Synthesis of cyclopent-2-enones from furans using a nebulizer-based continuous flow photoreactor

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Part A: Reactor Set-up

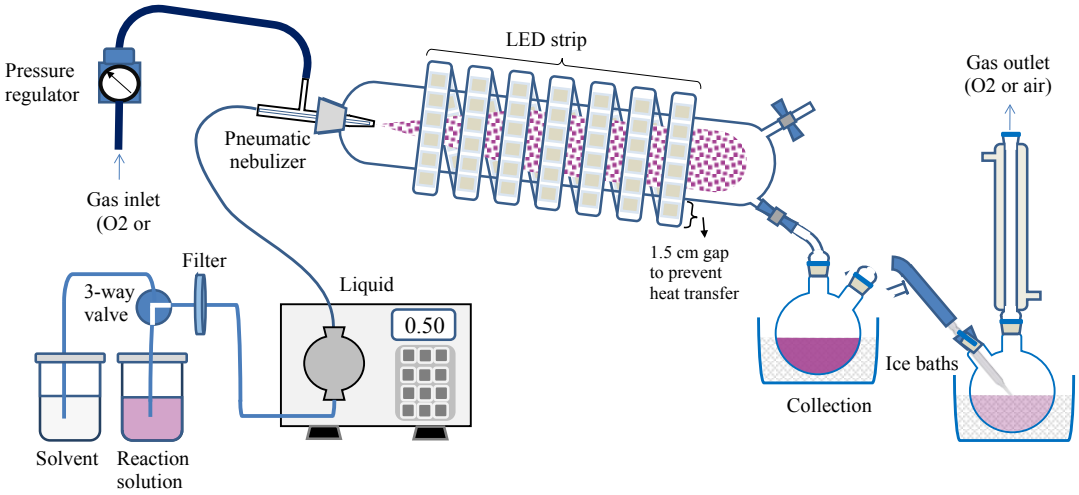


Figure 1. Schematic representation of NebPhotOX reactor.

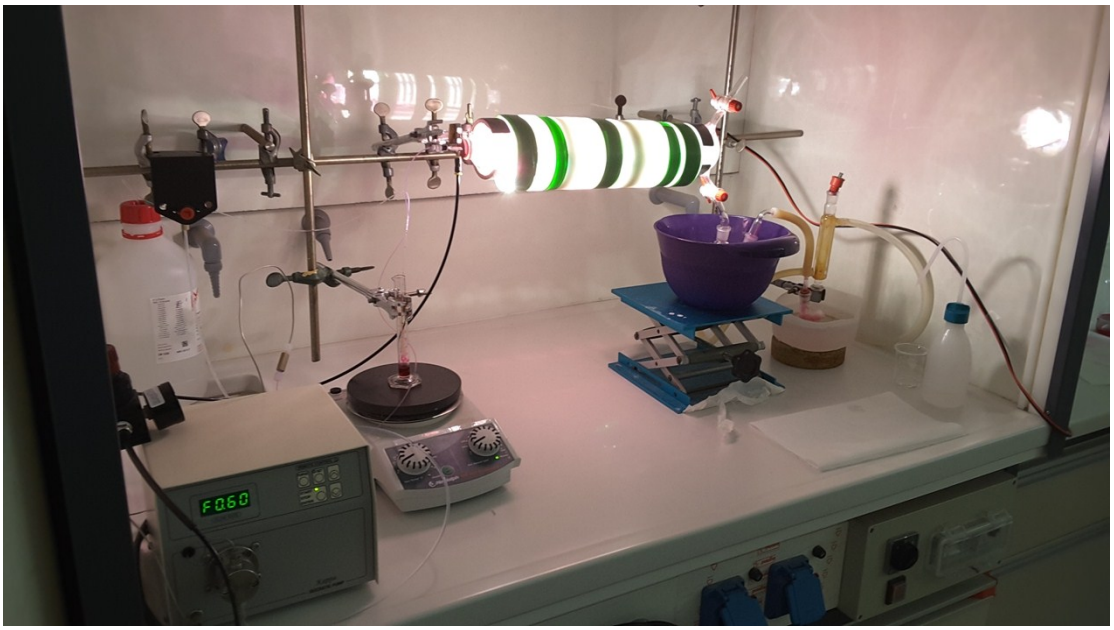


Figure 2. NebPhotOX in action.

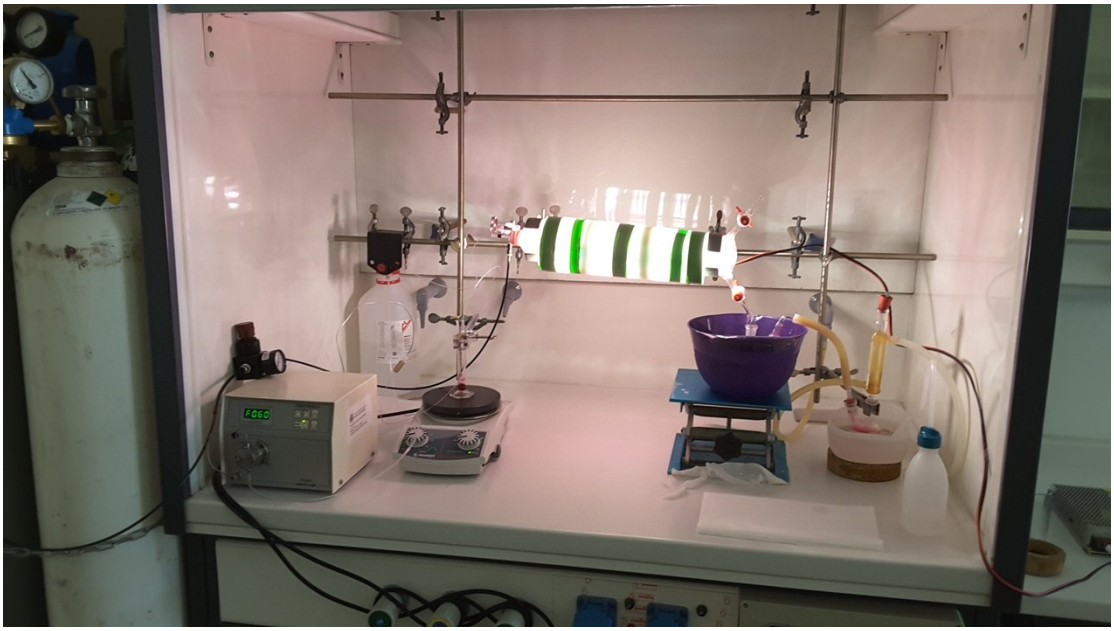


Figure 3. NebPhotOX in action.

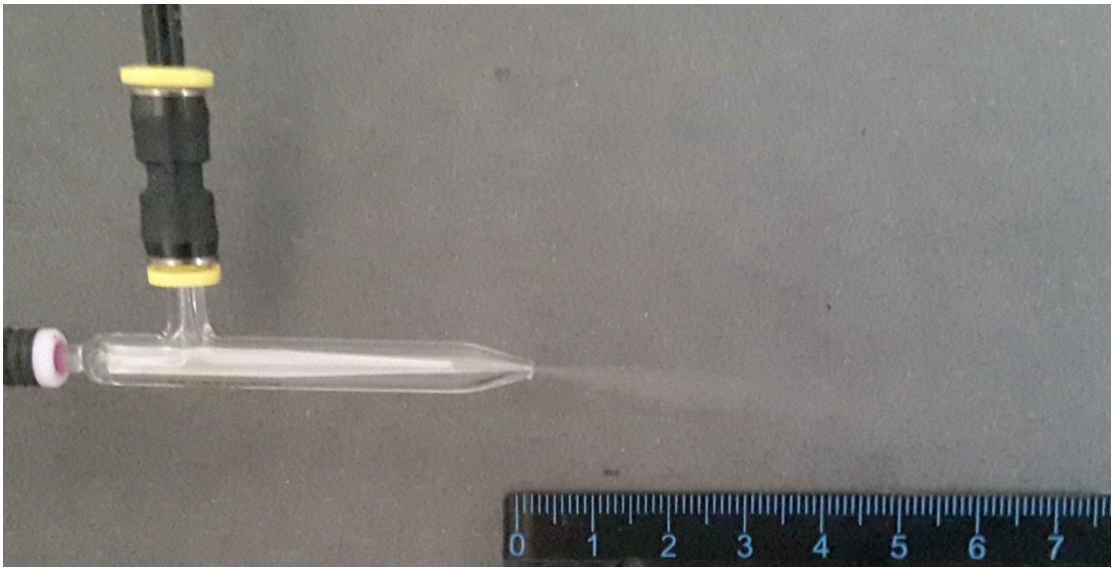


Figure 4. The cone angle of the nebulizer.

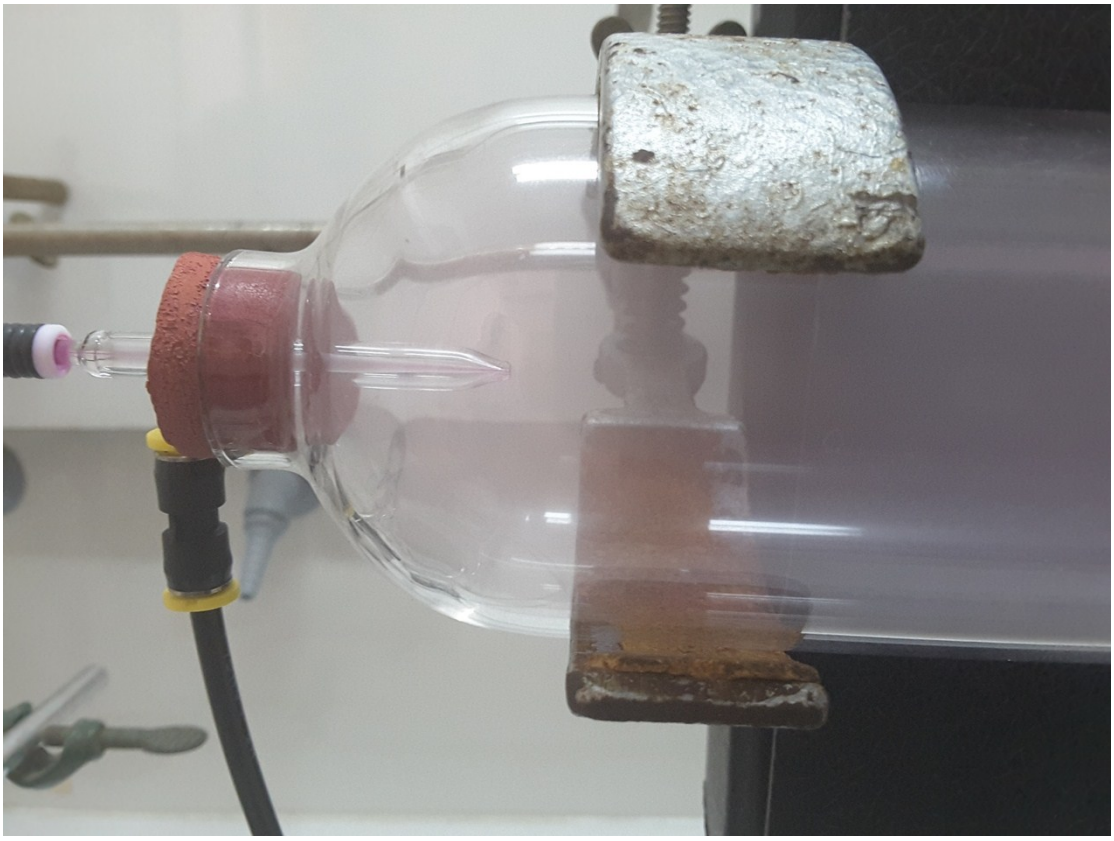


Figure 5. The aerosol "cloud" formed after 10 sec of nebulization.

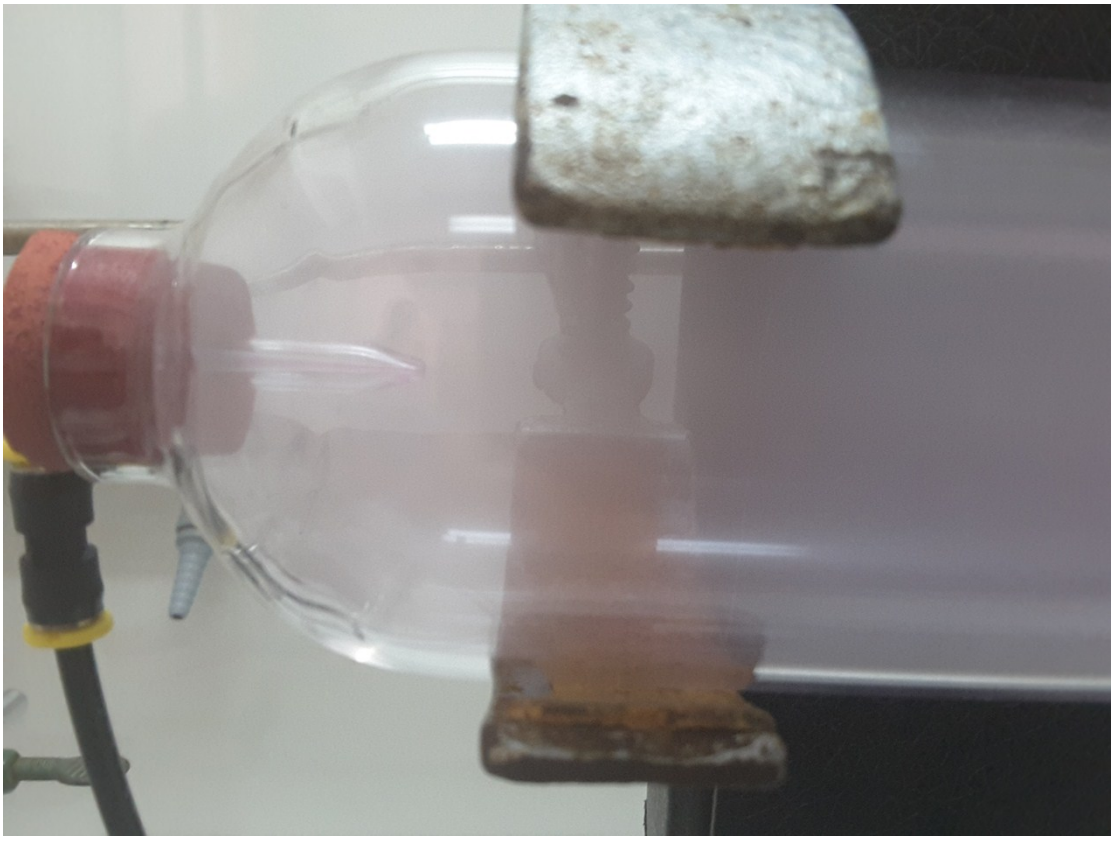


Figure 6. The aerosol "cloud" formed after 20 sec of nebulization.

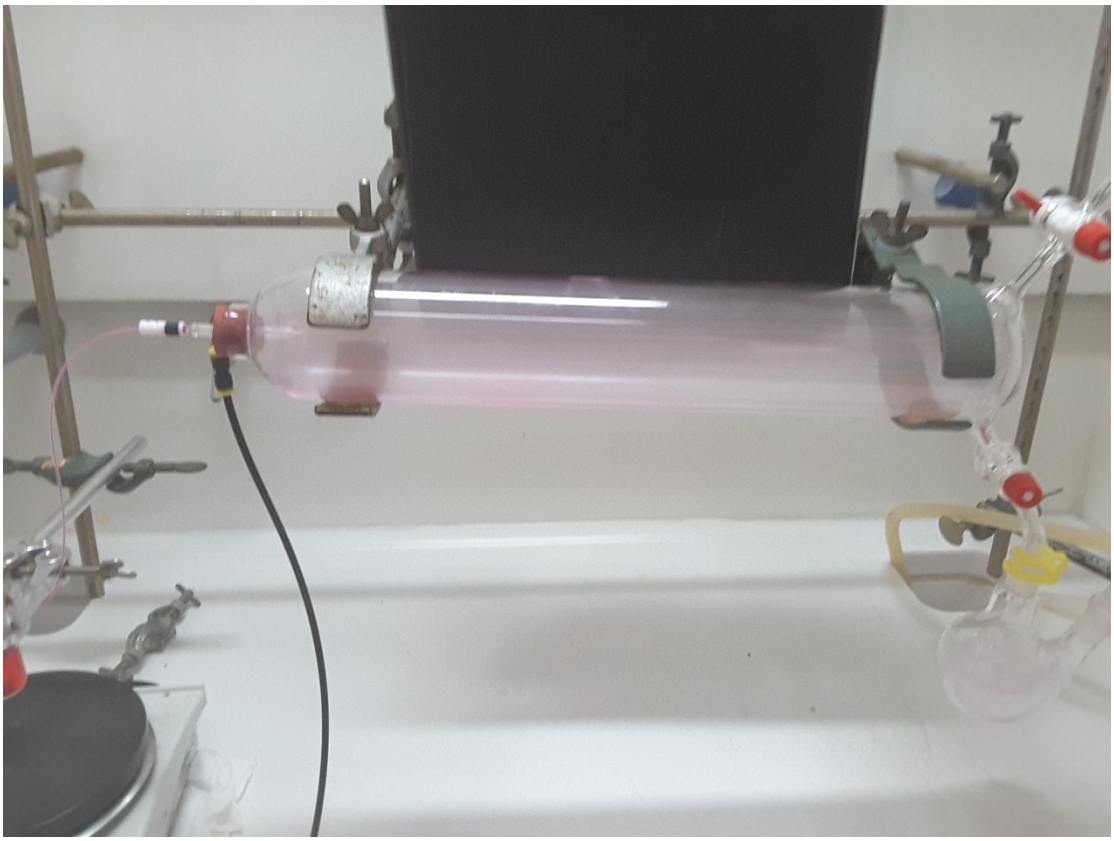
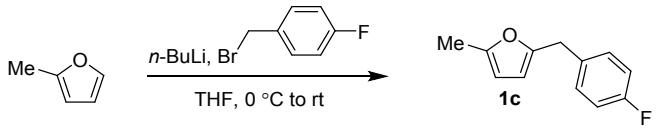


Figure 7. The aerosol "cloud" formed after 30 sec of nebulization. For better viewing of the aerosol the LED strip lights have been omitted.

SAFETY CAUTION: Measures were taken to eliminate all possible ignition sources from the fumehood area (sparks or flames, e.g. the electricity transformer for the LEDs was kept outside of the fumehood) in which the NebPhotOX system was operated. This included operating the reactor at room temperature and pressure conditions without any significant heat input from the low power LEDs used. In addition, the fumehood was always adequately ventilated with a high air flow. System operating conditions prevented oxygen stagnation in the system. Additional cautions included that the operator wears safety glasses with side shields and flame resistant safety clothing. For the fast reduction of the initially formed hydroperoxides of type A and B (Scheme 1), the two cooled collection flasks placed in series were prefilled with excess of Me_2S in MeOH (3 equiv in the first flask and 1 equiv in the second flask). Even higher excesses of the reducing agent can be used.

Part B: Experimental procedures

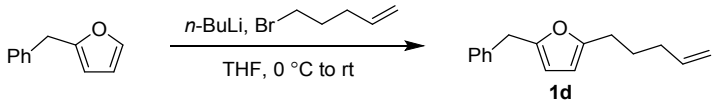
Known compounds. The following compounds were prepared as previously reported: **1a**,[1] **1b**,[2] **1f**.[3]



Synthesis of 2-(4-fluorobenzyl)-5-methylfuran (1c)

To a solution of 2-methylfuran (4.1 mL, 45 mmol) in anhydrous THF (20 mL), at 0 °C and under argon atmosphere, was added a solution of *n*-BuLi (12.2 mL, 1.6 M in hexanes, 19.5 mmol). The solution was stirred for 30 min at the same temperature and subsequently 1-(bromomethyl)-4-fluorobenzene (1.87 mL, 15 mmol) was added. The reaction solution was warmed to room temperature and stirred for a further 2 hours. The reaction was quenched with a saturated solution of NH_4Cl (20 mL) and the resulting mixture extracted with Et_2O (30 mL). The organic layer was separated and dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 100:1). Yield 95% (2.71 g).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.19 (dd, J_1=8.4 Hz, J_2=5.5 Hz, 2H), 6.98 (t, J=8.7 Hz, 2H), 5.85 (s, 2H), 3.88 (s, 2H), 2.24 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.6 (d, J=243.8 Hz, F-Ph-C(ipso)), 152.4, 151.1, 134.1 (d, J=2.9 Hz, F-Ph-C(para)), 130.1 (d, J=8.0 Hz, F-Ph-C(meta), 2C), 115.2 (d, J=21.1 Hz, F-Ph-C(ortho), 2C), 106.9, 106.0, 33.7, 13.5 ppm.



