Visible Light Photoredox Catalysis

A versatile tool for the activation of small molecules

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Meiner Familie

„Es kommt nicht darauf an, mit dem Kopf durch die Wand zu rennen, sondern mit den Augen die Tür zu finden“

Werner von Siemens

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1. Introduction

At the end of the 19th century, Giacomo Ciamician (1857-1922) and Paul Silber (1851-1930) studied the reduction of nitrobenzene to aniline and 2-methylquinoline as a first example for a light mediated reaction.[1] Both, as well as other scientists before, e.g. J. Priestley (1733-1800), N. T. de Saussure (1767-1845) or Sir H. Davy (1778-1829), recognized the diversity of sunlight and its potential for applications as the most abundant and sustainable energy source.[2] The concept of harvesting, storing and using this inexhaustible energy source in ubiquitous biological photosynthesis by nature, was an initial signal for chemists to engage in the development of new strategies to become more independent from fossil resources.[3] Efficient methods for the conversion of light into electrical energy[4,5] have been developed, however, utilization of sunlight in photochemical reactions is limited owing to the insufficient absorption of the visible part of the spectrum by most organic molecules.[6] The excitation of such compounds generally requires short wavelength (λ) ultra-violet (UV) irradiation, which is problematic due to the instability of most chemical bonds under such conditions. Therefore, suitable sensitizers or photocatalysts[7] have been introduced to promote chemical transformations by visible light.

Irradiation of a sensitizer chromophore or a photoredox catalyst *via* visible light at λ = 400 – 800 nm leads to an excited species. As a result of a significant electron density shift, this state can transfer energy[8] or an electron to an organic substrate.[9] In this process, the substrate should not get excited by the irradiation, thus it does not react until activation by the catalyst occurs. Therefore, side reactions that are often associated in reactions with high energetic UV light can be minimized.[10] Similar to UV light, photoredox catalysts can utilize the visible part of the electromagnetic spectrum to drive chemical reactions, although the energy content of visible light is considerably lower.[3] In principle, photoredox catalysis operates as a versatile tool for oxidation and reduction processes. Both can be simplified depicted by two different catalytic cycles, an oxidative and a reductive quenching process, in which single electron transfer steps occur, respectively (Figure 1). Irradiation of the visible light photocatalyst (PCat) populates a stable and short-lived singlet excited state (PCat*) *via* metal to ligand charge transfer (MLCT). The following intersystem crossing (ISC) leads to a more stable triplet state.[11] Compared to the ground state, the excited species can be easier reduced or oxidized and operates either as electron donor or acceptor to close the catalytic cycle. In general, the photoredox catalyst is involved in two single electron transfer (SET) steps, i.e the quenching process after excitation

and subsequently the regeneration of the catalyst itself. Depending on the reaction conditions, both single electron transfer steps can be utilized for chemical transformations.[6]

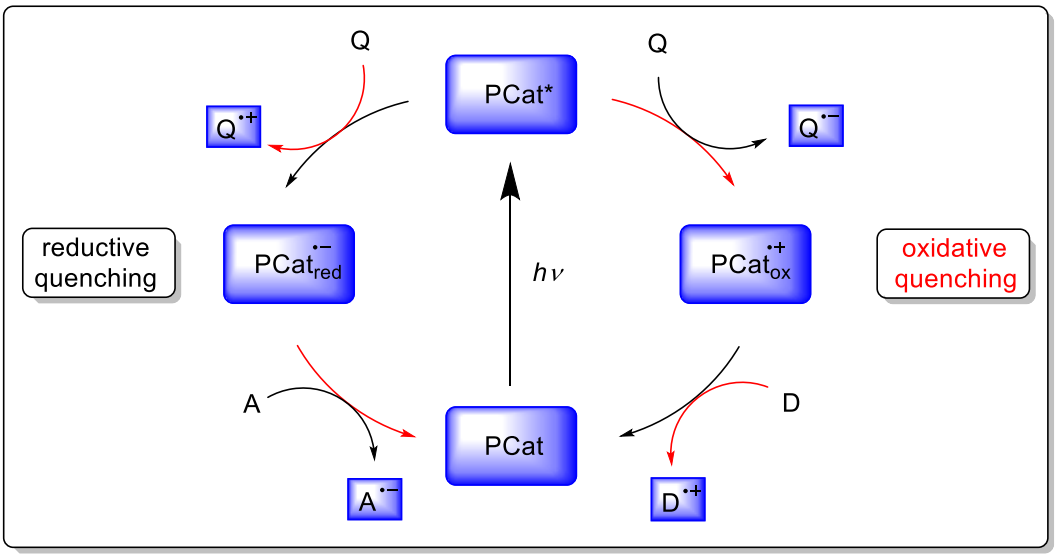
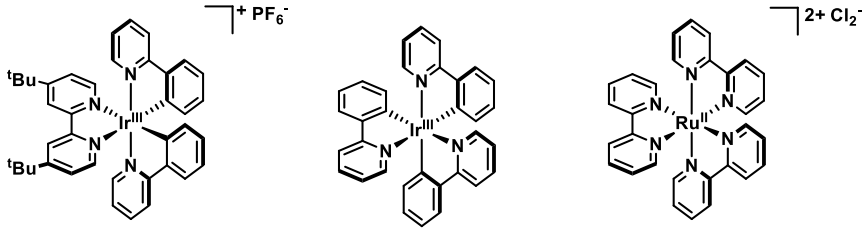


Figure 1. General paradigm of the photoredox catalysis by reduction or oxidation cycle. Oxidative process illustrated in red, reduction process in black. PCat = photoredox catalyst, A = acceptor, D = donor, Q = quencher.

Ruthenium and iridium based polypyridyl complexes are used for the majority of light mediated chemical processes due to their ease of synthesis, superior photoredox properties and excellent stability in an oxygen atmosphere compared to other inorganic complexes.[10] Commercially available $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ **1** (ppy = phenylpyridine, dtb-bpy = 4,4'-di-*tert*-butyl-2,2'-bipyridine),[12-14] *fac*-$Ir(ppy)_3$[14-17] **2** and $Ru(bpy)_3Cl_2$ **3** (bpy = 2,2'-bipyridine)[18,19] are arguably the most common photoredox catalysts and were employed in this thesis, too. Notable properties of these catalysts are their high oxidation and reduction potentials for single electron transfer, as well as the sufficient long lifetimes of their excited triplet states, and their emission maximas for the choice of suitable lightning devices (Table 1). Hence, the most suitable catalyst has to be selected considering the reduction (E_{Red}) or oxidation (E_{Ox}) potential of the compounds that are desired to be transformed, either following a reductive (Chapter 3) or an oxidative quenching cycle (Chapter 4 and 5). Furthermore, the redox potentials of the photocatalysts can be further tuned by modification of the ligands.[20]

Table 1. Redox potentials and selected photophysical properties of the visible light photoredox catalysts used in this thesis.[11]



		1	2	3
		$[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$	*fac*-$Ir(ppy)_3$	$[Ru(bpy)_3]Cl_2$
$E_{1/2}$ (M^+/M^*)	oxidative	-0.96	-1.73	-0.81
$E_{1/2}$ (M^+/M)	oxidative	+1.21	+0.77	+1.29
$E_{1/2}$ (M^*/M^-)	reductive	+0.66	+0.31	+0.77
$E_{1/2}$ (M/M^-)	reductive	-1.51	-2.19	-1.33
excited-state lifetime τ (ns)		557	1900	1100
excitation λ_{max} (nm)			375	452
emission λ_{max} (nm)		581	494[a]	615

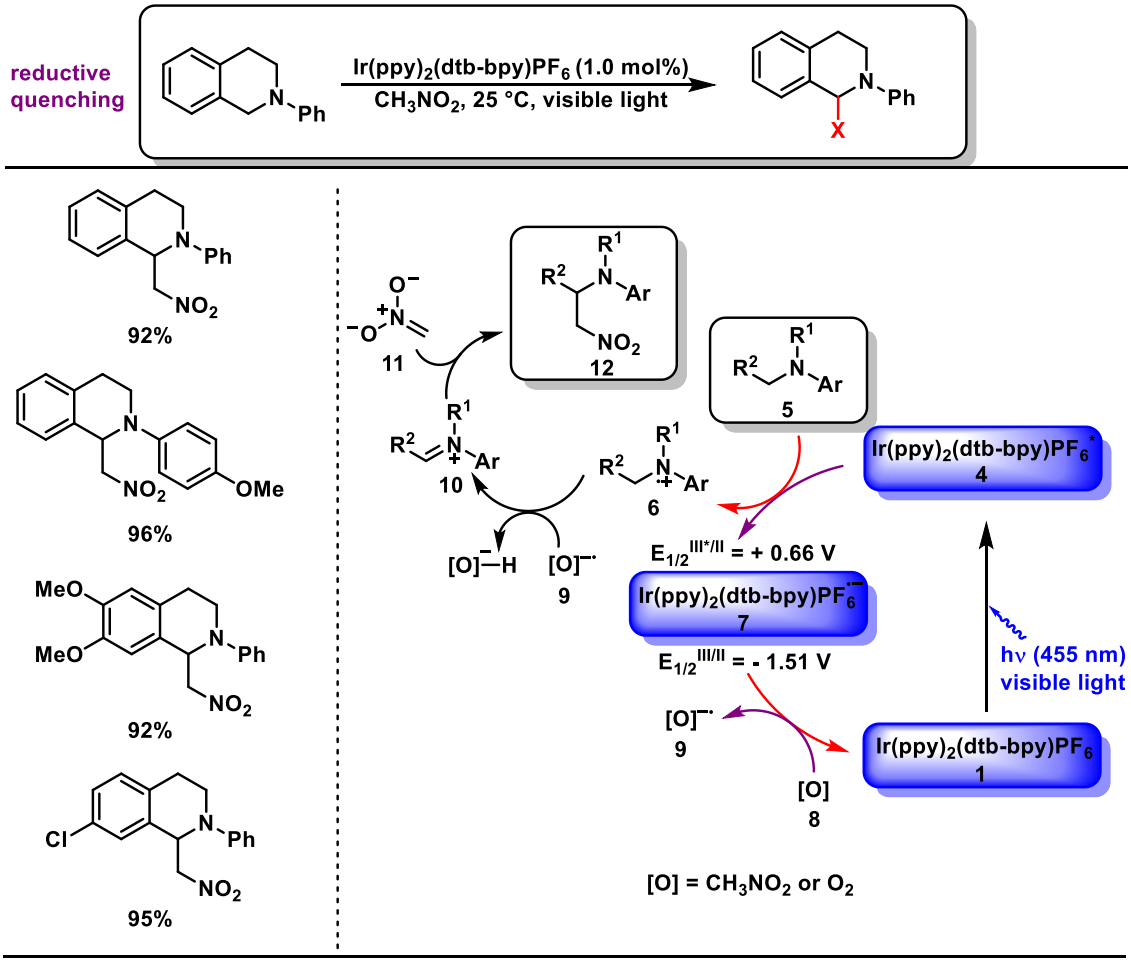
Redox potentials for the oxidative quenching process framed in red, reductive quenching process in black. Other photophysical properties framed in blue. All potentials are given in V vs. saturated calomel electrode (SCE) in CH_3CN at ambient temperature. [a]Determined in 1:1 EtOH/MeOH mixture at 77 K.

During the last years, the number of applications for chemical transformations based on visible light has increased considerably. Up to now, a broad variety of approaches have been developed for the activation of small molecules based on this catalytic method. Two examples have been chosen to illustrate the usage of these photocatalysts for a detailed presentation of aforementioned catalytic quenching processes.

1.1 Photoredox catalyzed aza – Henry reaction *via* carbon – hydrogen bond functionalization on a reductive quenching cycle of $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ (1)

In 2010 Stephenson *et al*.[21] published a light mediated amine functionalization *via* catalytic oxidation of sp^3 hybridized carbon – hydrogen bonds (Scheme 1).[22,23] High chemical yields were achieved for the oxidative coupling of nitroalkanes with tertiary *N*-arylamines using only 1.0 mol% catalyst **1**. Irradiation of the photoredox catalyst **1** with visible light induces its excited state **4**. A single electron transfer from the electron donor **5** to the excited species of the catalyst **4** forms the oxidized radical cation **6** and the reduced radical anion of the catalyst **7** by reductive quenching of **4**. This generated catalyst species **7** is a strong reducing agent (E_{Red} Ir^{3+}/Ir^{2+} = - 1.51 V vs SCE). Through a second single electron transfer from **7** to reagent **8**, the catalytic cycle will

be closed. Therefore, the catalyst will be oxidized and gives the regenerated catalyst **1**, whereas nitromethane and/or adventitious oxygen will be reduced to their corresponding radical anion **9**. Iminium ion **10** formation results from subsequent hydrogen abstraction of this radical anion **9** from the oxidized trialkylammonium radical cation **6**. Intermolecular carbon – carbon bond formation of **11** with the iminium ion **10** gives the desired product **12**.

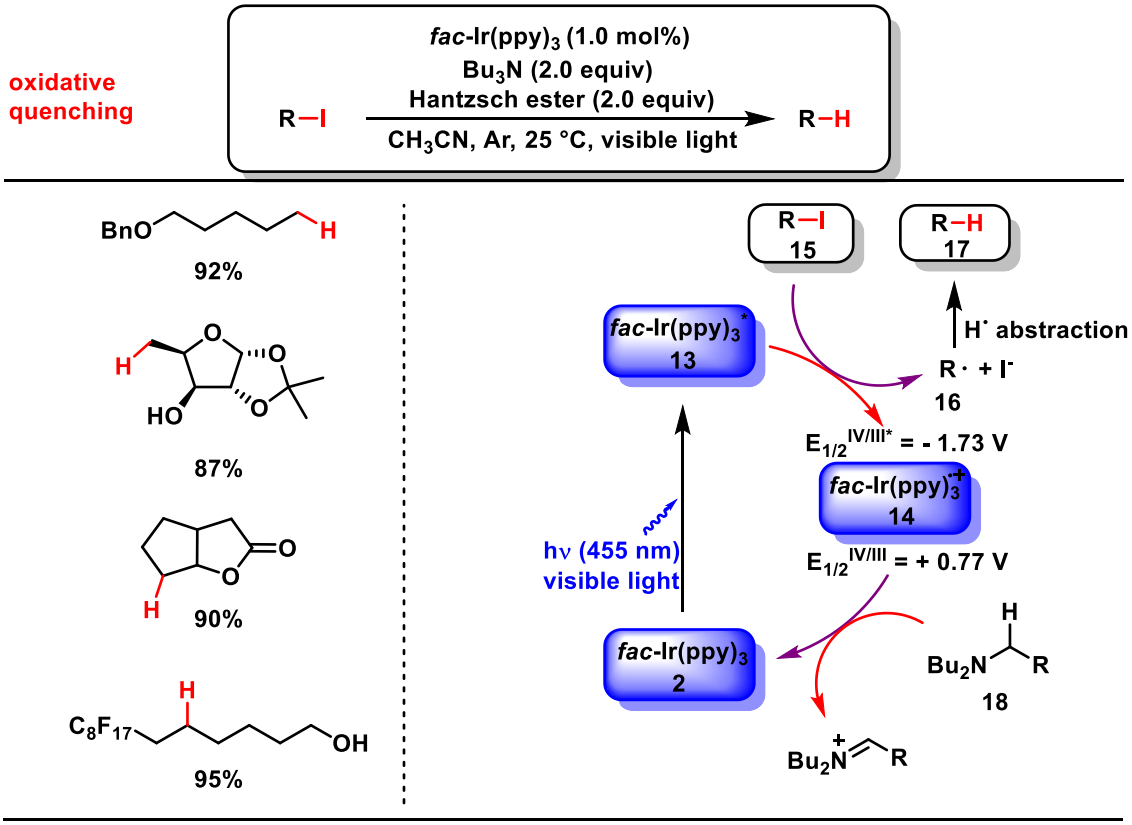


Scheme 1. Examples of visible light driven aza - Henry reaction of tertiary *N*-arylamines with nitroalkanes in very good yields depicted on the left. Proposed mechanism on the reductive quenching cycle of $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ **1** on the right. Oxidation steps marked in red, reduction steps in violet. Photoredox catalyst blue framed.

1.2 Photoredox catalyzed reduction of unactivated alkyl iodides utilizing an oxidative quenching cycle of *fac*-Ir(ppy)$_3$ (2)

The reductive deiodination of unactivated alkyl, alkenyl and aryl iodides is another visible light mediated activation of small organic molecules, reported by the group of Stephenson.[20] As an example, the catalytic carbon – iodide defunctionalization of primary and secondary alkyl iodides and its proposed mechanistic pathway is depicted (Scheme 2). This light mediated reaction is applicable to a broad substrate scope with high functional group tolerance under mild reaction conditions and only utilizes inexpensive reagents. Therefore, this method is superior to common iodide bond cleavages which employ metal – halogen exchanges[24,25] or hydride sources[26] and often lead to undesired side reactions.

The proposed mechanism involves the oxidative quenching of the excited *fac*-Ir(ppy)$_3^*$ **13** by a single electron transfer to the alkyl iodide **15**. By reductive carbon – iodide bond cleavage a carbon – centered radical **16** and oxidized Ir^{4+} species **14** will be generated. Subsequent hydrogen abstraction from Hantzsch ester/trialkylamine combination, which acts as an effective electron /hydrogen atom donor system, leads to the desired deiodinated product **17**. The catalytic cycle will be closed by reduction of Ir^{4+} to the Ir^{3+} ground state **2** in the presence of tributylamine **18** and/or Hantzsch ester that will be oxidized simultaneously.



Scheme 2. Examples of visible light catalyzed deiodination of unactivated alkyl iodides in very good yields depicted on the left. Proposed mechanism on the oxidative quenching cycle of *fac*-Ir(ppy)$_3$ **2** on the right. Oxidation steps marked in red, reduction steps in violet. Photoredox catalyst blue framed.

1.3 Setup for photoreactions

For the performance of photoredox catalyzed reactions lighting devices are necessary. Commonly used fluorescent household bulbs have been partially replaced by more efficient LEDs (light-emitting diode). Their narrow emission peak at a specific wavelength is advantageous, since they can be adapted to each photoredox catalyst. Based on the absorption maximum of the catalyst, LEDs with different wavelengths, typically blue (λ = 455 nm) or green light (λ = 530 nm), are installed. Moreover, utilization of LED devices lead to higher light intensities and a more efficient energy transfer.

A common setup for a photoreaction is build up by a snap cap vail or a round-bottom flask including the reaction mixture and an external irradiation system (Figure 2).

Figure 2. Common setup for photoreactions with a round-bottom flask while irradiation with six blue high power LED takes place from below.

In our group, Dr. Peter Kreitmeier developed an improved device which allows direct irradiation of the reaction solution *via* an optical fiber (Figure 3). Internal irradiation is beneficial in several aspects. Higher light intensities and more photon emission by the photoredox catalyst are ensured due to less light scattering on the glass wall of the vessel, as well as an easier setup of inert reaction conditions by utilizing enclosed Schlenk flask systems. Moreover, installation of the LED source from above facilitates the temperature control from below.

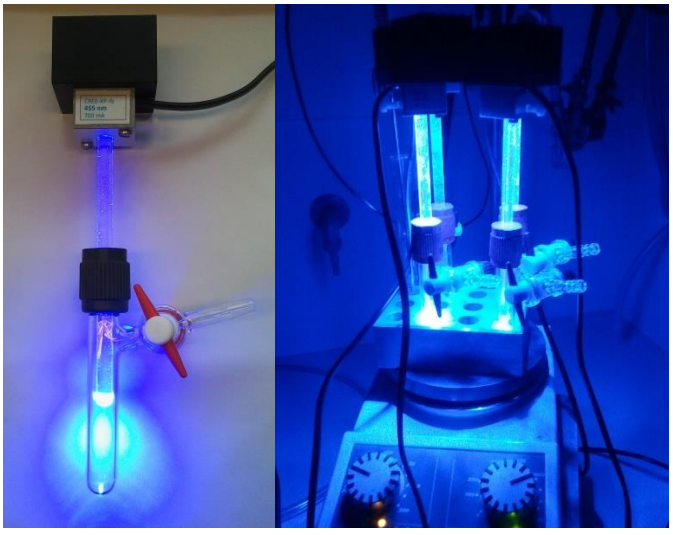


Figure 3. Developed irradiation system. Blue light (455 nm) generated from a high power LED is channeled through a glass rod directly in the reaction solution from above while magnetic stirring and heating in a metal block is applied from below.

Furthermore, industrially applied micro flow reactor technologies were adapted for light mediated reactions (Figure 4). Therefore, the microreactor was encased by a metal block which ensures demand-orientated temperature control. The light source is installed from above and enables irradiation by eight LEDs. The reaction time can be easily controlled by the help of a syringe pump and the adjustment of an accurate pump speed. Considering the precise installation of the light source on the metal block, exposure of the reaction mixture before and after trespassing the flow reactor is avoided. Thus, undesired side and over-reactions can be minimized. The high surface area of the flow reactor leads to shorter reaction times as well as a decrease of the catalyst loading due to a beneficial number of excited molecules of the catalyst simultaneously.

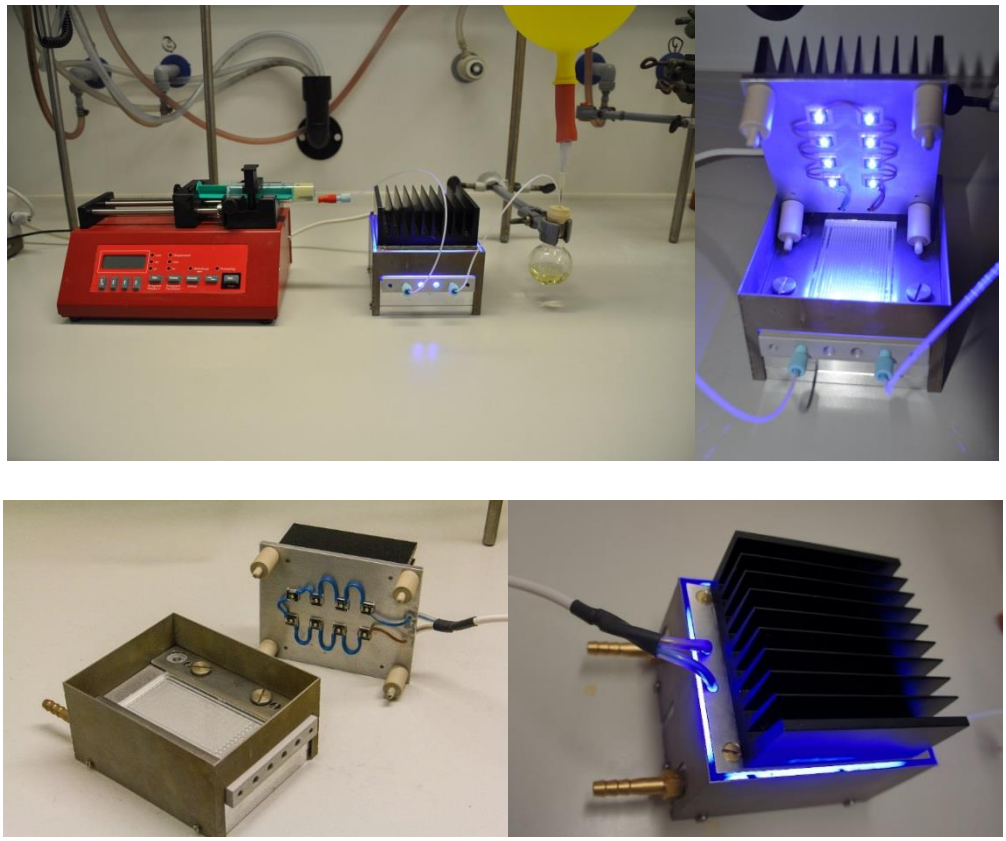


Figure 4. Developed microreactor irradiation system. Blue light (455 nm) generated from 8 high power LEDs exposures directly the reaction solution in the flow reactor. Heating or cooling will be controlled by a modified metal case. Pumping speed and therefore reaction time is adjusted by a syringe pump.

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2. Aim of this work

During the last years visible light photoredox catalysis emerged as a versatile tool for the activation of small molecules. As a mild and environmentally friendly alternative to literature known protocols, the broad applicability of visible light photoredox catalysis for new bond formations with various functionalization patterns as well as in natural product synthesis motivates scientist to further investigate this scientific field.

The aim of this work was the development of new and efficient visible light mediated synthetic applications of various photoredox catalysts *via* single electron transfer. In my thesis I investigated deoxygenations as well as couplings of photochemically generated vinyl radicals.

2.1 Deoxygenation of alcohols by iridium photoredox catalysts using oxidative and reductive quenching cycles

The defunctionalization of carbon – oxygen bonds in molecules stemming from renewable feedstock offers a potential access to products that are normally manufactured from fossil resources.[1] However, efficient and environmentally friendly methods for the chemical conversion of this highly functionalized carbohydrates are rare. Compared to previous reported protocols, e.g. the deoxygenation under Barton McCombie conditions, we were interested in the development of a mild and environmentally benign protocol for the defunctionalization of carbon – oxygen single bonds of alcohols. Due to the high carbon – oxygen bond strength and accordingly the minor tendency for the direct reduction of this bond, for the defunctionalization of alcohols, this group has to be activated by suitable auxiliaries.[2] Nevertheless, strong reductive agents have still to be used for the cleavage of an activated carbon – oxygen bond. Therefore, in my thesis I investigated iridium based photoredox catalysts are chosen as potential strong reducing reagents[3,4] for the visible light mediated carbon – oxygen bond cleavage (Chapter 3 and 4).

2.2 Visible light mediated vinyl radical generation following acrylamide preparation *via* intermolecular carbon – carbon bond formation with 1-isocyano-2,4-dimethoxybenzene

Vinyl radicals are known as highly reactive species, which can be utilized for various applications involving new bond formations.[5] These radicals can be generated under thermal[6,7] as well as under photochemical[8] conditions. Based on our interest and our previous results in the visible light mediated reductive debromination[9] of *vic*-dibromoalkene, we utilized α-bromochalcones as vinyl radical sources for chemical transformations. Depending on the trapping reagents, we envisioned new synthetic pathways for the preparation of inter- and intramolecular carbon – carbon bond formations. Thus, alternative concepts for the synthesis of polycyclic frameworks *via* cascade reactions or annulations have been established.[10,11]

To enlarge the field of applications for the utilization of vinyl radicals, we wanted to investigate 1-isocyano-2,4-dimethoxybenzene as alternative trapping reagent. Thereby, potentially bioactive acrylamide derivatives can be synthesized and subjected to pharmaceutical tests (Chapter 5).

2.3 References

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3. Visible light photoredox catalyzed one-pot deoxygenation of alcohols

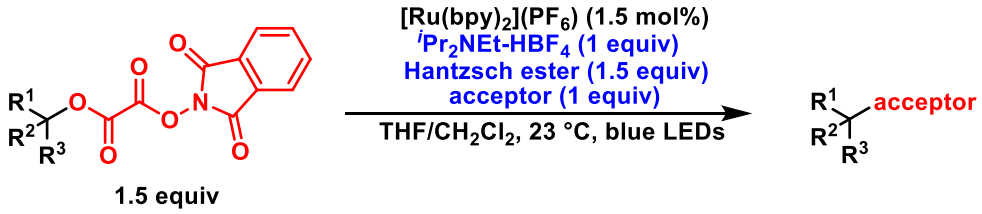
3.1 Introduction

The development of strategies for the control, conversion and utilization of chemicals stemming from renewable feedstock into fine chemicals is an important aspect in industrial research. The rising energy consumption and the increase in population worldwide have forced scientists to rethink their ideas concerning sustainable development over the last decades. On behalf of sustainability, fine chemicals must be harnessed from renewable feedstock.[1] Contradictory to fossil resources, renewable feedstock based on carbohydrates is characterized by a relative high number of identical functional groups, which complicates further chemical transformation. The defunctionalization of carbon – oxygen single bonds in natural materials to their respective carbon – hydrogen bonds leads to increased compatibility for further chemical transformations in accordance with established oil based protocols used by the chemical industry.[2] The direct reduction of alcohols to the corresponding alkanes is difficult considering the strong carbon – oxygen bond. In accordance to the poor nucleofugality of the hydroxyl group, a modification, e.g. to an ester or halide function is required.[3] Despite the usage of superstoichiometric amounts of highly noxious chemicals and the production of difficult to separate toxic tin-byproducts, the Barton McCombie[4] reaction is still the classical radical deoxygenation method of alcohols due to its broad substrate scope. Alternative protocols performed electrochemically[5-7] or photochemically[2,8-13] require an activation of the alcohol group *via* esterification or transformation into the corresponding halide to decrease the reduction potential.

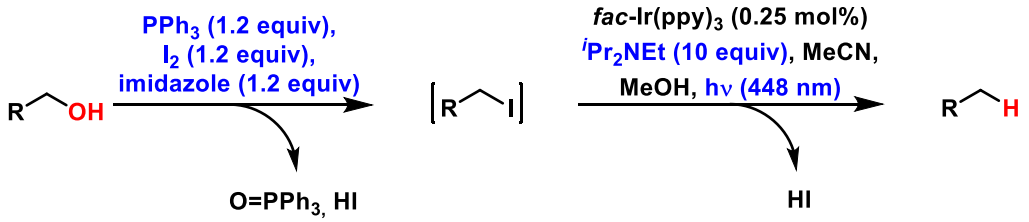
Related to this work, Overman *et al*. elegantly succeeded in the visible light mediated deoxygenation of tertiary alcohols followed by subsequent intermolecular carbon – carbon bond formation with electron-deficient alkenes by their conversion into *N*-phthalimidoyl oxalates (Scheme 1).[10] This protocol is applicable to a broad range of tertiary alcohols, however, the sensibility of the oxalates to aqueous workup and silica gel chromatography makes the operation of this reaction difficult. Moreover, the preparation of $^{i}Pr_2NEt{\cdot}HBF_4$ as electron donor to ensure the stability of the *N*-phthalimidoyl oxalates during the reaction, requires additional effort compared to the use of commercially available $^{i}Pr_2NEt$. In a second report, Stephenson *et al*. showed the deoxygenation of primary and secondary alcohols by their *in situ* conversion to iodides followed by visible light mediated reduction in the presence of an amine as a sacrificial electron donor and *fac*-Ir(ppy)$_3$ (ppy = 2-phenylpyridine) as photoredox catalyst.[14,15] This protocol for the deoxygenation of alcohols still suffers from the production of byproducts owing

to stoichiometric transformations of triphenylphosphine to triphenylphosphine oxide and iodine to iodide (Scheme 1). A more convenient method including the recovery and reuse of the auxiliary activation group, a redox economic deoxygenation of alcohols under visible light photocatalysis was investigated by Reiser *et al*.[2] However, the preparation of the expensive 3,5-bis(trifluoromethyl)benzoic anhydride as activation group involves multiple preparation steps (Scheme 1).

Overman et al.



Stephenson et al.



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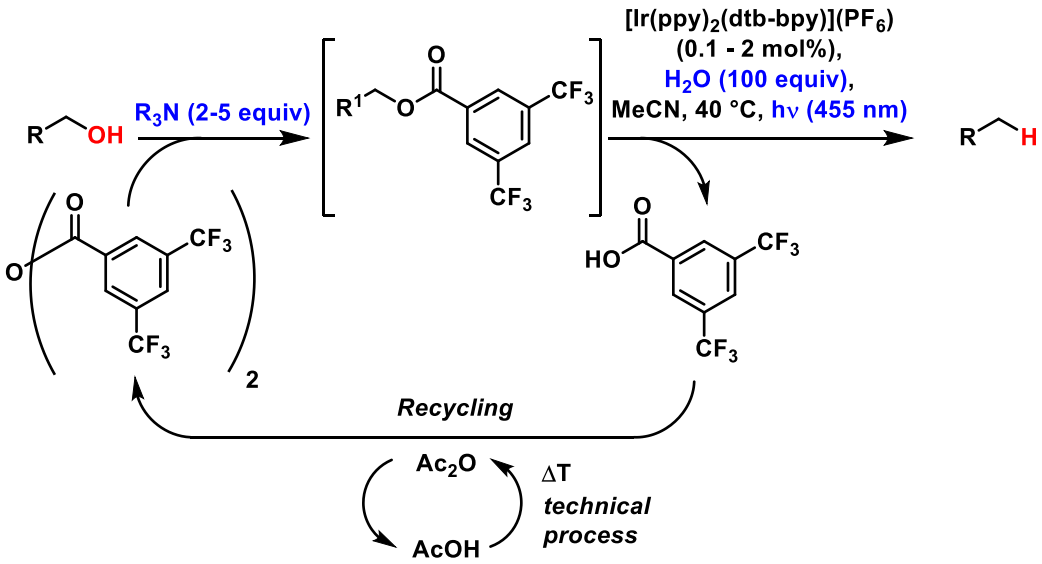
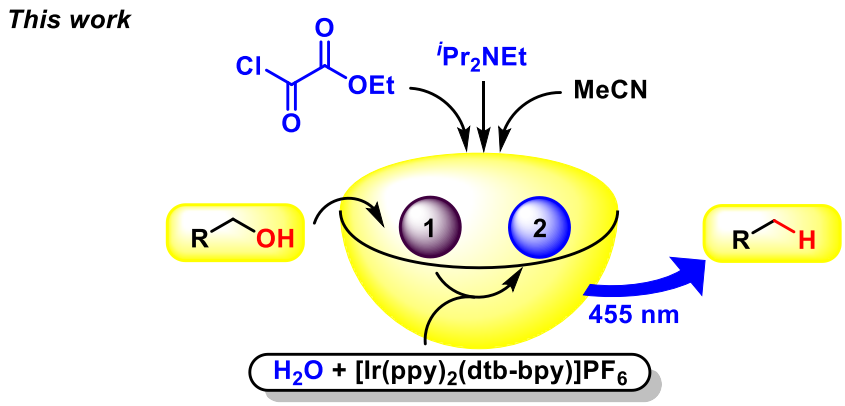




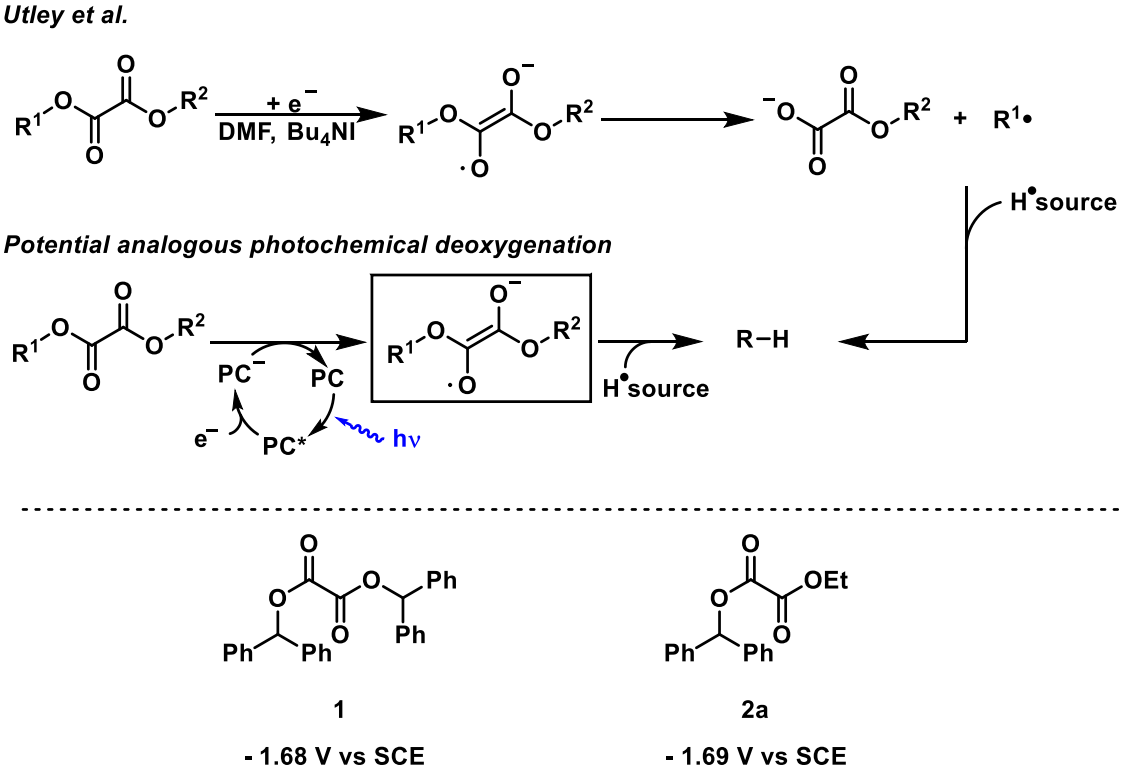
Scheme 1. Strategies on visible light mediated deoxygenation processes of alcohols (reagents needed in superstoichiometric amounts are depicted in blue).[2,10,14,15] One-pot deoxygenation of alcohols *via* in situ generated oxalate esters (first step) followed by light mediated carbon – oxygen bond cleavage in the presence of water and catalyst (second step).

Here we report an inexpensive, simple, and rapid deoxygenation method of alcohols, in which formation of radicals is achieved under mild visible light photocatalyzed conditions using ethyl oxalyl chloride for the alcohol esterification. The reaction can be performed in one-pot without additional isolation of the oxalate derivatives. This protocol ultimately requires a tertiary amine and ethyl oxalyl chloride as stoichiometric reagents and leads to high yields for the deoxygenation of benzylic and allylic alcohols, as well as α-hydroxyl carbonyls after short irradiation times and under mild reaction conditions (Figure 1). Moreover, the development of an one-pot method ensures significant savings in solvent, energy, and time.

3.2 Literature precedent

Following the electrochemical strategy for the deoxygenation of oxalate esters published by Utley *et al*.[3] and the use of methyl oxalyl ester intermediates in natural products[16] and sugar analogues[17] for the Barton-McCombie deoxygenation, we envisioned oxalyl ester derivatives as suitable substrates for initial photochemical test reactions. Ethyl oxalyl esters were chosen for the activation of alcohols due to their promising reduction potentials and the low price of ethyl oxalyl chloride as esterification reagent. Based on the Utley protocol, we assumed a related deoxygenation process under photoredox catalyzed conditions would be possible, including an electron transfer to the carboxylic moiety followed by subsequent defragmentation and hydrogen abstraction (Scheme 2). Due to the comparability between the deoxygenation under visible light photoredox catalyzed and electrochemical conditions, test substrate **1**, which was

also used by Utley *et al*. as initial oxalate ester, was synthesized. Moreover, the Utley group reported only partial cleavage of both diphenyl moieties and the generation of the stable $Ph_2CHOC.CO_2^-$ anion species. Due to incomplete defragmentation of the second diphenyl moiety only 70% yield of the deoxygenated product **3a** was achieved under electrochemical conditions by the use of 1 equivalent of dibenzhydryl oxalate **1**. Thus, mono-substituted ethyl oxalate ester **2a** was synthesized. Thereby, a possible partial cleavage of the ethyl moiety should have no effect on the yield. This modification of the test substrate could lead to a complete deoxygenation of the diphenyl moiety and hence, to an increased yield of the deoxygenated product **3a**.



Scheme 2. Comparison of the proposed deoxygenation process under electrochemical[3] and photochemical conditions. Reduction potentials of oxalate esters in **1** and **2a** in DMF.

3.3 Initial screening experiments

Initial experiments were carried out with isolated oxalate derivatives **1** and **2a**, either $Ru(bpy)_3Cl_2 \bullet 6H_2O$ (bpy = 2,2'-bipyridine) or $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ (ppy = phenylpyridine, dtb-bpy = 4,4'-di-*tert*-butyl-2,2'-bipyridine) as photocatalyst, Hantzsch ester (diethyl 1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate) as hydrogen source, and $^{i}Pr_2NEt$ as sacrificial electron donor in CH_3CN (Figure 1).

Irradiation was ensured by a high power blue LED (455 nm) bundled through a glas rod directly into the reaction solution while heating was enabled from below in a metal block. The reaction mixture was degassed by freeze - pump - thaw technique using a Schlenk tube and a lockable screw cap including a Teflon inlet.

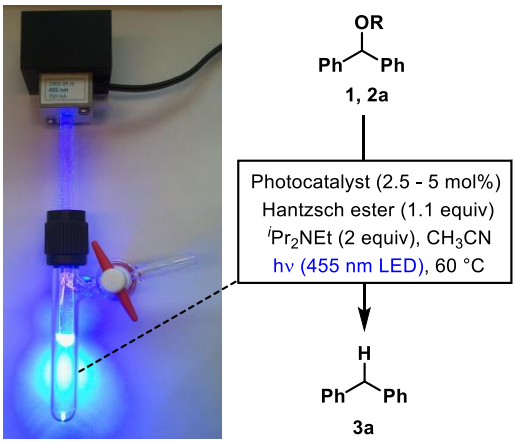
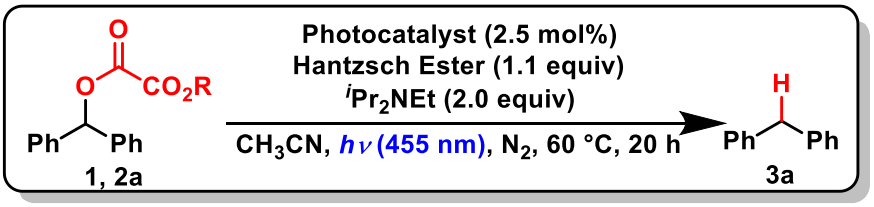


Figure 1. Initial reaction conditions for the deoxygenation of **1** and **2a**.

Cyclovoltammetric measurements gave the half-wave reduction potential of E_{Red} = -1.68 V for test compound **1** and E_{Red} = -1.69 V for **2a** (Scheme 2), which is in the same range as $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ (E_{Red} Ir^{3+}/Ir^{2+} = -1.51 V). Initial test reactions revealed the Ir complex is a superior photoredox catalyst in comparison to $Ru(bpy)_3Cl_2 \bullet 6H_2O$ (E_{Red} Ru^{2+}/Ru^{+}= -1.31 V) owing to the increased reduction potential.[14] Appliying $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ and using a combination of Hantzsch ester and Hünigs base as sacrificial donors, compound **2a** yielded 92% of the corresponding deoxygenated compound **3a** after 20 h, whereas only 68% could be obtained for **1** (Table 1). The lower yield for substrate **1** is fully in agreement with the reported yield under electrochemical conditions (lit. 70%) and can be explained by only partial cleavage of both diphenyl moieties and the generation of the stable $Ph_2CHO_2C.CO_2^-$ anion species (Scheme 2).

Table 1. Deoxygenation comparison of different esters **1** and **2a** in the presence of various photoredox catalysts.



Photoredox catalyst	Compound yield [%][a]	
	1	**2a**
$Ru(bpy)_3Cl_2$	-	9
$[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$	68	91

[a]all yields were determined by GC – FID analysis with naphthalene as internal standard. All reactions were degassed and performed under an N_2 atmosphere.

Considering the moderate yield for test substrate **1** and the promising initial reaction for ester **2a** (Table 1), optimization experiments were carried out for **2a** by variation of temperatures, catalyst loadings and potential hydrogen sources (Figure 2 and 3). Water/Hünig's base as an alternative hydrogen source system compared to Hantzsch ester/Hünig's base turned out to lead to faster deoxygenation processes. Deoxygenation using 10 equiv water was performed at ambient temperature and 60 °C. Both experiments gave the desired corresponding diphenylmethane **3a** in high yields after shorter irradiation times compared to the reaction with Hantzsch ester. Moreover, using only 1 mol% of catalyst still resulted in 85% yield of **3a** after 30 min., being comparable to the profile obtained when 2.5 mol% of catalyst were employed.

Noteworthy, further decrease to 0.1 mol% still yielded 75% after slightly prolonged irradiation (90 min.), however, full conversion was not observed even after 20 h (Figure 2), pointing to a deactivation of the catalyst with time.

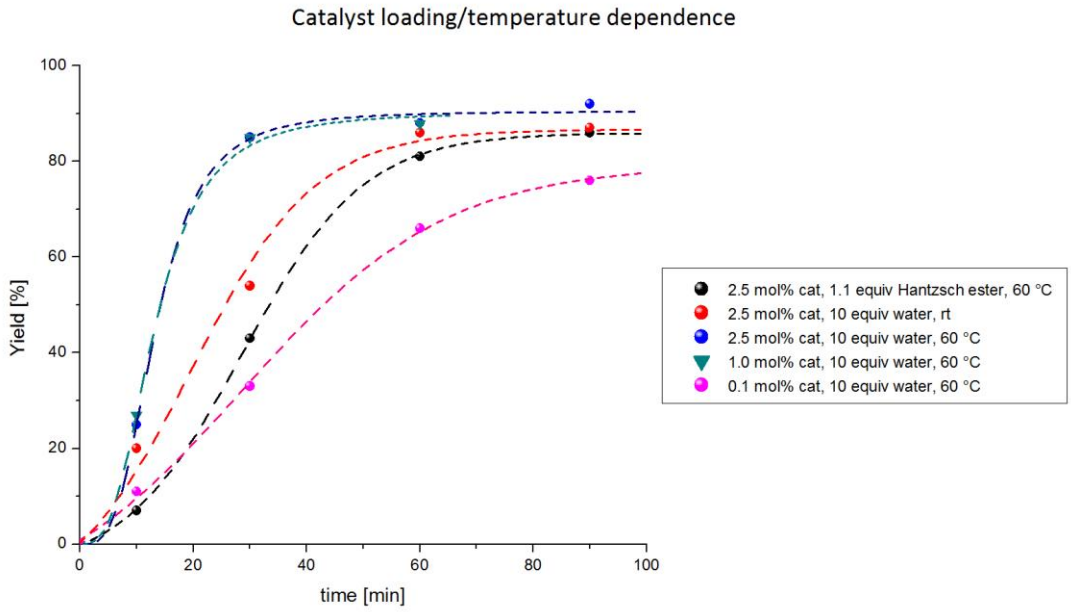


Figure 2. Catalyst loading and temperature dependence for the visible light mediated deoxygenation of **2a** with Hantzsch ester and water as hydrogen sources. *Reaction conditions*: ethyl oxalate ester **2a** (0.1 mmol), Hünig's base (2.0 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ (0.1 – 2.5 mol%), CH_3CN (c = 0.1 M), ΔT. All yields were determined by GC – FID analysis with naphthalene as internal standard. All reactions were degassed and performed under an N_2 atmosphere.

Further experiments elucidated the need for utilizing higher temperatures (Figure 3). Leaving out Hantzsch ester or water as an additional hydrogen source resulted in a slower deoxygenation of **2a**, especially at ambient temperature compared to 60 °C. However, addition of 1 equiv water and notably 10 equiv water was superior considering the reaction time and yield, whereas 100 equiv water yielded only 12% and mainly hydrolysis of the starting material **2a** was observed. ^{i}PrOH/Hünig's base as a hydrogen source system at 60 °C did not have any impact on the rate of product formation compared to the reaction using exclusively Hünig's base as hydrogen source (Figure 3).

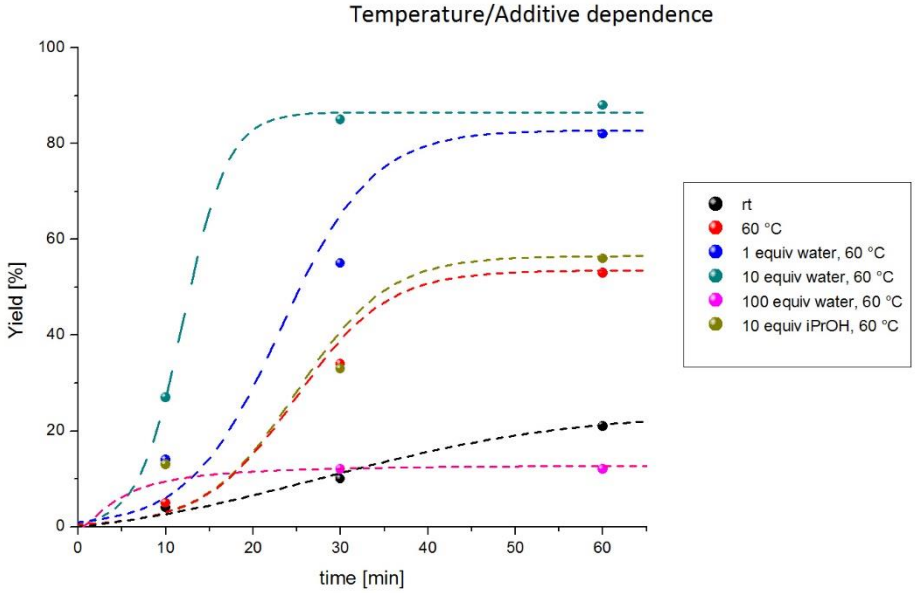
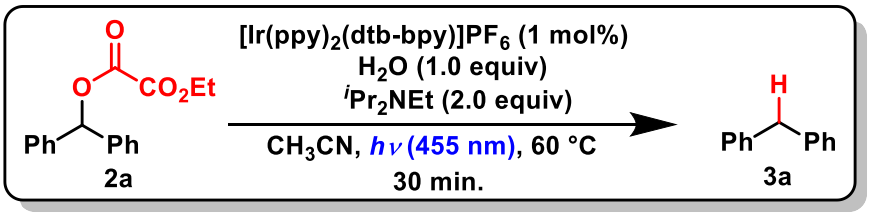


Figure 3. Temperature and additive equivalent dependence for the visible light mediated deoxygenation of **2a** with water and ^{i}PrOH as hydrogen sources at 1 mol% catalyst loading. *Reaction conditions*: ethyl oxalate ester **2a** (0.1 mmol), Hünig's base (2.0 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ (0.1 – 2.5 mol%), CH_3CN (c = 0.1 M), ΔT. All yields were determined by GC – FID analysis with naphthalene as internal standard. All reactions were degassed and performed under an N_2 atmosphere.

Solvent analogy and control experiments for benzhydryl ethyl oxalate **2a** were carried out. As expected, aprotic polar solvents, e.g. CH_3CN and DMF (Table 3, entry 1 and 2) turned out to be superior for visible light mediated deoxygenation, whereas almost no conversion was observed for the less polar solvent CH_2Cl_2 (Table 3, entry 3). Control experiments revealed that the deoxygenation of **2a** is indeed a photochemically induced process (Table 3, entry 4 and 5). When either photocatalyst (Table 3, entry 4) or the light source (Table 3, entry 5) were absent, no reaction was observed even for prolonged reaction times of up to 20 h. Leaving out Hünig's base resulted in no conversion (Table 3, entry 6). Moreover, degassing can be omitted, which economizes time and effort, and appears surprisingly considering the literature known quenching process of the excited triplet state of the photoredox catalyst by oxygen. Even higher yield of 96% could be achieved for **3a** without previous degassing of the reaction mixture (Table 3, entry 7), which can be explained by the formation of $OOH^{\cdot}$ radicals as hydrogen donors during the reaction in the presence of O_2. Reduction of O_2 *via* photocatalytic electron transfer gives $O_2^{\cdot-}$ radical anions which will be subsequent protonated by water to give $OOH^{\cdot}$ radicals (see 3.6 proposed mechanism).

Table 3. Solvent dependence and control experiments of the deoxygenation reaction of compound **2a**[a].



Entry	Solvent, modification	Yield [%][a]
1	none	85
2	DMF	36
3	CH_2Cl_2	3
4	CH_3CN, w/o photocatalyst	0[b]
5	CH_3CN, w/o light source	0[b]
6	CH_3CN, w/o Hünig's base	0[b]
7	CH_3CN, not degassed	96

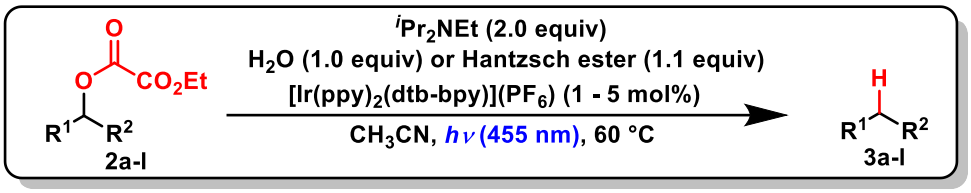
[a]Determined by GC – FID analysis using Naphthalene as internal standard. 0.3 mmol scale. Reactions were degassed by freeze – pump – thaw cycle (5x). [b]reaction time 20 h.

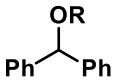
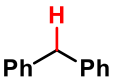
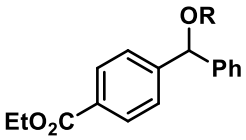
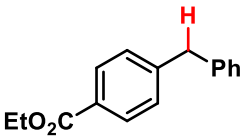
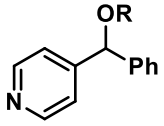
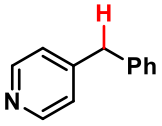
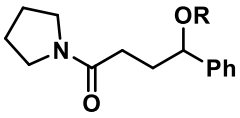
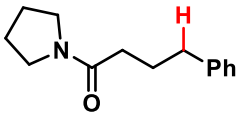
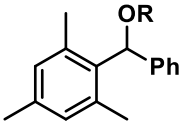
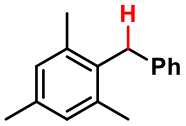
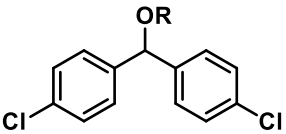
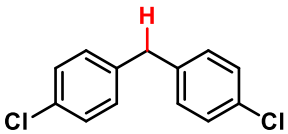
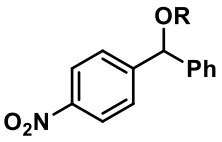
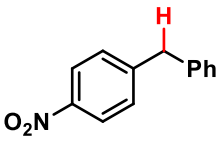
3.4 Photoredox catalyzed deoxygenation of oxalate esters

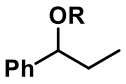
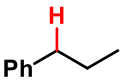
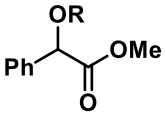
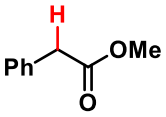
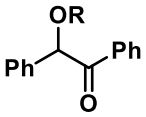
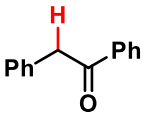
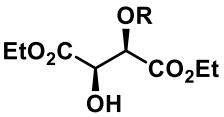
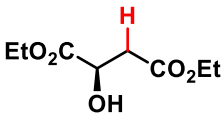
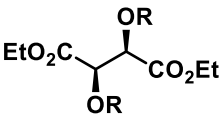
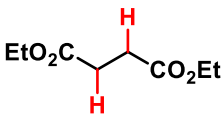
Initial deoxygenation (Table 4, entry 1-3) was performed under the aforementioned conditions using Hantzsch ester as additional hydrogen source. Both, an electron withdrawing ester containing compound **2b** and an electron deficient heteroaromatic dibenzylic oxalate ester **2c** were tested and furnished the respective deoxygenated products **3b** and **3c** in very good isolated yields (Table 4, entry 2 and 3). Variation to a mono-benzylic oxalate ester **3d** gave acceptable yield of 66% for **3d** (Table 4, entry 4). Having the newly optimized reaction conditions in hand using water as hydrogen source instead of Hantzsch ester (Table 3), different dibenzylic alcohol derivatives were investigated (Table 4, entry 4 - 12). Using 10 equiv of water yielded in 96% for the deoxygenation of diphenyl oxalate ester **2a**. However, the amount of water had to be adapted to 1 equiv for the remaining dibenzylic-, monobenzylic ester and α-carbonyl compounds (**2e – 2l**) in order to achieve good yields. Sterically demanding groups (Table 4, entry 5), as well as aryl chlorides (Table 4, entry 6) were well tolerated and gave the corresponding deoxygenated products in high yields. Moreover, compound **2g** containing an electron withdrawing *p*-nitro substituent yielded the corresponding deoxygenated product **3g** in 48% (Table 4, entry 7). Modification to mono-benzylic phenylpropane ester **2h** gave an acceptable yield of 75% for **3h** (Table 4, entry 8). In addition, α-carbonyl substituted benzylic ester, and especially acetylated derivative **2i** gave excellent yield of methyl 2-phenylacetate **3i** (Table 4, entry 9), whereas, the deoxygenated benzoin derivative **3j** was isolated in moderate 57% after prolonged reaction time of 3 h (Table 4, entry 10), as already observed by Utley *et al*. for electrochemical deoxygenations. Interestingly, the substrate scope could be extended to non-benzylic α-carbonyl compounds **2k** and **2l**, and in particularly the conversion from (+)-diethyl tartrate to unnatural (+)-diethyl malate **3k** on even larger scale is noteworthy (Table 4, entry 11 and 12).

Simple alkyl-substituted alcohols (primary, secondary and tertiary), however, did not show any conversion.

Table 4. Visible light mediated deoxygenation process of ethyl oxalate ester derivatives.



Entry	Substrate	Product	Yield [%][a]
1	 2a	 3a	96[b]
2	 2b	 3b	96[c]
3	 2c	 3c	92[c]
4	 2d	 3d	66[d]
5	 2e	 3e	98
6	 2f	 3f	89
7	 2g	 3g	48

8	 **2h**	 **3h**	75[e]
9	 **2i**	 **3i**	99
10	 **2j**	 **3j**	57
11	 **2k**	 **3k**	65/74[f]
12	 **2l**	 **3l**	35

[a]Isolated yields on a 0.3 - 1.0 mmol scale. [b]10 equiv H_2O. [c]5 mol% catalyst loading, Hantzsch ester. [d]2.5 mol% catalyst loading, Hantzsch ester. [e]GC-FID analysis using naphthalene as internal standard. [f] ^1H NMR yield (5 mmol scale). R = $(CO)_2OEt$

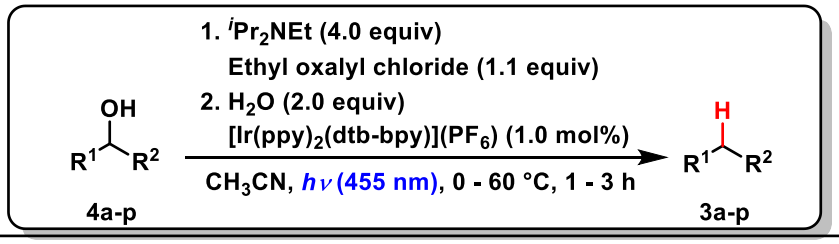
3.5 Visible light mediated deoxygenation of alcohols in one – pot *via* in situ generated oxalate esters

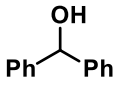
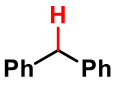
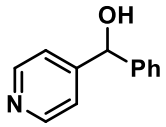
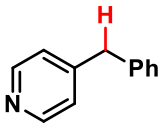
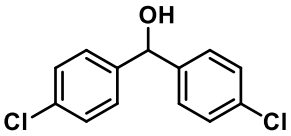
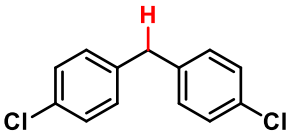
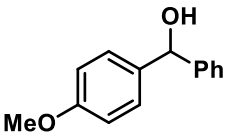
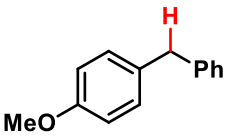
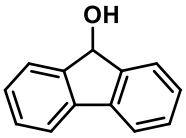
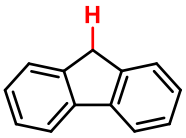
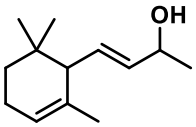
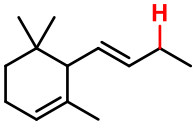
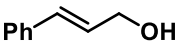
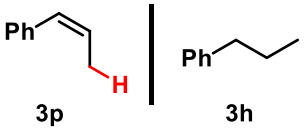
Having established a visible light mediated deoxygenation process for isolated oxalate esters, a direct deoxygenation of benzylic and allylic alcohols in an one pot procedure *via in situ* generated esters as activating species, was performed. This approach is more ecologically worthwhile than a foregoing reaction step. Advantageously, solvent consumption, additional work up and purification steps, the associated labor time, as well as energy loss can be minimized. Therefore, large scale applications appear more economic and environmentally sustainable.

Uniformly good yields after short reaction times were achieved in case of dibenzylic and allylic alcohols derivatives (Table 5). To examine a certain range of compounds with different electronic properties, benzylic alcohols with e.g., an electron deficient heteroaromatic system (Table 5, entry 2), chlorinated (Table 5, entry 3) and electron donating *p*-methoxy substituted aryls (Table 5, entry 4), as well as a rigid fluorenol compound (Table 5, entry 5), were investigated and well tolerated, giving the corresponding deoxygenated products in good yields after short reaction times (1 – 2 h) by filtration through a short plug of SiO_2 gel.

Moving to allylic alcohols resulted in good to very good yields (Table 5, entry 6 and 7). Assuming a possible 5-exo trig or 6-endo trig cyclization for α-Jonone **4o** after radical induction, exclusively deoxygenated product was observed. The deoxygenation process turns out to be faster compared to a competitive intramolecular cyclization (Table 5, entry 6). Furthermore, cinnamyl alcohol **4p** resulted in a very good yield of 86% as determined by GC analysis. Surprisingly, 59% of the deoxygenated product was identified as the isomerized cis species, whereas only 17% trans configuration and 24% allylbenzene were detected as minor products (Table 5, entry 7). Addition of Pd/C under H_2 atmosphere after complete alcohol deoxygenation accomplished a hydrogenation of the double bond as a third step in one pot in moderate 62% yield of **3h** (Table 5, entry 7).

Table 5. Visible light mediated deoxygenation process of alcohols following a carbon – hydrogen bond formation in one-pot.



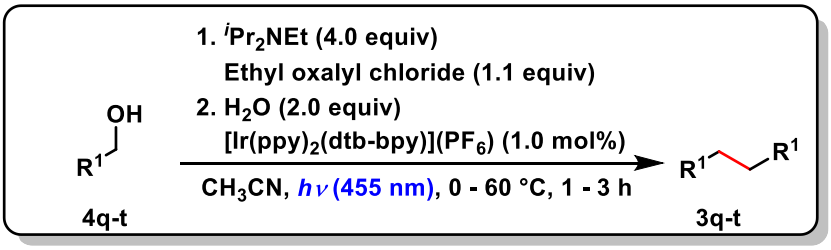
Entry	Substrate	Product	Yield [%][a]
1	 4a	 3a	91[b]
2	 4c	 3c	64
3	 4f	 3f	73
4	 4m	 3m	76
5	 4n	 3n	81
6	 4o	 3o	74
7	 4p	 3p 3h	86[b,c] / 62[b,d]

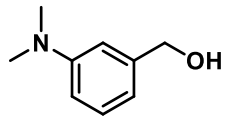
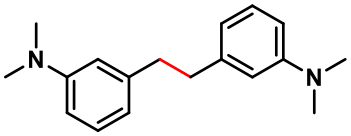
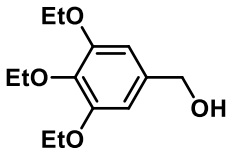
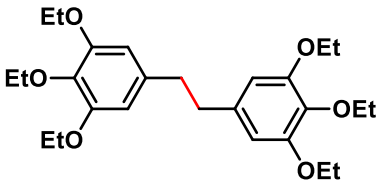
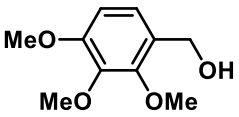
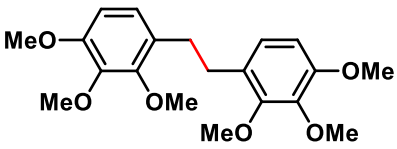
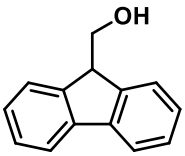
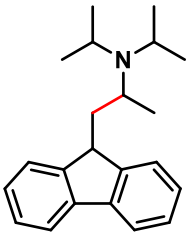
[a]Isolated yields on a 1.0 mmol scale. [b]Determined by GC-FID with naphthalene as internal standard. [c]Mixture of isomeric products (cis:trans:allybenzene = 59:17:24). [d]Hydrogenation with Pd/C and H_2 in a third step after deoxygenation.

Unlike aforementioned deoxygenation and corresponding carbon – hydrogen bond formation, benzylic alcohols with strong electron donating substituents induced carbon – carbon bond formation yielding dimerized products (Table 6, entry 1, 2 and 3). Thus, it can be assumed that the crucial electrophilic character and the stability of the radical is reduced, thereby a radical - radical recombination is favored.

Although we acknowledged that the deoxygenation for simple alkyl-substituted alcohols was not successful, fluorene methanol **4t** as a primary alcohol turned out to be an exception (Table 6, entry 4). The formation of the product **3t** could be possible explained by radical addition of the nucleophilic α-aminoalkyl radical of the oxidized $^{i}Pr_2NEt$ species with the induced electron deficient alkene radical of the deoxygenated compound **4t**.[18-22]

Table 6. Visible light mediated deoxygenation process of alcohols following a carbon – carbon bond formation in one-pot.

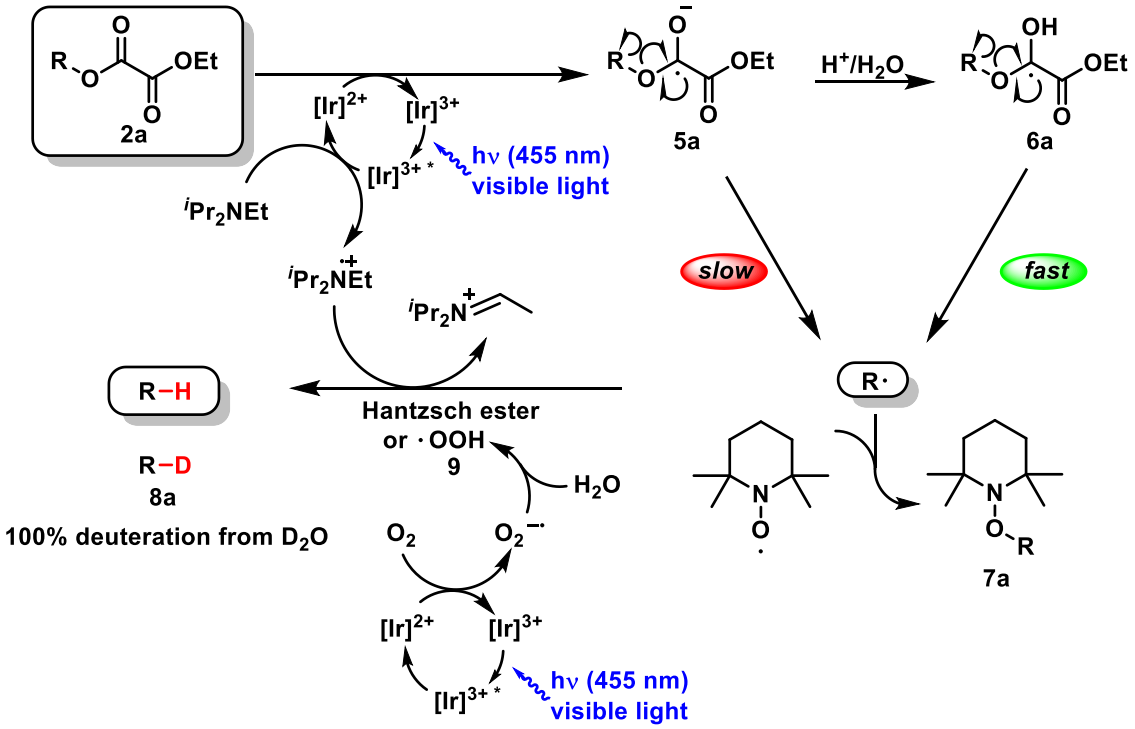


Entry	Substrate	Product	Yield [%][a]
1	 4q	 3q	35
2	 4r	 3r	56
3	 4s	 3s	51
4	 4t	 3t	36

[a]Isolated yields on a 1.0 mmol scale.

3.6 Proposed Mechanism

We assumed that the mechanism of the deoxygenation process involves an electron uptake by the ester moiety from the reductively quenched Ir^{2+} species *via* Hünig's base followed by several defragmentation steps und subsequent hydrogen abstraction from the generated $^{i}Pr_2NEt$ radical cation or Hantzsch ester as additional hydrogen source. Without further degassing of the reaction mixture, we assume that O_2 can be reduced by a second excited species of the catalyst to the radical anion $O_2^{\cdot-}$. This reactive species will be protonated in the presence of H_2O to give ·OOH **9**, which acts as an additional hydrogen donor. Aforementioned GC-FID kinetic measurements (Figure 2 and 3) indicate an electron density shift towards the carbon – oxygen bond which has to be cleaved, by generating a neutral radical species **6a** *via* protonation of **5a** in the presence of water. Therefore, faster defragmentation is achieved. Emerging radical species were characterized by trapping with TEMPO (2,2,6,6-Tetramethylpiperdinyloxyl) to give **7a**. In presence of 10 equiv D_2O exclusively deuterated diphenylmethane **8a** was observed (Scheme 3). In contrast to a photochemical induced deoxygenation, alternatively a simple Ir-catalyzed hydrogenation in the presence of H_2 would be conceivable. However, this reaction pathway could be eliminated, as exclusion of light and performance under the same reaction conditions yielded no deoxygenation product, even after three days of reaction time.



Scheme 3. Proposed visible light mediated mechanism with and without additional water. Trapping of the radical species with TEMPO and exclusive hydrogen abstraction with D_2O.

3.7 Conclusion

In summary, a mild and environmentally friendly protocol for the deoxygenation of benzylic and allylic alcohols, as well as α-carbonyl compounds was established under visible light photoredox catalysis. Alcohol activation was ensured by esterification with the suitable, commercially inexpensive ethyl oxalyl chloride, which is manufactured industrially on large scales. Moreover, *in situ* activation of alcohols and exclusion of inert conditions is possible, and therefore facile reaction setup and performance is ensured. As a result of technical feasibility, deoxygenation of alcohols by activation with oxalate auxiliaries could become attractive for large scale applications.

3.8 Experimental part

Experimental details, characterization data and spectra

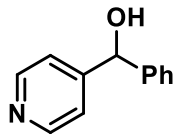
3.8.1 General information

All chemicals were used as received or purified according to Purification of Common Laboratory Chemicals. Glassware was dried in an oven at 110 °C or flame dried and cooled under a dry atmosphere prior to use. All reactions were performed using Schlenk techniques. Blue light irradiation in batch processes was performed using a CREE XLamp XP-E D5-15 LED (λ = 450-465 nm). Analytical thin layer chromatography was performed on Merck TLC aluminum sheets silica gel 60 F 254. Reactions were monitored by TLC and visualized by a short wave UV lamp and stained with a solution of potassium permanganate, p-anisaldehyde, or Seebach's stain. Column flash chromatography was performed using Merck flash silica gel 60 (0.040-0.063 mm). Automatic column purification was conducted by AnaLogix IntelliFlash 310 using Merck flash silica gel 60 (0.040-0.063 mm). The melting points were measured on an automated melting point system (MPA 100) with digital image processing technology by Stanford Research Systems. ATR-IR spectroscopy was carried out on a Biorad Excalibur FTS 3000 spectrometer, equipped with a Specac Golden Gate Diamond Single Reflection ATR-System. NMR spectra were recorded on Bruker Avance 300 and Bruker Avance 400 spectrometers. Chemical shifts for ^{1}H NMR were reported as δ, parts per million, relative to the signal of $CHCl_3$ at 7.26 ppm. Chemical shifts for ^{13}C NMR were reported as δ, parts per million, relative to the center line signal of the $CDCl_3$ triplet at 77 ppm. Coupling constants *J* are given in Hertz (Hz). The following notations indicate the multiplicity of the signals: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, p = quintet, sept = septet, and m = multiplet. Mass spectra were recorded at the Central Analytical Laboratory at the Department of Chemistry of the University of Regensburg on a Varian MAT 311A, Finnigan MAT 95, Thermoquest Finnigan TSQ 7000 or Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS. Gas chromatographic analyses were performed on a Fisons Instruments gas chromatograph equipped with a capillary column (30 m × 250 µm × 0.25 µm) and a flame ionization detector. Irradiation was performed with Cree XLamp XP-E LEDs (royal blue). Yields reported are referred to the isolated compounds unless otherwise stated.

3.8.2 Synthesis of alcohols

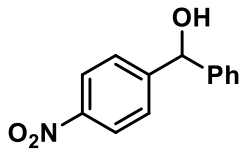
General procedure *GPI* for alcohol preparation according to reported procedure[23]

A 100 mL round bottom flask equipped with a magnetic stir bar was charged with ketone (20.0 mmol, 1.00 equiv), dissolved in MeOH (50 mL, 0.40 M) and treated with $NaBH_4$ (1.89 g, 50.0 mmol, 2.50 equiv) was added in portions. Water was added after the reaction completed (as judged by TLC) and solvent evaporated under reduced pressure. The obtained residue was dissolved in Et_2O (50 mL), phases were separated, the aqueous layer was extracted with Et_2O (3 x 50 mL), and the combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure. The obtained oil was purified by flash column chromatography.



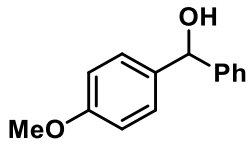
Phenyl(pyridin-4-yl)methanol (4c)[23,24]

Following general procedure ***GPI*** using phenyl(pyridin-4-yl)methanone (3.66 g, 20 mmol, 1.00 equiv) gave 3.70 g (20.0 mmol, quant.) of a white solid without further purification. ^{1}H NMR (300 MHz, $CDCl_3$): 8.49 (dd, *J* = 4.5, 1.6 Hz, 2H), 7.39 – 7.28 (m, 7H), 5.80 (s, 1H), 3.06 (bs, 1H).



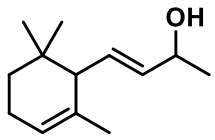
(4-Nitrophenyl)(phenyl)methanol (4g)[23,25]

Following general procedure ***GPI*** using (4-nitrophenyl)(phenyl)methanone (2.27 g, 10.0 mmol, 1.00 equiv), MeOH (60 mL) and CH_3CN (20 mL), $NaBH_4$ (946 mg, 25.0 mmol, 2.5 equiv) gave 2.22 g (9.68 mmol, 97%) of an orange oil after column purification (hexanes / EtOAc 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): 8.23 – 8.16 (m, 2H), 7.61 – 7.54 (m, 2H), 7.41 – 7.28 (m, 5H), 5.93 (s, 1H), 2.37 (s, 1H).



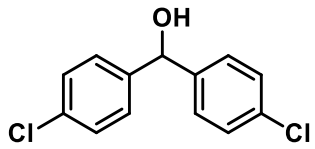
(4-methoxyphenyl)(phenyl)methanol (4m)[23,26]

Following general procedure ***GPI*** using (4-methoxyphenyl)(phenyl)methanone (4.24 g, 20.0 mmol, 1.00 equiv), MeOH (30 mL, 0.67 M), $NaBH_4$ (1.89 g, 50.0 mmol, 2.50 equiv) gave 4.01 g (18.7 mmol, 94%) of a white solid without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): 7.42 – 7.33 (m, 4H), 7.33 – 7.25 (m, 3H), 6.88 (d, *J* = 8.4 Hz, 2H), 5.75 (s, 1H), 3.79 (s, 3H), 2.77 (bs, 1H).



(*E*)-4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-ol (4o)[23,27]

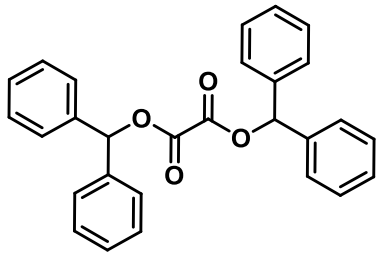
Following general procedure ***GPI*** using (*E*)-4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one (3.85 g, 20.0 mmol, 1.00 equiv), MeOH (50 mL, 0.4 M), $NaBH_4$ (2.27 g, 60.0 mmol, 3.00 equiv) gave 3.79 g (19.5 mmol, 98%) of a colorless oil without further purification. ^{1}H NMR (300 MHz, $CDCl_3$): 5.57 – 5.34 (m, 3H), 4.30 (p, *J* = 6.3 Hz, 1H), 2.07 (d, *J* = 8.7 Hz, 1H), 2.04 – 1.94 (m, 2H), 1.61 – 1.54 (m, 3H), 1.48 – 1.36 (m, 2H), 1.27 (dd, *J* = 6.3, 1.0 Hz, 3H), 1.16 (dt, *J* = 12.2, 4.7 Hz, 1H), 0.88 (d, *J* = 1.5 Hz, 3H), 0.81 (d, *J* = 6.7 Hz, 3H).



Bis(4-chlorophenyl)methanol (4f)[28]

A 25 mL Schlenk flask equipped with a magnetic stir bar was charged with $LiAlH_4$ (75.6 mg, 1.99 mmol, 0.50 equiv), dry THF (10 mL) under N_2 atmosphere and cooled to 0 °C. Bis(4-chlorophenyl)methanone (1.00 g, 3.98 mmol, 1.00 equiv) was added in portions. The reaction mixture was allowed to warm up to 25 °C, stirred for an additional hour and quenched with sat. NH_4Cl and H_2O. The aqueous layer was extracted with Et_2O (3 x 30 mL), and the organic layers were dried over Na_2SO_4 and evaporated under reduced pressure gave 955 mg (3.77 mmol, 95%) of a white solid without further purification. ^{1}H NMR (300 MHz, $CDCl_3$): 7.34 – 7.21 (m, 8H), 5.74 (s, 1H), 2.36 (bs, 1H).

3.8.3 Synthesis of Dibenzhydryl oxalate



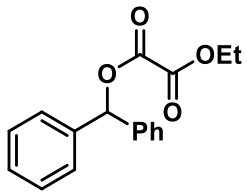
Dibenzhydryl oxalate (1)

Diphenylmethanol (4.27 g, 23.16 mmol, 2.0 equiv.) and $^{i}Pr_2NEt$ (4.33 mL, 3.29 g, 25.47 mmol, 1.1 equiv.) were dissolved in DMF (50 mL). Oxalyl chloride (1.47 g, 11.58 mmol, 1.0 equiv.) was added slowly at 0 °C. After complete esterification (as judged by TLC) solvent was removed by distillation under reduced pressure. Recrystallization with Et_2O overnight in the fridge yielded white crystals in 83%. ^{1}H NMR (400 MHz, $CDCl_3$): 7.44 – 7.27 (m, 10H), 6.99 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): 156.90, 138.90, 128.81, 128.56, 127.31, 79.80.

3.8.4 Synthesis of ethyl oxalate esters[3]

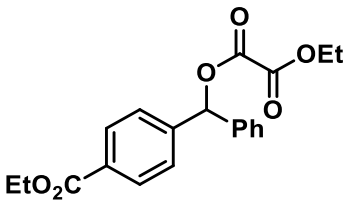
General procedure for the synthesis of oxalate esters *GPII*

A 500 mL round bottom flask equipped with a magnetic stir bar was charged with an alcohol (5.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (935 μL, 711 mg, 5.50 mmol, 1.10 equiv), and dry CH_2Cl_2 (50 mL, 0.10 M). The mixture was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (616 μL, 751 mg, 5.50 mmol, 1.10 equiv) was added dropwise. The reaction mixture was allowed to warm to 25 °C, quenched with H_2O, and evaporated under reduced pressure. Et_2O (25 mL) was added to the obtained residue, phases were separated, the organic layer was extracted with 1% HCl (10 mL), sat. $NaHCO_3$ (10 mL), and water (2 x 10 mL). The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The obtained residue was purified by flash column chromatography.



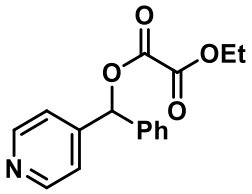
Benzhydryl ethyl oxalate (2a)

Following general procedure ***GPII*** using diphenylmethanol (4.61 g, 25.0 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (9.36 mL, 7.11 mg, 55.0 mmol, 2.2 equiv), ethyl 2-chloro-2-oxoacetate (6.16 mL, 7.51 mg, 55.0 mmol, 2.20 equiv) and dry CH_2Cl_2 (500 mL, 0.10 M) gave 7.01 g (24.7 mmol, 99%) of a colorless oil after flash column purification (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 3:1): 0.65; IR (neat): 2987, 1741, 1496, 1453, 1373, 1301, 1152, 1015, 954, 862, 756, 696, 603, 544, 425 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.43 – 7.28 (m, 10H), 6.99 (s, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): 157.88, 157.20, 138.89, 128.80, 128.54, 127.38, 79.62, 63.35, 14.09; HRMS (EI) m/z calculated for $C_{17}H_{16}NaO_4$ ([M+Na^+) 307.0941, found 307.0947.



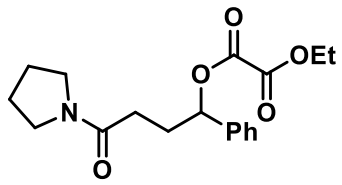
(4-(ethoxycarbonyl)phenyl)(phenyl)methyl ethyl oxalate (2b)

Following general procedure ***GPII*** using ethyl 4-(hydroxy(phenyl)methyl)benzoate[29] (500 mg, 1.95 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (365 μL, 277 mg, 2.15 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (240 μL, 293 mg, 2.15 mmol, 1.10 equiv), and dry THF (10 mL) gave 646 mg (1.81 mmol, 93%) of a colorless oil after flash column purification (hexanes / EtOAc, 7:1). R_f (hexanes / EtOAc, 3:1): 0.67; Ir (neat): 2983, 1767, 1744, 1714, 1613, 1455, 1415, 1368, 1273, 1154, 1102, 1020, 957, 860, 759, 697, 618, 546, 407 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 8.07 – 8.01 (m, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.43 – 7.28 (m, 5H), 7.00 (s, 1H), 4.37 (qd, *J* = 7.1, 1.1 Hz, 4H), 1.38 (td, *J* = 7.1, 2.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 166.23, 157.65, 157.04, 143.55, 138.22, 130.61, 130.07, 128.95, 128.90, 127.55, 127.01, 79.09, 63.49, 61.23, 14.45, 14.08; HRMS (EI) m/z calculated for $C_{20}H_{21}O_6$ ($[M+H)]^+$ 357.1333, found 357.1322.



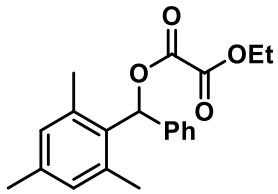
Ethyl (phenyl(pyridin-4-yl)methyl) oxalate (2c)

Following general the procedure ***GPII*** using phenyl(pyridin-4-yl)methanol **4c** (1.50 g, 8.10 mmol, 1.00 equiv.), $^{i}Pr_2NEt$ (997 μL, 1.20 g, 8.91 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (1.51 mL, 1.15 g, 8.91 mmol, 1.10 equiv), and dry THF (25 mL, 0.32 M) gave 1.84 g (6.46 mmol, 80%) of an orange oil after flash column purification (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 3:1): 0.18; IR (neat): 2985, 1729, 1634, 1598, 1494, 1450, 1408, 1280, 1198, 1056, 1023, 862, 787, 747, 699, 647, 422 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 8.61 (dd, *J* = 4.5, 1.6 Hz, 2H), 7.41 – 7.33 (m, 5H), 7.32 – 7.28 (m, 2H), 6.91 (s, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): 157.46, 156.91, 150.33, 147.53, 137.37, 129.30, 129.10, 127.82, 121.45, 78.09, 77.48, 77.16, 76.84, 63.58, 14.06; HRMS (EI) m/z calculated for $C_{16}H_{16}NO_4$ ($[M+H]^+$) 286.1074, found 286.1079.



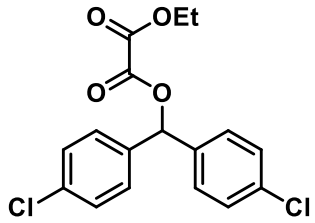
Ethyl (4-oxo-1-phenyl-4-(pyrrolidin-1-yl)butyl) oxalate (2d)

Following general procedure ***GPII*** using 4-hydroxy-4-phenyl-1-(pyrrolidin-1-yl)butan-1-one[30] (400 mg, 1.71 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (371 µL, 244 mg, 1.89 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (211 µL, 258 g, 1.89 mmol, 1.10 equiv) and dry THF (17 mL, 0.1 M) gave 570 g (1.71 mmol, 100%) of an slightly orange oil without further purification. R_f (hexanes / EtOAc, 3:1): 0.38; IR (neat): 2982, 2470, 1770, 1728, 1639, 1455, 1329, 1299, 1174, 1141, 1020, 985, 940, 891, 755, 699, 530, 480 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.45 – 7.27 (m, 5H), 6.03 – 5.91 (m, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.44 (t, *J* = 6.8 Hz, 2H), 3.31 (t, *J* = 6.7 Hz, 2H), 2.44 – 2.21 (m, 4H), 1.88 (dp, *J* = 26.4, 6.7 Hz, 4H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): 170.03, 158.04, 157.48, 138.82, 128.77, 128.64, 126.76, 78.75, 63.23, 46.60, 45.83, 31.19, 30.36, 26.18, 24.50, 14.07; HRMS (EI) m/z calculated for $C_{15}H_{22}NaO_4$ ($[M+Na]$)$^+$ 289.1410, found 289.1414.



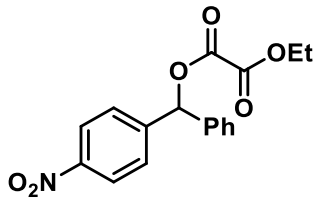
Ethyl (mesityl(phenyl)methyl)oxalate (2e)

Following general procedure ***GPII*** using mesityl(phenyl)methanol (1.08 g, 4.76 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (891 µL, 677 mg, 5.24 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (586 µL, 715 mg, 5.24 mmol, 1.10 equiv) and dry THF (25 mL) gave 1.13 g (3.47 mmol, 73%) of a white solid after flash column purification (hexanes / EtOAc, 20:1). R_f (hexanes / EtOAc, 7:1): 0.60; m.p.: 98 °C; Ir (neat): 2982, 2927, 1760, 1742, 1610, 1448, 1370, 1320, 1291, 1187, 1112, 1017, 946, 852, 820, 775, 732, 700, 641, 603, 497 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.45 (s, 1H), 7.36 – 7.27 (m, 3H), 7.18 (dd, *J* = 10.9, 4.2 Hz, 2H), 6.87 (s, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.30 (d, *J* = 11.1 Hz, 9H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 157.86, 157.51, 138.59, 138.31, 138.31, 138.05, 131.64, 130.08, 128.59, 127.66, 125.81, 75.77, 63.27, 21.10, 20.58, 14.08; HRMS (EI) m/z calculated for $C_{20}H_{22}NaO_4$ ($[M+Na]^+$) 349.1410, found 349.1413.



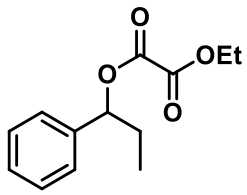
Bis(4-chlorophenyl)methyl ethyl oxalate (2f)

Following general procedure ***GPII*** using bis(4-chlorophenyl)methanol **4f** (1.27 g, 5.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (616 µL, 751 mg, 5.50 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (935 µL, 711 mg, 5.00 mmol, 1.10 equiv) and dry CH_2Cl_2 (50 mL, 0.1 M) gave 1.53 g (4.35 mmol, 87%) of a colorless oil after flash column purification (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 3:1) 0.80; IR (neat): 2985, 1767, 1742, 1596, 1491, 1412, 1296, 1153, 1089, 1014, 960, 859, 812, 771, 731, 677, 520, 441 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.36-7.28 (m, 8 H), 6.90 (s, 1 H), 4.37 (q, *J* = 7.1, 2 H), 1.38 (t, *J* = 7.1, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$): 157.53, 156.95, 136.91, 134.79, 129.15, 128.72, 128.00, 78.15, 63.56, 14.07.; HRMS (EI) m/z calculated for $C_{17}H_{14}Cl_2NaO_4$ ($[M+Na]^+$) 375.0161, found 375.0163.



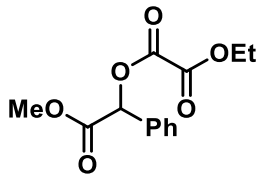
Ethyl ((4-nitrophenyl)(phenyl)methyl) oxalate (2g)

Following general procedure ***GPII*** using (4-nitrophenyl)(phenyl)methanol **4g** (1.15 g, 5.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (935 µL, 711 mg, 5.50 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (616 µL, 751 mg, 5.50 mmol, 1.10 equiv.) and dry THF (25 mL, 0.2 M) gave 1.64 g (4.97 mmol, 99%) of a slightly yellow oil without any further purification. R_f (hexanes / EtOAc, 3:1): 0.62; IR (neat): 2988, 2206, 1763, 1743, 1608, 1520, 1455, 1347, 1301, 1152, 1110, 1015, 965, 845, 743, 699, 617 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 8.25 – 8.19 (m, 2H), 7.62 – 7.55 (m, 2H), 7.42 – 7.33 (m, 5H), 7.02 (s, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 157.88, 157.33, 148.27, 146.24, 137.86, 129.60, 129.48, 128.19, 127.86, 124.37, 78.46, 63.57, 13.66; HRMS (EI) m/z calculated for $C_{17}H_{19}N_2O_6$ ($[M+NH_4]^+$) 347.1238, found 347.1240.



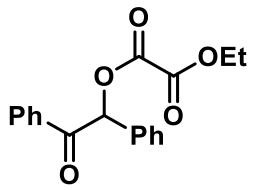
Ethyl (1-phenylpropyl) oxalate (2h)

Following general procedure ***GPII*** using 1-phenylpropan-1-ol (1.00 g, 7.34 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (1.37 mL, 1.04 g, 8.08 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (904 µL, 1.10 g, 8.08 mmol, 1.10 equiv) and dry THF (25 mL, 0.3 M) gave 1.28 g (5.42 mmol, 74%) of a colorless oil after flash column purification (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 5:1): 0.56; ^{1}H NMR (300 MHz, $CDCl_3$): 7.41 – 7.27 (m, 5H), 5.79 (t, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 2.19 – 1.84 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 158.10, 157.55, 138.96, 128.69, 128.55, 126.92, 80.71, 63.21, 29.15, 14.07, 10.01; HRMS (EI) m/z calculated for $C_{13}H_{16}NaO_4$ ($[M+Na]$)$^+$ 259.0941, found 259.0943.



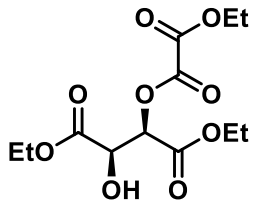
Ethyl (2-methoxy-2-oxo-1-phenylethyl) oxalate (2i)

Following general procedure ***GPII*** using methyl 2-hydroxy-2-phenylacetate (1.66 g, 10.0 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (3.74 mL, 2.84 g, 22.0 mmol, 2.20 equiv), ethyl 2-chloro-2-oxoacetate (2.46 mL, 3.00 g, 22.0 mmol, 2.20 equiv) and dry CH_2Cl_2 (100 mL, 0.1 M) gave 2.29 g (7.33 mmol, 73%) of a colorless oil after automatic column purification on SiO_2 (hexanes / EtOAc, 100:0 - 0:100). R_f (hexanes / EtOAc, 3:1): 0.52; IR (neat): 2986, 2959, 1770, 1742, 1438, 1315, 1272, 1220, 1150, 1011, 963, 859, 734, 696, 527 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 7.54 – 7.46 (m, 2H), 7.45 – 7.39 (m, 3H), 6.04 (s, *J* = 4.8 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.76 (s, *J* = 2.2 Hz, 3H), 1.39 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 168.07, 157.17, 157.04, 132.59, 129.87, 129.10, 127.91, 76.30, 63.65, 53.14, 14.06; HRMS (EI) m/z calculated for $C_{18}H_{17}O_5$ ($[M+H]^+$) 313.1071, found 313.1074.



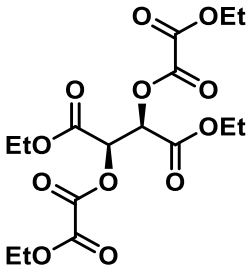
Ethyl (2-oxo-1,2-diphenylethyl) oxalate (2j)[31]

Following general procedure ***GPII*** using methyl 2-hydroxy-2-phenylacetate (1.06 g, 5.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (935 µL, 710 mg, 5.50 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (615 µL, 750 mg, 5.00 mmol, 1.10 equiv), and dry CH_2Cl_2 (50 mL, 0.1 M) gave 1.56 g (5.00 mmol, 100%) of a white solid after filtration through a short plug of flash silica gel (hexanes/ EtOAc, 2:1). R_f (hexanes / EtOAc, 5:1): 0.34; m.p.: 86 °C, IR (neat): 2984, 1757, 1694, 1596, 1496, 1449, 1374, 1325, 1257, 1230, 1199, 1115, 1011, 938, 858, 761, 697, 597, 534 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 7.96 – 7.89 (m, 2H), 7.56 – 7.35 (m, 8H), 6.94 (s, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): 191.89, 157.35, 157.31, 134.29, 133.90, 132.52, 129.95, 129.44, 129.06, 129.03, 128.87, 79.93, 77.48, 77.16, 76.84, 63.52, 14.05; HRMS (EI) m/z calculated for $C_{18}H_{17}O_5$ ($[M+H]^+$) 313.1071, found 313.1075.



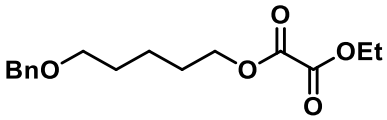
(*2R,3R*)-diethyl 2-(2-ethoxy-2-oxoacetoxy)-3-hydroxysuccinate (2k)

Following general procedure ***GPII*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate (10.31 g, 50.0 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (9.35 mL, 7.11 g, 55.0 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (6.16 mL, 7.51 mg, 55.0 mmol, 1.10 equiv) and dry CH_2Cl_2 (500 mL, 0.1 M) gave 7.77 g (25.4 mmol, 51%) of a colorless oil after flash column purification (hexanes / EtOAc, 5:1 - 2:1). R_f (hexanes / EtOAc, 2:1): 0.49; IR (neat): 3497, 2986, 1740, 1470, 1449, 1371, 1298, 1261, 1173, 1153, 1055, 1012, 932, 859, 764, 703 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 5.54 (d, *J* = 2.3 Hz, 1H), 4.81 (dd, *J* = 7.1, 2.1 Hz, 1H), 4.38 – 4.25 (m, 6H), 3.29 (d, *J* = 7.4 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.28 (dd, *J* = 14.0, 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): 170.12, 165.31, 156.80, 156.74, 74.96, 70.45, 63.62, 62.96, 62.74, 14.17, 14.14, 13.98; HRMS (EI) m/z calculated for $C_{12}H_{19}O_9$ ($[M+H]^+$) 307.1024, found 307.1020.



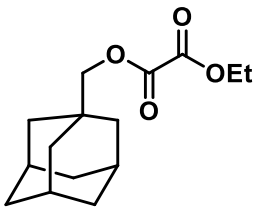
O,O'-((*2R,3R*)-1,4-diethoxy-1,4-dioxobutane-2,3-diyl) diethyl dioxalate (2l)

Following general procedure ***GPII*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate (10.31 g, 50.0 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (9.35 mL, 7.11 g, 55.0 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (6.16 mL, 7.51 mg, 55.0 mmol, 1.10 equiv) and dry CH_2Cl_2 (500 mL, 0.1 M) gave 2.23 g (5.49 mmol, 11%) of a colorless oil after flash column purification (hexanes / EtOAc, 5:1 - 2:1). R_f (hexanes / EtOAc, 2:1): 0.70; IR (neat): 2988, 2951, 1744, 1470, 1372, 1302, 1272, 1212, 1143, 1049, 1011, 858, 762, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 5.88 (s, 2H), 4.37 (q, *J* = 7.1 Hz, 4H), 4.32 – 4.21 (m, 4H), 1.37 (t, *J* = 7.1 Hz, 6H), 1.27 (t, *J* = 7.1 Hz, 6H).; ^{13}C NMR (75 MHz, $CDCl_3$): 164.16, 156.74, 156.59, 72.25, 63.71, 63.15, 14.10, 13.99; HRMS (EI) m/z calculated for $C_{16}H_{23}O_{12}$ ($[M+H]^+$) 407.1184, found 407.1185.



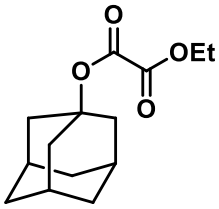
5-(benzyloxy)pentyl ethyl oxalate (2u)

Following general procedure ***GPII*** using 5-(benzyloxy)pentan-1-ol[32] (583 mg, 3.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (561 µL, 427 mg, 3.30 mmol, 1.10 equiv), ethyl 2-chloro-2-oxoacetate (369 µL, 451 mg, 3.30 mmol, 1.10 equiv) and dry THF (25 mL, 0.12 M) gave 884 mg (3.00 mmol, 100%) of a slightly yellowish oil without further purification. R_f (hexanes / EtOAc, 3:1): 0.69. IR (neat): 2939, 2862, 1741, 1636, 1454, 1363, 1313, 1174, 1098, 1025, 911, 733, 698, 612, 460 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.37 – 7.26 (m, 5H), 4.50 (s, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 4.29 (t, *J* = 6.7 Hz, 2H), 3.48 (t, *J* = 6.4 Hz, 2H), 1.81 – 1.71 (m, 2H), 1.70 – 1.62 (m, 2H), 1.54 – 1.43 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): 158.15, 158.03, 138.67, 128.51, 127.76, 127.68, 73.09, 70.09, 67.15, 63.24, 29.43, 28.25, 22.66, 14.06. HRMS (EI) m/z calculated for $C_{16}H_{23}O_5$ ($[M+H]^+$) 295.1540, found 295.1541.



(*3r,5r,7r*)-adamantan-1-ylmethyl ethyl oxalate (2v)

Following the general procedure ***GPII*** using (*3r,5r,7r*)-adamantan-1-ylmethanol (1.66 g, 10.0 mmol, 1.00 equiv), 4-DMAP (122 mg, 100 μmol, 0.100 equiv), $^{i}Pr_2NEt$ (3.40 mL, 2.58 g, 20.0 mmol, 2.00 equiv), ethyl 2-chloro-2-oxoacetate (2.24 mL, 2.73 g, 20.0 mmol, 2.00 equiv), and dry CH_2Cl_2 (50 mL, 0.2 M) gave 2.48 g (9.32 mmol, 93%) of a white solid after flash column purification (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 5:1): 0.64; m.p.: 47 °C; IR (neat): 2904, 2853, 1759, 1731, 1453, 1401, 1326, 1274, 1172, 1111, 1016, 962, 914, 866, 804, 592 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): 4.34 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 2H), 1.99 (s, 3H), 1.68 (dd, *J* = 30.2, 11.8 Hz, 6H), 1.56 (d, *J* = 2.5 Hz, 6H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): 158.41, 158.14, 76.27, 63.08, 39.12, 36.91, 33.50, 28.03, 14.05; HRMS (EI) m/z calculated for $C_{15}H_{22}NaO_4$ ($[M+Na]^+$) 289.1410, found 289.1414.



(*3s,5s,7s*)-adamantan-1-yl ethyl oxalate (2w)

Following general procedure ***GPII*** using (*3s,5s,7s*)-adamantan-1-ol (1.52 g, 10.0 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (5.61 mL, 4.26 g, 33.0 mmol, 3.30 equiv), ethyl 2-chloro-2-oxoacetate (3.69 mL, 4.51 g, 33.0 mmol, 3.30 equiv), and dry CH_2Cl_2 (100 mL, 0.1 M) gave 0.85 g (3.35 mmol, 34%) of a white solid after automatic column purification on SiO_2 (hexanes / EtOAc, 100:0 - 0:100). R_f (hexanes / EtOAc, 3:1): 0.42; m.p.: 32 °C; IR (neat): 2911, 2854, 1761, 1734, 1457, 1370, 1330, 1299, 1176, 1155, 1104, 1045, 1017, 964, 920, 876, 822, 788, 556, 445 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 4.31 (q, *J* = 7.1 Hz, 2H), 2.20 (d, *J* = 6.1 Hz, 9H), 1.73 – 1.63 (m, 6H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): 158.82, 156.86, 85.07, 62.88, 41.06, 36.09, 31.10, 14.08; HRMS (EI) m/z calculated for $C_{14}H_{20}NaO_4$ $([M+Na])^+$ 276.1288, found 276.1291.

3.8.5 General procedures for photoreactions *GPIII*

a. Procedure for the deoxygenation of dibenzhydryl oxalate (**1**)

A Schlenk tube equipped with a magnetic stir bar was charged with dibenzhydryl oxalate **1** (55.5 mg, 0.13 mmol, 1.00 equiv.) and $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (3.00 mg, 4.00 µmol, 2.50 mol%), Hantzsch ester (36.5 mg, 0.140 mmol, 1.10 equiv.), $^{i}Pr_2NEt$ (44.2 µL, 0.260 mmol, 2.00 equiv.), naphthalene (33.3 mg 0.260 mmol, 2.00 equiv.) as internal standard, dissolved in CH_3CN and sealed with a screw-cap. The reaction mixture was degassed by freeze-pump-thaw (5x) and the screw-cap was replaced with a Teflon sealed inlet for a glass rod, through which irradiation with a 455 nm high power LED took place from above while the reaction was magnetically stirred and heated at 60 °C in an aluminum block from below. Afterwards the reaction mixture was evaporated under reduced pressure and the residue was purified by filtration through a short plug of flash silica gel with a mixture of hexanes and ethyl acetate to give 68% GC – FID yield using naphthalene as internal standard.

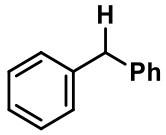
b. General procedure for the deoxygenations of oxalate esters with H_2O as additive ***GPIV***.

A Schlenk tube equipped with a magnetic stir bar was charged with oxalate ester (1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 10.0 µmol, 1.00 mol%), H_2O (18.0 µL, 18.0 mg, 1.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (340 µL, 259 mg, 2.00 mmol, 2.00 equiv), dissolved in CH_3CN (10.0 mL, 0.1 M) and sealed with a Teflon inlet for a glass rod, through which irradiation with a 455 nm high power LED took place from above while the reaction was magnetically stirred and heated at 60 °C in an aluminum block from below. Afterwards the reaction mixture was evaporated under reduced pressure and the residue was purified by filtration through a short plug of flash silica gel with a mixture of hexanes and ethyl acetate.

c. General procedure for the deoxygenations of oxalate esters with Hantzsch ester as additive ***GPV***.

A Schlenk tube equipped with a magnetic stir bar was charged with oxalate ester (1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (22.9 mg, 10.0 µmol, 2.50 mol%) and Hantzsch ester (279 mg, 1.10 mmol, 1.10 equiv). CH_3CN (10.0 mL, 0.1 M) and $^{i}Pr_2NEt$ (340 µL, 259 mg, 2.00 mmol, 2.00 equiv) was added. The reaction mixture was degassed by freeze-pump-thaw (5x) and the

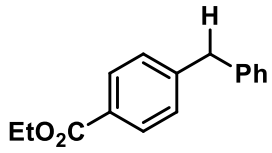
screw-cap was replaced with a Teflon sealed inlet for a glass rod, through which irradiation with a 455 nm high power LED took place from above while the reaction was magnetically stirred and heated at 60 °C in an Aluminum block from below. Afterwards the reaction mixture was evaporated under reduced pressure and the residue was purified by filtration through a short plug of flash silica gel with a mixture of hexanes and ethyl acetate.



Diphenylmethane (3a)[33,34]

a. Following general procedure ***GPIV*** using benzhydryl ethyl oxalate **2a** (284 mg, 1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 10.0 μmol, 1.00 mol%), H_2O (180 μL, 180 mg, 10.0 mmol, 10.0 equiv), $^{i}Pr_2NEt$ (340 μL, 258 mg, 2.00 mmol, 2.00 equiv), and CH_3CN (10 mL, 0.1 M) gave 153 mg (910 μmol, 91%) of a colorless oil after filtration through a short plug of flash silica gel with hexanes.
b. Following general procedure ***GPV*** using benzhydryl ethyl oxalate **2a** (284 mg, 1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (45.7 mg, 50.0 μmol, 5.00 mol%), Hantzsch ester (279 mg, 1.10 mmol, 1.10 equiv), $^{i}Pr_2NEt$ (340 μL, 259 mg, 2.00 mmol, 2.00 equiv), and CH_3CN (10 mL, 0.1 M) gave 143 mg (850 μmol, 85%) of a colorless oil after filtration through a short plug of flash silica gel with hexanes.

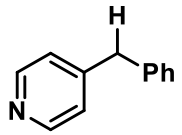
   ^1H NMR (400 MHz, $CDCl_3$): 7.33 – 7.27 (m, 4H), 7.24 – 7.16 (m, 6H), 4.00 (s, 2H).



Ethyl 4-benzylbenzoate (3b)[33,34]

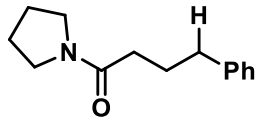
Following general procedure ***GPV*** using (4-(ethoxycarbonyl)phenyl)(phenyl)methyl ethyl oxalate **2b** (100 mg, 281 μmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (12.8 mg, 14.0 μmol, 5.00 mol%), Hantzsch ester (78.2 mg, 309 μmol, 1.10 equiv), $^{i}Pr_2NEt$ (95.4 μL, 72.5 mg, 561 μmol, 2.00 equiv), and CH_3CN (2.8 mL, 0.1 M) gave 64.8 mg (270 μmol, 96%) of a colorless oil after flash column

chromatography (hexanes / EtOAc 5:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.99 – 7.93 (m, 2H), 7.34 – 7.14 (m, 7H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.03 (s, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).



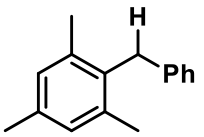
4-benzylpyridine (3c)[35]

Following general procedure ***GPV*** using ethyl (phenyl(pyridin-4-yl)methyl) oxalate **2c** (100 mg, 351 μmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (16 mg, 17.6 μmol, 5.00 mol%), Hantzsch ester (97.7 mg, 386 μmol, 1.10 equiv), ^{i}Pr$_2$NEt (119 μL, 90.6 mg, 701 μmol, 2.00 equiv), and CH_3CN (3 mL, 0.12 M) gave 54.7 mg (323 μmol, 92%) of a colorless oil after flash column chromatography (hexanes / EtOAc 5:1). ^{1}H NMR (300 MHz, $CDCl_3$): 8.50 (dd, *J* = 4.4, 1.6 Hz, 2H), 7.36 – 7.25 (m, 3H), 7.18 (dd, *J* = 5.2, 3.0 Hz, 2H), 7.10 (dd, *J* = 4.4, 1.6 Hz, 2H), 3.97 (s, 2H).



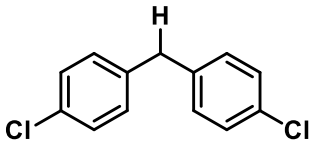
4-phenyl-1-(pyrrolidin-1-yl)butan-1-one (3d)[36]

Following general procedure ***GPV*** using ethyl (4-oxo-1-phenyl-4-(pyrrolidin-1-yl)butyl) oxalate **2d** (100 mg, 300 μmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (6.86 mg, 7.50 μmol, 2.50 mol%), Hantzsch ester (83.6 mg, 330 μmol, 1.10 equiv), ^{i}Pr$_2$NEt (102 μL, 77.5 mg, 600 μmol, 2.00 equiv), and CH_3CN (3.0 mL, 0.1 M) gave 43.0 mg (198 μmol, 66%) of a slightly yellow oil after flash column chromatography (hexanes / EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): 7.30 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 3.45 (t, *J* = 6.8 Hz, 2H), 3.32 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 2.26 (t, *J* = 7.5 Hz, 2H), 2.02 – 1.80 (m, 6H).



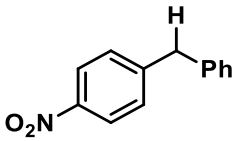
2-benzyl-1,3,5-trimethylbenzene (3e)[35]

Following general procedure ***GPIV*** using ethyl (mesityl(phenyl)methyl)oxalate **2e** (326 mg, 1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 10.0 μmol, 1.00 mol%), H_2O (18.0 μL, 18.0 mg, 1.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (340 μL, 259 mg, 2.00 mmol, 2.00 equiv), and CH_3CN (10 mL, 0.1 M) gave 207 mg (980 μmol, 98%) of a colorless oil after filtration through a short plug of flash silica gel (hexanes / EtOAc, 95:5). ^1H NMR (400 MHz, $CDCl_3$): 7.26 – 7.02 (m, 5H), 6.90 (s, 2H), 4.03 (s, 2H), 2.30 (s, 3H), 2.21 (s, 6H).



Bis(4-chlorophenyl)methane (3f)[37]

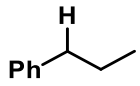
Following general procedure ***GPIV*** using bis(4-chlorophenyl)methyl ethyl oxalate **2f** (352 mg, 1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 10.0 μmol, 1.00 mol%), H_2O (18.0 μL, 18.0 mg, 1.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (340 μL, 258 mg, 2.00 mmol, 2.00 equiv), and CH_3CN (10 mL, 0.1 M) gave 210 mg (890 μmol, 89%) of a colorless oil after filtration through a short plug of flash silica gel (hexanes / EtOAc, 95:5). ^1H NMR (300 MHz, $CDCl_3$). 7.31 – 7.25 (m, 2H), 7.14 – 7.08 (m, 2H), 3.93 (s, 1H).



1-benzyl-4-nitrobenzene (3g)[38]

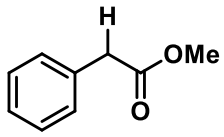
Following general procedure ***GPIV*** using ethyl ((4-nitrophenyl)(phenyl)methyl) oxalate **2g** (117 mg, 355 μmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (3.24 mg, 3.55 μmol, 1.00 mol%), H_2O (6.40 μL, 6.40 mg, 1.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (121 μL, 91.8 mg, 711 mmol, 2.00 equiv), and CH_3CN (3.5 mL, 0.1 M) gave 36.5 mg (171 μmol, 48%) of a colorless oil after filtration through a short

plug of flash silica gel (hexanes / EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): 8.18 – 8.11 (m, 2H), 7.37 – 7.29 (m, 4H), 7.25 (dt, *J* = 7.1, 3.5 Hz, 1H), 7.17 (dd, *J* = 7.8, 0.9 Hz, 2H), 4.08 (s, 2H).



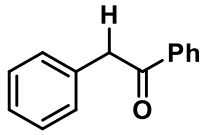
Propylbenzene (3h)[39]

Following general procedure ***GPV*** using ethyl (1-phenylpropyl) oxalate **2h** (100 mg, 423 μmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (19.3 mg, 21.2 μmol, 5.00 mol%), Hantzsch ester (118 mg, 466 μmol, 1.10 equiv), $^i Pr_2NEt$ (144 μL, 109 mg, 847 μmol, 2.00 equiv), and CH_3CN (3.0 mL, 0.14 M) gave 75% GC – FID yield using naphthalene as internal standard.



Methyl 2-phenylacetate (3i)[40]

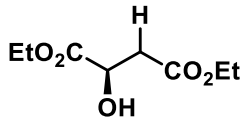
Following general procedure ***GPIV*** using ethyl (2-methoxy-2-oxo-1-phenylethyl) oxalate **2i** (266 mg, 1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 10.0 μmol, 1.00 mol%), H_2O (18.0 μL, 18.0 mg, 1.00 mmol, 1.00 equiv), $^i Pr_2NEt$ (340 μL, 258 mg, 2.00 mmol, 2.00 equiv), and CH_3CN (10 mL, 0.1 M) gave 148 mg (990 μmol, 99%) of a colorless oil after filtration through a short plug of flash silica gel (hexanes / EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): 7.36 – 7.26 (m, 5H), 3.70 (s, 3H), 3.63 (s, 2H).



