yield as colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 5.6, 1.2 Hz, 1H), 7.77 (dd, *J* = 8.1, 1.2 Hz, 1H), 4.30 – 4.08 (m, 4H), 1.36 (td, *J* = 7.1, 0.5 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 141.6 (CH, d, *J* = 6.4 Hz), 137.1 (CH, d, *J* = 12.4 Hz), 132.2 (C, d, *J* = 208.5 Hz), 114.1 (C, d, *J* = 1.3 Hz), 112.2 (C, d, *J* = 21.2 Hz), 63.5 (CH_2, d, *J* = 5.6 Hz), 16.4 (CH_3, d, *J* = 6.4 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 7.87 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_9H_{12}NO_3PS$: 246.0348, found: 246.0344.

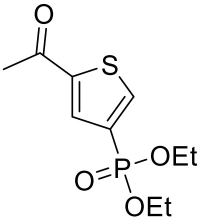
3k. Diethyl (4-cyanothiophen-3-yl)phosphonate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 4-bromo-3-thiophenecarbonitrile (9.7 mg, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 8 hours, obtaining **63%** product yield according to GC-FID analysis (51% isolated yield as colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 8.5, 3.1 Hz, 1H), 8.05 (t, *J* = 3.1 Hz, 1H), 4.32 – 4.06 (m, 4H), 1.37 (td, *J* = 7.1, 0.4 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 138.3 (CH, d, *J* = 15.2 Hz), 138.0 (CH, d, *J* = 16.2 Hz), 132.08 (C, d, *J* = 197.8 Hz), 113.67 (C, s), 112.55 (C, d, *J* = 12.4 Hz), 63.27 (CH_2, d, *J* = 5.9 Hz), 16.38 (CH_3, d, *J* = 6.4 Hz).
^{31}P NMR (162 MHz, $CDCl_3$) δ 7.14 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_9H_{12}NO_3PS$: 246.0348, found: 246.0346.

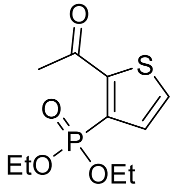
3l. Diethyl (5-acetylthiophen-3-yl)phosphonate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (2.4 mg, 10 µmol, 0.2 equiv.), 2-acetyl-4-bromothiophene (6.4 µL, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 1000 µmol, 20 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 21 hours, obtaining **29%** product yield according to GC-FID analysis (22% isolated yield as white powder). Using 2-acetyl-4-chlorothiophene, the gel mixture was irradiated for 24 hours, obtaining **12%** product yield according to GC-FID analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 5.7, 1.3 Hz, 1H), 8.02 (dd, *J* = 8.2, 1.3 Hz, 1H), 4.25 – 4.10 (m, 4H), 2.55 (s, 3H), 1.35 (td, *J* = 7.1, 0.5 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.6 (C, s), 146.7 (C, d, *J* = 15.6 Hz), 141.8 (CH, d, *J* = 16.2 Hz), 134.0 (CH, d, *J* = 15.8 Hz), 131.4 (C, d, *J* = 197.0 Hz), 62.7 (CH_2, d, *J* = 5.6 Hz), 27.0 (CH_3, s), 16.5 (CH_3, d, *J* = 6.5 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 9.80 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{10}H_{15}O_4PS$: 263.0501, found: 263.0497.

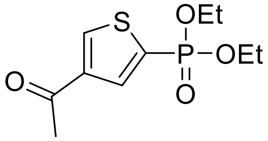
3m. Diethyl (2-acetylthiophen-3-yl)phosphonate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 2-acetyl-3-bromothiophene (10.6 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 8 hours, obtaining **89%** product yield according to GC-FID analysis (70% isolated yield as yellow oil). Using 2-acetyl-3-chlorothiophene, the gel mixture was irradiated for 24 hours, obtaining **48%** product yield according to GC-FID analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 5.0, 2.8 Hz, 1H), 7.51 (t, *J* = 4.9 Hz, 1H), 4.32 – 4.19 (m, 4H), 2.71 (s, 3H), 1.36 (td, *J* = 7.1, 0.5 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.4 (C, d, *J* = 2.6 Hz), 149.1 (C, d, *J* = 15.9 Hz), 134.9 (CH, d, *J* = 14.2 Hz), 132.2 (C, d, *J* = 194.0 Hz), 130.31 (CH, d, *J* = 19.6 Hz), 63.02 (CH_2, d, *J* = 6.0 Hz), 29.4 (CH_3, d, *J* = 1.6 Hz),16.5 (CH_3, d, *J* = 6.5 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 7.14 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{10}H_{15}O_4PS$: 263.0501, found: 263.0498.

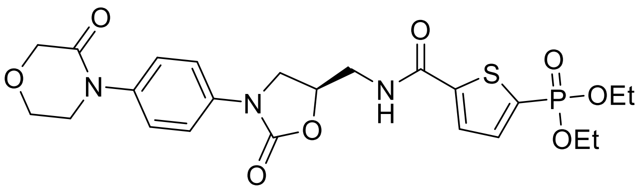
3n. Diethyl (4-acetylthiophen-2-yl)phosphonate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 3-acetyl-5-chlorothiophene (8.0 mg, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 1000 µmol, 20 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 24 hours, obtaining **26%** product yield according to GC-FID analysis (19% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 8.0, 1.2 Hz, 1H), 7.87 (dd, J = 4.5, 1.2 Hz, 1H), 4.21 – 4.06 (m, 4H), 2.58 (s, 3H), 1.35 (t, J = 7.2 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.7 (C, s), 143.4 (C, d, *J* = 17.4 Hz), 138.7 (CH, d, *J* = 6.8 Hz), 136.0 (CH, d, *J* = 12.0 Hz), 129.1 (C, d, *J* = 211.2 Hz), 63.2 (CH_2, d, *J* = 5.4 Hz), 27.9 (CH_3, s), 16.4 (CH_3, d, *J* = 6.6 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 10.98 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{10}H_{15}O_4PS$: 263.0501, found: 263.0502

3o. Diethyl (R)-(5-(((2-oxo-3-(4-(3-oxomorpholino)phenyl)oxazolidin-5-yl)methyl)carbamoyl)thiophen-2-yl)phosphonate

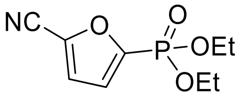


The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (2.4 mg, 10 µmol, 0.2 equiv.), rivaroxaban (21.8 mg, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 1000 µmol, 20 equiv.), DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 24 hours, obtaining **70%** (18.9 mg) isolated product yield as pale-yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (t, *J* = 6.0 Hz, 1H), 7.58 (t, *J* = 3.5 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.48 (dd, *J* = 8.1, 3.8 Hz, 1H), 7.33 – 7.28 (m, 2H), 4.83 (td, *J* = 11.5, 5.1 Hz, 1H), 4.32 (s, 2H), 4.23 – 4.06 (m, 4H), 4.06 – 3.98 (m, 3H), 3.83 (dd, *J* = 9.2, 6.6 Hz, 1H), 3.79 – 3.66 (m, 4H), 1.38 – 1.25 (m, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2 (C, s), 162.1 (C, d, *J* = 2.2 Hz), 154.6 (C, s), 145.8 (C, d, *J* = 8.0 Hz), 137.4 (C, s), 136.9 (C, s),136.6 (CH, d, *J* = 11.4 Hz), 132.9 (C, d, *J* = 205.3 Hz), 129.0 (CH, d, *J* = 17.2 Hz), 126.5 (CH, s), 119.2 (CH, s), 71.7 (CH, s), 68.6 (CH_2, s), 64.2 (CH_2, s), 63.3 (CH_2, dd, *J* = 5.4, 2.4 Hz), 49.9 (CH_2, s), 47.8 (CH_2, s), 42.6 (CH_2, s), 16.4 (CH_3, d, *J* = 6.7 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 9.80 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{23}H_{28}N_3O_8PS$: 538.1374, found: 538.1375.

FURANS

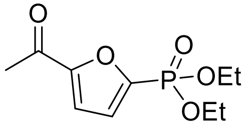
10a. Diethyl (5-cyanofuran-2-yl)phosphonate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 5-bromo-2-furancarbonitrile (5 µL, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 3 hours, obtaining **85%** product yield according to GC-FID analysis (77% isolated yield as yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 3.6, 2.0 Hz, 1H), 7.14 (dd, *J* = 3.6, 2.2 Hz, 1H), 4.32 – 4.10 (m, 4H), 1.37 (td, *J* = 7.1, 0.5 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 150.4 (C, d, *J* = 232.0 Hz), 130.4 (C, d, *J* = 13.4 Hz), 122.4 (d, *J* = 23.2 Hz), 121.8 (d, *J* = 10.4 Hz), 110.5 (C, d, *J* = 2.5 Hz), 63.9 (d, *J* = 5.7 Hz), 16.4 (d, *J* = 6.3 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 0.19 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_9H_{12}NO_4P$: 230.0577, found: 230.0574.

10b. Diethyl (5-acetylfuran-2-yl)phosphonate

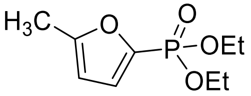


The compound (CAS: 261365-06-4) was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 2-acetyl-5-bromofuran (9.9 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 4 hours, obtaining **96%** product yield according to GC-FID analysis (82% isolated yield as pale-yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 3.6, 2.4 Hz, 1H), 7.14 (dd, *J* = 3.6, 1.8 Hz, 1H), 4.26 – 4.10 (m, 4H), 2.51 (s, 3H), 1.34 (q, *J* = 6.9 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 187.3 (C, d, *J* = 1.0 Hz), 156.4 (C, d, *J* = 9.5 Hz), 147.9 (C, d, *J* = 236.5 Hz), 123.3 (CH, d, *J* = 24.0 Hz), 116.0 (CH, d, *J* = 10.7 Hz), 63.5 (CH_2, d, *J* = 5.6 Hz), 26.5 (CH_3, d, *J* = 1.6 Hz), 16.4 (CH_3, d, *J* = 6.2 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 2.15 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{10}H_{15}O_5P$: 247.0730, found: 247.0729.

Spectral data were consistent with the literature.[2]

10c. Diethyl (5-methylfuran-2-yl)phosphonate

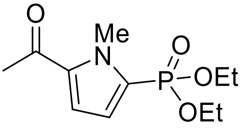


The compound (CAS: 70519-53-8) was prepared according to the general procedure using 9-10-dicyanoanthracene (2.4 mg, 10 µmol, 0.2 equiv.), 2-bromo-5-methylfuran (5.5 µL, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 1000 µmol, 20 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 24 hours, obtaining **30%** product yield according to GC-FID analysis (19% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (dd, *J* = 2.9, 2.2 Hz, 1H), 6.08 (ddd, *J* = 3.4, 2.7, 0.9 Hz, 1H), 4.26 – 4.16 (m, 4H), 2.36 (s, 3H), 1.34 (td, *J* = 7.1, 0.5 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (C, d, *J* = 242.8 Hz), 143.2 (C, s), 124.4 (d, *J* = 26.2 Hz), 107.2 (CH, d, *J* = 11.8 Hz), 62.8 (CH_2, d, *J* = 3.0 Hz), 16.4 (CH_3, d, *J* = 7.04 Hz), 14.2 (CH_3, s) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 5.02 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_9H_{15}O_4P$: 219.0781, found 219.0779.

PYRROLE

11a. Diethyl (5-acetyl-1-methyl-1H-pyrrol-2-yl)phosphonate



The compound (CAS: 1394991-86-6) was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 2-acetyl-5-bromo-*N*-methylpyrrole (10.1 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 4 hours, obtaining **92%** product yield according to GC-FID analysis (76% isolated yield as pale-yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (t, *J* = 4.1 Hz, 1H), 6.76 (dd, *J* = 4.1, 3.2 Hz, 1H), 4.21 – 4.10 (m, 4H), 4.09 (d, *J* = 0.8 Hz, 3H), 2.48 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 6H) ppm.

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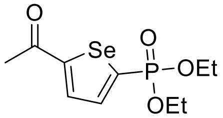
[2] Qun Dang, Srinivas Rao Kasibhatla, K. Raja Reddy, Tao Jiang, M. Rami Reddy, Scott C. Potter, James M. Fujitaki, Paul D. van Poelje, Jingwei Huang, William N. Lipscomb, and Mark D. Erion. *J. Am. Chem. Soc.* **2007**, 129, *50*, 15491–15502

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.0 (C, d, *J* = 1.3 Hz), 135.7 (C, d, *J* = 11.5 Hz), 128.2 (C, d, *J* = 219.2 Hz), 119.6 (CH, d, *J* = 17.0 Hz), 118.1 (CH, d, *J* = 13.9 Hz), 62.8 (CH_2, dd, *J* = 5.3, 2.1 Hz), 36.1 – 36.0 (CH_3, m), 28.6 – 28.1 (CH_3, m), 16.4 (CH_3, d, *J* = 6.5 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 8.33 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{11}H_{18}NO_4P$: 260.1046, found: 260.1046.
Spectral data were consistent with the literature.[3]

SELENOPHENE

12a. Diethyl (5-acetylselenophen-2-yl)phosphonate

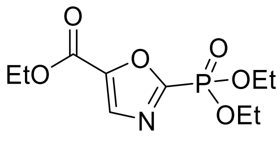


The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 2-acetyl-5-bromoselenophene (12.6 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The gel mixture was irradiated for 4 hours, obtaining **86%** product yield according to GC-FID analysis (71% isolated yield as yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 8.4, 3.0 Hz, 1H), 7.89 (t, *J* = 2.9 Hz, 1H), 4.24 – 4.08 (m, 4H), 2.59 (s, 3H), 1.34 (td, *J* = 7.1, 0.5 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.0 (C, d, *J* = 1.2 Hz), 158.4 (C, d, *J* = 5.5 Hz), 142.4 (C, d, *J* = 197.7 Hz), 139.2 (CH, d, *J* = 10.5 Hz), 134.5 (CH, d, *J* = 18.7 Hz), 63.2 (CH_2, dd, *J* = 5.1, 2.2 Hz), 26.5 (CH_3, d, *J* = 2.1 Hz), 16.4 (CH_3, d, *J* = 6.6 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 12.02 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{10}H_{15}O_4PSe$: 310.9946, found: 310.9944.

OXAZOLE

13a. Ethyl 2-(diethoxyphosphoryl)oxazole-5-carboxylate



The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), ethyl 2-chloro-1,3-oxazole-5-carboxylate (6.6 µL, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10

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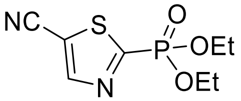
[3] Xiang, C. -, B.; et l. *J. Org. Chem.* **2012**, 77, *17*, 7706–7710.

mg/mL). The gel mixture was irradiated for 15 hours, obtaining **91%** product yield according to GC-FID analysis (76% isolated yield as pale-yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 1.2 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.38 – 4.30 (m, 4H), 1.42 (td, *J* = 7.1, 0.7 Hz, 6H), 1.40 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4 (C, d, *J* = 266.2 Hz), 157.2 (C, d, *J* = 0.5 Hz), 145.0 (C, d, *J* = 5.6 Hz), 133.9 (CH, d, *J* = 14.6 Hz), 64.9 (CH_2, d, *J* = 5.9 Hz), 62.2 (CH_2, s), 16.4 (CH_3, d, *J* = 6.3 Hz), 14.3 (CH_3, s) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ -4.19 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{10}H_{16}NO_6P$: 278.0788, found: 278.0787.

THIAZOLE

14a. Diethyl (5-cyanothiazol-2-yl)phosphonate

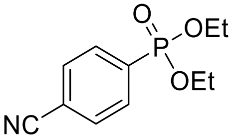


The compound was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), ethyl 2-bromo-1,3-thiazole-5-carbonitrile (9.5 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The reaction mixture was irradiated for 15 hours, obtaining **80%** product yield according to GC-FID analysis (72% isolated yield as pale-yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 1.5 Hz, 1H), 4.39 – 4.22 (m, 4H), 1.39 (td, J = 7.1, 0.7 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6 (C, d, *J* = 237.3 Hz), 153.8 (CH, d, *J* = 26.0 Hz), 111.5 (C, d, *J* = 1.7 Hz), 111.0 (C, d, *J* = 1.5 Hz), 64.9 (CH_2, d, *J* = 6.1 Hz), 16.4 (CH_3, d, *J* = 6.1 Hz) ppm.
^{31}P NMR (162 MHz, $CDCl_3$) δ 0.51 (s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_8H_{11}N_2O_3PS$: 247.0301, found: 247.0300.

6-MEMBERS HETEROARENES

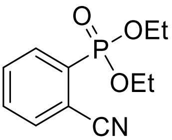
15a. Diethyl (4-cyanophenyl)phosphonate



The compound (CAS: 28255-72-3) was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 4-bromobenzonitrile (9.2 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The reaction mixture was irradiated for 2 hours, obtaining **98%** product yield according to GC-FID analysis (90% isolated yield as colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 13.1, 8.5 Hz, 1H), 7.75 (dd, J = 8.5, 3.6 Hz, 1H), 4.25 – 4.01 (m, 4H), 1.34 (t, J = 7.1 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 134.1 (C, d, J = 187.8 Hz), 132.4 (CH, d, J = 9.8 Hz), 132.1 (CH, d, J = 15.0 Hz), 118.0 (C, s), 116.2 (C, d, J = 3.6 Hz), 62.8 (CH_2, d, J = 5.6 Hz), 16.5 (CH_3, d, J = 6.3 Hz) ppm.
Spectral data were consistent with the literature.[4]

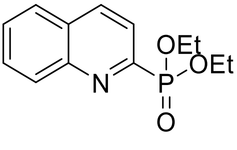
15b. Diethyl (2-cyanophenyl)phosphonate



The compound (CAS: 34595-07-8) was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), 2-bromobenzonitrile (9.2 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The reaction mixture was irradiated for 2 hours, obtaining **92%** product yield according to GC-FID analysis (83% isolated yield as colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 8.07 (m, 1H), 7.83 – 7.77 (m, 1H), 7.74 – 7.61 (m, 2H), 4.39 – 4.03 (m, 4H), 1.48 – 1.31 (m, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 134.7 (CH, d, J = 6.6 Hz), 134.6 (CH, d, J = 9.2 Hz), 132.5 (CH, d, J = 2.6 Hz), 132.5 (C, d, J = 188.0 Hz), 132.3 (CH, d, J = 14.0 Hz), 117.2 (C, d, J = 5.7 Hz), 114.8 (C, d, J = 5.0 Hz), 63.3 (CH_2, d, J = 6.0 Hz), 16.4 (CH_3, d, J = 6.3 Hz) ppm.
Spectral data were consistent with the literature.[5]

15c. diethyl quinolin-2-ylphosphonate



The compound (CAS: 37175-36-3) was prepared according to the general procedure using 9-10-dicyanoanthracene (2.4 mg, 10 µmol, 0.2 equiv.), 2-bromoquinoline (10.4 mg, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 1000 µmol, 20

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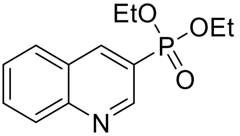
[4] Zhuang, R.; *Org. Lett.* **2011**, 13, *8*, 2110–2113.
[5] Ghosh, I.; Shaikh, R. S.; König, B.; *Angew. Chem. Int. Ed.* **2017**, *56*, 8544.
[5] Bai, Y.; et al. *Org. Lett.* **2019**, *21* (17), 6835-6838.

equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The reaction mixture was irradiated for 10 hours, obtaining **89%** product yield according to GC-FID analysis (74% isolated yield as colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, J = 7.9, 6.3 Hz, 2H), 8.00 (dd, J = 8.4, 4.7 Hz, 1H), 7.87 (dd, J = 8.2, 1.1 Hz, 1H), 7.78 (ddd, J = 8.5, 6.9, 1.4 Hz, 1H), 7.64 (dd, J = 11.1, 4.1 Hz, 1H), 4.39 – 4.22 (m, 4H), 1.38 (t, J = 7.1 Hz, 6H) ppm.
Spectral data were consistent with the literature.[5]

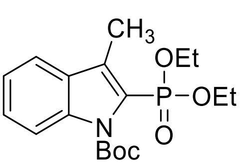
15d. Diethyl quinolin-3-ylphosphonate



The compound (CAS: 82594-50-1) was prepared according to the general procedure using 9-10-dicyanoanthracene (2.4 mg, 10 µmol, 0.2 equiv.), 3-bromoquinoline (6.9 µL, 50 µmol, 1.0 equiv.), triethylphosphite (180 µL, 1000 µmol, 20 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The reaction mixture was irradiated for 10 hours, obtaining **83%** product yield according to GC-FID analysis (69% isolated yield as pale-yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (dd, J = 4.5, 2.0 Hz, 1H), 8.71 (dd, J = 15.2, 1.3 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.92 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.85 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.64 (ddd, J = 8.1, 7.0, 1.0 Hz, 1H), 4.37 – 4.06 (m, 4H), 1.36 (td, J = 7.1, 0.4 Hz, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 150.7 (CH, d, J = 12.2 Hz), 149.5 (C, d, J = 1.2 Hz), 142.2 (CH, d, J = 8.6 Hz), 132.0 (CH, s), 129.7 (CH, d, J = 1.1 Hz), 128.8 (CH, s), 127.8 (CH, d, J = 1.1 Hz), 126.9 (C, d, J = 13.5 Hz), 122.1 (C, d, J = 189.3 Hz), 62.8 (CH_2, d, J = 5.5 Hz), 16.5 (CH_3, d, J = 6.4 Hz) ppm.
Spectral data were consistent with the literature.[4]

15e. Tert-butyl 2-(diethoxyphosphoryl)-3-methyl-1H-indole-1-carboxylate

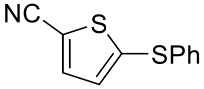


The compound (CAS: 2035049-93-3) was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), *N*-Boc-2-bromo-3-methylindole (16.0 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The reaction mixture was irradiated for 16 hours, obtaining **81%** product yield according to GC-FID analysis (65% isolated yield as yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.5 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.42 (dd, J = 8.2, 7.4 Hz, 1H), 7.30 – 7.25 (m, 1H), 4.32 – 4.01 (m, 4H), 2.60 (d, J = 2.2 Hz, 3H), 1.69 (s, 9H), 1.38 – 1.33 (m, 6H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 149.9 (C, s), 138.1 (C, d, J = 8.8 Hz), 132.1 (C, d, J = 16.9 Hz), 130.0 (C, d, J = 17.0 Hz), 127.3 (CH, s), 122.8 (CH, s), 122.3 (C, d, J = 220.5 Hz), 120.2 (CH, s), 115.4 (CH, s), 84.9 (C, s), 62.5 (CH_2, d, J = 5.5 Hz), 28.2 (CH_3, s), 16.5 (CH_3, d, J = 6.8 Hz), 11.1 (CH_3, s) ppm.
Spectral data were consistent with the literature.[6]

RADICAL TRAPPING

Tert-butyl 2-(diethoxyphosphoryl)-3-methyl-1H-indole-1-carboxylate



The compound (CAS: 1300106-13-1) was prepared according to the general procedure using 9-10-dicyanoanthracene (1.2 mg, 5 µmol, 0.1 equiv.), *N*-Boc-2-bromo-3-methylindole (16.0 mg, 50 µmol, 1.0 equiv.), triethylphosphite (45 µL, 250 µmol, 5 equiv.), diphenyl disulfide (47.5 mg, 250 µmol, 5 equiv.) as trapping agent, dodecanenitrile (12 µL, 50 µmol, 1.0 equiv.) as internal standard, DIPEA (10.5 µL, 60 µmol, 1.2 equiv.) and G1 (10 mg/mL). The reaction mixture was irradiated for 2.5 hours, obtaining **56%** product yield according to GC-FID analysis (41% isolated yield as colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 3.9 Hz, 1H), 7.41 – 7.31 (m, 5H), 7.10 (d, J = 3.9 Hz, 1H) ppm.
^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4 (C, s), 137.9 (CH, s), 134.8 (C, s), 131.9 (CH, s), 130.8 (CH, s), 129.8 (CH, s), 128.5 (CH, s), 113.7 (C, s), 112.1 (C, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{11}H_7NS_2$: 218.0093, found: 218.0089.
Spectral data were consistent with the literature.

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[4] I. Ghosh, R. S. Shaikh, B. König. *Angew. Chem. Int. Ed.* **2017**, *56*, 8544.

[6] Shaikh, Rizwan S.; Duesel, Simon J. S.; Koenig, Burkhard. *ACS Catalysis* **2016**, *6*(12), 8410-8414.

Chapter 6

Effective Formation of New C(sp^2)–S Bonds via Photoactivation of Alkylamine-based Electron Donor–Acceptor Complexes

Jorge C. Herrera-Luna, María Carmen Pérez-Aguilar, Leon Gerken, Olga García Mancheño,* M. Consuelo Jiménez* and Raúl Pérez-Ruiz*

Submitted

Effective Formation of New C(sp^2)–S Bonds via Photoactivation of Alkylamine-based Electron Donor-Acceptor Complexes

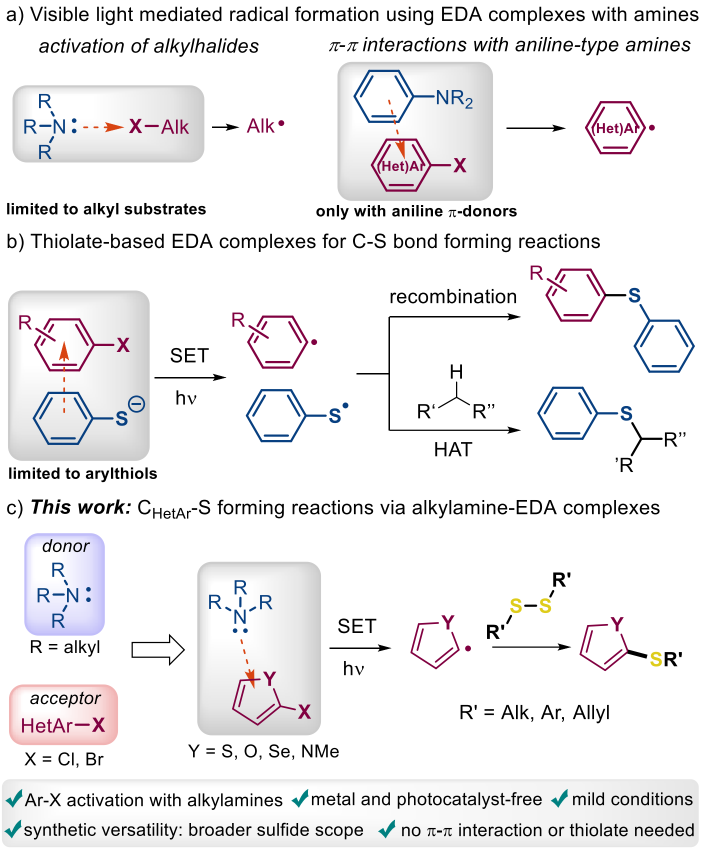
6.1 Abstract

A novel visible light promoted production of C$_{Aryl}$–S bonds through electron donor–acceptor (EDA) complexes of alkylamines with 5- and 6-membered (hetero)arene halides is presented. This represents the first EDA-based thiolation method not relying on π–π or a thiolate-anion-π interactions and provides a readily access to heteroarene radicals, which can be suitably trapped by disulfide derivatives to form the corresponding versatile arylsulfides. Mechanistic investigations on the aspects of the whole process have been conducted by spectroscopic measurements, demonstrating the hypothesized EDA complex formation. Moreover, the strength of this method has been proven by a gram-scale experiment and the late-stage derivatization of an anticoagulant drug.

6.2 Introduction

The electron donor–acceptor (EDA) complex photochemistry allows the mild and selective formation of radicals under visible light irradiation and has recently provided fresh prospects in synthetic chemistry, emerging as an active area of research.[1] This approach relies on the association of an electron-rich donor and an electron-poor acceptor to give rise to a new molecular aggregation in the ground state, the so-called EDA complex.[2] Appearance of a new (and usually weak) absorption band at longer wavelengths (visible light regime), which is not present in the spectra of the individual partners, is a general feature of these species. Direct photolysis then induces an intramolecular single-electron-transfer (SET) event, generating the desired radical intermediates under mild conditions. This approach has been hence employed for the controlled generation of C-centered radicals by activation of colorless organic compounds with visible light, opening new opportunities in organic synthesis. In particular, it has been well-established that tertiary alkylamines such as *N,N*-diisopropylethylamine (DIPEA, the Hünig's base)[3] can be involved in EDA complexes with alkylhalides, generating the corresponding alkyl radicals in subsequent SET reactions under visible light (**Scheme 1a**, left).[4] Moreover, electron rich aromatic amines such as anilines can also form EDA complex-es by π–π-interactions with aromatic substrates (**Scheme 1a**, right).[5] However, these methods are limited in the type of substrates or N-based donors that can be involved. Therefore, many scientists have been recently devoted to the development of more general EDA-based synthetic strategies, being new C-heteroatom bond forming reactions of particular interest.

Scheme 1. Amine-based EDA complexes and C–S bond forming approaches.



In this regard, organosulfur compounds occupy a pivotal role in nature[6] and drug discovery,[7] for which there is a continuous demand on new, efficient methods towards C–S forming-bond reactions. Besides many potent, classical coupling approaches based on transition metal catalysis that often still suffer from catalyst deactivation, harsh conditions or multi-step synthesis,[8] more lately photocatalysis have recently emerged as a powerful alternative strategy for the formation of C–S bonds induced by visible light. Within this respect, the photocatalytic thiolene reaction between thiols and alkenes or alkynes mediated by visible light towards aliphatic thioethers represents one of the most prominent approaches.[9] Regarding aromatic thioethers, the thiolation of six-membered rings,[10] indoles[11] and benzimidazoles[12] have also been successfully achieved using visible light photoredox catalysis.

In spite of the efforts directed to investigate the fabrication of new C–S bonds, novel methodologies that implies the EDA complex photochemistry using visible light in the absence of both photoredox catalysts and transition metals remains still scarce (**Scheme 1b**).[13] Furthermore, the existing approaches rely on EDAs formed by π–π interactions between the donor and acceptor or a thiolate-anion-π interaction, as well as the often incorporation of both the donor and acceptor units in the product, which limit the structural diversity of the methods. To overcome some of the current limitations, we envisioned the use of simple tertiary alkylamines as donors for the formation of EDA complexes with (hetero)arylhalides towards C(sp^2)-functionalization.

In the present work, a simple and effective approach for the direct thiolation of five-membered heteroarenes involving visible-light-absorbing EDA complexes between heteroarene halides and an alkylamine is reported for the first time. After generation of the heteroarene radical upon light irradiation, this open shell intermediate could be now trapped by an external sulfur-substrate, in this case a disulfide derivative, providing a remarkable synthetic versatility (**Scheme 1c**). Our strategy would evade not only π–π interactions but also the need to select highly polarized reagents with donor and acceptor properties that ultimately end up in the product skeleton.

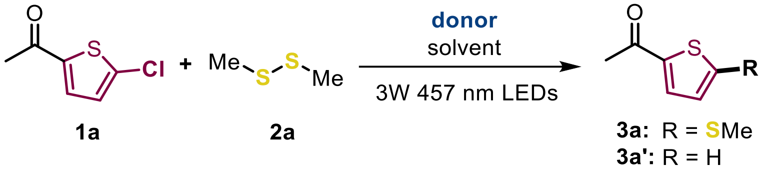
6.3 Results & Discussion

6.3.1 Optimization

To address the stated hypothesis, we focused on the photocoupling reaction between 2-acetyl-5-chlorothiophene (**1a**) and dimethyl disulfide (**2a**) using DIPEA as sacrificial donor (**Table 1**). For initial optimizations, an aerated anhydrous acetonitrile (anhACN) solution of **1a** (0.1 mmol), **2a** (0.3 mmol) and DIPEA (0.3 mmol) was photolyzed with blue LEDs (λ ~ 457 nm) for 2.5 hours observing no changes in the starting materials (entry 1). This result could indicate the deactivation of any excited intermediate in the process by dissolved molecular oxygen, which rapidly diffuses into the organic medium. Accordingly, a nearly complete conversion of **1a** was observed in argon atmosphere affording the desired product **3a** with very good yield (entry 2). A set of control experiments documented the essential role of the donor and light in this coupling reaction (entries 3–4). Utilization of more eco-friendly standard analytical grade ACN led to similar result than that obtained in anh ACN (entry 5 vs entry 2), whereas other solvents did not improve the corresponding yields of **3a** (entries 6–8). Changing the sacrificial donor (e.g. use of Et_3N, DIPA or DABCO) did not provide better outputs (entries 9–11). On the basis of literature data,[14] the model reaction was carried out in the presence of K_2CO_3 in order to enhance the selectivity. Complete conversion of **1a** was then observed after 2.5 hours of irradiation, leading to the desired product **3a** in 89% yield (entry 12); indeed, the amount for both donor (DIPEA) and base (K_2CO_3) were optimized to 0.6 equiv. and 1.5 equiv., respectively (entry 13), obtaining an excellent yield and selectivity (93% for both cases).

To check whether the dechlorination of **1a** could be mediated by the photochemistry of an EDA complex with DIPEA using blue LEDs at room temperature, we performed the model reaction in the absence of **2a** (entry 14). Although prolongated irradiation time was required, the corresponding photoreduced compound **3a’** was obtained as sole product within a 33% conversion. Furthermore, the interaction between **1a** and DIPEA was also demonstrated by employing chloroform ($CHCl_3$) as solvent, as the occurrence of $CHCl_3$ may or may not deactivate the **1a** dehalogenation process. The result clearly indicated that formation of **3a’** was negligible (entry 15), and $CHCl_3$ totally inhibited the process; in other words, the interaction between $CHCl_3$ and DIPEA was predominant under these conditions.[4b] Finally, the thioaryl bromide or iodide derivative were also submitted to this procedure, obtaining the coupling product **3a** in good yields (entries 16–17). Therefore, the optimized conditions involved low loadings of all components related to **1a** (3 equiv. of **2a**, 1.5 equiv. of K_2CO_3 and catalytic amounts of DIPEA, 0.6 equiv.) and irradiation in the visible region at 457 nm with a blue LED in an anaerobic ACN solution for 2.5 hours (see Experimental section for further details).

Table 1. Optimizing the reaction conditions.[a]



Entry	Solvent	Donor	Conv[b] %	3a/3a'[b]	3a Yield[b] %
1[c]	anhACN	DIPEA	0	-	0
2	anhACN	DIPEA	98	76/24	74
3	anhACN	-	0	-	0
4[d]	anhACN	DIPEA	0	-	0
5	ACN	DIPEA	96	75/25	72
6	DMA	DIPEA	91	15/85	14
7	Acetone	DIPEA	97	54/46	52
8	MeOH	DIPEA	95	3/97	3
9	ACN	Et$_3$N	21	81/19	17
10	ACN	DIPA	87	68/32	59
11	ACN	DABCO	0	-	0
12[e]	ACN	DIPEA+K_2CO_3	100	89/11	89
13[f]	**ACN**	**DIPEA+K_2CO_3**	**100**	**93/7**	**93(70)[g]**
14[h]	ACN	DIPEA+K_2CO_3	33	0/100	-
15[i]	CHCl$_3$	DIPEA	0	-	-
16[j]	ACN	DIPEA+K_2CO_3	68	84/16	57
17[k]	ACN	DIPEA+K_2CO_3	91	75/25	68

[a] **1a** (0.1 mmol), **2a** (0.3 mmol), DIPEA (0.3 mmol) in 3 mL of N_2/solvent; irradiation with 3W blue (~457 nm) LEDs at 23 °C for 2.5 hours unless otherwise indicated. [b] Conv = **1a** conversion; determined by GC-FID using internal 1-dodecanonitrile. Estimated error from randomly duplicated experiments independently ±3% (further detail in the S.I.). [c] Under aerobic conditions. [d] Heating (50 °C) in dark. [e] DIPEA (0.1 mmol) + K_2CO_3 (0.3 mmol). [f] DIPEA (0.06 mmol) + K_2CO_3 (0.15 mmol). [g] Isolated yield in parentheses. [h] DIPEA (0.06 mmol) + K_2CO_3 (0.15 mmol) without **2a**. [i] Without **2a**. [j] 2-Acetyl-5-bromothiophene (0.1 mmol), **2a** (0.3 mmol), DIPEA (0.06 mmol) + K_2CO_3 (0.15 mmol). [k] 2-Acetyl-5-iodothiophene (0.1 mmol), **2a** (0.3 mmol), DIPEA (0.06 mmol) + K_2CO_3 (0.15 mmol).

6.3.2 EDA complex formation in the ground state.

In order to confirm the formation of the EDA complex between **1a** and DIPEA in an unambiguous way, absorptivity measurements of different mixtures in acetonitrile at room temperature were performed. Thus, the UV-visible absorption spectra of **1a** at a fixed concentration were recorded in the presence of increasing amounts of DIPEA, and then difference spectra (**1a** + DIPEA)–**1a** were obtained. A new broad band was clearly observed from 345 nm to 500 nm, which was attributed to the EDA complex absorption (see Figure S1 in the S.I.). The equilibrium constant of EDA complex formation (K_{EDA}) was estimated spectrophotometrically by the Benesi-Hildebrand procedure (equation 1, see typical plot in the inset of **Figure E1** in the Experimental section).[15]

$$[\mathbf{1a}]/\mathrm{Abs}_{EDA} = [1/(K_{EDA}\ \varepsilon_{EDA}[\mathrm{DIPEA}])] + (1/\varepsilon_{EDA}) \qquad (1)$$

Here, Abs_{EDA} means the absorbance due to the EDA band at 457 nm, at different concentrations of DIPEA, and ε_{EDA} represents the molar absorption coefficient. The ε_{EDA} value in acetonitrile was calculated from the intercept and found to be 0.2 $M^{-1}cm^{-1}$. The corresponding K_{EDA} value, as determined from the slope, was 9.53 M^{-1}. Hence, this value was found to be compatible with previous similar systems,[5,16] indicating a significant intermolecular interaction between **1a** and DIPEA in the ground state. To further support this feature, NMR titration experiments showed that the ^{1}H NMR resonance signals of the protons at the ring in the thiophene-type halide **1a** shifted upfield upon addition of 10 eq of DIPEA (Figure 1A). Assuming that this interaction could also induce some effects on DIPEA, the most relevant part of the ^{1}H NMR spectrum revealed again an upfield-shifted variation of the signals corresponded to the protons at the centered CH and protons at the methyl of the isopropyl groups of DIPEA in the presence of 10 eq of **1a** (**Figure 1B**).

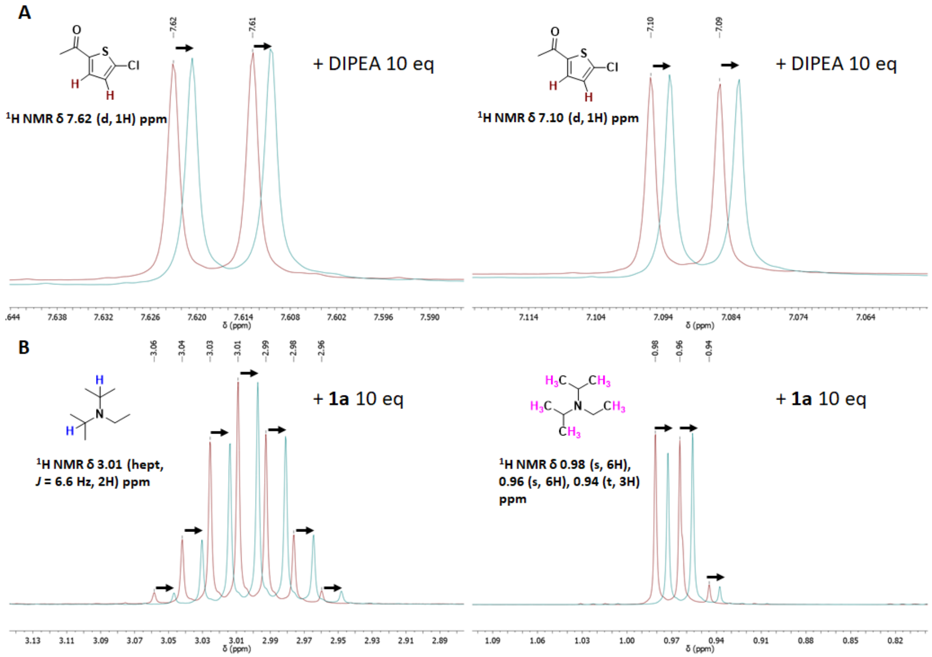


Figure 1. A: Relevant part of the ^{1}H NMR spectra of the starting material 1a (0.033 M) in the absence (red) and in the presence of 10 eq of DIPEA (green). **B**: Relevant part of the ^{1}H NMR spectrum of DIPEA (0.033 M) in the absence (red) and in the presence of 10 eq of **1a** (green). Measurements were carried out in deuterated acetonitrile CD_3CN.

6.3.3 Single electron transfer (SET) upon direct excitation of the EDA complex.

As abovementioned, the involvement of DIPEA in other EDA complex systems and subsequent SET processes upon visible light irradiation was already reported.[4] In these cases, color changes from colorless to deep yellow in the corresponding dehalogenation reactions were observed which was safely attributed to the formation of streptocyanine dyes[17] through an iminium ion intermediate. Interestingly, formation of the iminium ion from DIPEA was directly detected by monitoring time-resolved ^{1}H NMR spectroscopy in $CDCl_3$ where its characteristic peaks were observed at δ = 9.79 ppm and δ = 2.20 ppm. This fact proved unequivocally that a SET process had proceeded from the EDA complex irradiation. Inspired by these findings, the question arose whether our EDA complex system behaved at similar manner. As a matter of fact, new absorption band of a mixture of **1a** and DIPEA during blue light irradiation (λ ~ 457 nm) started to evolve, and after 300 seconds the solution was deep yellow (**Figure 2A**).

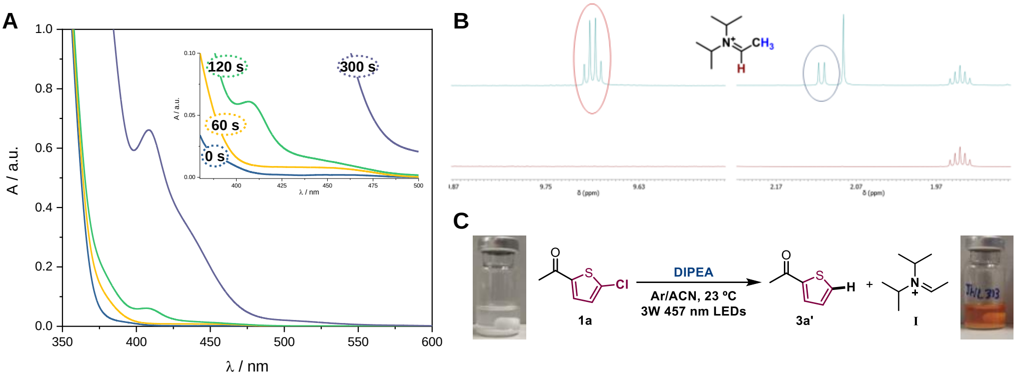


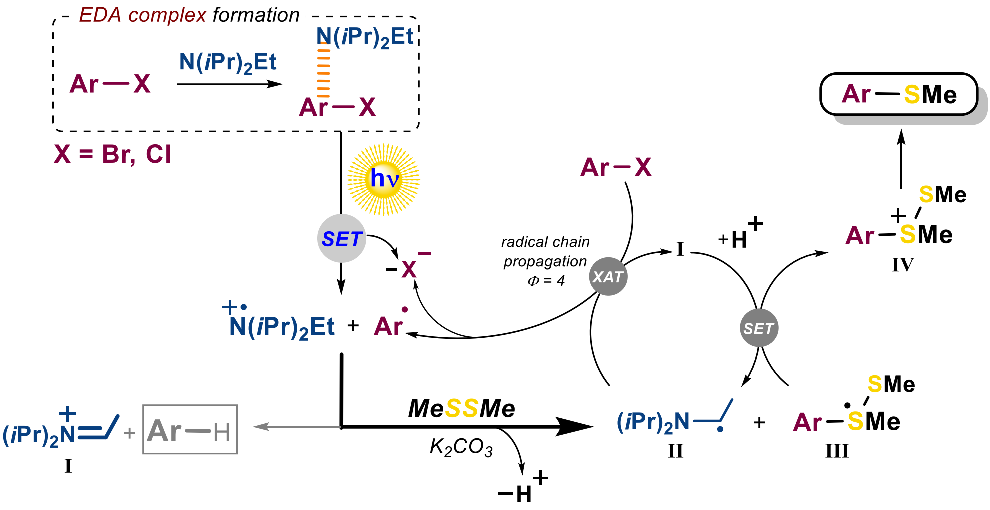
Figure 2. A: Time-dependent UV-Vis. spectra of dechlorination reaction of **1a** (0.033 M) in the presence of DIPEA (0.1 M) recorded in Ar/ACN under blue light (λ ~ 457 nm). **B**: Time-dependent ^{1}H NMR of **1a** (0.016 mmol) in the presence of DIPEA (10 eq) before (bottom) and after (top) irradiation at 420 nm during 90 min in Ar/CD_3CN. **C:** Photograph of the mixture solution containing **1a** + DIPEA showing coloration caused by formation of the iminium ion (**Table 1**, entry 14).

The long wavelength absorption band with maximum at 412 nm exactly matched as previously detected.[4b] In addition, a ^{1}H NMR experiment showed unequivocally the production of the corresponding iminium ion due to appearance of the characteristic peaks (Figure 2B). Therefore, some conclusions could be drawn from these data: *i*) a SET process occurred upon direct photolysis of the EDA complex, leading to the corresponding radical ion pairs; and *ii*) the unstable radical anion **1a**$^{\bullet-}$ fragmented rapidly to afford the thiophene-type radical that was capable to abstract a H-atom from the DIPEA radical cation, giving rise the formal reduction product **3a'** and the corresponding iminium ion (**I**). The latter was confirmed by the steady-state irradiation (Table 1, entries 14 and 15) that indeed an orange-colored solution was obtained (**Figure 2C**).

6.3.4 Mechanism.

With these premises, we proposed a plausible general mechanism for the thiolation of **1a** through EDA complex (Scheme 2).

Scheme 2. Visible-light-powered thiolation of heteroarenes through EDA complexes



First, the interaction between the thiophene-type halide **1a** and DIPEA in the ground state led to the formation of an EDA complex which was capable to absorb at the visible region (400–500 nm). Upon visible-light irradiation, a SET process occurred from the donor moiety (DIPEA) to the acceptor (**1a**), generating the DIPEA radical cation (DIPEA$^{\bullet+}$) and **1a** radical anion (**1a**$^{\bullet-}$). The latter then underwent fast irreversible fragmentation to give the anion Cl$^-$ and the aryl radical Ar$^\bullet$ that could be properly trapped by a nucleophile agent such as **2a** to produce the resultant trivalent sulfur-based radical adduct **III**.

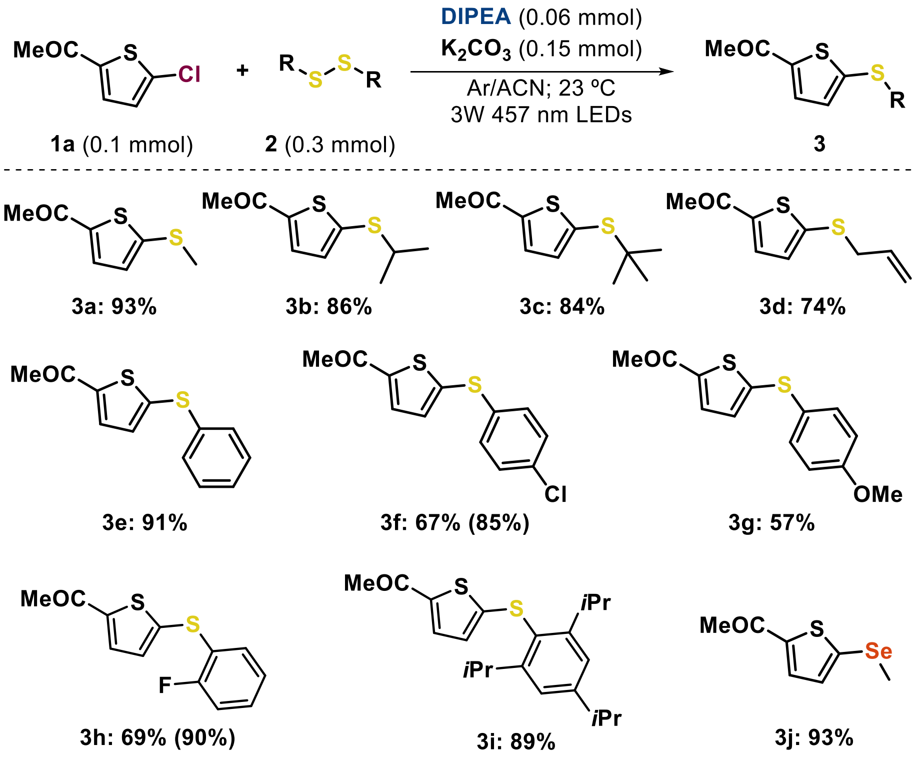
The selectivity of the process was controlled by the addition of K_2CO_3 as base that effectively deprotonated the DIPEA$^{\bullet+}$ to form the α-aminoalkyl radical **II**. This species might be now involved in the homolytic sp^2 C–Cl bond cleavage of **1a** via halogen-atom transfer (XAT)[18a] creating again Ar$^\bullet$ and the iminium ion **I**. A chain-propagating process could be therefore taken place and, certainly, the quantum yield of the model reaction was found to be 4 (see details in the Experimental section).[18b]

Based on previously data,[10a,e] systems close to adduct **III** were found to act as reducing agents to promote electron transfer to several photocatalyst radical cations such as eosinY$^{\bullet+}$ ($E°[EY^{\bullet+}/EY]$ = + 0.78 V vs SCE) or *fac*-Ir(ppy)$_3^{\bullet+}$ ([$E°[Ir^{IV}/Ir^{III}]$ = + 0.76 V vs SCE). Given thus similar reduction potential of DIPEA$^{\bullet+}$

(E°[DIPEA$^{\bullet+}$/DIPEA] = + 0.86 V vs SCE),[19] oxidation of adduct **III** by the protonated **I** gave rise intermediate **IV** and DIPEA, allowing both the electronic balance of the whole process and employment of the amine in substoichiometric amounts (see optimal conditions); indeed, catalytic amounts of DIPEA (0.2 mol %) produced significant 72% yield of **3a** (see details in the Experimental section). This fact was supported by the employment of DABCO as donor (**Table 1**, entry 11) resulted in a negligible **3a** production since this amine contains two bridgehead nitrogen atoms, and therefore the acidity of its radical cation is markedly lower. Finally, the electrophilic species **IV** evolved to the desired thioether product by S–S bond cleavage.

6.3.5 Scope

Scheme 3. Reaction scope of **1a** and disulfide derivatives through EDA complexes[a]



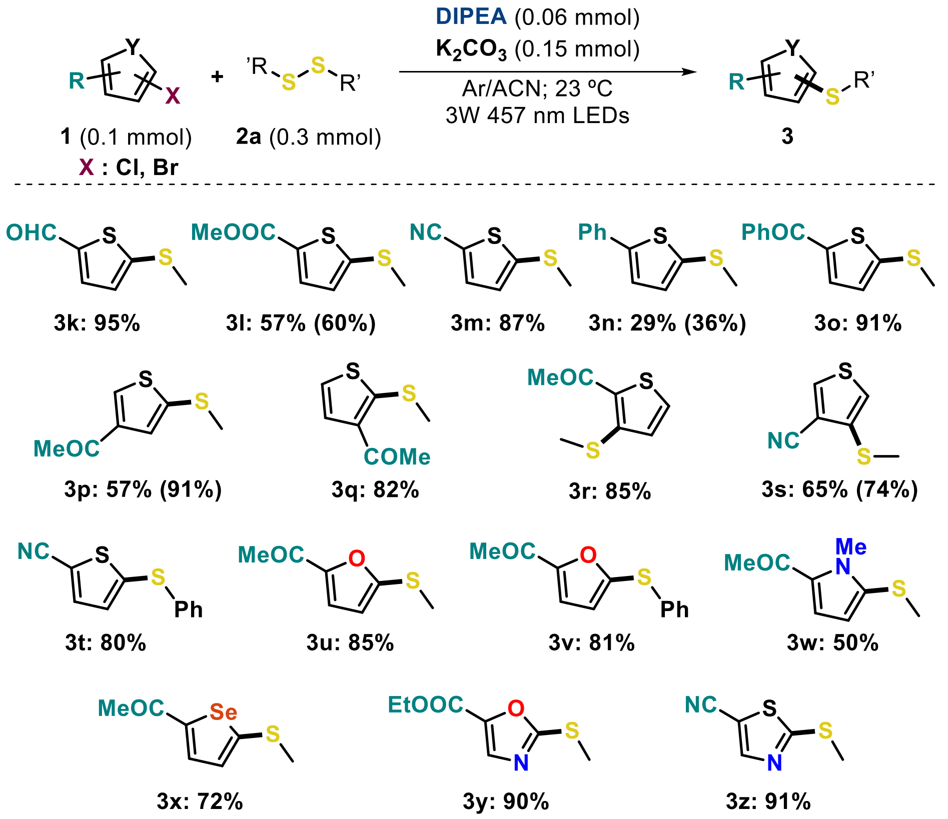
[a]For detailed information on the reaction conditions, see the Supporting Information. Full conversion of compound **1a** in all cases unless otherwise indicated in brackets.

Having standardized the reaction conditions and understood the methodology, the substrate scope for the thiolation of heteroarene halides through an EDA complex was explored (**Scheme 3**).

As the first step, the starting material **1a** was then submitted to blue irradiation in the presence of a diverse set of commercially available disulfide derivatives bearing different alkyl chains such as isopropyl (*i*Pr), *tert*-butyl or allyl under the standard reaction conditions. Gratifyingly, the corresponding coupling products (**3b**–**3d**) were obtained in high yields (74-86%) together with full conversion of the starting material. Disulfide derivatives with aromatic rings also efficiently underwent the present reaction to afford the corresponding products **3e**–**3i** from good to excellent yields (57%–91%). Functional groups such as halogen (F, Cl), OMe or *i*Pr could be well tolerated under mild reaction conditions. In addition, the thiolation of **1a** worked equally well with substrates possessing substituents at *ortho* and *para* positions (**3f** and **3h**). To further demonstrate the utility of the method, we performed our EDA complex strategy using the dimethyl diselenide as trapping agent, affording the desired product **3j** in an excellent yield of 93%.

Encouraged by these results, we set out to study the substrate scope of this milder protocol to encompass 5-membered thiophenes bearing different substitutions (**Scheme 4**). The derivatives presenting an aldehyde, ester, nitrile, phenyl or benzoyl group were capable to react with **2a** under the previously optimized conditions, providing the corresponding products **3k**–**3o** in moderate to excellent yields (29%–95%). Moreover, the reaction tolerated all possible positions of the halogen leaving group, as well as activating unit. Thus, the products **3p**–**3t** were successfully obtained in good to high yields from the thiolation of thiophene halides having the acetyl or the nitrile group shifted from position 2 to 3 or 4 in the heteroarene ring, or when the halogen atom is also in position 2 or 3. The feasibility of this novel procedure was also explored with other five-membered haloheterocycles such as furan, pyrrole, selenophene, oxazole or thioxazole halides. The outcomes indicated that the coupling reaction of **2a** or **2e** with the corresponding heteroarenes brilliantly succeeded (**3u**–**3z**), with excellent yields in some cases (for instance, 90% and 91% for **3y** and **3z**, respectively).

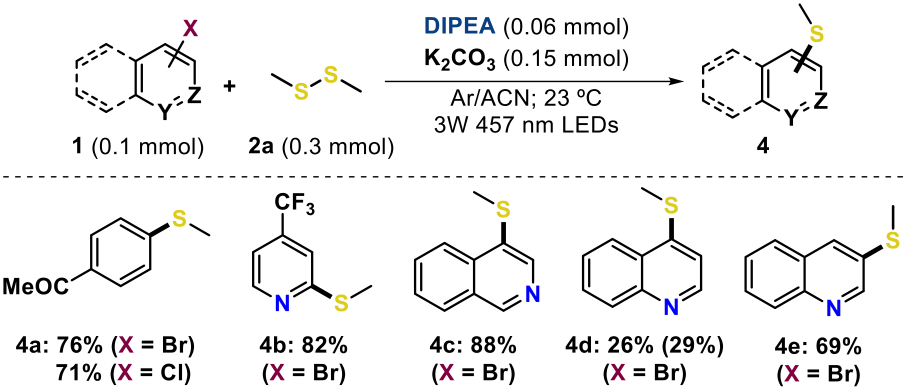
Scheme 4. Reaction scope of 5-membered heteroarene halides and dimethyl disulfide through EDA complexes[a]



[a] For detailed information on the reaction conditions, see the Experimental section. Full conversion of starting materials **1** in all cases unless otherwise indicated in brackets.

To check the generality of our procedure, the study was expanded to the thiolation of 6-membered ring (hetero)aryl halides (**Scheme 5**). To our delight, the simple 4-bromo and 4-chloro acetophenones were also reactive under the standard conditions using the DIPEA-K_2CO_3 system, leading to the thioanisole derivative **4a** in 76% and 71%, respectively. Moreover, other types of 6-membered nitrogen-containing haloarenes were also compatible under the optimized conditions. Hence, the reaction of 2-bromo-4-trifluoromethyl pyridine, 4-bromo isoquinoline and 4-bromo quinoline provided the corresponding heteroaromatic methylsulfide products **4b**–**4d**, which were obtained in moderate to high yields (26%–88%).

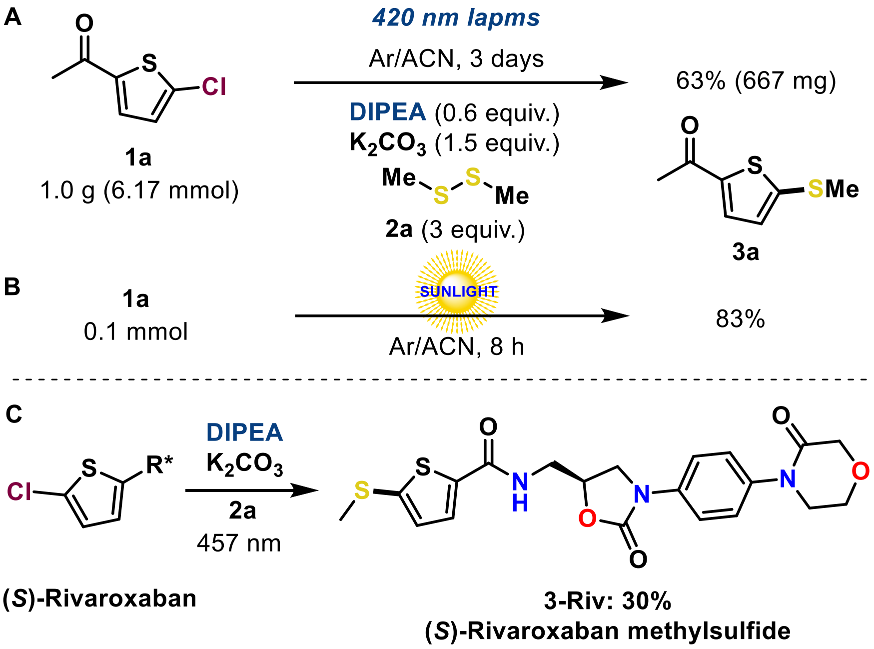
Scheme 5. Reaction scope of 6-membered (hetero)arene halides and dimethyl disulfide through EDA complexes[a]



[a] For detailed information on the reaction conditions, see the Experimental section. Full conversion of starting materials **1** in all cases unless otherwise indicated in brackets.

In addition, the practicability and scalability of this protocol were successfully demonstrated by performing the model reaction at 1 gram scale under the standard conditions for 3 days, resulting in a **3a** yield of 63% (**Scheme 6A**; see Experimental section for more details). Moreover, the reaction could also be performed under sunlight irradiation, which led to the desired product **3a** in 83% yield after 8 hours of a whole sunny day (**Scheme 6B**; see Experimental section for details). Finally, the synthetic potential of the developed photochemical transformation through EDA complex was demonstrated by applying this method to the late stage thiolation of (*S*)-rivaroxaban, an oral anticoagulant agent for the prevention and treatment of thromboembolic disorders.[20] The corresponding thioether product **3-Riv** was isolated in 30% yield (**Scheme 6C**).

Scheme 6. A: Upscaling of the model reaction. **B**: Use of sunlight irradiation. **C**: Application of a late-stage thiolation[a]



[a] See the Experimental section for detailed information.

6.4 Conclusion

In summary, a simple and effective metal-free, visible light-mediated thiolation of heteroarenes has been successfully achieved through an EDA complex approach with substoichiometric amounts of readily available trialkylamines. Selective photolysis to the EDA complex leads to the generation of the heteroarene radical that is suitably trapped by a disulfide derivative. This simple approach provides a potent, versatile, synthetic technique for the effective production of new C(sp^2)–S bonds that avoids the need of arylthiolates and/or π–π interactions for the generation of the photoactive EDA complex. In particular, DIPEA showed the best performance as electron donor in the presence of K_2CO_3 as base, allowing for the dehalogenative thiolation of a number of 5- and 6-membered (hetero)arene halides in up to 95% yield. Mechanistic aspects of the whole process have been demonstrated by spectroscopic measurements, whereas the strength of this novel method has been proven by a gram-scale experiment, the efficient use of sunlight irradiation, and the late-stage derivatization of the anticoagulant drug (*S*)-rivaroxaban.

6.5 References

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6.6 Experimental section

6.6.1 Materials and methods

All reagents (≥97% purity) and solvents (≥99% purity) were purchased from commercial suppliers (Merck, TCI, Apollo Scientific, Fluorochem, Scharlab) and used as received unless otherwise indicated. Reactions were carried out in Metria®-Crimp Headspace clear vial flat bottom (10 mL, Ø 20 mm) sealed with Metria®-aluminium crimp cap with moulded septum butyl/natural PTFE (Ø 20 mm).

Irradiation was performed with a 3W blue LEDs (455-460 nm) from Avonec. TLC was performed on commercial SiO_2-coated aluminium and plastic sheets (DC60 F254, Merck). Visualization was done by UV-light (254nm).

Product were isolated materials after column flash chromatography or TLC on silica gel (Merck, mesh 35-70, 60 Å pore size) and their corresponding yields were determined by quantitative GC-FID measurements on an Agilent 8860 GC-System with N_2 as carrier gas. 1-Dodecanenitrile was employed as an internal standard in the GC-FID quantitative measurements; yield products were estimated as: [conversion × selectivity]/mass balance.

Determination of purity and structure confirmation of the literature known products was performed by ^{1}H NMR, ^{13}C NMR, and high-resolution mass spectrometry (HRMS) in case of unknown products. NMR spectral data were measured on a Bruker Advance 400 (400 MHz for ^{1}H, 101 MHz for ^{13}C) spectrometer at 20 °C. Chemical shifts are reported in δ/ppm, coupling constants J are given in Hertz. Solvent residual peaks were used as internal standard for all NMR measurements. The quantification of ^{1}H cores was obtained from integrations of appropriate resonance signals. Abbreviations used in NMR spectra: s – singlet, d – doublet, t – triplet, q – quartet, m – multiplet, dd – doublet of doublet, ddd – doublet of doublet of doublet, td – triplet of doublet and dq – doublet of quartet.

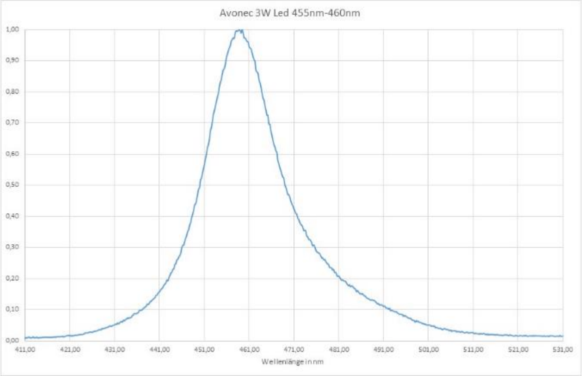
HRMS was carried out was performed in the mass facility of SCSIE University of Valencia. Absorption spectra were recorded on a JASCO V-630 spectrophotometer.

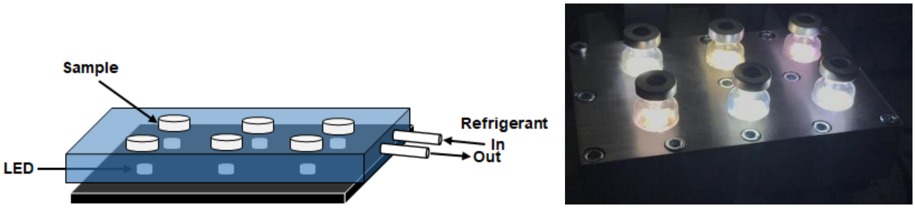
The fluorescence spectra were recorded on an FS5 Edinburgh instrument spectrofluorometer with a SC-05 standard cuvette holder module.

6.6.2 Standard procedure

A vial (10 mL) with a stir bar was loading with the corresponding five-membered heteroarene halide (100 µmol, 1.0 equiv.) and anhydrous K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.). Then, DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) and 1-dodecanenitrile (22.1 µL, 100 µmol, 1.0 equiv.) were injected with a microsyringe. The vial was hermetically sealed with a cap septum. After that, the mixture was purged with argon bubbling for 8 minutes. The reaction was irradiated with an external blue LED (Avonec 3W 455-460 nm) through the plain bottom side of the vial at 22 °C until totally conversion of the starting material.

Finally, brine (1 mL) was added, and the aqueous phase was extracted with ethyl acetate (3 x 2 mL). The reaction was examined by GC-FID analysis. The organic phase was dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuum. The crude was purified via TLC plastic sheet (20 x 20 cm) or flash column chromatography utilizing a hexane/ethyl acetate mixture as the mobile phase.

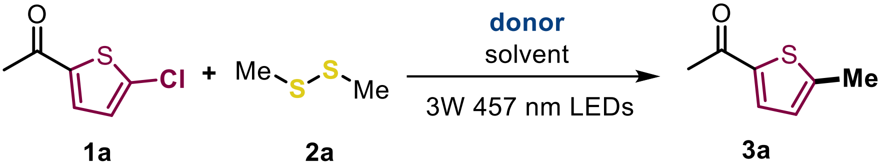




Irradiation setup

6.6.3 Searching for the optimal conditions

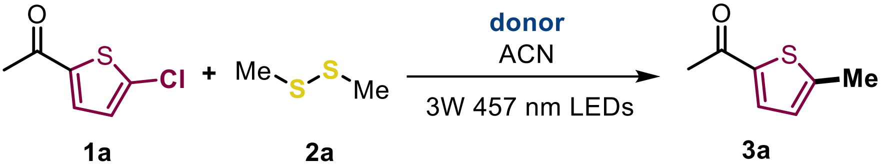
Table E1. Searching for the optimal conditions: Solvent and donor screening.[a]



Entry	Solvent / mL	Donor / Equiv.	*1a Conv / %*	*3a Yield / %*
1	Anh. ACN	-	-	-
2[b]	Anh. ACN	DIPEA (3)	-	-
3[c]	Anh. ACN	DIPEA (3)	-	-
4[d]	Anh. ACN	-	-	-
5	Anh. ACN	DIPEA (3)	98.1	74.6
6[e]	Anh. ACN	DIPEA (3)	-	-
7	**ACN**	**DIPEA** (3)	**96.2**	**72.6**
8	$CHCl_3$	DIPEA (3)	-	-
9	DMF	DIPEA (3)	63.6	12.2
10	DMA	DIPEA (3)	91.4	14
11	Acetone	DIPEA (3)	96.8	52
12	Toluene	DIPEA (3)	0	0
13	DMSO	DIPEA (3)	0	0
14	ACN/H_2O 9/1	DIPEA (3)	100	0
15	EtOAc	DIPEA (3)	0	0
16	MeOH	DIPEA (3)	95.2	2.4
17	ACN	Et_3N (3)	21.6	17.5
18	ACN	DIPA (3)	87	59
19	ACN	**DBU** (3)	100	78.6
20	ACN	DABCO (3)	1.5	1.3
21	ACN	K_2CO_3 (3)	0	0
22	ACN	Ph_3N (3)	47.8	26.4
23	ACN	Ph_3P (3)	8.9	8.9

[a] **1a** (16.2 mg, 0.1 mmol), solvent 4 mL; dimethyl disulfide (26.7 µL, 0.3 mmol, 3 equiv.) and irradiation with 3W blue LEDs (455-460 nm) at 22 °C for 2.5 hours unless otherwise indicated. [b] Reaction carried out without dimethyl disulfide and no irradiation source. [c] Reaction carried out without dimethyl disulfide and no irradiation source at 50 °C. [d] Reaction carried out without dimethyl disulfide, without DIPEA and no irradiation source. [e] Reaction carried out with 3W 515 nm LEDs.

Table E2. Donor-Base combination screening.[a]



Entry	Donor / Equiv.	Base / Equiv.	*1a Conv / %*	*3a Yield / %*
1	**DBU (1)**	**K$_2$CO$_3$ (3)**	**100**	**89**
2	**DIPEA (1)**	**K$_2$CO$_3$ (3)**	**100**	**89.2**
3	DIPEA (0.2)	K$_2$CO$_3$ (3)	76.7	72.3
4	DIPEA (0.6)	K$_2$CO$_3$ (3)	100	91.0
5	DIPEA (1.2)	K$_2$CO$_3$ (3)	100	90.4
6	DIPEA (0.6)	K$_2$CO$_3$ (2)	100	90.6
7	**DIPEA (0.6)**	**K$_2$CO$_3$ (1.5)**	**100**	**91.1**
8	DIPEA (0.6)	K$_2$CO$_3$ (1.2)	96.3	88.1
9	DIPEA (0.6)	K$_2$CO$_3$ (1.5)	85	79.4
10[b]	DIPEA (0.6)	K$_2$CO$_3$ (1.5)	72	68.6
11[c]	DIPEA (0.6)	K$_2$CO$_3$ (1.5)	81.4	76.4
12[d]	**DIPEA (0.6)**	**K$_2$CO$_3$ (1.5)**	**100**	**93.3**
13[e]	DIPEA (0.6)	K$_2$CO$_3$ (1.5)	100	91.1
14[f]	DIPEA (0.6)	K$_2$CO$_3$ (1.5)	100	90.6
15[g]	DIPEA (0.6)	K$_2$CO$_3$ (1.5)	100	88.5
16[h]	DIPEA (0.6)	K$_2$CO$_3$ (1.5)	*48.7*	*46.2*
17[i]	DIPEA (0.6)	K$_2$CO$_3$ (1.5)	56.5	53.1
18[j]	DIPEA (0.6)	K$_2$CO$_3$ (1.5)	87	81.5
19[k]	DIPEA (0.6)	K$_2$CO$_3$ (1.5)	90.2	85.1
20[l]	**DIPEA (0.6)**	**K$_2$CO$_3$ (1.5)**	**100**	**93**

[a] **1a** (16.2 mg, 0.1 mmol), solvent 4 mL; dimethyl disulfide (26.7 µL, 0.3 mmol, 3 equiv.) and irradiation with 3W blue LEDs (455-460 nm) at 22 °C for 2.5 hours unless otherwise indicated. [b] ACN 1 mL. [c] ACN 2 mL. [d] ACN 3 mL. [e] ACN 4 mL. [f] ACN 5 mL. [g] ACN 8 mL. [h] ACN 3 mL in 15 min of irradiation. [i] ACN 3 mL in 30 min of irradiation. [j] ACN 3 mL in 1 hour of irradiation. [k] ACN 3 mL in 1.5 hours of irradiation. [l] ACN 3 mL in 2 hours of irradiation.

6.6.4 Spectroscopical measurement

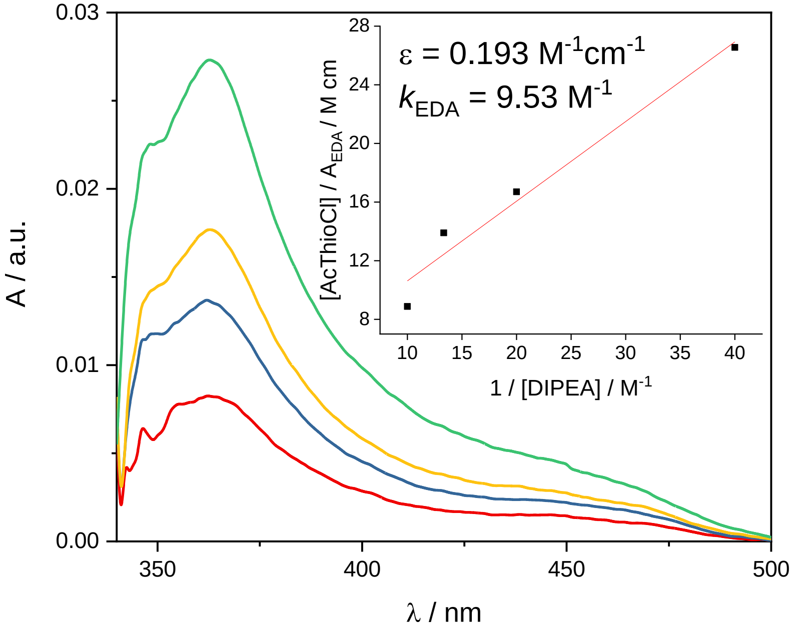
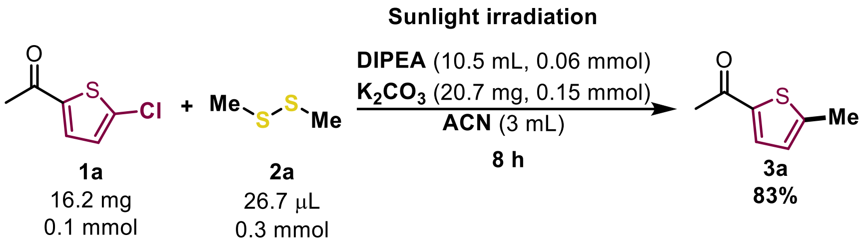


Figure E1. EDA complex formation recorded with the difference among the absorption spectrum of 2-acetyl-5-chlorothiophene 33 mM with DIPEA, the absorption spectrum of 2-acetyl-5-chlorothiophene 33 mM, and the absorption spectra of the corresponding amount of DIPEA in ACN. a) spectrum of a mixture of 2-acetyl-5-chlorothiophene 33 mM + DIPEA 24.75 mM minus spectrum of 2-acetyl-5-chlorothiophene 33 mM, and minus spectrum of DIPEA 24.75 mM in ACN (red), b) spectrum of a mixture of 2-acetyl-5-chlorothiophene 33 mM + DIPEA 49.5 mM minus spectrum of 2-acetyl-5-chlorothiophene 33 mM, and minus spectrum of DIPEA 49.5 mM in ACN (blue), c) spectrum of a mixture of 2-acetyl-5-chlorothiophene 33 mM + DIPEA 74.25 mM minus spectrum of 2-acetyl-5-chlorothiophene 33 mM, and minus spectrum of DIPEA 74.25 mM in ACN (yellow), and d) spectrum of a mixture of 2-acetyl-5-chlorothiophene 33 mM + DIPEA 99 mM minus spectrum of 2-acetyl-5-chlorothiophene 33 mM, and minus spectrum of DIPEA 99 mM in ACN (green).

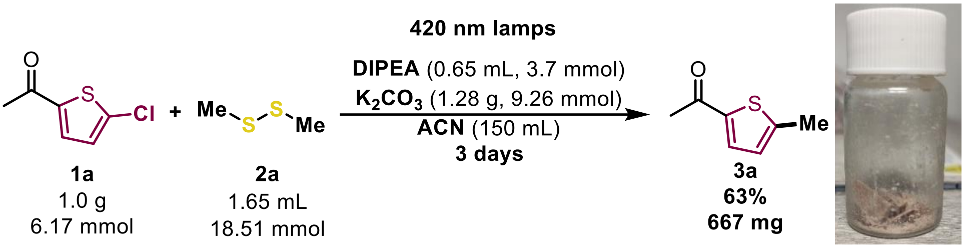
6.6.5 Sunlight irradiation



The compound **3a** was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.1 µL, 100 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) and K_2CO_3 (20.7 mg, 1.5 equiv) in ACN 3 mL. The mixture was irradiated with sunlight for 8 hours, giving an 83% product yield according to GC-FID analysis (65% isolated yield as brown solid).

Location: Camí de Vera S/N, Chemistry Department, Universitat Politècnica de València (UPV), Valencia, Spain (coordinate: 39.482917, -0.341642), temperature: 27 °C, from 9:00 to 17:00. Date: 24/06/2022

6.6.6 Gram scale



1a 1.0 g 6.17 mmol

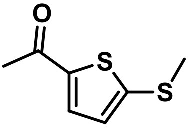
2a 1.65 mL 18.51 mmol

3a **63%** **667 mg**

To scale-up the procedure from 16.2 mg (0.1 mmol to 6.17 mmol), we performed the reaction following the general procedure in a 250 mL flask under 420 nm lamps irradiation for 3 days using 2-acetyl-5-chlorothiophene (1.0 g, 6.17 mmol, 1.0 equiv.), dimethyl disulfide (1.65 mL, 18.51 mmol, 3 equiv.), DIPEA (0.65 mL, 3,7 mmol, 0.6 equiv.) and K_2CO_3 (1.28 g, 9.26 mmol, 1.5 equiv.) in ACN 150 mL. Then, brine (100 mL) was added, and the aqueous phase was extracted with ethyl acetate (3 x 100 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuum. The crude was purified via flash column chromatography using a hexane/ethyl acetate mixture as the mobile phase obtaining 667 mg, 62.7% isolated yield.

6.6.7 Compounds characterization

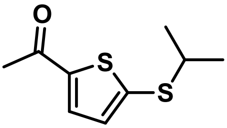
3a. 1-(5-(Methylthio)thiophen-2-yl)ethan-1-one



The compound (CAS: 22102-48-3) was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 2 hours, giving a **93%** product yield according to GC-FID analysis (77% isolated yield as brown powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 4.0 Hz, 1H), 6.92 (d, *J* = 4.0 Hz, 1H), 2.59 (s, 3H), 2.50 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 189.6 (C, s), 150.5 (C, s), 143.5 (C, s), 133.2 (CH, s), 126.8 (CH, s), 26.4 (CH_3, s), 19.6 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_7H_9OS_2$: 173.0089, found: 173.0089.

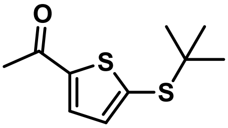
3b. 1-(5-(Isopropylthio)thiophen-2-yl)ethan-1-one



The compound (CAS: 98954-26-8) was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 µmol, 1.0 equiv.), diisopropyl disulfide (49.8 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 2.5 hours, giving an 86% product yield according to GC-FID analysis (78% isolated yield as brown-yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 3.9 Hz, 1H), 7.04 (d, *J* = 3.9 Hz, 1H), 3.34 (dt, *J* = 13.4, 6.7 Hz, 1H), 2.52 (s, 3H), 1.34 (s, 3H), 1.33 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 190.0 (C, s), 146.0 (C; s), 145.6 (C, s), 132.8 (CH, s), 132.7 (CH, s), 41.9 (CH, s), 26.6 (CH_3, s), 23.2 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_9H_{13}OS_2$: 201.0402, found: 201.0400.

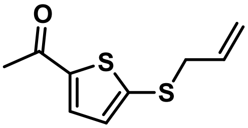
3c. 1-(5-(*tert*-Butylthio)thiophen-2-yl)ethan-1-one



The compound (CAS: 2567707-98-4) was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 4 hours, giving an 84% product yield according to GC-FID analysis (72% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 3.8 Hz, 1H), 7.13 (d, *J* = 3.8 Hz, 1H), 2.54 (s, 3H), 1.35 (s, 9H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 190.2 (C, s), 148.0 (C, s), 142.4 (C, s), 137.3 (CH, s), 132.3 (CH, s), 48.3 (C, s), 30.86 (CH_3, s), 26.82 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{10}H_{15}OS_2$: 215.0559, found: 215.0552.

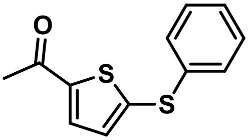
3d. 1-(5-(Allylthio)thiophen-2-yl)ethan-1-one



The compound was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 µmol, 1.0 equiv.), diallyl disulfide (54.4 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 2.5 hours, giving a 74% product yield according to GC-FID analysis (65% isolated yield as brown-yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 3.8 Hz, 1H), 6.84 (dt, *J* = 3.8, 0.9 Hz, 1H), 5.97 (ddt, *J* = 16.7, 10.0, 6.7 Hz, 1H), 5.17 (ddq, *J* = 9.8, 6.7, 1.4 Hz, 2H), 3.59 (dd, *J* = 6.7, 1.1 Hz, 2H), 2.51 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 190.7 (C, s), 153.0 (C, s), 142.9 (C, s), 135.2 (CH, s), 133.0 (CH, s), 126.2 (CH, s), 117.6 (CH, s), 34.9 (CH_2, s), 26.7 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_9H_{11}OS_2$: 199.0246, found: 199.0244.

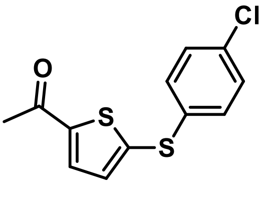
3e. 1-(5-(Phenylthio)thiophen-2-yl)ethan-1-one



The compound (CAS: 90680-26-5) was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 µmol, 1.0 equiv.), diphenyl disulfide (66.2 mg, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 2.5 hours, giving a 91% product yield according to GC-FID analysis (79% isolated yield as yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 3.9 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.36 – 7.29 (m, 3H), 7.09 (d, *J* = 3.9 Hz, 1H), 2.50 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 190.0 (C, s), 146.3 (C, s), 145.7 (C, s), 135.2 (C, s), 132.8 (CH, s), 132.1 (CH, s), 130.8 (CH, s), 129.6 (CH, s), 128.2 (CH, s), 26.6 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{11}OS_2$: 235.0246, found: 235.0239.

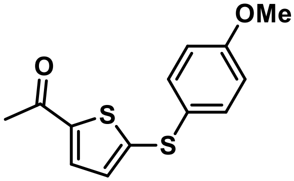
3f. 1-(5-((4-Chlorophenyl)thio)thiophen-2-yl)ethan-1-one



The compound was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 µmol, 1.0 equiv.), 1,2-bis(4-chlorophenyl) disulfide (88.8 mg, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 22 hours, giving a 67% product yield according to GC-FID analysis (59% isolated yield as pale-yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 3.9 Hz, 1H), 7.34 – 7.27 (m, 4H), 7.11 (d, *J* = 3.9 Hz, 1H), 2.51 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 190.0 (C, s), 146.8 (C, s), 144.5 (C, s), 134.4 (C, s), 133.9 (C, s), 132.8 (CH, s), 132.7 (CH, s), 131.9 (CH, s), 129.8 (CH, s), 26.7 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{10}ClOS_2$: 268.9856, found: 268.9854.

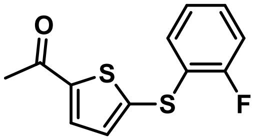
3g. 1-(5-((4-Methoxyphenyl)thio)thiophen-2-yl)ethan-1-one



The compound (CAS: 1542495-11-3) was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 µmol, 1.0 equiv.), 1,2-bis(4-methoxyphenyl) disulfide (86.1 mg, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 15 hours, giving a 57% product yield according to GC-FID analysis (51% isolated yield as yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 3.9 Hz, 1H), 7.48 – 7.44 (m, 2H), 6.93 (d, *J* = 3.9 Hz, 1H), 6.92 – 6.88 (m, 2H), 3.82 (s, 3H), 2.46 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 189.8 (C, s), 160.7 (C, s), 150.3 (C, s), 144.5 (C, s), 135.1 (CH, s), 133.0 (CH, s), 128.4 (CH, s), 124.2 (C, s), 115.4 (CH, s), 55.6 (CH_3, s), 26.4 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{13}H_{13}O_2S_2$: 265.0351, found: 265.0351.

3h. 1-(5-((4-Methoxyphenyl)thio)thiophen-2-yl)ethan-1-one

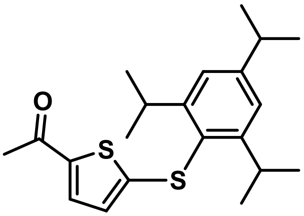


The compound was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 µmol, 1.0 equiv.), 2,2’-difluorodiphenyldisulfide (56.4 µL, 300 µmol, 3.0 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (41.5 mg, 300 µmol, 3.0 equiv.) and DIPEA (17.4 µL, 100 µmol, 1.0 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving a 69% product yield according to GC-FID analysis (68% isolated yield as pale-yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 4.0 Hz, 1H), 7.40 – 7.28 (m, 2H), 7.18 – 7.02 (m, 3H), 2.50 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) 190.0 (C, s), 162.3-159.8 (C, d, *J* = 248.1 Hz), 146.6 (C), 143.7 (C, d, *J* = 1.4 Hz), 133.3 (CH, s), 132.8 (CH, s), 132.6 (CH, s), 130.7 (CH, d, *J* =

7.9 Hz), 125.1 (CH, d, *J* = 3.9 Hz), 122.2 (C, d, *J* = 17.6 Hz), 116.4 (CH, d, *J*= 21.9 Hz), 26.6 (CH_3, s) ppm.
^{19}F NMR (377 MHz) δ -108.71 ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{10}FOS_2$: 253.0152, found: 253.0152.

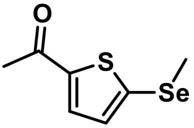
3i. 1-(5-((2,4,6-Triisopropylphenyl)thio)thiophen-2-yl)ethan-1-one



The compound was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 μmol, 1.0 equiv.), bis(2,4,6-triisopropylphenyl) disulfide (141.3 mg, 300 μmol, 3.0 equiv.), dodecanenitrile (22.15 μL, 100 μmol, 1.0 equiv.) as internal standard, K_2CO_3 (41.5 mg, 300 μmol, 3.0 equiv.) and DIPEA (17.4 μL, 100 μmol, 1.0 equiv.). in ACN 3 mL. The mixture was irradiated for 24 hours, giving an 89% product yield according to GC-FID analysis (53% isolated yield as colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 4.0 Hz, 1H), 7.10 (s, 2H), 6.71 (d, *J* = 4.0 Hz, 1H), 3.67 (hept, *J* = 6.8 Hz, 2H), 2.92 (hept, *J* = 6.9 Hz, 1H), 2.44 (s, 3H), 1.28 (d, *J* = 6.9 Hz, 6H), 1.19 (d, *J* = 6.9 Hz, 12H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 189.6 (C, s), 153.9 (C, s), 153.2 (CH, s), 151.9 (C, s), 142.3 (C, s), 133.5 (CH, s), 125.4 (C, s), 124.5 (CH, s), 122.8 (CH, s), 34.5 (CH, s), 32.0 (CH, s), 26.2 (CH_3, s), 24.4 (CH_3, s), 24.0 (CH_3, s) ppm.
HRMS (EI): m/z $(M+Na)^+$ = calcd. for $C_{21}H_{28}OS_2Na$: 383.1471, found: 383.1474.

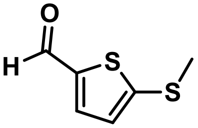
3j. 1-(5-(Methylselanyl)thiophen-2-yl)ethan-1-one



The compound (CAS: 29421-88-3) was prepared according to the general procedure using 2-acetyl-5-chlorothiophene (16.2 mg, 100 μmol, 1.0 equiv.), dimethyl diselenide (29.6 μL, 300 μmol, 3 equiv.), dodecanenitrile (22.15 μL, 100 μmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 μmol, 1.5 equiv.) and DIPEA (10.5 μL, 60 μmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 5 hours, giving a 93% product yield according to GC-FID analysis (82% isolated yield as yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 3.9 Hz, 1H), 7.08 (d, *J* = 3.9 Hz, 1H), 2.51 (s, 3H), 2.46 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7 (C, s), 146.6 (C, s), 139.0 (C, s), 133.2 (CH, s), 131.4 (CH, s), 26.6 (CH_3, s), 10.8 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for C_7H_9OSSe: 220.9534, found: 220.9533.

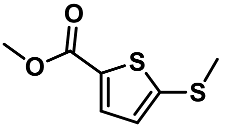
3k. 5-(Methylthio)thiophene-2-carbaldehyde



The compound (CAS: 24445-35-0) was prepared according to the general procedure using 5-bromo-2-thiophenecarbaldehyde (12.5 µL, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 2.5 hours, giving a 95% product yield according to GC-FID analysis (82% isolated yield as brown-yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.61 (d, *J* = 4.0 Hz, 1H), 6.98 (d, *J* = 4.0 Hz, 1H), 2.62 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 181.5 (C, s), 153.1 (C, s), 142.4 (C, s), 137.3 (CH, s), 126.2 (CH, s), 19.2 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_6H_7OS_2$: 158.9933, found: 158.9930.

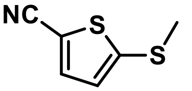
3l. Methyl 5-(methylthio)thiophene-2-carboxylate



The compound (CAS: 773873-78-2) was prepared according to the general procedure using methyl 5-chlorothiophene-2-carboxylate (13.2 µL, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 22 hours, giving a 57% product yield according to GC-FID analysis (49% isolated yield as yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 3.9 Hz, 1H), 6.93 (d, *J* = 3.9 Hz, 1H), 3.86 (s, 3H), 2.57 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2 (C, s), 147.5 (C, s), 134.1 (CH, s), 132.7 (C, s), 127.9 (CH, s), 52.3 (CH_3, s), 20.2 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_7H_9O_2S_2$: 189.0038, found: 189.0034.

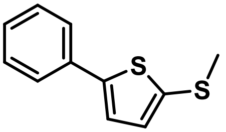
3m. 5-(Methylthio)thiophene-2-carbonitrile



The compound (CAS: 175205-78-4) was prepared according to the general procedure using 5-bromo-2-thiophenecarbonitrile (11.1 µL, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 2.5 hours, giving an 87% product yield according to GC-FID analysis (76% isolated yield as brown-yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 3.9 Hz, 1H), 6.93 (d, *J* = 3.9 Hz, 1H), 2.59 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2 (C, s), 138.0 (CH, s), 127.5 (CH, s), 114.0 (C, s), 109.1 (C, s), 20.33 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_6H_6NS_2$: 155.9936, found: 155.9929.

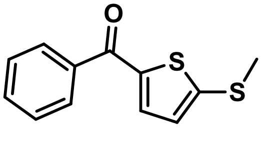
3n. 2-(Methylthio)-5-phenylthiophene



The compound (CAS: 478945-57-2) was prepared according to the general procedure 2-bromo-5-phenylthiophene (23.91 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (41.5 mg, 0.3 mmol, 3.0 equiv.) and DIPEA (17.4 µL, 0.10 mol, 1.0 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving a 29% product yield according to GC-FID analysis (23% isolated yield as colorless oil).

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.58–7.54 (m, 2H), 7.41–7.35 (m, 2H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.19 (d, *J* = 3.8 Hz, 1H), 7.05 (d, *J* = 3.8 Hz, 1H), 2.52 (s, 3H) ppm.
^{13}C NMR (100 MHz, CD_2Cl_2) δ 146.7 (C, s), 137.3 (C, s), 134.4 (C, s), 132.2 (CH, s), 129.4 (CH, s), 128.1 (CH, s), 125.9 (CH, s), 123.8 (CH, s), 22.3 (CH_3, s) ppm.
HRMS (EI): m/z $(M)^+$ = calcd. for $C_{11}H_{10}S_2$: 206.0218, found: 206.0218.

3o. (5-(Methylthio)thiophen-2-yl)(phenyl)methanone

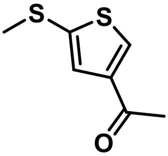


The compound (CAS: 22108-34-5) was prepared according to the general procedure using (5-bromothiophen-2-yl)(phenyl)methanone (27.3 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 2 hours, giving a 91% product yield according to GC-FID analysis (85% isolated yield as yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.57 (ddd, *J* = 6.8, 4.6, 1.3 Hz, 1H), 7.51 – 7.46 (m, 3H), 6.95 (d, *J* = 4.0 Hz, 1H), 2.63 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ 187.1 (C, s), 151.2 (C, s), 142.6 (C, s), 138.1 (C, s), 135.7 (CH, s), 132.2 (CH, s), 129.1 (CH, s), 128.6 (CH, s), 126.6 (CH, s), 19.5 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{12}H_{11}OS_2$: 235.0246, found: 235.0248.

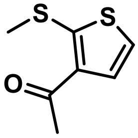
3p. 1-(5-(Methylthio)thiophen-3-yl)ethan-1-one



The compound was prepared according to the general procedure using 3-acetyl-5-chlorothiophene (16.2 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving a 57% product yield according to GC-FID analysis (51% isolated yield as yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 1.4 Hz, 1H), 7.45 (d, *J* = 1.4 Hz, 1H), 2.51 (s, 3H), 2.49 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 191.9 (C, s), 142.9 (C, s), 139.6 (C, s), 134.0 (CH, s), 129.7 (CH, s), 27.3 (CH_3, s), 21.7 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_7H_9OS_2$: 173.0089, found: 173.0084.

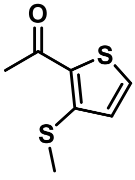
3q. 1-(2-(Methylthio)thiophen-3-yl)ethan-1-one



The compound (CAS: 42108-16-7) was prepared according to the general procedure using 3-acetyl-2-bromothiophene (20.5 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 17 hours, giving an 82% product yield according to GC-FID analysis (75% isolated yield as pale-yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 5.5 Hz, 1H), 7.10 (d, *J* = 5.5 Hz, 1H), 2.58 (s, 3H), 2.50 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 192.6 (C, s), 153.4 (C, s), 134.21 (C, s), 129.3 (CH, s), 121.6 (CH, s), 28.7 (CH_3, s), 18.7 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_7H_9OS_2$: 173.0089, found: 173.0088.

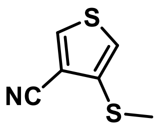
3r. 1-(3-(Methylthio)thiophen-2-yl)ethan-1-one



The compound (CAS: 74598-24-6) was prepared according to the general procedure using 2-acetyl-3-bromothiophene (21.1 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 6 hours, giving an 85% product yield according to GC-FID analysis (77% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 5.2 Hz, 1H), 7.03 (d, *J* = 5.2 Hz, 1H), 2.54 (s, 3H), 2.52 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 189.9 (C, s), 145.6 (C, s), 131.2 (CH, s), 126.4 (CH, s), 28.9 (CH_3, s), 16.73 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_7H_9OS_2$: 173.0089, found: 173.0089.

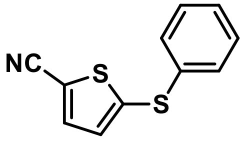
3s. 4-(Methylthio)thiophene-3-carbonitrile



The compound was prepared according to the general procedure using 4-bromo-3-thiophenecarbonitrile (18.8 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving an 65% product yield according to GC-FID analysis (61% isolated yield as pale-yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 3.2 Hz, 1H), 7.09 (d, *J* = 3.2 Hz, 1H), 2.53 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 137.0 (C, s), 136.7 (CH, s), 122.4 (CH, s), 114.1 (C, s), 113.2 (C, s), 17.9 (CH_3, s) ppm.
HRMS (EI): m/z $(M+Na)^+$ = calcd. for $C_6H_5NS_2Na$: 177.9761, found: 177.9764.

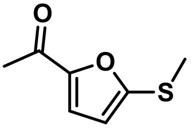
3t. 5-(Phenylthio)thiophene-2-carbonitrile



The compound (CAS: 1300106-13-1) was prepared according to the general procedure using 5-bromo-2-thiophenecarbonitrile (11.1 µL, 100 µmol, 1.0 equiv.), diphenyl disulfide (66.2 mg, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 4 hours, giving an 80% product yield according to GC-FID analysis (73% isolated yield as colorless oil).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.50 (d, *J* = 3.9 Hz, 1H), 7.41 – 7.31 (m, 5H), 7.10 (d, *J* = 3.9 Hz, 1H) ppm.
^{13}C NMR (100 MHz, CDCl$_3$) δ 144.4 (C, s), 137.9 (CH, s), 134.8 (C, s), 131.9 (CH, s), 130.8 (CH, s), 129.8 (CH, s), 128.5 (CH, s), 113.7 (C, s), 112.1 (C, s) ppm.
HRMS (EI): m/z (M+H)$^+$ = calcd. for $C_{11}H_8NS_2$: 218.0093, found: 218.0089.

3u. 1-(5-(Methylthio)furan-2-yl)ethan-1-one

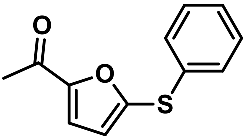


The compound (CAS: 934-64-5) was prepared according to the general procedure using 2-acetyl-5-bromofuran (19.9 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K$_2$CO$_3$ (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 6 hours, giving an 85% product yield according to GC-FID analysis (79% isolated yield as pale-yellow powder).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.16 (d, *J* = 3.6 Hz, 1H), 6.37 (d, *J* = 3.6 Hz, 1H), 2.54 (s, 3H), 2.45 (s, 3H) ppm.

^{13}C NMR (100 MHz, CDCl$_3$) δ 185.7 (C, s), 155.0 (C, s), 154.0 (C, s), 119.3 (CH, s), 112.3 (CH, s), 25.9 (CH$_3$, s), 16.5 (CH$_3$, s) ppm.
HRMS (EI): m/z (M+H)$^+$ = calcd. for $C_7H_9O_2S$: 157.0311, found: 157.0318.

