Supporting Information

Butyrolactone Synthesis via Polar Radical Crossover Cycloaddition Reactions: Diastereoselective Syntheses of Methylenolactocin and Protolichesterinic Acid

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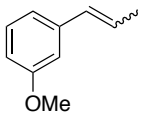
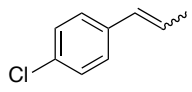
General Methods and Materials

Infrared (IR) spectra were obtained using a Jasco 260 Plus Fourier transform infrared spectrometer. Proton and carbon magnetic resonance spectra (1H NMR and 13C NMR) were recorded on a Bruker model DRX 400, DRX 500, or a Bruker AVANCE III 600 CryoProbe (1H NMR at 400 MHz, 500 MHz or 600 MHz and 13C NMR at 101, 126, or 151 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR: $CDCl_3$ at 7.26 ppm; ^{13}C NMR: $CDCl_3$ at 77.0 ppm). ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, ddt = doublet of doublet of triplets, ddd = doublet of doublet of doublets, dddd = doublet of doublet of doublet of doublets m = multiplet, brs = broad singlet), coupling constants (Hz), and integration. Mass spectra were obtained using a Micromass (now Waters Corporation, 34 Maple Street, Milford, MA 01757) Quattro-II, Triple Quadrupole Mass Spectrometer, with a Z-spray nano-Electrospray source design, in combination with a NanoMate (Advion 19 Brown Road, Ithaca, NY 14850) chip based electrospray sample introduction system and nozzle. Cyclic voltammograms were obtained with a platinum disc working electrode, Ag/AgCl reference electrode, a platinum wire auxillary, and CHI-760 potentiostat using 1 mM solutions of analyte in acetonitrile with 0.1 M tetrabutylammonium perchlorate as supporting electrolyte. Thin layer chromatography (TLC) was performed on SiliaPlate 250 μm thick silica gel plates provided by Silicycle. Visualization was accomplished with short wave UV light (254 nm), aqueous basic potassium permanganate solution, or cerium ammonium molybdate solution followed by heating. Flash chromatography was performed using SiliaFlash P60 silica gel (40-63 μm) purchased from Silicycle. Tetrahydrofuran, diethyl ether, dichloromethane, and toluene were dried by passage through a column of neutral alumina under nitrogen prior to use. Irradiation of photochemical reactions was carried out using a 15W PAR38 blue LED floodlamp purchased from EagleLight (Carlsbad, CA), with borosilicate glass vials purchased from Fisher Scientific. All other reagents were obtained from commercial sources and used without further purification unless otherwise noted.

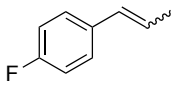
Preparation of Alkene Substrates:



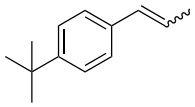
1-methoxy-3-(prop-1-en-1-yl)benzene: Prepared according to a published procedure; spectral data were in agreement with literature values.[1]



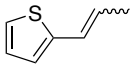
1-chloro-4-(prop-1-en-1-yl)benzene: Prepared according to a published procedure; spectral data were in agreement with literature values.[2]



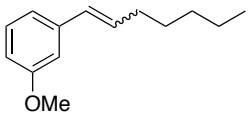
1-fluoro-4-(prop-1-en-1-yl)benzene: Prepared according to a published procedure; spectral data were in agreement with literature values.[2]



1-(*tert*-butyl)-4-(prop-1-en-1-yl)benzene: Prepared according to a published procedure; spectral data were in agreement with literature values.[3]

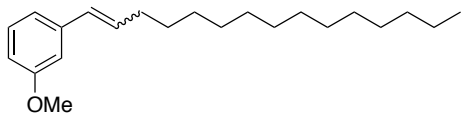


2-(prop-1-en-1-yl)thiophene: Prepared according to a published procedure; spectral data were in agreement with literature values.[4]



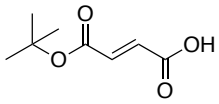
1-(hept-1-en-1-yl)-3-methoxybenzene: To a flame dried 250 mL round bottom flask equipped with a stir bar was added hexyltriphenylphosphonium bromide (11.32 g, 26.5 mmol, 1.05 equiv) and 65 mL dry THF. The solution was cooled to 0 ^{o}C, and potassium *tert*-butoxide (3.6 g, 26.5 mmol, 1.05 equiv) was added. The reaction turned bright orange, and was allowed to stir under N_2 for 45 minutes. *m*-anisaldehyde (3.07 mL, 25.2 mmol, 1.0 equiv) was dissolved in 16 mL THF, and the resulting solution was added dropwise to the reaction at 0 ^{o}C. By the end of the addition, the reaction had lost its orange color. The mixture was allowed to react at room temperature over night, at which point the solvent was evaporated. The product was purified via column chromatography, resulting in a clear, colorless oil (3.7 g, 72%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 (t, J = 7.9 Hz, 1H), 6.93-6.88(m, 1H), 6.84 (t, *J* = 2.0 Hz, 1H), 6.79 (ddd, *J* = 8.2, 2.7, 0.9 Hz, 1H), 6.40 (dt, *J* = 11.7, 1.9 Hz,

1H), 5.69 (dt, *J* = 11.6, 7.3 Hz, 1H), 3.83 (s, 3H), 2.35 (dq, *J* = 7.4, 1.9 Hz, 2H), 1.57-1.40 (m, 2H), 1.41-1.22 (m, 4H), 0.97-0.80 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.36, 139.20, 133.54, 129.01, 128.55, 121.31, 114.29, 111.92, 55.13, 31.59, 31.57, 29.66, 28.69, 22.65, 22.56, 14.11, 14.03. Spectral data were in agreement with literature values.[5]

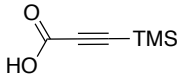


1-methoxy-3-(pentadec-1-en-1-yl)benzene: To a flame dried 500 mL round bottom flask equipped with a stir bar was added triphenyl(tetradecyl)phosphonium bromide (15 g, 27.9 mmol, 1.3 equiv) and 150 mL dry THF. The solution was cooled to 0 ^{o}C, and nBuLi (1.25 equiv) was added. The reaction turned red. The reaction was then cooled to -60 ^{o}C, and *m*-anisaldehyde (2.6 mL, 1 equiv) was added dropwise. The mixture was allowed to react at room temperature overnight, at which point it was quenched with the addition of H_2O, and extracted with Et_2O, washed with Brine, and dried over $MgSO_4$. The product was purified by column chromatography (1% Acetone in Hexanes), resulting in a clear, colorless oil (5.8 g, 87%, 1.7:1 *cis*:*trans*). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.26-7.14 (m, 1H), 6.94 (dt, *J* = 7.7, 1.2 Hz, 1H), 6.91-6.84 (m, 1H), 6.82 (t, *J* = 2.0 Hz, 1H), 6.76 (dddd, *J* = 16.3, 8.2, 2.6, 0.9 Hz, 1H), 6.42-6.28 (m, 1H), 6.22 (dt, *J* = 15.8, 6.9 Hz, 1H), 5.66 (dt, *J* = 11.7, 7.3 Hz, 1H), 3.81 (s, 3H), 2.32 (dq, *J* = 7.4, 1.8 Hz), 2.27-2.18 (m, 1H), 1.54-1.34 (m, 2H), 1.39-1.16 (m, 20H), 0.88 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.74, 159.32, 139.42, 139.19, 133.58, 131.62, 129.38, 129.01, 128.51, 121.30, 118.57, 114.26, 112.34, 111.91, 111.20, 55.15, 33.01, 31.92, 31.58, 30.92, 29.97, 29.68, 29.66, 29.64, 29.52, 29.23, 28.72, 22.69, 22.65, 14.12.

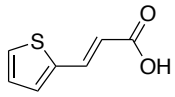
Preparation of Unsaturated Acid Substrates:



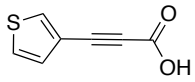
Mono-*tert*-butylfumarate: Prepared according to a published procedure; spectral data were in agreement with literature values.[6]



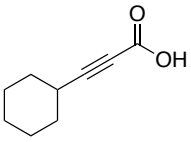
3-(trimethylsilyl)propiolic acid: Prepared according to a published procedure; spectral data were in agreement with literature values.[7]



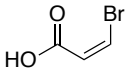
(*E*)-3-(thiophen-2-yl)acrylic acid: To a flame dried 25 mL round bottom flask equipped with a stir bar was added thiophene-2-carbaldehyde (0.6 mL, 6.5 mmol, 1 equiv), malonic acid (1.35 g, 13 mmol, 2 equiv) in pyridine (0.7 M, 9.3 mL). Piperidine (20 mol%, 130 μL, 1.3 mmol). The mixture was allowed to react for 4 hours, at which point it was poured into H_2O and acidified with 6M HCl. The mixture was cooled to 0 ^oC, and the resulting precipitate was filtered and further purified by silica chromatography (20% acetone in hexanes). Spectral data were in agreement with literature values.[8]



3-(thiophen-3-yl)propiolic acid: To a flame dried 25 mL round bottom flask equipped with a stir bar was added 3-ethynylthiophene (700 mg, 6.5 mmol, 1 equiv) in dry THF (5 mL, 1.3 M). Methylmagnesium bromide was added slowly at 0 ^oC, and the mixture was stirred for 3 hours. The reaction was cooled to -5 ^oC, and CO_2 was bubbled through the reaction. 1 mL additional THF was added to promote stirring, and the mixture was allowed to react for an additional 3 hours, at which point dilute HCl was slowly added to quench the reaction, and the mixture was extracted with Et_2O and dried over $MgSO_4$. The product was purified via flash silica chromatography (10% acetone in hexanes, followed by 20% acetone). The product was isolated as a brown solid (0.7 mg, 71%). Spectral data were in agreement with literature values.[9]



3-cyclohexylpropiolic acid: Prepared according to a published procedure;[10] spectral data were in agreement with literature values.[11]



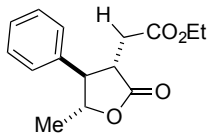
(*Z*)-3-bromoacrylic acid: Prepared according to a published procedure; spectral data were in agreement with literature values.[12]

General Procedures for the Polar Radical Crossover Cycloaddition Reactions:

General Procedure A. To a flame-dried two dram vial equipped with a magnetic stir bar was added the alkene (1 equiv.), α,β-unsaturated acid (1.1 equiv.), NMA*BF_4 (2.5 mol%), phenyl disulfide (10 mol%), and 2,6-lutidine (10 mol%). The vial was purged with N_2 and sparged dichloromethane was added to achieve a concentration of 0.15 M with respect to substrate, and sealed with a septum screwcap. The reaction was irradiated with a 450 nm lamp and stirred at room temperature for 24 hours. Upon completion, the reaction was passed through a silica plug to remove the catalyst and eluted with dichloromethane. The product was further purified by flash chromatography with acetone/hexanes as the eluent.

General Procedure B. To a flame-dried two dram vial equipped with a magnetic stir bar was added the alkene (2-3 equiv.), α,β-unsaturated acid (1 equiv.), NMA*BF_4 (2.5 mol%), and phenyl disulfide (15 mol%). The vial was purged with N_2 and sparged dichloromethane was added to achieve a concentration of 0.15 M with respect to substrate, and sealed with a septum screwcap and Teflon tape. The reaction was irradiated with a 450 nm lamp and stirred at room temperature for the indicated time period. Upon completion, the reaction was dry loaded and further purified by flash column chromatography with acetone/hexanes as the eluent mixture.

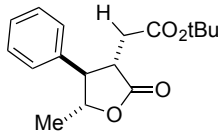
General Procedure C. To a flame-dried two dram vial equipped with a magnetic stir bar was added the alkene (2-3 equiv.), α,β-unsaturated acid (1 equiv.), NMA*BF_4 (2.5 mol%), 2,6-lutidine (10 mol%) and phenyl disulfide (15 mol%). The vial was purged with N_2 and sparged dichloromethane was added to achieve a concentration of 0.15 M with respect to substrate, and sealed with a septum screwcap and Teflon tape. The reaction was irradiated with a 450 nm lamp and stirred at room temperature for the indicated time period. Upon completion, the reaction was dry loaded and further purified by flash column chromatography with acetone/hexanes as the eluent mixture.



12a

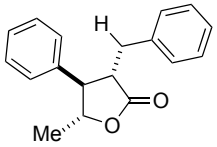
Ethyl 2-(5-methyl-2-oxo-4-phenyltetrahydrofuran-3-yl)acetate (12a) The lactone was prepared according to General procedure A using 65 μL of β-methylstyrene, 79.3 mg of mono-ethylfumarate, 10.9 mg phenyl disulfide, 5.2 mg NMA*BF_4, and 6 μL of 2,6-lutidine. Yield was 66% (2.2:1 dr). The major and minor diastereomers could be separated via column chromatography (3% acetone in hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$) δ major: 7.39-7.23 (m, 5H), 4.50 (dq, J = 6.1, 9.9 Hz, 1H),

3.95 (m, 2H), 3.25 (dt, J = 6.0, 12.0 Hz, 1H), 3.08 (dd, J = 9.8, 12.3 Hz, 1H), 2.70 (dd, J = 5.2, 16.5 Hz, 1H), 2.56 (dd, J = 6.4, 16.5 Hz, 1H), 1.39 (d, J = 6.1 Hz, 3H), 1.13 (t, J = 7.2 Hz, 3H). δ minor: 7.33-7.06 (m, 5H), 4.90 (dq, J = 6.4, 1.1 Hz, 1H), 4.08 (dq, J = 7.2, 1.8 Hz, 2H), 3.55 (m, 2H), 2.63 (dd, J = 2.9, 17.2 Hz, 1H), 1.92 (dd, J = 9.9, 17.8 Hz, 1H), 1.53 (d, J = 6.5 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ major: 175.95, 170.61, 136.26, 129.10, 128.12, 127.80, 81.03, 60.84, 55.58, 45.13, 32.84, 18.56, 13.95. δ minor: 177.08, 171.45, 138.45, 129.08, 127.79, 127.54, 81.55, 60.79, 50.01, 40.01, 31.14, 20.67, 14.06. **MS** (+ESI) Calculated *m/z* for $[M+H]^{+}$ = 263.12. Experimental *m/z* for $[M+H]^{+}$ = 263.16. **IR** (Thin Film, cm^{-1}) 3056, 2983, 1772, 1733, 1540, 1266.



12b

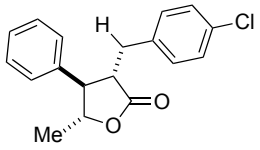
***tert*-Butyl 2-(5-methyl-2-oxo-4-phenyltetrahydrofuran-3-yl)acetate (12b)** The lactone was prepared according to General Procedure A using 65 μL of β-methylstyrene, 94.7 mg of mono-*tert*-butylfumarate, 10.9 mg phenyl disulfide, 5.2 mg NMA*BF_4, and 6 μL 2,6-lutidine. Yield was 74% (2.3:1 dr). The major and minor diastereomers could be separated via column chromatography (3% acetone in hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$) δ major: 7.24-7.38 (m, 5H), 4.49 (m, 1H), 3.22 (m, 1H), 3.05 (dd, J = 9.9, 12.3 Hz, 1H), 2.62 (dd, J = 5, 16.5 Hz, 1H), 2.50 (dd, J = 6.4, 16.5 Hz, 1H) 1.38 (d, J = 6.1 Hz, 3H), 1.31 (s, 9H). δ minor: 7.33-7.08 (m, 5H), 4.87 (dq, J = 1.4, 6.5 Hz, 1H), 3.50 (m, 2H), 2.57 (dd, J = 3.8, 17.9 Hz, 1H), 1.83 (dd, J = 10.2, 18 Hz, 1H), 1.51 (d, J = 6.5 Hz, 3H), 1.37 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ major: 176.13, 169.71, 136.37, 129.11, 128.05, 127.84, 81.28, 80.94, 55.70, 45.28, 34.12, 27.79, 18.53. δ minor: 177.26, 170.74, 138.62, 129.02, 127.69, 127.57, 81.49, 80.96, 49.97, 40.01, 32.12, 27.89, 20.65. **MS** (+ESI) Calculated *m/z* for $[M+H]^{+}$ = 291.15. Experimental *m/z* for $[M+H]^{+}$ = 291.19. **IR** (Thin Film, cm^{-1}) 3055, 2982, 2933, 2306, 1770, 1724, 1368, 1266.



12c

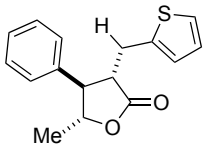
3-benzyl-5-methyl-4-phenyldihydrofuran-2(3H)-one (12c) The lactone was prepared according to General Procedure B using 194 μL of β–methylstyrene, 74 mg of cinnamic acid, 16 mg of phenyl disulfide, and 5 mg of NMA*BF_4. The reaction was carried out at room temperature for 24 hours and purified via flash chromatography. Yield was 108 mg (81%, 4.7:1 dr) of the desired adduct as a clear

oil. Characterizations include major and minor diastereomers. **^{1}H NMR** (600 MHz, $CDCl_3$) δ major: 7.27–6.78 (m, 10H), 4.3 (dq, *J* = 9.67, 6.61 Hz, 1H) 3.17 (m, 1H), 3.04 (ddd, J=4.8, 5.4, 14.4 Hz, 1H), 2.89 (dd, J =5.9, 14.3 Hz, 1H), 2.74, (dd, J=9.5, 12.1 Hz, 1H), 1.18 (d J=6.6 Hz, 3H). Minor: 7.27–6.78 (m, 10H), 4.71, (dq, J=1.8, 6.6 Hz, 1H), 3.30-3.2 (m, 3H), 2.28, (dd, J= 9.9, 14.7 Hz, 1H) 1.42 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ177.71, 176.74, 138.57, 137.19, 136.80, 129.64, 127.76, 126.56, 126.34, 81.25, 81.08, 54.25, 50.39, 49.41, 33.50, 31.59, 20.39, 18.46. **MS** (GC-MS) Calculated *m/z* for $[M]^+$ = 266. Experimental *m/z* for $[M]^+$ = 266. **IR** (Thin Film, cm^{-1}): 3062, 3029, 2976, 2923, 1770, 1602, 1496.



12d

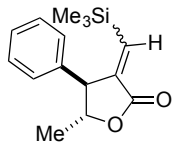
3-(4-chlorobenzyl)-5-methyl-4-phenyldihydrofuran-2(3H)-one (12d): The lactone was prepared according to General Procedure B using 155 μL of β–methylstyrene, 73 mg of *p*-chlorocinnamic acid, 13 mg of phenyl disulfide, and 4 mg of NMA*BF_4. Reaction was carried out at room temperature for 24 hours and purified via flash chromatography. Yield was 98 mg (82%, 5.2:1 dr) of the desired adduct as a clear oil. Characterizations include major and minor diastereomers. **^{1}H NMR** (600 MHz, $CDCl_3$) δ major: 7.34-7.0 (m, 9H), 4.4 (dq, 6, 12.6 Hz, 1H), 3.22-3.16 (m, 1H), 3.07 (dd, J=4.8, 14.4 Hz, 1H), 2.9 (5.9, 14.3 Hz, 1H), 2.7 (dd, J =9.9, 12.1 Hz, 1H), 1.25 (d J=6.6 Hz, 3H). Minor: 7.27–6.78 (m, 9H), 4.76 (dq, J = 8.8 Hz, 1H), 3.3 -3.0 (m, 3H), 2.31(dd, J= 9,14.4 Hz, 1H), 1.48 (d, J= 6.6 Hz, 3H).). **^{13}C NMR** (151 MHz, $CDCl_3$) δ177.43, 136.38, 135.68, 132.41, 130.98, 130, 129.05, 128.88, 128.41, 128.38, 127.91, 127.85, 127.70, 81.07, 50.39, 44.70, 31.12, 30.92, 30.24, 29.65, 20.40. **MS** (GC-MS) Calculated *m/z* for $[M]^+$ = 300. Experimental *m/z* for $[M]^+$ = 300. **IR** (Thin Film, cm^{-1}): 3063, 3030, 2977, 2928, 2359, 1771, 1600, 1491.



12e

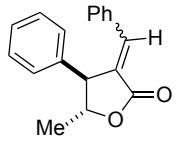
5-methyl-4-phenyl-3-(thiophen-2-ylmethyl)dihydrofuran-2(3H)-one (12e): The lactone was prepared according to General Procedure B using 155 μL of β-methylstyrene 61.6mg of (*E*)-3-(thiophen-2-yl)acrylic acid, 13 mg of phenyl disulfide, and 4 mg of NMA*BF_4. Reaction was carried out at room temperature for 2 days and purified via flash chromatography. Yield was 69 mg (63%, 2.7:1) of the desired adduct as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ *major*: 7.39-7.09 (m, 7H),

6.91 (dd, J= 3.3, 5.1 Hz, 1H), 6.81 (d, J = 3.3 Hz, 1H), 4.48, (m 1H), 3.39 (dd, J= 4.6, 15.2 Hz, 1H), 3.21 (dt, J = 5, 12.1 Hz, 1H), 3.1 (dd, J= 5.5, 15 Hz, 1H), 2.92 (dd, J = 9.9, 12.1 Hz, 1H), 3.54 (d, J = 6.24 Hz, 3H). *minor*: 7.36- 7.25 (m, 3H) 7.15 (dd, J=1.10, 5.14 Hz, 1H), 7.09 (m, 2H), 6.89 (dd, J=3.3, 5.14 Hz, 1H), 6.57 (d, J=3.3 Hz, 1H), 4.92 (dq, J =1.7, 6.5 Hz, 1H), 3.39 (m, 2H), 3.25 (dd, J = 3.9, 15.6 Hz, 1H), 2.55 (dd, J= 9.9, 15.4 Hz, 1H), 1.53 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) *major:* 176.29, 138.69, 136.74, 129.35, 129.08, 127.40, 126.93, 124.48, 80.96, 53.63, 49.84, 27.33, 20.45. *minor:* 176.98, 141.22, 138.34, 128.89, 127.91, 127.74, 126.74, 125.52, 123.70, 81.47, 50.49, 45.26, 26.20, 20.48. **MS** (GC-MS) Calculated *m/z* for $[M]^+$ = 272. Experimental *m/z* for $[M]^+$ = 272. **IR** (Thin Film, cm^{-1}): 3734, 3648, 3055, 2980, 2925, 2359, 2341, 1770, 1732, 1716, 1652, 1558, 1507, 1455.



12f

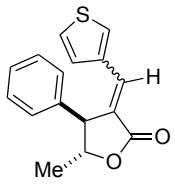
***trans*-(*E*/*Z*)-5-methyl-4-phenyl-3-((trimethylsilyl)methylene)dihydrofuran-2(3H)-one (12f)**: The lactone was prepared according to General Procedure B using 194 μL of β-methylstyrene, 71 mg of 3-(trimethylsilyl)propiolic acid, 16 mg of phenyl disulfide, and 5 mg of NMA*BF_4. Reaction was carried out at room temperature for 24 hours and purified via flash chromatography. Yield was 101 mg (78%, 1.3:1 *E*:*Z*) of the desired adduct as a clear oil. Characterizations include *Z* and *E* products. **^{1}H NMR** (600 MHz, $CDCl_3$) δ *E*: 7.34-7.15 (m, 5H), 4.41 (dq, J= 4.5, 6.3Hz, 1H), 3.77 (dd, J= 2.8, 4.3 Hz, 1H), 1.47 (d, J = 6.3 Hz, 3H), -0.13 (s, 9H). *Z*: 7.40-7.32 (m, 3H), 7.18-7.17 (m, 2H), 6.13 (d, J=2.93 Hz, 1H), 4.49 (dq, J= 6.17, 7.89 Hz, 1H), 3.69 (dd, J= 2.93, 8.07 Hz, 1H), 1.45 (d, J= 6.2 Hz, 3H), 0.20 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ *E*: δ169.99, 143.96, 143.73, 141.75, 129.07, 127.88, 127.58, 82.23, 52.70, 21.42, -1.49. *Z*: δ169.98, 143.71, 141.70, 129.04, 127.85, 82.22, 52.63, 21.39, -1.52. **MS** (GC-MS) Calculated *m/z* for $[M]^+$ = 260. Experimental *m/z* for $[M]^+$ = 260. **IR** (Thin Film, cm^{-1}): 3058, 3030, 2957, 2360, 2341, 1750, 1455, 1266, 1249, 1194.



12g

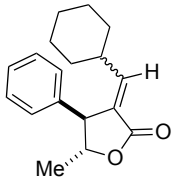
***trans*-3-((Z/E)-benzylidene)-5-methyl-4-phenyldihydrofuran-2(3H)-one (12g):** The lactone was prepared according to General Procedure C using 103.6 μL of β-methylstyrene 58.4 mg of 3-

phenylpropiolic acid, 13 mg of phenyl disulfide, 4.7 μL of 2,6-lutidine, and 4 mg of NMA*BF_4. Reaction was carried out at room temperature for 4 days and purified via flash chromatography. Yield was 53 mg (49%, 1.5:1) of the desired adduct as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ *Z*: 7.83, (m, 2H), 7.44-7.27 (m, 9H), 6.59, (d, J = 2.6 Hz, 1H), 4.61-4.58 (m, 1H), 3.92 (dd, J = 2.9, 8.1 Hz, 1H), 1.5 (d, J = 6.2 Hz, 3H). δ *E:* 7.8 (d, J = 2.6 Hz, 1H), 7.28 (m, 11H), 4.57 (qd, J = 3.5, 6.3 Hz, 1H), 4.17, (t, J = 2.8 Hz, 1H), 1.52 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ *Z:* 168.29, 141.30, 138.90, 133.40, 130.81, 130.28, 129.70, 129.21, 128.82, 128.10, 127.96, 80.94, 57.44, 19.81. *E:* 172.02, 139.79, 139.77, 133.41, 130.50, 129.91, 129.22, 128.46, 127.52, 127.19, 82.61, 52.14, 21.84. **MS** (GC-MS) Calculated *m/z* for $[M]^+$ = 264. Experimental *m/z* for $[M]^+$ = 264. **IR** (Thin Film, cm^{-1}): 3734, 3648, 3566, 2359, 1771, 1716, 1698, 1683, 1670, 1558, 1540, 1507.



12h

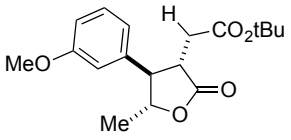
***trans*-3-(Z/E)-5-methyl-4-phenyl-3-(thiophen-3-ylmethylene)dihydrofuran-2(3H)-one (12h):** The lactone was prepared according to General Procedure C using 103.6 μL of β-methylstyrene, 60.4 mg of 3-(thiophen-2-yl)propiolic acid, 13 mg of phenyl disulfide, 4.7 μL of 2,6-lutidine, and 4 mg of NMA*BF_4. Reaction was carried out at room temperature for 4 days and purified via flash chromatography. Yield was 48 mg (44%, 1.5:1) of the desired adduct as a clear oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ *Z*: 8.24, (m, 1H), 7.64, (dd, J = 5.14, 1.10 Hz, 1H), 7.22-7.45, (m, 8H), 6.43 (d, J = 2.93 Hz, 1H), 4.55 (dq, J = 6.13, 8.02 Hz, 1H), 3.87 (dd, J = 2.57, 8.07 Hz, 1H), 1.43-1.49 (m, 3H). δ *E:* 7.87 (s, 1H), 7.37-7.19 (m, 8H), 6.9 (m, 1H), 4.56-4.53 (m, 1H), 4.08 (m, 1H), 1.55 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ *Z:* 168.81, 135.37, 133.69, 131.42, 129.21, 128.81, 125.05, 81.14, 57.17, 19.87. *E*: 172.10, 140.04, 135.83, 133.10, 130.23, 129.40, 126.90, 126.20, 82.53, 52.00, 22.05. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$= 271.07. Experimental *m/z* for $[M+H]^+$ = 271.12. **IR** (Thin Film, cm^{-1}): 3085, 3054, 2985, 2305, 1748, 1636, 1558, 1540, 1519, 1265.



12i

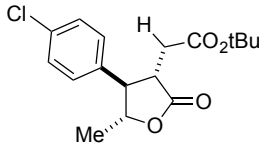
***trans-3*-(Z/E)-3-(cyclohexylmethylene)-5-methyl-4-phenyldihydrofuran-2(3H)-one (12i):** The lactone was prepared according to General Procedure C using 103.6 μL of β-methylstyrene, 60.8 mg

of 3-cyclohexylpropiolic acid, 13 mg of phenyl disulfide, 4.7 μL of 2,6-lutidine, and 4 mg of NMA*BF_4. Reaction was carried out at room temperature for 4 days and purified via flash chromatography. Yield was 99 mg (92%, 1:1) of the desired adduct as a clear oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ *Z:* 7.41-7.15 (m, 5H), 5.68, (dd, J = 2.6, 9.9 Hz, 1H), 4.40 (m, 1H), 3.67 (dd, J = 2.57, 8.07 Hz, 1H), 2.51 (m, 1H), 1.66 (m, 5H), 1.41 (m, 3H), 1.35 (m, 2H), 1.11 (m, 1H), 0.99 (m, 1H). *E*: 7.38-7.20 (m, 5H), 6.75-6.70 (dd, J = 2.75, 10.45 Hz, 1H), 4.56-4.47 (m, 1H), 3.78 (dd, J = 2.93, 5.14 Hz, 1H), 1.89 (m, 1H), 1.73-1.50 (m, 4H), 1.48 (d, J = 6.24 Hz, 3H), 1.08 (m, 4H), 0.90 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) *Z:* 169.20, 151.02, 139.27, 128.97, 128.51, 127.61, 81.17, 55.49, 35.70, 32.40, 32.02, 25.74, 25.22, 19.74. *E:* 171.09, 148.55, 141.32, 129.00, 127.49, 82.33, 51.67, 38.48, 31.32, 30.72, 25.57, 25.20, 24.98, 21.26. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 271.16. Experimental *m/z* for $[M+H]^+$ = 271.12. **IR** (Thin Film, cm^{-1}): 3853, 3749, 3648, 2927, 2852, 2359, 1750, 1716, 1698, 1683, 1559, 1554, 1507.



