Organic Syntheses

Fragment Coupling and Formation of Quaternary Carbons by Visible-Light Photoredox Catalyzed Reaction of *tert*-Alkyl Hemioxalate Salts and Michael Acceptors

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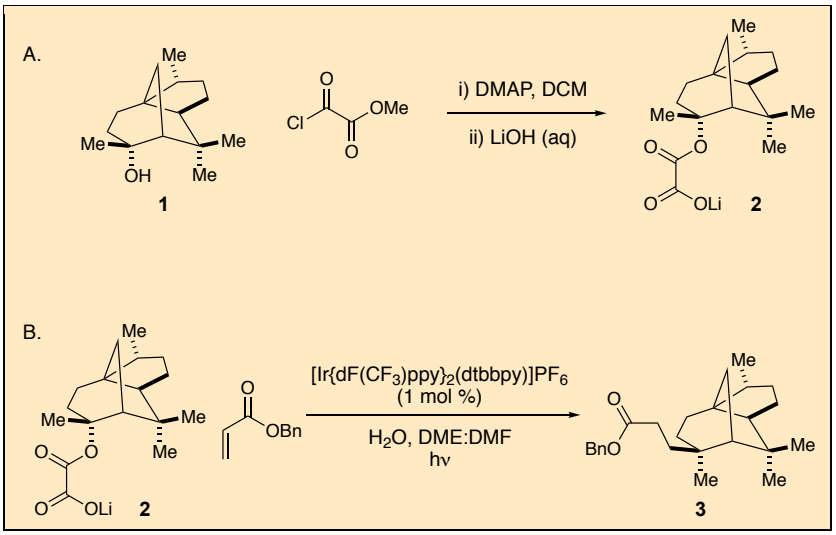

Procedure

A. *Cedrol lithium oxalate (***2***).* A 100 mL one-necked (24/40 joint) round-bottomed flask equipped with a Teflon-coated magnetic stir bar (oval, 25 mm x 10 mm) is charged with cedrol (**1**) (2.22 g, 10.0 mmol, 1.0 equiv) (Note 1), 4-dimethylaminopyridine (1.34 g, 11.0 mmol, 1.1 equiv) (Note 2), and dichloromethane (40 mL) (Note 3). The flask, which is open to air, is

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immersed in a room temperature water bath, and the mixture is rapidly stirred under ambient atmosphere. A disposable plastic syringe is used to add methyl chlorooxoacetate (960 μL, 10.5 mmol, 1.05 equiv) (Note 4) dropwise over the course of 2 min (Note 5). The resulting pale yellow solution is maintained for 2 h at room temperature (Figure 1). A fritted glass funnel (6 cm diameter x 10 cm height) with a vacuum adapter is packed with 35 g of silica gel (Note 6) as a slurry in dichloromethane. The crude reaction mixture is poured onto the silica gel plug (Figure 1). A mild vacuum (~10 mmHg) is applied, and the filtrate is collected. The 100 mL round-bottomed flask is rinsed with dichloromethane (2 x 10 mL), and the washings are also poured onto the silica gel plug. The silica gel plug is washed with additional dichloromethane (4 x 50 mL), and the combined organic washes are concentrated under reduced pressure (23 °C, 12 mmHg) in a 500 mL round-bottomed flask to yield the crude methyl oxalate as a clear oil (2.85–3.00 g).

Figure 1. Left: reaction turns pale yellow following the addition of methyl chlorooxoacetate; Right: reaction mixture is filtered over the silica gel plug

This crude product is dissolved in 10 mL of THF (Note 7) and transferred from the 500 mL round-bottomed flask to a 250 mL separatory funnel. The 500 mL round-bottomed flask is rinsed with an additional 10 mL of THF, and the washings are added to the separatory funnel. An aqueous solution of 0.5 M LiOH (18 mL, 9.0 mmol, 0.90 equiv) (Note 8) is added to the organic layer. The separatory funnel is briefly shaken to ensure efficient mixing, then the homogenous solution is allowed to stand for 5 min. Hexanes (60 mL) (Note 9) are then added, and the mixture is shaken. The phases are allowed to separate (Note 10), then the aqueous phase is collected in a 1 L round-bottomed flask. The organic layer is washed with a second portion of deionized water (20 mL), and the combined aqueous phases are concentrated under reduced pressure (12 mmHg, water was removed by distillation as an azeotrope with three 100 mL portions of toluene at 23 ºC) (Note 11). The resulting solid is then dried on a vacuum manifold (0.2 mmHg, 23 ºC) overnight to yield the desired product **2** as a colorless solid (2.56 g, 85% yield, 98% purity) (Note 12).

B. *Cedrol benzyl acrylate addition product (**3**).* On the bench under ambient atmosphere, six 8-mL scintillation vials (Note 13), each equipped with a magnetic stir bar (oval, 12 mm x 2 mm), are charged with benzyl acrylate (97 mg, 0.60 mmol, 1.0 equiv) (Note 14), cedrol lithium oxalate **2** (198 mg, 0.660 mmol, 1.1 equiv), and $[Ir\{dF(CF_3)ppy\}_2(dtbbpy)]PF_6$ (7 mg, 0.006 mmol, 0.01 equiv) (Note 15). A 3:1 mixture of dimethoxyethane/dimethylformamide (6 mL, 0.1 M) (Note 16) is added, followed by deionized water (110 μL, 6.0 mmol, 10 equiv) (Note 17), (Note 18). The vials are then sealed with screw caps bearing Teflon septa. Each septum of the sealed vials is pierced with a 21 gauge x 1.5" needle that is inserted just barely through the septum with the tip of the needle kept above the fluid level inside the vial (Figure 2). A separate 21 gauge x 3" needle attached to a flow of argon is also pierced through the septum, and the tip of the needle is pushed to the bottom of the vial and submersed in the fluid. The reaction mixtures are deoxygenated by sparging with argon for 15 min (Note 19).