Synthesis of 2-benzyl-5-(pent-4-en-1-yl)furan (1d)

To a solution of 2-benzylfuran (**1a**, 2.98 g, 18.83 mmol) in anhydrous THF (14 mL), at 0 °C and under argon atmosphere, was added a solution of *n*-BuLi (11.8 mL, 1.6 M in hexanes, 18.83 mmol). The solution was stirred for 30 min at the same temperature and subsequently 5-bromopent-1-ene (2.0 mL, 16.94 mmol) was added. The reaction solution was warmed to room temperature and stirred for a further 12 hours. The reaction was quenched with a saturated solution of NH_4Cl (20 mL) and the resulting mixture extracted with Et_2O (30 mL). The organic layer was separated, dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 100:1). Yield 94% (3.6 g).

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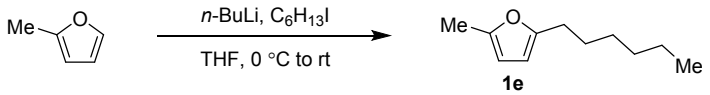
[1] D. Kalaitzakis, T. Montagnon, I. Alexopoulou and G. Vassilikogiannakis, *Angew. Chem. Int. Ed.*, 2012, **51**, 8868.

[2] D. Kalaitzakis, M. Triantafyllakis, I. Alexopoulou, M. Sofiadis and G. Vassilikogiannakis, *Angew. Chem. Int. Ed.*, 2014, **53**, 13201.

[3] G. Vassilikogiannakis, I. Alexopoulou, M. Tofi and T. Montagnon, *Chem. Commun.*, 2011, **47**, 259.

^{1}H NMR (500 MHz, $CHCl_3$): δ = 7.30 (m, 2H), 7.21 (m, 3H), 5.87 (d, *J*=3.0 Hz, 1H), 5.85 (d, *J*=3.0 Hz, 1H), 5.80 (m, 1H), 5.01 (dq, J_1=17.1 Hz, J_2=1.6 Hz, 1H), 4.96 (m, 1H), 3.92 (s, 2H), 2.58 (t, *J*=7.6 Hz, 2H), 2.09 (q, *J*=7.2 Hz, 2H), 1.71 (quin, *J*=7.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.0, 152.6, 138.5, 138.3, 128.6 (2C), 128.4 (2C), 126.3, 114.8, 106.6, 105.3, 34.5, 33.1, 27.4, 27.2 ppm.

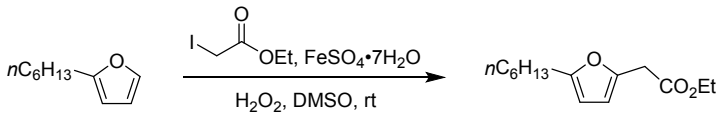


1e

Synthesis of 2-hexyl-5-methylfuran (1e)

To a solution of 2-methylfuran (2.57 mL, 28.5 mmol) in anhydrous THF (14 mL), at 0 °C and under argon atmosphere, was added a solution of *n*-BuLi (7.72 mL, 1.6 M in hexanes, 12.35 mmol). The solution was stirred for 30 min at the same temperature and subsequently a solution of 1-iodohexane (1.40 mL, 9.5 mmol) in anhydrous THF (5 mL) was added. The reaction solution was warmed to room temperature and stirred for a further 2 hours. The reaction was quenched with a saturated solution of NH_4Cl (20 mL) and the resulting mixture was extracted with Et_2O (30 mL). The organic layer was separated, dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 100:1). Yield 95% (1.5 g).

^{1}H NMR (500 MHz, $CHCl_3$): δ = 5.84 (s, 2H), 2.56 (t, *J*=7.6 Hz, 2H), 2.26 (s, 3H), 1.61 (quin, *J*=7.4 Hz, 2H), 1.38-1.28 (m, 6H), 0.89 (t, *J*=6.9 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.8, 149.9, 105.7, 105.0, 31.6, 28.9, 28.1 (2C), 22.6, 14.0, 13.5 ppm.



1g

Synthesis of ethyl 2-(5-hexylfuran-2-yl)acetate (1g)

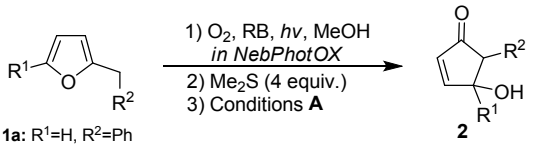
To a solution of 2-hexylfuran[4] (2.59 g, 17.0 mmol) in high purity DMSO (120 mL) was added ethyl iodoacetate (2.0 mL, 17.0 mmol). Then $FeSO_4$•$7H_2O$ (2.36 g, 8.5 mmol) and a solution of H_2O_2 30% wt. (8.7 mL, 85 mmol) were added in four equal portions every 30 min, while the reaction flask was placed in a water bath at rt. The mixture was stirred at rt for a further 12 hours. Afterwards, a saturated aqueous solution of NaCl (20 mL) was added and the resulting mixture was extracted with Et_2O (3× 40 mL). The combined organic layers were washed with H_2O (2× 60 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 40:1). Yield 54% (2.18 g).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.09 (d, *J*=3.0 Hz, 1H), 5.90 (d, *J*=3.0 Hz, 1H), 4.17 (q, *J*=7.1 Hz, 2H), 3.62 (s, 2H), 2.57 (t, *J*=7.6 Hz, 2H), 1.60 (quin, *J*=7.5 Hz, 2H) 1.36-1.22 (m, 6H), 1.26 (t, *J*=7.1 Hz, 3H), 0.88 (t, *J*=6.8 Hz, 3H) ppm; ^{13}C NMR (125

[4] G. I. Ioannou, D. Kalaitzakis and G. Vassilikogiannakis, *Eur. J. Org. Chem.* 2016, 3304.

MHz, $CDCl_3$): δ = 169.7, 156.1, 145.6, 108.3, 105.4, 61.0, 34.2, 31.5, 28.8, 28.0, 27.9, 22.5, 14.1, 14.0 ppm.

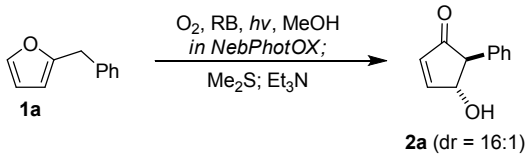
General procedure for the preparation of 4-hydroxy-cyclopent-2-enones of type 2



1a: R^1=H, R^2=Ph
1b: R^1=Me, R^2=Ph
1c: R^1=Me, R^2=*p*F-Ph
1d: R^1=pent-4-enyl, R^2=Ph
1f: R^1=Me, R^2=CO_2Et
1g: R^1=nC_6H_{13}, R^2=CO_2Et

Substituted furans **1a-d** and **1f-g** (2.5 mmol for **1a** or 5.0 mmol for **1b-d** and **1f-g**) and rose Bengal (1 mol%, 25.4 mg in case of **1a** or 50.8 mg in case of **1b-d** and **1f-g**) were dissolved in MeOH (total volume 5 mL, 0.5 M for **1a** or 1.0 M for **1b-d** and **1f-g**). The resulting solution was transferred to the nebulizer via a liquid pump (flow rate set at 0.5 mL/min) and timing was initiated for calculation of the exact flow rate. The solution was dispersed by the nebulizer into the reaction cylinder irradiated by the LEDs (natural white light 3800 - 4200 K, 10 W/m, 1050 Lm/m) using oxygen as the nebulizing gas (50 psi backpressure). When all the solution had been dispersed the exact flow rate was calculated and the three-way valve on the uptake line was switched to pure MeOH (2 mL) to flush out the system. The crude mixture was collected in the two cooled spherical flasks placed in series. A small sample of the crude mixture was concentrated *in vacuo* for the measurement of the conversions by ^{1}H NMR. Then, Me_2S (4 equiv, 730 μL, 10 mmol in case of **1a** or 1.46 mL, 20 mmol in case of **1b-d** and **1f-g**) was added and the solution was stirred for 1 h at rt. In many cases for the rapid reduction of hydroperoxide intermediates, the two cooled collection flasks were prefilled with excess of Me_2S in MeOH (see below). When the reduction was completed, as indicated by tlc, Et_3N (0.3 equiv, 105 μL, 0.75 mmol in case of **1a** or 209 μL, 1.5 mmol in case of **1b-d** and **1f-g**) was added and the mixture was stirred for 0.5 - 1 h at the same temperature. After completion of the reaction, a saturated aqueous solution of NH_4Cl (20 mL) was added and the mixture was extracted with EtOAc (3× 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc) to afford the corresponding 4-hydroxy-cyclopent-2-enones of type **2**.

For furan **1b** the same protocol was applied on a larger scale (50 mmol) with very similar results. The two cooled collection flasks placed in series were prefilled with excess of Me_2S in MeOH (3 equiv in the first flask and 1 equiv in the second flask), for the fast reduction of the initially formed hydroperoxides of type A and B (Scheme 1).

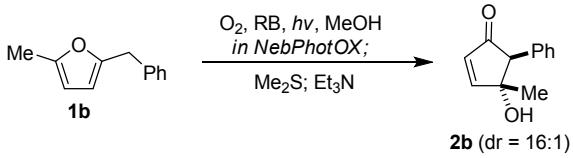


4-Hydroxy-5-phenylcyclopent-2-enone (2a)[2,5]

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1a** (395 mg, 2.5 mmol). Consumption of the 5 mL reaction solution took 8.45 min (actual flow rate = 0.59 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting solution was stirred at rt for a further 1 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 3:1). Yield 76% (330 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64 (dd, J_1=5.8 Hz, J_2=2.2 Hz, 1H), 7.36 (m, 2H), 7.30 (m, 1H), 7.15 (m, 2H), 6.36 (dd, J_1=5.8 Hz, J_2=1.3 Hz, 1H), 5.02 (m, 1H), 3.47 (d, J=2.9 Hz, 1H), 2.24 (d, J=6.1 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.4, 163.1, 136.5, 133.1, 128.4 (2C), 127.9 (2C), 126.9, 78.0, 61.3 ppm.

The relative configuration was assigned by comparing the reported NMR data from the literature[2,5] with our data.



4-Hydroxy-4-methyl-5-phenylcyclopent-2-enone (2b)[2,6]

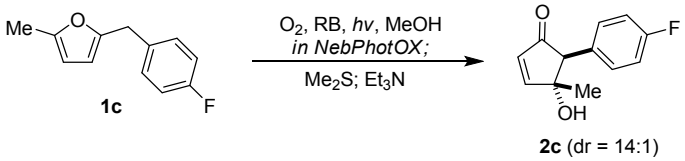
The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1b** (860 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.20 min (actual flow rate = 0.54 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the solution stirred at rt for a further 1h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 4:1). Yield 70% (658 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (d, J=5.8 Hz, 1H), 7.35 (m, 2H), 7.30 (m, 1H), 7.12 (m, 2H), 6.29 (d, J=5.8 Hz, 1H), 3.82 (s, 1H), 2.02 (brs, 1H), 1.07 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.1, 165.6, 135.2, 132.2, 129.8 (2C), 128.5 (2C), 127.4, 80.3, 65.5, 25.7 ppm.

The relative configuration was assigned by comparing the reported NMR data from the literature[2,6] with our data.

[5] G. Piancatelli, A. Scettri and S. Barbadoro, *Tetrahedron Lett.*, 1976, **17**, 3555.

[6] a) G. Piancatelli, A. Scettri, G. David and M. D'Auria, *Tetrahedron* 1978, **34**, 2775; b) M. D'Auria, *Heterocycles*, 2000, **52**, 185.



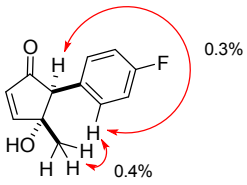
2c (dr = 14:1)

5-(4-Fluorophenyl)-4-hydroxy-4-methylcyclopent-2-enone (2c)

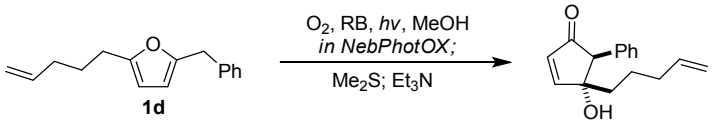
The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1c** (950 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 8.95 min (actual flow rate = 0.56 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting solution stirred at rt for a further 1h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 3:1). Yield 76% (784 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 (d, *J*=5.9 Hz, 1H), 7.10-7.02 (m, 4H), 6.25 (d, *J*=5.9 Hz, 1H), 3.79 (s, 1H), 2.37 (brs, 1H), 1.03 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.8, 165.7, 162.1 (d, *J*=246.1 Hz, F-Ph-C(ipso)), 132.0, 131.3 (d, *J*=8.0 Hz, F-Ph-C(meta), 2C), 130.9 (d, *J*=3.2 Hz, F-Ph-C(para)), 115.5 (d, *J*=21.3 Hz, F-Ph-C(ortho), 2C), 80.1, 64.7, 25.7 ppm; HRMS (TOF ESI): calcd for $C_{12}H_{12}FO_2$: 207.0816 $[M+H]^+$; found: 207.0816.

NOE



The relative configuration gives an upfield shift of the signal for the methyl group (1.03 ppm) as a result of the shielding effect from the aromatic ring when these two groups are *cis* configured.[6a]



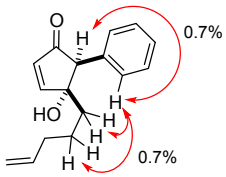
2d (dr = 8:1)

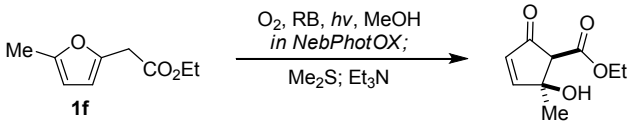
4-Hydroxy-4-(pent-4-enyl)-5-phenylcyclopent-2-enone (2d)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1d** (1.13 g, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.83 min (actual flow rate = 0.51 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting solutions stirred at rt for a further 1h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 8:1). Yield 67% (811 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 (d, *J*=5.9 Hz, 1H), 7.35 (m, 2H), 7.30 (m, 1H), 7.16 (m, 2H), 6.33 (d, *J*=5.9 Hz, 1H), 5.58 (m, 1H), 4.86 (m, 2H), 3.84 (s, 1H), 2.08 (brs, 1H), 1.82 (m, 2H), 1.40-1.23 (m, 4H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.4, 164.1, 137.8, 134.5, 132.9, 129.9 (2C), 128.4 (2C), 127.4, 114.9, 82.5, 66.0, 38.5, 33.7, 23.0 ppm; HRMS (TOF ESI): calcd for $C_{16}H_{19}O_2$: 243.1380 $[M+H]^+$; found: 243.1371.

NOE





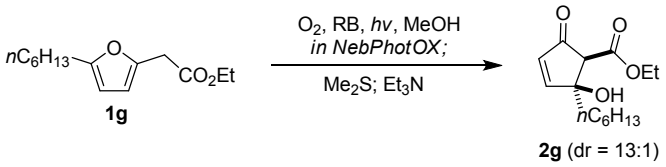
Ethyl 2-hydroxy-2-methyl-5-oxocyclopent-3-enecarboxylate (2f)[2]

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1f** (840 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.27 min (actual flow rate = 0.49 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting solution stirred at rt for a further 0.5 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 2:1). Yield 61% (561 mg). The diastereomeric ratio of the easily epimerizable product **2f** was determined as being 5:1 in the crude reaction mixture and 2:1 after the chromatographic purification.

For this substrate (**1f**), the procedure was repeated a number of times using air as the nebulizing gas for different initial substrate concentrations (Table 2 in main text of paper). These latter experiments were conducted with the pyrex reaction chamber placed in a vertical position. Exact flow rates were between 0.55 – 0.62 mL/min and isolated yields varied from 48 – 69 % (see, Table 2). In all other aspects these procedures were identical to the one described above.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 (d, *J*=5.7 Hz, 1H for major), 7.42 (d, *J*=5.7 Hz, 1H for minor), 6.12 (d, *J*=5.7 Hz, 1H for minor plus 1H for major), 4.20 (m, 2H for major plus 2H for minor), 3.78 (s, 1H for major), 3.46 (s, 1H for minor), 3.38 (s, 1H for major), 1.53 (s, 3H for major), 1.48 (s, 3H for minor), 1.28 (t, *J*=7.2 Hz, 3H for major), 1.26 (t, *J*=7.2 Hz, 3H for minor) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 201.0 (minor), 200.1 (major), 168.3 (1C for major plus 1C minor), 167.5 (major), 165.9 (minor), 131.8 (1C for major plus 1C minor), 78.8 (minor), 77.2 (major), 64.3 (minor), 62.4 (major), 62.0 (major), 61.3 (minor), 27.4 (major), 23.9 (minor), 14.1 (minor), 14.0 (major) ppm.

The relative configuration was assigned by comparing the reported NMR data from the literature.[2]

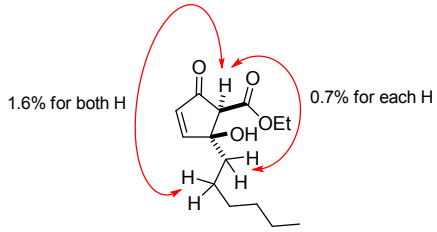


Ethyl 2-hexyl-2-hydroxy-5-oxocyclopent-3-enecarboxylate (2g)

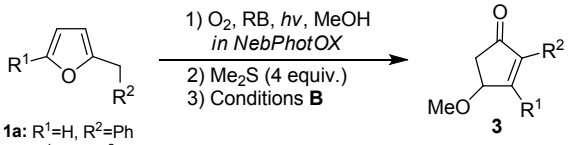
The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1g** (1.19 g, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.90 min (actual flow rate = 0.46 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting solution stirred at rt for a further 1h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 2:1). Yield 47% (597 mg). The diastereomeric ratio of the easily epimerizable product **2g** was determined as being 3:1 in the crude reaction mixture and 13:1 after the chromatographic purification.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (d, *J*=5.7 Hz, 1H), 6.18 (d, *J*=5.7 Hz, 1H), 4.24 (q, *J*=7.1 Hz, 2H), 3.70 (s, 1H), 3.44 (s, 1H), 1.81 (m, 1H), 1.69 (m, 1H), 1.43-1.24 (m, 8H), 1.31 (t, *J*=6.8, 3H), 0.88 (t, *J*=6.9, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 200.1, 168.7, 167.2, 132.3, 79.8, 62.1, 60.9, 40.3, 31.6, 29.4, 23.8, 22.5, 14.0 (2C) ppm; HRMS (TOF ESI): calcd for $C_{14}H_{21}O_4$: 253.1445 $[M-H]^-$; found: 253.1435.