1,2-diphenylethanone (3j)[41]

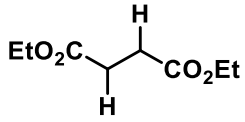
Following general procedure ***GPIV*** using ethyl (2-oxo-1,2-diphenylethyl) oxalate **2j** (312 mg, 1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 10.0 μmol, 1.00 mol%), H_2O (18.0 μL, 18.0 mg, 1.00 mmol, 1.00 equiv), $^i Pr_2NEt$ (340 μL, 258 mg, 2.00 mmol, 2.00 equiv), and CH_3CN (10 mL,

0.1 M) gave 112 mg (570 μmol, 57%) of an orange solid after filtration through a short plug of flash silica gel (hexanes / EtOAc, 95:5). ^{1}H NMR (400 MHz, $CDCl_3$): 8.13 (dt, *J* = 8.5, 1.6 Hz, 2H), 7.65 – 7.59 (m, 1H), 7.53 – 7.45 (m, 2H).



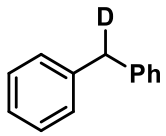
(*R*)-diethyl 2-hydroxysuccinate (3k)[34]

Following general procedure ***GPIV*** using (*2R,3R*)-diethyl 2-(2-ethoxy-2-oxoacetoxy)-3-hydroxysuccinate **2k** (306 mg, 1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 10.0 μmol, 1.00 mol%), H_2O (18.0 μL, 18.0 mg, 1.00 mmol, 1.00 equiv), ^{i}Pr$_2$NEt (340 μL, 258 mg, 2.00 mmol, 2.00 equiv), and CH_3CN (10 mL, 0.1 M) gave 124 mg (650 μmol, 65%) of a colorless oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 10:1). α_D^{20} = +12.4° (lit. α_D^{23} +11.2° c = 2.15, EtOH);[42] ^{1}H NMR (300 MHz, $CDCl_3$): 4.48 (dd, *J* = 10.3, 5.5 Hz, 1H), 4.32 – 4.22 (m, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.22 (d, *J* = 5.4 Hz, 1H), 2.89 – 2.73 (m, 2H), 1.28 (dt, *J* = 10.8, 7.1 Hz, 6H).



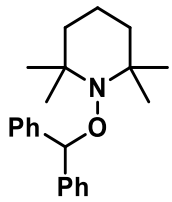
Diethyl succinate (3l)[34]

Following general procedure ***GPIV*** using O,O'-((*2R,3R*)-1,4-diethoxy-1,4-dioxobutane-2,3-diyl) diethyl dioxalate **2l** (406 mg, 1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 10.0 μmol, 1.00 mol%), H_2O (18.0 μL, 18.0 mg, 1.00 mmol, 1.00 equiv), ^{i}Pr$_2$NEt (340 μL, 258 mg, 2.00 mmol, 2.00 equiv), and CH_3CN (10 mL, 0.1 M) gave 60 mg (345 μmol, 35%) of a colorless oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 95:5). ^{1}H NMR (400 MHz, $CDCl_3$): 4.14 (q, *J* = 7.1 Hz, 2H), 2.61 (s, 2H), 1.25 (t, *J* = 7.1 Hz, 3H).



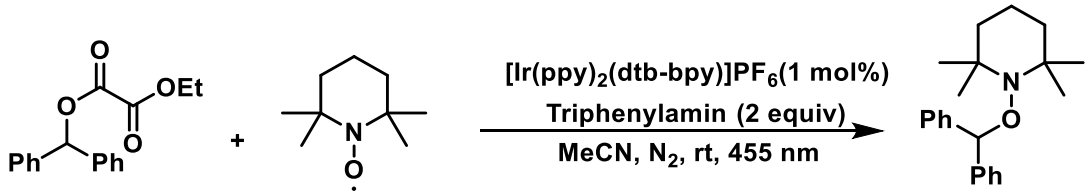
Diphenylmethane-d (8a)

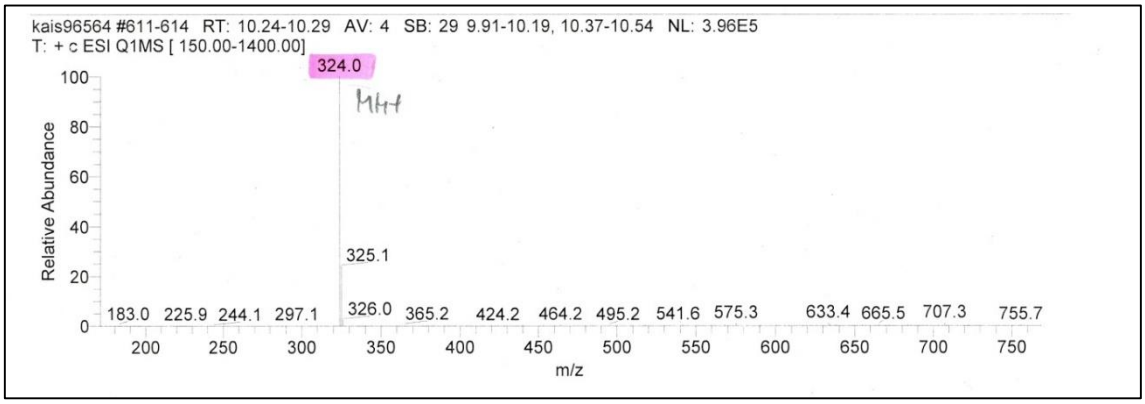
Following general procedure ***GPIV*** using benzhydryl ethyl oxalate **2a** (284 mg, 1.00 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 10.0 μmol, 1.00 mol%), D_2O (200 μL, 200 mg, 10.0 mmol, 10.0 equiv), $^{i}Pr_2NEt$ (340 μL, 258 mg, 2.00 mmol, 2.00 equiv), and CH_3CN (10 mL, 0.1 M) gave 140 mg (830 μmol, 83%) of a colorless oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 95:5). ^1H NMR (400 MHz, $CDCl_3$): 7.51 – 7.43 (m, 4H), 7.43 – 7.35 (m, 6H), 4.17 (d, *J* = 8.0 Hz, 1H).



1-(benzhydryloxy)-2,2,6,6-tetramethylpiperidine (7a)[43]

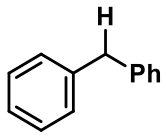
Following general procedure ***GPV*** using benzhydryl ethyl oxalate **2a** (85.3 mg, 0.30 mmol, 1.00 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (2.70 mg, 3.00 μmol, 1.00 mol%), TEMPO (188 mg, 1.20 mmol, 4.00 equiv), triphenylamine (147 mg, 0.60 mmol, 2.00 equiv) and MeCN (1.5 mL). The reaction mixture was degassed by freeze-pump-thaw (5x) and the screw-cap was replaced with a Teflon sealed inlet for a glass rod, through which irradiation with a 455 nm high power LED took place from above while the reaction was magnetically stirred. After 91 h of irradiation, TEMPO trapped compound **7a** was detected by mass spectra. Exact Mass = 323.22 g/mol.


OEt
Ph
Ph
+
[Ir(ppy)2(dtb-bpy)]PF6(1 mol%)
Triphenylamin (2 equiv)
MeCN, N2, rt, 455 nm
Ph
Ph


kais96564 #611-614 RT: 10.24-10.29 AV: 4 SB: 29 9.91-10.19, 10.37-10.54 NL: 3.96E5
T: + c ESI Q1MS [150.00-1400.00]
324.0
MH+
325.1
326.0
Relative Abundance
m/z
183.0 225.9 244.1 297.1 365.2 424.2 464.2 495.2 541.6 575.3 633.4 665.5 707.3 755.7

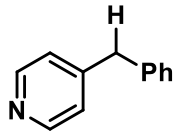
3.8.6 General procedure for an "one-pot" *in situ* esterification following a photoredox catalyzed deoxygenation of alcohols *GPIV*.

A 35 mL Schlenk flask equipped with a magnetic stir bar was charged with an alcohol (1.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (680 μL, 4.00 mmol, 4.00 equiv), dissolved in CH_3CN (10.0 mL, 0.1 M) and cooled to 0 °C. Ethyl 2-chloro-2-oxoacetate (123 μL, 1.10 mmol, 1.10 equiv) was added dropwise. The reaction mixture was allowed to warm up to 25 °C. After complete esterification (as judged by TLC), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 1.00 mol%) and H_2O (180 μL, 10.0 mmol, 10.0 equiv) was added. The Schlenk flask was sealed with a Teflon inlet for a glass rod, through which irradiation with a 455 nm high power LED took place from above while the reaction was magnetically stirred and heated at 60 °C in an aluminum block from below. Afterwards the reaction mixture was evaporated under reduced pressure and the residue was purified by filtration through a short plug of flash silica gel with a mixture of hexanes and ethyl acetate.



Diphenylmethane (3a)[33,34]

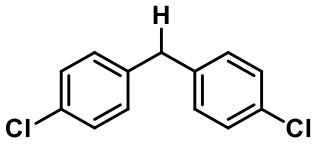
Following general procedure ***GPIV*** using benzhydrol **4a** (184 mg, 1.00 mmol, 1.00 equiv) gave 91% GC-FID yield using naphthalene as internal standard (mole ratio 1:1).



4-Benzylpyridine (3c)[35]

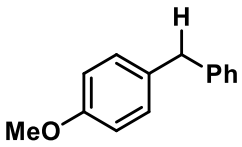
Following general procedure ***GPIV*** using phenyl(pyridin-4-yl)methanol **4c** (185 mg, 1.00 mmol, 1.00 equiv) $^{i}Pr_2NEt$ (680 μL, 4.00 mmol, 4.00 equiv), CH_3CN (10.0 mL, 0.1 M), Ethyl 2-chloro-2-oxoacetate (123 μL, 1.10 mmol, 1.10 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 1.00 mol%) and H_2O (36 μL, 2.00 mmol, 2.00 equiv) gave 107.9 mg (0.64 mmol, 64%) of a slightly yellow oil after filtration through a short plug of flash silica gel (hexanes/ EtOAc 95:5). ^1H NMR (300 MHz, $CDCl_3$):

8.50 (dd, *J* = 4.4, 1.6 Hz, 2H), 7.36 – 7.25 (m, 3H), 7.18 (dd, *J* = 5.2, 3.0 Hz, 2H), 7.10 (dd, *J* = 4.4, 1.6 Hz, 2H), 3.97 (s, 2H).



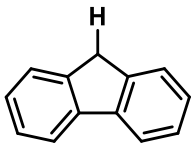
Bis(4-chlorphenyl)methane (3f)[37]

Following general procedure ***GPIV*** using bis(4-chlorophenyl)methanol **4f** (253 mg, 1.00 mmol, 1.00 equiv) gave 173 mg (0.73 mmol, 73%) of a colorless oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 95:5). ^{1}H NMR (300 MHz, $CDCl_3$). 7.31 – 7.25 (m, 4H), 7.14 – 7.08 (m, 4H), 3.93 (s, 2H).



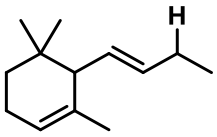
1-benzyl-4-methoxybenzene (3m)[35]

Following general procedure ***GPIV*** using (4-methoxyphenyl)(phenyl)methanol **4m** (214 mg, 1.00 mmol, 1.00 equiv) ^{i}Pr$_2$NEt (680 μL, 4.00 mmol, 4.00 equiv), CH_3CN (10.0 mL, 0.1 M), ethyl 2-chloro-2-oxoacetate (123 μL, 1.10 mmol, 1.10 equiv), [Ir(ppy)$_2$(dtb-bpy)](PF$_6$) (9.14 mg, 1.00 mol%) and H_2O (36 μL, 2.00 mmol, 2.00 equiv) gave 150 mg (0.76 mmol, 76%) of a colorless oil after filtration through a short plug of flash silica gel with hexanes. ^{1}H NMR (400 MHz, $CDCl_3$): 7.31 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 7.13 – 7.09 (m, 2H), 6.86 – 6.81 (m, 2H), 3.93 (s, 2H), 3.79 (s, 3H).



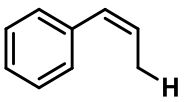
9*H*-fluorene (3n)[44]

Following general procedure ***GPIV*** using 9*H*-fluoren-9-ol **4n** (182 mg, 1.00 mmol, 1.00 equiv) $^{i}Pr_2NEt$ (680 μL, 4.00 mmol, 4.00 equiv), 4-DMAP (12.2 mg, 100 μmol, 0.100 equiv), CH_3CN (10.0 mL, 0.1 M), ethyl 2-chloro-2-oxoacetate (123 μL, 1.10 mmol, 1.10 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 1.00 mol%) and H_2O (36 μL, 2.00 mmol, 2.00 equiv) gave 135 mg (0.81 mmol, 81%) of a colorless oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 95:5). ^1H NMR (400 MHz, $CDCl_3$): 7.83 (d, *J* = 7.5 Hz, 2H), 7.58 (d, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.1 Hz, 2H), 7.35 (td, *J* = 7.4, 1.2 Hz, 2H), 3.94 (s, 2H).



(*E*)-6-(but-1-en-1-yl)-1,5,5-trimethylcyclohex-1-ene (3o)[45]

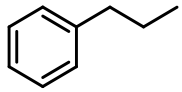
Following general procedure ***GPIV*** using α-Jonon **4o** (194 mg, 1.00 mmol, 1.00 equiv) $^{i}Pr_2NEt$ (680 μL, 4.00 mmol, 4.00 equiv), CH_3CN (10.0 mL, 0.1 M), ethyl 2-chloro-2-oxoacetate (123 μL, 1.10 mmol, 1.10 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 1.00 mol%) and H_2O (36 μL, 2.00 mmol, 2.00 equiv) gave 132 mg (0.74 mmol, 74%) of a colorless oil after filtration through a short plug of flash silica gel (petrol ether / EtOAc 95:5). ^1H NMR (300 MHz, $CDCl_3$): 5.44 – 5.08 (m, 3H), 2.20 – 1.93 (m, 4H), 1.62 – 1.53 (m, 3H), 1.49 – 1.11 (m, 3H), 0.99 – 0.77 (m, 9H).



(*Z*)-prop-1-en-1-ylbenzene (3p)[46]

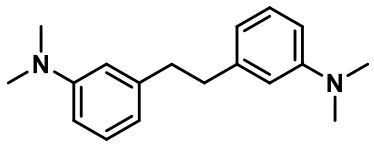
Following general procedure ***GPIV*** using (*E*)-3-phenylprop-2-en-1-ol **4p** (134 mg, 1.00 mmol, 1.00 equiv) $^{i}Pr_2NEt$ (680 μL, 4.00 mmol, 4.00 equiv), CH_3CN (10.0 mL, 0.1 M), ethyl 2-chloro-2-oxoacetate (123 μL, 1.10 mmol, 1.10 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 1.00 mol%) and

H_2O (36.0 μL, 2.00 mmol, 2.00 equiv) gave 86% (cis : trans: allylbenzene 17: 59: 24) GC-FID yield using naphthalene as internal standard (mole ratio 1:1).



Propylbenzene (3h)[39]

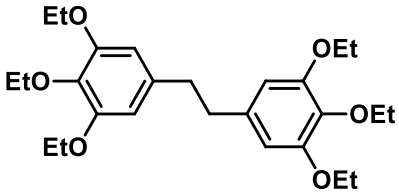
A Schlenk flask equipped with a magnetic stir bar was charged with (*E*)-3-phenylprop-2-en-1-ol **4p** (134 mg, 1.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (680 μL, 4.00 mmol, 4.00 equiv), dissolved in CH_3CN (10.0 mL, 0.1 M) and cooled to 0 °C. Ethyl 2-chloro-2-oxoacetate (123 μL, 1.10 mmol, 1.10 equiv) was added dropwise. The reaction mixture was allowed to warm up to 25 °C. After complete esterification (as judged by TLC), $[Ir(ppy)_2(dtbbpy)](PF_6)$ (9.14 mg, 1.00 mol%) and H_2O (36.0 μL, 2.00 mmol, 2.00 equiv) were added. The Schlenk flask was sealed with a Teflon inlet for a glass rod, through which irradiation with a 455 nm high power LED took place from above while the reaction was magnetically stirred and heated in an aluminum block from below. Afterwards a spatula Pd/C (1 wt%) was added to the reaction mixture and a H_2 balloon was placed on the Schlenk flask overnight gave 62% GC-FID yield using naphthalene as internal standard (mole ratio 1:1).



3,3'-(ethane-1,2-diyl)bis(N,N-dimethylaniline) (3q)

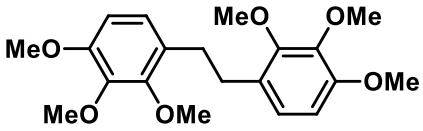
Following general procedure ***GPIV*** using (3-(dimethylamino)phenyl)methanol **4q** (151 mg, 1.00 mmol, 1.00 equiv) $^{i}Pr_2NEt$ (680 μL, 4.00 mmol, 4.00 equiv), 4-DMAP (12.2 mg, 100 μmol, 0.100 equiv), CH_3CN (10.0 mL, 0.1 M), Ethyl 2-chloro-2-oxoacetate (185 μL, 1.60 mmol, 1.60 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 1.00 mol%) and H_2O (36 μL, 2.00 mmol, 2.00 equiv) gave 47 mg (0.35 mmol, 35%) of a dark green oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc, 5:1): 0.26; IR (neat): 2926, 2858, 2802, 1677, 1601, 1497, 1439, 1345, 1227, 1177, 1114, 1061, 995, 847, 773, 695 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 7.24 – 7.16 (m, 2H), 6.70 – 6.61 (m, 6H), 2.96 (s, *J* = 5.7 Hz, 12H), 2.91 (s, 4H); ^{13}C NMR (75 MHz,

$CDCl_3$): 150.73, 143.19, 129.16, 117.34, 113.21, 110.71, 40.99, 38.73; HRMS (EI) m/z calculated for $C_{18}H_{25}N_2$ ($[M+H]^+$) 269.2012, found 269.2015.



1,2-bis(3,4,5-triethoxyphenyl)ethane (3r)

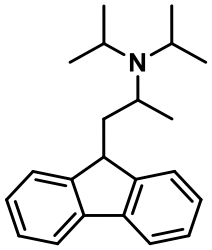
Following general procedure ***GPIV*** using (3,4,5-triethoxyphenyl)methanol **4r** (240 mg, 1.00 mmol, 1.00 equiv) $^{i}Pr_2NEt$ (680 μL, 4.00 mmol, 4.00 equiv), 4-DMAP (12.2 mg, 100 μmol, 0.100 equiv), CH_3CN (10.0 mL, 0.1 M), ethyl 2-chloro-2-oxoacetate (123 μL, 1.10 mmol, 1.10 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 1.00 mol%) and H_2O (36 μL, 2.00 mmol, 2.00 equiv) gave 126 mg (0.56 mmol, 56%) of a white solid after filtration through a short plug of flash silica gel (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc, 5:1): 0.36; m.p. 120 °C; IR (neat): 2974, 2931, 2881, 1585, 1504, 1435, 1389, 1329, 1226, 1096, 1041, 905, 823, 636, 533, 501 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 6.33 (s, *J* = 3.4 Hz, 4H), 4.06 – 3.98 (m, 12H), 2.79 (s, 4H), 1.42 – 1.32 (m, 18H); ^{13}C NMR (101 MHz, $CDCl_3$): 152.72, 136.94, 107.39, 68.76, 64.65, 38.23, 15.62, 15.02; HRMS (EI-MS, APCI) m/z calculated for $C_{26}H_{39}O_6$ ($[M+H]^+$) 447.2741, found 447.2742.



1,2-bis(2,3,4-trimethoxyphenyl)ethane (3s)[47]

Following general procedure ***GPIV*** using (2,3,4-trimethoxyphenyl)methanol **4s** (198 mg, 1.00 mmol, 1.00 equiv) $^{i}Pr_2NEt$ (680 μL, 4.00 mmol, 4.00 equiv), 4-DMAP (12.2 mg, 100 μmol, 0.100 equiv), CH_3CN (10.0 mL, 0.1 M), ethyl 2-chloro-2-oxoacetate (123 μL, 1.10 mmol, 1.10 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 1.00 mol%) and H_2O (36 μL, 2.00 mmol, 2.00 equiv) gave 93 mg (0.51 mmol, 51%) of a white solid after filtration through a short plug of flash silica gel (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc, 5:1): 0.26; ^1H NMR (300 MHz, $CDCl_3$): 6.83 (d, *J* = 8.5 Hz, 2H), 6.60 (d, *J* = 8.5 Hz, 2H), 3.88 (d, *J* = 0.5 Hz, 12H), 3.84 (s, 6H), 2.79 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): 152.17, 152.12, 142.46, 128.39, 124.05, 107.31, 77.48, 77.16, 76.84, 61.06, 60.87,

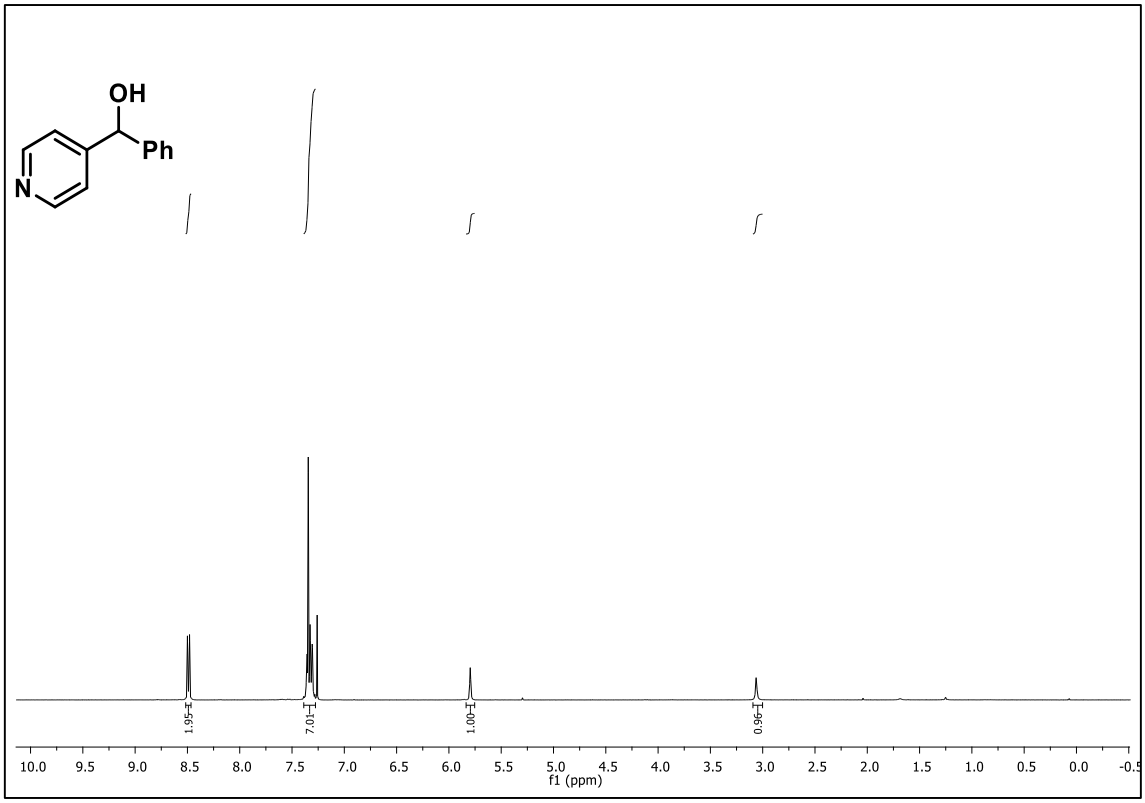
56.18, 31.40; HRMS (EI-MS, MAT95) m/z calculated for $C_{20}H_{26}O_6$ ([M]*) 362.1729, found 362.1732.

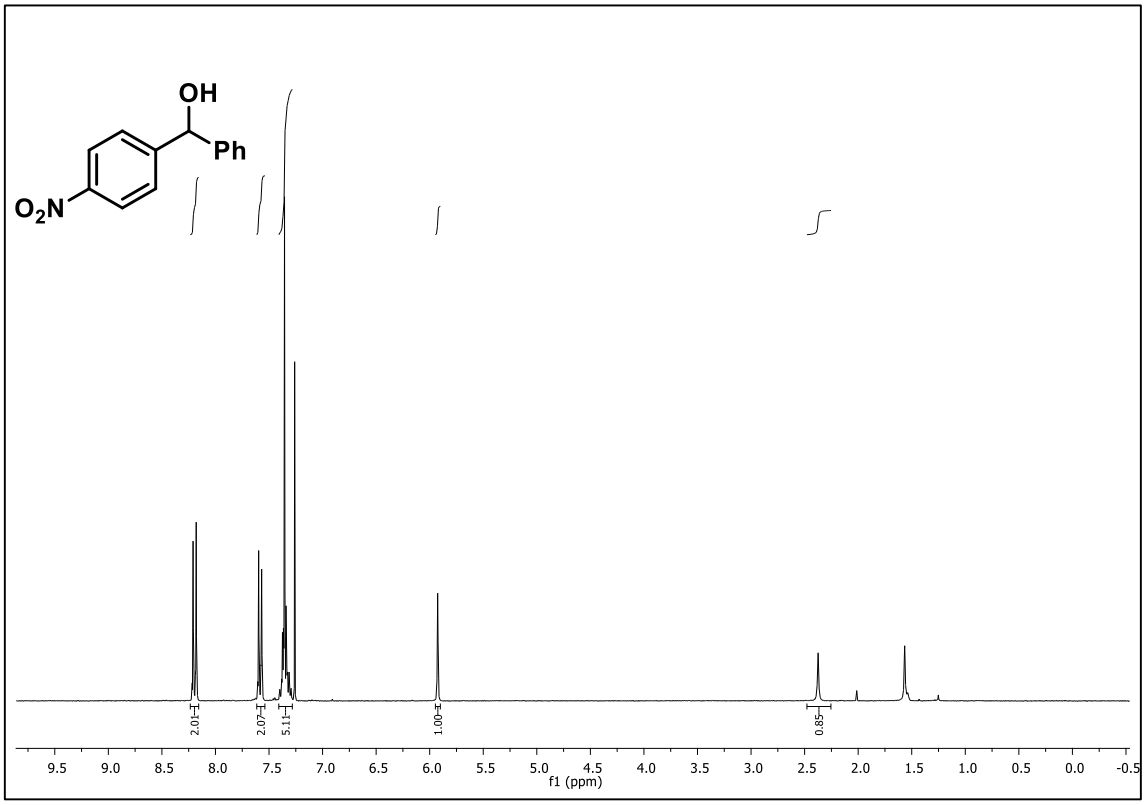


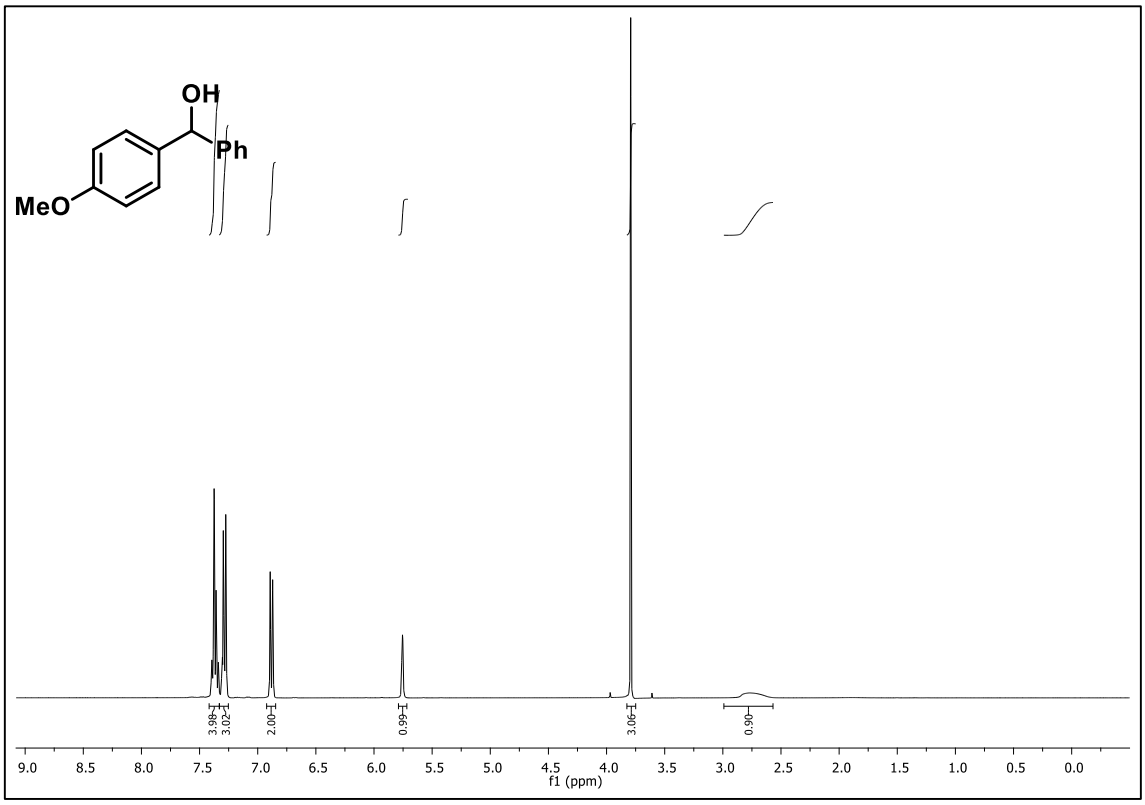
1-(9*H*-fluoren-9-yl)-*N,N*-diisopropylpropan-2-amine (3t)

Following general procedure ***GPIV*** using (3-(dimethylamino)phenyl)methanol **4t** (196 mg, 1.00 mmol, 1.00 equiv) $^{i}Pr_2NEt$ (680 μL, 4.00 mmol, 4.00 equiv), 4-DMAP (12.2 mg, 100 μmol, 0.100 equiv), CH_3CN (10.0 mL, 0.1 M), ethyl 2-chloro-2-oxoacetate (185 μL, 1.60 mmol, 1.60 equiv), $[Ir(ppy)_2(dtb\text{-}bpy)](PF_6)$ (9.14 mg, 1.00 mol%) and H_2O (36 μL, 2.00 mmol, 2.00 equiv) gave 106 mg (0.36 mmol, 36%) of a blue solid after filtration through a short plug of flash silica gel with hexanes. R_f (hexanes / EtOAc, 5:1): 0.68; m.p. 97 °C; IR (neat): 2968, 2929, 1736, 1444, 1392, 1365, 1166, 1134, 1030, 1002, 737, 622, 577, 539, 425 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 7.82 (td, *J* = 6.5, 1.5 Hz, 2H), 7.69 (d, *J* = 7.5 Hz, 1H), 7.59 – 7.49 (m, 1H), 7.45 – 7.36 (m, 4H), 4.27 (dd, *J* = 8.2, 3.7 Hz, 1H), 3.57 – 3.46 (m, 1H), 3.37 (hept, *J* = 6.7 Hz, 2H), 2.14 (ddd, *J* = 12.1, 7.9, 3.1 Hz, 1H), 1.74 – 1.62 (m, 1H), 1.24 – 1.15 (m, 15H); ^{13}C NMR (101 MHz, $CDCl_3$): 149.60, 149.53, 140.96, 140.80, 127.02, 126.96, 126.72, 126.67, 124.29, 124.22, 119.94, 119.81, 48.44, 44.93, 44.36, 41.20, 24.59, 22.54, 21.46; ^{13}C NMR (DEPT-135, 101 MHz, $CDCl_3$): 126.96, 126.90, 126.66, 126.61, 124.24, 124.17, 119.88, 119.76, 48.39, 44.86, 44.30, 41.14, 24.53, 22.49, 21.41; HRMS (EI-MS, MAT95) m/z calculated for $C_{22}H_{29}N$ ([M]*) 307.2300, found 307.2298.

3.8.7 Spectra of compounds



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Ph
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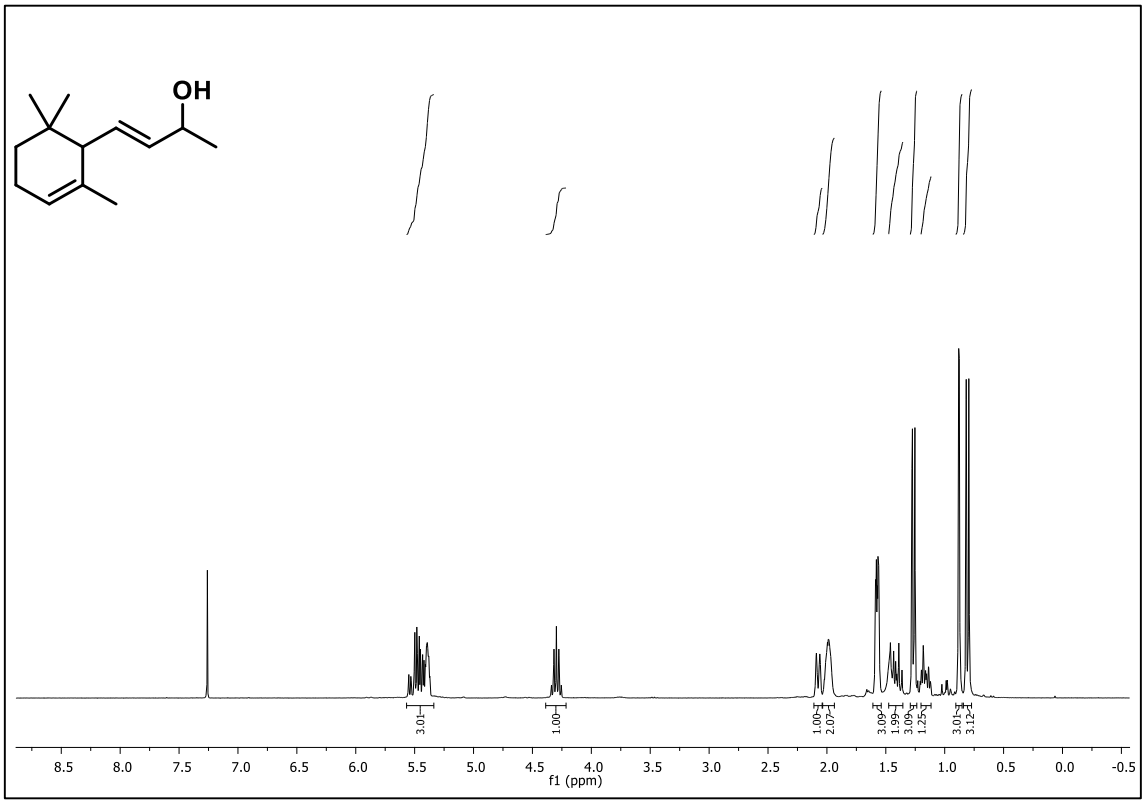
3.02
2.00
0.99
3.06
0.90
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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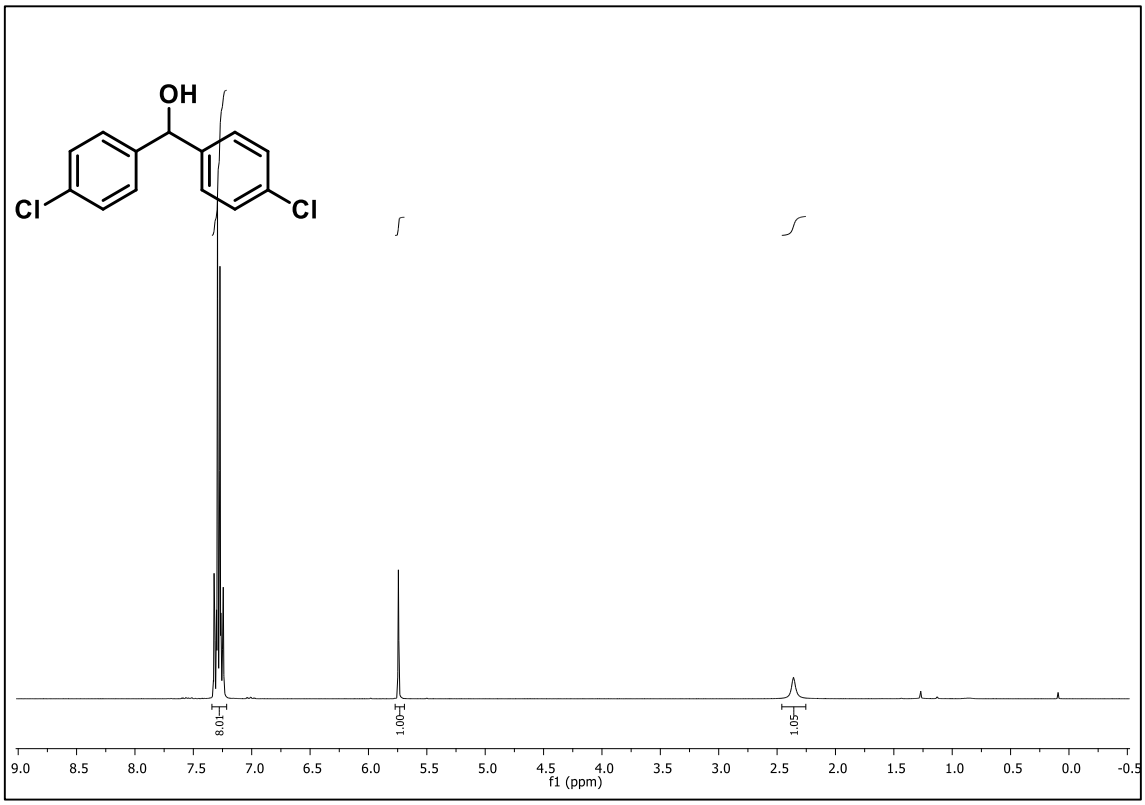
1.00
1.00
2.07
3.09
1.09
3.09
1.25
3.01
3.12
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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Cl
Cl
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1.05
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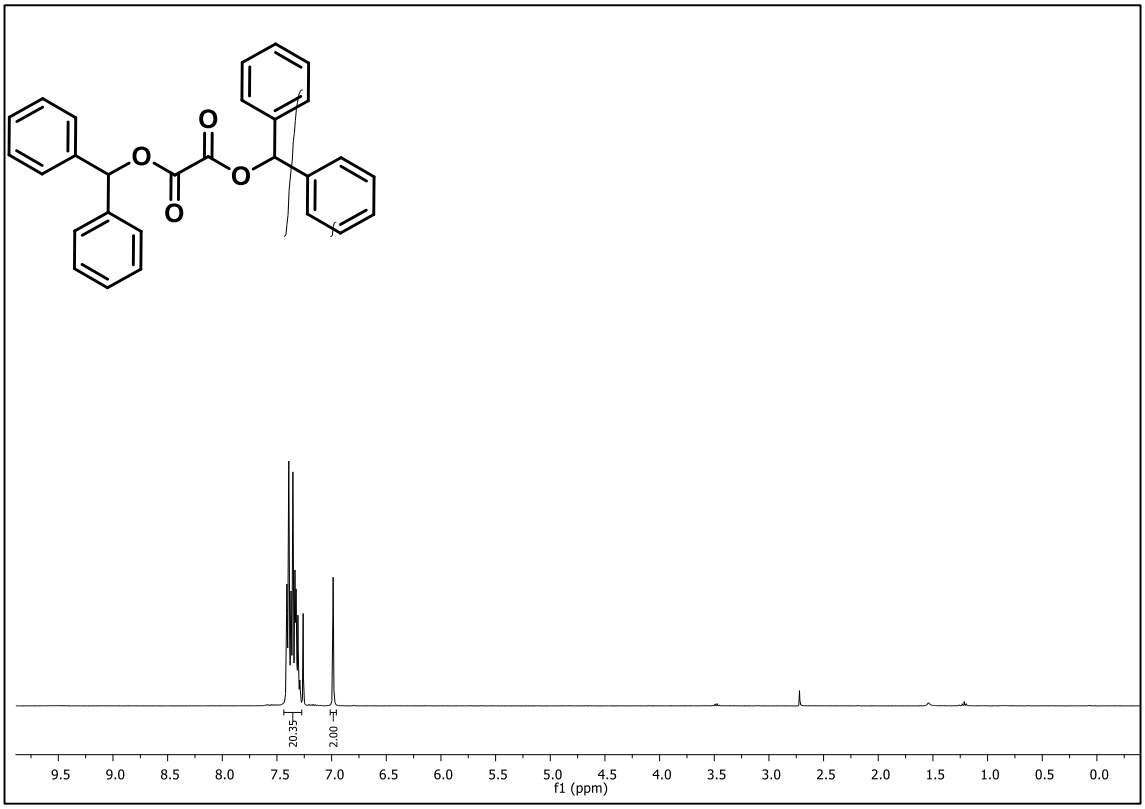
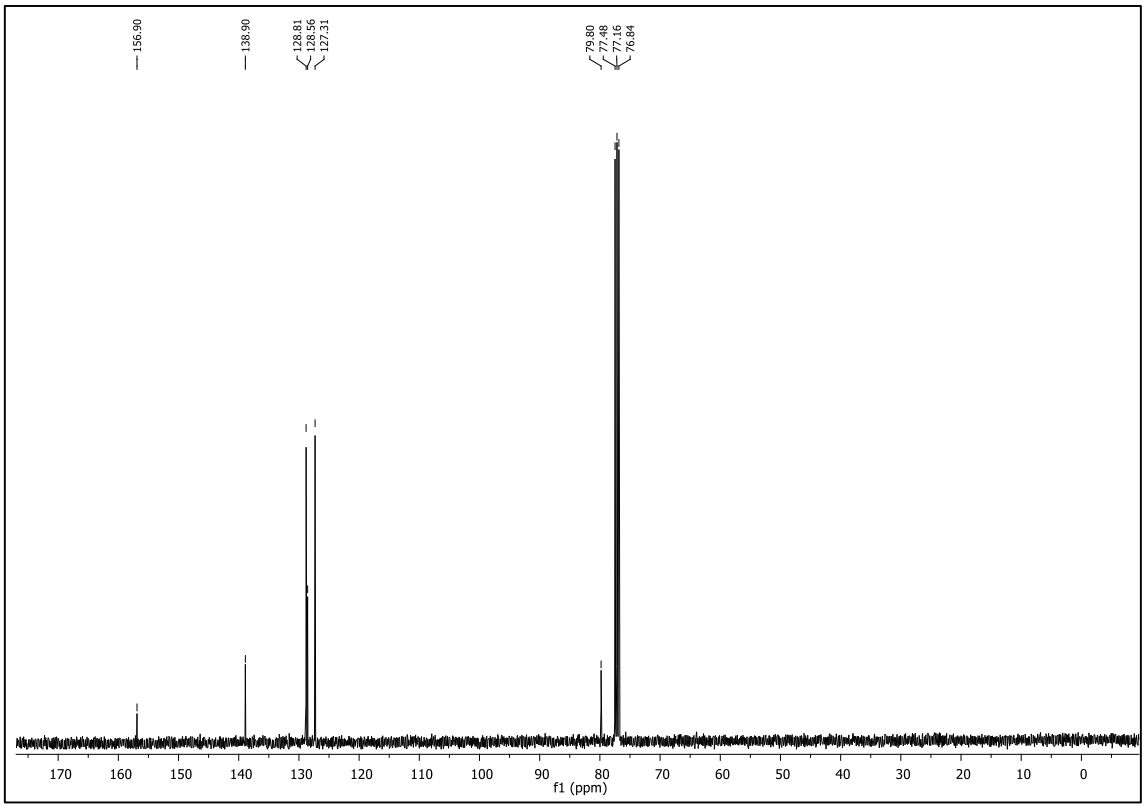
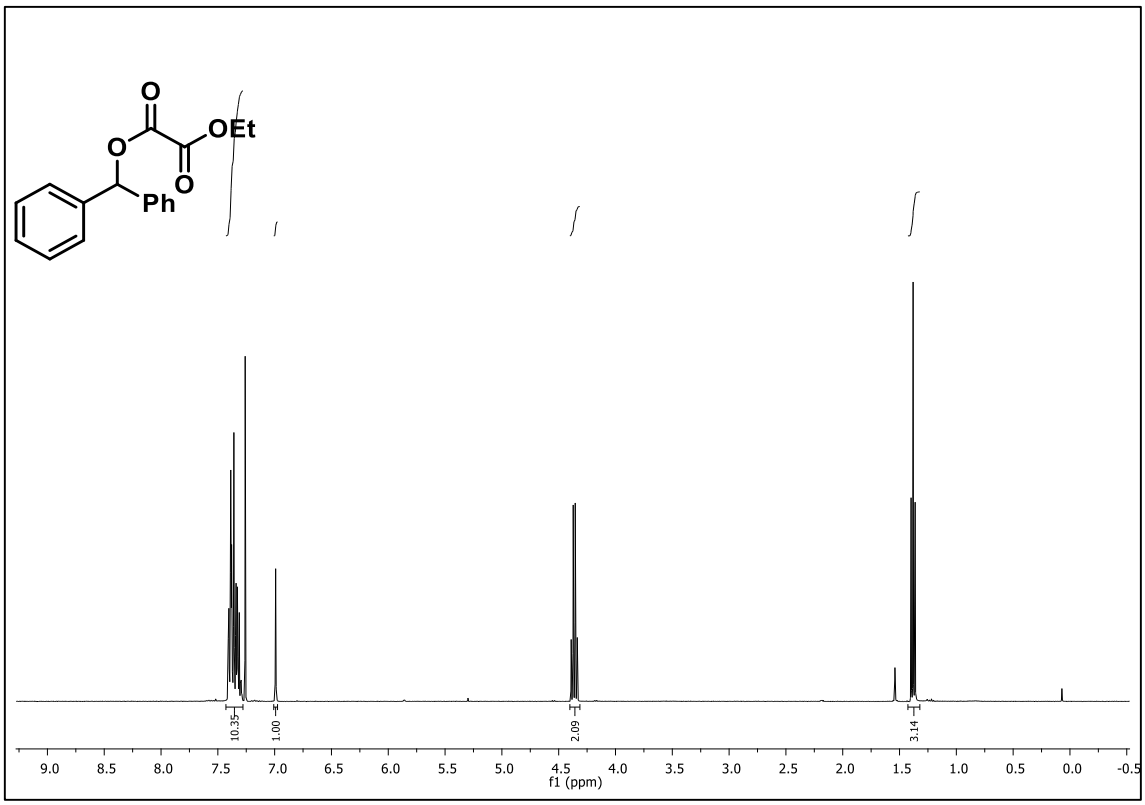
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


O
O
O
O
20.35
2.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


156.90
138.90
128.81
128.56
127.31
79.80
77.48
77.16
76.84
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
O
OEt
O
Ph
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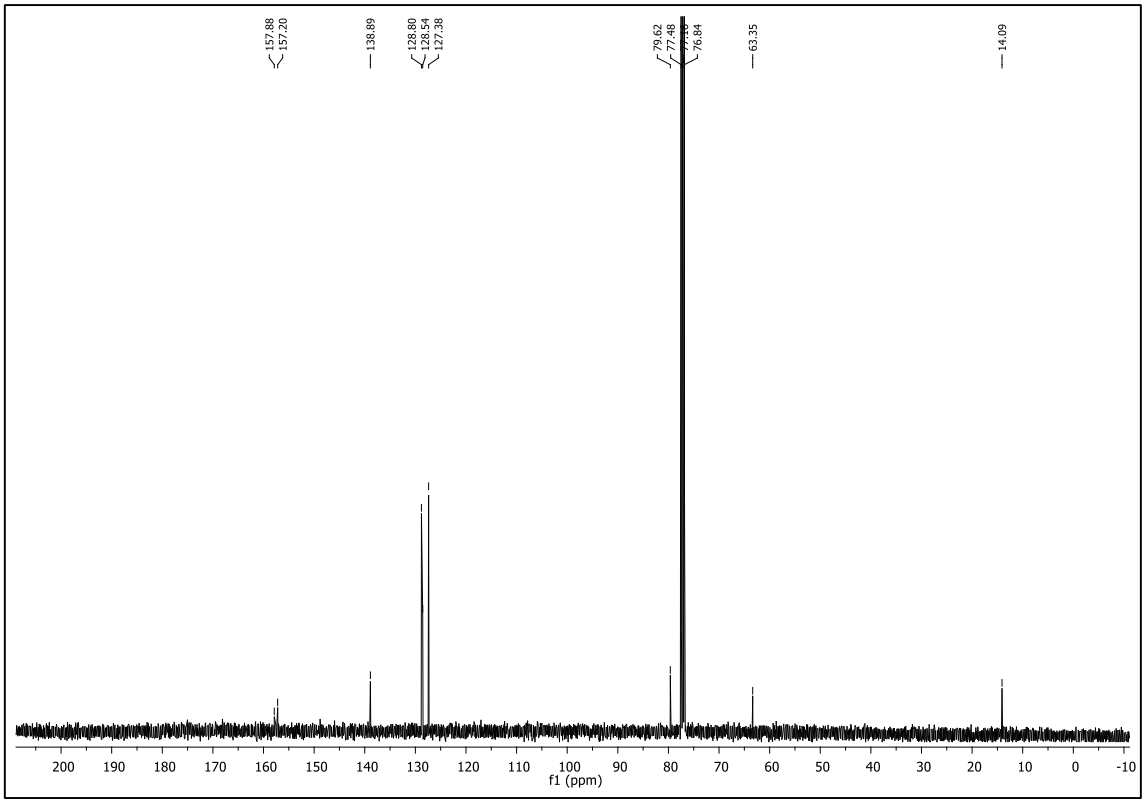
1.00
2.09
3.14
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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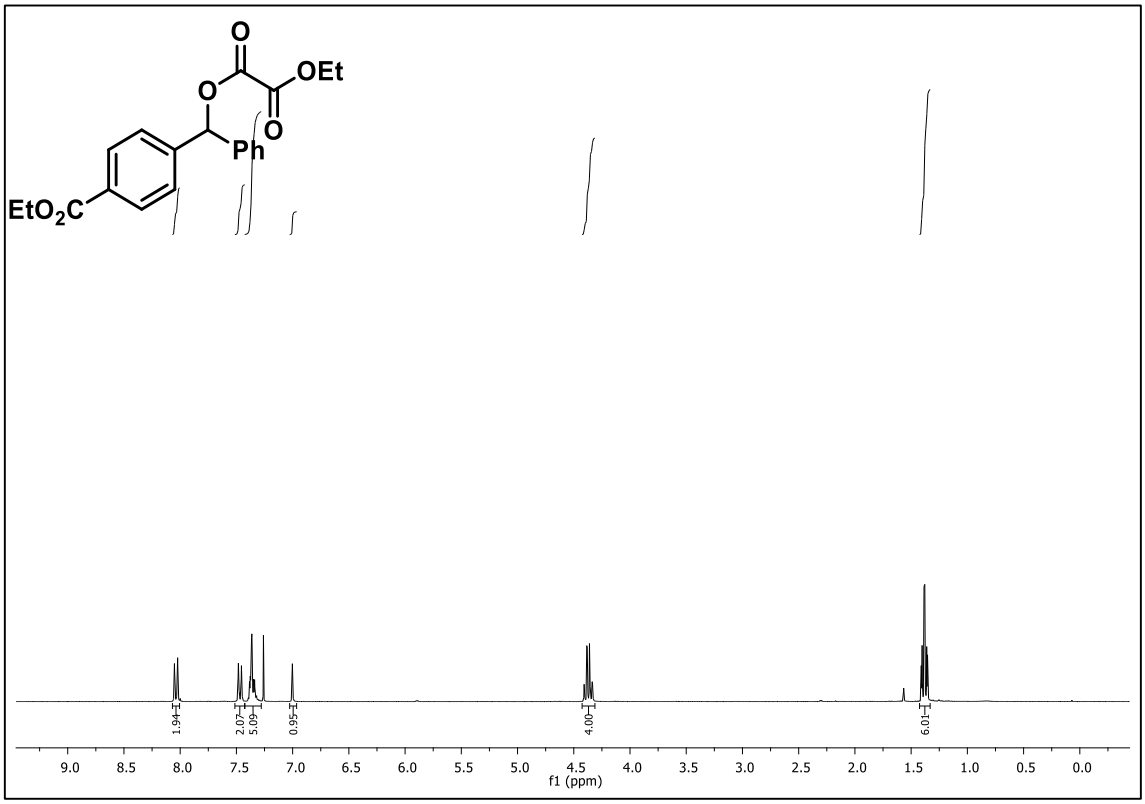
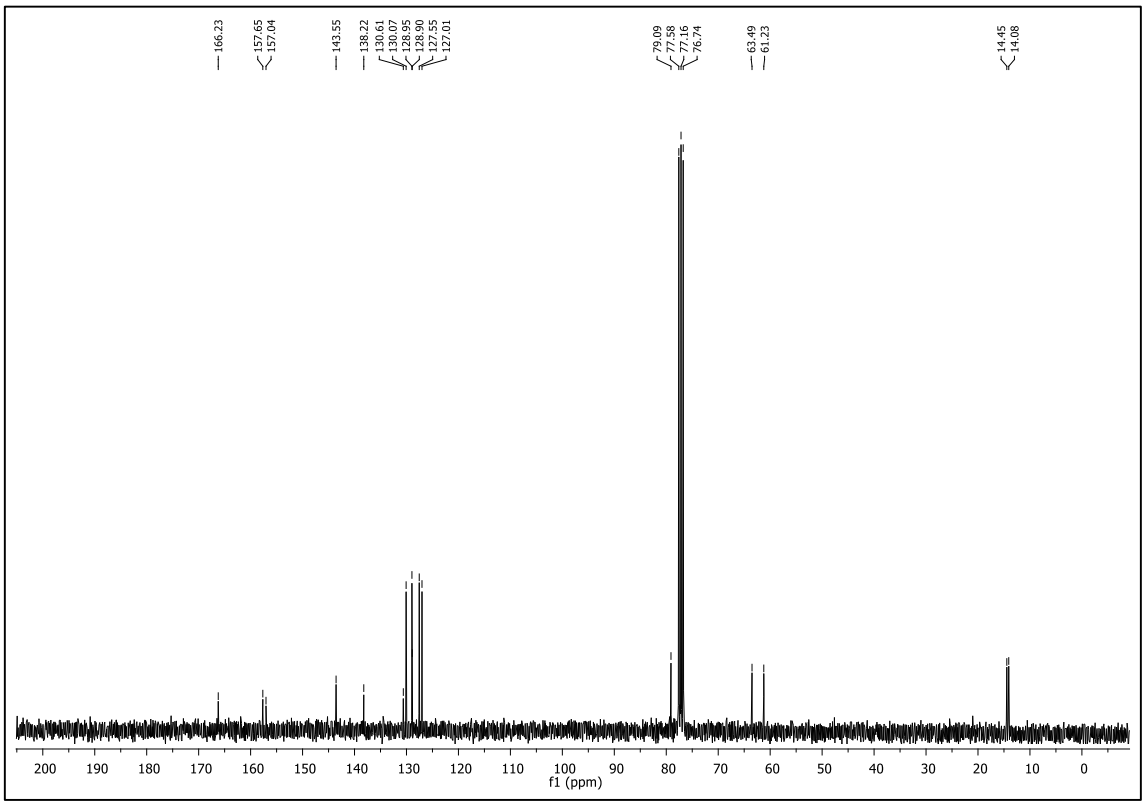
157.20
138.89
128.80
128.54
127.38
79.62
77.48
76.84
63.35
14.09
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OEt
O
O
Ph
EtO2C
1.94
2.07
5.09
0.95
4.00
6.01
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)


166.23
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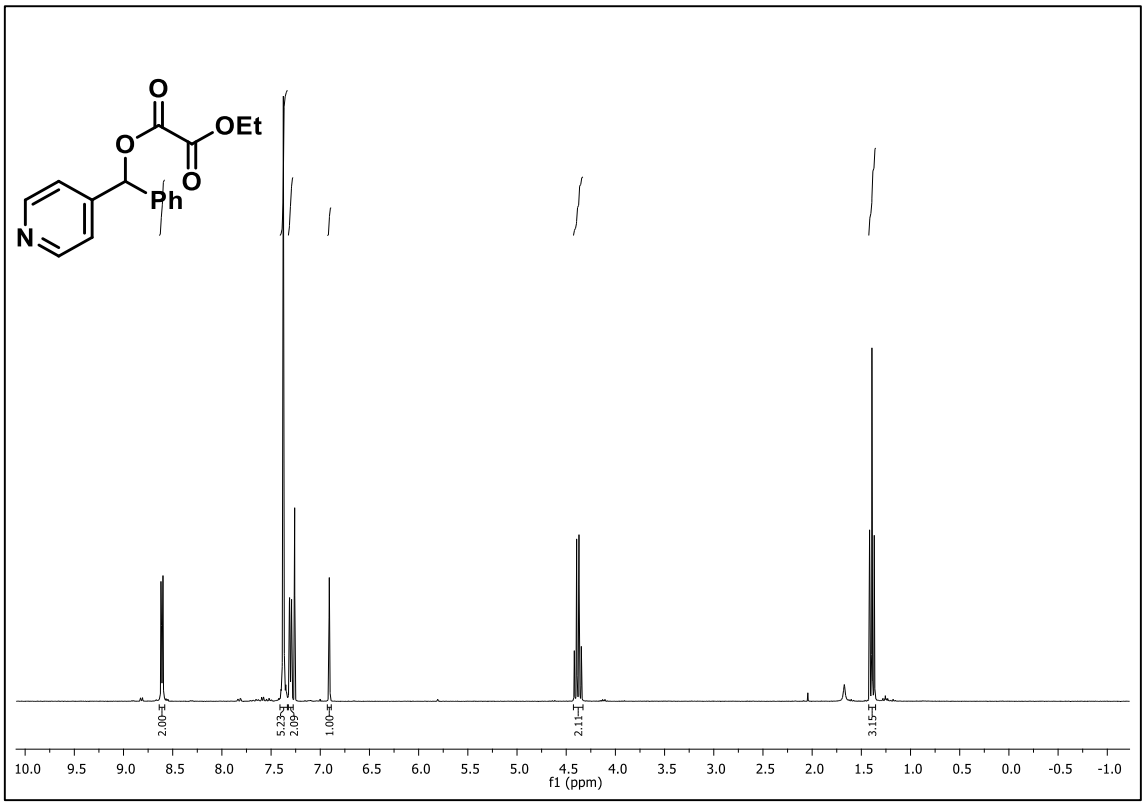
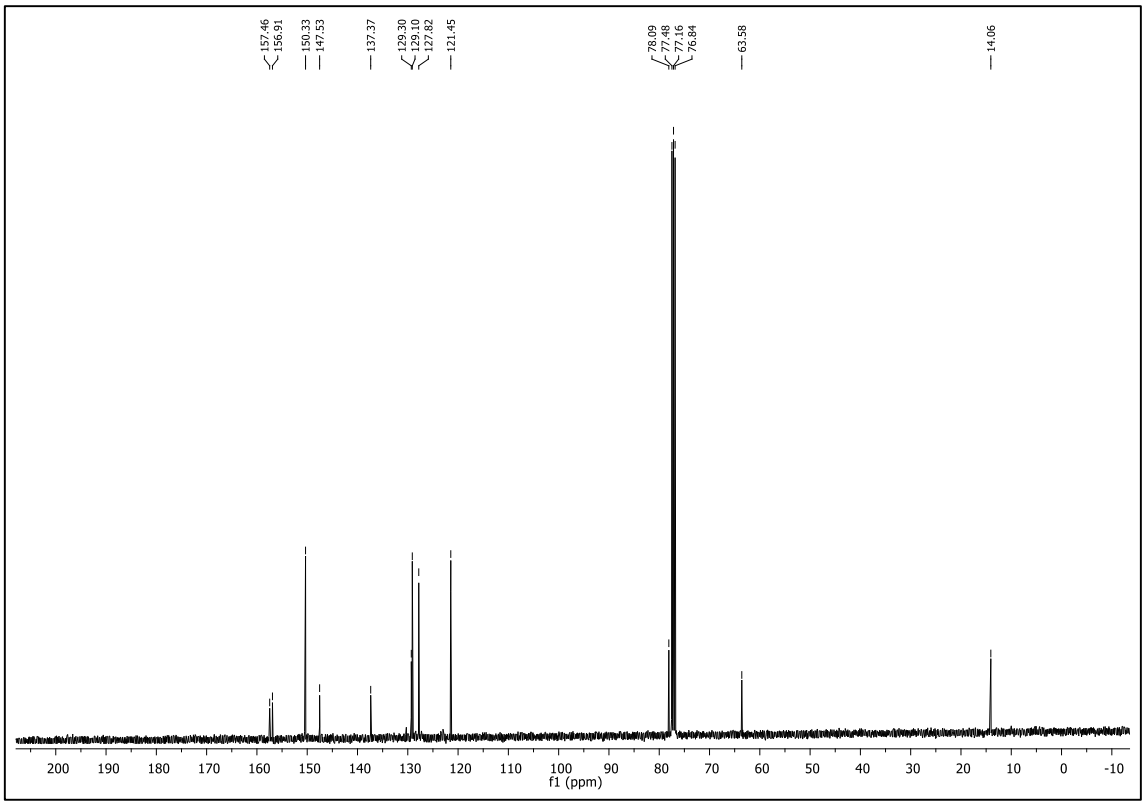
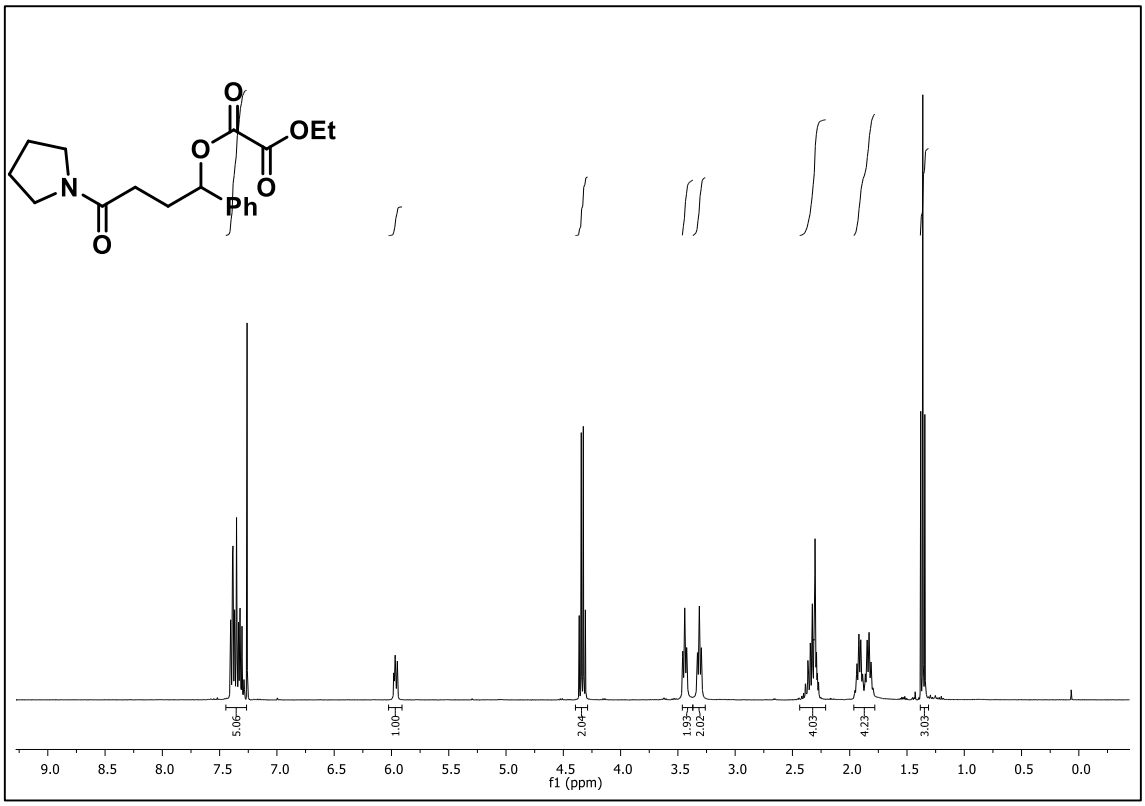
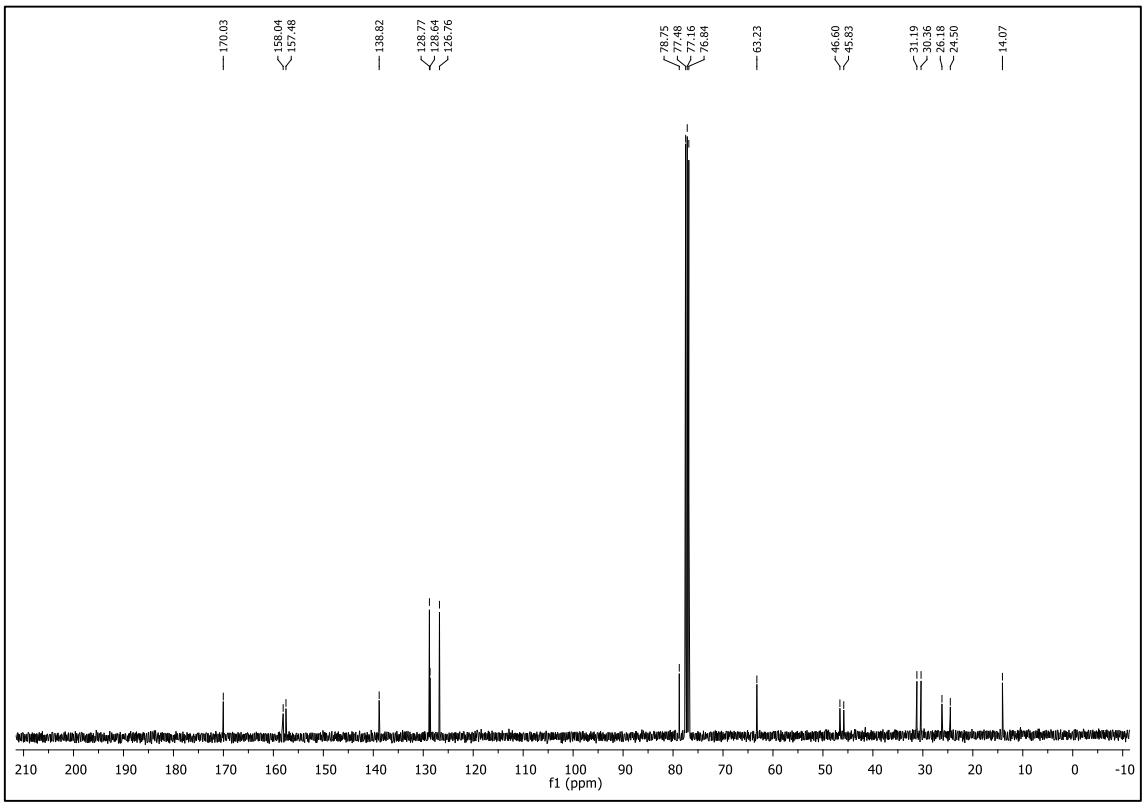
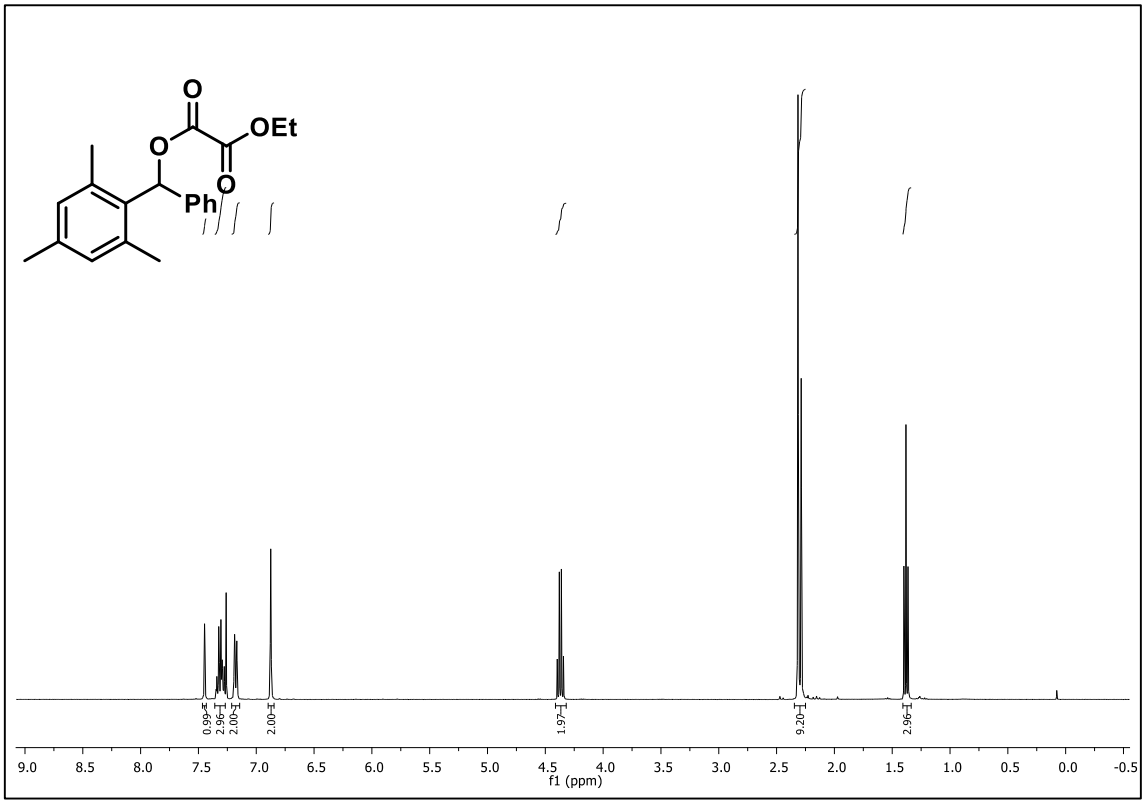
157.04
143.55
138.22
130.61
130.07
128.95
128.90
127.55
127.01
79.09
77.58
77.16
76.74
63.49
61.23
14.45
14.08
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

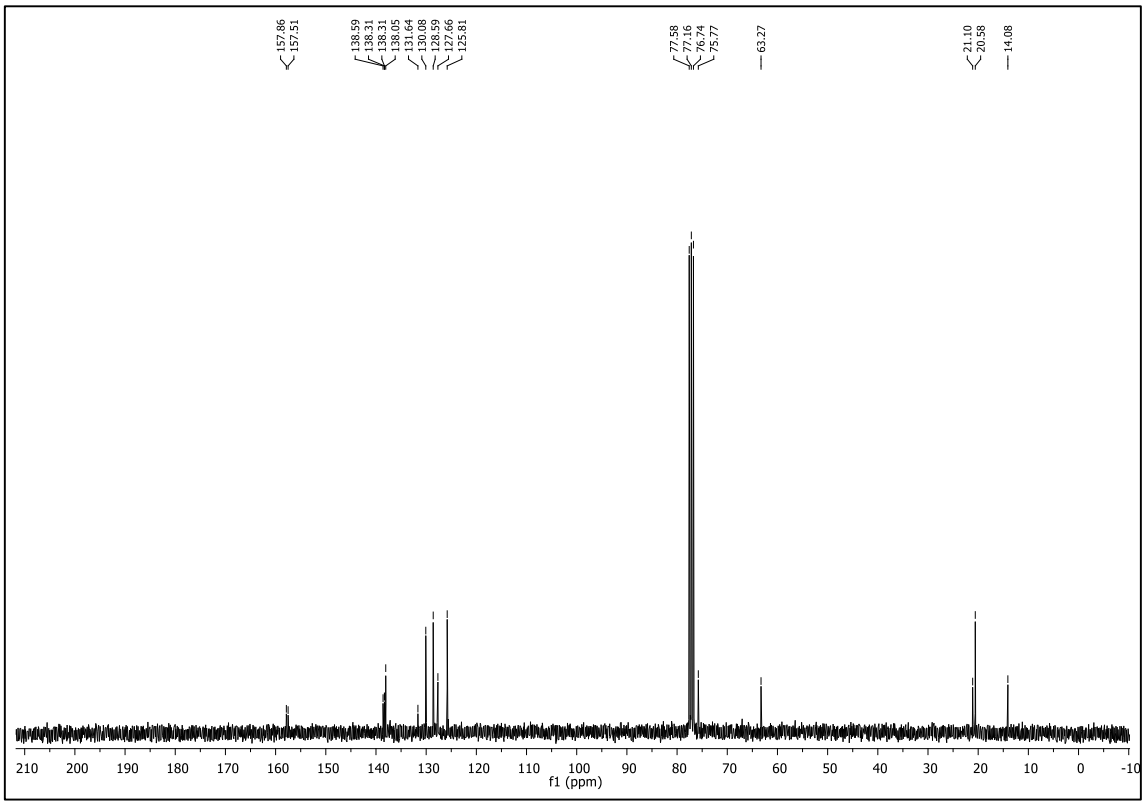

O
OEt
O
O
Ph
N
2.00
5.23
2.09
1.00
2.11
3.15
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

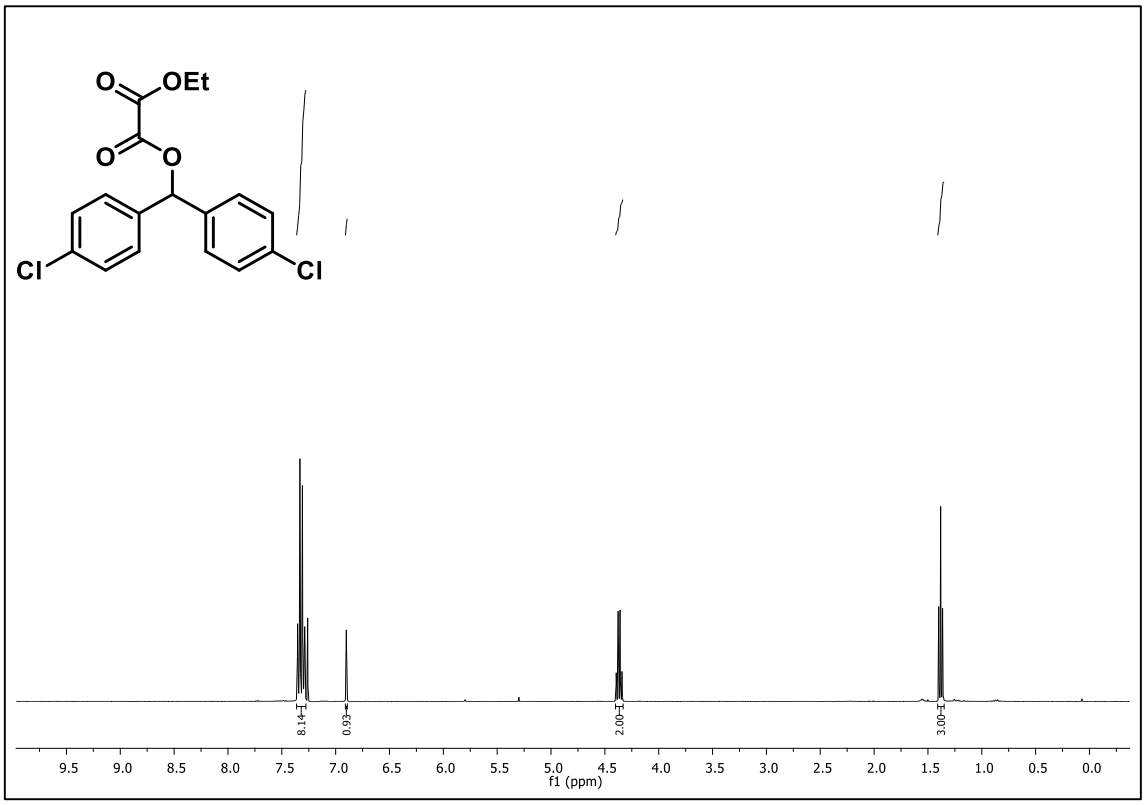

157.46
156.91
150.33
147.53
137.37
129.30
129.10
127.82
121.45
78.09
77.48
77.16
76.84
63.58
14.06
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

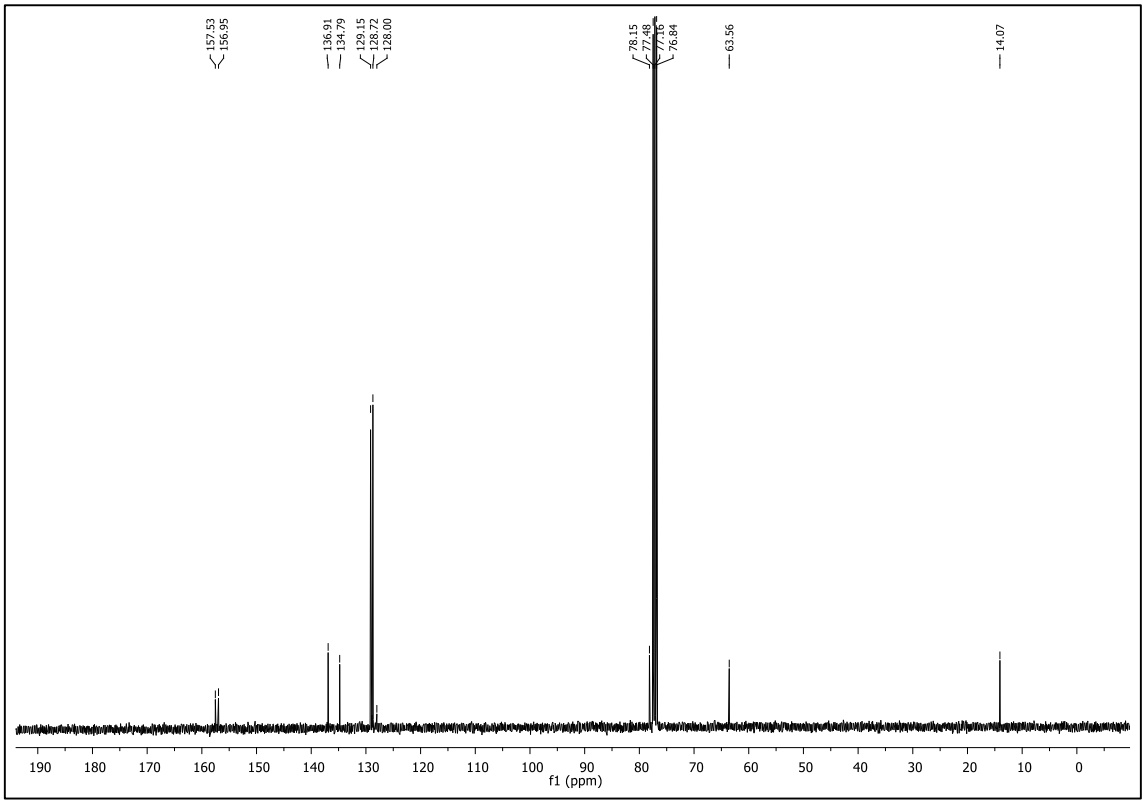

O
OEt
O
O
N
Ph
O
5.06
1.00
2.04
1.93
2.02
4.03
4.23
3.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

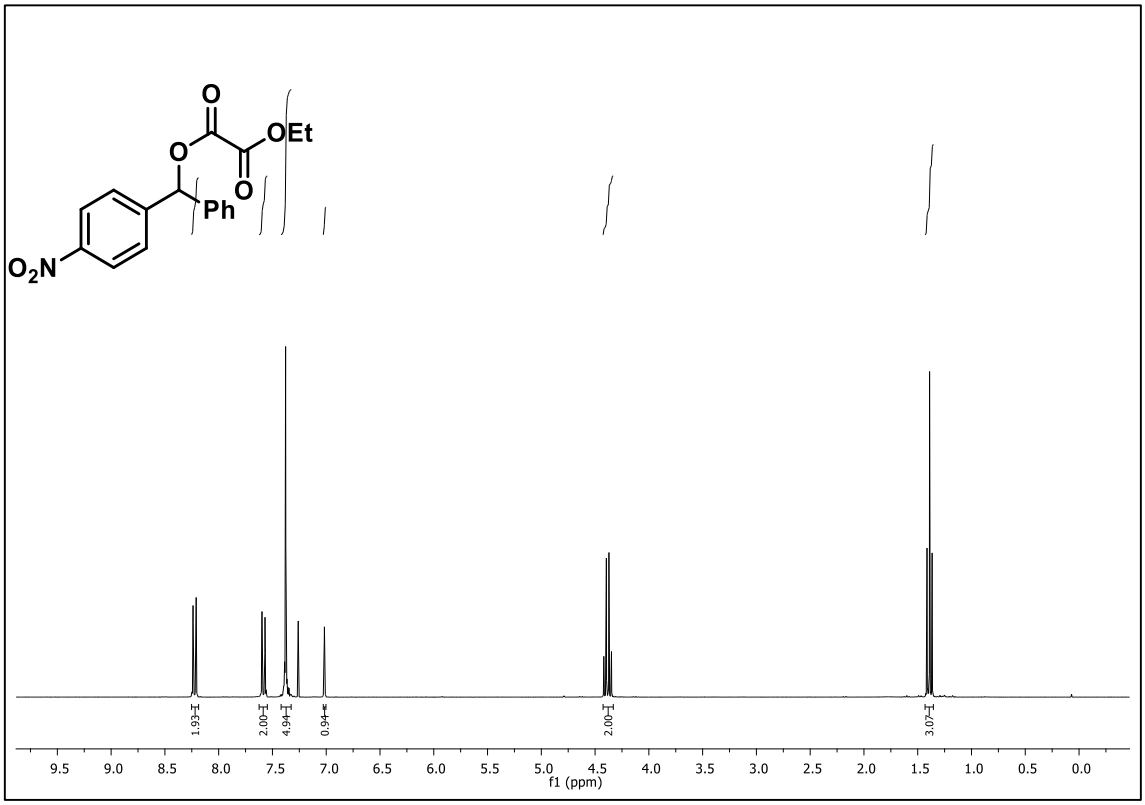

170.03
158.04
157.48
138.82
128.77
128.64
126.76
78.75
77.48
77.16
76.84
63.23
46.60
45.83
31.19
30.36
26.18
24.50
14.07
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

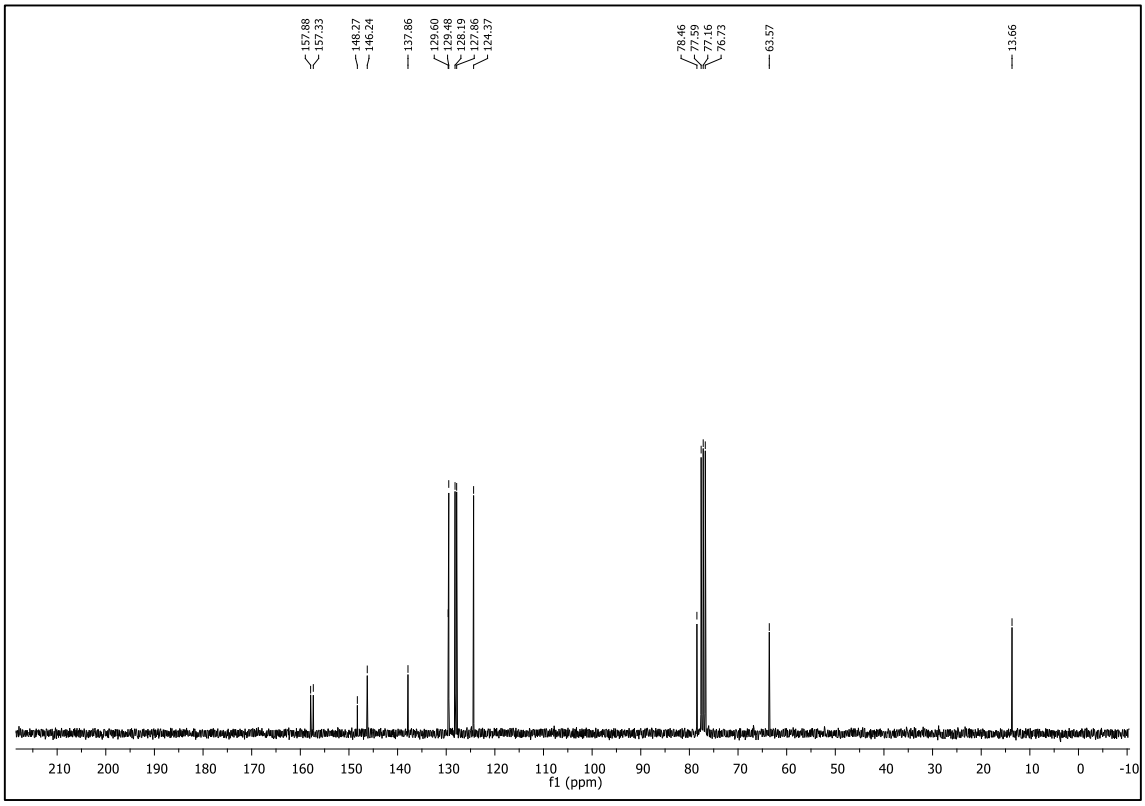

O
OEt
O
O
Ph
0.99
2.96
2.00
2.00
1.97
9.20
2.96
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

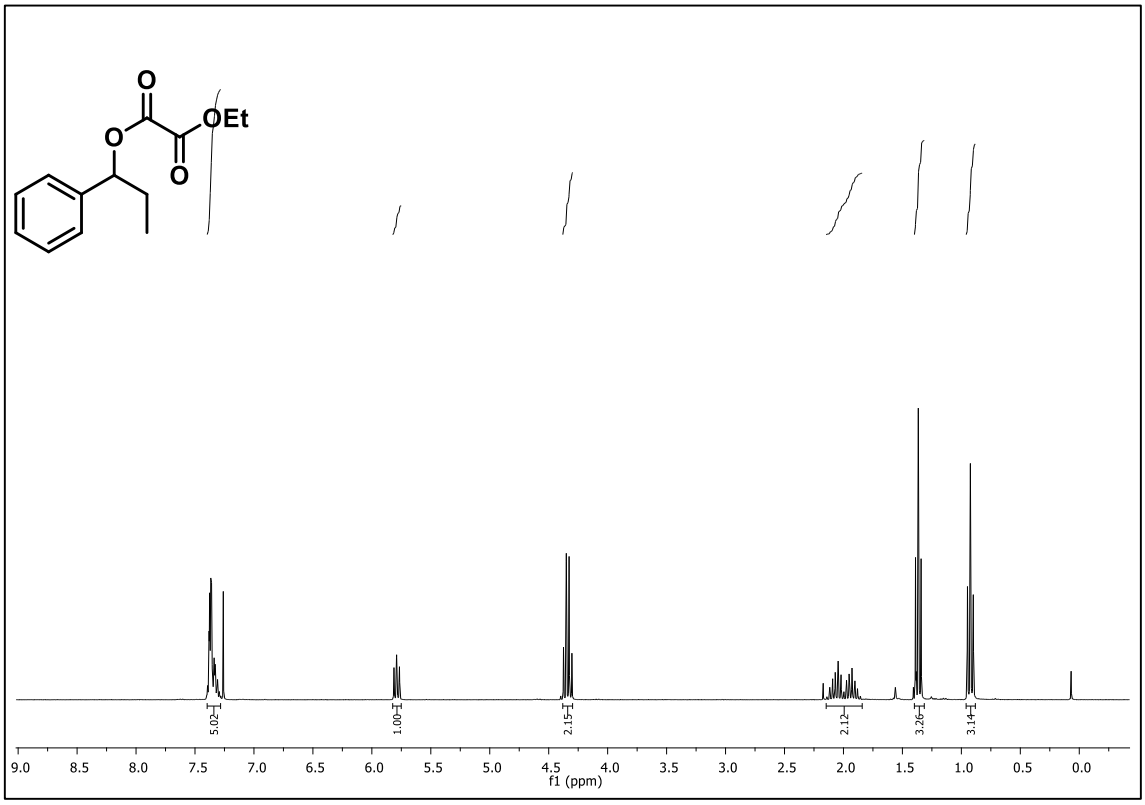

157.86
157.51
138.59
138.31
138.31
138.05
131.64
130.08
128.59
127.66
125.81
77.58
77.16
76.74
75.77
63.27
21.10
20.58
14.08
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

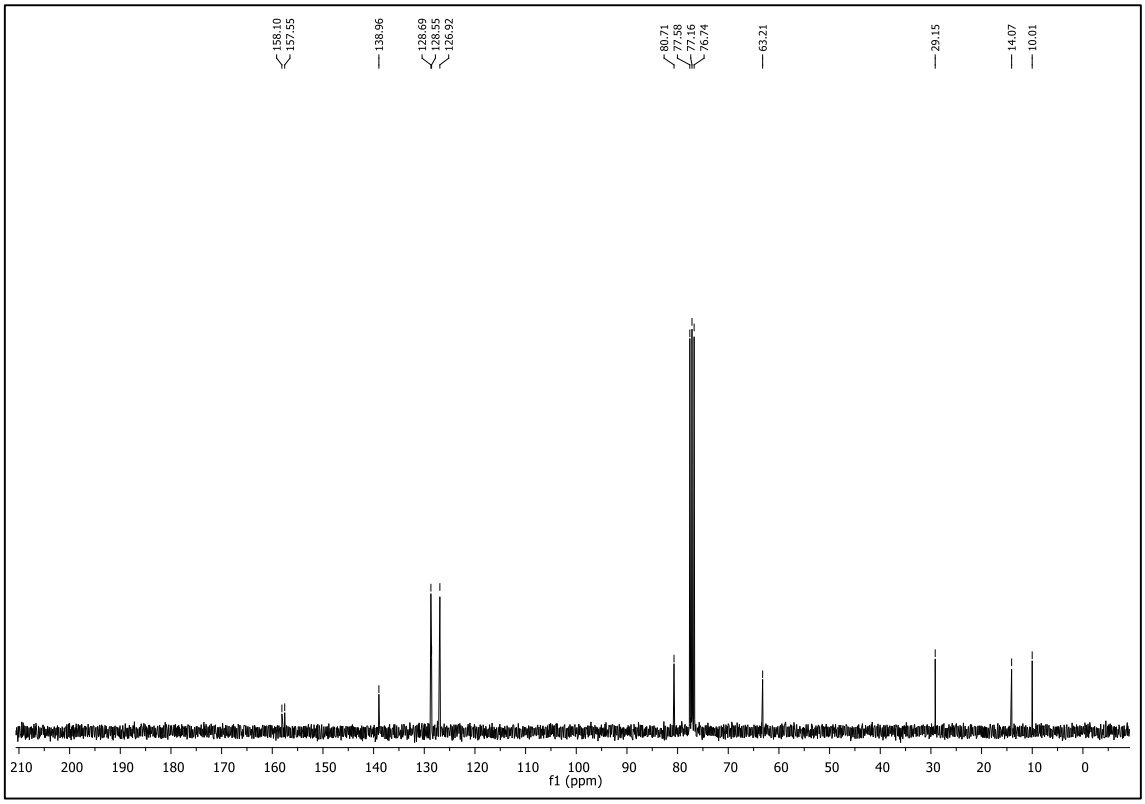

O
OEt
O
O
Cl
Cl
8.14
0.93
2.00
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

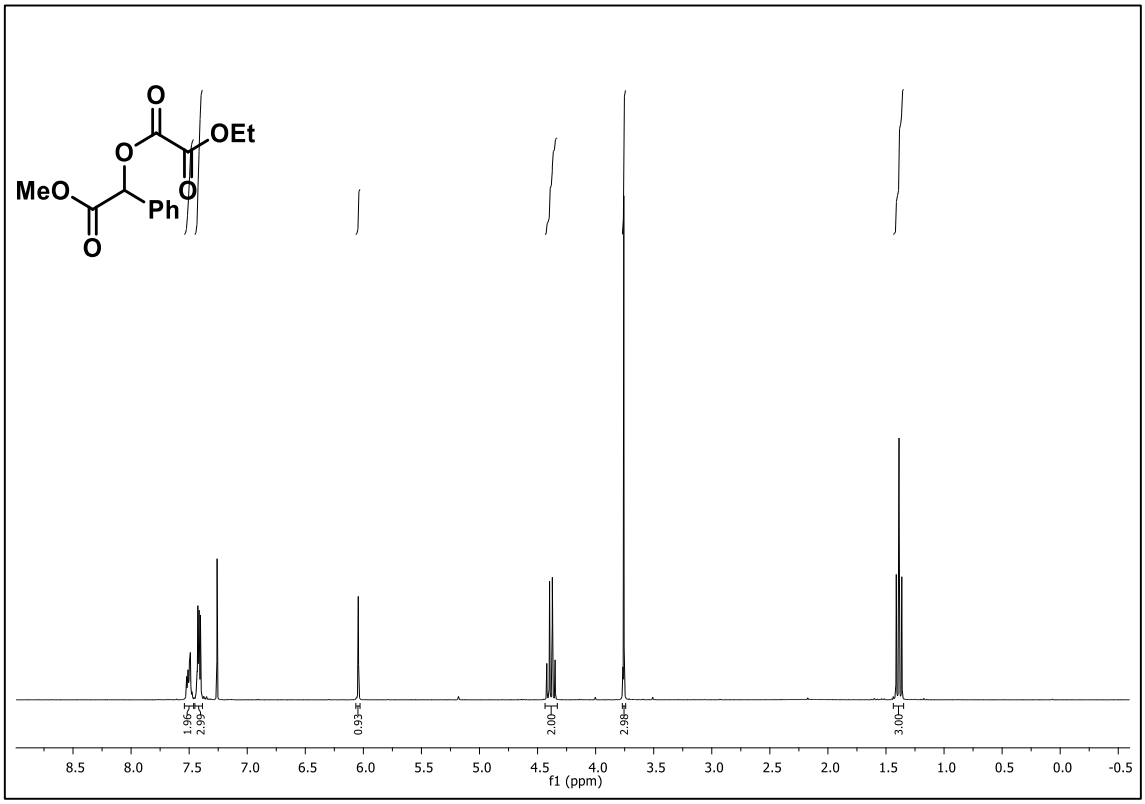

157.53
156.95
136.91
134.79
129.15
128.72
128.00
78.15
77.48
77.16
76.84
63.56
14.07
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

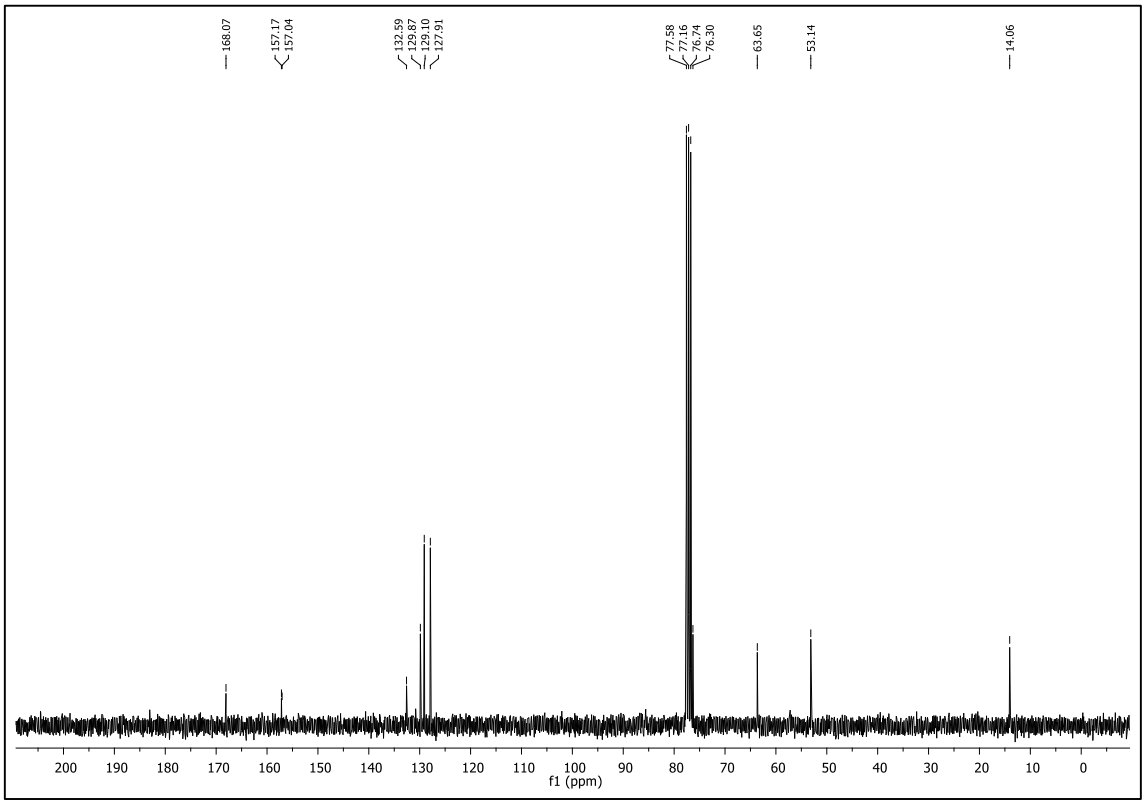

O
OEt
O
O
Ph
O2N
1.93
2.00
4.94
0.94
2.00
3.07
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

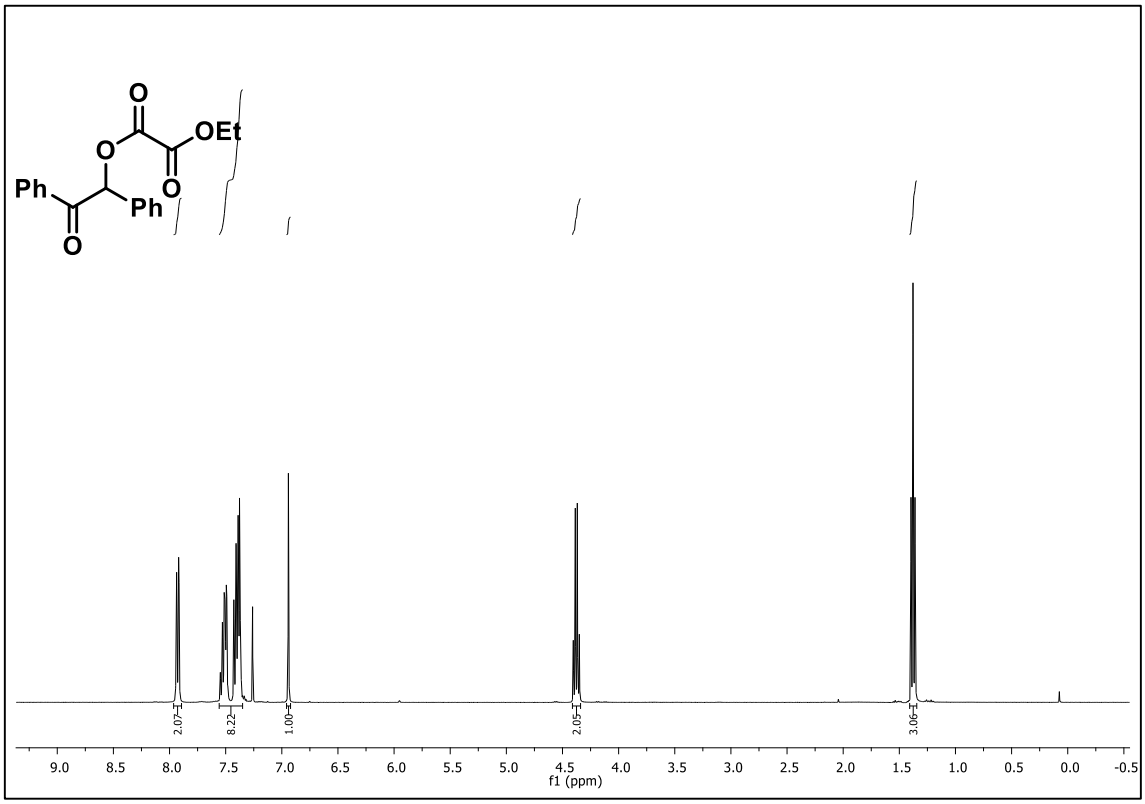

157.88
157.33
148.27
146.24
137.86
129.60
129.48
128.93
127.86
124.37
78.46
77.59
77.16
76.73
63.57
13.66
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

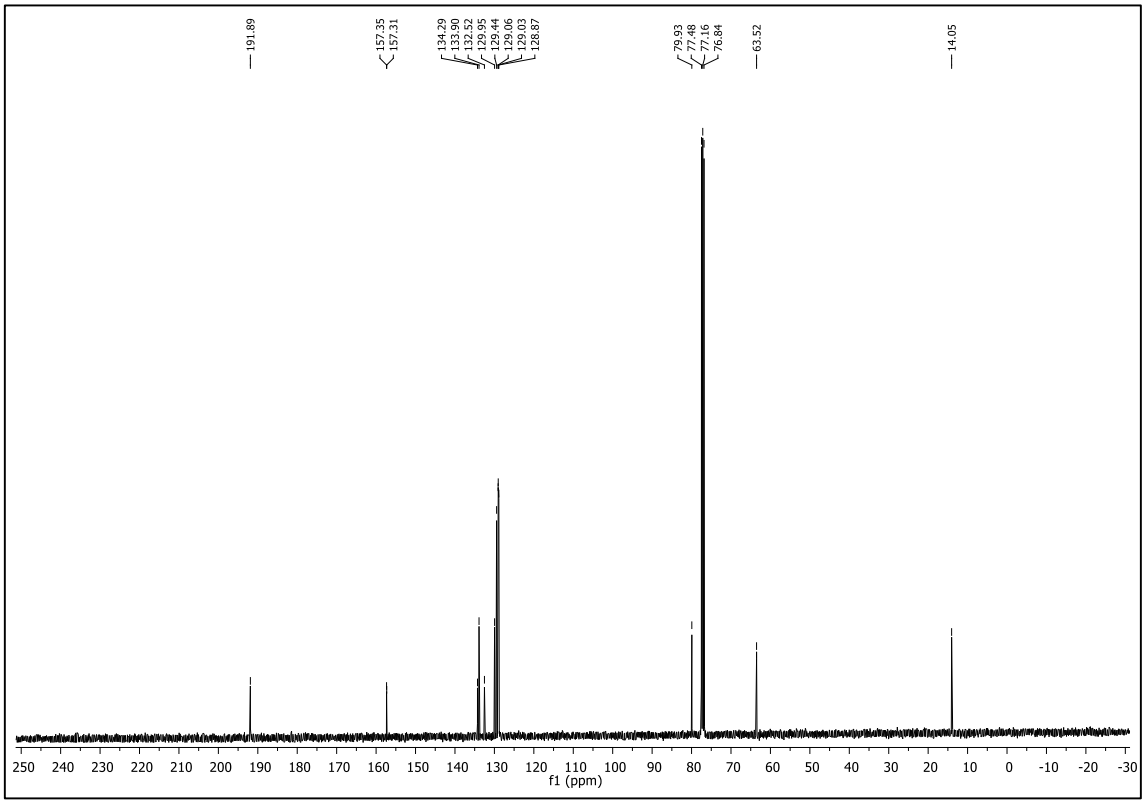

O
O
OEt
O
5.02
1.00
2.15
2.12
3.26
3.14
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

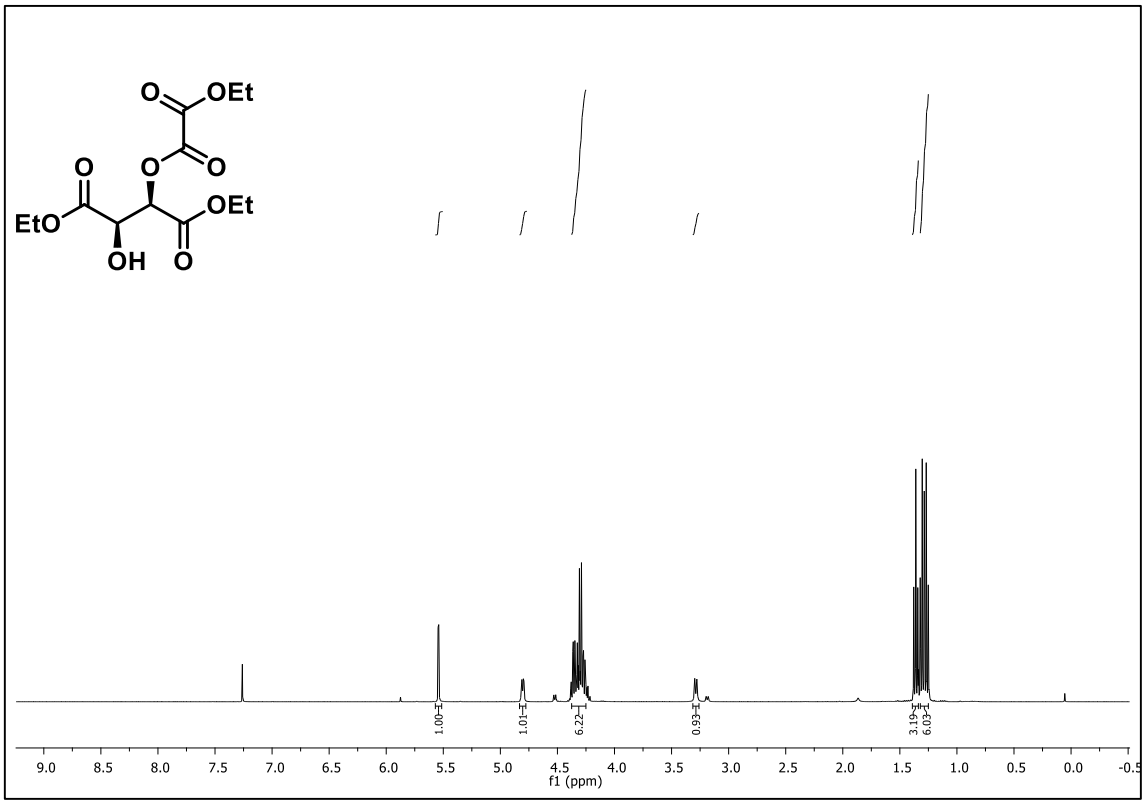

158.10
157.55
138.96
128.69
128.55
126.92
80.71
77.58
77.16
76.74
63.21
29.15
14.07
10.01
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

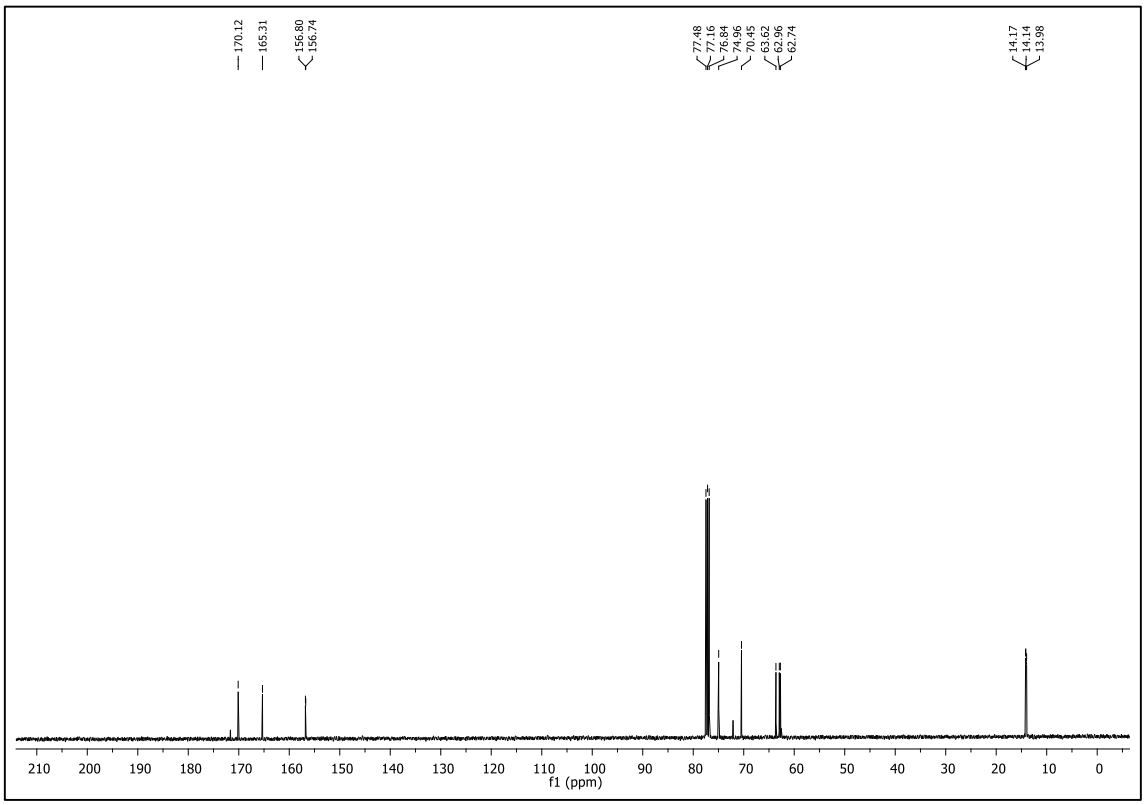

O
OEt
O
MeO
Ph
O
O
1.96
2.99
0.93
2.00
2.98
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

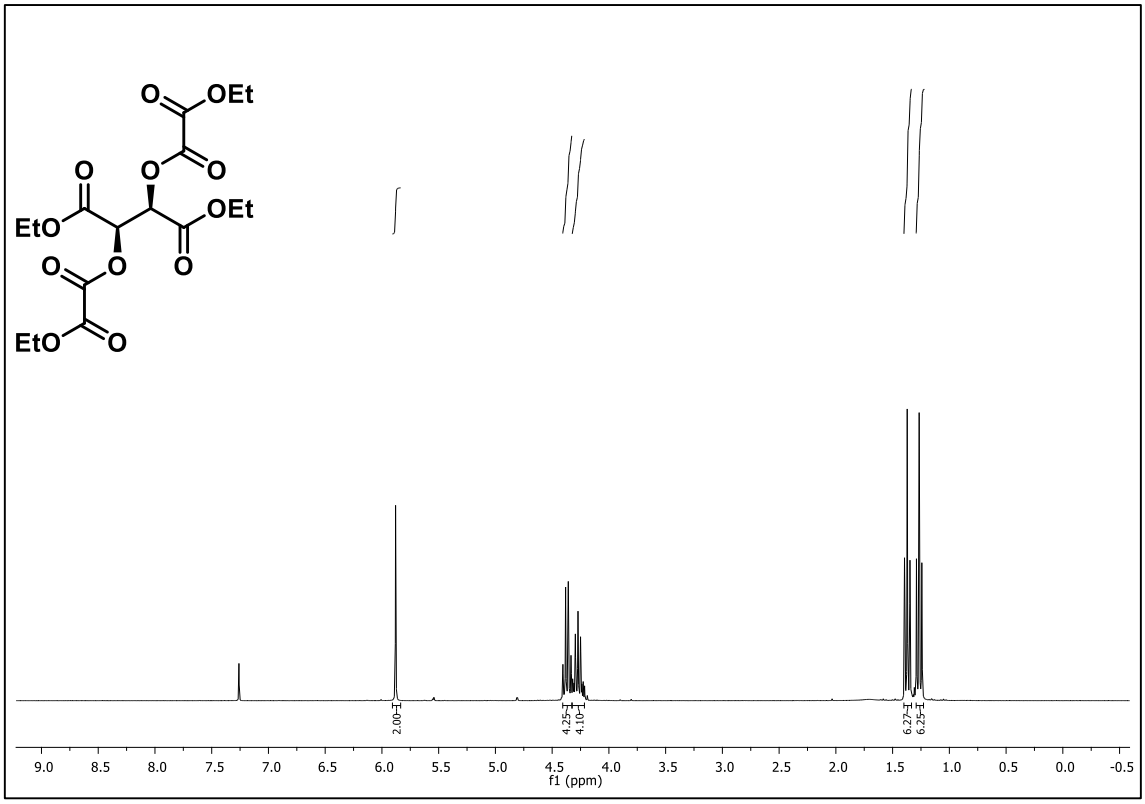

168.07
157.17
157.04
132.59
129.87
129.10
127.91
77.58
77.16
76.74
76.30
63.65
53.14
14.06
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