3v. 1-(5-(Phenylthio)furan-2-yl)ethan-1-one



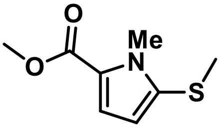
The compound (CAS: 28569-36-0) was prepared according to the general procedure using 2-acetyl-5-bromofuran (19.9 mg, 100 µmol, 1.0 equiv.), diphenyl disulfide (66.2 mg, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K$_2$CO$_3$ (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 6 hours, giving an 81% product yield according to GC-FID analysis (71% isolated yield as brown-yellow powder).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.41–7.25 (m, 5H), 7.17 (d, *J* = 3.5 Hz, 1H), 6.63 (d, *J* = 3.5 Hz, 1H), 2.45 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ 186.5 (C, s), 155.1 (C, s), 150.6 (C, s), 133.2 (C, s), 130.3 (CH, s), 129.6 (CH, s), 127.9 (CH, s), 118.6 (CH, s), 118.3 (CH, s), 26.1 (CH_3, s) ppm.

Analytical data is in accordance with the previously reported in literature.[1]

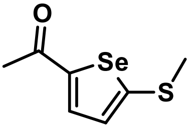
3w. Methyl 1-methyl-5-(methylthio)-1*H*-pyrrole-2-carboxylate



The compound was prepared according to the general procedure using methyl 1-methyl-5-bromo-1*H*-pyrrole-2-carboxylate (21.8 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving a 50% product yield according to GC-FID analysis (43% isolated yield as pale-yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (d, *J* = 4.3 Hz, 1H), 6.63 (d, *J* = 4.3 Hz, 1H), 4.16 (s, 3H), 3.85 (s, 3H), 2.97 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2 (C, s), 138.8 (C, s), 127.1 (C, s), 117.1 (CH, s), 109.9 (CH, s), 51.8 (CH_3, s), 39.9 (CH_3, s), 34.1 (CH_3, s) ppm.
HRMS (EI): m/z $(M)^+$ = calcd. for $C_8H_{11}NO_2S$: 185.0505, found: 185.0497.

3x. 1-(5-(Methylthio)selenophen-2-yl)ethan-1-one



The compound was prepared according to the general procedure using 2-acetyl-5-bromoselenophene (25.2 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 6 hours, giving a 72% product yield according to GC-FID analysis (66% isolated yield as yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 4.2 Hz, 1H), 7.05 (d, *J* = 4.2 Hz, 1H), 2.61 (s, 3H), 2.50 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 190.8 (C, s), 157.4 (C, s), 149.2 (C, s), 135.7 (CH, s), 127.4 (CH, s), 25.6 (CH_3, s), 20.6 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for C_7H_9OSSe: 220.9534, found: 220.9530.

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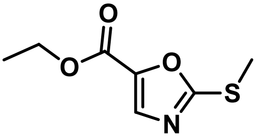
[1] Herrera-Luna, J.C.; *et al. Org. Lett.* **2021**, *23* (6), 2320–2325.

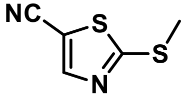
3y. Ethyl 2-(methylthio)oxazole-5-carboxylate



The compound (CAS: 2117579-63-0) was prepared according to the general procedure using ethyl 2-chlorooxazole-5-carboxylate (13.2 µL, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving a 90% product yield according to GC-FID analysis (74% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.69 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2 (C, s), 157.6 (C, s), 144.1 (C, s), 135.4 (CH, s), 61.6 (CH_2, s), 14.7 (CH_3, s), 14.4 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_7H_{10}NO_3S$: 188.0376, found 188.0376.

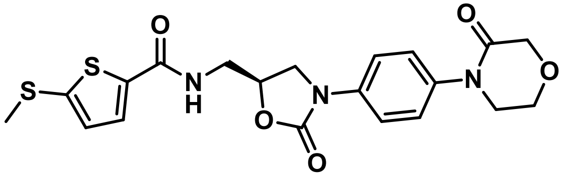
3z. 2-(Methylthio)thiazole-5-carbonitrile



The compound (CAS: 2110748-59-7) was prepared according to the general procedure using 2-bromo-5-thiazolecarbonitrile (18.9 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 2 hours, giving a 91% product yield according to GC-FID analysis (78% isolated yield as white powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 2.75 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6 (C, s), 151.9 (CH, s), 111.8 (C, s), 104.6 (C, s), 16.6 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_5H_4N_2S_2$: 156.9889, found: 156.9883.

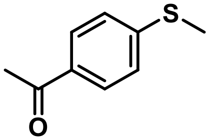
3-Riv. (*S*)-5-(Methylthio)-*N*-((2-oxo-3-(4-(3-oxomorpholino)phenyl)oxazolidin-5-yl)methyl)thiophene-2-carboxamide



The compound was prepared according to the general procedure using (*S*)-5-chloro-*N*-((2-oxo-3-(4-(3-oxomorpholino)phenyl) oxazolidin-5-yl)methyl)thiophene-2-carboxamide (43.6 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving a 30% isolated product yield as white powder.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.52 (m, 2H), 7.37 (d, *J* = 3.9 Hz, 1H), 7.35–7.31 (m, 2H), 6.9 (d, *J* = 3.9 Hz, 1H), 6.50 (t, *J* = 6.2 Hz, 1H), 4.85 (dtd, *J* = 9.9, 6.6, 3.4 Hz, 1H), 4.33 (s, 2H), 4.09 (t, *J* = 9.0 Hz, 1H), 4.03 (dd, *J* = 5.8, 4.3 Hz, 2H), 3.89 – 3.82 (m, 2H), 3.75 (dd, *J* = 11.3, 6.1 Hz, 3H), 2.55 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0 (C, s), 162.1 (C, s), 154.5 (C, s), 145.8 (C, s), 137.5 (C, s), 137.4 (C, s), 136.8 (C, s), 129.2 (CH, s), 128.5 (CH, s), 126.4 (CH, s), 119.2 (CH, s), 72.1 (CH, s), 68.7 (CH_2, s), 64.3 (CH_2, s), 49.8 (CH_2, s), 47.8 (CH_2, s), 42.5 (CH_2, s), 14.3 (CH_3, s) ppm.
HRMS (EI): m/z $(M+H)^+$ = calcd. for $C_{20}H_{21}N_3O_5S_2$: 448.0995, found: 448.0986.

4a. 1-(4-(Methylthio)phenyl)ethan-1-one

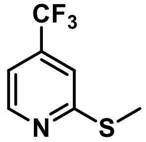


The compound (CAS: 1778-09-2) was prepared according to the general procedure using 1-(4-bromophenyl)ethan-1-one (19.9 mg, 100 µmol, 1.0 equiv.) or 1-(4-chlorophenyl)ethan-1-one (15.5 mg, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (41.5 mg, 300 µmol, 3.0 equiv.) and DIPEA (17.4 µL, 100 µmol, 1.0 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving a 76% (71% from 1-(4-chlorophenyl)ethan-1-one) product yield according to GC-FID analysis (65% isolated yield as pale-yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 2.57 (s, 3H), 2.52 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3 (C, s), 146.0 (C, s), 133.7 (C, s), 128.9 (CH, s), 125.1 (CH, s), 26.6 (CH_3, s), 14.9 (CH_3, s) ppm.
Analytical data is in accordance with the previously reported in literature.[2]

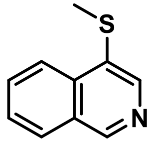
4b. 2-(Methylthio)-4-(trifluoromethyl)pyridine



The compound (CAS: 1865010-28-1) was prepared according to the general procedure using 2-bromo-4-(trifluoromethyl)pyridine (22.6 mg, 100 µmol, 1.0 equiv.), dimethyldisulfide (177.7 µL, 2.0 mmol, 20.0 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (41.5 mg, 300 µmol, 3.0 equiv.) and DIPEA (17.4 µL, 100 µmol, 1.0 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving an 82% product yield according to GC-FID analysis (39% isolated yield as colorless oil). Note: This compound is highly volatile and unstable.

^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.59 (d, *J* = 5.2 Hz, 1H), 7.39 (s, 1H), 7.18 (d, *J* = 5.2 Hz, 1H), 2.59 (s, 3H) ppm.
^{19}F-NMR (377 MHz, CD_2Cl_2) δ -65.44 ppm.
HRMS (EI): m/z $(M)^+$ = calcd. for $C_7H_6NSF_3$: 193.0168, found: 193.0160.

4c. 4-(Methylthio)isoquinoline



The compound (CAS: 38896-71-8) was prepared according to the general procedure using 4-bromoisoquinoline (20.8 mg, 100 µmol, 1.0 equiv.), dimethyldisulfide (177.7 µL, 2.0 mmol, 20.0 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (41.5 mg, 300 µmol, 3.0 equiv.) and DIPEA (52.3 µL, 300 µmol, 3.0 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving an 88% product yield according to GC-FID analysis (45% isolated yield as pale-yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.44 (s, 1H), 8.22 (dd, *J* = 8.4, 0.9 Hz, 1H), 7.97 (d, *J* = 8.2, 1H), 7.76 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.65 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 2.61 (s, 3H). ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6 (CH, s), 141.0 (CH, s), 134.7 (C, s), 130.7 (CH, s), 130.6 (C, s), 128.3 (CH, s), 127.8 (CH, s), 123.7 (CH, s), 16.5 (CH_3, s) ppm.
HRMS (ESI): m/z $(M+H)^+$ = calcd. for $C_{10}H_{10}NS$: 176.0529, found: 176.0528.
Analytical data is in accordance with the previously reported in literature.[3]

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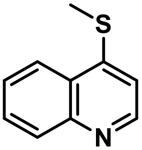
[2] Ruan, J.; Li,X.; Saidi, O.; Xiao, J. *J. Am. Chem. Soc*. **2008**, *130*, 2424 – 2425.

[3] Wang, Y.; Wu, X.; Yang, M. *Synlett* **2020**, *31*, 1226–1230.

4d. 4-(Methylthio)quinoline



The compound (CAS: 46000-25-3) was prepared according to the general procedure using 4-bromoquinoline (20.8 mg, 100 µmol, 1.0 equiv.), dimethyldisulfide (177.7 µL, 2.0 mmol, 20.0 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (41.5 mg, 300 µmol, 3.0 equiv.) and DIPEA (52.3 µL, 300 µmol, 3.0 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving a 26% product yield according to GC-FID analysis (31% isolated yield as pale-yellow powder).

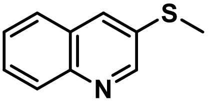
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.9 Hz, 1H), 8.10 (ddd, *J* = 7.9, 6.1, 1.6 Hz, 2H), 7.73 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.56 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.14 (d, *J* = 4.9 Hz, 1H), 2.63 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4 (C, s), 149.2 (CH, s), 147.0 (C, s), 130.0 (CH, s), 129.9 (CH, s), 126.5 (CH, s), 126.4 (C, s), 123.5 (CH, s), 114.9 (CH, s), 14.2 (CH_3, s) ppm.

HRMS (ESI) m/z $(M+H)^+$ = calcd. for $C_{10}H_9NSH$: 176.0529, found: 176.0528.

Analytical data is in accordance with the previously reported in literature.[4]

4e. 3-(Methylthio)quinoline



The compound (CAS: 51934-46-4) was prepared according to the general procedure using 3-bromoquinoline (13.9 µL, 100 µmol, 1.0 equiv.), dimethyl disulfide (26.7 µL, 300 µmol, 3 equiv.), dodecanenitrile (22.15 µL, 100 µmol, 1.0 equiv.) as internal standard, K_2CO_3 (20.8 mg, 150 µmol, 1.5 equiv.) and DIPEA (10.5 µL, 60 µmol, 0.6 equiv.) in ACN 3 mL. The mixture was irradiated for 24 hours, giving a 69% product yield according to GC-FID analysis (56% isolated yield as pale-yellow powder).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 2.4 Hz, 1H), 8.06 (d, *J* = 8.7 Hz, 1H), 7.90 (d, *J* = 2.2 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.64 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.57 – 7.51 (m, 1H), 2.61 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1 (s), 146.1 (s), 132.8 (s), 131.6 (s), 129.5 (s), 128.8 (s), 128.5 (s), 127.4 (s), 126.9 (s), 16.0 (s) ppm.

Analytical data is in accordance with the previously reported in literature.[5]

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[4] Wang, M.; Qiao, Z.; Zhao, J.; Jiang, X. *Org. Lett.* **2018**, *20* (19), 6193–6197.

[5] Reeves, J.T., Camara, K.; Han, S.Z.; Xu, Y.; Lee, H.; Busacca, C.A., Senanayake, C.H. *Org. Lett.* **2014**, *16* (4), 1196-1199.

Chapter 7
Conclusions

Conclusions

This doctoral thesis has focused on the utilization of visible light as a cheap, clean, and inexhaustible source of energy for relevant chemical transformations such as production of new C–heteroatom bonds with widespread applications and, hence, to have an immediate impact on the current state of industrial manufacture. Moreover, the use of nanostructured gel matrices as alternative reaction media to enhance high-tech visible light-induced processes has been well exploited.

At first approach, the formation of borylated-like thiophenes by means of visible light (cold-white LEDs) as an energy source has been reported. The method does not require the presence of a photocatalyst and proceeds via the *in-situ* generation of a ground-state complex that, after visible-light absorption, evolves to the formation of the corresponding borylation of the thiophene core. The corresponding proposed reaction mechanism has been elucidated by spectroscopic measurements and theoretical calculations. The scope and the versatility of the procedure have been successfully proven, obtaining 20 products with yields up to 97%. This challenging coupling reaction offers a novel route toward synthetic highly valuable heteroarene boronates with a new, likely exploitable mechanistic paradigm.

The mandatory anaerobic atmosphere and the high loading of the trapping agent fostered us to further develop the previous protocol to improve the conditions for the construction of new C–B bonds. Thus, utilization of supramolecular viscoelastic gels has allowed us: i) to protect against oxygen poisoning; ii) to drop down the trapping agent loading; and iii) to accelerate the reaction relative to standard conditions. An attractive and efficient methodology for building five-membered heteroarene boronate esters under very mild conditions has been reported. A wide variety of products (52 examples) have been obtained with good to excellent yields (up to 91%) that may act as versatile precursors for further synthetic work.

In view of the potential of supramolecular gels as reaction media to carry out aerobic visible-light reactions, fabrication of new C–P bonds to obtain five-membered heteroarene phosphonates has been afforded using the ConPET photoredox catalysis (in our case dichromatic photoredox catalysis). The procedure involves visible aerobic irradiation of a mixture containing the heteroarene halide, trisubstituted phosphite, *N*,*N*-diisopropylethylamine (DIPEA) as sacrificial agent, and catalytic amounts of 9,10-dicyanoanthracene (DCA) in the presence of an adequate gelator, which permits a faster process than at the homogeneous phase. A broad scope with the production of 27 phosphonylated products has been obtained whereas the synthetic potential of this dichromatic photocatalyzed transformation has been demonstrated by its application in the late-stage phosphonylation of the anticoagulant rivaroxaban. Spectroscopic and thermodynamic studies have supported the involvement of the strongly reducing excited radical anion $DCA^{\bullet-*}$ in the proposed reaction mechanism.

Despite the fact that EDA complex photochemistry is nowadays considered a useful synthetic tool in organic synthesis, fabrication of new C–S bonds that implies the EDA complex photochemistry using visible light remains still scarce. Herein, a simple and effective approach for the direct thiolation of five-membered heteroarenes involving visible-light-absorbing EDA complexes between a heteroarene halide and an alkylamine is reported for the first time. The experimental results are consistent with the reaction taking place from an electron donor–acceptor (EDA) complex between an alkylamine and the heteroarene halide. Selective photolysis to the EDA complex has allowed to generate the heteroarene radical that is suitably trapped by disulfide derivatives, providing a potent synthetic versatility. Mechanistic aspects of the whole process have been demonstrated by spectroscopic measurements whereas the strength of this novel method has been proven by gram-scale experiment and late-stage derivatization.

ANNEX I

Publications & Congresses

PUBLICATIONS

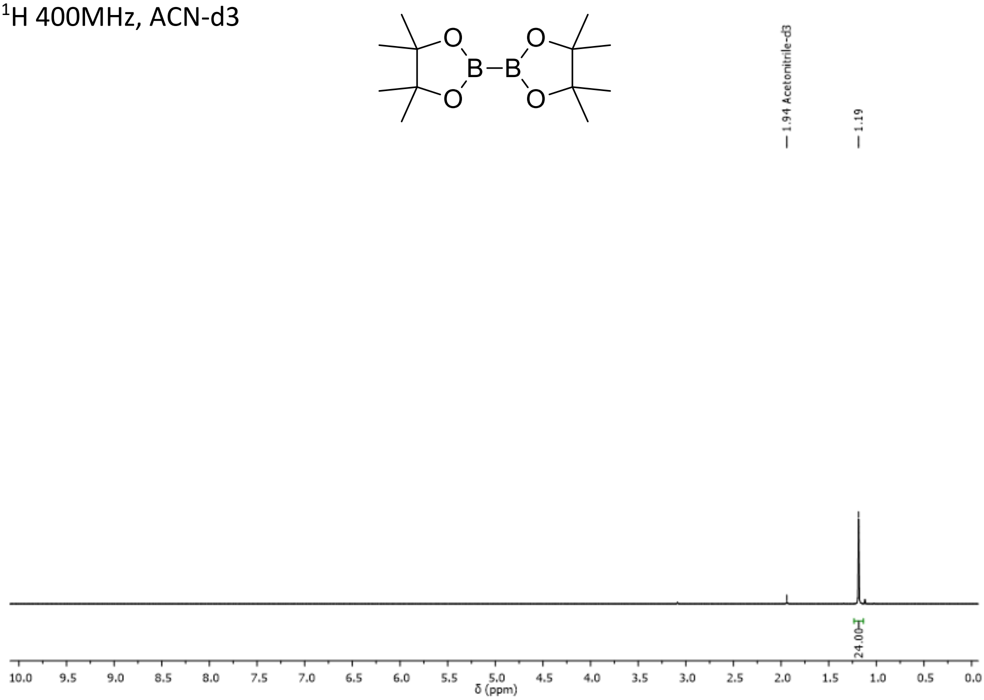
1. Jorge C. Herrera-Luna, María Carmen Pérez-Aguilar, Leon Gerken, Olga García Mancheño*, M. Consuelo Jiménez* and Raúl Pérez-Ruiz*
   Effective Formation of New C(sp^2)–S Bonds via Photoactivation of Alkylamine-based Electron Donor–Acceptor Complexes
   Submitted
2. Jorge C. Herrera-Luna, David Díaz Díaz, M. Consuelo Jiménez* and Raúl Pérez-Ruiz*
   Highly Efficient Production of Heteroarene Phosphonates by Dichromatic Photoredox Catalysis
   ACS Appl. Mater. Interfaces **2021**, *13*, 41, 48784–48794.
   DOI: 10.1021/acsami.1c14497
   9.229 Q1
3. Jorge C. Herrera-Luna, David Díaz Díaz, Alex Abramov, Susana Encinas, M. Consuelo Jiménez* and Raúl Pérez-Ruiz*
   Aerobic Visible-Light-Driven Borylation of Heteroarenes in a Gel Nanoreactor
   Org. Lett. **2021**, *23*, 6, 2320–2325.
   DOI: 10.1021/acs.orglett.1c00451
   6.005 Q1
4. Jorge Castellanos-Soriano‡, Jorge C. Herrera-Luna‡, David Díaz Díaz, M. Consuelo Jiménez and Raúl Pérez-Ruiz*
   Recent applications of biphotonic processes in organic synthesis
   Org. Chem. Front., **2020**, *7*, 1709-1716.
   DOI: 10.1039/D0QO00466A
   5.281 Q1
5. Jorge C. Herrera-Luna, Diego Sampedro, M. Consuelo Jiménez* and Raúl Pérez-Ruiz*
   Rapid Access to Borylated Thiophenes Enabled by Visible Light
   Org. Lett. **2020**, *22*, 8, 3273–3278.
   DOI: 10.1021/acs.orglett.0c01076
   6.005 Q1
6. Miguel Espinosa, Jorge Herrera, Gonzalo Blay*, Luz Cardona, M. Carmen Muñoz, and José R. Pedro*
   Copper-catalysed enantioselective Michael addition of malonic esters to β-trifluoromethyl-α,β-unsaturated imines
   Org. Biomol. Chem., **2017**,*15*, 3849-3853.
   DOI: 10.1039/C7OB00595D
   3.876 Q2

CONGRESS PARTICIPATION

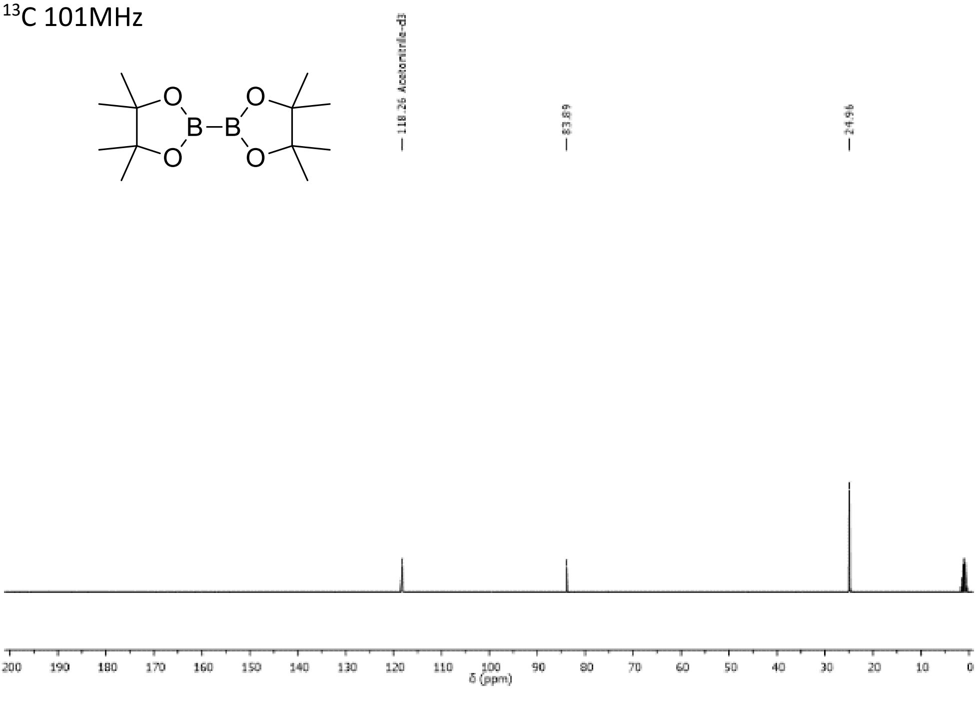
1. Oral Communication
   X REQOMED
   Place and date: Valencia (Spain) 20/10/2022
2. Poster Communication
   VII Iberian conference on photochemistry
   Place and date: Alcalá de Henares (Spain) 05/09/2022
3. Poster Communication
   XXVIII Bienal RSEQ 2022
   Place and date: Granada (Spain) 27/06/2022
4. Oral Communication
   Iberian Symposium of Young Photochemists (RSEQ)
   Place and date: Online 18/10/2021
5. Poster Communication
   RSEQ Symposium 2021
   Place and date: Online 27/09/2021
6. Poster Communication
   AEBIN Photochemistry School 2020
   Place and date: Online 07/09/2020
7. Oral Communication
   XVI Symposium of young researchers of Royal Spanish Society of Chemistry (RSEQ)-Sigma Aldrich (Merck)
   Place and date: Valencia (Spain) 04/11/2019
8. Poster Communication
   XXXVII Bienal RSEQ 2019
   Place and date: San Sebastian (Spain) 26/05/2019

ANNEX II
NMR Spectra

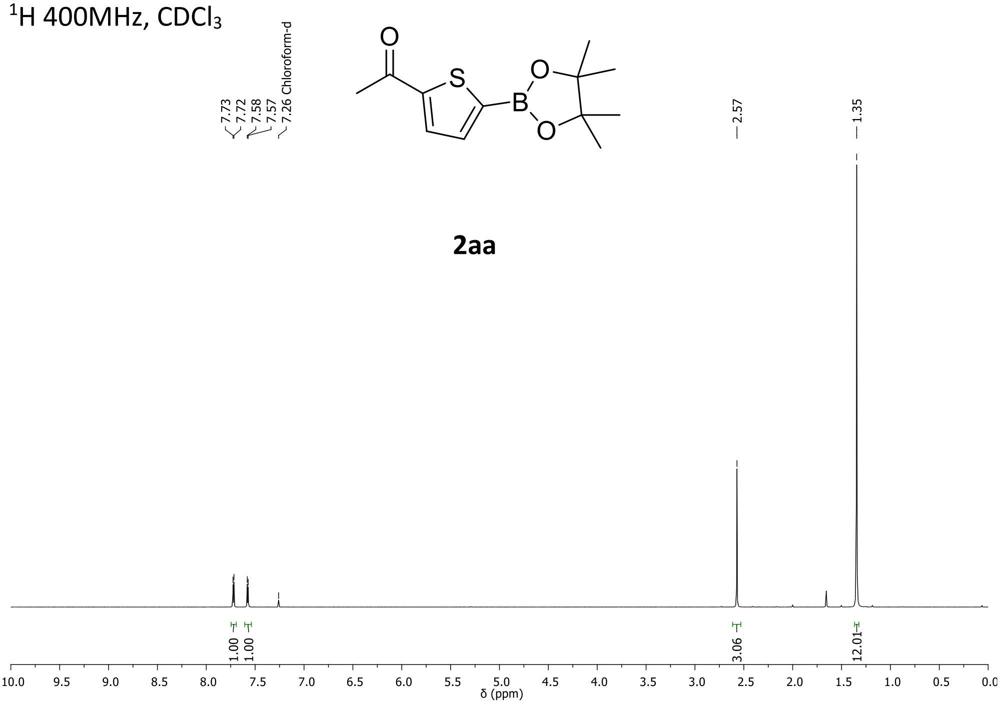
^{1}H 400MHz, ACN-d3



^{13}C 101MHz

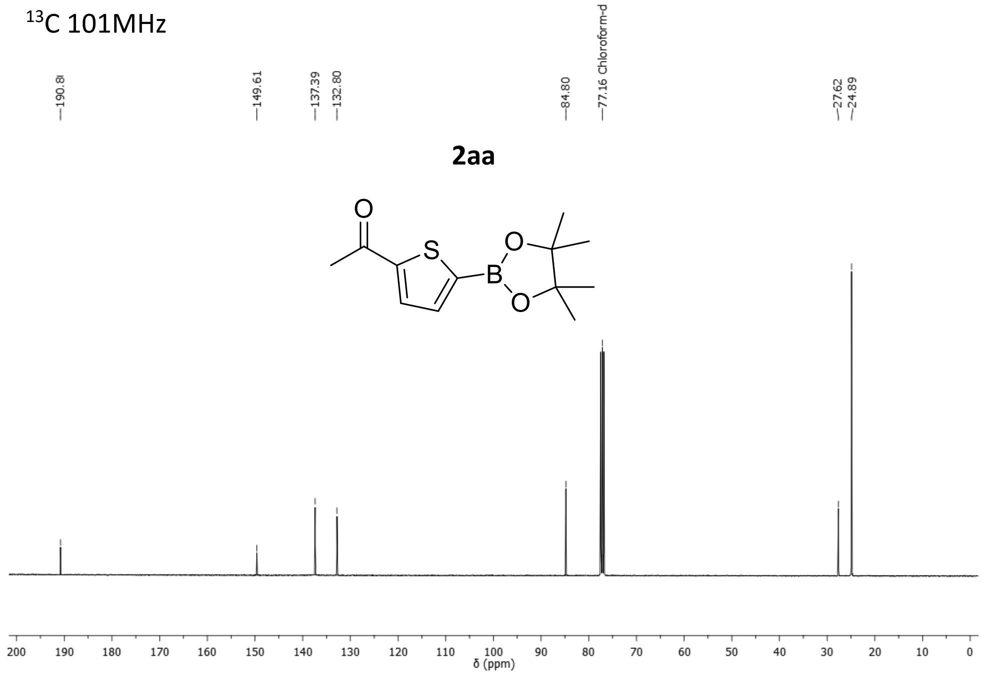


^{1}H 400MHz, CDCl$_3$



2aa

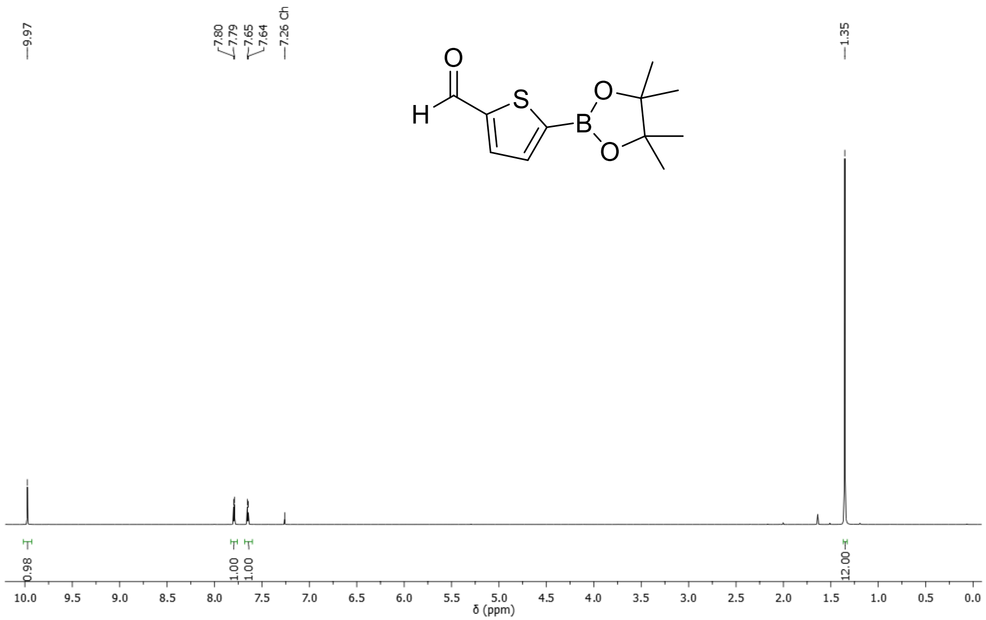
^{13}C 101MHz



2aa

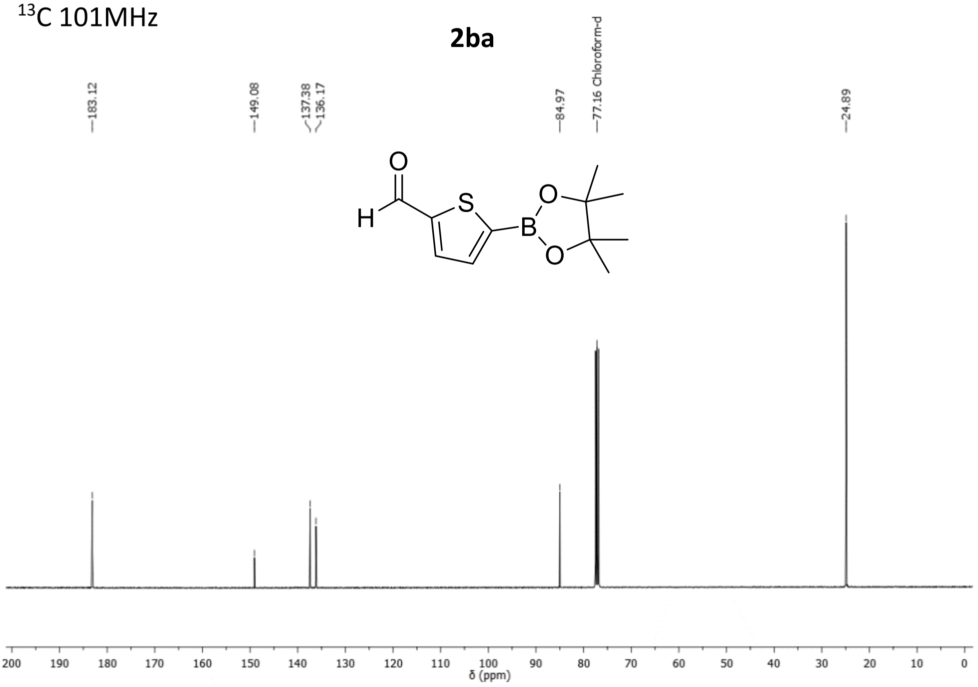
^{1}H 400MHz, $CDCl_3$

2ba



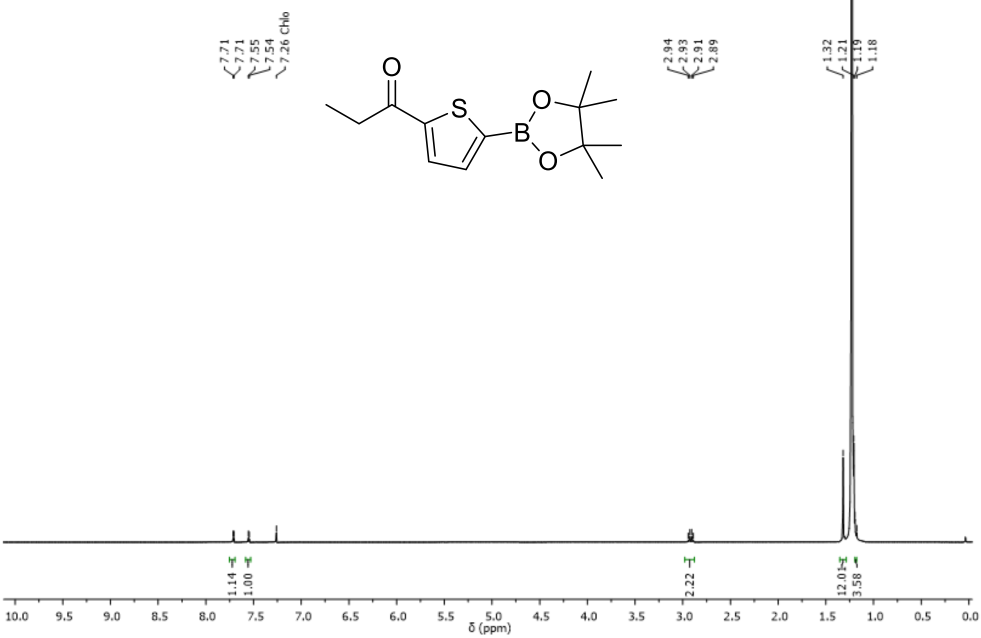
^{13}C 101MHz

2ba



^{1}H 400MHz, $CDCl_3$

2ca

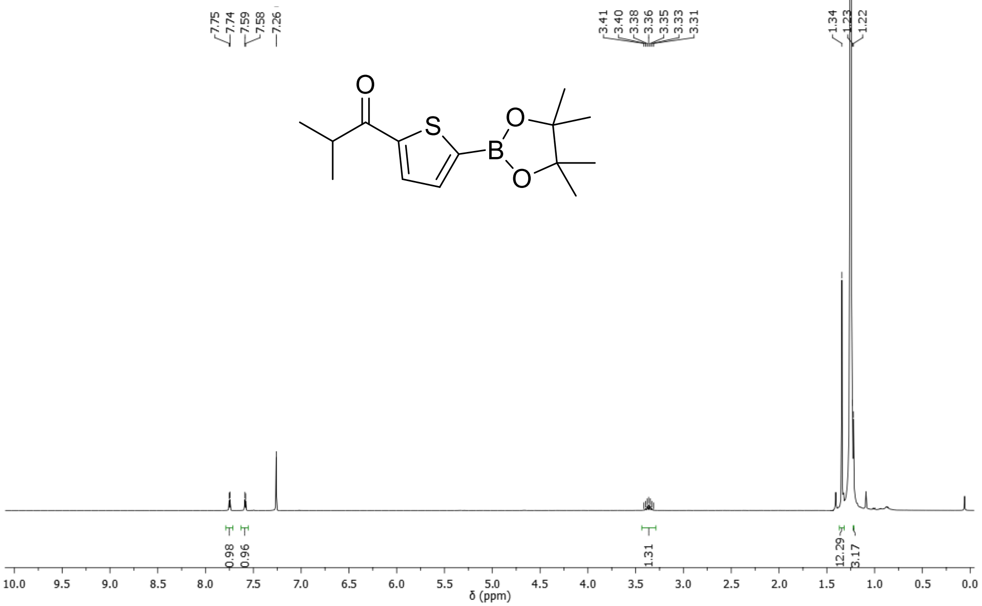


^{13}C 101MHz

2ca

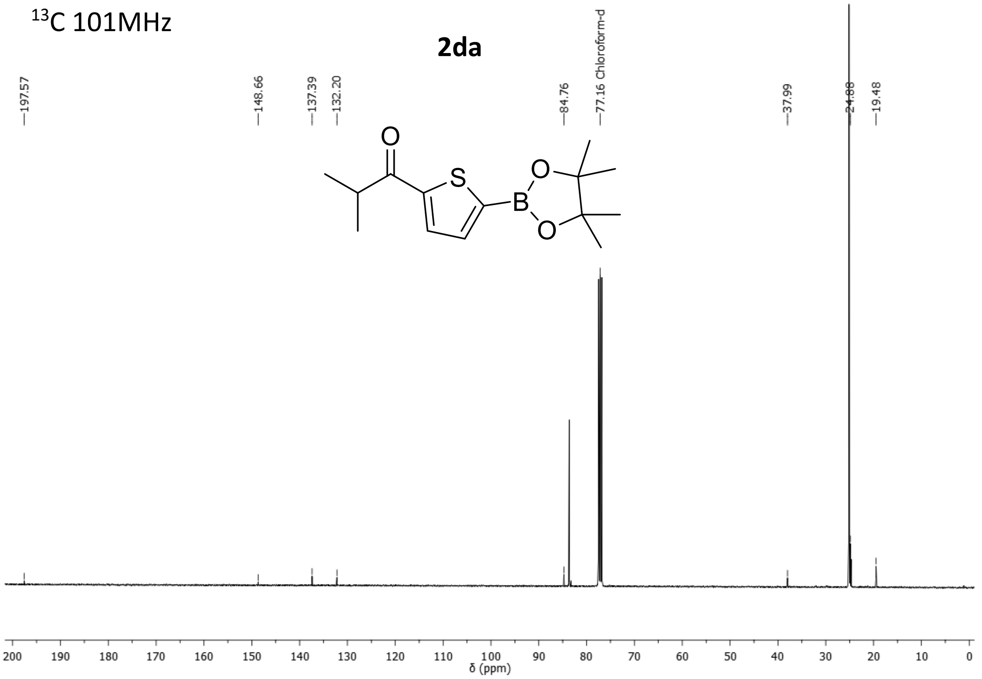
^{1}H 400MHz, CDCl$_3$

2da



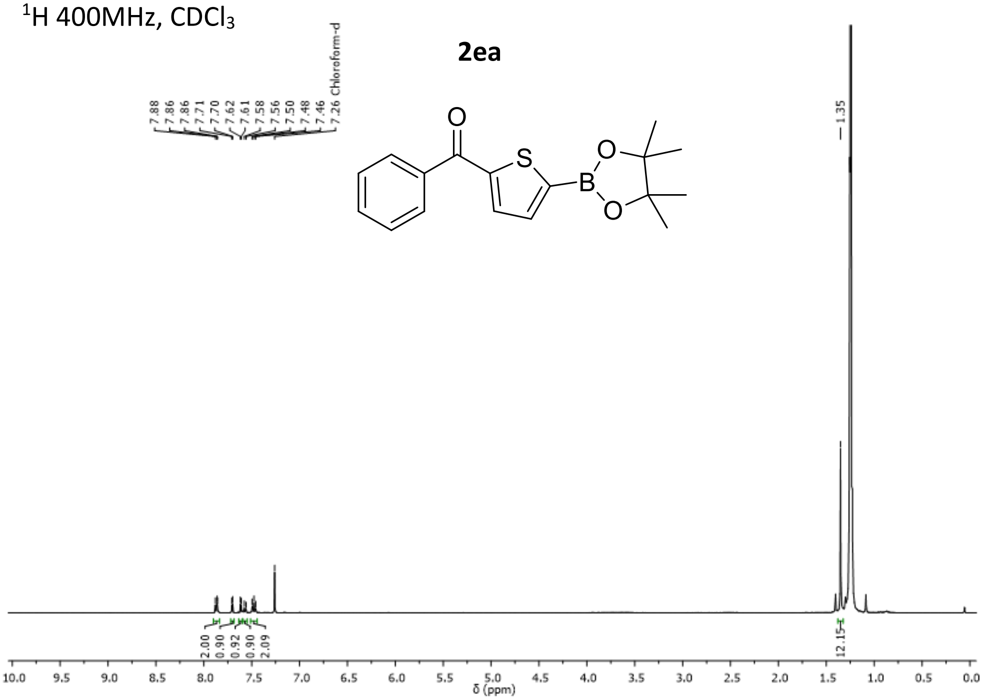
^{13}C 101MHz

2da



^{1}H 400MHz, CDCl$_3$

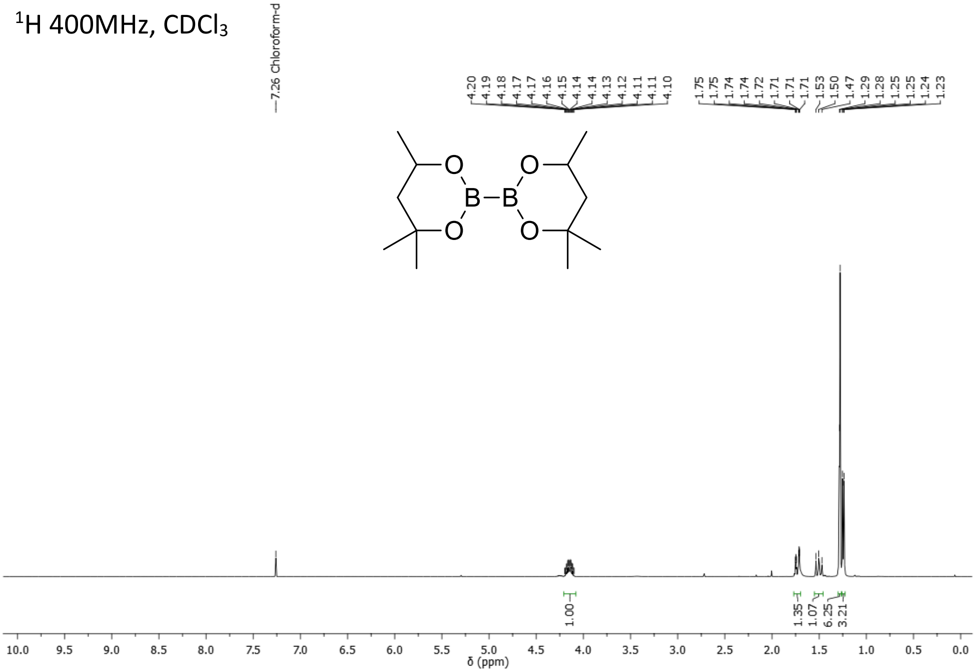
2ea



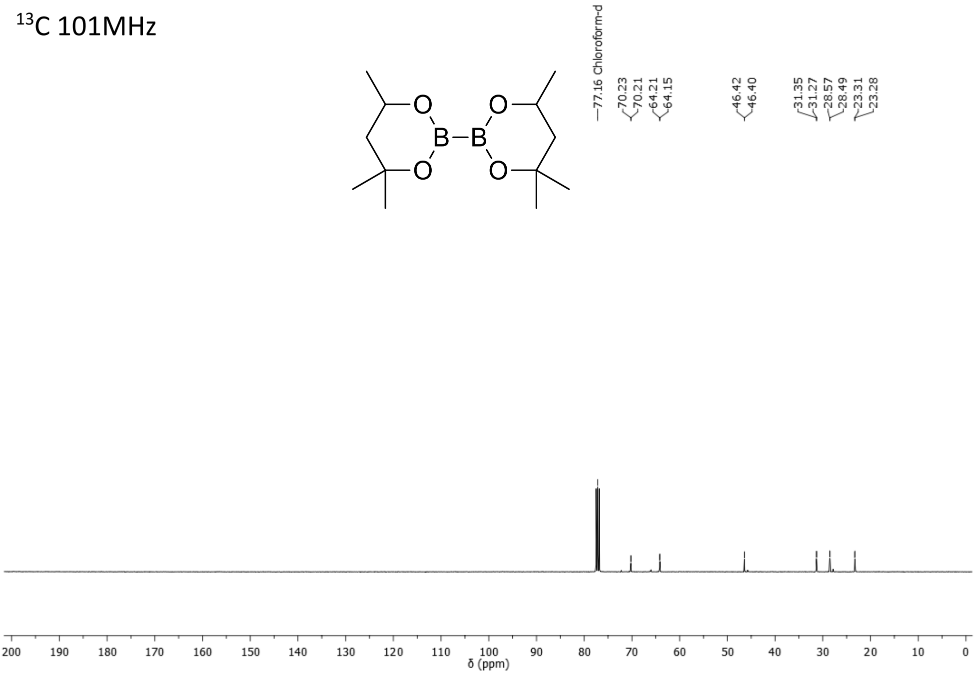
^{13}C 101MHz

2ea

^{1}H 400MHz, $CDCl_3$

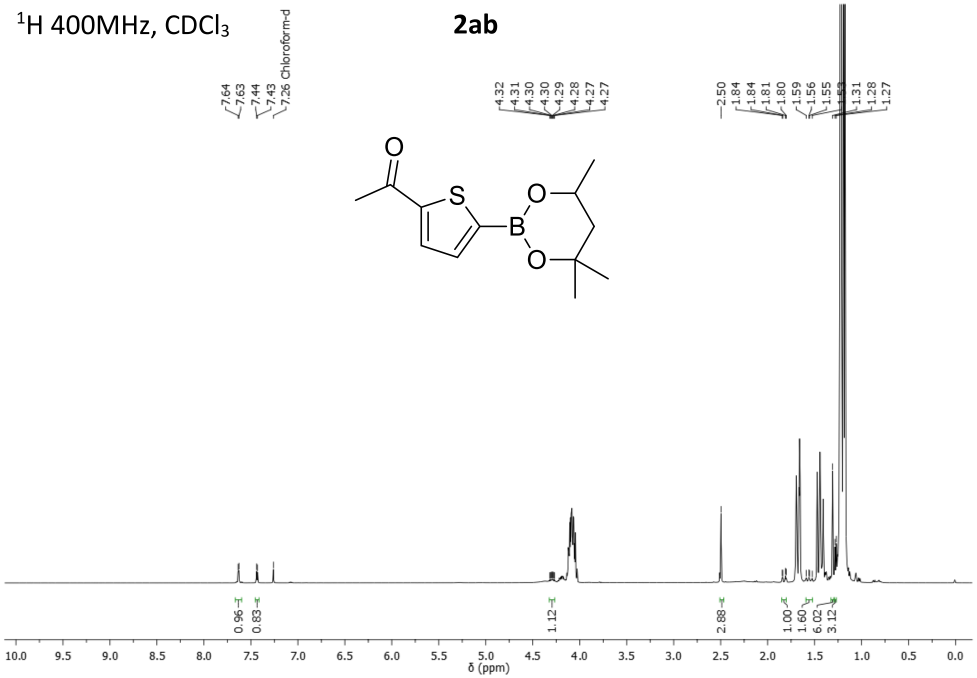


^{13}C 101MHz



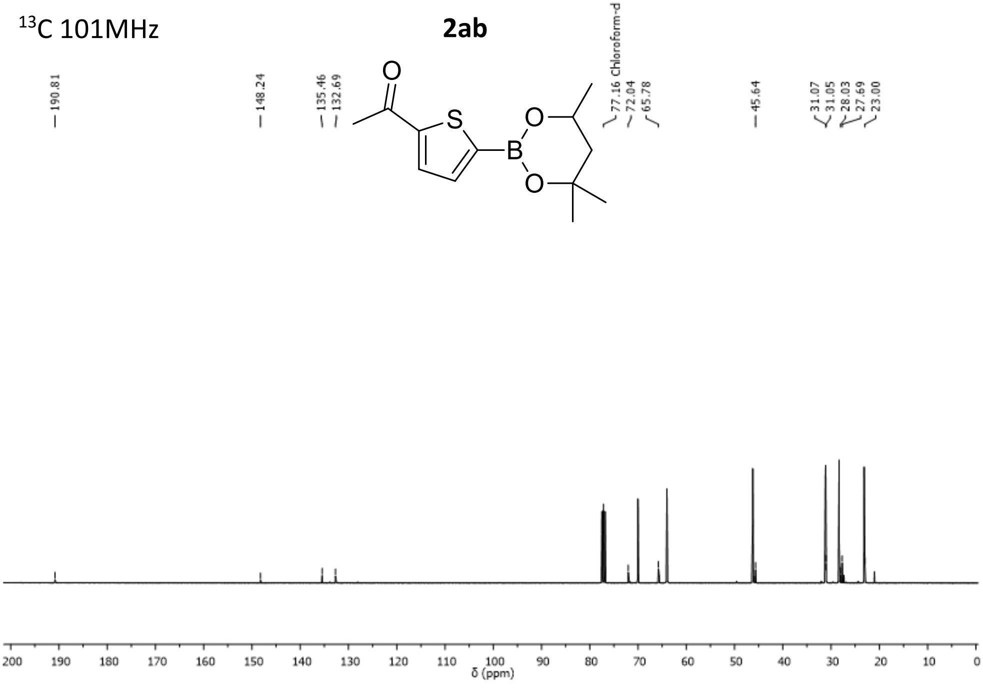
^{1}H 400MHz, CDCl$_3$

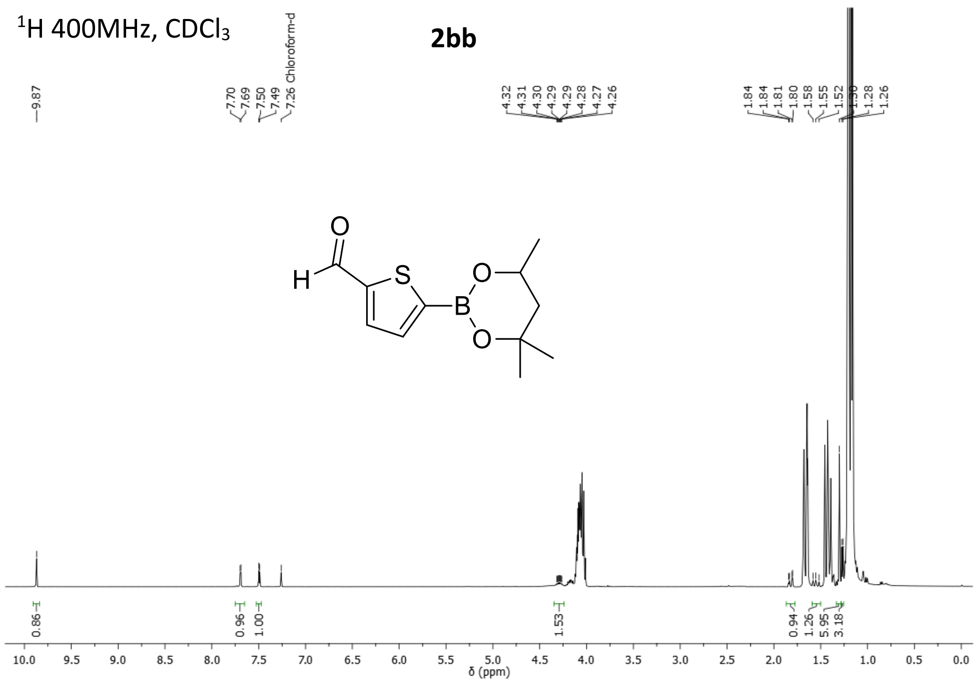
2ab

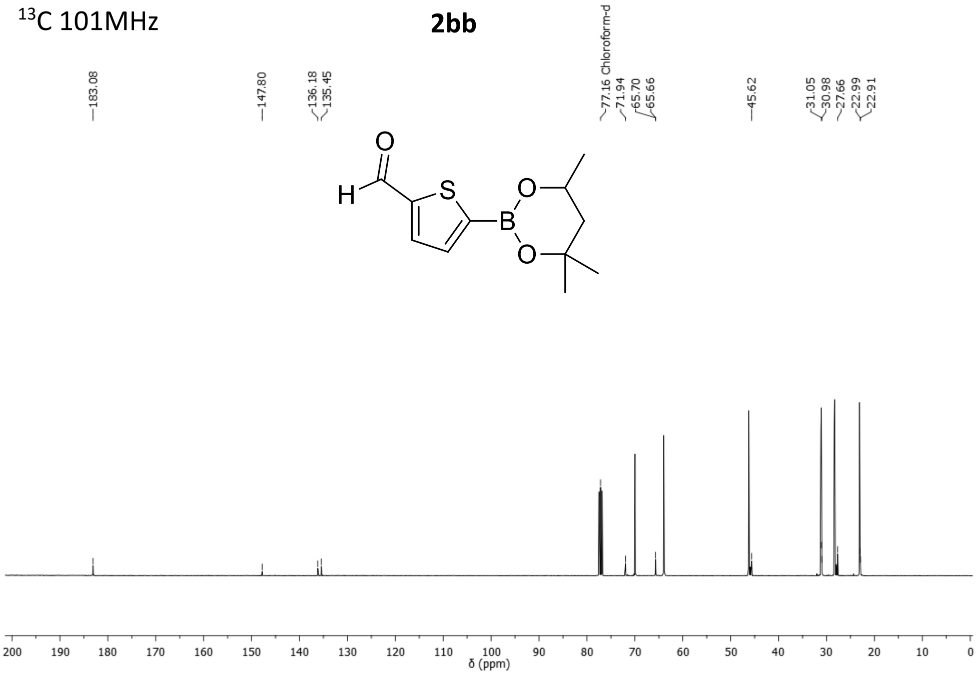


^{13}C 101MHz

2ab

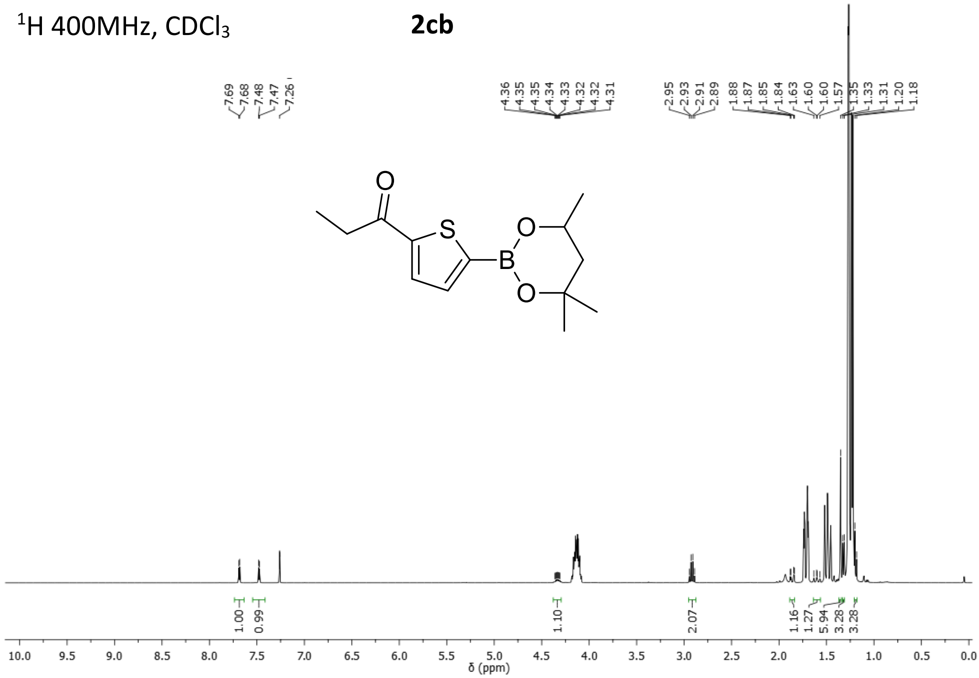



^{1}H 400MHz, CDCl$_3$
2bb
9.87
7.70
7.69
7.50
7.49
7.26 Chloroform-d
4.32
4.31
4.30
4.29
4.29
4.28
4.27
4.26
1.84
1.84
1.81
1.80
1.58
1.55
1.52
1.30
1.28
1.26
O
H
S
O
B
O
0.86
0.96
1.00
1.53
0.94
1.26
5.95
3.18
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)


^{13}C 101MHz
2bb
183.08
147.80
136.18
135.45
77.16 Chloroform-d
71.94
65.70
65.66
45.62
31.05
30.98
27.66
22.99
22.91
O
H
S
O
B
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

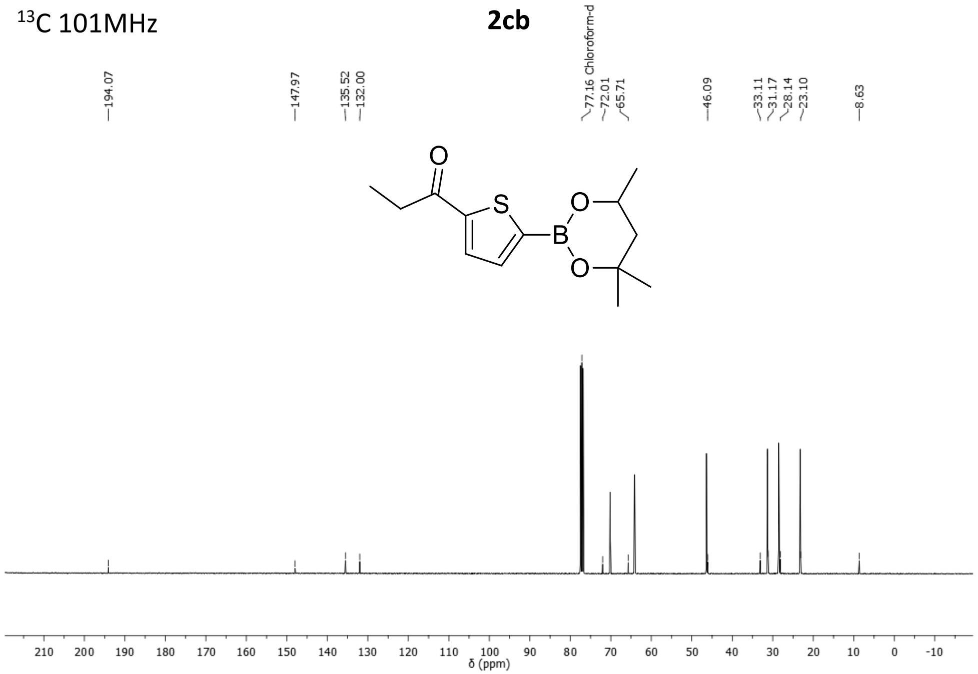
^{1}H 400MHz, CDCl$_3$

2cb



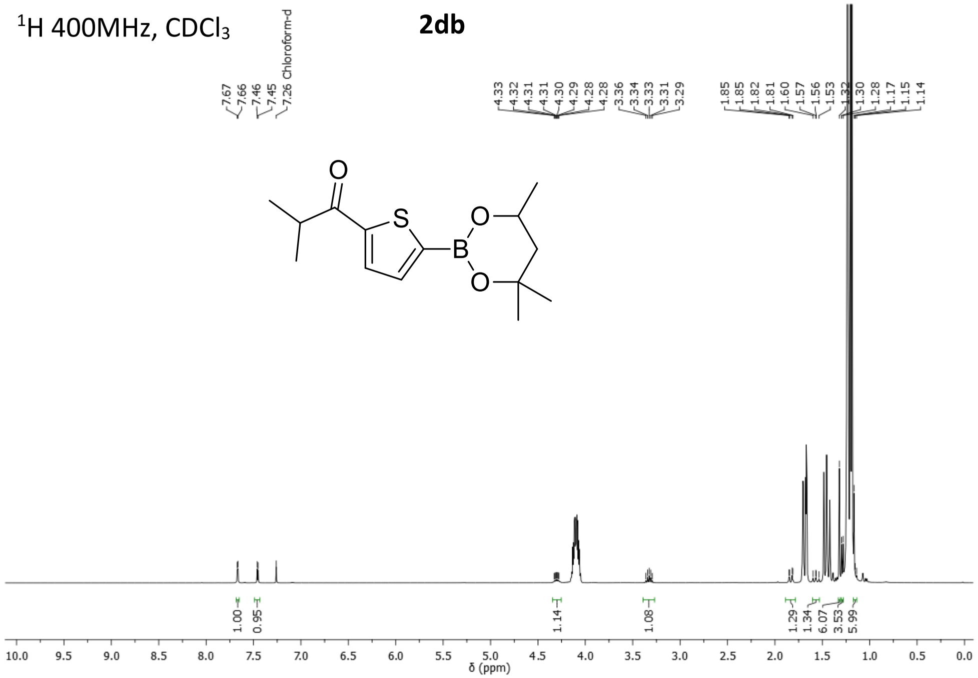
^{13}C 101MHz

2cb



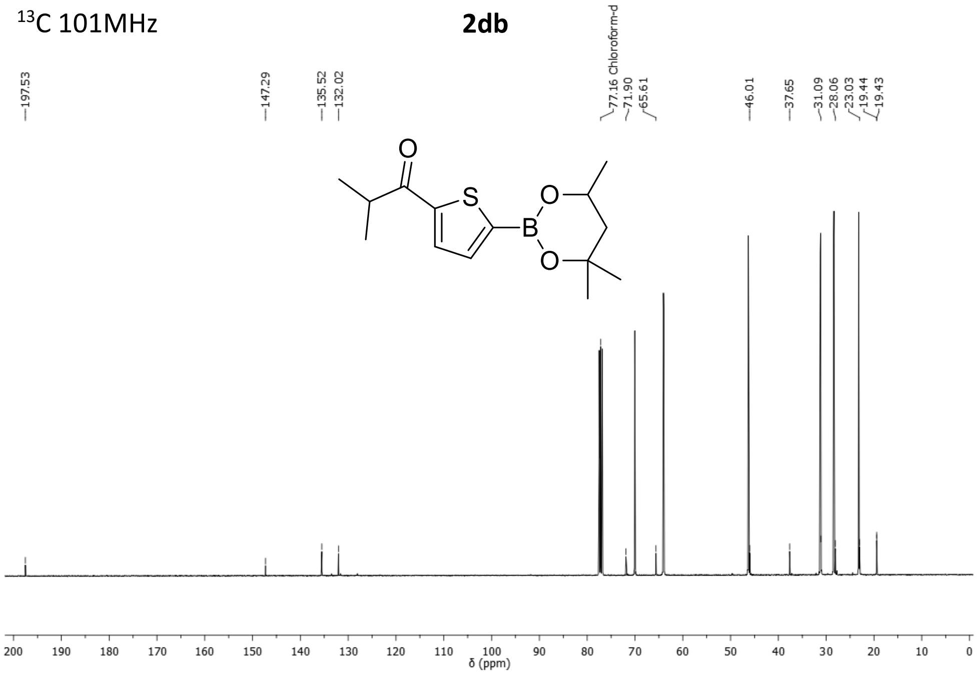
^{1}H 400MHz, CDCl$_3$

2db



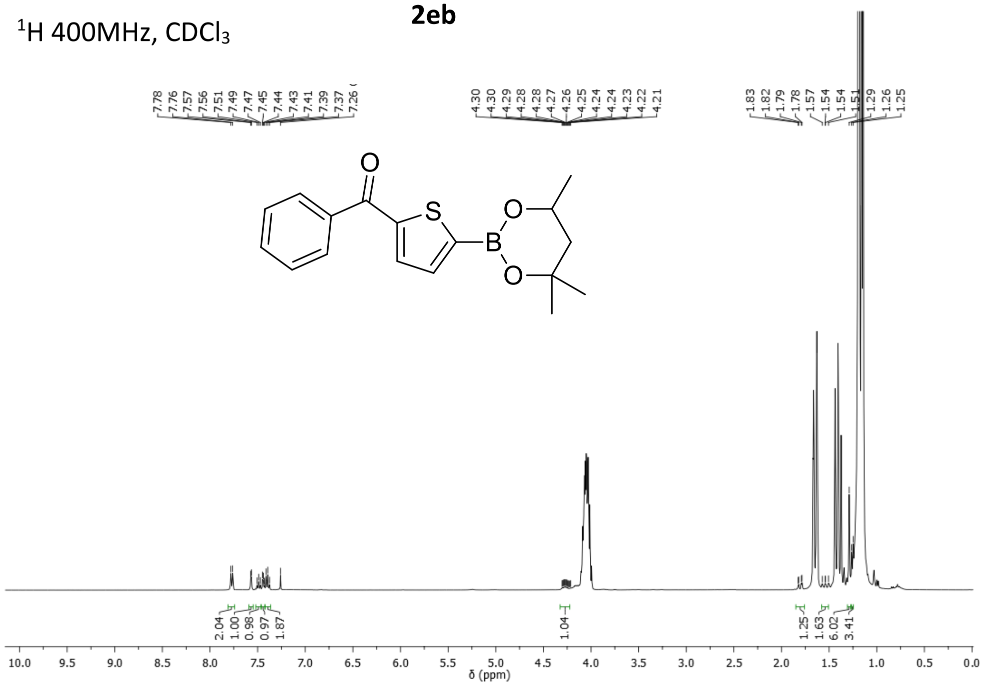
^{13}C 101MHz

2db



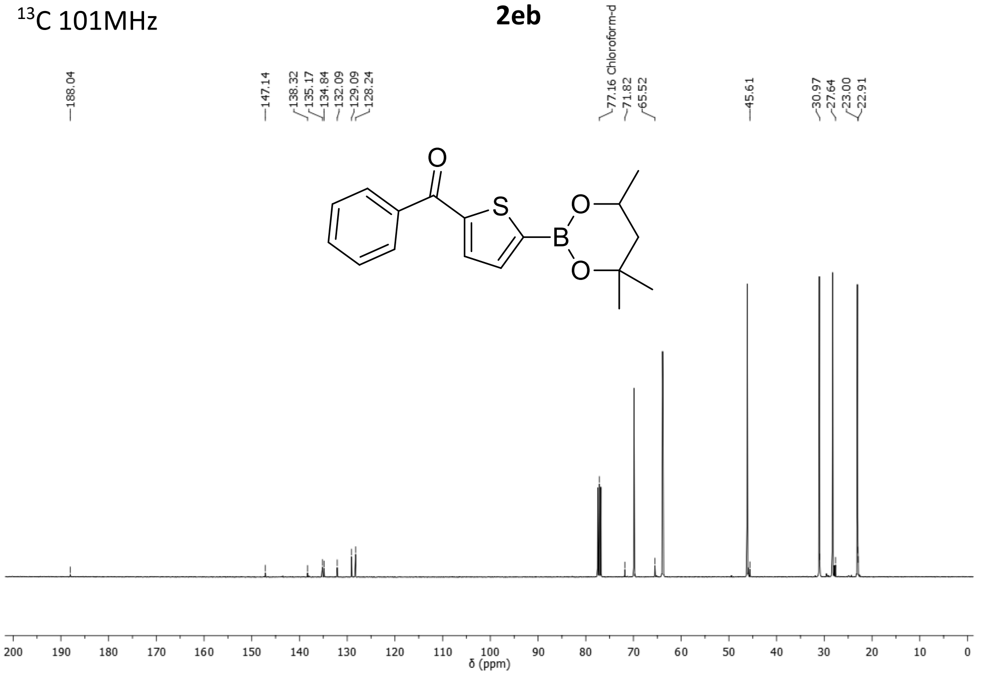
^{1}H 400MHz, $CDCl_3$

2eb

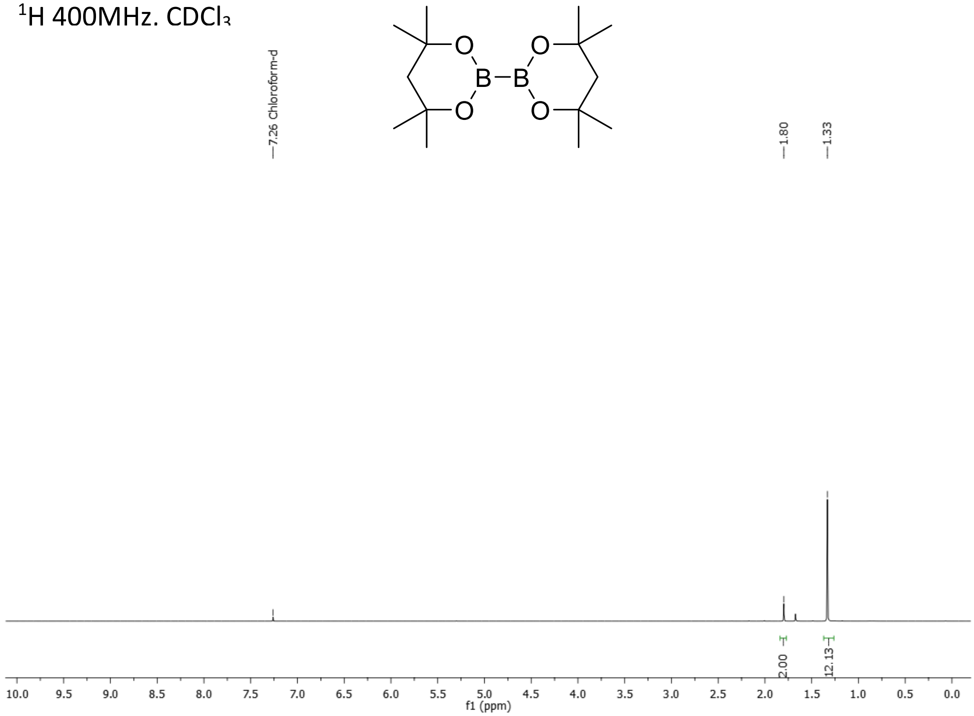


^{13}C 101MHz

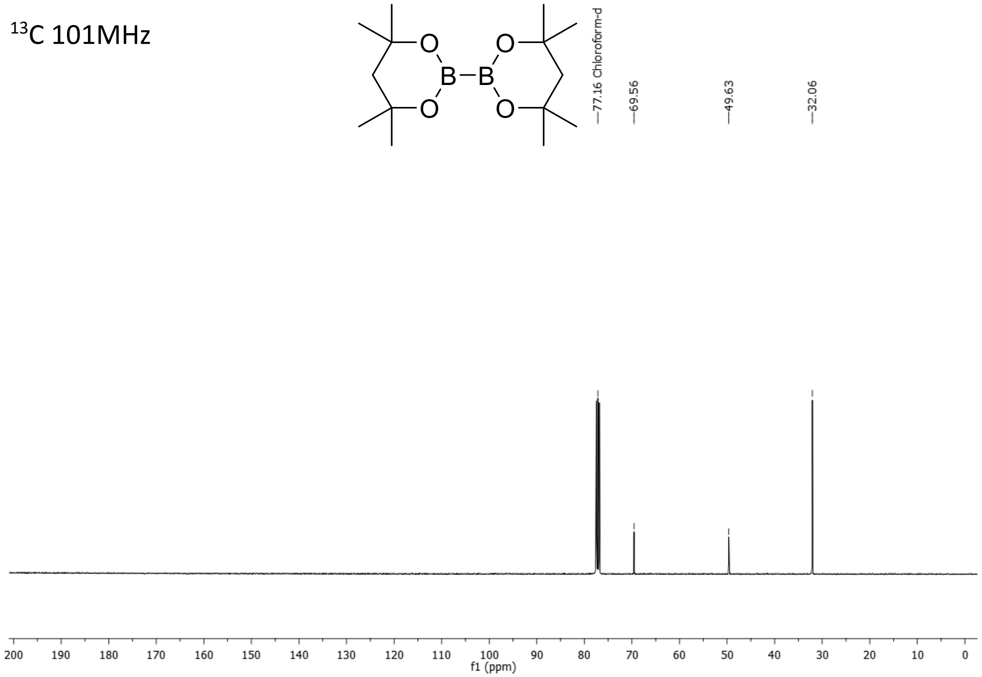
2eb

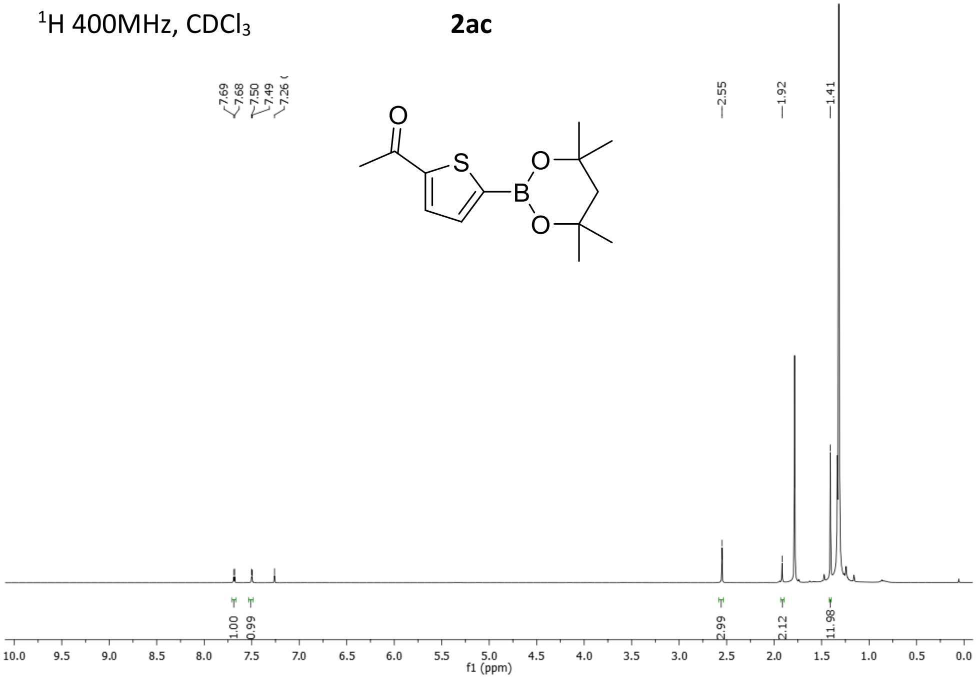


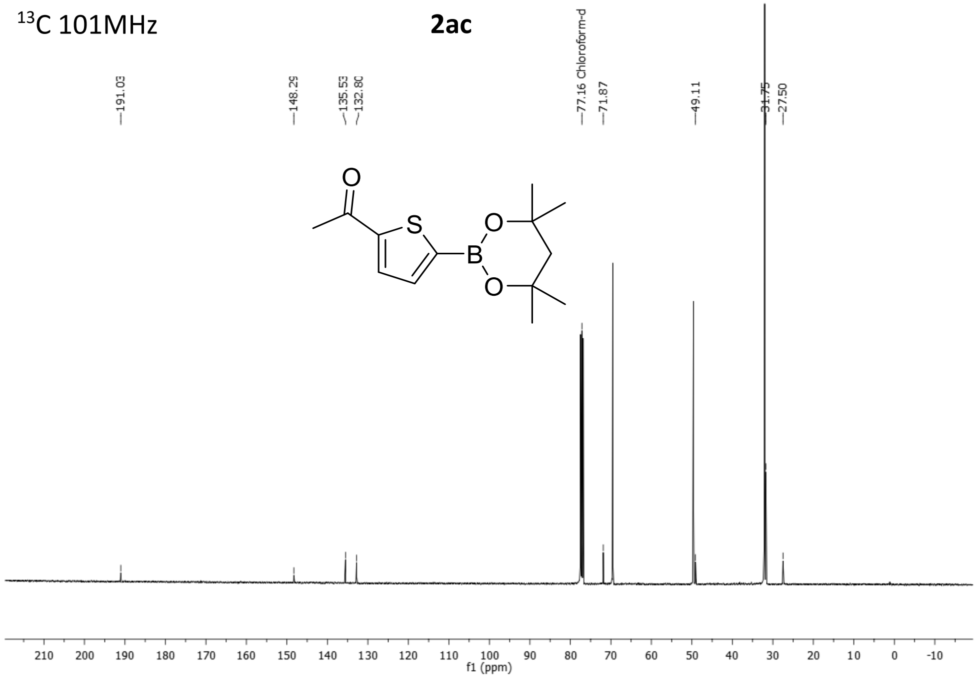
^{1}H 400MHz. CDCl$_3$



^{13}C 101MHz

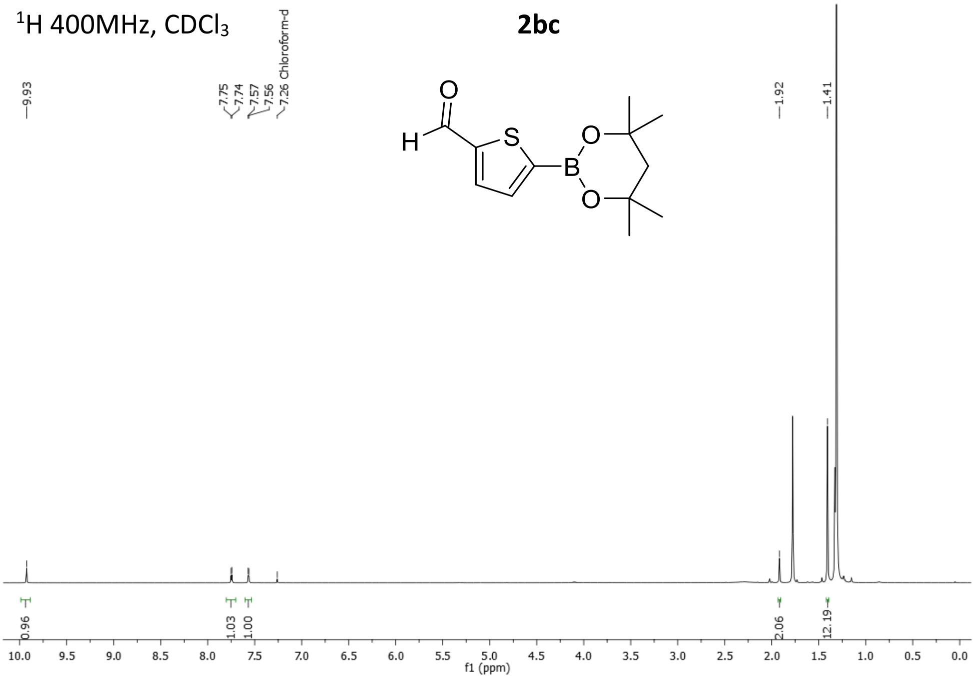



^{1}H 400MHz, CDCl$_3$
2ac
7.69
7.68
7.50
7.49
7.26
2.55
1.92
1.41
1.00
0.99
2.99
2.12
11.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


^{13}C 101MHz
2ac
191.03
148.29
135.53
132.80
77.16 Chloroform-d
71.87
49.11
31.75
27.50
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

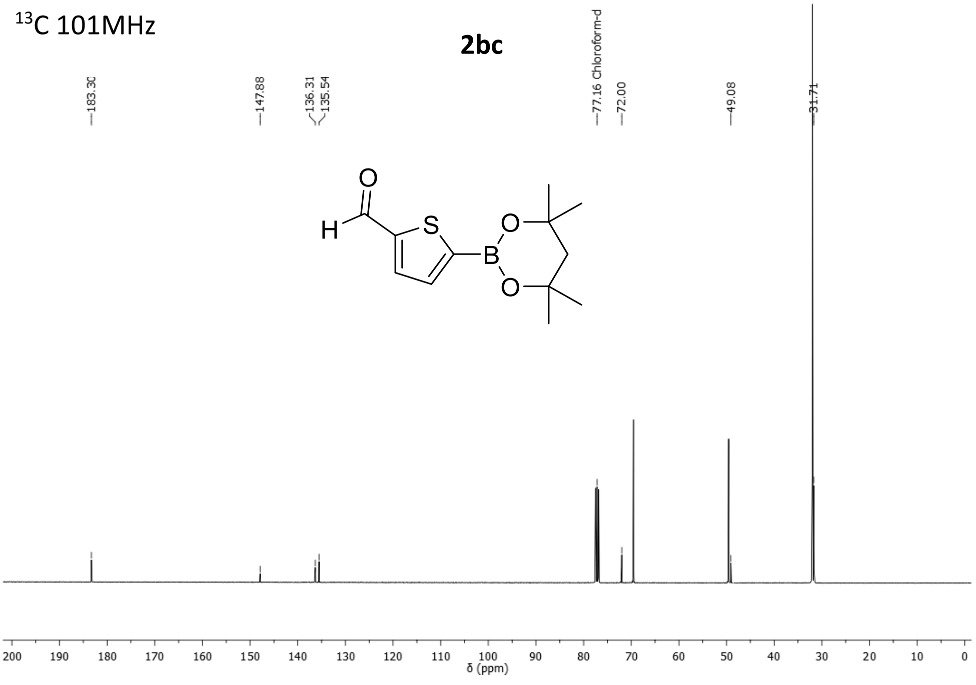
^{1}H 400MHz, $CDCl_3$

2bc



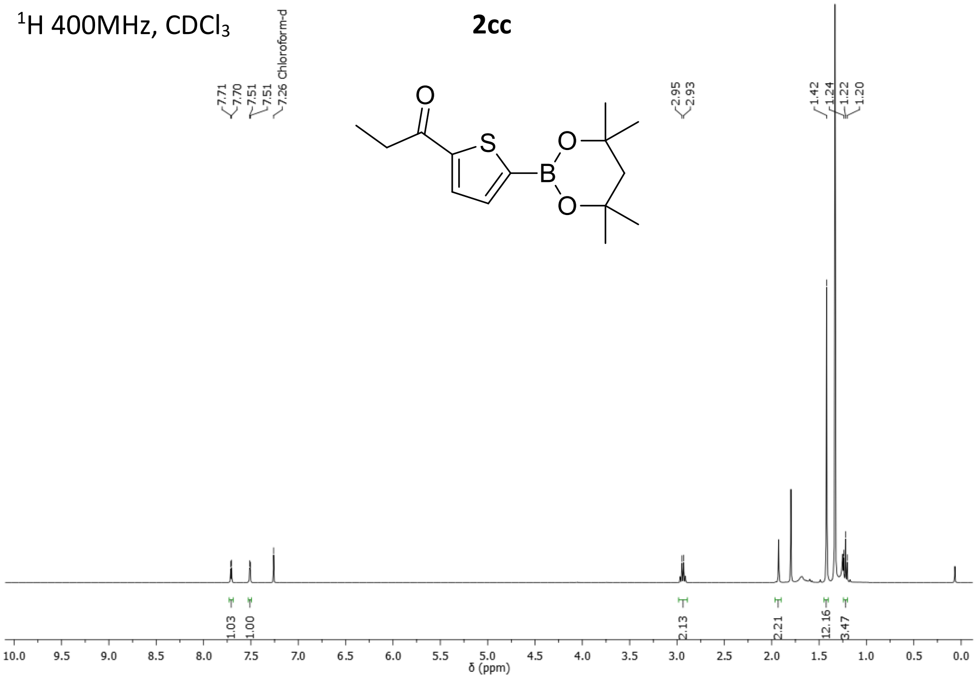
^{13}C 101MHz

2bc



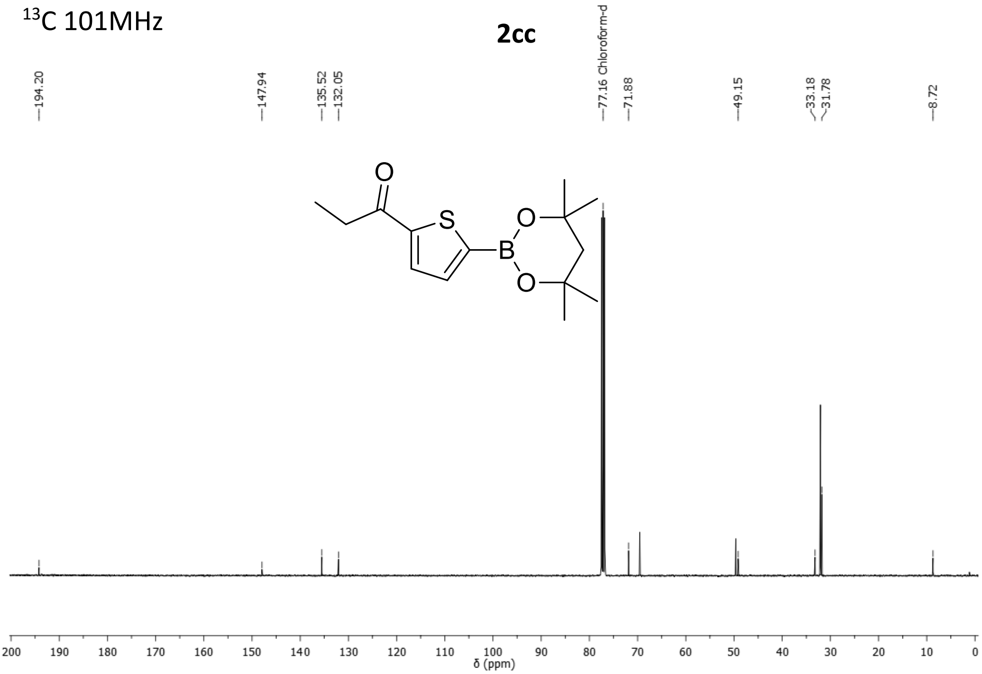
^{1}H 400MHz, CDCl$_3$

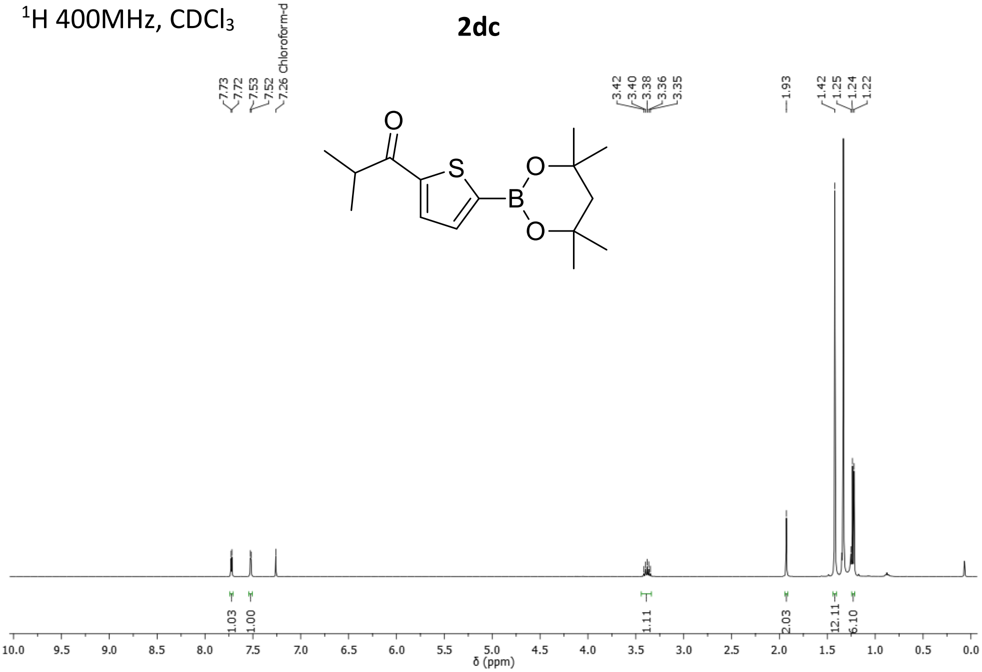
2cc

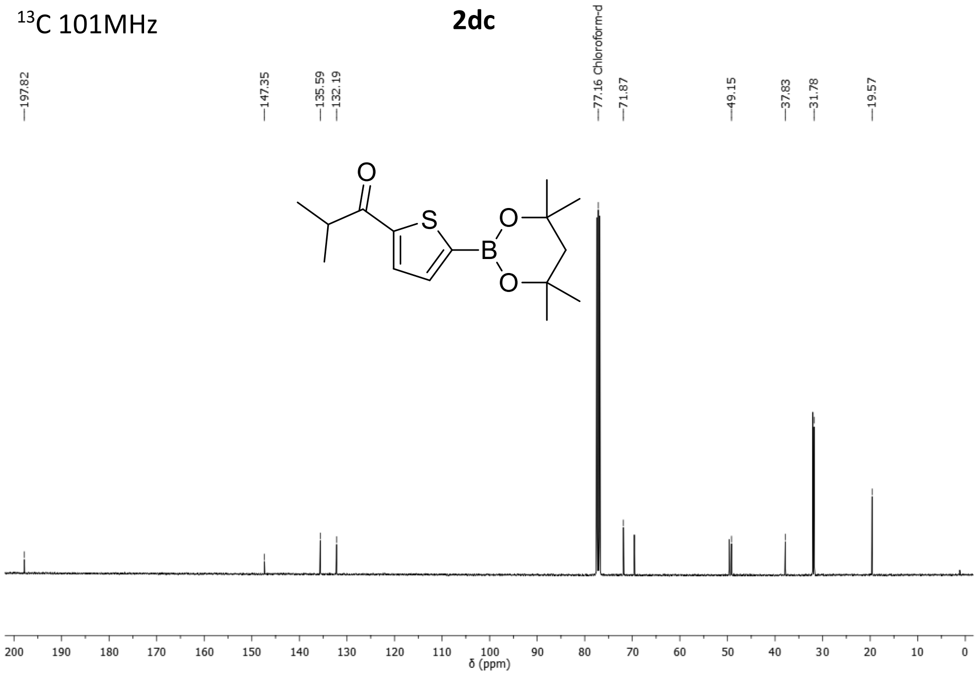


^{13}C 101MHz

2cc

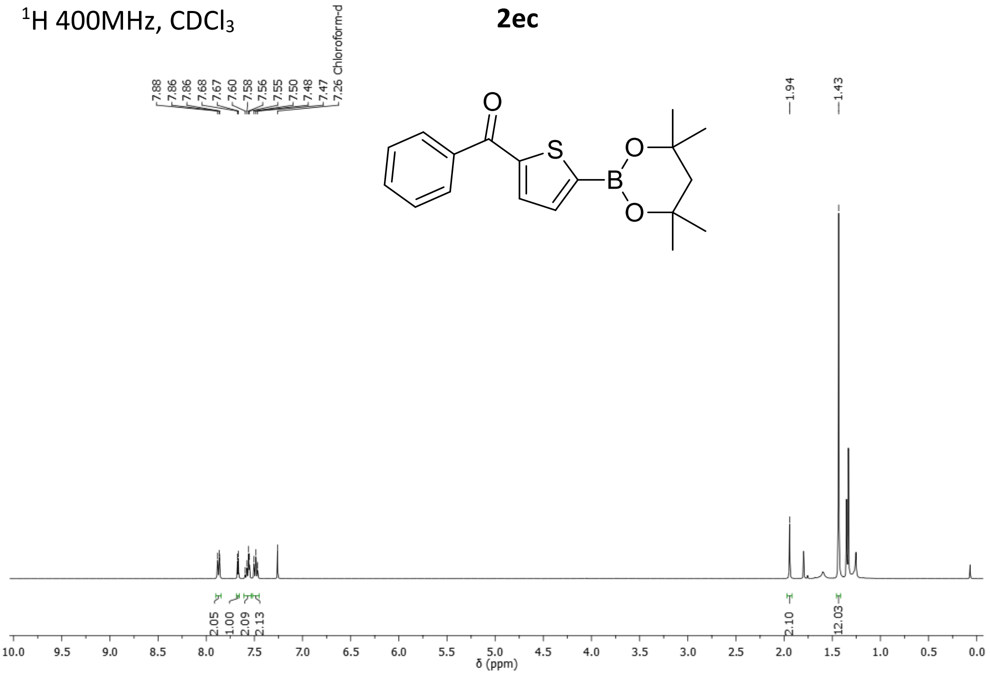



^{1}H 400MHz, CDCl$_3$
2dc
7.73
7.72
7.53
7.52
7.26 Chloroform-d
3.42
3.40
3.38
3.36
3.35
1.93
1.42
1.25
1.24
1.22
O
S
B
O
O
1.03
1.00
1.11
2.03
12.11
6.10
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)


^{13}C 101MHz
2dc
197.82
147.35
135.59
132.19
77.16 Chloroform-d
71.87
49.15
37.83
31.78
19.57
O
S
B
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