Both needles are removed, and the sealed vials are then placed on a stir plate equipped with 2 x 34 W blue LED lamps (Notes 20 and 21) and a rack to hold the vials inside of a cardboard box to block light pollution from entering the lab (Figure 3). The vials are placed in two parallel rows of 3 vials approximately 4 cm from the lamps and stirred vigorously. The samples are irradiated by the lamps for 24 h inside the closed box, and the

air inside the box rises to 40–45 °C because of heat given off from the LEDs (Notes 22, 23, and 24).

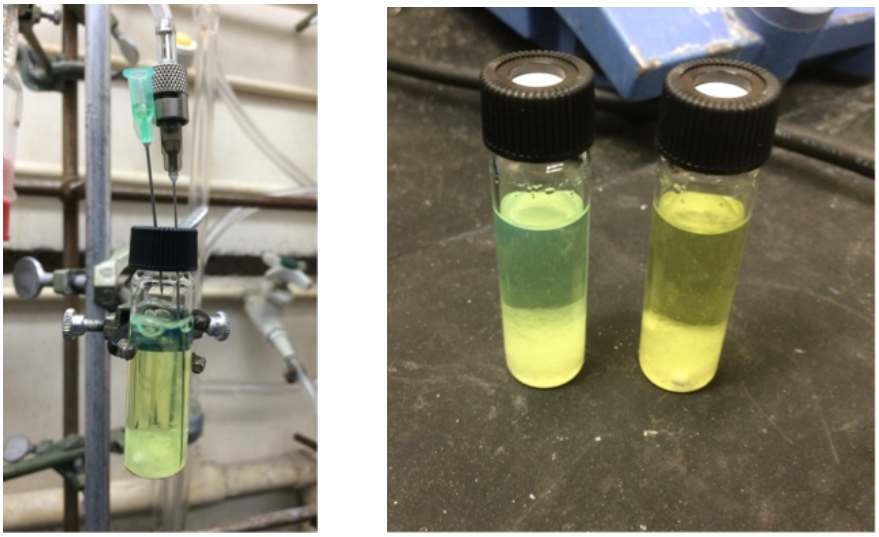

Figure 2. Left: reaction mixture is being sparged with argon. Right: reaction mixture before (right) and after (left) being sparged with argon

The reactions are allowed to cool to rt, then all six are opened and poured into the same 500 mL separatory funnel. The vials are each rinsed with 5 mL of diethyl ether, and the washings are also added to the separatory funnel. The mixture is further diluted with 200 mL of additional diethyl ether. The organic solution is washed with an aqueous mixture of 2:1 saturated aqueous LiCl/deionized water (150 mL) (Note 25). The layers are separated and the organic phase is washed with deionized water (100 mL). The combined aqueous phases are extracted again with fresh diethyl ether (100 mL). The layers are separated, and the organic phase is washed with deionized water (100 mL). The combined ethereal extracts are dried with $MgSO_4$ (s) (4 g). The mixture is vacuum filtered through a fritted glass funnel (5 cm OD x 6 cm height), and the solids washed with diethyl ether (2 x 30 mL). The filtrate is concentrated under reduced pressure on a rotary evaporator (23 °C, 12 mmHg). The crude material is charged on a column (3 cm OD x 12.5 cm height) of 45 g of silica gel (Note 26) and eluted with 500 mL of 98:2 hexanes/Et_2O solvent mixture. The eluent is collected over 25 fractions, with the desired product obtained in fractions 13–22

(Note 27). The fractions containing the product are concentrated under reduced pressure (23 °C, 12 mmHg) to give the desired product **3** as a yellow oil (1.04 g, 78% yield, 99% purity) (Notes 28, 29, and 30).

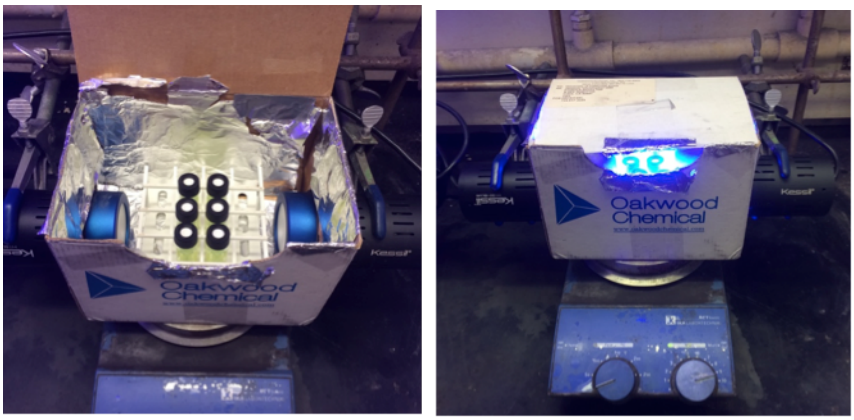

Figure 3. Visible light reaction set-up

Notes

1. Cedrol (98%) was purchased from TCI America and used as received. "Redistilled Cedrol" is commercially available in cheap, bulk quantities, but the purity (~60%) is not sufficient for these studies.
2. DMAP (99%) was purchased from Oakwood Chemical and used as received.
3. Dichloromethane (99.9%) was purchased from Fisher Scientific Company and used as received.
4. Methyl chlorooxoacetate was purchased from Alfa Aesar and used as received. The batch used by the submitters was from a bottle without an air-free septum and was used periodically over the course of a year before being used in the reported procedure.
5. The reaction is mildly exothermic. A clear, pale yellow homogeneous solution is observed after addition of all reagents.
6. Geduran Si 60 (40–63 μm) silica gel was purchased from EMD Millipore Corporation.
7. Tetrahydrofuran (99.9%) was purchased from Fisher Scientific Company and used as received.