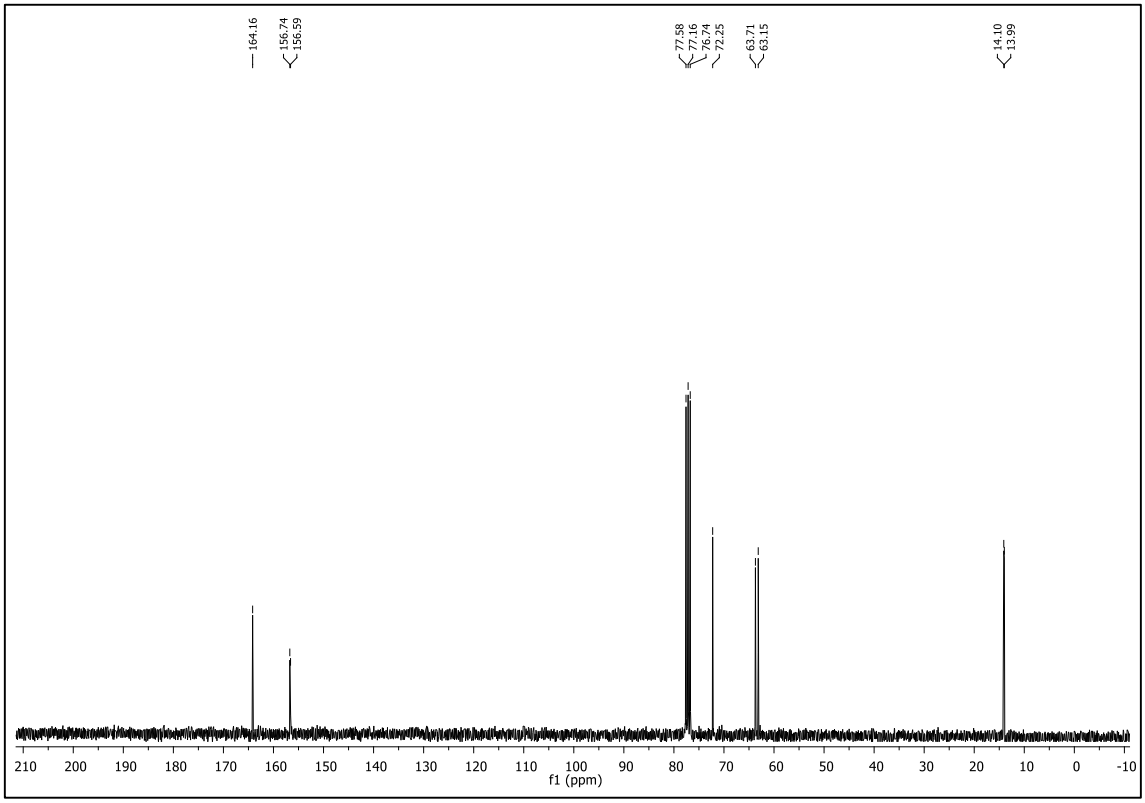

O
OEt
O
O
Ph
Ph
O
2.07
8.22
1.00
2.05
3.06
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

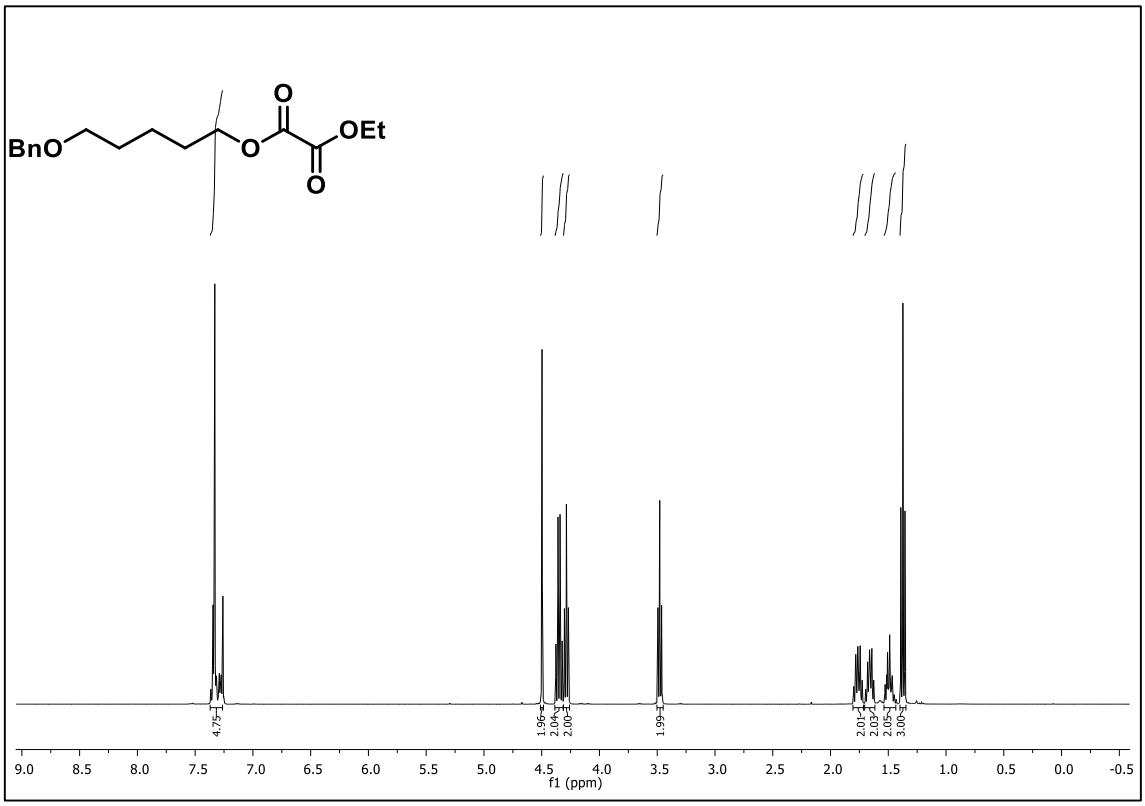

191.89
157.35
157.31
134.29
133.90
132.52
129.95
129.44
129.06
129.03
128.87
79.93
77.48
77.16
76.84
63.52
14.05
250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

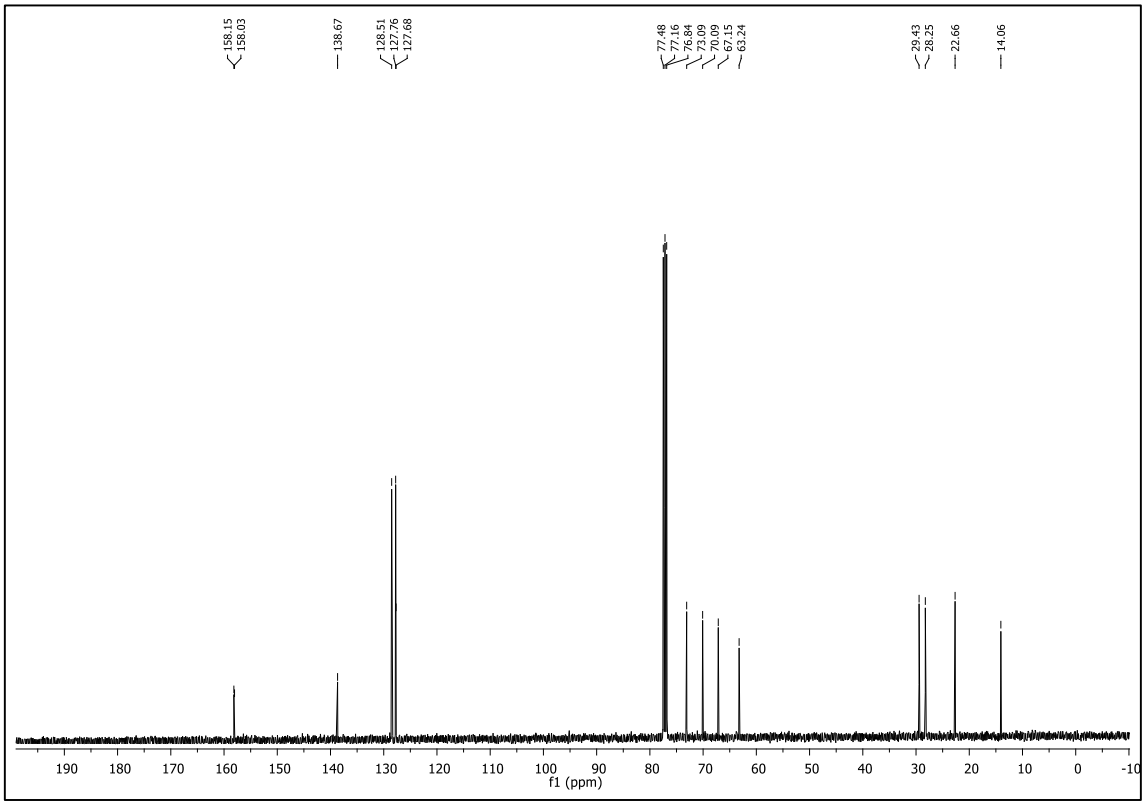

OEt
O
O
O
O
EtO
OEt
OH
O
1.00
1.01
6.22
0.93
3.19
6.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

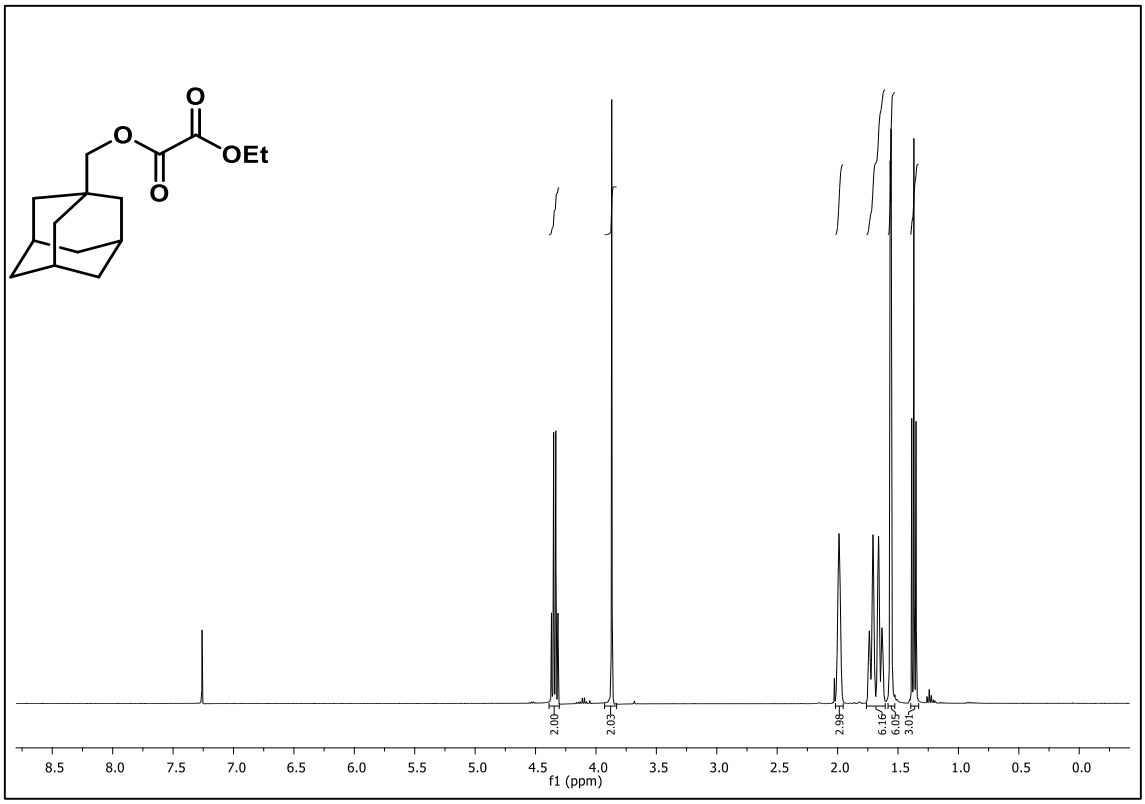

170.12
165.31
156.80
156.74
77.48
77.16
76.84
74.96
70.45
63.62
62.96
62.74
14.17
14.14
13.98
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

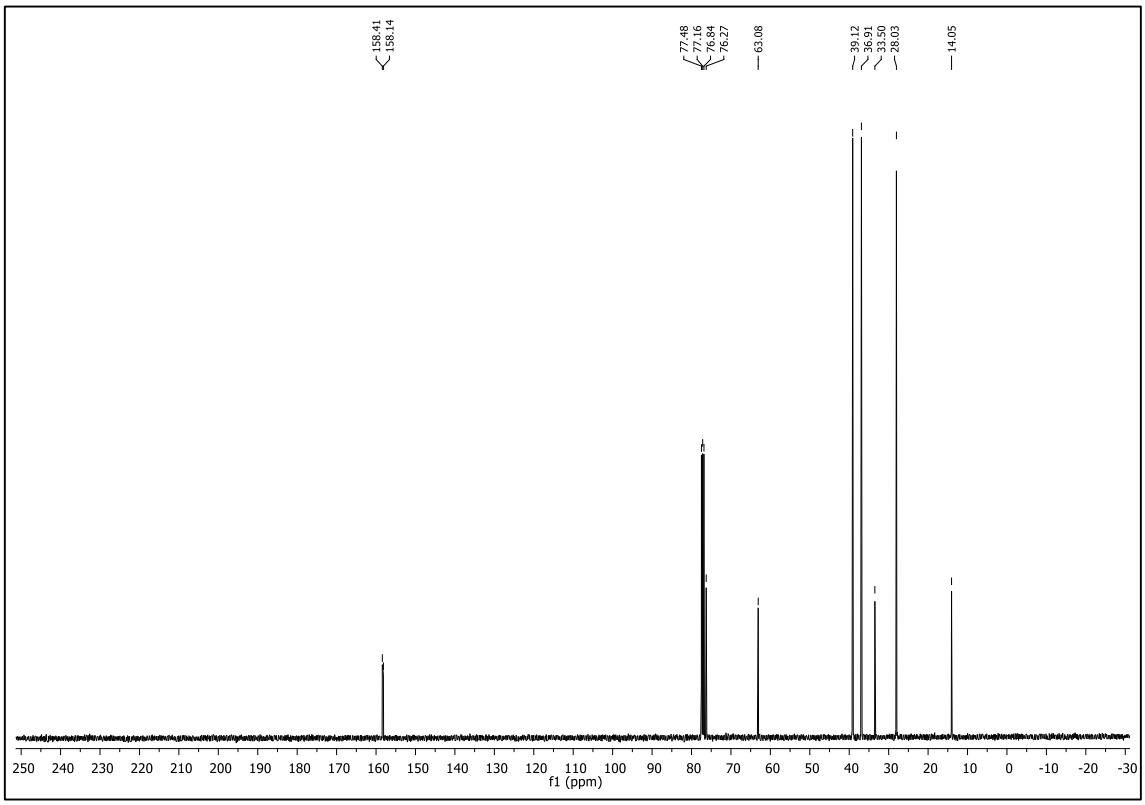

OEt
O
O
O
O
EtO
OEt
O
O
O
EtO
O
2.00
4.25
4.10
6.27
6.25
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

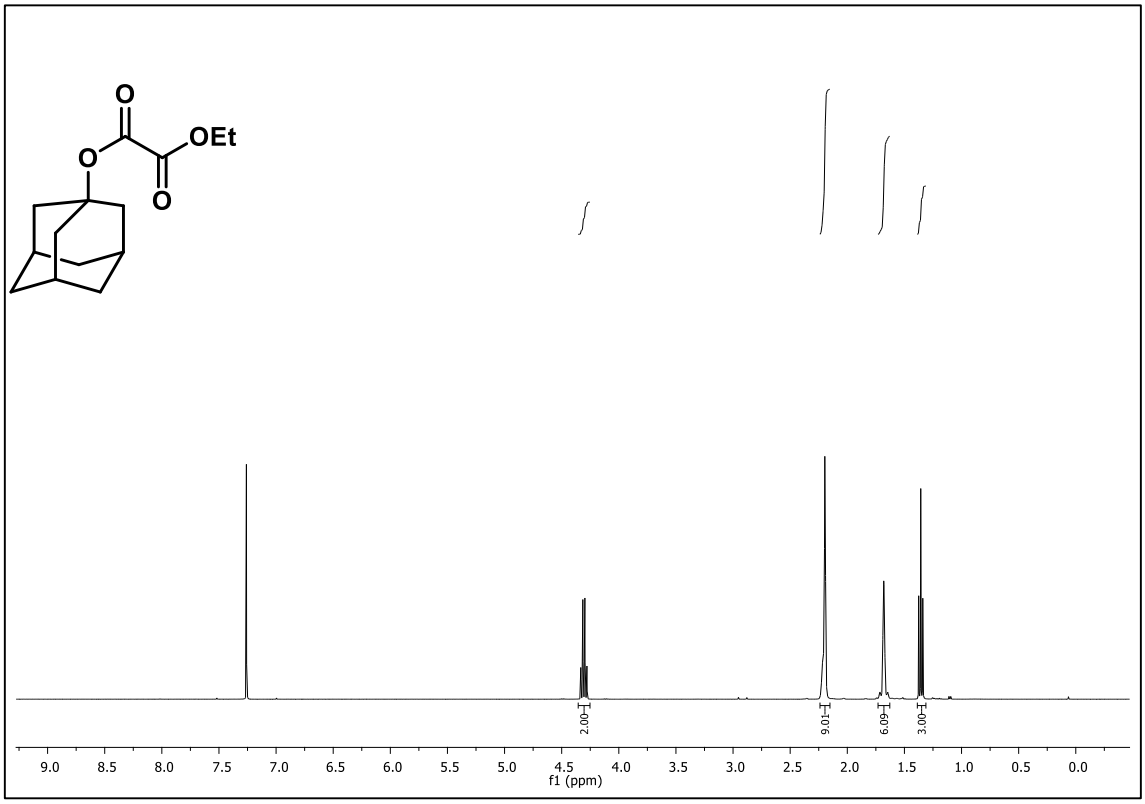

164.16
156.74
156.59
77.58
77.16
76.74
72.25
63.71
63.15
14.10
13.99
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

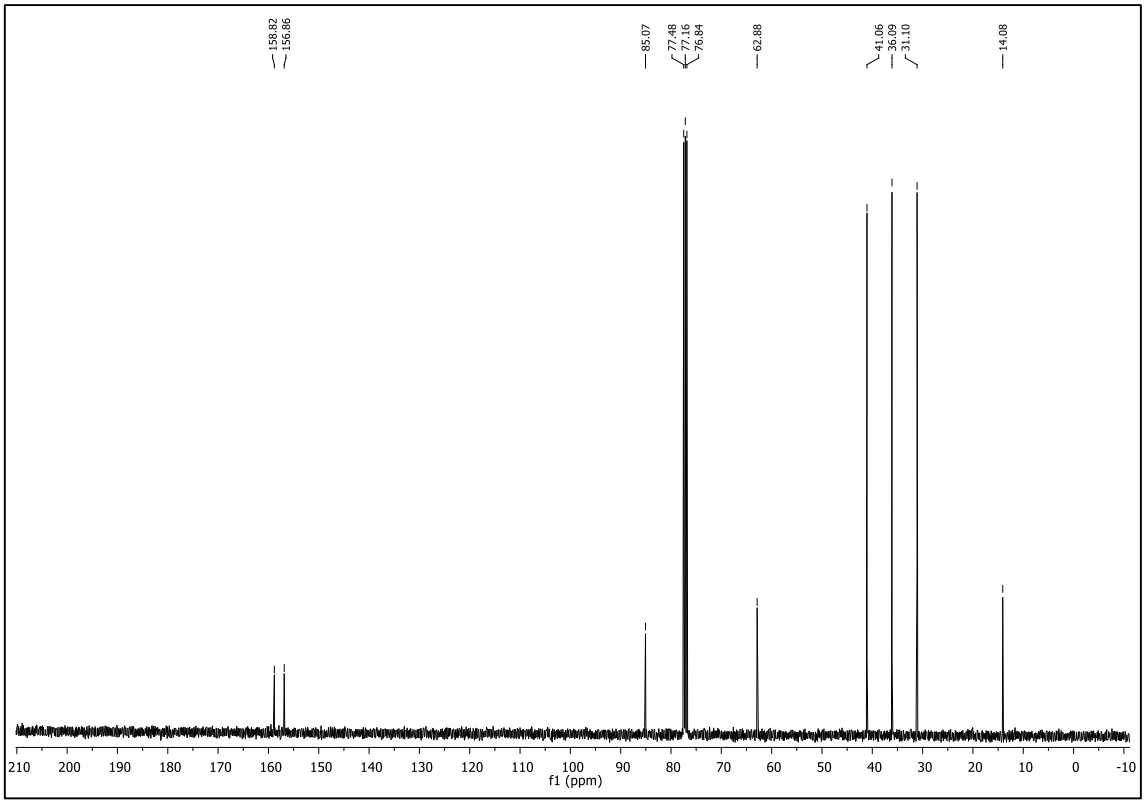

BnO
O
OEt
O
O
4.75
1.96
2.04
2.00
1.99
2.01
2.03
2.05
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

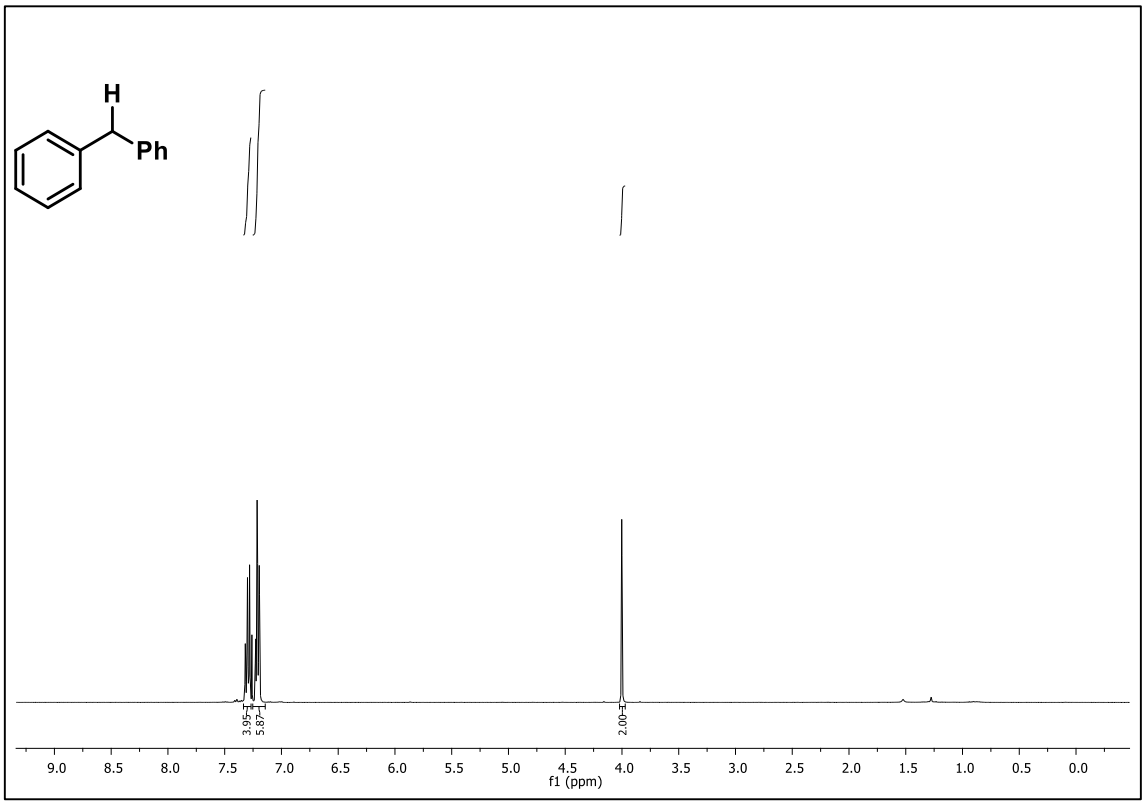

158.15
158.03
138.67
128.51
127.76
127.68
77.48
77.16
76.84
73.09
70.09
67.15
63.24
29.43
28.25
22.66
14.06
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

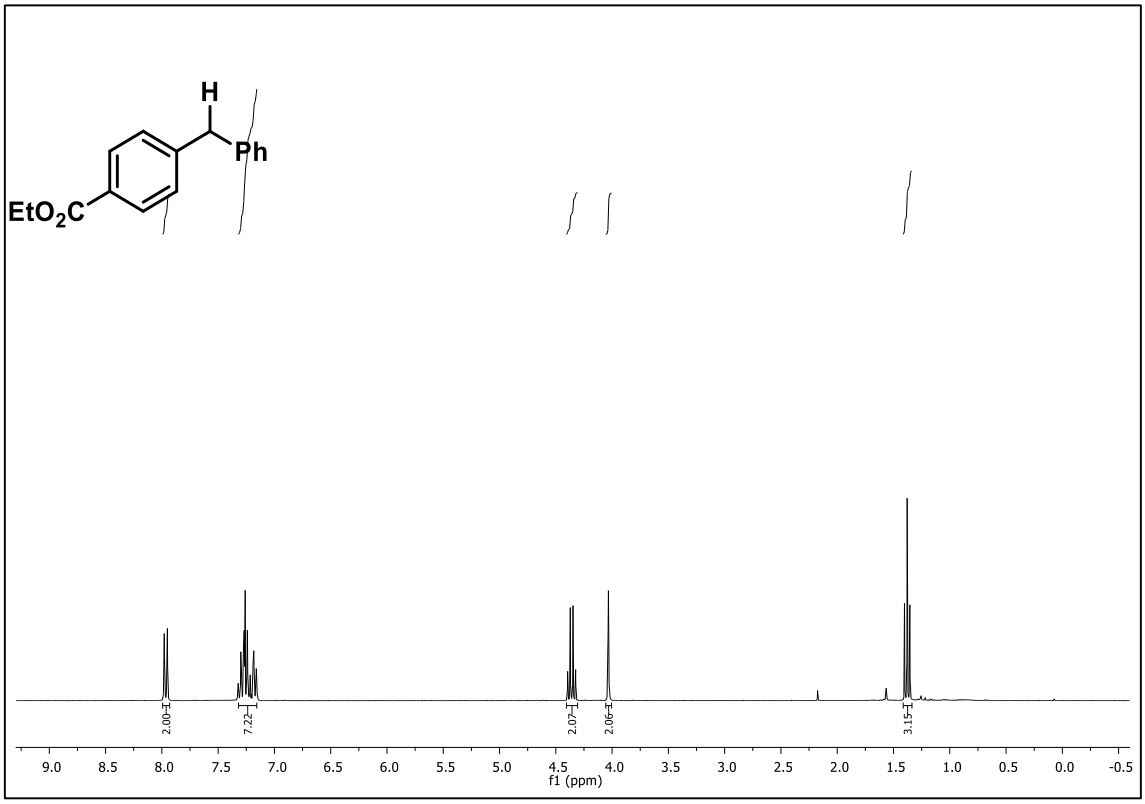

O
O
OEt
O
2.00
2.03
2.99
6.16
6.05
3.01
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

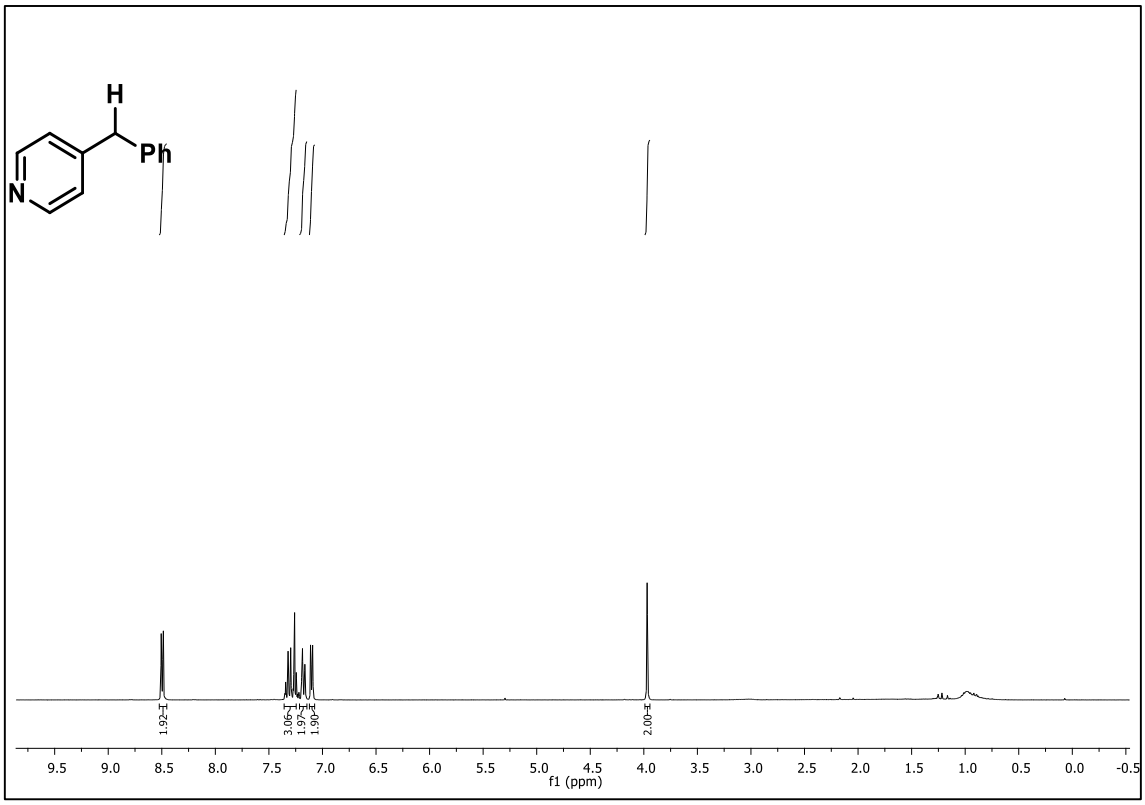

158.41
158.14
77.48
77.16
76.84
76.27
63.08
39.12
36.91
33.50
28.03
14.05
250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

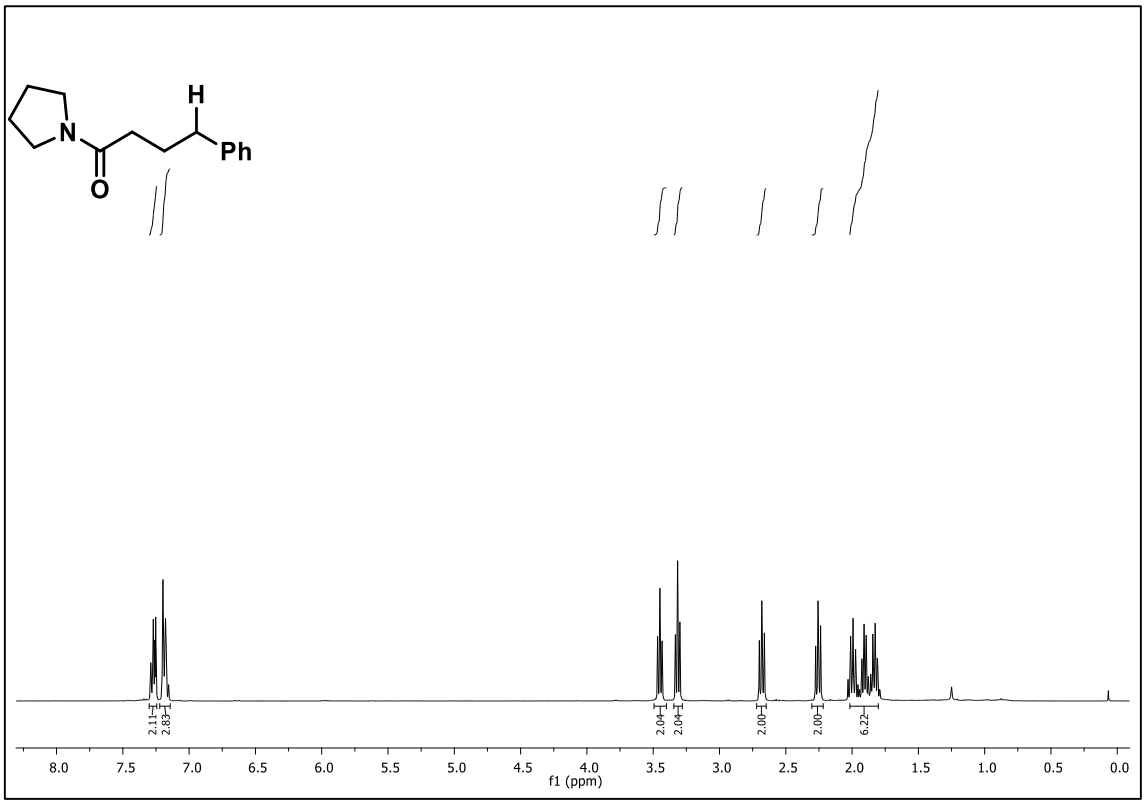

O
OEt
O
O
2.00
9.01
6.09
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

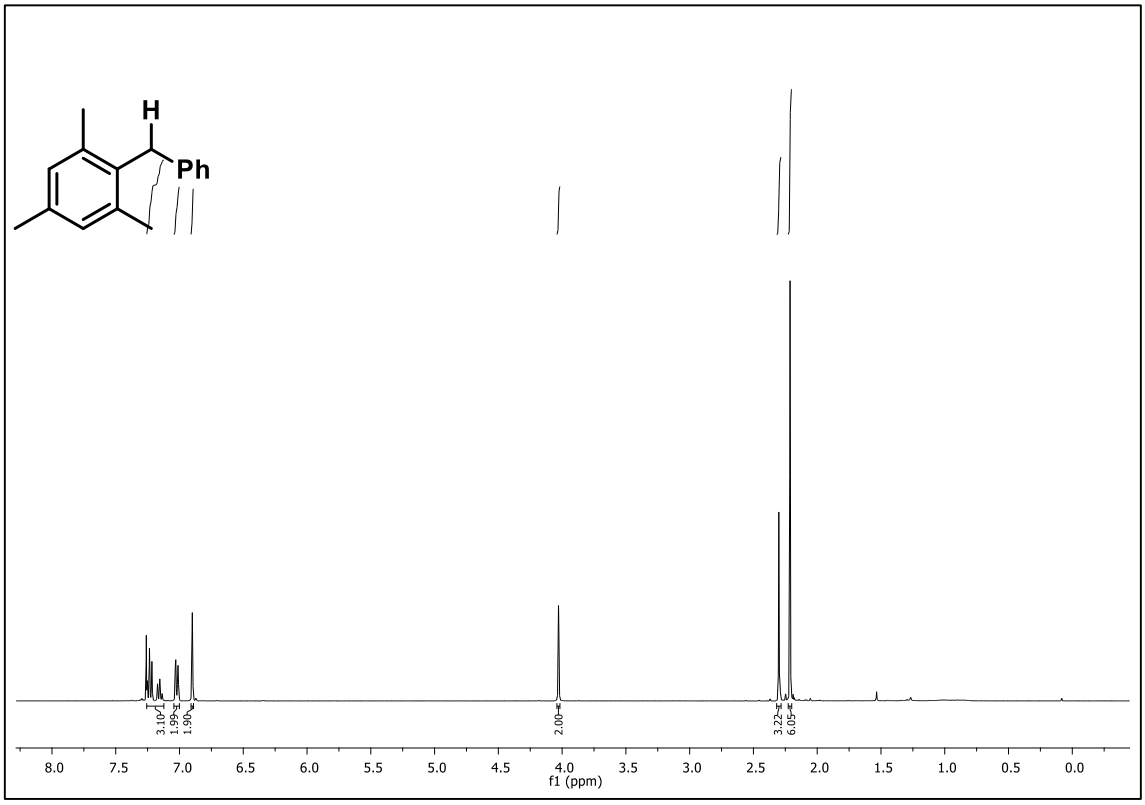

158.82
156.86
85.07
77.48
77.16
76.84
62.88
41.06
36.09
31.10
14.08
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

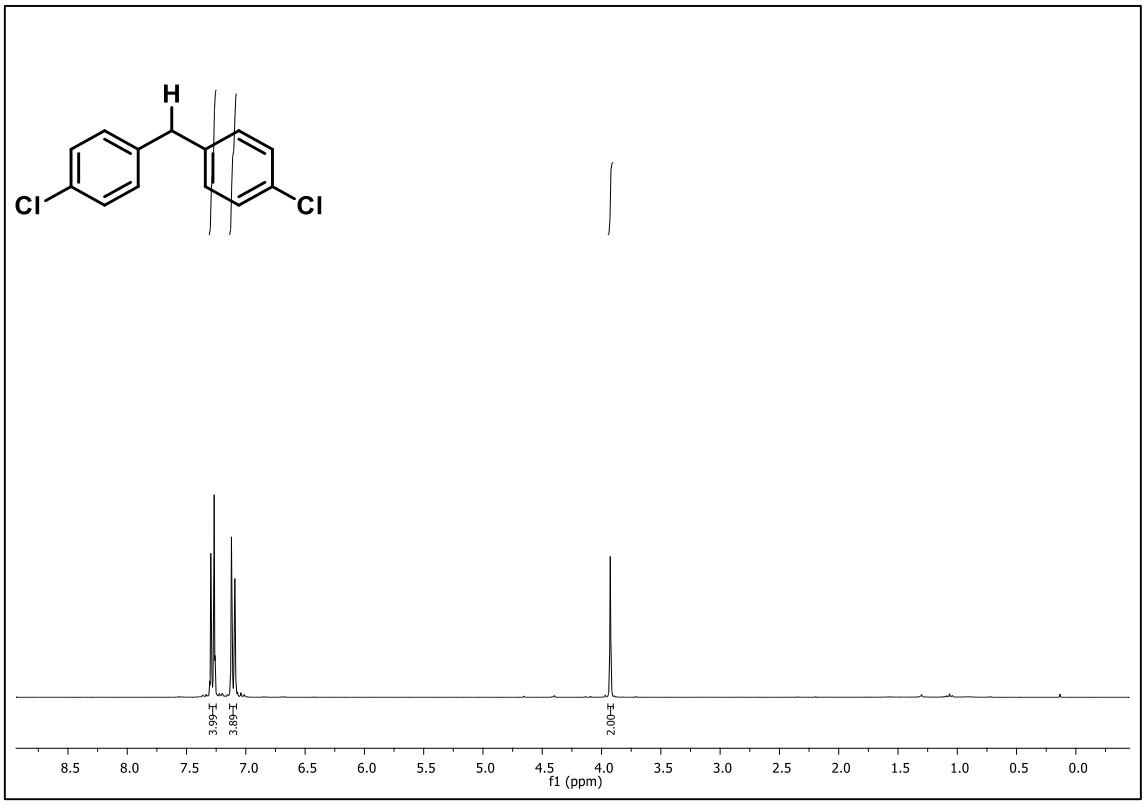

H
Ph
3.95
5.87
2.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

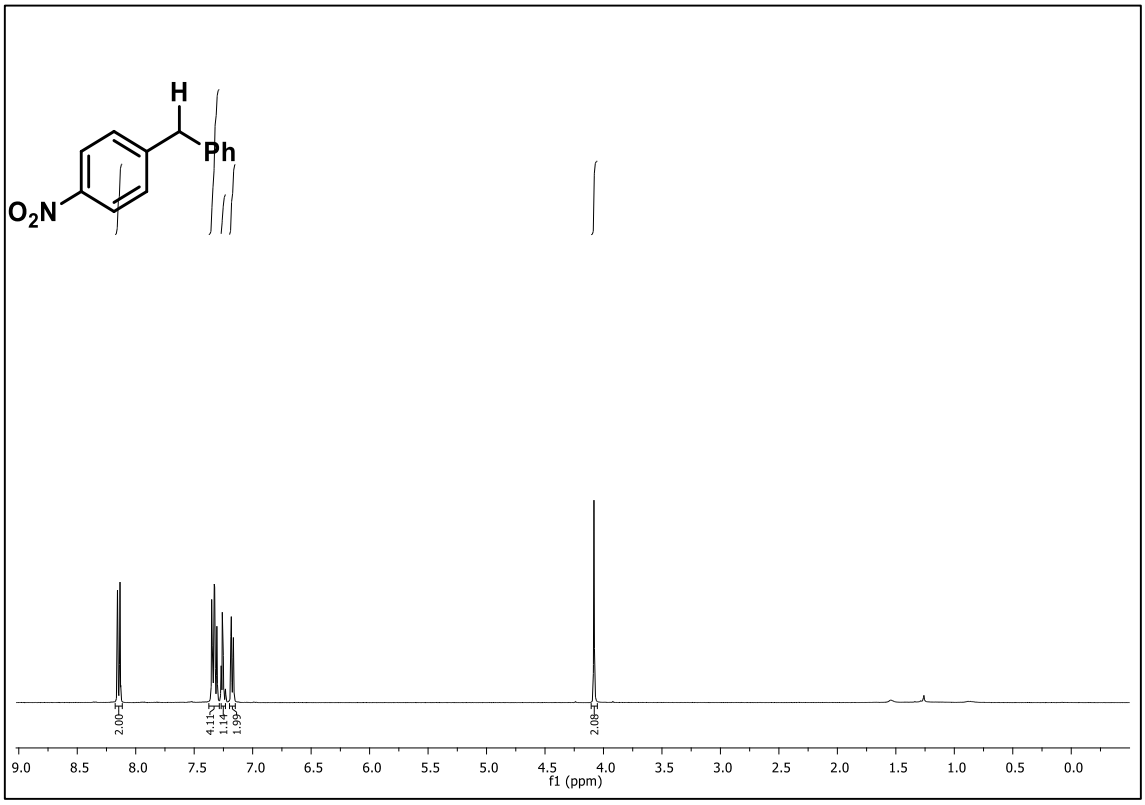

H
Ph
EtO2C
2.00
7.22
2.07
2.06
3.15
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

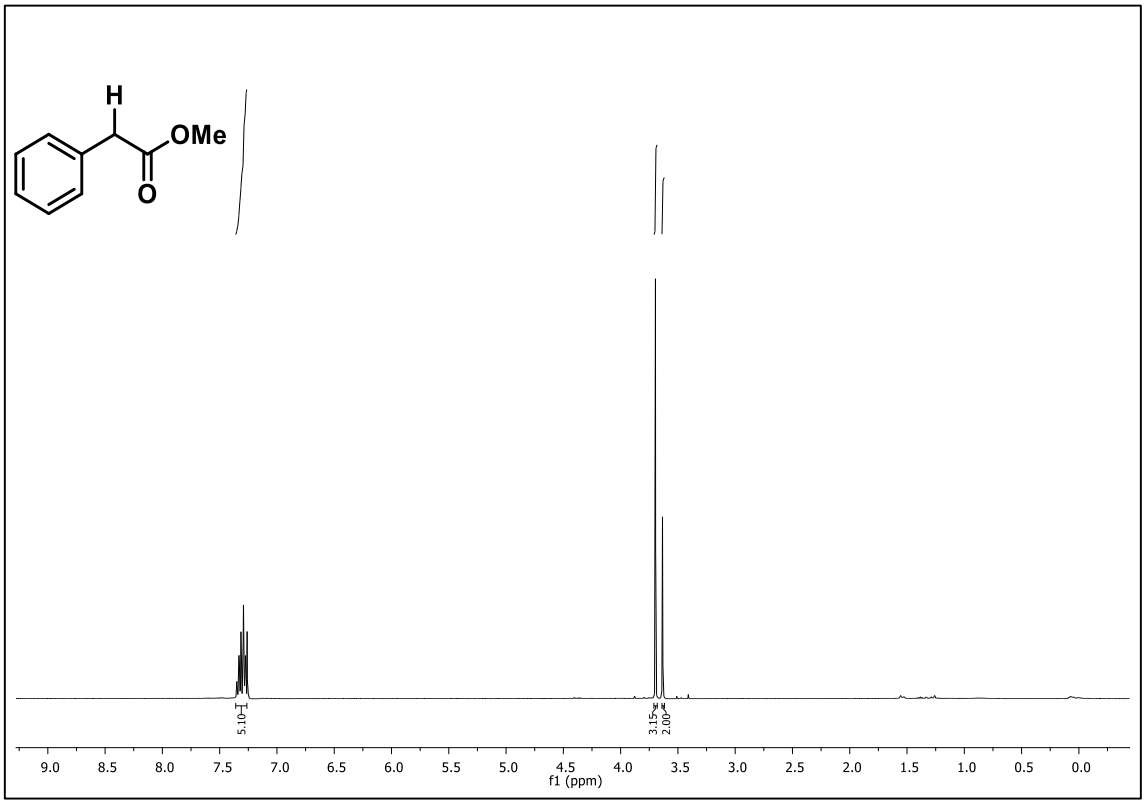

H
Ph
N
1.92
3.06
1.97
1.90
2.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

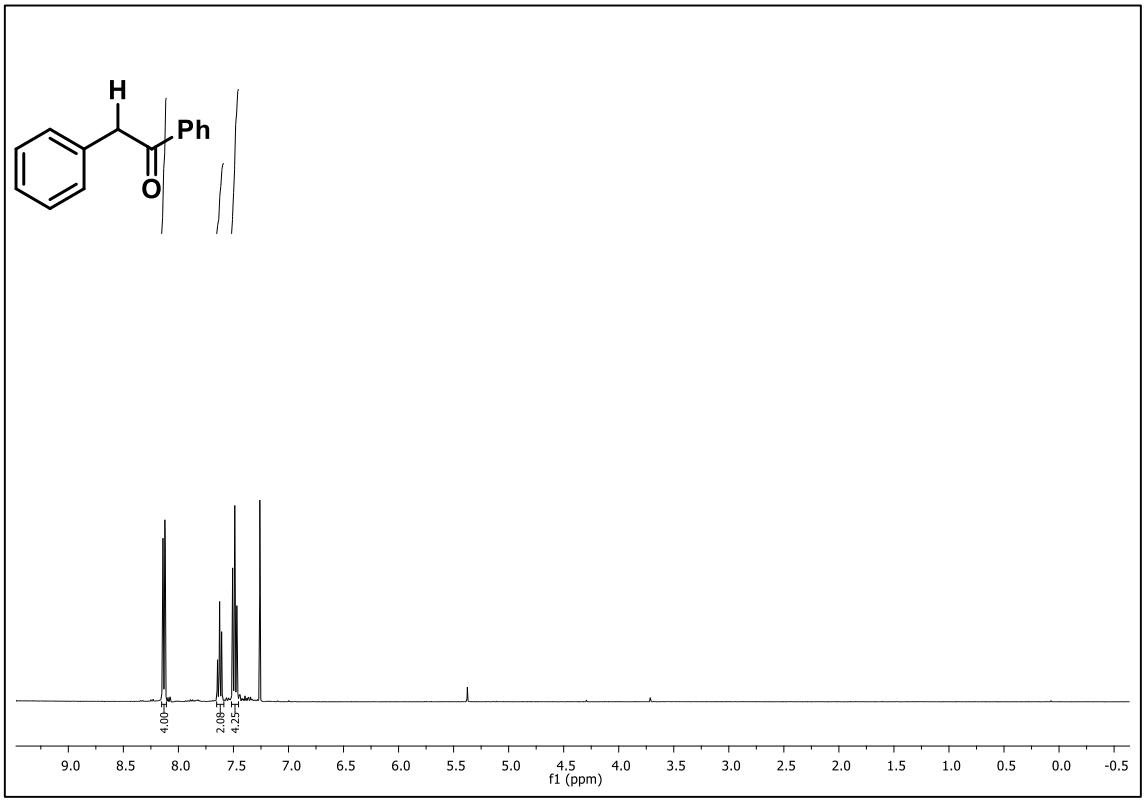

H
N
Ph
O
2.11
2.83
2.04
2.04
2.00
2.00
6.22
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

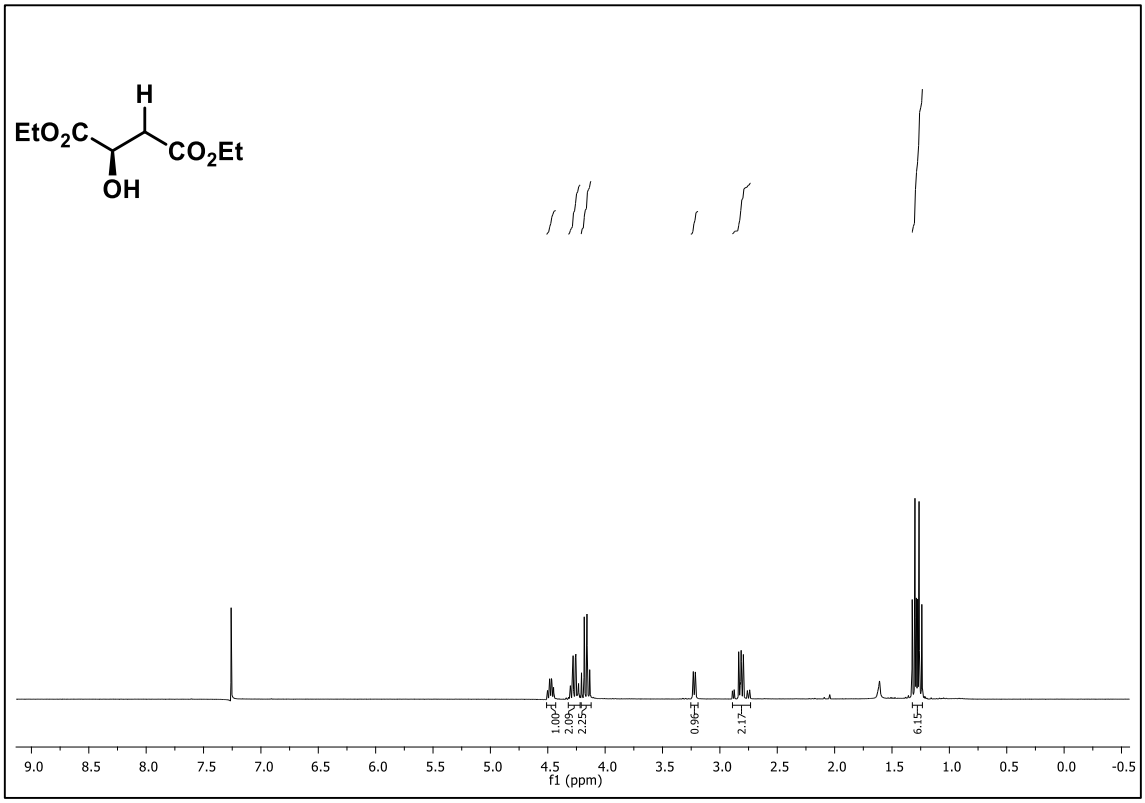

H
Ph
3.10
1.99
1.90
2.00
3.22
6.05
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


H
Cl
Cl
3.99
3.89
2.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


H
Ph
O2N
2.00
4.11
1.14
1.99
2.08
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)


H
OMe
O
5.10
3.15
2.00
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)


H
Ph
O
4.00
2.09
4.25
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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OH
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2.17
6.16
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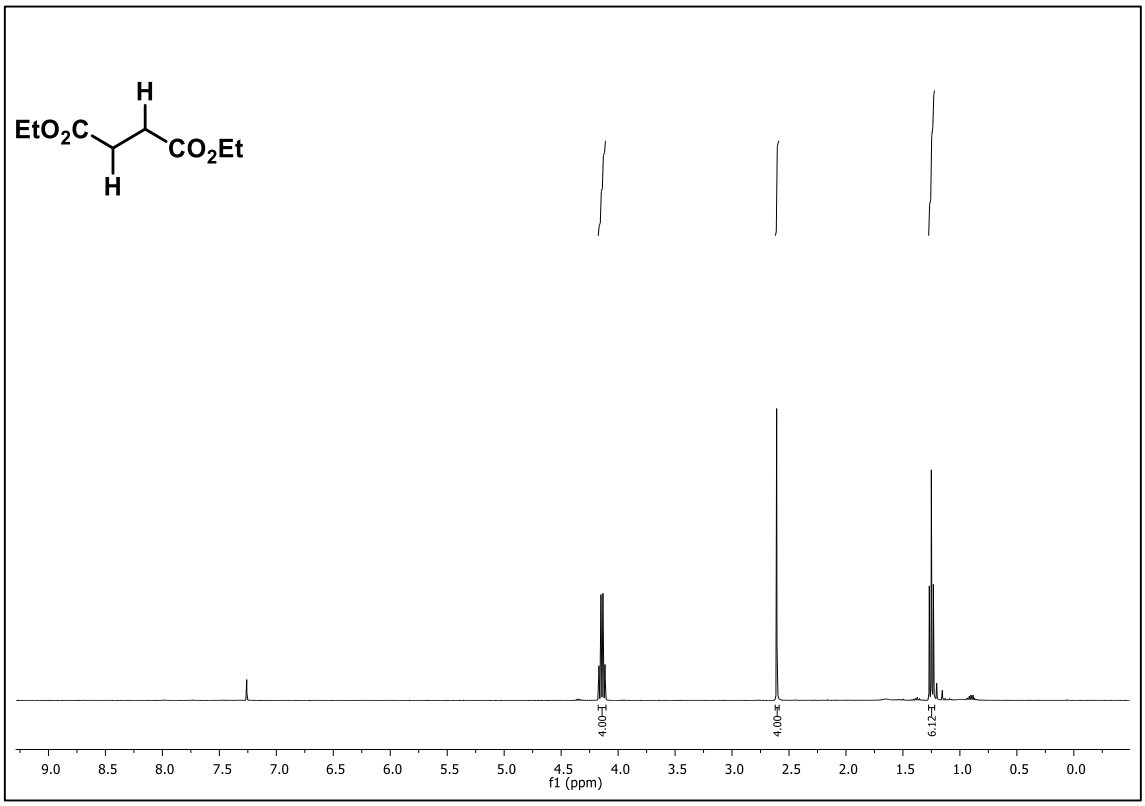
f1 (ppm)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4.00
6.12
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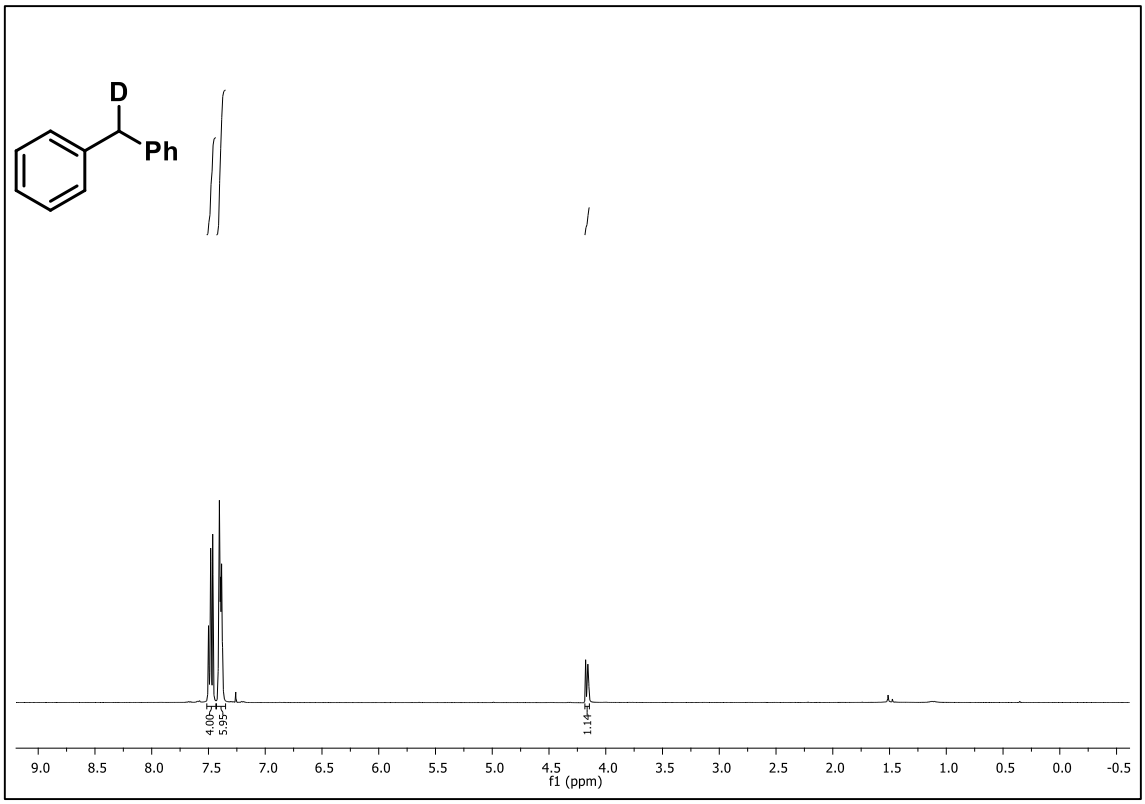
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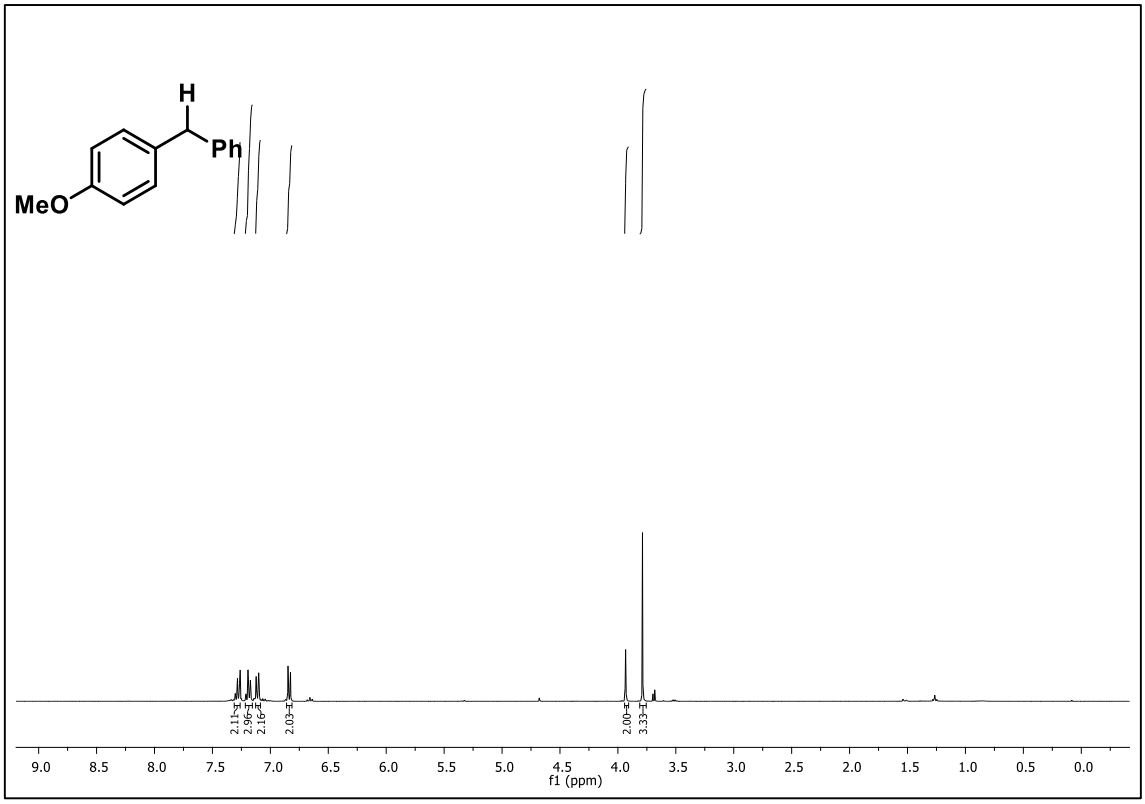
f1 (ppm)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3.33
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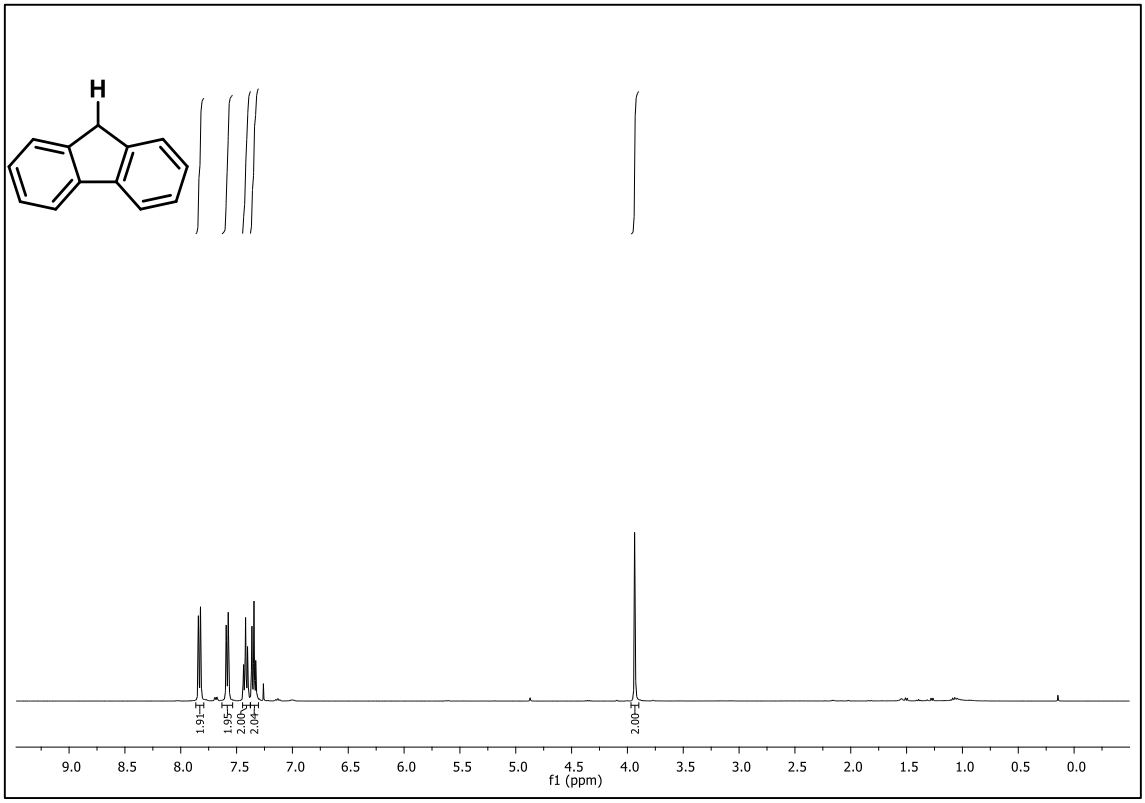
f1 (ppm)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2.04
2.00
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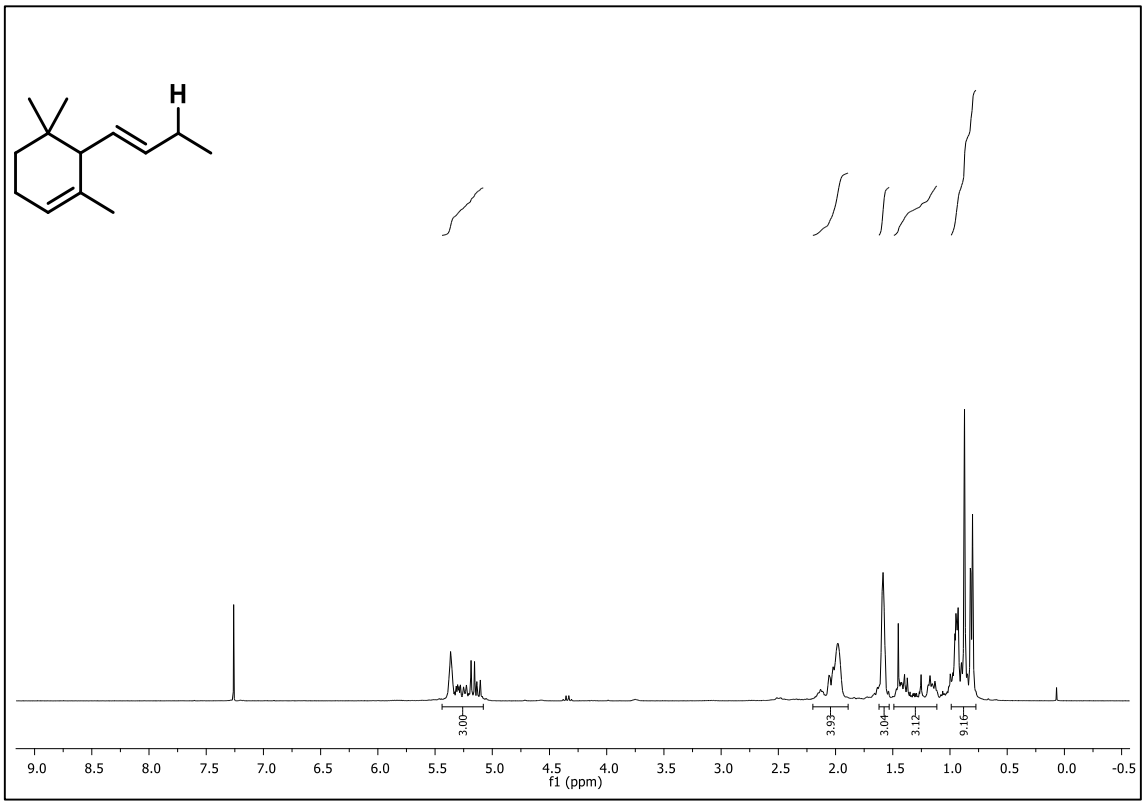
f1 (ppm)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3.12
9.16
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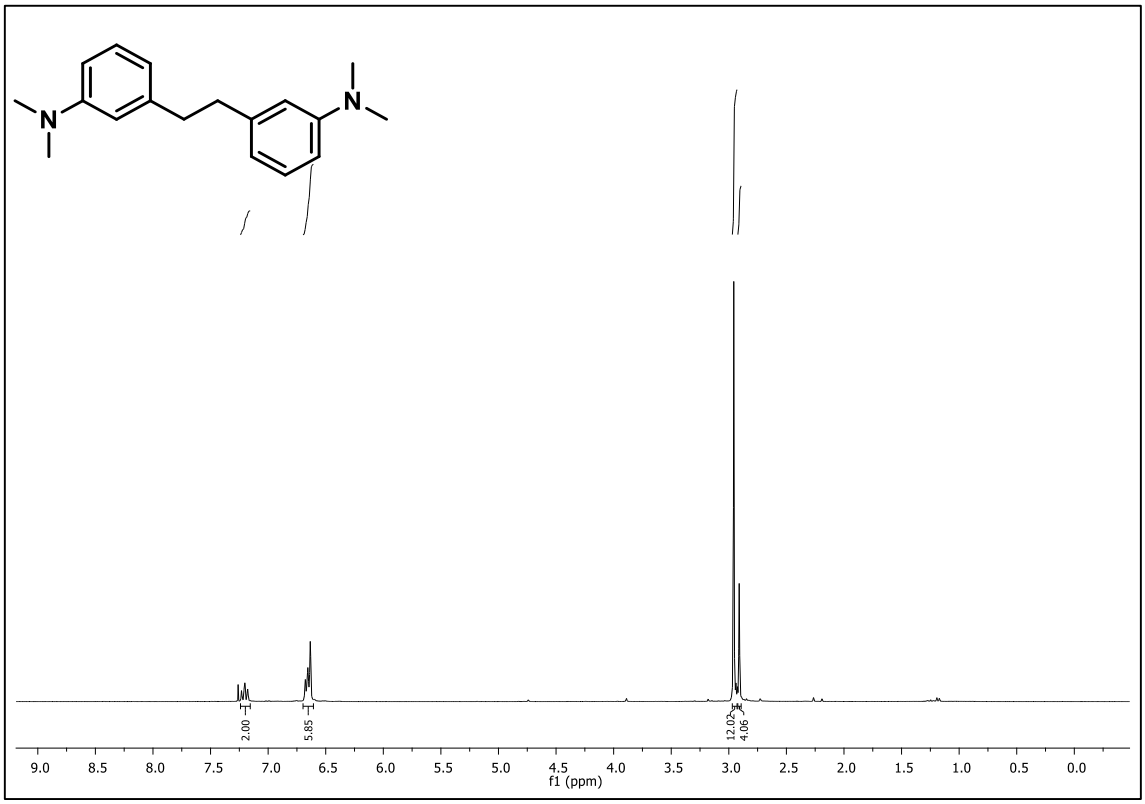
f1 (ppm)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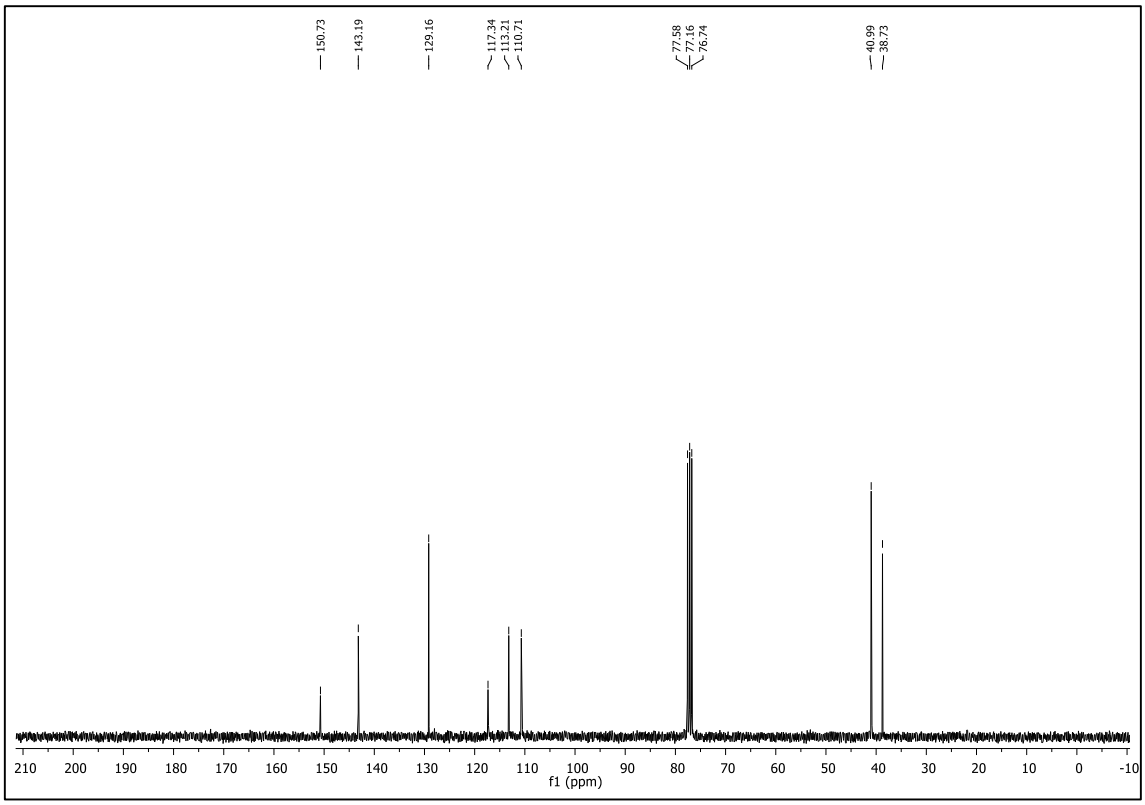
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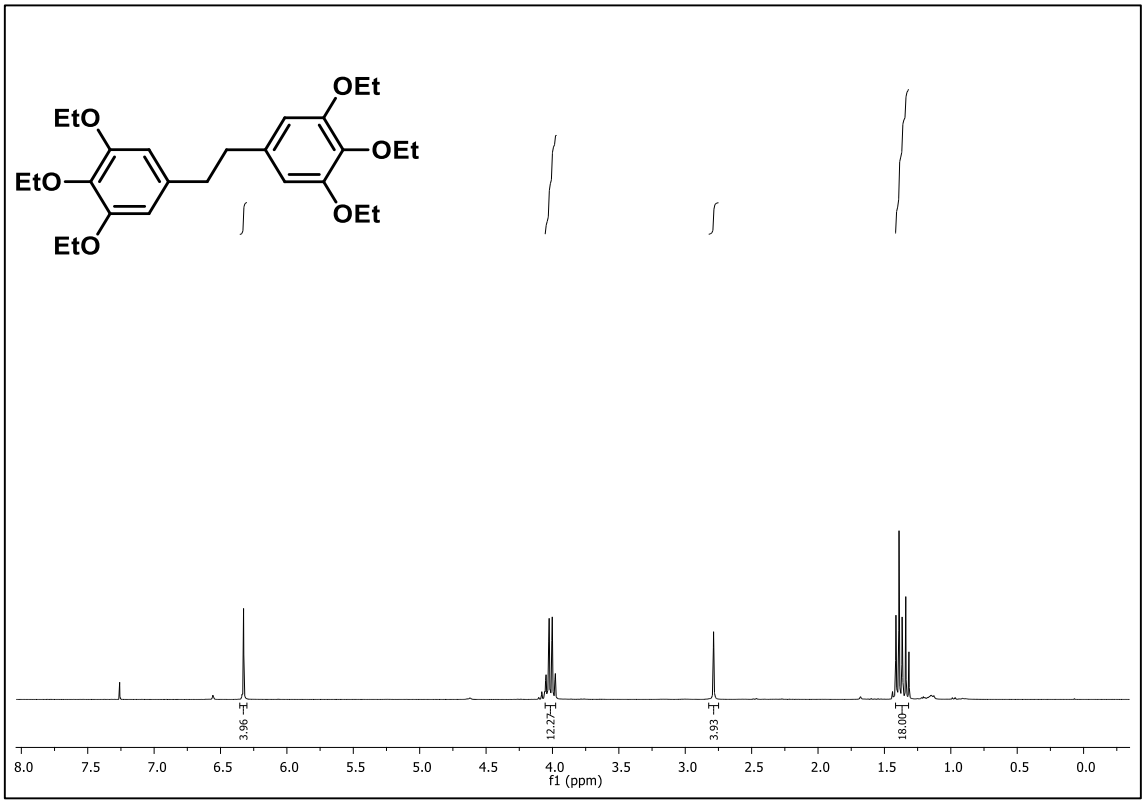
40.99
38.73
f1 (ppm)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EtO
OEt
EtO
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3.93
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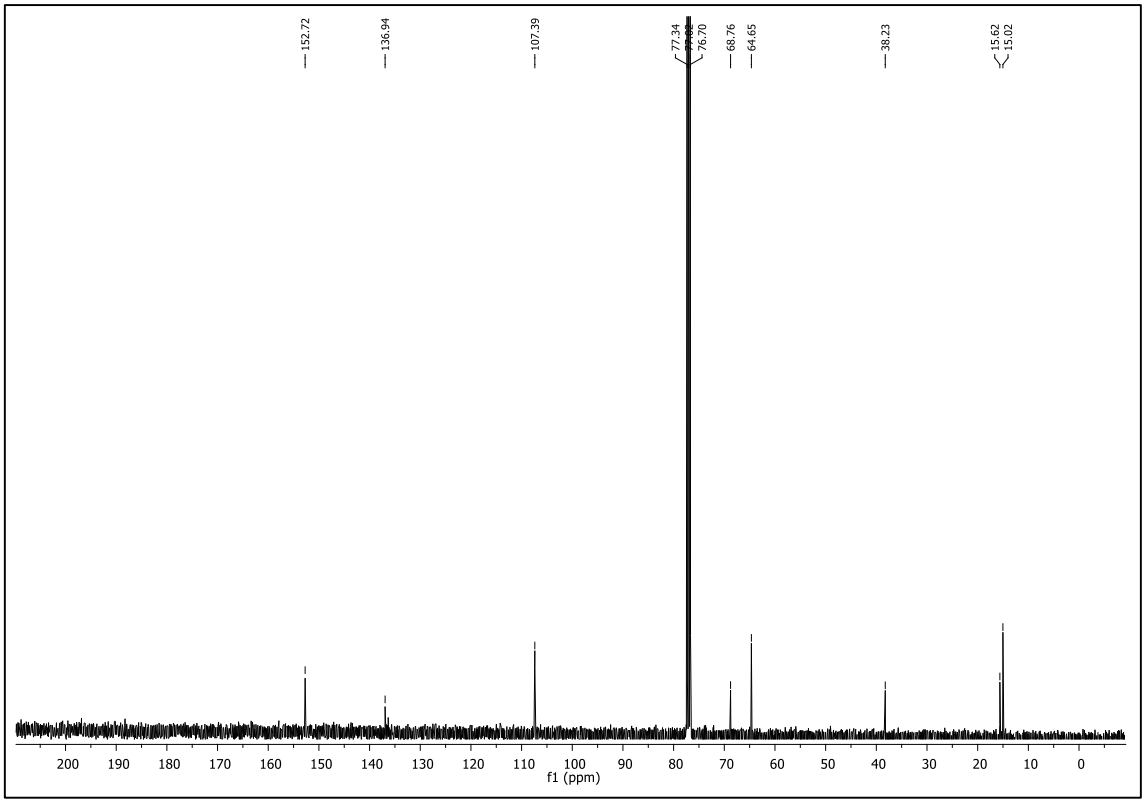
f1 (ppm)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68.76
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15.02
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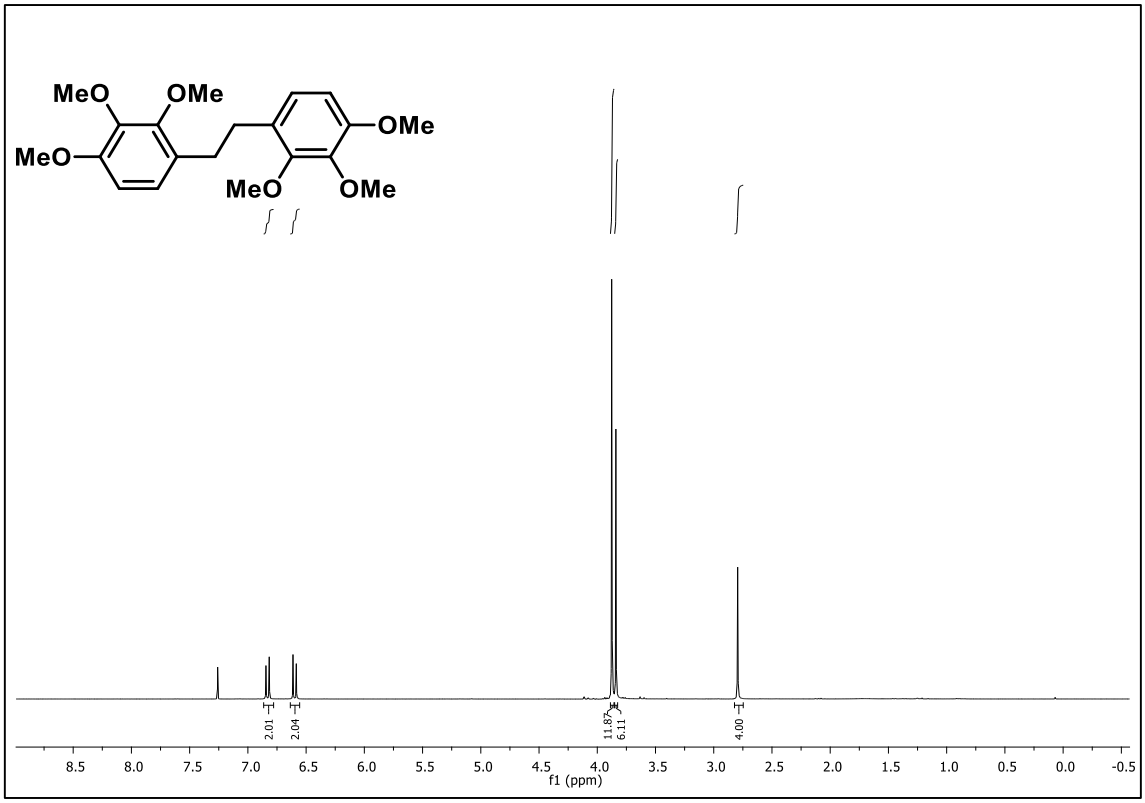
f1 (ppm)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MeO
OMe
MeO
OMe
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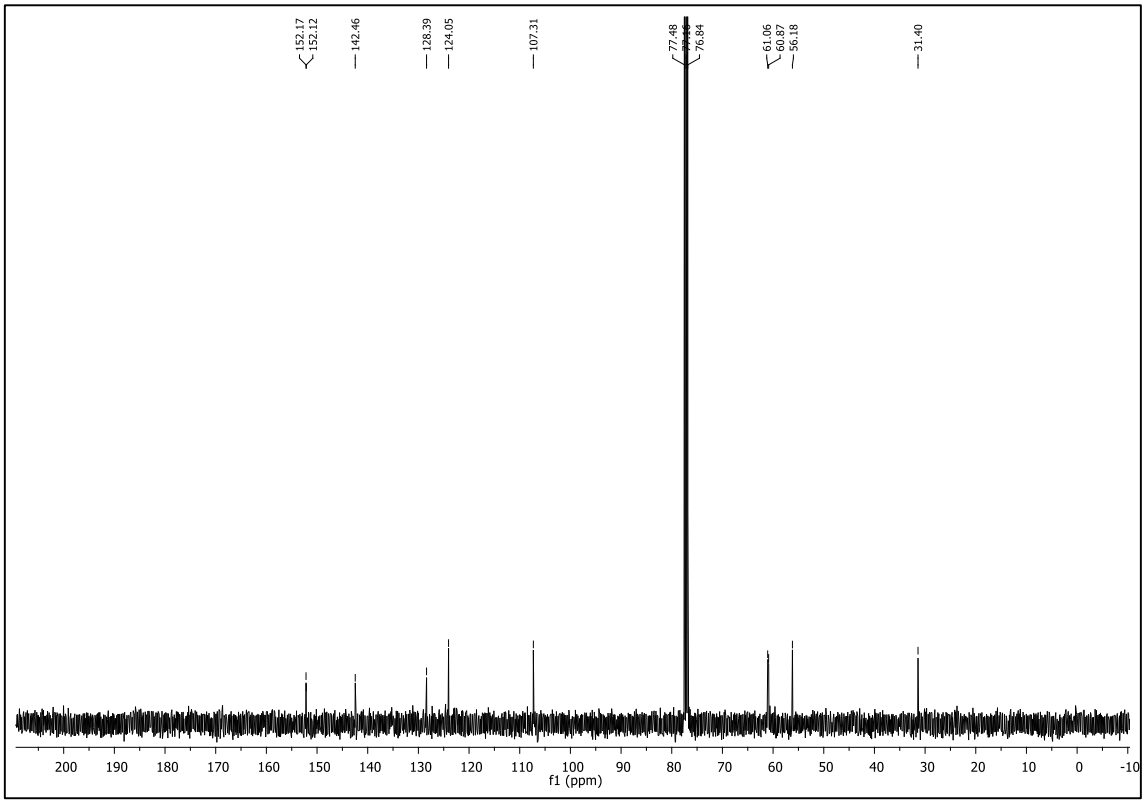
2.04
11.87
6.11
4.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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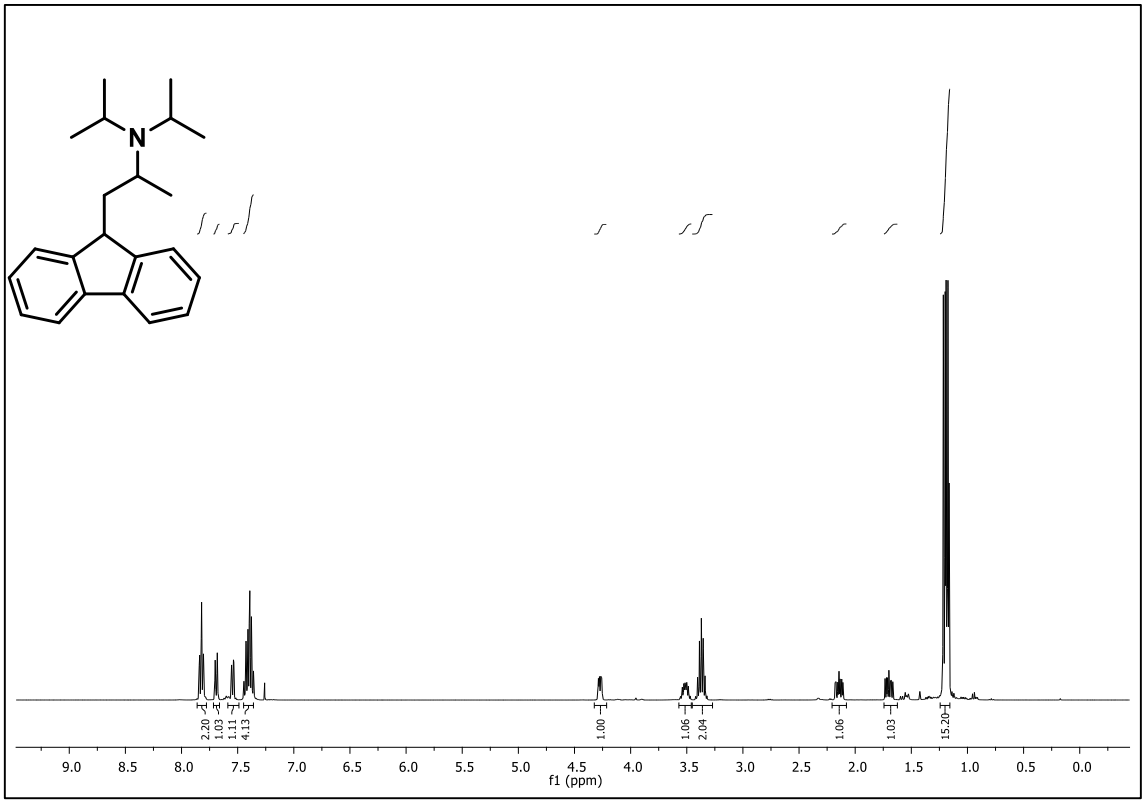
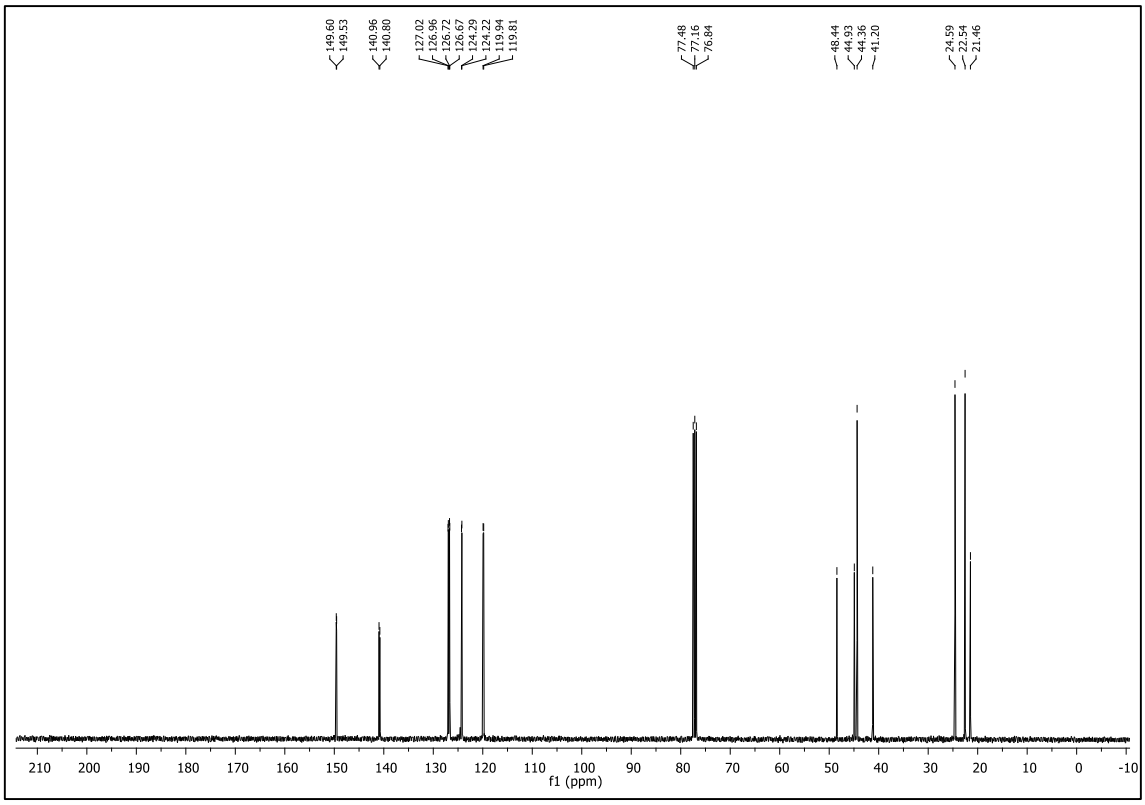
f1 (ppm)


N
2.20
1.03
1.11
4.13
1.00
1.06
2.04
1.06
1.03
15.20
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)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77.48
77.16
76.84
48.44
44.93
44.36
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24.59
22.54
21.46
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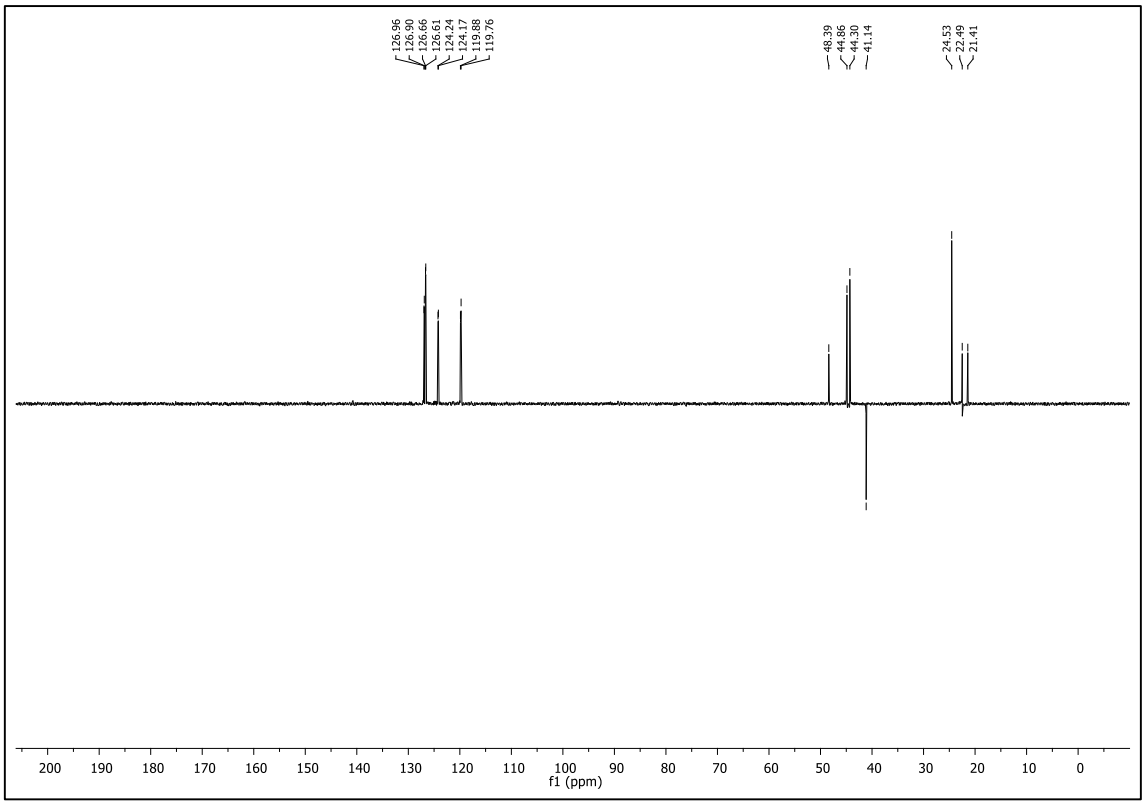
f1 (ppm)



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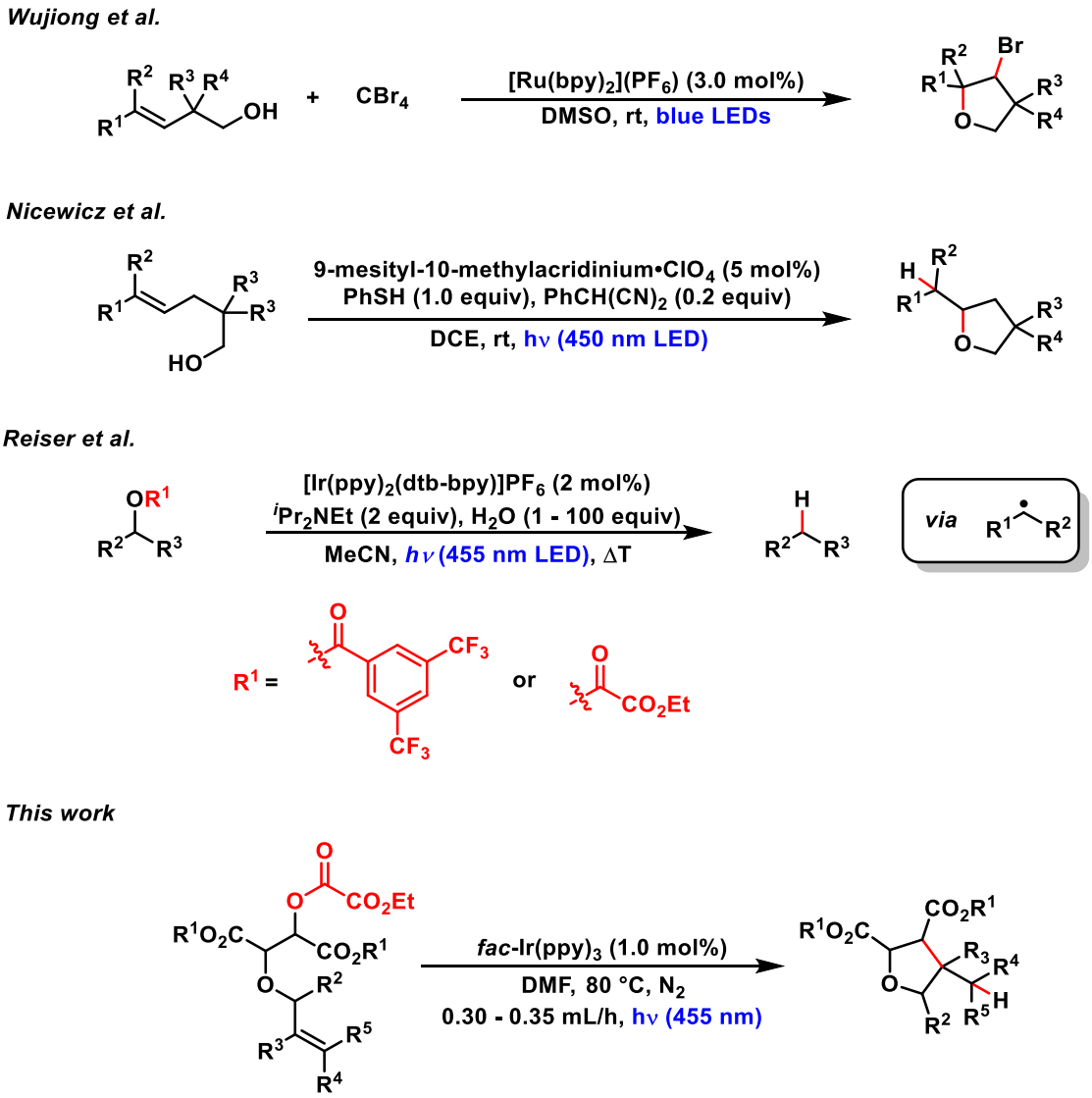
4. Visible light photoredox catalyzed synthesis of chiral tetrahydrofuranes

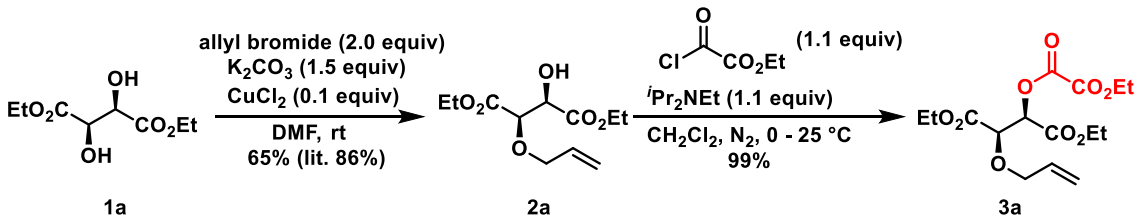
4.1 Introduction

Due to their broad biological activity, tetrahydrofurans represent an important class of heterocycles. A huge variety of natural products and pharmaceuticals bear a chiral tetrahydrofuran ring as a structural element.[1,2] Recently, Wujiong *et al*. reported the synthesis of β-bromotetrahydrofurans and –tetrahydropyrans using alkenols and tetrabromomethane *via* bromine addition to the alkene followed by an intramolecular nucleophilic cyclization under visible light photocatalysis (Scheme 1).[3] Moreover, Nicewicz *et al.* elegantly showed the facile visible light mediated synthesis of butyrolactones[4] and highly substituted tetrahydrofurans by polar radical crossover cycloaddition (Scheme 1).[5,6] Based on our recent studies on the deoxygenation of alcohols *via* 3,5-bis(trifluoromethyl)benzoate[7] and the feasible deoxygenation with ethyl oxalate auxiliaries (Chapter 3), we intended to expand this methodology for the preparation of chiral tetrahydrofuran derivatives utilizing the simple deoxygenation of activated mono-allylated succinates, followed by an intramolecular carbon – carbon bond formation (Scheme 1).



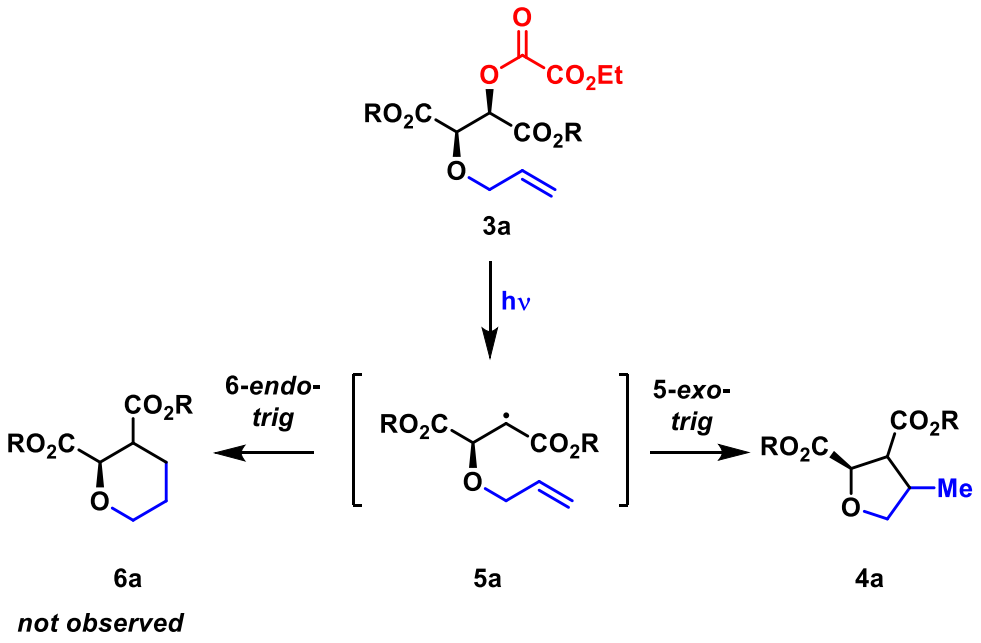
Scheme 1. Strategies on visible light mediated carbon - carbon and carbon – hydrogen bond formations.[3-8]

Owing to the excellent radical deoxygenation behavior of activated tartrates, we started our investigations looking into intramolecular cyclization capabilities of modified tartrate derivatives. Starting from the commercially available low cost (+)-diethyl tartrate **1a**, we performed an initial mono-allylation in the presence of copper(II) chloride as coordinating Lewis acid, potassium carbonate as base and allyl bromide as coupling reagent in DMF yielding **2a** (Scheme 2). In a second reaction step, the esterification of the remaining alcohol group was achieved in quantitative yield for the corresponding product **3a**, using ethyl oxalyl chloride and Hünig's base in CH_2Cl_2.



Scheme 2. Two-step synthesis for the preparation of the starting material **3a**.[9]

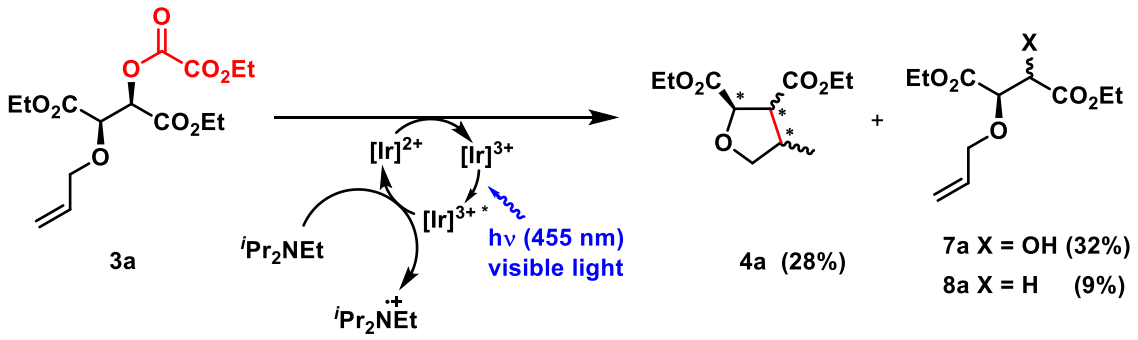
Two plausible cyclization products could emerge from test compound **3a**. After visible light induced deoxygenation of the ethyl oxalyl ester moiety, the generated α-carbonyl radical **5a** can interact with the nearby allyl group in an intramolecular cyclization, giving rise either to a kinetically favored chiral tetrahydrofuran derivative **4a** *via* 5-*exo* trig ring closure, or alternatively to a conceivable tetrahydropyran product **6a** *via* 6-*endo* trig cyclization (Scheme 3).



Scheme 3. Possible product cyclization pathways for an intramolecular ring closure. R = Et, ^{i}Pr.

4.2 Initial experiment

The first attempt to synthesize a chiral tetrahydrofuran starting from ethyl oxalate activated *O*-allylated tartrate **3a** was performed under the established conditions for the deoxygenation process (Chapter 3) using $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ (ppy = phenylpyridine, dtb-bpy = 4,4'-di-*tert*-butyl-2,2'-bipyridine) as photoredox catalyst and $^{i}Pr_2NEt$ as sacrificial electron donor in CH_3CN at 60 °C (Scheme 4). As the presence of water as additional hydrogen source greatly increases the deoxygenation of oxalate esters (as shown in chapter 3), these reaction conditions were adapted: The addition of water was omitted to favor the reaction pathway of kinetically slower intramolecular cyclization over faster competitive simple reduction of the initially formed radical in the presence of water. The irradiation was carried out by a high power blue LED (455 nm), channeled through a glass rod directly into the reaction solution while heating was enabled from below in a metal block. Cyclized product **4a** was obtained in 28% yield and a diastereomeric ratio of 62:28:8:2. Nevertheless, the starting material **3a** gave also simple deoxygenated product **7a** in 9% as well as hydrolyzed succinate derivative 8a in **32%** yield. The results were not fully satisfactory and leave room for further improvement.

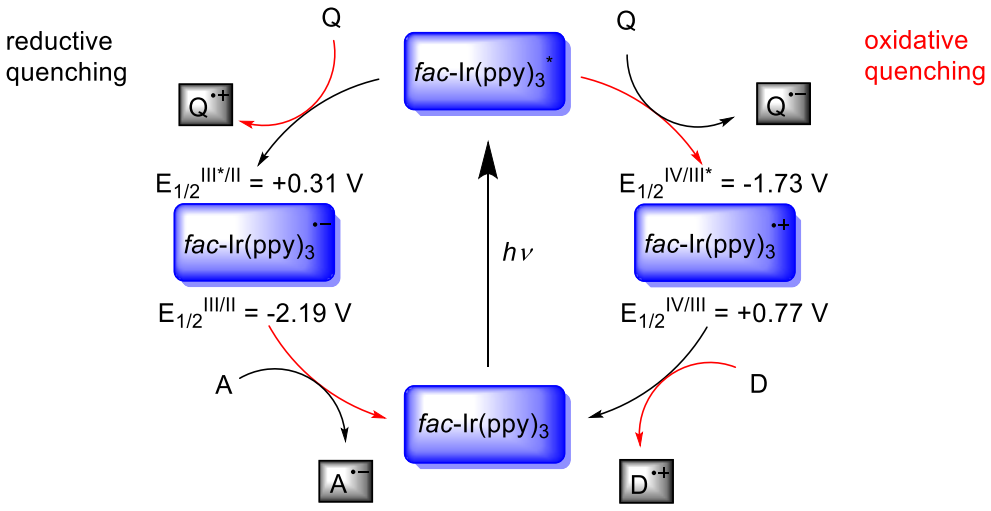


Scheme 4. Photoredox catalyzed deoxygenation process in a reductive quenching process.

4.3 Change of the catalytic cycle and screening investigations

The competitive hydrolysis and deoxygenation of **3a** occurs in the presence of an external sacrificial electron donor ($^{i}Pr_2NEt$). After irradiation, $^{i}Pr_2NEt$ will be oxidized by transferring an electron to the excited Ir_3^{+}* species of the catalyst to form the reduced Ir^{2+}. This oxidized species acts as an additional hydrogen source and leads to the formation of the byproducts **7a** and **8a**.

Therefore, an alternative oxidative quenching pathway was investigated (Schema 5). Instead of electron transfer by Hünig's base, the electron can be directly donated from the excited species of the photoredox catalyst into the ester moiety of the oxalates. In that case, Hünig's base can be omitted and consequently, competitive hydrolysis and simple deoxygenation can be minimized.

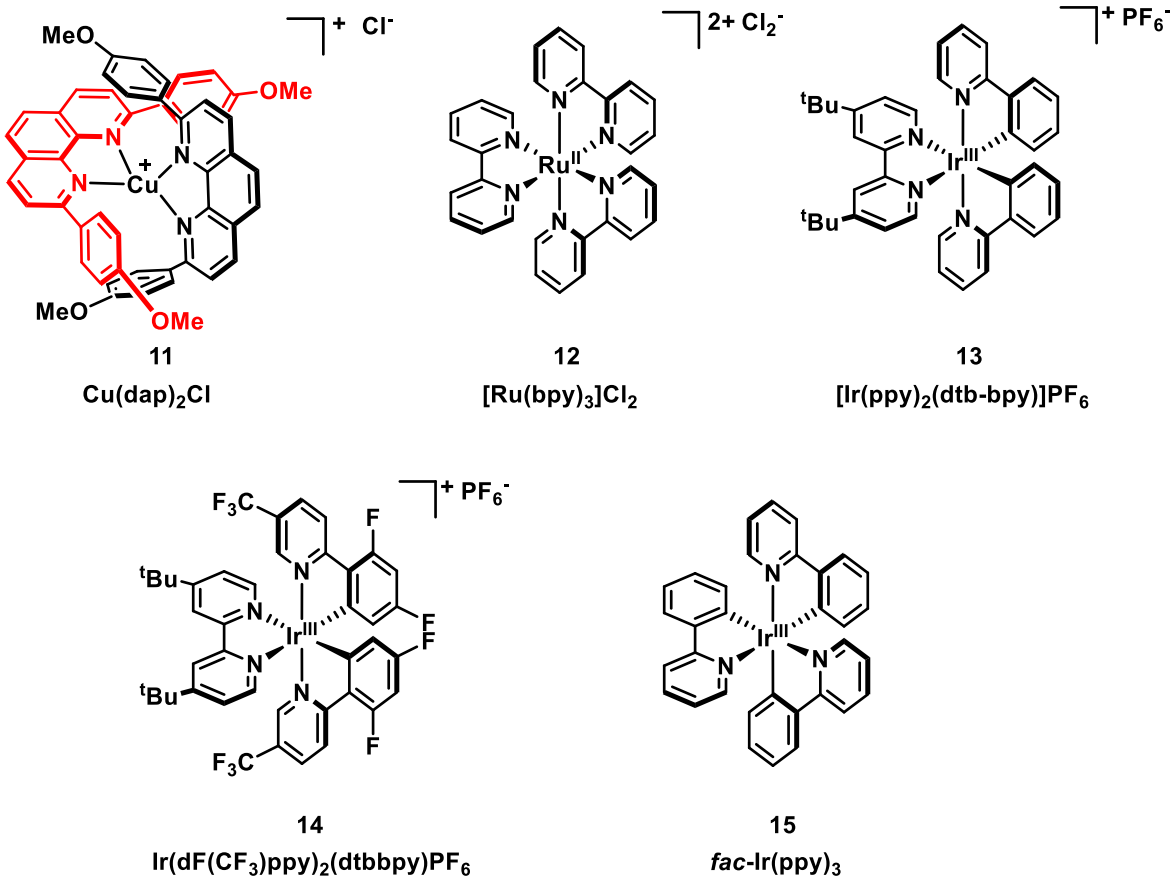


Scheme 5. General pathways for single electron transfers induced by visible light either *via* reductive or oxidative quenching process for the *fac*-$Ir(ppy)_3$ photoredox catalyst. Q = quencher, A = acceptor, D = donor, $E_{1/2}$ = half potential. Oxidative quenching process marked in red, reductive quenching process in black.

To ensure a first electron transfer to the oxalate moiety, feasible catalysts based on the reduction potential of **3a** (E_{Red} = -1.65 V vs SCE in DMF) were investigated (Table 1). Initial screenings were carried out with mono-allylated oxalate derivative **3a**, using well established photoredox catalysts for the oxidative quenching cycle (Scheme 6), i.e. $Cu(dap)_2Cl$ **11** (E_{Red} Cu^{+*}/Cu^{2+} = -1.43 V vs SCE,[10] dap = 2,9-bis(4-anisyl)-1,10-phenanthroline, entry 1) or $Ru(bpy)_3Cl_2$ **12** (E_{Red} Ru^{2+}/Ru^{+} = -1.33 V,[11] bpy = 2,2'-bipyridine, entry 2). Both catalysts gave no conversion at 80 °C in DMF, suggesting that the reduction potentials are not sufficient to transfer an electron

to the oxalate ester moiety. However, switch to iridium based catalysts was more promising. $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ **13** (E_{Red} Ir^{3+}/Ir^{2+} = -1.51 V,[12] ppy = phenylpyridine, dtb-bpy = 4,4'-di-*tert*-butyl-2,2'-bipyridine, entry 3) and $Ir[dF(CF_3)ppy]_2(dtb\text{-}bpy)PF_6$ **14** (E_{Red} Ir^{3+*}/Ir^{4+} = -1.21 V,[12] $dF(CF_3)ppy$ =2-(2,4-difluorophenyl)-5-trifluoromethylpyridine, dtb-bpy = 4,4'-di-*tert*-butyl-2,2'-bipyridine, entry 4) led to 22% and 44% conversion, respectively, although their reduction potentials are lower compared to $Cu(dap)_2Cl$ **11**. Fluorinated iridium catalyst **14** yielded negligible 5% of the 5-membered cyclized product **4a**. The best results could be achieved for highly reducing *fac*–$Ir(ppy)_3$ photoredox catalyst **15** (E_{Red} Ir^{3+*}/Ir^{4+} = -1.73 V vs SCE,[13] ppy = phenylpyridine, entry 5, scheme 7). Full conversion and 70% yield of the chiral tetrahydrofuran product **4a**, in a diastereomeric ratio of 62:28:8:2 was obtained after 20 h of irradiation, while no tetrahydropyran formation was observed. Having identified *fac*–$Ir(ppy)_3$ **15** as most promising photoredox catalyst, different reaction temperatures were examined to increase the yield. Ambient temperature (Table 1, entry 6) as well as an elevated temperature of 40 °C (Table 1, entry 7) gave no conversion of starting material **3a** at all. A further increase of the temperature was identified as crucial parameter for the photoinduced cyclization, since 89% conversion and 51% yield were achieved at 60 °C after 20 h irradiation time. A prolonged reaction time of up to 44 h gave full conversion and yielded 81% (Table 1, entry 8, scheme 7). This could be rationalized by the elevated temperature, which increases the rotational freedom of the substrate and thus, may lead to an increased population of the conformation needed for the cyclization. Addition of 2 equivalents of water to provide an additional hydrogen source and therefore, an accelerated product formation due to faster hydrogen abstraction, surprisingly led to lower conversion of only 53% and yielded 36% of **4a** after a prolonged reaction time of 24 h (Table 1, entry 9, scheme 7). Decrease of the catalyst loading to 0.1 mol% gave 64% conversion and poor 18% yield after 20 h irradiation time (Table 1, entry 10). Constant increase in conversion and yield was observed using 0.2 mol%, 0.5 mol%, and 1.0 mol% catalyst loading (Table 1, entry 11, 12 and 13). Despite similar conversions of 74% and 75%, higher yield of 38% was achieved for 0.5 mol% catalyst loading compared to 23% for 0.2 mol%. Moreover, a catalyst loading of 1.0 mol% gave 80% conversion and yielded 47% of the corresponding cyclized product **4a** (Table 1, entry 13). Control experiments corroborated our assumption that the deoxygenation of **3a** is indeed a photochemically induced process (Table 1, entry 15 and 16). When either light (Table 1, entry 15) or the photocatalyst (Table 1, entry 16) were absent, no reaction was observed. The performance of the reaction without prior degassing gave 26% conversion and 8% yield. This result was not surprising, due to the literature known quenching process of the excited triplet state of the photoredox catalyst in the presence of oxygen atmosphere (Table 1, entry 17). In

addition, DMF turned out to be superior for visible light mediated intramolecular cyclization compared to CH_3CN (Table 1, entry 17). Only 34% conversion of **3a** and 1% yield for the desired tetrahydrofuran derivative **4a** was observed using CH_3CN (Table 1, entry 18).



