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Electronic complementarity permits hindered butenolide heterodimerization and discovery of novel cGAS/STING pathway antagonists

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Supplementary Information

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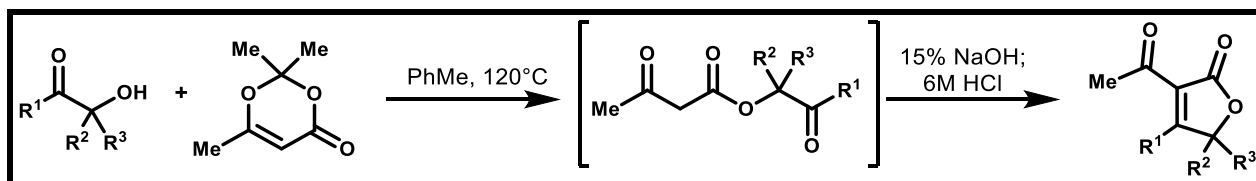
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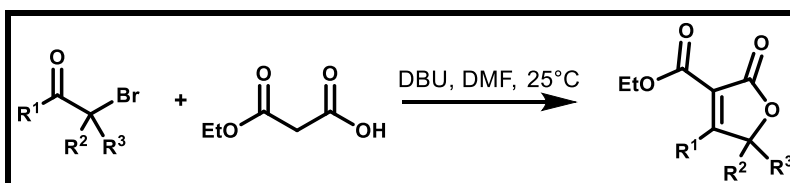
Materials and Methods. All reactions were carried out under positive pressure of argon unless otherwise stated. Anhydrous tetrahydrofuran (THF) was purchased from Sigma Aldrich. Diisopropylamine was purchased from Acros Organics and freshly distilled over CaH_2 . *n*-Butyllithium solution (*n*-BuLi, 2.5 M in hexanes) was purchased from Sigma Aldrich. Reactions were monitored by thin layer chromatography (TLC) using precoated silica gel plates from EDM Chemicals (TLC Silica gel 60 F₂₅₄, 250 μm thickness). Flash column chromatography was performed over Silica gel 60 (particle size 0.04-0.063 mm) from EDM Chemicals. ^1H and ^{13}C NMR spectra were recorded on Bruker DPX-400, Bruker DPX-500, or Bruker DPX-600 (equipped with cryoprobe) spectrometers using residual solvent peaks as an internal standard (CDCl_3 at 7.26 ppm ^1H NMR, 77.16 ^{13}C NMR). NMR data are denoted with apparent multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, and combinations thereof.

Experimental Procedures:

Lithium diisopropylamide (LDA) preparation. A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried, backfilled with argon, and charged with 2.95 mL of anhydrous THF. Next, freshly distilled diisopropylamine (2.14 mmol, 0.300 mL, 1.1 equiv) was added and the resulting solution was cooled to -78°C using a dry ice/acetone bath. After allowing the solution to cool for 10 minutes, *n*-BuLi (1.94 mmol, 0.712 mL of a 2.73 M solution, 1.0 equiv) was added dropwise over 5 minutes. The resulting 0.49 M solution of LDA was allowed to stir at -78°C for 1 hour before use.

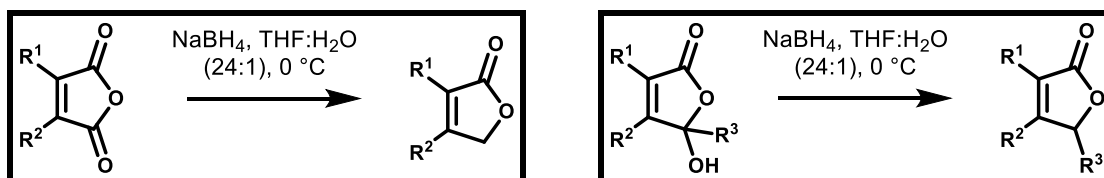


General Procedure A. The title compound was prepared by heating a mixture of α -hydroxy ketone (5 mmol) and 2,2,6-trimethyl-4H-1,3-dioxin-4-one (5.1 mmol) in anhydrous toluene (12.5 mL) at 120°C . The reaction was monitored by TLC and, upon completion, concentrated *in vacuo*. The crude material can be used in the next step without purification (however, higher yields were obtained using purified material). Next, the crude material was transferred to a separatory funnel using a minimal amount of organic solvent (Et_2O) followed by addition of 15% NaOH (ratio: (1 mmol) 2-oxopropyl 3-oxobutanoate: (25.0 mL) 15% NaOH solution). The resulting mixture was shaken vigorously for 2 minutes (carefully vent every 10-15 seconds). 6 M HCl was then carefully added until pH = 0. The solution was shaken vigorously for an additional 60 seconds (carefully vent every 5-10 seconds). Organic solvent (Et_2O) was added and the mixture was extracted three times (**Caution:** care should be taken when extracting, vent often.) The combined organics were dried over MgSO_4 , concentrated *in vacuo*, and purified via column chromatography.

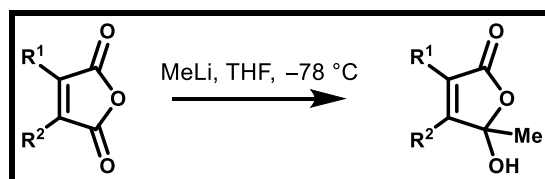


General Procedure B. To a flame-dried flask equipped with a magnetic stir bar was added α -bromo ketone (1.0 mmol). After purging the flask with argon, dry DMF (10 mL) and 3-ethoxy-3-oxopropanoic acid (1.0 mmol) were added. Then, DBU (3.0 mmol) was added dropwise at 25°C and the reaction mixture was stirred for 16 hours at 25°C . The reaction mixture was diluted with

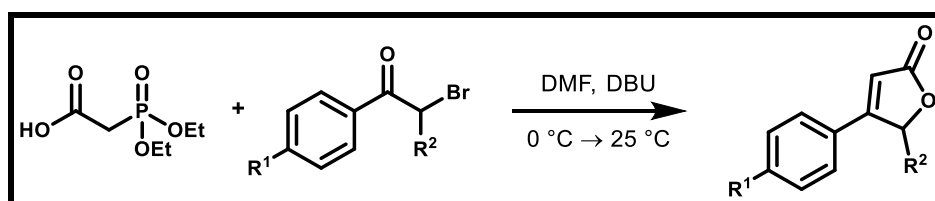
saturated NH_4Cl (aq.) and extracted with EtOAc. The combined organic layers were washed with H_2O and brine, dried over MgSO_4 , concentrated *in vacuo*, and purified via column chromatography.



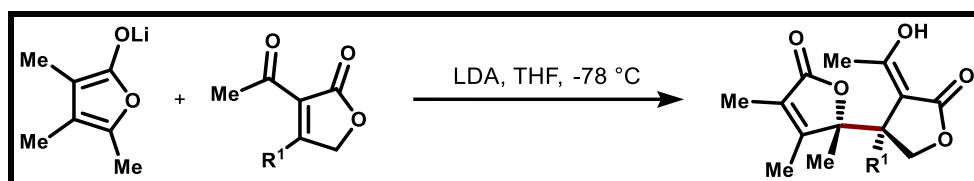
General Procedure C. The title compound was prepared using an adapted procedure from Kimpe and coworkers.¹ To a solution of hydroxy-furan-2(5H)-one **or** unsubstituted maleic anhydride (1.00 mmol) in THF (16.6 mL) and water (0.694 mL) (THF/ H_2O 24:1) was added sodium borohydride (3.00 mmol) in portions at 0 °C. The solution was stirred at 0 °C for 2 hours and then the reaction mixture was quenched by addition of 1 M HCl (6 mL). The mixture was extracted with EtOAc, washed with brine, dried over MgSO_4 , concentrated *in vacuo*, and purified via column chromatography.



General procedure D. The title compound was prepared using an adapted procedure from Kimpe and coworkers.¹ Substituted maleic anhydride (8.00 mmol) was added to a flame dried flask and dissolved in anhydrous THF (50 mL). The solution was cooled to -78 °C and MeLi (1.6M in THF, 8 mmol, 2.5 mL) was added dropwise over 15 minutes. The reaction was monitored by TLC, quenched with saturated ammonium chloride (20 mL), and extracted with EtOAc. The combined organics were washed with brine, dried over MgSO_4 , concentrated *in vacuo*, and purified via column chromatography.

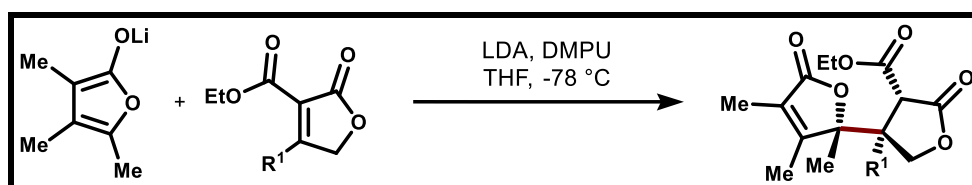


General Procedure E. The title compound was prepared by adding 2-(diethoxyphosphoryl)acetic acid (1.00 mmol) to a mixture of phenacyl bromide derivative (1.00 mmol) in DMF (10 mL). The reaction mixture was cooled to 0 °C and DBU (3 mmol) was added. The mixture was stirred for 30 minutes at 0 °C then warmed to 25 °C and allowed to stir an additional 30 minutes. The reaction was quenched with 1 M HCl (20 mL), extracted with EtOAc, dried over MgSO_4 , concentrated *in vacuo*, and purified via column chromatography.





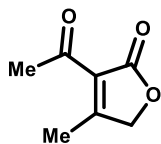
General Procedure F. A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to $-78\text{ }^{\circ}\text{C}$ and charged with LDA (0.11 mmol, 0.224 mL, 1.1eq). Next, nucleophilic butenolide (0.11 mmol, 1.1 eq) was dissolved in 0.388 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, electrophilic butenolide (0.10 mmol, 1.0 eq), dissolved in 0.388 mL of anhydrous THF, was added dropwise (ca. 5 minutes). After stirring for 1 hour the reaction was quenched with sat. NH_4Cl , and extracted with EtOAc (3x 3 mL). The combined organics were washed with brine, dried with MgSO_4 , and concentrated *in vacuo*. Compounds were purified via preparative TLC.



General Procedure G. A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to $-78\text{ }^{\circ}\text{C}$ and charged with LDA (0.12 mmol, 0.224 mL, 1.1eq). Next, nucleophilic butenolide (0.11 mmol, 1.1 eq) was dissolved in 0.270 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, electrophilic butenolide (0.10 mmol, 1.0 eq) and DMPU (0.200 mL), dissolved in 0.270 mL of anhydrous THF, were added dropwise (ca. 5 minutes). After stirring for 1 hour the reaction was quenched with sat. NH_4Cl , and extracted with EtOAc (3x 3 mL). The combined organics were washed with brine, dried with MgSO_4 , and concentrated *in vacuo*. Compounds were purified via preparative TLC.

Substrate Characterization

Electrophiles



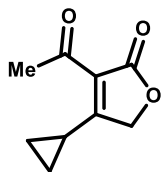
3-acetyl-4-methylfuran-2(5H)-one (SI-1) [Compound (6) in manuscript]. The title compound was obtained as a yellow oil using **General Procedure A** (62% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 4.76 (t, *J* = 0.7 Hz, 2H), 2.56 (d, *J* = 0.6 Hz, 3H), 2.42 (d, *J* = 0.6 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 194.80, 174.32, 171.20, 125.25, 72.49, 30.21, 14.80.

LC-MS (ESI) Calculated [C₇H₉O₃]⁺: 141.1, found: 141.1;

R_f 0.5 (Hexanes:EtOAc = 1:1).



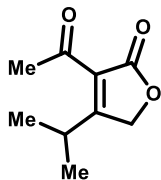
3-acetyl-4-cyclopropylfuran-2(5H)-one (SI-2). The title compound was obtained as a yellow solid using **General Procedure A** (46% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 4.50 (d, *J* = 0.6 Hz, 2H), 3.27 – 3.14 (m, 1H), 2.59 (s, 3H), 1.37 – 1.31 (m, 2H), 0.97 – 0.91 (m, 2H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 195.22, 180.88, 171.55, 124.56, 67.77, 30.28, 12.69, 12.61.

LC-MS (ESI) Calculated [C₉H₁₁O₃]⁺: 167.1, found: 167.1;

R_f 0.60 (Hexanes:EtOAc = 1:1).



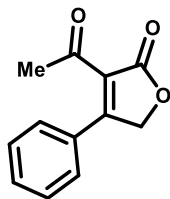
3-acetyl-4-isopropylfuran-2(5H)-one (SI-3). The title compound was obtained as a yellow oil using **General Procedure A** (76% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 4.84 (d, *J* = 0.7 Hz, 2H), 3.84 – 3.75 (m, 1H), 2.56 (d, *J* = 0.6 Hz, 3H), 1.19 (d, *J* = 7.0 Hz, 6H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 194.92, 183.54, 171.58, 123.59, 68.75, 30.41, 28.15, 20.87, 20.87.

LC-MS (ESI) Calculated [C₉H₁₃O₃]⁺: 169.1, found: 169.1;

R_f 0.3 (Hexanes:EtOAc = 7:3).



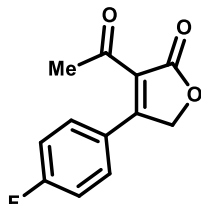
3-acetyl-4-phenylfuran-2(5H)-one (SI-4). The title compound was obtained as a purple solid using **General Procedure A** (44% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 7.58 – 7.54 (m, 2H), 7.54 – 7.51 (m, 1H), 7.49 – 7.45 (m, 2H), 5.16 (s, 2H), 2.57 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 196.05, 170.90, 164.89, 132.20, 129.42, 129.08, 128.13, 126.01, 70.75, 30.70.

LC-MS (ESI) Calculated [C₁₂H₁₁O₃]⁺: 203.1, found: 203.1;

R_f 0.8 (Hexanes:EtOAc = 1:1).



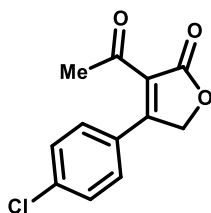
3-acetyl-4-(4-fluorophenyl)furan-2(5H)-one (SI-5). The title compound was obtained as a yellow solid using **General Procedure A** (65% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 7.64 (dd, *J* = 9.0, 5.2 Hz, 2H), 7.18 – 7.14 (m, 2H), 5.14 (s, 2H), 2.59 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 195.46, 170.43, 165.28, 163.59, 163.40, 130.32, 130.26, 125.16, 115.97, 115.82, 70.18, 30.25.

LC-MS (ESI) Calculated [C₁₂H₁₀FO₃]⁺: 221.1, found: 221.1;

R_f 0.6 (DCM:Ether = 7:3).



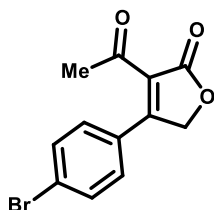
3-acetyl-4-(4-chlorophenyl)furan-2(5H)-one (SI-6). The title compound was obtained as a purple solid using **General Procedure A** (27% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 7.56 – 7.53 (m, 2H), 7.46 – 7.43 (m, 2H), 5.13 (s, 2H), 2.59 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 195.91, 170.86, 163.97, 138.74, 129.74, 129.51, 127.93, 126.30, 70.74, 30.84.

LC-MS (ESI) Calculated [C₁₂H₁₀ClO₃]⁺: 237.1, found: 237.1;

R_f 0.75 (Hexanes:EtOAc = 1:1).



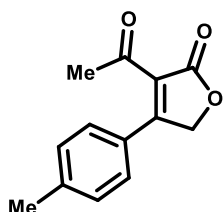
3-acetyl-4-(4-bromophenyl)furan-2(5H)-one (SI-7). The title compound was obtained as a purple solid using **General Procedure A** (48% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 5.12 (s, 2H), 2.58 (d, *J* = 0.8 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 195.86, 170.83, 164.08, 132.47, 129.81, 128.36, 127.17, 126.36, 70.68, 30.81.

LC-MS (ESI) Calculated [C₁₂H₁₀BrO₃]⁺: 280.1, found: 280.1;

R_f 0.2 (Hexanes:EtOAc = 4:1).



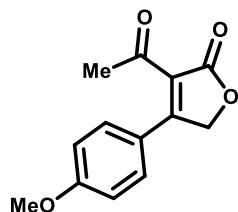
3-acetyl-4-(p-tolyl)furan-2(5H)-one (SI-8). The title compound was obtained as a green solid using **General Procedure A** (71% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 7.48 – 7.44 (m, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 5.13 (s, 2H), 2.55 (s, 3H), 2.40 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 196.47, 171.25, 164.92, 143.34, 129.86, 128.28, 126.64, 125.15, 70.75, 30.81, 21.73.

LC-MS (ESI) Calculated [C₁₃H₁₃O₃]⁺: 217.1, found: 217.1;

R_f 0.8 (Hexanes:EtOAc = 1:1).



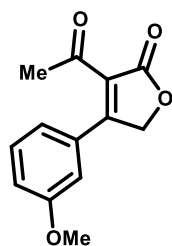
3-acetyl-4-(4-methoxyphenyl)furan-2(5H)-one (SI-9). The title compound was obtained as a orange solid using **General Procedure A** (72% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 7.64 – 7.61 (m, 2H), 6.98 – 6.94 (m, 2H), 5.15 (s, 2H), 3.87 (s, 3H), 2.59 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 196.78, 171.65, 163.16, 130.61, 123.71, 121.91, 114.59, 114.59, 70.61, 55.69, 30.95.

LC-MS (ESI) Calculated [C₁₃H₁₃O₄]⁺: 233.1, found: 233.1;

R_f 0.8 (Hexanes:EtOAc = 1:1).



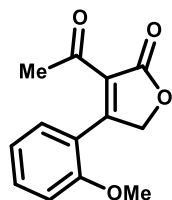
3-acetyl-4-(3-methoxyphenyl)furan-2(5H)-one (SI-10). The title compound was obtained as a purple solid using **General Procedure A** (52% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 7.37 (t, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 2.1 Hz, 1H), 7.07 (dddd, *J* = 13.5, 8.4, 2.2, 0.9 Hz, 2H), 5.13 (s, 2H), 3.84 (s, 3H), 2.56 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 195.67, 170.40, 164.04, 159.35, 130.12, 129.69, 125.82, 119.71, 117.35, 113.35, 70.34, 55.00, 30.25.

LC-MS (ESI) Calculated [C₁₃H₁₃O₄]⁺: 233.1, found: 233.1;

R_f 0.2 (Hexanes:EtOAc = 4:1).



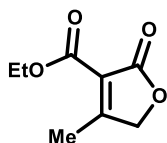
3-acetyl-4-(2-methoxyphenyl)furan-2(5H)-one (SI-11). The title compound was obtained as a purple solid using **General Procedure A** (52% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 7.46 (ddd, *J* = 8.4, 7.4, 1.7 Hz, 1H), 7.28 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.04 (td, *J* = 7.6, 1.0 Hz, 1H), 6.98 (dd, *J* = 8.5, 0.9 Hz, 1H), 5.13 (s, 2H), 3.83 (s, 3H), 2.50 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 195.69, 171.00, 162.53, 156.54, 133.09, 129.44, 127.33, 121.11, 119.03, 111.71, 71.45, 55.37, 30.16.

LC-MS (ESI) Calculated [C₁₃H₁₃O₄]⁺: 233.1, found: 233.1;

R_f 0.25 (Hexanes:EtOAc = 7:3).



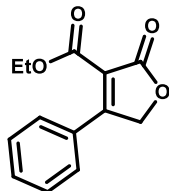
Ethyl 4-methyl-2-oxo-2,5-dihydrofuran-3-carboxylate (SI-12). The title compound was obtained as a yellow oil using **General Procedure B** (45%).

¹H NMR (600 MHz, Chloroform-*d*) δ 4.77 (d, *J* = 1.3 Hz, 2H), 4.40 – 4.35 (m, 2H), 2.41 (d, *J* = 3.5 Hz, 3H), 1.38 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 173.74, 169.06, 161.34, 119.69, 72.20, 61.47, 14.61, 14.32.

LC-MS (ESI) Calculated [C₈H₁₁O₄]⁺: 171.1, found: 171.1;

R_f 0.25 (Hexanes:EtOAc = 7:3).



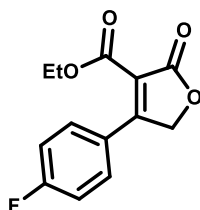
Ethyl 2-oxo-4-phenyl-2,5-dihydrofuran-3-carboxylate (SI-13). The title compound was obtained as a yellow oil using **General Procedure B** (46%).

¹H NMR (600 MHz, CDCl₃): δ (ppm) = 7.57 – 7.51 (m, 3H), 7.51 – 7.45 (m, 2H), 5.17 (s, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H);

¹³C NMR (151 MHz, CDCl₃): δ (ppm) = 169.6, 164.2, 162.5, 132.2, 129.4, 129.2, 127.9, 119.9, 70.6, 62.2, 14.1;

LC-MS (ESI) Calculated [C₁₃H₁₃O₄]⁺: 233.1, found: 233.0;

R_f 0.37 (Hexanes:EtOAc = 2:1).



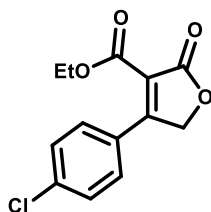
Ethyl 4-(4-fluorophenyl)-2-oxo-2,5-dihydrofuran-3-carboxylate (SI-14). The title compound was obtained as a yellow oil using **General Procedure B** (49%).

¹H NMR (600 MHz, CDCl₃): δ (ppm) = 7.61 – 7.56 (m, 2H), 7.21 – 7.15 (m, 2H), 5.15 (2, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.33 (s, 3H);

¹³C NMR (151 MHz, Chloroform-*d*) δ 169.45, 165.78, 164.09, 163.11, 162.39, 130.45, 130.39, 125.59, 119.62, 116.68, 116.53, 70.51, 62.27, 14.15.

LC-MS (ESI) Calculated [C₁₃H₁₂FO₄]⁺: 251.1, found: 251.1;

R_f 0.37 (Hexanes:EtOAc = 2:1).



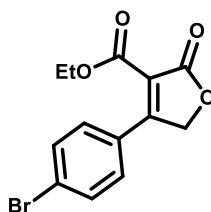
Ethyl 4-(4-chlorophenyl)-2-oxo-2,5-dihydrofuran-3-carboxylate (SI-15). The title compound was obtained as a yellow oil using **General Procedure B** (29%).

¹H NMR (600 MHz, CDCl₃): δ (ppm) = 7.53 – 7.48 (m, 2H), 7.48 – 7.44 (m, 2H), 5.14 (s, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H);

¹³C NMR (151 MHz, CDCl₃): δ (ppm) = 169.3, 163.0, 162.2, 138.6, 129.6, 129.3, 127.8, 120.2, 70.4, 62.3, 14.2;

LC-MS (ESI) Calculated [C₁₃H₁₂ClO₄]⁺: 267.0, found: 267.0;

R_f 0.44 (Hexanes:EtOAc = 2:1).



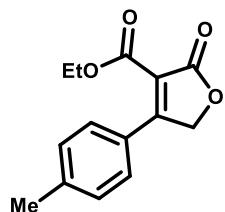
Ethyl 4-(4-bromophenyl)-2-oxo-2,5-dihydrofuran-3-carboxylate (SI-16). The title compound was obtained as an orange solid using **General Procedure B** (64%).

¹H NMR (600 MHz, CDCl₃): δ (ppm) = 7.65 – 7.60 (m, 2H), 7.45 – 7.40 (m, 2H), 5.13 (s, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (151 MHz, CDCl₃): δ (ppm) = 169.3, 163.2, 162.2, 132.6, 129.4, 128.2, 127.0, 120.3, 70.4, 62.3, 14.2;

LC-MS (ESI) Calculated [C₁₃H₁₂BrO₄]⁺: 311.0, found: 311.0;

R_f 0.39 (Hexanes:EtOAc = 2:1).



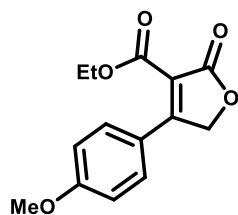
Ethyl 2-oxo-4-(p-tolyl)-2,5-dihydrofuran-3-carboxylate (SI-17). The title compound was obtained as a yellow solid using **General Procedure B** (30%).

¹H NMR (600 MHz, CDCl₃): δ (ppm) = 7.45 – 7.42 (m, 2H), 7.30 – 7.27 (m, 2H), 5.16 (s, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 2.42 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (151 MHz, CDCl₃): δ (ppm) = 169.9, 164.0, 162.8, 143.2, 130.0, 128.0, 126.5, 118.9, 70.6, 62.1, 21.8, 14.2;

LC-MS (ESI) Calculated [C₁₄H₁₅O₄]⁺: 247.1, found: 247.1;

R_f 0.41 (Hexanes/EtOAc = 2:1).



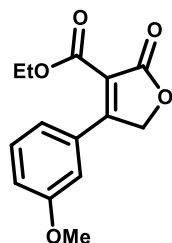
Ethyl 4-(4-methoxyphenyl)-2-oxo-2,5-dihydrofuran-3-carboxylate (SI-18). The title compound was obtained as a yellow solid using **General Procedure B** (35%).

¹H NMR (600 MHz, CDCl₃): δ (ppm) = 7.58 – 7.53 (m, 2H), 6.99 – 6.95 (m, 2H), 5.16 (s, 2H), 4.39 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (151 MHz, CDCl₃): δ (ppm) = 170.1, 163.4, 163.1, 162.9, 130.1, 121.7, 117.4, 114.7, 70.4, 62.1, 55.7, 14.2;

LC-MS (ESI) Calculated [C₁₄H₁₅O₅]⁺: 263.1, found: 263.1;

R_f 0.22 (Hexanes:EtOAc = 2:1).



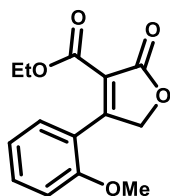
Ethyl 4-(3-methoxyphenyl)-2-oxo-2,5-dihydrofuran-3-carboxylate (SI-19). The title compound was obtained as a yellow oil using **General Procedure B** (52%).

¹H NMR (600 MHz, CDCl₃): δ (ppm) = 7.41 – 7.36 (m, 1H), 7.12 – 7.04 (m, 3H), 5.15 (s, 2H), 4.37 (q, *J* = 7.2 Hz, 3H), 3.84 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (151 MHz, CDCl₃): δ (ppm) = 169.6, 163.9, 162.5, 160.0, 130.5, 130.3, 120.1, 120.1, 117.7, 113.7, 70.7, 62.2, 55.6, 14.1;

LC-MS (ESI) Calculated [C₁₄H₁₅O₅]⁺: 263.1, found: 263.1;

R_f 0.30 (Hexanes:EtOAc = 2:1).



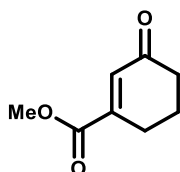
Ethyl 4-(2-methoxyphenyl)-2-oxo-2,5-dihydrofuran-3-carboxylate (SI-20). The title compound was obtained as an orange oil using **General Procedure B** (51%).

¹H NMR (600 MHz, CDCl₃): δ (ppm) = 7.50 – 7.44 (m, 1H), 7.32 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.03 (td, *J* = 7.6, 1.0 Hz, 1H), 6.98 (dd, *J* = 8.4, 1.0 Hz, 1H), 5.17 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 3H), 3.84 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (151 MHz, CDCl₃): δ (ppm) = 169.8, 163.6, 162.4, 157.0, 133.1, 129.5, 121.0, 120.9, 119.0, 111.5, 71.5, 61.6, 55.5, 14.1;

LC-MS (ESI) Calculated [C₁₄H₁₅O₅]⁺: 263.1, found: 263.0;

R_f 0.21 (Hexanes:EtOAc = 2:1).

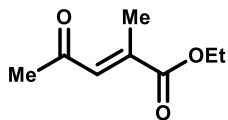


methyl 3-oxocyclohex-1-ene-1-carboxylate (SI-21). The title compound was prepared using an adapted procedure from Zhai and coworkers.² To a 500 mL three-necked flask equipped with a stir bar, an ammonia gas outlet, and a cold-finger condenser were added *m*-Anisic acid (115 mmol, 17.5g) and H₂O (22.5 mL). Ammonia (200 mL) was collected through the condenser containing dry ice and acetone. Lithium wire (350 mmol, 2.4g) was added in small pieces over 1 hour and the reaction was stirred for 6 hours. Stirring was then stopped and the reaction was allowed to warm to 25 °C overnight. Then, KOH (145 mL, 1M aq.) was added and stirring was restarted. The solution was heated for 4 hours at 60 °C and then cooled to 0 °C. Next, concentrated HCl (18 mL) was added until pH = 2. The aqueous solution was extracted with DCM/PrOH (3:1). The combined organics were dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was used in the next step without purification.

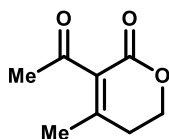
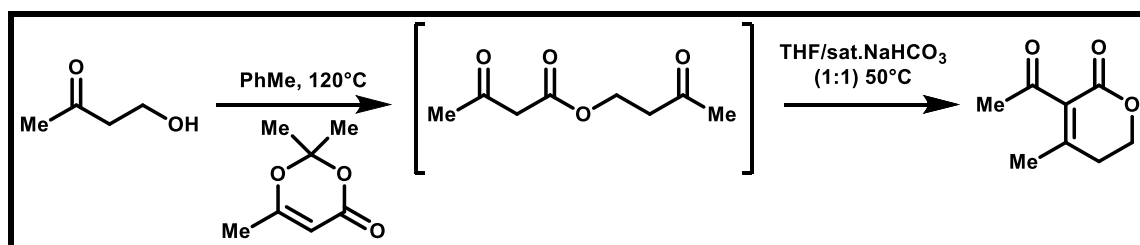
To a solution of crude product (61 mmol, 8.614g) in MeOH (100 mL) was added SOCl₂ (70 mmol, 5.0 mL) at 0 °C. The solution was warmed to 25 °C and stirred overnight. The mixture was concentrated *in vacuo*, diluted with EtOAc, washed with NaHCO₃ aq. and brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Crude oil (3.050 g) was used in the next step without purification.

To a solution of crude product (19.4 mmol, 3.050 g) in CHCl₃ (200 mL) was added DBU (22.3 mmol, 3.33 mL) at 0 °C. The solution was stirred at 25 °C for 12 hours and then washed

with 1.0 M HCl aq. and brine. The organic layer was dried over Na₂SO₄, filtered, concentrated *in vacuo*, and purified via column chromatography. The product was obtained as a yellow oil (15% over five steps). The spectral data for the title compound matched those that were previously reported.²



ethyl (E)-2-methyl-4-oxopent-2-enoate (SI-22). The title compound was prepared using an adapted procedure from Taylor and coworkers.³ To a solution of hydroxyacetone (2.0 mmol 0.139 mL) in DCM (7 mL) was added MnO₂ (20 mmol 1.78 g) and ethyl 2-(triphenyl-λ⁵-phosphanylidene)propanoate (2.0 mmol, 724 mg). The reaction mixture was stirred for 4 hours at 25 °C. The reaction mixture was then filtered over celite, concentrated *in vacuo*, and purified via column chromatography. The spectral data for the title compound matched those that were previously reported.⁴



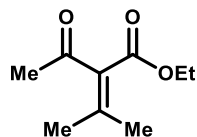
3-acetyl-4-methyl-5,6-dihydro-2H-pyran-2-one (SI-23). The title compound was prepared by heating a mixture of 4-hydroxybutan-2-one (26.2 mmol, 2.08 mL) and 2,2,6-trimethyl-4H-1,3-dioxin-4-one (26.2 mmol, 3.48 mL) in anhydrous toluene (50 mL) at 120 °C. The reaction was monitored by TLC and, upon completion, concentrated *in vacuo*. The crude material was dry loaded onto a column using silica and purified via column chromatography. Next, 3-oxobutyl 3-oxobutanoate (1.66 mmol, 286 mg) was dissolved in THF (14.3 mL), saturated NaHCO₃ (14.3 mL) was added, and the resulting mixture was heated to 50 °C. The reaction was monitored by TLC and, upon completion, diluted and extracted with EtOAc, washed with brine, dried over MgSO₄, concentrated *in vacuo*, and purified via column chromatography. The product was obtained as a yellow oil (21% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 4.35 (t, *J* = 6.2 Hz, 1H), 2.52 – 2.48 (m, 1H), 2.42 (s, 1H), 2.07 (d, *J* = 0.8 Hz, 1H).

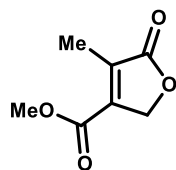
¹³C NMR (151 MHz, Chloroform-*d*) δ 200.33, 162.63, 158.19, 130.24, 65.25, 31.28, 31.02, 21.17.)

LC-MS (ESI) Calculated [C₈H₁₁O₃]⁺: 155.1, found: 155.1;

R_f 0.45 (Hexanes:EtOAc = 1:1).



ethyl 2-acetyl-3-methylbut-2-enoate (SI-24). The title compound can be prepared following a procedure published by Georgiadis and coworkers.⁵ The spectral data for the title compound matched those that were previously reported.⁵



methyl 4-methyl-5-oxo-2,5-dihydrofuran-3-carboxylate (SI-25). The title compound can be prepared following a procedure published by Georgiadis and coworkers.⁶

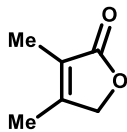
¹H NMR (600 MHz, Chloroform-*d*) δ 4.90 (q, *J* = 2.3 Hz, 1H), 3.89 (s, 1H), 2.23 (t, *J* = 2.4 Hz, 1H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 173.75, 162.41, 144.37, 137.74, 69.70, 52.56, 10.80.

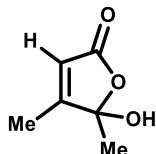
LC-MS (ESI) Calculated [C₇H₉O₄]⁺: 157.1, found: 157.1;

R_f 0.6 (Hexanes:EtOAc = 1:1).

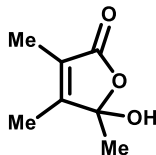
Nucleophiles



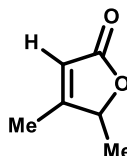
3,4-dimethylfuran-2(5H)-one (SI-26). The title compound was prepared following **General Procedure C**. The spectral data for the title compound matched those that were previously reported.⁷



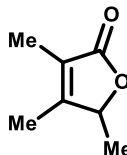
5-hydroxy-4,5-dimethylfuran-2(5H)-one (SI-27). The title compound was prepared following **General Procedure D**. The spectral data for the title compound matched those that were previously reported.⁸



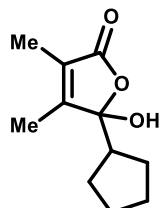
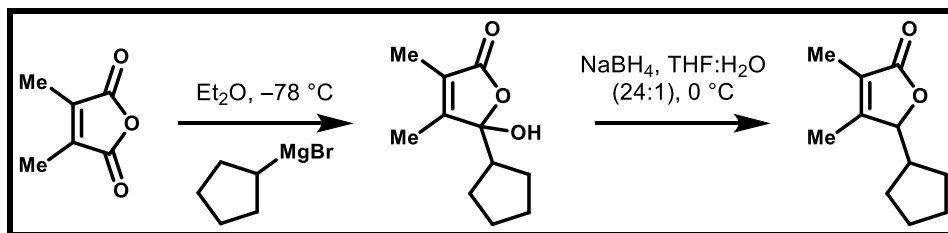
5-hydroxy-3,4,5-trimethylfuran-2(5H)-one (SI-28). The title compound was prepared following **General Procedure D**. The spectral data for the title compound matched those that were previously reported.¹



4,5-dimethylfuran-2(5H)-one (SI-29). The title compound was prepared by applying **General Procedure C** to **SI-27**. The spectral data for the title compound matched those that were previously reported.⁹



3,4,5-trimethylfuran-2(5H)-one (SI-30). The title compound was prepared by applying **General Procedure C** to **SI-28**. The spectral data for the title compound matched those that were previously reported.¹



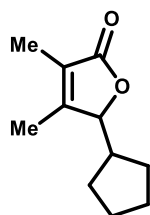
5-cyclopentyl-5-hydroxy-3,4-dimethylfuran-2(5H)-one (SI-31). To a suspension of Mg^0 (7.5 mmol, 182 mg) in anhydrous Et_2O (5 mL) was added bromocyclopentane (5.00 mmol, 0.540 mL) at r.t. After reflux for 2 hours, the grignard solution was added dropwise to a solution of 2,3-dimethylmaleic anhydride (5.00 mmol, 630 mg) in anhydrous ether (15 mL) at -78°C . The mixture was stirred for 1 hour at -78°C before quenching with a saturated solution of ammonium chloride. The mixture was extracted with EtOAc, washed with brine, dried over MgSO_4 , concentrated *in vacuo*, and purified via column chromatography (Hexanes:EtOAc 4:1). The product was obtained as colorless solid (1.27 mmol, 255 mg, 25%).

^1H NMR (600 MHz, CDCl_3): δ (ppm) = 2.92 (s, 1H), 2.43 – 2.35 (m, 1H), 1.95 (q, J = 1.1 Hz, 3H), 1.89 – 1.82 (m, 2H), 1.82 (q, J = 1.1 Hz, 3H), 1.76 – 1.56 (m, 3H), 1.54 – 1.43 (m, 2H), 1.04 – 0.96 (m, 1H);

^{13}C NMR (151 MHz, CDCl_3): δ (ppm) = 172.4, 158.1, 125.3, 108.1, 44.3, 27.3, 26.3, 26.1, 26.1, 11.1, 8.5;

LC-MS (ESI) Calculated $[\text{C}_{11}\text{H}_{17}\text{O}_3]^+$: 197.1, found: 197.1;

R_f 0.14 (Hexanes:EtOAc = 4:1).



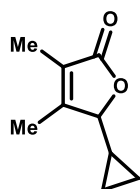
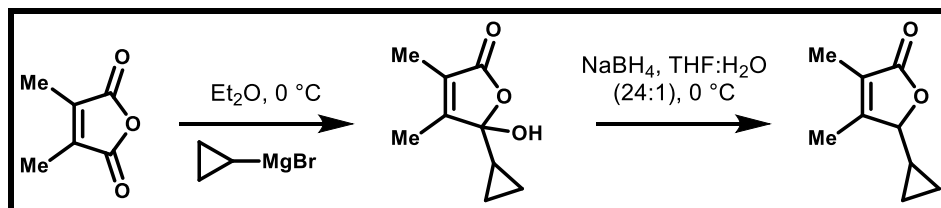
5-cyclopentyl-3,4-dimethylfuran-2(5H)-one (SI-32). The title compound was obtained after applying **General Procedure C** to SI-31. The product was isolated as a pale yellow oil (1.18 mmol, 214 mg, 93%).

^1H NMR (400 MHz, CDCl_3): δ (ppm) = 4.78 (d, J = 3.3 Hz, 1H), 2.31 – 2.18 (m, 1H), 1.96 – 1.91 (m, 3H), 1.90 – 1.83 (m, 1H), 1.81 (d, J = 1.4 Hz, 3H), 1.75 – 1.32 (m, 6H), 1.13 – 0.99 (m, 1H);

^{13}C NMR (151 MHz, CDCl_3): δ (ppm) = 175.1, 159.3, 124.0, 85.4, 40.8, 29.5, 26.0, 25.7, 24.6, 12.4, 8.5;

GC-MS (EI) Calculated $[\text{C}_{11}\text{H}_{16}\text{O}_2]^+$: 180.1, found: 180.1;

R_f 0.50 (Hexanes/EtOAc = 7:3).



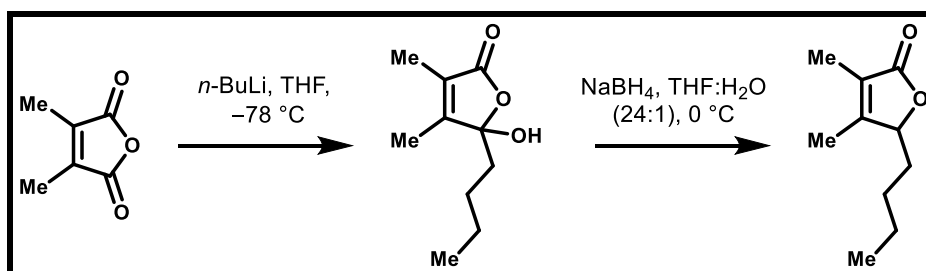
5-cyclopropyl-3,4-dimethylfuran-2(5H)-one (SI-33). To a suspension of Mg^0 (31.7 mmol, 738 mg) in anhydrous THF (5 mL) was added bromocyclopropane (7.90 mmol, 0.627 mL) at r.t. After the mixture was refluxed for 2 hours, the grignard solution was added dropwise to a solution of 2,3-dimethylmaleic anhydride (7.90 mmol, 1.0 g) in anhydrous THF (15 mL) at 0 °C. The mixture was stirred for 1 hour at 0 °C before quenching with a saturated solution of ammonium chloride. The mixture was extracted with EtOAc, washed with brine, dried over MgSO_4 , concentrated *in vacuo*, and the crude product was used in the next step without further purification. **General Procedure C** was applied to the crude reaction mixture and the product was obtained as a pale yellow oil (0.480 mmol, 73.0 mg, 6 %).

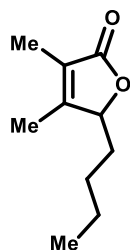
¹H NMR (600 MHz, Chloroform-*d*) δ 4.00 (d, J = 8.5 Hz, 1H), 1.97 (s, 3H), 1.73 (d, J = 1.8 Hz, 3H), 0.81 – 0.71 (m, 1H), 0.64 (tdd, J = 8.5, 6.0, 4.6 Hz, 1H), 0.57 – 0.48 (m, 1H), 0.45 (dq, J = 10.1, 4.9 Hz, 1H), 0.41 – 0.33 (m, 1H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 174.58, 159.52, 123.23, 87.12, 12.95, 12.46, 8.53, 2.50, 1.89.

LC-MS (ESI) Calculated $[\text{C}_9\text{H}_{13}\text{O}_2]^+$: 153.1, found: 153.1;

R_f 0.3 (Hexanes/EtOAc = 4:1).





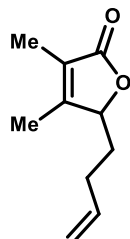
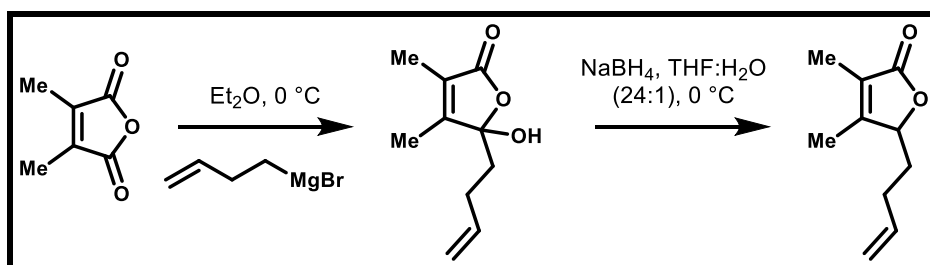
5-butyl-5-hydroxy-3,4-dimethylfuran-2(5H)-one (SI-34). A solution of n-BuLi (2.24 M in hexanes, 10.0 mmol, 4.50 mL) in THF was added dropwise to a solution of 2,3-dimethylmaleic anhydride (10.0 mmol, 1.26 g) in THF (20 mL) at -78 °C. The reaction was stirred for 1 hour at -78 °C and then quenched with a saturated ammonium chloride solution (5.0 mL). After warming to ambient temperature the layers were separated and the aqueous layer extracted with EtOAc. The combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. The crude product was used in the next step without further purification. **General Procedure C** was applied to the crude reaction mixture and the product was obtained as a pale yellow oil (9 % over two steps).

¹H NMR (400 MHz, CDCl₃): δ (ppm) = 4.72 (d, *J* = 7.8 Hz, 1H), 1.94 – 1.93 (m, 3H), 1.84 – 1.79 (m, 3H), 1.81 (d, *J* = 1.3 Hz, 3H), 1.51 – 1.23 (m, 6H), 0.93 – 0.88 (m, 3H).

¹³C NMR (151 MHz, CDCl₃): δ (ppm) = 174.9, 159.3, 123.6, 83.4, 32.0, 26.7, 22.6, 14.0, 12.1, 8.6.

GC-MS (EI) Calculated [C₁₀H₁₆O₂]⁺: 168.1, found: 168.1;

R_f 0.44 (Hexanes:EtOAc = 4:1).



5-(but-3-en-1-yl)-3,4-dimethylfuran-2(5H)-one (SI-35). To a suspension of Mg⁰ (40.2 mmol, 964 mg) in anhydrous THF (5 mL) was added 4-bromobut-1-ene (13.4 mmol, 1.58 mL) at r.t. After the mixture was refluxed for 2 hours, the grignard solution was added dropwise to a solution of 2,3-

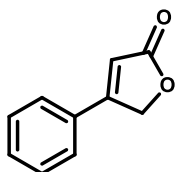
dimethylmaleic anhydride (13.4 mmol, 1.68 g) in anhydrous THF (15 mL) at 0 °C. The mixture was stirred for 1 hour at 0 °C before quenching with a saturated solution of ammonium chloride. The mixture was extracted with EtOAc, washed with brine, dried over MgSO₄, concentrated *in vacuo*, and the crude product was used in the next step without further purification. **General Procedure C** was applied to the crude reaction mixture and the product was obtained as a clear oil (41 % over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 5.83 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.09 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.06 – 5.02 (m, 1H), 4.80 – 4.73 (m, 1H), 2.24 – 2.19 (m, 2H), 2.03 – 1.98 (m, 1H), 1.97 (p, *J* = 1.1 Hz, 3H), 1.83 (dq, *J* = 2.1, 1.1 Hz, 3H), 1.58 – 1.51 (m, 1H).

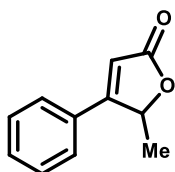
¹³C NMR (151 MHz, Chloroform-*d*) δ 174.69, 159.14, 137.14, 123.79, 116.01, 82.57, 31.67, 28.97, 12.14, 8.60.

LC-MS (ESI) Calculated [C₁₀H₁₅O₂]⁺: 167.1, found: 167.1;

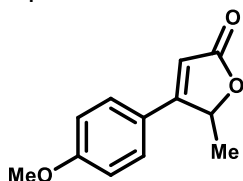
R_f 0.40 (Hexanes:EtOAc = 85:15).



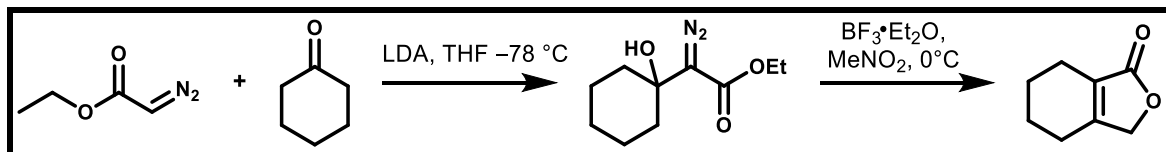
4-phenylfuran-2(5H)-one (SI-36). The title compound was prepared using **General Procedure E**. The spectral data for the title compound matched those that were previously reported.¹⁰

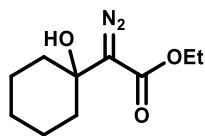


5-methyl-4-phenylfuran-2(5H)-one (SI-37). The title compound was prepared using **General Procedure E**. The spectral data for the title compound matched those that were previously reported.¹⁰

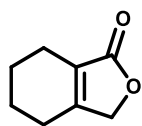


4-(4-methoxyphenyl)-5-methylfuran-2(5H)-one (SI-38). The title compound was prepared using **General Procedure E**. The spectral data for the title compound matched those that were previously reported.¹⁰

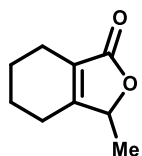




ethyl 2-diazo-2-(1-hydroxycyclohexyl)acetate (SI-39). The title compound was prepared using an adapted procedure from Pellicciari and coworkers.¹¹ To a stirring solution of ethyl 2-diazoacetate (10 mmol, 1.2 mL) and cyclohexanone (10 mmol, 1.04 mL) in anhydrous THF (10 mL) at -78 °C was added LDA (dropwise over 15 minutes). The reaction mixture was stirred for 1 hour at -78 °C then quenched with 30% ammonium chloride (20 mL). The reaction mixture was then extracted with EtOAc, dried over MgSO₄, concentrated *in vacuo*, and purified via column chromatography. The spectral data for the title compound matched those that were previously reported.¹¹



4,5,6,7-tetrahydroisobenzofuran-1(3H)-one (SI-40). The title compound was prepared using an adapted procedure from Pellicciari and coworkers.¹² To a solution of boron trifluoride-diethyl ether (2.00 mmol, 0.246 mL) in nitromethane (1 mL) was added ethyl 2-diazo-2-(1-hydroxycyclohexyl)acetate (1.33 mmol, 284 mg) in nitromethane (1 mL) at 0 °C (dropwise over 20 minutes). The reaction was stirred at 0 °C for 2 hours before dilution with DCM (5 mL) and quench with saturated ammonium chloride (2 mL). The mixture was extracted with DCM, dried over MgSO₄, concentrated *in vacuo*, and purified via column chromatography. The spectral data for the title compound matched those that were previously reported.¹³



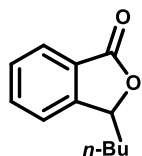
3-methyl-4,5,6,7-tetrahydroisobenzofuran-1(3H)-one (SI-41). The title compound was prepared by applying **General Procedure D** to 3,4-dimethylfuran-2,5-dione followed by application of **General Procedure C** (4% over two steps).

¹H NMR (600 MHz, Chloroform-*d*) δ 4.91 – 4.84 (m, 1H), 2.28 – 2.20 (m, 4H), 1.80 – 1.68 (m, 4H), 1.40 (d, *J* = 6.8 Hz, 3H).

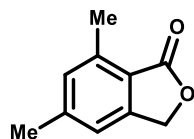
¹³C NMR (151 MHz, Chloroform-*d*) δ 173.59, 164.90, 126.09, 79.30, 24.87, 22.93, 21.68, 19.93, 18.35.

LC-MS (ESI) Calculated [C₉H₁₃O₂]⁺: 153.1, found: 153.1;

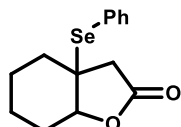
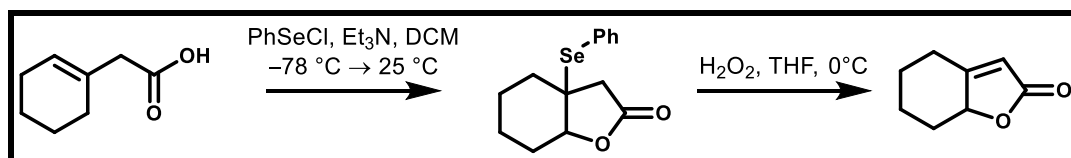
R_f 0.50 (Hexanes:EtOAc = 70:30).



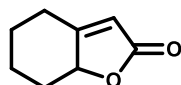
3-butylisobenzofuran-1(3H)-one (SI-42). The title compound was prepared using an adapted procedure from Zhang and coworkers.¹⁴ To a suspension of Mg^0 (20 mmol, 480 mg) in anhydrous ether (15 mL) was added 1-bromobutane (20 mmol, 2.14 mL) at r.t. After the mixture was refluxed for 2 hours, the grignard solution was added dropwise to a solution of 2-formylbenzoic acid (10 mmol, 1.5g) in anhydrous ether (15 mL) at 0 °C. The mixture was stirred for 5 hours at 0 °C before quenching with a saturated solution of ammonium chloride (10 mL). The mixture was extracted with ether, washed with brine, dried over MgSO_4 , and concentrated *in vacuo*. To the resulting crude material was added 1M HCl (15 mL) at 25 °C. The mixture was allowed to stir for 1 hour before it was extracted with ether, washed with brine, dried over MgSO_4 , concentrated *in vacuo*, and purified via column chromatography. The product was obtained as clear yellow oil (5.08 mmol, 967 mg, 51%). The spectral data for the title compound matched those that were previously reported.¹⁵



5,7-dimethylisobenzofuran-1(3H)-one (SI-43). The title compound can be prepared following a procedure published by Martin and coworkers.¹⁶ The spectral data for the title compound matched those that were previously reported.¹⁶



3a-(phenylselanyl)hexahydrobenzofuran-2(3H)-one (SI-44). The title compound was prepared using an adapted procedure from Nicolaou and coworkers.¹⁷ To a solution of 2-(cyclohex-1-en-1-yl)acetic acid (1.64 mmol, 230 mg) and Et_3N (1.80 mmol, 181 mg) in DCM (8 mL) at – 78 °C was added PhSeCl (1.80 mmol, 345 mg). After 2 hours at – 78 °C the reaction was brought to 25 °C and allowed to stir for 16 hours. The crude reaction mixture was concentrated on celite and purified via column chromatography. The spectral data for the title compound matched those that were previously reported.¹⁷

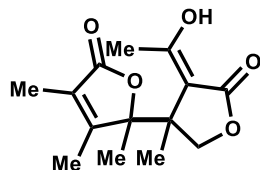


5,6,7,7a-tetrahydrobenzofuran-2(4H)-one (SI-45). The title compound was prepared using an adapted procedure from Nicolaou and coworkers.¹⁷ To a solution of 3a-(phenylselanyl)hexahydrobenzofuran-2(3H)-one (0.42 mmol, 125 mg) in THF (0.575 mL) at 0 °C was added H_2O_2 (30%, 0.63 mmol, 21.42 mg). The mixture was stirred at 0 °C for 2 hours then diluted with Et_2O (5.0 mL) and quenched with saturated $\text{Na}_2\text{S}_2\text{O}_3$ (2.0 mL). The mixture was

extracted with Et₂O, dried over MgSO₄, concentrated *in vacuo*, and purified via column chromatography. The spectral data for the title compound matched those that were previously reported.¹⁷

Product Characterization

Electrophile Scope



(Z)-5-(4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-46) [Compound (7) in manuscript]. The title compound was obtained as a white solid using **General Procedure F** (98 %).

Mixture of Diastereomers (85:15)

Major Diastereomer (Compound 10 in manuscript)

Major Enol:

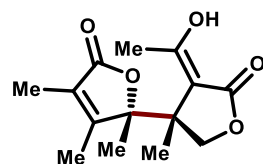
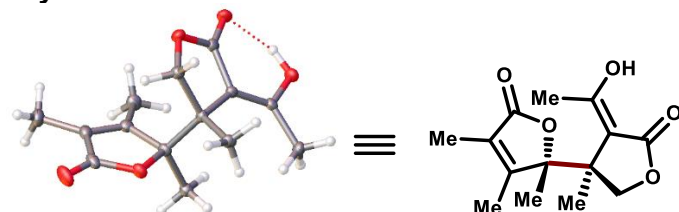
¹H NMR (600 MHz, Chloroform-*d*) δ 12.16 (q, *J* = 0.9 Hz, 1H), 4.28 (d, *J* = 9.9 Hz, 1H), 3.82 (d, *J* = 9.9 Hz, 1H), 2.20 (d, *J* = 0.9 Hz, 3H), 1.95 (q, *J* = 1.1 Hz, 3H), 1.83 (q, *J* = 1.1 Hz, 3H), 1.45 (s, 3H), 1.27 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 177.16, 174.30, 172.77, 161.12, 126.05, 100.04, 91.18, 74.26, 47.74, 20.88, 20.54, 19.82, 13.31, 8.88.

LC-MS (ESI) Calculated [C₁₄H₁₉O₅]⁺: 267.1, found: 267.1;

R_f 0.4 (Hexanes:EtOAc = 1:1).

Crystal Structure:



Minor Diastereomer (Mixture of Enol and Keto Tautomers 80:20) (Compound 11 in manuscript)

Minor Enol:

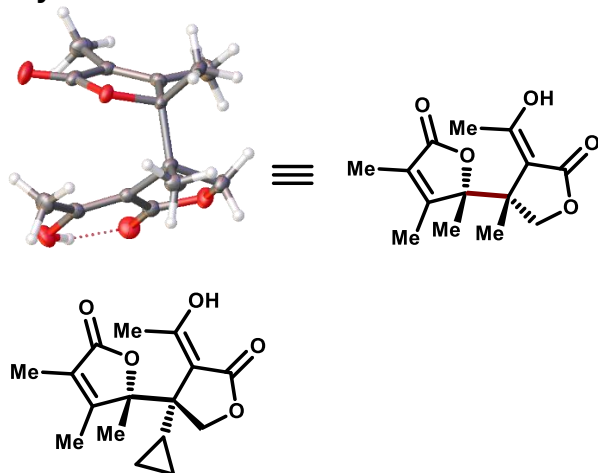
¹H NMR (600 MHz, Chloroform-*d*) δ 11.76 (q, *J* = 0.9 Hz, 1H), 4.46 (d, *J* = 10.1 Hz, 1H), 3.92 (d, *J* = 10.1 Hz, 1H), 2.16 (d, *J* = 0.8 Hz, 3H), 1.99 (d, *J* = 1.1 Hz, 2H), 1.75 (t, *J* = 1.1 Hz, 3H), 1.54 (s, 3H), 1.50 (s, 3H).

¹³C NMR

(151 MHz, Chloroform-*d*) δ 176.18, 174.24, 172.25, 160.61, 126.44, 99.26, 90.74, 73.59, 49.12, 21.60, 19.80, 18.77, 12.34, 8.86.

LC-MS (ESI) Calculated [C₁₄H₁₉O₅]⁺: 267.1, found: 267.1;

R_f 0.4 (Hexanes:EtOAc = 1:1).

Crystal Structure:

(S)-5-((S,Z)-3-cyclopropyl-4-(1-hydroxyethylidene)-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-47). The title compound was obtained as a white solid using General Procedure F (90 %).

Mixture of Diastereomers ([89:11](#)) and Tautomers:**Major Diastereomer (61:34 Enol:Keto):****¹H NMR**

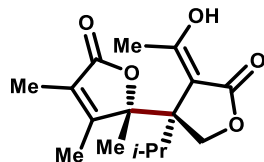
(600 MHz, Chloroform-*d*) δ 11.75 (s, 1H), 4.03 (d, *J* = 10.4 Hz, 1H), 3.31 (d, *J* = 10.5 Hz, 1H), 2.25 (s, 3H), 1.99 (q, *J* = 1.1 Hz, 3H), 1.76 (q, *J* = 1.1 Hz, 3H), 1.66 (ddd, *J* = 8.6, 5.6, 3.0 Hz, 1H), 1.64 (s, 3H), 0.81 – 0.74 (m, 1H), 0.62 (tt, *J* = 9.1, 5.6 Hz, 1H), 0.37 (dq, *J* = 9.4, 5.4 Hz, 1H), 0.25 (dq, *J* = 9.4, 5.9 Hz, 1H).

¹³C NMR

(151 MHz, Chloroform-*d*) δ 202.02, 176.83, 175.44, 172.86, 172.43, 172.31, 162.96, 161.70, 125.79, 125.71, 99.33, 92.14, 89.77, 32.06, 20.75, 20.58, 19.97, 14.26, 13.79, 12.41, 10.06, 8.79, 3.63, 3.15, 2.47, 0.33.

LC-MS (ESI) Calculated [C₁₆H₂₁O₅]⁺: 293.1, found: 293.1;

R_f 0.6 (Hexanes:EtOAc = 1:1).



(S)-5-((S,Z)-4-(1-hydroxyethylidene)-3-isopropyl-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-48). The title compound was obtained as a yellow oil using General Procedure F (90 %).

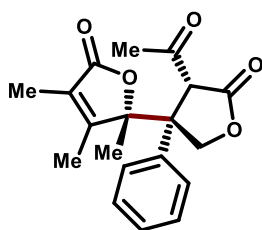
Single Diastereomer (>95:5):

¹H NMR (600 MHz, Chloroform-*d*) δ 12.51 (s, 1H), 4.05 (s, 2H), 2.37 (dq, *J* = 13.5, 6.7 Hz, 1H), 2.20 (s, 3H), 1.95 (q, *J* = 1.1 Hz, 3H), 1.82 (q, *J* = 1.1 Hz, 3H), 1.47 (s, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 177.89, 174.95, 174.82, 164.94, 125.90, 99.69, 93.17, 68.23, 56.07, 28.61, 21.31, 20.88, 20.47, 18.83, 14.55, 8.86.

LC-MS (ESI) Calculated [C₁₆H₂₃O₅]⁺: 295.1, found: 295.1;

R_f 0.4 (Hexanes:EtOAc = 1:1).



(S)-5-((3R,4R)-4-acetyl-5-oxo-3-phenyltetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-49). The title compound was obtained as a white solid using **General Procedure F** (91 %).

Mixture of Diastereomers (81:19) and Tautomers:

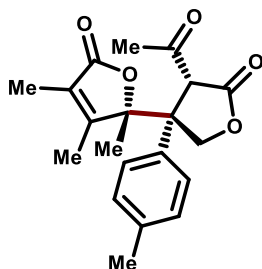
Major Diastereomer (8:92 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 7.25 – 7.17 (m, 3H), 6.91 – 6.84 (m, 2H), 5.20 (d, *J* = 9.5 Hz, 1H), 4.92 (d, *J* = 9.4 Hz, 1H), 4.70 (s, 1H), 2.35 (s, 3H), 1.94 (q, *J* = 1.0 Hz, 3H), 1.54 (s, 3H), 1.32 (q, *J* = 1.1 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 201.18, 172.20, 172.08, 160.10, 136.90, 128.58, 128.44, 128.11, 126.14, 89.09, 72.85, 60.33, 58.04, 33.28, 19.99, 13.45, 8.12.

LC-MS (ESI) Calculated [C₁₉H₂₁O₅]⁺: 329.1, found: 329.1;

R_f 0.55 (Hexanes:EtOAc = 1:1).



(S)-5-((3R,4R)-4-acetyl-5-oxo-3-(p-tolyl)tetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-50). The title compound was obtained as a white solid using **General Procedure F** (81 %).

Mixture of Diastereomers (81:19) and Tautomers:

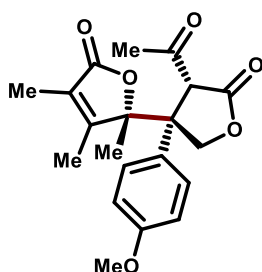
Major Diastereomer (16:84 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 7.04 – 6.99 (m, 2H), 6.78 – 6.74 (m, 2H), 5.17 (d, *J* = 9.5 Hz, 1H), 4.90 (d, *J* = 9.5 Hz, 1H), 4.68 (s, 1H), 2.35 (s, 3H), 2.24 (s, 3H), 1.93 (q, *J* = 1.1 Hz, 3H), 1.53 (s, 3H), 1.35 (q, *J* = 1.1 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 201.34, 172.37, 172.27, 160.25, 137.87, 133.78, 129.27, 129.17, 126.07, 89.25, 72.95, 60.37, 57.79, 33.37, 21.03, 20.04, 13.48, 8.20.

LC-MS (ESI) Calculated [C₂₀H₂₃O₅]⁺: 343.1, found: 343.1;

R_f 0.7 (Hexanes:EtOAc = 1:1).



(S)-5-((3R,4R)-4-acetyl-3-(4-methoxyphenyl)-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-51). The title compound was obtained as a white solid using General Procedure F (82 %).

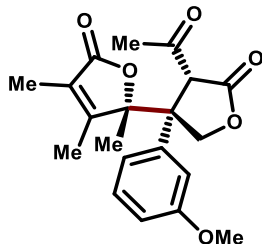
Mixture of Diastereomers (78:22) and Tautomers:
Major Diastereomer (8:92 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 6.83 – 6.78 (m, 2H), 6.74 (d, *J* = 9.0 Hz, 2H), 5.15 (d, *J* = 9.5 Hz, 1H), 4.89 (d, *J* = 9.5 Hz, 1H), 4.65 (s, 1H), 3.72 (s, 3H), 2.33 (s, 3H), 1.93 (q, *J* = 1.1 Hz, 3H), 1.52 (s, 3H), 1.37 (q, *J* = 1.0 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 201.30, 172.29, 160.30, 159.02, 128.71, 127.49, 126.11, 113.96, 113.84, 89.38, 72.94, 60.42, 57.43, 55.29, 33.35, 20.05, 13.47, 8.26.

LC-MS (ESI) Calculated [C₂₀H₂₃O₆]⁺: 359.1, found: 359.1;

R_f 0.5 (Hexanes:EtOAc = 1:1).



(S)-5-((3R,4R)-4-acetyl-3-(3-methoxyphenyl)-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-52). The title compound was obtained as a white solid using General Procedure F (89 %).

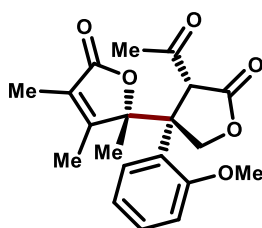
Mixture of Diastereomers (85:15) and Tautomers:
Major Diastereomer (15:85 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 7.13 (t, *J* = 8.0 Hz, 1H), 6.72 (ddd, *J* = 8.3, 2.5, 0.9 Hz, 1H), 6.44 (ddd, *J* = 7.8, 1.9, 0.8 Hz, 1H), 6.41 (t, *J* = 2.2 Hz, 1H), 5.18 (d, *J* = 9.5 Hz, 1H), 4.88 (d, *J* = 9.5 Hz, 1H), 4.68 (s, 1H), 3.73 (s, 3H), 2.35 (s, 3H), 1.94 (q, *J* = 1.1 Hz, 3H), 1.53 (s, 3H), 1.36 (q, *J* = 1.0 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 201.09, 172.35, 172.07, 160.12, 159.43, 138.36, 129.64, 126.03, 112.90, 89.05, 72.84, 60.33, 57.88, 55.37, 33.29, 20.04, 13.45, 8.21.

LC-MS (ESI) Calculated [C₂₀H₂₃O₆]⁺: 359.1, found: 359.1;

R_f 0.5 (Hexanes:EtOAc = 1:1).



(S)-5-((3R,4R)-4-acetyl-3-(2-methoxyphenyl)-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-53). The title compound was obtained as a clear oil using General Procedure F (80 %).

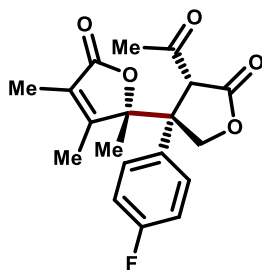
Mixture of Diastereomers (81:19) and:
Major Diastereomer (Keto):

¹H NMR (500 MHz, Chloroform-*d*) δ 7.28 – 7.24 (m, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.91 (dd, *J* = 7.9, 1.6 Hz, 1H), 6.80 (t, *J* = 8.5 Hz, 1H), 5.05 (s, 2H), 3.80 (s, 1H), 3.78 (s, 3H), 2.39 (s, 3H), 2.02 (t, *J* = 1.1 Hz, 3H), 1.51 (s, 2H), 1.49 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 197.00, 171.28, 171.00, 159.59, 130.16, 128.68, 124.24, 120.56, 120.33, 88.88, 74.58, 59.80, 52.83, 31.05, 22.10, 19.04, 13.51, 7.92.

LC-MS (ESI) Calculated [C₂₀H₂₃O₆]⁺: 359.1, found: 359.1;

R_f 0.4 (Hexanes:EtOAc = 1:1).



(S)-5-((3R,4R)-4-acetyl-3-(4-fluorophenyl)-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-54). The title compound was obtained as a white solid using **General Procedure F** (98 %).

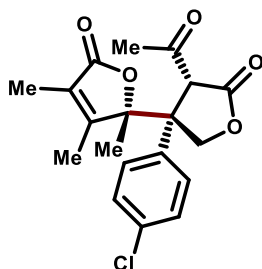
Mixture of Diastereomers (78:22) and Tautomers:
Major Diastereomer (12:88 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 6.93 (dd, *J* = 9.0, 8.2 Hz, 2H), 6.89 – 6.85 (m, 2H), 5.14 (d, *J* = 9.5 Hz, 1H), 4.90 (d, *J* = 9.4 Hz, 1H), 4.68 (s, 1H), 2.35 (s, 3H), 1.94 (q, *J* = 1.1 Hz, 3H), 1.53 (s, 3H), 1.37 (q, *J* = 1.1 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 201.03, 172.04, 171.77, 162.83, 161.18, 160.05, 132.92, 132.89, 126.35, 115.74, 115.59, 89.06, 72.70, 60.41, 57.47, 33.22, 20.03, 13.47, 8.20.

LC-MS (ESI) Calculated [C₁₉H₂₀FO₅]⁺: 347.1, found: 347.1;

R_f 0.55 (Hexanes:EtOAc = 1:1).



(S)-5-((3R,4R)-4-acetyl-3-(4-chlorophenyl)-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-55). The title compound was obtained as a white solid using **General Procedure F** (82 %).

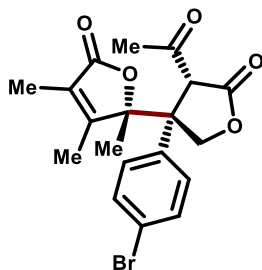
Mixture of Diastereomers (80:20) and Tautomers:
Major Diastereomer (17:83 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 7.23 – 7.19 (m, 2H), 6.84 – 6.80 (m, 2H), 5.14 (d, *J* = 9.5 Hz, 1H), 4.90 (d, *J* = 9.4 Hz, 1H), 4.69 (s, 1H), 2.37 (s, 3H), 1.95 (d, *J* = 1.1 Hz, 3H), 1.54 (s, 3H), 1.39 (d, *J* = 1.1 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 200.92, 171.99, 171.60, 159.92, 135.63, 134.13, 128.85, 128.74, 126.46, 88.95, 72.58, 60.38, 57.58, 33.21, 20.12, 13.50, 8.28.

LC-MS (ESI) Calculated [C₁₉H₂₀ClO₅]⁺: 363.1, found: 363.1;

R_f 0.5 (Hexanes:EtOAc = 1:1).



(S)-5-((S,Z)-3-(4-bromophenyl)-4-(1-hydroxyethylidene)-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-56) [Compound (13) in manuscript]. The title compound was obtained as a white solid using **General Procedure F** (89 %).

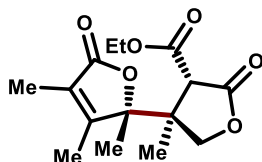
Mixture of Diastereomers (77:23) and Tautomers:
Major Diastereomer (15:85 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 7.38 – 7.35 (m, 2H), 6.78 – 6.73 (m, 2H), 5.13 (d, J = 9.4 Hz, 1H), 4.89 (d, J = 9.4 Hz, 1H), 4.69 (s, 1H), 2.36 (s, 3H), 1.94 (q, J = 1.0 Hz, 3H), 1.54 (s, 3H), 1.39 (q, J = 1.1 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 200.90, 171.97, 171.56, 159.91, 136.15, 131.78, 131.67, 126.47, 122.19, 88.86, 72.52, 60.33, 57.64, 33.20, 20.10, 13.50, 8.29.

LC-MS (ESI) Calculated $[C_{19}H_{20}BrO_5]^+$: 407.1, found: 407.1 and 409.1;

R_f 0.5 (Hexanes:EtOAc = 1:1).



Ethyl (3R,4S)-4-methyl-2-oxo-4-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)tetrahydrofuran-3-carboxylate (SI-57). The title compound was obtained as a clear oil using **General Procedure G** (83 %).

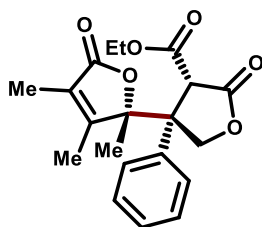
Single Diastereomer (>95:5):
Major Diastereomer:

¹H NMR (600 MHz,) δ 4.50 (d, J = 9.0 Hz, 1H), 4.29 – 4.13 (m, 2H), 4.04 (d, J = 9.1 Hz, 1H), 3.47 (s, 1H), 1.99 (q, J = 1.1 Hz, 3H), 1.83 (q, J = 1.0 Hz, 3H), 1.47 (s, 3H), 1.36 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H).

¹³C NMR (151 MHz,) δ 171.44, 170.75, 166.06, 160.24, 125.87, 88.02, 74.39, 61.65, 51.04, 49.66, 19.41, 17.43, 13.67, 13.12, 8.27.

LC-MS (ESI) Calculated $[C_{15}H_{21}O_6]^+$: 297.1, found: 297.1;

R_f 0.35 (Et₂O).



Ethyl (3R,4R)-2-oxo-4-phenyl-4-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)tetrahydrofuran-3-carboxylate (SI-58). The title compound was obtained as a clear oil using General Procedure G (73 %).

Mixture of Diastereomers ([88:12](#))

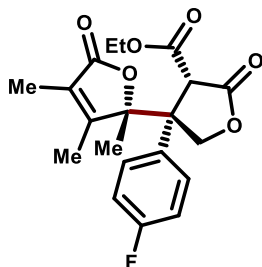
Major Diastereomer:

¹H NMR (600 MHz,) δ 7.25 – 7.21 (m, 2H), 7.04 – 6.99 (m, 2H), 5.18 (d, J = 9.5 Hz, 1H), 4.94 (d, J = 9.5 Hz, 1H), 4.38 (s, 1H), 3.98 – 3.82 (m, 2H), 1.97 – 1.94 (m, 3H), 1.54 (s, 3H), 1.37 (t, J = 1.1 Hz, 3H), 0.95 (t, J = 7.1 Hz, 3H).

¹³C NMR (151 MHz,) δ 171.62, 171.45, 165.76, 159.31, 135.93, 127.85, 127.80, 126.22, 125.84, 88.32, 71.95, 61.70, 57.01, 54.22, 19.32, 13.04, 12.90, 7.65.

LC-MS (ESI) Calculated $[\text{C}_{20}\text{H}_{23}\text{O}_6]^+$: 359.1, found: 359.1;

R_f 0.4 (Hexanes:EtOAc = 1:1).



Ethyl (3R,4R)-4-(4-fluorophenyl)-2-oxo-4-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)tetrahydrofuran-3-carboxylate (SI-59). The title compound was obtained as a clear oil using General Procedure G (74 %).

Mixture of Diastereomers ([80:20](#))

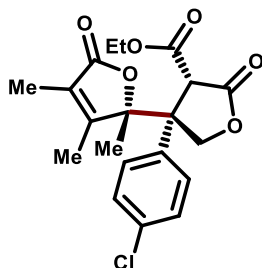
Major Diastereomer:

¹H NMR (600 MHz, Chloroform-*d*) δ 7.02 (q, J = 8.3 Hz, 3H), 6.99 – 6.93 (m, 2H), 5.13 (d, J = 9.5 Hz, 1H), 4.92 (d, J = 9.5 Hz, 1H), 4.36 (s, 1H), 4.02 – 3.83 (m, 2H), 1.96 (d, J = 1.3 Hz, 3H), 1.54 (s, 3H), 1.42 (d, J = 1.2 Hz, 3H), 0.99 (t, J = 7.1 Hz, 3H).

¹³C NMR (151 MHz,) δ 171.35, 171.28, 165.66, 162.54, 160.89, 159.23, 131.87, 128.06, 126.03, 114.97, 114.82, 88.25, 71.75, 61.85, 56.53, 54.24, 19.36, 13.13, 12.90, 7.72.

LC-MS (ESI) Calculated $[\text{C}_{20}\text{H}_{22}\text{FO}_6]^+$: 377.1, found: 377.1;

R_f 0.48 (Et₂O).



Ethyl (3R,4R)-4-(4-chlorophenyl)-2-oxo-4-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)tetrahydrofuran-3-carboxylate (SI-60). The title compound was obtained as a clear oil using General Procedure G (79 %).

Mixture of Diastereomers (75:25)

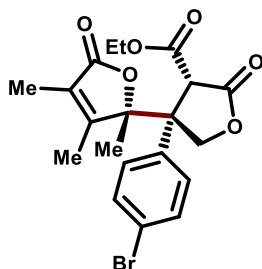
Major Diastereomer:

¹H NMR (600 MHz, Chloroform-*d*) δ 7.26 – 7.22 (m, 2H), 6.97 (d, J = 8.3 Hz, 2H), 5.12 (d, J = 9.5 Hz, 1H), 4.91 (d, J = 9.5 Hz, 1H), 4.35 (s, 1H), 3.98 (dq, J = 11.2, 7.2 Hz, 1H), 3.94 – 3.87 (m, 1H), 1.96 (q, J = 1.2 Hz, 3H), 1.54 (d, J = 1.0 Hz, 3H), 1.43 (q, J = 1.2 Hz, 3H), 1.01 (t, J = 7.1 Hz, 3H).

¹³C NMR (151 MHz,) δ 171.81, 171.80, 166.20, 159.72, 135.11, 134.51, 128.65, 128.43, 126.69, 88.73, 72.20, 62.50, 57.22, 54.70, 19.97, 13.73, 13.49, 8.36.

LC-MS (ESI) Calculated [C₂₀H₂₂ClO₆]⁺: 393.1, found: 393.1;

R_f 0.70 (Et₂O).



Ethyl (3R,4R)-4-(4-bromophenyl)-2-oxo-4-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)tetrahydrofuran-3-carboxylate (SI-61). The title compound was obtained as a clear oil using General Procedure G (66 %).

Mixture of Diastereomers (74:26)

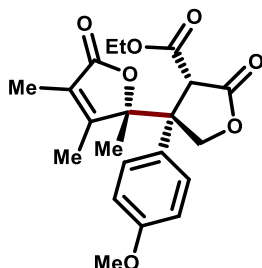
Major Diastereomer:

¹H NMR (600 MHz, Chloroform-*d*) δ 7.42 – 7.37 (m, 2H), 6.91 (d, J = 8.2 Hz, 2H), 5.12 (d, J = 9.5 Hz, 1H), 4.91 (d, J = 9.5 Hz, 1H), 4.35 (s, 1H), 3.98 (dq, J = 11.3, 7.1 Hz, 1H), 3.91 (tq, J = 10.8, 7.2 Hz, 1H), 1.96 (d, J = 1.3 Hz, 3H), 1.54 (s, 3H), 1.45 – 1.42 (m, 3H), 1.02 (t, J = 7.1 Hz, 3H).

¹³C NMR (151 MHz,) δ 171.22, 171.18, 165.61, 159.12, 135.06, 131.03, 130.81, 126.13, 122.04, 88.07, 71.57, 61.94, 56.70, 54.06, 19.39, 13.16, 12.91, 7.79.

LC-MS (ESI) Calculated $[\text{C}_{20}\text{H}_{22}\text{BrO}_6]^+$: 437.1, found: 437.1;

R_f 0.65 (Et₂O).



Ethyl (3R,4R)-4-(4-methoxyphenyl)-2-oxo-4-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)tetrahydrofuran-3-carboxylate (SI-62). The title compound was obtained as a clear oil using General Procedure G (82 %).

Mixture of Diastereomers (87:13)

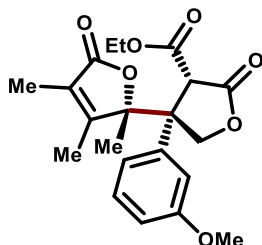
Major Diastereomer:

¹H NMR (600 MHz, Chloroform-*d*) δ 6.94 (d, *J* = 8.4 Hz, 2H), 6.78 – 6.74 (m, 2H), 5.13 (d, *J* = 9.5 Hz, 1H), 4.91 (d, *J* = 9.5 Hz, 1H), 4.34 (s, 1H), 3.96 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.91 – 3.84 (m, 1H), 3.75 (s, 3H), 1.96 – 1.93 (m, 3H), 1.53 (s, 3H), 1.41 (q, *J* = 1.1 Hz, 3H), 0.98 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 171.79, 171.56, 165.81, 159.49, 158.69, 127.78, 127.43, 125.77, 113.12, 88.57, 72.05, 61.66, 56.43, 54.76, 54.35, 19.39, 13.14, 12.90, 7.76.

LC-MS (ESI) Calculated $[\text{C}_{21}\text{H}_{25}\text{O}_7]^+$: 389.1, found: 389.1;

R_f 0.68 (Et₂O).



Ethyl (3R,4R)-4-(3-methoxyphenyl)-2-oxo-4-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)tetrahydrofuran-3-carboxylate (SI-63). The title compound was obtained as a clear oil using General Procedure G (80 %).

Mixture of Diastereomers (87:13)

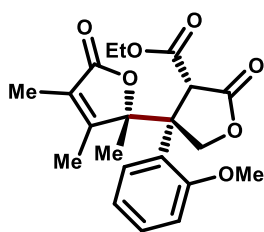
Major Diastereomer:

¹H NMR (600 MHz, Chloroform-*d*) δ 7.15 (t, *J* = 8.0 Hz, 1H), 6.80 – 6.73 (m, 1H), 6.60 (s, 1H), 6.53 (d, *J* = 7.7 Hz, 1H), 5.17 (d, *J* = 9.5 Hz, 1H), 4.91 (d, *J* = 9.5 Hz, 1H), 4.38 (s, 1H), 3.97 (dq, *J* = 11.1, 7.1 Hz, 1H), 3.91 – 3.83 (m, 1H), 3.76 (s, 3H), 1.96 (q, *J* = 1.1 Hz, 3H), 1.54 (s, 3H), 1.40 (q, *J* = 1.1 Hz, 3H), 0.96 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz,) δ 172.20, 172.15, 166.35, 159.93, 159.28, 137.93, 129.40, 126.26, 112.90, 88.87, 72.50, 62.30, 57.47, 55.44, 54.81, 19.91, 13.60, 13.45, 8.28.

LC-MS (ESI) Calculated [C₂₁H₂₅O₇]⁺: 389.1, found: 389.1;

R_f 0.55 (Et₂O).



Ethyl (3R,4R)-4-(2-methoxyphenyl)-2-oxo-4-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)tetrahydrofuran-3-carboxylate (SI-64). The title compound was obtained as a clear oil using General Procedure G (64 %).

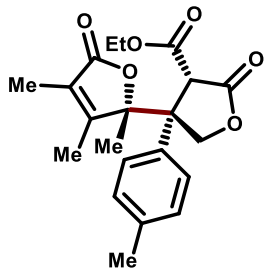
Mixture of Diastereomers (85:15):
Major Diastereomer:

¹H NMR (500 MHz, Chloroform-*d*) δ 7.21 (dd, *J* = 20.2, 7.9 Hz, 2H), 6.91 (t, *J* = 7.5 Hz, 1H), 6.84 (s, 5H), 6.78 (d, *J* = 8.3 Hz, 1H), 5.13 (d, *J* = 88.0 Hz, 6H), 4.05 – 3.87 (m, 5H), 3.75 (s, 4H), 2.00 (d, *J* = 1.1 Hz, 5H), 1.52 (s, 3H), 1.47 – 1.38 (m, 10H), 1.02 (q, *J* = 7.4, 5.8 Hz, 8H).

¹³C NMR (126 MHz, Chloroform-*d*) δ 171.85, 171.65, 166.06, 160.81, 160.53, 129.68, 125.96, 120.85, 120.79, 111.23, 89.44, 73.52, 62.02, 54.68, 20.01, 19.77, 13.77, 13.24, 8.37.

LC-MS (ESI) Calculated [C₂₁H₂₅O₇]⁺: 389.1, found: 389.1;

R_f 0.50 (Et₂O).



Ethyl (3R,4R)-2-oxo-4-(p-tolyl)-4-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)tetrahydrofuran-3-carboxylate (SI-65). The title compound was obtained as a clear oil using **General Procedure G** (74 %).

Mixture of Diastereomers (95:5)

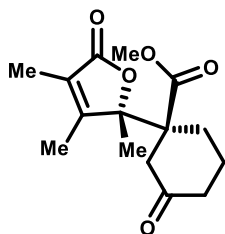
Major Diastereomer:

¹H NMR (600 MHz,) δ 7.05 – 7.02 (m, 2H), 6.89 (d, J = 7.9 Hz, 2H), 5.15 (d, J = 9.5 Hz, 1H), 4.92 (d, J = 9.5 Hz, 1H), 4.35 (s, 1H), 3.95 (dq, J = 11.0, 7.2 Hz, 1H), 3.91 – 3.82 (m, 1H), 2.26 (s, 3H), 1.95 (d, J = 1.5 Hz, 3H), 1.53 (s, 3H), 1.40 – 1.37 (m, 3H), 0.98 (t, J = 7.1 Hz, 3H).

¹³C NMR (151 MHz,) δ 172.37, 172.17, 166.44, 160.05, 138.13, 133.40, 129.04, 126.66, 126.29, 89.04, 72.65, 62.23, 57.33, 54.83, 21.04, 19.92, 13.66, 13.48, 8.28.

LC-MS (ESI) Calculated $[C_{21}H_{25}O_6]^+$: 373.1, found: 373.1;

R_f 0.71 (Et₂O).



Methyl (S)-3-oxo-1-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)cyclohexane-1-carboxylate (SI-66). The title compound was obtained as a clear oil by applying **General Procedure F** to **SI-21** (92 %).

Mixture of Diastereomers (80:20)

Major Diastereomer:

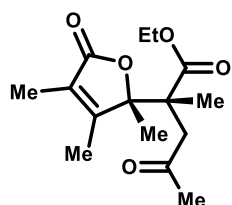
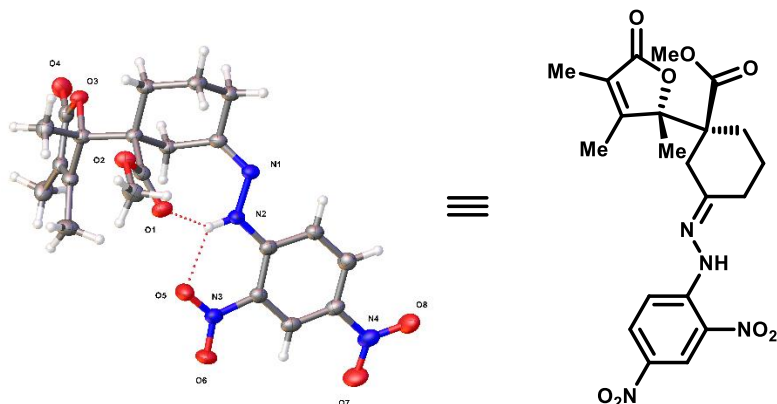
¹H NMR (600 MHz, Chloroform-*d*) δ 3.72 (s, 3H), 2.48 – 2.31 (m, 3H), 2.19 (dddd, J = 15.5, 13.3, 6.6, 0.9 Hz, 1H), 2.12 – 2.04 (m, 3H), 1.78 (s, 6H), 1.65 (s, 3H), 1.49 – 1.39 (m, 1H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 208.06, 173.08, 172.81, 161.25, 125.16, 89.34, 56.16, 52.68, 42.97, 39.83, 29.63, 21.70, 20.44, 12.05, 8.67.

LC-MS (ESI) Calculated $[C_{15}H_{21}O_5]^+$: 281.1, found: 281.1;

R_f 0.35 (Hexanes:EtOAc = 1:1).

Crystal (see [procedure](#))



Ethyl (S)-2-methyl-4-oxo-2-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)pentanoate (SI-67). The title compound was obtained as a clear oil by applying **General Procedure F** to **SI-22** (98 %).

Single Diastereomer (>95:5):
Major Diastereomer:

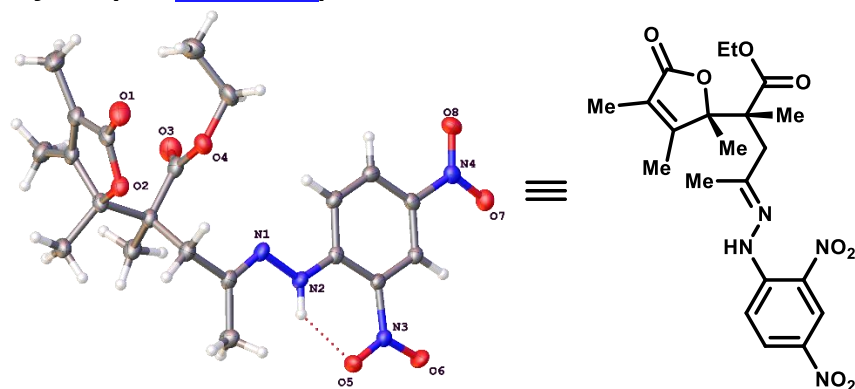
¹H NMR (600 MHz, Chloroform-*d*) δ 4.01 (q, *J* = 7.1 Hz, 2H), 3.35 (d, *J* = 18.3 Hz, 1H), 2.61 (d, *J* = 18.3 Hz, 1H), 2.09 (s, 3H), 2.00 (d, *J* = 1.3 Hz, 3H), 1.75 (d, *J* = 1.3 Hz, 3H), 1.45 (s, 3H), 1.41 (d, *J* = 1.0 Hz, 3H), 1.15 (t, *J* = 7.2 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 205.61, 172.78, 172.75, 162.22, 124.81, 89.31, 61.22, 50.47, 47.89, 30.58, 19.86, 19.31, 14.02, 13.63, 8.69.

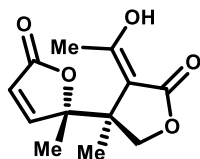
LC-MS (ESI) Calculated [C₁₅H₂₃O₅]⁺: 283.1, found: 283.1;

R_f 0.50 (Hexanes:EtOAc = 1:1).

Crystal (see [procedure](#))



Nucleophile Scope



(S)-5-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-5-methylfuran-2(5H)-one (SI-68). The title compound was obtained as a clear oil using **General Procedure F** (80 %).

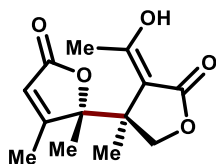
Mixture of Diastereomers (90:10) and Tautomers (63:37 Enol:Keto):
Major Diastereomer:

¹H NMR (600 MHz, Chloroform-*d*) δ 12.08 (s, 1H), 7.54 (d, *J* = 5.7 Hz, 1H), 7.38 (d, *J* = 5.7 Hz, 1H), 6.17 (d, *J* = 5.7 Hz, 1H), 6.07 (dd, *J* = 5.7, 1.6 Hz, 1H), 4.38 (d, *J* = 9.0 Hz, 1H), 4.18 (d, *J* = 9.9 Hz, 1H), 4.04 (d, *J* = 8.9 Hz, 1H), 3.87 (d, *J* = 9.9 Hz, 1H), 3.55 (s, 1H), 2.33 (s, 2H), 2.19 (s, 3H), 1.48 (s, 2H), 1.46 (s, 3H), 1.44 (s, 2H), 1.31 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 200.96, 176.14, 173.55, 170.98, 170.64, 170.56, 158.62, 157.10, 122.08, 120.31, 98.90, 91.75, 88.70, 73.61, 73.55, 55.45, 49.27, 46.78, 31.55, 19.92, 19.73, 19.71, 19.71, 17.21.

LC-MS (ESI) Calculated [C₁₂H₁₅O₅]⁺: 239.1, found: 239.1;

R_f 0.3 (Hexanes:EtOAc = 6:4).



(S)-5-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-4,5-dimethylfuran-2(5H)-one (SI-69) [Compound (12) in manuscript]. The title compound was obtained as a clear oil using **General Procedure F** (87 %).

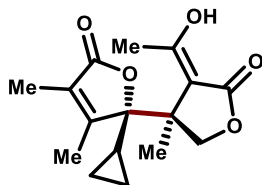
Mixture of Diastereomers (88:12) and Tautomers:
Major Diastereomer (73:27 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 12.22 – 12.11 (m, 1H), 11.82 (s, 0H), 5.87 (q, *J* = 1.5 Hz, 1H), 5.82 (q, *J* = 1.5 Hz, 0H), 4.48 – 4.46 (m, 0H), 4.34 (d, *J* = 9.9 Hz, 1H), 4.02 (d, *J* = 9.0 Hz, 0H), 3.86 (d, *J* = 9.9 Hz, 1H), 3.75 (s, 0H), 2.34 (s, 1H), 2.20 (s, 3H), 2.17 (d, *J* = 1.5 Hz, 1H), 2.08 (d, *J* = 1.6 Hz, 3H), 1.49 (s, 1H), 1.48 (s, 3H), 1.37 – 1.35 (m, 1H), 1.28 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 201.43, 176.44, 174.17, 171.32, 171.07, 170.51, 169.96, 169.92, 119.03, 118.29, 99.01, 92.09, 89.44, 73.99, 73.47, 55.63, 49.85, 46.88, 31.90, 20.17, 19.97, 19.36, 19.28, 16.48, 15.27, 14.79.

LC-MS (ESI) Calculated [C₁₃H₁₇O₅]⁺: 253.1, found: 253.1;

R_f 0.35 (Hexanes:EtOAc = 1:1).



(S)-5-cyclopropyl-5-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-3,4-dimethylfuran-2(5H)-one (SI-70). The title compound was obtained as a clear oil using **General Procedure F** (84 %).

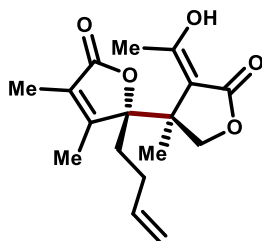
Mixture of Diastereomers (88:12) and Tautomers:
Major Diastereomer (55:45 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 12.05 (q, *J* = 0.9 Hz, 1H), 4.52 (d, *J* = 9.2 Hz, 1H), 4.34 (d, *J* = 9.9 Hz, 1H), 4.11 (d, *J* = 9.3 Hz, 1H), 3.84 – 3.82 (m, 2H), 2.29 (s, 2H), 2.18 (d, *J* = 0.9 Hz, 3H), 2.08 (q, *J* = 1.1 Hz, 2H), 1.99 (q, *J* = 1.1 Hz, 3H), 1.81 (t, *J* = 1.1 Hz, 3H), 1.78 (d, *J* = 1.1 Hz, 2H), 1.34 (s, 2H), 1.31 (s, 3H), 0.80 (dtd, *J* = 9.9, 5.4, 5.0, 1.2 Hz, 1H), 0.77 – 0.72 (m, 1H), 0.72 – 0.60 (m, 2H), 0.40 (dddd, *J* = 9.4, 8.4, 5.9, 4.9 Hz, 1H), 0.31 (dddd, *J* = 9.3, 8.3, 6.0, 4.8 Hz, 1H), - 0.10 (ddt, *J* = 10.0, 6.1, 5.1 Hz, 1H), -0.19 (ddt, *J* = 9.8, 6.1, 5.0 Hz, 1H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 202.43, 177.28, 173.22, 173.20, 172.71, 172.09, 124.93, 124.47, 100.81, 90.08, 87.81, 74.39, 72.48, 57.17, 52.07, 48.71, 32.78, 21.17, 20.29, 17.13, 13.86, 13.35, 12.73, 12.29, 8.64, 8.48, 5.03, 4.48, -0.68, -0.96.

LC-MS (ESI) Calculated [C₁₆H₂₁O₅]⁺: 293.1, found: 293.1;

R_f 0.4 (Hexanes:EtOAc = 1:1).



(S)-5-(but-3-en-1-yl)-5-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-3,4-dimethylfuran-2(5H)-one (SI-71). The title compound was obtained as a clear oil using **General Procedure F** (70 %).

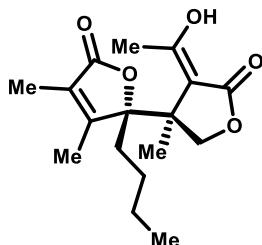
Single Diastereomer (94:6) and Tautomers:
Major Diastereomer (66:44 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 12.16 (d, *J* = 1.0 Hz, 1H), 5.74 – 5.63 (m, 2H), 5.01 – 4.92 (m, 3H), 4.47 (dd, *J* = 8.9, 0.8 Hz, 1H), 4.33 (d, *J* = 9.9 Hz, 1H), 3.99 (d, *J* = 8.8 Hz, 0H), 3.82 (d, *J* = 9.8 Hz, 1H), 3.65 (s, 0H), 2.27 (s, 1H), 2.20 (d, *J* = 0.7 Hz, 3H), 2.04 – 2.00 (m, 1H), 2.00 – 1.98 (m, 2H), 1.91 (q, *J* = 1.1 Hz, 3H), 1.84 (q, *J* = 1.0 Hz, 3H), 1.80 (q, *J* = 1.1 Hz, 2H), 1.42 – 1.40 (m, 1H), 1.24 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 201.83, 177.14, 174.42, 172.94, 172.46, 171.58, 160.63, 158.63, 136.77, 136.31, 127.88, 127.16, 116.23, 115.86, 100.03, 93.52, 90.66, 74.97, 74.20, 55.97, 51.79, 48.16, 32.45, 29.97, 29.64, 27.12, 26.98, 20.97, 20.60, 17.34, 14.17, 13.56, 8.78, 8.63.

LC-MS (ESI) Calculated [C₁₇H₂₃O₅]⁺: 307.1, found: 307.1;

R_f 0.5 (Hexanes:EtOAc = 1:1).



(S)-5-butyl-5-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-3,4-dimethylfuran-2(5H)-one (SI-72). The title compound was obtained as a clear oil using **General Procedure F** (77 %).

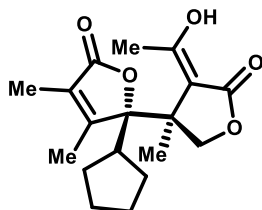
Single Diastereomer (>95:5) and Tautomers:
Major Diastereomer (71:29 Enol:Keto):

¹H NMR (600 MHz, Benzene-*d*₆) δ 3.94 (d, *J* = 8.6 Hz, OH), 3.79 (d, *J* = 9.8 Hz, 1H), 3.46 (s, OH), 3.30 (d, *J* = 8.6 Hz, OH), 3.07 (d, *J* = 9.8 Hz, 1H), 1.94 (s, 3H), 1.85 (s, 1H), 1.51 (d, *J* = 1.2 Hz, 3H), 1.47 – 1.43 (m, 2H), 1.29 (d, *J* = 1.3 Hz, 1H), 1.12 (d, *J* = 1.2 Hz, 3H), 0.70 (t, *J* = 7.2 Hz, 1H), 0.64 (t, *J* = 7.1 Hz, 3H), 0.56 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 201.91, 177.20, 174.28, 173.14, 172.66, 171.71, 160.90, 158.93, 127.51, 126.82, 100.13, 93.87, 91.01, 75.00, 74.26, 56.04, 51.74, 48.09, 32.47, 30.30, 29.99, 24.68, 24.55, 22.71, 22.61, 20.99, 20.57, 17.35, 14.05, 13.98, 13.46, 8.73, 8.60.

LC-MS (ESI) Calculated [C₁₇H₂₅O₅]⁺: 309.1, found: 309.1;

R_f 0.5 (Hexanes:EtOAc = 1:1).



(S)-5-cyclopentyl-5-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-3,4-dimethylfuran-2(5H)-one (SI-73). The title compound was obtained as a clear oil using **General Procedure F** (50 %).

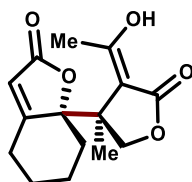
Mixture of Diastereomers (88:12) and Tautomers:
Major Diastereomer (62:38 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 12.19 (s, 1H), 4.60 (d, *J* = 9.8 Hz, 1H), 4.54 (dd, *J* = 8.6, 1.1 Hz, 1H), 4.00 (d, *J* = 8.6 Hz, 1H), 3.88 (d, *J* = 9.9 Hz, 1H), 3.48 (s, 1H), 2.19 (s, 2H), 2.19 (s, 3H), 1.95 (t, *J* = 1.2 Hz, 5H), 1.82 (d, *J* = 1.2 Hz, 2H), 1.77 (q, *J* = 1.1 Hz, 3H), 1.63 (d, *J* = 0.9 Hz, 3H), 1.62 – 1.42 (m, 4H), 1.35 – 1.23 (m, 2H), 1.11 (s, 2H), 0.95 – 0.84 (m, 1H), 0.84 – 0.76 (m, 0H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 200.89, 176.69, 173.78, 173.13, 172.72, 170.33, 163.79, 160.12, 125.33, 124.65, 100.80, 93.09, 90.07, 76.09, 73.80, 54.61, 53.05, 47.17, 41.32, 40.79, 32.16, 28.69, 26.79, 26.71, 26.54, 25.17, 24.96, 23.93, 23.22, 22.12, 19.91, 17.46, 14.03, 13.53, 7.85, 7.78,

LC-MS (ESI) Calculated [C₁₈H₂₅O₅]⁺: 338.1, found: 338.1;

R_f 0.55 (Hexanes:EtOAc = 1:1).



(S)-7a-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-5,6,7,7a-tetrahydrobenzofuran-2(4H)-one (SI-74). The title compound was obtained as a clear oil using General Procedure F (82 %).

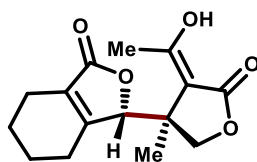
Mixture of Diastereomers (73:27) and Tautomers:
Major Diastereomer (63:37 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 12.01 (s, 1H), 5.90 (d, *J* = 1.6 Hz, 1H), 5.81 (d, *J* = 1.5 Hz, 1H), 4.63 (dd, *J* = 9.0, 0.8 Hz, 1H), 4.41 (d, *J* = 9.9 Hz, 1H), 4.04 (d, *J* = 8.9 Hz, 1H), 3.76 (d, *J* = 9.9 Hz, 1H), 3.68 (s, 1H), 2.96 – 2.83 (m, 2H), 2.64 – 2.53 (m, 3H), 2.44 – 2.38 (m, 1H), 2.30 – 2.25 (m, 1H), 2.18 (s, 2H), 1.92 – 1.72 (m, 3H), 1.68 – 1.51 (m, 4H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 201.96, 177.09, 176.22, 174.37, 173.74, 171.55, 171.44, 170.98, 116.95, 115.68, 100.42, 90.29, 87.97, 74.80, 74.07, 57.12, 51.10, 48.40, 37.13, 36.92, 32.16, 30.00, 29.59, 28.96, 28.33, 22.94, 22.87, 21.13, 20.29, 18.76.

LC-MS (ESI) Calculated [C₁₅H₁₉O₅]⁺: 279.1, found: 279.1;

R_f 0.3 (Hexanes:EtOAc = 1:1).



(S)-3-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-4,5,6,7-tetrahydroisobenzofuran-1(3H)-one (SI-75). The title compound was obtained as a clear oil using **General Procedure F** (72 %).

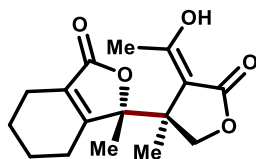
Mixture of Diastereomers (71:29) and Tautomers:
Major and Minor Diastereomers:

¹H NMR (600 MHz, Chloroform-*d*) δ 11.93 (s, 1H), 11.82 (s, 1H), 5.62 (t, *J* = 2.1 Hz, OH), 5.26 (d, *J* = 2.5 Hz, 1H), 4.97 – 4.92 (m, 1H), 4.86 – 4.81 (m, 1H), 4.76 – 4.71 (m, 1H), 4.57 (d, *J* = 8.3 Hz, 1H), 4.49 (d, *J* = 9.2 Hz, OH), 4.33 (d, *J* = 9.2 Hz, OH), 4.25 (d, *J* = 9.8 Hz, 1H), 4.12 (d, *J* = 9.2 Hz, OH), 4.09 – 4.05 (m, 2H), 3.97 (d, *J* = 9.8 Hz, 1H), 3.94 (d, *J* = 9.9 Hz, 1H), 3.91 (d, *J* = 9.2 Hz, OH), 3.81 – 3.78 (m, 1H), 3.76 (s, OH), 2.49 (s, 2H), 2.48 (s, 1H), 2.41 (s, 1H), 2.37 (s, 1H), 2.36 – 2.26 (m, 2H), 2.20 (ddt, *J* = 11.8, 5.8, 3.1 Hz, 1H), 2.17 (s, 3H), 2.13 (s, 2H), 1.93 – 1.75 (m, 9H), 1.71 – 1.59 (m, 1H), 1.58 (s, 2H), 1.55 (s, 3H), 1.29 (s, 1H), 1.16 (s, 1H), 1.08 (s, 1H), 1.00 (s, 2H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 202.43, 201.32, 200.95, 200.70, 175.87, 175.63, 173.12, 171.91, 171.76, 171.66, 171.57, 171.44, 171.28, 171.21, 171.13, 170.83, 160.09, 159.61, 159.58, 159.51, 159.18, 158.95, 130.06, 129.76, 129.67, 129.61, 129.35, 128.98, 99.62, 97.50, 86.93, 85.05, 84.11, 83.31, 82.03, 81.61, 75.37, 73.92, 73.45, 73.07, 72.07, 71.79, 62.68, 61.87, 57.28, 57.27, 47.07, 46.02, 45.93, 44.86, 44.57, 43.29, 32.48, 32.18, 31.20, 30.74, 25.19, 25.08, 24.74, 24.12, 23.92, 23.56, 23.36, 23.08, 21.40, 21.33, 21.27, 21.18, 20.99, 20.80, 20.77, 20.67, 20.64, 20.62, 20.61, 19.84, 19.81, 19.67, 19.63, 19.05, 19.03, 18.98, 18.75, 16.57, 14.69, 13.60.

LC-MS (ESI) Calculated [C₁₅H₁₉O₅]⁺: 279.1, found: 279.1;

R_f 0.3 (Hexanes:EtOAc = 1:1).



(S)-3-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-3-methyl-4,5,6,7-tetrahydroisobenzofuran-1(3H)-one (SI-76). The title compound was obtained as a clear oil using **General Procedure F** (88 %).

Mixture of Diastereomers (64:36) and Tautomers:
Major and Minor Diastereomer (78:22):

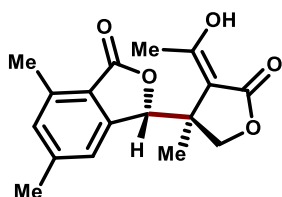
¹H NMR (600 MHz, Chloroform-*d*) δ 12.15 (s, 1H), 11.77 (s, 1H), 4.45 (d, *J* = 9.0 Hz, 1H), 4.38 (d, *J* = 10.1 Hz, OH), 4.00 (d, *J* = 8.9 Hz, 1H), 3.93 (d, *J* = 9.7 Hz, OH), 3.91 (d, *J* = 10.1 Hz, OH), 3.83 (d, *J* = 9.8 Hz, 1H), 3.75 (s, OH), 3.70 (s, 1H), 2.37 (s, 1H), 2.36 – 2.30 (m, 1H), 2.29 (s, 2H), 2.20 (s, 3H), 2.16 (s, 1H), 2.15 – 2.06 (m, 1H), 1.92 – 1.84 (m, 1H), 1.80 (dddd, *J* = 17.1, 12.3, 6.7, 3.4 Hz, 2H), 1.73 – 1.67 (m, OH), 1.66 – 1.55 (m, 6H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 202.11, 202.02, 177.15, 176.19, 174.55, 174.25, 172.37, 172.03, 171.95, 171.58, 171.51, 171.43, 166.41, 165.01, 164.69, 129.10,

128.94, 128.51, 128.05, 99.74, 99.26, 91.43, 90.92, 89.14, 88.78, 77.37, 74.77, 74.17, 73.86, 73.45, 58.41, 56.14, 50.72, 49.48, 48.86, 47.39, 32.64, 32.51, 25.13, 24.73, 24.68, 23.55, 22.21, 22.18, 22.15, 22.10, 21.54, 21.31, 21.25, 21.22, 21.08, 20.76, 20.53, 20.52, 20.30, 20.27, 19.98, 19.97, 19.78.

LC-MS (ESI) Calculated $[C_{16}H_{21}O_5]^+$: 293.1, found: 293.1;

R_f 0.45 (Hexanes:EtOAc = 7:3).



(S)-3-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-5,7-dimethylisobenzofuran-1(3H)-one (SI-77). The title compound was obtained as a clear oil using General Procedure F (62 %).

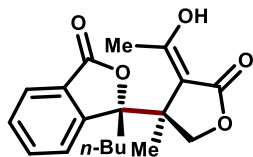
Mixture of Diastereomers (70:30) and Tautomers:
Major Diastereomer (75:25 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 12.08 (d, *J* = 0.9 Hz, 1H), 7.18 (s, 0H), 7.13 – 7.11 (m, 1H), 6.84 – 6.80 (m, 1H), 6.76 (s, 0H), 5.34 (s, 1H), 5.29 (s, 0H), 4.32 (d, *J* = 9.2 Hz, 0H), 4.16 (d, *J* = 9.3 Hz, 0H), 3.85 (s, 0H), 3.81 (d, *J* = 9.9 Hz, 1H), 3.78 (dd, *J* = 9.9, 0.8 Hz, 1H), 2.64 (s, 4H), 2.55 (s, 1H), 2.41 (s, 1H), 2.38 (s, 3H), 2.23 (d, *J* = 0.8 Hz, 3H), 2.08 (d, *J* = 0.8 Hz, 1H), 1.64 (s, 3H), 1.55 (s, 1H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 203.28, 176.53, 172.77, 171.67, 170.00, 169.25, 147.26, 146.81, 145.64, 145.13, 140.01, 139.84, 133.28, 133.06, 132.96, 132.87, 122.12, 120.87, 100.55, 83.46, 82.21, 74.61, 72.86, 63.24, 45.95, 44.72, 33.20, 24.07, 22.20, 21.87, 19.68, 19.60, 17.52, 16.52.

LC-MS (ESI) Calculated $[C_{17}H_{19}O_5]^+$: 303.1, found: 303.1;

R_f 0.55 (Hexanes:EtOAc = 1:1).



(S)-3-butyl-3-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)isobenzofuran-1(3H)-one (SI-78). The title compound was obtained as a clear oil using General Procedure F (90 %).

Mixture of Diastereomers (78:22) and Tautomers:
Major and Minor Diastereomer (Major: (70:30 Enol:Keto), Minor:(81:19 Enol:Keto)):

¹H NMR (600 MHz, Chloroform-*d*) δ 12.22 (s, 1H), 11.55 (s, 0H), 7.92 (dd, *J* = 10.1, 7.6 Hz, 1H), 7.82 (d, *J* = 7.5 Hz, 0H), 7.72 (t, *J* = 7.4 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.62 (dq, *J* = 7.4, 3.9 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 0H),

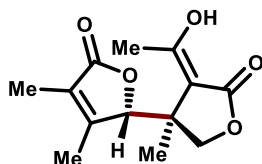
7.48 (t, $J = 8.6$ Hz, 0H), 7.38 (t, $J = 8.0$ Hz, 1H), 4.79 (d, $J = 10.1$ Hz, 0H), 4.55 (d, $J = 9.0$ Hz, 0H), 4.44 (d, $J = 9.9$ Hz, 1H), 4.11 (d, $J = 9.1$ Hz, 0H), 4.07 (d, $J = 9.6$ Hz, 0H), 4.03 – 3.96 (m, 0H), 3.83 (d, $J = 9.9$ Hz, 1H), 3.72 (s, 0H), 3.66 (d, $J = 9.6$ Hz, 0H), 2.47 (s, 0H), 2.39 (s, 0H), 2.17 – 2.09 (m, 5H), 2.09 – 1.88 (m, 2H), 1.85 (s, 1H), 1.55 (s, 1H), 1.45 (s, 1H), 1.24 (d, $J = 10.3$ Hz, 5H), 1.19 – 1.03 (m, 1H), 0.98 (dtd, $J = 17.1, 8.8, 8.0, 4.6$ Hz, 1H), 0.87 (ddt, $J = 19.6, 15.5, 7.5$ Hz, 1H), 0.74 (dt, $J = 14.9, 7.3$ Hz, 6H), 0.55 – 0.33 (m, 2H).

¹³C NMR

(151 MHz, Chloroform-*d*) δ 202.37, 201.63, 177.20, 176.16, 174.02, 173.36, 172.06, 169.71, 169.40, 169.20, 149.26, 148.42, 134.83, 134.44, 134.05, 130.42, 129.98, 129.89, 127.86, 126.25, 125.65, 123.05, 122.51, 122.01, 100.22, 100.22, 100.07, 93.29, 93.09, 90.69, 74.55, 74.31, 73.98, 65.98, 58.23, 56.29, 52.28, 51.36, 49.60, 48.94, 33.69, 33.23, 32.74, 32.40, 32.02, 29.83, 25.36, 25.00, 24.92, 22.74, 22.69, 22.57, 22.57, 21.25, 20.97, 20.38, 19.84, 17.75, 13.93, 13.88.

LC-MS (ESI) Calculated $[\text{C}_{19}\text{H}_{23}\text{O}_5]^+$: 331.1, found: 331.1;

R_f 0.6 (Hexanes:EtOAc = 1:1).



(R)-5-((3S,4R)-4-acetyl-3-methyl-5-oxotetrahydrofuran-3-yl)-3,4-dimethylfuran-2(5H)-one (SI-79). The title compound was obtained as a clear oil using **General Procedure F** (83 %).

Mixture of Diastereomers (79:21) and Tautomers:

Major Diastereomer (57:43 Enol:Keto):

¹H NMR

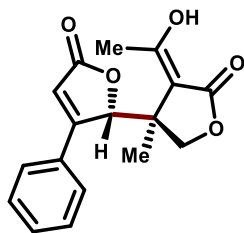
(600 MHz, Chloroform-*d*) δ 11.93 (s, 1H), 5.22 (dq, $J = 2.2, 1.1$ Hz, 1H), 4.82 – 4.77 (m, 1H), 4.68 – 4.64 (m, 1H), 4.11 (d, $J = 8.1$ Hz, 1H), 3.92 (d, $J = 9.9$ Hz, 1H), 3.78 (dd, $J = 9.9, 0.8$ Hz, 1H), 3.59 (s, 1H), 2.49 (s, 2H), 2.18 (s, 3H), 1.90 (q, $J = 1.1$ Hz, 2H), 1.87 (p, $J = 1.1$ Hz, 3H), 1.85 (dq, $J = 2.1, 1.1$ Hz, 4H), 1.84 (q, $J = 1.1$ Hz, 1H), 1.56 (s, 3H), 0.96 (d, $J = 0.7$ Hz, 2H).

¹³C NMR

(151 MHz, Chloroform-*d*) δ 203.00, 176.38, 173.28, 173.20, 171.93, 170.84, 156.60, 155.59, 127.92, 126.74, 100.49, 85.71, 82.60, 74.90, 72.60, 63.52, 46.65, 44.19, 33.04, 24.43, 19.63, 19.10, 13.92, 12.50, 8.88, 8.73.

LC-MS (ESI) Calculated $[\text{C}_{13}\text{H}_{17}\text{O}_5]^+$: 253.1, found: 253.1;

R_f 0.3 (Hexanes:EtOAc = 7:3).



(S)-5-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-4-phenylfuran-2(5H)-one (SI-80). The title compound was obtained as a clear oil using **General Procedure F** (80 %).

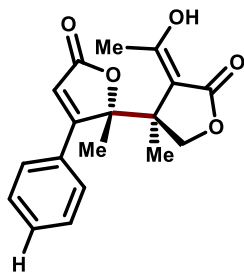
Mixture of Diastereomers (83:17) and Tautomers:
Major Diastereomer (50:50 Enol:Keto):

¹H NMR (600 MHz, Chloroform-*d*) δ 7.57 – 7.47 (m, 5H), 7.45 – 7.35 (m, 7H), 7.23 – 7.19 (m, 2H), 6.27 (d, *J* = 1.5 Hz, 1H), 6.23 (d, *J* = 1.6 Hz, 1H), 6.06 (d, *J* = 1.5 Hz, 1H), 5.50 (d, *J* = 1.4 Hz, 1H), 4.59 – 4.53 (m, 1H), 4.05 (d, *J* = 10.0 Hz, 1H), 3.66 (dd, *J* = 9.9, 0.7 Hz, 1H), 3.61 (s, 1H), 3.24 (d, *J* = 8.5 Hz, 1H), 2.52 (s, 3H), 2.17 (s, 3H), 1.58 (s, 3H), 0.94 (d, *J* = 0.8 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 202.92, 176.27, 175.27, 173.51, 171.29, 170.56, 167.89, 166.99, 131.89, 131.33, 130.95, 130.41, 129.77, 129.12, 128.92, 127.47, 127.24, 127.03, 119.42, 118.12, 100.51, 84.89, 81.74, 75.20, 71.79, 63.65, 47.05, 45.20, 32.82, 23.73, 19.61, 19.02.

LC-MS (ESI) Calculated [C₁₇H₁₇O₅]⁺: 301.1, found: 301.1;

R_f 0.25 (Hexanes:EtOAc = 65:35).



(S)-5-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-5-methyl-4-phenylfuran-2(5H)-one (SI-81). The title compound was obtained as a clear oil using **General Procedure F** (65 %).

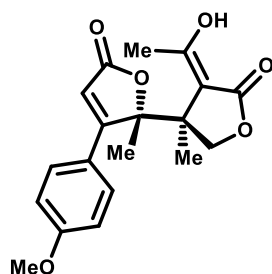
Mixture of Diastereomers (74:26):
Major Diastereomer (Enol):

¹H NMR (600 MHz, Chloroform-*d*) δ 12.04 (s, 1H), 7.51 – 7.43 (m, 3H), 7.40 – 7.36 (m, 2H), 6.12 (s, 1H), 4.03 (d, *J* = 10.2 Hz, 1H), 3.48 (d, *J* = 10.2 Hz, 1H), 2.24 (s, 3H), 1.85 (s, 3H), 1.32 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 176.78, 174.42, 171.75, 170.55, 132.61, 130.70, 129.50, 127.45, 120.61, 99.90, 93.54, 73.39, 48.21, 20.89, 20.69, 20.48.

LC-MS (ESI) Calculated $[\text{C}_{18}\text{H}_{19}\text{O}_5]^+$: 315.1, found: 315.1;

R_f 0.25 (Hexanes:Ether = 4:6).



(S)-5-((S,Z)-4-(1-hydroxyethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-4-(4-methoxyphenyl)-5-methylfuran-2(5H)-one (SI-82). The title compound was obtained as a clear oil using **General Procedure F** (75 %).

Mixture of Diastereomers (71:29):

Major and Minor Diastereomers (50:50):

¹H NMR (600 MHz, Chloroform-*d*) δ 12.04 – 11.98 (m, 1H), 11.94 (d, *J* = 0.9 Hz, 1H), 7.37 (dd, *J* = 8.6, 1.7 Hz, 2H), 7.34 – 7.31 (m, 2H), 7.02 (d, *J* = 8.8 Hz, 0H), 6.98 – 6.95 (m, 2H), 6.94 – 6.91 (m, 2H), 6.06 (s, 1H), 6.00 (s, 1H), 4.32 (d, *J* = 9.9 Hz, 1H), 4.13 (d, *J* = 10.2 Hz, 1H), 3.86 (s, 2H), 3.84 (s, 2H), 3.71 (d, *J* = 10.0 Hz, 1H), 3.49 (d, *J* = 10.2 Hz, 1H), 2.23 (d, *J* = 0.8 Hz, 3H), 1.99 (d, *J* = 0.8 Hz, 3H), 1.92 (s, 3H), 1.84 (s, 3H), 1.51 (s, 3H), 1.30 (s, 3H).

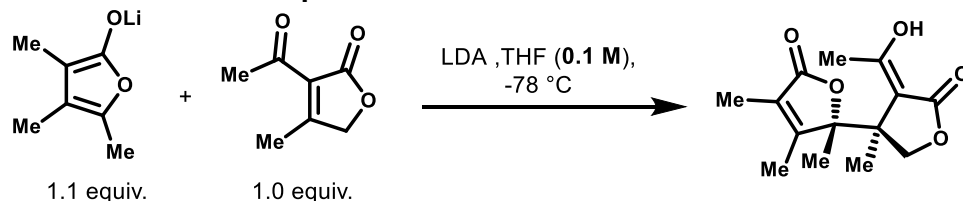
¹³C NMR (151 MHz, Chloroform-*d*) δ 176.14, 175.87, 173.59, 173.46, 170.91, 170.24, 169.97, 169.72, 169.60, 161.26, 161.03, 160.91, 128.60, 128.30, 123.92, 123.88, 118.44, 118.16, 114.25, 113.91, 99.45, 98.78, 92.61, 91.89, 73.10, 72.83, 55.00, 54.92, 48.74, 47.69, 20.89, 20.25, 20.21, 20.15, 19.84, 19.04.

LC-MS (ESI) Calculated $[\text{C}_{19}\text{H}_{21}\text{O}_6]^+$: 345.1, found: 345.1;

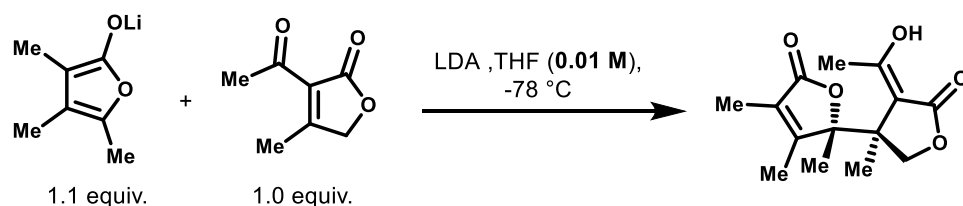
R_f 0.3 (Hexanes:EtOAc = 70:30).

Rapid Quenching Experiments

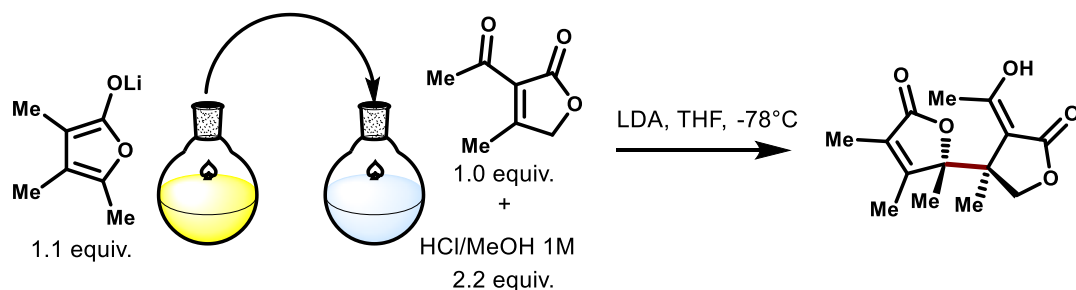
Figure 3a of the main manuscript file



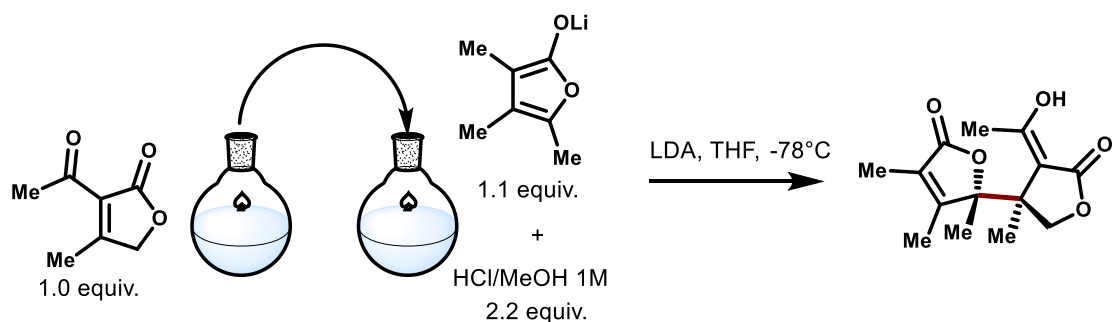
Entry 1 Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.11 mmol, 0.224 mL). Next, **SI-30** (0.11 mmol, 13.8 mg) was dissolved in 0.388 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, the enolate solution was rapidly injected (<1 second) into a solution of **SI-1** (0.10 mmol, 1.0 eq), dissolved in 9.4 mL of anhydrous THF at -78 °C. The reaction was rapidly stirred for 5 seconds before rapid injection (<1 second) of 1M HCl/MeOH (0.22 mmol, 0.220 mL). The mixture was then diluted with water (1 mL), and extracted with EtOAc (3x 3 mL). The combined organics were washed with brine, dried with MgSO₄, and concentrated *in vacuo*. **SI-46** was isolated via preparative TLC (98 % yield).



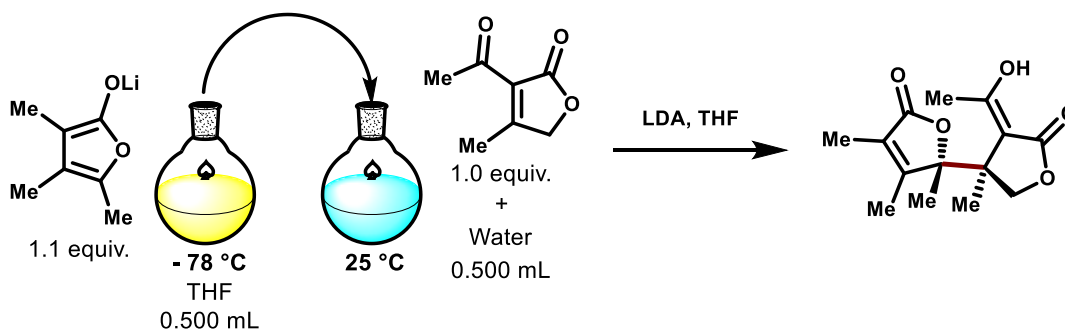
Entry 2 Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.11 mmol, 0.224 mL). Next, **SI-30** (0.11 mmol, 13.8 mg) was dissolved in 0.388 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, the enolate solution was rapidly injected (<1 second) into a solution of **SI-1** (0.10 mmol, 1.0 eq), dissolved in 9.4 mL of anhydrous THF at -78 °C. The reaction was rapidly stirred for 5 seconds before rapid injection (<1 second) of 1M HCl/MeOH (0.22 mmol, 0.220 mL). The mixture was then diluted with water (1 mL), and extracted with EtOAc (3x 3 mL). The combined organics were washed with brine, dried with MgSO₄, and concentrated *in vacuo*. 1,3,5-trimethoxybenzene (0.063 mmol, 10.6 mg) was added as an internal standard and the yield was determined from the crude ¹H NMR spectrum (98 % yield). ([1H NMR](#))



Entry 3 Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.11 mmol, 0.224 mL). Next, **SI-30** (0.11 mmol, 13.8 mg) was dissolved in 0.388 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, the enolate solution was rapidly injected (<1 second) into a solution of **SI-1** (0.10 mmol, 1.0 eq) in 0.180 mL anhydrous THF, and 1M HCl/MeOH (0.22 mmol, 0.220 mL) at -78 °C. The reaction was rapidly stirred for 5 seconds. Next, the mixture was diluted with water (1 mL), and extracted with EtOAc (3x 3 mL). The combined organics were washed with brine, dried with MgSO₄, and concentrated *in vacuo*. Mesitylene (0.1 mmol) was added as an internal standard and the yield was determined from the crude ¹H NMR spectrum (30 % yield). ([1H NMR](#))

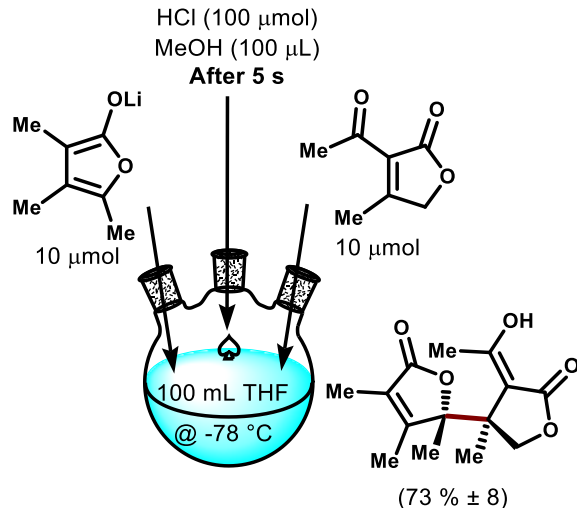


Entry 4 Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78°C and charged with LDA (0.11 mmol, 0.224 mL). Next, **SI-30** (0.11 mmol, 13.8 mg) was dissolved in 0.388 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, 1M HCl/MeOH (0.22 mmol, 0.220 mL) was added to the enolate solution. After 30 seconds, a solution of **SI-1** (0.10 mmol, 1.0 eq) in 0.180 mL anhydrous THF was rapidly injected (<1 second) and the resulting mixture was stirred for an additional 5 s. Next, the mixture was diluted with water (1 mL), and extracted with EtOAc (3x 3 mL). The combined organics were washed with brine, dried with MgSO_4 , and concentrated *in vacuo*. Mesitylene (0.1 mmol) was added as an internal standard and the yield was determined from the crude ^1H NMR spectrum ($<1\%$ yield/ NR). ([1H NMR](#))

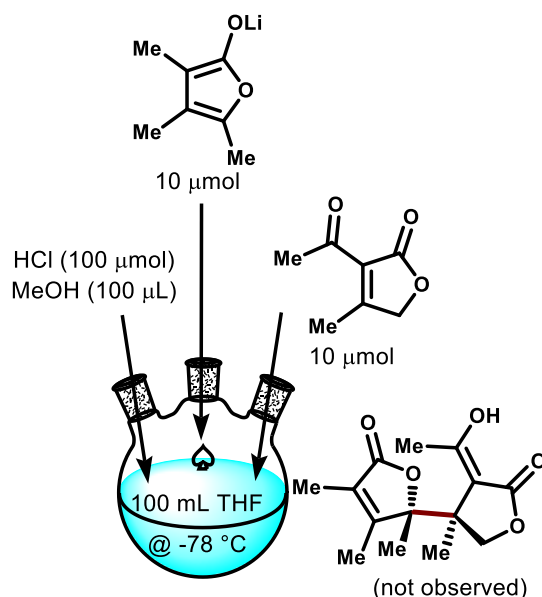


Entry 5 Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.11 mmol, 0.224 mL). Next, **SI-30** (0.11 mmol, 13.8 mg) was dissolved in 0.288 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, the enolate solution was rapidly injected (<1 second) into a solution of **SI-1** (0.10 mmol, 14.0 mg) in 0.500 mL H₂O at 25 °C. The reaction was rapidly stirred for 5 seconds before rapid injection (<1 second) of 1M HCl/MeOH (0.22 mmol, 0.220 mL). The mixture was then diluted with water (1 mL), and extracted with EtOAc (3x 3 mL). The combined organics were washed with brine, dried with MgSO₄, and concentrated *in vacuo*. Mesitylene (0.1 mmol) was added as an internal standard and the yield was determined from the crude ¹H NMR spectrum (35 % yield). (¹H NMR)

Figure 3c of the main manuscript file



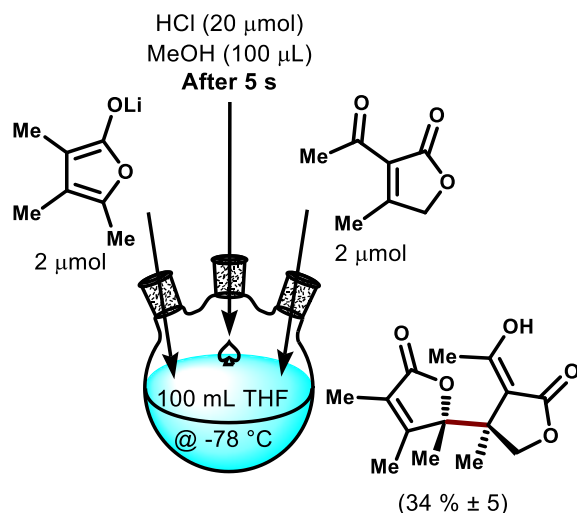
100 μ M Rapid Quench Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.10 mmol, 0.204 mL). Next, **SI-30** (0.10 mmol, 12.6 mg) was dissolved in 0.296 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, the enolate solution was diluted with anhydrous THF (0.500 mL) to a final concentration of 0.1 M. Next, the enolate solution (0.01 mmol, 0.100 mL) and a solution of **SI-1** (0.01 mmol) in anhydrous THF (0.100 mL) were simultaneously and rapidly injected (< 1s) into 100 mL of anhydrous THF at -78 °C. The reaction was stirred vigorously for 5 seconds before rapid injection (< 1s) of 1M HCl/MeOH (0.1 mmol, 0.100 mL). After 90 seconds, 1M NaHCO₃ aq. (0.15 mmol, 0.150 mL) was added and the reaction mixture was warmed to 25 °C. Next, 1,3,5-trimethoxybenzene (0.006 mmol, 0.100 mL, .063 M solution in THF) was added as an internal standard, the mixture was concentrated *in vacuo*, and the yield was determined from the crude ¹H NMR spectrum. This experiment was repeated in quadruplicate with an average yield of 74 % $\pm$ 8. (Replicate 1: [1H NMR](#), Replicate 2: [1H NMR](#), Replicate 3: [1H NMR](#), Replicate 4: [1H NMR](#))



A control reaction was conducted to ensure proton transfer from 10 equiv. of 1M HCl in MeOH outcompeted product formation.

Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 $^{\circ}\text{C}$ and charged with LDA (0.10 mmol, 0.204 mL). Next, **SI-30** (0.10 mmol, 12.6 mg) was dissolved in 0.296 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, the enolate solution was diluted with anhydrous THF (0.500 mL) to a final concentration of 0.1 M. Next, **Li•SI-30** (.01 mmol, 0.100 mL) was rapidly injected (< 1s) into a premixed solution of **SI-1** (.01 mmol) and 1M HCl/MeOH (0.1 mmol) in anhydrous THF (100 mL) at -78 $^{\circ}\text{C}$. After 90 seconds, 1M NaHCO_3 aq. (0.15 mmol, 0.150 mL) was added and the reaction mixture was warmed to 25 $^{\circ}\text{C}$. Next, 1,3,5-trimethoxybenzene (0.006 mmol, 0.100 mL, .063 M solution in THF) was added as an internal standard, the mixture was concentrated *in vacuo*, and the yield was determined from the crude ^1H NMR spectrum (0 %, no product observed). ([\$^1\text{H}\$ NMR](#))

Note: The presence of unreacted electrophile in the crude ^1H NMR spectrum excluded decomposition of starting material as an alternative explanation for the absence of product.



20 μ M Rapid Quench Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.10 mmol, 0.204 mL). Next, **SI-30** (0.10 mmol, 12.6 mg) was dissolved in 0.296 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, the enolate solution was diluted with anhydrous THF to a final concentration of 0.020 M. Next, the enolate solution (2.0 μ mol, 0.100 mL, 0.020M) and a solution of **SI-1** (2.0 μ mol, 0.100 mL, 0.020M) in anhydrous THF (0.100 mL) were simultaneously and rapidly injected (< 1s) into 100 mL of anhydrous THF at -78 °C. The reaction was stirred vigorously for 5 seconds before rapid injection (< 1s) of 1M HCl/MeOH (20 μ mol, 0.100 mL, 0.2 M). After 90 seconds, 0.2 M NaHCO₃ aq. (30 μ mol, 0.150 mL) was added and the reaction mixture was warmed to 25 °C. Next, 1,3,5-trimethoxybenzene (18.6 μ mol, 0.200 mL, 0.093 M solution in THF) was added as an internal standard, the mixture was concentrated *in vacuo*, and the yield was determined from the crude ¹H NMR spectrum. This experiment was repeated in triplicate with an average yield of 34 % $\pm$ 5. (Replicate 1: [1H NMR](#), Replicate 2: [1H NMR](#), Replicate 3: [1H NMR](#))

Rate Calculation

The relative amounts of **Li•SI-30** and **SI-1** were kinetically modeled on an Excel™ spreadsheet by a least-squares fitting of a single observation data point (73 $\pm$ 8% conversion) to the rate law rate = $k[\text{Li}\cdot\text{SI-30}][\text{SI-1}]$. The $[\text{Li}\cdot\text{SI-30}]$ was calculated from the percent conversion, assuming no other processes were taking place. The bimolecular rate constant was $k = 5.4 \pm 2 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$. The half-life was determined using equation 1, the half-life for a second order reaction. The half-life according to equation 1 is $t_{1/2} = 1.9 \pm 0.8 \text{ s}$, where $[\text{Li}\cdot\text{SI-30}]_0 = 100 \text{ } \mu\text{M}$.

(1)

$$t_{1/2} = \frac{1}{k [\text{Li}\cdot\text{SI-30}]}$$

The free energy of activation $\Delta G^\ddagger$ was calculated from the Eyring equation. The following form¹⁸ of the equation was used to convert the rate constant into a free energy barrier (equation 2) where $T = 195 \text{ K}$ (-78 °C), $k = 5.4 \pm 2 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$, and $\kappa = 1$. $\Delta G^\ddagger = 7.9 \pm 0.2 \text{ kcal/mol}$.

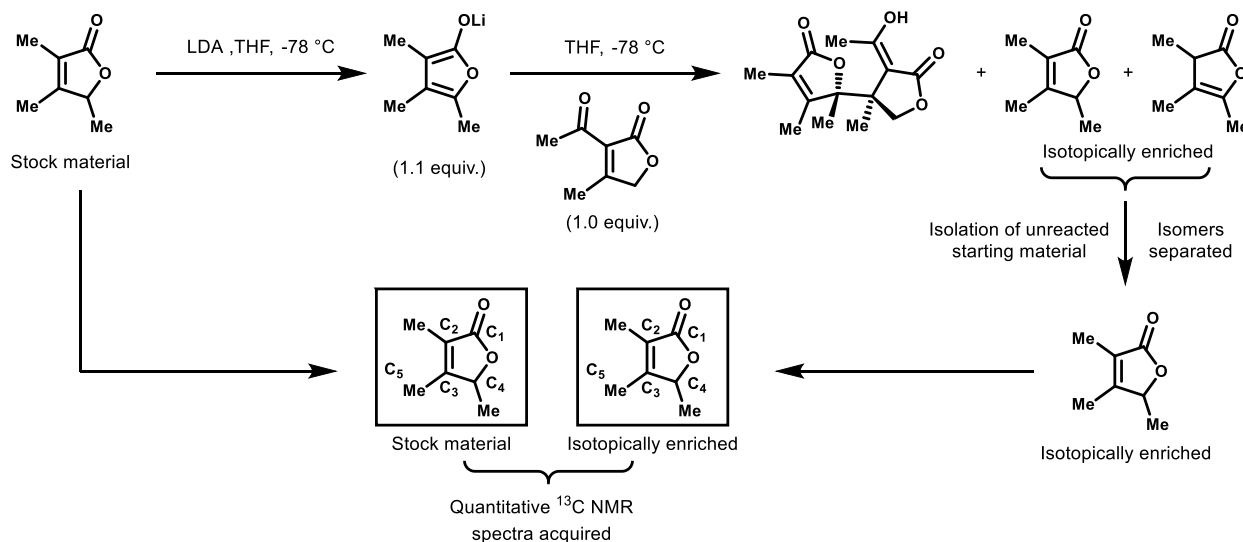
(2)

$$\Delta G^\ddagger = 4.576 \cdot T \cdot [10.319 + \log(\frac{T}{k})]$$

Replication of this was calculated at $33 \pm 7\%$ conversion, giving a rate constant $k = 5.0 \pm 2 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$, and a half-life $t_{1/2} = 10 \pm 3 \text{ s}$, where $[\text{Li}\cdot\text{SI-30}]_0 = 20 \text{ }\mu\text{M}$. The free energy of activation $\Delta G^\ddagger = 8.0 \pm 0.2 \text{ kcal/mol}$ with $T = 195 \text{ K}$ ($-78 \text{ }^\circ\text{C}$), $k = 5.0 \pm 2 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$, and $\kappa = 1$.

KIE Analysis

KIE Reaction Procedure



Procedure for SI-30 KIE: A 100 mL flask with a Teflon stir bar was flame dried and backfilled with argon. Next, a solution of diisopropylamine (1.37 mL, 9.7 mmol) in anhydrous THF (13.5 mL) was added and the flask was cooled to -78 °C. *n*-BuLi (8.88 mmol, 3.252 mL, 2.73 M) was then added dropwise (ca. 5 minutes) and the solution was allowed to stir for 1 hour at -78 °C. After 1 hour, **SI-30** (8.88 mmol, 1.118 g, 1.12 equiv.) in anhydrous THF (13 mL) was added dropwise (ca. 5 minutes) and the solution was allowed to stir for 1 hour at -78 °C. Next, **SI-1** (7.9 mmol, 1.106 g, 1.0 equiv.) in anhydrous THF was added dropwise (ca. 5 minutes). After 1 hour, the reaction was quenched with 1 M HCl/MeOH (8.88 mmol, 1M, 1.12 equiv.) and 1,3,5-trimethoxybenzene was added as an internal standard. Next, the mixture was diluted with water (10 mL), and extracted 3x with EtOAc (15 mL). The combined organics were washed with brine, dried with MgSO₄, and concentrated in vacuo. A crude ¹H NMR spectrum was then taken and the relative intensities of remaining **SI-30** and its olefin isomer to the internal standard were used to determine the fractional conversion (Replicate 1: ¹H NMR, Replicate 2: ¹H NMR). Next, unreacted **SI-30** was recovered from the reaction mixture via column chromatography. Samples for isotopically enriched and stock material were prepared (see below) and quantitative ¹³C NMR spectra were acquired. The above procedure was repeated in duplicate.

Procedure for SI-1 KIE: A 100 mL flask with a Teflon stir bar was flame dried and backfilled with argon. Next, a solution of diisopropylamine (2.47 mL, 17.5 mmol) in anhydrous THF (32 mL) was added and the flask was cooled to -78 °C. *n*-BuLi (15.97 mmol, 5.91 mL, 2.70 M) was then added dropwise (ca. 5 minutes) and the solution was allowed to stir for 1 hour at -78 °C. After 1 hour, **SI-30** (15.94 mmol, 1.708 g, 1.00 equiv.) in anhydrous THF (12 mL) was added dropwise (ca. 5 minutes) and the solution was allowed to stir for 1 hour at -78 °C. Next, a flame dried 100 mL flask with a Teflon stir bar was charged with **SI-1** (17.53 mmol, 2.457 g, 1.10 equiv.) and anhydrous THF (44 mL) and cooled to -78 °C. The solution of **SI-30** enolate was then cannulated under positive pressure (ca. 1 min) into the rapidly stirring solution of **SI-1**. After 1 hour, the reaction was quenched with 1 M HCl/MeOH (8.88 mmol, 1M, 1.12 equiv.) and 1,3,5-trimethoxybenzene was added as an internal standard. Next, the mixture was diluted with water (10 mL), and extracted 3x with EtOAc (30 mL). The combined organics were washed with brine, dried with MgSO₄, and concentrated in vacuo. A crude ¹H NMR spectrum was then taken and the relative intensities of

remaining **SI-1** to the internal standard was used to determine the fractional conversion (¹H NMR). Next, unreacted **SI-1** was recovered from the reaction mixture via preparative HPLC. Samples for isotopically enriched and stock material were prepared (see below) and quantitative ¹³C NMR spectra were acquired.

Note: Given that the reaction achieves high conversion within 5 seconds under dilute conditions, (see [Kinetics](#)) a slight excess of the analyte (**SI-30** or **SI-1**) was required to ensure enough material could be recovered for quantitative ¹³C NMR measurements. Thus, although the fractional conversions of **SI-30** and **SI-1** were 80 ± 1.6%, 83 ± 1.4%, and 87 ± 1.6% the yields relative to the limiting reagent were 90 ± 1.6%, 93 ± 1.4%, and 96 ± 1.6%.

Quantitative NMR Measurements

Quantitative NMR measurements were performed on a Bruker AVIII HD-600 equipped with a 5mm DCH Cryoprobe. All samples were prepared using a constant amount of analyte (77.0 mg) in 5 mm NMR tubes filled with chloroform-d to a constant height of 5.0 cm. The ¹³C spectra were recorded at 150.92 MHz with inverse-gated decoupling. A T₁ measurement was performed on each sample to ensure that the relaxation rates did not change from sample to sample. Integrations were determined numerically using a constant integration region for each peak of 10 times the width at half-height. A zeroth order baseline correction was generally applied but in no case was the first order (tilt) correction applied.

The ¹³C spectra of **SI-30** were taken at a controlled temperature of 298.0 K using 200-s delay (200 seconds > 5*T₁) between calibrated 90° pulses. To obtain a minimal digital resolution of 5 points across the peak at half-height, a 14.9999-s acquisition time was used and 999996 points were collected. The digital resolution was zero-filled to 2048K points before Fourier transformation.

Calculations and Results

The NMR data was processed off-line using MestReNova software. No baseline correction was applied, no apodization (line-broadening) was applied, and in no case was a linear correction applied for bias (zeroth order) nor slope (first order). The raw data was zero-filled to 2048K points before Fourier transformation. The fractional conversion, raw integrations, R/R₀'s, and KIEs and all their respective deviations and errors are shown in the following series of tables. The integrations for peaks in **SI-30** were set to relative integrations of 1.0000 for the C₅ methyl carbon (see above), and the averaged results from six spectra for each compound are shown in the tables. The relative changes in isotopic composition (R/R₀) at each position in “*enrich*” **SI-30** were calculated as the ratio of average integrations relative to the “*stock*” **SI-30**. The standard deviations Δ(R/R₀) were calculated from equation 1. In this equation *enrich* is the average integration for each carbon in the isotopically enriched ¹³C **SI-30**, *stock* is the average integration for each carbon in starting material **SI-30** from the original batch, and Δ*enrich* and Δ*stock* are the standard deviations in the integrations for the *enrich* and *stock*, respectively.

$$D(R/R_0) = (R/R_0) \times \sqrt{\left(\frac{\Delta \text{enrich}}{\text{enrich}}\right)^2 + \left(\frac{\Delta \text{stock}}{\text{stock}}\right)^2} \quad (1)$$

All KIEs for **SI-30** were based on analyses of recovered starting materials. In such cases, the KIEs were calculated from equation 2, with the standard deviations calculated, and it varies from 0 to 1.¹⁹ From equation 2, F denotes the fractional amount of reaction or %conversion/100, and R/R₀ denotes isotope ratios of the unreacted substrate (recovered **SI-30**) and the initial substrate (**SI-30** from the original batch). Error analysis on equation 2 is shown in equations 3, 4, and 5.

$$\text{KIE}_{\text{calcd}} = \frac{\ln(1 - F)}{\ln[(1 - F)R/R_0]} \quad (2)$$

$$\text{DKIE}_F = \frac{\partial \text{KIE}}{\partial F} = - \frac{1}{1 - F} \times \frac{\ln(R/R_0)}{\ln^2[(1 - F)R/R_0]} \quad (3)$$

$$\text{DKIE}_R = \frac{\partial \text{KIE}}{\partial (R/R_0)} = - \frac{1}{R/R_0} \times \frac{\ln(1 - F)}{\ln^2[(1 - F)R/R_0]} \quad (4)$$

$$\text{DKIE} = \text{KIE} \times \sqrt{\left(\frac{\text{DKIE}_R}{\text{KIE}}\right)^2 + \left(\frac{\text{DKIE}_F}{\text{KIE}}\right)^2} \quad (5)$$

The uncertainties obtained in this way are approximately 95% confidence limits when based on six spectra. Actual 95% confidence limits may be obtained by multiplying the uncertainties by 1.0496.

Table S1. Conversion, Integrations, R/R₀'s ¹³C KIEs, and Uncertainties for SI-30, Set 1.

BH3_049 Intermolecular recovered starting material KIEs

F	0.83
1-F	0.17
DF	0.014

Reisolated Starting Material BH3_049_Enrich

Peak d(ppm)	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
174.5	0.9296	0.9296	0.934	0.933	0.9288	0.9291	0.931	0.002
161.0	0.9264	0.9347	0.9339	0.9345	0.9235	0.9267	0.930	0.005
122.9	0.9463	0.9441	0.9559	0.9473	0.9488	0.9587	0.950	0.006
79.9	0.9474	0.9449	0.9456	0.9494	0.9445	0.9491	0.947	0.002
18.4	0.9693	0.9693	0.9833	0.9734	0.9723	0.9796	0.975	0.006
11.9	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.000	0.000
8.6	1.0241	1.0237	1.0236	1.0232	1.0213	1.0247	1.023	0.001

Starting Matieral from Original Bottle BH3_049_Stock

Peak d(ppm)	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
174.5	0.9379	0.9326	0.924	0.9304	0.9259	0.9351	0.931	0.005
161.0	0.9304	0.9294	0.9295	0.9302	0.9322	0.9297	0.930	0.001
122.9	0.9413	0.9475	0.9415	0.9423	0.9435	0.9499	0.944	0.004
79.9	0.963	0.964	0.9506	0.9452	0.9472	0.9544	0.954	0.008
18.4	0.9720	0.9729	0.9687	0.9708	0.9706	0.9780	0.972	0.003
11.9	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.000	0.000
8.6	1.0115	1.0229	1.0165	1.0079	1.0096	1.0207	1.015	0.006

Calculated KIEs and Uncertainties

Peak d(ppm)	KIE	DKIE _F	R/R ₀	D(R/R ₀)	DKIE _R	DKIE
174.5	1.000	0.0000	1.000	0.006	0.004	0.004
161.0	1.000	0.0000	1.000	0.005	0.003	0.003
122.9	1.003	-0.0002	1.006	0.007	0.004	0.004
79.9	0.996	0.0002	0.992	0.009	0.005	0.005
18.4	1.001	-0.0001	1.002	0.007	0.004	0.004
11.9	1.000	0.0000	1.000	0.000	0.000	0.000
8.6	1.005	-0.0002	1.008	0.006	0.004	0.004

Table S2. Conversion, Integrations, R/R₀'s, ¹³C KIEs, and Uncertainties for SI-30, Set 2.

BH3_045 Intermolecular recovered starting material KIEs

F	0.8
1-F	0.2
DF	0.016

Reisolated Starting Material BH3_045_Enrich

Peak d(ppm)	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
174.5	0.9849	0.9890	0.9873	0.9862	0.9840	0.9820	0.986	0.002
161.0	1.0274	1.0189	1.0237	1.0248	1.0233	1.0211	1.023	0.003
122.9	1.0715	1.0699	1.0703	1.0680	1.0663	1.0676	1.069	0.002
79.9	1.1257	1.1304	1.1237	1.1249	1.1258	1.1252	1.126	0.002
18.4	0.9533	0.9556	0.9562	0.9534	0.9550	0.9608	0.956	0.003
11.9	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.000	0.000
8.6	1.0372	1.0365	1.0387	1.0319	1.0295	1.0349	1.035	0.003

Starting Material from Original Bottle BH3_045_Stock

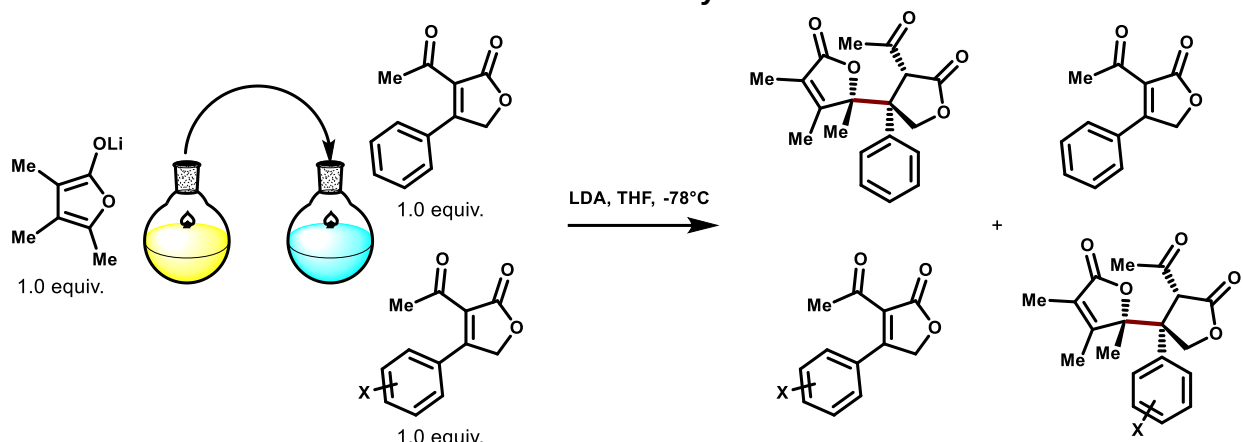
Peak d(ppm)	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
174.5	0.9821	0.9819	0.9812	0.9812	0.9788	0.9744	0.980	0.003
161.0	1.0255	1.0196	1.0122	1.0104	1.0162	1.0117	1.016	0.006
122.9	1.0663	1.0683	1.0628	1.0630	1.0644	1.0629	1.065	0.002
79.9	1.1375	1.1362	1.1382	1.1343	1.1340	1.1252	1.134	0.005
18.4	0.9620	0.9549	0.9609	0.9617	0.9636	0.9562	0.960	0.003
11.9	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.000	0.000
8.6	1.0041	0.9974	1.0015	0.9966	1.0032	0.9971	1.000	0.003

Calculated KIEs and Uncertainties

Peak d(ppm)	KIE	DKIE _F	R/R ₀	D(R/R ₀)	DKIE _R	DKIE
174.5	1.004	-0.0002	1.006	0.004	0.002	0.002
161.0	1.004	-0.0002	1.007	0.006	0.004	0.004
122.9	1.003	-0.0001	1.004	0.003	0.002	0.002
79.9	0.995	0.0002	0.993	0.005	0.003	0.003
18.4	0.997	0.0001	0.996	0.005	0.003	0.003
11.9	1.000	0.0000	1.000	0.000	0.000	0.000
8.6	1.022	-0.0011	1.035	0.005	0.003	0.003

Table S3 Conversion, Integrations, R/R ₀ , 13C KIEs, and Uncertainties for SI-1								
F	0.87							
1-F	0.13							
Delta F	0.112							
Reisolated Starting Material								
Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
194	1.0552	1.0585	1.0575	1.0547	1.0504	1.0535	1.055	0.003
174	1.0625	1.0612	1.0594	1.0606	1.0653	1.0622	1.062	0.002
171	1.0822	1.085	1.0806	1.0836	1.0856	1.0819	1.083	0.002
124	1.0421	1.0418	1.042	1.0462	1.0398	1.0427	1.042	0.002
72	1.0276	1.0318	1.0293	1.0287	1.0245	1.0287	1.028	0.002
29	1.0056	1.0074	1.0017	1.0097	1.0057	1.0054	1.006	0.003
14	1	1	1	1	1	1	1.000	0.000
Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
194	1.0427	1.0425	1.0413	1.0426	1.0409	1.0446	1.042	0.001
174	1.0514	1.0533	1.0525	1.0527	1.0536	1.0489	1.052	0.002
171	1.0879	1.0868	1.0871	1.0883	1.0843	1.0872	1.087	0.001
124	1.0421	1.0454	1.0411	1.0416	1.0429	1.0393	1.042	0.002
72	1.0464	1.0389	1.0394	1.0396	1.0424	1.0425	1.042	0.003
29	1.0118	1.0182	1.0138	1.0157	1.0153	1.0109	1.014	0.003
14	1	1	1	1	1	1	1.000	0.000
Calculated KIEs and Uncertainties								
Peak	KIE	ΔKIE_F	R/R ₀	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE		
194	1.006	-0.0025	1.012	0.003	0.001	0.003		
174	1.005	-0.0019	1.009	0.003	0.001	0.002		
171	0.998	0.0007	0.997	0.002	0.001	0.001		
124	1.000	-0.0001	1.000	0.003	0.001	0.001		
72	0.994	0.0026	0.987	0.004	0.002	0.003		
29	0.996	0.0017	0.992	0.004	0.002	0.002		
14	1.000	0.0000	1.000	0.000	0.000	0.000		

Hammett Analysis



Competition Hammett Procedure: Hammett plots were generated using an adapted procedure from Yamataka and coworkers.²⁰ A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.10 mmol, 0.204 mL, 0.49 M). To the solution of LDA was added **SI-30** (0.10 mmol, 12.6 mg) in 0.296 mL anhydrous THF. The resulting mixture was stirred for 1 hour at -78 °C. Next, an additional 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with both (X = H) **SI-4** (0.1 mmol, 20.2 mg) in 0.250 mL anhydrous THF and an aromatic-substituted butenolide electrophile (**SI-5**, **SI-6**, **SI-7**, **SI-8**, or **SI-9**) (0.1 mmol) in 0.250 mL anhydrous THF. Next, the solution containing **Li•SI-30** was rapidly transferred (< 5 seconds) to the stirring solution of competing aromatic butenolide electrophiles. After stirring for 1 hour, the reaction was quenched with 0.220 mL of 1M HCl/MeOH. Next, 1,3,5-trimethoxybenzene was added as an internal standard and the mixture was diluted with water (0.5 mL) and extracted 3x with EtOAc (3 mL). The combined organics were washed with brine, dried with MgSO₄, and concentrated in vacuo. The relative intensities of the remaining electrophiles to the internal standard (determined by ¹H NMR) were used to determine the fraction of reaction, *f*, and the rate ratio was calculated according to the equation:

$$\frac{k_x}{k_H} = \frac{\log(1 - f_x)}{\log(1 - f_H)}$$

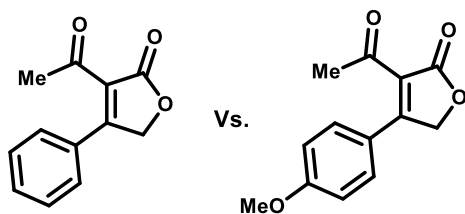
Where,

$$f_x = \frac{P_x}{P_x + P_H}$$

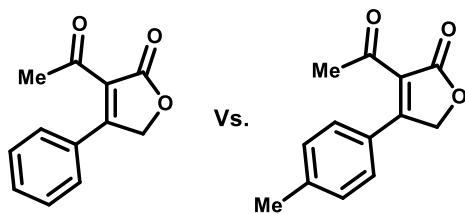
$$f_x = \frac{(0.1 - E_x)}{((0.1 - E_x) + (0.1 - E_H))}$$

Where, *P_x* and *P_H* are the amounts of product after competition and *E_x* and *E_H* are the amounts of remaining electrophiles (in mmol) after competition. The competition reaction was repeated in triplicate for each substituted electrophile (X = *p*-OMe, *p*-Me, *p*-F, *p*-Cl, and *p*-Br).

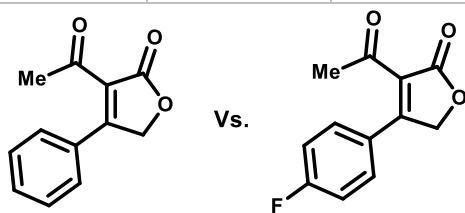
Results



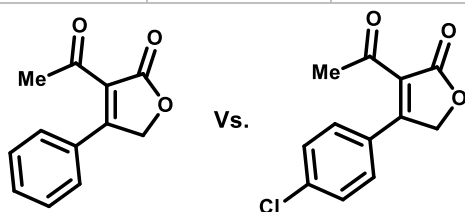
	E_H (mmol)	f_H	E_{OMe} (mmol)	f_{OMe}
Replicate 1	0.043	0.564	0.056	0.435
Replicate 2	0.044	0.560	0.056	0.440
Replicate 3	0.040	0.555	0.052	0.444
Average	0.0423	0.559	0.054666667	0.440
Std. Dev.	0.00169	0.00359	0.00188	0.0036



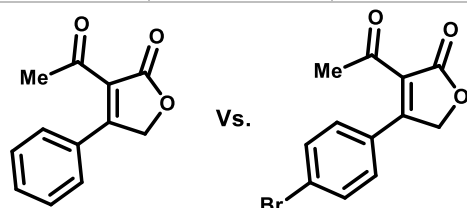
	E_H (mmol)	f_H	E_{Me} (mmol)	f_{Me}
Replicate 1	0.050	0.537	0.057	0.462
Replicate 2	0.050	0.526	0.055	0.473
Replicate 3	0.053	0.566	0.064	0.433
Average	0.051	0.543	0.0586	0.456
Std. Dev.	0.00141	0.0168	0.0038	0.0168



	E_H (mmol)	f_H	E_F (mmol)	f_F
Replicate 1	0.051	0.449	0.040	0.550
Replicate 2	0.049	0.463	0.041	0.536
Replicate 3	0.051	0.466	0.044	0.533
Average	0.050	0.459	0.0416	0.540
Std. Dev.	0.00094	0.007	0.0016	0.0074

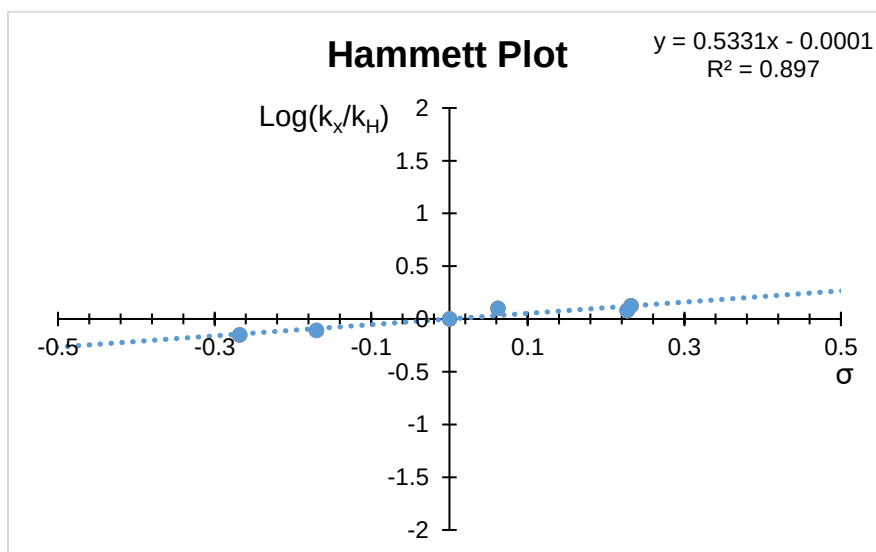


	E_H (mmol)	f_H	E_{Cl} (mmol)	f_{Cl}
Replicate 1	0.053	0.456	0.044	0.543
Replicate 2	0.054	0.464	0.047	0.535
Replicate 3	0.049	0.485	0.046	0.514
Average	0.052	0.468	0.0456	0.531
Std. Dev.	0.0021	0.012	0.0012	0.012



	E_H (mmol)	f_H	E_{Br} (mmol)	f_{Br}
Replicate 1	0.060	0.439	0.049	0.560
Replicate 2	0.053	0.470	0.047	0.530
Replicate 3	0.066	0.441	0.057	0.558
Average	0.059	0.450	0.051	0.549
Std. Dev.	0.0053	0.0138	0.00432	0.0139

$p-X$	σ	Avg. f_H	Avg. f_x	k_x/k_H	$\log(k_x/k_H)$
$p\text{-OMe}$	-0.268	0.559	0.440	0.706	-0.151
$p\text{-Me}$	-0.170	0.543	0.456	0.777	-0.109
$p\text{-H}$	0	0.5	0.5	1	0
$p\text{-F}$	0.062	0.459	0.540	1.260	0.101
$p\text{-Cl}$	0.227	0.468	0.531	1.196	0.0780
$p\text{-Br}$	0.232	0.450	0.549	1.332	0.124

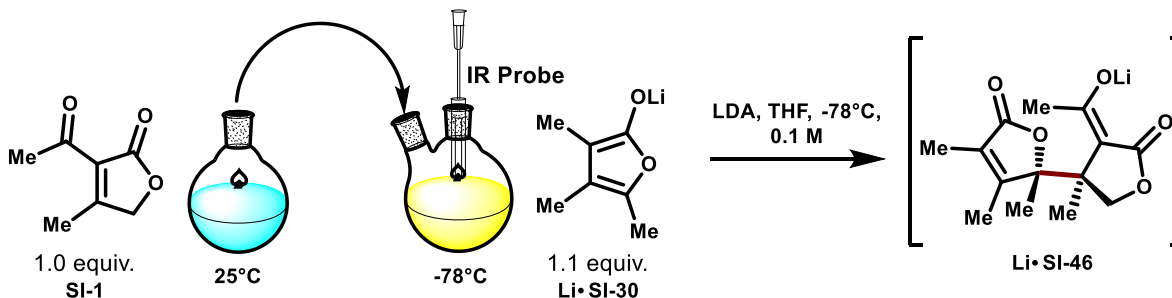


In Situ Infrared Spectroscopy

Instrumentation

In-situ FT-IR analysis was performed using a Mettler-Toledo ReactIR™ 45m instrument fitted with a DST 6.35 mm DiComp ATR probe. The ReactIR instrument's MCT detector cooled with liquid nitrogen and purged with dry gaseous nitrogen for at least two hours before use. The ReactIR recorded spectra using rapid-scan mode, allowing the instrument to record a spectrum approximately every one second (~1 s). Real time progress could not be observed during this rapid-scan mode.