8. LiOH monohydrate was purchased from Sigma-Aldrich and used as received. The salt is dissolved in deionized water to form a stock solution. The stock solution was titrated with 1 N HCl (aq) using phenolphthalein as an indicator to determine the exact concentration of this stock solution. More than 0.9 equiv LiOH (aq) can be judiciously used to consume all of the methyl oxalate, but adding too much is detrimental to the purity of the product. The use of other alkali hydroxides is possible, and the resulting oxalates couple with similar efficiency.[2] In general, lithium and cesium oxalates have the most favorable physical properties (i.e., non-hygroscopic, non-deliquescent, and stable solid compounds) and perform well in the photoredox-catalyzed coupling reaction.
9. Hexanes (98.5%) was purchased from Fisher Scientific Company and used as received.
10. The lithium oxalate is not completely soluble in the aqueous phase because of the large hydrophobic backbone of cedrol, so some insoluble product is observed at the interface of the layers. The second aqueous extraction dissolves this insoluble material. This poor solubility is not generally observed for lithium oxalates derived from other alcohols, but is in fact specific to cedrol.
11. The use of a 1 L round bottom is highly recommended, as the mixture tends to bump during concentration. It is also advised to dry the sample on the rotary evaporator for at least an hour to remove as much water as possible before placing it under high vacuum. After drying, the material can either be scraped out of the vessel or transferred to a smaller vessel by dissolving in methanol. It is important to thoroughly dry the salt under high vacuum to remove all methanol before use.
12. A reaction performed on half scale provided 1.27 g (85%) of product **2**. The lithium oxalate **2** is 98% pure as measured by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard. No melting or decomposition apparent at 360 ºC. ^{1}H NMR (400 MHz, CD_3OD) δ 0.87 (d, J = 7.1, 3H), (1.00, (s, 3H), 1.23 (s, 3H), 1.27–1.35 (m, 1H), 1.40–1.59 (m, 5H), 1.60 (s, 3H), 1.66–1.73 (m, 2H), 1.85–1.95 (m, 2H), 2.08–2.12 (m, 2H), 2.52 (d, J = 5.2 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ: 15.8, 26.2, 26.3, 27.7, 28.9, 32.3, 34.2, 38.0, 42.1, 42.8, 44.5, 55.2, 58.1, 58.2, 88.8, 165.9, 166.7; IR (ATR) 2950, 1701, 1663, 1249 cm^{-1}; HRMS (ESI–TOF) (m/z) calculated for $C_{17}H_{25}LiO_4$ [M − Li]$^-$ 293.1753; found 293.1761; $[\alpha]^{23}_D$ +27.9 (c 1.0, MeOH).

13. The 8-mL vials (Kimble Glass Screw-Thread Sample Vials with PTFE/Silicone Septa and Open-Top Polypropylene Closure, 60942A8) were purchased from Fisher Scientific Company. The dimensions of the reaction vessel are important for maximizing surface area exposed to the light source.
14. Benzyl acrylate was purchased from Alfa Aesar and used as received. Commercial Michael acceptors often contain ppm concentration of various radical inhibitors that are generally not detrimental to the reaction. This is consistent with the proposed photoredox mechanism that does not involve radical chain reactions.
15. $[Ir\{dF(CF_3)ppy\}_2(dtbbpy)]PF_6$ may be purchased from Sigma Aldrich or Strem Chemicals in high purity. The complex can alternatively be synthesized for a fraction of the price.[8a] An *Organic Syntheses* procedure is also available for the preparation of $[Ir\{dF(CF_3)ppy\}_2(dtbbpy)]PF_6$.[8b]
16. Dimethoxyethane (99%) and dimethylformamide (99.8%) were purchased from Fisher Scientific Company and used as received.
17. The addition of deionized water is highly beneficial. Presumably, the water both assists in solubilizing the oxalate salt and provides a proton source to quench the intermediate lithium enolate after radical coupling and reduction. The exact equiv of water used is an important but is not an absolutely critical variable. A diminished isolated yield (59%) was obtained for a reaction run with 50 equiv of water, which corresponds to a reaction solution that is roughly 10% water by volume. As a corollary, the use of rigorously dried solvents and flame-dried glassware is generally not necessary.
18. It is important to add the deionized water last. If the water is added to the oxalate before the other solvents, a gel may form that impedes stirring in the reactions.
19. The reaction is moderately air sensitive. A 46% ^{1}H NMR yield was observed when the reaction was run under an air atmosphere with no attempt to deoxygenate the reaction mixture at all.
20. If a standard 20 W CFL bulb is used in place of the 34 W blue LED, a 41% ^{1}H NMR yield is observed after 24 h. Blue LED lamps were purchased from Kessil on Amazon.com (http://www.amazon.com/Kessil-KSH150B-Grow-Light-Blue/dp/B004GB441K). During the course of our studies, the Kessil KSH150B lamps became unavailable. Ostensibly equivalent Kessil models A160WE and Kessil H150W can be purchased on Amazon.com (http://www.amazon.com/Kessil-A160WE-Controllable-Aquarium-

Light/dp/B00QHC6D7O, http://www.amazon.com/Kessil-Angle-Light-Discontinued-Manufacturer/dp/B00598HIEO). The Checkers used two Kessil A160WE "Tuna Blue" lamps described above at the full blue setting.