11 **12** **13**

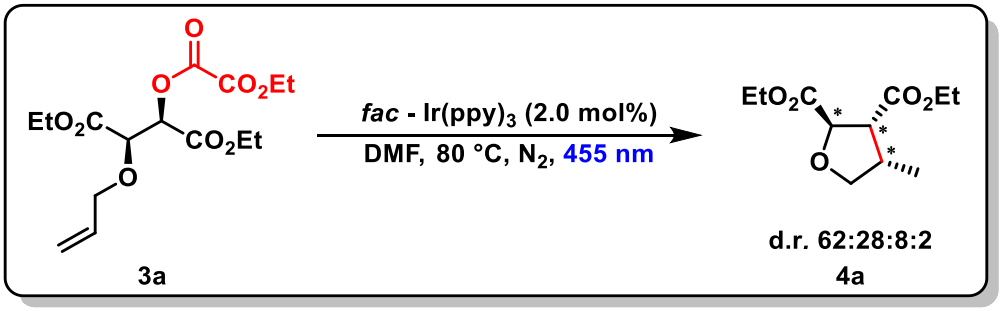
Cu(dap)$_2$Cl **[Ru(bpy)$_3$]Cl$_2$** **[Ir(ppy)$_2$(dtb-bpy)]PF$_6$**

14 **15**

Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)PF$_6$ ***fac*-Ir(ppy)$_3$**

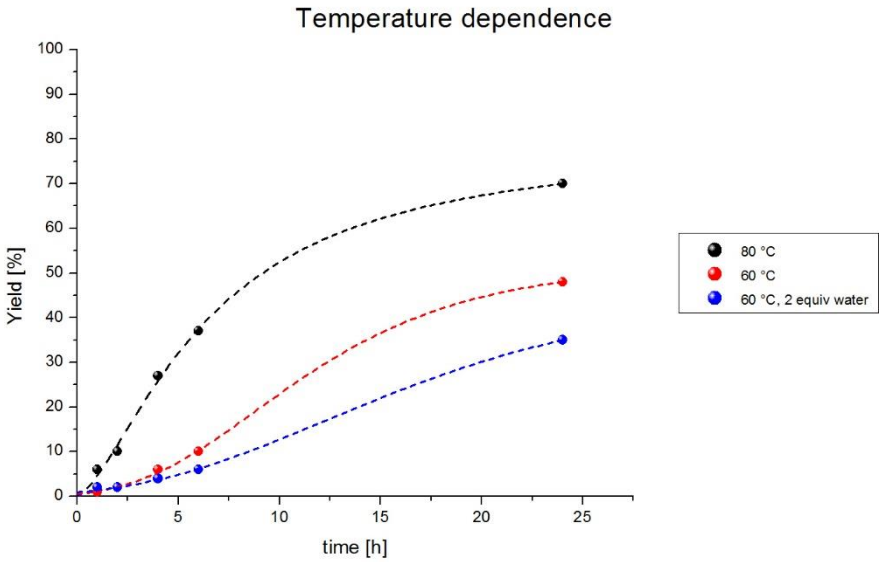
Scheme 6. Various photoredox catalysts used for the initial screening experiments for the light mediated chiral tetrahydrofuran synthesis.

Table 1. Catalyst screening, solvent/temperature dependence and control experiments of the cyclization reaction of compound **3a**.



Entry	Catalyst, solvent, modification	Conversion [%][a]	Yield 4a [%][a]
1	$Cu(dap)_2Cl_2$ **11**	2	0
2	$Ru(bpy)_3Cl_2$ **12**	6	0
3	$[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ **13**	22	0
4	$Ir[dF(CF_3)ppy]_2(dtb\text{-}bpy)PF_6$ **14**	44	5
5	*fac*–$Ir(ppy)_3$ **15**	100	70
6	25 °C	0	0
7	40 °C	0	0
8	60 °C	89/100[b]	51/81[b]
9	60 °C	53[c]	36[c]
10	0.1 mol% **15**	64	18
11	0.2 mol% **15**	74	23
12	0.5 mol% **15**	75	38
13	1.0 mol% **15**	80	47
15	no light	1	0
16	no catalyst	5	0
17	oxygen atmosphere	26	8
18	CH_3CN	34	1

[a]2 mol% photoredox catalyst, **3a** (0.1 mmol), DMF (c = 0.1 M), 80 °C, 20 h. GC – FID Yield (Naphthalene as internal standard). [b]44 h, [c]2 equiv water, 24 h.



Scheme 7. Temperature dependence for the intramolecular cyclization of **4a** at 60 °C and 80 °C. *Reaction conditions*: 2 mol% photoredox catalyst **15**, **3a** (0.1 mmol), DMF (c = 0.1 M), N_2. GC – FID Yield (Naphthalene as internal standard).

4.4 Comparison of batch and microreactor systems

Having identified the best reaction conditions using 1.0 mol% *fac*–Ir(ppy)$_3$ as photoredox catalyst, we scaled up from 0.1 mmol to a preparative scale of 1.0 mmol, while keeping all other parameters constant. Since the light intensity decreases in a larger reaction flask, prolonged reaction times of 7 days were required to achieve full conversion and 54% isolated yield of **4a** (Table 2, entry 1).

Setting up the reaction in a microreactor would give numerous advantages compared to conventional batch mode, as was already discussed on multiple occasions in the context of photochemistry.[14,15] The higher surface and improved miscibility of the continuous flow mode, typically offers shorter reaction times, higher yields, lower catalyst loadings, and makes upscaling trivial. By performance of the reaction in a microreactor, full conversion was achieved after only 28 h at a pump rate of 0.35 mL/h and yielded 73% of **4a**, which is a 19% increase compared to the batch reaction system (Table 2, entry 2).

Table 2. Comparison of yield and reaction time in a batch reaction and microreactor.

Entry	Reaction system	Time	Conversion 3a [%][a]	Yield 4a [%][b]
1	batch	7 d	100	54
2	microreactor[c]	28 h	100	73

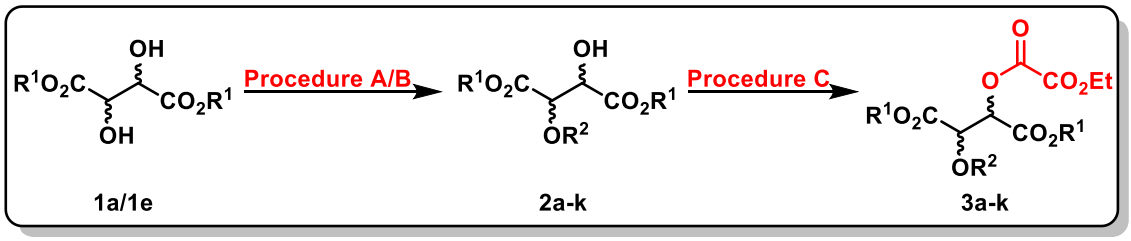
[a]Oxalate ester (1 mmol) **3a** , *fac*–Ir(ppy)$_3$ (1.0 mol%), DMF (c = 0.1 M), 80 °C, 455 nm LED irradation, N_2 atmosphere. GC-FID yield using naphthalene as internal standard [b]isolated yields [c]flow rate 0.35 mL/h.

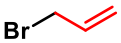
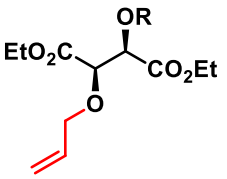
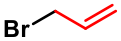
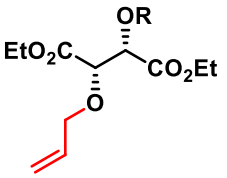
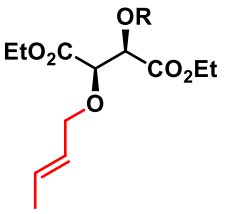
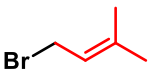
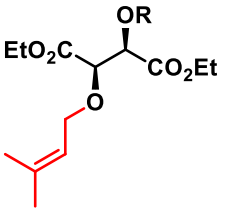
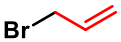
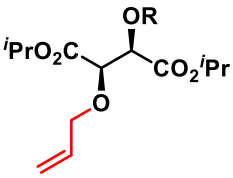
4.5 Preparation of starting materials

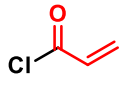
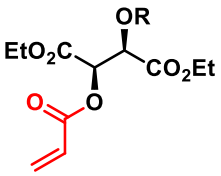
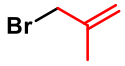
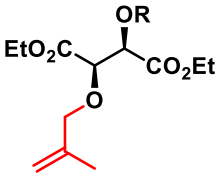
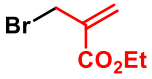
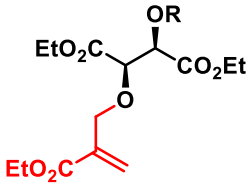
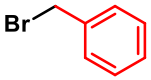
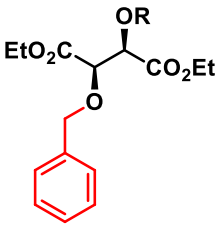
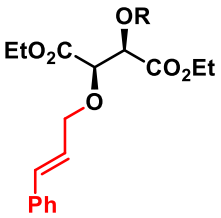
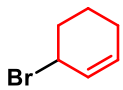
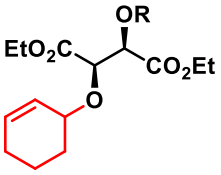
Having identified the best reaction conditions for the visible light mediated tetrahydrofuran preparation in a microreactor system, multiple allylated tartrate derivatives were synthesized to explore the substrate scope (Table 3). Both enantiomers, (+)-diethyl tartrate **1a** and (-)-diethyl tartrate **1b** gave good yields of the mono-allylated products **2a** and **2b** following the procedure of Onomura *et al*.[9] using K_2CO_3 as base, copper(II) chloride as Lewis acid and allyl bromide as coupling reagent in DMF at ambient temperature (Table 3, entry 1 and 2). In order to improve the diastereomeric ratio of the initial test compound **3a**, slightly sterically more demanding allyl groups were investigated. Reaction of (+)-diethyl tartrate **1a** with crotyl bromide or 1-bromo-3-methylbut-2-ene gave compounds **2c** and **2d** in 48% and 60% yield, respectively (Table 3, entry 3 and 4). Moreover, (+)-diethyl tartrate **1a** was replaced by (+)-diisopropyl tartrate **1e** to increase bulkiness (Table 3, entry 5). Acryloyl chloride as coupling reagent yielded 46% of the corresponding allylated hydroxysuccinate **2f** including an additional carbonyl group at the allylic moiety (Table 3, entry 6). So far, three possible stereocenters could be generated for the chiral tetrahydrofurans by using the aforementioned allylated tartrates. Therefore, substituted coupling reagents in β-position ensure a reduction to two stereocenters by creating a tertiary carbon center in a 5-*exo*-trig cyclization (Table 3, entry 7 and 8). Allylated alcohol **2g** with an additional methyl group in β-position yielded moderate 42% (Table 3, entry 7), whereas improved yield of 65% was achieved for α,β-unsaturated ester **2h** (Table 3, entry 8). Considering a possible limitation of the visible light mediated cyclization, mono-benzoylation of (+)-diethyl tartrate **1a** was performed in 46% yield (Table 3, entry 9). The five membered ring cyclization of its corresponding oxalate ester **2i** could lead to a dearomatization of the energetically more favored benzyl ring. Furthermore, 18% and 52% yield were achieved for the cinnamyl hydroxysuccinate **2j** and cyclohexene derivative **2k** by treatment of (+)-diethyl tartrate **1a** with silver(I) oxide in Et_2O (Table 3, entry 9 and 10).[16] Both compounds are contemplable as limitations due to their steric hindrance and additional conjugation in case of cinnamyl

hydroxysuccinate **2j**. In a second synthesis step, the remaining hydroxyl group was esterified in a S_N2 reaction by ethyl 2-chloro-2-oxoacetate in the presence of $^{i}Pr_2NEt$ as base in dry CH_2Cl_2 (Table 3, Procedure C). The oxalate moiety ensures the photoinduced carbon – oxygen bond cleavage and subsequent radical formation at the α-carbonyl position from where radical cyclization can occur. In general, esterification of the mono-allylated compounds gave excellent yields after very short reaction times of 10 - 30 min. (Table 3, entry 1-5 and 8-11). In case of (*2R,3R*)-diethyl 2-(2-ethoxy-2-oxoacetoxy)-3-((2-methylallyl)oxy)succinate **3g** (Table 3, entry 7) only 46% yield could be achieved, whereas no isolation was possible for the corresponding oxalate ester of **3f** (Table 3, entry 6). The product immediately polymerized after solvent evaporation. Moreover, attempts for a photoredox catalyzed ring formation by *in situ* generated oxalate ester **3f** and subsequent performance of the photoreaction were not successful.

Table 3. Synthesis of allylated alcohols **2a-k** and continuative ethyl oxalate esters **3a-k**.



Entry	Coupling reagent	Product	Yield [%]	
			R = H[a]	R = Oxalate[c]
1		 2a/3a	65	99
2		 2b/3b	70	89
3		 2c/3c	48	99
4		 2d/3d	60	95
5		 2e/3e	38	100

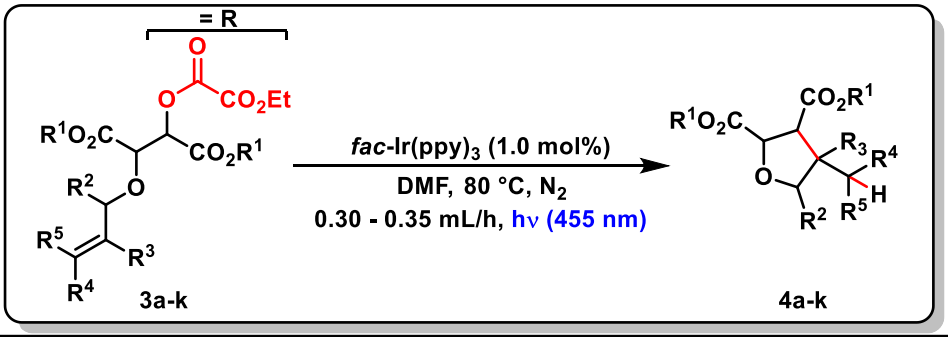
6		 2f/3f	46	0
7		 2g/3g	42	46
8		 2h/3h	65	100
9		 2i/3i	46	97
10		 2j/3j	18[b]	93
11		 2k/3k	52[b]	89

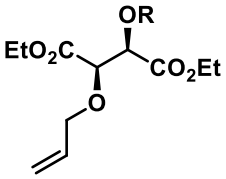
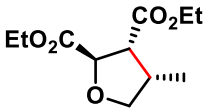
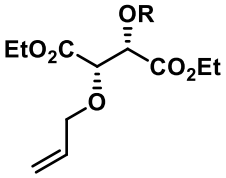
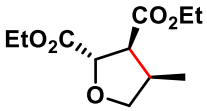
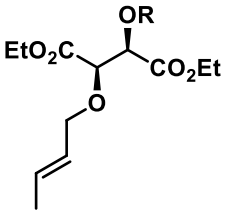
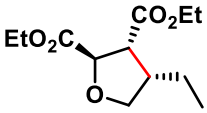
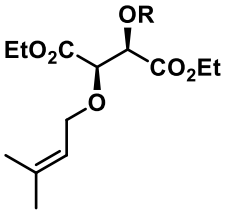
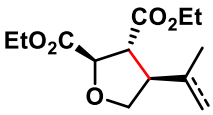
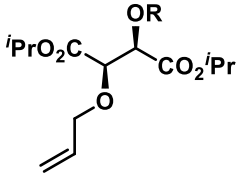
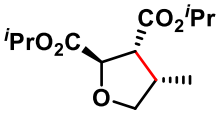
[a]**Procedure A**: Dihydroxysuccinate **1a** or **1e** (1.0 equiv), $CuCl_2$ (0.1 equiv), K_2CO_3 (1.5 equiv), coupling reagent (2.0 equiv), DMF (c = 0.5 M), 25 °C, isolated yields [b]**Procedure B**: Dihydroxysuccinate **1a** (1.0 equiv), Ag_2O (2.6 equiv), coupling reagent (1.0 equiv), dry Et_2O (c = 0.25 M), reflux, isolated yields [c]**Procedure C**: Hydroxysuccinate **2a-k** (1.0 equiv), $^iPr_2NEt$ (1.1 equiv), Ethyl 2-chloro-2-oxoacetate (1.1 equiv), dry CH_2Cl_2, N_2, 0 °C – 25 °C, isolated yields. R^1 = Et, ^{i}Pr, R^2 = allyl group.

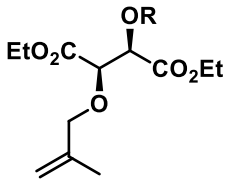
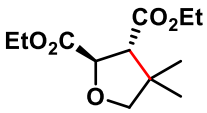
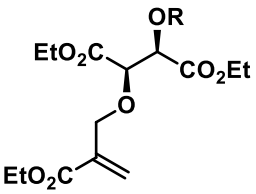
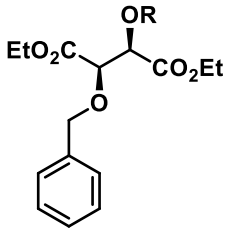
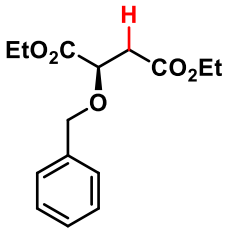
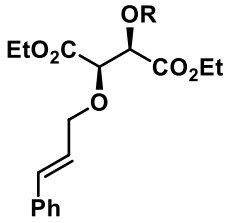
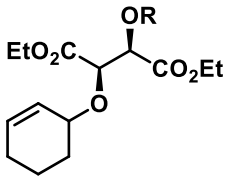
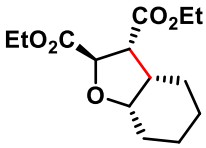
4.6 Visible light mediated deoxygenation following an intramolecular 5-*exo* trig cyclization

The photoinduced cyclization of chiral tetrahydrofurans was performed in a microreactor using *fac*–Ir(ppy)$_3$ **15** as photoredox catalyst in DMF at 80 °C (Table 4). The aforementioned allyloxy succinate **3a** yielded 73% of the corresponding tetrahydrofuran **4a** in a diastereomeric ratio of 62:28:8:2 (Table 4, entry 1) at a flow rate of 0.35 mL/h in analytical pure form after filtration through a short plug of silica. The second enantiomer **3b** was prepared to verify that the induced stereocenter of the allylic moiety has no effect on the stereoselectivity (Table 4, entry 2). 71% yield of the inverted tetrahydrofuran **4b** at a diastereomeric ratio of 57:37:6 was isolated. Chirality at the allylated hydroxyl function during the photoredox process is preserved as is evident from the comparison of chiral HPLC analysis of **4a** and **4b**. Concerning steric hindrance, allylic succinate derivative **3c** including an additional methyl group at the γ-position yielded 75% of **4c**, however, no improvement of the diasteromeric ratio (60:34:5:1) was observed (Table 4, entry 3). A further increase of steric bulk in γ-position with a second methyl group, on the one hand diminished the product yield from 75% to 53%, while on the other hand also inverting the stereochemistry in 3-position, exclusively gave the all-trans configured tetrahydrofuran derivative **4d** (Table 4, entry 4). Moreover, major amounts of alkene were observed, originating from a hydrogen elimination rather than an abstraction after cyclization. Replacement of ethyl ester backbone structure by more bulky isopropyl esters yielded 65% of the cyclized diisopropyl containing product **4e**, although the diastereoselectivity prevalence remained unchanged with a ratio of 60:32:5:3 (Table 4, entry 5). Methyl substitution in β-position in **3g** again gave good product yield of 70% of the corresponding tetrahydrofuran derivative **4g** with excellent diastereomeric induction (Table 4, entry 6). By construction of a quaternary carbon, only two diastereomeric centers are formed. Considering the induced stereocenter and the steric hindrance of the ethyl ester groups, only one enantiomer was detected. α,β-unsaturated compound **4h** containing an electron withdrawing ester group at the γ-position did not give the desired cyclized product and decomposed during the photocatalyzed reaction (Table 4, entry 7). For benzylated succinate derivative **3i** only simple deoxygenation was observed, hence 5-membered as well as 6-membered ring cyclization was not feasible as it would have required dearomatization of the energetically favorable π system (Table 4, entry 8). Neither deoxygenation nor light mediated cyclization was observed for conjugated cinnamyl including succinate **3j** (Table 4, entry 9). Bulky cyclohexenated derivative **3k** yielded 54% of the corresponding cyclohexenyl annulated tetrahydrofuran **4k** in a diasteromeric ratio of 57:43 *via* carbon – carbon bond formation (Table 4, entry 10).

Table 4. Photoredox catalyzed synthesis of chiral tetrahydrofurans.



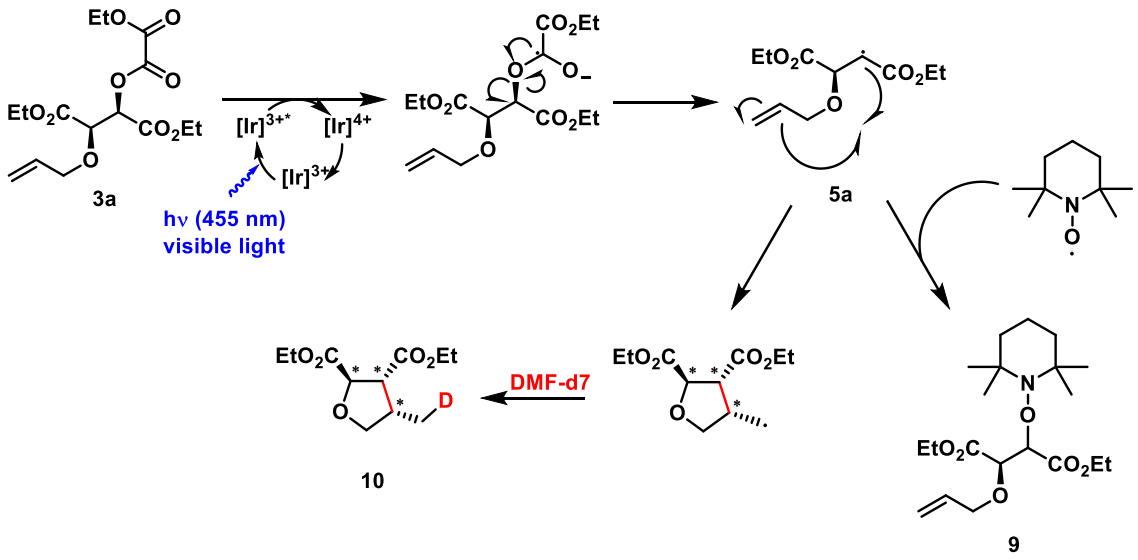
Entry	Substrate	Product	Yield [%][a]
1	 3a	 d.r. 62:28:8:2 4a	73
2	 3b	 d.r. 57:37:6 4b	71
3	 3c	 d.r. 60:34:5:1 4c	75
4	 3d	 4d	53[b]
5	 3e	 d.r. 60:32:5:3 4e	65

6	 **3g**	 **4g**	**70**
7	 **3h**		**decomp.**
8	 **3i**	 **4i**	**64**
9	 **3j**		**0**
10	 **3k**	 **d.r. 57:43** **4k**	**54**

[a]isolated yields. [b]alkane/alkene ratio (25 : 75). R^1 = Et, ^{i}Pr; R^2 = H, cyclohexen; R^3 = H, Me, CO_2Et; R^4 = H, Me, Ph; R^5 = H, Me.

4.7 Proposed reaction mechanism

We assumed that the mechanism of the 5-*exo*-trig cyclization process involves an electron uptake by the oxalate ester moiety from the visible light mediated excited triplet state of the Ir^{3+*} species followed by several defragmentation steps and the generation of an α-carbonyl radical **5a**, which undergoes an intramolecular cyclization with the opposite allylic moiety. After carbon – carbon bond formation subsequent hydrogen abstraction from the solvent takes place. Regeneration of the photocatalyst is accomplished by reduction with either ethyl oxalate[17] or solvent. Emerging radical species were characterized by trapping with TEMPO (2,2,6,6-tetramethylpiperdinyloxyl) to give **9**. In the presence of DMF-d7 chiral tetrahydrofuran **10** was observed by deuteration at the terminal methyl group (Scheme 8).



Scheme 8. Proposed mechanism for a visible light mediated deoxygenation of **3a** following a 5-*exo*-trig cyclization for the synthesis of chiral tetrahydrofuran. Trapping of the radical species with TEMPO and hydrogen abstraction from DMF-d7.

4.8 Conclusion

In summary, a mild protocol for the preparation of chiral tetrahydrofuran derivatives was developed based on the visible light mediated deoxygenation of mono-allylated succinates followed by an intramolecular 5-*exo* trig cyclization. The method features inexpensive, naturally occurring, chiral starting materials (tartrates) and a sustainable activation of the hydroxyl group. Radical reaction was realized by the transformation of the remaining hydroxyl group into ethyl oxalate ester in very good yield. Continuative photoredox catalyzed reaction for sugar analogues under mild reaction conditions only requires heat, photoredox catalyst and visible light. Moreover, improvement in yield and reaction time was achieved by the use of microreactor technology.

4.9 Experimental part

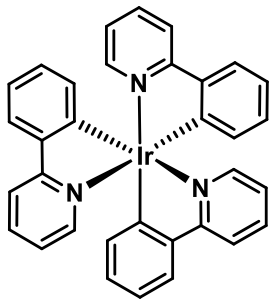
Experimental details, characterization data and spectra

4.9.1 General information

All chemicals were used as received or purified according to Purification of Common Laboratory Chemicals. Glassware was dried in an oven at 110 °C or flame dried and cooled under a dry atmosphere prior to use. All reactions were performed using Schlenk techniques. Blue light irradiation in batch processes was performed using a CREE XLamp XP-E D5-15 LED (λ = 450-465 nm). In micro reactor processes 8 OSRAM OSLON Black Series LD H9GP LEDs (λ = 455±10 nm) were employed. Analytical thin layer chromatography was performed on Merck TLC aluminum sheets silica gel 60 F 254. Reactions were monitored by TLC and visualized by a short wave UV lamp and stained with a solution of potassium permanganate, *p*-anisaldehyde, or Seebach's stain. Column flash chromatography was performed using Merck flash silica gel 60 (0.040-0.063 mm). The melting points were measured on an automated melting point system (MPA 100) with digital image processing technology by Stanford Research Systems. ATR-IR spectroscopy was carried out on a Biorad Excalibur FTS 3000 spectrometer, equipped with a Specac Golden Gate Diamond Single Reflection ATR-System. NMR spectra were recorded on Bruker Avance 300 and Bruker Avance 400 spectrometers. Chemical shifts for ^{1}H NMR were reported as δ, parts per million, relative to the signal of $CHCl_3$ at 7.26 ppm. Chemical shifts for ^{13}C NMR were reported as δ, parts per million, relative to the center line signal of the $CDCl_3$ triplet at 77 ppm. Coupling constants *J* are given in Hertz (Hz). The following notations indicate the multiplicity of the signals:

s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, p = quintet, sept = septet, and m = multiplet. DEPT-135 for Avance 400 CH_3, CH peaks down, CH_2 peaks up. DEPT-135 for Avance 300 CH_3, CH peaks up, CH_2 peaks down. Mass spectra were recorded at the Central Analytical Laboratory at the Department of Chemistry of the University of Regensburg on a Varian MAT 311A, Finnigan MAT 95, Thermoquest Finnigan TSQ 7000 or Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS. Gas chromatographic analyses were performed on a Fisons Instuments gas chromatograph equipped with a capillary column (30 m × 250 µm × 0.25 µm) and a flame ionization detector. The yields reported are referred to the isolated compounds unless otherwise stated.

4.9.2 Synthesis of *fac*-Ir(ppy)$_3$[1,2] photoredox catalyst



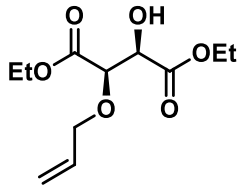
***fac*-Ir(ppy)$_3$**[18]

Following the literature procedure using 2-phenylpyridine (1.05 g, 6.75 mmol, 5.00 equiv), tetrakis(2-phenylpyridine-*C2*,*N'*)(*µ*-dichloro)diiridium[19] (1.45 g, 1.35 mmol, 1.00 equiv), AgOTf (694 mg, 2.84 mmol, 2.00 equiv) and 2-ethoxyethanol (130 mL), refluxed for 24 h to give 1.51 g (85%) as a yellow solid after flash column purification (CH_2Cl_2 / hexanes 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.88 (d, *J* = 8.3 Hz, 3H), 7.65 (d, *J* = 7.4 Hz, 3H), 7.62 – 7.57 (m, 3H), 7.56 – 7.51 (m, 3H), 6.94 – 6.80 (m, 12H).

4.9.3 General procedure *GPI* & *GPII* for the synthesis of monoallylated compounds[9,16]

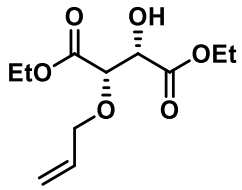
a. GPI[9]

A 25 mL round bottom flask equipped with a magnetic stir bar was charged with dihydroxysuccinate (5.00 mmol, 1.00 equiv), 67.2 mg $CuCl_2$ (500 μmol, 0.100 equiv), 1.04 g K_2CO_3 (7.50 mmol, 1.50 equiv) and dissolved in DMF (10.0 mL, 0.5 M). Allylating reagent (10.0 mmol, 2.00 equiv) was added dropwise at 25 °C. After stirring for three days, the mixture was poured into water (100 mL) and extracted with EtOAc (4 x 100 mL). The organic layers were combined, dried over Na_2SO_4 and evaporated under reduced pressure. The obtained residue was purified by automatic flash silica gel column chromatography.



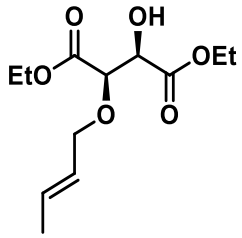
(*2R,3R*)-diethyl 2-(allyloxy)-3-hydroxysuccinate (2a)[9]

Following general procedure ***GPI*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate **1a** (10.3 g, 50.0 mmol, 1.00 equiv), $CuCl_2$ (672 mg, 5.00 mmol, 0.100 equiv), K_2CO_3 (10.4 g, 75.0 mmol, 15.0 equiv), DMF (100 mL, 0.5 M) and allyl bromide (8.65 mL, 12.1 g, 100 mmol, 2.00 equiv) gave 8.05 g (32.7 mmol, 65%) of (*2R,3R*)-diethyl 2-(allyloxy)-3-hydroxysuccinate as a colorless oil after automatic column purification (hexanes / EtOAc 100:0 – 0:100). ^{1}H NMR (300 MHz, $CDCl_3$): 5.81 (dddd, *J* = 17.0, 10.3, 6.5, 5.3 Hz, 1H), 5.32 – 5.12 (m, 2H), 4.59 (s, 1H), 4.39 – 4.19 (m, 6H), 3.92 (ddt, *J* = 12.7, 6.6, 1.2 Hz, 1H), 3.08 (bs, 1H), 1.31 (td, *J* = 7.1, 0.9 Hz, 6H).



(*2S,3S*)-diethyl 2-(allyloxy)-3-hydroxysuccinate (2b)

Following general procedure ***GPI*** using (*2S,3S*)-diethyl 2,3-dihydroxysuccinate **1b** (1.03 g, 5.00 mmol, 1.00 equiv), $CuCl_2$ (67.2 mg, 500 μmol, 0.100 equiv), K_2CO_3 (1.04 g, 7.50 mmol, 1.50 equiv), DMF (10.0 mL, 0.5 M) and allyl bromide (865 μL, 1.21 g, 10.0 mmol, 2.00 equiv) gave 867 mg (3.52 mmol, 70%) of (*2S,3S*)-diethyl 2-(allyloxy)-3-hydroxysuccinate as a colorless oil after automatic column purification (hexanes / EtOAc 100:0 – 0:100). R_f (hexanes / EtOAc 1:1) = 0.73; IR (neat): 3512, 2988, 2937, 2162, 1983, 1946, 1745, 1464, 1369, 1254, 1195, 1139, 1089, 1021, 1020, 929, 860, 816, 691, 577, 470, 431 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 5.82 (dddd, *J* = 17.0, 10.3, 6.5, 5.3 Hz, 3H), 5.31 – 5.15 (m, 6H), 4.60 (d, *J* = 2.3 Hz, 3H), 4.39 – 4.19 (m, 18H), 3.92 (ddt, *J* = 12.7, 6.5, 1.2 Hz, 3H), 3.05 (s, 2H), 1.32 (td, *J* = 7.1, 0.9 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): 171.28, 169.49, 133.52, 118.57, 78.40, 72.48, 72.33, 62.25, 61.71, 14.34; ^{13}C NMR (DEPT-135, 75 MHz, $CDCl_3$): 133.40, 118.45, 78.28, 72.36, 72.21, 62.13, 61.59, 14.22; HRMS (ESI) m/z calculated for $C_{11}H_{19}O_6$ ($[M+H]^+$) 247.1176, found 247.1175.



(*2R,3R*)-diethyl 2-((*E*)-but-2-en-1-yloxy)-3-hydroxysuccinate (2c)

Following general procedure ***GPI*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate **1a** (1.03 g, 5.00 mmol, 1.00 equiv), $CuCl_2$ (67.2 mg, 500 μmol, 0.100 equiv), K_2CO_3 (1.04 g, 7.50 mmol, 1.50 equiv), DMF (10.0 mL, 0.5 M) and crotyl bromide (1.03 mL, 1.35 g, 10.0 mmol, 2.00 equiv) gave 396 mg (1.52 mmol, 30%) of (*2R,3R*)-diethyl 2-((*E*)-but-2-en-1-yloxy)-3-hydroxysuccinate as a colorless oil as a mixture *E* / *Z* = 75:25 after automatic column purification (hexanes / EtOAc 100:0 – 0:100). R_f (hexanes / EtOAc 1:1) = 0.78; IR (neat): 2981, 2944, 2086, 1988, 1748, 1448, 1374, 1261, 1196, 1134, 1090, 1020, 968, 915, 869, 518, 426 cm^{-1}; HRMS (ESI) m/z calculated for $C_{12}H_{20}NaO_6$ ($[M+Na]^+$) 283.1152, found 283.1155.

^{1}H NMR (*E* - Isomer, 300 MHz, $CDCl_3$): 5.76 – 5.58 (m, 1H), 5.53 – 5.37 (m, 1H), 4.58 (s, 1H), 4.36 – 4.13 (m, 6H), 3.94 – 3.79 (m, 1H), 3.06 (bs, 1H), 1.69 (ddd, *J* = 6.4, 2.4, 1.1 Hz, 3H), 1.31 (td, *J* = 4.6, 2.3 Hz, 6H).

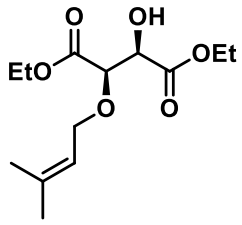
^{1}H NMR (*Z* - Isomer, 300 MHz, $CDCl_3$): 5.76 – 5.58 (m, 1H), 5.53 – 5.37 (m, 1H), 4.58 (s, 1H), 4.36 – 4.13 (m, 6H), 4.13 – 4.01 (m, 1H), 3.06 (bs, 1H), 1.64 – 1.27 (m, 3H), 1.31 (td, *J* = 7.1, 1.2 Hz, 6H).

^{13}C NMR (*E* - Isomer, 75 MHz, $CDCl_3$): 171.33, 169.68, 131.28, 126.40, 125.44, 77.80, 72.49, 71.99, 62.17, 61.63, 17.91, 14.34.

^{13}C NMR (*Z* - Isomer, 75 MHz, $CDCl_3$): 171.28, 169.66, 129.67, 125.44, 78.04, 72.52, 71.99, 66.13, 62.17, 61.63, 14.34, 13.21.

^{13}C NMR (*E* - Isomer, 75 MHz, $CDCl_3$): 131.17, 126.28, 77.68, 72.38, 71.88, 62.06, 61.52, 17.80, 14.23.

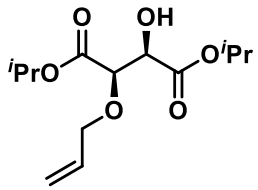
^{13}C NMR (*Z* - Isomer, 75 MHz, $CDCl_3$): 131.17, 125.33, 77.92, 72.41, 66.01, 62.06, 61.52, 17.80, 13.10.



(*2R,3R*)-diethyl 2-hydroxy-3-((3-methylbut-2-en-1-yl)oxy)succinate (2d)

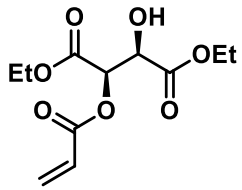
Following general procedure ***GPI*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate **1a** (2.06 g, 10.0 mmol, 1.00 equiv), $CuCl_2$ (134 mg, 1.00 mmol, 0.100 equiv), K_2CO_3 (2.07 g, 15.0 mmol, 1.50 equiv), DMF (20.0 mL, 0.5 M) and 1-bromo-3-methylbut-2-ene (2.31 mL, 2.98 g, 20.0 mmol, 2.00 equiv) gave 1.63 g (5.95 mmol, 60%) of (*2R,3R*)-diethyl 2-hydroxy-3-((3-methylbut-2-en-1-yl)oxy)succinate as a colorless oil after automatic column purification (hexanes / EtOAc 100:0 – 0:100). R_f (hexanes / EtOAc 1:1) = 0.68; IR (neat): 3675, 3501, 2979, 2910, 2205, 2126, 1976, 1744, 1738, 1450, 1373, 1259, 1199, 1135, 1090, 1017, 861, 781, 697, 605, 437 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 5.19 (ttd, *J* = 6.7, 2.8, 1.4 Hz, 1H), 4.51 (dd, *J* = 9.0, 7.2 Hz, 1H), 4.27 – 4.13 (m, 6H), 4.00 – 3.85 (m, 1H), 3.09 (d, *J* = 8.4 Hz, 1H), 1.74 – 1.64 (m, 3H), 1.58 (s, 3H), 1.26 (tt, *J* = 4.2, 2.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 171.21, 169.67, 138.78, 119.71, 77.63, , 72.39, 67.19,

61.97, 61.43, 25.80, 17.90, 14.21, 14.19; ^{13}C NMR (DEPT-135, 75 MHz, $CDCl_3$): 119.67, 77.59, 72.36, 67.15, 61.94, 61.39, 25.76, 17.86, 14.18, 14.16; HRMS (ESI) m/z calculated for $C_{13}H_{22}NaO_6$ ($[M+Na]^+$) 297.1309, found 297.1308.



(*2R,3R*)-diisopropyl 2-(allyloxy)-3-hydroxysuccinate (2e)

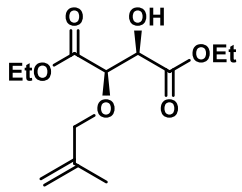
Following general procedure ***GPI*** using (*2R,3R*)-diisopropyl 2,3-dihydroxysuccinate **1e** (1.17 g, 5.00 mmol, 1.00 equiv), $CuCl_2$ (67.2 mg, 500 μmol, 0.100 equiv), K_2CO_3 (1.04 g, 7.50 mmol, 1.50 equiv), DMF (10.0 mL, 0.5 M) and allyl bromide (865 μL, 1.21 g, 10.0 mmol, 2.00 equiv) gave 525 mg (1.91 mmol, 38%) of (*2R,3R*)-diisopropyl 2-(allyloxy)-3-hydroxysuccinate as a colorless oil after automatic column purification (hexanes / EtOAc 100:0 – 0:100). R_f (hexanes / EtOAc 1:1) = 0.74; IR (neat): 3489, 2984, 1745, 1467, 1375, 1264, 1204, 1144, 1101, 1000, 935, 823, 722, 425 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 5.92 – 5.75 (m, 1H), 5.24 (ddd, *J* = 17.3, 3.0, 1.4 Hz, 1H), 5.21 – 5.10 (m, 3H), 4.54 (d, *J* = 2.1 Hz, 1H), 4.33 – 4.22 (m, 2H), 3.91 (dd, *J* = 12.5, 6.4 Hz, 1H), 3.05 (s, 1H), 1.29 (dd, *J* = 9.1, 4.4 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$): 170.86, 169.03, 133.67, 118.38, 78.73, 77.48, 72.39, 70.16, 69.45, 21.99, 21.94, 21.93, 21.91; ^{13}C NMR (DEPT-135, 101 MHz, $CDCl_3$): 133.53, 118.25, 78.58, 72.40, 72.26, 70.02, 69.32, 21.85, 21.80, 21.79, 21.77; HRMS (ESI) m/z calculated for $C_{13}H_{23}O_6$ ($[M+H]^+$) 276.1523, found 276.1523.



(*2R,3R*)-diethyl 2-(acryloyloxy)-3-hydroxysuccinate (2f)

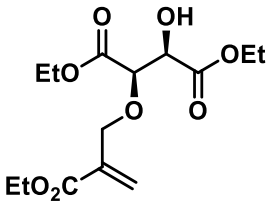
Following general procedure ***GPI*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate **1a** (1.03 g, 5.00 mmol, 1.00 equiv), $CuCl_2$ (67.2 mg, 500 μmol, 0.100 equiv), K_2CO_3 (1.04 g, 7.50 mmol, 1.50 equiv), DMF (10.0 mL, 0.5 M) and acryloyl chloride (812 μL, 905 mg, 10.0 mmol, 2.00 equiv) gave 602 mg (2.31 mmol, 46%) of (*2R,3R*)-diethyl 2-(acryloyloxy)-3-hydroxysuccinate as a colorless oil after automatic column purification (hexanes / EtOAc 100:0 – 0:100). R_f (hexanes / EtOAc 2:1) = 0.73; IR (neat): 3493, 2985, 1731, 1637, 1473, 1451, 1407, 1370, 1253, 1172, 1132, 1068, 1017,

985, 927, 858, 808, 702, 584, 445 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 6.49 (dd, *J* = 17.3, 1.3 Hz, 1H), 6.18 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.93 (dd, *J* = 10.4, 1.3 Hz, 1H), 5.52 (d, *J* = 2.3 Hz, 1H), 4.78 (d, *J* = 1.2 Hz, 1H), 4.34 – 4.14 (m, 4H), 3.18 (bs, 1H), 1.28 (dt, *J* = 15.8, 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 170.84, 166.61, 164.82, 132.98, 127.05, 73.16, 70.69, 62.79, 62.36, 14.23, 14.21; ^{13}C NMR (DEPT-135, 75 MHz, $CDCl_3$): 132.87, 126.93, 73.04, 70.57, 62.67, 62.24, 14.11, 14.09; HRMS (ESI) m/z calculated for $C_{11}H_{17}O_7$ ($[M+H]^+$)261.0969, found 261.0970.



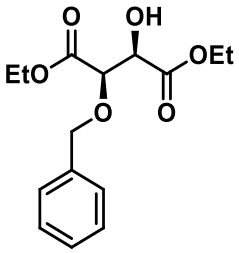
(*2R,3R*)-diethyl 2-hydroxy-3-((2-methylallyl)oxy)succinate (2g)

Following general procedure ***GPI*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate **1a** (1.03 g, 5.00 mmol, 1.00 equiv), $CuCl_2$ (67.2 mg, 500 μmol, 0.100 equiv), K_2CO_3 (1.04 g, 7.50 mmol, 1.50 equiv), DMF (10.0 mL, 0.5 M) and 3-bromo-2-methylprop-1-ene (1.01 mL, 1.35 g, 10.00 mmol, 2.00 equiv) gave 545 mg (2.10 mmol, 42%) of (*2R,3R*)-diethyl 2-hydroxy-3-((2-methylallyl)oxy)succinate as a colorless oil after automatic column purification (hexanes / EtOAc 100:0 – 0:100). R_f (hexanes / EtOAc 3:1) = 0.64; IR (neat): 3499, 2983, 2370, 2209, 2019, 1742, 1452, 1371, 1258, 1196, 1135, 1096, 1023, 908, 862, 550, 472 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 4.90 (dd, *J* = 1.9, 0.9 Hz, 2H), 4.59 (d, *J* = 2.2 Hz, 1H), 4.35 – 4.17 (m, 6H), 3.81 (d, *J* = 12.0 Hz, 1H), 3.03 (bs, 1H), 1.69 (s, 3H), 1.31 (td, *J* = 7.1, 2.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 171.31, 169.44, 140.99, 113.96, 78.60, 75.34, 72.50, 62.24, 61.67, 19.55, 14.34, 14.29; ^{13}C NMR (DEPT-135, 75 MHz, $CDCl_3$): 113.84, 78.48, 75.22, 72.38, 62.12, 61.56, 19.43, 14.22, 14.17; HRMS (ESI) m/z calculated for $C_{12}H_{21}O_6$ ($[M+H]^+$) 261.1333, found 261.1334.



(*2R,3R*)-diethyl 2-((2-(ethoxycarbonyl)allyl)oxy)-3-hydroxysuccinate (2h)

Following general procedure ***GPI*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate **1a** (1.03 g, 5.00 mmol, 1.00 equiv), $CuCl_2$ (67.2 mg, 500 μmol, 0.100 equiv), K_2CO_3 (1.04 g, 7.50 mmol, 1.50 equiv), DMF (10.0 mL, 0.5 M) and ethyl 2-(bromomethyl)acrylate (693 μL, 965 mg, 5.00 mmol, 1.00 equiv) gave 1.03 g (3.24 mmol, 65%) of (*2R,3R*)-diethyl 2-((2-(ethoxycarbonyl)allyl)oxy)-3-hydroxysuccinate as a colorless oil after automatic column purification (hexanes / EtOAc 100:0 – 0:100). R_f (hexanes / EtOAc 1:1) = 0.7; IR (neat): 3493, 2983, 1726, 1640, 1260, 1189, 1138, 1098, 1017, 959, 861, 593, 471, 440 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 6.34 – 6.26 (m, 1H), 5.85 (q, *J* = 1.6 Hz, 1H), 4.61 (d, *J* = 2.4 Hz, 1H), 4.56 – 4.50 (m, 1H), 4.37 (d, *J* = 2.4 Hz, 1H), 4.34 – 4.16 (m, 6H), 4.12 (ddd, *J* = 4.9, 3.4, 2.1 Hz, 1H), 3.11 (bs, 1H), 1.30 (dtd, *J* = 9.0, 7.1, 1.9 Hz, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): 171.23, 169.20, 165.63, 136.56, 126.77, 79.84, 72.43, 69.68, 62.31, 61.79, 60.96, 14.33, 14.29; ^{13}C NMR (DEPT-135, 101 MHz, $CDCl_3$): 126.64, 79.70, 72.29, 69.54, 62.18, 61.66, 60.83, 14.19, 14.16; HRMS (ESI) m/z calculated for $C_{14}H_{23}O_8$ ($[M+H]^+$) 319.1387, found 319.1387.



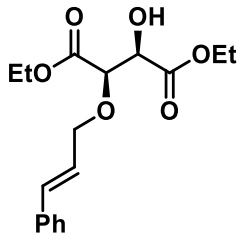
(*2R,3R*)-diethyl 2-(benzyloxy)-3-hydroxysuccinate (2i)[20]

Following general procedure ***GPI*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate **1a** (1.03 g, 5.00 mmol, 1.00 equiv), $CuCl_2$ (67.2 mg, 500 μmol, 0.100 equiv), K_2CO_3 (1.04 g, 7.50 mmol, 1.50 equiv), DMF (10.0 mL, 0.5 M) and (bromomethyl)benzene (1.19 mL, 1.71 g, 10.0 mmol, 2.00 equiv) gave 685 mg (2.31 mmol, 46%) of (*2R,3R*)-diethyl 2-(benzyloxy)-3-hydroxysuccinate as a colorless oil after automatic column purification (hexanes / EtOAc 100:0 – 0:100). R_f (hexanes / EtOAc 1:1) = 0.78; IR (neat): 3530, 2978, 2352, 2314, 2197, 2169, 2116, 2051, 1745, 1455, 1367,

1260, 1196, 1136, 1093, 1023, 862, 744, 699, 588, 434 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): 7.37 – 7.21 (m, 5H), 4.85 (d, *J* = 11.9 Hz, 1H), 4.57 (s, *J* = 15.0 Hz, 1H), 4.40 (d, *J* = 11.9 Hz, 1H), 4.34 – 4.14 (m, 4H), 4.03 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.19 (d, *J* = 6.7 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 171.15, 169.38, 136.79, 128.43, 128.31, 128.15, 78.15, 72.93, 72.36, 62.07, 61.63, 14.24, 14.05; ^{13}C NMR (DEPT-135, 75 MHz, $CDCl_3$): 128.41, 128.29, 128.13, 78.12, 72.90, 72.34, 62.05, 61.61, 14.22, 14.03; HRMS (ESI) m/z calculated for $C_{15}H_{20}NaO_6$ ($[M+Na]^+$) 319.1152, found 319.1155.

b. *GPII*[16]

A solution of dihydroxysuccinate (5.00 mmol, 1.00 equiv) and allylating reagent (5.00 mmol, 1.00 equiv) in dry Et_2O (20.0 mL, 0.25 M) was gently refluxed in the dark. Within 10 min., 3.01 g silver(I) oxide (13.0 mmol, 2.60 equiv) was added in three portions. After refluxing for 3 h the reaction mixture was stirred for 24 h. The residue was separated with water (20 mL) and washed repeatedly with Et_2O. The combined organic layers were dried over $NaSO_4$ and evaporated under reduced pressure. The obtained residue was purified by automatic flash silica gel column purification.



(*2R,3R*)-diethyl 2-(cinnamyloxy)-3-hydroxysuccinate (2j)

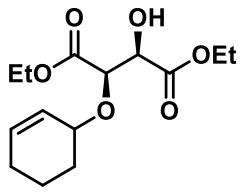
Following general procedure ***GPII*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate **1a** (1.03 g, 5.00 mmol, 1.00 equiv), (*E*)-(3-chloroprop-1-en-1-yl)benzene (686 μL, 762 mg, 5.00 mmol, 1.00 equiv), dry Et_2O (20.0 mL, 0.25 M) and silver(I) oxide (3.01 g, 13.0 mmol, 2.60 equiv) gave 289 mg (900 μmol, 18%) of (*2R,3R*)-diethyl 2-(cinnamyloxy)-3-hydroxysuccinate as a colorless oil as a mixture *E / Z* = 92 : 18 after automatic column purification (hexanes / EtOAc, 100:0 – 0:100). R_f (hexanes / EtOAc 3:1) = 0.26; IR (neat): 3497, 2982, 2196, 2014, 1963, 1741, 1449, 1394, 1369, 1261, 1196, 1138, 1103, 1024, 969, 912, 862, 804, 732, 693, 591 cm^{-1}; HRMS (ESI) m/z calculated for $C_{17}H_{23}O_6$ ($[M+H]^+$) 323.1489, found 323.1476.

^{1}H NMR (E - Isomer, 400 MHz, $CDCl_3$): 7.40 – 7.22 (m, 5H), 6.56 (d, *J* = 15.9 Hz, 1H), 6.19 (ddd, *J* = 15.9, 6.9, 5.8 Hz, 1H), 4.62 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.45 (ddd, *J* = 12.6, 5.8, 1.4 Hz, 1H), 4.37 (d, *J* = 2.4 Hz, 1H), 4.34 – 4.21 (m, 4H), 4.11 (ddd, *J* = 12.5, 7.0, 1.2 Hz, 1H), 3.11 (d, *J* = 8.6 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{1}H NMR (Z - Isomer, 400 MHz, $CDCl_3$): 7.40 – 7.22 (m, 5H), 6.62 (d, *J* = 15.9 Hz, 1H), 6.37 (dt, *J* = 15.9, 5.7 Hz, 1H), 4.62 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.45 (ddd, *J* = 12.6, 5.8, 1.4 Hz, 1H), 4.37 (d, *J* = 2.4 Hz, 1H), 4.34 – 4.21 (m, 4H), 4.11 (ddd, *J* = 12.5, 7.0, 1.2 Hz, 1H), 3.11 (d, *J* = 8.6 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): 171.31, 169.56, 136.45, 133.94, 128.74, 128.13, 126.67, 124.65, 78.35, 72.53, 72.03, 62.27, 61.73, 14.35, 14.29.

^{13}C NMR (DEPT-135, 101 MHz, $CDCl_3$): 133.82, 128.62, 128.00, 126.54, 124.52, 78.22, 72.40, 71.91, 62.15, 61.61, 14.22, 14.16.



(*2R,3R*)-diethyl 2-(cyclohex-2-en-1-yloxy)-3-hydroxysuccinate (2k)

Following general procedure ***GPII*** using (*2R,3R*)-diethyl 2,3-dihydroxysuccinate **1a** (1.03 g, 5.00 mmol, 1.00 equiv), 3-bromocyclohex-1-ene (575 μL, 804 mg, 5.00 mmol, 1.00 equiv), dry Et_2O (20.0 mL, 0.25 M) and silver(I) oxide (3.01 g, 13.0 mmol, 2.60 equiv) gave 746 mg (2.60 mmol, 52%) of (*2R,3R*)-diethyl 2-(cyclohex-2-en-1-yloxy)-3-hydroxysuccinate as a colorless oil as a mixture of diastereomers (d.r.: 75 : 25) after automatic column purification (hexanes / EtOAc 100:0 – 0:100). R_f (hexanes / EtOAc 3:1) = 0.24; IR (neat): 3496, 2938, 2369, 1752, 1741, 1443, 1402, 1373, 1258, 1195, 1134, 1089, 1067, 1022, 962, 863, 802, 753, 725, 659, 533, 499 cm^{-1}; HRMS (ESI) m/z calculated for $C_{14}H_{23}O_6$ ($[M+H]^+$) 287.1489, found 287.1484.

^{1}H NMR (Major Diastereomer, 300 MHz, $CDCl_3$): 5.93 – 5.78 (m, 2H), 4.60 (dd, *J* = 5.2, 2.2 Hz, 1H), 4.42 (dd, *J* = 9.3, 2.3 Hz, 1H), 4.36 – 4.07 (m, 4H), 4.02 – 3.78 (m, 1H), 3.05 (s, 1H), 2.06 – 1.50 (m, 6H), 1.31 (m, 6H).

^{1}H NMR (Minor Diastereomer, 300 MHz, $CDCl_3$): 5.66 (ddd, *J* = 10.2, 5.3, 2.1 Hz, 2H), 4.60 (dd, *J* = 5.2, 2.2 Hz, 1H), 4.42 (dd, *J* = 9.3, 2.3 Hz, 1H), 4.36 – 4.07 (m, 4H), 4.02 – 3.78 (m, 1H), 3.05 (s, 1H), 2.06 – 1.50 (m, 6H), 1.31 (m, 6H).

^{13}C NMR (Major Diastereomer, 75 MHz, $CDCl_3$): 171.37, 170.20, 131.75, 127.14, 77.47, 73.05, 72.79, 62.22, 61.66, 27.32, 25.20, 18.54, 14.33, 14.30.

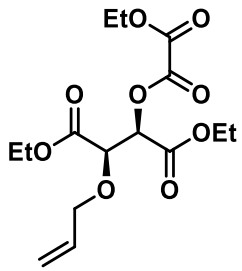
^{13}C NMR (Minor Diastereomer, 75 MHz, $CDCl_3$): 171.37, 170.22, 132.42, 125.68, 77.36, 73.48, 72.79, 62.17, 61.64, 29.06, 25.33, 18.88, 14.33, 14.30.

^{13}C NMR (DEPT-135, Major Diastereomer, 75 MHz, $CDCl_3$): 131.64, 127.01, 77.35, 72.93, 72.68, 62.10, 61.54, 27.20, 25.09, 18.42, 14.22, 14.19.

^{13}C NMR (DEPT-135, Minor Diastereomer, 75 MHz, $CDCl_3$): 132.31, 125.56, 77.05, 73.36, 72.68, 62.06, 61.54, 28.94, 25.21, 18.77, 14.22, 14.19.

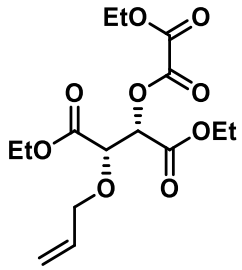
4.9.4 General procedure *GPIII* for the synthesis of ethyl oxalyl esters *via* acylation with ethyl 2-chloro-2-oxoacetate

A 50 mL Schlenk flask equipped with a magnetic stir bar was charged with monoallylated substrate (2.00 mmol, 1.00 equiv) and dissolved in dry CH_2Cl_2 (20.0 mL, 0.1 M) under N_2 atmosphere. $^{i}Pr_2NEt$ (374 μL, 284 mg, 2.20 mmol, 1.10 equiv) was added and the reaction mixture cooled down to 0 °C. Ethyl 2-chloro-2-oxoacetate (246 μL, 300 mg, 2.20 mmol, 1.10 equiv) was added dropwise and the reaction mixture was allowed to warm to room temperature. After complete esterification (as judged by TLC) the reaction mixture was quenched with water (10 mL) and extracted with EtOAc (30 mL). The organic layer was extracted with two portions of water (2 x 10 mL), dried over Na_2SO_4 and evaporated under reduced pressure. The obtained residue was purified by filtration through a short plug of flash silica gel.



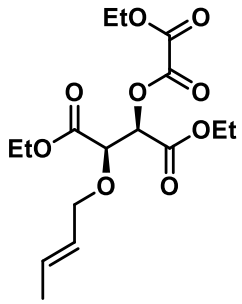
(*2R,3R*)-diethyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate (3a)

Following general procedure ***GPIII*** using (*2R,3R*)-diethyl 2-(allyloxy)-3-hydroxysuccinate **2a** (4.92 g, 20.0 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (3.74 mL, 2.84 g, 22.00 mmol, 1.10 equiv), dry CH_2Cl_2 (200 mL, 0.1 M) and ethyl 2-chloro-2-oxoacetate (2.46 mL, 3.00 g, 22.0 mmol, 1.10 equiv) gave 6.85 g (19.8 mmol, 99%) of (*2R,3R*)-diethyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate as an orange oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 3:1). R_f (hexanes / EtOAc 1:1) = 0.77; IR (neat): 2985, 1742, 1463, 1372, 1301, 1274, 1176, 1157, 1070, 1018, 928, 861, 815, 701, 460 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 5.92 – 5.78 (m, 1H), 5.67 (d, *J* = 3.5 Hz, 1H), 5.33 – 5.17 (m, 2H), 4.58 (d, *J* = 3.5 Hz, 1H), 4.40 – 4.18 (m, 7H), 4.04 (dd, *J* = 12.7, 6.7 Hz, 1H), 1.39 – 1.24 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): 167.99, 165.18, 156.96, 156.73, 133.15, 118.65, 75.97, 74.47, 72.73, 63.25, 62.31, 61.74, 13.97, 13.92, 13.73; ^{13}C NMR (DEPT-135, 101 MHz, $CDCl_3$): 133.18, 118.70, 75.99, 74.50, 72.77, 63.29, 62.35, 61.78, 14.02, 13.96, 13.77; HRMS (ESI) m/z calculated for $C_{15}H_{23}O_9$ ($[M+H]^+$) 347.1337, found 347.1339.



(*2S,3S*)-diethyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate (3b)

Following general procedure ***GPIII*** using (*2S,3S*)-diethyl 2-(allyloxy)-3-hydroxysuccinate **2b** (493 mg, 2.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (374 μL, 284 mg, 2.20 mmol, 1.10 equiv), dry CH_2Cl_2 (20 mL, 0.1 M) and ethyl 2-chloro-2-oxoacetate (246 μL, 300 mg, 2.20 mmol, 1.10 equiv) gave 620 mg (1.79 mmol, 89%) of (*2S,3S*)-diethyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate as an colorless oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc 1:1) = 0.86; IR (neat): 2983, 2362, 2216, 2048, 1775, 1748, 1453, 1372, 1307, 1270, 1179, 1155, 1071, 1016, 935, 859, 456, 434 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 5.84 (dddd, *J* = 17.1, 10.3, 6.7, 5.4 Hz, 1H), 5.66 (d, *J* = 3.4 Hz, 1H), 5.32 – 5.16 (m, 2H), 4.58 (d, *J* = 3.4 Hz, 1H), 4.41 – 4.18 (m, 7H), 4.03 (ddt, *J* = 12.7, 6.7, 1.1 Hz, 1H), 1.40 – 1.24 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): 168.26, 165.45, 157.20, 156.94, 133.30, 119.14, 76.08, 74.75, 73.01, 63.54, 62.60, 62.02, 14.25, 14.18, 14.01; ^{13}C NMR (DEPT-135, 75 MHz, $CDCl_3$): 133.18, 119.03, 75.95, 74.63, 72.89, 63.42, 62.48, 61.90, 14.13, 14.06, 13.89; HRMS (ESI) m/z calculated for $C_{15}H_{23}O_9$ ($[M+H]^+$) 348.1371, found 348.1369;



(*2R,3R*)-diethyl 2-((*E*)-but-2-en-1-yloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate (3c)

Following general procedure ***GPIII*** using (*2R,3R*)-diethyl 2-((*E*)-but-2-en-1-yloxy)-3-hydroxysuccinate **2c** (521 mg, 2.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (374 μL, 284 mg, 2.20 mmol, 1.10 equiv), dry CH_2Cl_2 (20 mL, 0.1 M) and ethyl 2-chloro-2-oxoacetate (246 μL, 300 mg, 2.20 mmol, 1.10 equiv) gave 711 mg (1.97 mmol, 99%) of (*2R,3R*)-diethyl 2-((*E*)-but-2-en-1-yloxy)-3-(2-

ethoxy-2-oxoacetoxy)succinate as a slightly yellowish oil as a mixture *E / Z* = 75:25 after filtration through a short silica plug (hexanes / EtOAc 3:1). R_f (hexanes / EtOAc 1:1) = 0.84; IR (neat): 2985, 2231, 2099, 1745, 1467, 1450, 1371, 1302, 1271, 1182, 1151, 1061, 1016, 970, 859 cm^{-1}; HRMS (ESI) m/z calculated for $C_{16}H_{25}O_9$ ($[M+H]^+$) 361.1493, found 361.1486.

^1H NMR (*E* – Isomer, 400 MHz, $CDCl_3$): 5.81 – 5.59 (m, 2H), 5.56 – 5.41 (m, 1H), 4.56 (d, *J* = 3.5 Hz, 1H), 4.38 – 4.17 (m, 8H), 1.71 (dd, *J* = 6.4, 1.2 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.32 – 1.24 (m, 6H).

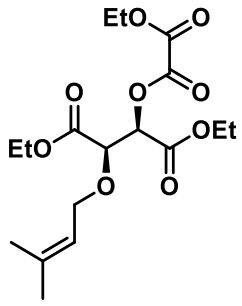
^1H NMR (Z – Isomer, 400 MHz, $CDCl_3$): 5.81 – 5.59 (m, 2H), 5.56 – 5.41 (m, 1H), 4.56 (d, *J* = 3.5 Hz, 1H), 4.38 – 4.17 (m, 7H), 3.98 (dd, *J* = 11.9, 7.3 Hz, 1H), 1.66 – 1.62 (m, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.32 – 1.24 (m, 6H).

^{13}C NMR (*E* - Isomer, 101 MHz, $CDCl_3$): 168.45, 165.49, 157.26, 156.99, 131.78, 126.25, 75.61, 74.81, 72.68, 63.47, 62.51, 61.93, 17.89, 14.26, 14.18, 14.00.

^{13}C NMR (*Z* - Isomer, 101 MHz, $CDCl_3$): 168.44, 165.49, 157.26, 156.99, 130.03, 125.27, 75.86, 74.81, 66.79, 63.47, 62.54, 61.95, 17.89, 14.26, 14.00, 13.22.

^{13}C NMR (*E* - Isomer, DEPT-135, 101 MHz, $CDCl_3$): 131.66, 126.12, 75.48, 74.69, 72.55, 63.35, 62.39, 61.81, 17.76, 14.14, 14.05, 13.88.

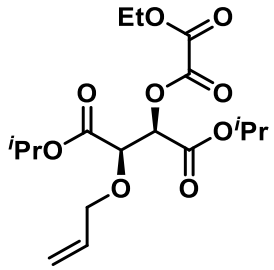
^{13}C NMR (*Z* - Isomer, DEPT-135, 101 MHz, $CDCl_3$): 129.91, 125.14, 75.72, 74.69, 66.66, 63.35, 62.42, 61.83, 17.76, 14.14, 13.88, 13.09.



(*2R,3R*)-diethyl 2-(2-ethoxy-2-oxoacetoxy)-3-((3-methylbut-2-en-1-yl)oxy)succinate 3d

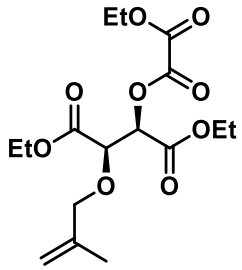
Following general procedure ***GPIII*** using (*2R,3R*)-diethyl 2-hydroxy-3-((3-methylbut-2-en-1-yl)oxy)succinate **2d** (549 mg, 2.00 mmol, 1.00 equiv), $^iPr_2NEt$ (374 μL, 284 mg, 2.20 mmol, 1.10 equiv), dry CH_2Cl_2 (20 mL, 0.1 M) and ethyl 2-chloro-2-oxoacetate (246 μL, 300 mg, 2.20 mmol, 1.10 equiv) gave 711 mg (1.90 mmol, 95%) of (*2R,3R*)-diethyl 2-(2-ethoxy-2-oxoacetoxy)-3-((3-

methylbut-2-en-1-yl)oxy)succinate as a slightly yellowish oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 3:1). R_f (hexanes / EtOAc 3:1) = 0.56; IR (neat): 2980, 1998, 1744, 1455, 1370, 1300, 1270, 1174, 1150, 1068, 1014, 857, 705, 600, 552 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 5.63 (d, *J* = 3.4 Hz, 1H), 5.26 (ttd, *J* = 6.6, 2.7, 1.3 Hz, 1H), 4.55 (d, *J* = 3.4 Hz, 1H), 4.41 – 4.19 (m, 7H), 4.10 (dd, *J* = 11.7, 7.9 Hz, 1H), 1.74 (s, 3H), 1.64 (s, 3H), 1.40 – 1.24 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): 168.57, 165.49, 157.26, 156.98, 139.47, 119.56, 75.50, 74.86, 67.99, 63.49, 62.51, 61.92, 25.97, 18.07, 14.26, 14.16, 13.99; ^{13}C NMR (DEPT-135, 75 MHz, $CDCl_3$): 119.45, 75.39, 74.75, 67.88, 63.38, 62.41, 61.81, 25.86, 17.97, 14.16, 14.05, 13.88. HRMS (ESI) m/z calculated for $C_{17}H_{27}O_9$ ($[M+H]^+$) 375.1650, found 375.1630.



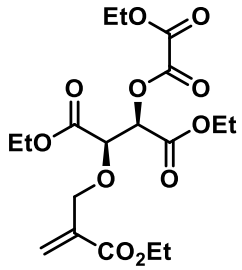
(*2R,3R*)-diisopropyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate 3e

Following general procedure ***GPIII*** using (*2R,3R*)-diisopropyl 2-(allyloxy)-3-hydroxysuccinate **2e** (549 mg, 2.00 mmol, 1.00 equiv), $^iPr_2NEt$ (374 μL, 284 mg, 2.20 mmol, 1.10 equiv), dry CH_2Cl_2 (20 mL, 0.1 M) and ethyl 2-chloro-2-oxoacetate (246 μL, 300 mg, 2.20 mmol, 1.10 equiv) gave 749 mg (2.00 mmol, 100%) of (*2R,3R*)-diisopropyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate as a slightly yellowish oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 3:1). R_f (hexanes / EtOAc 1:1) = 0.82; IR (neat): 2986, 2194, 2018, 1779, 1747, 1468, 1376, 1272, 1211, 1175, 1154, 1101, 1064, 1010, 934, 821, 763, 721, 495 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 5.92 – 5.80 (m, 1H), 5.62 (dd, *J* = 3.3, 1.1 Hz, 1H), 5.31 – 5.18 (m, 2H), 5.15 – 5.05 (m, 2H), 4.53 (dd, *J* = 3.3, 0.8 Hz, 1H), 4.42 – 4.27 (m, 3H), 4.03 (ddd, *J* = 12.5, 6.5, 1.1 Hz, 1H), 1.35 (td, *J* = 7.1, 0.9 Hz, 3H), 1.31 – 1.20 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$): 167.72, 164.91, 157.37, 157.08, 133.45, 118.89, 76.31, 74.88, 73.06, 70.69, 69.92, 63.40, 21.82, 21.80, 21.75, 14.00; ^{13}C NMR (DEPT-135, 101 MHz, $CDCl_3$): 133.31, 118.77, 76.17, 74.75, 72.93, 70.56, 69.79, 63.28, 21.70, 21.68, 21.63, 13.87; HRMS (ESI) m/z calculated for $C_{17}H_{27}O_9$ ($[M+H]^+$) 375.165, found 375.1655.



(*2R,3R*)-diethyl 2-(2-ethoxy-2-oxoacetoxy)-3-((2-methylallyl)oxy)succinate (3g)

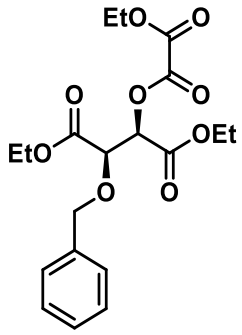
Following general procedure ***GPIII*** using (*2R,3R*)-diethyl 2-hydroxy-3-((2-methylallyl)oxy)succinate **2g** (260 mg, 1.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (187 μL, 142 mg, 1.10 mmol, 1.10 equiv), dry CH_2Cl_2 (10 mL, 0.1 M) and ethyl 2-chloro-2-oxoacetate (123 μL, 150 mg, 1.10 mmol, 1.10 equiv) gave 164 mg (455 μmol, 46%) of (*2R,3R*)-diethyl 2-(2-ethoxy-2-oxoacetoxy)-3-((2-methylallyl)oxy)succinate as an colorless oil after flash column purification (hexanes / EtOAc 3:1). R_f (hexanes / EtOAc 1:1) = 0.79; IR (neat): 2992, 2184, 1746, 1448, 1372, 1303, 1271, 1180, 1153, 1075, 1052, 1015, 910, 862, 762 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 5.64 (d, *J* = 3.7 Hz, 1H), 4.94 (d, *J* = 5.9 Hz, 2H), 4.54 (d, *J* = 3.7 Hz, 1H), 4.40 – 4.32 (m, 2H), 4.30 – 4.20 (m, 5H), 3.92 (d, *J* = 12.1 Hz, 1H), 1.72 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.28 (td, *J* = 7.1, 4.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): 168.17, 165.50, 157.27, 156.98, 140.78, 114.55, 76.34, 75.96, 74.74, 63.48, 62.56, 61.95, 19.55, 14.26, 14.14, 14.01; ^{13}C NMR (DEPT-135, 101 MHz, $CDCl_3$): 114.42, 76.20, 75.83, 74.61, 63.36, 62.43, 61.82, 19.42, 14.13, 14.01, 13.88; HRMS (ESI) m/z calculated for $C_{16}H_{25}O_9$ ($[M+H]^+$) 361.1493, found 361.1494.



(*2R,3R*)-diethyl 2-(2-ethoxy-2-oxoacetoxy)-3-((2-(ethoxycarbonyl)allyl)oxy)succinate (3h)

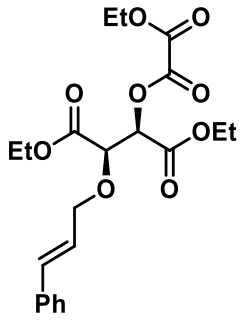
Following general procedure ***GPIII*** using (*2R,3R*)-diethyl 2-((2-(ethoxycarbonyl)allyl)oxy)-3-hydroxysuccinate **2h** (318 mg, 1.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (187 μL, 143 mg, 1.10 mmol, 1.10 equiv), dry CH_2Cl_2 (10 mL, 0.1 M) and ethyl 2-chloro-2-oxoacetate (123 μL, 150 mg, 1.10 mmol, 1.10 equiv) gave 419 mg (1.00 mmol, 100%) of (*2R,3R*)-diethyl 2-(2-ethoxy-2-oxoacetoxy)-3-((2-(ethoxycarbonyl)allyl)oxy)succinate as a slightly yellowish oil after filtration through a short plug

of flash silica gel (hexanes / EtOAc 3:1). R_f (hexanes / EtOAc 1:1) = 0.76; IR (neat): 2987, 2945, 2363, 1744, 1648, 1471, 1451, 1391, 1371, 1303, 1271, 1180, 1147, 1072, 1015, 859, 764, 485 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 6.28 (d, *J* = 1.2 Hz, 1H), 5.87 (q, *J* = 1.5 Hz, 1H), 5.63 (d, *J* = 3.5 Hz, 1H), 4.62 (d, *J* = 3.5 Hz, 1H), 4.55 (dt, *J* = 13.7, 1.4 Hz, 1H), 4.35 – 4.14 (m, 9H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.29 – 1.21 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): 167.89, 165.52, 165.23, 157.09, 156.82, 136.21, 127.07, 77.51, 74.53, 70.17, 63.44, 62.51, 62.01, 60.89, 14.19, 14.15, 14.06, 13.91; ^{13}C NMR (75 MHz, $CDCl_3$): 127.00, 77.44, 74.46, 70.11, 63.37, 62.44, 61.94, 60.82, 14.13, 14.09, 13.99, 13.84; HRMS (ESI) m/z calculated for $C_{18}H_{27}O_{11}$ ($[M+H]^+$) 420.1582, found 420.1580.



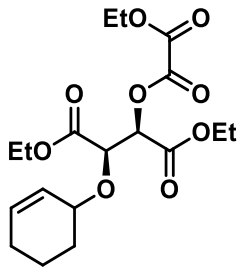
(*2R,3R*)-diethyl 2-(benzyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate (3i)

Following general procedure ***GPIII*** using (*2R,3R*)-diethyl 2-(benzyloxy)-3-hydroxysuccinate **2i** (538 mg, 1.81 mmol, 1.00 equiv), $^iPr_2NEt$ (339 μL, 258 mg, 2.00 mmol, 1.10 equiv), dry CH_2Cl_2 (18 mL, 0.1 M) and ethyl 2-chloro-2-oxoacetate (223 μL, 272 mg, 2.00 mmol, 1.10 equiv) gave 695 mg (1.75 mmol, 97%) of (*2R,3R*)-diethyl 2-(benzyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate as a slightly yellowish oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 3:1). R_f (hexanes / EtOAc 1:1) = 0.82; IR (neat): 2986, 1743, 1471, 1371, 1302, 1271, 1175, 1151, 1066, 1014, 920, 859, 746, 698, 623, 580 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 7.42 – 7.27 (m, 5H), 5.64 (d, *J* = 3.4 Hz, 1H), 4.92 (d, *J* = 11.9 Hz, 1H), 4.56 (dd, *J* = 11.4, 7.6 Hz, 2H), 4.40 – 4.05 (m, 6H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* =y 7.1 Hz, 3H), 1.18 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 168.19, 165.34, 136.54, 128.59, 128.57, 128.38, 76.10, 74.73, 73.66, 63.54, 62.56, 62.05, 14.28, 14.06, 14.03; ^{13}C NMR (DEPT-135, 75 MHz, $CDCl_3$): 128.47, 128.45, 128.26, 75.97, 74.61, 73.54, 63.42, 62.44, 61.93, 14.16, 13.93, 13.90; HRMS (ESI) m/z calculated for $C_{19}H_{25}O_9$ ($[M+H]^+$) 397.1493, found 397.1490.



(*2R,3R*)-diethyl 2-(cinnamyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate (3j)

Following general procedure ***GPIII*** using (*2R,3R*)-diethyl 2-(cinnamyloxy)-3-hydroxysuccinate **2j** (258 mg, 800 μmol, 1.00 equiv), $^{i}Pr_2NEt$ (218 μL, 165 mg, 880 μmol, 1.60 equiv), dry CH_2Cl_2 (8 mL, 0.1 M) and ethyl 2-chloro-2-oxoacetate (143 μL, 175 mg, 880 μmol, 1.60 equiv) gave 315 mg (746 μmol, 93%) of (*2R,3R*)-diethyl 2-(cinnamyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate as a slightly yellowish oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc 3:1) = 0.51. IR (neat): 2989, 2164, 1743, 1449, 1370, 1304, 1268, 1179, 1149, 1112, 1063, 1013, 972, 922, 858, 747, 694, 509, 424 cm^{-1};.^{1}H NMR (300 MHz, $CDCl_3$): 7.40 – 7.26 (m, 5H), 6.59 (d, *J* = 15.9 Hz, 1H), 6.21 (ddd, *J* = 15.9, 6.9, 6.0 Hz, 1H), 5.68 (d, *J* = 3.3 Hz, 1H), 4.64 (d, *J* = 3.3 Hz, 1H), 4.50 (ddd, *J* = 12.6, 5.9, 1.2 Hz, 1H), 4.38 – 4.19 (m, 7H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.25 (dt, *J* = 8.5, 7.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): 168.34, 165.51, 157.23, 156.98, 136.40, 134.38, 128.75, 128.18, 126.73, 124.45, 76.10, 74.76, 72.74, 63.52, 62.62, 62.05, 14.26, 14.15, 14.02; ^{13}C NMR (DEPT-135, 101 MHz, $CDCl_3$): 134.26, 128.62, 128.05, 126.60, 124.31, 75.96, 74.63, 72.61, 63.39, 62.50, 61.92, 14.14, 14.02, 13.89; HRMS (ESI) m/z calculated for $C_{21}H_{26}KO_9$ ($[M+K]^+$) 461.1208, found 461.1207.



(*2R,3R*)-diethyl 2-(cyclohex-2-en-1-yloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate (3k)

Following general procedure ***GPIII*** using (*2R,3R*)-diethyl 2-(cyclohex-2-en-1-yloxy)-3-hydroxysuccinate **2k** (573 mg, 2.00 mmol, 1.00 equiv), $^{i}Pr_2NEt$ (374 μL, 284 mg, 2.20 mmol, 1.10 equiv), dry CH_2Cl_2 (20 mL, 0.1 M) and ethyl 2-chloro-2-oxoacetate (246 μL, 300 mg, 2.20 mmol,

1.10 equiv) gave 690 mg (1.79 mmol, 89%) of (*2R,3R*)-diethyl 2-(cyclohex-2-en-1-yloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate as a slightly yellowish oil as a mixture of diastereomers (d.r.: 56:43) after filtration through a short plug of flash silica gel (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc 3:1) = 0.63; IR (neat): 2986, 2943, 1949, 1744, 1453, 1398, 1371, 1306, 1268, 1182, 1152, 1062, 1015, 969, 931, 905, 858, 771, 729, 582, 511, 448, 399 cm^{-1}; HRMS (ESI) m/z calculated for $C_{18}H_{30}O_9$ ($[M+NH_4]^+$) 404.1915, found 404.1915.

^{1}H NMR (Major Diastereomer, 400 MHz, $CDCl_3$): 5.90 – 5.66 (m, 2H), 5.64 (d, *J* = 3.8 Hz, 1H), 4.63 (d, *J* = 3.8 Hz, 1H), 4.36 – 4.18 (m, 6H), 3.98 (t, *J* = 3.6 Hz, 1H), 2.07 – 1.88 (m, 2H), 1.83 – 1.61 (m, 3H), 1.57 – 1.43 (m, 1H), 1.37 – 1.25 (m, 9H).

^{1}H NMR (Minor Diastereomer, 400 MHz, $CDCl_3$): 5.90 – 5.66 (m, 2H), 5.64 (d, *J* = 3.8 Hz, 1H), 4.66 (d, *J* = 4.0 Hz, 1H), 4.36 – 4.18 (m, 6H), 4.10 – 4.03 (m, 1H), 2.07 – 1.88 (m, 2H), 1.83 – 1.61 (m, 3H), 1.57 – 1.43 (m, 1H), 1.37 – 1.25 (m, 9H).

^{13}C NMR (Major Diastereomer, 101 MHz, $CDCl_3$): 168.86, 165.63, 157.38, 157.38, 131.85, 127.12, 75.65, 75.02, 74.28, 63.38, 61.89, 61.88, 27.37, 25.19, 18.70, 14.24, 14.12, 13.99.

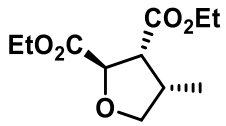
^{13}C NMR (Minor Diastereomer, 101 MHz, $CDCl_3$): 168.88, 165.60, 157.09, 157.06, 132.54, 125.82, 75.56, 75.07, 74.80, 63.26, 62.54, 62.46, 28.92, 25.29, 18.91, 14.24, 14.14, 14.05.

^{13}C NMR (Major Diastereomer, DEPT-135, 101 MHz, $CDCl_3$): 131.74, 126.99, 75.52, 74.90, 74.16, 63.27, 62.42, 61.78, 27.25, 25.07, 18.58, 14.12, 14.01, 13.86.

^{13}C NMR (Minor Diastereomer, DEPT-135, 101 MHz, $CDCl_3$): 132.42, 125.69, 75.44, 74.96, 74.68, 63.15, 62.34, 61.76, 28.79, 25.17, 18.79, 14.12, 14.02, 13.93.

4.9.5 General procedure *GPIV* for photoreactions in a batch scale

A Schlenk tube equipped with a magnetic stir bar was charged with ethyl oxalate ester (346 mg, 1.00 mmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (6.55 mg, 10.0 μmol, 1.00 mol%), dissolved in DMF (10 mL, 0.1M), sealed with a screw-cap and subsequently evacuated for 15 min. and backfilled with N_2. The screw-cap was replaced with a Teflon sealed inlet for a glass rod, through which irradiation with a 455 nm high power LED took place from above while the reaction was magnetically stirred and heated in an aluminum block at 80 °C from below. The reaction was monitored by TLC. Afterwards the reaction mixture was diluted with EtOAc (300 mL) and extracted with water (5 x 100 mL). The combined organic layers were dried over $NaSO_4$, the solvent evaporated under reduced pressure and the residue purified by flash column chromatography.



Diethyl 4-methyltetrahydrofuran-2,3-dicarboxylate (4a)

Following general procedure ***GPIV*** using (*2R,3R*)-diethyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate **3a** (346 mg, 1.00 mmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (6.55 mg, 10.0 μmol, 1.00 mol%) and DMF (10 mL, 0.1M) gave 125 mg (543 μmol, 54%) of a colorless oil as a mixture of diastereomers (d.r.: 62:28:8:2) after flash column purification (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc 1:1) = 0.81; IR (neat): 2979, 2939, 2877, 2190, 1731, 1464, 1372, 1275, 1180, 1095, 1027, 939, 858, 462 cm^{-1}; HRMS (ESI) m/z calculated for $C_{11}H_{18}O_5$ ([M+H]$^+$) 231.1227, found 231.1230.

^{1}H NMR (Major Diastereomer, 400 MHz, $CDCl_3$): 4.80 (d, *J* = 6.1 Hz, 1H), 4.26 – 4.16 (m, 4H), 4.16 – 4.08 (m, 1H), 3.63 (dd, *J* = 8.3, 6.2 Hz, 1H), 3.24 (dd, *J* = 8.3, 6.1 Hz, 1H), 2.67 (dp, *J* = 13.4, 6.8 Hz, 1H), 1.32 – 1.23 (m, 6H), 1.01 (d, *J* = 7.0 Hz, 3H).

^{1}H NMR (Minor Diastereomer 1, 400 MHz, $CDCl_3$): 4.72 (d, *J* = 7.4 Hz, 1H), 4.26 – 4.16 (m, 4H), 4.16 – 4.08 (m, 1H), 3.58 (t, *J* = 8.7 Hz, 1H), 2.77 (dt, *J* = 11.1, 5.6 Hz, 1H), 2.62 – 2.51 (m, 1H), 1.32 – 1.23 (m, 6H), 1.16 – 1.10 (m, 3H).

^{1}H NMR (Minor Diastereomer 2, 400 MHz, $CDCl_3$): 4.65 (d, *J* = 8.3 Hz, 1H), 4.26 – 4.16 (m, 4H), 4.16 – 4.08 (m, 1H), 3.48 (t, *J* = 8.0 Hz, 1H), 2.95 (t, *J* = 8.4 Hz, 1H), 2.67 (dp, *J* = 13.4, 6.8 Hz, 1H), 1.32 – 1.23 (m, 6H), 1.01 (d, *J* = 7.0 Hz, 3H).

^{1}H NMR (Minor Diastereomer 3, 400 MHz, $CDCl_3$): 4.59 (d, *J* = 2.3 Hz, 1H), 4.26 – 4.16 (m, 4H), 4.16 – 4.08 (m, 1H), 3.41 (d, *J* = 7.3 Hz, 1H), 2.77 (dt, *J* = 11.1, 5.6 Hz, 1H), 2.62 – 2.51 (m, 1H), 1.32 – 1.23 (m, 6H), 1.01 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (Major Diastereomer, 101 MHz, $CDCl_3$): 171.98, 171.17, 78.74, 75.67, 61.45, 61.13, 52.28, 36.87, 14.42, 14.29, 13.40.

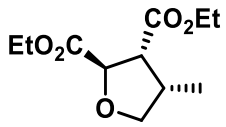
^{13}C NMR (Minor Diastereomer 1, 101 MHz, $CDCl_3$): 172.16, 171.90, 79.85, 76.02, 61.44, 61.36, 55.81, 39.80, 15.85, 14.34, 14.29.

^{13}C NMR (Major Diastereomer, DEPT-135, 101 MHz, $CDCl_3$): 78.61, 75.54, 61.33, 61.00, 52.61, 36.75, 14.30, 14.16, 13.27.

^{13}C NMR (Minor Diastereomer 1, DEPT-135, 101 MHz, $CDCl_3$): 79.72, 75.89, 61.33, 61.24, 55.68, 39.67, 15.73, 14.22, 14.10.

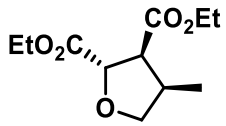
4.9.6 General procedure *GPV* for photoreactions in a microreactor

A Schlenk tube equipped with a magnetic stir bar was charged with ethyl oxalate ester (1.00 mmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (6.55 mg, 10.0 μmol, 1.00 mol%) and dissolved in DMF (10 mL, 0.1 M). The reaction mixture was degassed by sparging with N_2 through a needle and a septum for 30 min. and pumped through a micro reactor (which was sparged with N_2 too) equipped with 8 LED's at a flow rate of 0.35 mL/h *via* a syringe pump while heated at 80 °C. Afterwards the reaction mixture was diluted with EtOAc (300 mL) and extracted with water (5 x 100 mL). The combined organic layers were dried over $NaSO_4$, the solvent evaporated under reduced pressure and the residue purified by flash column chromatography.



Diethyl (*2R,3R,4S*)-4-methyltetrahydrofuran-2,3-dicarboxylate (4a)

Following general procedure ***GPV*** using (*2R,3R*)-diethyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate **3a** (346 mg, 1.00 mmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (6.55 mg, 10.0 μmol, 1.00 mol%) and DMF (10 mL, 0.1 M) gave 167 mg (725 μmol, 73%) of a colorless oil as a mixture of diastereomers (d.r.: 62 : 28 : 8:2) after filtration through a short plug of flash silica gel (hexanes / EtOAc 5:1). (NMR information see General procedure *GPIV* for photoreactions in a batch scale above)



Diethyl (*2R,3R,4S*)-4-methyltetrahydrofuran-2,3-dicarboxylate (4b)

Following general procedure ***GPV*** using (*2S,3S*)-diethyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate **3b** (346 mg, 1.00 mmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (6.55 mg, 10.0 μmol, 1.00 mol%) and DMF (10 mL, 0.1 M) gave 163 mg (711 μmol, 71%) of a colorless oil as a mixture of diastereomers (d.r.: 57:37:6) after filtration through a short plug of flash silica gel (hexanes / EtOAc 5:1).

^{1}H NMR (Major Diastereomer, 300 MHz, $CDCl_3$): 4.75 (d, *J* = 6.1 Hz, 1H), 4.23 – 4.02 (m, 5H), 3.63 – 3.48 (m, 1H), 3.20 (dd, *J* = 8.3, 6.1 Hz, 1H), 2.68 – 2.44 (m, 1H), 1.30 – 1.17 (m, 6H), 0.96 (d, *J* = 7.0 Hz, 3H).

^{1}H NMR (Minor Diastereomer 1, 300 MHz, $CDCl_3$): 4.68 (d, *J* = 7.4 Hz, 1H), 4.23 – 4.02 (m, 5H), 3.63 – 3.48 (m, 1H), 2.73 (dd, *J* = 8.8, 7.4 Hz, 1H), 2.68 – 2.44 (m, 1H), 1.30 – 1.17 (m, 6H), 1.08 (dd, *J* = 6.6, 3H).

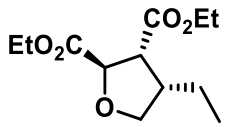
^{1}H NMR (Minor Diastereomer 2, 300 MHz, $CDCl_3$): 4.61 (d, *J* = 8.3 Hz, 1H), 4.23 – 4.02 (m, 5H), 3.44 (t, *J* = 8.0 Hz, 1H), 2.91 (t, *J* = 8.4 Hz, 1H), 2.68 – 2.44 (m, 1H), 1.30 – 1.17 (m, 6H), 1.07 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (Major Diastereomer, 75 MHz, $CDCl_3$): 172.00, 171.19, 78.71, 75.66, 61.48, 61.15, 52.26, 36.87, 14.43, 14.30, 13.40.

^{13}C NMR (Minor Diastereomer 1, 75 MHz, $CDCl_3$): 172.17, 171.92, 79.82, 76.02, 61.48, 61.39, 55.79, 39.82, 15.84, 14.35, 13.40.

^{13}C NMR (Major Diastereomer, DEPT-135, 75 MHz, $CDCl_3$): 78.59, 75.54, 61.36, 61.03, 52.14, 36.75, 14.31, 14.18, 13.28.

^{13}C NMR (Minor Diastereomer 1, DEPT-135, 75 MHz, $CDCl_3$): 79.70, 75.90, 61.36, 61.27, 55.67, 39.70, 15.72, 14.23, 13.28.



Diethyl (*2R,3R,4S*)-4-ethyltetrahydrofuran-2,3-dicarboxylate (4c)

Following general procedure ***GPV*** using (*2R,3R*)-diethyl 2-((*E*)-but-2-en-1-yloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate **3c** (360mg, 1.00 mmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (6.55 mg, 10.0 μmol, 1.00 mol%) and DMF (10 mL, 0.1 M) at a flow rate of 0.3 mL/h gave 183mg (750 μmol, 75%) of a colorless oil as a mixture of diastereomers (d.r.: 60 : 34 : 5 : 1) after flash column purification (hexanes / EtOAc 3:1). R_f (hexanes / EtOAc 1:1) = 0.92; IR (neat): 2970, 2938, 2878, 1729, 1464, 1372, 1266, 1179, 1135, 1095, 1028, 943, 857, 433 cm^{-1}; HRMS (ESI) m/z calculated for $C_{12}H_{21}O_5$ ($[M+H]^+$) 245.1384, found 245.1388.

^{1}H NMR (Major Diastereomer, 300 MHz, $CDCl_3$): 4.71 (d, *J* = 5.0 Hz, 1H), 4.18 – 4.08 (m, 5H), 3.64 (dt, *J* = 13.8, 8.2 Hz, 1H), 3.21 (dd, *J* = 8.4, 5.0 Hz, 1H), 2.48 – 2.32 (m, 1H), 1.66 – 1.28 (m, 2H), 1.27 – 1.20 (m, 6H), 0.88 (ddd, *J* = 7.5, 6.1, 3.9 Hz, 3H).

^{1}H NMR (Minor Diastereomer 1, 300 MHz, $CDCl_3$): 4.64 (d, *J* = 7.2 Hz, 1H), 4.18 – 4.08 (m, 5H), 3.64 (dt, *J* = 13.8, 8.2 Hz, 1H), 2.82 – 2.74 (m, 1H), 2.48 – 2.32 (m, 1H), 1.66 – 1.28 (m, 2H), 1.27 – 1.20 (m, 6H), 0.88 (ddd, *J* = 7.5, 6.1, 3.9 Hz, 3H).

^{1}H NMR (Minor Diastereomer 2, 300 MHz, $CDCl_3$): 4.52 (d, *J* = 3.4 Hz, 1H), 4.18 – 4.08 (m, 5H), 3.64 (dt, *J* = 13.8, 8.2 Hz, 1H), 2.82 – 2.74 (m, 1H), 2.48 – 2.32 (m, 1H), 1.66 – 1.28 (m, 2H), 1.27 – 1.20 (m, 6H), 0.88 (ddd, *J* = 7.5, 6.1, 3.9 Hz, 3H).

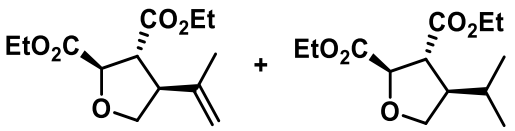
^{1}H NMR (Minor Diastereomer 3, 300 MHz, $CDCl_3$): 4.58 (d, *J* = 8.3 Hz, 1H), 4.18 – 4.08 (m, 5H), 3.55 – 3.47 (m, 1H), 2.98 (t, *J* = 8.1 Hz, 1H), 2.48 – 2.32 (m, 1H), 1.66 – 1.28 (m, 2H), 1.27 – 1.20 (m, 6H), 0.88 (ddd, *J* = 7.5, 6.1, 3.9 Hz, 3H).

^{13}C NMR (Major Diastereomer, 75 MHz, $CDCl_3$): 171.87, 171.37, 79.11, 73.29, 61.36, 61.00, 51.55, 44.06, 21.00, 14.28, 14.18, 12.75.

^{13}C NMR (Minor Diastereomer 1, 75 MHz, $CDCl_3$): 172.51, 171.63, 79.93, 74.32, 61.33, 61.26, 54.16, 46.48, 25.09, 14.28, 14.18, 12.37.

^{13}C NMR (Major Diastereomer, DEPT-135, 75 MHz, $CDCl_3$): 79.06, 73.23, 61.31, 61.08, 60.94, 51.49, 44.01, 20.94, 14.22, 14.13, 12.70.

^{13}C NMR (Minor Diastereomer, DEPT-135, 75 MHz, $CDCl_3$): 79.88, 74.26, 61.27, 61.21, 60.94, 54.11, 46.43, 25.03, 14.22, 14.13, 12.32.



75 : **25**

Diethyl (*2R,3R,4S*)-4-(prop-1-en-2-yl)tetrahydrofuran-2,3-dicarboxylate (4d)

Following general procedure ***GPV*** using (*2R,3R*)-diethyl 2-((*E*)-but-2-en-1-yloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate **3d** (374mg, 1.00 mmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (6.55 mg, 10.0 μmol, 1.00 mol%) and DMF (10 mL, 0.1 M) gave 137mg (530 μmol, 53%) of a colorless oil after flash column purification (hexanes / EtOAc 7:1). R_f (hexanes / EtOAc 3:1) = 0.49; IR (neat): 2970, 2938, 2878,

1729, 1464, 1372, 1266, 1179, 1135, 1095, 1028, 943, 857, 433 cm^{-1}; IR (neat): 2982, 1732, 1464, 1379, 1269, 1217, 1183, 1102, 1026, 913, 858, 729, 650, 532, 454, 428 cm^{-1}. HRMS (ESI) m/z calculated for major product $C_{13}H_{21}O_5$ ($[M+H]^+$) 257.1384, found 257.1391.

^1H NMR (Major product, 400 MHz, $CDCl_3$): 4.85 (dd, *J* = 4.0, 2.6 Hz, 2H), 4.69 (d, *J* = 7.5 Hz, 1H), 4.27 – 4.09 (m, 5H), 3.84 (t, *J* = 8.8 Hz, 1H), 3.26 – 3.16 (m, 1H), 3.13 (dd, *J* = 9.3, 7.5 Hz, 1H), 1.73 (s, 3H), 1.30 – 1.23 (m, 6H).

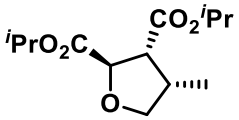
^1H NMR (Minor product, 400 MHz, $CDCl_3$): 4.61 (d, *J* = 7.1 Hz, 1H), 4.27 – 4.09 (m, 5H), 3.75 (t, *J* = 8.6 Hz, 1H), 2.94 – 2.84 (m, 1H), 2.39 (p, *J* = 8.3 Hz, 1H), 1.69 – 1.61 (m, 1H), 1.30 – 1.23 (m, 6H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (Major product, 101 MHz, $CDCl_3$): 172.03, 171.43, 141.06, 113.45, 80.22, 73.01, 61.50, 61.43, 52.44, 51.81, 20.21, 14.30, 14.26.

^{13}C NMR (Minor product, 101 MHz, $CDCl_3$): 173.17, 171.54, 80.83, 73.07, 61.40, 61.33, 52.72, 51.66, 30.76, 21.03, 20.83, 14.26, 14.23.

^{13}C NMR (Major product, DEPT-135, 101 MHz, $CDCl_3$): 113.34, 80.10, 72.89, 61.39, 61.31, 61.22, 52.32, 51.69, 20.09, 14.19, 14.15.

^{13}C NMR (Minor product, DEPT-135, 101 MHz, $CDCl_3$): 80.71, 72.96, 61.29, 61.22, 52.61, 51.55, 30.64, 20.91, 20.72, 14.15, 14.11.



Diisopropyl (*2R,3R,4S*)-4-methyltetrahydrofuran-2,3-dicarboxylate (4e)

Following general procedure ***GPV*** using (*2R,3R*)-diisopropyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate **3e** (374mg, 1.00 mmol, 1.00 equiv), *fac*-$Ir(ppy)_3$ (6.55 mg, 10.0 μmol, 1.00 mol%) and DMF (10 mL, 0.1 M) at a flow rate of 0.3 mL/h gave 168 mg (650 μmol, 65%) of a colorless oil as a mixture of diastereomers (d.r.: 60 : 32 : 5 : 3) after flash column purification (hexanes / EtOAc 3:1). R_f (hexanes / EtOAc 1:1) = 0.83; IR (neat): 2980, 2940, 2879, 1727, 1469, 1375, 1273, 1180, 1145, 1103, 989, 944, 902, 829 cm^{-1}. HRMS (ESI) m/z calculated for $C_{13}H_{23}O_5$ ($[M+H]^+$) 259.1540, found 259.1545.

^{1}H NMR (Major Diastereomer, 300 MHz, $CDCl_3$): 5.10 – 4.91 (m, 2H), 4.69 (d, *J* = 6.3 Hz, 1H), 4.07 (ddd, *J* = 8.3, 6.7, 4.3 Hz, 1H), 3.64 – 3.47 (m, 1H), 3.11 (dd, *J* = 8.4, 6.3 Hz, 1H), 2.71 – 2.55 (m, 1H), 1.25 – 1.13 (m, 12H), 0.96 (d, *J* = 7.0 Hz, 3H).

^{1}H NMR (Minor Diastereomer 1, 300 MHz, $CDCl_3$): 5.10 – 4.91 (m, 2H), 4.61 (d, *J* = 7.6 Hz, 1H), 4.07 (ddd, *J* = 8.3, 6.7, 4.3 Hz, 1H), 3.64 – 3.47 (m, 1H), 2.71 – 2.55 (m, 1H), 2.55 – 2.40 (m, 1H), 1.25 – 1.13 (m, 12H), 0.96 (d, *J* = 7.0 Hz, 3H).

^{1}H NMR (Minor Diastereomer 2, 300 MHz, $CDCl_3$): 5.10 – 4.91 (m, 2H), 4.54 (d, *J* = 8.2 Hz, 1H), 4.07 (ddd, *J* = 8.3, 6.7, 4.3 Hz, 1H), 3.42 (t, *J* = 8.0 Hz, 1H), 2.85 (t, *J* = 8.3 Hz, 1H), 2.71 – 2.55 (m, 1H), 2.85 (t, *J* = 8.3 Hz, 1H), 1.25 – 1.13 (m, 12H), 0.96 (d, *J* = 7.0 Hz, 3H).

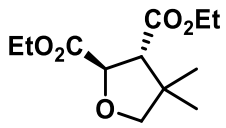
^{1}H NMR (Minor Diastereomer 3, 300 MHz, $CDCl_3$): 5.10 – 4.91 (m, 2H), 4.49 (d, *J* = 3.3 Hz, 1H), 4.07 (ddd, *J* = 8.3, 6.7, 4.3 Hz, 1H), 3.64 – 3.47 (m, 1H), 2.71 – 2.55 (m, 2H), 1.25 – 1.13 (m, 12H), 0.96 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (Major Diastereomer 1, 75 MHz, $CDCl_3$): 171.41, 170.52, 78.70, 75.60, 68.80, 68.56, 52.33, 36.69, 21.92, 21.89, 21.77, 21.71, 13.29.

^{13}C NMR (Major Diastereomer 2, 75 MHz, $CDCl_3$): 171.54, 171.38, 79.79, 75.92, 68.77, 68.63, 56.05, 39.81, 21.92, 21.82, 21.77, 21.71, 15.51.

^{13}C NMR (Major Diastereomer 1, DEPT-135, 75 MHz, $CDCl_3$): 78.65, 75.55, 68.75, 68.51, 52.27, 36.64, 21.87, 21.83, 21.72, 21.66, 13.24.

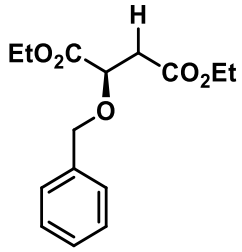
^{13}C NMR (Major Diastereomer 2, DEPT-135, 75 MHz, $CDCl_3$): 79.74, 75.87, 68.72, 68.57, 55.99, 39.76, 21.87, 21.76, 21.72, 21.66, 15.46.



Diethyl (*2R,3R*)-4,4-dimethyltetrahydrofuran-2,3-dicarboxylate (4g)

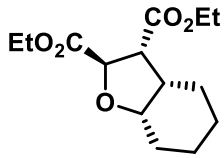
Following general procedure ***GPV*** using (*2R,3R*)-diethyl 2-(2-ethoxy-2-oxoacetoxy)-3-((2-methylallyl)oxy)succinate **3g** (144 mg, 400 μmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (2.62 mg, 4.00 μmol, 1.00 mol%) and DMF (4 mL, 0.1 M) gave 68 mg (278 μmol, 70%) of a colorless oil after filtration through a short plug of flash silica gel (hexanes / EtOAc 3:1). R_f (hexanes / EtOAc 1:1) = 0.8, IR (neat): 2978, 2874, 1729, 1466, 1371, 1337, 1264, 109, 1179, 1093, 1028, 968, 940, 860, 716,

441 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 4.89 (d, *J* = 8.0 Hz, 1H), 4.27 – 4.12 (m, 4H), 3.69 (s, 2H), 2.89 (d, *J* = 8.0 Hz, 1H), 1.31 – 1.23 (m, 6H), 1.20 (s, *J* = 3.9 Hz, 3H), 1.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 172.26, 170.64, 81.59, 78.79, 61.38, 61.10, 58.11, 43.68, 24.90, 21.99, 14.43, 14.26; ^{13}C NMR (DEPT-135, 75 MHz, $CDCl_3$): 81.48, 78.69, 61.28, 61.01, 58.01, 24.80, 21.89, 14.33, 14.16; HRMS (ESI) m/z calculated for $C_{12}H_{21}O_5$ ($[M+H]^+$) 245.1384, found 245.1388.



(*R*)-diethyl 2-(benzyloxy)succinate (4i)[21]

Following general procedure ***GPV*** using (*2R,3R*)-diethyl 2-(benzyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate **3i** (396 mg, 1.00 mmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (6.55 mg, 10.0 μmol, 1.00 mol%) and DMF (10 mL, 0.1 M) at a flow rate of 0.3 mL/h gave 170 mg (640 μmol, 64%) of a colorless oil after flash column purification (hexanes / EtOAc 5:1).R_f (hexanes / EtOAc 1:1) = 0.86; ^1H NMR (400 MHz, $CDCl_3$): 7.37 – 7.25 (m, 5H), 4.77 (d, *J* = 11.4 Hz, 1H), 4.54 (d, *J* = 11.4 Hz, 1H), 4.39 (dd, *J* = 7.8, 5.1 Hz, 1H), 4.25 – 4.10 (m, 4H), 2.85 – 2.71 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C (101 MHz, $CDCl_3$): 171.43, 170.12, 137.40, 128.43, 128.15, 127.98, 74.76, 73.11, 61.29, 60.92, 38.15, 14.24, 14.19.



Diethyl (*2R,3R,3aS,7aS*)-octahydrobenzofuran-2,3-dicarboxylate (4k)

Following general procedure ***GPV*** using (*2R,3R*)-diethyl 2-(cyclohex-2-en-1-yloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate **3k** (386 mg, 1.00 mmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (6.55 mg, 10.0 μmol, 1.00 mol%) and DMF (10 mL, 0.1 M) gave 170 mg (629 μmol, 63%) of a colorless oil as a mixture of diastereomers (d.r.: 57:43) after flash column purification (hexanes / EtOAc 6:1).R_f (hexanes / EtOAc 3:1) = 0.6; IR (neat): 2970, 2938, 2878, 1729, 1464, 1372, 1266, 1179, 1135, 1095, 1028, 943, 857, 433 cm^{-1}; IR (neat): 2992, 2935, 2866, 1730, 1449, 1370, 1271, 1221, 1183, 1115, 1093,

1025, 1000, 938, 858, 491, 440 cm^{-1}; HRMS (ESI) m/z calculated for $C_{14}H_{23}O_5$ ($[M+H]^+$) 271.1540, found 271.1543.

^1H NMR (Major Diastereomer, 300 MHz, $CDCl_3$): 4.91 (d, *J* = 8.4 Hz, 1H), 4.23 – 4.14 (m, 4H), 3.36 (dd, *J* = 8.3, 6.5 Hz, 1H), 2.37 – 2.27 (m, 1H), 2.15 – 2.05 (m, 1H), 1.75 – 1.29 (m, 7H), 1.28 – 1.22 (m, 6H).

^1H NMR (Minor Diastereomer, 300 MHz, $CDCl_3$): 4.72 (d, *J* = 5.9 Hz, 1H), 4.23 – 4.14 (m, 4H), 3.01 (dd, *J* = 5.7, 4.9 Hz, 1H), 2.37 – 2.27 (m, 1H), 1.91 – 1.79 (m, 1H), 1.75 – 1.29 (m, 7H), 1.28 – 1.22 (m, 6H).

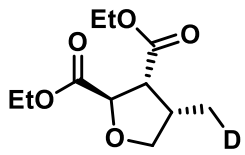
^{13}C NMR (Major Diastereomer, 75 MHz, $CDCl_3$): 172.98, 170.31, 79.15, 76.39, 61.31, 61.07, 53.33, 41.29, 27.71, 24.18, 23.24, 19.77, 14.38, 14.28.

^{13}C NMR (Minor Diastereomer, 75 MHz, $CDCl_3$): 172.94, 171.96, 78.66, 78.34, 61.41, 61.31, 53.22, 42.72, 28.13, 26.97, 23.30, 21.04, 14.31, 14.28.

^{13}C NMR (Major Diastereomer, DEPT-135, 75 MHz, $CDCl_3$): 79.05, 76.30, 61.22, 60.98, 53.24, 41.19, 27.62, 24.09, 23.14, 19.68, 14.29, 14.19.

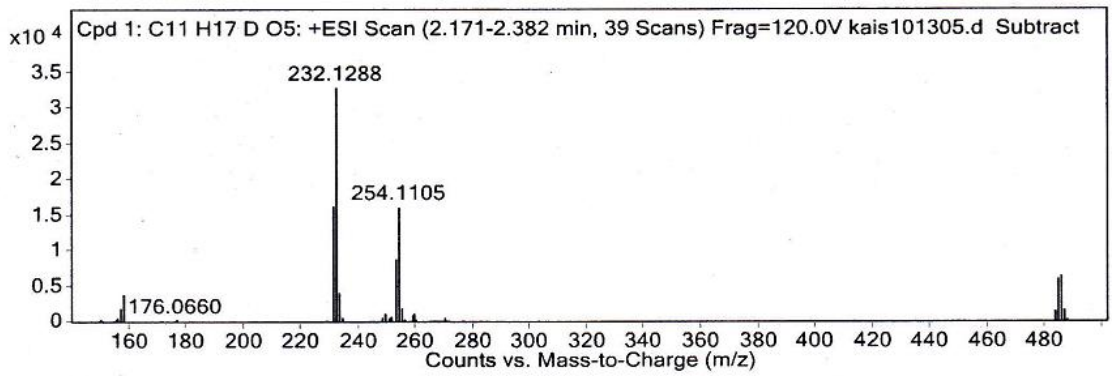
^{13}C NMR (Minor Diastereomer, DEPT-135, 75 MHz, $CDCl_3$): 78.56, 78.25, 61.32, 61.22, 53.13, 42.63, 28.04, 26.88, 23.20, 20.95, 14.22, 14.19.

4.9.7 Trapping reactions



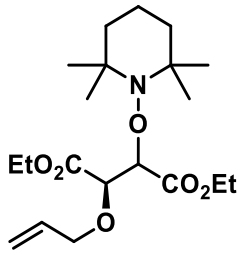
Diethyl (*2R,3R,4S*)-4-(methyl-d)tetrahydrofuran-2,3-dicarboxylate (7)

Following general procedure ***GPIV*** using (*2R,3R*)-diethyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate **3a** (34.6 mg, 100 μmol, 1.00 equiv), *fac*-Ir(ppy)$_3$ (1.31 mg, 2.00 μmol, 2.00 mol%) and DMF-d7 (1.0 mL, 0.1M) gave deuterated compound **7** detected by mass spectroscopy. HRMS (ESI) m/z calculated for $C_{11}H_{18}DO_5$ ([M+H]$^+$) 232.1290, found 232.1288.



