Supporting Information

Vinylogous Addition of Siloxyfurans to Benzopyryliums: A Concise Approach to the Tetrahydroxanthone Natural Products

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I. General Information

A. Instrumentation and methods

^{1}H NMR spectra were recorded at 400 MHz at ambient temperature with $CDCl_3$ (Cambridge Isotope Laboratories, Inc.) as the solvent unless otherwise stated. ^{13}C NMR spectra were recorded at 100.0 MHz at ambient temperature with $CDCl_3$ as the solvent unless otherwise stated. Chemical shifts are reported in parts per million relative to $CDCl_3$ (^{1}H, δ 7.26; ^{13}C, δ 77.0). Data for ^{1}H NMR are reported as follows: chemical shift, integration, multiplicity (app = apparent, br = broad, par obsc = partially obscure, ovrlp = overlapping, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constants. All ^{13}C NMR spectra were recorded with complete proton decoupling. Infrared spectra were recorded on a Nicolet Nexus 670 FT-IR spectrophotometer. High-resolution mass spectra were obtained in the Boston University Chemical Instrumentation Center using a Waters Q-TOF mass spectrometer. Melting points were recorded on a Mel-temp (Laboratory Devices). Analytical thin layer chromatography was performed using 0.25 mm silica gel 60-F plates. Flash chromatography was performed using 200-400 mesh silica gel (Sorbent Technologies, Inc.). Preparative TLC was conducted with glass backed 1000 μm silica gel 60-F plates (Silicycle, Inc.) Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. All other reactions were carried out in oven-dried glassware under an argon atmosphere unless otherwise noted. The Arthur™ Suite Reaction Planner (Symyx Technologies, Inc.) was used for experimental procedure planning.

B. Reagents and solvents

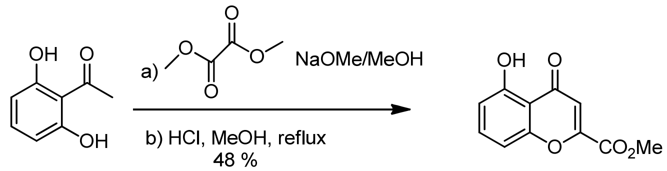
HPLC grade tetrahydrofuran, methylene chloride, diethyl ether and hexanes were purchased from Fisher and VWR and were purified and dried by passing through a PURE SOLV® solvent purification system (Innovative Technology, Inc.). Methanol was purchased from Fisher and used without further purification.

5 % Rhodium on alumina and nickel (II) chloride hexahydrate were purchased from Strem Chemicals. All other chemicals and reagents were used as received

from Sigma-Aldrich. Oxoammonium salt **43** (50 wt% on SiO_2) was prepared according to the literature procedure.[S1] CD_2Cl_2 (^1H, δ 5.32) was purchased from Cambridge Isotope Laboratories, Inc.

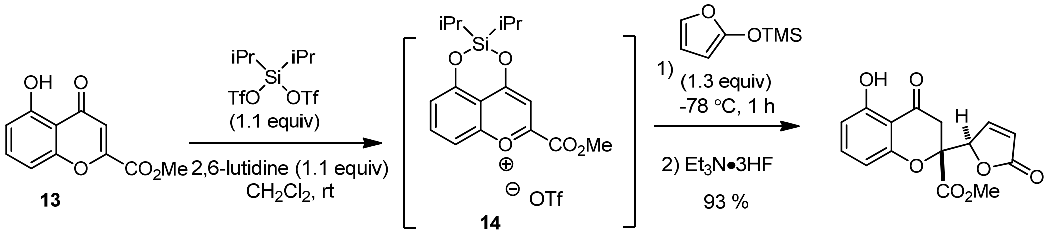
[S1] Bobbitt, J. M. *J. Org. Chem.* **1998**, *63*, 9367.

II. Experimental Procedures and Compound Characterization



13

Chromone 13: 2, 6-Dihydroxyacetophenone (1.5 g, 9.9 mmol) and dimethyl oxalate (5.8 g, 49.3 mmol, 5 equiv) were dissolved in 100 mL MeOH/MeONa solution (freshly prepared by dissolving Na (1.1 g, 49.3 mmol, 5 equiv) in 100 mL of MeOH), and the reaction was heated to reflux overnight. The reaction was cooled, solvent removed *in vacuo*, and 100 mL H_2O was added. A yellow precipitate was formed immediately upon acidification with conc. HCl. The resulting solid was collected by vacuum filtration and dissolved in 50 mL of MeOH. An additional 10 mL of conc. HCl was added again, and the solution was refluxed at 85 °C for 2 h. The aqueous phase was extracted three times with EtOAc. The combined organic phase was washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography (hexanes/EtOAc = 8: 1) which afforded **13** (1.05 g, 48 %) as a bright yellow solid. NMR, IR, and MS spectra were found to be identical with previously published data.[S2]

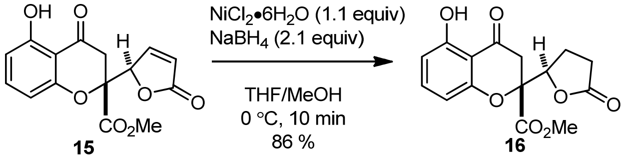


dr = 15: 1
single diastereomer
after recrystallization

15

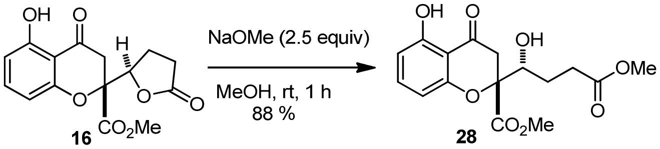
[S2] Wu, L.; Lal, J.; Simon, K. A.; Burton, E. A.; Luk, Y.-Y. *J. Am. Chem. Soc.* **2009**, *131*, 7430.

Chromone butenolide 15: To a flame-dried flask under argon containing chromone **13** (150 mg, 0.68 mmol) and 2, 6-lutidine (87 µL, 0.75 mmol) was added 10 mL of anhydrous CH_2Cl_2 followed by diisopropylsilyl *bis*(trifluoromethanesulfonate) (221 µL, 0.75 mmol) dropwise. The resulting solution was stirred at rt for 30 min during which time a dark red solution was observed. The solution was cooled to -78 °C and 2-trimethylsiloxyfuran (146 µL, 0.89 mmol) was added dropwise. The mixture was stirred at -78 °C for 1 h at which time 320 µL of $Et_3N{\cdot}3HF$ was added dropwise. The reaction was stirred for an additional 30 min and was quenched at -78 °C with 10 mL of saturated NH_4Cl solution. The mixture was extracted three times with EtOAc and the combined extracts washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was analyzed by ^1H NMR analysis to be a 15: 1 mixture of diastereomers.[S3] Compound **15** was found to decompose on silica gel. However, the gummy solid was dissolved in THF and slowly evaporated which led to crystallization from solution. Subsequently, the crystals were washed with MeOH to afford colorless crystals of chromone butenolide **15** (192 mg, 93 %) (Single diastereomer by ^1H NMR analysis). $R_f = 0.34$ (hexanes/EtOAc = 1: 1); mp 157-159 °C (THF); IR (thin film): ν_{max} 3104, 3022, 2958, 1791, 1759, 1651, 1628, 1463, 761 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 11.43 (s, 1H), 7.51 (dd, J = 5.8, 1.4 Hz, 1H), 7.38 (t, J = 8.3 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 6.45 (d, J = 8.2 Hz, 1H), 6.34 (dd, J = 5.8, 2.0 Hz, 1H), 5.38 (s, 1H), 3.78 (s, 3H), 3.26 (d, J = 17.1 Hz, 1H), 3.16 (d, J = 17.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 194.2, 170.9, 168.5, 161.8, 158.4, 150.7, 138.8, 124.2, 110.8, 107.4(1), 107.3(6), 83.0, 82.3, 53.9, 39.5; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{13}O_7$, 305.0661; found, 305.0660.



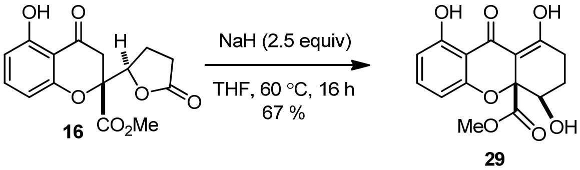
[S3] Yield was determined by ^1H NMR based on addition of 1,3,5-trimethoxybenzene as internal standard to a solution of the crude product after workup.

Chromone lactone 16: Butenolide chromone **15** (40 mg, 0.13 mmol) and nickel chloride hexahydrate (34.3 mg, 0.14 mmol, 1.1 equiv) were dissolved in THF/MeOH (3: 1, 4 mL). After cooling to 0 °C, $NaBH_4$ (10.5 mg, 0.28 mmol, 2.1 equiv) was added in one portion. After 10 min, the reaction was quenched with saturated NH_4Cl and extracted twice with 20 mL of EtOAc. The combined organic phase was washed twice with brine, dried over sodium sulfate, filtered, and concentrated. The crude product was purified by silica gel chromatography (hexanes/EtOAc = 3: 1) to afford chromone lactone **16** (34.8 mg, 86 %) as a colorless gum. $R_f = 0.31$ (hexanes/EtOAc = 1: 1); mp 131-133 °C (CH_2Cl_2); IR (thin film): ν_{max} 3024, 2965, 1792, 1757, 1652, 1629, 1464, 762 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 11.45 (s, 1H), 7.40 (t, *J* = 8.3 Hz, 1H), 6.55 (dd, *J* = 8.4, 0.9 Hz, 1H), 6.51 (dd, *J* = 8.2, 0.9 Hz, 1H), 4.78 (dd, *J* = 8.6, 4.3 Hz, 1H), 3.74 (s, 3H), 3.48 (d, *J* = 17.3 Hz, 1H), 3.10 (d, *J* = 17.3 Hz, 1H), 2.81 (m, 1H), 2.58 (m, 1H), 2.51 (m, 1H), 2.34 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 194.8, 175.9, 169.0, 161.8, 159.1, 138.8, 110.5, 107.4(5), 107.4(3), 84.6, 79.7, 53.7, 40.5, 27.8, 21.7; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{15}O_7$, 307.0818; found, 307.0814.

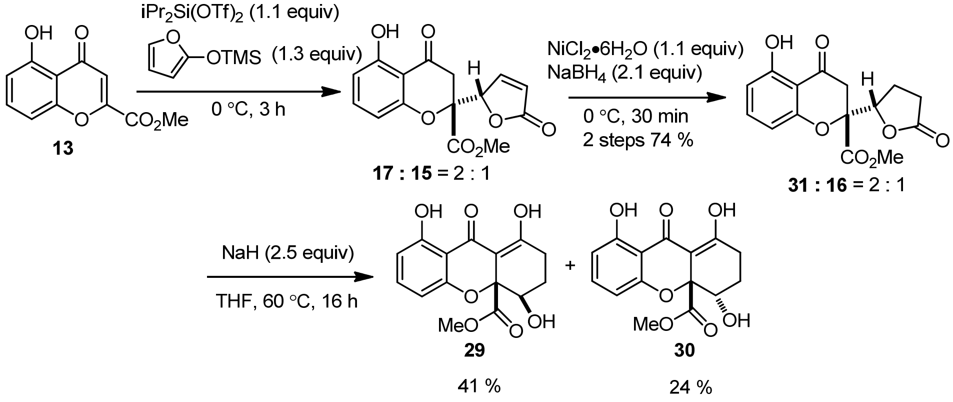


Hydroxy ester 28: Chromone lactone **16** (35.8 mg, 0.117 mmol) was dissolved in 6 mL of MeOH, and NaOMe (15.8 mg, 0.292 mmol, 2.5 equiv) was added in one portion. After stirring for one hour, the reaction was quenched with aqueous 2M HCl, and was extracted with EtOAc (10 mL×2). The combined organic phase was washed with brine, dried over sodium sulfate, filtered, and concentrated. The crude mixture was purified by silica gel chromatography (hexanes/EtOAc = 3: 1 or CH_2Cl_2/EtOAc = 20: 1) to afford hydroxy ester **28** (34.6 mg, 88 %) as a colorless oil. $R_f = 0.34$ (hexanes/EtOAc = 1: 1); 0.30 (CH_2Cl_2/EtOAc = 20: 1); IR (thin film): ν_{max} 3472, 2955, 1732, 1646, 1627, 1462, 1356, 1226, 1203, 1174, 1056, 731 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 11.54 (s, 1H), 7.39 (t, *J* = 8.3 Hz, 1H), 6.54 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.53 (dd, *J* = 8.3, 0.9 Hz, 1H), 3.94 (ddd, *J* = 10.6, 8.0, 2.5 Hz, 1H), 3.71 (s, 6H), 3.36 (d, *J* = 17.3 Hz, 1H), 3.11 (d, *J* = 17.3 Hz, 1H), 2.68 (d, *J* = 8.0 Hz, 1H), 2.60 (t, *J* = 6.6 Hz, 2H), 2.01 (m, 1H), 1.88 (m, 1H) ; ^{13}C

NMR ($CDCl_3$, 100 MHz) : δ 195.9, 174.3, 170.2, 161.8, 159.5, 138.6, 110.2, 107.6, 107.5, 86.0, 74.1, 53.2, 51.9, 40.3, 30.5, 26.0; HRMS−ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{19}O_8$, 339.1080; found, 339.1094.