NOE



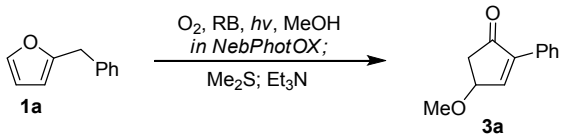
General procedure for the preparation of 4-methoxy-2-cyclopentenones of type 3



1a: R^1=H, R^2=Ph
1b: R^1=Me, R^2=Ph
1c: R^1=Me, R^2=*p*F-Ph
1d: R^1=pent-4-enyl, R^2=Ph
1e: R^1=Me, R^2=nC_5H_{11}
1f: R^1=Me, R^2=CO_2Et
1g: R^1=nC_6H_{13}, R^2=CO_2Et

Substituted furans **1a-1g** (2.5 mmol for **1a** or 5.0 mmol for **1b-1g**) and rose Bengal (1 mol%, 25.4 mg in case of **1a** or 50.8 mg in case of **1b-1g**) were dissolved in MeOH (total volume 5 mL, 0.5 M for **1a** or 1.0 M for **1b-1g**). The resulting solution was transferred to the nebulizer via a liquid pump (flow rate set at 0.5 mL/min) and timing was initiated for calculation of the exact flow rate. The solution was dispersed by the nebulizer into the reaction cylinder irradiated by the LEDs (natural white light 3800 - 4200 K, 10 W/m, 1050 Lm/m) using oxygen as the nebulizing gas (50 psi backpressure). When all the solution had been dispersed the exact flow rate was calculated and the three-way valve on the uptake line was switched to pure MeOH (2

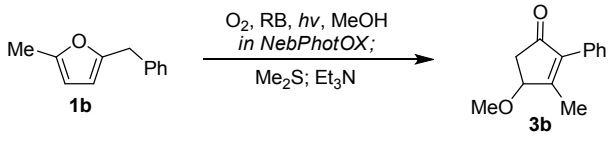
mL) to flush out the system. The flow rate was measured based on the time needed for the nebulization of 5 mL of photooxidation solution. The crude solution was collected in the two cooled spherical flasks placed in series. A small sample of the crude solution was concentrated *in vacuo* for the measurement of the conversion by ^{1}H NMR. Then, Me_2S (4.0 equiv, 730 µL, 10 mmol in case of **1a** or 1.46 mL, 20 mmol in case of **1b-1g**) was added and the solution was stirred for 1 h at rt. In many cases for the rapid reduction of hydroperoxide intermediates, the two cooled collection flasks were prefilled with excess of Me_2S in MeOH. When the reduction was completed, as indicated by tlc, Et_3N (0.5 equiv, 348 µL, 2.5 mmol in case of **1b-1d** and **1f**, or 174 µL, 1.25 mmol in case of **1a** or 1.0 equiv, 696 µL, 5.0 mmol in case of **1g**) or NaOH (1.5 equiv, 300 mg, 7.5 mmol in case of **1e**) was added and the solution was stirred for 1 - 12 h at the same temperature. After the completion of the reaction, a saturated aqueous solution of NH_4Cl (20 mL) was added and the mixture was extracted with EtOAc (3× 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc) to afford the corresponding 4-methoxy-cyclopent-2-enones of type **3**.



4-Methoxy-2-phenylcyclopent-2-enone (3a)[2,7]

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1a** (395 mg, 2.5 mmol). Consumption of the 5 mL reaction solution took 9.15 min (actual flow rate = 0.55 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting solution stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 6:1). Yield 65% (306 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.70 (m, 3H), 7.39 (m, 3H), 4.62 (dt, J_1=5.9 Hz, J_2=2.4 Hz, 1H), 3.48 (s, 3H), 2.91 (dd, J_1=18.3 Hz, J_2=5.9 Hz, 1H), 2.54 (dd, J_1=18.2 Hz, J_2=2.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.4, 154.0, 144.5, 130.4, 128.9, 128.3 (2C), 127.4 (2C), 75.9, 56.8, 42.7 ppm.



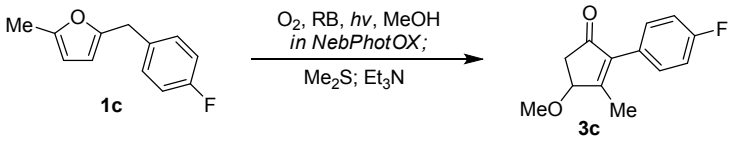
4-Methoxy-3-methyl-2-phenylcyclopent-2-enone (3b)[2,8]

[7] K. Tanaka and G. C. Fu, *J. Am. Chem. Soc.*, 2003, **125**, 8078.

[8] C. A. Challener, W. D. Wulff, B. A. Anderson, S. Chamberlin, K. L. Faron, O. K. Kim, C. K. Murray, Y.-C. Xu, D. C. Yang and S. D. Darling, *J. Am. Chem. Soc.*, 1993, **115**, 1359.

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1b** (860 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.25 min (actual flow rate = 0.54 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting solution stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 6:1). Yield 75% (757 mg).

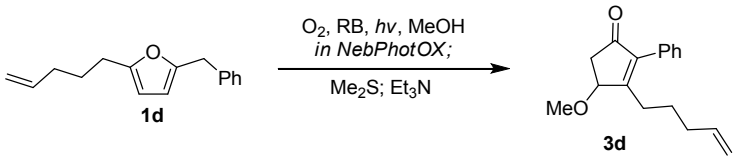
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41 (m, 2H), 7.32 (m, 3H), 4.46 (m, 1H), 3.47 (s, 3H), 2.81 (dd, J_1=18.1 Hz, J_2=5.9 Hz, 1H), 2.49 (dd, J_1=18.1 Hz, J_2=2.1 Hz, 1H), 2.20 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.2, 168.2, 141.7, 130.7, 129.1 (2C), 128.2 (2C), 128.0, 79.6, 57.3, 40.9, 14.9 ppm.



2-(4-Fluorophenyl)-4-methoxy-3-methylcyclopent-2-enone (3c)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1c** (950 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.22 min (actual flow rate = 0.54 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting solution stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 3:1). Yield 69% (759 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30 (m, 2H), 7.10 (m, 2H), 4.44 (m, 1H), 3.47 (s, 3H), 2.80 (dd, J_1=18.1 Hz, J_2=6.0 Hz, 1H), 2.48 (dd, J_1=18.1 Hz, J_2=2.2 Hz, 1H), 2.19 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.1, 168.2, 162.5 (d, J=247.5 Hz, F-Ph-C(ipso)), 140.7, 130.9 (d, J=8.2 Hz, F-Ph-C(meta), 2C), 126.7 (d, J=3.4 Hz, F-Ph-C(para)), 115.3 (d, J=21.6 Hz, F-Ph-C(ortho), 2C), 79.6, 57.4, 40.9, 15.0 ppm; HRMS (TOF ESI): calcd for $C_{13}H_{14}FO_2$: 221.0972 $[M+H]^+$; found: 221.0976.

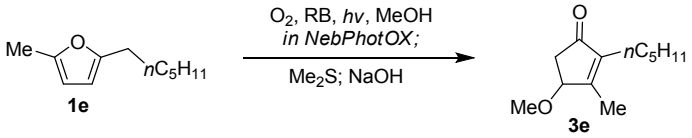


4-Methoxy-3-(pent-4-enyl)-2-phenylcyclopent-2-enone (3d)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1d** (1.13 g, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.63 min (actual flow rate = 0.52 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting solution stirred at rt for further 12 h. The product was purified by

flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1). Yield 71% (909 mg).

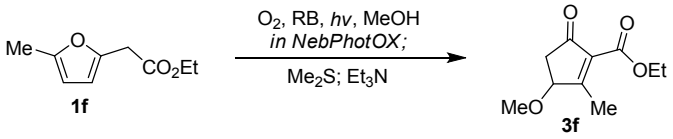
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41 (m, 2H), 7.34 (m, 1H), 7.25 (m, 2H), 5.75 (m, 1H), 4.96 (m, 2H), 4.58 (dd, J_1=6.0 Hz, J_2=2.1 Hz, 1H), 3.46 (s, 3H), 2.81 (dd, J_1=18.1 Hz, J_2=5.9 Hz, 1H), 2.59 (m, 2H), 2.48 (dd, J_1=18.1 Hz, J_2=2.2 Hz, 1H), 2.07 (m, 2H), 1.74 (m, 1H), 1.59 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.2, 171.6, 141.9, 137.5, 130.8, 128.9 (2C), 128.1 (2C), 127.9, 115.1, 77.4, 57.2, 40.8, 33.5, 27.6, 26.5 ppm; HRMS (TOF ESI): calcd for $C_{17}H_{21}O_2$: 257.1536 $[M+H]^+$; found: 257.1531.



2-Hexyl-4-methoxy-3-methylcyclopent-2-enone (3e)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1e** (830 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.58 min (actual flow rate = 0.47 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by NaOH and the resulting solution stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1). Yield 50% (490 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.30 (brd, J=5.7 Hz, 1H), 3.38 (s, 3H), 2.61 (dd, J_1=18.1 Hz, J_2=5.9 Hz, 1H), 2.26 (dd, J_1=18.1 Hz, J_2=1.7 Hz, 1H), 2.16 (m, 2H), 2.04 (s, 3H), 1.37 (m, 2H), 1.27 (m, 4H), 0.86 (t, J=7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.1, 166.8, 142.9, 79.7, 56.9, 40.5, 31.7, 27.7, 22.8, 22.4, 13.9 (2C) ppm; HRMS (TOF ESI): calcd for $C_{12}H_{21}O_2$: 197.1536 $[M+H]^+$; found: 197.1528.

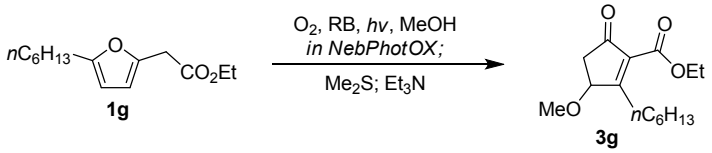


Ethyl 3-methoxy-2-methyl-5-oxocyclopent-1-enecarboxylate (3f)[2]

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1f** (840 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.22 min (actual flow rate = 0.49 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting solution stirred at rt for a further 1 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 3:1). Yield 57% (564 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.37 (dd, J_1=6.1 Hz, J_2=2.6 Hz, 1H), 4.32 (q, J=7.1 Hz, 2H), 3.43 (s, 3H), 2.74 (dd, J_1=18.1 Hz, J_2=6.1 Hz, 1H), 2.41 (dd, J_1=18.1 Hz,

J_2=2.6 Hz, 1H), 2.35 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.7, 179.1, 162.5, 133.6, 79.0, 60.8, 57.4, 41.0, 15.5, 13.9 ppm.

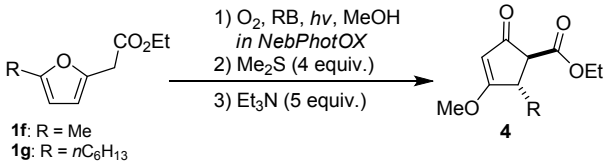


Ethyl 2-hexyl-3-methoxy-5-oxocyclopent-1-enecarboxylate (3g)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1g** (1.19 g, 5.0 mmol). Consumption of the 5 mL reaction solution took 9.83 min (actual flow rate = 0.51 mL/min). Then Me_2S (1.46 mL, 20 mmol, 4.0 equiv.) was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N (696 µL, 5 mmol, 1 equiv.) and the resulting solution stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 6:1). Yield 40% (536 mg).

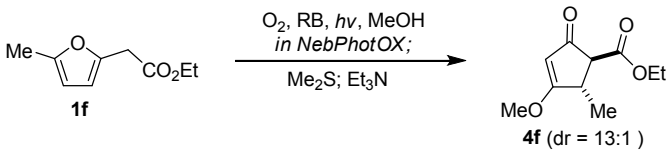
^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.46 (dd, J_1=6.1 Hz, J_2=2.6 Hz, 1H), 4.31 (q, J=7.1 Hz, 2H), 3.41 (s, 3H), 2.81 (ddd, J_1=12.7 Hz, J_2=9.6 Hz, J_3=6.5 Hz, 1H), 2.74 (dd, J_1=18.1 Hz, J_2=6.1 Hz, 1H), 2.63 (ddd, J_1=12.7 Hz, J_2=9.6 Hz, J_3=5.6 Hz, 1H), 2.40 (dd, J_1=18.1 Hz, J_2=2.6 Hz, 1H), 1.57 (m, 2H), 1.39-1.26 (m, 6H), 1.33 (t, J = 7.1 Hz, 3H), 0.88 (t, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 199.2, 182.3, 162.9, 133.9, 77.6, 61.1, 57.6, 41.3, 31.4, 29.5, 29.0, 27.7, 22.5, 14.1, 14.0 ppm; HRMS (TOF ESI): calcd for $C_{15}H_{25}O_4$: 269.1747 $[M+H]^+$; found: 269.1753.

General procedure for the preparation of ethyl 4-methoxy-2-oxocyclopent-3-enecarboxylate of type 4



Substituted furans **1f** or **1g** (5.0 mmol) and rose Bengal (1 mol%, 50.8 mg) were dissolved in MeOH (total volume 5 mL, 1 M final concentration). The resulting solution was transferred to the nebulizer via a liquid pump (flow rate set at 0.5 mL/min) and timing was initiated for calculation of the exact flow rate. The solution was dispersed by the nebulizer into the reaction cylinder irradiated by the LEDs (natural white light 3800 - 4200 K, 10 W/m, 1050 Lm/m) using oxygen as the nebulizing gas (50 psi backpressure). When all the solution had been dispersed the exact flow rate was calculated and the three-way valve on the uptake line was switched to pure MeOH (2 mL) to flush out the system. The crude mixture was collected in the two cooled spherical flasks placed in series. A small sample of the crude mixture was concentrated *in vacuo* for the measurement of the conversion by ^{1}H NMR. Then, Me_2S (4.0 equiv, 1.46 mL, 20 mmol) was added and the solution was stirred for 1 h at rt. In many cases for the rapid reduction of hydroperoxide intermediates, the two cooled collection flasks were prefilled with excess of Me_2S in

MeOH. When the reduction was completed as indicated by tlc, Et_3N (5.0 equiv, 3.48 mL, 25 mmol) was added and the mixture was stirred for 12 – 48 h at the same temperature. After completion of the reaction, a saturated aqueous solution of NH_4Cl (20 mL) was added and the mixture was extracted with EtOAc (3× 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, petroleum ether:EtOAc) to afford the corresponding ethyl 4-methoxy-2-oxocyclopent-3-enecarboxylates of type **4**.

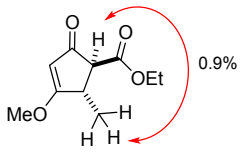


Ethyl 3-methoxy-2-methyl-5-oxocyclopent-3-ene-1-carboxylate (4f)

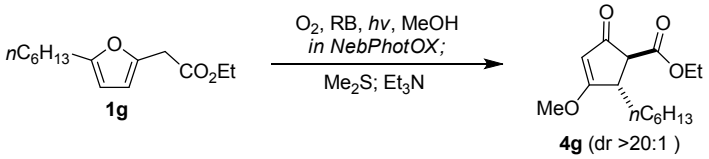
The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1f** (840 mg, 5.0 mmol). Consumption of the 5 mL reaction solution took 10.18 min (actual flow rate = 0.49 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N and the resulting mixture stirred at rt for further 12 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 3:1). Yield 62% (614 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.23 (s, 1H), 4.22 (q, *J*=7.1 Hz, 2H), 3.87 (s, 3H), 3.26 (qd, J_1=7.1 Hz, J_2=3.0 Hz, 1H), 3.11 (d, *J*=3.0 Hz, 1H), 1.30 (t, *J*=7.1 Hz, 3H), 1.27 (d, *J*=7.3 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.1, 193.3, 169.0, 101.7, 61.5, 60.2, 59.1, 39.2, 17.0, 14.1 ppm; HRMS (TOF ESI): calcd for $C_{10}H_{15}O_4$: 199.0965 $[M+H]^+$; found: 199.0963.

NOE



The *J* coupling of 3.0 Hz for the hydrogen at 3.11 ppm indicates a *trans* relative configuration.[5]



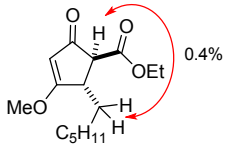
Ethyl 2-hexyl-3-methoxy-5-oxocyclopent-3-ene-1-carboxylate (4g)

The reaction was accomplished according to the general experimental procedure described above, utilizing furan **1g** (1.19 g, 5.0 mmol), Consumption of the 5 mL reaction solution took 10.68 min (actual flow rate = 0.47 mL/min). Then Me_2S was added followed later, after completion of the reduction (as indicated by tlc), by Et_3N

and the resulting mixture stirred at rt for further 48 h. The product was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1). Yield 47% (630 mg).

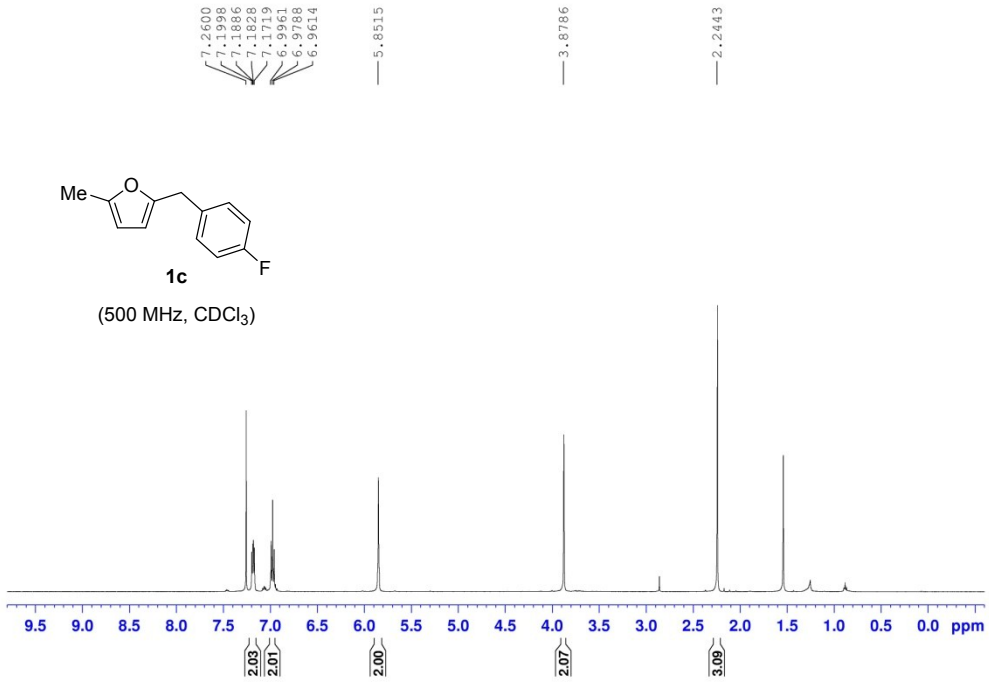
^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.24 (d, *J*=0.8 Hz, 1H), 4.22 (q, *J*=7.1 Hz, 2H), 3.86 (s, 3H), 3.20 (m, 1H), 3.17 (d, *J*=3.0 Hz, 1H), 1.83 (m, 1H), 1.38 (m, 1H), 1.29 (t, *J*=7.0 Hz, 3H), 1.26 (m, 8H), 0.88 (t, *J*=6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.4, 192.8, 169.3, 102.1, 61.4, 59.1, 58.2, 44.5, 31.5, 31.2, 28.9, 26.5, 22.4, 14.1, 13.9 ppm; HRMS (TOF ESI): calcd for $C_{15}H_{25}O_4$: 269.1747 $[M+H]^+$; found: 269.1747 .