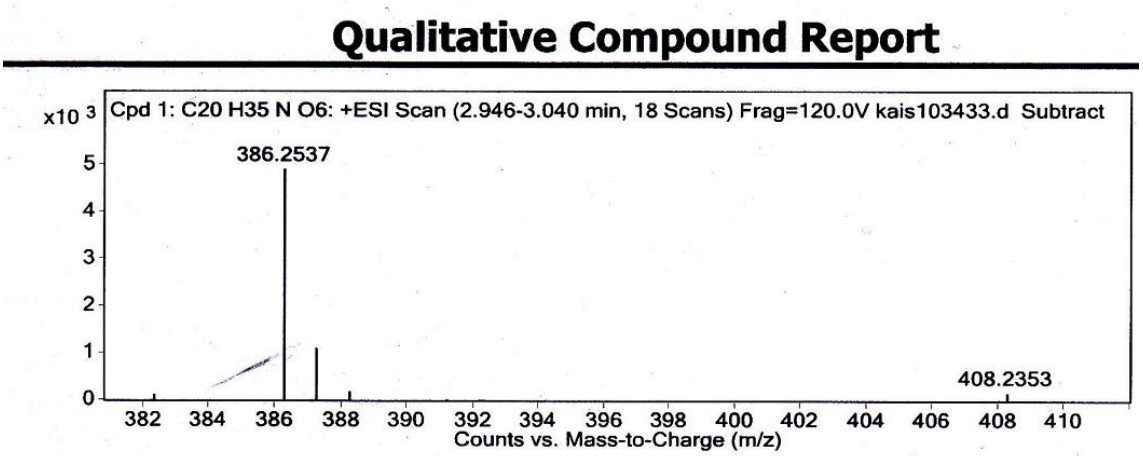
MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
154.0599	154.0585	9.09	1	67.47	C6H9DNaO3	(M+Na)+[-C5H8O2]
176.066	176.0664	-2.23	1	125.51	C7H10DO5	(M+H)+[-C4H8]
232.1288	232.129	-0.94	1	32841.09	C11H18DO5	(M+H)+
233.132	233.1324	-1.54	1	4034.07	C11H18DO5	(M+H)+
249.1549	249.1555	-2.67	1	1117.79	C11H21DNO5	(M+NH4)+
254.1105	254.1109	-1.79	1	16121.74	C11H17DNaO5	(M+Na)+
255.1144	255.1143	0.19	1	2040.36	C11H17DNaO5	(M+Na)+
270.0845	270.0849	-1.21	1	566.18	C11H17DKO5	(M+K)+
485.2319	485.2326	-1.48	1	6437.03	C22H34D2NaO10	(2M+Na)+
486.235	486.236	-2.21	1	1685.95	C22H34D2NaO10	(2M+Na)+



Diethyl (2*R*)-2-(allyloxy)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)succinate (8)

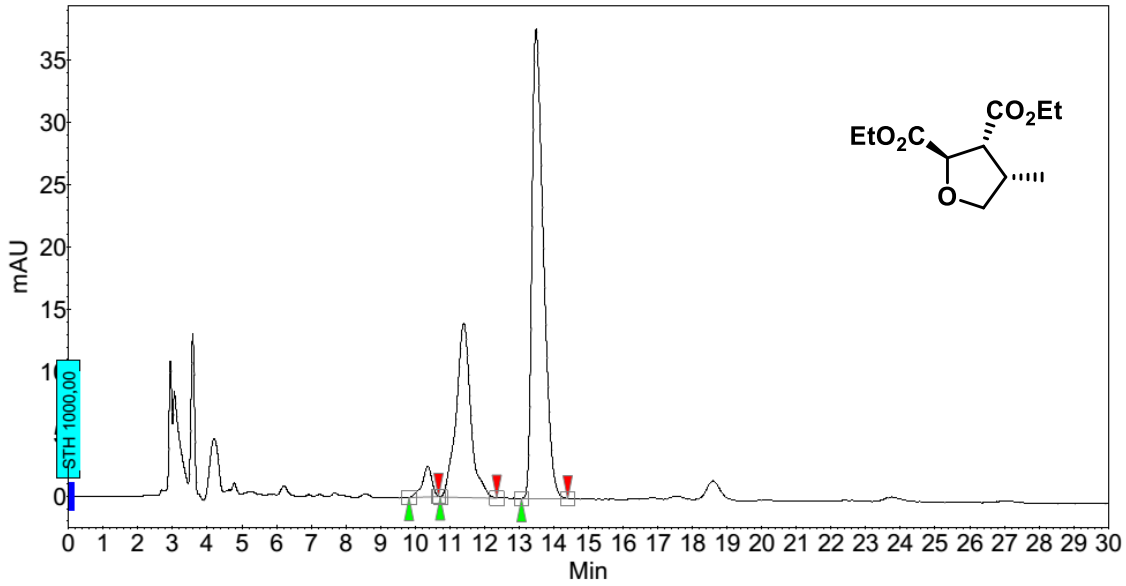
Following general procedure ***GPIV*** using (*2R,3R*)-diethyl 2-(allyloxy)-3-(2-ethoxy-2-oxoacetoxy)succinate **3a** (34.6 mg, 100 μmol, 1.00 equiv), TEMPO (31.3 mg, 200 μmol, 2.00 equiv), *fac*-Ir(ppy)$_3$ (1.31 mg, 2.00 μmol, 2.00 mol%) and DMF (1.0 mL, 0.1 M) gave TEMPO trapped compound **8**. HRMS (ESI) m/z calculated for $C_{20}H_{36}NO_6$ ([M+H]$^+$) 386.2537, found 386.2537.

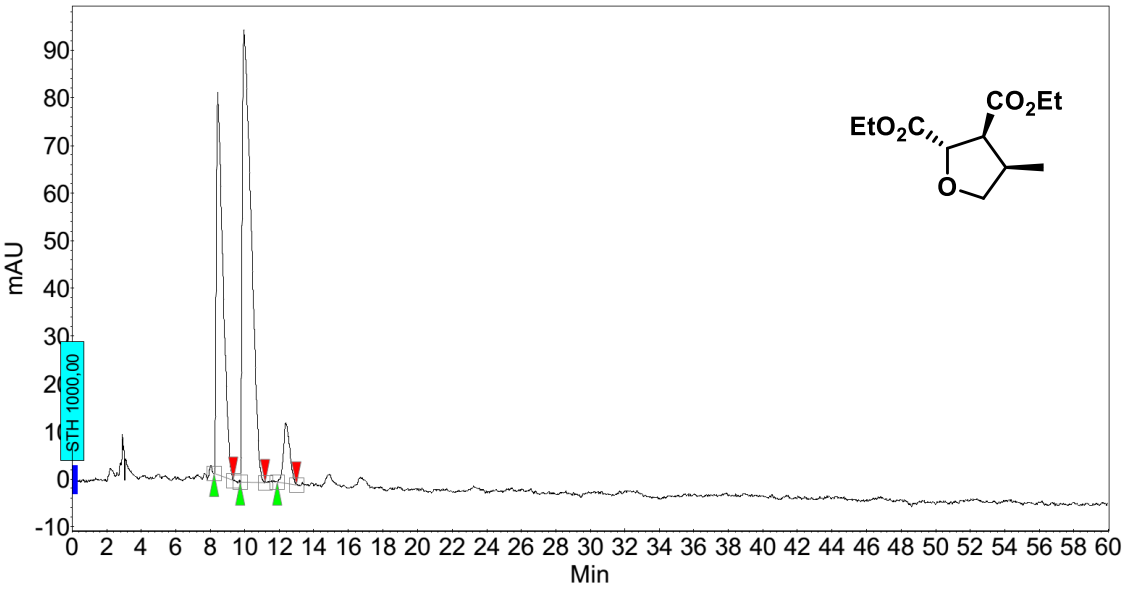


MS Spectrum Peak List

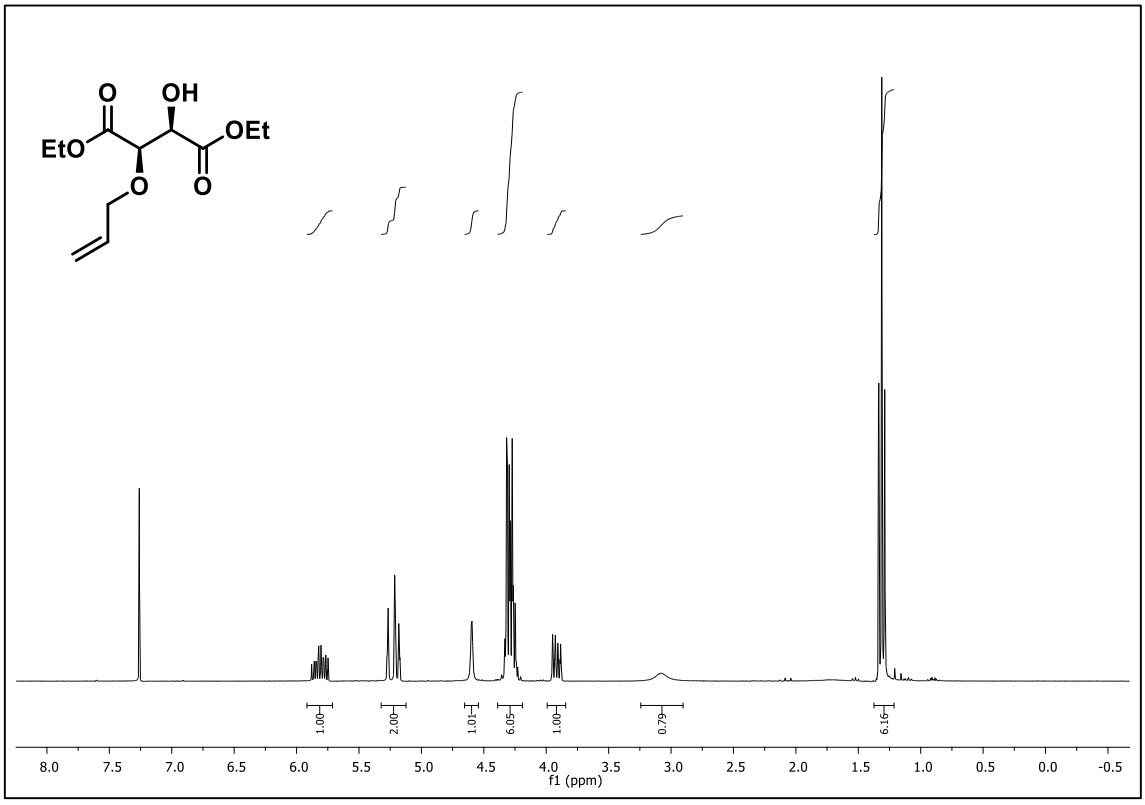
m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
386.2537	386.2537	-0.15	1	4926.16	C20H36NO6	(M+H)+
387.2565	387.257	-1.45	1	1132.44	C20H36NO6	(M+H)+
388.2597	388.2595	0.36	1	203.61	C20H36NO6	(M+H)+
408.2353	408.2357	-0.9	1	184.21	C20H35NNaO6	(M+Na)+

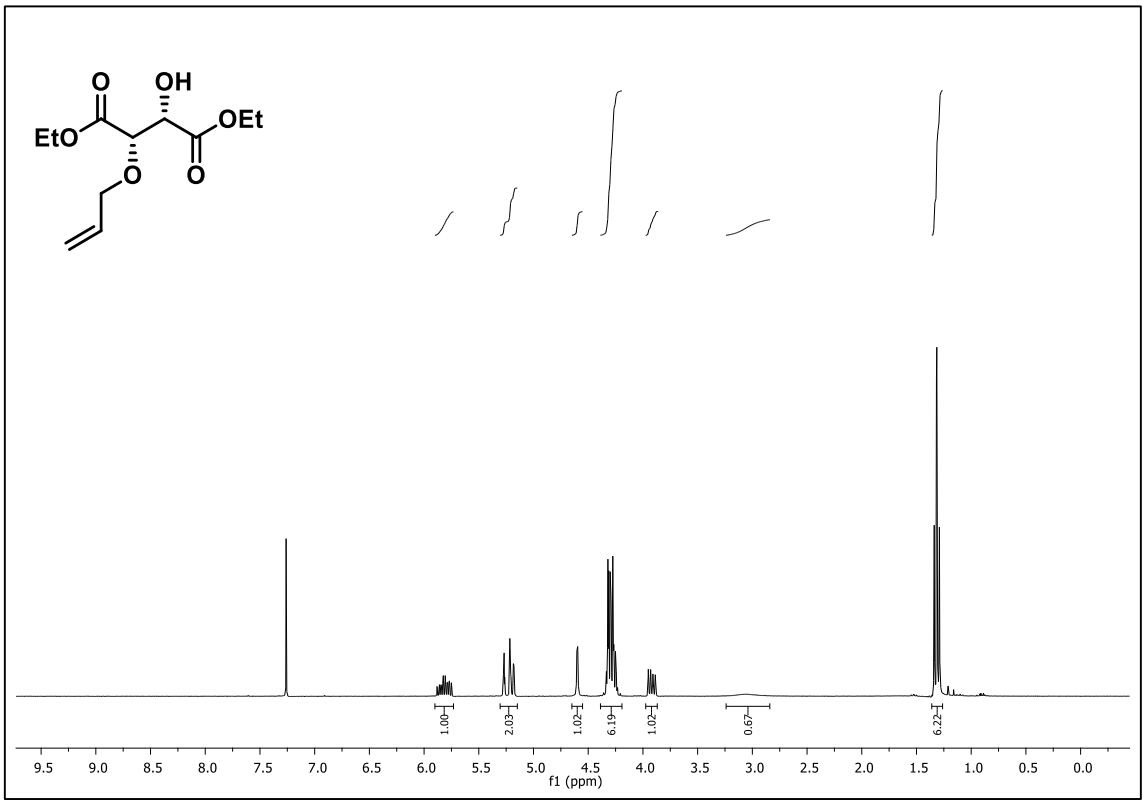
Chiral HPLC

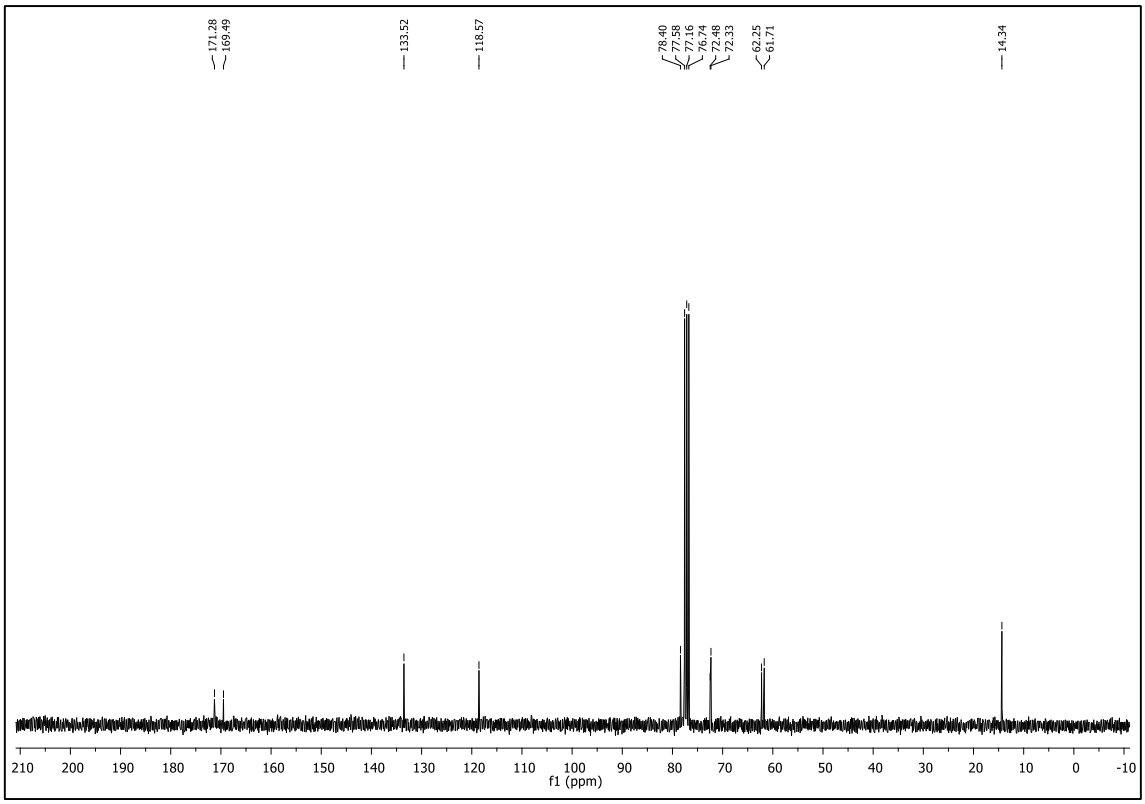

mAU
STH 1000,00
Min
CO_2Et
EtO_2C
O

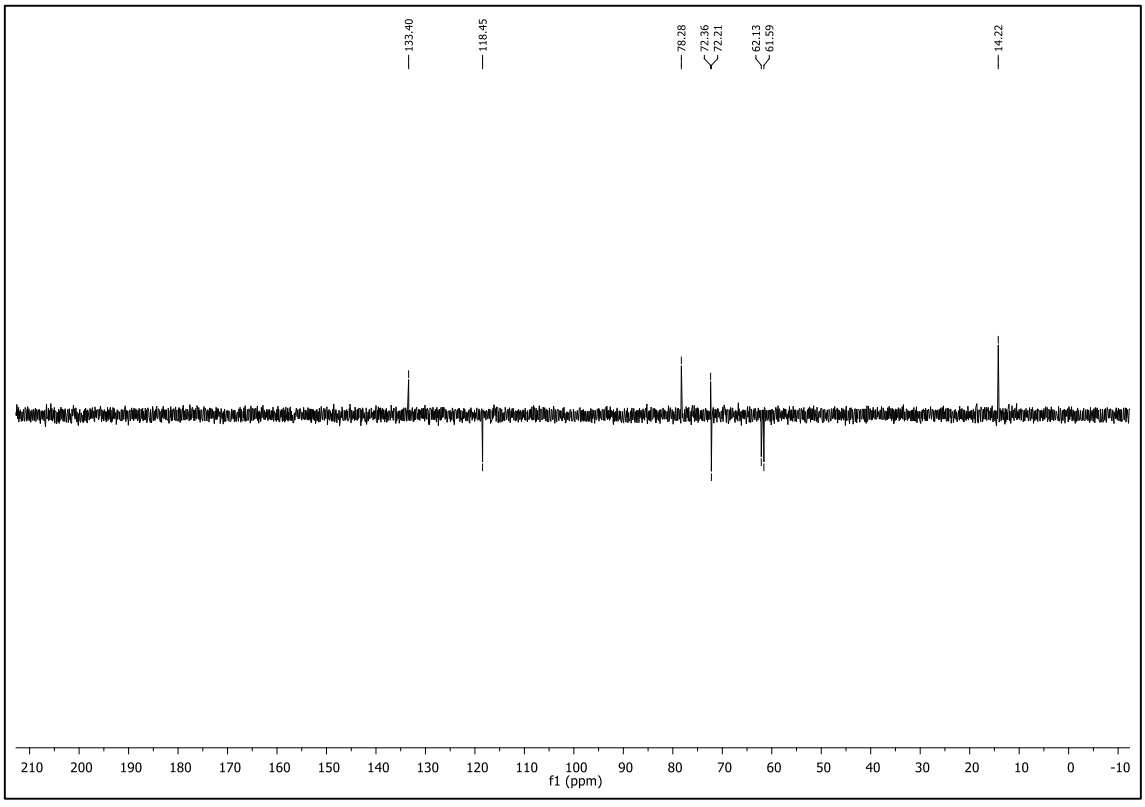

mAU
STH 1000,00
Min
CO_2Et
EtO_2C
O

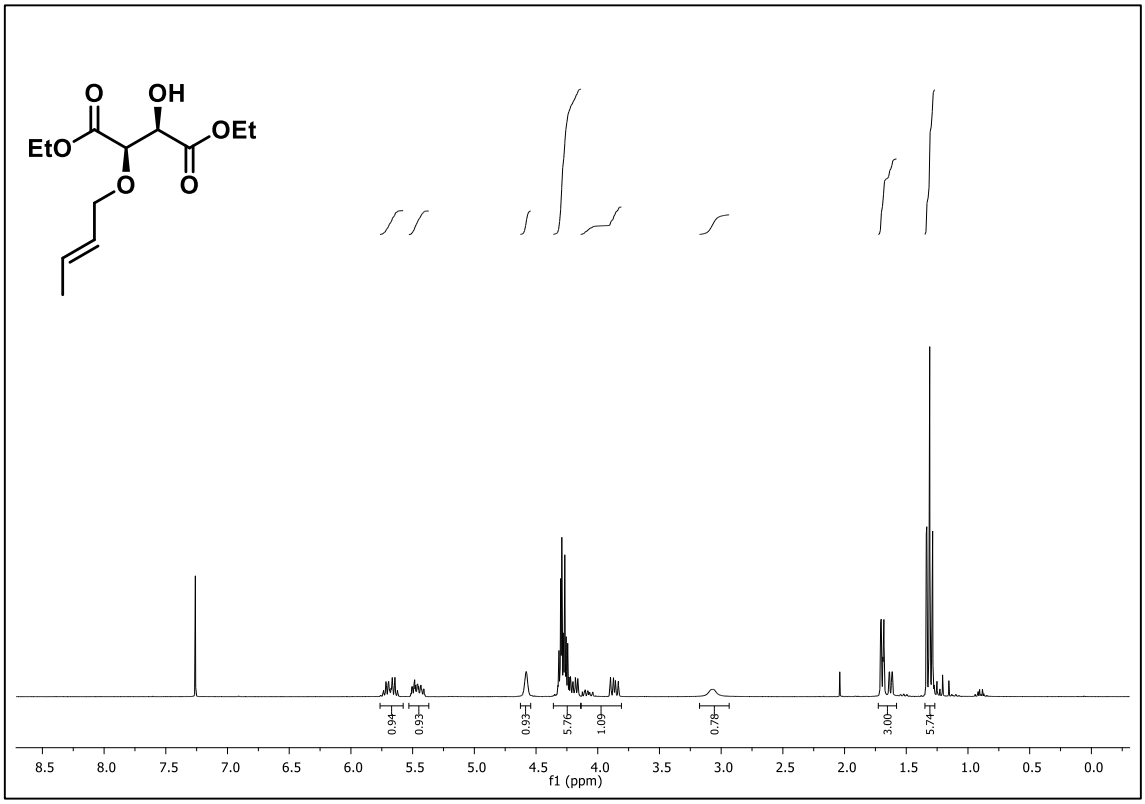
4.9.8 Spectra of compounds






171.28
169.49
133.52
118.57
78.40
77.58
77.16
76.74
72.48
72.33
62.25
61.71
14.34
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)


133.40
118.45
78.28
72.36
72.21
62.13
61.59
14.22
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)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OH
EtO
OEt
O
O
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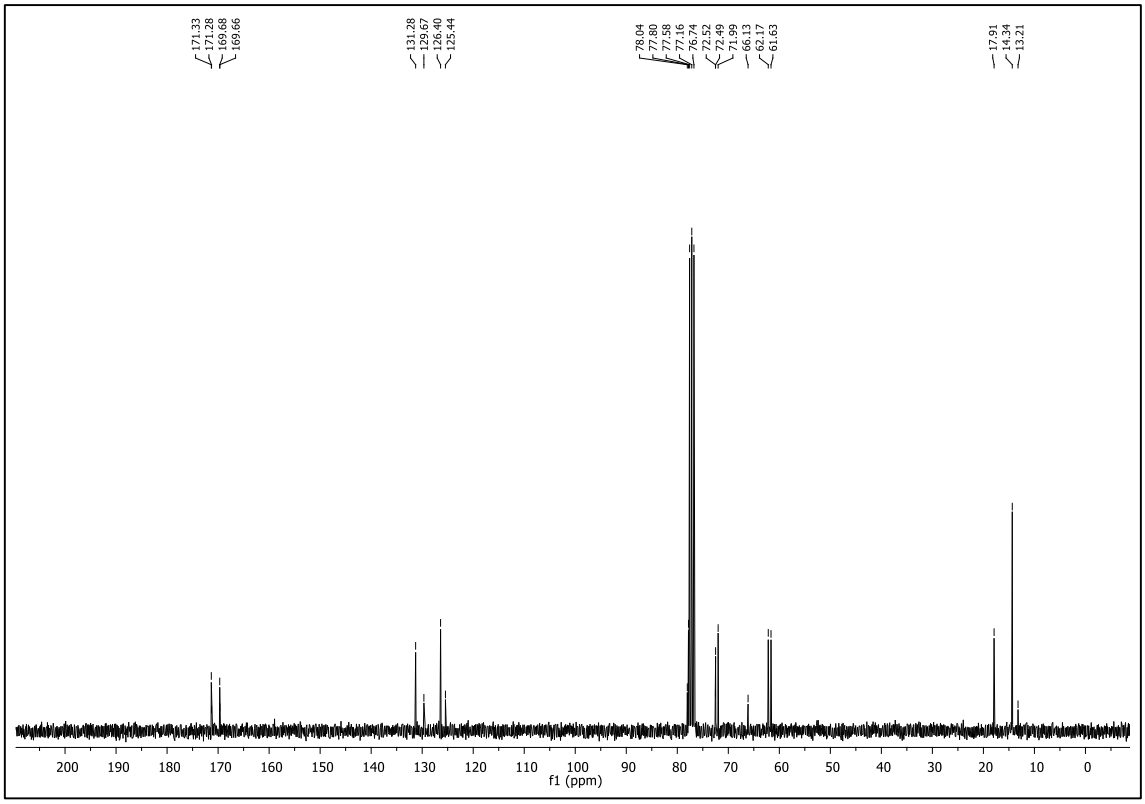
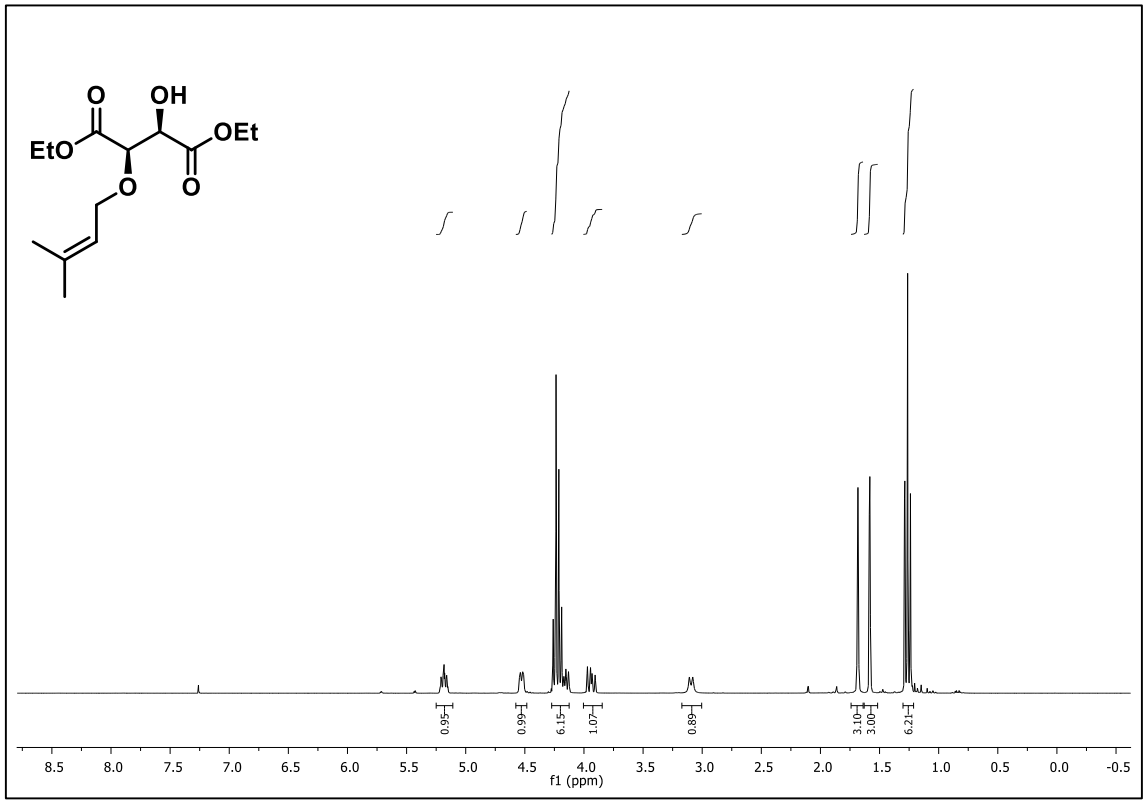
0.93
0.93
5.76
1.09
0.78
3.00
5.74
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


171.33
171.28
169.68
169.66
131.28
129.67
126.40
125.44
78.04
77.80
77.58
77.16
76.74
72.52
72.49
71.99
66.13
62.17
61.63
17.91
14.34
13.21
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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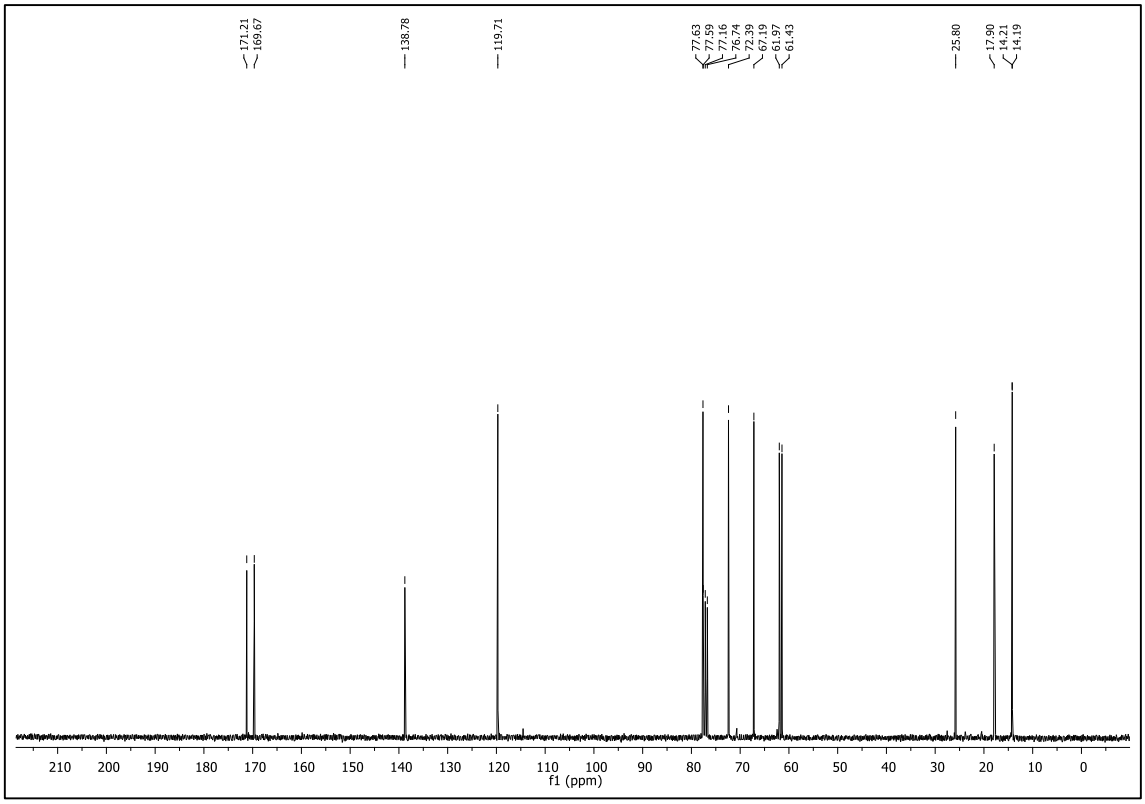
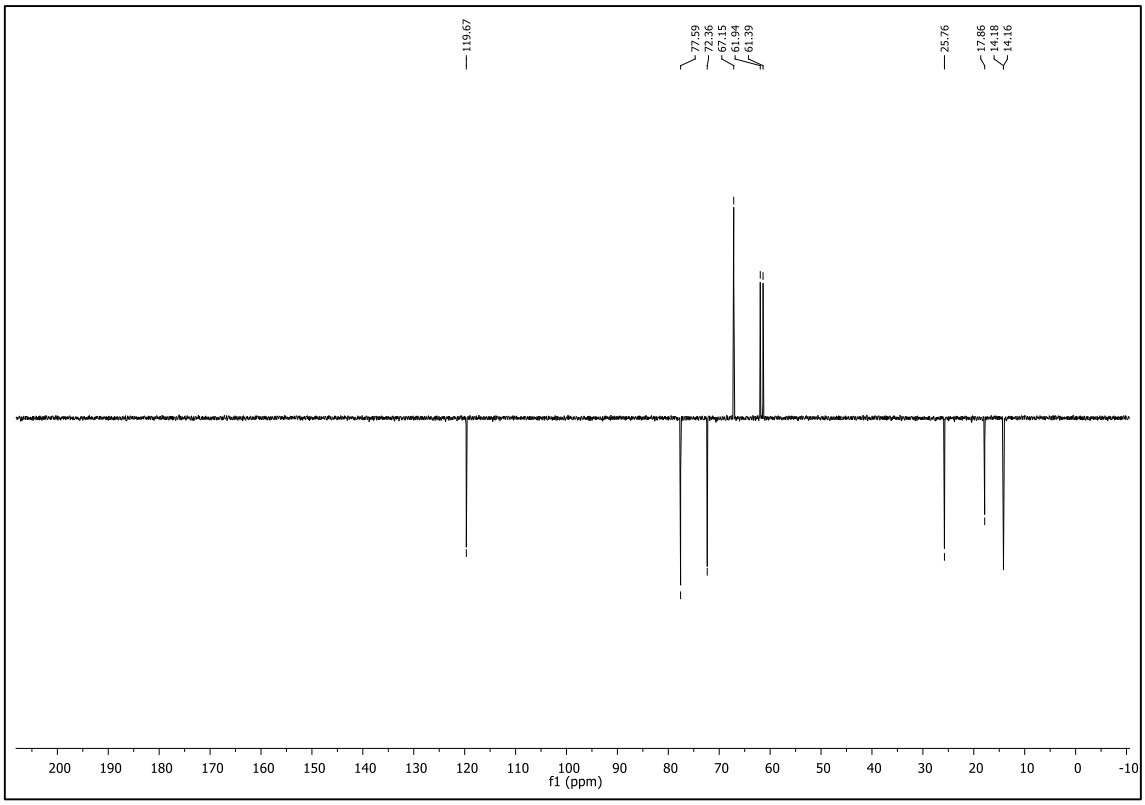
OH
EtO
OEt
O
O
0.95
0.99
6.15
1.07
0.89
3.10
3.00
6.21
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


171.21
169.67
138.78
119.71
77.63
77.59
77.16
76.74
72.39
67.19
61.97
61.43
25.80
17.90
14.21
14.19
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


119.67
77.59
72.36
67.15
61.94
61.39
25.76
17.86
14.18
14.16
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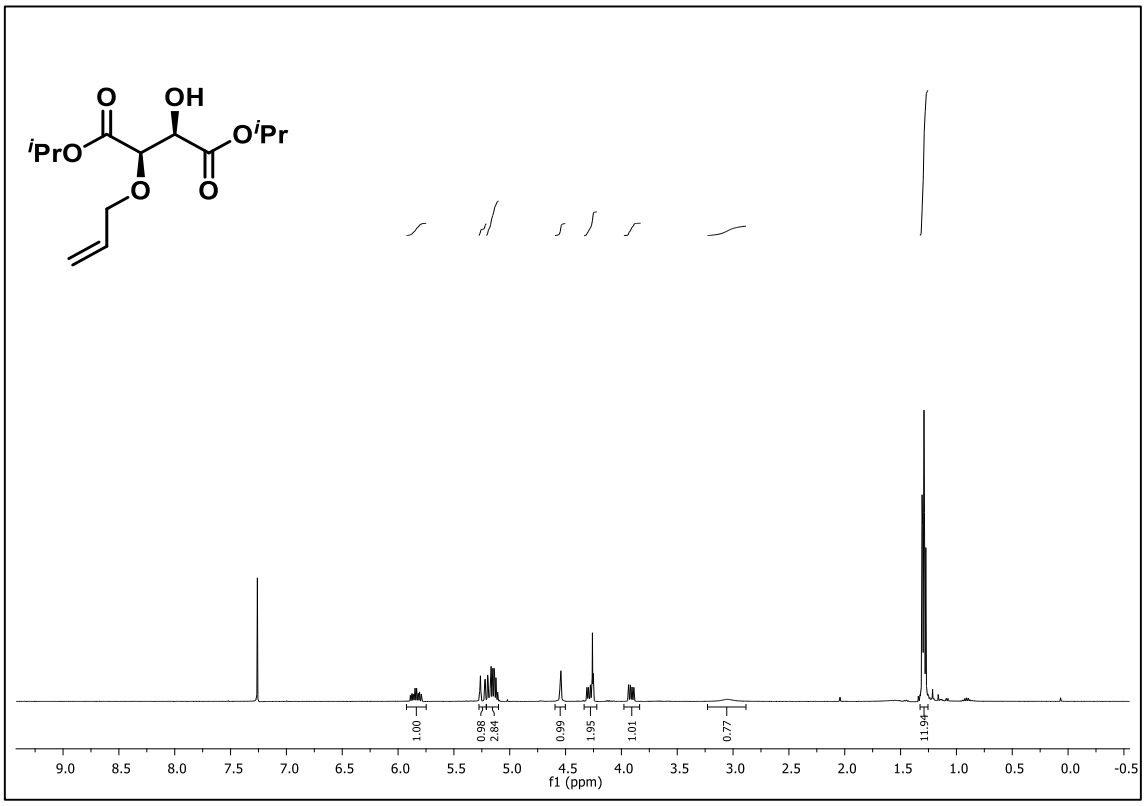
f1 (ppm)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OH
iPrO
OiPr
O
O
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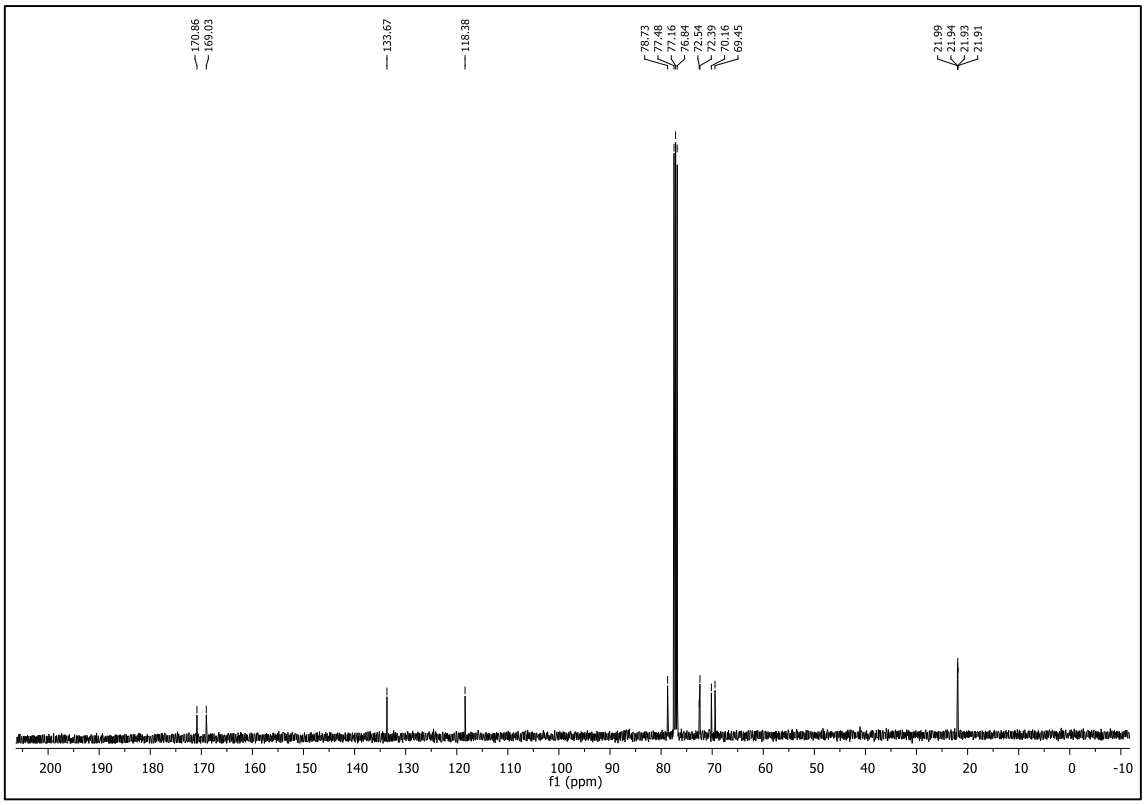
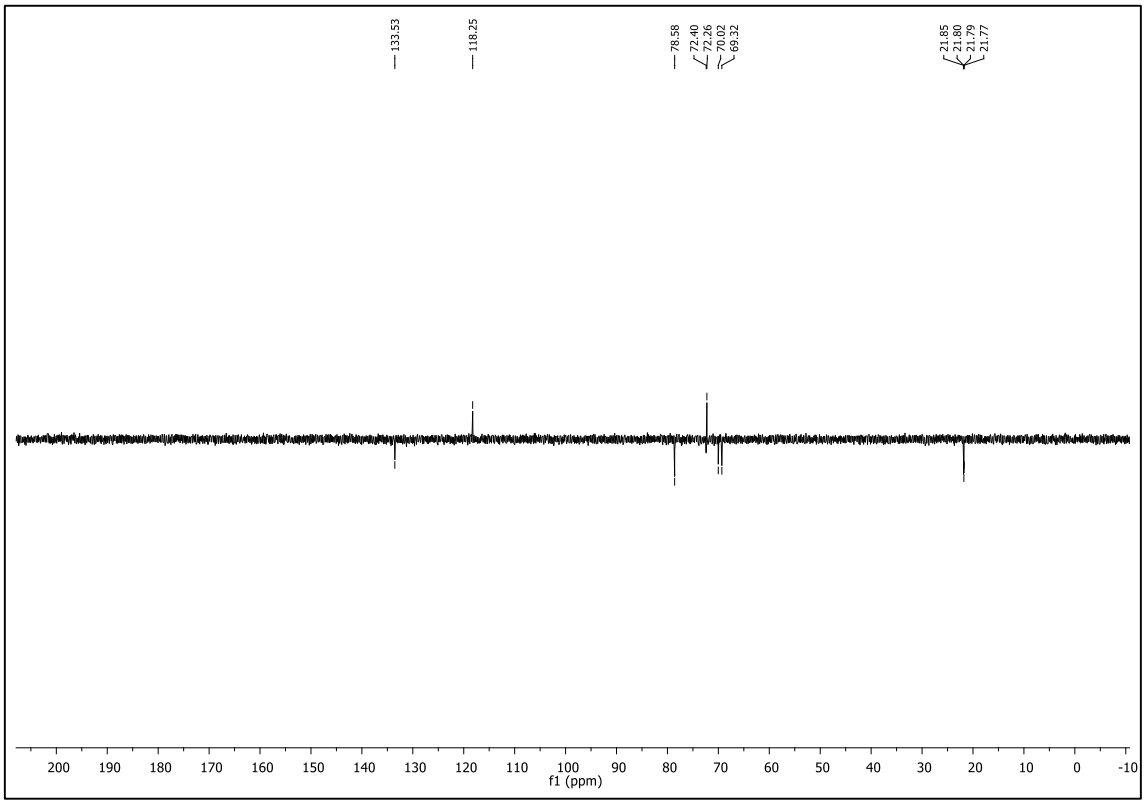
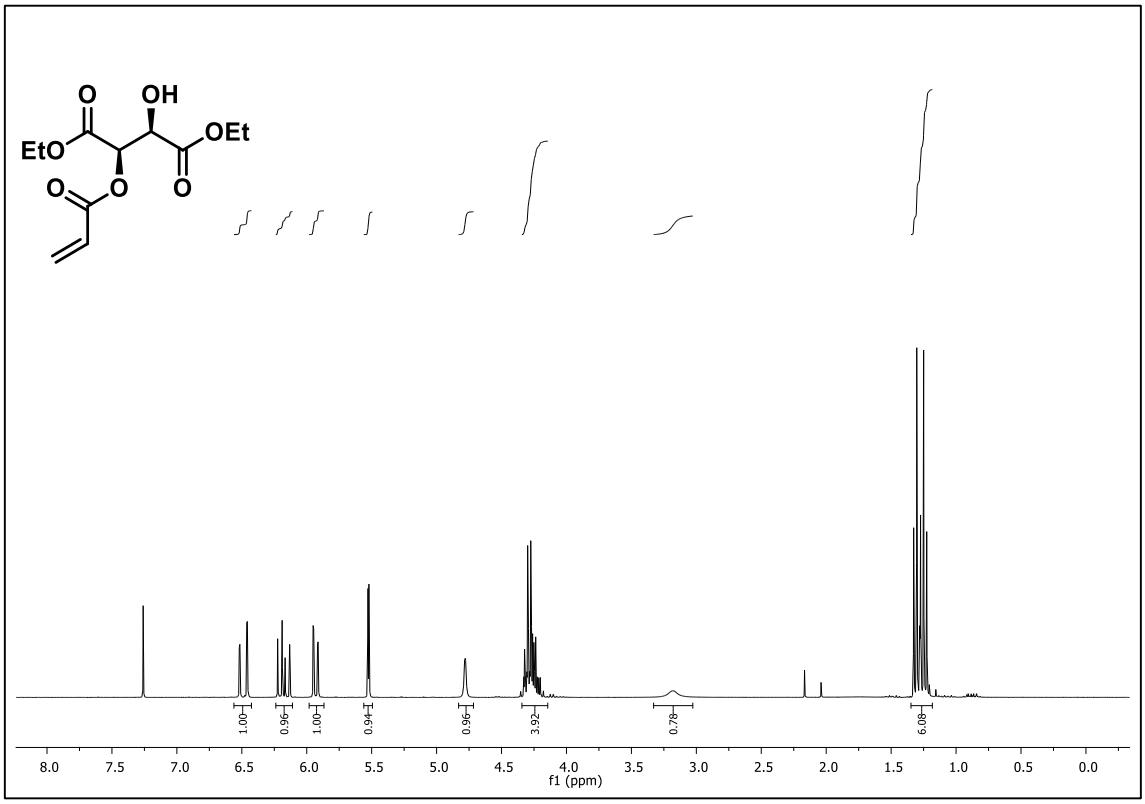
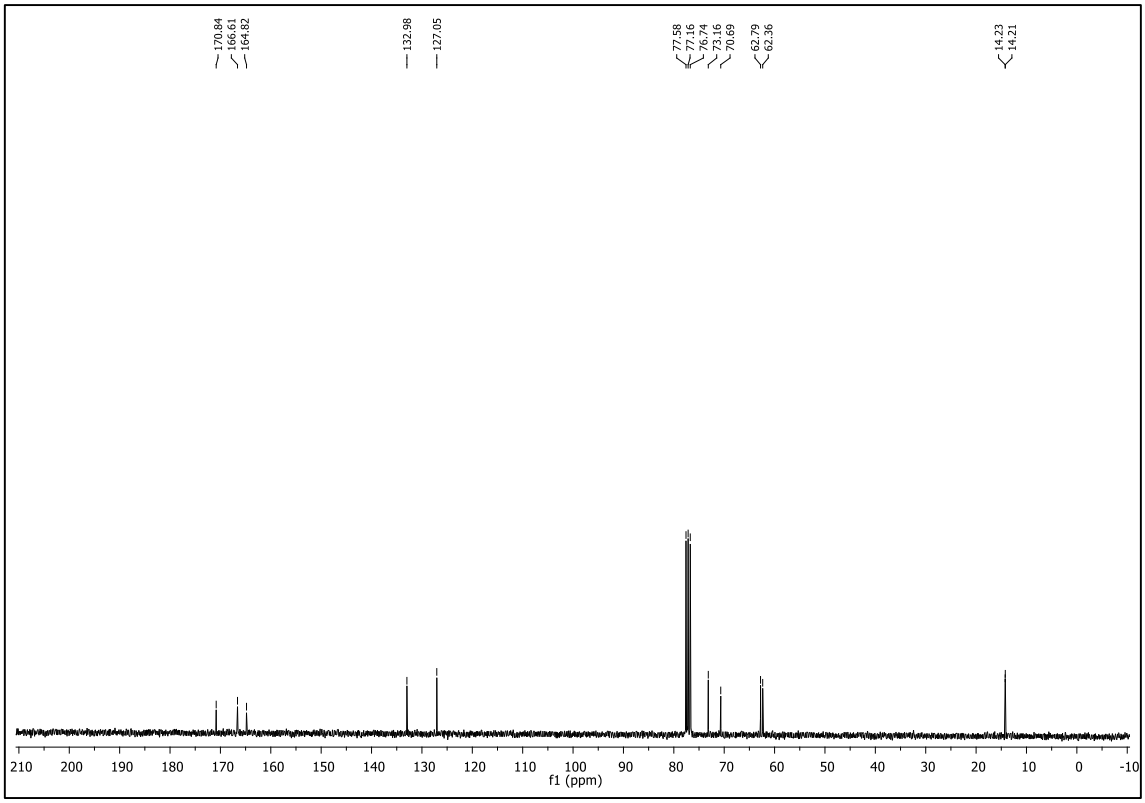
0.98
2.84
0.99
1.95
1.01
0.77
11.94
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


170.86
169.03
133.67
118.38
78.73
77.48
77.16
76.84
72.54
72.39
70.16
69.45
21.99
21.94
21.93
21.91
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


133.53
118.25
78.58
72.40
72.26
70.02
69.32
21.85
21.80
21.79
21.77
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OH
EtO
OEt
O
O
O
1.00
0.96
1.00
0.94
0.96
3.92
0.78
6.08
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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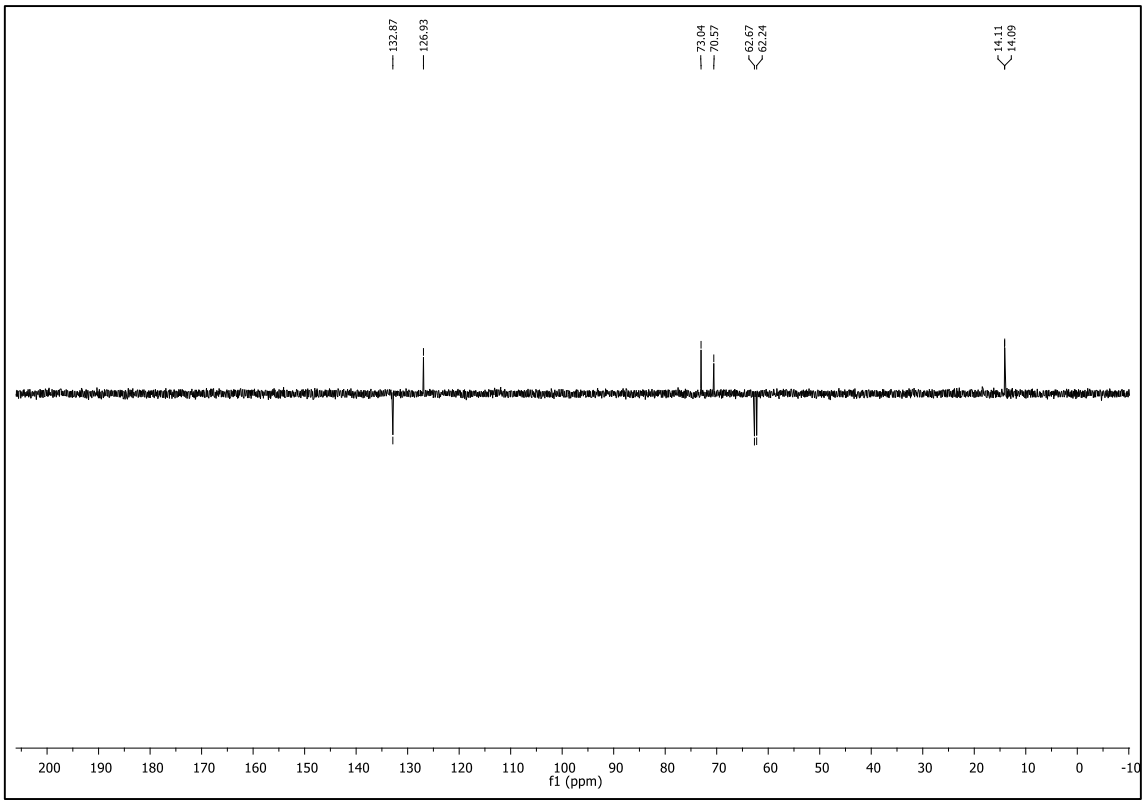
166.61
164.82
132.98
127.05
77.58
77.16
76.74
73.16
70.69
62.79
62.36
14.23
14.21
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


132.87
126.93
73.04
70.57
62.67
62.24
14.11
14.09
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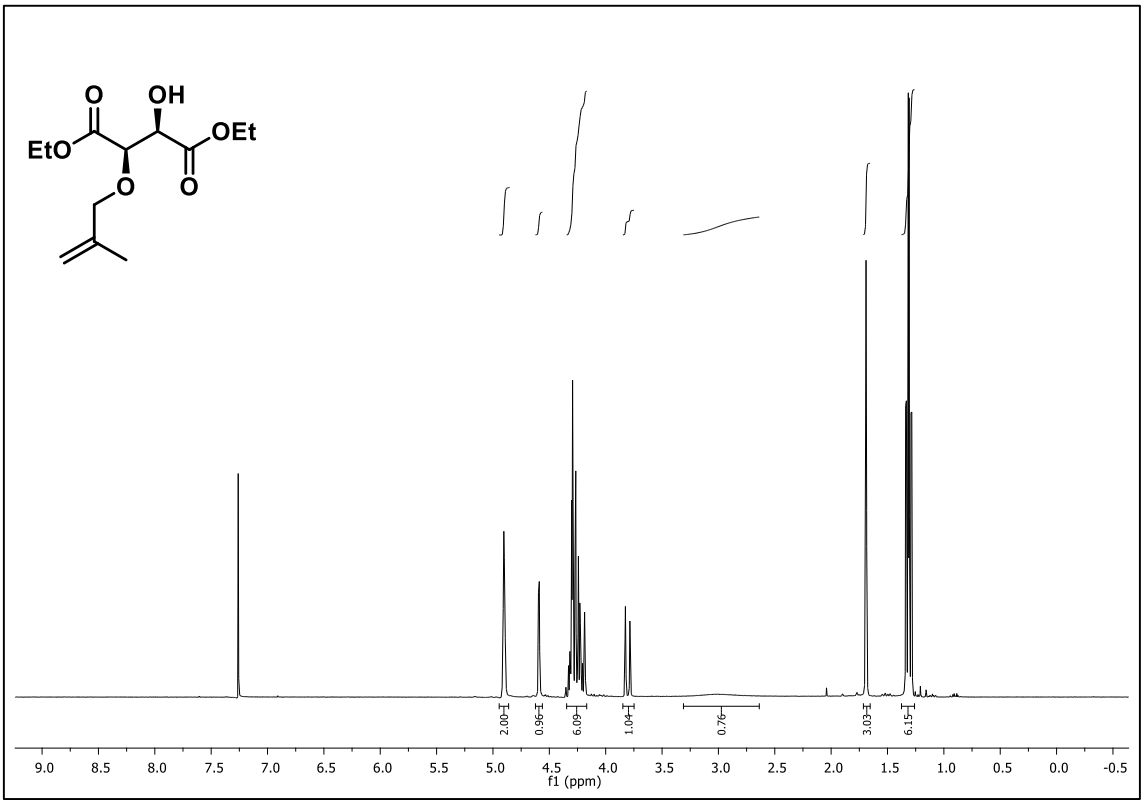
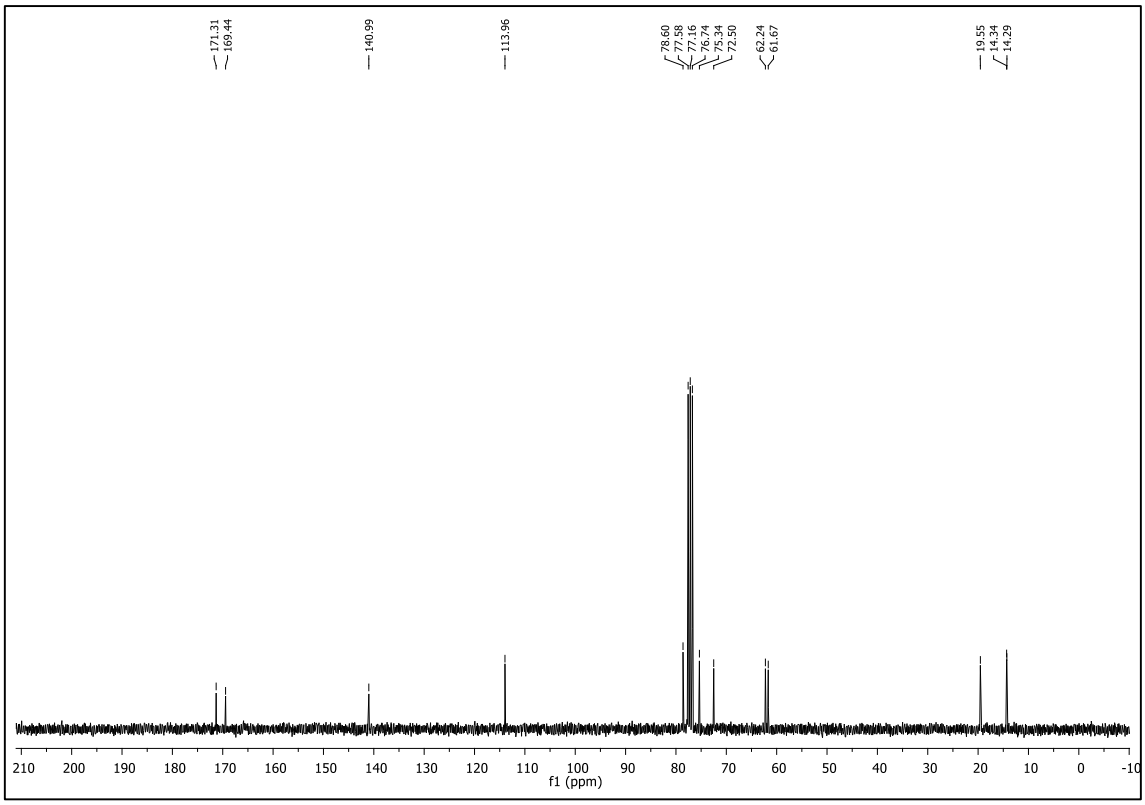
f1 (ppm)


O
OH
EtO
OEt
O
O
2.00
0.96
6.09
1.04
0.76
3.03
6.15
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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140.99
113.96
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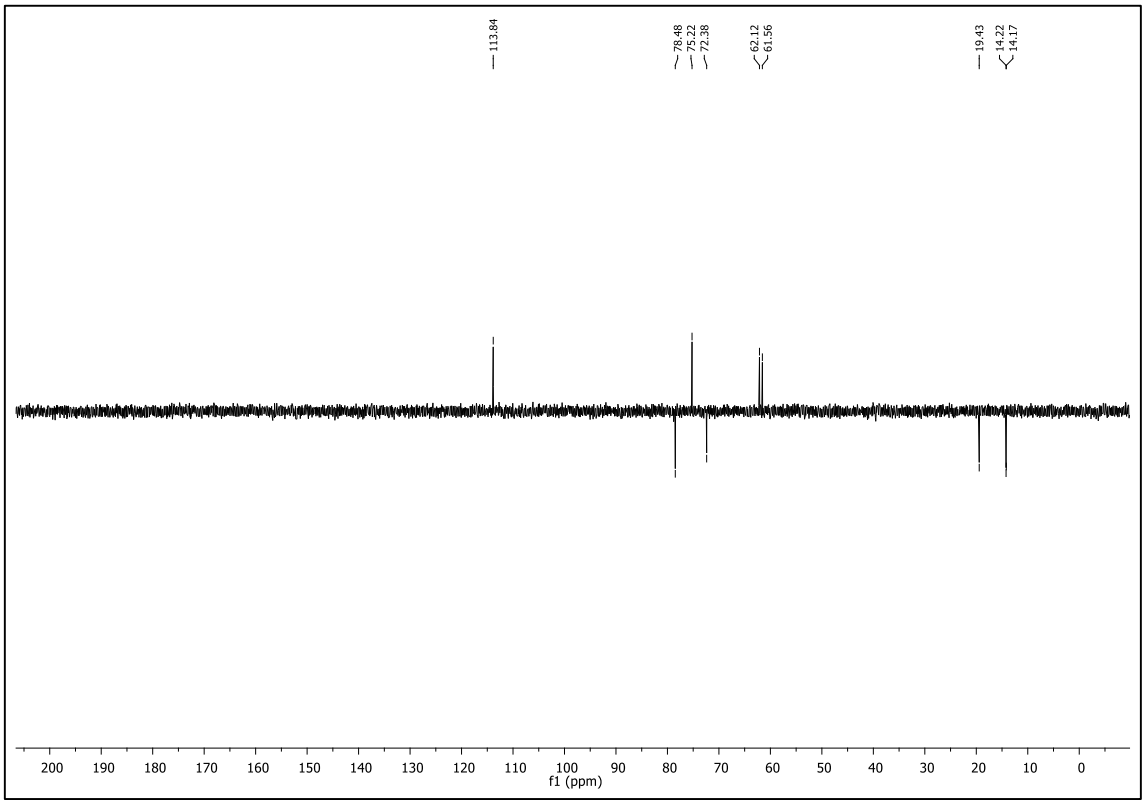
76.74
75.34
72.50
62.24
61.67
19.55
14.34
14.29
f1 (ppm)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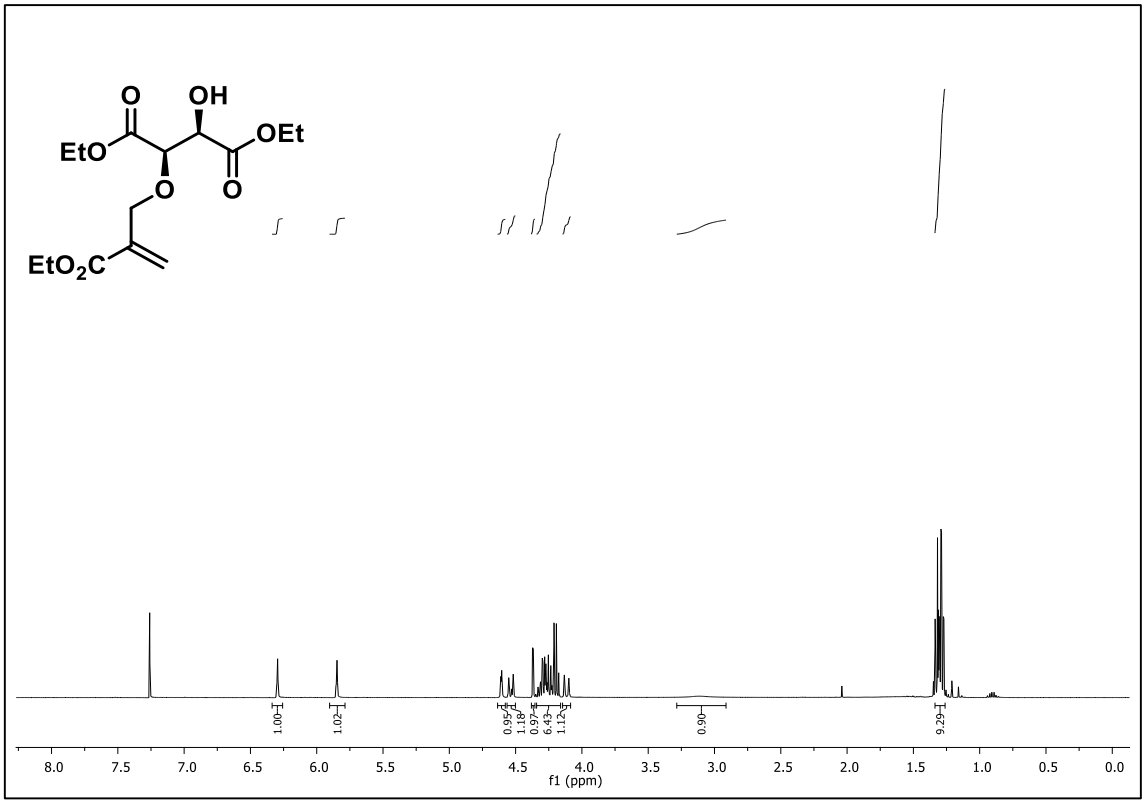
61.56
19.43
14.22
14.17
f1 (ppm)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OH
EtO
OEt
O
O
EtO2C
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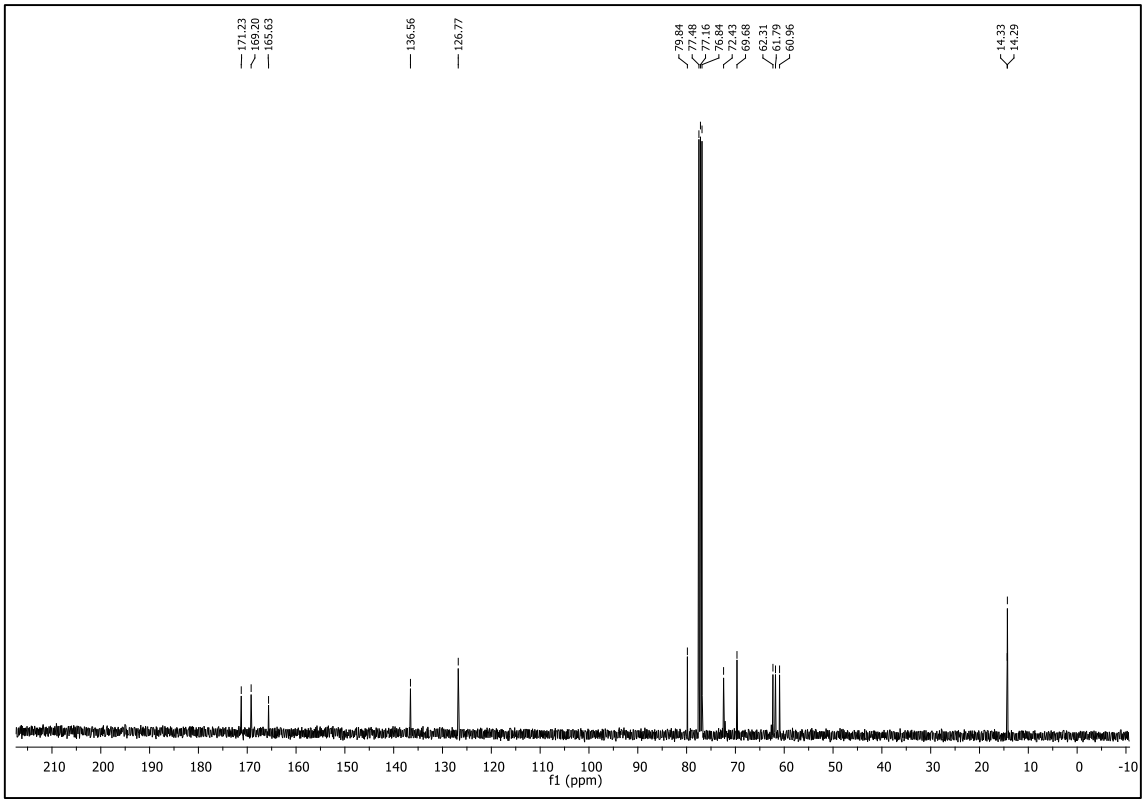
1.02
0.95
1.18
0.97
6.43
1.12
0.90
9.29
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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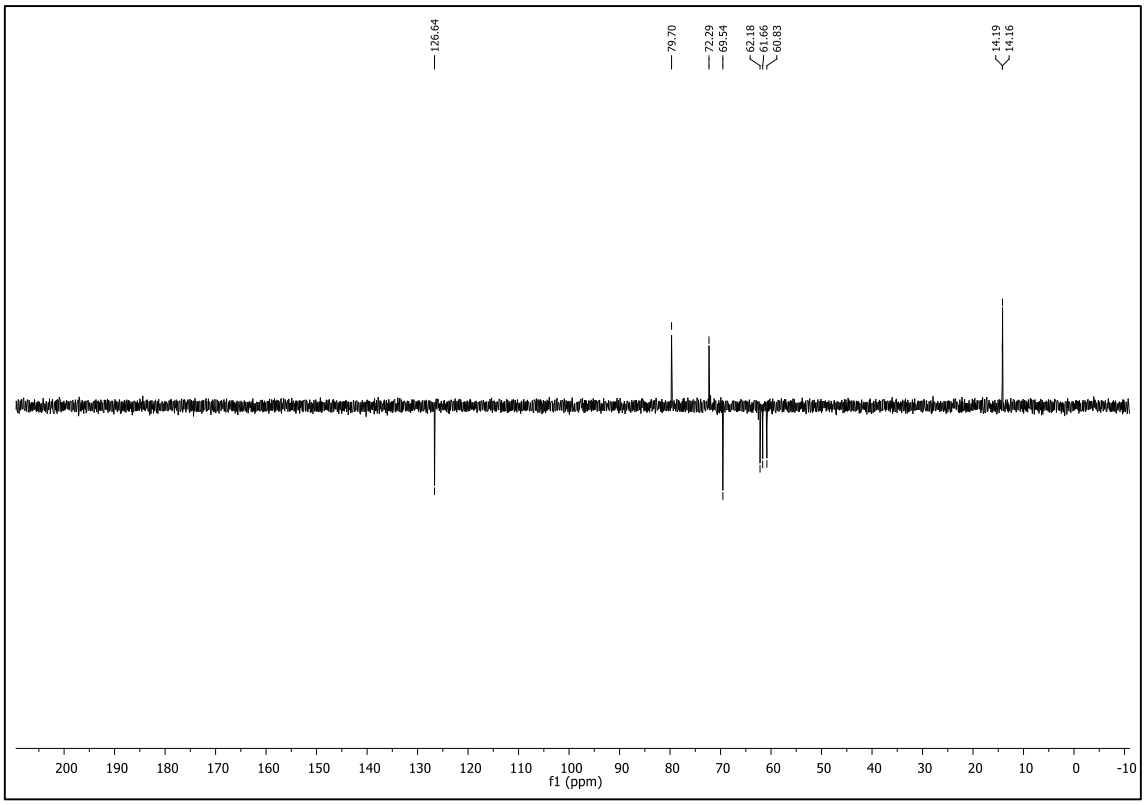
136.56
126.77
79.84
77.48
77.16
76.84
72.43
69.68
62.31
61.79
60.96
14.33
14.29
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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61.66
60.83
14.19
14.16
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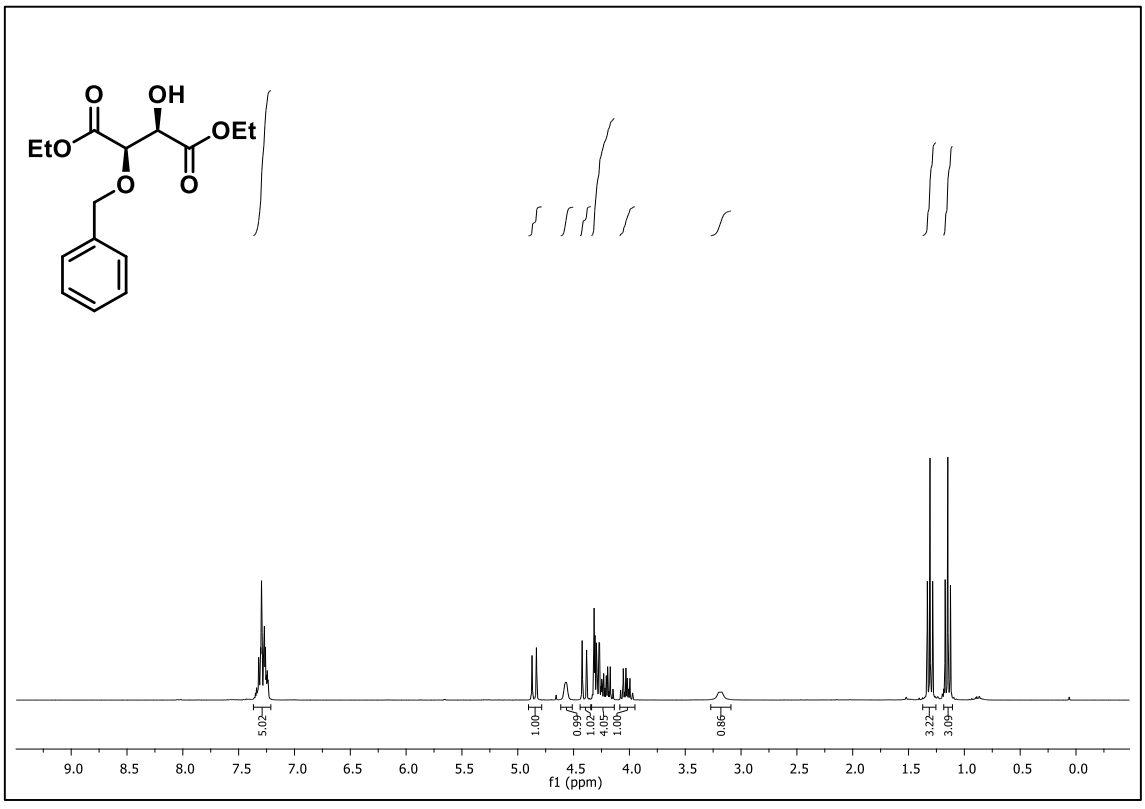
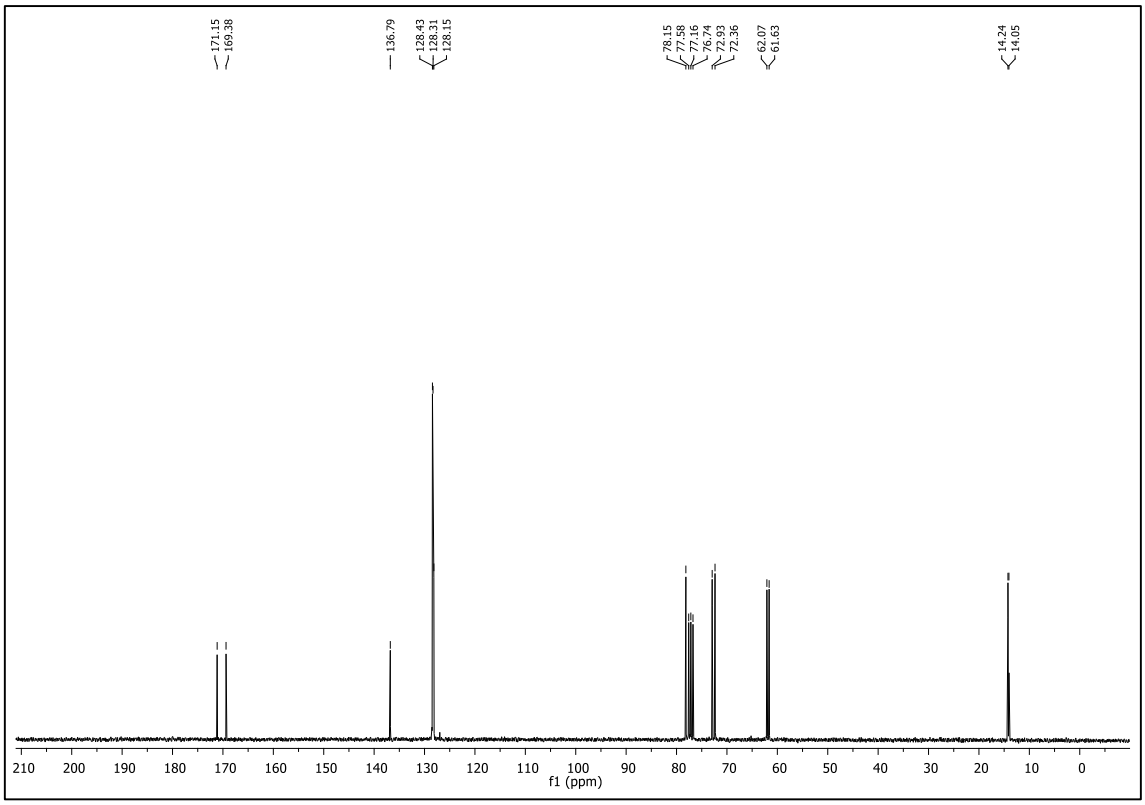
f1 (ppm)


O
OH
EtO
OEt
O
O
5.02
1.00
0.99
1.02
4.05
1.00
0.86
3.22
3.09
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)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128.43
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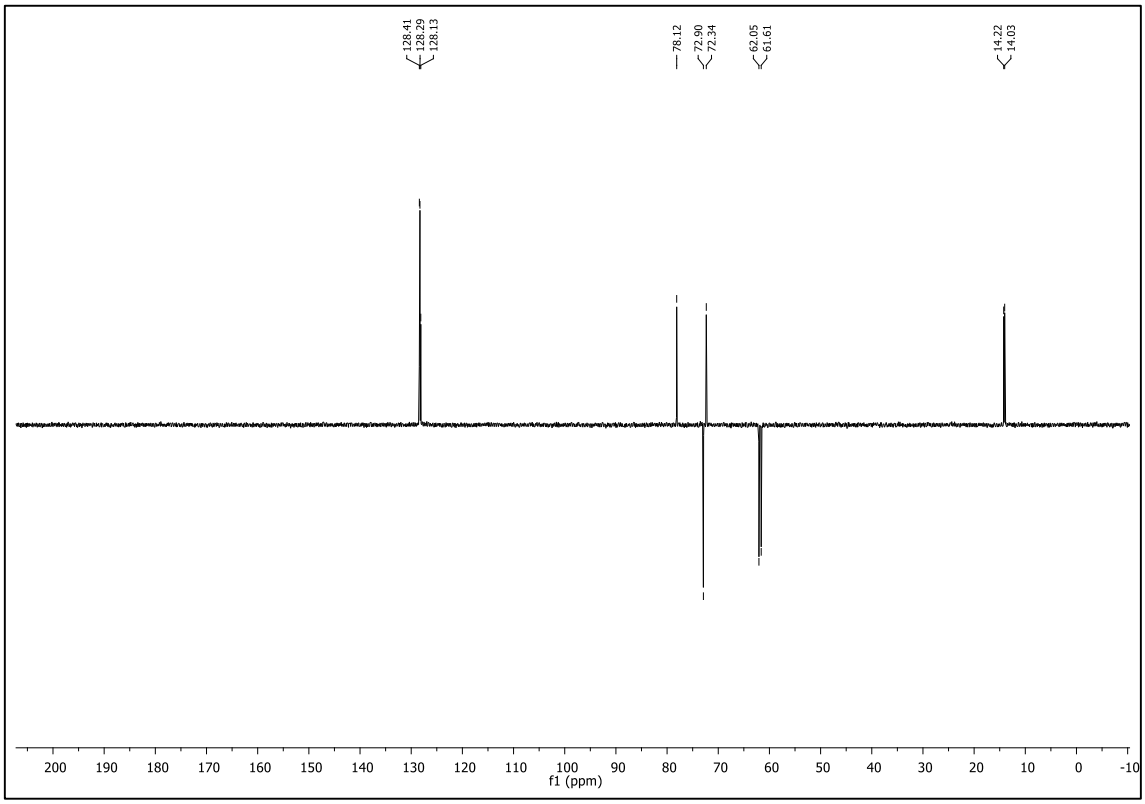
76.74
72.93
72.36
62.07
61.63
14.24
14.05
f1 (ppm)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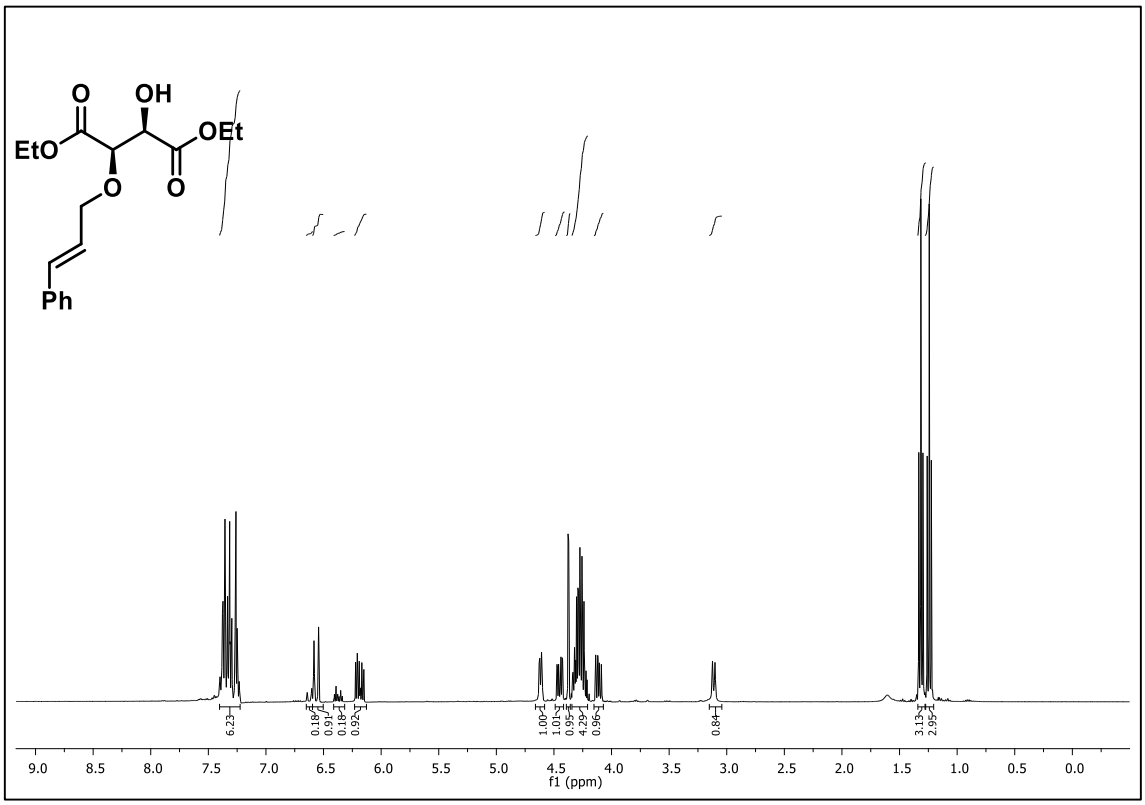
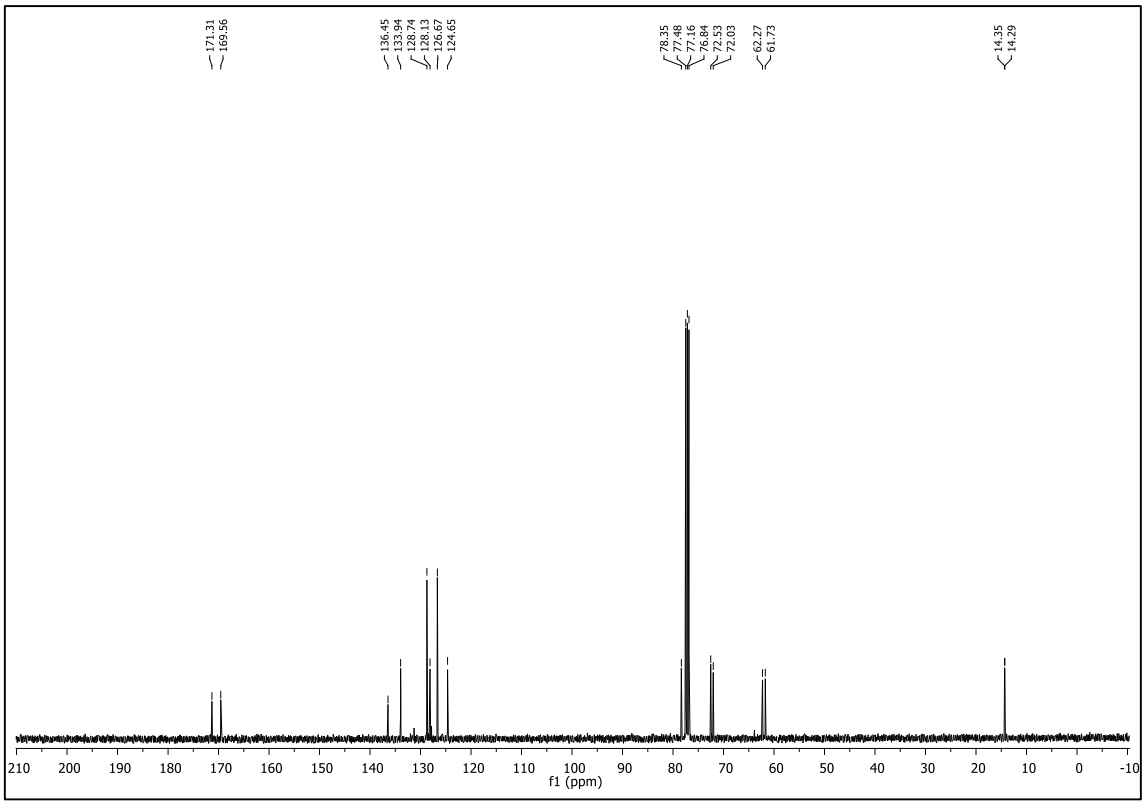
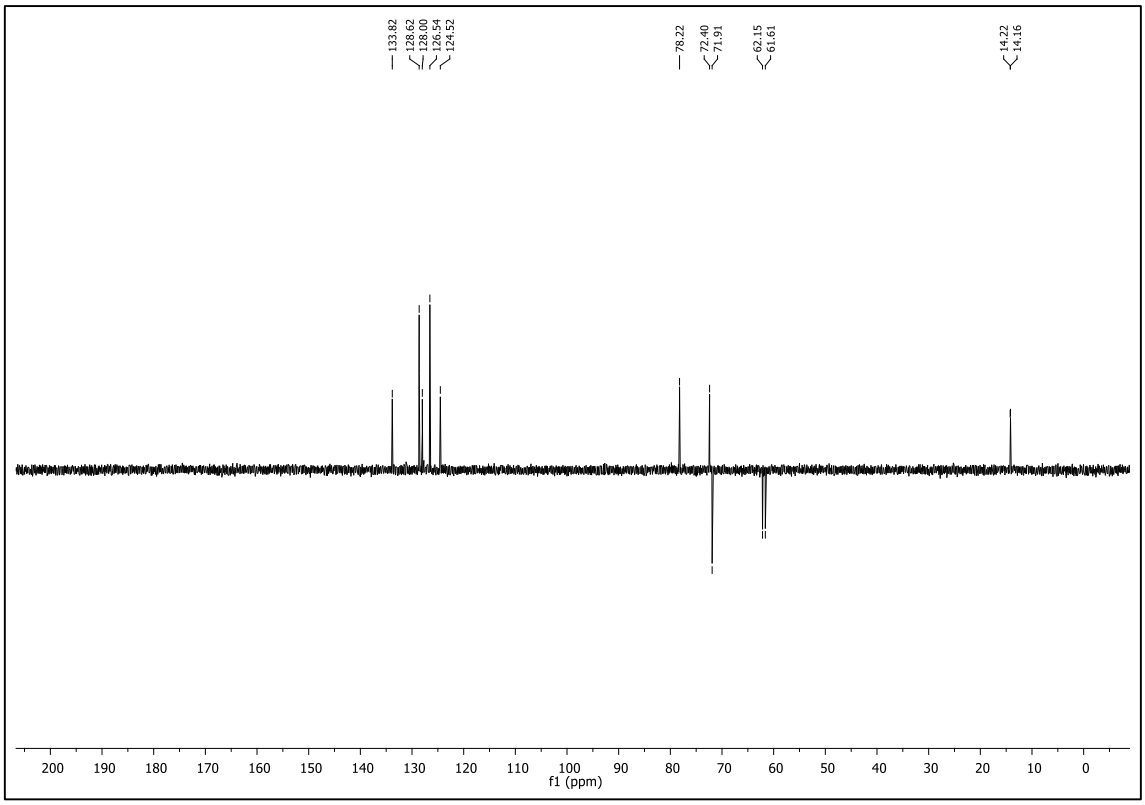
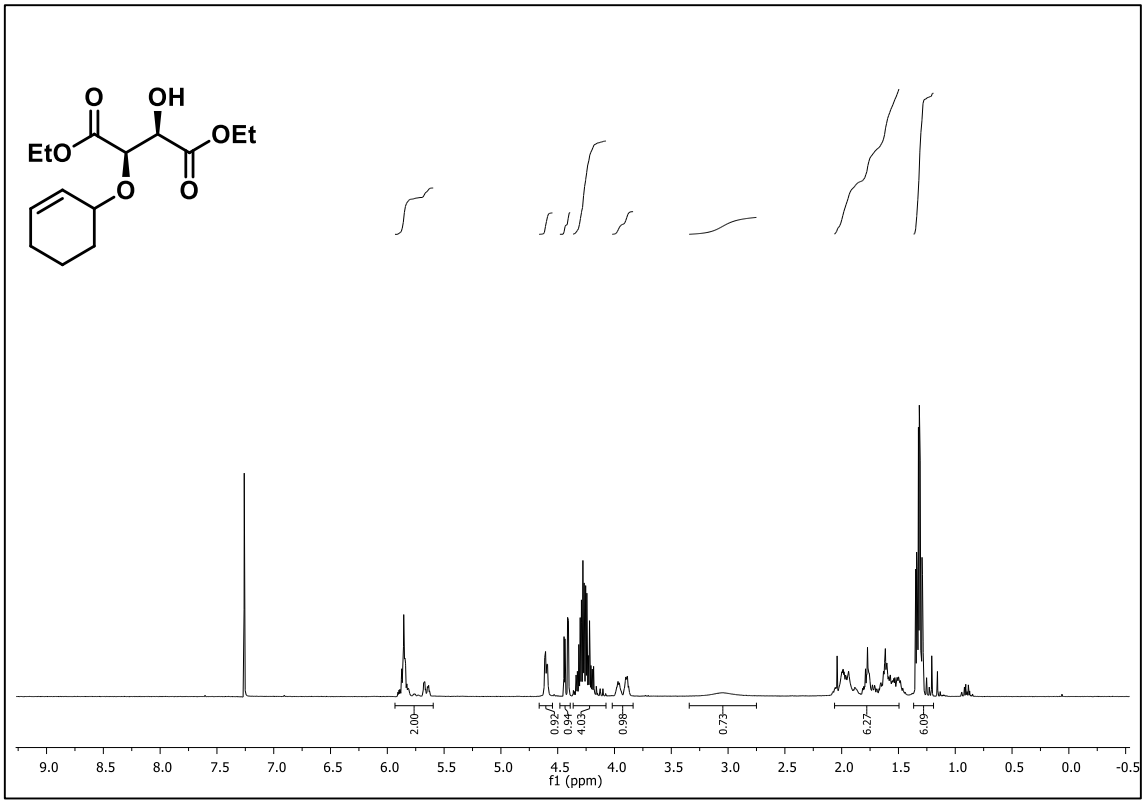
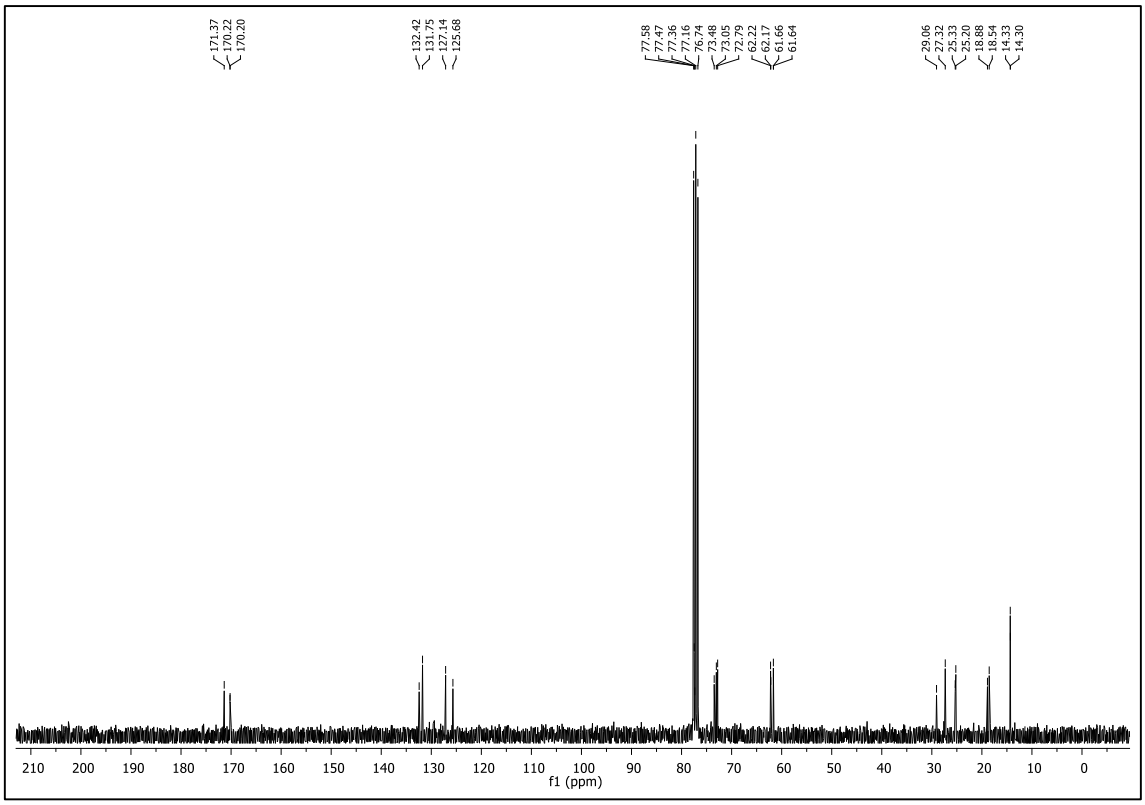
72.90
72.34
62.05
61.61
14.22
14.03
f1 (ppm)

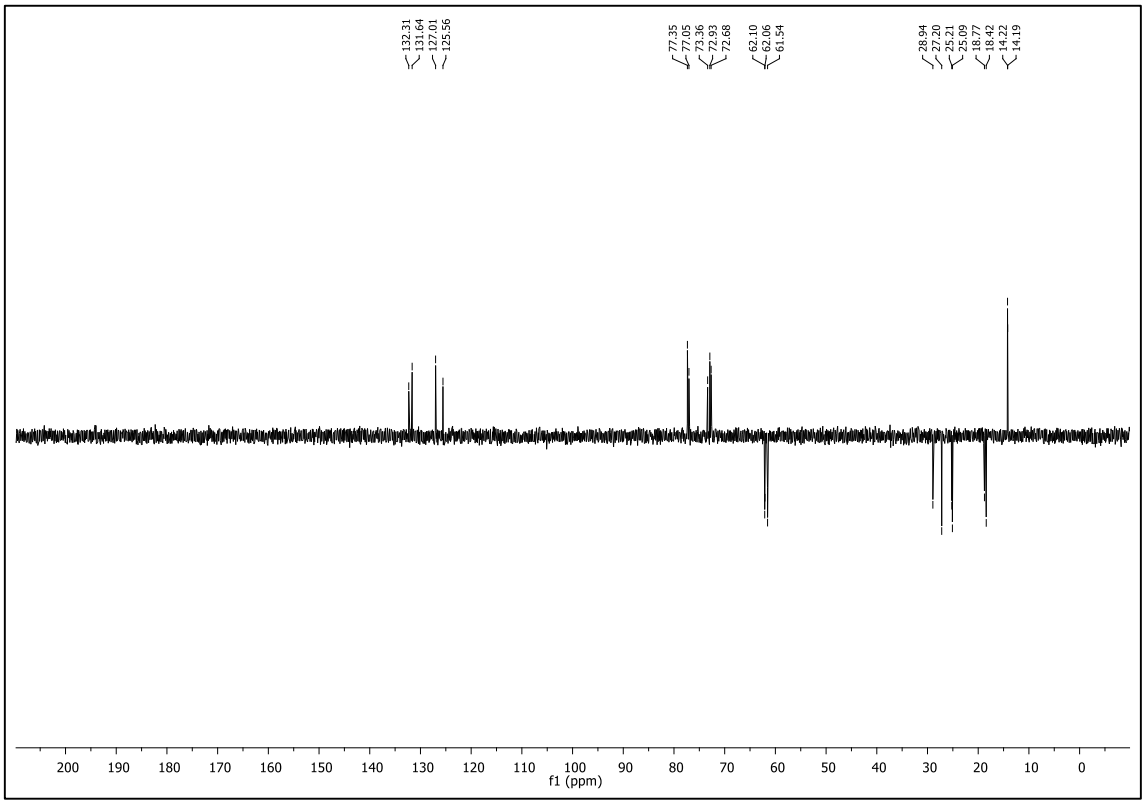

O
OH
EtO
OEt
O
O
Ph
6.23
0.18
0.91
0.18
0.92
1.00
1.01
0.95
4.29
0.96
0.84
3.13
2.95
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

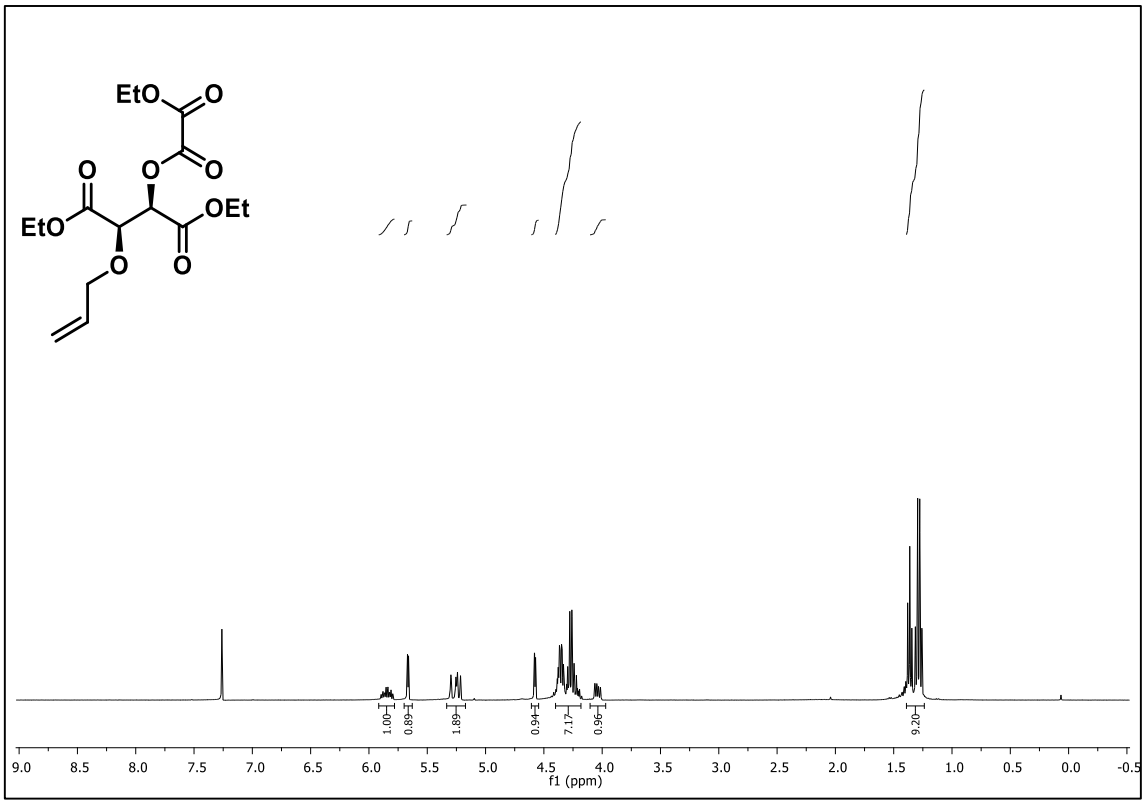

171.31
169.56
136.45
133.94
128.74
128.13
126.67
124.65
78.35
77.48
77.16
76.84
72.53
72.03
62.27
61.73
14.35
14.29
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

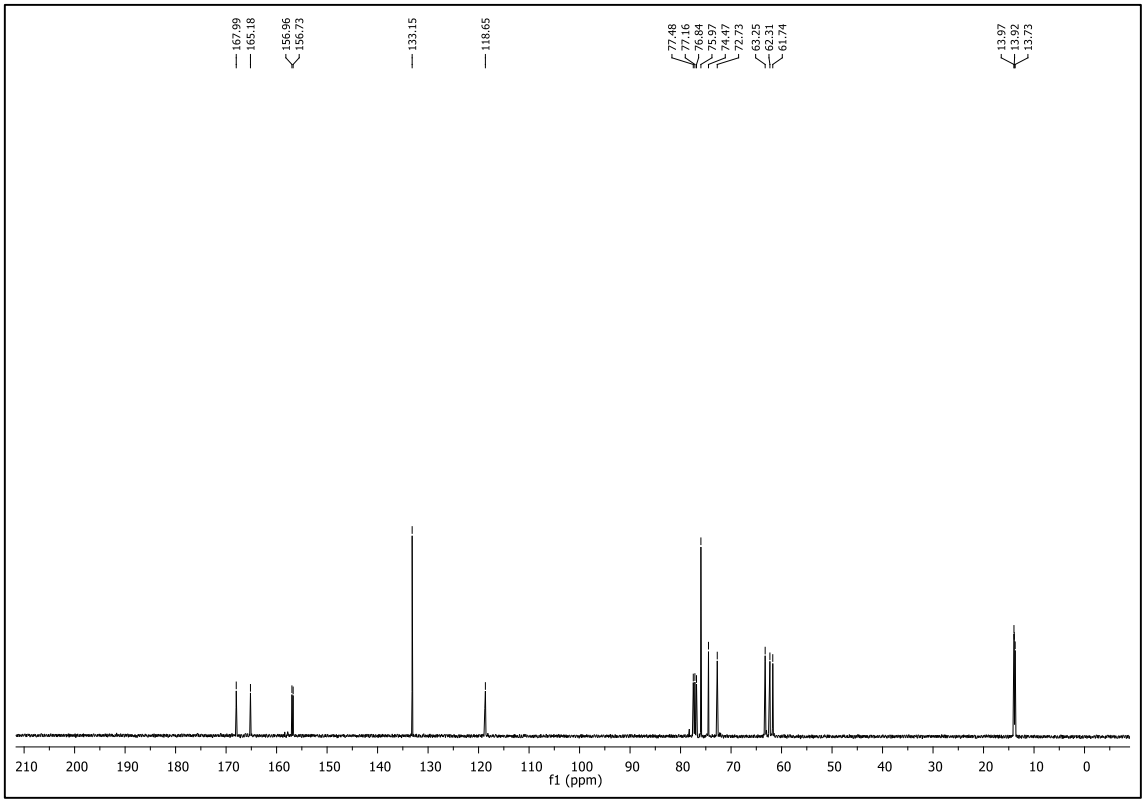

133.82
128.62
128.00
126.54
124.52
78.22
72.40
71.91
62.15
61.61
14.22
14.16
f1 (ppm)

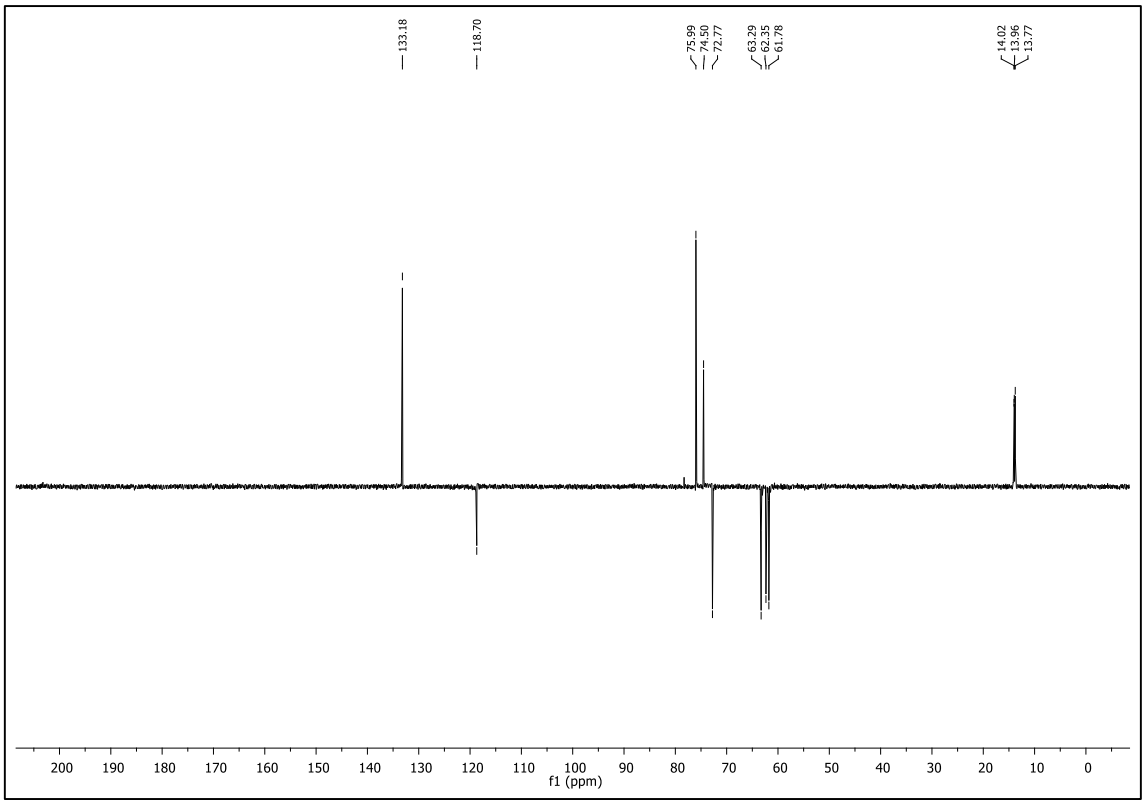

O
OH
EtO
OEt
O
O
2.00
0.92
0.94
4.03
0.98
0.73
6.27
6.09
f1 (ppm)

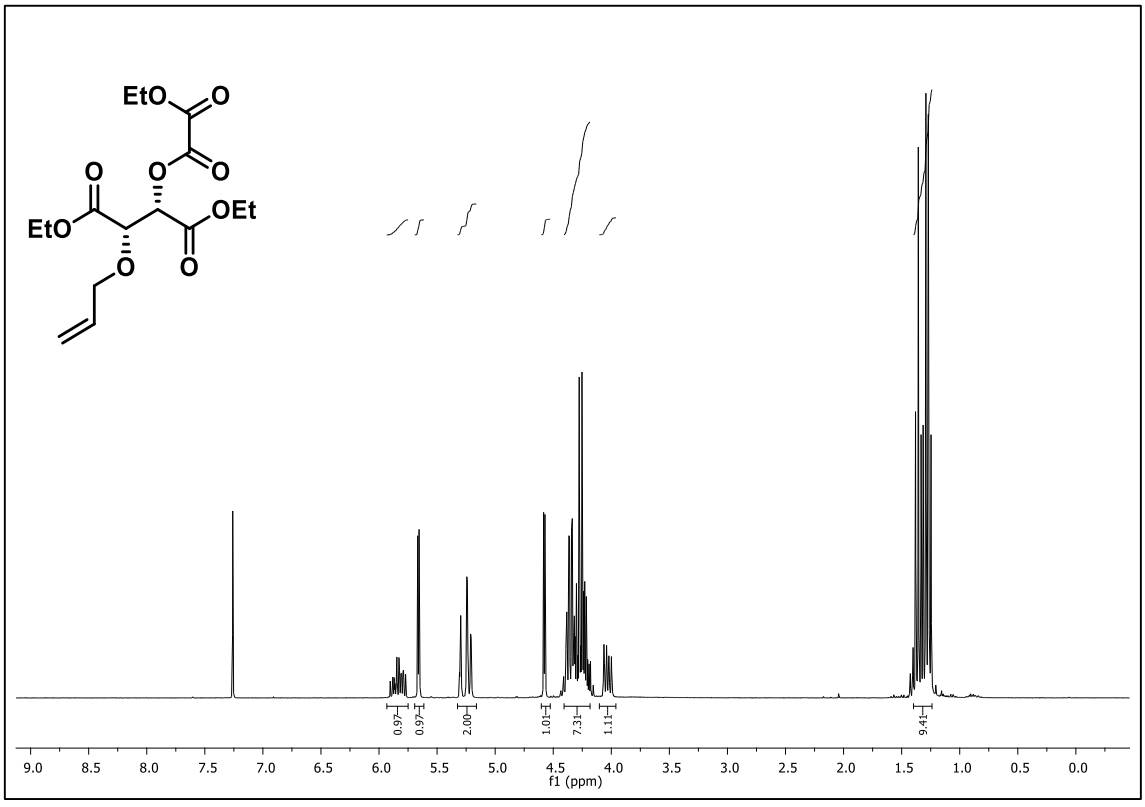

171.37
170.22
170.20
132.42
131.75
127.14
125.68
77.58
77.47
77.36
77.16
76.74
73.48
73.05
72.79
62.22
62.17
61.66
61.64
29.06
27.32
25.33
25.20
18.88
18.64
14.33
14.30
f1 (ppm)

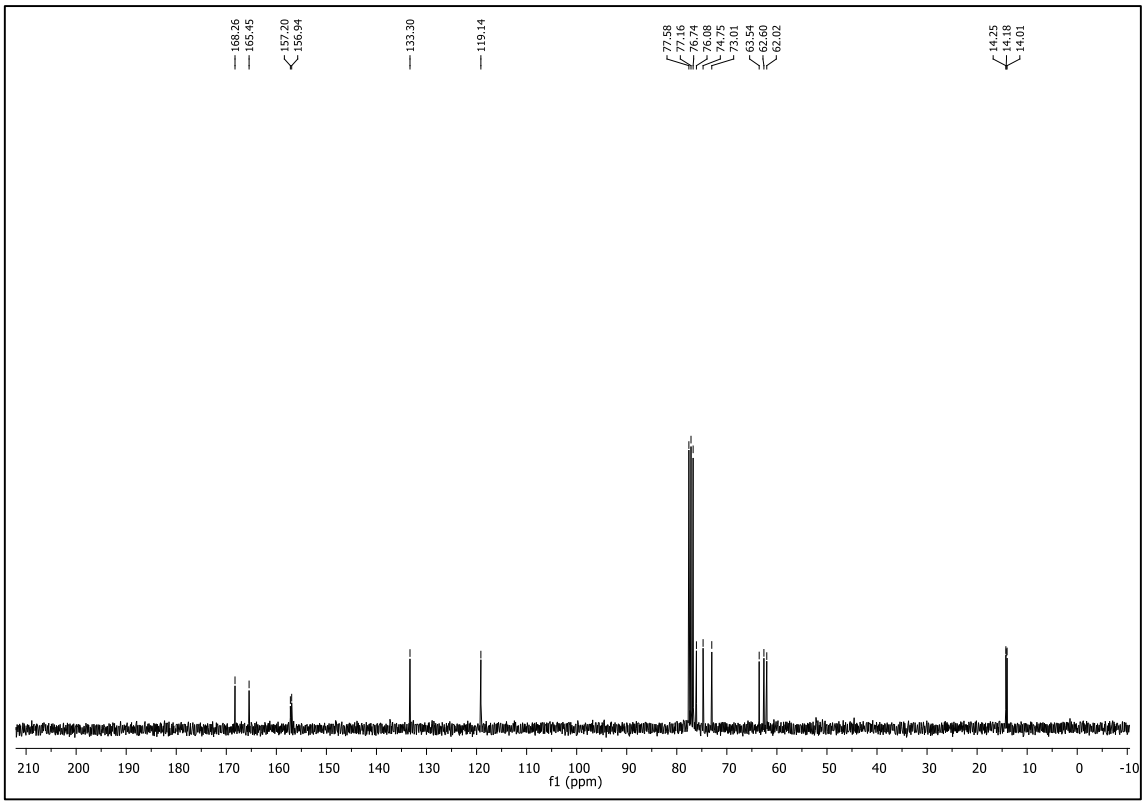

132.31
131.64
127.01
125.56
77.35
77.05
73.36
72.93
72.68
62.10
62.06
61.54
28.94
27.20
25.21
25.09
18.77
18.42
14.22
14.19
f1 (ppm)