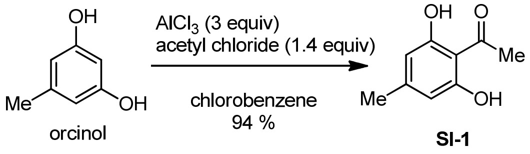
Tetrahydroxanthone 29: Chromone lactone **16** (40 mg, 0.13 mmol) and NaH (13.1 mg, 0.33 mmol, 2.5 equiv) were placed into a flask under a N_2 atmosphere. 4 mL of THF was next added into the flask which was warmed up to 60 °C and stirred for 16 h. After cooling to room temperature, the reaction was quenched with aqueous 2M HCl and extracted twice with 10 mL of EtOAc. The organic phase was combined, washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. Purification by column chromatography (CH_2Cl_2/EtOAc = 20: 1) afforded product **29** (26.9 mg, 67 %) as a white powder. R_f = 0.30 (hexanes/EtOAc = 1: 1); 0.30 (CH_2Cl_2/EtOAc = 10: 1); mp 179-181 °C (CH_2Cl_2); IR (thin film): ν_{max} 3499, 3014, 2954, 2894, 1736, 1612, 1585, 1465, 1355, 1297, 1217, 1053, 815, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 13.95 (s, 1H), 11.22 (s, 1H), 7.36 (t, *J* = 8.3 Hz, 1H), 6.55 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.54 (dd, *J* = 8.3, 0.9 Hz, 1H), 4.32 (ddd, *J* = 12.4, 5.0, 2.6 Hz, 1H), 3.70 (s, 3H), 2.85 (d, *J* = 2.7 Hz, 1H), 2.67 (m, 2H), 2.19 (m, 1H), 2.09 (m, 1H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 187.0, 178.3, 170.1, 162.0, 158.7, 138.0, 110.7, 107.9, 107.0, 101.4, 84.4, 71.9, 53.2, 27.6, 23.8; HRMS−ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{15}O_7$, 307.0818 ; found, 307.0822.



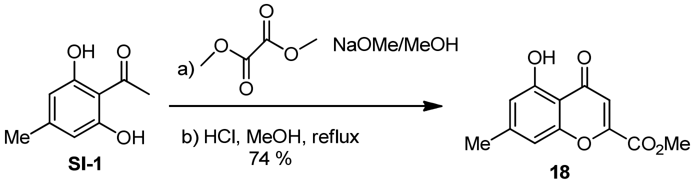
Tetrahydroxanthones 29 and 30: To a flame-dried flask under argon containing compound **13** (150 mg, 0.68 mmol) and 2,6-lutidine (87 µL, 0.75 mmol, 1.1 equiv) was added 10 mL of anhydrous CH_2Cl_2 followed by diisopropylsilyl *bis*(trifluoromethanesulfonate) (221 µL, 0.75 mmol, 1.1 equiv) dropwise. The resulting solution was stirred at rt for 30 min during which time a dark red solution was formed. The solution was cooled to 0 ^oC and 2-trimethylsiloxyfuran (146 µL, 0.89 mmol, 1.3 equiv) was added dropwise. The mixture was stirred at 0 ^oC for 3 h at which time 320 µL of $Et_3N·3HF$ was added dropwise. The reaction was stirred for 30 min and was quenched with 10 mL of saturated NH_4Cl solution at 0 ^oC. After warming to rt, the reaction mixture was extracted three times with 20 mL EtOAc. The combined extracts were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*.

The crude product was directly dissolved in a solution of THF/MeOH (3: 1, 8 mL) and nickel chloride hexahydrate (178 mg, 0.75 mmol, 1.1 equiv) was added to the solution. After cooling the reaction mixture to 0 ^oC, $NaBH_4$ (54 mg, 1.43 mmol, 2.1 equiv) was added in one portion. After stirring for 30 min, the reaction was quenched with saturated NH_4Cl, extracted with EtOAc (20 mL×2), washed with brine, and dried over sodium sulfate, filtered, and concentrated. The crude product was purified by silica gel chromatography (hexanes/EtOAc = 3: 1) to afford a mixture (154.2 mg, 74 %) of two diastereomers, **31** and **16** (2: 1 ratio by ^1H NMR analysis).

The mixture of compounds **31** and **16** (130 mg, 0.43 mmol) and NaH (42.4 mg, 1.06 mmol, 2.5 equiv) were placed into a flask under a N_2 atmosphere. 8 mL of THF was next added into the flask which was warmed up to 60 ^oC and stirred for 16 h. After cooling to room temperature, 2M HCl was used to quench the reaction which was extracted twice with 20 mL EtOAc. The organic phase was combined, washed with brine, and dried over sodium sulfate. Purification by column chromatography (hexanes/EtOAc= 3: 1) afforded tetrahydroxanthone **30** (30.6 mg, 24 %) as a white powder as well as a mixture of starting material and tetrahydroxanthone **29**. The mixture was further separated by column chromatography (CH_2Cl_2/EtOAc = 20: 1) to afford tetrahydroxanthone **29** (52.6 mg, 41 %) as a white powder. Tetrahydroxanthone **30**: R_f = 0.34 (hexanes/EtOAc = 1: 1); 0.51 (CH_2Cl_2/EtOAc = 20: 1); mp 158-159 °C; IR (thin film): ν_{max} 3505, 2953, 1737, 1613, 1583, 1465, 1360, 1236, 1059, 1021, 731 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 14.07 (s, 1H), 11.33 (s, 1H), 7.32 (t, *J* = 8.3 Hz, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 6.49 (d, *J* = 8.2 Hz, 1H), 4.33 (d, *J* = 1.4 Hz, 1H), 3.68 (s, 3H), 2.83 (ddd, *J* =19.2, 11.3, 7.2 Hz, 1H), 2.75 (s, 1H), 2.40 (dd, *J* = 19.3, 6.8 Hz, 1H), 2.14 (m, 1H), 1.95 (m, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) : δ 187.3, 179.8, 171.1, 162.0, 157.7, 137.6, 111.2, 107.8, 107.0, 100.3, 83.8, 66.9, 53.4, 24.4, 23.0; HRMS−ESI (m/z): [M+H]$^+$ calcd for $C_{15}H_{15}O_7$, 307.0818; found, 307.0805.



Acetophenone SI-1: Aluminum trichloride (32.2 g, 0.242 mol, 3 equiv) and orcinol (10.0 g, 81 mmol) were dissolved in 100 mL of chlorobenzene. Acetyl chloride (0.80 mL, 0.113 mol, 1.4 equiv) was added dropwise to the solution at 40 °C and stirred for 30 min. Subsequently, the temperature was raised to 70 °C and the reaction mixture was stirred for an additional hour. The reaction was cooled to room temperature, and 35 % aqueous solution was added until pH<1. The aqueous phase was extracted with EtOAc (150 mL×2) and the combined organic phase washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The final product (12.6 g, 94 %) was obtained by recrystallization from toluene. NMR, IR, and MS spectra were found to be identical with previously published data.[S4,S5]



Chromone 18: 4-Methyl-2,6-dihydroxyacetophenone **SI-1** (500 mg, 3 mmol) and dimethyl oxalate (1.78 g, 15 mmol, 5 equiv) were dissolved in 50 mL of MeOH/NaOMe

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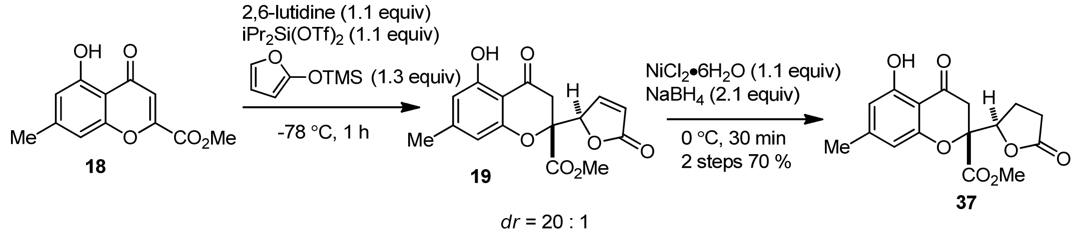
[S4] Tsujihara, K.; Hongu, M.; Saito, K.; Kawanishi, H.; Kuriyama, K.; Matsumoto, M.; Oku, A.; Ueta, K.; Tsuda, M.; Saito, A. *J. Med. Chem.* **1999**, *42*, 5311.

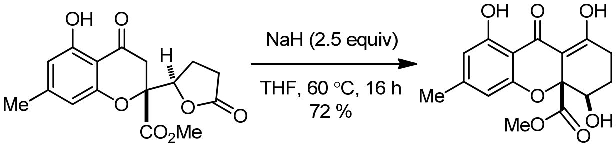
[S5] Kuraoka, S.; Matuyama, K.; Ishida, M. *Jpn. Kokai Tokkyo Koho* **2004**, **15** pp. JP 2004-091426.

solution (freshly prepared by dissolving Na metal (277 mg, 12 mmol, 4 equiv) in 50 mL of MeOH), and the reaction was heated to reflux overnight. The reaction was cooled, solvent removed *in vacuo*, and 100 mL H_2O was added. A yellow precipitate was formed immediately upon acidification with conc. HCl. The resulting solid was collected by vacuum filtration and dissolved in 50 mL of MeOH. An additional 5 mL conc. HCl was added and the solution was refluxed at 85 °C for 2 h. The aqueous phase was extracted with EtOAc (50 mL×2) and combined organic phase washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography (hexanes/EtOAc = 8: 1) to afford chromone **18** (520 mg, 76 %) as a bright yellow solid. R_f= 0.31 (hexanes/EtOAc = 4: 1); mp 167-168 °C (EtOAc); IR (thin film): ν_{max} 3091, 3026, 2954, 1778, 1742, 1658, 1627, 1441, 1251, 1213, 762 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 12.27 (s, 1H), 7.52 (s, 1H), 7.11 (s, 1H), 6.93 (s, 1H), 4.26 (s, 3H), 2.68(s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 183.1, 160.5, 160.3, 156.0, 152.5, 148.7, 113.6, 112.9, 109.8, 108.1, 53.4, 22.5; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{12}H_{11}O_5$, 235.0606; found, 235.0615.



Chromone lactone 37: To a flame-dried flask under argon containing chromone **18** (150 mg, 0.64 mmol) and 2,6-lutidine (82 μL, 0.70 mmol, 1.1 equiv) was added 10 mL of anhydrous CH_2Cl_2 followed by diisopropylsilyl *bis*(trifluoromethanesulfonate) (208 μL, 0.70 mmol, 1.1 equiv) dropwise. The resulting solution was stirred at rt for 30 min during which time a dark red solution was formed. The solution mixture was cooled to -78 ^oC and 2-trimethylsiloxyfuran (137 μL, 0.83 mmol, 1.3 equiv) was added dropwise. The mixture was stirred at -78 ^oC for 1 h at which time 320 μL of $Et_3N{\cdot}3HF$ was added dropwise. The reaction was stirred for an additional 30 min and was quenched with 10 mL of saturated NH_4Cl solution at -78 ^oC and warmed to room temperature. The mixture was extracted three times with 20 mL EtOAc and the combined extracts were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*.