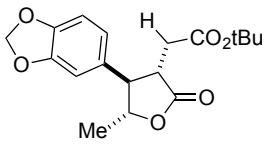
13a

***tert*-Butyl 2-(4-(3-methoxyphenyl)-5-methyl-2-oxotetrahydrofuran-3-yl)acetate (13a)** The lactone was prepared according to General Procedure A using 77 μL 1-methoxy-3-(prop-1-en-1-yl)benzene, 94.7 mg mono-*tert*-butylfumarate, 10.9 mg phenyl disulfide, 5.2 mg NMA*BF_4, and 6 μL 2,6-lutidine. Yield was 76% (2.8:1 dr). The major and minor diastereomers could be separated via column chromatography (3% acetone in hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$) δ major: 7.28 (t, J = 7.9 Hz, 1H), 6.84 (m, 2H), 6.77 (t, J = 1.9 Hz, 1H), 4.48 (m, 1H), 3.81 (s, 3H), 3.19 (m, 1H), 3.03 (dd, J = 9.9, 12.3 Hz, 1H), 2.60 (dd, J = 5.1, 16.5 Hz), 2.51 (dd, J = 6.2, 16.6 Hz, 1H) 1.38 (s, 9H). δ minor: (400 MHz, CDCl3) 7.23 (t, J = 8 Hz, 1H), 6.81 (dd, J = 2.1, 8.3 Hz, 1H), 6.66 (d, J = 7.6 Hz, 1H), 6.62 (t, J = 2.2 Hz, 1H), 4.85 (dq, J = 1, 6.6 Hz, 1H), 3.77 (s, 3H), 3.48 (m, 2H), 2.58 (dd, J = 3.5, 18.4 Hz, 1H), 1.87 (dd, J = 9.5, 17.6 Hz, 1H), 1.51 (d, J = 6.6 Hz, 3H), 1.37 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$). δ major: 176.05, 169.70, 160.04, 138.05, 130.17, 119.98, 114.00, 112.88, 81.28, 80.77, 55.58, 55.24, 45.31, 34.02, 27.83, 18.62. δ minor: (101 MHz, CDCl3) 177.19, 170.79, 159.98, 140.16, 130.10, 119.73, 113.56, 112.78, 81.32, 80.98, 55.14, 55.01, 39.97, 32.10, 27.90, 20.63. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 221.16. Experimental *m/z* for $[M+H]^+$ = 221.19. **IR** (Thin Film, cm^{-1}) 2976, 2932, 2837, 1775, 1728, 1601, 1586, 1489, 1456, 1367, 1266.



13b

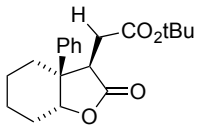
***tert*-Butyl 2-(4-(4-chlorophenyl)-5-methyl-2-oxotetrahydrofuran-3-yl)acetate (13b)** The lactone was prepared according to General Procedure A using 72 µL *p*-Cl-β-methylstyrene, 94.7 mg mono-*tert*-butylfumarate, 10.9 mg phenyl disulfide, 5.2 mg NMA*BF_4, and 6 µL 2,6-lutidine. Yield was 77% (2.3:1 dr). The major and minor diastereomers could be separated via column chromatography (3% acetone in hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$) δ major: 7.33 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 4.43 (m, 1H), 3.17 (m, 1H), 3.03 (dd, J = 9.8, 12.2 Hz, 1H), 2.60 (dd, J = 4.8, 16.5 Hz, 1H), 2.47 (dd, J = 6.3, 16.5 Hz, 1H), 1.36 (d, J = 6.1 Hz, 3H), 1.31 (s, 9H). δ minor: 7.28 (d, J = 8.4 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 4.81 (dq, J = 1.6, 6.5 Hz, 1H), 3.55-3.44 (m, 2H), 2.60 (dd, J = 3.7, 18 Hz, 1H), 1.82 (dd, J = 10.3, 18, 1H), 1.51 (d, J = 6.6 Hz, 3H), 1.38 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ major: 175.69, 169.59, 134.92, 133.88, 129.24, 129.16, 81.36, 80.61, 55.06, 45.19, 33.97, 27.76, 18.42. δ minor: (125 MHz, CDCl3) 176.88, 170.61, 137.11, 133.61, 129.18, 128.97, 81.30, 81.20, 49.42, 39.89, 32.03, 27.90, 20.59. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 325.11. Experimental *m/z* for [M+H]+ = 325.09. **IR** (Thin Film, cm^{-1}) 3057, 2979, 2931, 1776, 1726, 1494, 1368, 1266.



13c

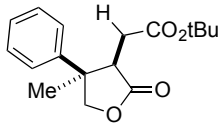
***tert*-Butyl 2-(4-(benzo[d][1,3]dioxol-5-yl)-5-methyl-2-oxotetrahydrofuran-3-yl)acetate (13c)** The lactone was prepared according to General Procedure A using 72.5 µL isosafrole, 94.7 mg mono-*tert*-butylfumarate, 10.9 mg phenyl disulfide, 5.2 mg NMA*BF_4, and 6 µL 2,6-lutidine. Yield was 65% (4.3:1 dr). The major and minor diastereomers could be separated via column chromatography (5% acetone in hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$) δ major: 6.79 (d, J = 7.9 Hz, 1H), 6.70 (m, 2H), 5.97 (s, 2H), 4.41 (m, 1H), 3.11 (m, 1H), 2.98 (dd, J = 9.8, 12.3, 1H), 2.90 (dd, J = 5, 16.5 Hz, 1H), 2.49 (dd, J = 6.1, 16.5 Hz, 1H), 1.37 (d, J = 6.1 Hz, 1.36 (s, 9H). δ minor: 6.73 (d, J = 7.9 Hz, 1H), 6.54 (m, 2H), 5.96 (s, 2H), 4.81 (q, J = 6.3 Hz, 1H), 3.43 (m, 2H), 2.59 (dd, J = 3.4, 18 Hz, 1H), 1.89 (dd, J = 10.2, 17.9 Hz, 1H), 1.50 (d, J = 6.5 Hz, 3H), 1.39 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ major: 175.96, 169.71, 148.25, 147.38, 129.99, 121.43, 108.68, 107.55, 101.24, 81.28, 80.84, 55.37, 45.33, 33.88, 27.84, 18.44. δ minor: 177.18, 170.85, 148.24, 147.02, 132.34, 120.87, 108.55, 107.73, 101.19, 81.55, 81.07, 49.73, 40.09, 32.08, 27.95, 20.61. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ =

335.14. Experimental *m/z* for $[M+H]^+$ = 335.17. **IR** (Thin Film, cm^{-1}) 3056, 2980, 2932, 2307, 1773, 1726, 1506, 1489, 1446, 1368, 1266.



13d

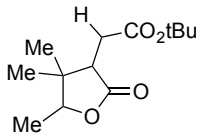
***tert*-Butyl 2-(2-oxo-3a-phenyloctahydrobenzovuran-3-yl)acetate (13d)** The lactone was prepared according to General Procedure A using 80 μL 1-phenylcyclohexene, 94.7 mg mono-*tert*-butylfumarate, 10.9 mg phenyl disulfide, 5.2 mg NMA*BF_4, and 6 μL 2,6-lutidine. The mixture was allowed to react for 30 hours instead of the typical 24. Yield was 64% (5:1 dr). The major and minor diastereomers could not be separated, and the product was isolated as a mixture of isomers following column chromatography (2% acetone in hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$) δ major: 7.42-7.33 (m, 5H), 4.95 (bs, 1H), 3.38 (t, J = 7 Hz, 1H), 2.57 (dd, J = 7.4, 16.2 Hz, 1H), 2.28 (d, J = 13.2 Hz, 1H) 2.20 (dd, J = 6.2, 16.2 Hz, 1H), 2.10 (d, J = 13.6 Hz, 1H), 1.70-1.37 (m, 6H), 1.26 (s, 9H). δ minor: 7.29-7.22 (m, 5H), 5.01 (t, J = 4.4 Hz, 1H), 3.17 (t, J = 6.8 Hz, 1H), 2.17 (dd, J = 6.8, 16.3 Hz, 1H), 2.1-1.9 (m, 3H), 1.7-1.4 (m, 6H), 1.33 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ major: 176.37, 170.09, 138.34, 128.94, 127.22, 126.62, 81.79, 80.92, 53.37, 47.64, 29.86, 27.74, 26.42, 24.63, 21.04, 19.36. minor: 177.46, 169.96, 139.65, 128.78, 127.13, 127.06, 81.11, 79.46, 48.67, 48.29, 34.91, 32.98, 31.52, 27.85, 26.61, 22.59, 20.34, 14.06. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 331.18. Experimental *m/z* for $[M+H]^+$ = 331.15. **IR** (Thin Film, cm^{-1}) 3054, 2360, 2341, 1771, 1507, 1266.



13e

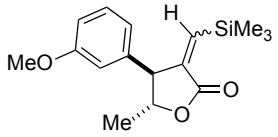
***tert*-Butyl 2-(4-methyl-2-oxo-4-phenyltetrahydrofuran-3-yl)acetate (13e)** The lactone was prepared using General Prodedure A, however a 3:1 ratio of alkene:acid was employed, and the mixture was allowed to react for 48 hours instead of the typical 24. The lactone was prepared using 195 μL α-methylstyrene, 86.1 mg mono-*tert*-butylfumarate, 10.9 mg phenyl disulfide, 5.2 mg NMA*BF_4, and 6 μL 2,6-lutidine. The major and minor diastereomers could not be separated, and the product was isolated in an 81% yield (1.3:1 dr) following column chromatography (3% acetone in hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$) δ major: 7.43-7.22 (m, 5H), 4.28 (d, J = 8.9 Hz, 1H), 4.21 (d, J = 8.9 Hz, 1H), 3.61 (dd, J = 5.1, 8.4 Hz, 1H), 2.61 (dd, J = 8.4, 16.1 Hz, 1H), 2.38 (dd, J = 5.2, 16.2 Hz, 1H), 1.43 (s, 3H), 1.38 (s, 9H). δ minor: 7.43-7.22 (m, 5H), 4.71 (d, J = 9.3 Hz, 1H), 4.28 (d, J = 9.3 Hz, 1H), 3.19 (dd, J = 6, 7.4 Hz, 1H), 2.30 (dd, J = 6, 17 Hz, 1H), 1.89 (dd, J = 7.4, 17 Hz, 1H),

1.64 (s, 3H), 1.42 (s,9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ major: 177.05, 170.26, 141.45, 129.02, 127.52, 125.64, 81.35, 78.17, 46.48, 46.22, 31.43, 27.87, 20.82. δ minor: 177.58, 170.58, 141.16, 128.95, 127.52, 126.04, 81.13, 78.31, 48.18, 46.41, 32.71, 27.94, 24.59. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 291.15. Experimental *m/z* for $[M+H]^+$ = 291.19. **IR** (Thin Film, cm^{-1}) 3058, 2979, 2932, 2306, 1775, 1728, 1498, 1455, 1368, 1266.



13f

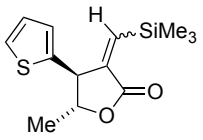
***tert*-Butyl 2-(4,4,5-trimethyl-2-oxotetrahydrofuran-3-yl)acetate (13f)** The lactone was prepared according to a modified General Procedure B. The lactone was prepared using 159 μL of 2-methyl-2-butene (3 equiv.), 86.1 mg of mono-*tert*-butylfumarate (1 equiv.), 5.2 mg NMA*BF_4, 3.8 mg *p*-nitrothiophenol (5 mol%), and 6 μL 2,6-lutidine. The major and minor diastereomers could not be separated, and relative stereochemistry could not be determined. The yield was 55% (2.7:1 d.r.) following column chromatography (5% acetone in hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$) δ major: 4.18 (q, J = 6.5 Hz, 1H), 2.90 (t, J = 6.9 Hz, 1H), 2.58 (dd, J = 6.8, 16.3 Hz, 1H), 2.23 (dd, J = 7.1, 16.4 Hz, 1H), 1.45 (s, 9H), 1.25 (d, J = 6.5 Hz, 3H), 1.06 (s, 3H), 0.79 (s, 3H). δ minor: 4.21 (q, J = 6.7 Hz, 1H), 2.91 (t, J overlap, 1H), 2.55 (dd, J = 6.3, 16.3 Hz, 1H), 2.29 (dd, J = 7.8, 16.4 Hz, 1H), 1.44 (s, 9H), 1.26 (d, J = 6.6 Hz, 3H), 1.04 (s, 3H), 0.98 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ major: 176.93, 170.74, 83.20, 81.14, 48.87, 42.43, 30.85, 27.96, 23.18, 15.81, 13.00. δ minor: 177.31, 170.73, 84.03, 81.23, 45.31, 40.74, 31.20, 27.94, 22.86, 22.11, 15.56. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 243.15. Experimental *m/z* for $[M+H]^+$ = 243.18. **IR** (Thin Film, cm^{-1}) 3056, 2980, 2360, 1771, 1731, 1497, 1266.



13g

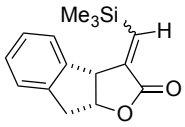
(*E/Z*)-4-(3-methoxyphenyl)-5-methyl-3-((trimethylsilyl)methylene)dihydrufran-2-(3H)-one (13g) The lactone was prepared using General Procedure A using 77 μL *m*-methoxy-β-methylstyrene, 76 μL 3-(trimethylsilyl)propiolic acid, 10.9 mg phenyl disulfide, 5.2 mg NMA*BF_4, and 6 μL 2,6-lutidine. Yield was 73% (0.8:1 *E*:*Z*). The *E*- and *Z*- isomers could be separated via column chromatography (3% acetone in hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$) δ *E*: 7.24 (t, J = 7.9 Hz, 1H), 7.19 (d, J = 2,6 Hz, 1H), 6.80 (dd, J = 2.4, 8.2 Hz, 1H), 6.72 (d, J = 7.6 Hz, 1H), 6.65 (t, J = 2 Hz,

1H), 4.40 (m, 1H), 3.77 (s, 3H), 3.74 (dd, J = 2.6, 4.4 Hz, 1H), 1.46 (d, J = 6.3 Hz, 3H), -0.11 (s, 9H). δ *Z*: 7.30 (t, J = 8 Hz, 1H), 6.85 (m, 1H), 6.75 (d, J = 7.6 Hz, 1H), 6.69 (t, J = 1.8 Hz, 1H), 6.15 (d, J = 2.9 Hz, 1H), 4.49 (m, 1H), 3.81 (s, 3H), 3.64 (dd, J = 2.9, 8 Hz, 1H), 1.44 (d, J = 6.2 Hz, 3H), 0.19 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ *E*: 169.93, 160.01, 143.85, 143.64, 143.12, 130.06, 120.16, 113.57, 112.71, 82.08, 55.23, 52.59, 21.44, -1.49. δ *Z*: 169.29, 159.97, 145.95, 145.37, 140.47, 130.09, 120.89, 114.60, 112.63, 81.27, 57.25, 55.23, 20.04, -0.79. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 291.13. Experimental *m/z* for $[M+H]^+$ = 291.12. **IR** (Thin Film, cm^{-1}) 3055, 2956, 2837, 2306, 1757, 1600, 1585, 1490, 1455, 1266.



13h

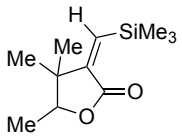
(*E/Z*)-5-methyl-4-(thiophen-2-yl)-3-((trimethylsilyl)methylene)dihydrofuran-2(3H)-one (13h): The lactone was prepared according to General Procedure B using 149 mg of *t*-2-propenethiophene, 57 mg of 3-(trimethylsilyl)propiolic acid, 13 mg of phenyl disulfide, and 4 mg of NMA BF_4^-. Reaction was carried out at room temperature for 3 days and purified via flash chromatography. Yield was 83 mg (78%, 1.4:1 *E*: *Z*) of the desired adduct as a purple oil. Characterizations include *Z* and *E* products. **^{1}H NMR** (600 MHz, $CDCl_3$) δ mixture of *Z* and *E*: 7.28-7.22 (m, 6H *E*+*Z*), 7.05 (m, 1H *Z*), 6.97 (ddd, J=3.5, 4.8, 8.6 Hz, 1H *E*), 6.86 (d, J= 4Hz, 1H *Z*), 6.35 (d, J= 2.9Hz, 1H *Z*), 4.51 (m, 2H *E*+*Z*), 4.07 (dd, J= 3, 6Hz, 1H *E*), 4.01 (dd, J= 3, 7.8 Hz, 1H *Z*). 1.5 (m, 6H *E*+*Z*), 0.22 (s, 3H *Z*), 0.02 (s, 3H *E*). **^{13}C NMR** (151 MHz, $CDCl_3$) mixture of *Z* and *E*: 169.34, 168.84, 145.59, 145.40, 143.02, 144.5, 140.94, 127.27, 127.06, 126.59, 125.45, 125.29, 125.01, 82.20, 81.51, 52.11, 49.38, 21.37, 19.80, -0.78, -1.42. **MS** (GC-MS) Calculated *m/z* for $[M]^+$ = 266. Experimental *m/z* for $[M]^+$ = 266. **IR** (Thin Film, cm^{-1}): 2952, 2899, 1763, 1385, 1307, 1245.



13i

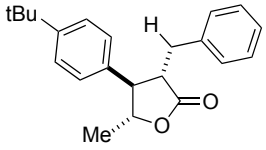
(*E/Z*)-3-((trimethylsilyl)methylene)-3,3a,8,8a-tetrahydro-2H-indeno[2,1-b]furan-2-one (13i): The lactone was prepared according to General Procedure B using 174 μL of indene, 71 mg of 3-(trimethylsilyl)propiolic acid, 16 mg of phenyl disulfide, and 5 mg of NMA BF_4^-. Reaction was carried out at room temperature for 4 days and purified via flash chromatography. Yield was 98 mg (76%, 1.3:1 *E*: *Z*) of the desired adduct as a purple oil. Characterizations include *Z* and *E* products.

^{1}H NMR (600 MHz, $CDCl_3$) δ *E*: 7.29-7.20 (m, 2H), 7.19 (d, J=7 Hz, 2H), 6.9 (d, J= 1.1Hz, 1H), 5.18 (m, 1H), 4.53 (d, J=5.1 Hz, 1H), 3.37 (m, 2H), 0.35 (s, 9H). δ *Z*: 7.25 (s, 4H), 6.73 (d, J= 1.47 Hz, 1H), 5.29 (dq, J 1.6, 5.8 Hz, 1H), 4.38 (dd, J=1.3, 6 Hz, 1H), 3.34 (m, 2H), 0.22 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ *E*: 169.98, 142.45, 140.17, 138.68, 128.38, 127.43, 125.49, 125.06, 81.90, 50.33, 38.48, -0.64. δ *Z*: 169.43, 144.22, 141.03, 139.98, 128.26, 127.54, 124.17, 81.22, 53.28, 39.03, -0.78. **MS** (GC-MS) Calculated *m/z* for $[M]^+$ = 258. Experimental *m/z* for $[M]^+$ = 258. **IR** (Thin Film, cm^{-1}): 3069, 2955, 2901, 1759, 1636, 1558, 1479, 1311, 1265.



13j

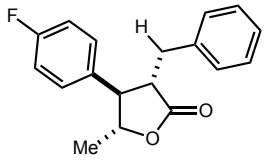
(E)-4,4,5-trimethyl-3-((trimethylsilyl)methylene)dihydrofuran-2(3H)-one (13j): The lactone was prepared according to General Procedure B using 212 μL of 2-methyl-2-butene, 71 mg of 3-(trimethylsilyl)propiolic acid, 16 mg of phenyl disulfide, and 5 mg of NMA BF_4^-. Reaction was carried out at room temperature for 48 hours and purified via flash chromatography. Yield was 58 mg (55%, *Z*) of the desired adduct as a clear oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.19 (s, 1H), 4.21 (q, J=6.6 Hz, 1H), 1.26 (d, J= 6.6 Hz, 3H), 1.14 (s, 3H), 1.01 (s, 3H), 0.19 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) 170.03, 151.96, 139.96, 82.96, 43.73, 25.43, 22.68, 15.29, -0.75. **MS** (+ESI) Calculated *m/z* for $[M+Li]^+$ = 219.14. Experimental *m/z* for $[M+Li]^+$ = 219.18. **IR** (Thin Film, cm^{-1}): 2965, 2359, 1704, 1636, 1558, 1520, 1507, 1456.



13k

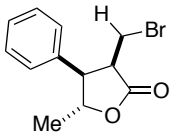
3-benzyl-4-(4-(tert-butyl)phenyl)-5-methyldihydrofuran-2(3H)-one (13k): The lactone was prepared according to General Procedure B using 108.8 mg of 1-(*tert*-butyl)-4-(prop-1-en-1-yl)benzene, 59.2 mg of cinnamic acid, 13 mg of phenyl disulfide, and 4 mg of NMA BF_4^-. Reaction was carried out at room temperature for 24 hours and purified via flash chromatography. Yield was 100 mg (78%, 4.9:1 dr) of the desired adduct as a white crystalline solid. Characterizations include major and minor diastereomers. **^{1}H NMR** (600 MHz, $CDCl_3$) δ major: 7.33 (d, J= 8.4 Hz, 2H), 7.22-7.05 (m, 7H), 7.39 (dq, J=6.1, 9.7 Hz, 1H), 3.21 (dt, J= 5.55, 12.01 Hz, 1H), 3.1 (m, 1H), 2.93 (dd, J= 5.9, 14.3 Hz, 1H), 2.78 (dd, J= 9.54, 12.10 Hz, 1H) 1.23 (d, J= 6 Hz, 3H). Minor: 7.2-7.05 (m, 5H), 6.98 (d, J= 8.4 Hz, 2H), 6.92 (d, 7.35 Hz, 2H), 4.78 (dq, J= 4.2, 6.6Hz, 1H), 3.3-3.24 (m, 2H), 3.05 (d, J=4.2, 14.4 Hz, 1H), 2.36, dd, J=9.5, 14.7Hz, 1H), 1.47 (d, J= 6.6 Hz, 3H).). **^{13}C NMR** (151 MHz,

$CDCl_3$) δ177.79, 176.80, 150.55, 137.29, 133.63, 129.67, 128.65, 128.23, 127.65, 127.39, 126.45, 125.79, 125.61, 81.05, 77.20, 76.99, 76.79, 53.74, 49.39, 34.44, 33.42, 31.26, 31.22, 20.31, 18.05. **MS** (GC-MS) Calculated *m/z* for $[M]^+$ = 322. Experimental *m/z* for $[M]^+$ = 322. **IR** (Thin Film, cm^{-1}): 3060, 3029, 2964, 2969, 2359, 1771, 1652, 1558, 1496.



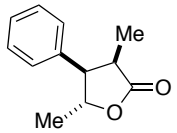
13l

3-benzyl-4-(4-fluorophenyl)-5-methyldihydrofuran-2(3H)-one (13l): The lactone was prepared according to General Procedure B using 108.8 mg of (E)-1-fluoro-4-(prop-1-en-1-yl)benzene, 59.2 mg of cinnamic acid, 13 mg of phenyl disulfide, and 4 mg of NMA BF_4^-. Reaction was carried out at room temperature for 24 hours and purified via flash chromatography. Yield was 89 mg (78%, 3.7:1 dr) of the desired adduct as a green oil. Characterizations include major and minor diastereomers. **^{1}H NMR** (600 MHz, $CDCl_3$) δ major: 7.19-6.97 (m, 9H), 4.34 (dq, J= 6.0, 9.77 Hz, 1H), 3.17 (m, 1H), 3.06, (dd, J = 6, 14.4 Hz, 1H), 2.97 (dd, J=6, 14.4Hz, 1H), 2.79, dd (J= 9.9, 12.1 Hz, 1H), 1.23 (d, J =6.6 Hz, 3H). minor: 7.22-6.89 (m, 9H), 4.72 (dq, J=1.8, 6.4 Hz, 1H), 3.37-3.05 (m, 3H), 2.28 (dd, 10.45, 14.86 Hz, 1H), 1.48 (d, J= 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ177.43, 176.44, 138.29, 136.96, 135.69, 132.41, 130.98, 138.42, 127.71, 81.21, 81.08, 54.36, 50.39, 49.25, 44.71, 32.74, 30.93, 30.25, 20.41, 18.36. **MS** (GC-MS) Calculated *m/z* for $[M]^+$ = 284. Experimental *m/z* for $[M]^+$ = 284. **IR** (Thin Film, cm^{-1}): 3063, 3029, 2977, 2927, 2360, 2341, 1711, 1604, 1511, 1455, 1386, 1711, 1604, 1511, 1455, 1386.

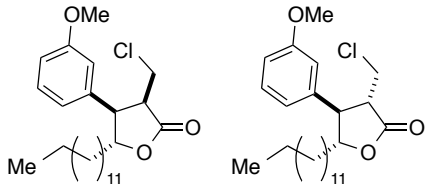


3-(bromomethyl)-5-methyl-4-phenyldihydrofuran-2(3*H*)-one (14): The lactone was prepared according to a modified General Procedure A, using 130 μL of β-methylstyrene (2 equiv), 75.5 mg (*Z*)-3-bromoacrylic acid (1 equiv), 10.9 mg phenyldisulfide, 5.2 mg NMA*BF_4, and 6 μL 2,6-Lutidine. The reaction was carried out at room temperature over 4 days. Due to degradation issues on silica chromatography, only one diastereomer could be isolated. The other major product observed was the elimination to the α-methylene-γ-butyrolactone. The indicated diastereomer was isolated in a 14% yield (19 mg) via silica chromatography (2% acetone in hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39-7.24 (m, 5H), 4.91 (dq, J = 1.8, 6.5 Hz, 1H), 3.58-3.45 (m, 3H), 2.76 (t, J = 10.12 Hz, 1H), 1.53 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.26, 136.97, 129.07, 128.06, 127.91,

81.37, 50.03, 46.85, 26.77, 20.40. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 271.01. Experimental *m/z* for $[M+H]^+$ = 271.02. **IR** (Thin Film, cm^{-1}) 3063, 3032, 2979, 2931, 2254, 1772, 1603, 1498, 1455, 1357.

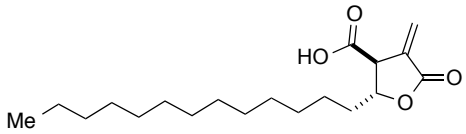


3,5-dimethyl-4-phenyldihydrofuran-2(3*H*)-one (15): The lactone was prepared by dehalogenation of 3-(bromomethyl)-5-methyl-4-phenyldihydrofuran-2(3*H*)-one (16 mg), using tributyltin hydride (80 μL, 5 equiv) and AIBN (3 mg, 0.3 equiv) in [0.2] benzene (0.3 mL). A 1-dram vial equipped with a stir bar and a Teflon septum screw cap was charged with the lactone, AIBN, tributyltin hydride, and benzene. The reaction mixture was capped and sparged with N_2 for 5 minutes, and then the vial was sealed with Teflon tape prior to heating at 65 ^oC for 2 hours. At this point, the solvent was evaporated under reduced pressure, and a crude ^1H NMR was taken to determine if any ring opening or isomerization products could be observed. The only observed product was the dehalogenated product 3,5-dimethyl-4-phenyldihydrofuran-2(3*H*)-one. The reaction was purified via silica chromatography, flushing with hexanes to remove the tributyltin hydride, followed by dichloromethane to isolate 8.2 mg (73%) of lactone Y. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 3H), 7.13 (dd, J = 1.4, 7.8 Hz, 2H), 4.87 (m, 1H), 3.34 (dd, J = 4.8, 8.7 Hz, 1H), 3.04 (m, 1H), 1.48 (d, J = 6.4 Hz, 3H), 0.89 (d, J = 7.5 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.96, 137.65, 128.87, 127.84, 127.50, 79.75, 52.07, 38.95, 20.12, 11.40. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 191.10. Experimental $[M+H]^+$ = 191.15. **IR** (Thin Film, cm^{-1}) 3031, 2978, 2935, 1771, 1456, 1206.



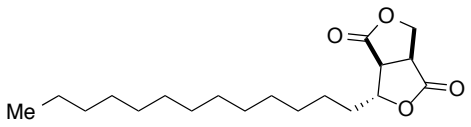
***cis-trans*-3-(chloromethyl)-4-(3-methoxyphenyl)-5-tridecyldihydrofuran-2(3*H*)-one:** The lactone was prepared according to modified General Procedure C using 94.8 mg of 1-methoxy-3-pentadec-1-en-1-yl)benzene, 60.8 mg of (*Z*)-chloroacrylic acid, 10 mg of phenyl disulfide, 3.5 μL of 2,6-lutidine, and 3 mg of NMA BF_4^-. Reaction was carried out at room temperature for 4 days and purified via flash chromatography. Yield was 174 mg (69%) of the desired adduct as a pink oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ *minor*: 7.27-7.25 (m, 1H), 6.86-6.77 (m, 3H), 4.75-4.71 (ddd, J = 2.5, 5.7, 8.3 Hz, 1H), 3.8 (s, 3H), 3.71-3.68 (dd, J = 3.4, 11.5 Hz, 2H), 3.55-3.53 (dd, J = 2.5, 8.6 Hz, 2H), 3.37 (m, 2H), 3.05 (dd, J = 9.8, 11.5 Hz, 2H), 1.86-1.66 (m, 5H), 1.56-1.1 (m, 25H), 0.88 (m, 3H).) δ *major*:

7.29 (m, 1H), 6.87-6.0 (m, 3H), 4.46 (dt, J = 6.0, 9.8 Hz, 1H), 4.02-3.98 (dd, J = 3.4, 11, 1H) 3.82 (s, 1H), 3.55 (dd, J = 3.4, 11.7 Hz, 1H), 3.43 (dd, J – 9.8 11.7 Hz, 1H), 3.16 (dt, J = 3.3, 11.7 Hz, 1H), 1.68 (m, 5H), 1.4-1.21 (m, 24H), 0.87 (t, J = 6.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ *minor*: 174.38, 159.91, 138.67, 130.15, 119.90, 114.00, 113.05, 85.30, 55.19, 48.41, 47.09, 39.87, 34.64, 31.86, 29.59, 29.31, 29.19, 25.57, 22.65, 10.08. *major:* 173.75, 160.17, 138.46, 130.37, 119.93, 114.08, 112.85, 84.32, 55.28, 50.88, 50.01, 40.66, 33.64, 31.90, 29.56, 29.46, 29.35, 29.28, 25.60, 22.68, 14.11. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 423.03. Experimental *m/z* for $[M+H]^+$ = 423.30. **IR** (Thin Film, cm^{-1}): 3054, 2926, 2851, 1777, 1469, 1265.