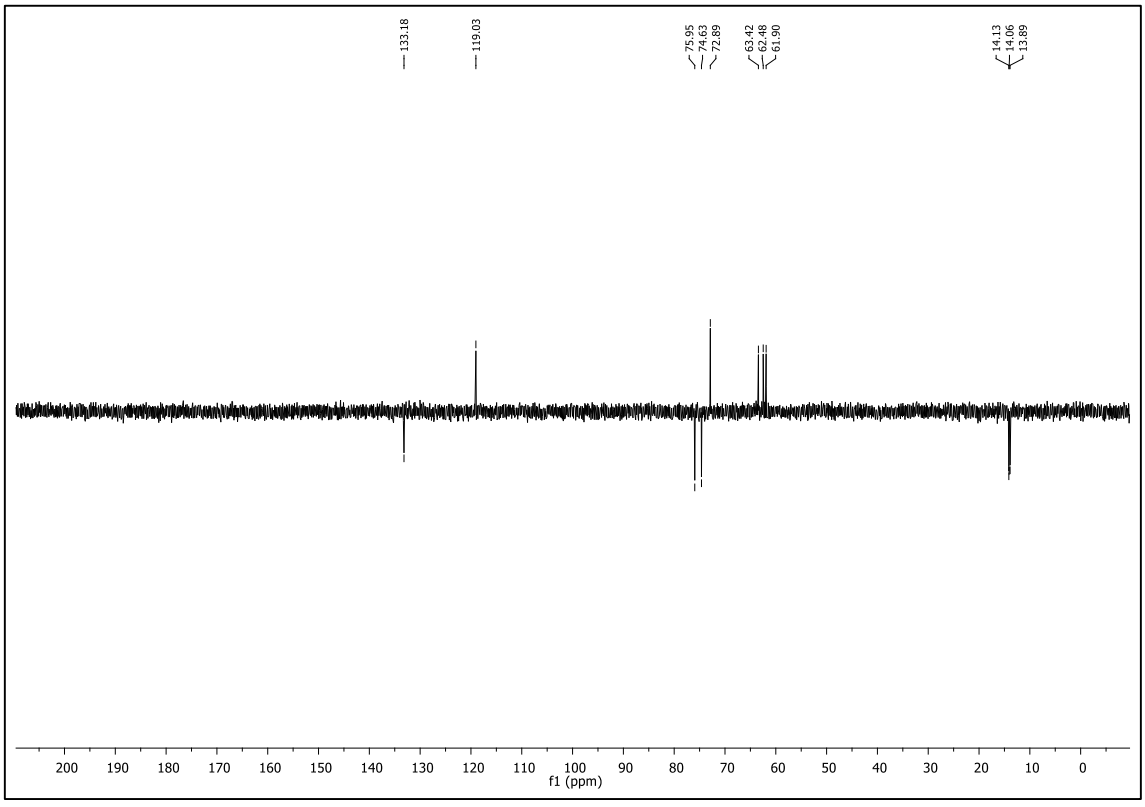

EtO
O
O
O
O
EtO
OEt
O
O
1.00
0.89
1.89
0.94
7.17
0.96
9.20
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

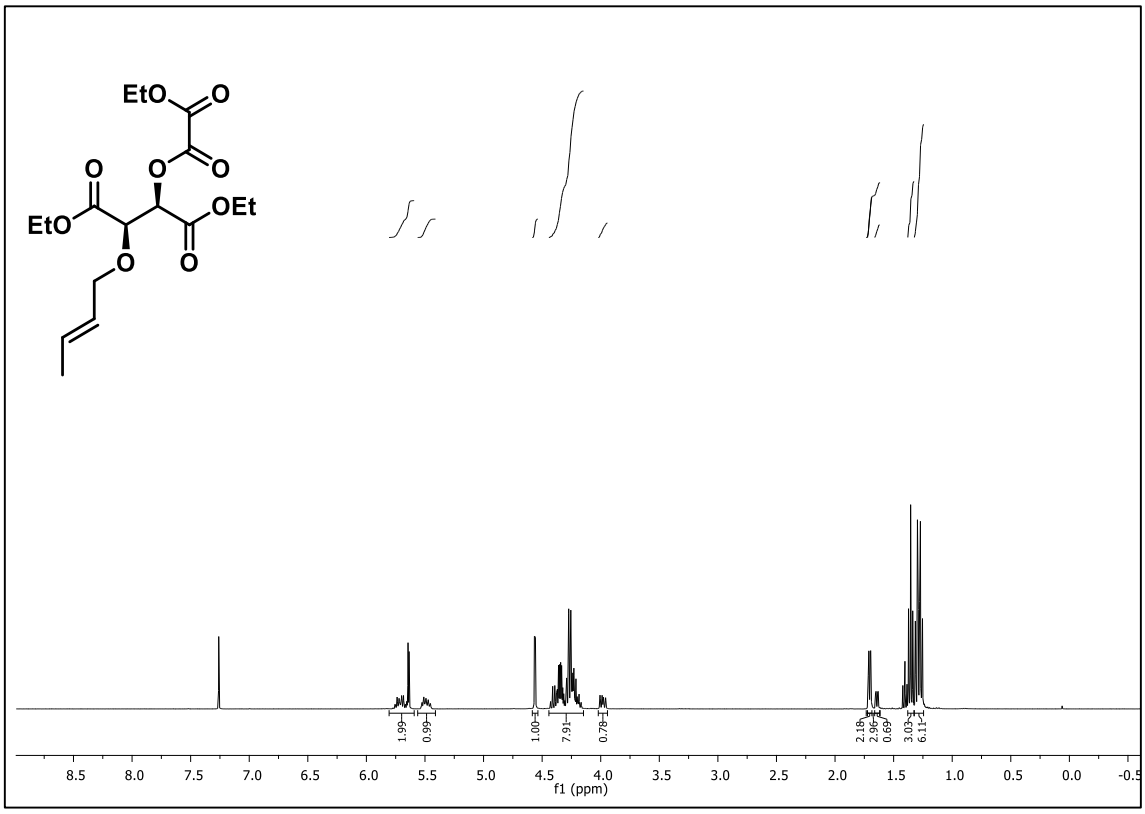

167.99
165.18
156.96
156.73
133.15
118.65
77.48
77.16
76.84
75.97
74.47
72.73
63.25
62.31
61.74
13.97
13.92
13.73
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

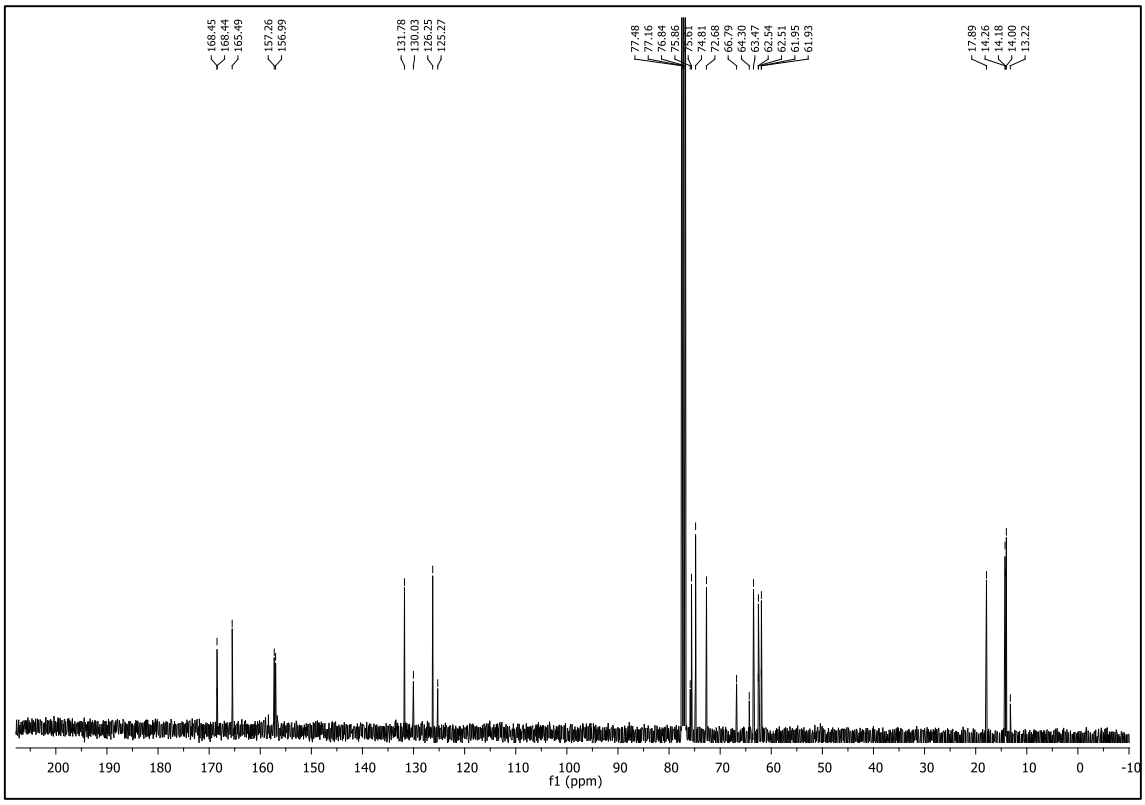

133.18
118.70
75.99
74.50
72.77
63.29
62.35
61.78
14.02
13.96
13.77
f1 (ppm)

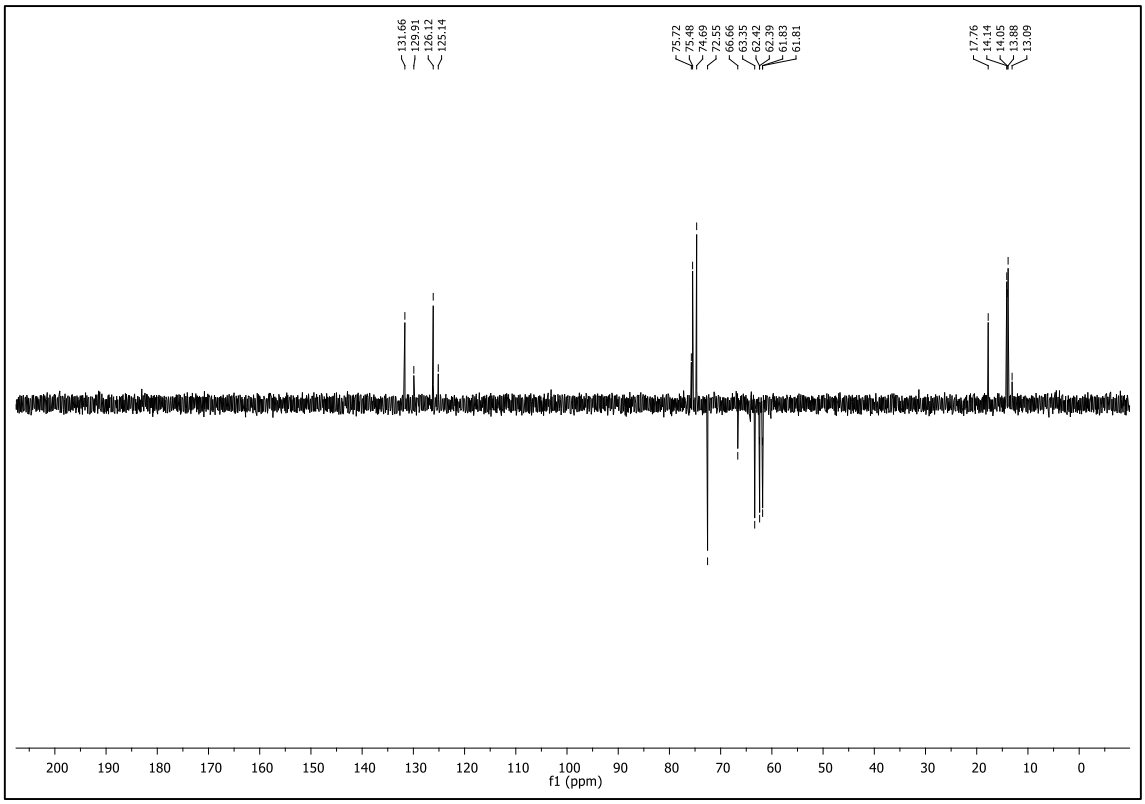

EtO
O
O
O
O
EtO
OEt
O
O
0.97
0.97
2.00
1.01
7.31
1.11
9.41
f1 (ppm)

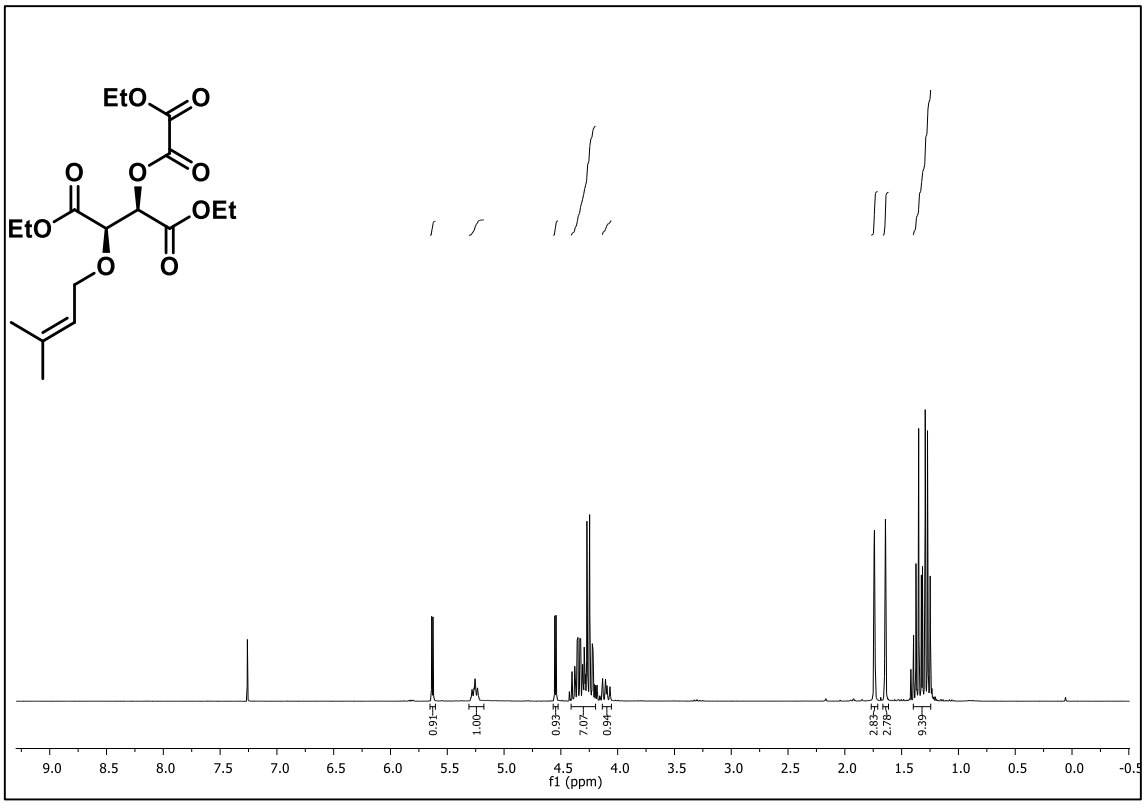

168.26
165.45
157.20
156.94
133.30
119.14
77.58
77.16
76.74
76.08
74.75
73.01
63.54
62.60
62.02
14.25
14.18
14.01
f1 (ppm)

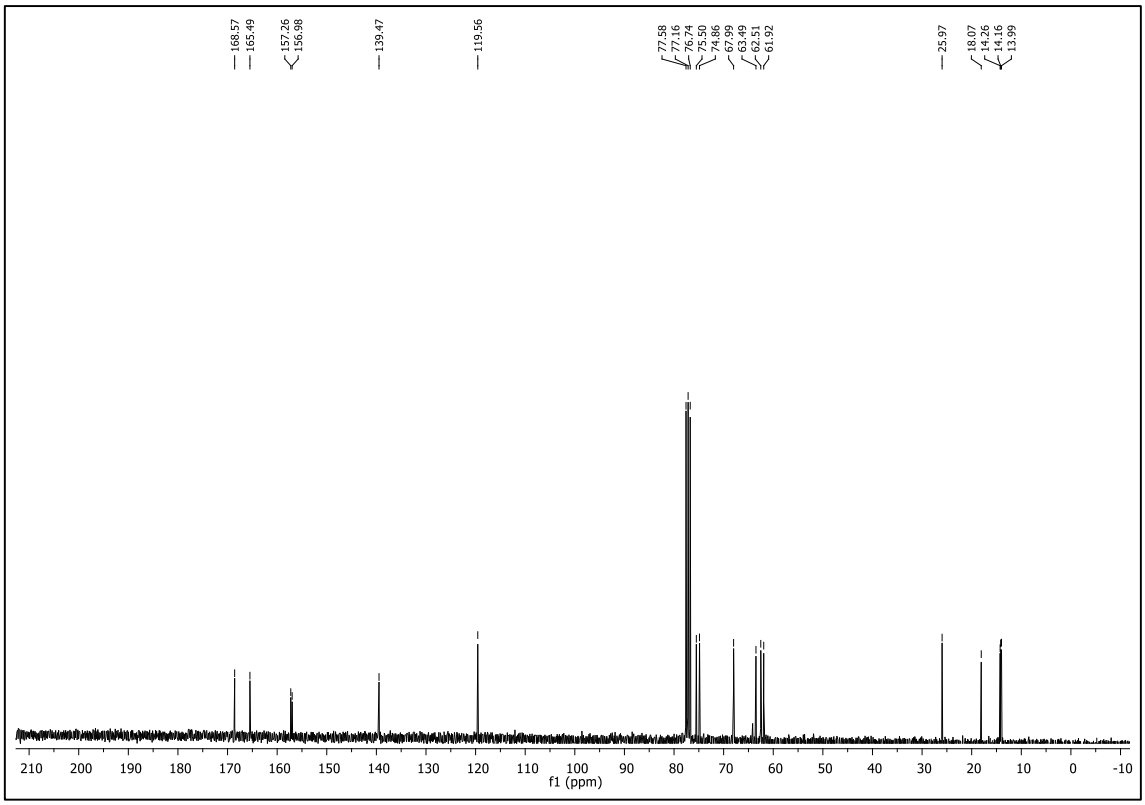

133.18
119.03
75.95
74.63
72.89
63.42
62.48
61.90
14.13
14.06
13.89
f1 (ppm)


EtO
O
O
O
O
EtO
OEt
O
O
1.99
0.99
1.00
7.91
0.78
2.18
2.96
0.69
3.03
6.11
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


168.45
168.44
165.49
157.26
156.99
131.78
130.03
126.25
125.27
77.48
77.16
76.84
75.86
75.61
74.81
72.68
66.79
64.30
63.47
62.64
62.51
61.95
61.93
17.89
14.26
14.18
14.00
13.22
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


131.66
129.91
126.12
125.14
75.72
75.48
74.69
72.55
66.66
63.35
62.42
62.39
61.83
61.81
17.76
14.14
14.05
13.88
13.09
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


EtO
O
O
O
O
EtO
OEt
O
O
0.91
1.00
0.93
7.07
0.94
2.83
2.78
9.39
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)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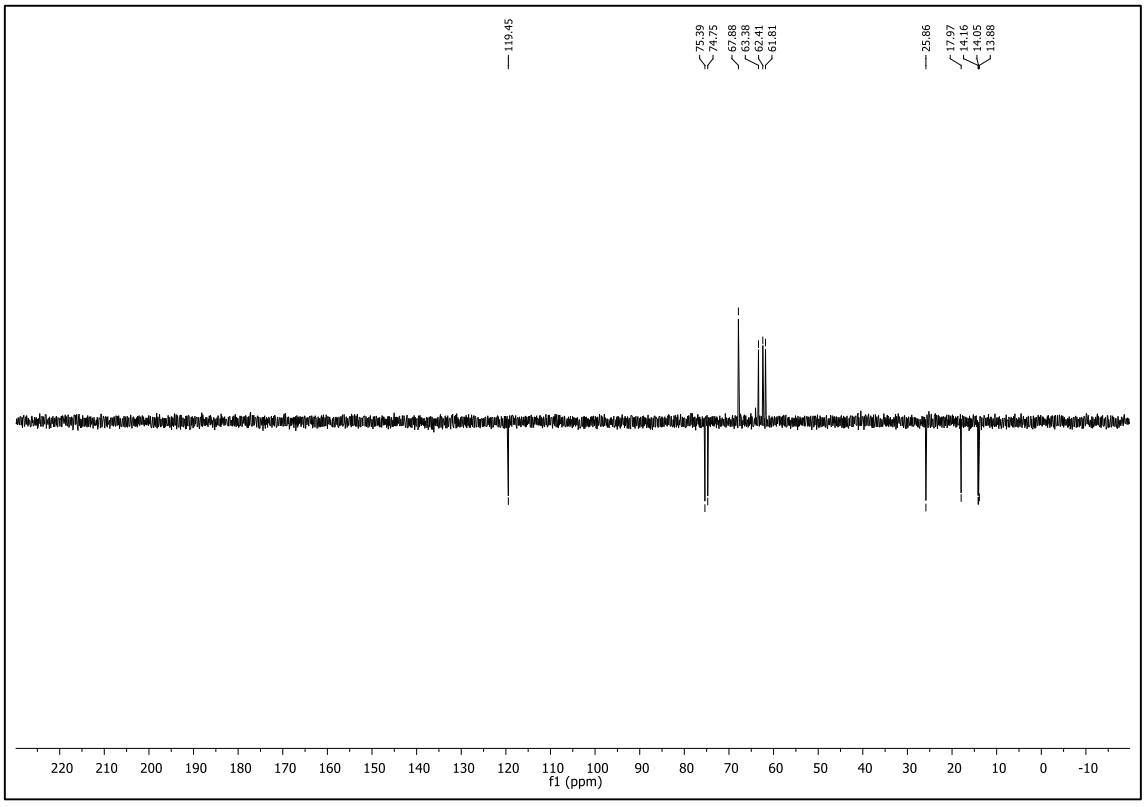
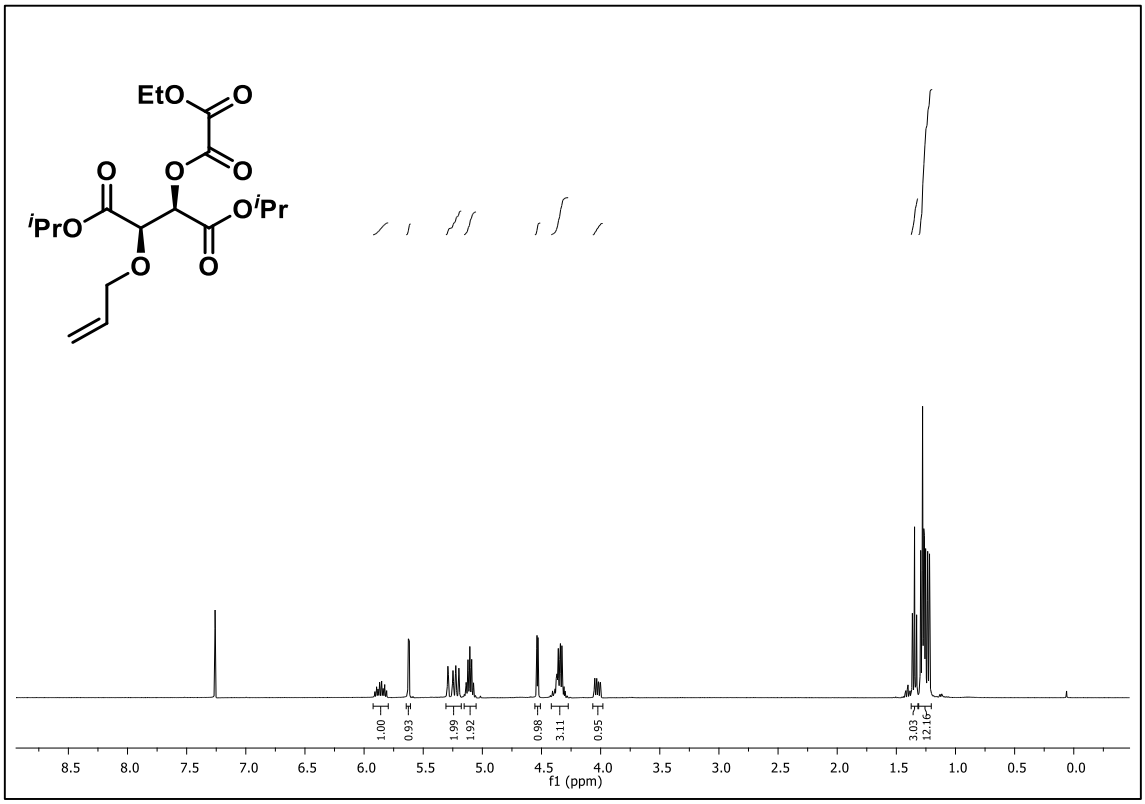
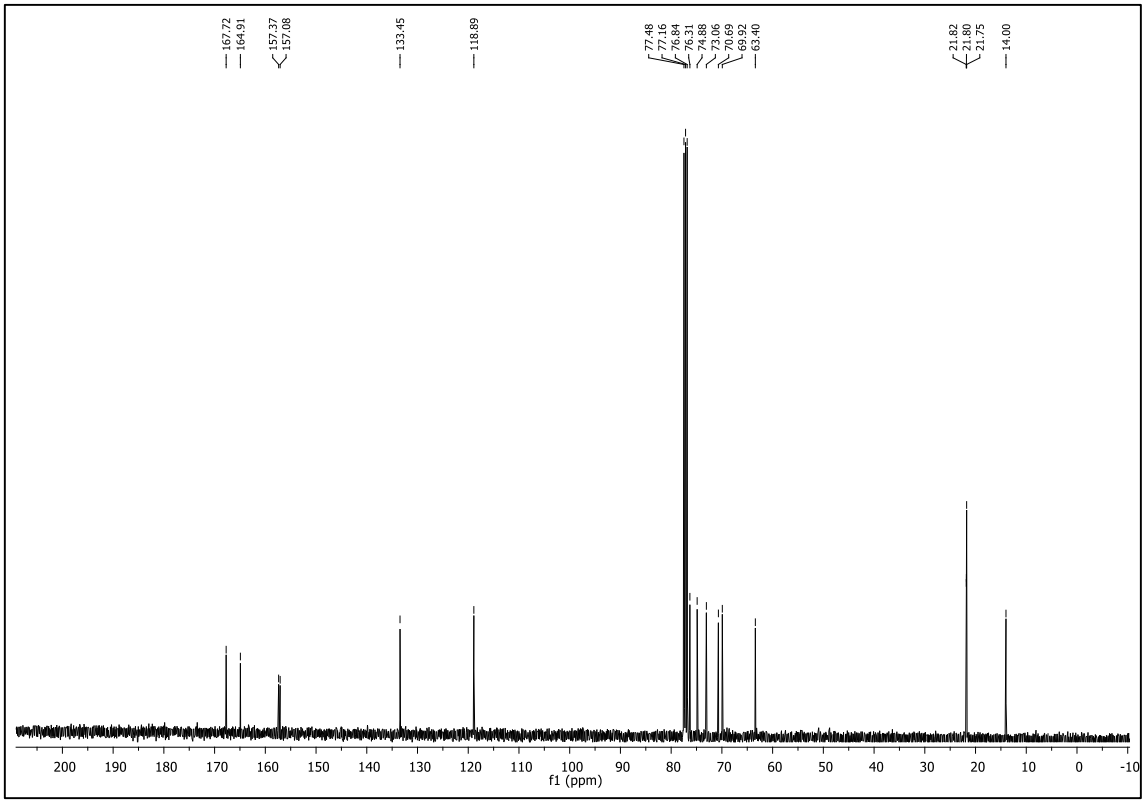
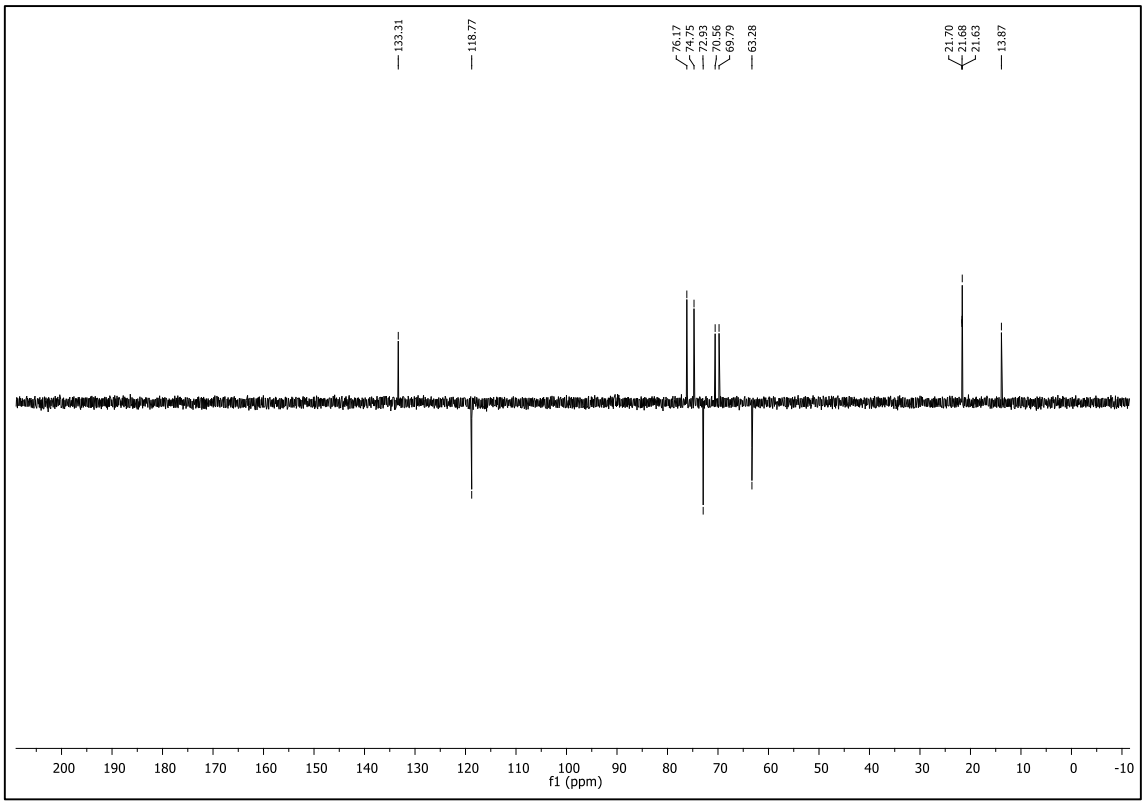
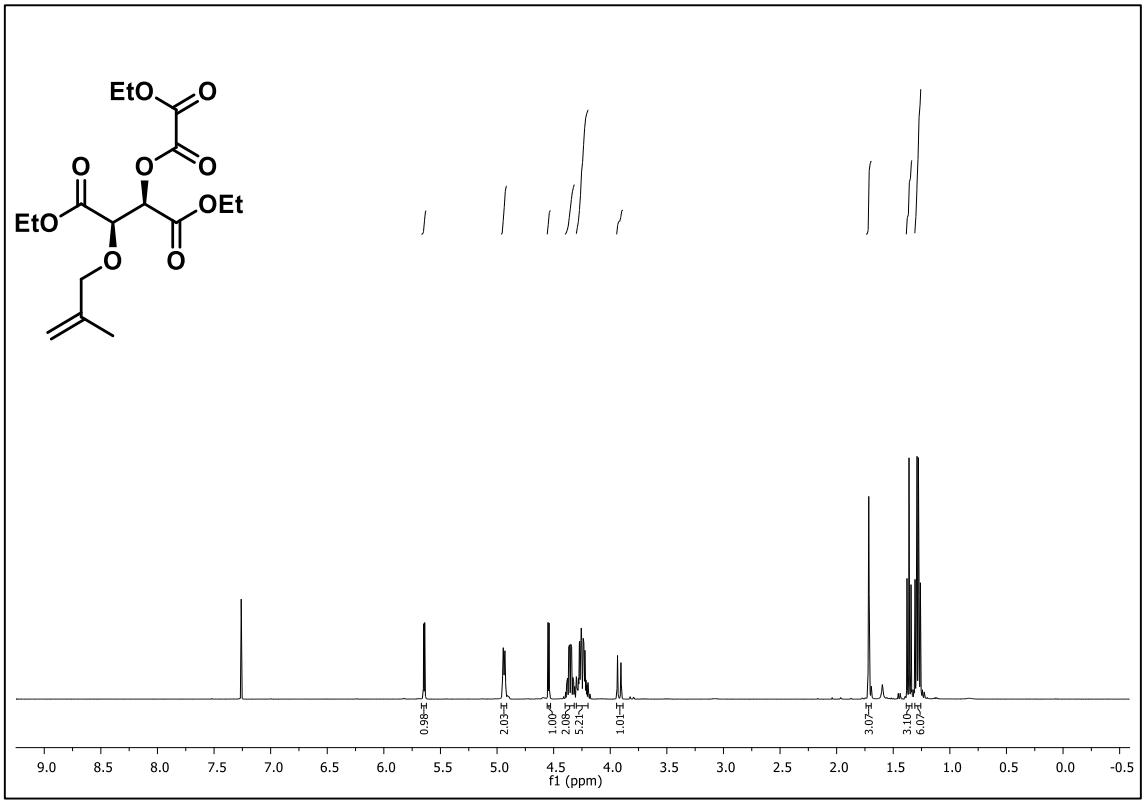
165.49
157.26
156.98
139.47
119.56
77.58
77.16
76.74
75.50
74.86
67.99
63.49
62.51
61.92
25.97
18.07
14.26
14.16
13.99
f1 (ppm)

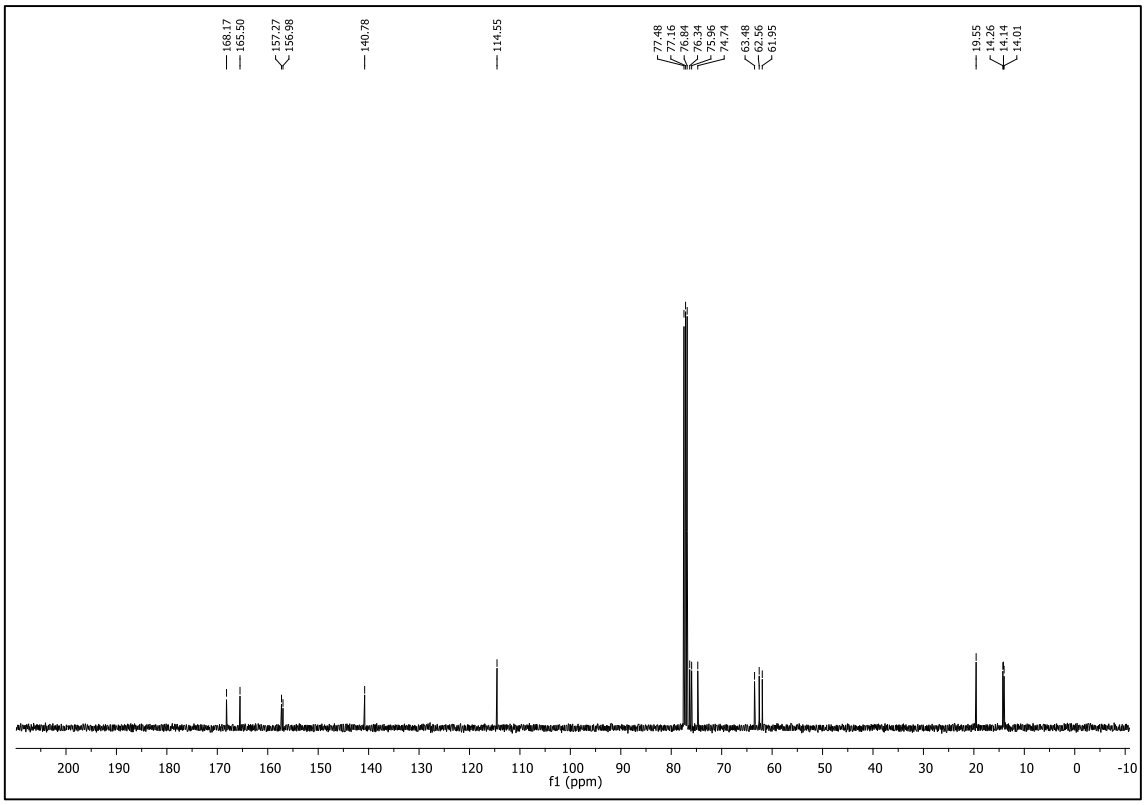

119.45
75.39
74.75
67.88
63.38
62.41
61.81
25.86
17.97
14.16
14.05
13.88
f1 (ppm)

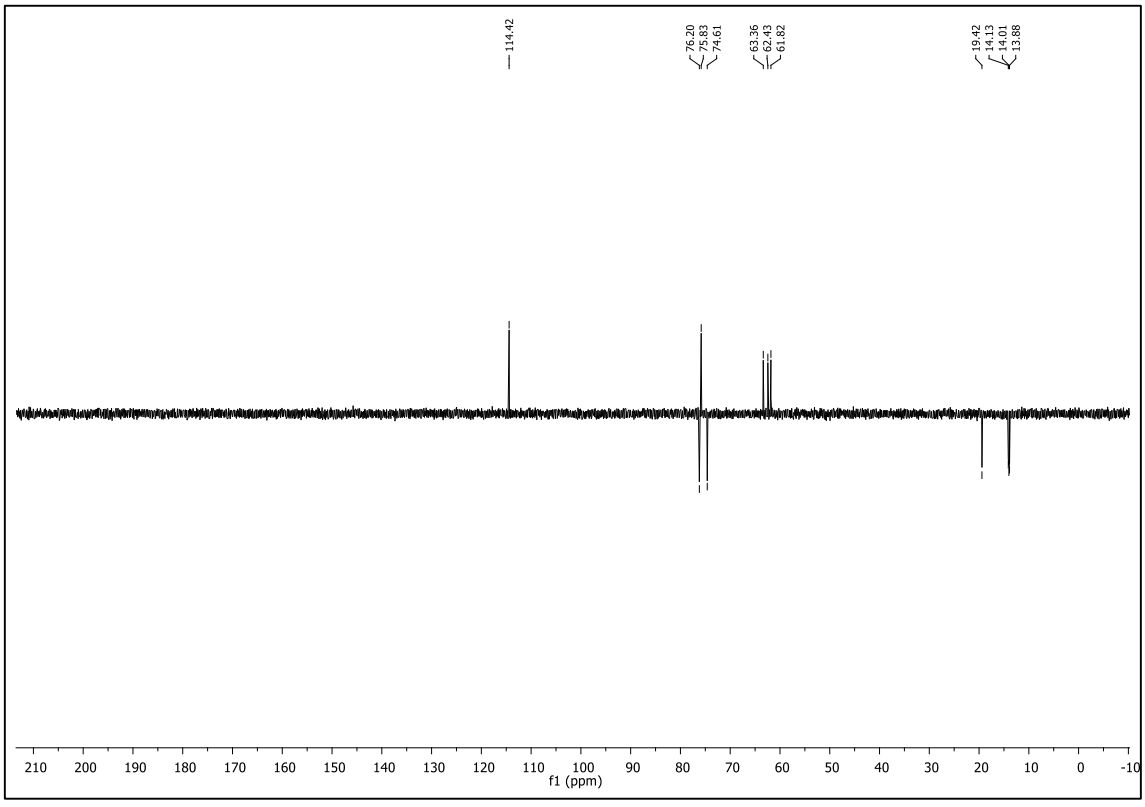

EtO
O
O
O
O
O
O
O
O
O
O
O
1.00
0.93
1.99
1.92
0.98
3.11
0.95
3.03
12.16
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

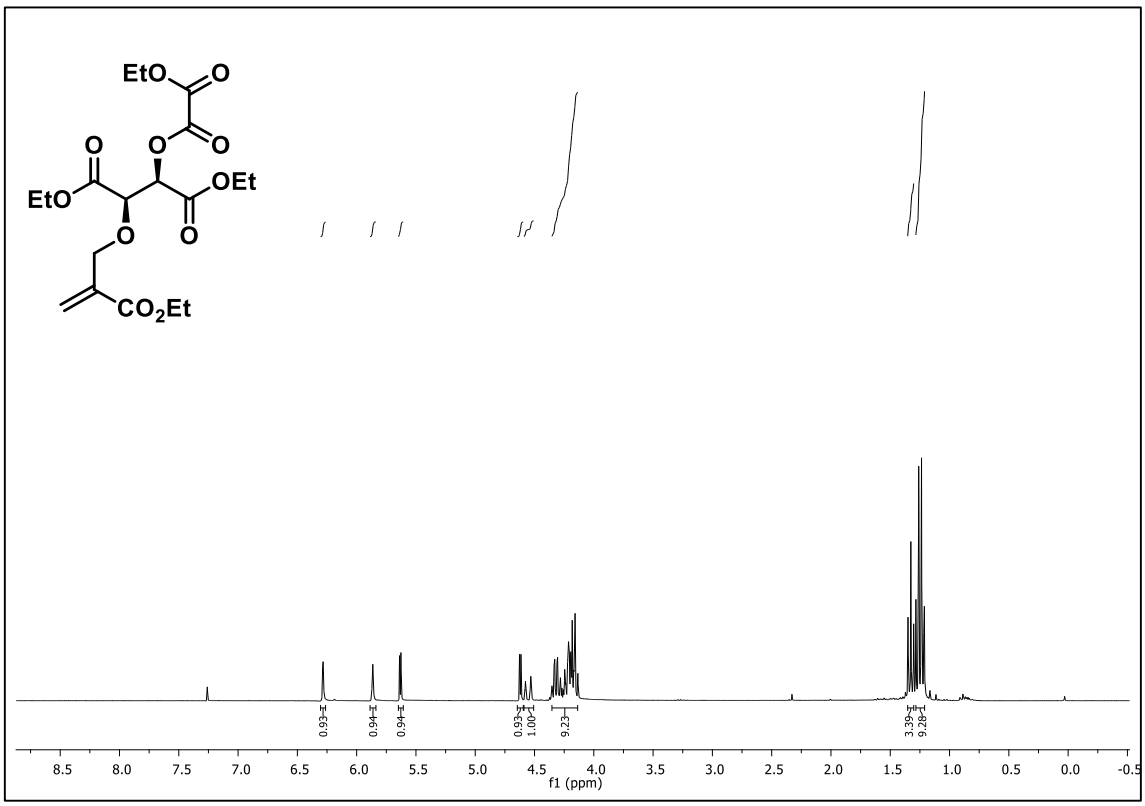

167.72
164.91
157.37
157.08
133.45
118.89
77.48
77.16
76.84
76.31
74.88
73.06
70.69
69.92
63.40
21.82
21.80
21.75
14.00
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

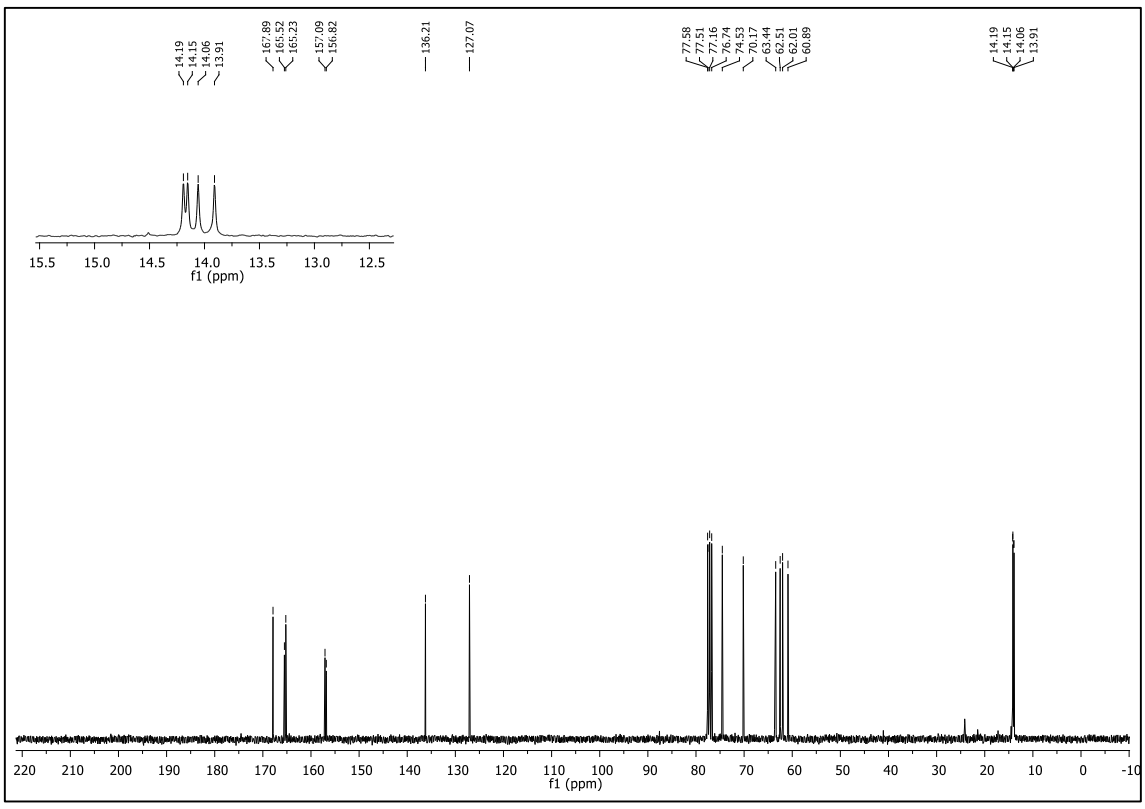

133.31
118.77
76.17
74.75
72.93
70.56
69.79
63.28
21.70
21.68
21.63
13.87
f1 (ppm)

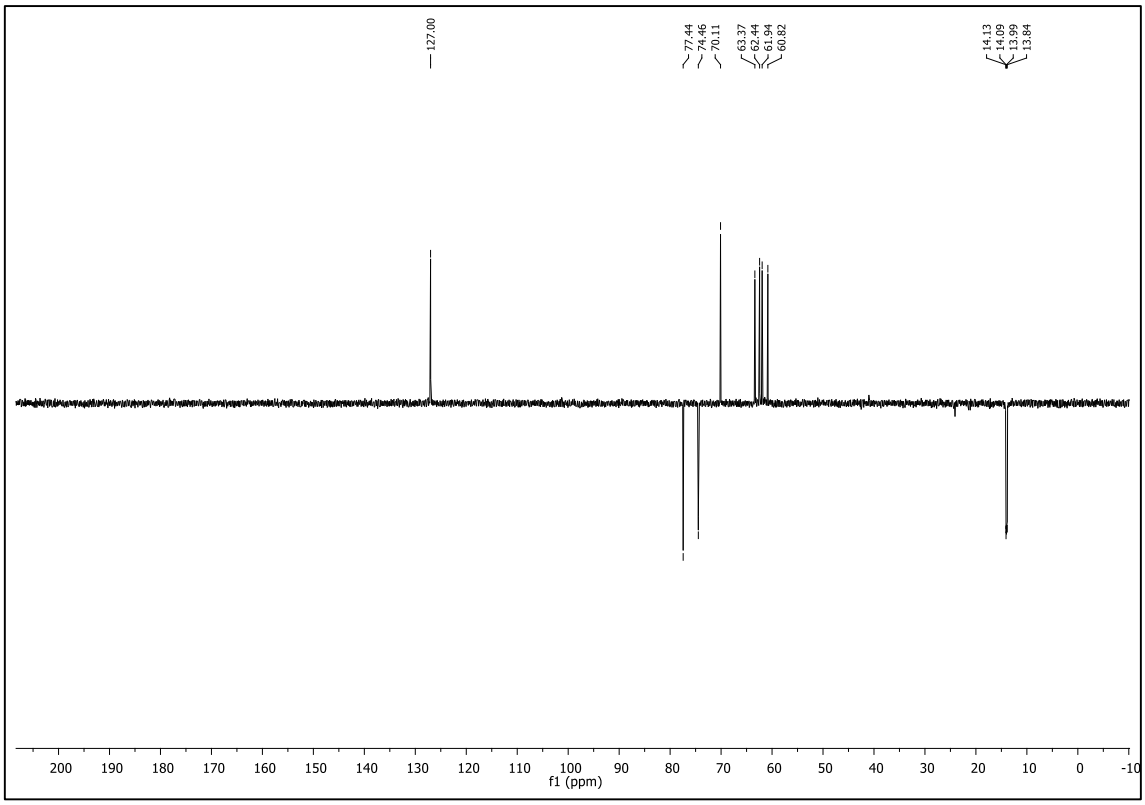

EtO
O
O
O
O
EtO
OEt
O
O
0.98
2.03
1.00
2.08
5.21
1.01
3.07
3.10
6.07
f1 (ppm)

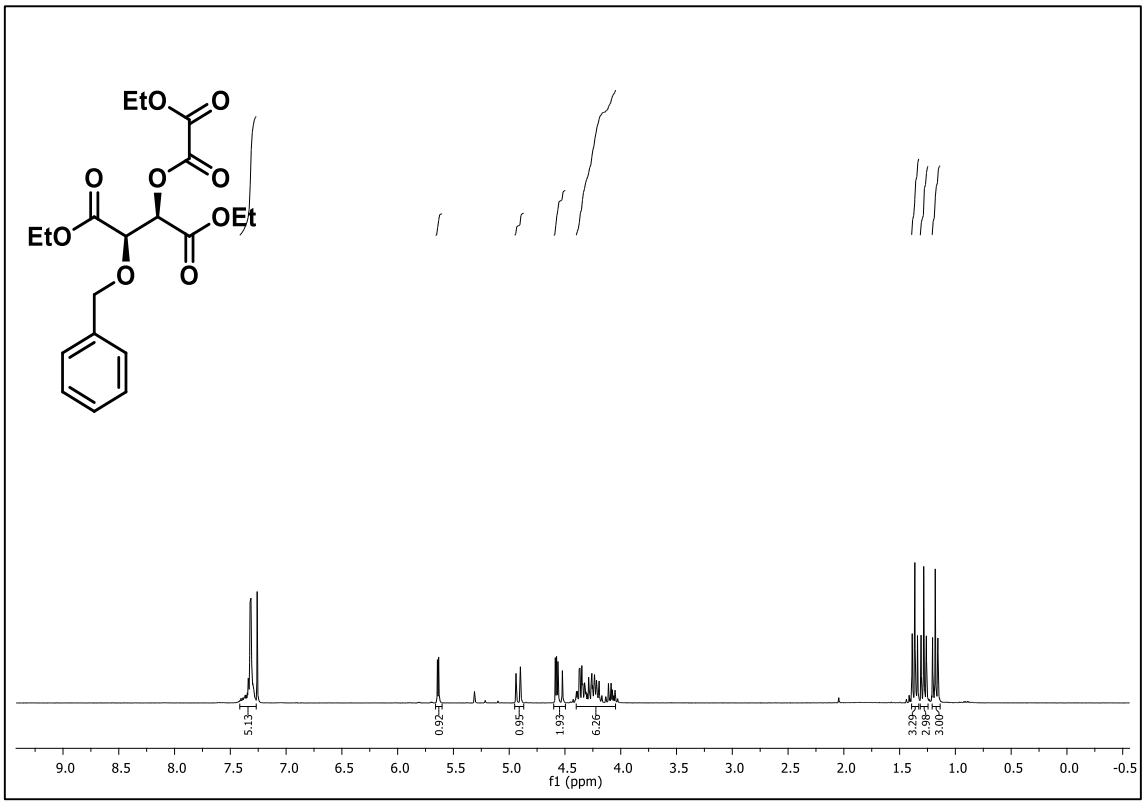

168.17
165.50
157.27
156.98
140.78
114.55
77.48
77.16
76.84
76.34
75.96
74.74
63.48
62.56
61.95
19.55
14.26
14.14
14.01
f1 (ppm)

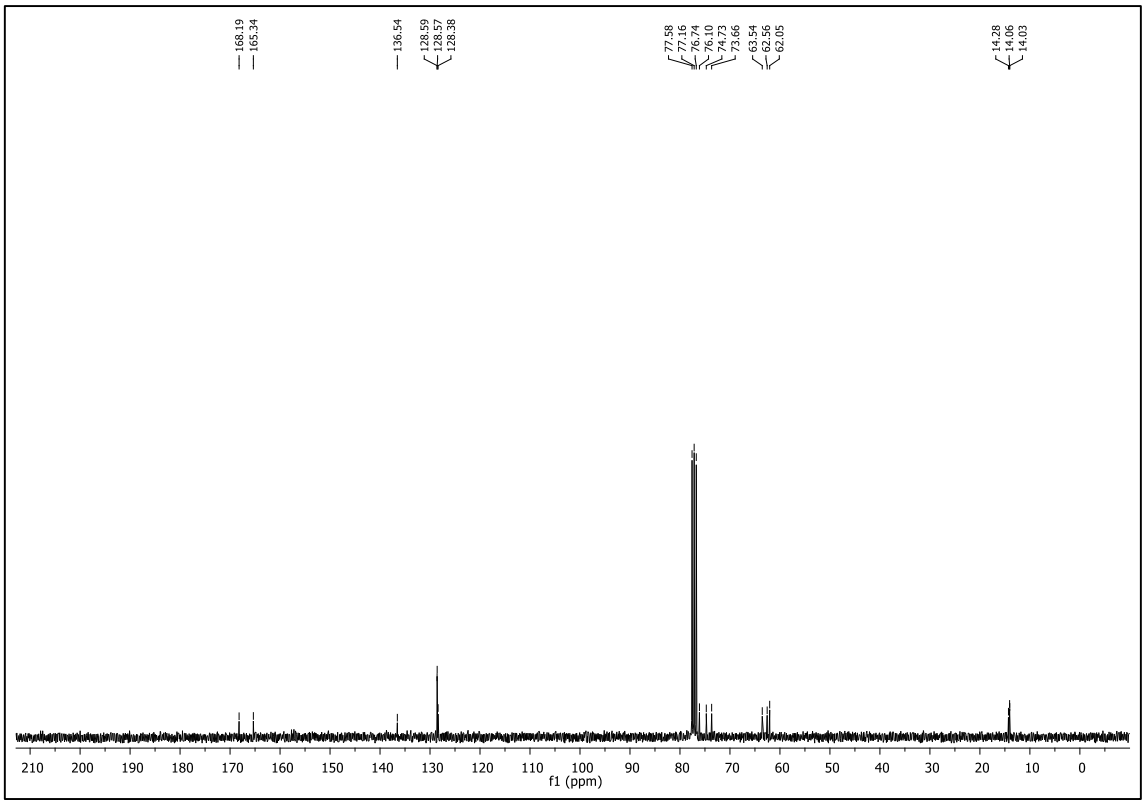

114.42
76.20
75.83
74.61
63.36
62.43
61.82
19.42
14.13
14.01
13.88
f1 (ppm)

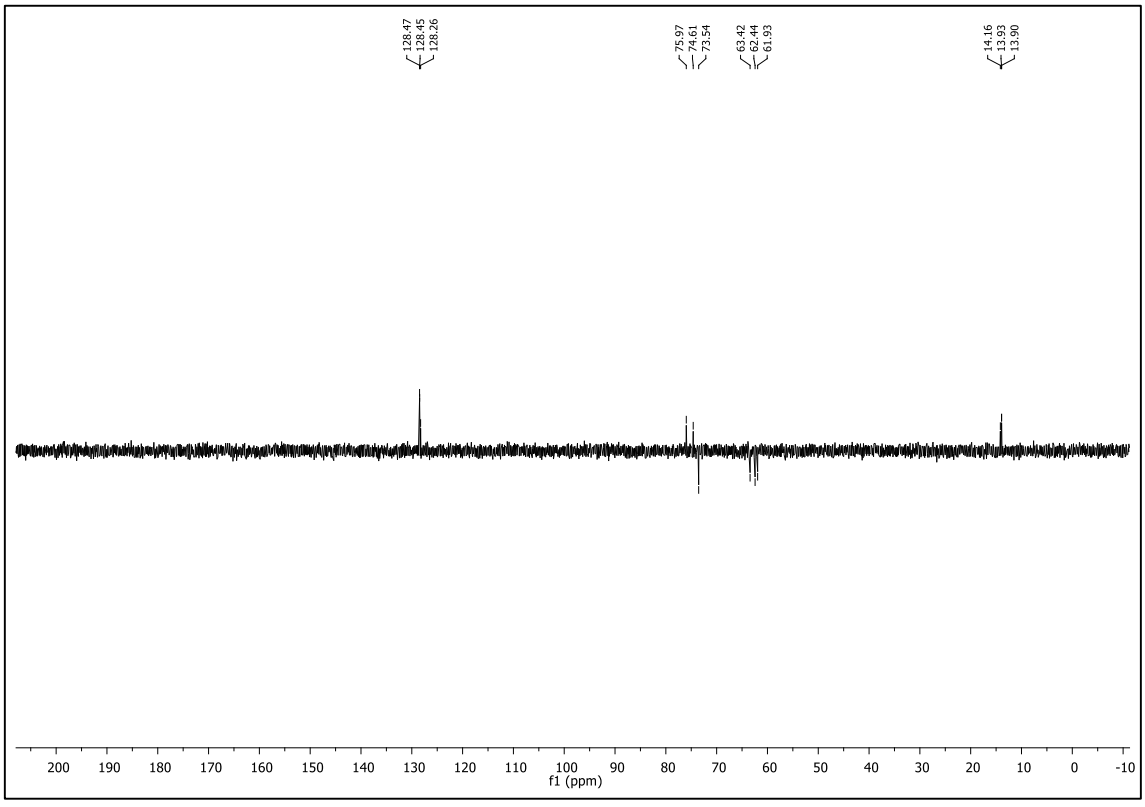

EtO
O
O
O
O
EtO
OEt
O
O
CO2Et
0.93
0.94
0.94
0.93
1.00
9.23
3.39
9.28
f1 (ppm)

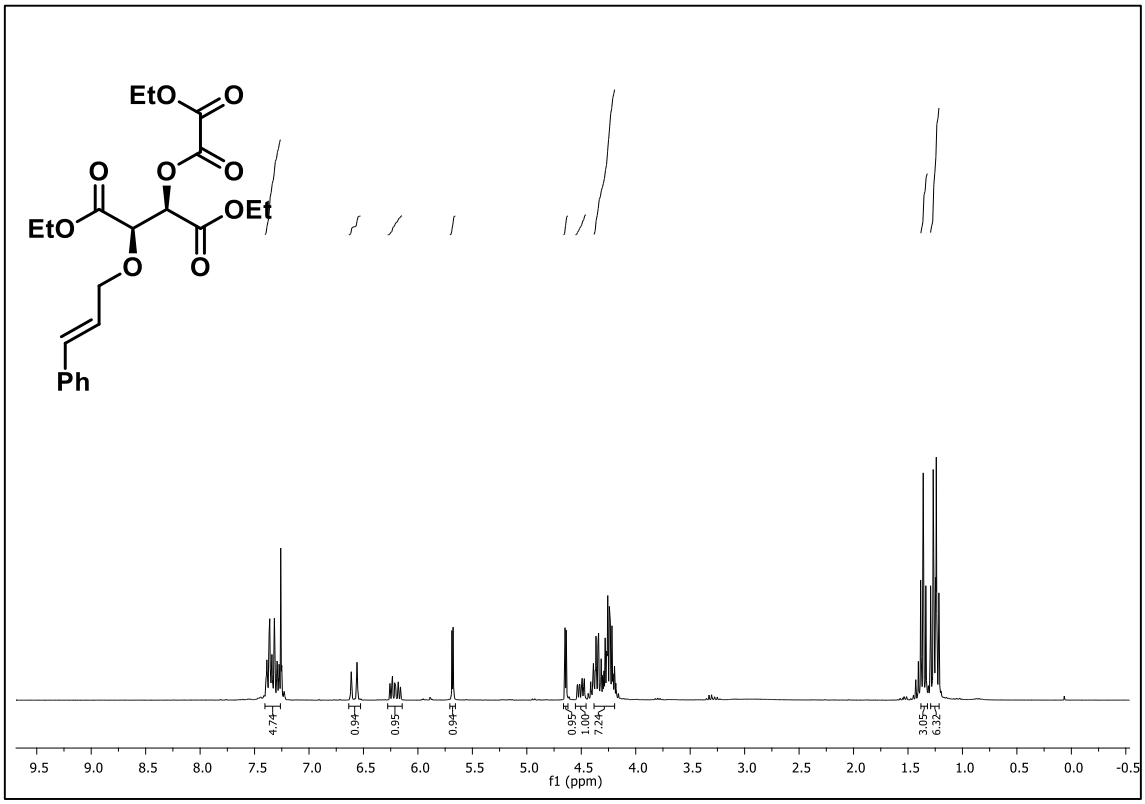

14.19
14.15
14.06
13.91
167.89
165.52
165.23
157.09
156.82
136.21
127.07
77.58
77.51
77.16
76.74
74.53
70.17
63.44
62.51
62.01
60.89
f1 (ppm)

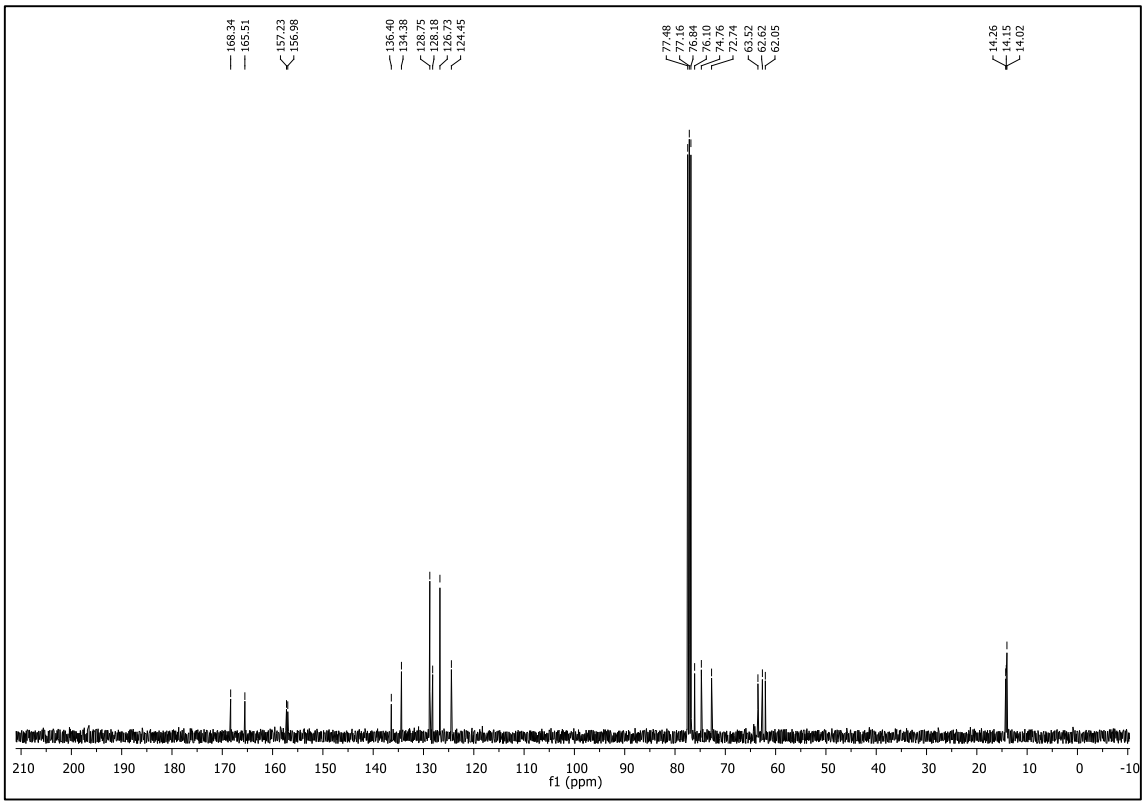

127.00
77.44
74.46
70.11
63.37
62.44
61.94
60.82
14.13
14.09
13.99
13.84
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

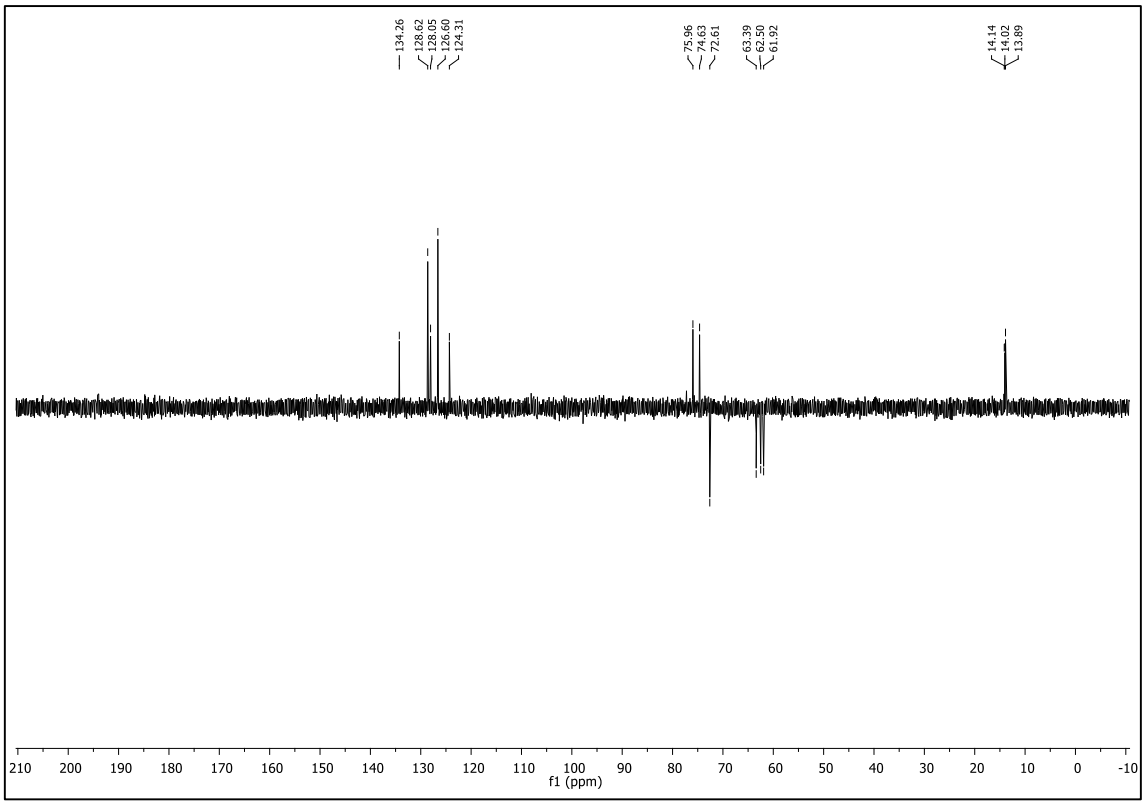

EtO
O
O
O
O
EtO
OEt
O
O
5.13
0.92
0.95
1.93
6.26
3.29
2.98
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

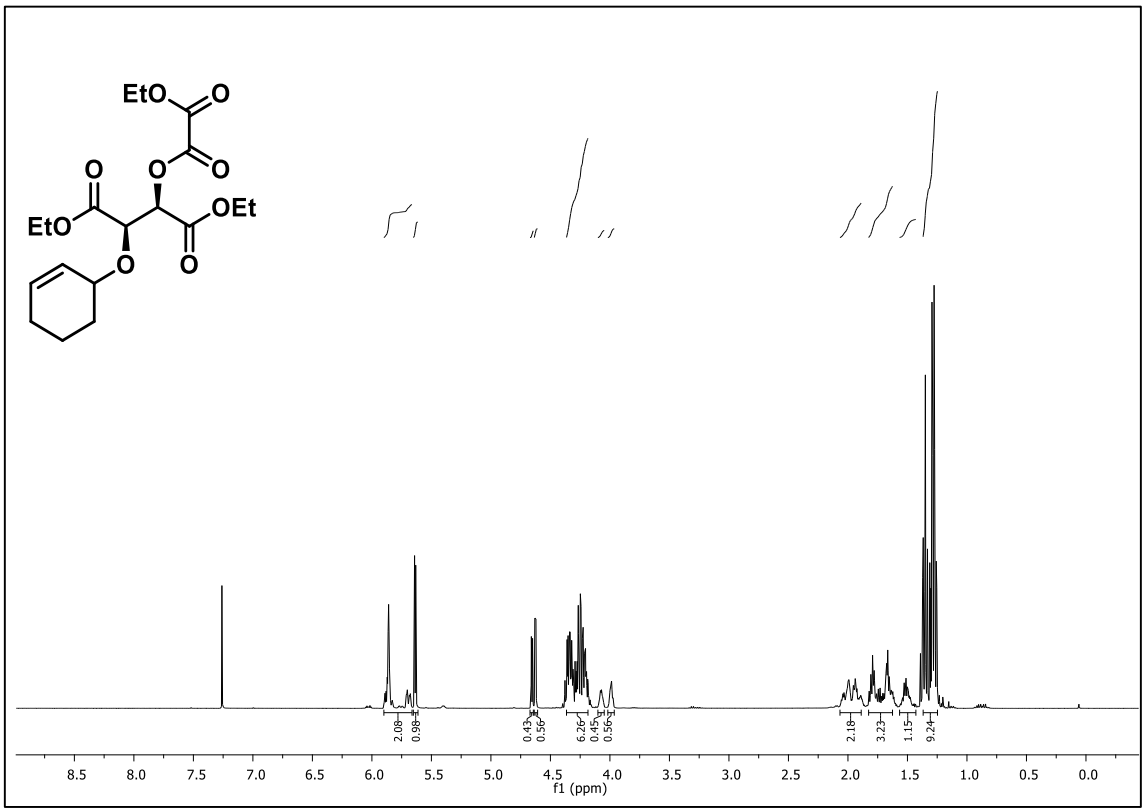

168.19
165.34
136.54
128.59
128.57
128.38
77.58
77.16
76.74
76.10
74.73
73.66
63.54
62.56
62.05
14.28
14.06
14.03
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

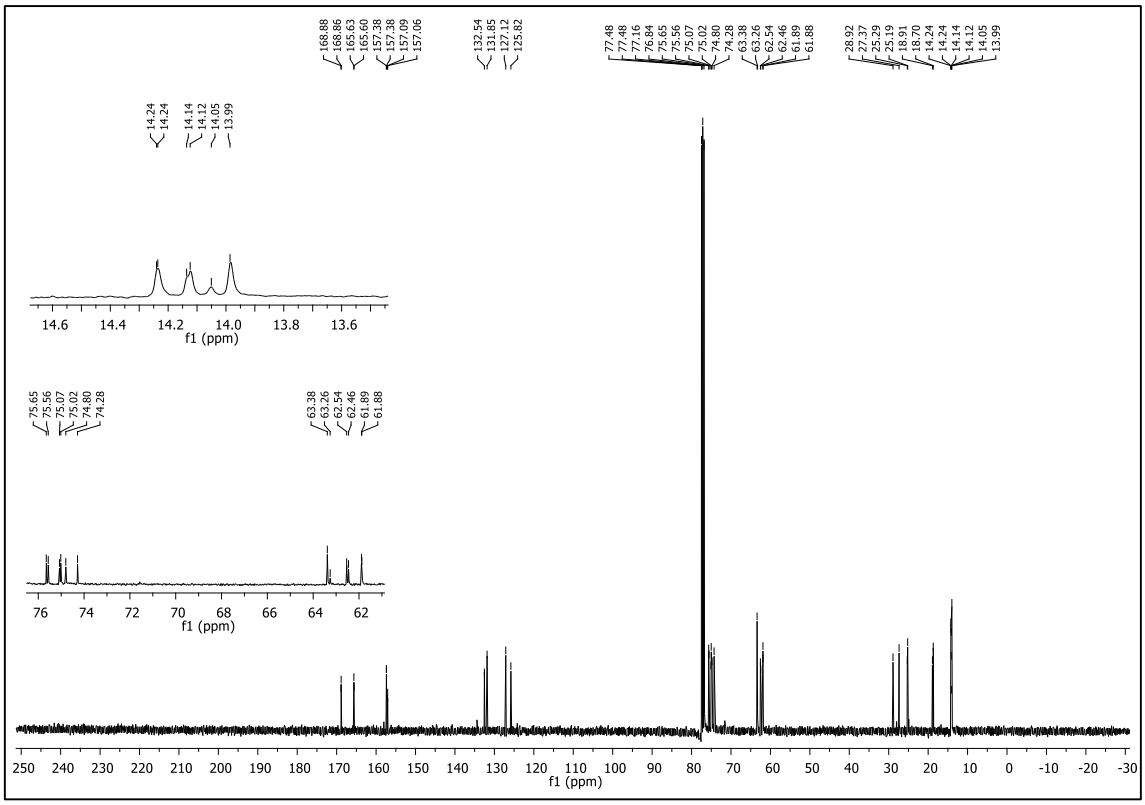

128.47
128.45
128.26
75.97
74.61
73.54
63.42
62.44
61.93
14.16
13.93
13.90
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

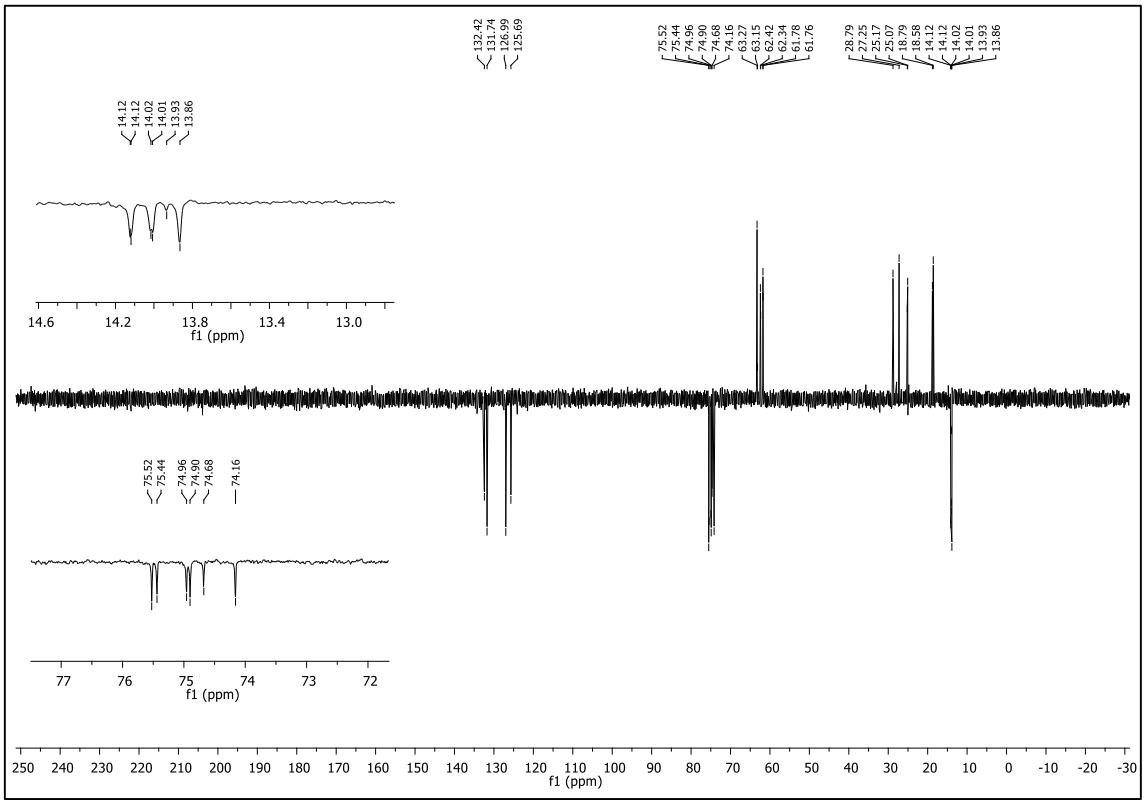

EtO
O
O
O
O
EtO
OEt
O
O
Ph
4.74
0.94
0.95
0.94
0.95
1.00
7.24
3.05
6.32
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

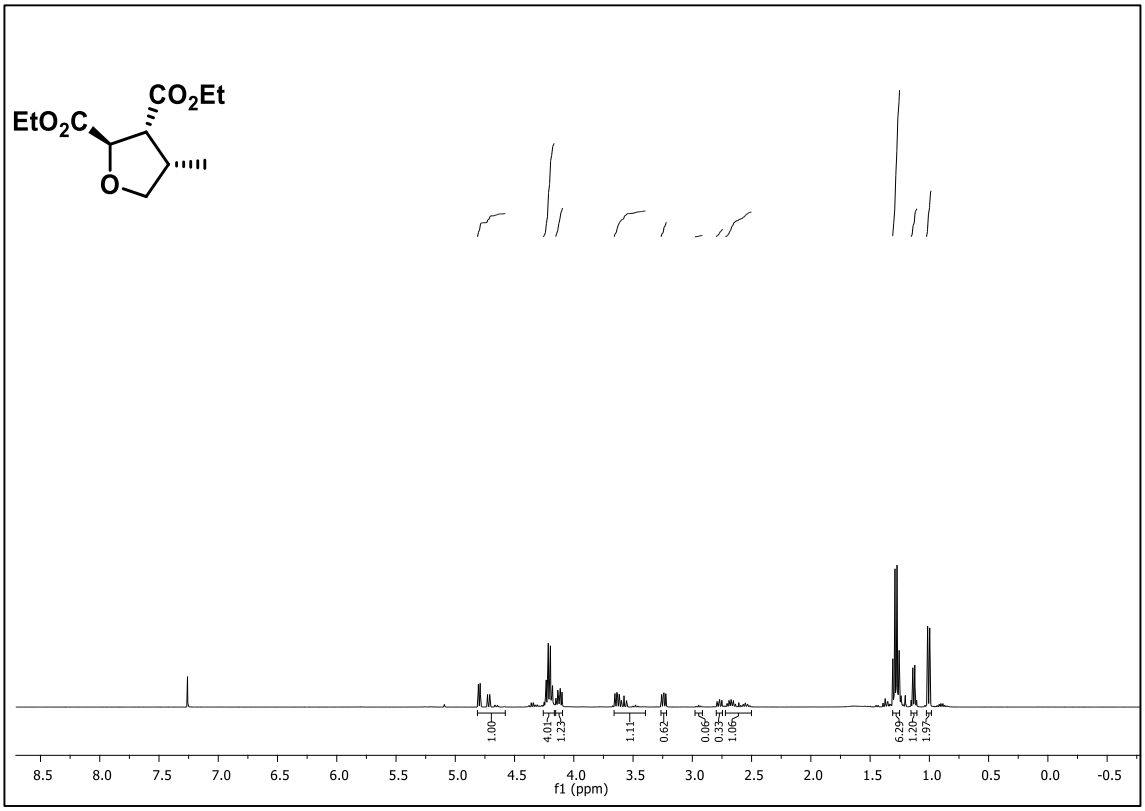

168.34
165.51
157.23
156.98
136.40
134.38
128.75
128.18
126.73
124.45
77.48
77.16
76.84
76.10
74.76
72.74
63.52
62.62
62.05
14.26
14.15
14.02
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

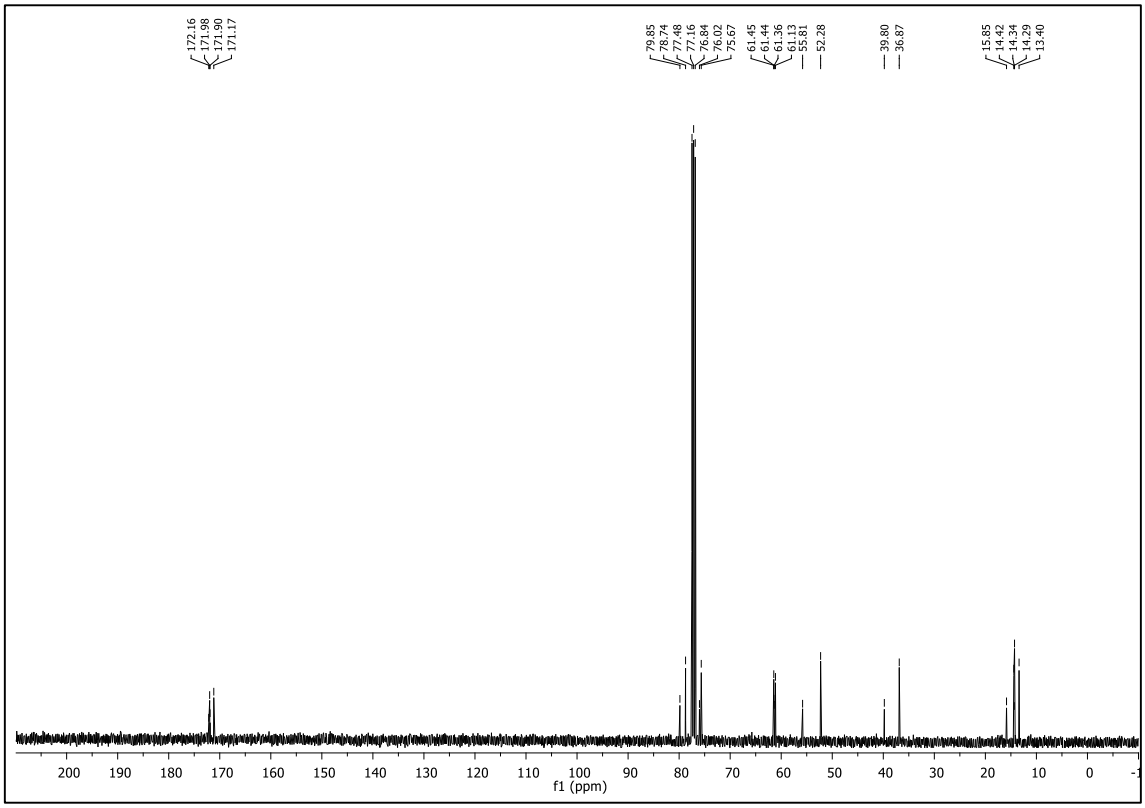

134.26
128.62
128.05
126.60
124.31
75.96
74.63
72.61
63.39
62.50
61.92
14.14
14.02
13.89
f1 (ppm)

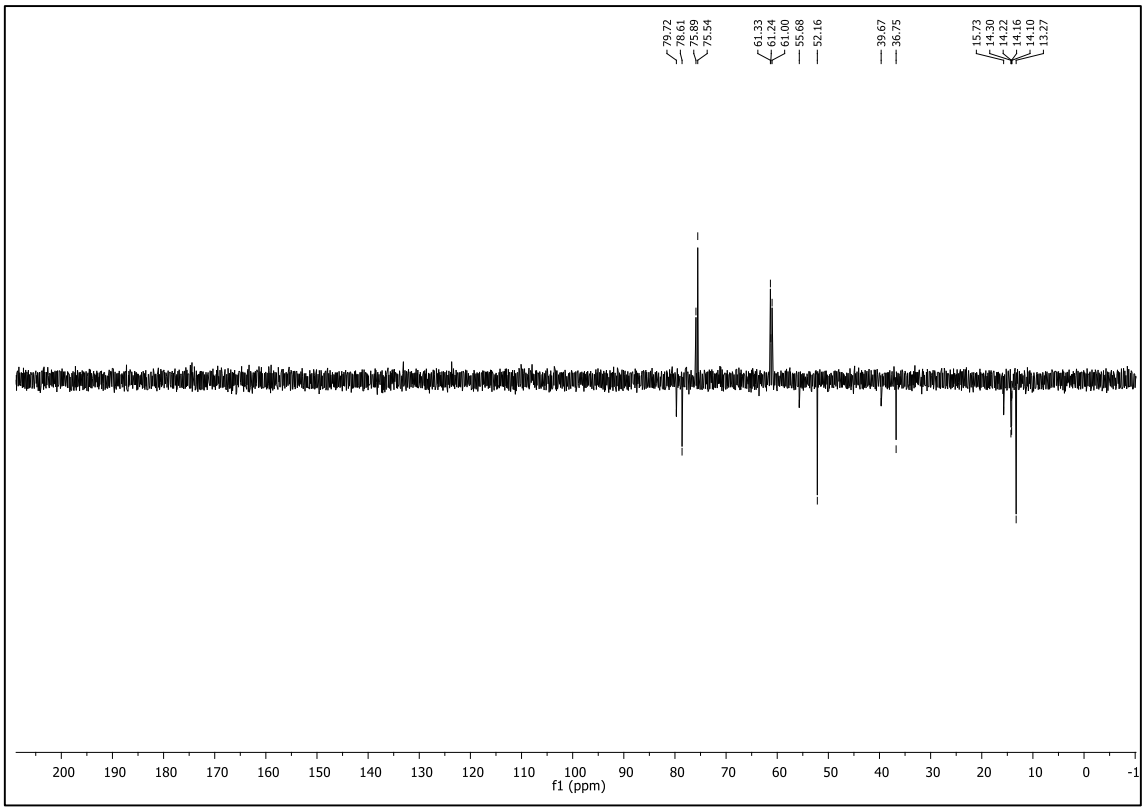

EtO
O
O
O
O
EtO
OEt
O
O
2.08
0.98
0.43
0.56
6.26
0.45
0.56
2.18
3.23
1.15
9.24
f1 (ppm)

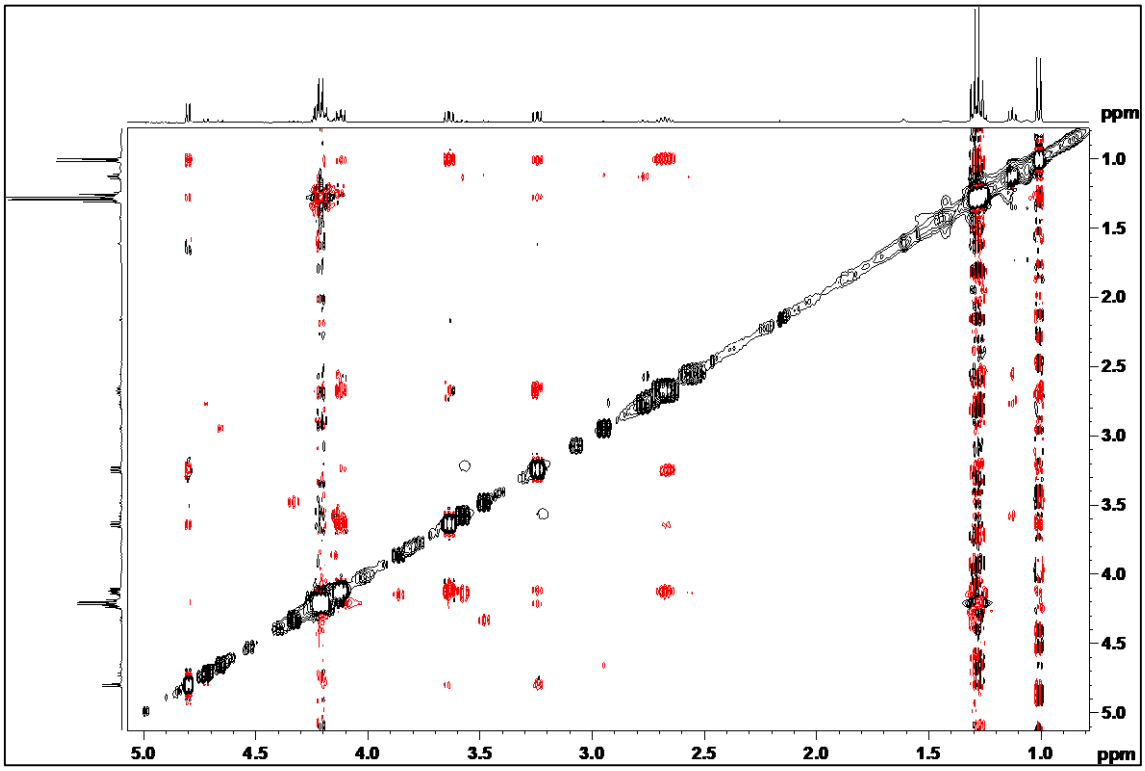

168.88
168.86
165.63
165.60
157.38
157.09
157.06
132.54
131.85
127.12
125.82
77.48
77.48
77.16
76.84
75.65
75.56
75.07
75.02
74.80
74.28
63.38
63.26
62.54
62.46
61.89
61.88
28.92
27.37
25.29
25.19
18.91
18.70
14.24
14.24
14.14
14.12
14.05
13.99
f1 (ppm)

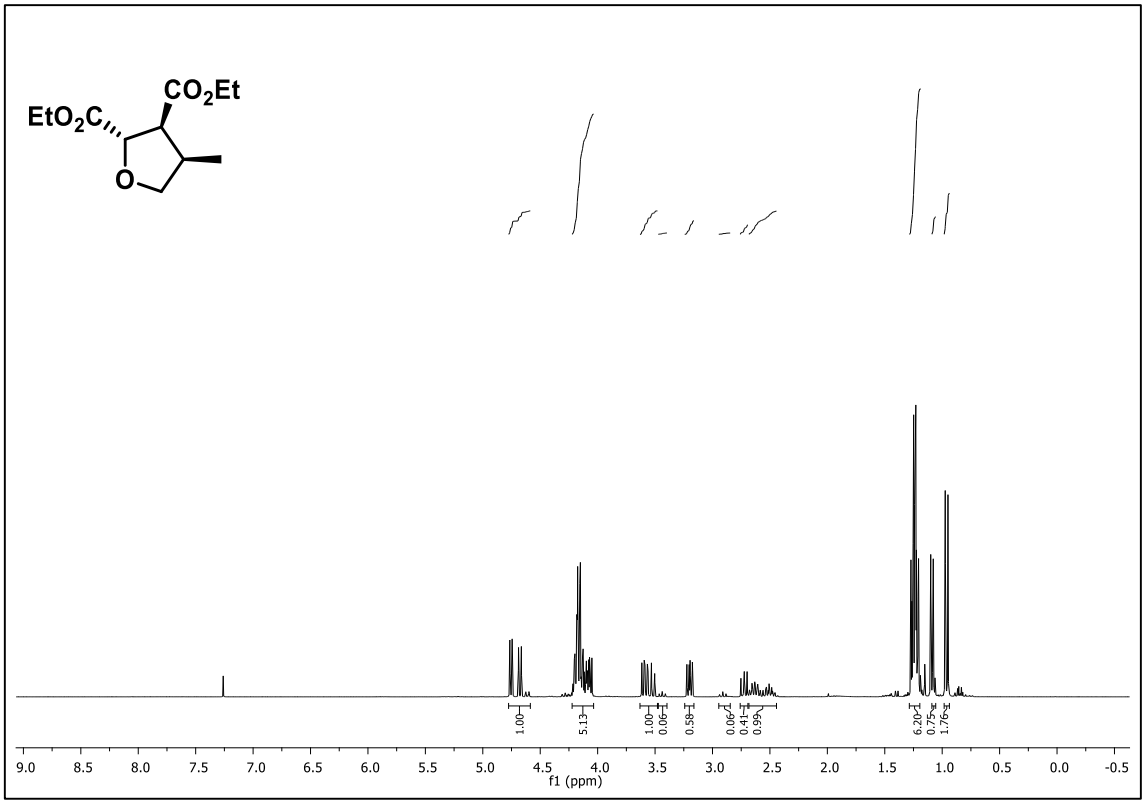

132.42
131.74
126.99
125.69
75.52
75.44
74.96
74.90
74.68
74.16
63.27
63.15
62.42
62.34
61.78
61.76
28.79
27.25
25.17
25.07
18.79
18.58
14.12
14.12
14.02
14.01
13.93
13.86
f1 (ppm)

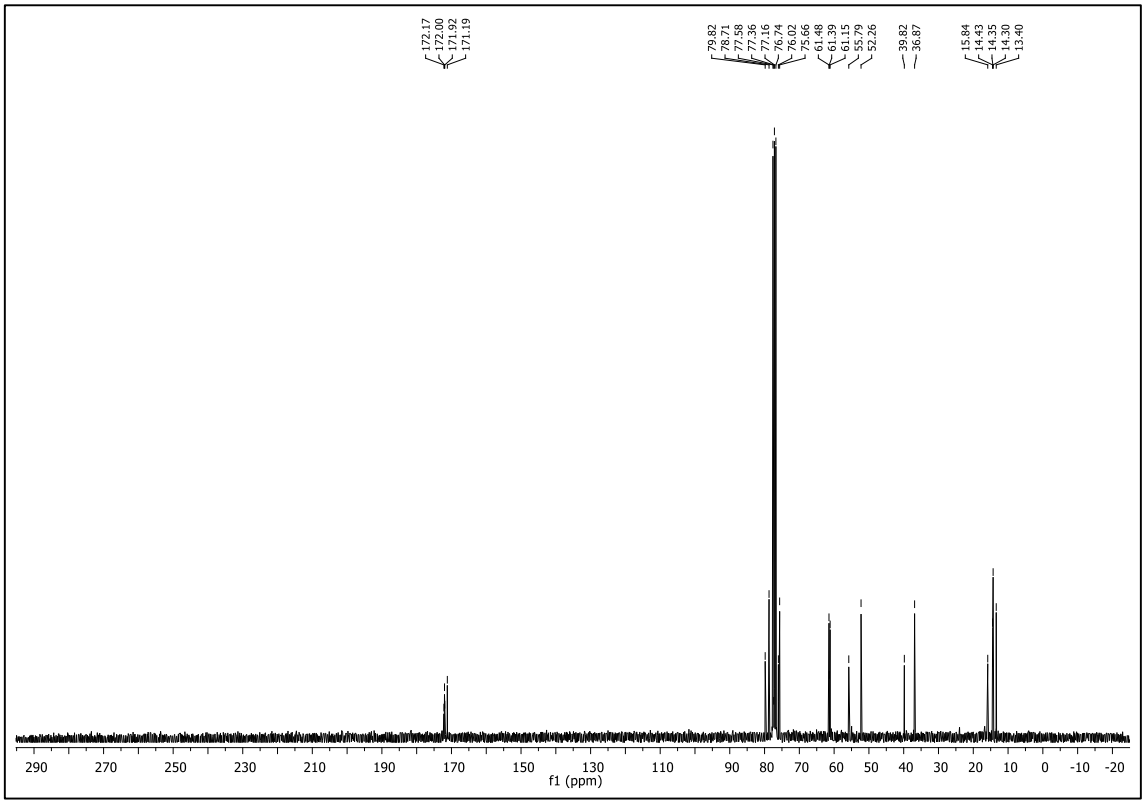

EtO2C
CO2Et
O
1.00
4.01
1.23
1.11
0.62
0.06
0.33
1.06
6.29
1.20
1.97
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

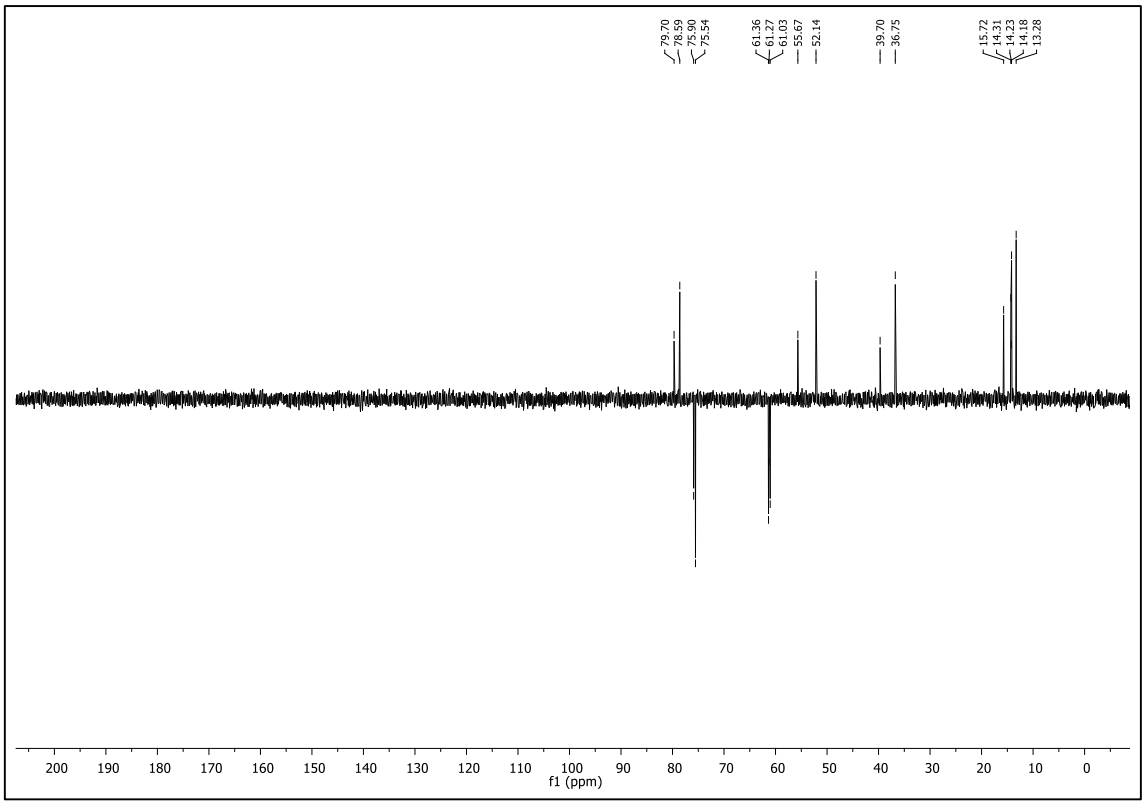

172.16
171.98
171.90
171.17
79.85
78.74
77.48
77.16
76.84
76.02
75.67
61.45
61.44
61.36
61.13
55.81
52.28
39.80
36.87
15.85
14.42
14.34
14.29
13.40
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

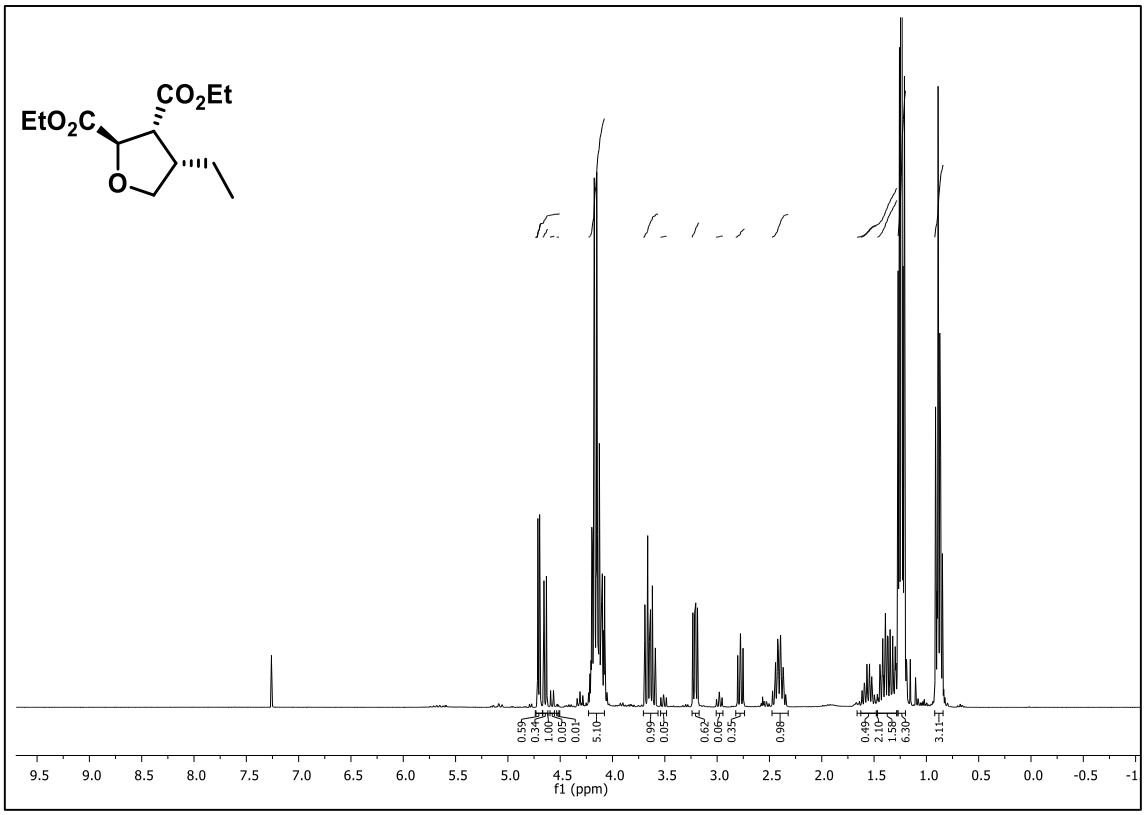

79.72
78.61
75.89
75.54
61.33
61.24
61.00
55.68
52.16
39.67
36.75
15.73
14.30
14.22
14.16
14.10
13.27
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

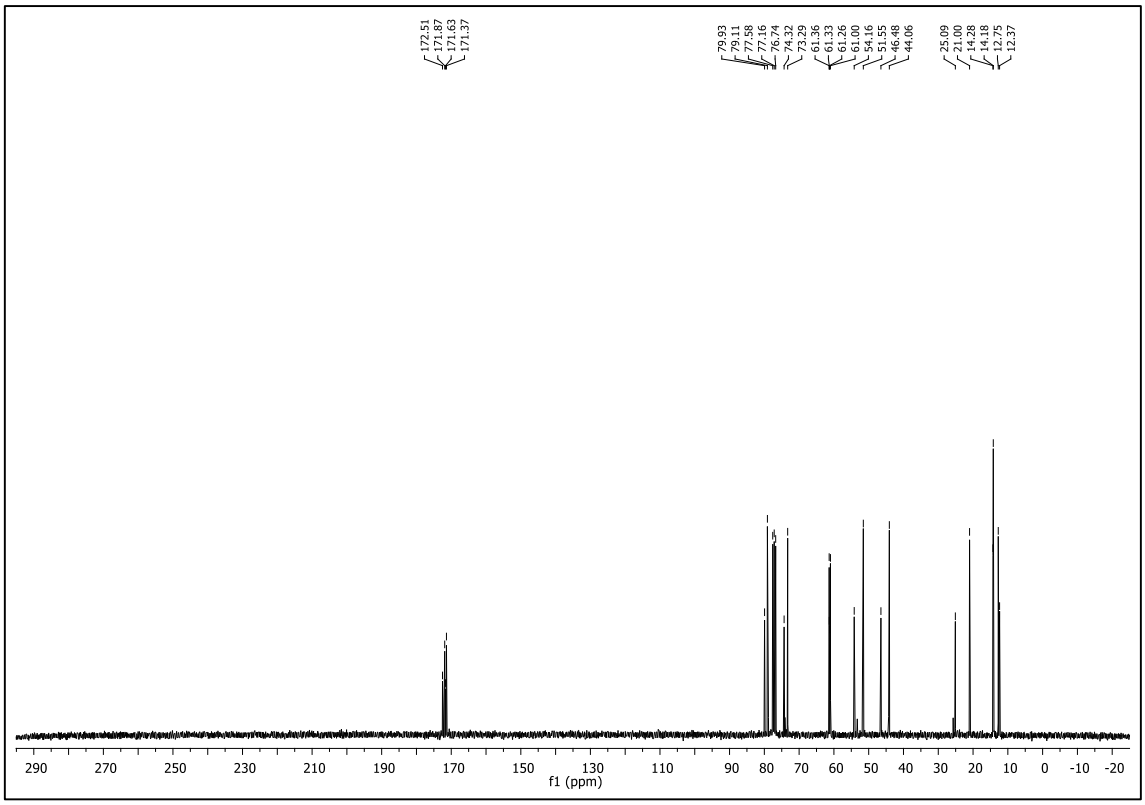

ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
ppm

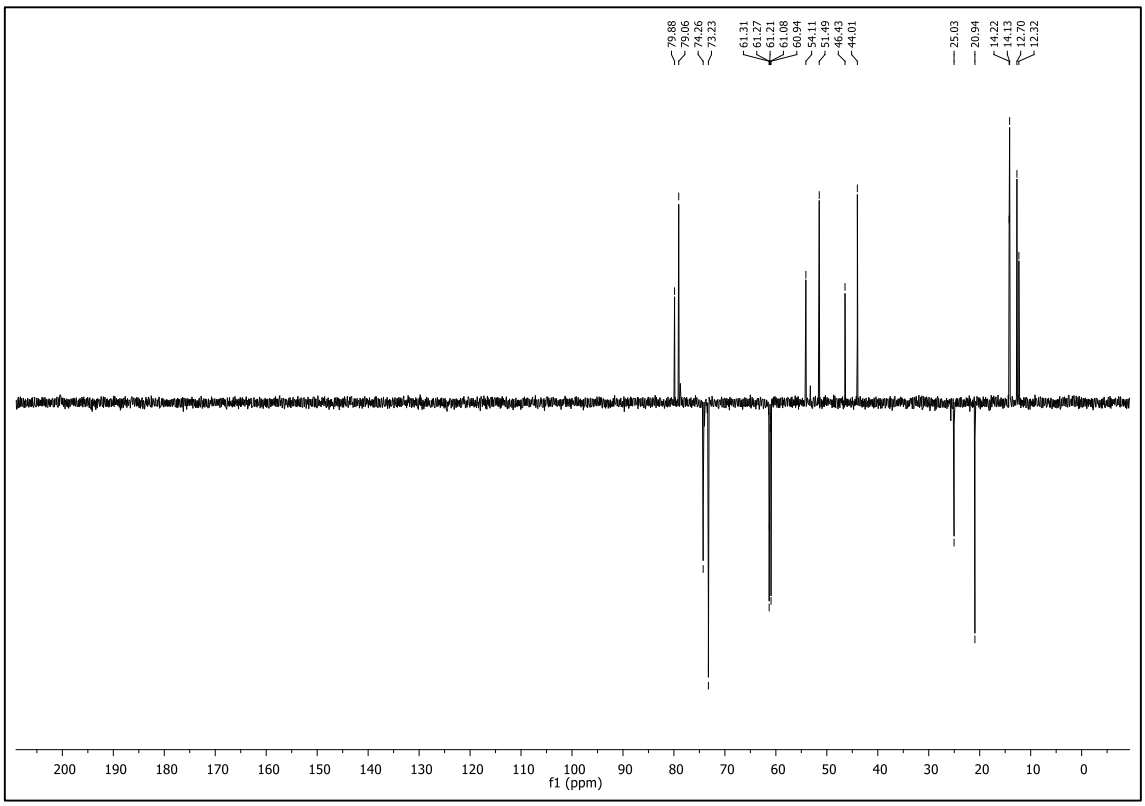

CO2Et
EtO2C
O
1.00
5.13
1.00
0.06
0.58
0.06
0.41
0.99
6.20
0.75
1.76
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

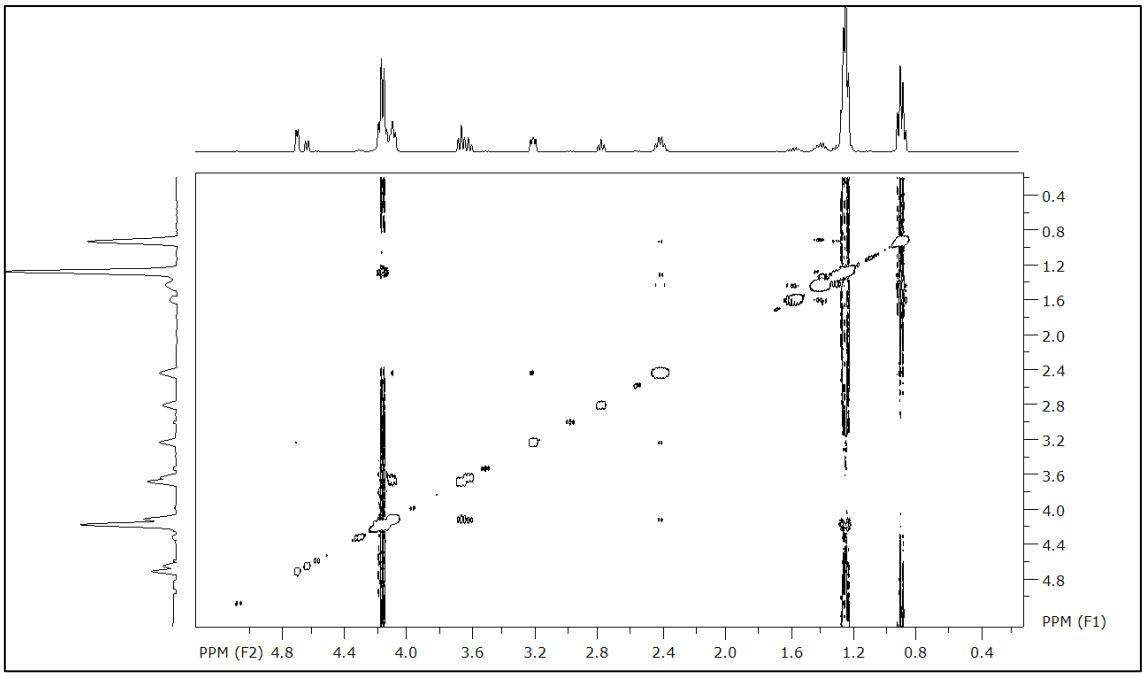

172.17
172.00
171.92
171.19
79.82
78.71
77.58
77.36
77.16
76.74
76.02
75.66
61.48
61.39
61.15
55.79
52.26
39.82
36.87
15.84
14.43
14.35
14.30
13.40
290 270 250 230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

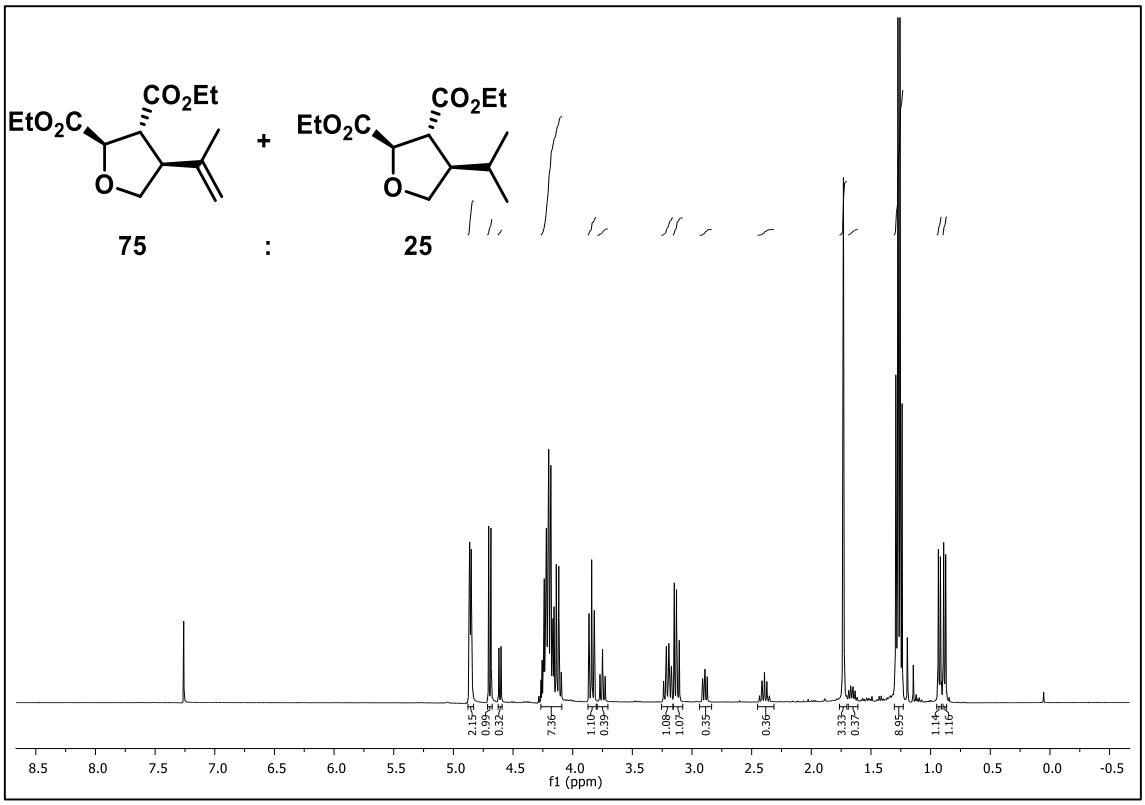

79.70
78.59
75.90
75.54
61.36
61.27
61.03
55.67
52.14
39.70
36.75
15.72
14.31
14.23
14.18
13.28
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