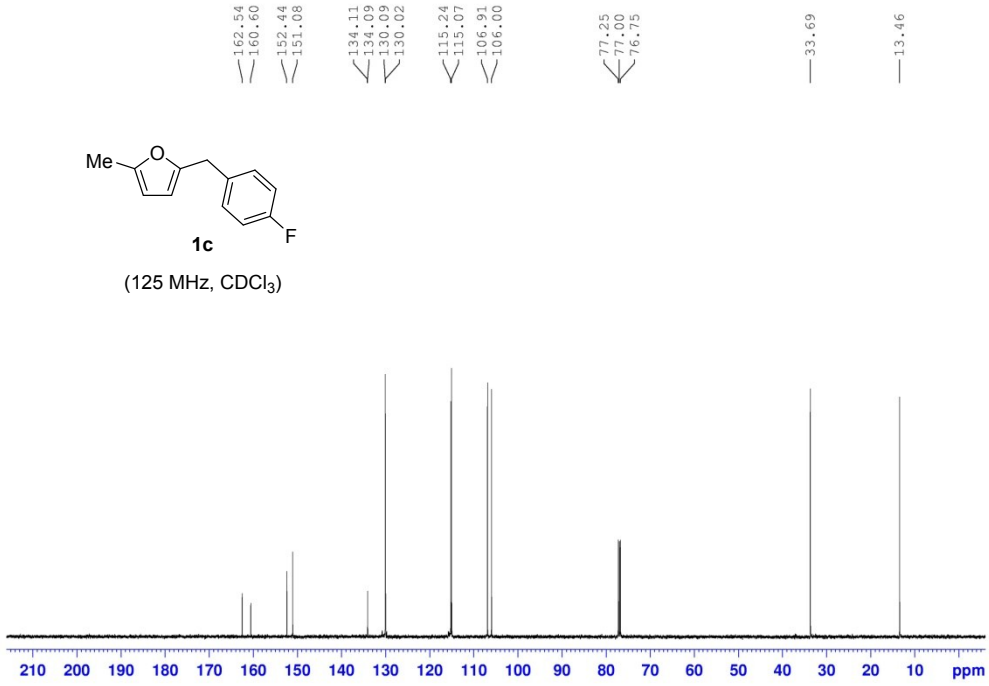
NOE

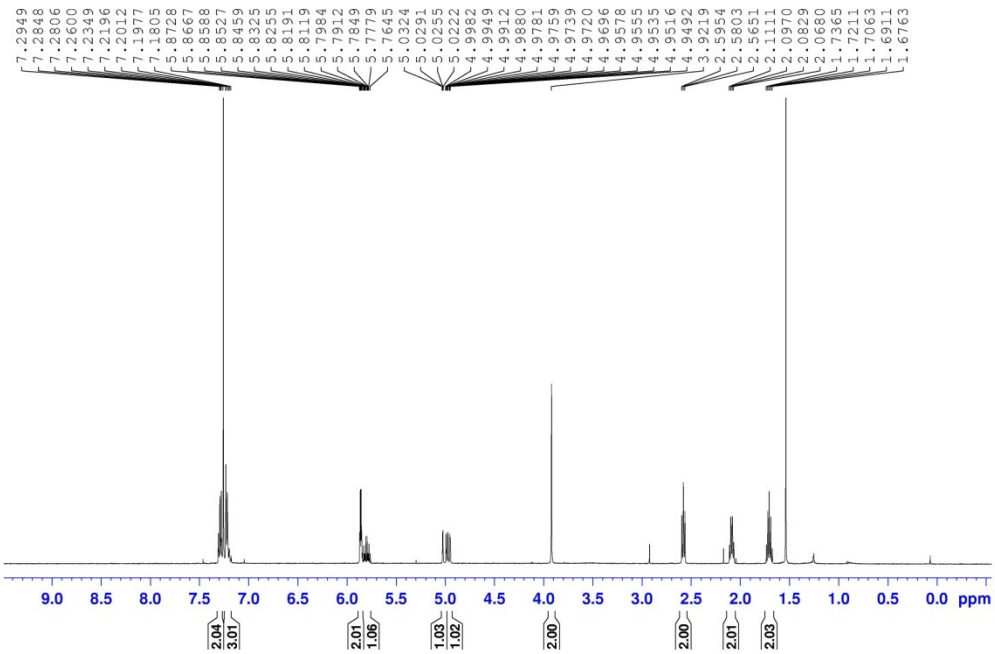


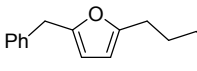
The *J* coupling of 3.0 Hz for the hydrogen at 3.17 ppm indicates a *trans* relative configuration.[5]

Part C: Copies of ^{1}H-NMR, ^{13}C-NMR and NOE spectra



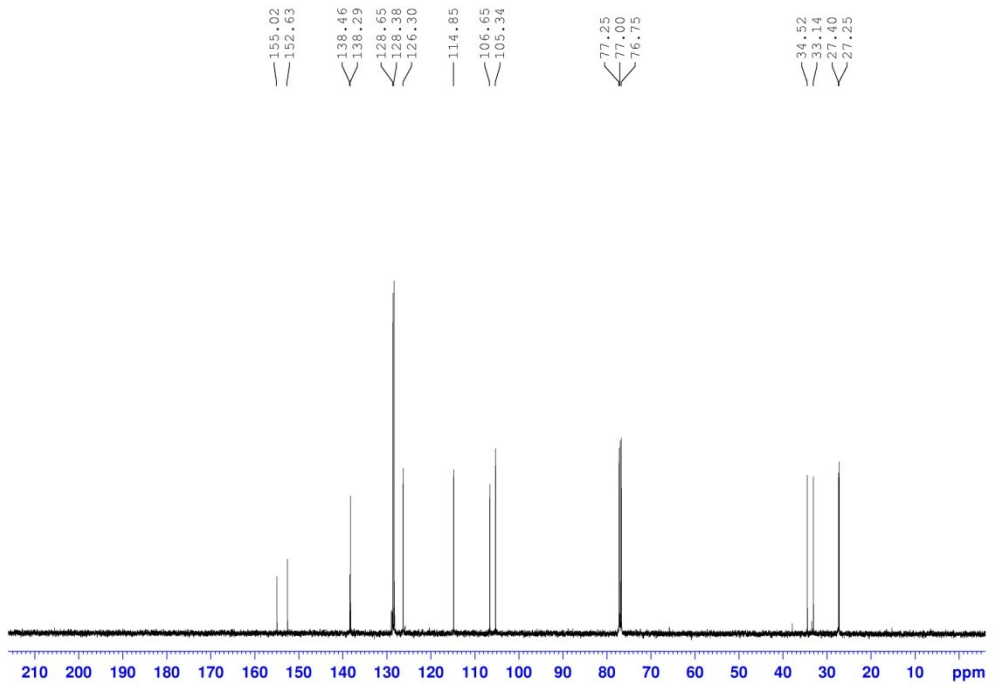


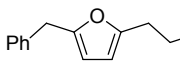




1d

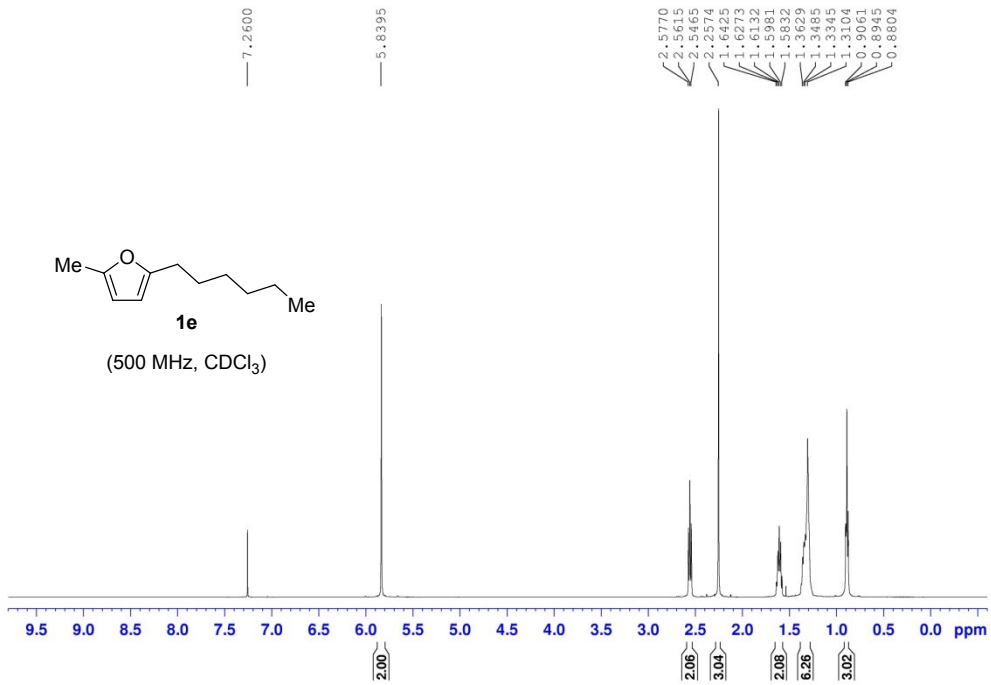
(500 MHz, $CDCl_3$)

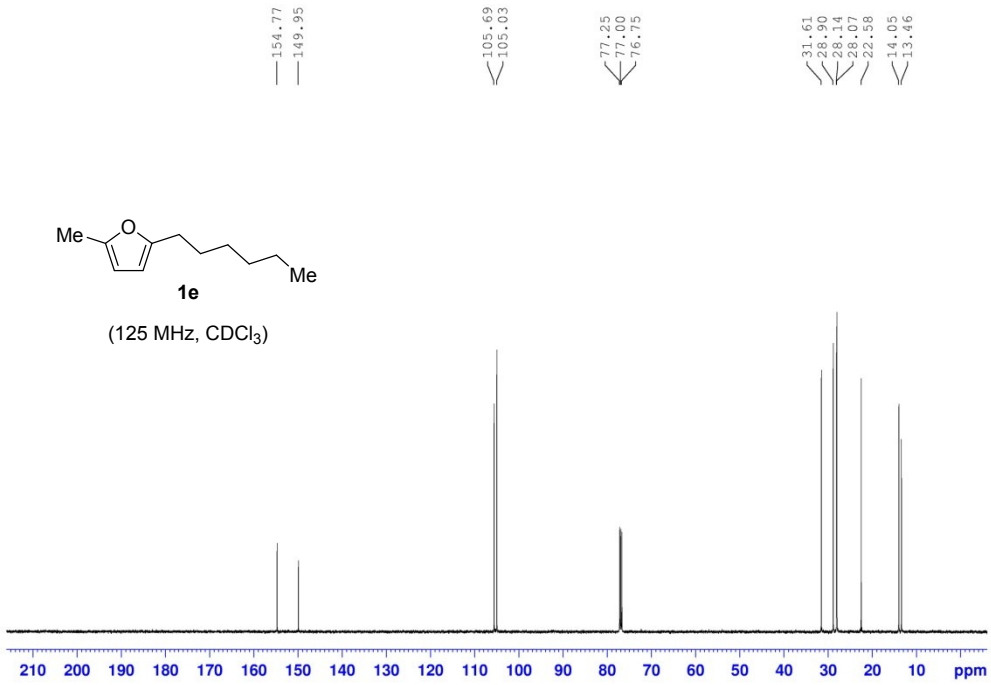


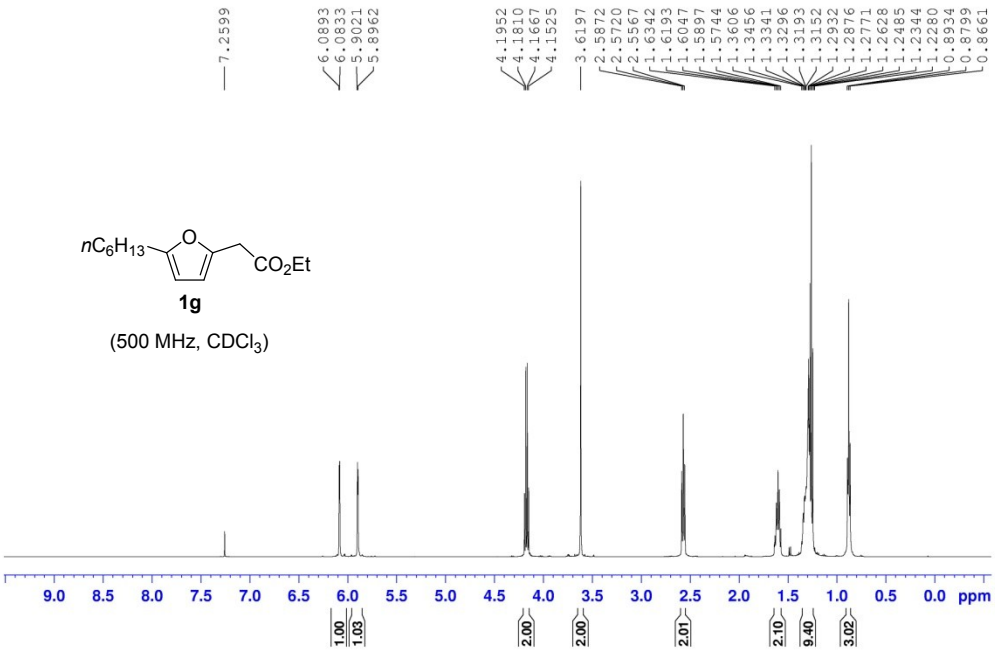


1d

(125 MHz, $CDCl_3$)

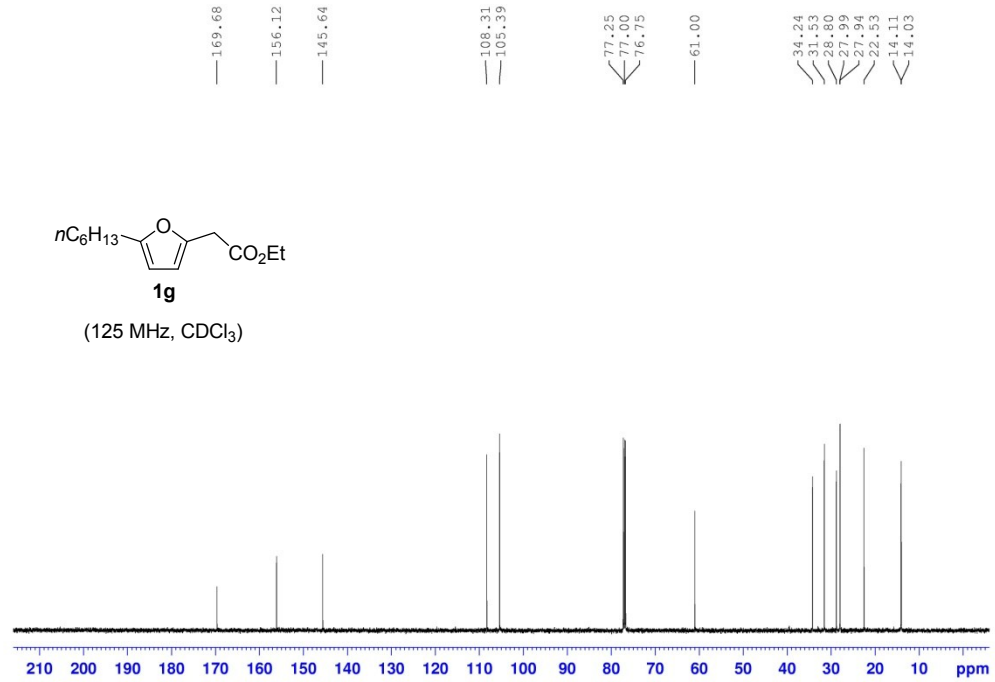

7.2600
5.8395
2.5770
2.5615
2.5465
2.2374
1.6425
1.6273
1.6132
1.5981
1.5832
1.3629
1.3485
1.3345
1.3104
0.9061
0.8945
0.8804
Me
O
Me
1e
(500 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.00
2.06
3.04
2.08
6.26
3.02


154.77
149.95
105.69
105.03
77.25
77.00
76.75
31.61
28.90
28.14
28.07
22.58
14.05
13.46
Me
O
Me
1e
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



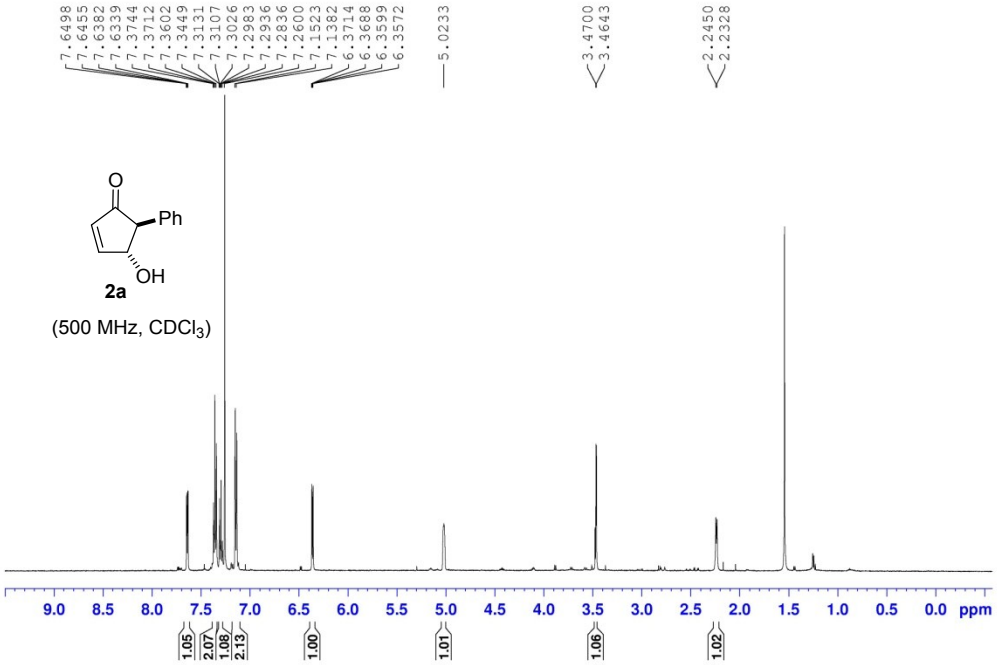
1g

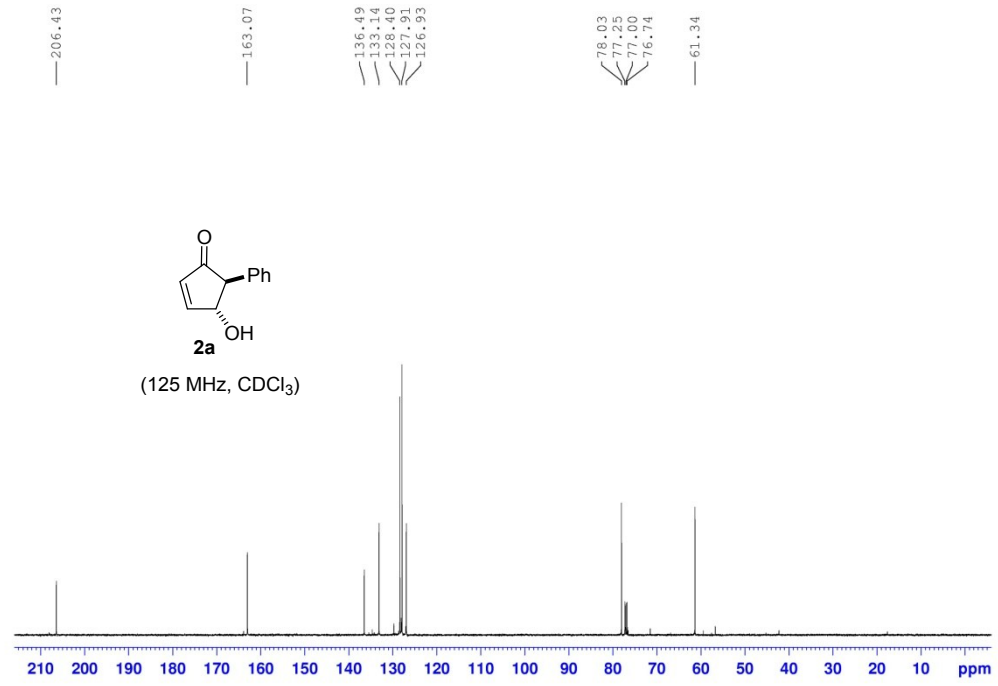
(500 MHz, $CDCl_3$)