21. Blue light from high-intensity LEDs can be damaging to eyesight. It is important that the reaction setup be surrounded by an appropriate shield to protect researchers from exposure to the light from the LED lamps. Researchers should wear blue-light blocking safety glasses when the lamps are in operation. The Submitters used Uvex Skyper Blue Computer Blocking Glasses (model #: S1933X).
22. The temperature of the reaction mixture after 24 h was measured by the use of a thermocouple to be 62 ºC, which is roughly 20 ºC warmer than the ambient air inside the cardboard box.
23. The increased temperature is generally beneficial to the reaction provided that the Michael acceptor is not particularly sensitive. If the reactions are cooled to rt by blowing a stream of rt air over them during irradiation, a 71% yield is observed by ^{1}H NMR after 24 h.
24. As the rate of the reaction is proportional to the amount of light exposure, it is important that each vial has maximum exposure to the light source. The reactions turn brown-black within 5 minutes, then become greenish-brown after 24 h. The lithium oxalate is not completely soluble in the reaction mixture and may collect near the surface of the solution. It is helpful to briefly shake the vials once or twice during the 24 h course of the reaction to dislodge this material; all of this material should be dissolved to ensure complete reaction and to allow maximum light flux into solution. The low solubility of the lithium oxalate is not a general feature of lithium oxalates and seems unique to the cedrol-based lithium oxalate **2**.
25. The purpose of the aqueous LiCl wash is to remove traces of DMF from the product. There are some solids at the interface between the phases during the LiCl (aq) wash. These dissolve during the subsequent wash with deionized water.
26. Geduran Si 60 (40–63 μm) silica gel was purchased from EMD Millipore Corporation.
27. The course of the chromatography can be monitored by TLC. Coupled product **3**: R_f = 0.42, 98:2 hexanes/EtOAc, visualized with KMnO stain. Benzyl acrylate: R_f = 0.37, 98:2 hexanes/EtOAc, visualized with $KMnO_4$ stain.

28. A reaction performed on half scale provided 0.52 g (78%) of product **3**. The coupled product **3** is 99% pure as measured by ^{1}H NMR using 1,2,4,5-tetrachlorobenzene as internal standard. ^{1}H NMR (400 MHz, $CDCl_3$) δ : 0.83 (d, J = 7.1, 3H), 0.98 (s, 3H), 1.03 (s, 3H), 1.20 (s, 3H), 1.22–1.40 (m, 6H), 1.46–1.57 (m, 4H), 1.60–1.69 (m, 2H), 1.73 (t, J = 8.2 Hz, 1H), 1.86 (dq, J = 11.8, 5.8 Hz, 1H), 2.08–2.17 (m, 1H), 2.23–2.32 (m, 2H), 5.11 (s, 2H), 7.40–7.30 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 15.6, 25.6, 26.9, 29.3, 29.4, 30.1, 30.4, 34.2, 36.9, 37.2, 37.6, 39.9, 42.0, 44.3, 53.9, 56.4, 57.7, 66.3, 128.3, 128.4, 128.7, 136.2, 174.7; IR (thin film): 2943, 2869, 1738, 1455, 1161 cm^{-1}; HRMS (FAB–TOF) (m/z) calculated for $C_{25}H_{36}O_2$ $[(M+H)–H_2]^+$ 367.2637; found 367.2645; $[\alpha]^{23}_D$ +25.6 (c 1.0, $CHCl_3$).
29. Trace amounts of benzyl acrylate may be present in the sample. The impurity can be removed via concentration on a vacuum manifold (0.2 mmHg, 23 °C) overnight.
30. Due to the reaction's requirement for a large surface area to volume ratio for efficient exposure to visible light, the gram-scale procedure detailed here is appropriate mainly for academic research or medicinal chemistry applications. Flow-chemistry has been utilized to great effect for photoredox-catalyzed reactions[11] and should be employed for large-scale preparations.

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The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that

procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

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Discussion

The reported method, which was developed in collaboration with the MacMillan group, allows for redox-neutral construction of quaternary carbon stereocenters by the coupling of tertiary radicals, generated from tertiary alcohol-derived oxalate salts, with electron-deficient alkenes under visible-light photoredox catalysis.[2] The most common alternative to the reported method for the generation of tertiary alkyl radicals from tertiary alcohols is the use of Barton's alkyl *N*-hydroxypyridine-2-thionyl oxalates.[3] While useful for primary and secondary alcohols, Barton oxalate derivatives of tertiary alcohols are fairly unstable, which prevents their isolation, and their light sensitivity makes their use challenging. Inspired by this Barton chemistry, the Overman group described the use of *tert*-alkyl *N*-phthalimidoyl oxalates as precursors of tertiary radicals.[4] These radical precursors are relatively stable to visible light and can be stored at –20 °C in a freezer indefinitely. However, the *N*-phthalimidoyl oxalate moiety presents complications during purification, resulting in decomposition upon silica gel chromatography or aqueous extraction. Other synthetically useful methods for generation of tertiary radicals utilize precursor functional groups such as alkenes,[5] carboxylic acids,[6] or *N*-(acyloxy)phthalimides.[7]