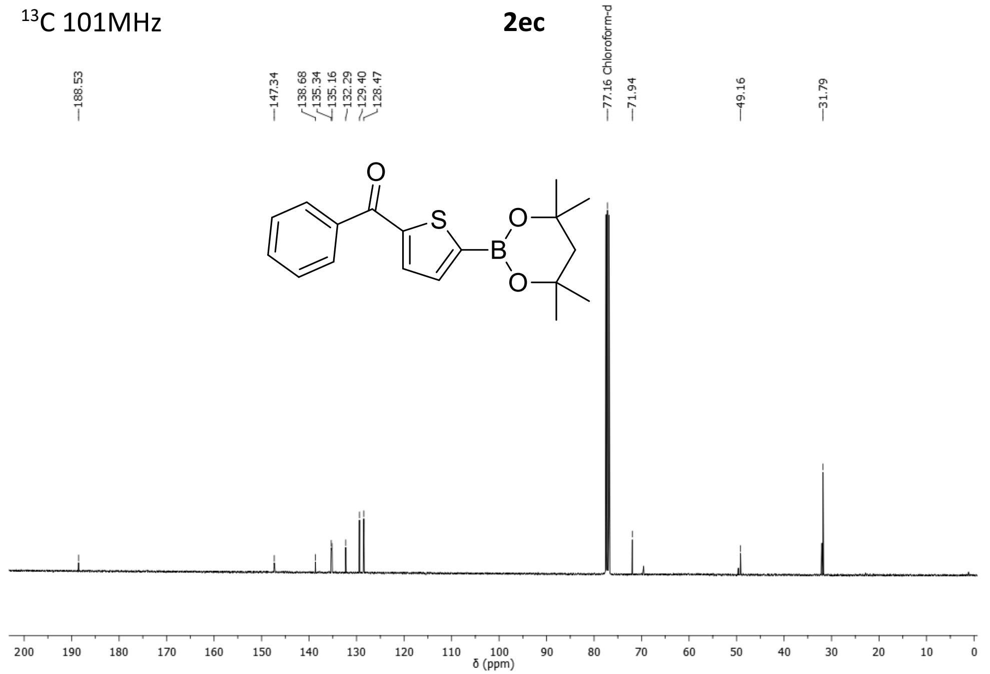
^1H 400MHz, $CDCl_3$

2ec

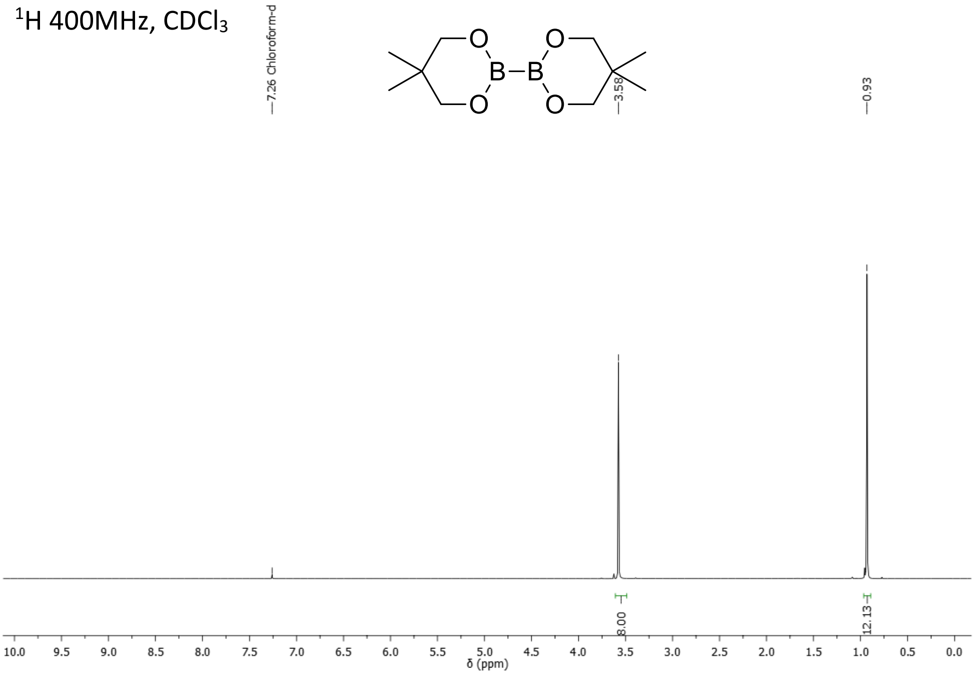


^{13}C 101MHz

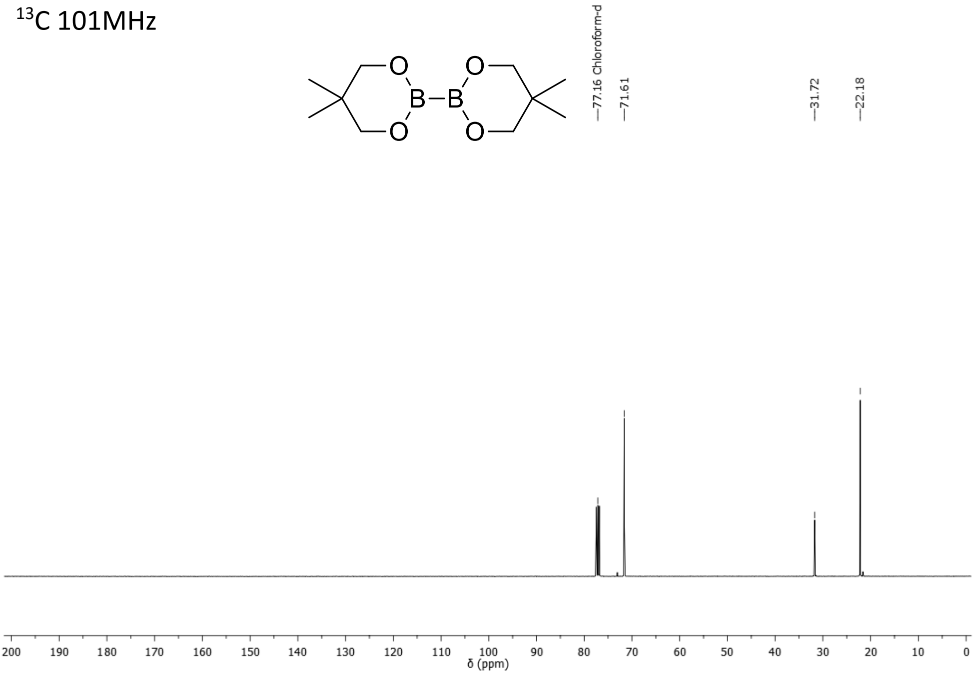
2ec

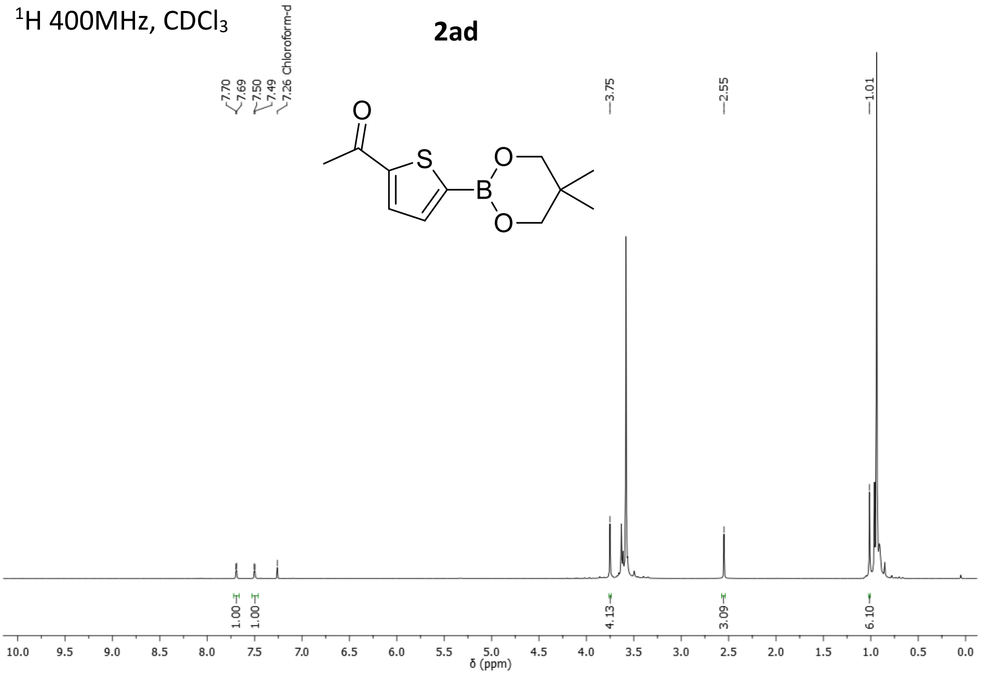


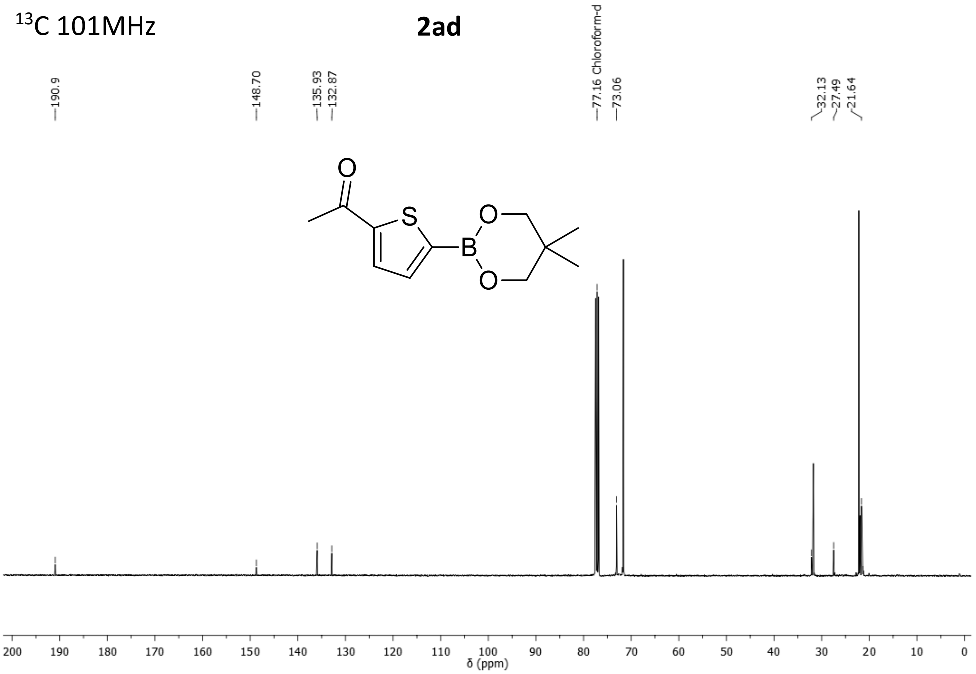
^{1}H 400MHz, CDCl$_3$



^{13}C 101MHz

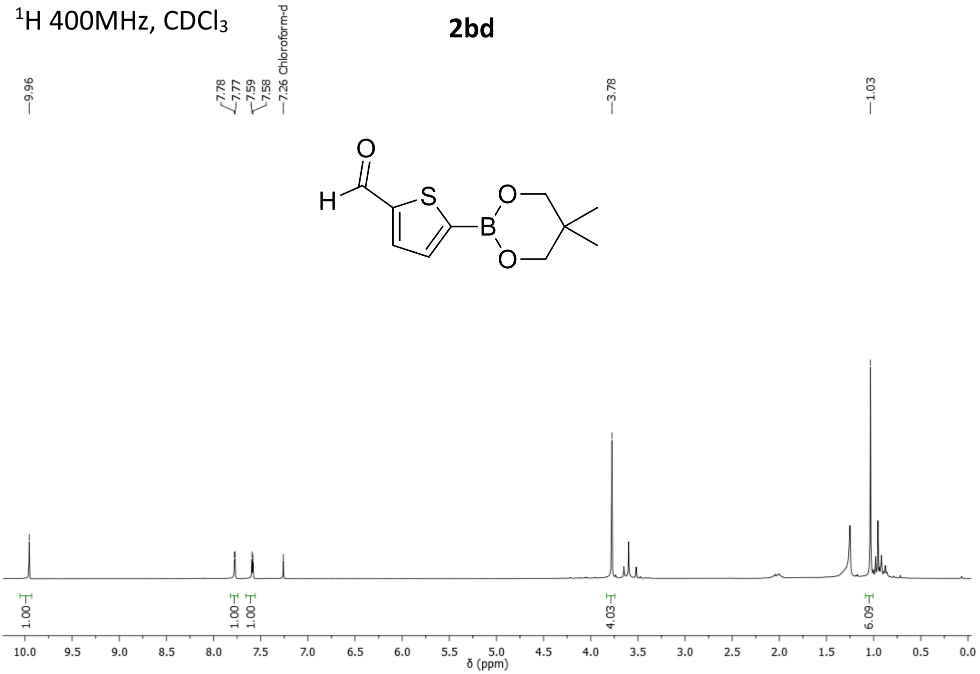



^{1}H 400MHz, CDCl$_3$
2ad
7.70
7.69
7.50
7.49
7.26 Chloroform-d
3.75
2.55
1.01
O
S
O
B
O
1.00
1.00
4.13
3.09
6.10
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)


^{13}C 101MHz
2ad
190.9
148.70
135.93
132.87
77.16 Chloroform-d
73.06
32.13
27.49
21.64
O
S
O
B
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

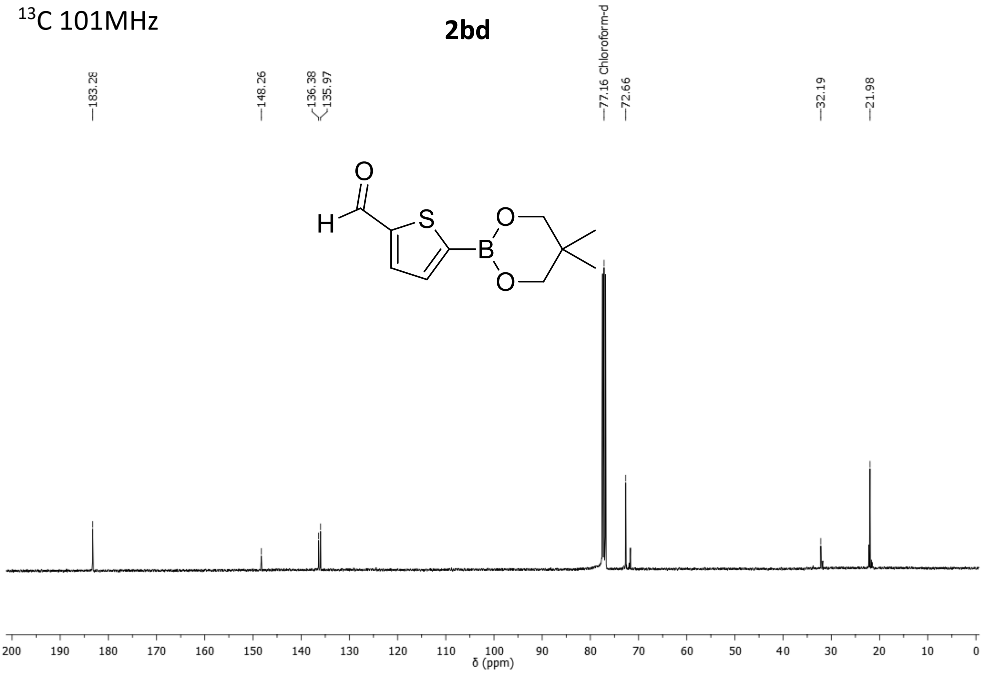
^{1}H 400MHz, CDCl$_3$

2bd



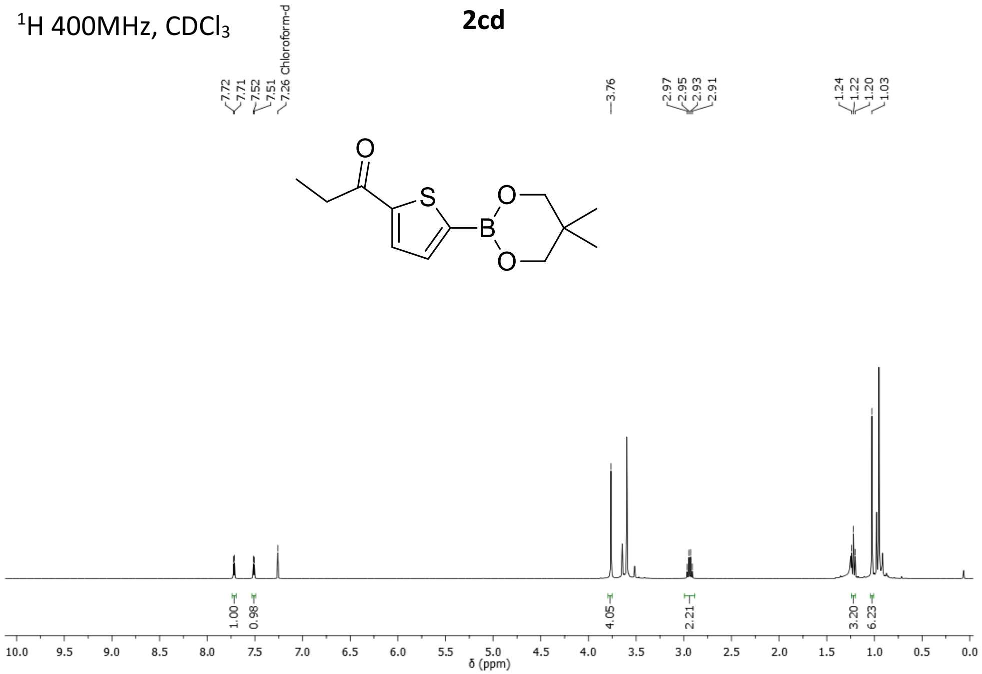
^{13}C 101MHz

2bd



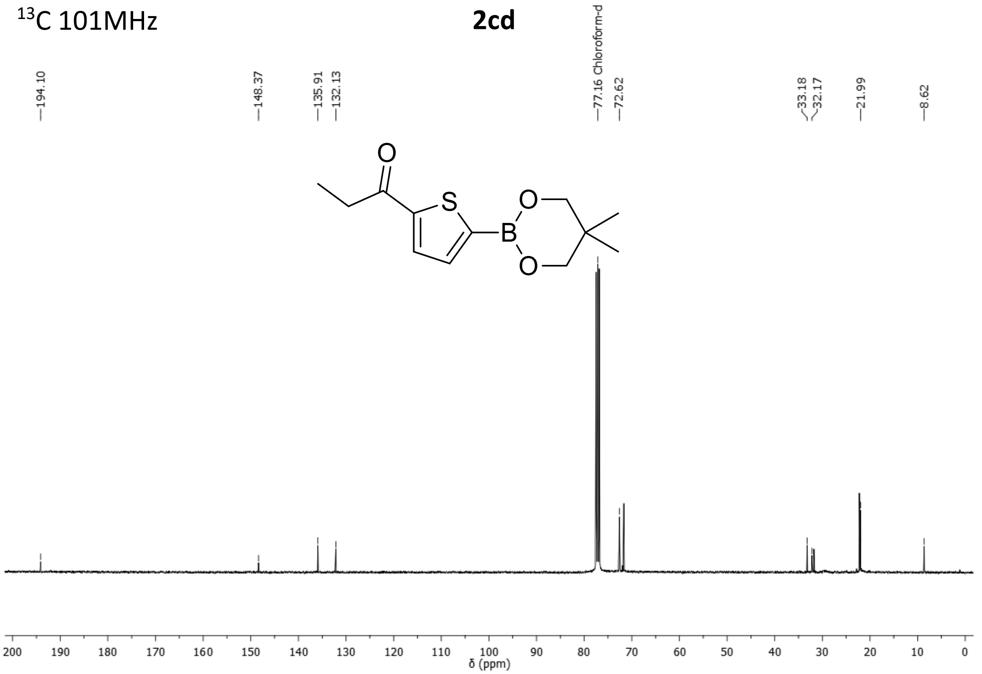
^{1}H 400MHz, CDCl$_3$

2cd



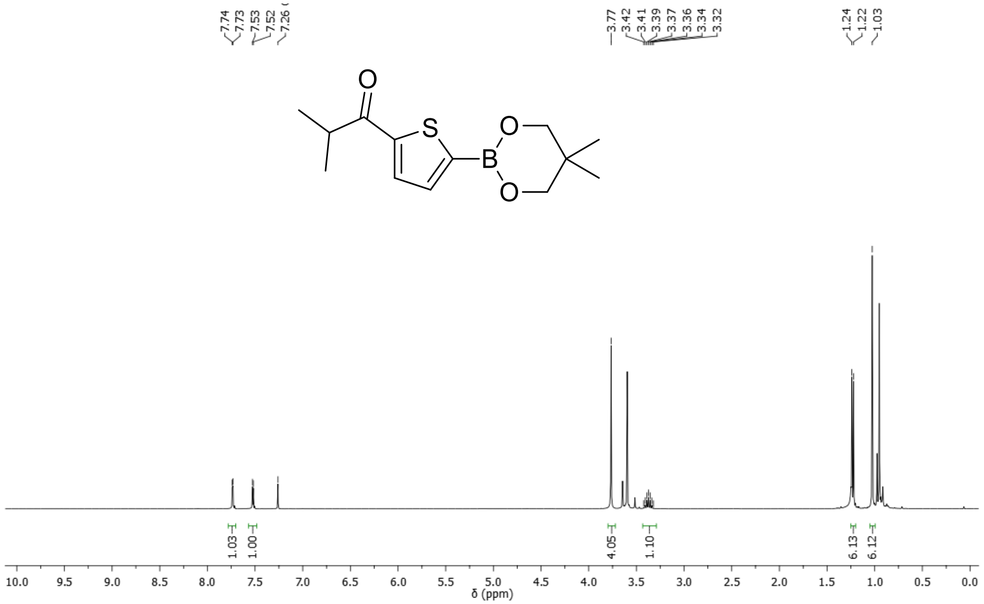
^{13}C 101MHz

2cd



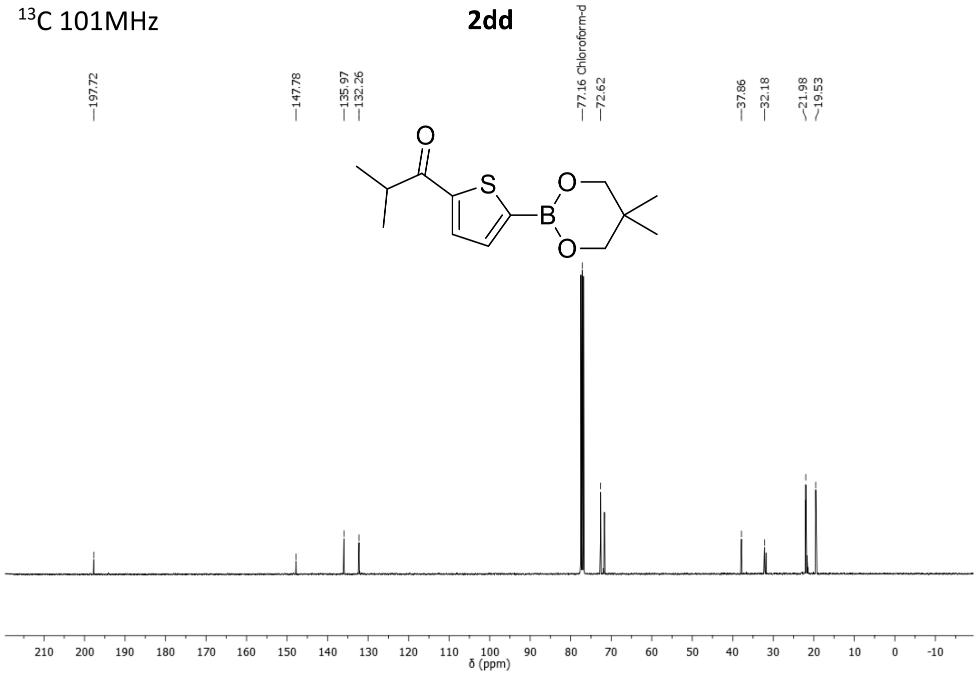
^{1}H 400MHz, $CDCl_3$

2dd



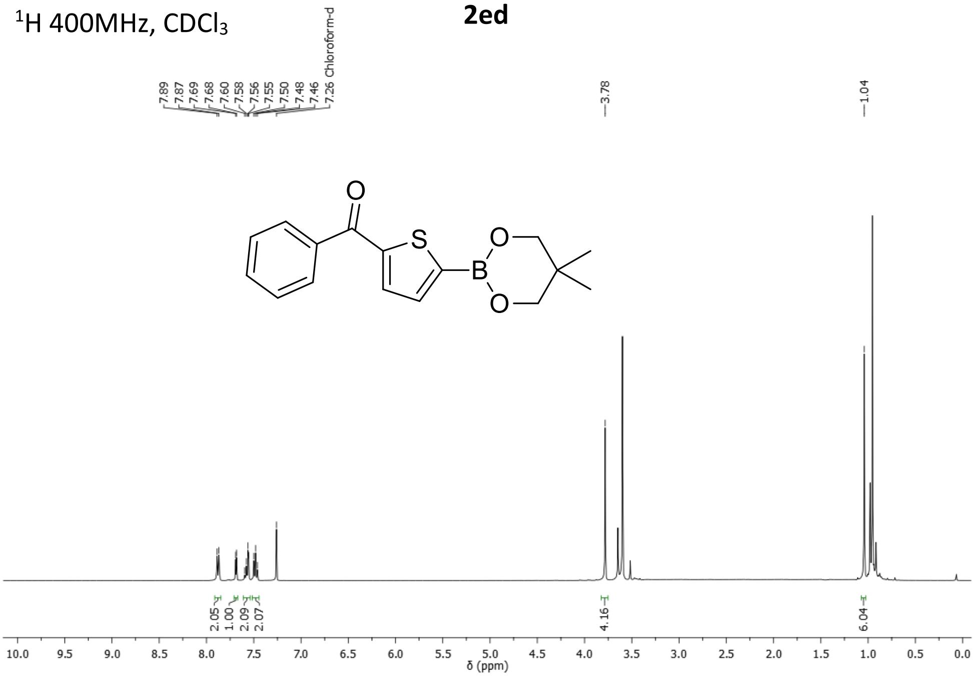
^{13}C 101MHz

2dd



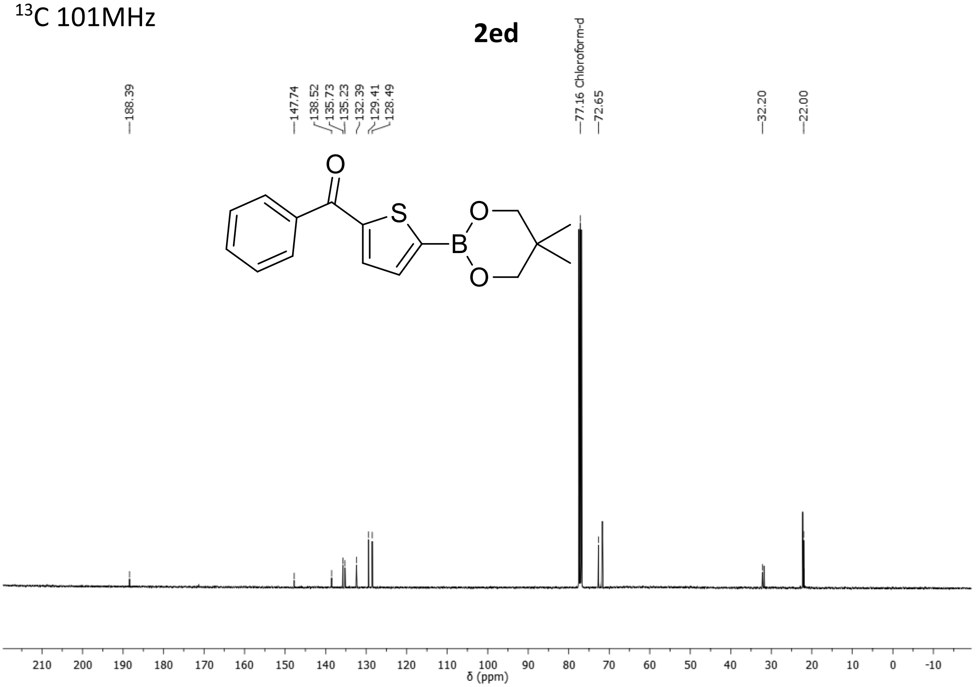
^{1}H 400MHz, CDCl$_3$

2ed

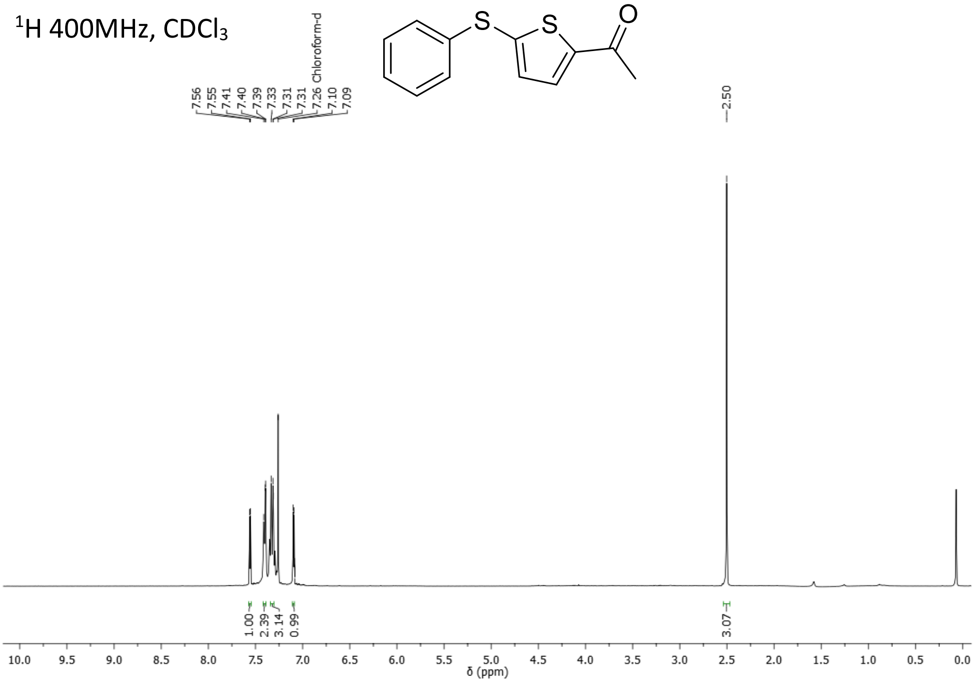


^{13}C 101MHz

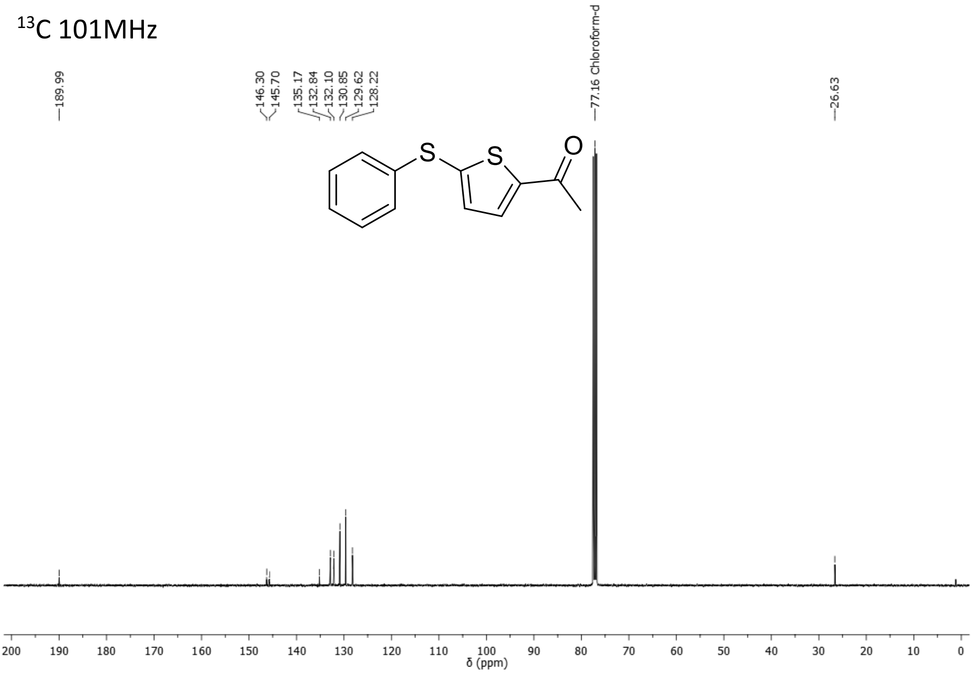
2ed



^{1}H 400MHz, $CDCl_3$

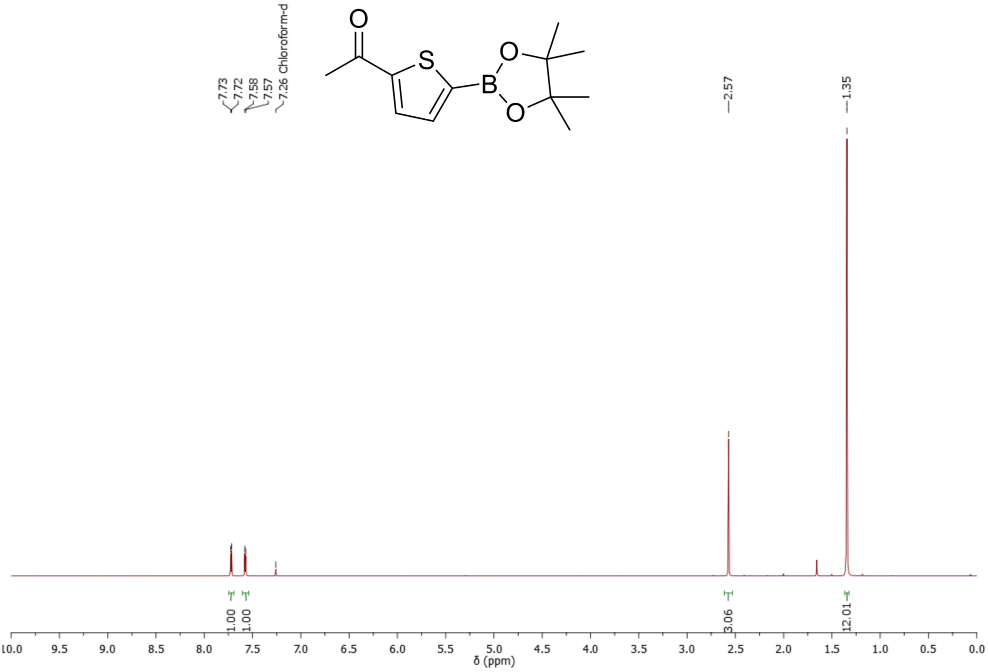


^{13}C 101MHz



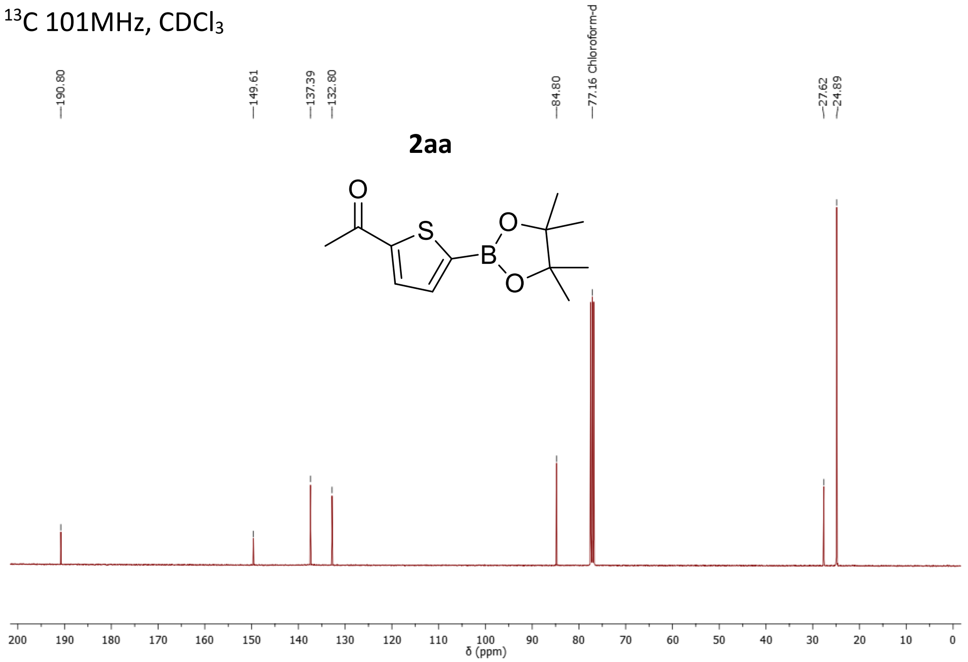
^{1}H 400MHz, CDCl$_3$

2aa

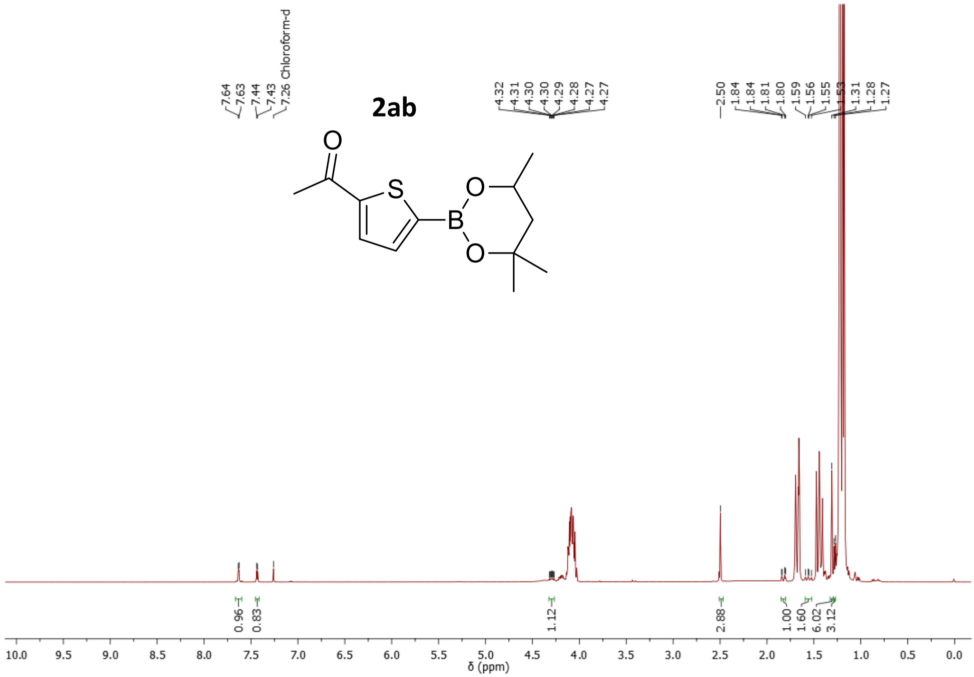


^{13}C 101MHz, CDCl$_3$

2aa

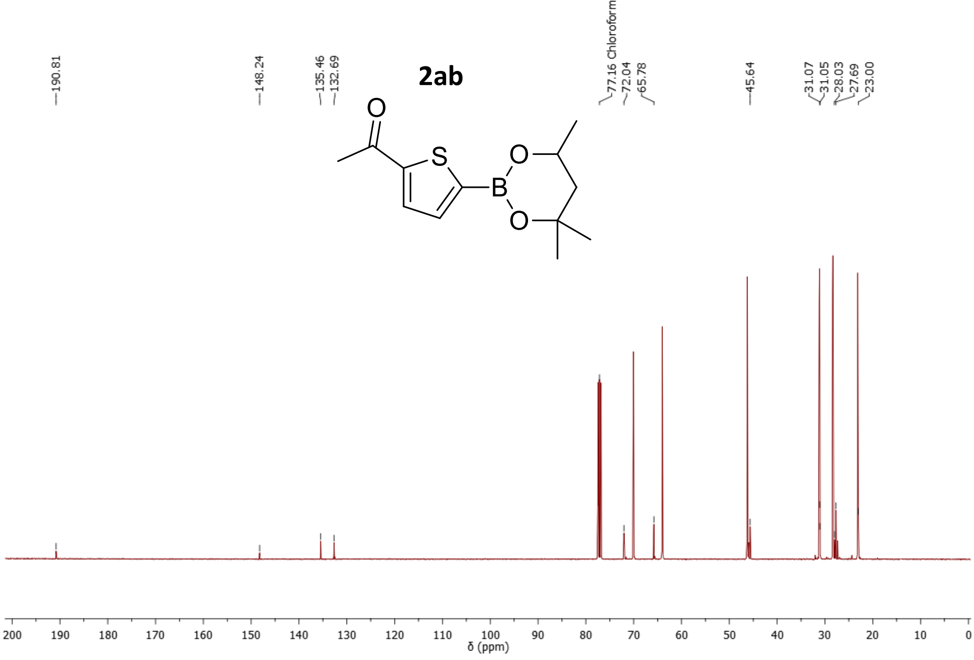


^{1}H 400MHz, CDCl$_3$



2ab

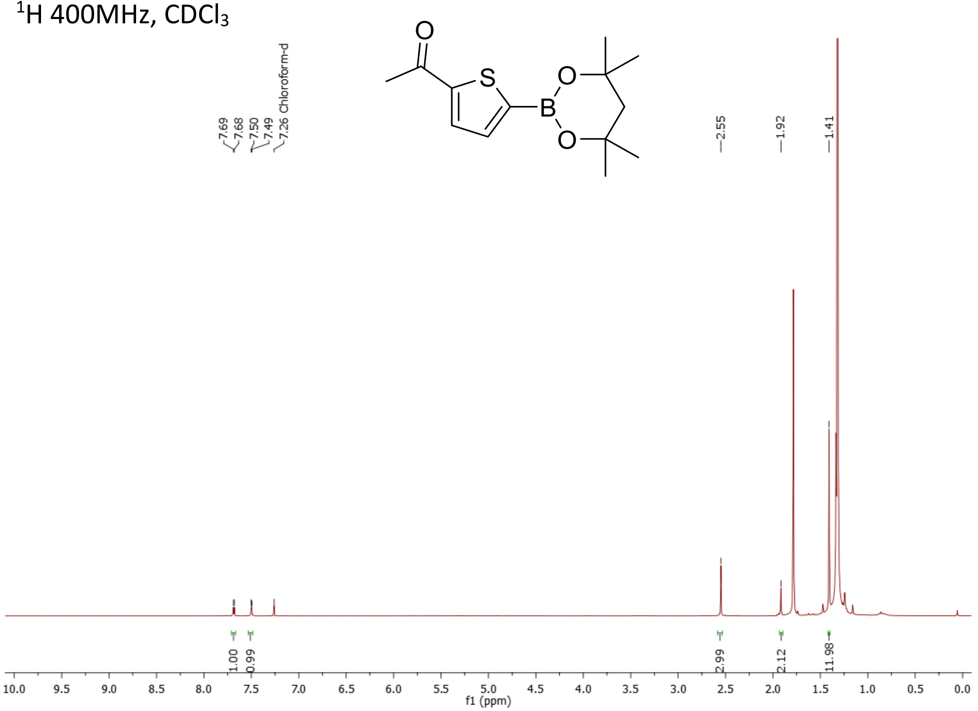
^{13}C 101MHz, CDCl$_3$



2ab

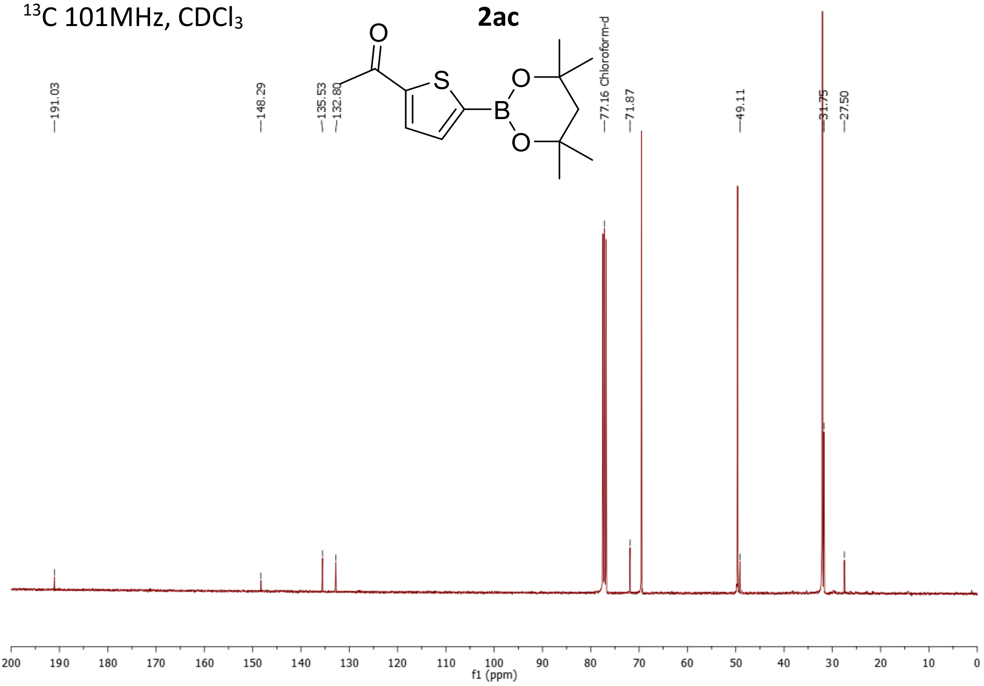
2ac

^{1}H 400MHz, $CDCl_3$

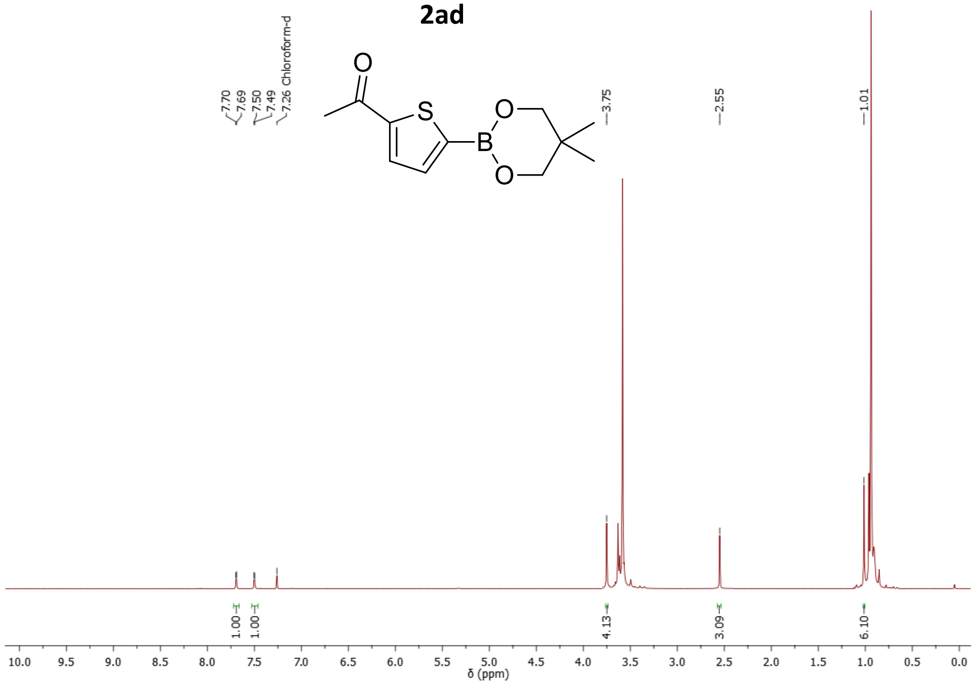


^{13}C 101MHz, $CDCl_3$

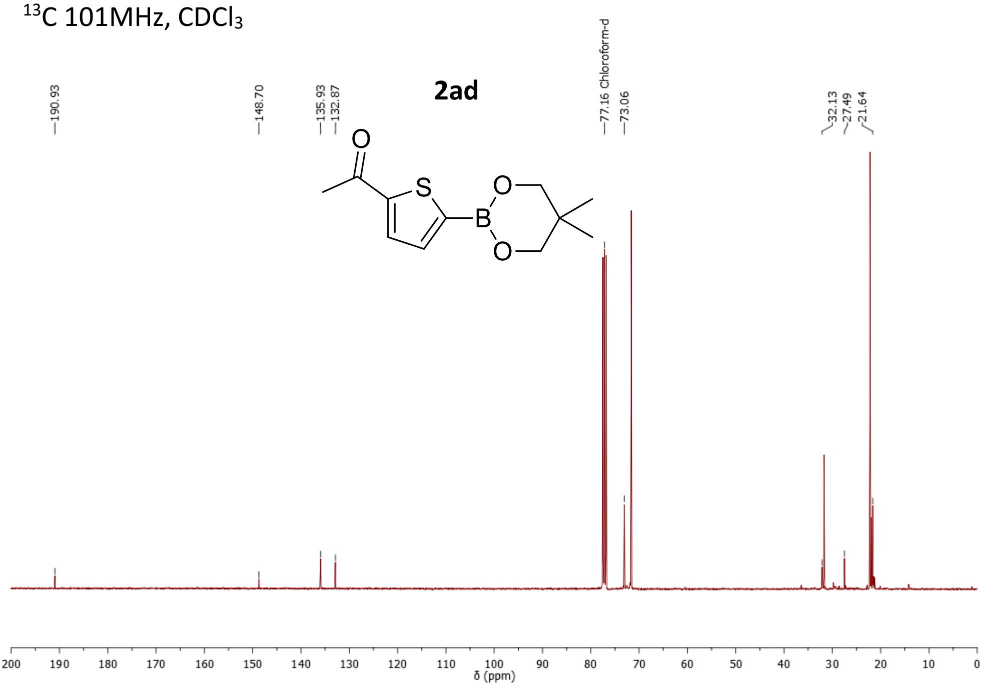
2ac



^{1}H 400MHz, CDCl$_3$

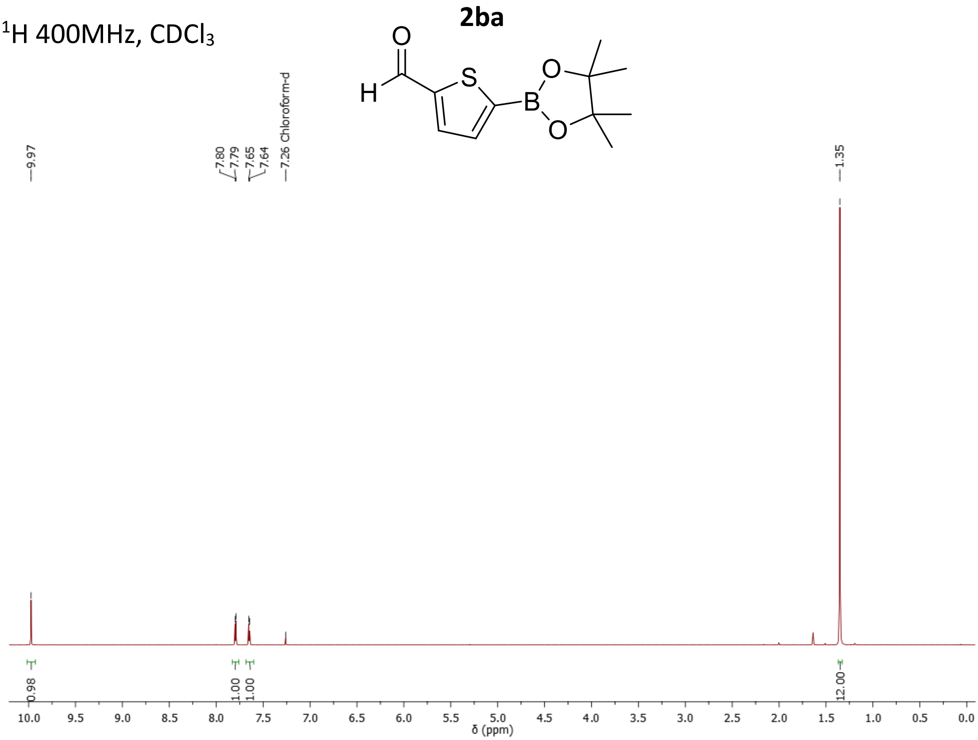


^{13}C 101MHz, CDCl$_3$



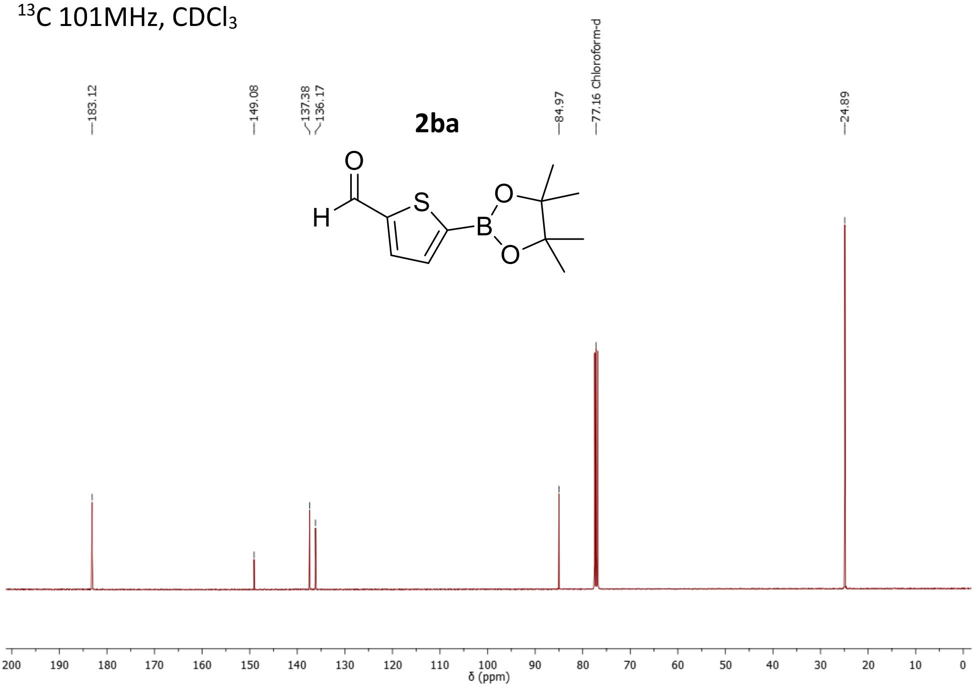
^1H 400MHz, $CDCl_3$

2ba

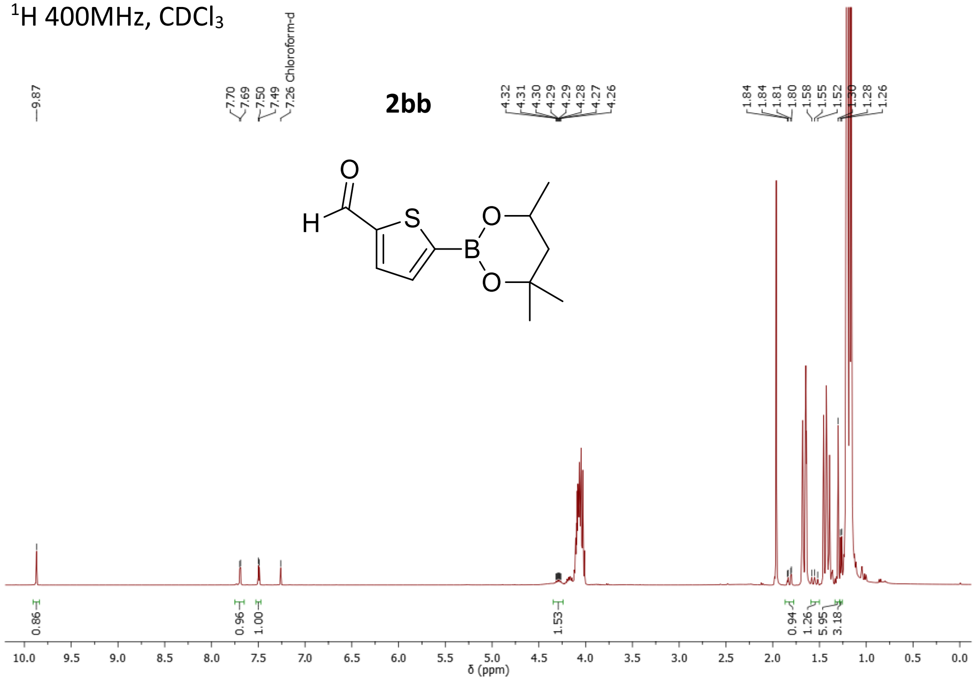


^{13}C 101MHz, $CDCl_3$

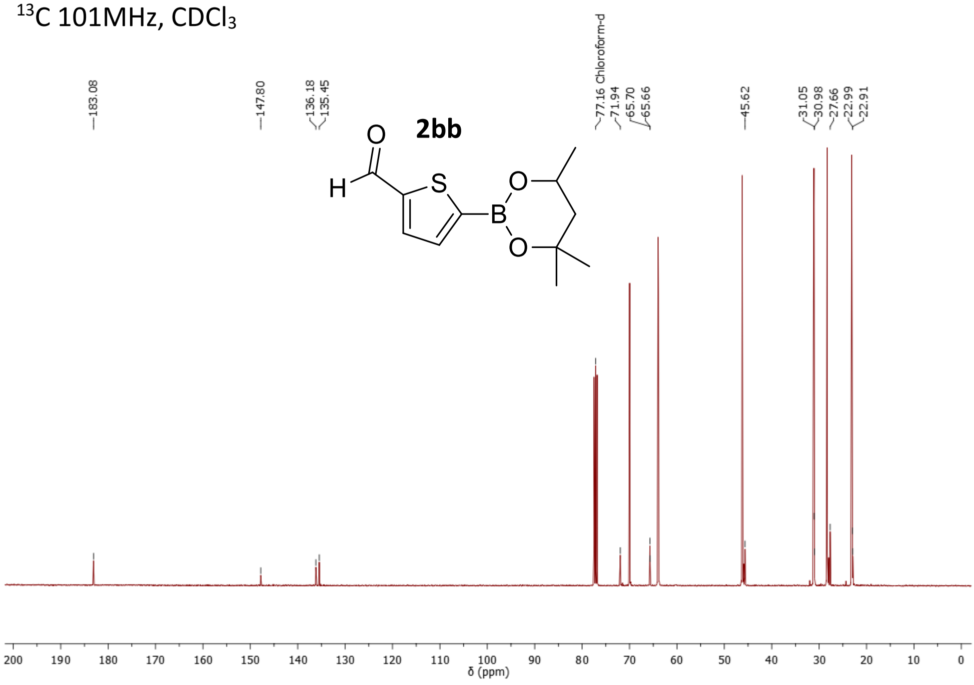
2ba



^{1}H 400MHz, CDCl$_3$

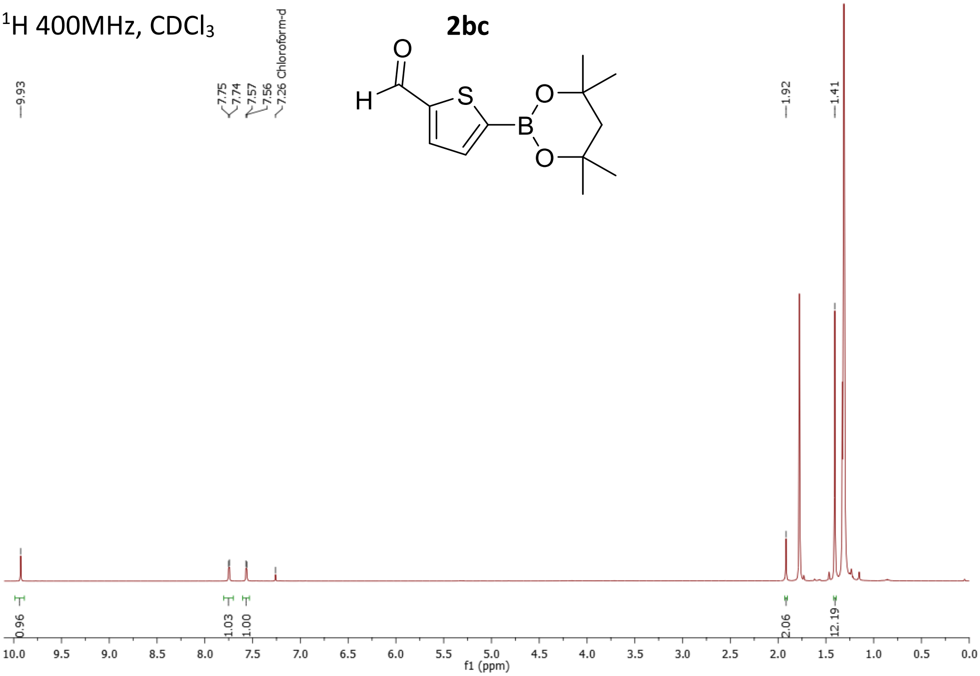


^{13}C 101MHz, CDCl$_3$



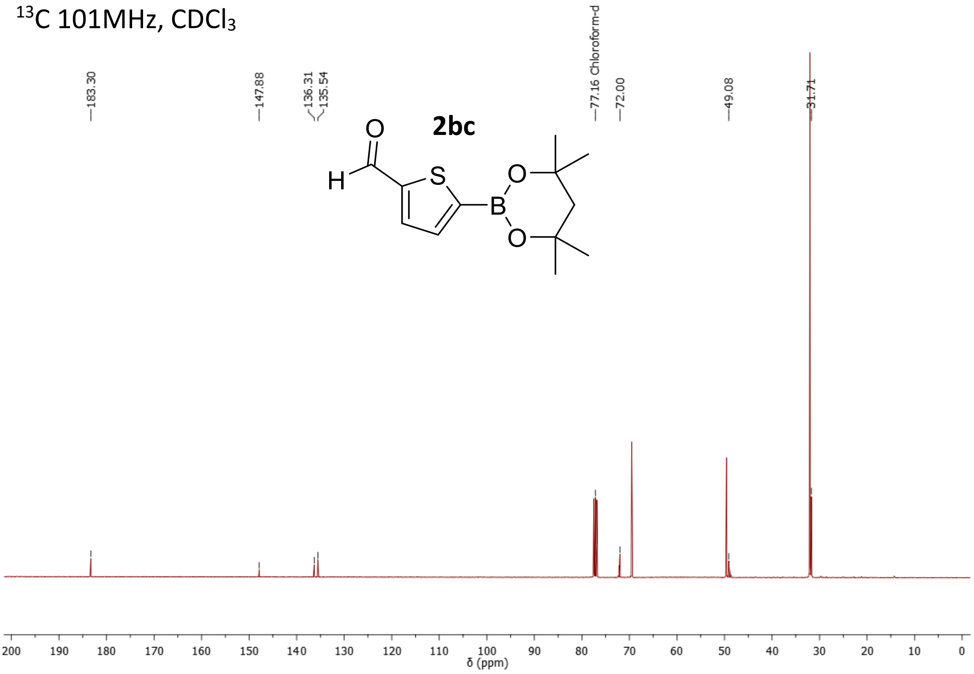
^1H 400MHz, $CDCl_3$

2bc



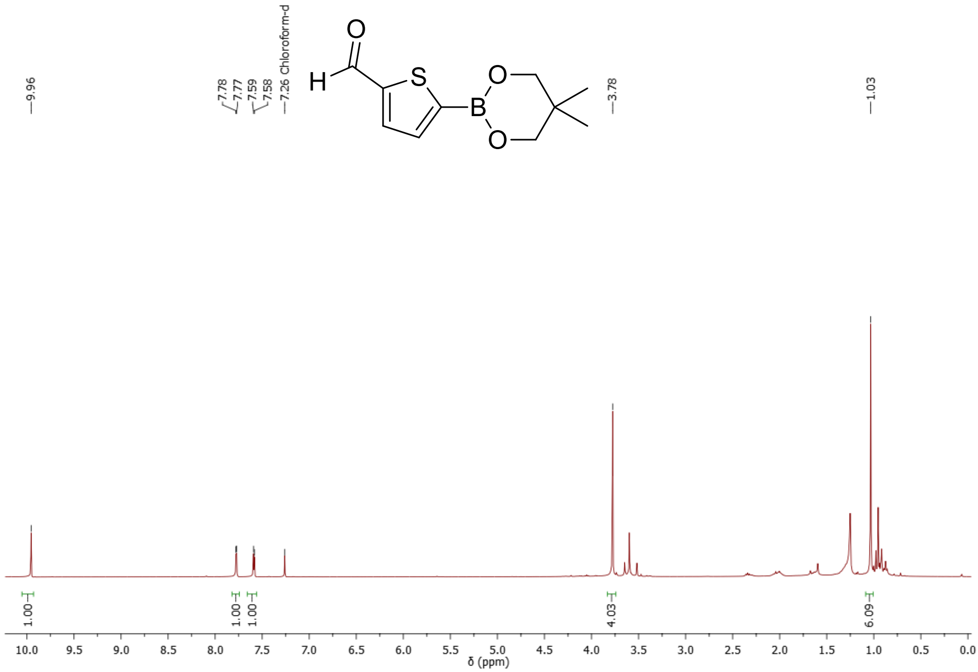
^{13}C 101MHz, $CDCl_3$

2bc

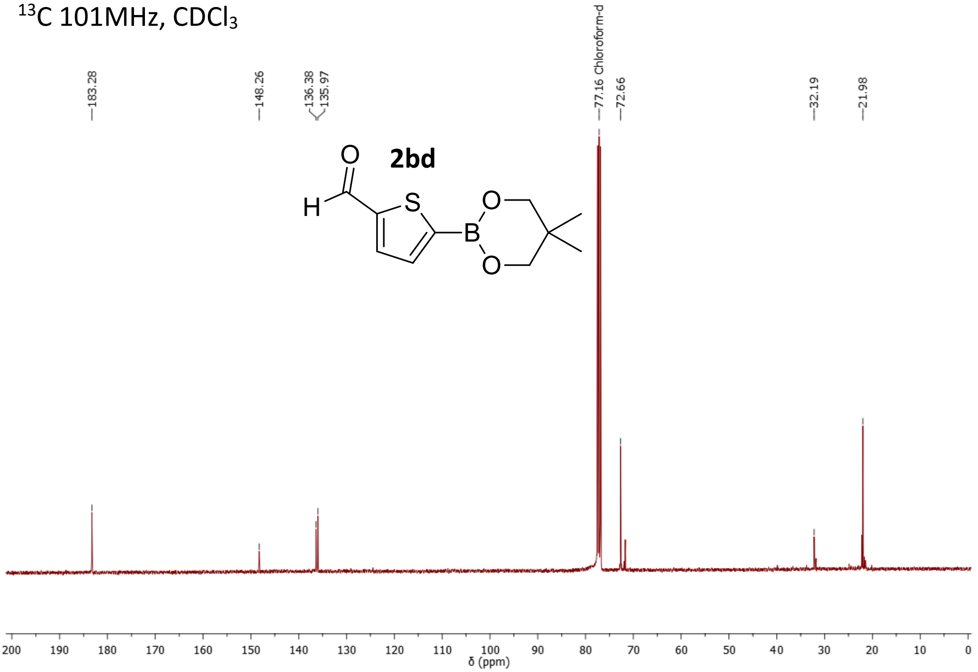


^{1}H 400MHz, $CDCl_3$

2bd

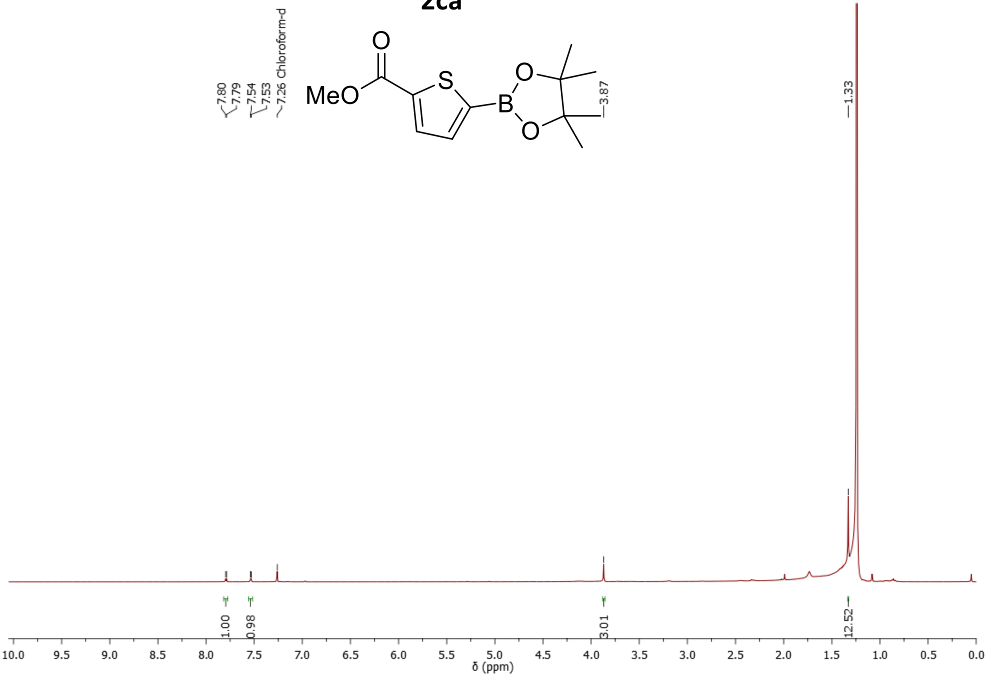


^{13}C 101MHz, $CDCl_3$



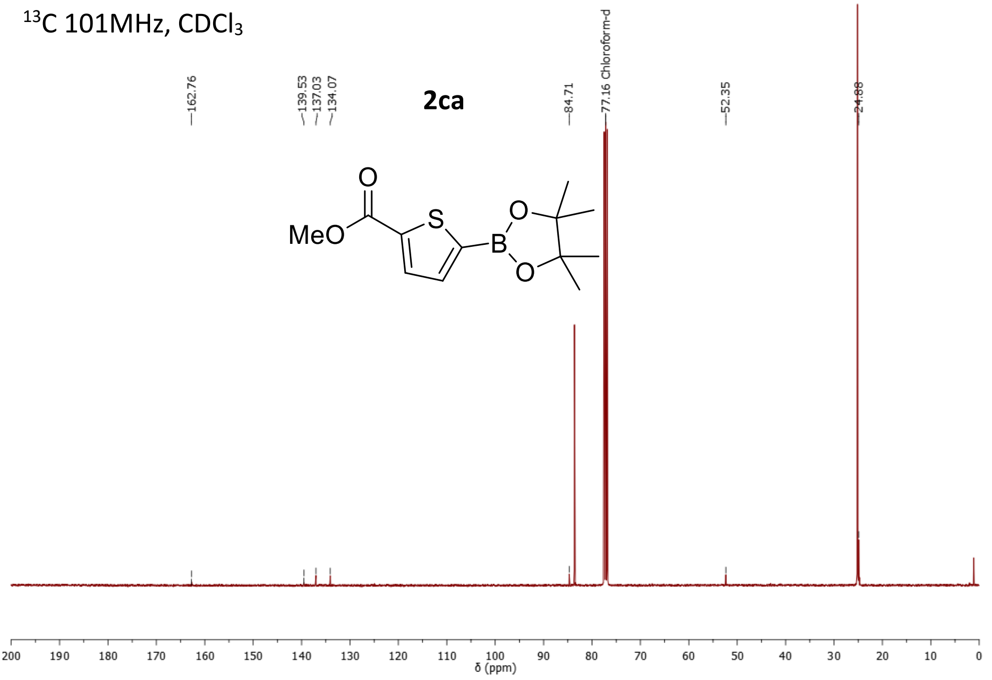
^1H 400MHz, $CDCl_3$

2ca



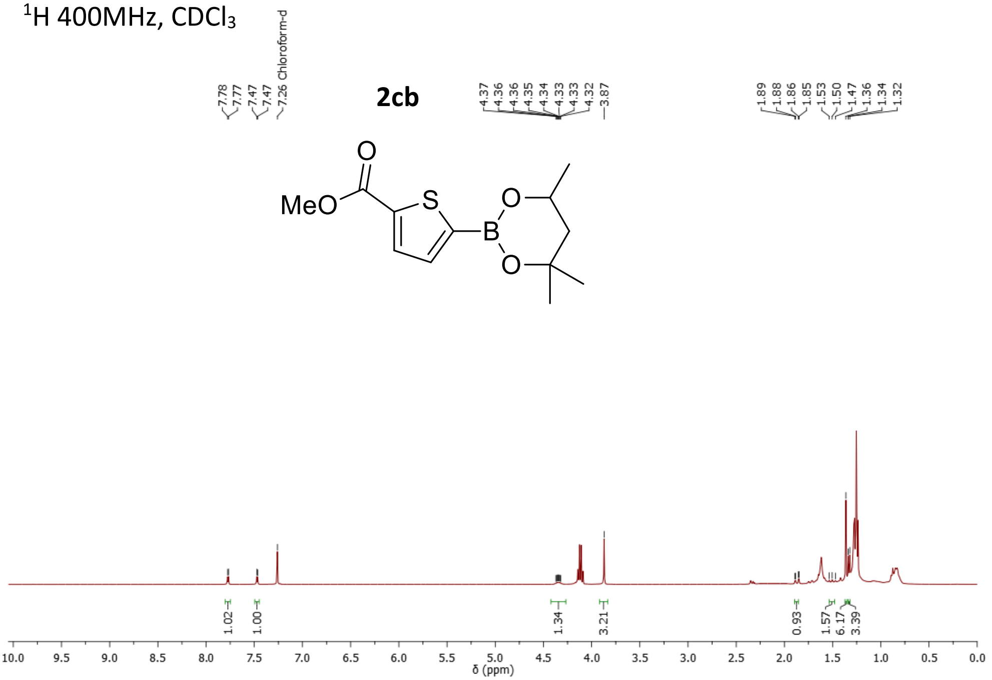
^{13}C 101MHz, $CDCl_3$

2ca



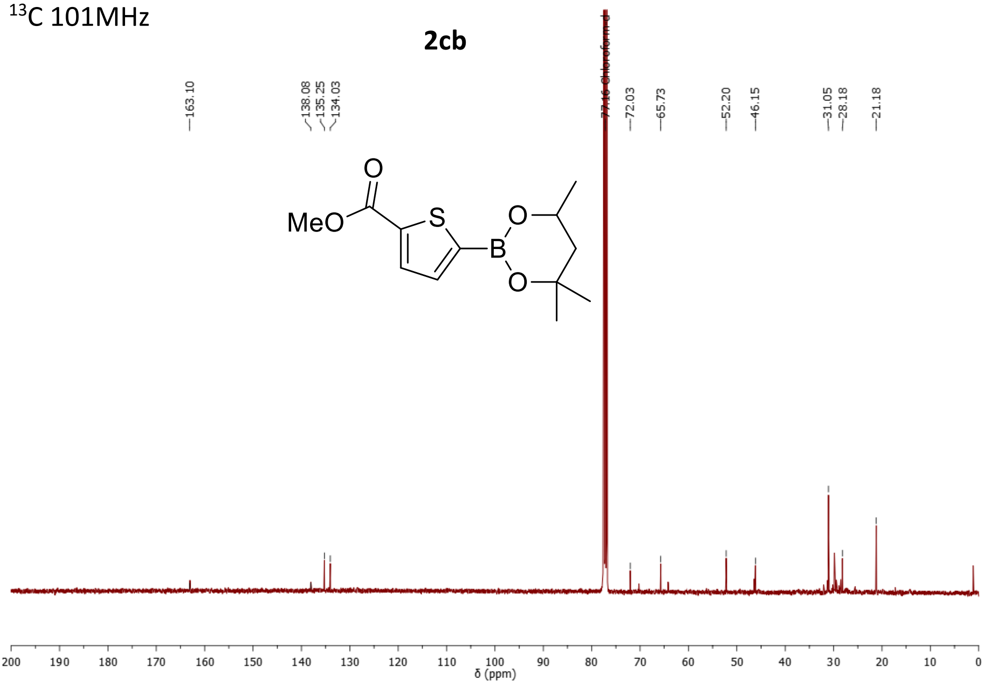
^{1}H 400MHz, $CDCl_3$

2cb



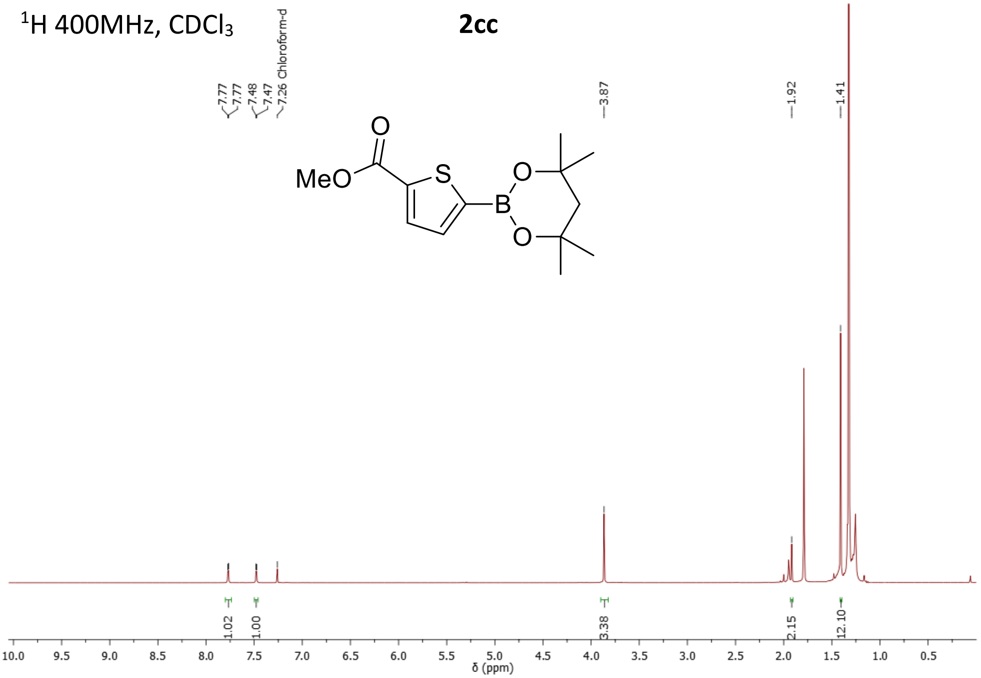
^{13}C 101MHz

2cb



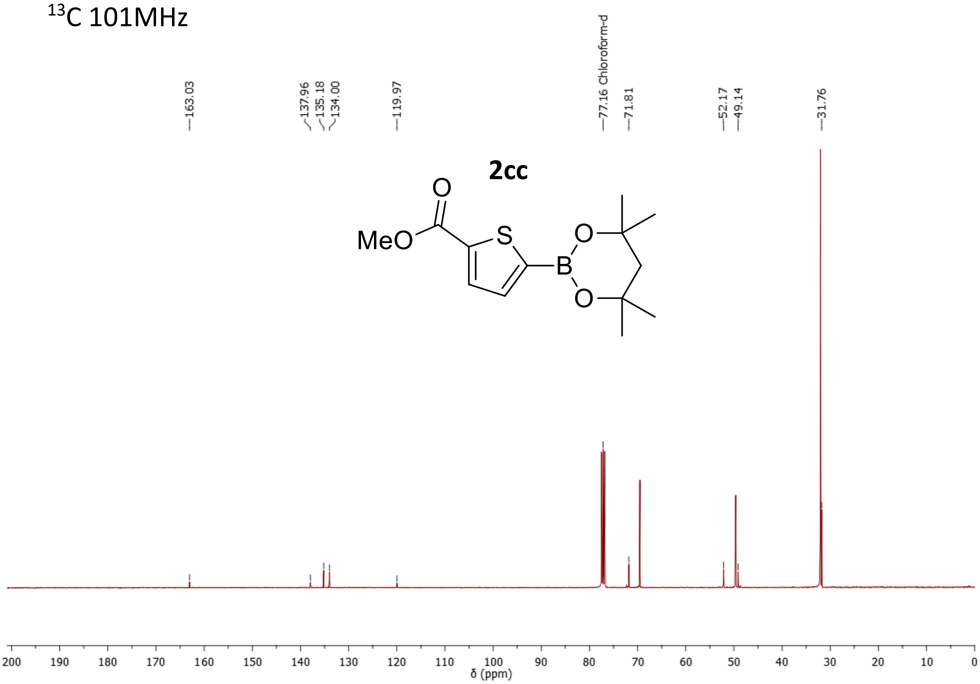
^{1}H 400MHz, $CDCl_3$

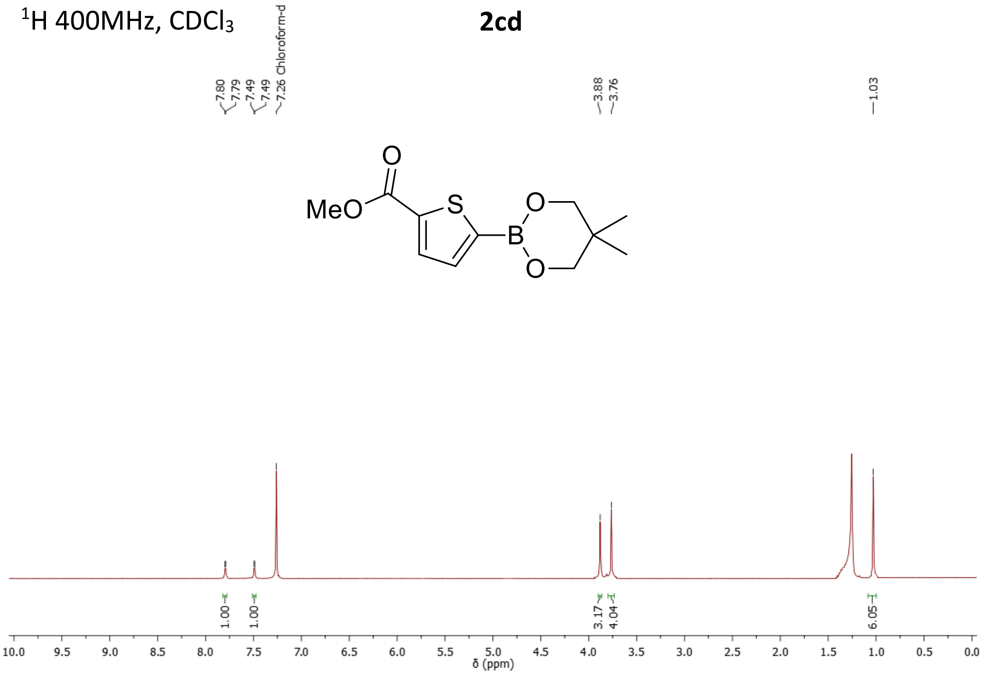
2cc

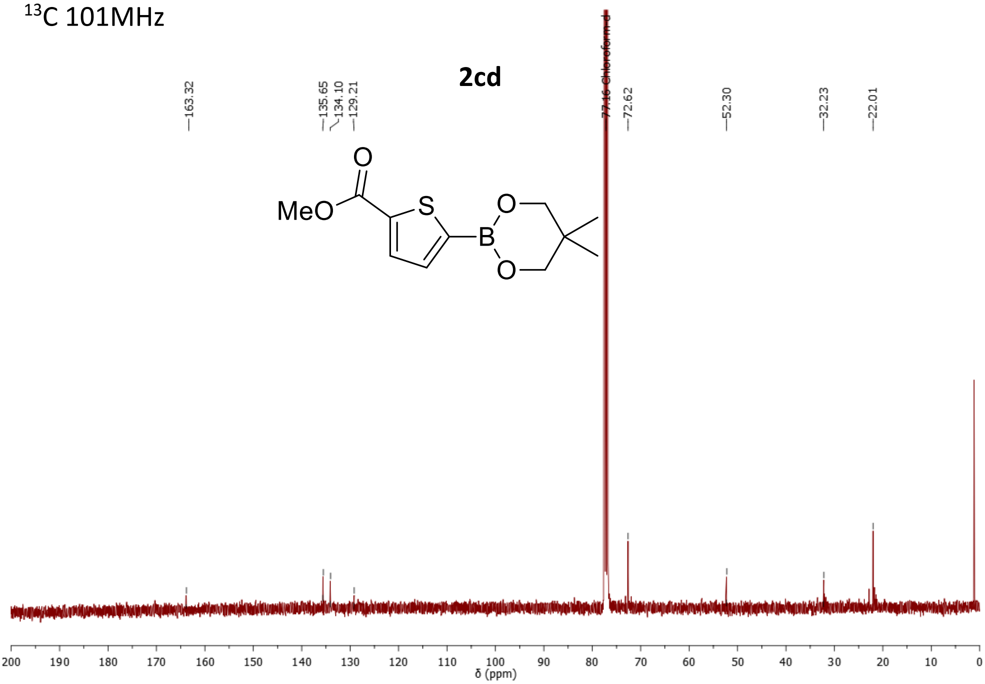


^{13}C 101MHz

2cc

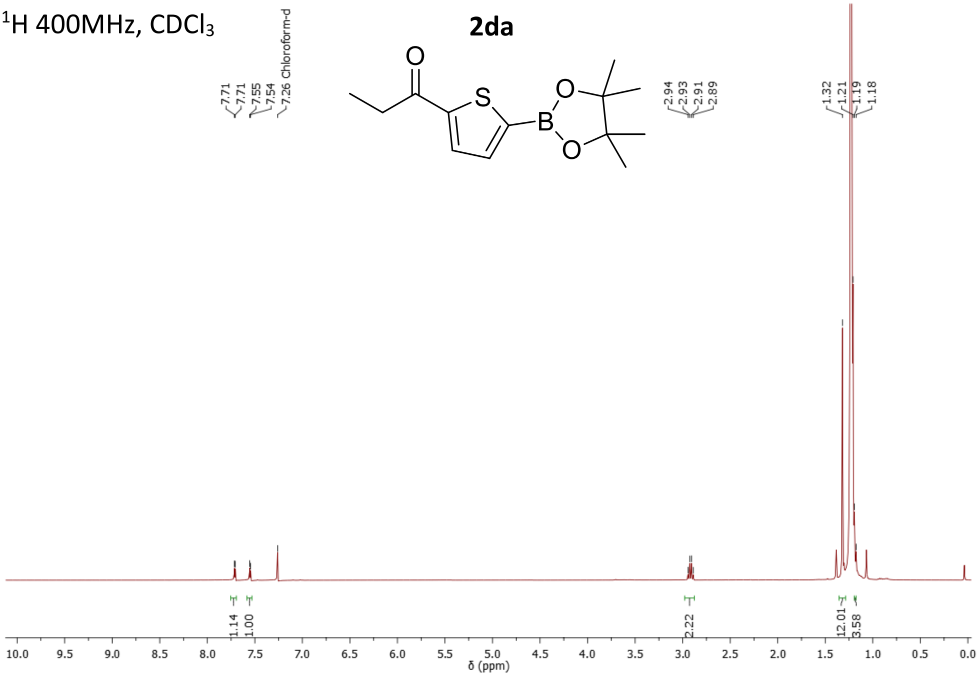



^{1}H 400MHz, CDCl$_3$
2cd
7.80
7.79
7.49
7.49
7.26 Chloroform-d
3.88
3.76
1.03
MeO
O
S
B
O
O
1.00
1.00
3.17
4.04
6.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)


^{13}C 101MHz
2cd
163.32
135.65
134.10
129.21
77.16 Chloroform-d
72.62
52.30
32.23
22.01
MeO
O
S
B
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

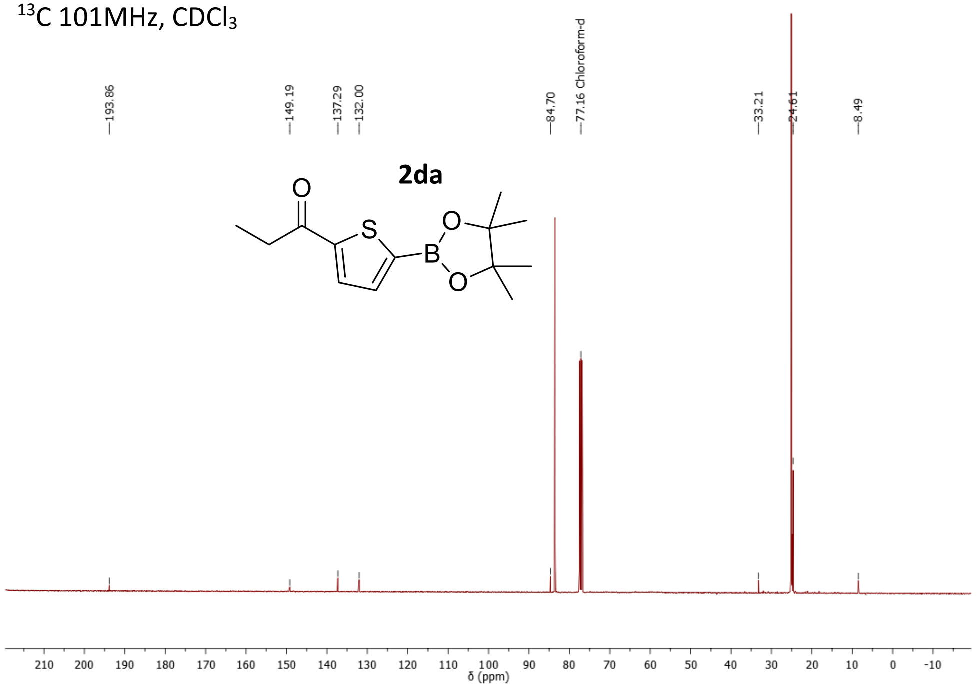
^{1}H 400MHz, $CDCl_3$

2da

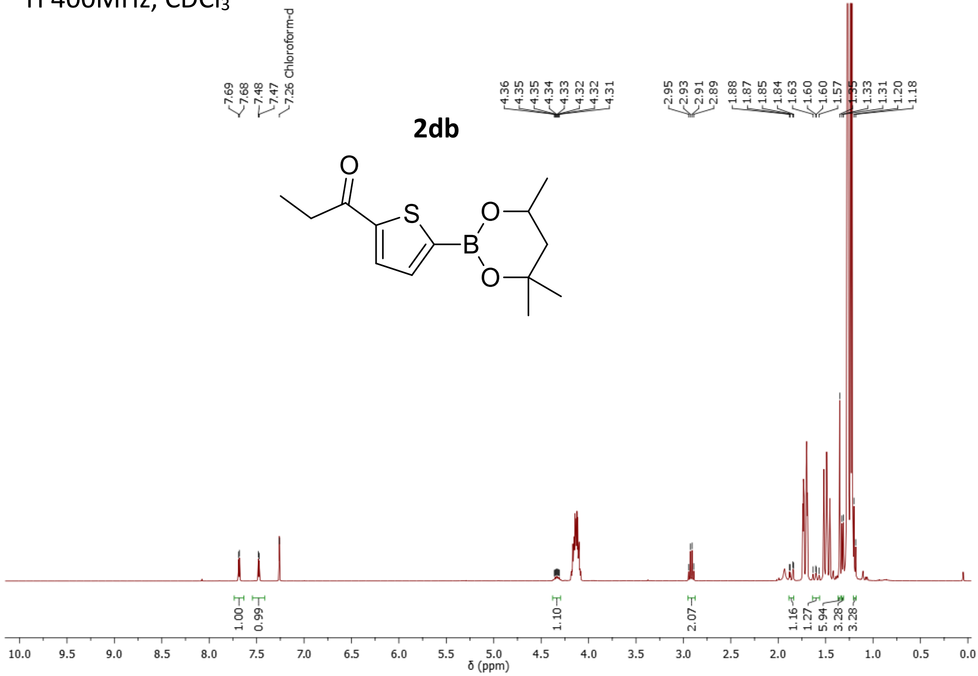


^{13}C 101MHz, $CDCl_3$

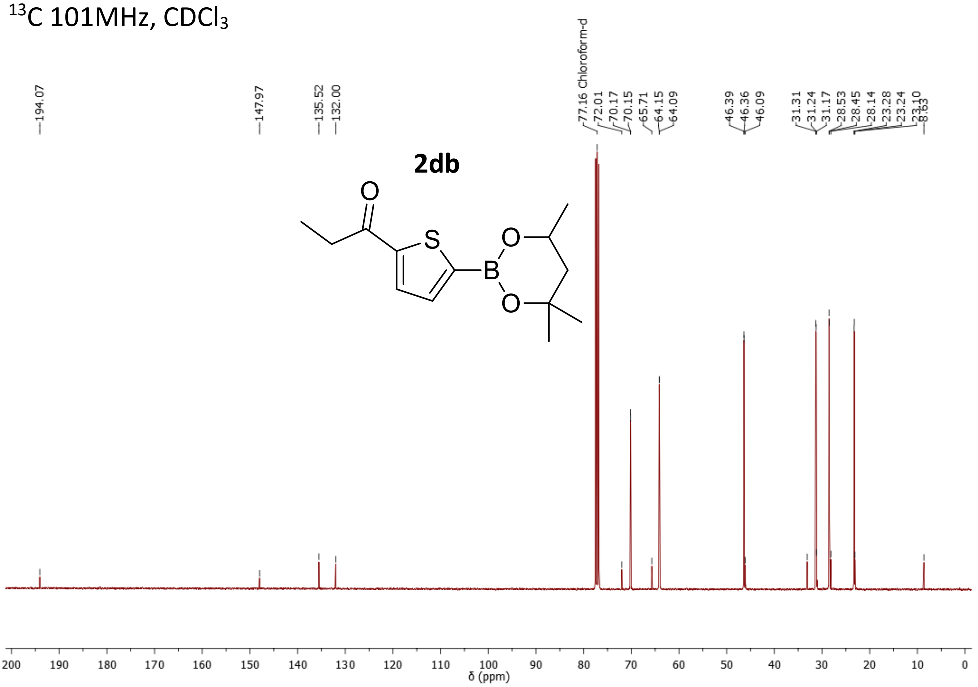
2da

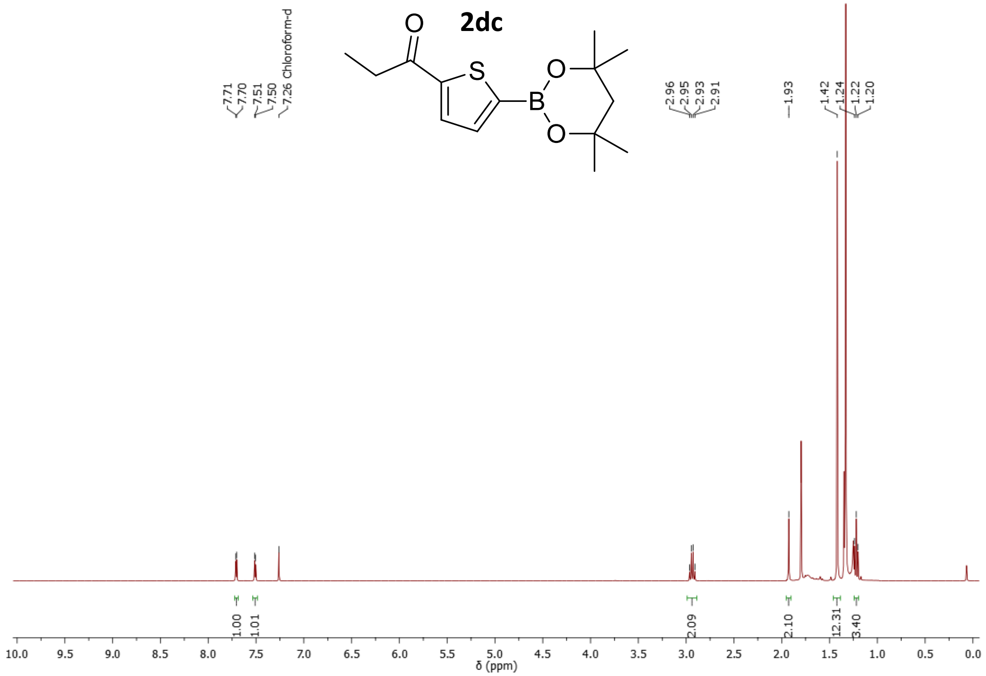


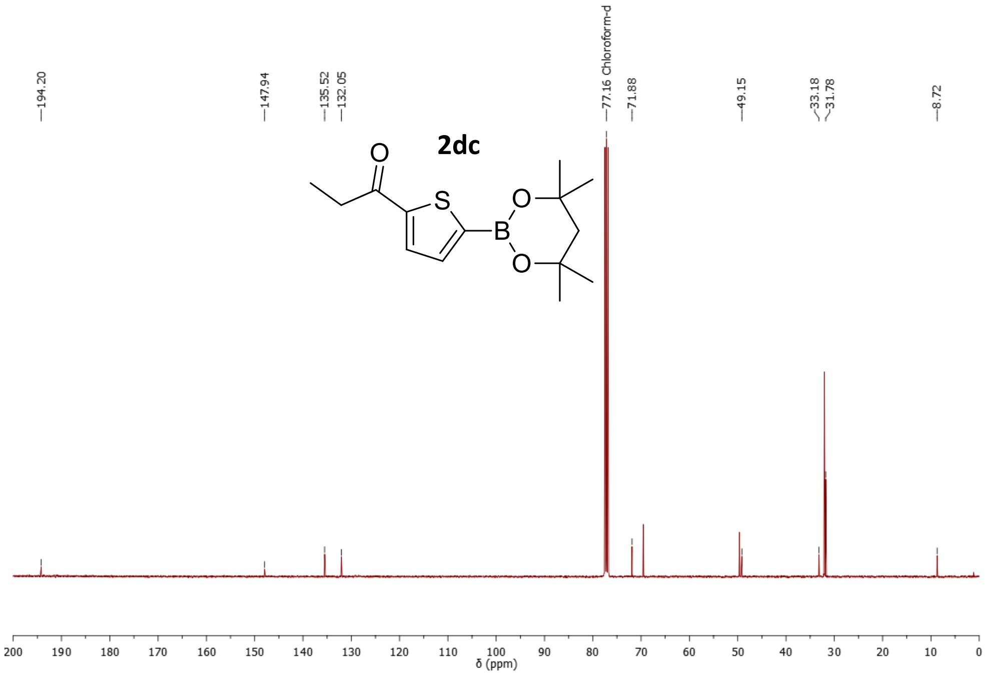
^{1}H 400MHz, $CDCl_3$



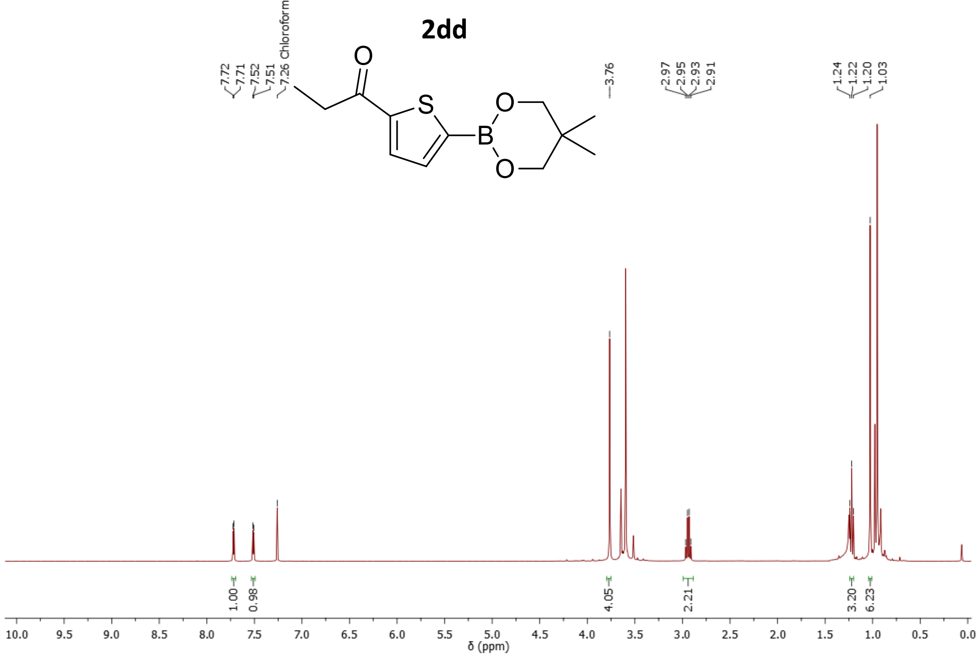
^{13}C 101MHz, $CDCl_3$



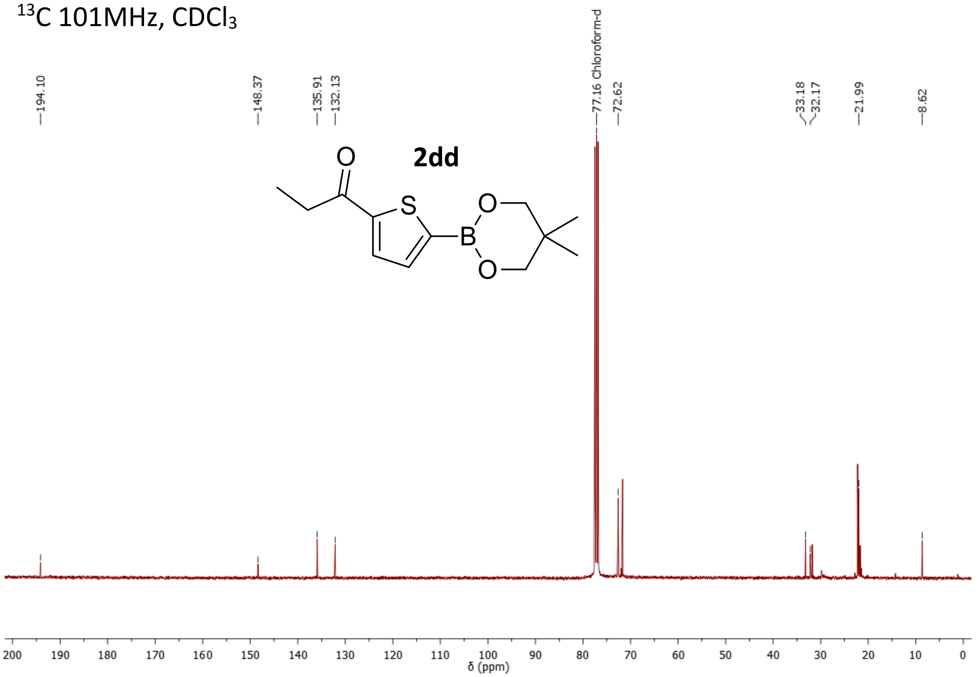

2dc
O
S
B
O
O
7.71
7.70
7.51
7.50
7.26 Chloroform-d
2.96
2.95
2.93
2.91
1.93
1.42
1.24
1.22
1.20
1.00
1.01
2.09
2.10
12.31
3.40
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)