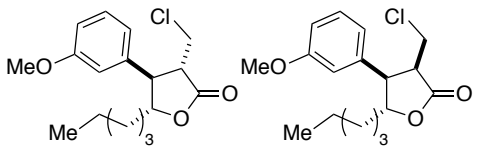
Protolichesterinic acid

Protolichesterinic Acid: 136 mg of *cis-trans*-3-(chloromethyl)-4-(3-methoxyphenyl)-5-tridecyldihydrofuran-2(3*H*)-one were combined and stirred in 2.7 mL of EtOAc, and 2.7 mL of MeCN. To this was added 8.26 mg $RuCl_3$ and 1.022 g $NaIO_4$, dissolved in 5.3 mL H_2O dropwise. Reaction was stirred for 4 hours. Following reaction completion, white precipitate was filtered through celite and was diluted with EtOAc. Washing with $Na_2S_2O_3$ (aq), and brine followed. The aqueous solution was acidified and extracted with EtOAc, which was then washed with brine. The combined organic layers were dried over $MgSO_4$ and dried. Crude material was then treated with 282 mg (5 equiv) K_2CO_3, 0.41 mL (1M), and 10.3 mL iPrOH. Reaction was stirred overnight. At the completion of the reaction, the solution was diluted with EtOAc, and acidified with 3 N HCl. The organics were washed with H_2O and brine, and were dried over $MgSO_4$. The desired product was purified via pipet column with 100% DCM, where byproduct 3-tridecyltetrahydrofuro[3,4-c]furan-1,4-dione was removed. Following the removal of the bicycle, the column was treated with 100% EtOAc to obtain the desired natural product as an off white solid (66mg, 54% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.47 (d, J = 2.93 Hz, 1H), 6.02 (d, J = 2.57) 4.81 (m, 1H), 3.63 (dt, J = 2.75, 5.50 Hz, 1H) 1.73 (m, 2H), 1.39 (m, 24 H), 0.88 (t, J = 7.15 Hz, 3H). **^{13}C NMR** (151 MHz) $CDCl_3$ d 174.39, 168.22, 132.34, 125.99, 78.84, 49.44, 35.73, 31.90, 29.66, 29.62, 29.59, 29.38, 29.34, 29.17, 24.74, 22.67, 14.11.

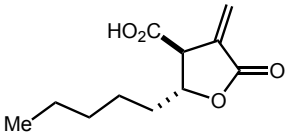


3-tridecyltetrahydrofluro[3,4-c]furan-1,4-dione: White solid **^{1}H NMR** (600 MHz,

$CDCl_3$) δ 4.83–4.78 (tq, J = 1.1, 6.6 Hz, 1H), 4.72-4.66 (dd, J = 1.5, 9.5 Hz, 1H), 4.57-4.51 (dd, J = 7.7, 9.9 Hz, 1H), 3.52 (ddd, J = 1.47, 7.79, 9.45 Hz, 1H), 3.20 (dd, J = 1.47, 9.54 Hz, 1H) 1.74 (m, 2H), 1.44 (m, 2H), 1.38-1.17 (m, 23H), 0.85-0.89 (t, J = 6.97 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$ δ 175.53, 175.35, 81.86, 69.00, 45.39, 40.69, 36.31, 31.90, 29.62, 29.36, 29.01, 24.61, 22.67, 14.11. **MS** (+ESI) Calculated *m/z* for $[M+H]^+$ = 325.23. Experimental *m/z* for $[M+H]^+$ = 325.24. **IR** (Thin Film, cm^{-1}): 3055, 2923, 2851, 1777, 1469, 1265.



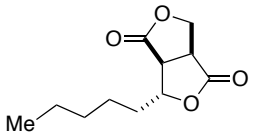
3-(chloromethyl)-4-(3-methoxyphenyl)-5-pentyldihydrofuran-2(3*H*)-one: The lactone was prepared according to modified General Procedure C using 58.5 mg (*Z*)-3-chloroacrylic acid, 108 µL 1-(hept-1-en-1-yl)-3-methoxybenzene, 5.2 mg NMA*BF_4, 16.3 mg phenyldisulfide, and 6 µL 2,6-lutidine. The diastereomers could be separated via column chromatography if using a gradient eluent. 2% acetone in hexanes was used until the minor diastereomer was observed, followed by 5% acetone in hexanes to isolate the all trans diastereomer. The all trans would eliminate on the column to the α-methylene if a less polar solvent was used. Using these conditions, elimination was minimized. Yield was 100.7 mg (65%), with a 1.1:1 d.r. **^{1}H NMR** (400 MHz, $CDCl_3$) δ major: 7.31 (t, J = 7.9 Hz, 1H), 6.85 (m, 2H), 6.80 (t, J = 1.9 Hz, 1H), 4.46 (ddd, J = 6.1, 9.8, 11.9 Hz, 1H), 4.00 (dd, J = 3.4, 11.6 Hz, 1H), 3.83 (s, 3H), 3.55 (dd, J = 3.4, 11.6 Hz, 1H), 3.43 (dd, J = 9.9, 11.7 Hz, 1H), 3.17 (dt, J = 3.4, 11.7 Hz, 1H), 1.68 (m, 2H), 1.51 (m, 1H), 1.35 (m, 1H), 1.25 (m, 4H), 0.84 (t, J = 6.9 Hz, 3H). δ minor: 7.29 (d, J = 7.9 Hz, 1H), 6.85 (m, 3H), 4.73 (ddd, J = 2.4, 5.5, 8.1 Hz, 1H), 3.80 (s, 3H), 3.70 (dd, J = 3.5, 11.4 Hz, 1H), 3.54 (dd, J = 2.4, 8.7 Hz, 1H), 3.36 (dt, J = 3.6, 9.8 Hz, 1H), 3.05 (dd, J = 9.9, 11.3 Hz, 1H), 1.85-1.25 (m, 8H), 0.88 (t, J = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ major: 173.71, 160.14, 138.41, 130.36, 119.91, 114.04, 112.83, 84.30, 55.27, 50.83, 49.99, 40.64, 33.58, 31.41, 25.26, 22.36, 13.89. δ minor: 174.42, 159.91, 138.66, 130.17, 119.91, 114.01, 113.07, 85.33, 55.22, 48.43, 47.12, 39.88, 34.62, 31.35, 25.27, 22.45, 13.92. **MS** (+ESI) calculated *m/z* for $[M+H]^+$ = 311.13. Experimental *m/z* for $[M+H]^+$ = 311.11. **IR** (Thin Film, cm^{-1}) 3055, 2957, 2932, 2859, 1773, 1601,1585, 1489, 1456, 1266.



Methylenolactocin

Methylenolactocin: 155 mg of 3-(chloromethyl-4-(3-methyphenyl)-5-pentyldihydrofuran-2(3*H*)-one

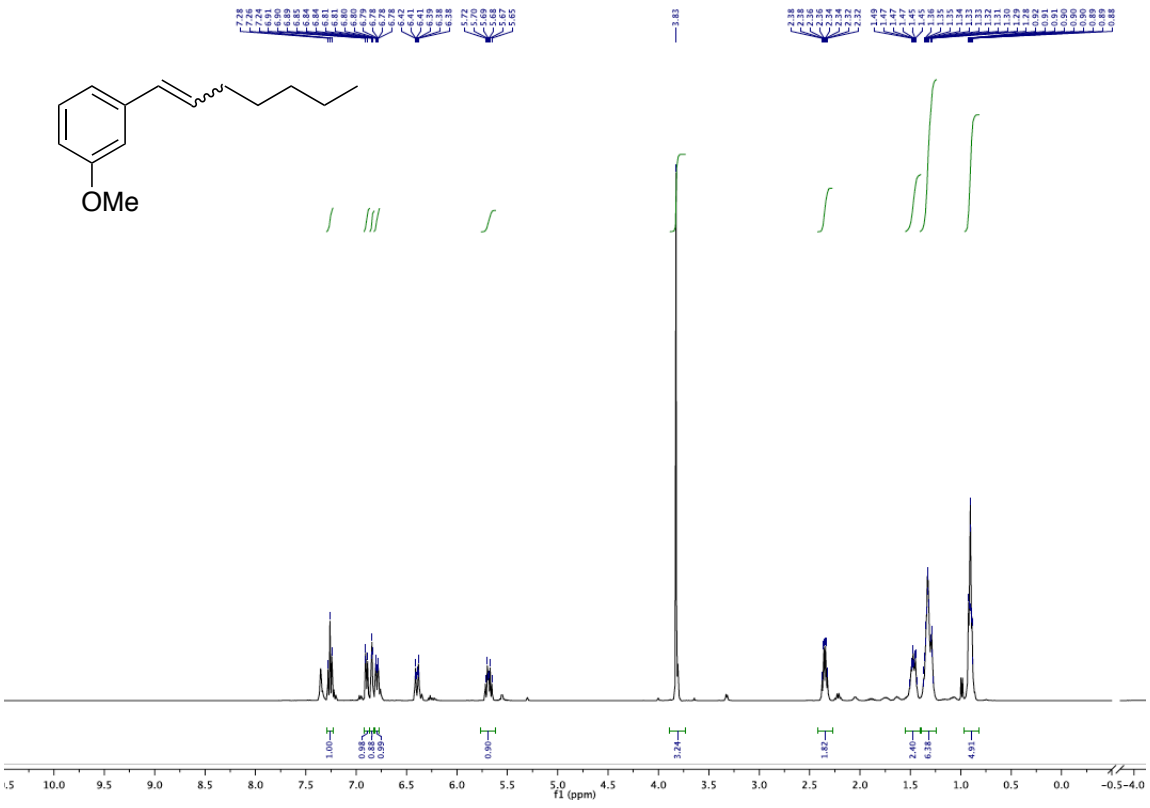
were stirred in 7.5 mL EtOAc and 7.5 mL MeCN. To this was added, fast dropwise, a solution of 13.1 mg $RuCl_3*3H_2O$ (10 mol%) and 1.6 g $NaIO_4$ (15 equiv) in 15 mL H_2O. The reaction was allowed to stir for 3 hours, after which the white precipitate was filtered over celite. The filtrate was diluted with EtOAc, and washed with sat. $NaHSO_3$. The aqueous solution was extracted with EtOAc and the combined organics were washed with H_2O and Brine, dried over $MgSO_4$, and evaporated under reduced pressure. The resulting product mixture was used in the next step without further purification. The lactone was dissolved in 2-propanol (12.5 mL, [0.04]) and 207 mg of K_2CO_3 (3 equiv) was added, followed by 0.5 mL NEt_3 (1M). The reaction was allowed to stir overnight, following which it was diluted with EtOAc and quenched with 3M HCl. The product was extracted with EtOAc, and washed with brine, and dried over Na_2SO_4. The product was purified on silica chromatography. The bicycle byproduct could be separated using dichloromethane as eluent, and the desired methylenolactocin could be isolated cleanly using 1% acetic acid in dichloromethane. The desired paraconic acid methylenolactocin was isolated in a 25% yield (27 mg) over these two steps. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.64 (bs, 1H), 6.46 (d, J = 2.3 Hz, 1H), 6.03 (d, J = 2.3 Hz, 1H), 4.81 (q, J = 5.8 Hz), 3.63 (m, 1H), 1.73 (m, 2H), 1.50-1.25 (m, 6H), 0.89 (t, J = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.58, 168.26, 132.34, 125.98, 78.87, 49.47, 35.66, 31.29, 24.40, 22.40, 13.90.



3-pentyltetrahydrofuro[3,4-*c*]furan-1,4-dione: White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.81 (dt, J = 1.2, 7.2 Hz, 1H), 4.69 (dd, J = 1.5, 9.7 Hz, 1H), 4.53 (dd, J = 7.7, 9.7 Hz, 1H), 3.52 (dt, J = 1.5, 9.7 Hz, 1H), 3.20 (dd, J = 1.4, 9.5 Hz, 1H), 1.75 (m, 2H), 1.46 (m, 2H), 1.34 (m, 4H), 0.90 (t, J = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.51, 175.33, 81.85, 68.99, 45.38, 40.68, 36.26, 31.15, 24.29, 22.40, 13.88. **MS** (+ESI) calculated *m/z* for $[M+H]^+$ = 213.10. Experimental *m/z* for $[M+H]^+$ = 213.10. **IR** (Thin Film, cm^{-1}) 2953, 2924, 2857, 1771, 1456, 1340.

General Procedure for Improving Lactone Diastereomeric Ratio:

A 25 mL round bottom flask equipped with a stir bar was charged with **12a** (108 mg, 0.4 mmol, 1 equiv), MeOH (10 mL, 0.04 M), triethylamine (1 ml, 0.4 M), and Potassium Carbonate (276 mg, 5 equiv). The mixture was allowed to react for 3 hours, at which point the reaction was diluted with Et_2O, and washed with H_2O and Brine, dried over $MgSO_4$, and the solvent was evaporated. The starting diastereomeric ratio for **12a** was 4.6:1 and the final ratio was >25:1 as determined by ^{1}H NMR. **12b** was subjected to the same conditions. The starting diastereomeric ratio was 2.3:1, and the final ratio was 13.5:1.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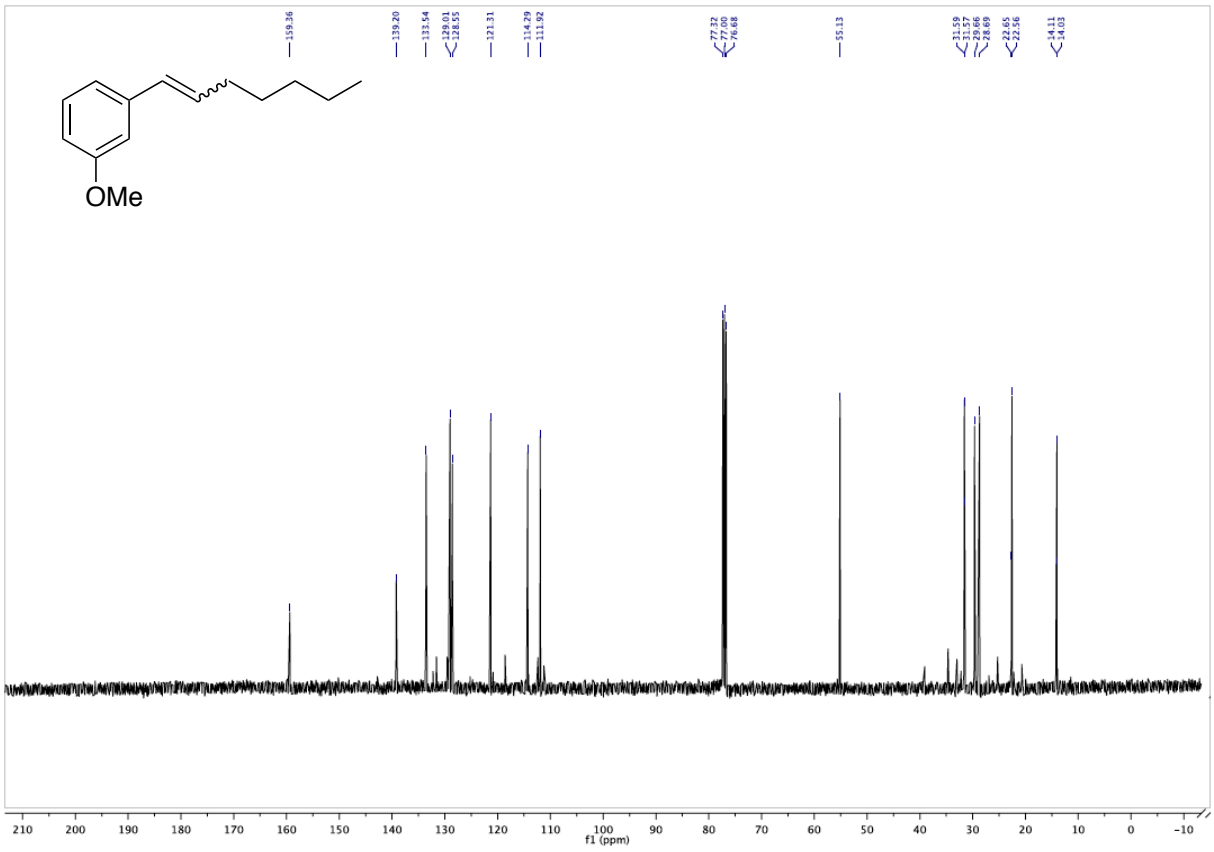
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130.01
129.65
121.31
114.29
111.92
77.32
77.00
76.68
55.13
31.59
31.57
30.66
28.69
22.65
22.56
14.11
14.03
OMe
210
200
190
180
170
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100
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80
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50
40
30
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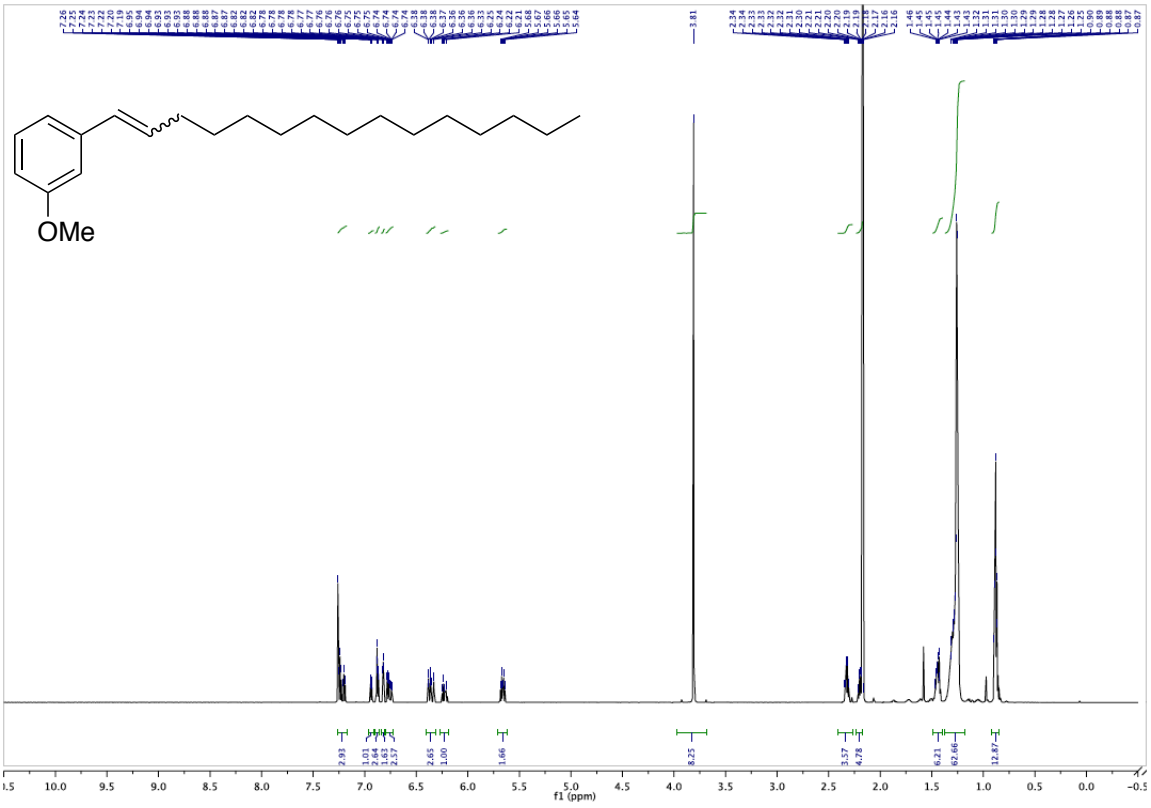
f1 (ppm)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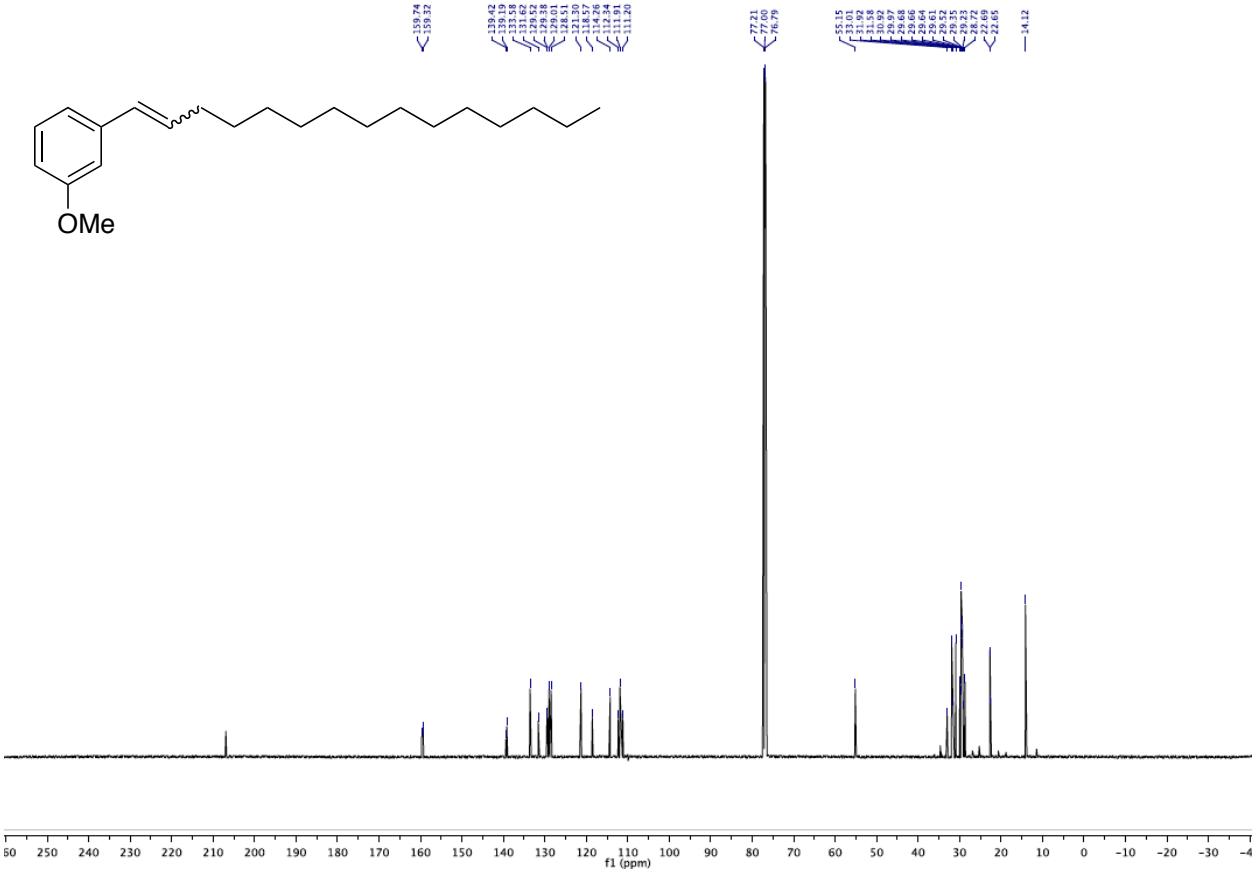
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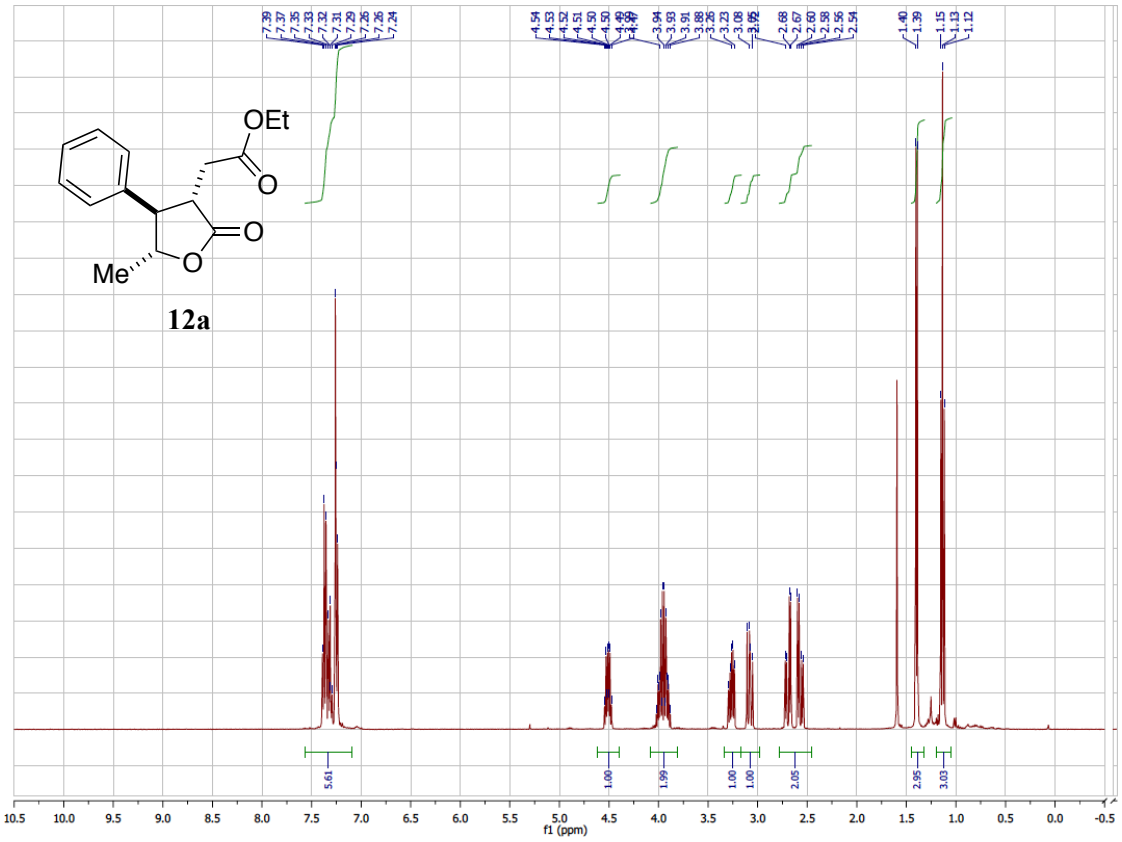
f1 (ppm)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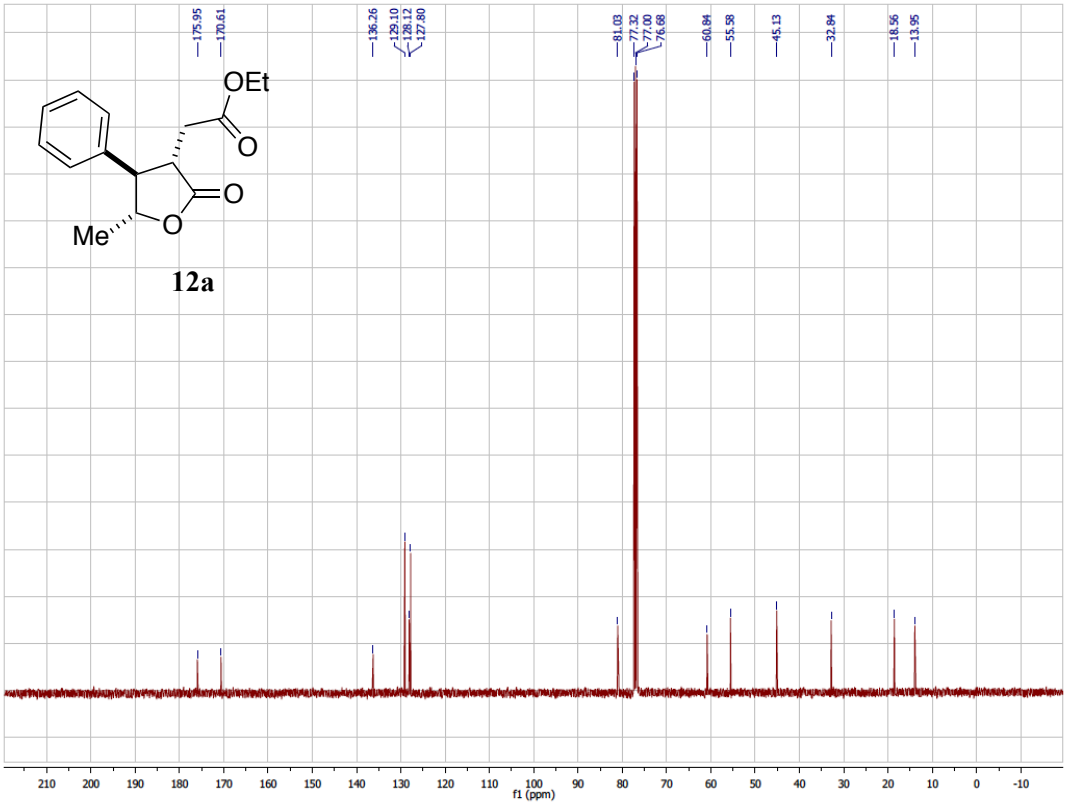
O
O
Me
O
12a
f1 (ppm)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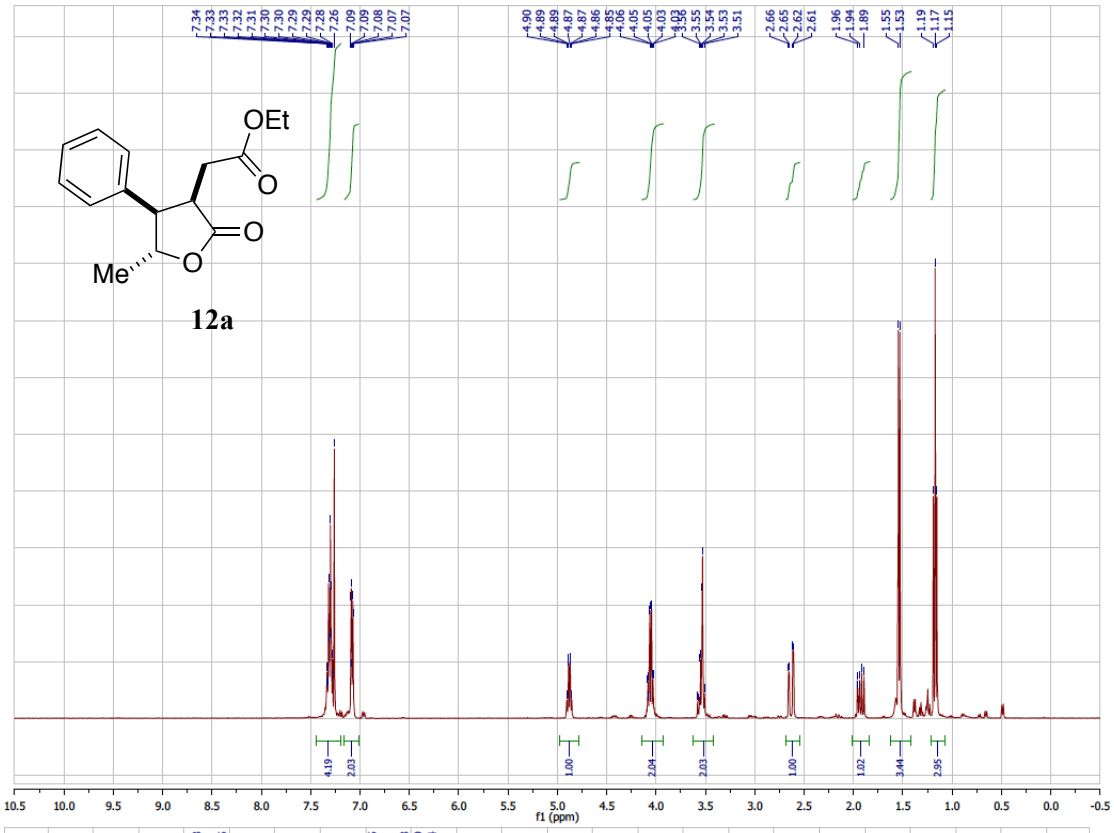
O
O
Me
O
12a
f1 (ppm)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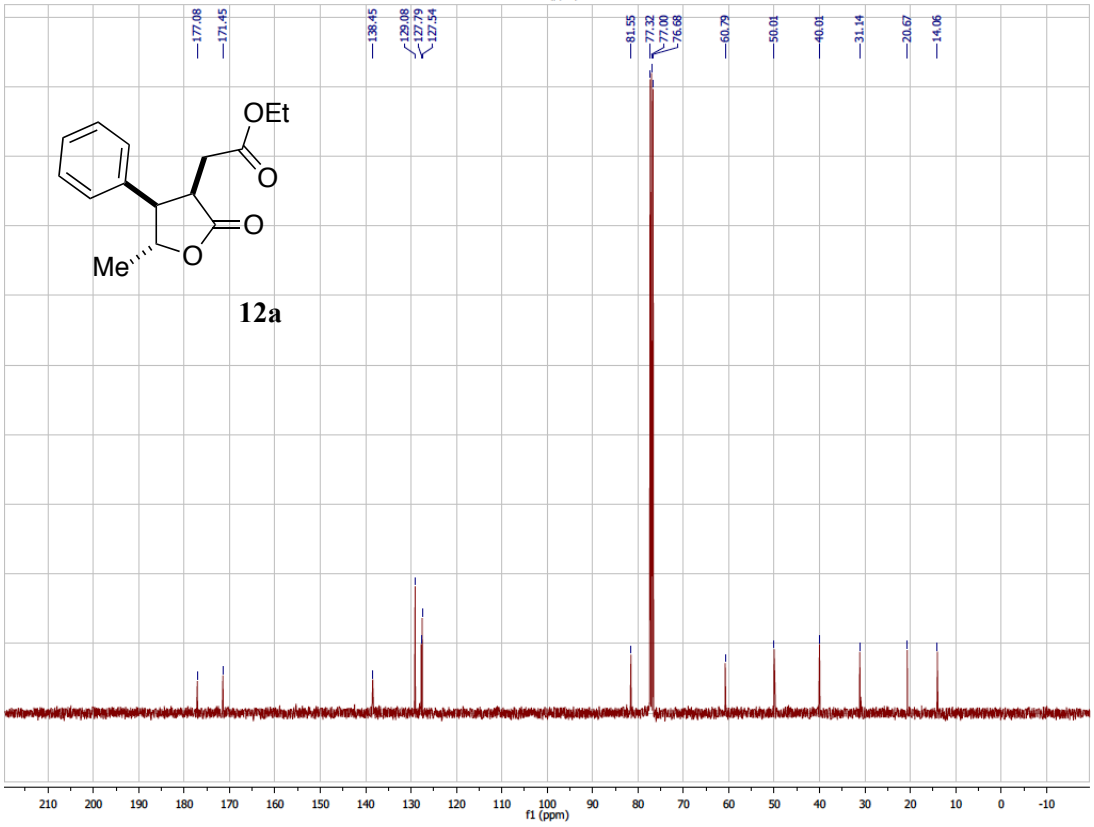
O
O
O
Me
12a
f1 (ppm)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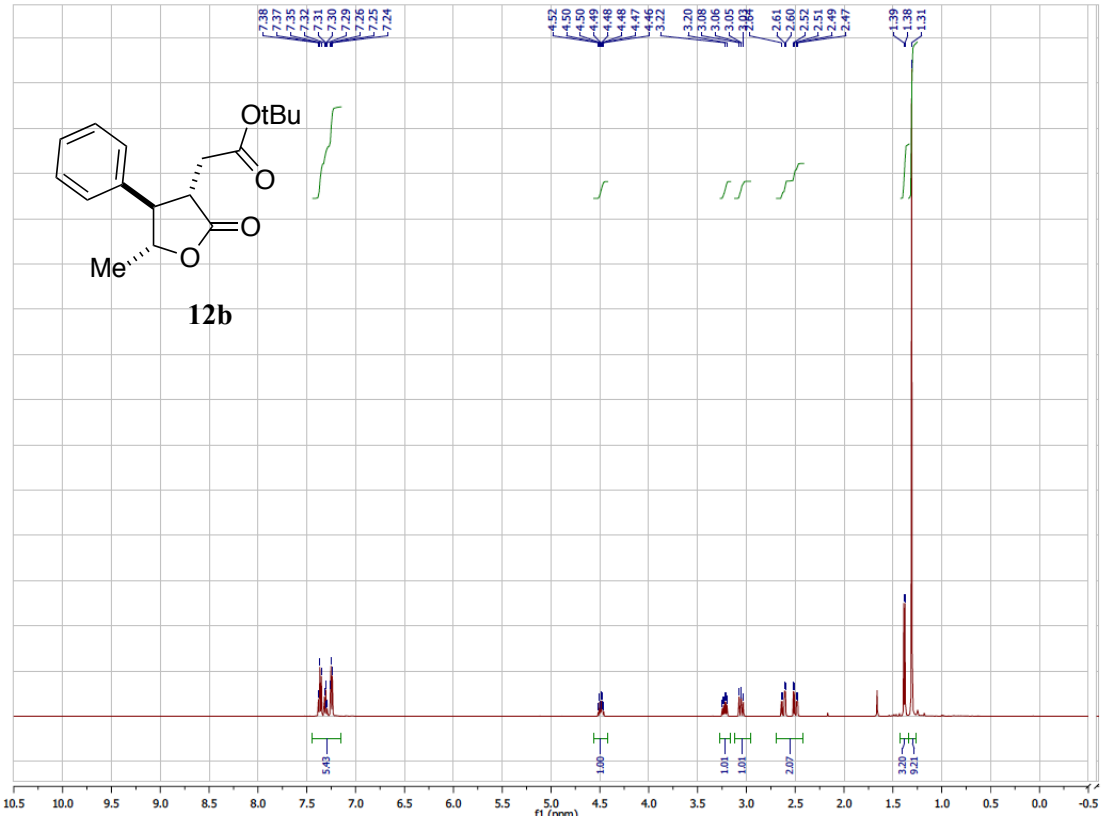
O
O
O
Me
12a
f1 (ppm)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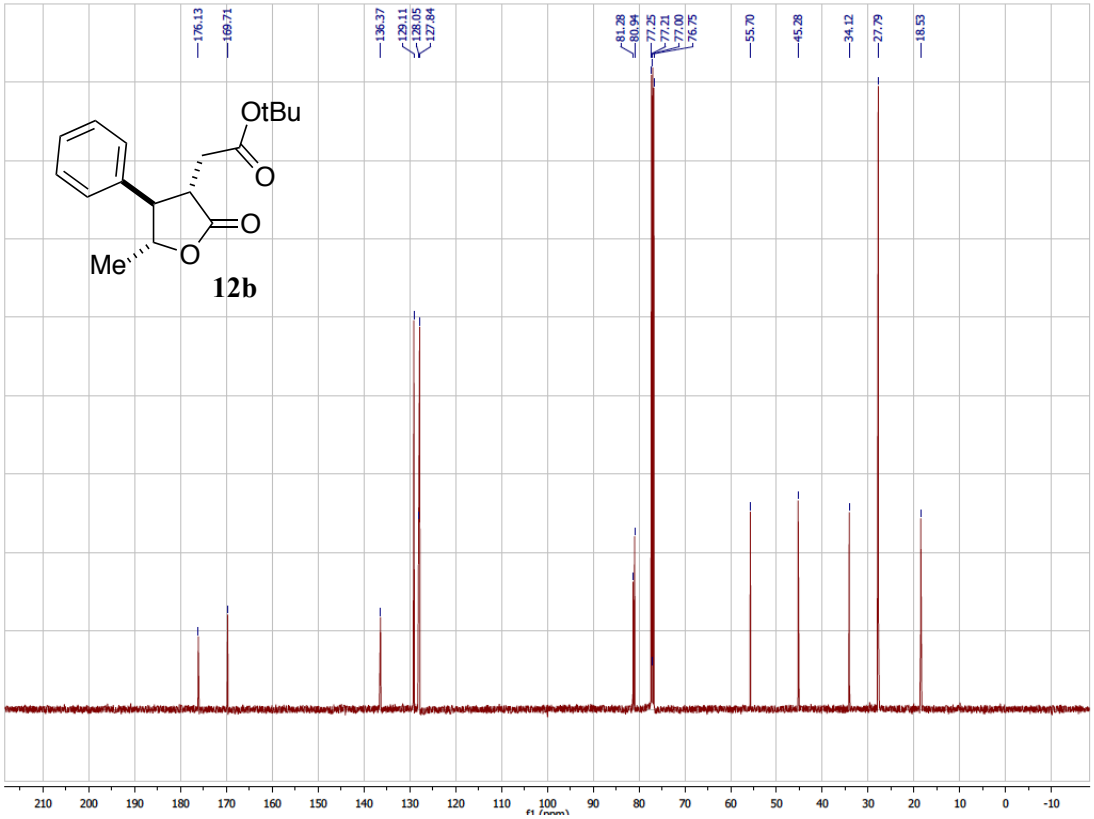
O
O
Me
O
12b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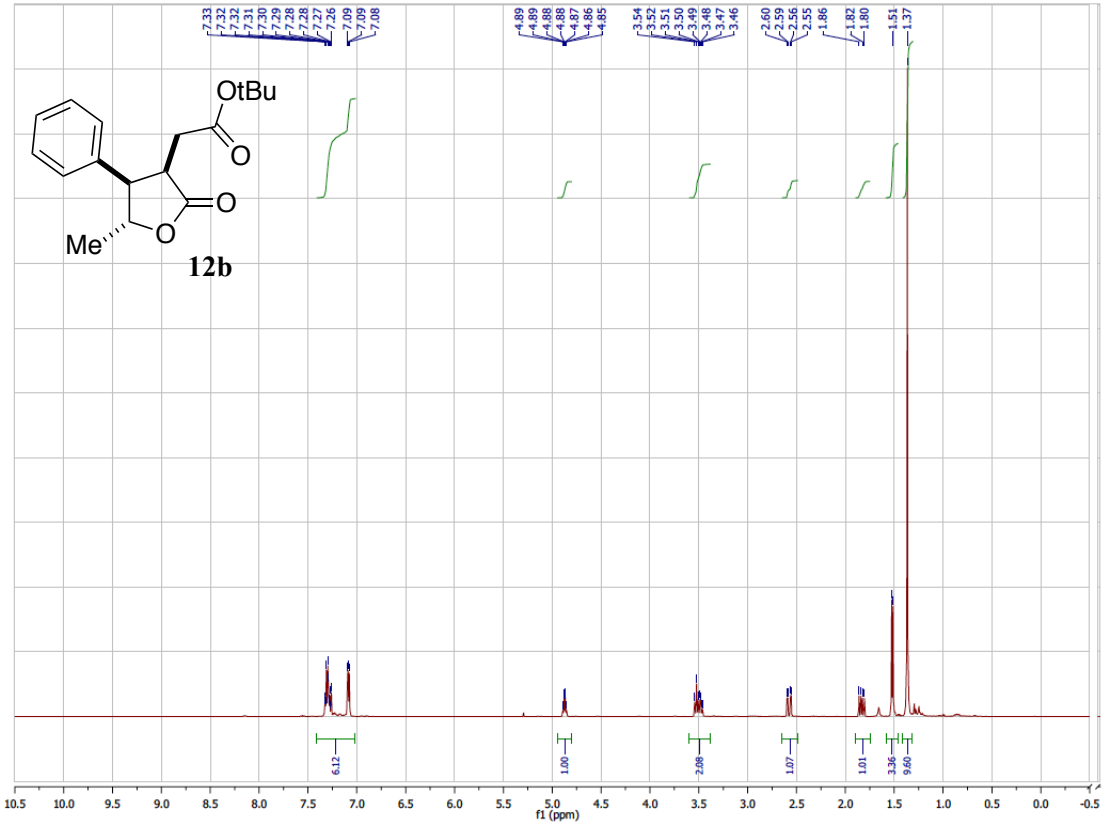
O
O
Me
O
12b