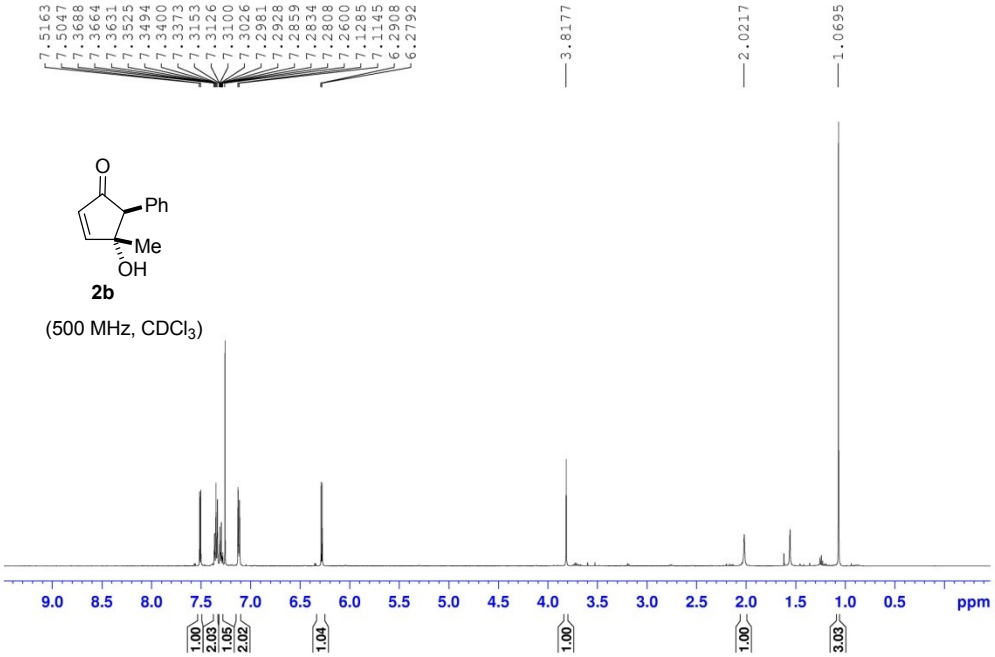


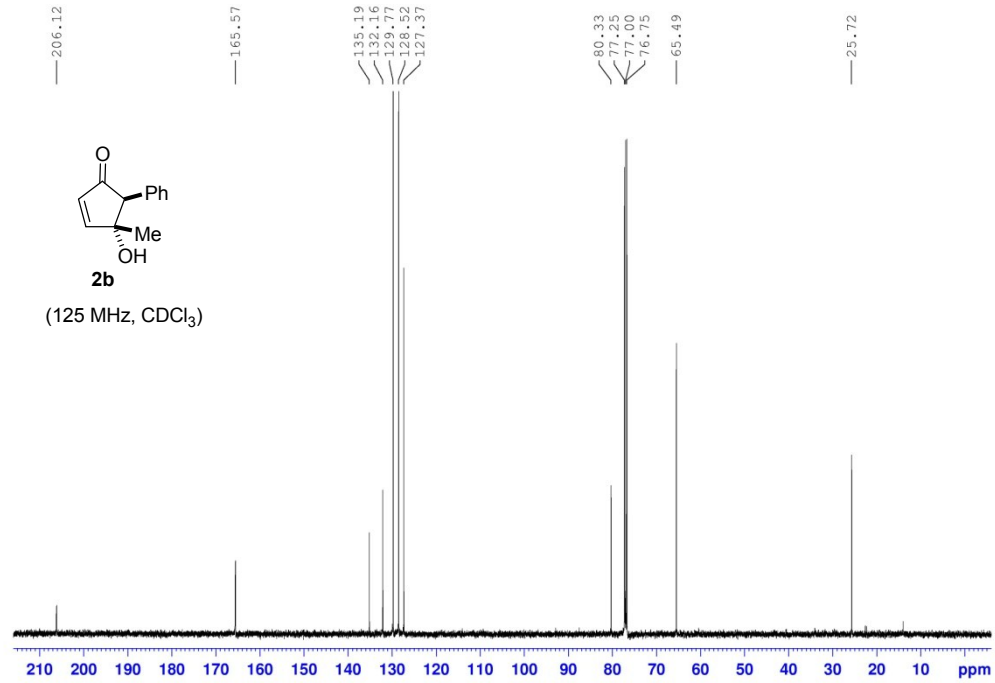
1g

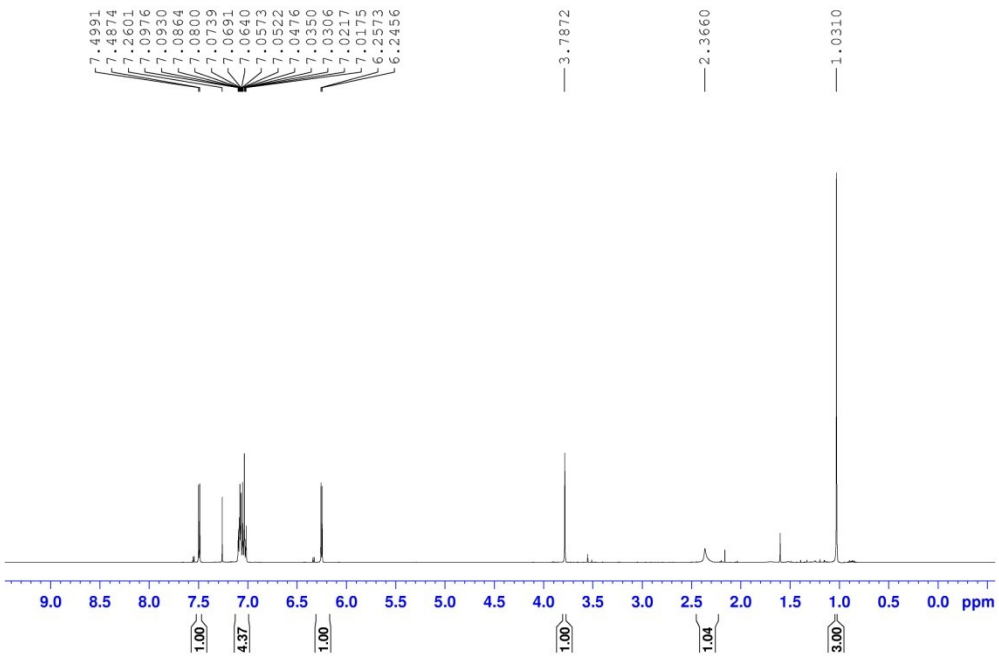
(125 MHz, $CDCl_3$)


7.6498
7.6455
7.6382
7.6339
7.3744
7.3712
7.3602
7.3449
7.3131
7.3107
7.3026
7.2983
7.2936
7.2836
7.2600
7.1523
7.1382
6.3714
6.3688
6.3599
6.3572
5.0233
3.4700
3.4643
2.2450
2.2328
O
Ph
OH
2a
(500 MHz, CDCl3)
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 ppm
1.05
2.07
1.08
2.13
1.00
1.01
1.06
1.02

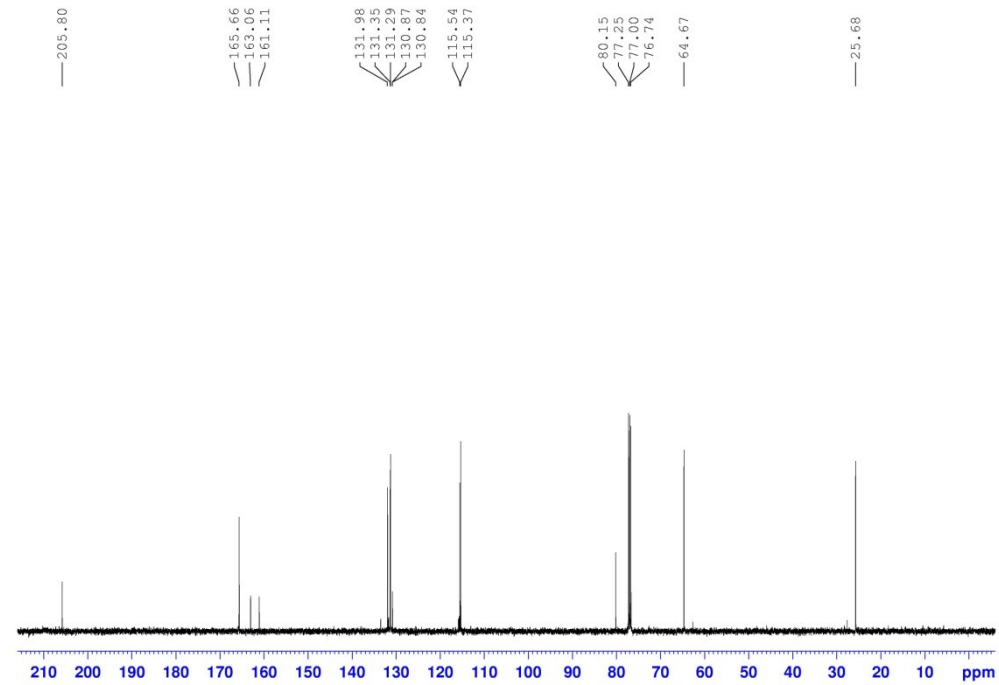

206.43
163.07
136.49
133.14
128.40
127.91
126.93
78.03
77.25
77.00
76.74
61.34
O
Ph
OH
2a
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.5163
7.5047
7.3688
7.3664
7.3631
7.3525
7.3494
7.3400
7.3373
7.3153
7.3126
7.3100
7.3026
7.2981
7.2928
7.2859
7.2834
7.2808
7.2600
7.1285
7.1145
6.2908
6.2792
3.8177
2.0217
1.0695
O
Ph
Me
OH
2b
(500 MHz, CDCl3)
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 ppm
1.00
2.03
1.05
2.02
1.04
1.00
1.00
3.03


206.12
165.57
135.19
132.16
129.77
128.52
127.37
80.33
77.25
77.00
76.75
65.49
25.72
O
Ph
Me
OH
2b
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

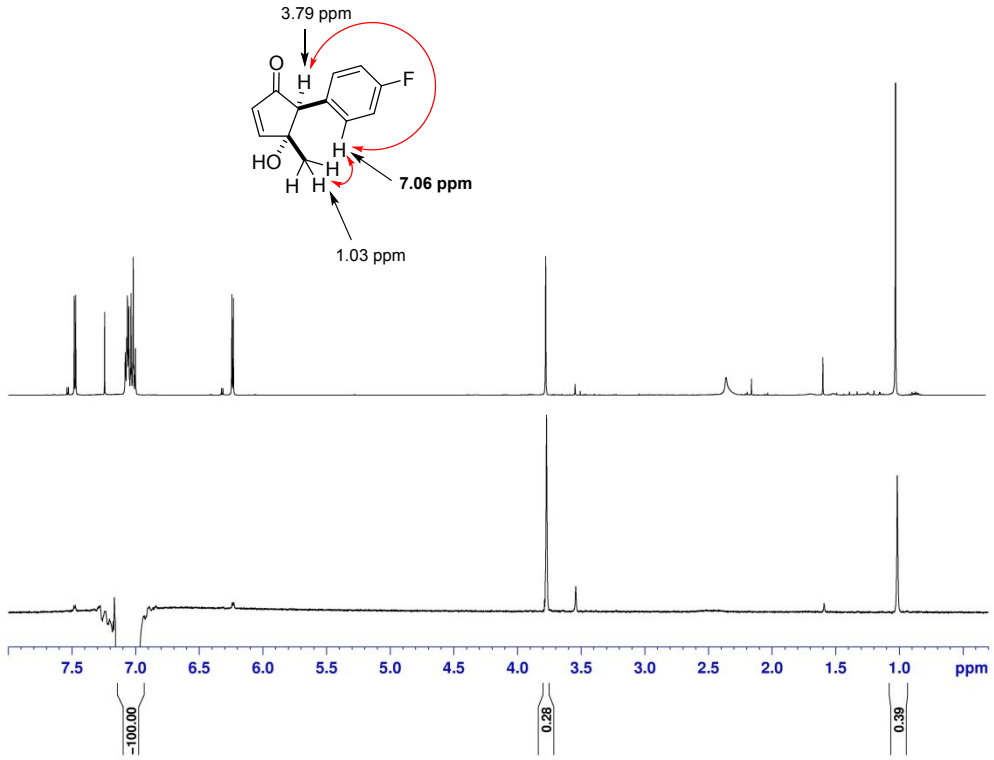

7.4991
7.4874
7.2601
7.0976
7.0930
7.0864
7.0800
7.0739
7.0691
7.0640
7.0573
7.0522
7.0476
7.0350
7.0306
7.0217
7.0175
6.2573
6.2456
3.7872
2.3660
1.0310
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
4.37
1.00
1.00
1.04
3.00

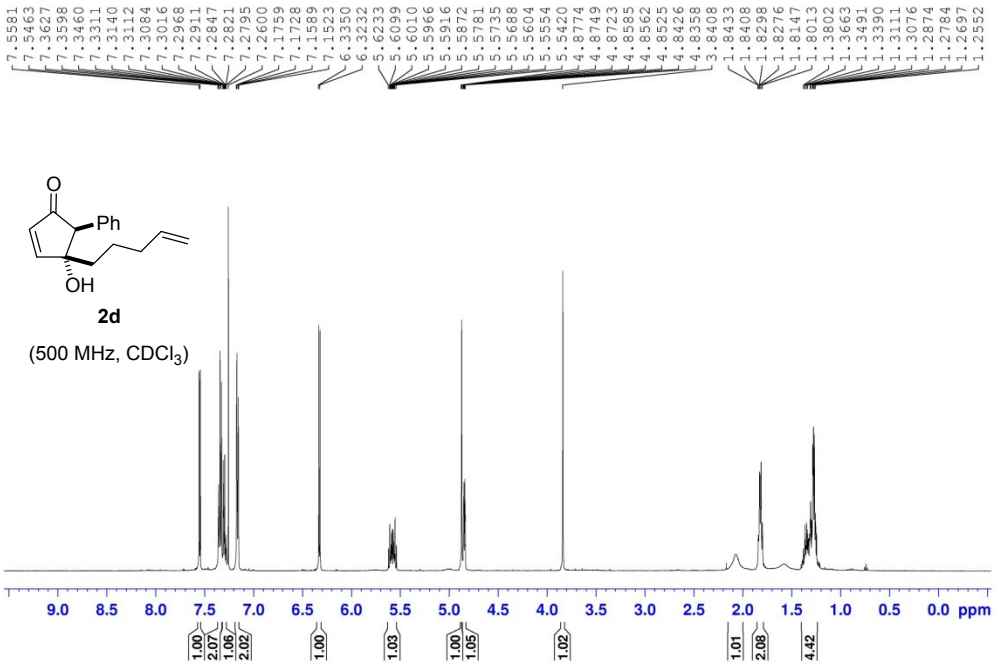
(500

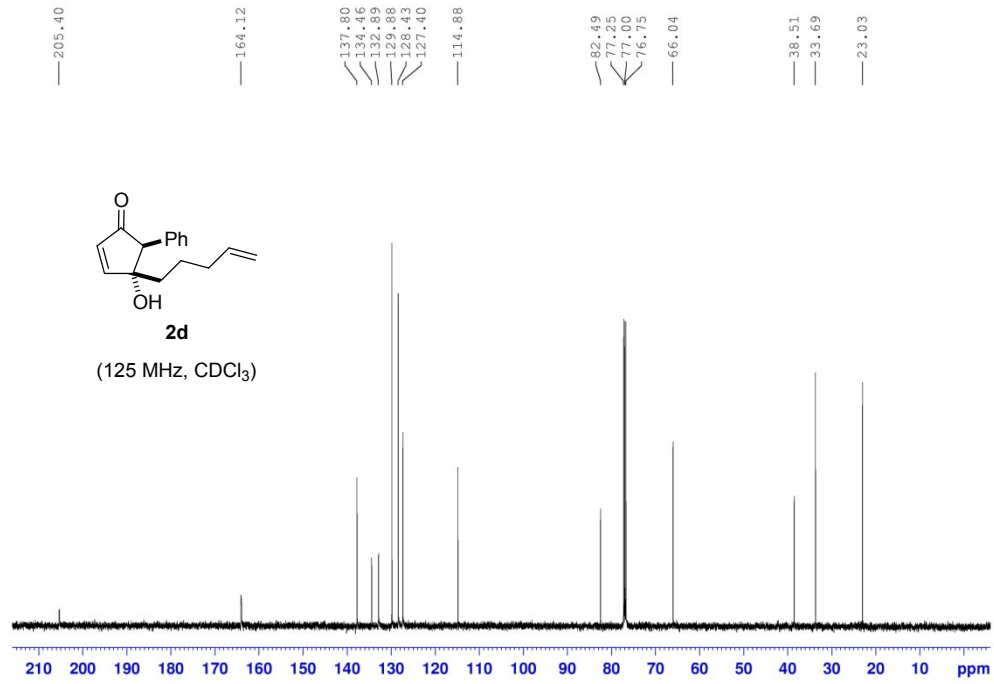

205.80
165.66
163.06
161.11
131.98
131.35
131.29
130.87
130.84
115.54
115.37
80.15
77.25
77.00
76.74
64.67
25.68
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

(125

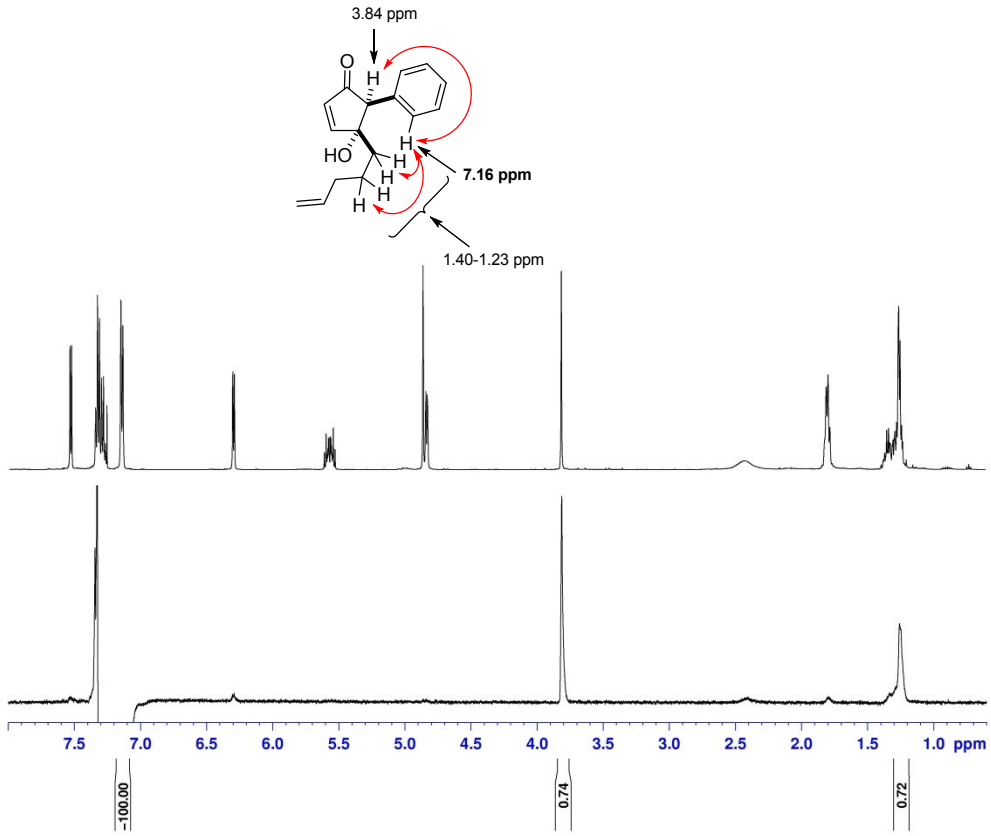
NOE experiment of compound **2c** at 7.06 ppm