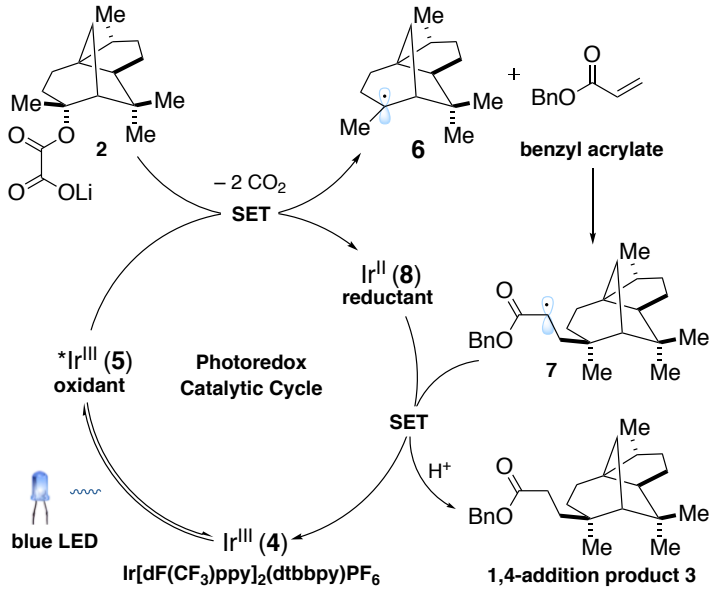
In the example detailed here, a commercially available, sterically congested tertiary alcohol, cedrol **1**, is coupled to a prototypical Michael acceptor, benzyl acrylate, to illustrate the efficiency and diastereoselective

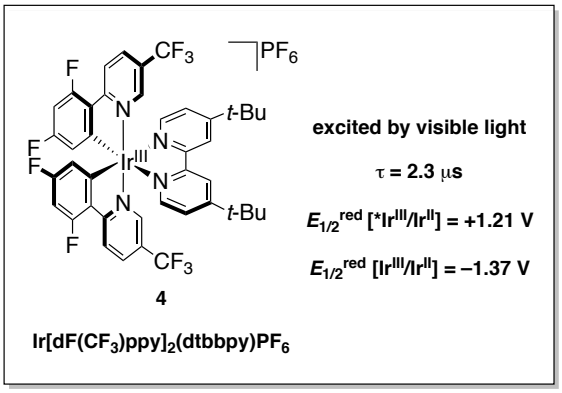
nature of the reaction in a complex setting. The resulting product is obtained as a single epimer at the newly formed quaternary carbon stereocenter in good yield using nearly equimolar amounts of the two coupling partners. The conditions reported are general and expected to be similarly efficient for a wide scope of coupling partners.

As shown in Scheme 1, the proposed mechanism of the coupling reaction involves irradiation of the heteroleptic photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (**4**) [$dF(CF_3)ppy$ = 2-(2,4-difluorophenyl)-5-trifluoromethylpyridine, dtbbpy = 4,4'-di-*tert*-butyl-2,2′ -bipyridine] with visible light to generate a long-lived ($\tau = 2.3$ μs) excited state $*Ir^{III}$ **5**, which is a strong oxidant ($E_{1/2}^{red}$ [$*Ir^{III}/Ir^{II}$] = +1.21 V vs. SCE in CH_3CN)[8] capable of oxidizing cedrol lithium oxalate **2** ($E_{1/2}^{red}$ = +1.28 V vs. SCE in CH_3CN for *t*-$BuOCOCO_2Cs$)[2] via single-electron transfer (SET). After oxidation, the oxalate radical spontaneously extrudes two molecules of CO_2 in a stepwise fashion to form the tertiary alkyl radical **6**. This nucleophilic carbon-centered radical **6** reacts with the electron-deficient alkene benzyl acrylate. Finally, the reduction of the resulting adduct radical **7** ($E_{1/2}^{red}$ = −0.59 to −0.73 V vs. SCE in MeCN)[9] by SET from the available Ir^{II} species **8** ($E_{1/2}^{red}$ [Ir^{III}/Ir^{II}] = –1.37 V vs. SCE in CH_3CN)[8] followed by protonation yields coupled product **3** and regenerates ground state photocatalyst **4**.

The addition of a nucleophilic tertiary carbon radicals to a π-bond has an early transition state and consequently a relatively long bond (~2.5 Å),[10] which reduces the enthalpic penalty incurred from steric strain as bulky fragments approach one another. As a result, the generation of sterically encumbered quaternary carbons is often facile and proceeds under mild conditions.[12] The efficiency and scope of the coupling procedure described in this procedure is illustrated by the selection of published examples grouped in (Table 1).[2] Steric bulk in the vicinity of the forming quaternary carbon is well tolerated, with adjacent isopropyl and *tert*-butyl groups not greatly reducing the efficiency of the reaction.

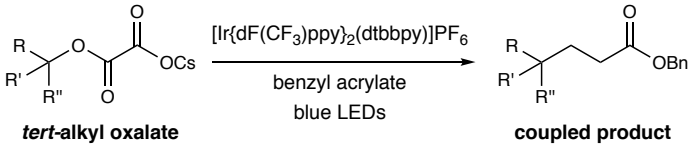
Additionally, stereoselection in the addition of tertiary radicals to alkenes can be quite large, as evinced by the high diastereoselectivity observed for the formation of quaternary stereocenters of coupled products **12–14** (Table 1).[2] The stereoselective nature of these reactions is somewhat surprising given the aforementioned long (~2.5 Å) forming bond in the transition state, which might be expected to translate to poor stereochemical control. Nevertheless, tertiary radicals are indeed large enough to impose significantly differentiated amounts of strain in diastereotopic transition states leading to excellent levels of stereoselectivity.