OtBu
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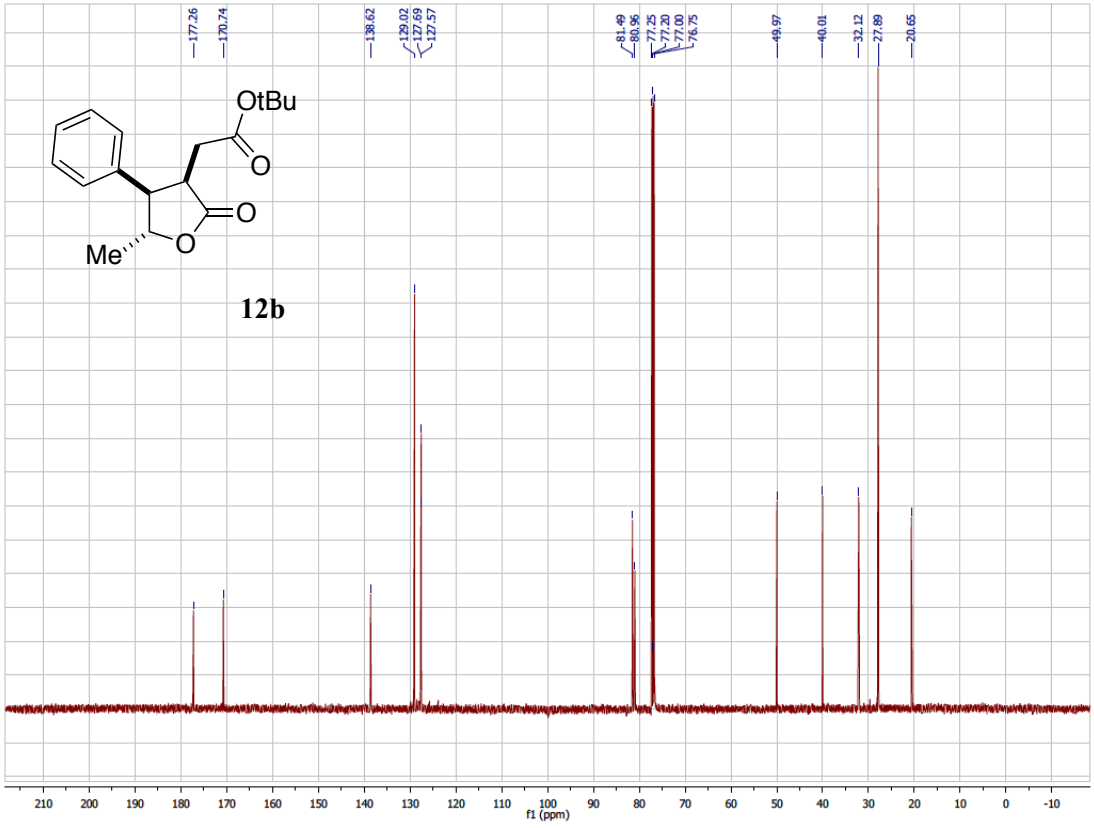
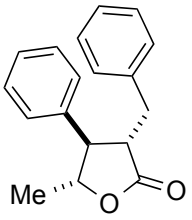
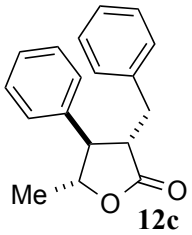
O
Me
O
12b
f1 (ppm)

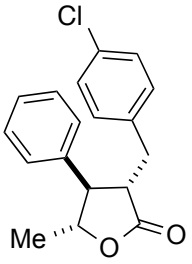

OtBu
O
O
Me
O
12b
f1 (ppm)



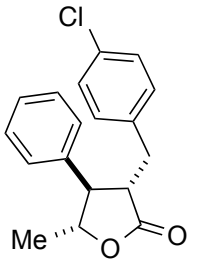
12c



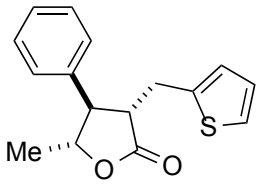
12c



12d



12d



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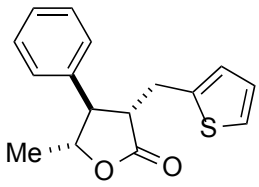

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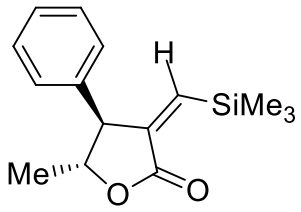
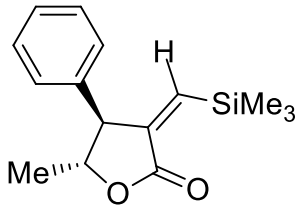

H
SiMe3
Me
O
O

12f

Chemical Shift (ppm)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SiMe3
Me
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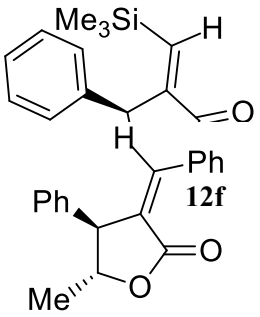
12f

Chemical Shift (ppm)


Me3Si
H
O
H
Ph
Ph
O
Me
O

12f

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4.59
4.58
4.61
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3.91
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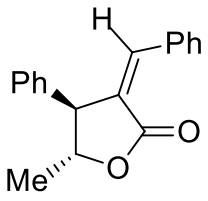
1.00
1.01
3.09
Chemical Shift (ppm)


H
Ph
Ph
O
Me
O

12f

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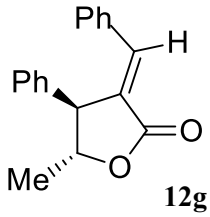
80.94
57.44
19.81
Chemical Shift (ppm)
Chemical Shift (ppm)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Ph
O
Me
O

12g

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7.31
7.23
7.22
4.59
4.58
4.58
4.57
4.56
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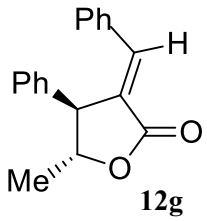
1.01
3.07
Chemical Shift (ppm)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12g

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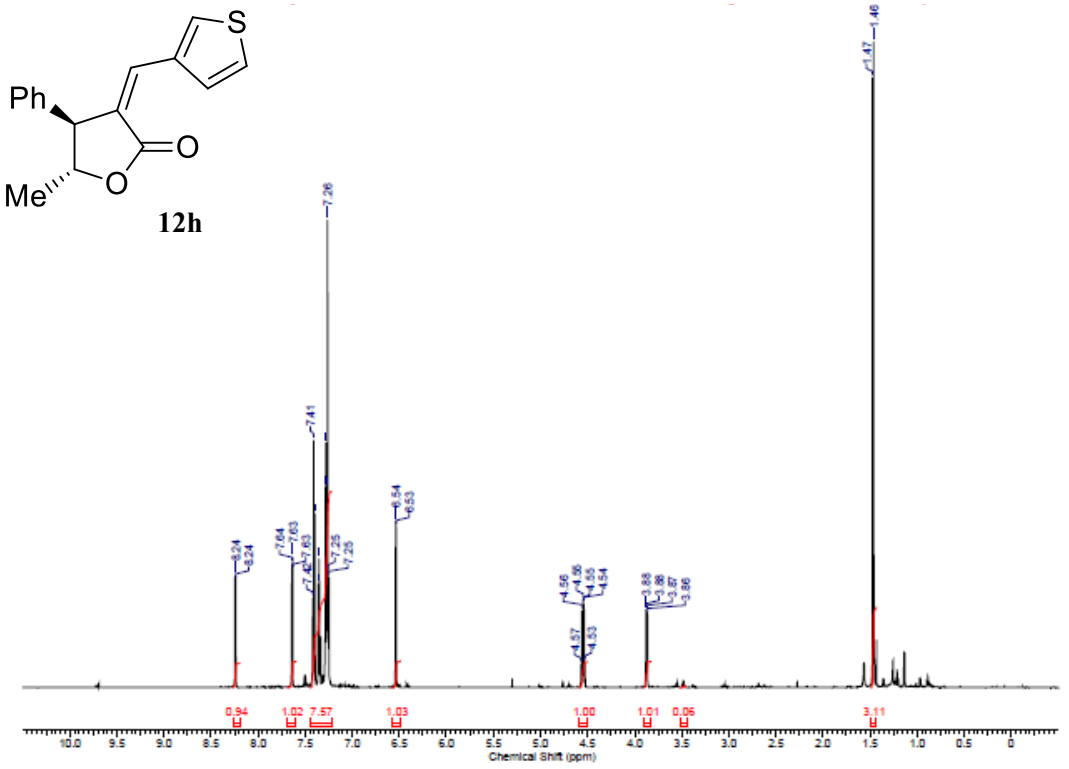
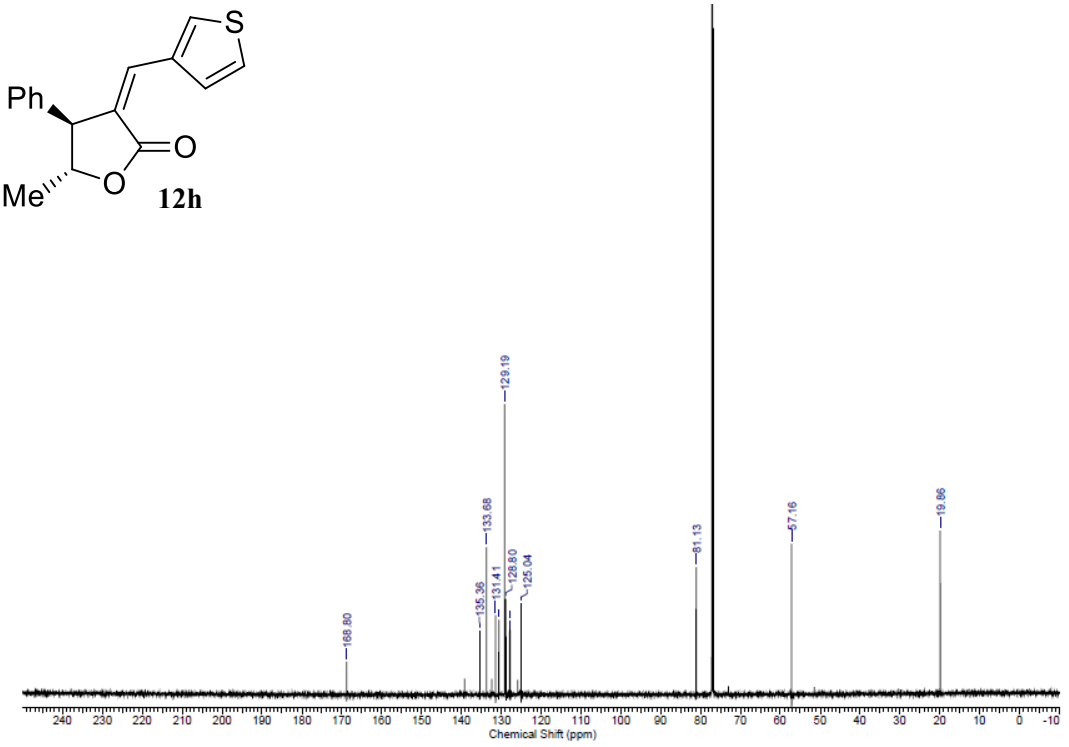
Chemical Shift (ppm)


Ph
Me
O
O
S
12h
Chemical Shift (ppm)


Ph
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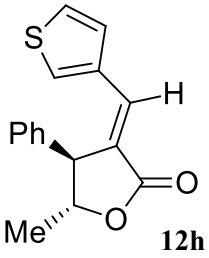
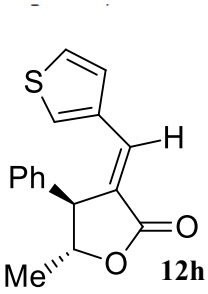
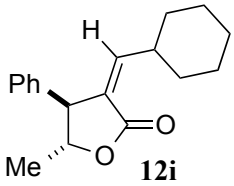
O
O
S
12h
Chemical Shift (ppm)



12h



12h


H
Ph
O
O
Me

12i

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1.63
1.69
1.43
1.36
1.35
1.34
1.11
1.13
0.98
0.97
0.97
0.96
0.94
0.93
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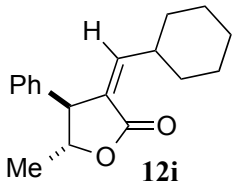
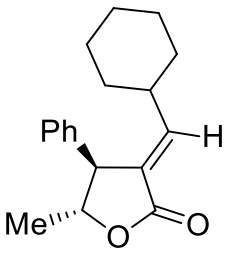
1.00
0.99
1.01 1.02
5.40 5.42 1.17 2.19
Chemical Shift (ppm)

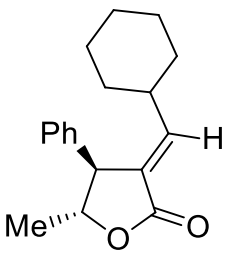

H
Ph
O
O
Me

12i

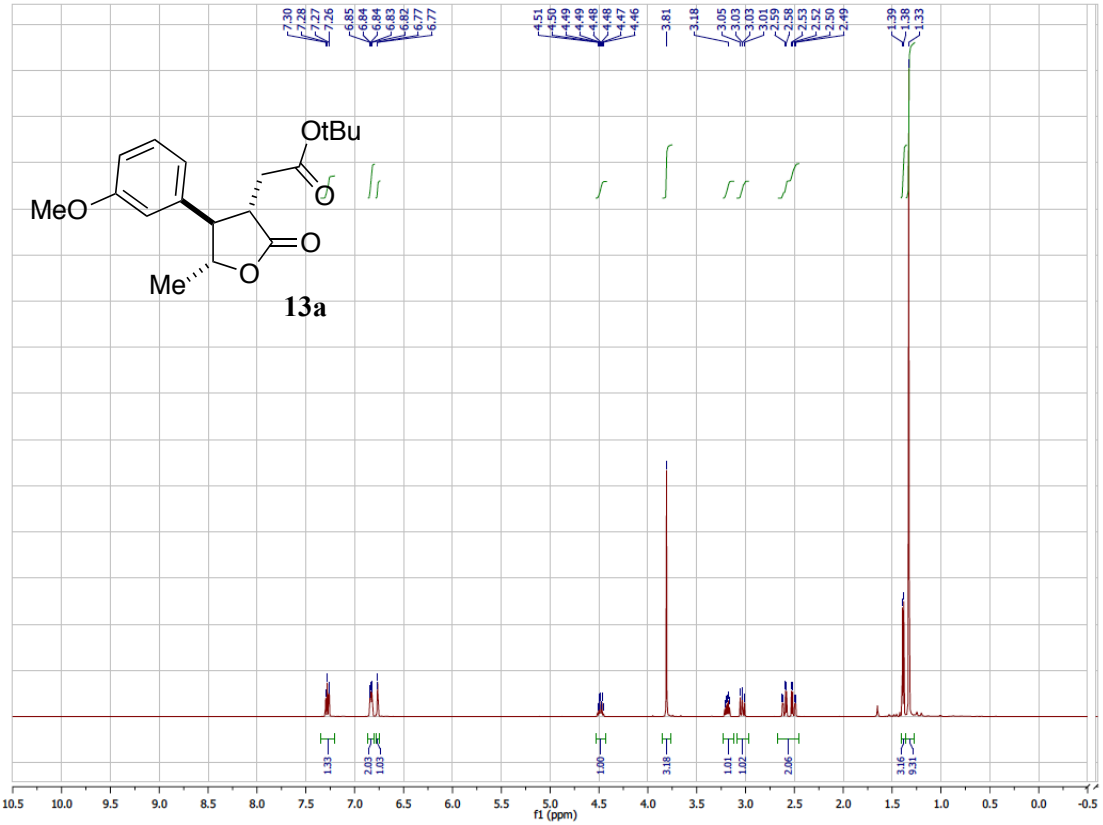
128.1
77.00
55.49
128.97
127.61
81.17
36.70
25.22
25.74
19.74
32.40
32.02
169.20
151.02
139.27
Chemical Shift (ppm)