The crude product was directly dissolved in THF/MeOH (3: 1, 8 mL) and nickel chloride hexahydrate (168 mg, 0.70 mmol, 1.1 equiv) was added to the solution. After cooling the solution to 0 ^{o}C, $NaBH_4$ (51 mg, 1.35 mmol, 2.1 equiv) was added in one portion. After stirring for 30 min, the reaction was quenched with saturated NH_4Cl, extracted with EtOAc (20 mL×2), washed with brine, dried over sodium sulfate, filtered, and concentrated. The crude product was purified by silica gel chromatography (hexanes/EtOAc = 3: 1) to afford chromone lactone **37** (143 mg, 70 %) as a colorless gum. R_f= 0.42 (hexanes/EtOAc = 2: 3); 0.64 (CH_2Cl_2/EtOAc = 20: 1); mp 176-178 °C (CH_2Cl_2); IR (thin film): ν_{max} 2958, 1785, 1754, 1648, 1572, 1456, 1367, 1202, 1164, 838, 733 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 11.39 (s, 1H), 6.34 (s, 2H), 4.75 (dd, *J* = 8.5, 4.2 Hz, 1H), 3.72 (s, 3H), 3.42 (d, *J* = 17.2 Hz, 1H), 3.04 (d, *J* = 17.3 Hz, 1H), 2.78 (m, 1H), 2.55 (m, 1H), 2.47 (m, 1H), 2.32 (m, 1H), 2.28 (s, 3H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 194.0, 176.0, 169.0, 161.6, 158.8, 151.1, 110.9, 108.2, 105.4, 84.5, 79.6, 53.6, 40.2, 27.7, 22.5, 21.6; HRMS–ESI (m/z): [M+H]$^{+}$ calcd for $C_{16}H_{17}O_7$, 321.0974; found, 321.0974.

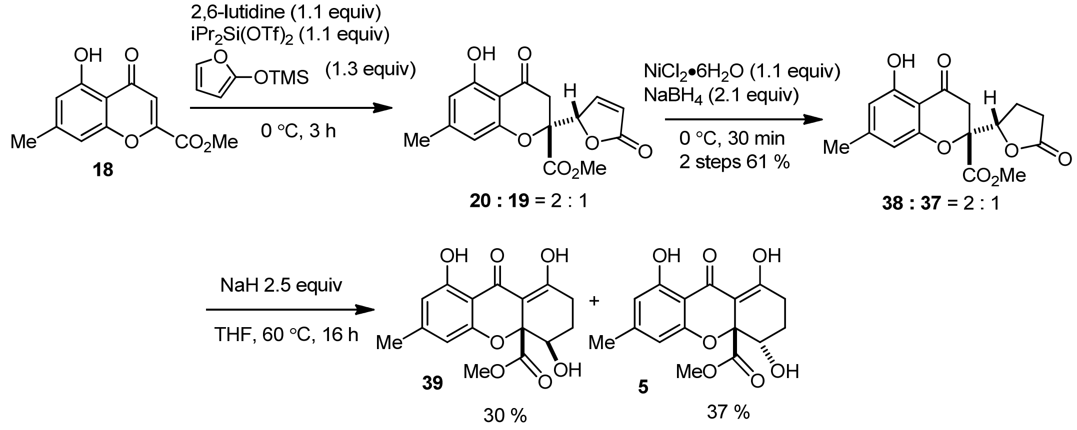


37

39

***Epi*-blennolide C 39:** Chromone lactone **37** (30 mg, 0.09 mmol) and NaH (9.4 mg, 0.23 mmol, 2.5 equiv) were placed into a flask under a N_2 atmosphere. 4 mL of THF was next added to the flask which was warmed up to 60 ^{o}C and stirred for 16 h. After cooling to room temperature, 2M HCl aqueous solution was used to quench the reaction which was further extracted twice with 10 mL of EtOAc. The organic phase was combined, washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. Purification by silica gel column chromatography (CH_2Cl_2/EtOAc = 20: 1) afforded tetrahydroxanthone **39** (21.7 mg, 72 %) as a white powder. R_f = 0.41 (hexanes/EtOAc = 2: 3); 0.30

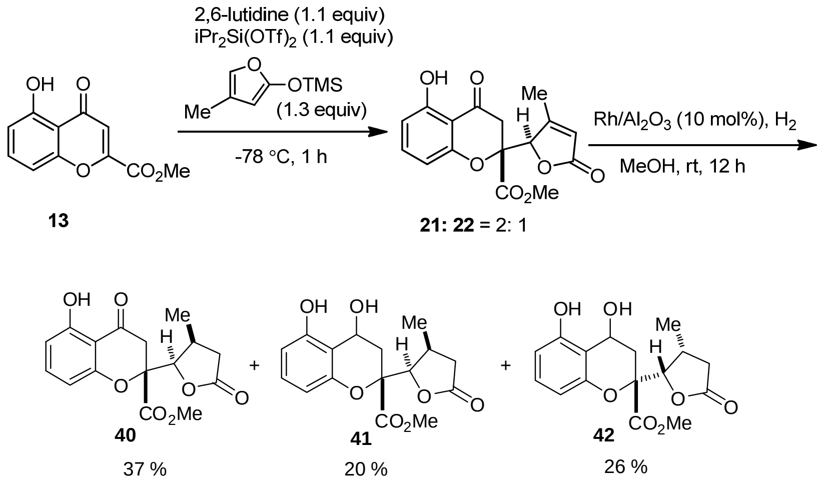
(CH_2Cl_2/EtOAc = 20: 1); mp 212-213 °C (CH_2Cl_2); IR (thin film): ν_{max} 3475, 2958, 1719, 1617, 1585, 1461, 1356, 1265, 1201, 1068, 860, 835 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 13.91 (s, 1H), 11.17 (s, 1H), 6.40 (d, J = 0.6 Hz, 1H), 6.36 (d, J = 0.7 Hz, 1H), 4.31 (dd, J = 12.2, 4.5 Hz, 1H), 3.71 (s, 3H), 2.79 (s, 1H), 2.66 (m, 2H), 2.30 (s, 3H), 2.19 (m, 1H), 2.09 (m, 1H) ; ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 186.6, 177.6, 170.1, 161.9, 158.5, 150.4, 111.3, 108.7, 104.9, 101.2, 84.4, 71.9, 53.2, 27.5, 23.8, 22.6; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{17}O_7$, 321.0974 ; found, 321.0959.



Blennolide C (5) and *epi*-blennolide C 39: To a flame-dried flask under argon containing chromone **18** (150 mg, 0.64 mmol) and 2,6-lutidine (82 μL, 0.70 mmol, 1.1 equiv) was added 10 mL of anhydrous CH_2Cl_2 followed by diisopropylsilyl *bis*(trifluoromethanesulfonate) (208 μL, 0.70 mmol, 1.1 equiv) dropwise. The resulting solution was stirred at rt for 30 min during which time a dark red solution was formed. The solution was cooled to 0 °C and 2-trimethylsiloxyfuran (137 μL, 0.83 mmol, 1.3 equiv) was added dropwise. The reaction mixture was stirred at 0 °C for 3 h at which time 320 μL of $Et_3N{\cdot}3HF$ was added dropwise. The reaction was stirred for an additional 30 min and was quenched at 0 °C with 10 mL of saturated NH_4Cl solution. After warming to rt, the reaction mixture was extracted three times with 20 mL of EtOAc. The combined extracts were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*.

The crude product was directly dissolved in THF/MeOH (3: 1, 8 mL), and nickel chloride hexahydrate (168 mg, 0.70 mmol, 1.1 equiv) was added to the solution. After cooling the reaction mixture to 0 ^oC, $NaBH_4$ (51 mg, 1.35 mmol, 2.1 equiv) was added in one portion. After stirring for 30 min, the reaction was quenched with saturated NH_4Cl, extracted with EtOAc (20 mL×2), washed with brine, dried over sodium sulfate, filtered, and concentrated. The crude product was purified by silica gel chromatography (hexanes/EtOAc = 3: 1) afford a mixture (124.2 mg, 61 %) of two diastereomers **37** and **38** (2: 1 ratio by ^1H NMR analysis).

The mixture of lactone compounds **37** and **38** (30 mg, 0.09 mmol) and NaH (9.37 mg, 0.23 mmol, 2.5 equiv) were placed into a flask under a N_2 atmosphere. 4 mL of THF was also added to the flask which was warmed up to 60 ^oC and stirred for 16 h. After cooling to room temperature, 2M HCl was used to quench the reaction which was extracted twice with 10 mL of EtOAc. The organic phase was combined, washed with brine, dried over sodium sulfate, filtered, and concentrated. Purification by column chromatography (hexanes/EtOAc = 3: 1) afforded blennolide C (**5**) (11.1 mg, 37 %) as a white powder as well as a mixture of starting material and *epi*-blennolide C **39**. The latter mixture was further separated by column chromatography (CH_2Cl_2/EtOAc= 20: 1) to afford *epi*-blennolide C **39** (9.0 mg, 30 %) as a white powder. Blennolide C (**5**): R_f = 0.51 (hexanes/EtOAc = 2: 3); 0.42 (CH_2Cl_2/EtOAc = 20: 1); mp 182-184 °C (CH_2Cl_2); IR (thin film): ν_{max} 3497, 2953, 1737, 1613, 1579, 1462, 1364, 1237, 1203, 879, 836, 730 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 14.03 (s, 1H), 11.26 (s, 1H), 6.36 (s, 1H), 6.33 (s, 1H), 4.31 (m, 1H), 3.69 (s, 3H), 2.82 (ddd, *J* = 19.2, 11.6, 7.2 Hz, 1H), 2.74 (s, 1H), 2.38 (ddd, *J* = 19.2, 6.8, 1.0 Hz, 1H), 2.28 (s, 3H), 2.14 (m, 1H), 1.95 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 186.9, 179.1, 171.2, 161.8, 157.5, 149.9, 111.7, 108.7, 104.8, 100.1, 83.8, 66.9, 53.4, 24.3, 23.0, 22.4; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{17}O_7$, 321.0974; found, 321.0966.



13

21: **22** = 2: 1

40 37 %

41 20 %

42 26 %

Chromone Lactone 40: To a flame-dried flask under argon containing chromone lactone **13** (150 mg, 0.68 mmol) and 2,6-lutidine (87 μL, 0.75 mmol, 1.1 equiv) was added 10 mL of anhydrous CH_2Cl_2 followed by diisopropylsilyl *bis*(trifluoromethanesulfonate) (221 μL, 0.75 mmol, 1.1 equiv) dropwise. The resulting solution was stirred at rt for 30 min during which time a dark red solution was formed. The solution was cooled to -78 ^{o}C and 4-methyl-2-trimethylsiloxyfuran (150.8 mg, 0.89 mmol, 1.3 equiv) was added dropwise. The mixture was stirred at -78 ^{o}C for 1 h at which time 320 of μL $Et_3N{\cdot}3HF$ was added dropwise. The reaction was stirred for an additional 30 min, was quenched with 10 mL of saturated NH_4Cl solution at -78 ^{o}C, and warmed to room temperature. The mixture was extracted 3× 20 mL EtOAc and the combined extracts were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*.