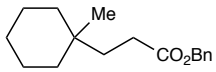
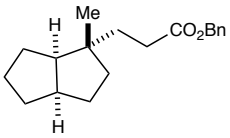
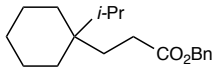
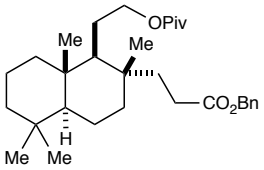
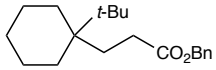
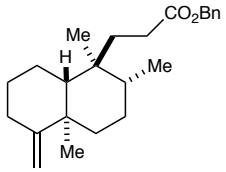


Scheme 1. Proposed mechanism for visible light photoredox-catalyzed coupling reaction

Table 1. Previously published examples of visible light photoredox catalyzed coupling reaction



***tert*-alkyl oxalate** **coupled product**

Product	Product
	
9 91% yield	**12 85% yield, >20:1 dr**
	
10 93% yield	**13 96% yield, >20:1 dr**
	
11 73% yield	**14 91% yield, >20:1 dr**

Finally, it is important to note that this visible-light photoredox catalyzed radical reaction proceeds with good efficiency in an intermolecular reaction utilizing nearly 1:1 stoichiometry of the coupling partners. The advantage of this feature is that it enables the union of complex fragments in the context of total synthesis, wherein it is not feasible to use a precious, complex intermediate in large excess. References 2 and 13 detail examples of utilizing this complex fragment coupling reaction to enable efficient total synthesis of *trans*-clerodane natural products. Two recent publications describe a one-pot procedure for transforming

secondary and tertiary alcohols to oxalate salts and employing them directly in visible-light photoredox coupling with carbon electrophiles.[14]

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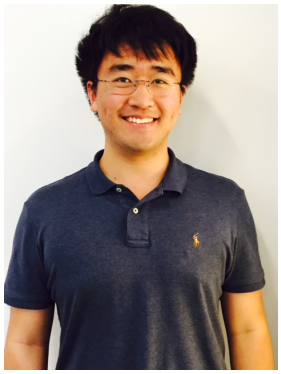
Appendix
Chemical Abstracts Nomenclature (Registry Number)

Cedrol: 1*H*-3a,7-Methanoazulen-6-ol, octahydro-3,6,8,8-tetramethyl-, (3*R*,3a*S*,6*R*,7*R*,8a*S*)-; (77-53-2)
4-dimethylaminopyridine: 4-Pyridinamine, *N*,*N*-dimethyl-; (1122-58-3)
Methyl chlorooxoacetate: Acetic acid, 2-chloro-2-oxo-, methyl ester; (5781-53-3)
Lithium hydroxide monohydrate-; (1310-66-3)
Benzyl acrylate: 2-Propenoic acid, phenylmethyl ester; (2495-35-4)
$[Ir\{dF(CF_3)ppy\}_2(dtbbpy)]PF_6$: Iridium(1+), [4,4'-bis(1,1-dimethylethyl)-2,2'-bipyridine-κ N^1,κ $N^{1'}$]bis[3,5-difluoro-2-[5-(trifluoromethyl)-2-pyridinyl-κ *N*]phenyl-κ *C*]-, (*OC*-6-33)-, hexafluorophosphate(1-) (1:1); (870987-63-6)
Dimethoxyethane: Ethane, 1,2-dimethoxy; (110-71-4)
Dimethylformamide: Formamide, *N*,*N*-dimethyl-; (68-12-2)
5,6-Dibromo-1,3-benzodioxole: 1, 3-Benzodioxole, 5,6-dibromo-; (5279-32-3)

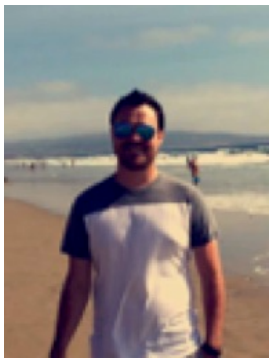
Larry Overman was born in Chicago, Illinois, in 1943 and raised in Hammond, Indiana. He obtained a B.A. degree from Earlham College in 1965 and completed his doctoral dissertation in 1969 with Professor Howard W. Whitlock, Jr. at the University of Wisconsin. After a NIH postdoctoral fellowship with Professor Ronald Breslow at Columbia University, he joined the faculty at the University of California, Irvine in 1971 where he is now Distinguished Professor of Chemistry. Professor Overman was Chair of the UC Irvine Department of Chemistry from 1990–1993.

Christopher R. Jamison received his B.S. in Biochemistry from the University of Nevada, Reno in 2007. He then earned a Ph. D. in Organic Chemistry at Princeton University under the supervision of Professor David MacMillan by developing enantioselective arylation reactions and applying them to the total synthesis of polypyrroloindoline natural products. In 2014, he started postdoctoral training at the University of California, Irvine with Professor Larry Overman to develop photoredox strategies for synthesizing quaternary stereocenters through complex fragment coupling.

Yuriy Slutskyy received his B. S. in Biochemistry from California State University, Sacramento in 2013. He then moved to University of California, Irvine to pursue his doctoral studies under the supervision of Professor Larry Overman. His initial graduate studies were aimed at the development of methods for visible light photoredox-catalyzed formation of quaternary carbon stereocenters. Currently, his research is focused on utilization of photoredox catalysis in complex molecule synthesis.



Anthony Y. Chen was born in Athens, Ohio, in 1993 and raised in Cupertino, California. He received a B. S. in Chemistry and B. A. in Molecular and Cell Biology in 2015 from the University of California, Berkeley, where he worked under the supervision of Professor Richmond Sarpong. He then moved to the California Institute of Technology to pursue his doctoral studies in the laboratory of Professor Brian M. Stoltz. His current research focuses on the total synthesis of alkaloid natural products.