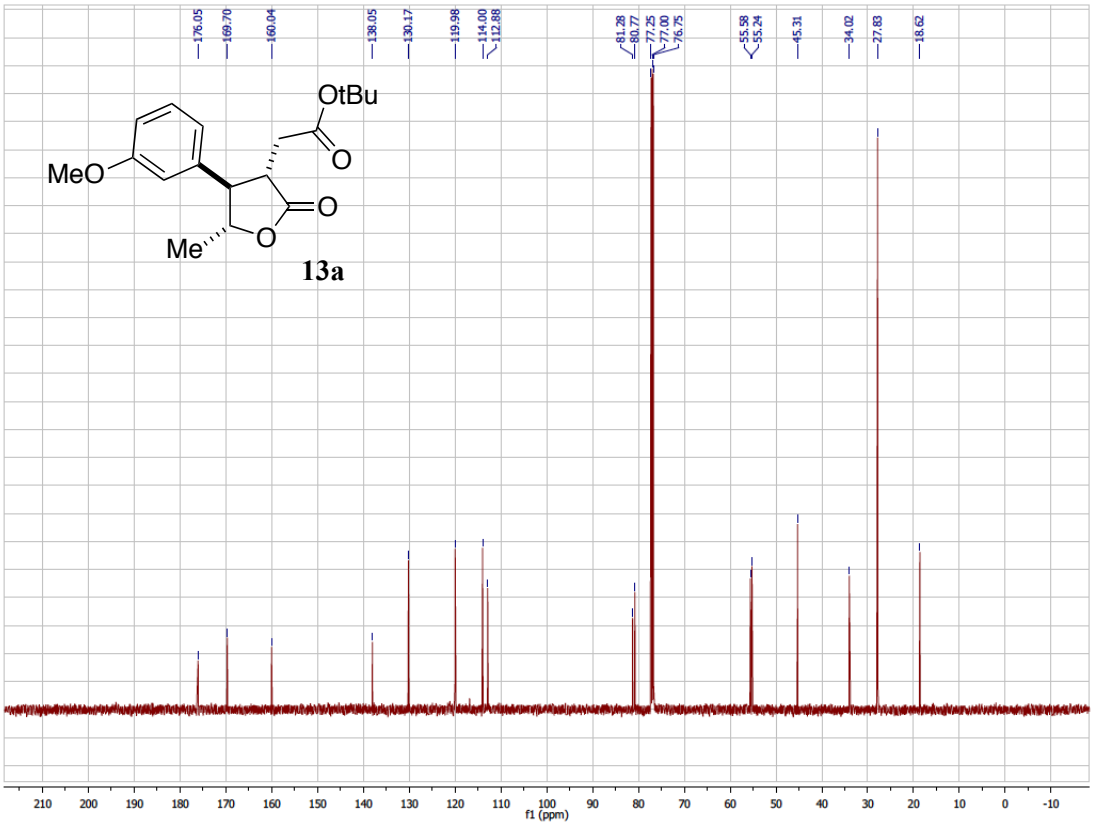


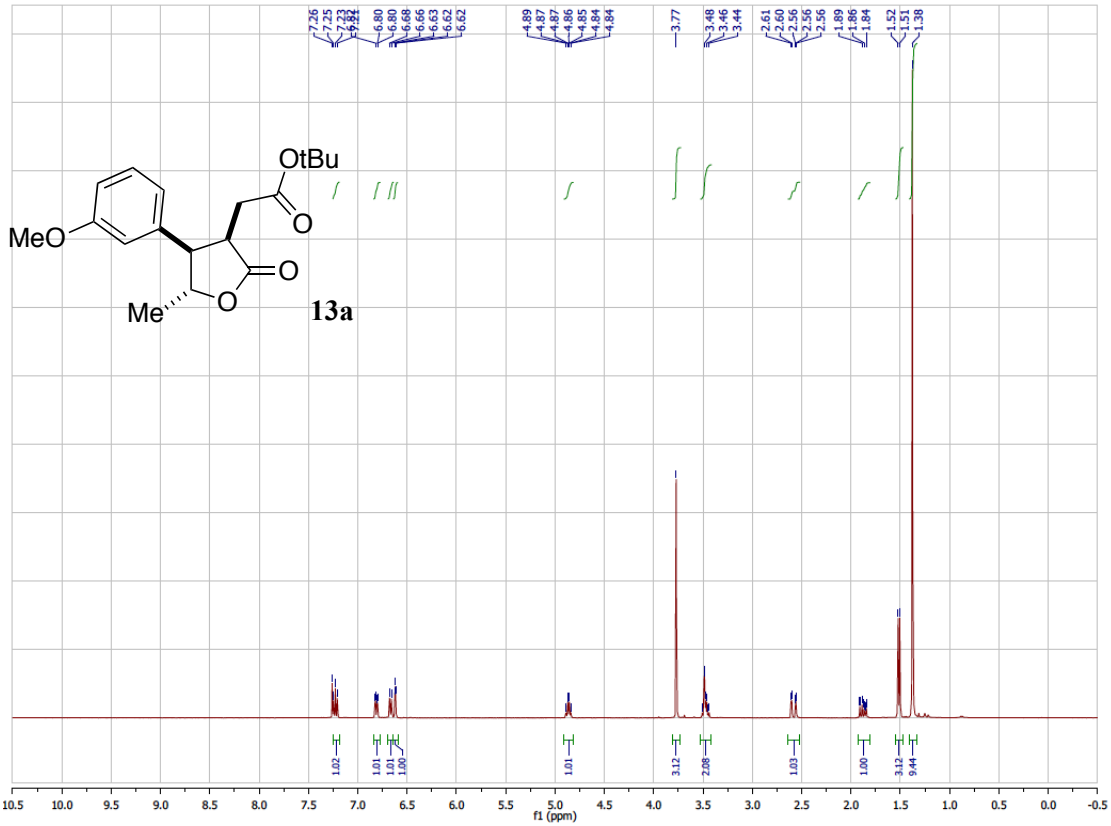
12i

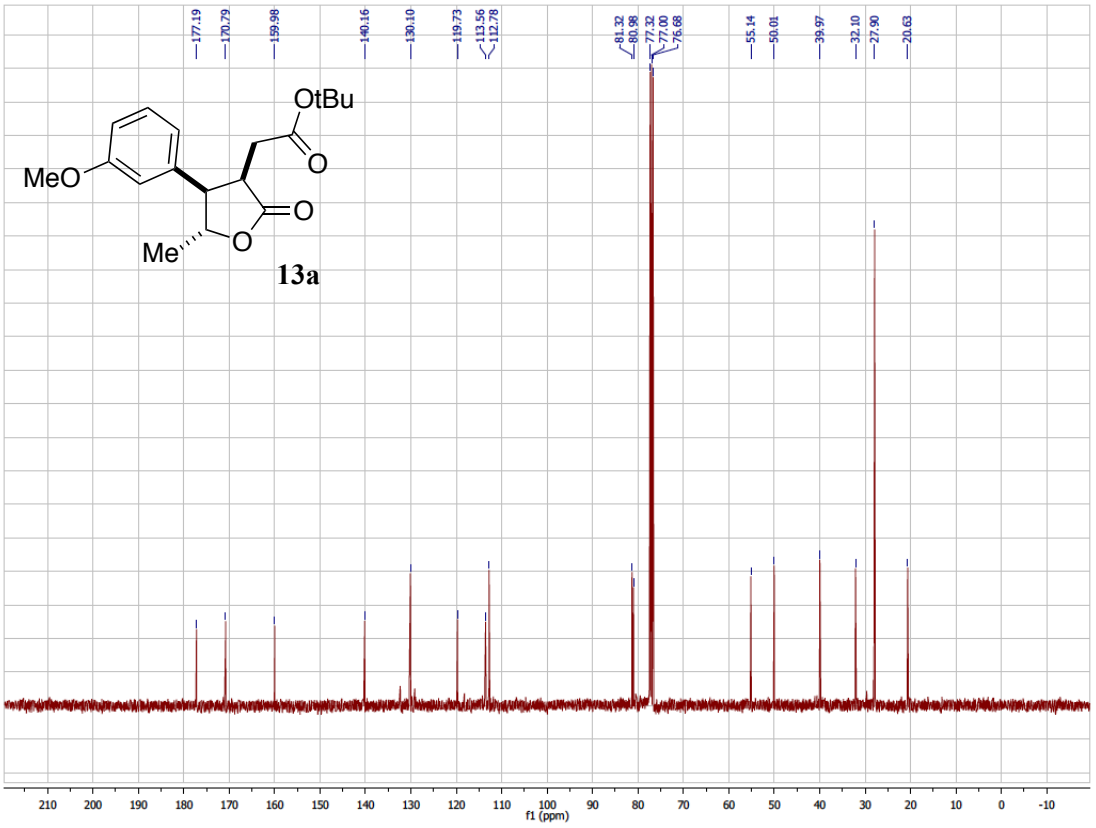


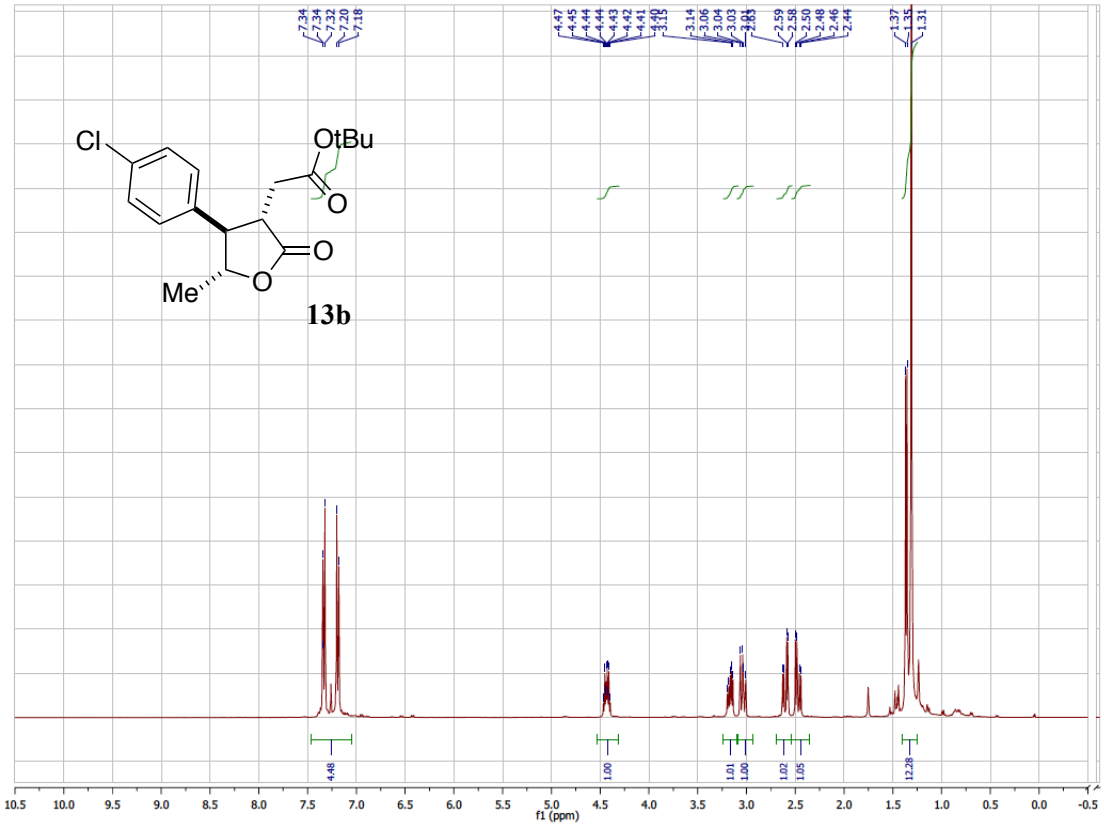
12i

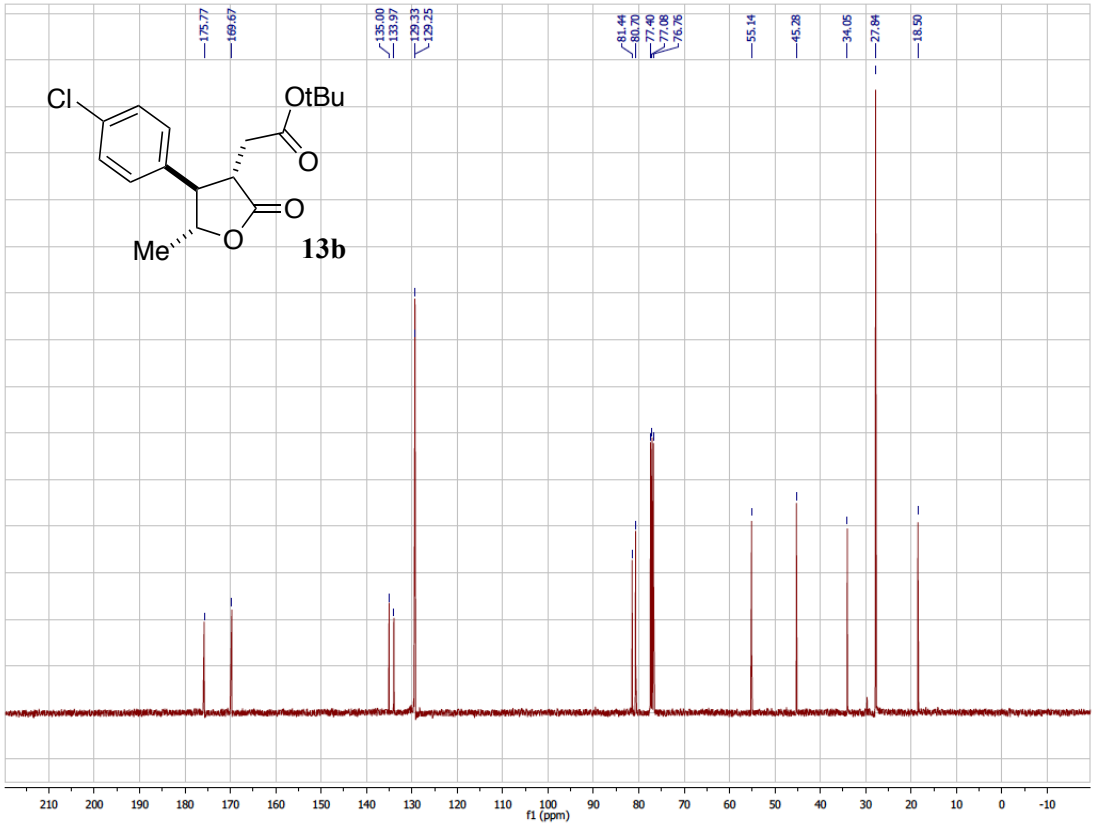

OtBu
MeO
O
O
O
Me
13a
f1 (ppm)

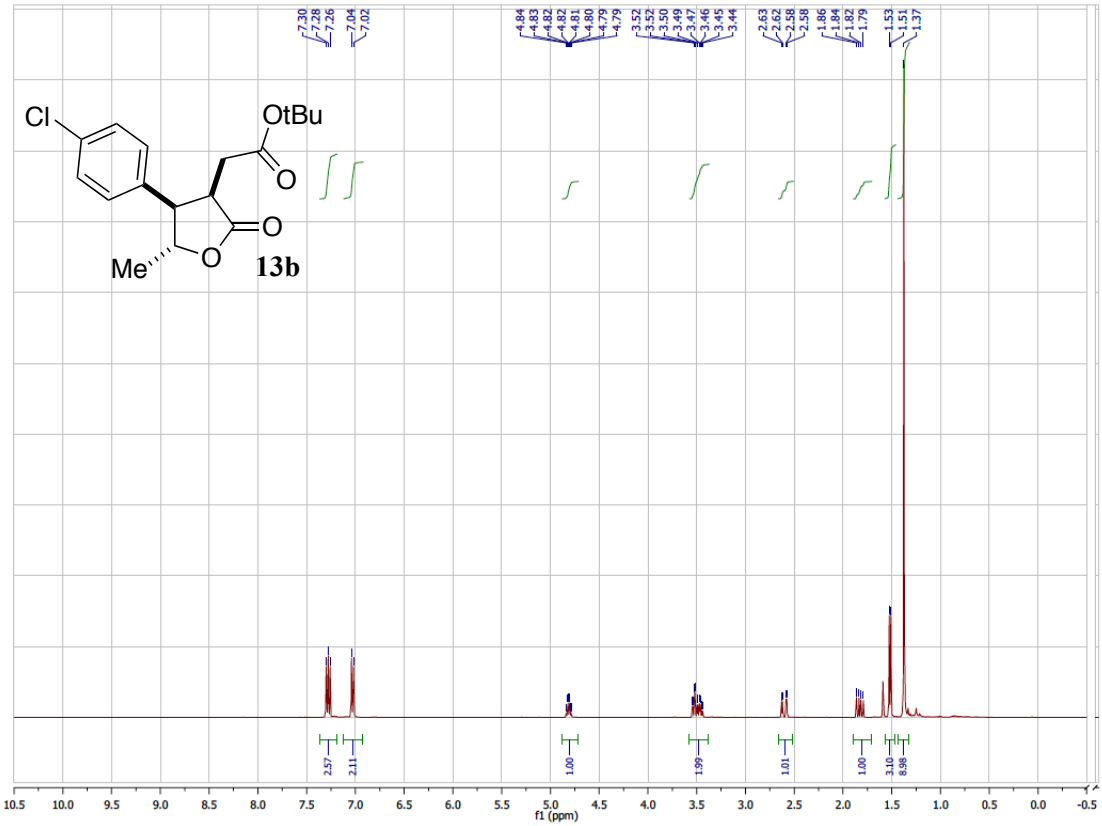

OtBu
MeO
O
O
O
Me
13a
f1 (ppm)

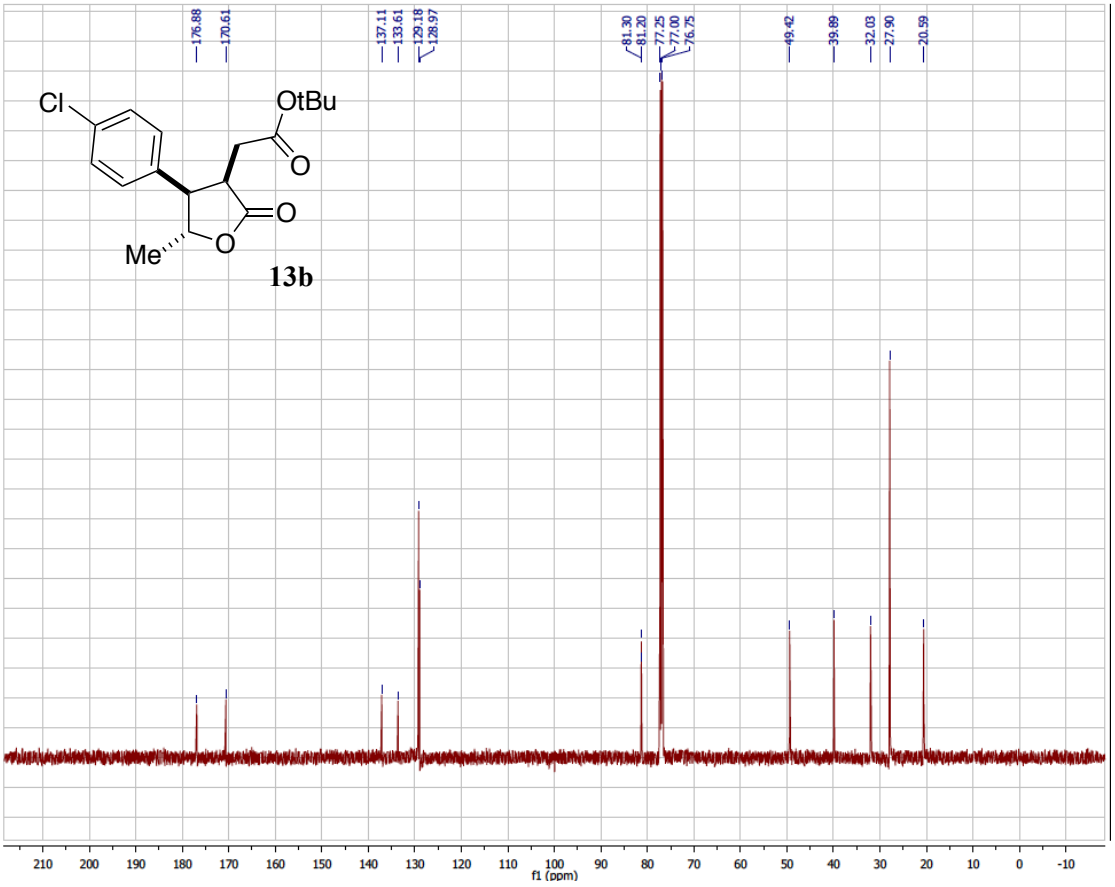

OtBu
MeO
O
O
Me
O
13a
f1 (ppm)

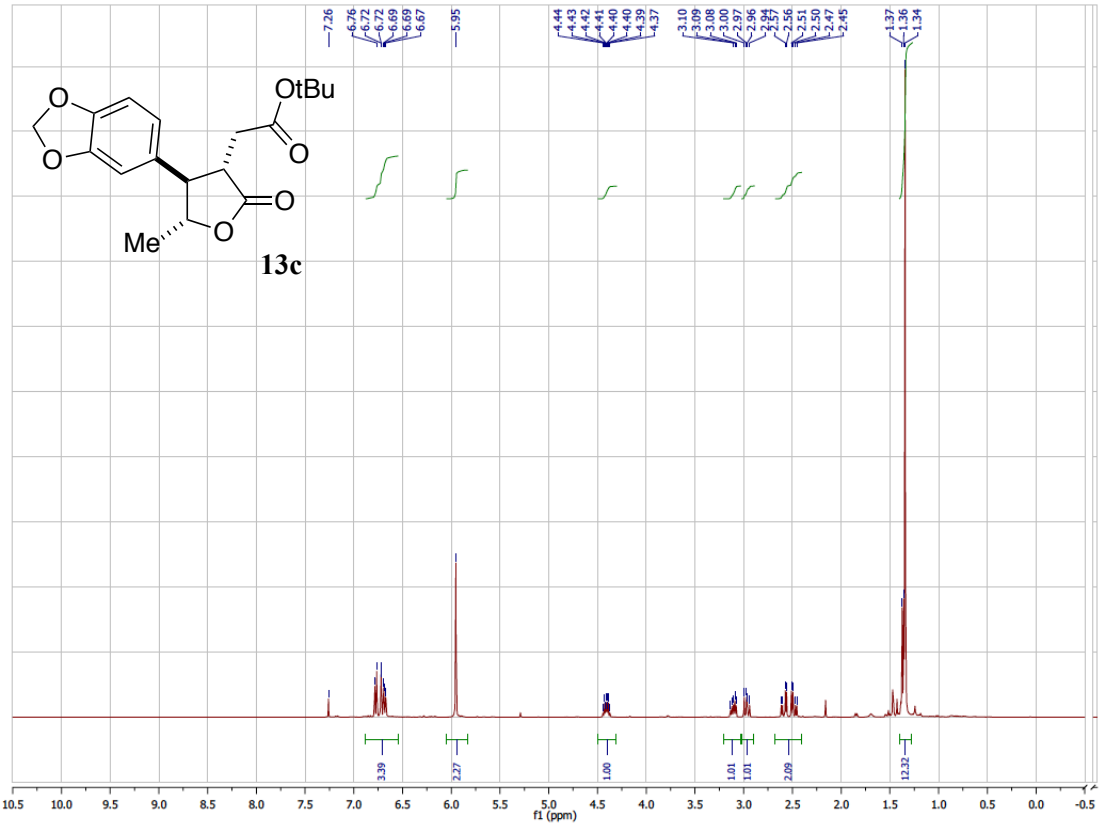

OtBu
MeO
O
O
Me
O
13a
f1 (ppm)

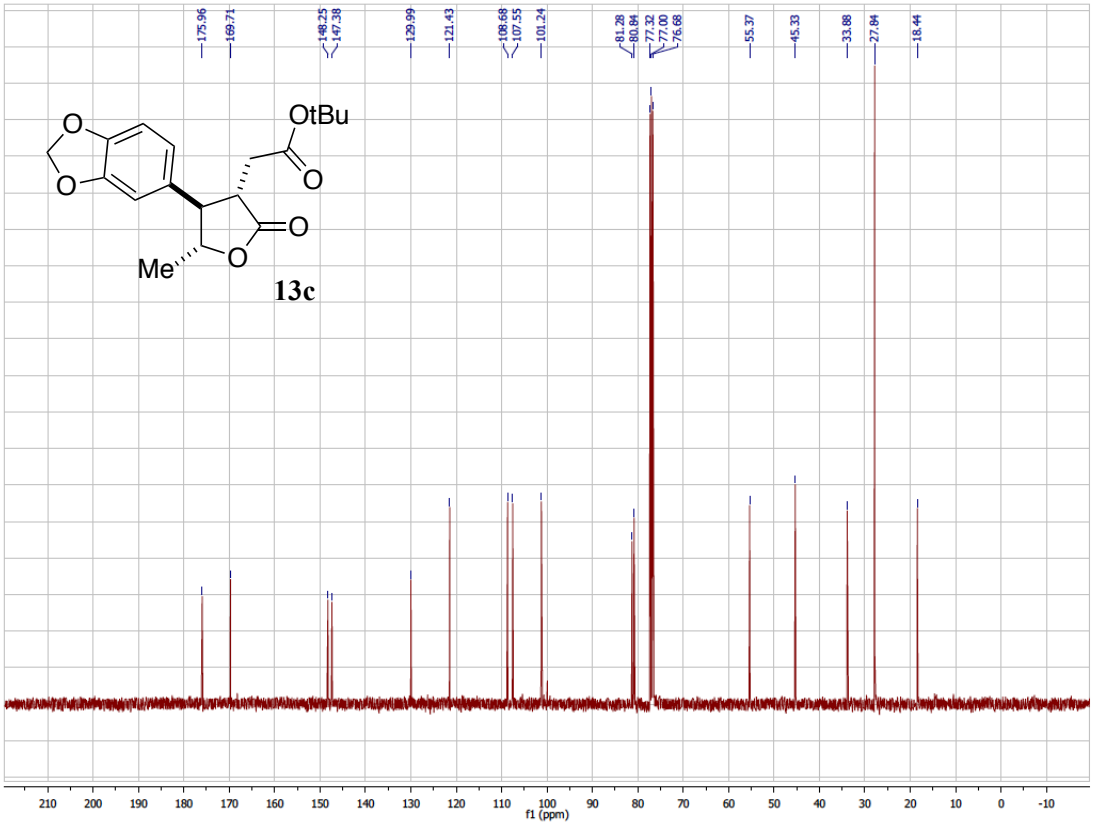

Cl
OtBu
O
O
O
Me
13b
f1 (ppm)

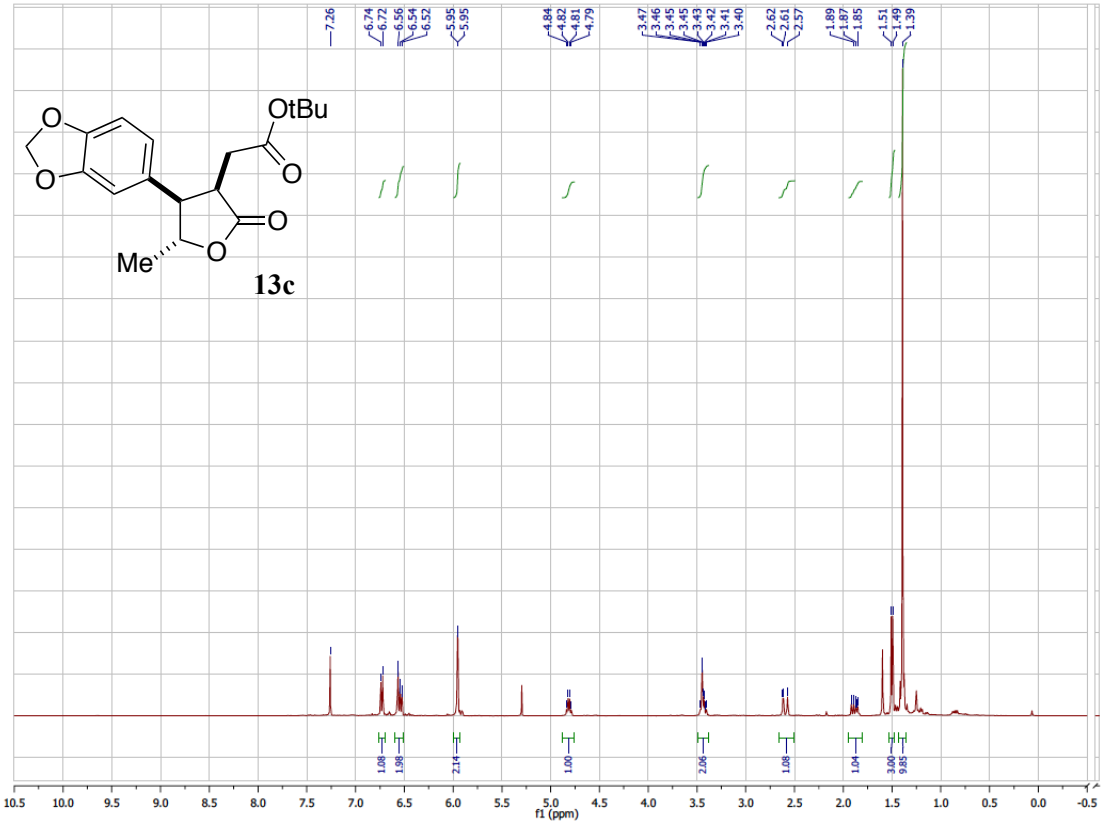

Cl
OtBu
O
O
O
Me
13b
f1 (ppm)