Normal Addition Procedure



The probe was cleaned, then placed through a Teflon fitting and then inserted into a 3-neck flask containing anhydrous THF (1 mL). The system was purged with argon prior to cooling to -78 °C. After allowing approximately 10 minutes for temperature equilibration, a background spectrum was recorded. **Li•SI-30** (0.33 mmol, 41.5 mg) in anhydrous THF (1 mL) prepared separately, was then added to the flask. After 10 minutes, **SI-1** (0.3 mmol, 42.0 mg) in anhydrous THF (1 mL) was rapidly injected into the flask. The reaction was quenched after 10 minutes and spectra were recorded for an additional two minutes. After this time, recording using rapid-scan mode was stopped.

It should be noted that proper stirring was ensured to maximize mixing. Care was also taken to ensure the needle was inside the solution when **SI-1** was rapidly injected.

Raw ReactIR absorbance data was obtained from the Mettler-Toledo iC IR software. No transformation (negative second derivative function) of the data was performed. The multi-component analysis algorithm, ConclRt, was not used. Raw absorbance data for **Li•SI-30** and **SI-1** was then normalized, scaled, and shifted so that it fit the initial and final concentrations, creating a concentration vs time profile for the reaction. The initial concentration was assumed to be the theoretical concentration at the start of reaction. The ending conversion was assumed to be complete conversion due to the absence of any reagent peaks. **Li•SI-30** can be described with three distinct bands (1755 cm⁻¹, 1650 cm⁻¹, and 1620 cm⁻¹) in the region from 1500 cm⁻¹ to 1800 cm⁻¹ with the 1620 cm⁻¹ band being the most intense. The reaction progress was monitored by FTIR using a single peak for **Li•SI-30** at 1620 cm⁻¹. Rates of disappearance of **Li•SI-30** were obtained by initial rates from the peak at 1620 cm⁻¹ and from shoulders (± 4 cm⁻¹) at 1624 cm⁻¹ and 1616 cm⁻¹. The rates of disappearance of **Li•SI-30** at 1624 cm⁻¹, 1620 cm⁻¹, and 1616 cm⁻¹ were 0.032 M s⁻¹, 0.033 M s⁻¹, and 0.036 M s⁻¹, respectively. The average rate of disappearance was 0.034 ± 0.001 M s⁻¹. The error was determined by taking the standard deviation and dividing by the square root of 3 (n = 3 samples).

The intermediate product (**Li•SI-46**) has three distinct peaks, 1747 cm⁻¹, 1669 cm⁻¹, and 1542 cm⁻¹, in the region from 1500 cm⁻¹ to 1800 cm⁻¹. The 1747 cm⁻¹ peak has a slight overlap with **SI-1** (1762 cm⁻¹). The 1669 cm⁻¹ peak has a slight overlap with **Li•SI-30** (1650 cm⁻¹). The 1542 cm⁻¹ band was isolated with no peaks in its vicinity. The rate of formation of **Li•SI-46** was determined from the 1542 cm⁻¹ band and from shoulders (± 4 cm⁻¹). The bands of 1546 cm⁻¹, 1542 cm⁻¹, 1538 cm⁻¹, and 1534 cm⁻¹ gave rates of product formation of 0.030 M s⁻¹, 0.030 M s⁻¹,

0.029 M s⁻¹, and 0.029 M s⁻¹, respectively. The average of these initial rates was 0.030 ± 0.001 M s⁻¹.

The combined average rate for disappearance of **Li•SI-30** and formation of **Li•SI-46** was 0.032 ± 0.001 M s⁻¹. This rate was converted to a bimolecular rate constant by dividing the rate by the concentration of **Li•SI-30** [**Li•SI-30**] = 0.1 M and by the concentration of **SI-1** [**SI-1**] = 0.1 M, to get a bimolecular rate constant, **k = 3.2 ± 0.1 M⁻¹ s⁻¹**. The half-life was determined using equation 1, the half-life for a second order reaction. The half-life according to equation 1 is **t_{1/2} = 3.1 s**, where [**Li•SI-30**]₀ = 0.1 M. t_{1/2}

(1)

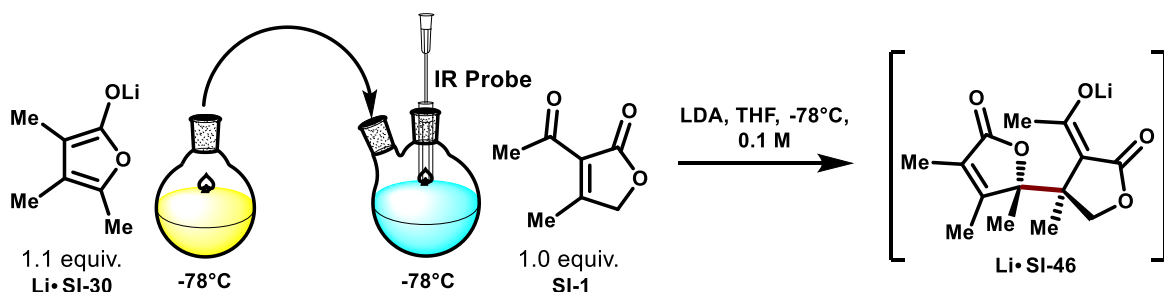
$$t_{1/2} = \frac{1}{k [\text{Li}\cdot\text{SI-30}]}$$

The free energy of activation ($\Delta G^\ddagger$) was calculated from the Eyring equation. The following form¹⁸ of the equation was used to convert the rate constant into a free energy barrier (equation 2) where T = 195 K (-78 °C), $k = 3.2 \pm 0.1 \text{ M}^{-1} \text{ s}^{-1}$, and $\kappa = 1$. **$\Delta G^\ddagger = 10.8 \pm 0.1 \text{ kcal/mol}$** .

(2)

$$\Delta G^\ddagger = 4.576 \cdot T \cdot [10.319 + \log(\frac{T}{k})]$$

Reverse Addition Procedure



In a similar fashion to the normal addition procedure, the reverse addition procedure was setup as follows. The probe was cleaned, then placed through a Teflon fitting and then inserted into a 3-neck flask containing anhydrous THF (1 mL). The system was purged with argon prior to cooling to -78°C . After allowing approximately 10 minutes for temperature equilibration, a background spectrum was recorded. **SI-1** (0.3 mmol, 42.0 mg) in anhydrous THF (1 mL), was then added to the flask. After 10 minutes, **Li•SI-30** (0.33 mmol, 41.5 mg), in anhydrous THF (1 mL), prepared separately, was rapidly injected into the flask. The reaction was quenched after 10 minutes and spectra were recorded for an additional two minutes. After this time, recording using rapid-scan mode was stopped.

Raw ReactIR absorbance data was obtained from the Mettler-Toledo iC IR software. No transformation (negative second derivative function) of the data was performed. The multi-component analysis algorithm, ConclRt, was not used. Raw absorbance data for electrophilic butenolide and product was then normalized, scaled, and shifted so that it fit the initial and final concentrations, creating a concentration versus time profile for the reaction. The initial concentration was assumed to be the theoretical concentration at the start of reaction. The ending conversion was assumed to be complete conversion due to the absence of any reagent peaks. The reaction progress was monitored by FTIR using multiple peaks for **SI-1** at 1788 cm^{-1} , 1762 cm^{-1} , 1691 cm^{-1} , and 1628 cm^{-1} . The largest intensity peak for **SI-1** was at 1762 cm^{-1} . The intermediate product (**Li•SI-46**) consists of three distinct peaks 1747 cm^{-1} , 1669 cm^{-1} , and 1542 cm^{-1} , in the region from 1500 cm^{-1} to 1800 cm^{-1} .

The most intense peak for **SI-1** (1762 cm^{-1}) was used to measure the rate of disappearance (initial rates) of **SI-1**. In this peak were three chemical shifts 1766 cm^{-1} , 1762 cm^{-1} , and 1758 cm^{-1} , that gave initial rates of 0.032 M s^{-1} , 0.037 M s^{-1} , and 0.044 M s^{-1} , respectively. The average of these initial rates was $0.038 \pm 0.004\text{ M s}^{-1}$. The error was determined by taking the standard deviation and dividing by the square root of 3 ($n = 3$ samples).

The rate of formation of **Li•SI-46** was determined from the 1542 cm^{-1} band and from shoulders ($\pm 4\text{ cm}^{-1}$). 1546 cm^{-1} , 1542 cm^{-1} , 1538 cm^{-1} , and 1534 cm^{-1} , gave initial rates of 0.030 M s^{-1} , 0.045 M s^{-1} , 0.045 M s^{-1} , and 0.045 M s^{-1} , respectively. The average of these initial rates was $0.041 \pm 0.004\text{ M s}^{-1}$.

The combined average rate for disappearance of **SI-1** and formation of **Li•SI-46** was $0.040 \pm 0.003\text{ M s}^{-1}$. This rate was converted to a bimolecular rate constant by dividing the rate by the concentration of **Li•SI-30** [**Li•SI-30**] = 0.1 M and by the concentration of **SI-1** [**SI-1**] = 0.1 M , to get a bimolecular rate constant $k = 4.0 \pm 0.3\text{ M}^{-1}\text{ s}^{-1}$. The half-life was determined using equation 1, the half-life for a second-order reaction. The half-life according to equation 1 is $t_{1/2} = 2.5\text{ s}$, where [**Li•SI-30**] $_0 = 0.1\text{ M}$.

(1)

$$t_{1/2} = \frac{1}{k [\text{Li•SI-30}]}$$

The free energy of activation ($\Delta G^\ddagger$) was calculated from the Eyring equation. The following form¹⁸ of the equation was used to convert the rate constant into a free energy barrier (equation 2) where $T = 195 \text{ K}$ (-78°C), $k = 4.0 \pm 0.3 \text{ M}^{-1} \text{ s}^{-1}$, and $\kappa = 1$. $\Delta G^\ddagger = 10.8 \pm 0.1 \text{ kcal/mol}$.

(2)

$$\Delta G^\ddagger = 4.576 \cdot T \cdot [10.319 + \log(\frac{T}{k})]$$

Combined Normal and Reverse Addition Results

The average of both normal and reverse addition experiments show a rate $k = 3.6 \pm 0.2 \text{ M}^{-1} \text{ s}^{-1}$. The $t_{1/2} = 2.8 \text{ s}$ with $[\text{Li}\cdot\text{SI-30}]_0 = 0.1 \text{ M}$. Using equation 2, this translates into a free energy barrier of $\Delta G^\ddagger = 10.8 \pm 0.1 \text{ kcal/mol}$, where $T = 195 \text{ K}$ (-78°C), $k = 3.6 \pm 0.2 \text{ M}^{-1} \text{ s}^{-1}$, and $\kappa = 1$.

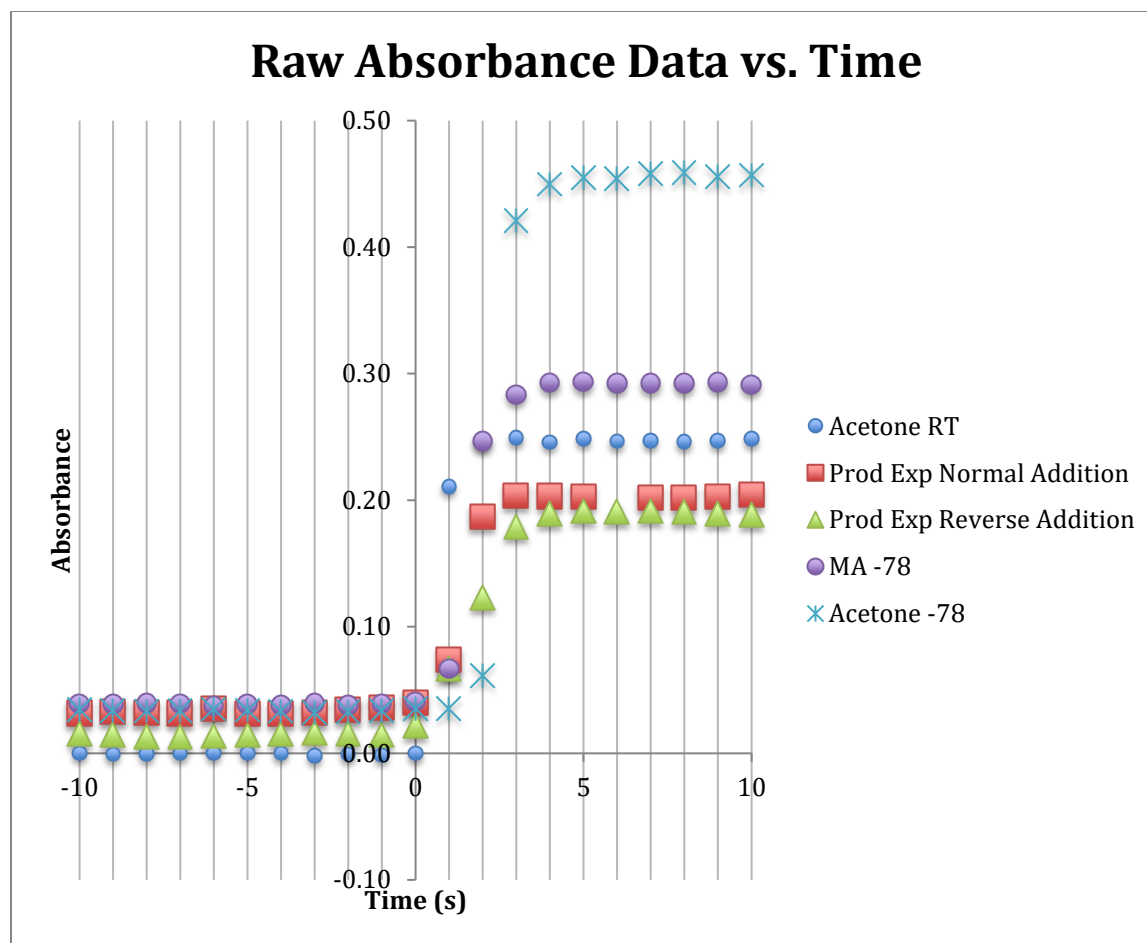
Analyte Signal Delay

Kinetic data acquired, via ReactIR spectroscopy for the “normal” addition reaction, shows **Li•SI-30** was present and immediately ($\sim 4 \text{ s}$) disappears upon addition of **SI-1**. **SI-1** does not appear to be seen in the spectrum when added to **Li•SI-30** (normal addition). The **SI-1** peak appears at 1762 cm^{-1} as it is an intense carbonyl stretch and should have been seen, however it was not observed. One explanation is that it overlapped with nearby intermediate product peak at 1747 cm^{-1} . In that case, the “reverse” was tried to see if the reagent that was being added could be observed.

A repeat of kinetic data was acquired via ReactIR spectroscopy for the “reverse” addition reaction. It shows **SI-1** present and immediately ($\sim 4 \text{ s}$) disappears upon addition of **Li•SI-30**. It was expected that **Li•SI-30** could be observed since it has a strong carbonyl stretch at 1620 cm^{-1} with no other reagent or product peaks in the vicinity, however it was not observed.

A series of control experiments showed that when a reagent such as acetone or methyl acrylate was added to the ReactIR probe, it took several ($\sim 4 \text{ s}$) to reach maximum signal. For instance, neat acetone ($25 \mu\text{L}$) was added to 4 mL of ethanol at 25°C and took $\sim 3 \text{ s}$ for the signal at 1714 cm^{-1} to reach its maximum intensity. In a separate experiment, 4 mL of ethanol was cooled to -78°C . The reactIR was used to look at the addition of a reagent to ethanol at -78°C . Using the same rapid-scan mode, $25 \mu\text{L}$ of neat acetone was injected into ethanol at -78°C . It took the carbonyl stretch at 1714 cm^{-1} $\sim 4 \text{ s}$ to reach a maximum signal strength. In a similar manner $25 \mu\text{L}$ of neat methyl acrylate was added to ethanol at -78°C and it took the carbonyl stretch at 1730 cm^{-1} $\sim 4 \text{ s}$ to reach a maximum signal. The acetone peak at 1714 cm^{-1} overlapped with methyl acrylate peak at 1730 cm^{-1} but the two were both distinguishable when both reagents were present.

The time it took for these reagents to reach maximum signal was also the same amount of time that it took for the reaction between **SI-1** and **Li•SI-30** to reach “observed completion”. Thus, the observed ReactIR results are equivalent to simply adding a solution of product (in this case **Li•SI-46**) to the ReactIR probe. This ultimately indicated that the reaction was complete within 4 seconds but an accurate rate could not be measured —since the addition of any reagent takes a few seconds to reach a maximum signal.



The graph above shows raw absorbance versus time for the series of experiments described above. The blue dots show acetone being added to ethanol at 25 °C. It has reached a maximum signal after 2-3 s. The purple dots and magenta stars correspond to methyl acrylate and acetone addition to ethanol at -78 °C, respectively. The formation of product (**Li•SI-46**) from the “normal” and “reverse” addition experiments are also plotted. All of these data indicate that it takes a few seconds (~4 s) for an analyte signal to stabilize and reach a maximum intensity. The rates of product formation (**Li•SI-46**) or rates of substrate disappearance (**Li•SI-30**, **SI-1**) were likely not accurate, rather these data suggests the reaction could have been complete in under a second and it took the signal intensities almost 4 seconds to finally reach their maximum intensity. It was concluded that the reaction is too fast for the capabilities of the ReactIR instrument.

Aggregation State Determination

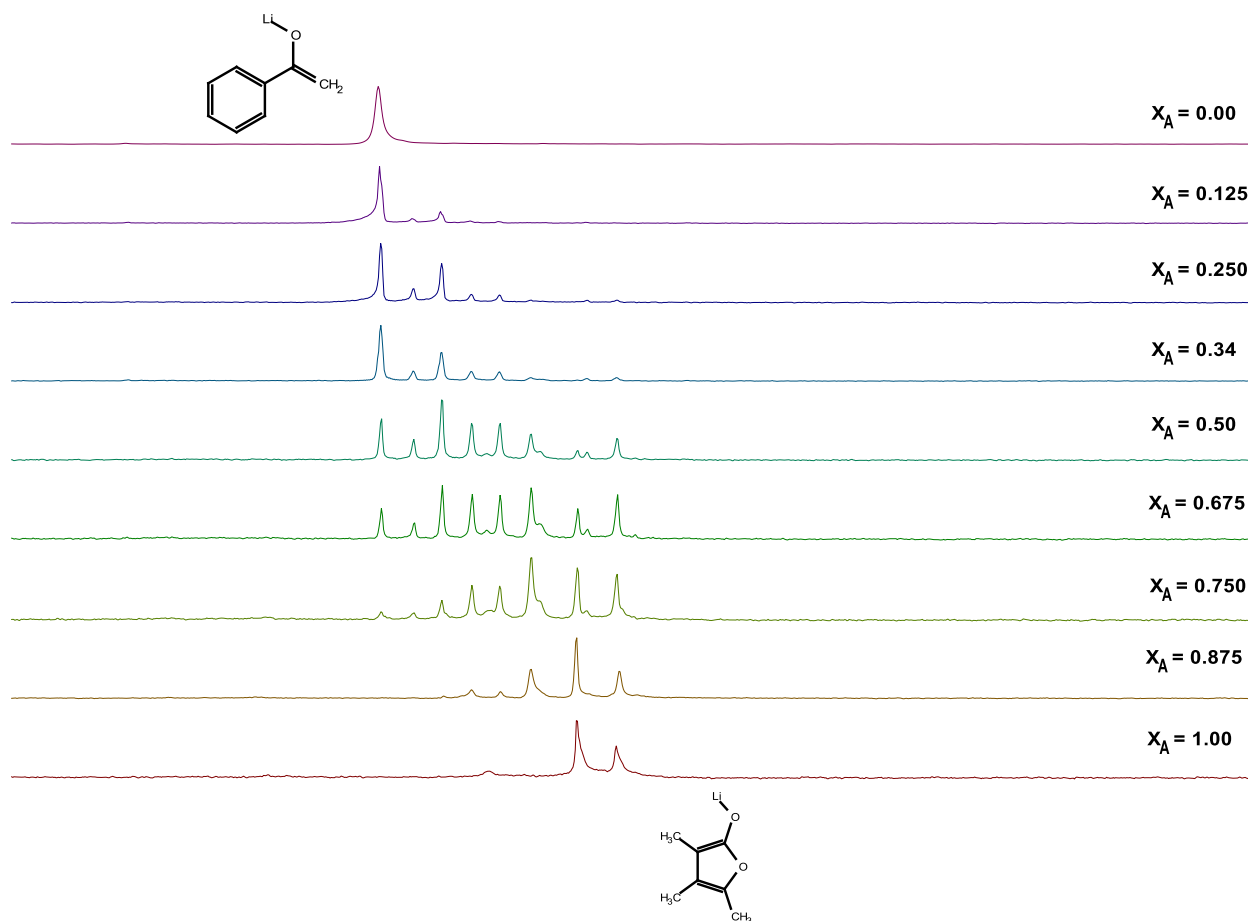
Materials

n-BuLi⁶ was prepared from ⁶Li-metal using Turner's procedure.²⁶ The reaction mixture was centrifuged under inert atmosphere to remove LiCl and the corresponding clear solution was transferred to a flame dried flask. The solution was titrated in triplicate prior to use. n-BuLi⁶ was used to generate ⁶Li-LDA according to the procedure highlighted above.

Sample Preparation

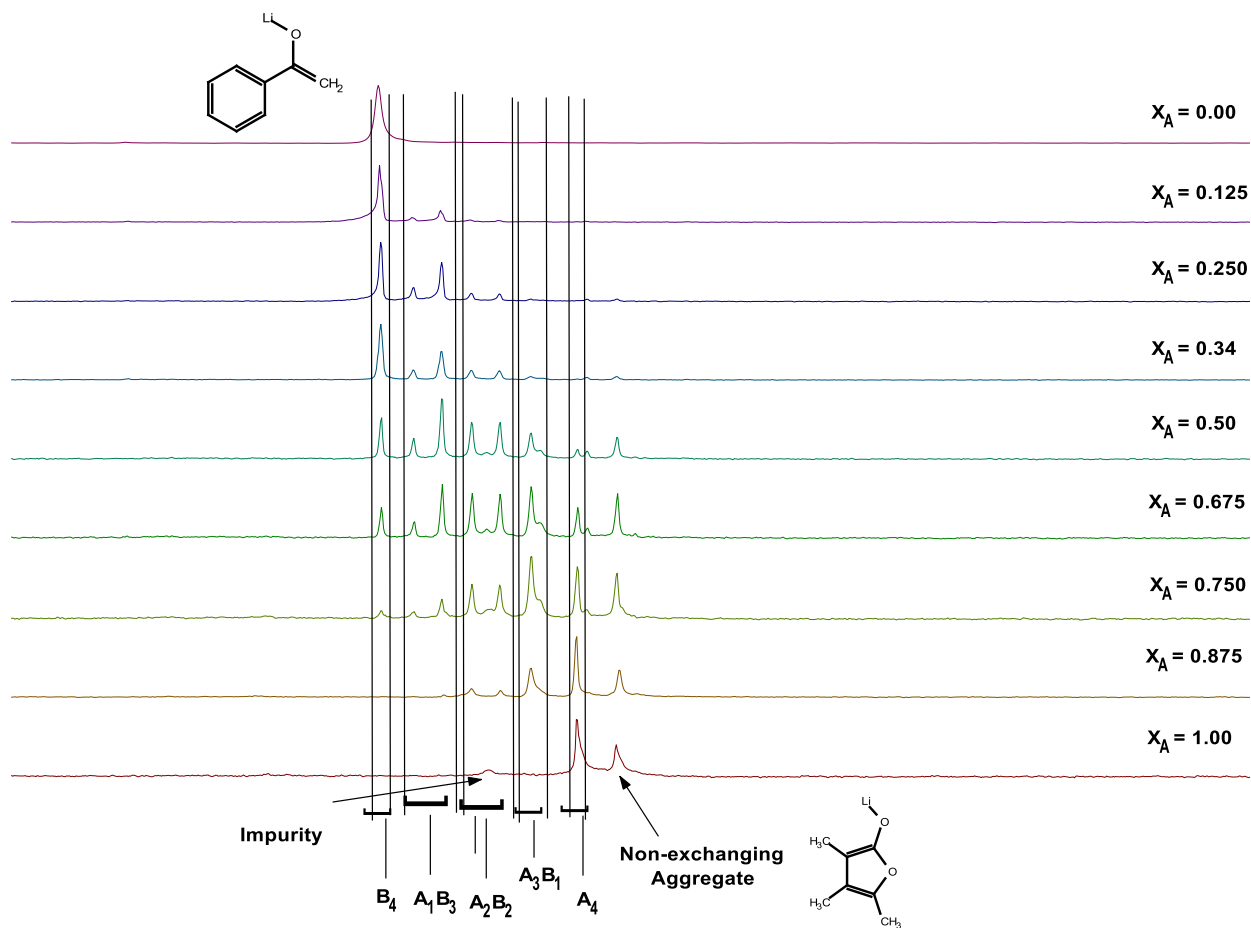
Two stock solutions of ⁶Li-acetophenone enolate (2.0 mmol, 0.3 M) in 2.35 mL anhydrous THF and ⁶Li-SI-30 (2.0 mmol, 0.3 M) in 2.59 mL anhydrous THF were prepared by adding ⁶Li-LDA (4.102 mL, 0.49 M) at -78 °C. Each stock solution was allowed to stir at -78 °C prior to sample preparation. Following adequate stirring, 9 5-mm NMR tubes fitted with septa were flame dried and backfilled with Argon. Each 5-mm NMR tube was cooled to -78 °C and each sample was prepared by adding appropriate amounts of stock solutions at -78 °C to a final volume of 1.00 mL (e.g: X_A = 0.5 was prepared by adding 500 μL of each stock solution to a dry 5-mm NMR tube). After addition of each solution, the mixture was vortexed for 5 seconds, cooled back to -78 °C for 20 seconds, sonicated for 5 seconds and cooled back to -78 °C. This process was repeated twice for each sample and care was taken to avoid excessive warming. Samples were stored at -78 °C for no longer than 10 minutes before ⁶Li-NMR analysis.

Spectra

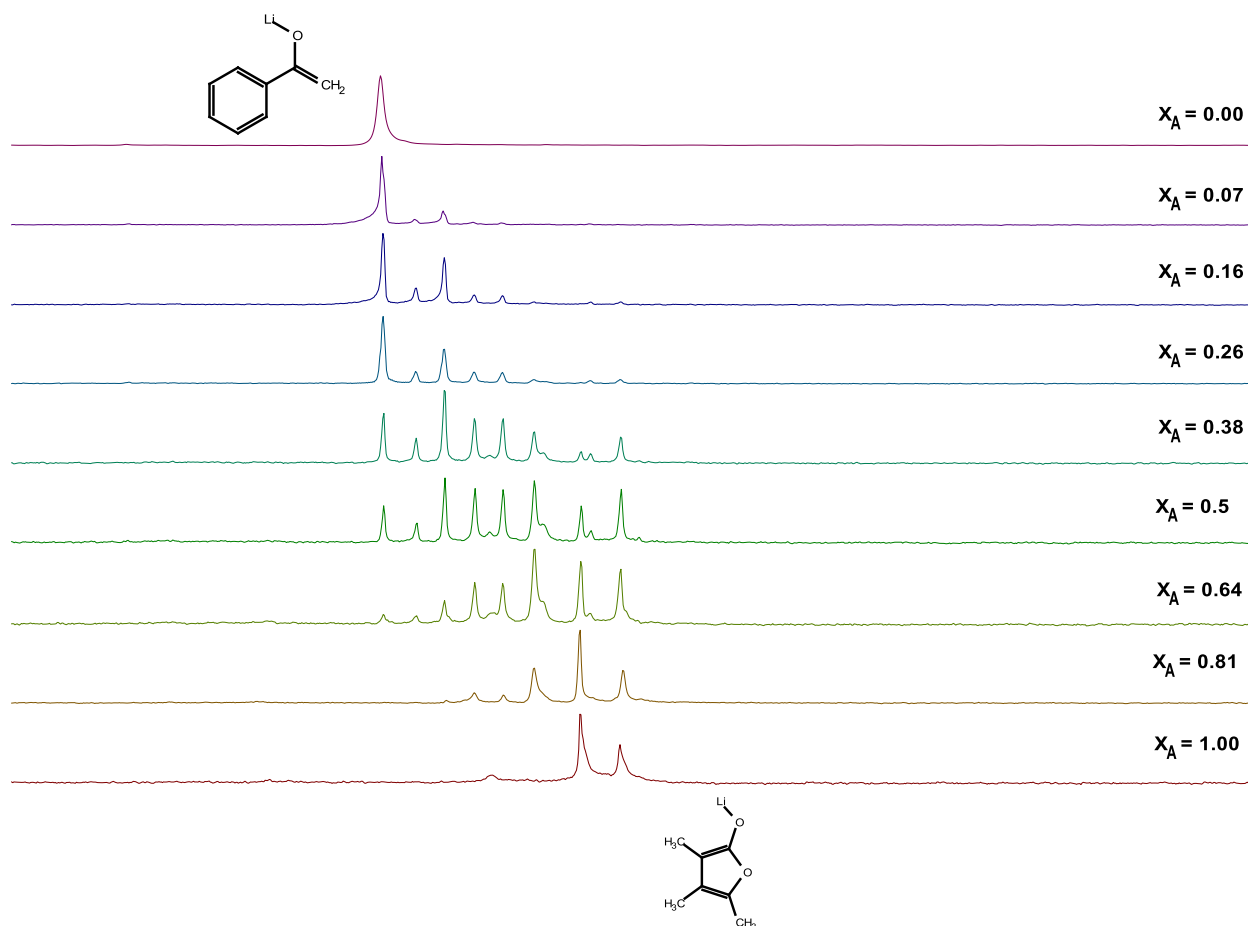


^6Li NMR spectra of mixtures of [^6Li] **SI-30** (**A**) and [^6Li] 1-phenylethen-1-olate (**B**) at various mole fractions in THF at $-78\text{ }^\circ\text{C}$. Samples were prepared to a total concentration of 0.3 M total enolate with 0.49 M $^6\text{Li-LDA}$.

Annotated Spectra



Two distinct ^6Li resonances in a ratio of 60:40 were observed in the pure ($X_A = 1.00$) spectrum of [^6Li] **SI-30**. The minor resonance did not exchange with [^6Li] 1-phenylethen-1-olate as evidenced by the adjusted job plot (see below).



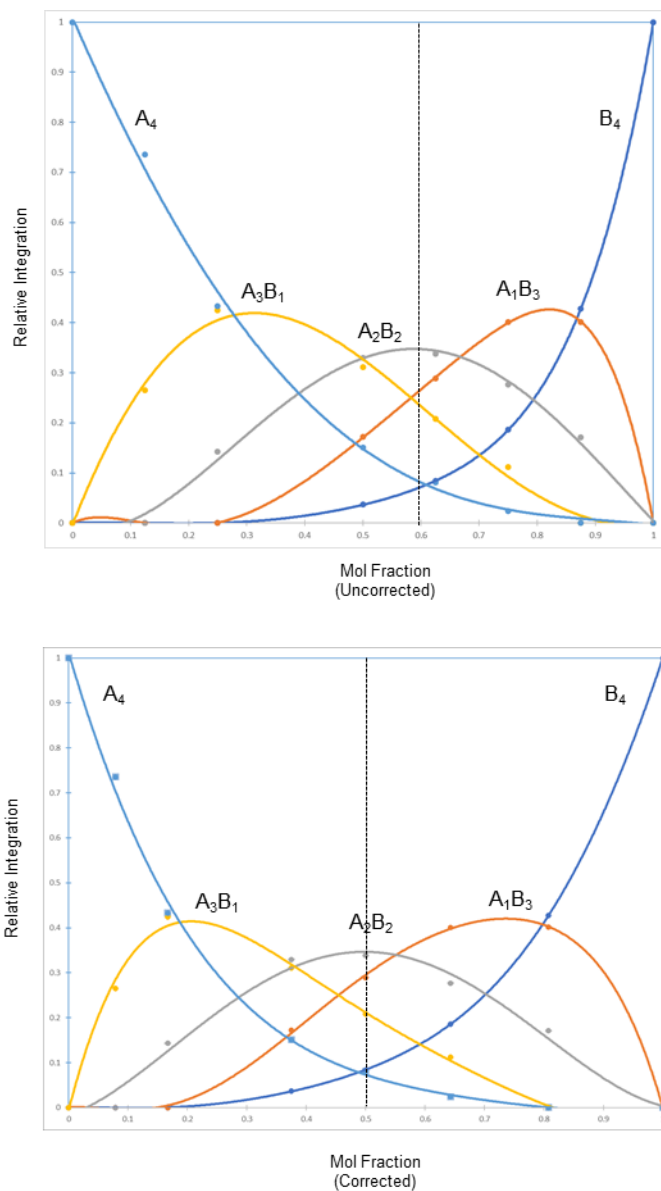
^6Li NMR spectra of mixtures of $[\text{}^6\text{Li}]$ **SI-30 (A)** and $[\text{}^6\text{Li}]$ 1-phenylethen-1-olate (**B**) at various mole fractions in THF at $-78\text{ }^\circ\text{C}$. Samples were prepared to a total concentration of 0.3 M total enolate with 0.49 M ^6Li -LDA. Adjusted mole fractions according to a 60:40 ratio are depicted on the right side of the spectrum.

Resonance Integrations

	Relative Integral Values				
Mol Fraction B	A4	A3B1	A2B2	A1B3	B4
1	0	0	0	0	1
0.875	0	0	0	0.264705882	0.735294118
0.75	0	0	0.142857143	0.424242424	0.432900433
0.625	0.036675952	0.171773445	0.329619313	0.311049211	0.15088208
0.5	0.083815029	0.289017341	0.338150289	0.208092486	0.080924855
0.25	0.186046512	0.40096231	0.276663994	0.112269447	0.024057739
0.125	0.427350427	0.401709402	0.170940171	0	0
0	1	0	0	0	0

	Relative Integral Values				
Adjusted Mol Fraction B	A4	A3B1	A2B2	A1B3	B4
1	0	0	0	0	1
0.807692308	0	0	0	0.264705882	0.735294118
0.642857143	0	0	0.142857143	0.424242424	0.432900433
0.5	0.036675952	0.171773445	0.329619313	0.311049211	0.15088208
0.375	0.083815029	0.289017341	0.338150289	0.208092486	0.080924855
0.166666667	0.186046512	0.40096231	0.276663994	0.112269447	0.024057739
0.078947368	0.427350427	0.401709402	0.170940171	0	0
0	1	0	0	0	0

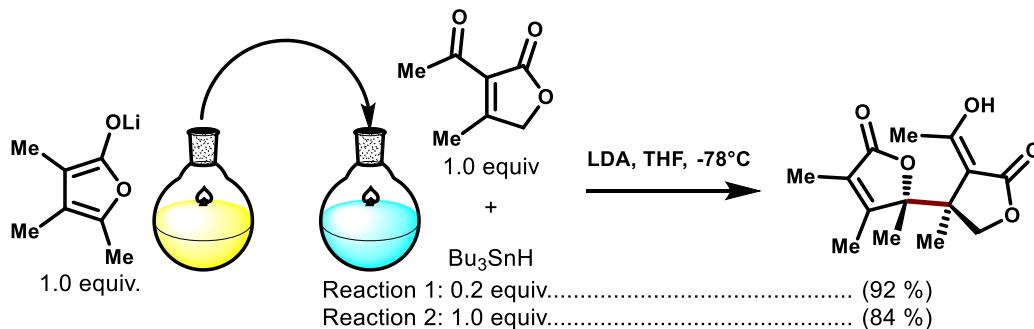
Job Plots



Plot of the relative integration versus the mole fraction of $[^6\text{Li}]$ 1-phenylethen-1-olate (**B**) for an ensemble of $[^6\text{Li}]$ **SI-30** (**A**) and $[^6\text{Li}]$ 1-phenylethen-1-olate (**B**) in THF at -78°C .

Additional Mechanistic Insight

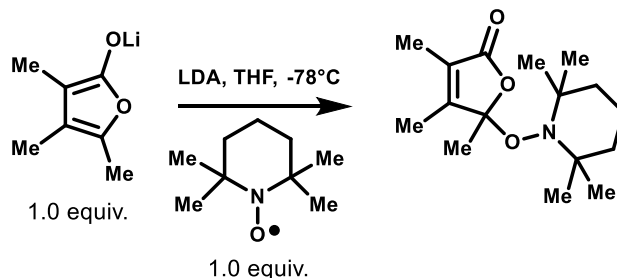
Radical Chain Termination



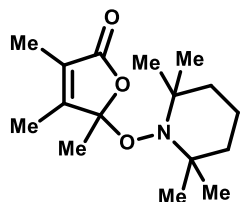
Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.10 mmol, 0.204 mL). Next, **SI-30** (0.10 mmol, 12.6 mg) was dissolved in 0.296 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, the enolate solution was added (<5 seconds) into a solution of **SI-1** (0.10 mmol, 14.0 mg) and Bu₃SnH (0.10 or 0.02 mmol) in anhydrous THF (0.500 mL) at -78 °C. The reaction was allowed to stir for 1 hour before quench with 1M HCl/MeOH (0.22 mmol, 0.220 mL). The mixture was then diluted with water (1 mL) and 1,3,5-trimethoxybenzene (0.093 mmol, 15.7 mg) was added as an internal standard before extraction with EtOAc (3x, 3 mL). The combined organics were washed with brine, dried with MgSO₄, concentrated *in vacuo*, and the yield was determined from the crude ¹H NMR spectrum. ([Reaction 1](#): 92 %, [Reaction 2](#): 84%)

Single-electron Oxidant Reactivity

Tempo Reactivity



Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.10 mmol, 0.204 mL). Next, **SI-30** (0.10 mmol, 12.6 mg) was dissolved in 0.296 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, TEMPO (0.20 mmol, 31.2 mg) in anhydrous THF (0.500 mL) was added dropwise (ca. 1 minute) at -78 °C. The reaction mixture was allowed to stir for 1 hour at -78 °C before quench with sat. NH₄Cl (1 mL). 1,3,5-trimethoxybenzene (0.107 mmol, 18.1 mg) was added as an internal standard prior to extraction with EtOAc (3x 3 mL). The combined organics were washed with brine, dried with MgSO₄, concentrated *in vacuo*, and the yield was determined from the crude ¹H NMR spectrum prior to purification via preparative TLC. (76 %, [1H NMR](#))



3,4,5-trimethyl-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)furan-2(5H)-one (SI-85)
[Compound (8) in manuscript]. The title compound was obtained as red oil.

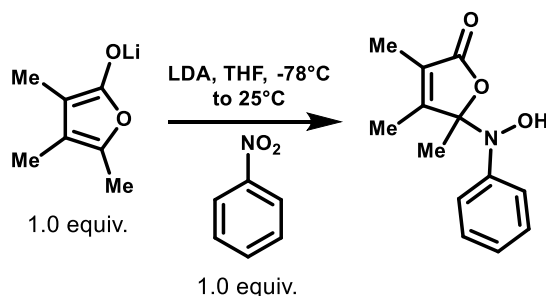
¹H NMR (600 MHz, Chloroform-*d*) δ 2.09 (d, *J* = 1.2 Hz, 1H), 1.91 – 1.88 (m, 1H), 1.80 (s, 1H), 1.64 – 1.54 (m, 2H), 1.45 (s, 1H), 1.26 (s, 1H), 1.20 (s, 1H), 1.16 (s, 1H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 170.66, 156.84, 123.95, 109.82, 59.57, 58.95, 40.44, 39.93, 33.01, 32.61, 19.39, 19.26, 19.05, 15.69, 11.13, 7.39.

LC-MS (ESI) Calculated [C₁₆H₂₈NO₃]⁺: 282.1, found: 282.1;

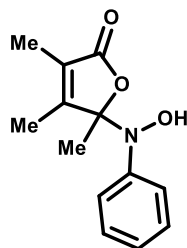
R_f 0.25 (Hexanes:EtOAc = 4:1).

Nitrobenzene Reactivity



Procedure:

A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.10 mmol, 0.204 mL). Next, **SI-30** (0.10 mmol, 12.6 mg) was dissolved in 0.296 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, nitrobenzene (0.10 mmol, 10.3 μ L) in anhydrous THF (0.500 mL) was added dropwise (ca. 1 minute) at -78 °C. The reaction mixture was brought to 25 °C and allowed to stir for 2.5 hours before quench with sat. NH_4Cl (1 mL). 1,3,5-trimethoxybenzene (0.082 mmol, 13.8 mg) was added as an internal standard prior to extraction with EtOAc (3x 3 mL). The combined organics were washed with brine, dried with MgSO_4 , concentrated *in vacuo*, and the yield was determined from the crude ^1H NMR spectrum prior to purification via preparative TLC. (36 %, [1H NMR](#))



5-(hydroxy(phenyl)amino)-3,4,5-trimethylfuran-2(5H)-one (SI-86) [Compound (9) in manuscript]. The title compound was obtained as a white solid.

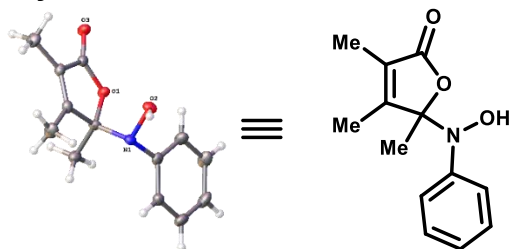
[1H NMR](#) (600 MHz, Chloroform-*d*) δ 7.44 – 7.40 (m, 2H), 7.35 – 7.31 (m, 2H), 7.27 – 7.23 (m, 2H), 2.06 (q, J = 1.1 Hz, 3H), 1.77 (q, J = 1.1 Hz, 3H), 1.46 (s, 3H).

[13C NMR](#) (151 MHz, Chloroform-*d*) δ 172.92, 158.74, 146.35, 128.66, 127.78, 126.40, 125.40, 101.58, 22.45, 11.67, 8.73.

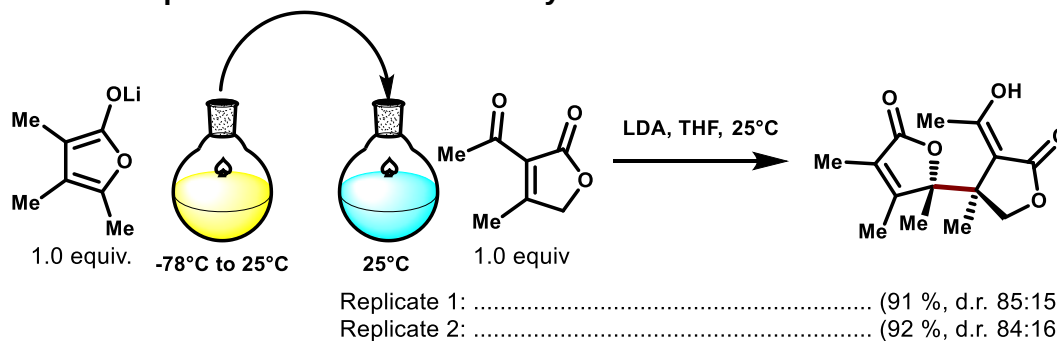
LC-MS (ESI) Calculated $[\text{C}_{13}\text{H}_{16}\text{NO}_3]^+$: 234.1, found: 234.1;

R_f 0.40 (Hexanes:EtOAc = 1:1).

Crystal

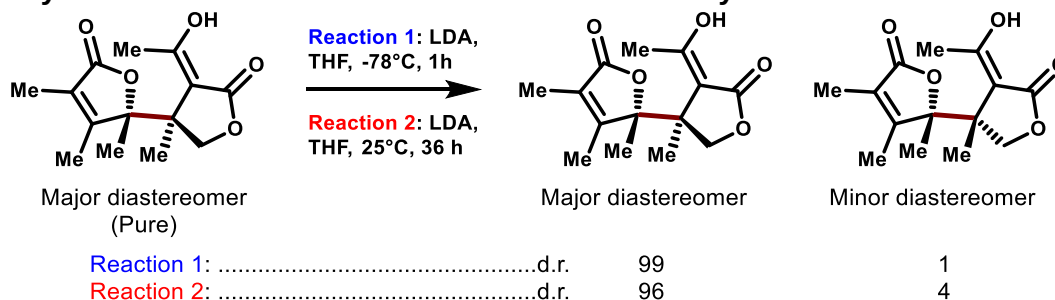


Temperature Independent Diastereoselectivity



Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.10 mmol, 0.204 mL). Next, **SI-30** (0.10 mmol, 12.6 mg) was dissolved in 0.296 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, the enolate solution was warmed to 25 °C and added (<5 seconds) into a solution of **SI-1** (0.10 mmol, 14.0 mg) in anhydrous THF (0.500 mL) at 25 °C. The reaction was allowed to stir for 1 hour before quench with 1M HCl/MeOH (0.22 mmol, 0.220 mL). The mixture was then diluted with water (1 mL) and extracted with EtOAc (3x, 3 mL). The combined organics were washed with brine, dried with MgSO₄, concentrated *in vacuo*, and the d.r. was determined from the crude ¹H NMR spectrum ([Replicate 1](#): (91 %, d.r. 85:15), [Replicate 2](#): (92 %, d.r. 84:16)). Products were purified via preparative TLC.

Thermodynamic vs. Kinetic Controlled Diastereoselectivity



Procedure (Reaction 1): A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.10 mmol, 0.204 mL). Next, **SI-46** (0.10 mmol, 26.0 mg) was dissolved in 0.796 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, the mixture was quenched with 1M HCl/MeOH (0.22 mmol, 0.220 mL). The mixture was then diluted with water (1 mL) and extracted with EtOAc (3x, 3 mL). The combined organics were washed with brine, dried with MgSO₄, concentrated *in vacuo*, and the d.r. was determined from the crude ¹H NMR spectrum (d.r. >99 : 1). ([¹H NMR](#))

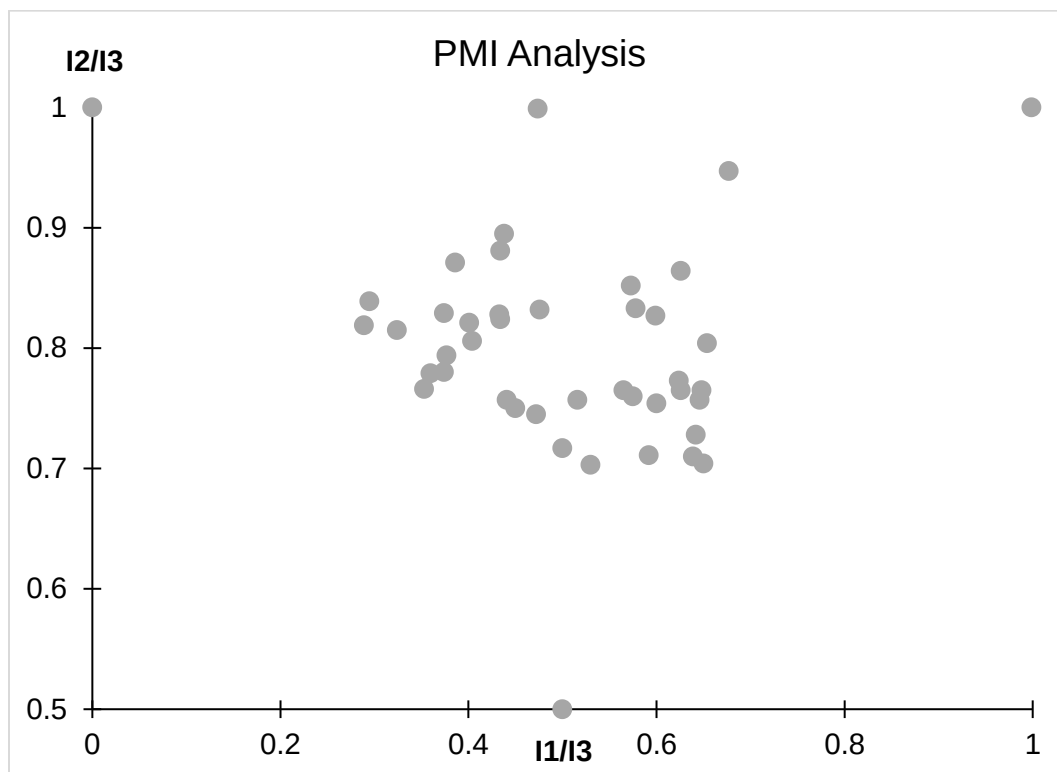
Procedure (Reaction 2): A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to -78 °C and charged with LDA (0.10 mmol, 0.204 mL). Next, **SI-46** (0.10 mmol, 26.0 mg) was dissolved in 0.796 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After, 5 minutes, the mixture was warmed to 25 °C and allowed to stir for an additional 36 hours. The mixture was quenched with 1M HCl/MeOH (0.22 mmol, 0.220 mL). The mixture was then diluted with water (1 mL) and extracted with EtOAc (3x, 3 mL). The combined organics were washed with brine, dried with MgSO₄, concentrated *in vacuo*, and the d.r. was determined from the crude ¹H NMR spectrum (d.r. 96 : 4). ([¹H NMR](#))

Principal Moment of Inertia

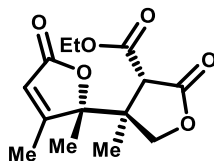
Results

Compound	PMI axis I1	PMI axis I2	PMI axis I3	PMI ratio I1/I3	PMI ratio I2/I3
SI-46	777.432	1637.274	2062.057	0.377	0.794
SI-47	967.578	1978.023	2210.944	0.438	0.895
SI-48	980.869	1992.885	2262.438	0.434	0.881
SI-49	1593.529	2199.192	2545.835	0.626	0.864
SI-50	1953.32	2305.817	3013.769	0.648	0.765
SI-51	2130.958	2676.225	3549.471	0.6	0.754
SI-52	2179.459	2472.772	3395.682	0.642	0.728
SI-53	1755.928	2528.831	3037.383	0.578	0.833
SI-54	1985.82	2325.519	3072.348	0.646	0.757
SI-55	2109.258	2790.068	3669.181	0.575	0.76
SI-56	2111.07	4007.035	4865.157	0.434	0.824
SI-57	778.802	1754.816	2015.364	0.386	0.871
SI-58	1813.517	2696.524	3163.258	0.573	0.852
SI-59	2251.766	2750.412	3595.138	0.626	0.765
SI-60	2630.371	2921.895	4118.042	0.639	0.71
SI-61	2708.555	3974.958	5252.362	0.516	0.757
SI-62	2614.469	2830.342	4021.899	0.65	0.704
SI-63	2499.87	3070.007	3820.107	0.654	0.804
SI-64	2145.297	3004.318	3171.092	0.677	0.947
SI-65	2213.914	2741.542	3546.693	0.624	0.773
SI-67	983.167	2012.785	2452.805	0.401	0.821
SI-68	639.073	1274.369	1581.618	0.404	0.806
SI-69	773.097	1328.591	1754.77	0.441	0.757
SI-70	1046.238	1831.335	2199.806	0.476	0.832
SI-71	1445.935	1956.871	2557.409	0.565	0.765
SI-72	1584.408	1902.429	2676.042	0.592	0.711
SI-73	1487.727	2056.193	2484.974	0.599	0.827
SI-74	1044.325	1742.919	2322.962	0.45	0.75
SI-75	862.88	2169.065	2661.204	0.324	0.815
SI-79	721.86	1563.597	2007.537	0.36	0.779
SI-80	1100.7	2390.069	3118.634	0.353	0.766
SI-81	1181.466	2461.301	3156.01	0.374	0.78
SI-82	1294.067	3662.831	4472.548	0.289	0.819
SI-87	1121.883	1770.134	2375.672	0.472	0.745
SI-88	1808.521	2594.262	3619.431	0.5	0.717
SI-89	1839.48	2438.697	3471.068	0.53	0.703
SI-90	1149.279	2550.269	3075.654	0.374	0.829
SI-91	1185.856	3374.547	4022.565	0.295	0.839
SI-92	866.071	1656.315	2001.582	0.433	0.828
SI-93	1361.49	1752.491	2548.43	0.534	0.688
Adamantane	302.067	302.197	302.292	0.999	1

Benzene	89.359	89.361	178.72	0.5	0.5
2,2'- dimethyl- 1,1'- biphenyl	582.274	1226.689	1227.689	0.474	0.9999
Acetylene	0.002	14.416	14.418	0	1



PMI Entries Not Included in Reaction Scope



ethyl (3R,4S)-4-((R)-2,3-dimethyl-5-oxo-2,5-dihydrofuran-2-yl)-4-methyl-2-oxotetrahydrofuran-3-carboxylate (**SI-87**). The title compound was obtained as a yellow oil using **General Procedure G** (33 %).

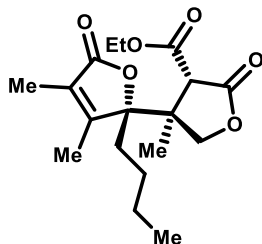
Isolated as a Single Diastereomers

¹H NMR (600 MHz, Chloroform-*d*) δ 5.88 (q, *J* = 1.5 Hz, 1H), 4.50 (d, *J* = 9.2 Hz, 1H), 4.23 (qd, *J* = 7.2, 2.6 Hz, 2H), 4.07 (d, *J* = 9.2 Hz, 1H), 3.55 (s, 1H), 2.12 (d, *J* = 1.5 Hz, 3H), 1.51 (s, 3H), 1.34 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 170.65, 169.70, 169.57, 166.01, 119.30, 89.53, 74.13, 61.74, 51.20, 49.11, 19.62, 17.20, 15.11, 13.62.

LC-MS (ESI) Calculated [C₁₄H₁₉O₆]⁺: 283.1, found: 283.1;

R_f 0.24 (Et₂O).



ethyl (3R,4S)-4-((R)-2-butyl-3,4-dimethyl-5-oxo-2,5-dihydrofuran-2-yl)-4-methyl-2-oxotetrahydrofuran-3-carboxylate (**SI-88**). The title compound was obtained as a yellow oil using **General Procedure G** (45 %).

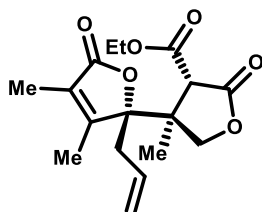
Isolated as a Single Diastereomers

¹H NMR (600 MHz, Chloroform-*d*) δ 4.50 (d, *J* = 8.9 Hz, 1H), 4.22 (dq, *J* = 10.9, 7.2 Hz, 1H), 4.14 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.02 (d, *J* = 8.9 Hz, 1H), 3.43 (s, 1H), 1.92 (d, *J* = 1.3 Hz, 3H), 1.90 – 1.86 (m, 1H), 1.83 (d, *J* = 1.3 Hz, 3H), 1.72 – 1.58 (m, 1H), 1.39 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.16 – 1.02 (m, 1H), 0.85 (t, *J* = 7.4 Hz, 3H), 0.81 – 0.71 (m, 1H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 172.46, 171.24, 166.69, 158.98, 127.78, 90.93, 75.26, 62.17, 51.54, 50.90, 30.55, 24.54, 22.61, 18.05, 14.26, 13.98, 13.87, 8.76.

LC-MS (ESI) Calculated [C₁₈H₂₇O₆]⁺: 339.1, found: 339.1;

R_f 0.68 (Et₂O).



ethyl (3R,4S)-4-((R)-2-(but-3-en-1-yl)-3,4-dimethyl-5-oxo-2,5-dihydrofuran-2-yl)-4-methyl-2-oxotetrahydrofuran-3-carboxylate (**SI-89**). The title compound was obtained as a yellow oil using **General Procedure G** (73 %).

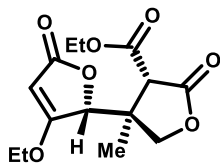
Isolated as a Single Diastereomers

¹H NMR (600 MHz, Chloroform-*d*) δ 5.37 (dddd, J = 16.6, 10.1, 7.7, 6.3 Hz, 1H), 5.15 – 5.08 (m, 2H), 4.52 (d, J = 9.0 Hz, 1H), 4.22 (dq, J = 10.9, 7.2 Hz, 1H), 4.15 (dq, J = 10.8, 7.1 Hz, 1H), 4.04 (d, J = 9.0 Hz, 1H), 3.46 (s, 1H), 2.60 (ddt, J = 14.2, 7.8, 0.9 Hz, 1H), 2.53 (ddt, J = 14.2, 6.3, 1.3 Hz, 1H), 1.93 (q, J = 1.1 Hz, 3H), 1.80 (q, J = 1.1 Hz, 3H), 1.41 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 172.13, 171.07, 166.58, 158.75, 129.13, 128.16, 120.87, 90.30, 75.13, 62.22, 51.57, 50.63, 35.55, 18.03, 14.26, 13.90, 8.69.

LC-MS (ESI) Calculated $[C_{17}H_{23}O_6]^+$: 323.1, found: 323.1;

R_f 0.68 (Et₂O).



ethyl (3R,4S)-4-((S)-3-ethoxy-5-oxo-2,5-dihydrofuran-2-yl)-4-methyl-2-oxotetrahydrofuran-3-carboxylate (**SI-90**). The title compound was obtained as a yellow oil using **General Procedure G** (58 %).

Isolated as a Mixture of Diastereomers (70:30)

Major Diastereomer:

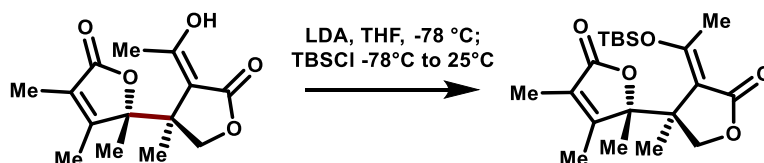
¹H NMR (600 MHz, Chloroform-*d*) δ 5.18 (d, J = 0.9 Hz, 1H), 4.70 (d, J = 0.9 Hz, 1H), 4.31 – 4.24 (m, 4H), 4.13 – 4.05 (m, 4H), 3.67 (s, 1H), 1.43 (t, J = 7.1 Hz, 5H), 1.34 – 1.31 (m, 4H), 1.29 (s, 3H).

¹³C NMR (151 MHz, Chloroform-*d*) δ 178.40, 171.47, 171.04, 166.36, 91.06, 80.57, 72.26, 69.81, 62.43, 53.52, 46.66, 17.05, 14.24, 13.83.

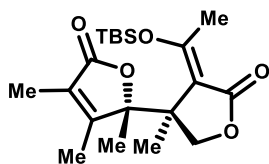
LC-MS (ESI) Calculated $[C_{14}H_{19}O_7]^+$: 299.1, found: 299.1;

R_f 0.36 (Et₂O).

Diversified Compounds



Procedure: A 10 mL flask fitted with a Teflon stir bar and rubber septum was flame dried and backfilled with argon. The flask was then cooled to -78°C and charged with LDA (0.902 mmol, 1.73 mL). Next, **SI-46** (0.751 mmol, 200 mg) in anhydrous THF (2.0 mL) was added to the flask and the resulting solution was allowed to stir at -78°C for 1 hour. After 1 hour, TBSCl (2.47 mmol, 371 mg) in anhydrous THF (3.0 mL) was added (ca. 2 minutes) at -78°C . After addition, the reaction was warmed to 25°C and allowed to stir overnight. The crude reaction was concentrated *in vacuo* and purified via column chromatography. **SI-91** was obtained as a white solid. (84 % yield)



(S)-5-((S,Z)-4-(1-((tert-butyldimethylsilyl)oxy)ethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-91). The title compound was obtained as a white solid.

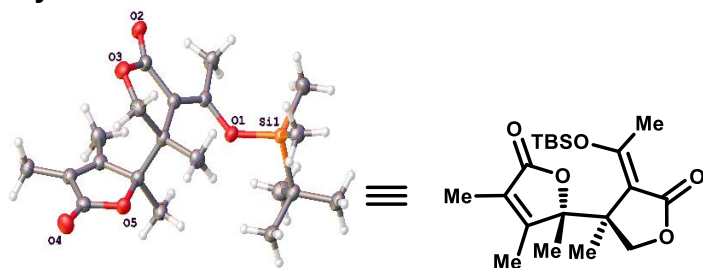
¹H NMR (600 MHz, Chloroform-*d*) δ 3.72 (d, J = 9.7 Hz, 1H), 3.53 (d, J = 9.7 Hz, 1H), 2.51 (s, 3H), 1.88 (q, J = 1.0 Hz, 3H), 1.80 (q, J = 1.1 Hz, 3H), 1.54 (s, 3H), 1.48 (s, 3H), 1.01 (s, 9H), 0.37 (s, 3H), 0.34 (s, 3H).

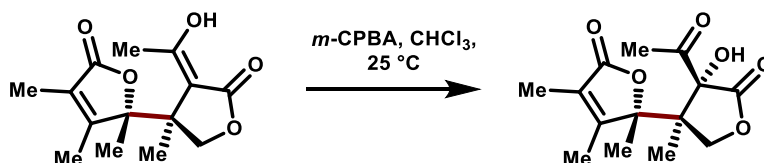
¹³C NMR (151 MHz, Chloroform-*d*) δ 173.31, 173.22, 167.34, 162.84, 125.16, 107.72, 90.92, 71.56, 50.06, 26.43, 25.71, 20.94, 20.86, 19.02, 13.14, 8.91, -2.06, -2.37.

LC-MS (ESI) Calculated $[\text{C}_{20}\text{H}_{33}\text{O}_5\text{Si}]^+$: 381.1, found: 381.1;

R_f 0.4 (Hexanes:EtOAc = 1:1).

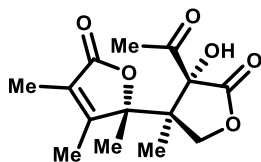
Crystal





Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then charged with *m*-CPBA (3.97 mmol, 678 mg). Next, **SI-46** (0.789 mmol, 300 mg) in CHCl₃ (4.0 mL) was added to the flask and the resulting solution was allowed to stir for 6 hours at 25 °C. After 6 hours, the reaction was quenched by addition of sat. Na₂S₂O₃ (1.0 mL) and sat. NaHCO₃ (1 mL) and extracted with EtOAc (3x, 3 mL). The combined organics were washed with brine, dried with MgSO₄, concentrated *in vacuo*, and purified via column chromatography. The title compound was obtained as a white solid. (90 % yield)

Note: CHCl₃ was filtered over basic alumina prior to reaction.



(S)-5-((3R,4R)-4-acetyl-4-hydroxy-3-methyl-5-oxotetrahydrofuran-3-yl)-3,4,5-trimethylfuran-2(5H)-one (SI-92). The title compound was obtained as a white solid.

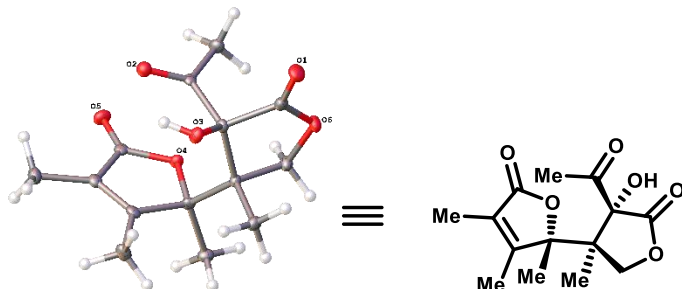
¹H NMR (600 MHz, Chloroform-*d*) δ 4.98 (dq, *J* = 9.1, 1.0 Hz, 1H), 4.30 (d, *J* = 9.1 Hz, 1H), 4.24 (s, 1H), 2.46 (s, 2H), 2.10 (q, *J* = 1.1 Hz, 3H), 1.78 (q, *J* = 1.1 Hz, 3H), 1.52 (d, *J* = 1.0 Hz, 3H), 1.43 (s, 3H).

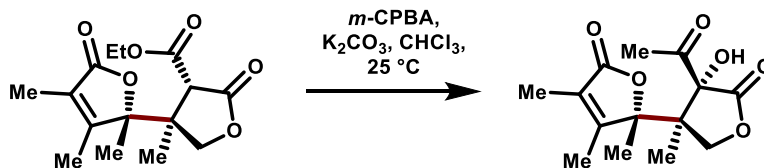
¹³C NMR (151 MHz, Chloroform-*d*) δ 201.11, 172.23, 170.84, 159.61, 125.12, 86.43, 85.15, 72.25, 54.55, 26.44, 21.98, 19.31, 13.78, 7.92.

LC-MS (ESI) Calculated [C₁₄H₁₉O₆]⁺: 283.1, found: 283.1;

R_f 0.25 (DCM:Et₂O = 9:1).

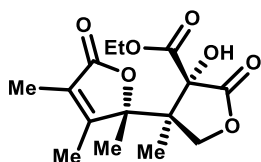
Crystal





Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then charged with *m*-CPBA (0.5 mmol, 86 mg), and K₂CO₃ (.312 mmol, 43.1 mg). Next, **SI-57** (0.10 mmol, 31 mg) in CHCl₃ (0.500 mL) was added to the flask and the resulting solution was allowed to stir for 24 hours at 25 °C. After 24 hours, the reaction was quenched by addition of sat. Na₂S₂O₃ (1.0 mL) and sat. NaHCO₃ (1 mL) and extracted with EtOAc (3x, 3 mL). The combined organics were washed with brine, dried with MgSO₄, concentrated *in vacuo*, and purified via column chromatography. The title compound was obtained as a white solid. (70 % yield)

Note: CHCl₃ was filtered over basic alumina prior to reaction.



ethyl (3R,4R)-3-hydroxy-4-methyl-2-oxo-4-((S)-2,3,4-trimethyl-5-oxo-2,5-dihydrofuran-2-yl)tetrahydrofuran-3-carboxylate (SI-93). The title compound was obtained as a white solid.

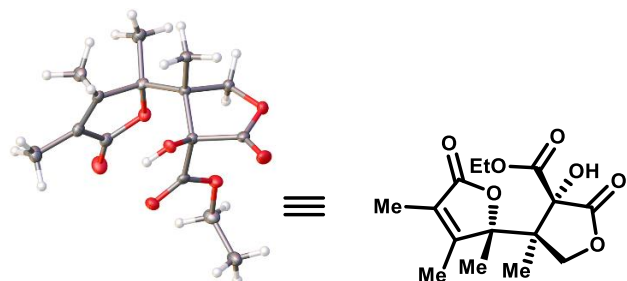
¹H NMR (600 MHz, Chloroform-*d*) δ 4.91 (d, *J* = 8.3 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 4.12 (d, *J* = 8.3 Hz, 1H), 3.64 (s, 1H), 2.10 (s, 3H), 1.77 (s, 3H), 1.45 (s, 3H), 1.40 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H).

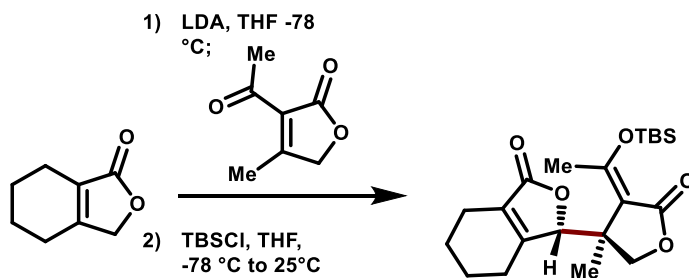
¹³C NMR (151 MHz, Chloroform-*d*) δ 172.56, 172.13, 169.15, 159.88, 125.88, 86.88, 79.54, 72.59, 65.11, 53.55, 22.76, 18.86, 14.37, 13.82, 8.64.

LC-MS (ESI) Calculated [C₁₅H₂₁O₇]⁺: 313.1, found: 313.1;

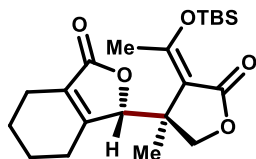
R_f 0.4 (Hexanes:EtOAc = 60:40).

Crystal





Procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. The flask was then cooled to $-78\text{ }^{\circ}\text{C}$ and charged with LDA (0.3 mmol, 0.612 mL). Next, **SI-40** (0.3 mmol, 41.4 mg) was dissolved in 0.300 mL of anhydrous THF and added dropwise (ca. 5 minutes) to the stirring LDA solution. After 1 hour of stirring, **SI-1** (0.30 mmol, 42 mg), dissolved in 0.700 mL of anhydrous THF, was added dropwise (ca. 5 minutes). After stirring for 1 hour, TBSCl (0.9 mmol, 135 mg) in anhydrous THF (1.0 mL) was added at $-78\text{ }^{\circ}\text{C}$. The reaction was brought to $25\text{ }^{\circ}\text{C}$ and allowed to stir for 24 hours. After 24 hours, the reaction was quenched with sat. NaHCO_3 and extracted with EtOAc (3x 3 mL). The combined organics were washed with brine, dried with MgSO_4 , and concentrated *in vacuo*. The title compound was obtained as a white solid via column chromatography. (57 % yield)



(R)-3-((S,Z)-4-(1-((tert-butyldimethylsilyl)oxy)ethylidene)-3-methyl-5-oxotetrahydrofuran-3-yl)-4,5,6,7-tetrahydroisobenzofuran-1(3H)-one (SI-94). The title compound was obtained as a white solid.

$^1\text{H NMR}$ (600 MHz, Chloroform-*d*) δ 5.28 (t, $J = 1.1\text{ Hz}$, 1H), 3.68 (d, $J = 9.7\text{ Hz}$, 1H), 3.63 (dd, $J = 9.7, 0.7\text{ Hz}$, 1H), 2.47 (s, 3H), 2.33 – 2.26 (m, 1H), 2.21 – 2.09 (m, 1H), 2.08 – 2.04 (m, 1H), 1.83 – 1.74 (m, 3H), 1.62 (s, 3H), 1.60 – 1.46 (m, 2H), 0.99 (s, 9H), 0.34 (s, 3H), 0.32 (s, 3H).

$^{13}\text{C NMR}$ (151 MHz, Chloroform-*d*) δ 172.96, 171.93, 167.20, 161.46, 130.01, 107.84, 84.48, 69.78, 45.56, 26.08, 25.00, 24.25, 22.02, 21.28, 20.35, 19.95, 18.63, -2.37, -2.66.

LC-MS (ESI) Calculated $[\text{C}_{21}\text{H}_{33}\text{O}_5\text{Si}]^+$: 393.1, found: 393.1;

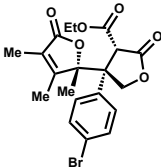
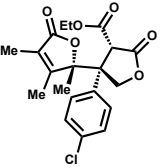
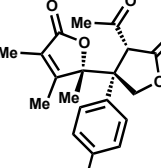
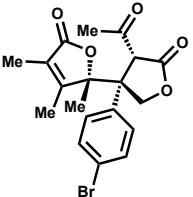
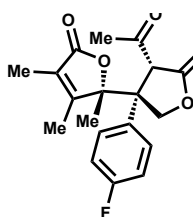
R_f 0.3 (Hexanes:EtOAc = 80:20).

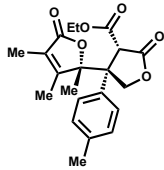
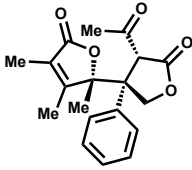
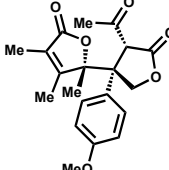
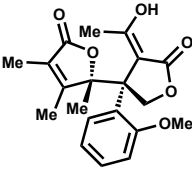
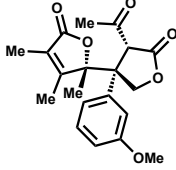
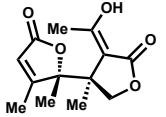
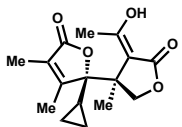
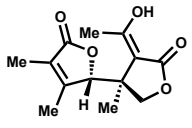
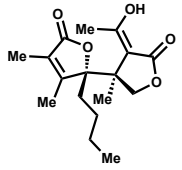
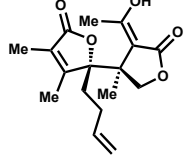
Cell Culture and Reporter Assay

Procedure

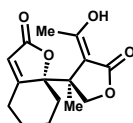
THP-1 Lucia ISG cells (cat. no. thpl-isg, Invivogen) were transiently transfected with viral dsDNA VacV70:LyoVec (cat. no. tlrl-vav70c, Invivogen) and treated with compounds or vehicle control (DMSO, 0.2% v/v). Following 24 h, luminescence was measured using an Envision plate reader (Perkin Elmer) set with an integration time of 0.1 seconds. Luminescence signals for test article samples were normalized to vehicle-treated samples and reported as relative light units (RLU). Using the same treatment conditions and incubation time, RNA was extracted from THP-1 cells and reverse-transcribed into cDNA. Gene expression was assessed using Taqman primers and probes with the Taqman Universal Mix II (cat. no. 4440038, ThermoFisher) following manufacturer's instructions. Gene expression was normalized using the delta-delta Ct method and was reported as fold change in expression.

Extended SAR Results

Identifier	Structure	ISRE-luciferase activity EC ₅₀ (μM)
SI-61		14.6
SI-60		16.2
SI-55		16.8
SI-56 Compound (13) in manuscript		19.6
SI-54		NA

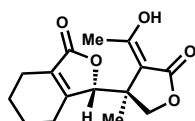
SI-65		NA
SI-49		NA
SI-51		NA
SI-53		NA
SI-52		NA
SI-69 Compound (12) in manuscript		NA
SI-70		NA
SI-79		NA
SI-72		NA
SI-71		NA

SI-74



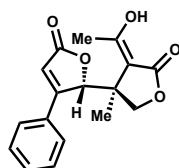
NA

SI-75



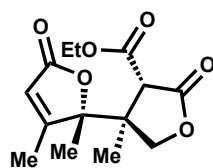
NA

SI-80



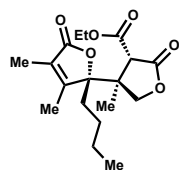
NA

SI-87



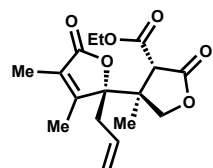
NA

SI-88



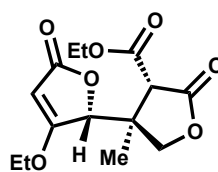
NA

SI-89



NA

SI-90



NA

Computational Study

Computational Methods

Computations were performed with Gaussian 09.¹ Molecular geometries were optimized using the ω B97XD² functional and the 6-31G(d) basis set. Solvation effects were included in the geometry optimizations using the SMD³ solvation model with tetrahydrofuran as the solvent. Frequency calculations were carried out at the same level of theory as for geometry optimization to characterize the stationary points as either minima (no imaginary frequencies) or saddle points (one imaginary frequency). Intrinsic reaction coordinate (IRC) calculations were performed to ensure that the transition states found connected the reactants and the products. Single-point energies were calculated with the ω B97XD functional and the 6-311++G(d,p) basis set. Solvation effects were included using the SMD solvation model with tetrahydrofuran as the solvent. Monte Carlo conformational searches were performed with the Merck molecular force field (MMFF) implemented in Spartan '16. Molecular structures were visualized using CYLview.⁴

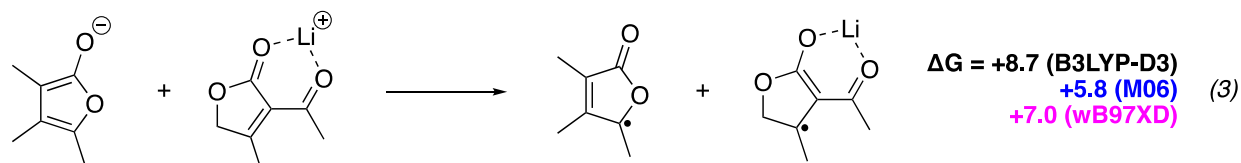
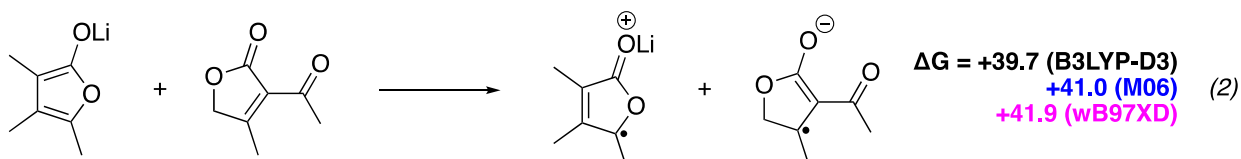
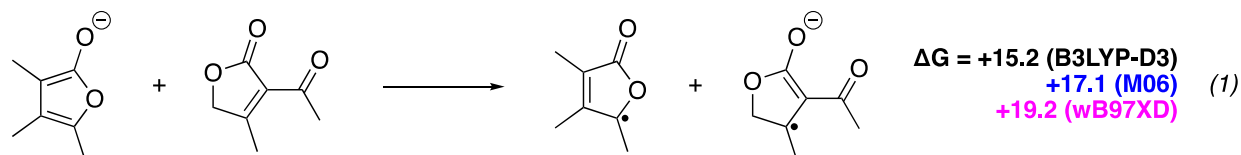
Distinguishing Michael Addition (Two-Electron) vs. SET (One-Electron) Pathways

The exceptionally facile C–C bond formation to furnish attached ring systems can be rationalized as either (1) a fast Michael addition preceded by rate-determining aggregation/deaggregation steps, or (2) rate-determining single electron transfer (SET) followed by rapid radical collapse.

To evaluate the energetic feasibility of the SET/radical collapse pathway, reaction free energies of the relevant intermolecular SET reactions were computed (Scheme S1). SET is calculated to be energetically uphill in all cases, even for reaction (3), in which electrostatic interactions between two segments (one cationic and the other anionic) are expected to be extremely favorable.

Scheme 1. Computed Reaction Free Energies for SET Reactions (in kcal/mol)

B3LYP-D3/6-311++G(d,p), SMD(THF) // B3LYP-D3/6-31+G(d), SMD (THF)
 M06/6-311++G(d,p), SMD(THF) // M06/6-31G(d), SMD (THF)
 wB97XD/6-311++G(d,p), SMD(THF) // wB97XD/6-31G(d), SMD (THF)



Attempts to locate singlet diradical transition states for the proposed radical collapse step did not find any open-shell transition states that are lower in energy than the two-electron Michael addition pathway (*vide infra*). These results, combined with the favorability of the Michael addition pathway (*vide infra*), effectively rule out the SET/radical collapse mechanism.

Aggregation States of Lithium Enolates and Michael Addition Transition States

Both the thermodynamics and the kinetics of lithium enolate aggregation can have a significant impact on reaction rates. We conducted a thorough computational investigation into the thermodynamic stability of tetrameric, dimeric and monomeric lithium enolate aggregates, as well as their corresponding Michael addition C–C bond forming transition states.

Figure 1 shows the computed lithium enolate tetramer structures solvated by different numbers of THF molecules. Calculated free energies indicate that THF solvation has a stabilizing effect, with the tetrasolvated tetramer being the lowest in energy.

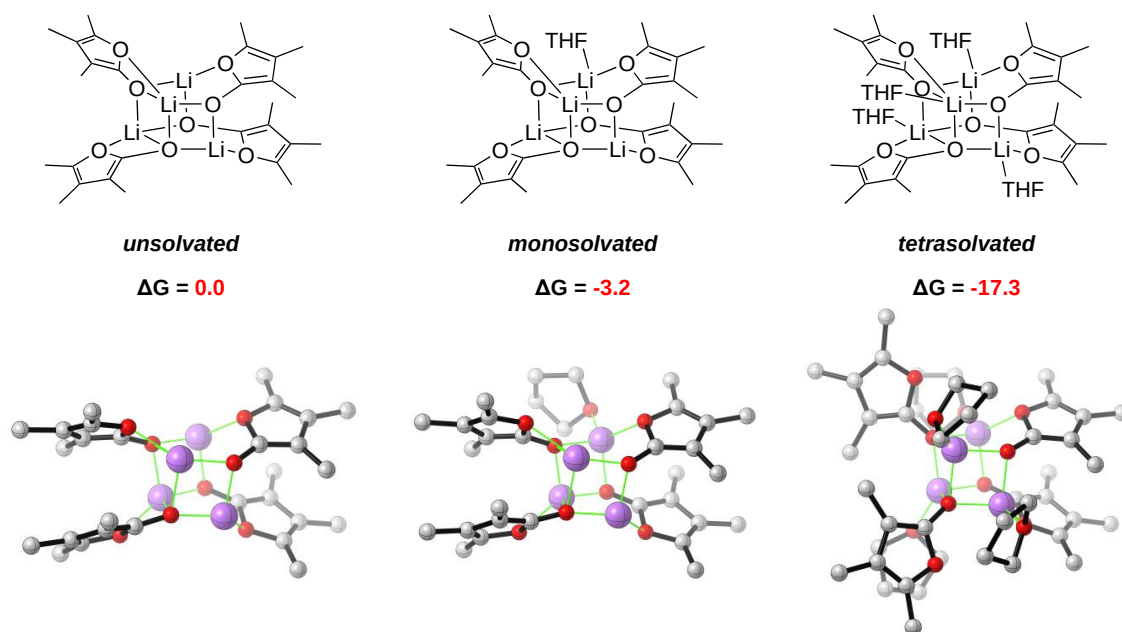


Figure 1. Computed structures and relative free energies of lithium enolate tetramers at the ω B97XD/6-311++G(d,p), SMD (THF) // ω B97XD/6-31G(d), SMD (THF) level of theory. Hydrogens are omitted from structures for clarity. Energies are in kcal/mol.

THF solvation has a similar stabilizing effect on lithium enolate dimers (Figure 2). The tetrasolvated dimer form was found to be the most stable.

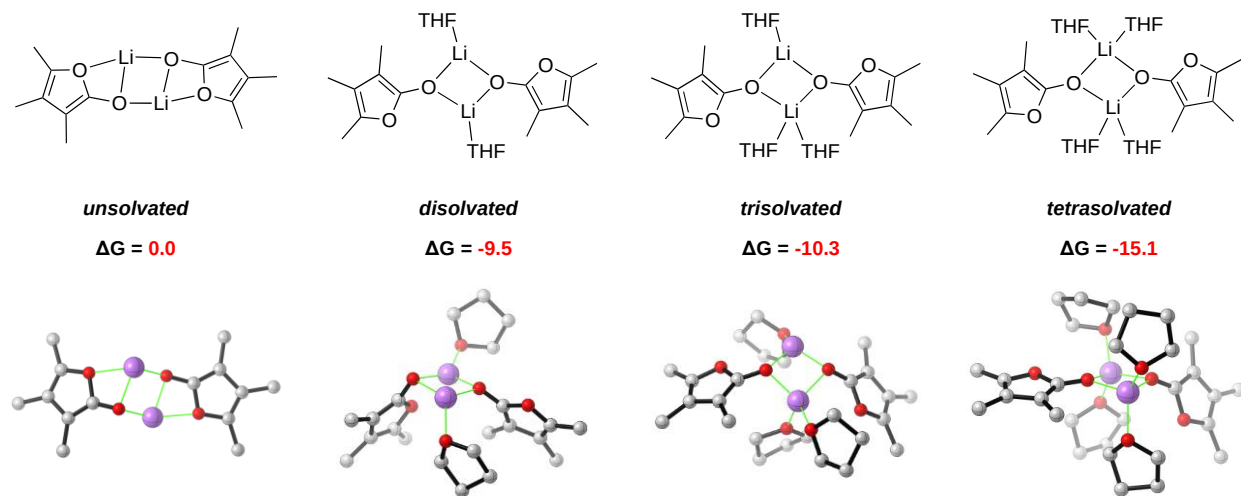


Figure 2. Computed structures and relative free energies of lithium enolate dimers at the ω B97XD/6-311++G(d,p), SMD (THF) // ω B97XD/6-31G(d), SMD (THF) level of theory. Hydrogens are omitted from structures for clarity. Energies are in kcal/mol.

For monomers, solvation stabilization peaks at 2–3 THF molecules per enolate (Figure 3).

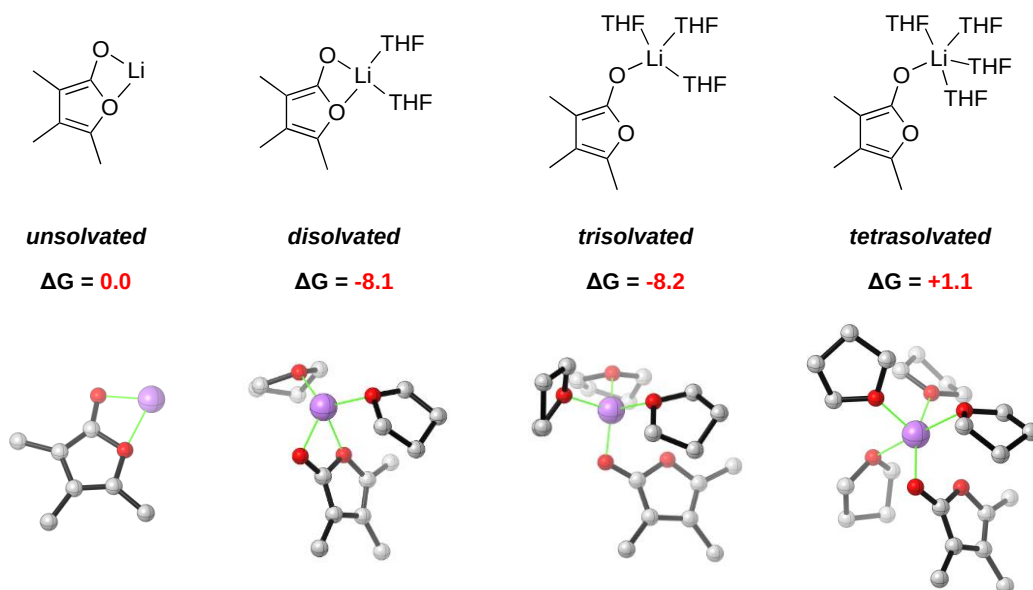
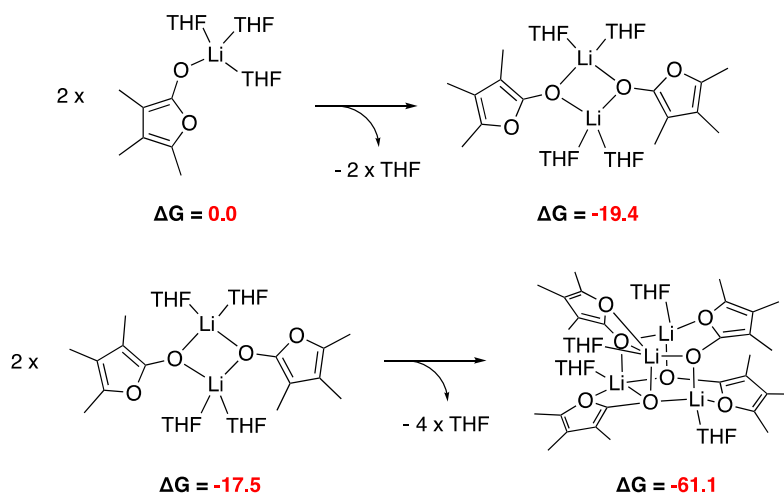


Figure 3. Computed structures and relative free energies of lithium enolate monomers at the ω B97XD/6-311++G(d,p), SMD (THF) // ω B97XD/6-31G(d), SMD (THF) level of theory. Hydrogens are omitted from structures for clarity. Energies are in kcal/mol.

Having established the most stable solvation states and free energies of the tetra-, di- and monomeric enolate forms, we computed the thermodynamics of their interconversion (Scheme 2). Relative free energy values show that the dimers are metastable and the tetramers are stable.

Scheme 2. Computed Thermodynamics of Interconversion Between Lithium Enolate Aggregates



Transition states involving mono, di- and tetrameric lithium enolates were obtained for the C–C bond formation step along the Michael addition pathway. Figure 4 shows the structures and free energies of the Michael addition of a monomeric lithium enolate. The free energy of activation was calculated to be 4.4 kcal/mol, indicating extremely facile C–C bond formation.

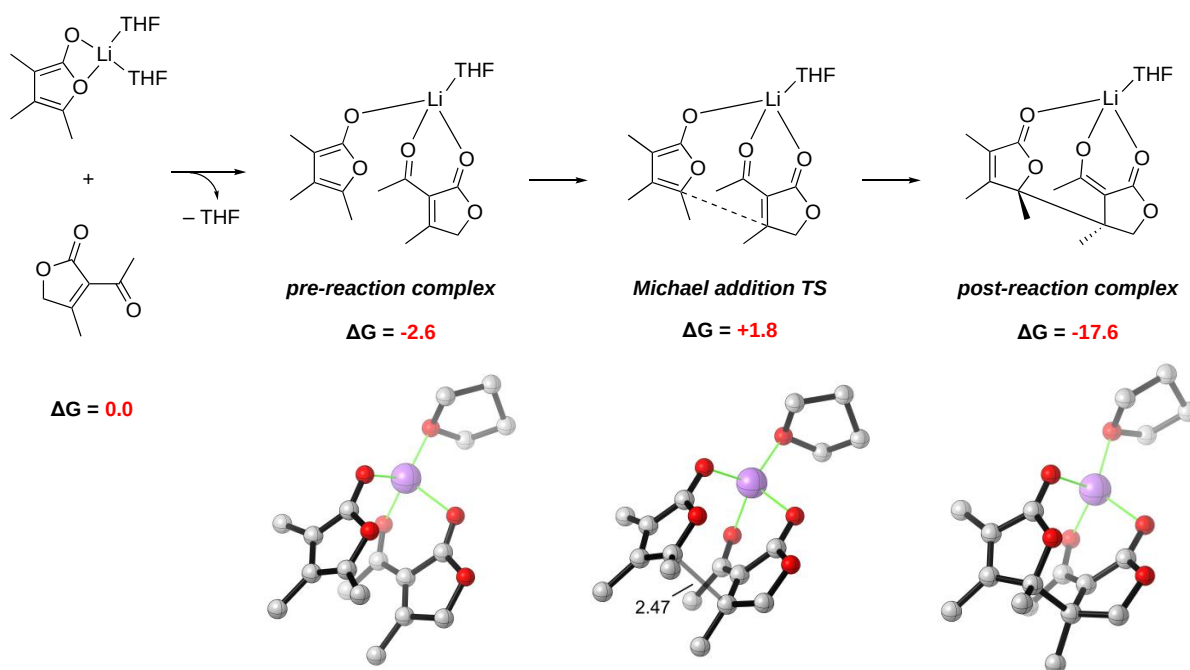


Figure 4. Calculated transition states for the Michael addition of a monomeric lithium enolate to a butenolide electrophile at the ω B97XD/6-311++G(d,p), SMD (THF) // ω B97XD/6-31G(d), SMD (THF) level of theory. Hydrogens are omitted from structures for clarity. Energies are in kcal/mol.

For the monomeric transition state, the addition of one THF molecule coordinating to the Li atom was found to be detrimental (Figure 5).

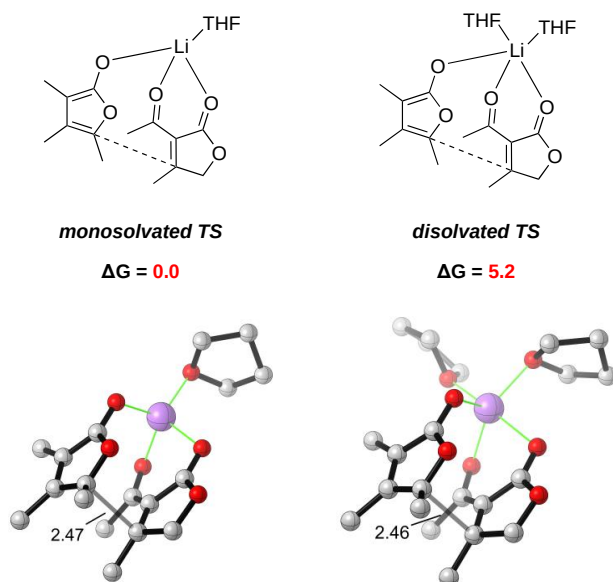


Figure 5. Michael addition transition states with different numbers of THF molecules solvating Li.

Michael addition of a dimeric enolate to the same butenolide electrophile was found to have a barrier of 12.1 kcal/mol (Figure 6). Both the tri- and tetrasolvated TS structures are higher in energy than the disolvated TS (Figure 7).

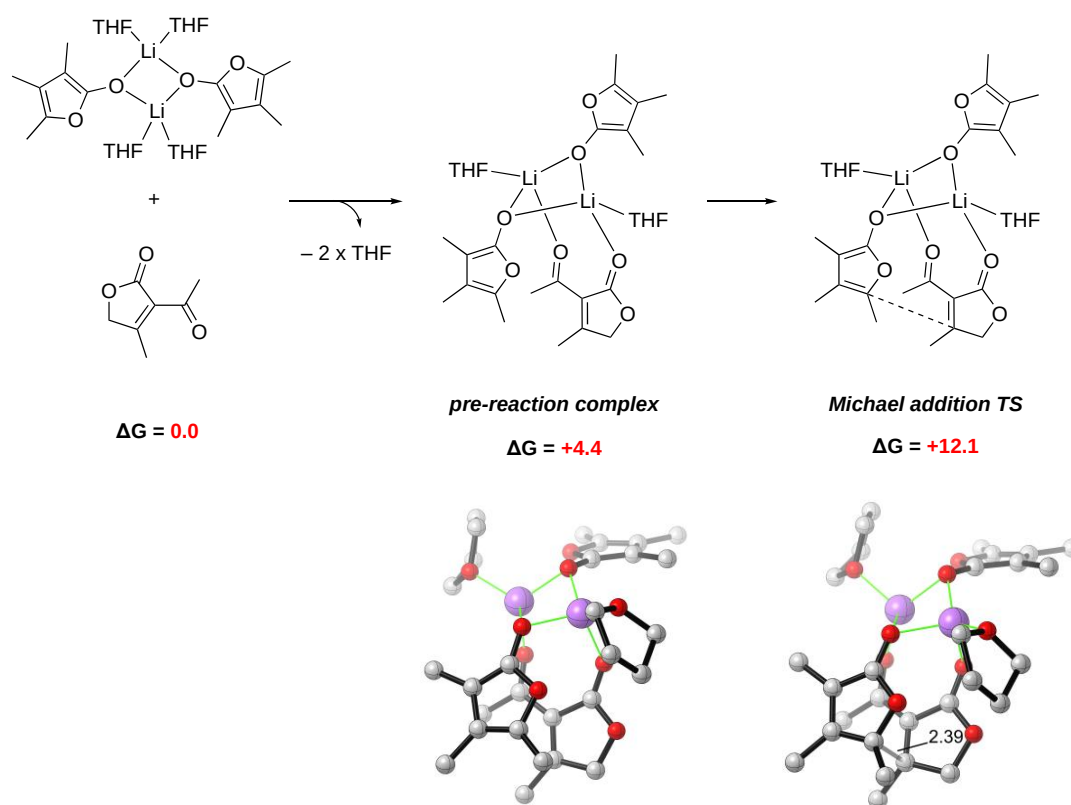


Figure 6. Calculated transition states for the Michael addition of a dimeric lithium enolate to a butenolide electrophile at the ω B97XD/6-311++G(d,p), SMD (THF) // ω B97XD/6-31G(d), SMD (THF) level of theory. Hydrogens are omitted from structures for clarity. Energies are in kcal/mol.

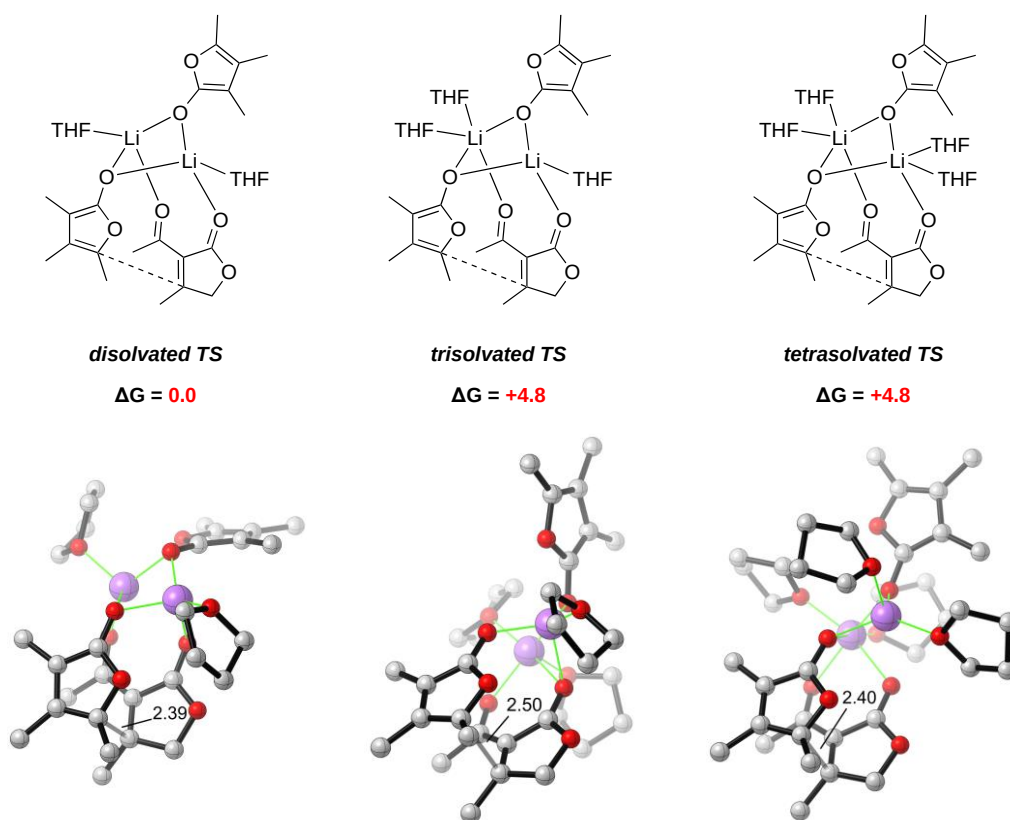


Figure 7. Michael addition transition states with different numbers of THF molecules solvating Li.

For the tetrameric transition state, the coordination of 3 THF molecules was found to be optimal. The C–C bond formation step has a barrier of 15.4 kcal/mol (Figure 8).

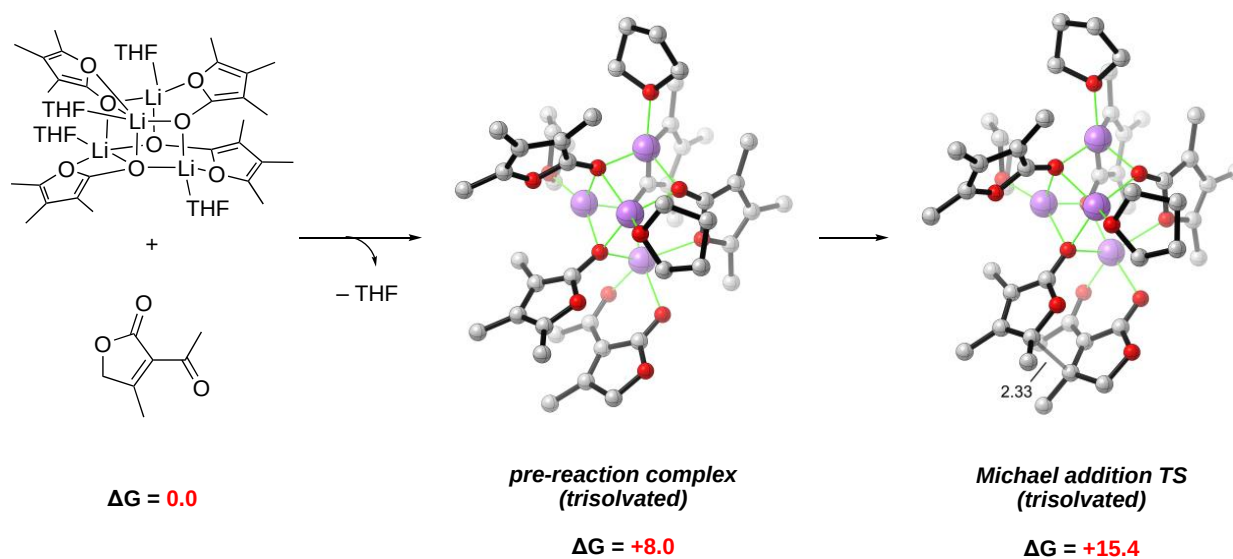


Figure 8. Calculated transition states for the Michael addition of a tetrameric lithium enolate to a butenolide electrophile at the ω B97XD/6-311++G(d,p), SMD (THF) // ω B97XD/6-31G(d), SMD (THF) level of theory. Hydrogens are omitted from structures for clarity. Energies are in kcal/mol.

For both the dimeric and the tetrameric enolate, the calculated free energy barrier of the Michael addition step exceed the experimentally measured barrier of 7.9–8.0 kcal/mol. We therefore concluded that the monomeric TS is most likely to be operational.

The Role of Dispersive Interactions in Facilitating Michael Addition

The extremely facile C–C bond formation in the Michael addition step can be attributed to stabilizing dispersive interactions (including π - π stacking interactions) between the conjugated π systems of the two reacting partners (Figure 9). To evaluate the magnitude of dispersion stabilization, we calculated the activation electronic energy, ΔE , of the Michael addition step using the B3LYP-D3 and B3LYP functionals. The difference between the B3LYP-D3 and B3LYP values is defined as the stabilizing contribution from dispersive interactions, termed $E_{\text{dispersion}}$ (see formula below).

$$E_{\text{B3LYP-D3}} = E_{\text{B3LYP}} + E_{\text{dispersion}}$$

Our results show that both the pre-reaction complex and the Michael addition transition state are stabilized by dispersive interactions (including π - π stacking). Furthermore, this stabilizing effect is stronger in the transition state than in the pre-reaction complex, resulting in an overall reduction of the barrier by 2.1 kcal/mol (Figure 9).

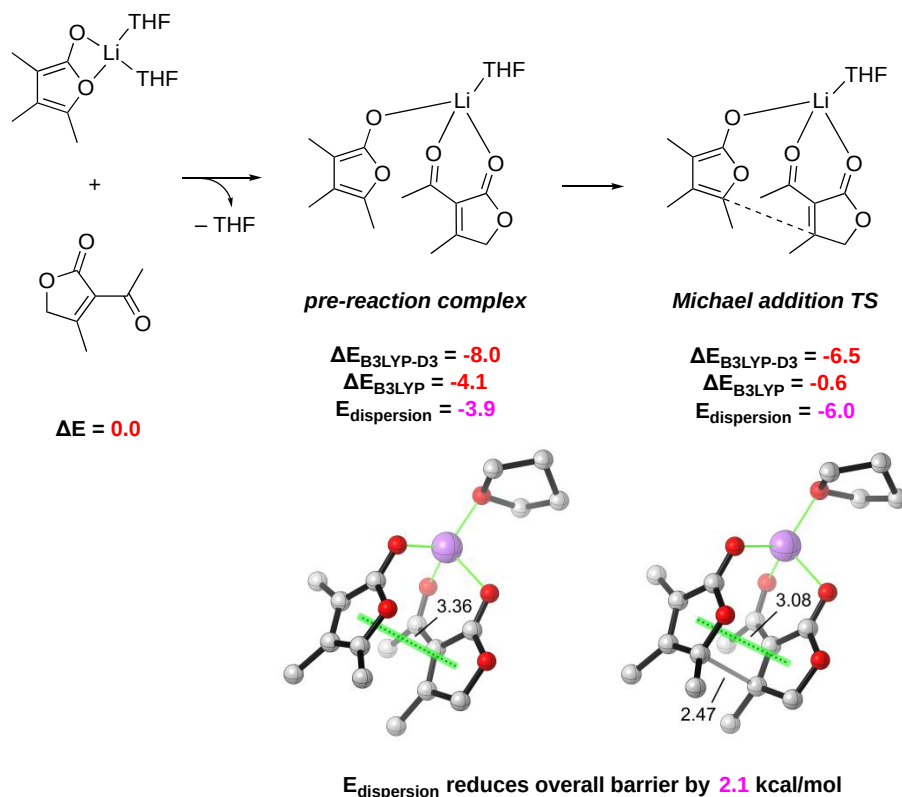


Figure 9. Evaluation of stabilizing dispersive interactions (including π - π stacking interactions) in the pre-reaction complex and the transition state. Activation electronic energies (in kcal/mol) are calculated at the B3LYP-D3/6-311G(d,p) or B3LYP/6-311G(d,p) level of theory employing the implicit SMD solvation model with THF as the solvent.

Origins of Diastereoselectivity in Michael Addition

We studied the diastereofacial selectivity of the Michael addition step by calculating the C–C bond forming transition state leading to the minor diastereomer (Figure 10). The TS leading to the minor diastereomer was found to be 2.9 kcal/mol higher in energy than the one yielding the major diastereomer. This difference in free energy can be partly attributed to unfavorable eclipsing interactions about the forming C–C bond in the TS leading to the minor diastereomer.

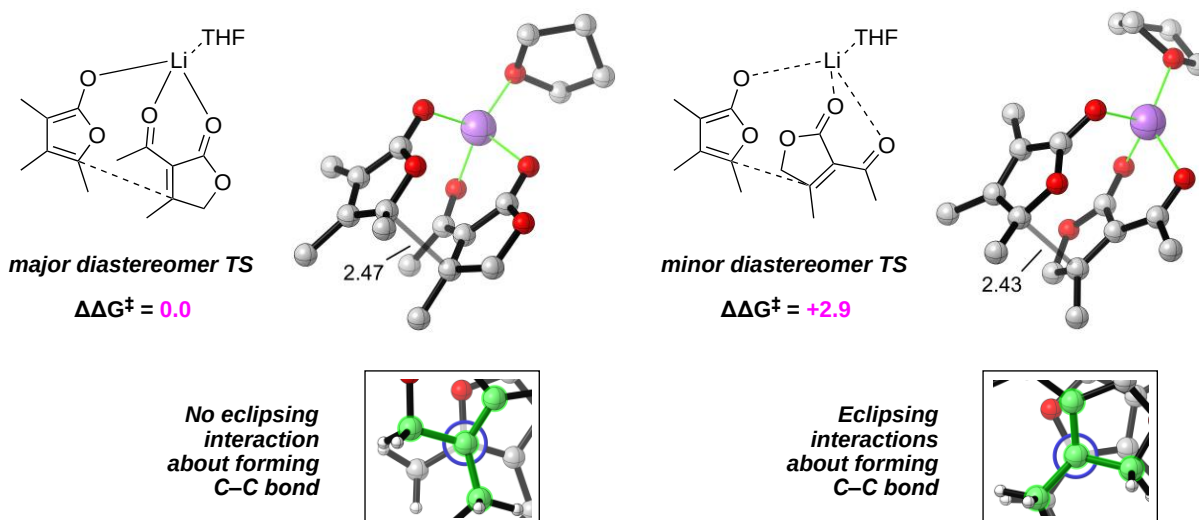


Figure 10. Computed Michael addition transition states leading to the major and minor diastereomeric products at the ω B97XD/6-311++G(d,p), SMD (THF) // ω B97XD/6-31G(d), SMD (THF) level of theory. Hydrogens are omitted from structures for clarity. Energies are in kcal/mol.

Superior alignment of charges in the major diastereomeric TS also contributes to stereodiscrimination (Figure 11). In the major diastereomeric TS, three favorable electrostatic interactions exist between the two reacting partners (C1–C2, C3–C4, C5–O6). In the minor diastereomeric TS, this alignment of negatively and positively charged moieties is significantly disrupted. For instance, the negatively charged O6 is unable to interact significantly with the positively charged C1, but is instead forced to interact with the negatively charged C3.

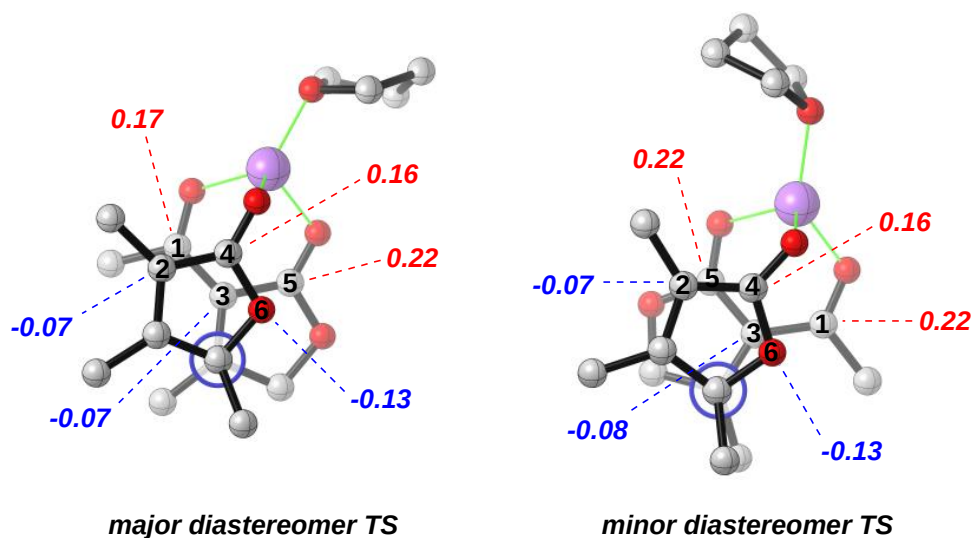
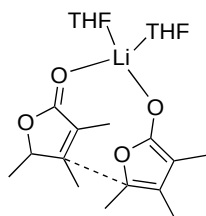


Figure 11. Calculated Hirshfeld charges for Michael addition transition states at the ω B97XD/6-31G(d), SMD (THF) level of theory. **[Major diastereomer TS is compound (10) in manuscript, Minor diastereomer TS is compound (11) in manuscript]**

Heterospecificity in Michael Addition

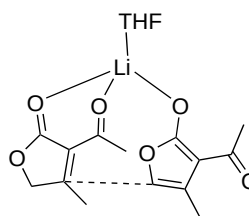
Our calculations confirm the experimentally observed heterospecificity of the Michael addition reaction. Homo-couplings of both the nucleophile and the electrophile have high C–C formation free energy barriers (Figure 12). The presence of the second carbonyl group in the butenolide electrophile significantly enhances electrophilicity and reduces nucleophilicity.

Nucleophile-Nucleophile Homo-Coupling



$$\Delta G^\ddagger = +19.7$$

Electrophile-Electrophile Homo-Coupling



$$\Delta G^\ddagger = +15.8$$

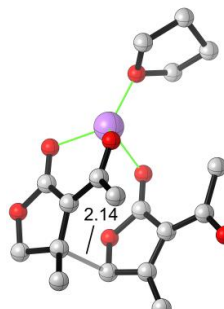
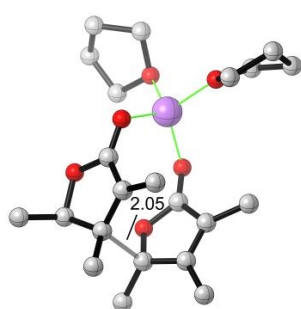


Figure 12. Computed C–C forming transition states for the homo-couplings at the ω B97XD/6-311++G(d,p), SMD (THF) // ω B97XD/6-31G(d), SMD (THF) level of theory. Hydrogens are omitted from structures for clarity. Energies are in kcal/mol.

Less Reactive Electrophiles

We computed the Michael addition transition states for two electrophiles that were experimentally not observed to undergo the Michael addition (Figure 13). Both show much higher free energies of activation than the standard butenolide electrophile.

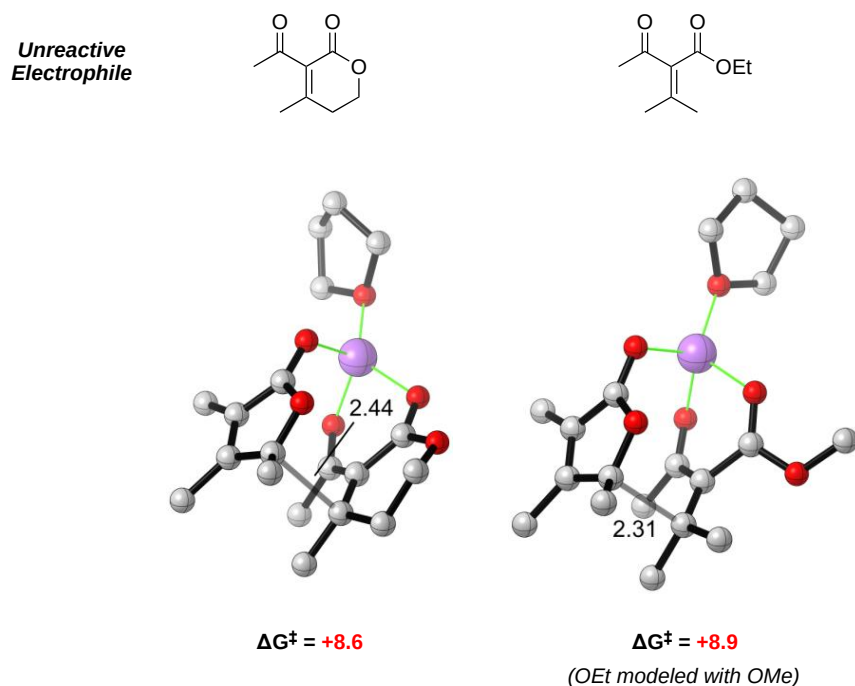


Figure 13. Calculated Michael addition transition states for experimentally unreactive electrophiles at the ω B97XD/6-311++G(d,p), SMD (THF) // ω B97XD/6-31G(d), SMD (THF) level of theory. Hydrogens are omitted from structures for clarity. Energies are in kcal/mol.

The lack of Michael addition reactivity by these two electrophiles can be rationalized both through orbital energies and sterics. Calculated molecular orbital energies for the experimentally reactive standard butenolide are shown in Figure 14. The two unreactive electrophiles were calculated to have higher-lying LUMOs (Figure 15), making them less electrophilic.

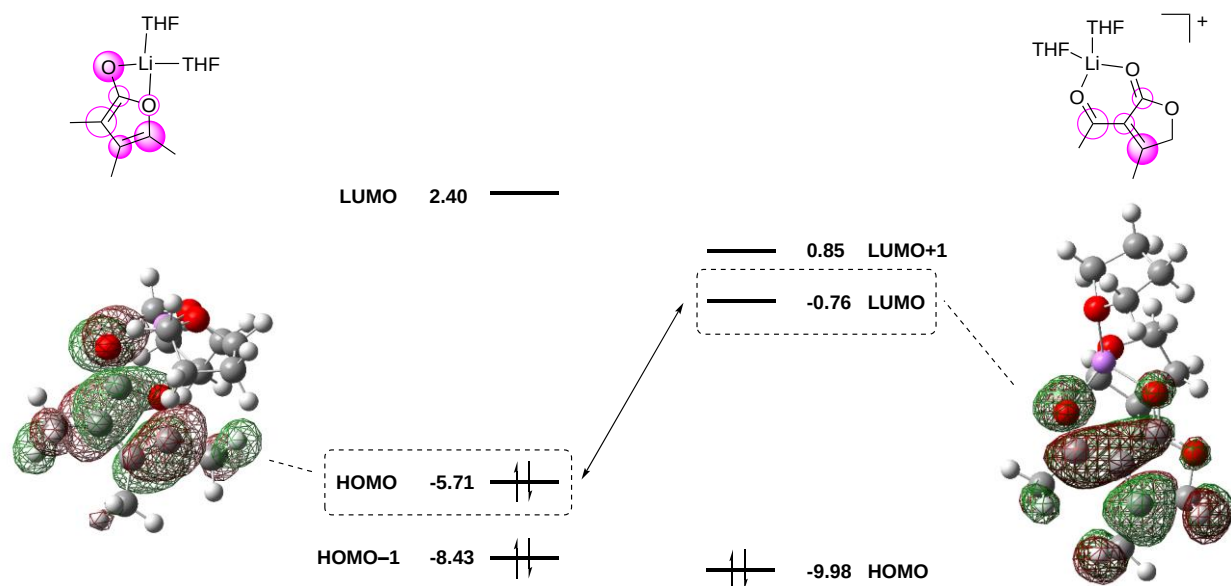


Figure 14. Calculated frontier and subadjacent molecular orbitals at the ω B97XD/6-31G(d), SMD (THF) level of theory. Orbital energies are in eV.

Unreactive Electrophiles:

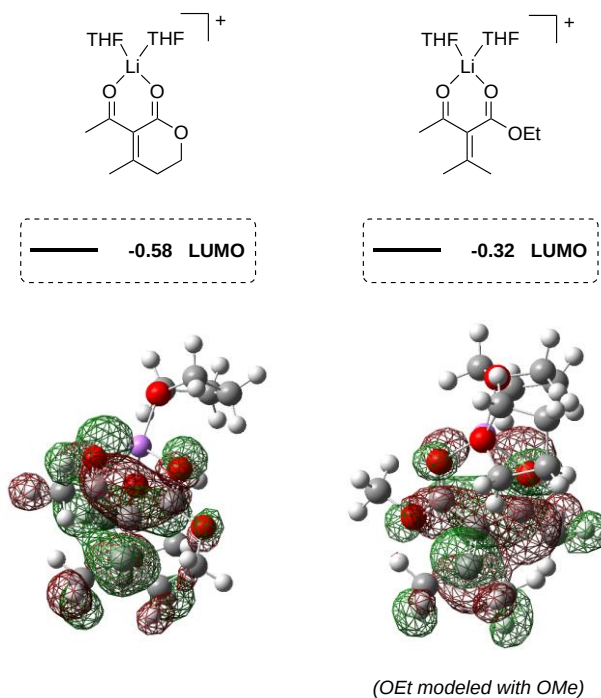


Figure 15. Calculated lowest unoccupied molecular orbitals (LUMOs) for unreactive electrophiles at the ω B97XD/6-31G(d), SMD (THF) level of theory. Orbital energies are in eV.

Calculated structures of the Michael addition transition states (Figure 16) show that the two unreactive electrophiles experience more 1,3-allylic strain than the reactive five-membered

butenolide electrophile, as indicated by shorter H...H contact distances between the ketone and vinylic methyl groups on the electrophile.

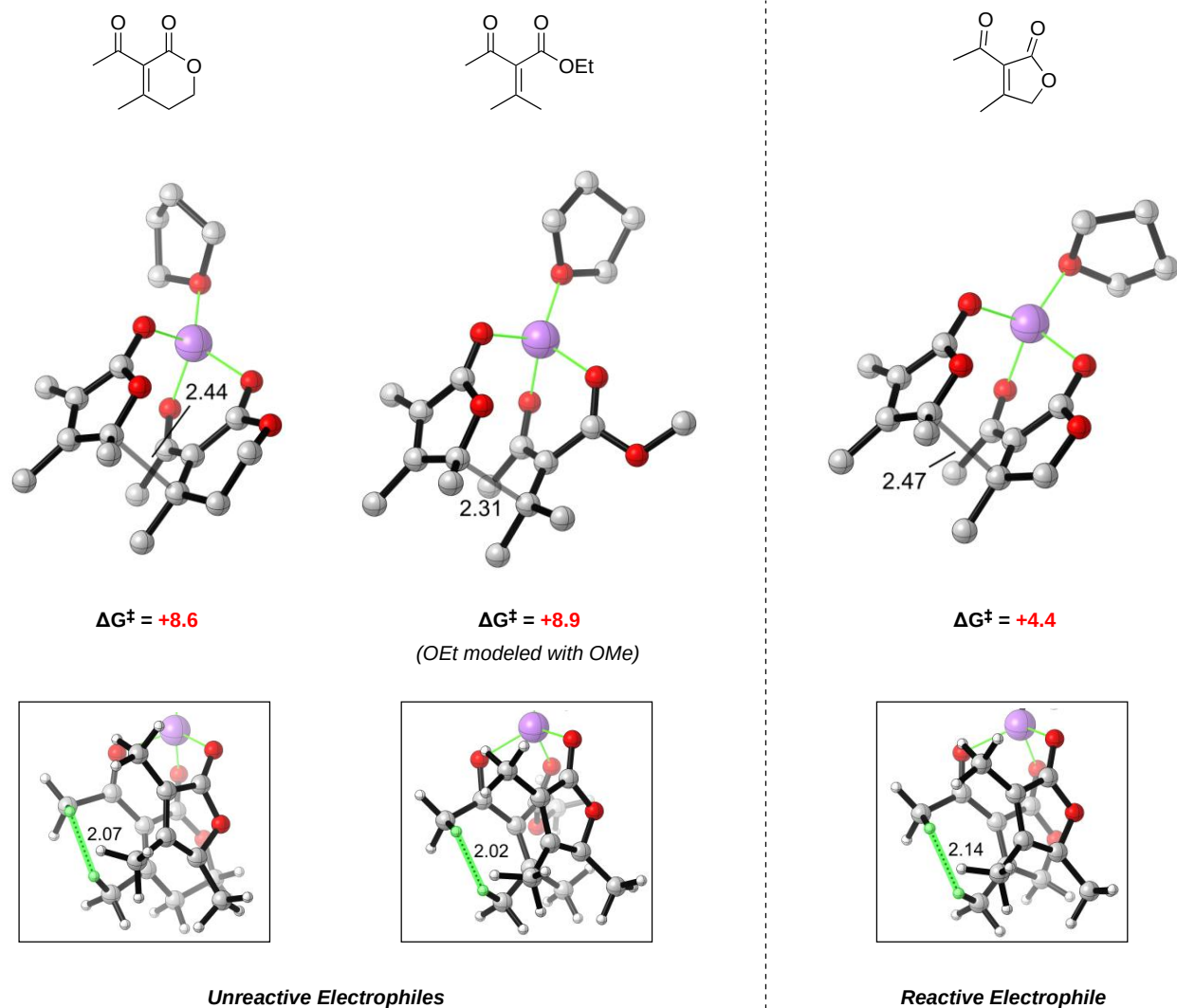


Figure 16. Shortest H...H contact distances in computed Michael addition transition states for unreactive and reactive electrophiles.

Calculated pKas

Because protonation of the nucleophile is suspected to be competing with C–C bond formation in certain cases, we also computed the pKas of select electrophiles and nucleophile precursors. The results are shown in Figure 17.

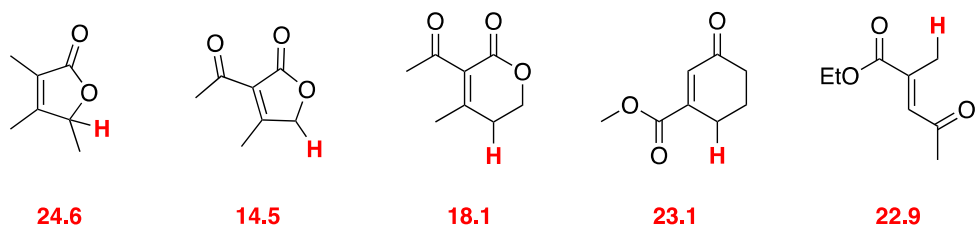


Figure 17. Calculated pKa values of highlighted protons at the ω B97XD/6-311++G(d,p), SMD (MeOH) // ω B97XD/6-31G(d), SMD (MeOH) level of theory using the pKa of AcOH in MeOH (9.7) as reference.

The calculated pKas indicate that the five-membered butenolide electrophile (pKa 14.5) is the most acidic, at 10.1 pKa units below the nucleophile precursor (pKa 24.6). The six-membered butenolide is less acidic than the five-membered butenolide, at 18.1.

Computational References

1. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09; Gaussian Inc.: Wallingford, CT, **2009**.
2. Chai, J. D.; Head-Gordon, M. Long-Range Corrected Hybrid Density Functionals with Damped Atom-Atom Dispersion Corrections. *Phys. Chem. Chem. Phys.* **2008**, *10*, 6615.
3. Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378.
4. Legault, C. Y. CYLview, 1.0b; Université de Sherbrooke, 2009; <http://www.cylview.org>.

References

- (1) Surmont, R.; Verniest, G.; Kimpe, N. De. *J. Org. Chem.* **2010**, 5750–5753.
- (2) Zhang, H.; Hu, L.; Ma, Z.; Li, R.; Zhang, Z.; Tao, C.; Cheng, B.; Li, Y.; Wang, H.; Zhai, H. *Angew. Chem. Int. Ed. Engl.* **2016**, 11638–11641.
- (3) Runcie, K. A.; Taylor, R. J. K. *chem. Commun.* **2002**, 974–975.
- (4) Dudzi, K.; Kwiatkowski, P. *Org. Lett.* **2012**, 2010–2013.
- (5) Kalyva, M.; Zografos, A. L.; Kapourani, E.; Giambazolias, E. *Chem. Eur. J.* **2015**, 3278–3289.
- (6) Abe, H.; Kawai, * Toshitaka; Komatsu, Y.; Mayu Kamimura; Yasuo Takeuchi; Horino, and Y. *Heterocycles* **2012**, 86 (1), 785–789.
- (7) Edmund P. Woo and Frank C. W. Cheng. *J. Org. Chem.* **1986**, No. 9, 3706–3707.
- (8) Kotzabasaki, V.; Vassilikogiannakis, G.; Stratakis, M. *J. Org. Chem.* **2016**, 4406–4411.
- (9) Chen, B.; Resch, V.; Otten, L. G.; Hanefeld, U. *Chem. Eur. J.* **2015**, 3020–3030.
- (10) Thombare, P.; Desai, J.; Argade, A.; Gite, S.; Shah, K.; Pavase, L.; Patel, P. *Synth. Commun.* **2009**, 7911, 2–9.
- (11) Pellicciari, R.; Natalini, B.; Cecchetti, S.; Fringuelli, R. *J. Chem. Soc. Perkin Trans. I* **1985**, No. 5, 493–497.
- (12) Pellicciari, R.; Natalini, B.; Sadeghpour, B. M.; Rosato, G. C.; Ursini, A. *J. Chem. Soc., Chem. Commun.* **1993**, No. 1798, 1798–1800.
- (13) Hue, B. T. B.; Dijkink, J.; Kuiper, S.; Schaik, S. Van; Maarseveen, J. H. Van; Hiemstra, H. *Eur. J. Org. Chem.* **2006**, 127–137.
- (14) Sheng, X.; Hua, K.; Yang, C.; Wang, X.; Ji, H.; Xu, J. *Bioorg. Med. Chem. Lett.* **2015**, 25 (17), 3535–3540.
- (15) Qiang, X.; Li, Y.; Yang, X.; Luo, L.; Xu, R.; Zheng, Y.; Cao, Z. *Bioorg. Med. Chem. Lett.* **2017**, 27, 718–722.
- (16) Novak, P.; Correa, A.; Gallardo-donaire, J.; Martin, R. *Angew. Chemie - Int. Ed.* **2011**, 12236–12239.
- (17) Nicolaou, K. C.; Seitz, S. P.; Sipio, W. J.; Blount, J. F. *J. Am. Chem. Soc.* **1979**, 101 (14), 3884–3893.
- (18) Anslyn, E.; Dougherty, D. *Modern Physical Organic Chemistry*; 2006.
- (19) Melander, L.; Saunders, W. H., J. *Reactions Rates of Isotopic Molecules*; 1980.
- (20) Yamataka, H.; Fujimura, N.; Kawafuji, Y.; Hanafusa, T. *J. Am. Chem. Soc.* **1987**, 4305–4308.
- (21) Frisch, et. al. .
- (22) Liptak, M.; Schields, G. *J. Am. Chem. Soc.* **2001**, 123, 7314–7319.
- (23) Saunders, M. et. al. *J. Am. Chem. Soc.* **1989**, 111, 8989–8994.
- (24) J., B. *J. Chem. Phys.* **1947**, 15, 261–267.
- (25) Bell, R. P. **1980**, No. Chapman and Hall, 60–63.
- (26) Turner, E. J. A., *Chem. Soc.* **1953**, 861

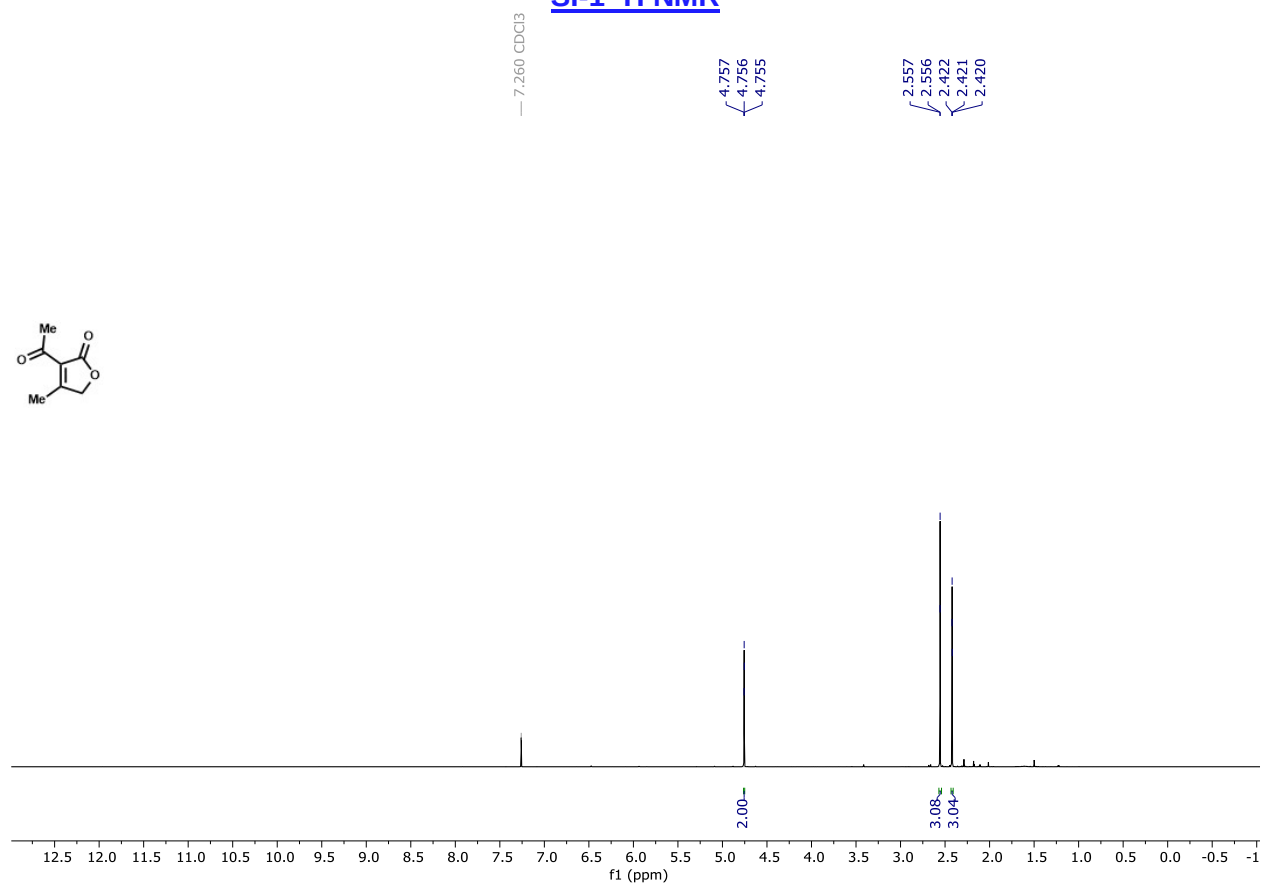
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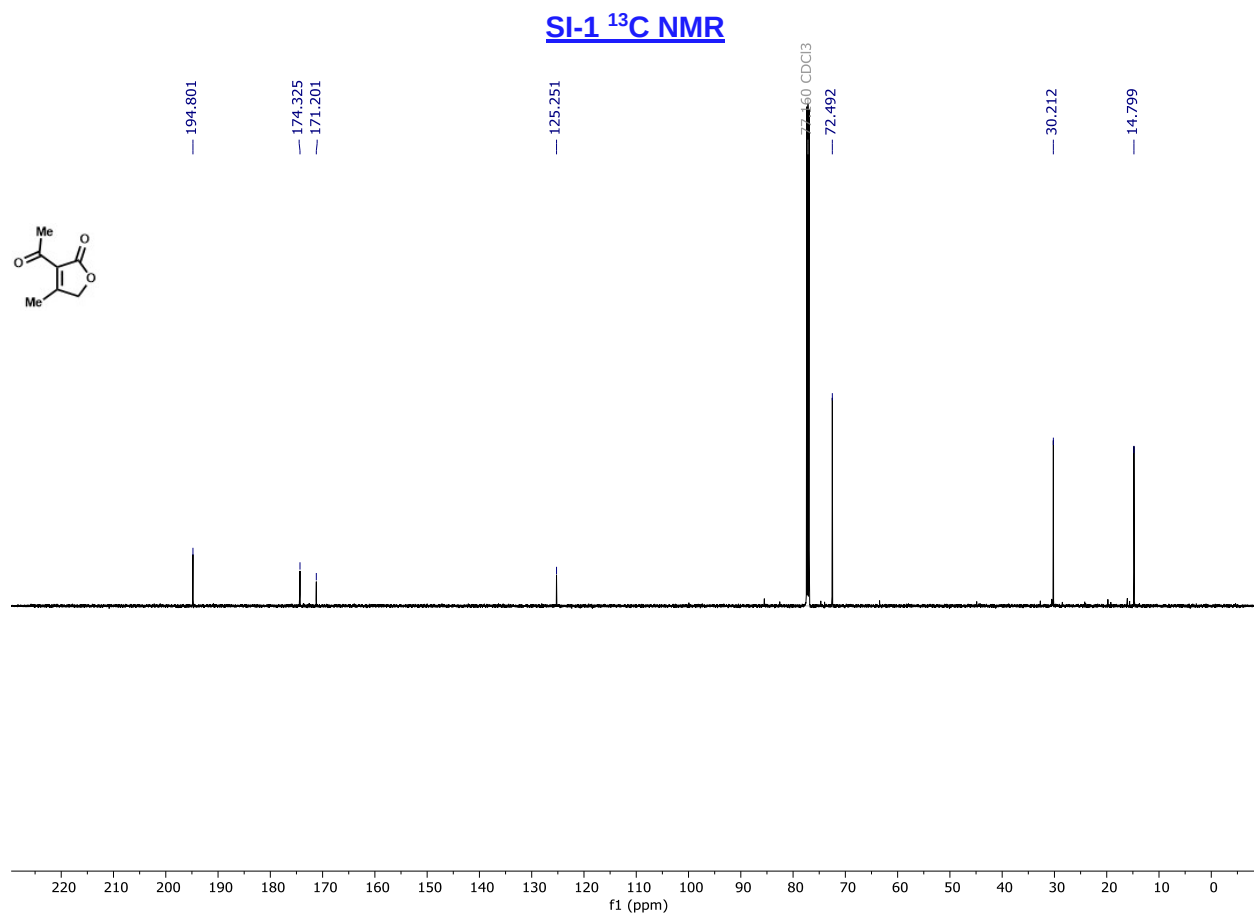
General comments:

- 1) Singlets between 1.55-1.60 ppm are the result of residual water within the NMR sample.
- 2) Minor peaks between 1.20 - 1.30 ppm are the result of residual grease within the NMR sample.
- 3) The singlet peak at 0.07 ppm is an artifact of silicon grease.