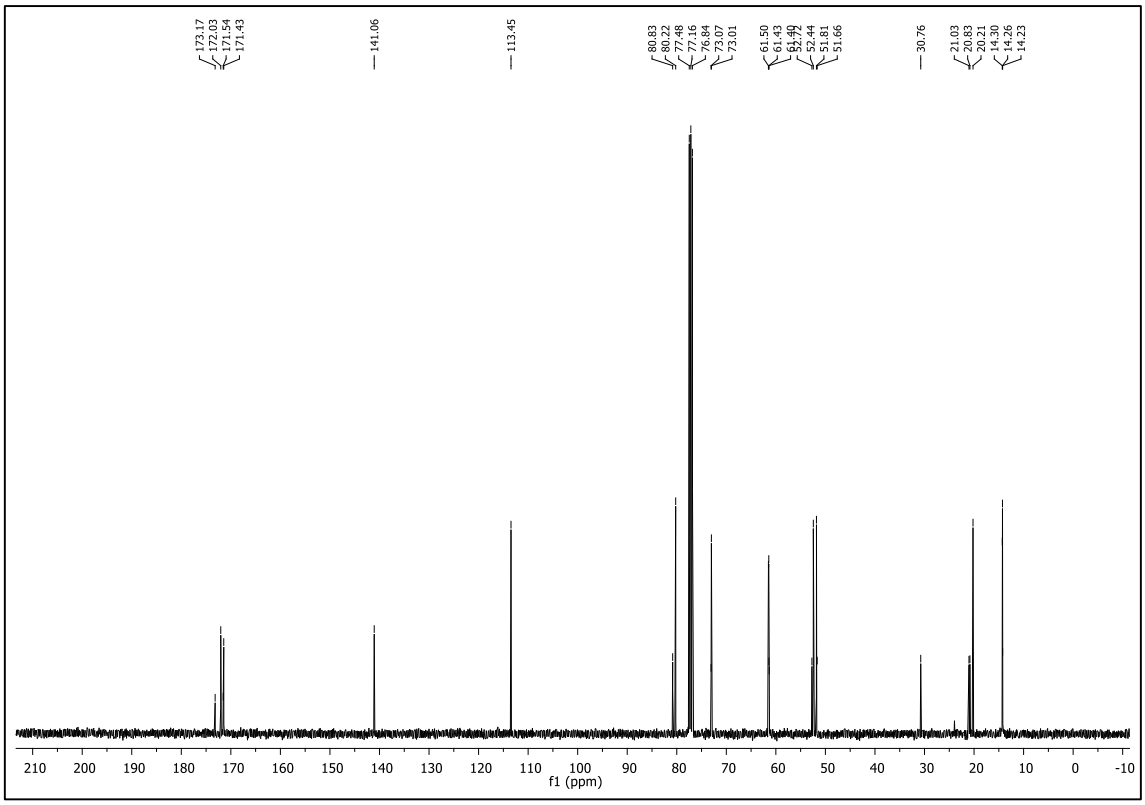

CO2Et
EtO2C
O
0.59
0.34
1.00
0.05
0.01
5.10
0.99
0.05
0.62
0.06
0.35
0.98
0.49
2.10
1.58
6.30
3.11
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

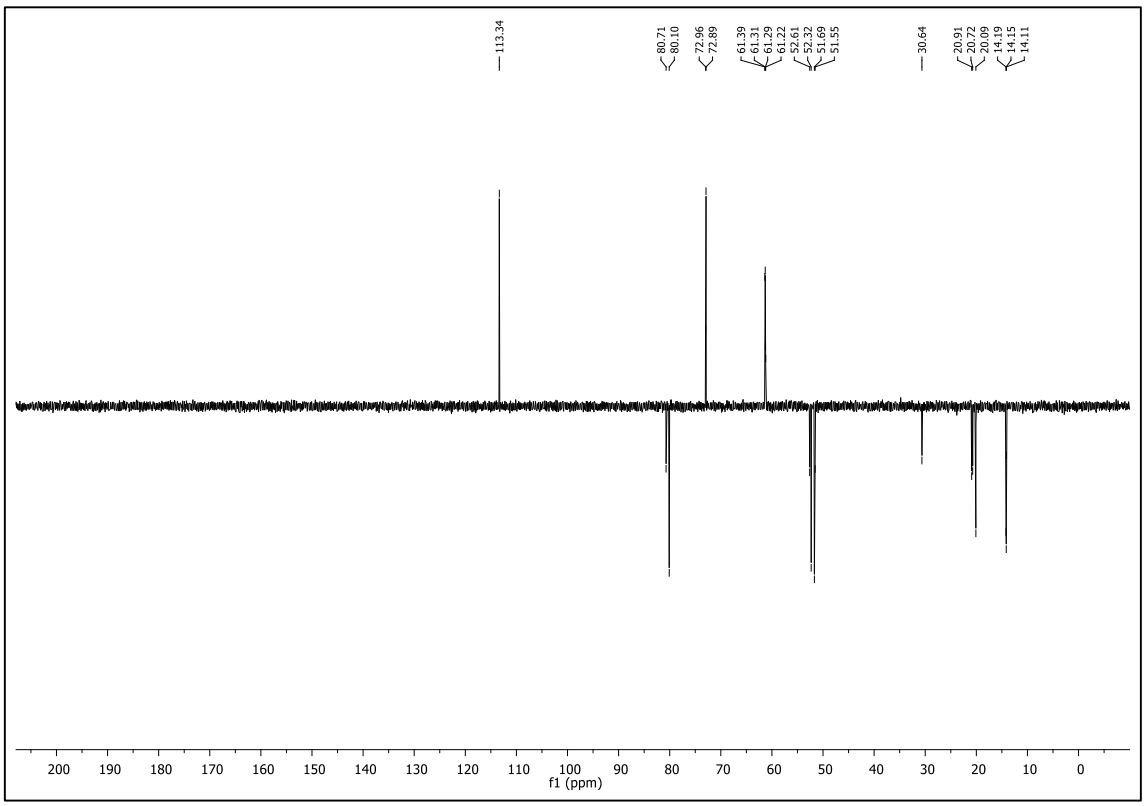

172.51
171.87
171.63
171.37
79.93
79.11
77.58
77.16
76.74
74.32
73.29
61.36
61.33
61.26
61.00
54.16
51.55
46.48
44.06
25.09
21.00
14.28
14.18
12.75
12.37
290 270 250 230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

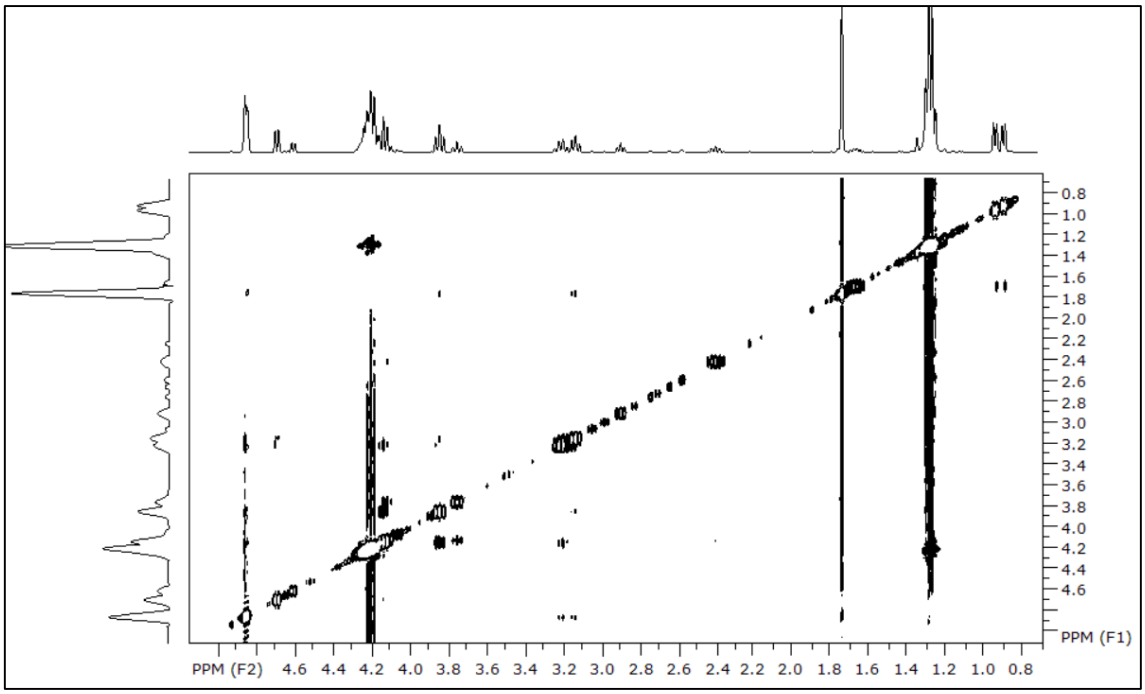

79.88
79.06
74.26
73.23
61.31
61.27
61.21
61.08
60.94
54.11
51.49
46.43
44.01
25.03
20.94
14.22
14.13
12.70
12.32
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

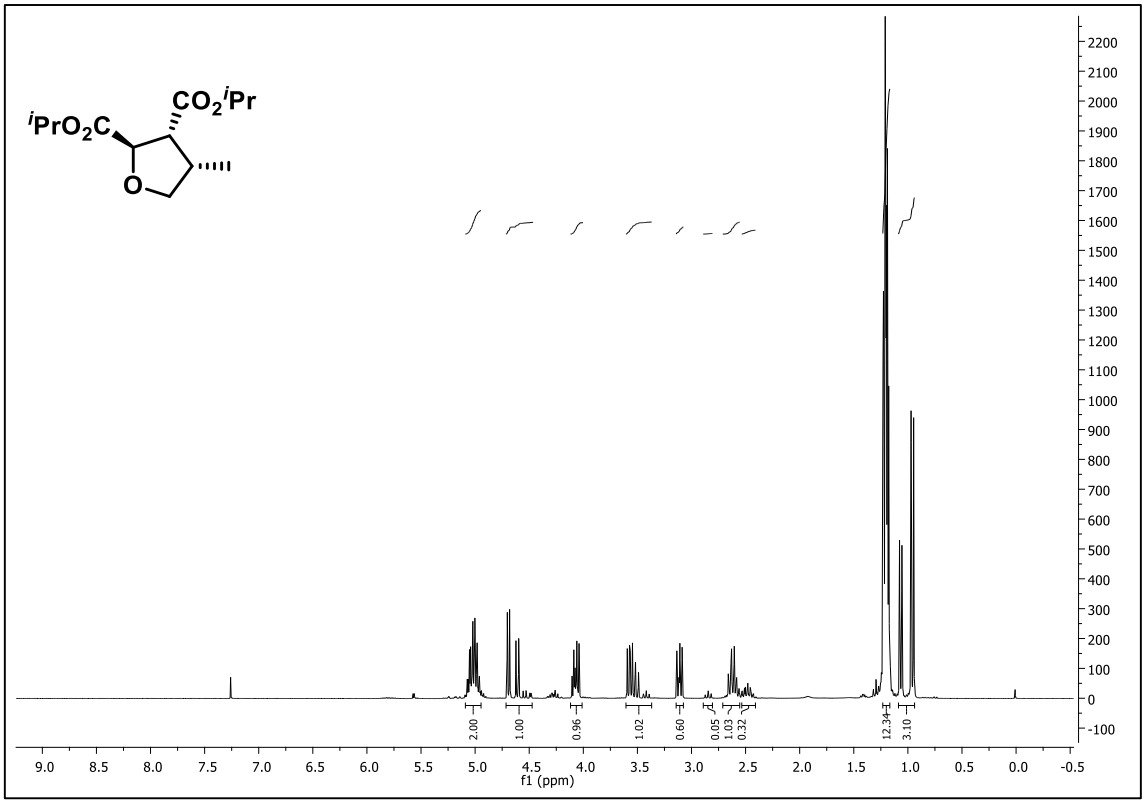

PPM (F2) 4.8 4.4 4.0 3.6 3.2 2.8 2.4 2.0 1.6 1.2 0.8 0.4
PPM (F1) 0.4 0.8 1.2 1.6 2.0 2.4 2.8 3.2 3.6 4.0 4.4 4.8

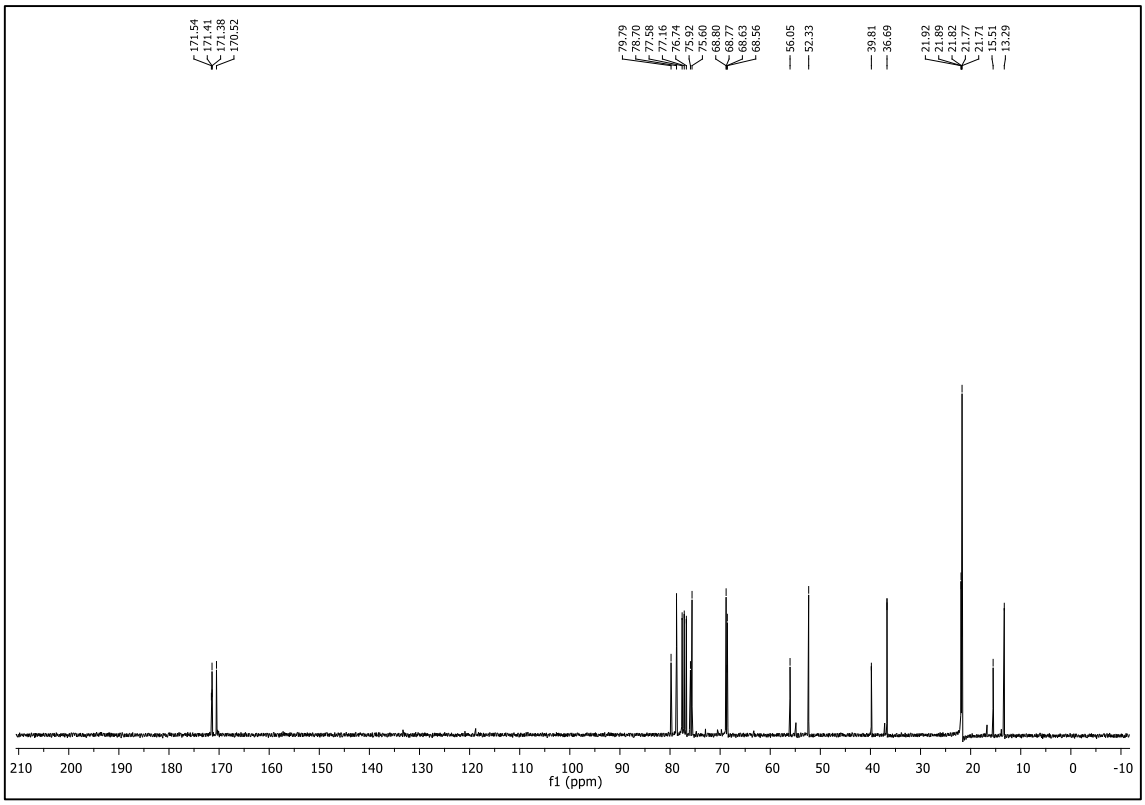

EtO2C
CO2Et
O
+
EtO2C
CO2Et
O
75 : 25
2.15 0.95 0.32 7.36 1.10 0.39 1.08 1.07 0.35 0.36 3.33 0.37 8.95 1.14 1.16
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

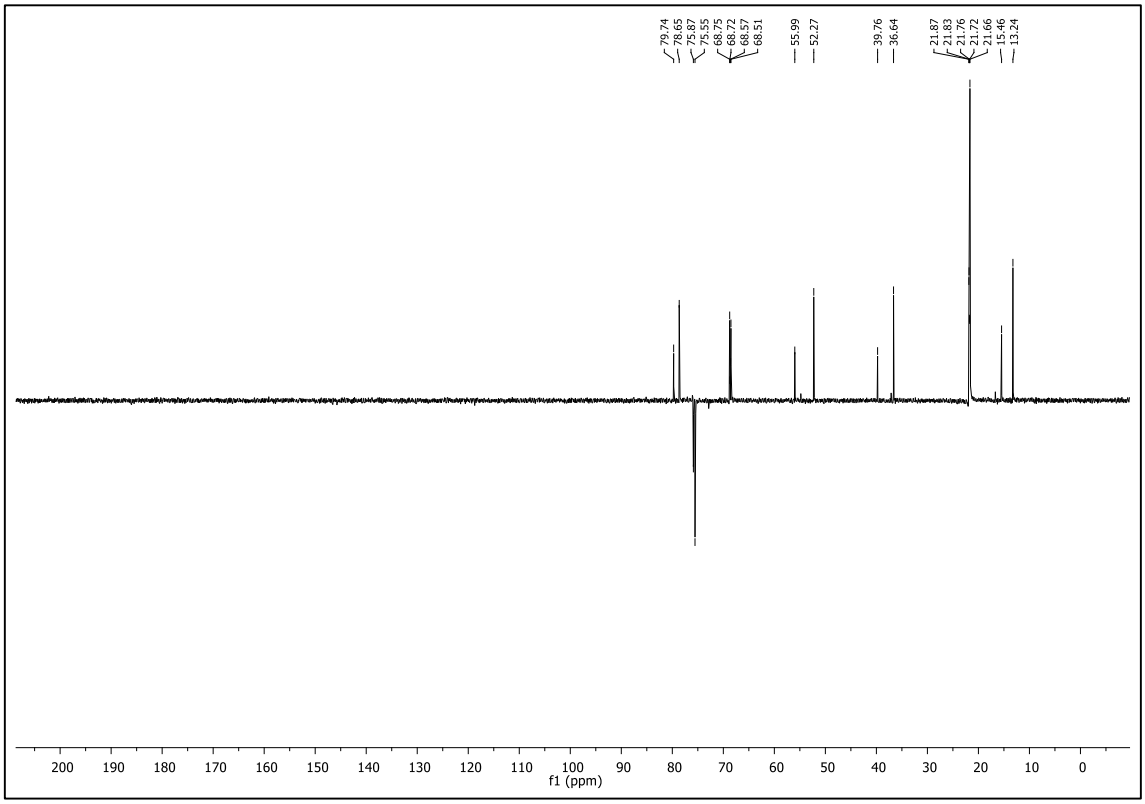

173.17
172.03
171.54
171.43
141.06
113.45
80.83
80.22
77.48
77.16
76.84
73.07
73.01
61.50
61.43
52.44
51.81
51.66
30.76
21.03
20.83
20.21
14.30
14.26
14.23
f1 (ppm)

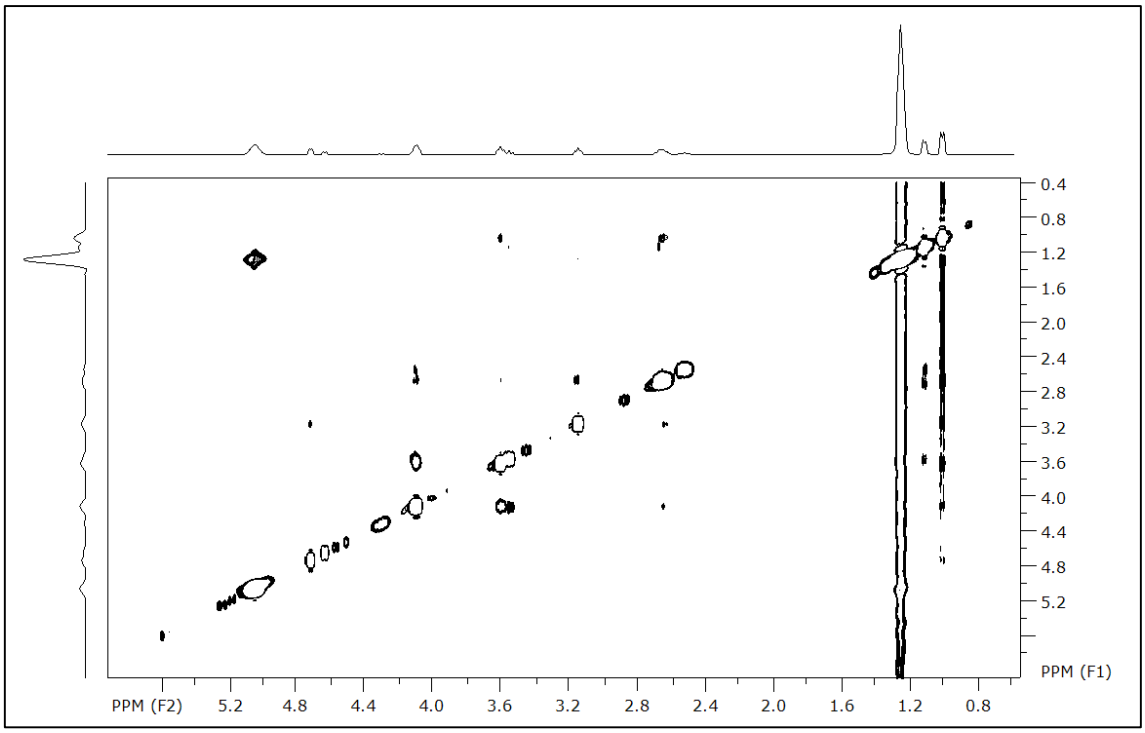

113.34
80.71
80.10
72.96
72.89
61.39
61.31
61.29
61.22
52.61
52.32
51.69
51.55
30.64
20.91
20.72
20.09
14.19
14.15
14.11
f1 (ppm)

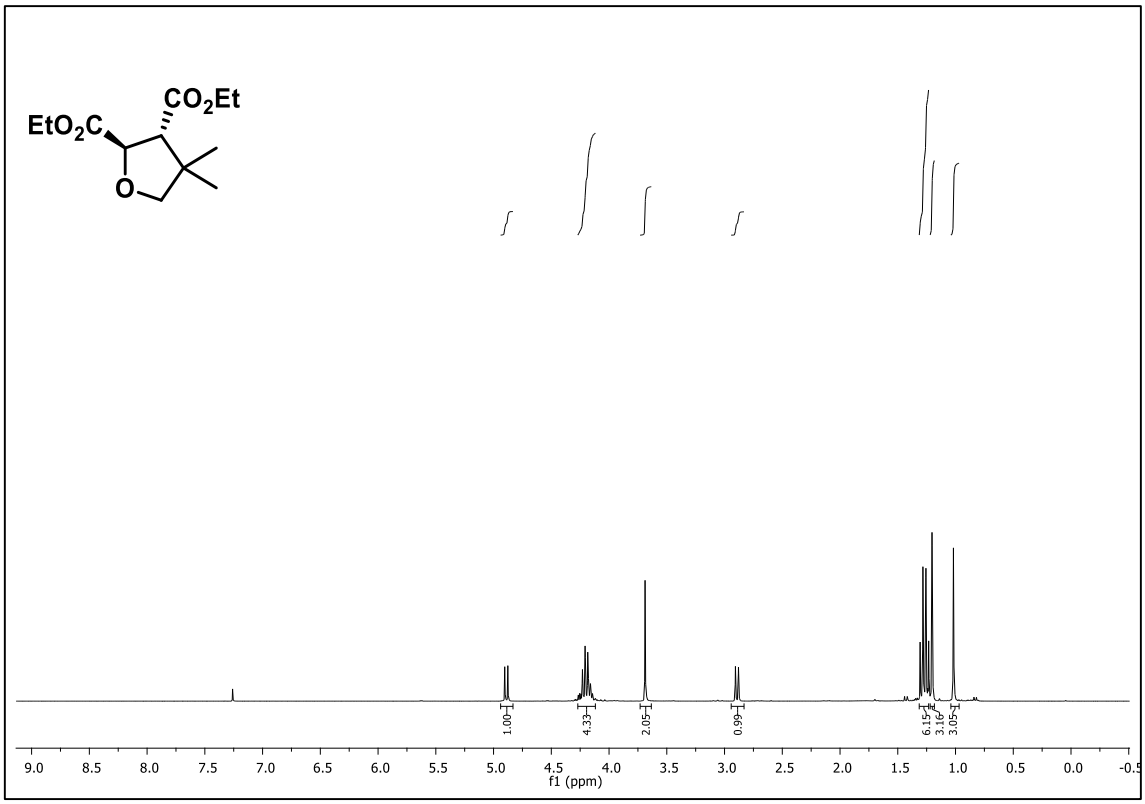

PPM (F2)
PPM (F1)

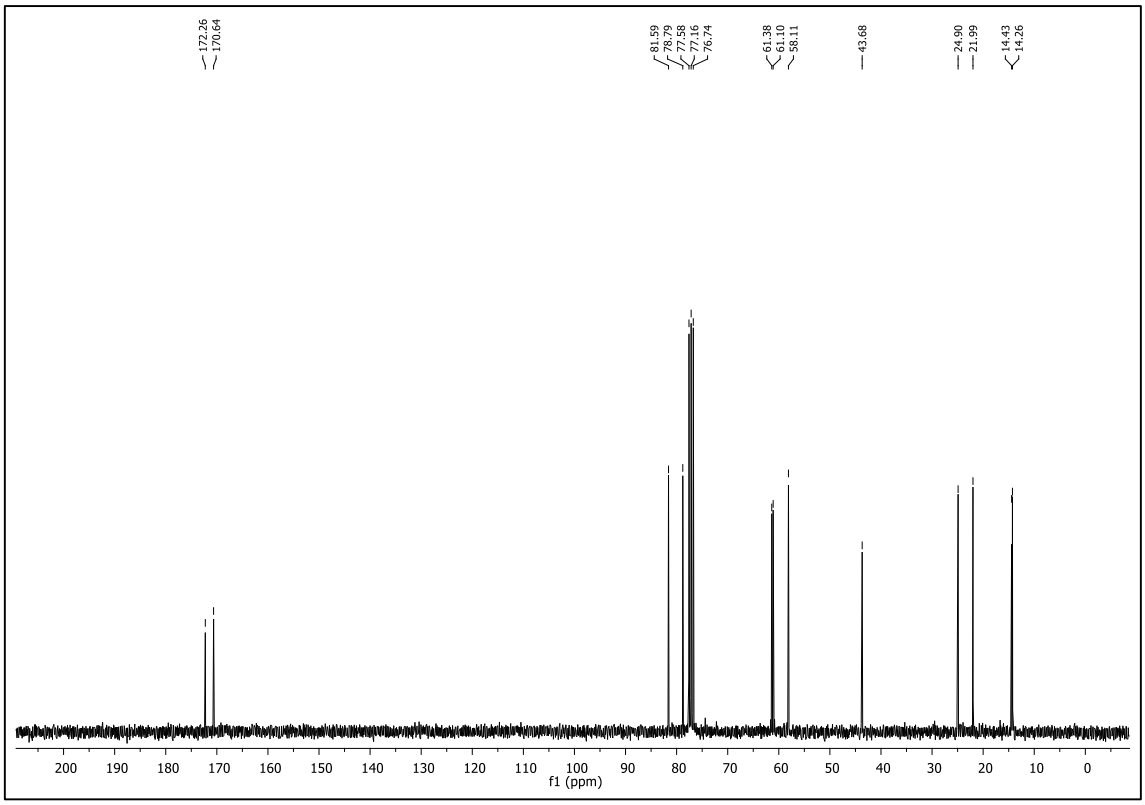

$^{i}PrO_2C$
$CO_2{}^{i}Pr$
O
f1 (ppm)

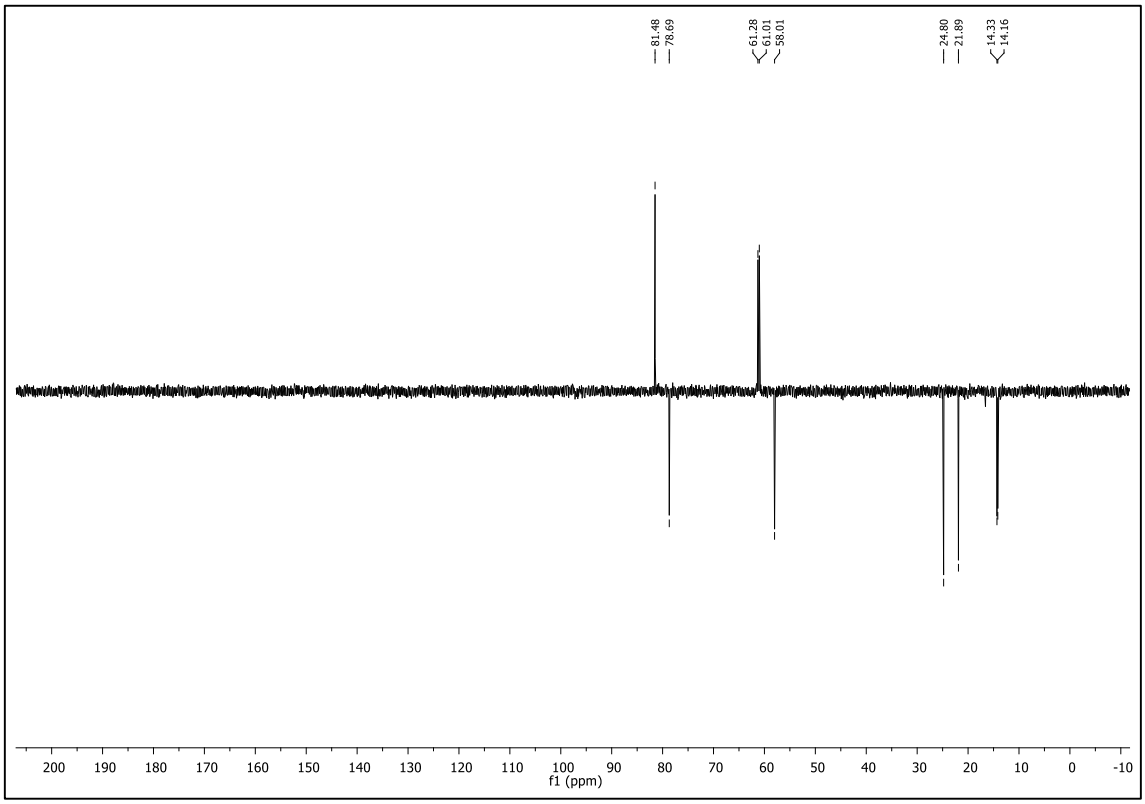

171.54
171.41
171.38
170.52
79.79
78.70
77.58
77.16
76.74
75.92
75.60
68.80
68.77
68.63
68.56
56.05
52.33
39.81
36.69
21.92
21.89
21.82
21.77
21.71
15.51
13.29
f1 (ppm)

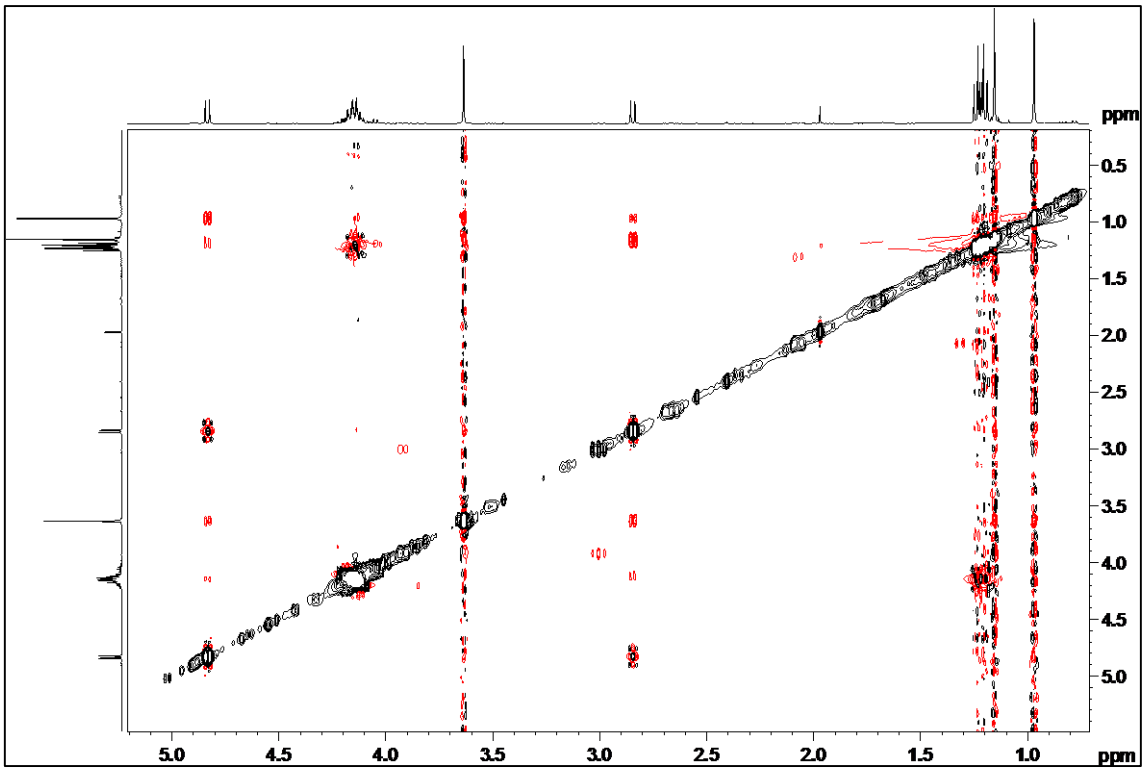

79.74
78.65
75.87
75.55
68.75
68.72
68.57
68.51
55.99
52.27
39.76
36.64
21.87
21.83
21.76
21.72
21.66
15.46
13.24
f1 (ppm)

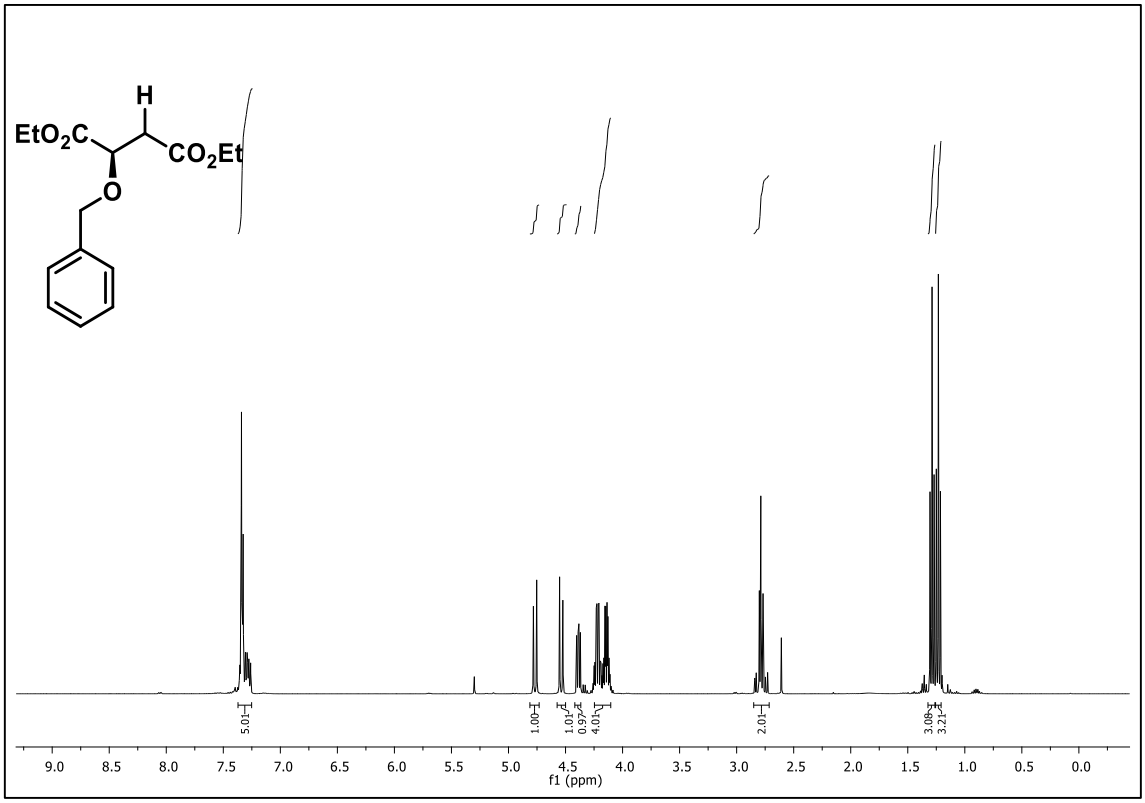

0.4
0.8
1.2
1.6
2.0
2.4
2.8
3.2
3.6
4.0
4.4
4.8
5.2
PPM (F1)
PPM (F2) 5.2 4.8 4.4 4.0 3.6 3.2 2.8 2.4 2.0 1.6 1.2 0.8

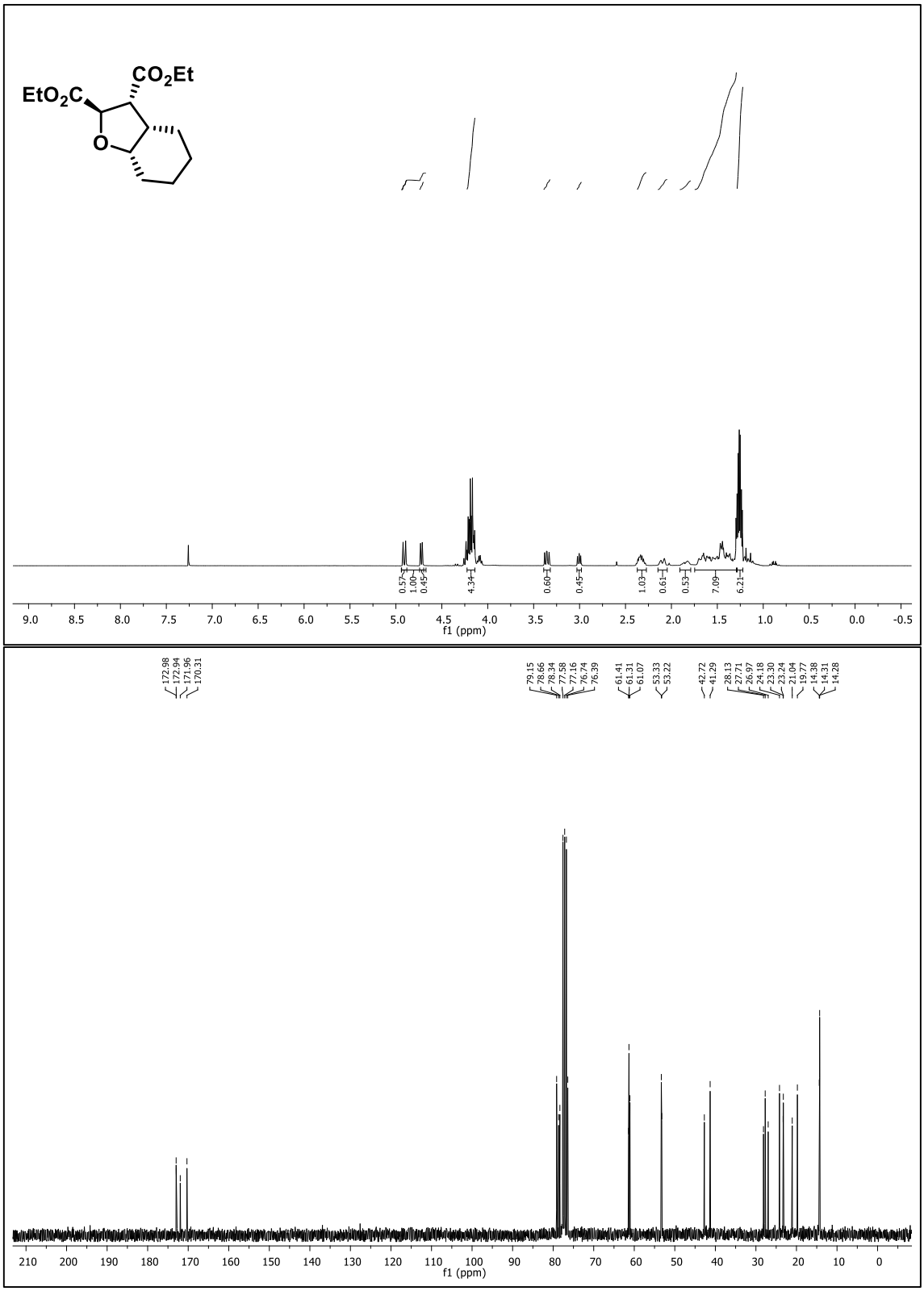

EtO2C
CO2Et
O
1.00
4.33
2.05
0.99
6.15
3.16
3.05
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

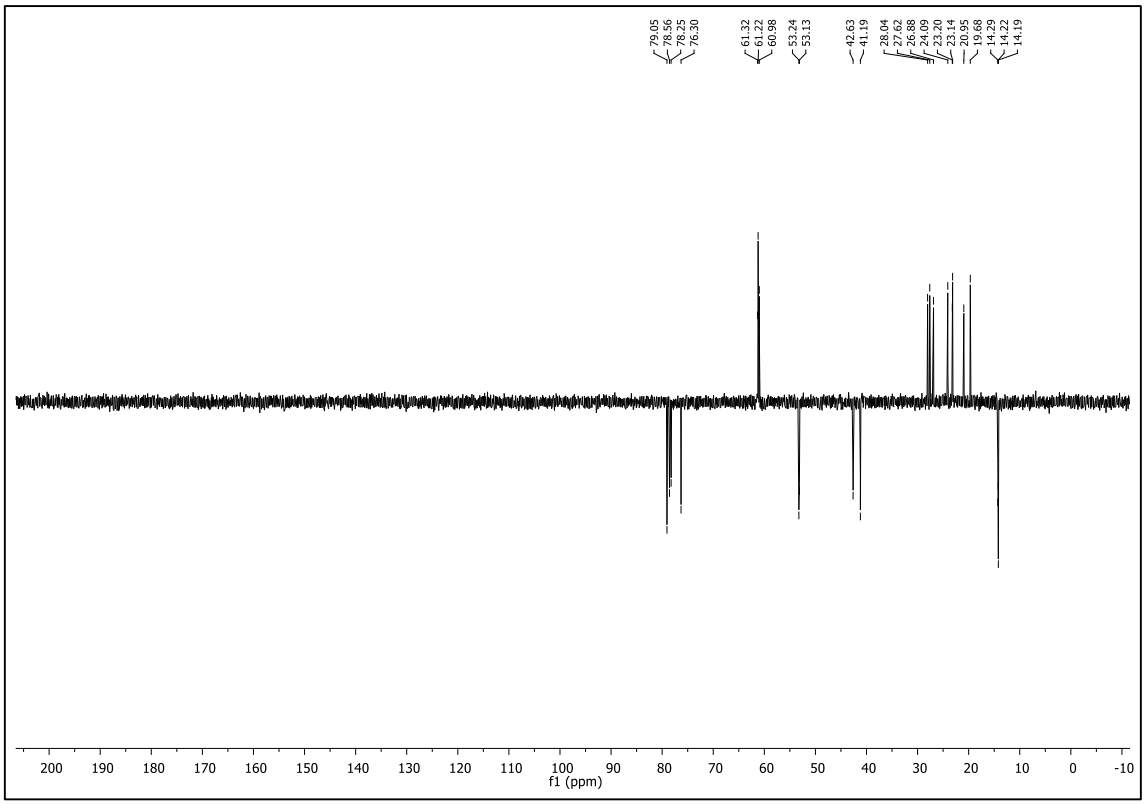

172.26
170.64
81.59
78.79
77.58
77.16
76.74
61.38
61.10
58.11
43.68
24.90
21.99
14.43
14.26
f1 (ppm)

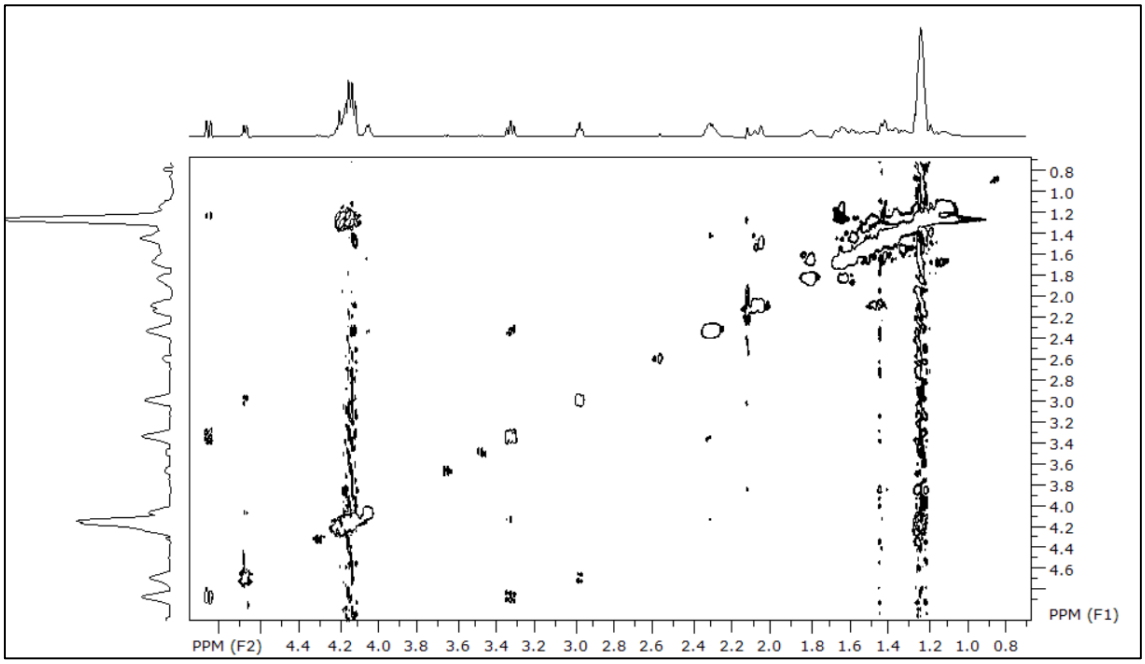

81.48
78.69
61.28
61.01
58.01
24.80
21.89
14.33
14.16
f1 (ppm)


ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm


H
EtO2C
CO2Et
O
5.01
1.00
1.01
0.97
4.01
2.01
3.08
3.21
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)


EtO2C
CO2Et
O
0.57
1.00
0.45
4.34
0.60
0.45
1.03
0.61
0.53
7.09
6.21
f1 (ppm)
172.98
172.94
171.96
170.31
79.15
78.66
78.34
77.58
77.16
76.74
76.39
61.41
61.31
61.07
53.33
53.22
42.72
41.29
28.13
27.71
26.97
24.18
23.30
23.24
21.04
19.77
14.38
14.31
14.28
f1 (ppm)


79.05
78.56
78.25
76.30
61.32
61.22
60.98
53.24
53.13
42.63
41.19
28.04
27.62
26.88
24.09
23.20
23.14
20.95
19.68
14.29
14.22
14.19
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


0.8 1.0 1.2 1.4 1.6 1.8 2.0 2.2 2.4 2.6 2.8 3.0 3.2 3.4 3.6 3.8 4.0 4.2 4.4 4.6
PPM (F1)
PPM (F2) 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8

4.10 References

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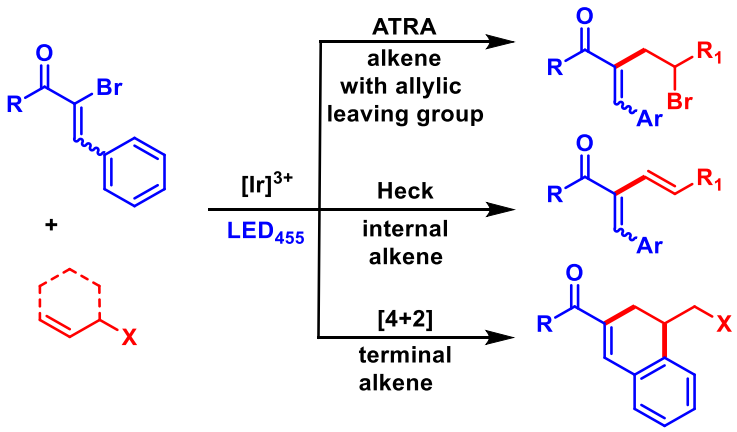
5 Photoredox catalyzed vinyl radical formation following acrylamide synthesis

5.1 Introduction

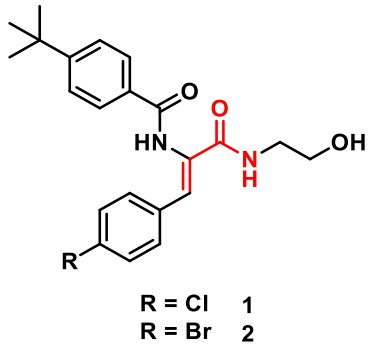
Stork *et al.* developed a strategy to use vinyl radicals as a versatile tool in a variety of synthetic organic transformations. Their applications range from cyclization processes to intermolecular carbon – carbon bond formations, and radical polymerization reactions.[1,2] The reactive radical intermediates were prepared thermically using tributyltin hydride and a radical initiator such as AIBN. As alternative, induction processes were carried out electrochemically[3,4] or by photolysis[5-7] of vinyl halides and are well established in the literature. Highly reactive and electrophilic vinyl radicals derived from α-bromochalcones *via* visible light photoredox catalysis have already been trapped by various alkenes to generate carbon – carbon bonds, as reported previously in our group. Alkenes with allylic leaving groups have been utilized in atomic transfer radical addition (ATRA) processes[8], whereas Heck-type couplings as well as cyclization cascades have been realized *via* internal and terminal alkenes (Scheme 1).[9,10]



Scheme 1. Coupling of α-bromochalcones with olefins – possible reaction pathways.[8-10]

Considering the aforementioned photoredox catalyzed couplings of α-bromochalcones to olefins, continuative studies on intermolecular carbon – carbon bond formation with 1-isocyano-2,4-dimethoxybenzene have been investigated. Thereby, acrylamide substrates were synthesized and subjected to pharmaceutical tests to examine their biological activity.

Acrylamides depict a broad substrate class for multiple industrial applications.[11] Especially their occurrence in food in predominantly heat treated carbohydrate-rich foods is monitored critically by the food industry, as they can act as potential toxicants *via* Maillard reaction[12,13].[14,15] Beyond, acrylamides are mainly used in water and wastewater treatment, mineral and paper processes,[11] as well as active compounds in the pharmaceutical industry, for e.g. anti-inflammation, anti-rheumatoid arthritis, anti-hypercalcemia, anti-osteoporosis and/or bone resorption-suppressing.[16] Moreover, acrylamide derivatives are useful as insecticides[17] in plant protection (Scheme 2).



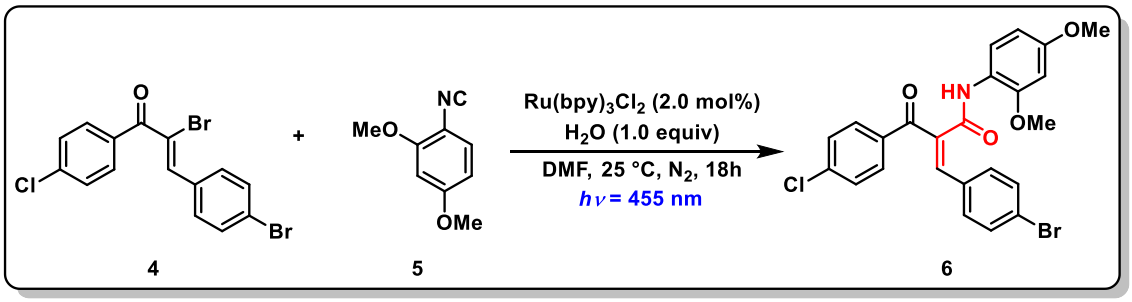
Scheme 2. Two examples for biologically active cinnamide compounds against insects and acarina **1**[17] and as bone resorption-suppressing agent **2**[16].

5.2 Initial screening experiments

We initiated our investigations with the visible light mediated reaction between α-bromochalcone **4** and isonitrile **5** in the presence of 2 mol% $Cu(dap)_2Cl$ as photoredox catalyst, 1 equivalent of water and DMF as solvent at ambient temperature and under N_2 atmosphere resulted in the formation of the desired acrylamide **6**, albeit in a yield of only 2% (Table 1, entry 1). Employing some other well established photoredox catalysts such as $Ir(ppy)_2(dtb\text{-}bpy)PF_6$ (Table 1, entry 2), *fac*-$Ir(ppy)_3$ (Table 1, entry 3) or $Ru(bpy)_3Cl_2$ (Table 1, entry 4) which all have been utilized in oxidative quenching processes successfully before, gave improved isolated yields of 13%, 45%, and 47% after 18 h irradiation time. Having identified $Ru(bpy)_3Cl_2$ as most suitable catalyst, commonly used solvents in photoredox reactions have been screened. The first applied polar CH_3CN or CH_2Cl_2 / THF (9:1) mixture yielded 16% and 15% (Table 1, entry 4 and 5). In the absence of THF using of exclusively non polar CH_2Cl_2, no product formation was detected (Table 1, entry 6). Polar aprotic DMF turned out to be superior towards acrylamide formation **6**

and yielded 47%. Considering the necessity of H_2O as nucleophile for the acrylamide **6** formation, no reaction took place in its absence (Table 1, entry 8). Moreover, control experiments proved that the acrylamide synthesis is indeed a photoredox catalyzed reaction. In the absence of light or catalyst no reaction takes place (Table 1, entry 9 and 10).

Table 1. Initial screening experiments for the visible light mediated acrylamide **6** formation.



Entry	Photoredox catalyst, solvent, modification	Yield [%][a]
1	$Cu(dap)_2Cl_2$	2
2	$Ir(ppy)_2(dtb\text{-}bpy)PF_6$	13
3	*fac*-$Ir(ppy)_3$	45
4	CH_3CN	16
5	CH_2Cl_2 / THF (9:1)	15
6	CH_2Cl_2	0
7	none	47
8	w/o water, *fac*-Ir(ppy) (2.0 mol%)	0
9	w/o light source	0
10	w/o photocatalyst	0

[a]*reaction conditions*: 0.3 mmol scale, photocatalyst (2.0 mol%), isonitrile **5** (2.0 equiv), H_2O (1.0 equiv), solvent (c = 0.15 M), 18 h, 25 °C, N_2, isolated yields.

Beside these screening experiments (Table 1), modifications of the amount of additives and other parameters were performed to obtain the best conditions (Table 2). The amount of H_2O was adapted while using *fac*-Ir(ppy)$_3$ instead of Ru-based photocatalyst. Increased quantity of H_2O equivalents to 5 and 10 yielded constantly 46% and 45% of **6** (Table 2, entry 1 and 2), whereas highly excess of 100 equiv H_2O gave poor yield of 17% of the desired product **6**. Since no improvement could be achieved, only a prolonged irradiation time of 72 h elevated the yield slightly to 51% (Table 2, entry 4). Surprisingly, addition of the original amount of catalyst, isonitrile **5** and H_2O after 20 h and prolonged reaction time of 48 h yielded only 40% (Table 2, entry 5). Further screenings to determine the optimal amount of coupling reagent **5** were performed. The use of 1 equiv isonitrile **5** decreased the yield of **6** to 32% (Table 2, entry 6) and a yield of 47% was achieved for excess of 3 equiv of **5** (Table 2, entry 7). The yield could further be improved to 52% using fourfold amount of isonitrile **5** (Table 2, entry 8). Moreover, experiments on the temperature dependence have been investigated. Cooling of the reaction mixture during irradiation to 0 °C (Table 2, entry 9) led to 26% yield for the product **6**. The performance of the reaction at an increased temperature at 40 °C gave 35% isolated yield (Table 2, entry 10), whereas further temperature increase to 60 °C (Table 2, entry 11) or even 80 °C (Table 2, entry 12) revealed the tendency of diminishing yields for photoinduced carbon – carbon bond coupling at higher temperatures . Modification of the catalyst loading to 1.0 mol% (Table 2, entry 13) yielded lower 22% and negligible increased yield of 53% was isolated for **6** at 3.0 mol% (Table 2, entry 14). The last parameter was the variation of the concentration in the photoreaction. Nevertheless, neither halving the concentration to 0.075 M (Table 2, entry 15) nor an increase to 0.3 M (Table 2, entry 16) were propitious. The variation to isonitrile **5** as limiting reactant and the use of α-bromochalcone **4** in an excess of 1.5 equiv (Table 1, entry 17) gave related 45% of the corresponding acrylamide **6** and 38% hydrolyzed *N*-(2,4-dimethoxyphenyl)formamide as byproduct. Albeit, no significant improvement in yield was achieved by the screening of various parameters, the best result for the photoredox catalyzed acrylamide synthesis was obtained using 2 mol% Ru(bpy)$_3$Cl$_2$, 2.0 equiv isonitrile **5**, 1.0 equiv H_2O in DMF at ambient temperature (Table 1).

Table 2. Advanced screening experiments for the visible light mediated acrylamide **6** formation.

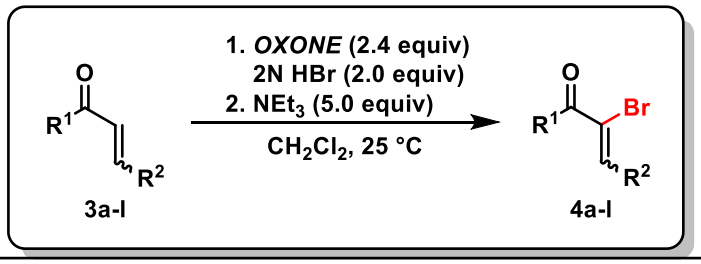
Entry	Changes from standard conditions	Yield [%][a]
1	H_2O (5.0 equiv), *fac*-Ir(ppy)$_3$ (2.0 mol%)	46
2	H_2O (10 equiv), *fac*-Ir(ppy)$_3$ (2.0 mol%)	45
3	H_2O (100 equiv), *fac*-Ir(ppy)$_3$ (2.0 mol%)	17
4	*fac*-Ir(ppy)$_3$ (2.0 mol%)[b]	51
5	*fac*-Ir(ppy)$_3$ (2.0 mol%)[c]	40
6	Isonitrile **5** (1.0 equiv)	32
7	Isonitrile **5** (3.0 equiv)	47
8	Isonitrile **5** (4.0 equiv)	52
9	0 °C	26
10	40 °C	35
11	60 °C	16
12	80 °C	7
13	Ru(bpy)$_3$Cl$_2$ (1.0 mol%)	22
14	Ru(bpy)$_3$Cl$_2$ (3.0 mol%)	53
15	c = 0.075 M	40
16	c = 0.3 M	34
17	α-bromochalcone **4** (1.5 equiv), isonitrile **5** (1.0 equiv)[d]	45

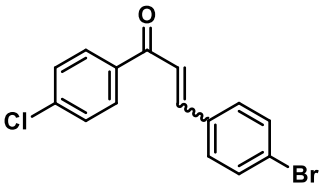
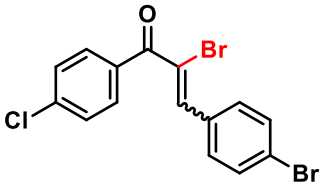
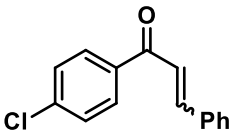
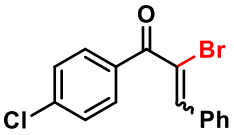
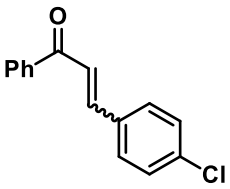
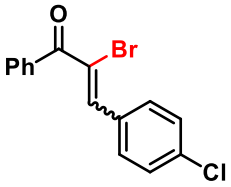
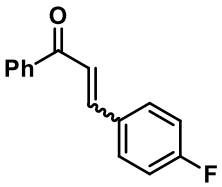
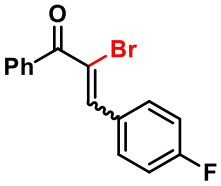
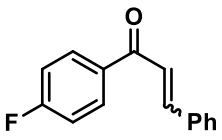
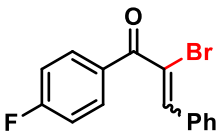
[a]*reaction conditions*: 0.3 mmol scale, Ru(bpy)$_3$Cl$_2$ (2.0 mol%), isonitrile **5** (2.0 equiv), H_2O (1.0 equiv), DMF (c = 0.15 M), 18 h, 25 °C, N_2, isolated yields. [b]72 h reaction time. [c]additional catalyst (2.0 mol%), isonitrile **5** (2.0 equiv) and H_2O (1.0 equiv) after 20 h, 48 h total reaction time. [d]38% *N*-(2,4-dimethoxyphenyl)formamide as byproduct.

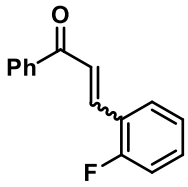
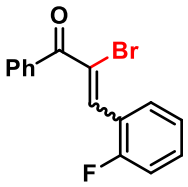
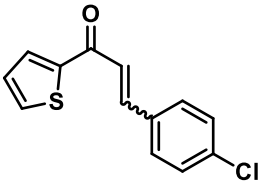
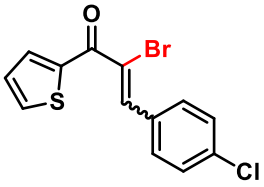
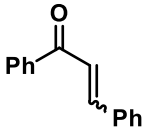
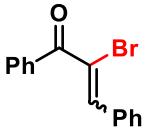
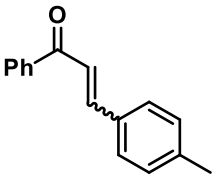
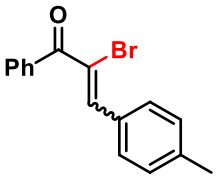
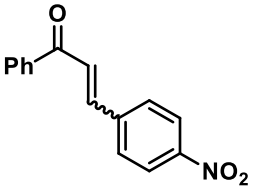
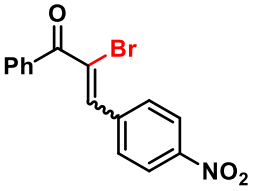
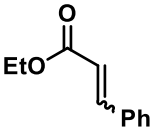
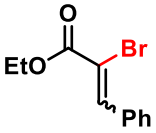
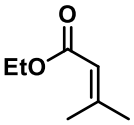
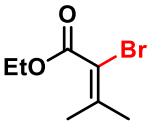
5.3 Starting material synthesis

After setting up the light mediated reaction conditions for acrylamide preparation, α-bromochalcones and bromoacrylates were prepared in the presence of chalcones, potassium salt *OXONE* as oxidizing agent in the presence of 2N HBr in CH_2Cl_2 at ambient temperature. After complete bromination of the alkene moiety, NEt_3 as base was added to give the desired products (Table 3). Chlorine substituted chalcones at the *para* position gave generally good yields of the corresponding products with various *E/Z* ratios (Table 3, entry 1-3). Moreover, moderate yields were achieved for *para* and *ortho* fluorinated compounds (Table 3, entry 4-6) and electron rich heteroaromatic thiophene derivative **4g** (Table 3, entry 7) with an excess of cis isomers. Chalcone **3h** (Table 3, entry 8) and *p*-methylated compound **3i** (Table 3, entry 9) yielded 87% and 74% of brominated compounds **4h** and **4i** with *E/Z* ratios 13:87 and 22:78. Compound **3j** containing an electron withdrawing *p*-nitro substituent yielded corresponding α-bromochalcone **4j** in 79% with *E/Z* ratio 36:64 (Table 3, entry 10). Replacement of one aryl group by an ethyl ester gave 78% yield of the mono-brominated ethyl 3-phenylacrylate **4k** (Table 3, entry 11). In addition, poor yield of 27% was achieved for aromatic free dimethylacrylate compound **4l** (Table 3, entry 12).

Table 3. Synthesis of α-bromochalcones and bromoacrylates as starting materials for the light mediated acrylamide preparation.



Entry	Acrolein	Product	*E/Z*	Yield [%][a]
1	 3a	 4a	9:91	87
2	 3b	 4b	36:64	82
3	 3c	 4c	53:47	85
4	 3d	 4d	19:81	76
5	 3e	 4e	34:66	67

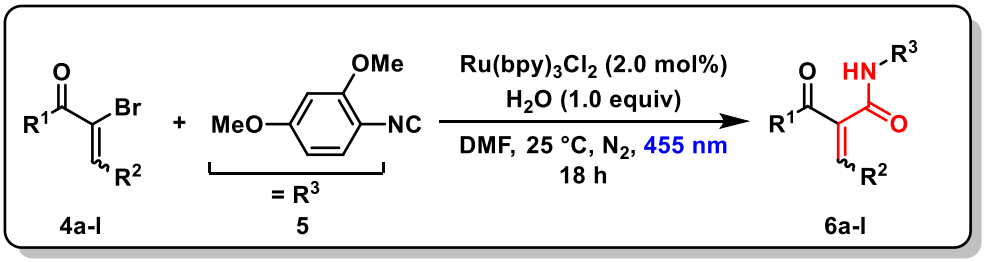
6	 **3f**	 **4f**	36:64	62
7	 **3g**	 **4g**	13:87	55
8	 **3h**	 **4h**	9:91	87
9	 **3i**	 **4i**	22:78	74
10	 **3j**	 **4j**	19:81	79
11	 **3k**	 **4k**	43:57	78
12	 **3l**	 **4l**		27

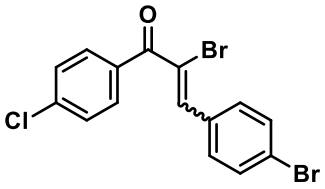
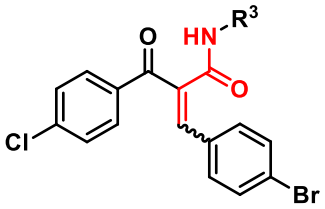
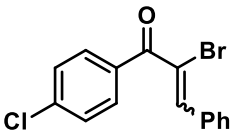
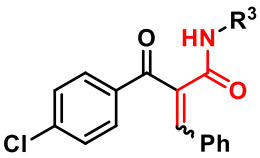
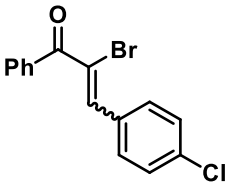
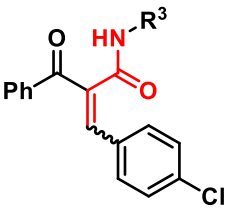
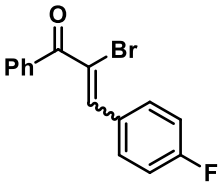
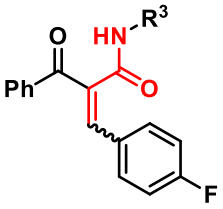
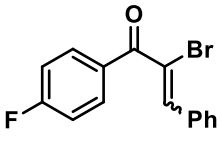
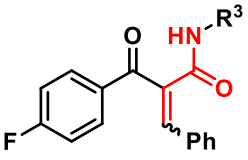
[a]isolated yields.

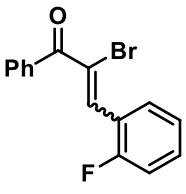
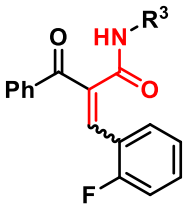
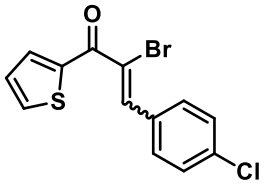
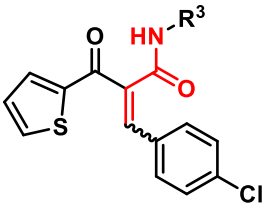
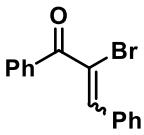
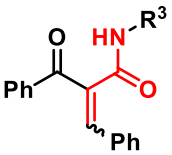
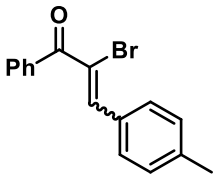
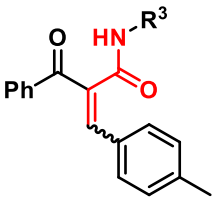
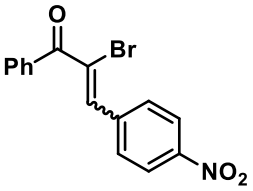
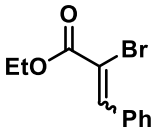
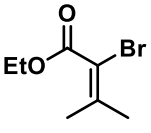
5.4 Visible light mediated acrylamide synthesis

Having α-bromochalcones in hand, light mediated acrylamide preparation was performed using $Ru(bpy)_3Cl_2$ as photoredox catalyst, 1-isocyano-2,4-dimethoxybenzene **5** as coupling reagent and H_2O as nucleophile in DMF at ambient temperature after 18 h reaction time (Table 4). Electron donating and withdrawing groups, as well as halides in either ring of the chalcone were examined. Previously screened α-bromochalcone **4a** yielded 47% of the corresponding acrylamide **6a** (*E/Z* = 15:85) in analytical pure form after column purification on flash silica (Table 4, entry 1). Further *p*-chlorinated **4b** (Table 4, entry 2) and **4c** (Table 4, entry 3) compounds, likewise gave 40% (*E/Z* = 16:84) and 49% (*E/Z* = 13:87) yield of the desired photoredox catalyzed products **6b** and **6c**. Respectively, 47% and 46% yield were achieved for acrylamide derivatives **6d** and **6e** by replacement of chlorine to fluorine at the para position (Table 4, entry 4 and 5). Modification to *o*-fluorine including α-bromochalcone **4f** yielded moderate 47% and an excess of trans isomer of 84% of the corresponding product **6f** (Table 4, entry 6). Substitution of an aryl group by an electron rich thiophene was also well tolerated and gave 43% isolated yield of **6g** (*E/Z* = 13:87; Table 4, entry 7). Moreover, slightly increased 55% yield of **6h** (E/Z = 13:87) was achieved for the photoinduced reaction of unsubstituted α-bromochalcone **4h** (Table 4, entry 8), whereas *p*-methylated derivative **4i** (Table 4, entry 9) yielded 47% yield of **6i** (E/Z = 11:89), similar to aforementioned substrates. However, the process was limited to electron withdrawing *p*-nitro compound **4j** as well as α-bromo acrylates **4k** and **4l**, where no conversion of the starting materials was observed (Table 4, entry 10 - 12)

Table 4. Photoredox catalyst carbon – carbon bond formation for acrylamide synthesis.



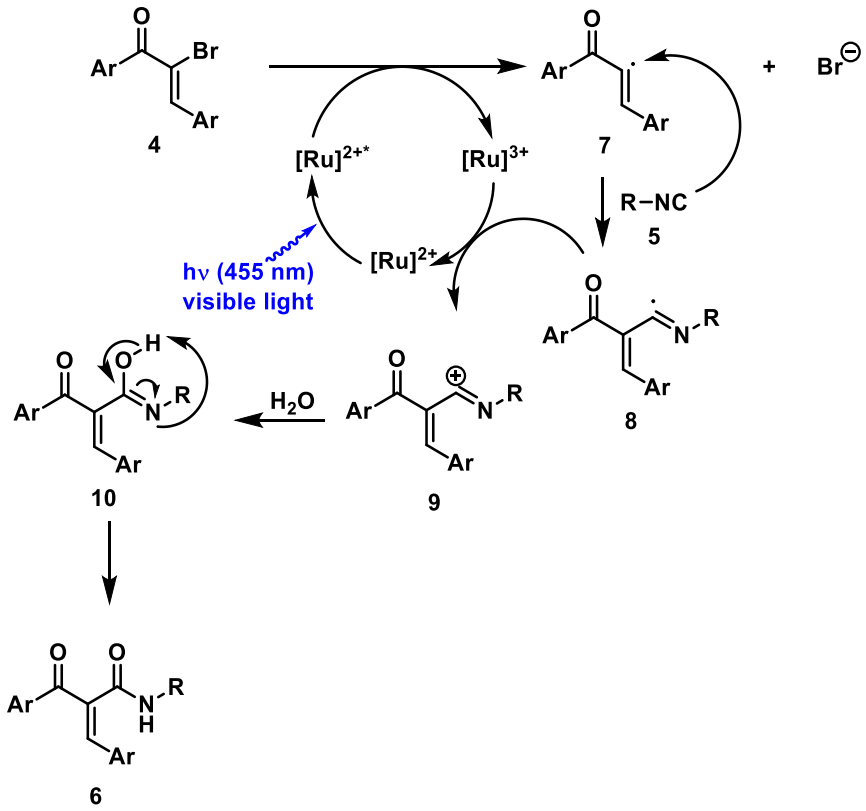
Entry	Substrate	Product	*E/Z*	Yield [%][a]
1	 4a	 6a	15:85	47
2	 4b	 6b	16:84	40
3	 4c	 6c	13:87	49
4	 4d	 6d	15:85	47
5	 4e	 6e	10:90	46

6	 **4f**	 **6f**	16:84	47
7	 **4g**	 **6g**	13:87	43
8	 **4h**	 **6h**	13:87	55
9	 **4i**	 **6i**	11:89	47
10	 **4j**			0
11	 **4k**			0
12	 **4l**			0

[a]*reaction conditions*: 0.3-0.5 mmol scale, $Ru(bpy)_3Cl_2$ (2.0 mol%), isonitrile **5** (2.0 equiv), H_2O (1.0 equiv), DMF (c = 0.15 M), 18 h, 25 °C, N_2, isolated yields.

5.5 Proposed reaction mechanism

Proposed mechanism for the above photoredox catalyzed transformation is in consistent with the oxidative quenching cycle of the $Ru(bpy)_3Cl_2$ catalyst, involving the formation of vinyl radical **7** by the transfer of an electron from the excited Ru^{2+*} species to α-bromochalcone **4** (Scheme 3). Isonitrile **5** then adds intermolecular to the induced electrophilic radical **7** to form a carbon – carbon bond and radical **8**. A back electron transfer from **8** to the oxidized Ir^{3+} species regenerates the catalyst and forms the cation intermediate **9**. In presence of H_2O as nucleophile, addition to the cation **9** and subsequent intramolecular hydrogen rearrangement **10** gives the desired acrylamide **6**.



Scheme 3. Proposed visible light mediated mechanism of the acrylamide formation in the presence of H_2O.

5.6 Biological activity

Synthesized acrylamide compounds have been tested in order to identify novel inhibitors of the ATP-binding cassete transporter ABCG2. Comparison of the activities of the compounds showed in all cases less inhibition (Table 4). Chlorinated acrylamides depicted 10-20% inhibition (Table 4, substrate 6a, 6b, 6c), whereas 20% was determined for **6a** with an additional *p*-bromo group. Less inhibition of 2-8% was detected for fluorinated test compounds, especially *o*-fluorinated acrylamide **6f** turned out to have low 2% (Table 4, substrate 6d, 6e and 6f). However, thiophene substituted acrylamide **6g** was identified as superior ABCG2 inhibitor with 26% (Table 4, substrate 6g). Non-functionalized compound **6h** emerged 12% inhibition (Table 4, substrate 6h), whereas improved 20% was detected for *p*-methylated substrate (Table 4, substrate 6i).

Table 4. Acrylamide compounds as potential ABCG2 inhibitors.

Substrate	$F_{Average}$	SD (F)	rel SD (F) [%]	Inhibition [%]
6a	14591	353	2	20
6b	12077	851	7	10
6c	12061	294	2	10
6d	11710	272	2	8
6e	11532	416	4	7
6f	10214	650	6	2
6g	16163	492	3	26
6h	12552	207	2	12
6i	14739	515	3	20

c = 10 μM. $F_{Average}$ = average fluorescence intensity, SD (F) = standard deviation fluorescence, rel SD (F) = relative standard deviation fluorescence.

5.7 Conclusion

In conclusion, a photoredox catalyzed synthesis of acrylamides has been achieved by intermolecular vinyl radial carbon – carbon bond formation with 1-isocyano-2,4-dimethoxybenzene **5** utilizing ruthenium photoredox catalyst and visible light. A diversity of halogenated as well as heteroaromatic, methylated and unsubstituted α-bromochalcones were tolerated giving rise to larger variety of acrylamides. Biological activity studies towards ABCG2 transporter depicted less inhibitory effects.

5.8 Experimental part

Experimental details, characterization data and spectra

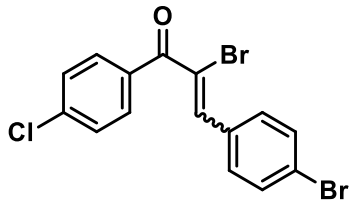
5.8.1 General information

All chemicals were used as received or purified according to Purification of Common Laboratory Chemicals. Glassware was dried in an oven at 110 °C or flame dried and cooled under a dry atmosphere prior to use. All reactions were performed using Schlenk techniques. Blue light irradiation processes was performed using a CREE XLamp XP-E D5-15 LED (λ = 450-465 nm). Analytical thin layer chromatography was performed on Merck TLC aluminum sheets silica gel 60 F 254. Reactions were monitored by TLC and visualized by a short wave UV lamp and stained with a solution of potassium permanganate, *p*-anisaldehyde, or Seebach's stain. Column flash chromatography was performed using Merck flash silica gel 60 (0.040-0.063 mm). The melting points were measured on an automated melting point system (MPA 100) with digital image processing technology by Stanford Research Systems. ATR-IR spectroscopy was carried out on a Biorad Excalibur FTS 3000 spectrometer, equipped with a Specac Golden Gate Diamond Single Reflection ATR-System. NMR spectra were recorded on Bruker Avance 300 and Bruker Avance 400 spectrometers. Chemical shifts for ^{1}H NMR were reported as δ, parts per million, relative to the signal of $CHCl_3$ at 7.26 ppm. Chemical shifts for ^{13}C NMR were reported as δ, parts per million, relative to the center line signal of the $CDCl_3$ triplet at 77 ppm. Coupling constants *J* are given in Hertz (Hz). The following notations indicate the multiplicity of the signals: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, p = quintet, sept = septet, and m = multiplet. Mass spectra were recorded at the Central Analytical Laboratory at the Department of Chemistry of the University of Regensburg on a Varian MAT 311A, Finnigan MAT 95, Thermoquest Finnigan TSQ 7000 or Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS. Gas chromatographic analyses were performed on a Fisons Instruments gas chromatograph equipped with a capillary column (30 m × 250 µm × 0.25 µm) and a flame ionization detector. The yields reported are referred to the isolated compounds unless otherwise stated.

5.8.2 Synthesis of α-bromochalcones

General procedure ***GPI*** for the preparation of α-bromo chalcone[9,10,18]

To a mixture of corresponding chalcone[19,20] (2.0 mmol, 1.00 equiv) and *OXONE* (2.40 mmol, 1.20 equiv) dissolved in CH_2Cl_2, 2 N HBr (10.0 mmol, 2.00 equiv) was added dropwise to give a dark red colored solution. The reaction mixture was stirred at 25 °C until full conversion (monitored by TLC) of the chalcone to dibromide. Triethylamine (10.0 mmol, 5.00 equiv) was added and continued stirring until full conversion. The reaction mixture was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers was washed with brine, dried over $NaSO_4$ and the solvent evaporated under reduced pressure. The residue was purified by flash column chromatography.

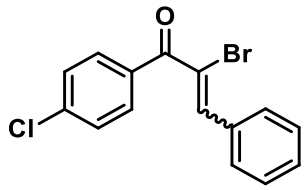


2-bromo-3-(4-bromophenyl)-1-(4-chlorophenyl)prop-2-en-1-one (4a)

Following general procedure ***GPI*** using (*E*)-3-(4-bromophenyl)-1-(4-chlorophenyl)prop-2-en-1-one (2.57 g, 8.00 mmol, 1.00 equiv), *OXONE* (5.91 g, 9.60 mmol, 1.20 equiv), 2 N HBr (1.30 mL, 1.94 g, 24.0 mmol, 3.00 equiv), triethylamine (6.70 mL, 4.86 g, 48.0 mmol, 6.00 equiv) in CH_2Cl_2 (40.0 mL, 0.2 M) gave 2.78 g (87%) as a white solid after flash column purification on silica gel as a mixture of *E/Z* = 9:91. R_f (hexanes/EtOAc 9:1) = 0.57.

^{1}H NMR (400 MHz, $CDCl_3$, E isomer): 7.87 (dd, *J* = 8.9, 2.1 Hz, 2H), 7.40 – 7.33 (m, 2H), 7.30 – 7.23 (m, 3H), 6.99 (d, *J* = 8.4 Hz, 2H).

^{1}H NMR (400 MHz, $CDCl_3$, Z isomer): 7.77 – 7.65 (m, 4H), 7.57 (s, 1H), 7.56 – 7.48 (m, 2H), 7.47 – 7.40 (m, 2H).

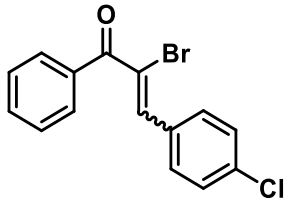


2-bromo-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one (4b)[21]

Following general procedure ***GPI*** using (*E*)-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one (485 mg, 2.00 mmol, 1.00 equiv), *OXONE* (1.48 g, 2.40 mmol, 1.20 equiv), 2 N HBr (217 μL, 324 mg, 4.00 mmol, 2.00 equiv), triethylamine (1.40 mL, 1.01 g, 10.0 mmol, 5.00 equiv) in CH_2Cl_2 (10.0 mL, 0.2 M) gave 530 mg (82%) as a white solid after flash column purification on silica gel as a mixture of *E/Z* = 36:64. R_f (hexanes/EtOAc 9:1) = 0.58.

^{1}H NMR (400 MHz, $CDCl_3$, E isomer): 7.92 – 7.90 (m, 1H), 7.90 – 7.88 (m, 1H), 7.40 – 7.38 (m, 2H), 7.38 – 7.35 (m, 1H), 7.21 – 7.10 (m, 5H).

^{1}H NMR (400 MHz, $CDCl_3$, Z isomer): 7.87 – 7.83 (m, 2H), 7.79 – 7.75 (m, 2H), 7.67 (s, 1H), 7.49 – 7.42 (m, 5H).

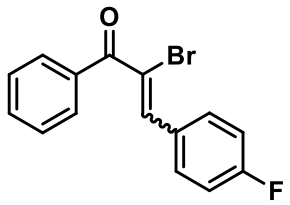


2-bromo-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (4c)[22]

Following general procedure ***GPI*** using (*E*)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (485 mg, 2.00 mmol, 1.00 equiv), *OXONE* (1.48 g, 2.40 mmol, 1.20 equiv), 2 N HBr (217 μL, 324 mg, 4.00 mmol, 2.00 equiv), triethylamine (1.40 mL, 1.01 g, 10.0 mmol, 5.00 equiv) in CH_2Cl_2 (10.0 mL, 0.2 M) gave 545 mg (85%) as a white solid after flash column purification on silica gel as a mixture of *E/Z* = 53:47. R_f (hexanes/EtOAc 9:1) = 0.52.

^{1}H NMR (300 MHz, $CDCl_3$, E isomer): 7.99 – 7.93 (m, 2H), 7.64 (s, 1H), 7.62 – 7.38 (m, 2H), 7.31 (s, 1H), 7.18 – 7.07 (m, 4H).

^{1}H NMR (300 MHz, $CDCl_3$, Z isomer): 7.83 – 7.77 (m, 4H), 7.62 – 7.38 (m, 6H),

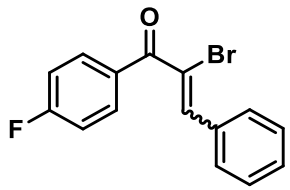


2-bromo-3-(4-fluorophenyl)-1-phenylprop-2-en-1-one (4d)[22]

Following general procedure ***GPI*** using (*E*)-3-(4-fluorophenyl)-1-phenylprop-2-en-1-one (453 mg, 2.00 mmol, 1.00 equiv), *OXONE* (1.48 g, 2.40 mmol, 1.20 equiv), 2 N HBr (217 μL, 324 mg, 4.00 mmol, 2.00 equiv), triethylamine (1.40 mL, 1.01 g, 10.0 mmol, 5.00 equiv) in CH_2Cl_2 (10.0 mL, 0.2 M) gave 465 mg (76%) as a yellow liquid after flash column purification on silica gel as a mixture of *E/Z* = 19:81. R_f hexanes/EtOAc 9:1) = 0.53.

^{1}H NMR (400 MHz, $CDCl_3$, E isomer): 7.97 (dt, *J* = 8.5, 1.5 Hz, 2H), 7.63 – 7.53 (m, 1H), 7.46 – 7.40 (m, 2H), 7.33 (s, 1H), 7.18 – 7.10 (m, 2H), 6.90 – 6.83 (m, 2H).

^{1}H NMR (400 MHz, $CDCl_3$, Z isomer): 7.91 – 7.84 (m, 2H), 7.80 (dt, *J* = 8.4, 1.6 Hz, 2H), 7.66 (s, 1H), 7.63 – 7.53 (m, 1H), 7.53 – 7.46 (m, 2H), 7.18 – 7.10 (m, 2H).

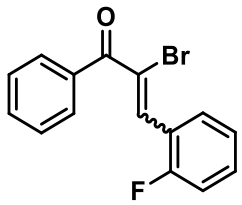


2-bromo-1-(4-fluorophenyl)-3-phenylprop-2-en-1-one (4e)[21]

Following general procedure ***GPI*** using (*E*)-1-(4-fluorophenyl)-3-phenylprop-2-en-1-one (453 mg, 2.00 mmol, 1.00 equiv), *OXONE* (1.48 g, 2.40 mmol, 1.20 equiv), 2 N HBr (217 μL, 324 mg, 4.00 mmol, 2.00 equiv), triethylamine (1.40 mL, 1.01 g, 10.0 mmol, 5.00 equiv) in CH_2Cl_2 (10.0 mL, 0.2 M) gave 410 mg (67%) as a yellow oil after flash column purification on silica gel as a mixture of *E/Z* = 34:66. R_f (hexanes/EtOAc 9:1) = 0.64.

^{1}H NMR (300 MHz, $CDCl_3$, E isomer): 8.03 – 7.95 (m, 2H), 7.38 (s, 1H), 7.23 – 7.12 (m, 5H), 7.12 – 7.03 (m, 2H).

^{1}H NMR (300 MHz, $CDCl_3$, Z isomer): 7.87 (ddt, *J* = 6.0, 4.9, 2.9 Hz, 4H), 7.68 – 7.62 (m, 1H), 7.49 – 7.40 (m, 3H), 7.23 – 7.12 (m, 2H).

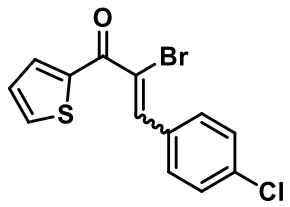


2-bromo-3-(2-fluorophenyl)-1-phenylprop-2-en-1-one (4f)

Following general procedure ***GPI*** using (*E*)-3-(2-fluorophenyl)-1-phenylprop-2-en-1-one (453 mg, 2.00 mmol, 1.00 equiv), *OXONE* (1.48 g, 2.40 mmol, 1.20 equiv), 2 N HBr (217 μL, 324 mg, 4.00 mmol, 2.00 equiv), triethylamine (1.40 mL, 1.01 g, 10.0 mmol, 5.00 equiv) in CH_2Cl_2 (10.0 mL, 0.2 M) gave 376 mg (62%) as a yellow oil after flash column purification on silica gel as a mixture of *E/Z* = 36:64. R_f (hexanes/EtOAc 9:1) = 0.64.

^{1}H NMR (300 MHz, $CDCl_3$, E isomer): 8.21 (t, *J* = 7.6 Hz, 2H), 7.99 – 7.91 (m, 2H), 7.65 – 7.56 (m, 2H), 7.25 (t, *J* = 7.6 Hz, 2H), 6.92 (dt, *J* = 15.8, 8.4 Hz, 2H).

^{1}H NMR (300 MHz, $CDCl_3$, Z isomer): 7.85 (d, *J* = 7.1 Hz, 3H), 7.56 – 7.36 (m, 5H), 7.14 (ddt, *J* = 15.5, 9.4, 7.7 Hz, 2H).

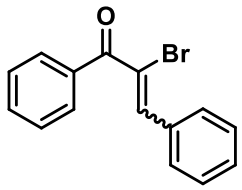


2-bromo-3-(4-chlorophenyl)-1-(thiophen-2-yl)prop-2-en-1-one (4g)

Following general procedure ***GPI*** using (*E*)-3-(4-chlorophenyl)-1-(thiophen-2-yl)prop-2-en-1-one (498 mg, 2.00 mmol, 1.00 equiv), *OXONE* (1.48 g, 2.40 mmol, 1.20 equiv), 2 N HBr (217 μL, 324 mg, 4.00 mmol, 2.00 equiv), triethylamine (1.40 mL, 1.01 g, 10.0 mmol, 5.00 equiv) in CH_2Cl_2 (10.0 mL, 0.2 M) gave 358 mg (55%) as a yellow liquid after flash column purification on silica gel as a mixture of *E/Z* = 13:87. R_f (hexanes/EtOAc 9:1) = 0.3.

^{1}H NMR (400 MHz, $CDCl_3$, E isomer): 7.67 (ddd, *J* = 5.0, 4.4, 1.1 Hz, 2H), 7.25 (s, 1H), 7.18 – 7.12 (m, 4H), 7.03 (dd, *J* = 4.9, 3.9 Hz, 1H).

^{1}H NMR (400 MHz, $CDCl_3$, Z isomer): 7.81 – 7.71 (m, 5H), 7.42 – 7.35 (m, 2H), 7.18 – 7.12 (m, 1H).

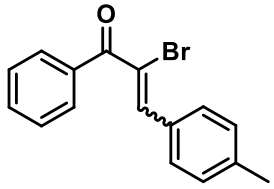


2-bromo-1,3-diphenylprop-2-en-1-one (4h)[22]

Following general procedure ***GPI*** using (*E*)-chalcone (416 mg, 2.00 mmol, 1.00 equiv), *OXONE* (1.48 g, 2.40 mmol, 1.20 equiv), 2 N HBr (217 μL, 324 mg, 4.00 mmol, 2.00 equiv), triethylamine (1.40 mL, 1.01 g, 10.0 mmol, 5.00 equiv) in CH_2Cl_2 (10.0 mL, 0.2 M) gave 511 mg (89%) as a slightly yellow solid after flash column purification on silica gel as a mixture of *E/Z* = 9:91. R_f (hexanes/EtOAc 9:1) = 0.61.

^{1}H NMR (400 MHz, $CDCl_3$, E isomer): 8.05 – 7.96 (m, 4H), 7.65 (dd, *J* = 6.8, 2.7 Hz, 2H), 7.38 (s, 1H), 7.19 – 7.16 (m, 4H).

^{1}H NMR (400 MHz, $CDCl_3$, Z isomer): 7.89 – 7.78 (m, 4H), 7.70 (s, 1H), 7.63 – 7.57 (m, 1H), 7.53 – 7.46 (m, 2H), 7.46 – 7.39 (m, 3H),

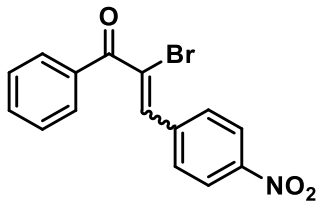


2-bromo-1-phenyl-3-(p-tolyl)prop-2-en-1-one (4i)[22]

Following general procedure ***GPI*** using (*E*)-1-phenyl-3-(p-tolyl)prop-2-en-1-one (445 mg, 2.00 mmol, 1.00 equiv), *OXONE* (1.48 g, 2.40 mmol, 1.20 equiv), 2 N HBr (217 μL, 324 mg, 4.00 mmol, 2.00 equiv), triethylamine (1.40 mL, 1.01 g, 10.0 mmol, 5.00 equiv) in CH_2Cl_2 (10.0 mL, 0.2 M) gave 443 mg (74%) as a white solid after flash column purification on silica gel as a mixture of *E/Z* = 22:78. R_f (hexanes/EtOAc 9:1) = 0.58.

^{1}H NMR (300 MHz, $CDCl_3$, E isomer): 8.02 – 7.94 (m, 2H), 7.62 – 7.36 (m, 3H), 7.33 (s, 1H), 7.06 (d, *J* = 8.2 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 2H), 2.22 (s, 3H).

^{1}H NMR (300 MHz, $CDCl_3$, Z isomer): 7.78 (dd, *J* = 5.2, 3.1 Hz, 4H), 7.70 (s, 1H), 7.62 – 7.36 (m, 3H), 7.25 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H).

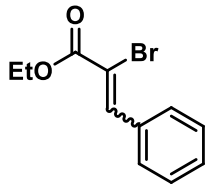


2-bromo-3-(4-nitrophenyl)-1-phenylprop-2-en-1-one (4j)[23]

Following general procedure ***GPI*** using (*E*)-3-(4-nitrophenyl)-1-phenylprop-2-en-1-one (507 mg, 2.00 mmol, 1.00 equiv), *OXONE* (1.48 g, 2.40 mmol, 1.20 equiv), 2 N HBr (217 μL, 324 mg, 4.00 mmol, 2.00 equiv), triethylamine (1.40 mL, 1.01 g, 10.0 mmol, 5.00 equiv) in CH_2Cl_2 (10.0 mL, 0.2 M) gave 528 mg (79%) as a an orange solid after flash column purification on silica gel as a mixture of *E/Z* = 19:81. R_f (hexanes/EtOAc 5:1) = 0.60.

^{1}H NMR (400 MHz, $CDCl_3$, Z isomer): 8.31 – 8.26 (m, 2H), 7.98 – 7.93 (m, 2H), 7.87 – 7.82 (m, 2H), 7.67 (d, *J* = 1.6 Hz, 1H), 7.66 – 7.60 (m, 1H), 7.55 – 7.49 (m, 2H).

^{1}H NMR (400 MHz, $CDCl_3$, E isomer): 8.31 – 8.26 (m, 2H), 8.22 – 8.18 (m, 1H), 8.04 (dt, *J* = 8.5, 1.6 Hz, 2H), 7.81 – 7.77 (m, 2H), 7.66 – 7.60 (m, 1H), 7.55 – 7.49 (m, 2H).

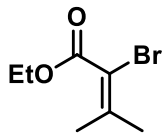


Ethyl 2-bromo-3-phenylacrylate (4k)[18]

Following general procedure ***GPI*** using ethyl cinnamate (881 mg, 5.00 mmol, 1.00 equiv), *OXONE* (7.39 g, 12.0 mmol, 2.40 equiv), 2 N HBr (1.09 mL, 1.62 g, 20.0 mmol, 4.00 equiv), triethylamine (14.0 mL, 10.1 g, 100 mmol, 20.0 equiv) in CH_2Cl_2 (25.0 mL, 0.2 M) gave 995 mg (78%) as a colorless liquid after flash column purification on silica gel as a mixture of *E/Z* = 43:57. R_f (hexanes/EtOAc 20:1) = 0.28.

^{1}H NMR (400 MHz, $CDCl_3$, E isomer): 8.22 (s, 1H), 7.85 (dd, *J* = 6.5, 3.1 Hz, 2H), 7.45 – 7.40 (m, 3H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H)

^{1}H NMR (400 MHz, $CDCl_3$, Z isomer): 7.36 (s, 1H), 7.35 – 7.31 (m, 3H), 7.30 – 7.26 (m, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H).

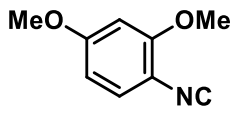


Ethyl 2-bromo-3-methylbut-2-enoate (4l)

Following general procedure ***GPI*** using Ethyl 3-methylbut-2-enoate (256 mg, 278 µL, 2.00 mmol, 1.00 equiv), *OXONE* (1.48 g, 2.40 mmol, 1.20 equiv), 2 N HBr (217 µL, 324 mg, 4.00 mmol, 2.00 equiv), triethylamine (1.40 mL, 1.01 g, 10.0 mmol, 5.00 equiv) in CH_2Cl_2 (10.0 mL, 0.2 M) gave 110 mg (27%) as a colorless oil after flash column purification on silica gel. R_f (hexanes/EtOAc 40:1) = 0.73.

^{1}H NMR (400 MHz, $CDCl_3$): 4.26 (q, *J* = 7.1 Hz, 2H), 2.12 (s, 3H), 2.04 (s, *J* = 5.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

5.8.2 Synthesis of 1-Isocyano-2,4-dimethoxybenzene (5)



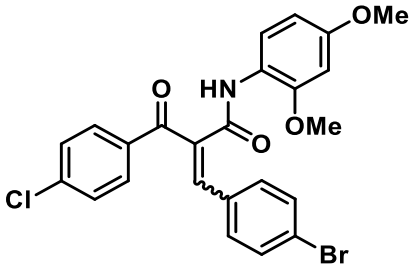
1-isocyano-2,4-dimethoxybenzene (5)[24]

A round bottom flask was charged with 2,4-dimethoxyaniline (7.60 g, 49.6 mmol, 1.00 equiv) and formic acid (5.50 mL, 6.71 g, 146 mmol, 2.94 equiv). The reaction mixture was heated for 15 h at 90 °C and extracted with EtOAc (3 x 400 mL), dried over $NaSO_4$ and the solvent evaporated under reduced pressure to give 8.64 g (95%) of a violet-brown solid after purification on SiO_2. R_f (hexanes / EtOAc 1:1) = 0.62. The formamide (7.69 g, 42.5 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (230 mL), triethylamine (17.8 mL, 12.9 g, 127 mmol, 3.00 equiv) was added and the reaction mixture was cooled to 0 °C. Distilled $POCl_3$ (4.65 mL, 7.81 g, 50.9 mmol, 1.20 equiv) dissolved in CH_2Cl_2 (20 mL) was added *via* syringe pump dropwise over 2 h under vigorous stirring. The reaction mixture was stirred for 20 h at 25 °C and quenched (carefully!) with aq. Na_2CO_3 solution at 0 °C. The organic layer was separated, dried over $NaSO_4$ and the solvent evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel to give 5.68 g (82%) of a brown solid. R_f (hexanes / EtOAc 1:1) = 0.85. ^{1}H NMR (300 MHz, $CDCl_3$): 7.26 (d, *J* = 8.6 Hz, 1H), 6.46 (d, *J* = 2.5 Hz, 1H), 6.42 (dd, *J* = 8.6, 2.5 Hz, 1H), 3.89 (s, 3H), 3.82 (s, 3H).

5.8.3 Visible light mediated coupling of α-bromochalcones with isonitrile (5)

General procedure for photoreactions *GPII*

A Schlenk tube equipped with a magnetic stir bar was charged with α-bromochalcone (500 μmol, 1.00 equiv), $[Ru(bpy)_3]Cl_2$ (6.41 mg, 10.0 μmol, 2.00 mol%), H_2O (9.00 μL, 9.00 mg, 500 μmol, 1.00 equiv), 1-isocyano-2,4-dimethoxybenzene **5** (163 mg, 1.00 mmol, 2.00 equiv), dissolved in DMF (3.30 mL, 0.15 M) and sealed with a screw-cap and subsequently evacuated for 15 min. and backfilled with N_2. The screw-cap was replaced with a Teflon inlet for a glass rod, through which irradiation with a 455 nm high power LED took place from above for 18 h while the reaction was magnetically stirred at 25 °C in an aluminum block from below. Afterwards the reaction mixture was diluted with EtOAc (100 mL) and extracted with water (5 x 20 mL). The combined organic layers were dried over $NaSO_4$, the solvent evaporated under reduced pressure and the residue purified by flash column chromatography.



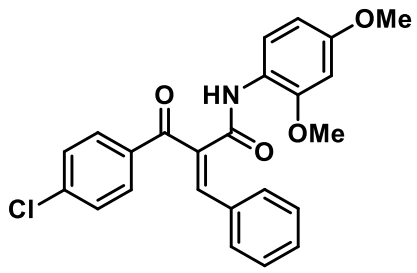
3-(4-bromophenyl)-2-(4-chlorobenzoyl)-*N*-(2,4-dimethoxyphenyl)acrylamide (6a)

Following general procedure ***GPII*** using **4a** (120 mg, 300 μmol, 1.00 equiv), $[Ru(bpy)_3]Cl_2$ (3.84 mg, 6.00 μmol, 2.00 mol%), H_2O (5.40 μL, 5.40 mg, 300 μmol, 1.00 equiv), 1-isocyano-2,4-dimethoxybenzene **5** (97.8 mg, 600 μmol, 2.00 equiv), dissolved in DMF (2.00 mL, 0.15 M) gave 71.0 mg (47%) of a yellow solid as a mixture of *Z/E* = 85:15 after flash column purification (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc, 3:1) = 0.38. m.p. = 186 °C, IR (neat): 3399, 2837, 2374, 2019, 1944, 1669, 1645, 1614, 1583, 1499, 1462, 1399, 1364, 1282, 1220, 1185, 1158, 1126, 1089, 1032, 1007, 950, 858, 829, 810, 710, 585, 552, 508, 450 cm^{-1}; HRMS (ESI) m/z calculated for $C_{24}H_{20}BrClNO_4$ ($[M+H]^+$) 502.0239, found 502.024.

^1H NMR (400 MHz, $CDCl_3$, E isomer): 9.03 (s, 1H), 8.29 (t, *J* = 9.5 Hz, 1H), 8.11 (s, 1H), 7.86 – 7.81 (m, 2H), 7.52 – 7.41 (m, 1H), 7.34 – 7.27 (m, 3H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.48 (dd, *J* = 11.7, 2.7 Hz, 2H), 3.87 (s, 3H), 3.80 (d, *J* = 3.5 Hz, 3H).

^{1}H NMR (400 MHz, $CDCl_3$, Z isomer): 8.69 (s, 1H), 8.29 (t, *J* = 9.5 Hz, 1H), 7.92 – 7.88 (m, 2H), 7.34 – 7.27 (m, 6H), 7.16 (s, 1H), 6.48 (dd, *J* = 11.7, 2.7 Hz, 2H), 3.80 (d, *J* = 3.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): 197.82, 164.33, 162.23, 160.27, 157.06, 150.12, 141.15, 141.11, 134.72, 134.40, 132.54, 132.02, 131.68, 131.43, 131.41, 131.18, 129.32, 129.12, 124.59, 121.06, 103.93, 98.82, 56.11, 55.68.



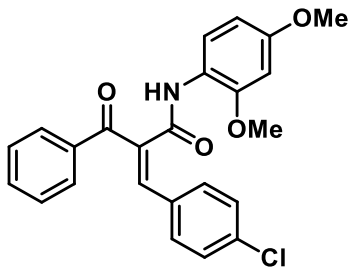
2-(4-chlorobenzoyl)-*N*-(2,4-dimethoxyphenyl)-3-phenylacrylamide (6b)

Following general procedure ***GPII*** using **4b** (161 mg, 500 μmol, 1.00 equiv), H_2O (45.0 μL, 45.9 mg, 2.50 mmol, 5.00 equiv) gave 84.0 mg (40%) of an orange oil as a mixture of *Z/E* = 84:16 after flash column purification (hexanes / EtOAc 4:1). R_f (hexanes / EtOAc, 3:1) = 0.49. IR (neat): 3338, 2959, 2836, 2050, 1999, 1670, 1602, 1585, 1524, 1464, 1415, 1365, 1282, 1207, 1157, 1128, 1090, 1032, 947, 870, 833, 752, 693, 632, 548, 493, 458 cm^{-1}; HRMS (ESI) m/z calculated for $C_{24}H_{21}ClNO_4$ ($[M+H]^+$) 422.1154, found 422.1152.

^{1}H NMR (300 MHz, $CDCl_3$, E isomer): 9.17 (s, 1H), 8.37 – 8.29 (m, 1H), 8.24 (s, 1H), 7.86 – 7.79 (m, 2H), 7.26 – 7.12 (m, 7H), 6.52 – 6.44 (m, 2H), 3.88 (s, 3H), 3.79 (s, 3H).

^{1}H NMR (300 MHz, $CDCl_3$, Z isomer): 8.63 (s, 1H), 8.37 – 8.29 (m, 1H), 7.93 – 7.87 (m, 2H), 7.57 (dd, *J* = 7.2, 2.2 Hz, 2H), 7.49 – 7.43 (m, 2H), 7.38 – 7.33 (m, 3H), 7.26 – 7.12 (m, 1H), 6.52 – 6.44 (m, 2H), 3.79 (s, 3H), 3.75 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): 198.10, 160.55, 156.88, 150.06, 143.13, 140.58, 134.63, 133.89, 133.61, 131.18, 130.06, 130.02, 129.03, 128.64, 121.19, 120.97, 103.78, 98.72, 56.07, 55.62.



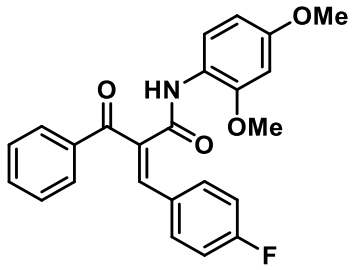
2-benzoyl-3-(4-chlorophenyl)-*N*-(2,4-dimethoxyphenyl)acrylamide (6c)

Following general procedure ***GPII*** using **4c** (139 mg, 432 μmol, 1.00 equiv), H_2O (38.9 μL, 38.9 mg, 2.16 mmol, 5.00 equiv) $[Ru(bpy)_3]Cl_2$) (5.66 mg, 8.64 μmol, 2.00 mol%), 1-isocyano-2,4-dimethoxybenzene **5** (141 mg, 864 μmol, 2.00 equiv), dissolved in DMF (2.90 mL, 0.15 M) gave 89.0 mg (49%) of an orange solid as a mixture of *Z/E* = 87:13 after flash column purification (hexanes / EtOAc 4:1). R_f (hexanes / EtOAc, 3:1) = 0.4. m.p. = 126 °C, IR (neat): 3354, 2844, 1667, 1615, 1604, 1528, 1496, 1449, 1416, 1360, 1285, 1209, 1181, 1156, 1129, 1093, 1039, 953, 916, 866, 817, 709, 670, 634, 506, 419 cm^{-1}; HRMS (ESI) m/z calculated for $C_{24}H_{21}ClNO_4$ ($[M+H]^+$) 422.1154, found 422.1152.

^1H NMR (300 MHz, $CDCl_3$, E isomer): 9.09 (s, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 8.14 (s, 1H), 7.96 – 7.87 (m, 2H), 7.55 – 7.43 (m, 1H), 7.35 – 7.27 (m, 2H), 7.15 (dd, *J* = 20.5, 8.6 Hz, 4H), 6.54 – 6.42 (m, 2H), 3.85 (s, 3H), 3.82 – 3.76 (m, 3H).

^1H NMR (300 MHz, $CDCl_3$, Z isomer): 8.85 (s, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 7.96 – 7.87 (m, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.55 – 7.43 (m, 4H), 7.35 – 7.27 (m, 2H), 7.15 (dd, *J* = 20.5, 8.6 Hz, 1H), 6.54 – 6.42 (m, 2H), 3.82 – 3.76 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): 199.11, 160.49, 156.91, 150.07, 141.00, 136.01, 135.82, 134.84, 134.44, 132.25, 131.25, 129.84, 128.86, 128.84, 121.17, 120.98, 103.78, 98.71, 56.05, 55.63.



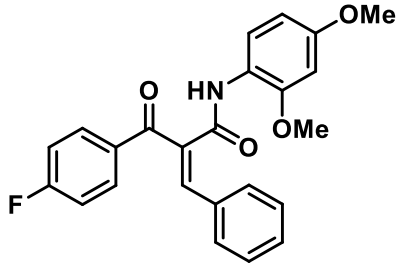
2-benzoyl-*N*-(2,4-dimethoxyphenyl)-3-(4-fluorophenyl)acrylamide (6d)

Following general procedure ***GPII*** using **4d** (153 mg, 500 μmol, 1.00 equiv) gave 96.0 mg (47%) of a yellow solid as a mixture of *Z/E* = 85:15 after flash column purification (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc, 3:1) = 0.32. m.p. = 125 °C, IR (neat): 3385, 2937, 2144, 1676, 1599, 1529, 1496, 1463, 1414, 1372, 1279, 1218, 1158, 1119, 1027, 952, 922, 828, 657, 545, 516 cm^{-1}; HRMS (ESI) m/z calculated for $C_{24}H_{21}FNO_4$ ($[M+H]^+$) 406.1449, found 406.1453.

^1H NMR (400 MHz, $CDCl_3$, E isomer): 9.11 (s, 1H), 8.33 (d, *J* = 8.7 Hz, 1H), 8.17 (s, 1H), 7.91 (dt, *J* = 8.5, 1.5 Hz, 2H), 7.54 – 7.43 (m, 1H), 7.35 – 7.27 (m, 2H), 7.27 – 7.19 (m, 2H), 6.87 – 6.79 (m, 2H), 6.49 (ddd, *J* = 7.8, 6.1, 3.2 Hz, 2H), 3.86 (s, 3H), 3.80 (s, 3H).

^1H NMR (400 MHz, $CDCl_3$, Z isomer): 8.84 (s, 1H), 8.33 (d, *J* = 8.7 Hz, 1H), 7.94 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.63 – 7.56 (m, 3H), 7.54 – 7.43 (m, 2H), 7.27 – 7.19 (m, 1H), 7.08 – 6.99 (m, 2H), 6.49 (ddd, *J* = 7.8, 6.1, 3.2 Hz, 2H), 3.82 (s, 3H), 3.81 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): 199.24, 164.63, 162.12, 160.66, 156.92, 150.12, 141.36, 136.16, 134.31, 134.23, 132.11, 132.03, 130.07, 129.86, 128.81, 128.70, 121.29, 121.04, 115.86, 115.65, 103.88, 98.78, 56.07, 55.65.



***N*-(2,4-dimethoxyphenyl)-2-(4-fluorobenzoyl)-3-phenylacrylamide (6e)**

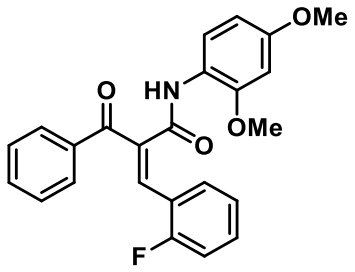
Following general procedure ***GPII*** using **4e** (153 mg, 500 μmol, 1.00 equiv), H_2O (45.0 μL, 45.9 mg, 2.50 mmol, 5.00 equiv) gave 93.0 mg (46%) of orange crystals as a mixture of *Z/E* = 90:10 after flash column purification (hexanes / EtOAc 4:1). R_f (hexanes / EtOAc, 3:1) = 0.51. m.p. =

142 °C, IR (neat): 3351, 2959, 1663, 1620, 2586, 1527, 1496, 1456, 1411, 1366, 1285, 1233, 1208, 1190, 1154, 1129, 1103, 1047, 1030, 949, 864, 824, 787, 761, 689, 611 cm^{-1}; HRMS (ESI) m/z calculated for $C_{24}H_{21}FNO4$ ($[M+H]^+$) 406.1449, found 406.1446.