Eric R. Welin was born in Columbus, Ohio, in 1987. He obtained his B. S. degree in Chemistry in 2010 from the Ohio State University, where he conducted undergraduate research in the laboratory of Professor James P. Stambuli. In the same year, he began his graduate studies at Princeton University under the supervision of Professor David W. C. MacMillan. At Princeton his research focused on developing new methods utilizing photoredox catalysis. He earned his Ph. D. in 2015, and later that year he joined the laboratory of Professor Brian M. Stoltz as an American Cancer Society postdoctoral fellow. His current research focuses on the total synthesis of bioactive natural products.

Tyler J. Fulton was born in Hazleton, Pennsylvania in 1994. He obtained his B. S. and M. S. degree in chemistry from Bucknell University in 2016 under the direction of Dr. Michael Krout. He then moved to Caltech to pursue his doctoral degree under the supervision of Dr. Brian Stoltz. His current research focuses on the total synthesis of natural products.

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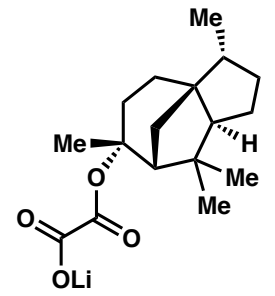
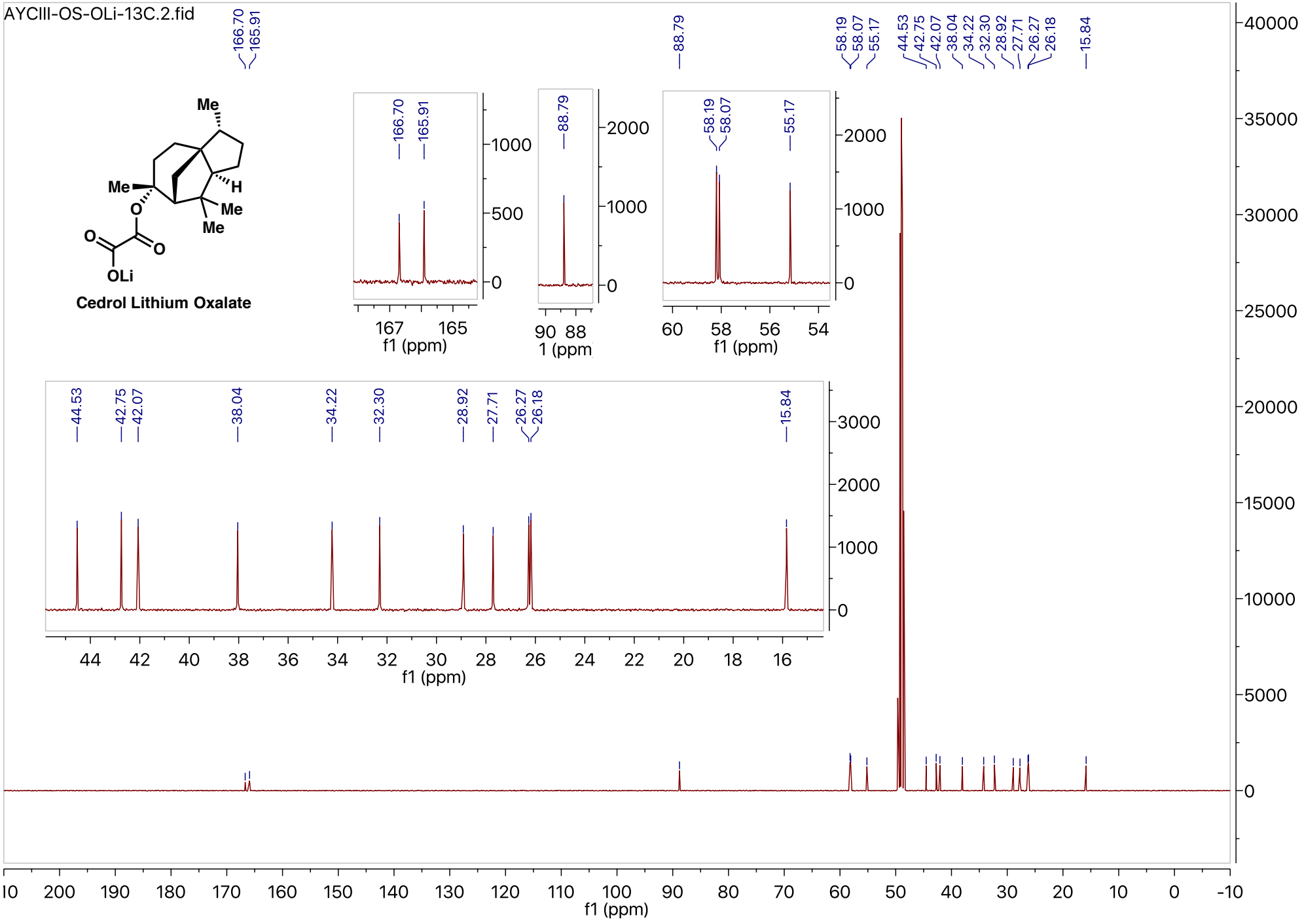


Cedrol Lithium Oxalate

f1 (ppm)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88.79
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58.07
55.17
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42.75
42.07
38.04
34.22
32.30
28.92
27.71
26.27
26.18
15.84
Me
Me
H
O
Me
Me
O
O
OLi
Cedrol Lithium Oxalate
f1 (ppm)
1 (ppm