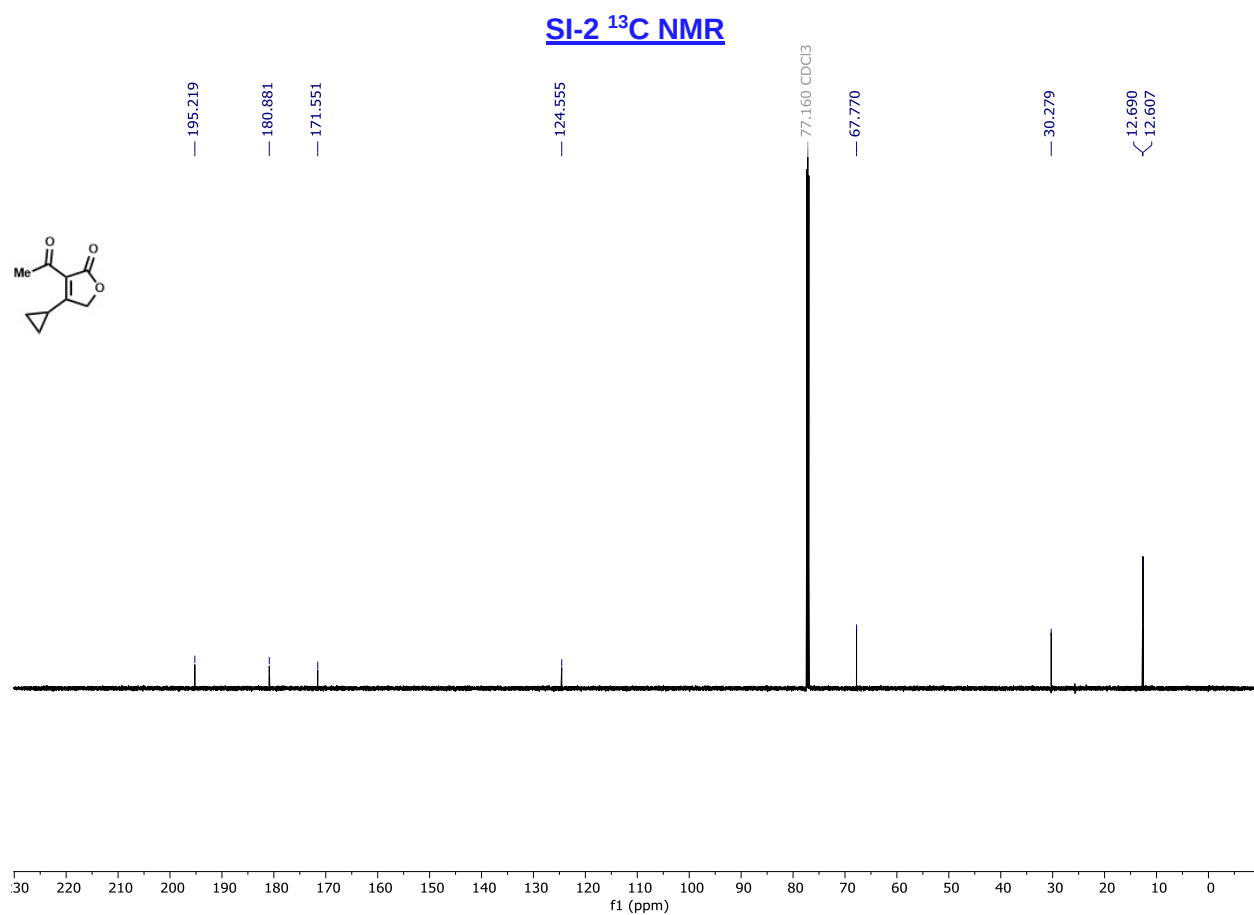
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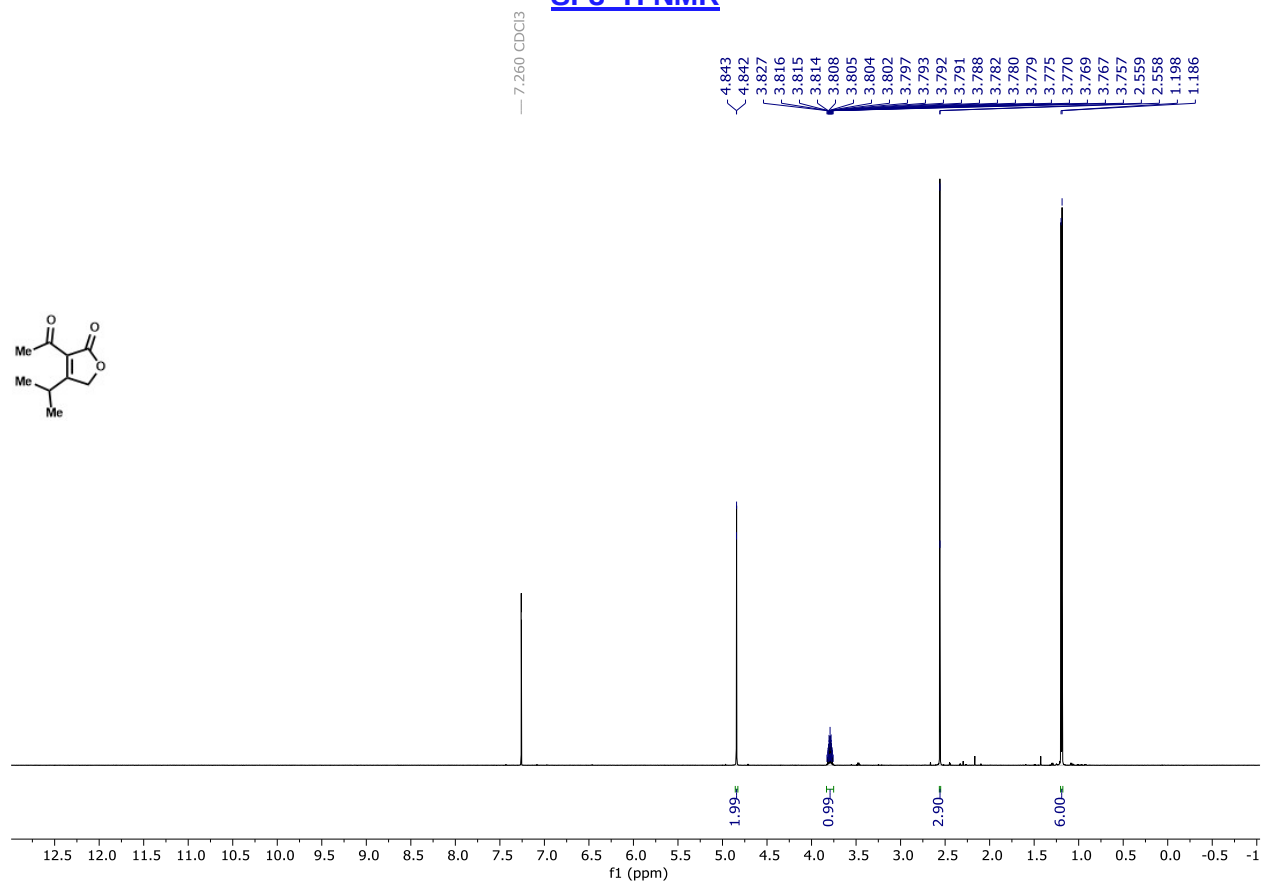
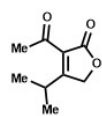
SI-1 ^1H NMR

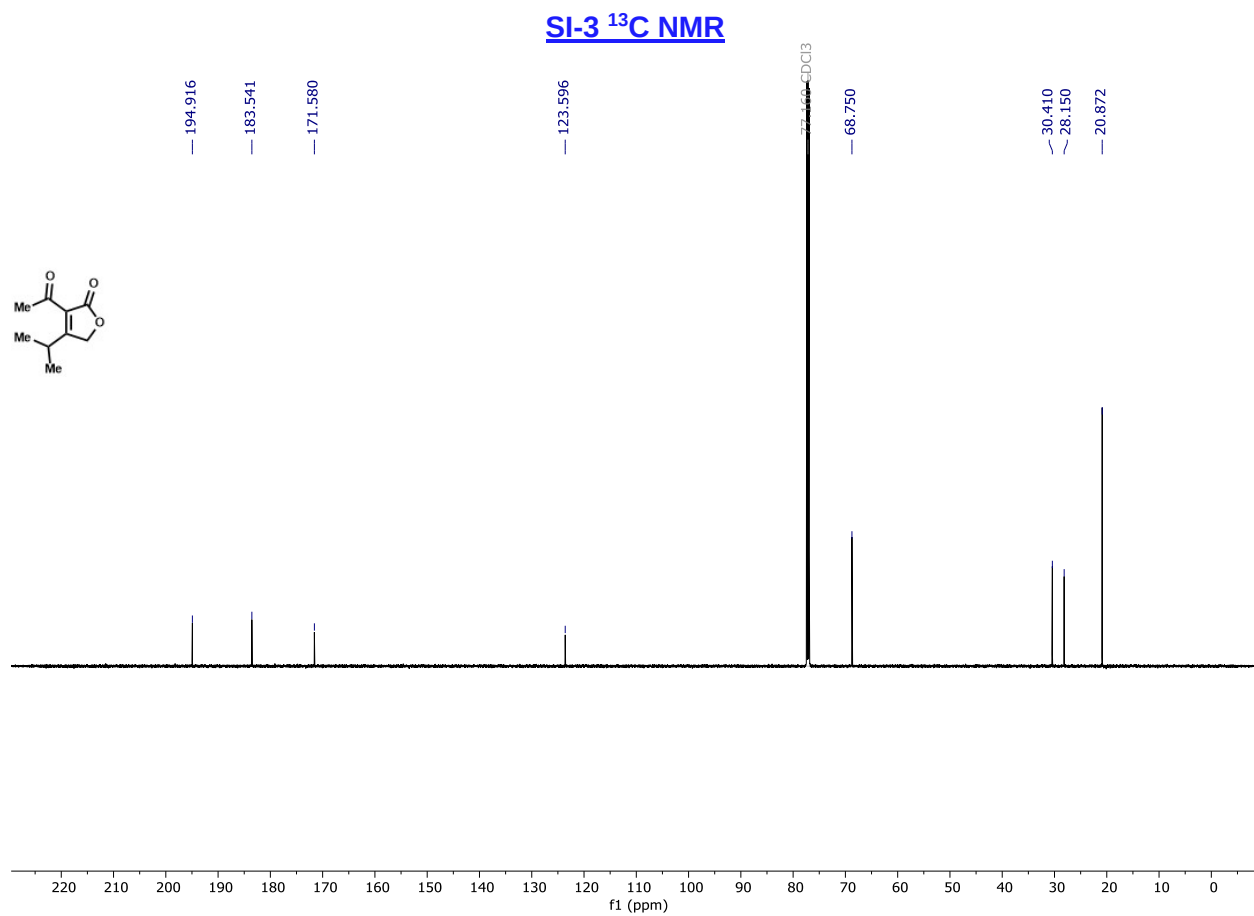


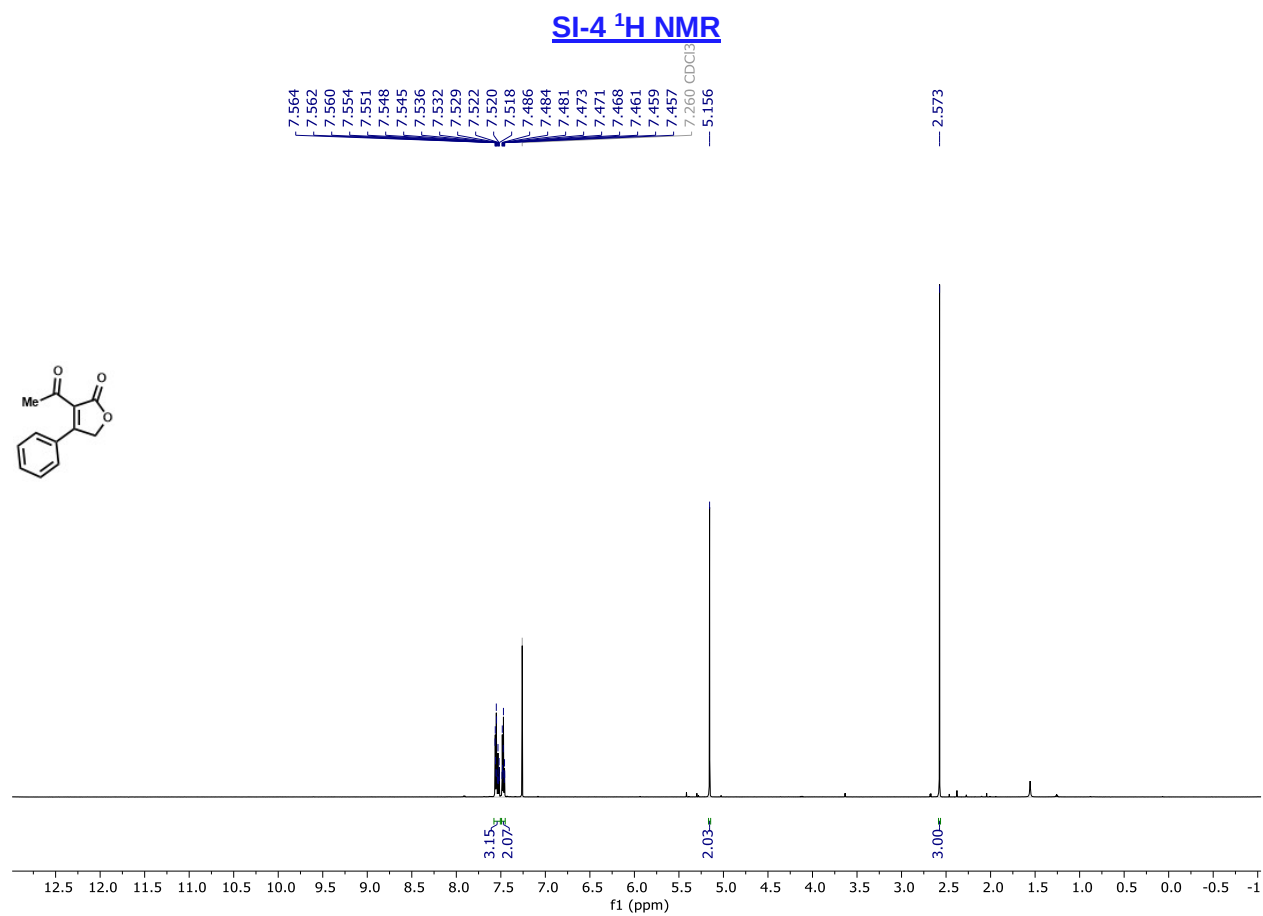
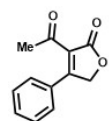




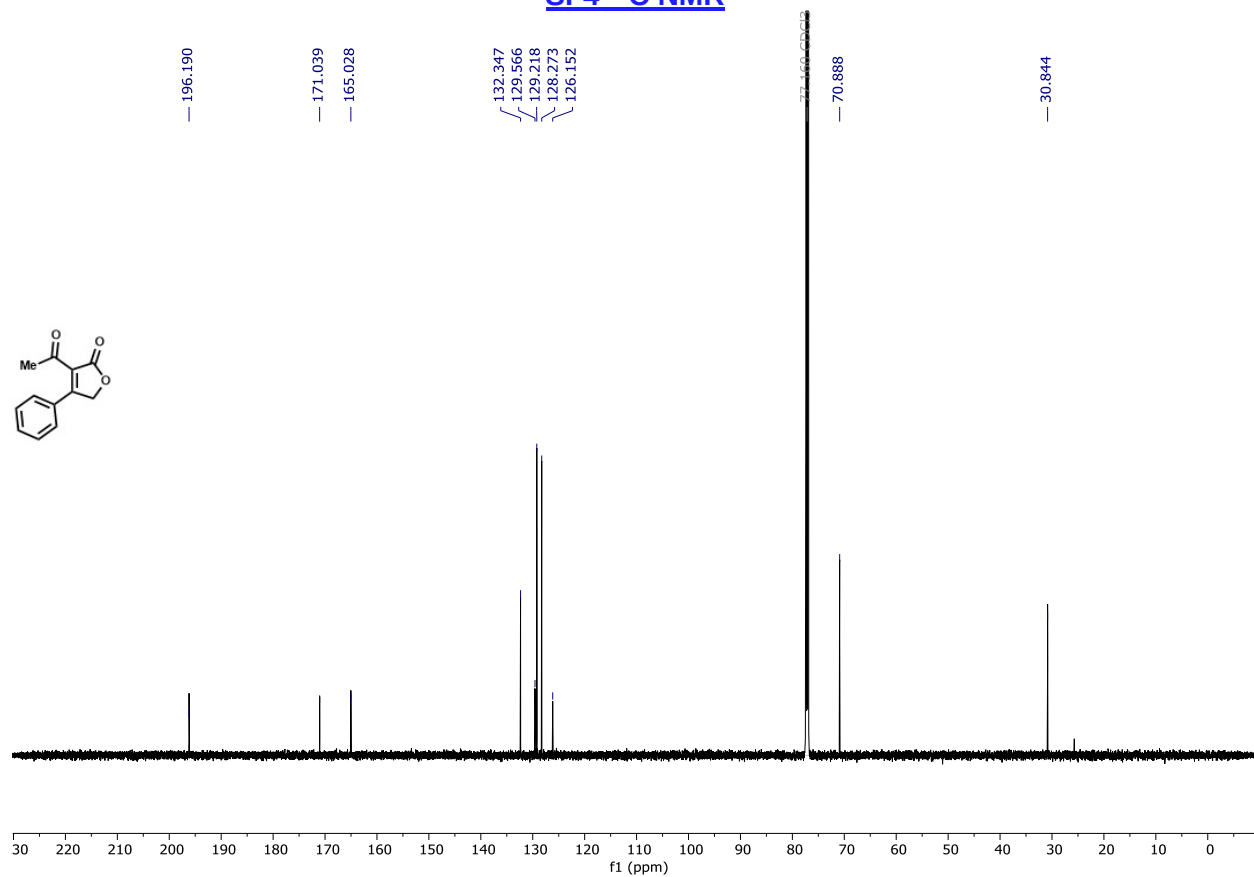


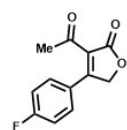




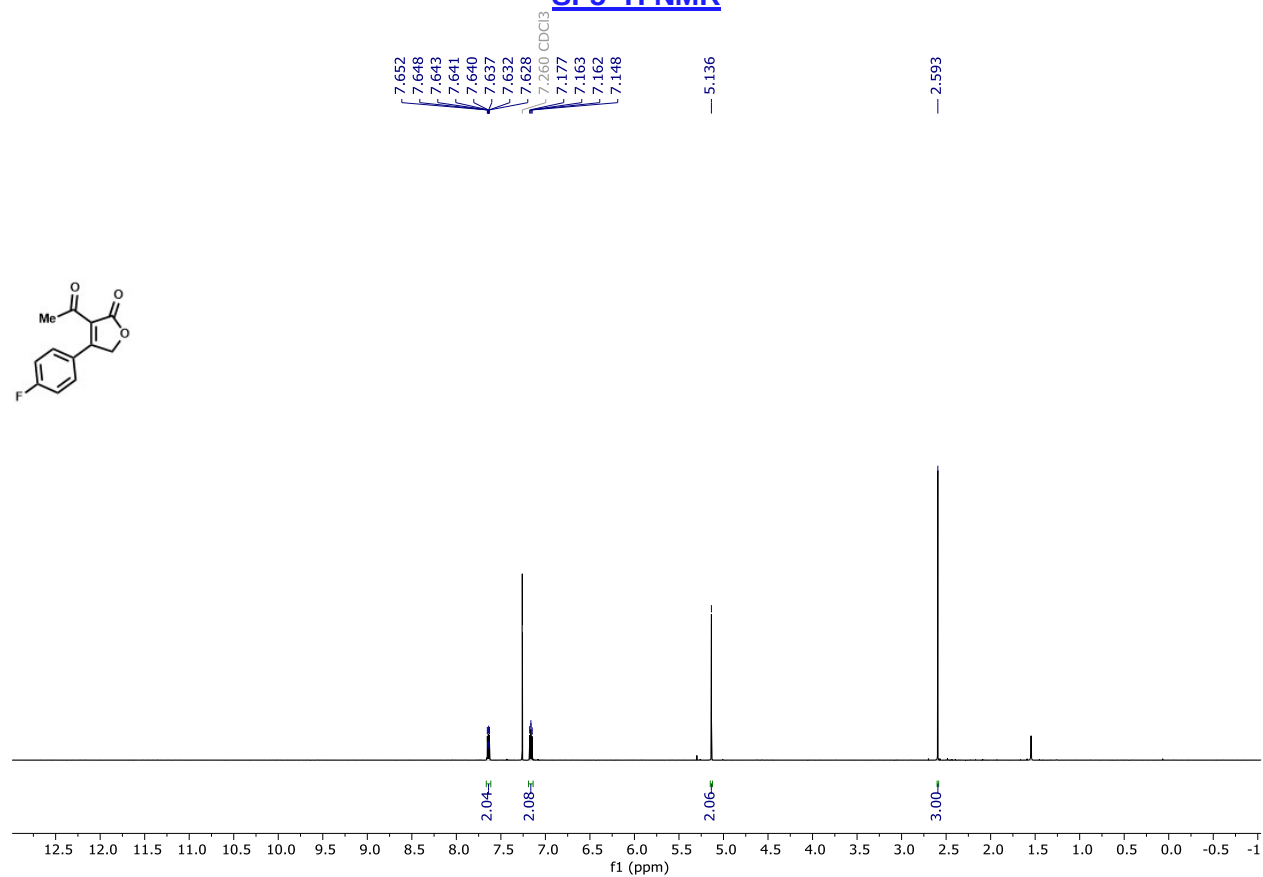


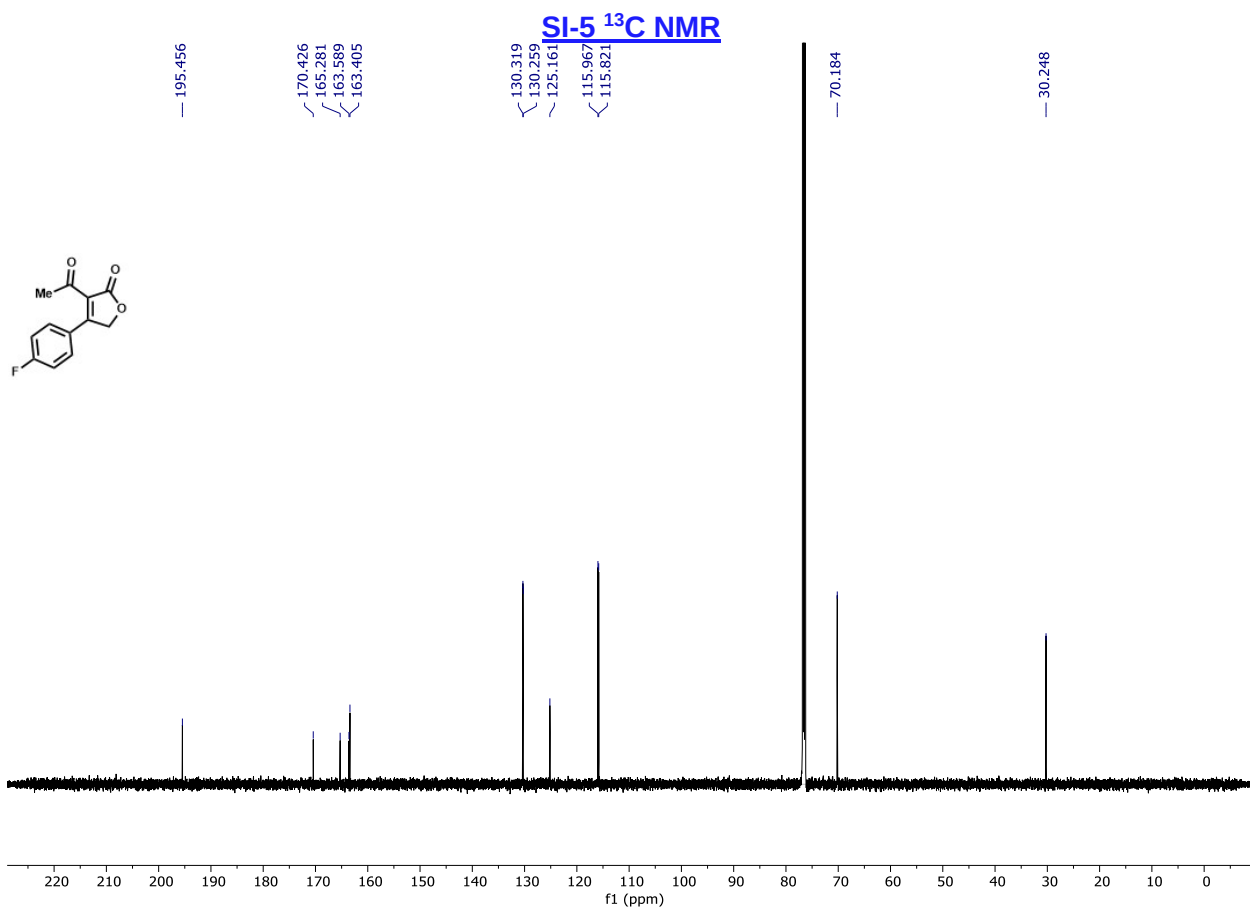
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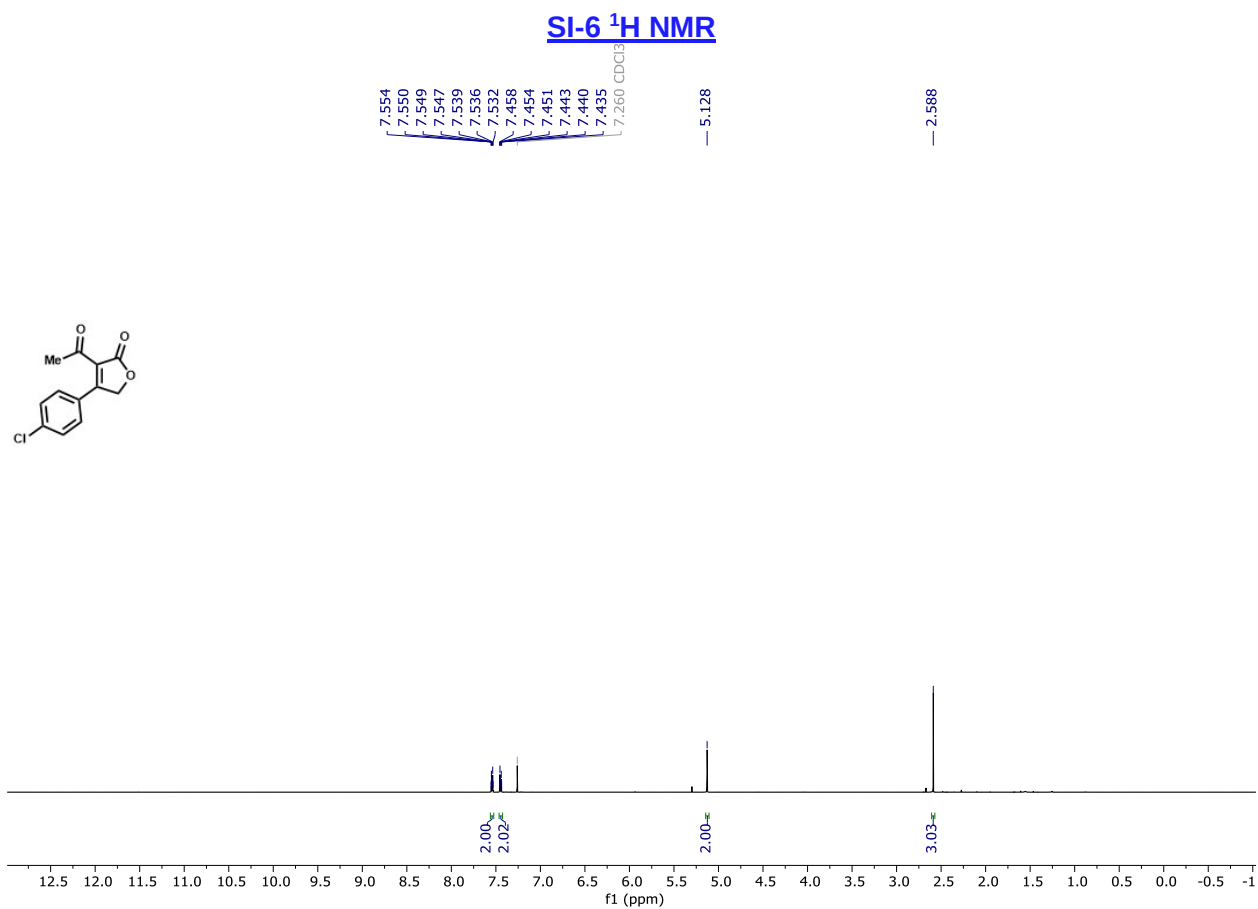




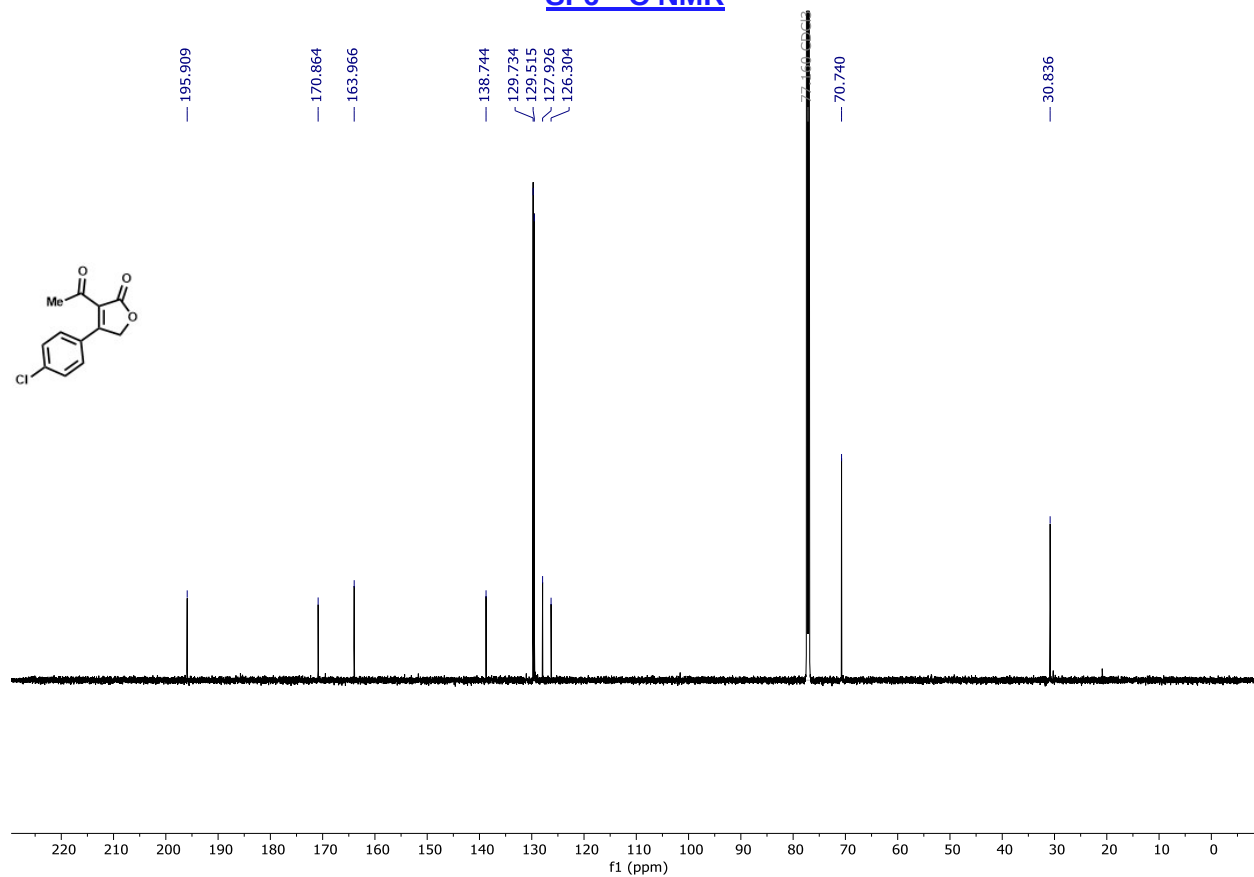
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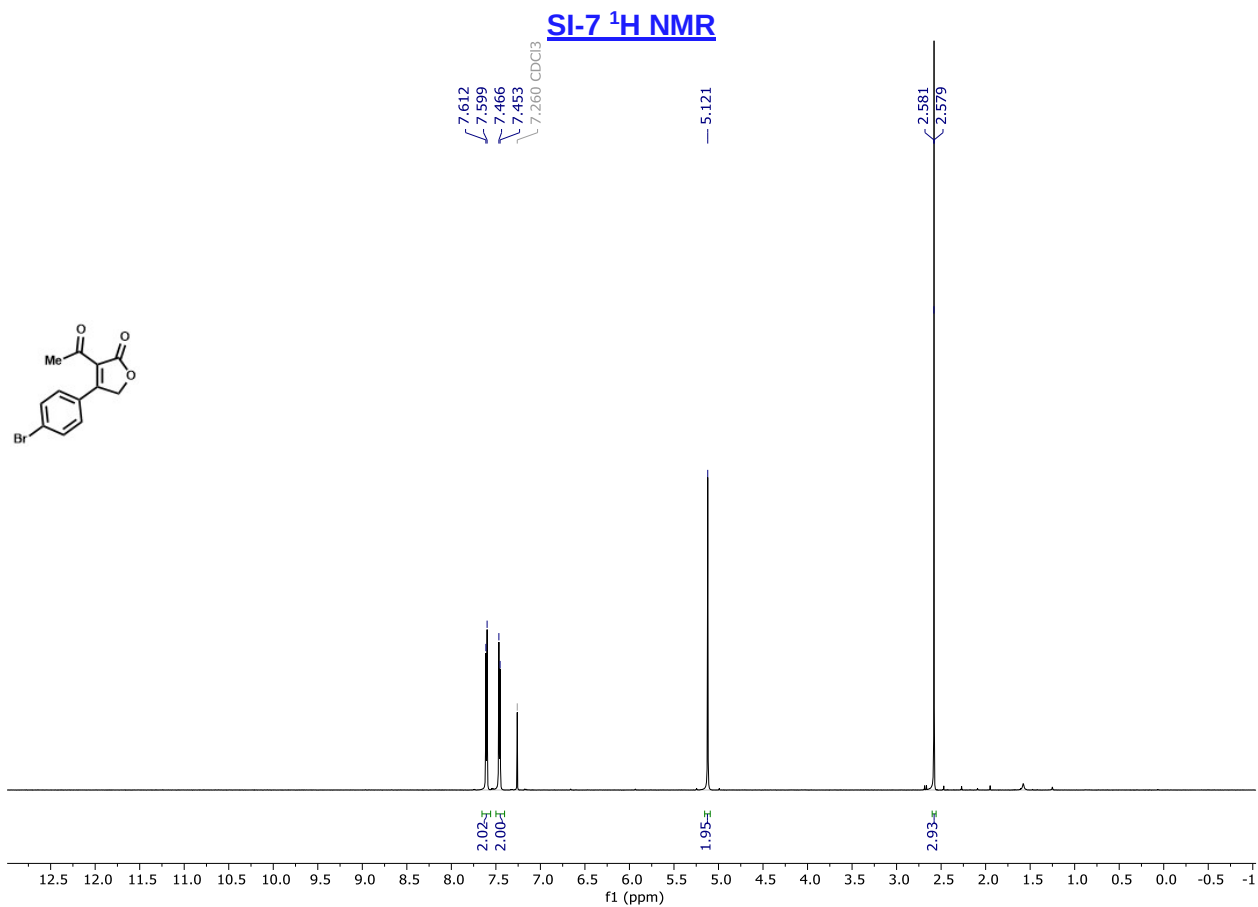




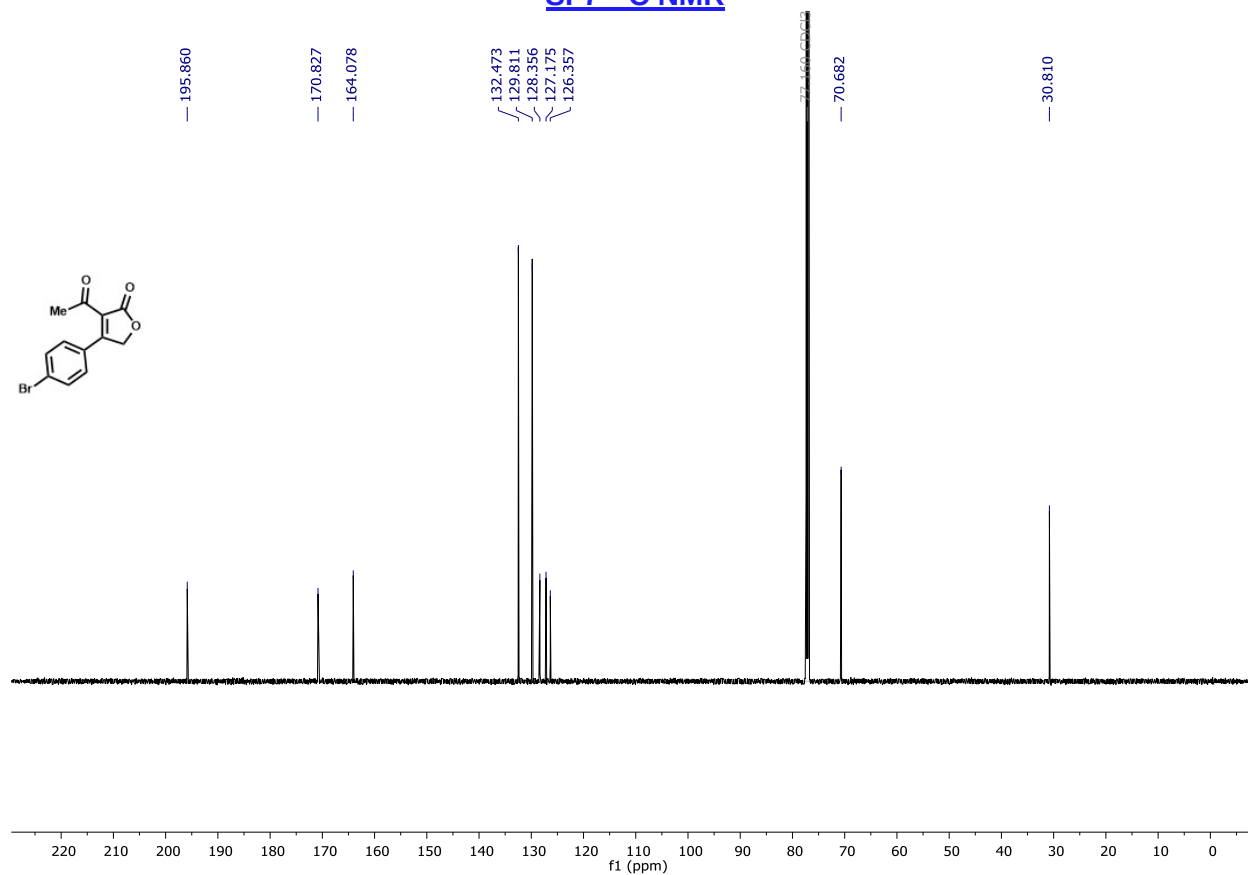


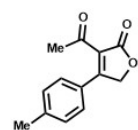
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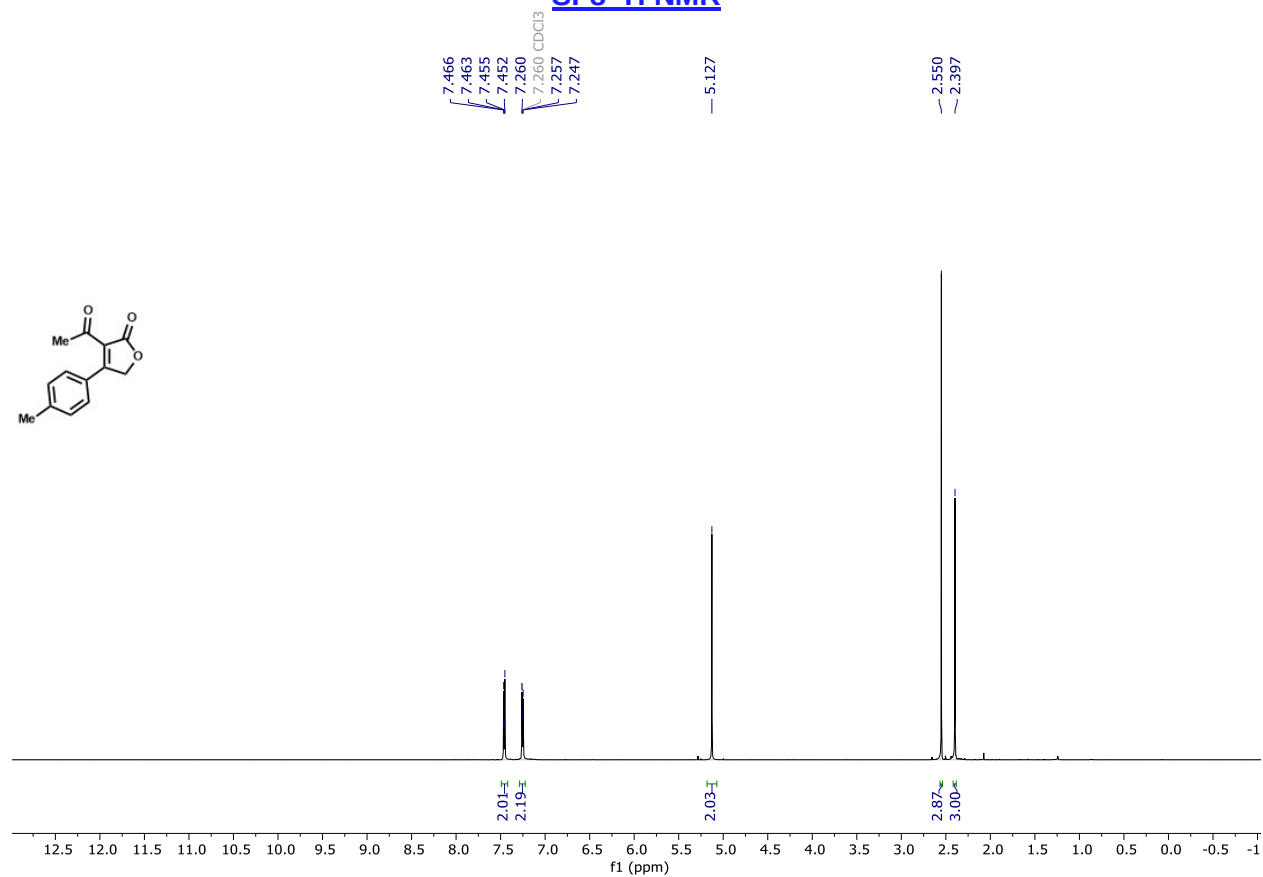


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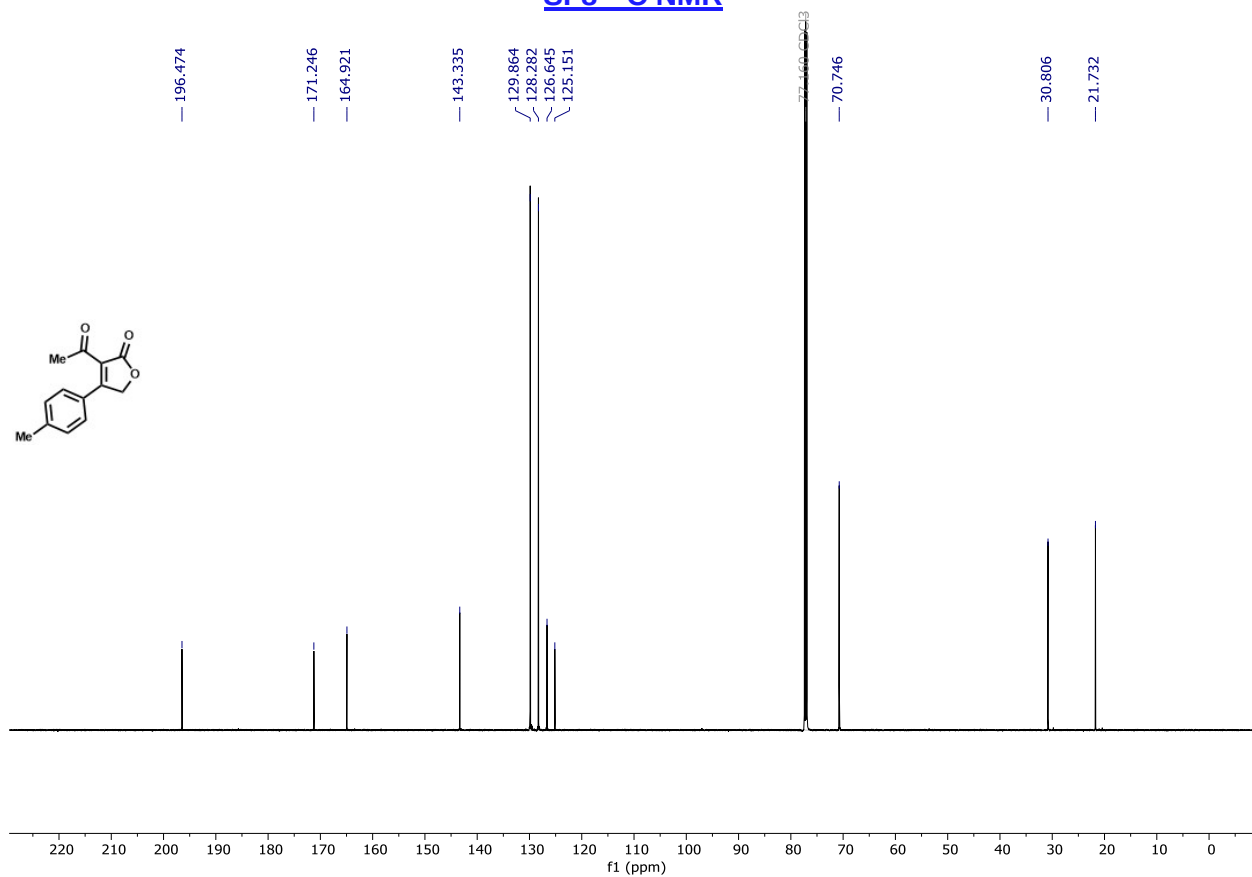


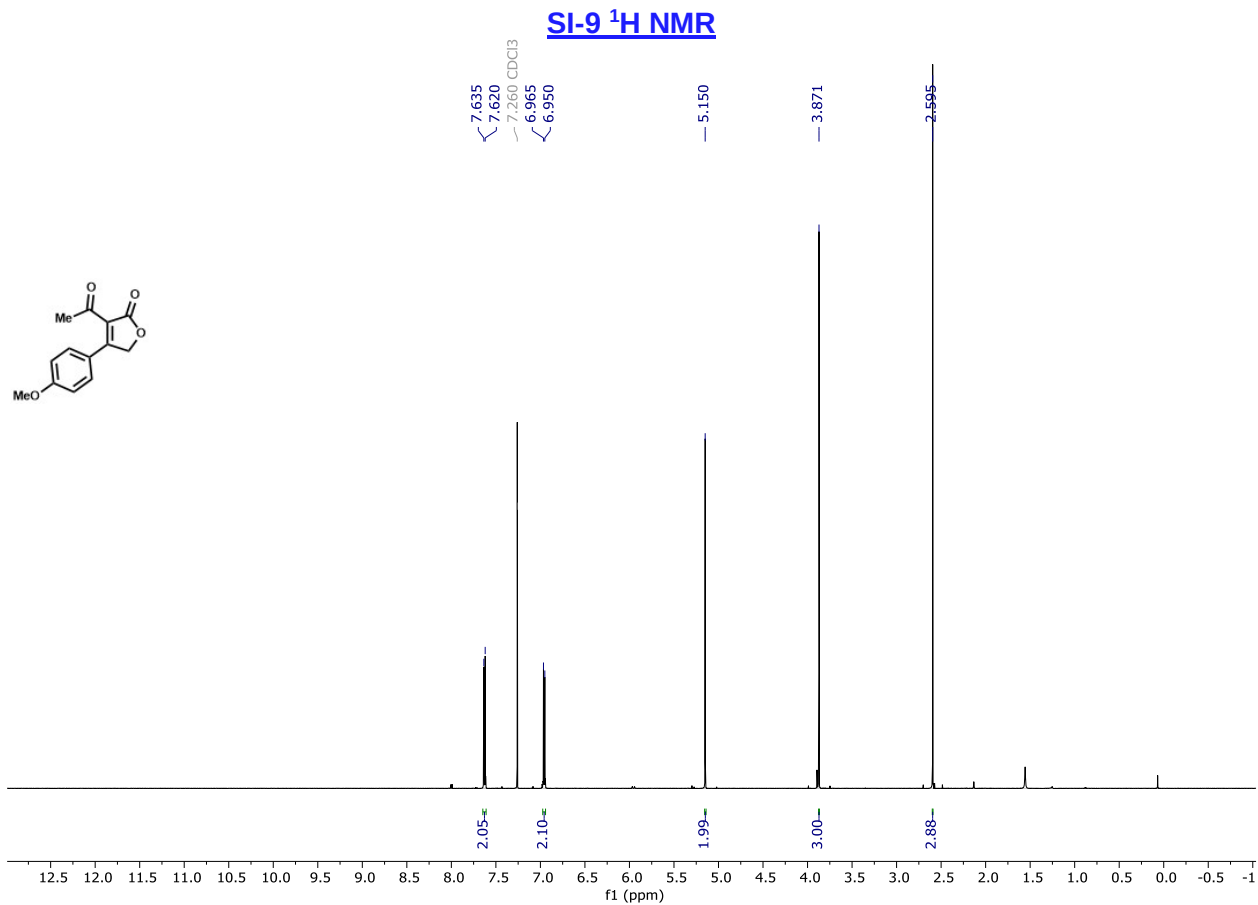


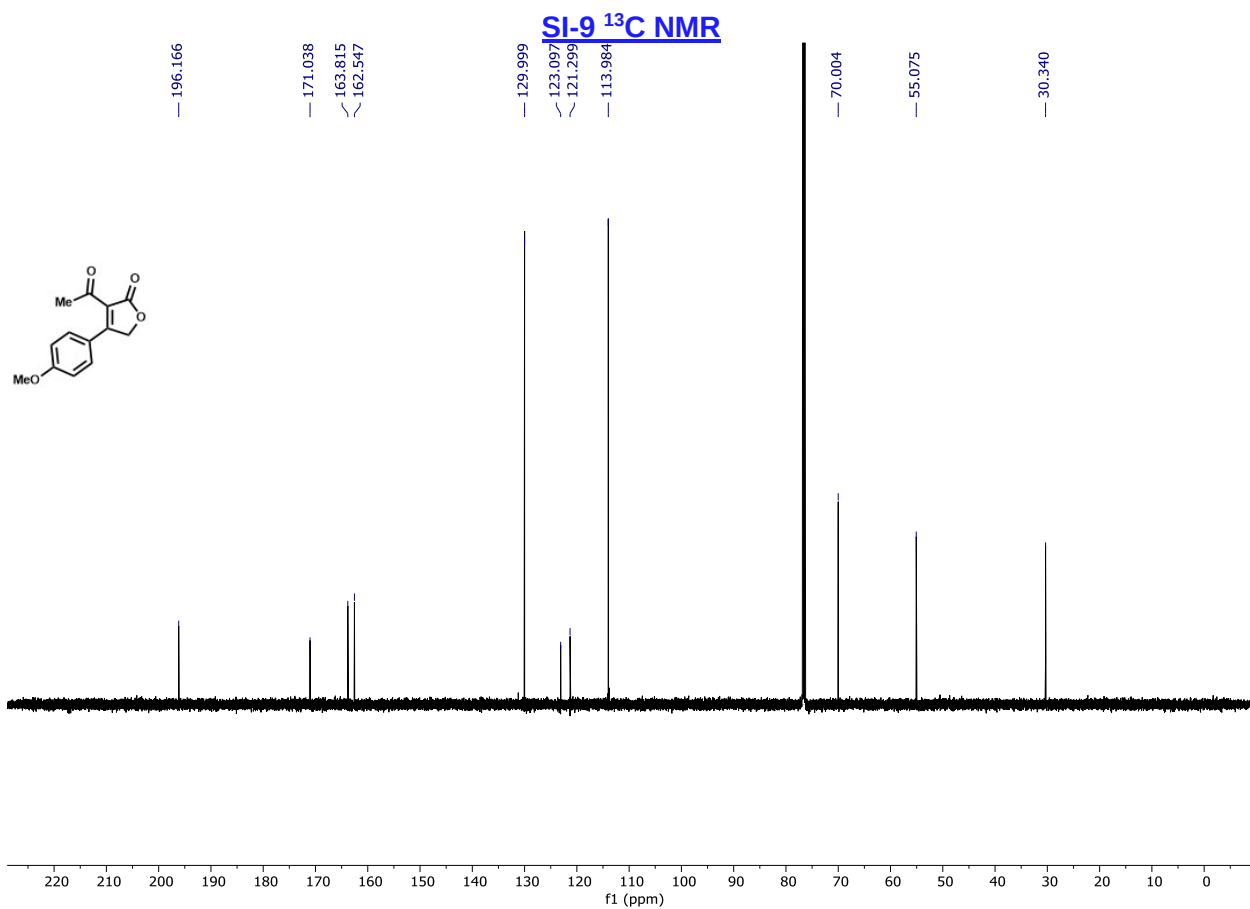
SI-8 ¹H NMR

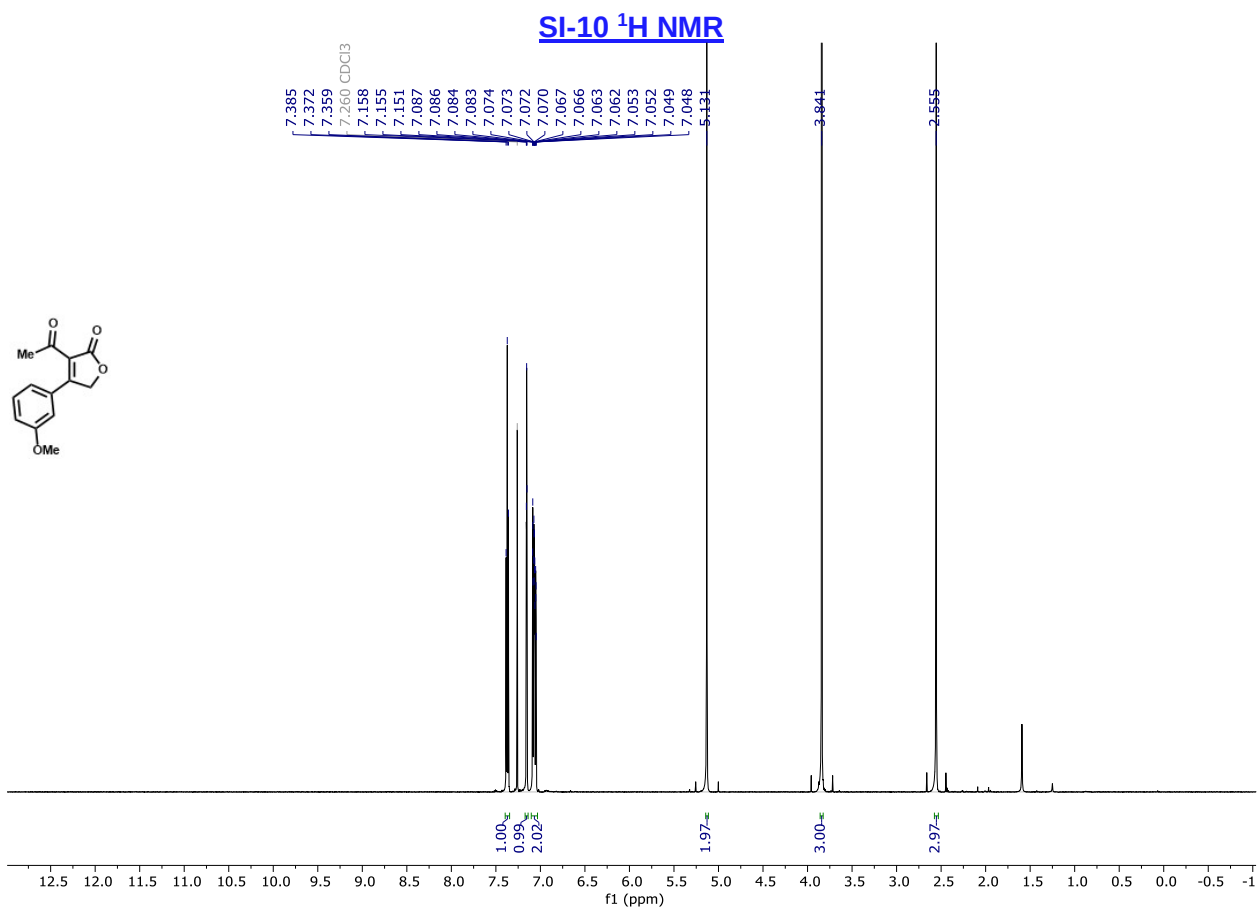


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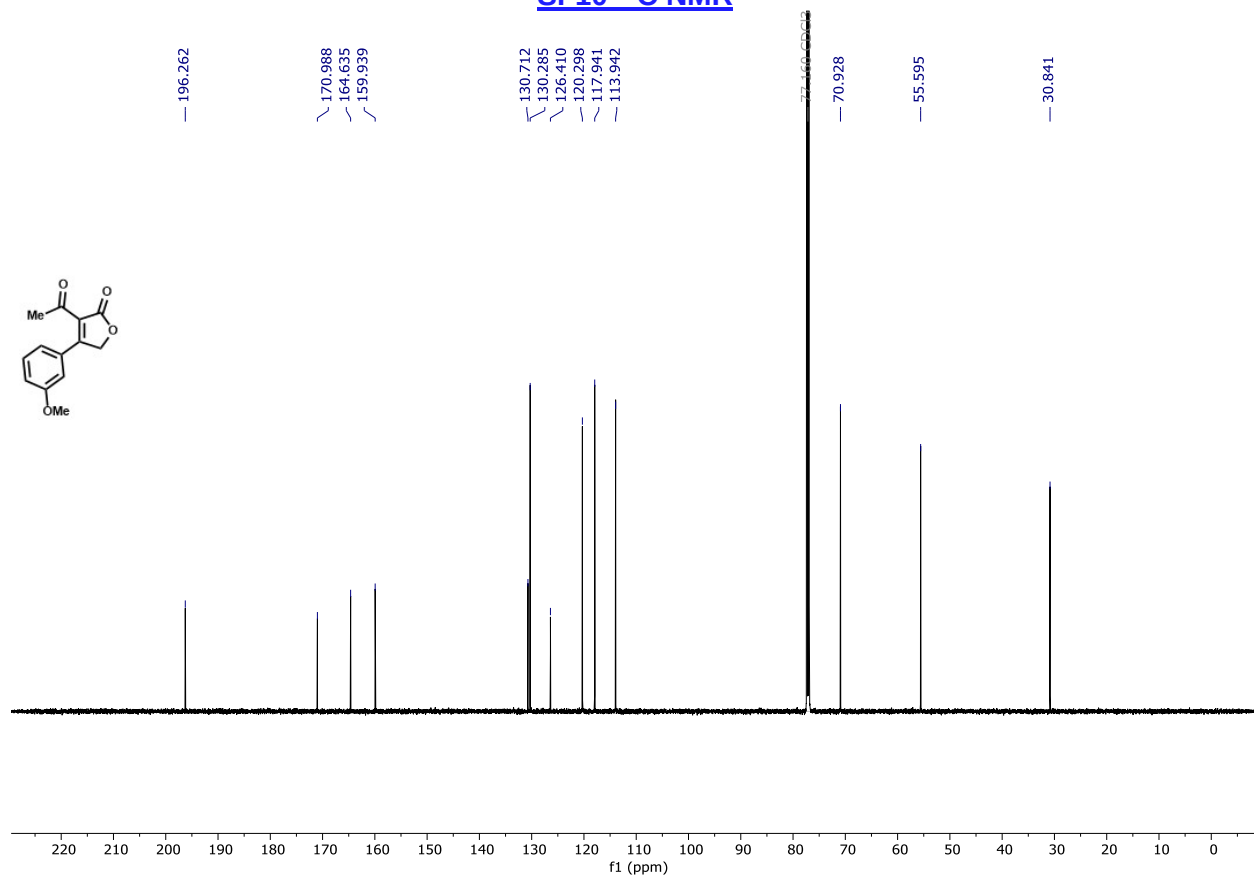


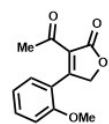




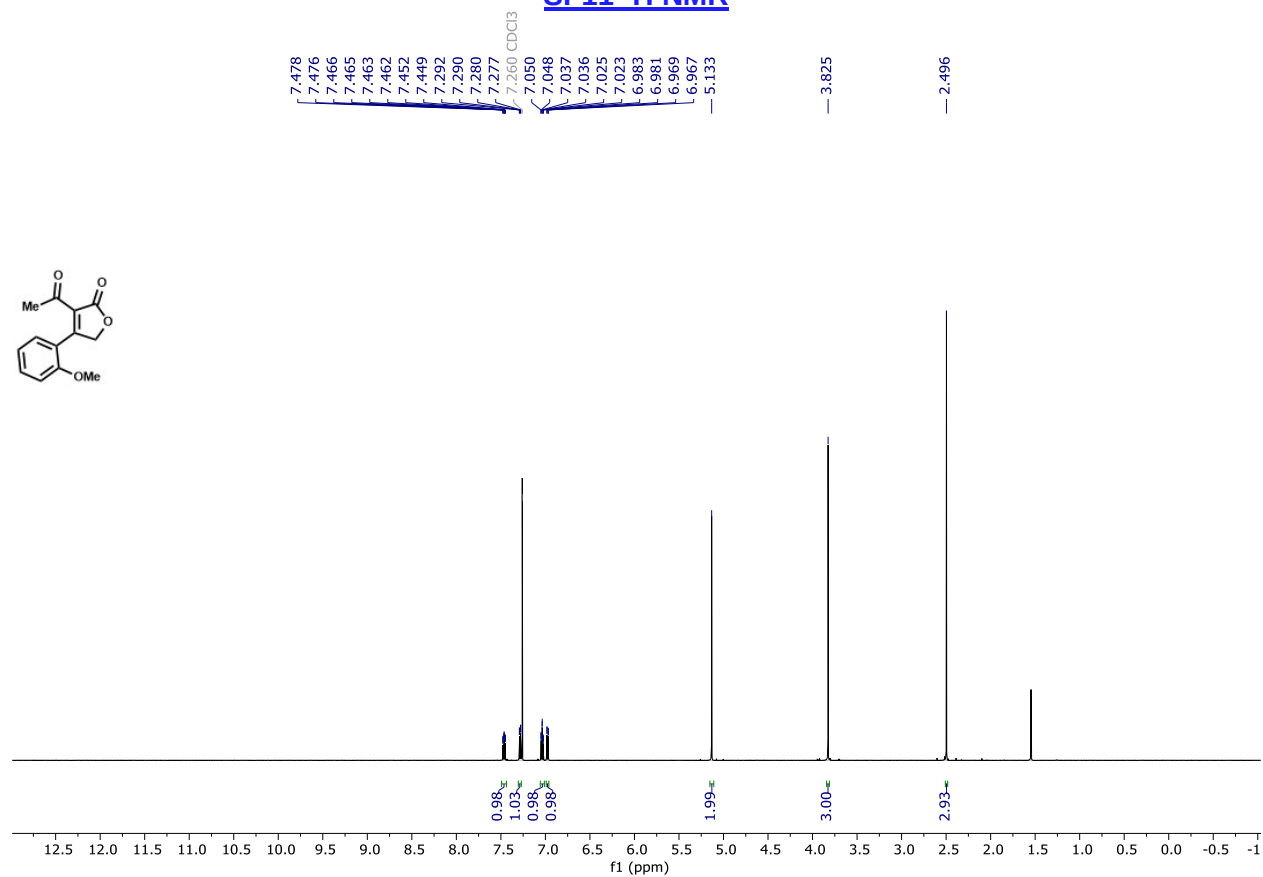


SI-10 ¹³C NMR

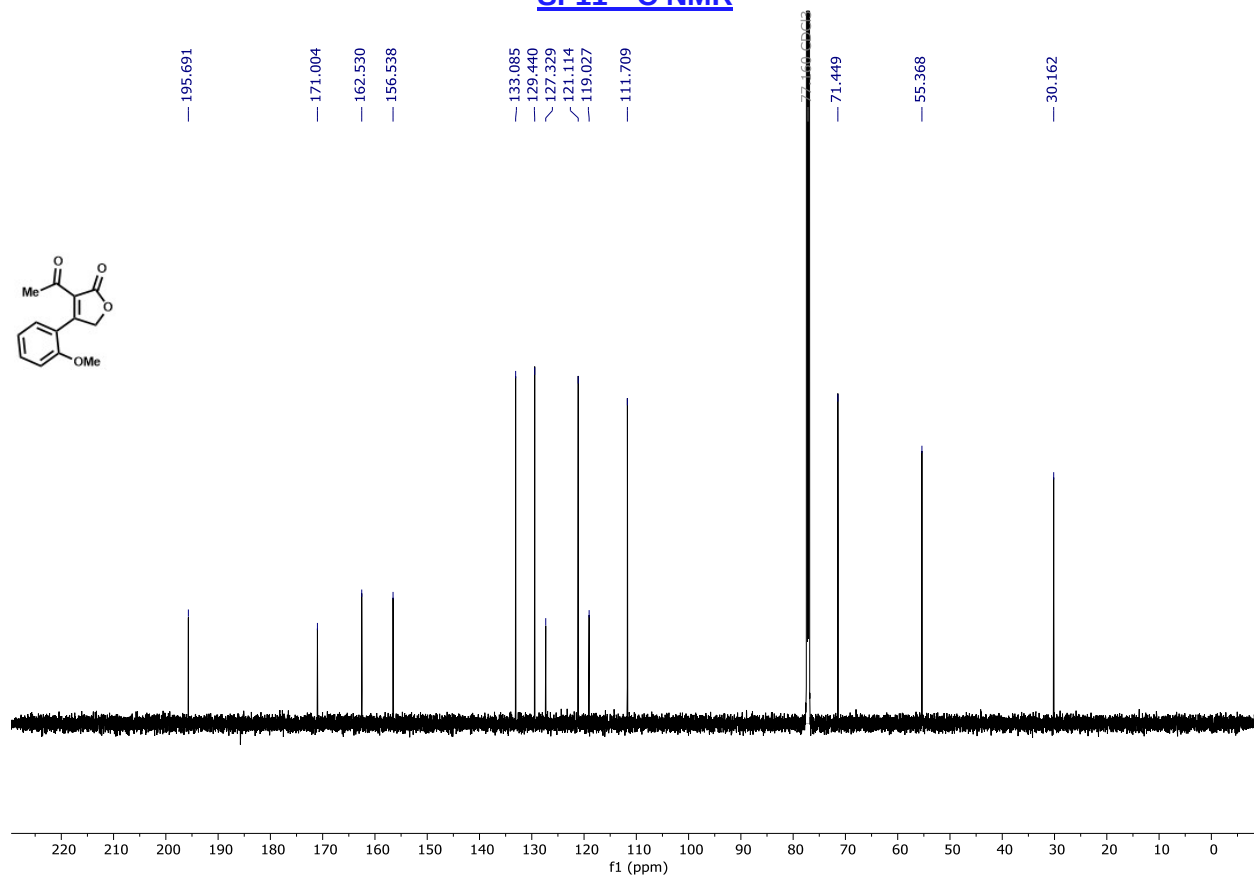


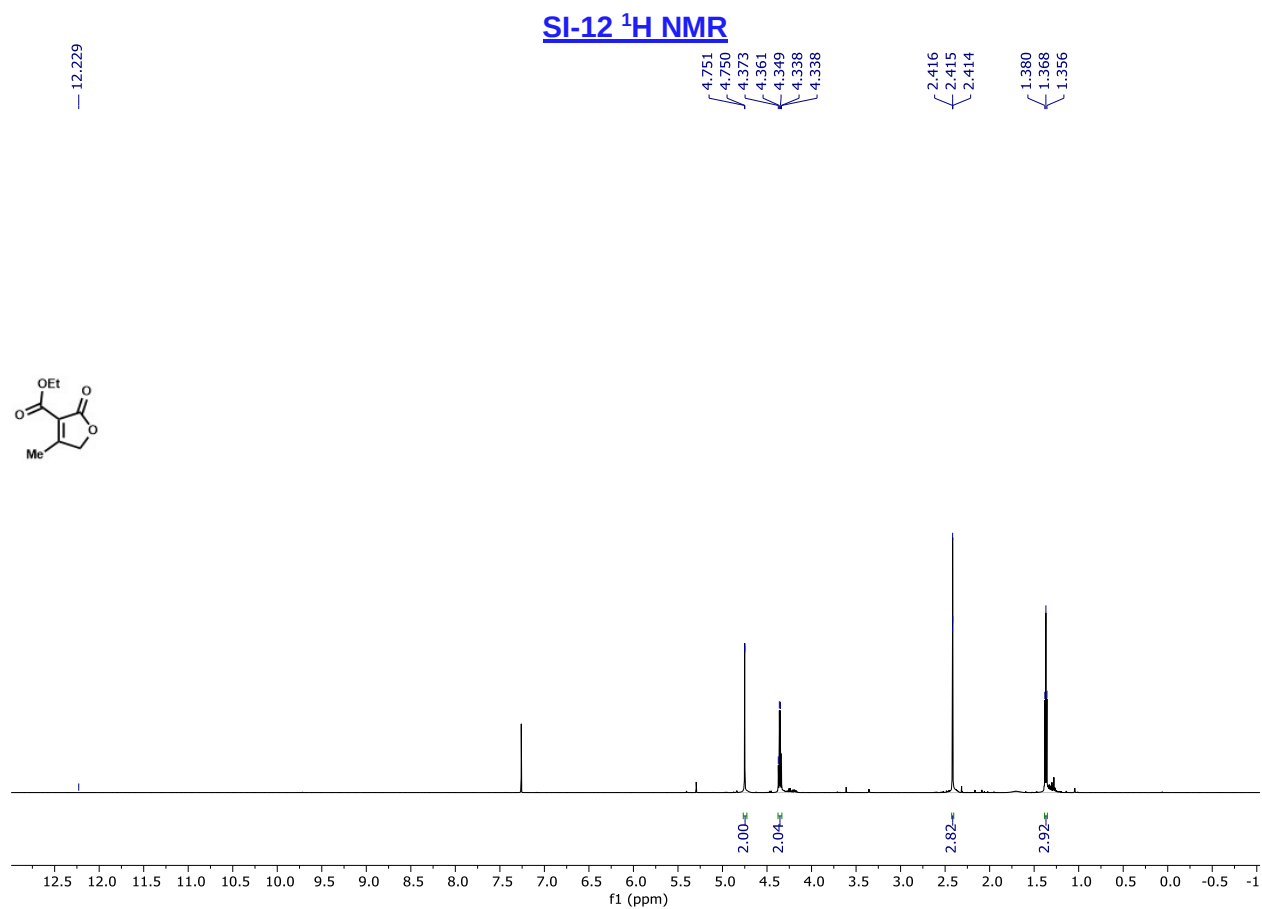


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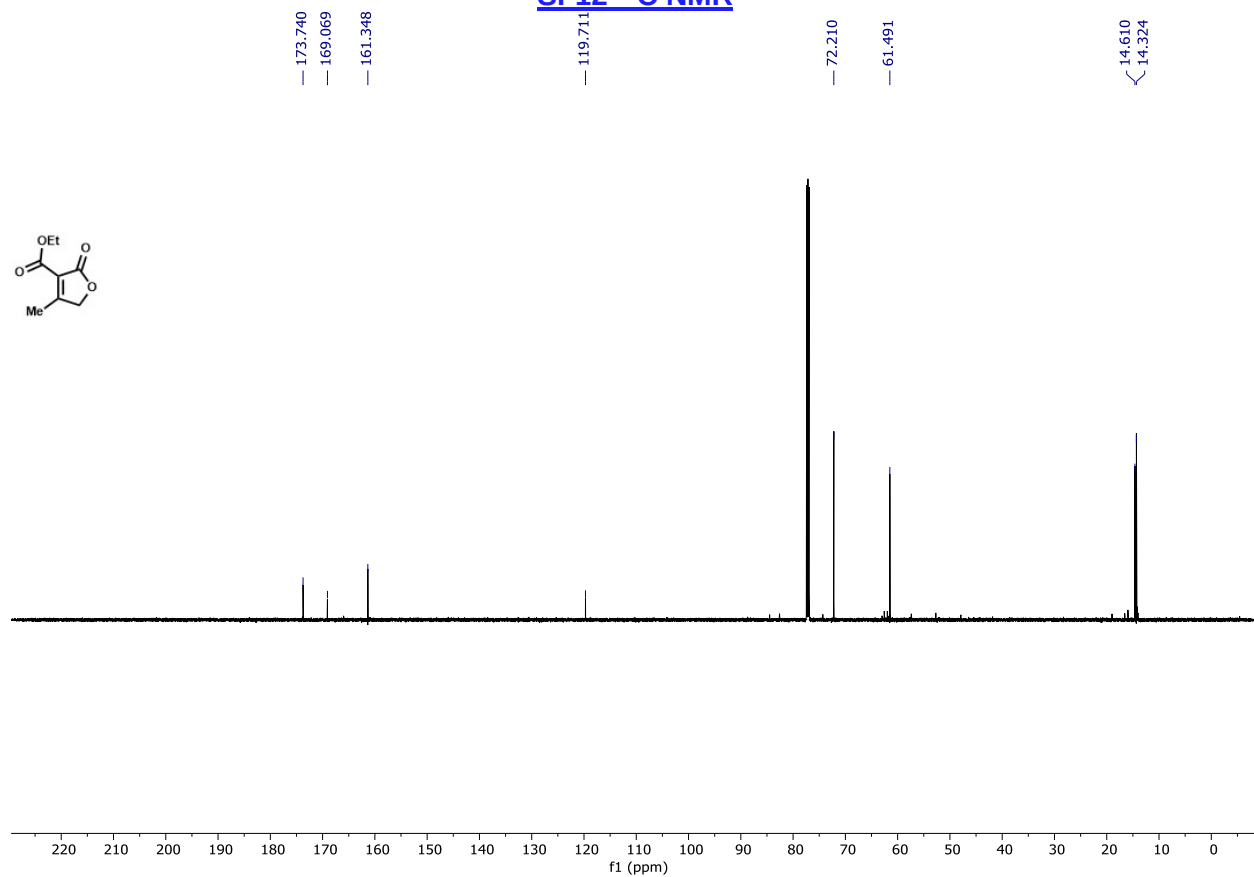


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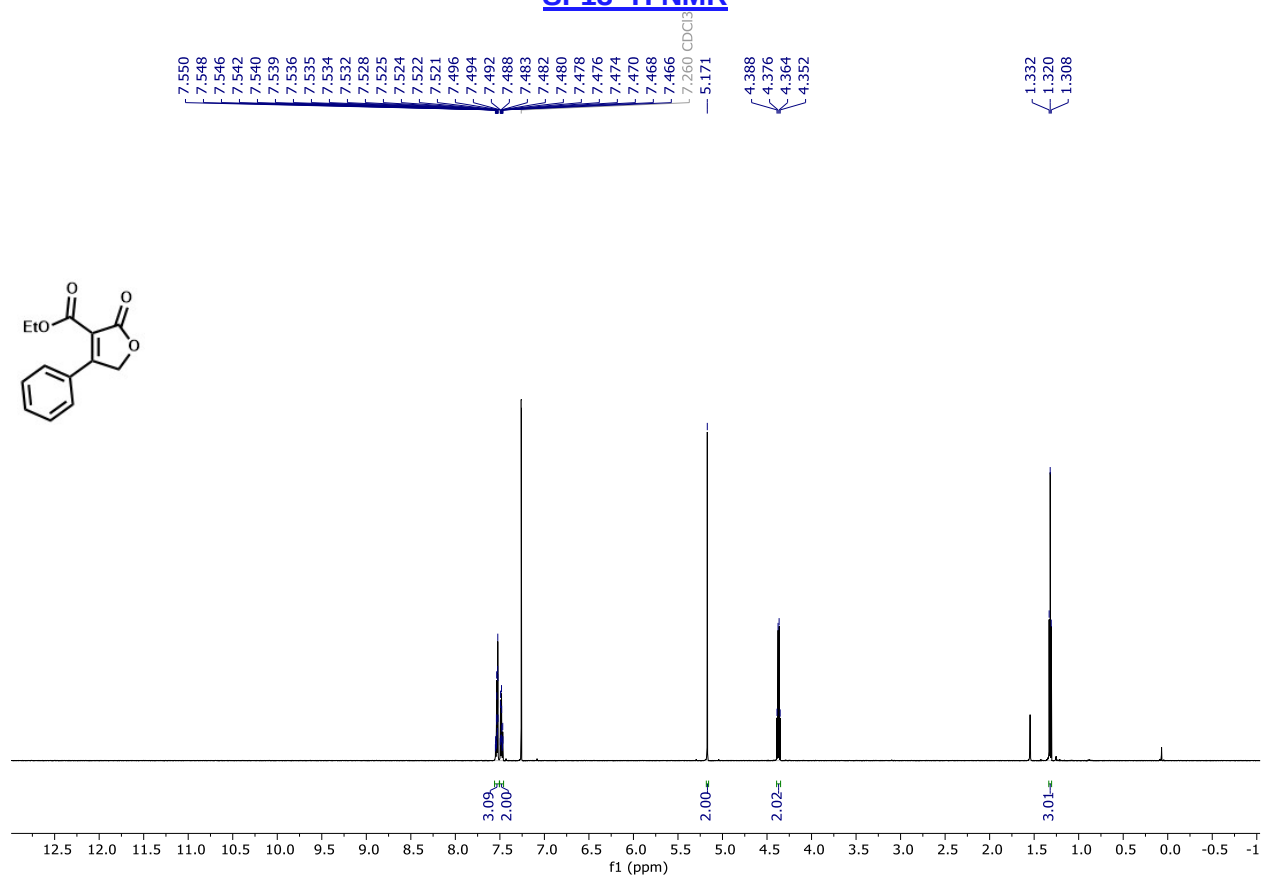


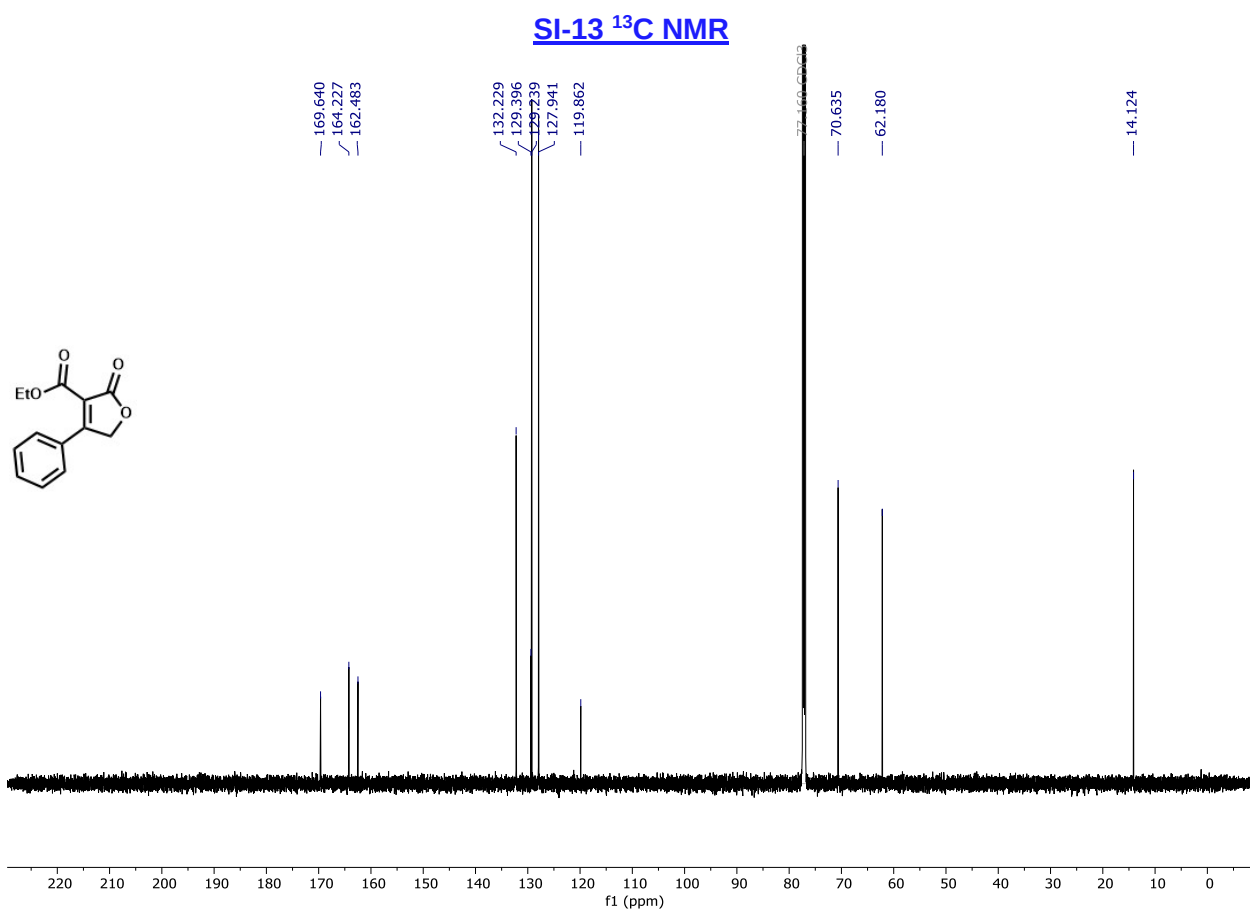


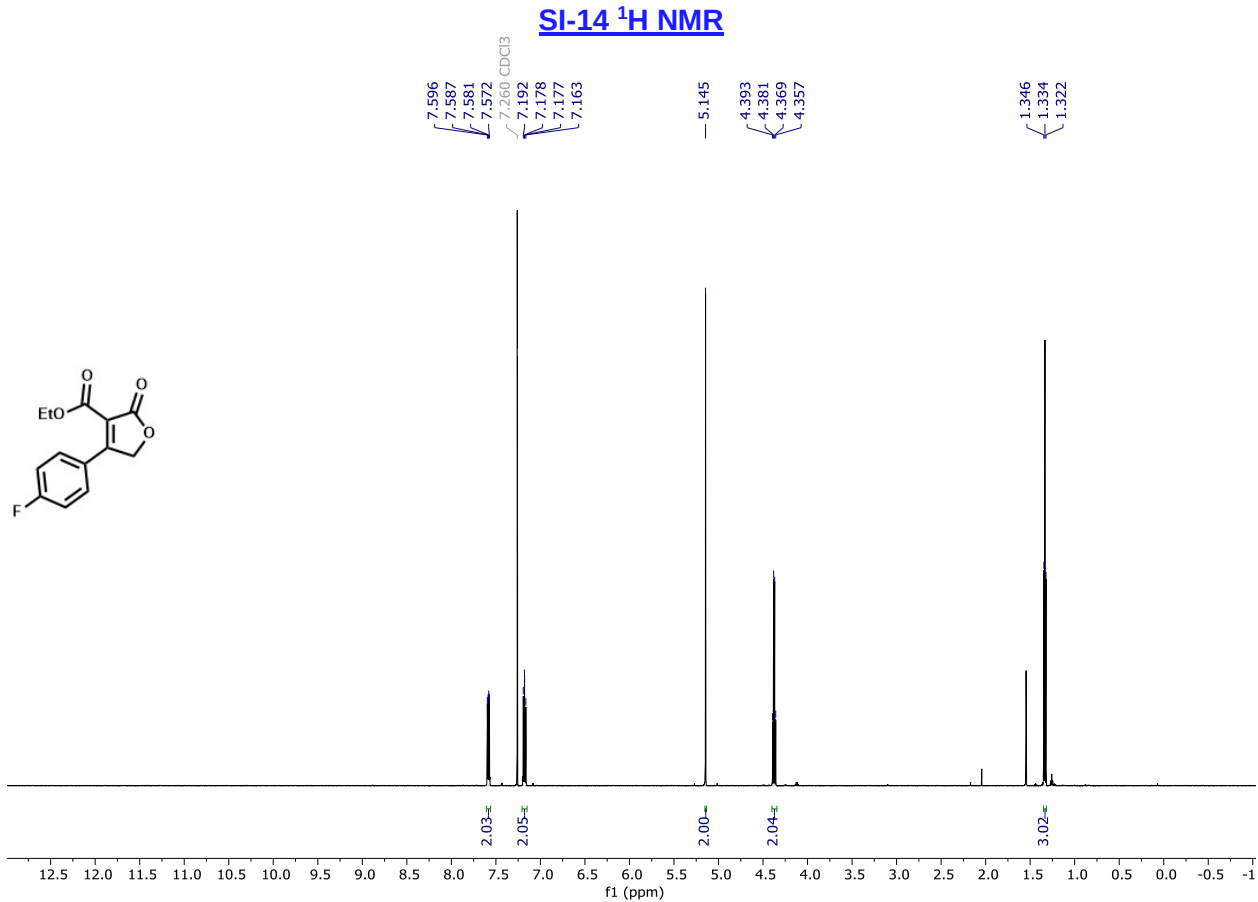
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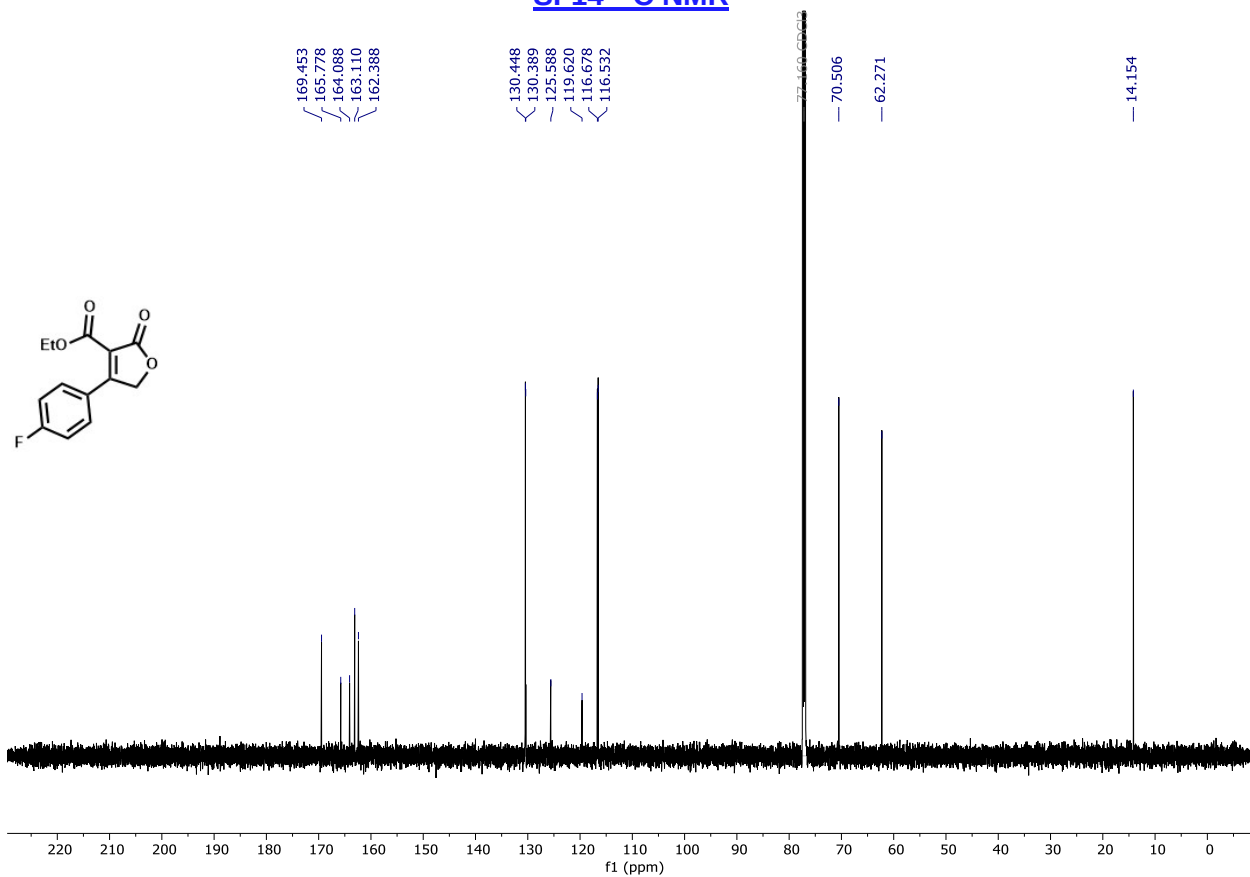
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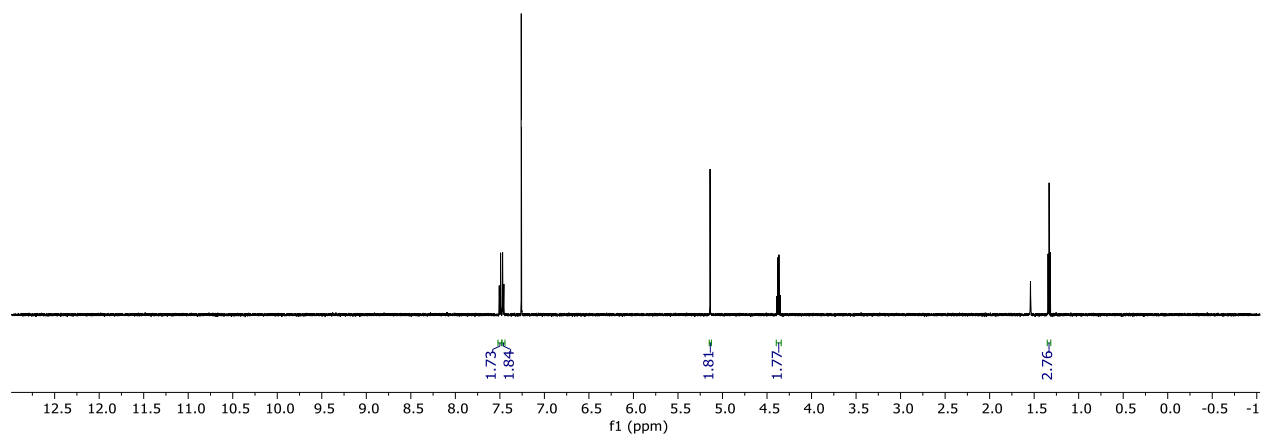
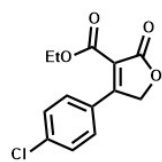


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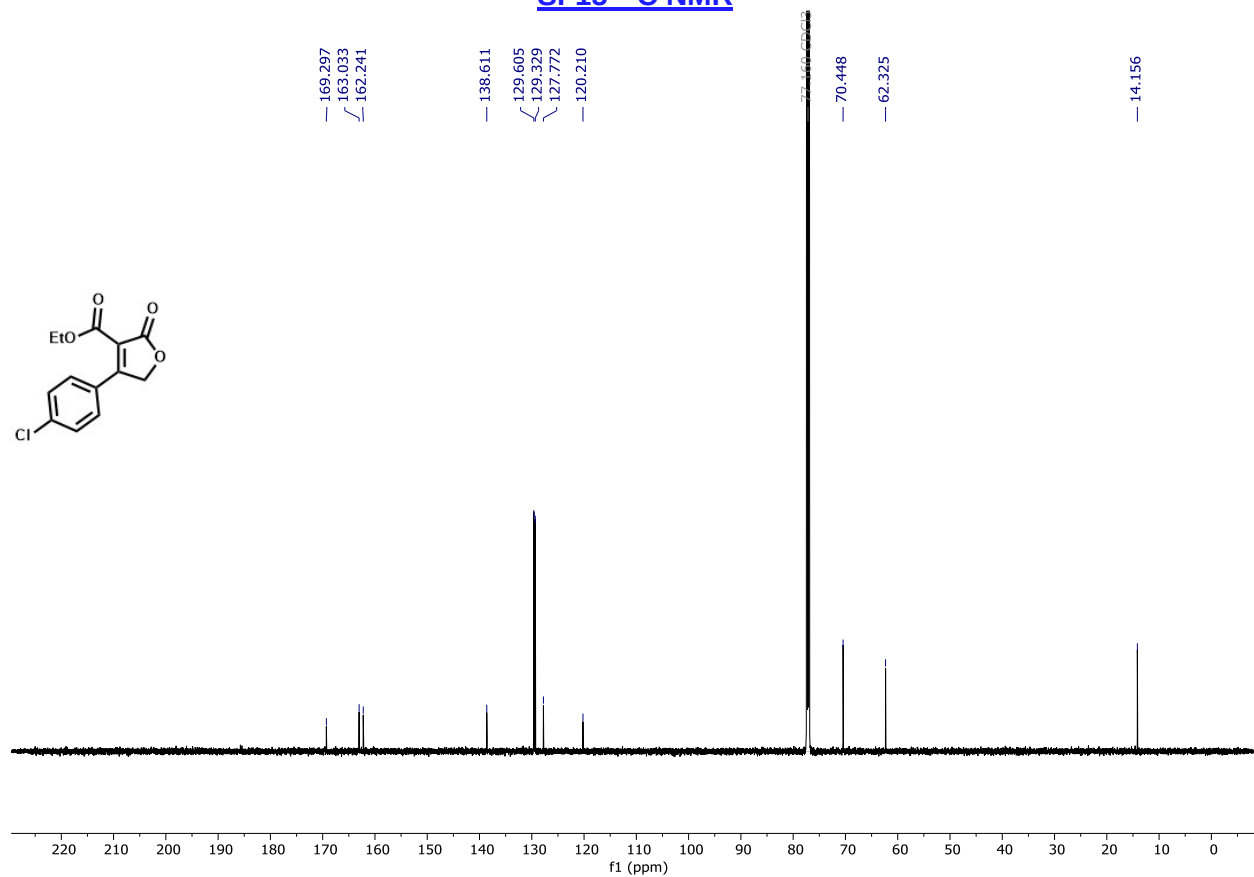


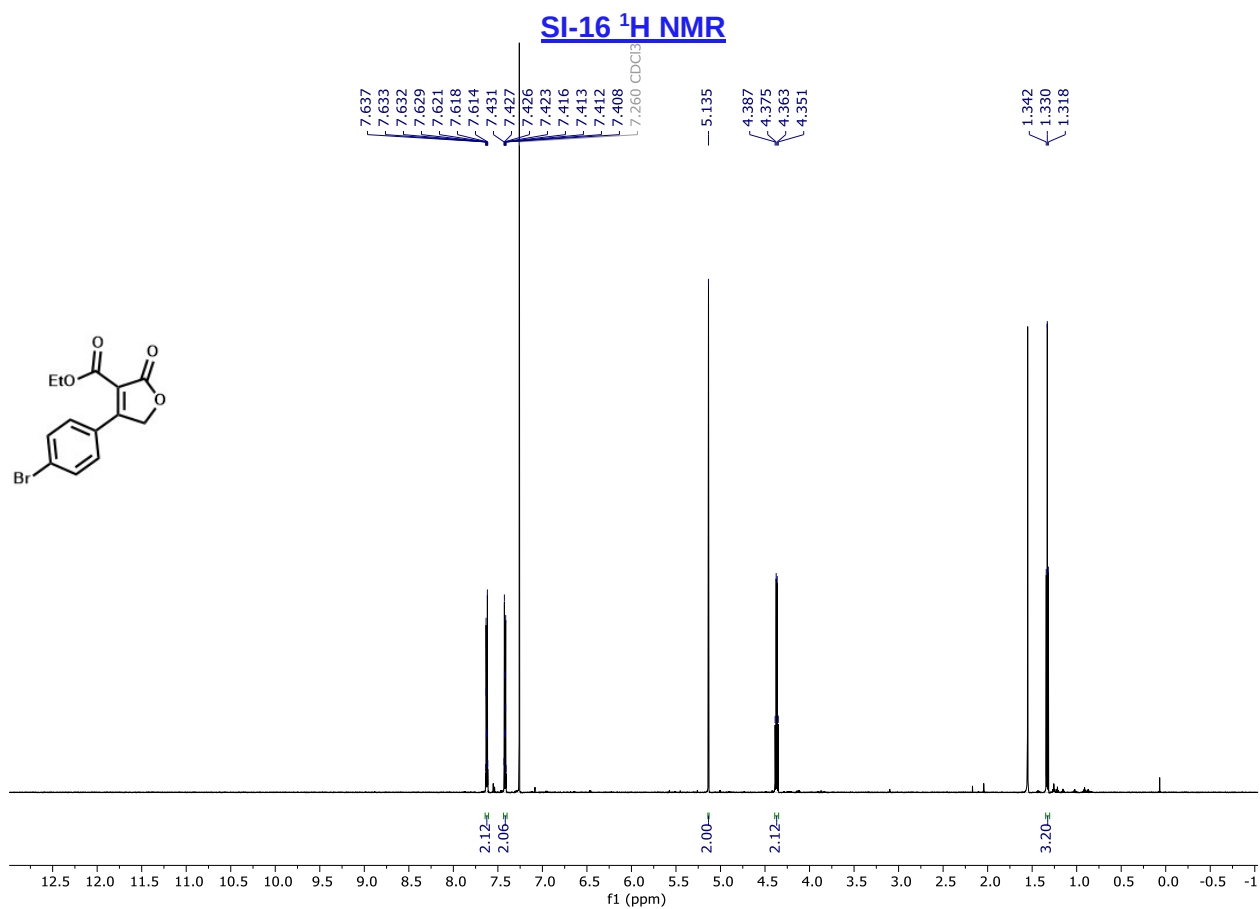
SI-15 ¹H NMR

— 7.260 CDCl₃

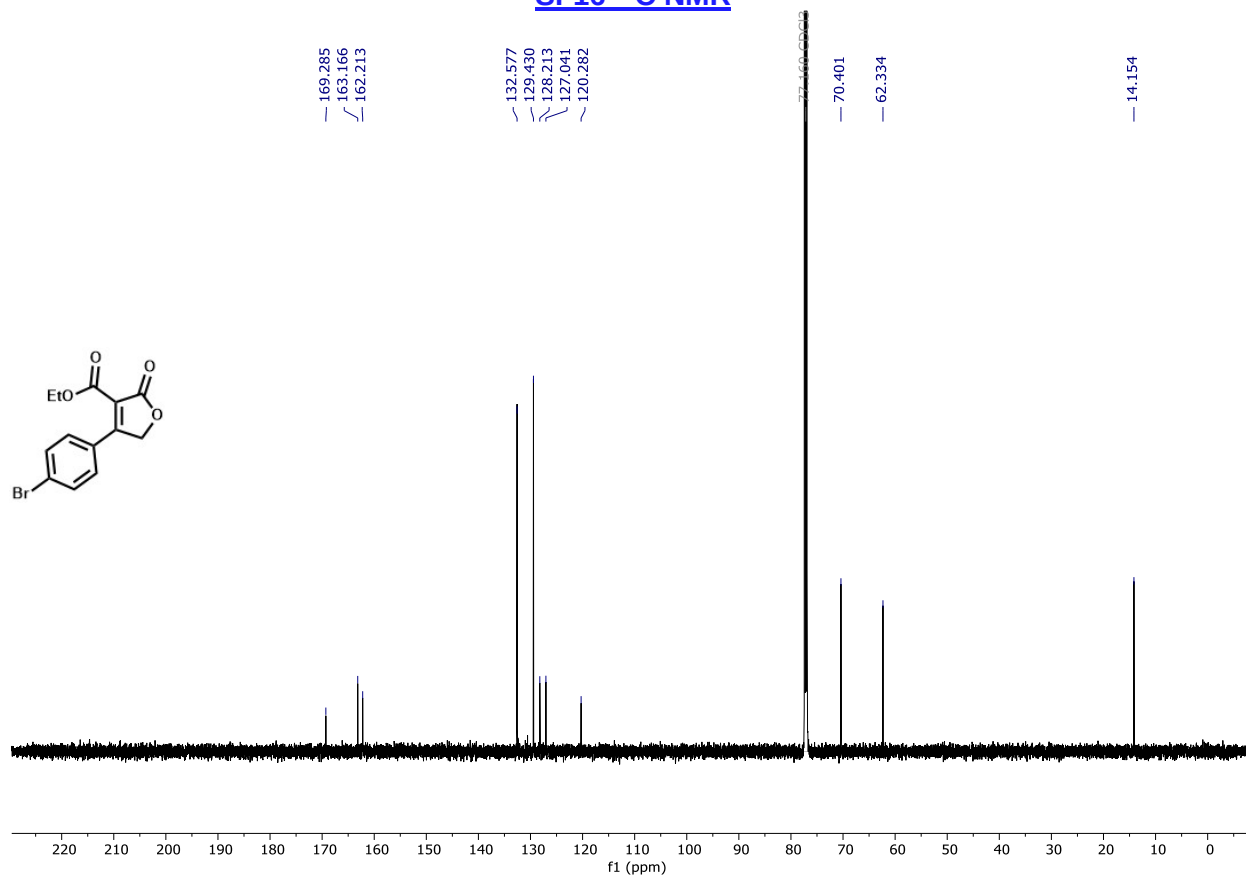


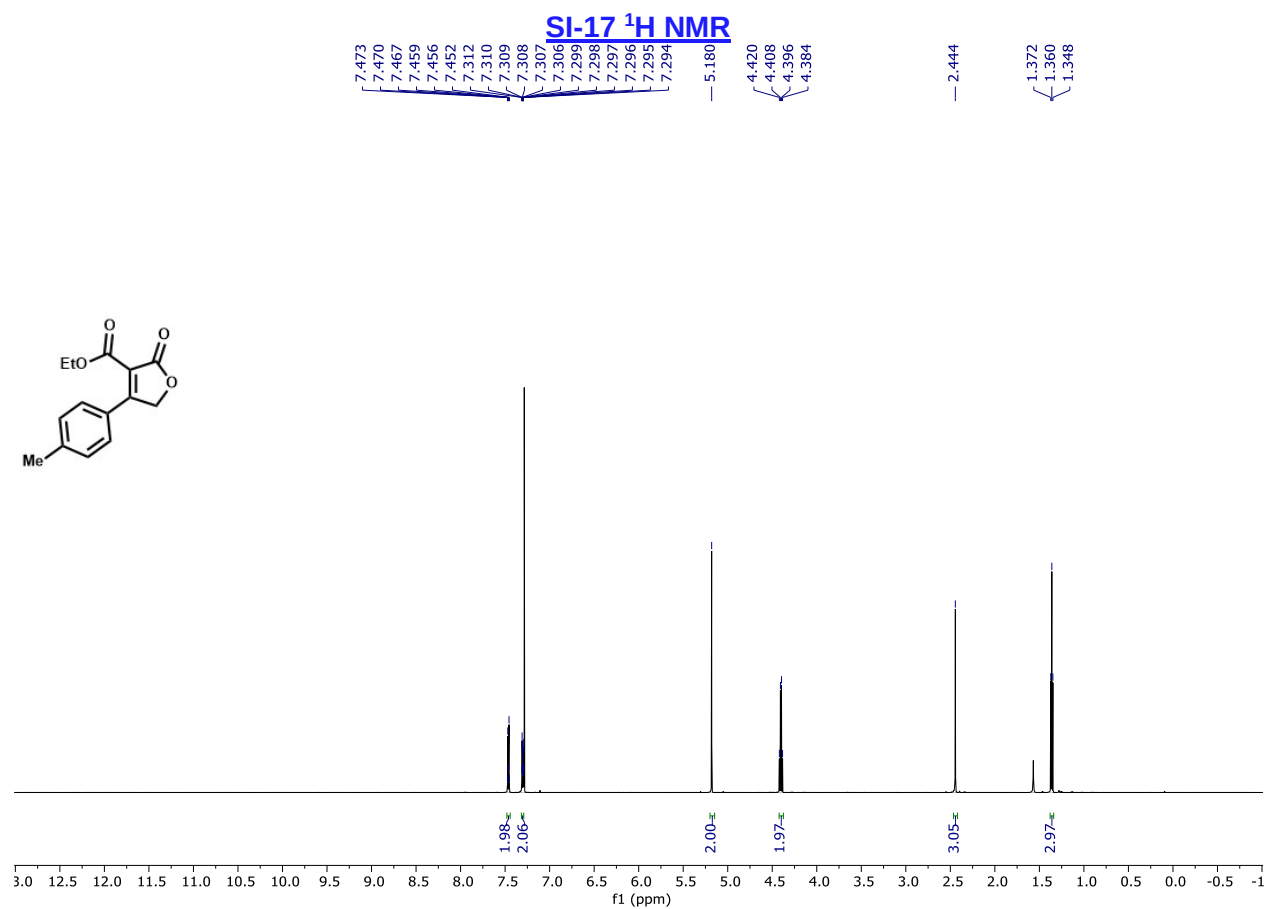
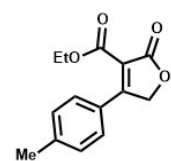
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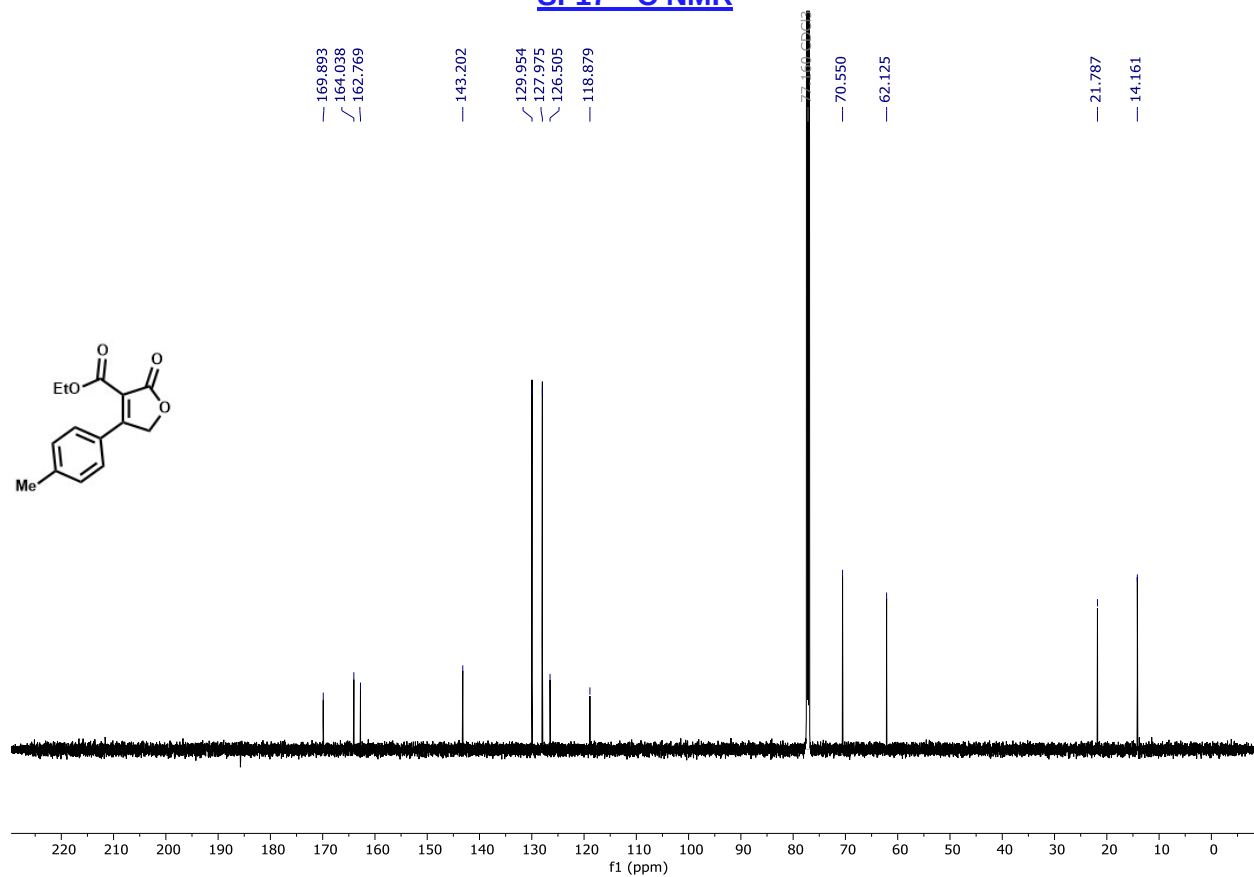


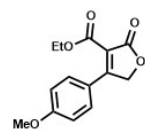
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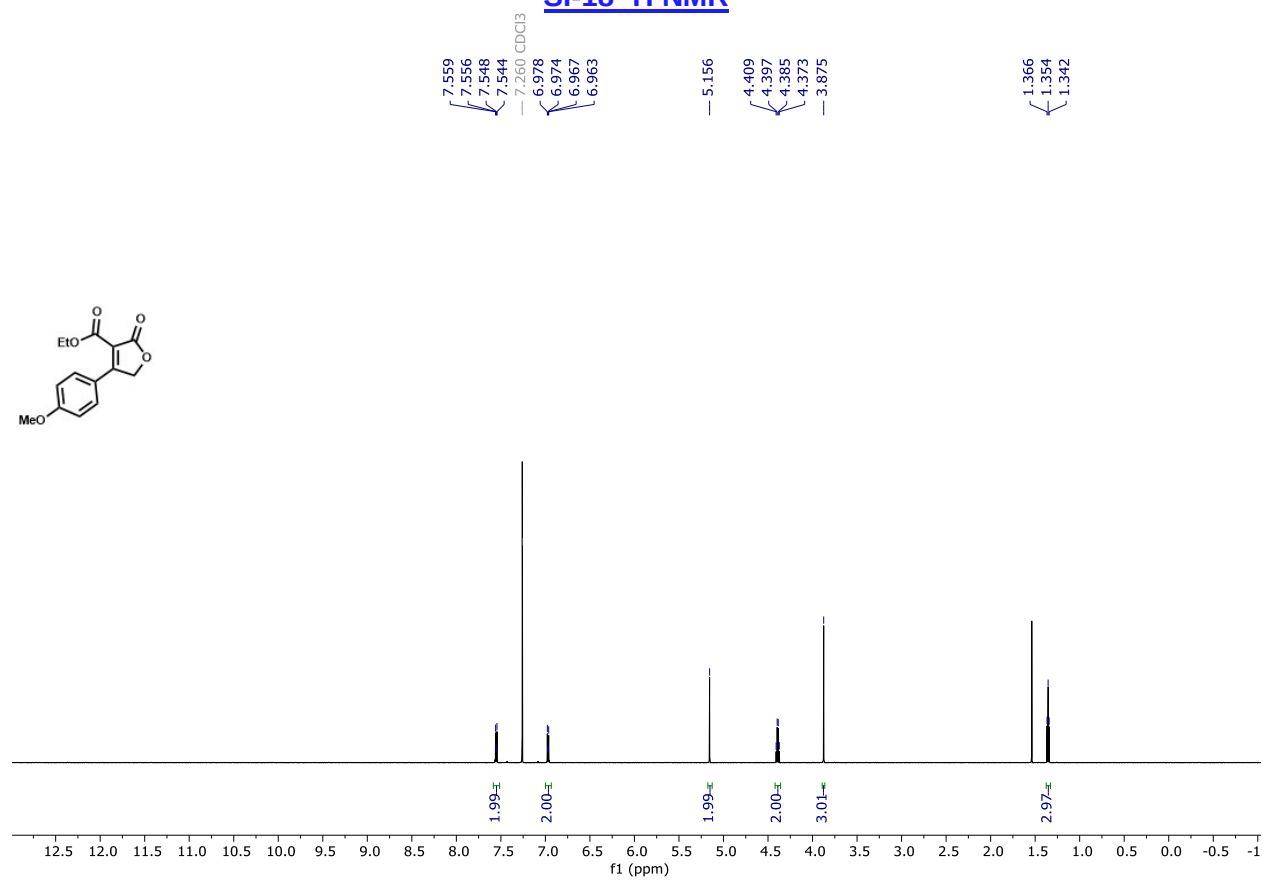


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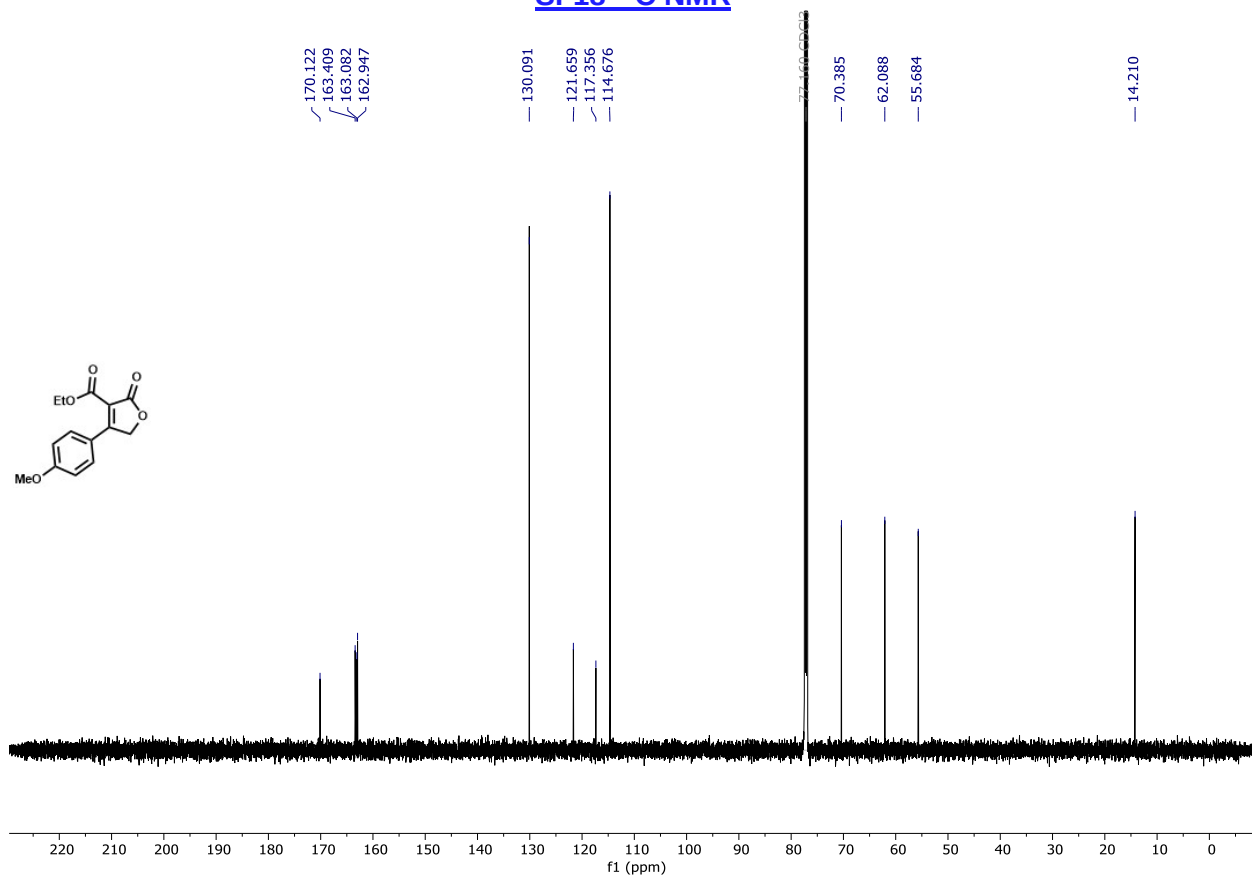


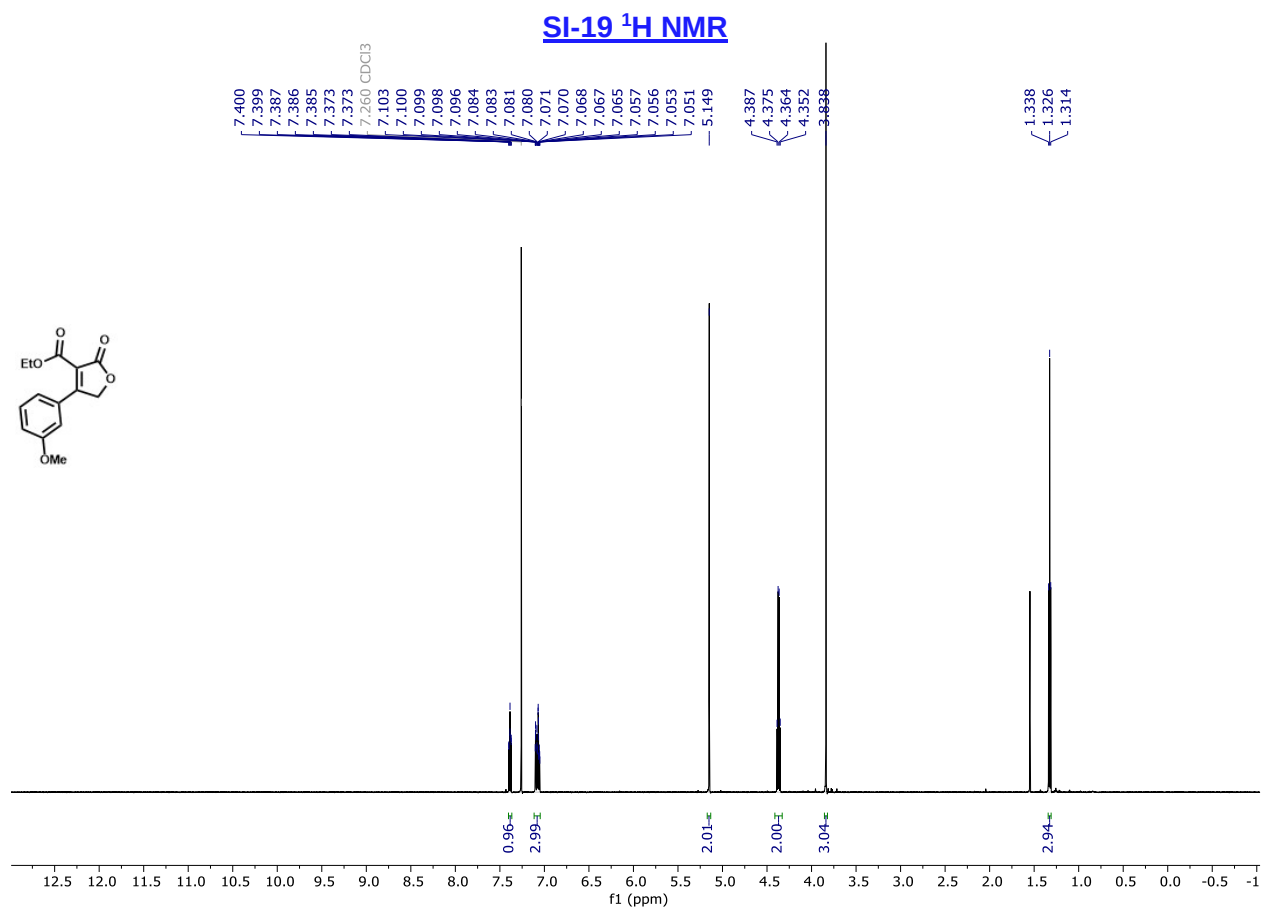


SI-18 ^1H NMR

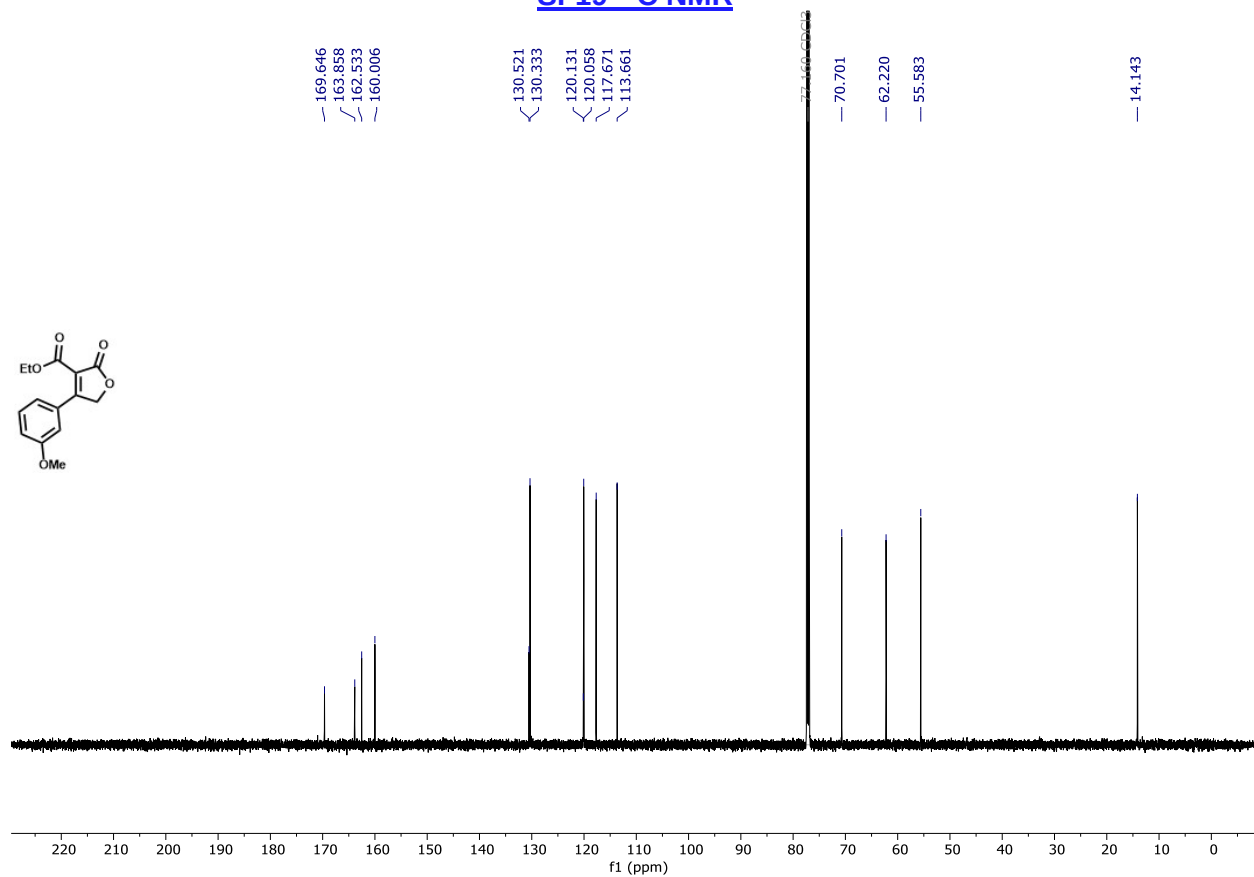


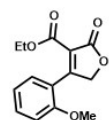
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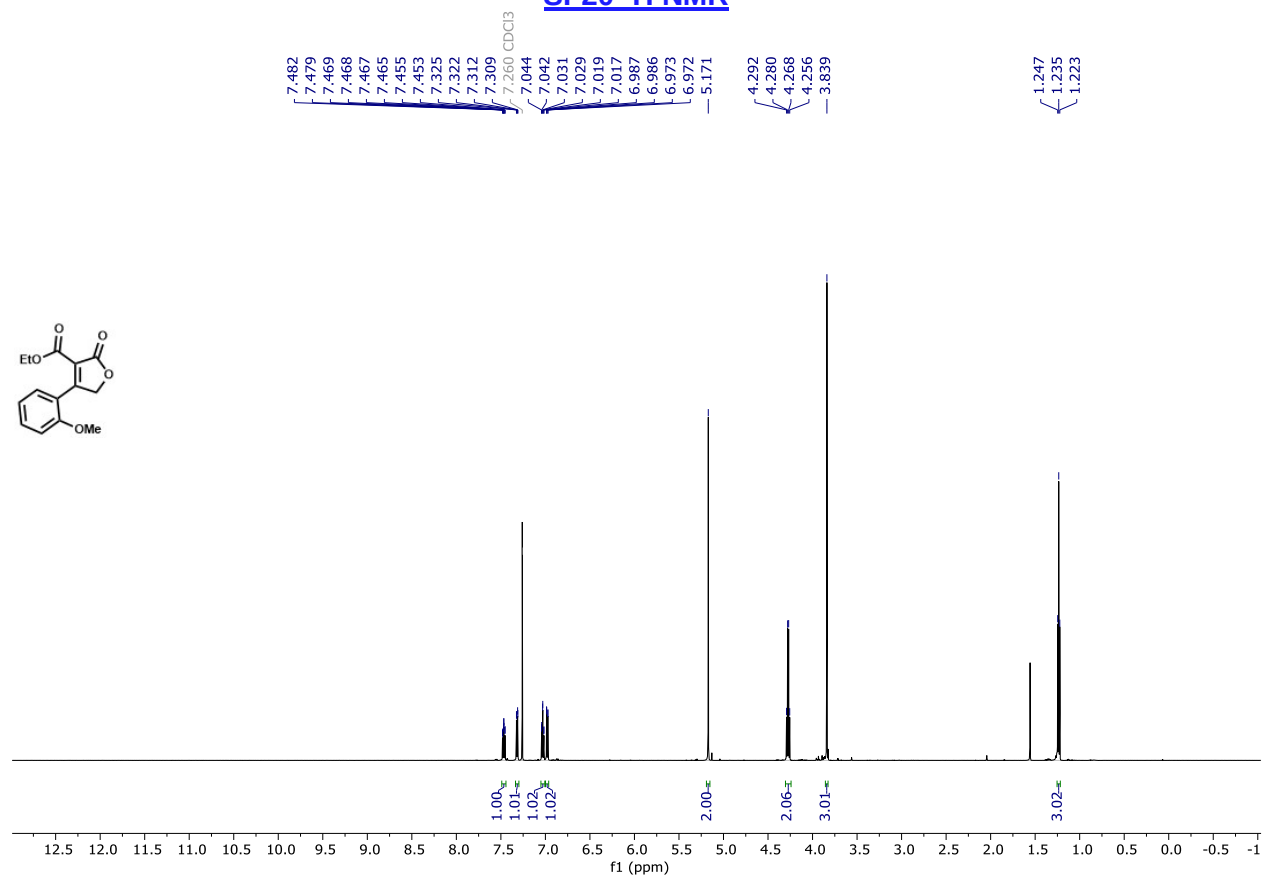


SI-19 ¹³C NMR

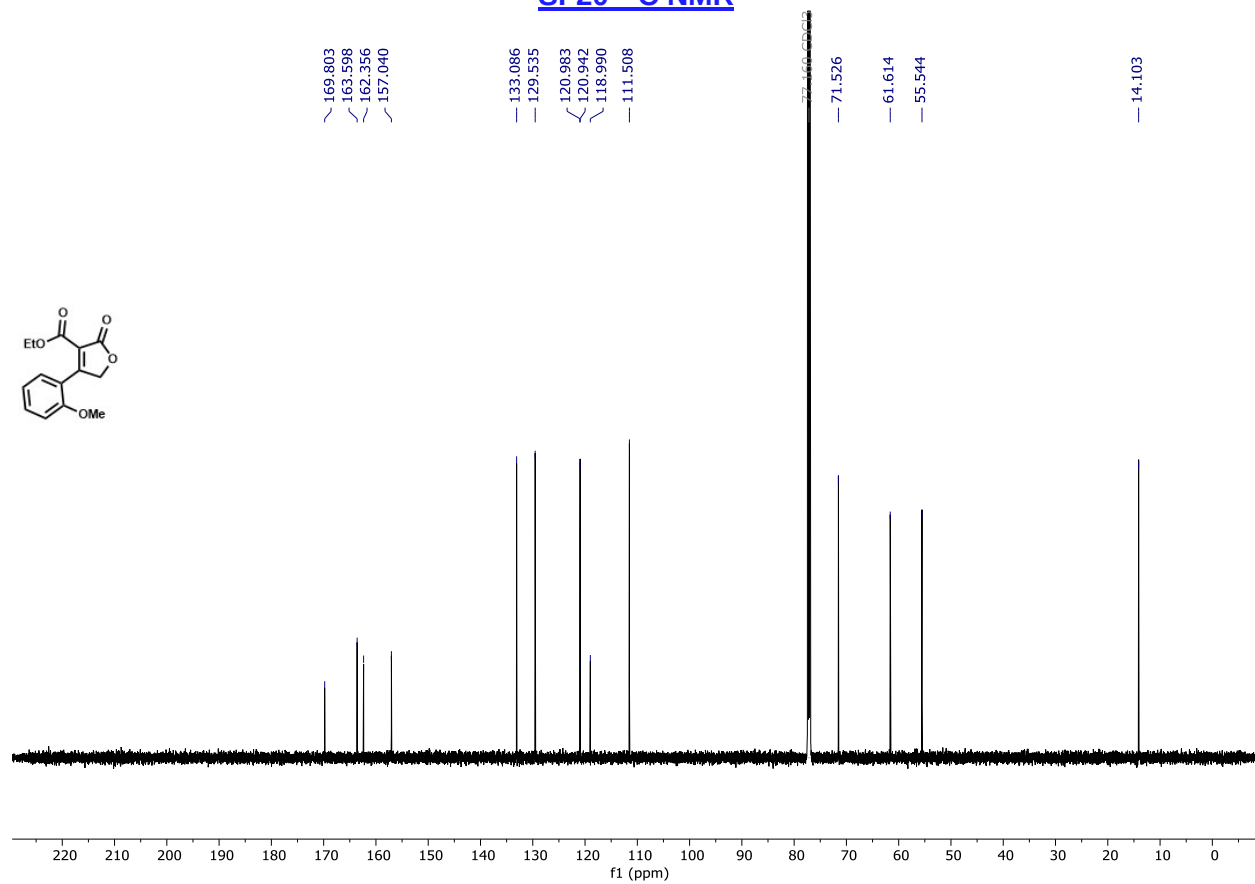




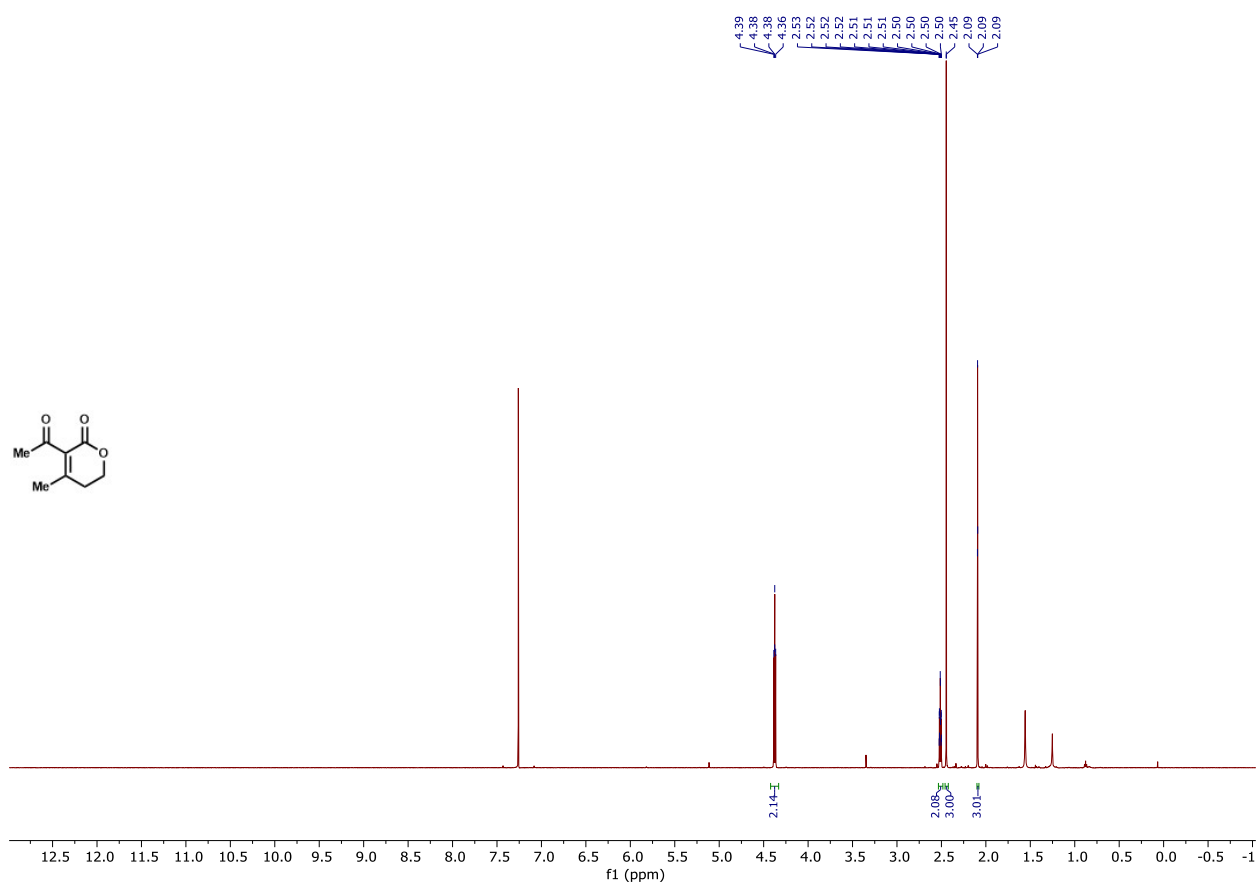
SI-20 ¹H NMR

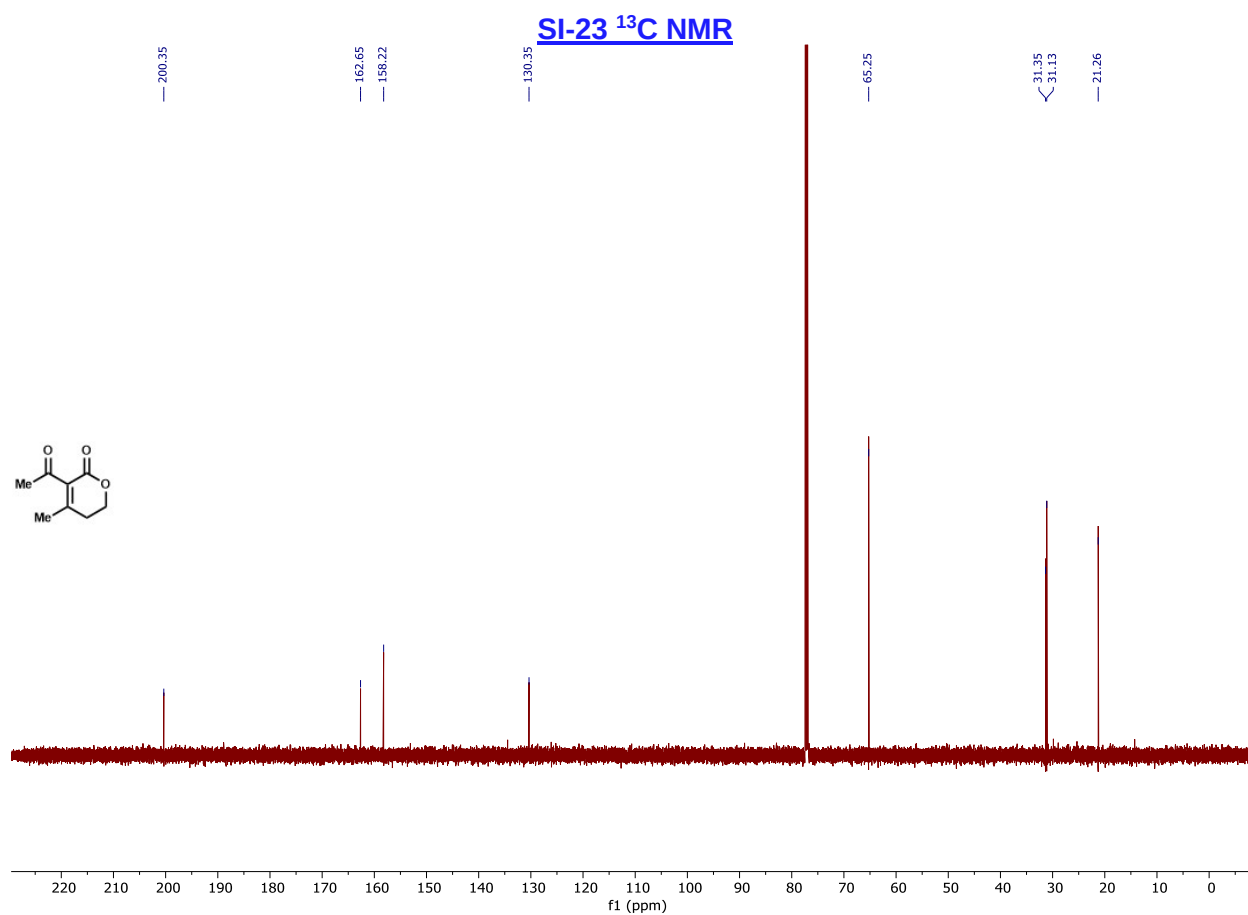


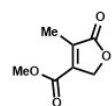
SI-20 ¹³C NMR



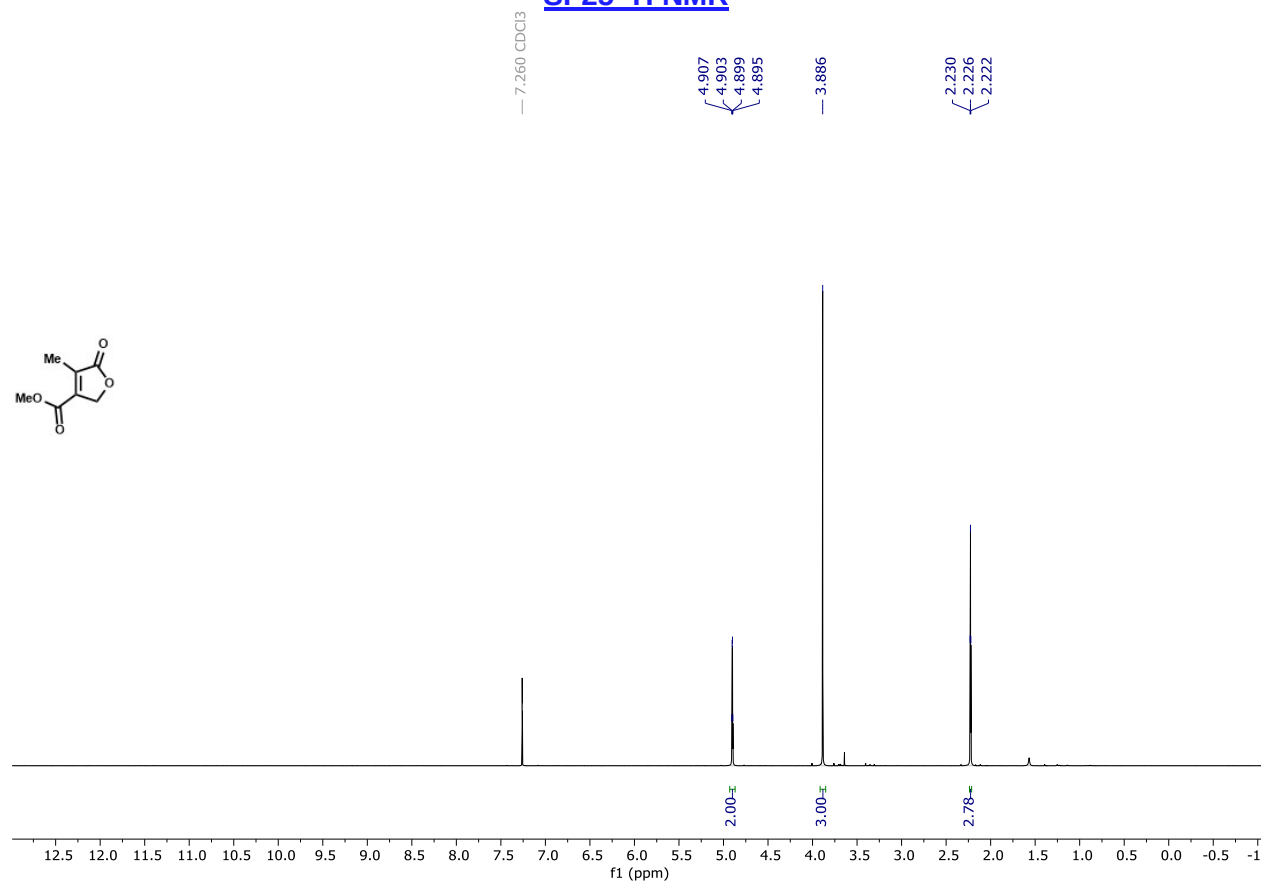
SI-23 ¹H NMR



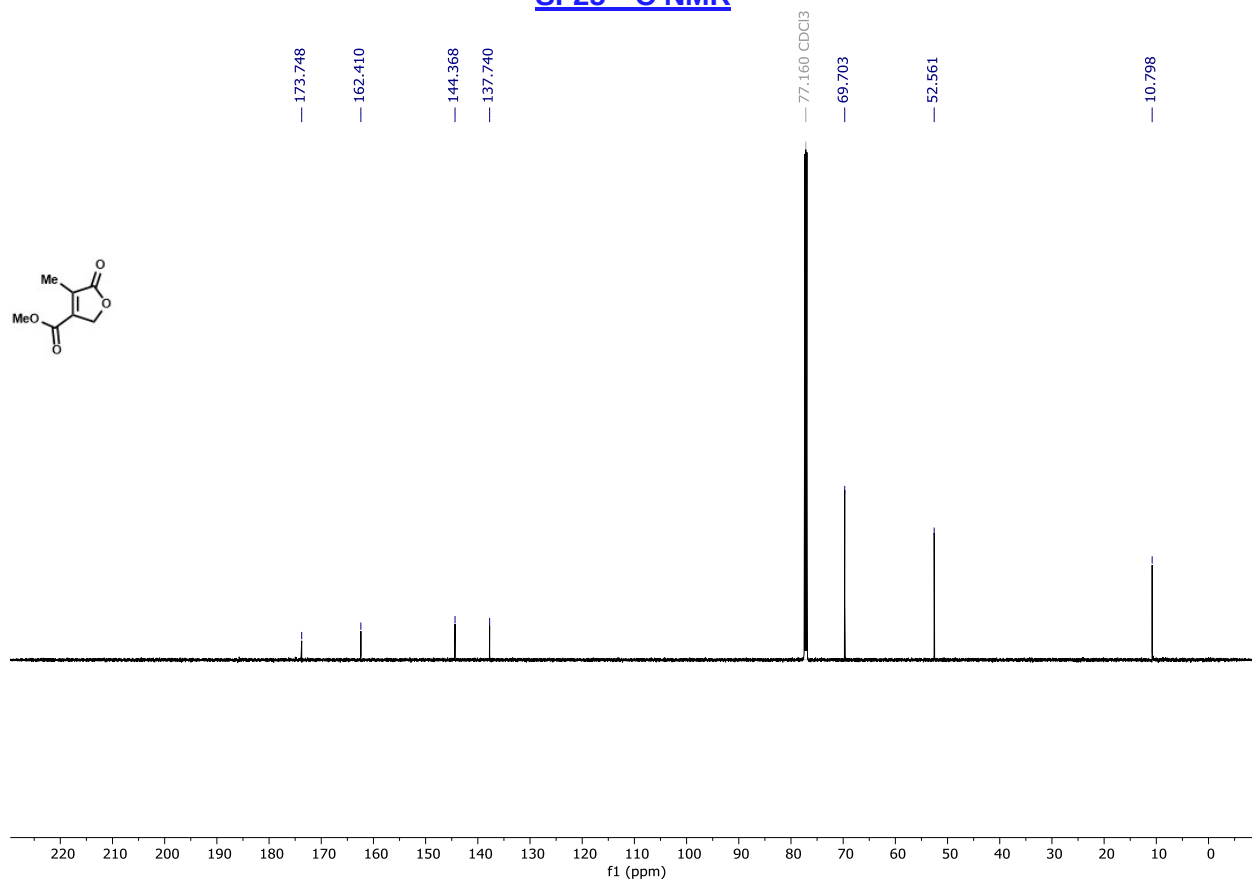




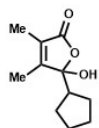
SI-25 ¹H NMR

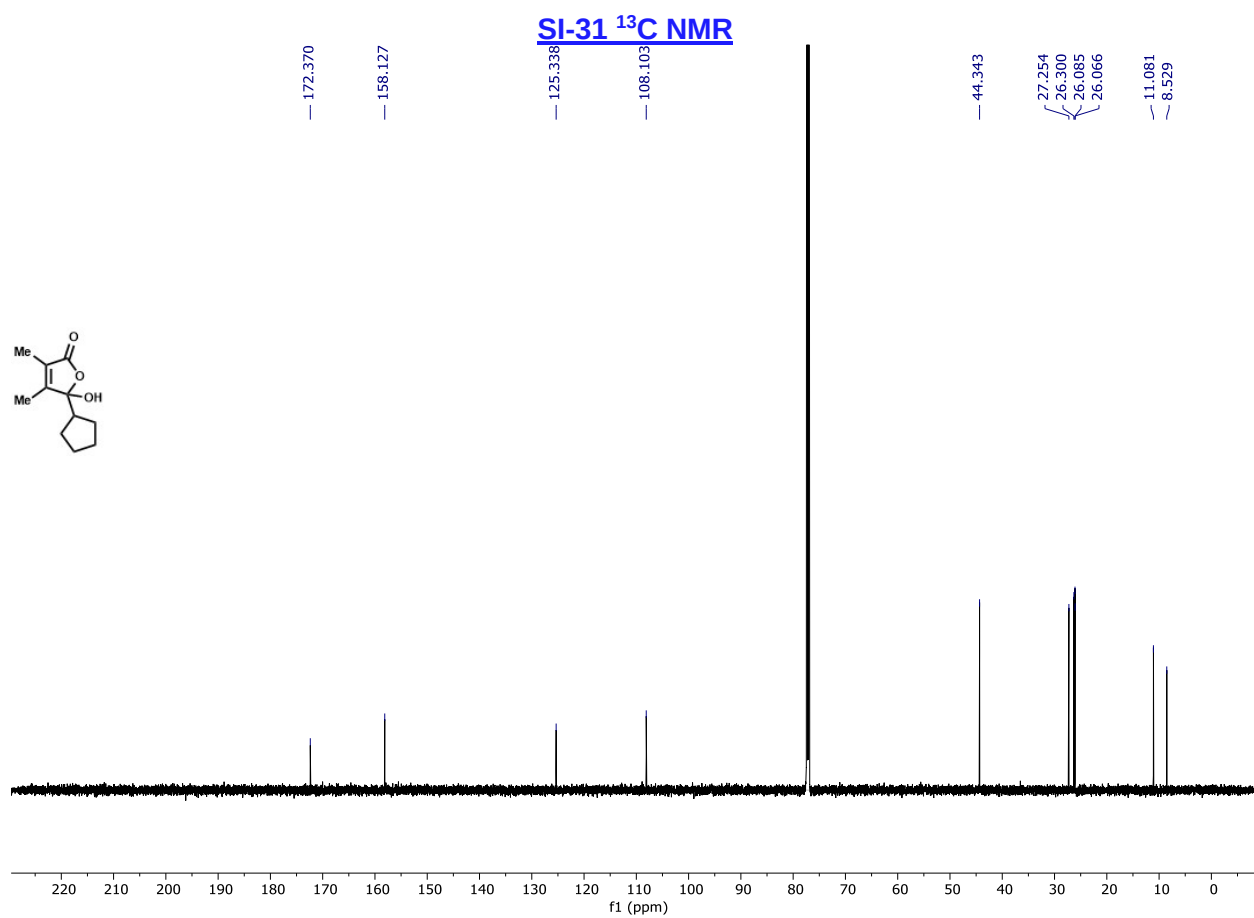


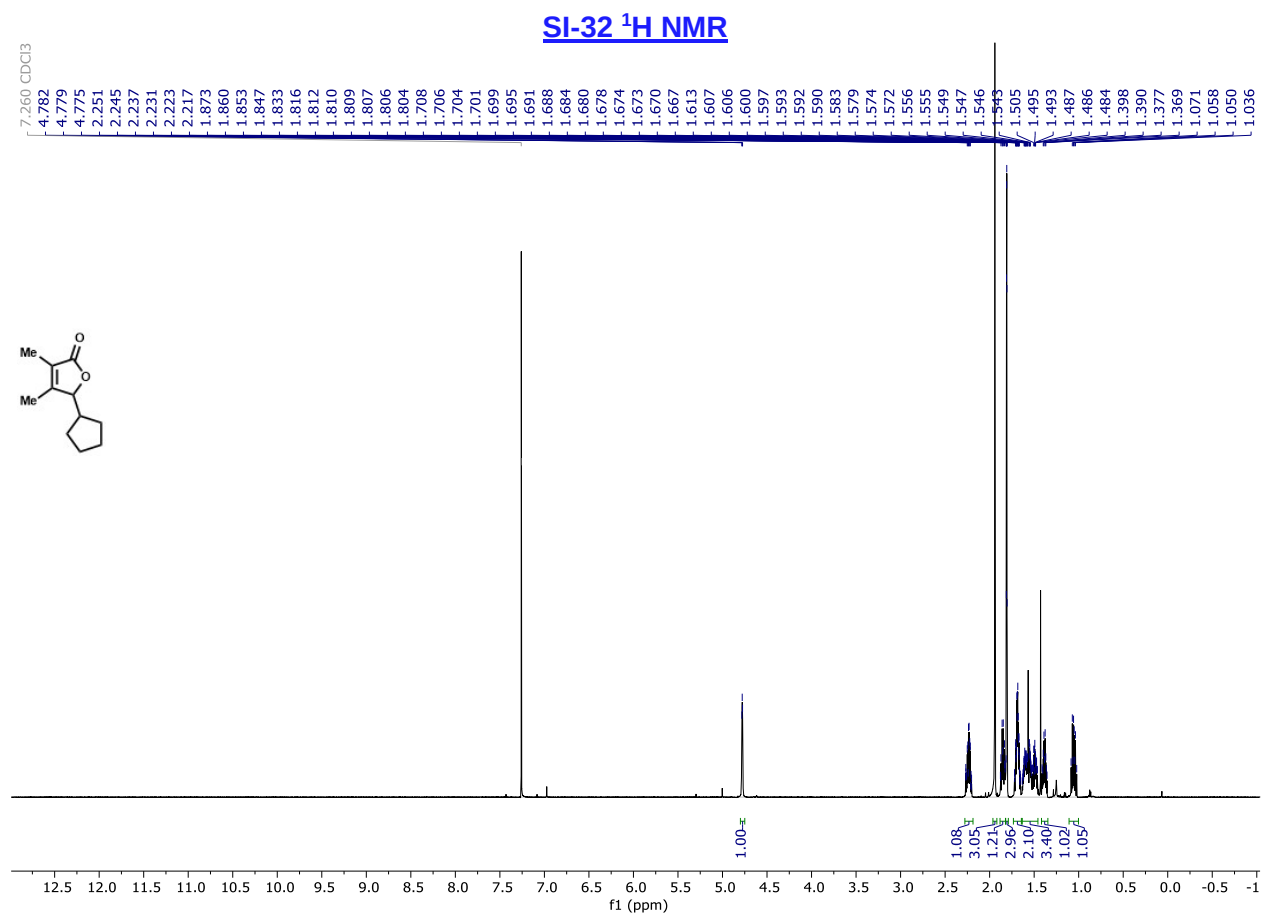
SI-25 ¹³C NMR



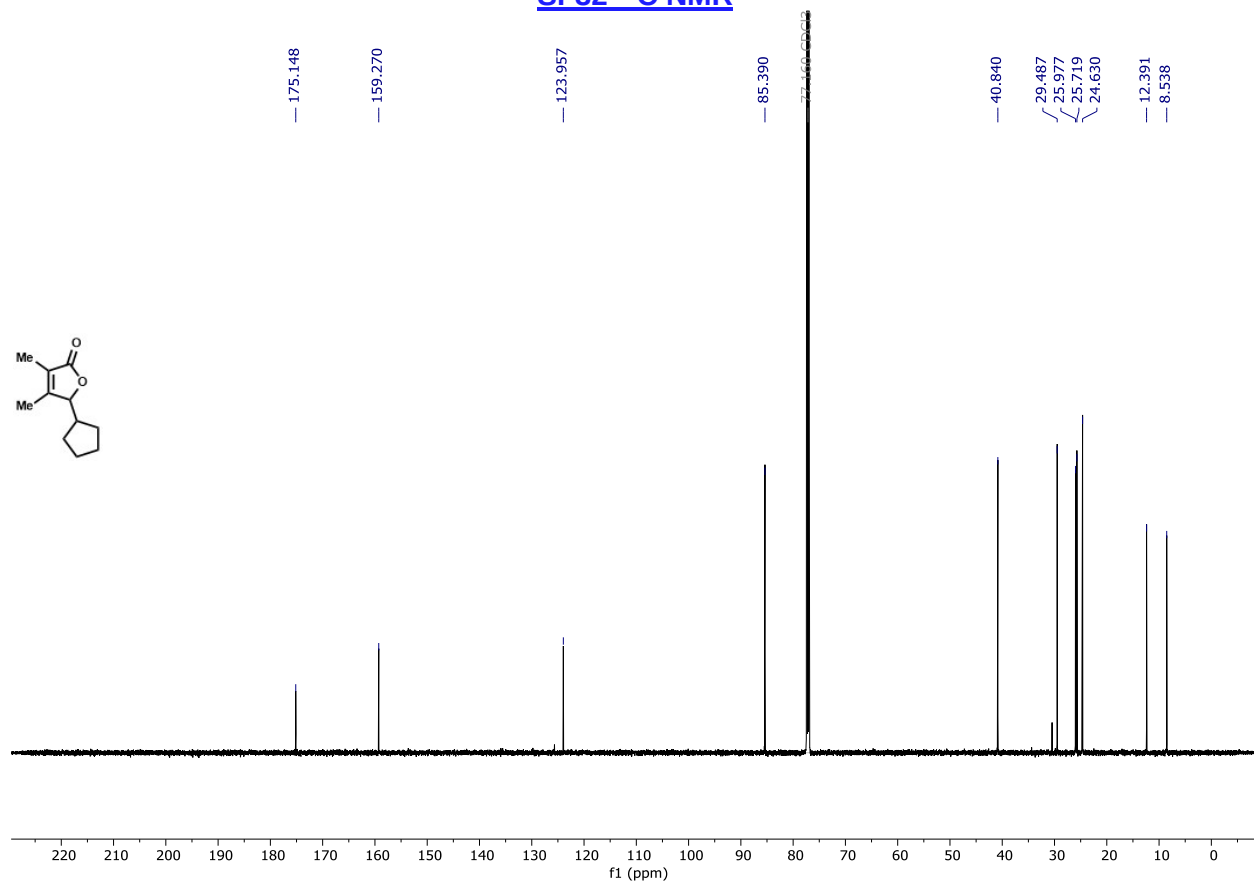
SI-31 ¹H NMR



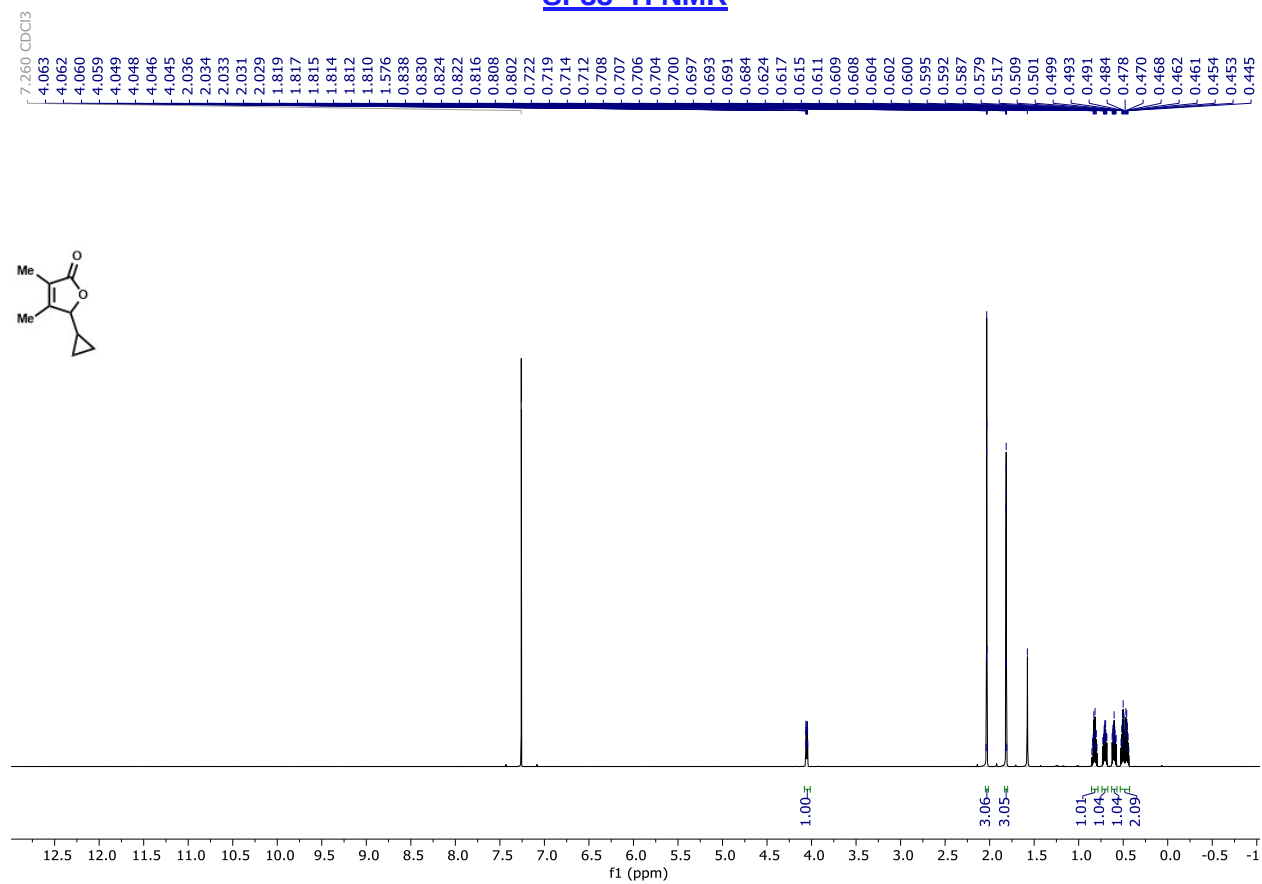


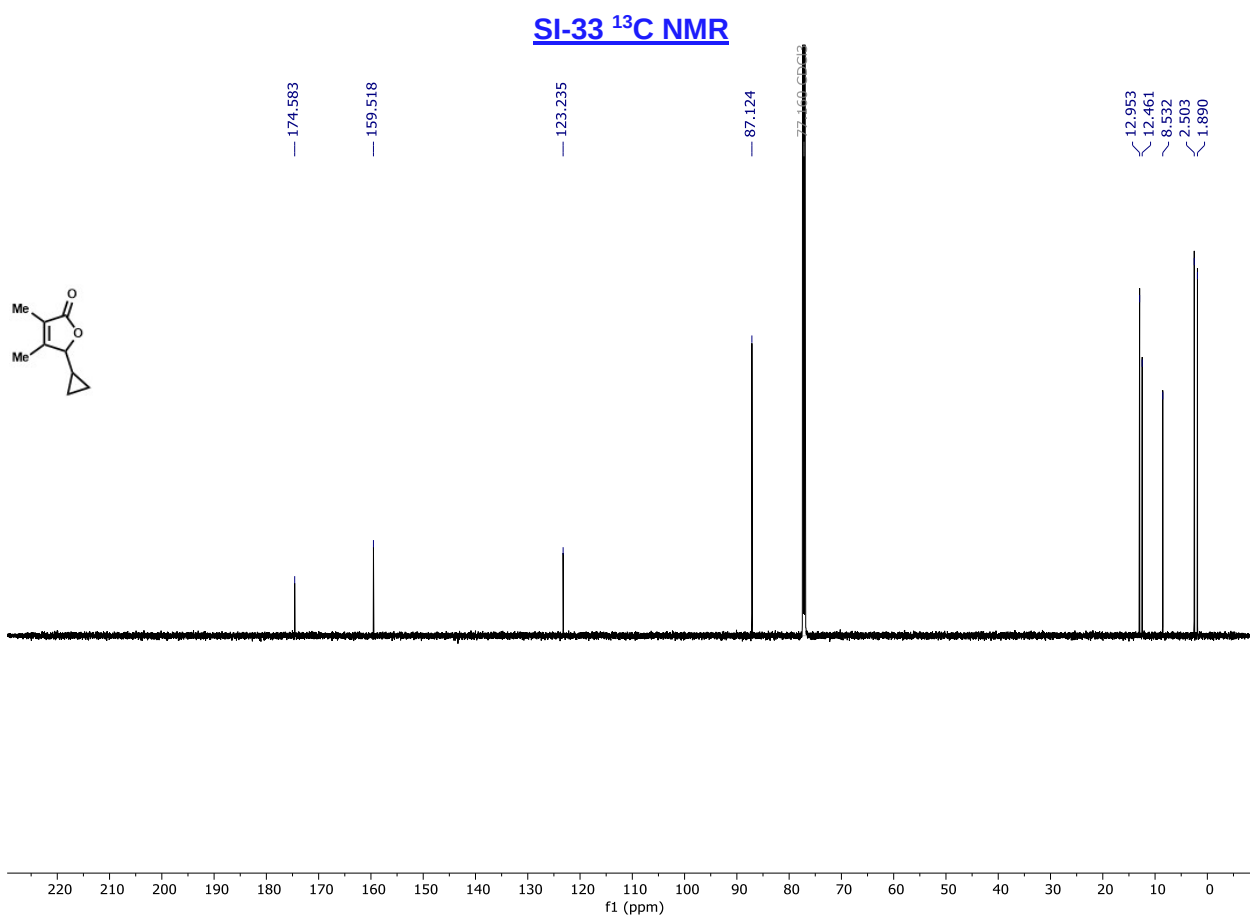


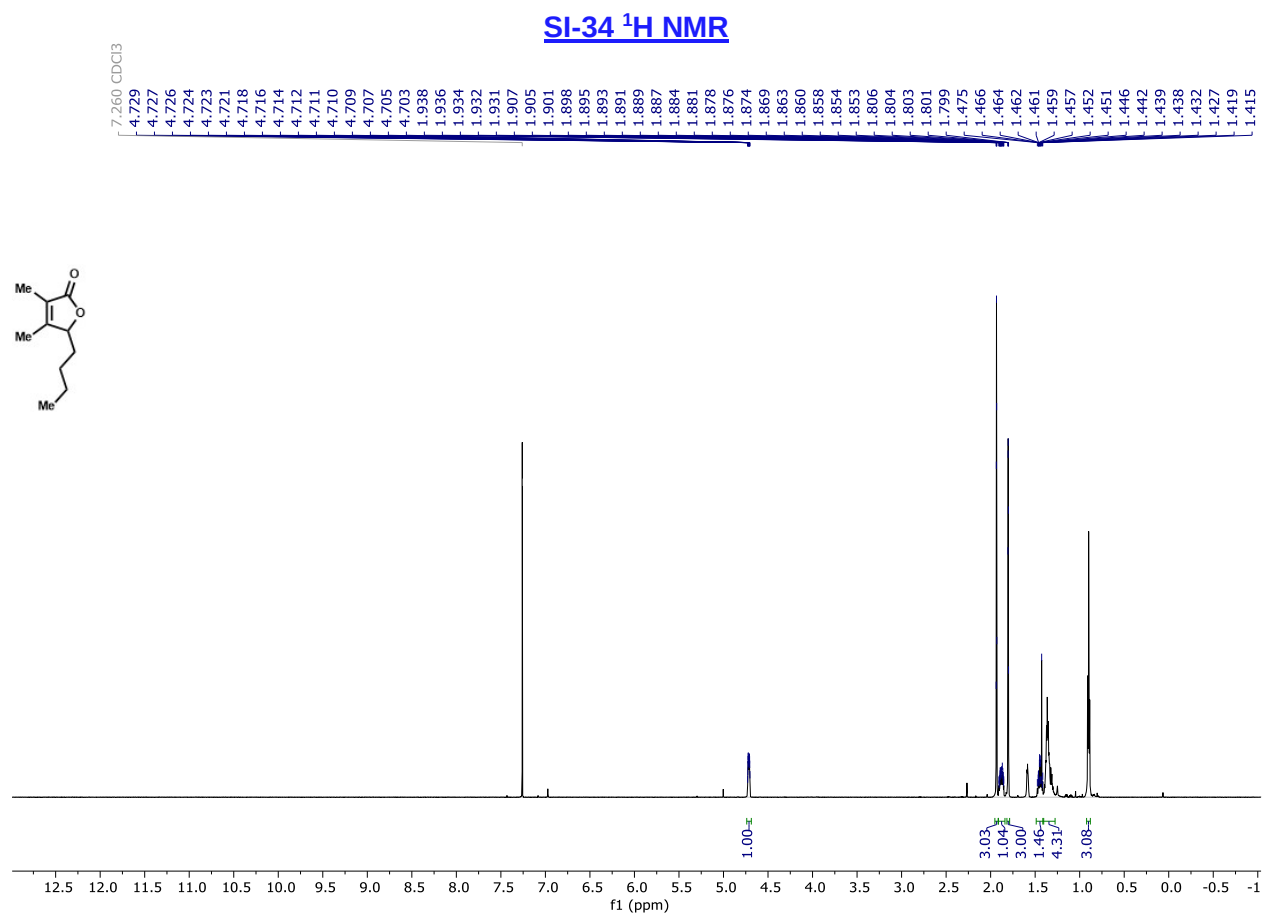
SI-32 ¹³C NMR



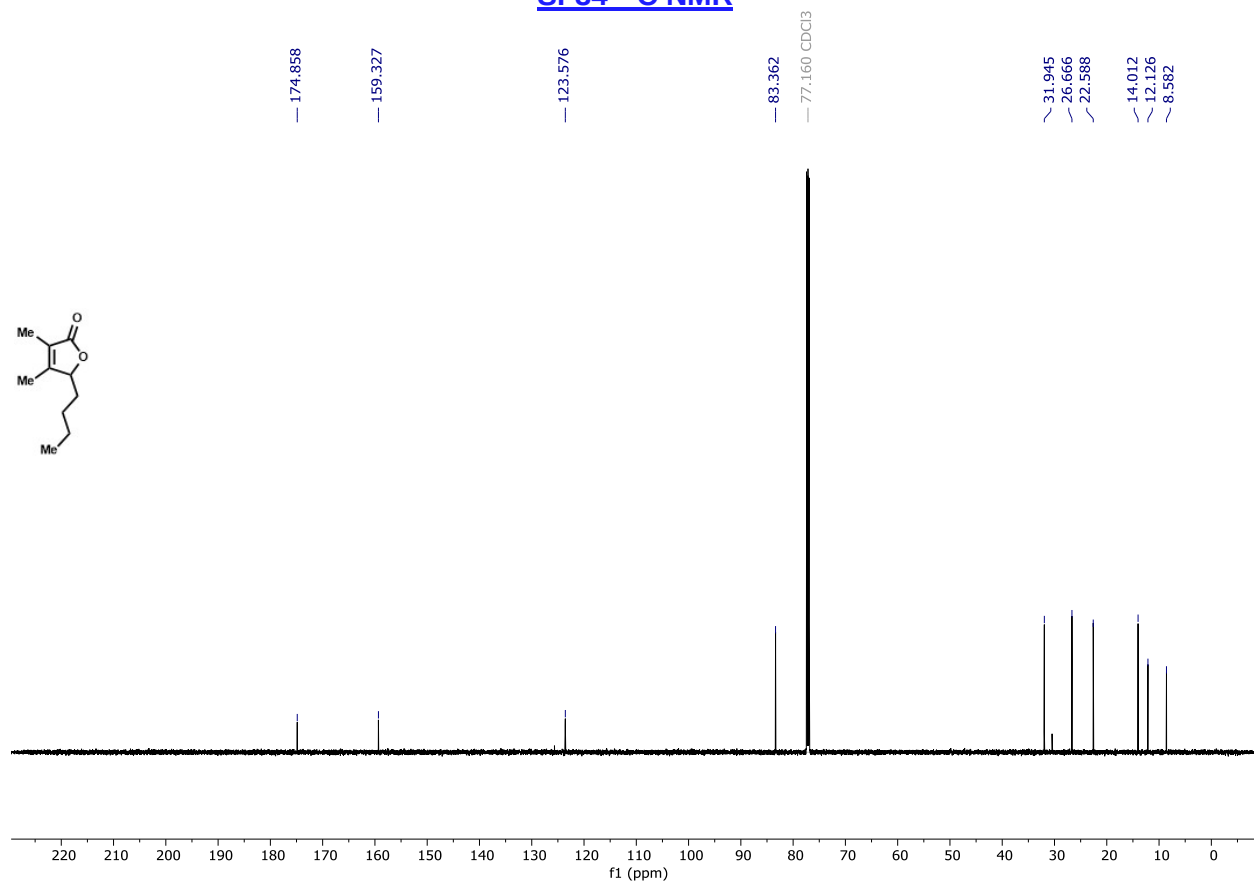
SI-33 ¹H NMR

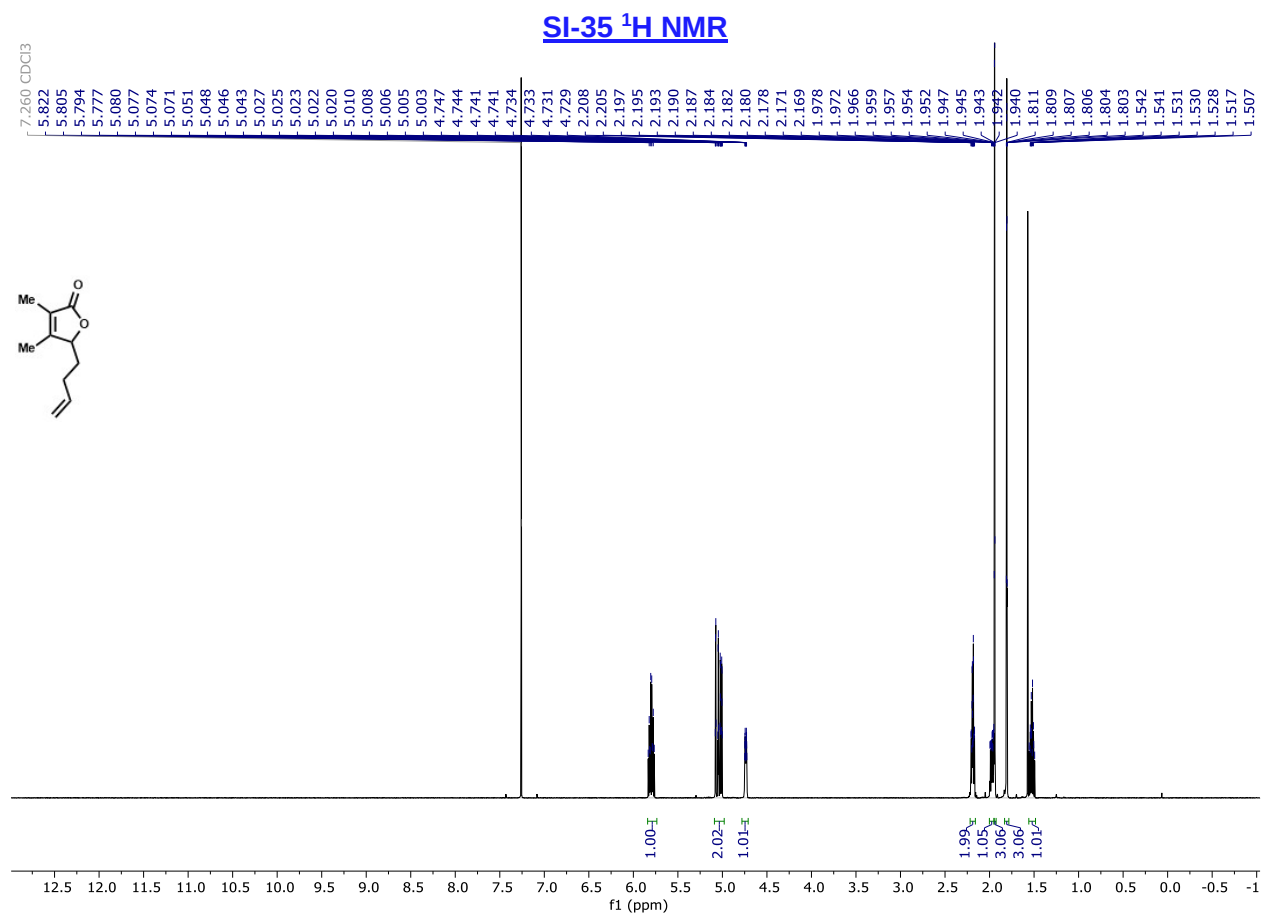




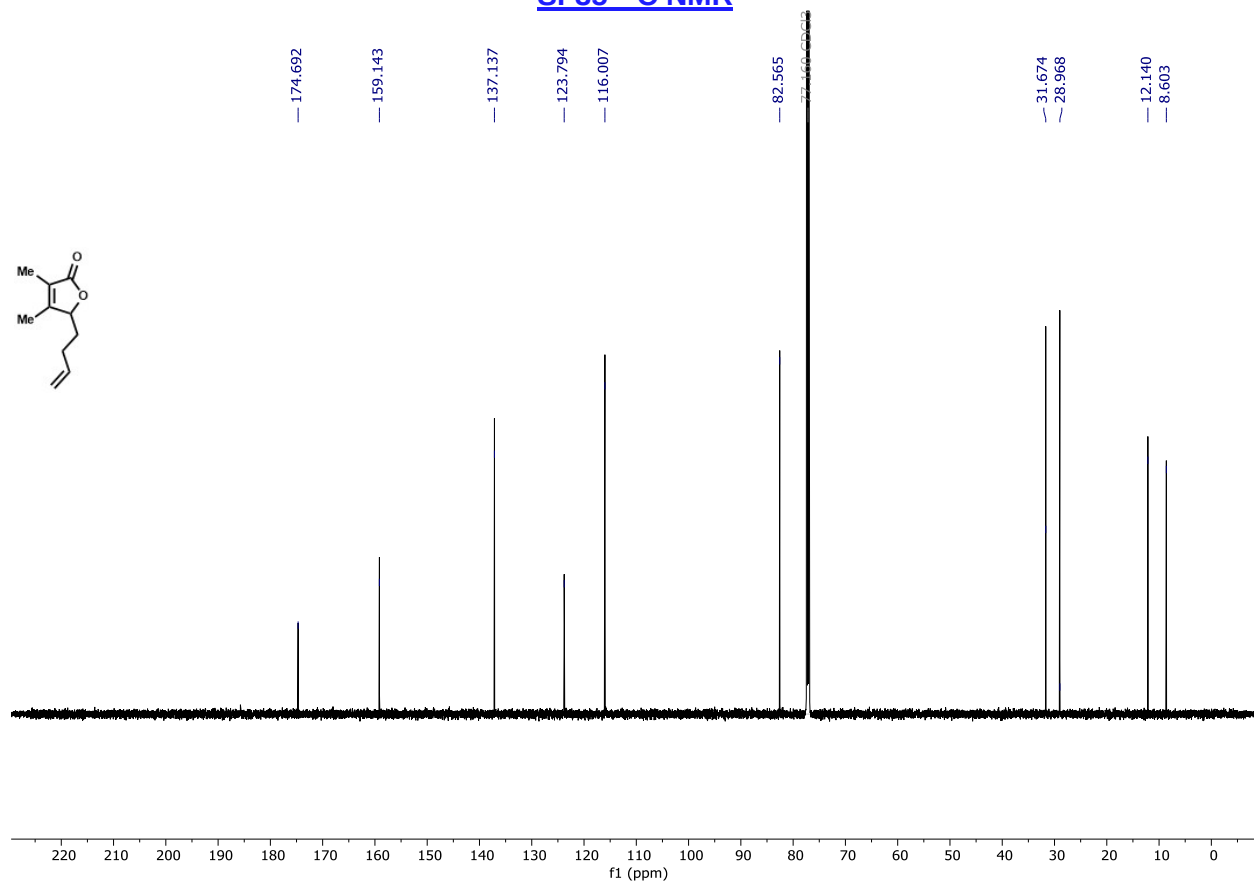


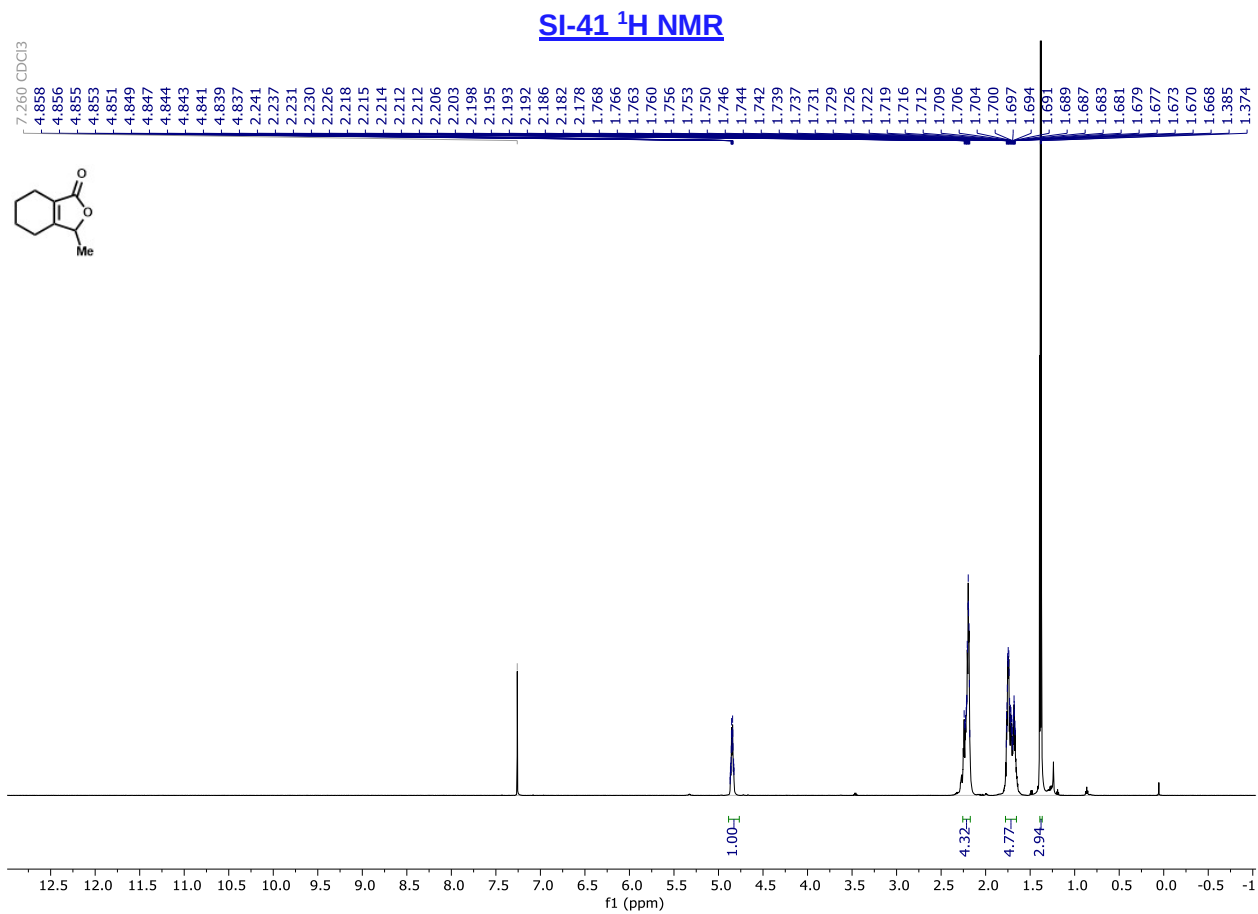
SI-34 ¹³C NMR



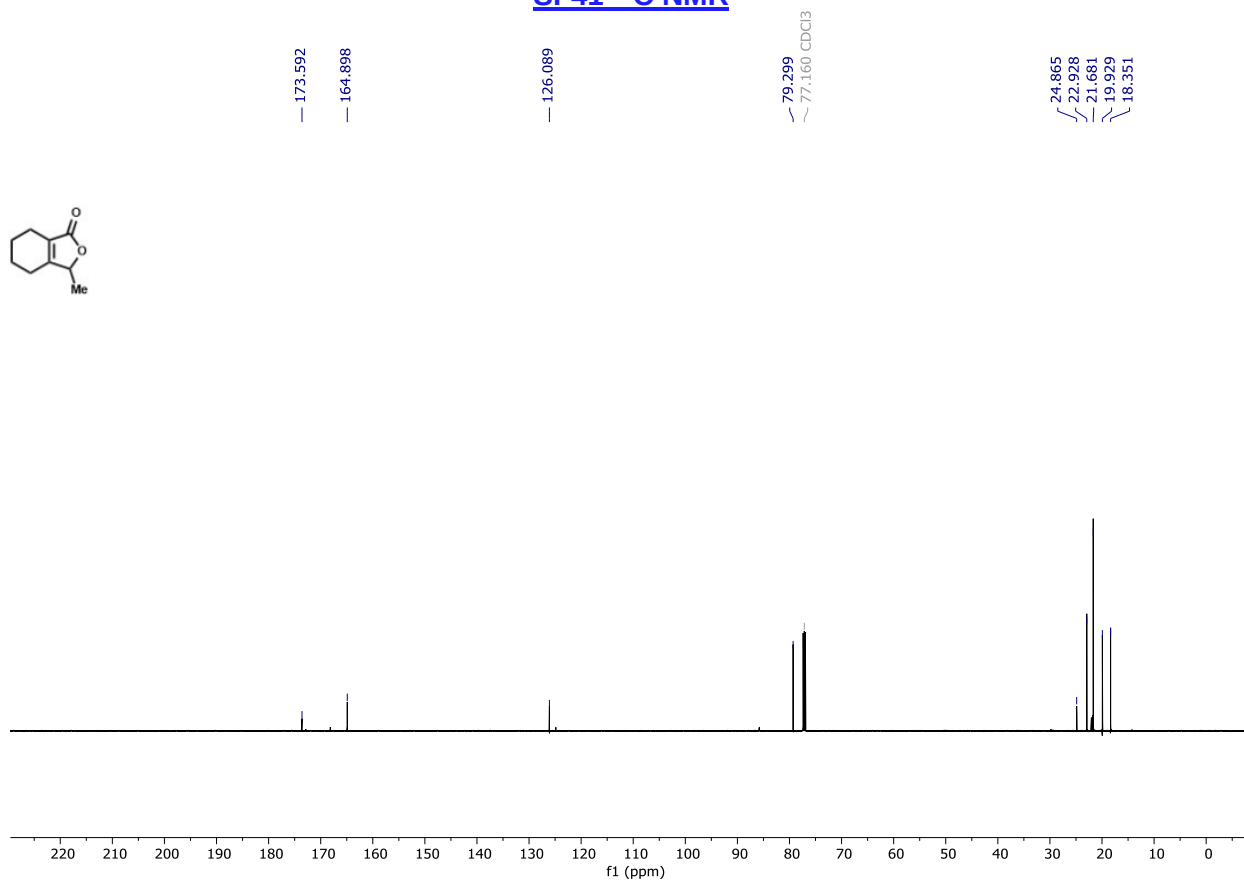


SI-35 ¹³C NMR



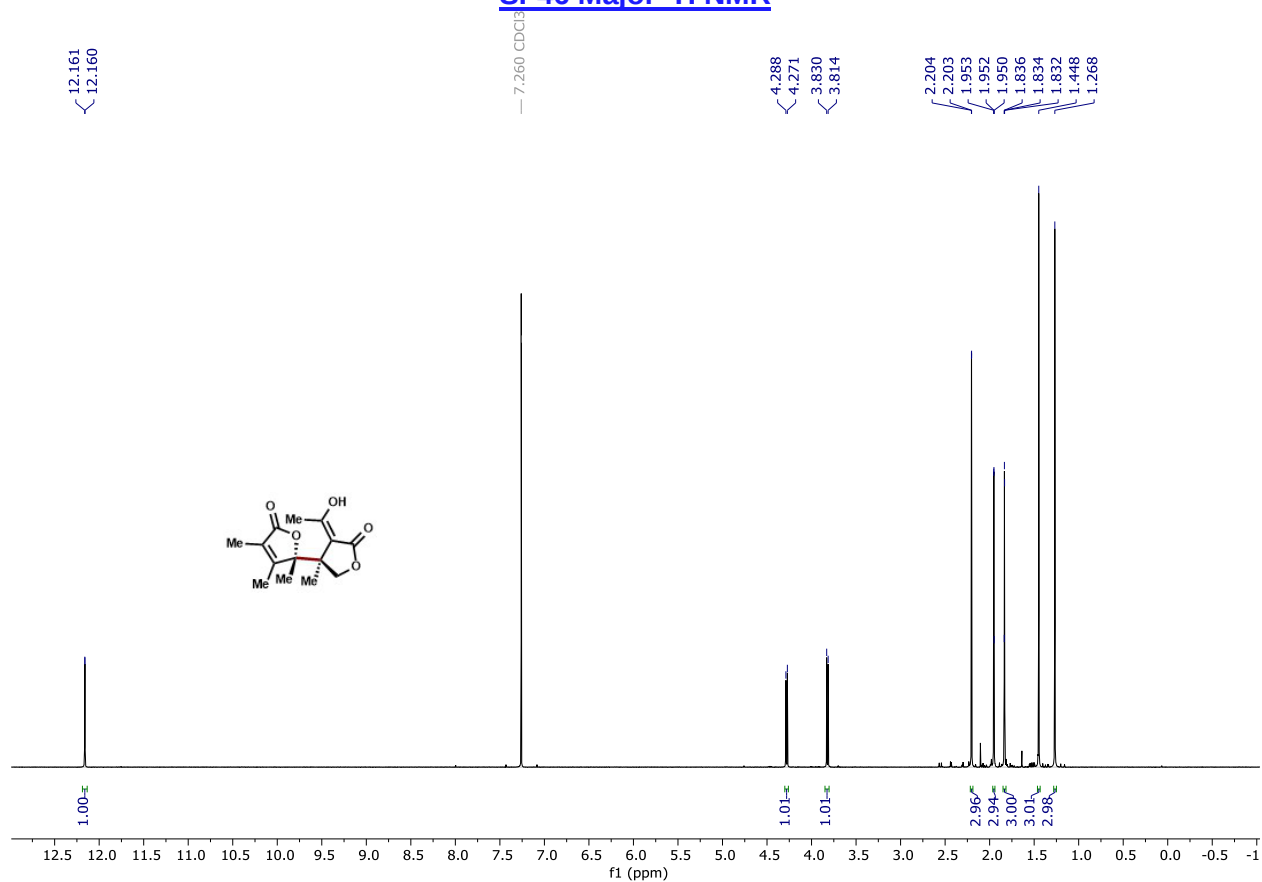


SI-41 ¹³C NMR



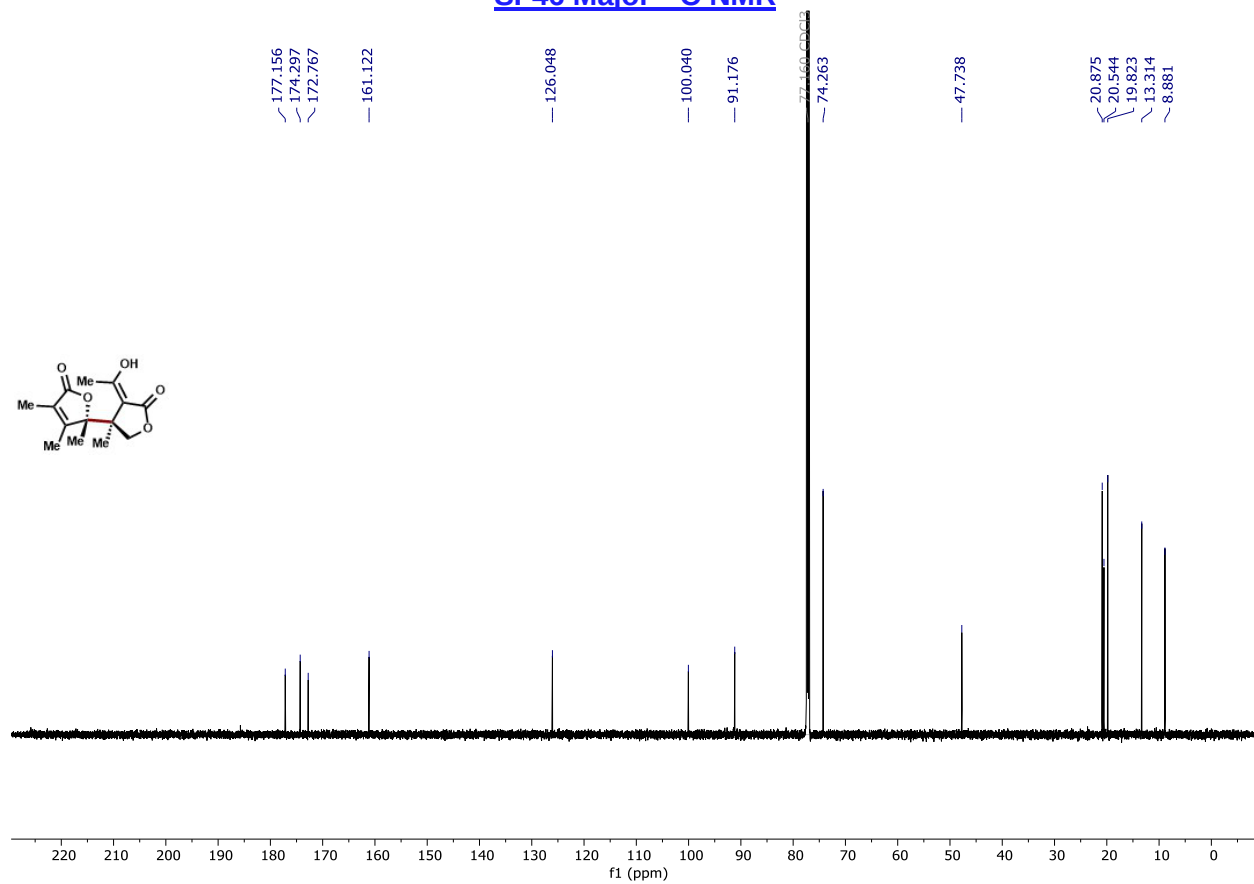
Electrophile Scope

SI-46 Major ^1H NMR



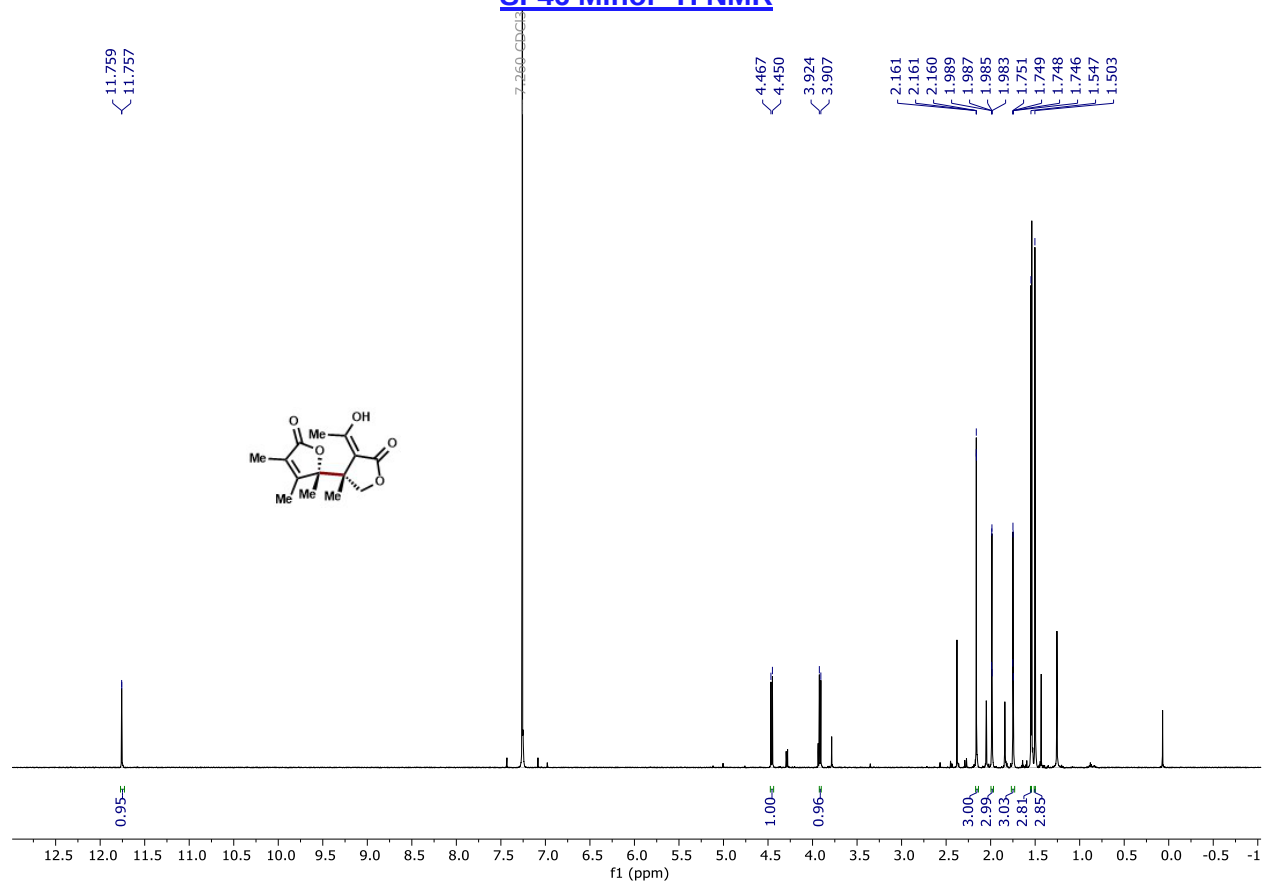
Note: The above spectrum was obtained from recrystallized material. In solution, the enol tautomer gradually equilibrates to a mixture of keto and enol tautomers.