2dc
O
S
B
O
O
194.20
147.94
135.52
132.05
77.16 Chloroform-d
71.88
49.15
33.18
31.78
8.72
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)

^{1}H 400MHz, $CDCl_3$

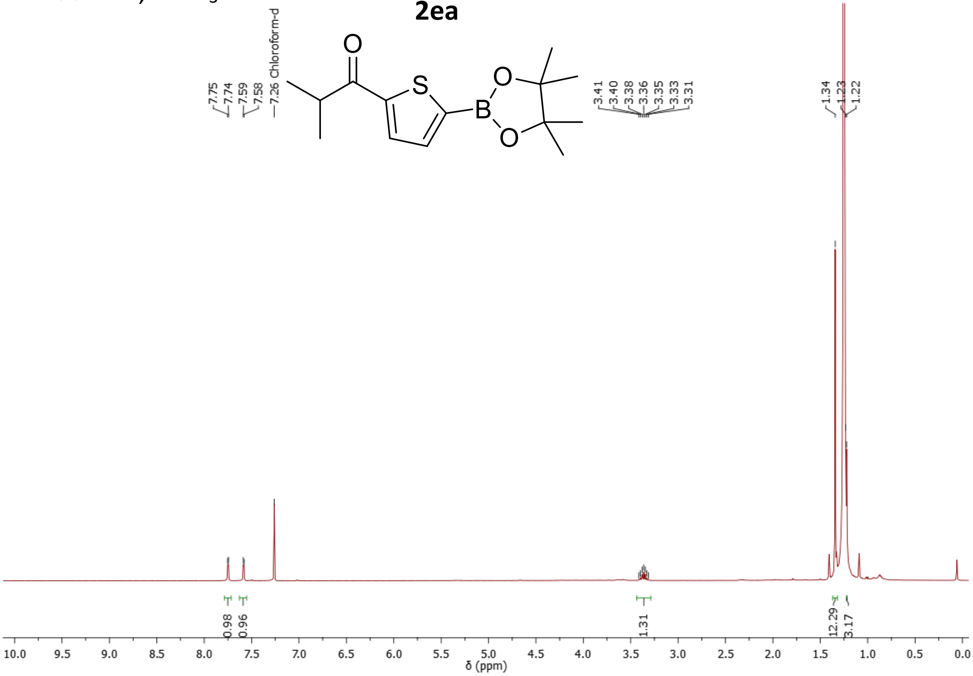


^{13}C 101MHz, $CDCl_3$



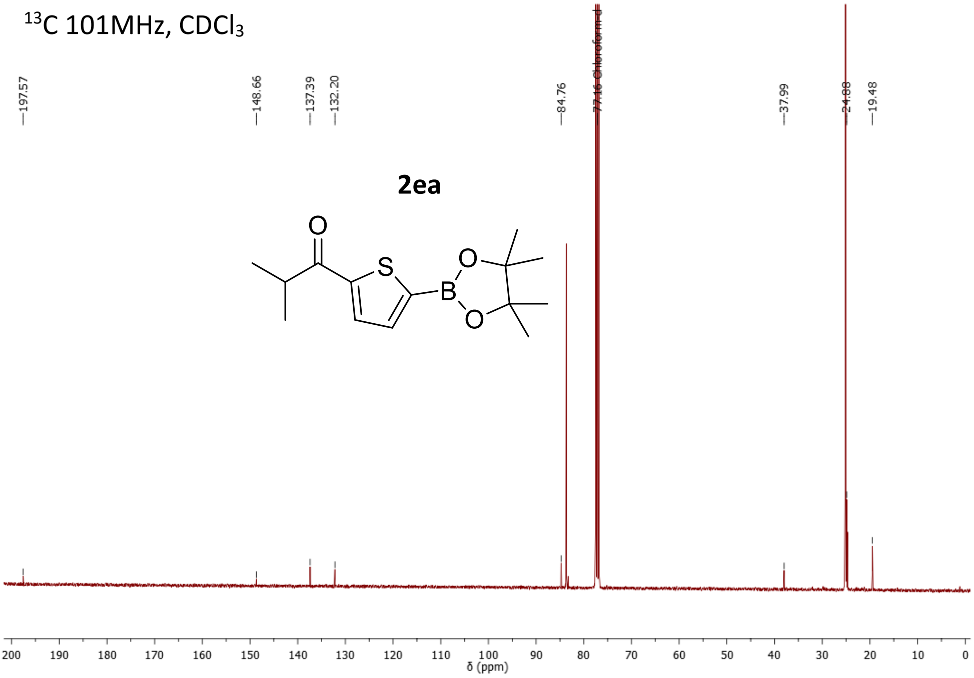
^{1}H 400MHz, $CDCl_3$

2ea

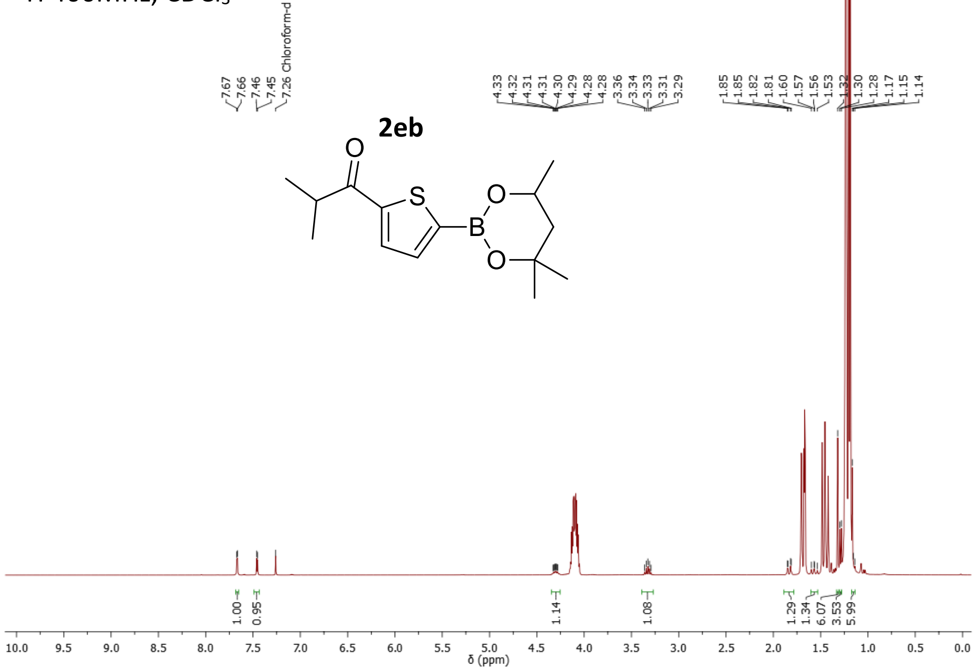


^{13}C 101MHz, $CDCl_3$

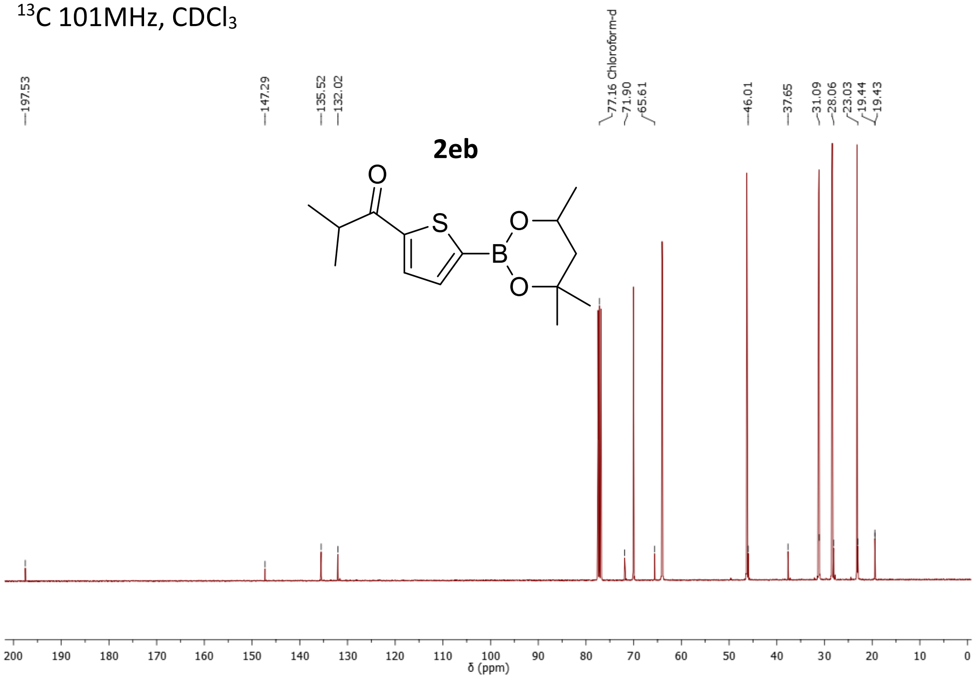
2ea



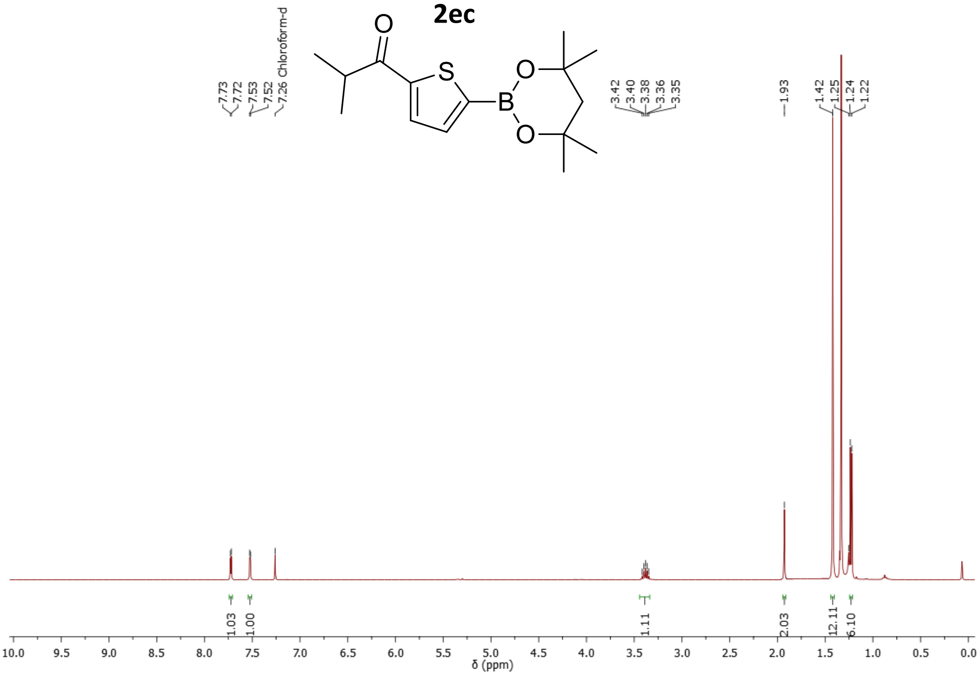
^{1}H 400MHz, CDCl$_3$


2eb

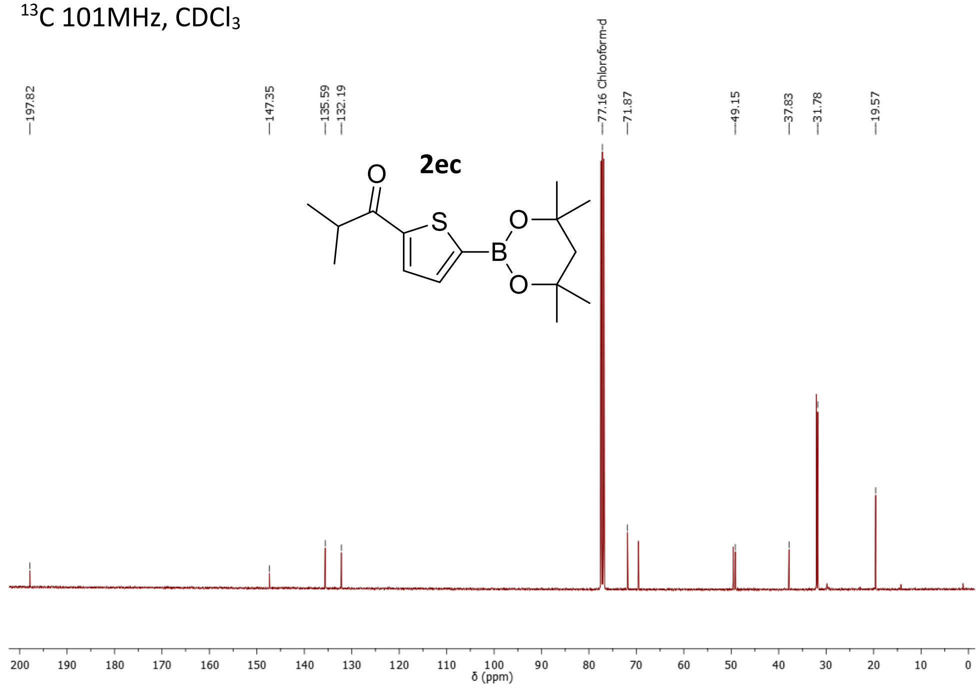
^{13}C 101MHz, CDCl$_3$


2eb

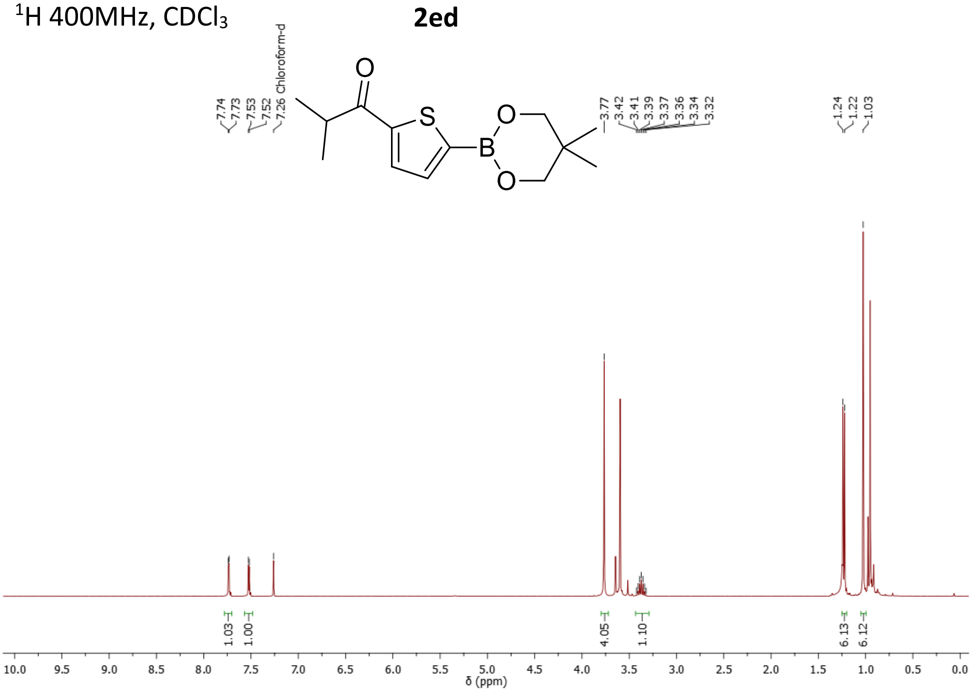
^{1}H 400MHz, CDCl$_3$



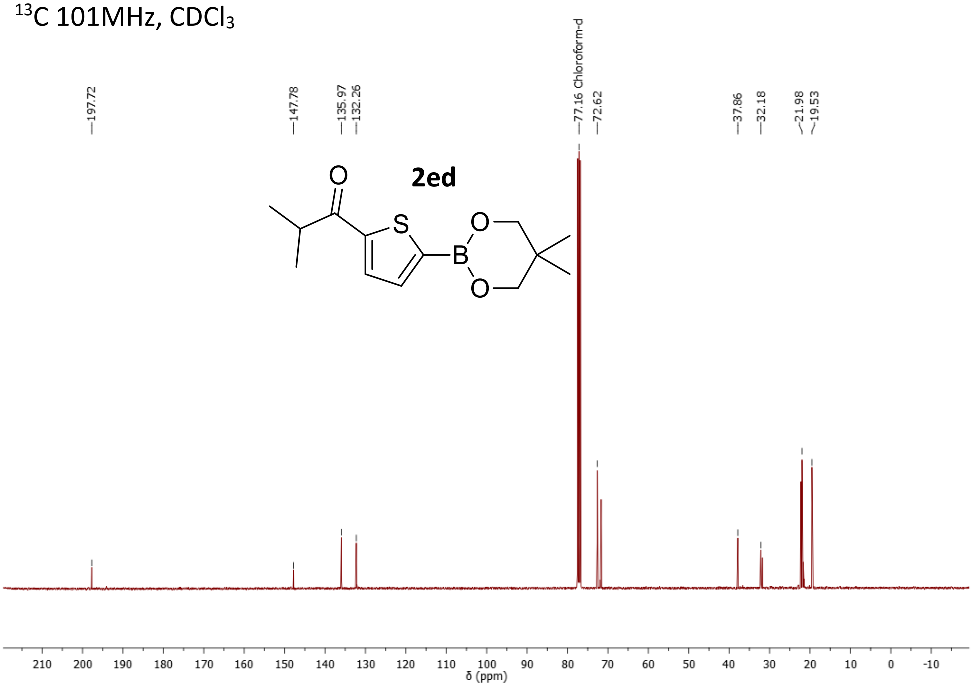
^{13}C 101MHz, CDCl$_3$



^{1}H 400MHz, $CDCl_3$

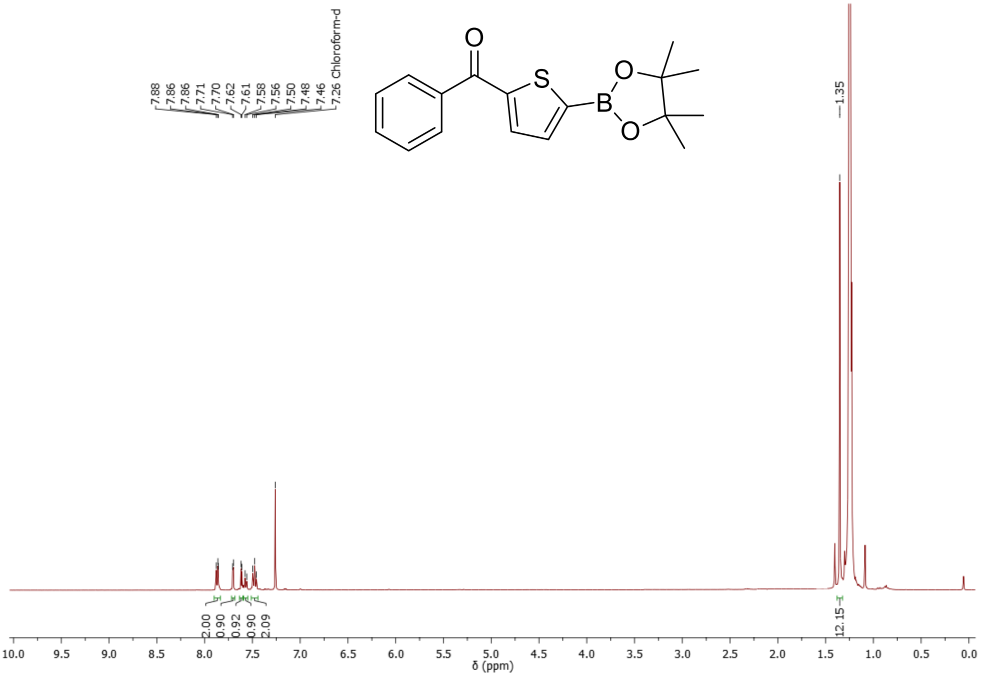


^{13}C 101MHz, $CDCl_3$

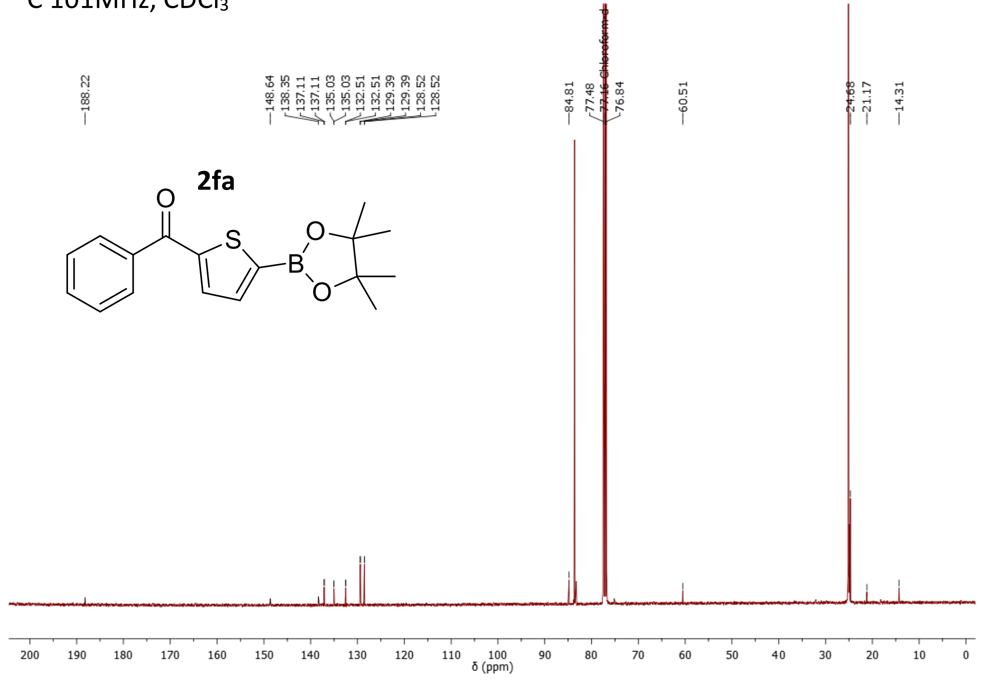


^{1}H 400MHz, $CDCl_3$

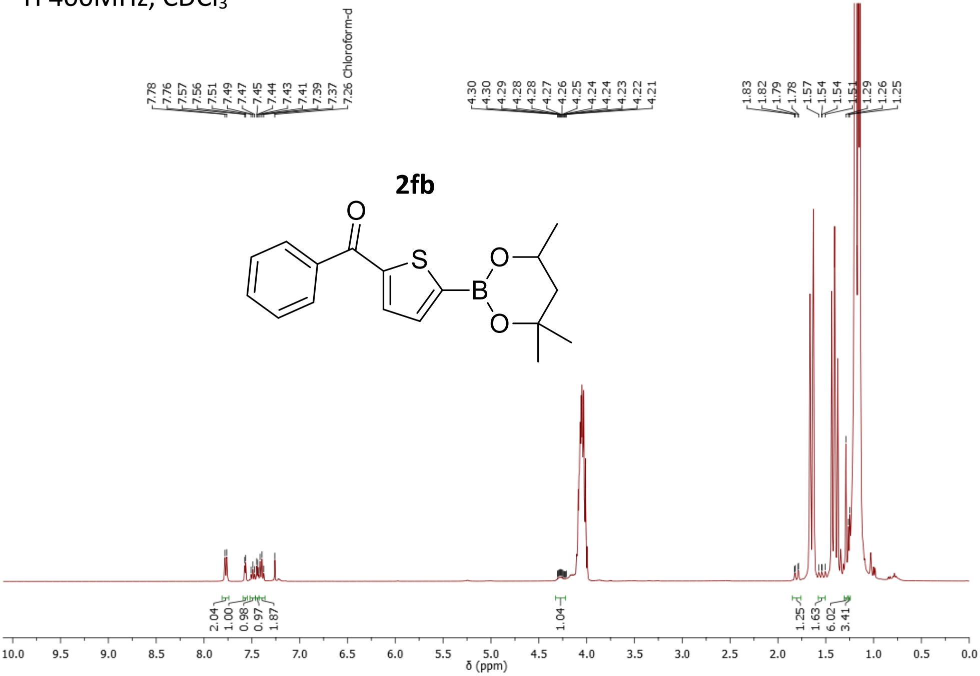
2fa



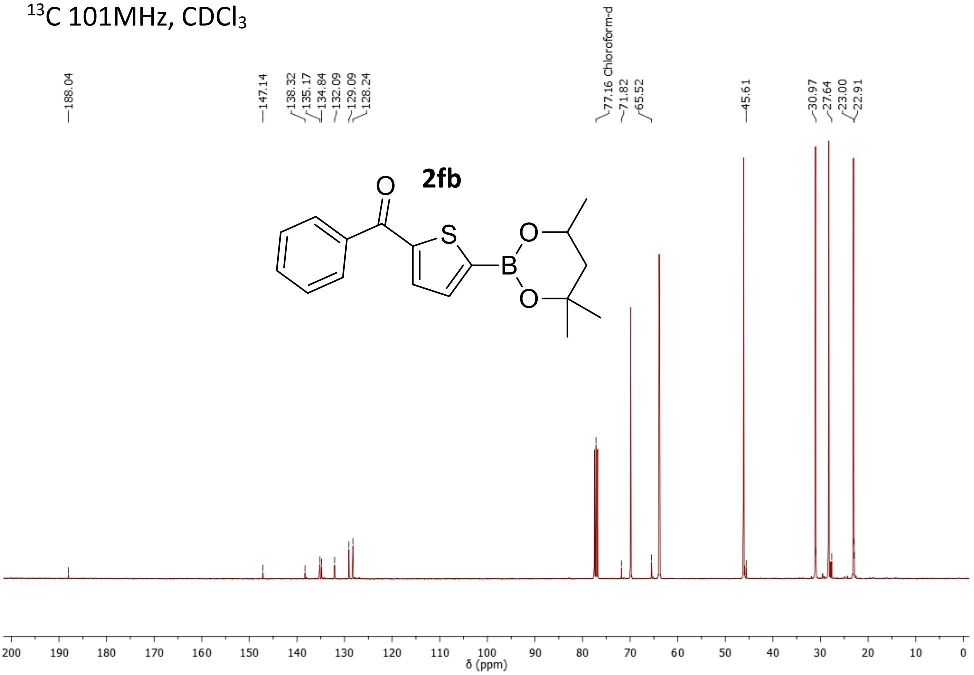
^{13}C 101MHz, $CDCl_3$



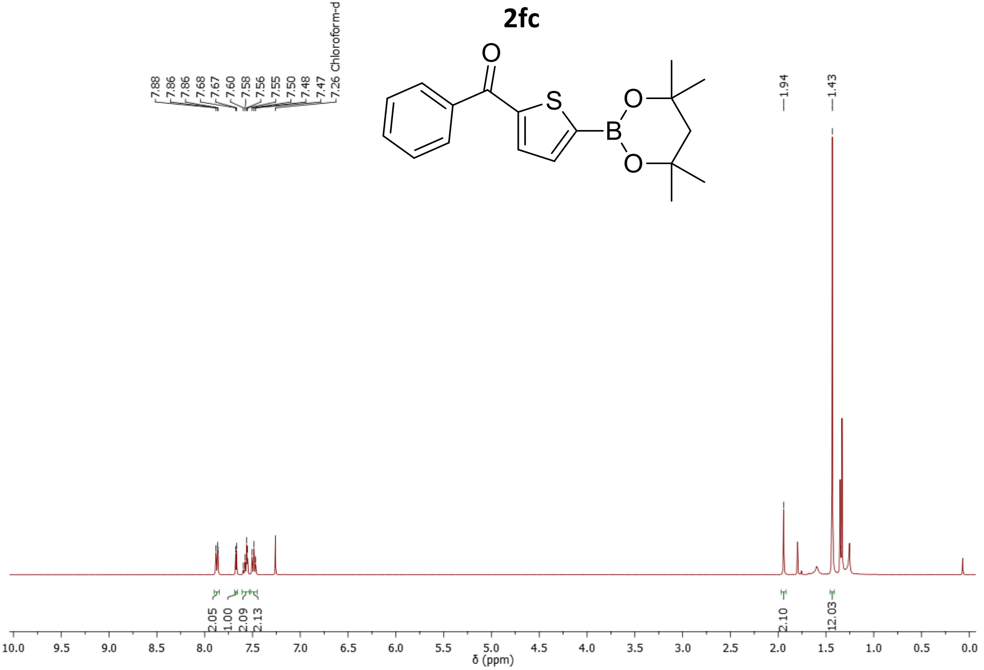
^{1}H 400MHz, $CDCl_3$



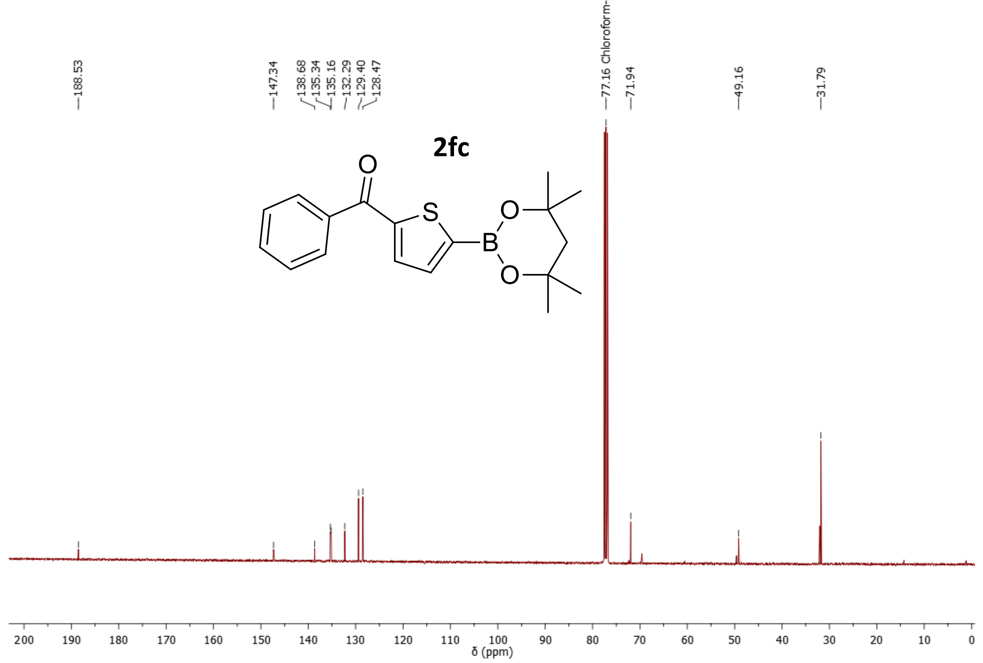
^{13}C 101MHz, $CDCl_3$



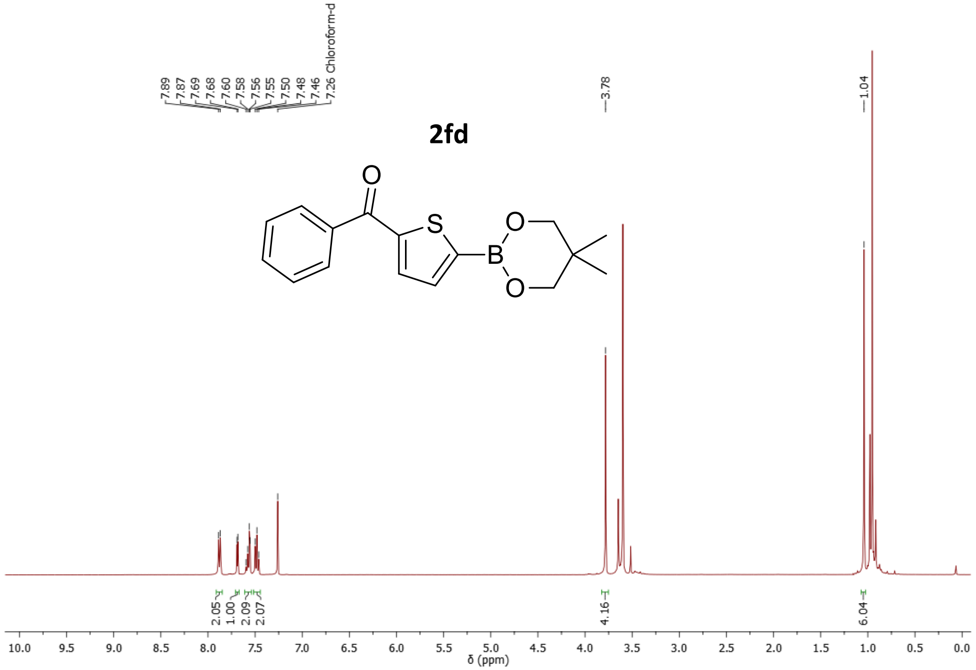
^{1}H 400MHz, $CDCl_3$



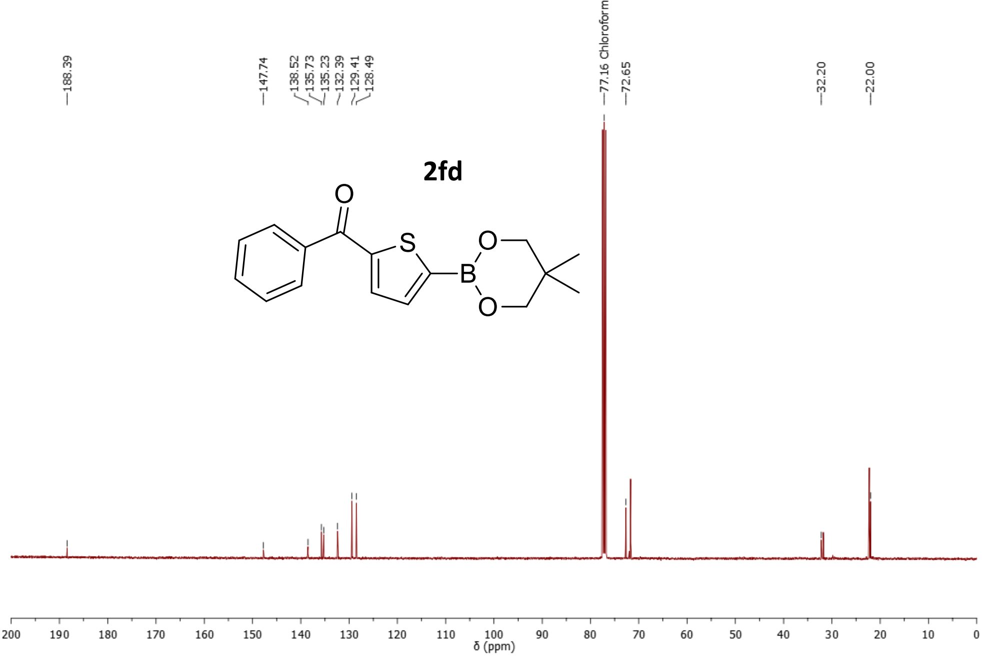
^{13}C 101MHz, $CDCl_3$



^{1}H 400MHz, $CDCl_3$

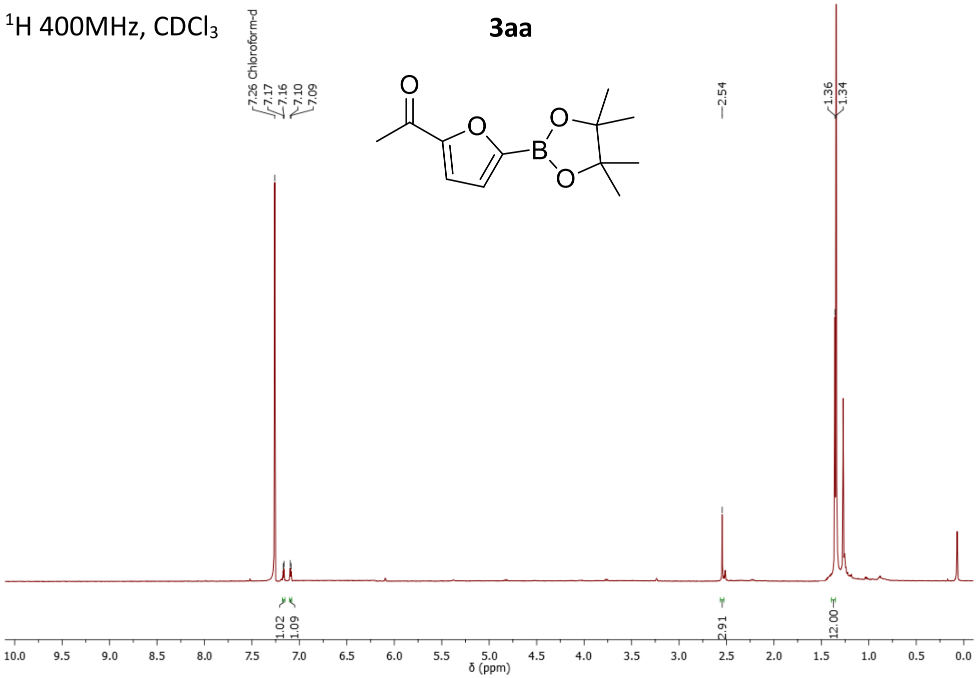


^{13}C 101MHz, $CDCl_3$



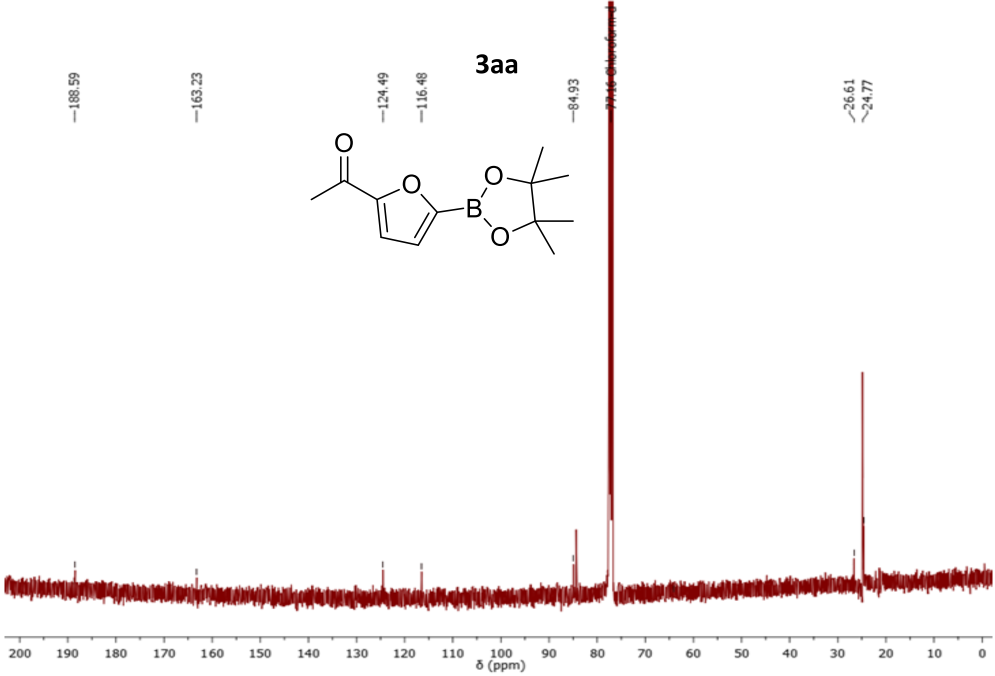
^1H 400MHz, $CDCl_3$

3aa



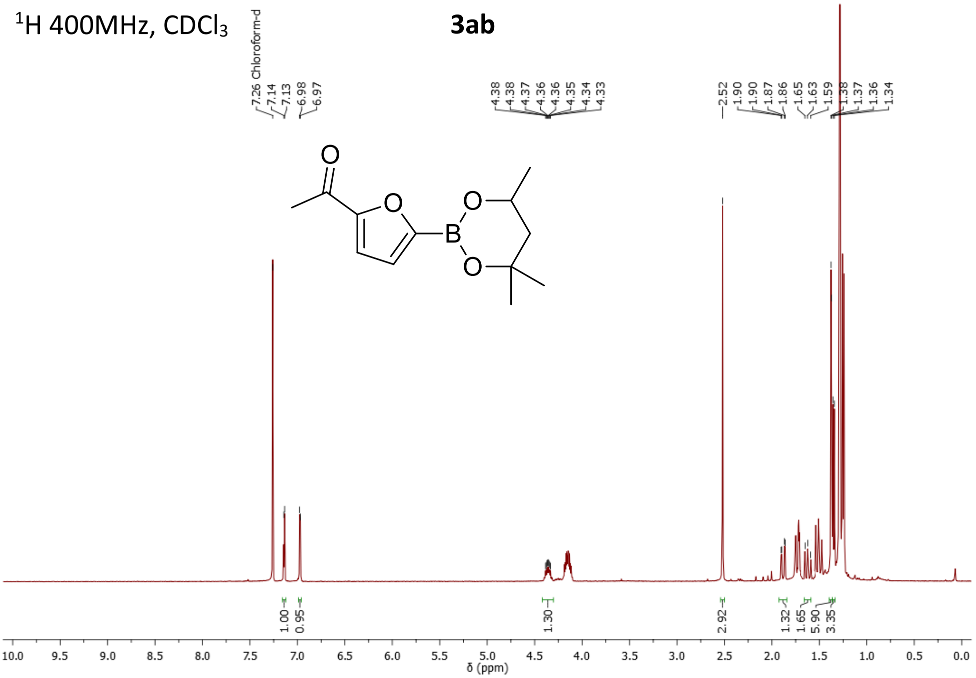
^{13}C 101MHz, $CDCl_3$

3aa



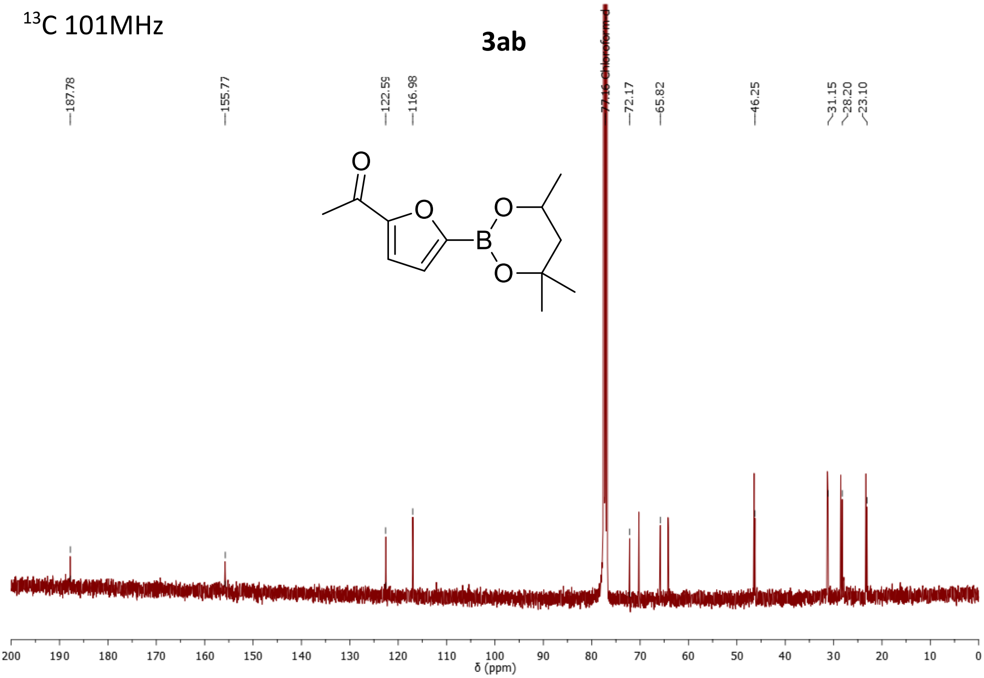
^{1}H 400MHz, CDCl$_3$

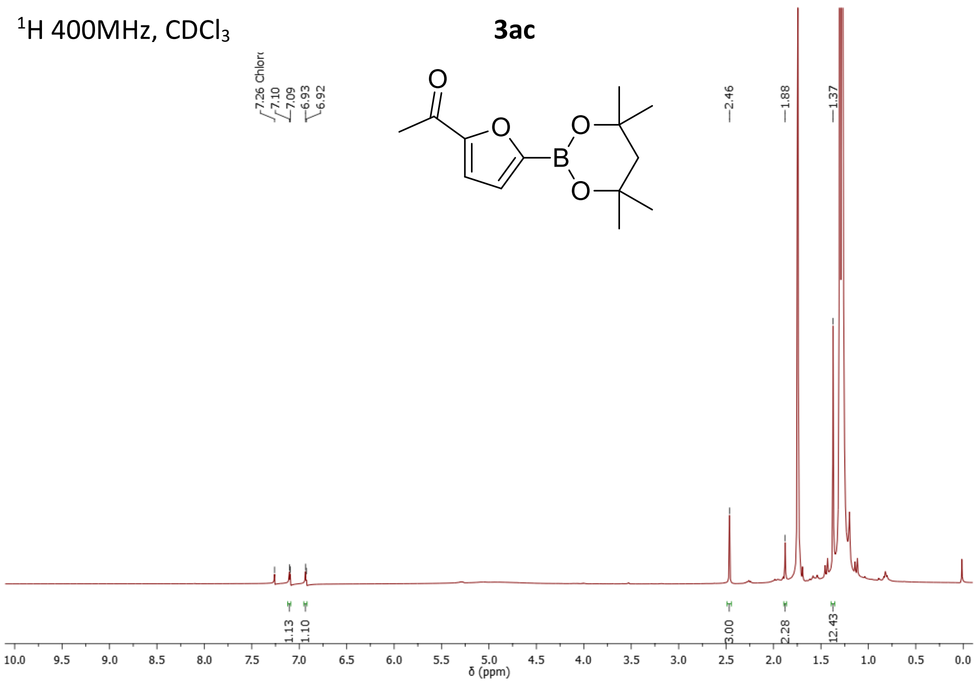
3ab

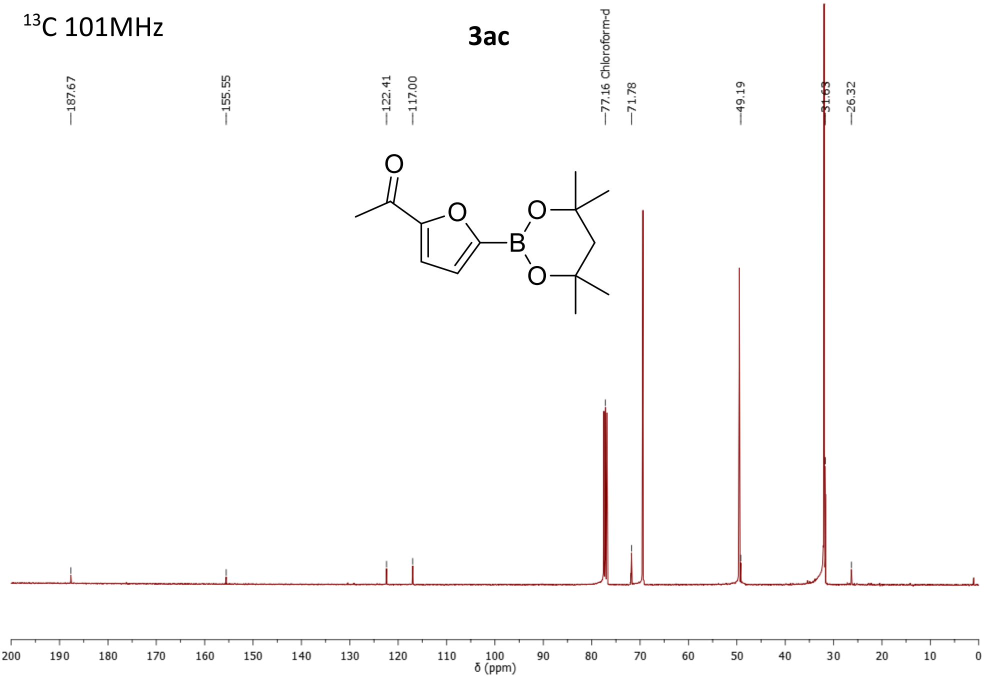


^{13}C 101MHz

3ab

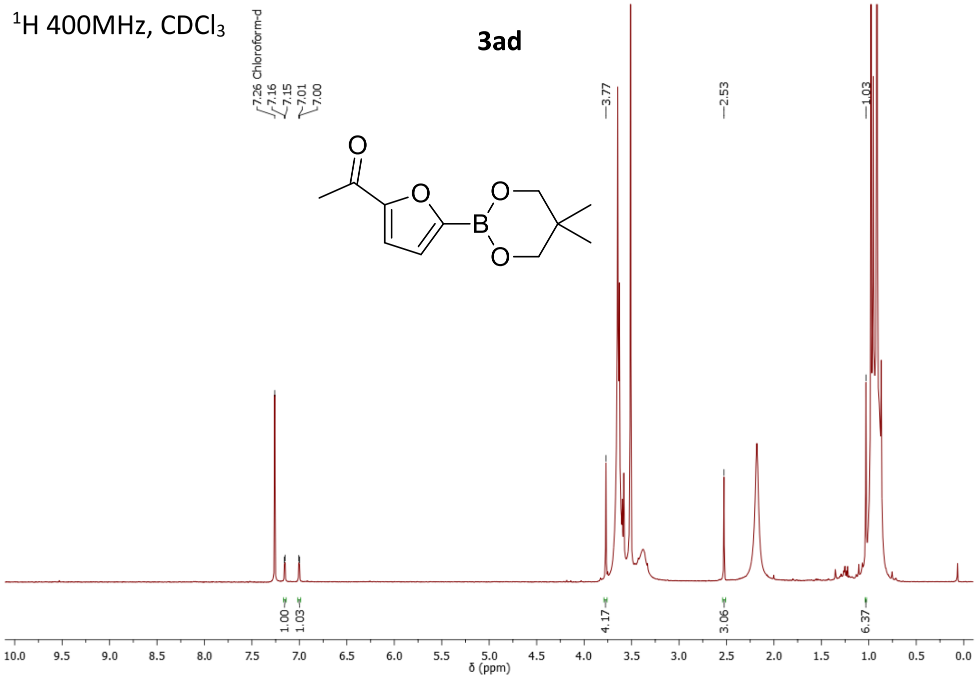



^{1}H 400MHz, CDCl$_3$
3ac
7.26 Chlorc
7.10
7.09
6.93
6.92
2.46
1.88
1.37
O
O
O
B
O
1.13
1.10
3.00
2.28
12.43
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)


^{13}C 101MHz
3ac
187.67
155.55
122.41
117.00
77.16 Chloroform-d
71.78
49.19
31.63
26.32
O
O
O
B
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

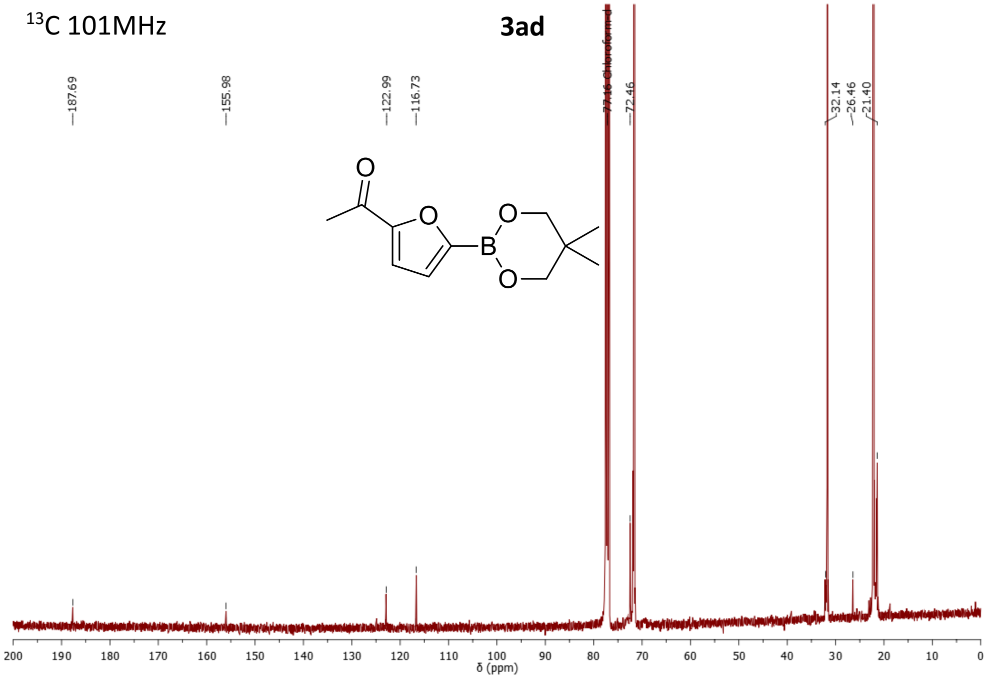
^{1}H 400MHz, CDCl$_3$

3ad



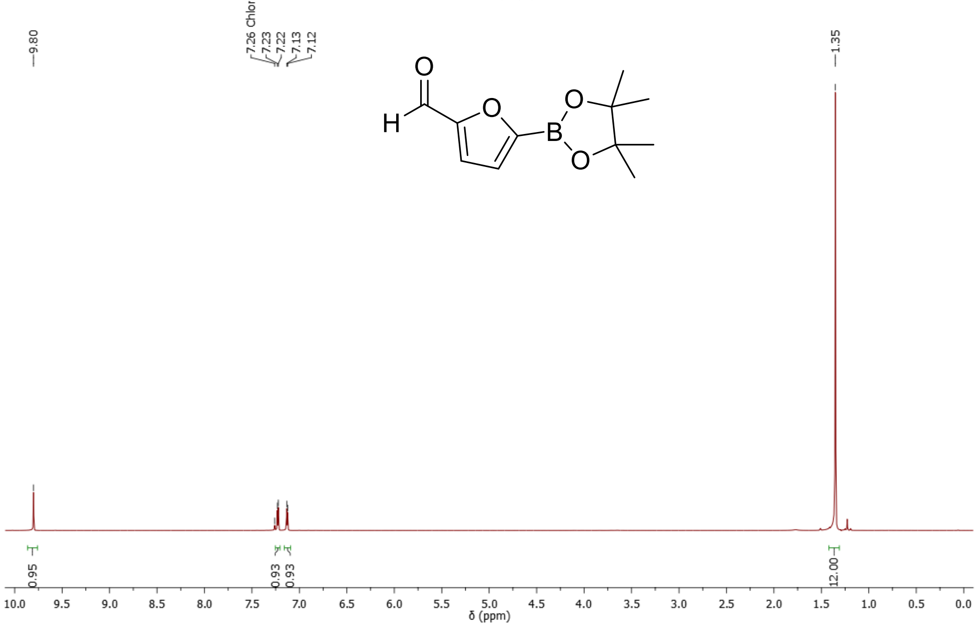
^{13}C 101MHz

3ad



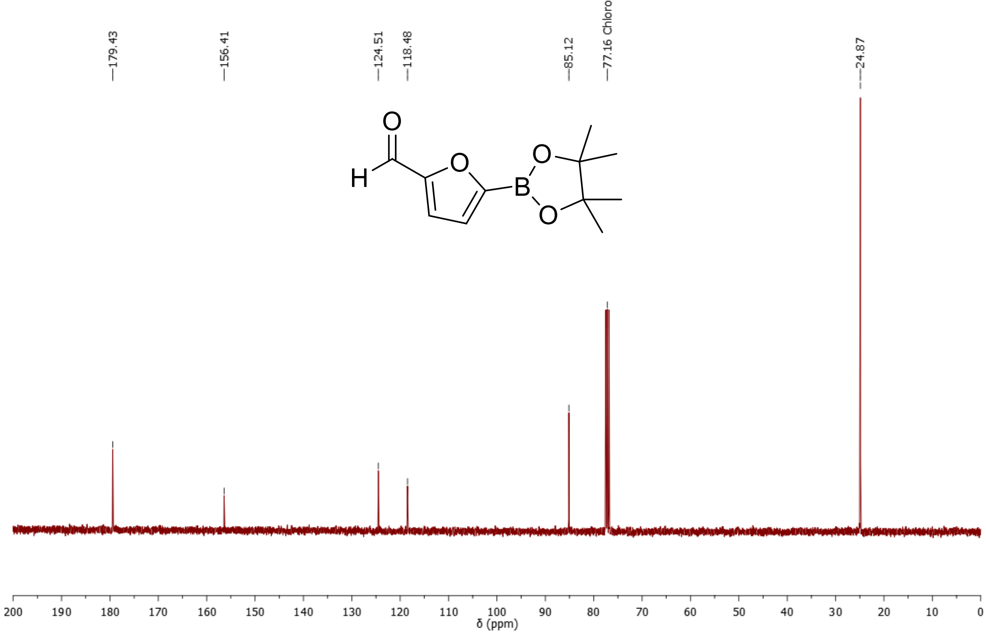
^{1}H 400MHz, CDCl$_3$

3ba



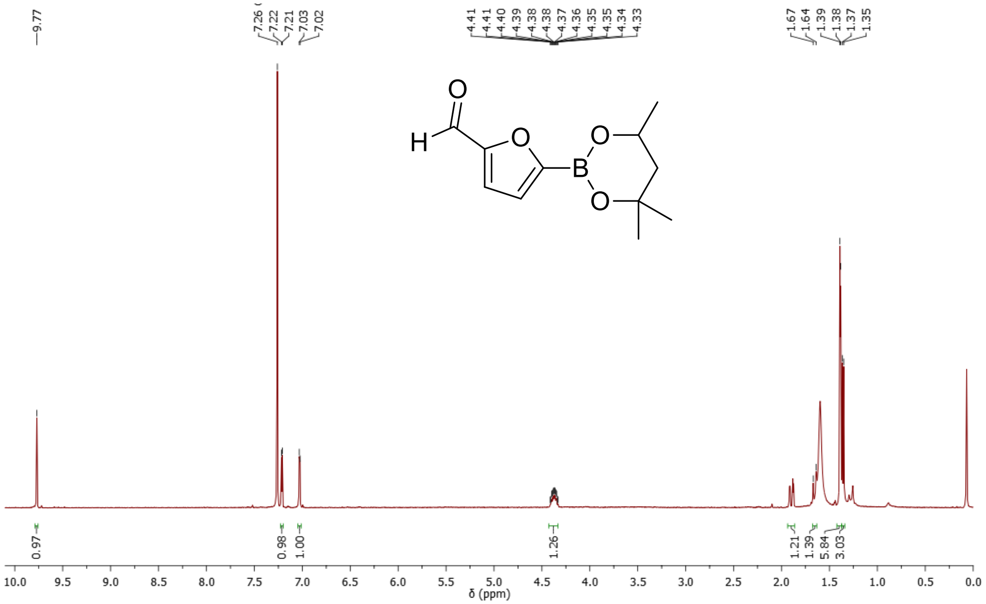
^{13}C 101MHz, CDCl$_3$

3ba



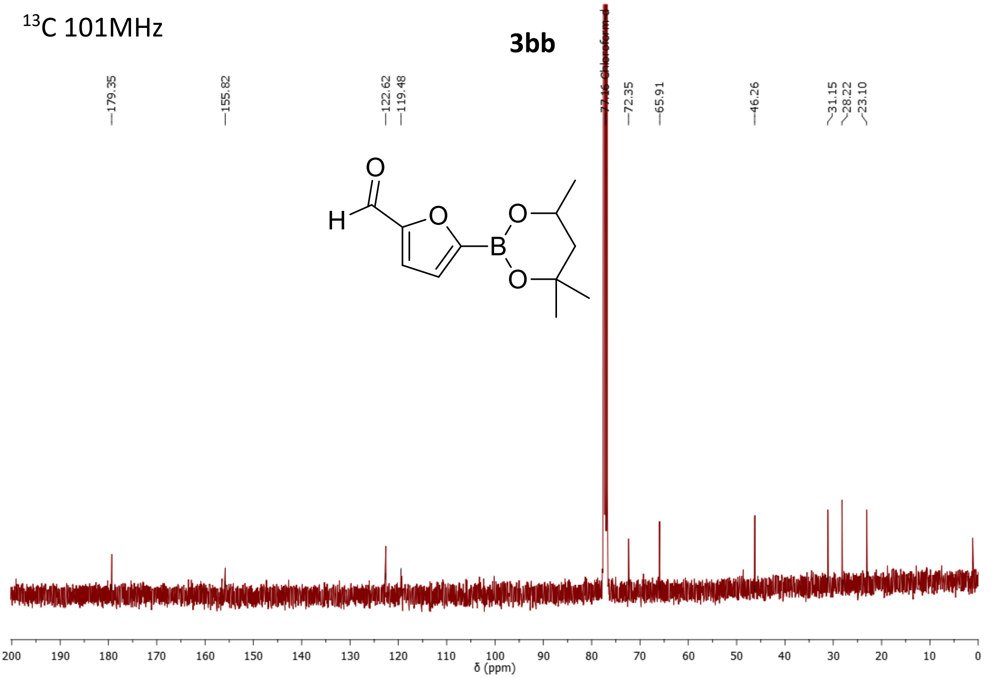
^1H 400MHz, $CDCl_3$

3bb



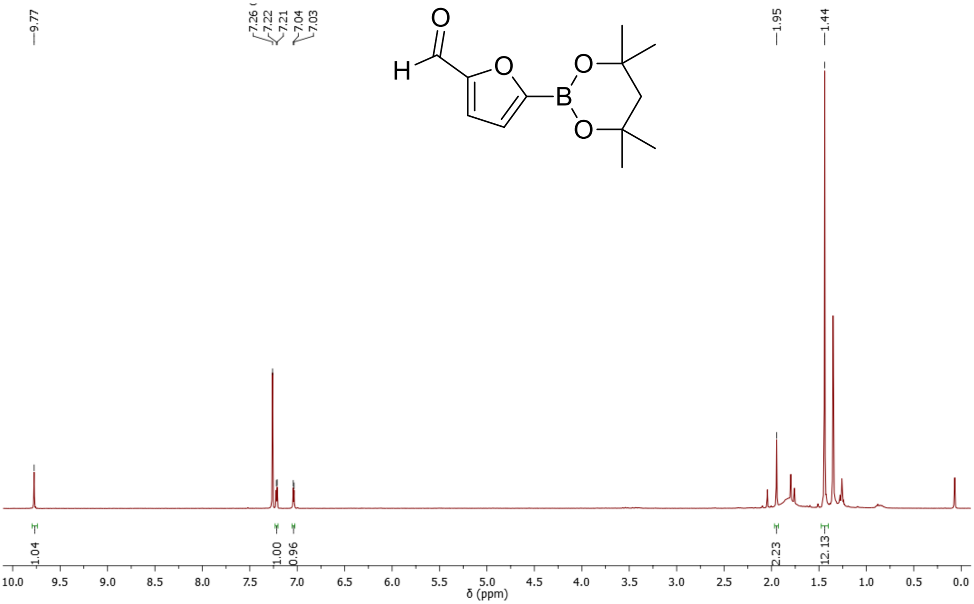
^{13}C 101MHz

3bb



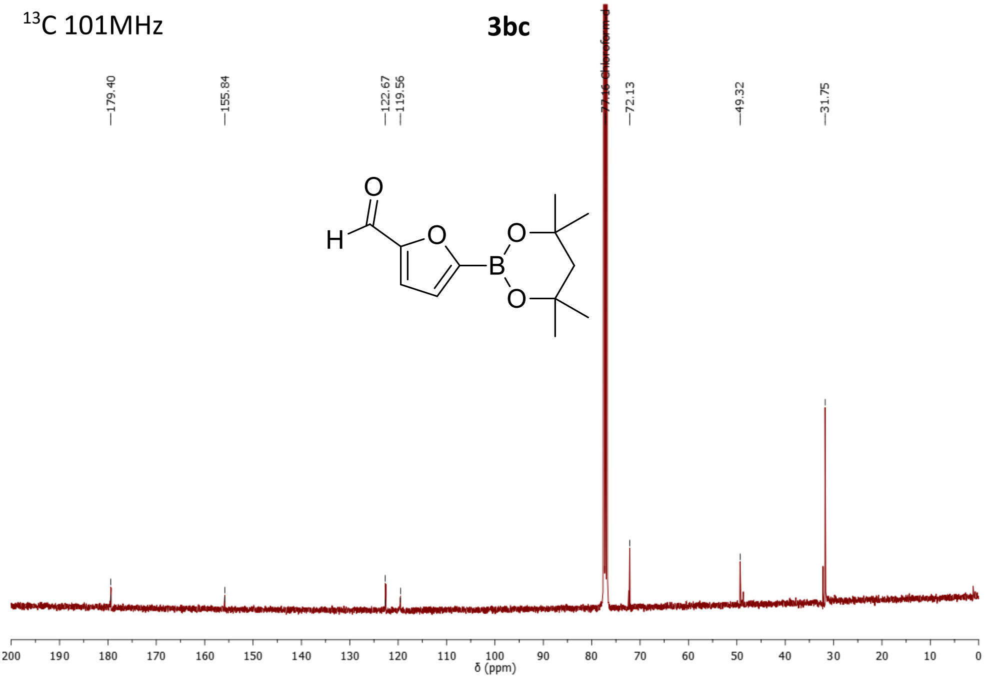
^{1}H 400MHz, $CDCl_3$

3bc



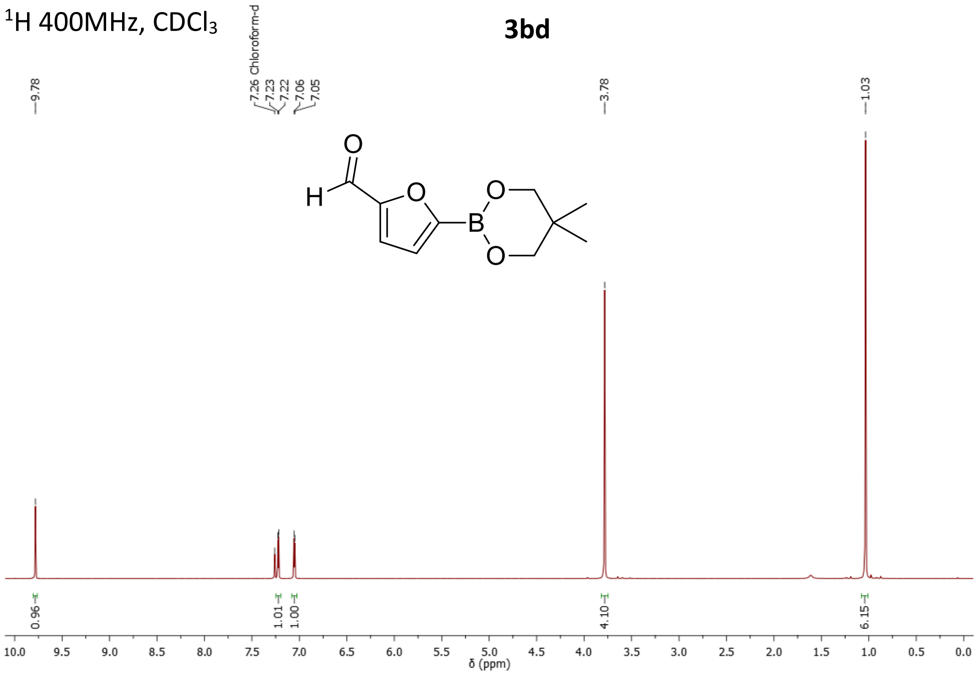
^{13}C 101MHz

3bc



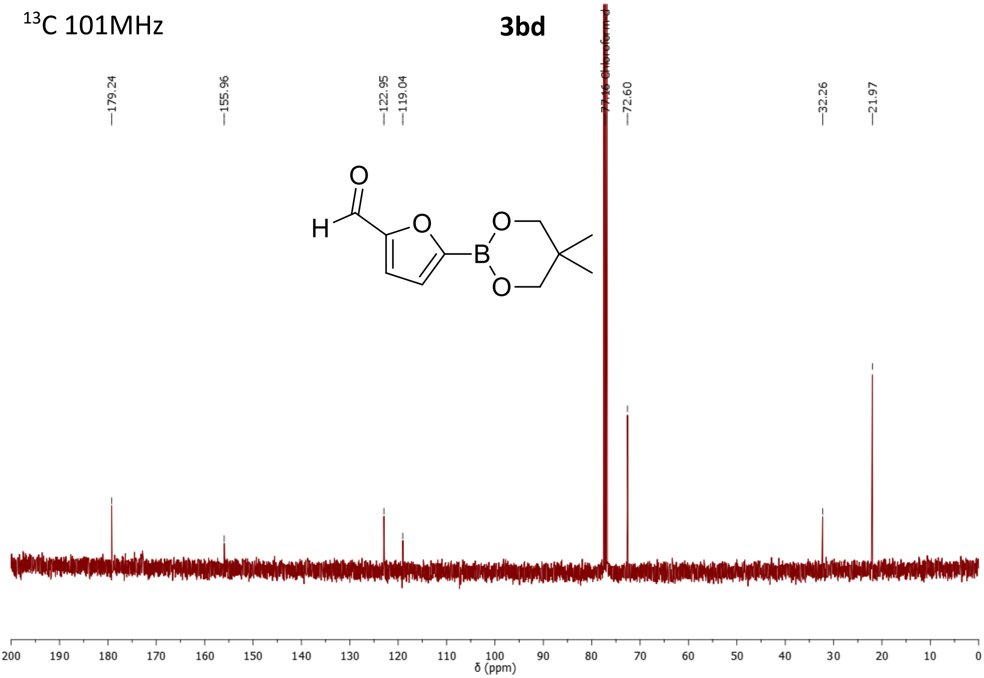
^{1}H 400MHz, $CDCl_3$

3bd



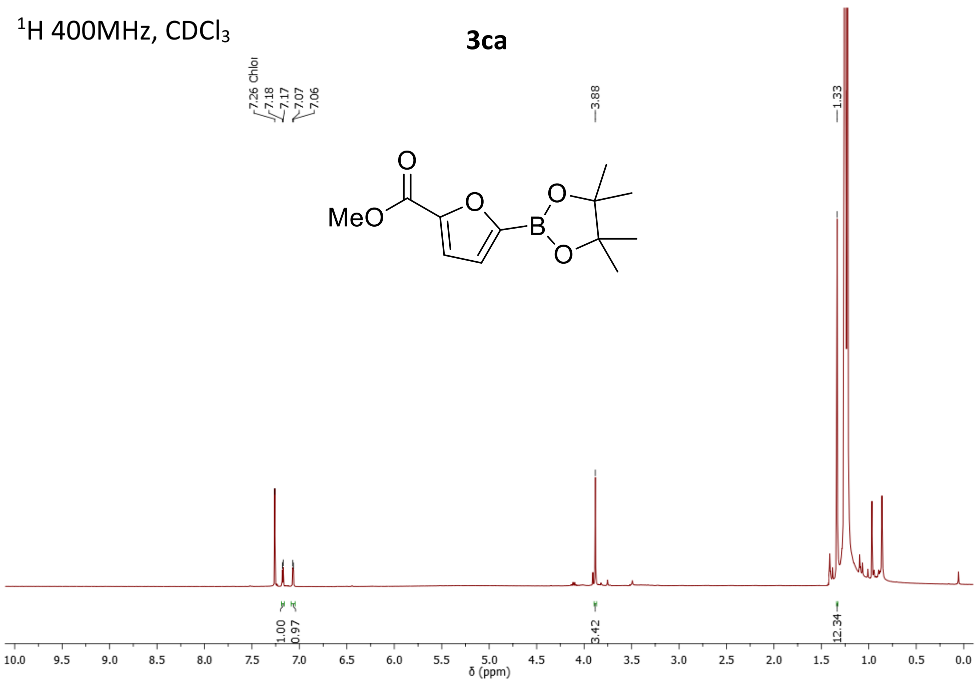
^{13}C 101MHz

3bd



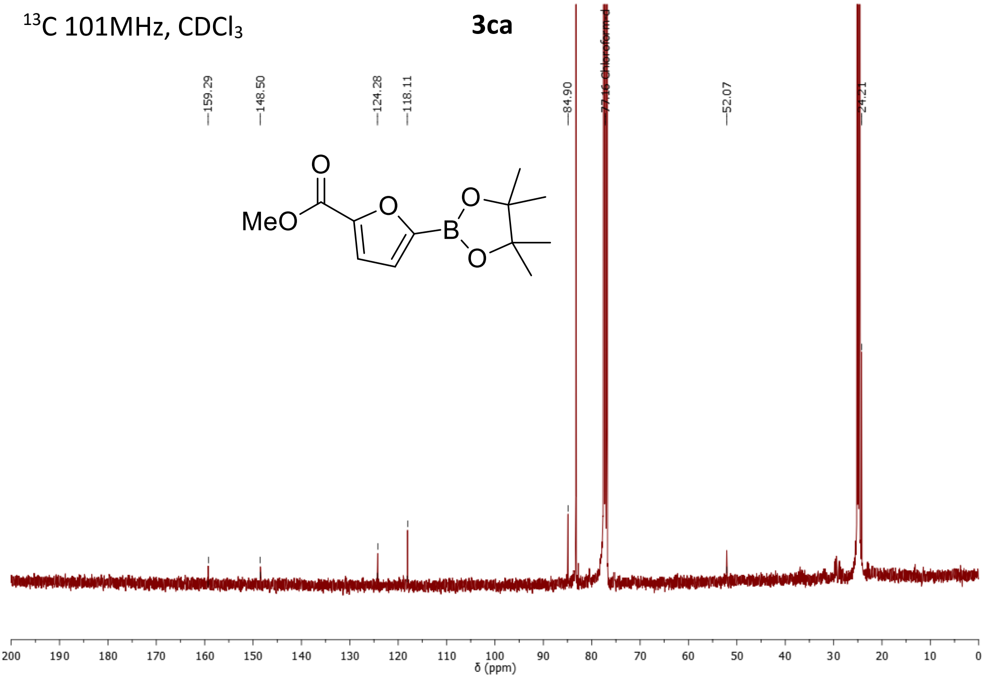
^{1}H 400MHz, CDCl$_3$

3ca



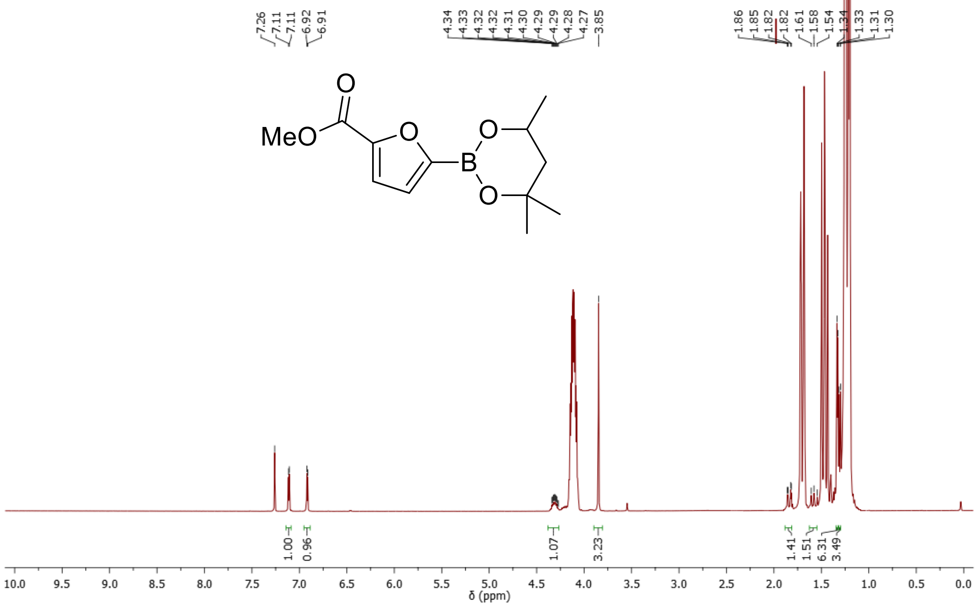
^{13}C 101MHz, CDCl$_3$

3ca



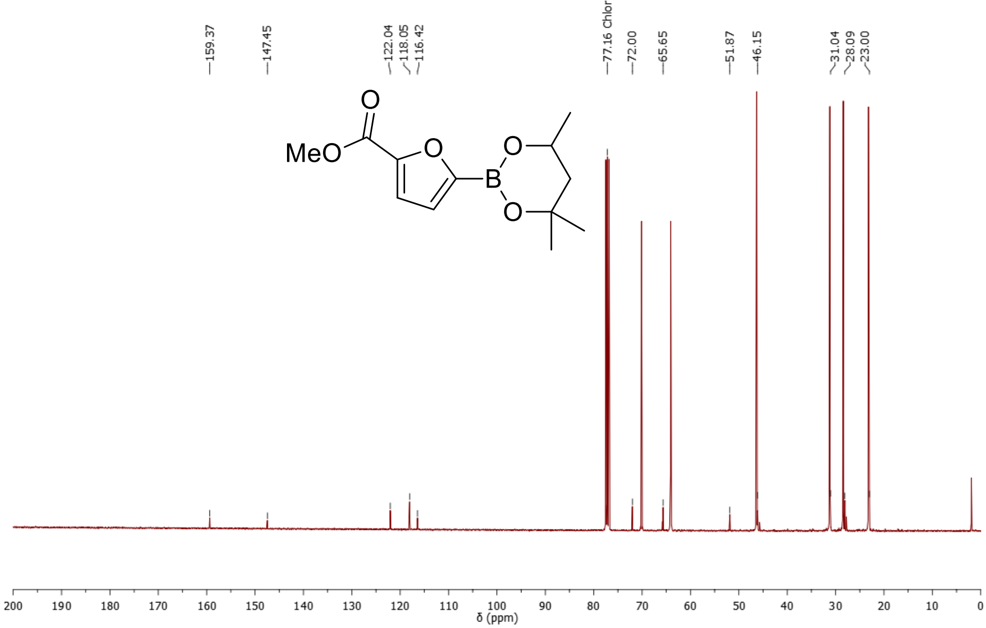
^{1}H 400MHz, $CDCl_3$

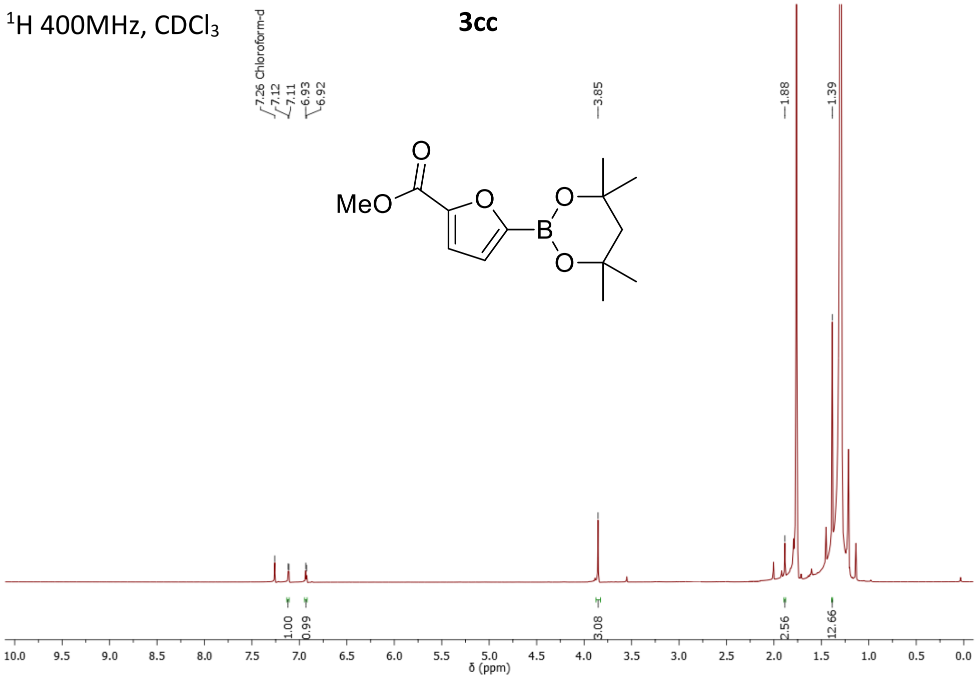
3cb

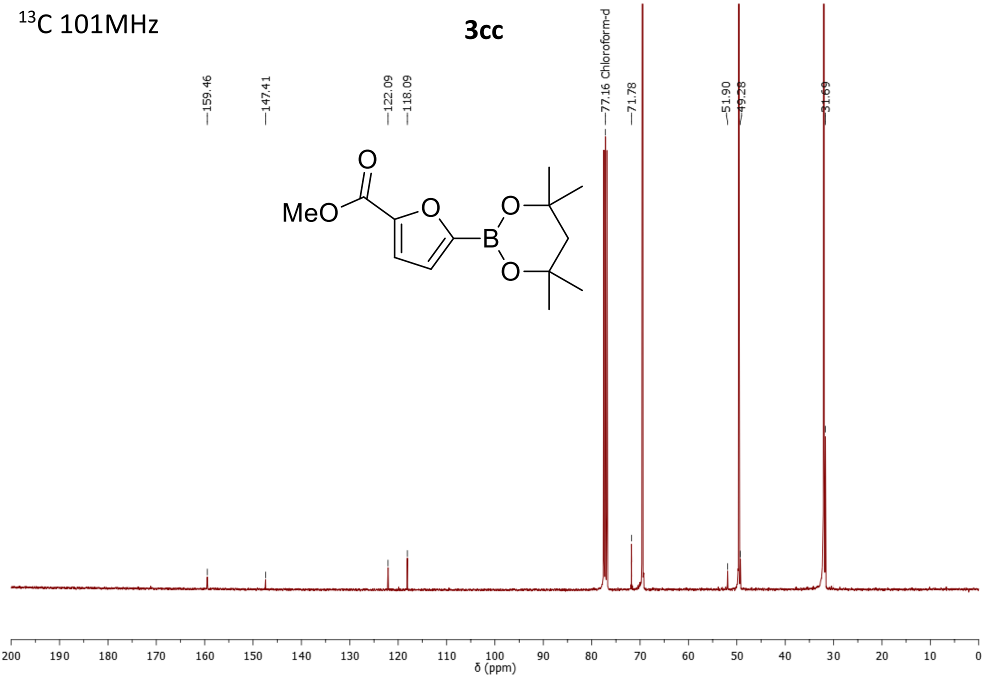


^{13}C 101MHz

3cb

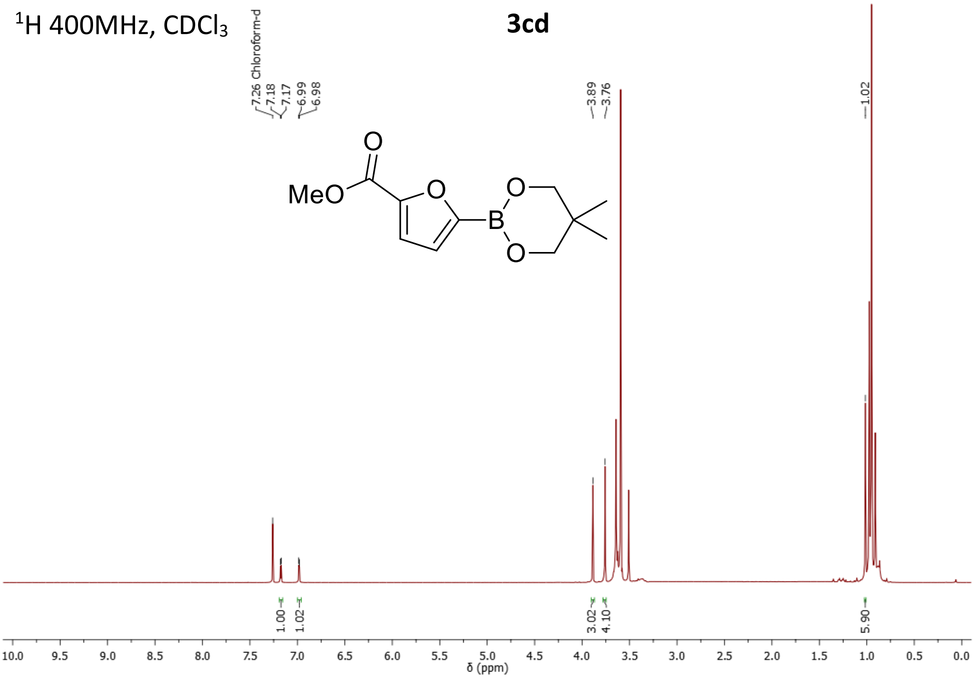



^{1}H 400MHz, CDCl$_3$
3cc
7.26 Chloroform-d
7.12
7.11
6.93
6.92
3.85
1.88
1.39
MeO
O
O
B
O
O
1.00
0.99
3.08
2.56
12.66
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)


^{13}C 101MHz
3cc
159.46
147.41
122.09
118.09
77.16 Chloroform-d
71.78
51.90
49.28
31.69
MeO
O
O
B
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