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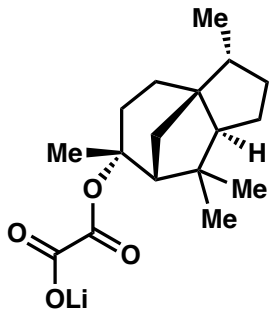
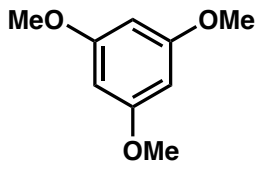


Cedrol Lithium Oxalate
25.2 mg (0.0839 mmol)

+



1,3,5-trimethoxybenzene
34.7 mg (0.206 mmol)

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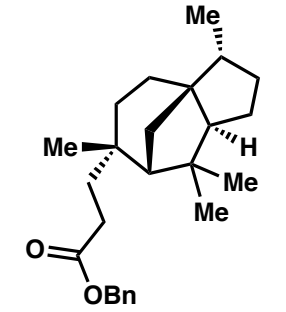
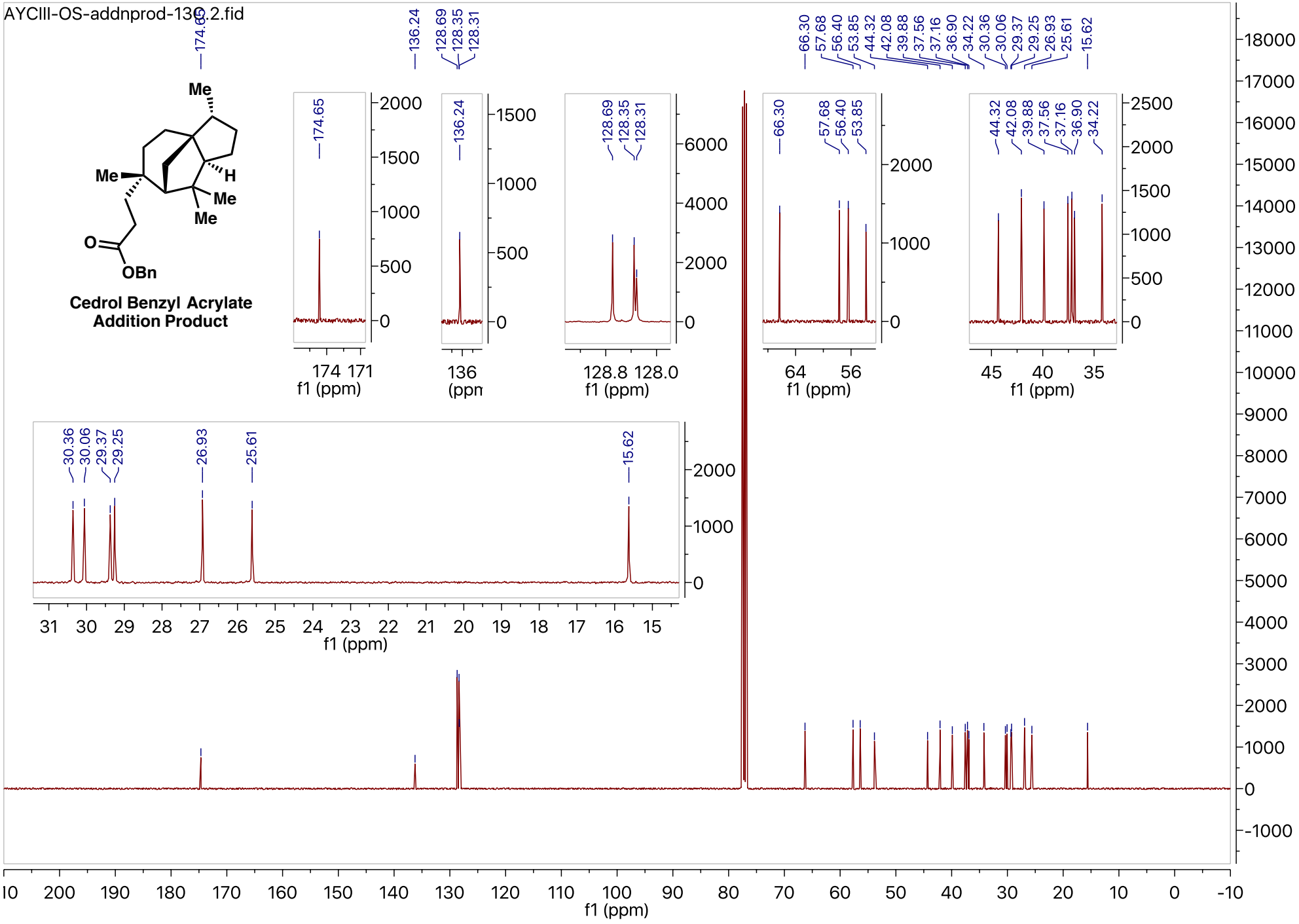


Cedrol Benzyl Acrylate Addition Product

f1 (ppm)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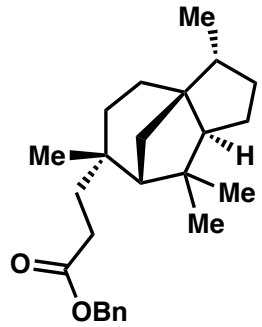
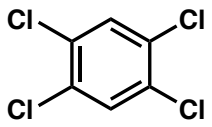
37.56
37.16
36.90
34.22
30.36
30.06
29.37
29.25
26.93
25.61
15.62
Me
Me
H
Me
Me
O
OBn
Cedrol Benzyl Acrylate
Addition Product
f1 (ppm)

AYCIII-cedroladdnpdt-qNMR.1.fid



Cedrol Benzyl Acrylate Addition Product
33.6 mg (0.0912 mmol)

+



1,2,4,5-tetrachlorobenzene
42.3 mg (0.196 mmol)