SI-46 Major ^{13}C NMR



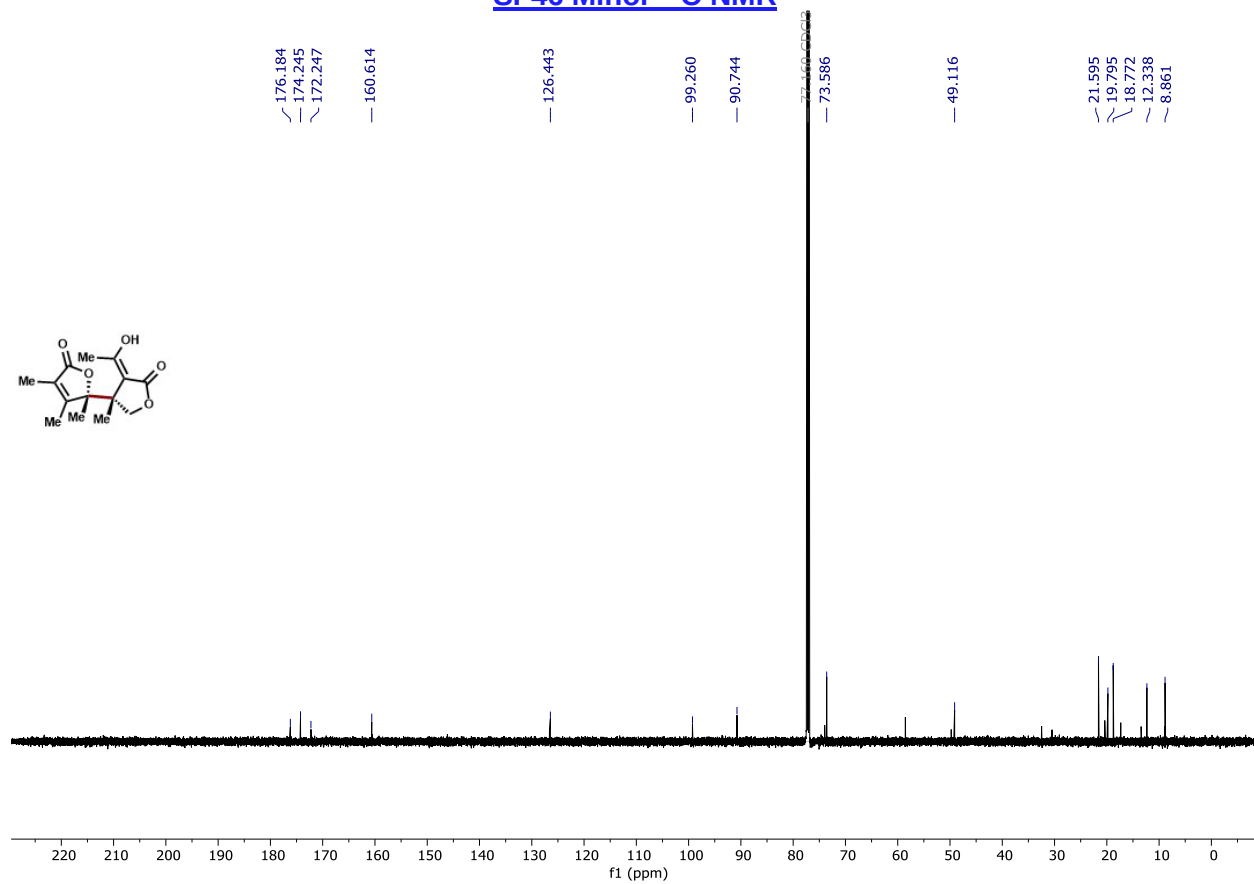
Note: The above spectrum was obtained from recrystallized material. In solution, the enol tautomer gradually equilibrates to a mixture of keto and enol tautomers.

SI-46 Minor ¹H NMR

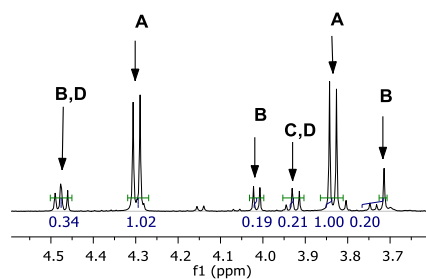


Minor peaks belong to the keto tautomer.

SI-46 Minor ¹³C NMR



SI-46 Crude ¹H NMR

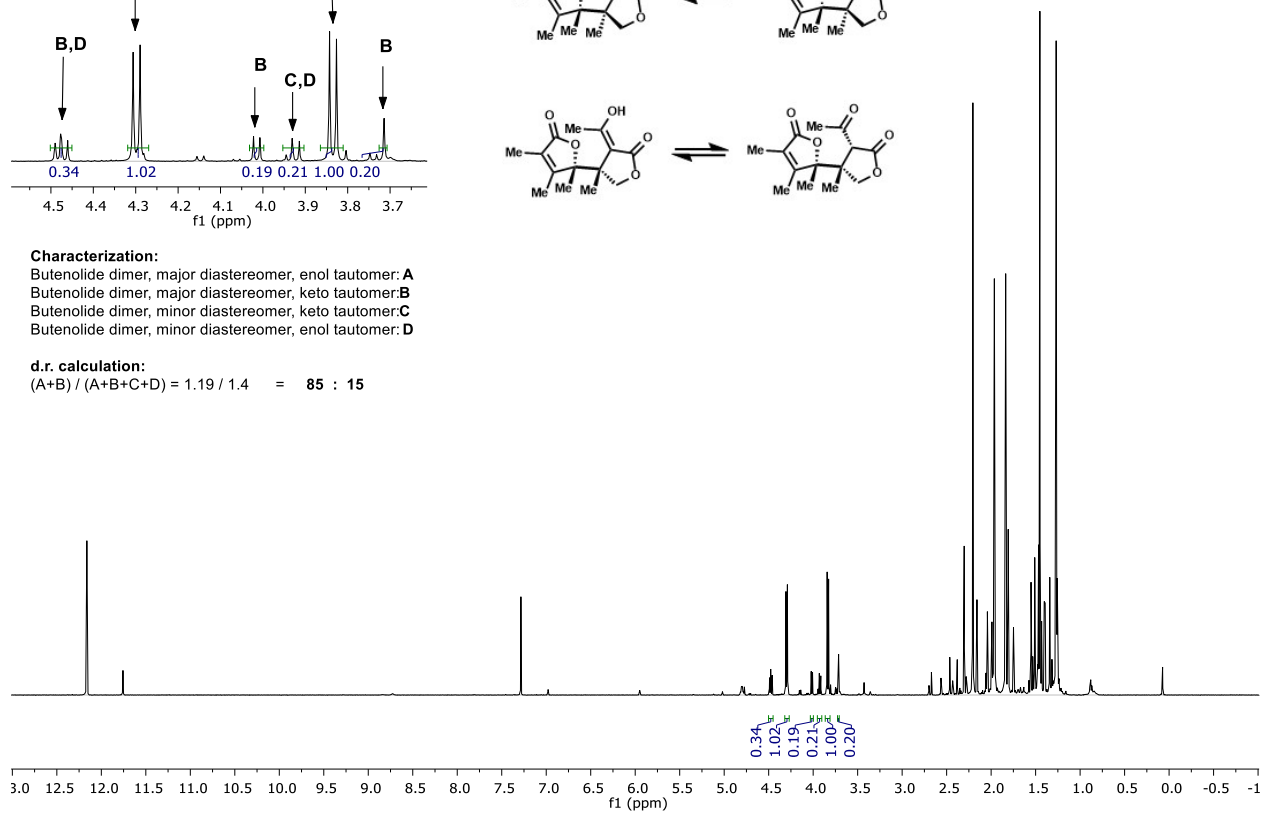
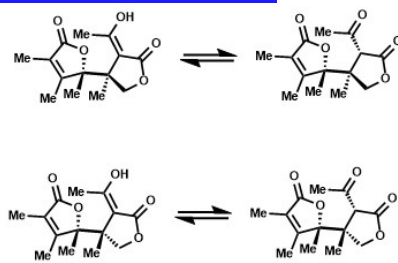


Characterization:

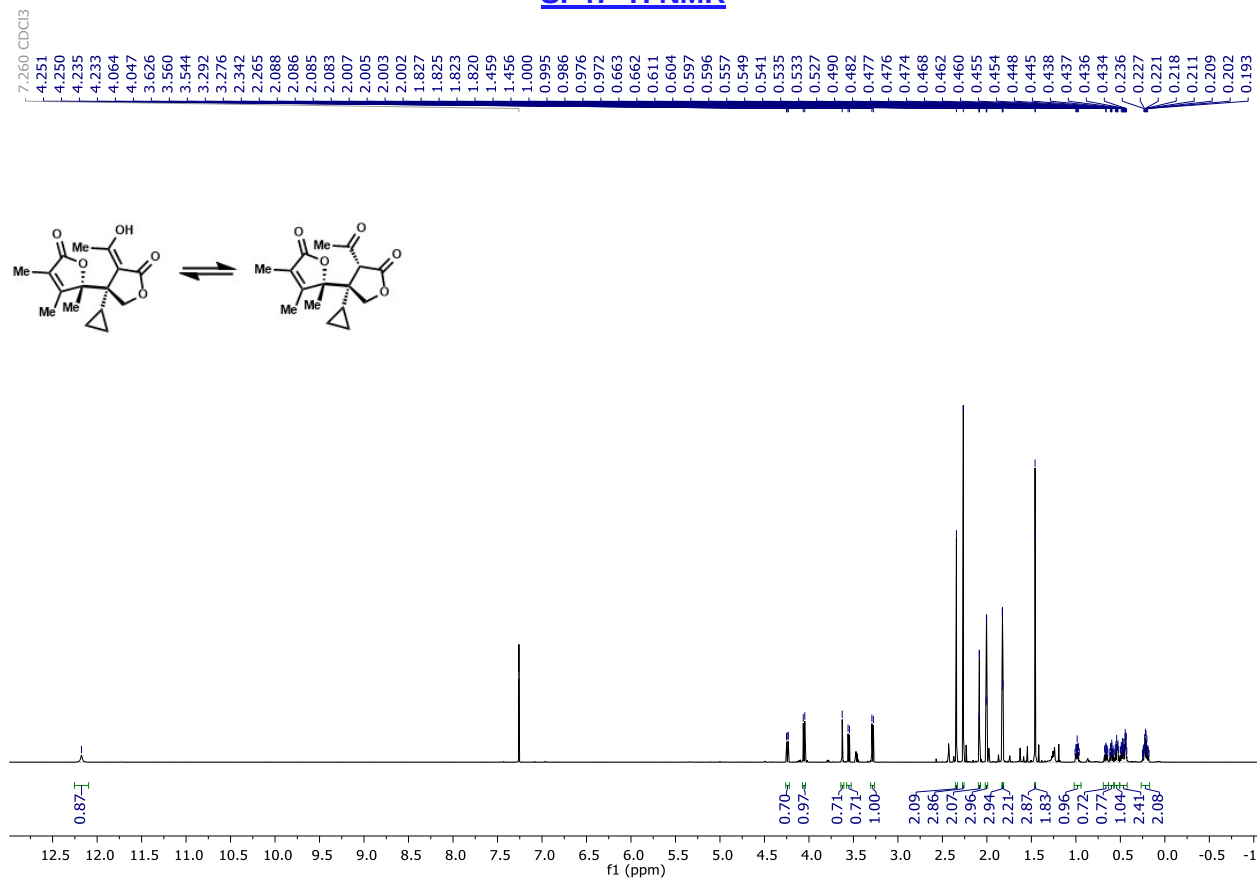
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

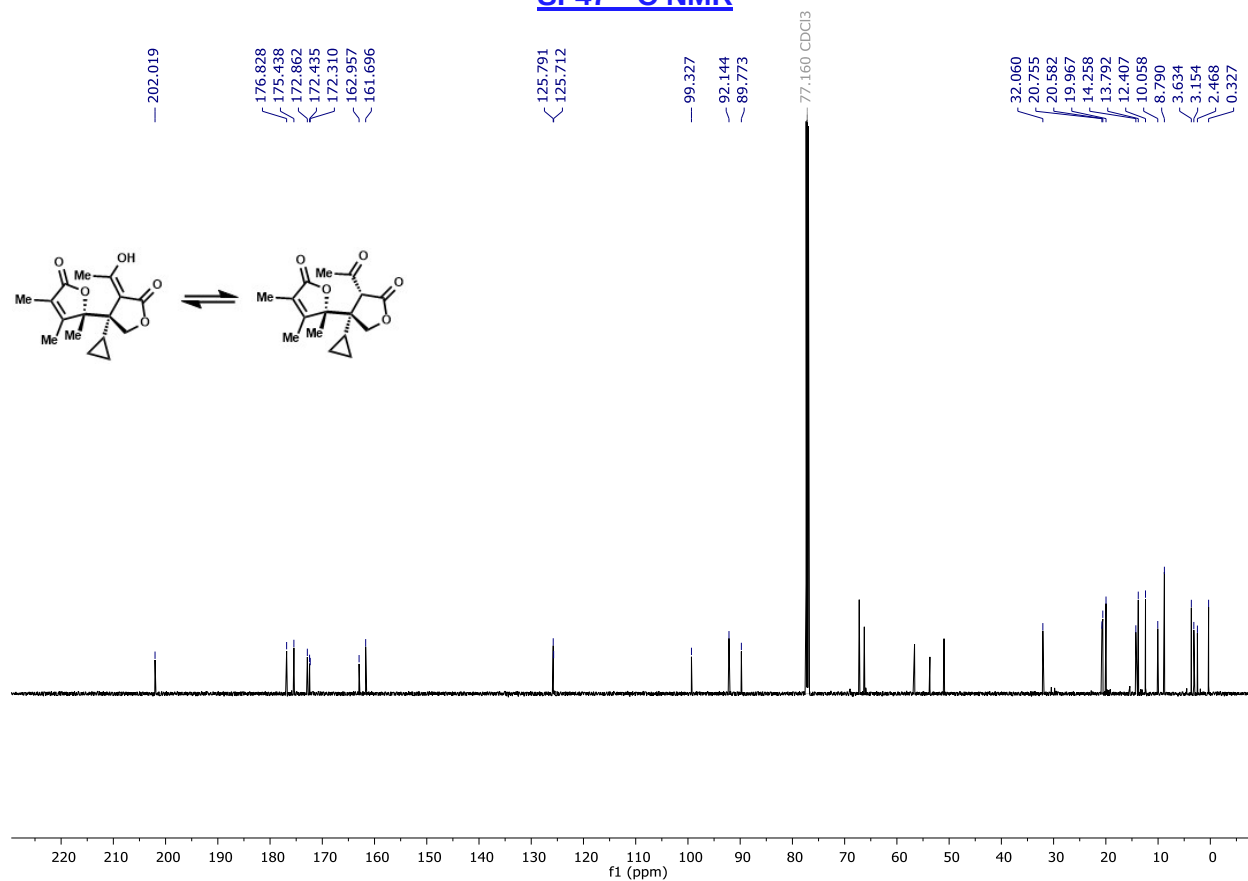
$$(A+B) / (A+B+C+D) = 1.19 / 1.4 = 85 : 15$$



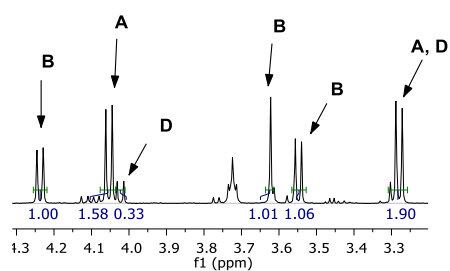
SI-47 ¹H NMR



SI-47 ¹³C NMR



SI-47 Crude ¹H NMR

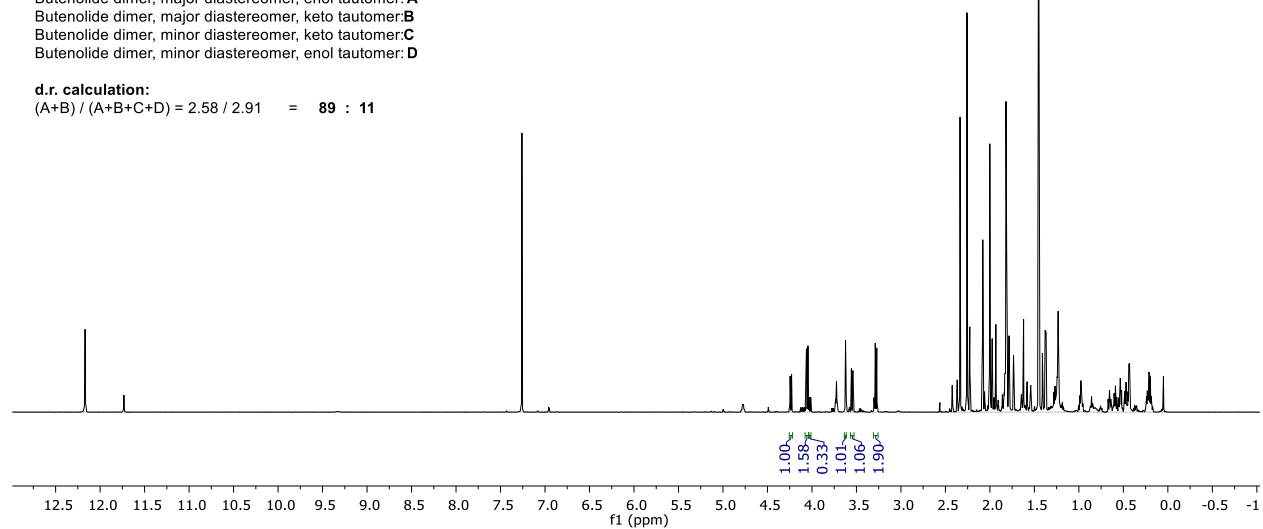
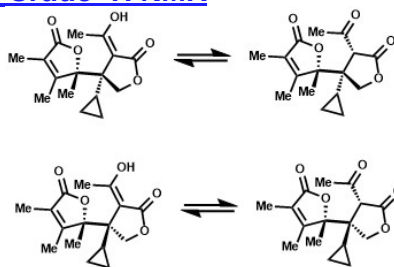


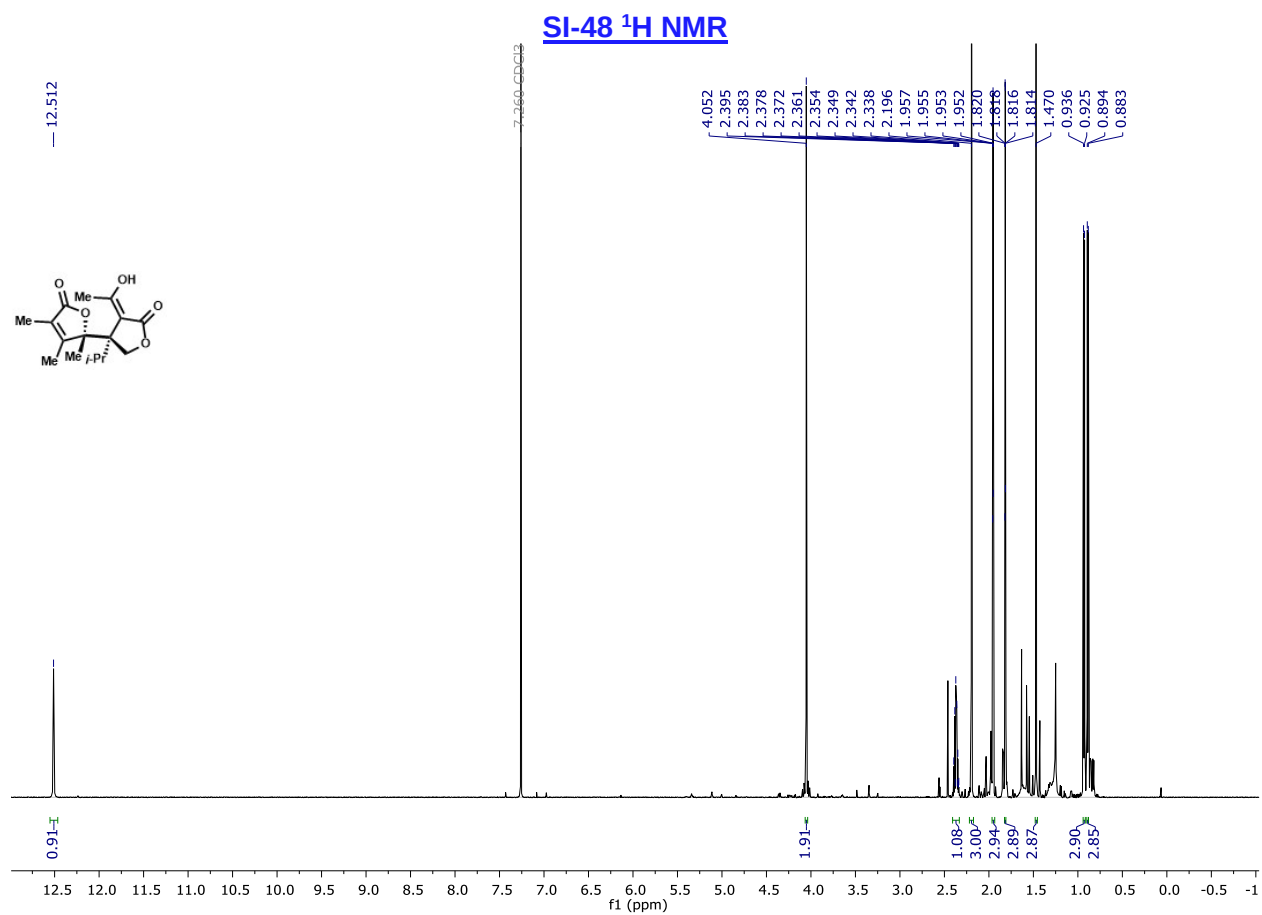
Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

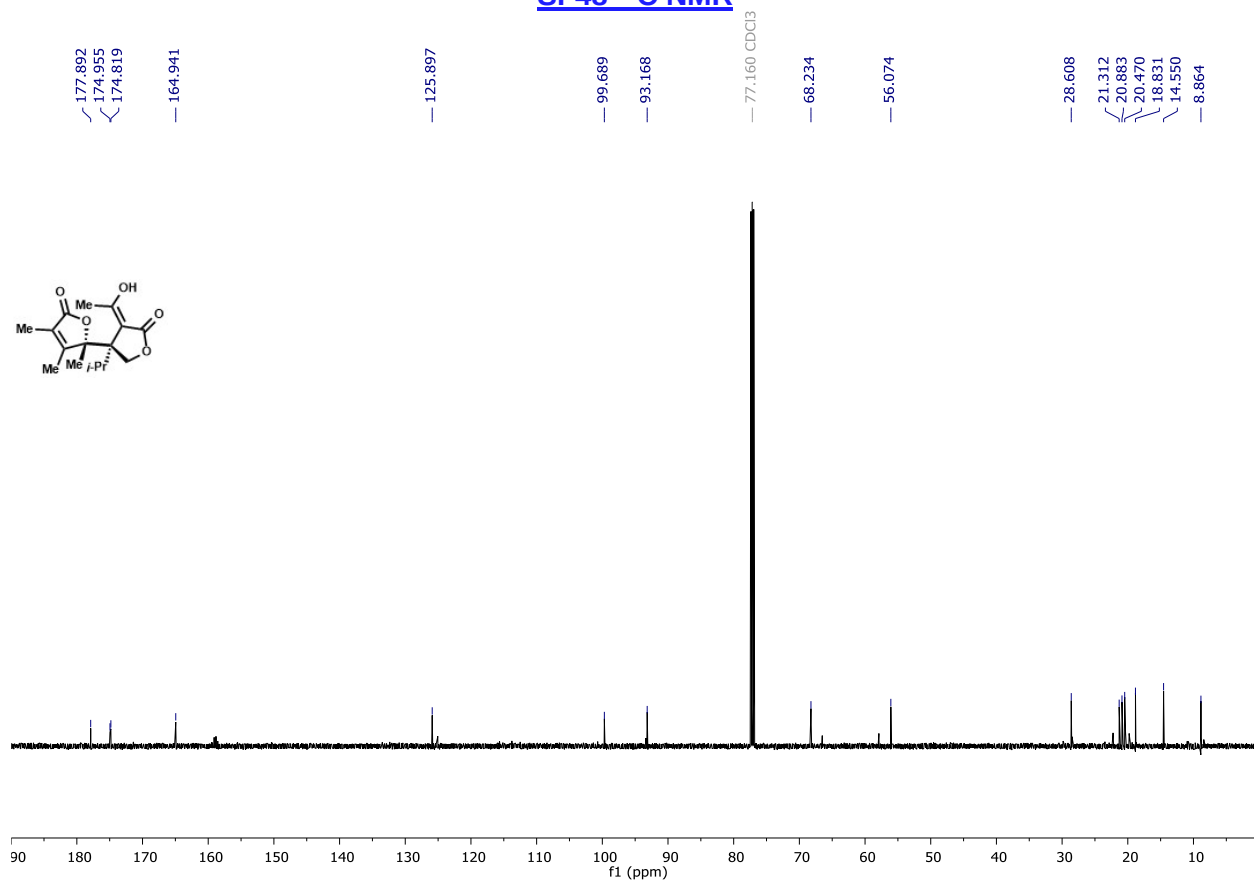
d.r. calculation:

$$(A+B) / (A+B+C+D) = 2.58 / 2.91 = 89 : 11$$

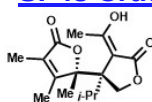
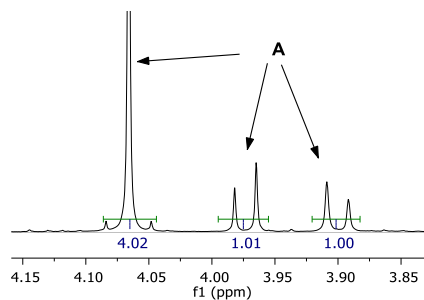




SI-48 ¹³C NMR



SI-48 Crude ¹H NMR

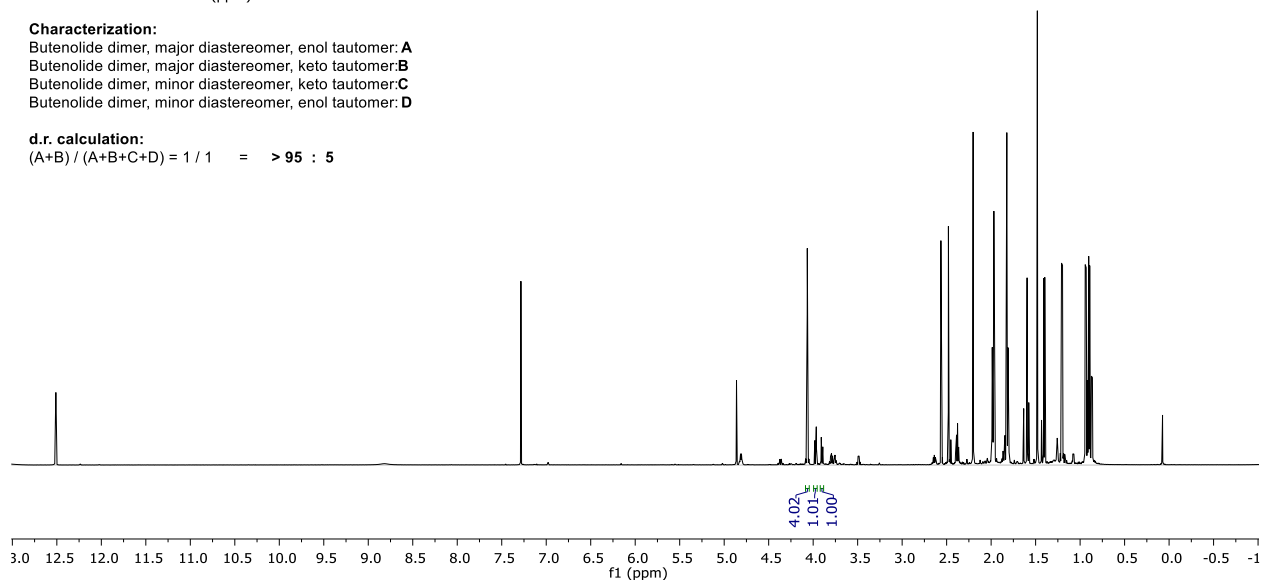


Characterization:

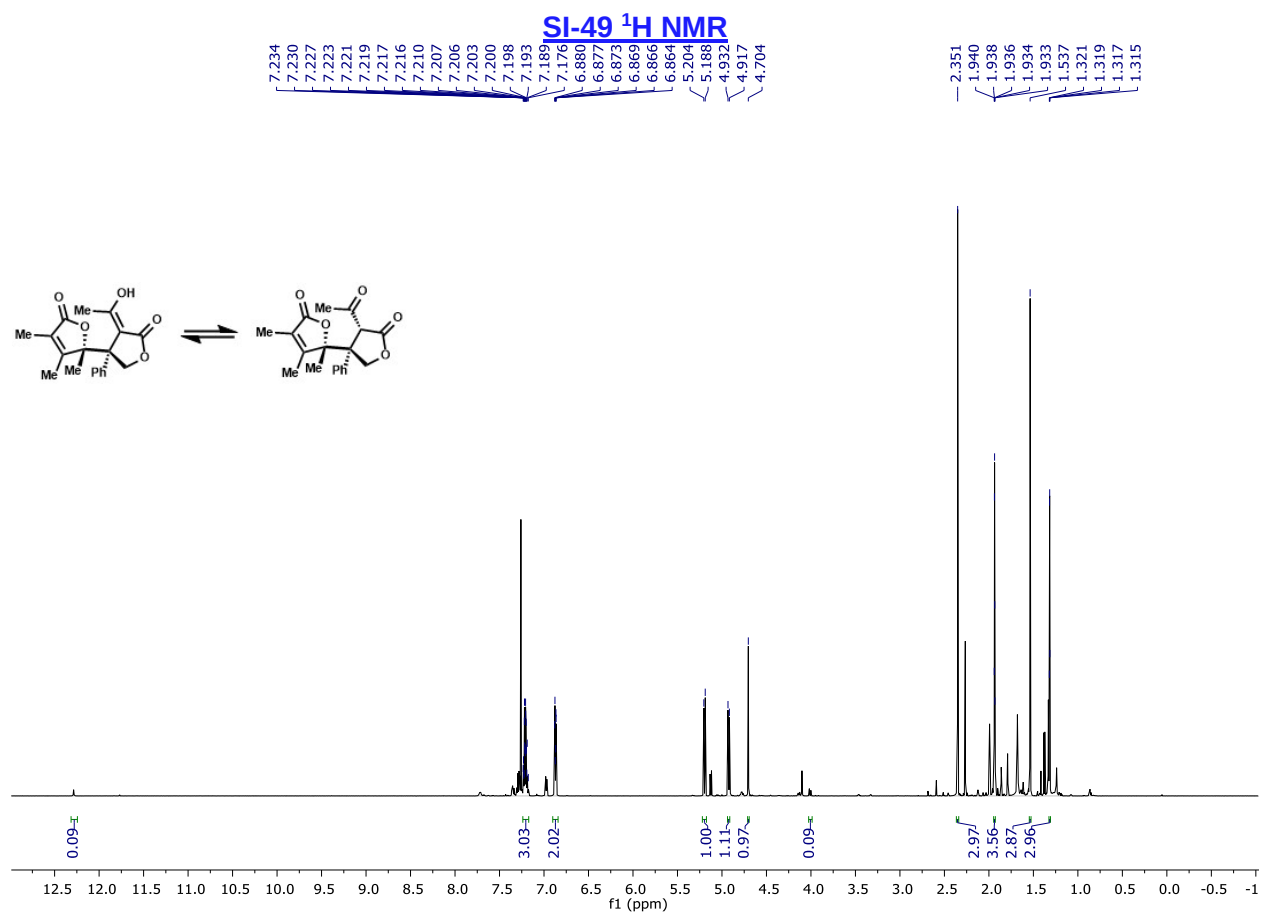
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

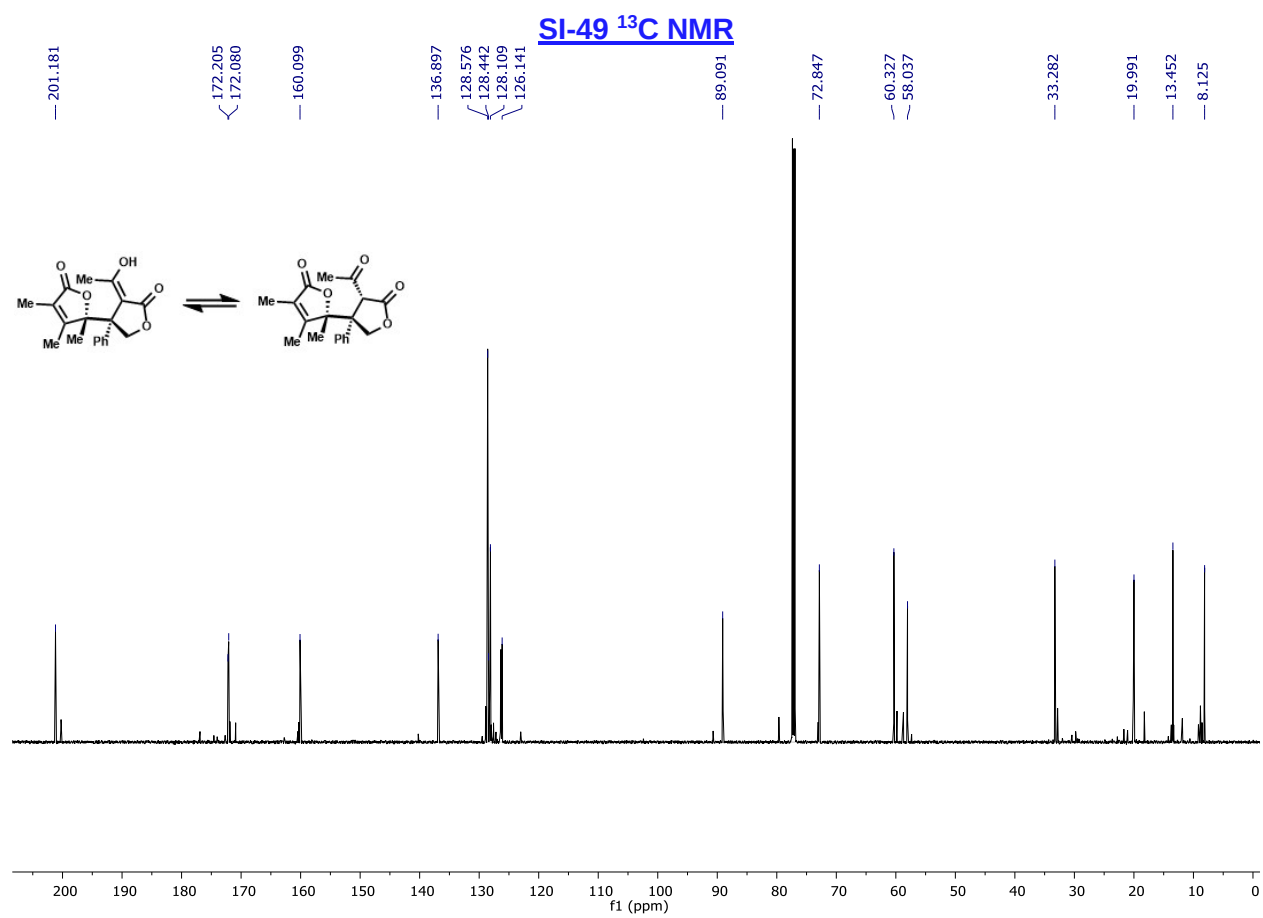
d.r. calculation:

$(A+B) / (A+B+C+D) = 1 / 1 = > 95 : 5$

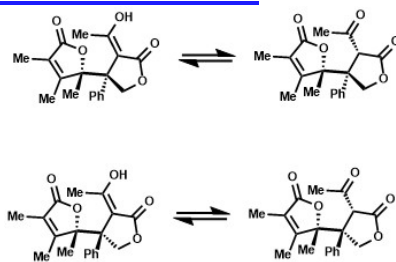
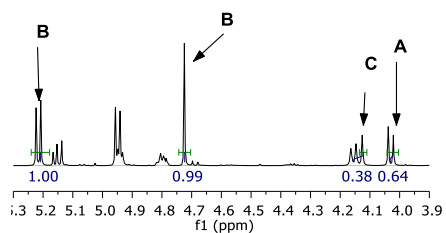


Note: Crude ¹H NMR spectrum showed two major products (ratio 66:33). These two products gradually coalesce in CDCl₃ and in the presence of TFA. The two major products are likely rotamers of the major diastereomer.





SI-49 Crude ¹H NMR

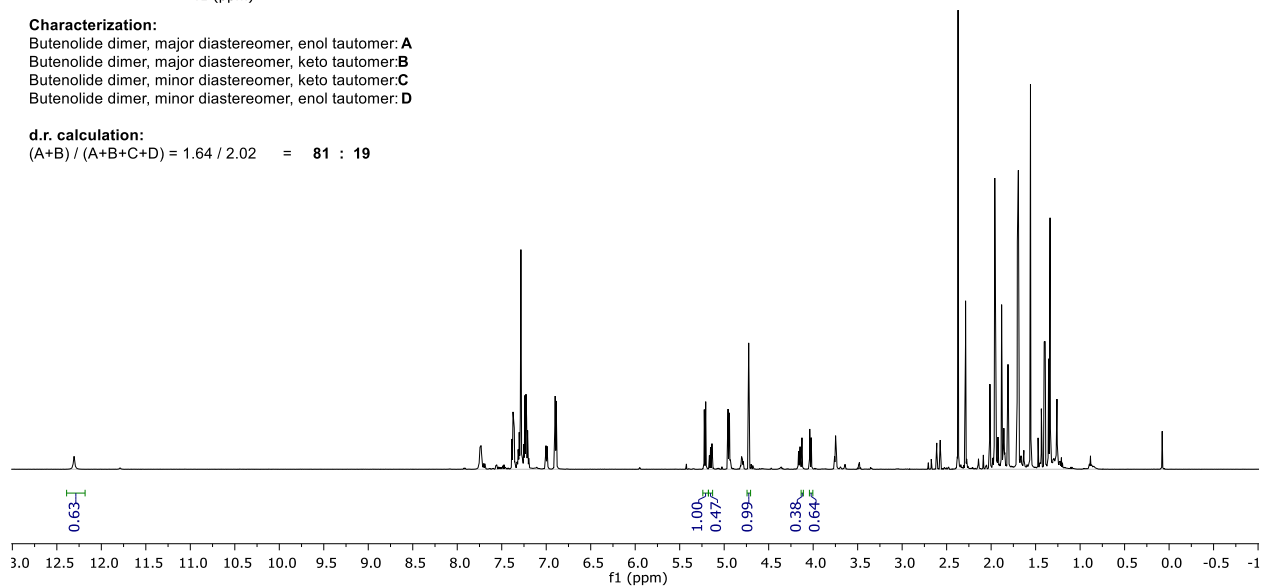


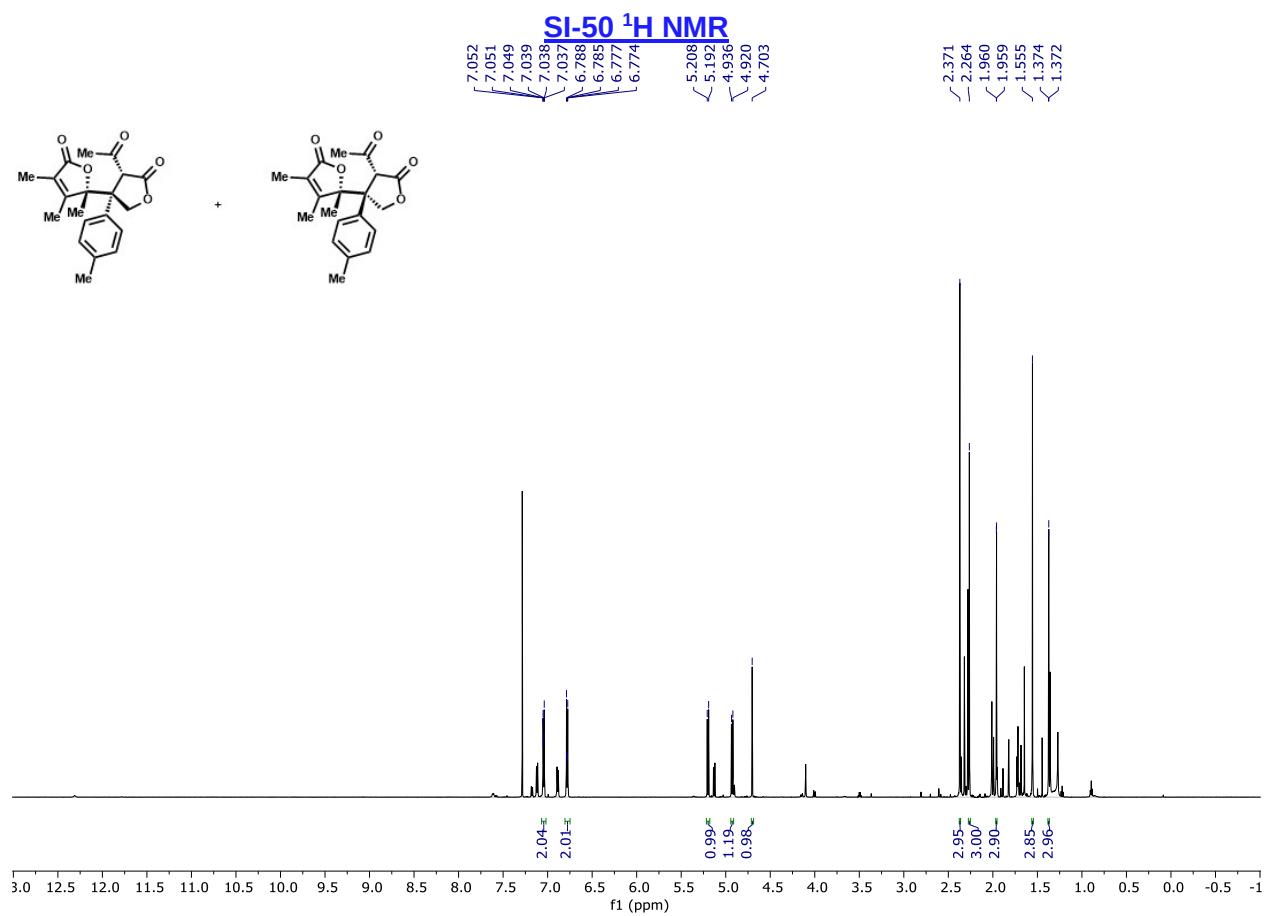
Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

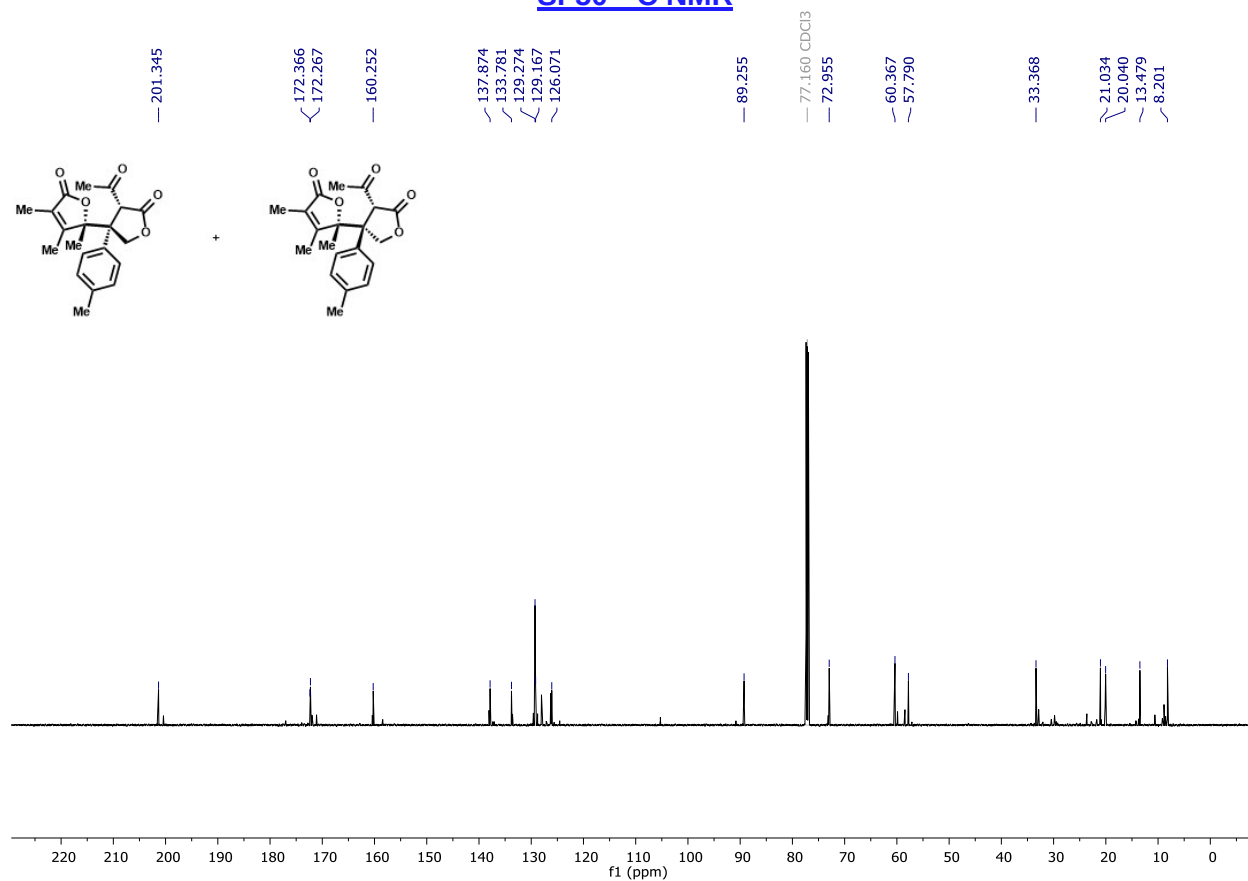
d.r. calculation:

$$(A+B) / (A+B+C+D) = 1.64 / 2.02 = 81 : 19$$

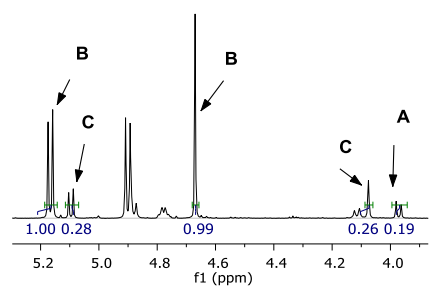




SI-50 ¹³C NMR



SI-50 Crude ¹H NMR



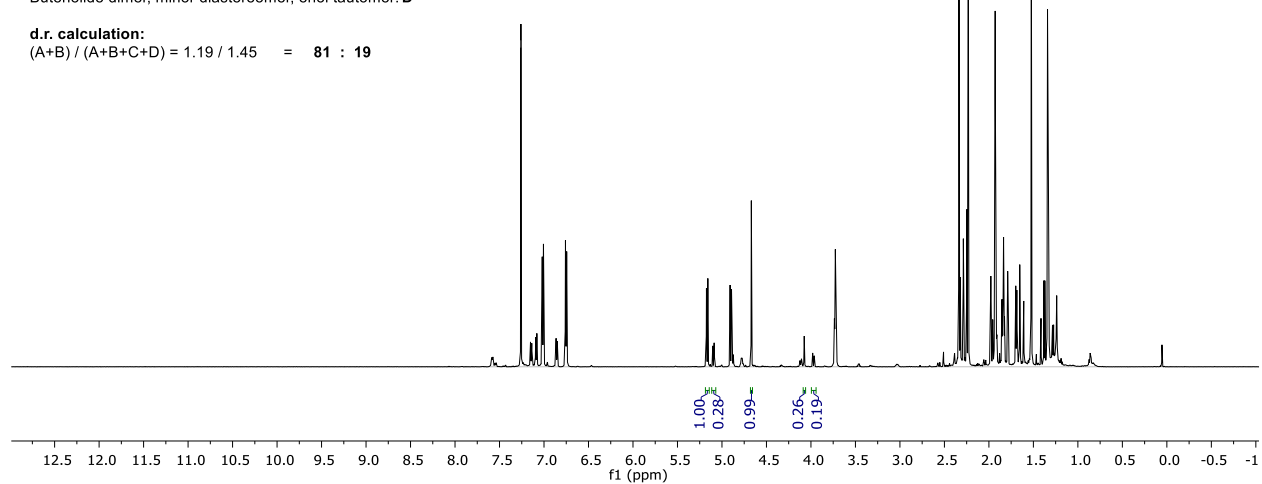
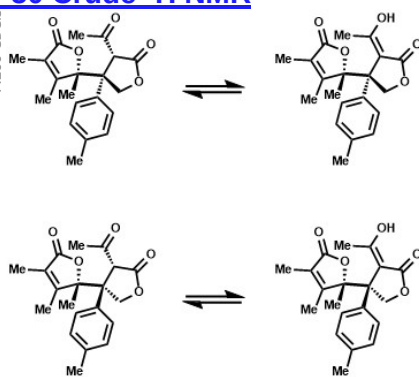
Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

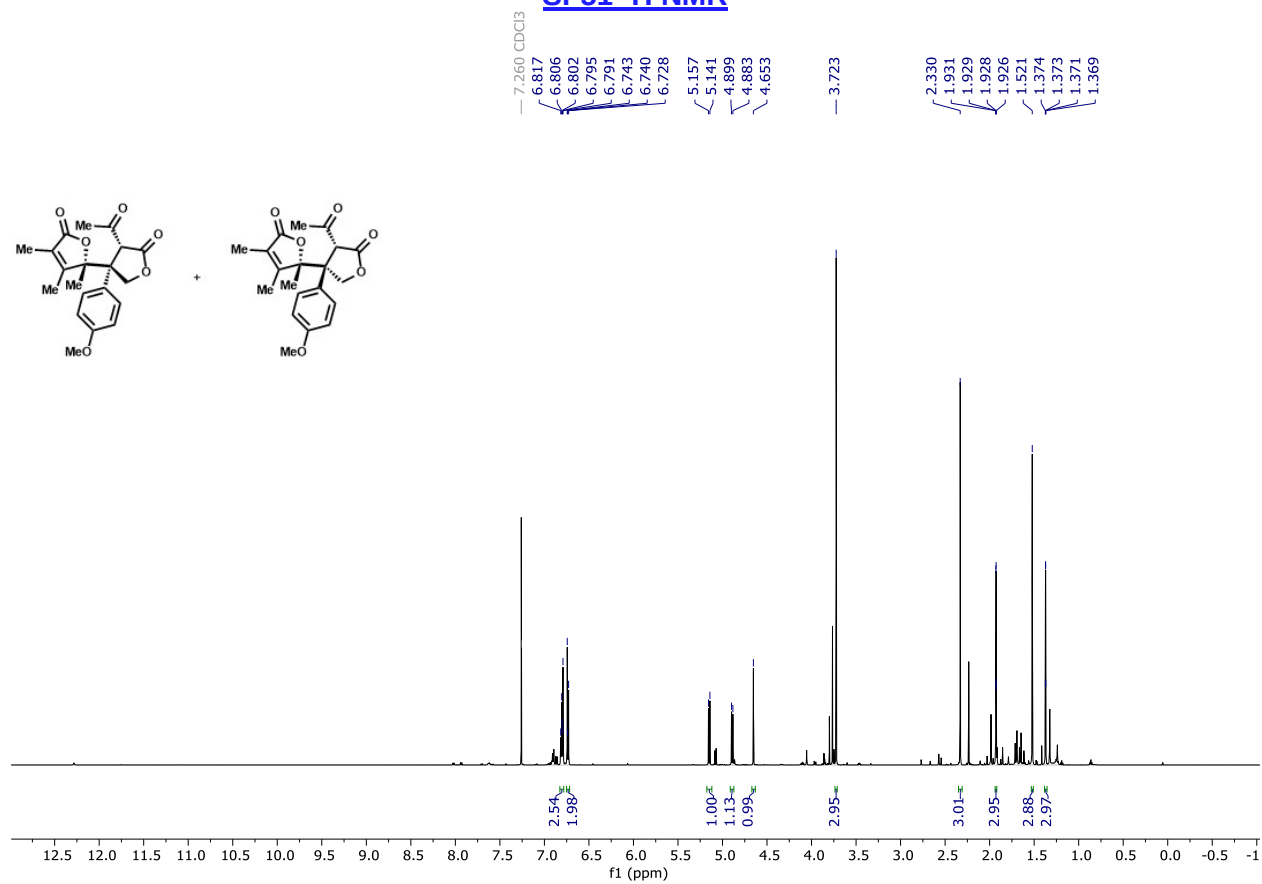
d.r. calculation:

(A+B) / (A+B+C+D) = 1.19 / 1.45 = **81 : 19**

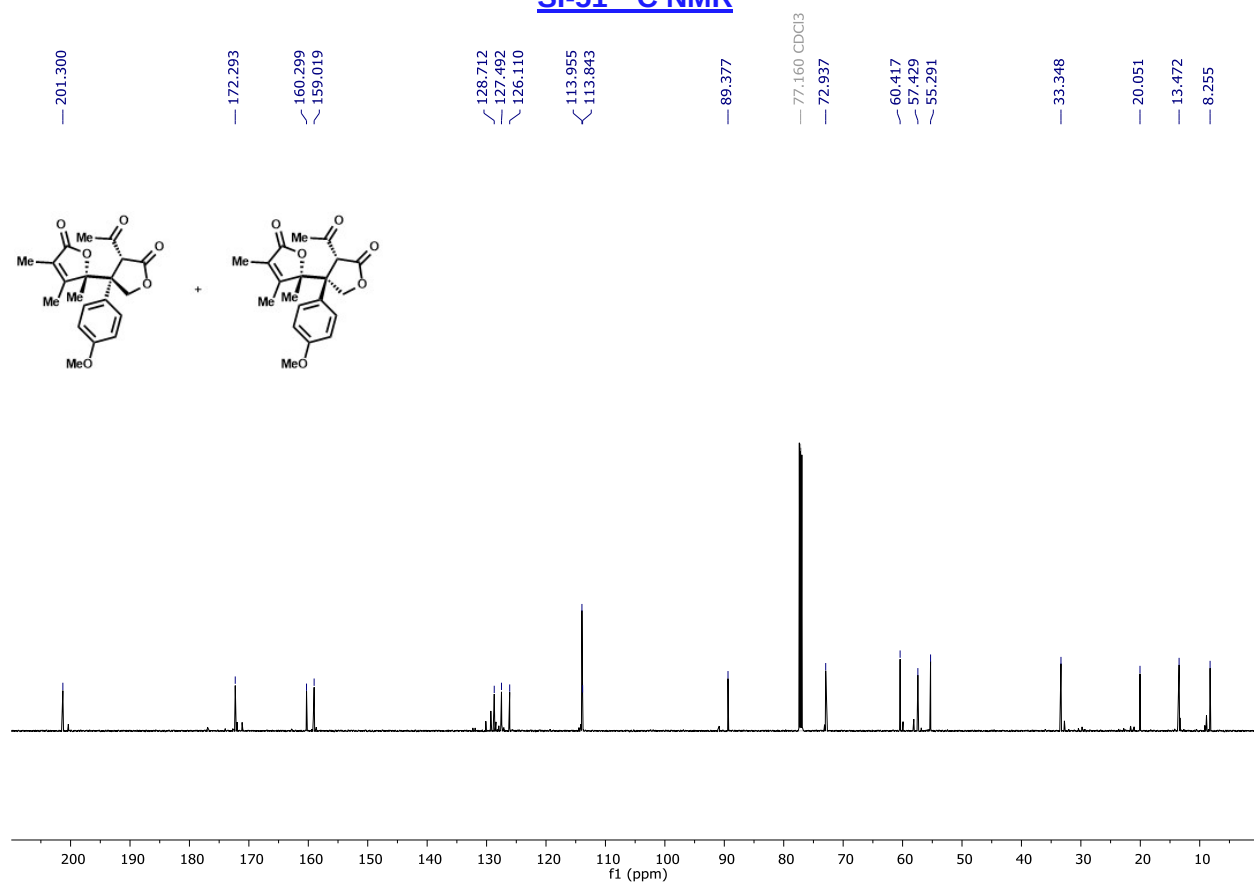
— 7.260 CDCl₃



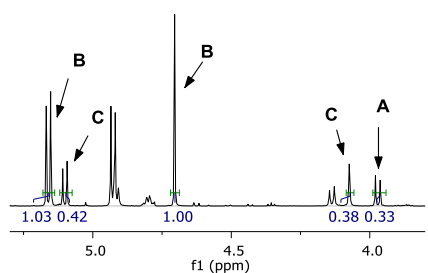
SI-51 ¹H NMR



SI-51 ¹³C NMR



SI-51 Crude ¹H NMR

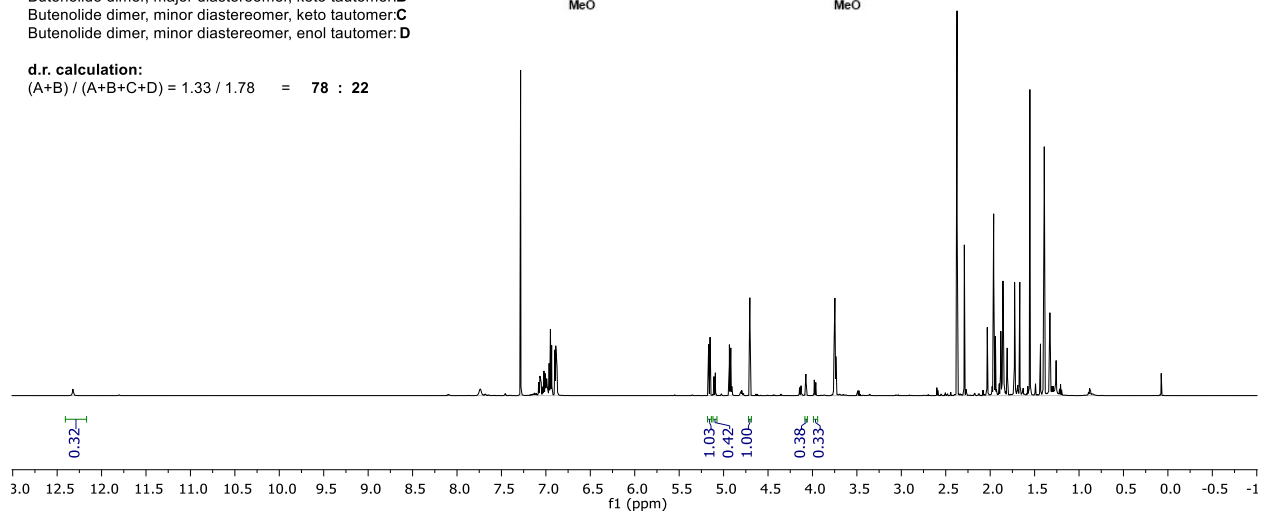
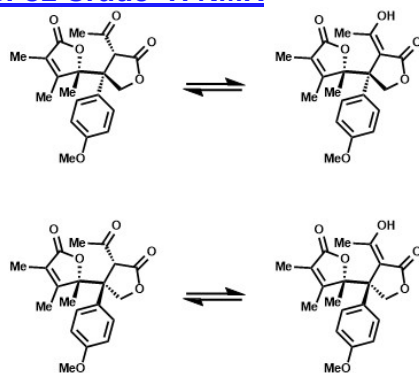


Characterization:

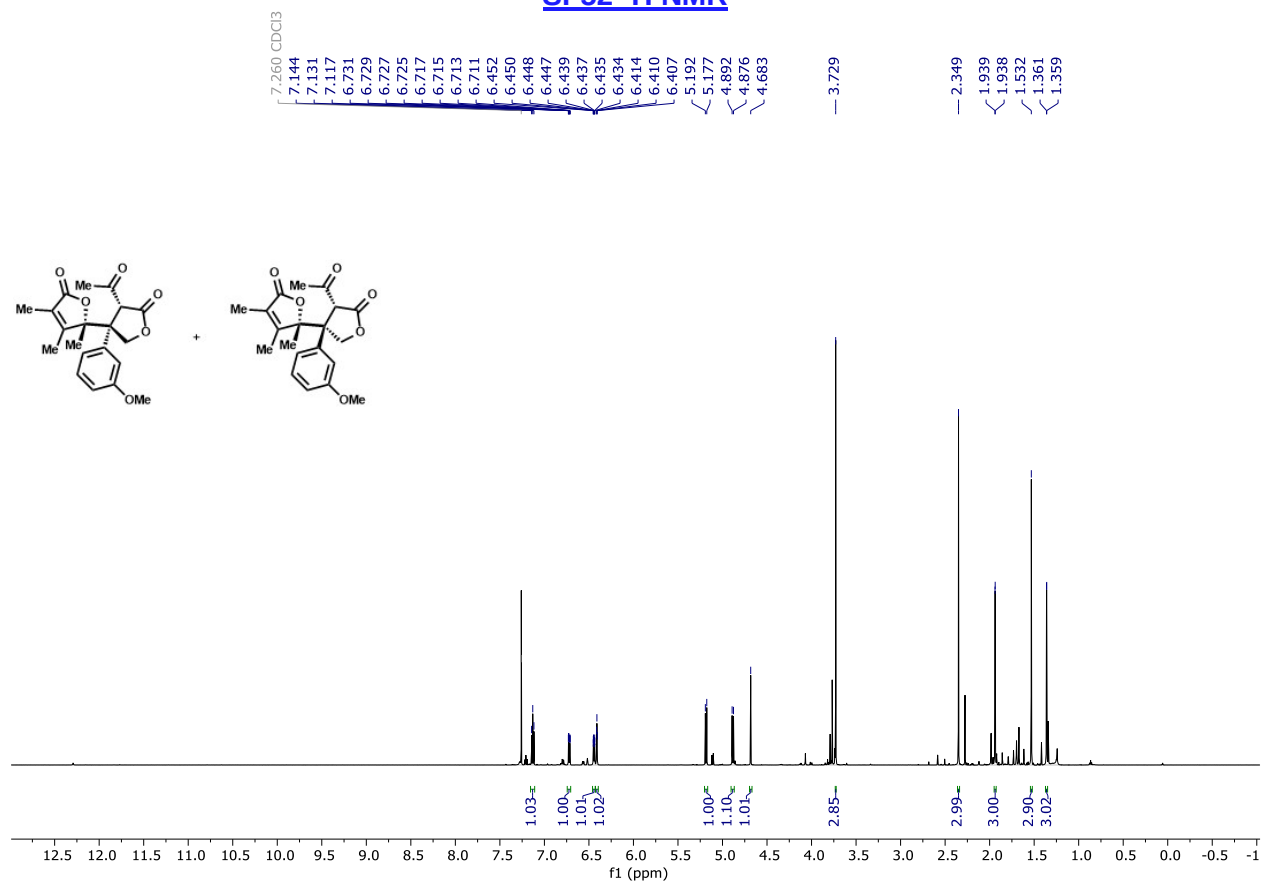
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

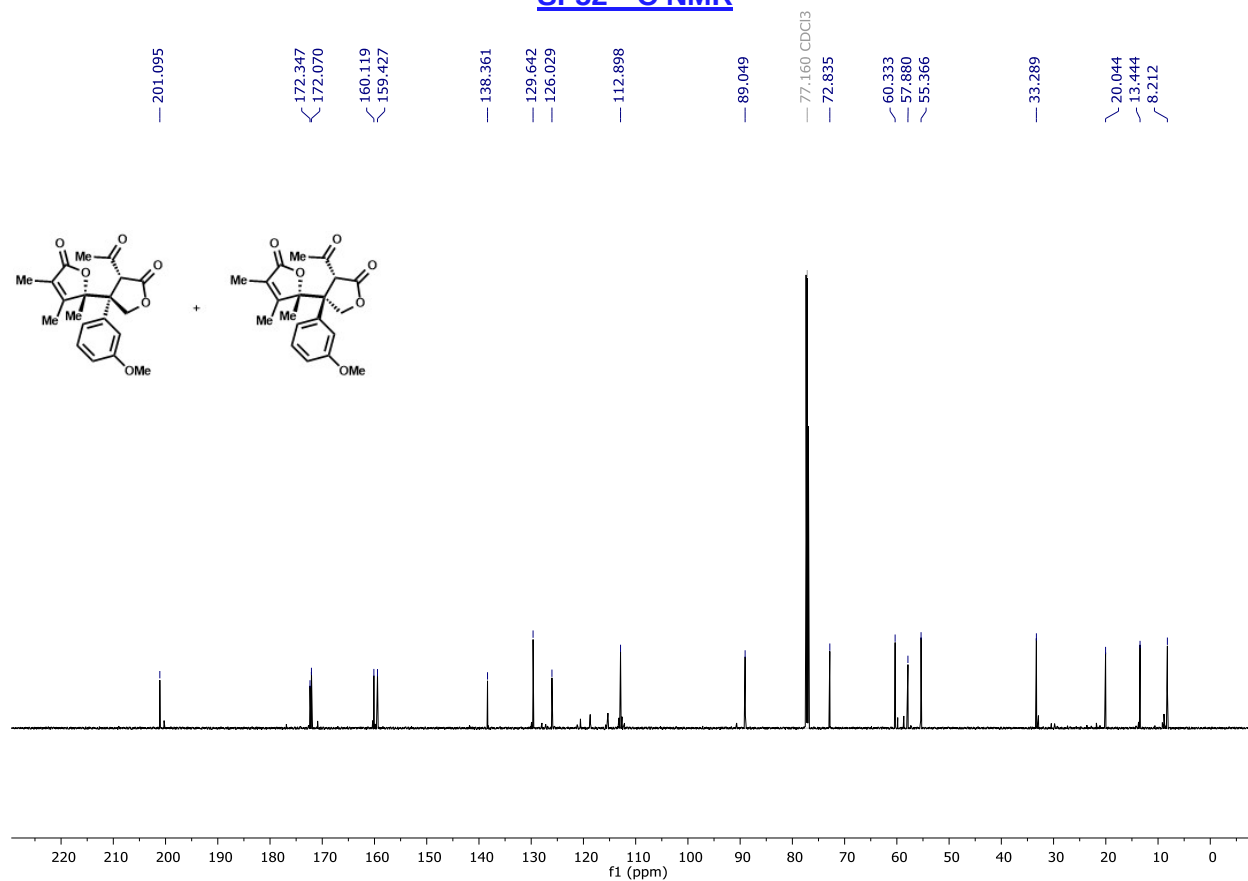
(A+B) / (A+B+C+D) = 1.33 / 1.78 = **78 : 22**



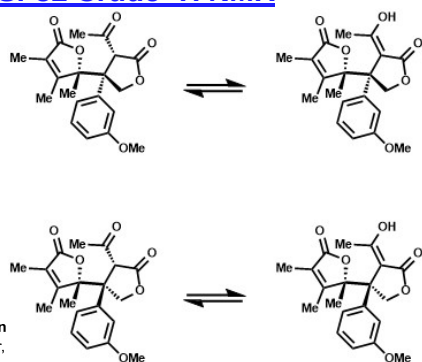
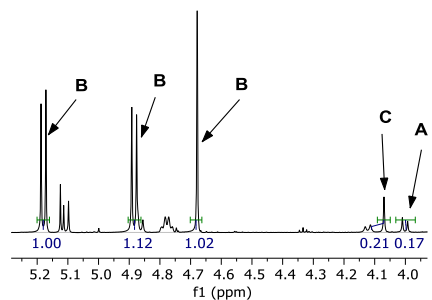
SI-52 ¹H NMR



SI-52 ¹³C NMR



SI-52 Crude ¹H NMR



Characterization

Butenolide dimer,

A

Butenolide dimer, major diastereomer, keto tautomer:

B

Butenolide dimer, minor diastereomer, keto tautomer:

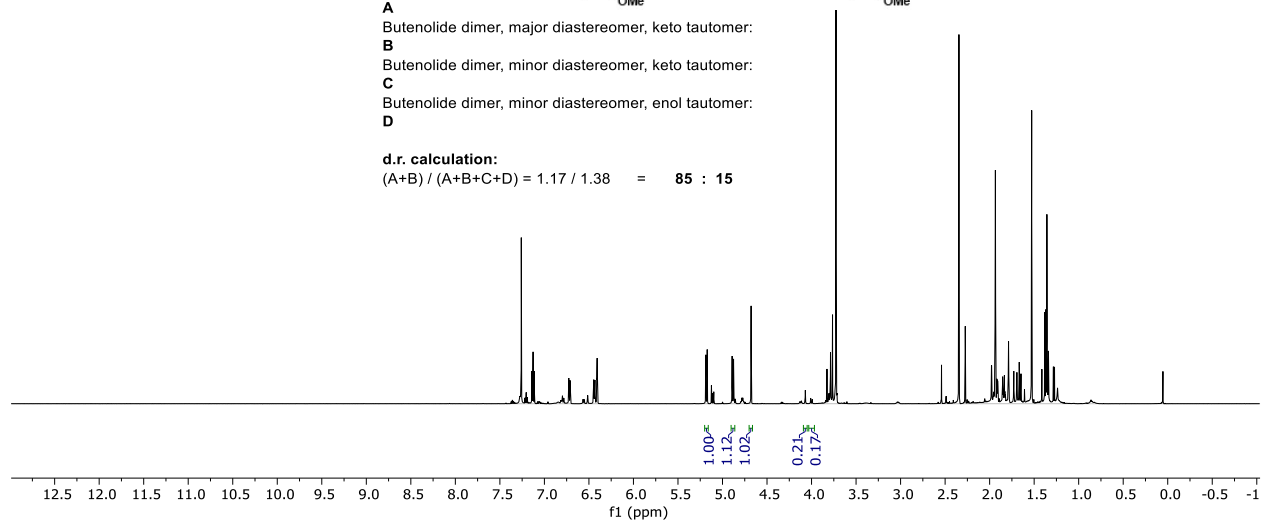
C

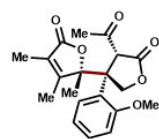
Butenolide dimer, minor diastereomer, enol tautomer:

D

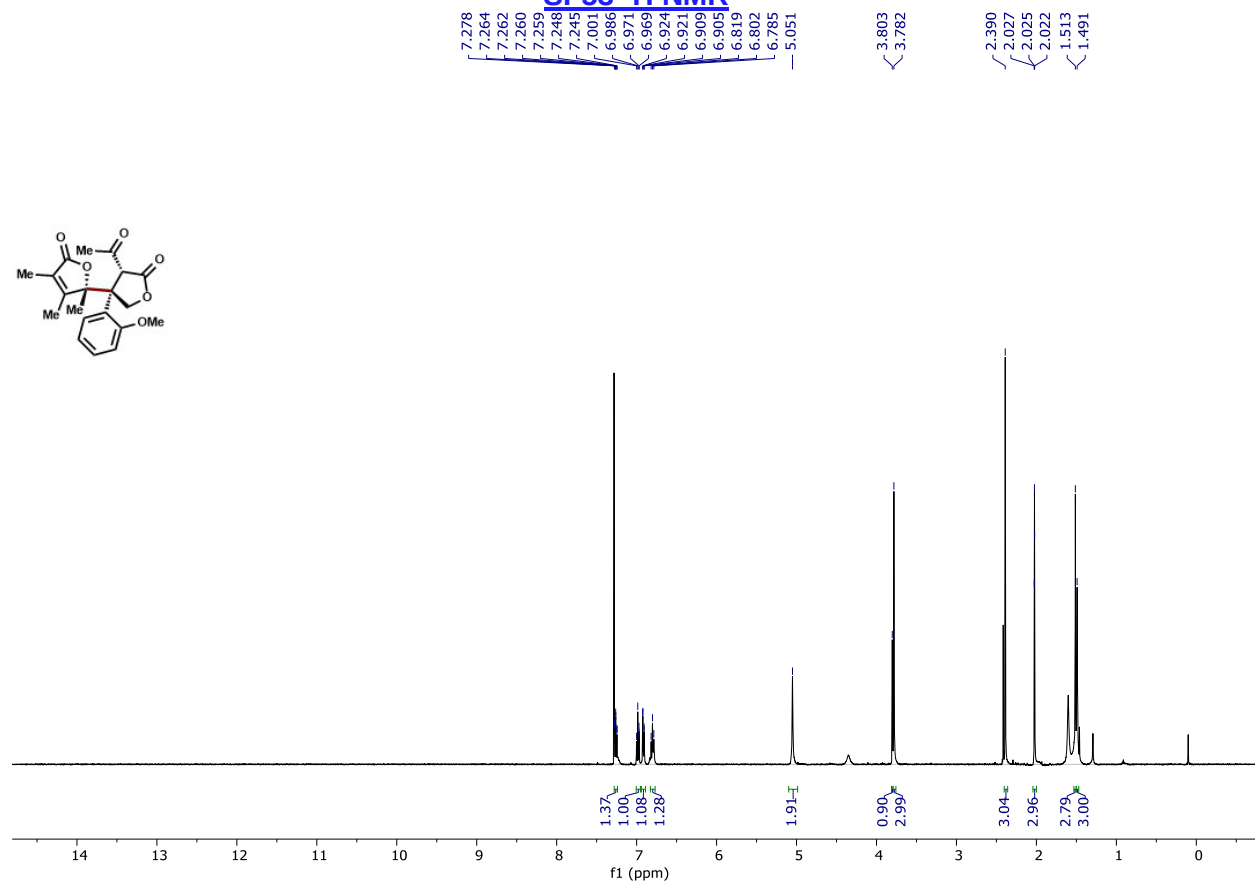
d.r. calculation:

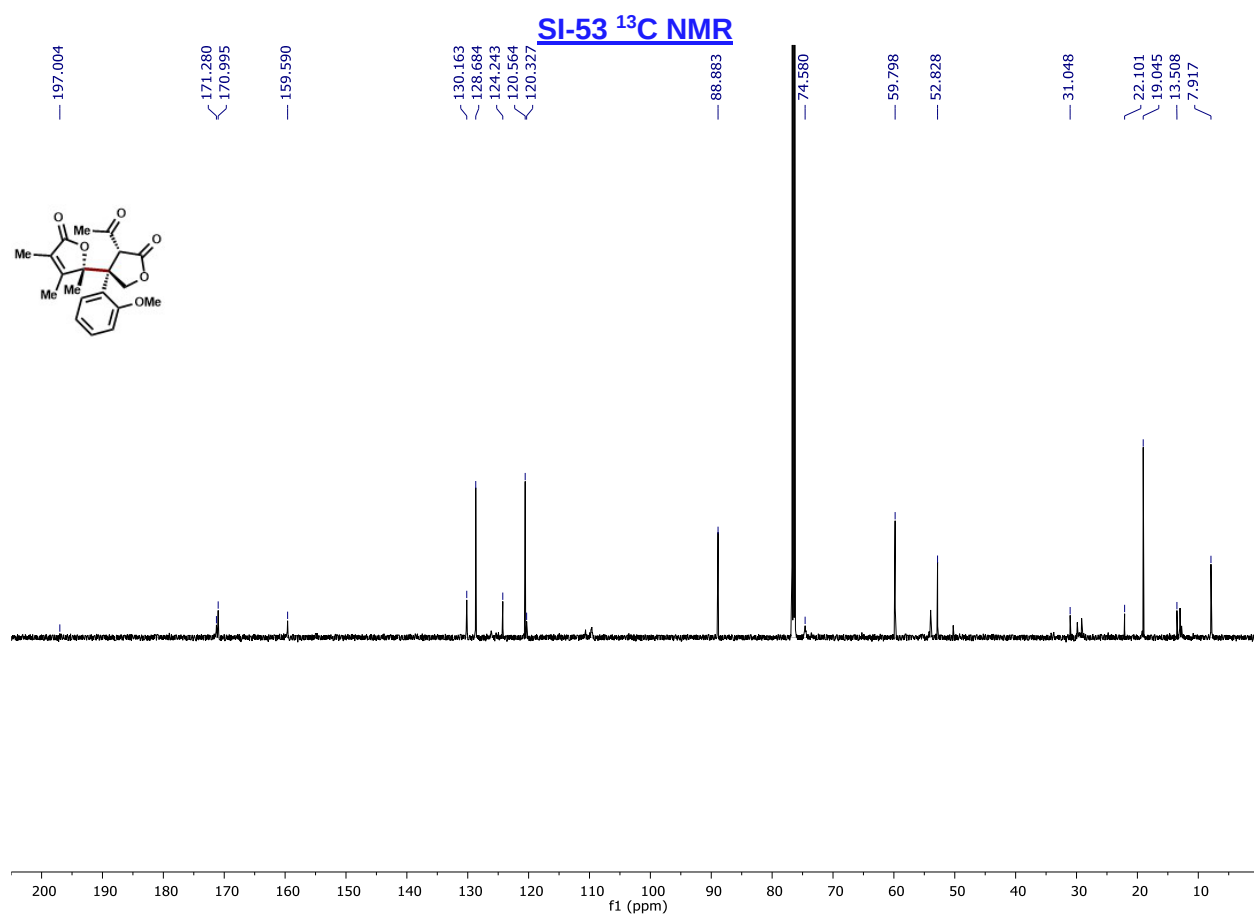
$$(A+B) / (A+B+C+D) = 1.17 / 1.38 = 85 : 15$$



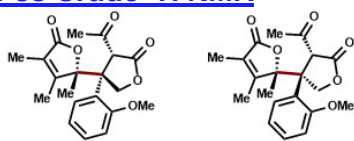
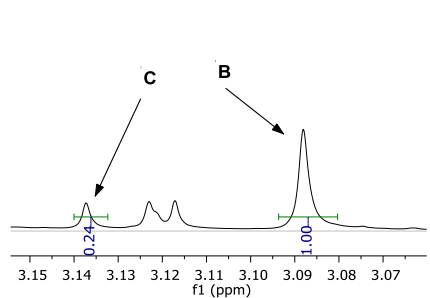


SI-53 ¹H NMR





SI-53 Crude ¹H NMR



Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**

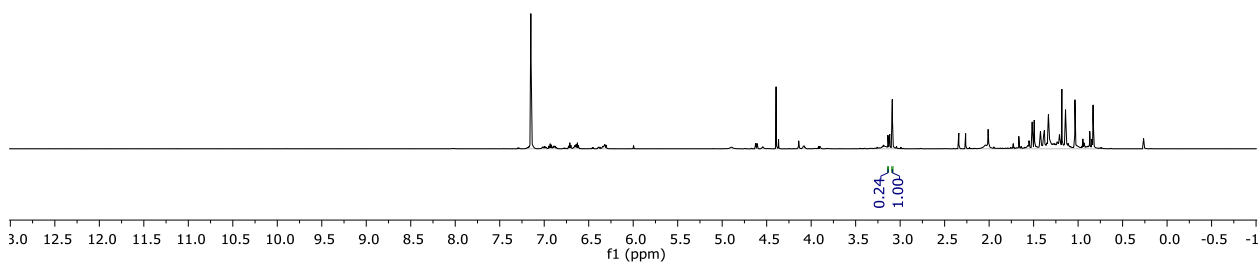
Butenolide dimer, major diastereomer, keto tautomer: **B**

Butenolide dimer, minor diastereomer, keto tautomer: **C**

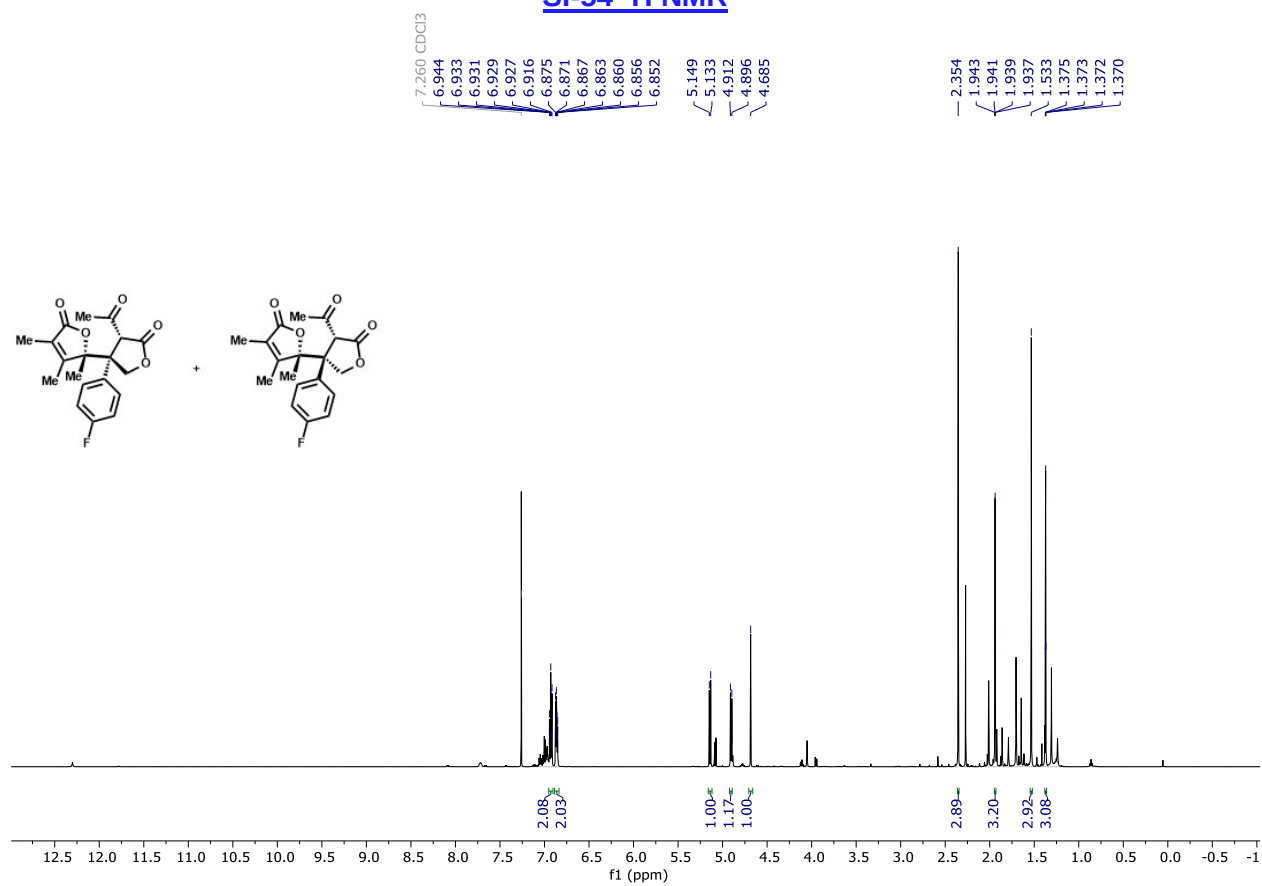
Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

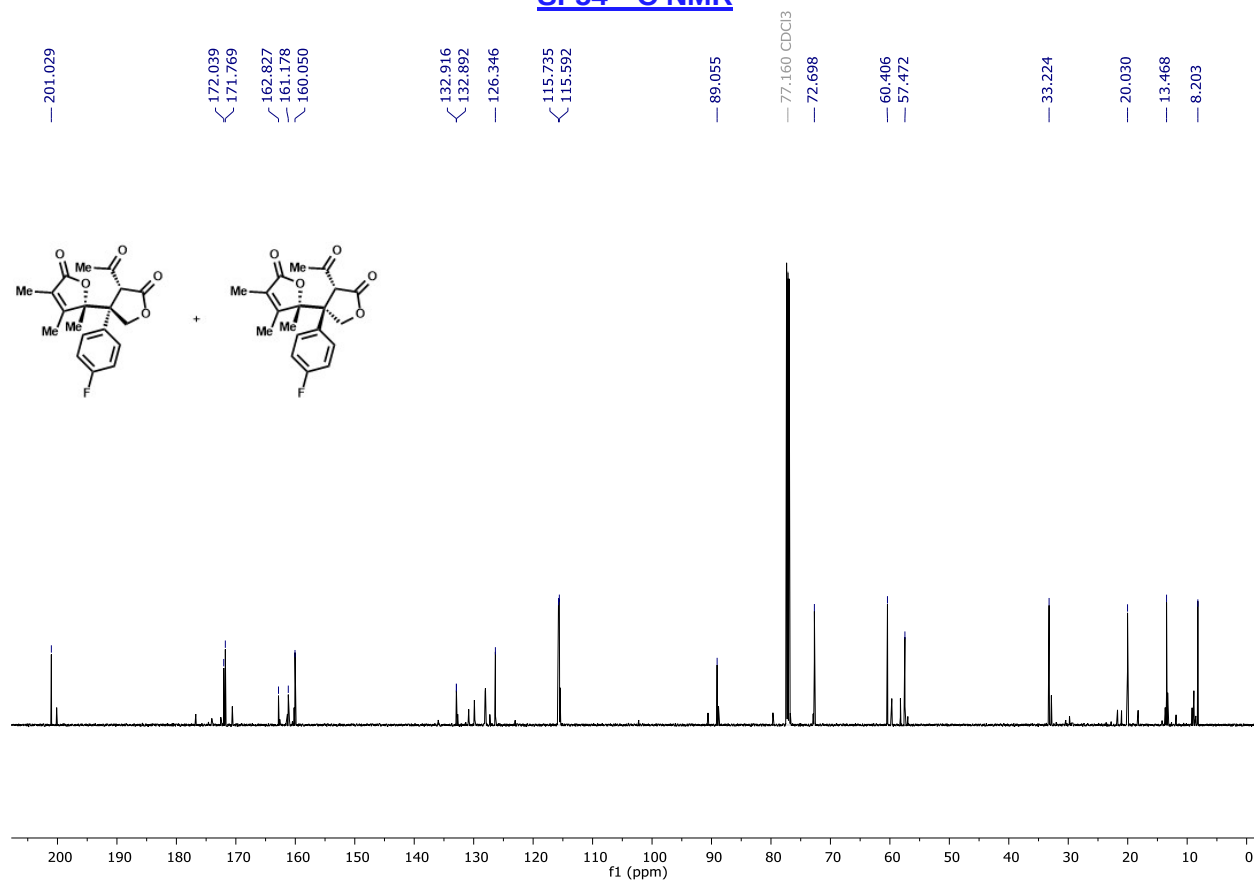
$$(A+B) / (A+B+C+D) = 1.00 / 1.24 = 81 : 19$$



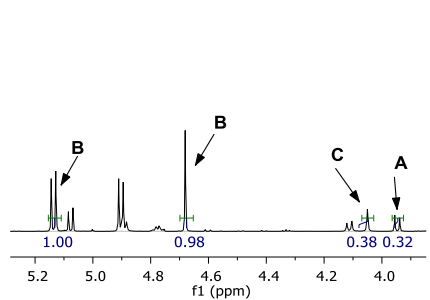
SI-54 ¹H NMR



SI-54 ¹³C NMR



SI-54 Crude ¹H NMR



Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**

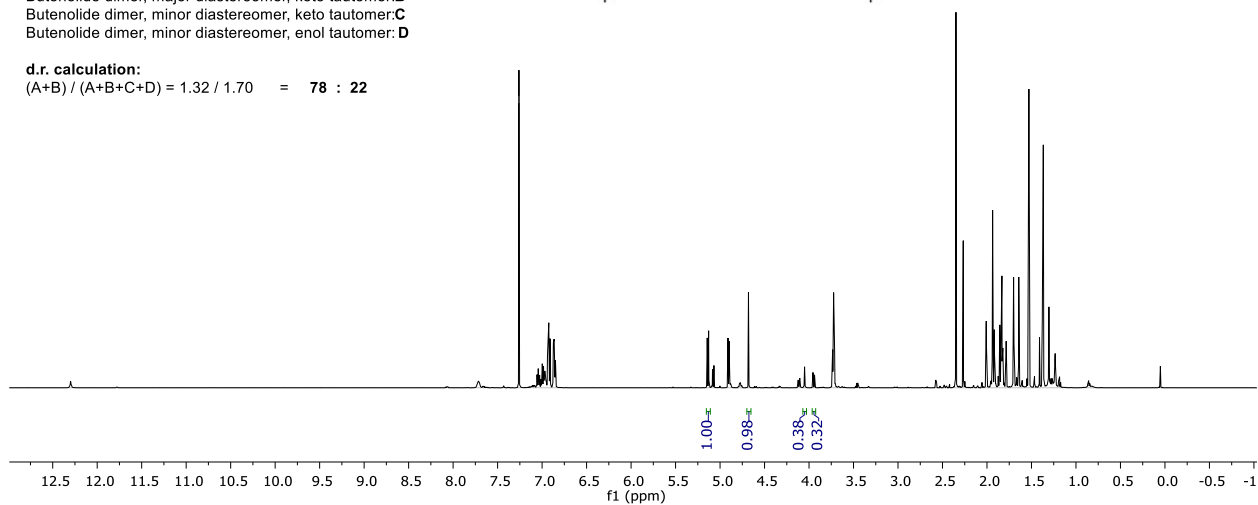
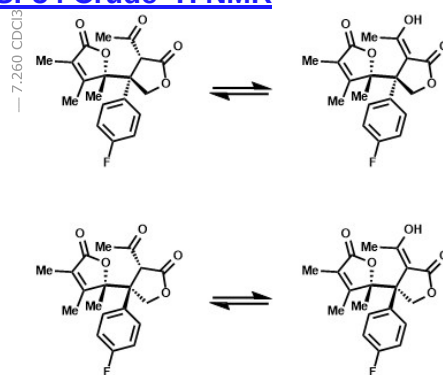
Butenolide dimer, major diastereomer, keto tautomer: **B**

Butenolide dimer, minor diastereomer, keto tautomer: **C**

Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

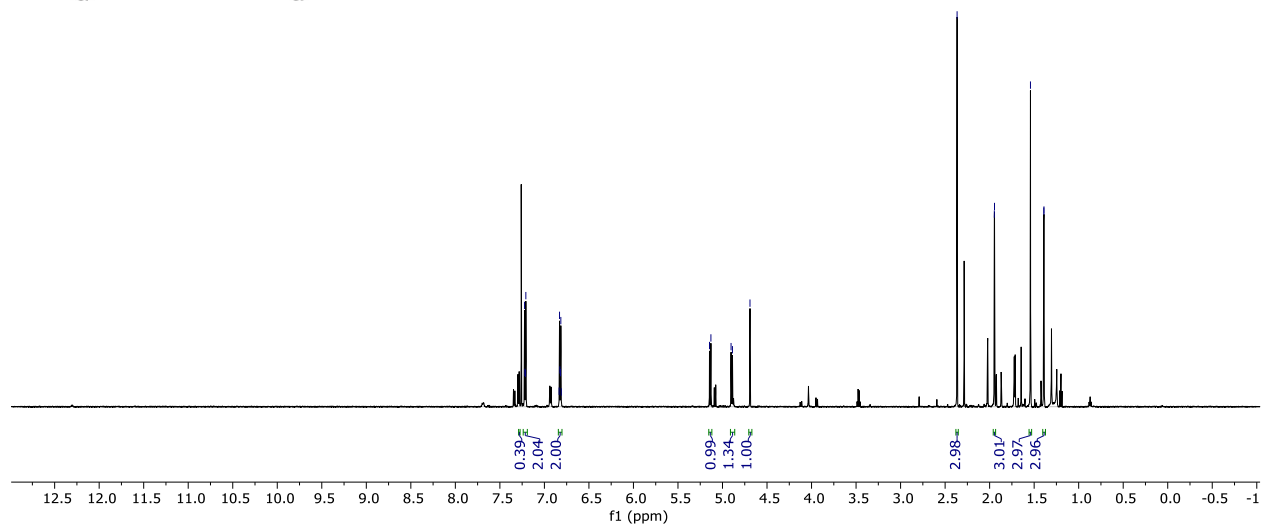
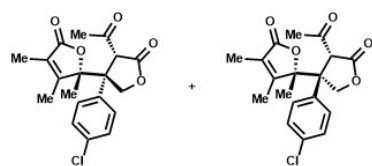
$$(A+B) / (A+B+C+D) = 1.32 / 1.70 = 78 : 22$$

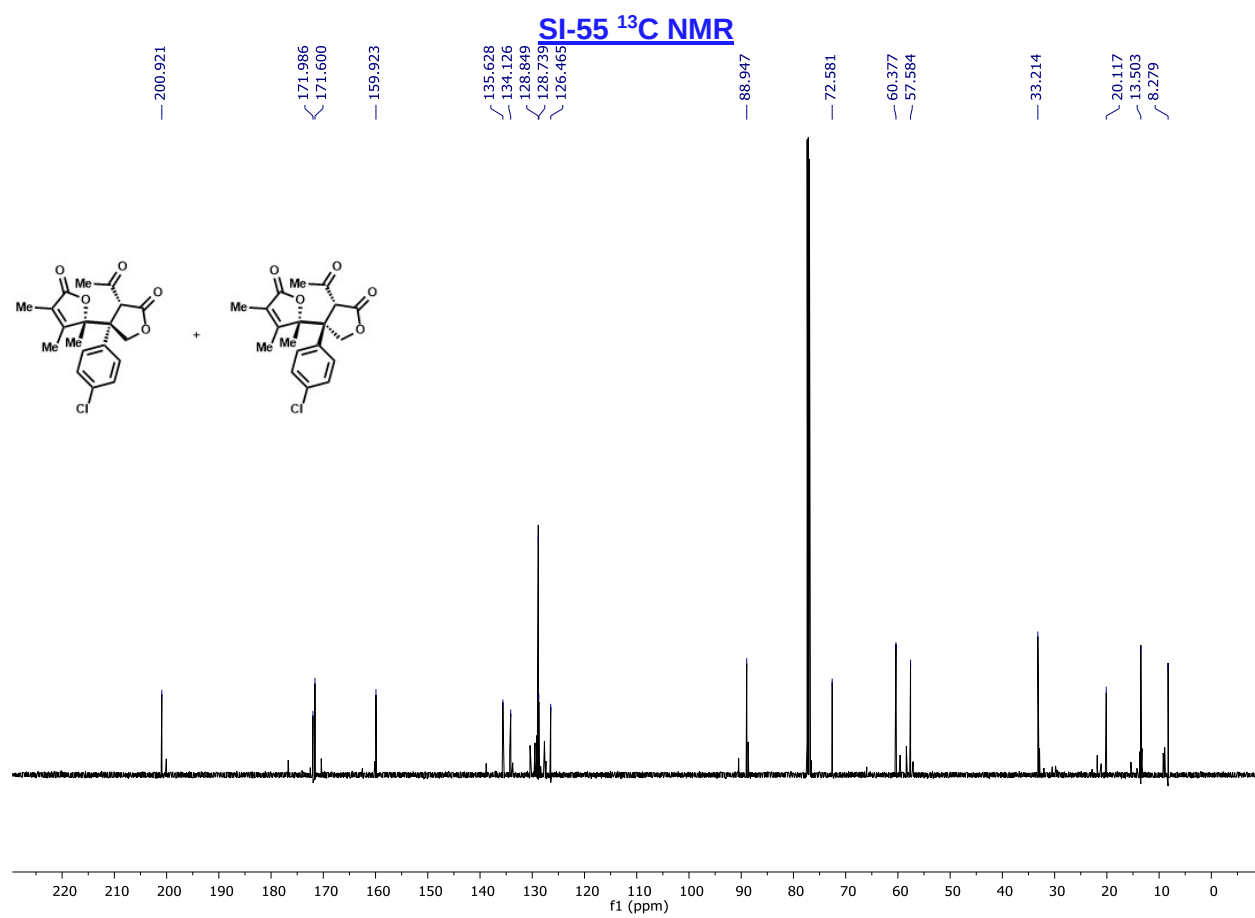


SI-55 ¹H NMR

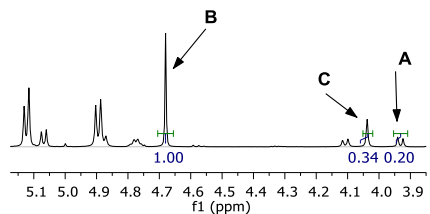
7.223
7.220
7.212
7.208
6.835
6.830
6.827
6.819
6.816
6.811
5.146
5.130
4.904
4.888
4.691

2.365
1.947
1.945
1.541
1.391
1.390





SI-55 Crude ¹H NMR

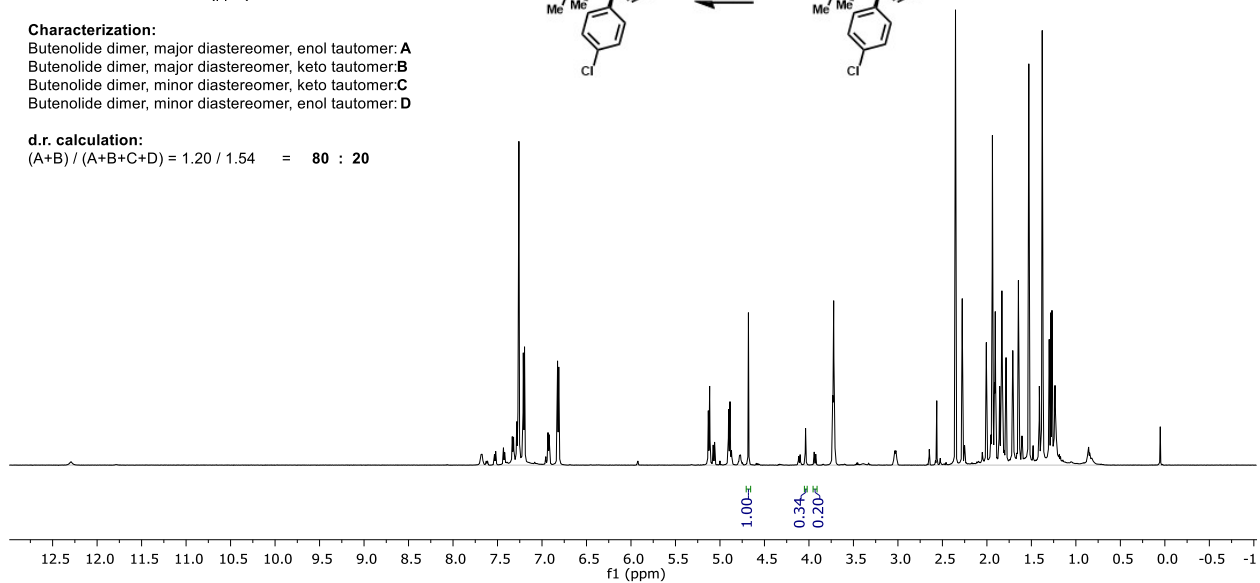
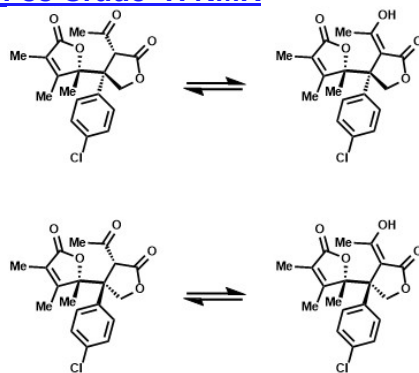


Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

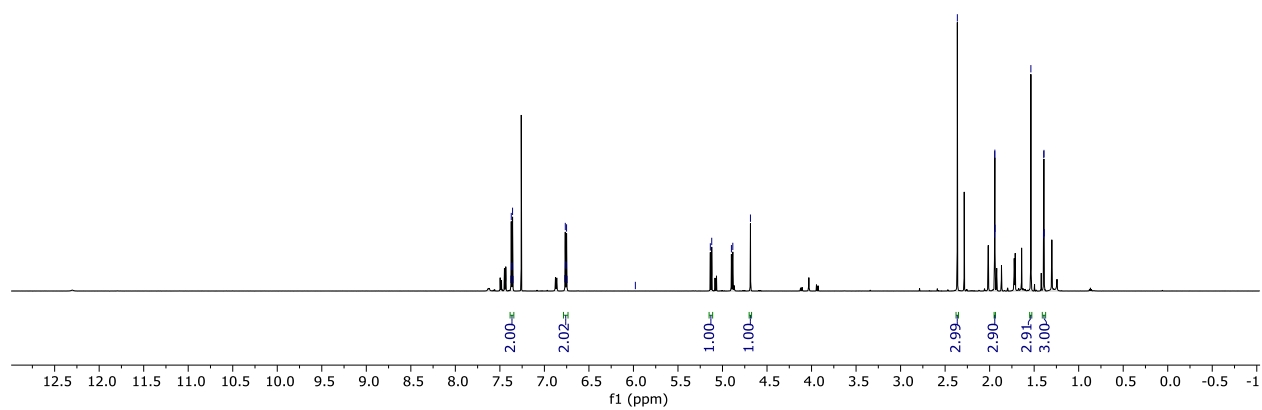
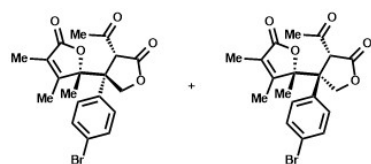
$(A+B) / (A+B+C+D) = 1.20 / 1.54 = 80 : 20$

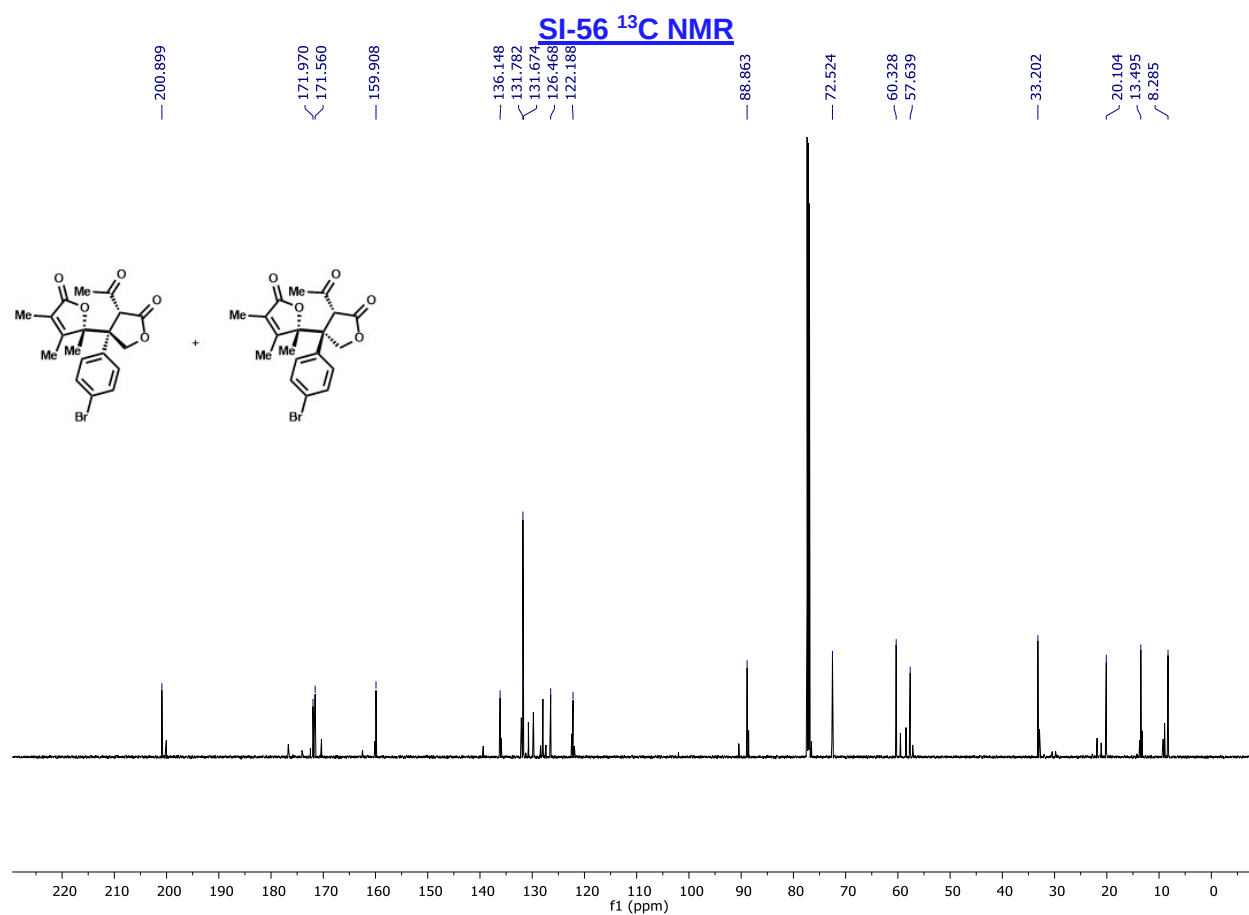


SI-56 ¹H NMR

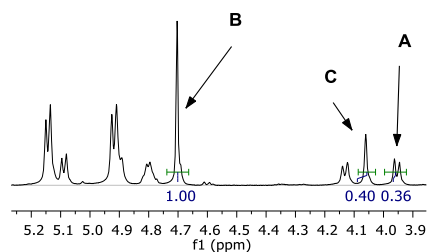
7.376
7.372
7.369
7.361
7.358
7.353
6.770
6.766
6.762
6.755
6.751
6.747
5.979
5.137
5.121
4.900
4.884
4.686

2.363
1.945
1.943
1.941
1.940
1.537
1.394
1.392
1.390
1.388





SI-56 Crude ¹H NMR

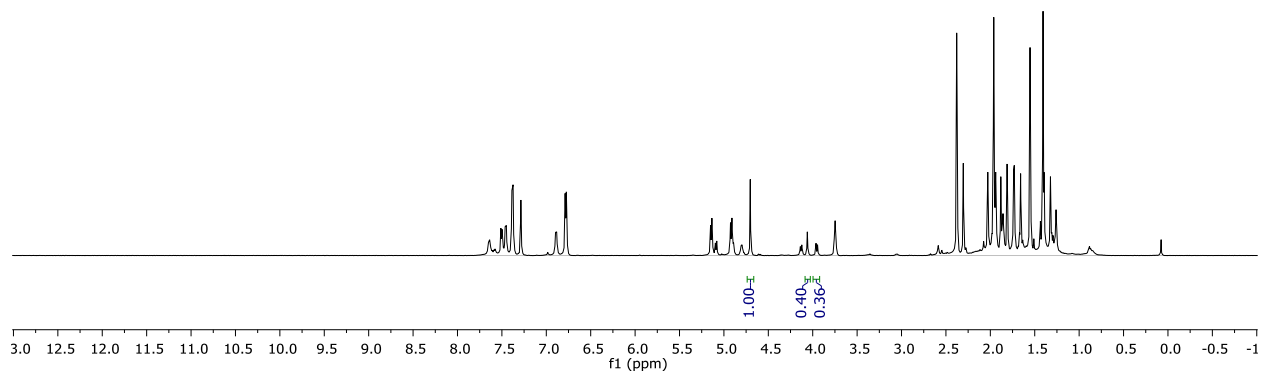
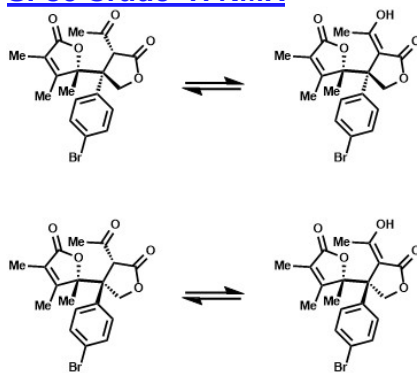


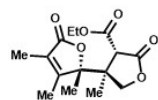
Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

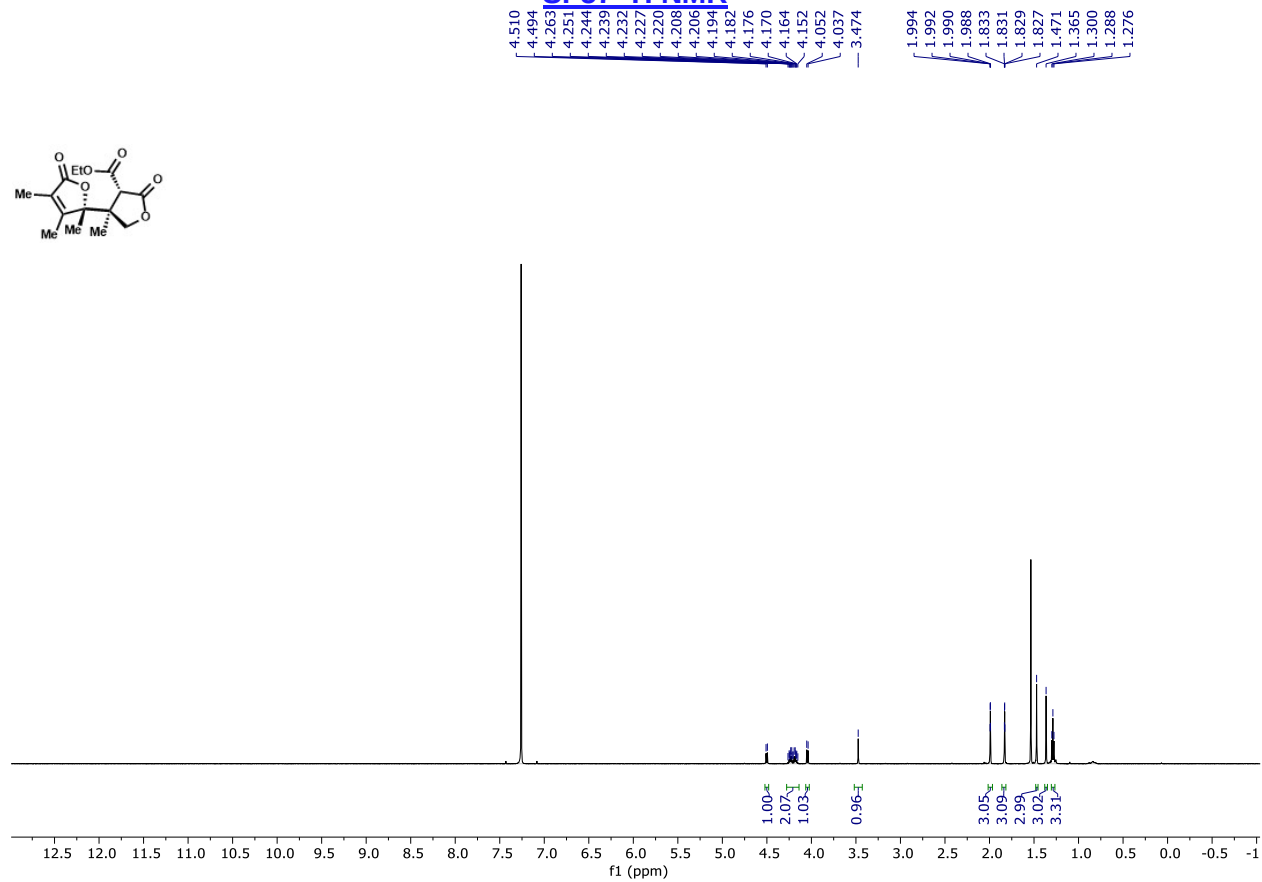
d.r. calculation:

(A+B) / (A+B+C+D) = 1.36 / 1.76 = 77 : 23

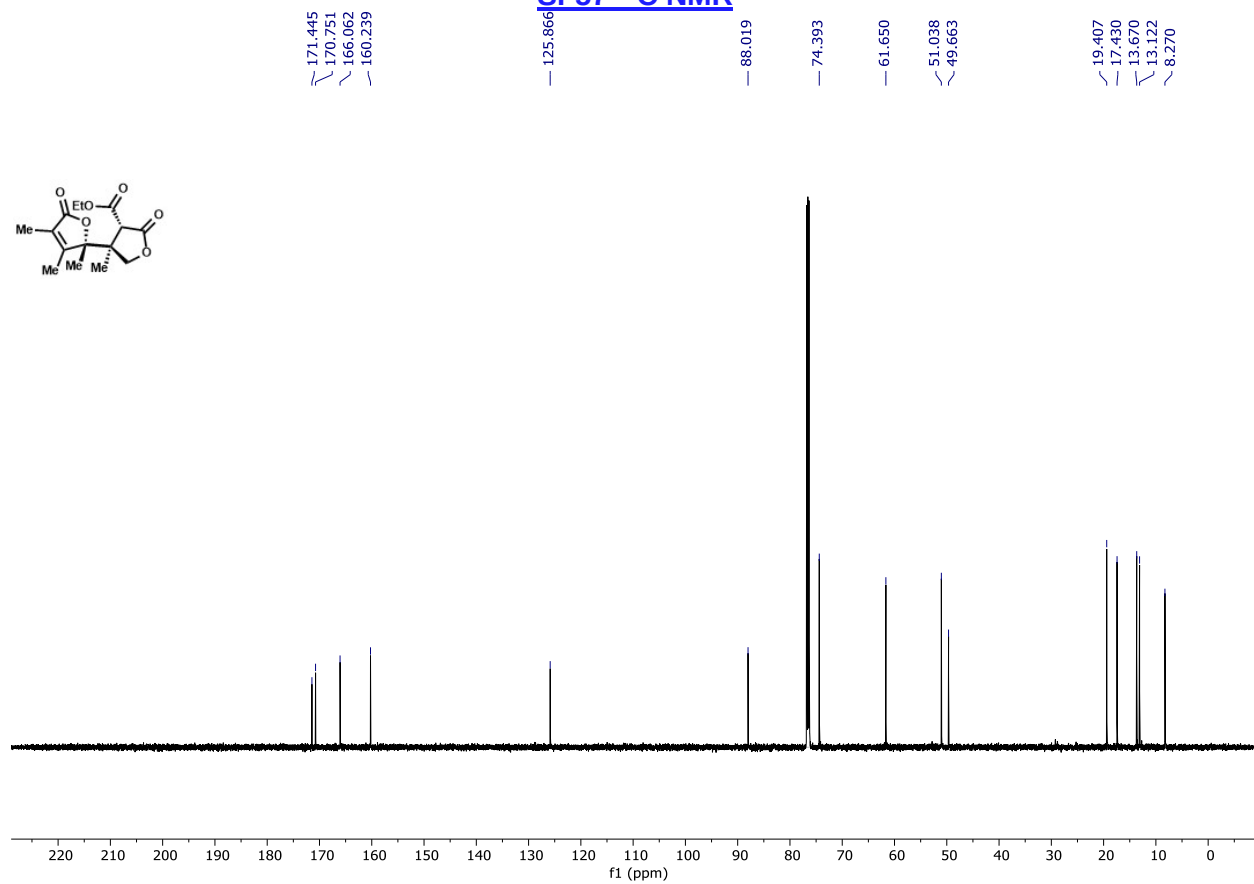




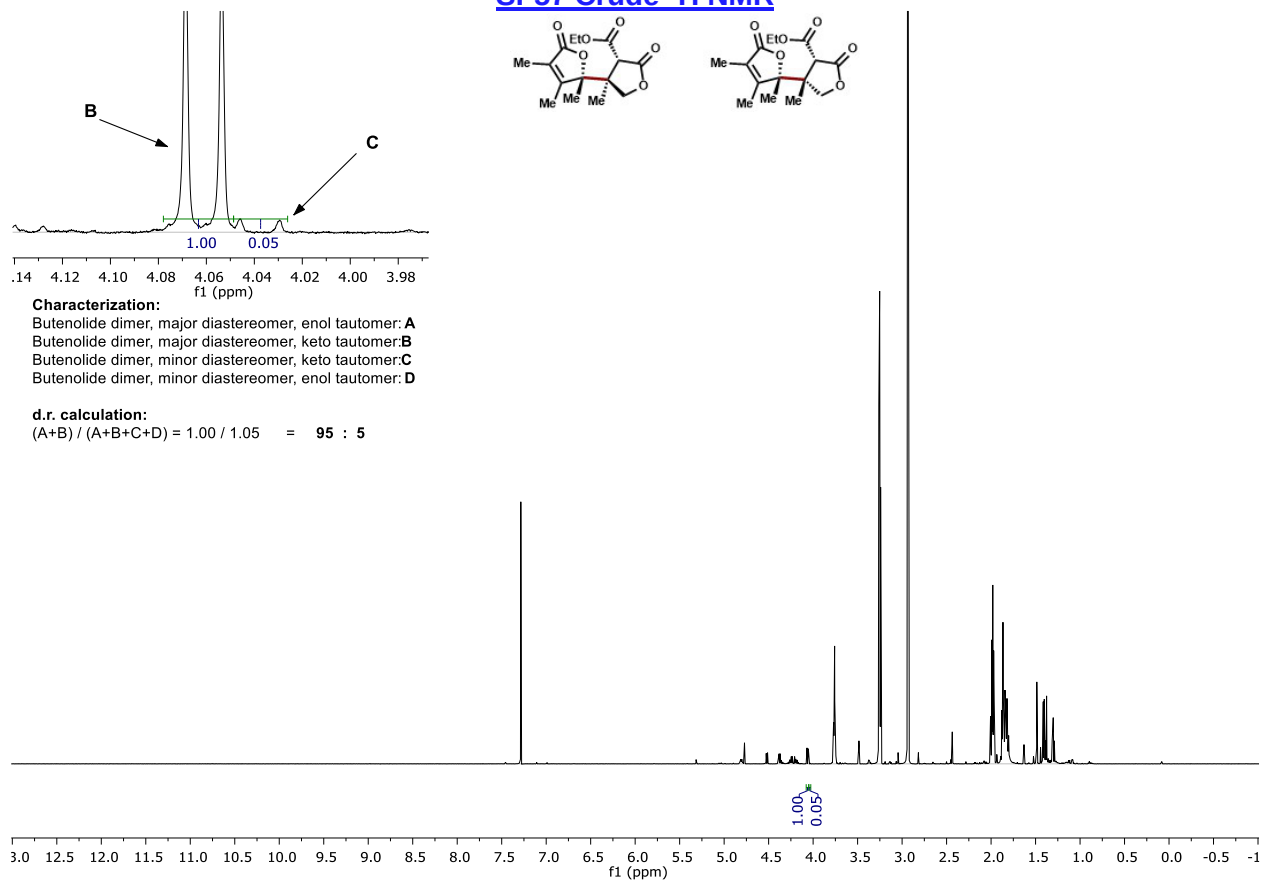
SI-57 ¹H NMR



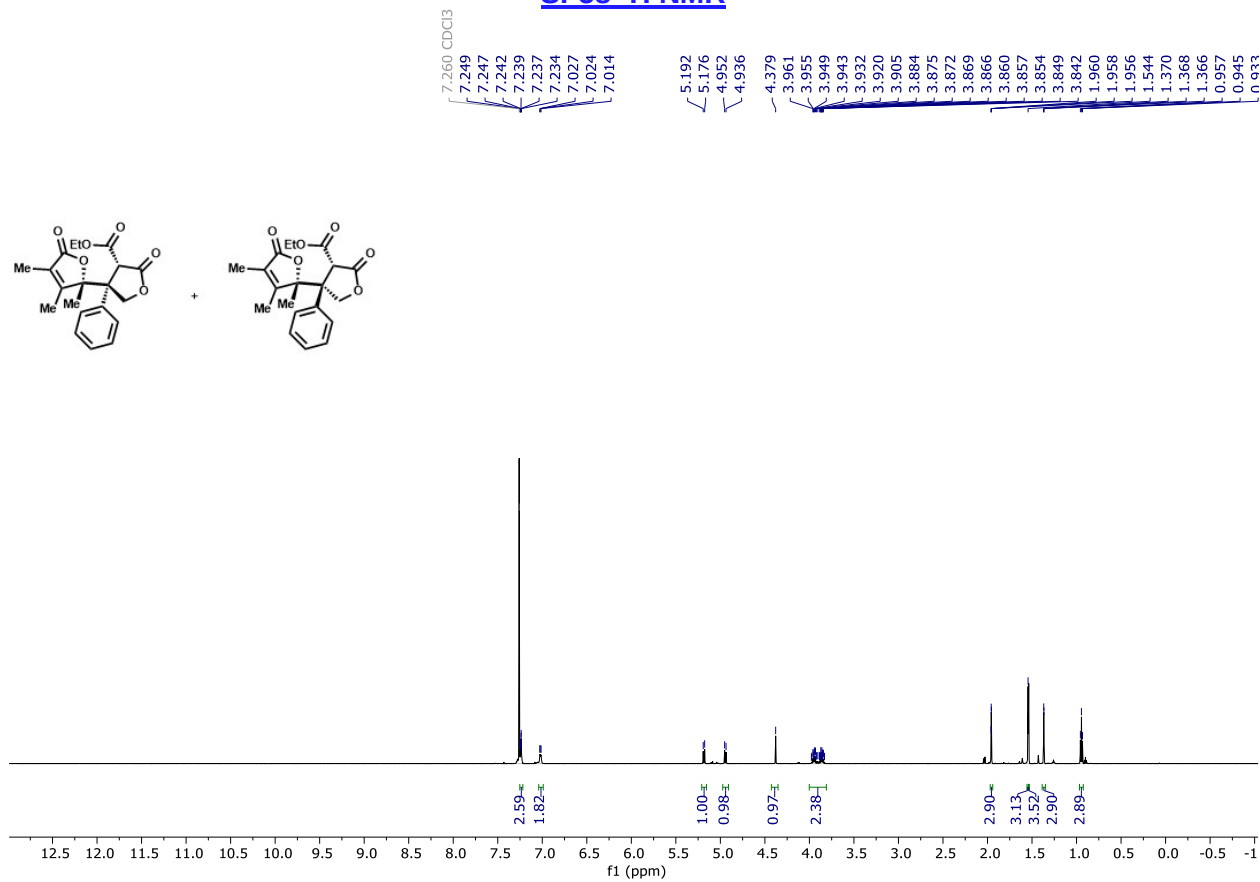
SI-57 ¹³C NMR



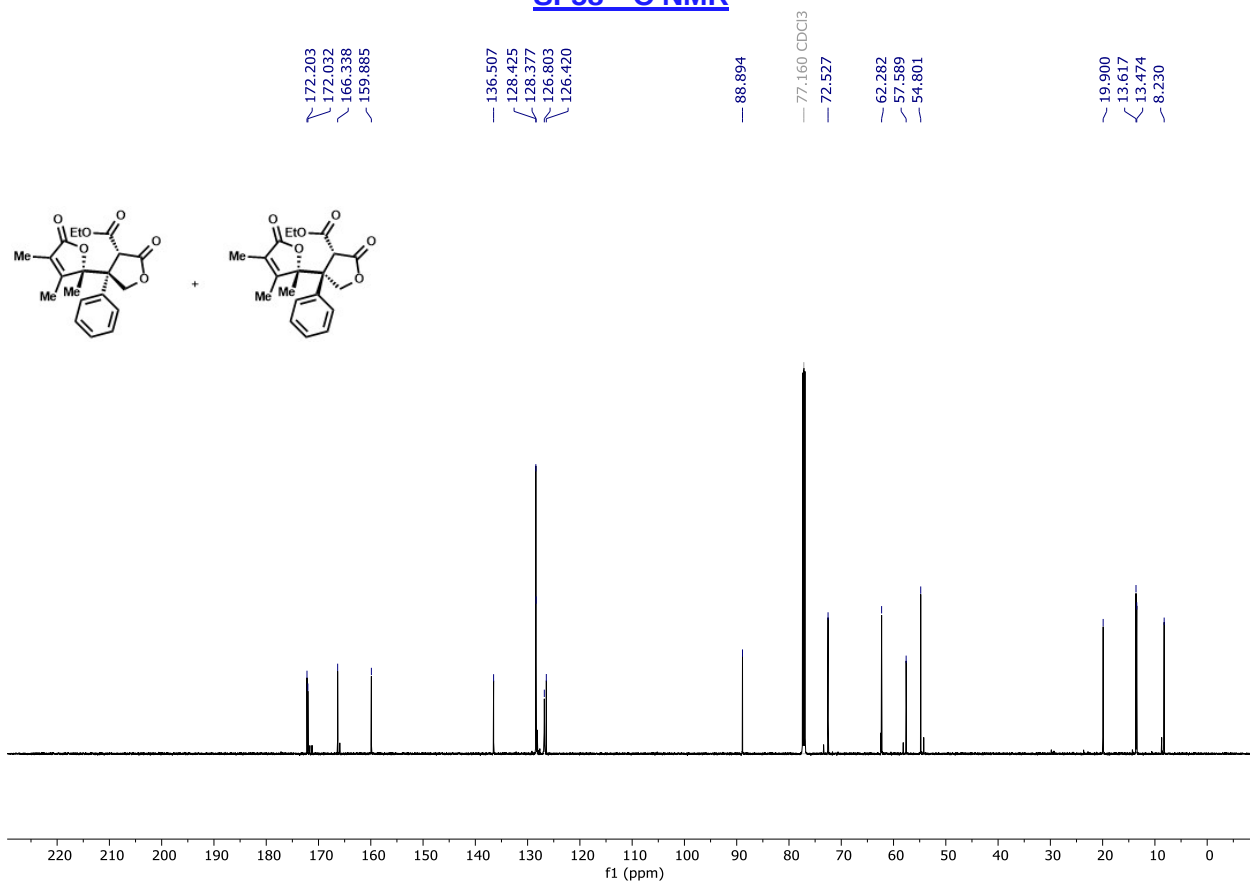
SI-57 Crude ¹H NMR



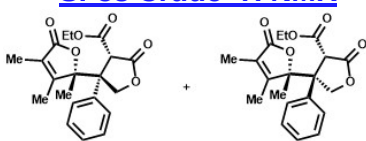
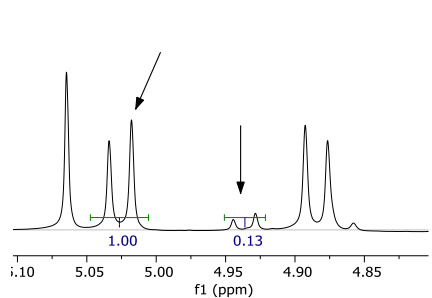
SI-58 ¹H NMR



SI-58 ¹³C NMR



SI-58 Crude ¹H NMR



Characterization:

Butenolide dimer, major diastereomer, enol tautomer:

A

Butenolide dimer, major diastereomer, keto tautomer:

B

Butenolide dimer, minor diastereomer, keto tautomer:

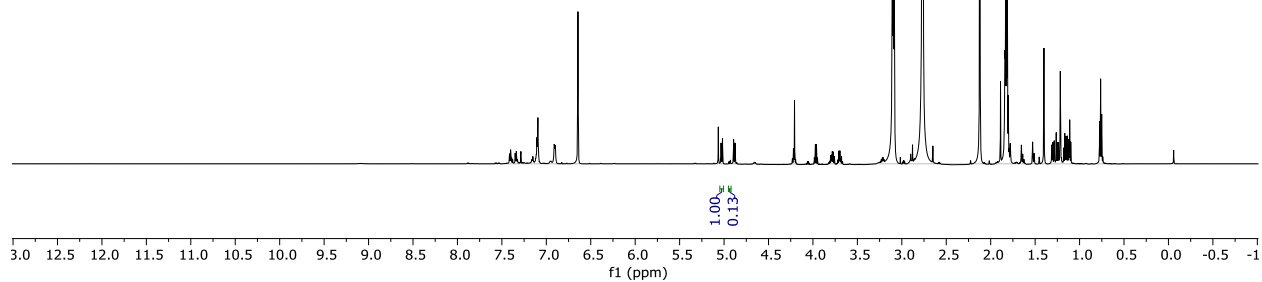
C

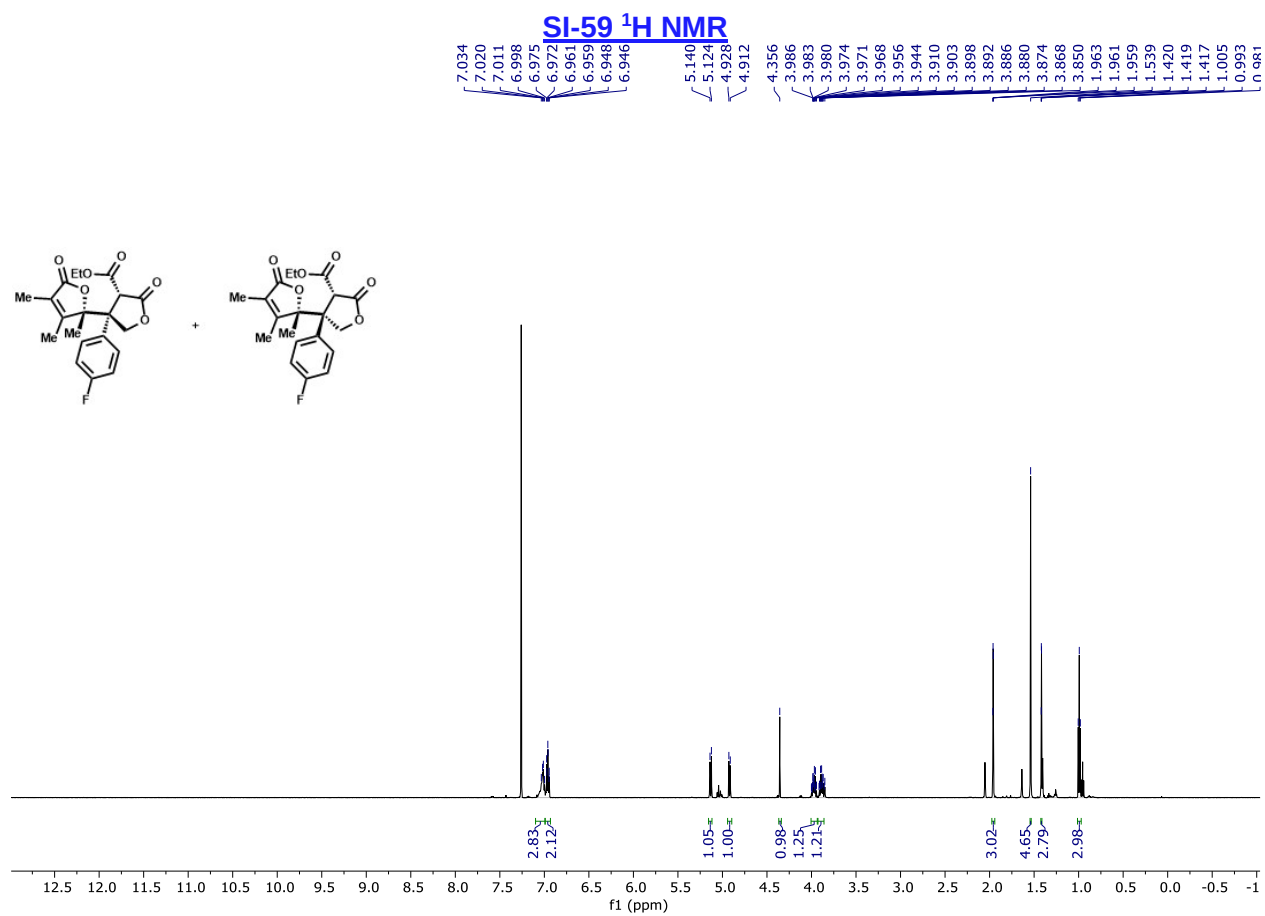
Butenolide dimer, minor diastereomer, enol tautomer:

D

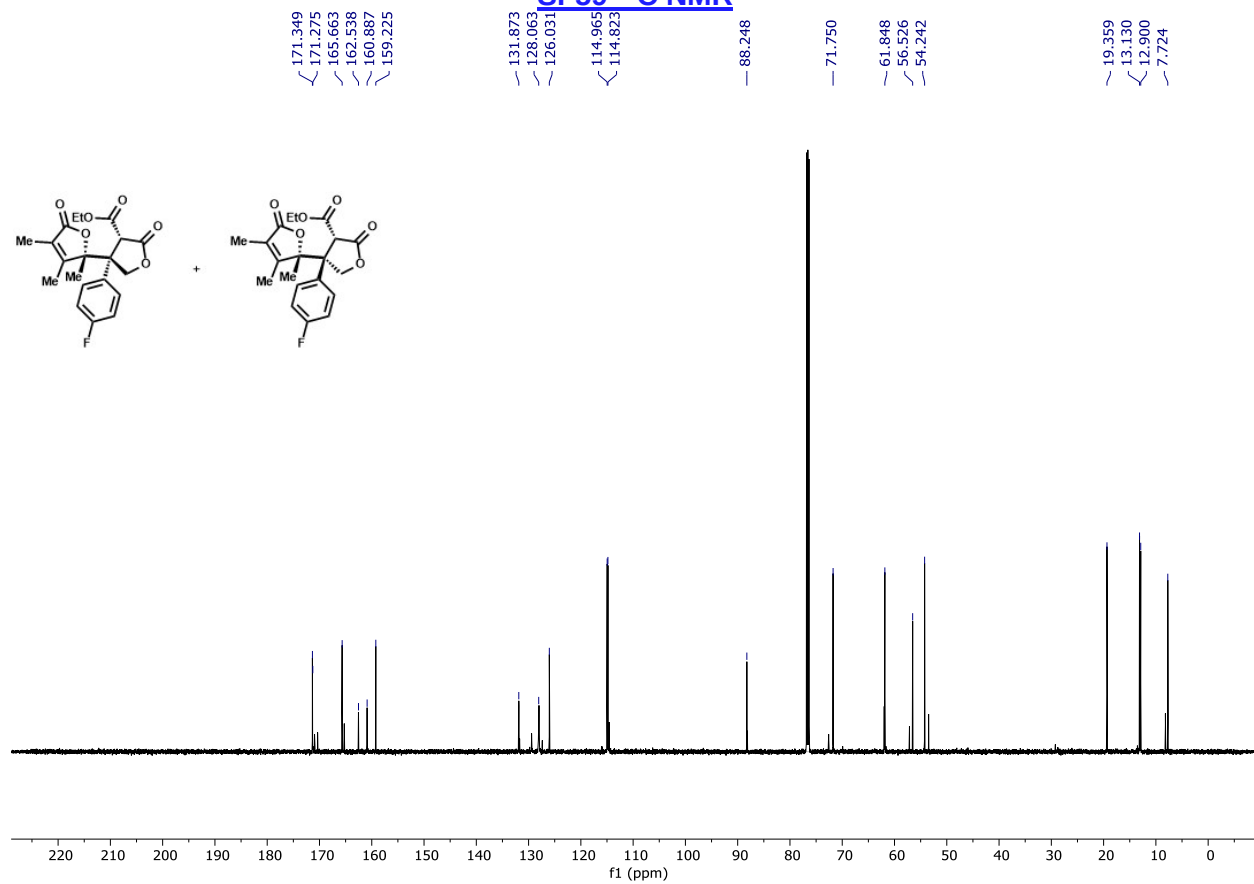
d.r. calculation:

$$(A+B) / (A+B+C+D) = 1.00 / 1.13 = 88 : 12$$

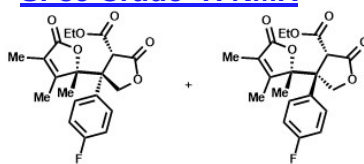
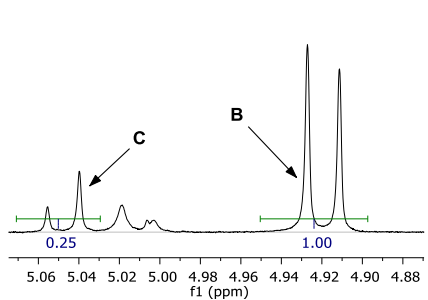




SI-59 ¹³C NMR



SI-59 Crude ¹H NMR

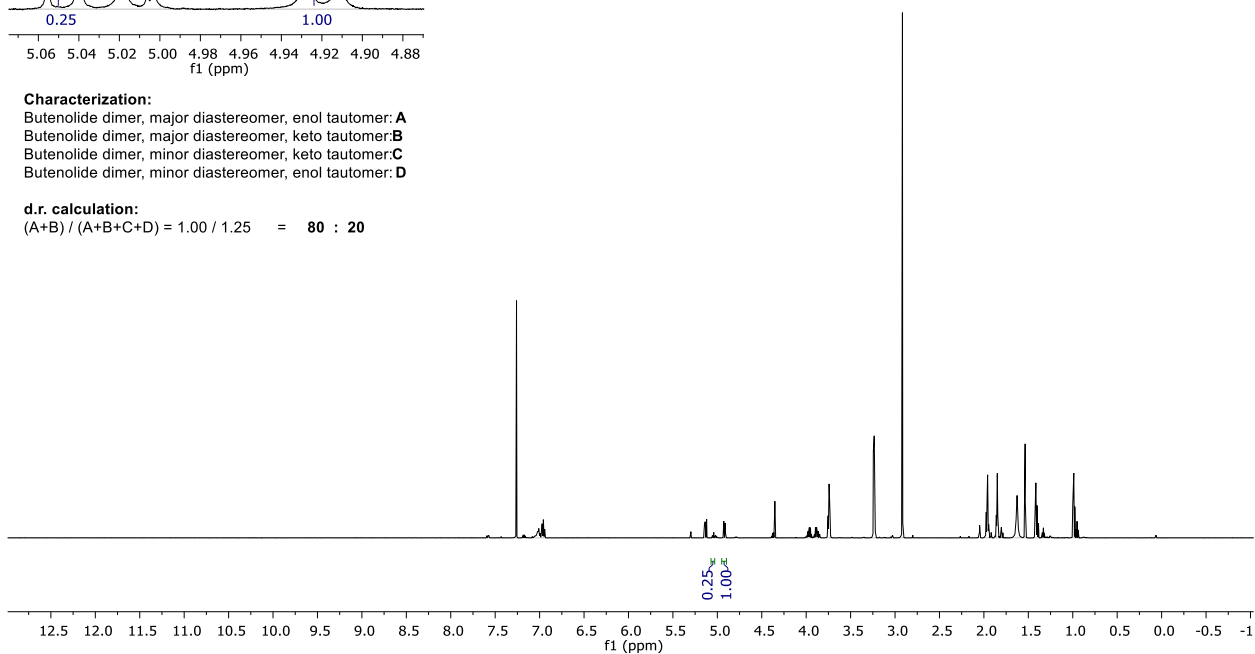


Characterization:

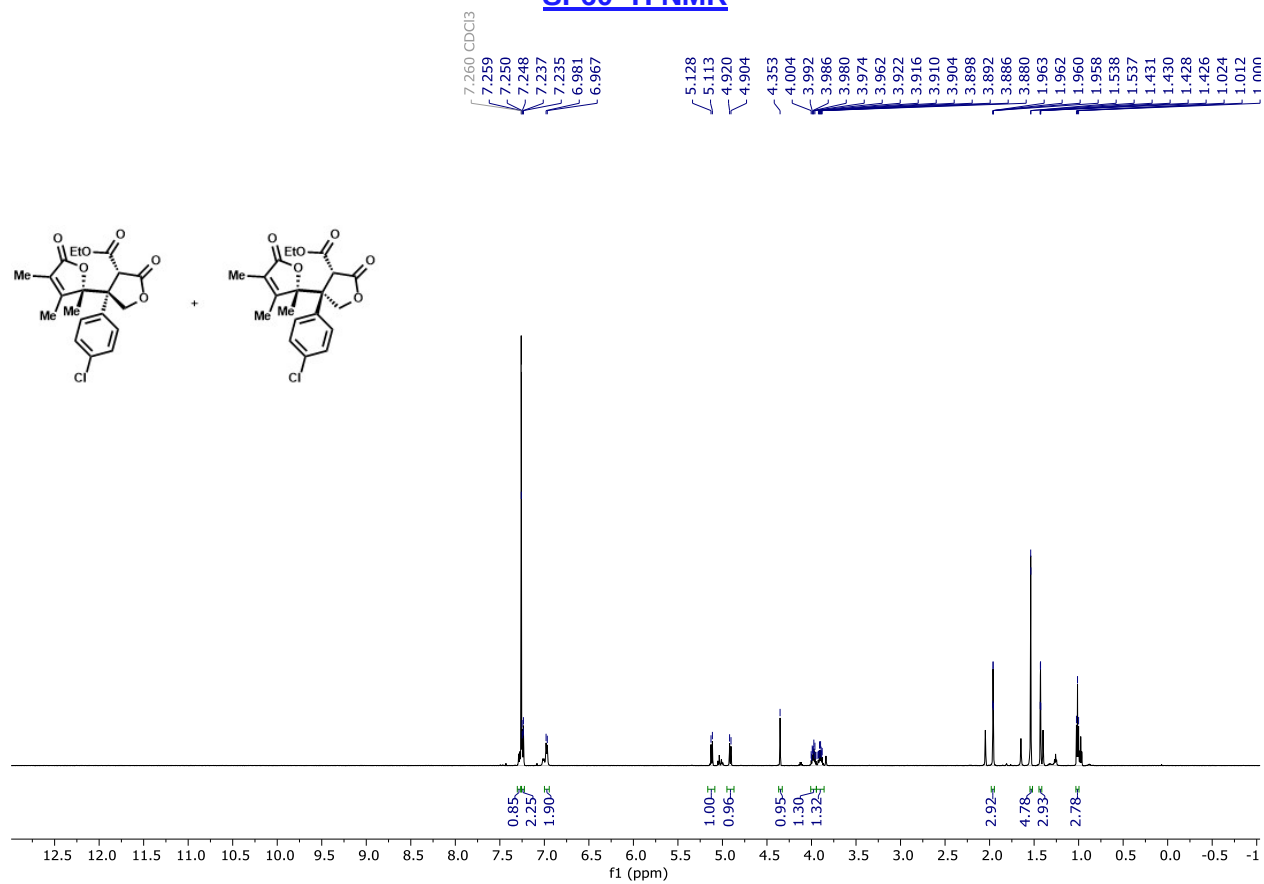
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

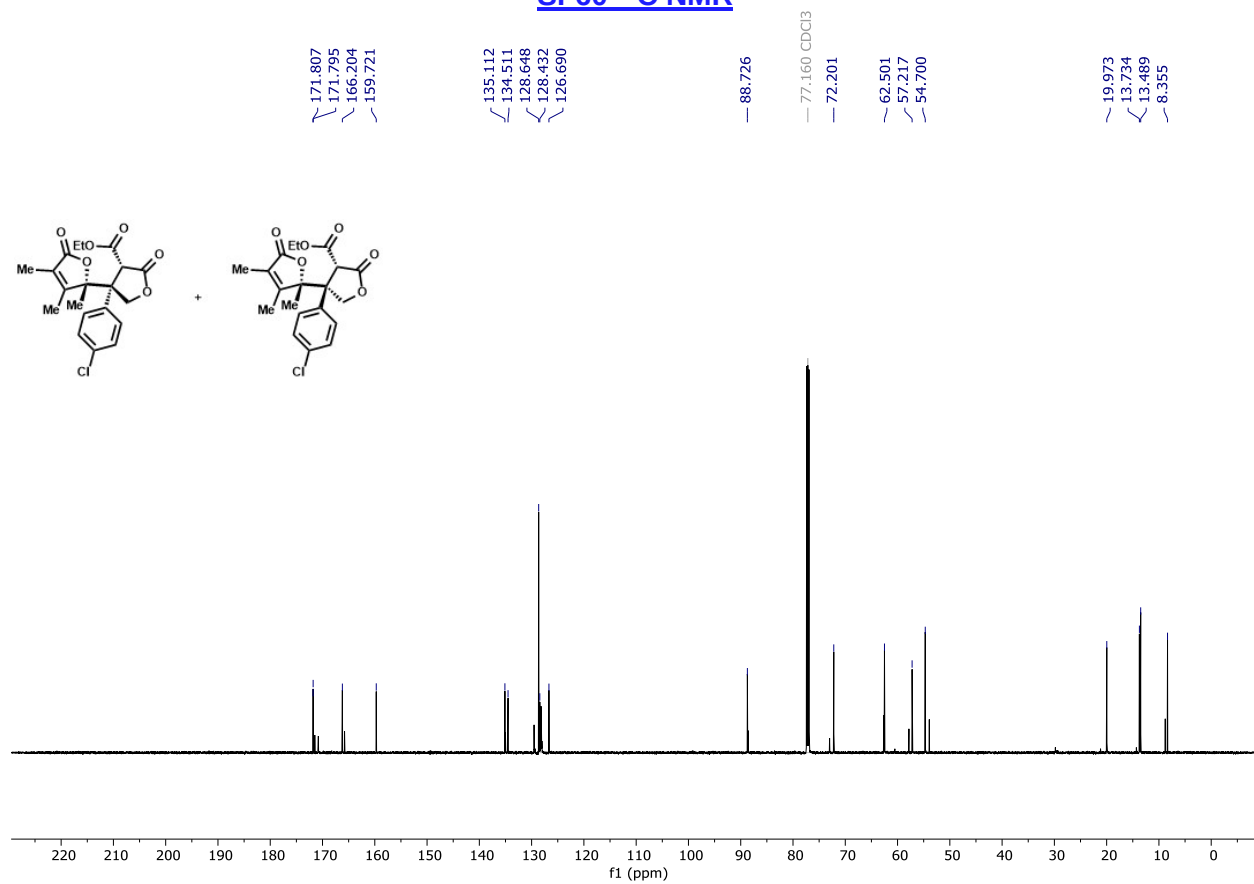
$$(A+B) / (A+B+C+D) = 1.00 / 1.25 = 80 : 20$$



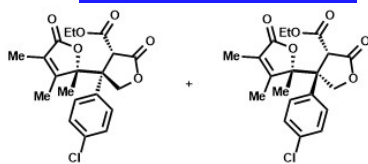
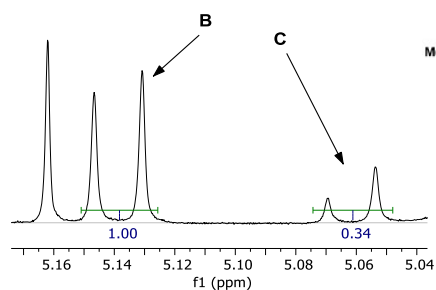
SI-60 ¹H NMR



SI-60 ¹³C NMR



SI-60 Crude ¹H NMR



Characterization:

Butenolide dimer, major diastereomer, enol tautomer:

A

Butenolide dimer, major diastereomer, keto tautomer:

B

Butenolide dimer, minor diastereomer, keto tautomer:

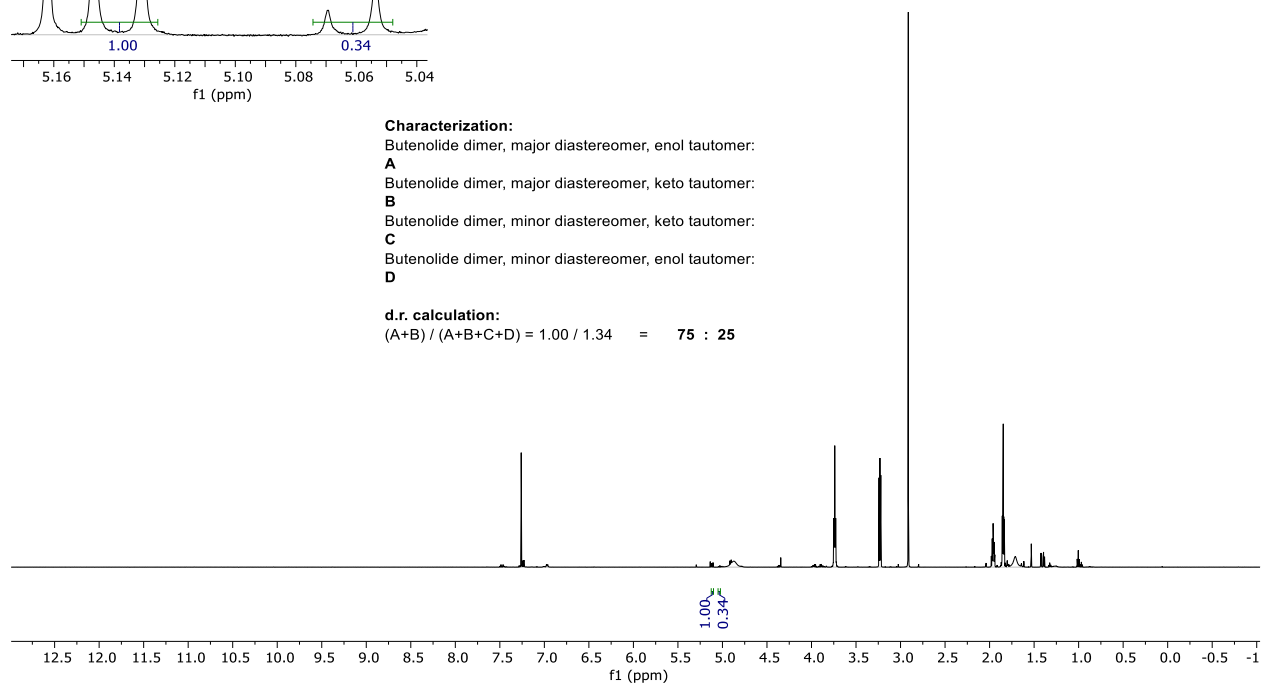
C

Butenolide dimer, minor diastereomer, enol tautomer:

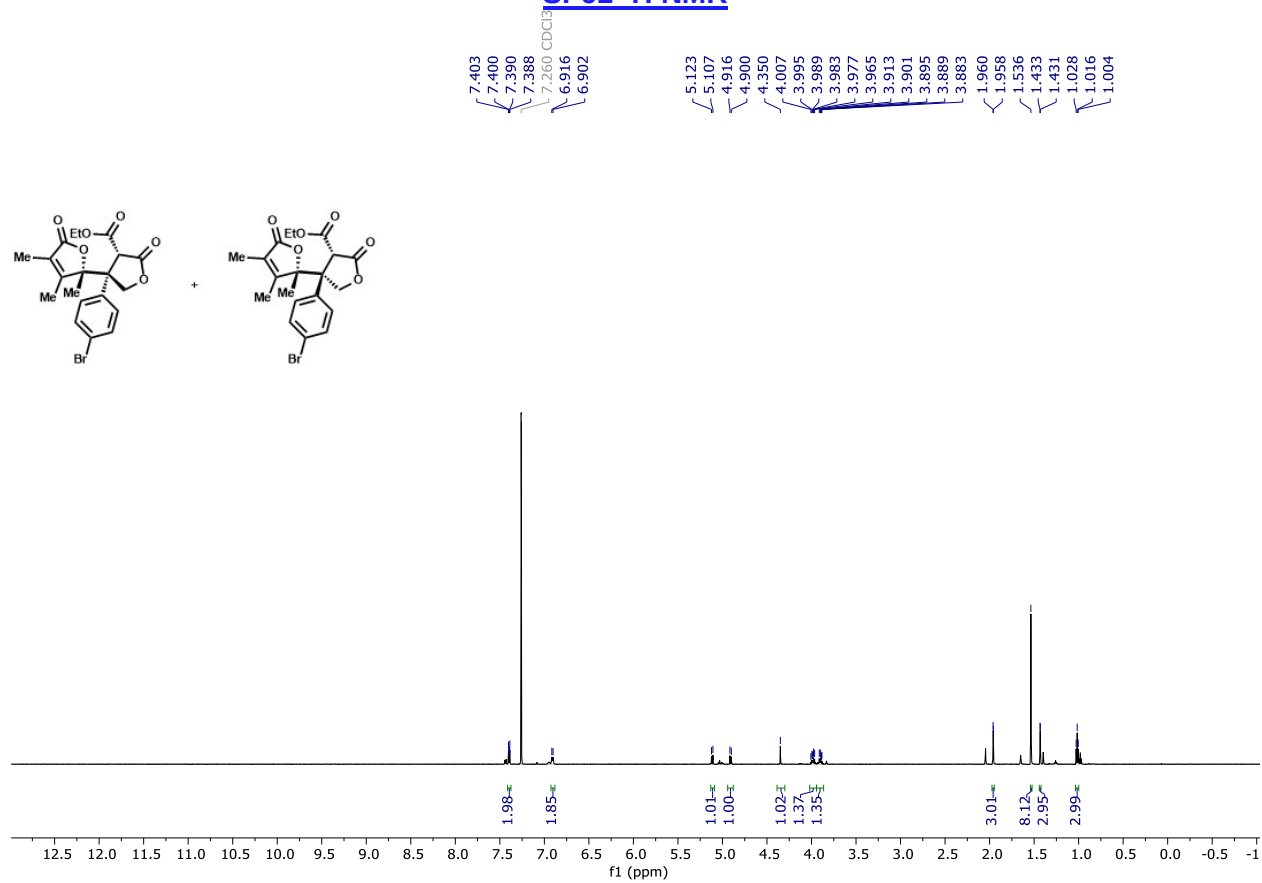
D

d.r. calculation:

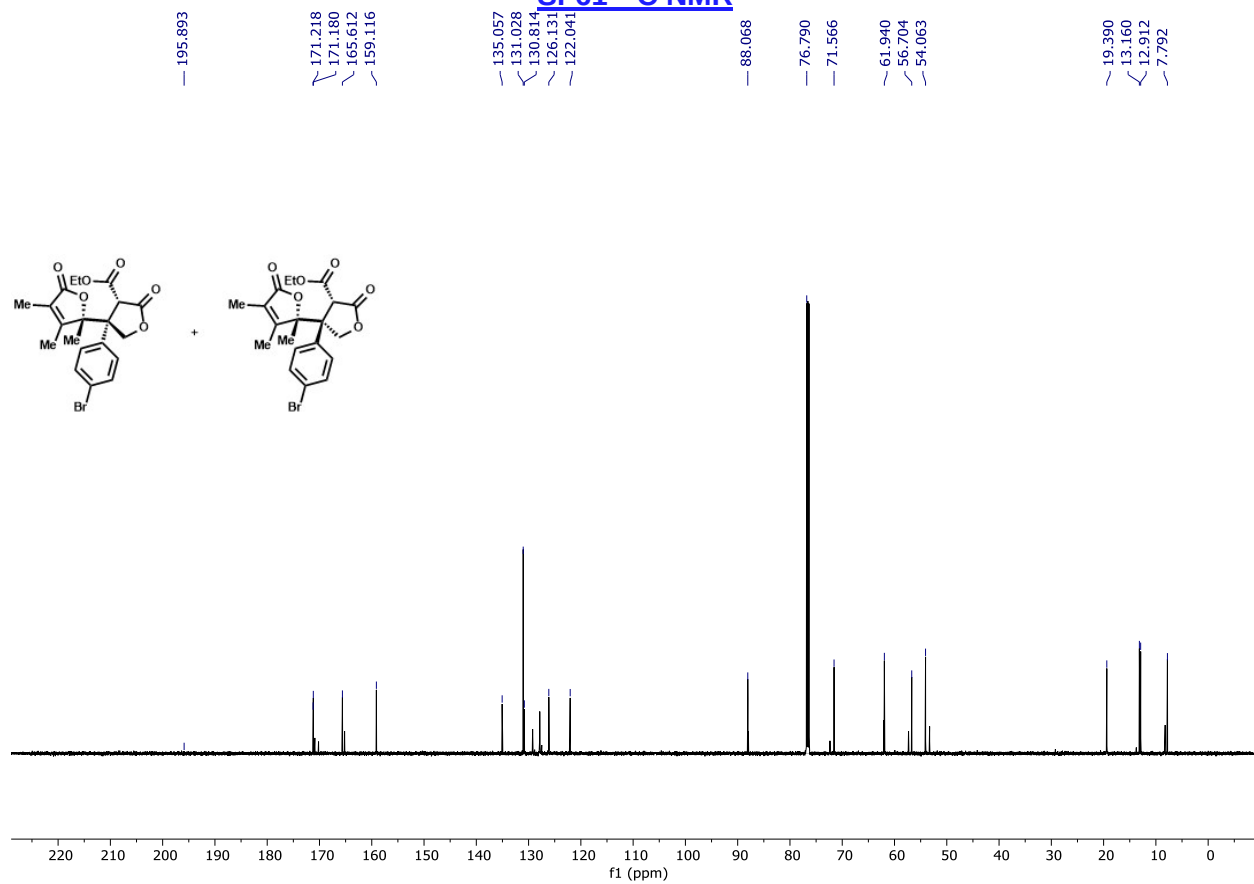
$$(A+B) / (A+B+C+D) = 1.00 / 1.34 = 75 : 25$$



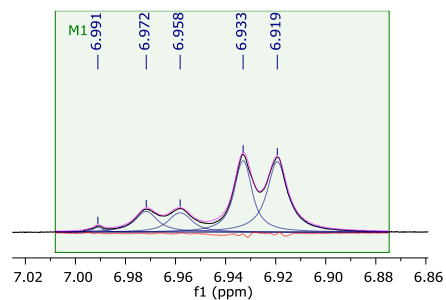
SI-61 ¹H NMR



SI-61 ¹³C NMR



SI-61 Crude ¹H NMR



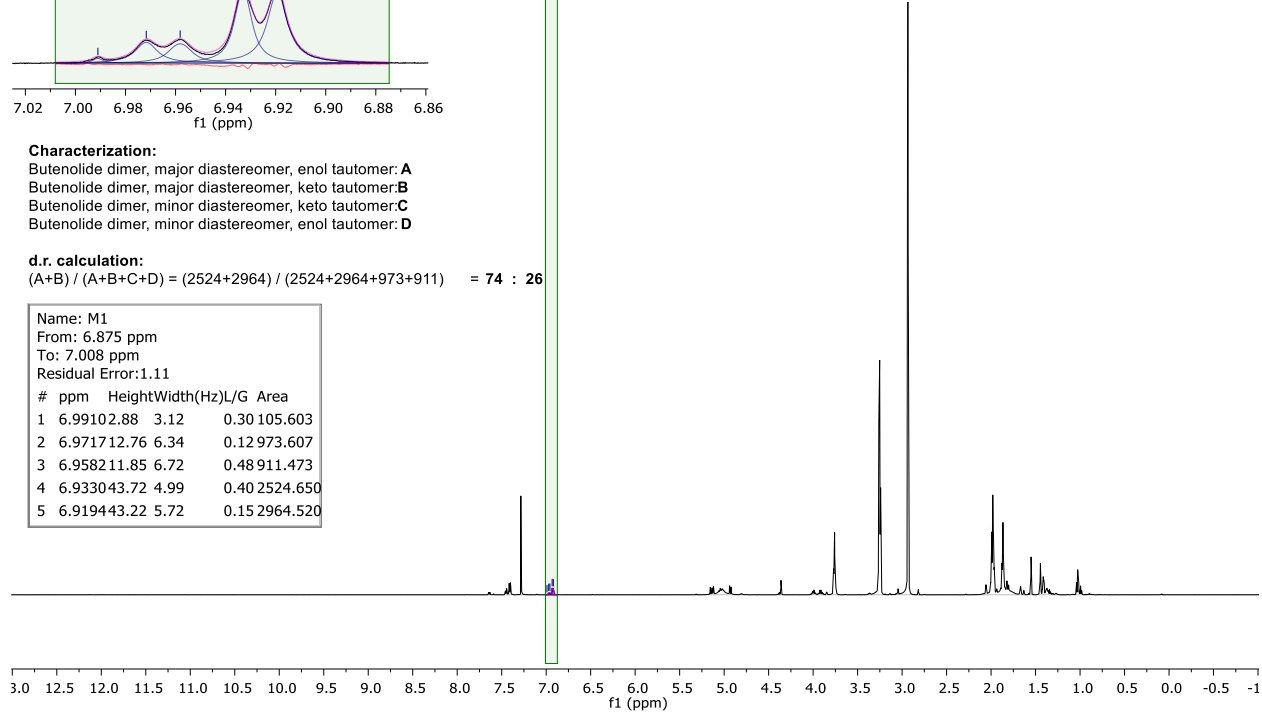
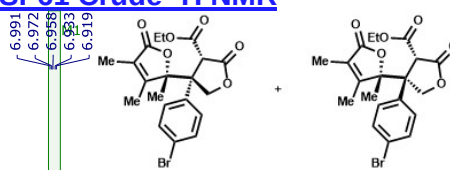
Characterization:

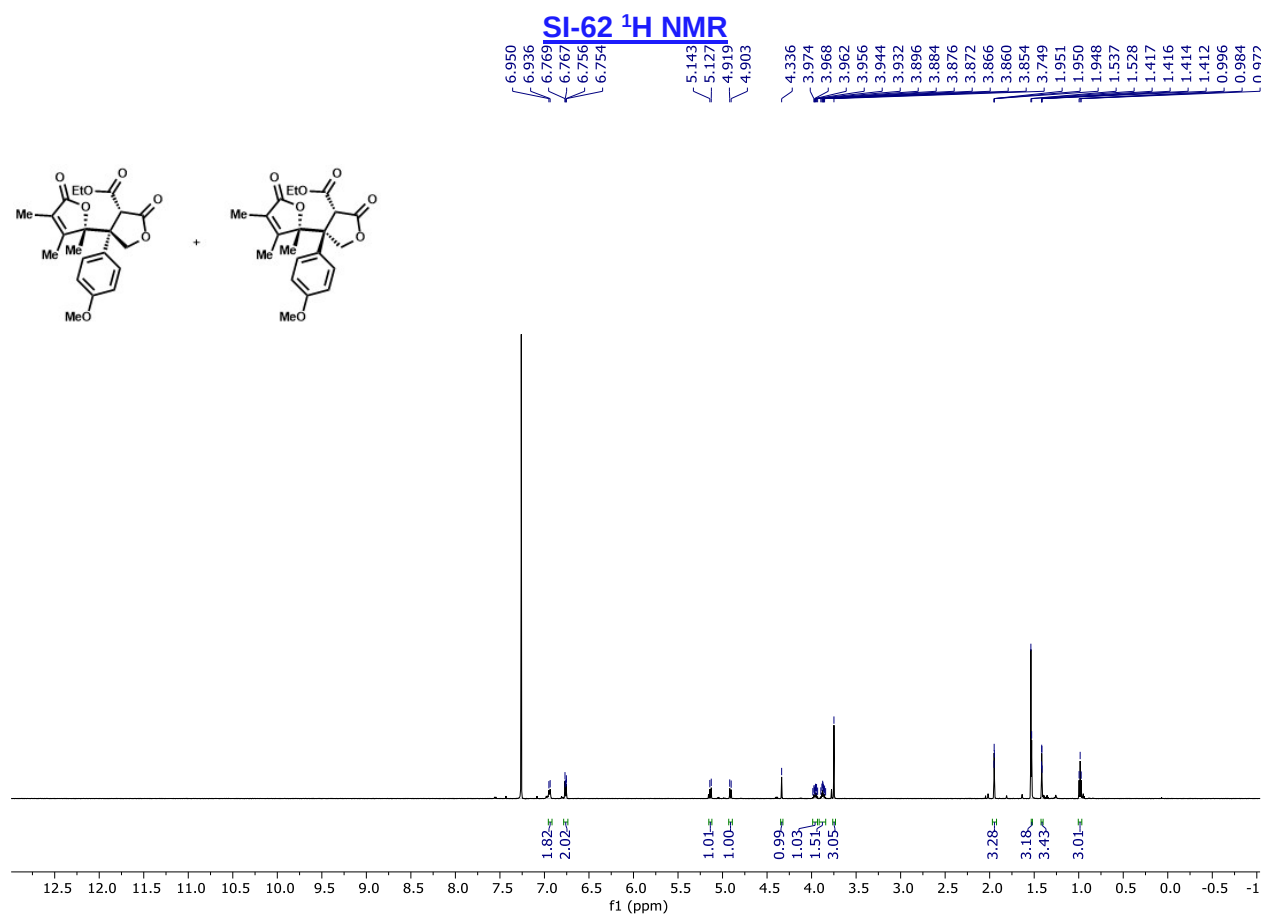
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

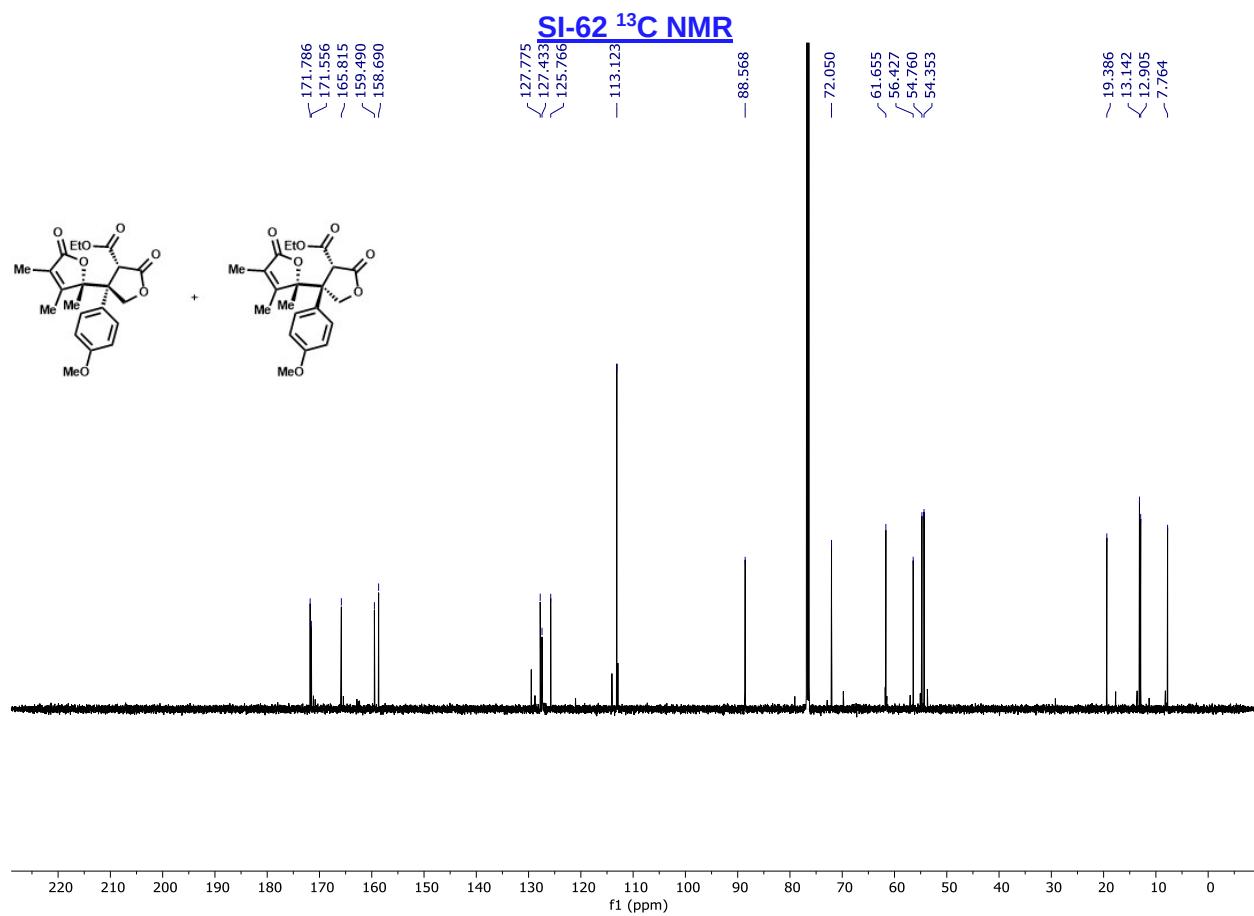
d.r. calculation:

$$(A+B) / (A+B+C+D) = (2524+2964) / (2524+2964+973+911) = 74 : 26$$

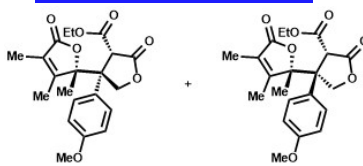
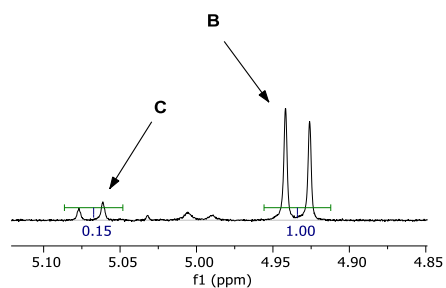
Name: M1				
From: 6.875 ppm				
To: 7.008 ppm				
Residual Error: 1.11				
#	ppm	Height	Width(Hz)	L/G Area
1	6.99102.88	3.12	0.30	105.603
2	6.971712.76	6.34	0.12	973.607
3	6.958211.85	6.72	0.48	911.473
4	6.933043.72	4.99	0.40	2524.650
5	6.919443.22	5.72	0.15	2964.520







SI-62 Crude ¹H NMR



Characterization:

Butenolide dimer, major diastereomer, enol tautomer:

A

Butenolide dimer, major diastereomer, keto tautomer:

B

Butenolide dimer, minor diastereomer, keto tautomer:

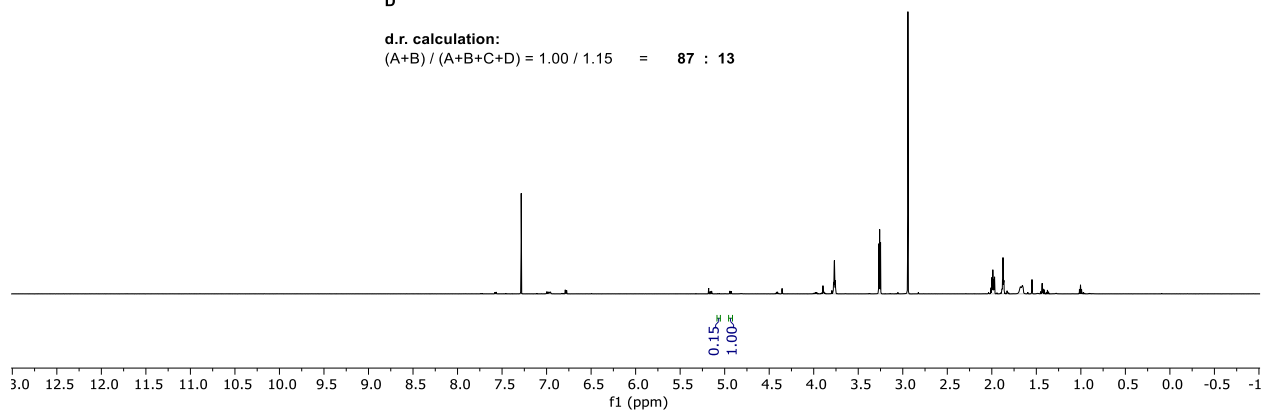
C

Butenolide dimer, minor diastereomer, enol tautomer:

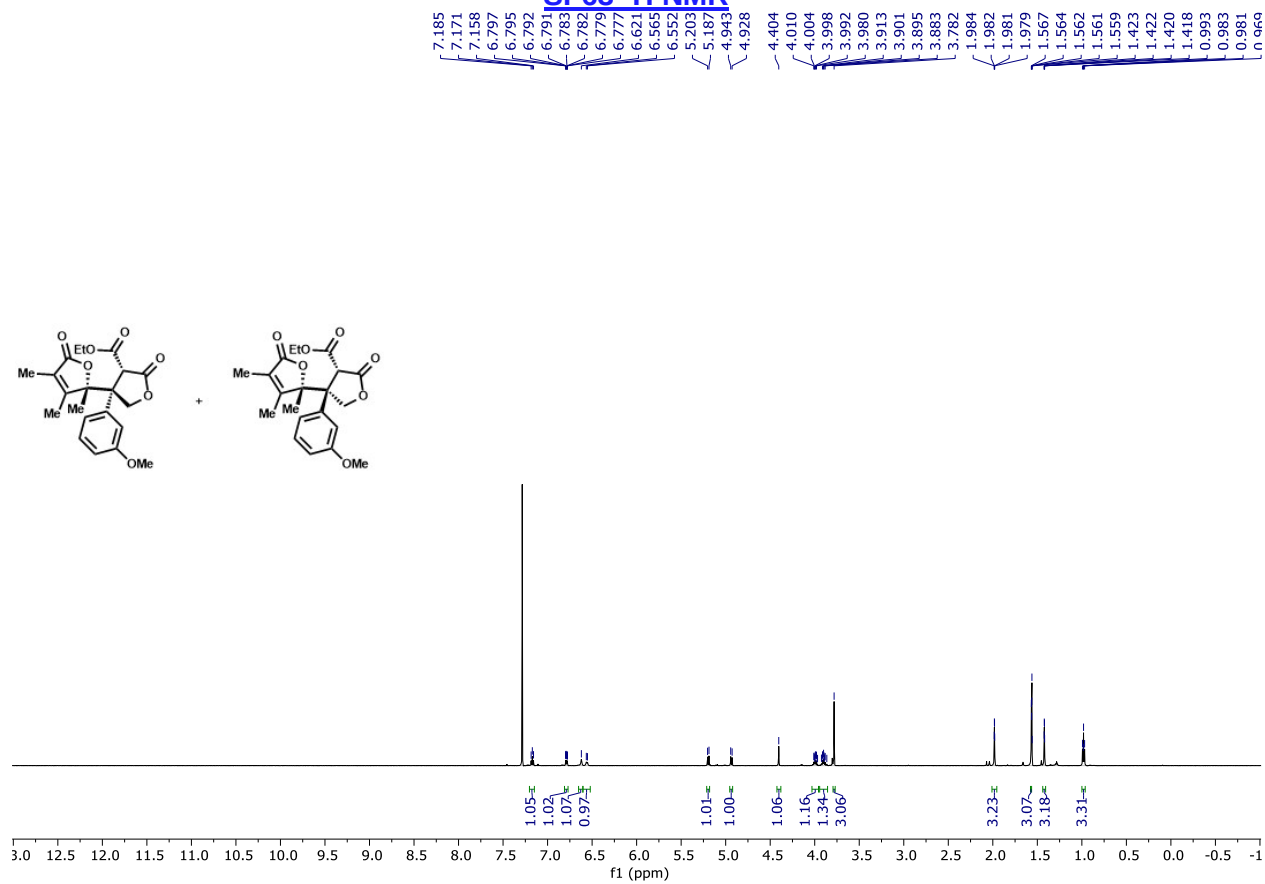
D

d.r. calculation:

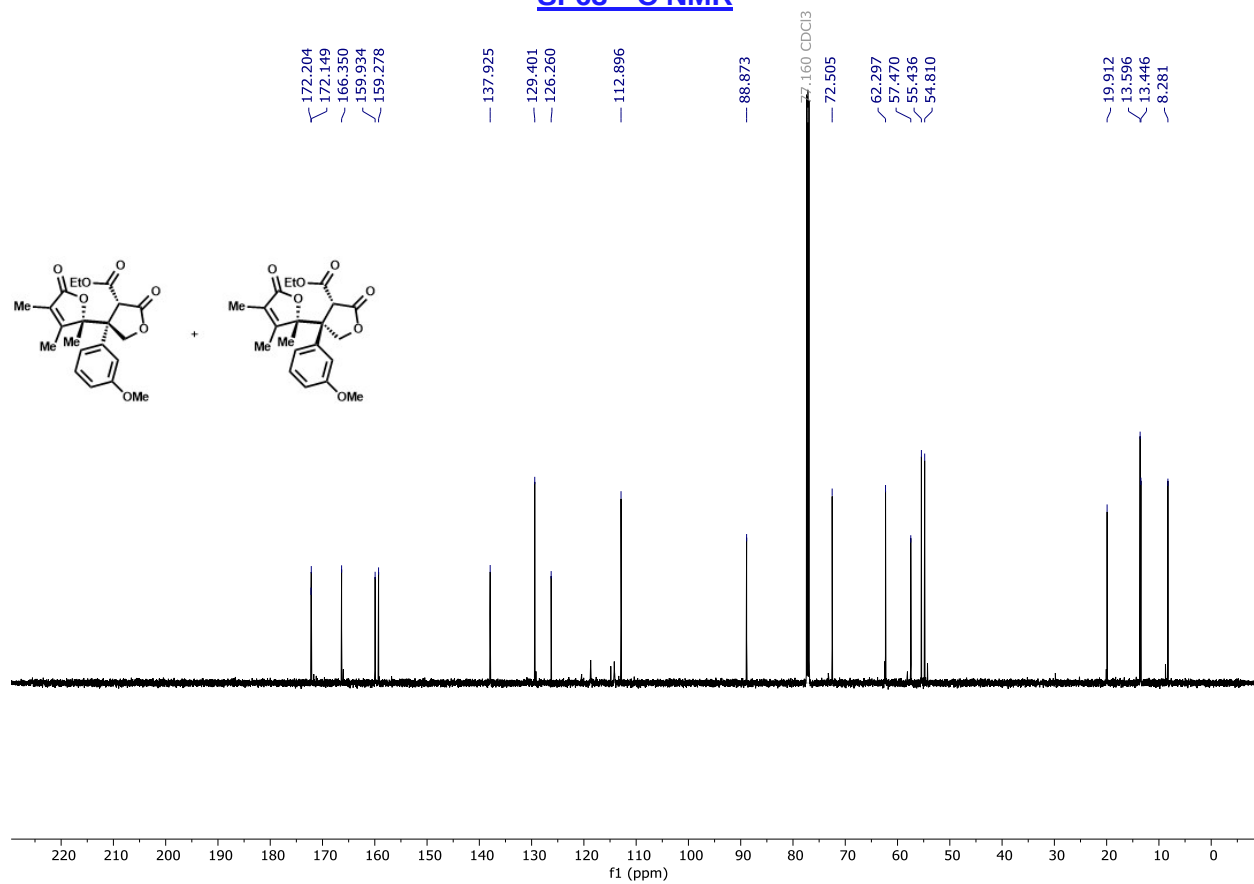
$$(A+B) / (A+B+C+D) = 1.00 / 1.15 = 87 : 13$$



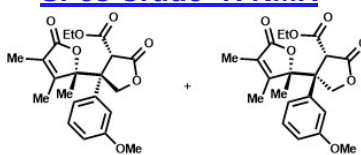
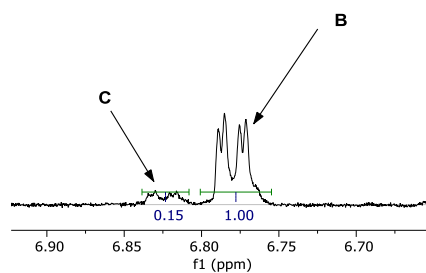
SI-63 ¹H NMR



SI-63 ¹³C NMR



SI-63 Crude ¹H NMR



Characterization:

Butenolide dimer, major diastereomer, enol tautomer:

A

Butenolide dimer, major diastereomer, keto tautomer:

B

Butenolide dimer, minor diastereomer, keto tautomer:

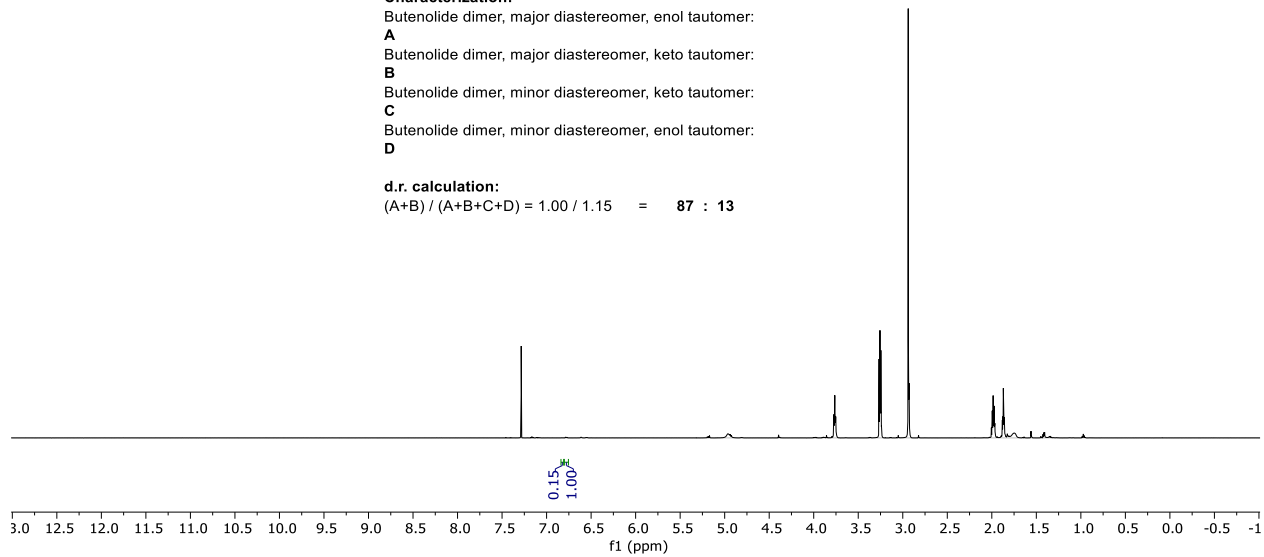
C

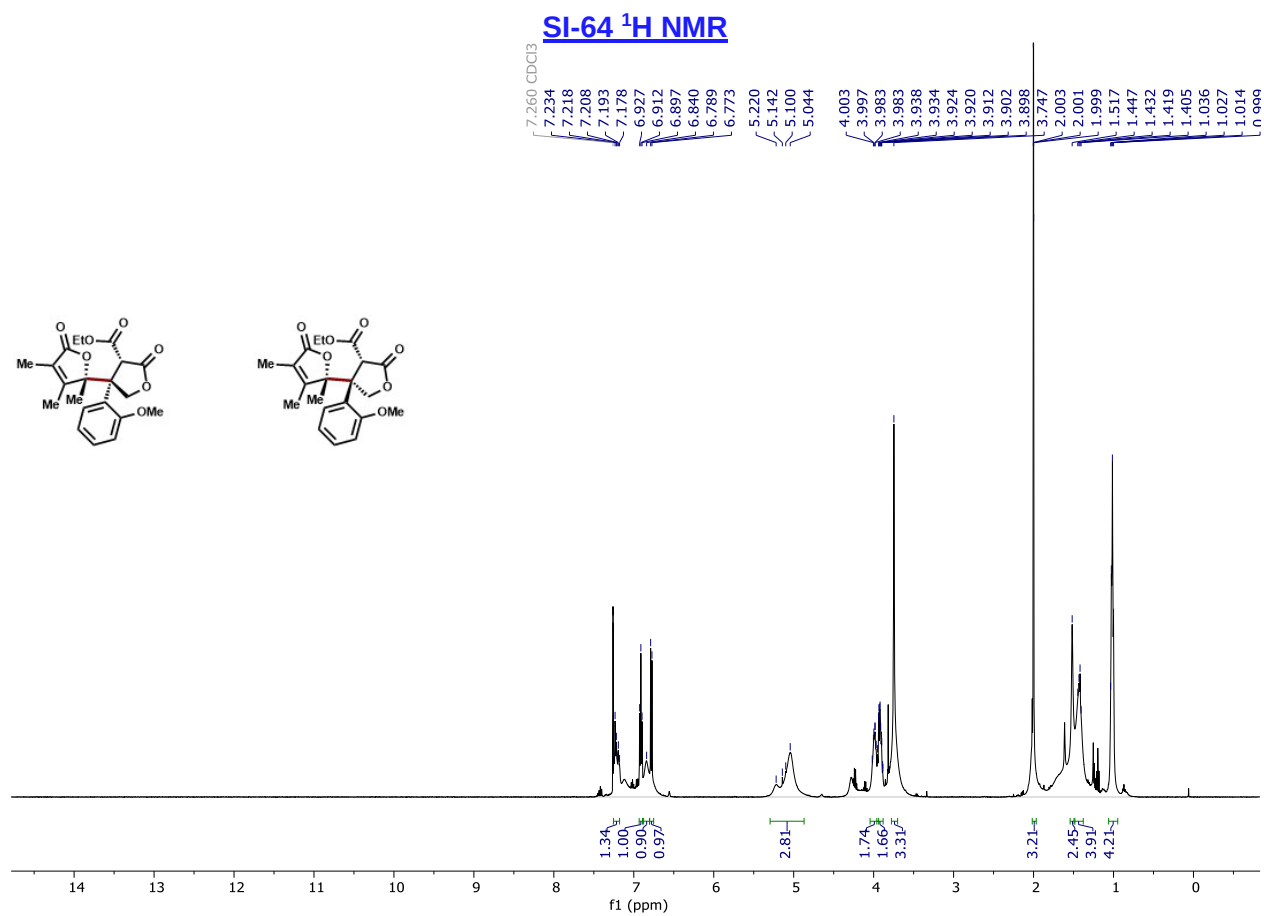
Butenolide dimer, minor diastereomer, enol tautomer:

D

d.r. calculation:

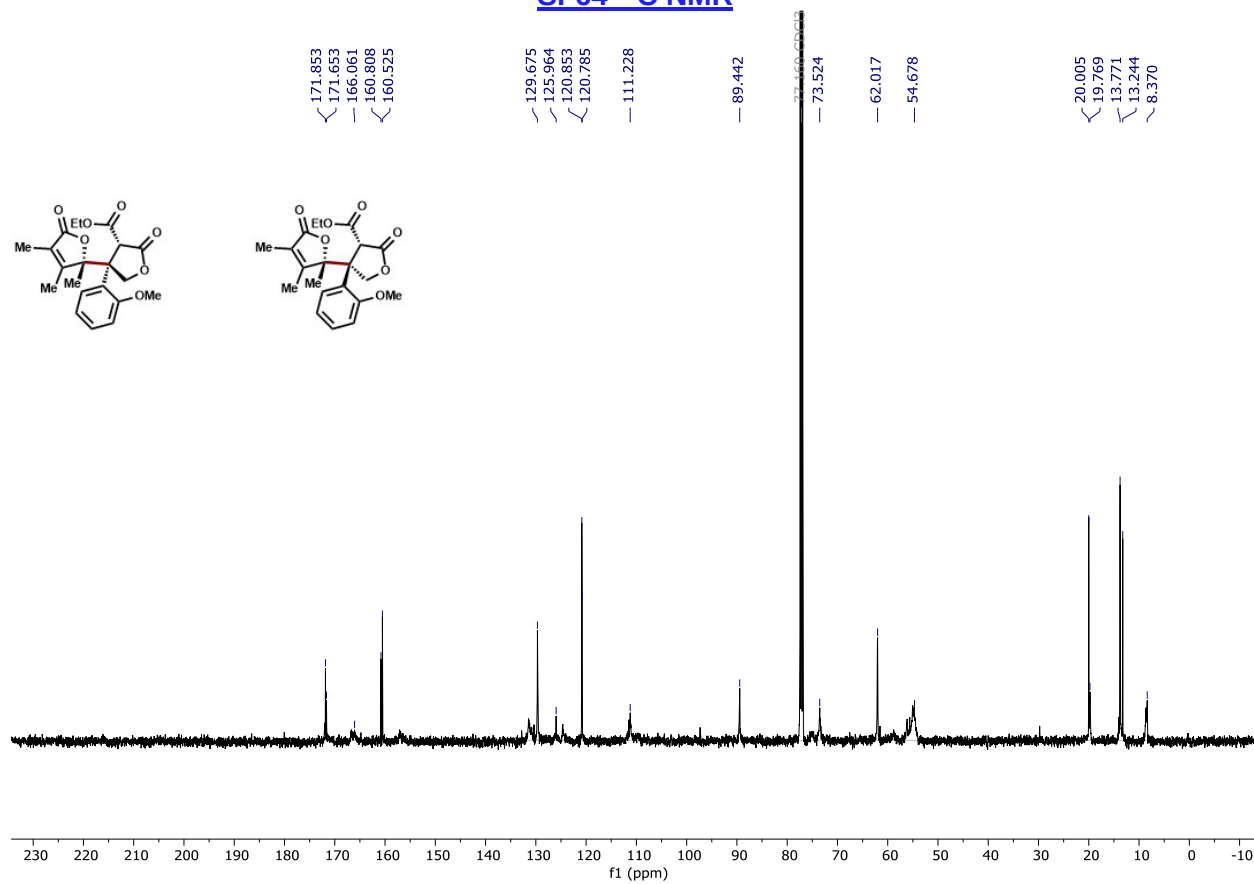
$$(A+B) / (A+B+C+D) = 1.00 / 1.15 = 87 : 13$$





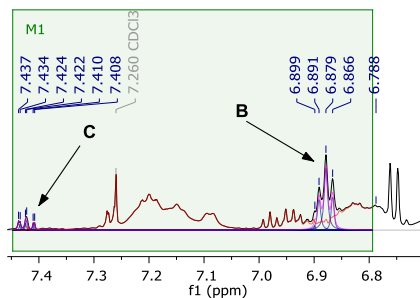
Note: Signal are broad likely due to atropisomerism.

SI-64 ¹³C NMR



Note: Signal are broad likely due to atropisomerism.

SI-64 Crude ¹H NMR

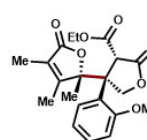
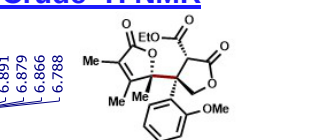


Characterization:

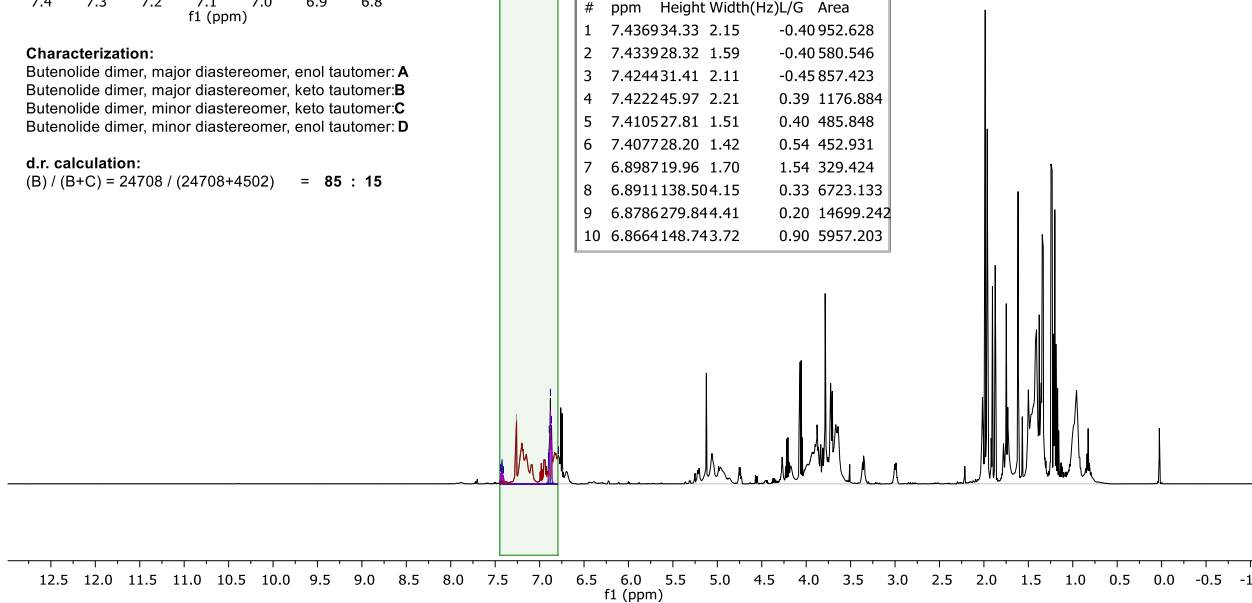
Butenolide dimer, major diastereomer, enol tautomer: **A**
Butenolide dimer, major diastereomer, keto tautomer: **B**
Butenolide dimer, minor diastereomer, keto tautomer: **C**
Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

$$(B) / (B+C) = 24708 / (24708+4502) = 85 : 15$$

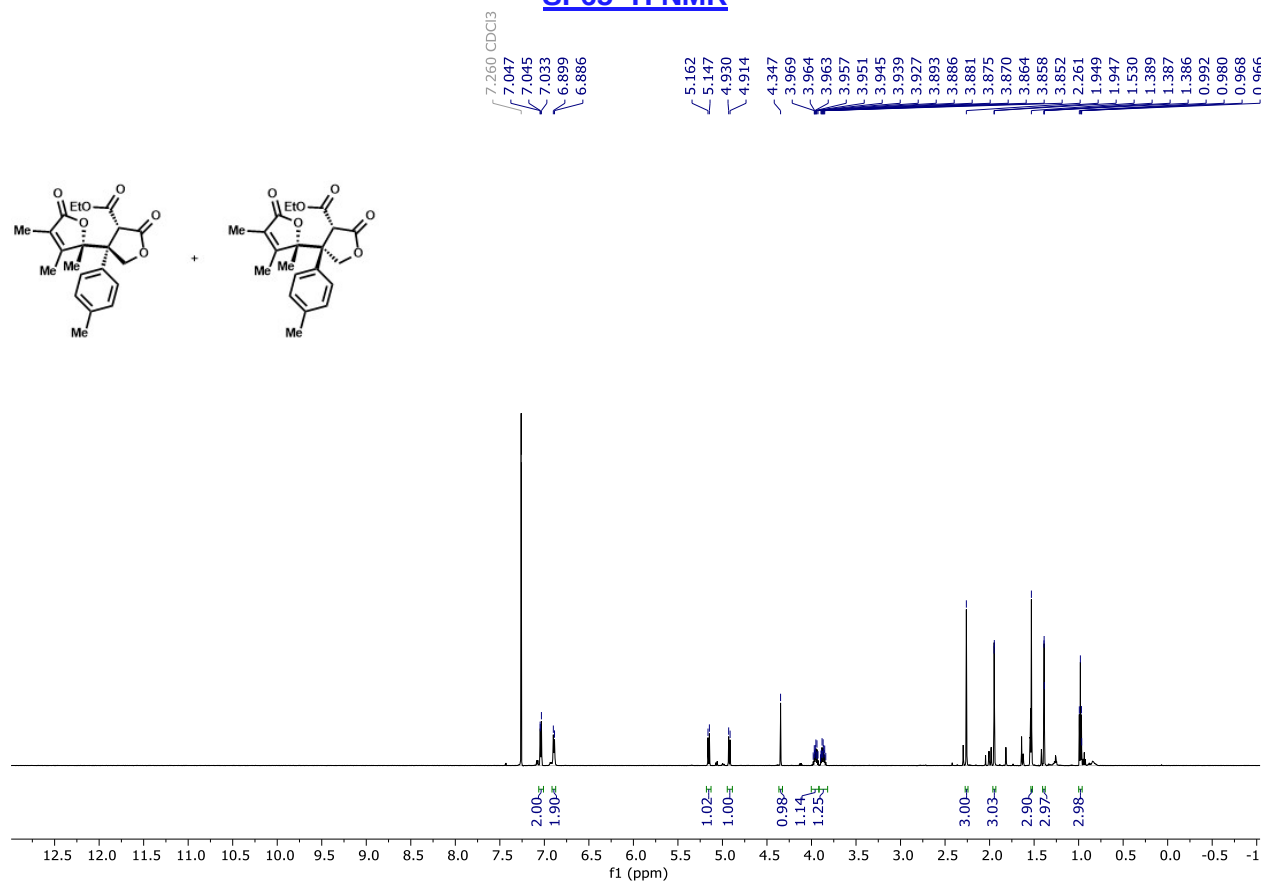


Name: M1				
From: 6.794 ppm				
To: 7.448 ppm				
Residual Error: 4.19e+03				
#	ppm	Height	Width(Hz)	L/G Area
1	7.4369	34.33	2.15	-0.40 952.628
2	7.4339	28.32	1.59	-0.40 580.546
3	7.4244	31.41	2.11	-0.45 857.423
4	7.4222	45.97	2.21	0.39 1176.884
5	7.4105	27.81	1.51	0.40 485.848
6	7.4077	28.20	1.42	0.54 452.931
7	6.8987	19.96	1.70	1.54 329.424
8	6.8911	138.50	4.15	0.33 6723.133
9	6.8786	279.84	4.41	0.20 14699.242
10	6.8664	148.74	3.72	0.90 5957.203

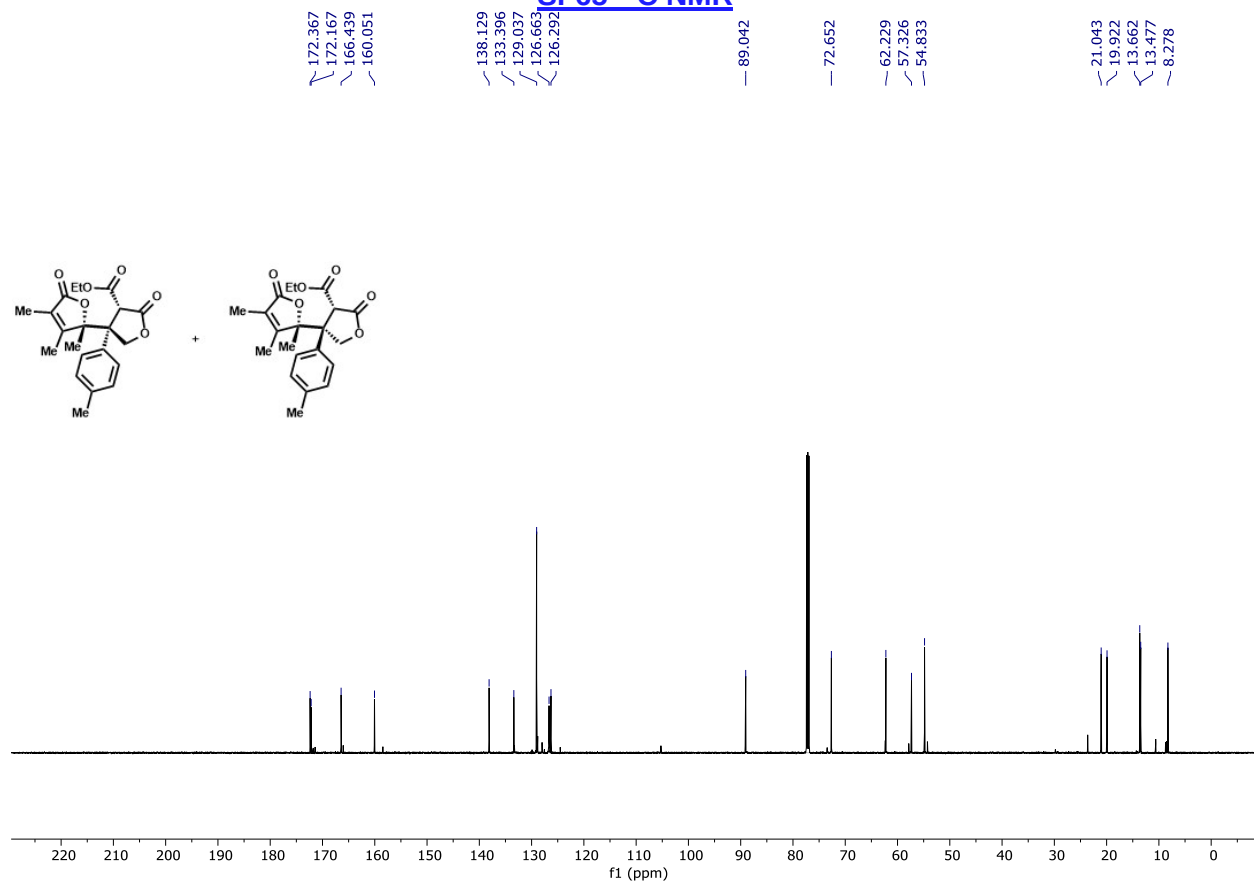


Note: Signal are broad likely due to atropisomerism.

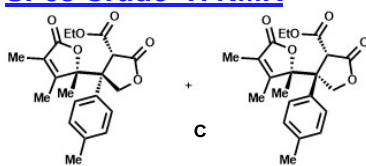
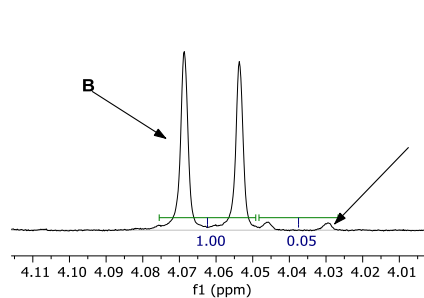
SI-65 ¹H NMR



SI-65 ¹³C NMR



SI-65 Crude ¹H NMR



Characterization:

Butenolide dimer, major diastereomer, enol tautomer:

A

Butenolide dimer, major diastereomer, keto tautomer:

B

Butenolide dimer, minor diastereomer, keto tautomer:

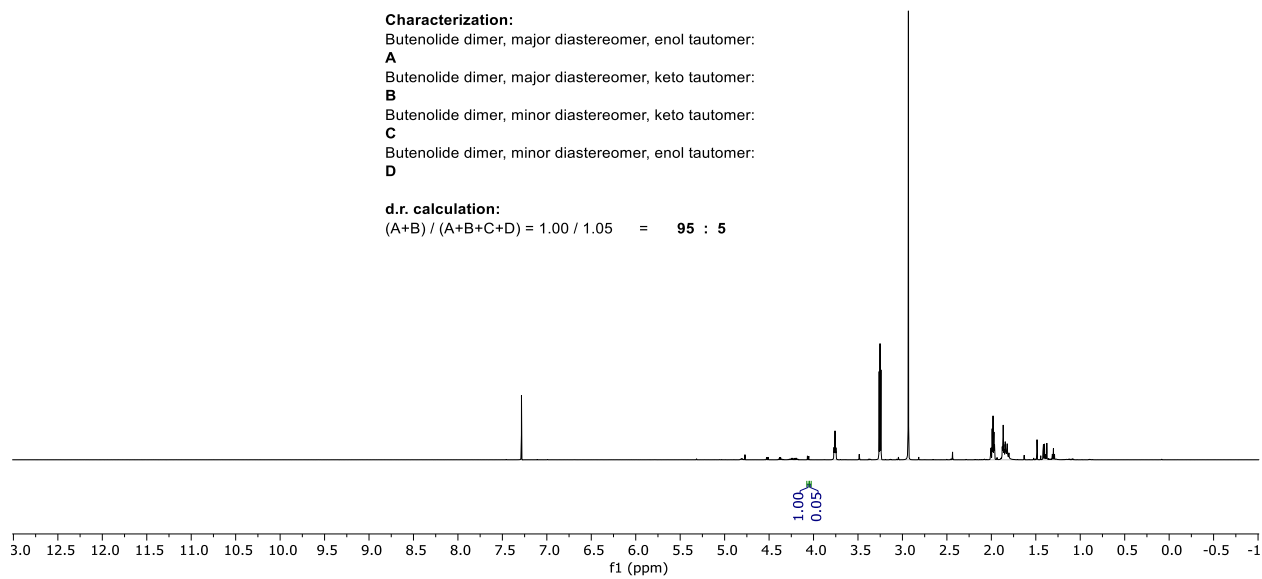
C

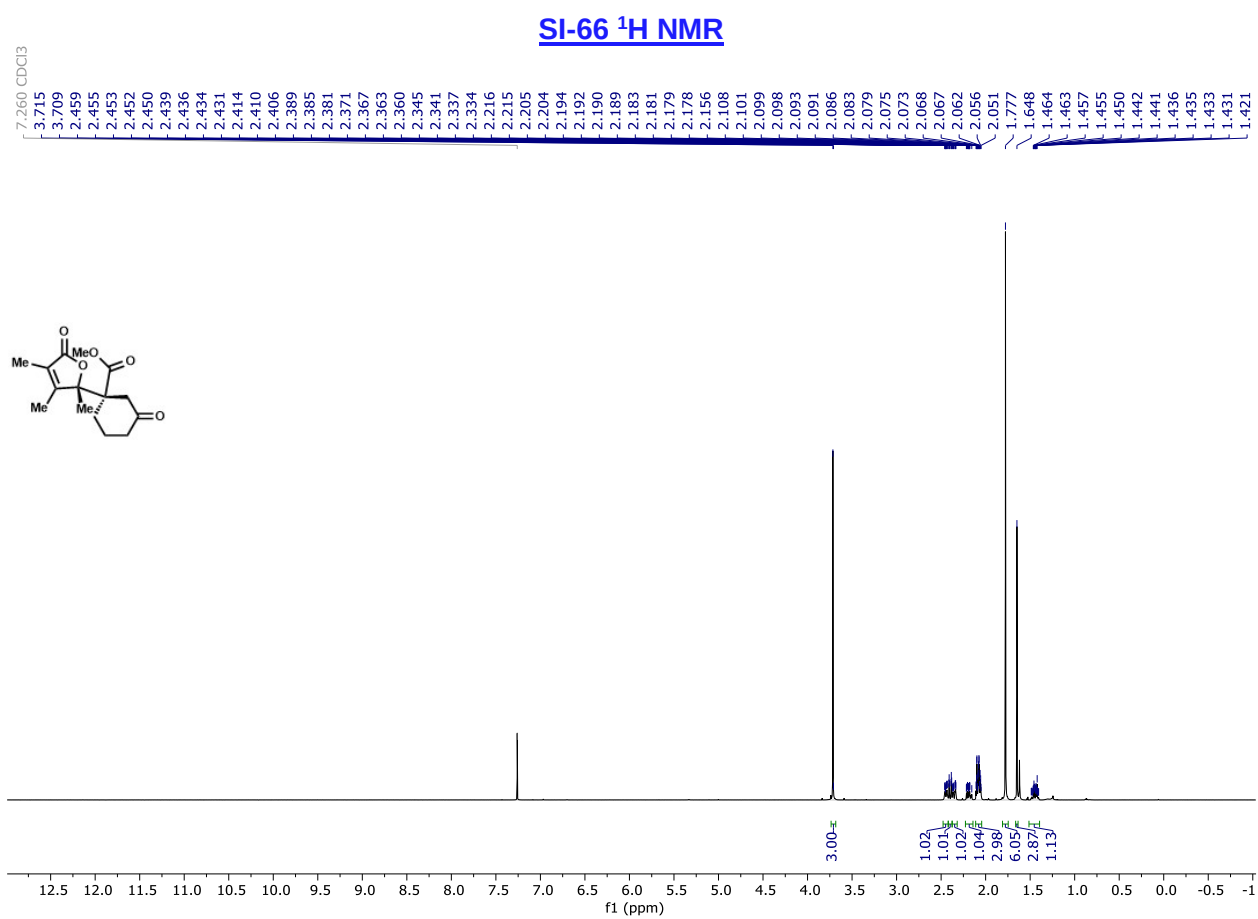
Butenolide dimer, minor diastereomer, enol tautomer:

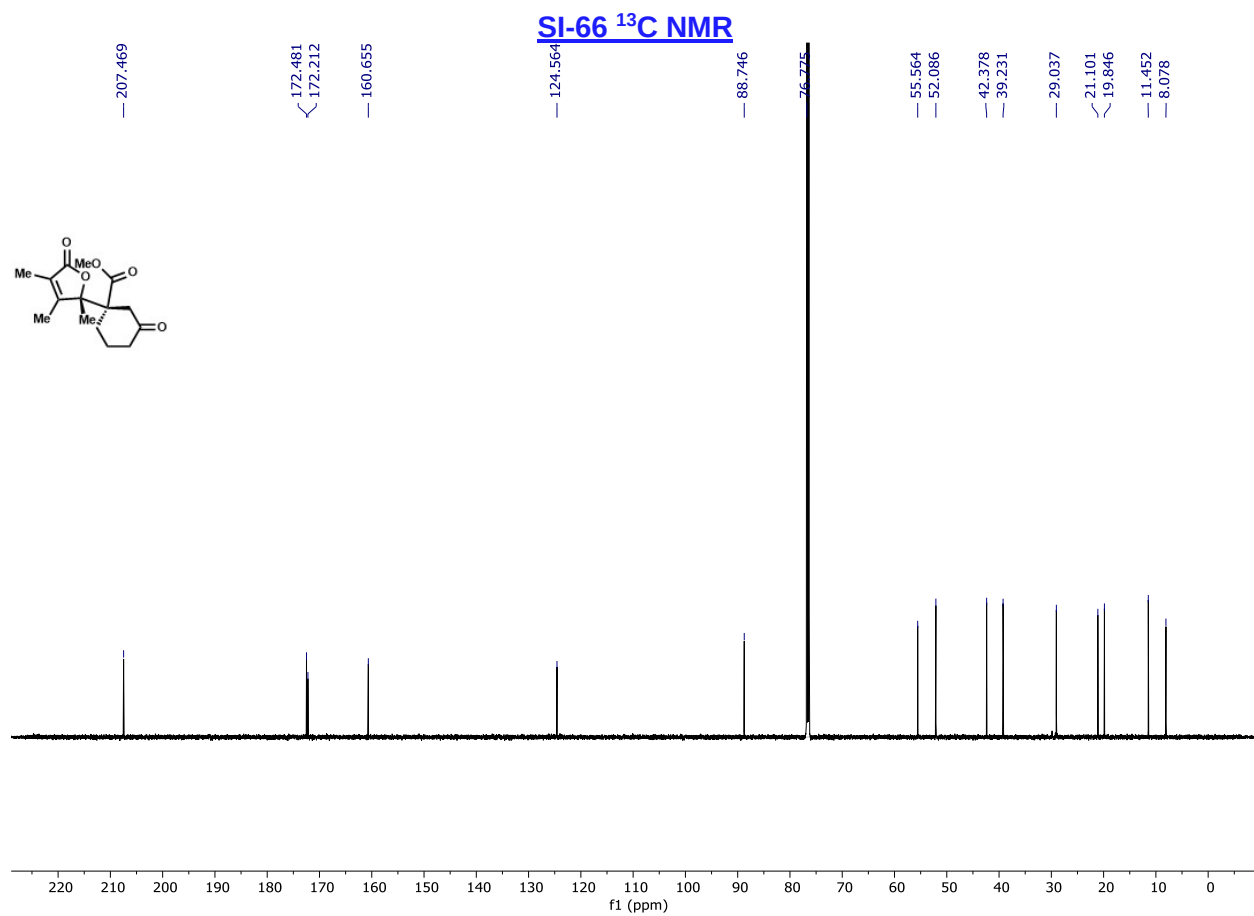
D

d.r. calculation:

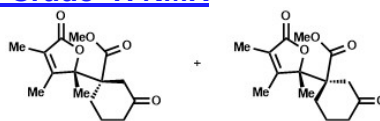
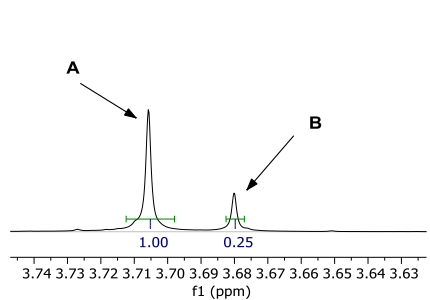
$$(A+B) / (A+B+C+D) = 1.00 / 1.05 = 95 : 5$$







SI-66 Crude ^1H NMR



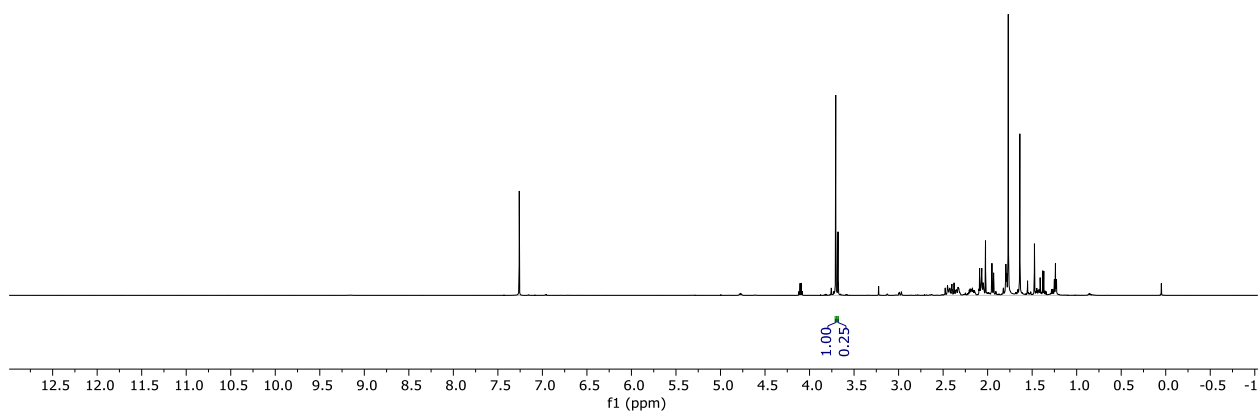
Characterization:

Butenolide dimer, major diastereomer: **A**

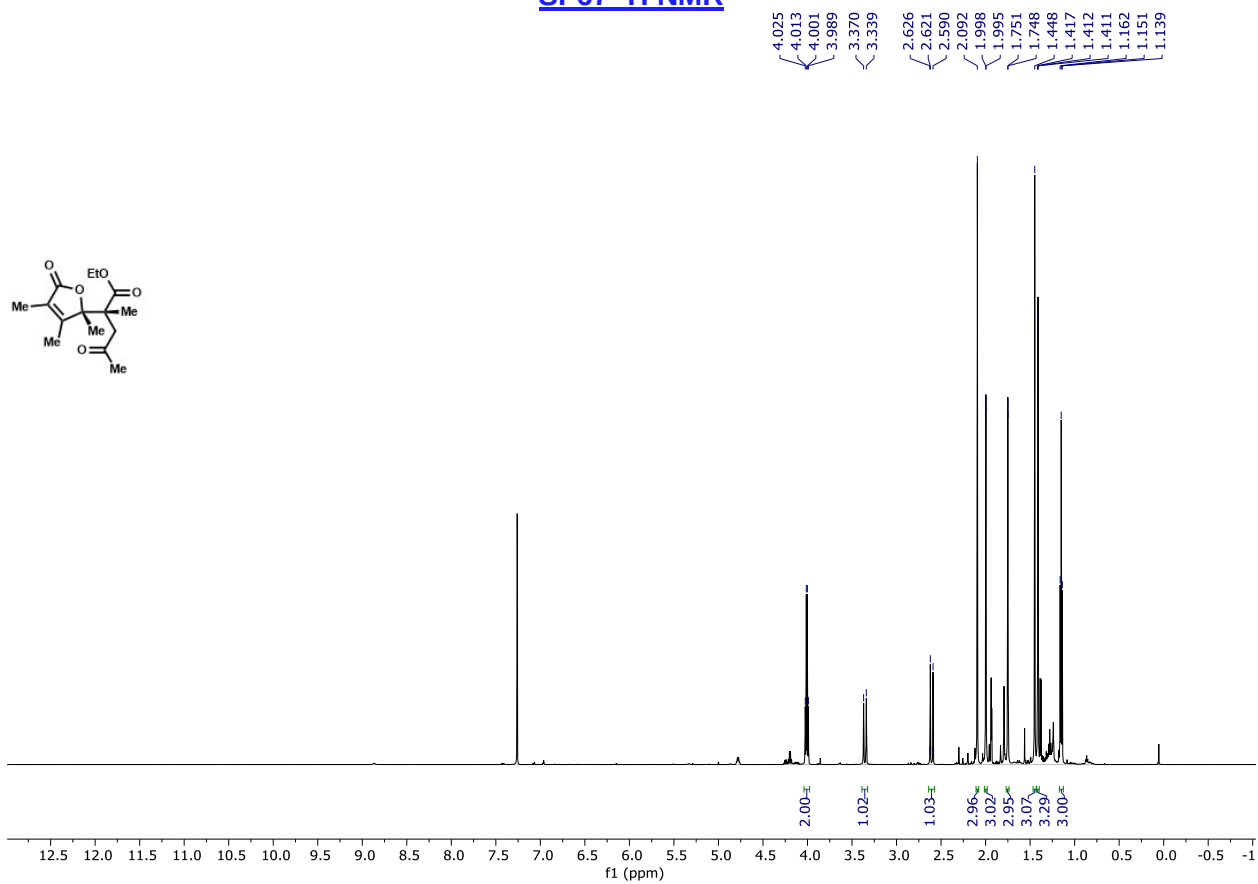
Butenolide dimer, minor diastereomer: **B**

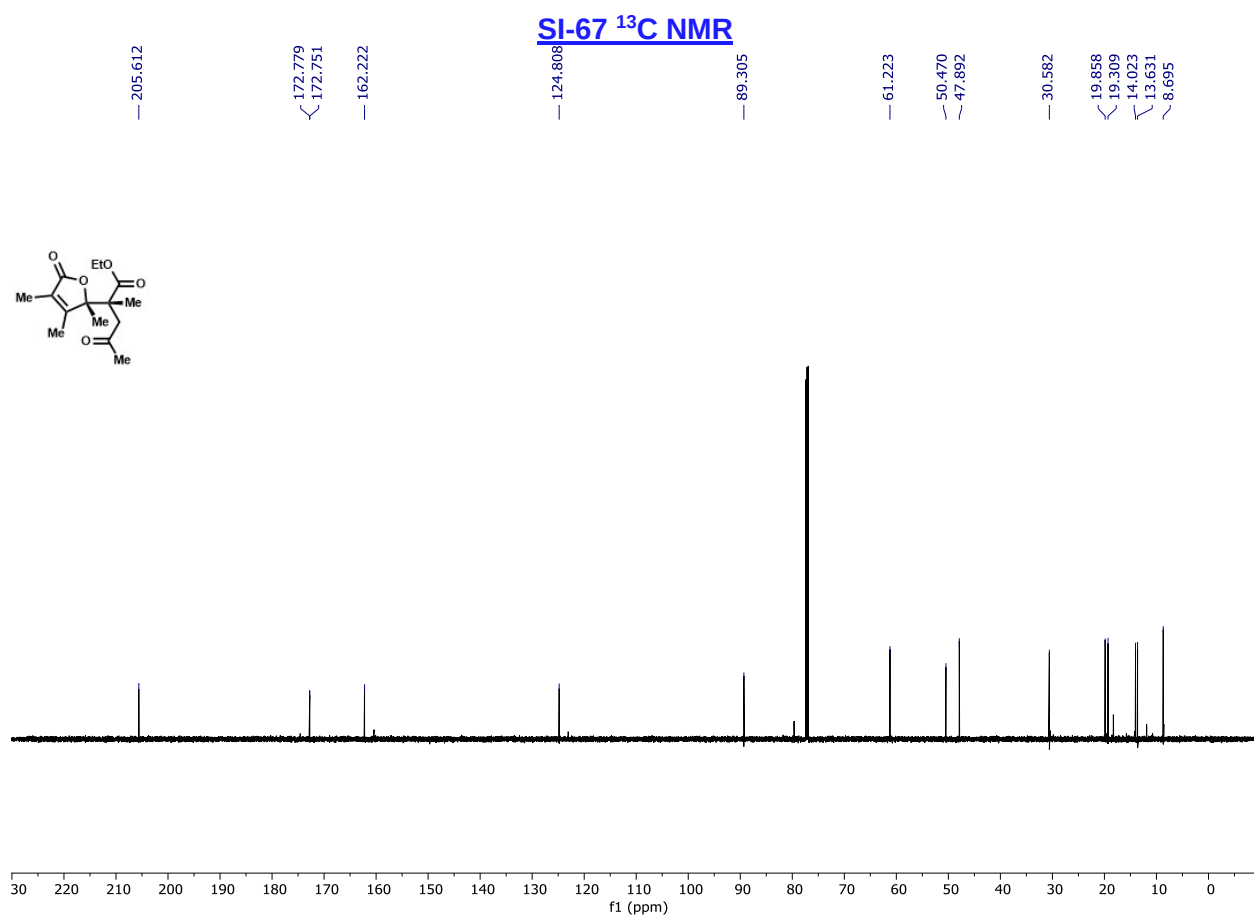
d.r. calculation:

$$(A) / (A+B) = 1.00 / 1.25 = 80 : 20$$

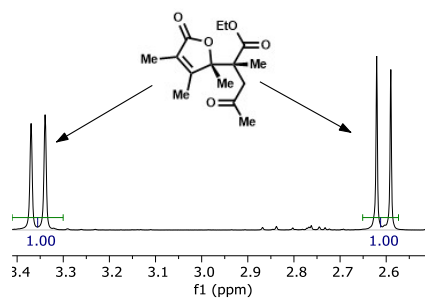


SI-67 ¹H NMR





SI-67 Crude ^1H NMR



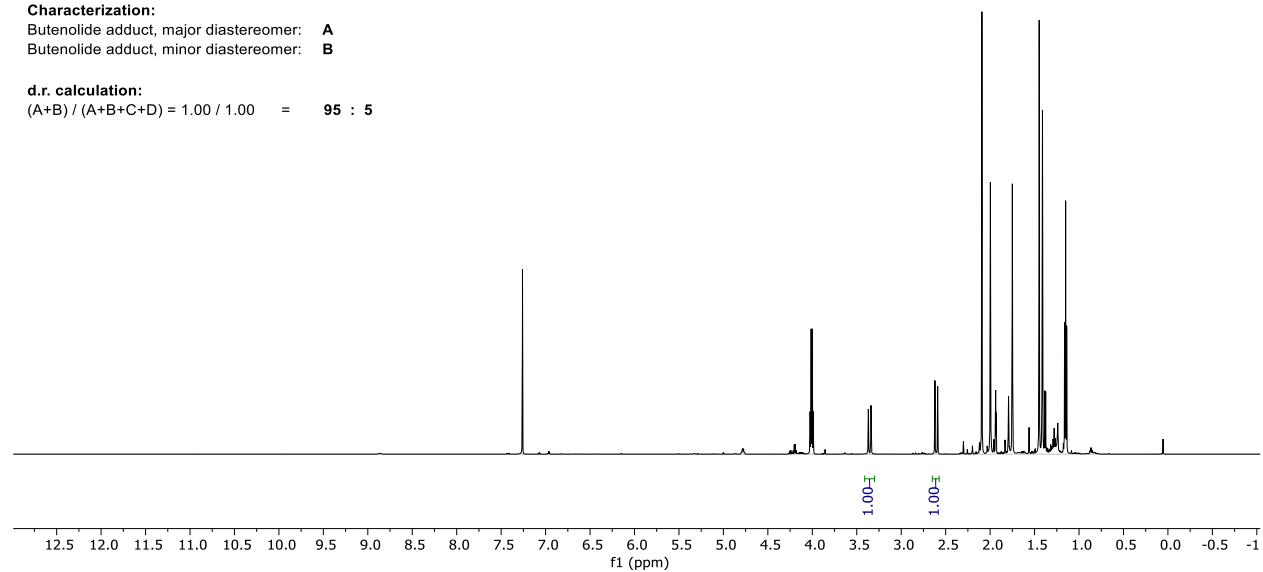
Characterization:

Butenolide adduct, major diastereomer: **A**

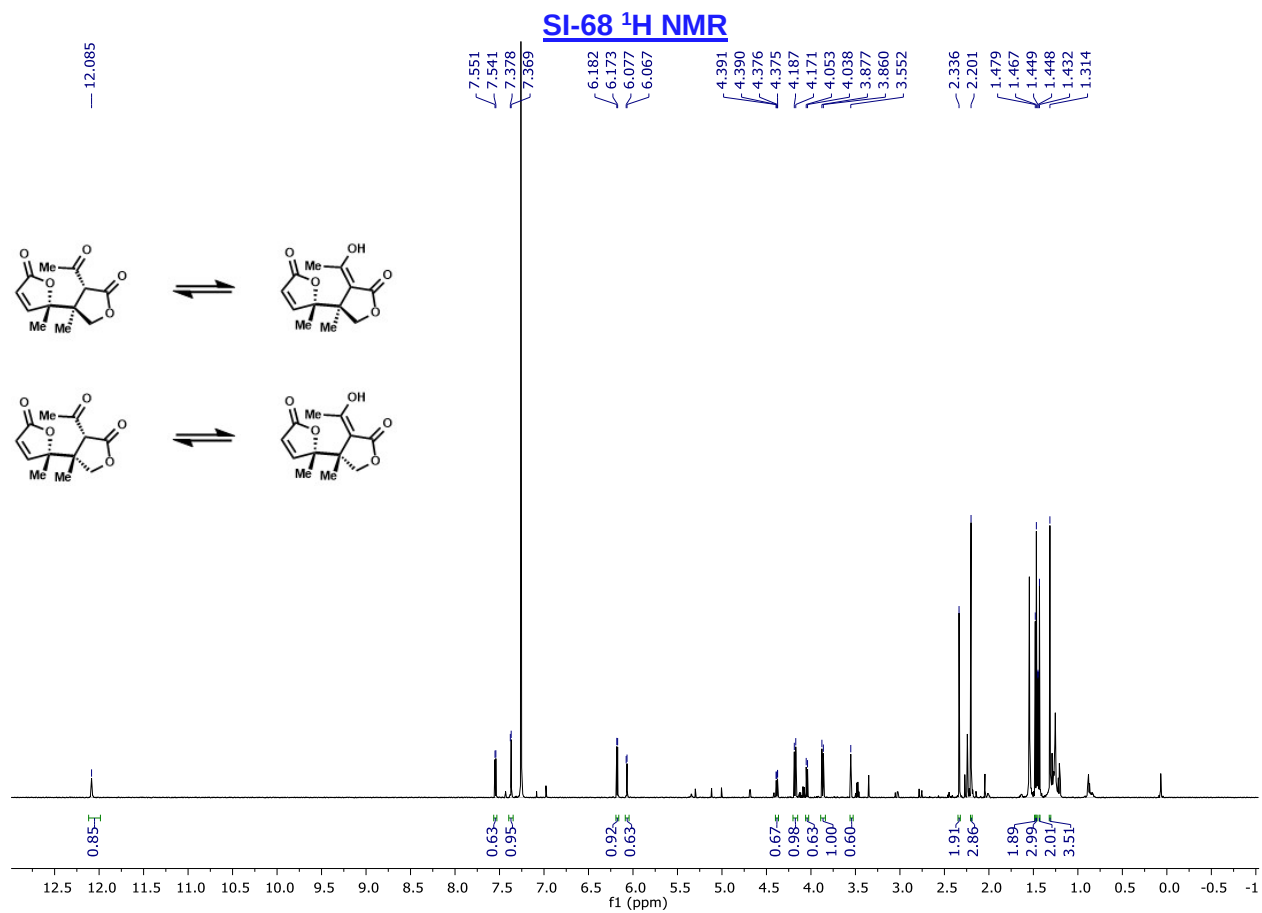
Butenolide adduct, minor diastereomer: **B**

d.r. calculation:

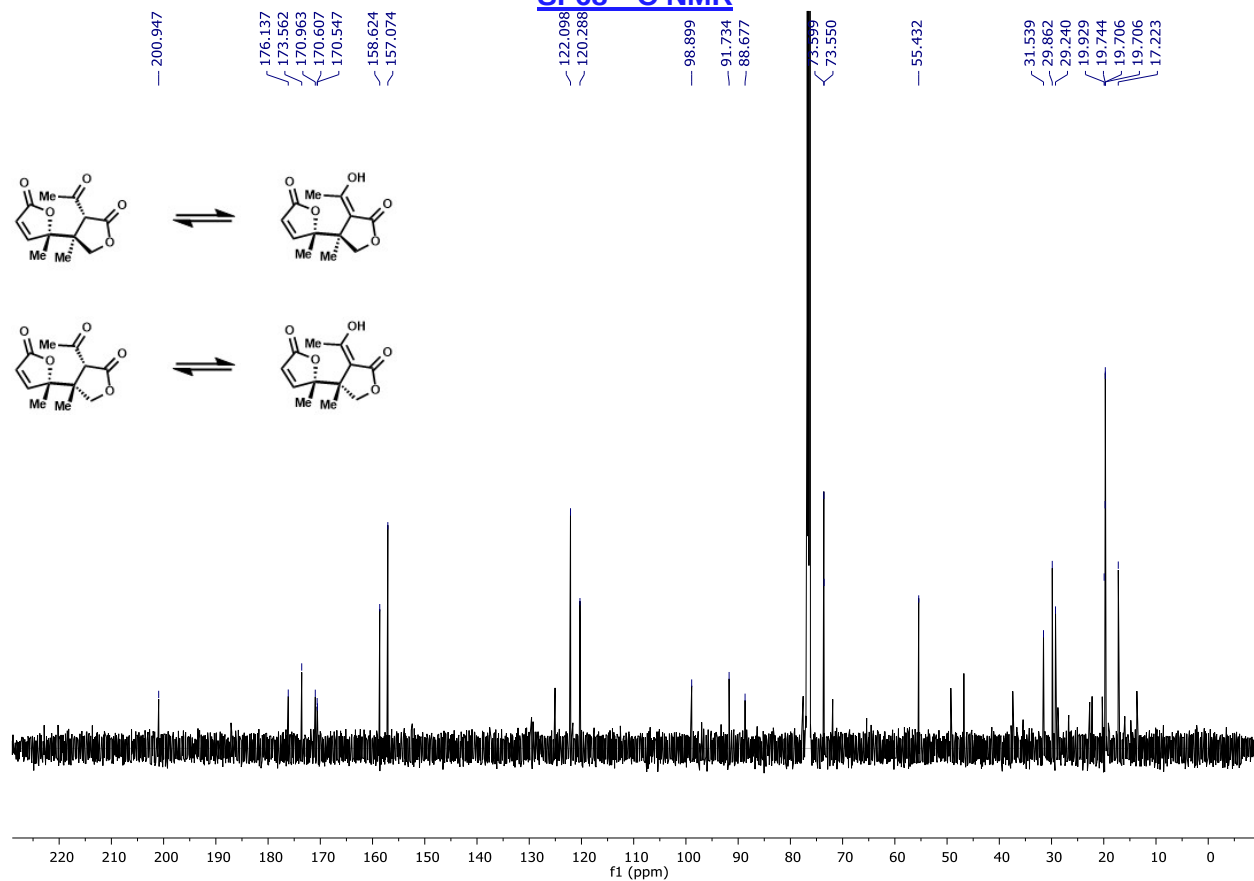
$$(A+B) / (A+B+C+D) = 1.00 / 1.00 = 95 : 5$$



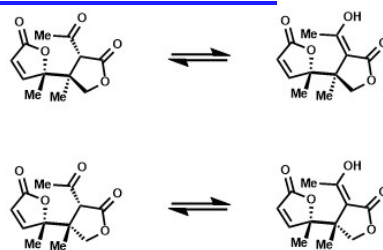
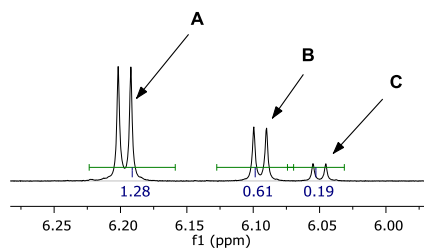
Nucleophile Scope



SI-68 ¹³C NMR



SI-68 Crude ¹H NMR

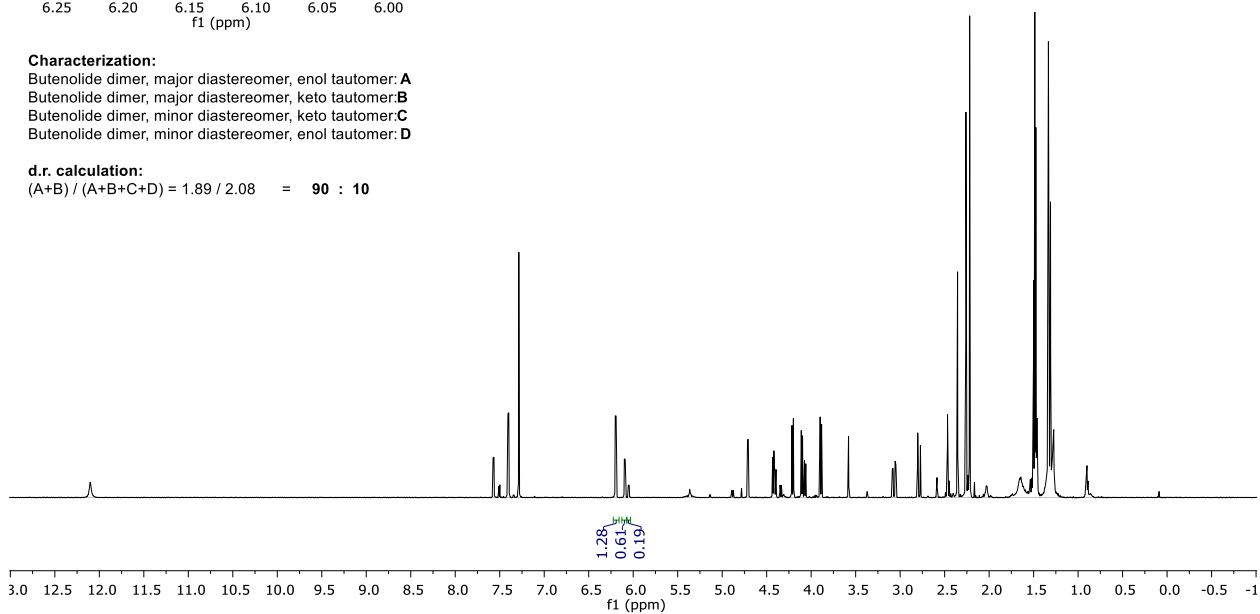


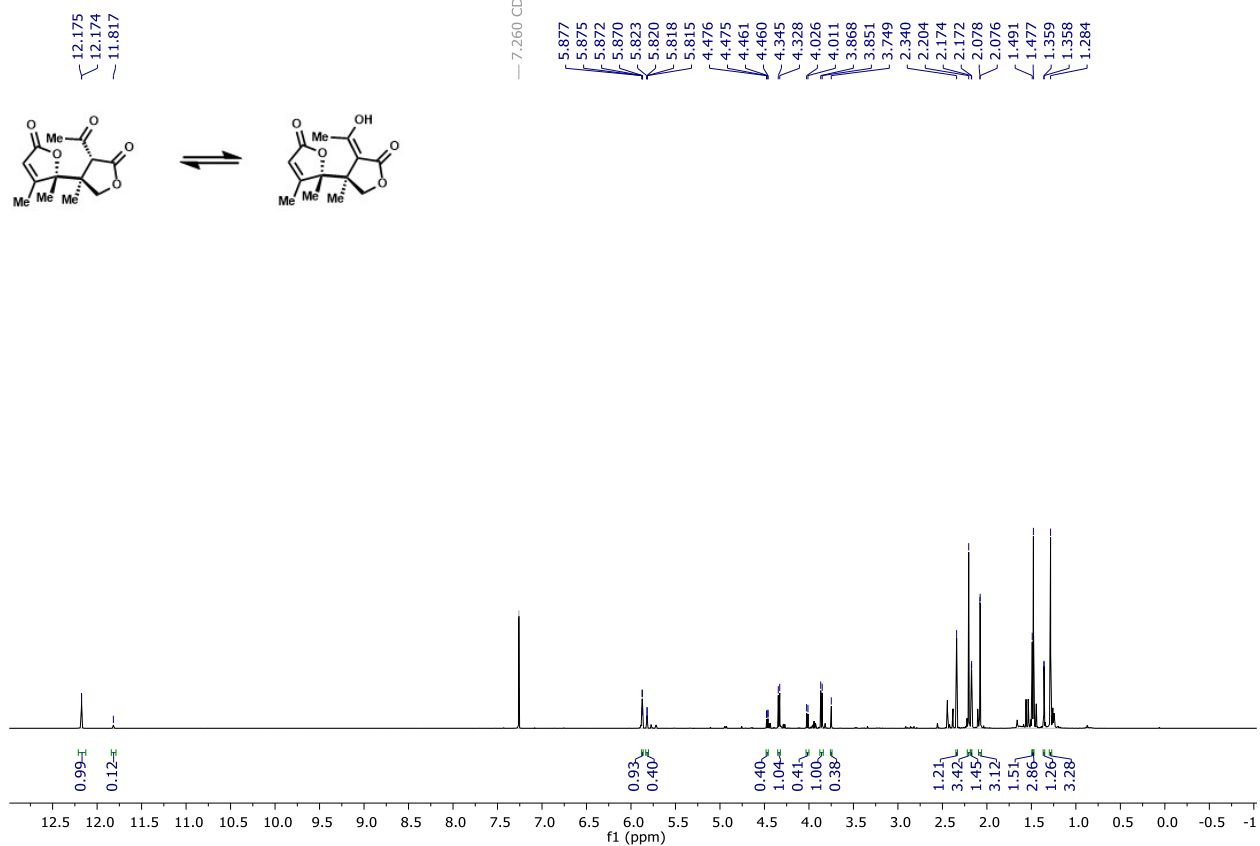
Characterization:

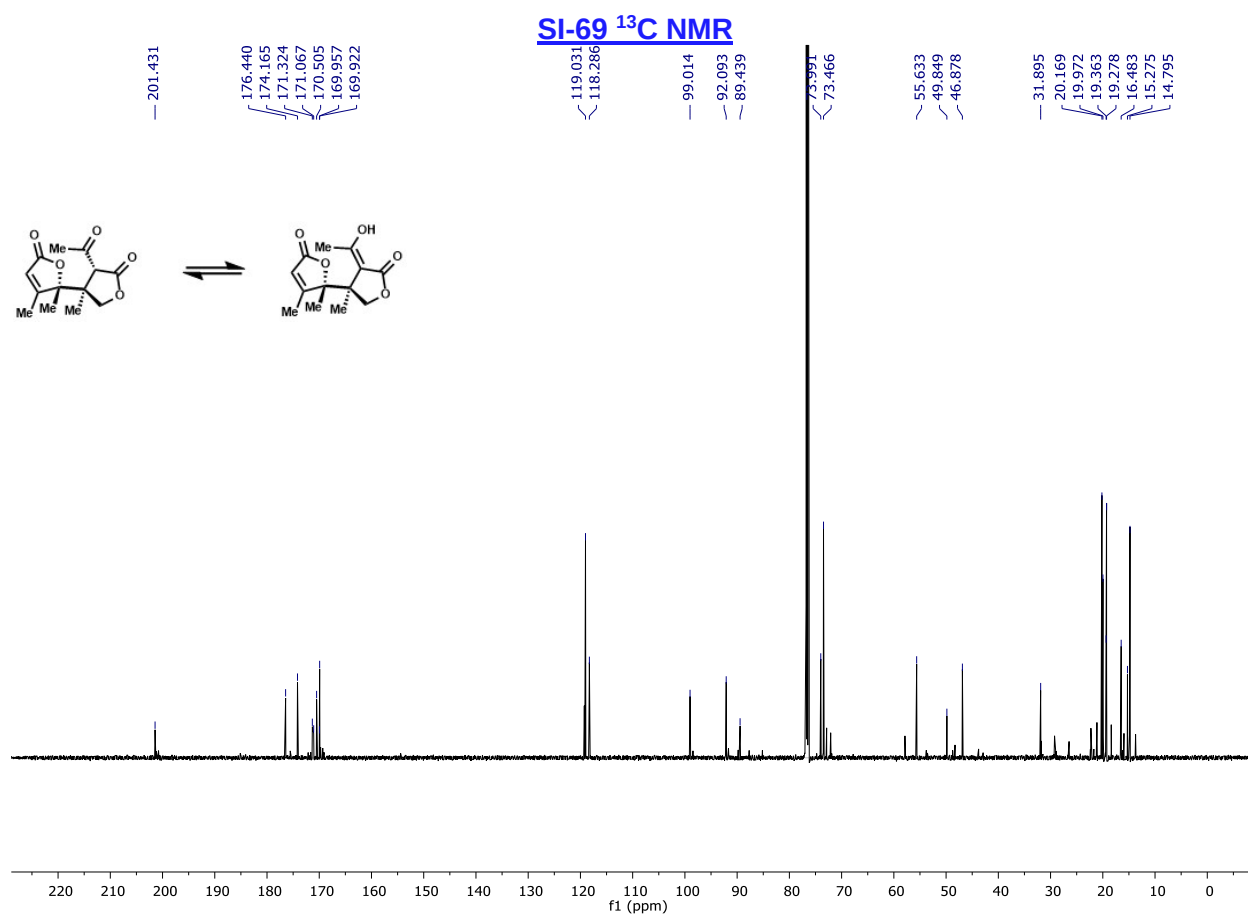
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

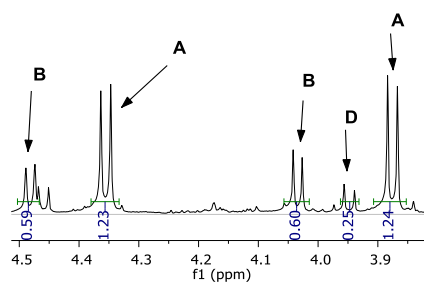
$$(A+B) / (A+B+C+D) = 1.89 / 2.08 = 90 : 10$$







SI-69 Crude ¹H NMR

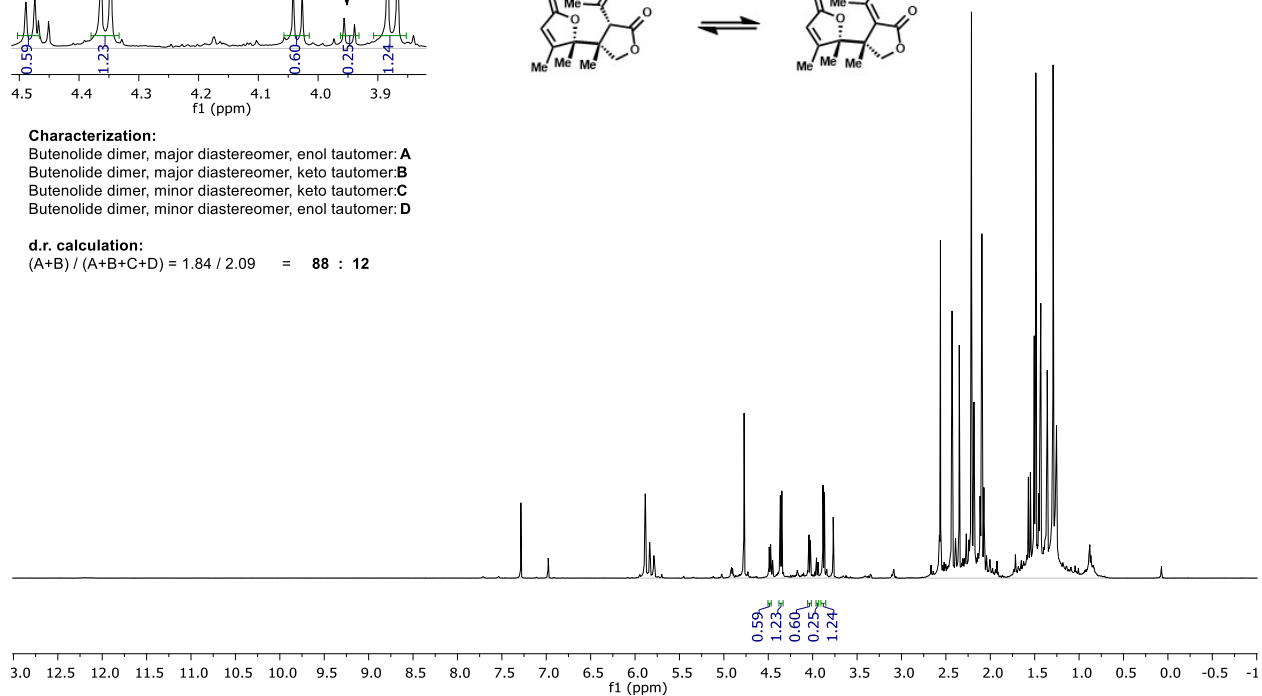
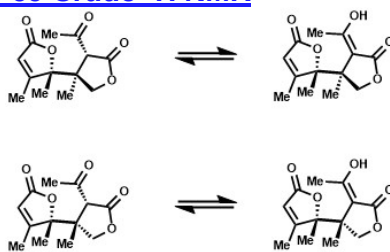


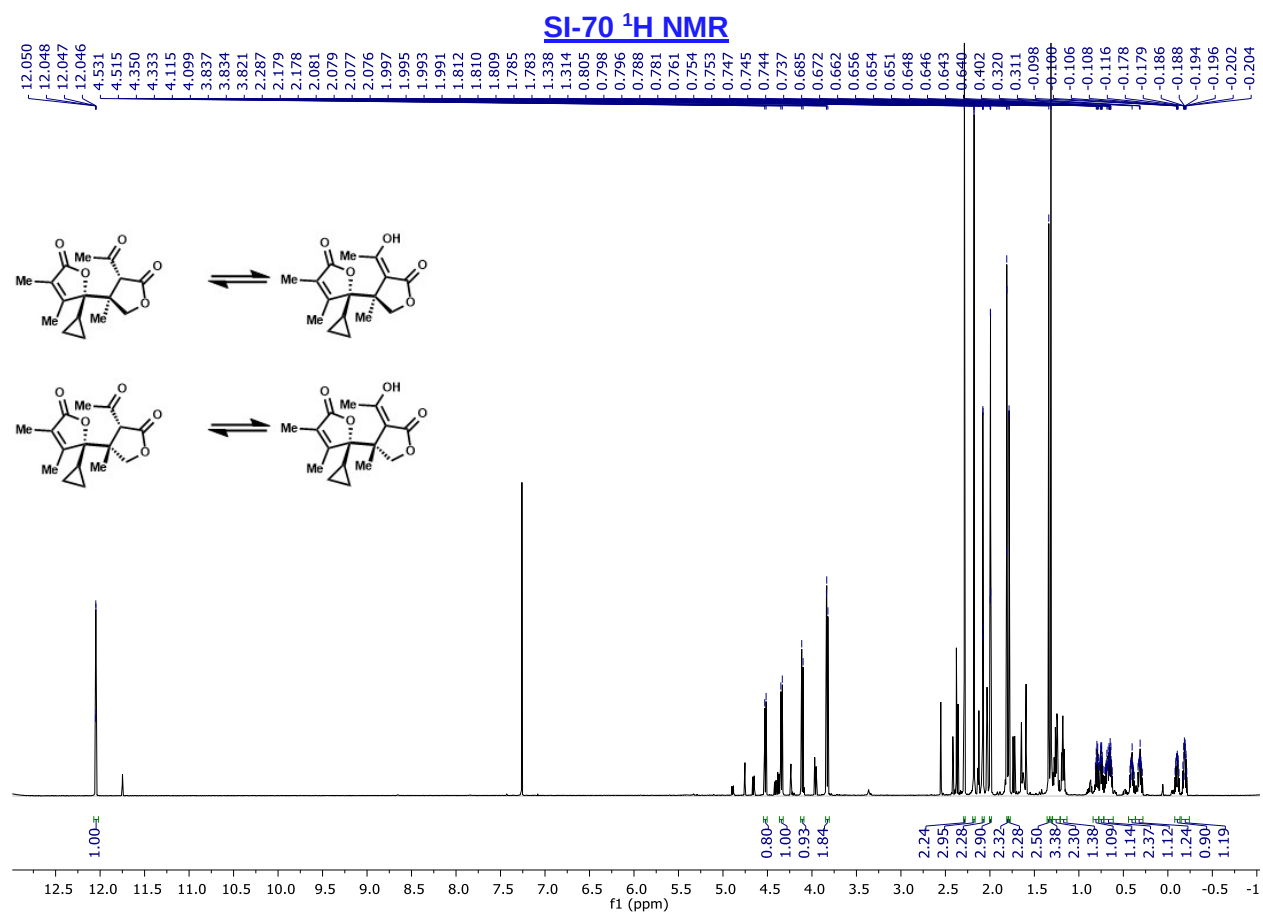
Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

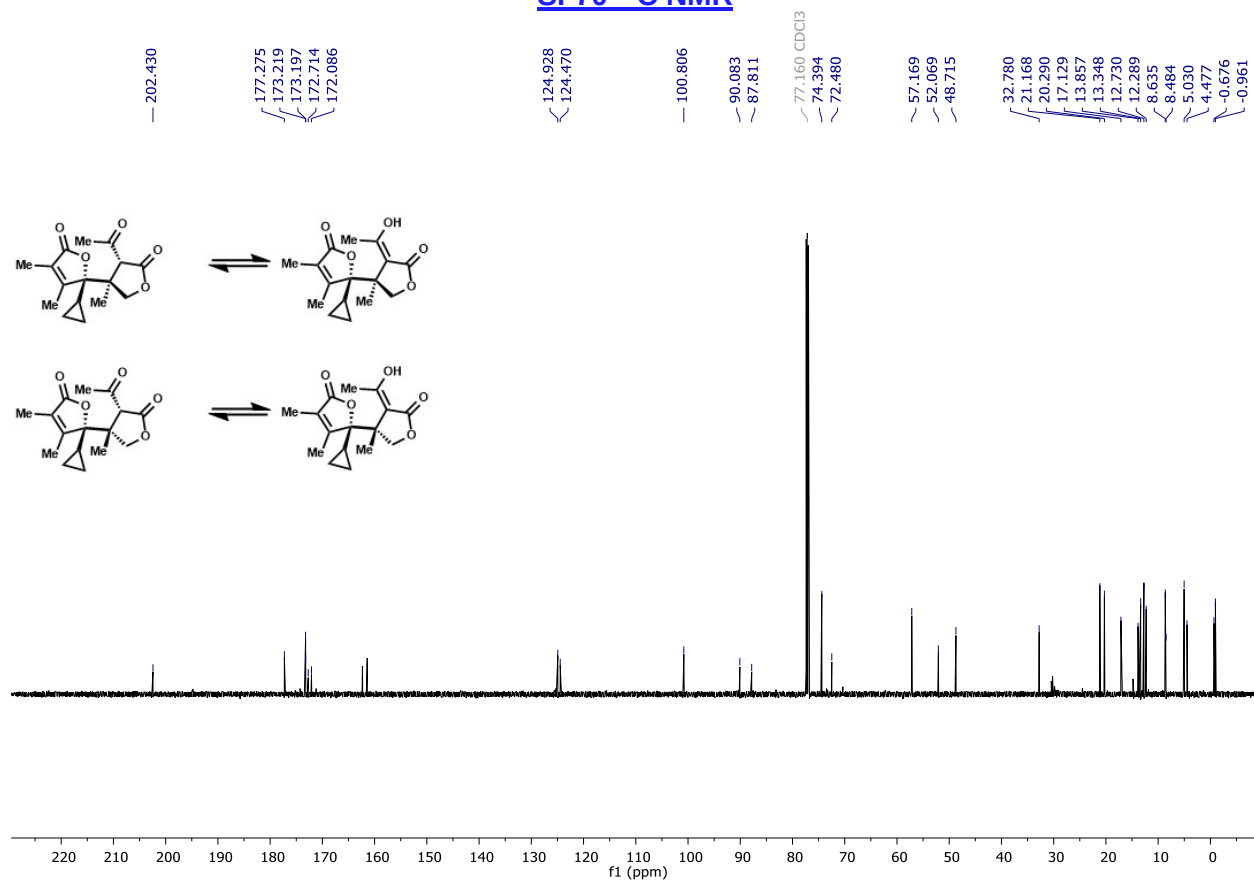
d.r. calculation:

$$(A+B) / (A+B+C+D) = 1.84 / 2.09 = 88 : 12$$

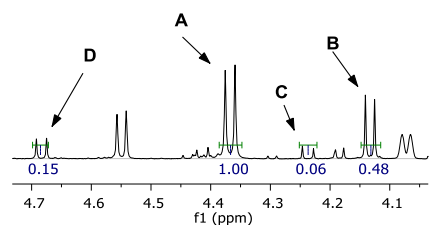




SI-70 ¹³C NMR



SI-70 Crude ^1H NMR

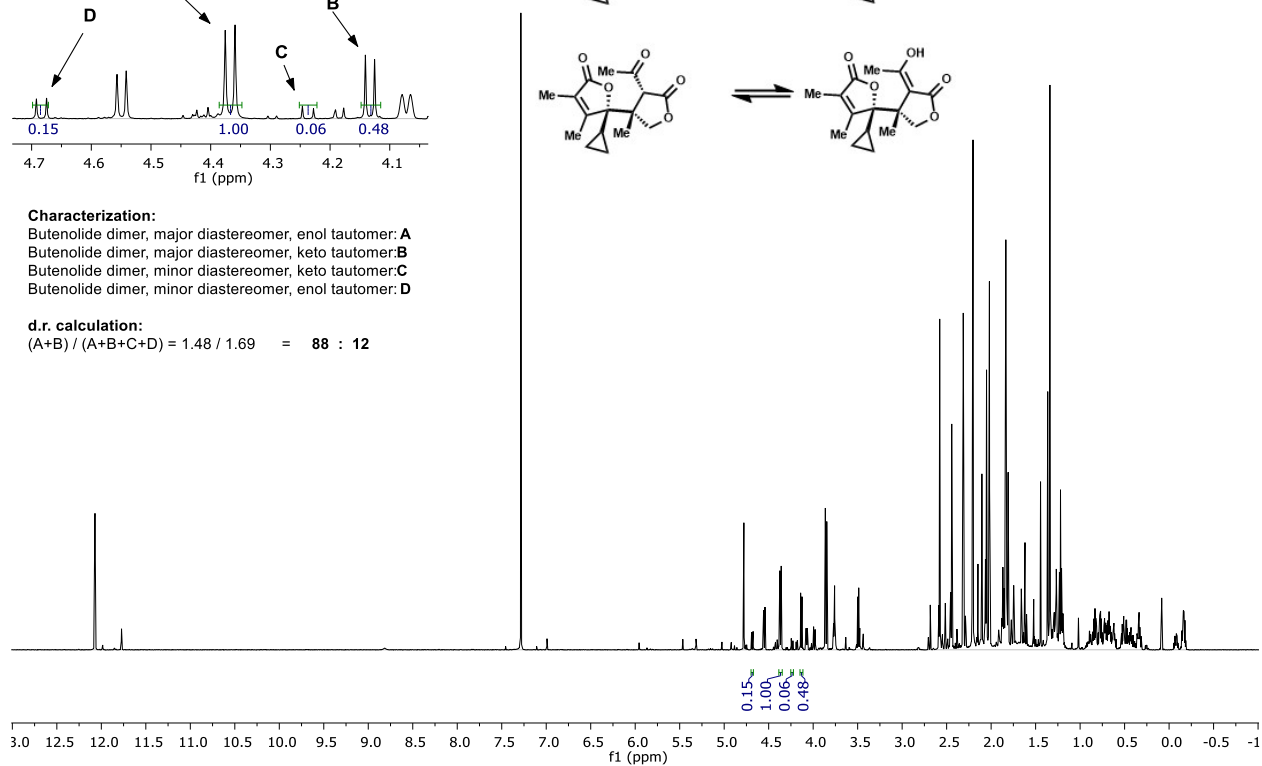
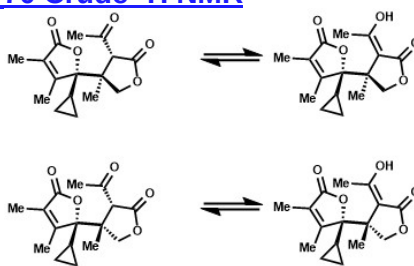


Characterization:

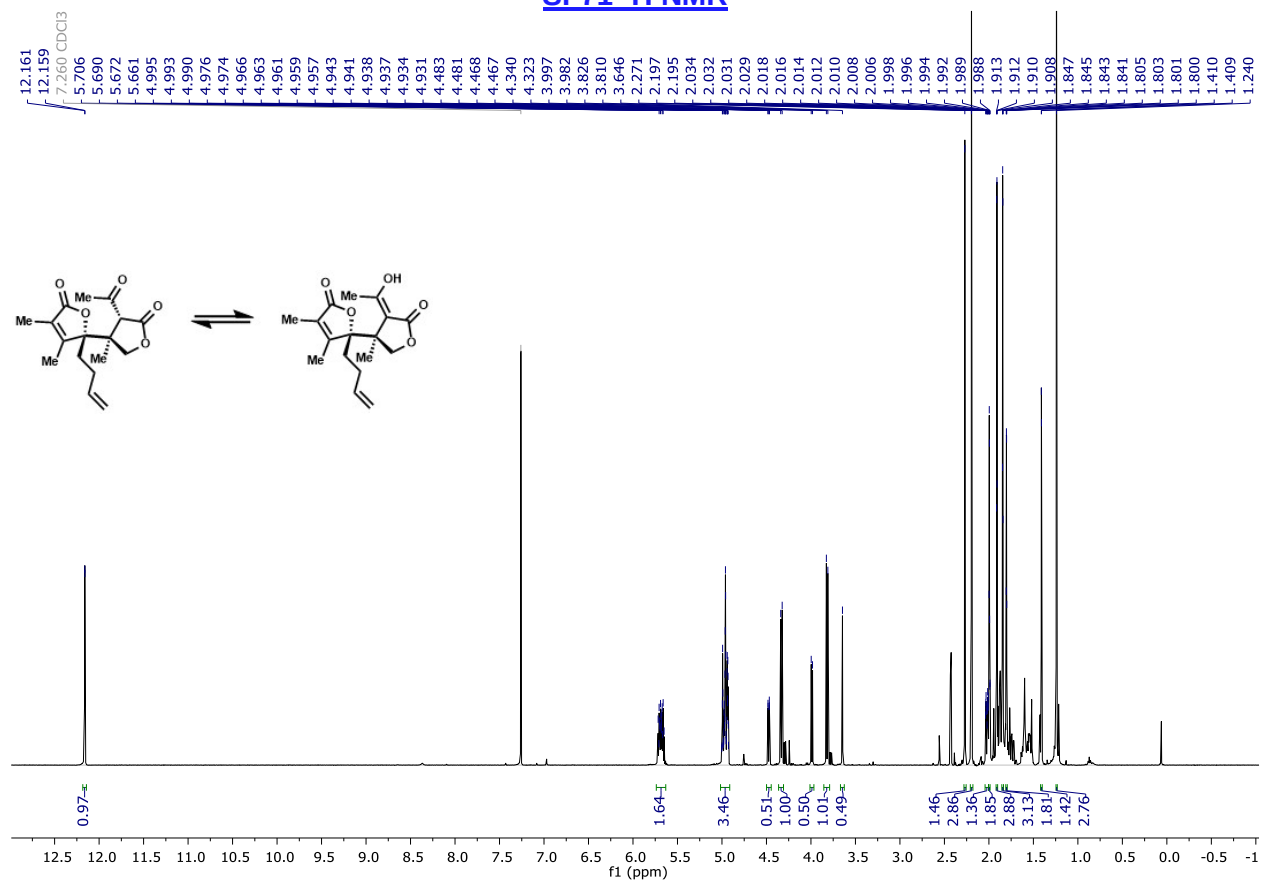
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

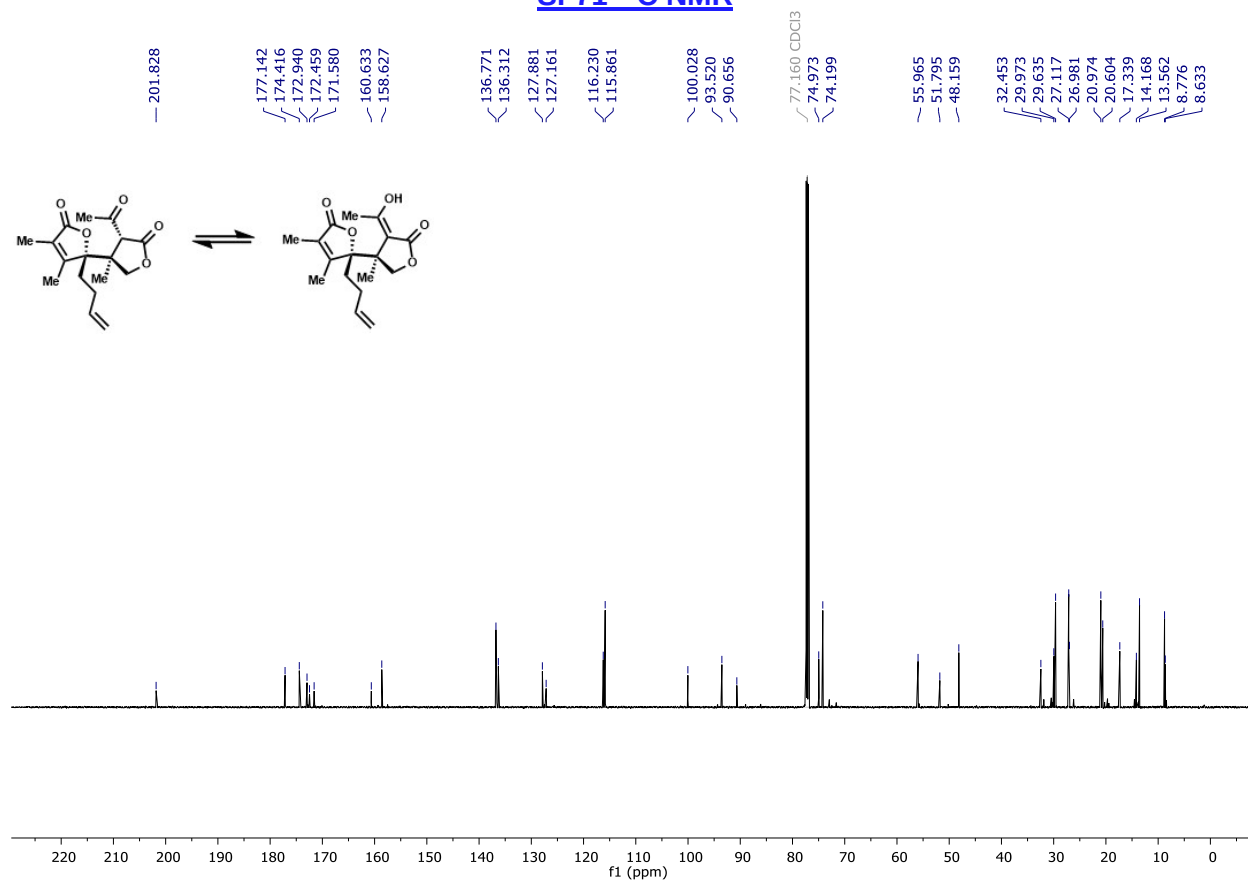
$$(A+B) / (A+B+C+D) = 1.48 / 1.69 = 88 : 12$$



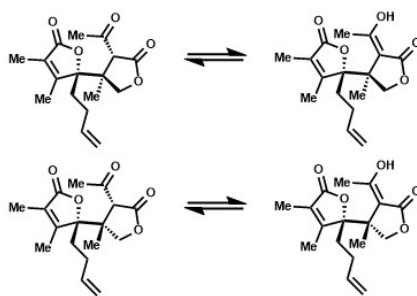
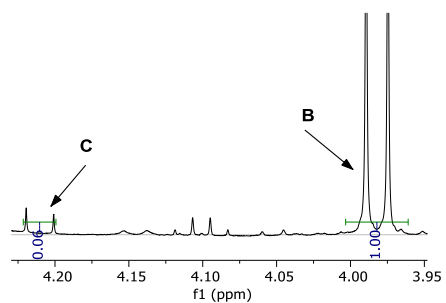
SI-71 ¹H NMR



SI-71 ¹³C NMR



SI-71 Crude ¹H NMR



Characterization:

Butenolide dimer, major diastereomer, enol tautomer:

A

Butenolide dimer, major diastereomer, keto tautomer:

B

Butenolide dimer, minor diastereomer, keto tautomer:

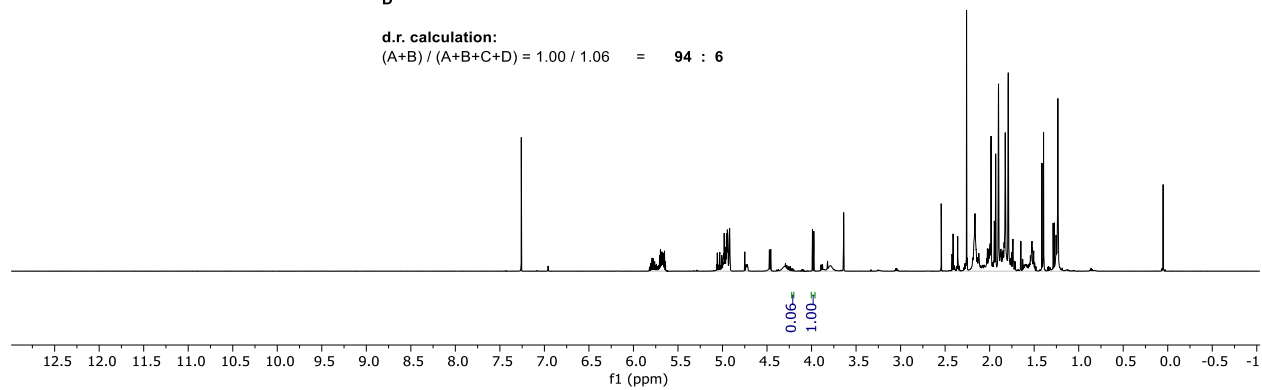
C

Butenolide dimer, minor diastereomer, enol tautomer:

D

d.r. calculation:

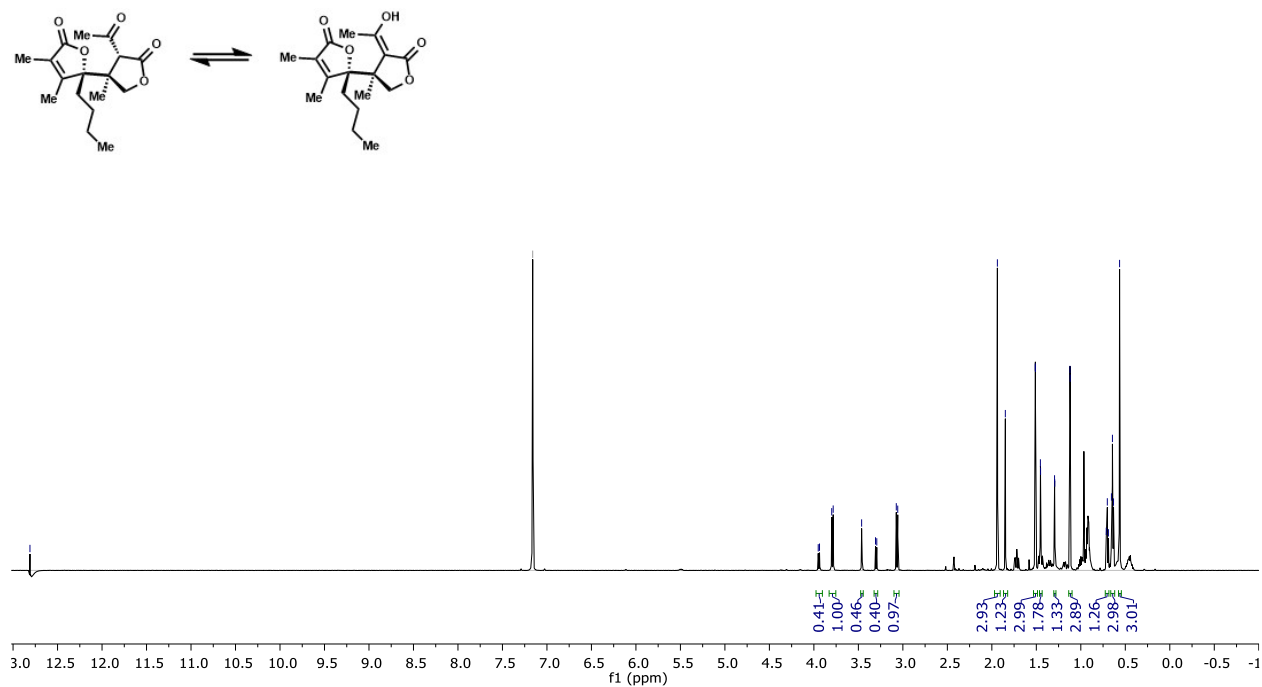
$$(A+B) / (A+B+C+D) = 1.00 / 1.06 = 94 : 6$$

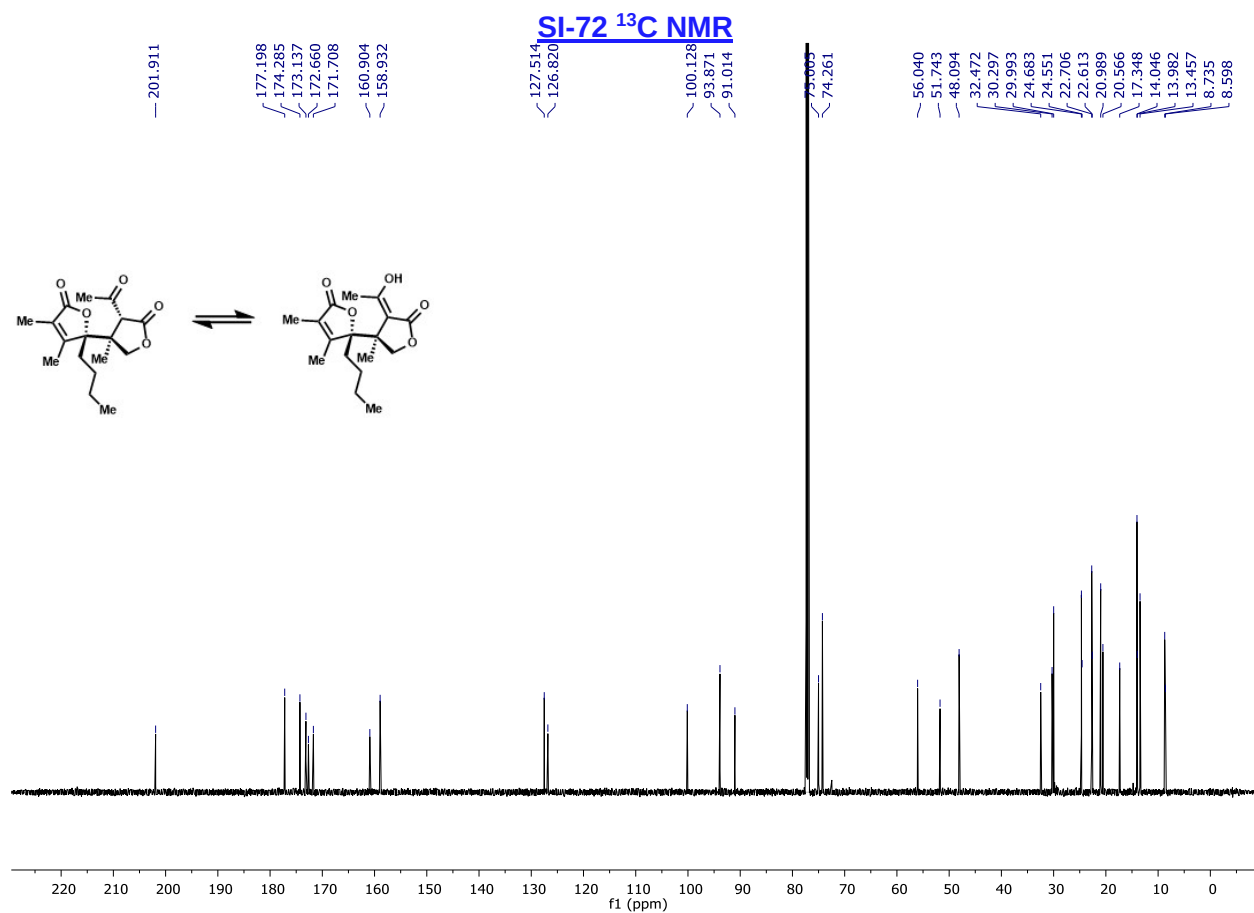


— 12.810

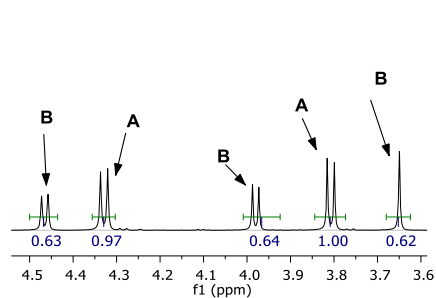
— 7.160 C6D6

SI-72 ¹H NMR





SI-72 Crude ¹H NMR

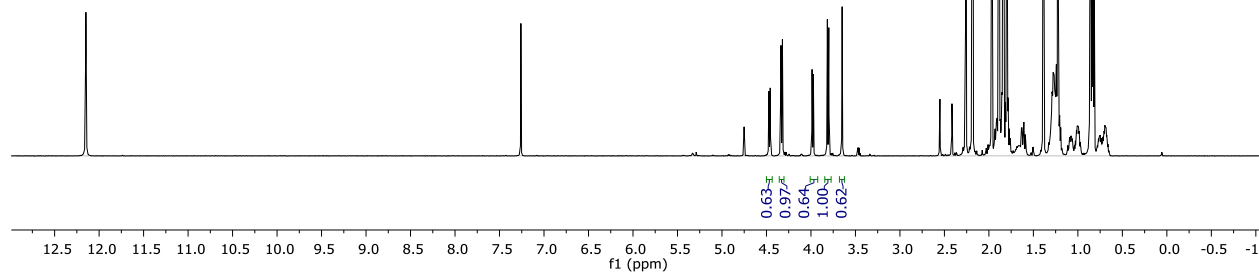
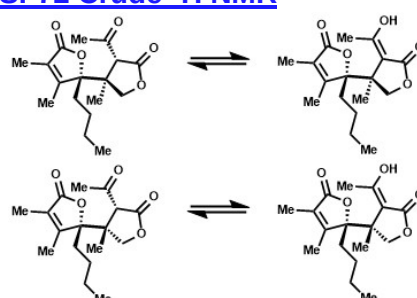


Characterization:

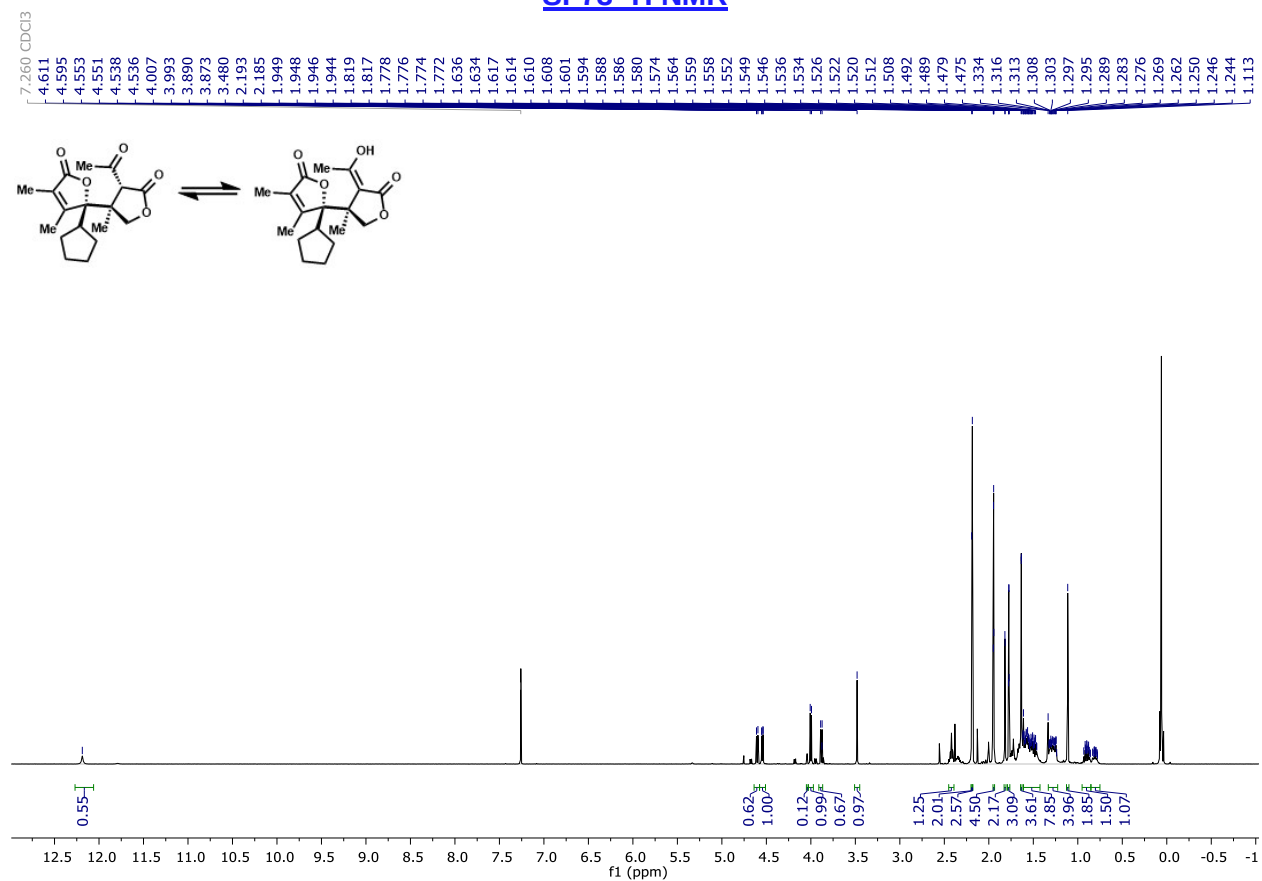
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

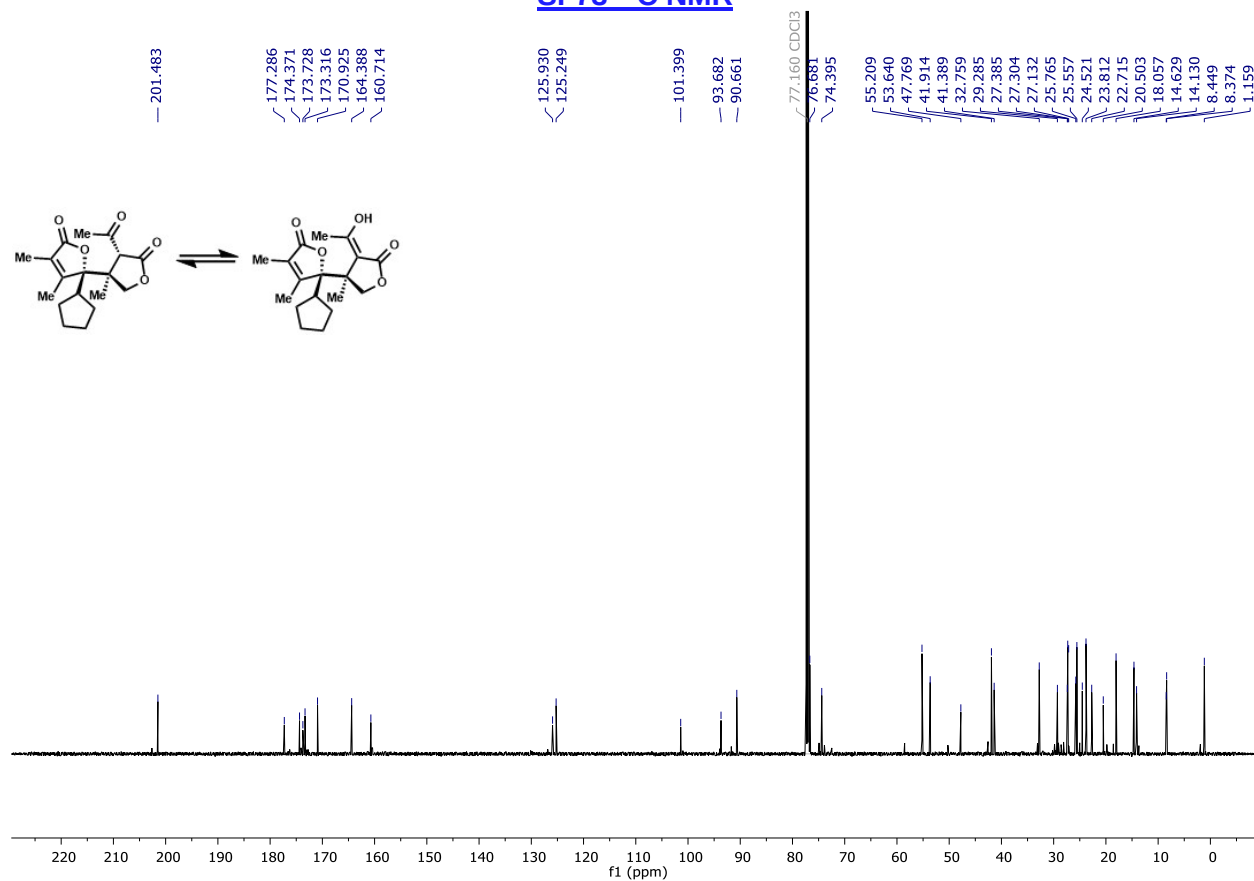
(A+B) / (A+B+C+D) = 1.64 / 1.64 = **100 : 0 (>95:5)**



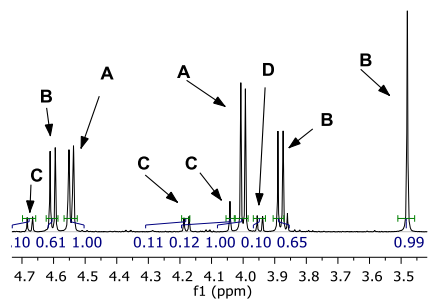
SI-73 ¹H NMR



SI-73 ¹³C NMR



SI-73 Crude ¹H NMR



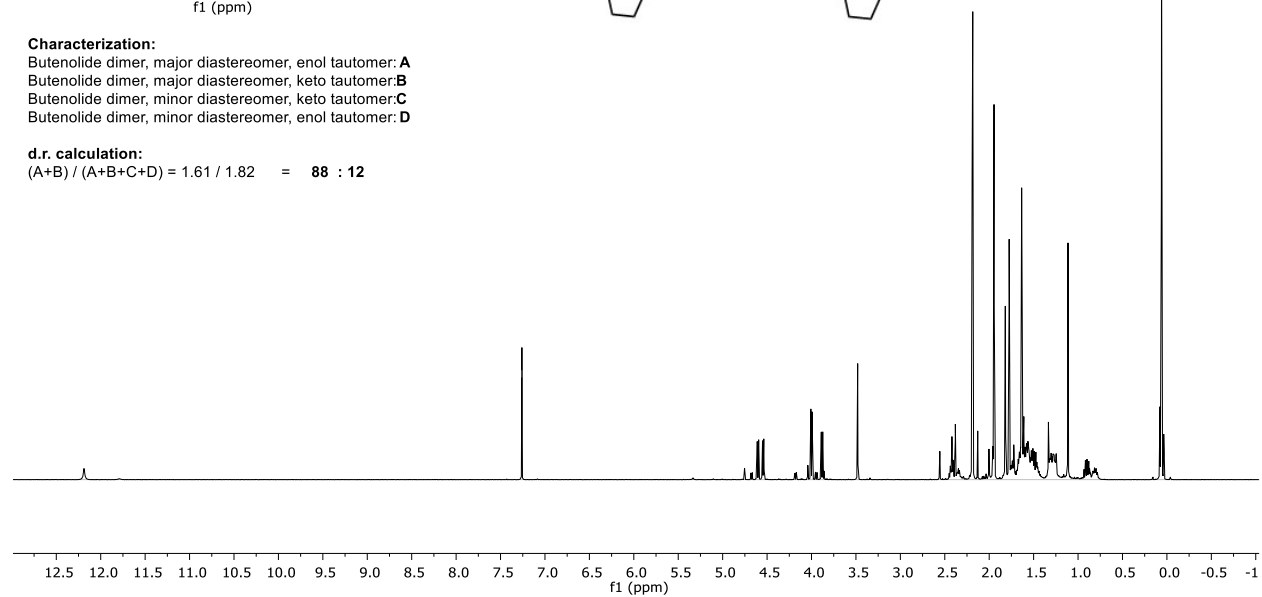
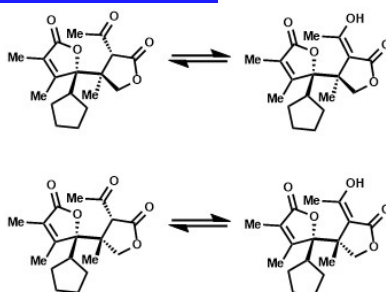
Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

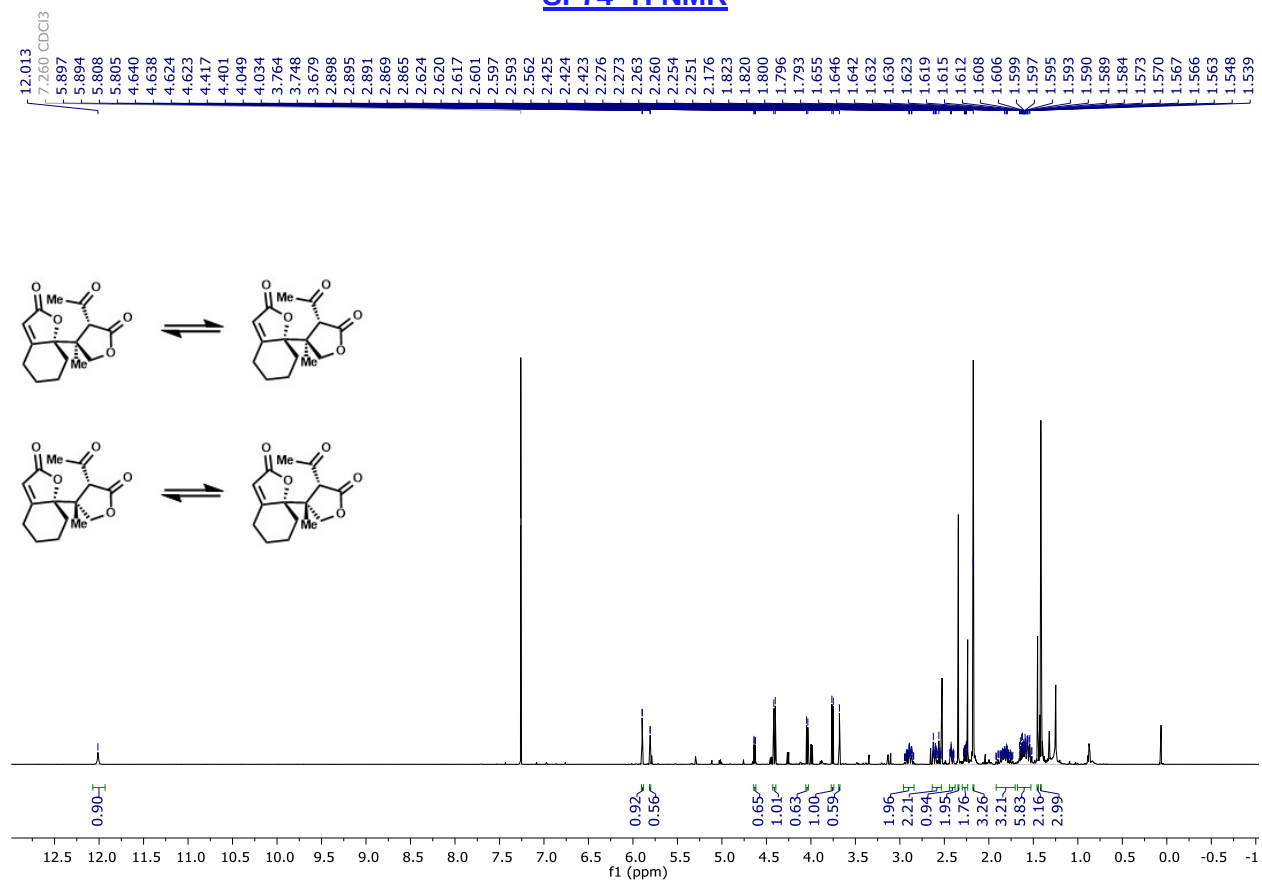
d.r. calculation:

(A+B) / (A+B+C+D) = 1.61 / 1.82 = **88 : 12**

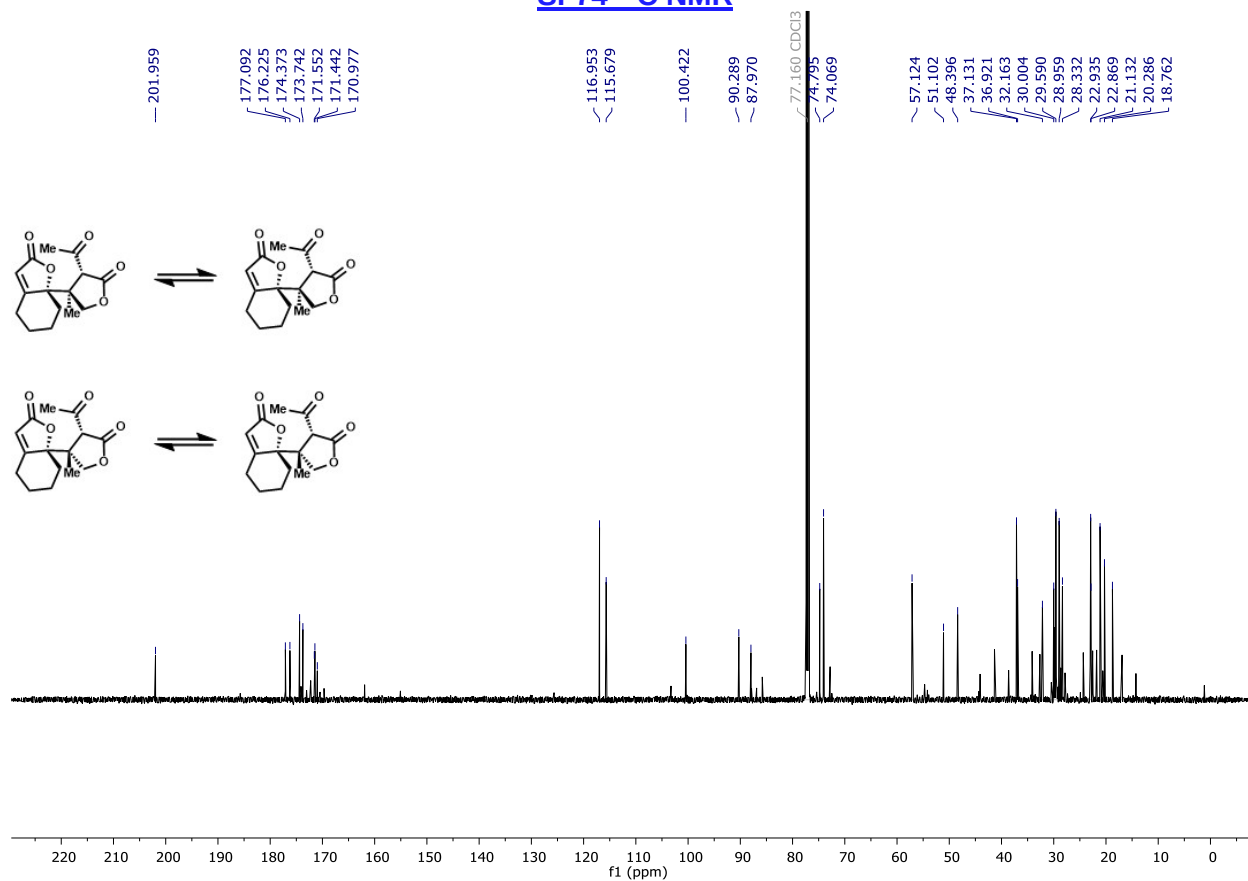
— 7.260 CDCl₃



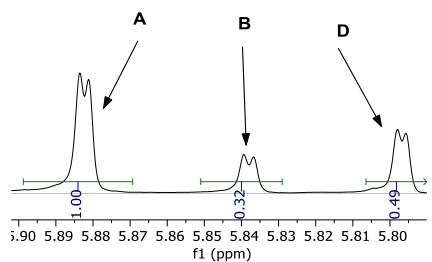
SI-74 ¹H NMR



SI-74 ¹³C NMR



SI-74 Crude ¹H NMR

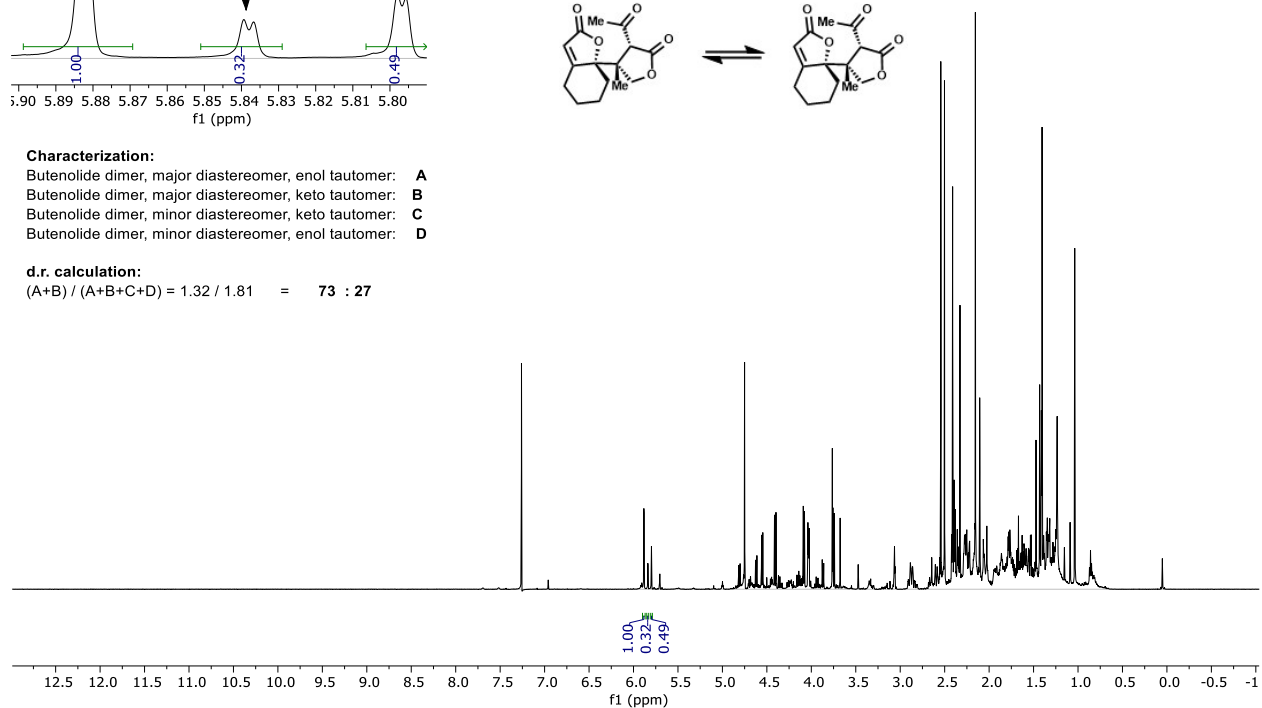
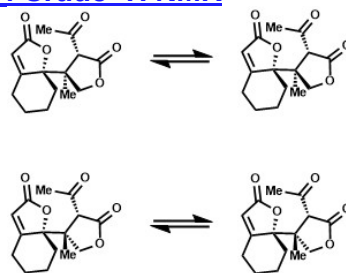


Characterization:

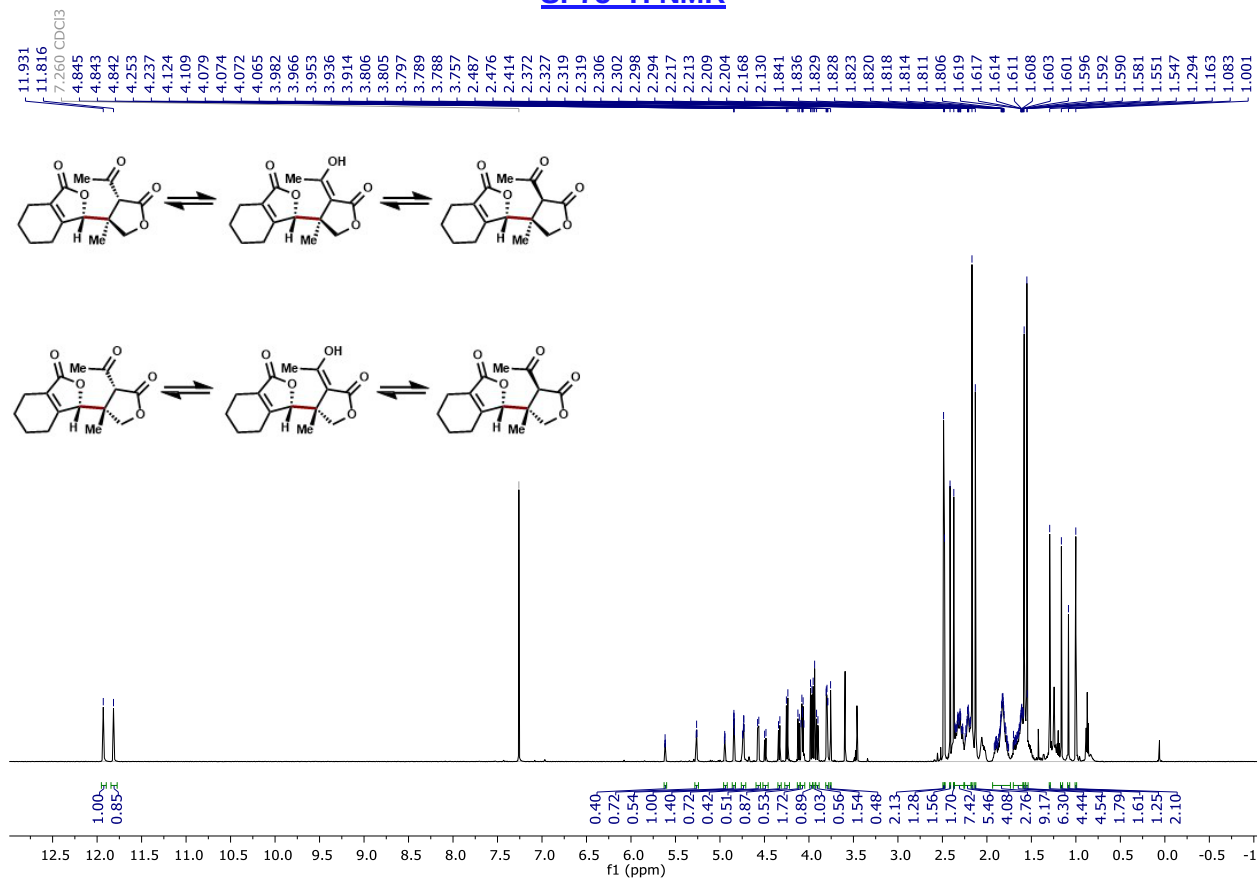
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

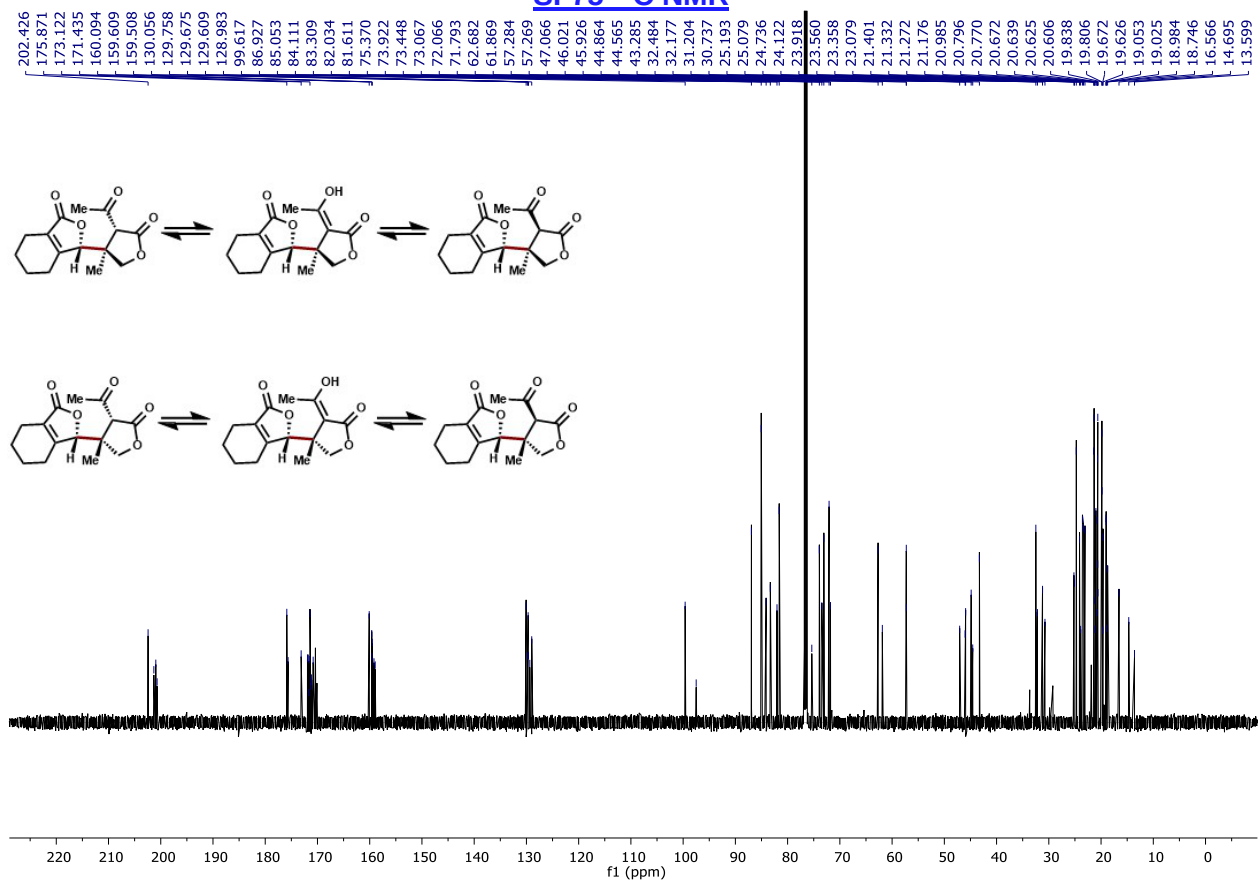
$$(A+B) / (A+B+C+D) = 1.32 / 1.81 = 73 : 27$$

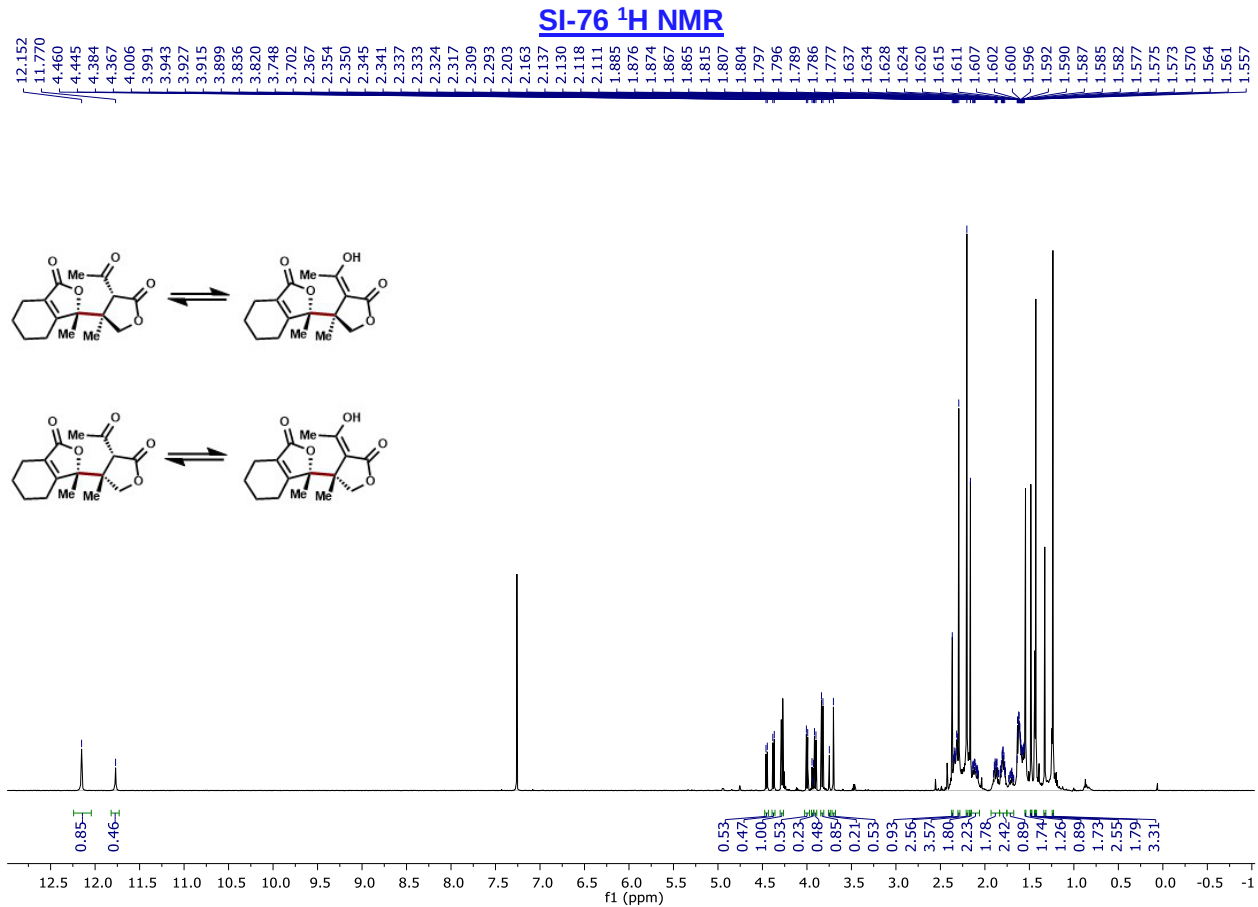


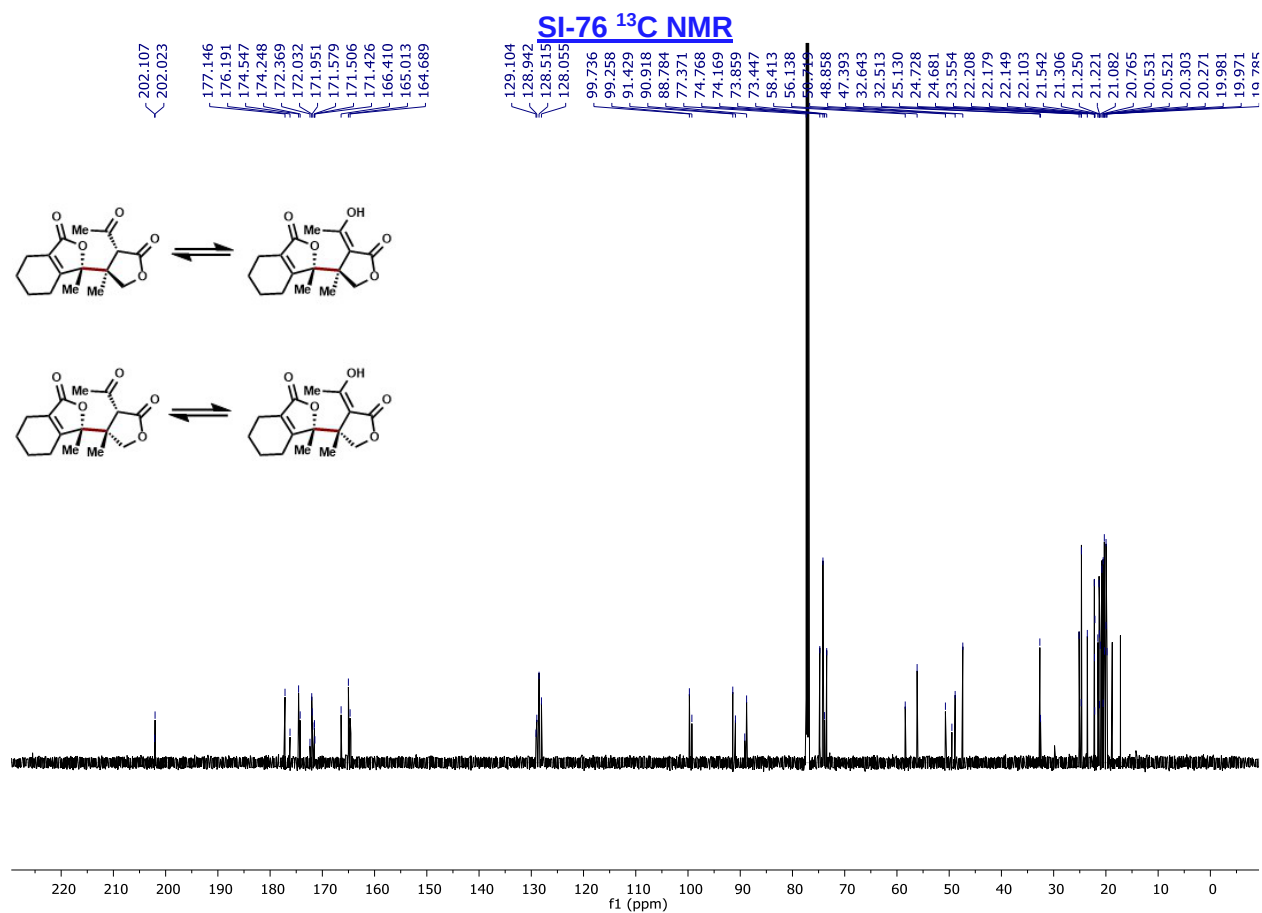
SI-75 ^1H NMR



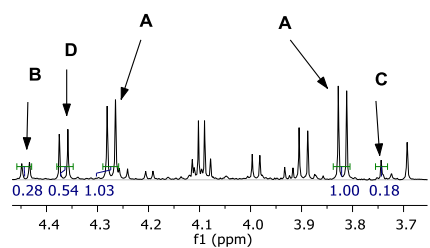
SI-75 ¹³C NMR







SI-76 Crude ¹H NMR

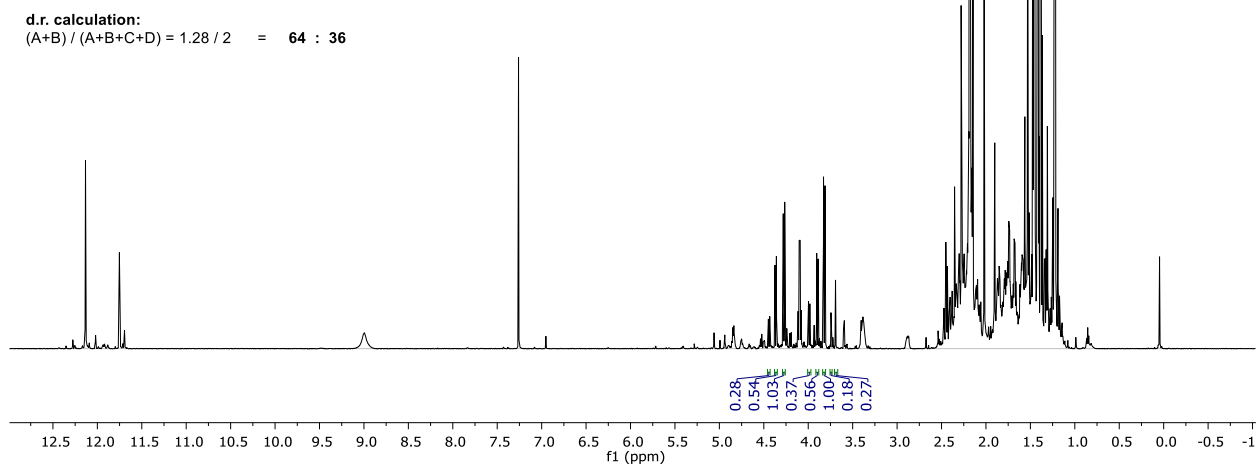
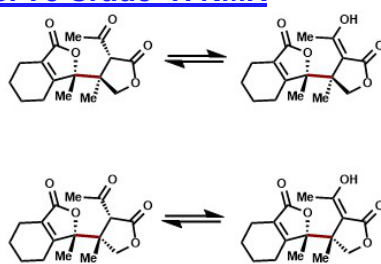


Characterization:

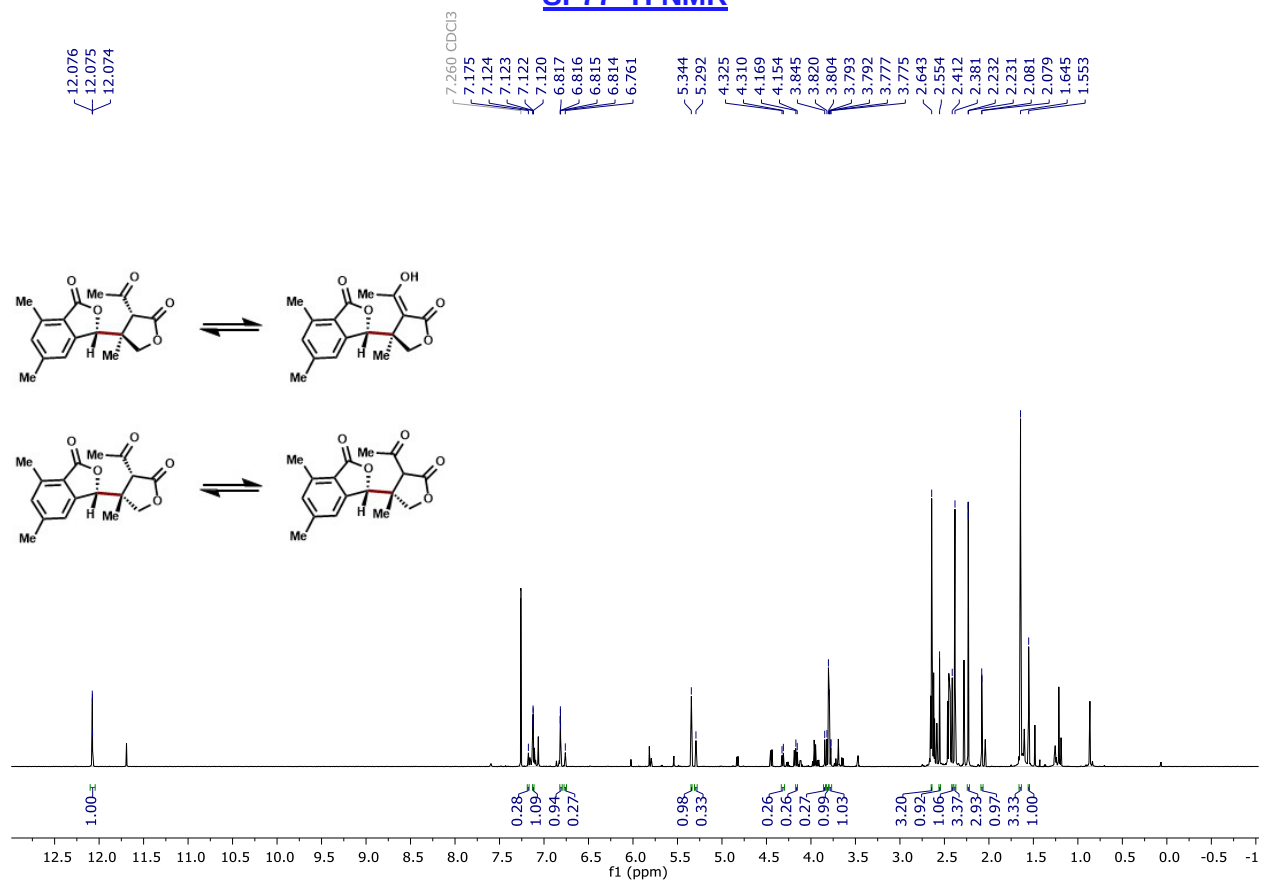
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

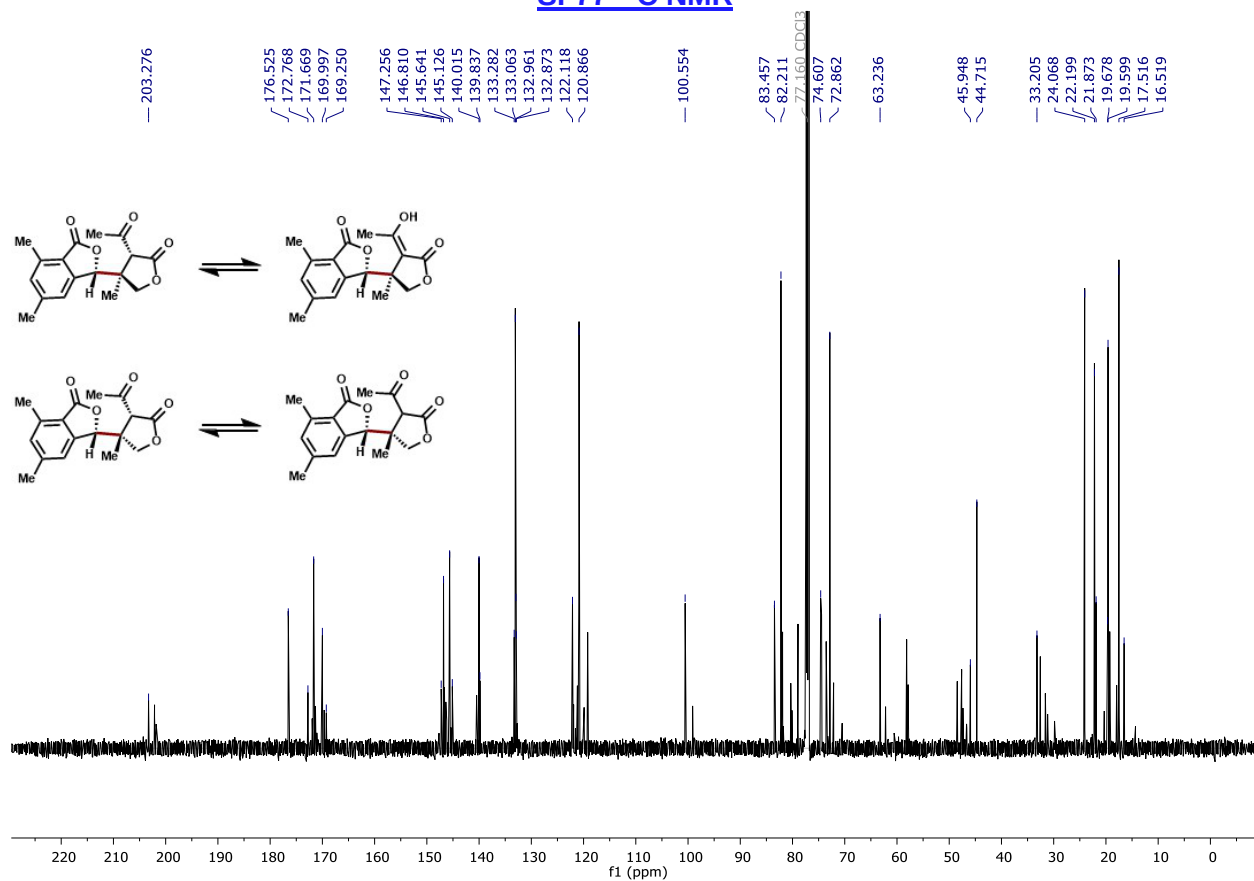
$$(A+B) / (A+B+C+D) = 1.28 / 2 = 64 : 36$$



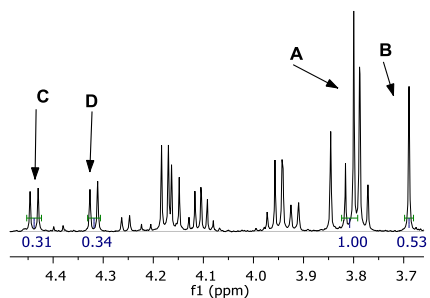
SI-77 ¹H NMR



SI-77 ¹³C NMR



SI-77 Crude ¹H NMR

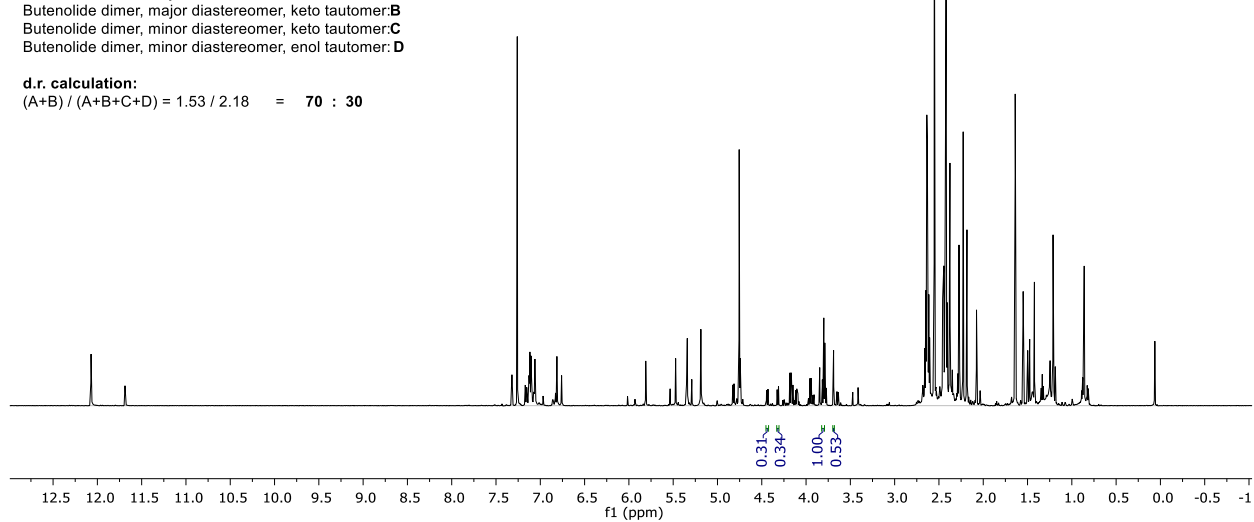
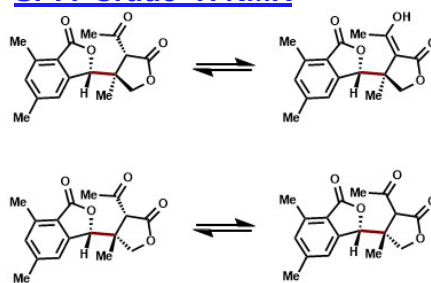


Characterization:

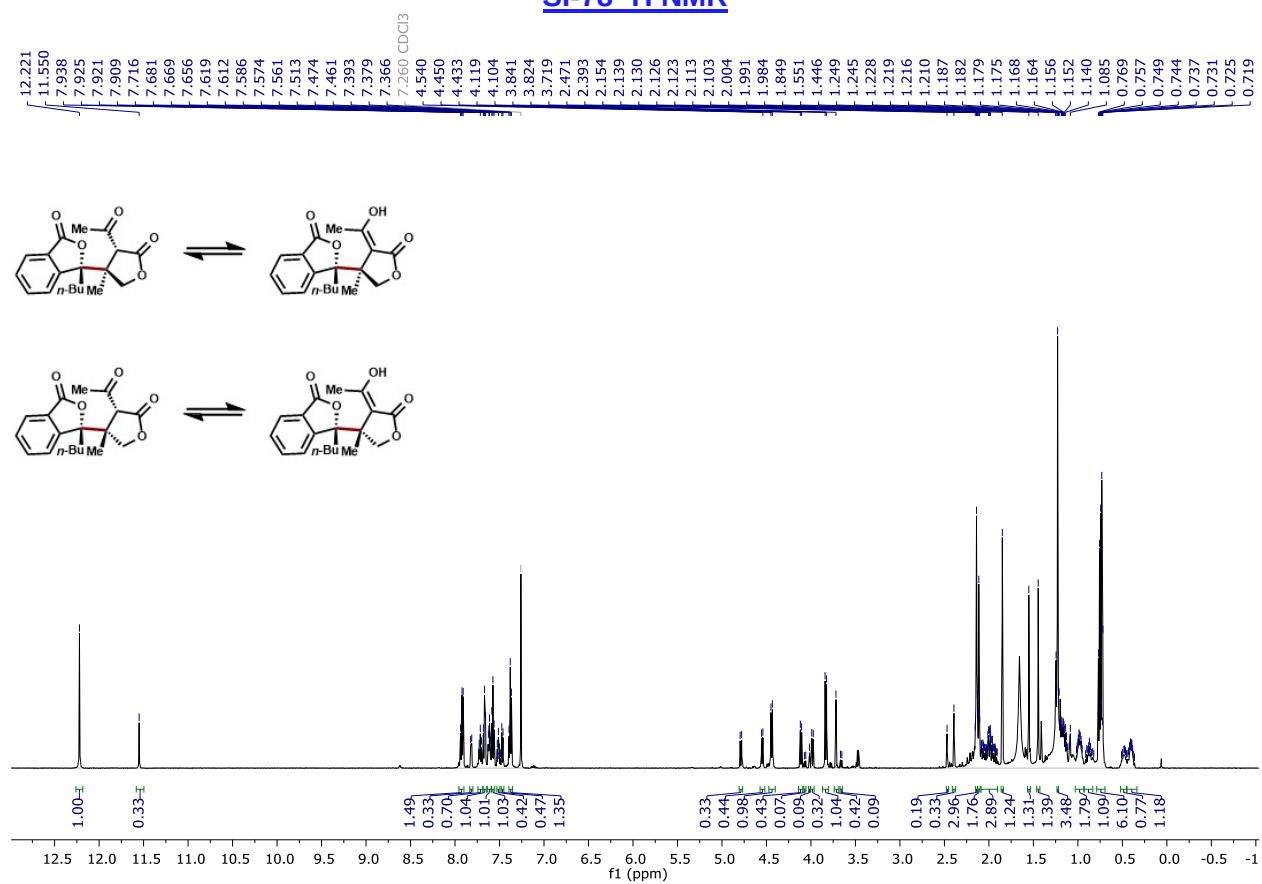
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

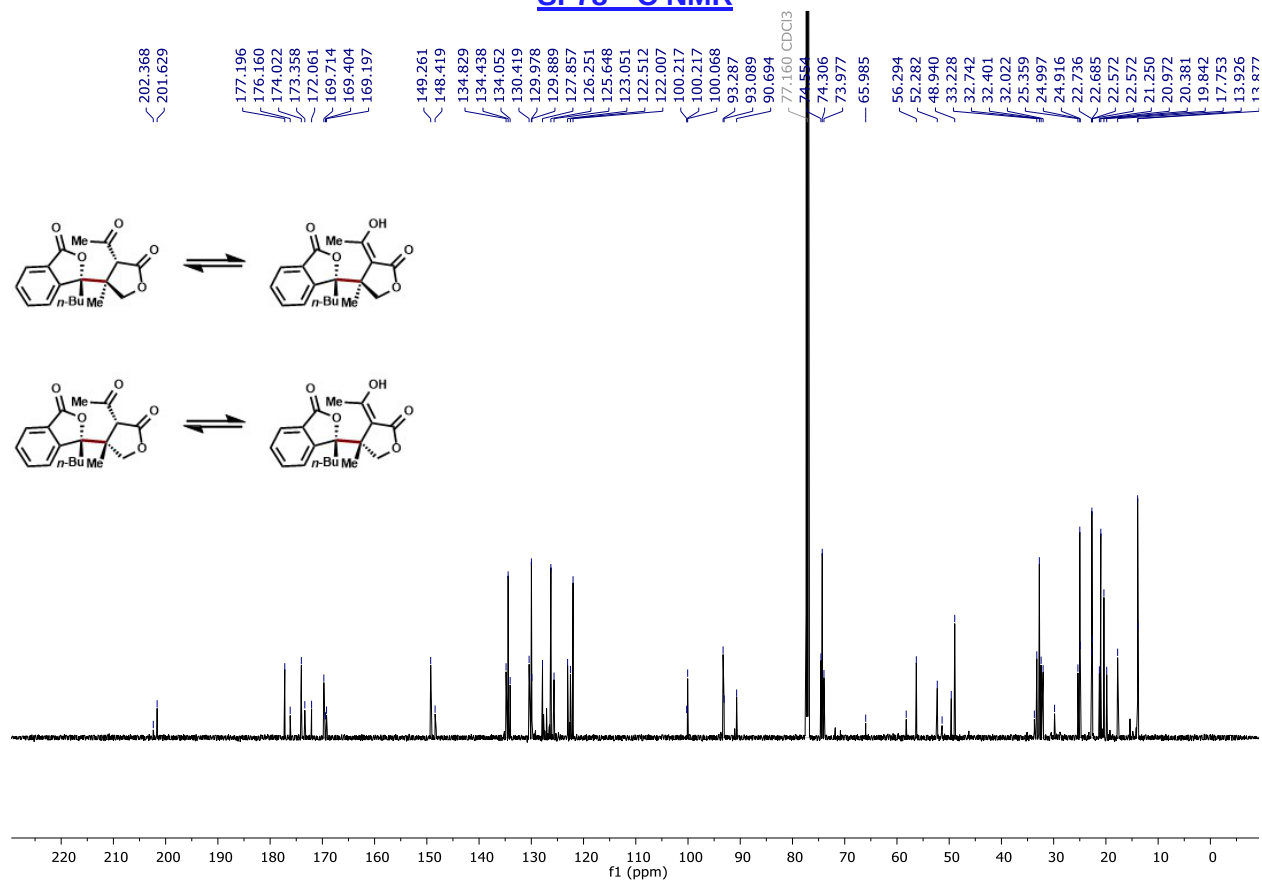
$$(A+B) / (A+B+C+D) = 1.53 / 2.18 = 70 : 30$$



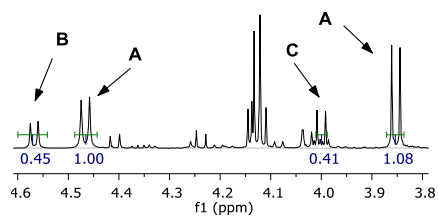
SI-78 ¹H NMR



SI-78 ¹³C NMR



SI-78 Crude ¹H NMR

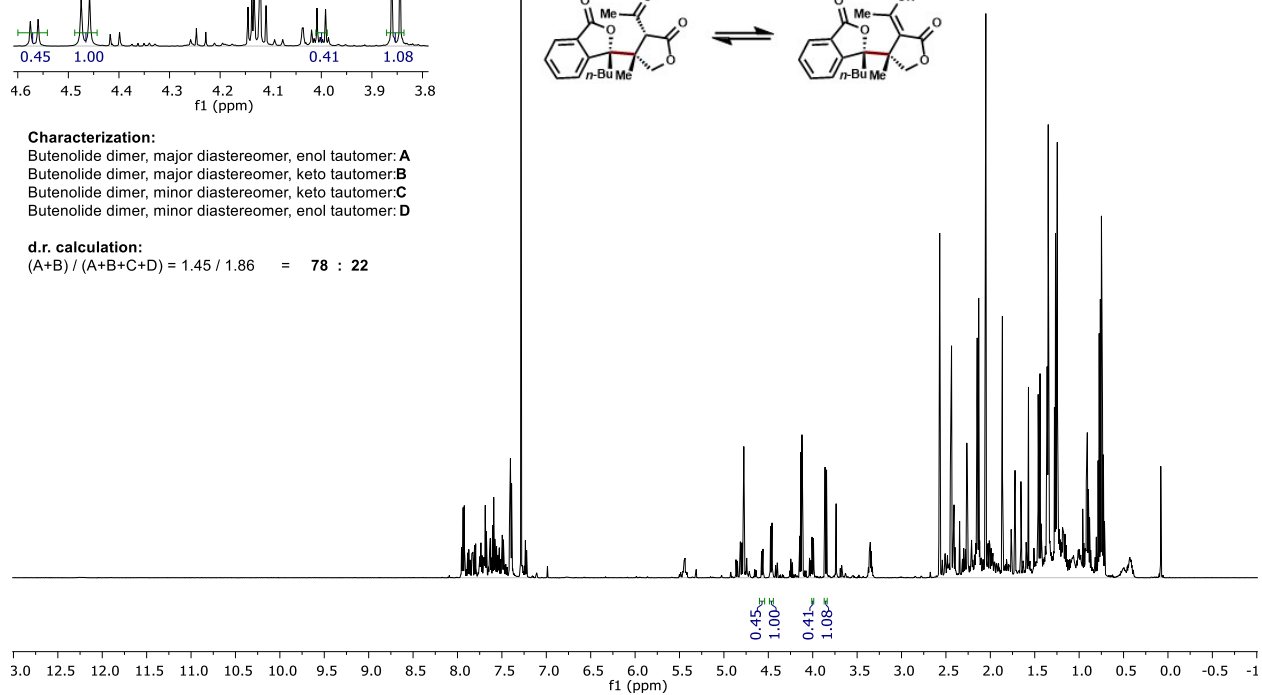
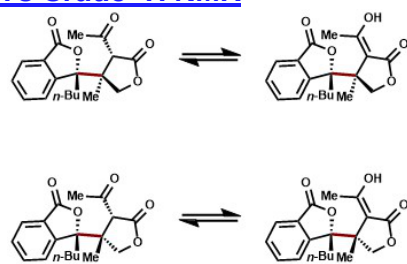


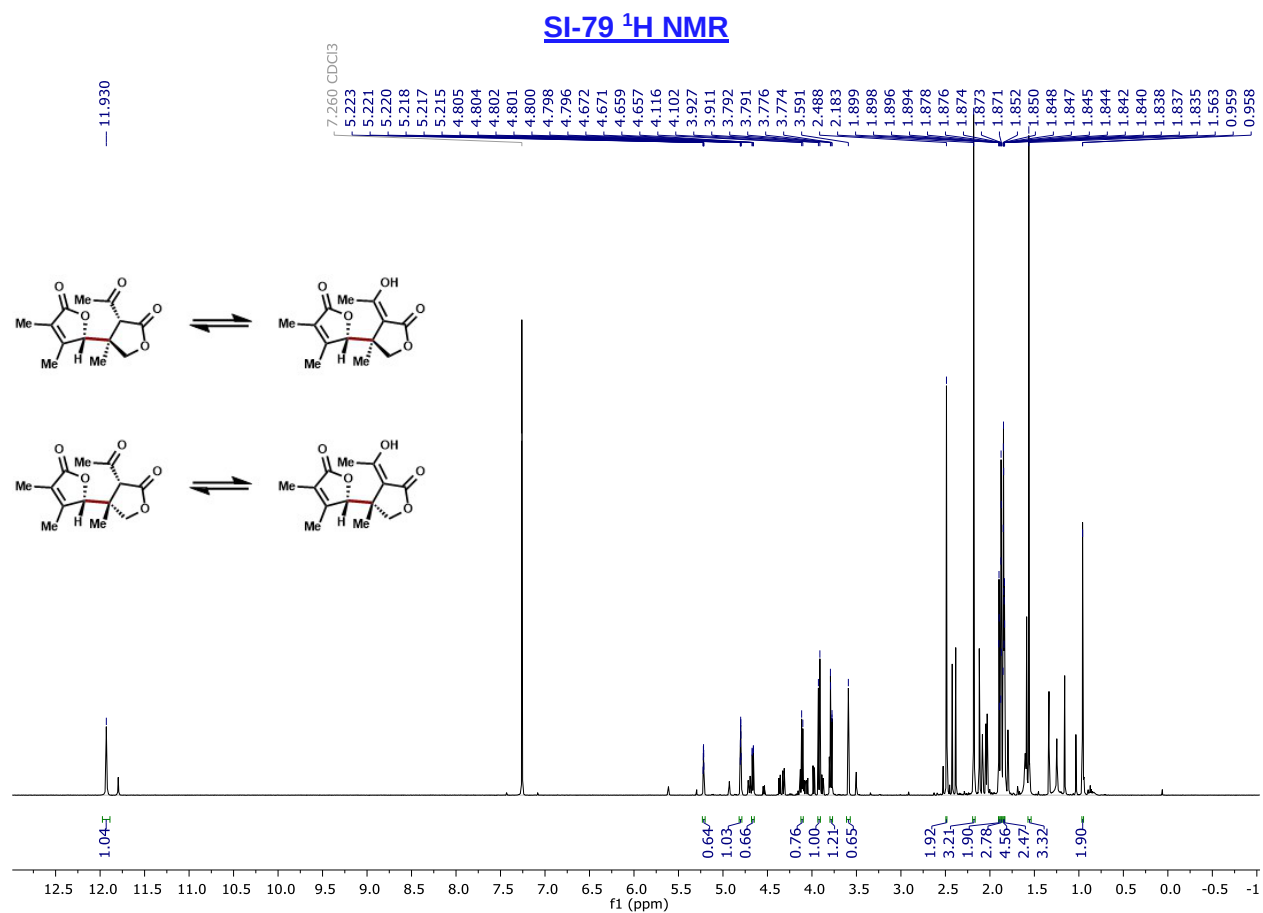
Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

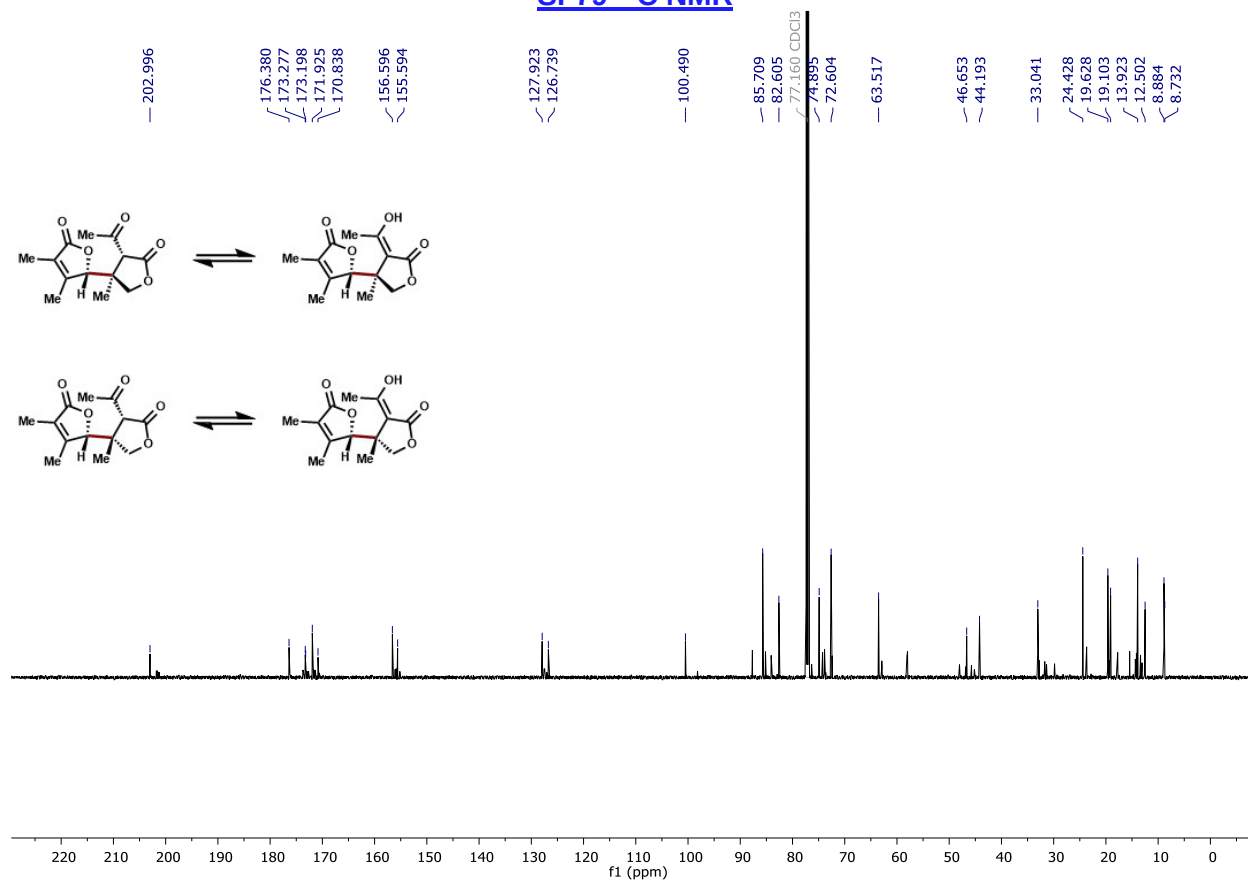
d.r. calculation:

$$(A+B) / (A+B+C+D) = 1.45 / 1.86 = 78 : 22$$

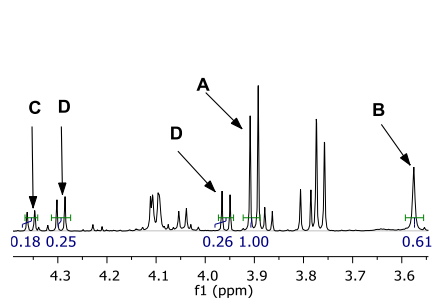




SI-79 ¹³C NMR



SI-79 Crude ¹H NMR



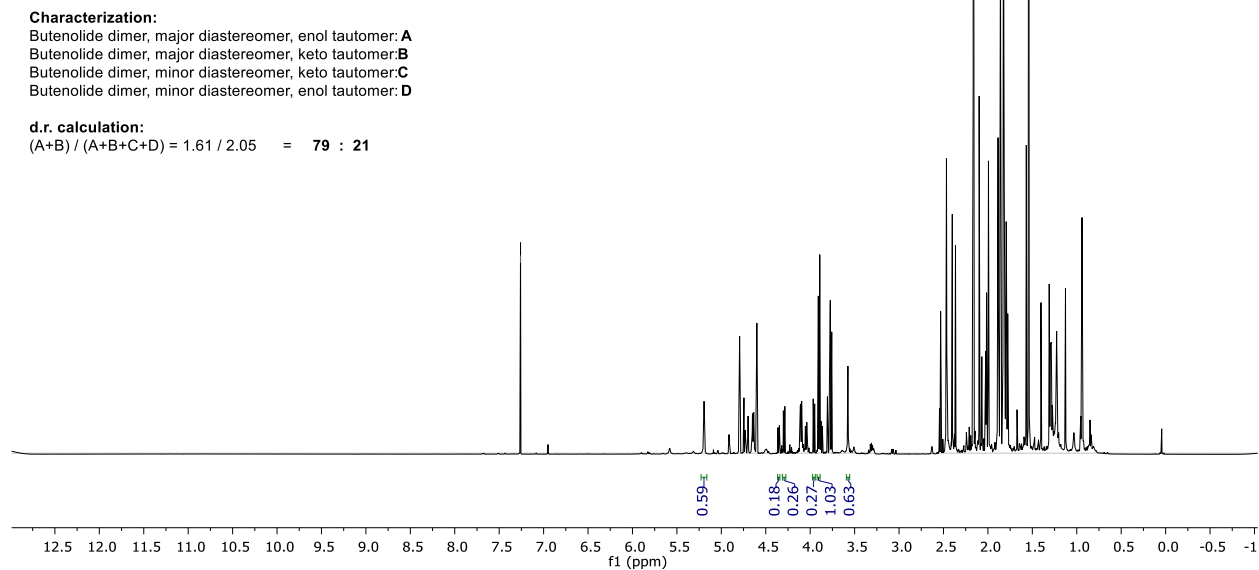
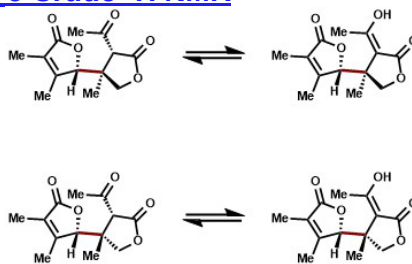
Characterization:

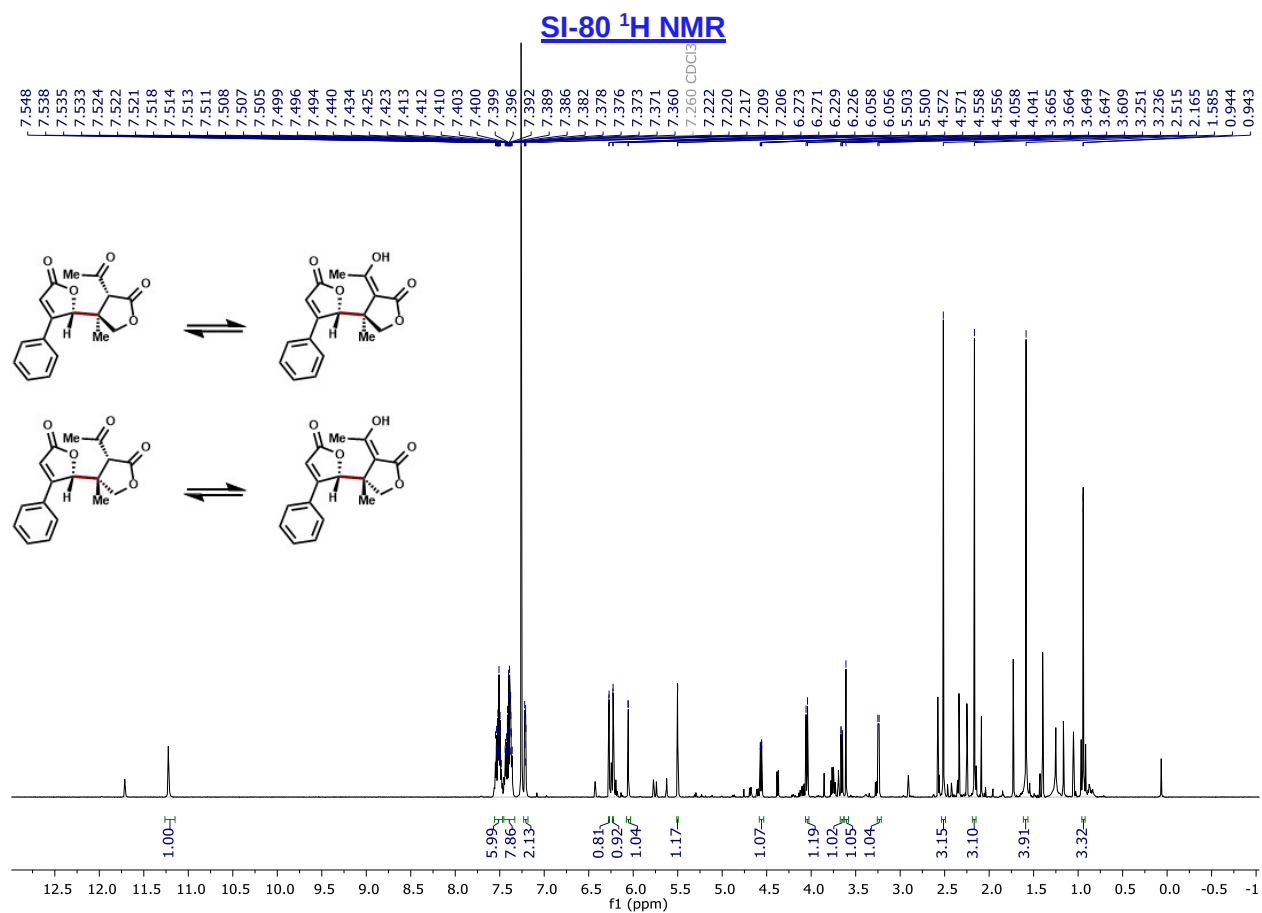
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

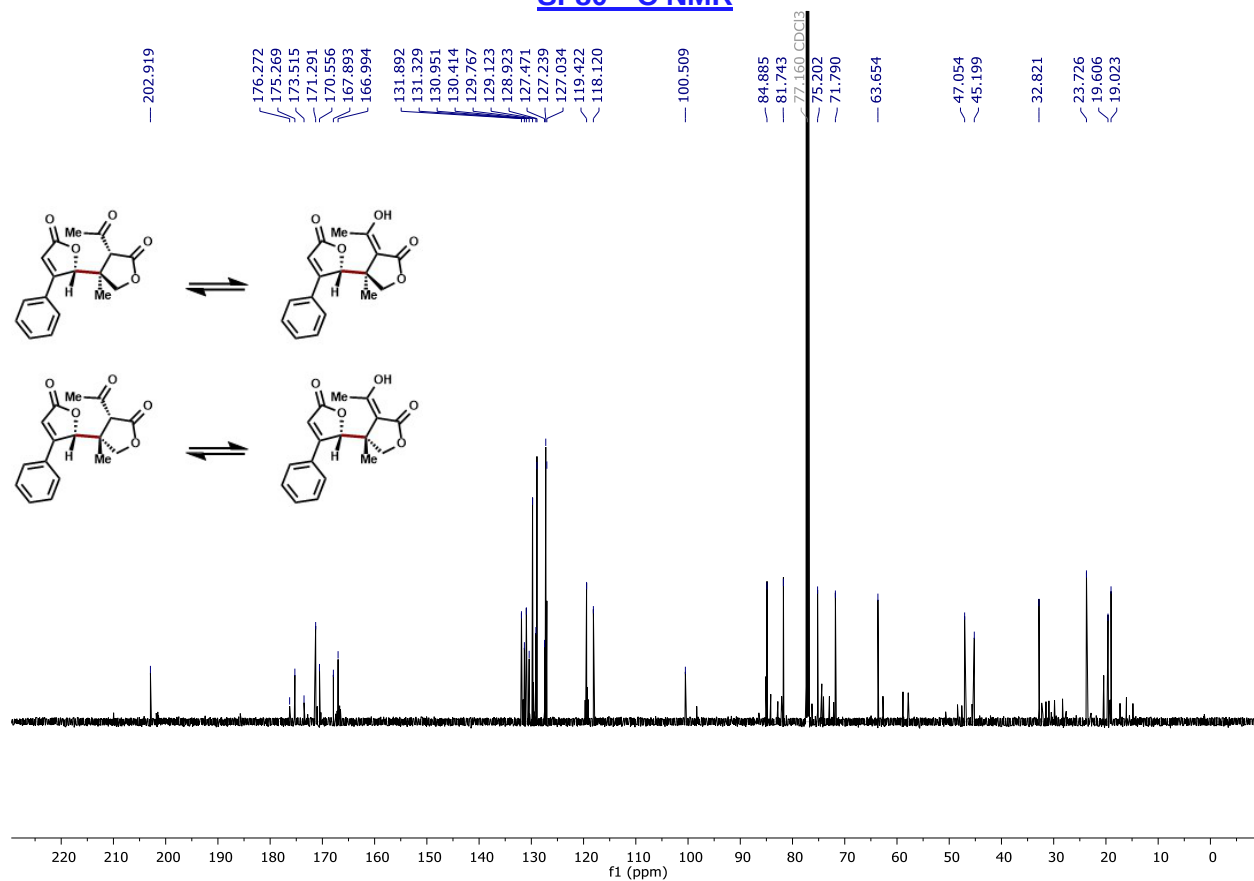
$$(A+B) / (A+B+C+D) = 1.61 / 2.05 = 79 : 21$$

— 7.260 CDCl₃

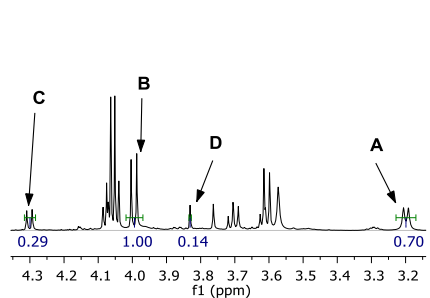




SI-80 ¹³C NMR



SI-80 Crude ¹H NMR

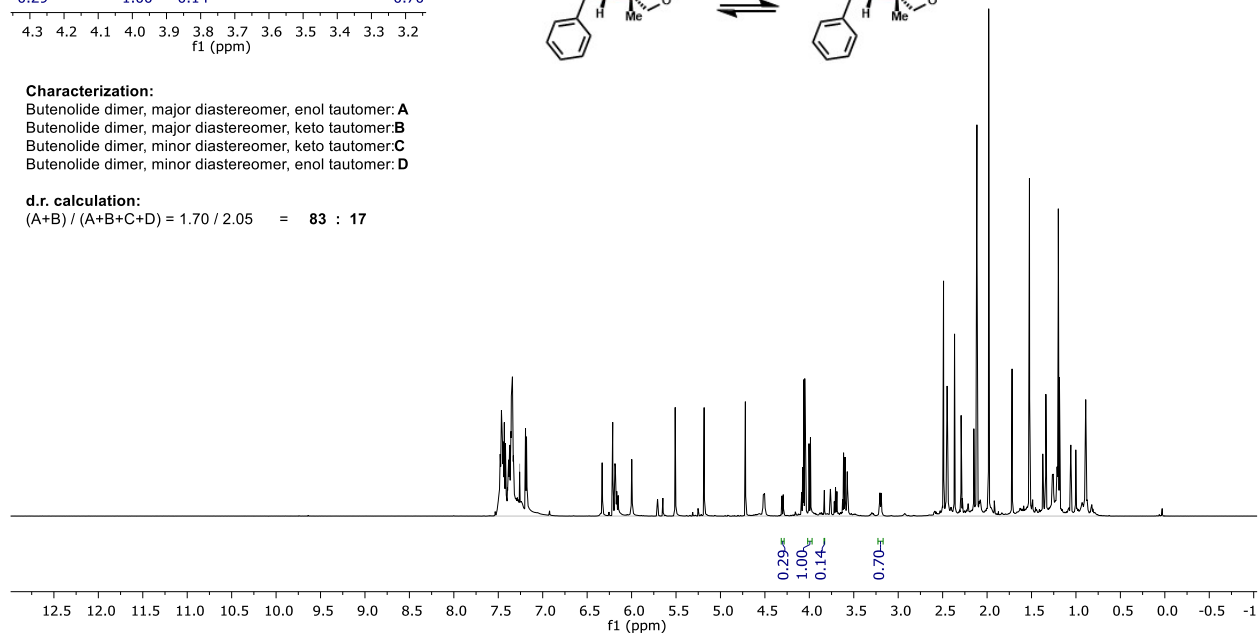
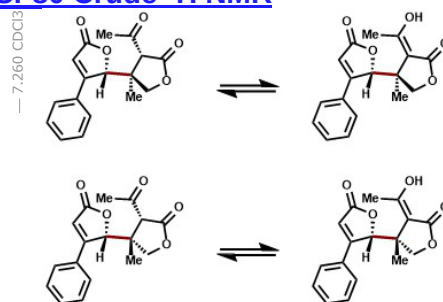


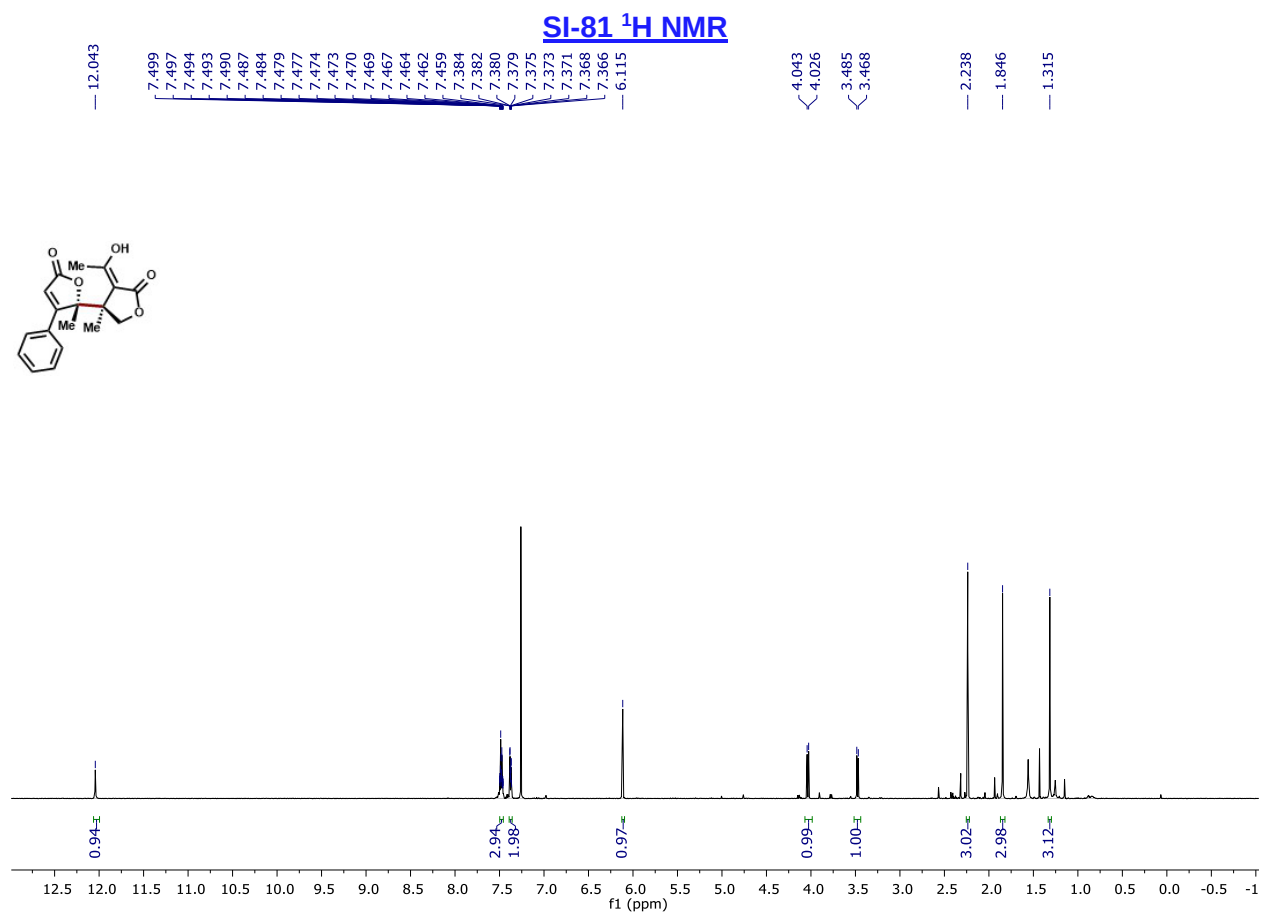
Characterization:

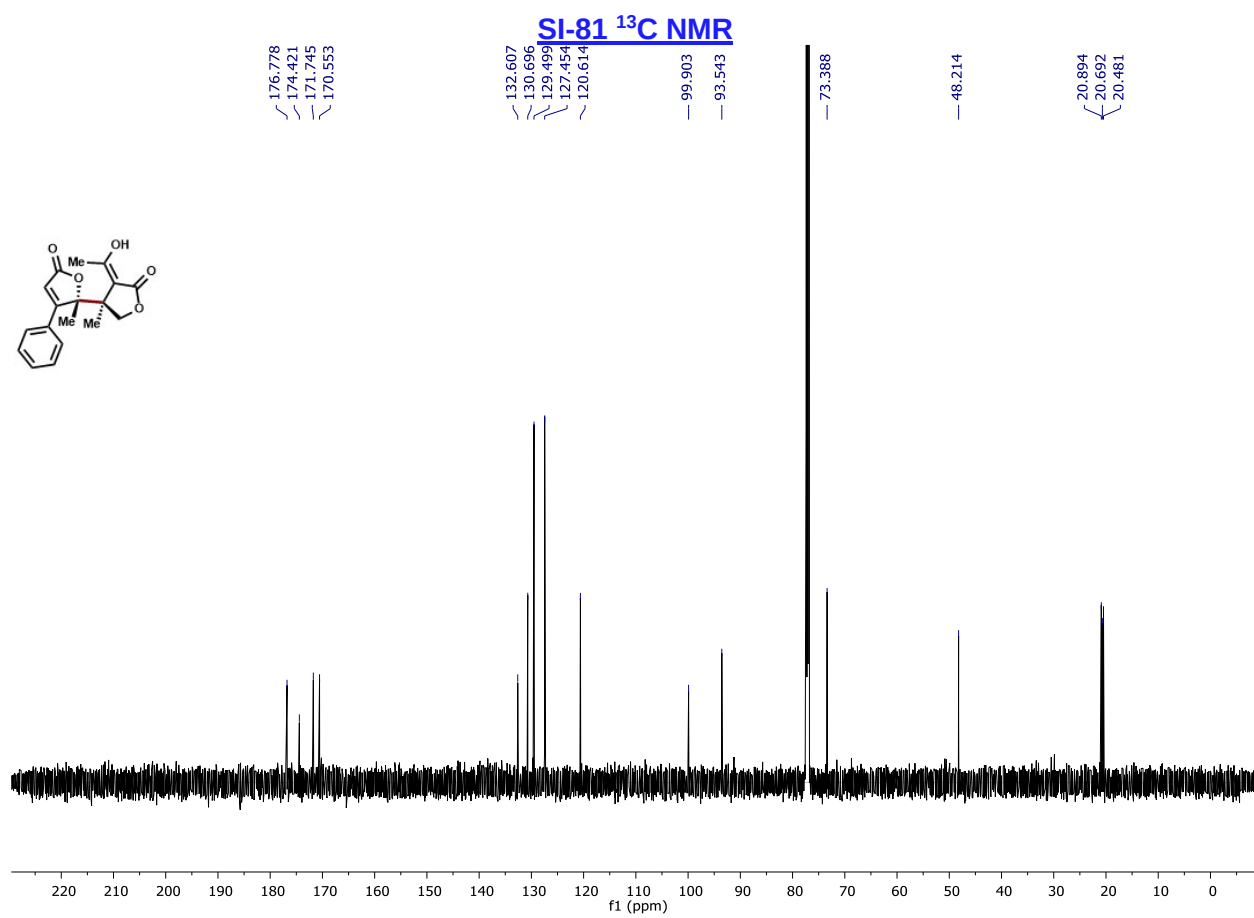
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

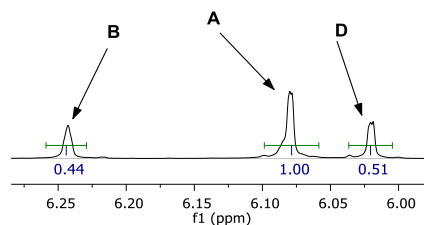
(A+B) / (A+B+C+D) = 1.70 / 2.05 = **83 : 17**







SI-81 Crude ¹H NMR

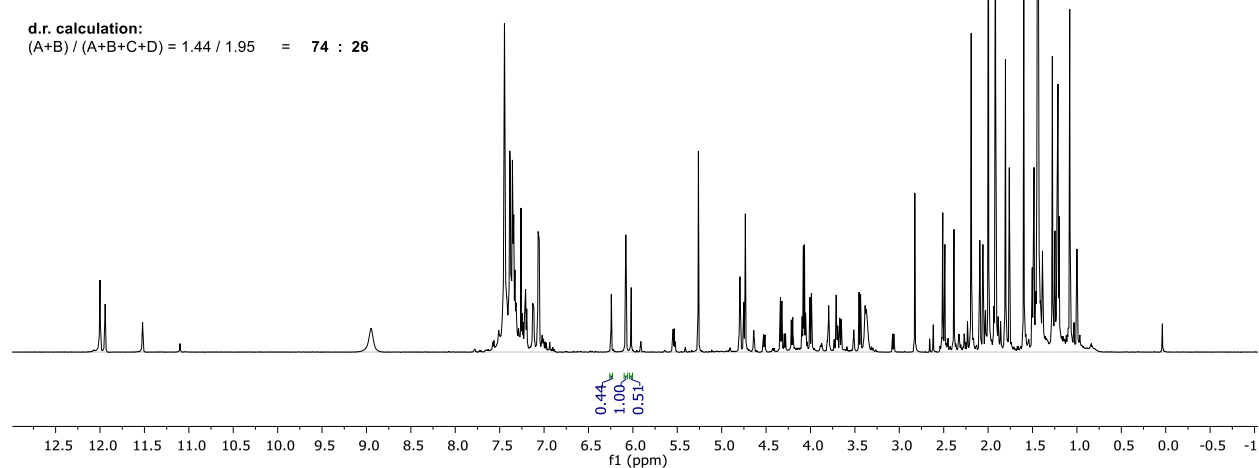
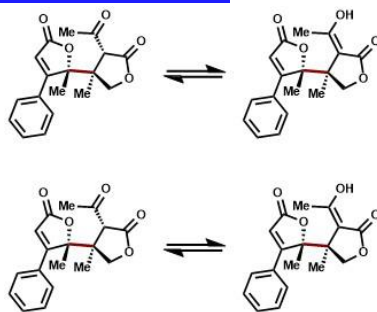


Characterization:

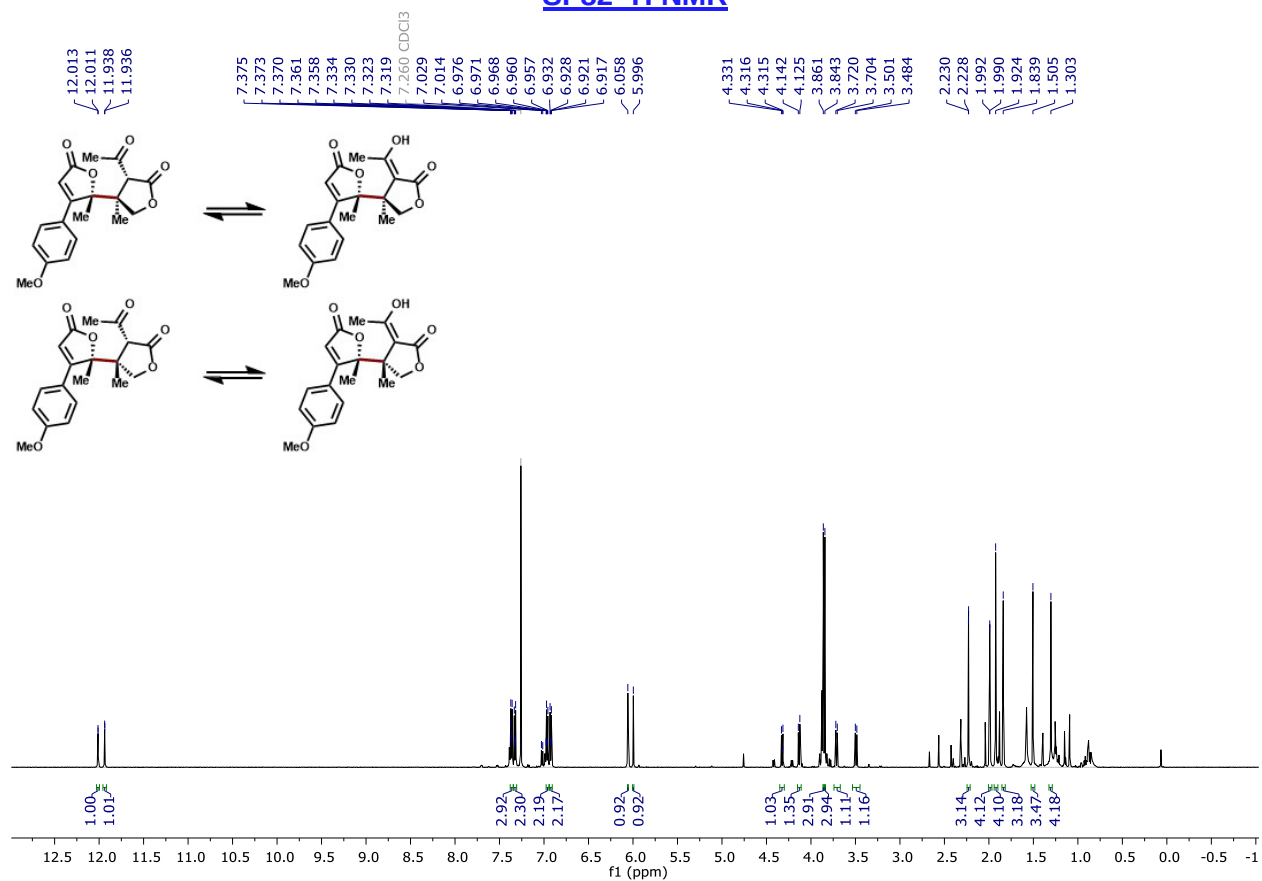
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

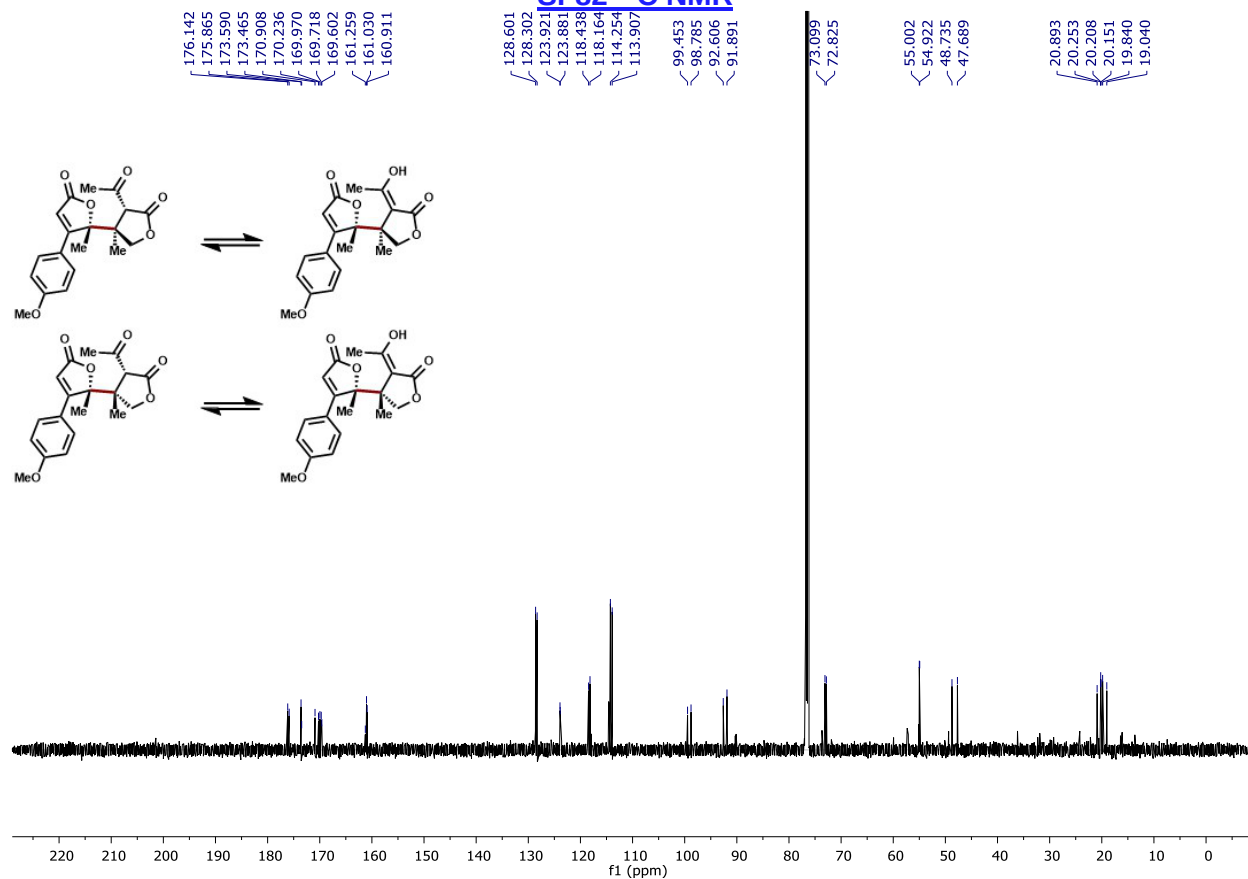
(A+B) / (A+B+C+D) = 1.44 / 1.95 = **74 : 26**



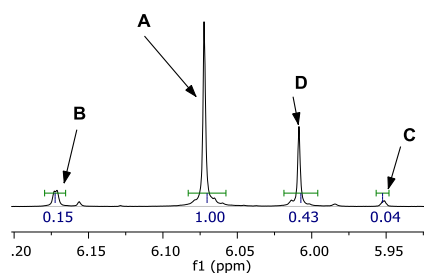
SI-82 ¹H NMR



SI-82 ¹³C NMR



SI-82 Crude ¹H NMR

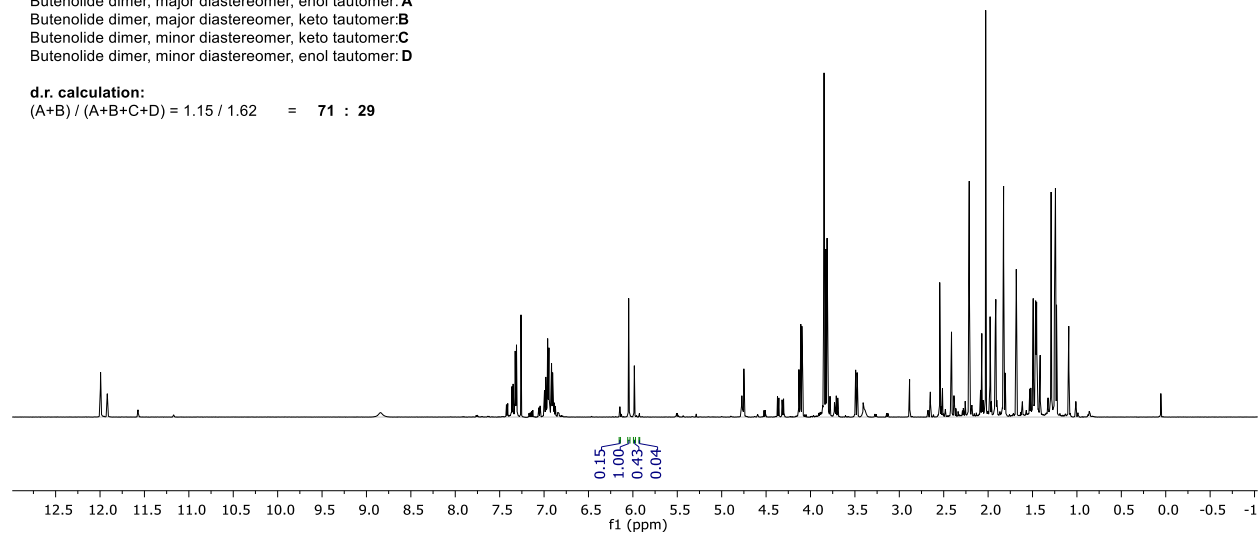
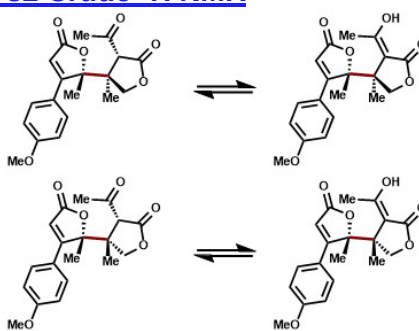


Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

$$(A+B) / (A+B+C+D) = 1.15 / 1.62 = 71 : 29$$



Rapid Quench

Figure 3a entry 2 (Crude ^1H NMR)

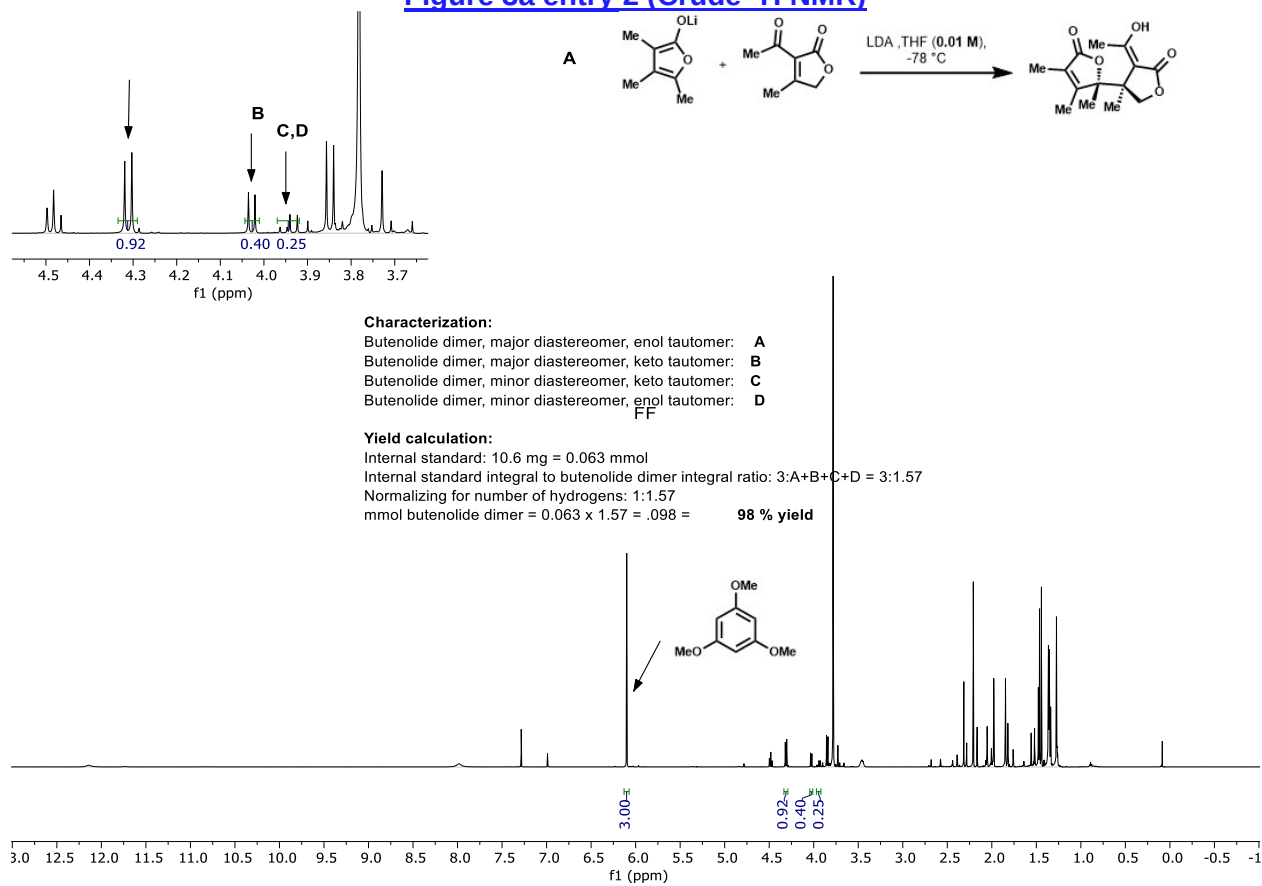
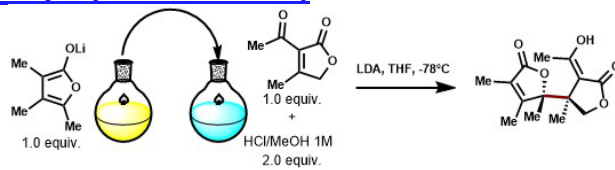
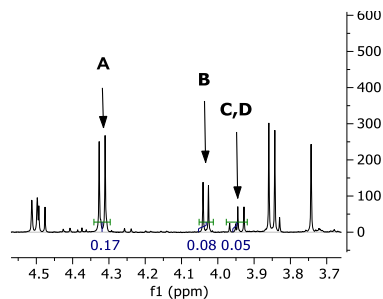


Figure 3a entry 3 (Crude ^1H NMR)



Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**

Butenolide dimer, major diastereomer, keto tautomer: **B**

Butenolide dimer, minor diastereomer, keto tautomer: **C**

Butenolide dimer, minor diastereomer, enol tautomer: **D**

Yield calculation:

Internal standard: 0.1 mmol

Internal standard integral to butenolide dimer integral ratio: $3:A+B+C+D = 3:0.30$

Normalizing for number of hydrogens: $1:0.30$

mmol butenolide dimer = $0.1 \times 0.30 = .030$

30 % yield

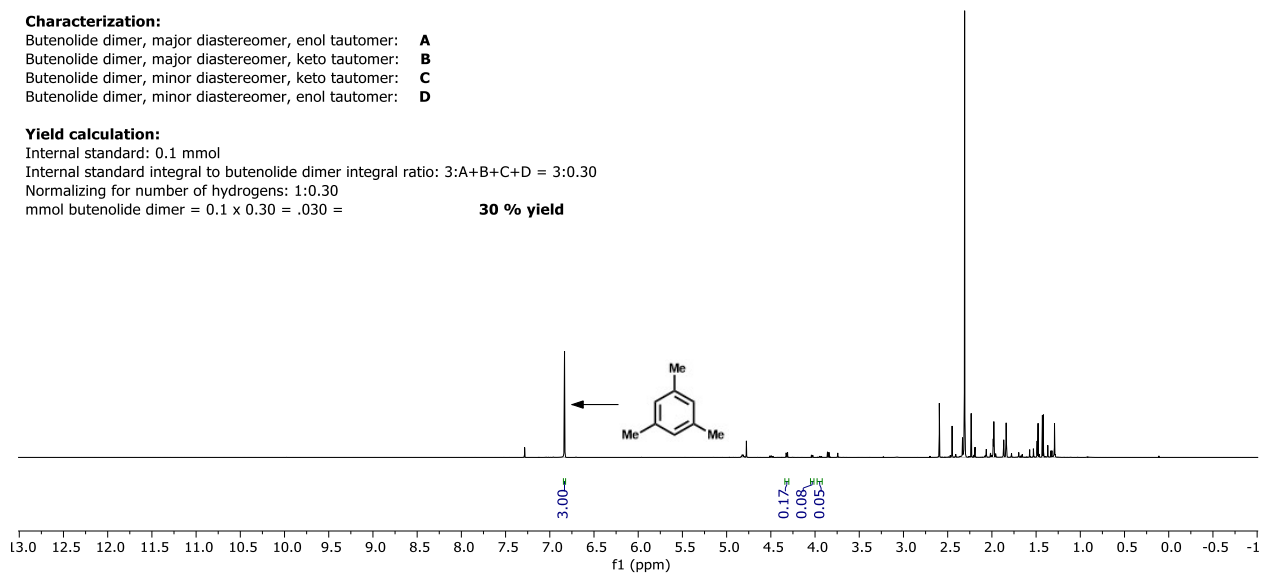


Figure 3a entry 4 (Crude ^1H NMR)

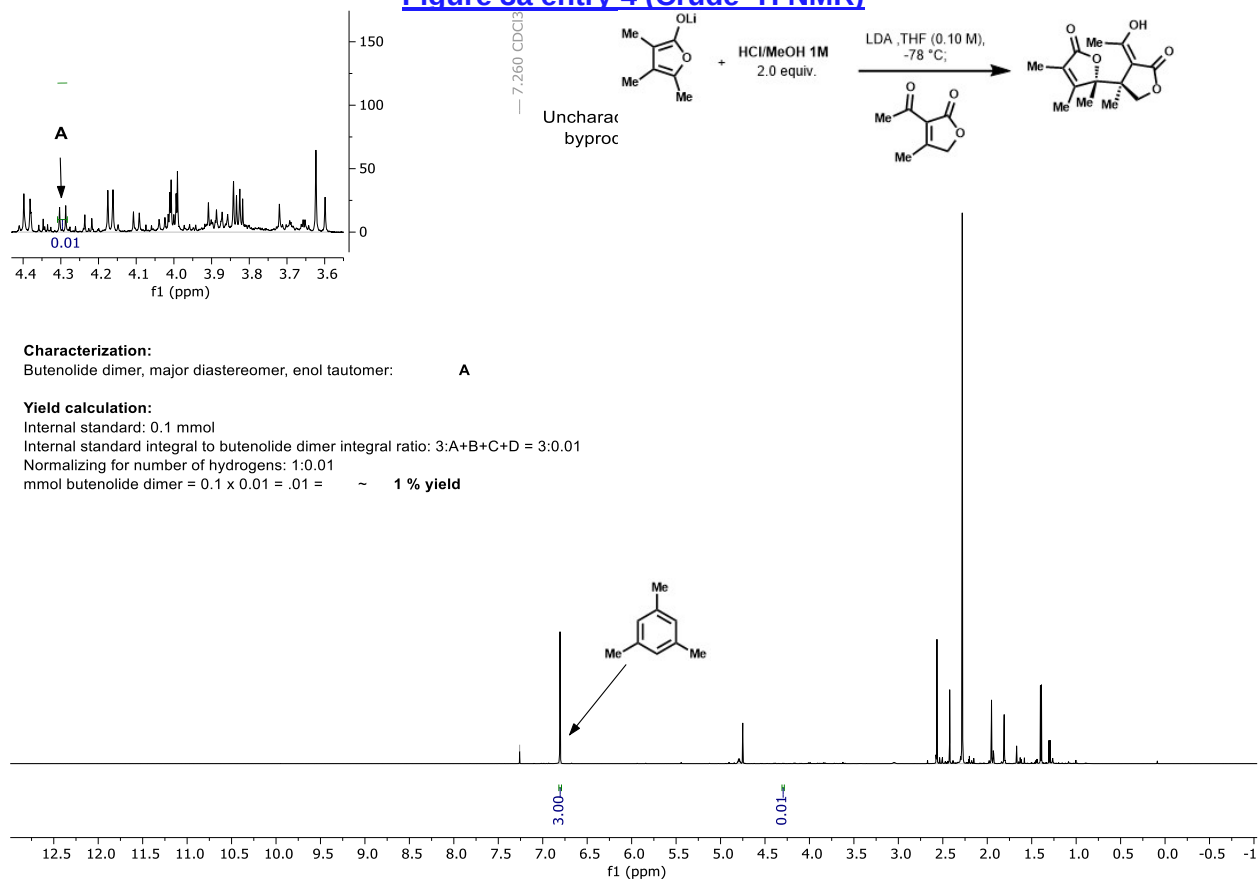
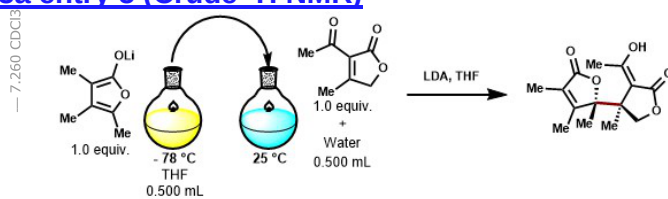
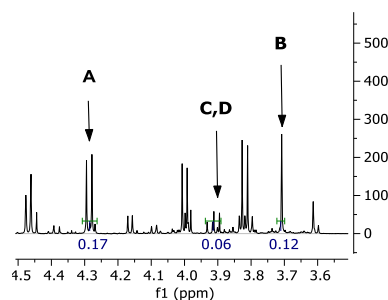


Figure 3a entry 5 (Crude ^1H NMR)



Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**

Butenolide dimer, major diastereomer, keto tautomer: **B**

Butenolide dimer, minor diastereomer, keto tautomer: **C**

Butenolide dimer, minor diastereomer, enol tautomer: **D**

Yield calculation:

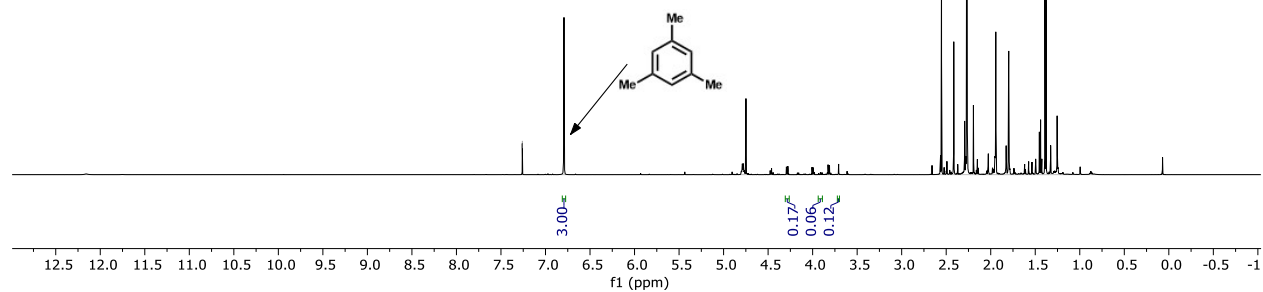
Internal standard: 0.1 mmol

Internal standard integral to butenolide dimer integral ratio: $3:A+B+C+D = 3:0.35$

3:0.35

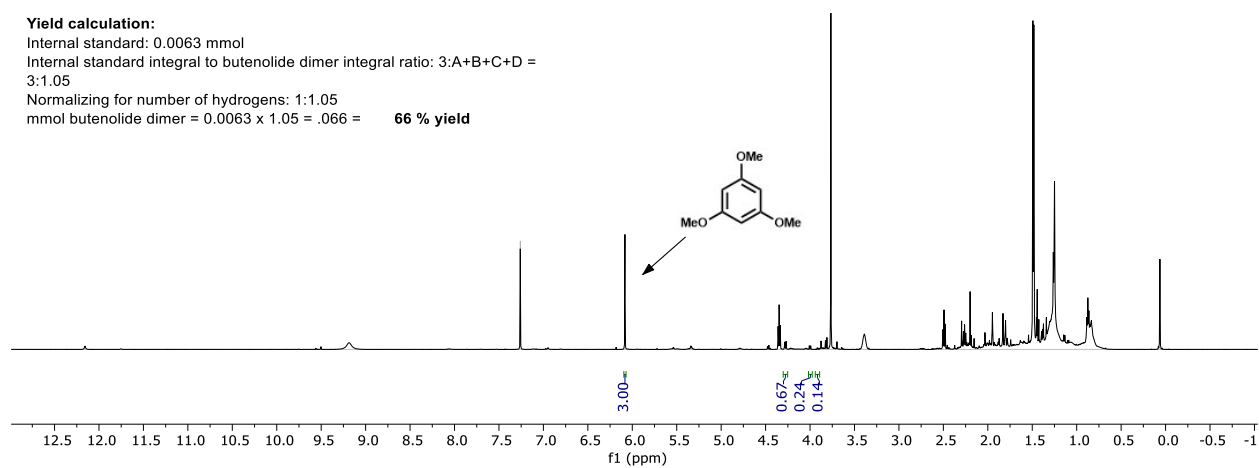
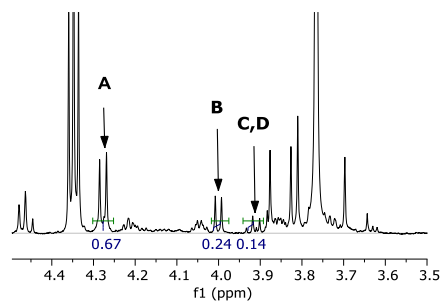
Normalizing for number of hydrogens: $1:0.35$

mmol butenolide dimer = $0.1 \times 0.35 = .035 = 35\% \text{ yield}$



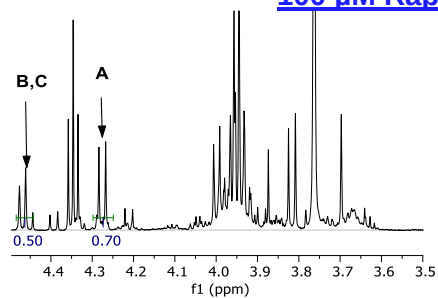
100 μ M Rapid Quench Replicate 1 (Crude ^1H NMR)

Replicate 1



100 μ M Rapid Quench Replicate 2 (Crude ^1H NMR)

Replicate 2



Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**

Butenolide dimer, major diastereomer, keto tautomer: **B**

Butenolide dimer, minor diastereomer, enol tautomer: **C**

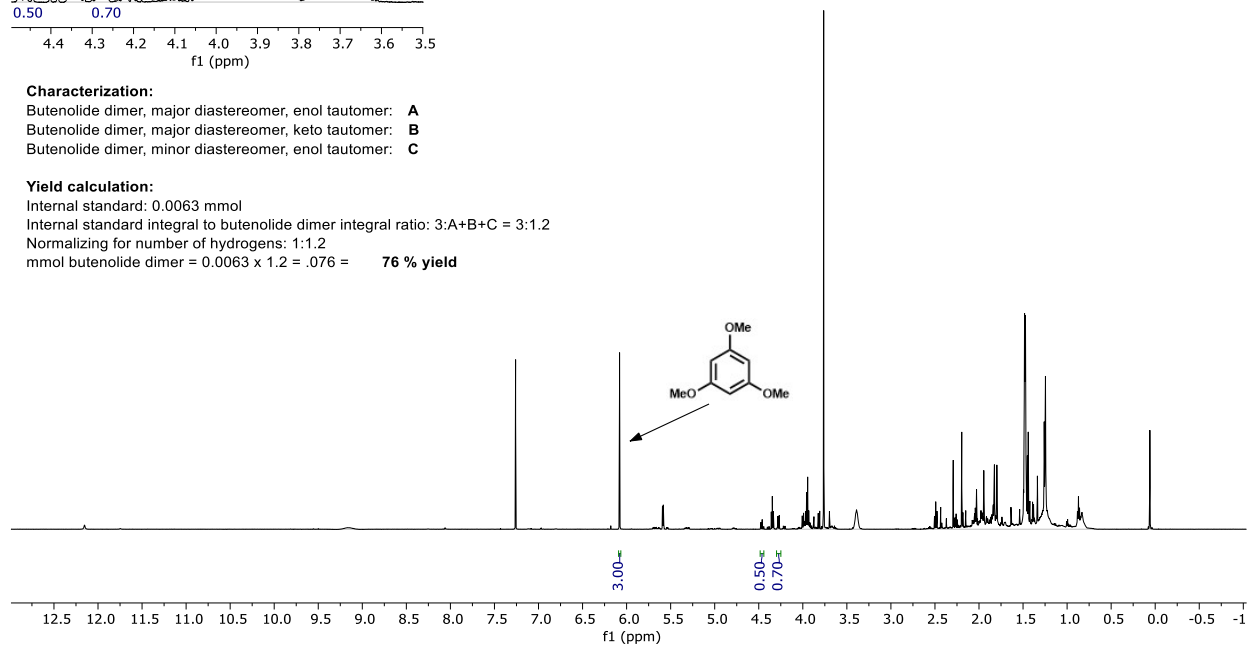
Yield calculation:

Internal standard: 0.0063 mmol

Internal standard integral to butenolide dimer integral ratio: 3:A+B+C = 3:1.2

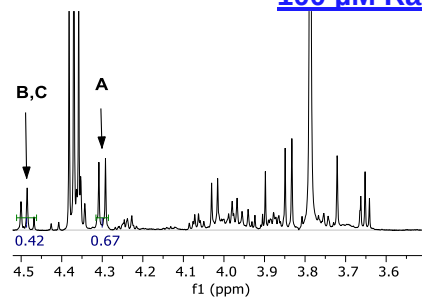
Normalizing for number of hydrogens: 1:1.2

mmol butenolide dimer = $0.0063 \times 1.2 = .0076$ = **76 % yield**



100 μ M Rapid Quench Replicate 3 (Crude ^1H NMR)

Replicate 3



Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**

Butenolide dimer, major diastereomer, keto tautomer: **B**

Butenolide dimer, minor diastereomer, enol tautomer: **C**

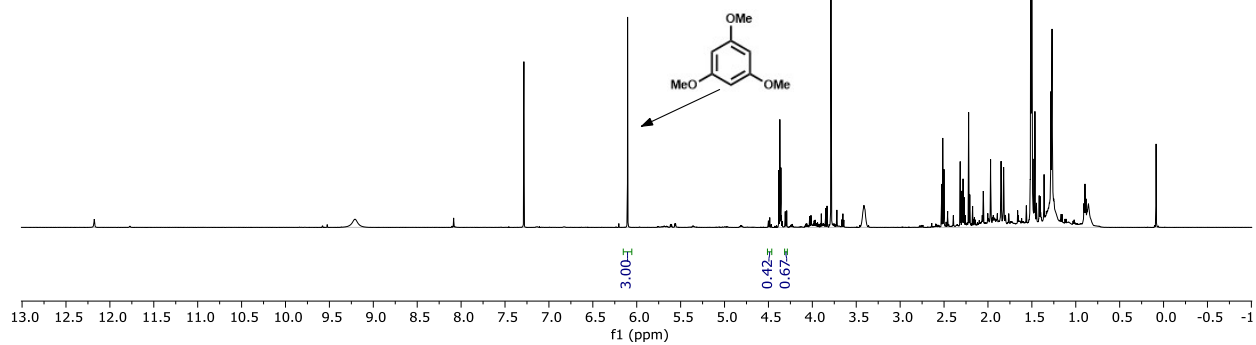
Yield calculation:

Internal standard: 0.0063 mmol

Internal standard integral to butenolide dimer integral ratio: $3:A+B+C = 3:1.09$

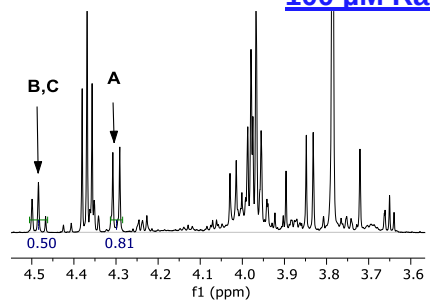
Normalizing for number of hydrogens: 1:1.09

mmol butenolide dimer = $0.0063 \times 1.09 = .0069$ = **69 % yield**



100 μ M Rapid Quench Replicate 4 (Crude ^1H NMR)

Replicate 4



Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**

Butenolide dimer, major diastereomer, keto tautomer: **B**

Butenolide dimer, minor diastereomer, enol tautomer: **C**

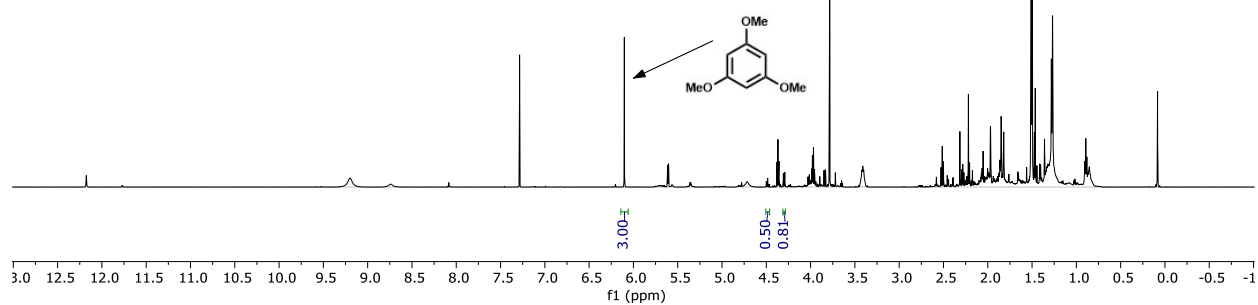
Yield calculation:

Internal standard: 0.0063 mmol

Internal standard integral to butenolide dimer integral ratio: $3:A+B+C = 3:1.31$

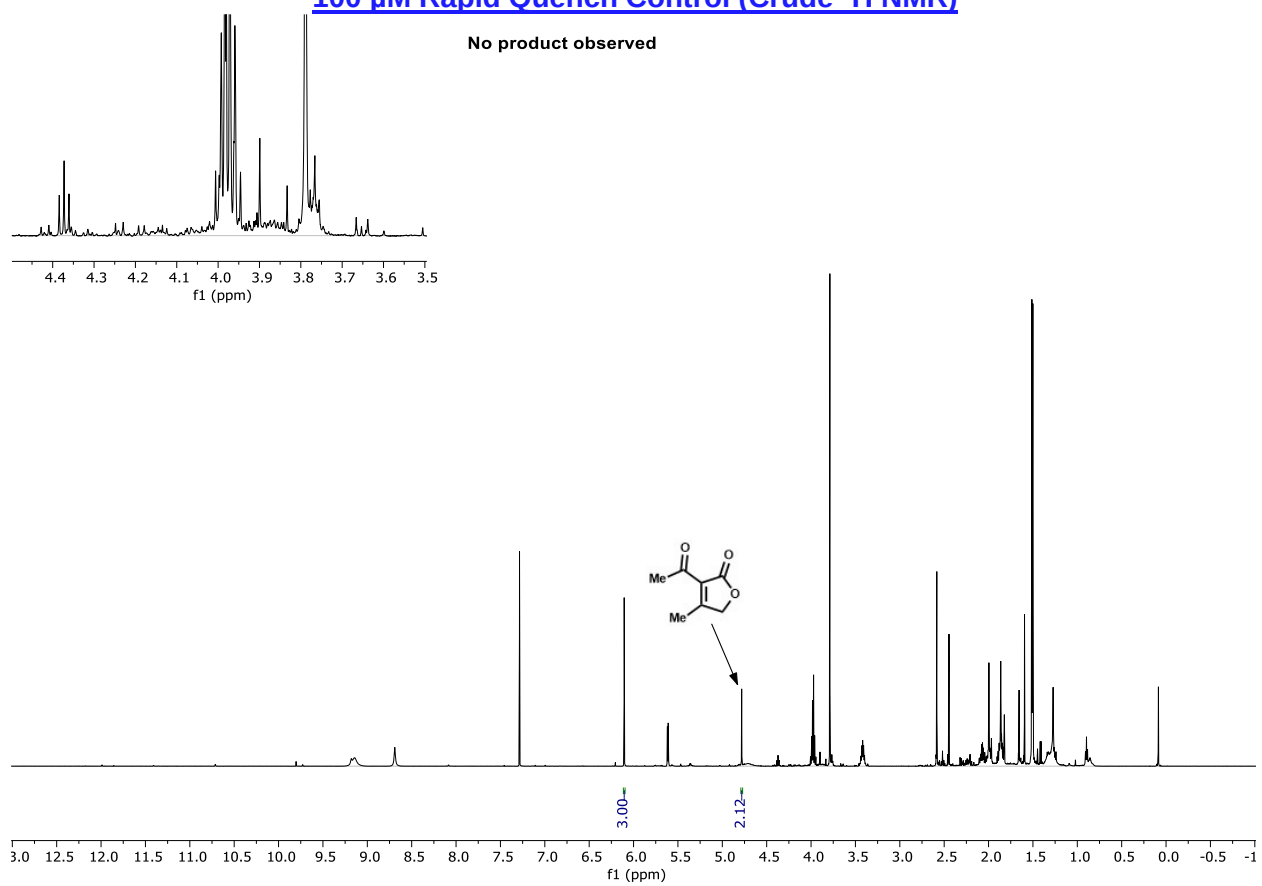
Normalizing for number of hydrogens: 1:1.31

mmol butenolide dimer = $0.0063 \times 1.31 = .0082$ = **82 % yield**



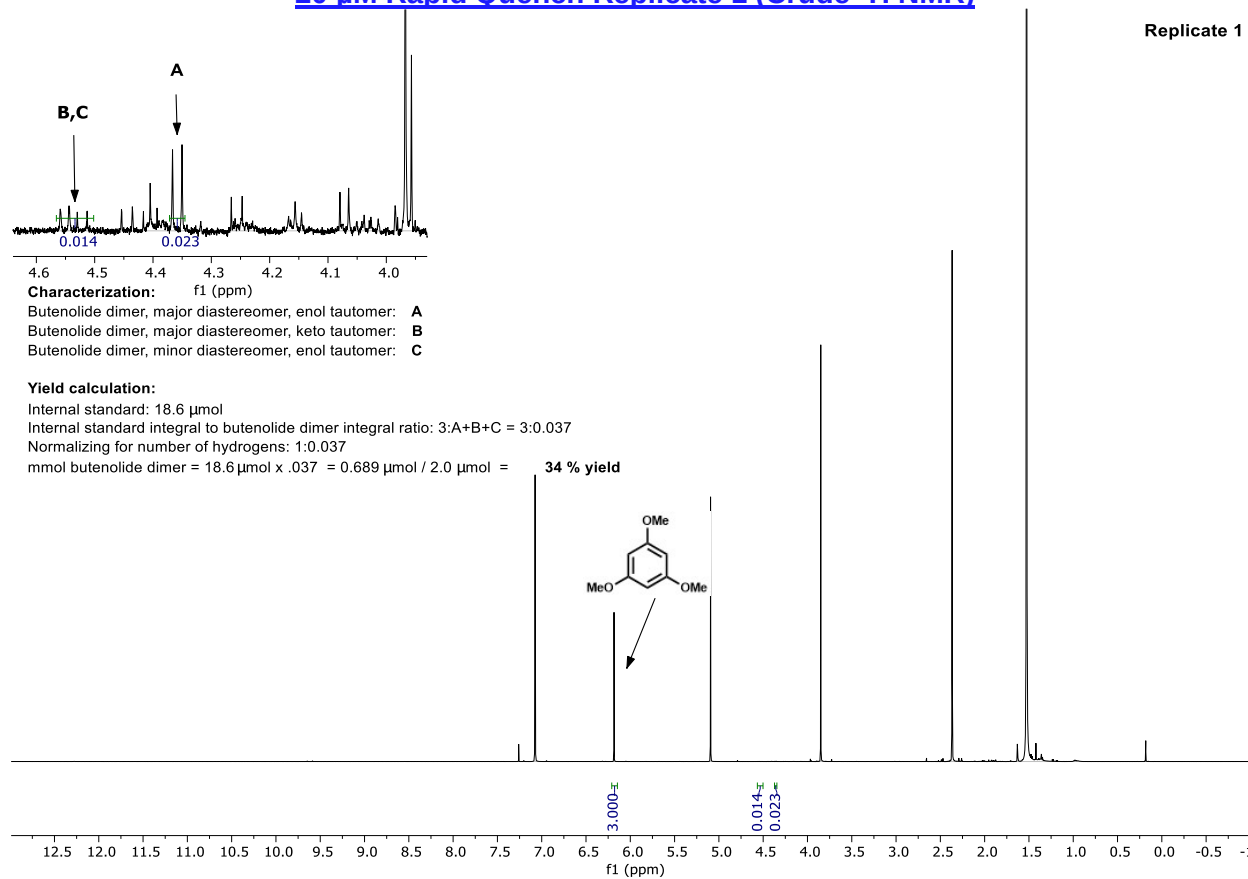
100 μ M Rapid Quench Control (Crude ^1H NMR)

No product observed



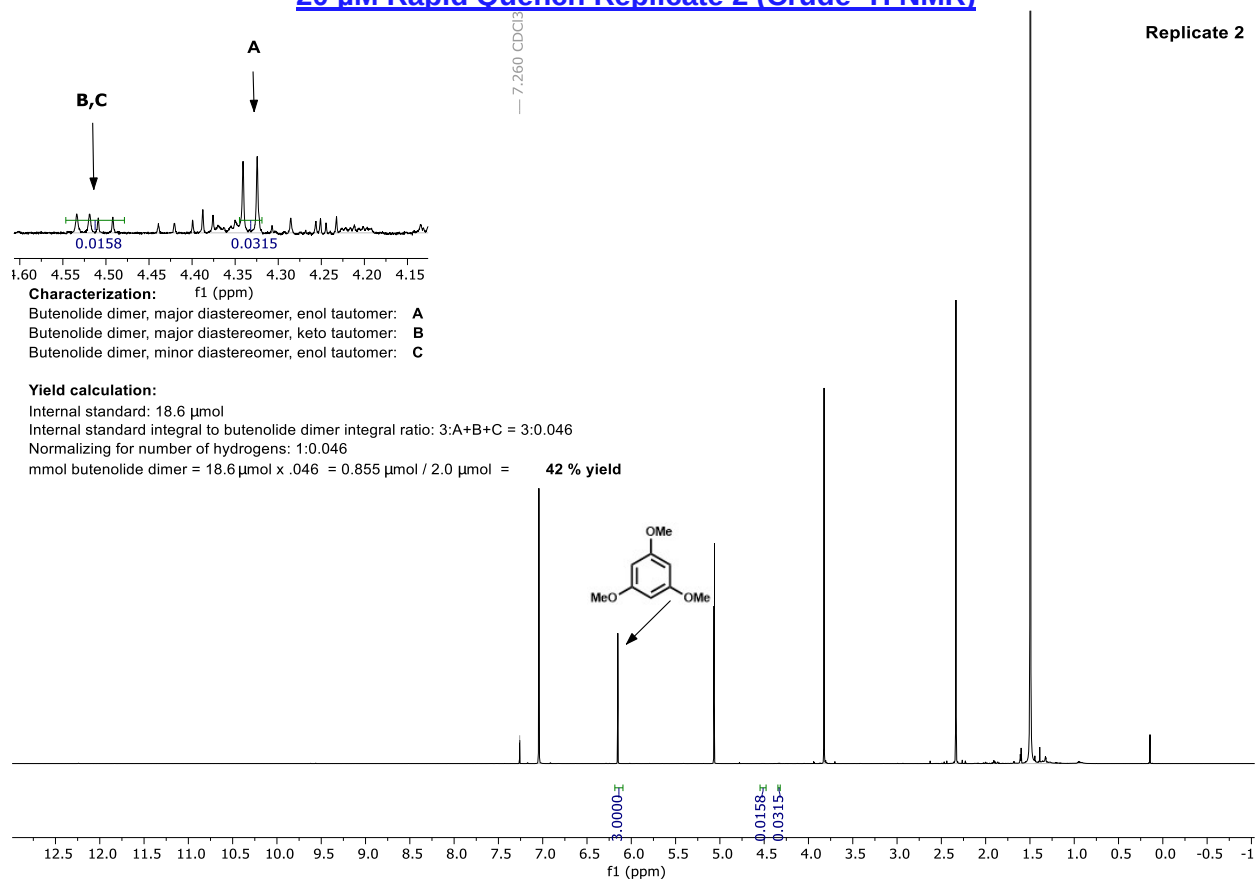
20 μ M Rapid Quench Replicate 1 (Crude ^1H NMR)

Replicate 1



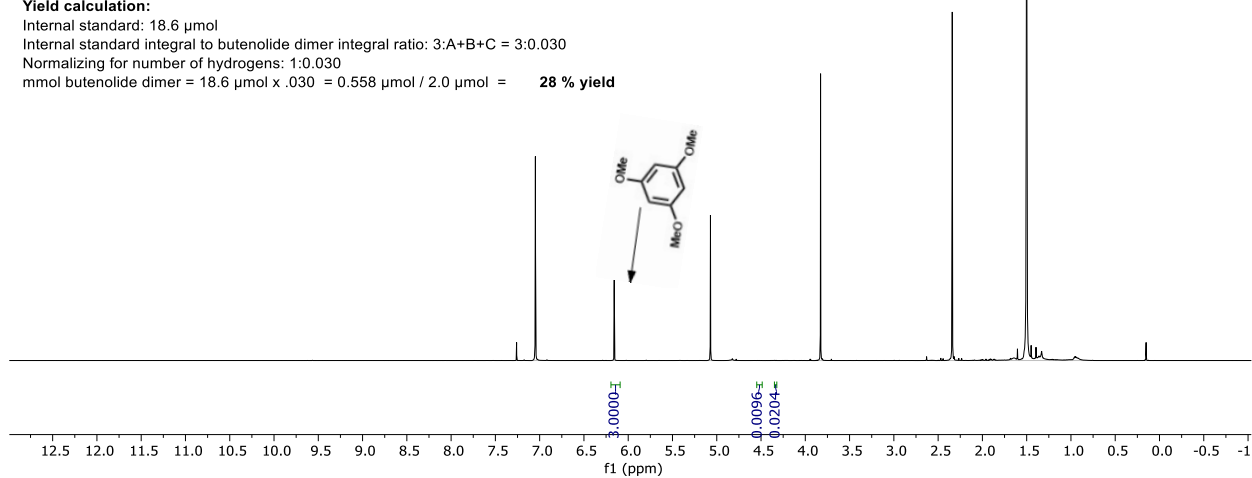
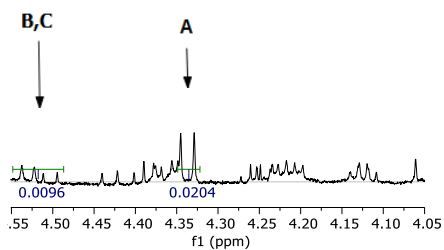
20 μ M Rapid Quench Replicate 2 (Crude ^1H NMR)

Replicate 2



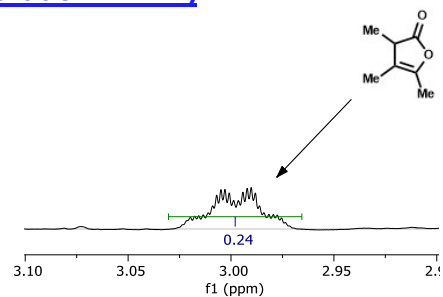
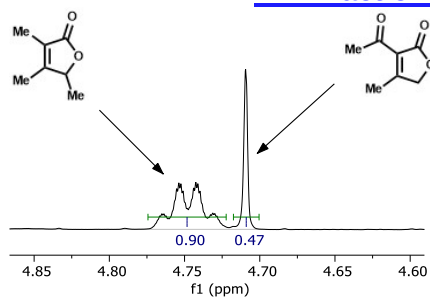
20 μ M Rapid Quench Replicate 3 (Crude ^1H NMR)

Replicate 3



KIE

KIE Fractional Conversion Replicate 1 (Crude ^1H NMR)



Fractional Conversion Calculation:

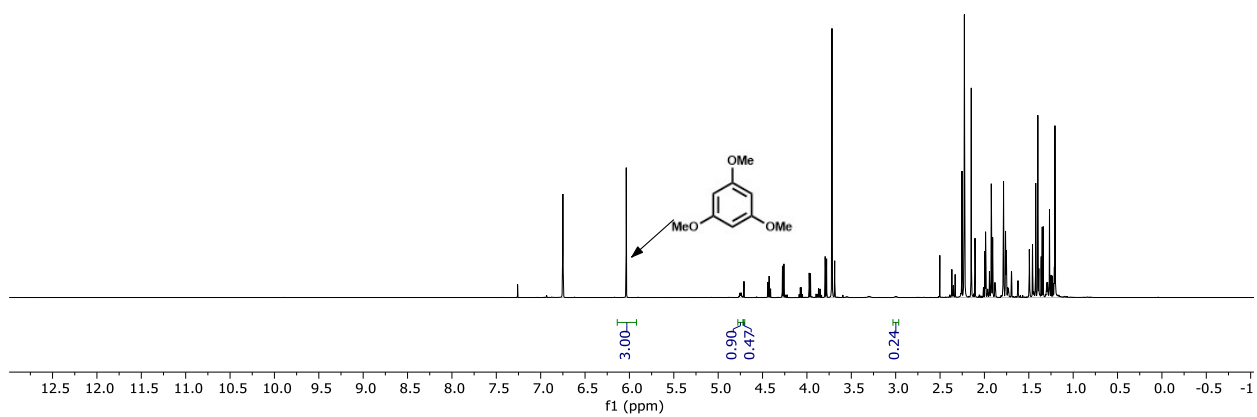
Internal standard: 1.58 mmol

Internal standard integral to Nucleophile: $3 : 0.90 + 0.24 = 3 : 1.14$

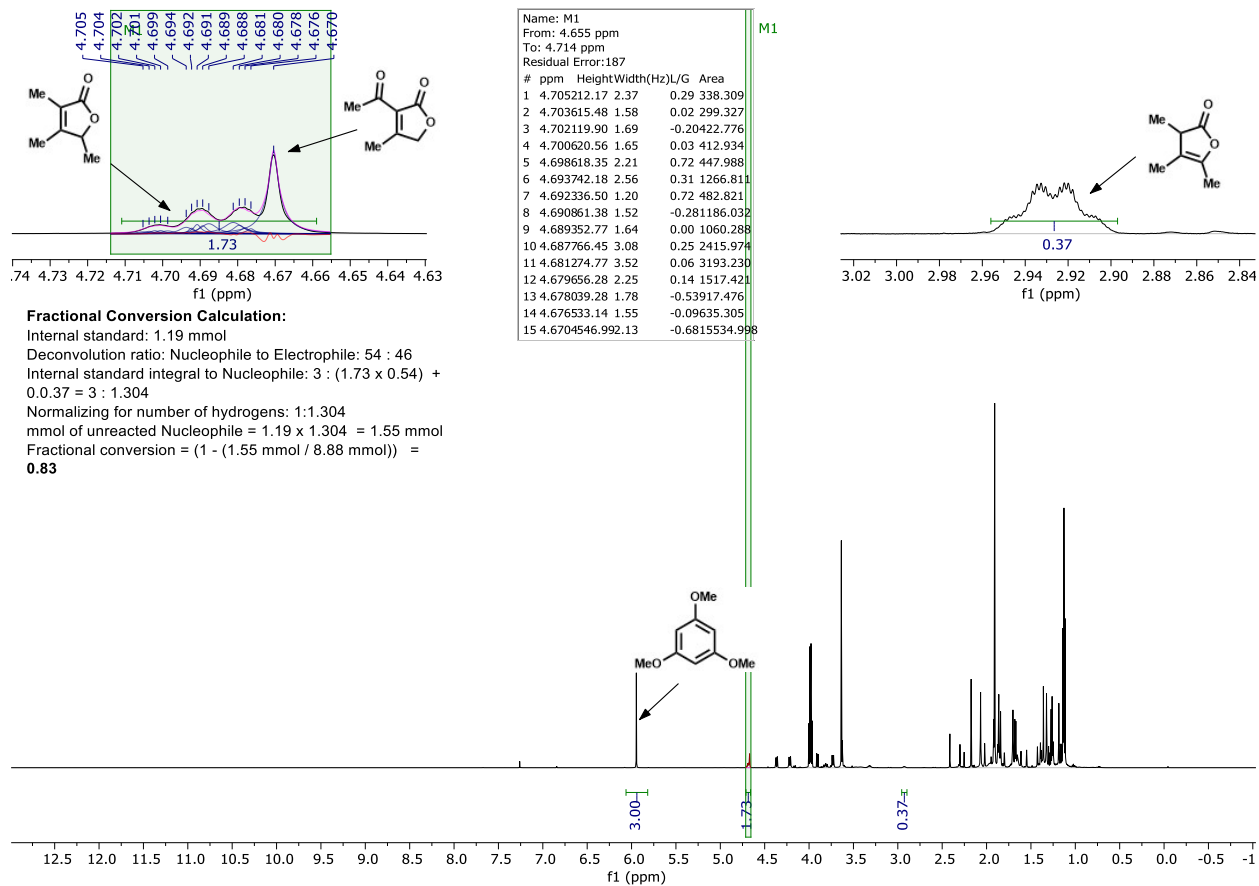
Normalizing for number of hydrogens: 1:1.14

mmol of unreacted Nucleophile = $1.58 \times 1.14 = 1.80$ mmol

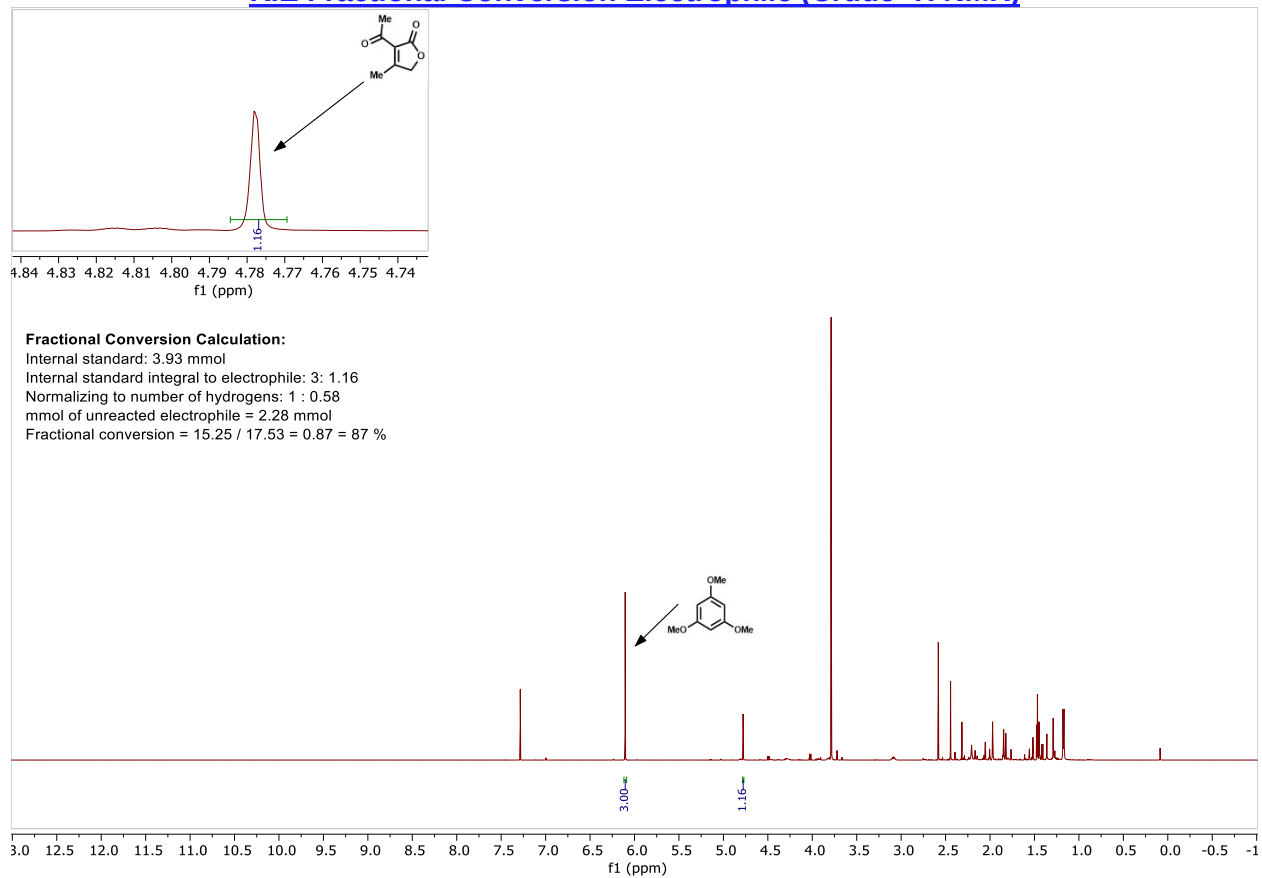
Fractional conversion = $(1 - (1.80 \text{ mmol} / 8.88 \text{ mmol})) = 0.80$



KIE Fractional Conversion Replicate 2 (Crude ^1H NMR)

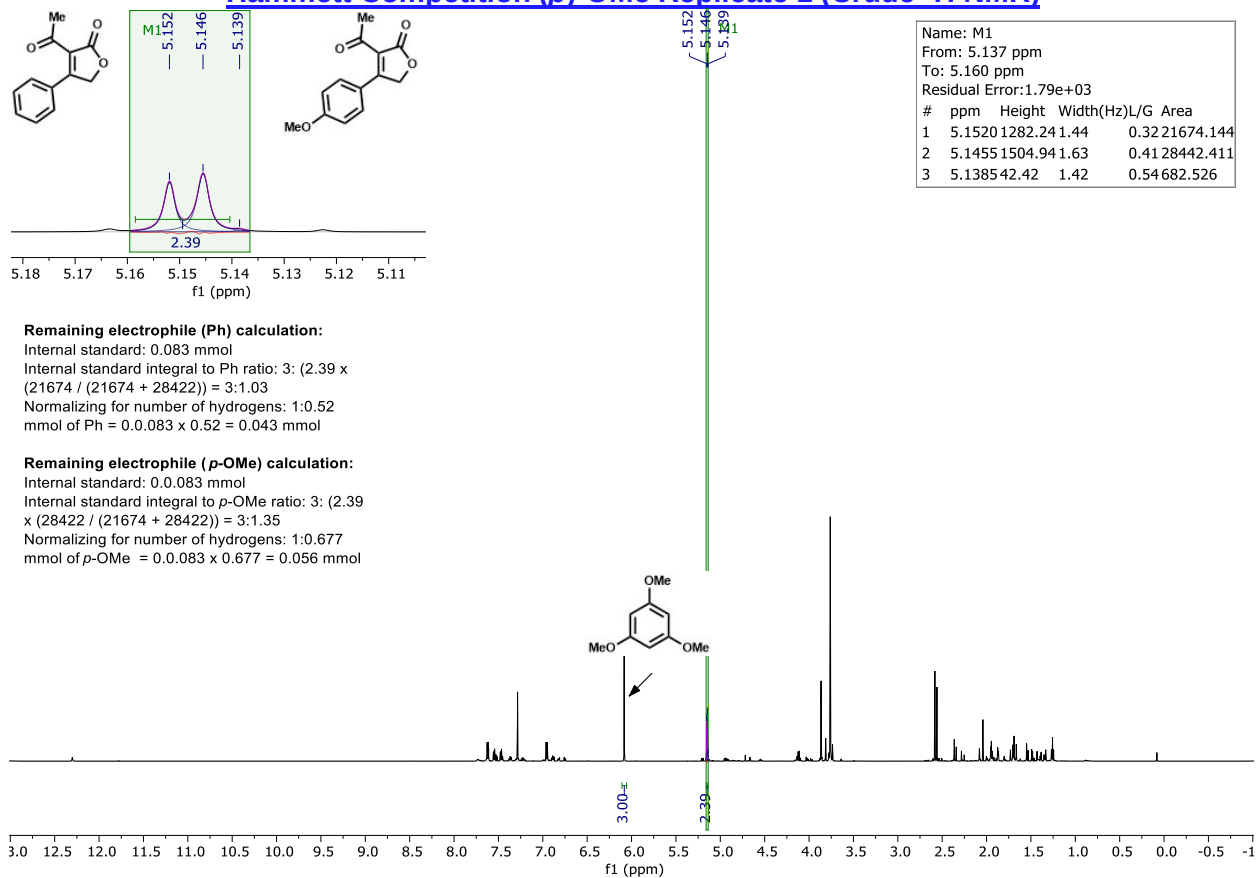


KIE Fractional Conversion Electrophile (Crude ^1H NMR)

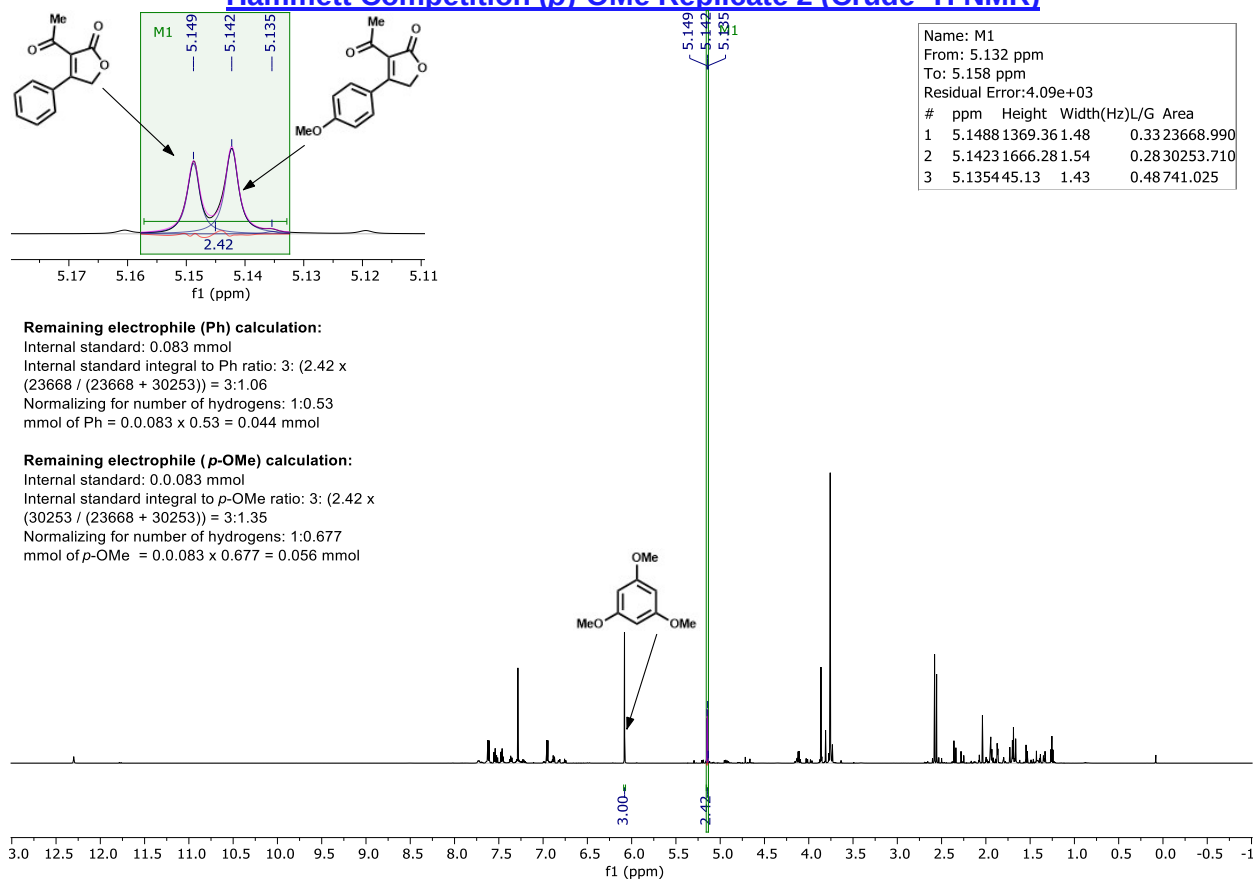


Hammett Analysis

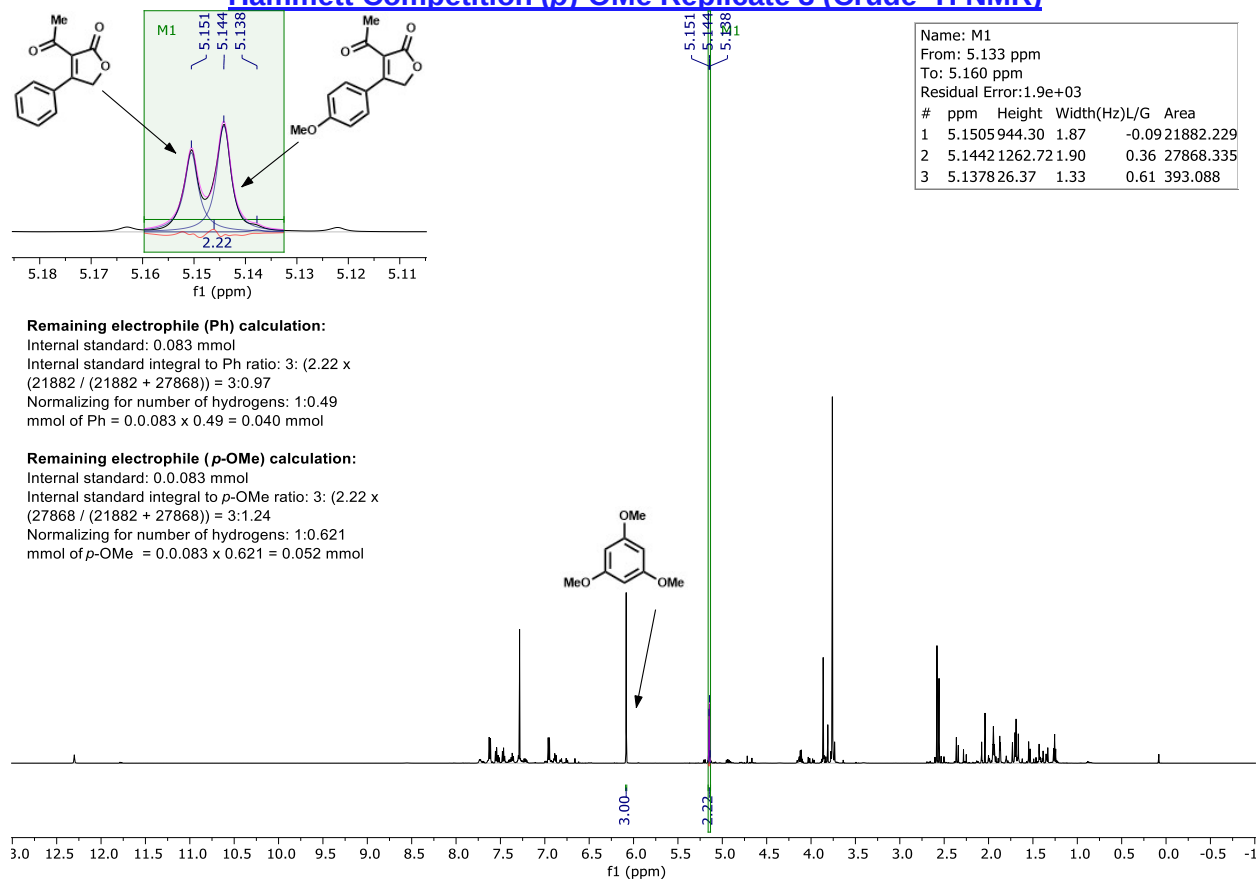
Hammett Competition (*p*-OMe Replicate 1 (Crude ^1H NMR))



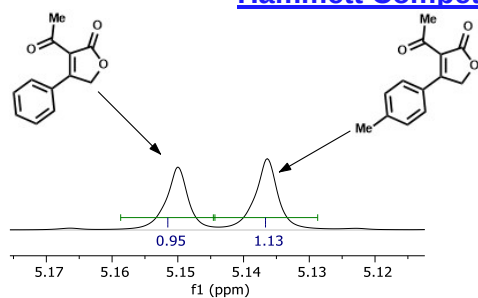
Hammett Competition (*p*-OMe Replicate 2 (Crude ¹H NMR))



Hammett Competition (*p*-OMe Replicate 3 (Crude ¹H NMR))



Hammett Competition (*p*-Me Replicate 1 (Crude ^1H NMR))



Remaining electrophile (Ph) calculation:

Internal standard: 0.101 mmol

Internal standard integral to Ph ratio: 3:0.95

Normalizing for number of hydrogens:

1:0.475

mmol of Ph = $0.101 \times 0.475 = 0.050$ mmol

Remaining electrophile (*p*-Me) calculation:

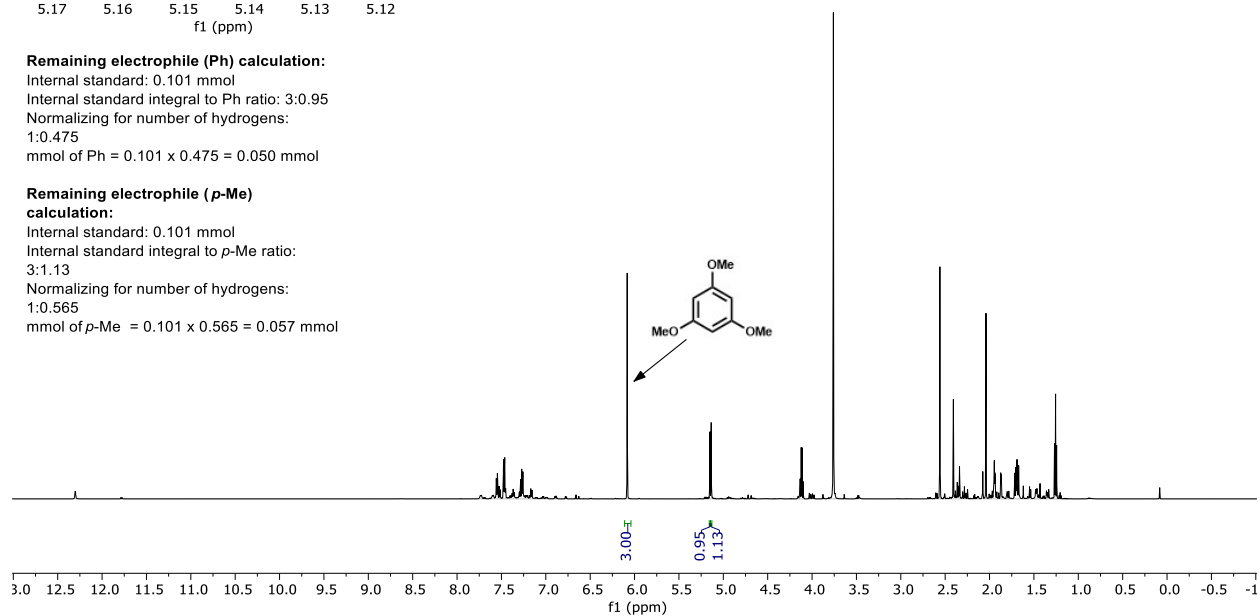
Internal standard: 0.101 mmol

Internal standard integral to *p*-Me ratio: 3:1.13

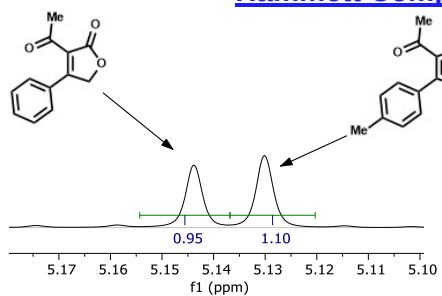
Normalizing for number of hydrogens:

1:0.565

mmol of *p*-Me = $0.101 \times 0.565 = 0.057$ mmol



Hammett Competition (*p*-Me Replicate 2 (Crude ^1H NMR))



Remaining electrophile (Ph) calculation:

Internal standard: 0.101 mmol

Internal standard integral to Ph ratio: 3:0.95

Normalizing for number of hydrogens:

1:0.475

mmol of Ph = $0.101 \times 0.475 = 0.050$ mmol

Remaining electrophile (*p*-Me) calculation:

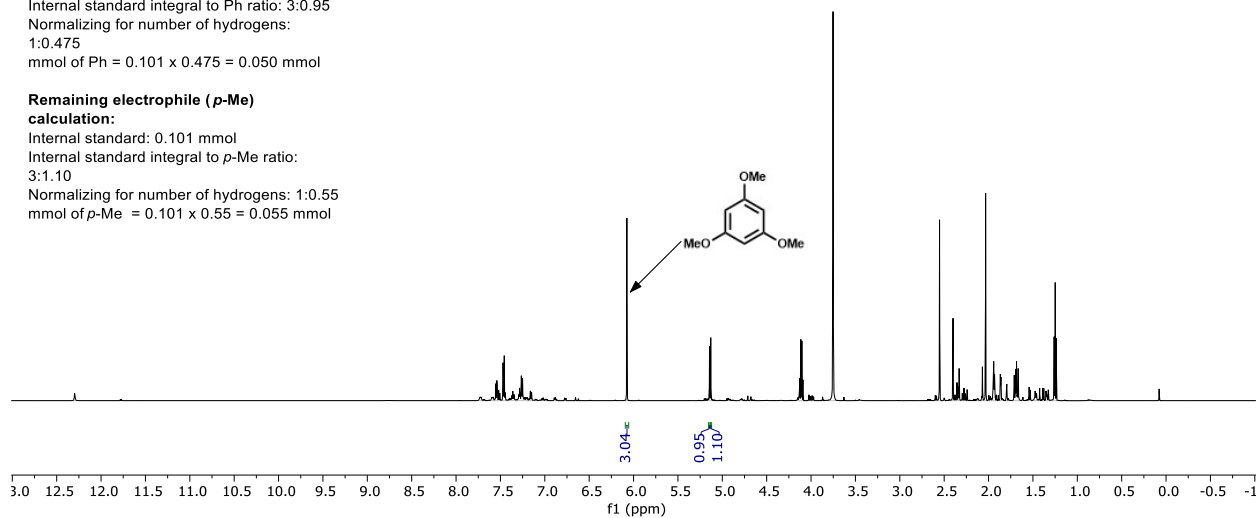
Internal standard: 0.101 mmol

Internal standard integral to *p*-Me ratio: 3:1.10

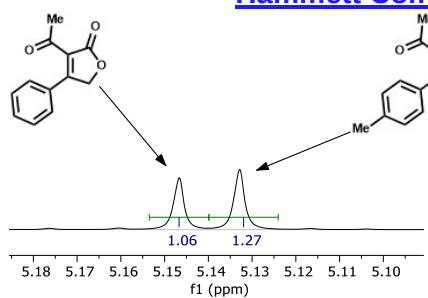
3:1.10

Normalizing for number of hydrogens: 1:0.55

mmol of *p*-Me = $0.101 \times 0.55 = 0.055$ mmol



Hammett Competition (*p*-Me Replicate 3 (Crude ^1H NMR))



Remaining electrophile (Ph) calculation:

Internal standard: 0.101 mmol

Internal standard integral to Ph ratio: 3:1.06

Normalizing for number of hydrogens: 1:0.53

mmol of Ph = $0.101 \times 0.53 = 0.053$ mmol

Remaining electrophile (*p*-Me) calculation:

Internal standard: 0.101 mmol

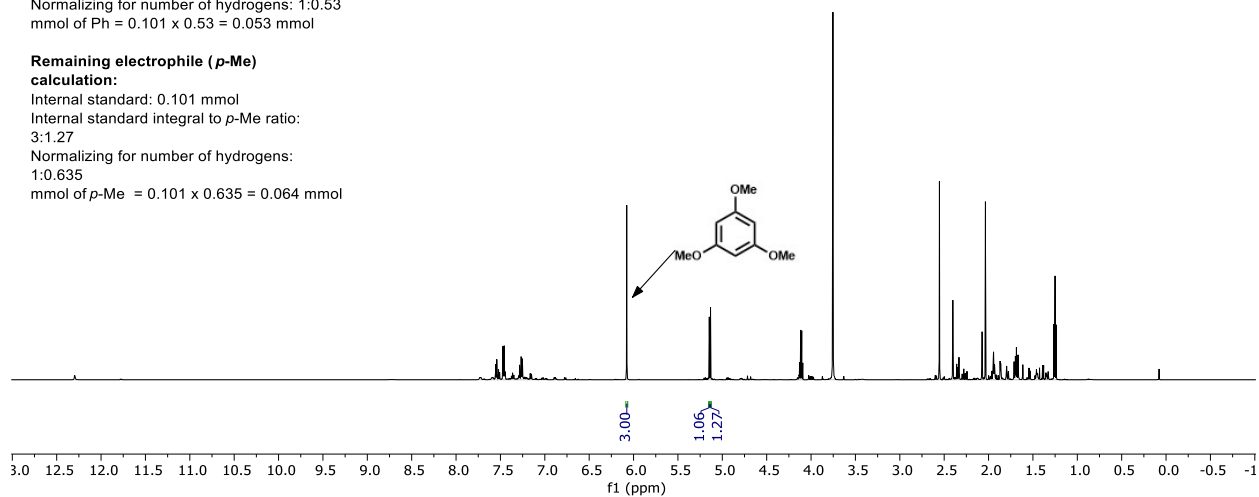
Internal standard integral to *p*-Me ratio:

3:1.27

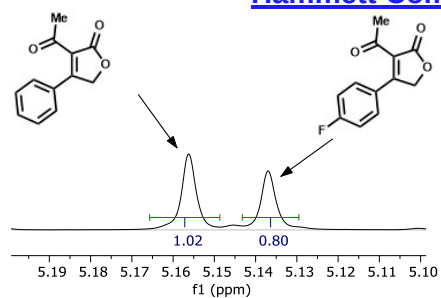
Normalizing for number of hydrogens:

1:0.635

mmol of *p*-Me = $0.101 \times 0.635 = 0.064$ mmol



Hammett Competition (*p*-F Replicate 1 (Crude ^1H NMR))



Remaining electrophile (Ph) calculation:

Internal standard: 0.101 mmol

Internal standard integral to Ph ratio: 3:1.02

Normalizing for number of hydrogens:

1:0.51

mmol of Ph = $0.101 \times 0.51 = 0.051$ mmol

Remaining electrophile (*p*-F) calculation:

Internal standard:

Internal standard: 0.101 mmol

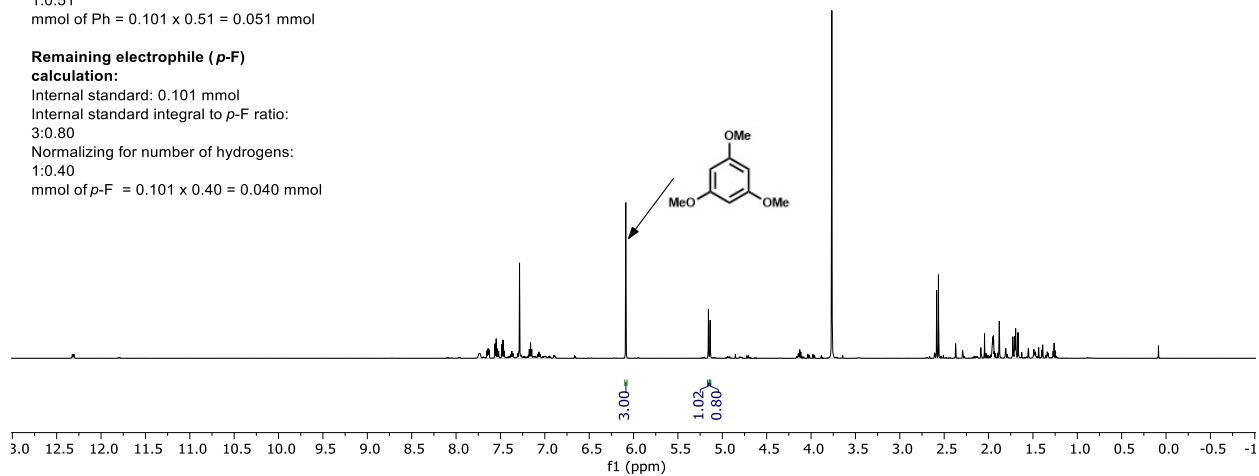
Internal standard integral to *p*-F ratio:

3:0.80

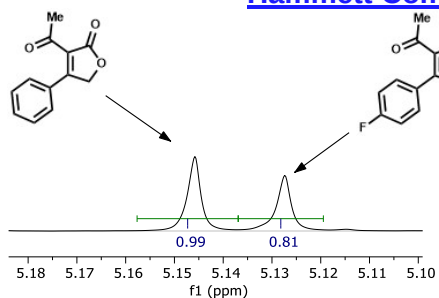
Normalizing for number of hydrogens:

1:0.40

mmol of *p*-F = $0.101 \times 0.40 = 0.040$ mmol



Hammett Competition (*p*-F Replicate 2 (Crude ^1H NMR))



Remaining electrophile (Ph)

calculation:

Internal standard: 0.101 mmol

Internal standard integral to Ph ratio: 3:0.99

Normalizing for number of hydrogens:

1:0.49

mmol of Ph = $0.101 \times 0.49 = 0.049$ mmol

Remaining electrophile (*p*-F)

calculation:

Internal standard: 0.101 mmol

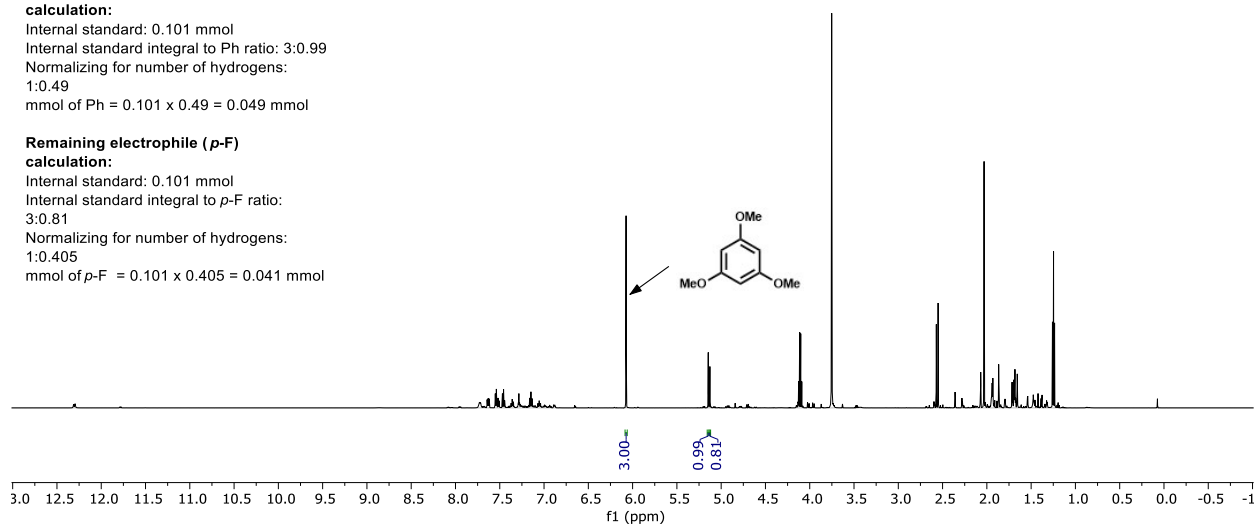
Internal standard integral to *p*-F ratio:

3:0.81

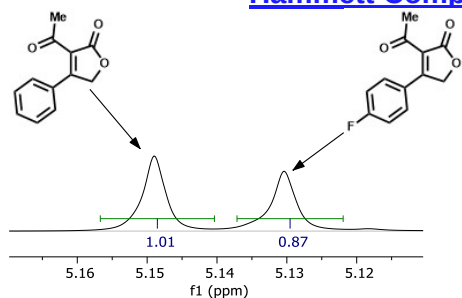
Normalizing for number of hydrogens:

1:0.405

mmol of *p*-F = $0.101 \times 0.405 = 0.041$ mmol



Hammett Competition (*p*-F Replicate 3 (Crude ^1H NMR))



Remaining electrophile (Ph) calculation:

Internal standard: 0.101 mmol

Internal standard integral to Ph ratio: 3:1.01

Normalizing for number of hydrogens:

1:0.505

mmol of Ph = $0.101 \times 0.505 = 0.051$ mmol

Remaining electrophile (*p*-F) calculation:

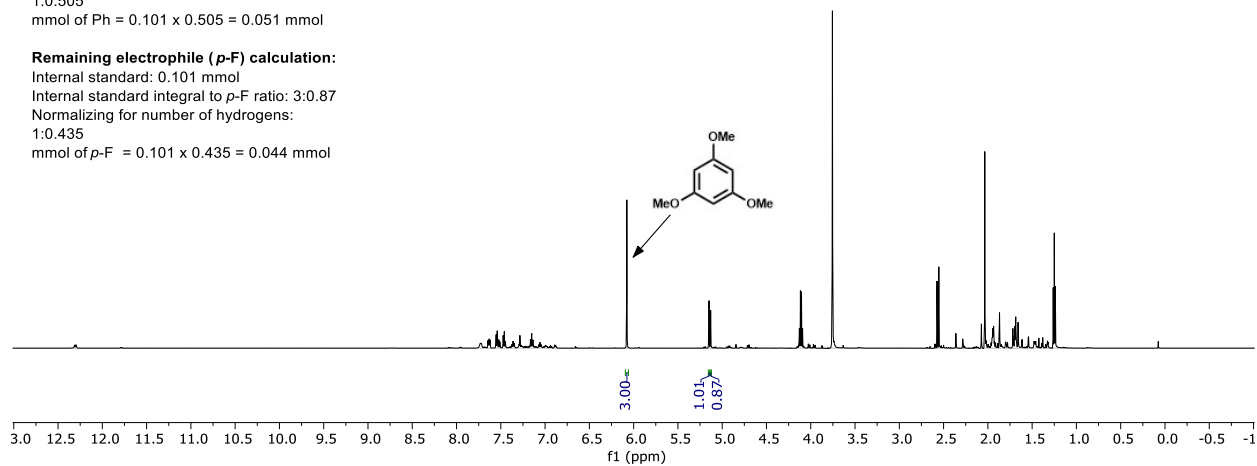
Internal standard: 0.101 mmol

Internal standard integral to *p*-F ratio: 3:0.87

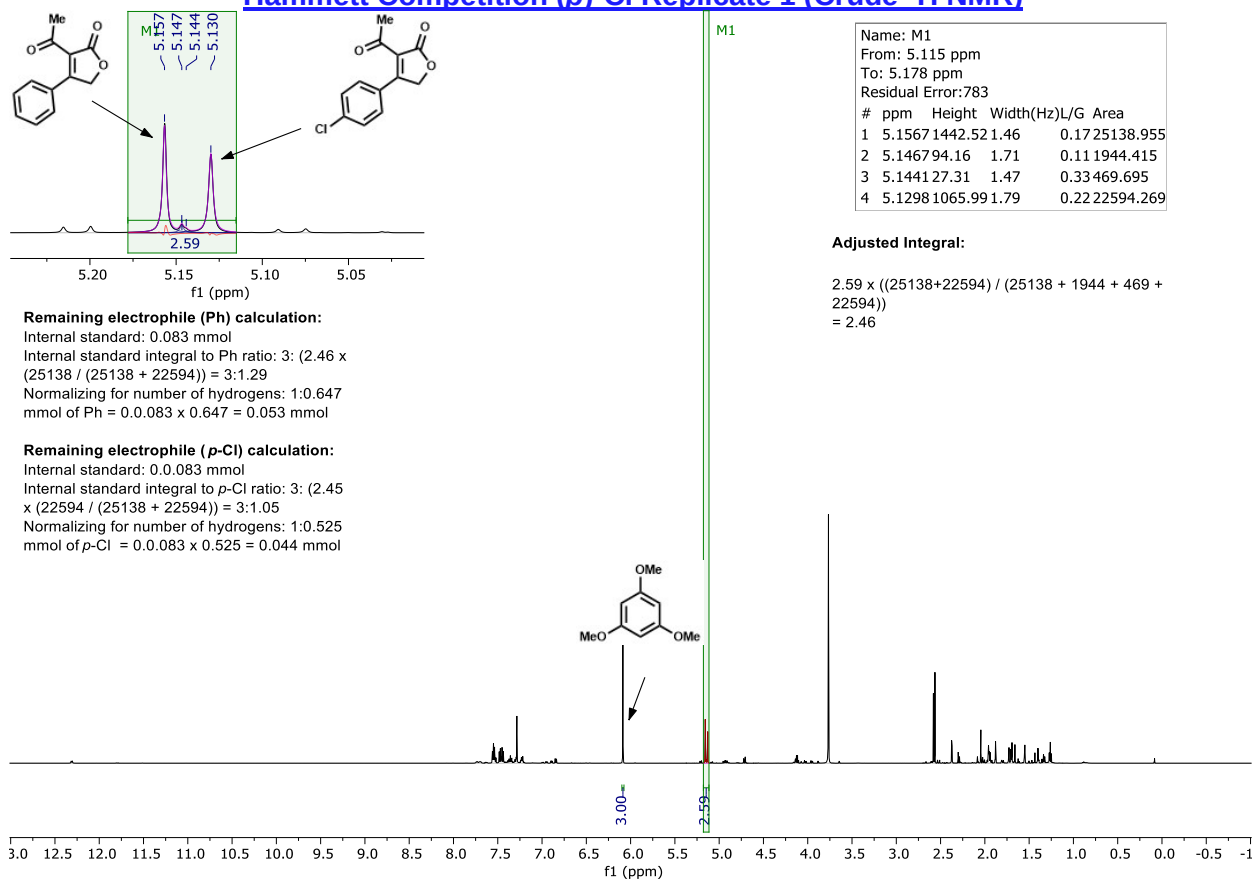
Normalizing for number of hydrogens:

1:0.435

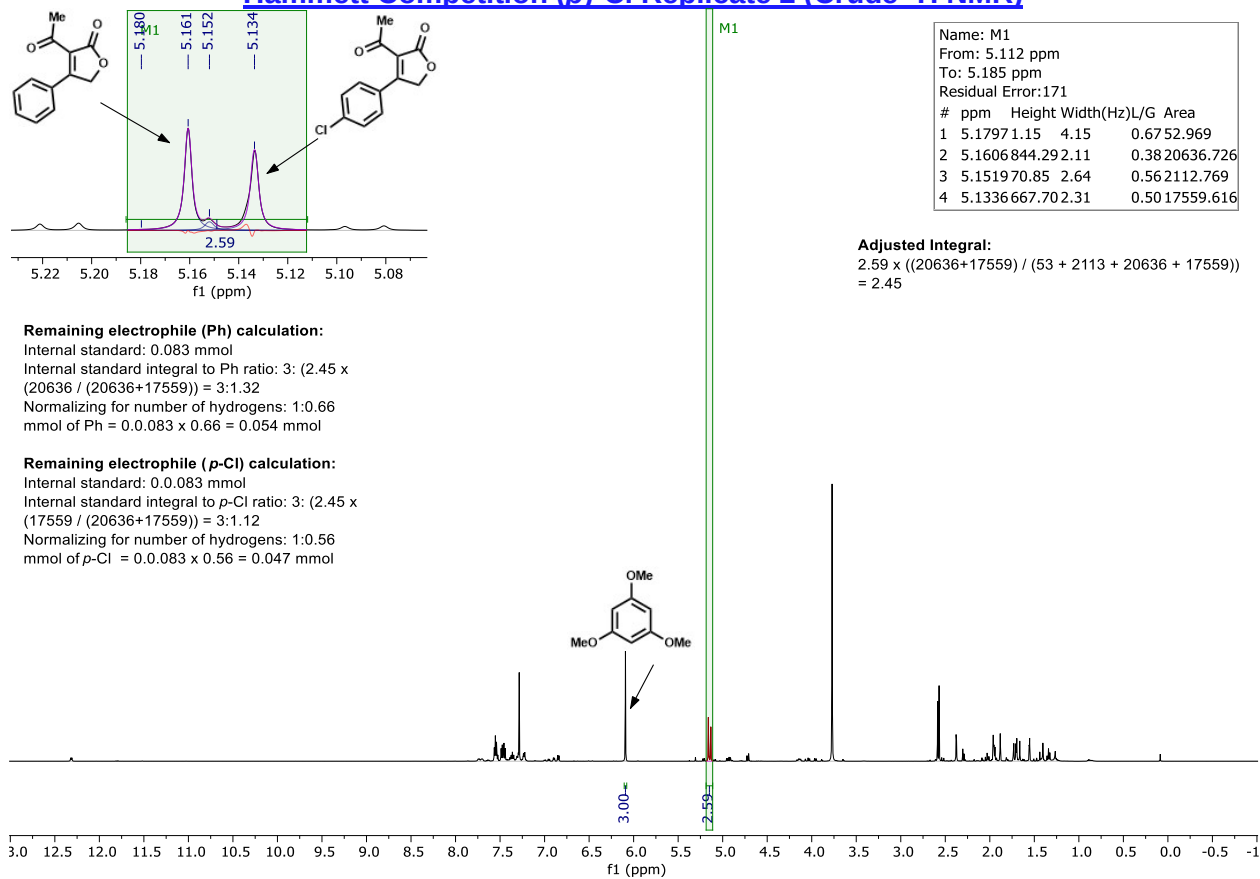
mmol of *p*-F = $0.101 \times 0.435 = 0.044$ mmol



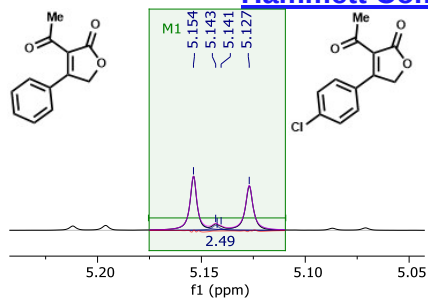
Hammett Competition (*p*-Cl Replicate 1 (Crude ¹H NMR))



Hammett Competition (*p*-Cl Replicate 2 (Crude ¹H NMR))



Hammett Competition (*p*-Cl Replicate 3 (Crude ¹H NMR))



Remaining electrophile (Ph) calculation:

Internal standard: 0.083 mmol
 Internal standard integral to Ph ratio: 3: (2.32 x
 (6341 / (6341+5960))) = 3:1.19
 Normalizing for number of hydrogens: 1:0.595
 mmol of Ph = 0.083 x 0.595 = 0.049 mmol

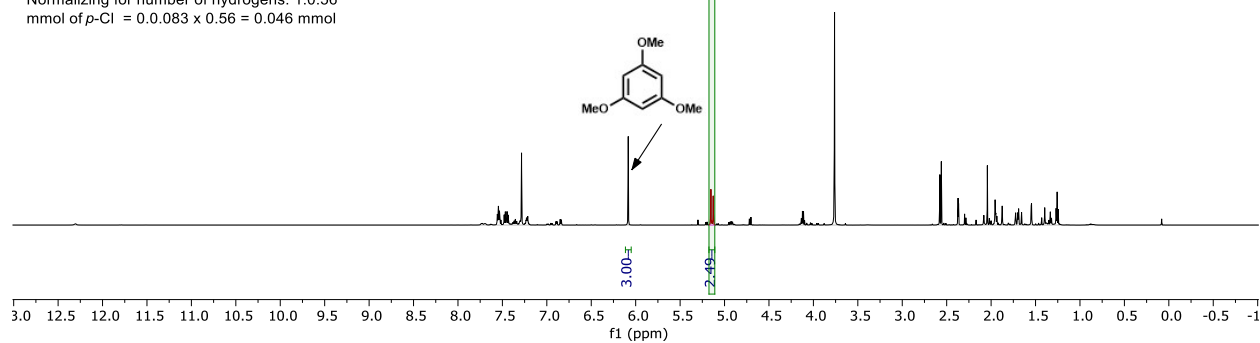
Remaining electrophile (*p*-Cl) calculation:

Internal standard: 0.083 mmol
 Internal standard integral to *p*-Cl ratio: 3: (2.32 x
 (5960 / (6341+5960))) = 3:1.12
 Normalizing for number of hydrogens: 1:0.56
 mmol of *p*-Cl = 0.083 x 0.56 = 0.046 mmol

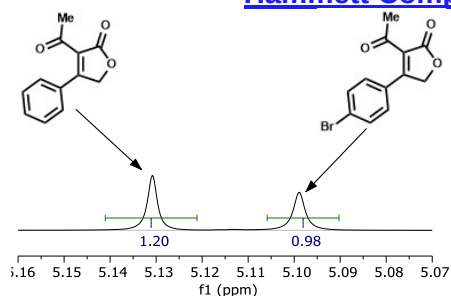
Name: M1				
From: 5.110 ppm				
To: 5.175 ppm				
Residual Error:18.7				
#	ppm	Height	Width(Hz)	L/G Area
1	5.1538	258.03	2.12	0.40 6341.972
2	5.1431	23.81	2.40	0.01 699.134
3	5.1405	6.16	2.15	-0.08 163.175
4	5.1270	214.36	2.35	0.24 5960.508

Adjusted Integral:

$$2.49 \times ((6341+5960) / (163 + 699 + 6341 + 5960)) = 2.32$$



Hammett Competition (*p*-Br Replicate 1 (Crude ^1H NMR))



Remaining electrophile (Ph) calculation:

Internal standard: 0.101 mmol

Internal standard integral to Ph ratio: 3:1.20

Normalizing for number of hydrogens: 1:0.6

mmol of Ph = $0.101 \times 0.6 = 0.060$ mmol

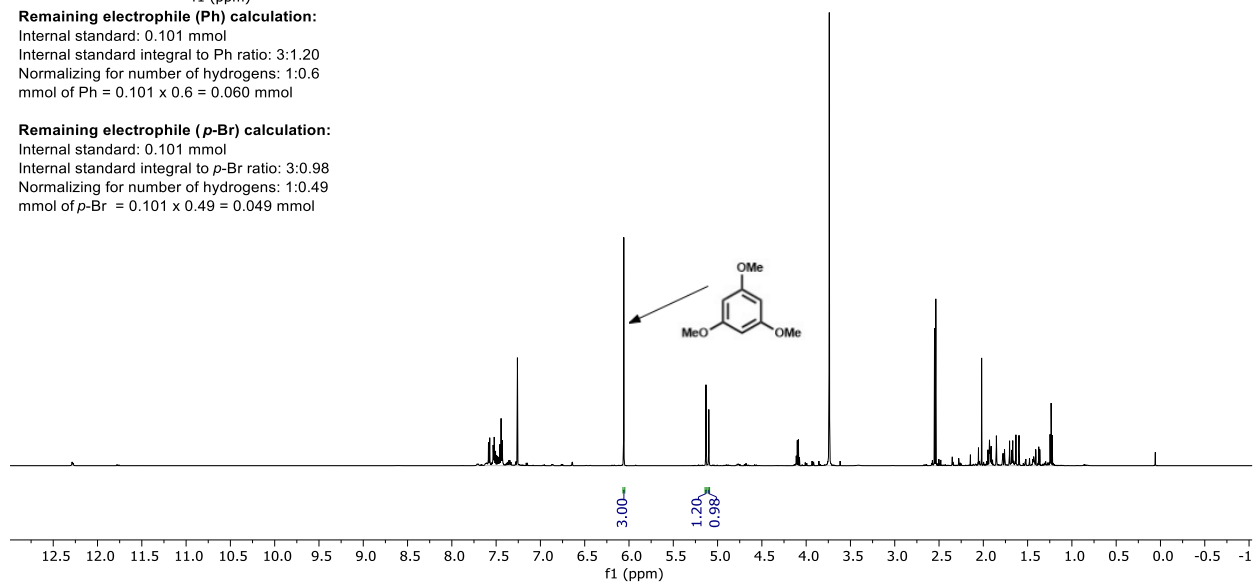
Remaining electrophile (*p*-Br) calculation:

Internal standard: 0.101 mmol

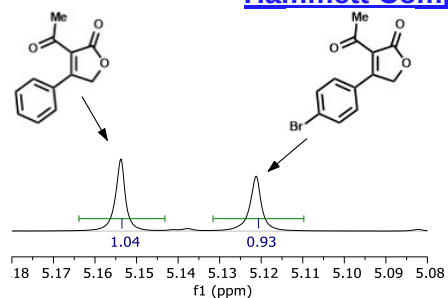
Internal standard integral to *p*-Br ratio: 3:0.98

Normalizing for number of hydrogens: 1:0.49

mmol of *p*-Br = $0.101 \times 0.49 = 0.049$ mmol



Hammett Competition (*p*-Br Replicate 2 (Crude ^1H NMR))

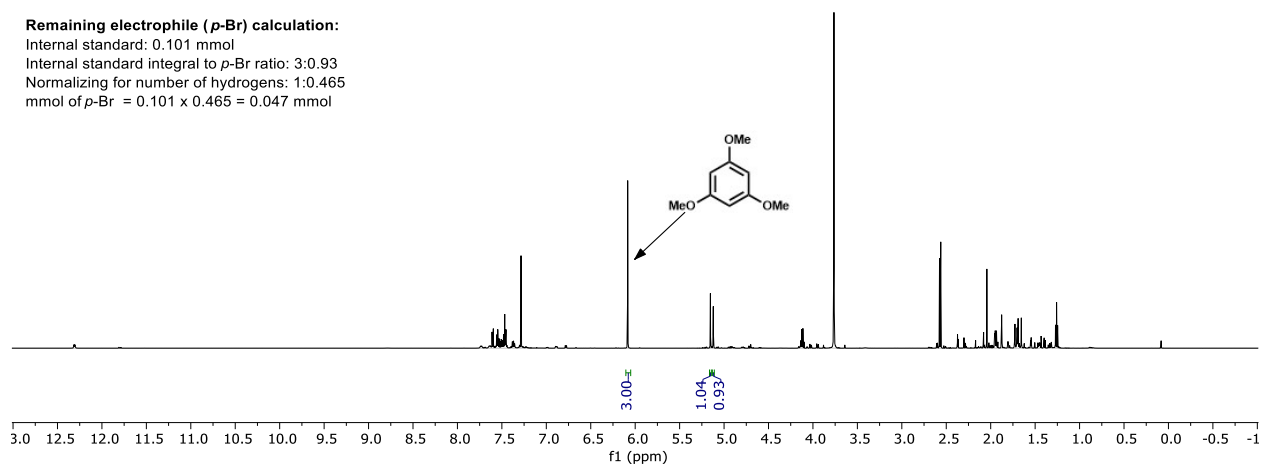


Remaining electrophile (Ph) calculation:

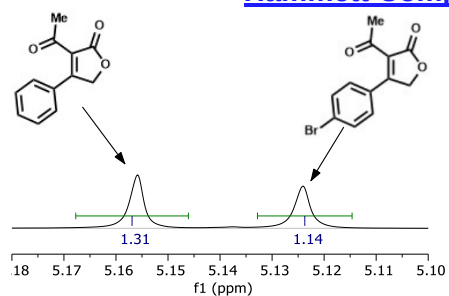
Internal standard: 0.101 mmol
 Internal standard integral to Ph ratio: 3:1.04
 Normalizing for number of hydrogens: 1:0.52
 mmol of Ph = $0.101 \times 0.52 = 0.053$ mmol

Remaining electrophile (*p*-Br) calculation:

Internal standard: 0.101 mmol
 Internal standard integral to *p*-Br ratio: 3:0.93
 Normalizing for number of hydrogens: 1:0.465
 mmol of *p*-Br = $0.101 \times 0.465 = 0.047$ mmol



Hammett Competition (*p*-Br Replicate 3 (Crude ^1H NMR))



Remaining electrophile (Ph) calculation:

Internal standard: 0.101 mmol

Internal standard integral to Ph ratio: 3:1.31

Normalizing for number of hydrogens: 1:0.65

mmol of Ph = $0.101 \times 0.65 = 0.066$ mmol

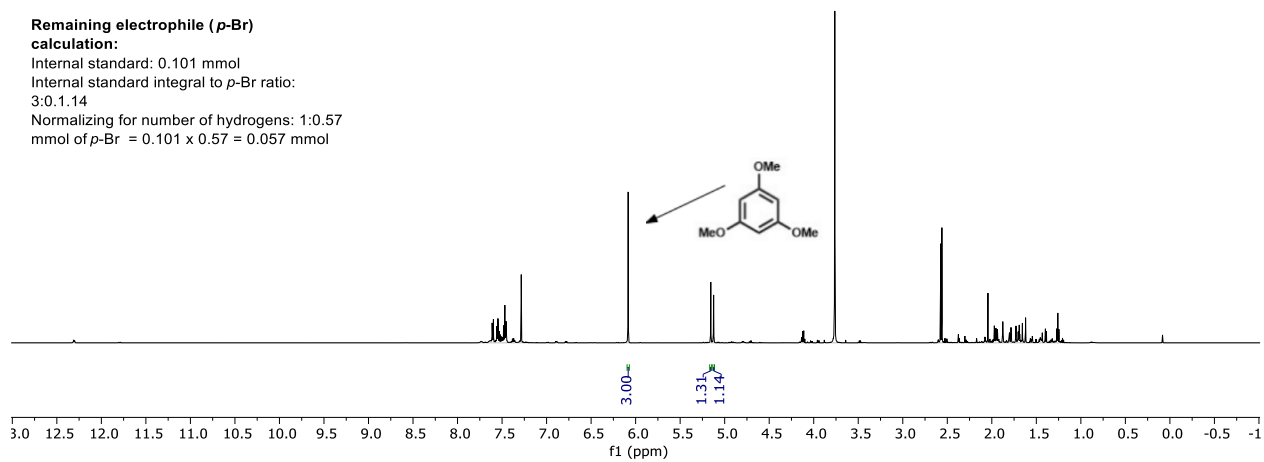
Remaining electrophile (*p*-Br) calculation:

Internal standard: 0.101 mmol

Internal standard integral to *p*-Br ratio: 3:0.114

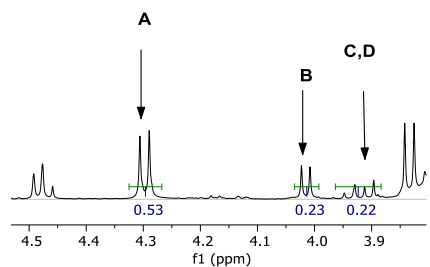
Normalizing for number of hydrogens: 1:0.57

mmol of *p*-Br = $0.101 \times 0.57 = 0.057$ mmol



Additional Mechanistic Insight

Radical Chain Termination Reaction 1 (Crude ^1H NMR)



Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**
Butenolide dimer, major diastereomer, keto tautomer: **B**
Butenolide dimer, minor diastereomer, keto tautomer: **C**
Butenolide dimer, minor diastereomer, enol tautomer: **D**

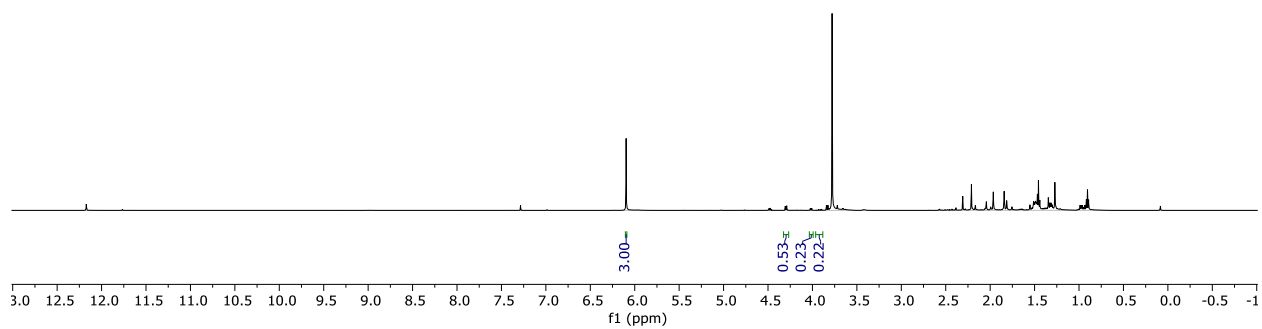
Yield calculation:

Internal standard: 15.7 mg = 0.093 mmol

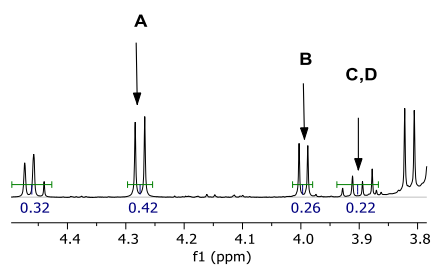
Internal standard integral to butenolide dimer integral ratio: $3:A+B+C+D = 3:0.98$

Normalizing for number of hydrogens: $1:0.98$

mmol butenolide dimer = $0.093 \times 0.98 = .092 = \mathbf{92\% \text{ yield}}$



Radical Chain Termination Reaction 2 (Crude ^1H NMR)



Characterization:

Butenolide dimer, major diastereomer, enol tautomer: **A**

Butenolide dimer, major diastereomer, keto tautomer: **B**

Butenolide dimer, minor diastereomer, keto tautomer: **C**

Butenolide dimer, minor diastereomer, enol tautomer: **D**

Yield calculation:

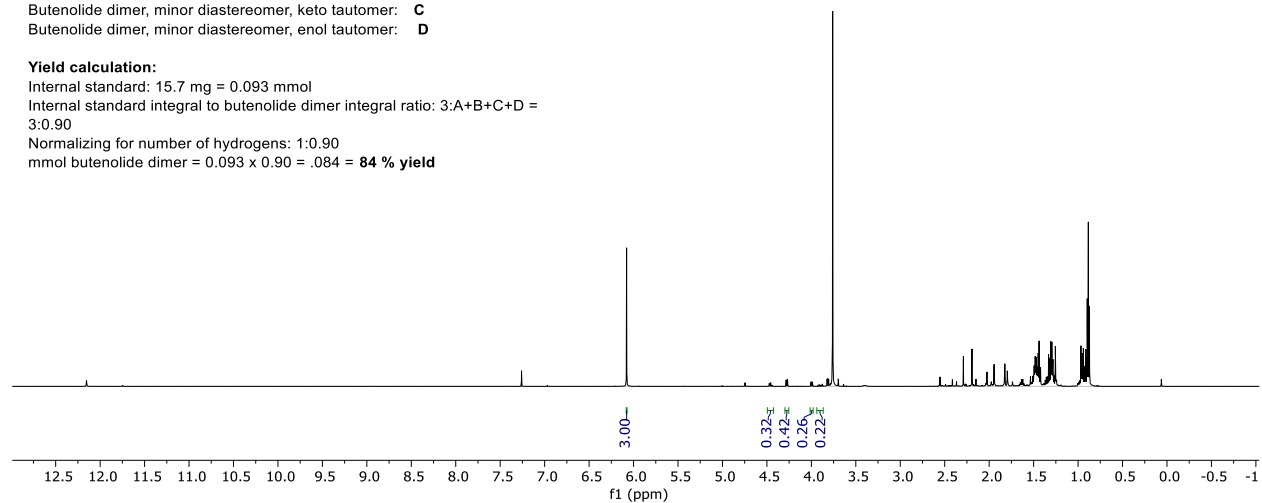
Internal standard: 15.7 mg = 0.093 mmol

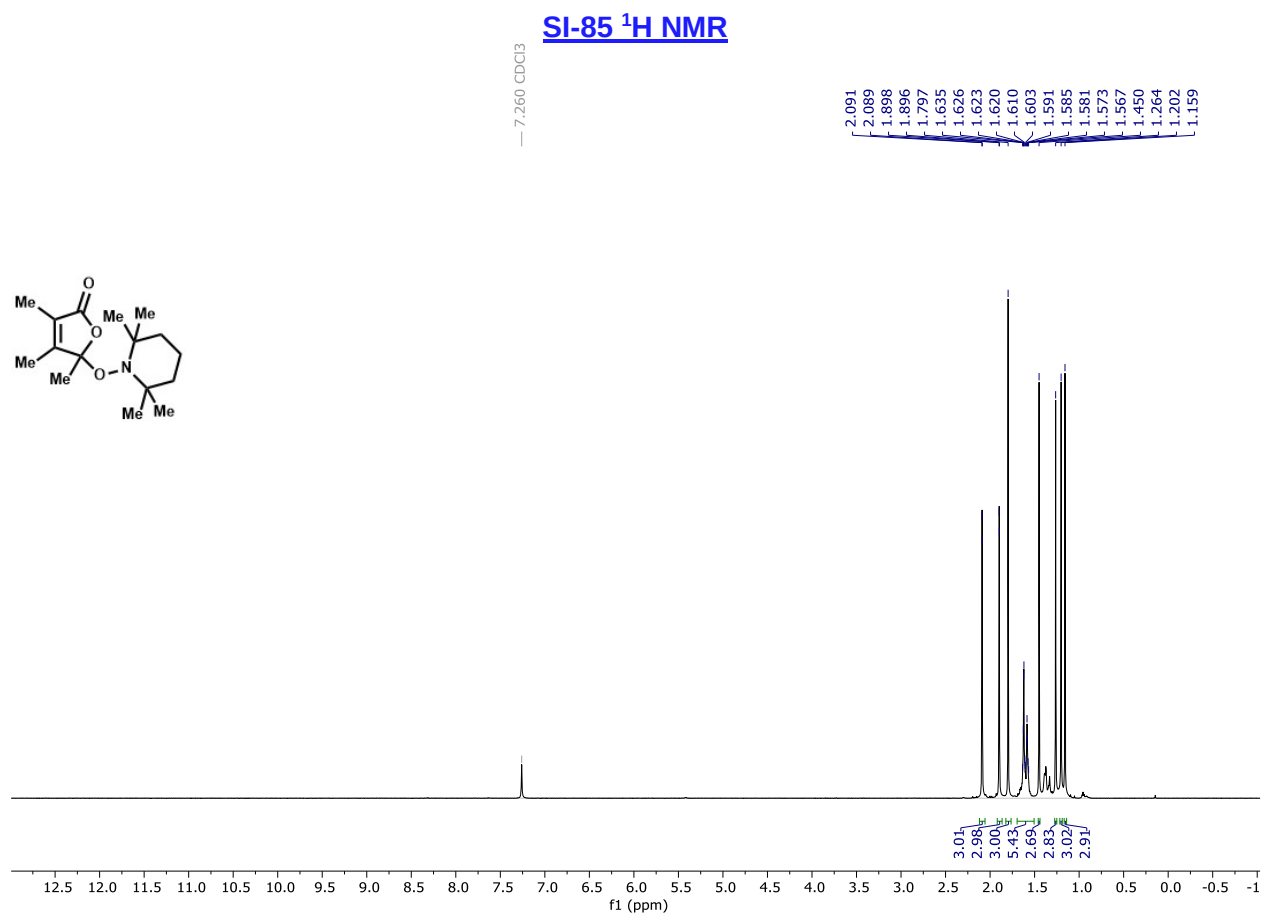
Internal standard integral to butenolide dimer integral ratio: 3:A+B+C+D =

3:0.90

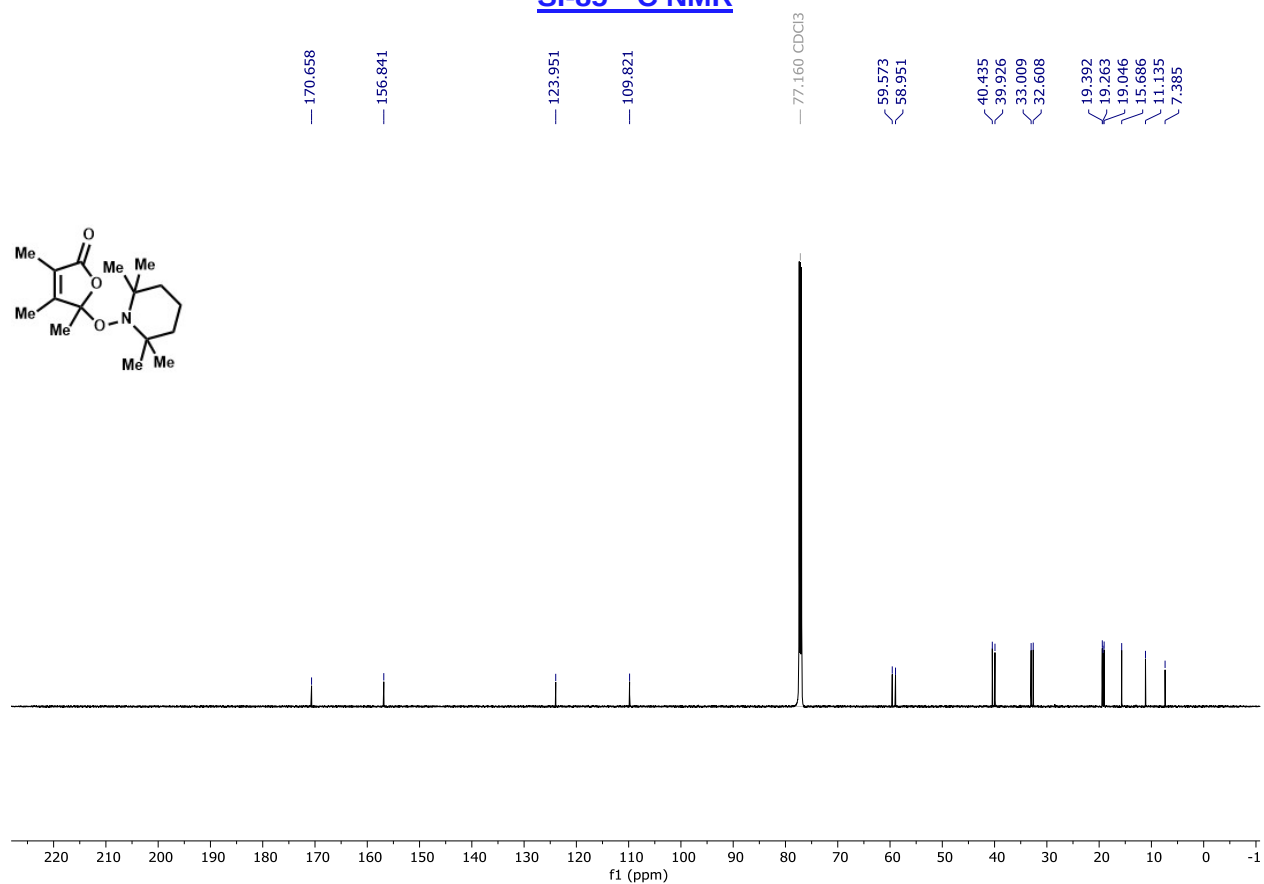
Normalizing for number of hydrogens: 1:0.90

mmol butenolide dimer = 0.093 x 0.90 = .084 = **84 % yield**

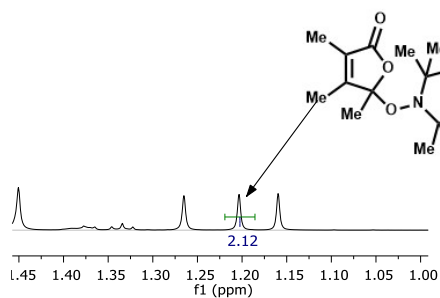




SI-85 ¹³C NMR



SI-85 Crude ^1H NMR



Yield calculation:

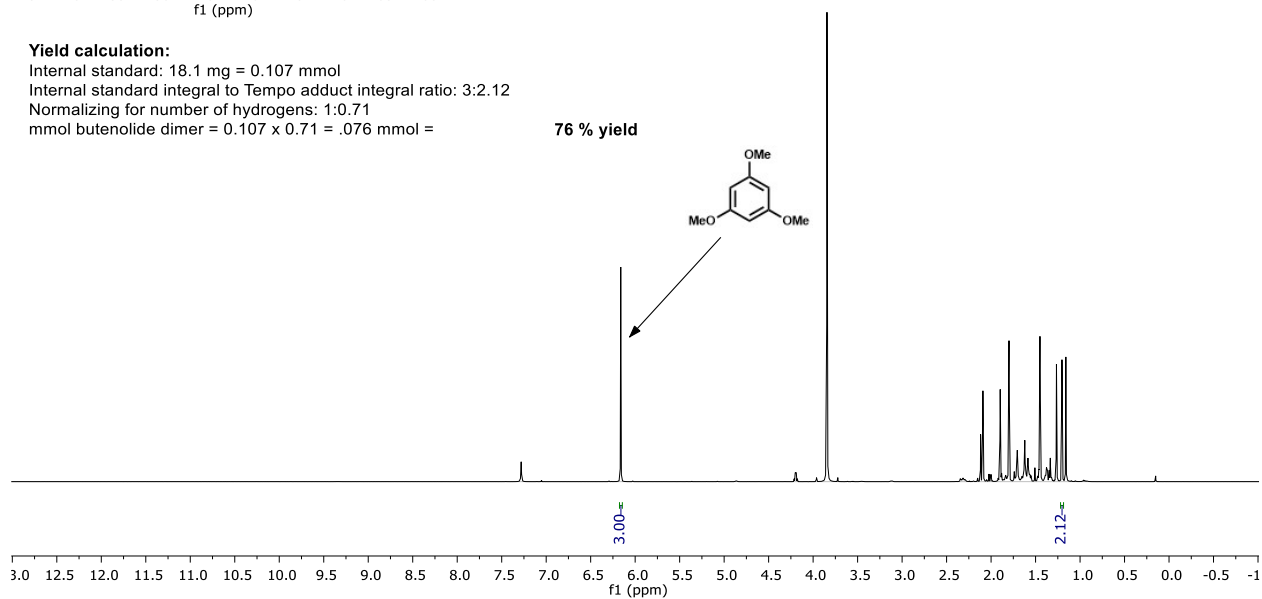
Internal standard: 18.1 mg = 0.107 mmol

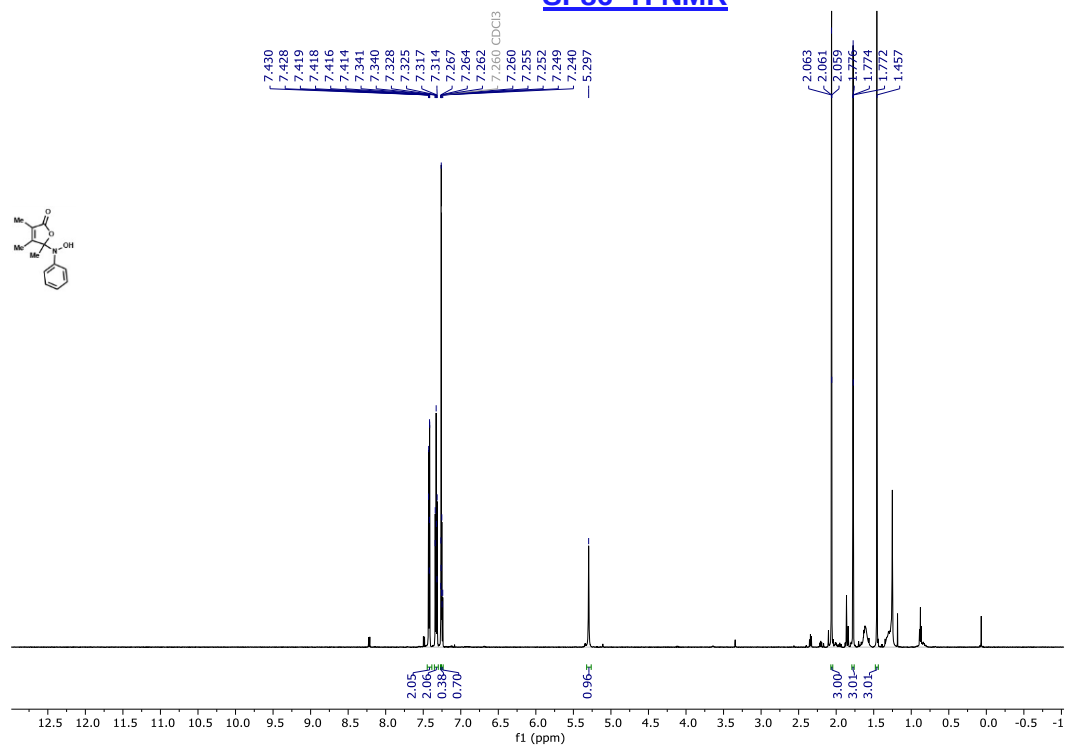
Internal standard integral to Tempo adduct integral ratio: 3:2.12

Normalizing for number of hydrogens: 1:0.71

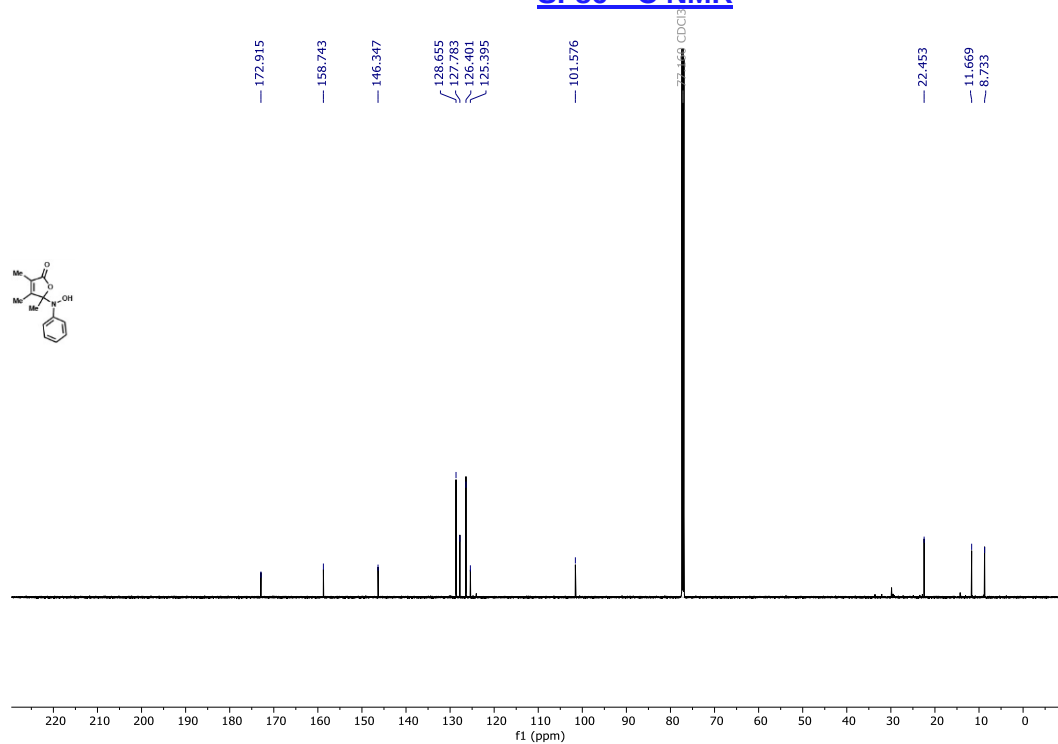
mmol butenolide dimer = $0.107 \times 0.71 = .076$ mmol =

76 % yield

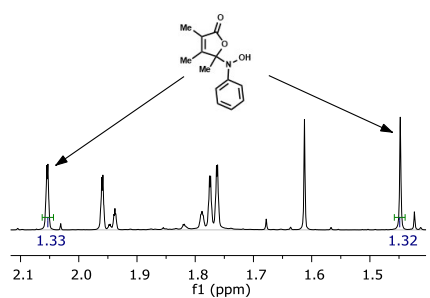




SI-86 ¹³C NMR



SI-86 Crude ¹H NMR



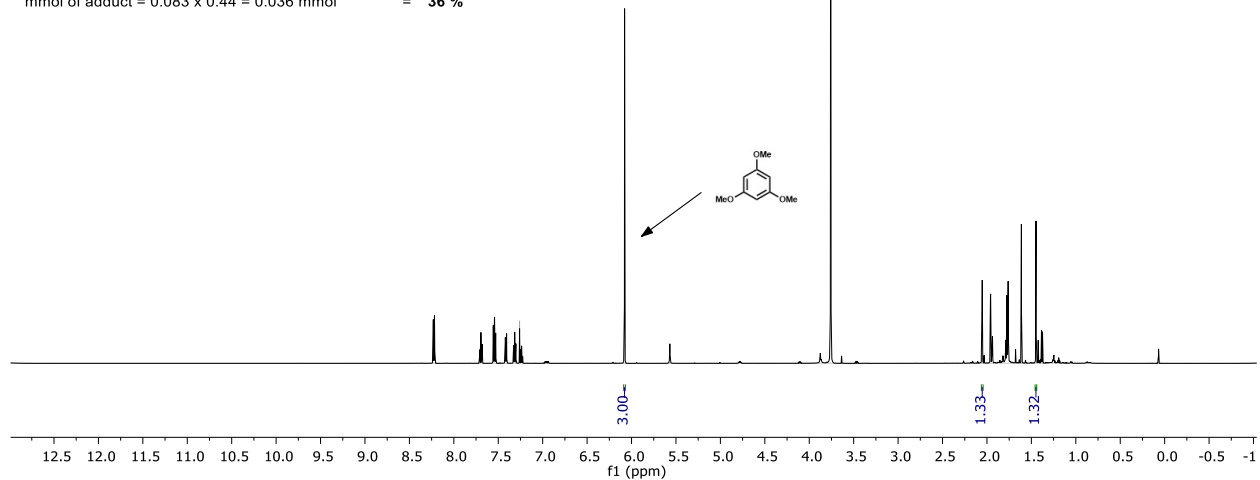
Yield calculation:

Internal standard: 0.083 mmol

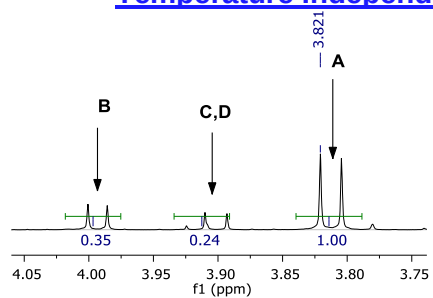
Internal standard integral to adduct ratio: 3:1.32

Normalizing for number of hydrogens: 1:0.44

mmol of adduct = 0.083 x 0.44 = 0.036 mmol = 36 %



Temperature Independent Diastereoselectivity Replicate 1 (Crude ^1H NMR)

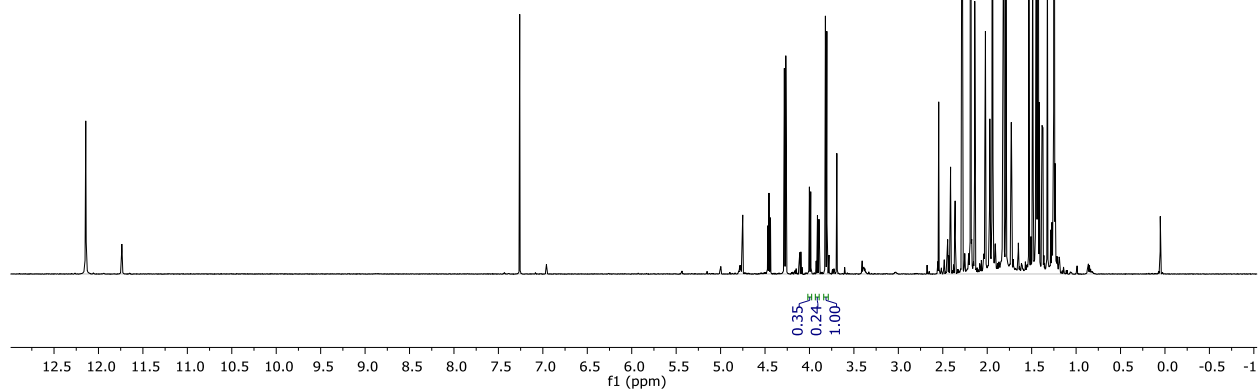


Characterization:

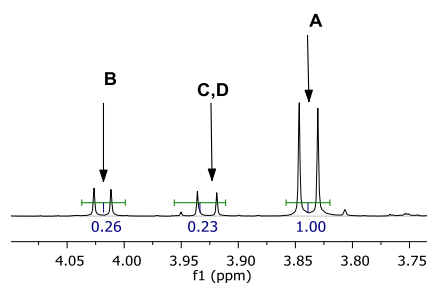
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, major diastereomer, keto tautomer: **B**
 Butenolide dimer, minor diastereomer, keto tautomer: **C**
 Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

$(A+B) / (A+B+C+D) = 1.35 / 1.59 ==$ **d.r. 85:15**



Temperature Independent Diastereoselectivity Replicate 2 (Crude ^1H NMR)

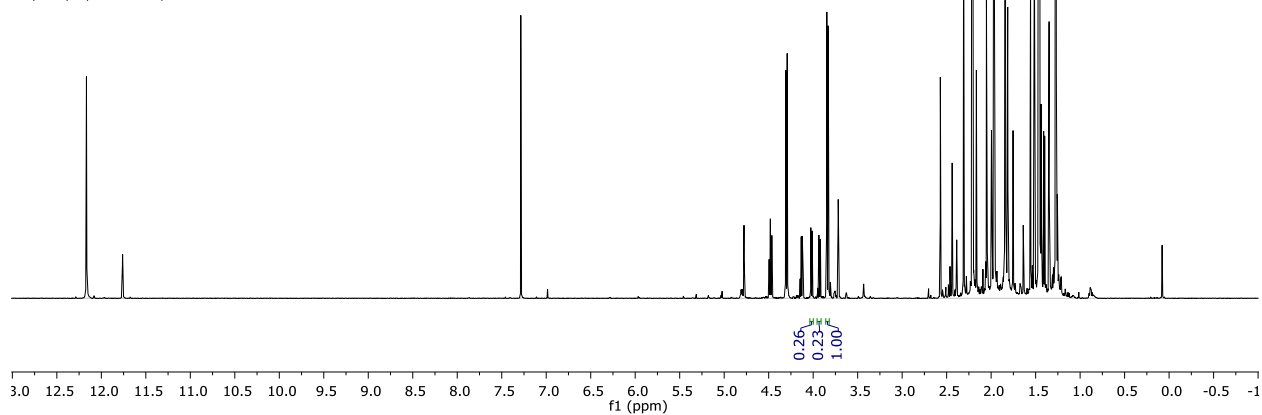


Characterization:

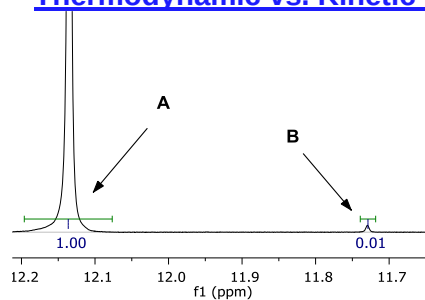
Butenolide dimer, major diastereomer, enol tautomer: **A**
Butenolide dimer, major diastereomer, keto tautomer: **B**
Butenolide dimer, minor diastereomer, keto tautomer: **C**
Butenolide dimer, minor diastereomer, enol tautomer: **D**

d.r. calculation:

$(A+B) / (A+B+C+D) = 1.26 / 1.49 ==$ **d.r. 84:16**



Thermodynamic vs. Kinetic Controlled Diastereoselectivity Reaction 1 (Crude ^1H NMR)

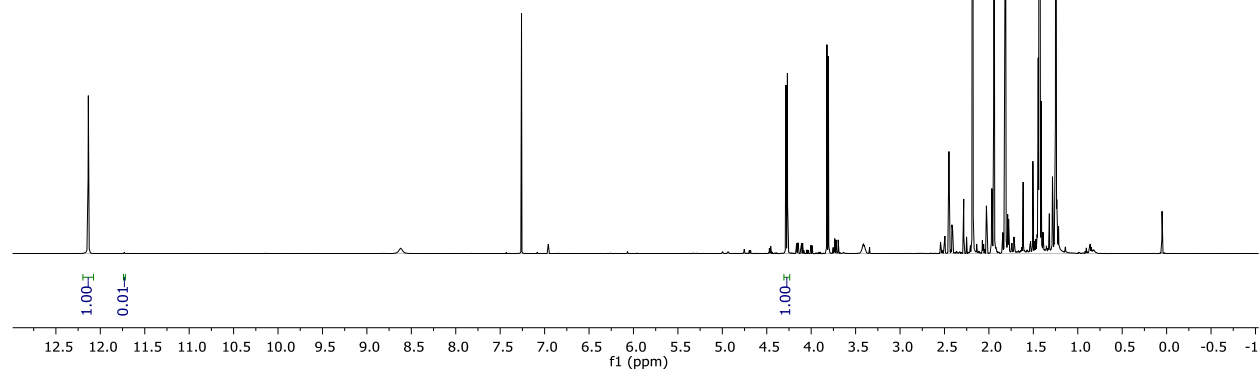


Characterization:

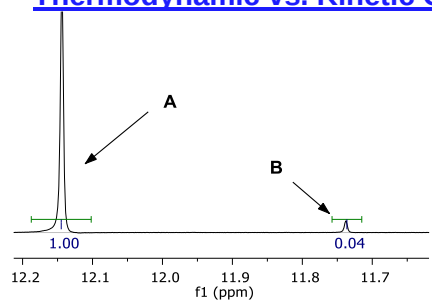
Butenolide dimer, major diastereomer, enol tautomer: **A**
 Butenolide dimer, minor diastereomer, enol tautomer: **B**

d.r. calculation:

$(A) / (A+B) = 1 / 1.01 ==$ d.r. 99 : 1



Thermodynamic vs. Kinetic Controlled Diastereoselectivity Reaction 2 (Crude ^1H NMR)

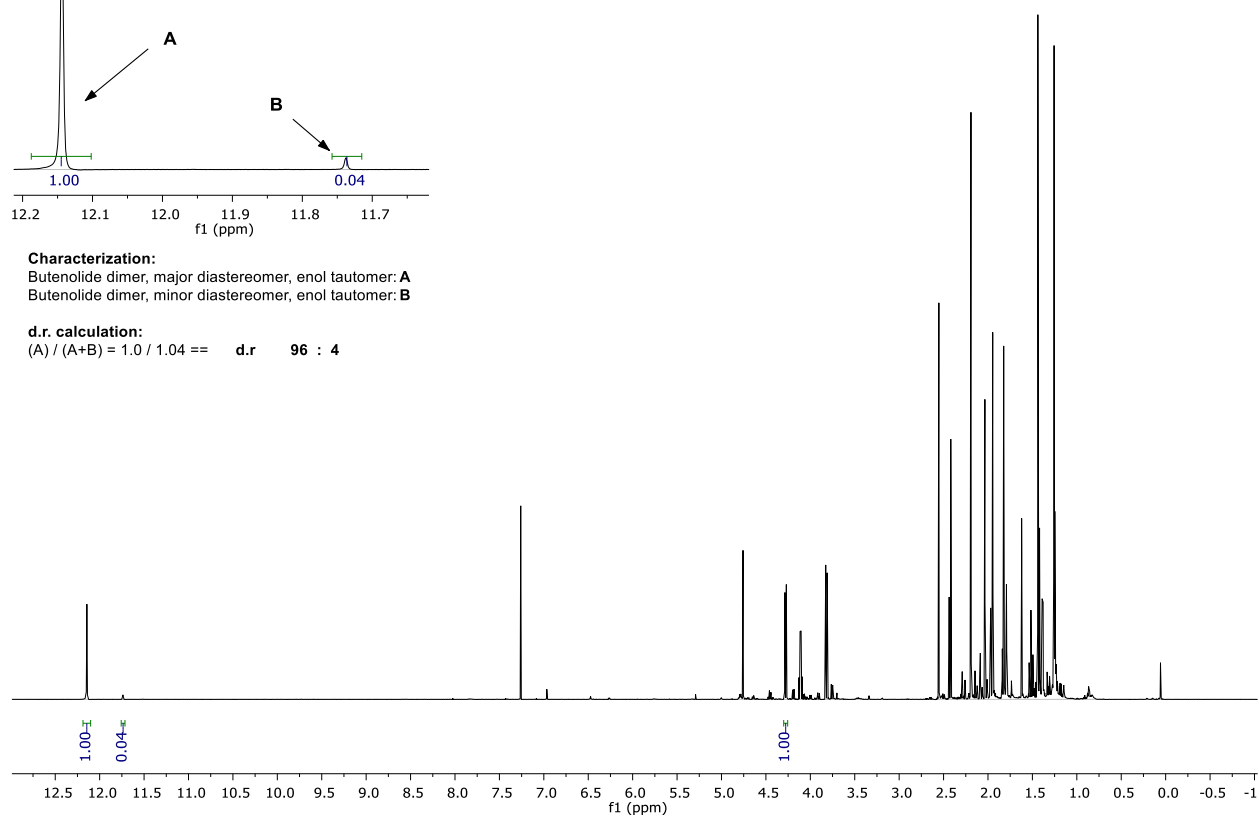


Characterization:

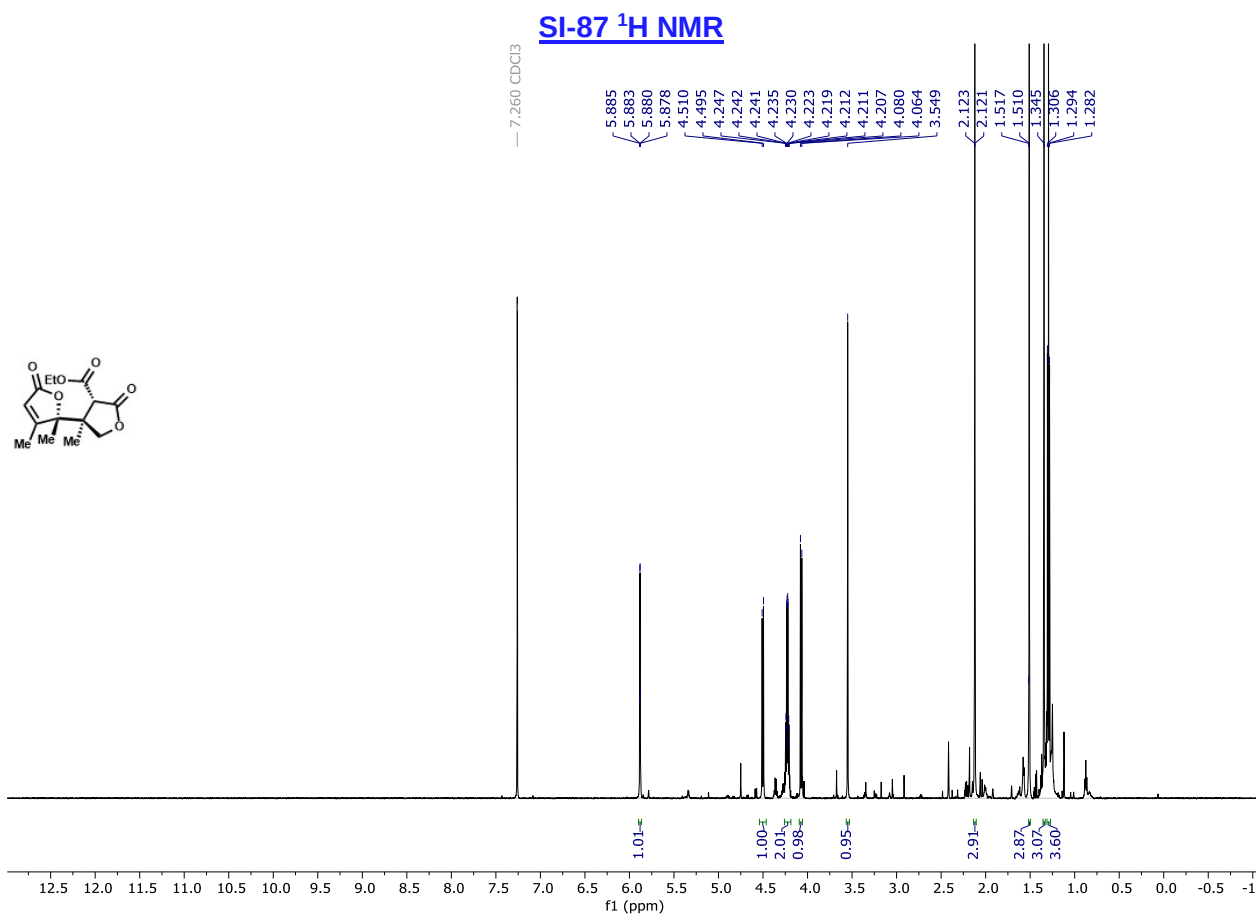
Butenolide dimer, major diastereomer, enol tautomer: A
Butenolide dimer, minor diastereomer, enol tautomer: B

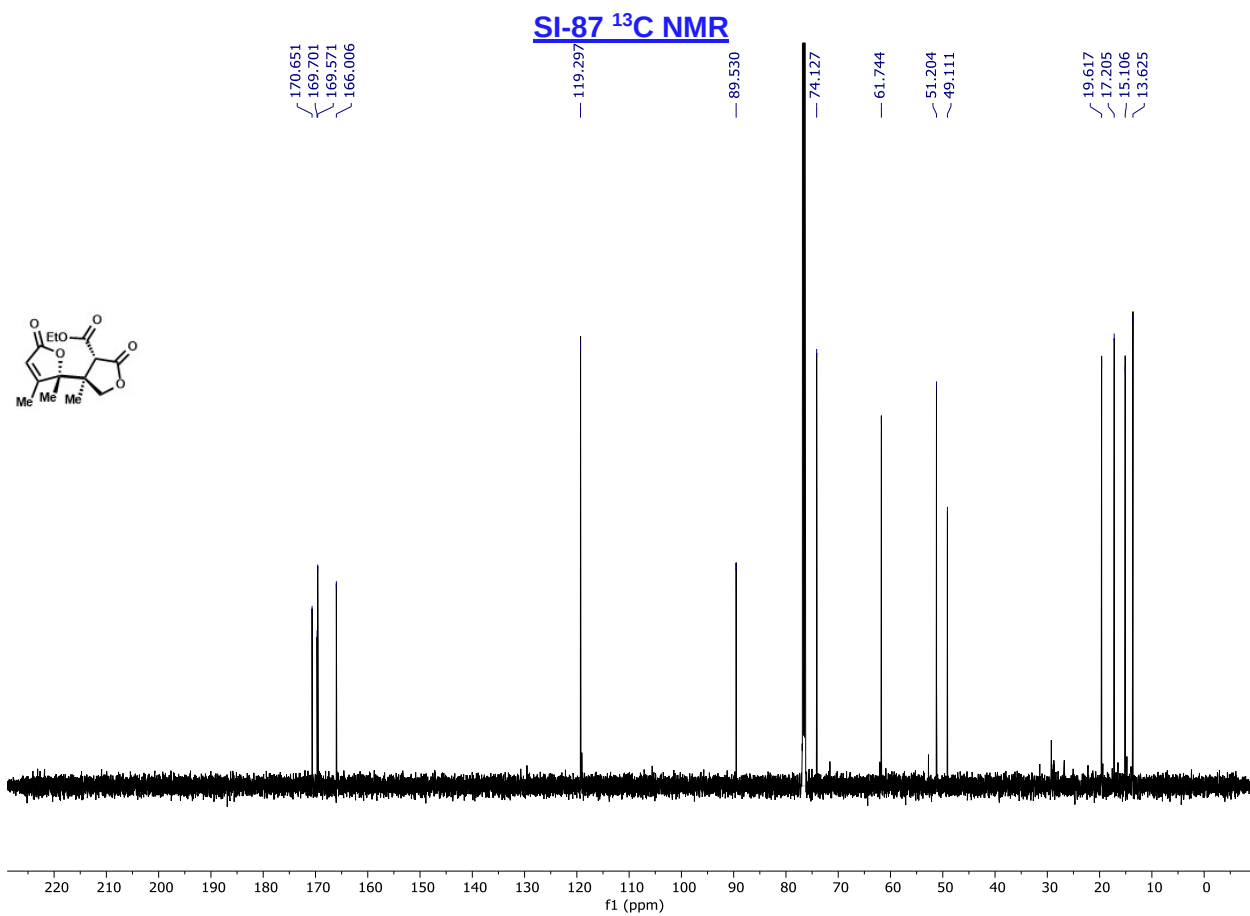
d.r. calculation:

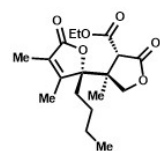
$(A) / (A+B) = 1.0 / 1.04 = \text{d.r. } 96 : 4$



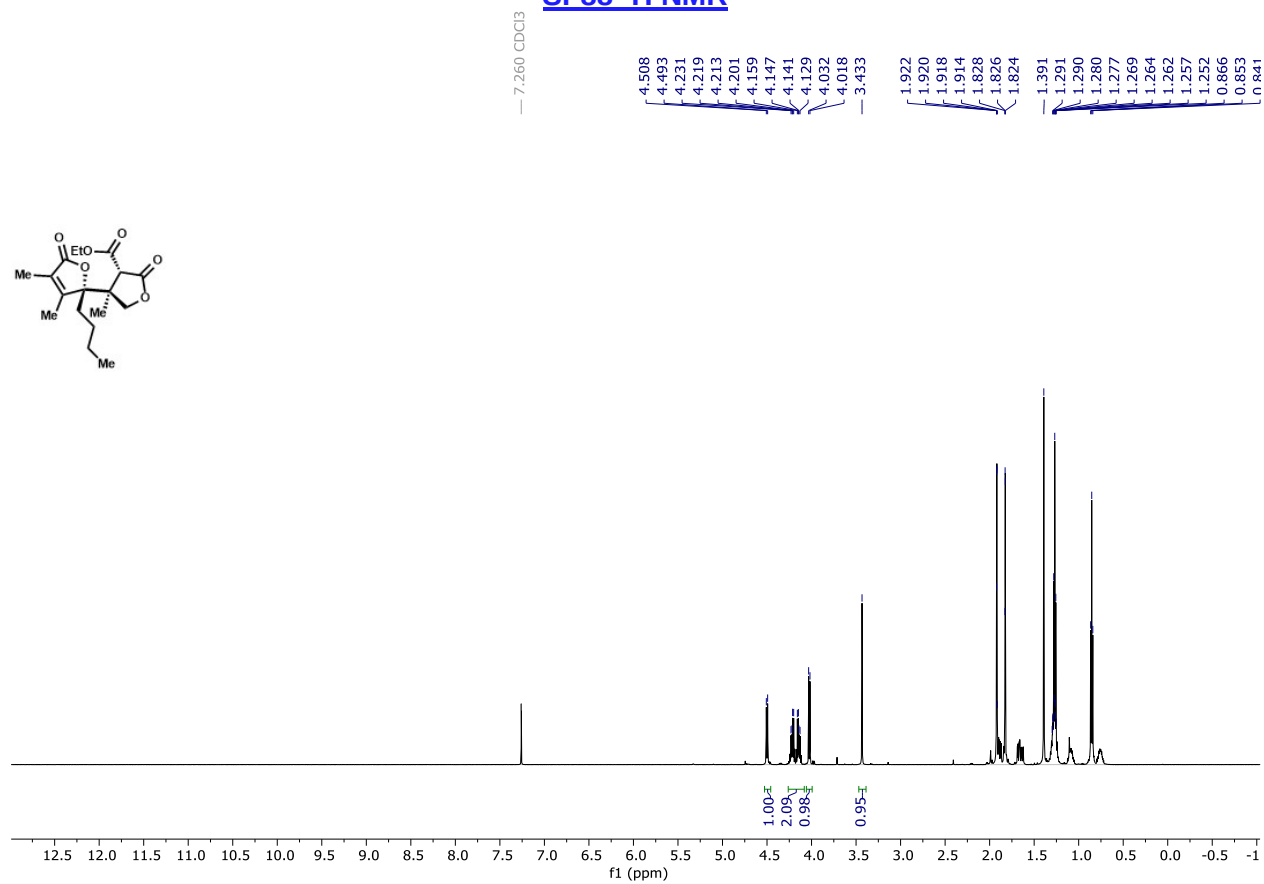
Principal Moment of Inertia



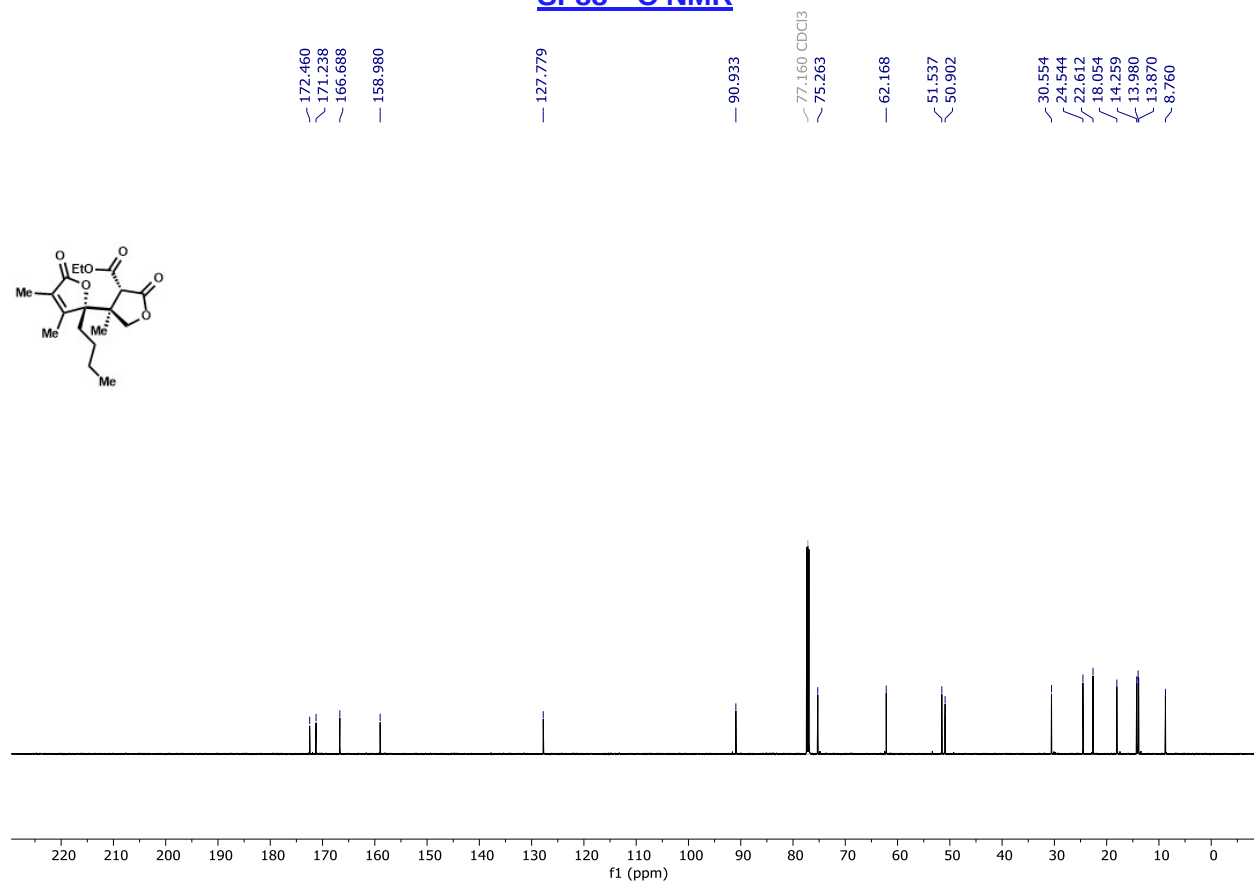




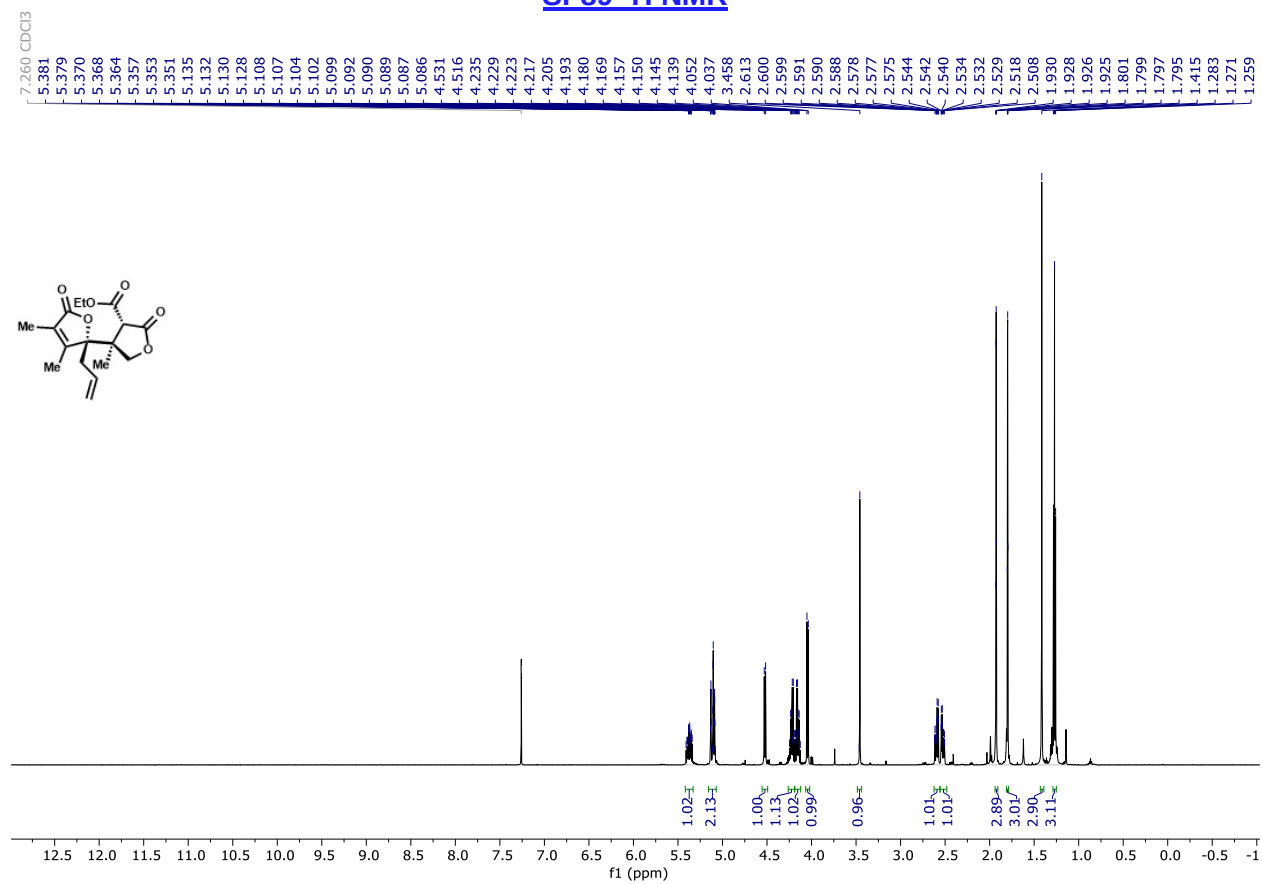
SI-88 ¹H NMR



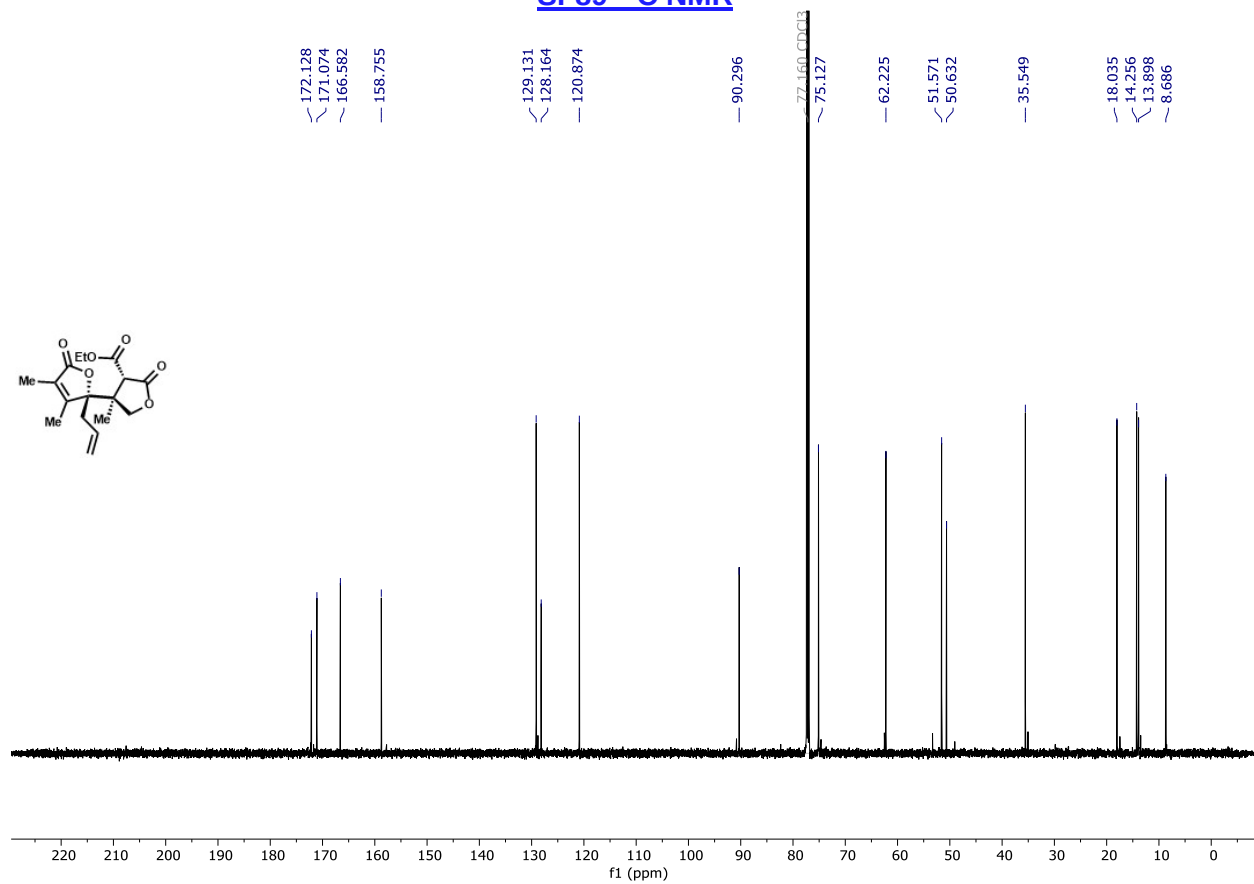
SI-88 ¹³C NMR

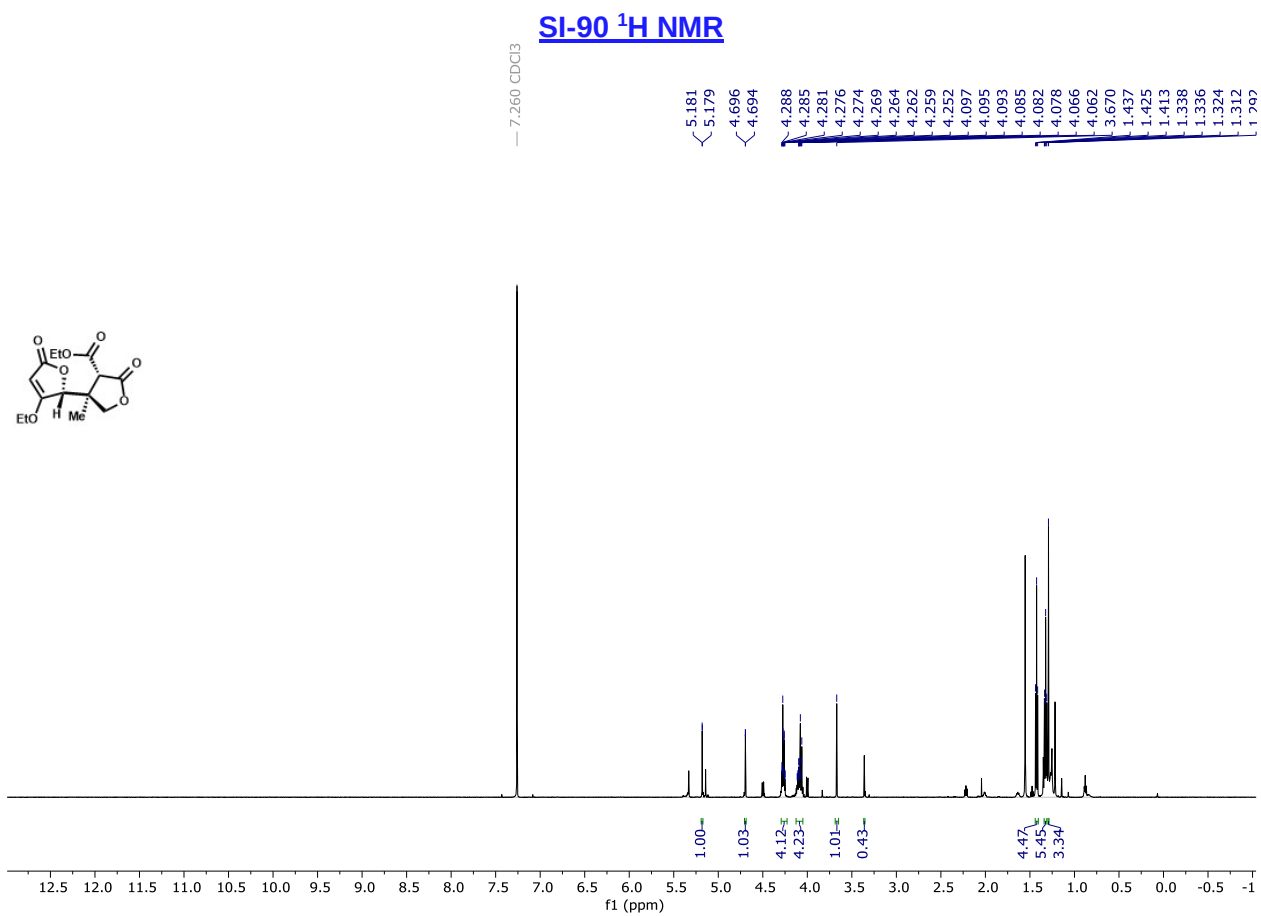


SI-89 ¹H NMR

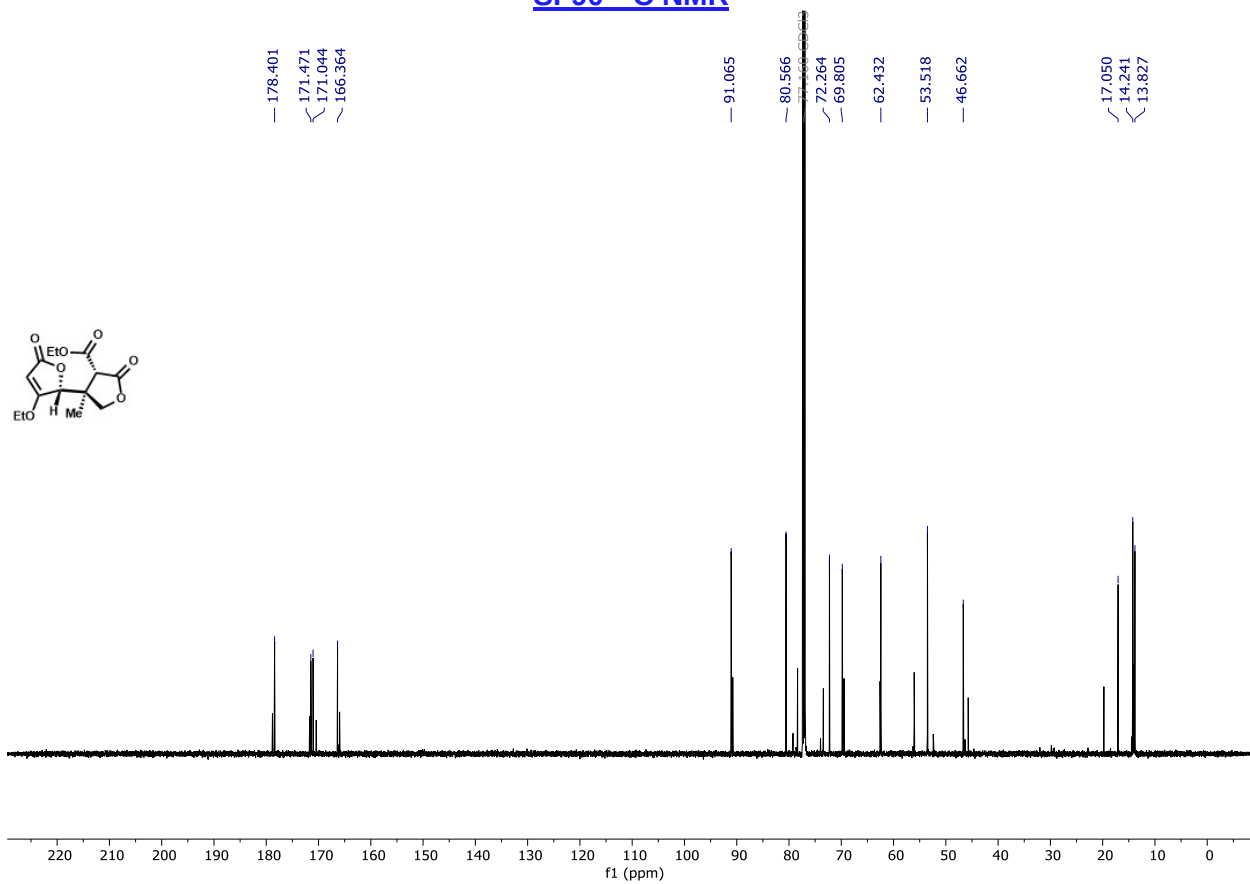


SI-89 ¹³C NMR



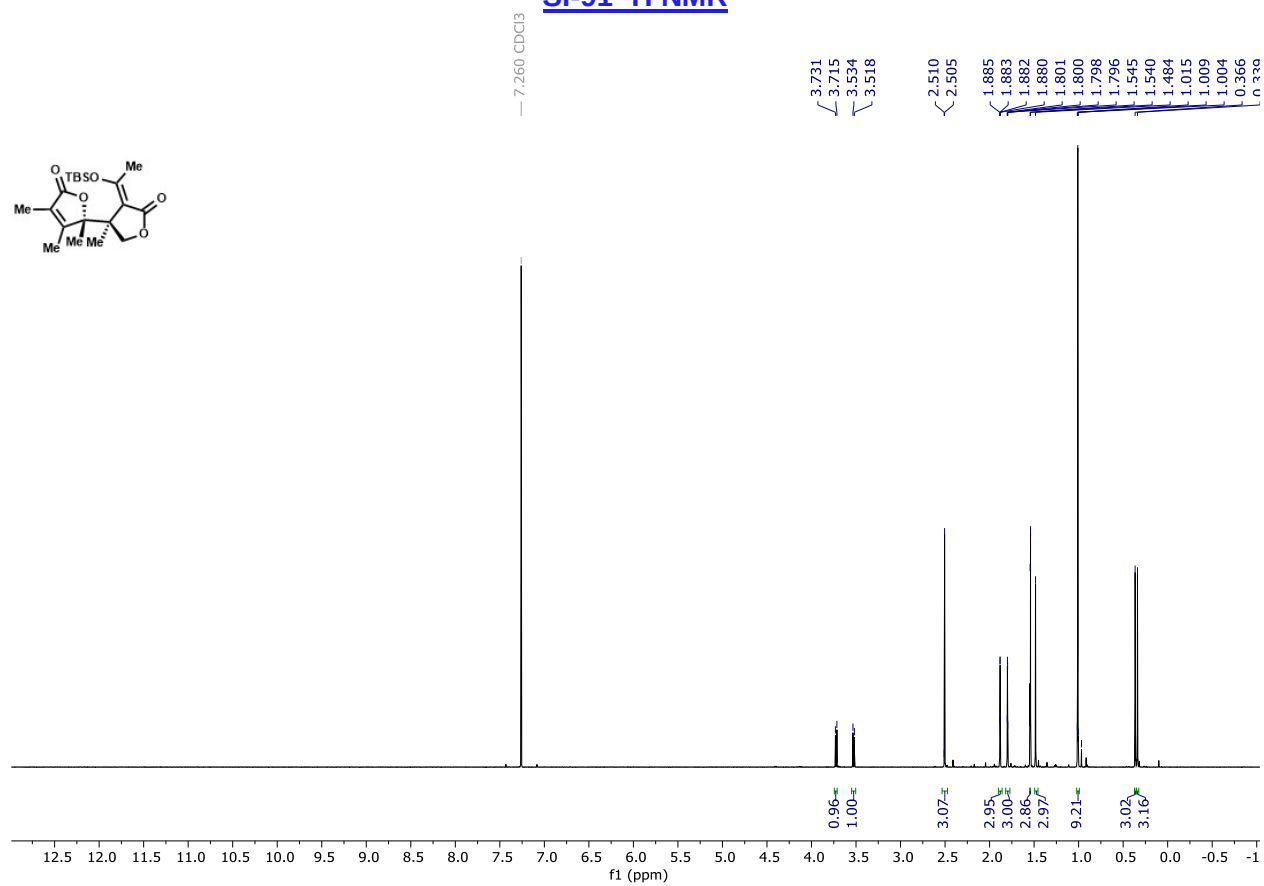


SI-90 ¹³C NMR

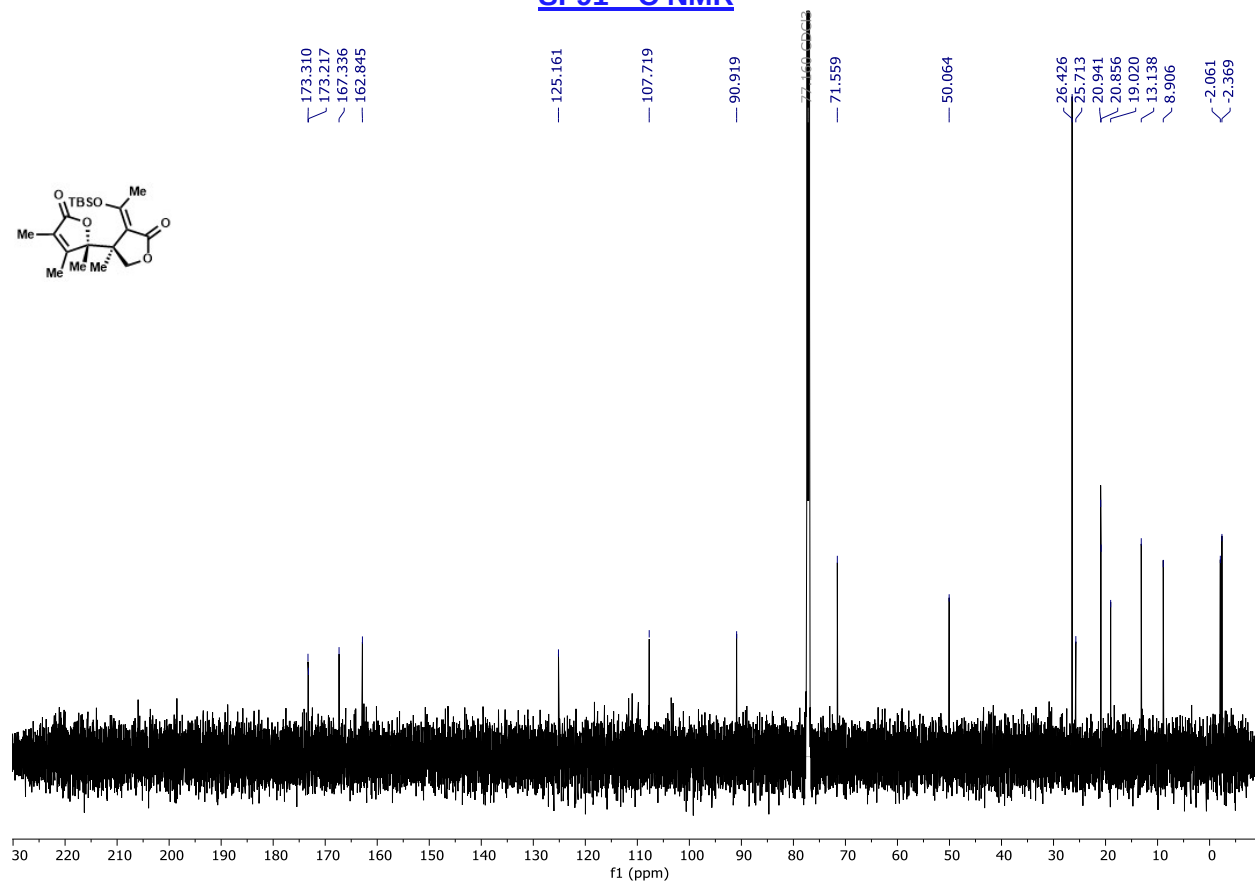
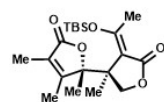


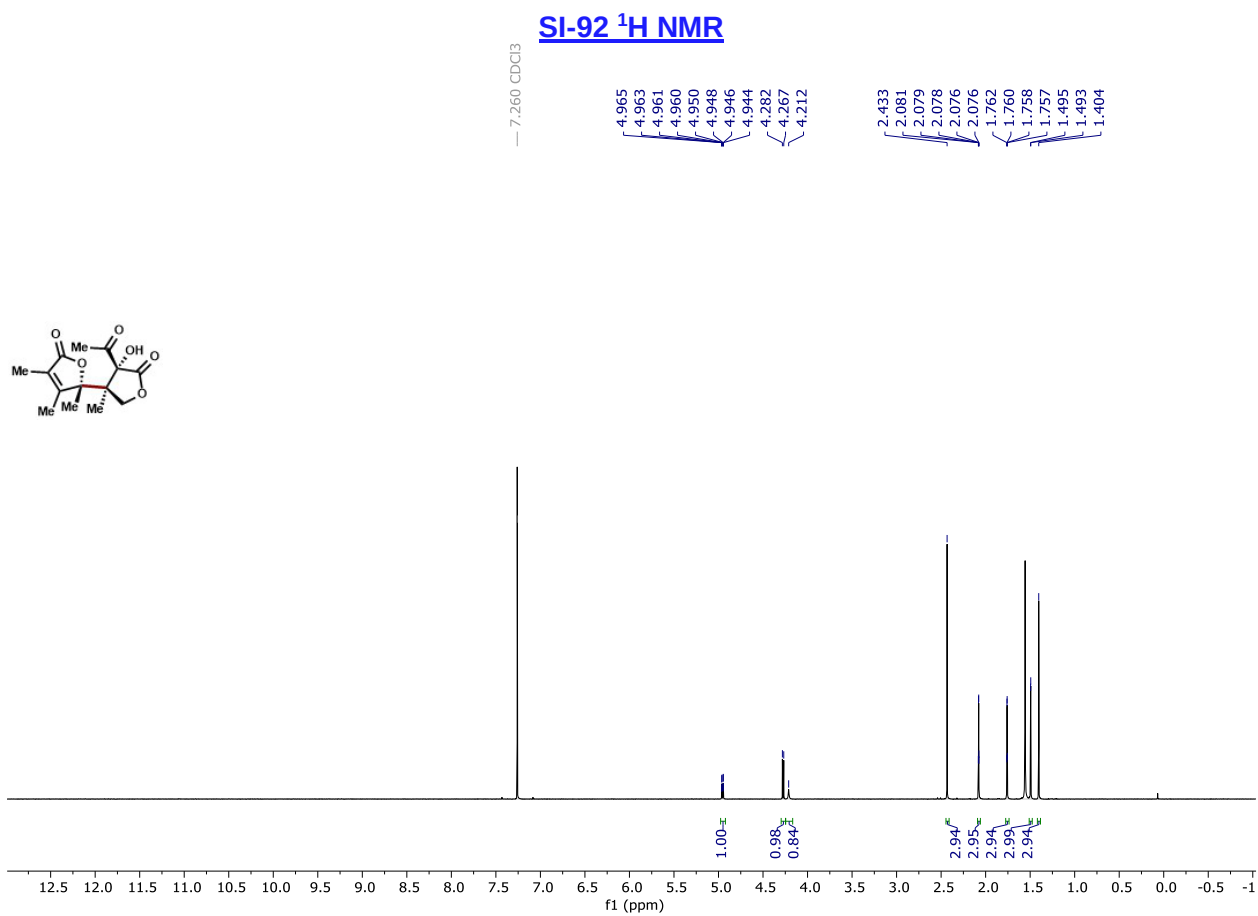
Diversified Compounds

SI-91 ¹H NMR

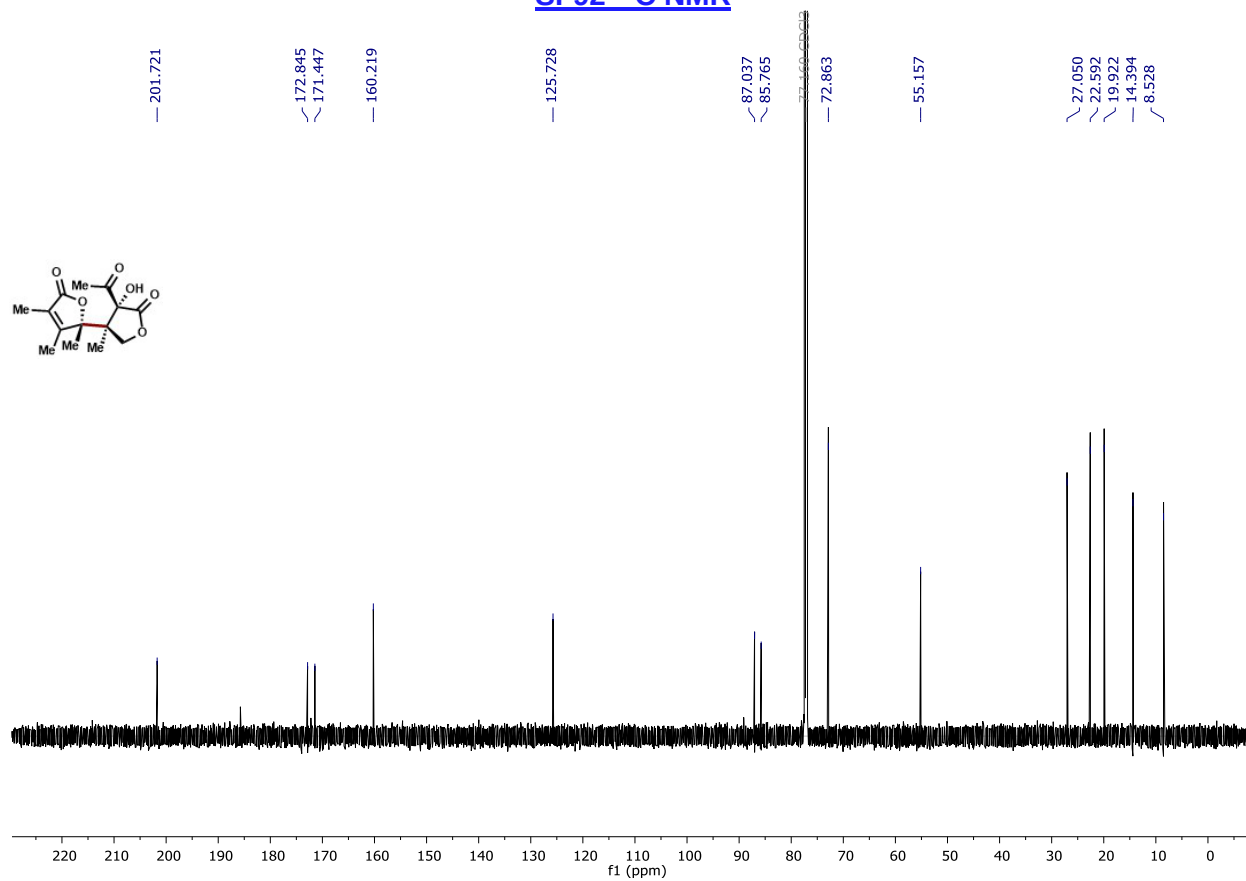


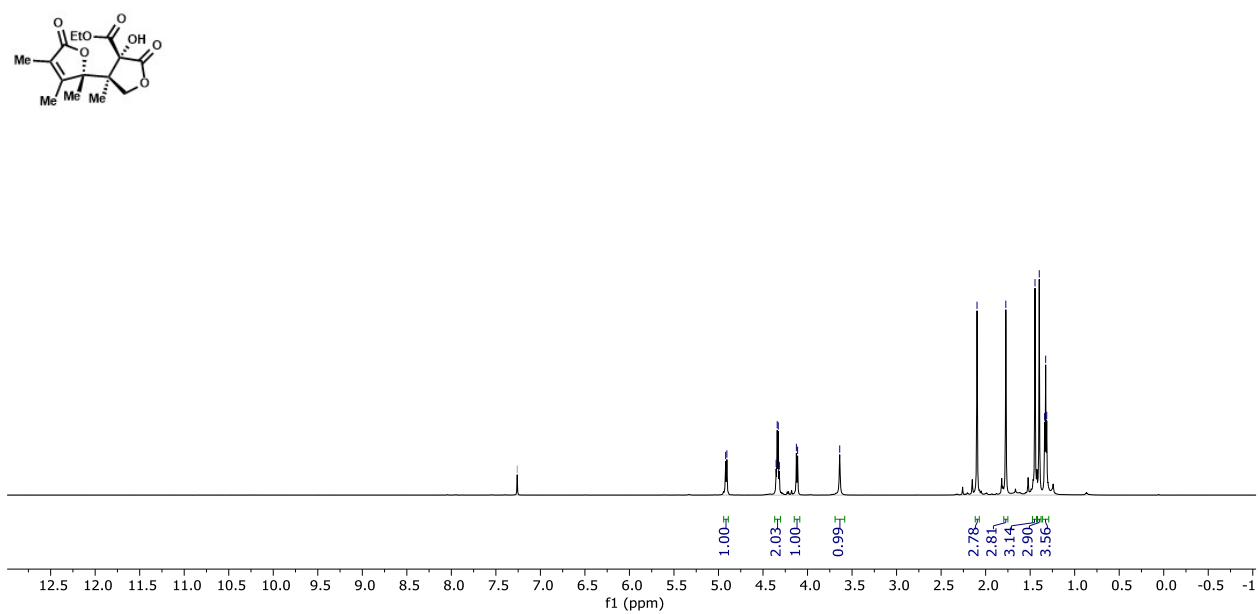
SI-91 ¹³C NMR



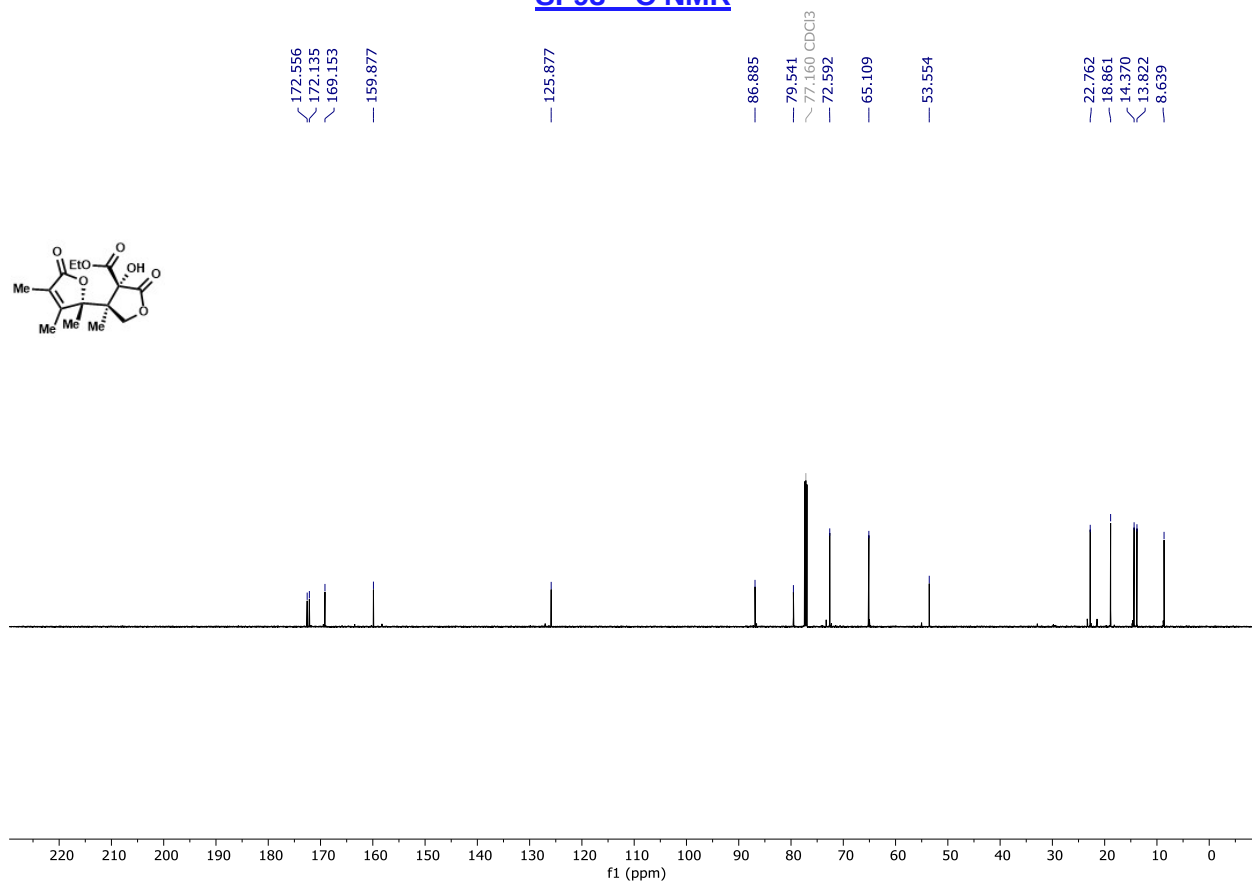


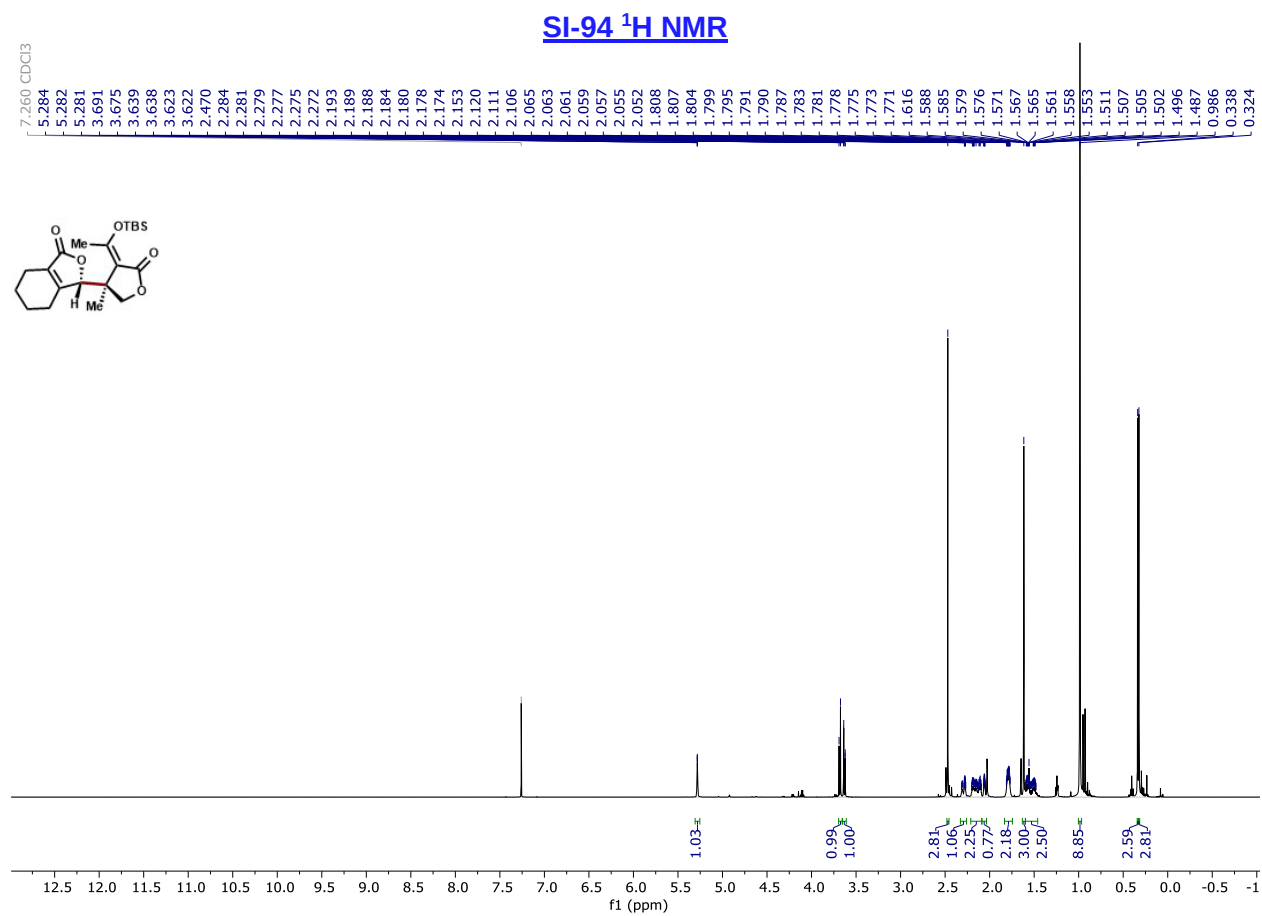
SI-92 ¹³C NMR



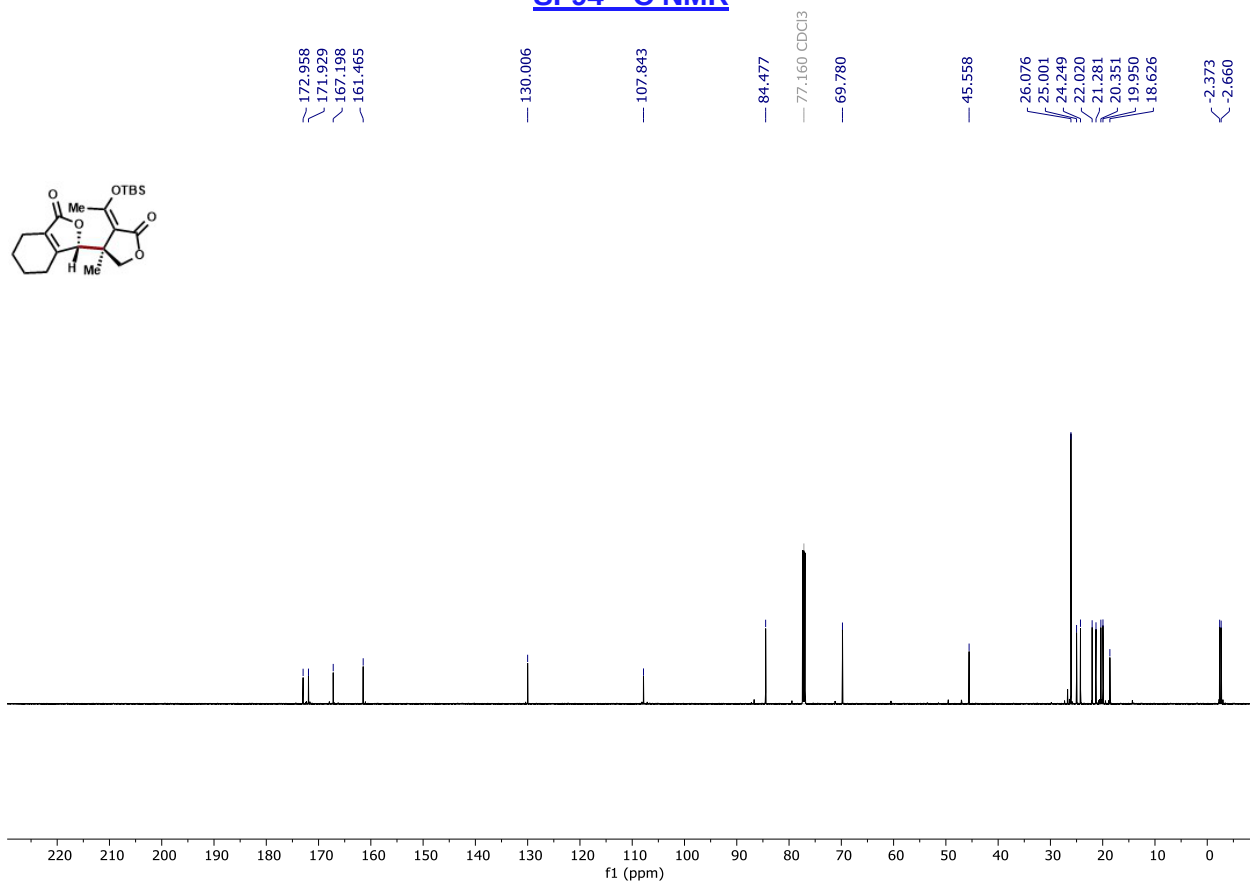


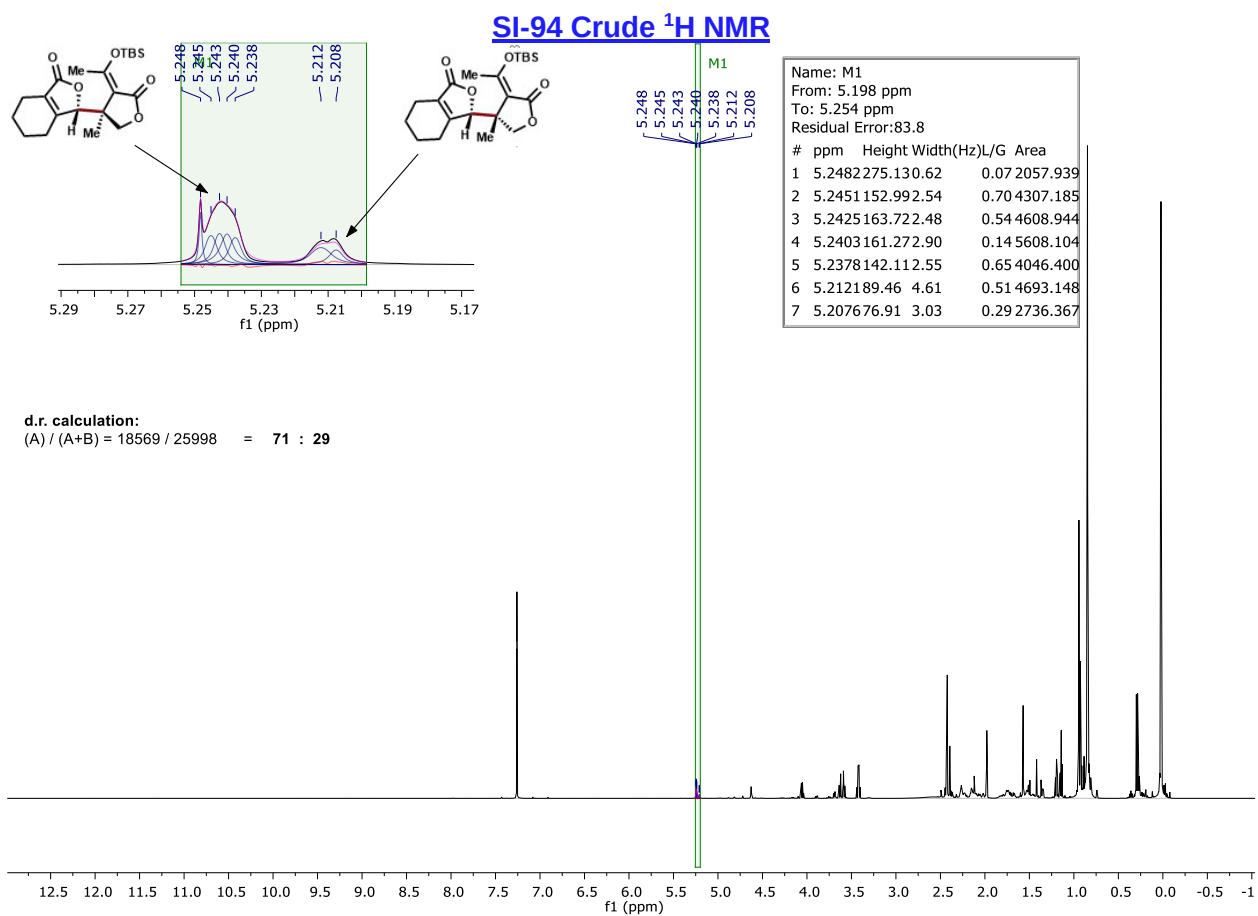
SI-93 ¹³C NMR





SI-94 ¹³C NMR

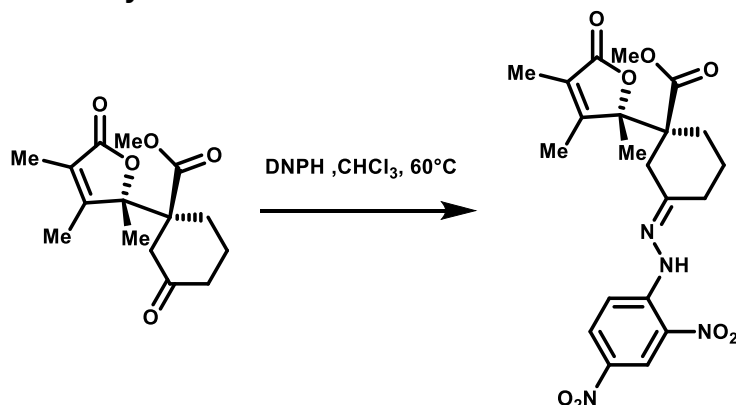




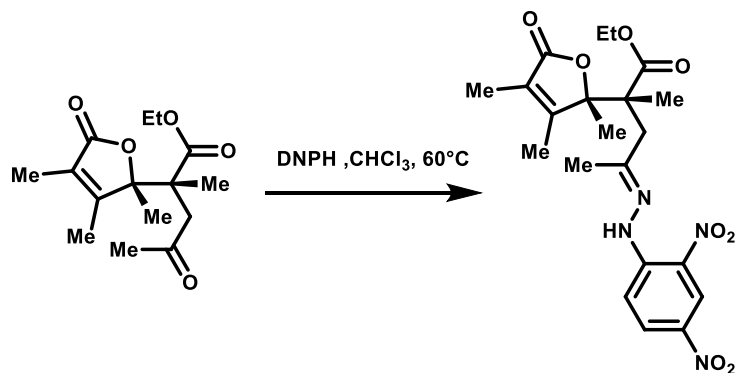
Note: Since **SI-75** could only be isolated as a mixture of diastereomers and tautomers (6 distinct compounds), crude **SI-75** was treated with TBSCl in an effort to determine the d.r. Treatment with TBSCl ablated a stereocenter and eliminated the possibility of tautomerism—thus simplifying the mixture from 6 to 2 diastereomers. (See [SI-94](#))

Crystal Data

DNPH Condensation for Crystalization

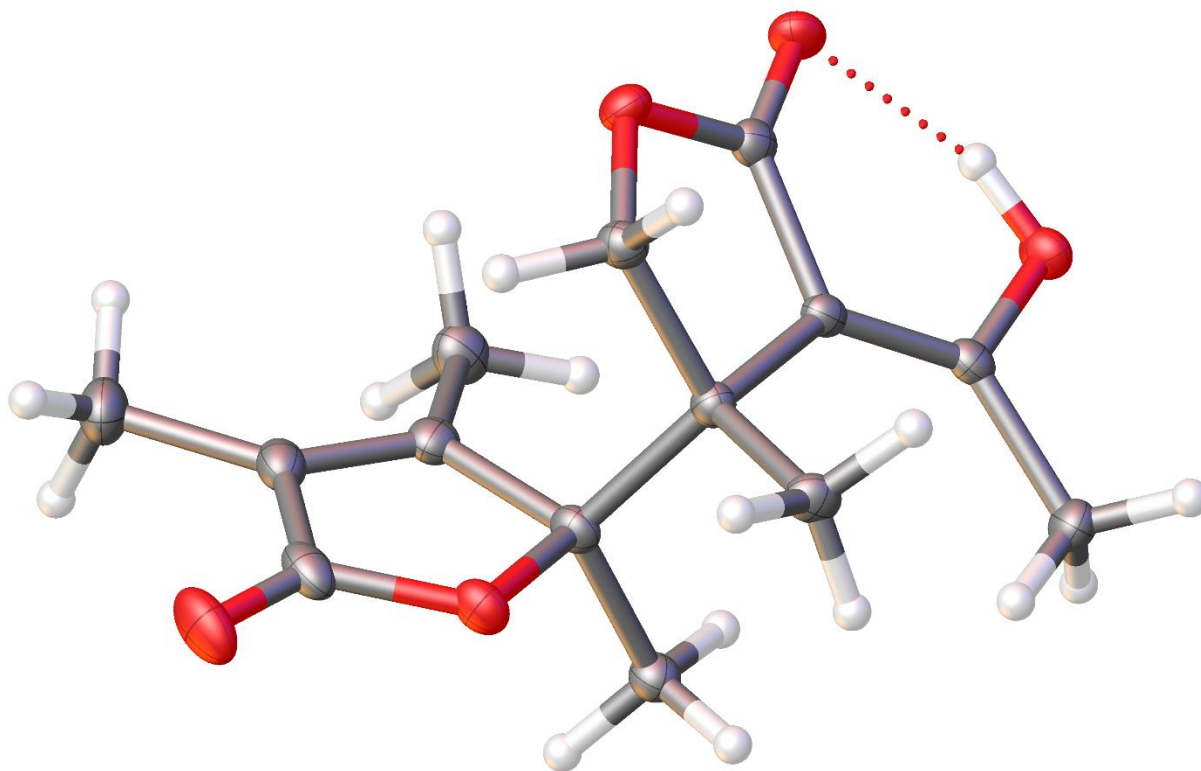


DNPH condensation procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. Next, the flask was charged with **SI-21** (0.1 mmol, 28.0 mg), recrystallized 2,4-dinitrophenylhydrazine (0.5 mmol, 99.0 mg) and CHCl₃ (1.0 mL). The reaction mixture was heated to 60 °C and allowed to stir for 36 hours. The reaction was then diluted with H₂O and extracted with EtOAc (3x 3 mL). The combined organics were dried over MgSO₄, concentrated *in vacuo*, and purified via column chromatography.



DNPH condensation procedure: A 13 x 100 mm test tube fitted with a Teflon stir bar and rubber lined screw cap septum was flame dried and backfilled with argon. Next, the flask was charged with **SI-22** (0.1 mmol, 28.0 mg), recrystallized 2,4-dinitrophenylhydrazine (0.5 mmol, 99.0 mg) and CHCl₃ (1.0 mL). The reaction mixture was heated to 60 °C and allowed to stir for 36 hours. The reaction was then diluted with H₂O and extracted with EtOAc (3x 3 mL). The combined organics were dried over MgSO₄, concentrated *in vacuo*, and purified via column chromatography.

SI-46 (Major)



CCDC: 1849244. The single crystal X-ray diffraction studies were carried out on a Bruker APEX II Ultra diffractometer equipped with Mo K $_{\alpha}$ radiation ($\lambda = 0.71073$). Crystals of the subject compound were used as received (grown from DCM/Pentane). A 0.200 x 0.22x 0.20 mm colorless block was mounted on a Cryoloop with Paratone oil.

Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ω scans. Crystal-to-detector distance was 40 mm using exposure times 1.0 second, with a scan width of 0.80°. Data collection was 100.0% complete to 25.242° in θ . A total of 15873 reflections were collected. 2448 reflections were found to be symmetry independent, with a R_{int} of 0.0553. Indexing and unit cell refinement indicated a **Primitive Monoclinic** lattice. The space group was found to be ***P2₁/c***. The data were integrated using the Bruker SAINT software program and scaled using the WINABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained

relative to their parent atom using the appropriate HFIX command in SHELXL-2014. All other hydrogen atoms (H-bonding) were located in the difference map. Their relative positions were restrained using DFIX commands and their thermal parameters freely refined. Crystallographic data are summarized in Table 1.

SI-46 (major)

Table 1 Data collection and refinement statistics (molecular replacement)

SI-46 Major	
Identification code	shenvi175_0m_a
Empirical formula	C ₂₂ H ₂₄ O ₆ S
Temperature	100.0 K
Wavelength (Å)	0.710
Crystal system	Monoclinic
Space group	P 1 21/c 1
Cell dimensions	
<i>a</i> , <i>b</i> , <i>c</i> (Å)	13.44, 7.08, 14.20
α , β , γ (°)	90, 108.46, 90
Volume	1283.53(14) Å ³
<i>Z</i>	4
Density (calculated)	1.378 Mg/m ³
Absorption coefficient	0.104 mm ⁻¹
<i>F</i> (000)	568
Crystal size	0.25 x 0.22 x 0.2 mm ³
Crystal color, habit	colorless block
Theta range for data collection	1.597 to 25.672°
Index ranges	-14 ≤ <i>h</i> ≤ 16, -
	8 ≤ <i>k</i> ≤ 8, -
	17 ≤ <i>l</i> ≤ 17
Reflections collected	15873
Independent reflections	2448 [R(int) =
	0.0553]
Completeness to theta = 25.242°	100.0%
Absorption correction	Semi-empirical from
	equivalents
Max. and min. transmission	0.4900 and 0.4503
Refinement method	Full-matrix least-
	squares on <i>F</i> ²
Data / restraints / parameters	2448 / 0 / 180
Goodness-of-fit on <i>F</i> ²	1.037
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> ₁ = 0.0380, <i>wR</i> ₂ =
	0.0934
<i>R</i> indices (all data)	<i>R</i> ₁ = 0.0428, <i>wR</i> ₂ =
	0.0971
Extinction coefficient	n/a
Largest diff. peak and hole	0.288 and -0.182 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for Shenvi88A. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
O(1)	10476(1)	2187(2)	5019(1)	19(1)
O(2)	9123(1)	3530(2)	3424(1)	20(1)
O(3)	7687(1)	4777(1)	3649(1)	18(1)
O(4)	6247(1)	2627(1)	5562(1)	19(1)
O(5)	4493(1)	2786(2)	4951(1)	30(1)
C(1)	10167(1)	1870(2)	6547(1)	19(1)
C(2)	9753(1)	2454(2)	5486(1)	15(1)
C(3)	8802(1)	3200(2)	4994(1)	14(1)
C(4)	8588(1)	3810(2)	3973(1)	16(1)
C(5)	7324(1)	5157(2)	4496(1)	17(1)
C(6)	7851(1)	3693(2)	5305(1)	14(1)
C(7)	8085(1)	4653(2)	6322(1)	18(1)
C(8)	7107(1)	1946(2)	5227(1)	16(1)
C(9)	7625(1)	303(2)	5897(1)	18(1)
C(10)	6550(1)	1261(2)	4185(1)	18(1)
C(11)	7084(1)	274(2)	3547(1)	22(1)
C(12)	5521(1)	1524(2)	3965(1)	20(1)
C(13)	4650(1)	977(3)	3051(1)	29(1)
C(14)	5315(1)	2373(2)	4830(1)	22(1)

Table 3. Bond lengths [Å] and angles [°] for Shenvi88A.

O(1)-C(2)	1.3521(17)	C(12)-C(14)	1.470(2)
O(1)-H(1)	0.88(2)	C(13)-H(13A)	0.9800
O(2)-C(4)	1.2317(17)	C(13)-H(13B)	0.9800
O(3)-C(4)	1.3403(17)	C(13)-H(13C)	0.9800
O(3)-C(5)	1.4603(16)		
O(4)-C(8)	1.4644(17)	C(2)-O(1)-H(1)	103.8(12)
O(4)-C(14)	1.3630(19)	C(4)-O(3)-C(5)	108.26(10)
O(5)-C(14)	1.2071(19)	C(14)-O(4)-C(8)	109.80(11)
C(1)-H(1A)	0.9800	H(1A)-C(1)-H(1B)	109.5
C(1)-H(1B)	0.9800	H(1A)-C(1)-H(1C)	109.5
C(1)-H(1C)	0.9800	H(1B)-C(1)-H(1C)	109.5
C(1)-C(2)	1.4900(19)	C(2)-C(1)-H(1A)	109.5
C(2)-C(3)	1.356(2)	C(2)-C(1)-H(1B)	109.5
C(3)-C(4)	1.4510(19)	C(2)-C(1)-H(1C)	109.5
C(3)-C(6)	1.5188(19)	O(1)-C(2)-C(1)	111.16(12)
C(5)-H(5A)	0.9900	O(1)-C(2)-C(3)	120.62(12)
C(5)-H(5B)	0.9900	C(3)-C(2)-C(1)	128.21(13)
C(5)-C(6)	1.5435(19)	C(2)-C(3)-C(4)	119.12(13)
C(6)-C(7)	1.5371(18)	C(2)-C(3)-C(6)	133.09(12)
C(6)-C(8)	1.5735(19)	C(4)-C(3)-C(6)	107.67(12)
C(7)-H(7A)	0.9800	O(2)-C(4)-O(3)	120.64(12)
C(7)-H(7B)	0.9800	O(2)-C(4)-C(3)	127.85(13)
C(7)-H(7C)	0.9800	O(3)-C(4)-C(3)	111.51(12)
C(8)-C(9)	1.5257(19)	O(3)-C(5)-H(5A)	110.3
C(8)-C(10)	1.5119(19)	O(3)-C(5)-H(5B)	110.3
C(9)-H(9A)	0.9800	O(3)-C(5)-C(6)	107.08(11)
C(9)-H(9B)	0.9800	H(5A)-C(5)-H(5B)	108.6
C(9)-H(9C)	0.9800	C(6)-C(5)-H(5A)	110.3
C(10)-C(11)	1.496(2)	C(6)-C(5)-H(5B)	110.3
C(10)-C(12)	1.331(2)	C(3)-C(6)-C(5)	99.74(10)
C(11)-H(11A)	0.9800	C(3)-C(6)-C(7)	115.77(12)
C(11)-H(11B)	0.9800	C(3)-C(6)-C(8)	111.90(11)
C(11)-H(11C)	0.9800	C(5)-C(6)-C(8)	110.18(11)
C(12)-C(13)	1.497(2)	C(7)-C(6)-C(5)	108.10(11)

C(7)-C(6)-C(8)	110.51(11)	H(13B)-C(13)-H(13C)	109.5
C(6)-C(7)-H(7A)	109.5	O(4)-C(14)-C(12)	108.67(12)
C(6)-C(7)-H(7B)	109.5	O(5)-C(14)-O(4)	121.42(15)
C(6)-C(7)-H(7C)	109.5	O(5)-C(14)-C(12)	129.89(15)
H(7A)-C(7)-H(7B)	109.5		
H(7A)-C(7)-H(7C)	109.5		
H(7B)-C(7)-H(7C)	109.5		
O(4)-C(8)-C(6)	105.50(11)		
O(4)-C(8)-C(9)	107.48(11)		
O(4)-C(8)-C(10)	103.07(11)		
C(9)-C(8)-C(6)	113.78(11)		
C(10)-C(8)-C(6)	115.39(11)		
C(10)-C(8)-C(9)	110.58(12)		
C(8)-C(9)-H(9A)	109.5		
C(8)-C(9)-H(9B)	109.5		
C(8)-C(9)-H(9C)	109.5		
H(9A)-C(9)-H(9B)	109.5		
H(9A)-C(9)-H(9C)	109.5		
H(9B)-C(9)-H(9C)	109.5		
C(11)-C(10)-C(8)	123.96(12)		
C(12)-C(10)-C(8)	109.90(13)		
C(12)-C(10)-C(11)	125.91(14)		
C(10)-C(11)-H(11A)	109.5		
C(10)-C(11)-H(11B)	109.5		
C(10)-C(11)-H(11C)	109.5		
H(11A)-C(11)-H(11B)	109.5		
H(11A)-C(11)-H(11C)	109.5		
H(11B)-C(11)-H(11C)	109.5		
C(10)-C(12)-C(13)	129.44(15)		
C(10)-C(12)-C(14)	108.55(13)		
C(14)-C(12)-C(13)	121.87(14)		
C(12)-C(13)-H(13A)	109.5		
C(12)-C(13)-H(13B)	109.5		
C(12)-C(13)-H(13C)	109.5		
H(13A)-C(13)-H(13B)	109.5		
H(13A)-C(13)-H(13C)	109.5		

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for Shenvi88A. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	15(1)	22(1)	20(1)	2(1)	8(1)	2(1)
O(2)	22(1)	25(1)	14(1)	-1(1)	9(1)	-2(1)
O(3)	18(1)	22(1)	14(1)	3(1)	4(1)	2(1)
O(4)	17(1)	20(1)	24(1)	-1(1)	11(1)	0(1)
O(5)	18(1)	27(1)	50(1)	-1(1)	16(1)	0(1)
C(1)	16(1)	22(1)	18(1)	3(1)	3(1)	0(1)
C(2)	15(1)	13(1)	17(1)	-1(1)	7(1)	-2(1)
C(3)	15(1)	14(1)	13(1)	-1(1)	5(1)	-2(1)
C(4)	16(1)	15(1)	15(1)	-2(1)	5(1)	-4(1)
C(5)	16(1)	18(1)	18(1)	1(1)	7(1)	1(1)
C(6)	13(1)	15(1)	14(1)	0(1)	4(1)	0(1)
C(7)	21(1)	19(1)	16(1)	-2(1)	9(1)	-1(1)
C(8)	14(1)	17(1)	18(1)	0(1)	8(1)	0(1)
C(9)	18(1)	17(1)	19(1)	1(1)	6(1)	-1(1)
C(10)	19(1)	15(1)	19(1)	2(1)	5(1)	-3(1)
C(11)	23(1)	23(1)	21(1)	-4(1)	8(1)	-4(1)
C(12)	17(1)	18(1)	23(1)	4(1)	4(1)	-3(1)
C(13)	20(1)	34(1)	28(1)	3(1)	0(1)	-6(1)
C(14)	16(1)	16(1)	34(1)	5(1)	9(1)	-1(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for Shenvi88A.

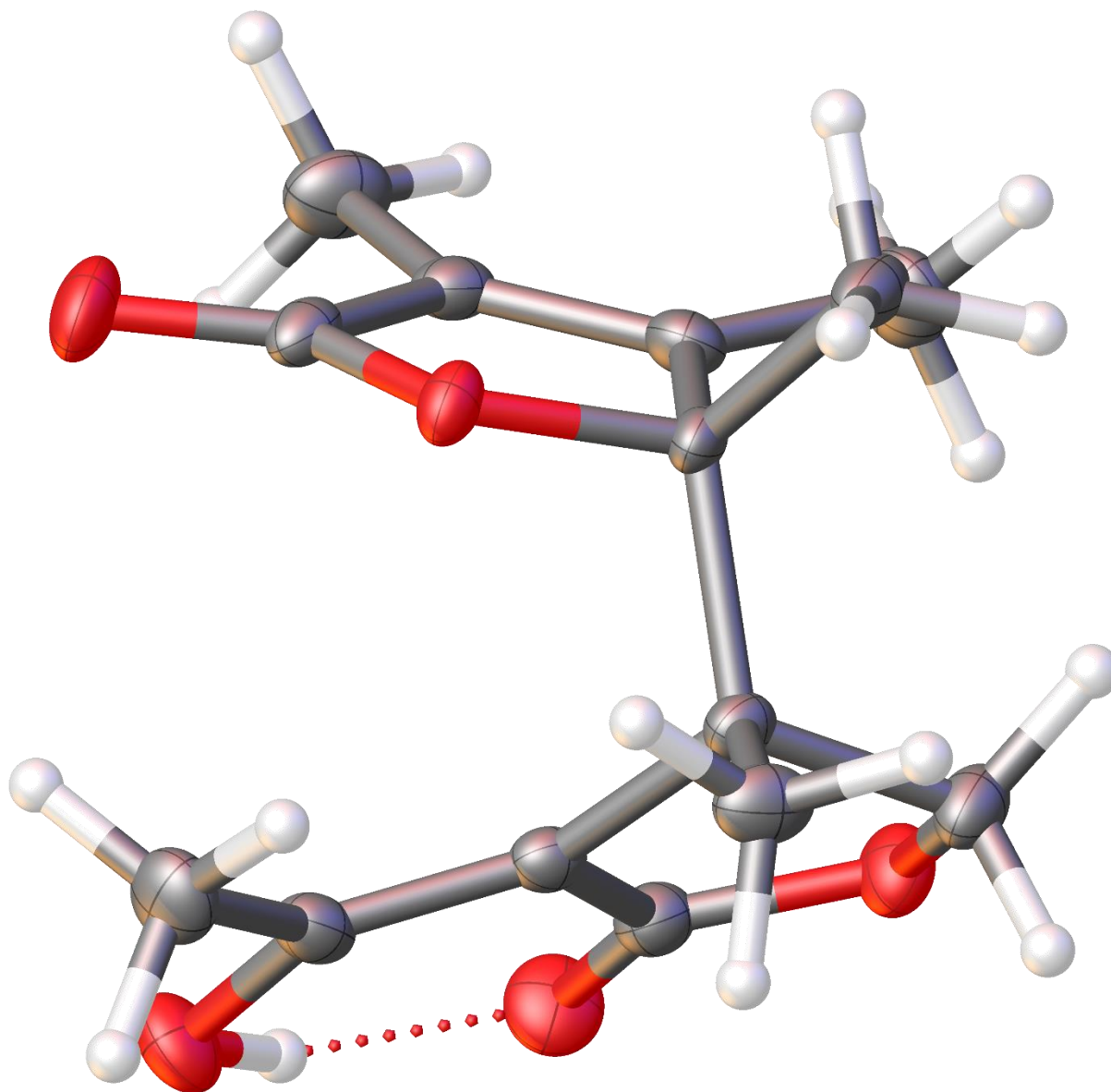
	x	y	z	U(eq)
H(1A)	10351	528	6586	29
H(1B)	9629	2081	6867	29
H(1C)	10791	2616	6885	29
H(5A)	6551	5040	4299	20
H(5B)	7521	6452	4748	20
H(7A)	8290	3696	6847	27
H(7B)	7456	5313	6355	27
H(7C)	8658	5560	6414	27
H(9A)	7882	733	6588	26
H(9B)	8214	-172	5698	26
H(9C)	7111	-709	5835	26
H(11A)	7057	1071	2975	34
H(11B)	6728	-924	3313	34
H(11C)	7817	30	3934	34
H(13A)	4889	1097	2470	43
H(13B)	4047	1808	2973	43
H(13C)	4445	-333	3112	43
H(1)	10159(15)	2580(30)	4409(15)	33

Table 6. Hydrogen bonds for Shenvi88A [$\text{\AA}$ and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	$\angle(\text{DHA})$
O(1)-H(1)...O(2)	0.88(2)	1.77(2)	2.5950(14)	156.1(18)

Symmetry transformations used to generate equivalent atoms:

SI-46 (Minor)



CCDC: 1849245. The single crystal X-ray diffraction studies were carried out on a Bruker APEX II Ultra diffractometer equipped with Mo K_{α} radiation ($\lambda = 0.71073$). Crystals of the subject compound were used as received (grown from DCM/Pentane). A 0.300 x 0.24 x 0.24 mm colorless block was mounted on a Cryoloop with Paratone oil.

Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ω scans. Crystal-to-detector distance was 40 mm using exposure times 0.5 second, with a scan width of 0.80°. Data collection was 100.0% complete to 25.242° in θ . A total of 34381 reflections were collected. 5008 reflections were found

to be symmetry independent, with a R_{int} of 0.0805. Indexing and unit cell refinement indicated a **Primitive Triclinic** lattice. The space group was found to be **P-1**. The data were integrated using the Bruker SAINT software program and scaled using the WINABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. All other hydrogen atoms (H-bonding) were located in the difference map. Their relative positions were restrained using DFIX commands and their thermal parameters freely refined. Crystallographic data are summarized in Table 1.

Table 1 Data collection and refinement statistics (molecular replacement)

SI-46 minor	
Identification code	shenvi88b
Empirical formula	C ₁₄ H ₁₈ O ₅
Temperature	100.0 K
Wavelength (Å)	0.710
Crystal system	Triclinic
Space group	P-1
Cell dimensions	
<i>a</i> , <i>b</i> , <i>c</i> (Å)	7.47, 13.71, 14.43
α , β , γ (°)	67, 81, 76
Volume	1320.87(13) Å ³
Z	4
Density (calculated)	1.339 Mg/m ³
Absorption coefficient	0.101 mm ⁻¹
F(000)	568
Crystal size	0.3 x 0.24 x 0.24 mm ³
Crystal color, habit	colorless block
Theta range for data collection	1.535 to 25.680°
Index ranges	-9 ≤ <i>h</i> ≤ 9, -
	16 ≤ <i>k</i> ≤ 16, -
	17 ≤ <i>l</i> ≤ 17
Reflections collected	34381
Independent reflections	5008 [R(int) =
	0.0805]
Completeness to theta = 25.242°	100.0%
Absorption correction	Semi-empirical from
	equivalents
Max. and min. transmission	0.4394 and 0.4128
Refinement method	

	Full-matrix least-squares on F ²
Data / restraints / parameters	
Goodness-of-fit on F ²	5008 / 0 / 360
Final R indices [I>2sigma(I)]	1.030
R indices (all data)	R1 = 0.0419, wR2 = 0.1072
	R1 = 0.0496, wR2 = 0.1136
Extinction coefficient	
Largest diff. peak and hole	0.0055(13)
	0.294 and -0.227 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for Shenvi88B. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
O(1)	10615(2)	3437(1)	7346(1)	29(1)
O(2)	8719(2)	3622(1)	5896(1)	29(1)
O(3)	6503(2)	2644(1)	6380(1)	25(1)
O(4)	10061(1)	156(1)	8593(1)	19(1)
O(5)	13069(2)	178(1)	8224(1)	30(1)
C(1)	10362(2)	2169(2)	8993(1)	28(1)
C(2)	9740(2)	2631(1)	7954(1)	21(1)
C(3)	8460(2)	2341(1)	7593(1)	17(1)
C(4)	7978(2)	2933(1)	6561(1)	21(1)
C(5)	5750(2)	1944(1)	7332(1)	24(1)
C(6)	7296(2)	1474(1)	8072(1)	18(1)
C(7)	6437(2)	1336(1)	9134(1)	26(1)
C(8)	8456(2)	362(1)	8040(1)	17(1)
C(9)	7456(2)	-575(1)	8572(1)	27(1)
C(10)	9282(2)	405(1)	7001(1)	21(1)
C(11)	8216(3)	399(2)	6208(1)	34(1)
C(12)	11097(2)	364(1)	6955(1)	21(1)
C(13)	12553(3)	412(2)	6111(1)	31(1)
C(14)	11586(2)	236(1)	7945(1)	20(1)
O(1')	7354(2)	5681(1)	9028(1)	25(1)
O(2')	6528(2)	4005(1)	8925(1)	24(1)
O(3')	3594(2)	4190(1)	8628(1)	20(1)
O(4')	3438(2)	7641(1)	6848(1)	21(1)
O(5')	6114(2)	8184(1)	6191(1)	27(1)
C(1')	5321(2)	7352(1)	8713(1)	26(1)
C(2')	5641(2)	6224(1)	8753(1)	19(1)
C(3')	4457(2)	5723(1)	8564(1)	16(1)
C(4')	5016(2)	4590(1)	8718(1)	18(1)
C(5')	1930(2)	5015(1)	8517(1)	19(1)
C(6')	2531(2)	6110(1)	8193(1)	16(1)

C(7')	1172(2)	6820(1)	8695(1)	22(1)
C(8')	2628(2)	6715(1)	7015(1)	19(1)
C(9')	740(2)	7135(2)	6578(1)	30(1)
C(10')	3981(2)	6116(1)	6424(1)	19(1)
C(11')	3625(2)	5183(1)	6240(1)	25(1)
C(12')	5407(2)	6618(1)	6034(1)	21(1)
C(13')	7043(2)	6384(1)	5366(1)	26(1)
C(14')	5123(2)	7552(1)	6336(1)	21(1)

Table 3. Bond lengths [Å] and angles [°] for Shenvi88B.

O(1)-C(2)	1.352(2)	C(12)-C(14)	1.463(2)
O(1)-H(1)	0.91(2)	C(13)-H(13A)	0.9800
O(2)-C(4)	1.224(2)	C(13)-H(13B)	0.9800
O(3)-C(4)	1.3472(19)	C(13)-H(13C)	0.9800
O(3)-C(5)	1.454(2)	O(1')-C(2')	1.3509(19)
O(4)-C(8)	1.4528(18)	O(1')-H(1')	0.99(2)
O(4)-C(14)	1.3557(19)	O(2')-C(4')	1.2239(19)
O(5)-C(14)	1.2104(19)	O(3')-C(4')	1.3490(19)
C(1)-H(1A)	0.9800	O(3')-C(5')	1.4514(19)
C(1)-H(1B)	0.9800	O(4')-C(8')	1.4553(18)
C(1)-H(1C)	0.9800	O(4')-C(14')	1.3645(19)
C(1)-C(2)	1.483(2)	O(5')-C(14')	1.2065(19)
C(2)-C(3)	1.355(2)	C(1')-H(1'A)	0.9800
C(3)-C(4)	1.445(2)	C(1')-H(1'B)	0.9800
C(3)-C(6)	1.520(2)	C(1')-H(1'C)	0.9800
C(5)-H(5A)	0.9900	C(1')-C(2')	1.487(2)
C(5)-H(5B)	0.9900	C(2')-C(3')	1.355(2)
C(5)-C(6)	1.542(2)	C(3')-C(4')	1.446(2)
C(6)-C(7)	1.527(2)	C(3')-C(6')	1.514(2)
C(6)-C(8)	1.581(2)	C(5')-H(5'A)	0.9900
C(7)-H(7A)	0.9800	C(5')-H(5'B)	0.9900
C(7)-H(7B)	0.9800	C(5')-C(6')	1.543(2)
C(7)-H(7C)	0.9800	C(6')-C(7')	1.538(2)
C(8)-C(9)	1.519(2)	C(6')-C(8')	1.573(2)
C(8)-C(10)	1.517(2)	C(7')-H(7'A)	0.9800
C(9)-H(9A)	0.9800	C(7')-H(7'B)	0.9800
C(9)-H(9B)	0.9800	C(7')-H(7'C)	0.9800
C(9)-H(9C)	0.9800	C(8')-C(9')	1.525(2)
C(10)-C(11)	1.495(2)	C(8')-C(10')	1.522(2)
C(10)-C(12)	1.337(2)	C(9')-H(9'A)	0.9800
C(11)-H(11A)	0.9800	C(9')-H(9'B)	0.9800
C(11)-H(11B)	0.9800	C(9')-H(9'C)	0.9800
C(11)-H(11C)	0.9800	C(10')-C(11')	1.492(2)
C(12)-C(13)	1.497(2)	C(10')-C(12')	1.337(2)

C(11')-H(11D)	0.9800	C(5)-C(6)-C(8)	111.53(13)
C(11')-H(11E)	0.9800	C(7)-C(6)-C(5)	108.99(13)
C(11')-H(11F)	0.9800	C(7)-C(6)-C(8)	110.56(13)
C(12')-C(13')	1.492(2)	C(6)-C(7)-H(7A)	109.5
C(12')-C(14')	1.469(2)	C(6)-C(7)-H(7B)	109.5
C(13')-H(13D)	0.9800	C(6)-C(7)-H(7C)	109.5
C(13')-H(13E)	0.9800	H(7A)-C(7)-H(7B)	109.5
C(13')-H(13F)	0.9800	H(7A)-C(7)-H(7C)	109.5
		H(7B)-C(7)-H(7C)	109.5
C(2)-O(1)-H(1)	104.8(12)	O(4)-C(8)-C(6)	104.41(11)
C(4)-O(3)-C(5)	108.50(12)	O(4)-C(8)-C(9)	107.68(12)
C(14)-O(4)-C(8)	109.26(12)	O(4)-C(8)-C(10)	103.44(11)
H(1A)-C(1)-H(1B)	109.5	C(9)-C(8)-C(6)	113.49(13)
H(1A)-C(1)-H(1C)	109.5	C(10)-C(8)-C(6)	114.45(13)
H(1B)-C(1)-H(1C)	109.5	C(10)-C(8)-C(9)	112.28(13)
C(2)-C(1)-H(1A)	109.5	C(8)-C(9)-H(9A)	109.5
C(2)-C(1)-H(1B)	109.5	C(8)-C(9)-H(9B)	109.5
C(2)-C(1)-H(1C)	109.5	C(8)-C(9)-H(9C)	109.5
O(1)-C(2)-C(1)	111.64(14)	H(9A)-C(9)-H(9B)	109.5
O(1)-C(2)-C(3)	120.48(15)	H(9A)-C(9)-H(9C)	109.5
C(3)-C(2)-C(1)	127.88(15)	H(9B)-C(9)-H(9C)	109.5
C(2)-C(3)-C(4)	119.35(14)	C(11)-C(10)-C(8)	123.96(14)
C(2)-C(3)-C(6)	132.65(14)	C(12)-C(10)-C(8)	109.02(14)
C(4)-C(3)-C(6)	107.99(13)	C(12)-C(10)-C(11)	126.83(15)
O(2)-C(4)-O(3)	120.59(15)	C(10)-C(11)-H(11A)	109.5
O(2)-C(4)-C(3)	128.38(15)	C(10)-C(11)-H(11B)	109.5
O(3)-C(4)-C(3)	111.03(13)	C(10)-C(11)-H(11C)	109.5
O(3)-C(5)-H(5A)	110.3	H(11A)-C(11)-H(11B)	109.5
O(3)-C(5)-H(5B)	110.3	H(11A)-C(11)-H(11C)	109.5
O(3)-C(5)-C(6)	107.23(12)	H(11B)-C(11)-H(11C)	109.5
H(5A)-C(5)-H(5B)	108.5	C(10)-C(12)-C(13)	131.39(16)
C(6)-C(5)-H(5A)	110.3	C(10)-C(12)-C(14)	108.24(14)
C(6)-C(5)-H(5B)	110.3	C(14)-C(12)-C(13)	120.36(15)
C(3)-C(6)-C(5)	99.35(12)	C(12)-C(13)-H(13A)	109.5
C(3)-C(6)-C(7)	116.36(13)	C(12)-C(13)-H(13B)	109.5
C(3)-C(6)-C(8)	109.60(12)	C(12)-C(13)-H(13C)	109.5

H(13A)-C(13)-H(13B)	109.5	C(6')-C(7')-H(7'A)	109.5
H(13A)-C(13)-H(13C)	109.5	C(6')-C(7')-H(7'B)	109.5
H(13B)-C(13)-H(13C)	109.5	C(6')-C(7')-H(7'C)	109.5
O(4)-C(14)-C(12)	109.35(13)	H(7'A)-C(7')-H(7'B)	109.5
O(5)-C(14)-O(4)	120.91(15)	H(7'A)-C(7')-H(7'C)	109.5
O(5)-C(14)-C(12)	129.72(15)	H(7'B)-C(7')-H(7'C)	109.5
C(2')-O(1')-H(1')	105.3(11)	O(4')-C(8')-C(6')	104.31(12)
C(4')-O(3')-C(5')	108.63(11)	O(4')-C(8')-C(9')	107.92(13)
C(14')-O(4')-C(8')	109.88(12)	O(4')-C(8')-C(10')	103.10(12)
H(1'A)-C(1')-H(1'B)	109.5	C(9')-C(8')-C(6')	113.48(13)
H(1'A)-C(1')-H(1'C)	109.5	C(10')-C(8')-C(6')	115.33(13)
H(1'B)-C(1')-H(1'C)	109.5	C(10')-C(8')-C(9')	111.58(13)
C(2')-C(1')-H(1'A)	109.5	C(8')-C(9')-H(9'A)	109.5
C(2')-C(1')-H(1'B)	109.5	C(8')-C(9')-H(9'B)	109.5
C(2')-C(1')-H(1'C)	109.5	C(8')-C(9')-H(9'C)	109.5
O(1')-C(2')-C(1')	111.65(13)	H(9'A)-C(9')-H(9'B)	109.5
O(1')-C(2')-C(3')	119.95(15)	H(9'A)-C(9')-H(9'C)	109.5
C(3')-C(2')-C(1')	128.40(15)	H(9'B)-C(9')-H(9'C)	109.5
C(2')-C(3')-C(4')	119.13(14)	C(11')-C(10')-C(8')	123.72(14)
C(2')-C(3')-C(6')	132.86(14)	C(12')-C(10')-C(8')	109.45(14)
C(4')-C(3')-C(6')	108.01(12)	C(12')-C(10')-C(11')	126.56(15)
O(2')-C(4')-O(3')	120.45(14)	C(10')-C(11')-H(11D)	109.5
O(2')-C(4')-C(3')	128.43(14)	C(10')-C(11')-H(11E)	109.5
O(3')-C(4')-C(3')	111.11(13)	C(10')-C(11')-H(11F)	109.5
O(3')-C(5')-H(5'A)	110.2	H(11D)-C(11')-H(11E)	109.5
O(3')-C(5')-H(5'B)	110.2	H(11D)-C(11')-H(11F)	109.5
O(3')-C(5')-C(6')	107.45(11)	H(11E)-C(11')-H(11F)	109.5
H(5'A)-C(5')-H(5'B)	108.5	C(10')-C(12')-C(13')	130.46(15)
C(6')-C(5')-H(5'A)	110.2	C(10')-C(12')-C(14')	108.44(14)
C(6')-C(5')-H(5'B)	110.2	C(14')-C(12')-C(13')	121.06(14)
C(3')-C(6')-C(5')	99.78(12)	C(12')-C(13')-H(13D)	109.5
C(3')-C(6')-C(7')	115.52(13)	C(12')-C(13')-H(13E)	109.5
C(3')-C(6')-C(8')	110.02(12)	C(12')-C(13')-H(13F)	109.5
C(5')-C(6')-C(8')	112.22(12)	H(13D)-C(13')-H(13E)	109.5
C(7')-C(6')-C(5')	109.13(12)	H(13D)-C(13')-H(13F)	109.5
C(7')-C(6')-C(8')	109.87(13)	H(13E)-C(13')-H(13F)	109.5

O(4')-C(14')-C(12')	108.71(13)
O(5')-C(14')-O(4')	121.27(14)
O(5')-C(14')-C(12')	130.02(15)

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for Shenvi88B. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	32(1)	27(1)	32(1)	-8(1)	-1(1)	-16(1)
O(2)	33(1)	25(1)	24(1)	0(1)	0(1)	-10(1)
O(3)	22(1)	24(1)	25(1)	-4(1)	-7(1)	-4(1)
O(4)	13(1)	21(1)	21(1)	-3(1)	-2(1)	-3(1)
O(5)	14(1)	33(1)	38(1)	-7(1)	-5(1)	-4(1)
C(1)	29(1)	34(1)	27(1)	-17(1)	-5(1)	-6(1)
C(2)	21(1)	19(1)	26(1)	-12(1)	2(1)	-5(1)
C(3)	16(1)	15(1)	20(1)	-7(1)	2(1)	-2(1)
C(4)	19(1)	18(1)	25(1)	-7(1)	-1(1)	-2(1)
C(5)	16(1)	20(1)	32(1)	-5(1)	-2(1)	-3(1)
C(6)	14(1)	16(1)	24(1)	-7(1)	2(1)	-2(1)
C(7)	25(1)	22(1)	28(1)	-9(1)	9(1)	-6(1)
C(8)	11(1)	15(1)	25(1)	-7(1)	-2(1)	-2(1)
C(9)	15(1)	16(1)	45(1)	-7(1)	0(1)	-3(1)
C(10)	22(1)	17(1)	26(1)	-12(1)	-2(1)	-3(1)
C(11)	31(1)	42(1)	39(1)	-26(1)	-6(1)	-6(1)
C(12)	20(1)	14(1)	27(1)	-9(1)	2(1)	-2(1)
C(13)	29(1)	29(1)	33(1)	-15(1)	10(1)	-6(1)
C(14)	14(1)	14(1)	28(1)	-4(1)	0(1)	-2(1)
O(1')	18(1)	31(1)	29(1)	-10(1)	-5(1)	-7(1)
O(2')	21(1)	22(1)	27(1)	-10(1)	-5(1)	4(1)
O(3')	22(1)	16(1)	24(1)	-8(1)	-3(1)	-5(1)
O(4')	20(1)	14(1)	26(1)	-5(1)	1(1)	-4(1)
O(5')	30(1)	23(1)	30(1)	-9(1)	6(1)	-12(1)
C(1')	31(1)	24(1)	28(1)	-12(1)	0(1)	-14(1)
C(2')	18(1)	24(1)	15(1)	-6(1)	1(1)	-7(1)
C(3')	15(1)	17(1)	14(1)	-6(1)	1(1)	-4(1)
C(4')	19(1)	20(1)	15(1)	-7(1)	0(1)	-4(1)
C(5')	16(1)	20(1)	22(1)	-8(1)	-1(1)	-6(1)
C(6')	14(1)	17(1)	19(1)	-7(1)	0(1)	-4(1)
C(7')	17(1)	22(1)	29(1)	-11(1)	4(1)	-3(1)
C(8')	19(1)	17(1)	21(1)	-4(1)	-3(1)	-5(1)
C(9')	22(1)	31(1)	29(1)	-2(1)	-8(1)	-2(1)
C(10')	23(1)	20(1)	13(1)	-4(1)	-5(1)	-4(1)
C(11')	32(1)	29(1)	19(1)	-11(1)	-2(1)	-11(1)
C(12')	23(1)	22(1)	17(1)	-6(1)	-3(1)	-3(1)
C(13')	26(1)	29(1)	26(1)	-13(1)	3(1)	-6(1)
C(14')	22(1)	19(1)	17(1)	-3(1)	0(1)	-4(1)

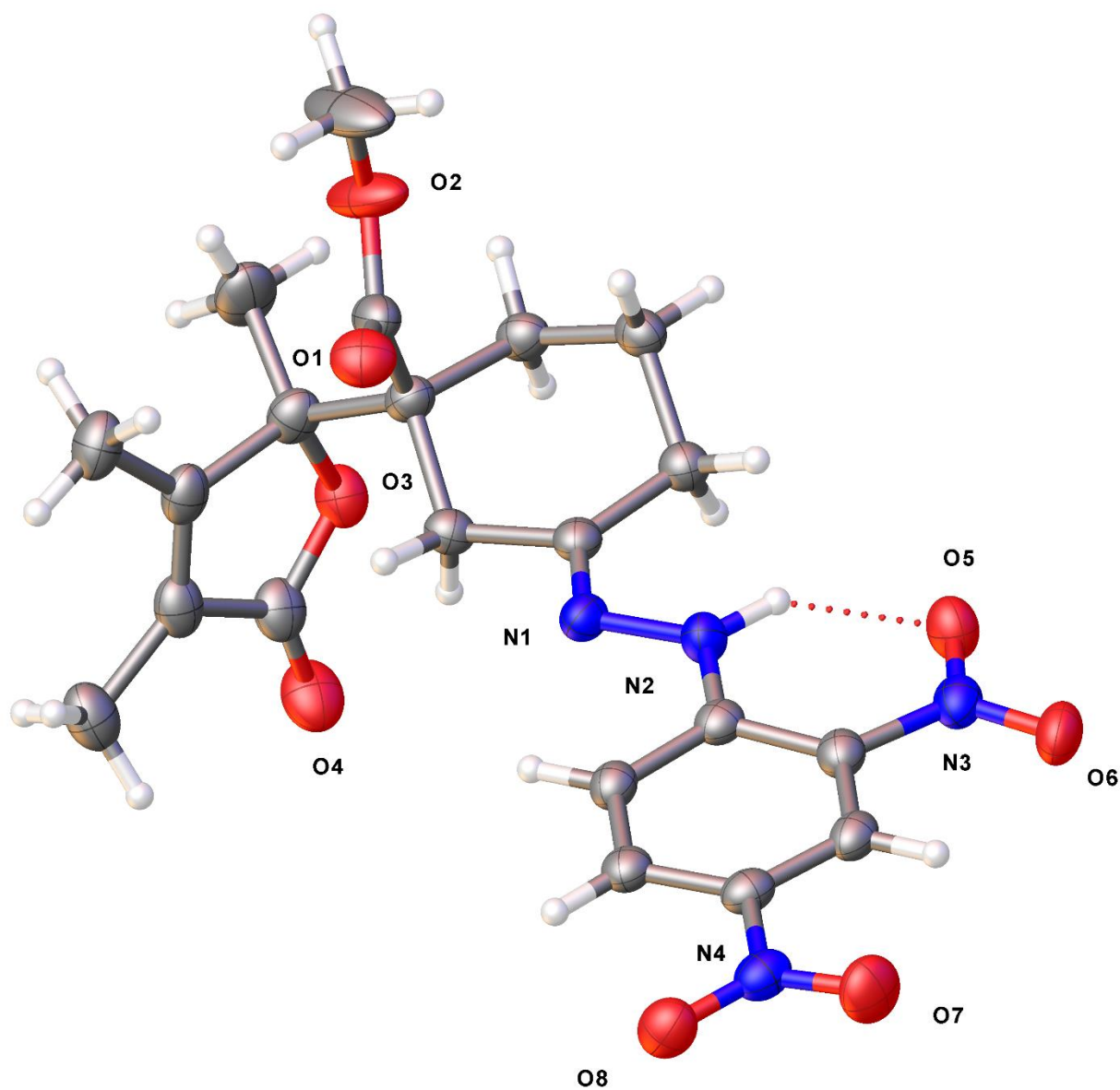
Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for Shenvi88B.

	x	y	z	U(eq)
H(1A)	11667	1820	8984	42
H(1B)	9625	1634	9426	42
H(1C)	10205	2746	9254	42
H(5A)	5344	1355	7235	29
H(5B)	4675	2360	7598	29
H(7A)	7356	891	9626	39
H(7B)	5377	982	9269	39
H(7C)	6026	2046	9190	39
H(9A)	8227	-1233	8507	40
H(9B)	6286	-417	8265	40
H(9C)	7208	-679	9287	40
H(11A)	7528	-191	6498	50
H(11B)	9070	295	5653	50
H(11C)	7351	1089	5952	50
H(13A)	11995	471	5515	46
H(13B)	13505	-247	6315	46
H(13C)	13114	1041	5952	46
H(1'A)	5770	7354	9316	39
H(1'B)	3997	7661	8687	39
H(1'C)	5985	7785	8110	39
H(5'A)	1173	4868	9164	23
H(5'B)	1186	5024	8001	23
H(7'A)	1383	6549	9413	34
H(7'B)	-97	6796	8618	34
H(7'C)	1362	7565	8374	34
H(9'A)	23	7682	6839	45
H(9'B)	85	6537	6772	45
H(9'C)	898	7458	5841	45
H(11D)	2580	5426	5815	38
H(11E)	3337	4625	6885	38
H(11F)	4725	4886	5899	38
H(13D)	6727	6734	4661	40
H(13E)	7410	5603	5538	40
H(13F)	8068	6663	5460	40
H(1')	7440(30)	4960(17)	9009(14)	31
H(1)	10130(30)	3669(16)	6736(16)	31

Table 6. Hydrogen bonds for Shenvi88B [$\text{\AA}$ and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1')-H(1')...O(2')	0.99(2)	1.66(2)	2.5804(17)	152.5(17)
O(1)-H(1)...O(2)	0.91(2)	1.75(2)	2.6016(18)	154.0(18)

Symmetry transformations used to generate equivalent atoms:



CCDC: 1849241. The single crystal X-ray diffraction studies were carried out on a Bruker D8 diffractometer equipped with a Dectris Eiger R 1M HPAD detector and Cu K_{α} radiation ($\lambda = 1.5478$). Crystals of the subject compound were grown by dissolving approximately 1mg of sample in 350 μ L of Dichloroethane, which was then vapor diffused with pentane over several days. A 0.217 x 0.053 x 0.051 mm piece of an orange rod was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ω scans. Crystal-to-detector distance was 40 mm and exposure time

was 5 seconds per frame using a scan width of 2.0°. Data collection was 99.9% complete to 68.00° in θ . A total of 44225 reflections were collected covering the indices, $-27 \leq h \leq 27$, $-25 \leq k \leq 26$, $-10 \leq l \leq 10$. 4203 reflections were found to be symmetry independent, with a R_{int} of 0.372. Indexing and unit cell refinement indicated an A-centered, orthorhombic lattice. The space group was found to be Aea2. The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

Table 1 Data collection and refinement statistics (molecular replacement)

	SI-66
Identification code	BH3-193-C
Empirical formula	C ₂₁ H ₂₄ N ₄ O ₈
Temperature	100.0 K
Wavelength (Å)	1.54178 Å
Crystal system	Orthorhombic
Space group	A e a 2
Cell dimensions	
<i>a</i> , <i>b</i> , <i>c</i> (Å)	22.1, 22.0032, 89.6
α , β , γ (°)	90, 90, 90
Volume	4268.0(3) Å ³
Z	8
Density (calculated)	1.433 Mg/m ³
Absorption coefficient	0.942 mm ⁻¹
F(000)	1936
Crystal size	0.217 x 0.053 x 0.051 mm ³
Crystal color, habit	Orange Rod
Theta range for data collection	3.971 to 72.553°.
Index ranges	$-27 \leq h \leq 27$, $-25 \leq k \leq 26$, $-10 \leq l \leq 10$
Reflections collected	44225
Independent reflections	4203 [R(int) = 0.0372, R(sigma) = 0.0190]
Completeness to theta = 68°	99.9%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.3241 and 0.2191
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	4203 / 2 / 306
Goodness-of-fit on F ²	1.039

Final R indices [I>2sigma(I)]	R1 = 0.0288, wR2 = 0.0752
R indices (all data)	R1 = 0.0298, wR2 = 0.0757
Extinction coefficient	n/a
Largest diff. peak and hole	0.144 and -0.159 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for Shenvi142. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
O(1)	3436(1)	3962(1)	6114(2)	42(1)
O(2)	4350(1)	4362(1)	5929(3)	61(1)
O(3)	4412(1)	3302(1)	1695(2)	36(1)
O(4)	4029(1)	2724(1)	-189(2)	50(1)
O(5)	3641(1)	1103(1)	8959(2)	41(1)
O(6)	3071(1)	505(1)	10281(2)	43(1)
O(7)	965(1)	578(1)	10151(2)	49(1)
O(8)	494(1)	1150(1)	8526(2)	43(1)
N(1)	3169(1)	2372(1)	6051(2)	30(1)
N(2)	3166(1)	1929(1)	7176(2)	31(1)
N(3)	3138(1)	919(1)	9352(2)	34(1)
N(4)	958(1)	958(1)	9122(2)	35(1)
C(1)	3691(1)	2572(1)	5653(2)	28(1)
C(2)	4295(1)	2391(1)	6287(3)	32(1)
C(3)	4715(1)	2934(1)	6418(3)	32(1)
C(4)	4768(1)	3267(1)	4887(3)	32(1)
C(5)	4153(1)	3512(1)	4347(3)	30(1)
C(6)	3691(1)	2992(1)	4288(2)	29(1)
C(7)	3926(1)	3966(1)	5546(3)	34(1)
C(8)	4192(2)	4767(2)	7173(5)	86(1)
C(9)	4204(1)	3793(1)	2675(3)	35(1)
C(10)	3602(1)	3961(1)	1949(3)	35(1)
C(11)	3480(1)	3587(1)	777(3)	36(1)
C(12)	3977(1)	3158(1)	648(3)	37(1)
C(13)	4659(1)	4301(1)	2521(4)	53(1)
C(14)	3239(1)	4489(1)	2465(3)	44(1)
C(15)	2954(1)	3552(1)	-296(3)	48(1)
C(16)	2638(1)	1680(1)	7615(2)	28(1)
C(17)	2604(1)	1197(1)	8698(2)	30(1)
C(18)	2056(1)	966(1)	9178(3)	31(1)
C(19)	1533(1)	1195(1)	8571(2)	30(1)

C(20)	1542(1)	1646(1)	7441(3)	30(1)
C(21)	2083(1)	1885(1)	6991(2)	29(1)

Table 3. Bond lengths [Å] and angles [°] for Shenvi142.

O(1)-C(7)	1.193(3)	C(20)-C(21)	1.368(3)
O(2)-C(7)	1.330(3)		
O(2)-C(8)	1.446(4)	C(7)-O(2)-C(8)	115.3(2)
O(3)-C(9)	1.457(3)	C(12)-O(3)-C(9)	109.88(16)
O(3)-C(12)	1.361(3)	C(1)-N(1)-N(2)	115.98(17)
O(4)-C(12)	1.211(3)	C(16)-N(2)-N(1)	119.61(17)
O(5)-N(3)	1.236(2)	O(5)-N(3)-C(17)	119.27(18)
O(6)-N(3)	1.230(2)	O(6)-N(3)-O(5)	122.33(18)
O(7)-N(4)	1.229(3)	O(6)-N(3)-C(17)	118.40(18)
O(8)-N(4)	1.228(3)	O(7)-N(4)-C(19)	118.41(19)
N(1)-N(2)	1.386(2)	O(8)-N(4)-O(7)	123.61(19)
N(1)-C(1)	1.287(3)	O(8)-N(4)-C(19)	117.98(19)
N(2)-C(16)	1.350(3)	N(1)-C(1)-C(2)	127.69(18)
N(3)-C(17)	1.451(3)	N(1)-C(1)-C(6)	115.10(17)
N(4)-C(19)	1.459(3)	C(2)-C(1)-C(6)	116.93(17)
C(1)-C(2)	1.502(3)	C(1)-C(2)-C(3)	110.89(17)
C(1)-C(6)	1.506(3)	C(4)-C(3)-C(2)	111.54(17)
C(2)-C(3)	1.532(3)	C(3)-C(4)-C(5)	111.52(17)
C(3)-C(4)	1.521(3)	C(4)-C(5)-C(6)	109.28(16)
C(4)-C(5)	1.543(3)	C(4)-C(5)-C(9)	110.67(17)
C(5)-C(6)	1.547(3)	C(6)-C(5)-C(9)	108.27(17)
C(5)-C(7)	1.533(3)	C(7)-C(5)-C(4)	108.65(17)
C(5)-C(9)	1.579(3)	C(7)-C(5)-C(6)	107.38(17)
C(9)-C(10)	1.523(3)	C(7)-C(5)-C(9)	112.49(17)
C(9)-C(13)	1.521(3)	C(1)-C(6)-C(5)	116.07(17)
C(10)-C(11)	1.339(4)	O(1)-C(7)-O(2)	123.1(2)
C(10)-C(14)	1.493(3)	O(1)-C(7)-C(5)	124.89(19)
C(11)-C(12)	1.465(3)	O(2)-C(7)-C(5)	111.95(19)
C(11)-C(15)	1.492(3)	O(3)-C(9)-C(5)	105.01(16)
C(16)-C(17)	1.427(3)	O(3)-C(9)-C(10)	102.86(18)
C(16)-C(21)	1.419(3)	O(3)-C(9)-C(13)	107.30(19)
C(17)-C(18)	1.383(3)	C(10)-C(9)-C(5)	114.28(17)
C(18)-C(19)	1.370(3)	C(13)-C(9)-C(5)	114.9(2)
C(19)-C(20)	1.401(3)	C(13)-C(9)-C(10)	111.24(19)

C(11)-C(10)-C(9)	109.66(19)
C(11)-C(10)-C(14)	127.3(2)
C(14)-C(10)-C(9)	122.9(2)
C(10)-C(11)-C(12)	108.1(2)
C(10)-C(11)-C(15)	131.5(2)
C(12)-C(11)-C(15)	120.4(2)
O(3)-C(12)-C(11)	109.2(2)
O(4)-C(12)-O(3)	121.2(2)
O(4)-C(12)-C(11)	129.6(2)
N(2)-C(16)-C(17)	122.68(18)
N(2)-C(16)-C(21)	120.85(18)
C(21)-C(16)-C(17)	116.46(18)
C(16)-C(17)-N(3)	122.21(18)
C(18)-C(17)-N(3)	116.22(19)
C(18)-C(17)-C(16)	121.56(19)
C(19)-C(18)-C(17)	119.3(2)
C(18)-C(19)-N(4)	118.62(19)
C(18)-C(19)-C(20)	121.39(19)
C(20)-C(19)-N(4)	119.99(19)
C(21)-C(20)-C(19)	119.36(19)
C(20)-C(21)-C(16)	121.75(19)

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for Shenvi142. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2}U^{11} + \dots + 2hka^*b^*U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	44(1)	45(1)	39(1)	-10(1)	6(1)	1(1)
O(2)	40(1)	39(1)	105(2)	-36(1)	-17(1)	3(1)
O(3)	31(1)	44(1)	34(1)	4(1)	6(1)	7(1)
O(4)	58(1)	58(1)	34(1)	-4(1)	3(1)	13(1)
O(5)	36(1)	45(1)	42(1)	7(1)	-1(1)	6(1)
O(6)	56(1)	32(1)	41(1)	8(1)	-4(1)	6(1)
O(7)	51(1)	50(1)	44(1)	14(1)	7(1)	-7(1)
O(8)	35(1)	40(1)	54(1)	2(1)	2(1)	0(1)
N(1)	34(1)	26(1)	28(1)	1(1)	0(1)	-2(1)
N(2)	33(1)	30(1)	30(1)	4(1)	-3(1)	0(1)
N(3)	41(1)	29(1)	30(1)	-1(1)	-1(1)	4(1)
N(4)	42(1)	29(1)	33(1)	-4(1)	6(1)	-3(1)
C(1)	32(1)	25(1)	26(1)	-4(1)	-2(1)	0(1)
C(2)	33(1)	31(1)	33(1)	-1(1)	-2(1)	0(1)
C(3)	29(1)	32(1)	34(1)	-4(1)	-3(1)	2(1)
C(4)	27(1)	31(1)	39(1)	-3(1)	0(1)	-1(1)
C(5)	28(1)	26(1)	36(1)	-1(1)	0(1)	-1(1)
C(6)	28(1)	31(1)	27(1)	-2(1)	0(1)	-2(1)
C(7)	34(1)	28(1)	40(1)	-3(1)	-9(1)	3(1)
C(8)	72(2)	59(2)	129(3)	-63(2)	-48(2)	26(2)
C(9)	31(1)	33(1)	42(1)	4(1)	4(1)	-2(1)
C(10)	32(1)	32(1)	42(1)	11(1)	6(1)	1(1)
C(11)	33(1)	41(1)	35(1)	11(1)	5(1)	2(1)
C(12)	39(1)	43(1)	29(1)	5(1)	6(1)	5(1)
C(13)	41(1)	48(2)	69(2)	18(1)	-1(1)	-14(1)
C(14)	46(1)	37(1)	48(1)	9(1)	6(1)	9(1)
C(15)	42(1)	60(2)	41(1)	10(1)	-4(1)	4(1)
C(16)	34(1)	24(1)	26(1)	-4(1)	1(1)	0(1)
C(17)	37(1)	27(1)	28(1)	-3(1)	-2(1)	3(1)

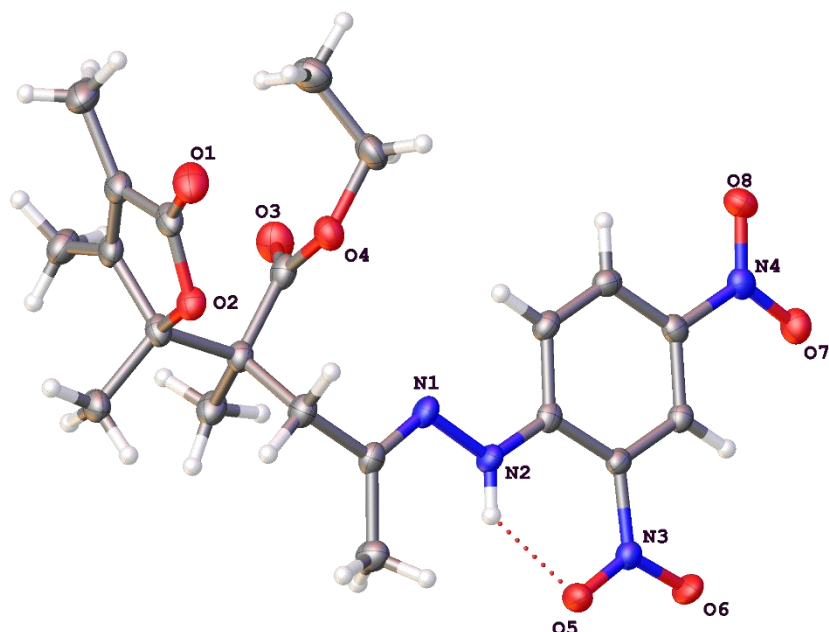
C(18)	44(1)	24(1)	26(1)	-2(1)	1(1)	0(1)
C(19)	36(1)	26(1)	29(1)	-4(1)	3(1)	-4(1)
C(20)	35(1)	25(1)	30(1)	-4(1)	-1(1)	0(1)
C(21)	37(1)	25(1)	27(1)	-1(1)	0(1)	2(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for Shenvi142.

	x	y	z	U(eq)
H(2)	3507(10)	1773(11)	7620(30)	41(7)
H(2A)	4480	2087	5598	38
H(2B)	4241	2207	7320	38
H(3A)	4558	3212	7217	38
H(3B)	5120	2798	6750	38
H(4A)	4930	2991	4091	39
H(4B)	5056	3604	5003	39
H(6A)	3283	3168	4188	35
H(6B)	3769	2754	3342	35
H(8A)	3783	4922	7006	130
H(8B)	4478	5102	7197	130
H(8C)	4207	4551	8160	130
H(13A)	5054	4164	2889	79
H(13B)	4526	4644	3143	79
H(13C)	4690	4421	1434	79
H(14A)	3151	4452	3572	65
H(14B)	2861	4504	1881	65
H(14C)	3469	4859	2281	65
H(15A)	3056	3749	-1275	71
H(15B)	2606	3753	173	71
H(15C)	2855	3129	-490	71
H(18)	2042	652	9921	37
H(20)	1177	1784	6991	36
H(21)	2087	2197	6241	35

Table 6. Hydrogen bonds for Shenvi142 [$\text{\AA}$ and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2)...O(5)	0.91(2)	1.91(2)	2.621(2)	133(2)

SI-67

CCDC: 1849243. The single crystal X-ray diffraction studies were carried out on a Bruker D8 diffractometer equipped with a Dectris Eiger R 1M HPAD detector and Cu K α radiation ($\lambda = 1.5478$). Crystals of the subject compound were grown by dissolving approximately 1mg of sample in 350 μ L of Dichloroethane, which was then vapor diffused with pentane over several days. A 0.217 x 0.053 x 0.051 mm piece of an orange rod was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ω scans. Crystal-to-detector distance was 40 mm and exposure time was 5 seconds per frame using a scan width of 2.0°. Data collection was 99.9% complete to 68.00° in θ . A total of 44225 reflections were collected covering the indices, $-27 \leq h \leq 27$, $-25 \leq k \leq 26$, $-10 \leq l \leq 10$. 4203 reflections were found to be symmetry independent, with a R_{int} of 0.372. Indexing and unit cell refinement indicated an A-centered, orthorhombic lattice. The space group was found to be Aea2. The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

Table 1 Data collection and refinement statistics (molecular replacement)

SI-67

Identification code	BH3-289 band 2
Empirical formula	C ₂₁ H ₂₆ N ₄ O ₈
Temperature	100.0 K
Wavelength (Å)	1.54178 Å
Crystal system	monoclinic
Space group	C 2/c
Cell dimensions	
<i>a</i> , <i>b</i> , <i>c</i> (Å)	10.7, 10.1, 40.0
α, β, γ (°)	90, 91, 90
Volume	4389.4(2) Å ³
<i>Z</i>	8
Density (calculated)	1.400 Mg/m ³
Absorption coefficient	0.917 mm ⁻¹
<i>F</i> (000)	1952
Crystal size	0.28 x 0.26 x 0.05 mm ³
Crystal color, habit	N/a
Theta range for data collection	2.207 to 68.521°.
Index ranges	-12 ≤ <i>h</i> ≤ 12, -12 ≤ <i>k</i> ≤ 12, -47 ≤ <i>l</i> ≤ 48
Reflections collected	13252
Independent reflections	3967 [R(int) = 0.0406]
Completeness to theta = 68°	98.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7531 and 0.6645
Refinement method	Full-matrix least-squares on <i>F</i> ²
Data / restraints / parameters	3967 / 1 / 315
Goodness-of-fit on <i>F</i> ²	1.089
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> 1 = 0.0531, <i>wR</i> 2 = 0.1500
<i>R</i> indices (all data)	<i>R</i> 1 = 0.0597, <i>wR</i> 2 = 0.1548
Extinction coefficient	n/a
Largest diff. peak and hole	0.326 and -0.277 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for shenvi149_0m_a. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> (eq)
O(1)	2135(2)	9194(2)	7080(1)	36(1)
O(2)	3845(1)	8383(2)	6850(1)	25(1)
O(3)	2894(2)	5119(2)	6309(1)	36(1)

O(4)	2360(2)	7248(2)	6304(1)	28(1)
O(5)	6230(1)	7172(2)	4866(1)	26(1)
O(6)	5682(1)	6406(2)	4380(1)	30(1)
O(7)	1746(2)	4618(2)	4138(1)	29(1)
O(8)	314(1)	4614(2)	4509(1)	29(1)
N(1)	4374(2)	7180(2)	5693(1)	23(1)
N(2)	4737(2)	6972(2)	5366(1)	21(1)
N(3)	5462(2)	6637(2)	4673(1)	21(1)
N(4)	1388(2)	4822(2)	4422(1)	23(1)
C(1)	2807(2)	8264(2)	7032(1)	27(1)
C(2)	2703(2)	6908(2)	7150(1)	27(1)
C(3)	3655(2)	6216(2)	7034(1)	25(1)
C(4)	4459(2)	7110(2)	6827(1)	24(1)
C(5)	1659(3)	6495(3)	7368(1)	36(1)
C(6)	3929(2)	4811(2)	7098(1)	33(1)
C(7)	5758(2)	7269(3)	6986(1)	29(1)
C(8)	4481(2)	6742(2)	6445(1)	22(1)
C(9)	5404(2)	5616(2)	6387(1)	29(1)
C(10)	4848(2)	7968(2)	6243(1)	25(1)
C(11)	5209(2)	7685(2)	5888(1)	22(1)
C(12)	6507(2)	8036(2)	5791(1)	28(1)
C(13)	3170(2)	6259(2)	6342(1)	26(1)
C(14)	1084(2)	6891(3)	6212(1)	35(1)
C(15)	333(2)	6580(3)	6513(1)	38(1)
C(16)	3950(2)	6435(2)	5140(1)	19(1)
C(17)	2745(2)	6004(2)	5231(1)	22(1)
C(18)	1931(2)	5476(2)	5002(1)	22(1)
C(19)	2270(2)	5349(2)	4668(1)	21(1)
C(20)	3425(2)	5727(2)	4567(1)	20(1)
C(21)	4258(2)	6258(2)	4799(1)	19(1)

Table 3. Bond lengths [Å] and angles [°] for shenvi149_0m_a.