Cl
OtBu
O
O
Me
O
13b
f1 (ppm)

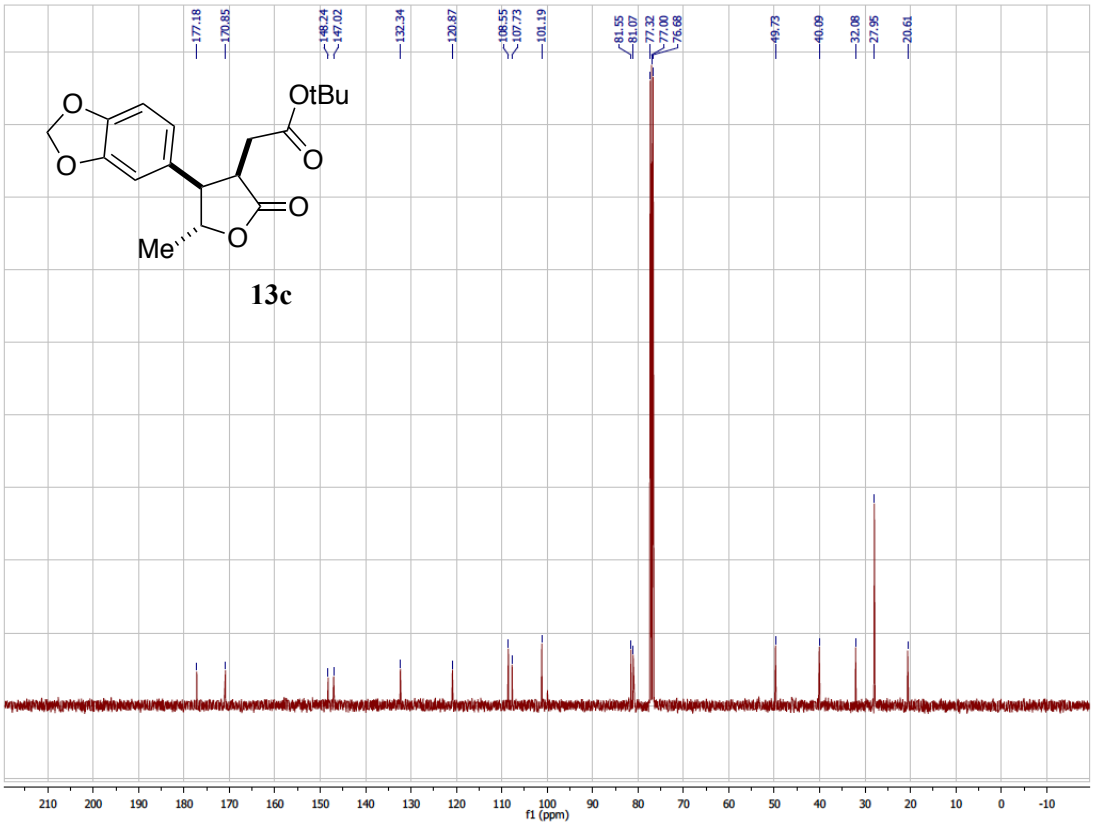

Cl
OtBu
O
O
Me
O
13b
f1 (ppm)


OtBu
O
O
O
O
O
Me
13c
f1 (ppm)

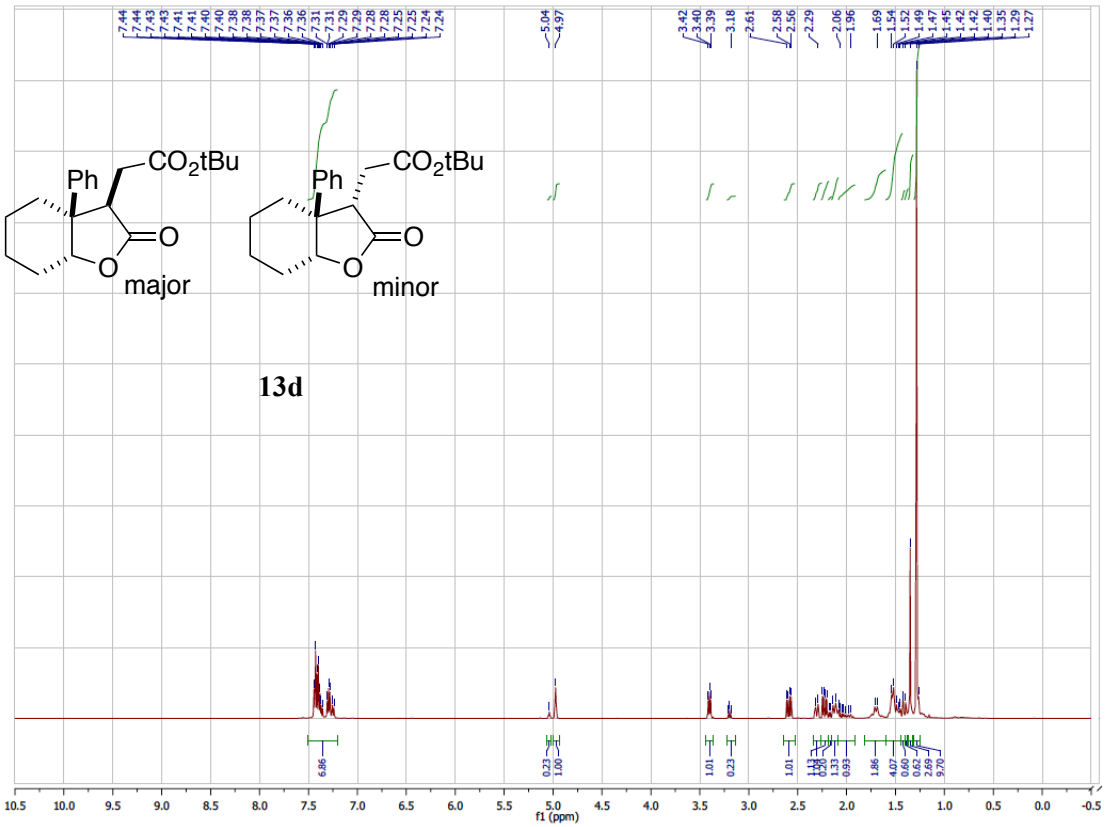

OtBu
O
O
O
O
O
Me
13c
f1 (ppm)

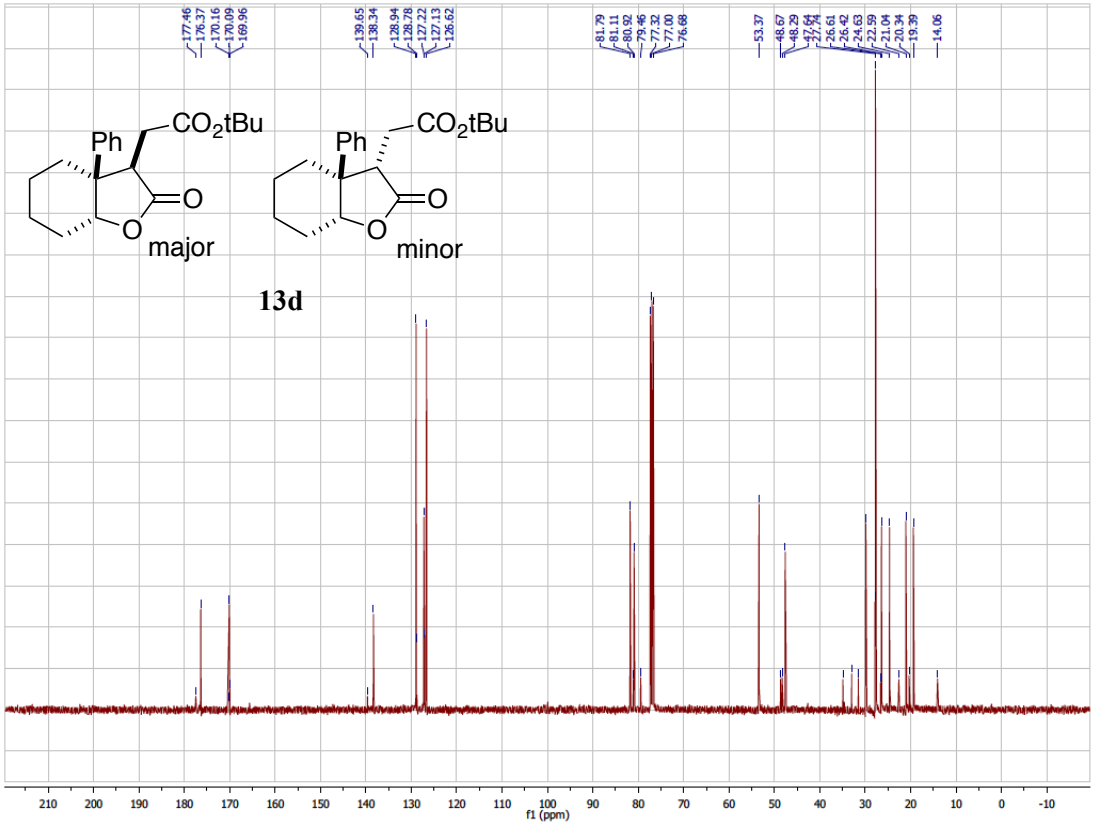

7.26
6.74
6.72
6.56
6.54
6.52
5.95
5.95
4.84
4.82
4.81
4.79
3.47
3.46
3.45
3.45
3.43
3.42
3.41
3.40
2.62
2.61
2.57
1.89
1.87
1.85
1.51
1.49
1.39
OtBu
O
O
O
O
Me
1.08
1.98
2.14
1.00
2.06
1.08
1.04
3.00
9.85
f1 (ppm)

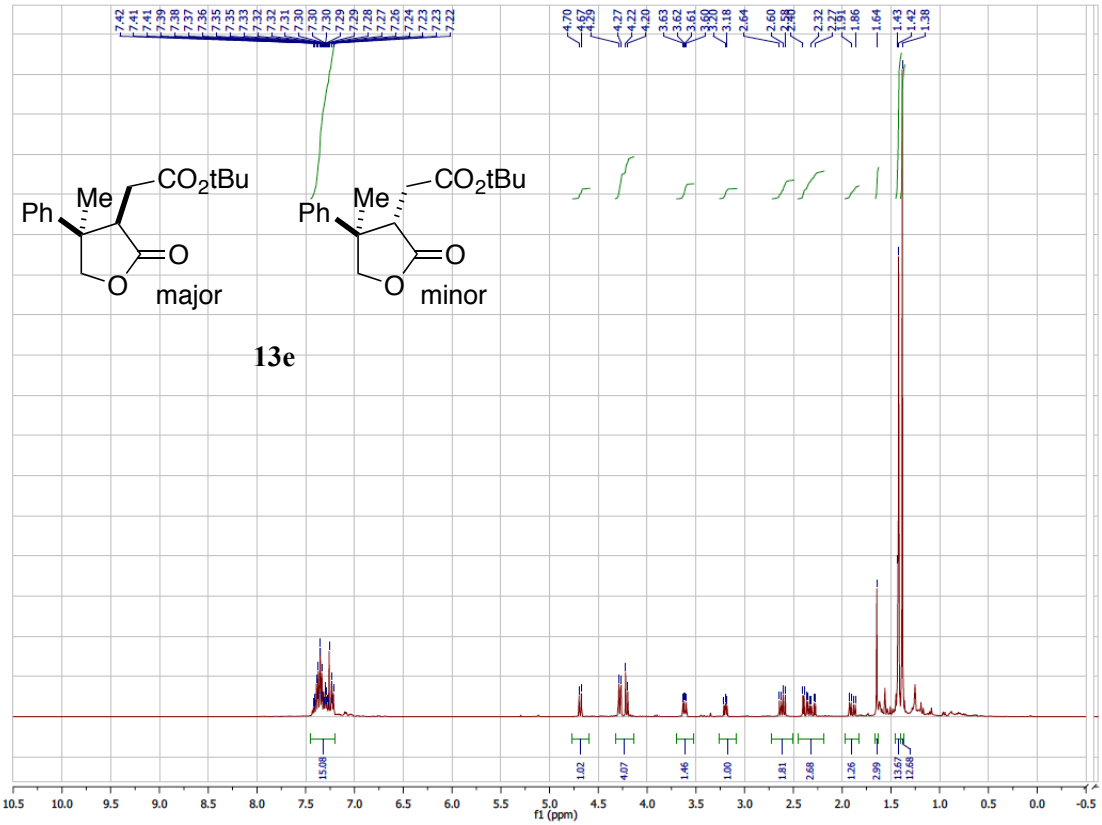
13c


177.18
170.85
148.24
147.02
132.34
120.87
108.55
107.73
101.19
81.55
81.07
77.32
77.00
76.68
49.73
40.09
32.08
27.95
20.61
OtBu
O
O
O
O
Me
f1 (ppm)

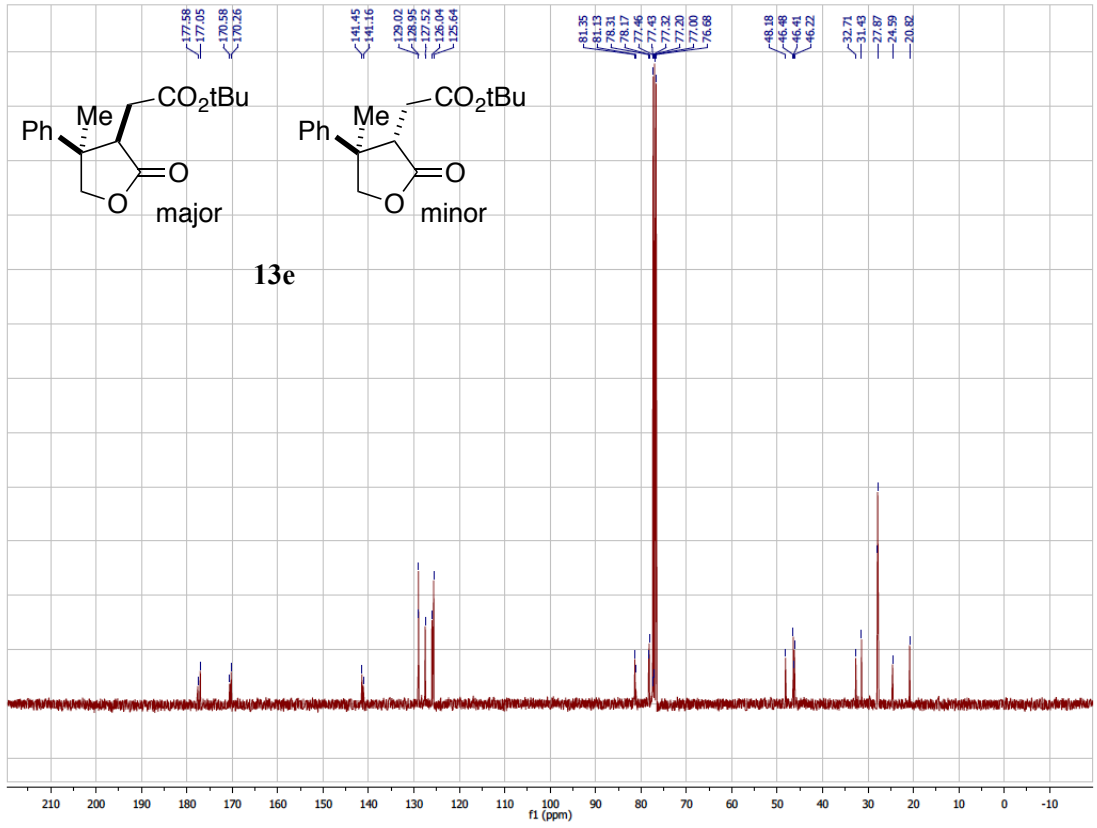
13c


Ph
CO2tBu
O
O
major
Ph
CO2tBu
O
O
minor
13d
f1 (ppm)

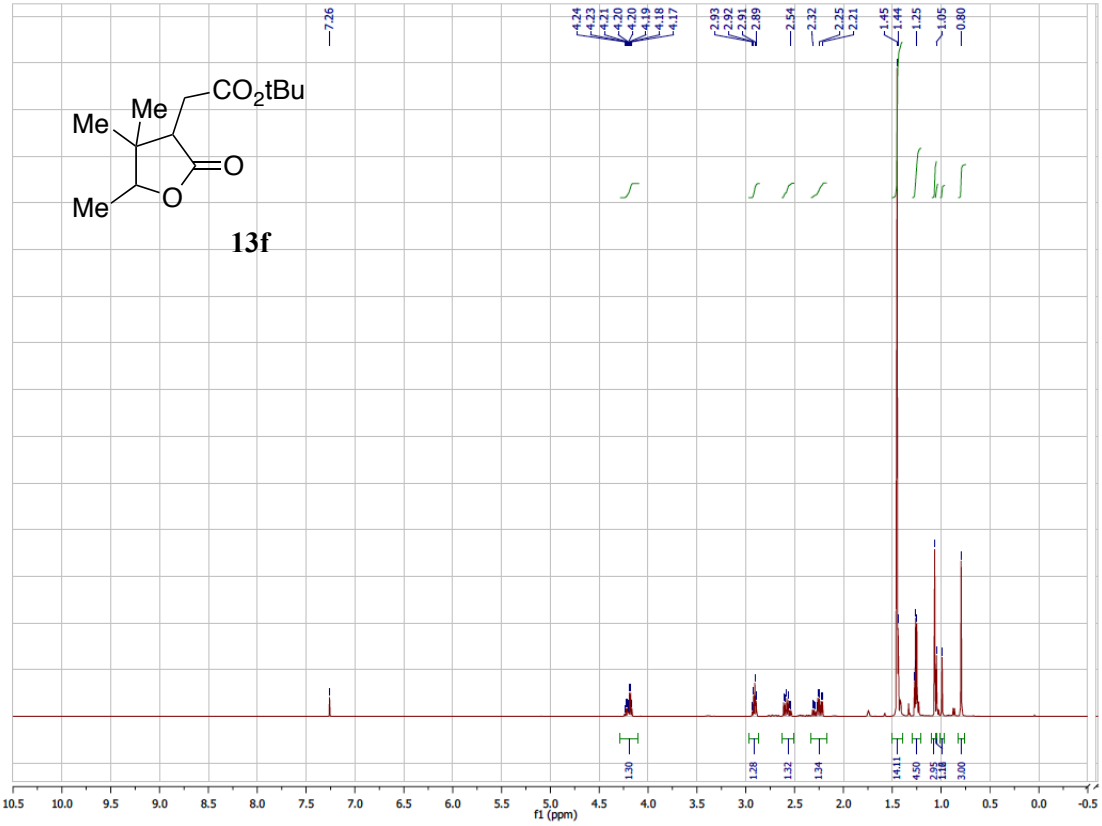

Ph
CO2tBu
O
O
major
Ph
CO2tBu
O
O
minor
13d
f1 (ppm)