The crude product was directly dissolved in 8 mL of MeOH. Rh/Al_2O_3 (5 wt% on alumina) (10 mol %, 140 mg, 0.068 mmol, 0.1 equiv) was added to the solution. Subsequently, atmosphere was changed to hydrogen and the reaction was stirred at rt for 12 h. The reaction vessel was purged with nitrogen, filtered through Celite to remove the catalyst, and the solvent removed *in vacuo*.[S6] Purification by silica gel column chromatography (hexanes/EtOAc = 3: 1) afforded chromone lactone **40** (81.6 mg, 37 %) as a colorless gum. R_f = 0.30 (hexanes/EtOAc = 1: 1); 0.62 (CH_2Cl_2/EtOAc = 10: 1); mp 147-149 °C (CH_2Cl_2/MeOH = 1: 1); IR (thin film): ν_{max} 3624, 2956, 1790, 1757, 1647,

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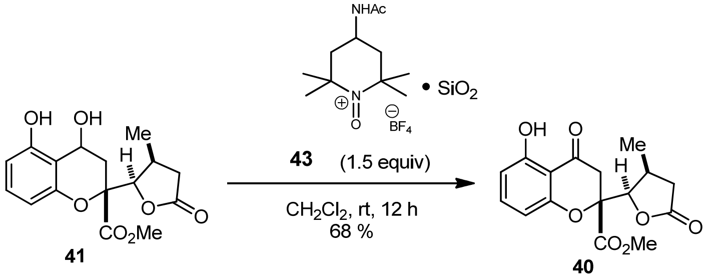
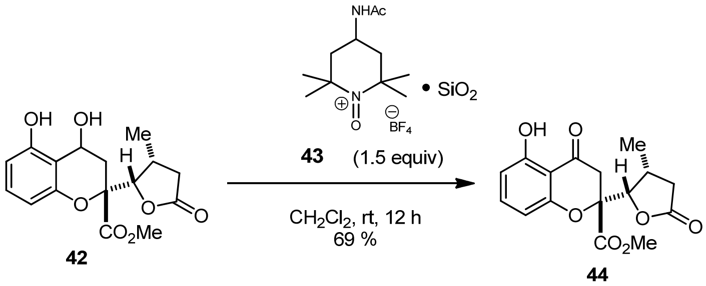
[S6] MeOH was immediately removed after filtration as chromone lactone **40** was found to be prone to ring-opening with MeOH after prolonged time.

1627, 1461, 1227, 1160, 1017, 759 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz): δ 11.38 (s, 1H), 7.40 (t, *J* = 8.3 Hz, 1H), 6.54 (dd, *J* = 8.4, 0.9 Hz, 1H), 6.46 (dd, *J* = 8.2, 0.9 Hz, 1H), 4.84 (d, *J* = 7.9 Hz, 1H), 3.73 (s, 3H), 3.65 (d, *J* = 17.4 Hz, 1H), 2.98 (m, 1H), 2.89 (d, *J* = 17.4 Hz, 1H), 2.60 (dd, *J* = 11.0, 2.0 Hz, 2H), 1.25 (d, *J* = 7.1 Hz, 3H) ; ^{13}C NMR (CDCl$_3$, 100 MHz) : δ 194.5, 175.5, 169.6, 161.7, 159.3, 138.7, 110.3, 107.3, 107.1, 84.5, 82.0, 53.3, 41.4, 35.8, 33.5, 13.4; HRMS–ESI (m/z): [M+H]$^+$ calcd for $C_{16}H_{17}O_7$, 321.0974 ; found, 321.0989. Further purification using silica gel chromatography (hexane/EtOAc = 1: 1) afforded the overreduced compounds **41** (44 mg, 20 %) and **42** (56.8 mg, 26 %).



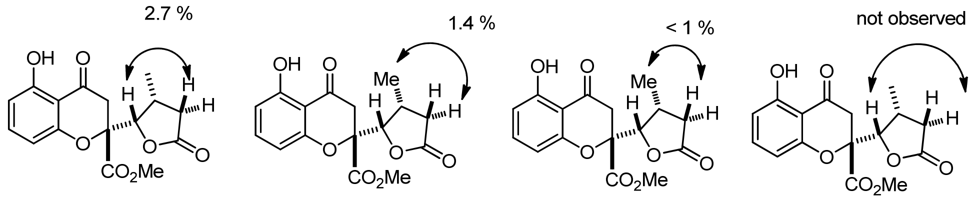
Chromone Lactone 40: Compound **41** (44 mg, 0.14 mmol, 1.0 equiv) was added into flame-dried flask with 3 mL CH$_2$Cl$_2$ which was followed by addition of oxoammonium salt **43** (50 wt% on SiO$_2$, 123 mg, 0.21 mmol, 1.5 equiv). The reaction was stirred for 12 h, filtered, and concentrated. Purification by column chromatography (hexanes/EtOAc = 3: 1) afforded chromone lactone **40** (29.8 mg, 68 %) as a colorless gum.



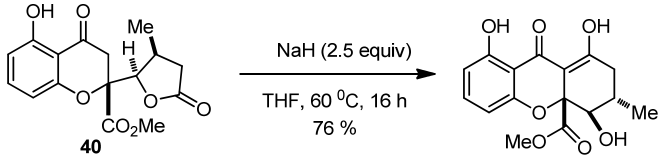
Chromone Lactone 44: Compound **42** (56.8 mg, 0.18 mmol, 1.0 equiv) was added into flame-dried flask with 3 mL CH$_2$Cl$_2$ which was followed by addition of oxoammonium salt **43** (50 wt% on SiO$_2$, 159 mg, 0.27 mmol, 1.5 equiv). The reaction was stirred for 12 h, filtered, and concentrated. Purification by column chromatography (hexanes/EtOAc =

3: 1) afforded chromone lactone **44** (38.8 mg, 69 %) as a colorless gum. R$_f$ = 0.30 (hexanes/EtOAc = 1: 1); mp 173-174 °C (CH_2Cl_2); IR (thin film): ν_{max} 2957, 1788, 1760, 1648, 1628, 1463, 1229, 1160, 1056, 732 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 11.44 (s, 1H), 7.41 (t, *J* = 8.3 Hz, 1H), 6.55 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.54 (dd, *J* = 8.2, 0.9 Hz, 1H), 4.79 (d, *J* = 6.8 Hz, 1H), 3.73 (s, 3H), 3.25 (d, *J* = 17.3 Hz, 1H), 3.18 (d, *J* = 17.3 Hz, 1H), 2.96 (m, 1H), 2.69 (dd, *J* = 17.3, 8.3 Hz, 1H), 2.46 (dd, *J* = 17.3, 7.9 Hz, 1H), 1.32 (d, *J* = 7.2 Hz, 3H) ; ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 193.9, 174.8, 169.0, 161.9, 158.8, 139.0, 110.5, 107.5(9), 107.5(7), 84.3, 82.7, 53.6, 39.8, 36.7, 33.4, 14.8; HRMS−ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{17}O_7$, 321.0974 ; found, 321.0981.

Selected NOE's for chromone lactone **44**:



(See S30 for X-ray crystal structure analysis for **44**)

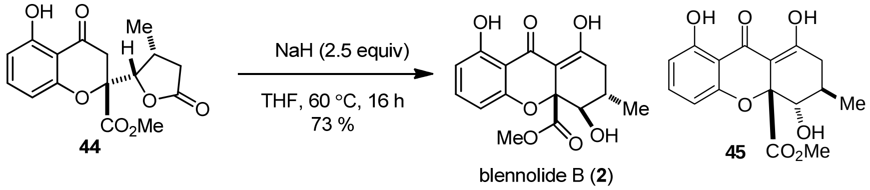


40

blennolide B (**2**)

Blennolide B (2): Chromone lactone **40** (59 mg, 0.18 mmol, 1.0 equiv) and NaH (18.4 mg, 0.46 mmol, 2.5 equiv) were placed into a flask under a N_2 atmosphere. 5 mL of THF was next added into the flask which was warmed up to 60 °C and stirred for 16 h. After cooling to rt, 2M aqueous HCl solution was used to quench the reaction which was further extracted twice with 10 mL of EtOAc. The organic phase was combined, washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. Purification by column chromatography (CH_2Cl_2/EtOAc = 20: 1) afforded blennolide B (**2**) (44.6 mg, 76 %) as a pale yellow solid. R$_f$ = 0.35 (CH_2Cl_2/EtOAc = 10: 1); mp 192-193 °C (CH_2Cl_2);

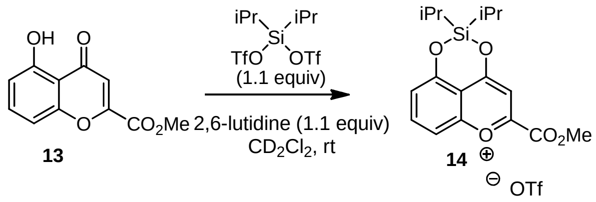
IR (thin film): ν_{max} 3471, 3024, 2958, 1740, 1619, 1584, 1465, 1222, 1058, 764 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz): δ 13.80 (s, 1H), 11.23 (s, 1H), 7.36 (t, *J* = 8.3 Hz, 1H), 6.55 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.53 (dd, *J* = 8.2, 0.8 Hz, 1H), 3.92 (dd, *J* = 11.2, 2.1 Hz, 1H), 3.69 (s, 3H), 2.77 (d, *J* = 2.4 Hz, 1H), 2.73 (dd, *J* = 19.1, 6.2 Hz, 1H), 2.42 (m, 1H), 2.30 (dd, *J* = 19.1, 6.2 Hz, 1H), 1.17 (d, *J* = 6.5 Hz, 3H) ; ^{13}C NMR (CDCl$_3$, 125 MHz) : δ 187.0, 177.5, 170.3, 162.0, 158.8, 138.0, 110.7, 107.9, 107.0, 101.6, 84.7, 77.0, 53.2, 36.2, 29.2, 18.0; HRMS–ESI (m/z): [M+H]$^+$ calcd for $C_{16}H_{17}O_7$, 321.0974 ; found, 321.0971.



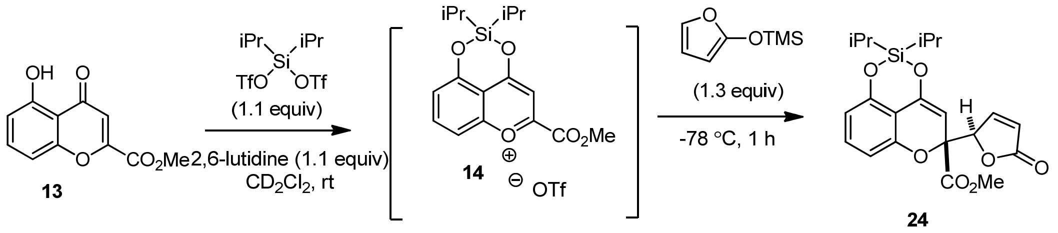
Blennolide B (**2**): Chromone lactone **44** (20.5 mg, 0.064 mmol, 1.0 equiv) and NaH (6.4 mg, 0.16 mmol, 2.5 equiv) were placed into a flask under a N_2 atmosphere. 2 mL of THF was also added into the flask which was warmed up to 60 ^{o}C and stirred for 16 h. After cooling to rt, 2M HCl aqueous solution was used to quench the reaction which was further extracted twice with 10 mL of EtOAc. The organic phase was combined, washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. Purification by column chromatography (CH_2Cl_2/EtOAc = 20: 1) afford blennolide B **2** (14.9 mg, 73 %) as a pale yellow solid. The ratio of blennolide B (**2**) to **44** was found to be 20: 1 by ^{1}H NMR analysis using this procedure.

III. Mechanistic Studies

A) Intermediate characterization:



Benzopyrylium 14: To a flame-dried flask under argon containing chromone **13** (20 mg, 0.09 mmol) and 2, 6-lutidine (12 µL, 0.10 mmol, 1.1 equiv) was added 1 mL of CD_2Cl_2 followed by diisopropylsilyl *bis*(trifluoromethanesulfonate) (30 µL, 0.10 mmol, 1.1 equiv) dropwise. The resulting solution was stirred at rt for 30 min during which time a dark red solution was formed. The solution was directly analyzed by ^{1}H NMR. HRMS–ESI (m/z): $[M]^+$ calcd for $C_{17}H_{21}O_5Si$, 333.1158; found, 333.1167.