O(1)-C(1)	1.211(3)
O(2)-C(1)	1.355(3)
O(2)-C(4)	1.460(3)
O(3)-C(13)	1.205(3)
O(4)-C(13)	1.339(3)
O(4)-C(14)	1.457(3)
O(5)-N(3)	1.242(2)
O(6)-N(3)	1.226(2)
O(7)-N(4)	1.229(2)
O(8)-N(4)	1.233(2)
N(1)-N(2)	1.393(2)
N(1)-C(11)	1.280(3)
N(2)-H(2)	0.8800
N(2)-C(16)	1.340(3)
N(3)-C(21)	1.454(3)
N(4)-C(19)	1.452(3)
C(1)-C(2)	1.467(3)
C(2)-C(3)	1.336(3)
C(2)-C(5)	1.499(3)
C(3)-C(4)	1.518(3)
C(3)-C(6)	1.484(3)
C(4)-C(7)	1.528(3)
C(4)-C(8)	1.578(3)
C(5)-H(5A)	0.95(5)
C(5)-H(5B)	0.96(5)
C(5)-H(5C)	0.9600(11)
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(6)-H(6C)	0.9800
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-C(9)	1.540(3)
C(8)-C(10)	1.545(3)

C(8)-C(13)	1.539(3)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(10)-C(11)	1.514(3)
C(11)-C(12)	1.501(3)
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900
C(14)-C(15)	1.502(4)
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(16)-C(17)	1.423(3)
C(16)-C(21)	1.425(3)
C(17)-H(17)	0.9500
C(17)-C(18)	1.361(3)
C(18)-H(18)	0.9500
C(18)-C(19)	1.401(3)
C(19)-C(20)	1.372(3)
C(20)-H(20)	0.9500
C(20)-C(21)	1.384(3)

C(1)-O(2)-C(4)	109.46(17)
C(13)-O(4)-C(14)	116.50(19)
C(11)-N(1)-N(2)	115.06(18)
N(1)-N(2)-H(2)	119.7
C(16)-N(2)-N(1)	120.68(17)
C(16)-N(2)-H(2)	119.7
O(5)-N(3)-C(21)	118.98(16)
O(6)-N(3)-O(5)	122.51(17)
O(6)-N(3)-C(21)	118.50(17)

O(7)-N(4)-O(8)	123.36(18)
O(7)-N(4)-C(19)	118.47(18)
O(8)-N(4)-C(19)	118.17(17)
O(1)-C(1)-O(2)	121.2(2)
O(1)-C(1)-C(2)	129.6(2)
O(2)-C(1)-C(2)	109.18(18)
C(1)-C(2)-C(5)	121.1(2)
C(3)-C(2)-C(1)	108.7(2)
C(3)-C(2)-C(5)	130.2(2)
C(2)-C(3)-C(4)	108.9(2)
C(2)-C(3)-C(6)	127.0(2)
C(6)-C(3)-C(4)	124.09(19)
O(2)-C(4)-C(3)	103.66(16)
O(2)-C(4)-C(7)	106.85(18)
O(2)-C(4)-C(8)	106.84(16)
C(3)-C(4)-C(7)	111.34(18)
C(3)-C(4)-C(8)	114.26(18)
C(7)-C(4)-C(8)	113.06(17)
C(2)-C(5)-H(5A)	109(3)
C(2)-C(5)-H(5B)	112(3)
C(2)-C(5)-H(5C)	114(3)
H(5A)-C(5)-H(5B)	102(4)
H(5A)-C(5)-H(5C)	119(4)
H(5B)-C(5)-H(5C)	100(4)
C(3)-C(6)-H(6A)	109.5
C(3)-C(6)-H(6B)	109.5
C(3)-C(6)-H(6C)	109.5
H(6A)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6C)	109.5
H(6B)-C(6)-H(6C)	109.5
C(4)-C(7)-H(7A)	109.5
C(4)-C(7)-H(7B)	109.5
C(4)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5

C(9)-C(8)-C(4)	110.51(17)
C(9)-C(8)-C(10)	110.53(17)
C(10)-C(8)-C(4)	108.93(17)
C(13)-C(8)-C(4)	107.39(16)
C(13)-C(8)-C(9)	108.10(18)
C(13)-C(8)-C(10)	111.33(18)
C(8)-C(9)-H(9A)	109.5
C(8)-C(9)-H(9B)	109.5
C(8)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(8)-C(10)-H(10A)	108.7
C(8)-C(10)-H(10B)	108.7
H(10A)-C(10)-H(10B)	107.6
C(11)-C(10)-C(8)	114.34(18)
C(11)-C(10)-H(10A)	108.7
C(11)-C(10)-H(10B)	108.7
N(1)-C(11)-C(10)	117.11(19)
N(1)-C(11)-C(12)	125.56(18)
C(12)-C(11)-C(10)	117.32(19)
C(11)-C(12)-H(12A)	109.5
C(11)-C(12)-H(12B)	109.5
C(11)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
O(3)-C(13)-O(4)	123.8(2)
O(3)-C(13)-C(8)	123.9(2)
O(4)-C(13)-C(8)	112.21(19)
O(4)-C(14)-H(14A)	109.2
O(4)-C(14)-H(14B)	109.2
O(4)-C(14)-C(15)	111.9(2)
H(14A)-C(14)-H(14B)	107.9
C(15)-C(14)-H(14A)	109.2
C(15)-C(14)-H(14B)	109.2

C(14)-C(15)-H(15A)	109.5
C(14)-C(15)-H(15B)	109.5
C(14)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
N(2)-C(16)-C(17)	121.12(18)
N(2)-C(16)-C(21)	122.72(19)
C(17)-C(16)-C(21)	116.15(18)
C(16)-C(17)-H(17)	119.2
C(18)-C(17)-C(16)	121.67(18)
C(18)-C(17)-H(17)	119.2
C(17)-C(18)-H(18)	120.0
C(17)-C(18)-C(19)	119.92(19)
C(19)-C(18)-H(18)	120.0
C(18)-C(19)-N(4)	120.02(19)
C(20)-C(19)-N(4)	118.90(18)
C(20)-C(19)-C(18)	121.08(19)
C(19)-C(20)-H(20)	120.4
C(19)-C(20)-C(21)	119.13(18)
C(21)-C(20)-H(20)	120.4
C(16)-C(21)-N(3)	122.04(18)
C(20)-C(21)-N(3)	115.93(17)
C(20)-C(21)-C(16)	122.02(19)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for shenvi149_0m_a. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

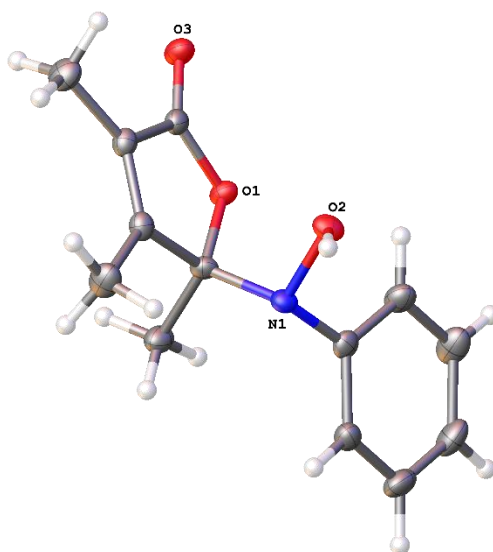
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	40(1)	40(1)	30(1)	-6(1)	3(1)	14(1)
O(2)	29(1)	26(1)	20(1)	-4(1)	2(1)	4(1)
O(3)	44(1)	28(1)	35(1)	-7(1)	-4(1)	-4(1)
O(4)	28(1)	32(1)	24(1)	-2(1)	-3(1)	2(1)
O(5)	22(1)	34(1)	21(1)	-3(1)	0(1)	-5(1)
O(6)	27(1)	45(1)	17(1)	-3(1)	6(1)	-2(1)
O(7)	32(1)	32(1)	22(1)	-5(1)	-1(1)	2(1)
O(8)	22(1)	34(1)	32(1)	0(1)	-2(1)	-3(1)
N(1)	29(1)	26(1)	15(1)	0(1)	3(1)	1(1)
N(2)	23(1)	26(1)	15(1)	-1(1)	4(1)	0(1)
N(3)	22(1)	24(1)	18(1)	1(1)	1(1)	1(1)
N(4)	25(1)	21(1)	23(1)	1(1)	-2(1)	2(1)
C(1)	27(1)	36(1)	17(1)	-6(1)	-1(1)	9(1)
C(2)	28(1)	37(1)	17(1)	-1(1)	1(1)	4(1)
C(3)	28(1)	33(1)	16(1)	0(1)	-1(1)	3(1)
C(4)	25(1)	28(1)	18(1)	-3(1)	-1(1)	8(1)
C(5)	32(1)	50(2)	28(1)	4(1)	8(1)	5(1)
C(6)	36(1)	35(1)	27(1)	6(1)	7(1)	5(1)
C(7)	27(1)	42(1)	20(1)	-2(1)	-2(1)	2(1)
C(8)	26(1)	25(1)	17(1)	-1(1)	1(1)	4(1)
C(9)	32(1)	33(1)	21(1)	0(1)	5(1)	8(1)
C(10)	31(1)	27(1)	18(1)	-2(1)	2(1)	0(1)
C(11)	30(1)	19(1)	18(1)	1(1)	1(1)	1(1)
C(12)	28(1)	32(1)	23(1)	-5(1)	2(1)	-3(1)
C(13)	35(1)	26(1)	16(1)	-1(1)	2(1)	3(1)
C(14)	28(1)	48(2)	30(1)	-4(1)	-9(1)	1(1)
C(15)	31(1)	45(2)	39(1)	-8(1)	-1(1)	-5(1)
C(16)	24(1)	16(1)	18(1)	1(1)	1(1)	5(1)
C(17)	26(1)	23(1)	18(1)	1(1)	4(1)	3(1)
C(18)	21(1)	22(1)	24(1)	2(1)	3(1)	1(1)
C(19)	21(1)	19(1)	22(1)	1(1)	-3(1)	3(1)

C(20)	23(1)	19(1)	17(1)	0(1)	1(1)	4(1)
C(21)	19(1)	21(1)	18(1)	2(1)	2(1)	4(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for shenvi149_0m_a.

	x	y	z	U(eq)
H(2)	5491	7196	5307	26
H(6A)	3633	4287	6907	49
H(6B)	3507	4526	7300	49
H(6C)	4829	4692	7130	49
H(7A)	6240	7887	6853	44
H(7B)	6180	6417	6992	44
H(7C)	5689	7605	7214	44
H(9A)	6257	5941	6417	43
H(9B)	5286	5279	6159	43
H(9C)	5257	4910	6547	43
H(10A)	4140	8588	6239	30
H(10B)	5556	8405	6361	30
H(12A)	6995	7233	5764	42
H(12B)	6896	8579	5966	42
H(12C)	6478	8524	5580	42
H(14A)	1091	6118	6063	42
H(14B)	686	7625	6088	42
H(15A)	-530	6399	6443	57
H(15B)	354	7329	6667	57
H(15C)	684	5808	6627	57
H(17)	2504	6087	5456	26
H(18)	1133	5194	5069	26
H(20)	3651	5625	4341	24
H(5A)	960(40)	7060(50)	7326(12)	102(15)
H(5B)	1330(40)	5650(50)	7305(11)	94(14)
H(5C)	1910(40)	6320(50)	7595(4)	129(19)

SI-86



CCDC: 1849246.

Table 1 Data collection and refinement statistics (molecular replacement)

SI-86	
Identification code	BH2-195
Empirical formula	C ₁₃ H ₁₅ N O ₃
Temperature	100.0 K
Wavelength (Å)	0.71073 Å
Crystal system	monoclinic
Space group	P 2 ₁ /c
Cell dimensions	
<i>a</i> , <i>b</i> , <i>c</i> (Å)	8.4, 12.9, 11.0
α , β , γ (°)	90, 91, 90
Volume	1193.6(14) Å ³
<i>Z</i>	4
Density (calculated)	1.298 Mg/m ³
Absorption coefficient	0.092 mm ⁻¹
<i>F</i> (000)	496
Crystal size	0.32 x 0.3 x 0.28 mm ³
Crystal color, habit	N/a
Theta range for data collection	2.893 to 26.449°.
Index ranges	-10 ≤ <i>h</i> ≤ 6, - 16 ≤ <i>k</i> ≤ 15, - 13 ≤ <i>l</i> ≤ 12
Reflections collected	6482
Independent reflections	2458 [R(int) = 0.0271]
Completeness to theta = 25°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.2602 and 0.2300
Refinement method	Full-matrix least- squares on <i>F</i> ²

Data / restraints / parameters	2458 / 0 / 161
Goodness-of-fit on F^2	1.023
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0393, wR2 = 0.0873
R indices (all data)	R1 = 0.0554, wR2 = 0.0953
Extinction coefficient	n/a
Largest diff. peak and hole	0.241 and -0.220 e. $\text{\AA}^{-3}$

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for shenvi113_0m. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	6119(1)	3373(1)	4469(1)	17(1)
O(2)	5509(1)	1690(1)	2996(1)	21(1)
O(3)	4193(1)	3776(1)	5745(1)	22(1)
N(1)	6725(1)	2416(1)	2658(1)	17(1)
C(1)	11336(2)	1421(1)	3700(2)	29(1)
C(2)	10119(2)	1311(1)	4511(1)	30(1)
C(3)	8579(2)	1614(1)	4191(1)	24(1)
C(4)	8264(2)	2022(1)	3043(1)	18(1)
C(5)	6326(2)	3420(1)	3144(1)	17(1)
C(6)	4722(2)	3794(1)	2663(1)	18(1)
C(7)	3778(2)	3984(1)	3582(1)	18(1)
C(8)	2132(2)	4411(1)	3608(1)	26(1)
C(9)	4650(2)	3712(1)	4707(1)	17(1)
C(10)	4428(2)	3950(1)	1334(1)	27(1)
C(11)	7638(2)	4199(1)	2929(1)	23(1)
C(12)	11002(2)	1796(1)	2544(2)	27(1)
C(13)	9469(2)	2084(1)	2215(1)	22(1)

Table 3. Bond lengths [Å] and angles [°] for shenvi113_0m.

O(1)-C(5)	1.4762(19)
O(1)-C(9)	1.3431(19)
O(2)-N(1)	1.4442(16)
O(2)-H(2)	0.93(2)
O(3)-C(9)	1.2192(19)
N(1)-C(4)	1.442(2)
N(1)-C(5)	1.445(2)
C(1)-H(1)	0.9500
C(1)-C(2)	1.384(2)
C(1)-C(12)	1.384(2)
C(2)-H(2A)	0.9500
C(2)-C(3)	1.388(2)
C(3)-H(3)	0.9500
C(3)-C(4)	1.387(2)
C(4)-C(13)	1.385(2)
C(5)-C(6)	1.513(2)
C(5)-C(11)	1.515(2)
C(6)-C(7)	1.326(2)
C(6)-C(10)	1.490(2)
C(7)-C(8)	1.491(2)
C(7)-C(9)	1.464(2)
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-H(12)	0.9500
C(12)-C(13)	1.379(2)
C(13)-H(13)	0.9500

C(9)-O(1)-C(5)	108.38(10)
N(1)-O(2)-H(2)	100.9(13)
O(2)-N(1)-C(5)	108.22(11)
C(4)-N(1)-O(2)	109.28(11)
C(4)-N(1)-C(5)	115.08(11)
C(2)-C(1)-H(1)	120.1
C(12)-C(1)-H(1)	120.1
C(12)-C(1)-C(2)	119.72(15)
C(1)-C(2)-H(2A)	119.7
C(1)-C(2)-C(3)	120.61(16)
C(3)-C(2)-H(2A)	119.7
C(2)-C(3)-H(3)	120.4
C(4)-C(3)-C(2)	119.26(15)
C(4)-C(3)-H(3)	120.4
C(3)-C(4)-N(1)	123.16(13)
C(13)-C(4)-N(1)	116.89(14)
C(13)-C(4)-C(3)	119.93(14)
O(1)-C(5)-C(6)	103.25(11)
O(1)-C(5)-C(11)	106.82(11)
N(1)-C(5)-O(1)	111.35(11)
N(1)-C(5)-C(6)	111.77(12)
N(1)-C(5)-C(11)	111.01(12)
C(6)-C(5)-C(11)	112.30(13)
C(7)-C(6)-C(5)	109.83(13)
C(7)-C(6)-C(10)	129.65(14)
C(10)-C(6)-C(5)	120.42(13)
C(6)-C(7)-C(8)	131.30(14)
C(6)-C(7)-C(9)	107.79(14)
C(9)-C(7)-C(8)	120.90(13)
C(7)-C(8)-H(8A)	109.5
C(7)-C(8)-H(8B)	109.5
C(7)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
O(1)-C(9)-C(7)	110.67(13)

O(3)-C(9)-O(1)	121.48(13)
O(3)-C(9)-C(7)	127.84(14)
C(6)-C(10)-H(10A)	109.5
C(6)-C(10)-H(10B)	109.5
C(6)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(5)-C(11)-H(11A)	109.5
C(5)-C(11)-H(11B)	109.5
C(5)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
C(1)-C(12)-H(12)	120.1
C(13)-C(12)-C(1)	119.89(15)
C(13)-C(12)-H(12)	120.1
C(4)-C(13)-H(13)	119.8
C(12)-C(13)-C(4)	120.46(15)
C(12)-C(13)-H(13)	119.8

Symmetry transformations used to generate equivalent atoms:

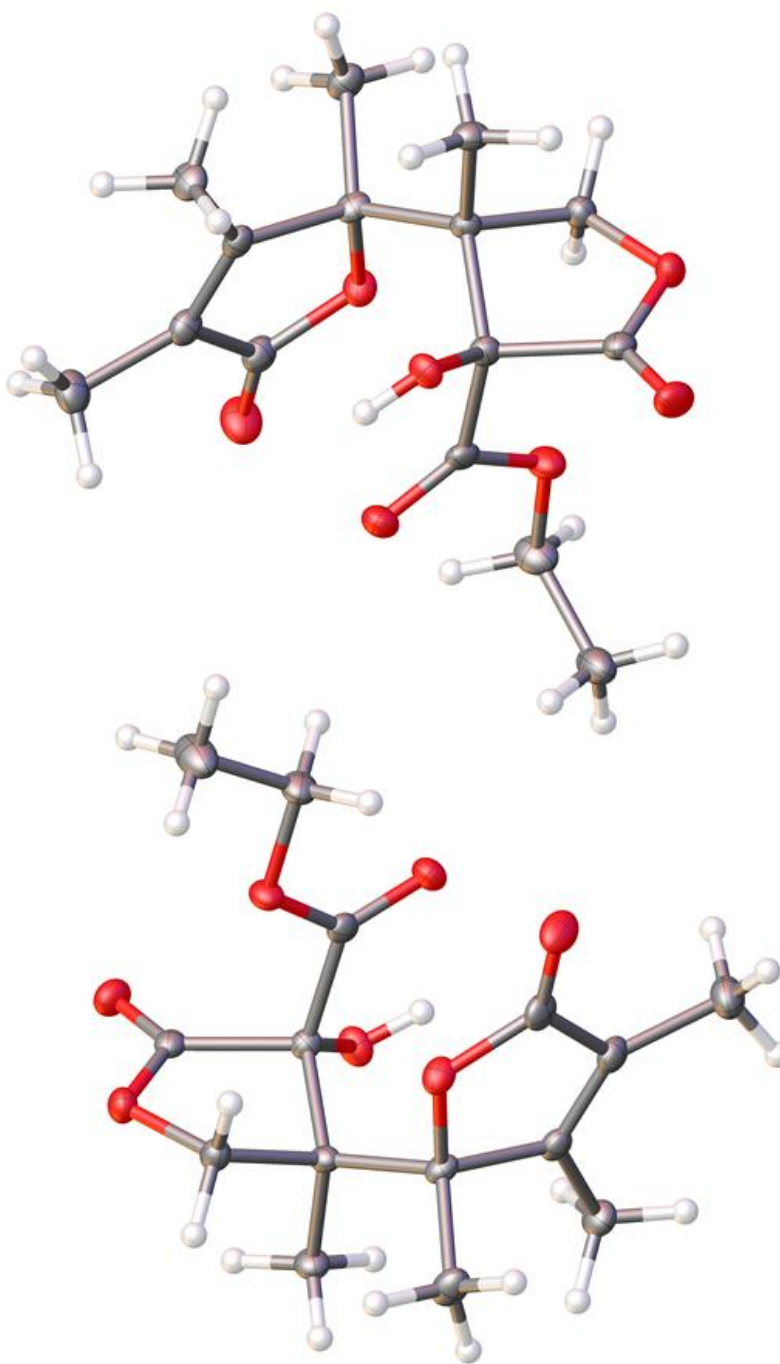
Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for shenvi113_0m. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	16(1)	22(1)	14(1)	-1(1)	1(1)	3(1)
O(2)	21(1)	21(1)	21(1)	0(1)	2(1)	-7(1)
O(3)	23(1)	26(1)	18(1)	1(1)	4(1)	6(1)
N(1)	15(1)	16(1)	18(1)	0(1)	3(1)	-3(1)
C(1)	24(1)	31(1)	32(1)	-6(1)	-3(1)	11(1)
C(2)	35(1)	35(1)	18(1)	-2(1)	-4(1)	11(1)
C(3)	26(1)	28(1)	17(1)	-1(1)	3(1)	5(1)
C(4)	21(1)	14(1)	19(1)	-4(1)	1(1)	1(1)
C(5)	17(1)	20(1)	13(1)	0(1)	3(1)	-1(1)
C(6)	20(1)	15(1)	19(1)	0(1)	-2(1)	-1(1)
C(7)	16(1)	16(1)	20(1)	-1(1)	-2(1)	1(1)
C(8)	20(1)	30(1)	27(1)	0(1)	-3(1)	4(1)
C(9)	18(1)	14(1)	20(1)	0(1)	2(1)	0(1)
C(10)	33(1)	31(1)	18(1)	1(1)	-2(1)	7(1)
C(11)	21(1)	20(1)	29(1)	-2(1)	6(1)	-2(1)
C(12)	23(1)	26(1)	33(1)	-5(1)	9(1)	4(1)
C(13)	26(1)	19(1)	20(1)	0(1)	5(1)	3(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for shenvi113_0m.

	x	y	z	U(eq)
H(1)	12395	1239	3937	35
H(2A)	10341	1027	5294	35
H(3)	7749	1543	4753	28
H(8A)	2154	5087	4014	39
H(8B)	1453	3935	4054	39
H(8C)	1707	4492	2775	39
H(10A)	3300	4108	1176	41
H(10B)	4711	3318	898	41
H(10C)	5080	4528	1055	41
H(11A)	8611	3981	3370	35
H(11B)	7312	4882	3220	35
H(11C)	7840	4236	2058	35
H(12)	11827	1855	1977	33
H(13)	9237	2326	1414	26
H(2)	5120(30)	1481(16)	2230(20)	54(6)

SI-93



CCDC: 1849242.

Table 1 Data collection and refinement statistics (molecular replacement)

SI-93	
Identification code	shenvi104
Empirical formula	C ₁₅ H ₂₀ O ₇
Temperature	100.0 K
Wavelength (Å)	1.54 Å

Crystal system	Orthorhombic
Space group	Pca2 ₁
Cell dimensions	
<i>a</i> , <i>b</i> , <i>c</i> (Å)	19.5, 13.9, 10.8
α , β , γ (°)	90, 90, 90
Volume	2966.61(13) Å ³
<i>Z</i>	8
Density (calculated)	1.399 Mg/m ³
Absorption coefficient	0.941 mm ⁻¹
F(000)	1328
Crystal size	0.25 x 0.15 x 0.05 mm ³
Crystal color, habit	colorless irregular
Theta range for data collection	3.165 to 70.130°.
Index ranges	-23 ≤ <i>h</i> ≤ 18, -13 ≤ <i>k</i> ≤ 17, -12 ≤ <i>l</i> ≤ 13
Reflections collected	23460
Independent reflections	5233 [R(int) = 0.0417]
Completeness to theta = 67°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.5220 and 0.4048
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	5233 / 1 / 411
Goodness-of-fit on F ²	1.052
Final R indices [I > 2σ(I)]	R1 = 0.0295, wR2 = 0.0775
R indices (all data)	R1 = 0.0300, wR2 = 0.0780
Extinction coefficient	0.00030(9)
Largest diff. peak and hole	0.293 and -0.166 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for Shenvi104. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
O(1)	4999(1)	5150(1)	6476(2)	24(1)
O(2)	3955(1)	4754(1)	5809(1)	17(1)
O(3)	2359(1)	6029(1)	4181(2)	17(1)
O(4)	2666(1)	6794(1)	2462(2)	21(1)
O(5)	3657(1)	5337(1)	2172(2)	17(1)
O(6)	4576(1)	6138(1)	3680(2)	18(1)
O(7)	3737(1)	6756(1)	4855(2)	17(1)
C(1)	4647(1)	4708(2)	5749(2)	17(1)
C(2)	4846(1)	4087(2)	4720(2)	17(1)
C(3)	5580(1)	3932(2)	4389(3)	25(1)
C(4)	4281(1)	3752(2)	4182(2)	15(1)
C(5)	4241(1)	3064(2)	3132(2)	19(1)
C(6)	3659(1)	4124(2)	4875(2)	14(1)
C(7)	3311(1)	3297(2)	5565(2)	21(1)
C(8)	3138(1)	4731(1)	4121(2)	13(1)
C(9)	2730(1)	4097(2)	3222(2)	17(1)
C(10)	2635(1)	5269(2)	4963(2)	16(1)
C(11)	2788(1)	6216(2)	3253(2)	14(1)
C(12)	3431(1)	5584(2)	3349(2)	13(1)
C(13)	3988(1)	6184(2)	3992(2)	14(1)
C(14)	4246(1)	7317(2)	5540(2)	20(1)
C(15)	3864(1)	8004(2)	6333(3)	31(1)
O(1')	5189(1)	10026(1)	3394(2)	26(1)
O(2')	6189(1)	10354(1)	4308(2)	16(1)
O(3')	7718(1)	9028(1)	6160(2)	18(1)
O(4')	7306(1)	8151(1)	7713(2)	25(1)
O(5')	6226(1)	9495(1)	7836(1)	15(1)
O(6')	5512(1)	8707(1)	5958(2)	21(1)
O(7')	6493(1)	8324(1)	4978(2)	21(1)
C(1')	5493(1)	10381(2)	4251(2)	18(1)
C(2')	5233(1)	10903(2)	5330(2)	17(1)
C(3')	4484(1)	11000(2)	5572(2)	23(1)
C(4')	5765(1)	11228(2)	5974(2)	15(1)
C(5')	5735(1)	11854(2)	7094(2)	20(1)
C(6')	6425(1)	10922(2)	5356(2)	14(1)
C(7')	6806(1)	11789(2)	4831(2)	18(1)
C(8')	6899(1)	10279(1)	6149(2)	13(1)
C(9')	7218(1)	10846(2)	7226(2)	16(1)
C(10')	7485(1)	9826(1)	5401(2)	16(1)
C(11')	7227(1)	8760(2)	6945(2)	16(1)
C(12')	6573(1)	9351(2)	6716(2)	14(1)
C(13')	6117(1)	8760(2)	5828(2)	16(1)
C(14')	6138(1)	7759(2)	4036(2)	24(1)
C(15')	6059(1)	6744(2)	4470(3)	27(1)

Table 3. Bond lengths [Å] and angles [°] for Shenvi104.

O(1)-C(1)	1.215(3)	O(3')-C(11')	1.339(3)
O(2)-C(1)	1.360(3)	O(4')-C(11')	1.200(3)
O(2)-C(6)	1.461(3)	O(5')-H(5')	0.8400
O(3)-C(10)	1.462(3)	O(5')-C(12')	1.406(3)
O(3)-C(11)	1.338(3)	O(6')-C(13')	1.197(3)
O(4)-C(11)	1.201(3)	O(7')-C(13')	1.327(3)
O(5)-H(5)	0.8400	O(7')-C(14')	1.467(3)
O(5)-C(12)	1.394(3)	C(1')-C(2')	1.469(3)
O(6)-C(13)	1.202(3)	C(2')-C(3')	1.498(3)
O(7)-C(13)	1.326(3)	C(2')-C(4')	1.333(3)
O(7)-C(14)	1.469(3)	C(3')-H(3'A)	0.9800
C(1)-C(2)	1.466(3)	C(3')-H(3'B)	0.9800
C(2)-C(3)	1.497(3)	C(3')-H(3'C)	0.9800
C(2)-C(4)	1.337(3)	C(4')-C(5')	1.498(3)
C(3)-H(3A)	0.9800	C(4')-C(6')	1.519(3)
C(3)-H(3B)	0.9800	C(5')-H(5'A)	0.9800
C(3)-H(3C)	0.9800	C(5')-H(5'B)	0.9800
C(4)-C(5)	1.491(3)	C(5')-H(5'C)	0.9800
C(4)-C(6)	1.523(3)	C(6')-C(7')	1.531(3)
C(5)-H(5A)	0.9800	C(6')-C(8')	1.552(3)
C(5)-H(5B)	0.9800	C(7')-H(7'A)	0.9800
C(5)-H(5C)	0.9800	C(7')-H(7'B)	0.9800
C(6)-C(7)	1.535(3)	C(7')-H(7'C)	0.9800
C(6)-C(8)	1.558(3)	C(8')-C(9')	1.544(3)
C(7)-H(7A)	0.9800	C(8')-C(10')	1.541(3)
C(7)-H(7B)	0.9800	C(8')-C(12')	1.570(3)
C(7)-H(7C)	0.9800	C(9')-H(9'A)	0.9800
C(8)-C(9)	1.541(3)	C(9')-H(9'B)	0.9800
C(8)-C(10)	1.540(3)	C(9')-H(9'C)	0.9800
C(8)-C(12)	1.564(3)	C(10')-H(10C)	0.9900
C(9)-H(9A)	0.9800	C(10')-H(10D)	0.9900
C(9)-H(9B)	0.9800	C(11')-C(12')	1.543(3)
C(9)-H(9C)	0.9800	C(12')-C(13')	1.551(3)
C(10)-H(10A)	0.9900	C(14')-H(14C)	0.9900
C(10)-H(10B)	0.9900	C(14')-H(14D)	0.9900
C(11)-C(12)	1.541(3)	C(14')-C(15')	1.501(4)
C(12)-C(13)	1.543(3)	C(15')-H(15D)	0.9800
C(14)-H(14A)	0.9900	C(15')-H(15E)	0.9800
C(14)-H(14B)	0.9900	C(15')-H(15F)	0.9800
C(14)-C(15)	1.490(3)		
C(15)-H(15A)	0.9800	C(1)-O(2)-C(6)	109.54(17)
C(15)-H(15B)	0.9800	C(11)-O(3)-C(10)	110.24(16)
C(15)-H(15C)	0.9800	C(12)-O(5)-H(5)	109.5
O(1')-C(1')	1.211(3)	C(13)-O(7)-C(14)	115.20(16)
O(2')-C(1')	1.366(3)	O(1)-C(1)-O(2)	120.8(2)
O(2')-C(6')	1.461(3)	O(1)-C(1)-C(2)	130.0(2)
O(3')-C(10')	1.458(3)	O(2)-C(1)-C(2)	109.24(19)

C(1)-C(2)-C(3)	121.6(2)	O(4)-C(11)-O(3)	122.92(19)
C(4)-C(2)-C(1)	108.6(2)	O(4)-C(11)-C(12)	126.5(2)
C(4)-C(2)-C(3)	129.8(2)	O(5)-C(12)-C(8)	114.71(17)
C(2)-C(3)-H(3A)	109.5	O(5)-C(12)-C(11)	109.82(17)
C(2)-C(3)-H(3B)	109.5	O(5)-C(12)-C(13)	108.84(17)
C(2)-C(3)-H(3C)	109.5	C(11)-C(12)-C(8)	99.99(16)
H(3A)-C(3)-H(3B)	109.5	C(11)-C(12)-C(13)	107.34(17)
H(3A)-C(3)-H(3C)	109.5	C(13)-C(12)-C(8)	115.49(18)
H(3B)-C(3)-H(3C)	109.5	O(6)-C(13)-O(7)	125.9(2)
C(2)-C(4)-C(5)	127.0(2)	O(6)-C(13)-C(12)	121.5(2)
C(2)-C(4)-C(6)	109.18(19)	O(7)-C(13)-C(12)	112.52(18)
C(5)-C(4)-C(6)	123.70(19)	O(7)-C(14)-H(14A)	110.3
C(4)-C(5)-H(5A)	109.5	O(7)-C(14)-H(14B)	110.3
C(4)-C(5)-H(5B)	109.5	O(7)-C(14)-C(15)	107.13(18)
C(4)-C(5)-H(5C)	109.5	H(14A)-C(14)-H(14B)	108.5
H(5A)-C(5)-H(5B)	109.5	C(15)-C(14)-H(14A)	110.3
H(5A)-C(5)-H(5C)	109.5	C(15)-C(14)-H(14B)	110.3
H(5B)-C(5)-H(5C)	109.5	C(14)-C(15)-H(15A)	109.5
O(2)-C(6)-C(4)	103.29(16)	C(14)-C(15)-H(15B)	109.5
O(2)-C(6)-C(7)	106.88(18)	C(14)-C(15)-H(15C)	109.5
O(2)-C(6)-C(8)	107.18(16)	H(15A)-C(15)-H(15B)	109.5
C(4)-C(6)-C(7)	109.90(17)	H(15A)-C(15)-H(15C)	109.5
C(4)-C(6)-C(8)	116.78(18)	H(15B)-C(15)-H(15C)	109.5
C(7)-C(6)-C(8)	111.97(18)	C(1')-O(2')-C(6')	109.58(16)
C(6)-C(7)-H(7A)	109.5	C(11')-O(3')-C(10')	110.32(16)
C(6)-C(7)-H(7B)	109.5	C(12')-O(5')-H(5')	109.5
C(6)-C(7)-H(7C)	109.5	C(13')-O(7')-C(14')	117.83(17)
H(7A)-C(7)-H(7B)	109.5	O(1')-C(1')-O(2')	121.0(2)
H(7A)-C(7)-H(7C)	109.5	O(1')-C(1')-C(2')	130.1(2)
H(7B)-C(7)-H(7C)	109.5	O(2')-C(1')-C(2')	108.95(19)
C(6)-C(8)-C(12)	117.12(16)	C(1')-C(2')-C(3')	121.6(2)
C(9)-C(8)-C(6)	111.03(17)	C(4')-C(2')-C(1')	108.3(2)
C(9)-C(8)-C(12)	106.82(18)	C(4')-C(2')-C(3')	130.0(2)
C(10)-C(8)-C(6)	111.94(17)	C(2')-C(3')-H(3'A)	109.5
C(10)-C(8)-C(9)	108.78(17)	C(2')-C(3')-H(3'B)	109.5
C(10)-C(8)-C(12)	100.42(16)	C(2')-C(3')-H(3'C)	109.5
C(8)-C(9)-H(9A)	109.5	H(3'A)-C(3')-H(3'B)	109.5
C(8)-C(9)-H(9B)	109.5	H(3'A)-C(3')-H(3'C)	109.5
C(8)-C(9)-H(9C)	109.5	H(3'B)-C(3')-H(3'C)	109.5
H(9A)-C(9)-H(9B)	109.5	C(2')-C(4')-C(5')	126.3(2)
H(9A)-C(9)-H(9C)	109.5	C(2')-C(4')-C(6')	109.8(2)
H(9B)-C(9)-H(9C)	109.5	C(5')-C(4')-C(6')	123.74(19)
O(3)-C(10)-C(8)	104.28(17)	C(4')-C(5')-H(5'A)	109.5
O(3)-C(10)-H(10A)	110.9	C(4')-C(5')-H(5'B)	109.5
O(3)-C(10)-H(10B)	110.9	C(4')-C(5')-H(5'C)	109.5
C(8)-C(10)-H(10A)	110.9	H(5'A)-C(5')-H(5'B)	109.5
C(8)-C(10)-H(10B)	110.9	H(5'A)-C(5')-H(5'C)	109.5
H(10A)-C(10)-H(10B)	108.9	H(5'B)-C(5')-H(5'C)	109.5
O(3)-C(11)-C(12)	110.53(18)	O(2')-C(6')-C(4')	103.10(17)

O(2')-C(6')-C(7')	107.10(18)	C(14')-C(15')-H(15F)	109.5
O(2')-C(6')-C(8')	107.80(16)	H(15D)-C(15')-H(15E)	109.5
C(4')-C(6')-C(7')	110.91(17)	H(15D)-C(15')-H(15F)	109.5
C(4')-C(6')-C(8')	115.37(18)	H(15E)-C(15')-H(15F)	109.5
C(7')-C(6')-C(8')	111.82(18)		
C(6')-C(7')-H(7'A)	109.5		
C(6')-C(7')-H(7'B)	109.5		
C(6')-C(7')-H(7'C)	109.5		
H(7'A)-C(7')-H(7'B)	109.5		
H(7'A)-C(7')-H(7'C)	109.5		
H(7'B)-C(7')-H(7'C)	109.5		
C(6')-C(8')-C(12')	116.82(17)		
C(9')-C(8')-C(6')	111.40(17)		
C(9')-C(8')-C(12')	106.96(17)		
C(10')-C(8')-C(6')	113.06(18)		
C(10')-C(8')-C(9')	107.87(17)		
C(10')-C(8')-C(12')	99.82(16)		
C(8')-C(9')-H(9'A)	109.5		
C(8')-C(9')-H(9'B)	109.5		
C(8')-C(9')-H(9'C)	109.5		
H(9'A)-C(9')-H(9'B)	109.5		
H(9'A)-C(9')-H(9'C)	109.5		
H(9'B)-C(9')-H(9'C)	109.5		
O(3')-C(10')-C(8')	104.46(17)		
O(3')-C(10')-H(10C)	110.9		
O(3')-C(10')-H(10D)	110.9		
C(8')-C(10')-H(10C)	110.9		
C(8')-C(10')-H(10D)	110.9		
H(10C)-C(10')-H(10D)	108.9		
O(3')-C(11')-C(12')	110.18(18)		
O(4')-C(11')-O(3')	123.2(2)		
O(4')-C(11')-C(12')	126.7(2)		
O(5')-C(12')-C(8')	114.64(18)		
O(5')-C(12')-C(11')	109.80(18)		
O(5')-C(12')-C(13')	109.53(17)		
C(11')-C(12')-C(8')	99.57(17)		
C(11')-C(12')-C(13')	107.09(17)		
C(13')-C(12')-C(8')	115.43(18)		
O(6')-C(13')-O(7')	127.1(2)		
O(6')-C(13')-C(12')	122.0(2)		
O(7')-C(13')-C(12')	110.82(18)		
O(7')-C(14')-H(14C)	109.7		
O(7')-C(14')-H(14D)	109.7		
O(7')-C(14')-C(15')	109.7(2)		
H(14C)-C(14')-H(14D)	108.2		
C(15')-C(14')-H(14C)	109.7		
C(15')-C(14')-H(14D)	109.7		
C(14')-C(15')-H(15D)	109.5		
C(14')-C(15')-H(15E)	109.5		

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for Shenvi104. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	27(1)	21(1)	24(1)	-4(1)	-13(1)	4(1)
O(2)	20(1)	16(1)	14(1)	-3(1)	-3(1)	3(1)
O(3)	14(1)	16(1)	20(1)	0(1)	1(1)	3(1)
O(4)	23(1)	16(1)	24(1)	4(1)	-4(1)	1(1)
O(5)	15(1)	24(1)	11(1)	-1(1)	2(1)	1(1)
O(6)	13(1)	19(1)	24(1)	0(1)	1(1)	-2(1)
O(7)	14(1)	17(1)	21(1)	-5(1)	-2(1)	-2(1)
C(1)	20(1)	14(1)	18(1)	4(1)	-4(1)	4(1)
C(2)	19(1)	14(1)	19(1)	1(1)	-3(1)	4(1)
C(3)	18(1)	25(1)	32(1)	-5(1)	-3(1)	4(1)
C(4)	18(1)	11(1)	16(1)	3(1)	2(1)	2(1)
C(5)	20(1)	17(1)	20(1)	-5(1)	2(1)	2(1)
C(6)	18(1)	11(1)	13(1)	-2(1)	0(1)	0(1)
C(7)	25(1)	16(1)	21(1)	4(1)	6(1)	1(1)
C(8)	12(1)	12(1)	14(1)	-2(1)	1(1)	-1(1)
C(9)	17(1)	16(1)	20(1)	-5(1)	-2(1)	-2(1)
C(10)	15(1)	14(1)	18(1)	1(1)	2(1)	1(1)
C(11)	14(1)	12(1)	17(1)	-3(1)	-3(1)	-1(1)
C(12)	15(1)	12(1)	11(1)	0(1)	0(1)	0(1)
C(13)	16(1)	12(1)	15(1)	4(1)	-2(1)	0(1)
C(14)	16(1)	18(1)	25(1)	-5(1)	-5(1)	-2(1)
C(15)	22(1)	33(2)	38(2)	-18(1)	0(1)	-2(1)
O(1')	25(1)	32(1)	23(1)	-8(1)	-8(1)	3(1)
O(2')	18(1)	18(1)	13(1)	-3(1)	-2(1)	2(1)
O(3')	14(1)	16(1)	24(1)	2(1)	-1(1)	2(1)
O(4')	23(1)	18(1)	33(1)	9(1)	-6(1)	-1(1)
O(5')	13(1)	20(1)	13(1)	0(1)	3(1)	-1(1)
O(6')	15(1)	19(1)	27(1)	1(1)	-1(1)	-3(1)
O(7')	18(1)	19(1)	25(1)	-6(1)	-1(1)	-3(1)
C(1')	21(1)	16(1)	17(1)	1(1)	-3(1)	2(1)
C(2')	20(1)	15(1)	15(1)	2(1)	-2(1)	3(1)
C(3')	19(1)	27(1)	23(1)	-1(1)	-4(1)	4(1)
C(4')	18(1)	11(1)	16(1)	2(1)	2(1)	2(1)
C(5')	21(1)	19(1)	19(1)	-7(1)	2(1)	2(1)
C(6')	19(1)	12(1)	11(1)	-3(1)	0(1)	-1(1)
C(7')	24(1)	16(1)	16(1)	3(1)	2(1)	1(1)
C(8')	14(1)	12(1)	13(1)	1(1)	1(1)	-2(1)
C(9')	18(1)	14(1)	17(1)	0(1)	-4(1)	-3(1)
C(10')	15(1)	15(1)	18(1)	2(1)	1(1)	1(1)
C(11')	16(1)	12(1)	20(1)	-1(1)	-2(1)	-2(1)
C(12')	15(1)	13(1)	15(1)	1(1)	0(1)	0(1)
C(13')	18(1)	10(1)	20(1)	3(1)	-1(1)	-2(1)
C(14')	24(1)	26(1)	21(1)	-8(1)	0(1)	-4(1)

C(15')	18(1)	25(1)	37(2)	-9(1)	3(1)	-3(1)
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Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for Shenvi104.

	x	y	z	U(eq)
H(5)	4082	5259	2184	25
H(3A)	5628	3319	3957	38
H(3B)	5856	3922	5142	38
H(3C)	5735	4452	3851	38
H(5A)	4163	3417	2364	28
H(5B)	3865	2615	3271	28
H(5C)	4671	2708	3072	28
H(7A)	3625	3034	6180	31
H(7B)	3184	2794	4978	31
H(7C)	2900	3536	5979	31
H(9A)	2371	4480	2830	26
H(9B)	2521	3566	3677	26
H(9C)	3036	3841	2589	26
H(10A)	2267	4837	5252	19
H(10B)	2872	5541	5689	19
H(14A)	4547	7666	4962	24
H(14B)	4531	6889	6054	24
H(15A)	3604	8446	5811	47
H(15B)	4187	8368	6839	47
H(15C)	3550	7651	6869	47
H(5')	5804	9501	7706	23
H(3'A)	4286	10365	5713	35
H(3'B)	4263	11299	4859	35
H(3'C)	4413	11400	6304	35
H(5'A)	5315	12236	7075	30
H(5'B)	6131	12283	7103	30
H(5'C)	5739	11454	7836	30
H(7'A)	7237	11577	4461	28
H(7'B)	6901	12246	5495	28
H(7'C)	6524	12099	4200	28
H(9'A)	7409	11448	6914	25
H(9'B)	7583	10465	7604	25
H(9'C)	6867	10985	7843	25
H(10C)	7319	9596	4591	19
H(10D)	7857	10294	5266	19
H(14C)	6401	7772	3257	28
H(14D)	5683	8041	3874	28
H(15D)	5906	6342	3782	40
H(15E)	5721	6720	5135	40
H(15F)	6499	6508	4775	40

Cartesian Coordinates of Computed Structures

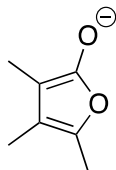
* Energies are in Hartrees. Frequencies are in cm^{-1} .

THF

C	1.08486100	-0.52564300	0.21418100
O	-0.06220200	-1.20864900	-0.25808200
C	-1.17644600	-0.39073600	0.07042300
C	-0.68174100	1.07517500	0.05159700
C	0.84056000	0.93708000	-0.15133000
H	1.18609100	-0.64516600	1.30617600
H	1.96289700	-0.96689300	-0.26487600
H	-1.96249100	-0.59461700	-0.66209800
H	-1.55937200	-0.65869600	1.06681700
H	-1.14639600	1.65224500	-0.75211500
H	-0.91448400	1.57431800	0.99661800
H	1.10660100	1.10394800	-1.19984800
H	1.42136800	1.62879800	0.46476300

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -232.448977619

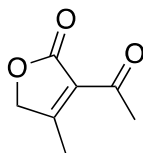
ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.090567



C	-1.15919400	-0.45290800	0.00056800
C	-0.51952800	0.74788600	-0.00089000
C	0.89454500	0.47626100	-0.00465300
C	1.06149900	-0.91329000	-0.00167300
O	-0.23846300	-1.47497100	-0.00033300
O	2.04343300	-1.68118900	-0.00142100
C	-2.59231400	-0.85543600	0.00339000
H	-3.24007600	0.02783100	0.00317000
H	-2.85904200	-1.45852500	-0.87752000
H	-2.85591300	-1.45574400	0.88717100
C	-1.13778600	2.11351900	-0.00305200
H	-0.83584200	2.69312400	-0.88661000
H	-2.23293600	2.07217800	0.00093400
H	-0.82909100	2.69949000	0.87385400
C	2.01778800	1.46491300	0.00523500
H	1.97156500	2.19367800	-0.82064000
H	2.08076000	2.06117600	0.93180100
H	2.97074800	0.93039400	-0.09168900

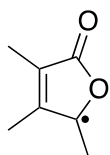
E [ω B97XD/6-311++G(d,p), SMD (THF)]: -422.700066621

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.111024



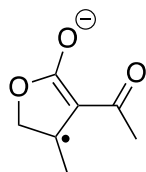
C	0.39554400	-1.35475700	-0.02087500
C	-0.10863400	0.04047900	-0.01048400
C	0.95594800	0.86929100	0.01562900
C	2.19483200	0.03437000	0.01980800
O	1.75377900	-1.31673100	-0.01005400
H	2.79375400	0.20196700	0.92220700
O	-0.20271200	-2.40295600	-0.03843100
H	2.82251700	0.23350700	-0.85640000
C	1.02465600	2.35344100	0.03444600
H	0.67855100	2.75605100	-0.92375900
H	0.36134400	2.76245400	0.80105300
H	2.04787100	2.69675100	0.21017700
C	-1.53512700	0.45225500	-0.01703900
C	-2.59133800	-0.61513600	0.08433400
H	-2.48230500	-1.34661000	-0.72200600
H	-2.47897100	-1.16798600	1.02338600
H	-3.57746400	-0.14909700	0.04204600
O	-1.82364000	1.63635000	-0.09296800

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -497.231099688
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.107092



C	1.14231300	-0.45974300	-0.00158000
C	0.48462900	0.76687500	-0.00607100
C	-0.88229100	0.48791800	-0.00513900
C	-1.02739800	-0.94839000	-0.00123200
O	0.26018400	-1.49068700	0.00028700
O	-2.00293000	-1.67241100	-0.00117500
C	2.57714200	-0.82216700	0.00423400
H	3.20553900	0.07076300	0.01232300
H	2.81782300	-1.42581200	0.88759200
H	2.82855600	-1.42005800	-0.88014100
C	1.10956500	2.12530900	-0.00216800
H	0.95324300	2.62554800	0.96076600
H	2.18611000	2.07962900	-0.18634000
H	0.66167100	2.75938600	-0.77520400
C	-2.02576400	1.43938600	0.00475000
H	-2.08330200	1.98106800	0.95757500
H	-1.92636200	2.19111000	-0.78736600
H	-2.97047400	0.90802900	-0.13886900

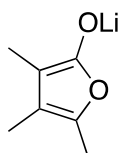
E [ω B97XD/6-311++G(d,p), SMD (THF)]: -422.589589389
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.112004



C	0.17905000	-1.34762500	-0.00744800
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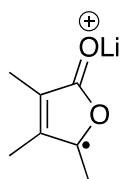
C	-0.12775000	0.06889300	-0.01706300
C	1.11202900	0.77099500	-0.05712400
C	2.20019200	-0.24968100	0.01259000
O	1.54659600	-1.52002100	-0.00664100
H	2.80604100	-0.18652600	0.93615300
O	-0.52909600	-2.34447900	-0.00421900
H	2.91258500	-0.21366200	-0.82974300
C	1.39689100	2.22914400	0.03096500
H	0.46710600	2.79111800	-0.07947500
H	1.85235300	2.51538900	0.99748700
H	2.10697100	2.56375800	-0.74385200
C	-1.44865000	0.61091500	-0.00572000
C	-2.64070300	-0.34176900	0.04108700
H	-2.74556500	-0.89837700	-0.89825400
H	-2.54742200	-1.09337400	0.83067000
H	-3.54466700	0.25429000	0.20033300
O	-1.68422000	1.84226800	-0.03877000

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -497.310999916
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.102760



C	-1.02318600	-0.70629100	-0.00132700
C	-0.82847800	0.63487300	-0.00110100
C	0.60080600	0.87996500	0.00010500
C	1.21416200	-0.34607200	0.00039100
O	0.21224300	-1.33560700	-0.00028900
O	2.40725600	-0.81200300	0.00075600
C	-2.21404200	-1.59461300	0.00037900
H	-3.12991000	-0.99664500	-0.00721500
H	-2.23811100	-2.25063000	-0.88009500
H	-2.24512900	-2.23824200	0.88982100
C	-1.87292800	1.70742700	0.00064700
H	-1.76404600	2.36787000	-0.86878700
H	-2.88646300	1.29463700	-0.02058500
H	-1.78974900	2.34046900	0.89313400
C	1.28450500	2.21173700	-0.00033900
H	1.03035600	2.81479100	-0.88356800
H	1.02693800	2.81715500	0.88025100
H	2.37179100	2.07943300	0.00183400
Li	1.90110000	-2.59003800	-0.00035300

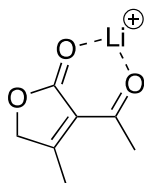
E [ω B97XD/6-311++G(d,p), SMD (THF)]: -430.188317873
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.110981



C	-0.92062100	-0.89789400	-0.00916800
C	-0.96774500	0.49660200	-0.00918500

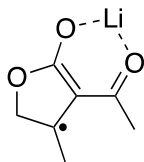
C	0.35262000	0.94418000	-0.00211100
C	1.17822000	-0.22539100	-0.00048700
O	0.37252100	-1.33386600	-0.00439500
O	2.40662900	-0.35880400	0.00331800
C	-1.96458700	-1.94041600	0.00606400
H	-2.95617000	-1.49585400	-0.09218100
H	-1.81063000	-2.65163700	-0.81326000
H	-1.92547100	-2.50494000	0.94593000
C	-2.18772600	1.35829000	0.00064400
H	-3.09499300	0.78668200	-0.20851100
H	-2.30922500	1.84267400	0.97612300
H	-2.10366100	2.15036400	-0.75076300
C	0.85540100	2.34335300	0.00345300
H	0.51982800	2.88041100	-0.89154300
H	0.47251200	2.88917500	0.87337100
H	1.94741400	2.36965200	0.03109200
Li	3.65127400	-1.73250400	0.00103400

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -430.038202188
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.111932



C	0.34927400	-1.34869900	0.00000000
C	-0.04438200	0.07531700	0.00000000
C	1.09798500	0.80879600	0.00000000
C	2.24823000	-0.13989900	0.00000000
O	1.67656600	-1.44715000	0.00000000
H	2.87289000	-0.02072400	0.89149400
O	-0.34738800	-2.35495600	0.00000000
H	2.87288900	-0.02072400	-0.89149500
C	1.34905700	2.27238400	0.00000000
H	0.90316300	2.74136600	-0.88296200
H	0.90316600	2.74136600	0.88296300
H	2.42155800	2.47960500	-0.00000200
C	-1.45352500	0.50830000	0.00000000
C	-1.78664000	1.96582100	0.00000100
H	-1.36279600	2.45432400	0.88394200
H	-1.36279800	2.45432400	-0.88394100
H	-2.87064500	2.08672600	0.00000200
O	-2.35826200	-0.33035600	0.00000000
Li	-2.23491700	-2.23623000	0.00000000

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -504.697924093
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.110063

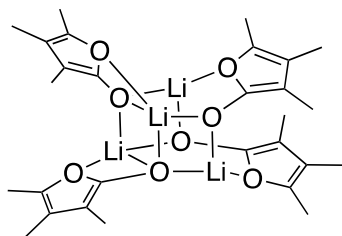


C	-0.14246000	-1.35249400	-0.00147400
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C	0.06507900	0.08302700	-0.01032300
C	-1.23414200	0.67067800	-0.03857800
C	-2.22576100	-0.44229200	0.05632500
O	-1.45055100	-1.65184100	0.03280400
H	-2.93722800	-0.47840400	-0.78070200
O	0.66653200	-2.29095100	-0.01268500
H	-2.81281300	-0.44352800	0.98799900
C	-1.68852700	2.08948000	-0.08135100
H	-1.68573700	2.57405900	0.90825100
H	-1.07103500	2.70837700	-0.74104000
H	-2.71961300	2.14376700	-0.45334200
C	1.35868000	0.65634600	0.01275000
C	1.51649800	2.15855400	0.08474400
H	1.37341500	2.61531100	-0.90291300
H	0.80067900	2.62063300	0.77066600
H	2.53134200	2.38978800	0.41874100
O	2.43666600	-0.02923500	-0.03488500
Li	2.46787200	-1.84452600	-0.07402900

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -504.815882627

Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.105403



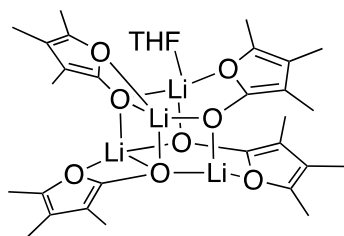
unsolvated tetramer

C	3.40157600	2.36272100	-0.46056900
C	4.30265500	1.91198000	0.44317400
C	3.57532800	1.17307300	1.45378200
C	2.25988400	1.20634500	1.09543800
O	2.13164500	1.95578600	-0.07123700
O	1.16775600	0.69800400	1.57062100
C	3.46727100	3.13886200	-1.72530500
H	2.89696500	4.07468200	-1.66491300
H	4.50555500	3.39372600	-1.95457500
H	3.07808300	2.56577700	-2.57901700
C	5.78630800	2.10064700	0.42484200
H	6.30487900	1.13452700	0.39647500
H	6.11263400	2.68010000	-0.44422900
H	6.13266200	2.62345100	1.32487500
C	4.16199900	0.45951000	2.62931400
H	4.85019400	-0.33887800	2.32098800
H	4.72544300	1.13616600	3.28542100
H	3.37248500	0.00086800	3.23502500
Li	0.87012600	1.16108200	-1.38025400
C	-3.66438000	2.18747400	0.74223800
C	-4.34580700	1.83524300	-0.37505700
C	-3.38055700	1.35395500	-1.34264400
C	-2.16517500	1.43900400	-0.73838600
O	-2.31427300	1.96368700	0.53446700
O	-0.94734800	1.07086800	-1.02604100
C	-4.03262100	2.79004900	2.04882100
H	-5.12042600	2.80746800	2.15984300

H	-3.61958900	2.21735300	2.88774900
H	-3.66883200	3.82182800	2.14082000
C	-5.82198000	1.89435900	-0.60810300
H	-6.07315200	2.60098000	-1.40908900
H	-6.20624500	0.91334700	-0.91376800
H	-6.36500000	2.20177400	0.29090100
C	-3.66760200	0.82286700	-2.70998200
H	-4.46018500	0.06552300	-2.68679900
H	-3.99342300	1.60951000	-3.40379700
H	-2.77398600	0.35741400	-3.14118300
Li	-0.62685300	0.85025800	1.07198400
C	-3.66560900	-2.18745100	-0.74208000
C	-4.34613700	-1.83509100	0.37573400
C	-3.38004700	-1.35399200	1.34257700
C	-2.16517800	-1.43928900	0.73734800
O	-2.31531500	-1.96388400	-0.53536500
O	-0.94704200	-1.07139200	1.02412900
C	-4.03499600	-2.78989900	-2.04839800
H	-5.12290700	-2.80749900	-2.15835800
H	-3.62287500	-2.21702100	-2.88765200
H	-3.67112400	-3.82159900	-2.14088100
C	-5.82214800	-1.89389400	0.60990000
H	-6.20596400	-0.91280900	0.91589700
H	-6.36591700	-2.20112600	-0.28871900
H	-6.07288900	-2.60049400	1.41103600
C	-3.66587900	-0.82286600	2.71015300
H	-4.45825600	-0.06528300	2.68761400
H	-3.99138800	-1.60944500	3.40418700
H	-2.77178800	-0.35769700	3.14068800
Li	-0.62646000	-0.85072500	-1.07277200
C	3.40209300	-2.36265400	0.46065400
C	4.30318600	-1.91199600	-0.44311700
C	3.57588200	-1.17307300	-1.45374000
C	2.26043700	-1.20626400	-1.09536400
O	2.13218900	-1.95567000	0.07132600
O	1.16829900	-0.69795400	-1.57055800
C	3.46772600	-3.13880700	1.72538800
H	2.89769900	-4.07478900	1.66485800
H	4.50602800	-3.39337500	1.95490500
H	3.07814300	-2.56582700	2.57899000
C	5.78681200	-2.10092000	-0.42488200
H	6.30557300	-1.13487400	-0.39744200
H	6.11317500	-2.67968300	0.44463900
H	6.13292000	-2.62457400	-1.32452000
C	4.16256400	-0.45928000	-2.62913100
H	4.85016600	0.33956600	-2.32064200
H	4.72666200	-1.13565900	-3.28495900
H	3.37299200	-0.00118100	-3.23517700
Li	0.87011000	-1.16111100	1.37985100

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1720.95896386

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.527781

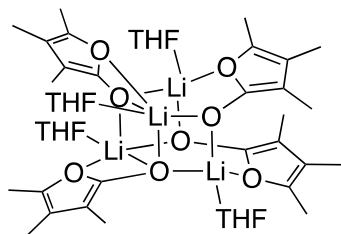


monosolvated tetramer

C	-3.68027200	0.65419600	2.16796400
C	-4.35859000	1.06220800	1.06729300
C	-3.39108700	1.25961600	0.00793900
C	-2.17750900	0.94854700	0.54141500
O	-2.33094300	0.58893600	1.86820300
O	-0.96317900	0.82190400	0.08921800
C	-4.05337800	0.33668000	3.56999200
H	-3.65184400	1.07488300	4.27649800
H	-5.14181400	0.33024800	3.67624300
H	-3.68044800	-0.64880400	3.87470700
C	-5.83212700	1.27298100	0.91961600
H	-6.22523300	0.69610000	0.07337800
H	-6.38020700	0.96676400	1.81599200
H	-6.06832800	2.32694900	0.72579400
C	-3.67088300	1.67494200	-1.40069200
H	-4.46836000	1.06787500	-1.84590300
H	-3.98601800	2.72483800	-1.47446800
H	-2.77696000	1.55608100	-2.02389000
Li	-0.57288300	-0.63205400	1.48115600
C	3.41180300	1.59859200	1.39888100
C	4.32236000	0.67217900	1.78074300
C	3.61427400	-0.56988100	2.00044500
C	2.30033500	-0.32425700	1.72860100
O	2.15367400	1.01107200	1.36687400
O	1.22436400	-1.04480700	1.72522500
C	3.47533900	3.03778100	1.03726600
H	4.51397100	3.37959100	1.06206400
H	3.08442700	3.22054800	0.02935800
H	2.90151700	3.66168700	1.73517700
C	5.79687300	0.85760200	1.95141700
H	6.10533400	0.67167000	2.98796100
H	6.35793800	0.15617700	1.32179200
H	6.11420300	1.87083100	1.68624300
C	4.21336400	-1.88379700	2.38878400
H	4.92628400	-2.24631000	1.63569500
H	4.75256400	-1.82935100	3.34403000
H	3.43318600	-2.64540800	2.49833300
Li	0.87596400	1.27661400	-0.21647700
C	3.57866500	-2.53916700	-1.11121700
C	4.39834900	-1.51853700	-1.45647600
C	3.57082000	-0.35665000	-1.70421600
C	2.28092200	-0.74095800	-1.48508300
O	2.26396200	-2.09025800	-1.13847200
O	1.13613900	-0.14260100	-1.49347900
C	3.76727300	-3.95837200	-0.71638800
H	4.83310500	-4.20173100	-0.69396200
H	3.36324300	-4.15937300	0.28554800
H	3.27990000	-4.64972200	-1.41608900
C	5.89070900	-1.53971100	-1.55104200
H	6.33629800	-0.80175900	-0.87280200

H	6.30176500	-2.52085900	-1.29411100
H	6.22971600	-1.28872400	-2.56377100
C	4.03459200	1.01960500	-2.06064400
H	4.74271200	1.41461300	-1.32016200
H	4.53555600	1.05401700	-3.03774700
H	3.18442300	1.71003400	-2.10276200
Li	0.94834900	-2.29727400	0.34484500
C	-3.64648900	-1.84955400	-1.79471200
C	-4.31743500	-2.24242300	-0.68439500
C	-3.33891000	-2.47337900	0.35827300
C	-2.12524500	-2.19997200	-0.19237800
O	-2.29012400	-1.82622600	-1.51707000
O	-0.90044500	-2.11358000	0.24288000
C	-4.03121100	-1.51523700	-3.18957500
H	-3.65644800	-2.25873000	-3.90510300
H	-5.12055800	-1.48373900	-3.28035400
H	-3.64092500	-0.53661600	-3.49507800
C	-5.79419300	-2.40650200	-0.51215100
H	-6.15294700	-1.82173800	0.34382700
H	-6.34732800	-2.07803600	-1.39749800
H	-6.06051600	-3.45329900	-0.31902500
C	-3.61086900	-2.88697300	1.76898500
H	-4.40848400	-2.28112800	2.21483100
H	-3.92302700	-3.93742800	1.84451100
H	-2.71525300	-2.76659700	2.38892100
Li	-0.63812300	-0.56090400	-1.20775500
C	0.21531300	3.98929500	0.00403100
O	0.82148800	3.09315800	-0.94849700
C	0.06267600	3.08299100	-2.17329300
C	-0.91336100	4.24831500	-2.06822100
C	-1.15931400	4.32588300	-0.55914900
H	0.17481500	3.48218900	0.97278700
H	0.85066900	4.87772200	0.09564600
H	0.76327800	3.16429000	-3.00765900
H	-0.46470700	2.12442500	-2.24385400
H	-0.44887700	5.17189800	-2.43034400
H	-1.82538300	4.07056800	-2.64379600
H	-1.50852600	5.30754700	-0.22922900
H	-1.88889200	3.57160700	-0.24818700

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1953.43775274
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.643042



tetrasolvated tetramer

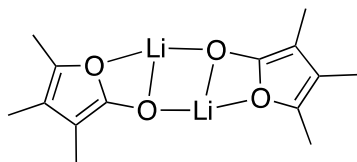
C	-3.98818700	-2.86472800	1.53413900
C	-3.56114300	-3.84485200	0.69585800
C	-2.46172700	-3.29517600	-0.06498000
C	-2.30116900	-2.00975200	0.37302100
O	-3.22270700	-1.73385900	1.34840000
O	-1.48378500	-1.05259000	0.04871100

C	-5.05811600	-2.76515900	2.56105100
H	-5.79407000	-1.99042200	2.30906800
H	-5.59080800	-3.71657900	2.64600800
H	-4.64974000	-2.52007800	3.54987300
C	-4.09949600	-5.23340200	0.54790800
H	-3.33243100	-5.98464700	0.77486000
H	-4.94867600	-5.41512400	1.21425200
H	-4.43558200	-5.42156100	-0.47967500
C	-1.66350200	-3.96296600	-1.13765700
H	-1.31830800	-4.96043900	-0.83725200
H	-2.22708300	-4.08612800	-2.07374600
H	-0.77416600	-3.36843300	-1.36895500
Li	-0.10094000	-0.53316100	1.26620000
C	-2.56690400	3.37959100	0.82889500
C	-1.67209800	4.35890900	1.10131200
C	-0.41958700	3.72200900	1.44021900
C	-0.62235600	2.37275900	1.34223700
O	-1.94982200	2.14593200	0.98290300
O	0.12637600	1.33543900	1.48030800
C	-3.98597800	3.34981800	0.39195500
H	-4.38351500	4.36791000	0.34685900
H	-4.09226800	2.90528600	-0.60570400
H	-4.61625900	2.77424500	1.08234500
C	-1.89078800	5.83772000	1.04255900
H	-1.69519200	6.31057000	2.01330300
H	-1.21293000	6.30562000	0.31758000
H	-2.91525400	6.08850600	0.74973000
C	0.87844800	4.39896600	1.74654800
H	1.11945700	5.16457400	0.99719600
H	0.88457000	4.89437800	2.72822400
H	1.69657200	3.67141600	1.73981600
Li	-2.02865200	0.71884000	-0.46435500
C	1.74011500	3.53111400	-1.56589300
C	0.70710900	4.24165300	-2.07971900
C	-0.41315200	3.33940300	-2.22216500
C	0.00453800	2.11702200	-1.77323300
O	1.33784600	2.21680100	-1.37847700
O	-0.55970500	0.97200800	-1.63286400
C	3.14311400	3.84508200	-1.19201700
H	3.34717300	4.90565600	-1.36618700
H	3.33673200	3.63205200	-0.13381900
H	3.86483100	3.26508800	-1.78331700
C	0.68369000	5.69649100	-2.42921000
H	-0.10710100	6.22046000	-1.87757800
H	1.63323000	6.18931700	-2.19734200
H	0.48059900	5.84957200	-3.49682500
C	-1.79361600	3.67255100	-2.69233900
H	-2.24784200	4.47460600	-2.09451600
H	-1.81845100	3.99947200	-3.74163600
H	-2.44327700	2.79372800	-2.60545400
Li	1.64770800	1.13762700	0.33093100
C	4.28064000	-2.38647000	-0.83225800
C	3.68090400	-3.44256700	-0.22422800
C	2.40002300	-2.97742500	0.26264100
C	2.31856700	-1.65740700	-0.08991200
O	3.45182900	-1.28795500	-0.76653600
O	1.41439900	-0.74061800	0.07640900
C	5.59406300	-2.17018300	-1.49397100
H	6.21444800	-1.44996500	-0.94394500
H	6.14788200	-3.11152100	-1.55181600
H	5.47704800	-1.78670600	-2.51582400
C	4.20702900	-4.83444300	-0.06555600

H	3.53785800	-5.56807100	-0.53285600
H	5.19605000	-4.95113000	-0.51990000
H	4.29198100	-5.11086600	0.99290300
C	1.34641600	-3.77966800	0.95980600
H	1.04261800	-4.65533300	0.37030800
H	1.68039400	-4.15711400	1.93600000
H	0.44748400	-3.17738800	1.13369800
Li	-0.03011300	-0.79724500	-1.24210900
C	-4.92501100	0.15741900	-0.81385200
O	-3.69805400	0.51025000	-1.47942300
C	-3.45220100	-0.38533000	-2.58054100
C	-4.77186900	-1.10582100	-2.82020300
C	-5.35228400	-1.18092200	-1.40547200
H	-4.73245800	0.11253900	0.26093800
H	-5.66289400	0.94347000	-1.01412600
H	-3.10880300	0.20945000	-3.42974500
H	-2.65768800	-1.08445200	-2.29261600
H	-5.41998500	-0.50912500	-3.47200800
H	-4.62571000	-2.08728300	-3.27856000
H	-6.43795600	-1.30741200	-1.38968000
H	-4.89732000	-2.00644700	-0.84949300
C	1.07469300	-1.41904900	3.62825300
O	-0.22336600	-1.42561300	3.00600900
C	-1.15420800	-0.67592500	3.80372800
C	-0.29670500	0.28264000	4.61441600
C	0.94436400	-0.57066200	4.89657500
H	1.37089600	-2.45136300	3.83572600
H	1.78358500	-0.99435000	2.90732300
H	-1.84940600	-0.18469800	3.11957100
H	-1.71638900	-1.36795400	4.44416300
H	-0.03914400	1.14931100	3.99810400
H	-0.79749500	0.62382400	5.52410700
H	1.83973000	0.02755200	5.08475700
H	0.77547000	-1.21273400	5.76742600
C	4.56520500	1.15044900	0.96447400
O	3.27559100	1.63187900	1.34772100
C	3.19370100	1.59075000	2.78156100
C	4.25530000	0.57725600	3.25345400
C	4.84170900	0.02152100	1.94515800
H	4.50316300	0.83284000	-0.07676100
H	5.30385700	1.95950200	1.05968100
H	3.39101600	2.59375700	3.17790900
H	2.16537500	1.31614700	3.02542300
H	5.02704300	1.08289800	3.84111100
H	3.82395600	-0.21075700	3.87604900
H	5.90548300	-0.21805600	2.02185100
H	4.30362100	-0.87772700	1.62968600
C	1.17354000	-2.91122000	-3.17585200
O	0.61560000	-1.60737500	-2.92921300
C	1.40046300	-0.59865600	-3.59444500
C	2.17459000	-1.34463600	-4.67013100
C	2.45035600	-2.68381400	-3.98251500
H	1.36591600	-3.40013500	-2.21703600
H	0.43229200	-3.49429000	-3.73445800
H	0.71359800	0.15750600	-3.97840300
H	2.07035200	-0.13211700	-2.86239200
H	1.55040900	-1.48722000	-5.55958600
H	3.08460200	-0.81549600	-4.96461300
H	2.64291100	-3.50031200	-4.68316200
H	3.30747400	-2.59774100	-3.30815200

E [ωB97XD/6-311++G(d,p), SMD (THF)]: -2650.87448635

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.982136

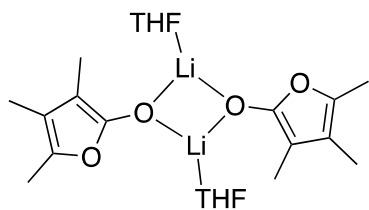


unsolvated dimer

C	-3.82062700	-1.12481200	0.19807500
C	-4.45797200	0.07086800	0.18018700
C	-3.45171600	1.10626600	0.03417800
C	-2.24874800	0.46640700	-0.02630000
O	-2.45857200	-0.90609600	0.07098900
O	-1.00279400	0.79447900	-0.13039900
C	-4.24878100	-2.54255900	0.30910500
H	-5.33352200	-2.59810100	0.43500900
H	-3.98541800	-3.12047200	-0.58649300
H	-3.78707300	-3.04008400	1.17172400
C	-5.92996300	0.31975500	0.28528300
H	-6.31147000	0.83062100	-0.60748700
H	-6.49149800	-0.61245500	0.40067900
H	-6.16490700	0.95999000	1.14460400
C	-3.68266300	2.58341800	-0.02306100
H	-4.33109800	2.86997700	-0.86161700
H	-4.15570700	2.96506900	0.89162100
H	-2.73241400	3.11426100	-0.14540200
Li	-0.35394700	-1.09276500	-0.12705900
C	3.77339300	1.13222100	0.08285700
C	4.37917400	-0.05777400	0.31393400
C	3.46936800	-1.10571900	-0.11078700
C	2.35216100	-0.47846000	-0.57946600
O	2.52441800	0.89783100	-0.46820600
O	1.21006500	-0.82563200	-1.08807200
C	4.13799200	2.55704600	0.29093700
H	5.13164900	2.63024200	0.74124400
H	4.15630600	3.11508900	-0.65417800
H	3.43033600	3.06314300	0.96013400
C	5.73595900	-0.29345800	0.89964100
H	6.36016400	-0.89271800	0.22534300
H	6.26361800	0.64496800	1.09581500
H	5.67019800	-0.84366400	1.84664400
C	3.71140400	-2.58169600	-0.06309600
H	4.59463700	-2.87384700	-0.64689100
H	3.87102200	-2.94640400	0.96026900
H	2.85322200	-3.12294000	-0.47594000
Li	0.50831900	1.04731400	-1.11244400

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -860.433241340

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.245656



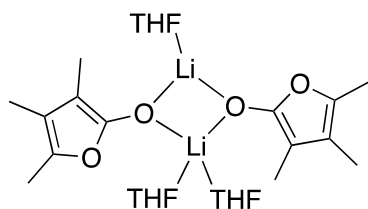
disolvated dimer

C	-3.74350000	-1.30597500	-0.00952400
C	-3.19430000	-1.17176400	1.22569300
C	-1.95406200	-0.44960200	1.05557700
C	-1.84351800	-0.18953000	-0.28785100
O	-2.92887200	-0.70713600	-0.94470200
O	-0.95498600	0.42200600	-1.00554700
C	-4.97928500	-1.94563900	-0.53331200
H	-5.55967600	-2.37475100	0.28837100
H	-5.62070900	-1.22585300	-1.05751300
H	-4.75002900	-2.75436900	-1.23949800
C	-3.72097300	-1.68555900	2.52926600
H	-3.83991400	-0.87649100	3.26091400
H	-4.69389800	-2.17330500	2.41203600
H	-3.03499500	-2.41793200	2.97434400
C	-0.97123600	-0.07841300	2.12184100
H	-0.63039000	-0.95357400	2.69228200
H	-0.07691100	0.38297100	1.68743500
H	-1.38068600	0.63504800	2.85080400
Li	0.44490000	-0.33400300	-1.97709700
C	3.09185600	0.43420300	1.45550500
C	4.08157700	-0.18349000	0.76373600
C	3.75977600	-0.07951100	-0.64592300
C	2.57883200	0.60489200	-0.72367700
O	2.16355700	0.93246300	0.56105000
O	1.77208600	0.98824200	-1.66318500
C	2.80815500	0.67463400	2.89420600
H	3.64585500	0.32963100	3.50689900
H	2.65641300	1.74152500	3.10138800
H	1.90756100	0.14393900	3.23050000
C	5.29361100	-0.86793200	1.31384500
H	6.21227200	-0.45671800	0.87744200
H	5.36538700	-0.76114500	2.40078200
H	5.28483200	-1.94142500	1.08530000
C	4.54201900	-0.64204000	-1.79043600
H	5.53345100	-0.17886400	-1.88989700
H	4.70531000	-1.72333600	-1.68635200
H	4.01104200	-0.48021200	-2.73475700
Li	0.33039800	1.66368000	-0.45286000
C	-0.23296600	4.38059500	-0.88438700
O	-0.31990800	3.38446500	0.15913800
C	-1.66868900	3.32043200	0.66365000
C	-2.53037700	3.90683400	-0.44209300
C	-1.62120500	5.01060900	-0.99068800
H	0.55027800	5.09466200	-0.61803500
H	0.05450700	3.87314900	-1.81315500
H	-1.89349400	2.27511500	0.88884600
H	-1.72982700	3.91031500	1.58629400
H	-2.72446000	3.14703800	-1.20689000
H	-3.48650500	4.28179600	-0.06888800
H	-1.86039600	5.29571600	-2.01787900
H	-1.68505900	5.90401100	-0.36073300

C	-0.47838500	-3.06249500	-1.95753100
O	0.65930700	-2.23234600	-1.64289900
C	1.06039600	-2.43563800	-0.27034800
C	0.34643400	-3.70201600	0.18054900
C	-0.94939500	-3.65268600	-0.63362100
H	-1.23523200	-2.43948000	-2.44349500
H	-0.14926200	-3.83671700	-2.65956200
H	2.14932200	-2.50724000	-0.24508900
H	0.74766000	-1.56348100	0.31757200
H	0.93628700	-4.58645700	-0.08468100
H	0.17355300	-3.71022200	1.25953900
H	-1.41127500	-4.63410600	-0.76774100
H	-1.67495900	-2.98928700	-0.15440800

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1325.39320348

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.473631



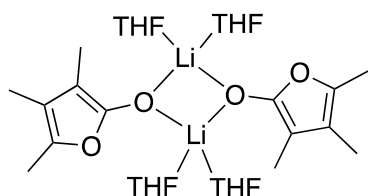
trisolvated dimer

C	4.08078800	-0.25817700	0.35620400
C	4.15989100	-1.58912300	0.10021300
C	3.04582100	-1.92268300	-0.76223200
C	2.35823700	-0.75314500	-0.97355300
O	2.99140300	0.26988200	-0.30049400
O	1.29000400	-0.42647800	-1.61718600
C	4.88052900	0.69994100	1.16387400
H	5.70595300	0.18074300	1.66002600
H	5.31330100	1.49851100	0.54676200
H	4.27443000	1.18177900	1.94303100
C	5.17929900	-2.56318100	0.60337300
H	5.71690200	-3.04201800	-0.22493800
H	5.92264300	-2.08083900	1.24618900
H	4.71011900	-3.36820400	1.18356700
C	2.71250000	-3.26803100	-1.32749700
H	2.65322300	-4.04254800	-0.55046900
H	1.74183500	-3.24095700	-1.83536000
H	3.45666300	-3.61340500	-2.05950900
Li	0.24841900	0.92092000	-0.64903700
C	-4.41559300	0.17107900	-0.11721900
C	-4.31656100	1.52121600	-0.01009200
C	-3.06312900	1.90280800	-0.61748500
C	-2.47571400	0.74230300	-1.05413400
O	-3.29732100	-0.32263500	-0.75791400
O	-1.35511400	0.48219400	-1.64125600
C	-5.43883800	-0.82635800	0.29395200
H	-6.32557300	-0.31615300	0.68167800
H	-5.75743100	-1.45212600	-0.54956100
H	-5.07647000	-1.49993700	1.08248500
C	-5.29203200	2.46945600	0.61495500
H	-5.62184200	3.23157100	-0.10226500
H	-6.18440500	1.95452500	0.98548000
H	-4.84288400	3.00405900	1.46209400

C	-2.48722600	3.28076300	-0.71260800
H	-3.08339300	3.94601200	-1.35370300
H	-2.41894600	3.76930100	0.27015800
H	-1.47256700	3.24339700	-1.12352600
Li	-0.39907100	-1.06031300	-2.01548600
C	-0.61856700	-2.72477100	0.08090500
O	-0.86692400	-2.81449800	-1.33581900
C	-2.15613300	-3.41565500	-1.57293500
C	-2.77445800	-3.65124600	-0.19733000
C	-1.54409500	-3.75452800	0.70756200
H	0.44473600	-2.91276000	0.24424800
H	-0.85558300	-1.70768000	0.41655600
H	-2.74972200	-2.73869700	-2.19384400
H	-1.99161000	-4.35185300	-2.11702000
H	-3.37799800	-2.78649100	0.08956200
H	-3.40441100	-4.54402600	-0.17765000
H	-1.76208600	-3.53419700	1.75593700
H	-1.09670700	-4.75256000	0.64588900
C	1.80339000	2.99496900	-1.81547500
O	0.99453700	2.74009500	-0.65100500
C	1.67803200	3.17326700	0.53324600
C	2.73987500	4.14910900	0.04599800
C	3.13660400	3.52660700	-1.29571000
H	1.90053700	2.05987900	-2.37372400
H	1.27986900	3.73265600	-2.43419600
H	0.93828800	3.61608300	1.20522200
H	2.13261400	2.30333000	1.02007000
H	2.30542400	5.14396600	-0.10267900
H	3.57499400	4.23374300	0.74647800
H	3.59107500	4.24103400	-1.98682800
H	3.83341300	2.69871400	-1.13636900
C	0.96046600	-0.24704300	2.07417400
O	-0.00176500	0.47111800	1.28586600
C	-1.22808100	0.63687700	2.01854700
C	-0.91195700	0.21210400	3.44817100
C	0.17125900	-0.84699500	3.22929900
H	1.44225500	-0.99124200	1.43658300
H	1.72161200	0.45788100	2.43100500
H	-1.54517800	1.67843800	1.92759500
H	-1.99642600	-0.00201400	1.56752000
H	-0.50863000	1.05578000	4.01889200
H	-1.79486600	-0.16818000	3.96778900
H	0.79443600	-1.02270700	4.10961900
H	-0.28005300	-1.79942800	2.92803300

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1557.86808228

Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.588838



tetrasolvated dimer

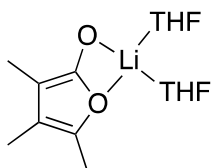
C	-4.39102900	-1.23452400	-0.66531800
C	-4.57352000	-1.19359600	0.67915200

C	-3.37205500	-0.62796600	1.25235100
C	-2.53102700	-0.35665000	0.19932800
O	-3.14828000	-0.72619500	-0.97617900
O	-1.35258900	0.14983000	0.10404700
C	-5.20958200	-1.70257100	-1.81452200
H	-6.16770500	-2.09503700	-1.46128600
H	-5.42319400	-0.89331100	-2.52537900
H	-4.70694500	-2.50298800	-2.37396200
C	-5.76968400	-1.64203500	1.45987700
H	-6.20469200	-0.81515400	2.03572200
H	-6.55502900	-2.04207300	0.81024600
H	-5.50520200	-2.42593500	2.18113400
C	-3.09815300	-0.37608900	2.70279400
H	-3.28044600	-1.26985000	3.31585600
H	-2.05131400	-0.09310300	2.85730800
H	-3.72484200	0.42479300	3.12159200
Li	0.06137800	0.08992800	-1.15162100
C	4.51125600	-0.33885700	0.27638400
C	4.74226500	0.48112700	-0.78106600
C	3.49716400	1.15501200	-1.07250500
C	2.57879100	0.68372800	-0.16766300
O	3.19468400	-0.22347600	0.66931000
O	1.32459500	0.90835500	0.02039500
C	5.34710600	-1.28860300	1.05758900
H	6.37603800	-1.27903600	0.68574100
H	5.37621700	-1.02850500	2.12391100
H	4.97714800	-2.32019200	0.98221000
C	6.02822100	0.68961800	-1.51885000
H	6.38570600	1.72238600	-1.41580600
H	6.82053500	0.02769400	-1.15442300
H	5.90623800	0.50160700	-2.59308100
C	3.23972300	2.15600300	-2.15474600
H	4.00817200	2.94038000	-2.17933500
H	3.21234900	1.70479900	-3.15703900
H	2.27269400	2.64569800	-1.99721800
Li	-0.01924600	0.69577200	1.32432400
C	0.22035500	-1.99487200	1.87130900
O	0.30569900	-0.76740600	2.60616800
C	1.49267400	-0.76656500	3.41784200
C	2.13905600	-2.14373700	3.23952100
C	0.98078900	-3.00147200	2.71888200
H	-0.83949000	-2.22101500	1.73115100
H	0.68921700	-1.85748700	0.88853200
H	2.14846200	0.04422000	3.08767500
H	1.18443200	-0.58113900	4.45215600
H	2.92739500	-2.08746400	2.48447500
H	2.57169000	-2.52074600	4.16975200
H	1.31535000	-3.86857700	2.14271300
H	0.35060900	-3.35347900	3.54308600
C	-0.63592900	2.52199400	-2.27033600
O	-0.31116700	1.21057100	-2.75206900
C	-1.43662200	0.66017900	-3.46449300
C	-2.55357700	1.70355300	-3.39003800
C	-2.15390700	2.54314300	-2.17220300
H	-0.12048600	2.64827500	-1.31448700
H	-0.26498200	3.27264500	-2.98162200
H	-1.12734000	0.43724600	-4.49044800
H	-1.72406300	-0.26983500	-2.96565500
H	-2.56361700	2.32305200	-4.29349400
H	-3.53536900	1.23745800	-3.27971200
H	-2.56336500	3.55651000	-2.19743200
H	-2.46674500	2.04933600	-1.24794400

C	-0.42178400	-2.79327800	-1.60028600
O	0.51146500	-1.71754600	-1.79425700
C	1.85990400	-2.21604000	-1.80588300
C	1.72967400	-3.72167300	-1.99702000
C	0.42155200	-4.01735900	-1.25791400
H	-1.12053100	-2.50421000	-0.81221400
H	-0.98198600	-2.93741000	-2.53179200
H	2.40043500	-1.71169900	-2.61036300
H	2.33778700	-1.97154100	-0.85035500
H	1.63203000	-3.96640400	-3.06044600
H	2.58842700	-4.26314300	-1.59235300
H	-0.05670100	-4.94730300	-1.57510400
H	0.59871100	-4.07185000	-0.17810200
C	0.60498400	3.40894900	2.00582000
O	-0.39328800	2.40028800	2.25551400
C	-1.70679800	2.92140800	1.98163700
C	-1.48201700	4.23091400	1.23633200
C	-0.16041500	4.71637000	1.83705300
H	1.30233700	3.41481800	2.84814200
H	1.15024500	3.12983000	1.09687600
H	-2.25292700	2.17427500	1.40037800
H	-2.22334900	3.08306000	2.93564500
H	-1.36383000	4.04228600	0.16412100
H	-2.30668500	4.93460900	1.37465900
H	0.37211400	5.42402700	1.19667500
H	-0.33335900	5.19033100	2.80959300

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1790.34283009

Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.697546

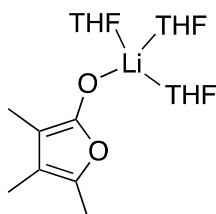


disolvated monomer

C	-0.97007500	-1.05324100	1.18372100
C	-1.96349200	-1.73234600	0.55604500
C	-1.73218000	-1.63231200	-0.86931300
C	-0.58912100	-0.88591900	-1.03803400
O	-0.11139400	-0.53302300	0.23352700
O	0.08929500	-0.42622700	-2.01855000
C	-0.61298100	-0.79258000	2.60278100
H	-1.34839900	-1.25436600	3.26818000
H	0.37182300	-1.20491300	2.86123600
H	-0.58819600	0.28130300	2.83328600
C	-3.10578100	-2.46631000	1.18727400
H	-3.06866500	-3.53859200	0.95589100
H	-3.10732500	-2.36236000	2.27713900
H	-4.06970500	-2.09486600	0.81689300
C	-2.58219800	-2.20187200	-1.96181000
H	-2.72953600	-3.28597300	-1.85740100
H	-3.58412400	-1.74994000	-2.00034100
H	-2.11157500	-2.02912200	-2.93587900
Li	1.00733300	0.90290900	-1.02072600
C	-1.32732500	2.46520300	-1.26285500
O	-0.03115300	2.51194500	-0.62960900

C	-0.18545100	2.76958500	0.78125300
C	-1.67805600	2.99098200	1.01585100
C	-2.31155000	2.20344800	-0.13417900
H	-1.51354900	3.43068900	-1.74949000
H	-1.29377800	1.67650200	-2.01784100
H	0.17543700	1.89102100	1.32658600
H	0.43194400	3.63204100	1.04714600
H	-1.99223800	2.64055000	2.00230500
H	-1.92518400	4.05479500	0.93225200
H	-2.34489300	1.13403600	0.10033900
H	-3.32200700	2.53934200	-0.38010600
C	3.01522200	0.40799200	0.95327100
O	2.85240000	0.62266200	-0.46005600
C	3.38943300	-0.50813400	-1.18988500
C	3.98442400	-1.44746700	-0.14262000
C	3.17982600	-1.09413900	1.11137700
H	3.90364000	0.95311600	1.29596900
H	2.13496200	0.81150100	1.46015000
H	2.55760300	-0.97043800	-1.73234000
H	4.12607500	-0.13582900	-1.90689400
H	3.88482500	-2.49559200	-0.43439400
H	5.04664600	-1.23087100	0.01243100
H	2.19921400	-1.57942300	1.08590600
H	3.68764300	-1.36153000	2.04140600

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -895.144125597
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.337087



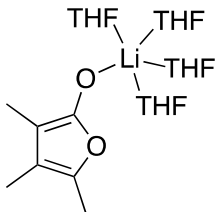
trisolvated monomer

C	3.03600100	0.34930900	0.07580600
C	3.37914900	-0.55617900	-0.87675600
C	2.19980600	-0.80365100	-1.67437100
C	1.19282400	-0.01725500	-1.15444800
O	1.71004500	0.69359100	-0.07738300
O	-0.03963200	0.16726800	-1.43443400
C	3.75057900	1.00081300	1.20532700
H	4.81305600	0.73996400	1.18560600
H	3.67494500	2.09513000	1.15569200
H	3.35273600	0.69212400	2.18276100
C	4.70893800	-1.21502800	-1.07808000
H	5.09871800	-1.03433700	-2.08806800
H	5.45700100	-0.85368300	-0.36446400
H	4.63581400	-2.30385500	-0.95705900
C	2.07366800	-1.73787900	-2.83663100
H	2.74024000	-1.47354700	-3.67076000
H	2.30263800	-2.78076800	-2.57171000
H	1.04837500	-1.71835100	-3.22345200
Li	-1.13595100	0.42353000	0.06682300
C	-0.32071900	-2.08761900	1.03030000
O	-0.65604500	-0.79526300	1.56783900
C	0.25082700	-0.44902500	2.62714600

C	1.00272600	-1.73167800	2.96160200
C	1.05156400	-2.42450600	1.59765900
H	-1.08253500	-2.80748400	1.35625200
H	-0.33589200	-2.01356600	-0.06032500
H	0.93628600	0.32107600	2.25995800
H	-0.33338100	-0.04752400	3.45973600
H	1.99181900	-1.53132900	3.38154600
H	0.43572900	-2.33487700	3.67955200
H	1.83624400	-1.98402400	0.97398400
H	1.21731000	-3.50278000	1.66382800
C	-0.28549100	3.02795100	1.08553300
O	-1.43943200	2.30322900	0.63282800
C	-1.98657800	2.94624300	-0.53846300
C	-1.10527700	4.16509000	-0.81603200
C	0.21197400	3.78403500	-0.13442800
H	-0.58390900	3.71036500	1.89281500
H	0.43477800	2.30456800	1.47097200
H	-1.95110500	2.22475000	-1.36126600
H	-3.03137200	3.20170900	-0.33953300
H	-0.99618900	4.35307300	-1.88688700
H	-1.52956800	5.06130800	-0.35064900
H	0.79838900	3.10873900	-0.76503500
H	0.82662100	4.64851100	0.13053000
C	-3.76972800	-0.84596300	0.58160700
O	-2.94760700	-0.23615500	-0.42803000
C	-2.98473100	-1.01581800	-1.63207600
C	-3.36771000	-2.41703900	-1.18055700
C	-4.35168000	-2.11739100	-0.04458500
H	-3.12848500	-1.06077600	1.44237800
H	-4.54064600	-0.13182000	0.88747000
H	-3.73981100	-0.59661100	-2.31131400
H	-1.99723200	-0.93690000	-2.09109300
H	-3.80936900	-3.00861400	-1.98659100
H	-2.48698600	-2.94662000	-0.80232200
H	-5.34894200	-1.92232600	-0.45277200
H	-4.43290800	-2.92994400	0.68185500

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1127.61535404

Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.449784

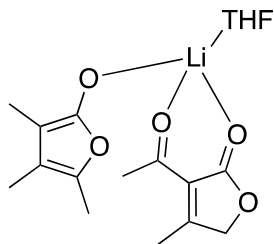


tetrasolvated monomer

C	-2.94465300	-0.21909700	0.94423400
C	-3.88097800	-0.08820100	-0.03052800
C	-3.18805100	0.24044500	-1.25484800
C	-1.83922000	0.30003900	-0.95457900
O	-1.69397000	0.01492000	0.40875000
O	-0.77478500	0.54111900	-1.60047600
C	-2.99209700	-0.55517000	2.39150200
H	-4.02739700	-0.71680400	2.70733000
H	-2.43152700	-1.47208700	2.62342000
H	-2.57904000	0.24673000	3.01945300

C	-5.36414600	-0.25035200	0.09957100
H	-5.74224000	-1.02645800	-0.57842400
H	-5.65939600	-0.52707600	1.11715700
H	-5.89278500	0.67708500	-0.15706800
C	-3.79569200	0.47389900	-2.60290100
H	-4.29705300	-0.41765800	-3.00877900
H	-4.54623700	1.27785100	-2.59796800
H	-3.01827300	0.76059400	-3.31992300
Li	0.68458100	0.26003700	-0.28486200
C	0.26940000	3.24522200	-0.57037400
O	0.61578800	2.31407300	0.45514400
C	-0.14418300	2.58969500	1.63758600
C	-1.06845300	3.76693600	1.30542800
C	-1.13516000	3.71622400	-0.22369800
H	0.98304400	4.08344500	-0.56083300
H	0.33016200	2.71897200	-1.52327100
H	-0.71310700	1.68989000	1.88487700
H	0.54285900	2.81509800	2.46134500
H	-2.04669500	3.66486200	1.78264000
H	-0.62396500	4.71239200	1.63568500
H	-1.86794600	2.97389200	-0.55543000
H	-1.37875600	4.68106900	-0.67716000
C	-0.14148000	-2.74256200	0.19712600
O	0.65883000	-1.99491400	-0.71830900
C	0.31189000	-2.34364200	-2.06774700
C	-0.74011900	-3.45150900	-1.97658800
C	-1.35488500	-3.20581000	-0.59670700
H	0.43677200	-3.59908200	0.57608700
H	-0.39897900	-2.08816000	1.03057900
H	-0.08228900	-1.44059000	-2.54161100
H	1.21760000	-2.66896600	-2.59140300
H	-1.47022500	-3.39114300	-2.78802200
H	-0.26734200	-4.43955500	-2.01272700
H	-2.09888400	-2.40432700	-0.64541600
H	-1.82189000	-4.09541300	-0.16486200
C	3.11114100	-0.32874600	-2.07715200
O	2.46455500	0.59355300	-1.19564800
C	3.40669100	1.54259500	-0.68214500
C	4.78221700	1.01587200	-1.07972800
C	4.47019200	0.28770100	-2.38920800
H	3.21578300	-1.29508900	-1.56820600
H	2.47766400	-0.46335600	-2.95768700
H	3.20779100	2.51977200	-1.13975200
H	3.25446700	1.62811600	0.39581800
H	5.51786900	1.81692400	-1.18940400
H	5.15410200	0.30565600	-0.33207600
H	4.38446000	1.00568400	-3.21245600
H	5.21626600	-0.46363800	-2.66002500
C	2.72727500	-1.12423000	1.53281600
O	1.55006000	-0.30858400	1.58037100
C	0.89719200	-0.45534600	2.84137800
C	1.43486600	-1.75220600	3.43288400
C	2.87873600	-1.73976200	2.92460600
H	2.58080200	-1.88171500	0.75626200
H	3.58087800	-0.49828300	1.25550800
H	1.14079000	0.40275700	3.48336600
H	-0.18058700	-0.46319100	2.66399300
H	1.35686500	-1.77774300	4.52288800
H	0.89237200	-2.61179900	3.02495100
H	3.49833800	-1.09987900	3.56271200
H	3.33525100	-2.73219200	2.88879700

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1360.07499003
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.565705



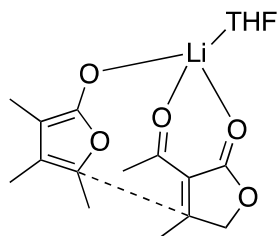
**pre-reaction complex
(monomeric)**

C	0.31656600	1.63991200	0.02722100
O	1.47474900	1.31701500	-0.16911700
O	-0.20893900	2.70345000	-0.60099700
C	-0.69988800	1.04323000	0.91954400
C	-1.85625300	1.72785600	0.72689000
C	-0.37807300	-0.06545400	1.83358200
C	-3.20225100	1.64669800	1.35795700
C	-1.57231900	2.84988700	-0.21843000
H	-3.95602100	2.07437600	0.69003500
H	-3.49167800	0.62547300	1.60000400
H	-3.21281000	2.23303300	2.28597900
H	-2.20001200	2.82809600	-1.11313200
H	-1.70317700	3.82266700	0.27074400
O	0.73221700	-0.60218100	1.80982200
C	-1.37353800	-0.45935100	2.89134000
H	-0.92145900	-1.20904300	3.54289500
H	-2.27466900	-0.87991300	2.43800600
H	-1.67126900	0.41174900	3.48523000
C	-2.47954200	-0.24367300	-1.56748400
C	-3.25922000	0.63577400	-2.47988500
O	-1.12908300	-0.33461100	-1.80820600
C	-2.84527100	-1.17728500	-0.63959600
C	-0.61116200	-1.33251600	-0.99760000
O	0.62946700	-1.57892800	-1.05612300
C	-1.65488700	-1.86919900	-0.24824600
C	-1.51981100	-3.01924400	0.69872300
H	-2.29936300	-3.00343600	1.47027500
H	-1.59392700	-3.99450500	0.19562400
H	-0.54825400	-2.99287200	1.20655600
C	-4.22652300	-1.45251500	-0.13130000
H	-4.94135100	-0.69016700	-0.45763300
H	-4.59693100	-2.42454900	-0.48192100
H	-4.25370000	-1.48485300	0.96586600
H	-3.41861400	0.17083200	-3.46305600
H	-4.24398800	0.85476500	-2.05534900
H	-2.74844300	1.58801900	-2.66512600
Li	1.74841100	-0.64728900	0.11099100
C	4.26474100	-0.97543700	-1.09713300
O	3.67193700	-0.95739500	0.21842000
C	4.31956900	0.03248200	1.03751200
C	5.05969900	0.94005800	0.06597400
C	5.47584500	-0.05006500	-1.02523600
H	4.51575100	-2.00984600	-1.34519900
H	3.51941900	-0.61278800	-1.81518500
H	3.54779900	0.54267600	1.61989800

H	5.00812300	-0.47440700	1.72468600
H	4.37587000	1.69287000	-0.33942900
H	5.90588800	1.44794200	0.53545900
H	5.68226000	0.42748600	-1.98599100
H	6.36644700	-0.60748900	-0.71559900

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1159.93644640

Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.359551



**Michael addition TS
(monomeric)**

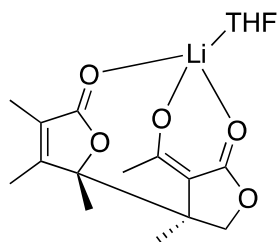
C	0.32689600	1.53259100	0.34260400
O	1.51814000	1.28587300	0.20327400
O	-0.17961000	2.67307200	-0.16106100
C	-0.72470600	0.77462700	1.02192100
C	-1.93011900	1.40923400	0.74562200
C	-0.42839300	-0.42581800	1.78095200
C	-3.26437500	1.32063000	1.41699300
C	-1.57102400	2.73925000	0.14119300
H	-4.03793100	1.76511500	0.78231700
H	-3.56063100	0.30120400	1.65529500
H	-3.24099600	1.89405100	2.35384200
H	-2.11763800	2.99762300	-0.76704800
H	-1.73144400	3.54053000	0.87524900
O	0.69208100	-0.96616500	1.74557300
C	-1.46972800	-0.99252000	2.71651600
H	-1.02365000	-1.81000500	3.28602200
H	-2.32632800	-1.37913600	2.15728300
H	-1.83753700	-0.22570500	3.40627500
C	-2.41517000	0.20005400	-1.34716100
C	-3.26612100	1.11796800	-2.16042600
O	-1.08810900	0.12237500	-1.72893400
C	-2.76993800	-1.00592500	-0.73890900
C	-0.55969000	-1.03074700	-1.20672600
O	0.66116500	-1.27415500	-1.33190100
C	-1.60525700	-1.76166900	-0.59122600
C	-1.41081100	-3.10151200	0.04024500
H	-2.31889500	-3.43728700	0.55194100
H	-1.14782900	-3.86700200	-0.70091600
H	-0.59589100	-3.07645800	0.77534700
C	-4.15278100	-1.40080000	-0.32536000
H	-4.84819800	-0.55784300	-0.37088100
H	-4.54191600	-2.18650000	-0.98456700
H	-4.17410600	-1.80131100	0.69518600
H	-3.61319800	0.63787500	-3.08526600
H	-4.15165800	1.43270600	-1.59825700
H	-2.71149100	2.01426600	-2.45428000
Li	1.76418100	-0.67926900	0.12675800
C	4.14981300	-0.63327800	-1.28106000
O	3.68292000	-1.01491000	0.03128300

C	4.38605800	-0.26690600	1.04070500
C	5.01780400	0.90785100	0.30845700
C	5.34667900	0.28375100	-1.05059600
H	4.39310300	-1.54330200	-1.83520200
H	3.33333400	-0.11444700	-1.79710300
H	3.66209000	0.02680700	1.80555200
H	5.14255900	-0.91703100	1.49701400
H	4.28527400	1.71295800	0.19252900
H	5.89550700	1.29918100	0.82869100
H	5.45581500	1.02205200	-1.84867700
H	6.27161000	-0.29992600	-0.98895600

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1159.93230740

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.362424

Imaginary Frequency: -259.83

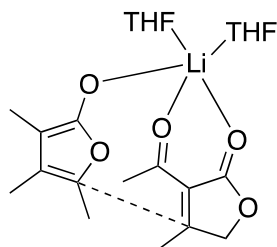


**post-reaction complex
(monomeric)**

C	-0.15059400	-1.68884500	0.29244200
O	-1.38613700	-1.60302000	0.30015700
O	0.40620200	-2.69283800	-0.42629200
C	0.85576300	-0.88914600	0.92653100
C	2.18059000	-1.22734800	0.26054600
C	0.50498400	0.17985600	1.78351400
C	3.44898100	-1.38213700	1.10856100
C	1.82305400	-2.62628600	-0.28909900
H	4.20486700	-1.95607000	0.55939900
H	3.90949700	-0.43549000	1.39319300
H	3.21466600	-1.93275700	2.02452600
H	2.26517200	-2.86344600	-1.25765500
H	2.13503500	-3.39256700	0.43069500
O	-0.67227900	0.63026500	1.89101100
C	1.53149700	0.84264700	2.67844300
H	1.16555000	0.77957300	3.70928600
H	1.60512400	1.90678400	2.42887800
H	2.52325600	0.39408000	2.63811000
C	2.42807700	-0.19193000	-0.94718600
C	3.51927200	-0.59155500	-1.92846300
O	1.16880500	-0.15334900	-1.66087700
C	2.57973000	1.23011400	-0.44996400
C	0.48497700	0.93063700	-1.25843500
O	-0.71737100	1.05127000	-1.44403100
C	1.40731900	1.86546900	-0.60262800
C	0.96387500	3.21674700	-0.16107100
H	1.79085200	3.79191900	0.26364400
H	0.52831400	3.78620200	-0.98907700
H	0.18692300	3.11433800	0.60717900
C	3.83608900	1.79951000	0.12515500
H	4.72250800	1.25508800	-0.21054400
H	3.94570700	2.84716500	-0.17214500

H	3.82260400	1.77505200	1.22038600
H	3.63439400	0.18318400	-2.69264800
H	4.47748000	-0.71269000	-1.41670800
H	3.28001800	-1.52940600	-2.43452700
Li	-1.75018500	0.30028300	0.34190700
C	-4.09763800	0.55120800	-1.20136700
O	-3.61002300	0.80513500	0.13268200
C	-4.47451400	0.18236000	1.10284400
C	-5.36106800	-0.76913500	0.31068600
C	-5.49425000	-0.03183900	-1.02441000
H	-4.07611200	1.49271100	-1.75519200
H	-3.42188100	-0.16163100	-1.68883400
H	-3.84736100	-0.31496300	1.84809600
H	-5.06011000	0.96562600	1.59844700
H	-4.85656200	-1.73047600	0.16732600
H	-6.31880300	-0.94804400	0.80545300
H	-5.77330000	-0.68584100	-1.85402100
H	-6.23772300	0.76914700	-0.94676700

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1159.96331771
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.362515



***disolvated TS
(monomeric)***

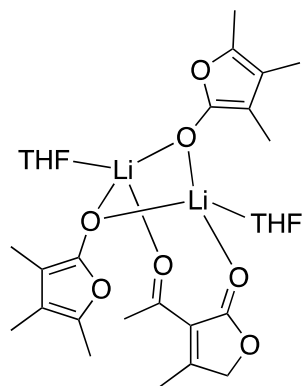
C	-0.82421800	1.84893900	0.63717000
O	0.38189800	2.01579800	0.55067900
O	-1.66965100	2.82521100	0.24132800
C	-1.58672400	0.71471100	1.15465400
C	-2.93050400	0.96016900	0.90487100
C	-0.90822700	-0.39573500	1.80101800
C	-4.16624400	0.38303200	1.52330000
C	-3.01022500	2.39613500	0.45559800
H	-5.04722400	0.64835800	0.92950800
H	-4.13393000	-0.70063500	1.62323300
H	-4.30991400	0.81075500	2.52537900
H	-3.57950000	2.55861200	-0.46101700
H	-3.45499000	3.01535900	1.24655500
O	0.32603700	-0.50325300	1.78309900
C	-1.71292700	-1.39672000	2.59658000
H	-1.03103900	-2.12011000	3.04816100
H	-2.41912100	-1.92848400	1.95455500
H	-2.28864000	-0.89688900	3.38338700
C	-3.08113400	-0.10953300	-1.30310500
C	-4.27956000	0.46294100	-1.98345800
O	-1.86108000	0.40449800	-1.70928900
C	-2.88244800	-1.42170600	-0.86825700
C	-0.88180600	-0.48605200	-1.35153000
O	0.31951900	-0.19226800	-1.52348500
C	-1.50606600	-1.64993600	-0.83008000

C	-0.75252600	-2.86326500	-0.38978800
H	-1.34986600	-3.47618100	0.29536400
H	-0.47358300	-3.50655900	-1.23643700
H	0.17464000	-2.57745300	0.12106800
C	-3.96246900	-2.39341500	-0.50734000
H	-4.93092200	-1.90002700	-0.38446300
H	-4.07635300	-3.15278200	-1.29122000
H	-3.73690100	-2.93062700	0.42156900
H	-4.37748400	0.08960900	-3.01234900
H	-5.19398700	0.19289800	-1.44618100
H	-4.23213700	1.55496200	-2.04614100
Li	1.36616500	0.16837200	0.12022500
C	2.86343100	2.09423300	-1.44416400
O	3.08120100	1.20107600	-0.33845700
C	3.55763500	1.93271700	0.79951100
C	3.36530800	3.40738000	0.46304300
C	3.54253800	3.40343300	-1.05788600
H	3.28144000	1.62977700	-2.34169100
H	1.78486700	2.22320300	-1.57782100
H	2.99181200	1.61036400	1.67935600
H	4.61735000	1.69106800	0.95552700
H	2.34978500	3.71868900	0.72257600
H	4.08122600	4.04867500	0.98383700
H	3.08339700	4.26572400	-1.54821400
H	4.60653700	3.37928400	-1.32037000
C	3.46453400	-1.83209900	1.12130100
O	2.42393100	-1.60757100	0.17786700
C	2.91093100	-2.05731600	-1.07896400
C	3.60321800	-3.37579000	-0.74824000
C	4.20929000	-3.09919500	0.64488300
H	4.13738900	-0.96337400	1.13722700
H	2.99728600	-1.93434900	2.10267400
H	2.05467200	-2.13572400	-1.74935100
H	3.61921400	-1.32044300	-1.48717600
H	2.85889800	-4.17648500	-0.69339400
H	4.35298800	-3.65478700	-1.49303800
H	4.05473100	-3.93990300	1.32580800
H	5.28516700	-2.91313000	0.58374000

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1392.39245051

Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.470478

Imaginary Frequency: -266.32

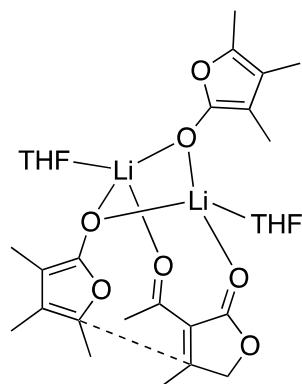


***pre-reaction complex
(dimeric)***

C	-3.88118000	-0.25366700	-0.58254100
C	-3.75851500	-1.60165200	-0.72657100
C	-2.40339500	-1.86125200	-1.13752800
C	-1.78229700	-0.63238500	-1.24066400
O	-2.68549400	0.35257600	-0.89686400
O	-0.60452200	-0.26314700	-1.57438200
C	-5.02076500	0.65884600	-0.29838900
H	-5.81011400	0.13329300	0.24841400
H	-4.70181500	1.51761900	0.30390100
H	-5.46914600	1.06357300	-1.21613400
C	-4.81667700	-2.63998100	-0.52002900
H	-4.47944700	-3.42498200	0.16978600
H	-5.73599000	-2.20877800	-0.11032600
H	-5.07572900	-3.13990600	-1.46189200
C	-1.78892700	-3.17714700	-1.49594800
H	-2.04592700	-3.49676000	-2.51630200
H	-0.69496000	-3.11991800	-1.44565600
H	-2.11312600	-3.97933200	-0.82170600
Li	0.22299500	1.33585500	-0.84301900
C	4.72966500	0.46267600	0.99148800
C	4.54978700	1.80333000	1.11471700
C	3.40136000	2.15122700	0.30812900
C	2.95551500	0.98116000	-0.25535500
O	3.76250600	-0.05521900	0.15788400
O	1.99204200	0.68541000	-1.05959100
C	5.69865700	-0.51492400	1.55399200
H	6.43164800	-0.00095100	2.18311300
H	5.20359100	-1.27426200	2.17448700
H	6.25037800	-1.04618200	0.76680700
C	5.36446900	2.76847200	1.91873700
H	4.75291800	3.27418600	2.67706900
H	6.19162400	2.27255300	2.43749000
H	5.79536800	3.55357400	1.28392400
C	2.79698000	3.50638400	0.11133000
H	2.34395100	3.91025800	1.02824000
H	3.53486700	4.24667700	-0.22920500
H	2.00917900	3.46239200	-0.65002800
Li	1.05991000	-0.97082000	-0.89165800
C	3.19327700	-2.21762500	-2.33799100
O	1.98149800	-2.56007200	-1.63944100
C	2.26312400	-3.65147200	-0.76214500
C	3.67769000	-3.38329000	-0.27161600
C	4.35658800	-2.82215200	-1.53044400
H	3.14230200	-2.62729400	-3.35309100
H	3.22626200	-1.12775600	-2.39017000
H	1.50612300	-3.63848700	0.02376500
H	2.19708000	-4.59864400	-1.31660600
H	3.65334100	-2.62241400	0.51294700
H	4.16562000	-4.28170500	0.11563400
H	5.10702300	-2.06793800	-1.28516200
H	4.84320900	-3.62153600	-2.09787200
C	-0.95407700	4.01866500	-0.72939200
O	-0.43317900	3.03596800	-1.62656200
C	-1.38567500	2.84815600	-2.68833500
C	-2.73589100	3.38088800	-2.17212900
C	-2.44983100	3.74459100	-0.70741800
H	-0.45775600	3.88118600	0.23272600
H	-0.73041200	5.02362600	-1.11494300
H	-1.04137000	3.39574000	-3.57314400
H	-1.40004900	1.77950900	-2.91094700
H	-3.03981200	4.26579400	-2.73972500

H	-3.52337500	2.62940400	-2.25991000
H	-3.02864900	4.60373600	-0.35761400
H	-2.65021700	2.89061800	-0.05524900
C	-1.25719400	0.86083100	1.64075500
O	-0.30741200	1.37421400	1.08698700
O	-2.21400500	1.63362400	2.19317700
C	-1.59604300	-0.56369500	1.87089700
C	-2.78763200	-0.59513000	2.51540300
C	-0.73120700	-1.67972200	1.43753400
C	-3.65180400	-1.70575700	3.00690300
C	-3.20885600	0.81038000	2.78317800
H	-4.48557900	-1.30663200	3.59121000
H	-4.06772500	-2.26811100	2.16521200
H	-3.09360600	-2.40610500	3.63378900
H	-4.18458100	1.04540700	2.34718700
H	-3.25270100	1.01364200	3.85961400
O	0.36158300	-1.46558100	0.91986200
C	-1.14798500	-3.09063700	1.75700300
H	-0.49288300	-3.78394900	1.22720500
H	-2.18540100	-3.28745200	1.48166800
H	-1.04189800	-3.26168000	2.83552400

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1822.65498400
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.609563



**Michael addition TS
(dimeric)**

C	-3.80197300	-0.19360700	-0.25048300
C	-3.71941200	-1.54492900	-0.61294700
C	-2.44612300	-1.76980400	-1.13238300
C	-1.79873700	-0.51316000	-1.17161400
O	-2.66446100	0.44393700	-0.72990500
O	-0.64335700	-0.18221100	-1.53657100
C	-5.02157700	0.66534400	-0.17648000
H	-5.75138100	0.24747900	0.52453300
H	-4.77251500	1.67770600	0.15576100
H	-5.51151500	0.75766900	-1.15458500
C	-4.80896800	-2.55623500	-0.44792900
H	-4.44348300	-3.47234000	0.03040800
H	-5.63718100	-2.16660600	0.15013600
H	-5.21251500	-2.84605900	-1.42563800
C	-1.81910100	-3.04278700	-1.59878500
H	-1.67311900	-3.05000100	-2.68623600

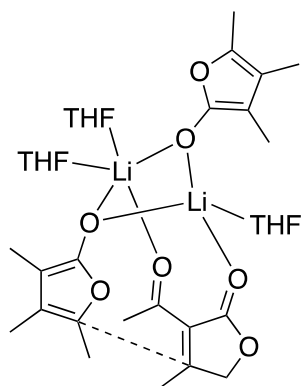
H	-0.82981500	-3.18316400	-1.14536100
H	-2.43984600	-3.90702100	-1.34082400
Li	0.33837500	1.40181600	-0.85990500
C	4.64094300	0.36234500	1.08800100
C	4.60966200	1.71987000	1.06580300
C	3.54845500	2.10442600	0.16163400
C	3.00009100	0.93765600	-0.30837400
O	3.66213900	-0.13222000	0.25330300
O	2.03960500	0.65653600	-1.12343400
C	5.46752500	-0.65061000	1.79595700
H	6.19942800	-0.15583900	2.44156000
H	4.85507800	-1.30603400	2.42957500
H	6.02157600	-1.29347300	1.09871700
C	5.48332600	2.66960600	1.82530200
H	4.88683000	3.33399800	2.46371800
H	6.19458100	2.14294300	2.47001300
H	6.06262000	3.31302800	1.15045900
C	3.08749200	3.48992400	-0.16859800
H	2.68664100	4.01997600	0.70745800
H	3.89197400	4.11801600	-0.57699100
H	2.28954600	3.45719200	-0.92029800
Li	1.04944100	-0.94431800	-0.59404700
C	3.07546000	-2.18988000	-2.30804600
O	1.91029200	-2.50447800	-1.53304000
C	2.20097100	-3.69411600	-0.80259300
C	3.64324800	-3.50714100	-0.34986600
C	4.28056900	-2.78512600	-1.55164000
H	2.96653900	-2.63703500	-3.30453700
H	3.10360200	-1.10349300	-2.39858800
H	1.47575700	-3.75924000	0.00910800
H	2.09585600	-4.56808000	-1.46304800
H	3.66641300	-2.86342600	0.53433300
H	4.13334600	-4.45443400	-0.10938000
H	4.97239300	-2.00484600	-1.22850900
H	4.82760200	-3.48516300	-2.19030000
C	-0.89343600	4.00378600	-0.42684000
O	-0.41654600	3.10867200	-1.43722500
C	-1.38821800	3.03645200	-2.49695200
C	-2.68919800	3.64682400	-1.94853600
C	-2.40401500	3.83065300	-0.45196800
H	-0.42734900	3.71085000	0.51627200
H	-0.59443100	5.03131300	-0.67558800
H	-1.00747400	3.58656800	-3.36395300
H	-1.48977800	1.98193700	-2.76237200
H	-2.88859600	4.61105500	-2.42592300
H	-3.54707100	2.99413200	-2.12793800
H	-2.92904700	4.68525400	-0.01718000
H	-2.66849700	2.92756600	0.10242400
C	-0.98915700	0.63644800	1.52110400
O	0.11347900	0.94414000	1.08785800
O	-1.81650300	1.60540000	1.97103600
C	-1.62943500	-0.66535000	1.65838800
C	-2.96952800	-0.43088900	1.97602700
C	-0.91645100	-1.90074000	1.40461600
C	-4.00472300	-1.33377900	2.57289000
C	-3.04164100	1.01429000	2.39304500
H	-4.99554500	-0.87508200	2.49175400
H	-4.04486600	-2.31720800	2.10933500
H	-3.79417100	-1.47169600	3.64193200
H	-3.87230800	1.57868800	1.96692900
H	-3.10801300	1.08493900	3.48682400
O	0.23315800	-1.91669200	0.93693700

C	-1.54533300	-3.21561000	1.80396800
H	-0.82994600	-4.01943700	1.61929700
H	-2.45281500	-3.41035800	1.22619400
H	-1.81871400	-3.21061400	2.86447800

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1822.64617968

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.612986

Imaginary Frequency: -294.77

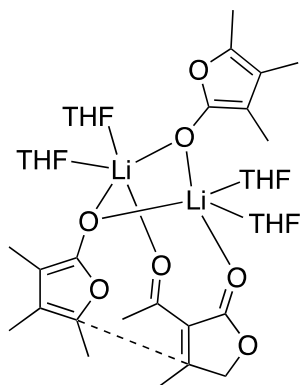


trisolvated TS
(dimeric)

C	-3.82340000	1.07634600	-0.95202200
C	-3.77201900	0.24364500	-2.06861100
C	-2.42579900	-0.02109400	-2.34065400
C	-1.66399300	0.74450800	-1.42670800
O	-2.53244000	1.46053500	-0.63450400
O	-0.43331800	0.86544200	-1.26100500
C	-4.89767100	2.02436900	-0.53765100
H	-5.86678100	1.51762300	-0.48379800
H	-4.68772400	2.46163400	0.44352700
H	-4.99862200	2.85864800	-1.24511500
C	-4.95713900	-0.26222900	-2.82929100
H	-4.89808000	-1.34231500	-3.00854300
H	-5.89406000	-0.05913800	-2.30278300
H	-5.01846700	0.22095400	-3.81218000
C	-1.81733400	-0.89008000	-3.39284300
H	-1.34853600	-0.30120500	-4.19188700
H	-1.03333100	-1.52742200	-2.96435100
H	-2.56784300	-1.53755200	-3.85896600
Li	0.43290300	1.33070900	0.39478300
C	3.91159900	2.75102800	-1.06775800
C	4.95902400	2.16114600	-0.43592100
C	4.41805300	1.09244200	0.37437400
C	3.05875300	1.09612000	0.16845100
O	2.74454500	2.11320700	-0.71199400
O	2.07574700	0.40657600	0.62748900
C	3.77413300	3.87906200	-2.02644700
H	3.10506900	4.66065700	-1.64201100
H	4.74912900	4.33884800	-2.21395800
H	3.36685400	3.54988200	-2.99197200
C	6.40890500	2.52413000	-0.52674300
H	7.01447800	1.67317400	-0.86476800
H	6.58082000	3.34913600	-1.22604800
H	6.80895900	2.82906900	0.44915800

C	5.18024500	0.14668100	1.24827200
H	4.48998000	-0.45762600	1.84769500
H	5.81058800	-0.55102800	0.67616500
H	5.84650000	0.67087300	1.94780400
Li	0.97178600	-1.17055400	0.10369400
C	3.52166300	-1.93720300	-1.11119300
O	2.13056100	-1.91825100	-1.47436000
C	1.78538200	-3.14381200	-2.12110000
C	2.79945500	-4.15975000	-1.61521400
C	4.06661000	-3.30294200	-1.54052600
H	4.02833400	-1.10176900	-1.60321300
H	3.57740900	-1.79175800	-0.03029300
H	0.74930500	-3.36698600	-1.86284100
H	1.86545400	-3.01977000	-3.21126100
H	2.51474500	-4.51407300	-0.61863000
H	2.89801400	-5.02251400	-2.27997900
H	4.80813200	-3.68710900	-0.83470700
H	4.53718300	-3.23834700	-2.52772700
C	-0.66707700	3.35733900	2.27937900
O	0.03801000	3.13135300	1.05938200
C	-0.46853700	4.02609300	0.05613600
C	-1.82118000	4.55043100	0.57295100
C	-2.07676500	3.72173200	1.84025500
H	-0.60498000	2.43918200	2.86688900
H	-0.18876900	4.17717200	2.83411000
H	0.25536400	4.83415700	-0.09690100
H	-0.55534200	3.44975600	-0.86739800
H	-1.75079300	5.61592300	0.81269500
H	-2.61269300	4.42063700	-0.16933900
H	-2.62638400	4.27112600	2.60948900
H	-2.61891400	2.80602500	1.59515200
C	-1.71301700	-0.30449600	1.43332900
O	-0.49807100	-0.16980400	1.51037300
O	-2.50773100	0.39975000	2.26488000
C	-2.52464200	-1.14373100	0.56118100
C	-3.84700400	-0.76167200	0.73937200
C	-1.91799200	-2.12059700	-0.32626500
C	-5.13101600	-1.43354200	0.37033200
C	-3.87038600	0.10869600	1.96517100
H	-5.95754200	-0.71733700	0.41759000
H	-5.11787900	-1.87936000	-0.62215600
H	-5.34778000	-2.22919900	1.09644800
H	-4.41471500	1.04786400	1.85108800
H	-4.30653500	-0.43634900	2.81259600
O	-0.68988900	-2.22768000	-0.43308800
C	-2.79574300	-3.11310300	-1.05234100
H	-2.16043900	-3.79879600	-1.61636600
H	-3.47888400	-2.61428400	-1.74337700
H	-3.39990200	-3.68446000	-0.33884500
C	1.86669300	-1.97880700	2.78833800
O	1.65077900	-2.56237500	1.50237900
C	0.91542100	-3.75920100	1.71716400
C	-0.10526000	-3.40147100	2.79559700
C	0.63350800	-2.34039200	3.63999600
H	2.78329900	-2.40269800	3.22273100
H	2.00456200	-0.91008200	2.62331900
H	0.47063800	-4.04984100	0.76443500
H	1.59631700	-4.55313900	2.06062700
H	-0.99610800	-2.97032000	2.32998700
H	-0.41184400	-4.27461200	3.37816300
H	0.00421200	-1.46450200	3.81075300
H	0.93715800	-2.73712000	4.61306400

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -2055.10947540
 ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.725625
Imaginary Frequency: -231.07



***tetrasolvated TS
(dimeric)***

C	4.20847900	0.79999000	0.87639300
C	4.34146000	-0.51921500	1.32835400
C	3.06649400	-1.07644700	1.38632700
C	2.15198100	-0.04194800	1.06276700
O	2.85648500	1.11344200	0.85726500
O	0.90846500	-0.04292800	0.97156400
C	5.12458500	1.94879700	1.14126200
H	6.15658300	1.68671600	0.88792600
H	4.84724900	2.83311200	0.55878200
H	5.10616400	2.24396800	2.19940400
C	5.63420500	-1.19522600	1.66297100
H	5.72045500	-2.17891000	1.18657200
H	6.49665400	-0.59705800	1.35513200
H	5.71457000	-1.35868600	2.74469000
C	2.63549500	-2.46725700	1.71836100
H	1.87055200	-2.80295400	1.00763100
H	3.47577200	-3.16929400	1.68132000
H	2.19800500	-2.53565900	2.72363000
Li	-0.42810000	1.27916800	0.48980100
C	-4.90399100	-0.79937700	0.50042600
C	-5.18291900	0.49375300	0.19164500
C	-3.93451200	1.11505900	-0.18469100
C	-2.96145500	0.14460900	-0.08358300
O	-3.55533500	-1.02823800	0.34535900
O	-1.69968300	0.12799500	-0.29621000
C	-5.71304000	-1.96838100	0.93680200
H	-6.76250000	-1.68375200	1.05837800
H	-5.67230200	-2.78786300	0.20617400
H	-5.36394100	-2.37258000	1.89669300
C	-6.51231400	1.18216700	0.22777300
H	-6.76107300	1.62349800	-0.74580300
H	-7.32216600	0.49582600	0.49640400
H	-6.51827700	2.00196200	0.95802900
C	-3.71898800	2.52593800	-0.63206900
H	-2.64784200	2.70931900	-0.76270000
H	-4.21109700	2.75247800	-1.58974500
H	-4.09148200	3.26197500	0.09522900

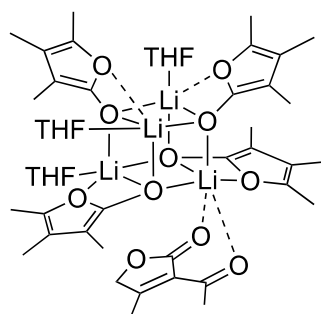
Li	-0.24808800	-1.10689900	-0.95976500
C	-0.98972300	-2.68529400	1.57505200
O	-0.71966900	-2.79139700	0.17352800
C	-0.50014300	-4.14958600	-0.19418000
C	-1.06440700	-4.97728500	0.95565200
C	-0.75130800	-4.07816900	2.15547300
H	-0.33128700	-1.91424700	1.98366400
H	-2.03098700	-2.36966800	1.69615600
H	-0.99550800	-4.32988400	-1.15241900
H	0.57542000	-4.32145200	-0.32638500
H	-2.14757200	-5.10041900	0.84146900
H	-0.60737900	-5.96836500	1.02266000
H	-1.38193100	-4.27863500	3.02619600
H	0.29607500	-4.20165200	2.45386600
C	0.06661700	1.90986300	3.30951600
O	-1.05033800	1.68135600	2.44758200
C	-1.86798700	0.62056500	2.97180900
C	-1.22272400	0.18176500	4.28758100
C	0.23262700	0.62608500	4.11196900
H	0.93155700	2.15048900	2.68531600
H	-0.14896900	2.76599400	3.96488700
H	-2.88802900	0.99613500	3.09993900
H	-1.87927200	-0.17974600	2.23135100
H	-1.68030100	0.70120400	5.13674000
H	-1.32650900	-0.89475900	4.45112400
H	0.75189400	0.78944300	5.06028200
H	0.78792100	-0.10687900	3.52022300
C	2.02595100	0.67687500	-1.84689400
O	0.80900900	0.58862500	-1.87672500
O	2.61465100	1.87490900	-2.09249900
C	3.05587200	-0.32631500	-1.59730300
C	4.27390200	0.33809900	-1.47988400
C	2.71399500	-1.73432300	-1.49408000
C	5.67729100	-0.17254200	-1.60843800
C	4.02631600	1.73523700	-1.98650500
H	6.39003900	0.58407600	-1.26435000
H	5.85702700	-1.08931500	-1.04978400
H	5.89913600	-0.37279400	-2.66575300
H	4.41065500	2.53216500	-1.34807800
H	4.46965900	1.85686200	-2.98436700
O	1.54077800	-2.11980900	-1.49979500
C	3.81663200	-2.77021600	-1.46639700
H	3.36291900	-3.76337800	-1.45418300
H	4.44271300	-2.65501200	-0.57846300
H	4.46319700	-2.67827400	-2.34574000
C	-1.33186200	-0.91807400	-3.78971500
O	-1.26610400	-1.85717900	-2.72326900
C	-2.59377400	-2.32857300	-2.47087500
C	-3.56446200	-1.28766200	-3.06635200
C	-2.63431400	-0.16567700	-3.55429200
H	-0.43612800	-0.29824300	-3.73217900
H	-1.34773400	-1.44753800	-4.75630400
H	-2.72336400	-3.31019800	-2.94764000
H	-2.69287100	-2.43558000	-1.39001000
H	-4.12071000	-1.71939100	-3.90498400
H	-4.28726400	-0.93345900	-2.32694000
H	-3.00321000	0.33442400	-4.45449200
H	-2.48629700	0.57730100	-2.76571800
C	-0.07718700	3.74438900	-1.31731200
O	-0.30568600	3.24117700	0.00781300
C	-0.88633400	4.26144100	0.83552200
C	-1.22317000	5.41825000	-0.09997700

C	-0.16291100	5.25975200	-1.19223800
H	0.88972600	3.37464600	-1.65669400
H	-0.85606100	3.35694800	-1.98711300
H	-1.75428700	3.84006400	1.34564800
H	-0.14625000	4.55752600	1.58942200
H	-2.22524200	5.28758100	-0.52382800
H	-1.18613100	6.38479400	0.40925700
H	-0.43448000	5.73938900	-2.13627200
H	0.79623000	5.67092100	-0.85649300

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -2287.57808416

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.835736

Imaginary Frequency: -276.95



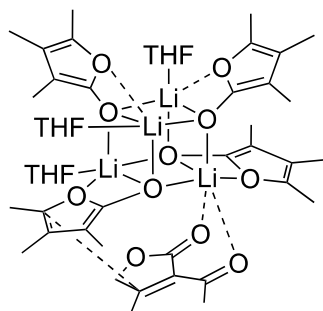
***pre-reaction complex
(tetrameric)***

C	0.77518300	-3.89129900	1.42047800
C	2.10730300	-4.00853100	1.64640100
C	2.62035800	-2.67860600	1.87962500
C	1.55643600	-1.82299100	1.76304700
O	0.41417300	-2.55805300	1.50374000
O	1.43027000	-0.54170100	1.82353200
C	-0.31152300	-4.85622700	1.11031800
H	-1.09374800	-4.85688200	1.87855800
H	0.10137800	-5.86743700	1.04330100
H	-0.79868700	-4.63277100	0.15230400
C	2.93369100	-5.25611500	1.62702000
H	3.72181500	-5.19280300	0.86563100
H	2.33065900	-6.14294700	1.40623100
H	3.43314900	-5.42451600	2.58981200
C	4.04211800	-2.28880300	2.12754100
H	4.71243500	-2.64305700	1.33269000
H	4.43494000	-2.68254900	3.07656700
H	4.13311900	-1.19760100	2.16930300
Li	-0.96858400	-1.76784700	-0.08559300
C	-4.64514900	1.38891800	0.43194200
C	-4.54725700	1.58183600	-0.91404000
C	-3.24734200	1.11454500	-1.30916600
C	-2.62885900	0.67838700	-0.15846500
O	-3.47257900	0.84612800	0.90643000
O	-1.46735600	0.16147100	0.04855400
C	-5.64152800	1.79794800	1.45703000
H	-6.62742400	1.93542900	1.00249200
H	-5.36446600	2.74338900	1.94299600
H	-5.73336000	1.04922700	2.25235100
C	-5.57789000	2.17478700	-1.82338900
H	-5.77378500	1.52455500	-2.68589700

H	-5.24974400	3.14158700	-2.22510400
H	-6.53016400	2.33567100	-1.30781700
C	-2.61026400	1.14347200	-2.66302200
H	-3.35837700	1.26392200	-3.45520800
H	-2.06825400	0.21003300	-2.86821000
H	-1.88704000	1.96207800	-2.76622800
Li	-0.04638700	0.57064800	1.29534700
C	-0.54631700	4.59231100	-0.73727600
C	0.22874900	5.09899400	0.25548800
C	1.03111100	4.00676900	0.76581100
C	0.67607300	2.90286600	0.03695100
O	-0.28152600	3.24930200	-0.88288500
O	1.01866500	1.65158800	0.04801500
C	-1.57951000	5.15085800	-1.64793400
H	-1.70199600	6.22333000	-1.47093000
H	-2.55514900	4.67250300	-1.49265500
H	-1.31076900	5.01268500	-2.70322300
C	0.27868900	6.50946200	0.75407500
H	0.04399700	6.56371200	1.82463700
H	-0.43241200	7.15279500	0.22600000
H	1.27798700	6.94524200	0.62546200
C	2.01123300	4.05343700	1.89483400
H	1.53320900	4.29386100	2.85440600
H	2.79637800	4.80532600	1.73456100
H	2.50224500	3.08099700	2.00527500
Li	-0.02037500	0.59353800	-1.27294800
C	3.97777600	-1.63323600	-1.41312900
C	3.61238700	-2.86024400	-1.86088200
C	2.16909900	-2.91802600	-1.84304200
C	1.73056000	-1.71130300	-1.36668500
O	2.83925300	-0.90436700	-1.11127700
O	0.58395300	-1.19826300	-1.12206300
C	5.28181900	-0.94794300	-1.22198900
H	5.43507200	-0.13218200	-1.94220000
H	6.09904000	-1.66286200	-1.35732400
H	5.36779200	-0.51956300	-0.21696000
C	4.50761800	-3.97484000	-2.30407400
H	4.28117500	-4.90154700	-1.76231600
H	5.56466400	-3.74319500	-2.13884200
H	4.37828100	-4.19175800	-3.37227900
C	1.30538900	-4.08835800	-2.19017700
H	1.46546100	-4.93804100	-1.51106100
H	1.48267000	-4.45623400	-3.21049700
H	0.24778100	-3.80932400	-2.12178000
Li	2.37952100	0.39888800	0.46394600
C	-3.63897300	-2.22732000	0.92679000
O	-2.48728000	-2.50920900	1.18250500
O	-4.57451700	-2.20008400	1.89595500
C	-4.27333300	-1.90270900	-0.36907100
C	-5.57321600	-1.61386900	-0.12659000
C	-3.51480400	-1.96010200	-1.63299400
C	-6.71262600	-1.24157100	-1.00977900
C	-5.82620100	-1.83121500	1.33064400
H	-7.48714400	-0.73037400	-0.43021900
H	-6.41036400	-0.59481300	-1.83293700
H	-7.16315600	-2.14657500	-1.43655600
H	-6.19984100	-0.93401500	1.83167100
H	-6.54692600	-2.64164400	1.49224100
O	-2.31255100	-2.21095600	-1.62966000
C	-4.24671300	-1.79509700	-2.93740400
H	-3.55278700	-1.97889600	-3.75951500
H	-4.64548400	-0.78028700	-3.02675100

H	-5.08791400	-2.49355800	-3.00212100
C	1.94344400	1.73257400	-3.02144500
O	0.64296700	1.12779400	-3.10964300
C	0.65596200	0.06855000	-4.08223100
C	2.11345400	-0.10028800	-4.50504600
C	2.67617800	1.30657000	-4.28595700
H	1.80714000	2.81179600	-2.92124700
H	2.44259700	1.35034300	-2.12654200
H	0.23739600	-0.82860600	-3.61840600
H	0.02069900	0.37026100	-4.92419600
H	2.61818300	-0.81818200	-3.85038000
H	2.20492700	-0.44969700	-5.53684200
H	3.76227600	1.32225200	-4.15960200
H	2.41377500	1.96332000	-5.12333000
C	4.38752800	2.38585000	-0.21875800
O	4.04672800	1.39628400	0.76581100
C	4.91722700	1.49005400	1.89998800
C	5.59458300	2.84885600	1.77935700
C	5.69245400	3.01424800	0.26051800
H	4.48330400	1.88960400	-1.18819500
H	3.56980800	3.11323500	-0.27236300
H	4.31438900	1.37462200	2.80467200
H	5.65128000	0.67453000	1.85718100
H	4.96081000	3.63060500	2.21011800
H	6.56546000	2.87108900	2.28030700
H	5.78704500	4.05592500	-0.05564100
H	6.55093200	2.45521900	-0.12787400
C	-1.54172200	0.04261600	3.47048700
O	-0.79413800	1.18951300	3.01286000
C	0.27186000	1.48036700	3.93275600
C	0.34482700	0.29093600	4.88225200
C	-1.11248400	-0.17636600	4.91520100
H	-2.60244900	0.26082800	3.34131500
H	-1.28585200	-0.82007200	2.84310800
H	1.19006300	1.62353700	3.35783400
H	0.02971100	2.41167700	4.45989400
H	0.98217900	-0.48627200	4.44944900
H	0.73640100	0.56830100	5.86472100
H	-1.22569500	-1.21948100	5.22188100
H	-1.70405700	0.45209800	5.59096400

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -2915.64990778
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 1.004717



**Michael addition TS
(tetrameric)**

C	0.95380600	-3.89042500	1.39313600
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C	2.29083700	-3.96750500	1.60805000
C	2.76234300	-2.62354600	1.85134800
C	1.66934000	-1.80293300	1.75376600
O	0.55200500	-2.57145300	1.49300600
O	1.49769400	-0.52672000	1.83565100
C	-0.10847500	-4.88163200	1.08059900
H	-0.88714300	-4.90520100	1.85195800
H	0.32867300	-5.88195400	1.00466200
H	-0.60657600	-4.66483400	0.12633900
C	3.15423600	-5.18922700	1.57210500
H	3.93617800	-5.09699200	0.80705100
H	2.57609000	-6.09124000	1.34647300
H	3.66393200	-5.35159100	2.53057400
C	4.17291300	-2.18854700	2.08843100
H	4.85335400	-2.55685200	1.30887400
H	4.57372600	-2.53454800	3.05273400
H	4.23696000	-1.09455800	2.08630900
Li	-0.90499000	-1.91159400	-0.11127300
C	-4.80198100	0.93096400	0.22991900
C	-4.60242600	1.18386800	-1.13719000
C	-3.27843300	0.87595200	-1.43118500
C	-2.66644500	0.53884300	-0.20481800
O	-3.55874000	0.68269300	0.80110100
O	-1.48596800	0.16049000	0.03412000
C	-5.78899700	1.58724300	1.14048200
H	-6.81642600	1.38145800	0.82336700
H	-5.65473200	2.67632200	1.15774700
H	-5.66949700	1.23129300	2.16750500
C	-5.64388000	1.68188800	-2.08773100
H	-5.63027400	1.12721400	-3.03294000
H	-5.46281800	2.73619900	-2.32997500
H	-6.64832000	1.60775500	-1.66220600
C	-2.54974800	0.88436900	-2.73429000
H	-3.24095700	0.98709000	-3.57698600
H	-1.99106100	-0.05115200	-2.87326600
H	-1.82870300	1.70809700	-2.79053700
Li	-0.03018800	0.50362100	1.30288100
C	-0.82010500	4.46886000	-0.73843800
C	-0.07407900	5.04399500	0.23903300
C	0.80808200	4.01927800	0.75847700
C	0.52747800	2.88282900	0.04953900
O	-0.46225200	3.14504400	-0.86650700
O	0.96067000	1.65954500	0.07013700
C	-1.89520800	4.94265100	-1.64843900
H	-2.08100300	6.00898000	-1.49082900
H	-2.83920400	4.40984300	-1.47459400
H	-1.62795700	4.80065800	-2.70352600
C	-0.12127400	6.46087600	0.71914200
H	-0.35526100	6.51110100	1.79003000
H	-0.87759200	7.04682700	0.18728200
H	0.84529300	6.96236500	0.58134200
C	1.80576600	4.15406600	1.86521800
H	1.33567900	4.42109200	2.82140500
H	2.56039400	4.92468700	1.65535200
H	2.33331400	3.20528800	2.00889000
Li	0.00340700	0.59514800	-1.29470300
C	4.01272200	-1.47063600	-1.41569100
C	3.69700000	-2.70540500	-1.87987100
C	2.25725900	-2.82233400	-1.85942900
C	1.77178600	-1.64275800	-1.36349700
O	2.84594500	-0.79409600	-1.09961100
O	0.60317500	-1.18169300	-1.10977200

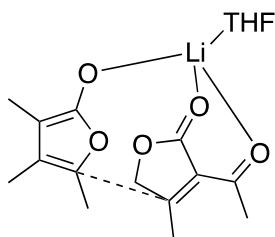
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H	6.13376700	-1.40520300	-1.37808000
H	5.36274600	-0.31684400	-0.21005300
C	4.63504700	-3.77583100	-2.34255300
H	4.44652200	-4.71910500	-1.81509900
H	5.68245100	-3.50531500	-2.17518600
H	4.51175000	-3.98090200	-3.41375400
C	1.43878800	-4.02041900	-2.22096500
H	1.63211600	-4.87115300	-1.55199900
H	1.62937300	-4.36782600	-3.24586900
H	0.37127900	-3.78270900	-2.14898400
Li	2.38719600	0.48464100	0.48689600
C	-3.46792700	-2.15845100	1.01979400
O	-2.32530500	-2.52214000	1.25167500
O	-4.34082600	-2.00236800	2.04018800
C	-4.12479000	-1.85859900	-0.24715000
C	-5.38172200	-1.32192700	0.05026800
C	-3.45340000	-2.10385100	-1.50693500
C	-6.61737100	-1.24619400	-0.79572300
C	-5.60736100	-1.62142800	1.51199600
H	-7.36612700	-0.60322700	-0.32148400
H	-6.43183800	-0.87132100	-1.80027800
H	-7.05684100	-2.24846600	-0.88604700
H	-6.00175900	-0.79332300	2.10153600
H	-6.29950900	-2.46870400	1.61148800
O	-2.25154700	-2.41302600	-1.55868500
C	-4.24465900	-2.06284700	-2.79389000
H	-3.58214100	-2.31296700	-3.62498500
H	-4.67256900	-1.07145700	-2.96469500
H	-5.07051900	-2.78197300	-2.76047600
C	1.94466800	1.82926000	-2.99615600
O	0.67486000	1.16340500	-3.09618500
C	0.73974800	0.11743000	-4.08260100
C	2.20709000	0.01406700	-4.48989600
C	2.70552700	1.44272300	-4.25686200
H	1.75748800	2.90077600	-2.89398100
H	2.45397600	1.46761100	-2.09844100
H	0.35110300	-0.80100600	-3.63439600
H	0.10166600	0.40485800	-4.92729200
H	2.73577300	-0.68524100	-3.83404200
H	2.32448300	-0.32398500	-5.52275300
H	3.78860600	1.50608200	-4.12130800
H	2.42169700	2.09274800	-5.09245200
C	4.30271800	2.58267300	-0.15154500
O	3.99555500	1.55668500	0.80656900
C	4.85165600	1.65931200	1.95087700
C	5.45068200	3.05775000	1.88193900
C	5.55814000	3.27649000	0.37020800
H	4.45105400	2.11206200	-1.12733900
H	3.44402000	3.26021300	-0.21303200
H	4.24933700	1.47761100	2.84470800
H	5.63091800	0.88837700	1.88658300
H	4.76773700	3.78779300	2.32803500
H	6.41279800	3.12012100	2.39633300
H	5.59108300	4.33184100	0.08852200
H	6.45548800	2.78508500	-0.02152800
C	-1.59536700	-0.00034700	3.44484500
O	-0.83583600	1.13790100	2.98184100
C	0.19539400	1.46027300	3.93017500
C	0.26035400	0.28155500	4.89263500
C	-1.19345600	-0.19799300	4.90067300

H	-2.65390100	0.21628600	3.29417700
H	-1.33209800	-0.87214800	2.83436200
H	1.12723200	1.61629100	3.38077700
H	-0.08068000	2.39111000	4.44127500
H	0.91408200	-0.49394000	4.48143200
H	0.62894100	0.57256200	5.88006300
H	-1.30450700	-1.23828700	5.21716200
H	-1.80321000	0.43307100	5.55758600

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -2915.64069564

Δ G [ω B97XD/6-31G(d), SMD (THF)]: 1.007246

Imaginary Frequency: -317.67



minor diastereomeric TS

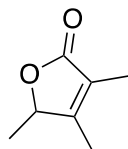
C	-0.10891200	0.42987300	1.42617500
O	1.11913400	0.39905700	1.37090000
O	-0.75858200	-0.35427700	2.31412800
C	-1.06745200	1.22652800	0.67546200
C	-2.34246200	0.74065400	0.97092200
C	-0.65306300	2.27974500	-0.23065400
C	-3.68367800	1.39017300	0.82641200
C	-2.16228900	-0.11899100	2.19635000
H	-4.47948900	0.67006500	1.03953000
H	-3.76911600	2.20203600	1.56151700
H	-3.86129300	1.81516100	-0.15991000
H	-2.49772700	0.43425200	3.08458800
H	-2.68416400	-1.07507200	2.17450300
O	0.54303200	2.48886600	-0.48507300
C	-1.68969300	3.16309100	-0.87496900
H	-1.18419400	3.95911400	-1.42530000
H	-2.36785300	3.60157500	-0.13711900
H	-2.28607200	2.57052400	-1.57698000
C	-2.50776400	-0.76403100	-0.92918500
C	-3.90613600	-0.70238500	-1.45185500
O	-1.57158300	-0.10612300	-1.70639600
C	-1.86951600	-1.85431500	-0.31361800
C	-0.33352200	-0.62775600	-1.41675900
O	0.70189900	-0.10935000	-1.89045900
C	-0.50688800	-1.74901700	-0.56996700
C	0.62397100	-2.56817100	-0.04273600
C	-2.54768800	-2.93387100	0.46825200
H	-3.59448500	-2.69346200	0.67606900
H	-2.53281100	-3.87672500	-0.09210000
H	-2.04110400	-3.11952400	1.42200000
H	0.25937500	-3.45905400	0.47861900
H	1.29042500	-2.90202000	-0.84729800
H	1.23064400	-1.98857600	0.66669100
H	-4.02062300	-1.32029100	-2.35290000
H	-4.61763300	-1.06616600	-0.70477500
H	-4.18944300	0.32021700	-1.71825100

Li	1.66762700	0.89737600	-0.49968000
C	4.34323800	1.06619500	0.50081400
O	3.59917700	0.72264800	-0.68705800
C	3.93166200	-0.61483500	-1.10062600
C	4.42973800	-1.29928700	0.16130600
C	5.19191700	-0.15982500	0.84553900
H	4.94191700	1.95751100	0.29214600
H	3.61942600	1.30038500	1.28802100
H	3.02851500	-1.05160300	-1.53305400
H	4.71361200	-0.56972000	-1.86976200
H	3.58190200	-1.62115600	0.77562500
H	5.05572300	-2.16873500	-0.05479600
H	5.29444100	-0.29635500	1.92465400
H	6.19375400	-0.06372200	0.41380700

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1159.92706449

Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.361123

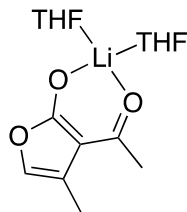
Imaginary Frequency: -282.41



C	-1.08883000	-0.84303300	-0.07008600
O	-2.15720700	-1.39641600	0.04749900
O	0.05391800	-1.52721200	-0.32228900
C	-0.77579500	0.59981000	0.01872000
C	0.54049100	0.74650700	-0.18135000
C	1.37413400	1.98141900	-0.19762200
C	1.15607000	-0.61135300	-0.39986200
H	1.98885800	2.01910000	-1.10469400
H	0.76255500	2.88627700	-0.15602100
H	2.06180400	1.99415600	0.65690400
C	2.21176300	-0.99506000	0.62480300
H	1.80712800	-0.91159100	1.63872100
H	2.54478600	-2.02319300	0.45785600
H	3.07970700	-0.33422300	0.53567300
C	-1.84774700	1.60108000	0.28855500
H	-2.61658500	1.56590400	-0.49136200
H	-2.34635000	1.38607000	1.24033500
H	-1.44803700	2.61748300	0.33402900
H	1.57193900	-0.68717400	-1.41207200

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -423.226541256

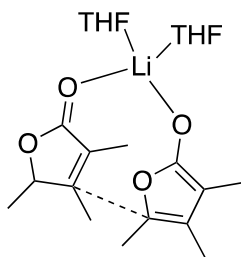
Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.126083



C	-3.51584200	-0.07488000	-1.33283000
O	-2.36586700	-0.04146300	-2.09391700
C	-3.25051500	-0.09290200	-0.01490700

C	-1.30047600	-0.03587900	-1.24223700
O	-0.15322300	-0.00607500	-1.72826400
C	-1.79307100	-0.06547500	0.09664200
C	-4.29378700	-0.15289800	1.05747500
H	-5.29244600	-0.09680100	0.61207400
H	-4.23627900	-1.08745800	1.62751500
H	-4.20030200	0.67117100	1.77272500
C	-0.93944800	-0.04265400	1.23138300
O	0.31293000	-0.00833100	1.14124100
C	-1.53178700	-0.03789400	2.62400300
H	-2.24310700	-0.85665100	2.76658800
H	-0.72550700	-0.12986400	3.35518700
H	-2.06681500	0.90076700	2.80755500
H	-4.44315100	-0.08624400	-1.88759900
Li	1.28437900	0.03265900	-0.50270700
C	1.51620700	2.75665200	-1.25293100
O	2.28226800	1.75544300	-0.57556500
C	2.51176700	2.25712900	0.74743100
C	1.28020100	3.10896300	1.11062800
C	0.49744800	3.21444700	-0.21556300
H	2.18252900	3.57573900	-1.55817500
H	1.07881200	2.29409400	-2.13872700
H	2.65594100	1.39489800	1.40174200
H	3.43148300	2.85583300	0.74382700
H	0.68140700	2.62542700	1.88510900
H	1.58781200	4.09189800	1.47785800
H	-0.35566400	2.52911500	-0.21391600
H	0.12838900	4.22376100	-0.41459600
C	1.71535600	-2.65481300	-1.26485100
O	2.41281900	-1.60691800	-0.58377200
C	2.67992700	-2.09835300	0.73603700
C	1.50955400	-3.03213900	1.09891700
C	0.73563100	-3.19164800	-0.22735600
H	1.24239100	-2.21719400	-2.14525700
H	2.43578700	-3.42283700	-1.57933400
H	3.63648300	-2.63579600	0.72582700
H	2.76977300	-1.23123100	1.39368400
H	1.88434100	-3.99131300	1.46680800
H	0.87848600	-2.59125800	1.87292800
H	0.44680100	-4.22601000	-0.43066600
H	-0.16870400	-2.57519500	-0.22186800

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -969.190909673
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.323728

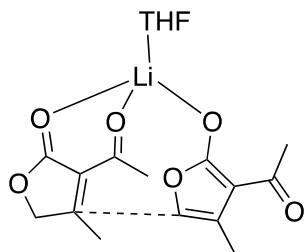


**nucleophile-nucleophile
homo-coupling TS**

C	-0.39755300	0.86917700	1.21473500
O	0.79443100	0.72311300	1.54188500

O	-0.74515900	1.98072900	0.50726400
C	-1.52576500	0.04793700	1.44180700
C	-2.60529800	0.56162300	0.70979500
C	-4.03842900	0.32446400	1.10728800
C	-2.16242500	1.95718800	0.27905100
H	-4.74608500	0.65011500	0.33912500
H	-4.21349000	-0.73589400	1.30897400
H	-4.27288600	0.87446500	2.02819700
C	-2.55028100	-0.44462700	-1.19614700
C	-3.61227200	0.14723900	-2.07381700
O	-1.25387000	-0.03852200	-1.53176100
C	-2.46801000	-1.81555000	-0.84047100
C	-0.38439900	-0.99552900	-1.11451900
O	0.84757700	-0.79492800	-1.18760100
C	-1.13032100	-2.14027700	-0.71344400
C	-0.52459700	-3.41488200	-0.22361000
H	-0.41893000	-3.42999600	0.87031500
H	-1.13784800	-4.27993300	-0.50117100
H	0.47283300	-3.56058100	-0.65102000
C	-3.62789200	-2.71954400	-0.56109500
H	-4.58230300	-2.18820900	-0.60834700
H	-3.66628800	-3.53383400	-1.29556400
H	-3.54924700	-3.18413900	0.42862800
H	-3.40217100	-0.04654000	-3.13335000
H	-4.58403400	-0.29741800	-1.84243400
H	-3.70606000	1.23250200	-1.95053900
Li	1.91407500	0.21991400	0.02750300
C	1.74168500	2.48286000	-1.61534900
O	2.74776200	1.76429300	-0.86925600
C	3.34918200	2.64637400	0.08556900
C	2.26414600	3.65741800	0.41803700
C	1.59329400	3.85542800	-0.94617800
H	2.06644900	2.55513500	-2.65860200
H	0.82249600	1.89407500	-1.56710600
H	3.67232200	2.03820500	0.93478000
H	4.22978200	3.12621900	-0.36362200
H	1.55843600	3.21405000	1.12562200
H	2.66828300	4.58281300	0.83726900
H	0.54353300	4.14317500	-0.85486900
H	2.11625900	4.62558800	-1.52294000
C	2.63880700	-2.04172600	1.38775400
O	3.33451200	-0.97890800	0.70273900
C	4.08109800	-1.51662900	-0.40234000
C	3.49253700	-2.89640500	-0.65764800
C	3.13365200	-3.34176800	0.76266900
H	2.84987200	-1.95702000	2.45705700
H	1.56448600	-1.90039800	1.22684900
H	3.97676100	-0.82476000	-1.24263100
H	5.14071200	-1.57280800	-0.12121800
H	2.58830200	-2.80051700	-1.26623600
H	4.19692100	-3.56544200	-1.15840400
H	2.37026300	-4.12358700	0.79087200
H	4.02420000	-3.70846300	1.28487300
C	-2.80637000	3.08290000	1.07601600
H	-2.65514800	2.93297300	2.15017800
H	-2.36133900	4.04093900	0.78999200
H	-3.88130300	3.13143600	0.87456900
C	-1.52280400	-1.13993600	2.34776400
H	-0.49662900	-1.46674300	2.54702000
H	-1.99320200	-0.92360400	3.31807300
H	-2.06562200	-1.98500700	1.90944500
H	-2.30148200	2.14284500	-0.78764500

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1318.37174937
 Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.495675
Imaginary Frequency: -397.75



**electrophile-electrophile
homo-coupling TS**

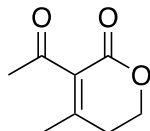
C	0.97244000	-2.29444400	-0.00456400
O	-0.15174600	-2.75275000	-0.17739100
O	2.03194400	-2.90954000	-0.56309500
C	1.41339900	-1.13057600	0.75822000
C	2.77125400	-0.92473400	0.46237400
C	0.49158500	-0.36212100	1.56630600
C	3.82319700	-0.22236100	1.26956000
C	3.21987500	-2.19623100	-0.22804000
H	4.74076000	-0.10884600	0.68376900
H	3.51367300	0.76061400	1.62002500
H	4.06491200	-0.83370000	2.14866700
H	3.80445100	-2.04709700	-1.13697200
H	3.80923900	-2.80497900	0.46963800
O	-0.73932200	-0.53883200	1.49128100
C	1.01507400	0.63269000	2.57323400
H	0.17862400	0.99520300	3.17423500
H	1.47710900	1.49012900	2.07411700
H	1.76582600	0.17668400	3.22610100
C	2.61294100	0.36340700	-1.33633200
O	1.51384400	-0.26017500	-1.90190400
C	2.21666000	1.57612300	-0.77361100
C	0.39488100	0.37815100	-1.44840100
O	-0.72275000	-0.10572200	-1.67347500
C	0.81456400	1.56520300	-0.75472800
C	3.14683200	2.61928700	-0.25427100
H	4.18939800	2.32183000	-0.39930600
H	2.97809500	3.56408300	-0.78133800
H	2.97515800	2.82622000	0.80579800
Li	-1.44003200	-1.25026200	-0.20719100
C	-4.01159300	-0.33212500	-1.20975300
O	-3.37399300	-1.11992200	-0.18540700
C	-4.00716000	-0.89087300	1.08845900
C	-5.29811700	-0.14581300	0.77399900
C	-4.90398800	0.65581200	-0.46956300
H	-3.22735400	0.13755900	-1.80782300
H	-4.59756900	-1.00347400	-1.84844900
H	-4.16237000	-1.86001100	1.56956500
H	-3.33216700	-0.29118200	1.70960600
H	-6.09949000	-0.85286400	0.53418600
H	-5.62421000	0.48082000	1.60774900
H	-5.75987700	0.96803400	-1.07305800
H	-4.33583800	1.54819200	-0.18487300

C	-0.05696600	2.53913100	-0.09996600
O	0.41362800	3.50137900	0.50081200
C	-1.55056600	2.31514700	-0.14870900
H	-1.80004900	1.39382400	0.39131000
H	-2.05260300	3.16288800	0.32296000
H	-1.90176700	2.19059900	-1.17707600
H	3.55741900	0.14671400	-1.81909800

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1233.95345805

Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.345912

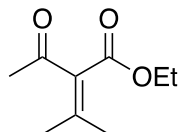
Imaginary Frequency: -404.90



C	-0.41751900	-1.31645700	0.00886200
O	0.19735900	-2.36049000	-0.06190100
O	-1.75998900	-1.36259500	0.02256100
C	0.23922600	0.01551200	0.04768700
C	-0.46646500	1.14391400	-0.16581700
C	1.73643700	0.04398900	0.24783700
C	0.12204900	2.51426600	-0.28580900
C	-1.95593100	1.03769400	-0.34561200
H	-0.15923100	3.11238400	0.58988200
H	1.21022700	2.51705800	-0.36586000
H	-0.30170100	3.01732000	-1.16304100
H	-2.44753000	1.93659300	0.04141200
H	-2.18928800	0.98123300	-1.41742300
O	2.20866800	0.63970100	1.19691700
C	2.59557300	-0.61995800	-0.79459700
H	3.65099900	-0.50074100	-0.54053800
H	2.39644200	-0.16086200	-1.77085300
H	2.33846400	-1.67940500	-0.87441600
C	-2.47956900	-0.17506800	0.39009200
H	-2.38655500	-0.03661200	1.47332400
H	-3.52295900	-0.38324100	0.15103100

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -536.536541276

Δ G [ω B97XD/6-31G(d), SMD (THF)]: 0.133792

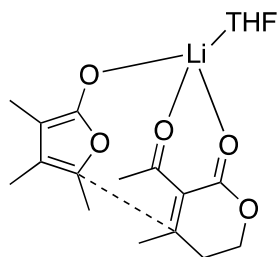


C	-1.01574300	-0.54176900	-0.02170000
O	-1.18008600	-1.73615100	-0.19392200
O	-2.02964200	0.31390500	0.14077600
C	0.33369100	0.06334600	0.05648100
C	0.65622500	1.36929300	-0.02669500
C	1.40410200	-1.00503400	0.21600500
C	2.08914200	1.82226700	0.05651400
H	2.18271300	2.59481500	0.82958400
H	2.79770400	1.02510900	0.29005700
H	2.38514000	2.28838500	-0.89150600
O	1.79178500	-1.34222300	1.31541800

C	1.94717500	-1.59279500	-1.05951400
H	2.67049500	-2.38207000	-0.84261500
H	2.42536500	-0.80156200	-1.64985800
H	1.12243700	-1.99255400	-1.65883500
C	-0.32513700	2.49807000	-0.21195400
H	0.19272200	3.38578100	-0.58766300
H	-1.13424600	2.24293300	-0.89716900
H	-0.78266300	2.76241100	0.74844200
C	-3.33982300	-0.25667200	0.06170600
H	-4.03006400	0.57481100	0.20384900
H	-3.50181600	-0.71961500	-0.91474900
H	-3.48202900	-1.00292200	0.84722600

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -537.733887520

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.152013



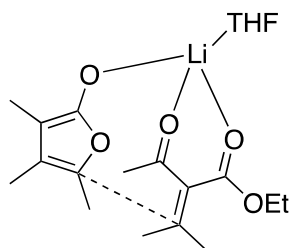
C	0.61512600	-2.07698300	0.38980300
O	-0.54424300	-2.45017500	0.56423600
O	1.36864900	-2.92812200	-0.32249600
C	1.21229800	-0.86013000	0.98053700
C	2.53798100	-0.52921200	0.65154700
C	0.34374000	-0.08687000	1.88345900
C	3.42697700	0.44698400	1.37846300
C	3.36898800	-1.59824500	-0.01925400
H	4.28278500	0.69871000	0.74484000
H	2.94482300	1.37378100	1.67065300
H	3.82773000	-0.02989100	2.28427200
H	4.20653900	-1.15703200	-0.56661000
H	3.81226000	-2.20748900	0.78295000
O	-0.89436000	-0.19241700	1.89340600
C	0.91038100	0.84739300	2.93360100
H	0.14409600	0.97007200	3.70215500
H	1.10123800	1.83407200	2.49747700
H	1.82945400	0.48218300	3.39437300
C	2.05449900	0.84932900	-1.32530500
C	3.24888800	0.78139200	-2.22039600
O	0.96486700	0.08484700	-1.71746600
C	1.57192000	1.96987000	-0.63935500
C	-0.15233200	0.59086900	-1.10948900
O	-1.24750700	-0.00498800	-1.21308800
C	0.20383200	1.79161700	-0.44428000
C	-0.77443400	2.65212800	0.28475800
H	-1.17429400	2.13857000	1.17003700
H	-0.31206200	3.58754700	0.61699400
H	-1.63184900	2.91185400	-0.34885800
C	2.38735300	3.14594000	-0.20054000
H	3.45901300	2.96774200	-0.32259800
H	2.12890900	4.03310600	-0.79176100
H	2.20592800	3.39744300	0.85080800
H	3.08465600	1.33205200	-3.15691300
H	4.12101800	1.22093100	-1.72629900

H	3.50106900	-0.24751300	-2.49289200
Li	-1.79914300	-0.97661900	0.37736100
C	-4.29353600	-1.15363300	-0.89613300
O	-3.75763400	-0.93746700	0.42279500
C	-4.14477600	0.36897800	0.90010200
C	-5.09478100	0.94080600	-0.14864700
C	-4.63193200	0.23158700	-1.42426900
H	-3.53530500	-1.67795600	-1.48396400
H	-5.18435800	-1.78894100	-0.81515600
H	-4.59882800	0.25346200	1.88785300
H	-3.23851400	0.97765000	0.99652100
H	-6.13168200	0.67425900	0.08322300
H	-5.02398800	2.02961200	-0.21166100
H	-5.39539800	0.20470500	-2.20578500
H	-3.72724900	0.70386000	-1.81887000
C	2.57142200	-2.47701500	-0.94447400
H	2.29364100	-1.95296600	-1.86167400
H	3.11993900	-3.38221900	-1.21106400

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1199.23058505

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.392854

Imaginary Frequency: -266.15



C	0.53032100	1.51568600	0.26246600
O	1.49207000	0.89317800	-0.17235400
O	0.59992500	2.84664100	0.37976700
C	-0.74252200	0.96159300	0.79646600
C	-1.96488600	1.47897400	0.31811500
C	-0.53687600	-0.09716600	1.77189400
C	-3.26408900	1.44648300	1.09038800
H	-4.10366300	1.65931300	0.42216700
H	-3.47576400	0.51337500	1.60181200
H	-3.24160500	2.24499600	1.84642600
O	0.56678300	-0.68011900	1.89042700
C	-1.58837800	-0.46664100	2.80070200
H	-1.10754500	-1.10009200	3.54910900
H	-2.40939400	-1.03179500	2.35218800
H	-2.00655100	0.41604400	3.29225200
C	-2.46466300	-0.12451400	-1.36039100
C	-3.26428400	0.55491400	-2.42674000
O	-1.14765100	-0.39069200	-1.71679300
C	-2.90514800	-1.17252800	-0.53231800
C	-0.71343600	-1.45121700	-0.97805400
O	0.47185300	-1.83915000	-1.05325000
C	-1.80328000	-1.95745300	-0.22187700
C	-1.69035500	-3.13942300	0.68335400
H	-2.61387900	-3.29795300	1.25010100
H	-1.48068500	-4.06250400	0.12781800
H	-0.87025500	-3.00453400	1.40096500
C	-4.31371200	-1.39742300	-0.08018900
H	-4.96217100	-0.55150800	-0.32277400

H	-4.73047800	-2.28679300	-0.56882000
H	-4.37217900	-1.56974500	1.00104000
H	-3.52469000	-0.14186400	-3.23557400
H	-4.19838000	0.95312900	-2.01754700
H	-2.70827400	1.38348300	-2.87376400
Li	1.57294500	-0.99957000	0.25510100
C	4.20644800	-0.39442400	1.00630900
O	3.48673000	-1.42353600	0.30367800
C	3.97719900	-1.53029800	-1.04990700
C	5.17975100	-0.59407100	-1.13951400
C	4.84973500	0.45766400	-0.07695900
H	3.48983300	0.14796200	1.62857900
H	4.95693400	-0.86575900	1.65321800
H	4.22283600	-2.57733100	-1.24591300
H	3.17166600	-1.22570400	-1.72804700
H	6.10071900	-1.12586500	-0.87709900
H	5.29695900	-0.17443900	-2.14164500
H	5.72777400	0.99875700	0.28450200
H	4.11972300	1.17594900	-0.46341500
C	-1.94636200	2.66856100	-0.62142000
H	-1.75911300	3.58517000	-0.04999100
H	-1.18046300	2.59783200	-1.39733500
H	-2.91783200	2.78538600	-1.10625200
C	1.77432300	3.47028700	-0.14208500
H	1.61206100	4.54186800	-0.02338800
H	2.65852300	3.16110200	0.42150900
H	1.91065900	3.22564800	-1.19866800

E [ω B97XD/6-311++G(d,p), SMD (THF)]: -1200.42420746

ΔG [ω B97XD/6-31G(d), SMD (THF)]: 0.407952

Imaginary Frequency: -286.95