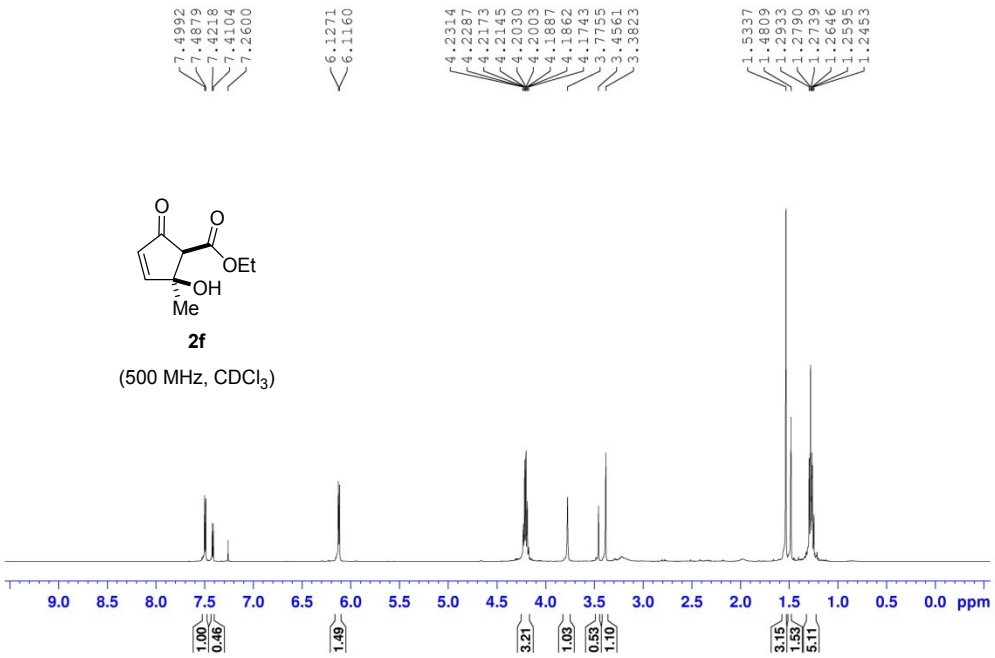


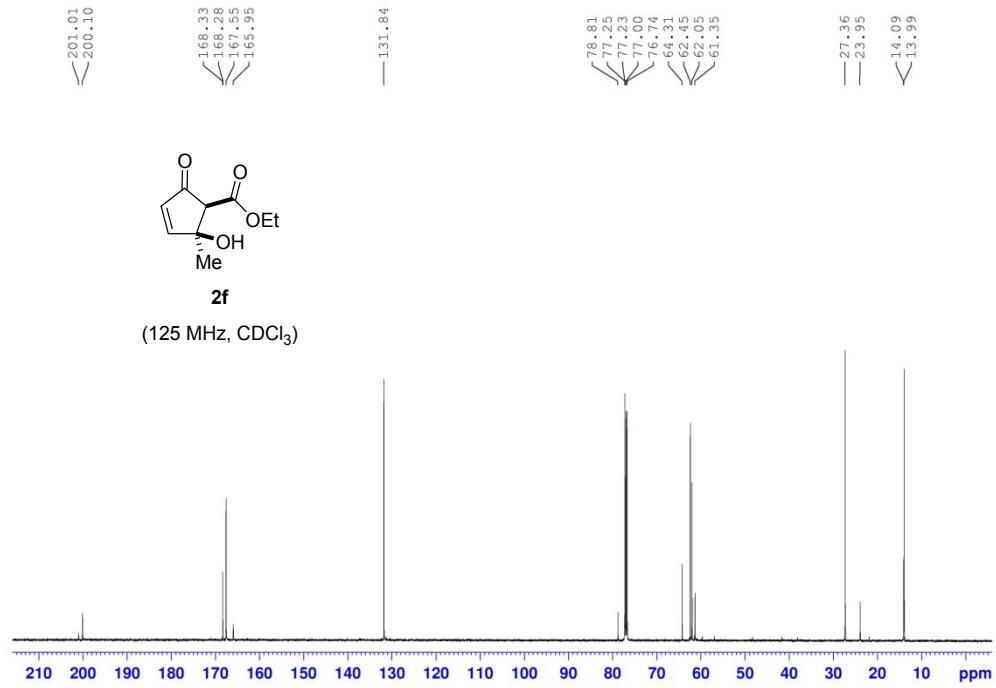

7.5581
7.5463
7.3627
7.3598
7.3460
7.3311
7.3140
7.3112
7.3084
7.3016
7.2968
7.2911
7.2847
7.2821
7.2795
7.2600
7.1759
7.1728
7.1589
7.1523
6.3350
6.3232
5.6233
5.6099
5.6010
5.5966
5.5916
5.5872
5.5781
5.5735
5.5688
5.5604
5.5554
5.5420
4.8774
4.8749
4.8723
4.8585
4.8562
4.8525
4.8426
4.8358
3.8408
1.8433
1.8408
1.8298
1.8276
1.8147
1.8013
1.3802
1.3663
1.3491
1.3390
1.3111
1.3076
1.2874
1.2784
1.2697
1.2552
O
Ph
OH
2d
(500 MHz, CDCl3)
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 ppm
1.00 2.07 1.06 2.02 1.00 1.03 1.00 1.05 1.02 1.01 2.08 4.42

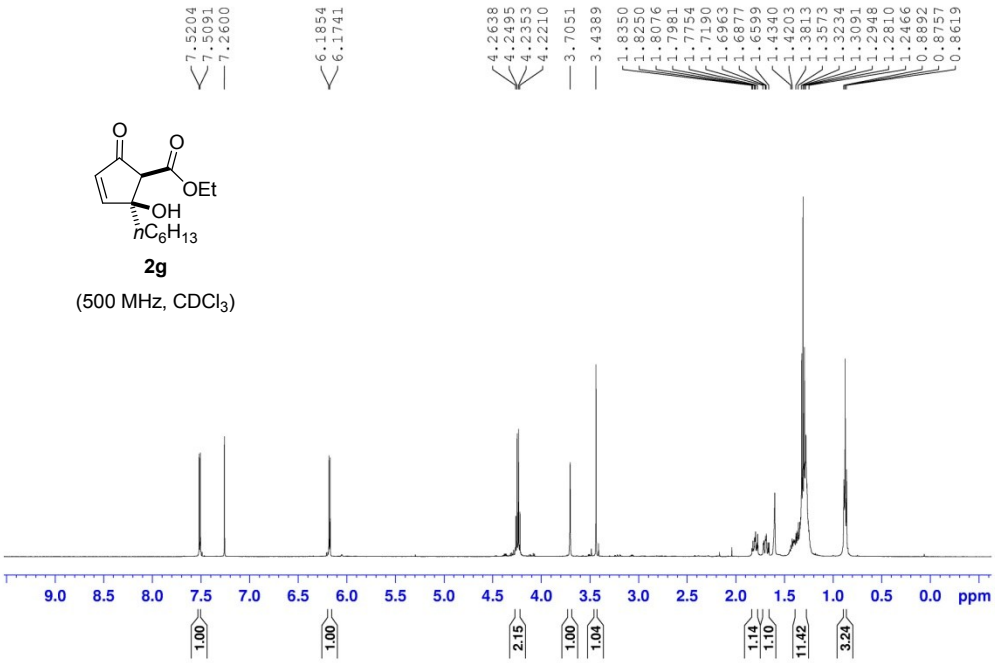

205.40
164.12
137.80
134.46
132.89
129.88
128.43
127.40
114.88
82.49
77.25
77.00
76.75
66.04
38.51
33.69
23.03
O
Ph
OH
2d
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

NOE experiment of compound **2d** at 7.16 ppm



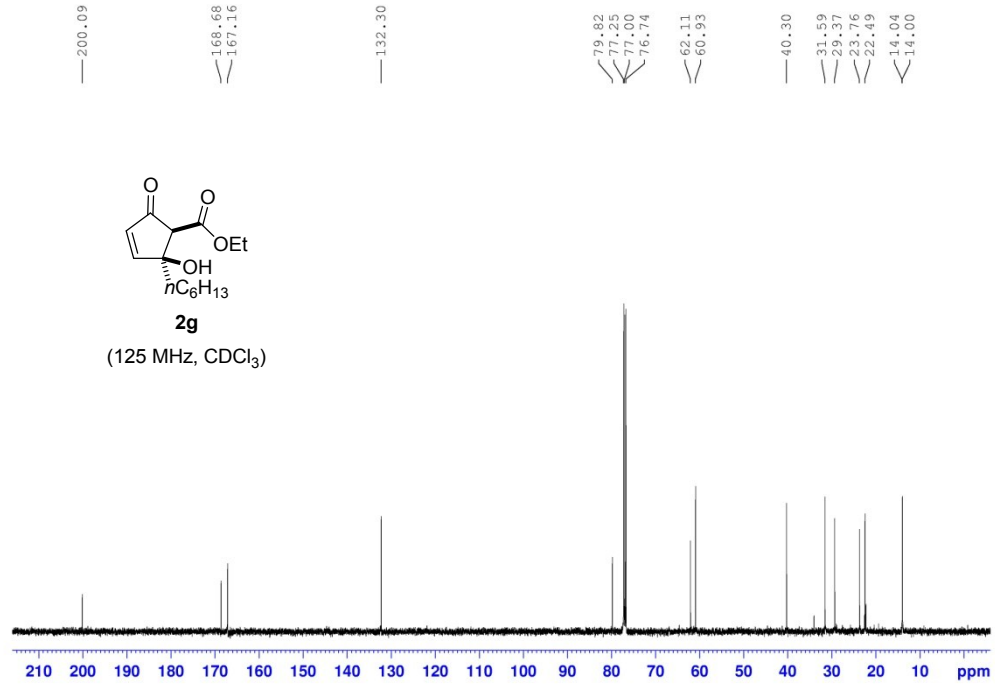

7.4992
7.4879
7.4218
7.4104
7.2600
6.1271
6.1160
4.2314
4.2287
4.2173
4.2145
4.2030
4.2003
4.1887
4.1862
4.1743
3.7755
3.4561
3.3823
1.5337
1.4809
1.2933
1.2790
1.2739
1.2646
1.2595
1.2453
O
O
OEt
OH
Me
2f
(500 MHz, CDCl3)
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
0.46
1.49
3.21
1.03
0.53
1.10
3.15
1.53
5.11


201.01
200.10
168.33
168.28
167.55
165.95
131.84
78.81
77.25
77.23
77.00
76.74
64.31
62.45
62.05
61.35
27.36
23.95
14.09
13.99
O
O
OEt
OH
Me
2f
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



2g

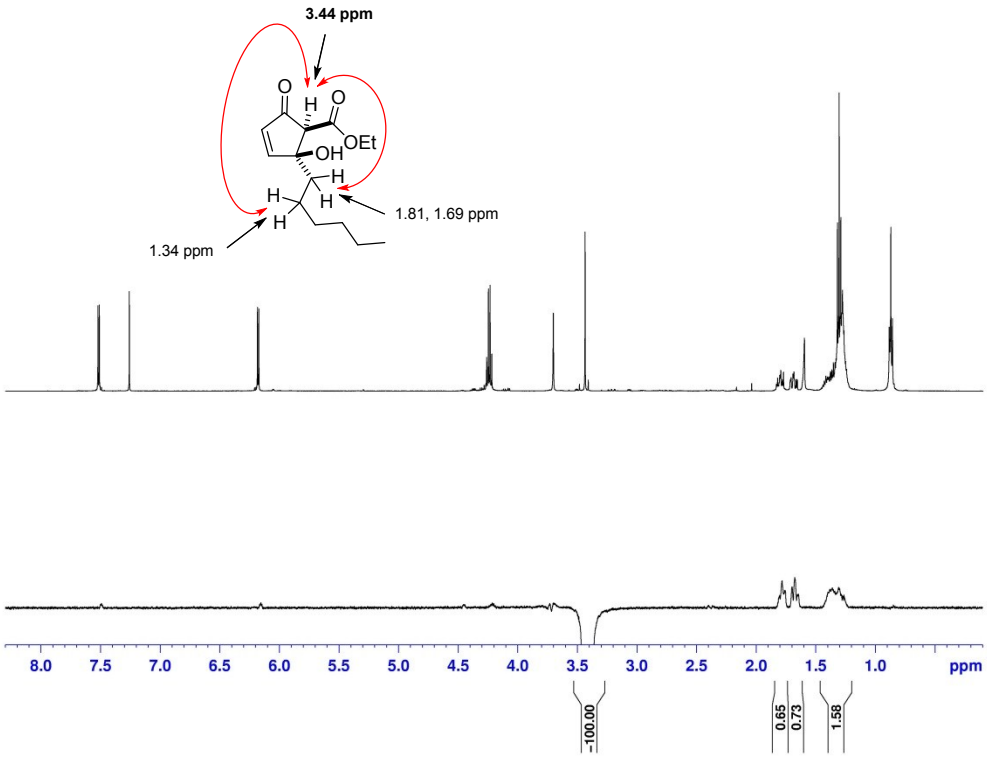
(500 MHz, $CDCl_3$)

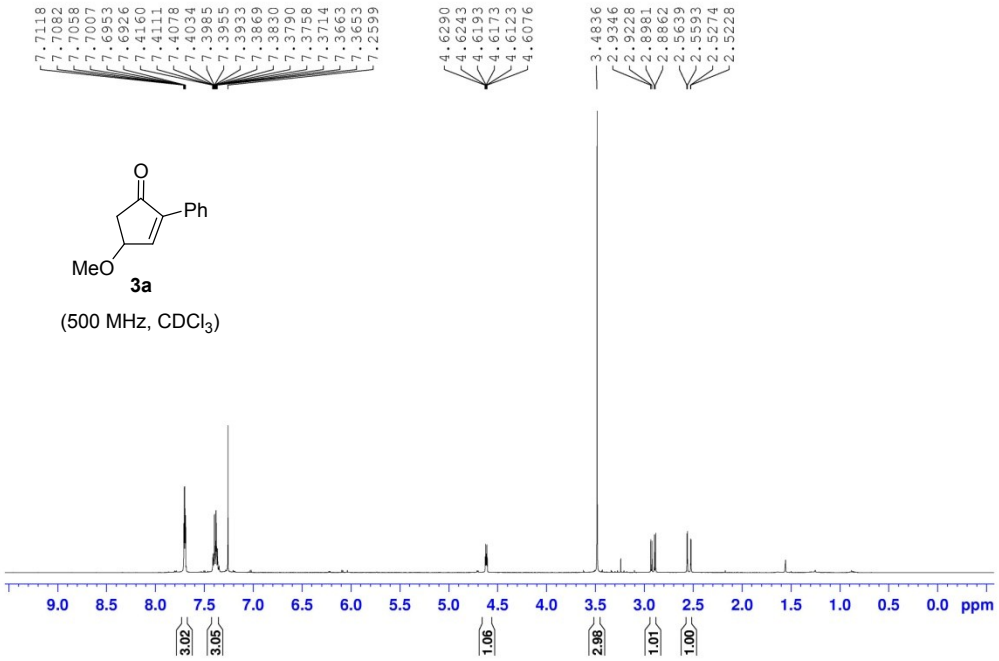


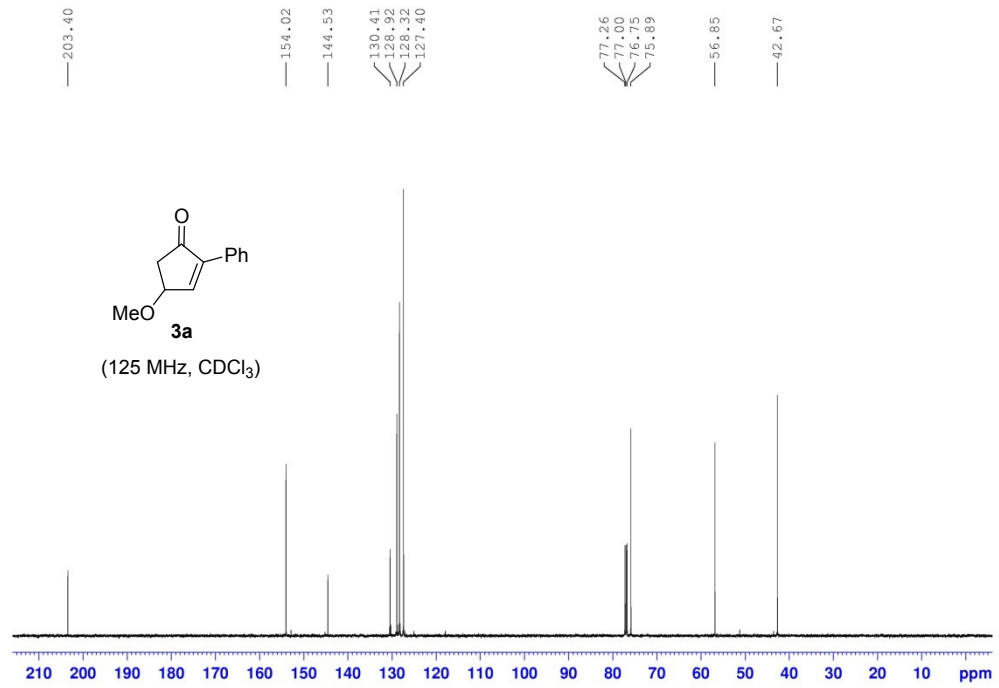
2g

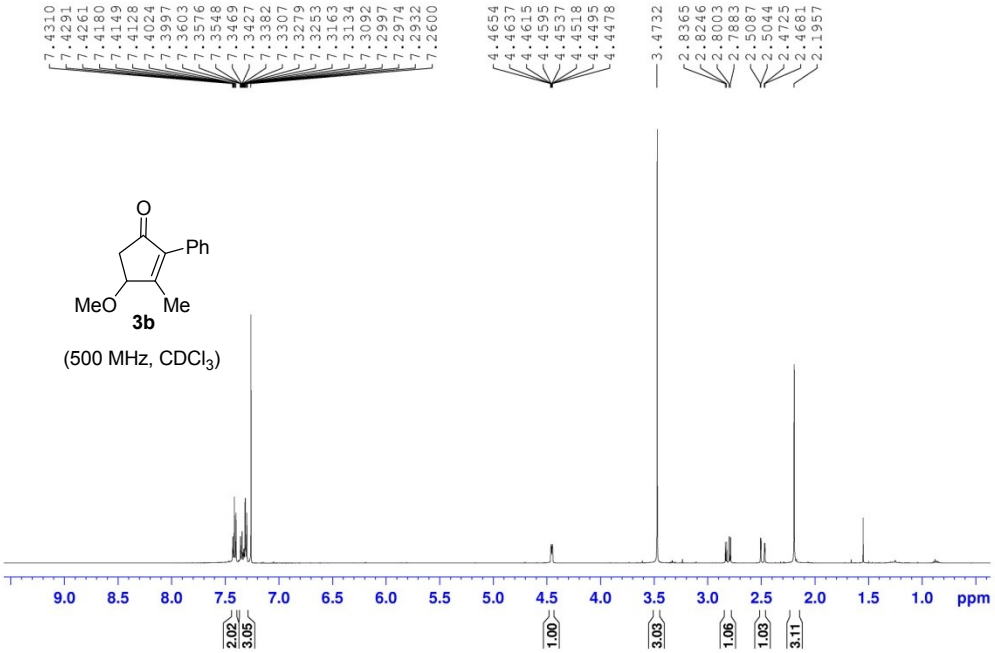
(125 MHz, $CDCl_3$)

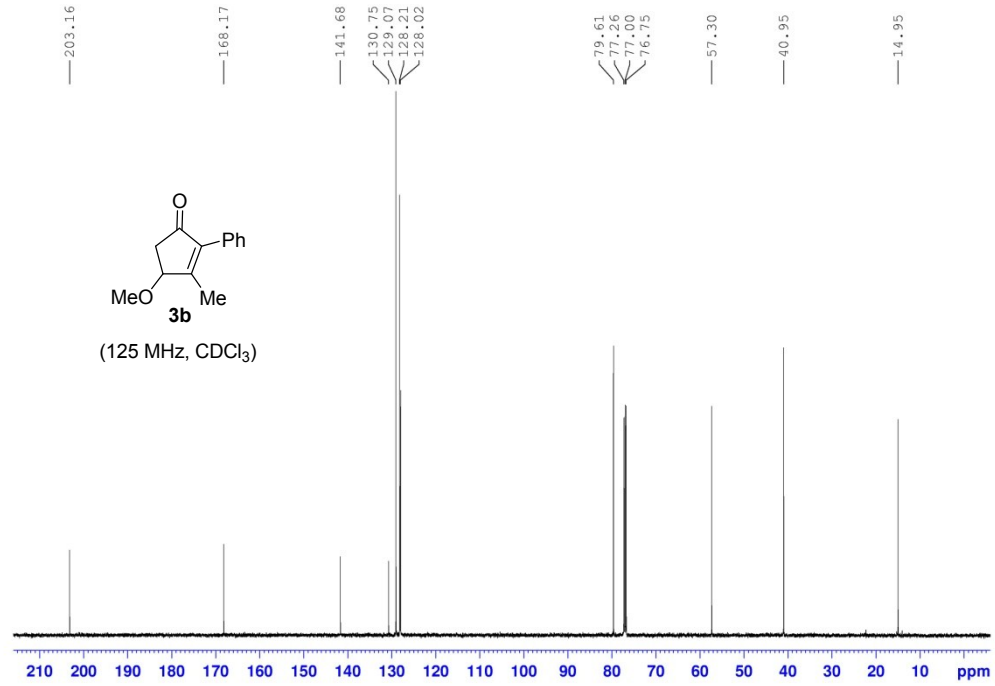
NOE experiment of compound **2g** at 3.44 ppm