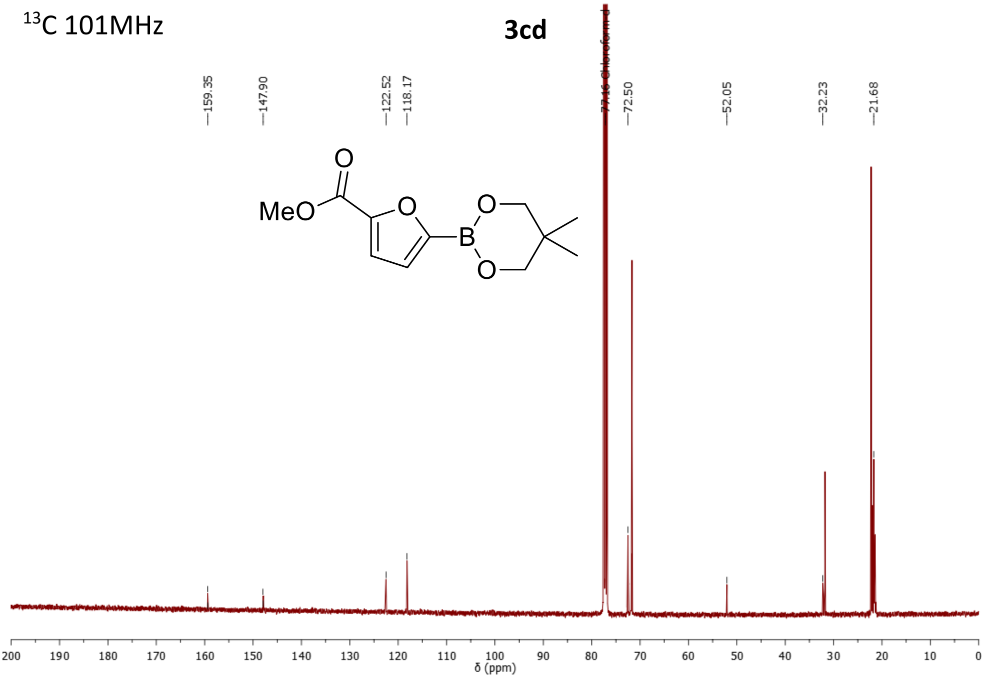
^{1}H 400MHz, $CDCl_3$

3cd

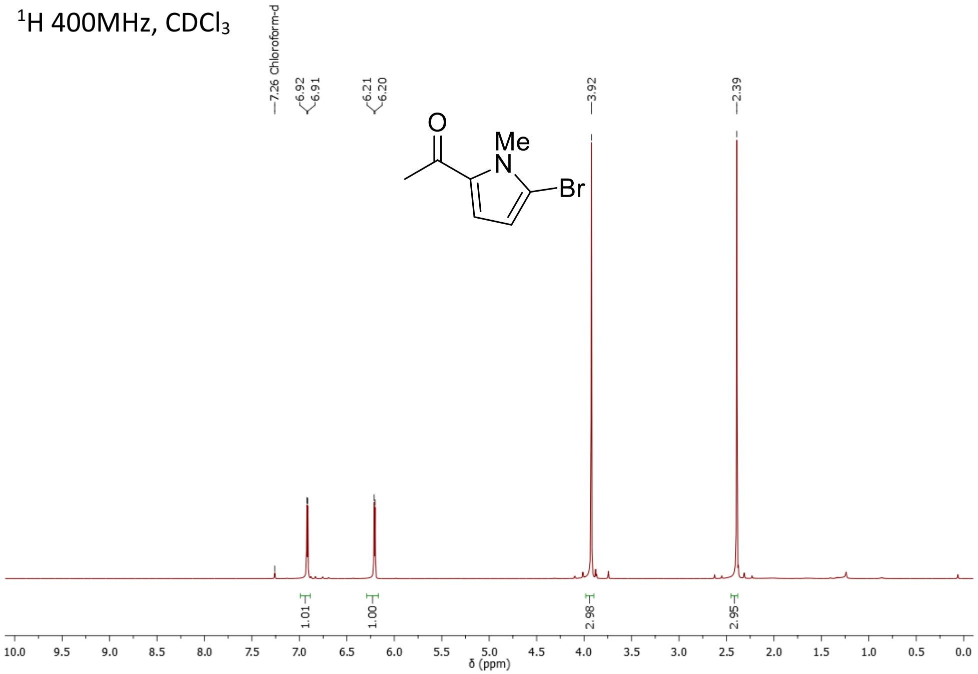


^{13}C 101MHz

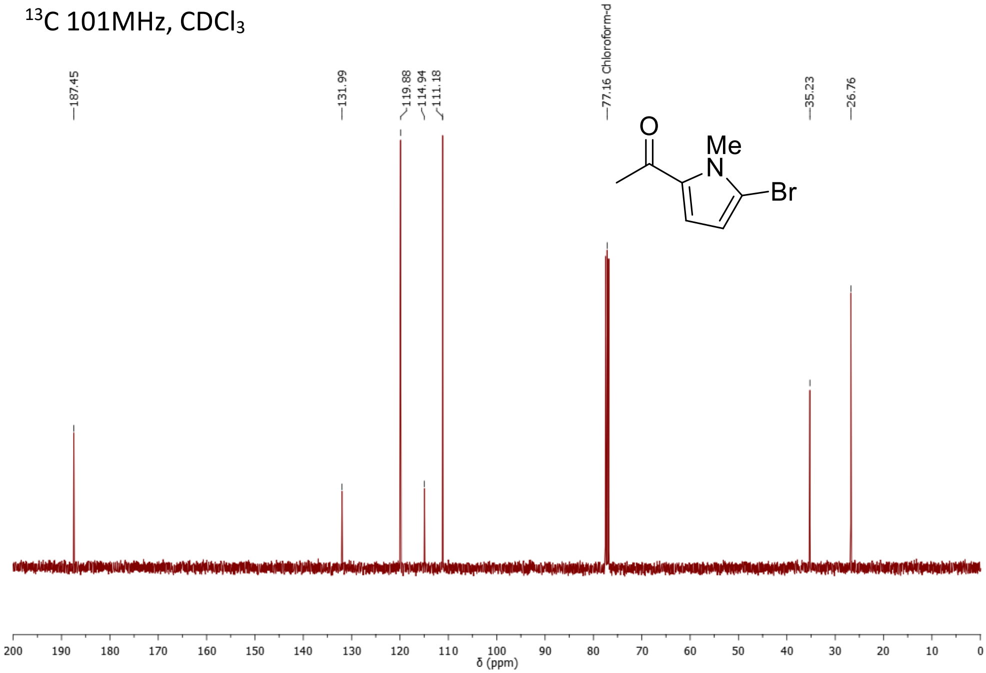
3cd



^{1}H 400MHz, CDCl$_3$

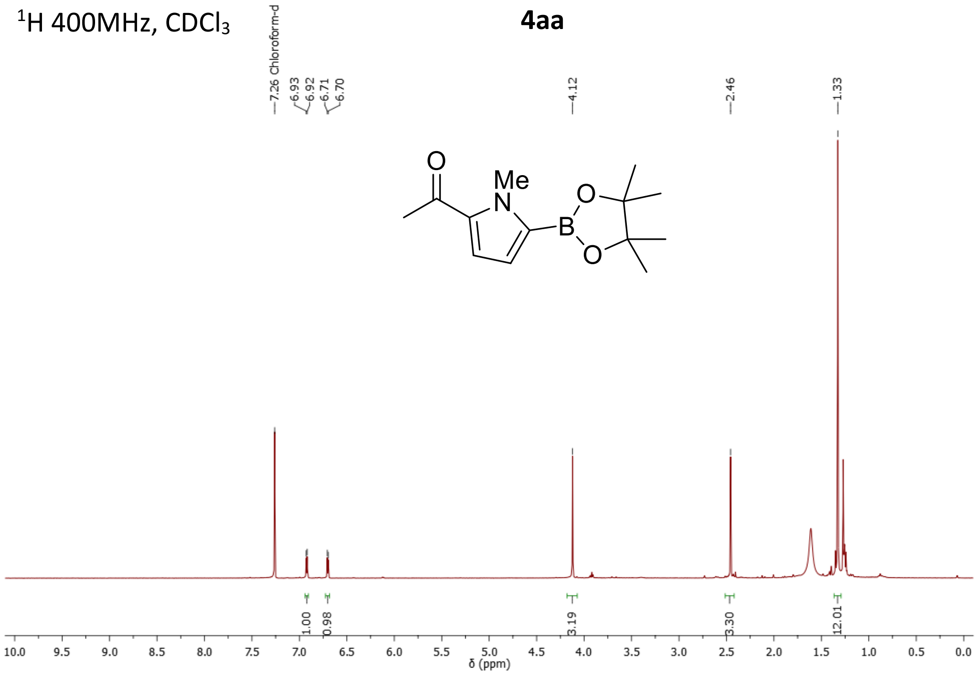


^{13}C 101MHz, CDCl$_3$



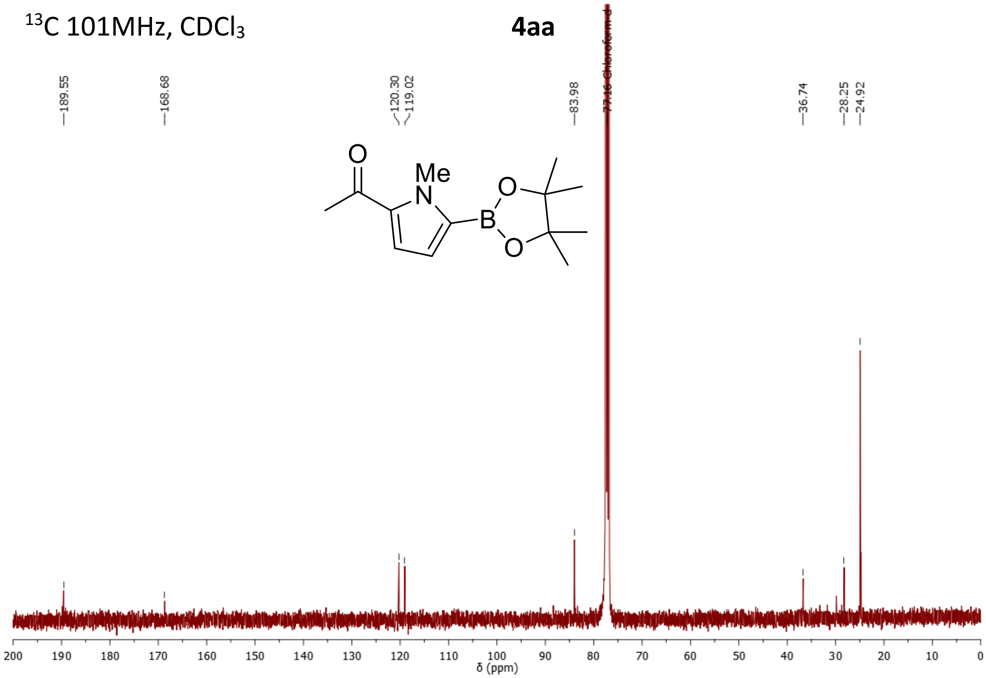
^{1}H 400MHz, CDCl$_3$

4aa



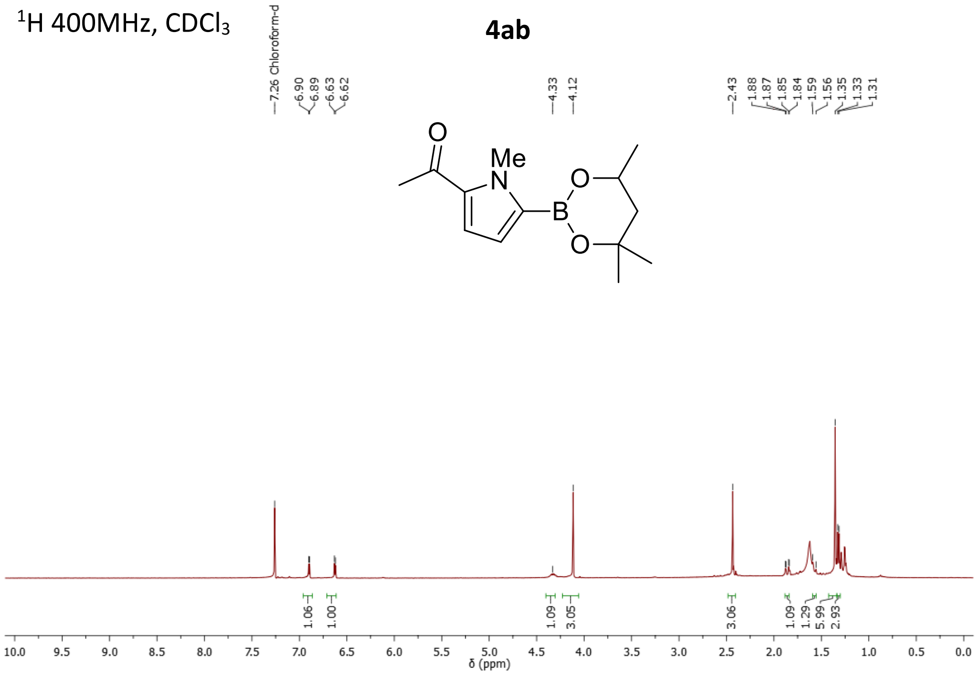
^{13}C 101MHz, CDCl$_3$

4aa



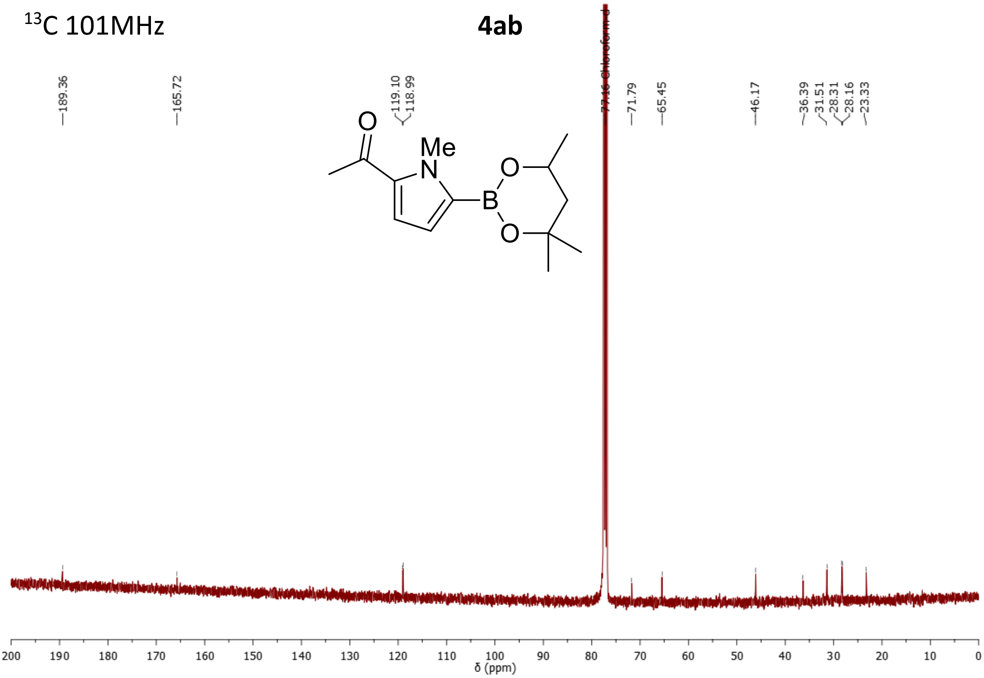
^{1}H 400MHz, $CDCl_3$

4ab



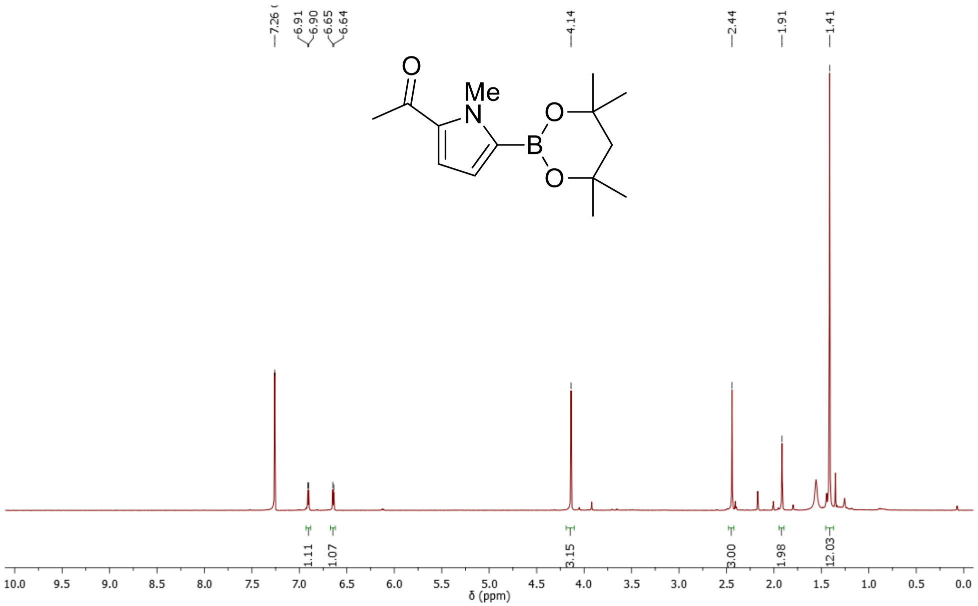
^{13}C 101MHz

4ab



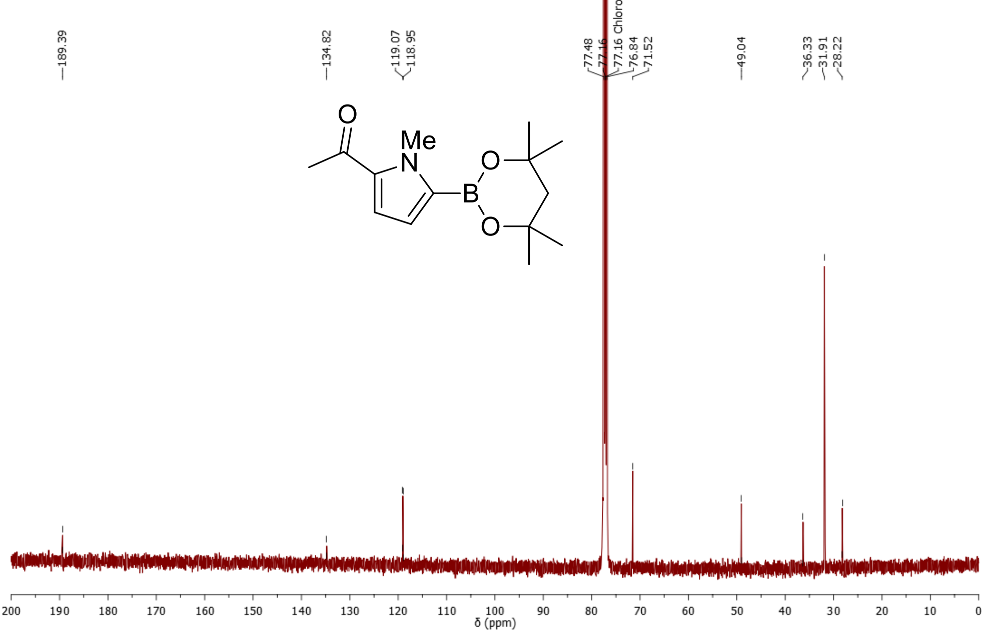
^{1}H 400MHz, CDCl$_3$

4ac



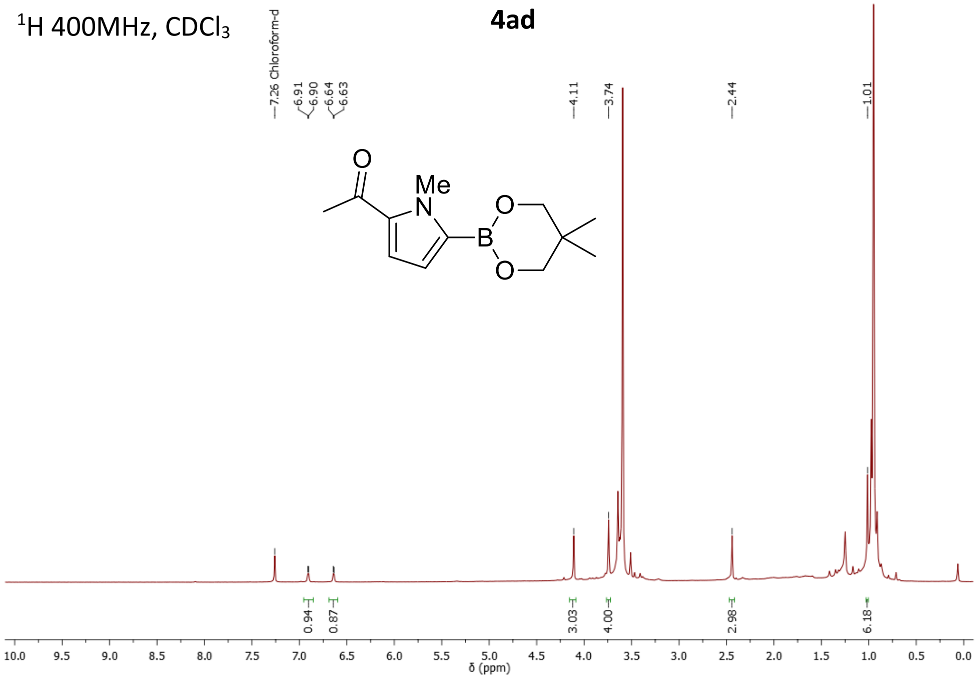
^{13}C 101MHz

4ac



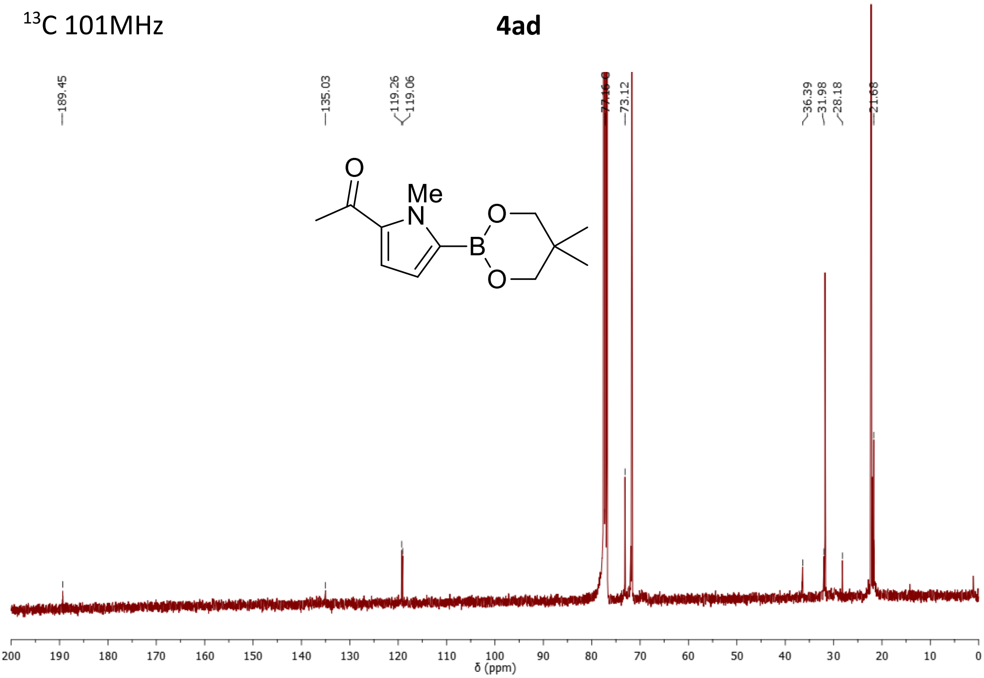
^{1}H 400MHz, CDCl$_3$

4ad



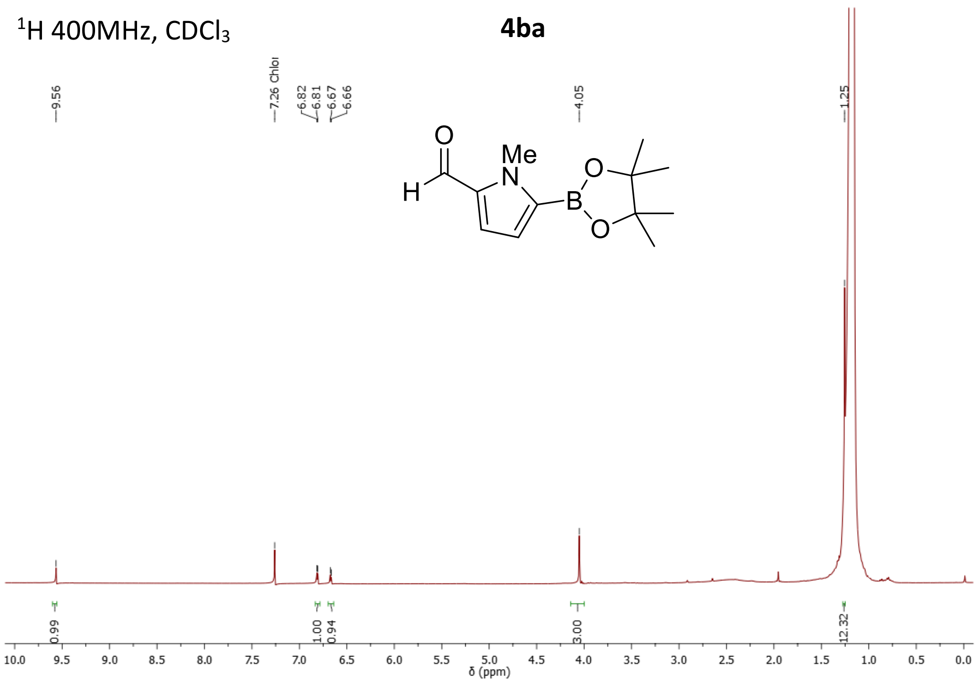
^{13}C 101MHz

4ad



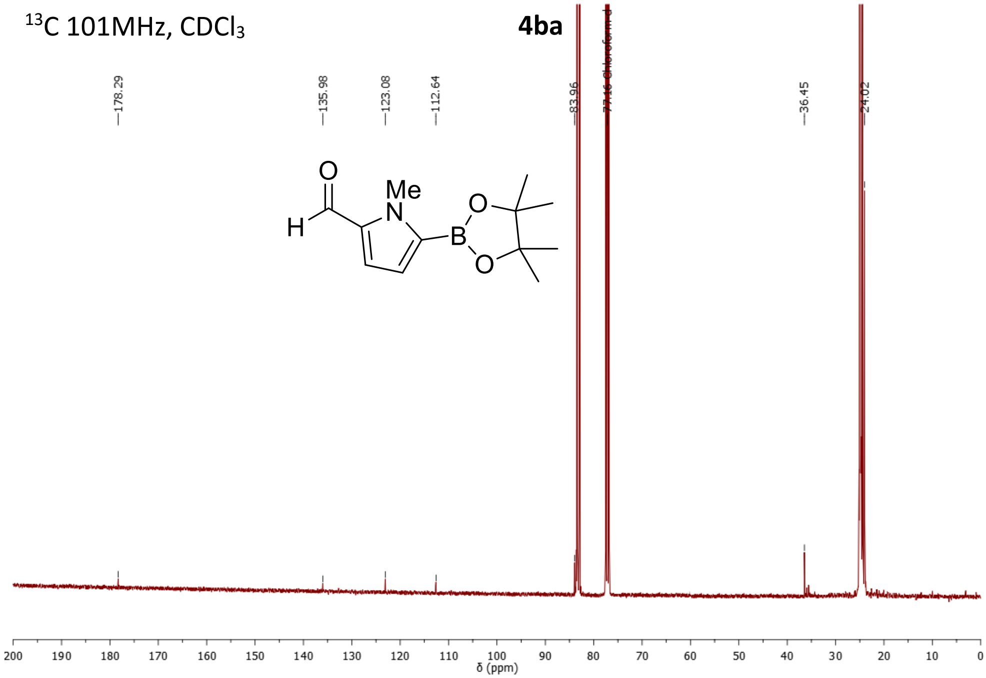
^{1}H 400MHz, $CDCl_3$

4ba



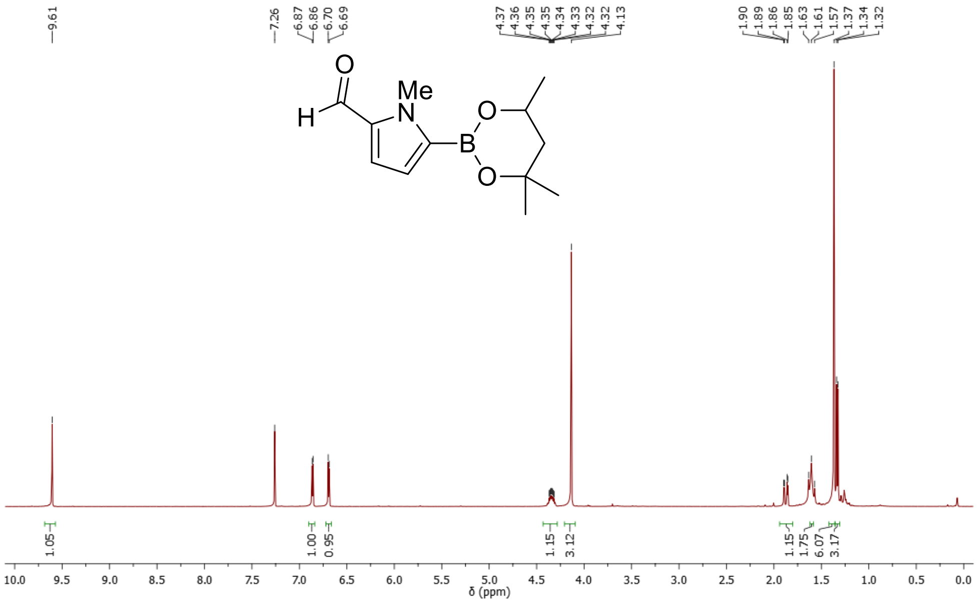
^{13}C 101MHz, $CDCl_3$

4ba

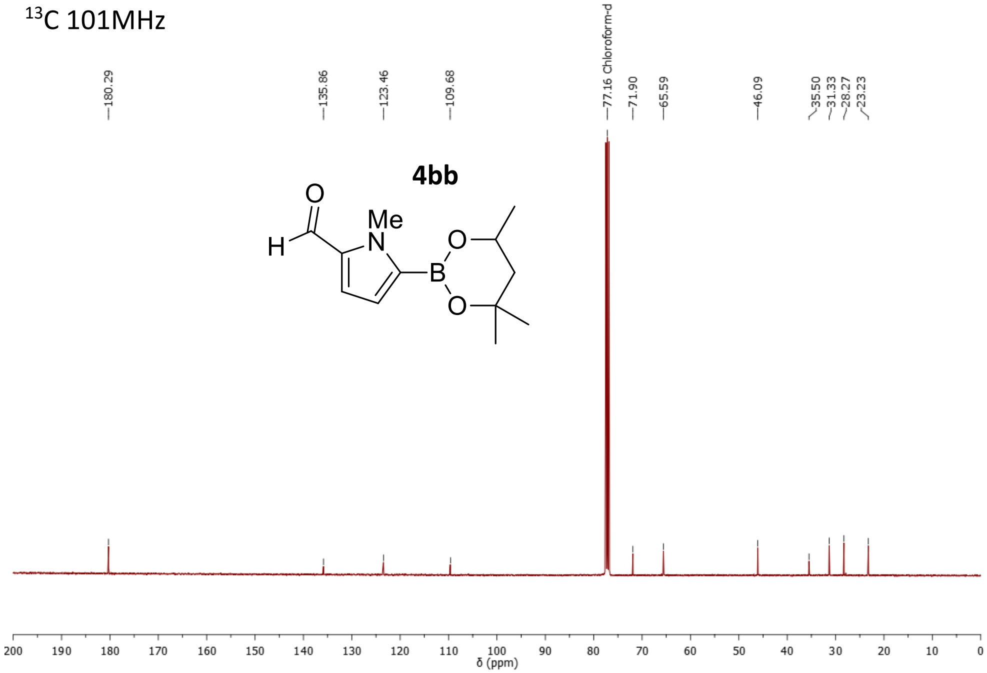


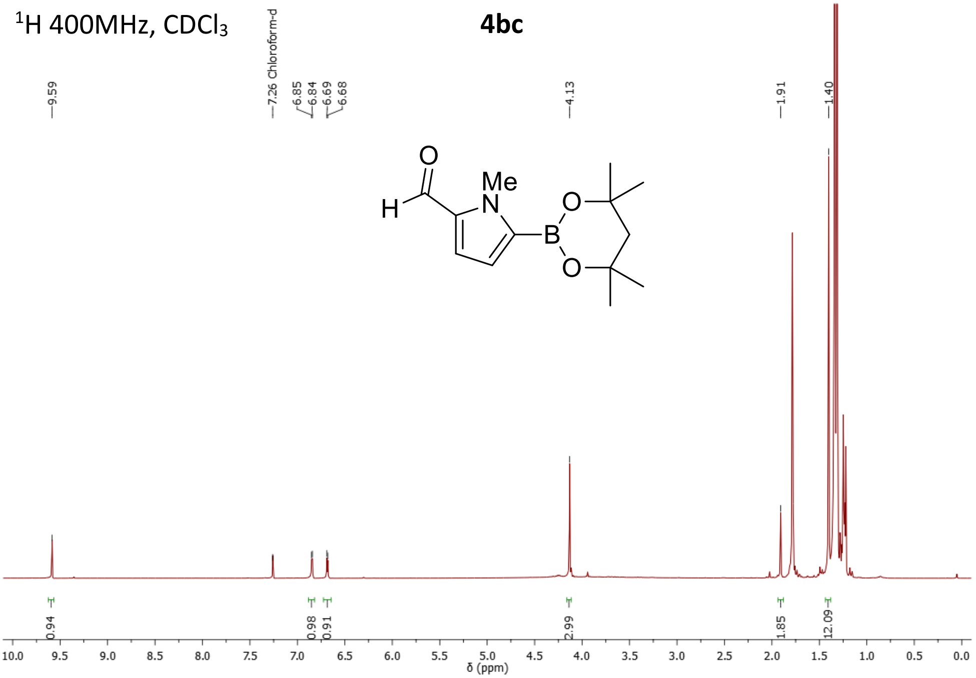
^{1}H 400MHz, $CDCl_3$

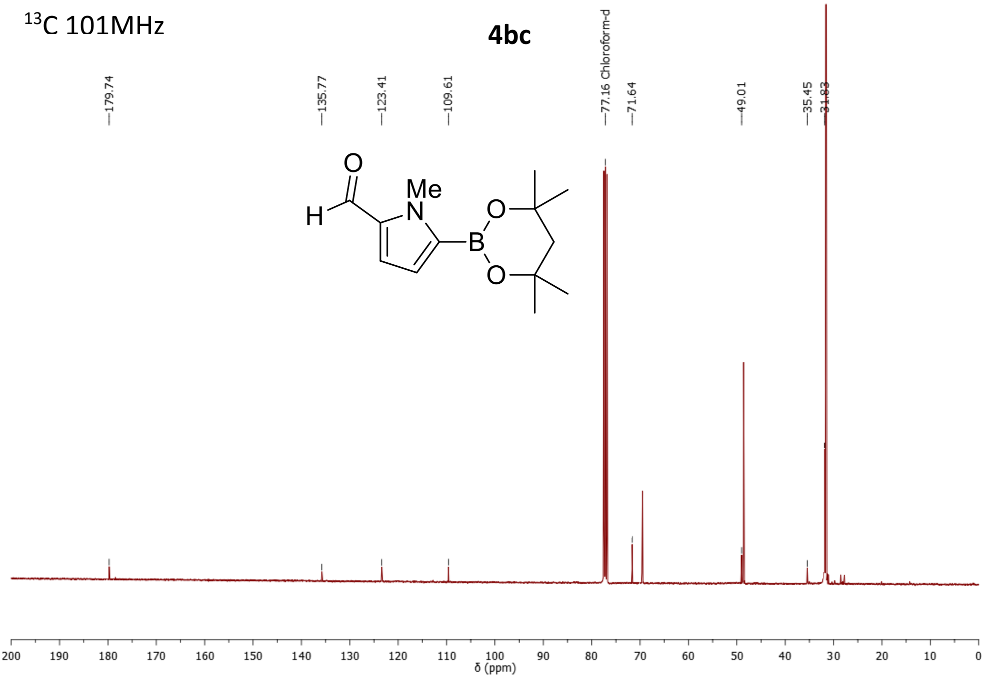
4bb



^{13}C 101MHz

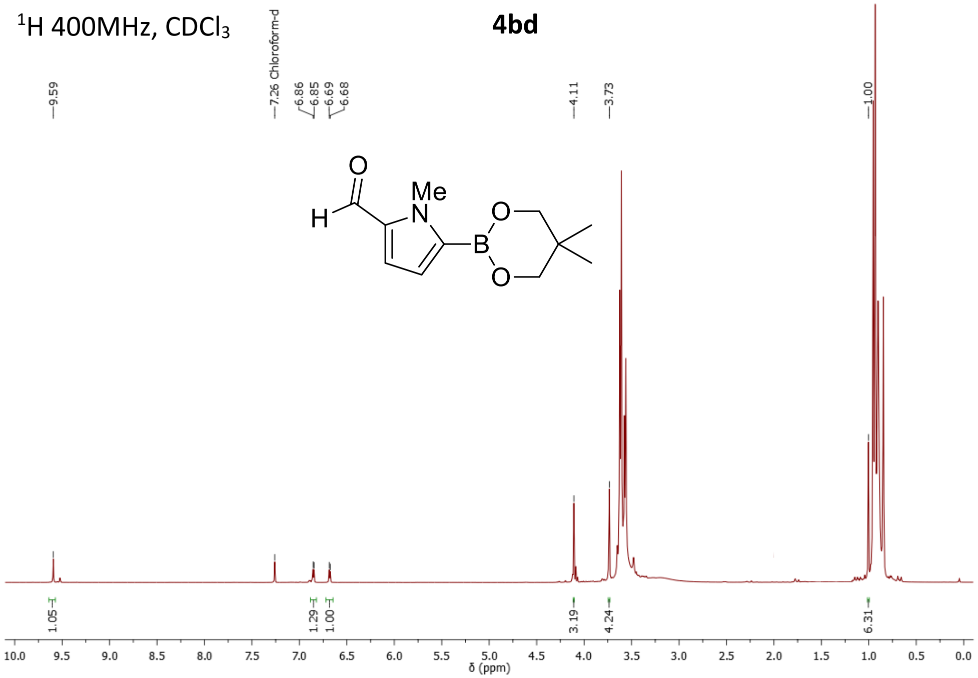



^{1}H 400MHz, CDCl$_3$
4bc
9.59
7.26 Chloroform-d
6.85
6.84
6.69
6.68
4.13
1.91
1.40
O
H
Me
N
O
B
O
0.94
0.98
0.91
2.99
1.85
12.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)


^{13}C 101MHz
4bc
179.74
135.77
123.41
109.61
77.16 Chloroform-d
71.64
49.01
35.45
31.83
O
H
Me
N
O
B
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

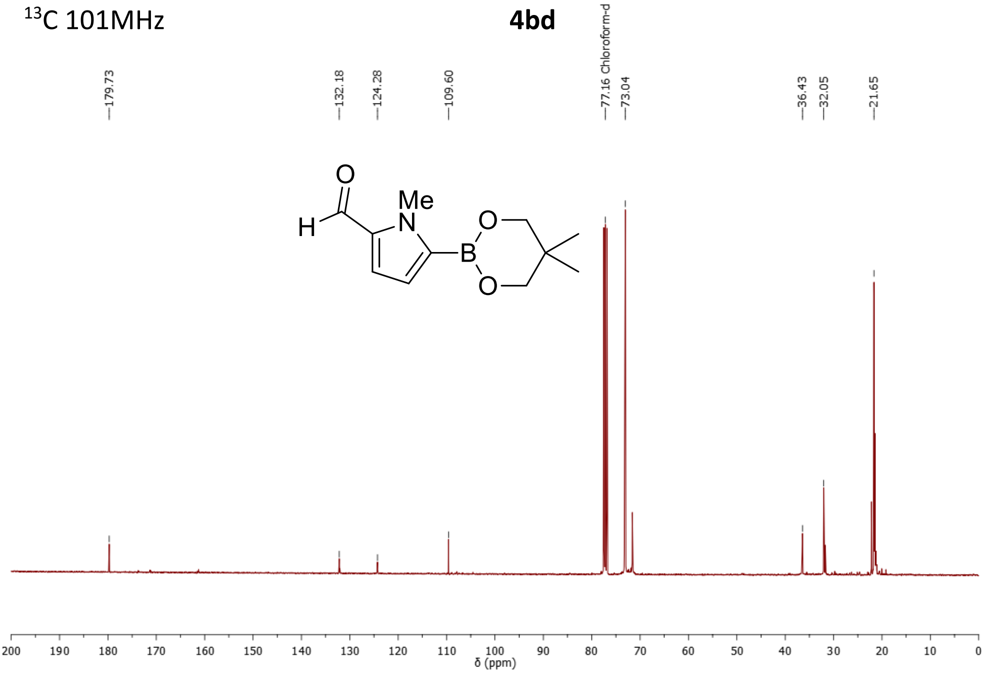
^{1}H 400MHz, CDCl$_3$

4bd

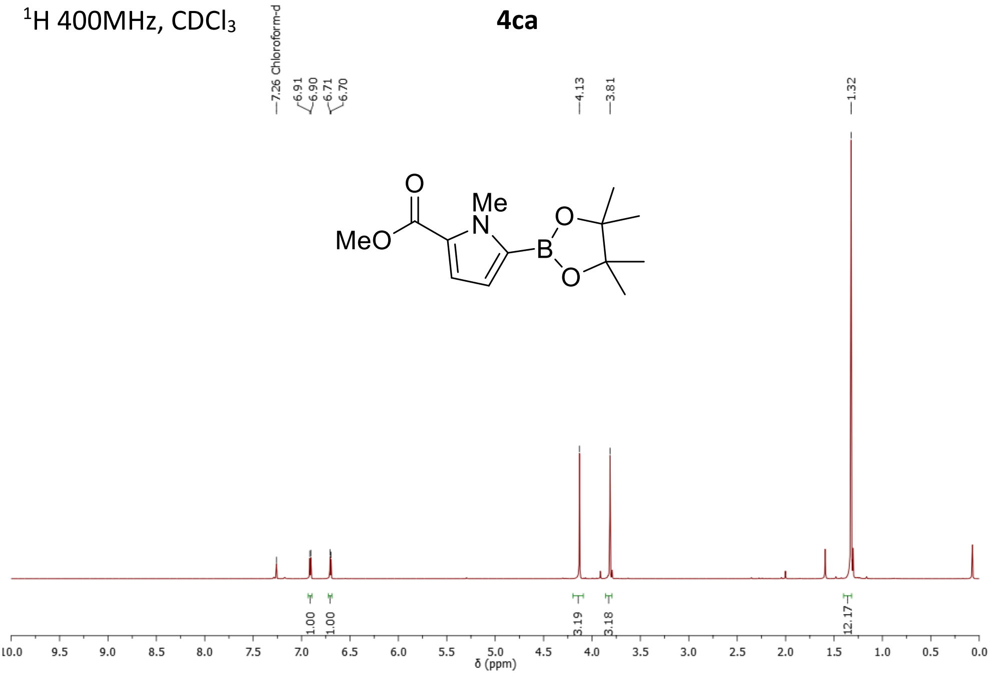


^{13}C 101MHz

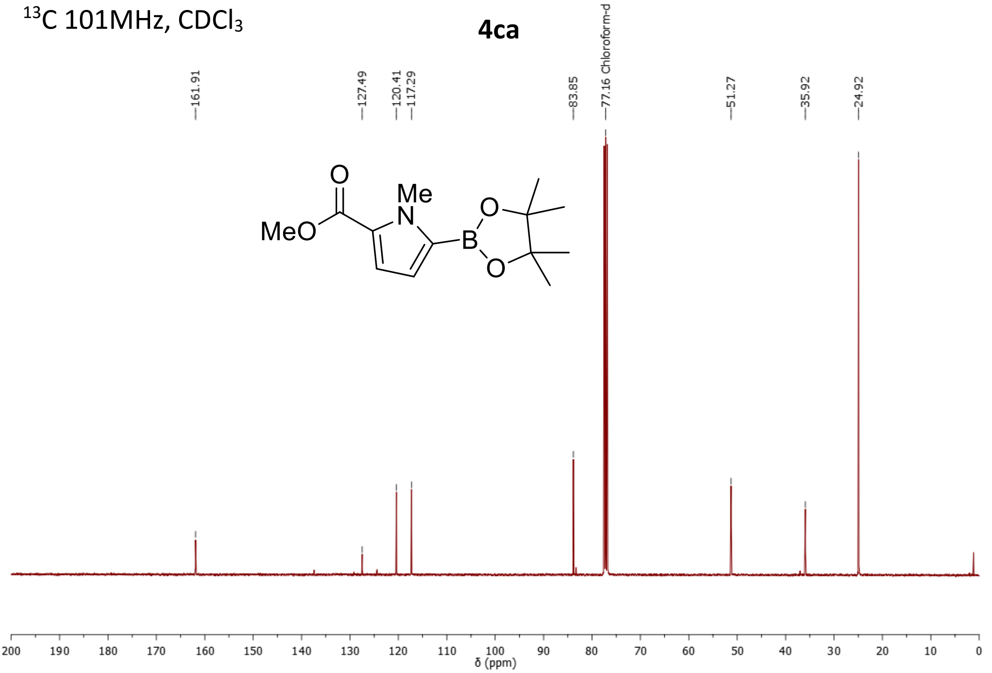
4bd



4ca

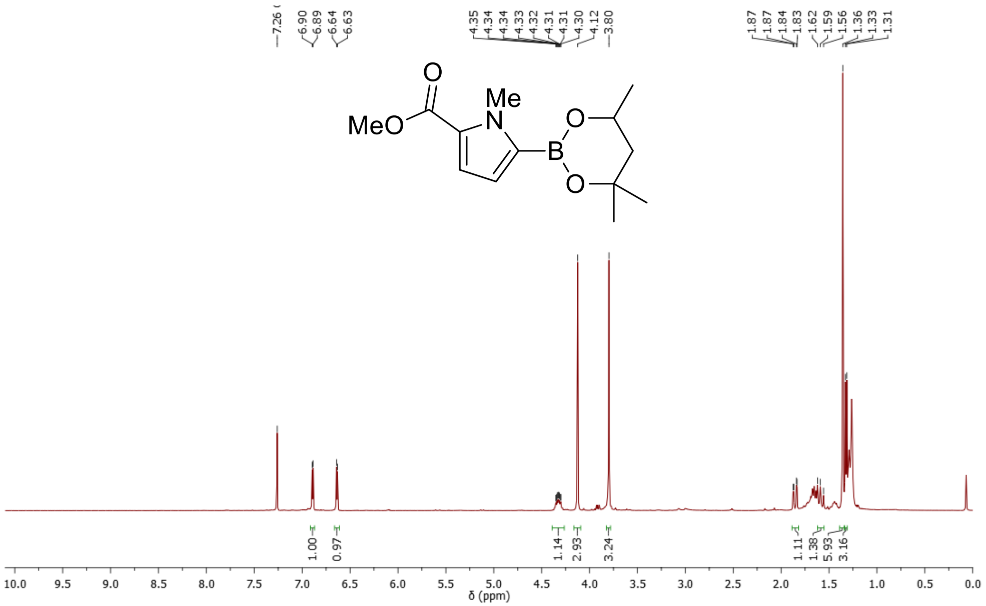

^{1}H 400MHz, CDCl$_3$
7.26 Chloroform-d
6.91
6.90
6.71
6.70
4.13
3.81
1.32
1.00
1.00
3.19
3.18
12.17
δ (ppm)
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
MeO
O
N
Me
B
O
O

4ca


^{13}C 101MHz, CDCl$_3$
161.91
127.49
120.41
117.29
83.85
77.16 Chloroform-d
51.27
35.92
24.92
δ (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
MeO
O
N
Me
B
O
O

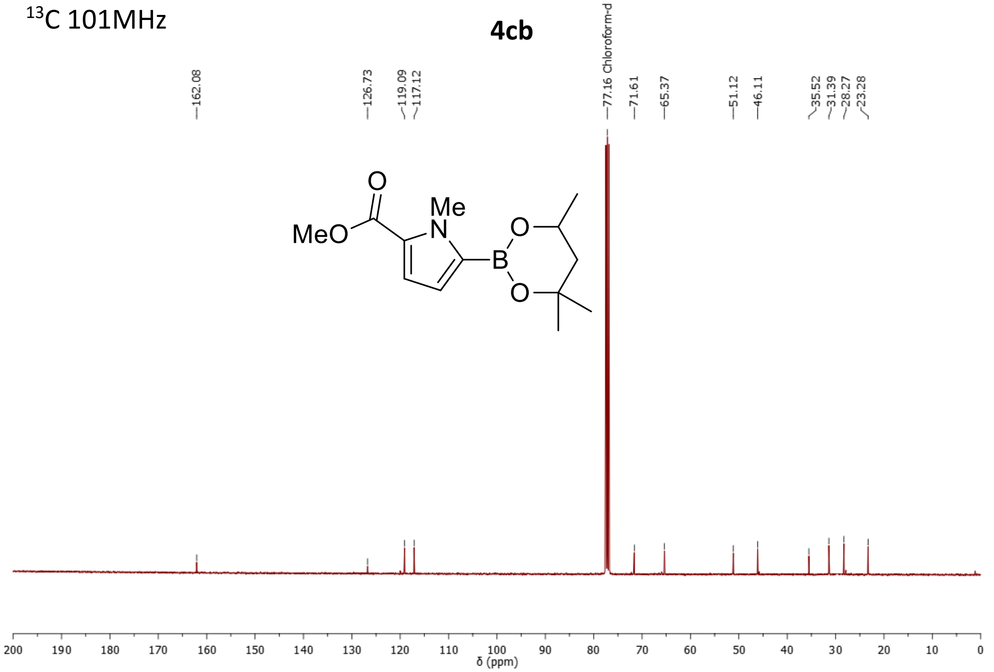
^{1}H 400MHz, $CDCl_3$

4cb



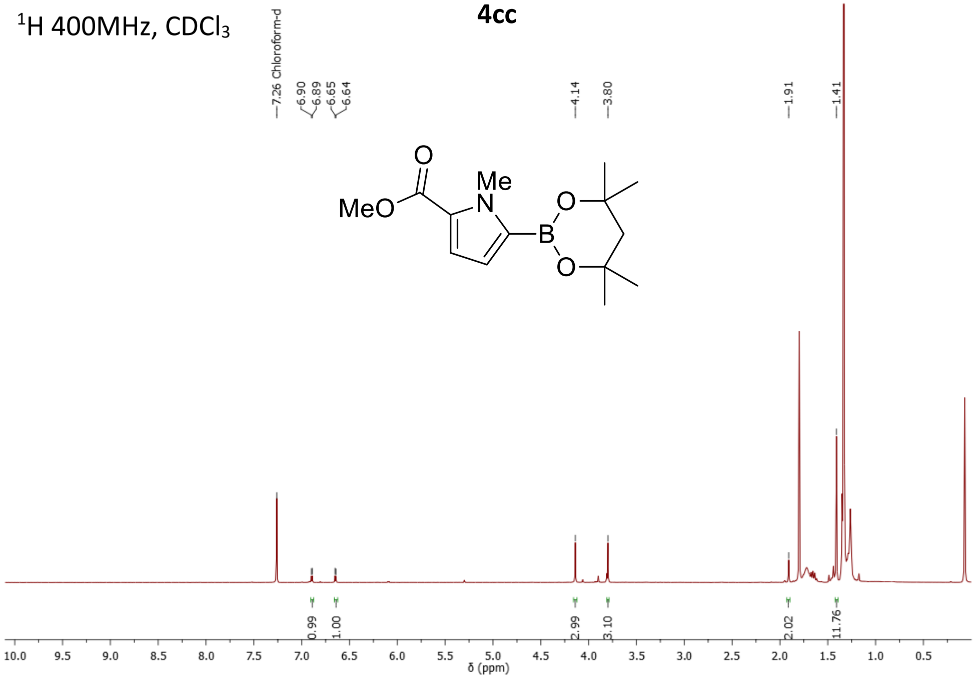
^{13}C 101MHz

4cb



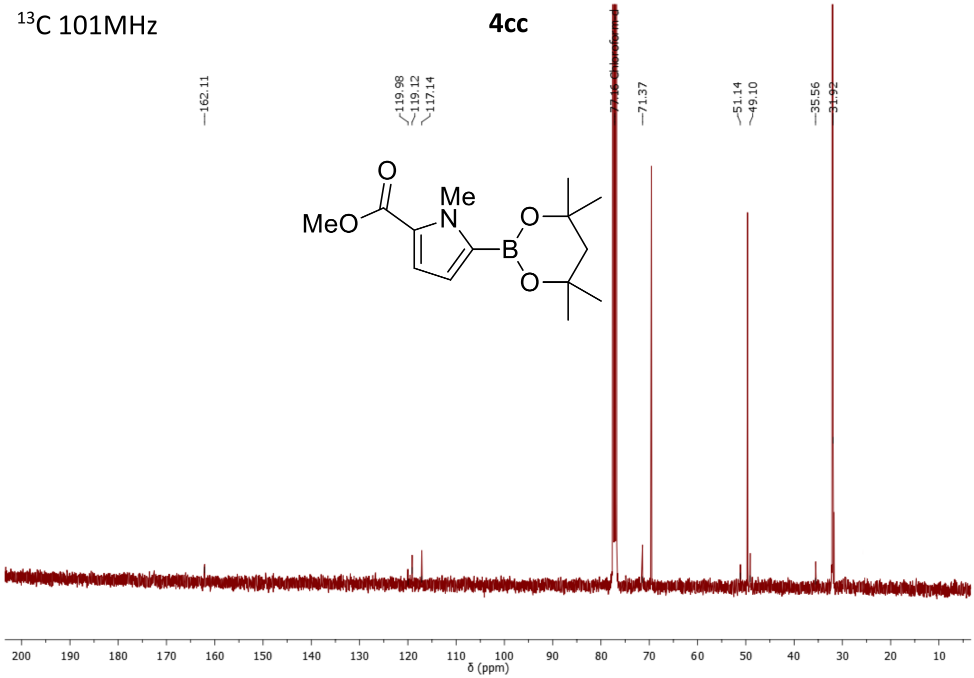
^{1}H 400MHz, $CDCl_3$

4cc



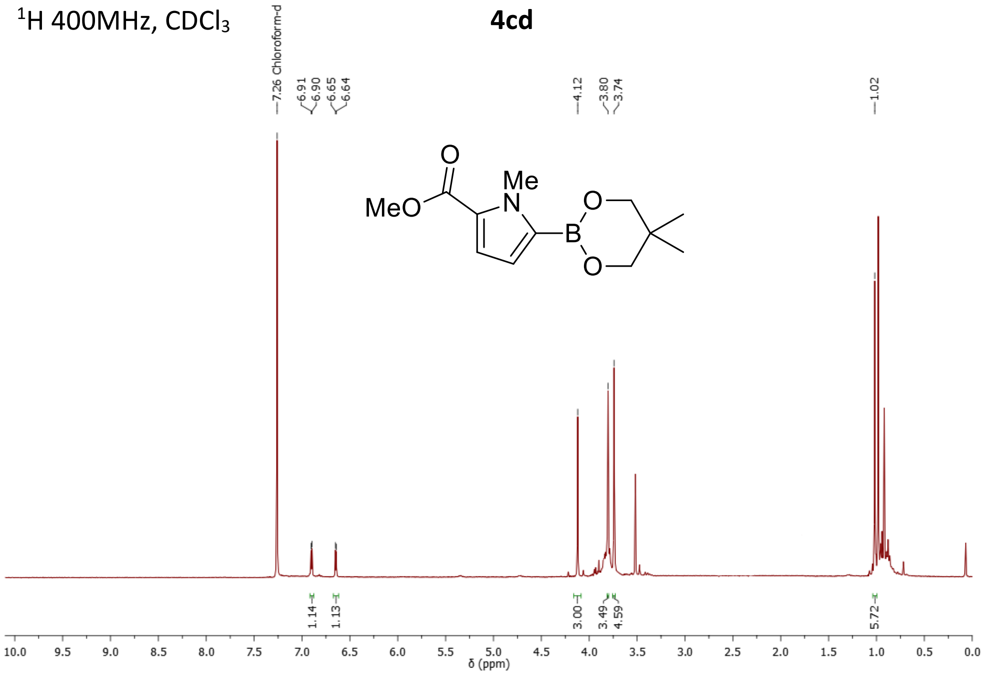
^{13}C 101MHz

4cc



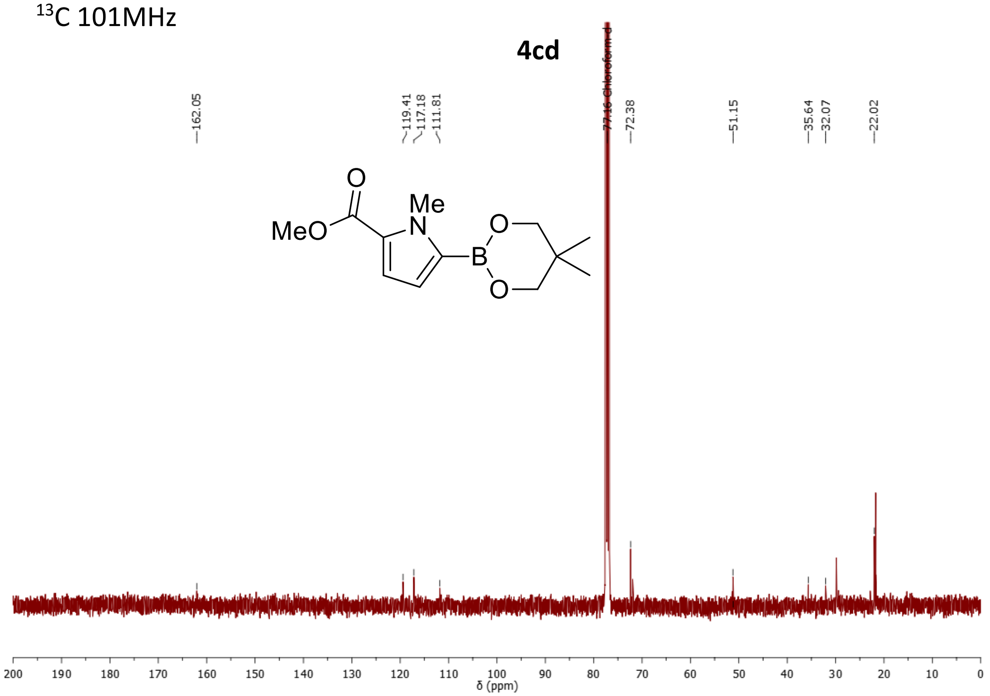
^{1}H 400MHz, $CDCl_3$

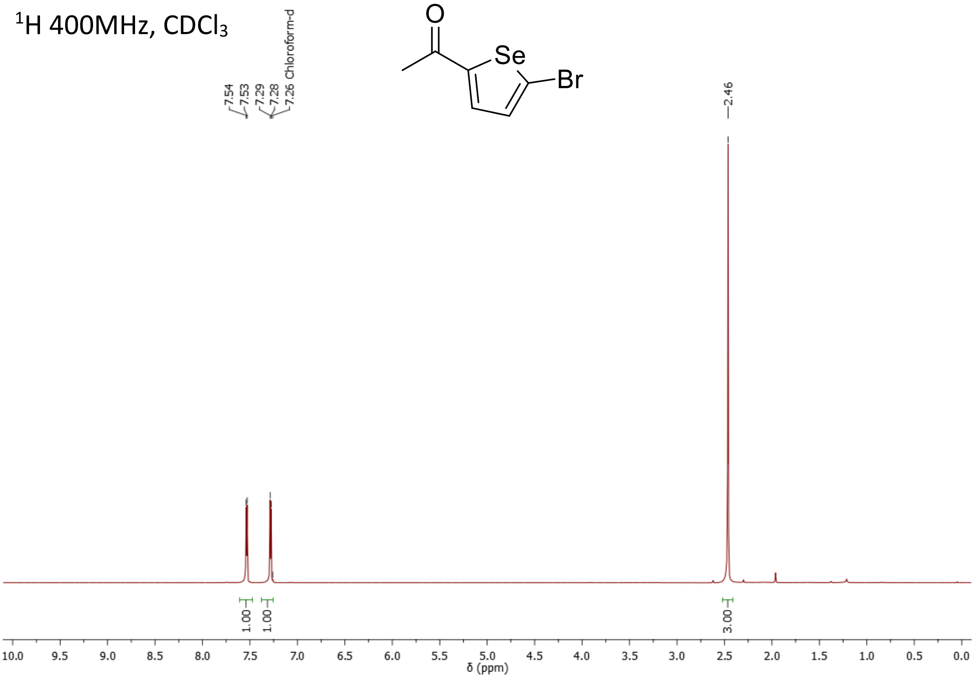
4cd



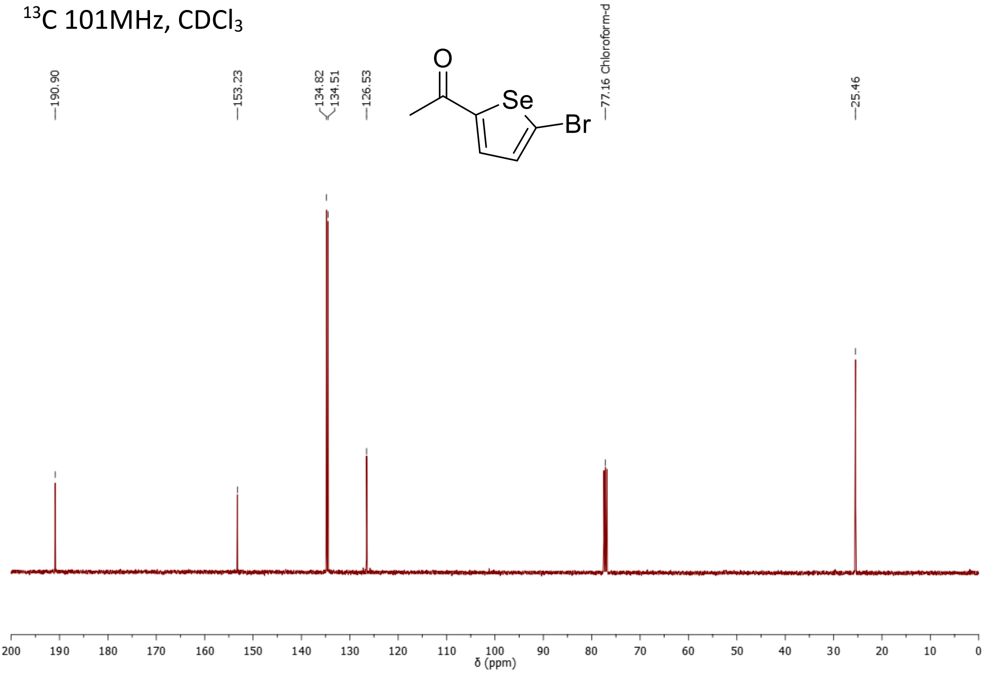
^{13}C 101MHz

4cd





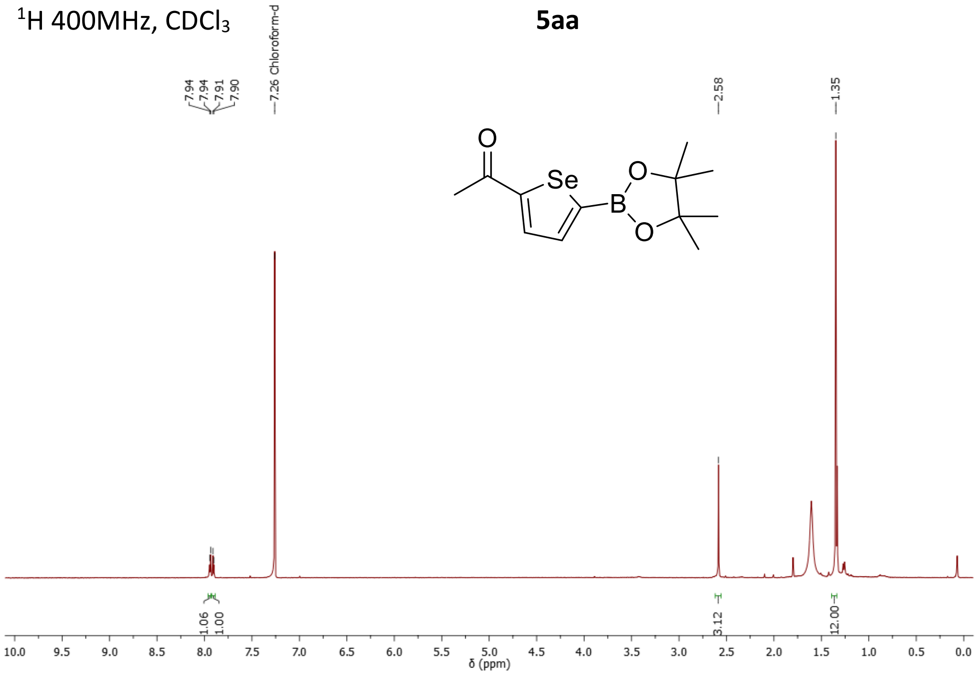
^{1}H 400MHz, $CDCl_3$



^{13}C 101MHz, $CDCl_3$

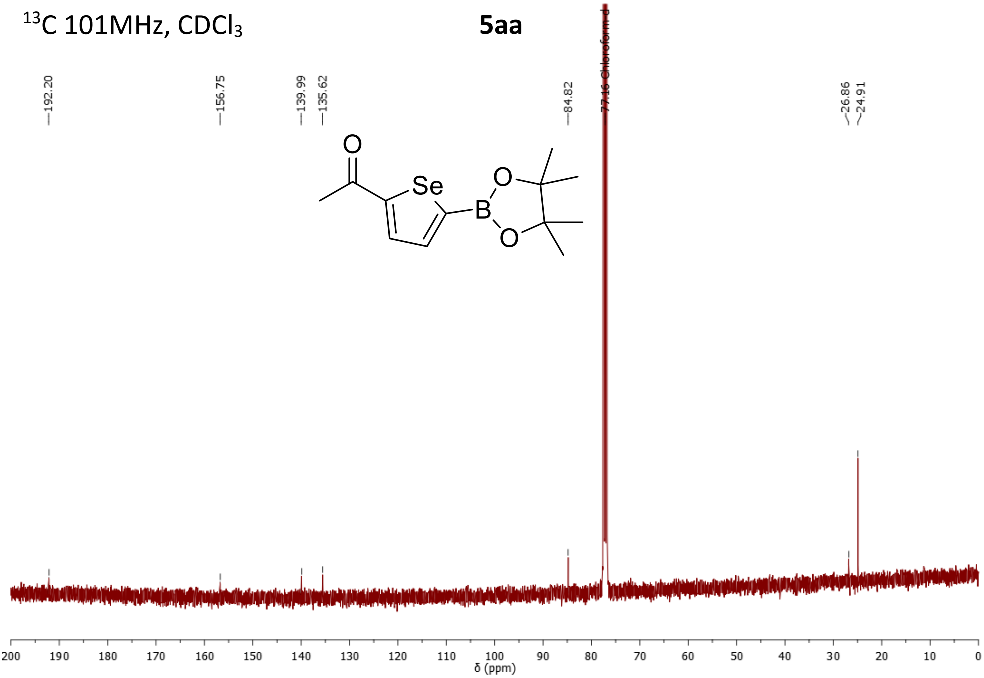
^{1}H 400MHz, $CDCl_3$

5aa



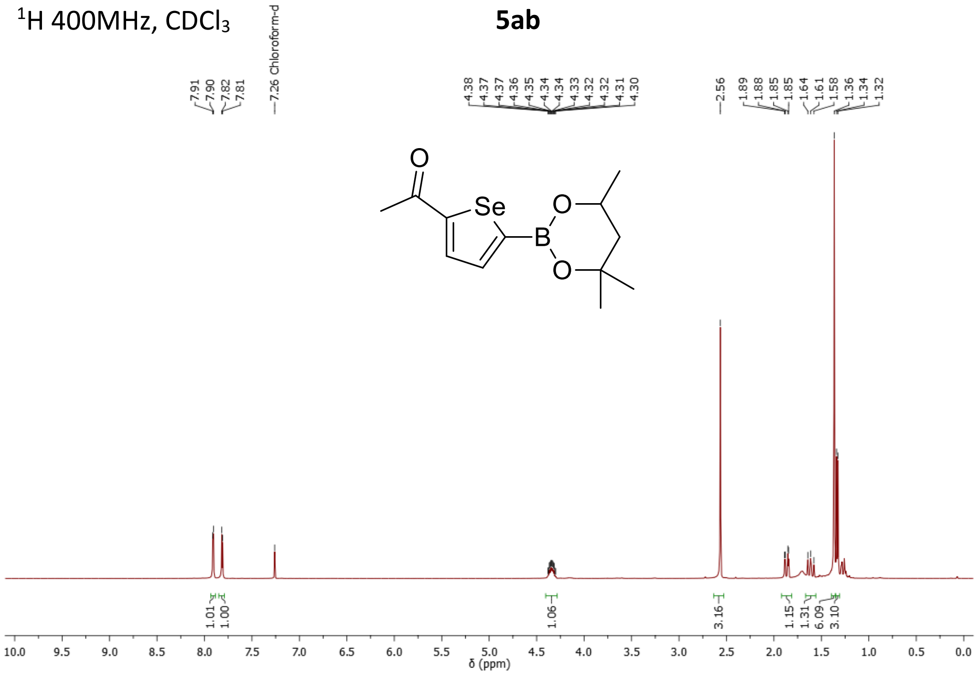
^{13}C 101MHz, $CDCl_3$

5aa



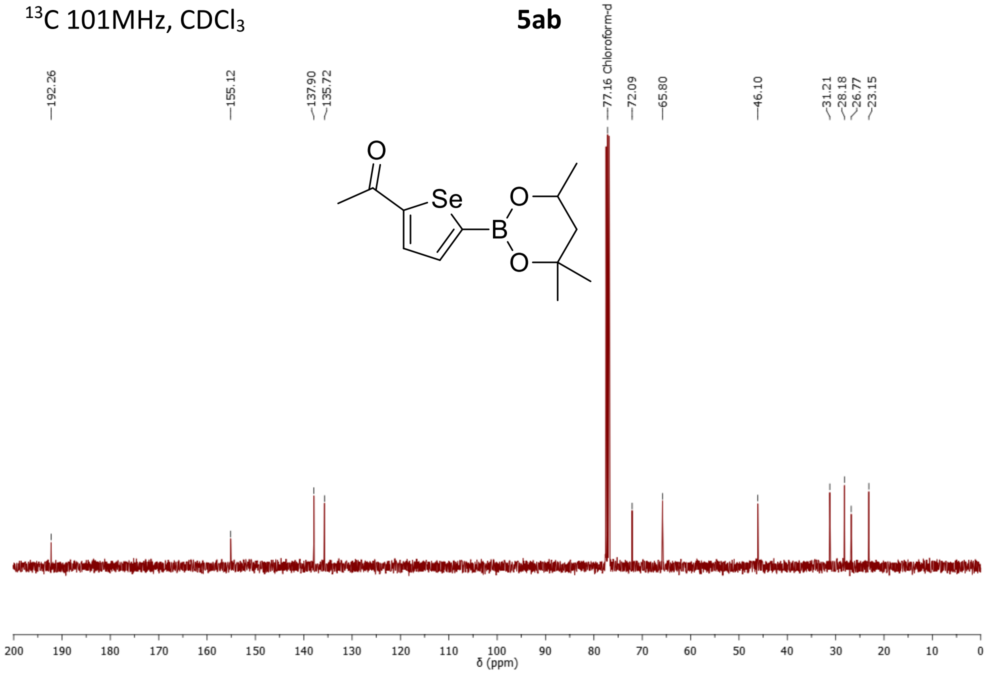
^{1}H 400MHz, CDCl$_3$

5ab

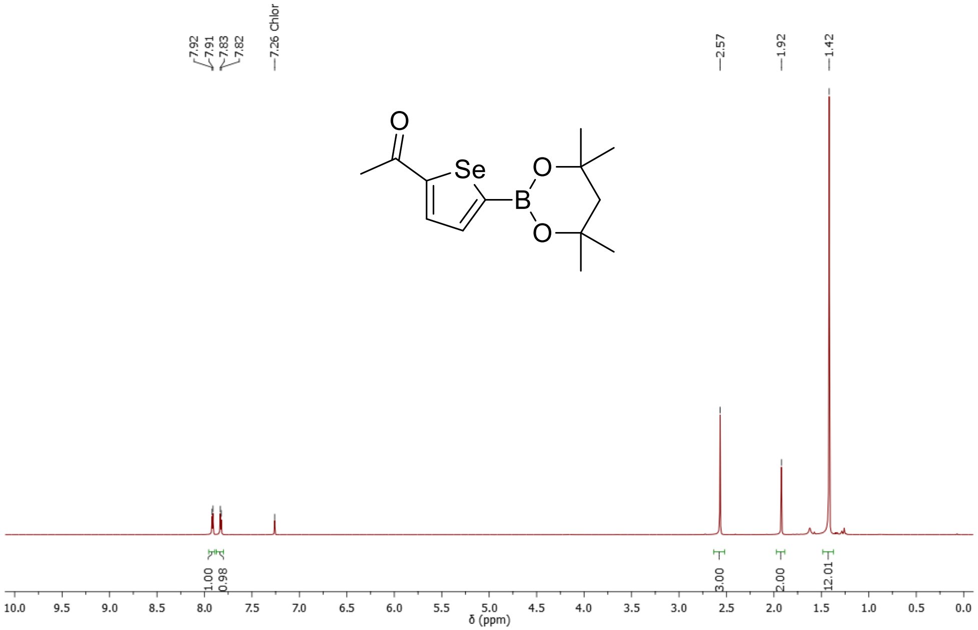


^{13}C 101MHz, CDCl$_3$

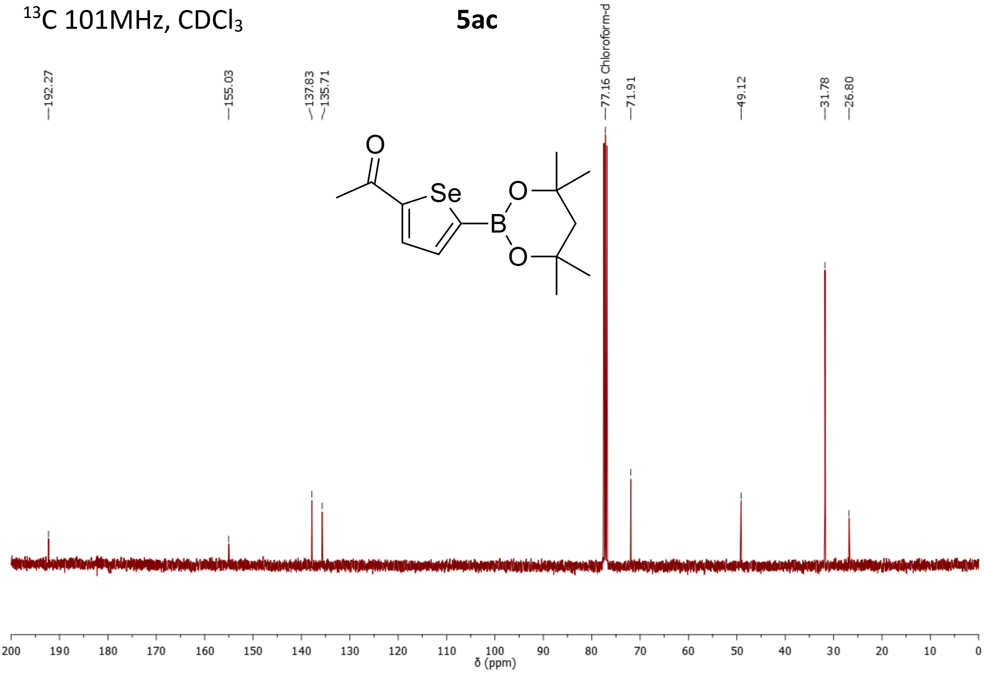
5ab



^{1}H 400MHz, $CDCl_3$ **5ac**

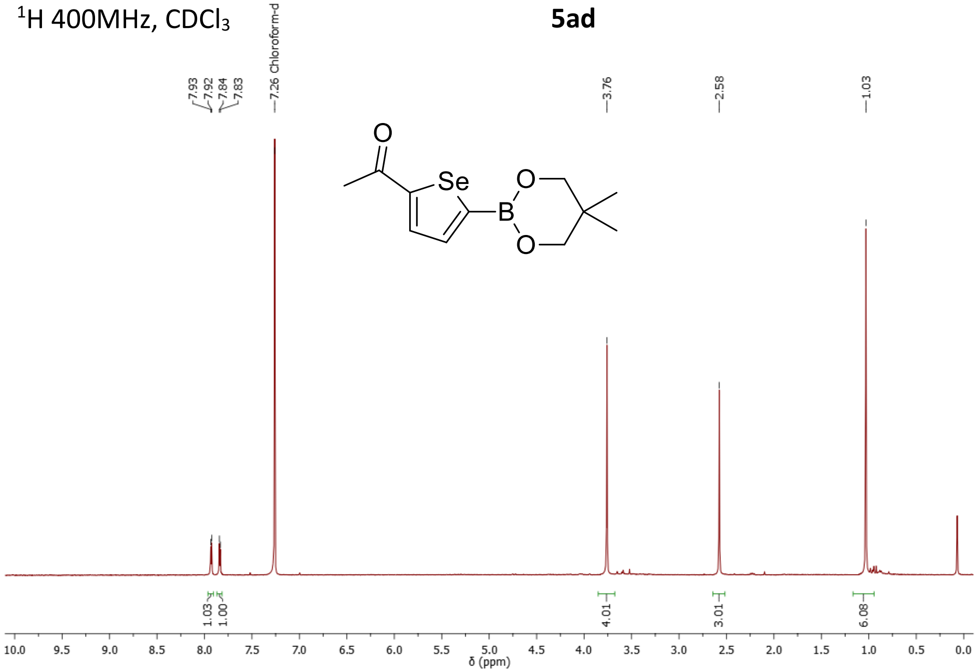


^{13}C 101MHz, $CDCl_3$ **5ac**



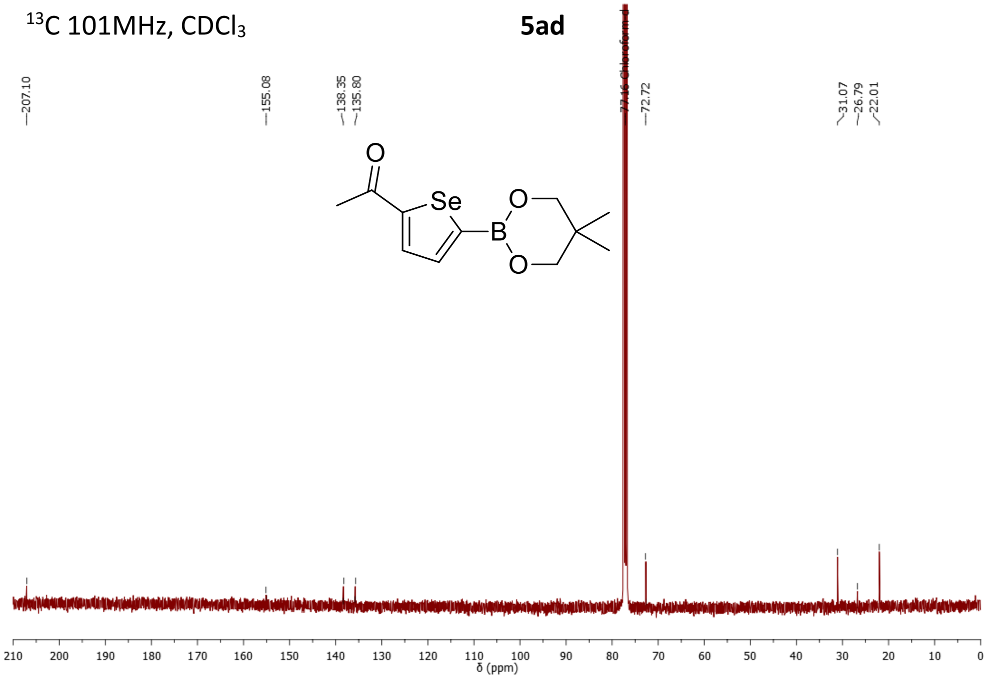
^{1}H 400MHz, CDCl$_3$

5ad

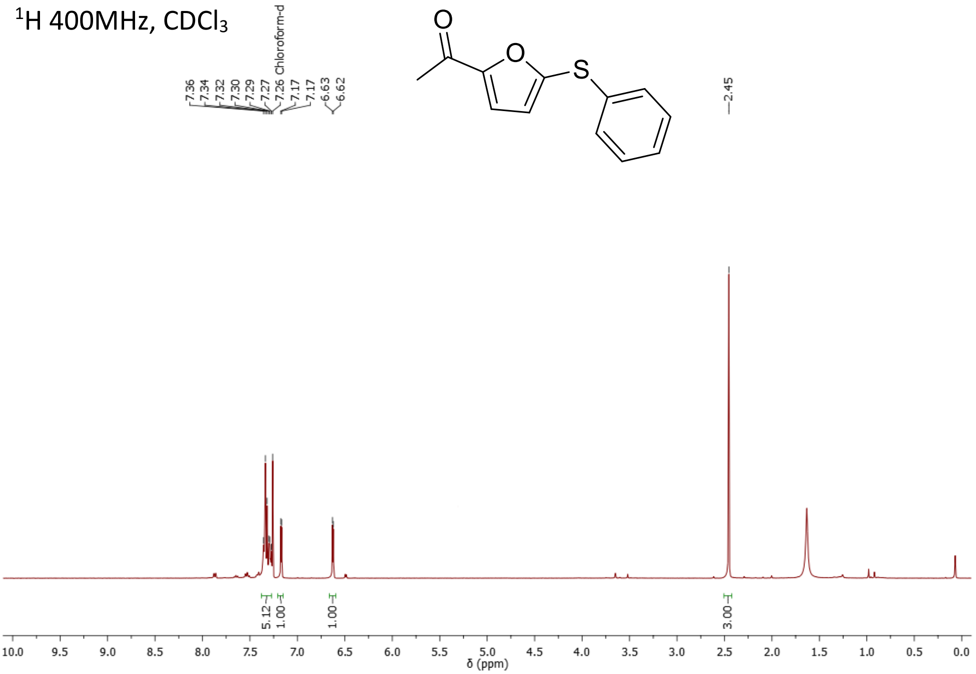


^{13}C 101MHz, CDCl$_3$

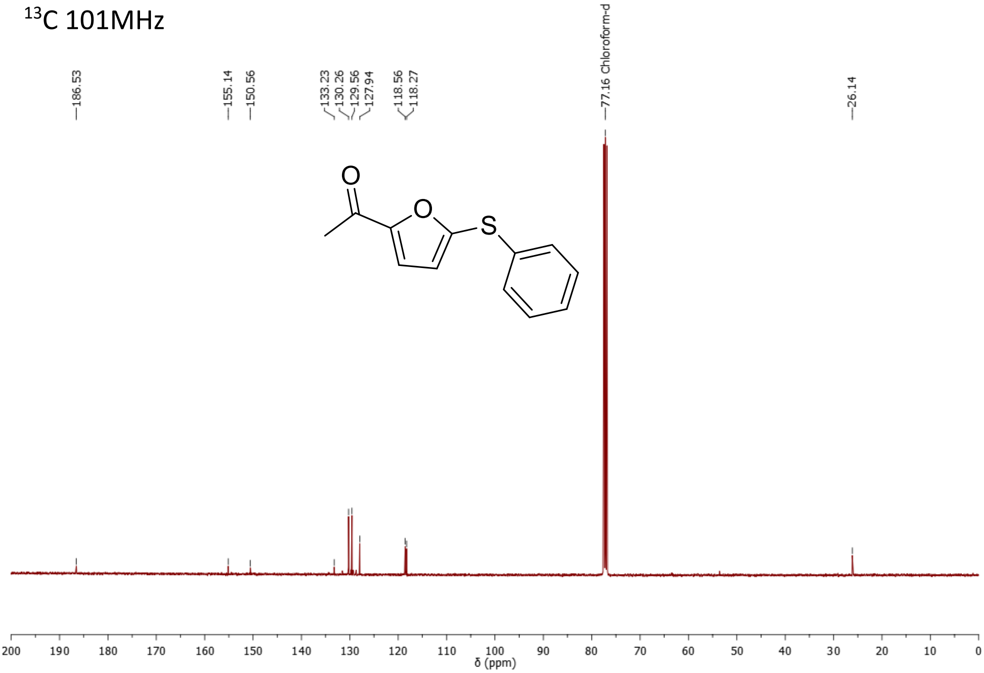
5ad



^{1}H 400MHz, $CDCl_3$

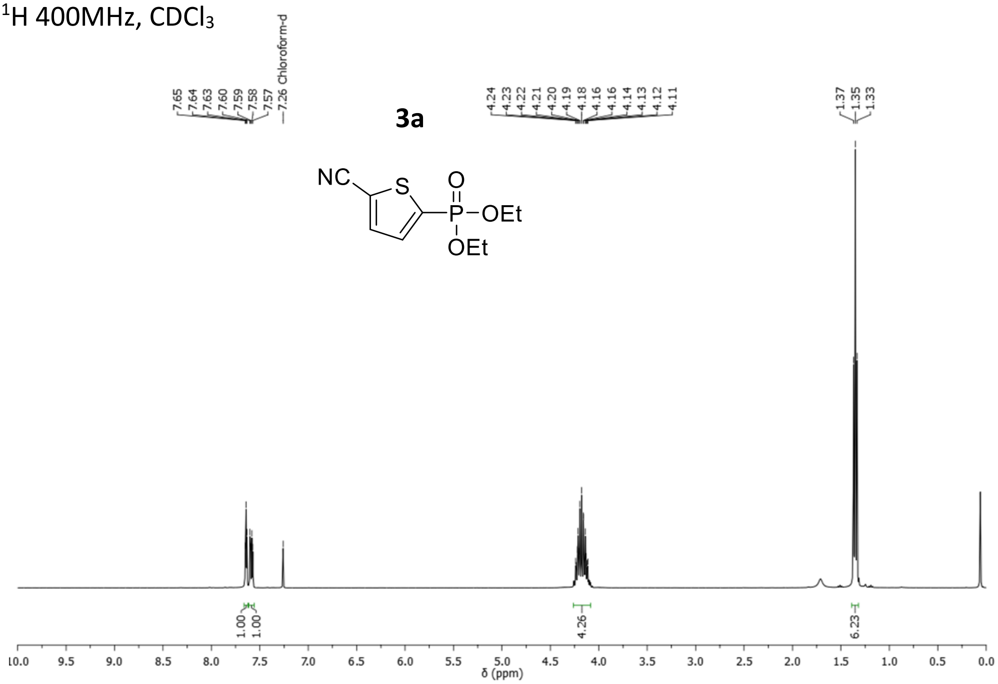


^{13}C 101MHz



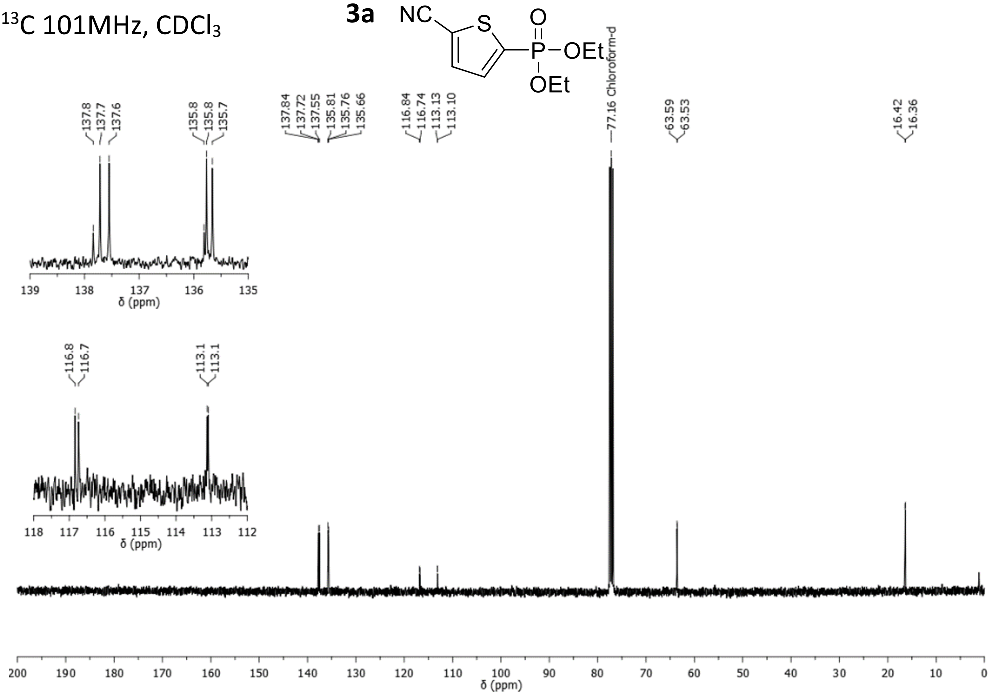
^{1}H 400MHz, CDCl$_3$

3a



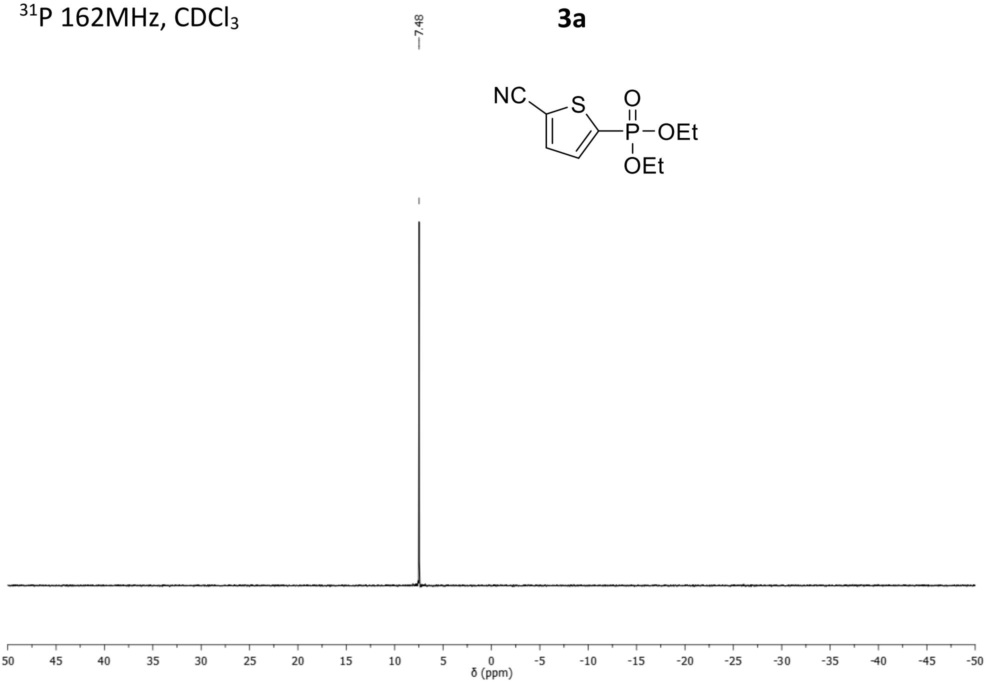
^{13}C 101MHz, CDCl$_3$

3a



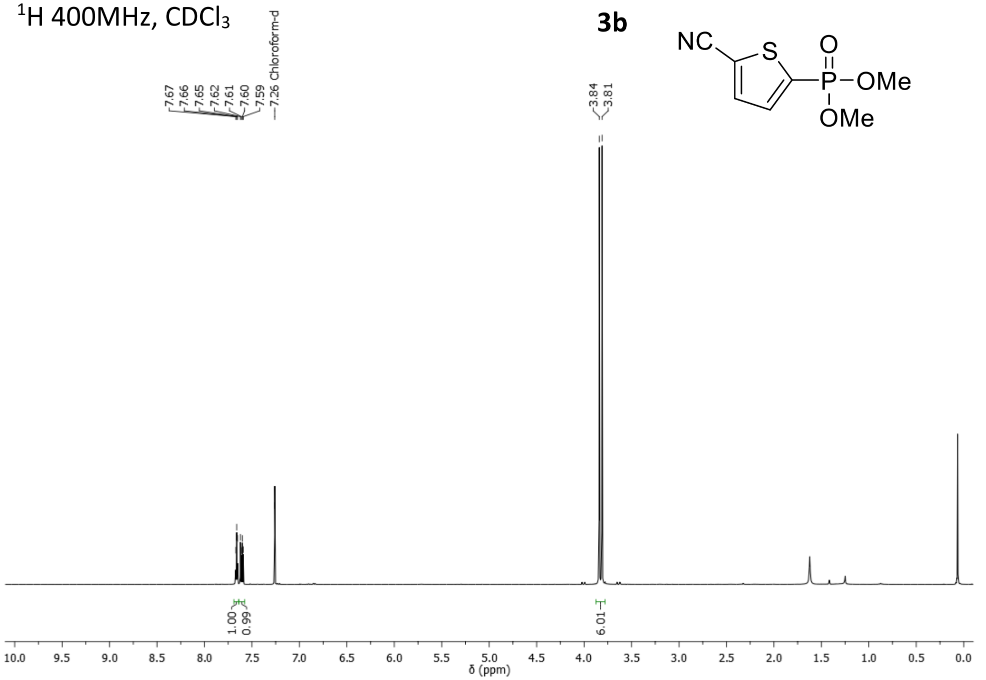
^{31}P 162MHz, $CDCl_3$

3a

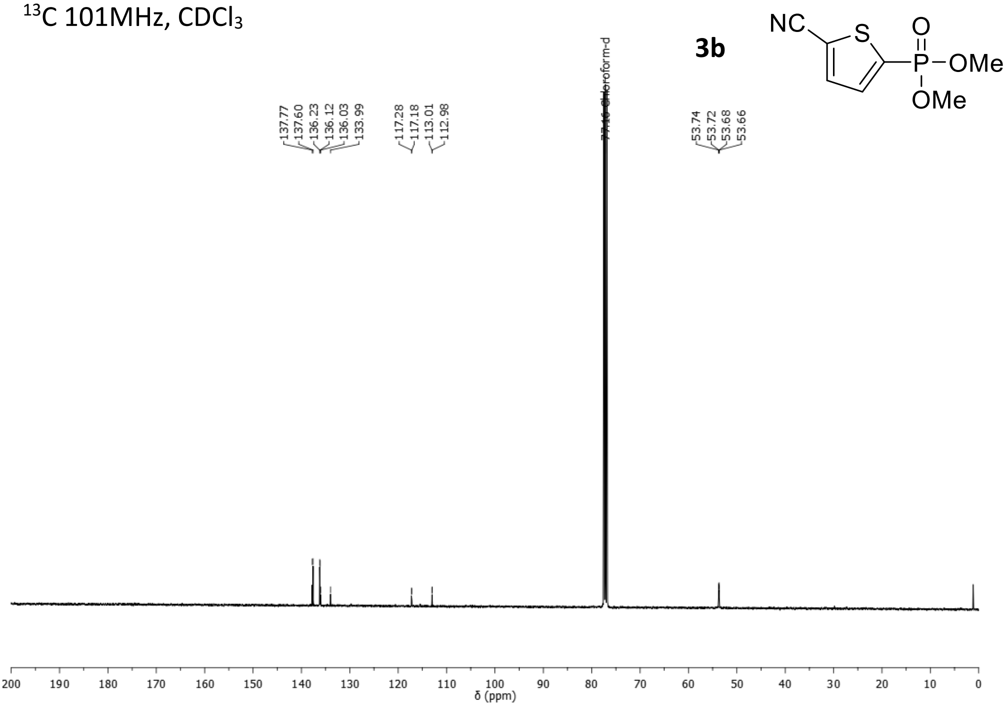


^{1}H 400MHz, $CDCl_3$

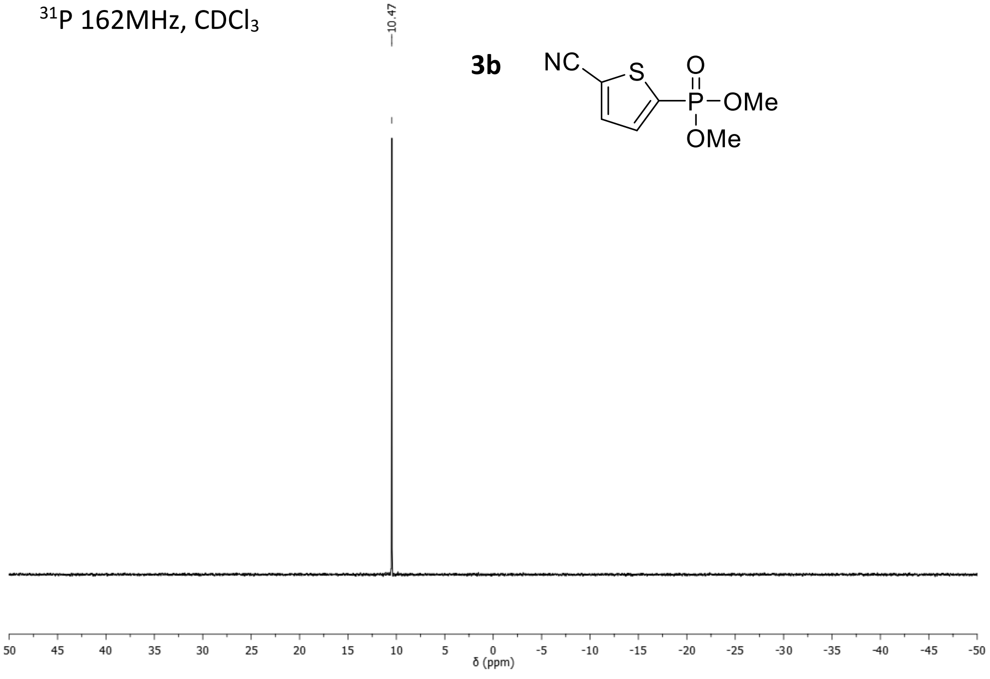
3b

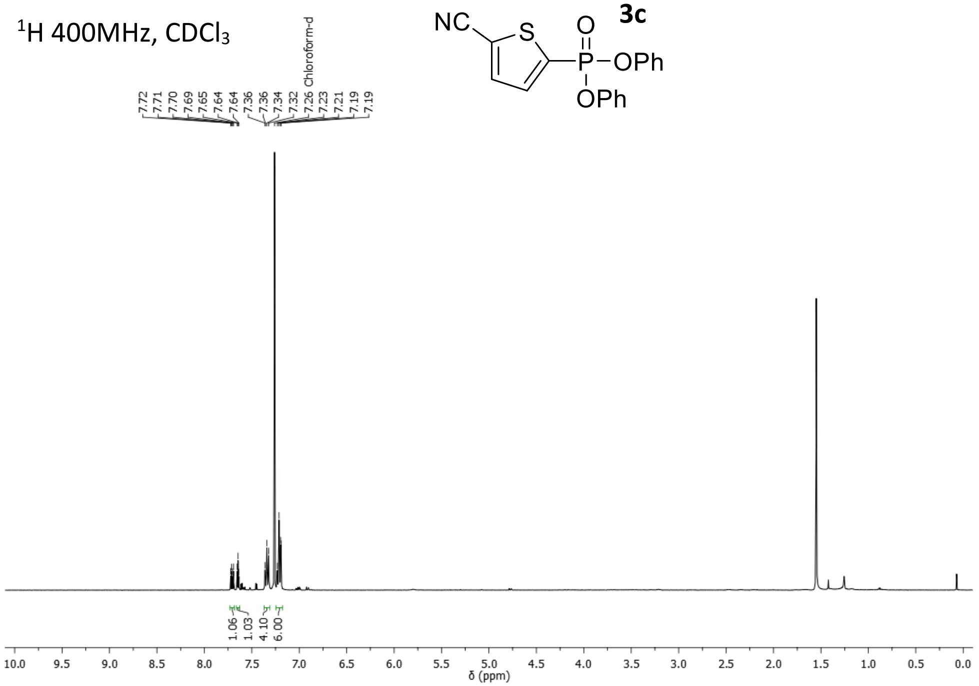


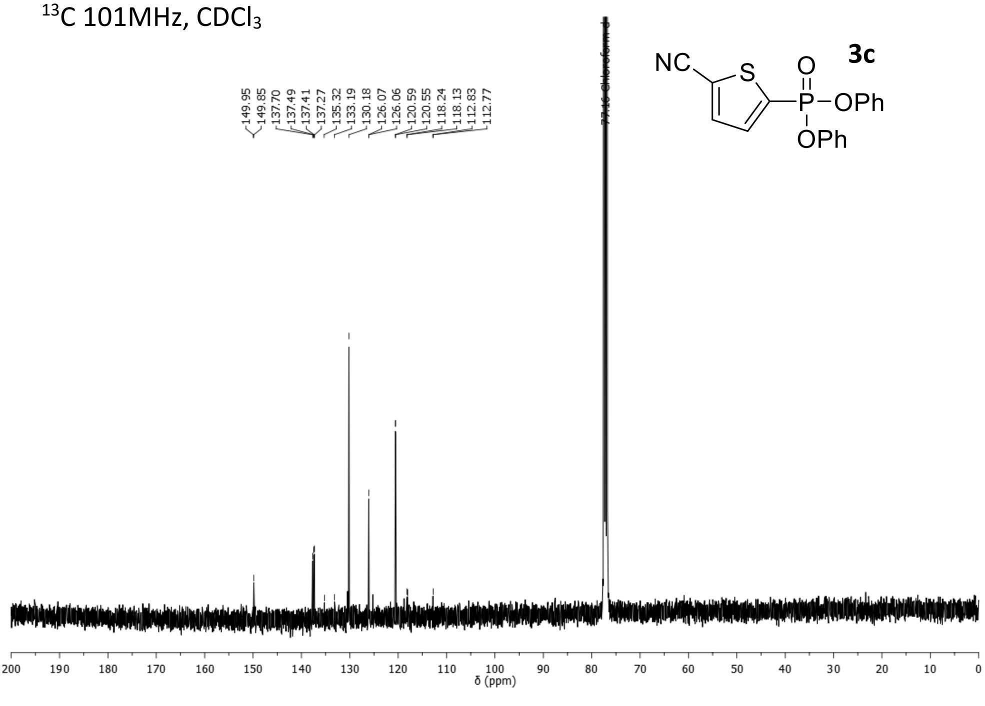
^{13}C 101MHz, CDCl$_3$



^{31}P 162MHz, CDCl$_3$

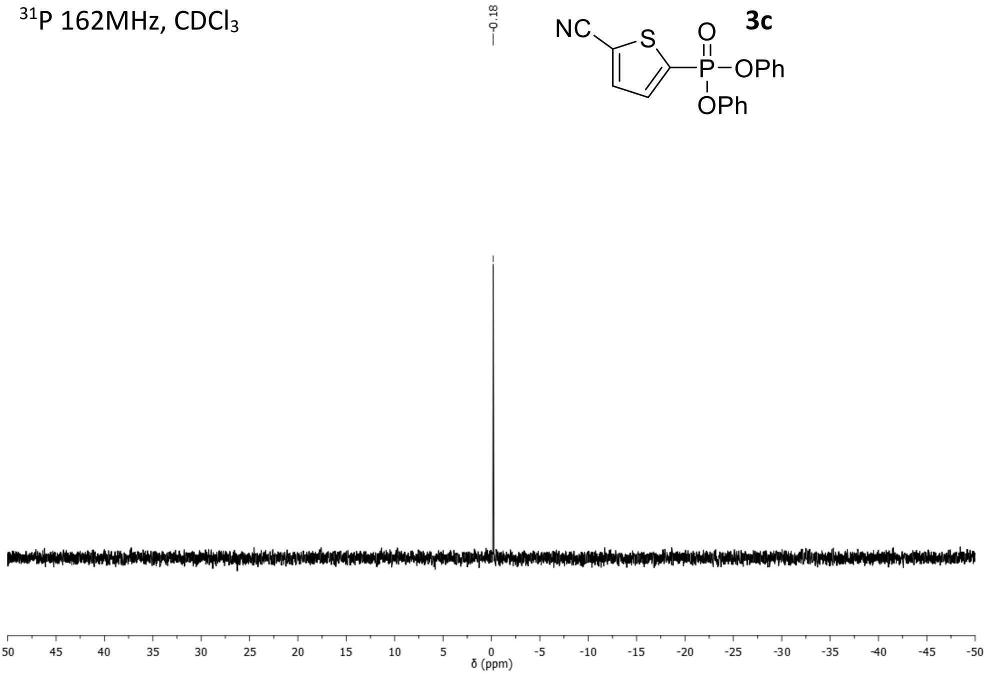



^{1}H 400MHz, CDCl$_3$
3c
NC
S
O
P
OPh
OPh
7.72
7.71
7.70
7.69
7.65
7.64
7.64
7.36
7.36
7.34
7.32
7.26 Chloroform-d
7.23
7.21
7.19
7.19
1.06
1.03
4.10
6.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)


^{13}C 101MHz, CDCl$_3$
3c
NC
S
O
P
OPh
OPh
149.95
149.85
137.70
137.49
137.41
137.27
135.32
133.19
130.18
126.07
126.06
120.59
120.55
118.24
118.13
112.83
112.77
77.16 Chloroform-d
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)