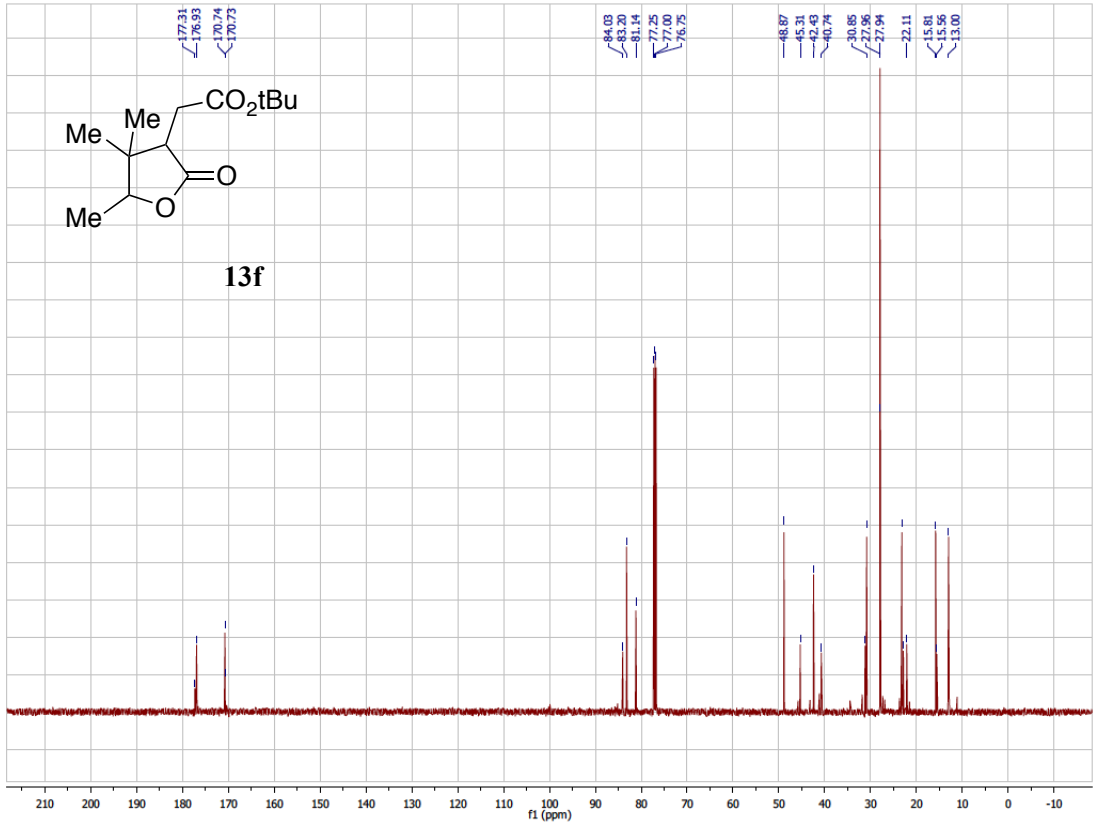

Ph
Me
CO2tBu
O
O
major
Ph
Me
CO2tBu
O
O
minor

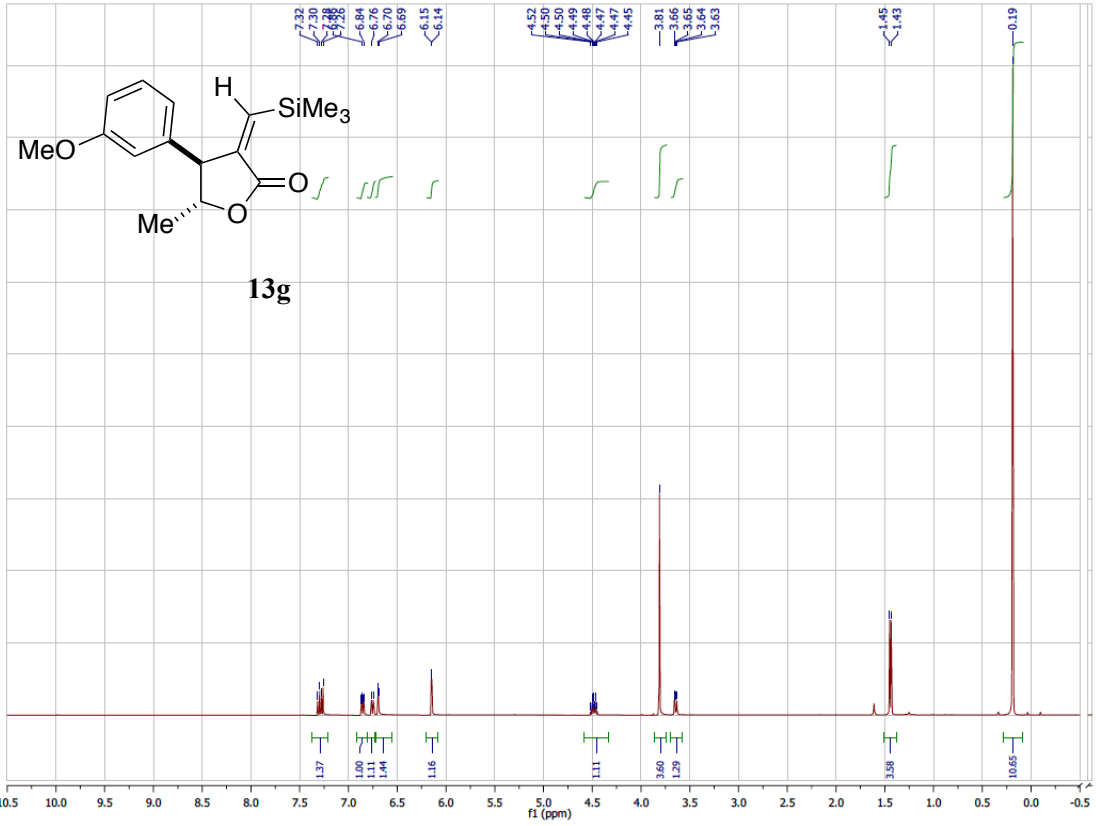
13e

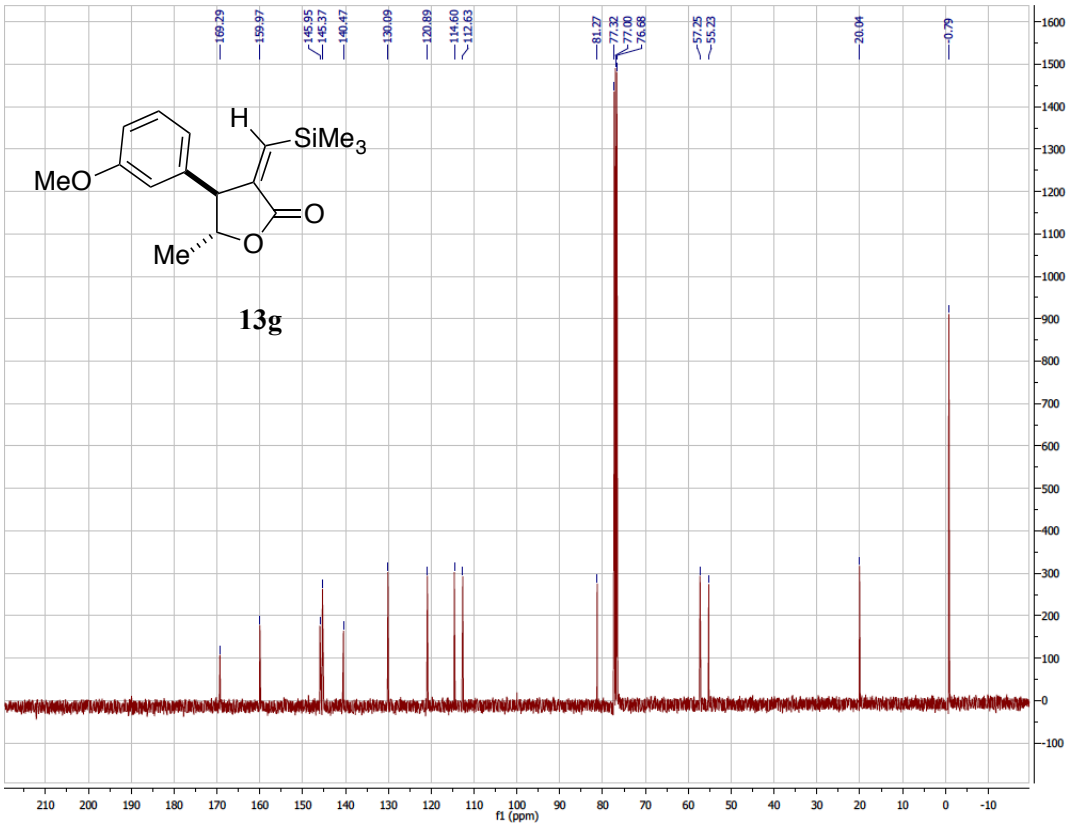

Ph
Me
CO2tBu
O
O
major
Ph
Me
CO2tBu
O
O
minor

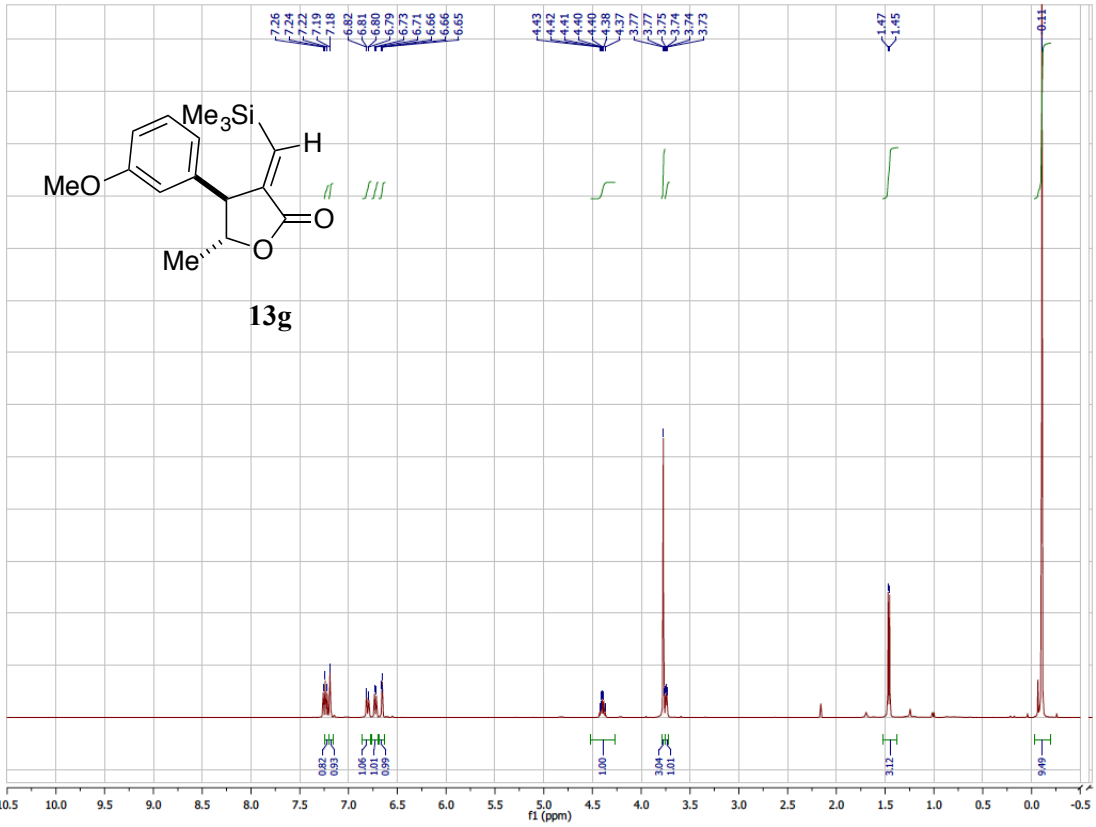
13e

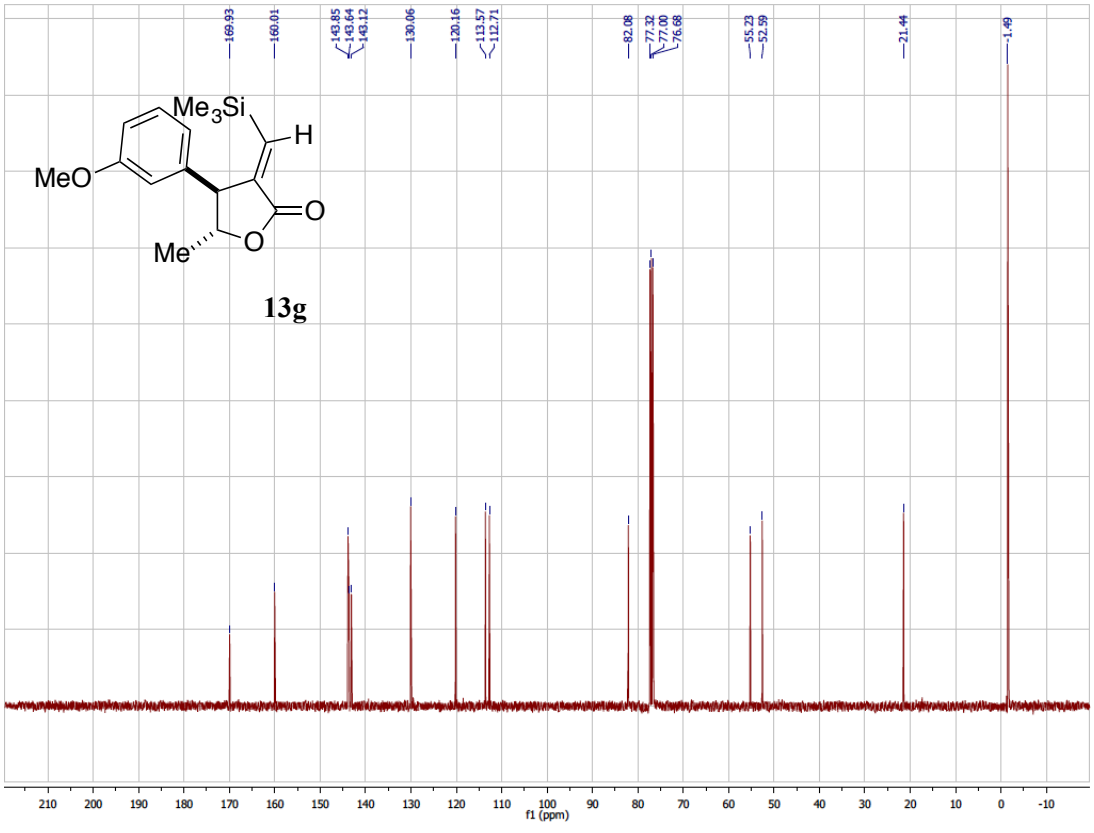

Me
Me
Me
CO2tBu
O
O
13f

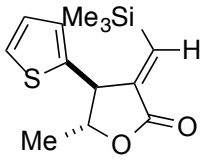

Me
Me
Me
CO2tBu
O
O
13f


H
SiMe3
MeO
O
Me
O
13g
f1 (ppm)


H
SiMe3
MeO
O
Me
O
13g
f1 (ppm)

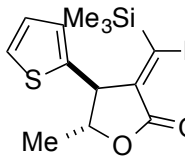

Me3Si
H
MeO
O
O
Me
13g


Me3Si
H
MeO
O
O
Me
13g


Me3Si
H
S
Me
O
O

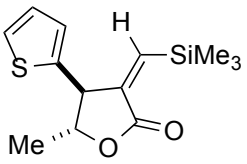
13h

-0.02
1.47
1.46
7.26
7.20
7.19
6.95
6.95
6.94
6.84
6.84
4.51
4.50
4.50
4.49
4.49
4.48
4.05
4.04
4.04
2.17
1.93
1.04
0.99
1.00
1.00
3.20
9.37
Chemical Shift (ppm)


Me3Si
H
S
Me
O
O

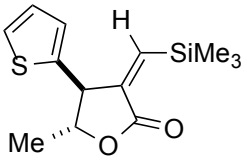
13h

1.50
47.34
21.31
82.14
125.21
127.00
144.52
142.90
124.93
169.31
Chemical Shift (ppm)


H
SiMe3
S
Me
O
O

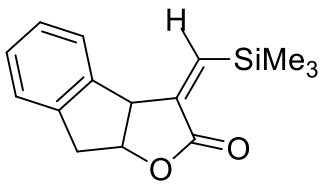
13h

Chemical Shift (ppm)


H
SiMe3
S
Me
O
O

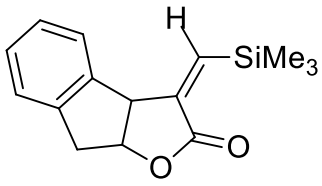
13h

Chemical Shift (ppm)


H
SiMe3
O
O

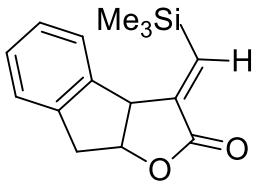
13i

7.26
0.22
6.73
6.73
5.31
5.31
5.29
5.28
5.28
4.39
4.38
4.37
4.37
3.36
3.35
3.33
1.59
4.57
0.99
1.00
0.99
2.12
9.26
Chemical Shift (ppm)


H
SiMe3
O
O

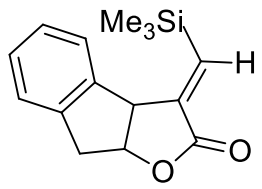
13i

0.79
169.42
144.21
141.02
139.97
128.25
127.53
125.26
124.16
81.21
53.27
39.02
Chemical Shift (ppm)


Me3Si
H
O
O

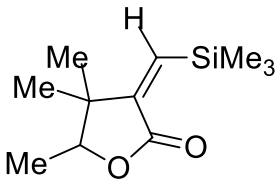
13i

0.35
3.36
6.90
7.28
7.26
7.19
7.18
7.29
5.19
5.18
4.53
4.52
3.35
3.48
1.06
0.95
1.00
1.00
2.11
9.25
Chemical Shift (ppm)


Me3Si
H
O
O

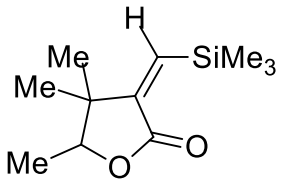
13i

0.64
169.98
142.45
138.68
128.38
125.49
125.06
51.90
50.33
38.48
Chemical Shift (ppm)


H
Me
SiMe3
Me
Me
O
O

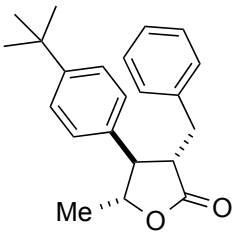
13j

6.19
4.23
4.22
4.21
4.20
1.27
1.25
1.14
1.01
0.19
1.01
1.00
3.42
3.54
3.25
10.31
Chemical Shift (ppm)

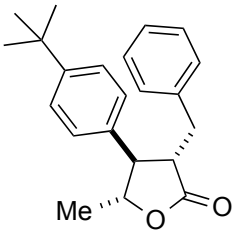

H
Me
SiMe3
Me
Me
O
O

13j

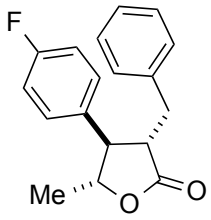
0.76
77.00
82.95
139.95
151.96
170.02
43.72
25.42
22.67
15.28
Chemical Shift (ppm)



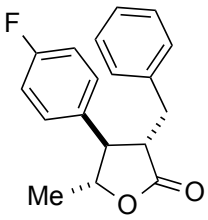
13k



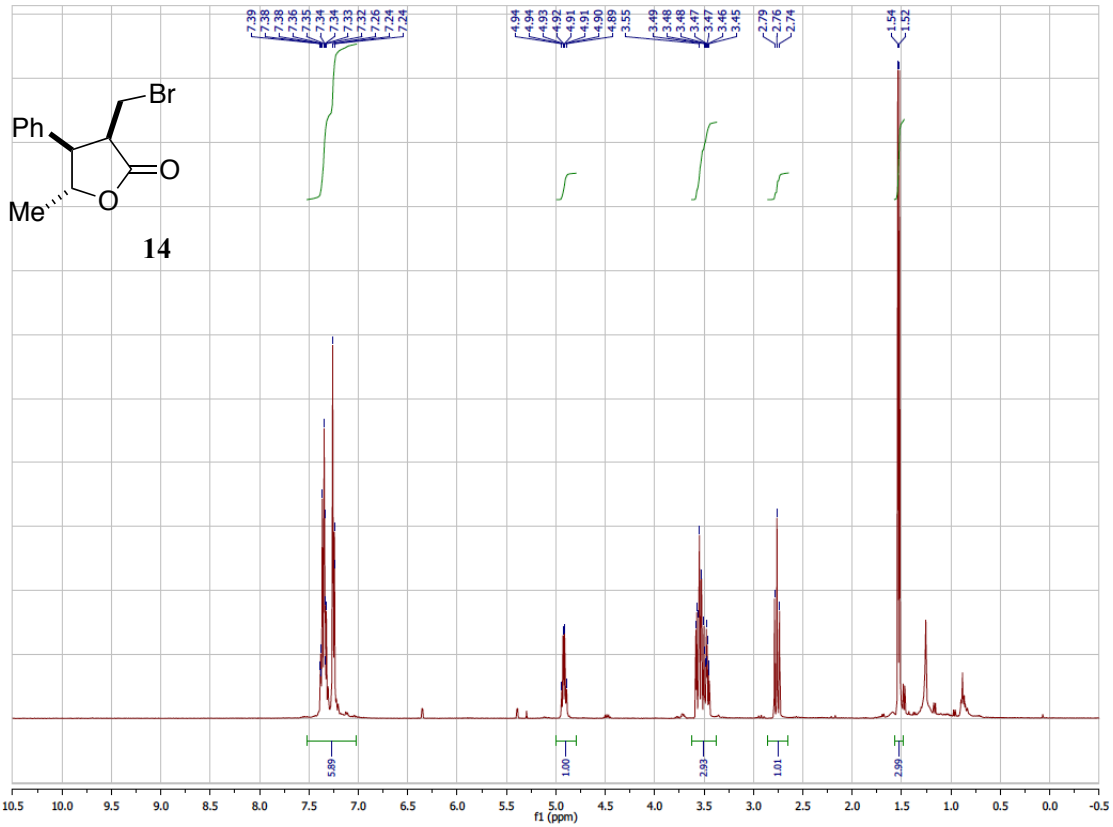
13k

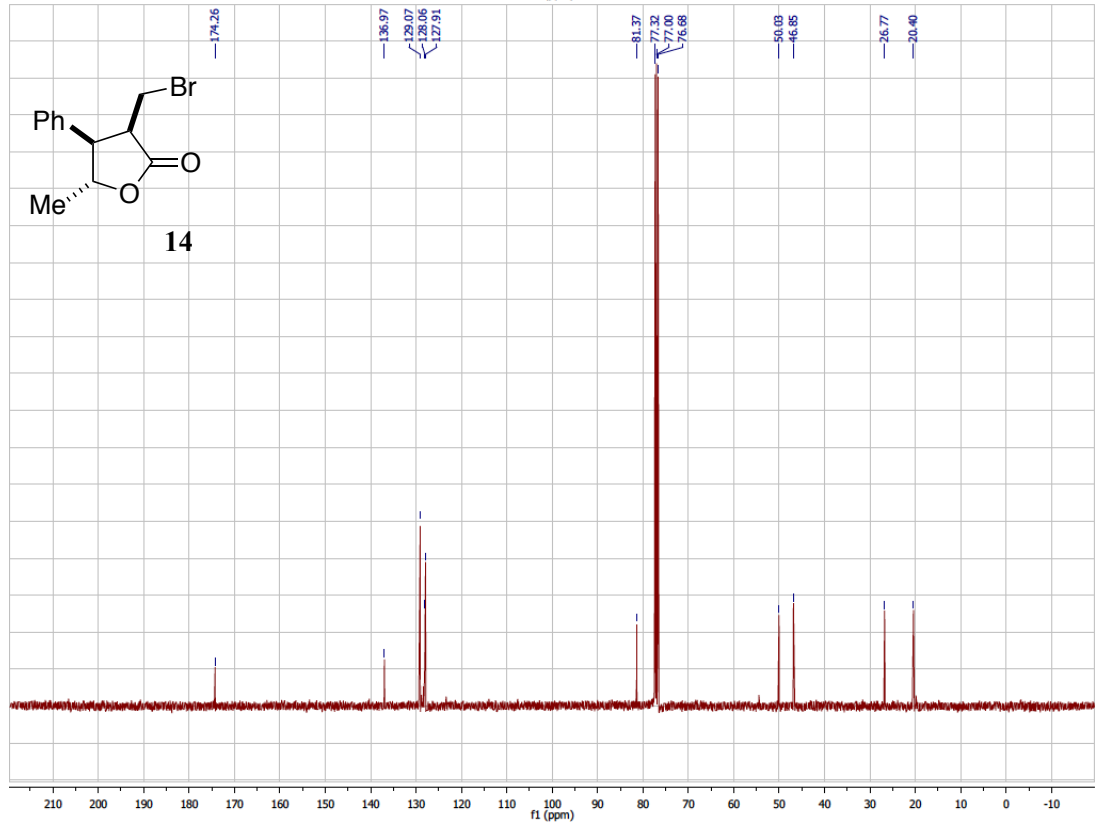


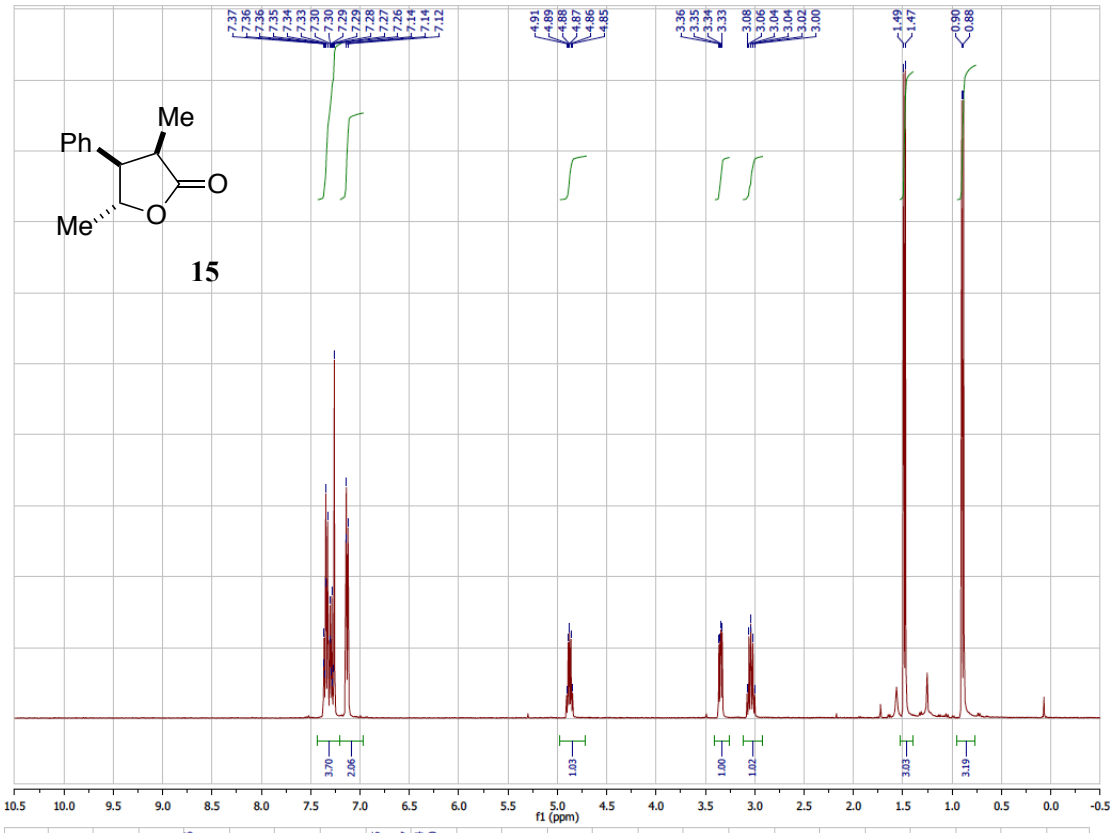
13l

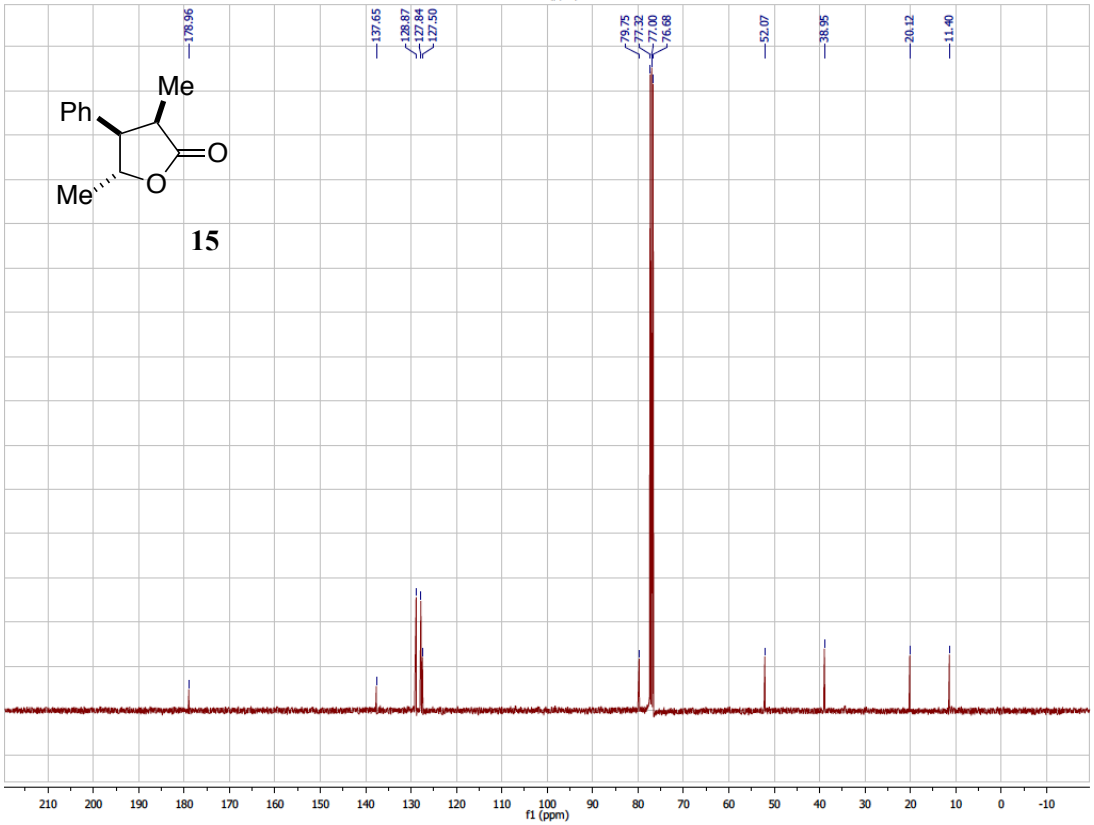


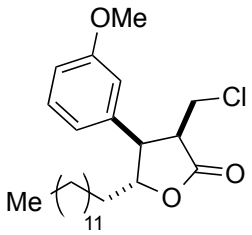
13l


Br
Ph
O
Me
O
14
7.39
7.38
7.38
7.36
7.35
7.34
7.34
7.33
7.32
7.26
7.24
7.24
4.94
4.94
4.93
4.92
4.91
4.91
4.90
4.89
3.55
3.49
3.48
3.48
3.47
3.47
3.46
3.45
2.79
2.76
2.74
1.54
1.52
5.89
1.00
2.93
1.01
2.99
f1 (ppm)

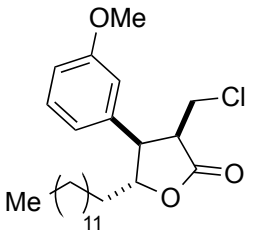

Br
Ph
O
Me
O
14
174.26
136.97
129.07
128.06
127.91
81.37
77.32
77.00
76.68
50.03
46.85
26.77
20.40
f1 (ppm)

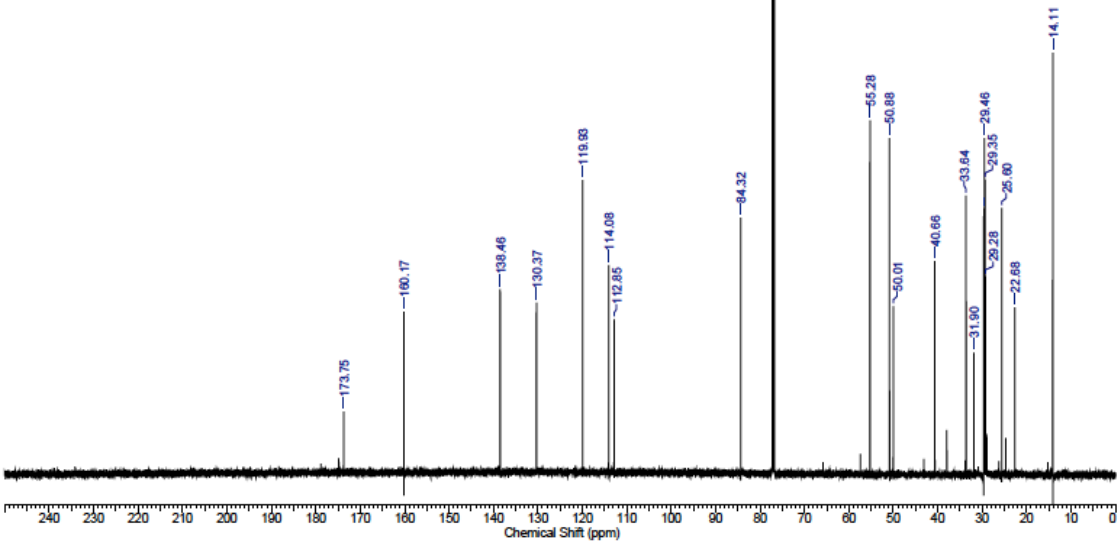

Me
Ph
O
Me
O
15
7.37
7.36
7.36
7.35
7.34
7.33
7.30
7.30
7.29
7.29
7.28
7.27
7.26
7.14
7.14
7.12
4.91
4.89
4.88
4.87
4.86
4.85
3.36
3.35
3.34
3.33
3.08
3.06
3.04
3.04
3.02
3.00
1.49
1.47
0.90
0.88
3.70
2.06
1.03
1.00
1.02
3.03
3.19
f1 (ppm)

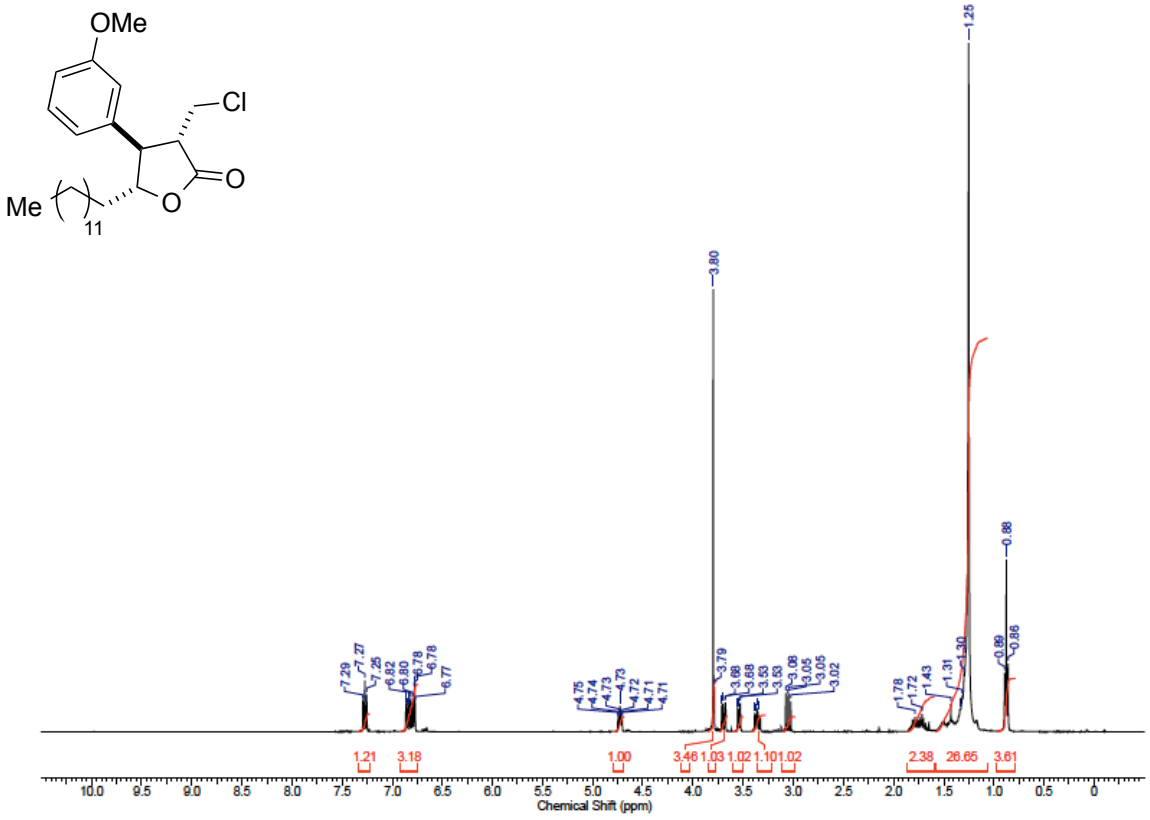

Me
Ph
O
Me
O
15
178.96
137.65
128.87
127.84
127.50
79.75
77.32
77.00
76.68
52.07
38.95
20.12
11.40
f1 (ppm)

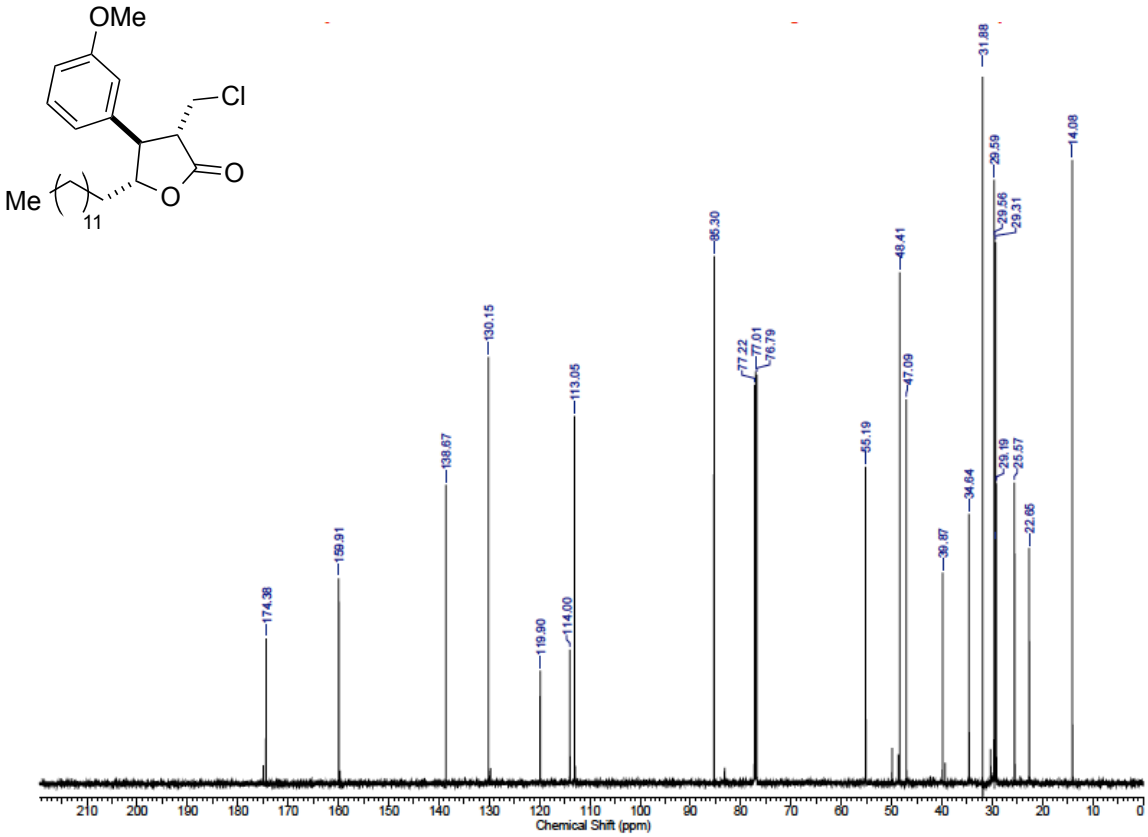

OMe
Cl
O
O
Me
11

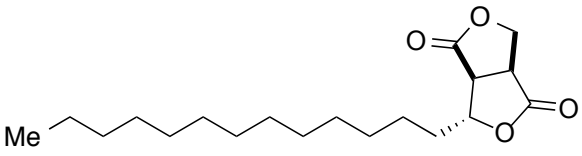
3.82
1.25
1.24
1.21
0.87
6.87
6.85
6.80
6.80
7.33
7.31
7.29
7.26
4.49
4.47
4.47
4.45
4.44
4.02
4.01
3.99
3.57
3.56
3.54
3.53
3.43
3.18
3.15
2.80
2.78
1.71
1.69
1.67
1.66
1.46
1.29
0.89
0.85
1.11
3.06
1.00
1.03
3.13
1.02
1.01
1.04
2.61
1.39
7.75
4.02
Chemical Shift (ppm)