Butenolides 24/27: To a flame-dried flask under argon containing chromone **13** (20 mg, 0.09 mmol) and 2, 6-lutidine (12 µL, 0.10 mmol, 1.1 equiv) was added 1 mL of CD_2Cl_2 followed by diisopropylsilyl *bis*(trifluoromethanesulfonate) (30 µL, 0.10 mmol, 1.1 equiv) dropwise. The resulting solution was stirred at rt for 30 min during which time a dark red solution was formed. The solution was cooled to -78 ^{o}C and 2-trimethylsiloxy furan (20 µL, 0.11 mmol, 1.3 equiv) was added dropwise. The mixture was stirred at -78 ^{o}C for 1 h and was directly analyzed by ^{1}H NMR. HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{21}H_{25}O_7Si$, 416.1370; found, 416.1382.

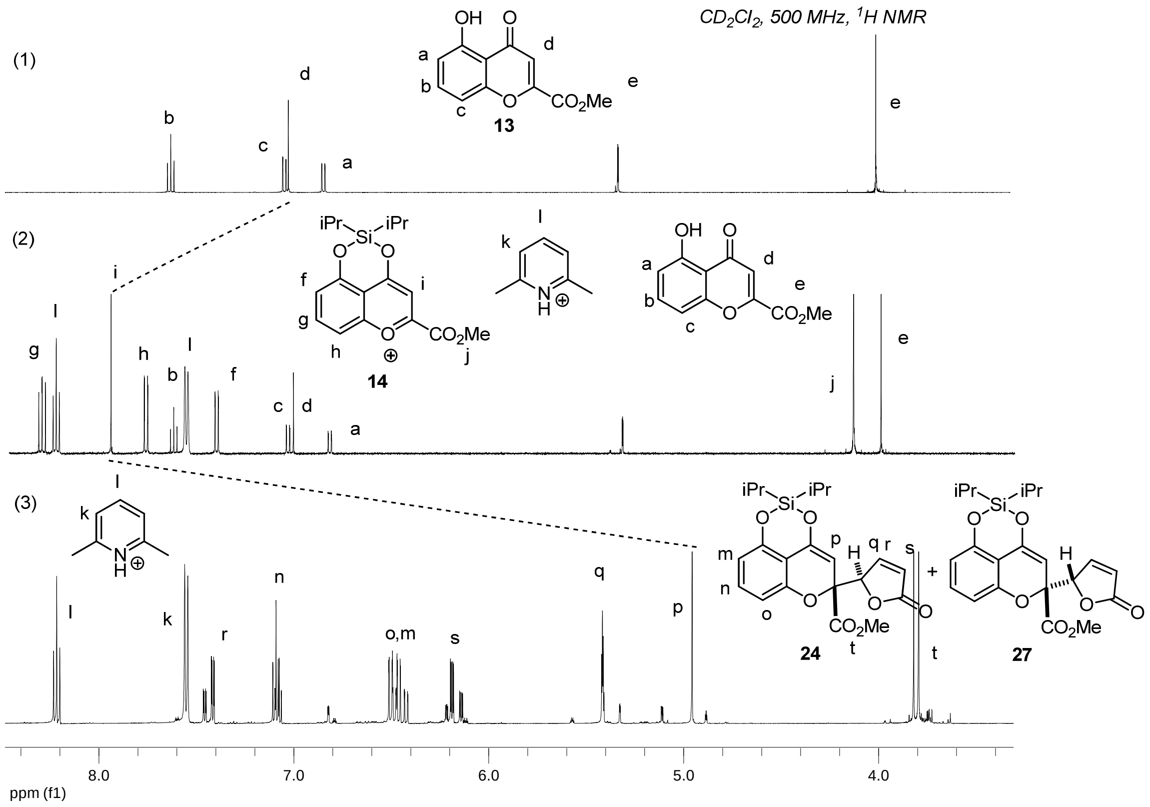


Figure SI-1. ^{1}H NMR spectra comparison of starting material and two intermediates.[S7]

From Figure SI-1 (2), we can clearly observe that H_i is shifted downfield in comparison with the chromone starting material (**13**) which supports benzopyrylium formation.[S8] After 2-trimethylsiloxyfuran was added to a solution of benzopyrylium (**14**), aromatic proton H_i shifted upfield to an alkene proton H_p. In spectrum SI-1 (3) which was taken at rt, two diastereomers (*dr* = 3: 2) were observed. This ratio was found to be lower than conditions performed at -78 °C (*dr* = 15: 1).

[S7] Protons f and h were not assigned.

[S8] Lee, Y.-G.; Ishimaru, K.; Iwasaki, H.; Ohkata, K.; Akib, K. *J. Org. Chem.* **1991**, *56*, 2058.

B) Epimerization Studies:

Following the procedure for **24**, the crude solution was directly measured by ^{1}H NMR analysis at rt and at 10 min intervals in which case epimerization was observed.

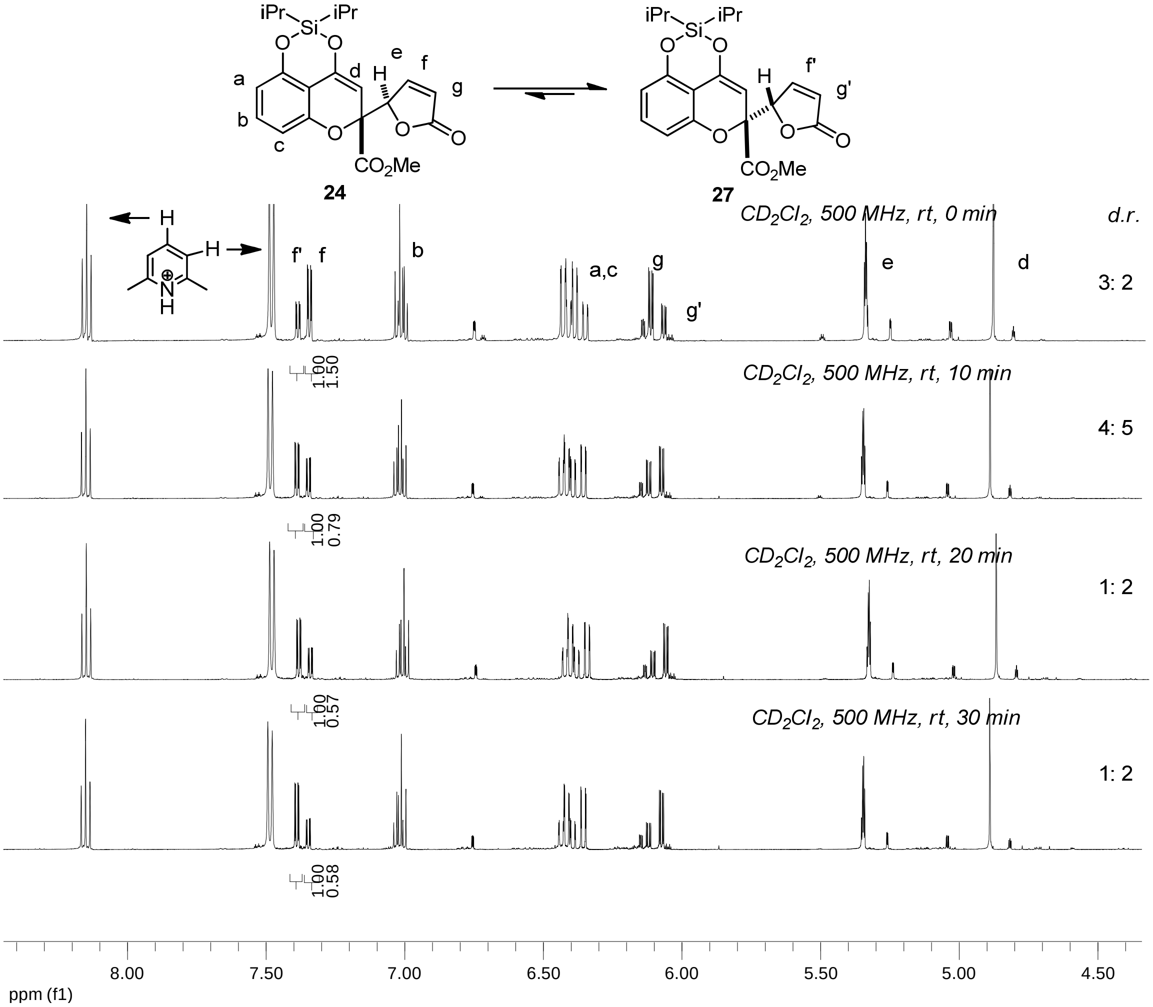
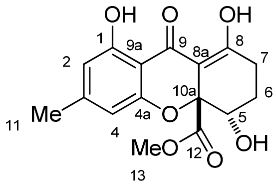


Figure SI-2. Epimerization observed by ^{1}H NMR.

IV. NMR Data Comparisons for the Blennolides

A) ^{1}H NMR spectrum of synthetic blennolide C in comparison with literature data:



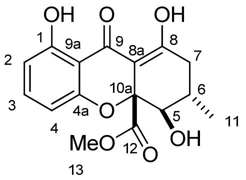
Position	δ ($J_{H\text{-}H}$ in Hz)		
	Natural Product Isolation (500 MHz, $CDCl_3$)[S9]	Synthetic (Nicolaou) (600 MHz, $CDCl_3$)[S10]	Synthetic (this work) (400 MHz, $CDCl_3$)
2	6.38 (s, 1H)	6.38 (s, 1H)	6.36 (s, 1H)
4	6.35 (d, J = 0.4, 1H)	6.35 (s, 1H)	6.33 (s, 1H)
5	4.31 (br s, 1H)	4.31 (dd, J = 3.7, 1.7, 1H)	4.31 (m, 1H)
6α	2.14 (m, 1H)	2.15 (ddd, J = 14.7, 6.6, 4.4, 1H)	2.14 (m, 1H)
6β	1.95 (m, 1H)	1.99-1.91(m, 1H)	1.95 (m, 1H)
7α	2.82 (ddd, J = 19.2, 11.7, 7.2, 1H)	2.87-2.77 (m, 1H)	2.82 (ddd, J =19.2, 11.6, 7.2, 1H)
7β	2.38 (dd, J = 19.2, 6.2, 1H)	2.39 (dd, J = 19.1, 6.8, 1H)	2.38 (ddd, J = 19.2, 6.8, 1.0, 1H)
11	2.29 (d, J = 0.4, 3H)	--	2.28 (s, 3H)
13	3.70 (s, 3H)	3.70 (s, 3H)	3.69 (s, 3H)
1-OH	11.27 (s, 1H)	11.28 (s, 1H)	11.26 (s, 1H)
5-OH	2.64 (d, J = 1.1, 1H)	2.66 (s, 1H)	2.74 (s, 1H)*
8-OH	14.03 (s, 1H)	14.04 (s, 1H)	14.03 (s, 1H)

*The chemical shift of the 5-OH peak was found to depend on concentration.

[S9] Zhang, W.; Krohn, K.; Ullah, Z.; Flörke, U.; Pescitelli, G.; Di Bari, L.; Antus, S.; Kurtán, T.; Rheinheimer, J.; Draeger, S.; Schulz, B. *Chem. Eur. J.* **2008**, *14*, 4913.

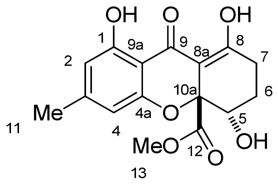
[S10] Nicolaou, K. C.; Li, A. *Angew. Chem. Int. Ed.* **2008**, *47*, 6579.