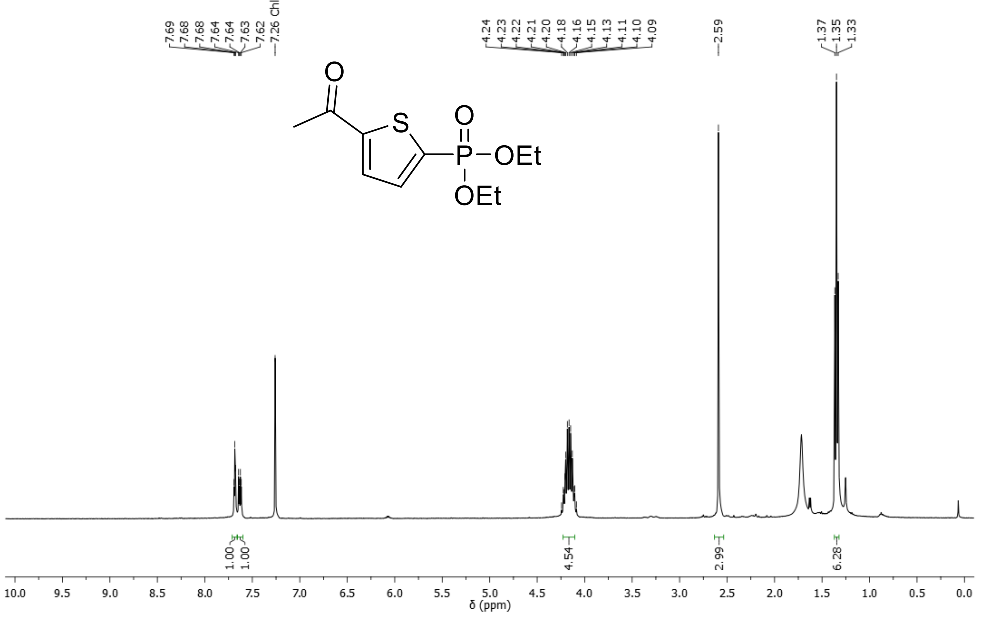
^{31}P 162MHz, CDCl$_3$

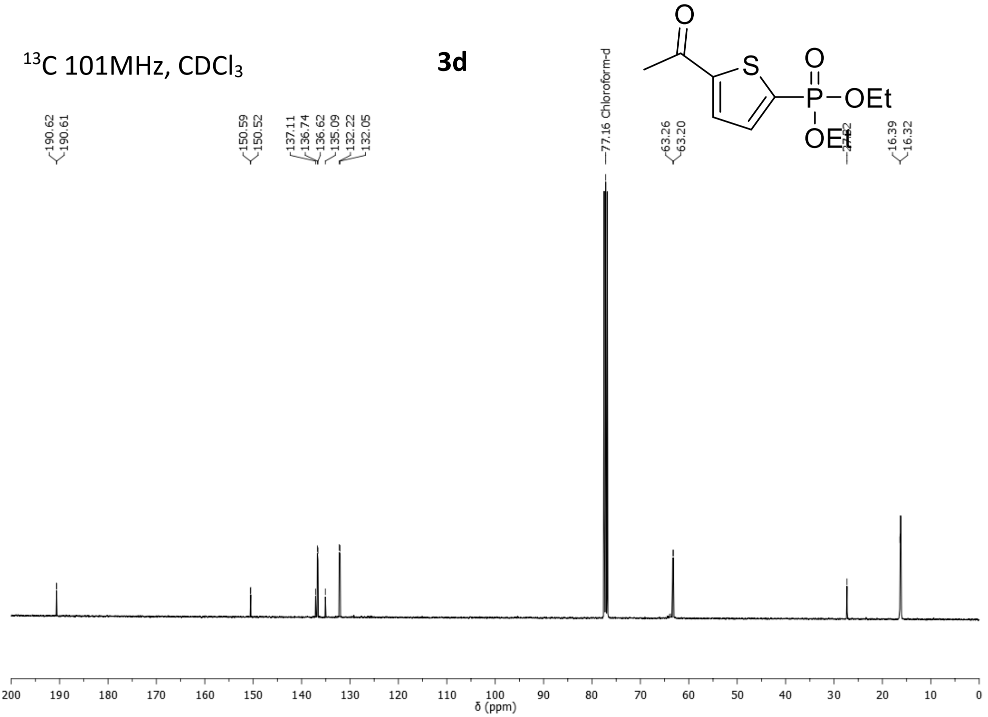
3c

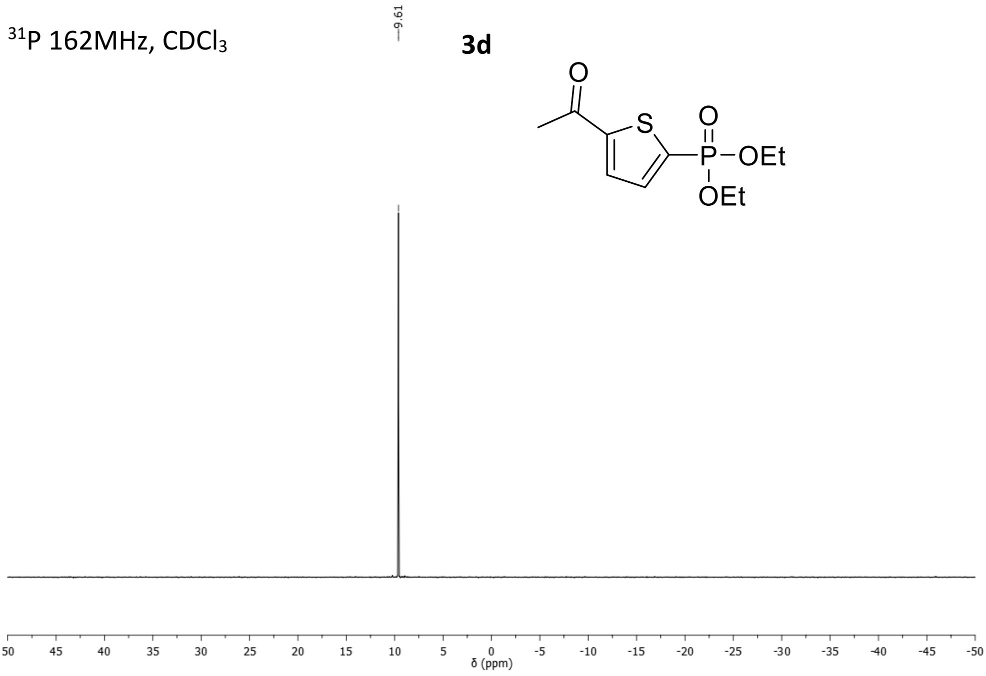


^{1}H 400MHz, CDCl$_3$

3d

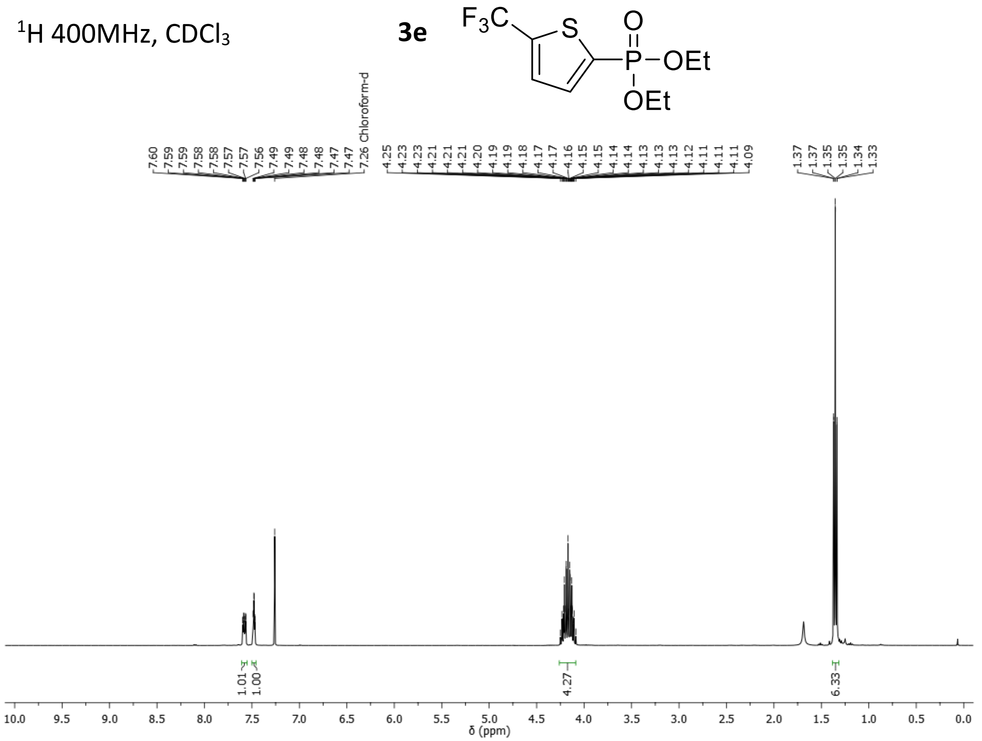



^{13}C 101MHz, CDCl$_3$
3d
190.62
190.61
150.59
150.52
137.11
136.74
136.62
135.09
132.22
132.05
77.16 Chloroform-d
63.26
63.20
16.39
16.32
O
S
O
P
OEt
OEt
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)


^{31}P 162MHz, CDCl$_3$
9.61
3d
O
S
O
P
OEt
OEt
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
δ (ppm)

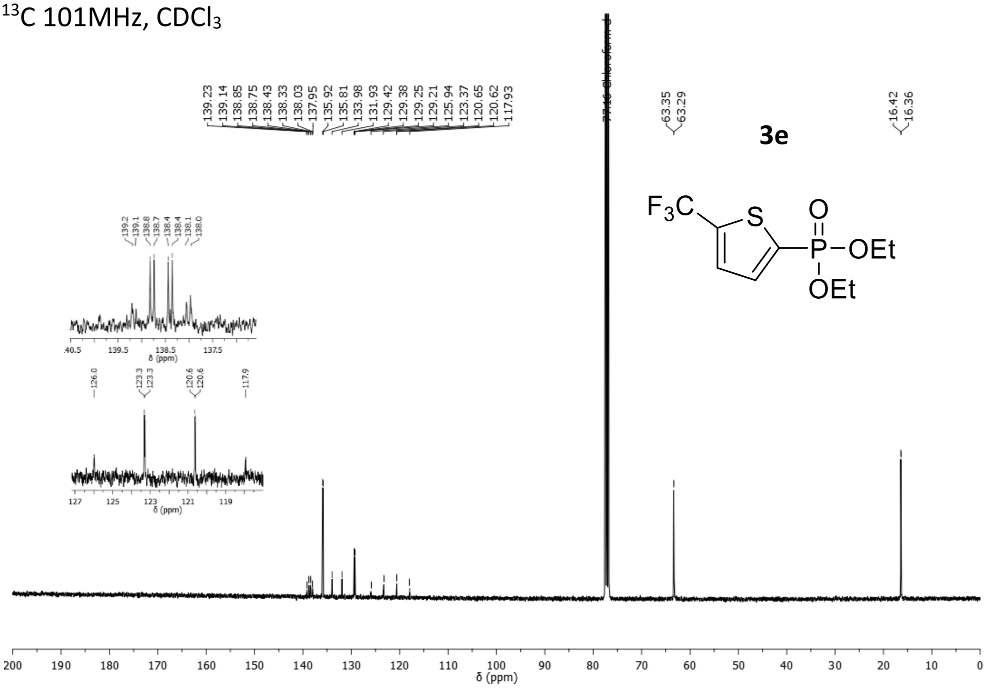
^{1}H 400MHz, CDCl$_3$

3e



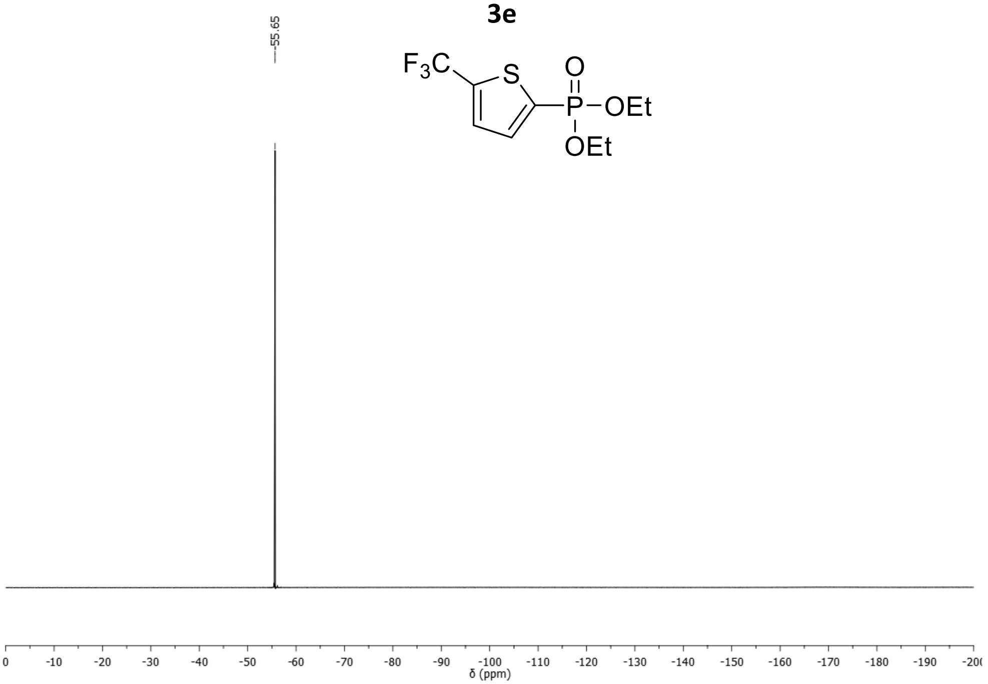
^{13}C 101MHz, CDCl$_3$

3e



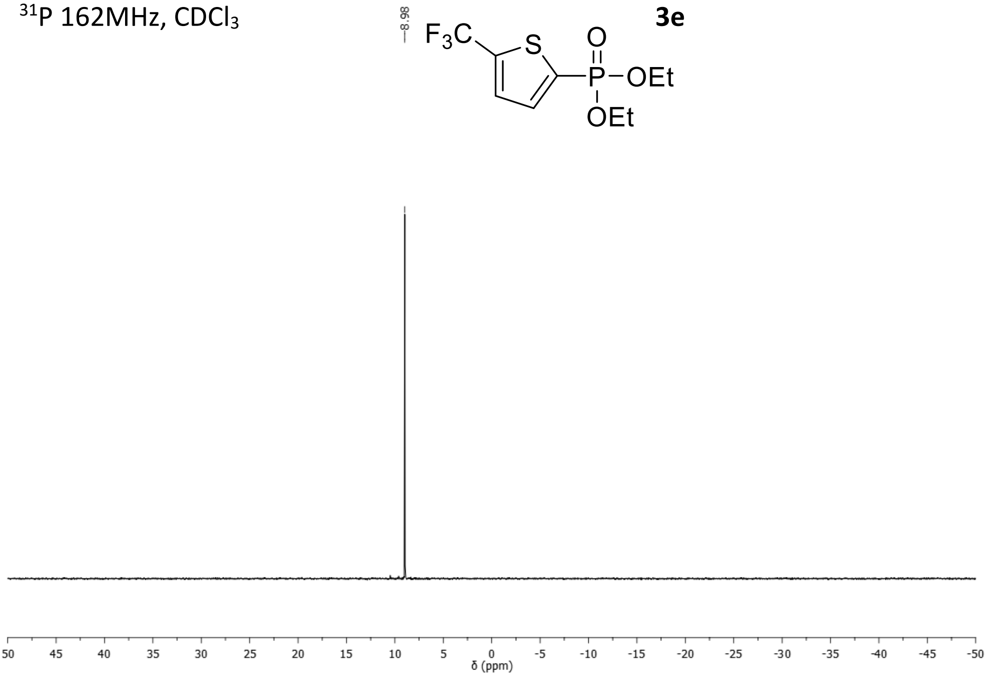
^{19}F 376 MHz, CDCl$_3$

3e

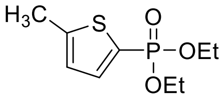


^{31}P 162MHz, CDCl$_3$

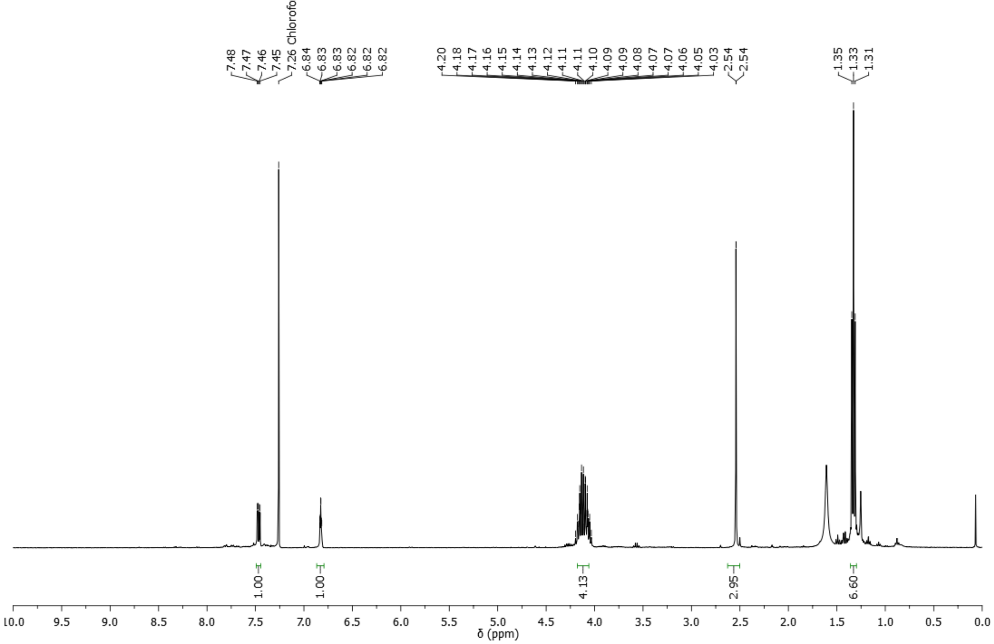
3e



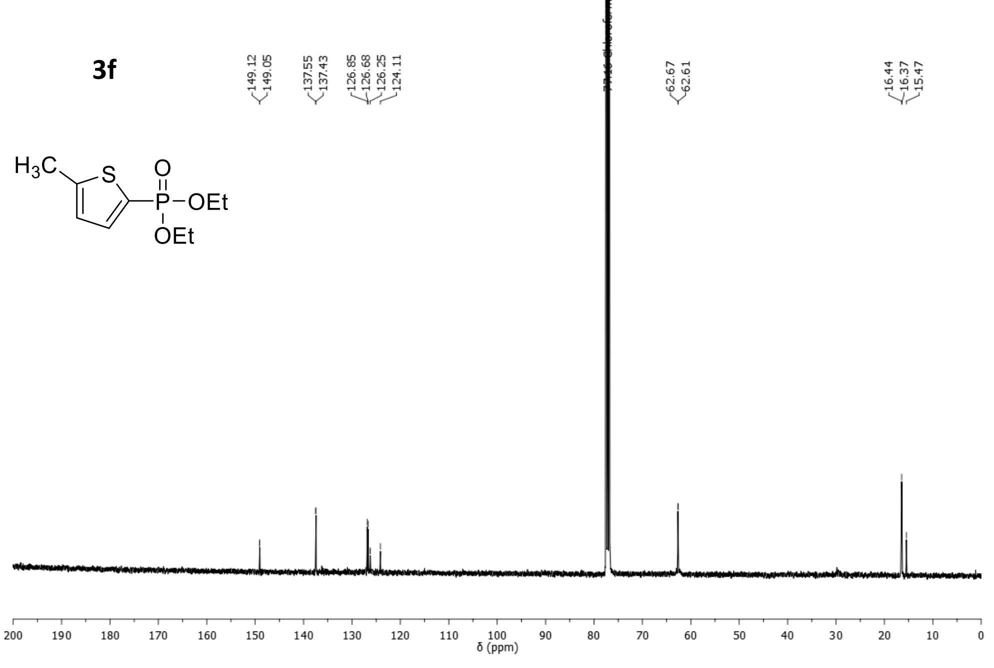
^{1}H 400MHz, CDCl$_3$



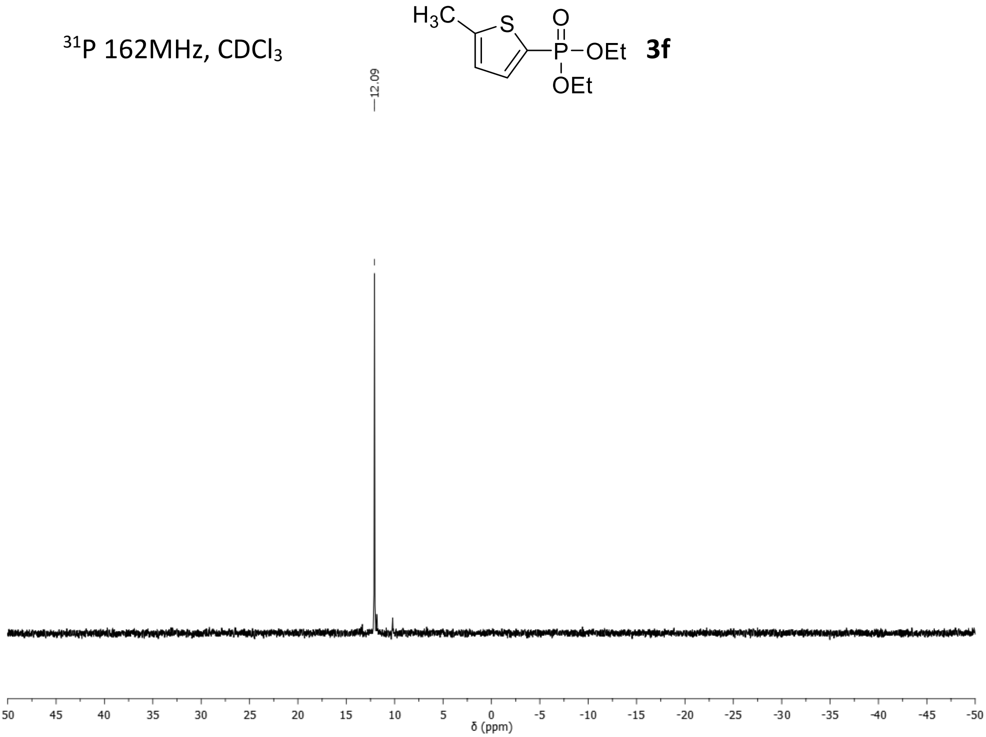
3f



^{13}C 101MHz, CDCl$_3$

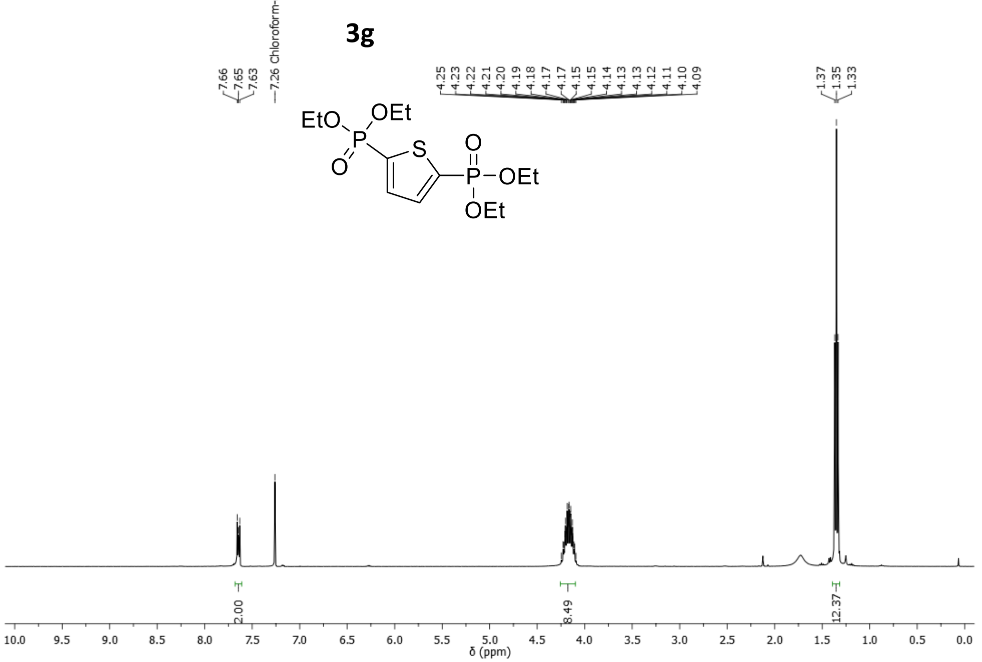


^{31}P 162MHz, CDCl$_3$



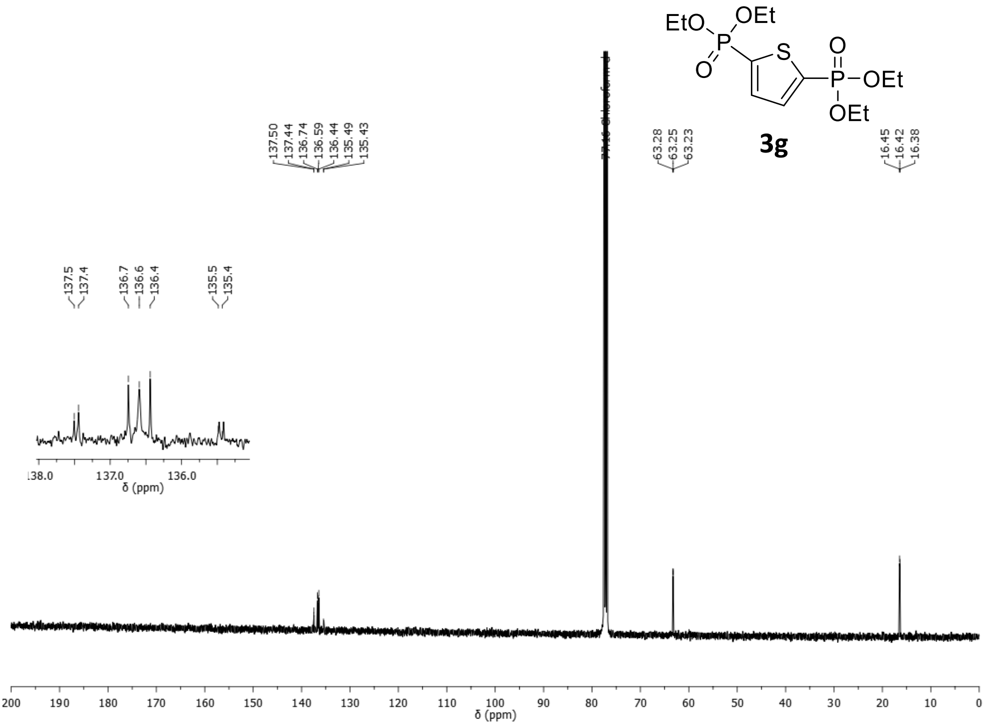
3f

^{1}H 400MHz, CDCl$_3$



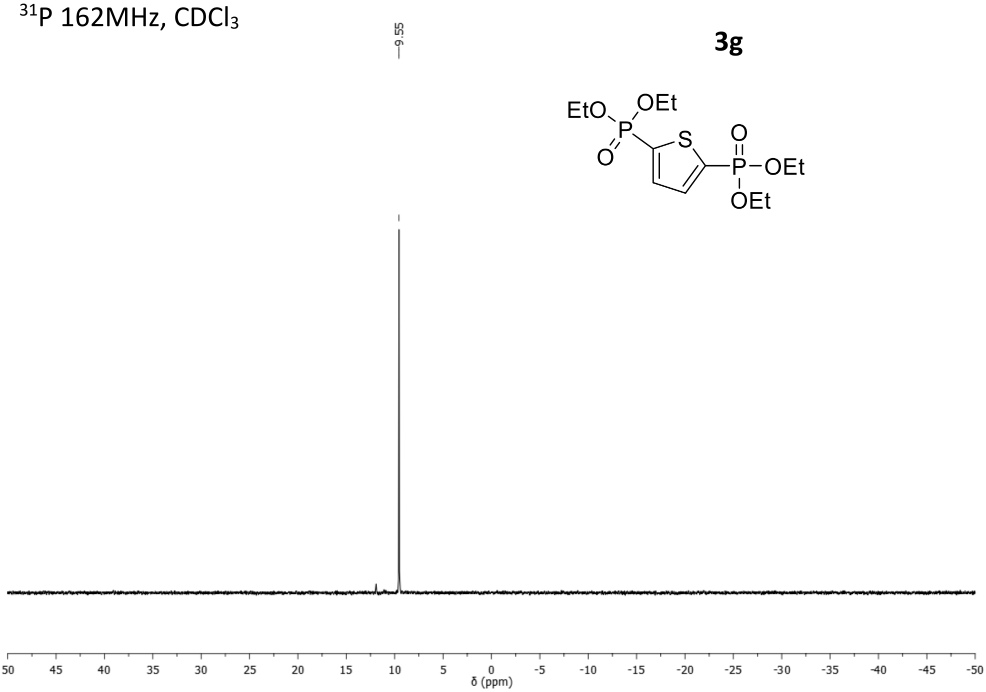
3g

^{13}C 101MHz, CDCl$_3$



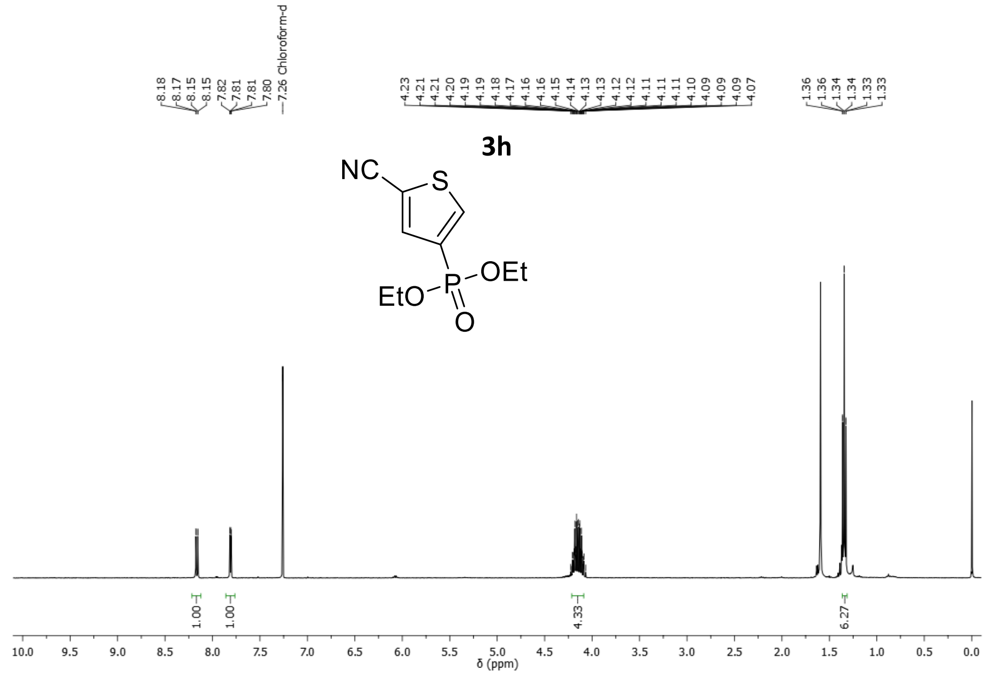
3g

^{31}P 162MHz, CDCl$_3$



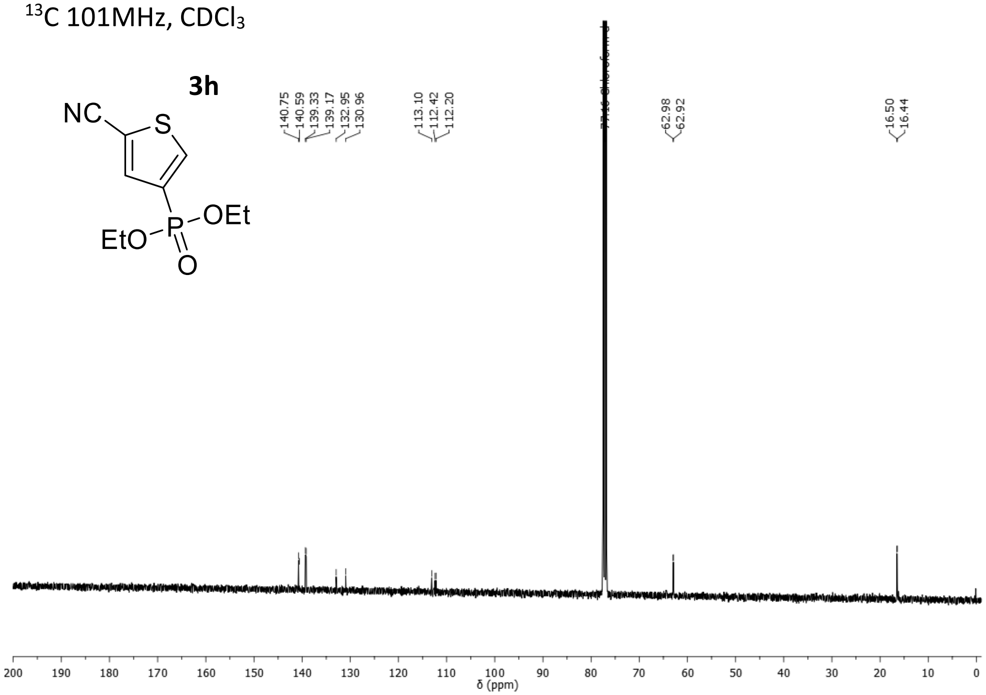
3g

^1H 400MHz, $CDCl_3$



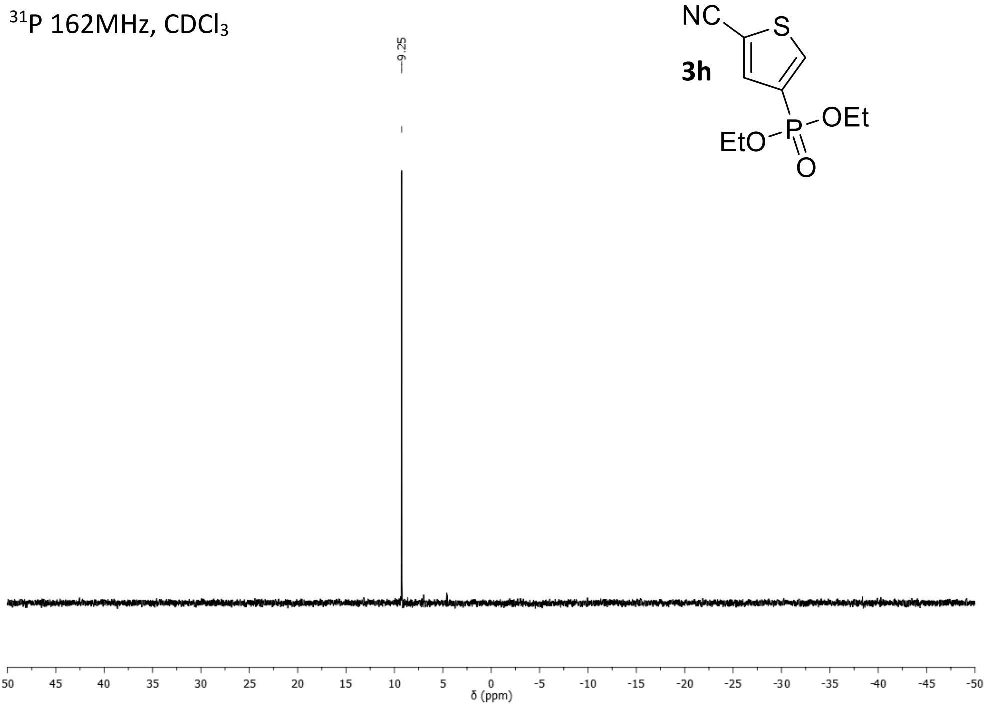
3h

^{13}C 101MHz, $CDCl_3$



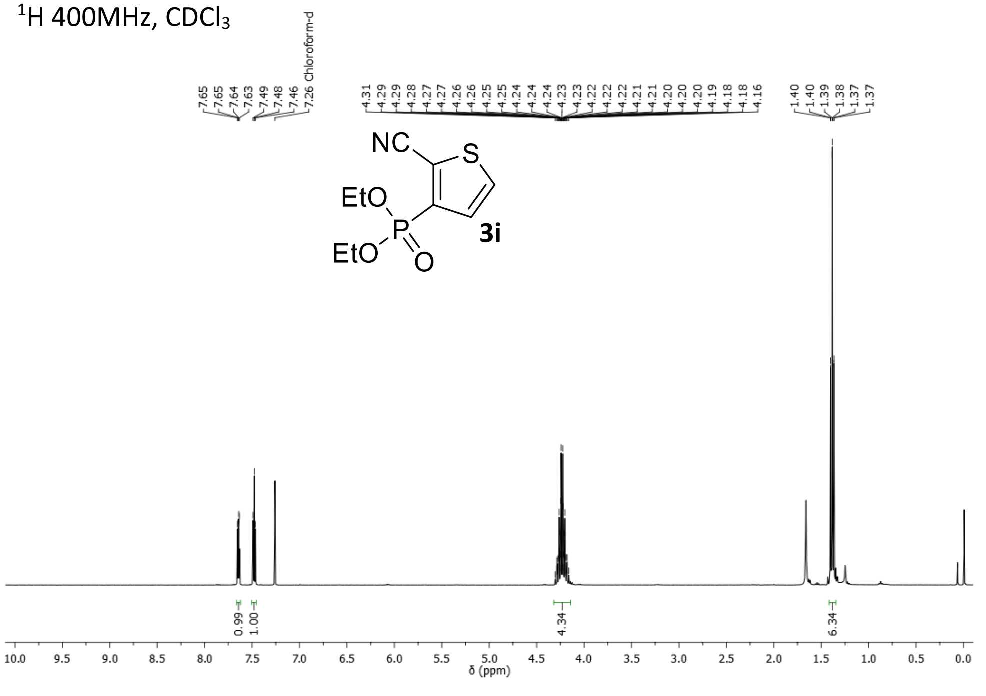
3h

^{31}P 162MHz, CDCl$_3$



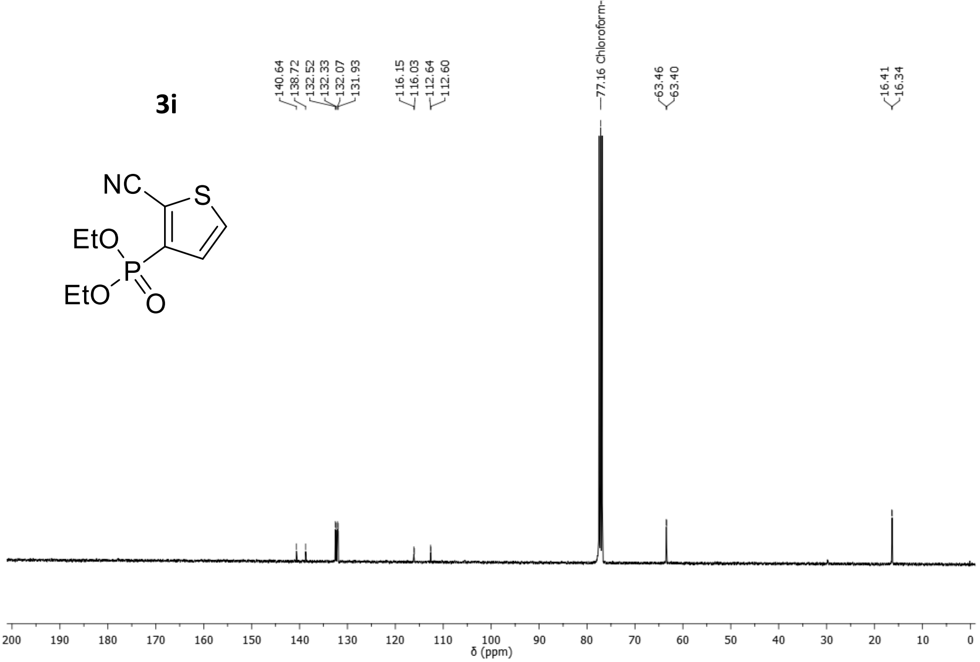
3h

^{1}H 400MHz, CDCl$_3$



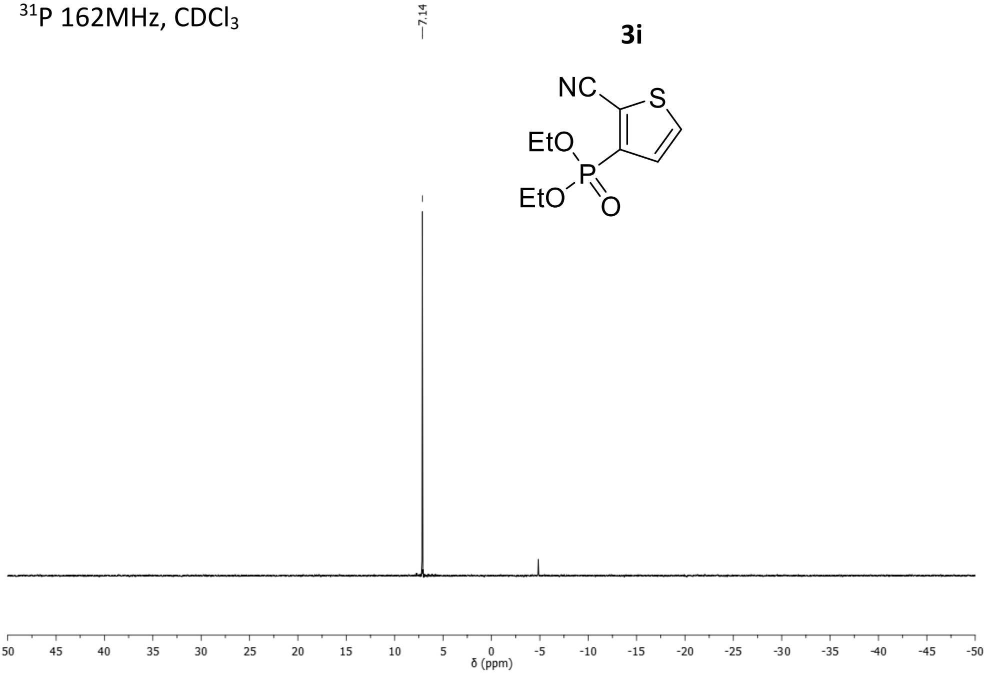
3i

^{13}C 101MHz, $CDCl_3$

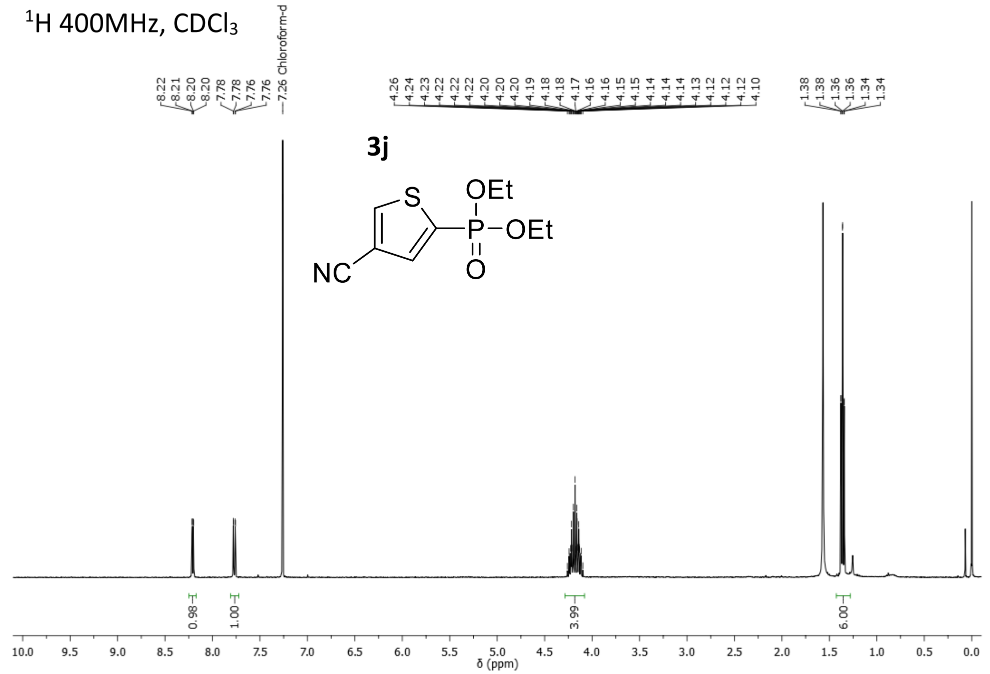


3i

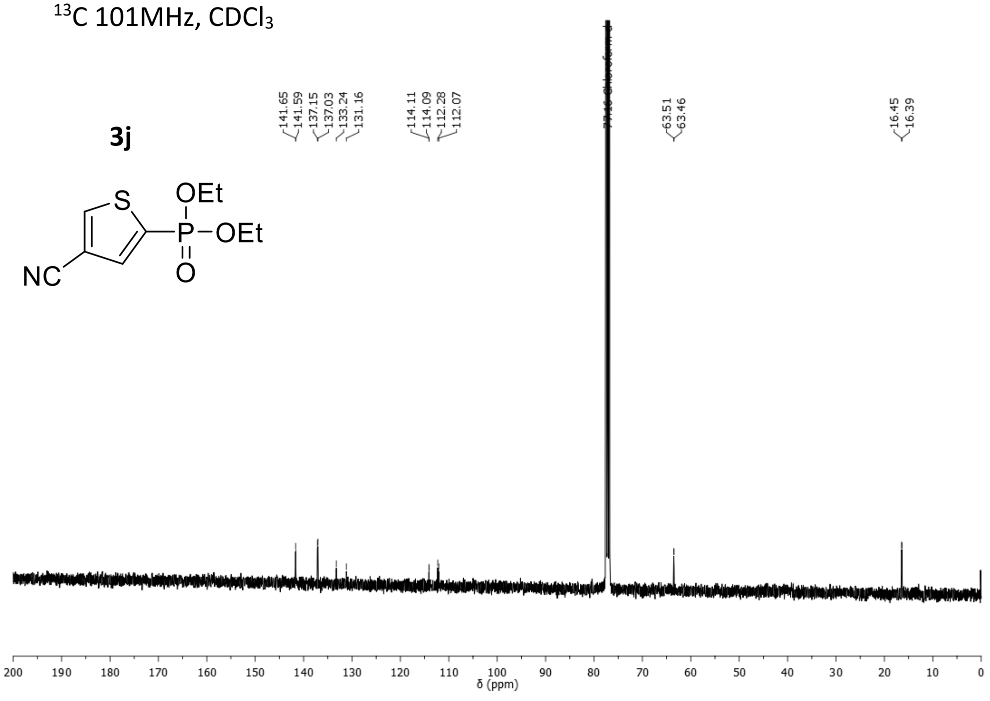
^{31}P 162MHz, $CDCl_3$



3i

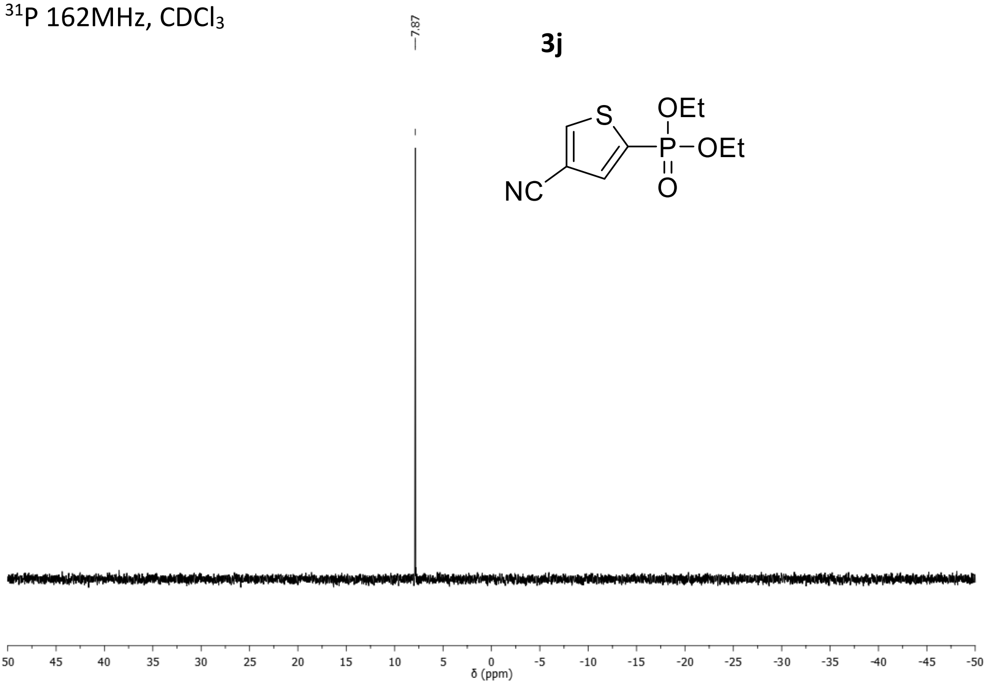

^{1}H 400MHz, $CDCl_3$

3j


^{13}C 101MHz, $CDCl_3$

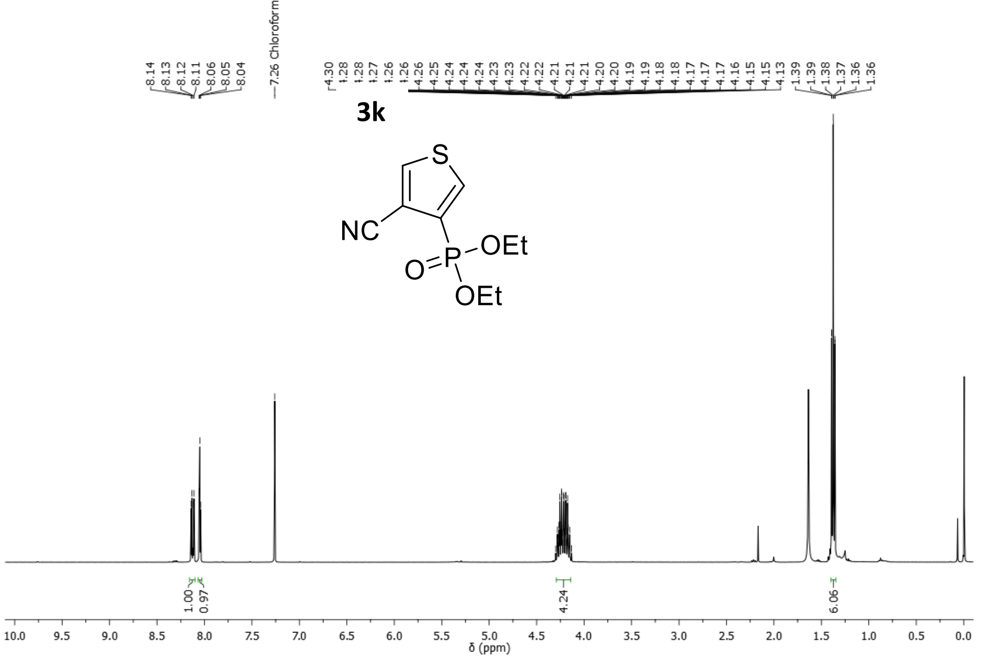
3j

^{31}P 162MHz, $CDCl_3$

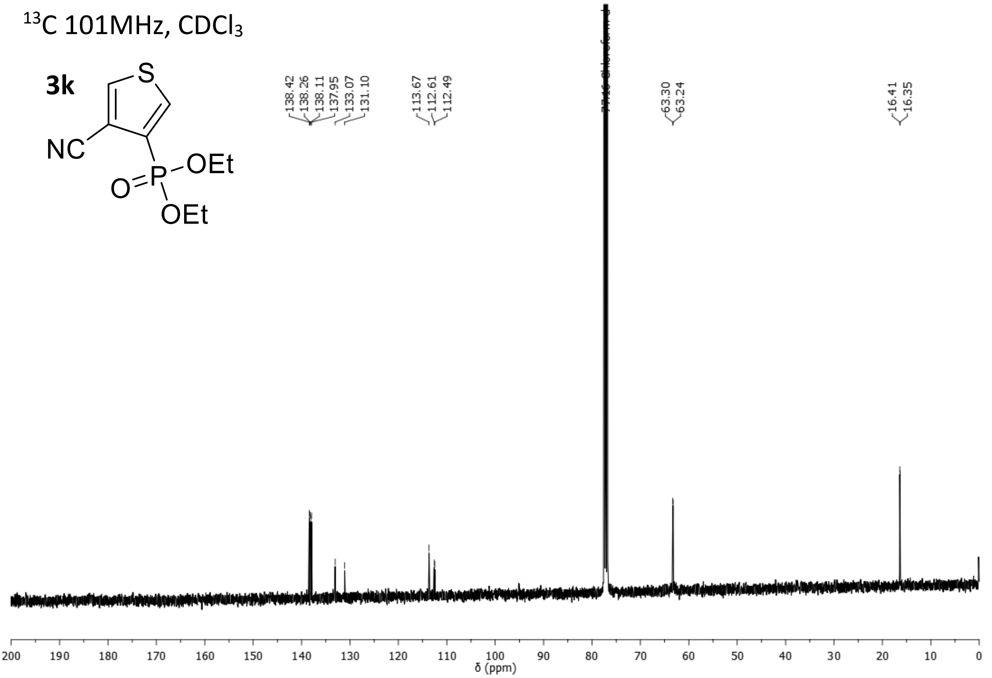


3j

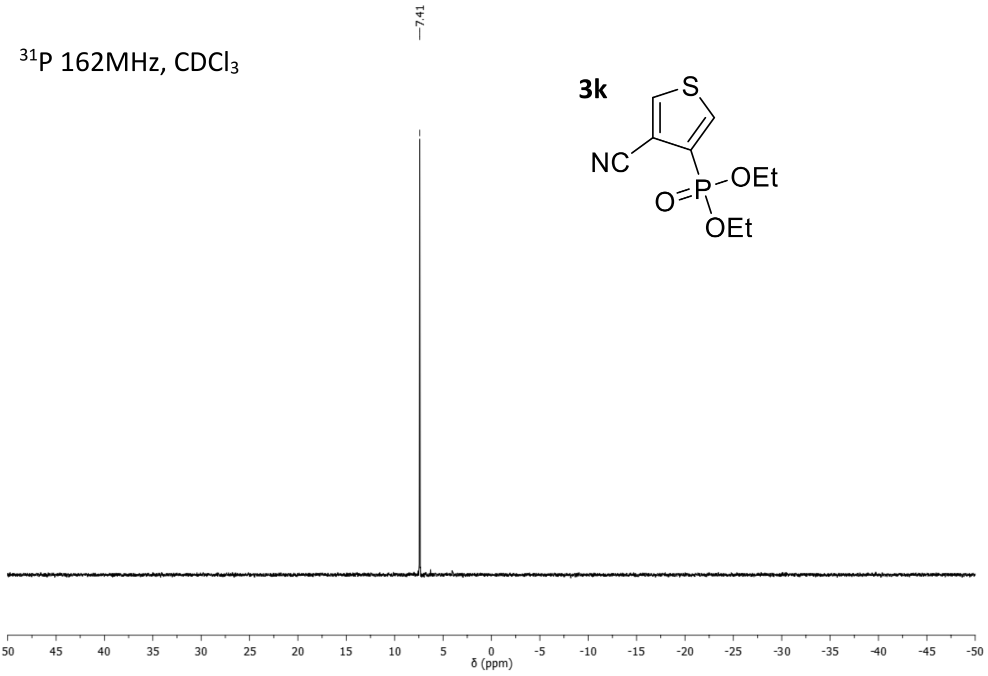
^{1}H 400MHz, $CDCl_3$



3k


^{13}C 101MHz, $CDCl_3$

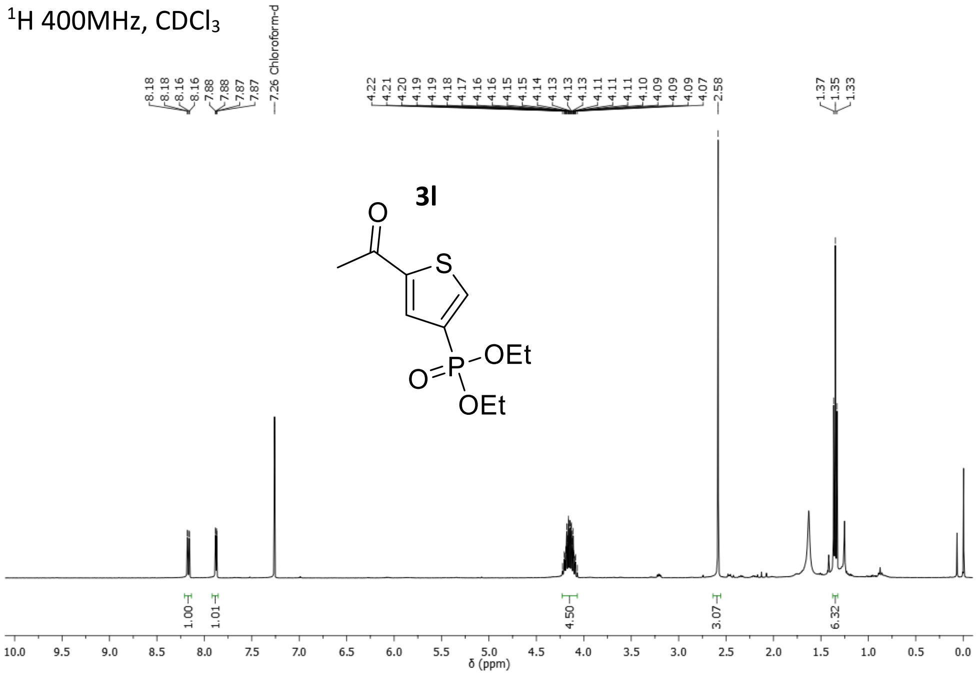
3k


^{31}P 162MHz, $CDCl_3$

3k

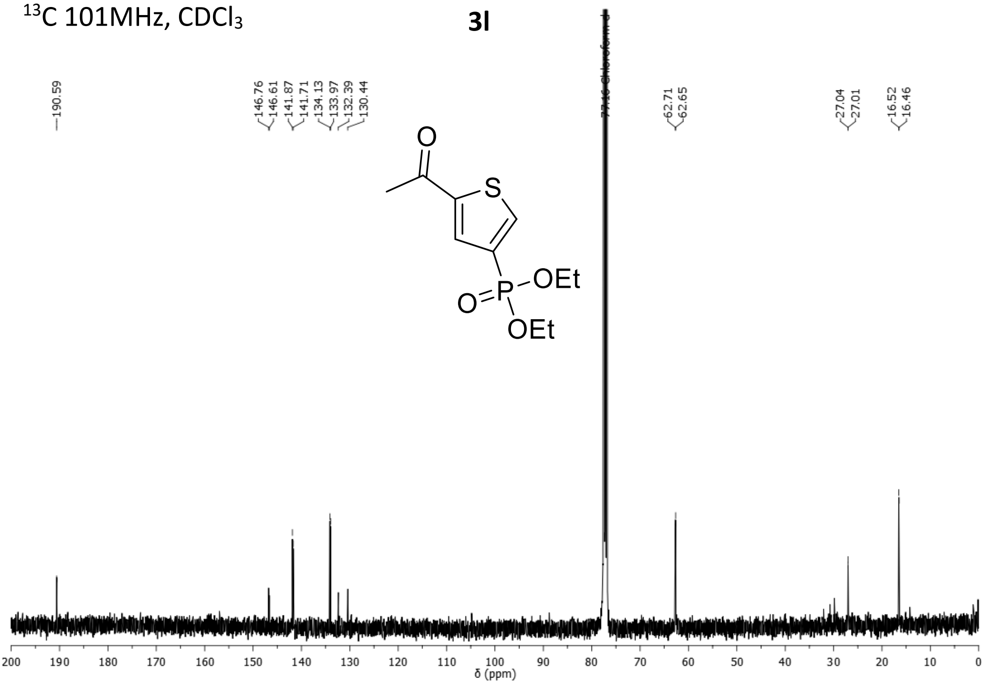
^{1}H 400MHz, $CDCl_3$

3l

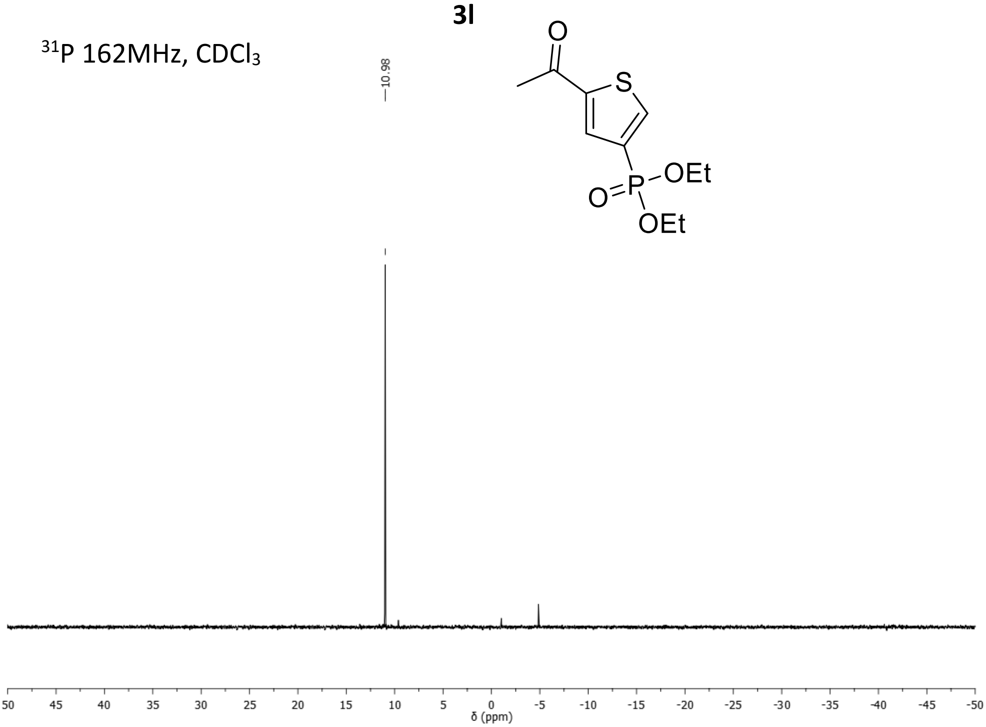


^{13}C 101MHz, $CDCl_3$

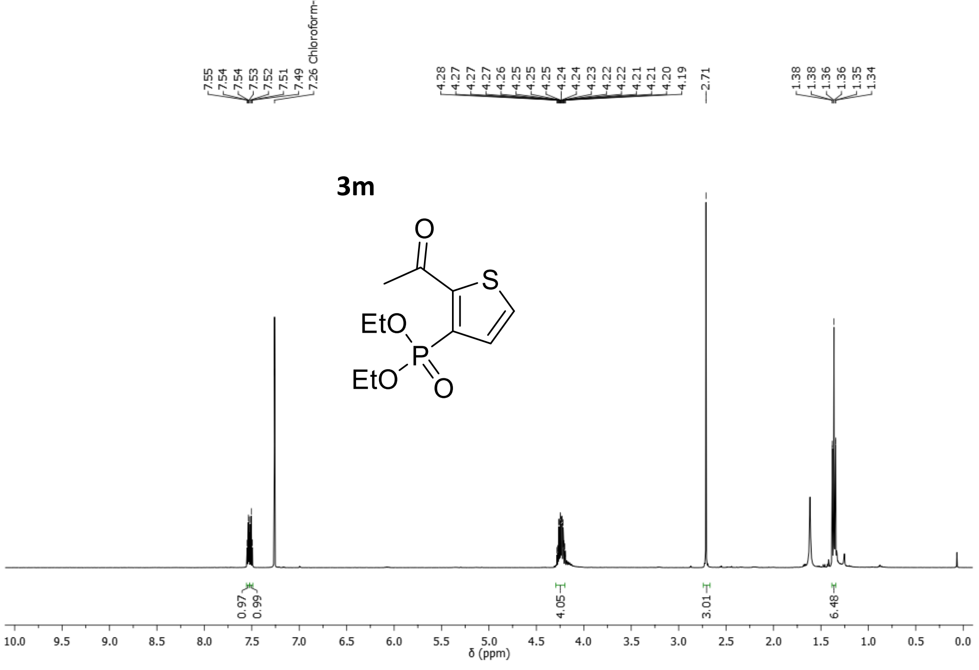
3l



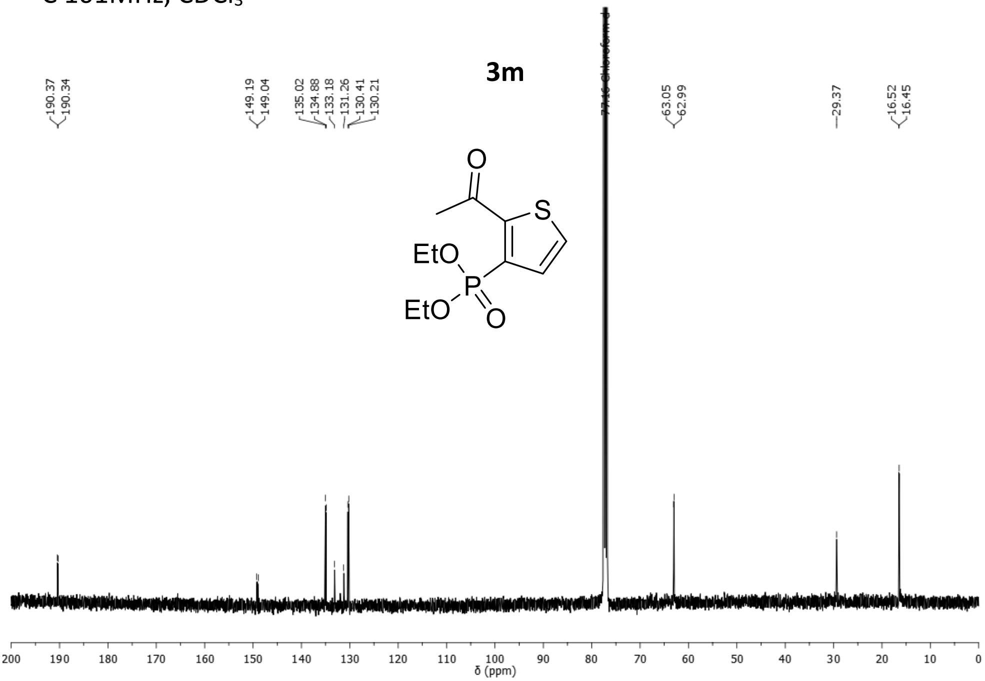
3l


^{31}P 162MHz, CDCl$_3$
10.98
O
S
O=P
OEt
OEt
50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50
δ (ppm)

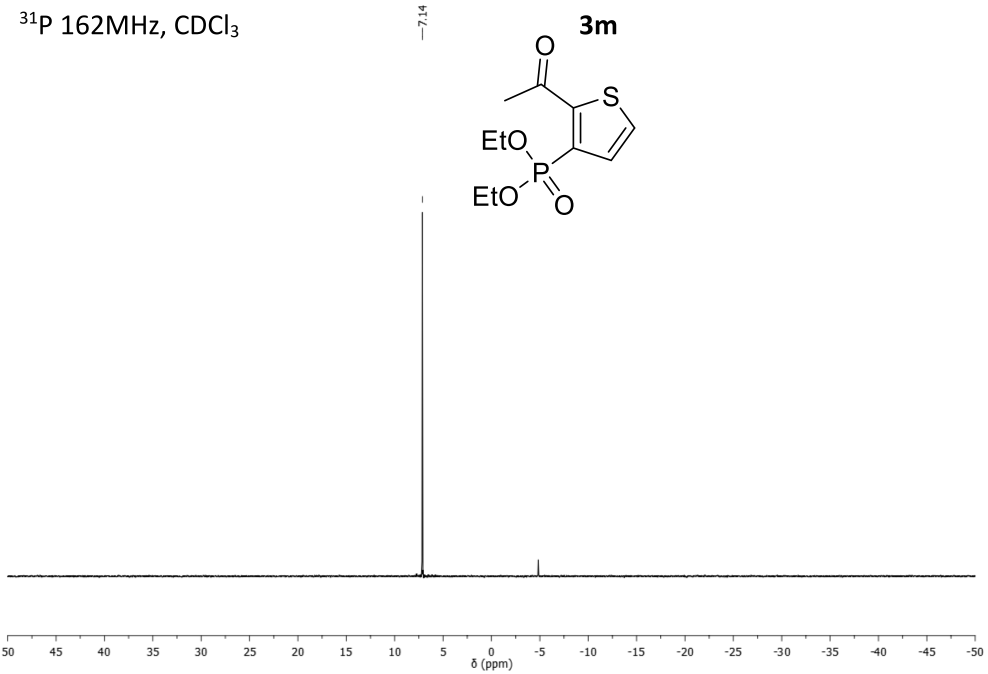
3m


^{1}H 400MHz, CDCl$_3$
7.55
7.54
7.54
7.53
7.52
7.51
7.49
7.26 Chloroform-d
4.28
4.27
4.27
4.27
4.26
4.25
4.25
4.25
4.24
4.24
4.23
4.22
4.22
4.21
4.21
4.20
4.19
2.71
1.38
1.38
1.36
1.36
1.35
1.34
O
S
EtO
P
EtO
O
0.97
0.99
4.05
3.01
6.48
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)

^{13}C 101MHz, CDCl$_3$

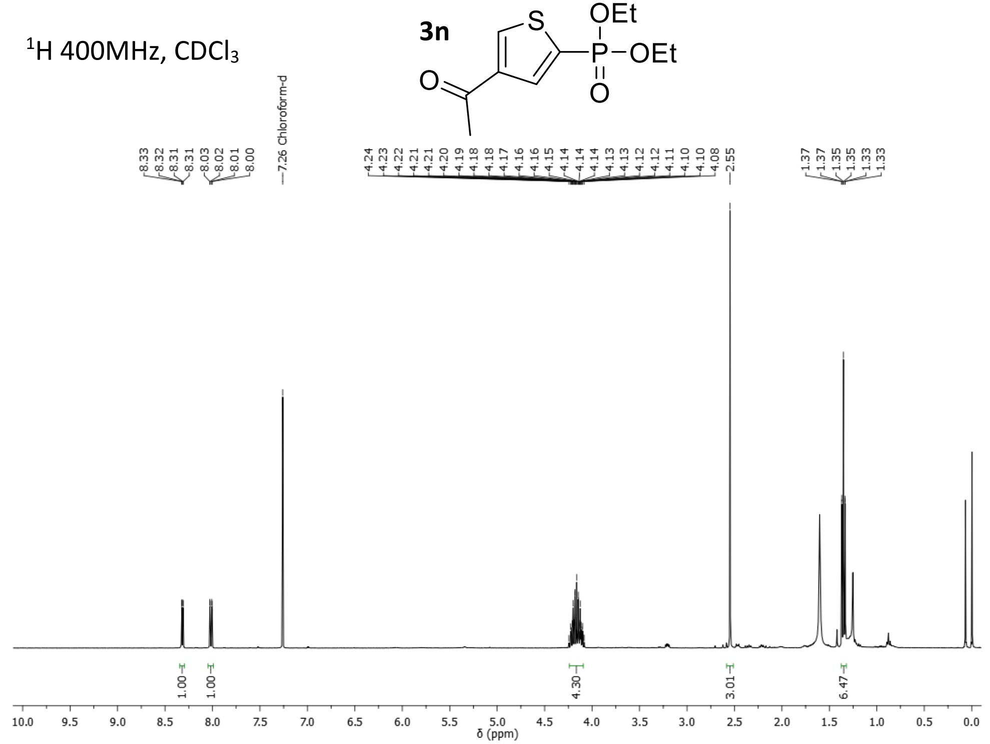


^{31}P 162MHz, CDCl$_3$



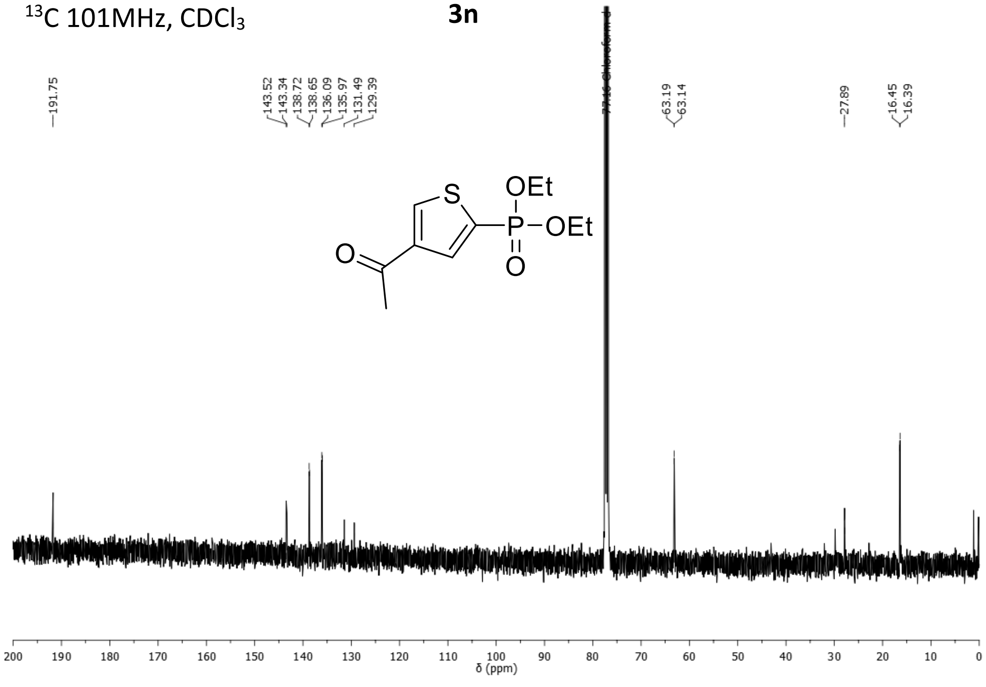
^{1}H 400MHz, $CDCl_3$

3n



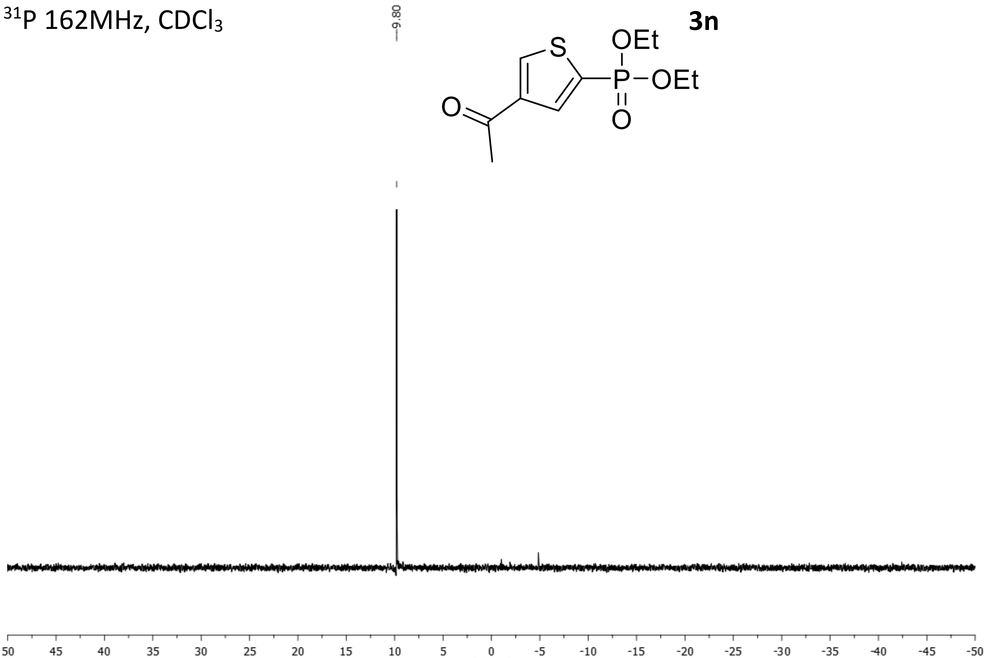
^{13}C 101MHz, $CDCl_3$

3n



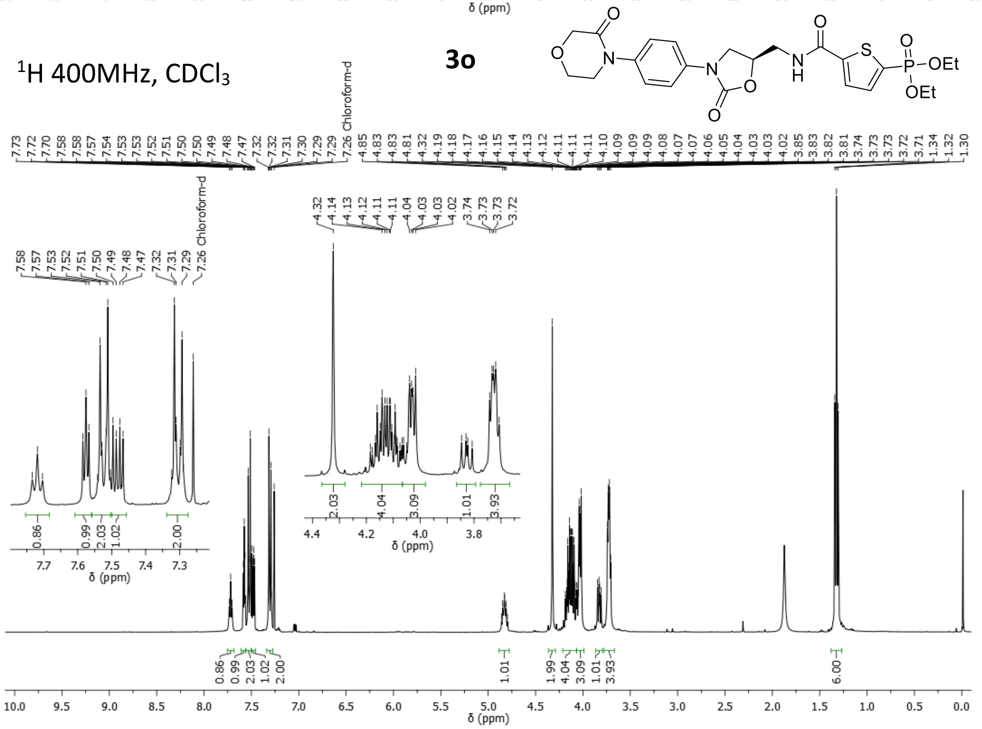
^{31}P 162MHz, $CDCl_3$

3n



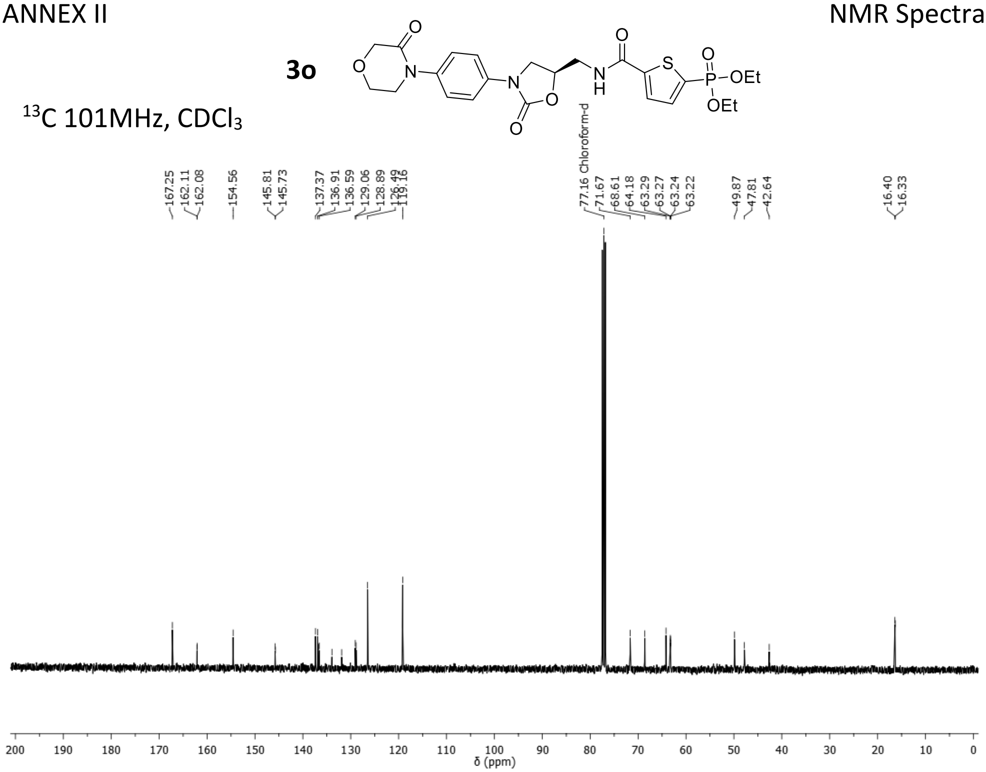
^{1}H 400MHz, $CDCl_3$

3o



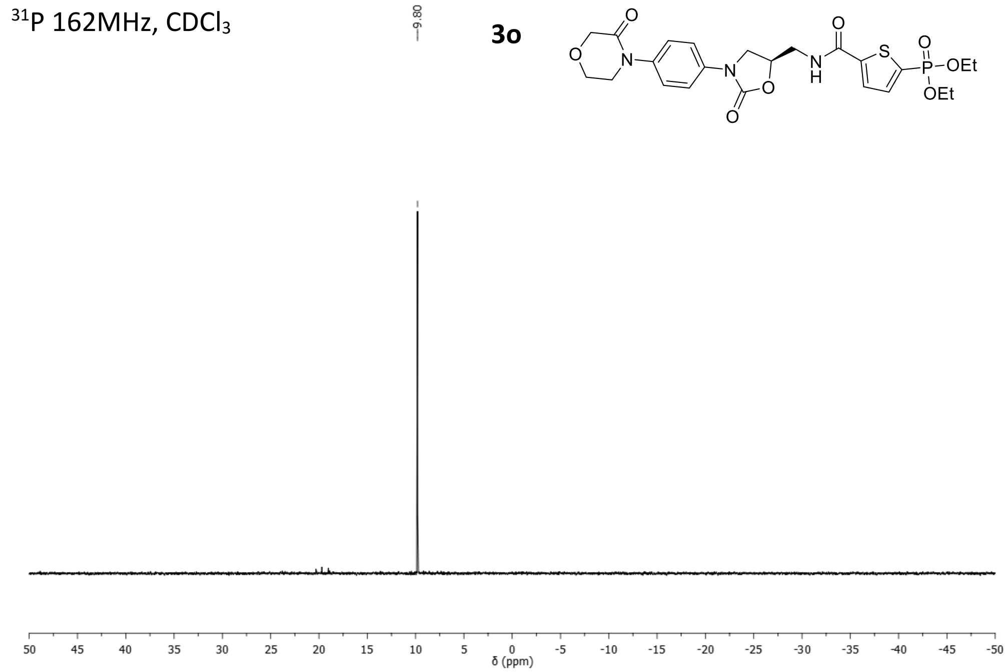
3o

^{13}C 101MHz, CDCl$_3$



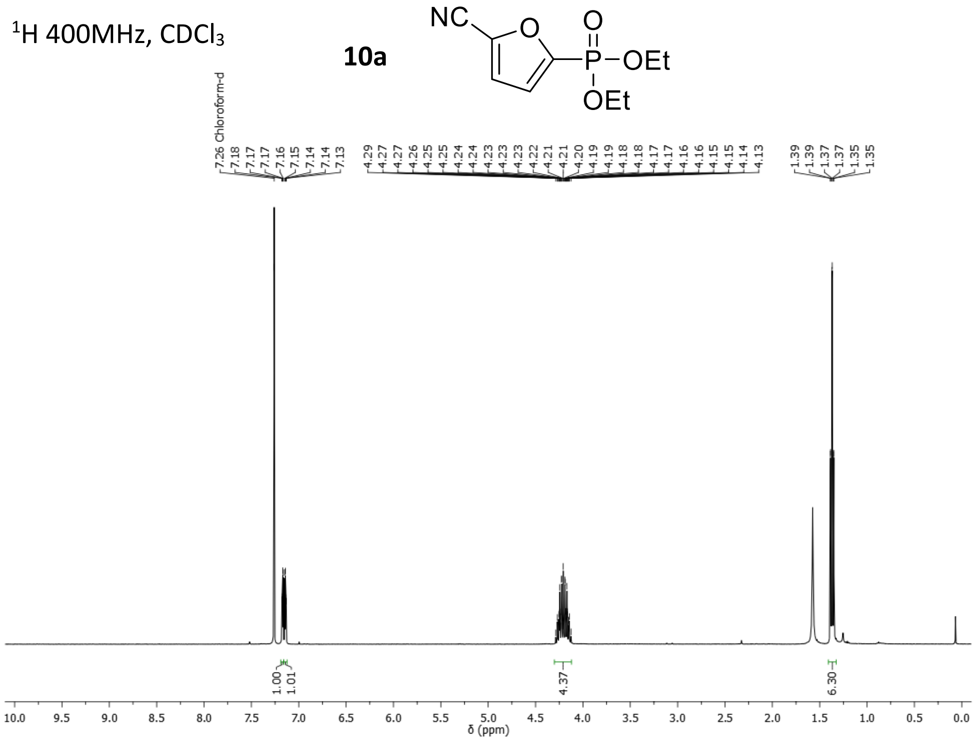
^{31}P 162MHz, CDCl$_3$

3o



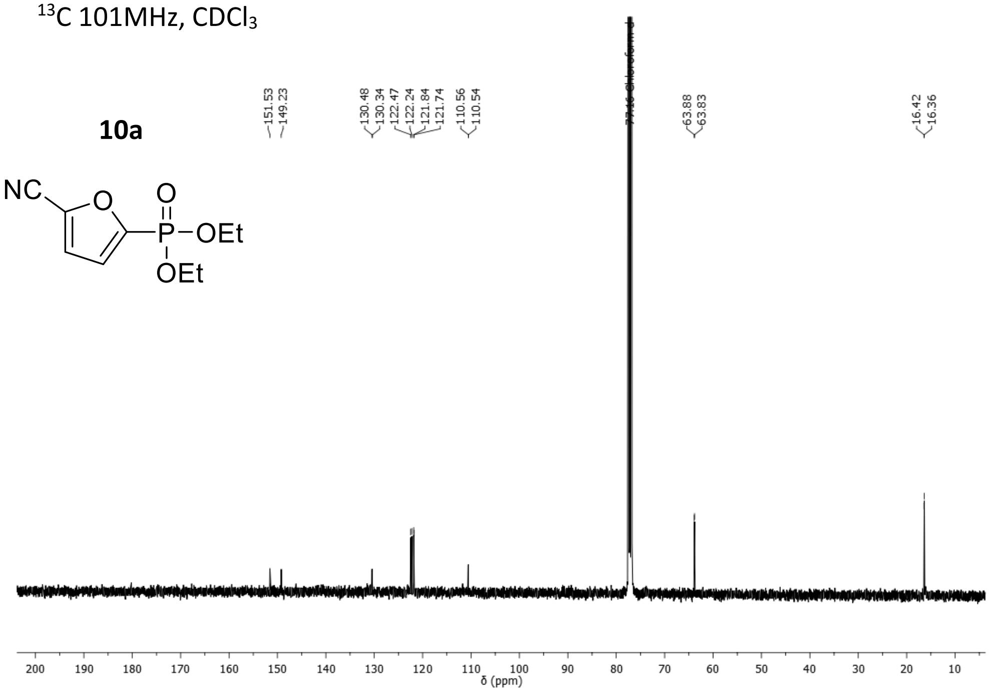
^{1}H 400MHz, CDCl$_3$

10a



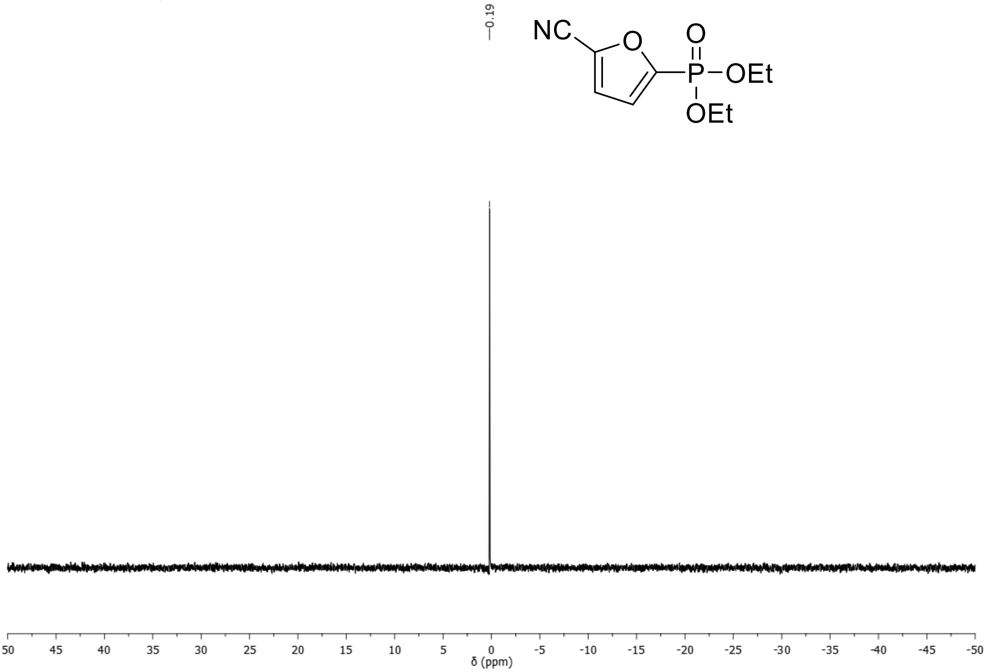
^{13}C 101MHz, CDCl$_3$

10a



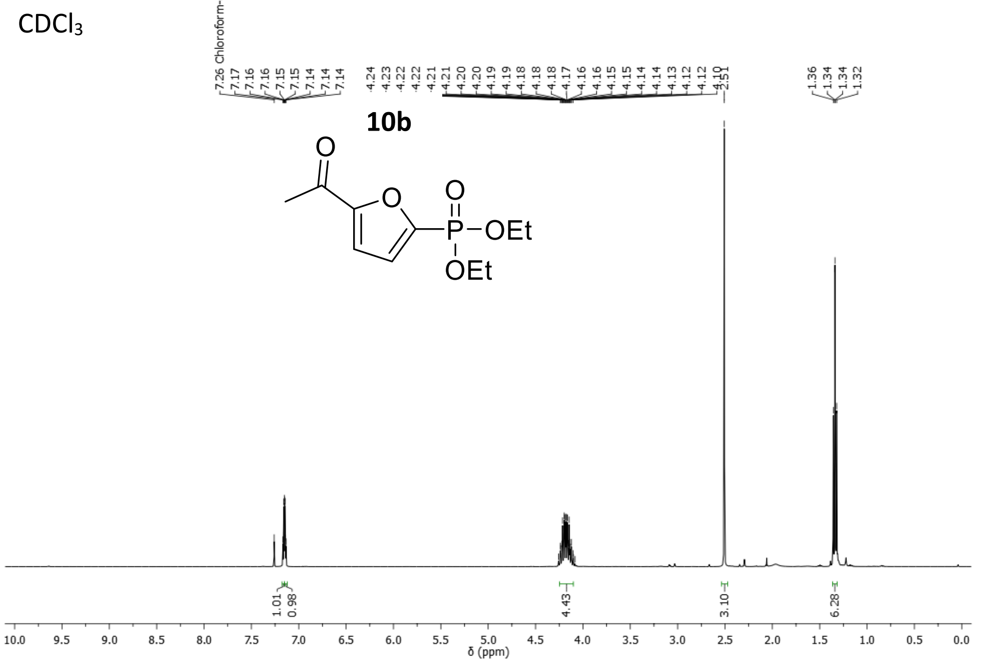
^{31}P 162MHz, CDCl$_3$

10a



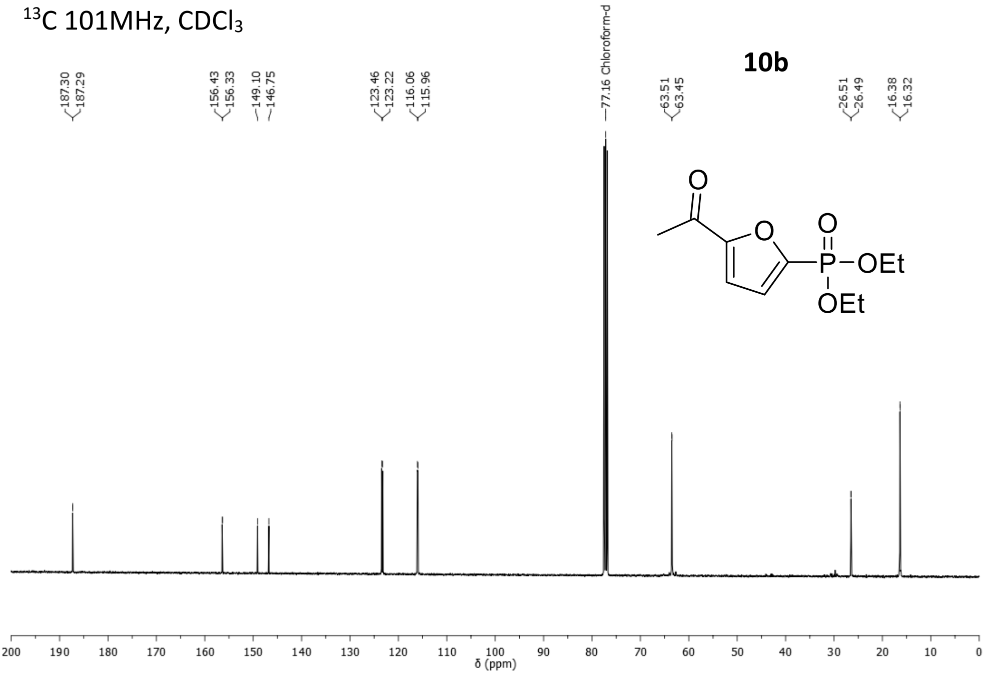
^{1}H 400MHz, CDCl$_3$

10b



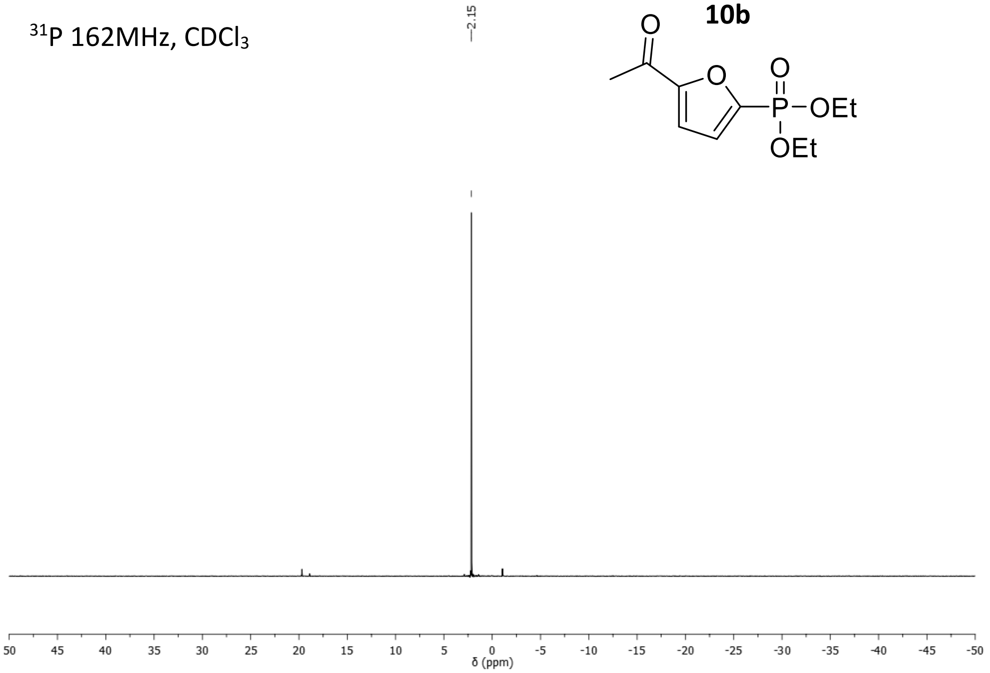
^{13}C 101MHz, $CDCl_3$

10b



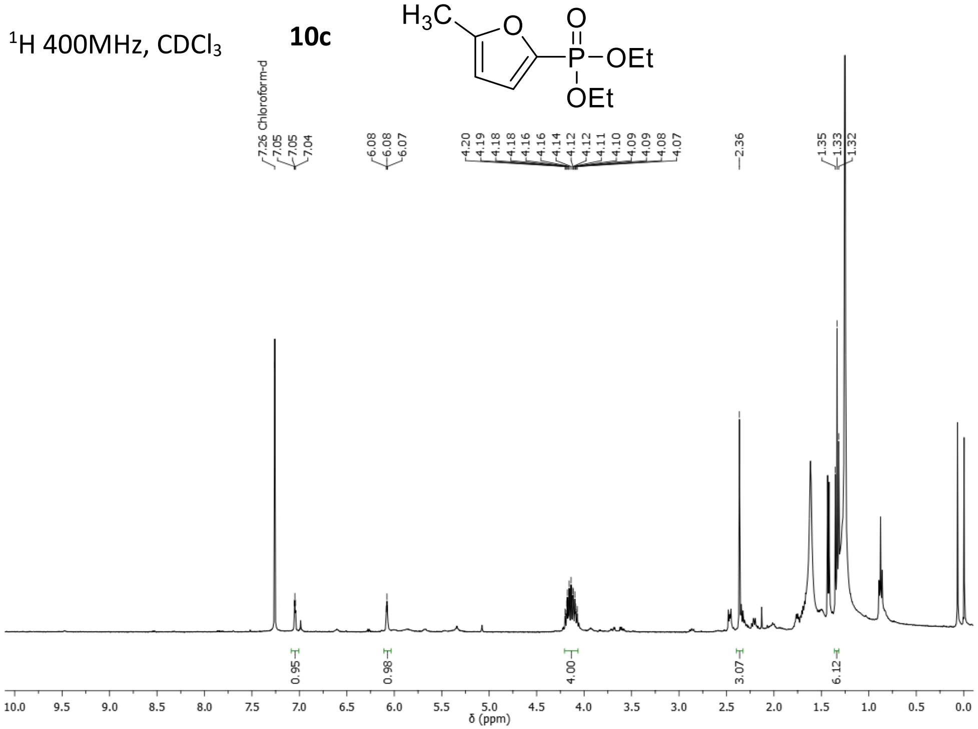
^{31}P 162MHz, $CDCl_3$

10b



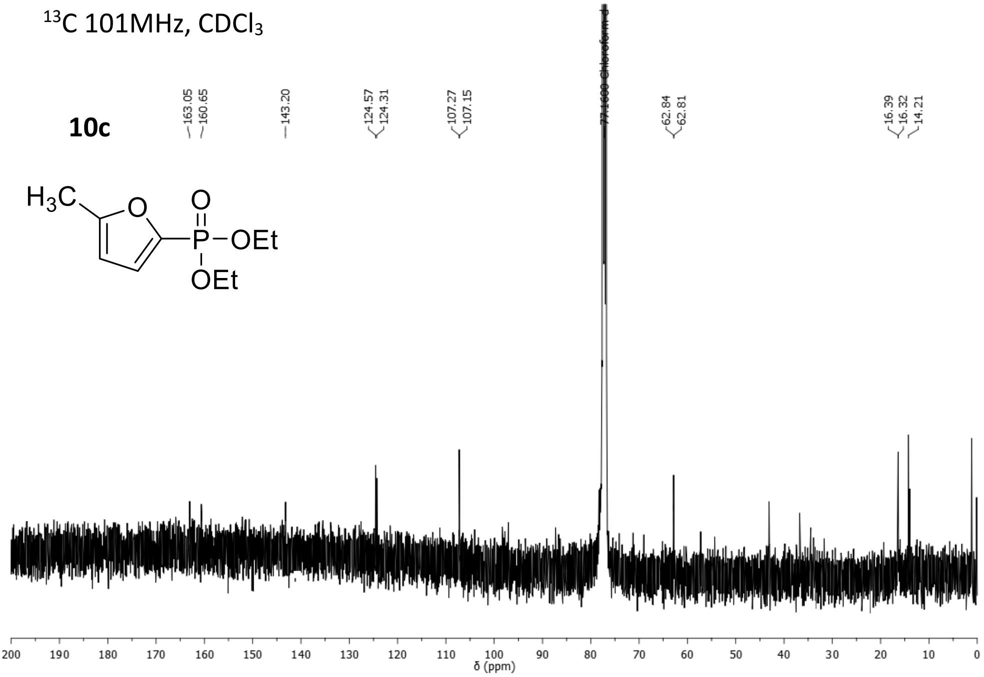
^{1}H 400MHz, CDCl$_3$

10c



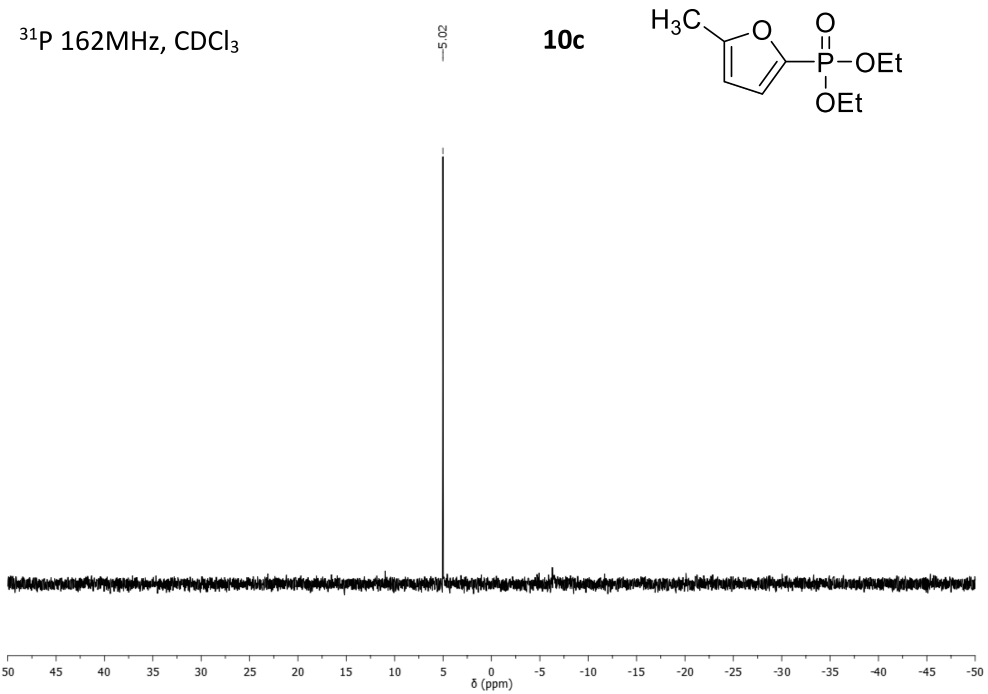
^{13}C 101MHz, CDCl$_3$

10c



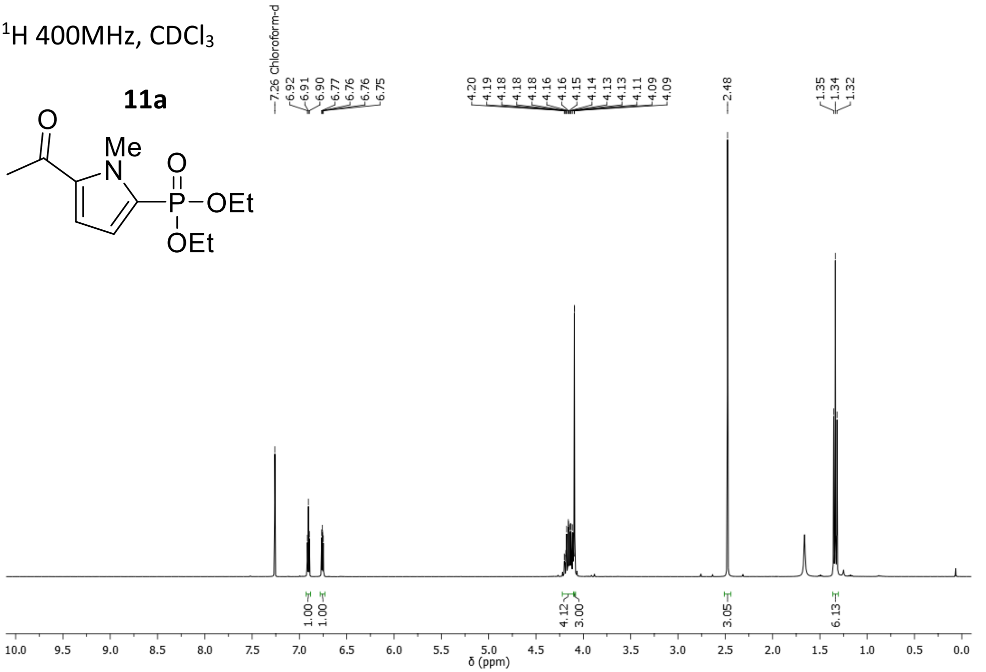
^{31}P 162MHz, $CDCl_3$

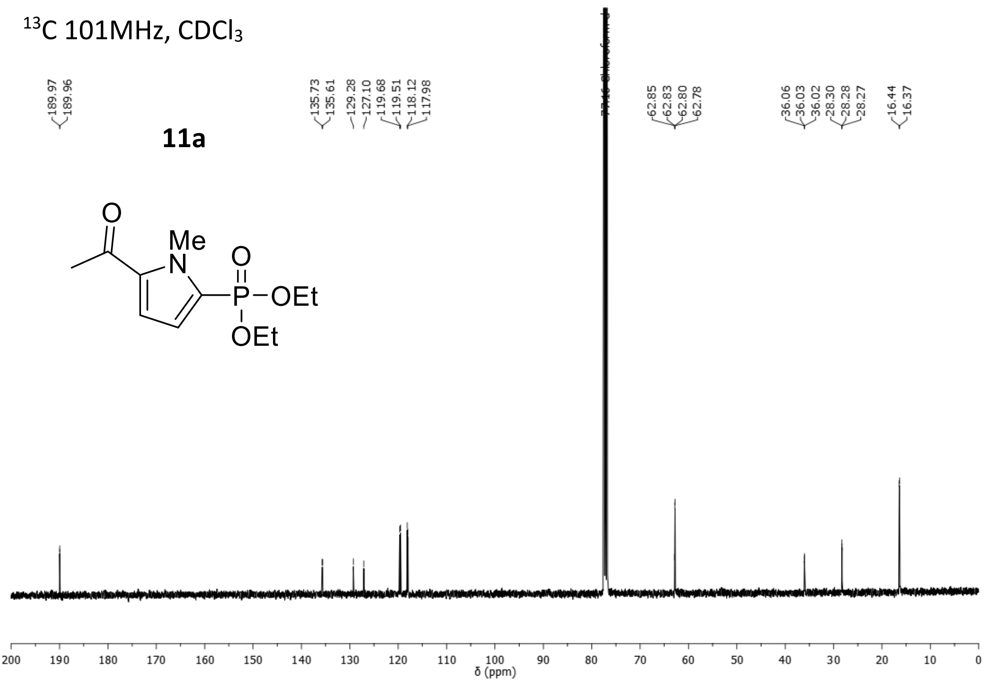
10c

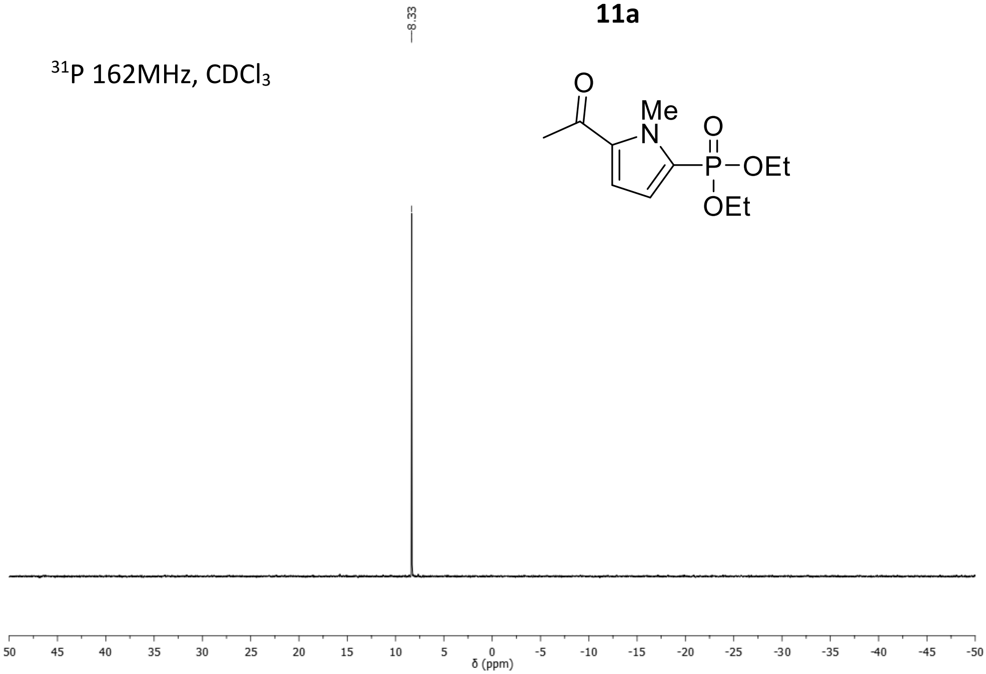


^1H 400MHz, $CDCl_3$

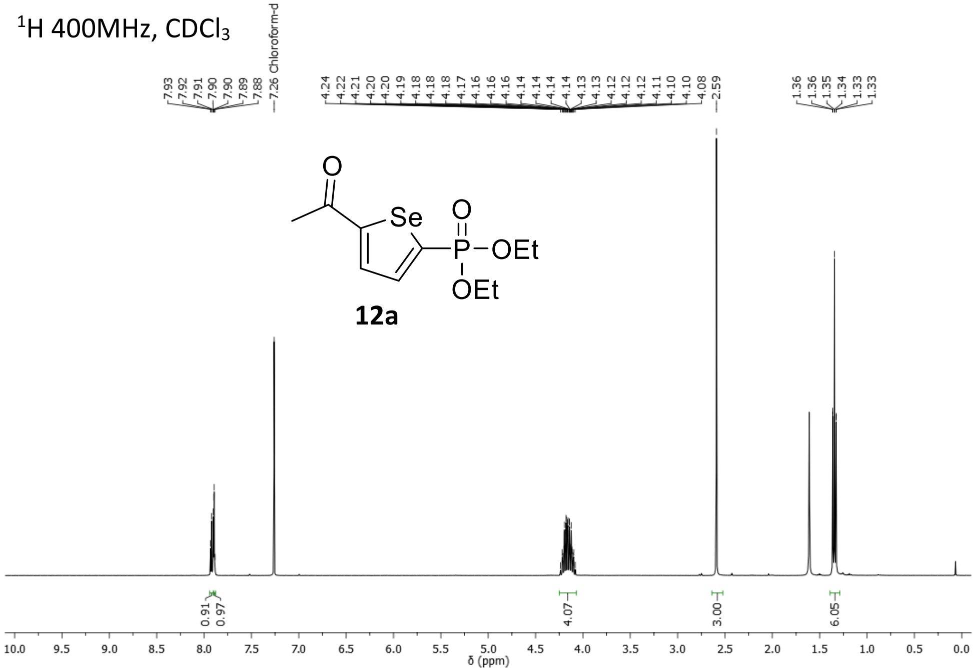
11a



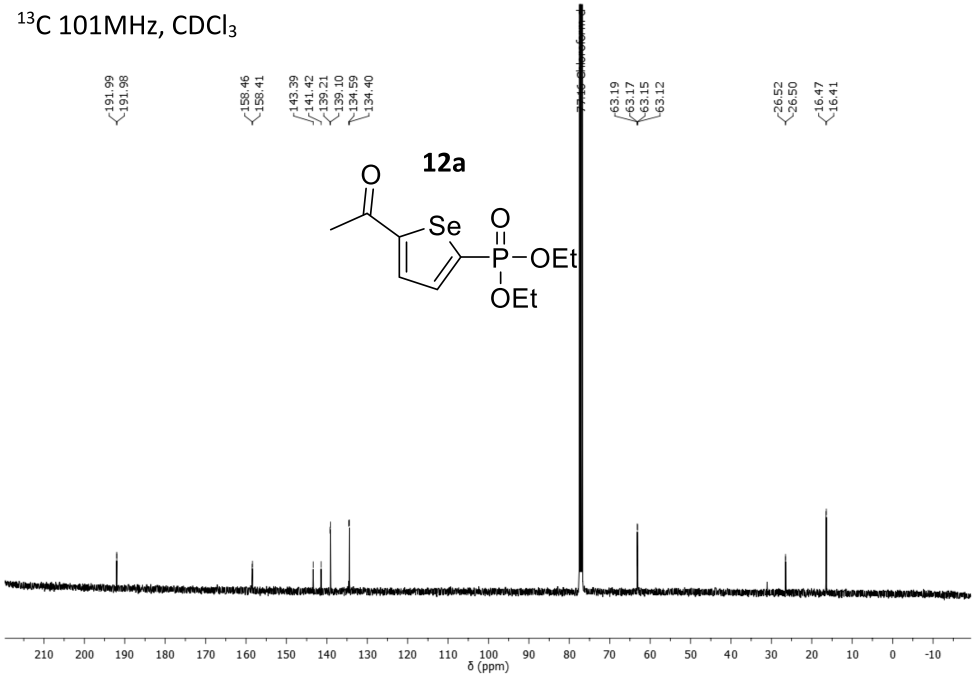

^{13}C 101MHz, CDCl$_3$
11a
189.97
189.96
135.73
135.61
129.28
127.10
119.68
119.51
118.12
117.98
77.16 chloroform-d
62.85
62.83
62.80
62.78
36.06
36.03
36.02
28.30
28.28
28.27
16.44
16.37
O
Me
N
O
P
OEt
OEt
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)