OMe
Cl
O
O
Me
11

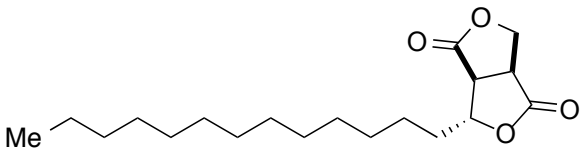

14.11
55.28
50.88
29.46
29.35
119.93
84.32
33.64
25.60
114.08
40.66
138.46
160.17
130.37
112.85
29.28
50.01
22.68
31.90
173.75
Chemical Shift (ppm)


OMe
Cl
O
Me
O
11
7.29
7.27
7.25
6.82
6.80
6.78
6.78
6.77
4.75
4.74
4.73
4.73
4.72
4.71
4.71
3.80
3.79
3.68
3.68
3.53
3.53
3.06
3.05
3.05
3.02
1.78
1.72
1.43
1.31
1.30
1.25
0.89
0.88
0.86
1.21
3.18
1.00
3.46
1.03
1.02
1.10
1.02
2.38
26.65
3.61
Chemical Shift (ppm)

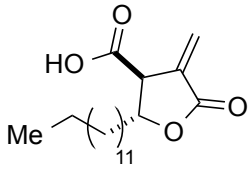

OMe
Cl
O
Me
O
11
174.38
159.91
138.67
130.15
119.90
114.00
113.05
86.30
77.22
77.01
76.79
55.19
48.41
47.09
39.87
34.64
31.88
29.59
29.56
29.31
29.19
25.57
22.65
14.08
Chemical Shift (ppm)


O
O
O
O
Me

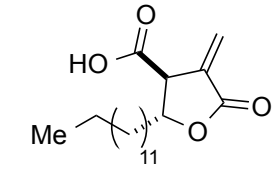
7.26
4.91
4.79
4.68
4.53
4.52
3.54
3.53
3.51
3.52
3.21
3.21
3.20
3.19
1.76
1.76
1.75
1.75
1.74
1.71
1.48
1.35
1.30
1.29
1.28
1.27
1.25
0.99
0.98
0.89
0.88
0.86
1.00 1.03 1.03
1.00 1.00
2.12 2.18 23.04 3.46
Chemical Shift (ppm)


O
O
O
O
Me

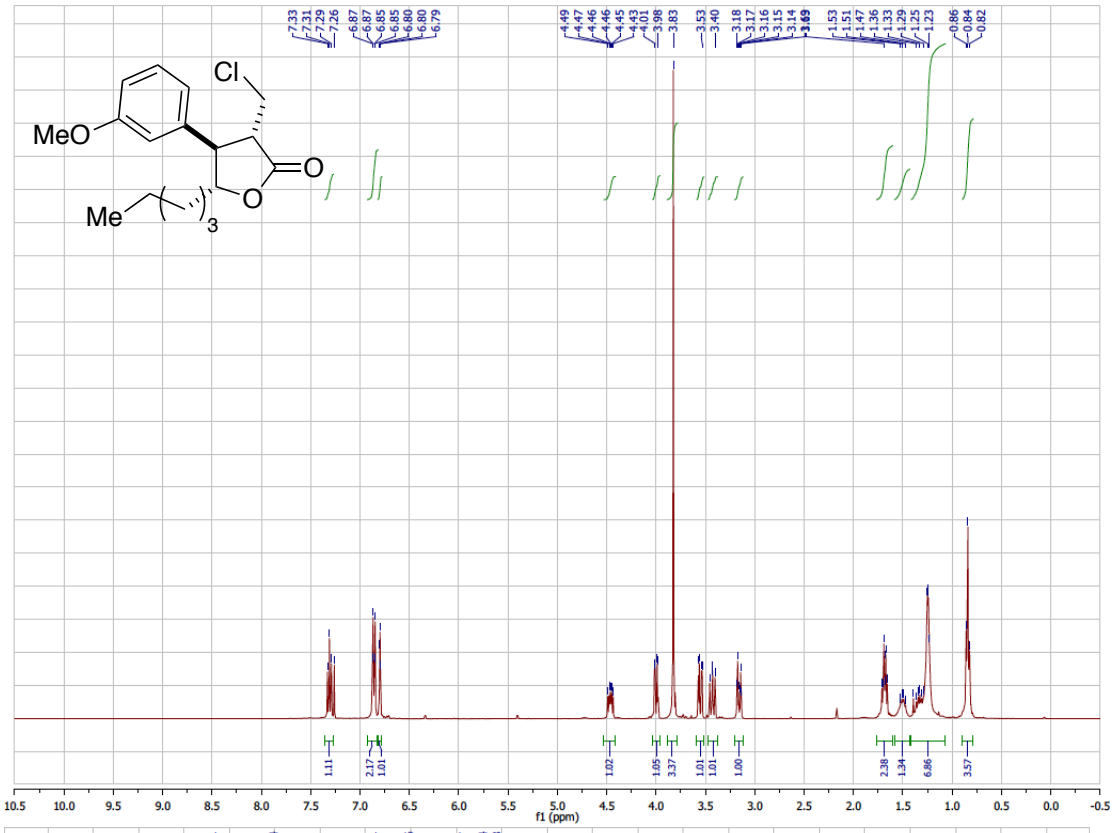
175.53
175.36
81.86
69.00
45.39
40.69
36.31
31.90
29.62
29.36
29.01
24.61
22.67
14.11
Chemical Shift (ppm)

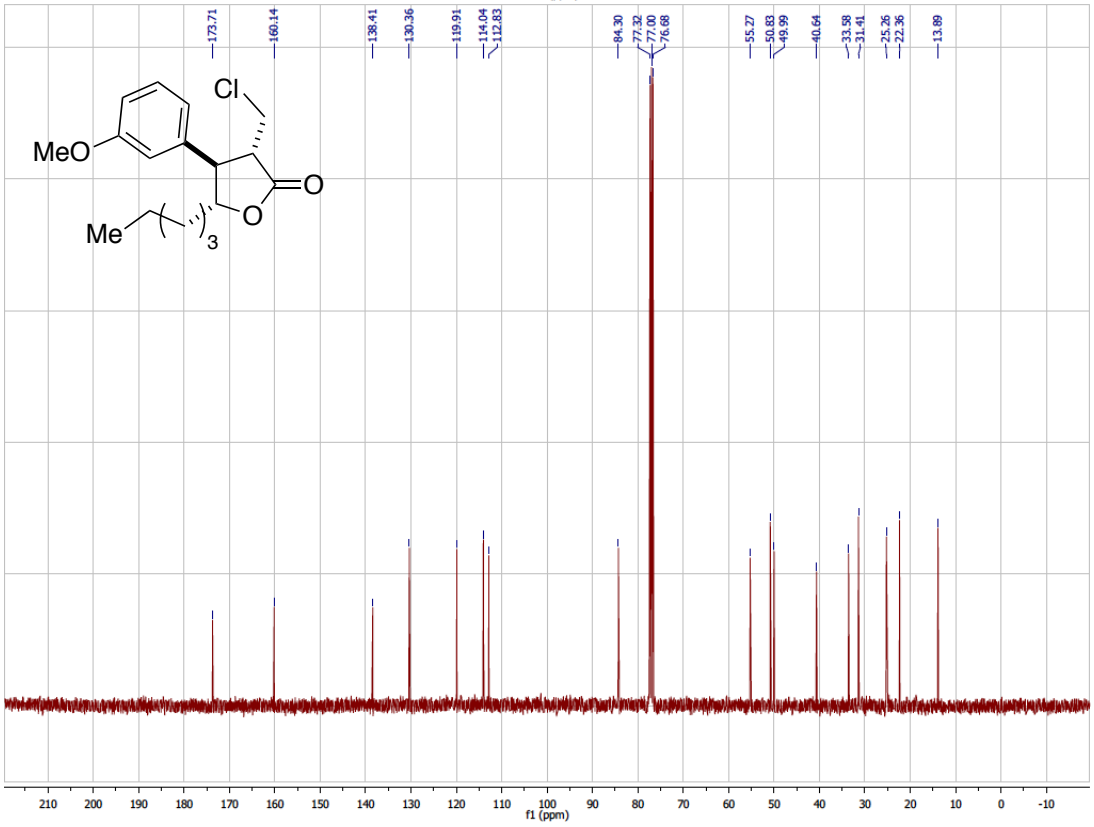


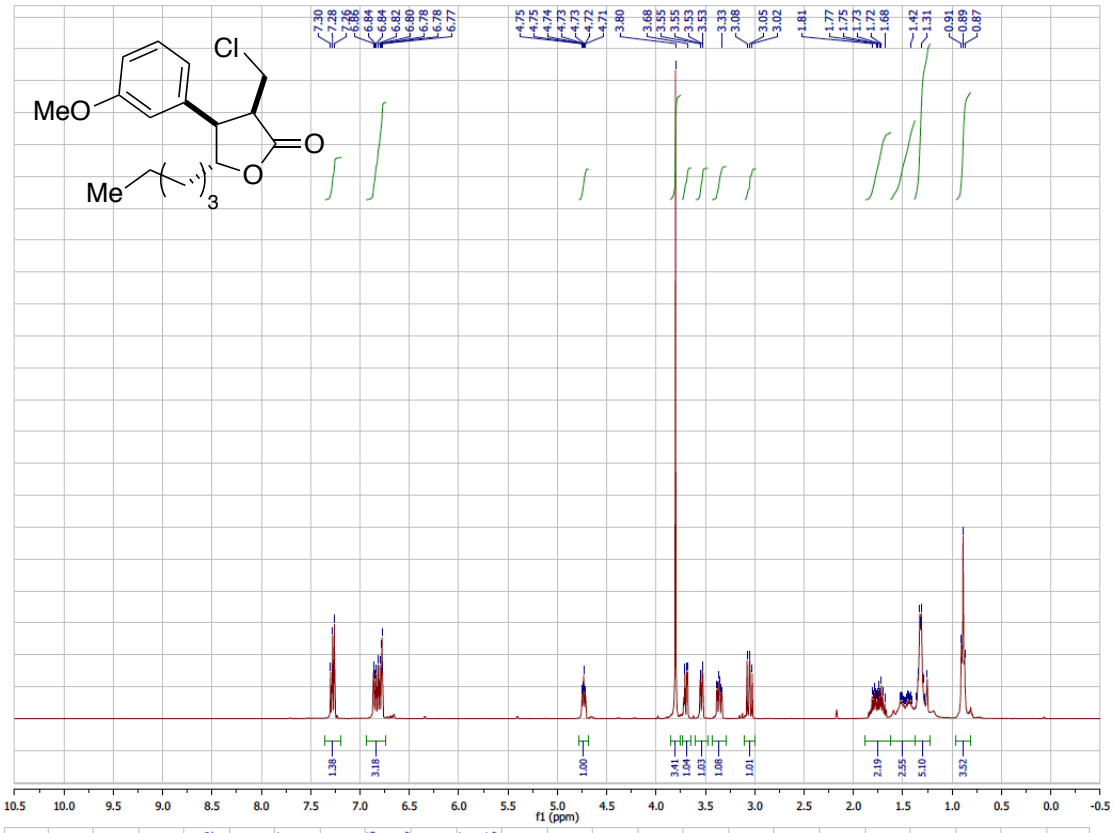
Protolichesterinic acid

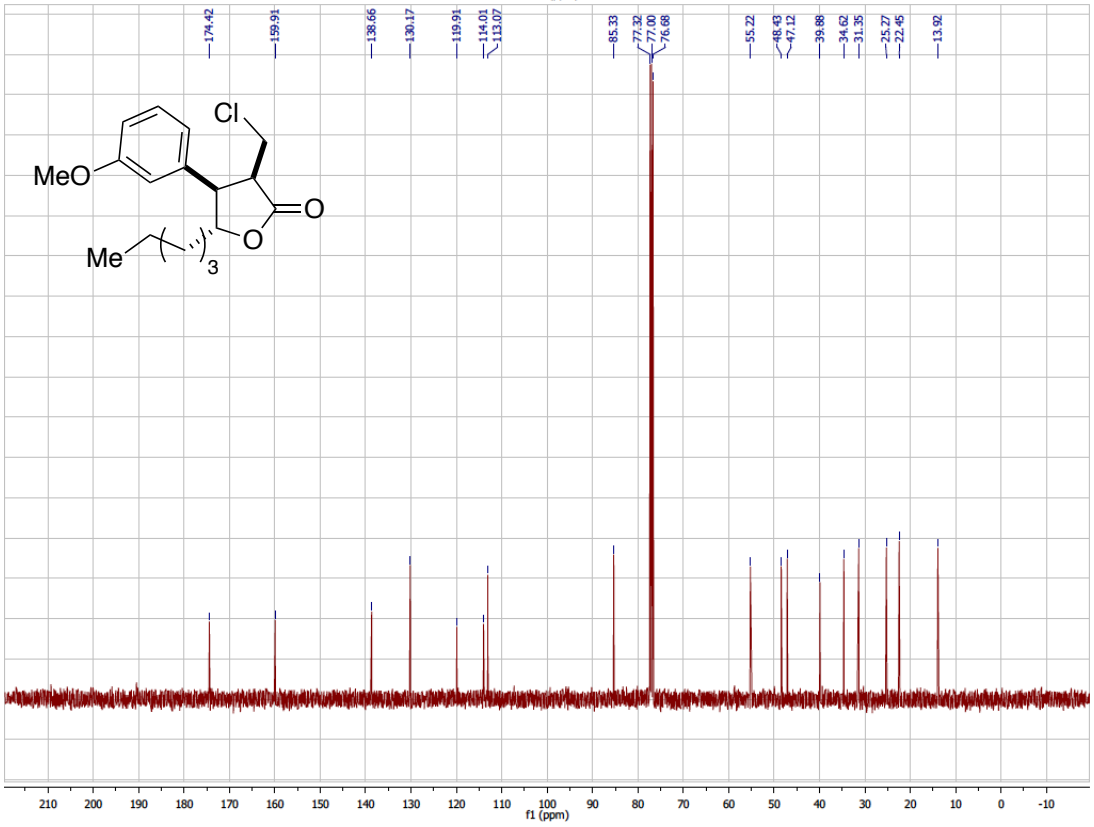


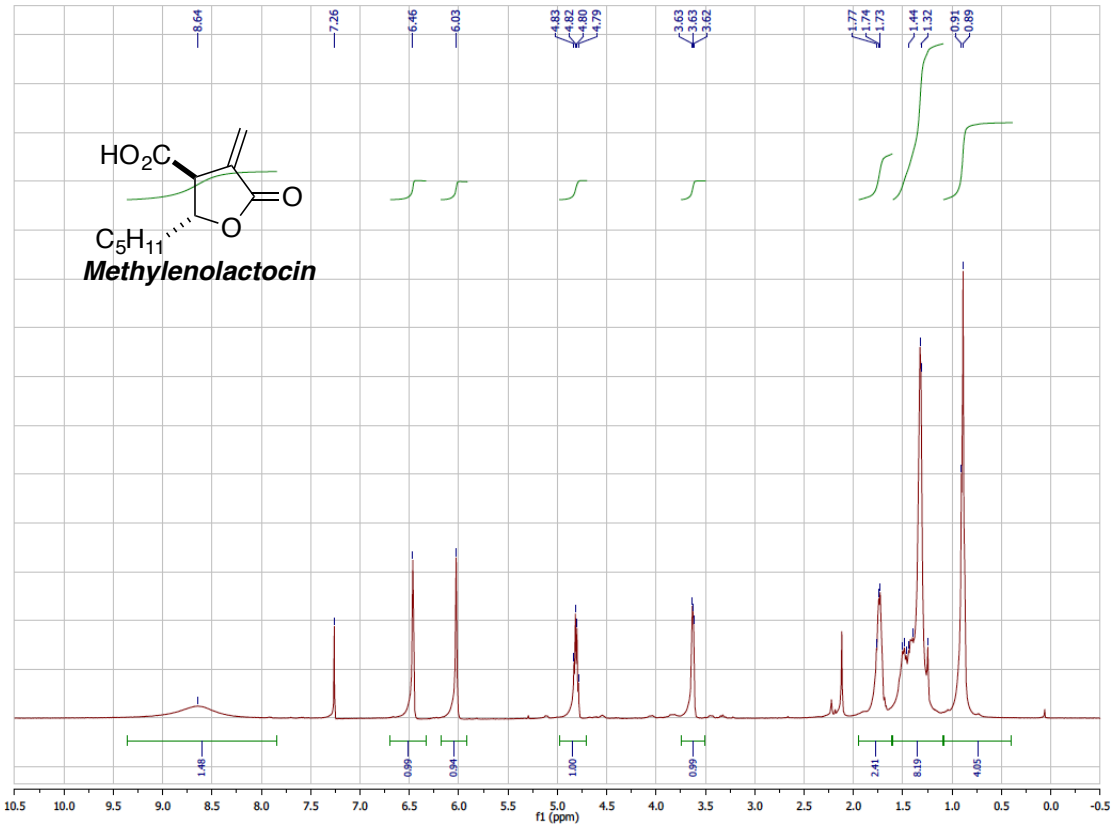
Protolichesterinic acid

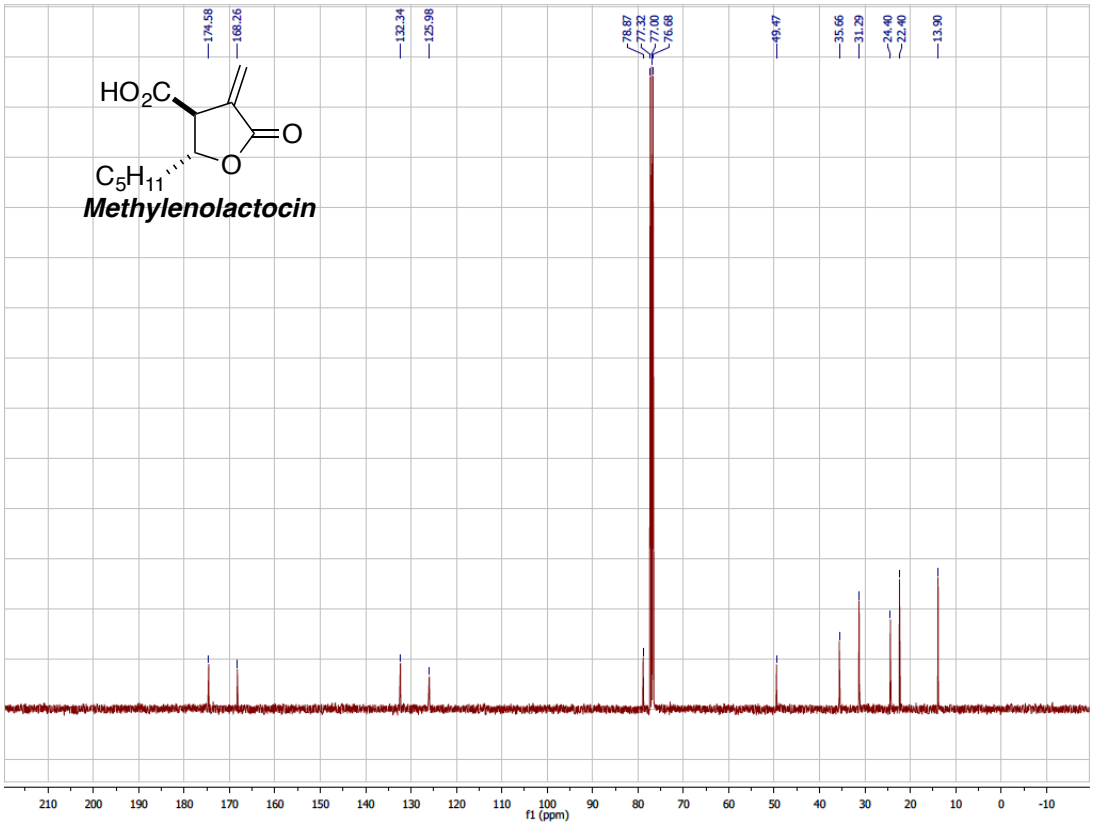

Cl
MeO
O
O
Me
3
f1 (ppm)

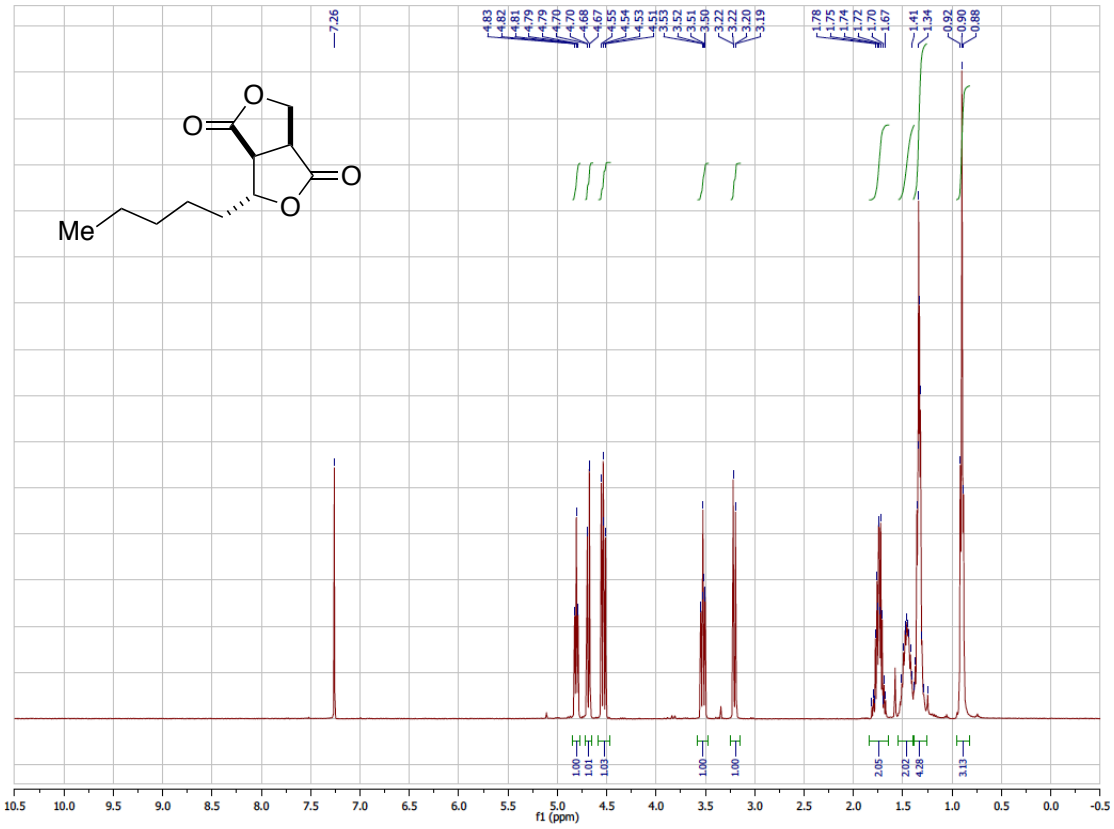

Cl
MeO
O
O
Me
3
f1 (ppm)

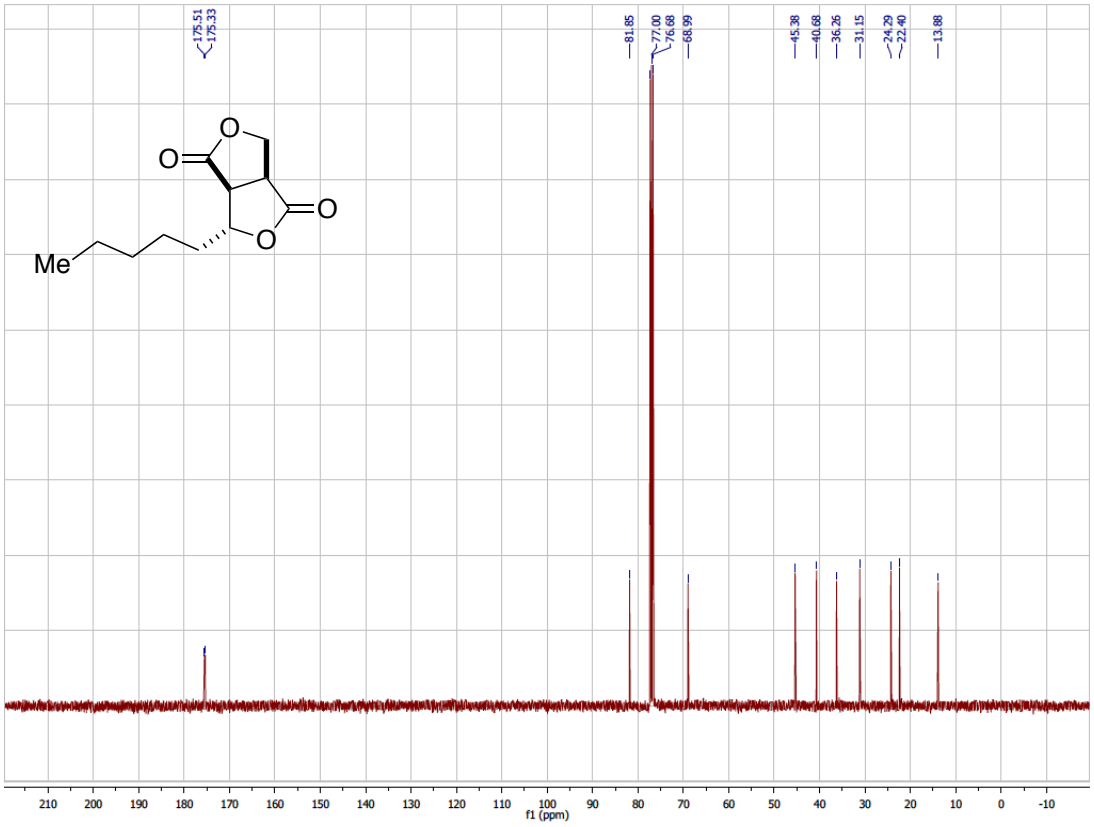

Cl
MeO
O
O
Me
3
7.30
7.28
7.26
6.86
6.84
6.84
6.82
6.80
6.78
6.78
6.77
4.75
4.75
4.74
4.74
4.73
4.73
4.72
4.71
3.80
3.68
3.55
3.55
3.53
3.53
3.33
3.08
3.05
3.02
1.81
1.77
1.75
1.73
1.72
1.68
1.42
1.31
0.91
0.89
0.87
1.38
3.18
1.00
3.41
1.04
1.03
1.08
1.01
2.19
2.55
5.10
3.52
f1 (ppm)


Cl
MeO
O
O
Me
3
174.42
159.91
138.66
130.17
119.91
114.01
113.07
85.33
77.32
77.00
76.68
55.22
48.43
47.12
39.88
34.62
31.35
25.27
22.45
13.92
f1 (ppm)


8.64
7.26
6.46
6.03
4.83
4.82
4.80
4.79
3.63
3.63
3.62
1.77
1.74
1.73
1.44
1.32
0.91
0.89
HO2C
O
O
C5H11
Methylenolactocin
1.48
0.89
0.94
1.00
0.99
2.41
8.19
4.05
f1 (ppm)


174.58
168.26
132.34
125.98
78.87
77.32
77.00
76.68
49.47
35.66
31.29
24.40
22.40
13.90
HO2C
O
O
C5H11
Methylenolactocin
f1 (ppm)


7.26
4.83
4.82
4.81
4.79
4.79
4.70
4.70
4.68
4.67
4.55
4.54
4.53
4.51
3.53
3.52
3.51
3.50
3.22
3.22
3.20
3.19
1.78
1.75
1.74
1.72
1.70
1.67
1.41
1.34
0.92
0.90
0.88
1.00
1.01
1.03
1.00
1.00
2.05
2.02
4.28
3.13
O
O
O
O
Me
f1 (ppm)


175.51
175.33
81.85
77.00
76.68
68.99
45.38
40.68
36.26
31.15
24.29
22.40
13.88
O
O
O
O
Me
f1 (ppm)

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