B) ^{1}H NMR spectrum of synthetic blennolide B in comparison with literature data:



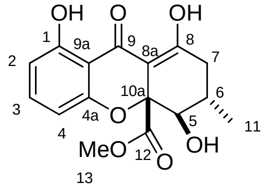
Position	δ ($J_{H\text{-}H}$ in Hz)	
	Natural Product Isolation (500 MHz, $CDCl_3$)[S9]	Synthetic (500 MHz, $CDCl_3$)
2	6.53 (dd, *J* = 8.3, 0.8, 1H)	6.53 (dd, *J* = 8.2, 0.8, 1H)
3	7.36 (t, *J* = 8.3, 1H)	7.36 (t, *J* = 8.3, 1H)
4	6.55 (dd, *J* = 8.2, 0.8, 1H)	6.55 (dd, *J* = 8.4, 0.8, 1H)
5	3.92 (dd, *J* = 11.2, 2.6, 1H)	3.92 (dd, *J* = 11.2, 2.1, 1H)
6	2.41 (m, 1H)	2.42 (m, 1H)
7α	2.30 (dd, *J* = 19.1, 10.6, 1H)	2.30 (dd, *J* = 19.1, 10.7, 1H)
7β	2.74 (dd, *J* =19.1, 6.2, 1H)	2.73 (dd, *J* = 19.1, 6.2, 1H)
11	1.17 (d, *J* = 6.5, 3H)	1.17 (d, *J* = 6.5, 3H)
13	3.69 (s, 3H)	3.69 (s, 1H)
1-OH	11.22 (s, 1H)	11.23 (s, 1H)
5-OH	--	2.77 (d, *J* = 2.4, 1H)
8-OH	13.80 (s, 1H)	13.80 (s, 1H)

C) ^{13}C NMR spectrum of synthetic blennolide C in comparison with literature data:



Position	δ		
	Natural Product Isolation (125 MHz, CDCl$_3$)[S9]	Synthetic (Nicolaou) (151 MHz, CDCl$_3$)[S10]	Synthetic (this work) (125 MHz, CDCl$_3$)
1	161.9	161.84	161.8
2	111.7	111.7	111.7
3	149.9	149.92	149.9
4	108.7	108.70	108.7
4a	157.6	157.55	157.5
5	67.0	66.95	66.9
6	23.1	23.02	23.0
7	24.3	24.32	24.3
8	179.1	179.07	179.1
8a	100.1	100.10	100.1
9	187.0	186.94	186.9
9a	104.9	104.86	104.8
10a	83.9	83.81	83.8
11	22.5	22.48	22.4
12	171.2	171.20	171.2
13	53.4	53.42	53.4

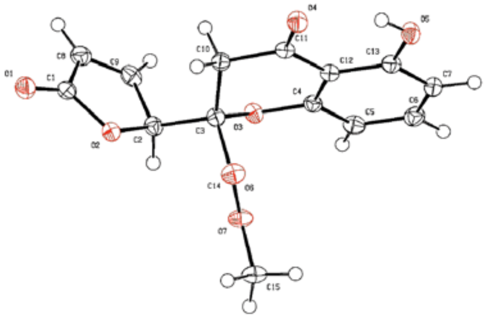
D) ^{13}C NMR spectrum of synthetic blennolide B in comparison with literature data:



Position	δ	
	Natural Product Isolation (125 MHz, $CDCl_3$)[S9]	Synthetic (125 MHz, $CDCl_3$)
1	162.1	162.0
2	110.7	110.7
3	138.0	138.0
4	107.9	107.9
4a	158.8	158.8
5	77.0	77.0
6	29.3	29.2
7	36.3	36.2
8	177.5	177.5
8a	101.7	101.6
9	187.1	187.0
9a	107.2	107.0
10a	84.7	84.7
11	18.0	18.0
12	170.3	170.3
13	53.1	53.2

V. X-ray Crystallographic Data

X-ray crystallographic data for compound **15**:



Crystals of compound **15** suitable for X-ray analysis were obtained by slow evaporation from THF. Crystallographic data have been deposited with the Cambridge Cystallograhic Data Centre (CCDC# 794127). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Table SI-1. Crystal data and structure refinement for **15**

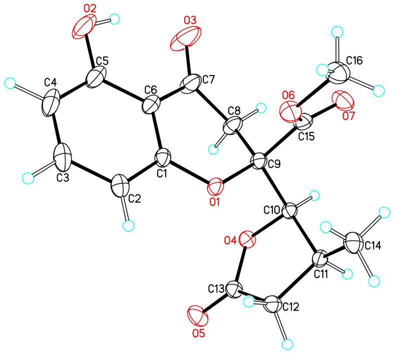
Identification code	Compound **15**	
Empirical formula	C15 H12 O7	
Formula weight	304.25	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P$\bar{1}$	
Unit cell dimensions	a = 7.8769(3) Å	α= 70.325(1)°.
	b = 8.1717(3) Å	β= 84.844(1)°.
	c = 11.1984(5) Å	γ = 78.875(1)°.
Volume	665.74(5) Å^3	
Z	2	
Density (calculated)	1.518 Mg/m^3	
Absorption coefficient	1.05 mm^{-1}	
F(000)	316	
Crystal size	0.2 x 0.05 x 0.03 mm^3	
Theta range for data collection	4.2 to 66.5°.	
Index ranges	-9<=h<=8, -9<=k<=9, -13<=l<=13	
Reflections collected	7724	

Independent reflections	2281 [R(int) = 0.023]
Completeness to theta = 66.5°	98.8 %
Absorption correction	Empirical (using intensity measurements)
Max. and min. transmission	0.753 and 0.663
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2281 / 0 / 201
Goodness-of-fit on F^2	0.91
Final R indices [I>2sigma(I)]	R1 = 0.030, wR2 = 0.083
R indices (all data)	R1 = 0.031, wR2 = 0.084
Largest diff. peak and hole	0.26 and -0.16 e.Å^{-3}

Table SI-2. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for compound **15**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
O(1)	1.26224 (11)	-0.04513 (12)	0.62965 (9)	0.0265 (2)
O(2)	1.00555 (11)	0.13372 (11)	0.62759 (8)	0.0199 (2)
O(3)	0.56916 (10)	0.16995 (11)	0.76095 (8)	0.0179 (2)
O(4)	0.80160 (11)	0.17678 (12)	1.07130 (8)	0.0220 (2)
O(5)	0.49743 (11)	0.30425 (12)	1.15338 (8)	0.0220 (2)
O(6)	0.84907 (11)	0.46428 (11)	0.73457 (8)	0.0227 (2)
O(7)	0.64381 (11)	0.47550 (11)	0.60267 (8)	0.0217 (2)
C(1)	1.10806 (16)	-0.02988 (16)	0.64581 (11)	0.0204 (3)
C(2)	0.82671 (15)	0.11249 (16)	0.64860 (11)	0.0188 (3)
C(3)	0.74602 (15)	0.19619 (15)	0.74965 (11)	0.0171 (3)
C(4)	0.46970 (16)	0.23199 (15)	0.84951 (11)	0.0174 (3)
C(5)	0.29446 (16)	0.28471 (16)	0.82923 (12)	0.0206 (3)
C(6)	0.19184 (16)	0.35006 (16)	0.91705 (12)	0.0216 (3)
C(7)	0.26032 (16)	0.35984 (16)	1.02358 (12)	0.0205 (3)
C(8)	0.99336 (17)	-0.16221 (17)	0.68226 (11)	0.0228 (3)
C(9)	0.83110 (17)	-0.08140 (17)	0.68513 (11)	0.0216 (3)
C(10)	0.83292 (15)	0.11114 (16)	0.87715 (11)	0.0178 (3)
C(11)	0.73098 (16)	0.17763 (15)	0.97728 (11)	0.0175 (3)
C(12)	0.54532 (15)	0.23746 (15)	0.95736 (11)	0.0175 (3)
C(13)	0.43619 (16)	0.30115 (15)	1.04568 (11)	0.0185 (3)
C(14)	0.75285 (15)	0.39536 (16)	0.69682 (11)	0.0172 (3)
C(15)	0.63985 (17)	0.66404 (16)	0.54117 (12)	0.0237 (3)

X-ray crystallographic data for compound **40**:



Crystals of compound **40** suitable for X-ray analysis were obtained by slow evaporation from a solution of CH_2Cl_2/methanol (1: 1). Crystallographic data have been deposited with the Cambridge Cystallograhic Data Centre (CCDC# 793890). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Table SI-3. Crystal data and structure refinement for **40**

Identification code	Compound **40**	
Empirical formula	C16 H16 O7	
Formula weight	320.29	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 13.2285(9) Å	α= 90°.
	b = 7.9453(5) Å	β= 104.118(3)°.
	c = 14.2764(9) Å	γ = 90°.
Volume	1455.19(16) $Å^3$	
Z	4	
Density (calculated)	1.462 Mg/m^3	
Absorption coefficient	0.116 mm^{-1}	
F(000)	672	
Crystal size	0.60 x 0.40 x 0.10 mm^3	
Theta range for data collection	1.88 to 30.51°.	
Index ranges	-18<=h<=18, -10<=k<=11, -20<=l<=18	

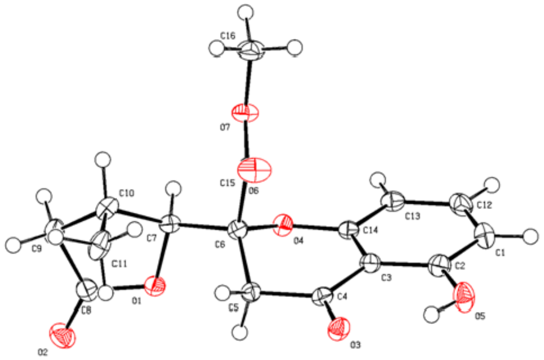
Reflections collected	15201
Independent reflections	4439 [R(int) = 0.0269]
Completeness to theta = 30.51°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9885 and 0.9337
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4439 / 0 / 272
Goodness-of-fit on F^2	1.053
Final R indices [I>2sigma(I)]	R1 = 0.0430, wR2 = 0.1163
R indices (all data)	R1 = 0.0542, wR2 = 0.1249
Largest diff. peak and hole	0.459 and -0.426 e.Å^{-3}

Table SI-4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for compound **40**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	1963(1)	7709(1)	-39(1)	21(1)
O(2)	4583(1)	6542(2)	-1782(1)	52(1)
O(3)	5060(1)	7655(2)	12(1)	66(1)
O(4)	2187(1)	6117(1)	1680(1)	21(1)
O(5)	961(1)	4160(1)	1288(1)	33(1)
O(6)	2390(1)	10911(1)	-123(1)	28(1)
O(7)	3428(1)	11003(1)	1375(1)	34(1)
C(1)	2281(1)	7150(1)	-826(1)	21(1)
C(2)	1502(1)	6611(2)	-1599(1)	27(1)
C(3)	1788(1)	6010(2)	-2413(1)	37(1)
C(4)	2814(1)	5968(2)	-2471(1)	39(1)
C(5)	3583(1)	6552(2)	-1708(1)	35(1)
C(6)	3332(1)	7123(2)	-855(1)	27(1)
C(7)	4139(1)	7495(2)	9(1)	34(1)
C(8)	3776(1)	7499(2)	924(1)	27(1)
C(9)	2710(1)	8344(1)	781(1)	20(1)
C(10)	2271(1)	7932(1)	1661(1)	19(1)
C(11)	1179(1)	8561(1)	1695(1)	20(1)

C(12)	472(1)	7120(1)	1239(1)	24(1)
C(13)	1177(1)	5625(1)	1389(1)	22(1)
C(14)	841(1)	10268(2)	1276(1)	28(1)
C(15)	2880(1)	10248(2)	717(1)	24(1)
C(16)	2487(1)	12727(2)	-196(1)	33(1)

X-ray crystallographic data for compound **44**:[S11]



Crystals of compound **44** suitable for X-ray analysis were obtained by slow evaporation at -40 °C from a solution of CH$_2$Cl$_2$. Crystallographic data have been deposited with the Cambridge Cystallograhic Data Centre (CCDC# 794128). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Table SI-5. Crystal data and structure refinement for **44**

Identification code	Compound **44**	
Empirical formula	C16 H16 O7	
Formula weight	320.29	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 8.8482(3) Å	α= 90°.
	b = 7.7305(2) Å	β= 98.759(1)°.
	c = 21.7938(6) Å	γ = 90°.
Volume	1473.33(7) Å^3	
Z	4	
Density (calculated)	1.444 Mg/m^3	
Absorption coefficient	0.97 mm^{-1}	
F(000)	672	
Crystal size	0.10 x 0.07 x 0.07 mm^3	

[S11] (a) Sheldrick, G. M. (1996). SADABS. University of Göttingen, Germany. (b) Sheldrick, G. M. (1997). SHELXL97. University of Göttingen, Germany. (c) Bruker (2006). SAINT. Bruker Analytical X-ray Instruments Inc., Madison, Wisconsin, USA. (d) Bruker (2006). APEX2. Bruker Analytical X-ray Instruments Inc., Madison, Wisconsin, USA. (e) Dolmanov, O.V. ; Bourhis, L. J.; Cildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339.