11a
8.33
^{31}P 162MHz, CDCl$_3$
O
Me
N
O
P
OEt
OEt
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
δ (ppm)

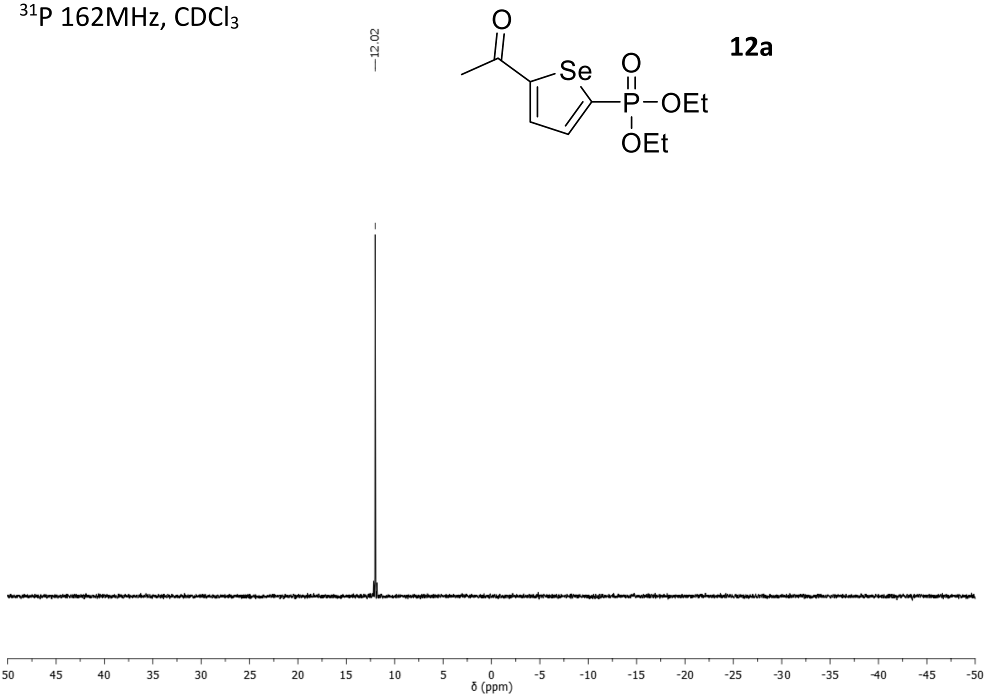
^{1}H 400MHz, $CDCl_3$



^{13}C 101MHz, $CDCl_3$

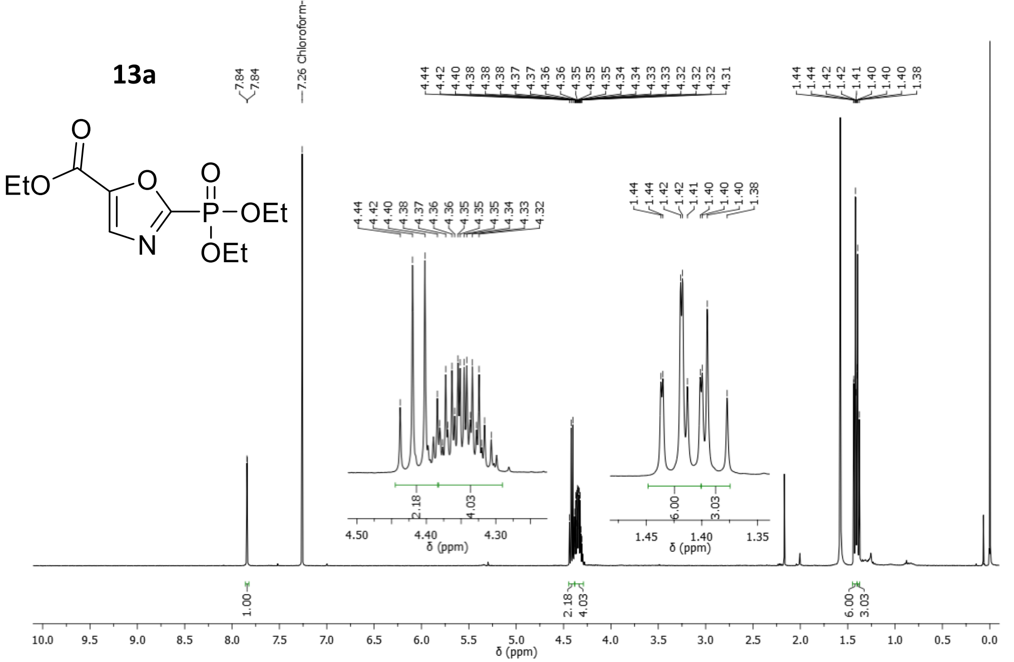


^{31}P 162MHz, $CDCl_3$



12a

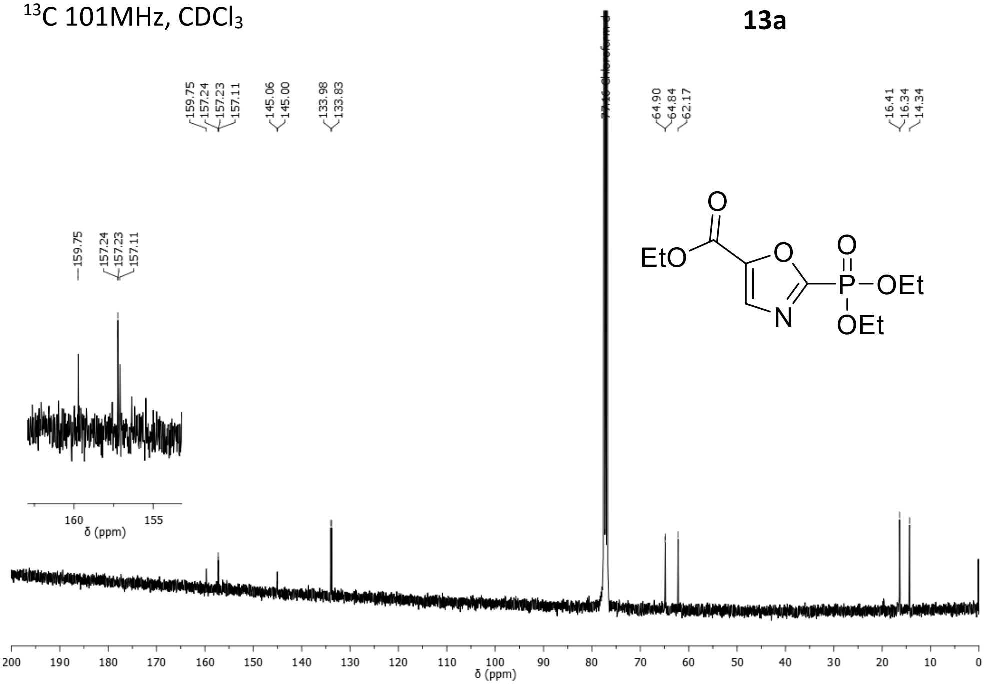
^{1}H 400MHz, $CDCl_3$



13a

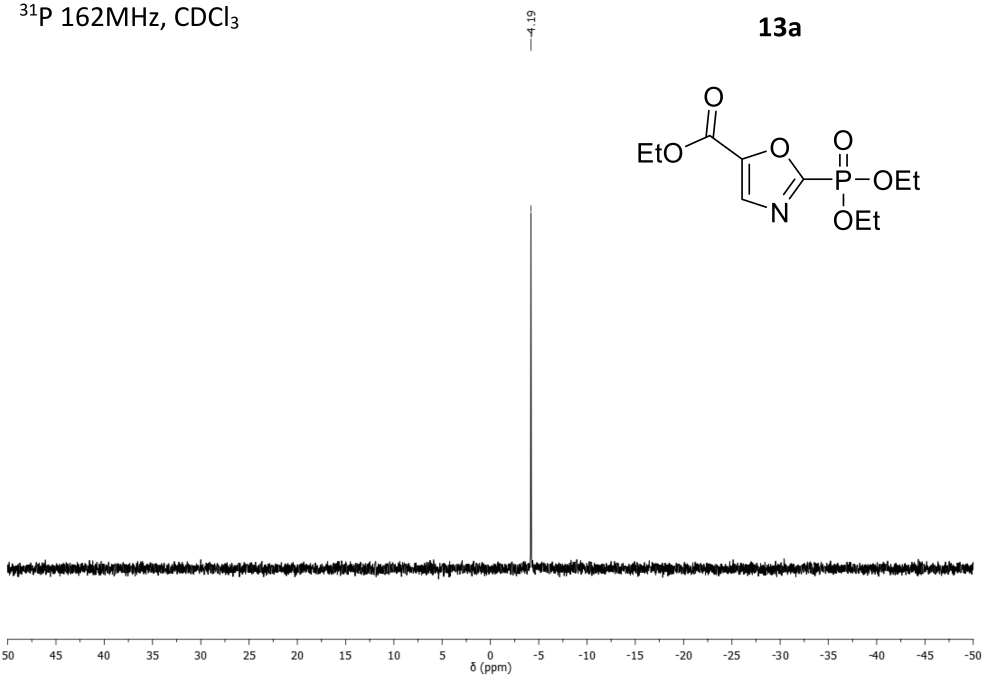
^{13}C 101MHz, CDCl$_3$

13a

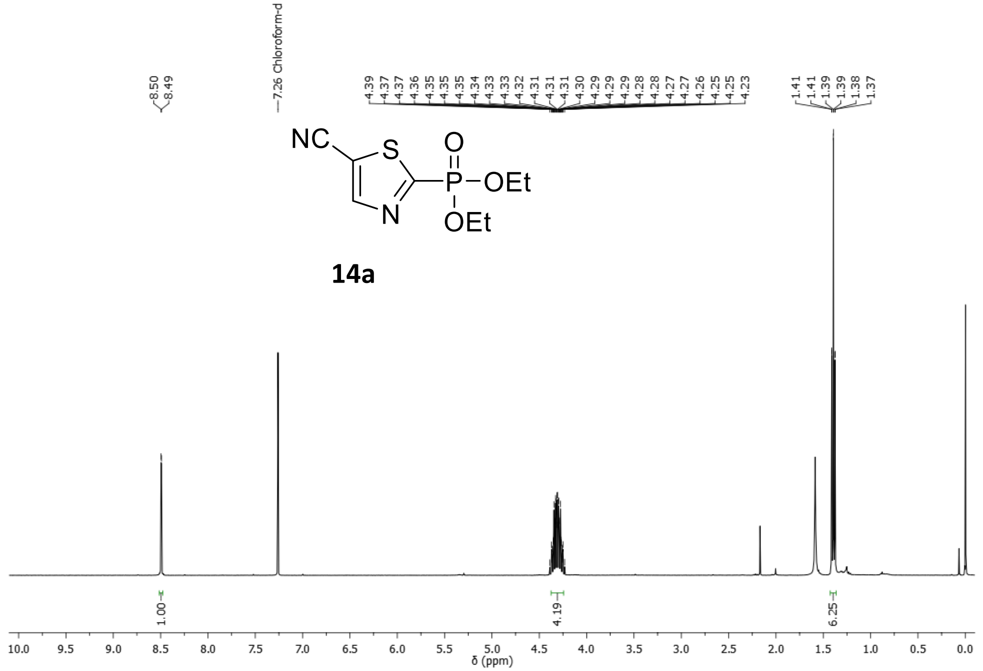


^{31}P 162MHz, CDCl$_3$

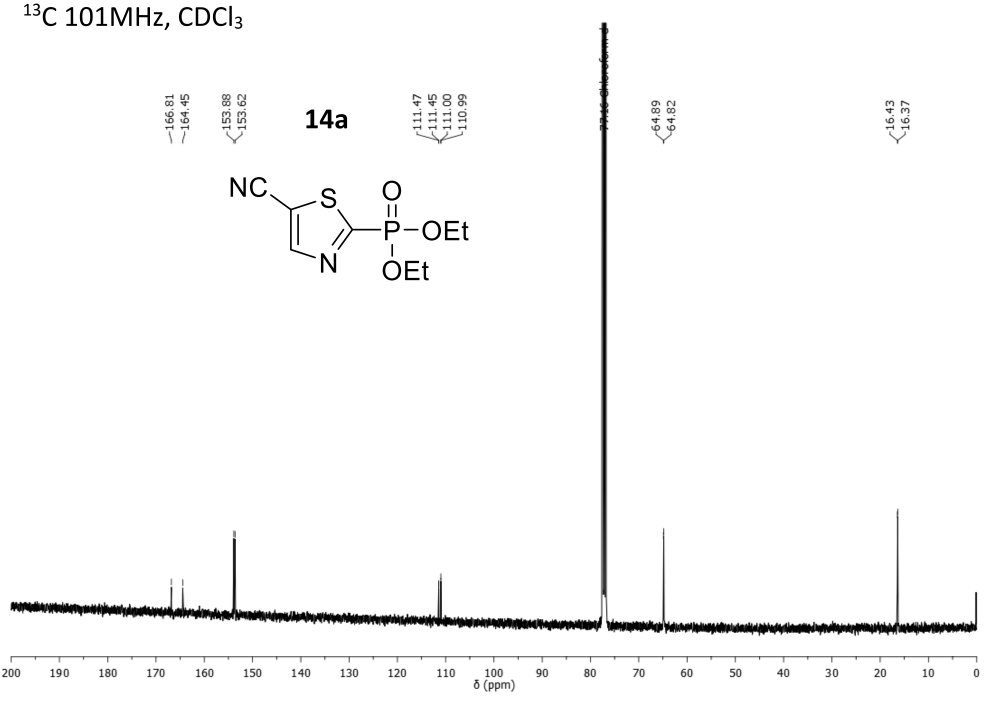
13a



^{1}H 400MHz, CDCl$_3$

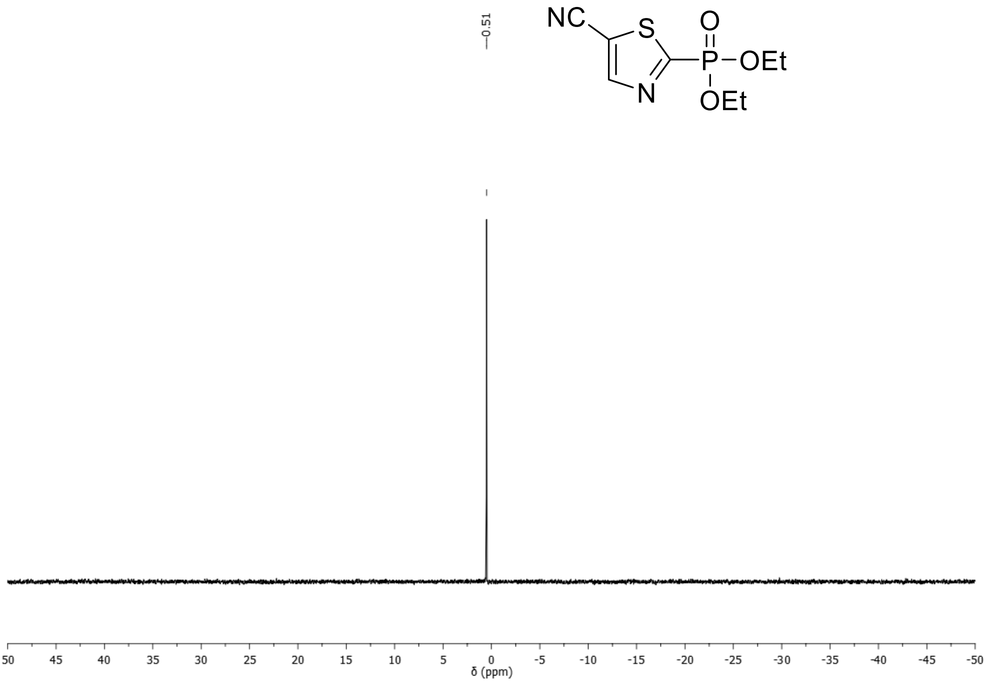


^{13}C 101MHz, CDCl$_3$



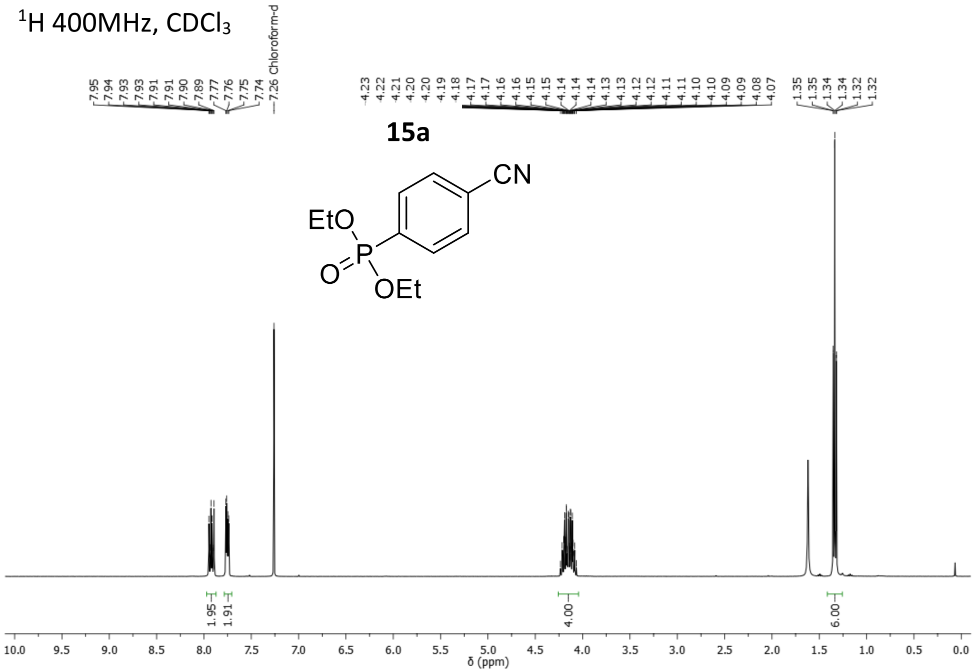
^{31}P 162MHz, $CDCl_3$

14a



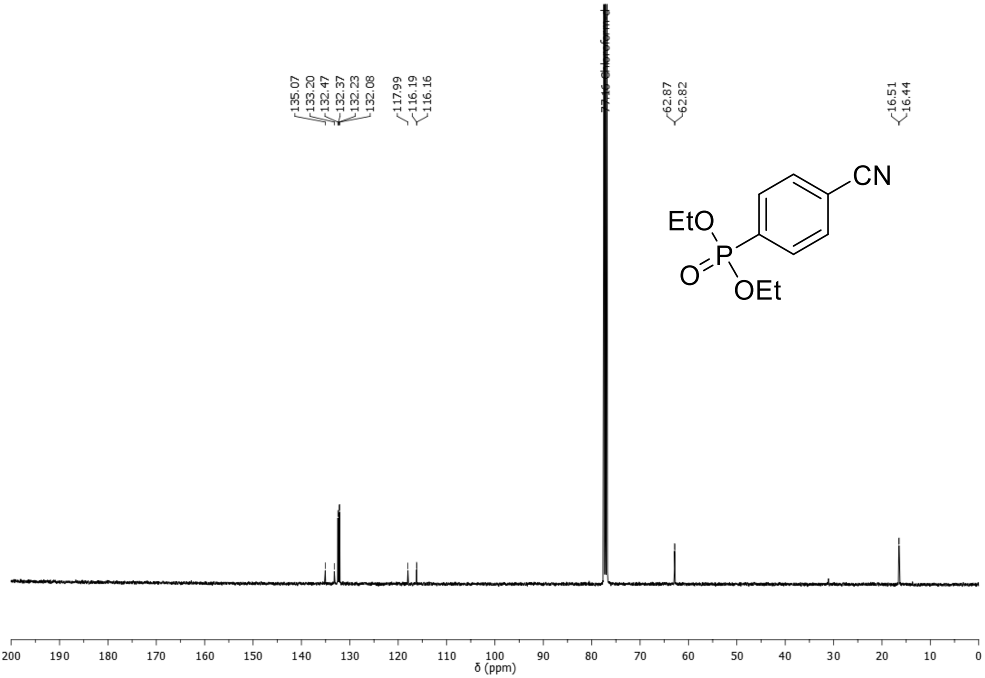
^{1}H 400MHz, $CDCl_3$

15a



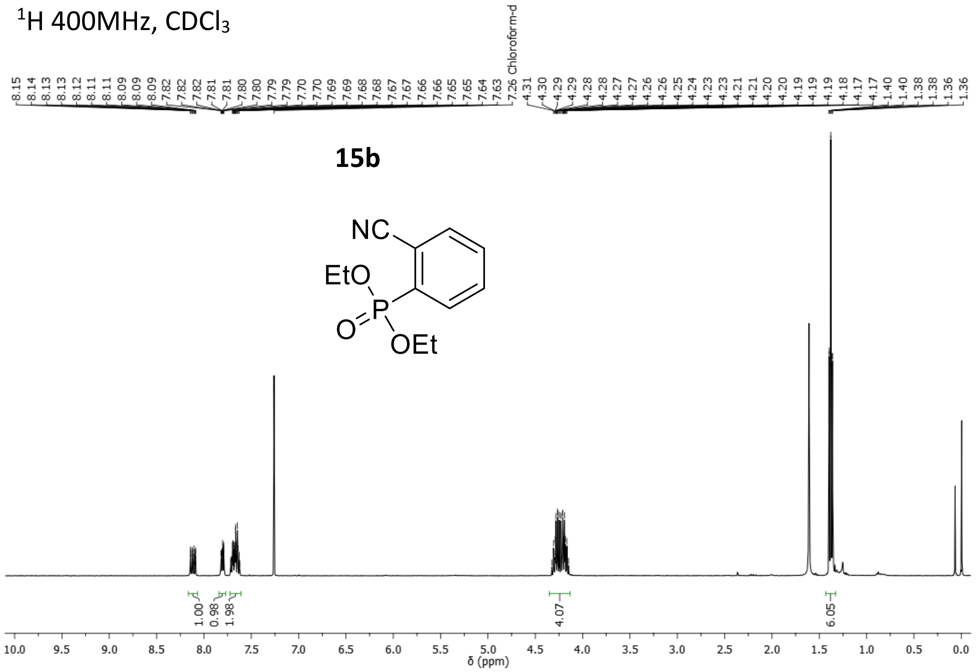
^{13}C 101MHz, CDCl$_3$

15a



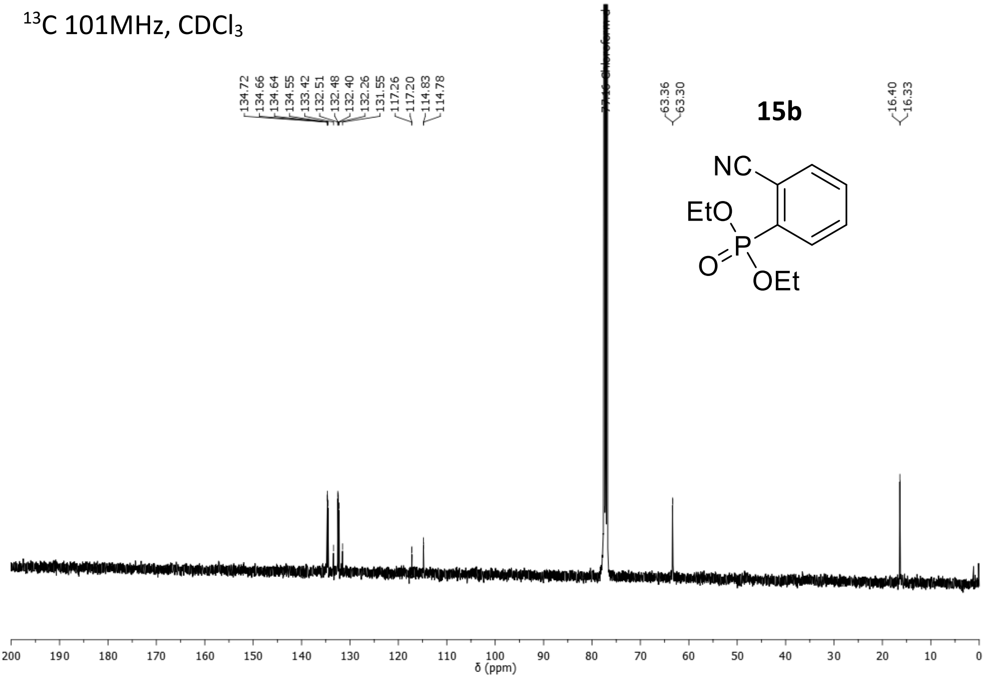
^{1}H 400MHz, CDCl$_3$

15b



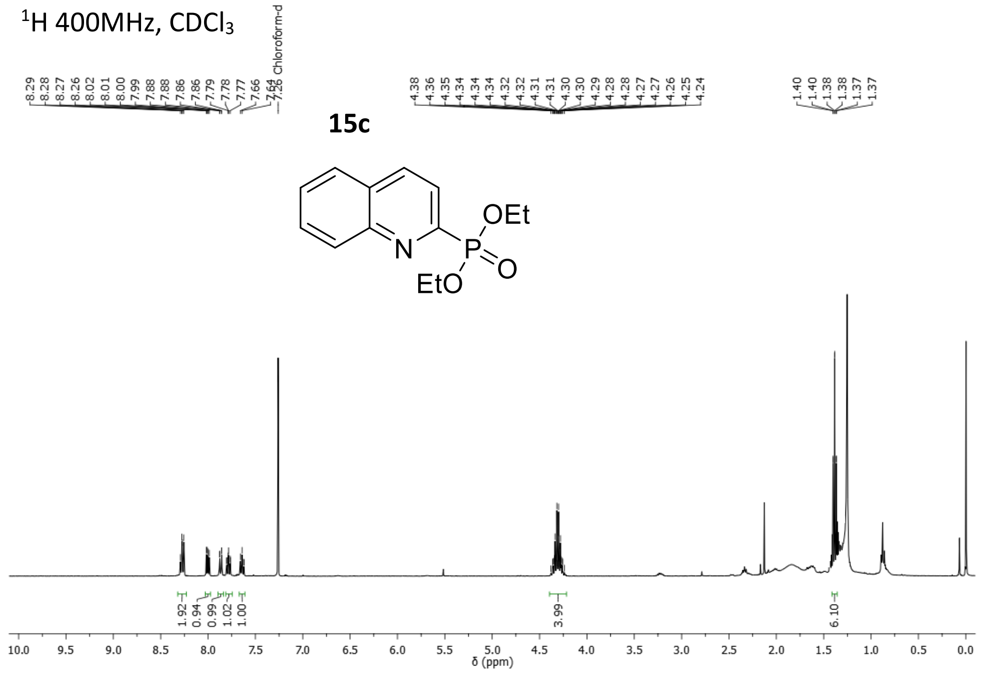
^{13}C 101MHz, CDCl$_3$

15b

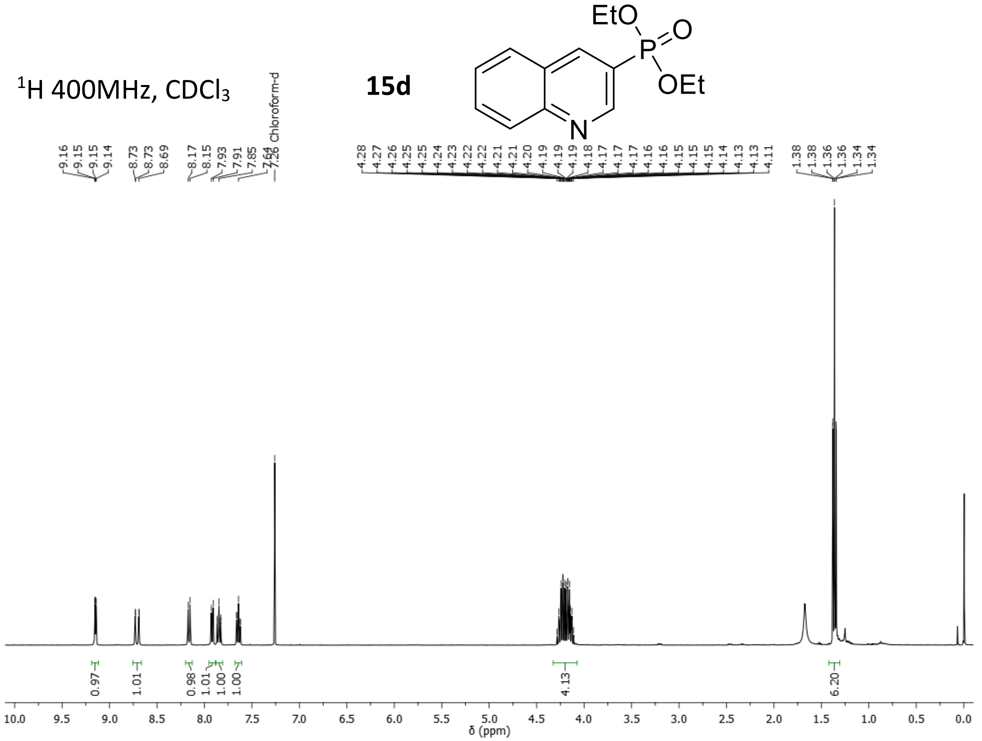


^{1}H 400MHz, CDCl$_3$

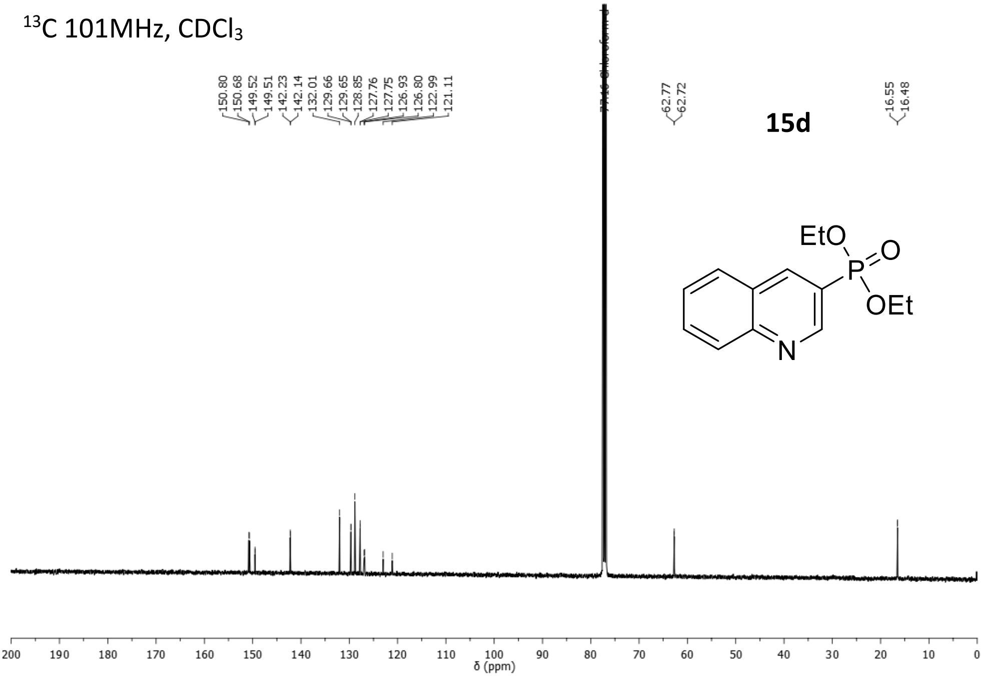
15c



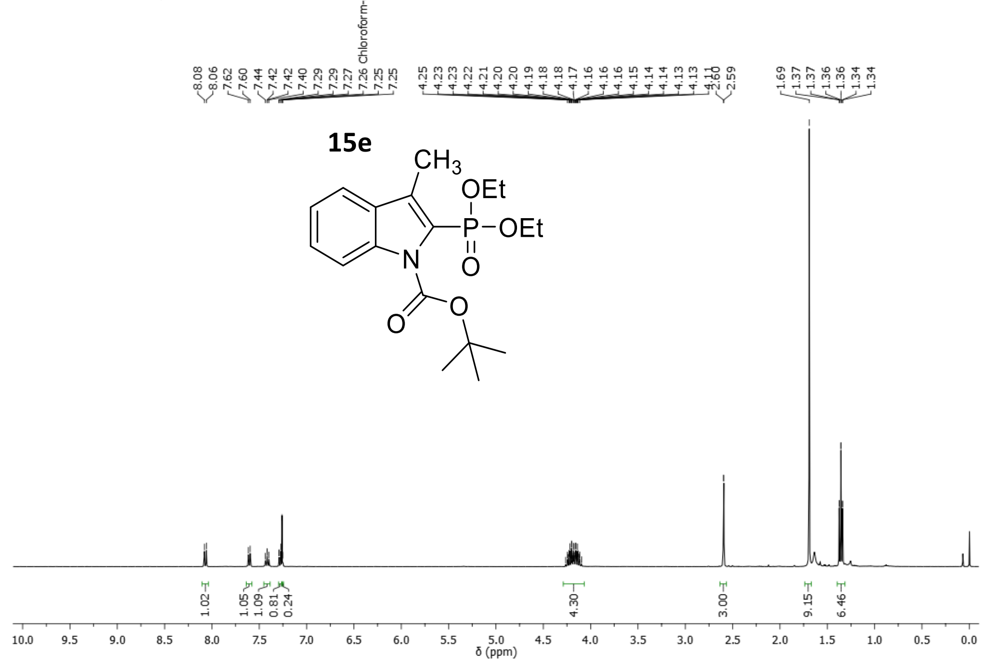
^{1}H 400MHz, $CDCl_3$



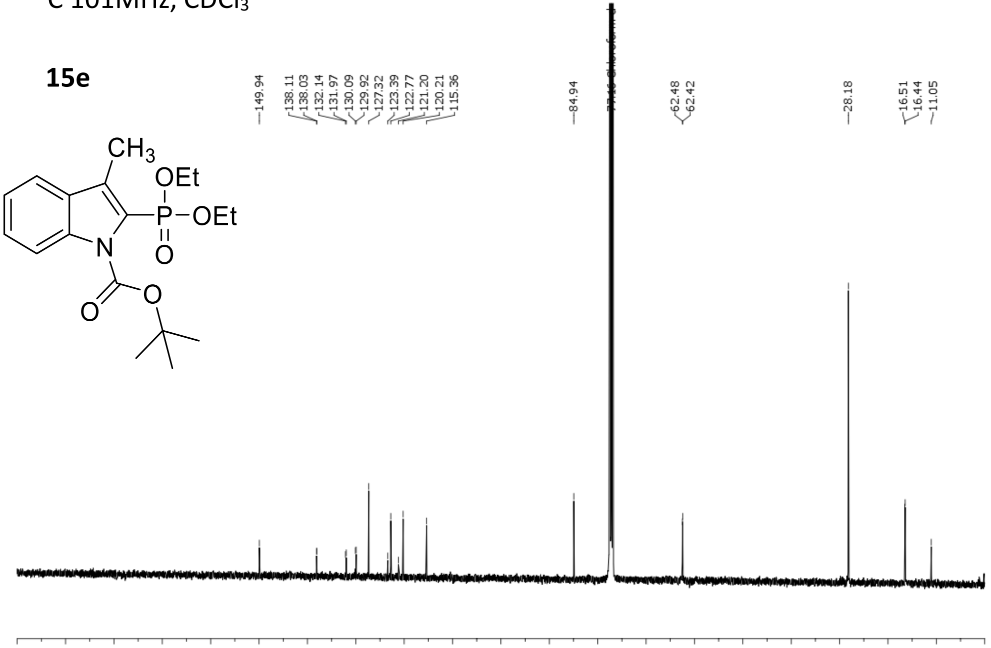
^{13}C 101MHz, $CDCl_3$



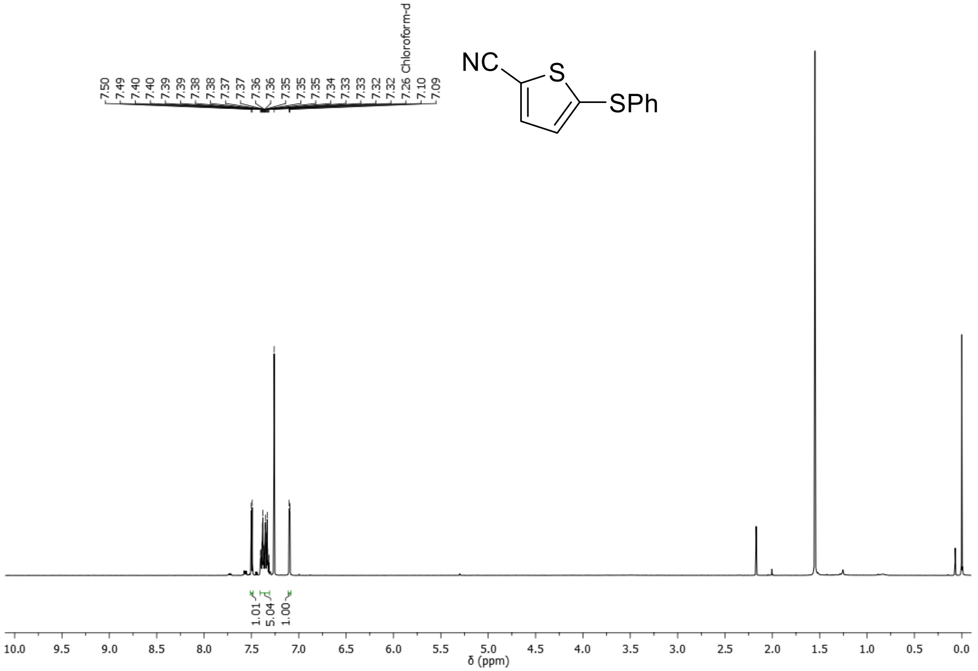
^{1}H 400MHz, CDCl$_3$



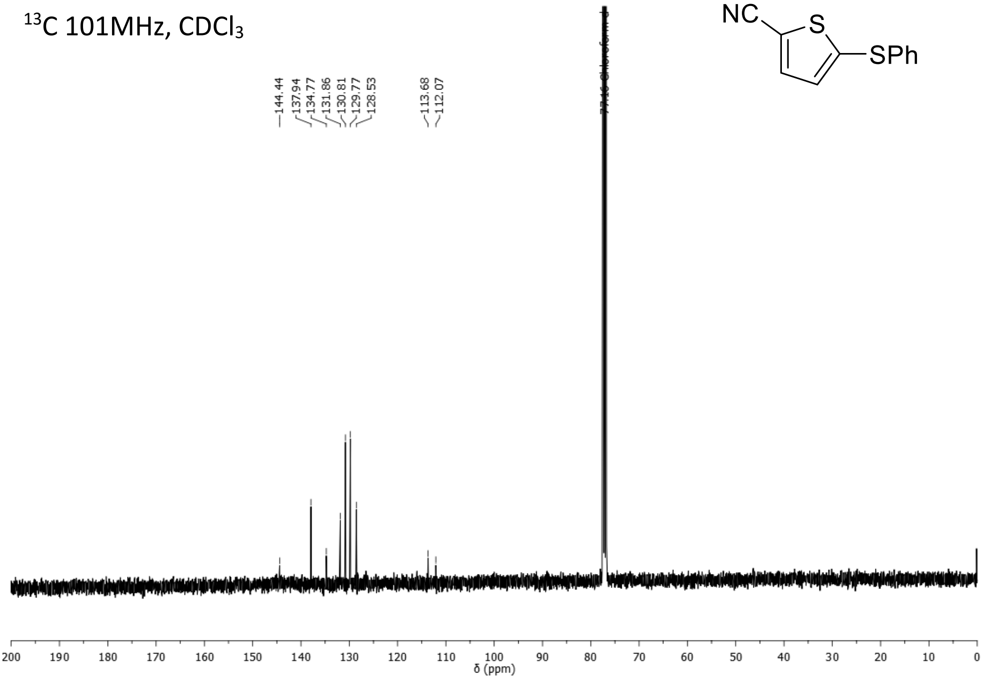
^{13}C 101MHz, CDCl$_3$



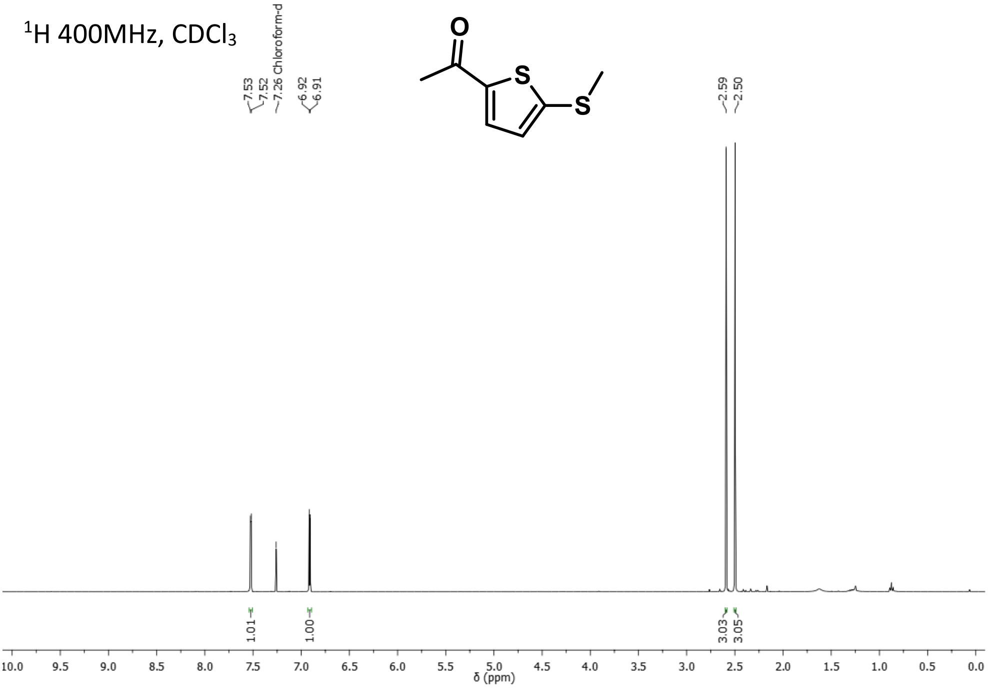
^{1}H 400MHz, CDCl$_3$



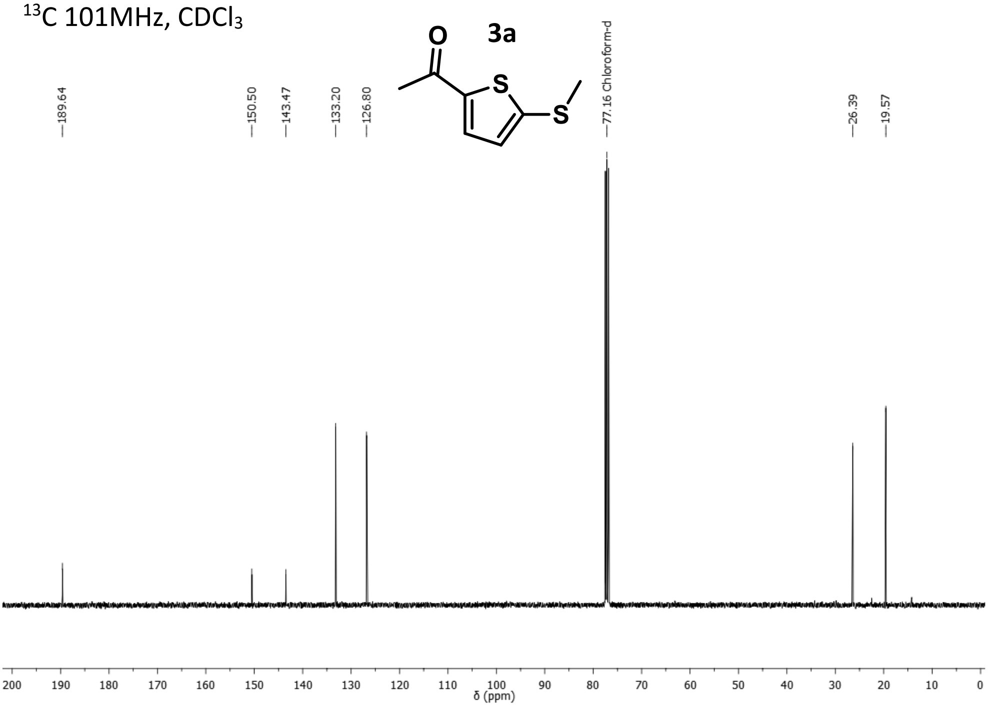
^{13}C 101MHz, CDCl$_3$



3a

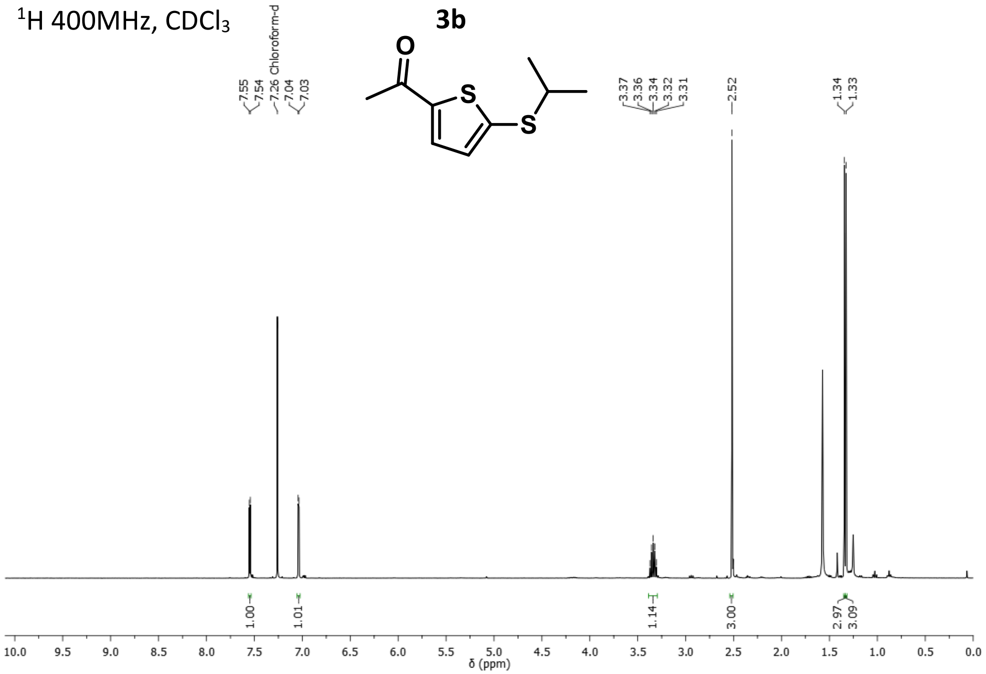

^{1}H 400MHz, CDCl$_3$
7.53
7.52
7.26 Chloroform-d
6.92
6.91
2.59
2.50
O
S
S
1.01
1.00
3.03
3.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)

3a


^{13}C 101MHz, CDCl$_3$
189.64
150.50
143.47
133.20
126.80
77.16 Chloroform-d
26.39
19.57
O
S
S
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)

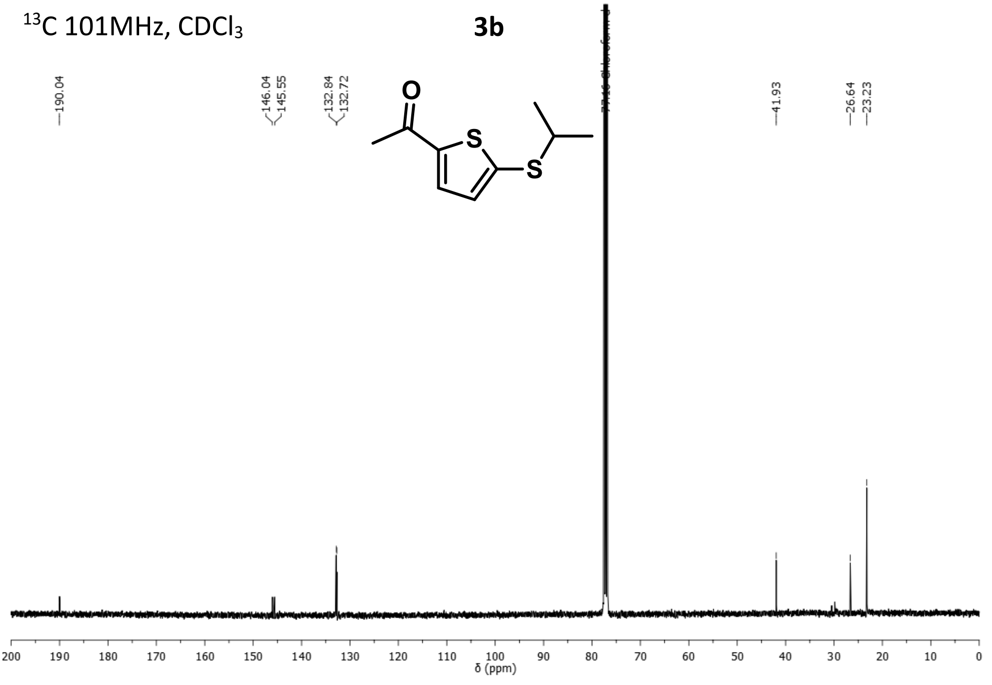
^{1}H 400MHz, CDCl$_3$

3b

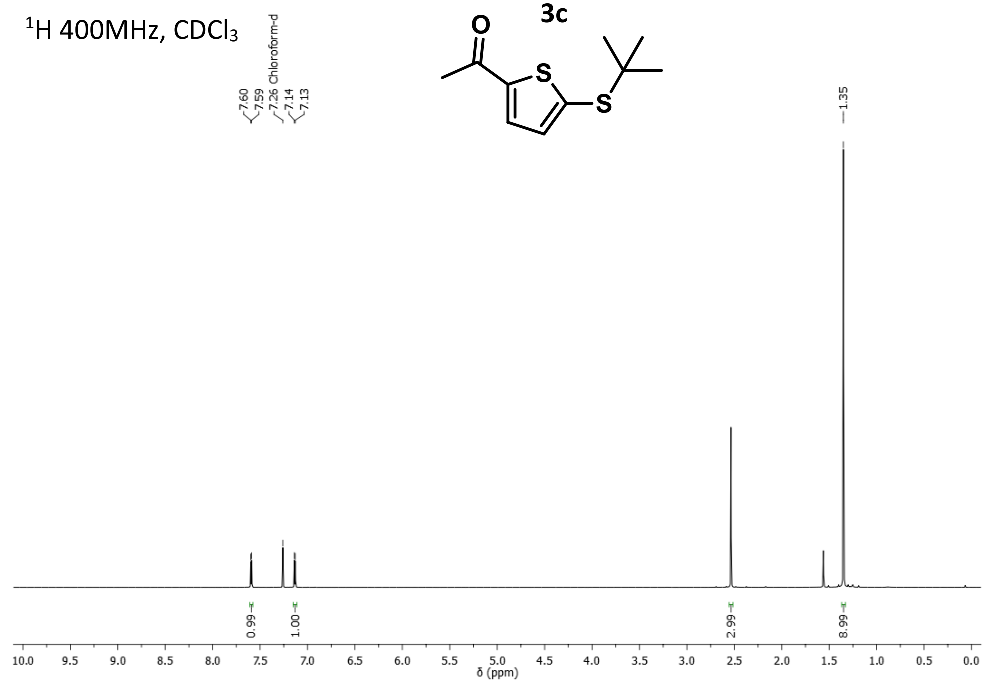


^{13}C 101MHz, CDCl$_3$

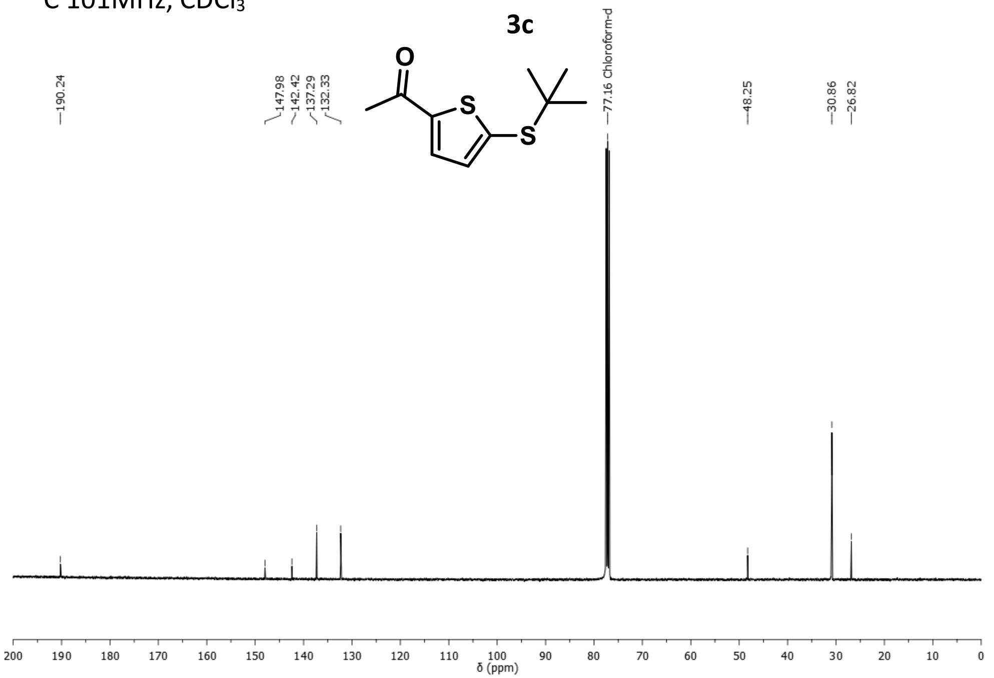
3b



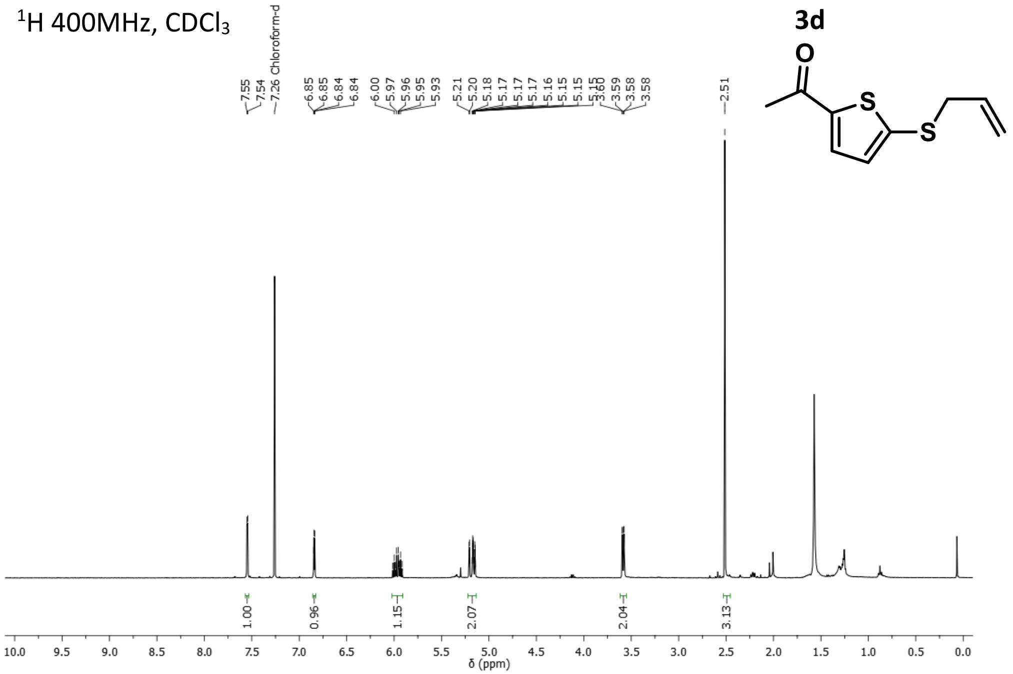
^1H 400MHz, $CDCl_3$



^{13}C 101MHz, $CDCl_3$

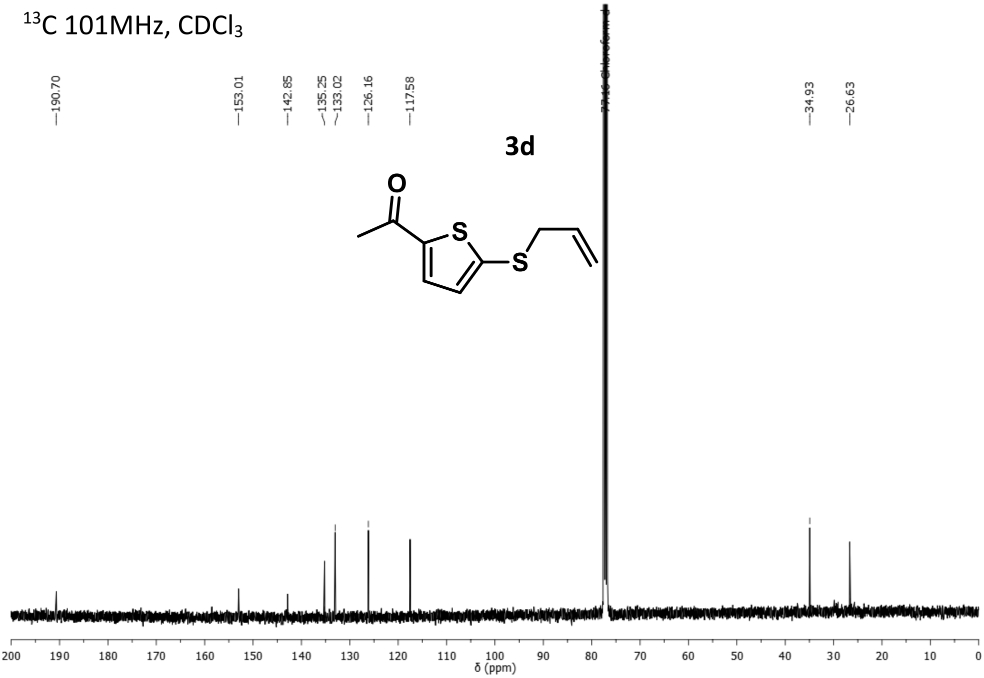


^{1}H 400MHz, $CDCl_3$

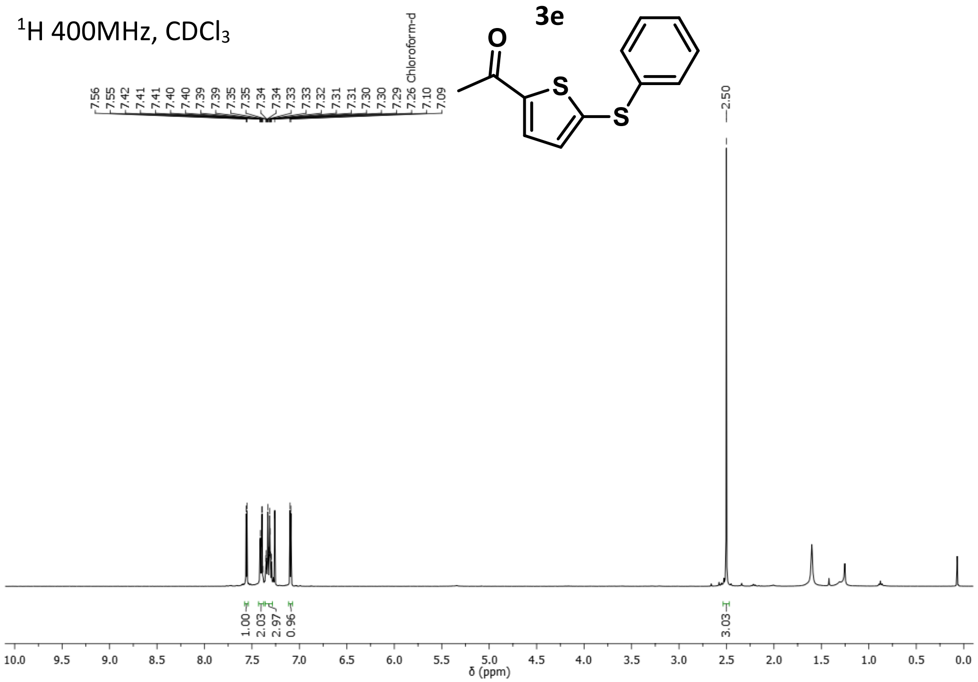


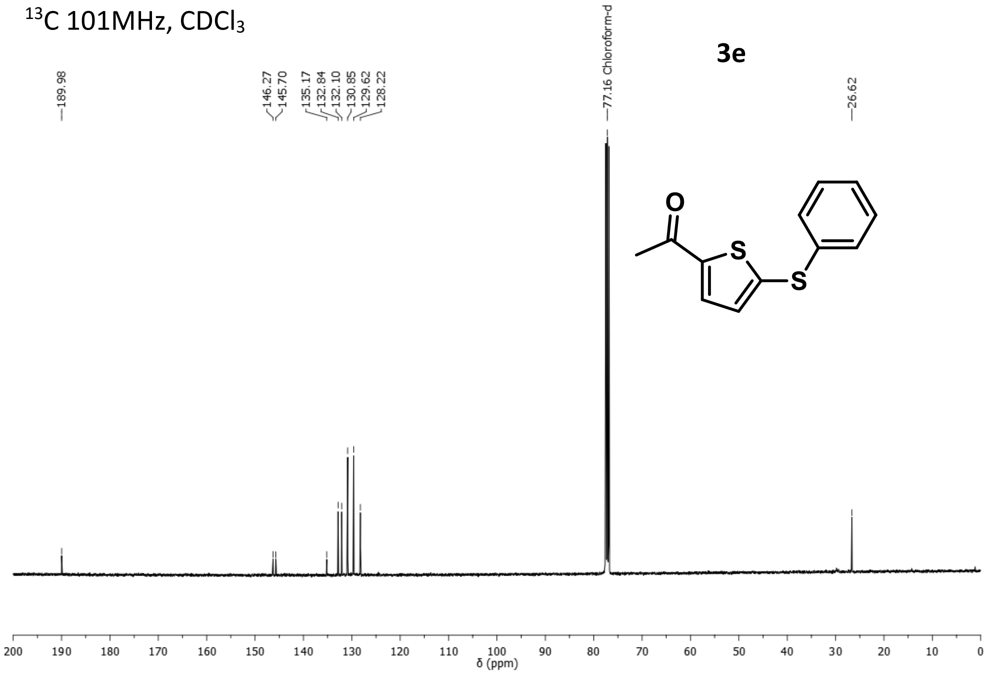
3d

^{13}C 101MHz, $CDCl_3$



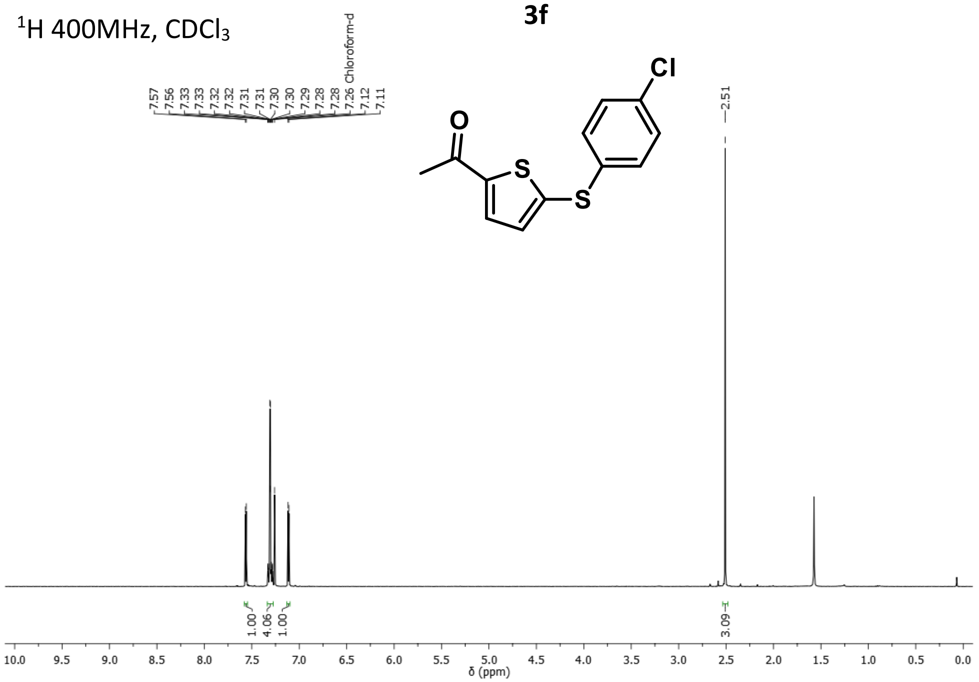
3d


^{1}H 400MHz, CDCl$_3$
3e
O
S
S
7.56
7.55
7.42
7.41
7.41
7.40
7.39
7.39
7.35
7.35
7.34
7.34
7.33
7.33
7.32
7.31
7.31
7.30
7.30
7.29
7.26 Chloroform-d
7.10
7.09
2.50
1.00
2.03
2.97
0.96
3.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)


^{13}C 101MHz, CDCl$_3$
3e
O
S
S
189.98
146.27
145.70
135.17
132.84
132.10
130.85
129.62
128.22
77.16 Chloroform-d
26.62
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)

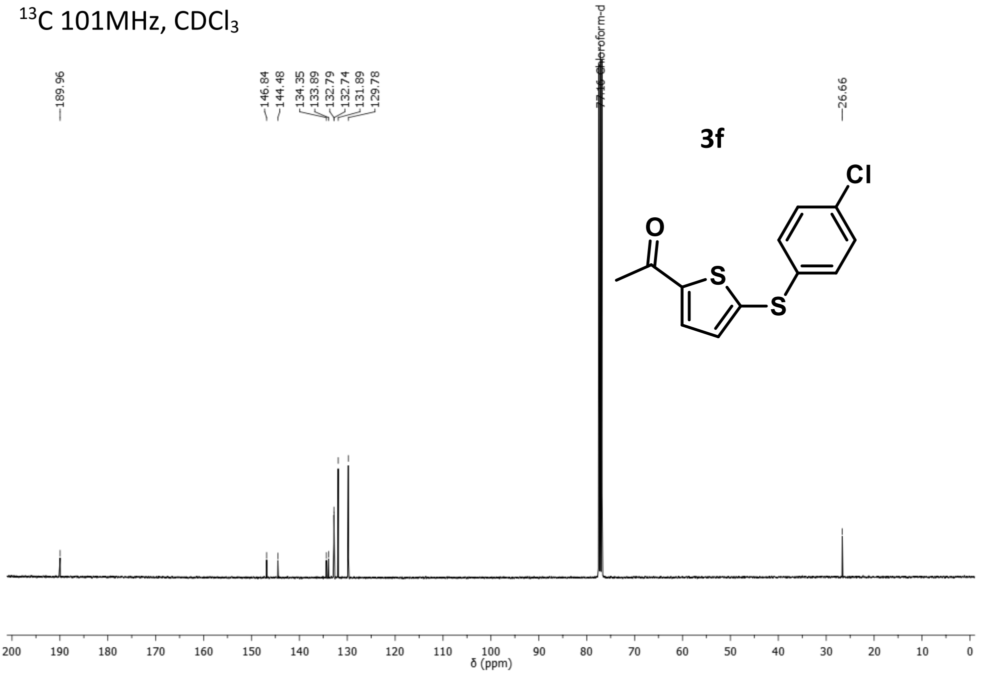
^1H 400MHz, $CDCl_3$

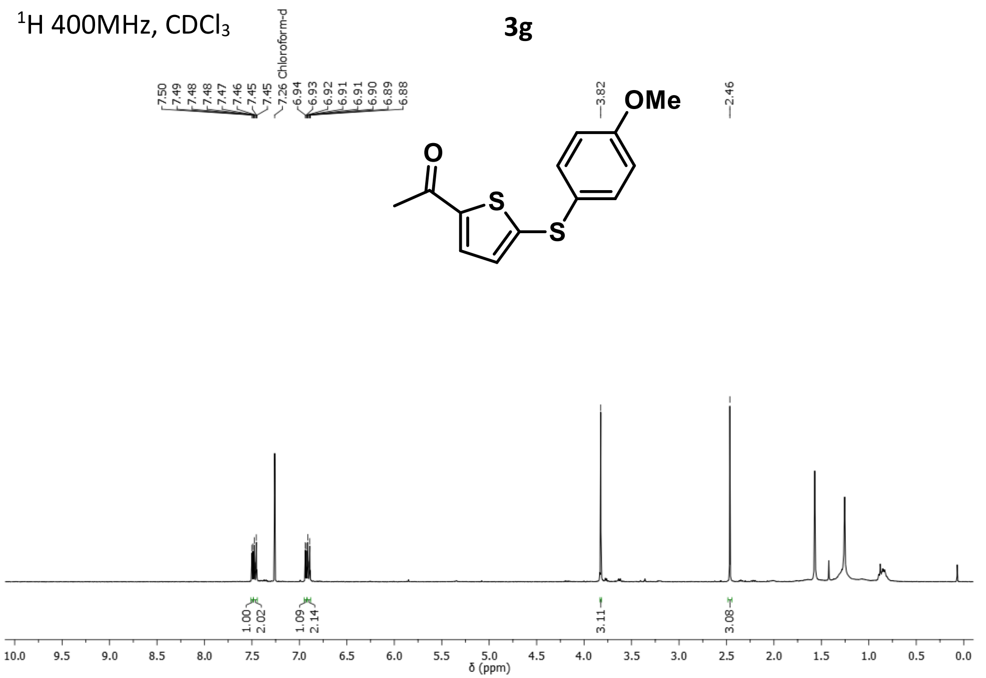
3f

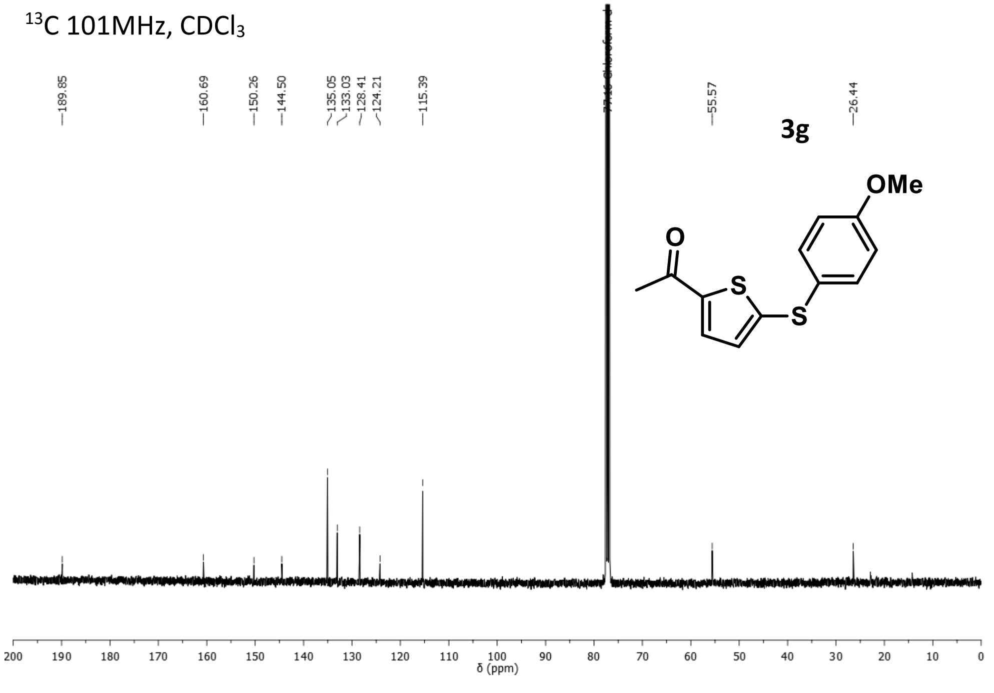


^{13}C 101MHz, $CDCl_3$

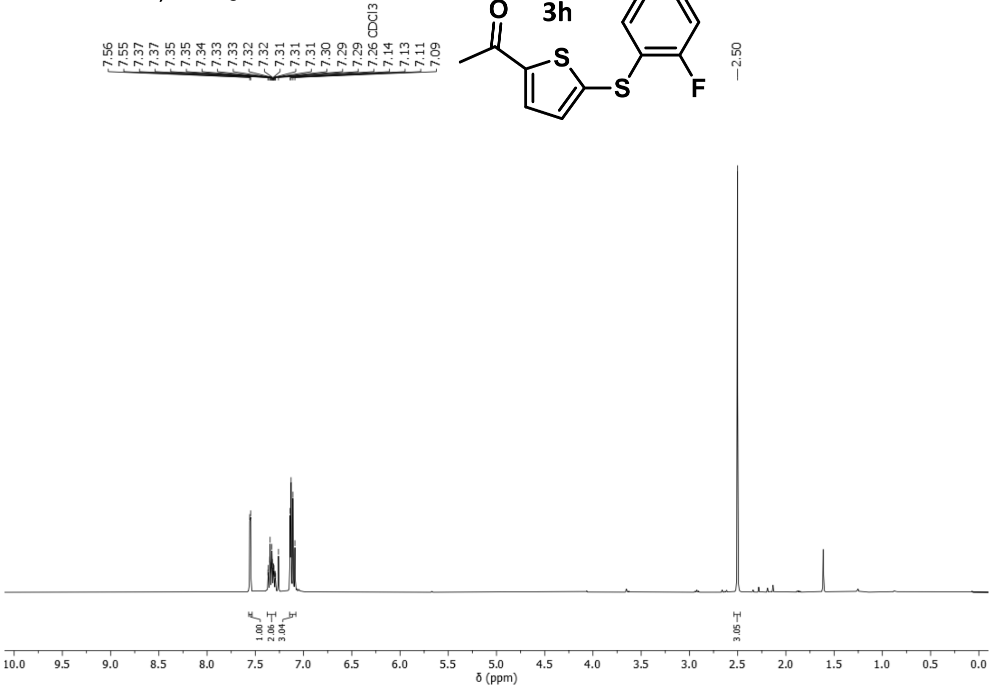
3f



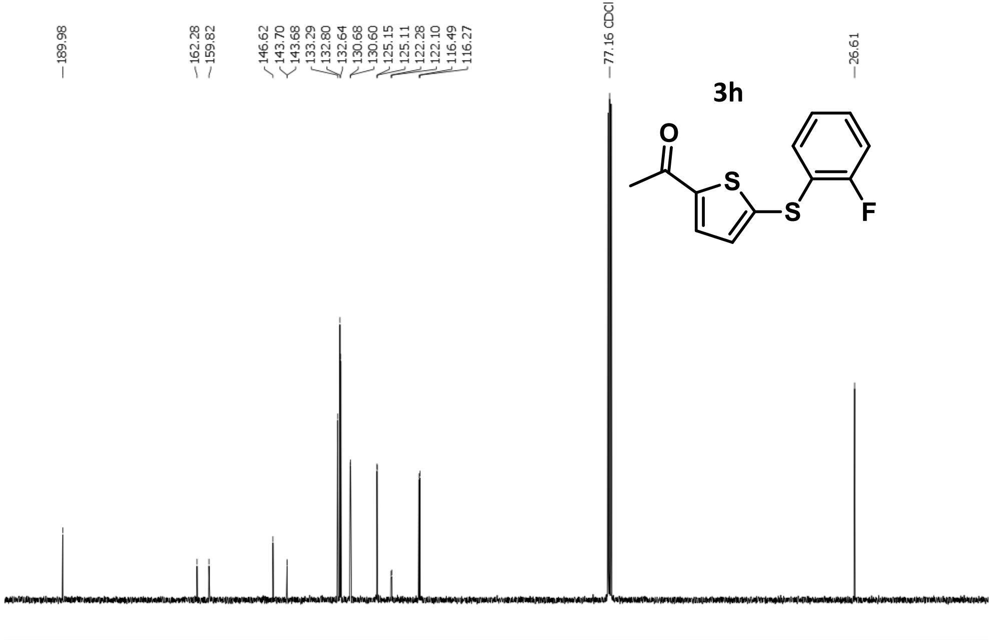

^{1}H 400MHz, CDCl$_3$
3g
7.50
7.49
7.48
7.48
7.47
7.46
7.45
7.45
7.26 Chloroform-d
6.94
6.93
6.92
6.91
6.91
6.90
6.89
6.88
3.82
2.46
OMe
O
S
S
1.00
2.02
1.09
2.14
3.11
3.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)


^{13}C 101MHz, CDCl$_3$
189.85
160.69
150.26
144.50
135.05
133.03
128.41
124.21
115.39
77.16 Chloroform-d
55.57
26.44
3g
OMe
O
S
S
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