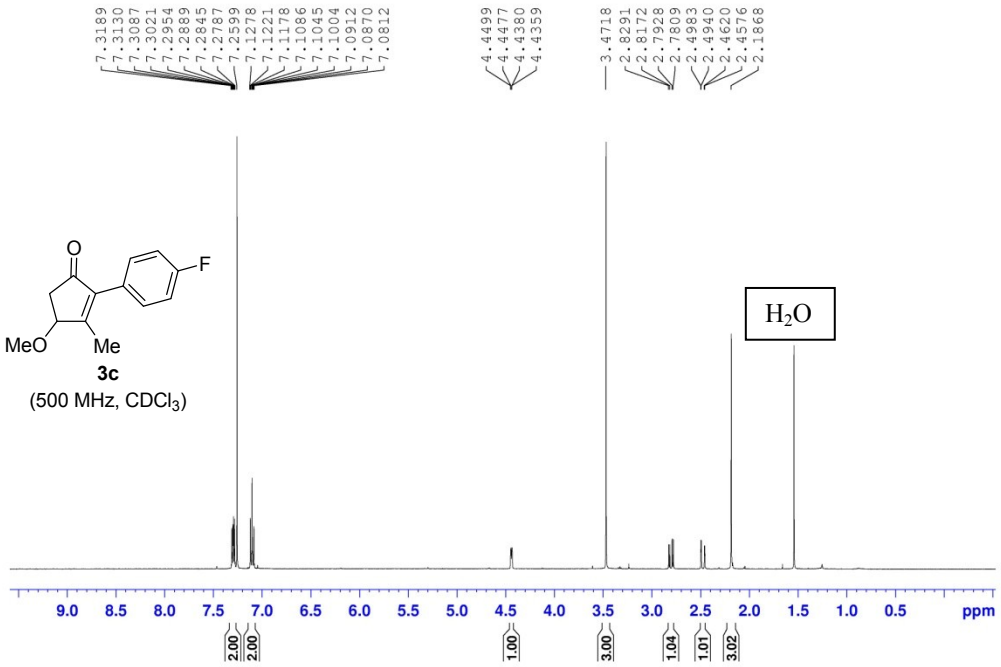


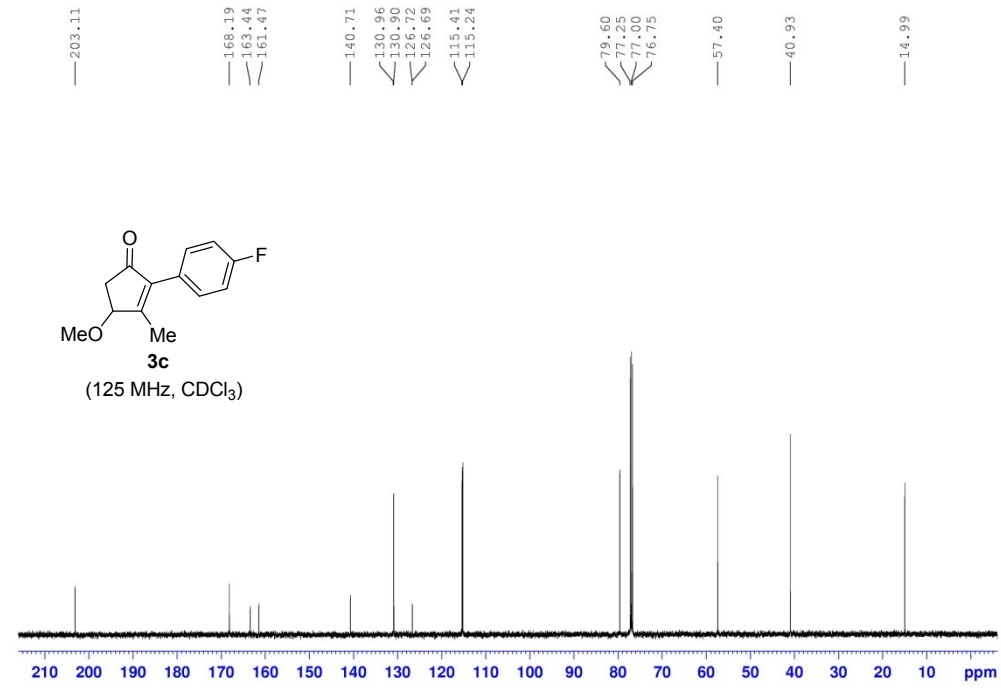

7.7118
7.7082
7.7058
7.7007
7.6953
7.6926
7.4160
7.4111
7.4078
7.4034
7.3985
7.3955
7.3933
7.3869
7.3830
7.3790
7.3758
7.3714
7.3663
7.3653
7.2599
4.6290
4.6243
4.6193
4.6173
4.6123
4.6076
3.4836
2.9346
2.9228
2.8981
2.8862
2.5639
2.5593
2.5274
2.5228
O
Ph
MeO
3a
(500 MHz, CDCl3)
9.0 8.5 8.0 7.5 7.0 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 ppm
3.02
3.05
1.06
2.98
1.01
1.00

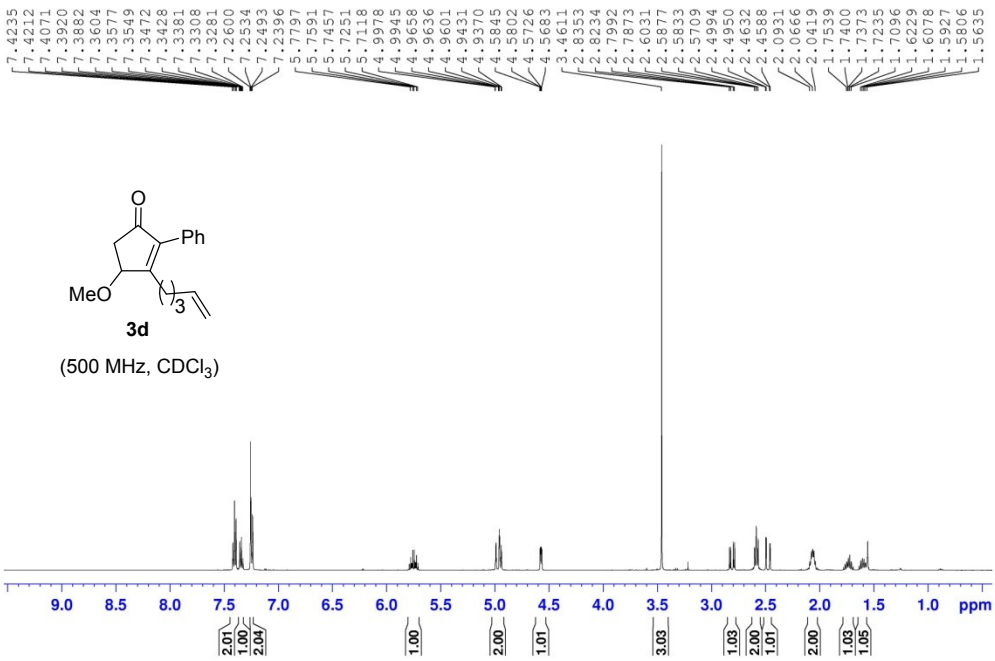

203.40
154.02
144.53
130.41
128.92
128.32
127.40
77.26
77.00
76.75
75.89
56.85
42.67
O
Ph
MeO
3a
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

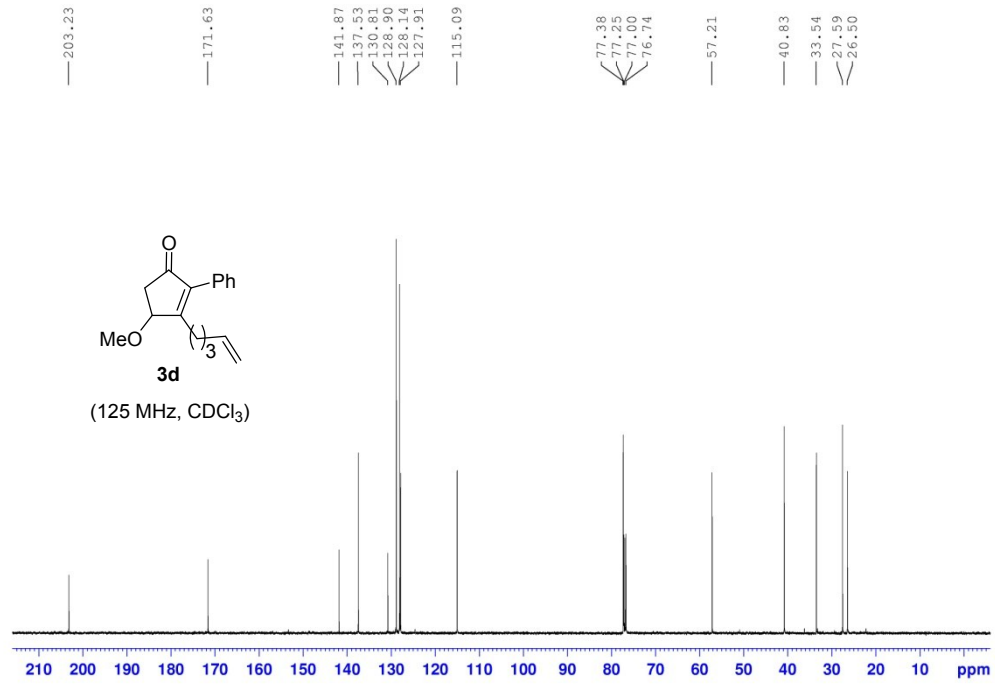

7.4310
7.4291
7.4261
7.4180
7.4149
7.4128
7.4024
7.3997
7.3603
7.3576
7.3548
7.3469
7.3427
7.3382
7.3307
7.3279
7.3253
7.3163
7.3134
7.3092
7.2997
7.2974
7.2932
7.2600
4.4654
4.4637
4.4615
4.4595
4.4537
4.4518
4.4495
4.4478
3.4732
2.8365
2.8246
2.8003
2.7883
2.5087
2.5044
2.4725
2.4681
2.1957
O
Ph
MeO
Me
3b
(500 MHz, CDCl3)
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
ppm
2.02
3.05
1.00
3.03
1.06
1.03
3.11

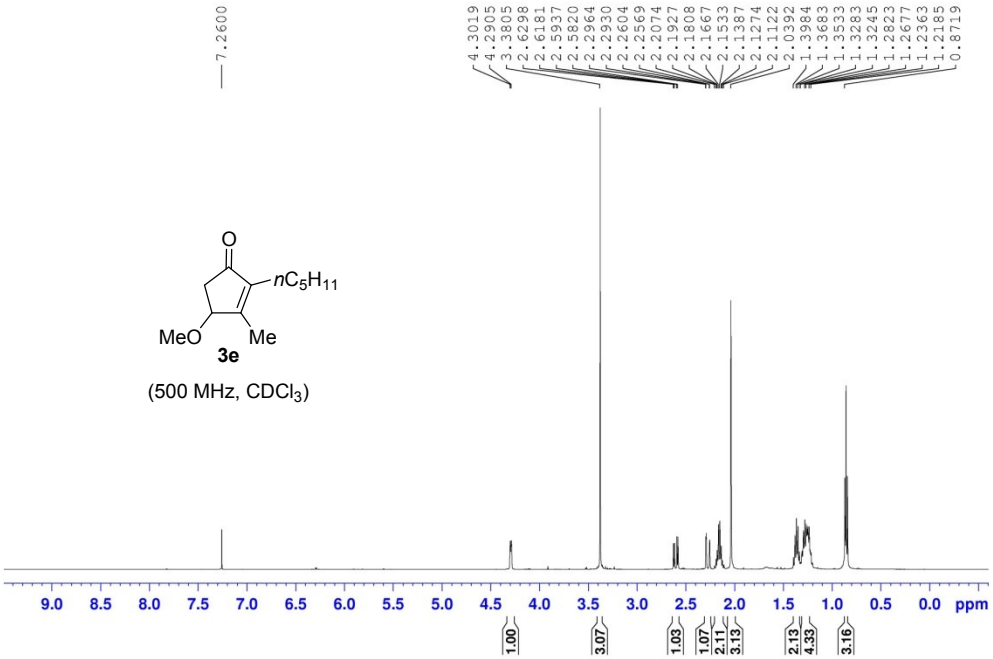

203.16
168.17
141.68
130.75
129.07
128.21
128.02
79.61
77.26
77.00
76.75
57.30
40.95
14.95
O
Ph
MeO
Me
3b
(125 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

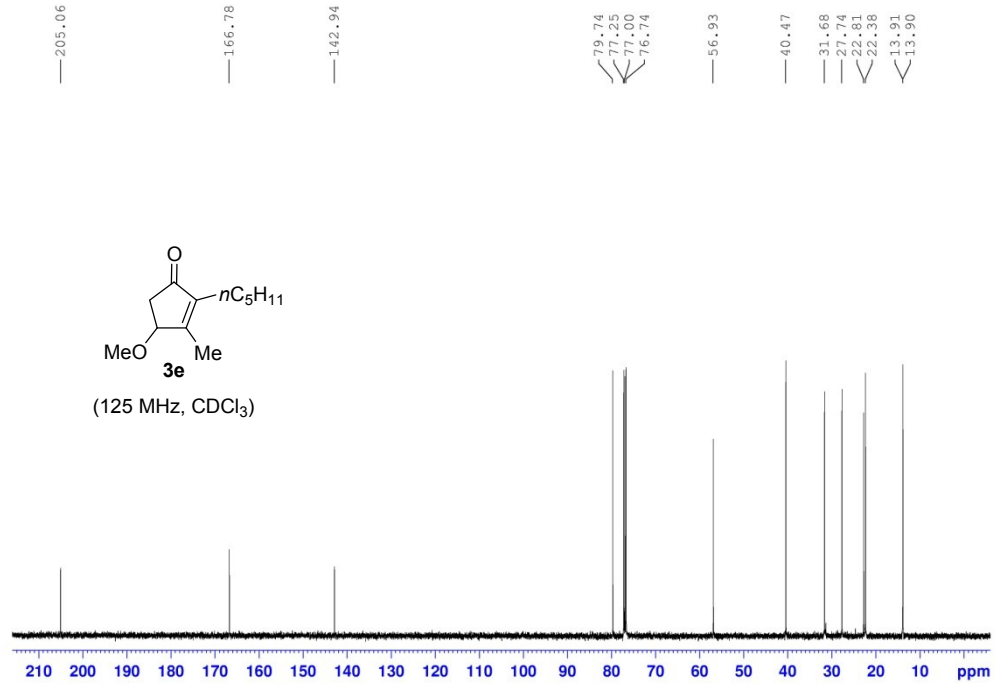

7.3189
7.3130
7.3087
7.3021
7.2954
7.2889
7.2845
7.2787
7.2599
7.1278
7.1221
7.1178
7.1086
7.1045
7.1004
7.0912
7.0870
7.0812
4.4499
4.4477
4.4380
4.4359
3.4718
2.8291
2.8172
2.7928
2.7809
2.4983
2.4940
2.4620
2.4576
2.1868
O
F
MeO
Me
3c
(500 MHz, CDCl3)
H2O
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.00
2.00
1.00
3.00
1.04
1.01
3.02

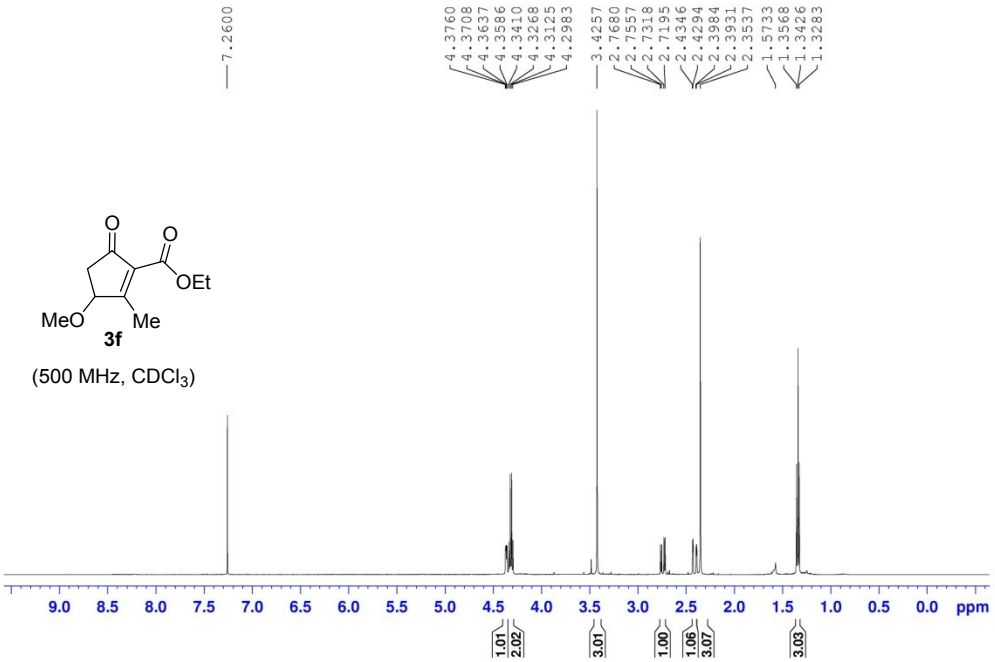

203.11
168.19
163.44
161.47
140.71
130.96
130.90
126.72
126.69
115.41
115.24
79.60
77.25
77.00
76.75
57.40
40.93
14.99
O
F
MeO
Me
3c
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

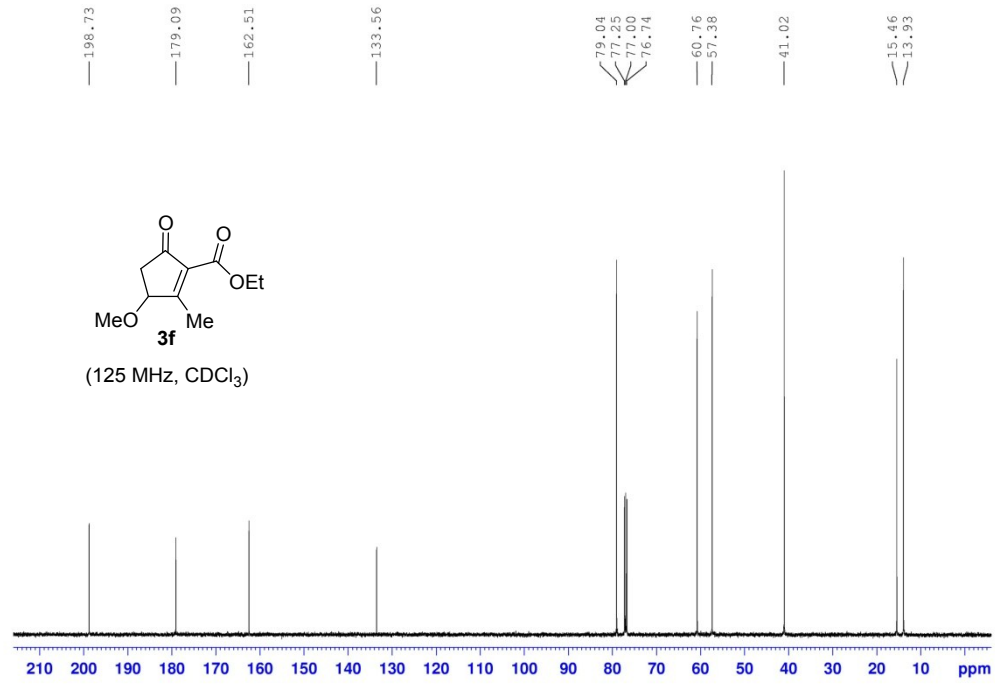

7.4235
7.4212
7.4071
7.3920
7.3882
7.3604
7.3577
7.3549
7.3472
7.3428
7.3381
7.3308
7.3281
7.2600
7.2534
7.2493
7.2396
5.7797
5.7591
5.7457
5.7251
5.7118
4.9978
4.9945
4.9658
4.9636
4.9601
4.9431
4.9370
4.5845
4.5802
4.5726
4.5683
3.4611
2.8353
2.8234
2.7992
2.7873
2.6031
2.5877
2.5833
2.5709
2.4994
2.4950
2.4632
2.4588
2.0931
2.0666
2.0419
1.7539
1.7400
1.7373
1.7235
1.7096
1.6229
1.6078
1.5927
1.5806
1.5635
O
Ph
MeO
3
3d
(500 MHz, CDCl3)
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 ppm
2.01 1.00 2.04 1.00 2.00 1.01 3.03 1.03 2.00 1.01 2.00 1.03 1.05