Theta range for data collection	4.1 to 66.5°.
Index ranges	-10<=h<=10, -8<=k<=9, -25<=l<=25
Reflections collected	63241
Independent reflections	2519 [R(int) = 0.035]
Completeness to theta = 66.5°	97.2 %
Absorption correction	multi-scan
Max. and min. transmission	0.753 and 0.712
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2519 / 0 / 211
Goodness-of-fit on F^2	1.08
Final R indices [I>2sigma(I)]	R1 = 0.032, wR2 = 0.0948
R indices (all data)	R1 = 0.0359, wR2 = 0.109
Largest diff. peak and hole	0.31 and -0.25 e.Å^{-3}

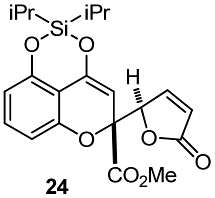
Table SI-6. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for compound **44**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	0.37511(11)	0.56253(14)	0.83172(5)	0.0187(3)
O(2)	0.17603(13)	0.45911(17)	0.76685(6)	0.0291(3)
O(3)	0.66530(12)	1.14590(14)	0.88073(5)	0.0213(3)
O(4)	0.58321(11)	0.65924(14)	0.94068(5)	0.0175(3)
O(5)	0.76948(14)	1.23362(15)	0.99609(5)	0.0271(3)
O(6)	0.87475(13)	0.75508(16)	0.85822(6)	0.0302(3)
O(7)	0.84016(11)	0.84016(14)	0.90995(5)	0.0218(3)
C(1)	0.75885(19)	1.0225(2)	1.07287(7)	0.0247(4)
C(2)	0.73491(17)	1.0708(2)	1.01072(7)	0.0210(3)
C(3)	0.67466(16)	0.9502(2)	0.96463(7)	0.0176(3)
C(4)	0.64192(16)	0.9987(2)	0.89927(7)	0.0178(3)
C(5)	0.57259(17)	0.8610(2)	0.85479(7)	0.0177(3)
C(6)	0.62004(16)	0.6820(2)	0.87866(6)	0.0165(3)
C(7)	0.53938(16)	0.5293(2)	0.84313(7)	0.0170(3)
C(8)	0.31206(18)	0.4634(2)	0.78284(7)	0.0208(4)

C(9)	0.43678(18)	0.3680(2)	0.75677(7)	0.0233(4)
C(10)	0.57966(18)	0.4745(2)	0.77977(7)	0.0211(4)
C(11)	0.6000(2)	0.6200(2)	0.73427(7)	0.0273(4)
C(12)	0.72038(17)	0.8565(2)	1.08912(7)	0.0234(4)
C(13)	0.66067(16)	0.7346(2)	1.04517(7)	0.0194(3)
C(14)	0.64008(15)	0.7824(2)	0.98318(7)	0.0170(3)
C(15)	0.79444(16)	0.6565(2)	0.88100(7)	0.0176(3)
C(16)	1.00180(17)	0.4686(2)	0.91294(8)	0.0264(4)

VI. Computational Studies

A) Calculations for Diastereomers 24 and 27:



24

For diastereomer **24**, we used Spartan '08 to perform calculations. First, a semi-empirical/AM1 level of theory was employed for a conformer search which resulted in 59 conformers. Energies for the 59 conformers were calculated at the DFT/B3LYP/6-31G* level of theory. The 9th conformer was found to have the lowest energy in dichloromethane (Figure SI-3)(-1023358.48 kcal/mol).

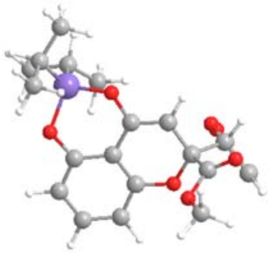
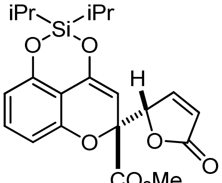


Figure SI-3. Lowest energy conformer for **24**



27

For diastereomer **27**, we employed Spartan '08 for calculations. First, semi-empirical/AM1 level was used for a conformer search which resulted in 65 conformers. Energies of the 65 conformers were calculated using the DFT/B3LYP/6-31G* level of theory. The 25th conformer had the lowest energy in dichloromethane (-1023359.45 kcal/mol, 0.97 kcal/mol more stable than diastereomer **24**).

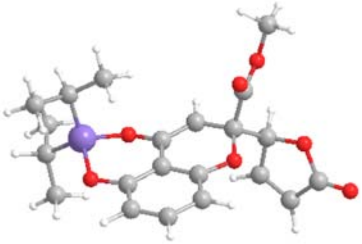
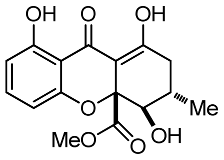


Figure SI-4. Lowest energy conformer for **27**

B) Lowest Energy Conformer Calculations for Diastereomers 2 and 45:



blennolide B (**2**)

For blennolide B (**2**), we employed Spartan '08 for energy calculations. First, the semi-empirical/AM1 level of theory was used to conduct a conformer search. Conformers were optimized at the DFT/B3LYP/6-31G* level of theory. The lowest energy conformer for compound **2** is shown in Figure SI-5.

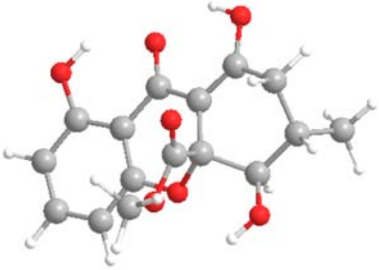
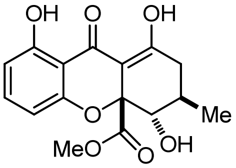


Figure SI-5. Lowest energy conformer for **2**



45

For diastereomer **45**, a semi-empirical/AM1 level of theory was first used for a conformer search. Next, conformers were optimized at the DFT/B3LYP/6-31G* level of theory. The ground state conformation for compound **45** is shown in Figure SI-6.

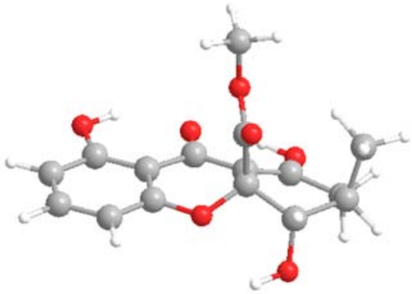


Figure SI-6. Lowest energy conformer for **45**

Optimized structures

Compound 2 **B3LYP/6-31G***

1	C	UNK	0001	3.365	-0.776	0.021
2	C	UNK	0001	2.542	1.621	-1.190
3	C	UNK	0001	1.984	-0.542	-0.158
4	C	UNK	0001	4.318	0.178	-0.398
5	C	UNK	0001	3.899	1.355	-0.999
6	C	UNK	0001	1.605	0.673	-0.767
7	H	UNK	0001	5.384	-0.037	-0.240
8	H	UNK	0001	4.645	2.095	-1.327
9	H	UNK	0001	2.203	2.552	-1.663
10	O	UNK	0001	3.896	-1.893	0.595
11	H	UNK	0001	3.194	-2.524	0.826
12	C	UNK	0001	0.946	-1.495	0.231
13	O	UNK	0001	1.223	-2.663	0.589
14	O	UNK	0001	0.289	0.972	-1.057
15	C	UNK	0001	-0.432	-1.028	0.179
16	C	UNK	0001	-1.506	-1.807	0.524
17	O	UNK	0001	-1.477	-3.099	0.914
18	H	UNK	0001	-0.562	-3.437	0.961
19	C	UNK	0001	-0.722	0.380	-0.223
20	C	UNK	0001	-2.890	-1.246	0.522
21	H	UNK	0001	-2.981	-0.605	1.447

22	H	UNK	0001	-3.644	-2.074	0.602
23	C	UNK	0001	-3.170	-0.406	-0.713
24	H	UNK	0001	-4.029	0.284	-0.460
25	C	UNK	0001	-1.989	0.479	-1.135
26	H	UNK	0001	-1.647	0.200	-2.175
27	C	UNK	0001	-0.912	1.273	1.006
28	O	UNK	0001	-1.349	0.969	2.116
29	O	UNK	0001	-0.566	2.571	0.771
30	C	UNK	0001	-0.731	3.486	1.859
31	H	UNK	0001	-1.802	3.512	2.174
32	H	UNK	0001	-0.404	4.465	1.429
33	H	UNK	0001	-0.085	3.176	2.714
34	O	UNK	0001	-2.474	1.811	-1.149
35	H	UNK	0001	-1.719	2.391	-1.326
36	C	UNK	0001	-3.598	-1.282	-1.874
37	H	UNK	0001	-2.795	-2.010	-2.140
38	H	UNK	0001	-3.822	-0.653	-2.769
39	H	UNK	0001	-4.519	-1.854	-1.603

Compound 45 B3LYP/6-31G*

1	C	UNK	0001	3.262	-0.647	0.126
2	C	UNK	0001	2.571	1.700	-1.255
3	C	UNK	0001	1.901	-0.399	-0.156
4	C	UNK	0001	4.261	0.262	-0.287
5	C	UNK	0001	3.909	1.412	-0.976
6	C	UNK	0001	1.588	0.798	-0.837
7	H	UNK	0001	5.311	0.033	-0.054
8	H	UNK	0001	4.691	2.116	-1.301
9	H	UNK	0001	2.283	2.616	-1.789
10	O	UNK	0001	3.734	-1.738	0.792
11	H	UNK	0001	3.002	-2.323	1.052

12	C	UNK	0001	0.824	-1.334	0.180
13	O	UNK	0001	1.061	-2.457	0.677
14	C	UNK	0001	-0.537	-0.912	-0.152
15	O	UNK	0001	0.294	1.139	-1.179
16	C	UNK	0001	-0.754	0.545	-0.387
17	C	UNK	0001	-1.583	-1.788	-0.245
18	O	UNK	0001	-1.533	-3.112	0.043
19	H	UNK	0001	-0.648	-3.380	0.352
20	C	UNK	0001	-2.040	0.867	-1.207
21	H	UNK	0001	-2.248	1.971	-1.099
22	C	UNK	0001	-3.245	0.053	-0.728
23	H	UNK	0001	-4.073	0.243	-1.473
24	C	UNK	0001	-2.944	-1.432	-0.757
25	H	UNK	0001	-3.720	-1.995	-0.172
26	H	UNK	0001	-2.988	-1.794	-1.823
27	C	UNK	0001	-3.719	0.510	0.633
28	H	UNK	0001	-2.980	0.237	1.427
29	H	UNK	0001	-4.694	0.025	0.879
30	H	UNK	0001	-3.857	1.619	0.647
31	O	UNK	0001	-1.859	0.551	-2.576
32	H	UNK	0001	-1.098	1.057	-2.890
33	C	UNK	0001	-0.825	1.354	0.915
34	O	UNK	0001	-1.111	2.548	1.017
35	O	UNK	0001	-0.544	0.655	2.051
36	C	UNK	0001	-0.590	1.386	3.280
37	H	UNK	0001	-1.623	1.776	3.449
38	H	UNK	0001	0.140	2.230	3.250
39	H	UNK	0001	-0.307	0.623	4.047

C) Transition State Calculations

a. Computational Methods

Computations were performed with Spartan ‘08[S12] or Gaussian 03.[S13] Transition state models for each addition stereochemistry were created in a Spartan ‘08 spreadsheet by carrying out a preliminary conformational search with a fixed 2.1 Å distance for the nascent bond, followed by AM1 optimization. Thirteen candidate structures were further optimized in Gaussian with B3LYP/6-31G(d) theory, followed by vibrational frequency analysis. Each TS structure yielded a single imaginary vibrational mode. Details for the reactants and two lowest energy transition state structures are presented below.

b. FMO Analysis

In this reaction, the dominant frontier MO interaction should occur between the HOMO of 2-trimethylsiloxyfuran and the LUMO of benzopyrylium ion **14**. Manuscript Figure 3 shows the B3LYP/6-31G(d) surfaces. These images support initial bonding between C5 of 2-trimethylsiloxyfuran and C2 of benzopyrylium ion **14** but also indicate additional bonding interactions across the ring, consistent with **TS-A** (manuscript Figure 4).