^1H NMR (300 MHz, $CDCl_3$, E isomer): 9.19 (s, 1H), 8.37 – 8.30 (m, 1H), 8.23 (s, 1H), 7.97 – 7.87 (m, 2H), 7.26 – 7.12 (m, 5H), 6.99 – 6.89 (m, 2H), 6.53 – 6.43 (m, 2H), 3.88 (s, 3H), 3.78 (d, *J* = 8.4 Hz, 3H).

^1H NMR (300 MHz, $CDCl_3$, Z isomer): 8.67 (s, 1H), 8.01 (dd, *J* = 8.8, 5.4 Hz, 2H), 7.61 – 7.55 (m, 2H), 7.38 – 7.33 (m, 3H), 7.26 – 7.12 (m, 4H), 6.53 – 6.43 (m, 2H), 3.78 (d, *J* = 8.4 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): 197.73, 167.98, 160.66, 156.88, 150.09, 142.90, 134.07, 133.69, 132.70, 132.68, 132.57, 130.03, 129.98, 128.61, 121.25, 120.98, 116.08, 115.79, 103.79, 98.74, 56.09, 55.65.



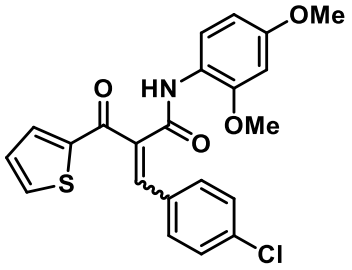
2-benzoyl-*N*-(2,4-dimethoxyphenyl)-3-(2-fluorophenyl)acrylamide (6f)

Following general procedure ***GPII*** using **4f** (153 mg, 500 μmol, 1.00 equiv), H_2O (45.0 μL, 45.9 mg, 2.50 mmol, 5.00 equiv) gave 95.6 mg (47%) of an orange solid as a mixture of *Z/E* = 84:16 after flash column purification (hexanes / EtOAc 4:1). R_f (hexanes / EtOAc, 3:1) = 0.44. m.p. = 118 °C, IR (neat): 3364, 2972, 2049, 1671, 1636, 1602, 1531, 1451, 1412, 1363, 1297, 1242, 1202, 1157, 1102 1028, 931, 856, 811, 760, 721, 684, 570, 452, 430, 415 cm^{-1}; HRMS (ESI) m/z calculated for $C_{24}H_{21}FNO4$ ($[M+H]^+$) 406.1449, found 406.1450.

^1H NMR (400 MHz, $CDCl_3$, E isomer): 9.32 (s, 1H), 8.36 (t, *J* = 4.3 Hz, 2H), 7.90 – 7.84 (m, 2H), 7.45 – 7.39 (m, 1H), 7.28 (dd, *J* = 10.9, 5.0 Hz, 2H), 7.17 – 7.05 (m, 2H), 6.92 – 6.82 (m, 2H), 6.52 – 6.46 (m, 2H), 3.88 (s, 3H), 3.80 (s, 3H).

^1H NMR (400 MHz, $CDCl_3$, Z isomer): 9.08 (s, 1H), 8.33 – 8.27 (m, 1H), 7.98 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.71 – 7.66 (m, 1H), 7.65 – 7.59 (m, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.45 – 7.39 (m, 1H), 7.35

(ddd, *J* = 15.3, 5.4, 1.7 Hz, 1H), 7.17 – 7.05 (m, 2H), 6.52 – 6.46 (d, *J* = 2.6 Hz, 2H), 3.83 (s, 3H), 3.80 (s, 3H).



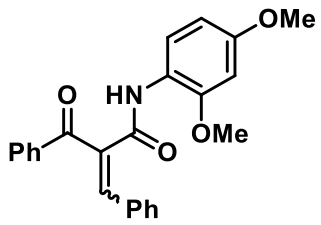
3-(4-chlorophenyl)-*N*-(2,4-dimethoxyphenyl)-2-(thiophene-2-carbonyl)acrylamide (6g)

Following general procedure ***GPII*** using **4g** (164 mg, 500 μmol, 1.00 equiv) gave 92.0 mg (43%) of yellow crystals as a mixture of *Z/E* = 87:13 after flash column purification (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc, 3:1) = 0.23. m.p. = 146 °C, IR (neat): 3329, 2057, 2015, 1912, 1666, 1616, 1532, 1490, 1460, 1410, 1360, 1282, 1256, 1206, 1156, 1129, 1091, 1031, 925, 831, 798, 720, 670, 625, 530, 500, 415 cm^{-1}; HRMS (ESI) m/z calculated for $C_{22}H_{19}ClNO_4S$ ($[M+H]^+$) 428.0718, found 428.0717.

^1H NMR (400 MHz, $CDCl_3$, E isomer): 9.10 (s, 1H), 8.33 – 8.27 (m, 1H), 8.10 (d, *J* = 5.5 Hz, 1H), 7.64 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.57 – 7.49 (m, 1H), 7.31 – 7.24 (m, 2H), 7.22 – 7.14 (m, 2H), 6.92 (dd, *J* = 4.8, 3.9 Hz, 1H), 6.54 – 6.45 (m, 2H), 3.88 (s, 3H), 3.80 (d, *J* = 3.0 Hz, 3H).

^1H NMR (400 MHz, $CDCl_3$, Z isomer): 8.78 (s, 1H), 8.33 – 8.27 (m, 1H), 7.89 (dd, *J* = 3.8, 1.0 Hz, 1H), 7.75 (dd, *J* = 4.9, 1.0 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.42 (s, 1H), 7.36 – 7.31 (m, 2H), 7.22 – 7.14 (m, 1H), 6.54 – 6.45 (m, 2H), 3.80 (d, *J* = 3.0 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): 190.51, 160.16, 157.02, 150.18, 143.36, 140.74, 136.65, 136.26, 135.97, 135.01, 132.42, 131.50, 131.24, 129.10, 129.04, 128.71, 121.21, 121.10, 103.91, 98.80, 56.12, 55.67.



2-benzoyl-*N*-(2,4-dimethoxyphenyl)-3-phenylacrylamide (6h)

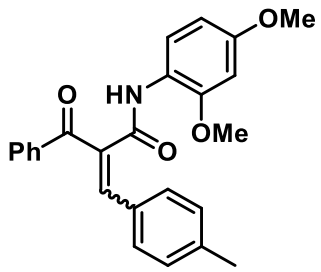
Following general procedure ***GPII*** using **4h** (144 mg, 500 μmol, 1.00 equiv) gave 106 mg (55%) of a yellow oil as a mixture of *Z/E* = 87:13 after flash column purification (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc, 3:1) = 0.22. IR (neat): 3341, 2934, 2005, 1667, 1597, 1522, 1459, 1416, 2371, 1281, 1206, 1157, 1128, 1029, 953, 933, 829, 805, 753, 689, 629, 489, 411 cm^{-1}; HRMS (ESI) m/z calculated for $C_{24}H_{21}NO_4Na$ ($[M+Na]^+$) 388.1543, found 388.1546.

^1H NMR (400 MHz, $CDCl_3$, E isomer): 9.15 (s, 1H), 8.38 – 8.32 (m, 1H), 8.22 (s, 1H), 7.98 – 7.87 (m, 2H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.30 - 7.22 (ddd, *J* = 11.3, 9.9, 6.7 Hz, 4H), 7.16 – 7.09 (m, 3H), 6.51 – 6.44 (m, 2H), 3.84 (s, 3H), 3.78 (d, *J* = 2.2 Hz, 3H).

^1H NMR (400 MHz, $CDCl_3$, Z isomer): 8.73 (s, 1H), 8.38 – 8.32 (m, 1H), 7.98 – 7.87 (m, 2H), 7.60 – 7.55 (m, 3H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.37 – 7.31 (m, 3H), 7.30 - 7.22 (ddd, *J* = 11.3, 9.9, 6.7 Hz, 1H), 6.51 – 6.44 (m, 2H), 3.78 (d, *J* = 2.2 Hz, 3H), 3.75 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, E isomer): 199.26, 160.74, 156.81, 150.03, 142.57, 136.21, 134.30, 134.04, 133.74, 130.61, 130.00, 129.95, 129.79, 129.72, 128.74, 128.62, 128.57, 128.44, 121.26, 120.93, 103.81, 98.68, 55.98, 55.54.

^{13}C NMR (101 MHz, $CDCl_3$, Z isomer): 195.14, 163.12, 156.91, 149.91, 144.01, 137.16, 136.25, 133.22, 133.05, 130.45, 130.16, 130.00, 129.95, 129.79, 129.72, 128.74, 128.57, 128.44, 121.23, 121.09, 103.81, 98.77, 55.83, 55.56.



2-Benzoyl-*N*-(2,4-dimethoxyphenyl)-3-(p-tolyl)acrylamide (6i)

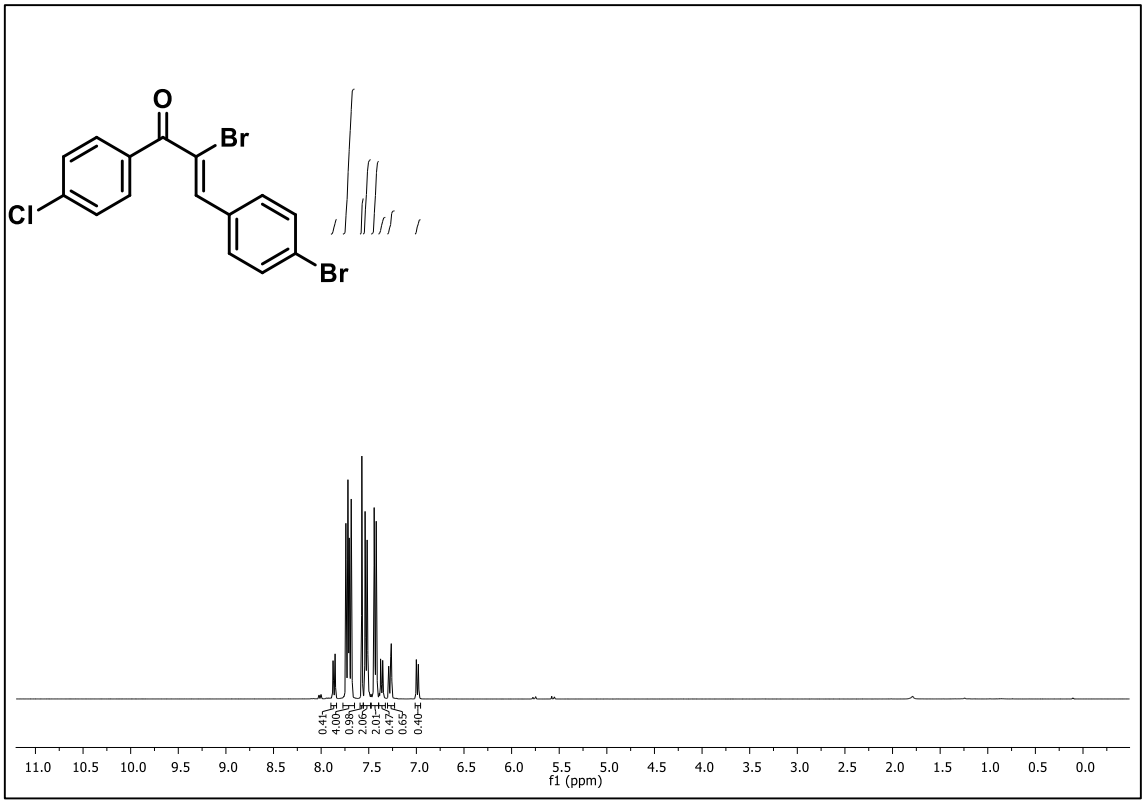
Following general procedure ***GPII*** using **4i** (151 mg, 500 μmol, 1.00 equiv) gave 95.0 mg (47%) of a yellow foam as a mixture of *Z/E* = 89:11 after flash column purification (hexanes / EtOAc 5:1). R_f (hexanes / EtOAc, 3:1) = 0.23. IR (neat): 3001, 2928, 2836, 2181, 1944, 1670, 1602, 1526, 1460, 1416, 1364, 1282, 1206, 1179, 1157, 1128, 1033, 955, 919, 872, 813, 749, 734, 690, 664, 580, 503, 411 cm^{-1}; HRMS (ESI) m/z calculated for $C_{24}H_{24}NO_4$ ($[M+H]^+$) 402.1700, found 402.1698.

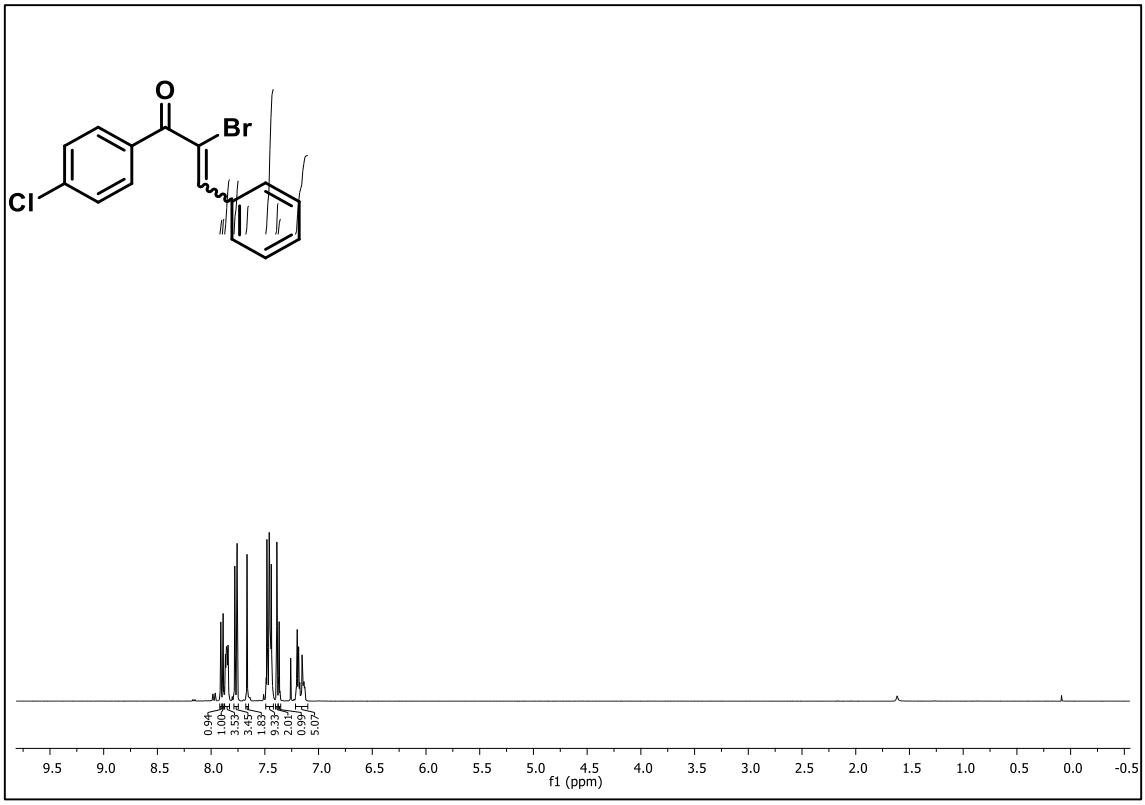
^1H NMR (400 MHz, $CDCl_3$, E isomer): 9.09 (s, 1H), 8.38 – 8.30 (m, 1H), 8.18 (s, 1H), 7.93 (dt, *J* = 7.3, 3.5 Hz, 2H), 7.52 – 7.41 (m, 1H), 7.30 (dd, *J* = 10.7, 4.9 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.52 – 6.44 (m, 2H), 3.86 (s, 3H), 3.80 (d, *J* = 5.2 Hz, 3H), 2.21 (s, 3H).

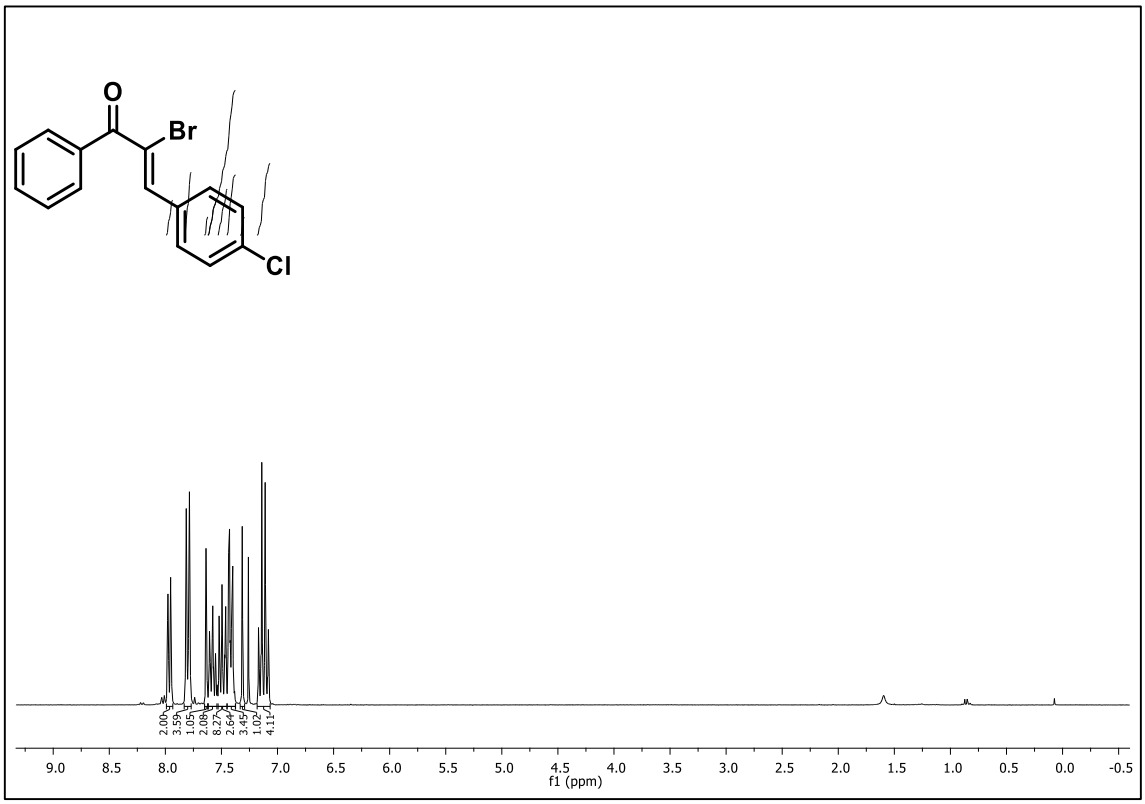
^1H NMR (400 MHz, $CDCl_3$, Z isomer): 8.74 (s, 1H), 8.38 – 8.30 (m, 1H), 7.93 (dt, *J* = 7.3, 3.5 Hz, 2H), 7.59 (dd, *J* = 10.5, 4.3 Hz, 1H), 7.52 – 7.41 (m, 4H), 7.30 (dd, *J* = 10.7, 4.9 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.52 – 6.44 (m, 2H), 3.80 (s, 6H), 2.34 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): 199.58, 161.06, 156.83, 150.12, 142.67, 140.27, 136.39, 134.07, 133.26, 130.95, 130.43, 130.31, 130.02, 129.91, 129.59, 129.31, 128.74, 128.63, 121.44, 121.03, 103.88, 98.78, 56.08, 55.65, 21.46.

5.8.4 Spectra of compounds



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Br
Cl
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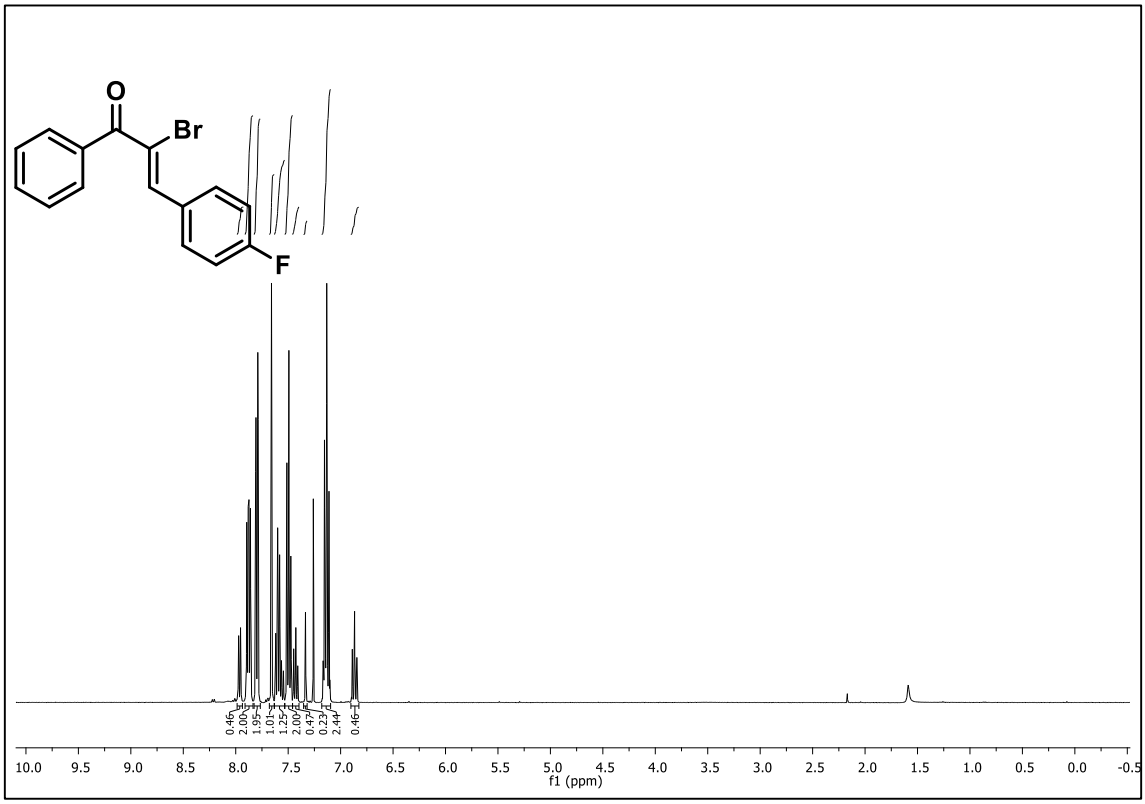
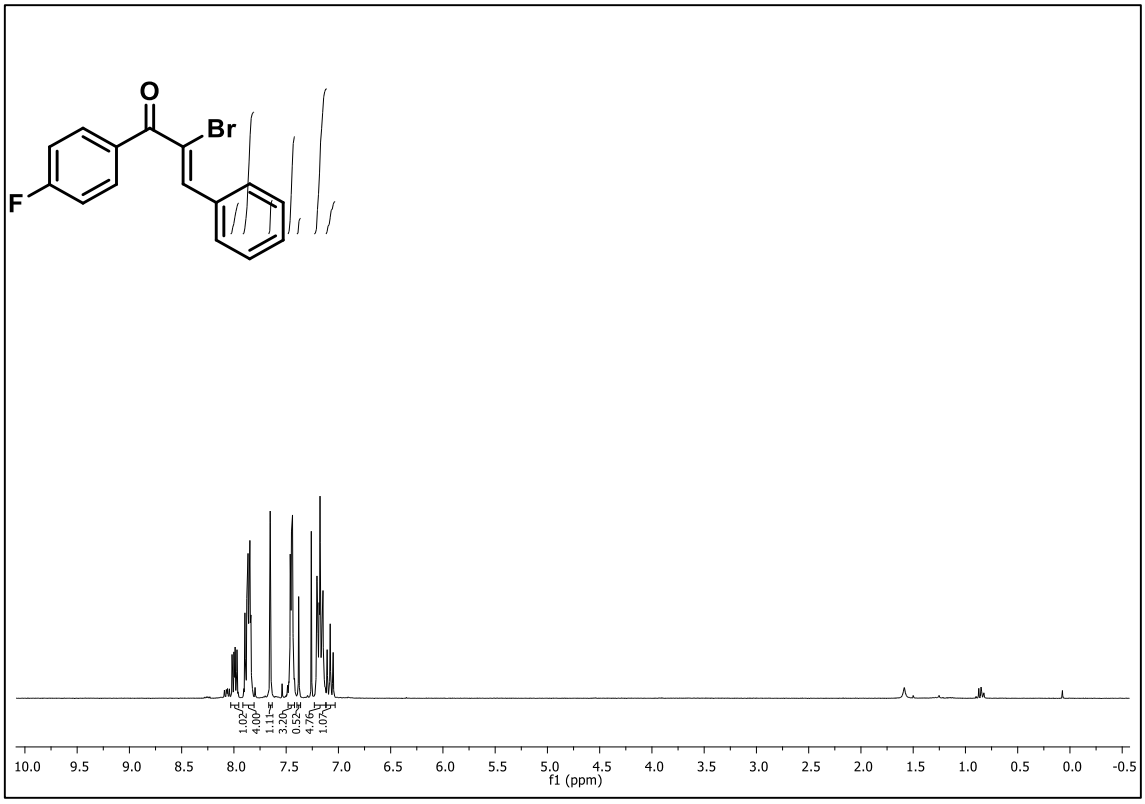

O
Br
F
f1 (ppm)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Br
F
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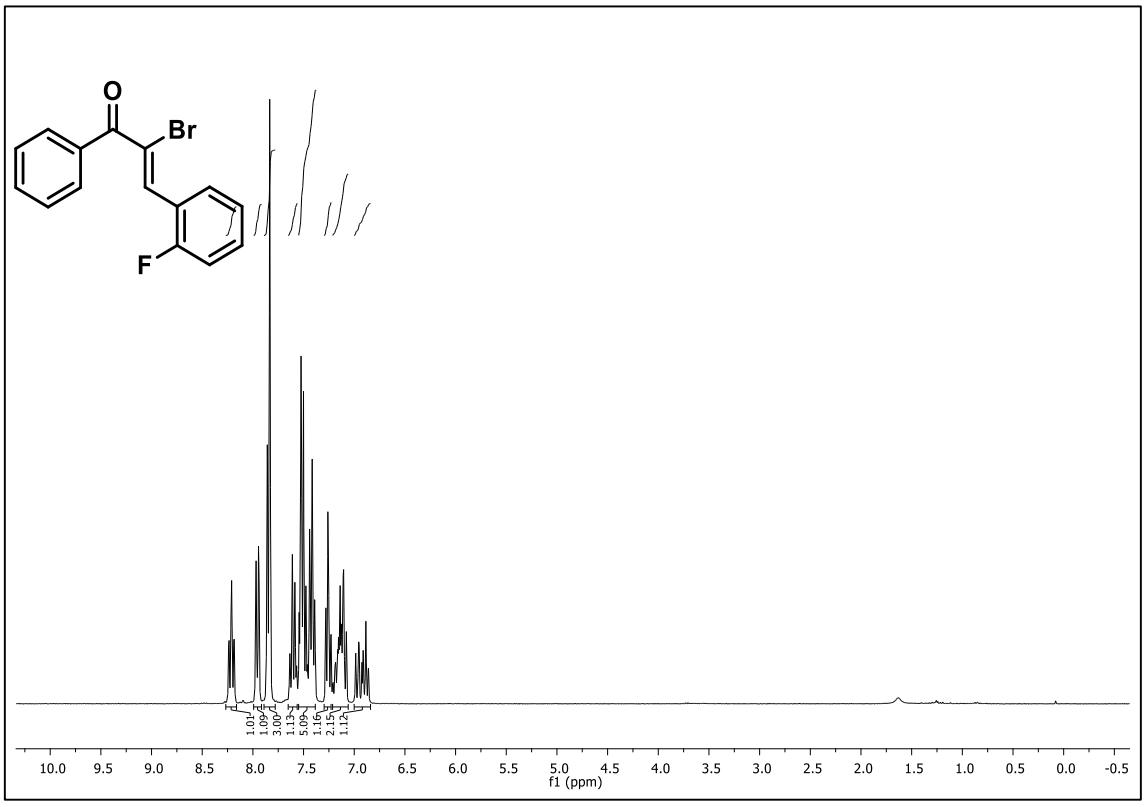
4.00
1.11
3.20
0.52
4.76
1.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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Br
F
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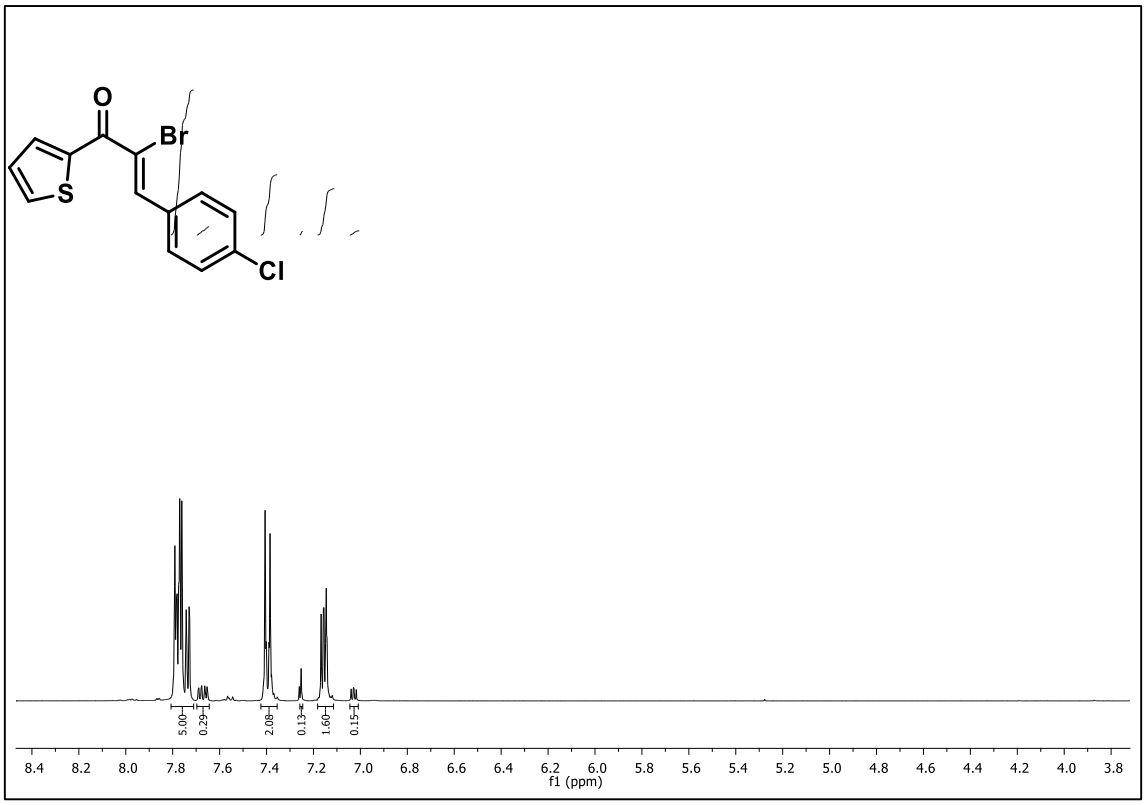
1.00
3.00
1.13
5.09
1.16
2.15
1.12
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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Br
S
Cl
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1.60
0.15
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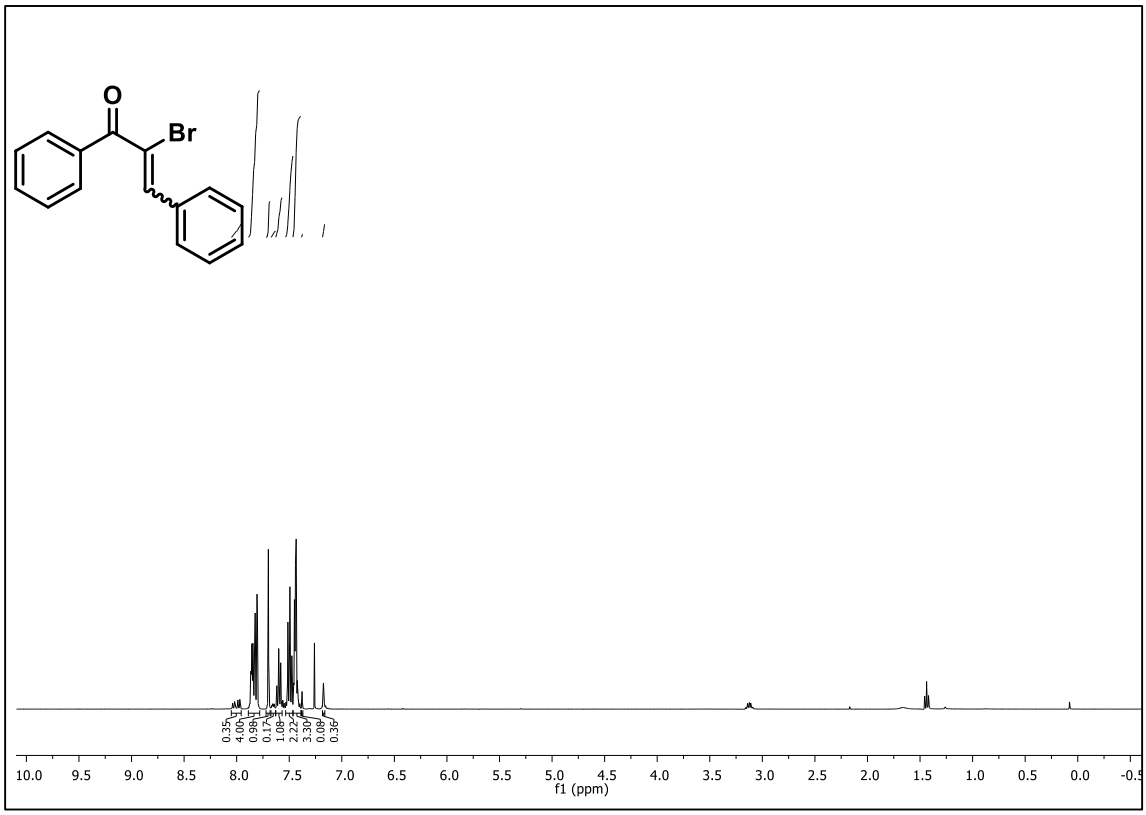
f1 (ppm)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0.36
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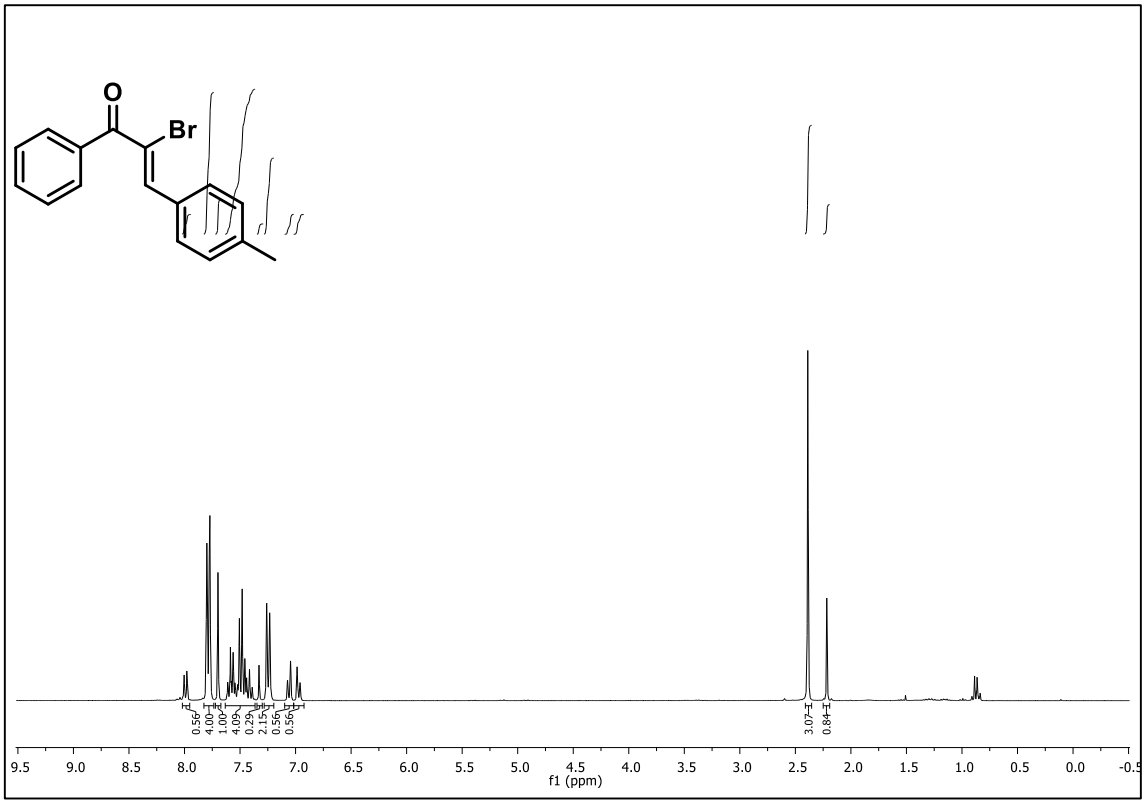
f1 (ppm)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3.07
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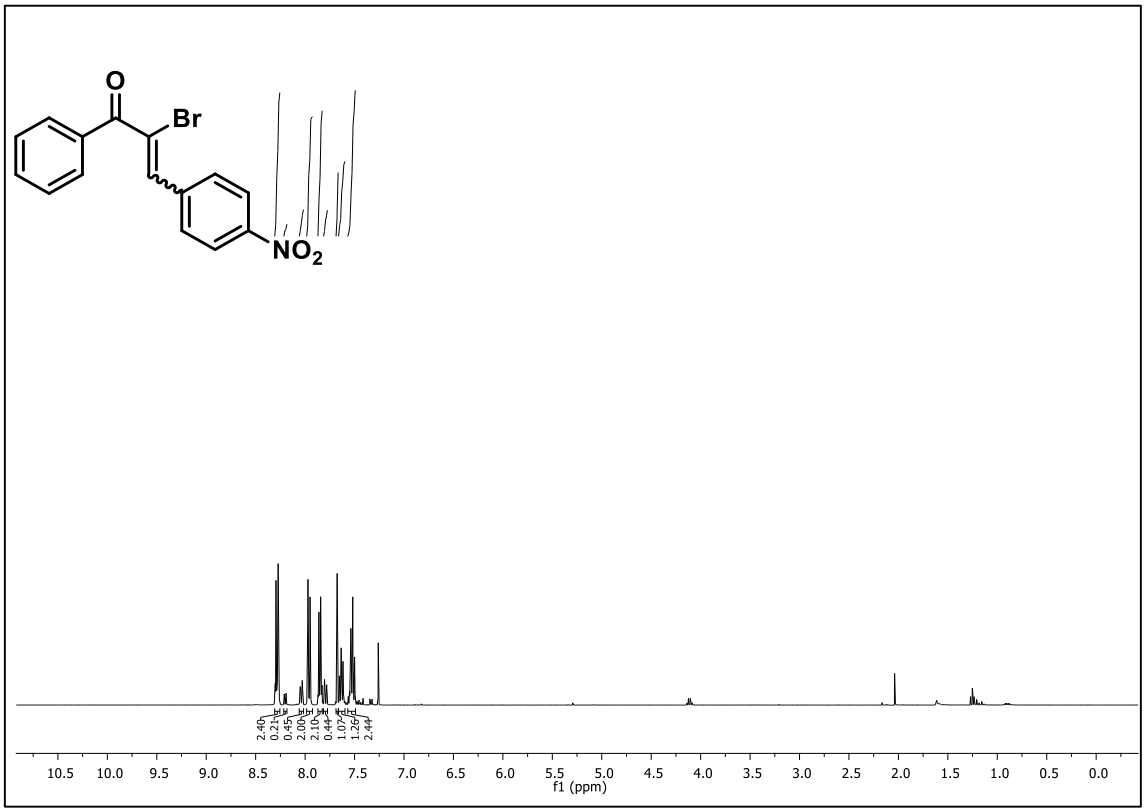
f1 (ppm)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0.44
1.07
1.26
2.44
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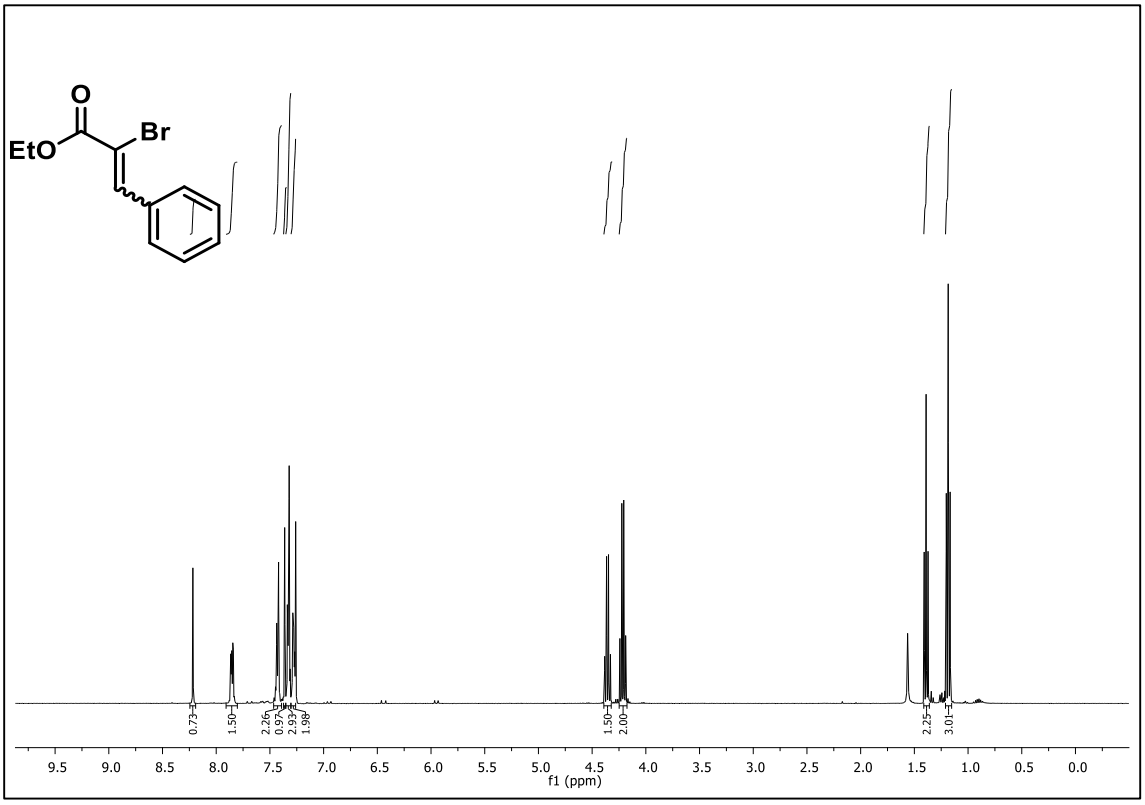
f1 (ppm)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Br
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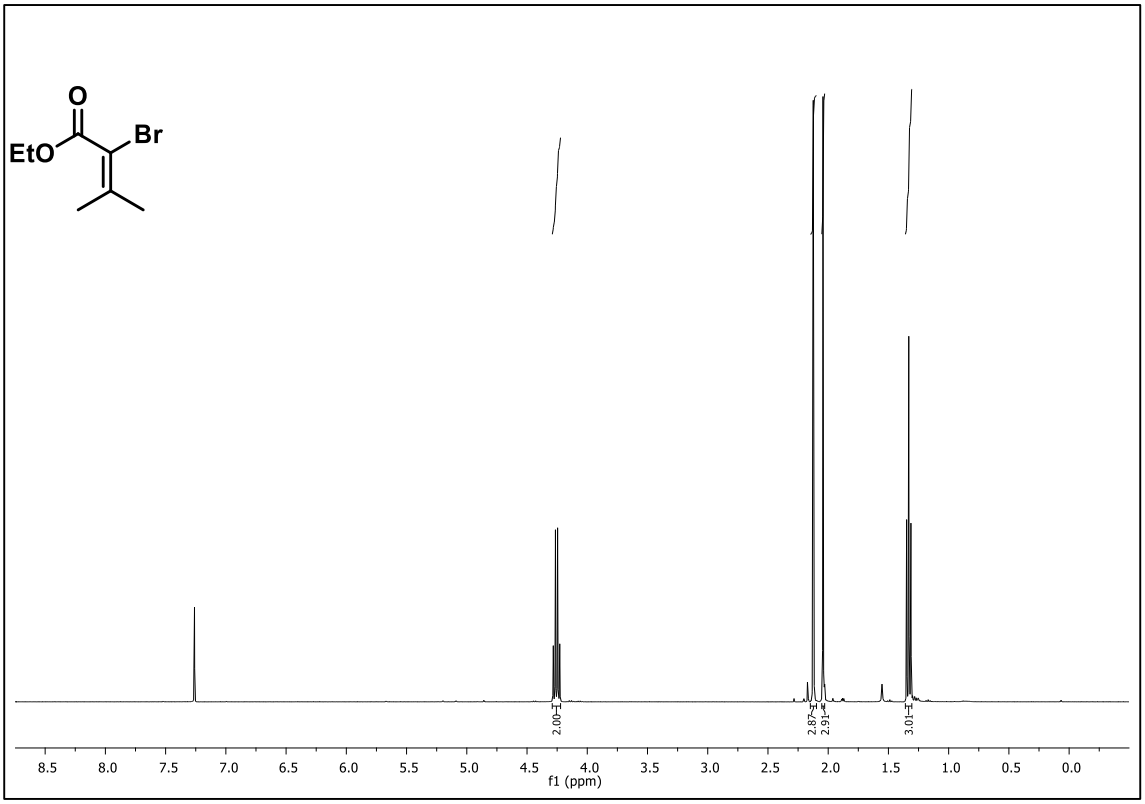
1.98
1.50
2.00
2.25
3.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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Br
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3.01
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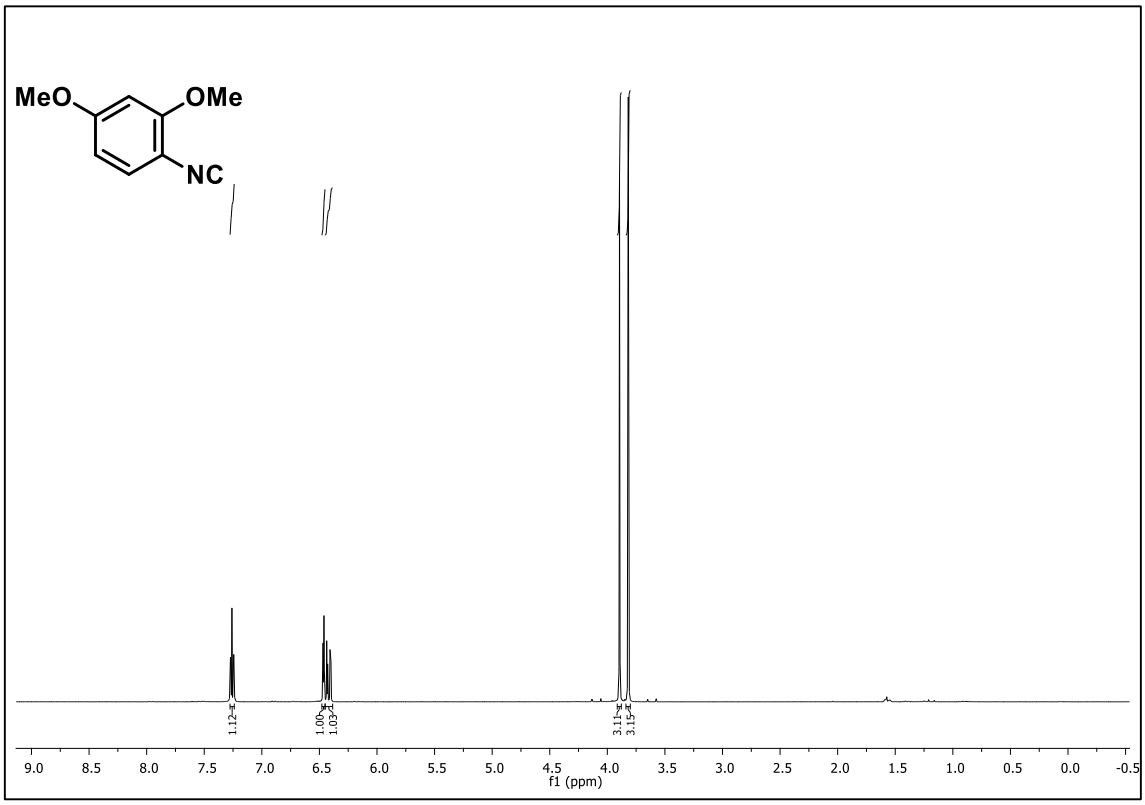
f1 (ppm)


MeO
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1.03
3.11
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8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.0
2.5
2.0
1.5
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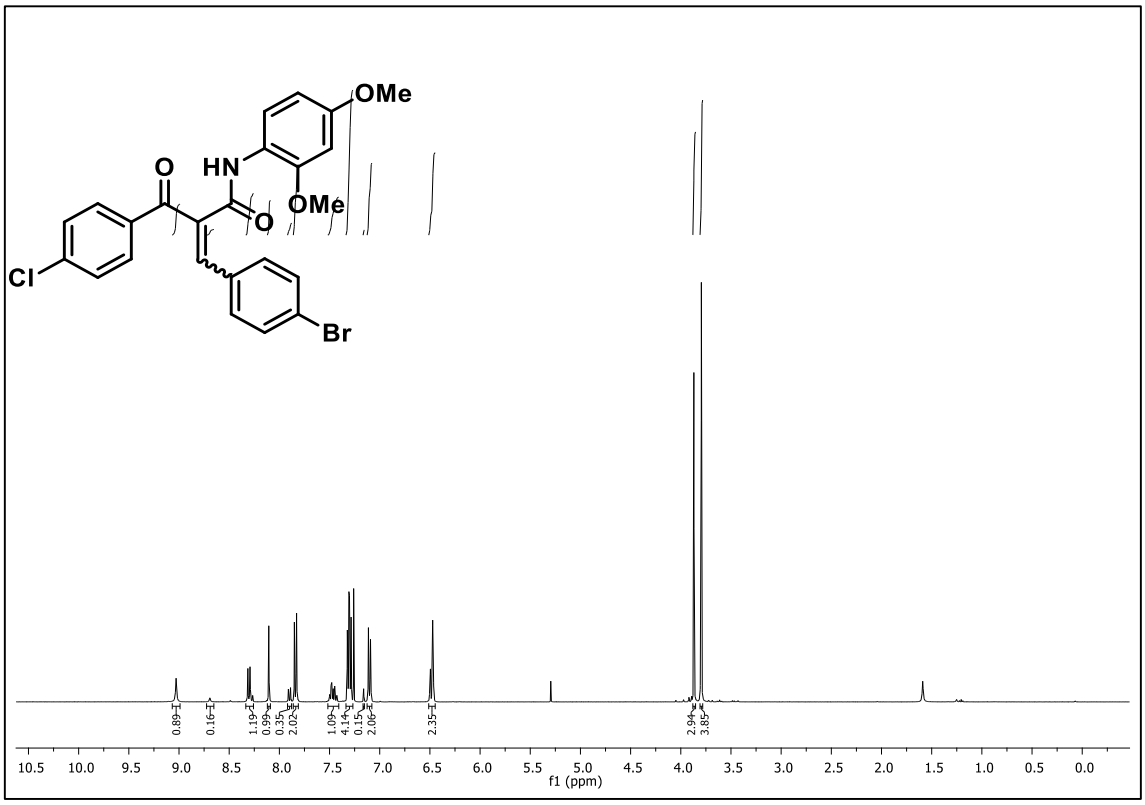
0.5
0.0
-0.5
f1 (ppm)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O
O
OMe
Cl
Br
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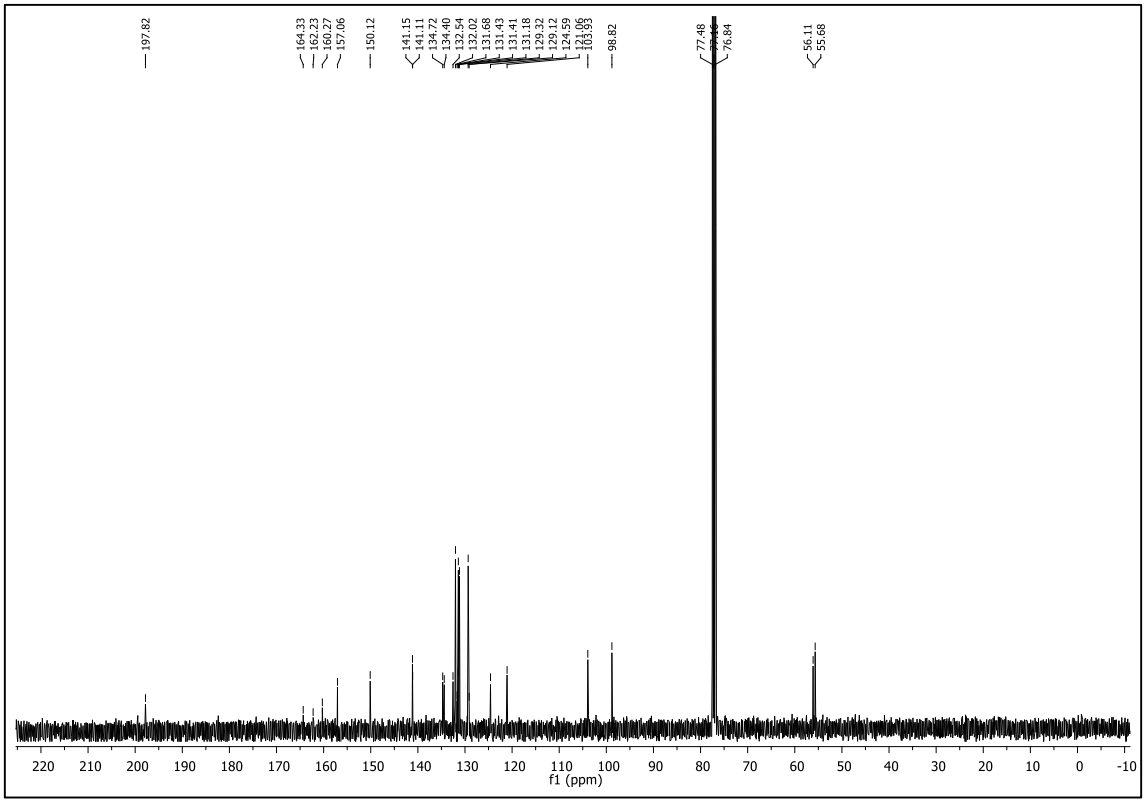
0.99
0.35
2.02
1.09
4.14
0.15
2.06
2.35
2.94
3.85
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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150.12
141.15
141.11
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132.54
132.02
131.68
131.43
131.41
131.18
129.32
129.12
124.59
121.06
103.93
98.82
77.48
77.16
76.84
56.11
55.68
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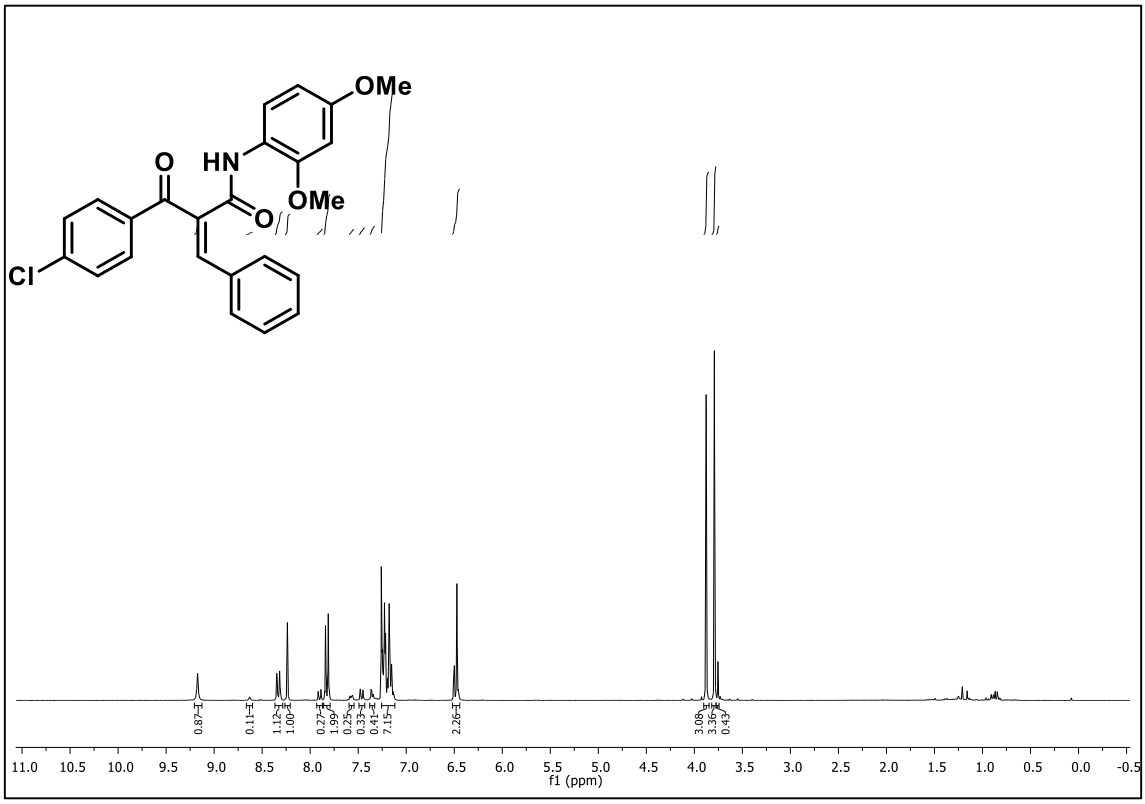
f1 (ppm)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1.00
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1.99
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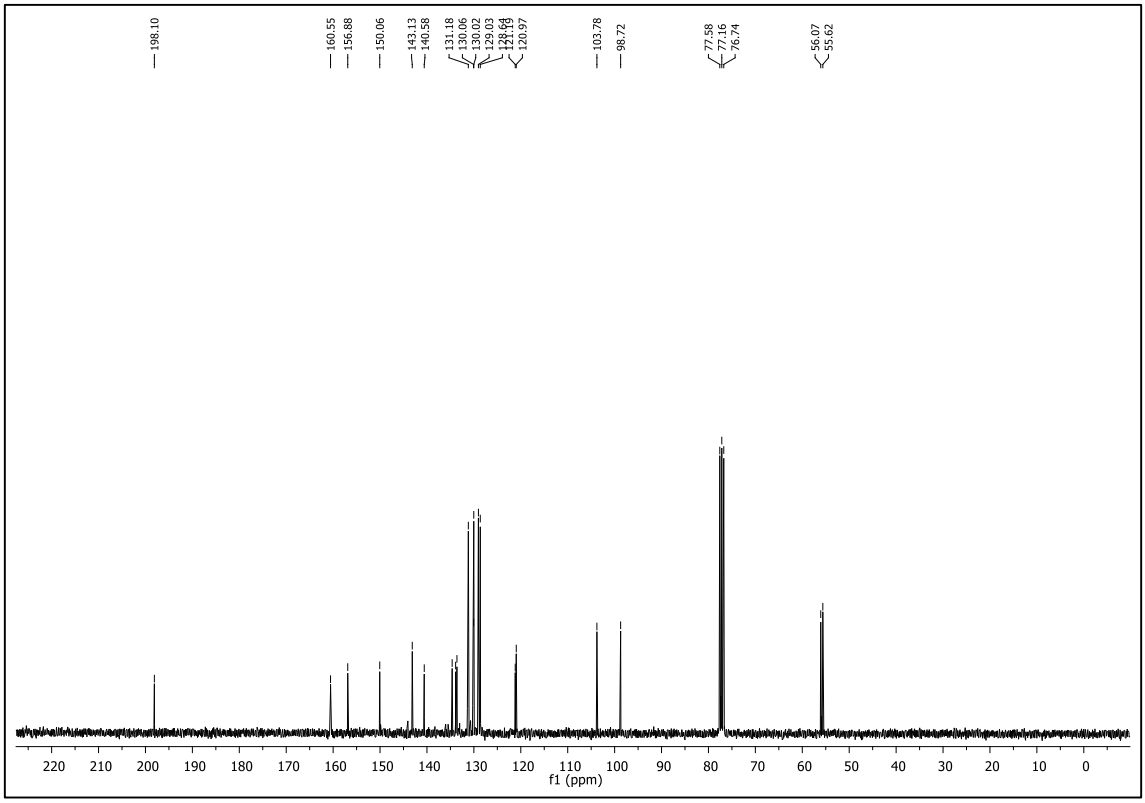
0.33
0.41
7.15
2.26
3.08
3.36
0.43
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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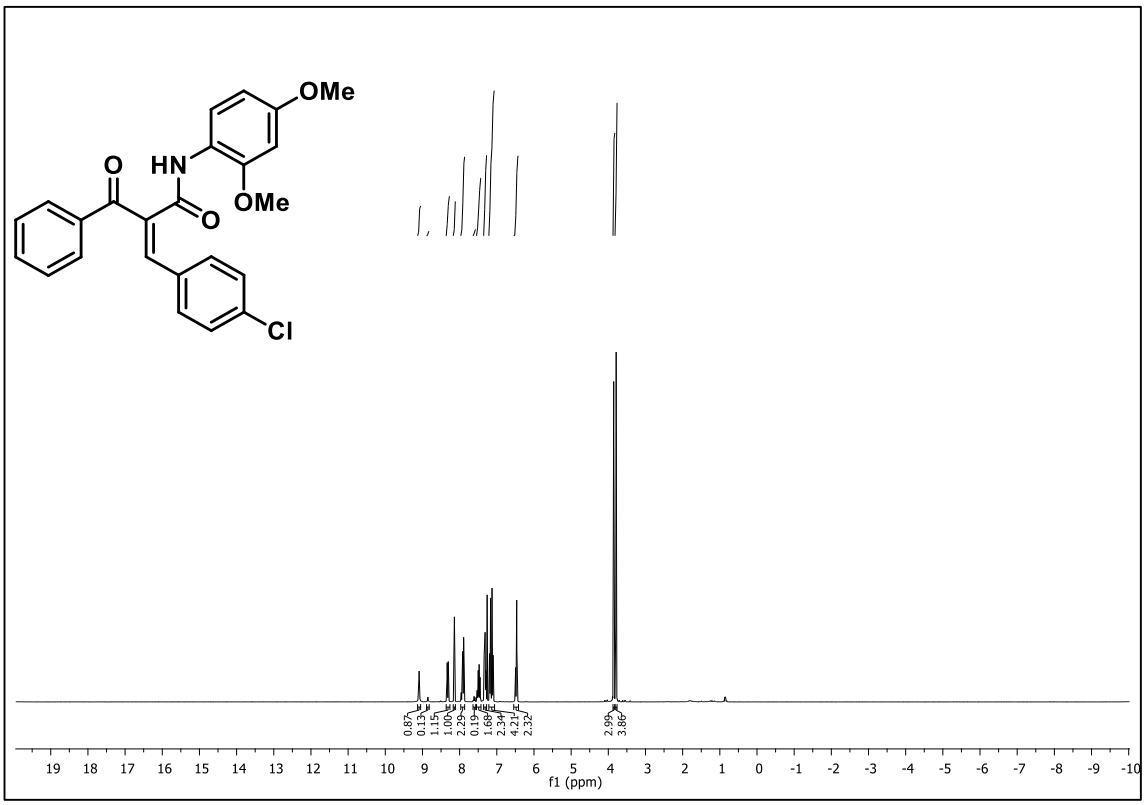
129.03
121.19
120.97
103.78
98.72
77.58
77.16
76.74
56.07
55.62
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


OMe
HN
O
OMe
O
Cl
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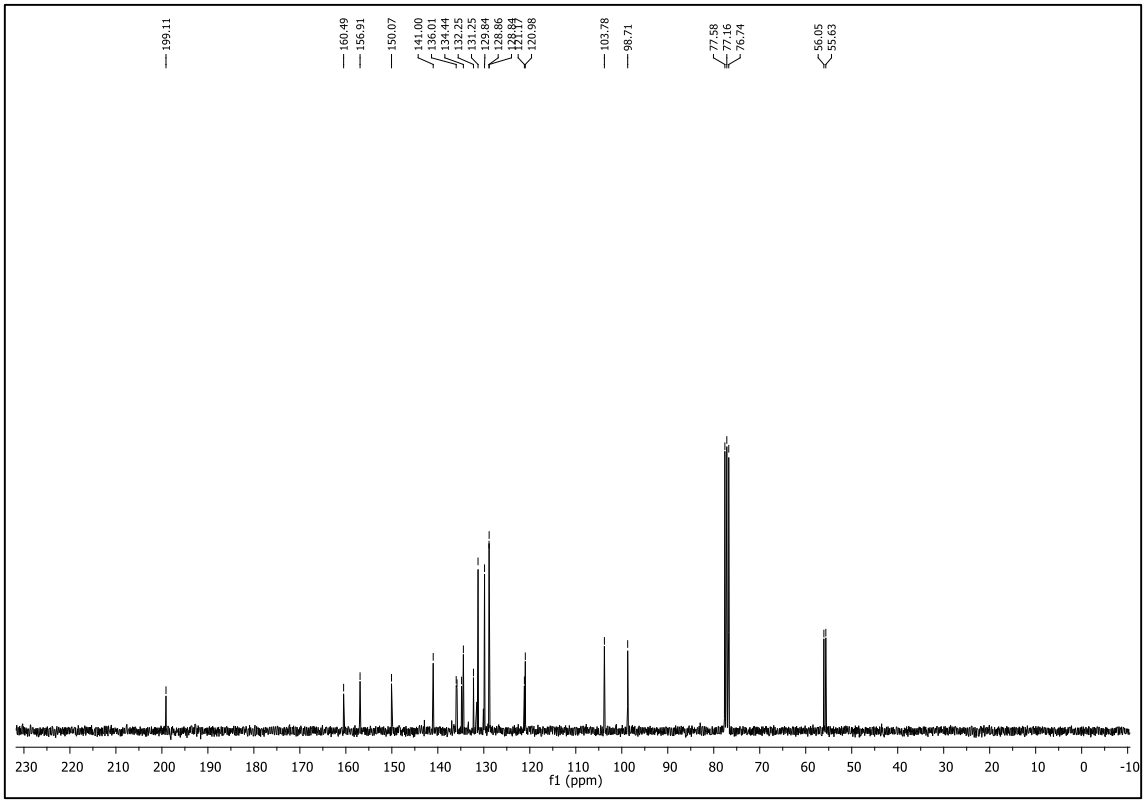
0.15
1.15
1.06
2.25
0.19
1.60
2.34
4.21
2.32
2.99
3.86
19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4 -5 -6 -7 -8 -9 -10
f1 (ppm)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136.01
134.44
132.25
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128.84
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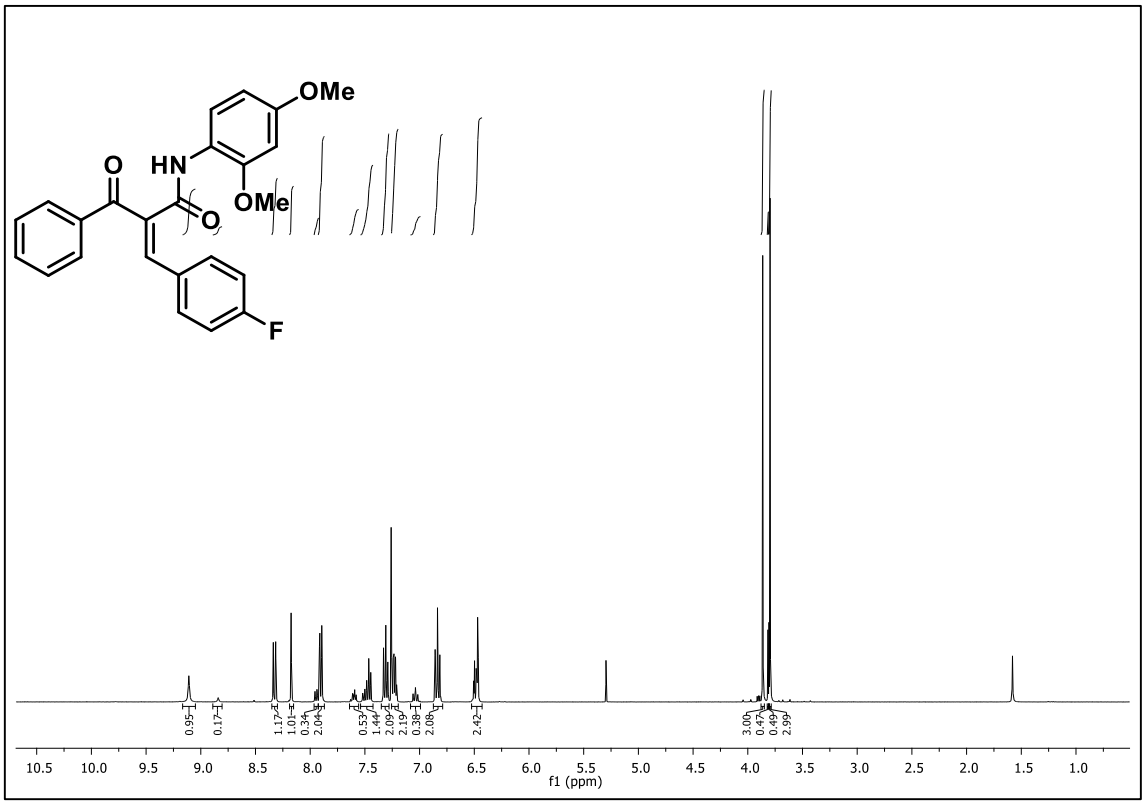
f1 (ppm)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HN
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O
F
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2.04
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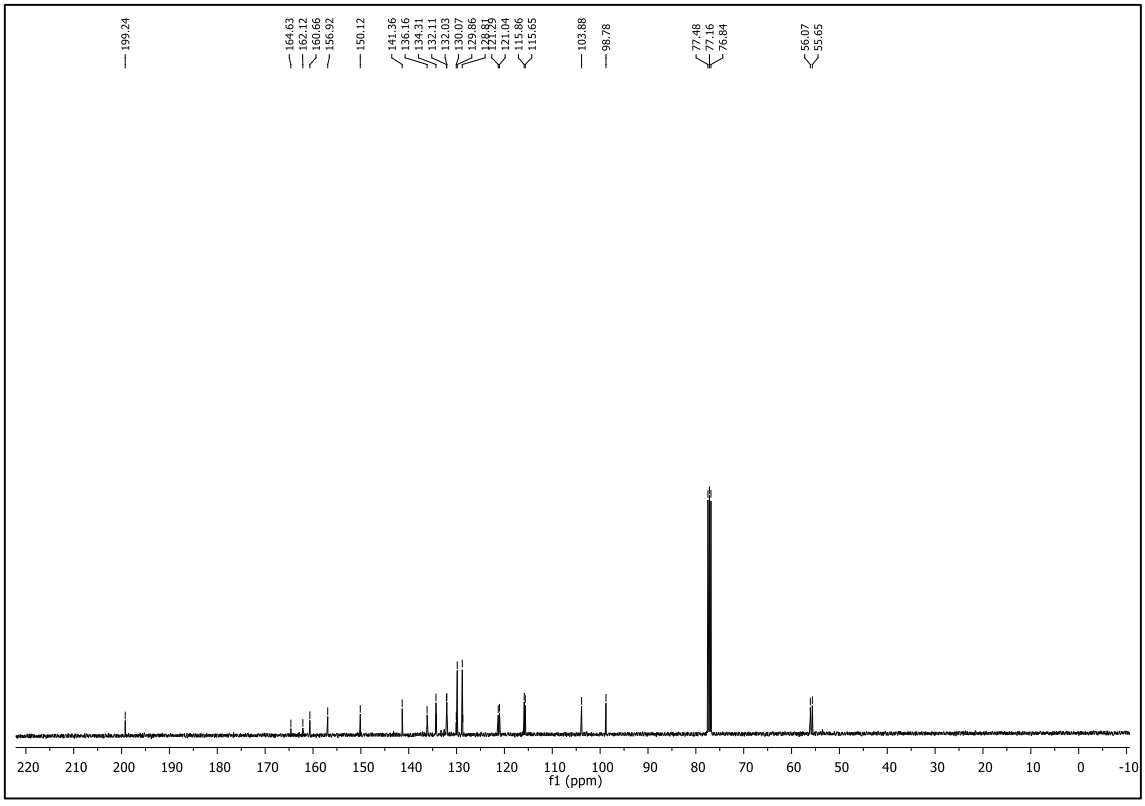
2.09
2.19
0.38
2.08
2.42
3.00
0.47
0.49
2.99
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)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128.81
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121.04
115.86
115.65
103.88
98.78
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56.07
55.65
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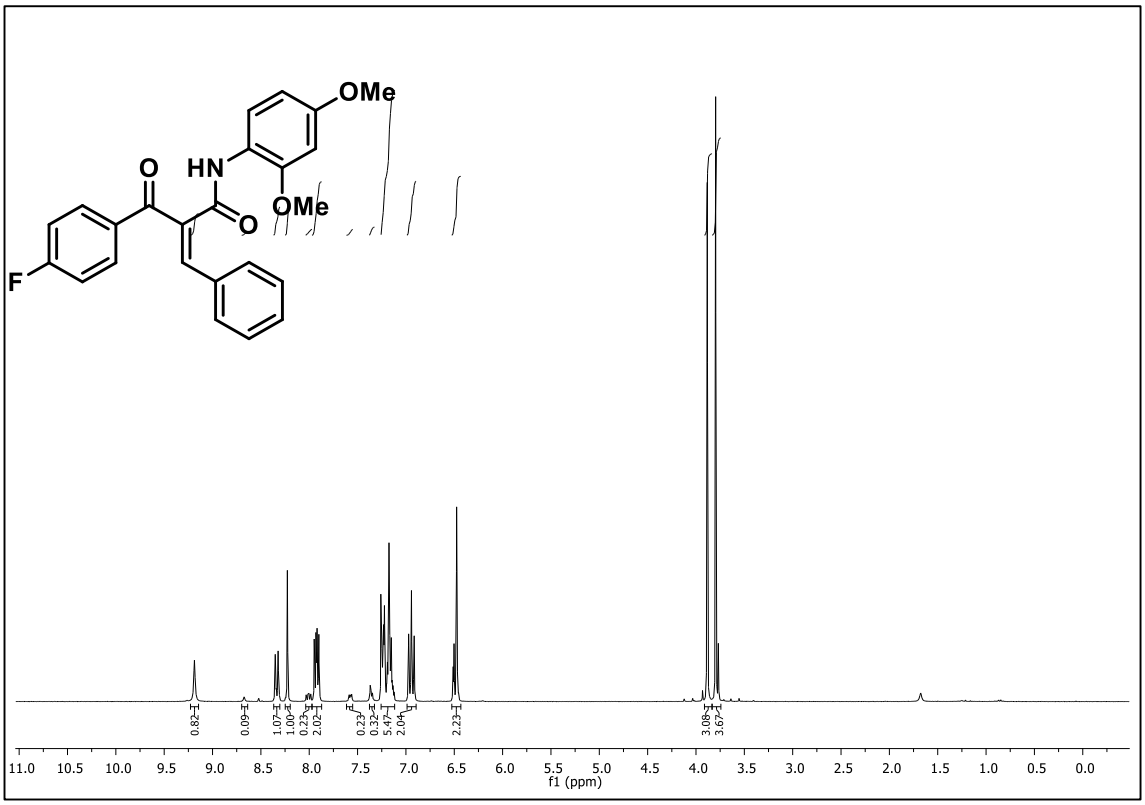
f1 (ppm)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O
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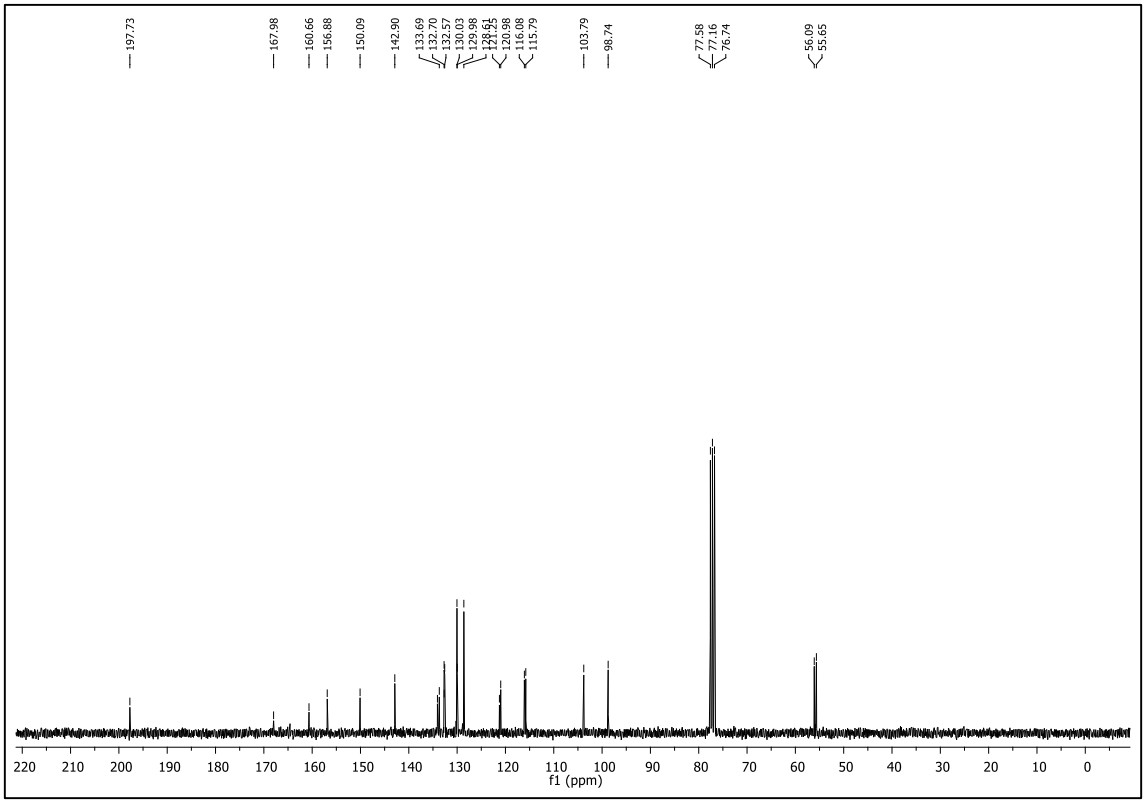
2.04
2.23
3.08
3.67
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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103.79
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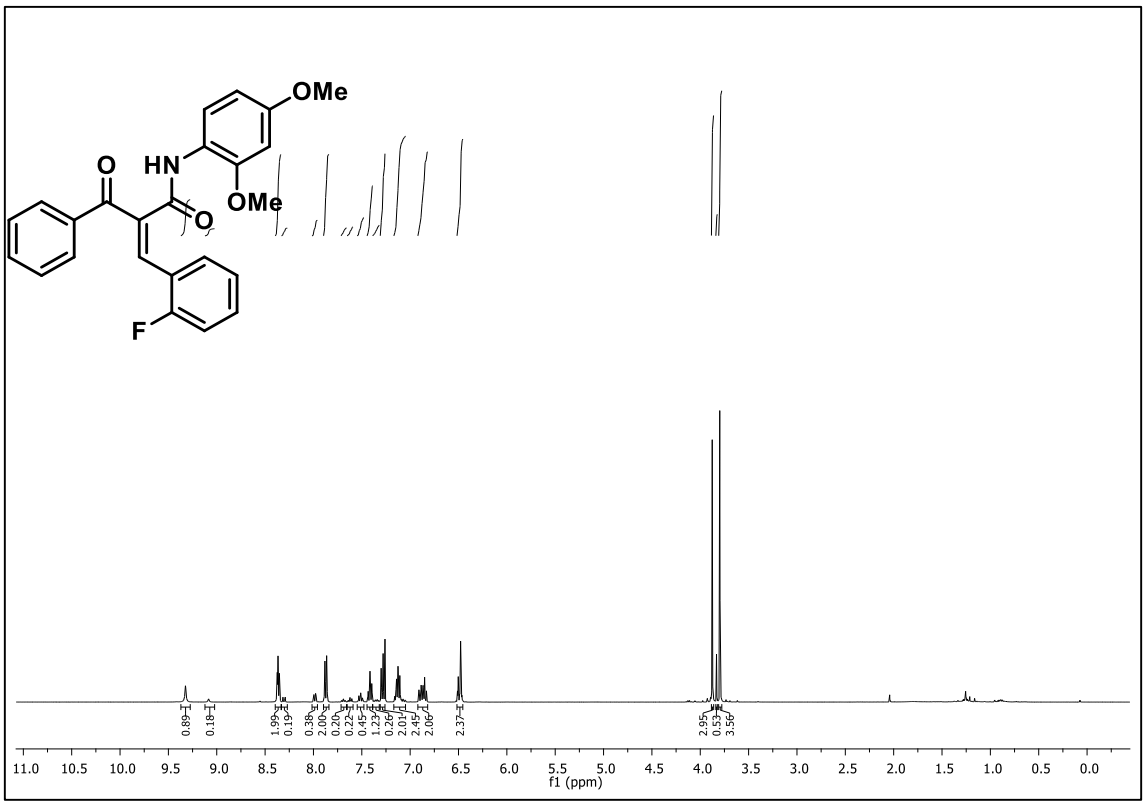
f1 (ppm)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1.22
0.20
2.01
2.49
2.06
2.37
2.95
0.52
3.56
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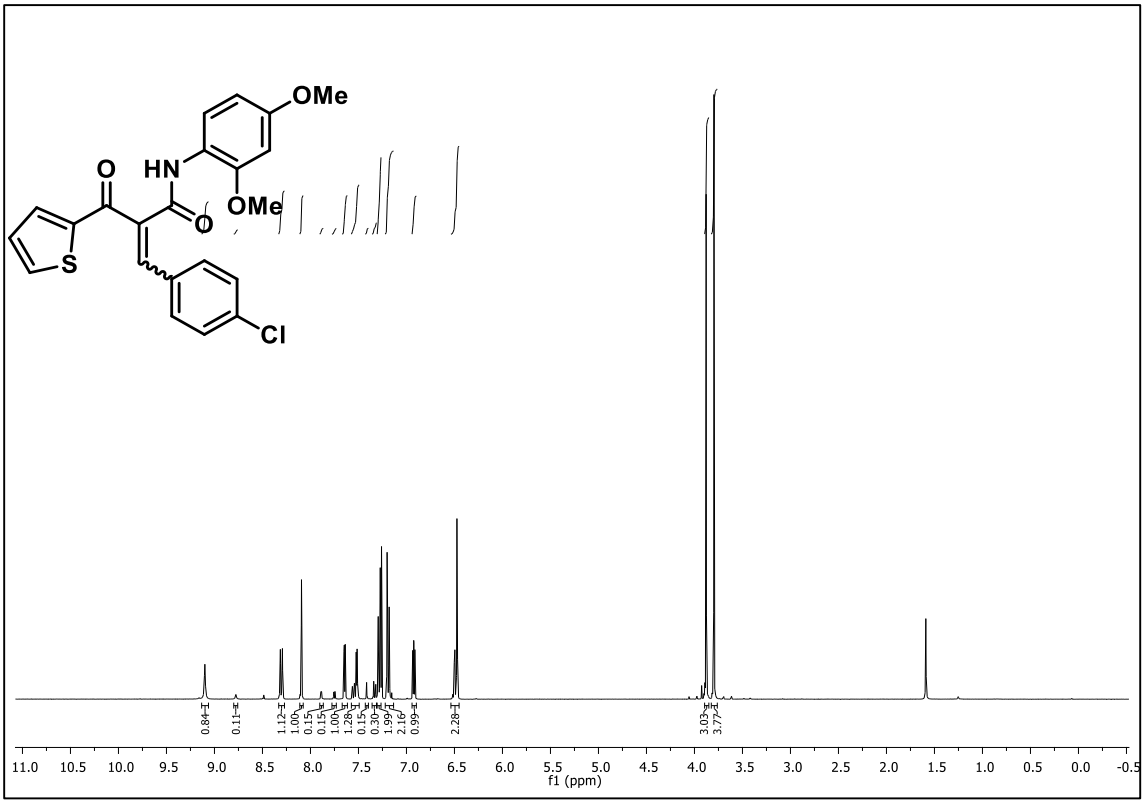
f1 (ppm)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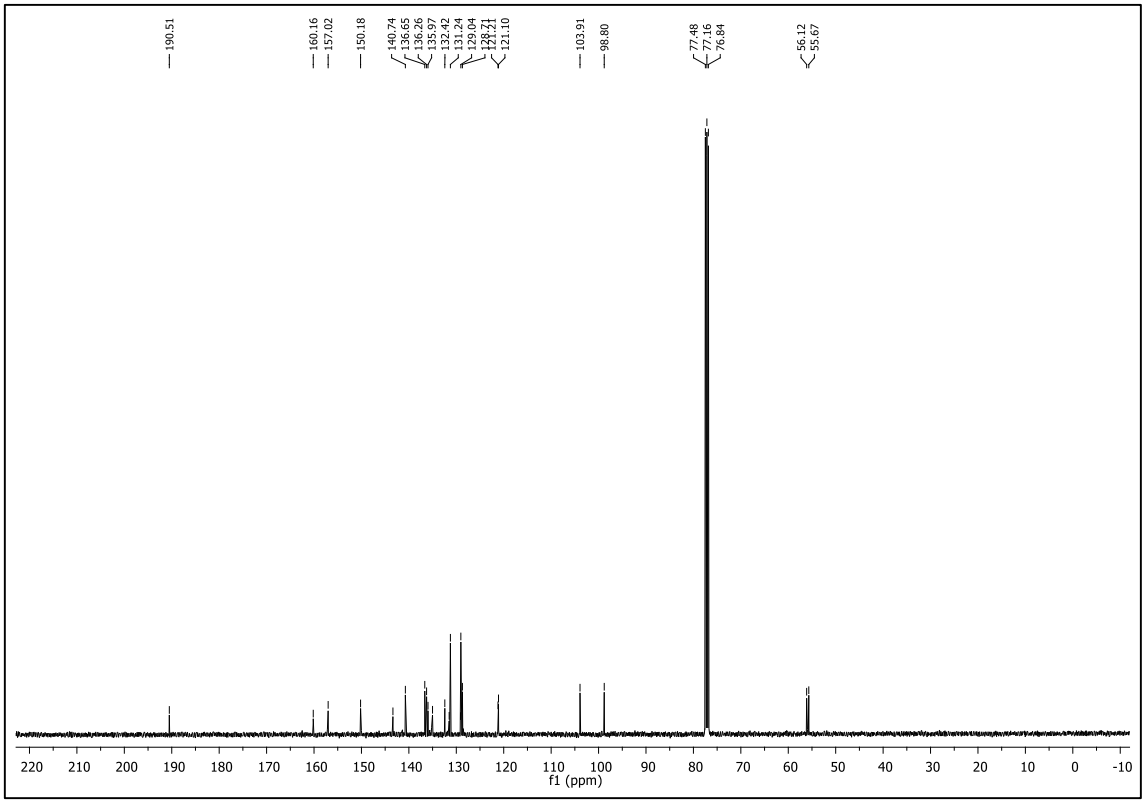
1.20
0.15
0.30
1.99
2.16
0.99
2.28
3.03
3.77
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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103.91
98.80
77.48
77.16
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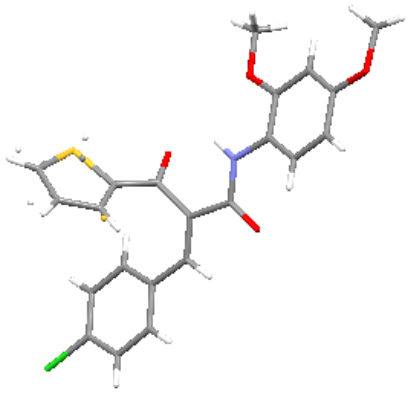
f1 (ppm)

X-Ray Data



Bond precision: C-C = 0.0020 A

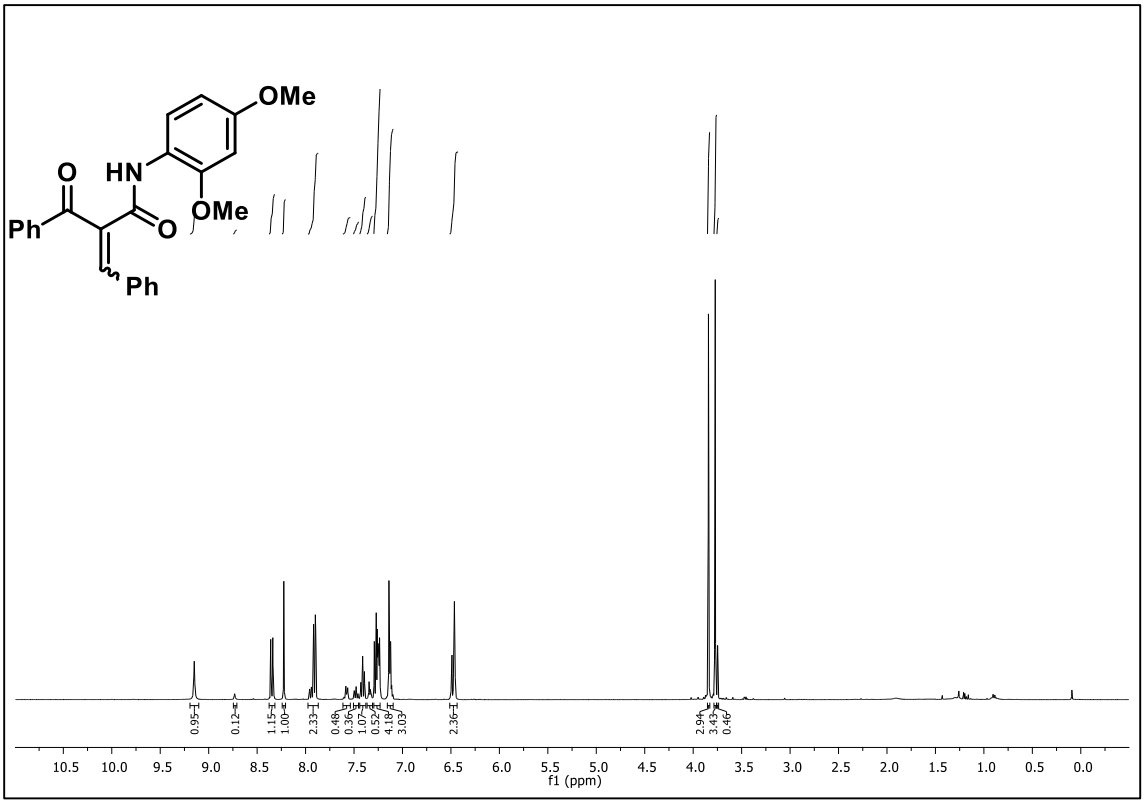
Wavelength=1.54184

Cell:	a=9.5087(4)	b=10.0290(4)	c=11.1468(4)
	alpha=84.025(3)	beta=68.125(4)	gamma=88.073(3)
Temperature:	123 K		

	Calculated		Reported
Volume	981.08(7)		981.08(7)
Space group	P -1		P -1
Hall group	-P 1		-P 1
Moiety formula	C22 H18 Cl	N O4 S	C22 H18 Cl N O4 S
Sum formula	C22 H18 Cl	N O4 S	C22 H18 Cl N O4 S
Mr	427.88		427.88
Dx,g cm-3	1.449		1.448
Z	2		2
Mu (mm-1)	2.974		2.974
F000	444.0		444.0
F000’	446.61		
h,k,lmax	11,12,13		11,12,13
Nref	4031		3923
Tmin,Tmax	0.531,0.700		0.396,1.000
Tmin’	0.403		

Correction method= MULTI-SCAN

Data completeness= 0.973 Theta(max)= 74.730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Ph
O
OMe
Ph
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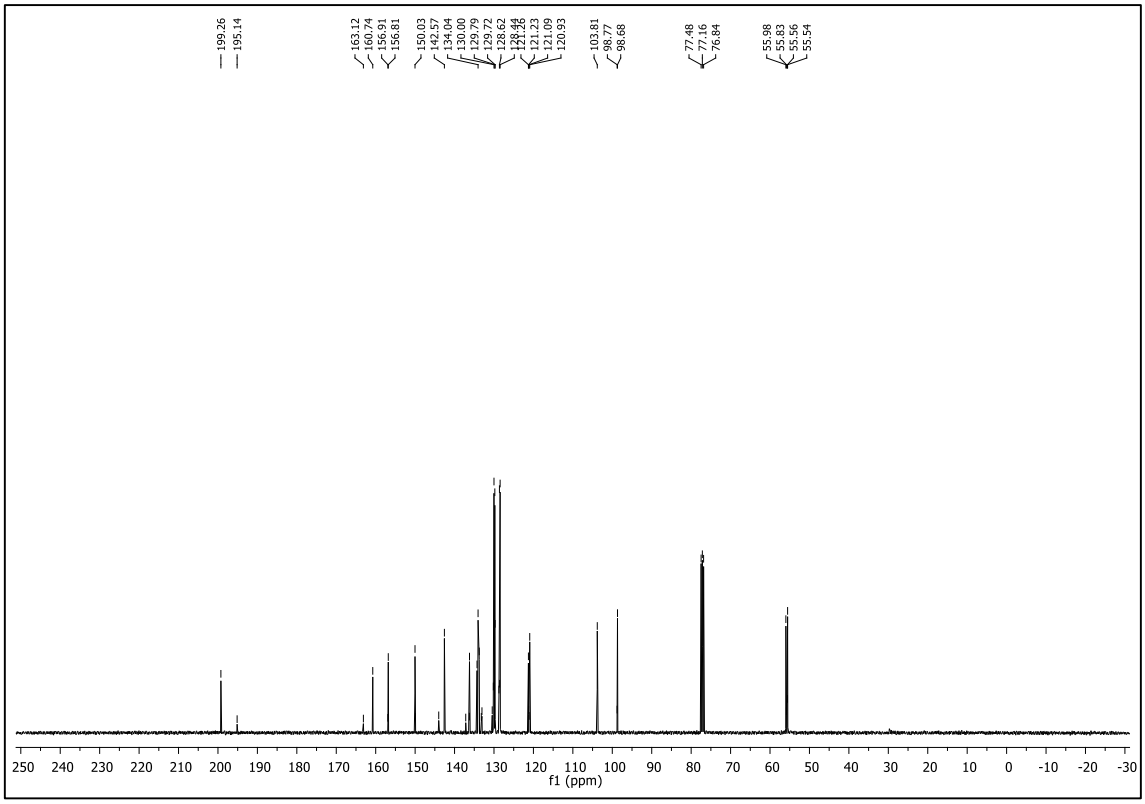
1.00
2.33
0.48
0.36
1.07
0.52
4.19
3.03
2.36
2.94
3.43
0.46
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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98.77
98.68
77.48
77.16
76.84
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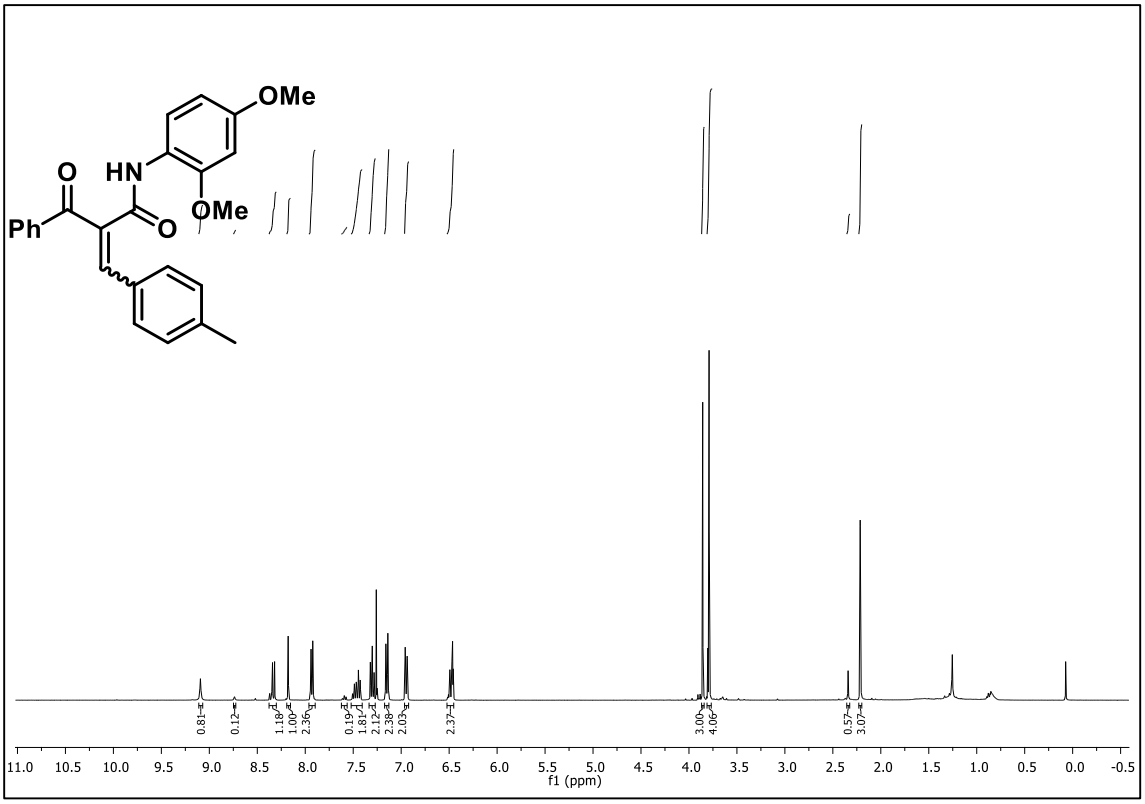
f1 (ppm)


OMe
HN
O
Ph
O
OMe
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1.18
1.00
2.36
0.19
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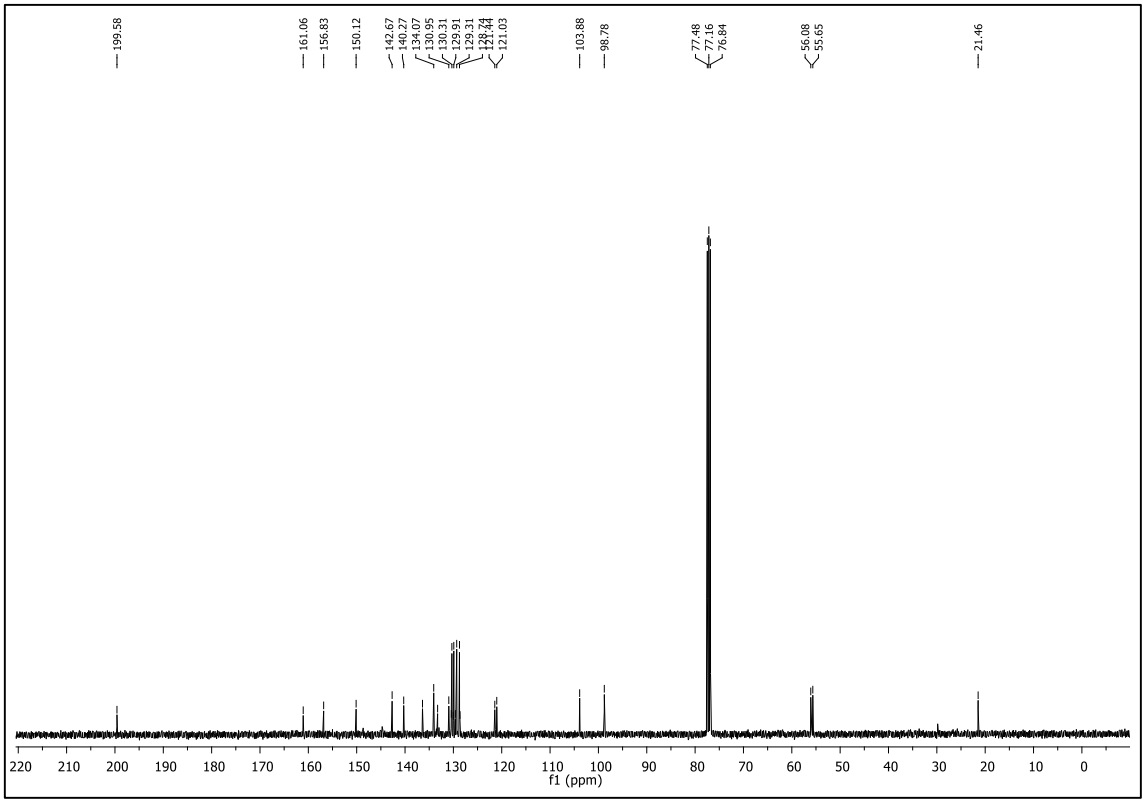
2.12
2.38
2.03
2.37
3.00
4.06
0.57
3.07
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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103.88
98.78
77.48
77.16
76.84
56.08
55.65
21.46
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

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6 Summary

This PhD thesis demonstrates the development of new methodologies for visible light mediated deoxygenation processes followed by new bond formations, as well as acrylamide synthesis *via* vinyl radical formation.

In chapter 3, a mild and environmentally benign protocol for the defunctionalization of carbon-oxygen single bonds of alcohols was outlined. Activation of the substrates, followed by reductive bond cleavage was accomplished in an one pot strategy under visible light photoredox catalysis. The minor tendency to the direct reduction of carbon-oxygen bonds of alcohols was solved by *in situ* generated activated ethyl oxalate esters. By irradiation with blue light in the presence of $[Ir(ppy)_2(dtb\text{-}bpy)]PF_6$ as visible light photocatalyst, $^{i}Pr_2NEt$ as sacrificial electron donor, water as hydrogen source gave generally good to excellent yields of the reduced compounds. Albeit its high functional group tolerance, the protocol reveals limitations for the defunctionalization of benzylic, α-carbonyl and allylic alcohols, exclusively.

In chapter 4, in analogy to the photoredox catalyzed deoxygenation process of (+)-diethyl tartrate to unnatural (+)-diethyl malate under visible light (Chapter 3), a strategy for carbon – carbon bond coupling reactions was developed, making use of the carbon radicals initially formed in the deoxygenation reaction. Thus, using monoallylated tartrates, a subsequent intramolecular 5-*exo* trig cyclization gave access to chiral tetrahydrofuran derivatives. The alcohol group of mono-allylated hydroxyl succinates was activated by conversion to their respective ethyl oxalyl esters. Consecutive irradiation with blue light in the presence of *fac*-$Ir(ppy)_3$ as visible light photoredox catalyst in DMF generally gave good yields of the desired cyclized products.

In chapter 5, the synthesis of sterically demanding acrylamides triggered by visible light was demonstrated. Therefore, we induced a highly reactive vinyl radical in the presence of $Ru(bpy)_3Cl_2$ as photoredox catalyst and visible light which was subsequently trapped intermolecular by 1-isocyano-2,4-dimethoxybenzene. Studies on biological inhibition of acrylamide compounds did not show any promising activity.

7 Abbreviations

ABC	ATP-binding cassette
AIBN	azobis(isobutyronitril)
Ar	aryl
ATP	Adenosintrtiphosphat
$CDCl_3$	deuterated chloroform
CH_2Cl_2	dichloromethane
CH_3CN	acetonitrile
CFL	compact fluorescent lamp
d.r.	diastereomeric ratio
DMF	dimethyl formamide
DMF-d^7	deuterated dimethyl formamide
EtOAc	ethyl acetate
EI	electron impact (MS)
equiv	equivalents
ESI	electronspray ionization
EtOH	ethanol
Et	ethyl
eV	electron volts
h	hour(s)
HRMS	high resolution mass spectrometry
^{i}Pr	*iso*-propyl
IR	infrared spectroscopy
ISC	intersystem crossing
LED	light-emitting diode
Me	methyl
MHz	mega hertz
min	minutes
mL	milliliter
MLCT	metal to ligand charge transfer
mmol	millimole
mol%	mole percent
m.p.	melting point
Na_2SO_4	sodium sulfate
nm	nanometer
hν	wavelength
NMR	nuclear magnetic resonance
o-	ortho
p-	para
Ph	phenyl
rt	room temperature
SCE	saturated calomel electrode
SET	single electron transfer
^{t}Bu	*tert*-butyl
TEMPO	(2,2,6,6,-Tetramethylpiperidin-1-yl)oxyl
TLC	thin layer chromatography
UV	ultraviolet
V	volt
W	watt

8 Curriculum Vitae

Education and Experience

10/2009 - 09/2011 **Master of Science, Chemistry**, University of Regensburg

Master thesis: *„Fullerene C_{60} – Photooxygenation reactions and their recycling by magnetic Co/C nanoparticle via π–π-stacking"* supervised by Prof. Dr. Oliver Reiser

Main subject: Organic Chemistry

Subsidiary subjects: Physical Chemistry, Inorganic Chemistry

10/2006 – 09/2009 **Bachelor of Science, Chemistry**, University of Regensburg

Bachelor thesis: „*Immobilization of homogeneous catalysts on heterogeneous supporter*" supervised by Dr. Sebastian Wittmann and Prof. Dr. Oliver Reiser

30/06/2006 **A levels** (Allgemeine Hochschulreife)

Wilhelm-Diess-Gymnasium, Pocking

International Experience

02/2012 – 04/2012 **Research internship**

INDIGO (Indian-German Graduate School of Advanced Organic Synthesis for a Sustainable Future) Program of the DAAD (Deutschen Akademiker Austausch Dienstes)

supervised by Dr. B. V. Subba Reddy, Indian Institute of Chemical Technology (IICT) Hyderabad, India

2012 – 2014 Participation at international conferences (Chennai, Istanbul, Marseille)

Additional Education

02/2015 – 06/2015 **Business Administration for Developer**

Advanced training of the „strategische Partnerschaft Sensorik e.V.", Regensburg

05/2014 **Business Administration for chemists**

GDCh-training 402/14, Leipzig

2009 Umfassende Sachkunde nach § 5, i. V. m. § 2 der Chemikalien Verbotsordnung

Work Experience

10/2011 – 02/2015 **Research associate**

Institute for Organic Chemistry, chair Prof. Dr. Oliver Reiser, University of Regensburg

- Instruction of scientific internship und bachelor thesis
- Supervision of internships in organic chemistry for beginners and advanced students in chemistry, biology und teaching profession chemistry/biology

08/2009 – 10/2010 **Voluntary social service**

Companions in the retirement home “Haus an der Rott” Pocking

Scholarships / Memberships

2012 - 2015 **Graduiertenkolleg Chemische Photokatalyse GRK 1626**

Deutsche Forschungsgemeinschaft (DFG)

2012 – 2015 **Indian-German Graduate School of Advanced Organic Synthesis for a Sustainable Future INDIGO**

IPID Programm des DAAD, funded by the Bundesministerium für Bildung und Forschung (BMBF)

2013 & 2014 **Karl-Ziegler Stiftung & August-Wilhelm-von-Hofmann Stiftung**

Gemeinschaft Deutscher Chemiker (GDCh)

Miscellaneous

Languages German (native), English (fluency), Russian (A2 level), French (basic)

EDV Knowledge SciFinder, ChemDraw, Mestrec, MestreNova, SpinWorks, MS Office (Word, Excel, Power Point), Origin, Topspin, ISIS Draw

Hobbies

Traveling, culinary art & culture, guitar, music, reading, bicycling (all-mountain)

Reference

Prof. Dr. Oliver Reiser

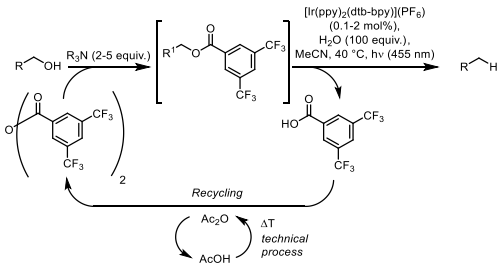
Institute for Organic Chemistry, University of Regensburg

Oliver.Reiser@ur.de

Publications

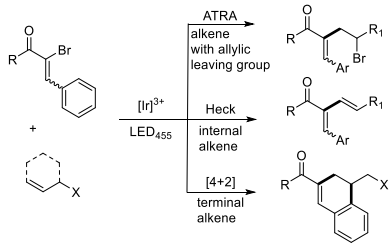
[1] Daniel Rackl, Viktor Kais, Peter Kreitmeier, Oliver Reiser

"*Visible Light Photoredoxcatalyzed Deoxygenation of Alcohols*", *Beilstein J. Org. Chem*. **2014**, *10*, 2157-5165.



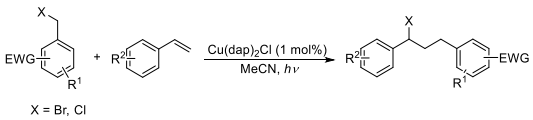
[2] Suva Paria, Viktor Kais, Oliver Reiser

"Visible Light-Mediated Coupling of α-Bromochalcones with Alkenes", *Adv. Synth. Catal.* **2014**, *356*, 2853-2858.



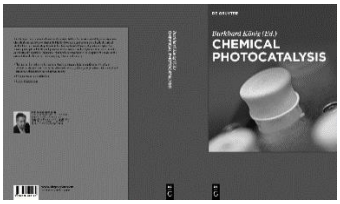
[3] Suva Paria, Michael Pirtsch, Viktor Kais, Oliver Reiser

"Visible Light Induced Intermolecular Atom Transfer Radical Addition of Benzyl Halides to Olefins: Facile Synthesis of Tetrahydroquinolines", *Synthesis* ***2013***, *45*, 2689-2698.



[4] Burkhard König (Ed.)

Bookchapter *"Chemical Photocatalysis"* (Book), *De Gruyter* **2013**



Posters / Oral Presentation

[1] Viktor Kais, Oliver Reiser

"Visible Light Photoredoxcatalyzed Deoxygenation of Benzylic and Allylic Alcohols"

(5th EuCheMS Chemie Kongress), **2014**, Istanbul, Türkei

[2] Viktor Kais, Oliver Reiser

"Visible Light Photoredoxcatalyzed Deoxygenation of Benzylic Alcohols"

GDCh Wissenschaftsforum **2013**, Darmstadt, Deutschland

[3] Viktor Kais, Raghavendra Ramachanderan, Oliver Reiser

"C-O bond Activation towards C-H bond formation under Visible Light Photocatalysis"

18th European Symposium on Organic Chemistry (ESOC), **2013**, Marseille, Frankreich

[4] Viktor Kais, Daniel Rackl, Raghavendra Ramachanderan, Peter Kreitmeier, Oliver Reiser

"Visible Light Photoredoxcatalyzed Deoxygenation of Benzylic Alcohols"

IPID Doctoral Conference **2013**, Köln, Deutschland

[5] Viktor Kais, Georgii Kachkovskyi, Paul Kohls, Suva Paria, Hana Seo, Daniel Rackl, Oliver Reiser

"Homogeneous Photocatalysis"

Chemical Photocatalysis - GRK 1626 Meeting, **2012**, München

[6] Viktor Kais, Dr. Subba Reddy, Oliver Reiser

"Visible Light Photocatalysis – C-O Activation – Generation of Oxocarbenium Ion following a Prins Cyclization"

Präsentation auf der 3rd Indian-German Graduate School of Advance Organic Synthesis for Sustainable Future (INDIGO) Konferenz, **2012**, Chennai, Indien

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10 Declaration

Herewith I declare that this present thesis is a presentation of my original work prepared single-handed. Wherever contributions from others are involved, all of them are marked clearly, with reference to the literature, license and acknowledgement of collaborative research.

Regensburg, 30. Juni 2015

Viktor Kais