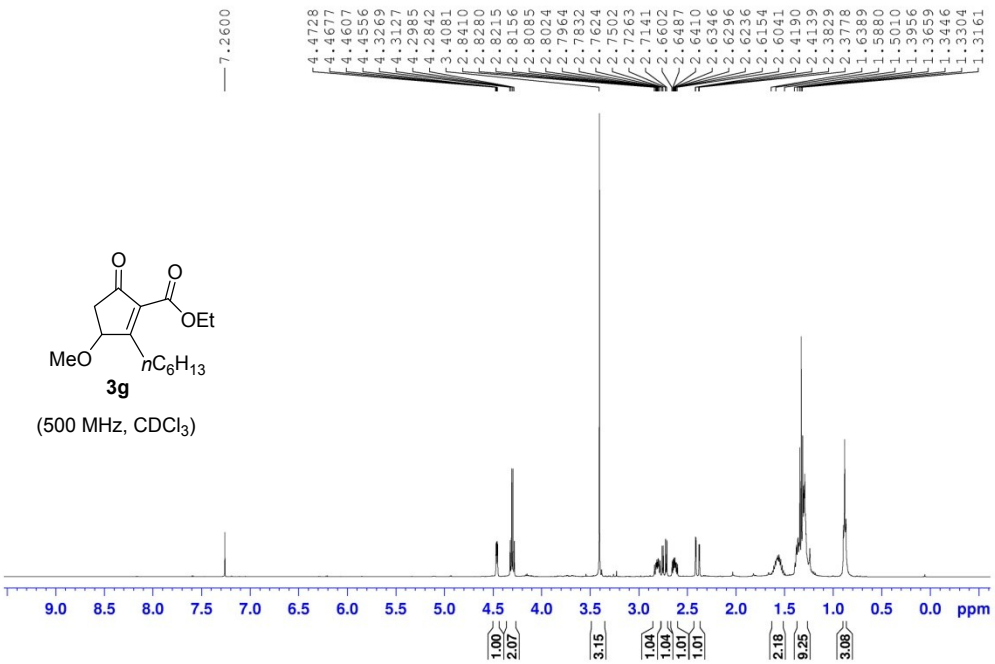

203.23
171.63
141.87
137.53
130.81
128.90
128.14
127.91
115.09
77.38
77.25
77.00
76.74
57.21
40.83
33.54
27.59
26.50
O
Ph
MeO
3
3d
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

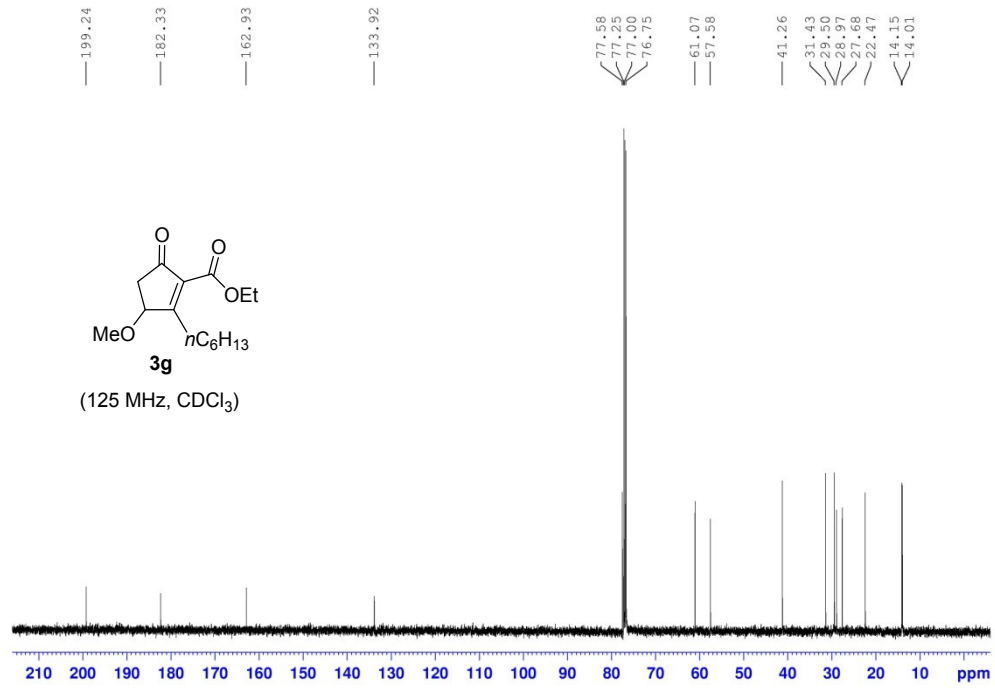

7.2600
4.3019
4.2905
3.3805
2.6298
2.6181
2.5937
2.5820
2.2964
2.2930
2.2604
2.2569
2.2074
2.1927
2.1808
2.1667
2.1533
2.1387
2.1274
2.1122
2.0392
1.3984
1.3683
1.3533
1.3283
1.3245
1.2823
1.2677
1.2363
1.2185
0.8719
O
nC5H11
MeO
Me
3e
(500 MHz, CDCl3)
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
3.07
1.03
1.07
2.11
3.13
2.13
4.33
3.16

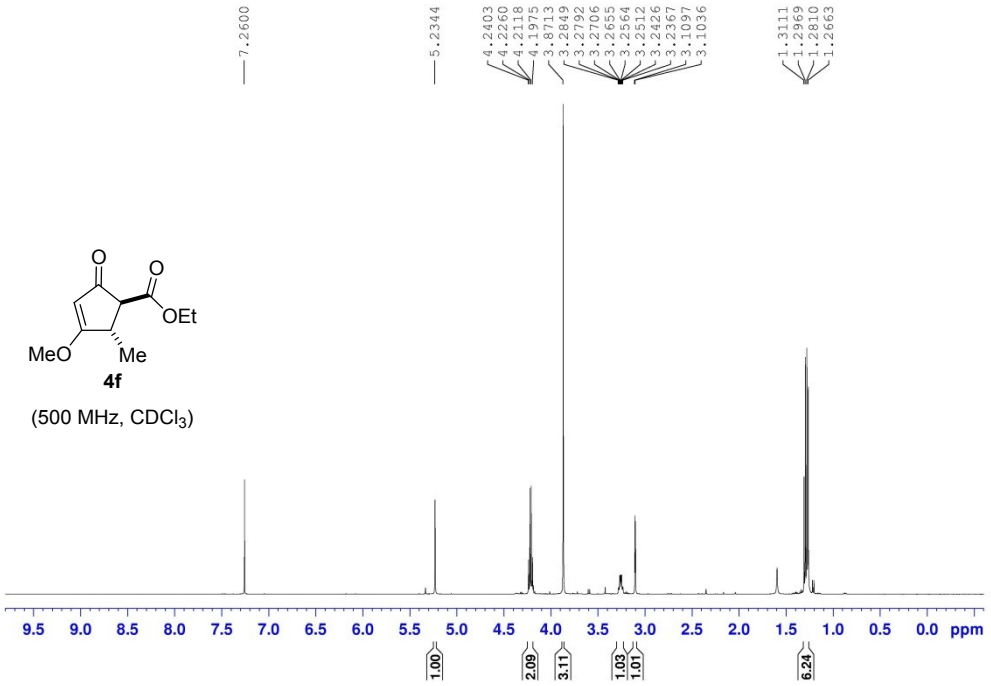

205.06
166.78
142.94
79.74
77.25
77.00
76.74
56.93
40.47
31.68
27.74
22.81
22.38
13.91
13.90
O
nC5H11
MeO
Me
3e
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

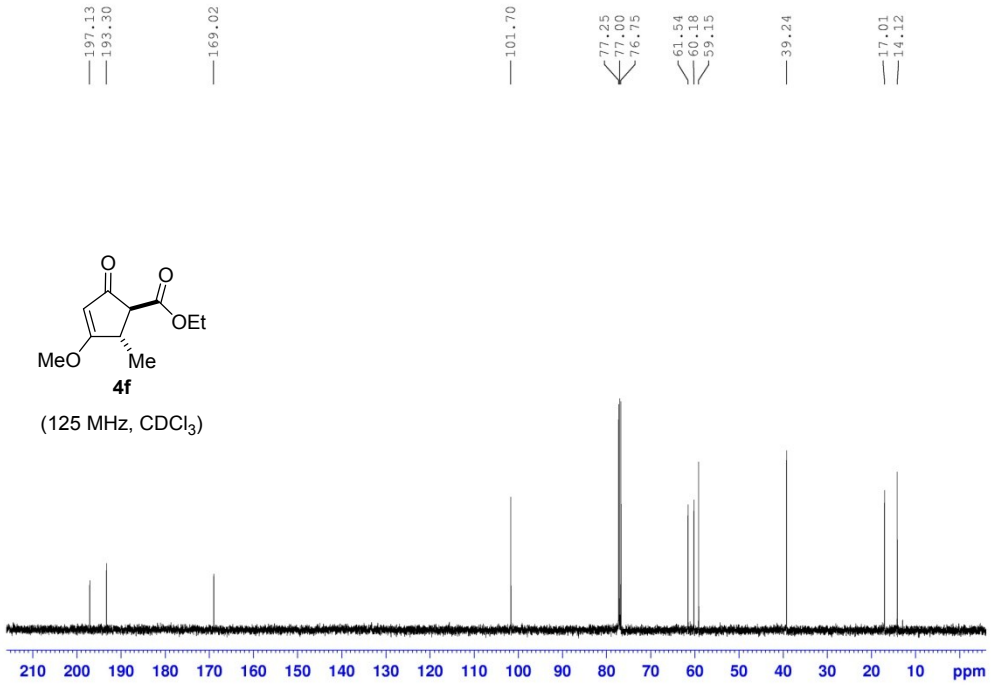

7.2600
4.3760
4.3708
4.3637
4.3586
4.3410
4.3268
4.3125
4.2983
3.4257
2.7680
2.7557
2.7318
2.7195
2.4346
2.4294
2.3984
2.3931
2.3537
1.5733
1.3568
1.3426
1.3283
O
O
OEt
MeO
Me
3f
(500 MHz, CDCl3)
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.01
2.02
3.01
1.00
1.06
3.07
3.03


198.73
179.09
162.51
133.56
79.04
77.25
77.00
76.74
60.76
57.38
41.02
15.46
13.93
O
O
OEt
MeO
Me
3f
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

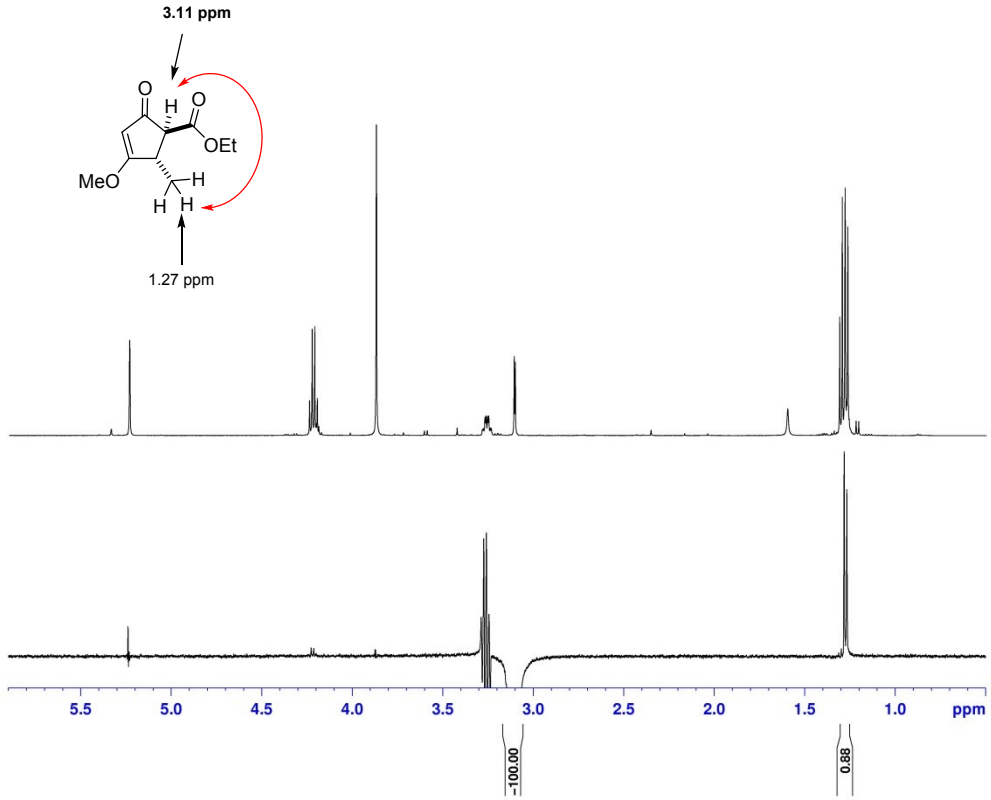

7.2600
4.4728
4.4677
4.4607
4.4556
4.3269
4.3127
4.2985
4.2842
3.4081
2.8410
2.8280
2.8215
2.8156
2.8085
2.8024
2.7964
2.7832
2.7624
2.7502
2.7263
2.7141
2.6602
2.6487
2.6410
2.6346
2.6296
2.6236
2.6154
2.6041
2.4190
2.4139
2.3829
2.3778
1.6389
1.5880
1.5010
1.3956
1.3659
1.3446
1.3304
1.3161
O
O
OEt
MeO
nC6H13
3g
(500 MHz, CDCl3)
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 ppm
1.00
2.07
3.15
1.04
1.04
1.01
1.01
2.18
9.25
3.08

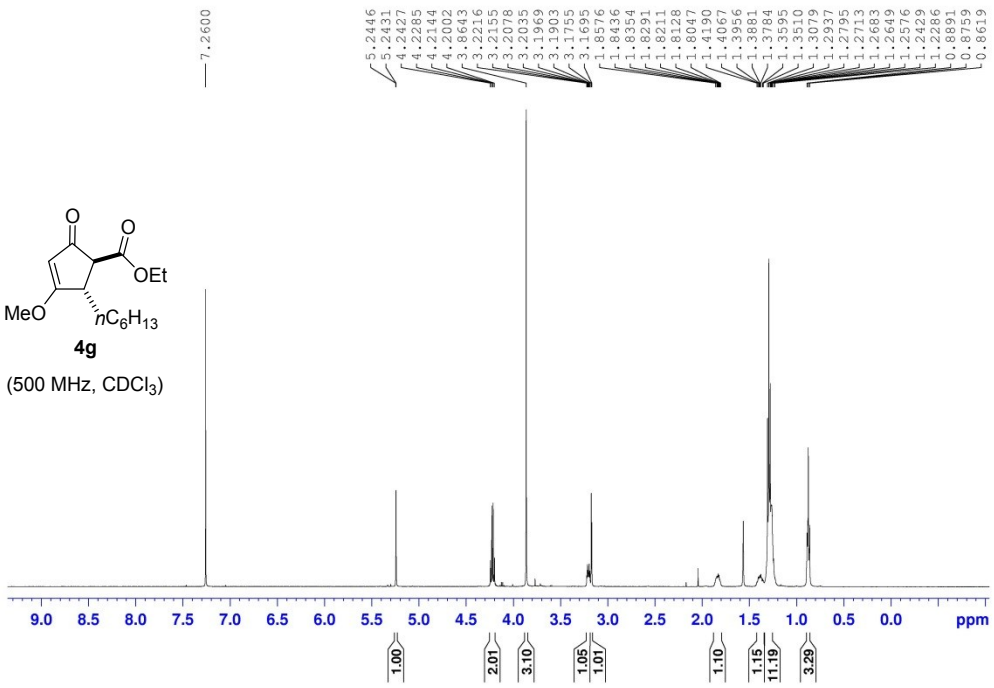

199.24
182.33
162.93
133.92
77.58
77.25
77.00
76.75
61.07
57.58
41.26
31.43
29.50
28.97
27.68
22.47
14.15
14.01
O
O
OEt
MeO
nC6H13
3g
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

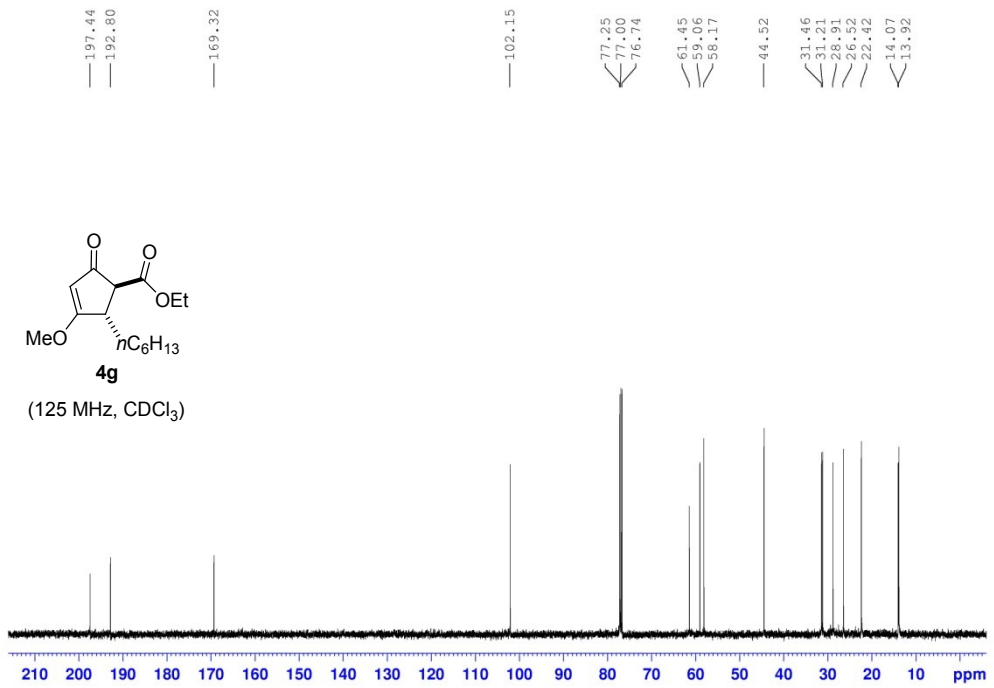

7.2600
5.2344
4.2403
4.2260
4.2118
4.1975
3.8713
3.2849
3.2792
3.2706
3.2655
3.2564
3.2512
3.2426
3.2367
3.1097
3.1036
1.3111
1.2969
1.2810
1.2663
O
O
OEt
MeO
Me
4f
(500 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
2.09
3.11
1.03
1.01
6.24


197.13
193.30
169.02
101.70
77.25
77.00
76.75
61.54
60.18
59.15
39.24
17.01
14.12
O
O
OEt
MeO
Me
4f
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

NOE experiment of compound **4f** at 3.11 ppm




7.2600
5.2446
5.2431
4.2427
4.2285
4.2144
4.2002
3.8643
3.2216
3.2155
3.2078
3.2035
3.1969
3.1903
3.1755
3.1695
1.8576
1.8436
1.8354
1.8291
1.8211
1.8128
1.8047
1.4190
1.4067
1.3956
1.3881
1.3784
1.3595
1.3510
1.3079
1.2937
1.2795
1.2713
1.2683
1.2649
1.2576
1.2429
1.2286
0.8891
0.8759
0.8619
O
O
OEt
MeO
nC6H13
4g
(500 MHz, CDCl3)
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 ppm
1.00
2.01
3.10
1.05
1.01
1.10
1.15
11.19
3.29


197.44
192.80
169.32
102.15
77.25
77.00
76.74
61.45
59.06
58.17
44.52
31.46
31.21
28.91
26.52
22.42
14.07
13.92
O
O
OEt
MeO
nC6H13
4g
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

NOE experiment of compound **4g** at 1.83 ppm