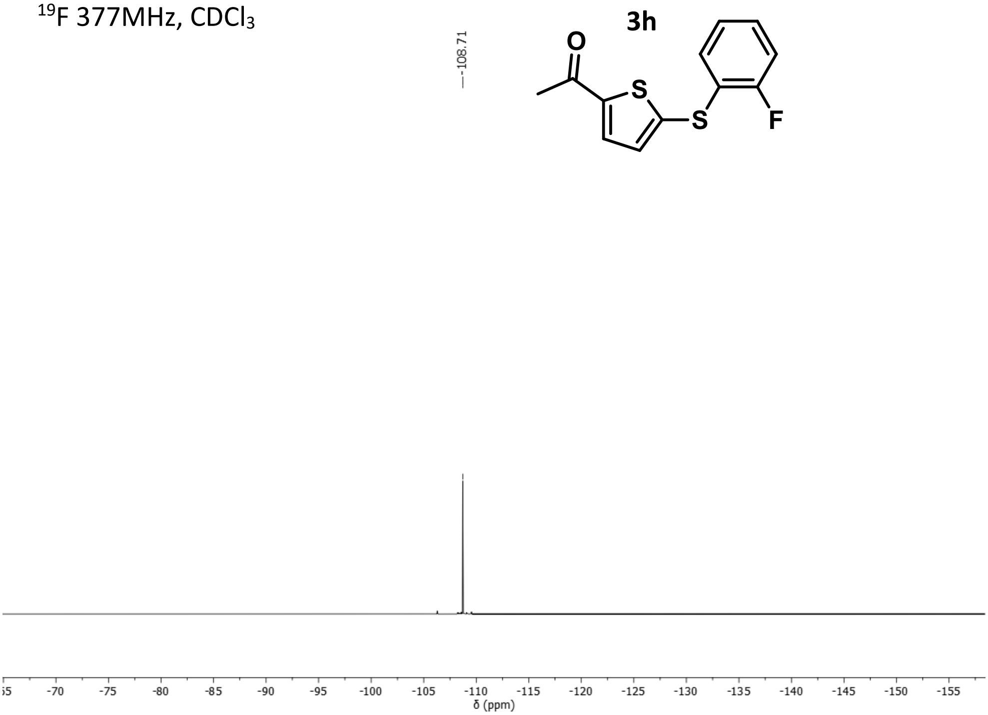
^{1}H 400MHz, $CDCl_3$



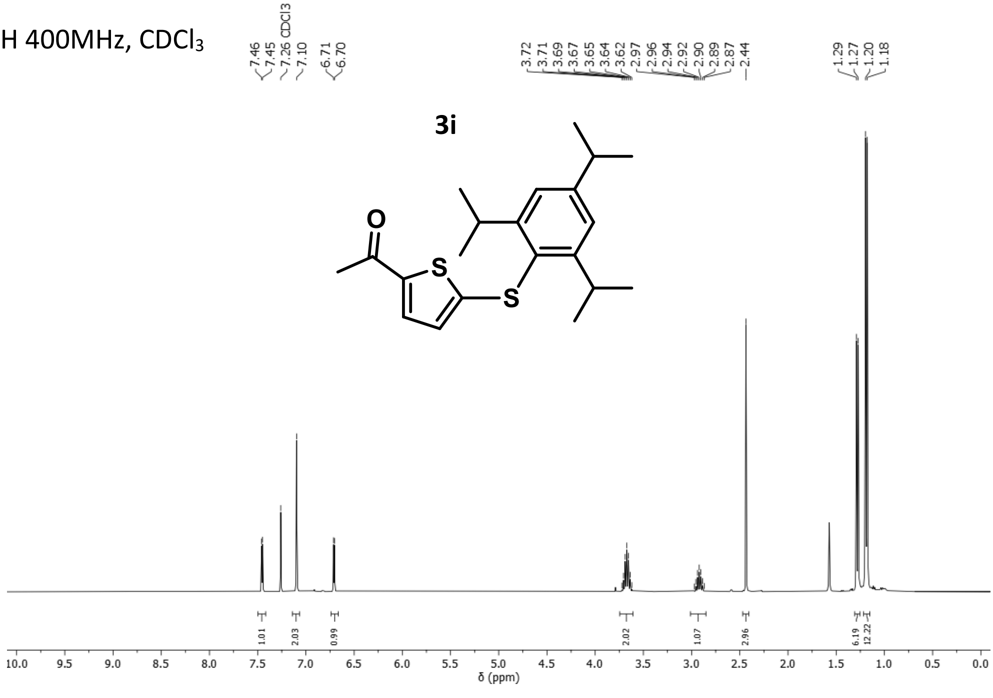
^{13}C 101MHz, $CDCl_3$



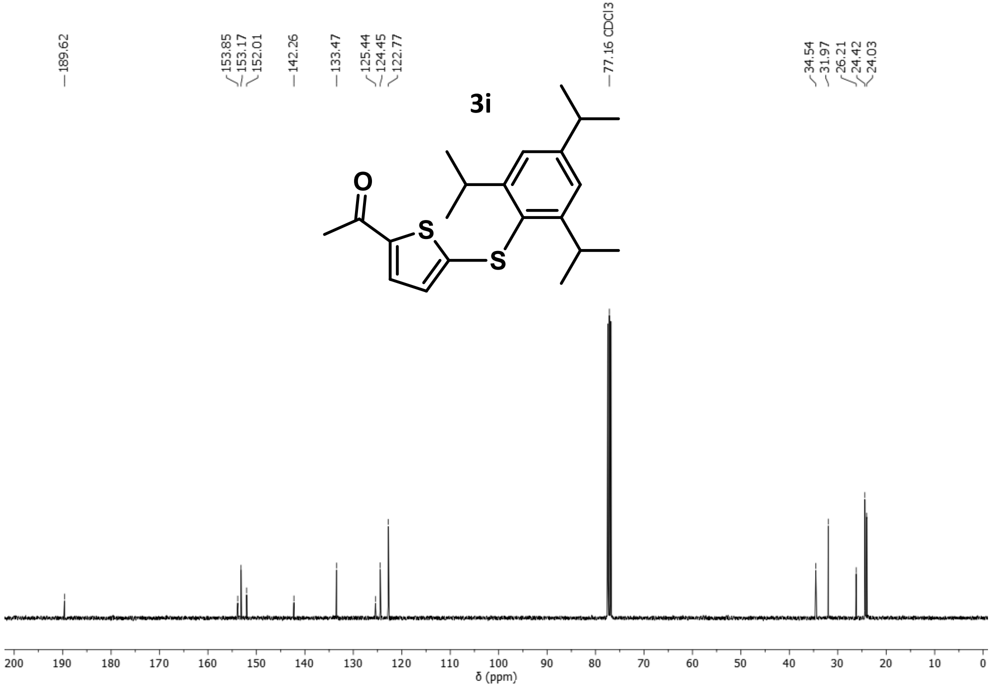
^{19}F 377MHz, CDCl$_3$



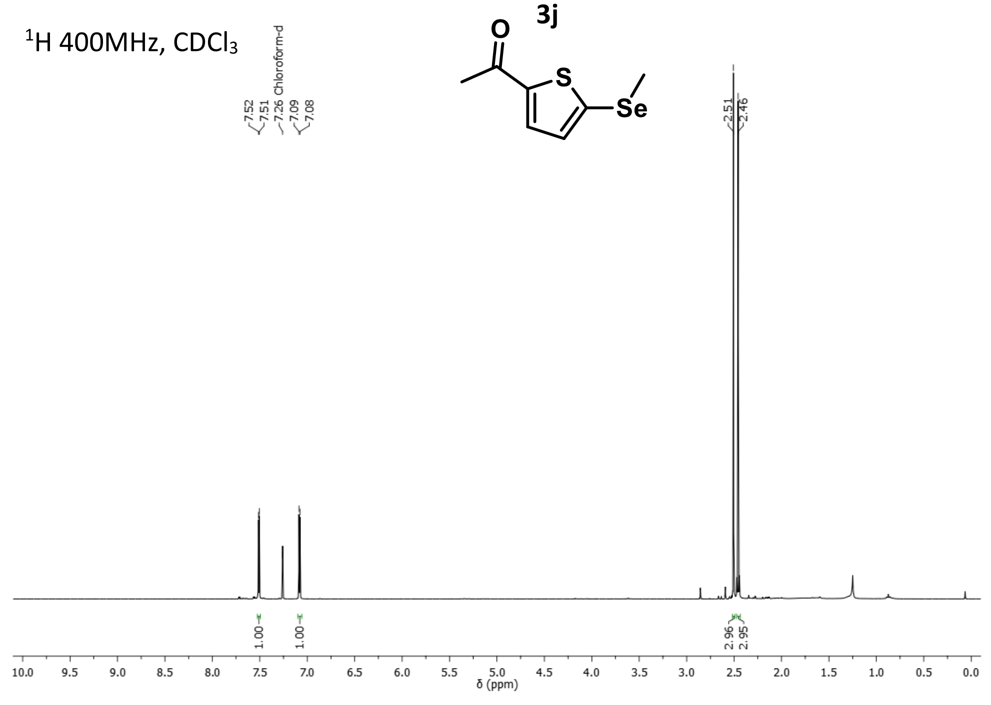
^{1}H 400MHz, CDCl$_3$



^{13}C 101MHz, CDCl$_3$

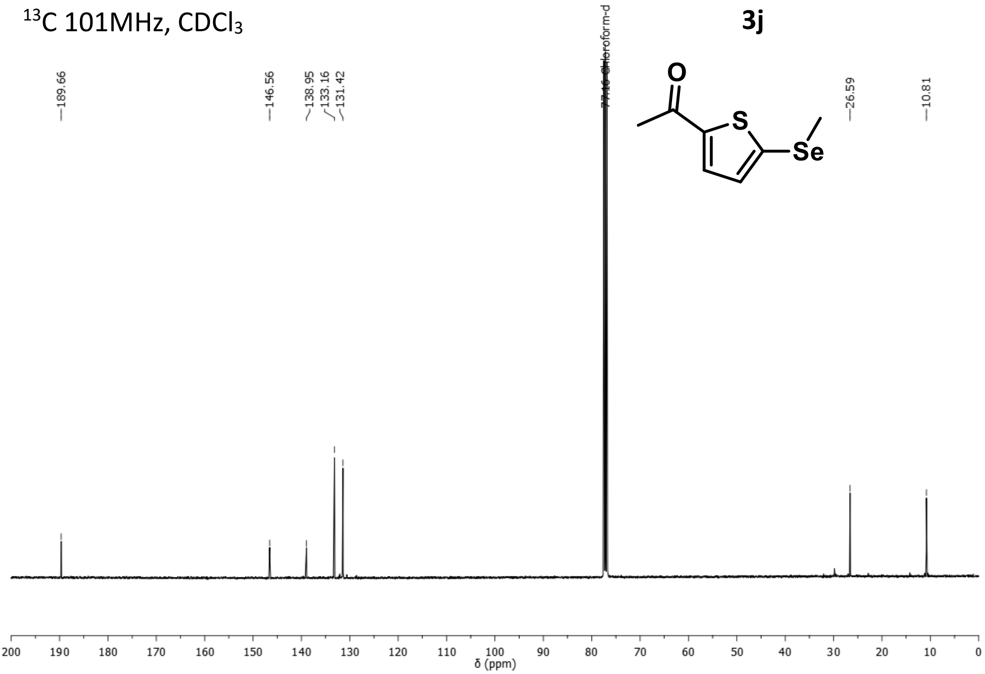


^{1}H 400MHz, CDCl$_3$



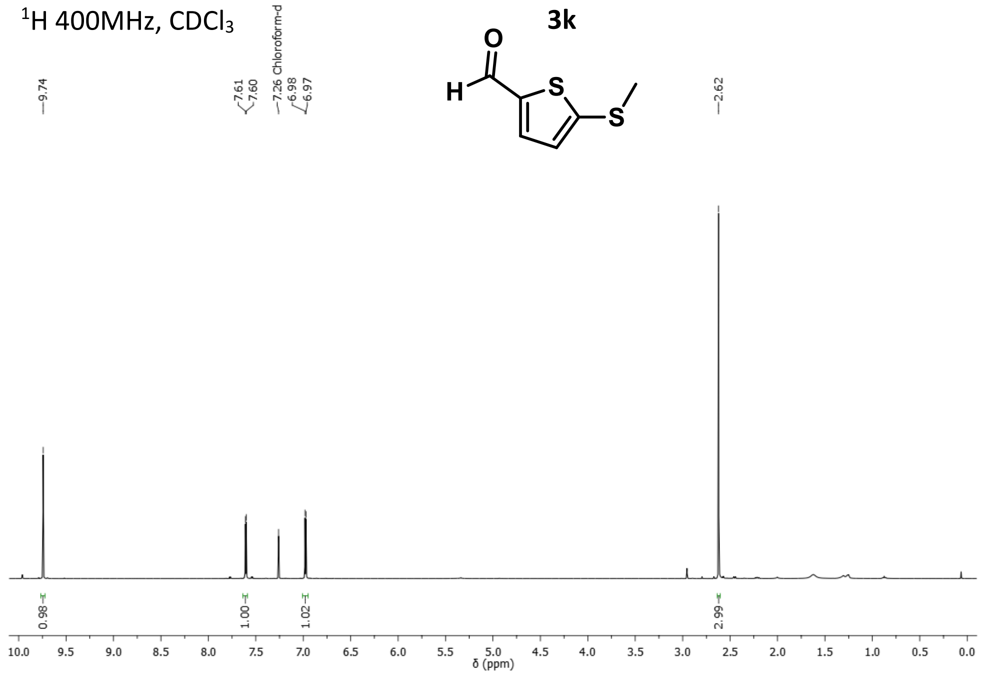
^{13}C 101MHz, $CDCl_3$

3j



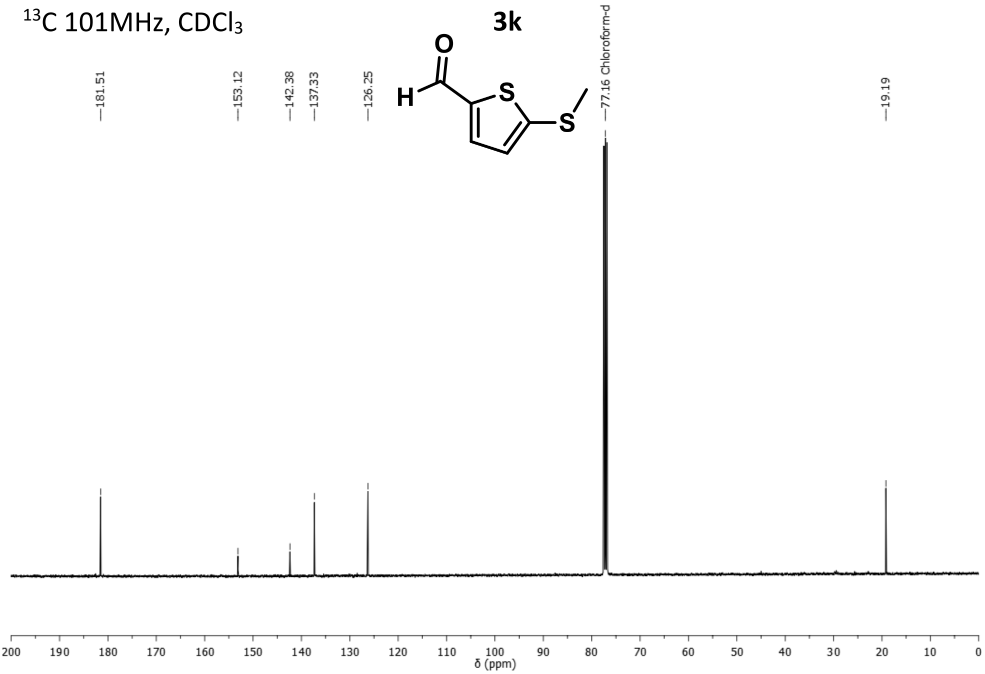
^{1}H 400MHz, $CDCl_3$

3k



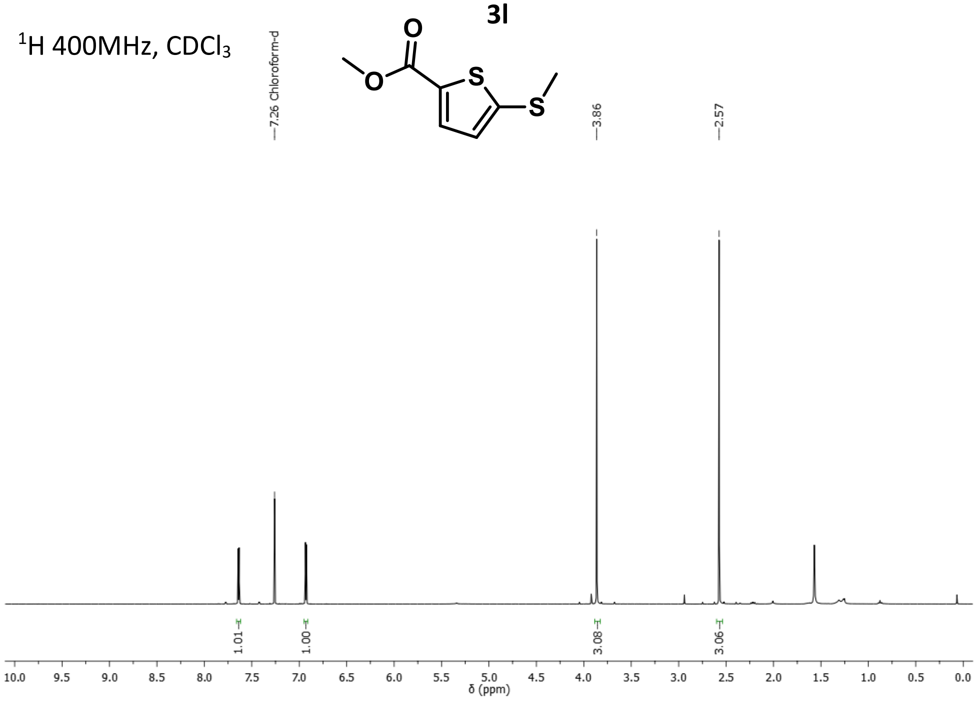
^{13}C 101MHz, CDCl$_3$

3k



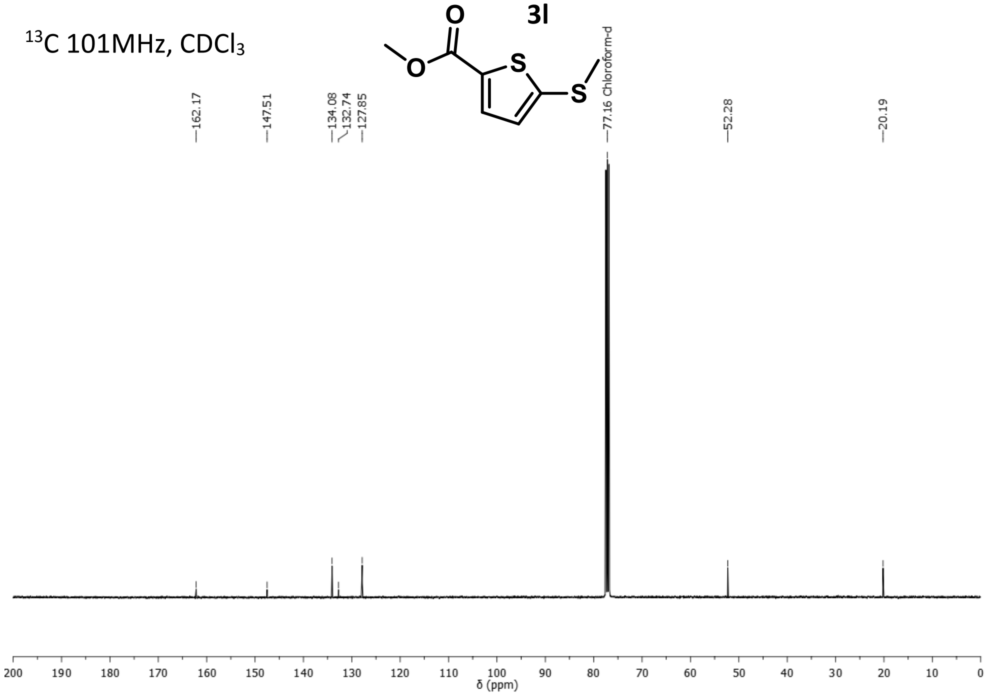
3l

^{1}H 400MHz, CDCl$_3$



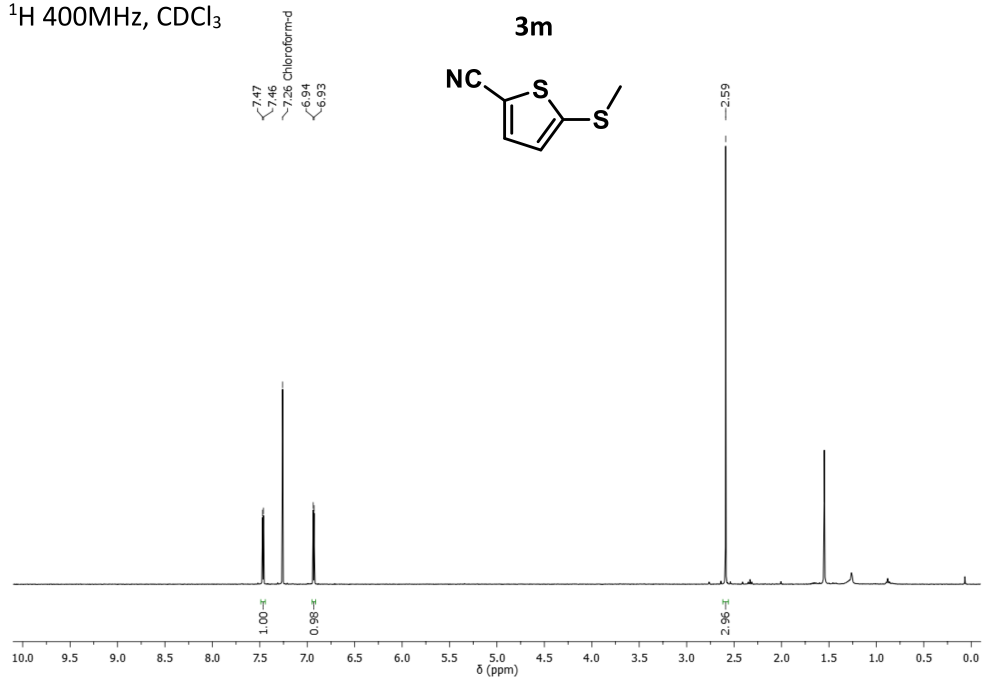
^{13}C 101MHz, CDCl$_3$

3l



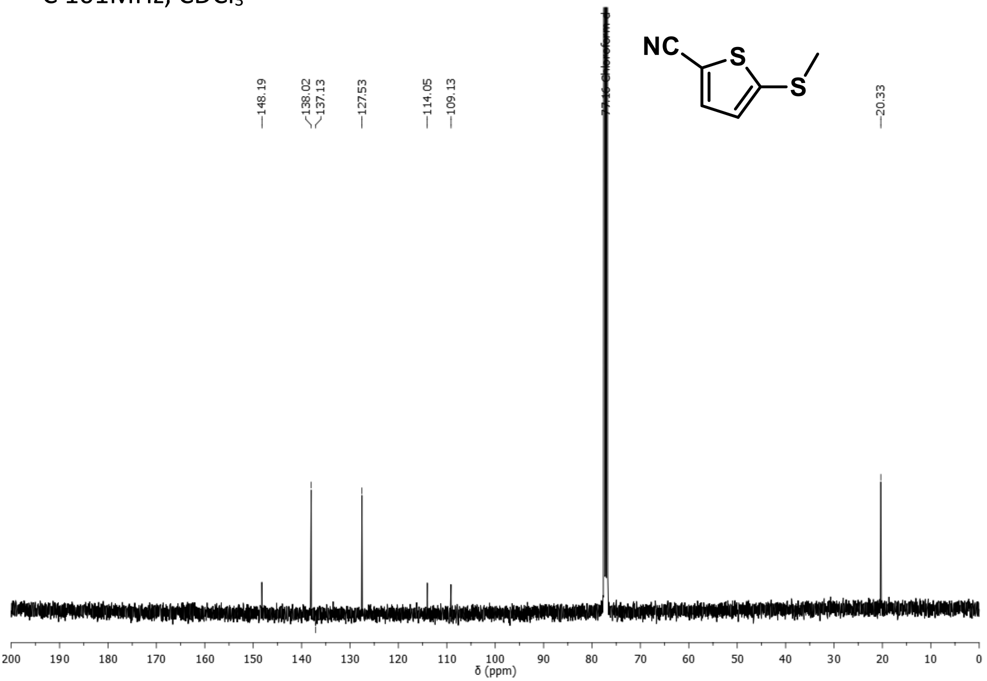
^{1}H 400MHz, CDCl$_3$

3m



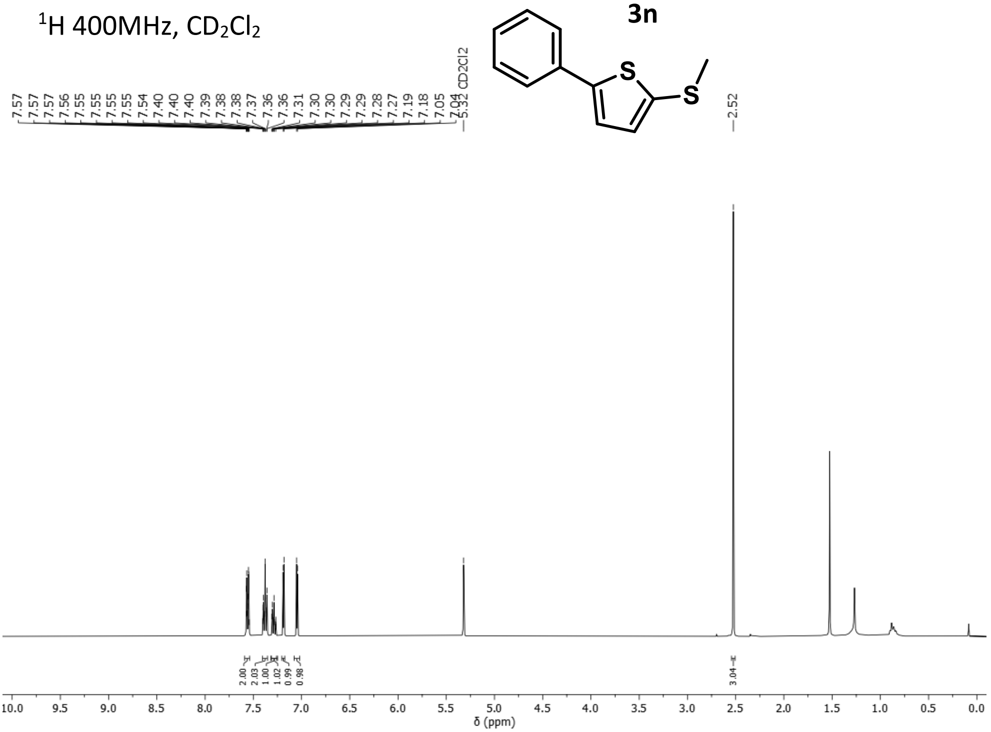
^{13}C 101MHz, CDCl$_3$

3m



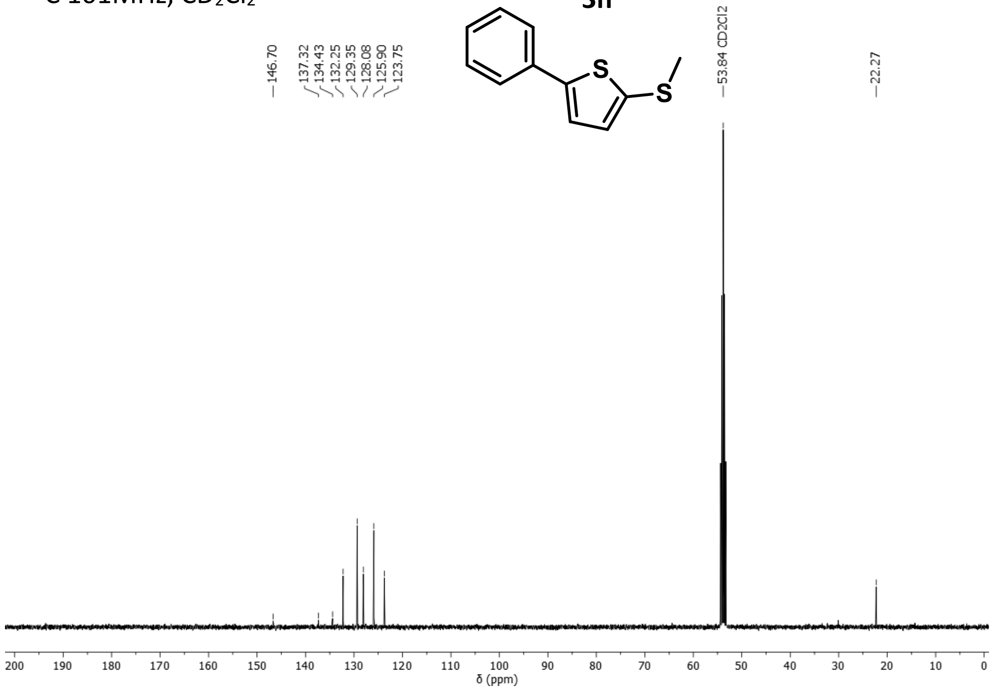
^{1}H 400MHz, CD$_2$Cl$_2$

3n



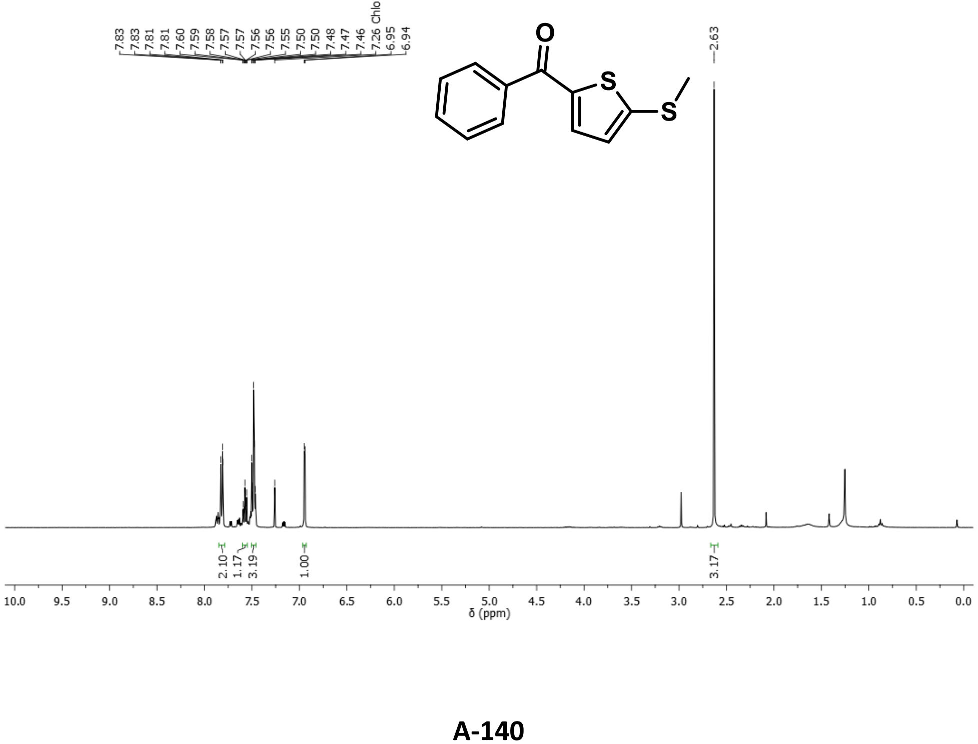
^{13}C 101MHz, CD$_2$Cl$_2$

3n

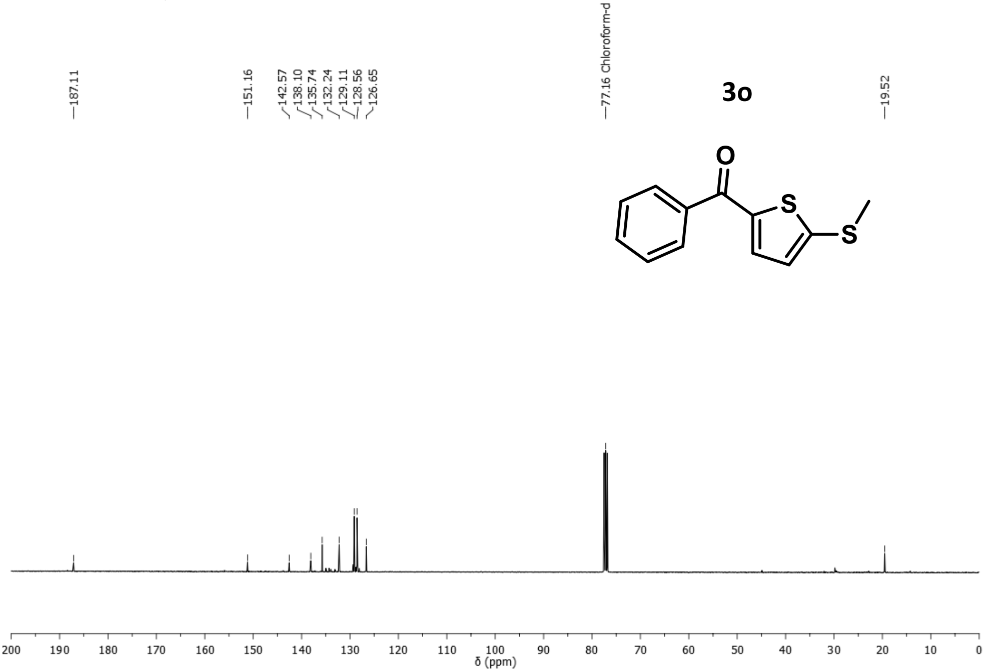


^{1}H 400MHz, CDCl$_3$

3o

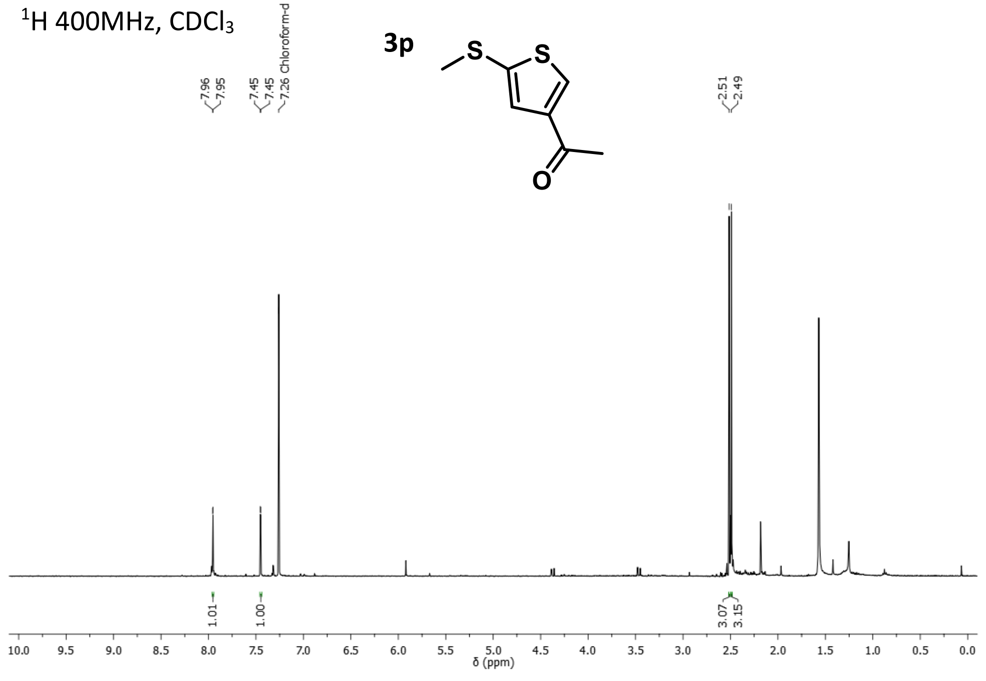


^{13}C 101MHz, CDCl$_3$



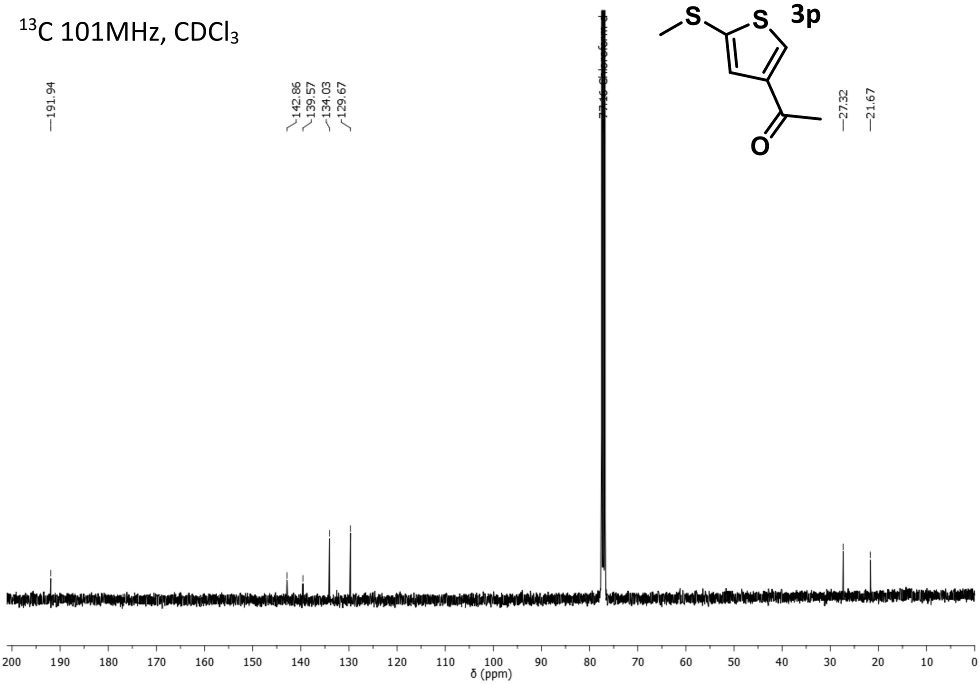
3o

^{1}H 400MHz, CDCl$_3$



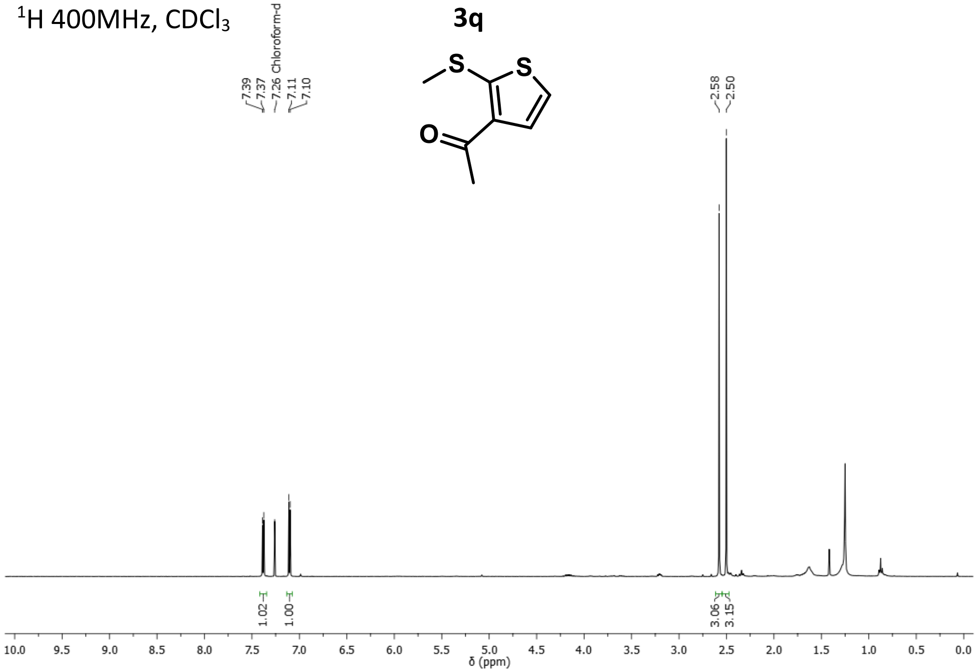
3p

^{13}C 101MHz, CDCl$_3$



3p

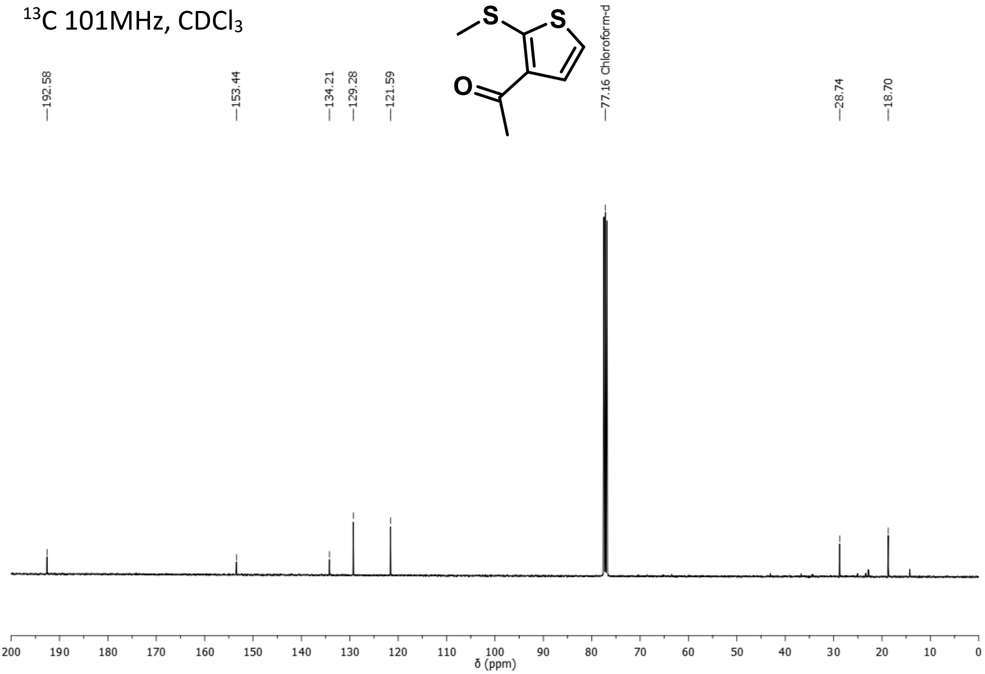
^{1}H 400MHz, CDCl$_3$



3q

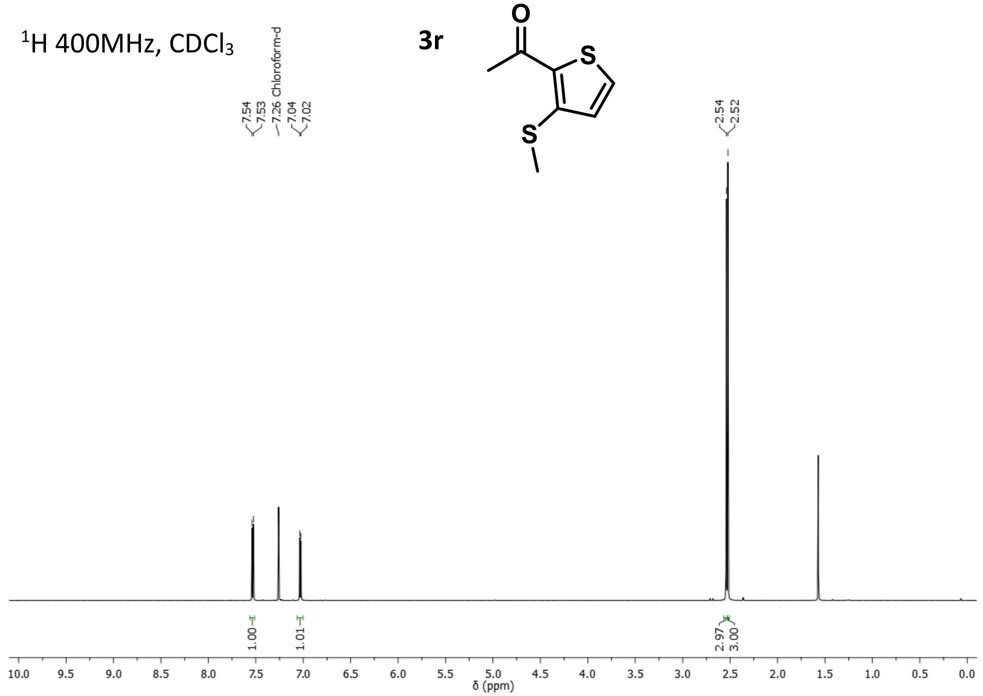
3q

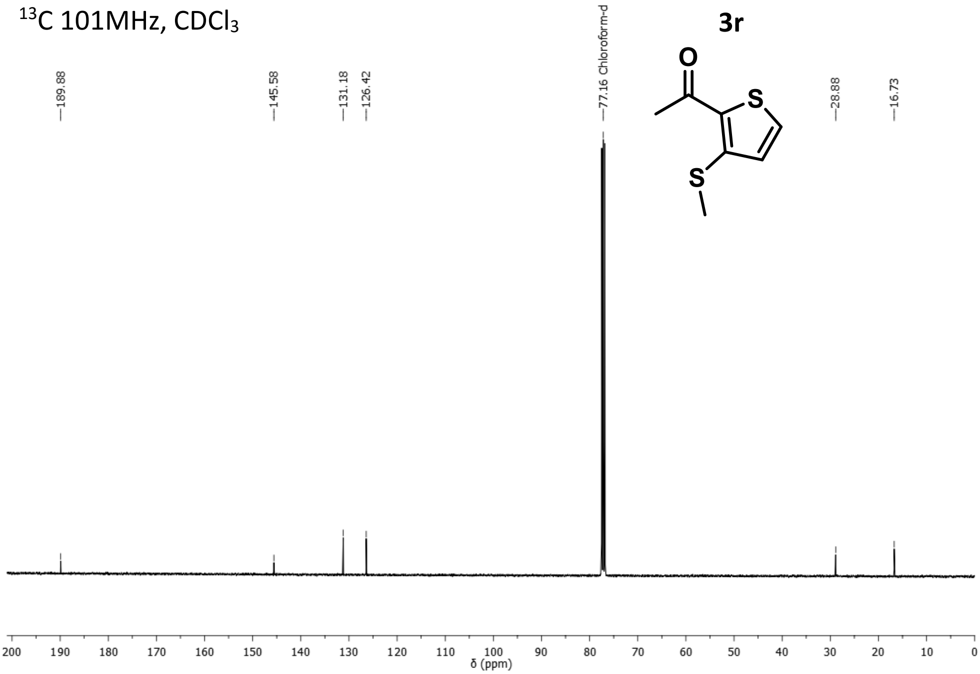
^{13}C 101MHz, CDCl$_3$

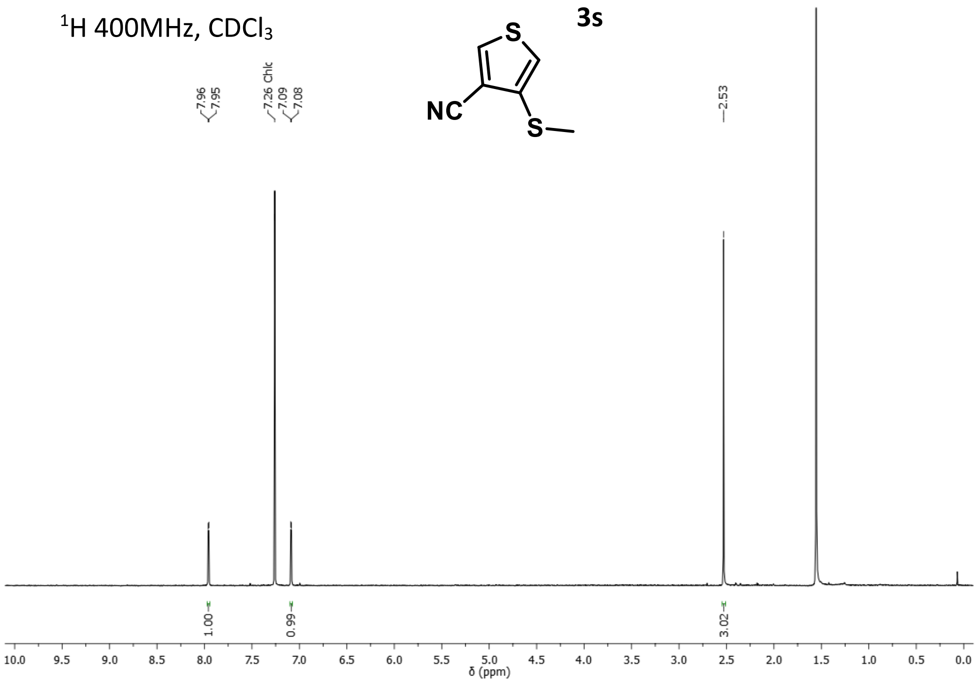


^{1}H 400MHz, CDCl$_3$

3r

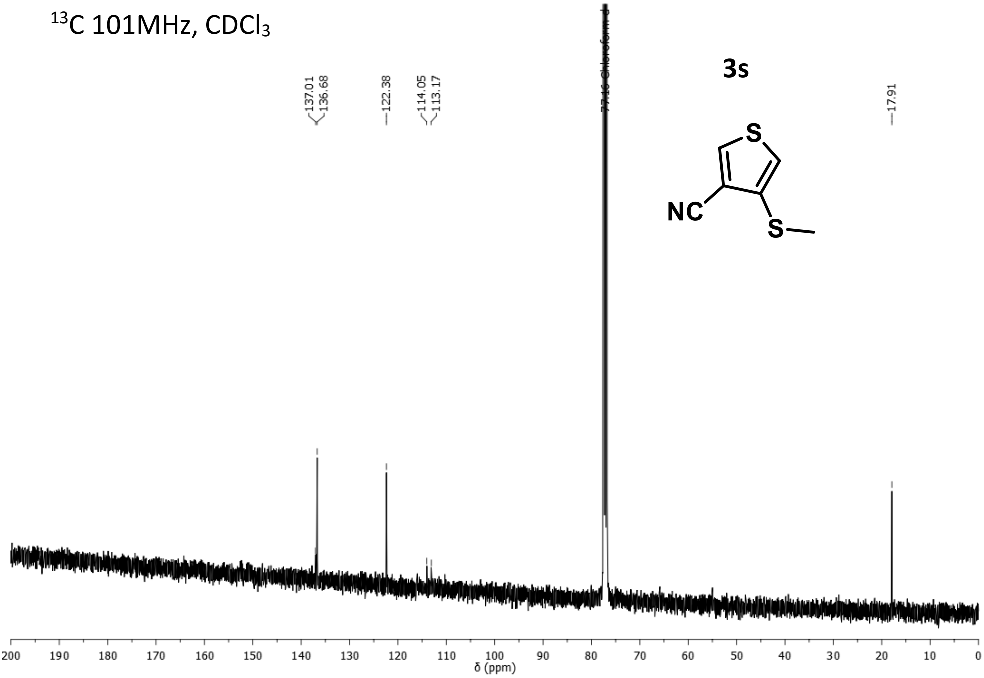



^{13}C 101MHz, CDCl$_3$
3r
O
S
S
189.88
145.58
131.18
126.42
77.16 Chloroform-d
28.88
16.73
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)


^{1}H 400MHz, CDCl$_3$
3s
S
NC
S
7.96
7.95
7.26 Chlc
7.09
7.08
2.53
1.00
0.99
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)

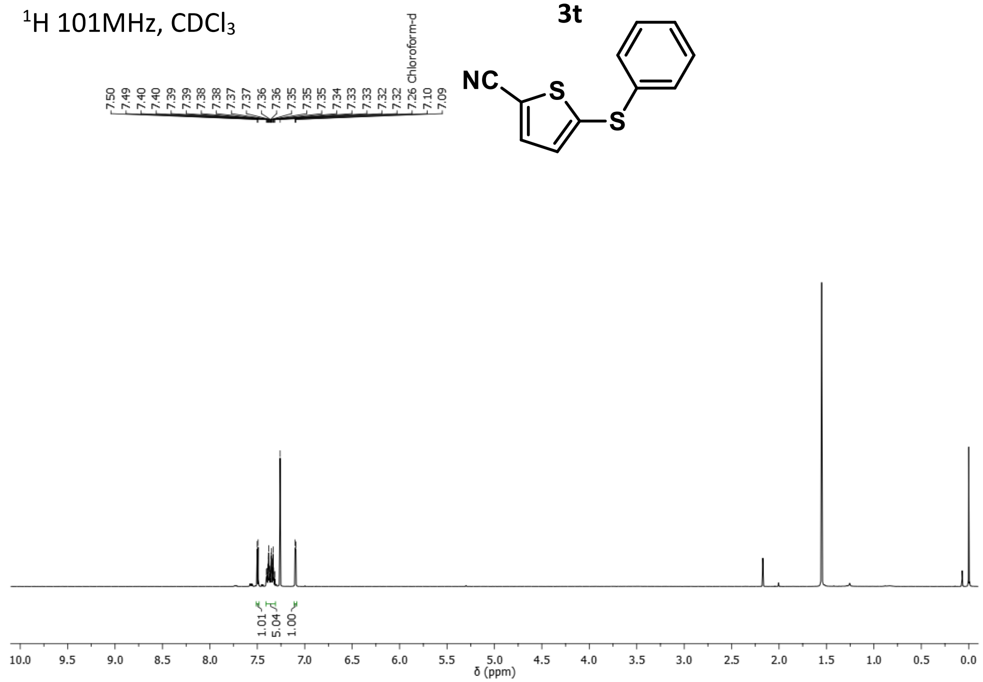
^{13}C 101MHz, $CDCl_3$

3s

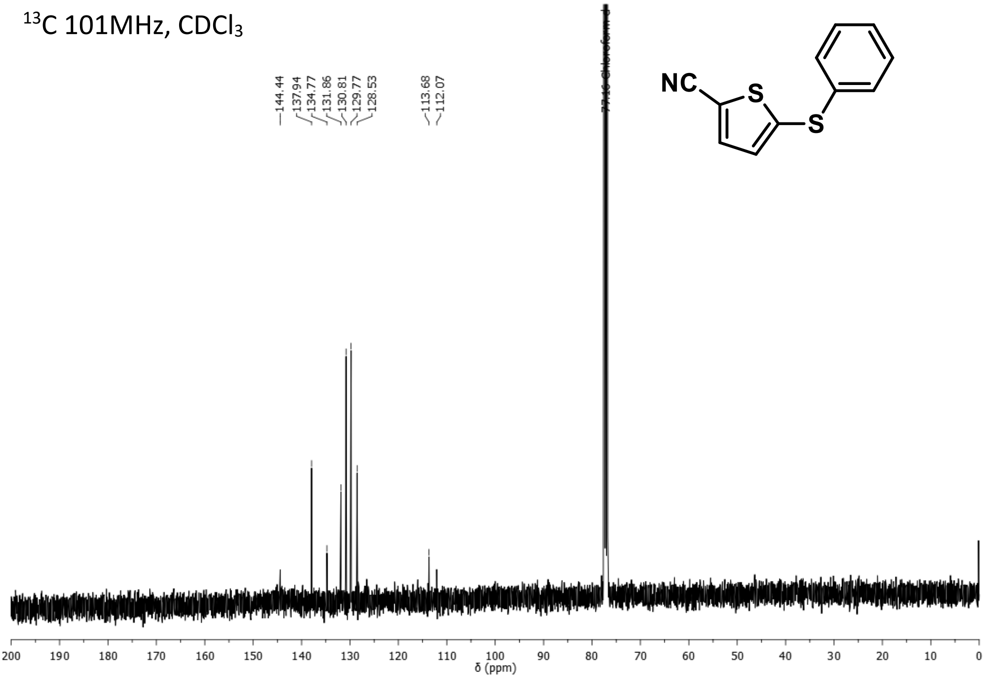


^1H 101MHz, $CDCl_3$

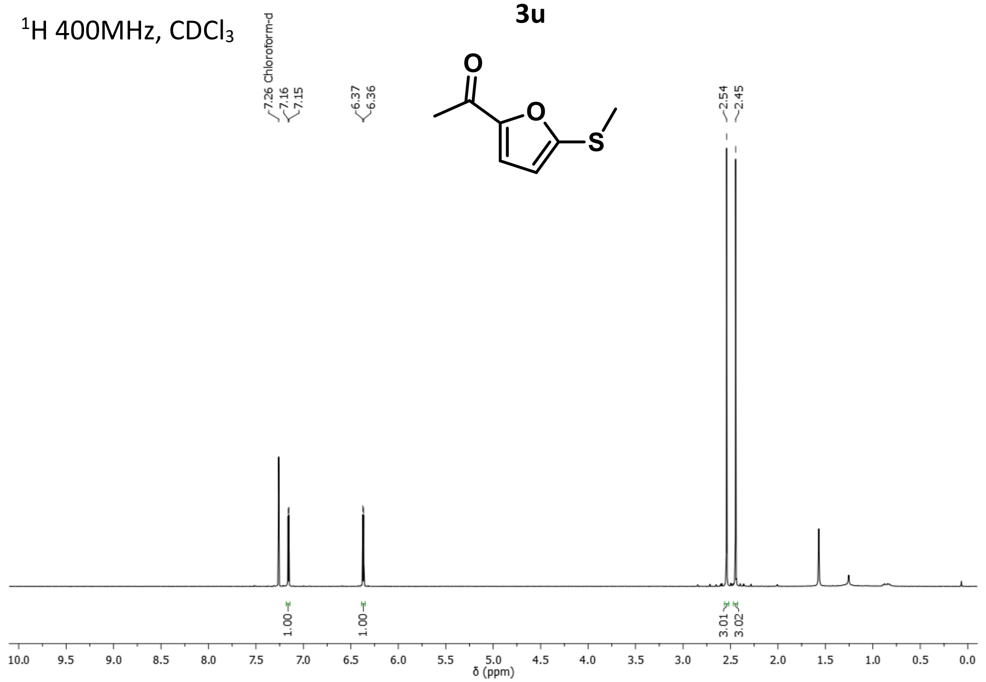
3t



3t

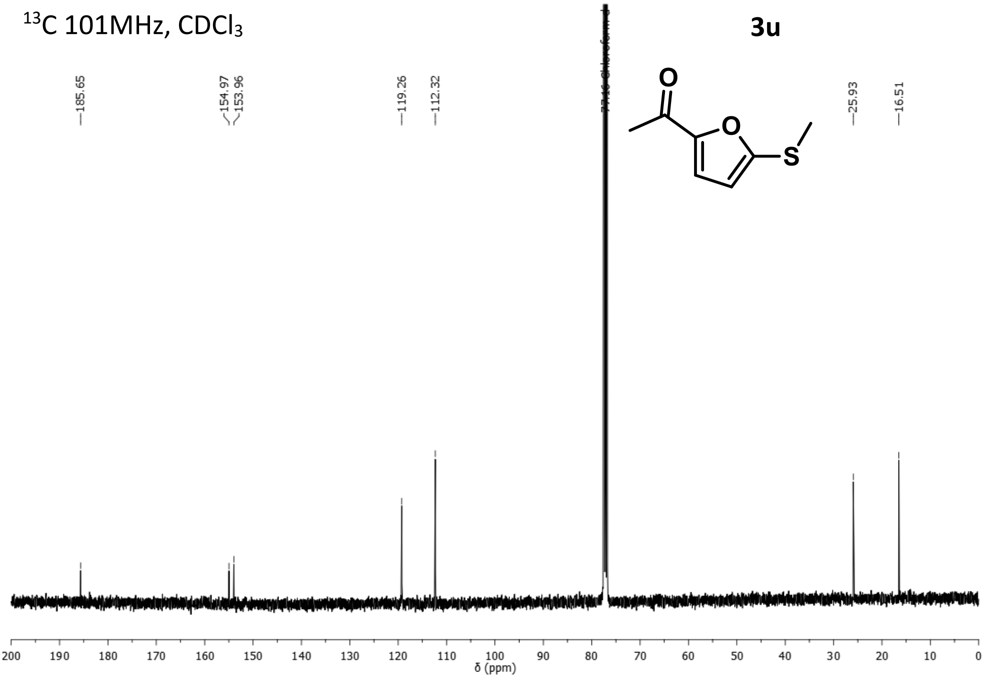

13C 101MHz, CDCl3
144.44
137.94
134.77
131.86
130.81
129.77
128.53
113.68
112.07
77.16 Chloroform-d
NC
S
S
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

3u


1H 400MHz, CDCl3
7.26 Chloroform-d
7.16
7.15
6.37
6.36
O
O
S
2.54
2.45
1.00
1.00
3.01
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)

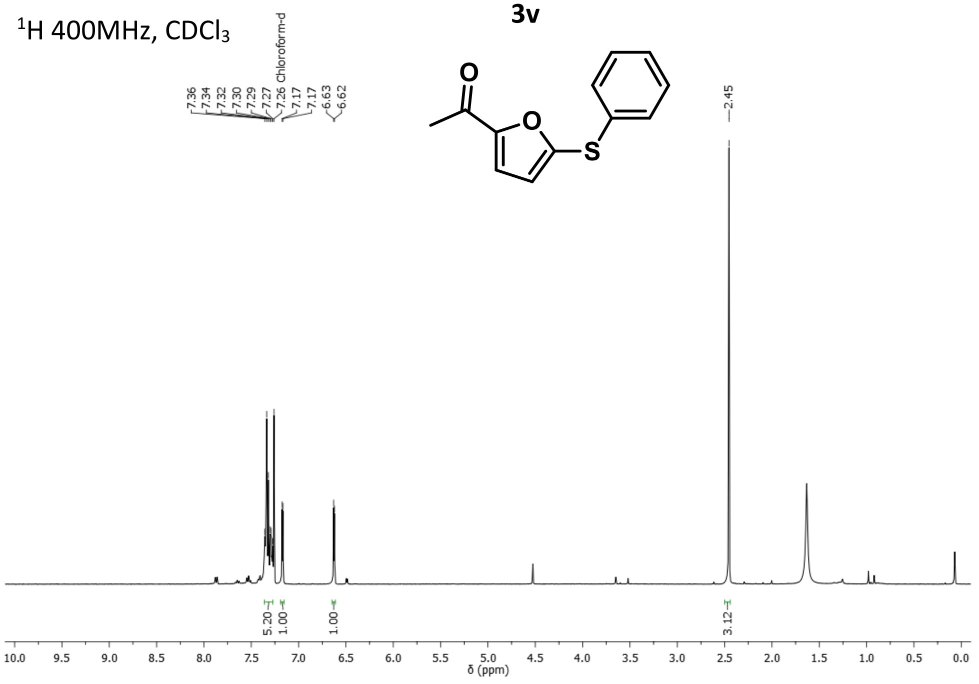
^{13}C 101MHz, CDCl$_3$

3u



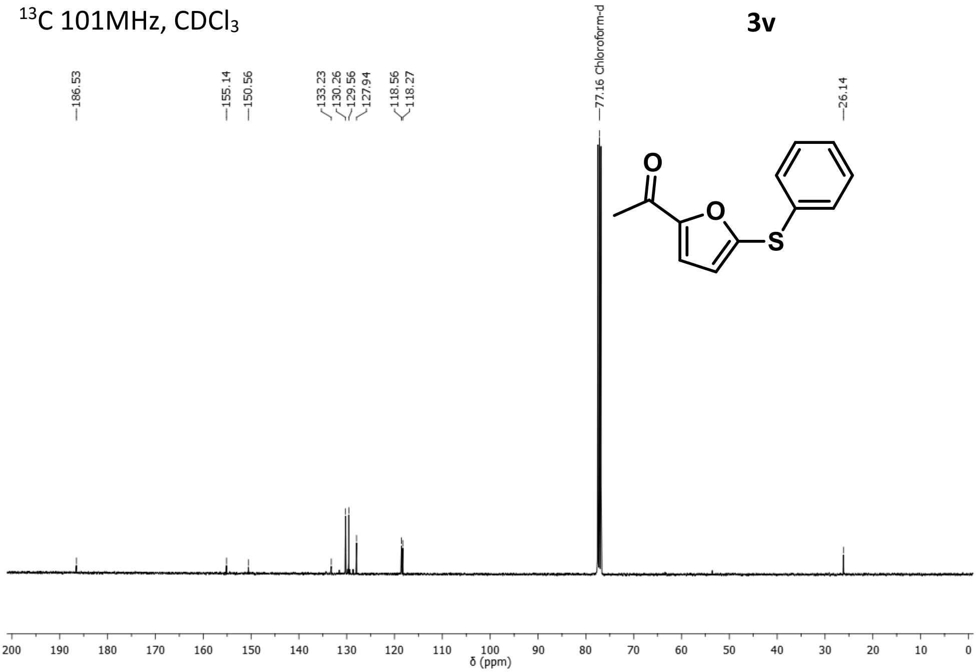
^{1}H 400MHz, CDCl$_3$

3v



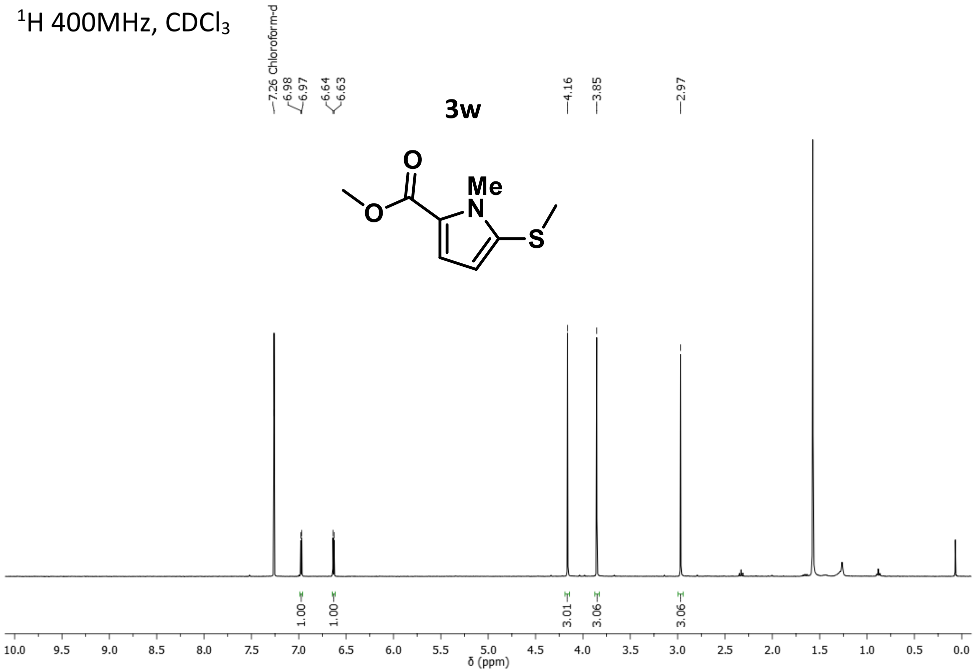
^{13}C 101MHz, $CDCl_3$

3v



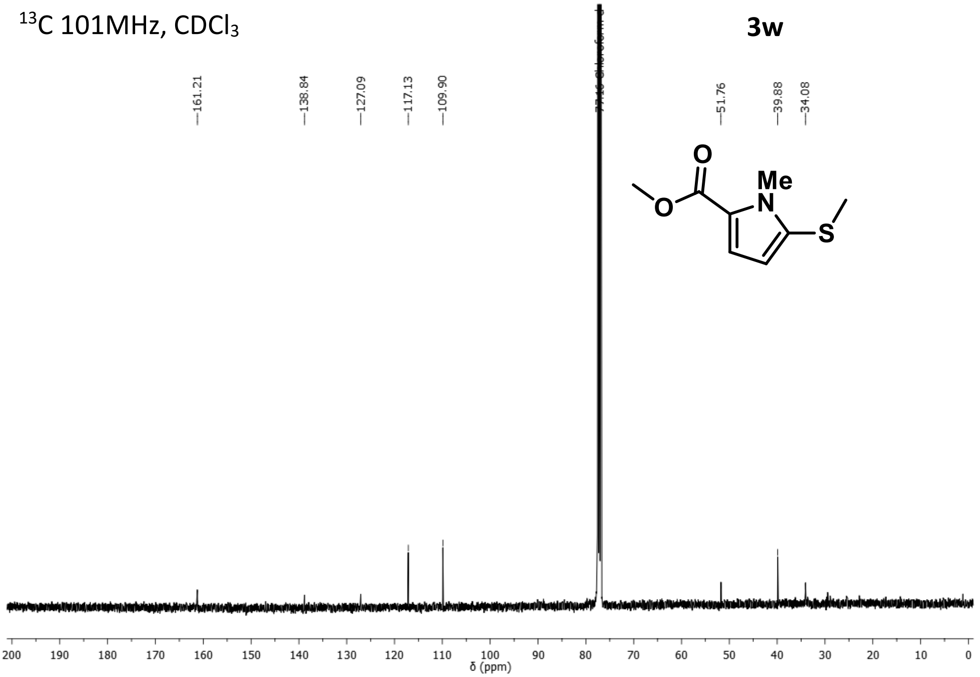
^{1}H 400MHz, $CDCl_3$

3w



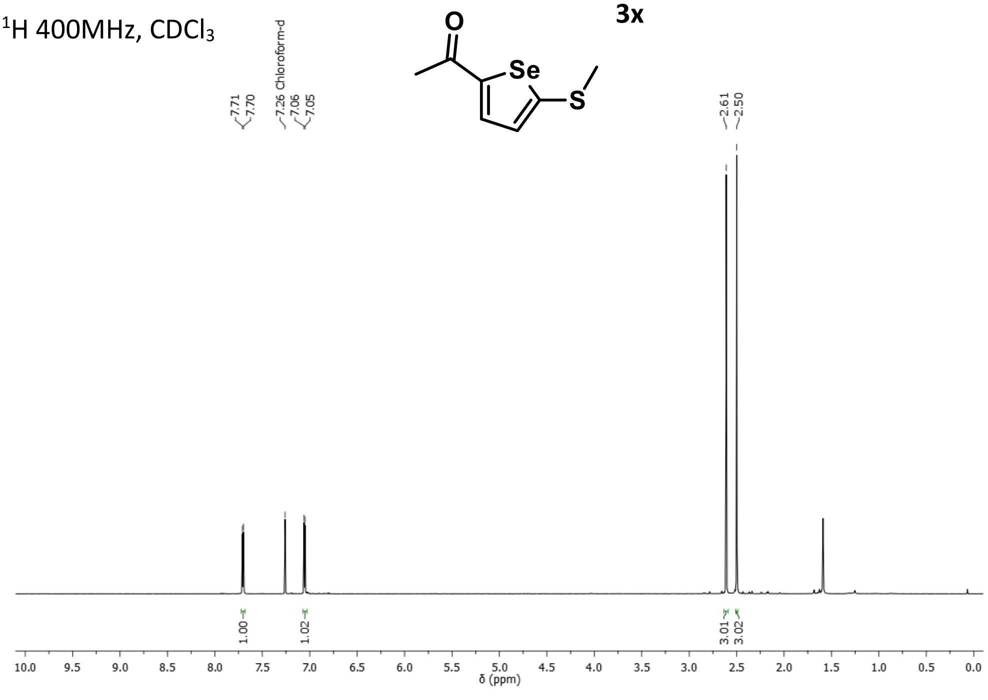
^{13}C 101MHz, CDCl$_3$

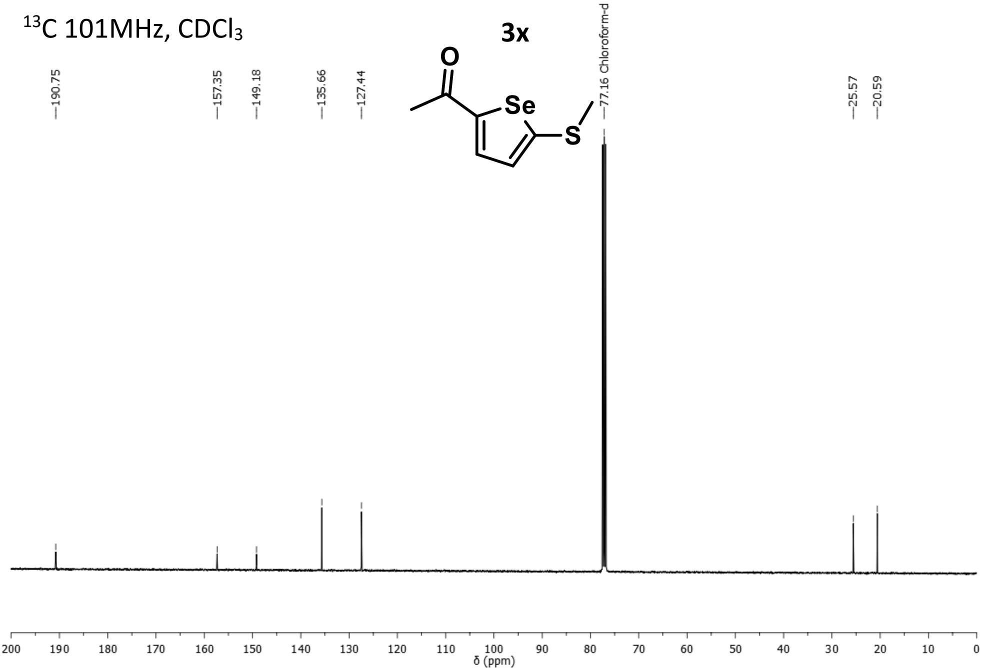
3w

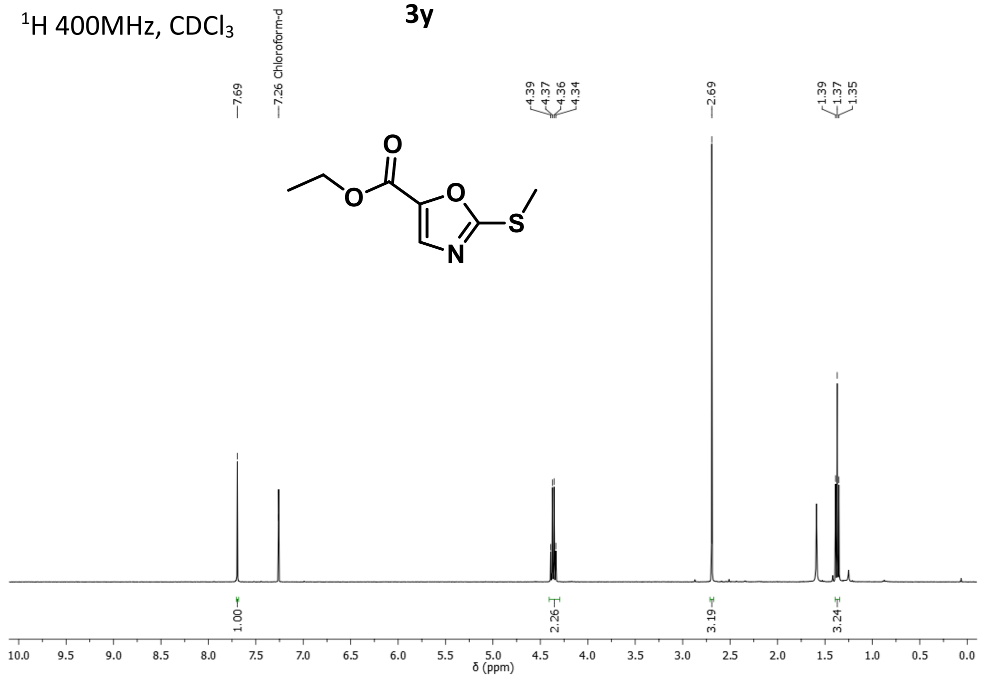


^{1}H 400MHz, CDCl$_3$

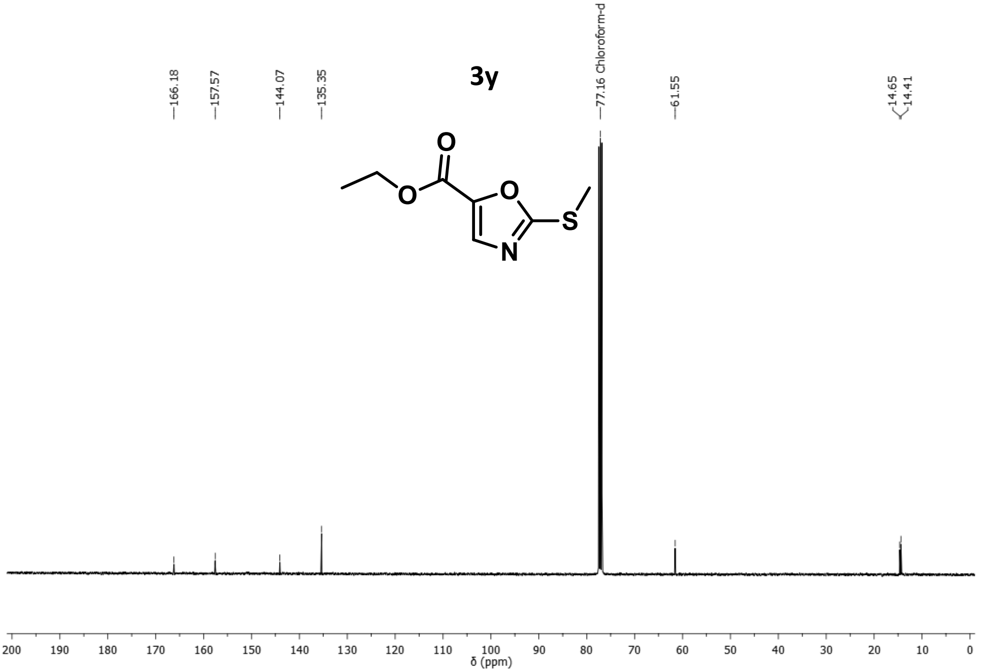
3x




^{13}C 101MHz, CDCl$_3$
3x
O
Se
S
190.75
157.35
149.18
135.66
127.44
77.16 Chloroform-d
25.57
20.59
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)

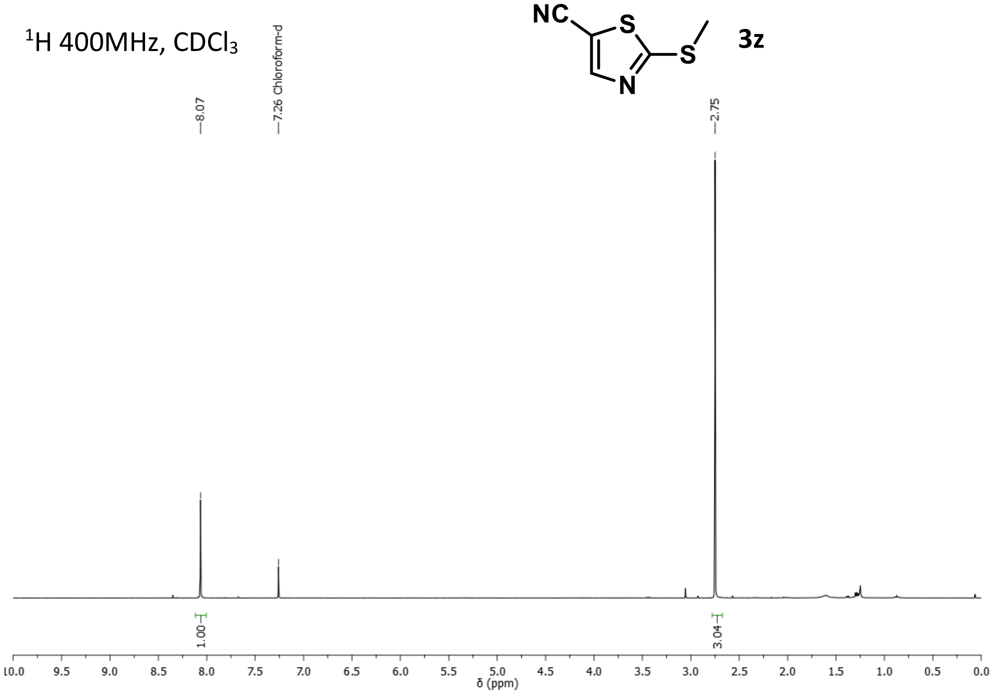

^{1}H 400MHz, CDCl$_3$
3y
O
O
O
S
N
7.69
7.26 Chloroform-d
4.39
4.37
4.36
4.34
2.69
1.39
1.37
1.35
1.00
2.26
3.19
3.24
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
δ (ppm)

^{13}C 101MHz, $CDCl_3$



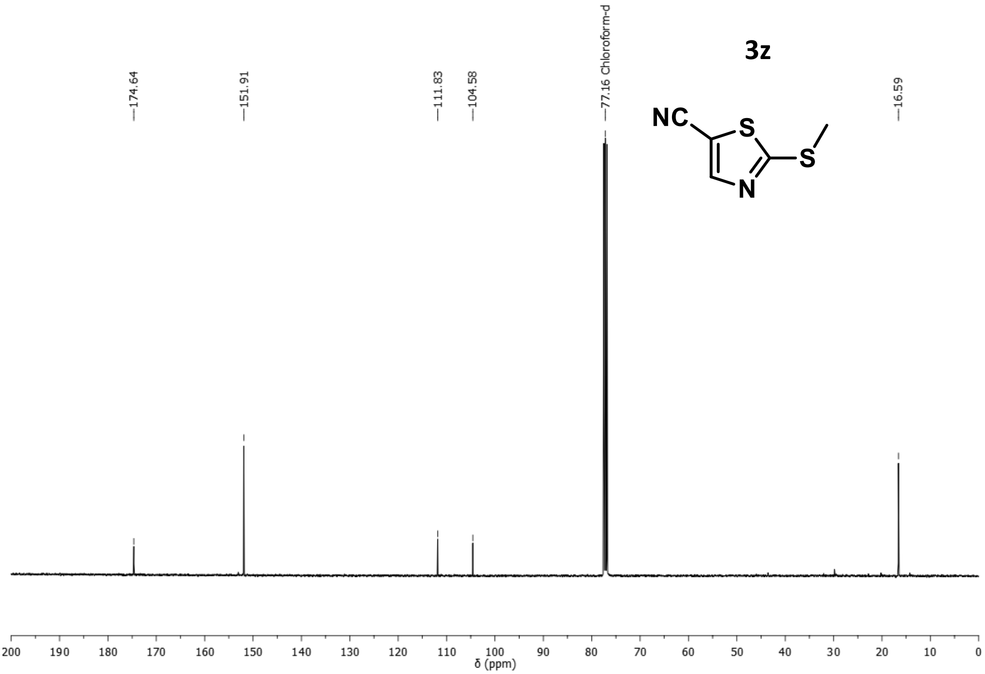
3y

^{1}H 400MHz, $CDCl_3$



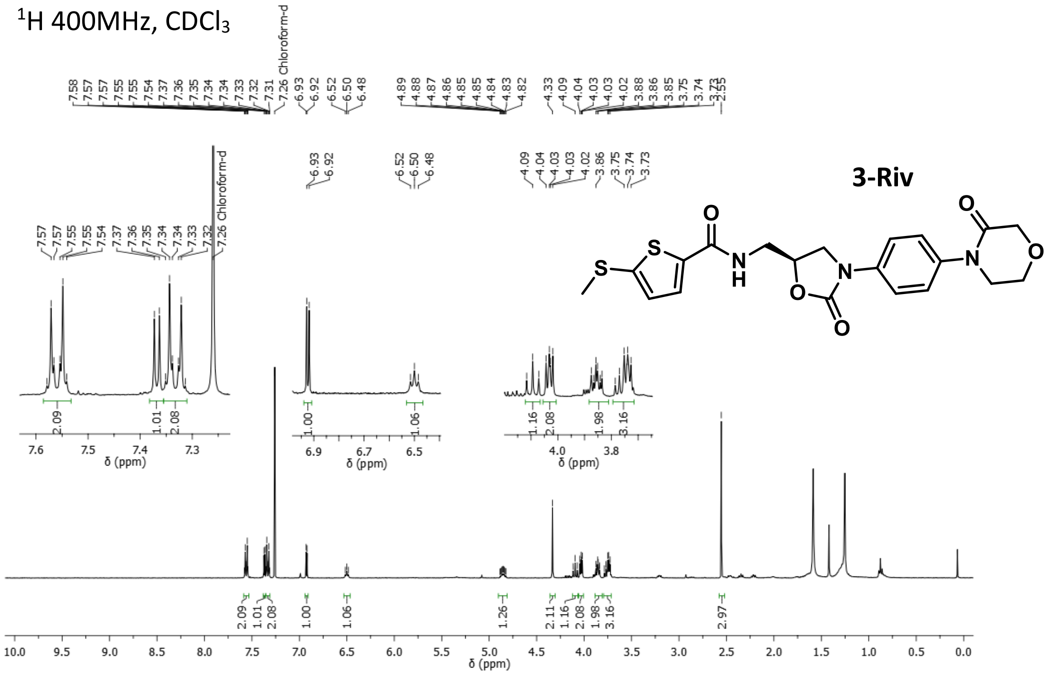
3z

^{13}C 101MHz, CDCl$_3$



3z

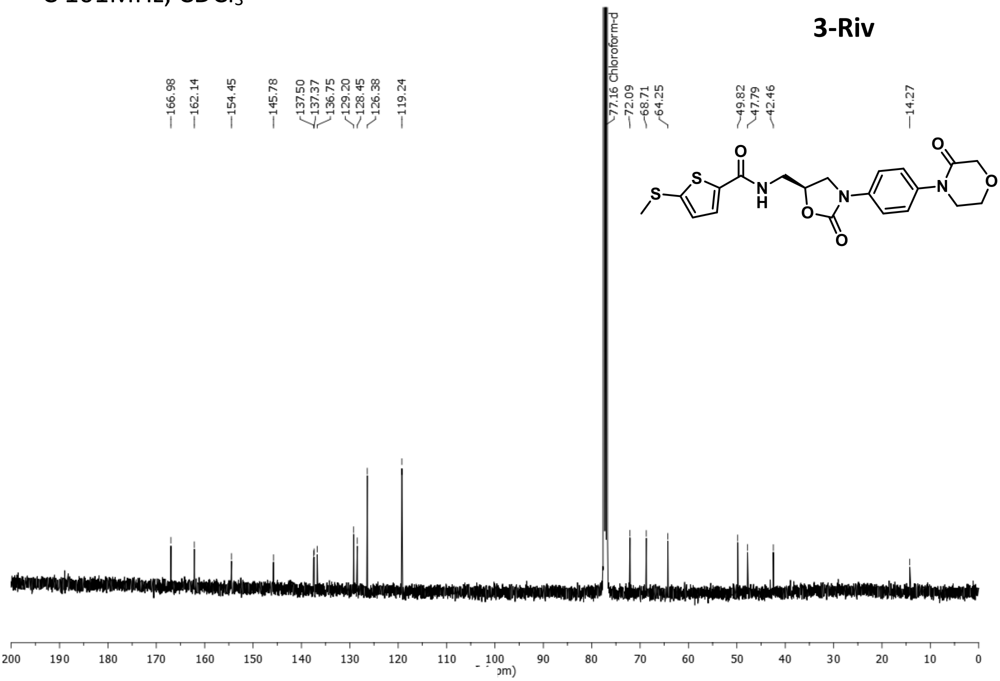
^{1}H 400MHz, CDCl$_3$



3-Riv

^{13}C 101MHz, CDCl$_3$

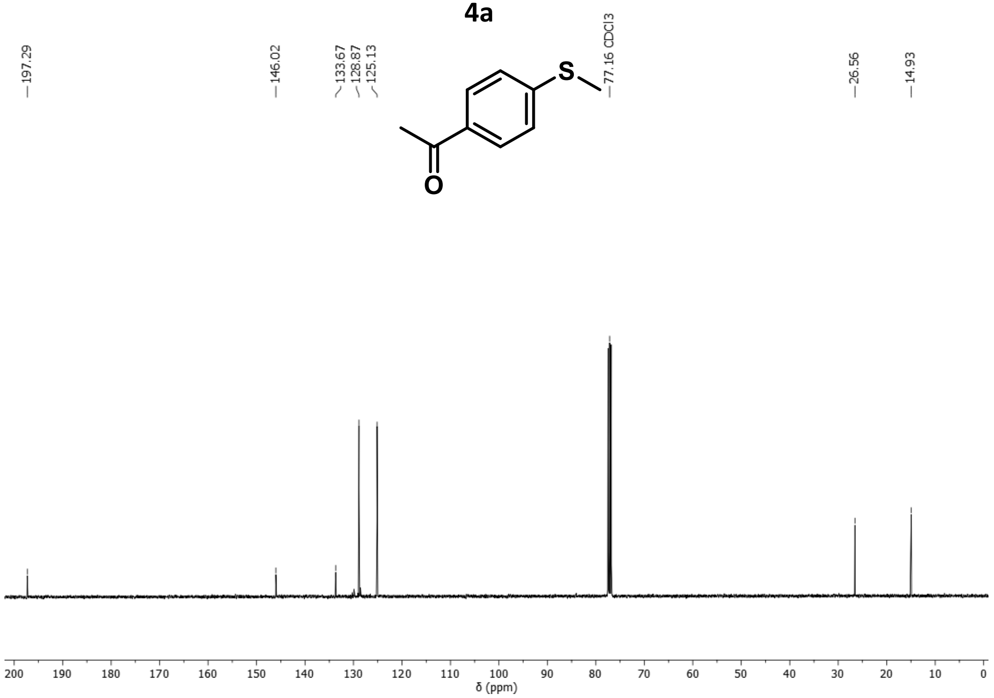
3-Riv



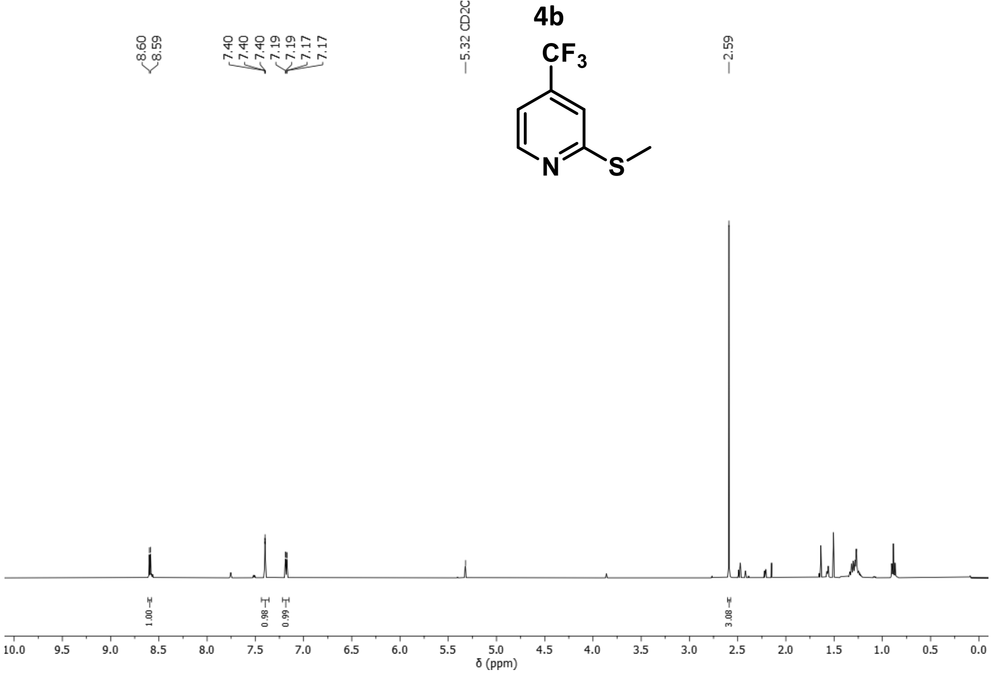
^{1}H 400MHz, CDCl$_3$

4a

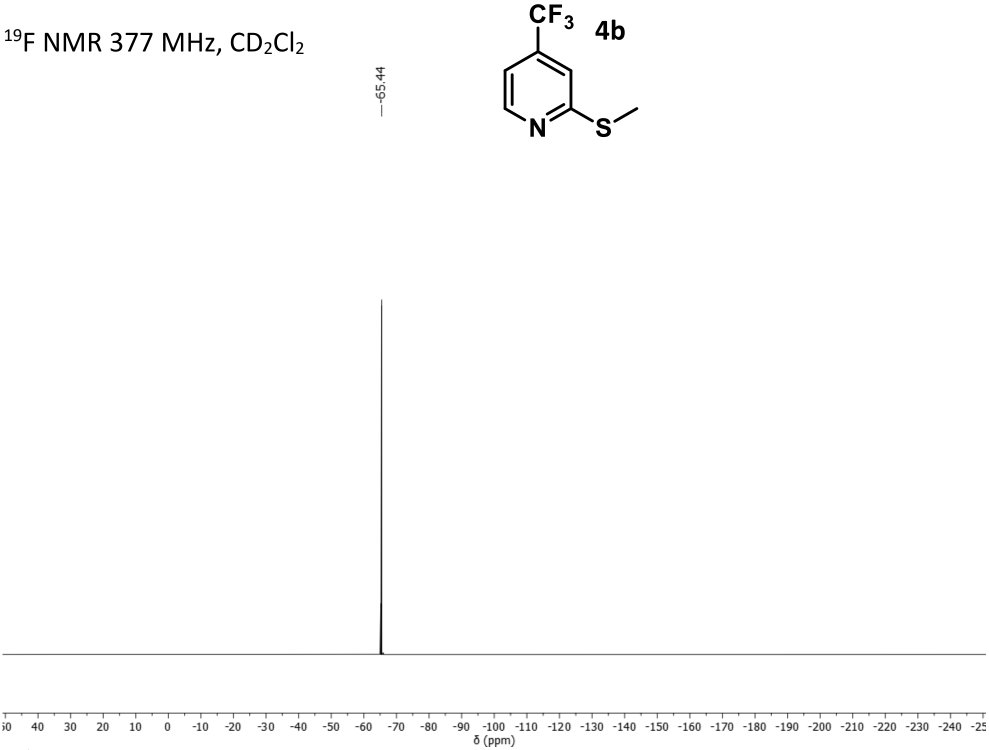
^{13}C 101MHz, $CDCl_3$



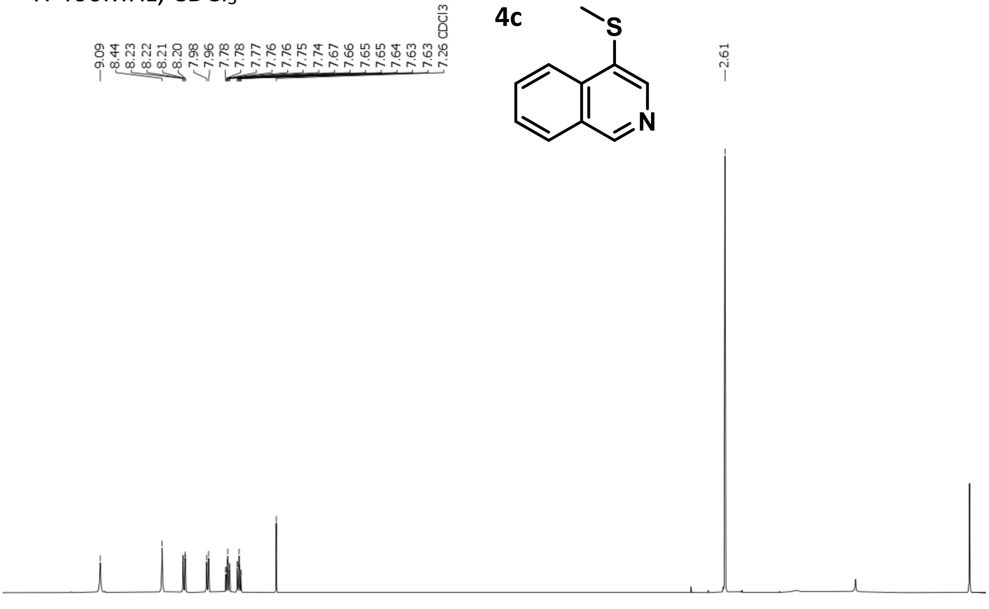
^1H 400MHz, CD_2Cl_2



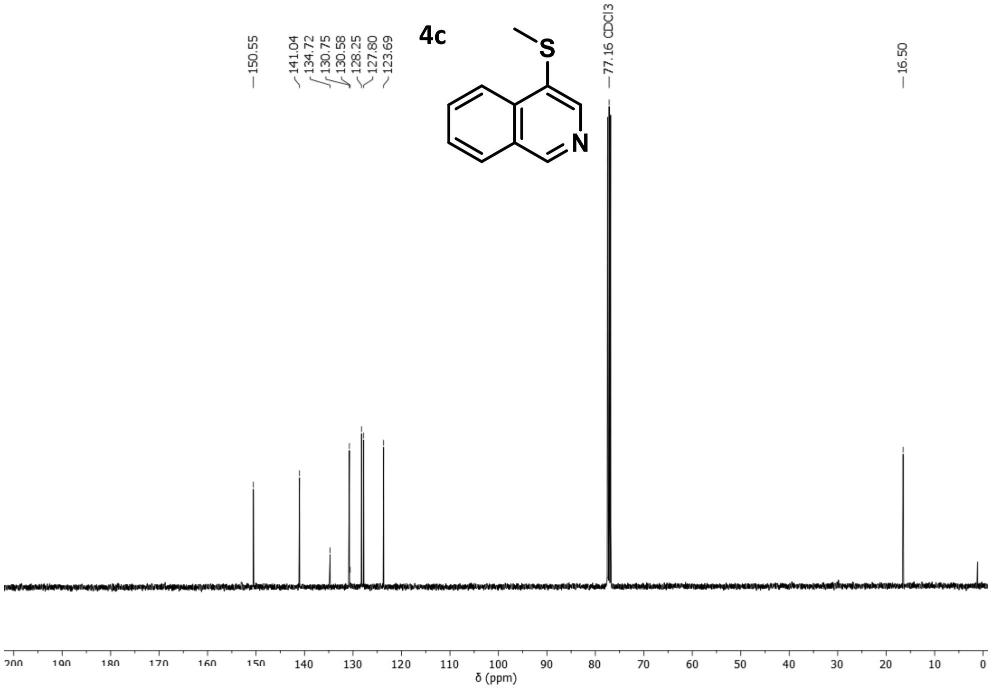
^{19}F NMR 377 MHz, CD_2Cl_2



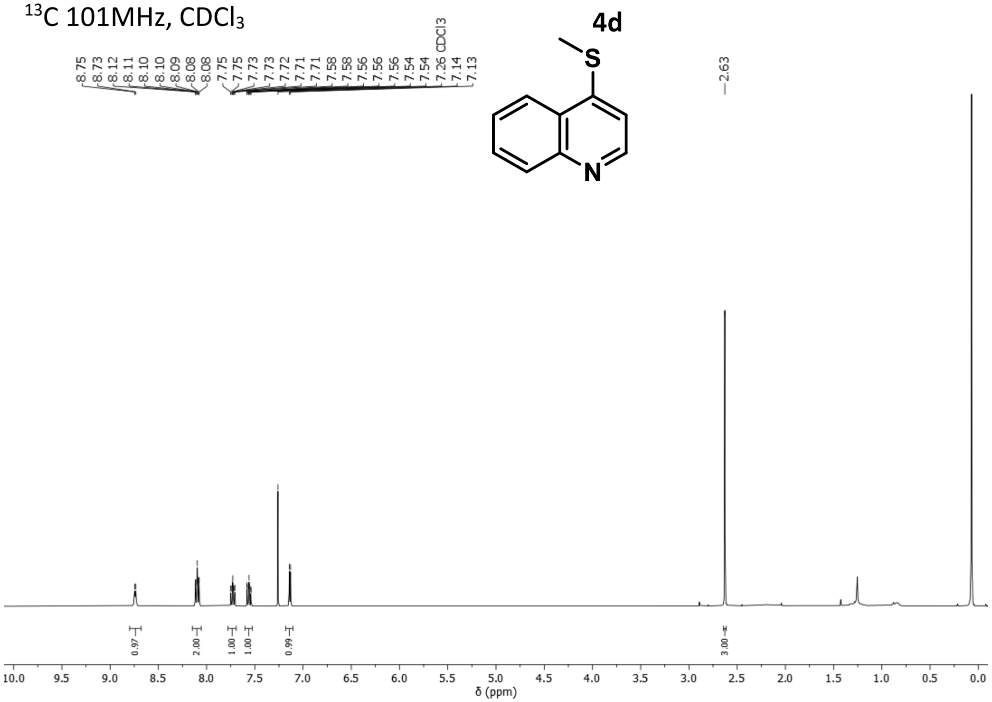
^{1}H 400MHz, $CDCl_3$



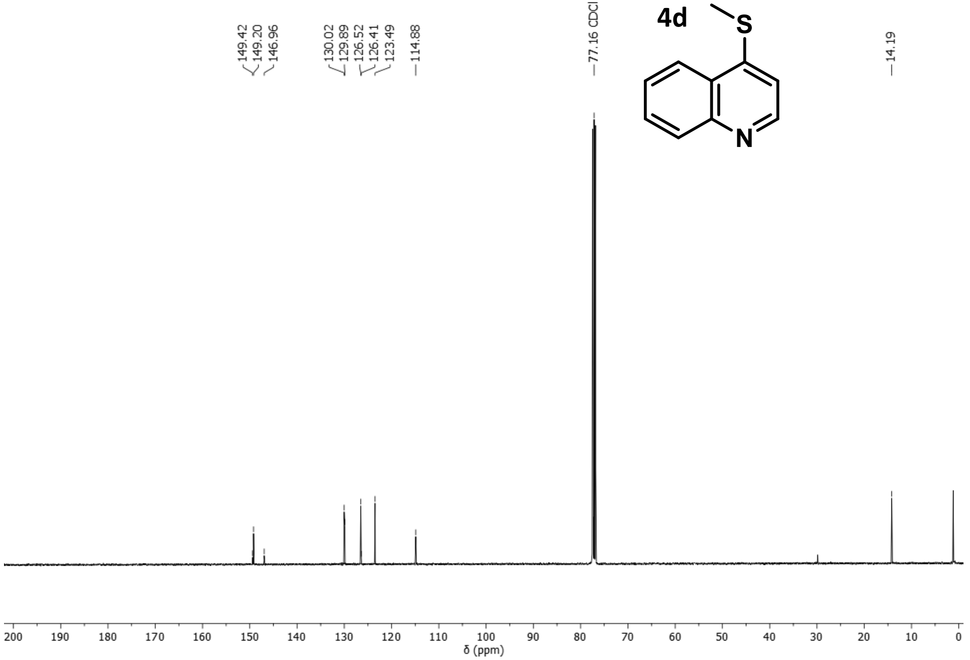
^{13}C 101MHz, CDCl$_3$



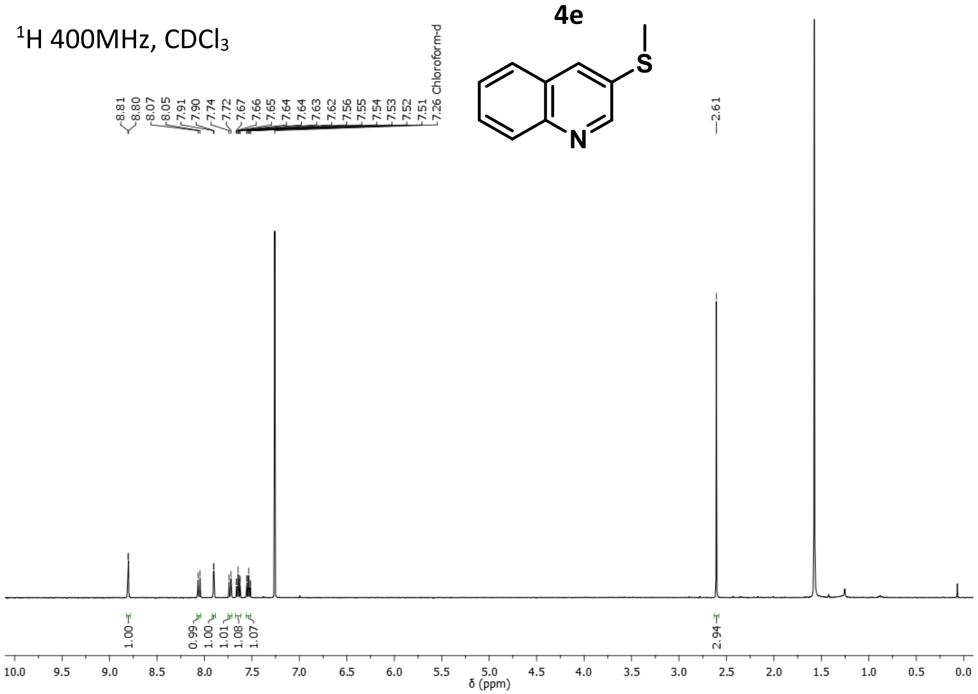
^{13}C 101MHz, CDCl$_3$



^{13}C 101MHz, $CDCl_3$



^{1}H 400MHz, $CDCl_3$



^{13}C 101MHz, $CDCl_3$