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[12] Spartan 08, Wavefunction Inc. , Irvine, CA.

[13] Gaussian 03, Revision E.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, Jr., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; 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.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; and Pople, J. A.; Gaussian, Inc., Wallingford CT, 2004.

Intermediate calculation and surface results

Optimized structures

Benzopyrylium Ion 14 B3LYP/6-31G(d)

Charge = 1 Multiplicity = 1

C,	0,	-0.011278693,	0.0282384954,	0.0090267218
C,	0,	-0.0120560793,	0.0219297238,	1.4236787403
O,	0,	2.3623958964,	0.005174791,	-0.0279430645
C,	0,	1.2369607164,	0.0052968388,	2.1063328194
C,	0,	1.1848890337,	0.0191708494,	-0.6535913849
C,	0,	2.4297848144,	-0.0028813593,	1.3363311545
C,	0,	1.3473829454,	-0.0066295979,	3.5292533167
H,	0,	4.5761372426,	-0.0261986219,	1.2977944165
C,	0,	2.6053279712,	-0.0245685307,	4.1156914941
H,	0,	2.6793960647,	-0.0339752949,	5.1973881091
C,	0,	3.7545908427,	-0.031058873,	3.3117313436
H,	0,	4.7279708616,	-0.0452553218,	3.792099304
C,	0,	3.6892872501,	-0.0204407453,	1.9203230626
O,	0,	0.2463727889,	-0.002971049,	4.3044562348
O,	0,	-1.1593129684,	0.0299705957,	2.0550307159
Si,	0,	-1.3750131525,	0.0238193414,	3.7934837595
C,	0,	-2.222780412,	-1.5815216919,	4.2474758013
H,	0,	-2.2375232148,	-1.594213276,	5.3485930029
C,	0,	-1.4347611784,	-2.8186187189,	3.7690404196
H,	0,	-1.3954879088,	-2.870819563,	2.6742458894
H,	0,	-1.9265241908,	-3.7336300691,	4.1175915093
H,	0,	-0.4087110639,	-2.8310631928,	4.1526788642
C,	0,	-3.6859679843,	-1.60914539,	3.749649049

H,	0,	-3.7407563319,	-1.5699400646,	2.6553992917
H,	0,	-4.2805380936,	-0.7798793541,	4.1485022155
H,	0,	-4.1702513778,	-2.539496962,	4.0666736132
C,	0,	-2.1782609834,	1.642793186,	4.2788011566
H,	0,	-3.1815905414,	1.6247501095,	3.8264923015
C,	0,	-2.3464043941,	1.7218220429,	5.814576613
H,	0,	-2.856429757,	2.6528334623,	6.0862644102
H,	0,	-1.376679869,	1.7194028217,	6.3255320433
H,	0,	-2.9434193434,	0.8947800379,	6.2150132065
C,	0,	-1.4247231944,	2.8707530552,	3.7278954224
H,	0,	-1.950109384,	3.7898899605,	4.0105475772
H,	0,	-1.3552056864,	2.8587070698,	2.6344054437
H,	0,	-0.4102426895,	2.9381232773,	4.1382083566
C,	0,	1.2392677796,	0.0227557267,	-2.1632868966
O,	0,	0.219034338,	0.0345526627,	-2.8136472276
O,	0,	2.4844692916,	0.0106933275,	-2.6157381421
C,	0,	2.6279022095,	0.0109768875,	-4.0614135357
H,	0,	3.7015716191,	0.0014162407,	-4.2384408919
H,	0,	2.1671915242,	0.9089201829,	-4.4776146117
H,	0,	2.1511280392,	-0.8777243488,	-4.4794172588
H,	0,	-0.934152228,	0.0393127401,	-0.5569998461

E(RB+HF-LYP) = -1325.96264842

Zero-point correction= 0.356682 (Hartree/Particle)
Thermal correction to Energy= 0.380542
Thermal correction to Enthalpy= 0.381487
Thermal correction to Gibbs Free Energy= 0.301919
Sum of electronic and zero-point Energies= -1325.605966
Sum of electronic and thermal Energies= -1325.582106
Sum of electronic and thermal Enthalpies= -1325.581162

Sum of electronic and thermal Free Energies= -1325.660730

2-Trimethylsiloxy Furan B3LYP/6-31G(d)

Charge = 0 Multiplicity = 1

O,	0,	0.9773669383,	-0.7187333509,	1.9226526372
C,	0,	0.0743750775,	0.2329196033,	1.5453149427
C,	0,	0.6054015966,	1.0585091553,	0.5989855718
C,	0,	1.9423671387,	0.5798873386,	0.3730359095
C,	0,	2.124892849,	-0.4890731407,	1.1885975894
H,	0,	0.1066922022,	1.8931155135,	0.1299893467
H,	0,	2.6697753344,	0.9892897943,	-0.3147689997
O,	0,	-1.1255961569,	0.2164597974,	2.1241914752
Si,	0,	-1.7319543361,	-0.852837244,	3.3120690271
C,	0,	-0.6923724884,	-0.7182915686,	4.8745974023
H,	0,	0.3424155089,	-1.0262214807,	4.692600889
H,	0,	-1.1003823511,	-1.357066528,	5.6680399801
H,	0,	-0.67708811,	0.3110118085,	5.2513067008
C,	0,	-3.4746497963,	-0.2096793885,	3.5898980429
H,	0,	-3.4619652442,	0.8289343888,	3.9389321205
H,	0,	-3.9999229725,	-0.8098176432,	4.3428979997
H,	0,	-4.0613331665,	-0.244778476,	2.6650864464
C,	0,	-1.7469118848,	-2.6083694344,	2.6351650459
H,	0,	-2.1846940793,	-3.3015282996,	3.3645047463
H,	0,	-0.7342576595,	-2.955672847,	2.405744393
H,	0,	-2.3420136758,	-2.672450867,	1.7168231703
H,	0,	2.9401249356,	-1.168835521,	1.377997443

E(RB3LYP) = -713.959872101

Zero-point correction= 0.176639 (Hartree/Particle)
Thermal correction to Energy= 0.189201
Thermal correction to Enthalpy= 0.190145
Thermal correction to Gibbs Free Energy= 0.137308
Sum of electronic and zero-point Energies= -713.783233
Sum of electronic and thermal Energies= -713.770671
Sum of electronic and thermal Enthalpies= -713.769727
Sum of electronic and thermal Free Energies= -713.822564

Transition State TS-A (manuscript, Figure 4) **B3LYP/6-31G(d)**

Charge = 1 Multiplicity = 1

C,	0,	-0.1858803496,	0.0793882792,	0.1547498271
C,	0,	-0.1178347134,	0.0652683826,	1.5272564124
O,	0,	2.2203301163,	0.185454589,	-0.0001650654
C,	0,	1.1744924377,	-0.0458930908,	2.1659190653
C,	0,	1.0153378721,	-0.0596937554,	-0.6068051168
C,	0,	2.3290386737,	0.0303377835,	1.3541141301
C,	0,	1.3463500952,	-0.1633009274,	3.5694655534
H,	0,	4.4717044999,	0.0677245369,	1.236642594
C,	0,	2.626061303,	-0.2217109555,	4.112812061
H,	0,	2.7340707175,	-0.3212277816,	5.1871614809
C,	0,	3.7423929186,	-0.1392074603,	3.2739035386
H,	0,	4.7353630592,	-0.1780200488,	3.7110636791
C,	0,	3.6121253456,	-0.0073212941,	1.8927223161
O,	0,	0.2731504722,	-0.239594502,	4.3958568616
O,	0,	-1.2315204218,	0.1893092031,	2.2537720454
Si,	0,	-1.3063486856,	0.2071289687,	3.9717513805

C,	0,	-2.4852751699,	-1.1416170093,	4.5266835182
H,	0,	-2.3786158143,	-1.1878223376,	5.6215257404
C,	0,	-2.1017872209,	-2.5218900783,	3.9567289598
H,	0,	-2.1925039389,	-2.5370990571,	2.8634939005
H,	0,	-2.7703958606,	-3.2957192696,	4.3520494296
H,	0,	-1.0763521746,	-2.8025966349,	4.2217248845
C,	0,	-3.953138429,	-0.7849770347,	4.2054147191
H,	0,	-4.1174284756,	-0.6951117911,	3.1247350351
H,	0,	-4.2661634041,	0.1556017459,	4.6721383832
H,	0,	-4.6230958648,	-1.5709271895,	4.5732868049
C,	0,	-1.682079239,	1.9557028653,	4.5412013541
H,	0,	-2.6750057504,	2.19509914,	4.1295904651
C,	0,	-1.7720208439,	2.0326890689,	6.0818566492
H,	0,	-2.0272050808,	3.0517167909,	6.3951020434
H,	0,	-0.8155569837,	1.7763791517,	6.5525851139
H,	0,	-2.5383173652,	1.3642380426,	6.4905172613
C,	0,	-0.6764560001,	2.9844637763,	3.9848934359
H,	0,	-0.9610555248,	3.997328367,	4.2931553334
H,	0,	-0.6369945408,	2.9741438022,	2.8899214715
H,	0,	0.3355834422,	2.8021316291,	4.3654069853
C,	0,	0.960425002,	0.4613679187,	-2.035226282
O,	0,	-0.0867908756,	0.6016096574,	-2.6281317782
O,	0,	2.1740959203,	0.6918025465,	-2.5307357301
C,	0,	2.2116528533,	1.2050607817,	-3.8855424184
H,	0,	3.2690495531,	1.3290739648,	-4.1130538557
H,	0,	1.6869698365,	2.1611659881,	-3.9356830805
H,	0,	1.7433243663,	0.4942908539,	-4.5697158844
O,	0,	-0.0979055819,	-2.3184682024,	-1.5978798797
C,	0,	-0.7442072933,	-2.9843330715,	-0.6311620575
C,	0,	0.1266863569,	-3.2889824605,	0.4369999093
C,	0,	1.3566764564,	-2.764815476,	0.0872199937

C,	0,	1.1946269204,	-2.0320956622,	-1.1188458705
H,	0,	-0.1499667834,	-3.8516948092,	1.316219884
H,	0,	2.2793848075,	-2.8332030503,	0.6475342484
O,	0,	-1.9884166619,	-3.2796837486,	-0.7712216825
Si,	0,	-3.0942875784,	-3.0188151121,	-2.141195596
C,	0,	-3.3206031368,	-1.1688586141,	-2.311587453
H,	0,	-3.7238894923,	-0.730155609,	-1.3913879859
H,	0,	-4.0409147891,	-0.958890277,	-3.1123658305
H,	0,	-2.3871477117,	-0.6547771399,	-2.5643741394
C,	0,	-2.3102605849,	-3.8287843796,	-3.6368816991
H,	0,	-3.0030734705,	-3.7793112495,	-4.4861514062
H,	0,	-2.0936215847,	-4.887301801,	-3.4541228917
H,	0,	-1.3824052062,	-3.3326519046,	-3.9385311867
C,	0,	-4.621403172,	-3.9087439232,	-1.5367249413
H,	0,	-4.4259027785,	-4.9742525181,	-1.3740557401
H,	0,	-5.4276739462,	-3.8284606016,	-2.2756893298
H,	0,	-4.9901934633,	-3.4837396598,	-0.5968357275
H,	0,	1.9336318364,	-1.9545066116,	-1.9068981454
H,	0,	-1.1249318897,	0.2129085159,	-0.3645111251

E(RB+HF-LYP) = -2039.92365397

Imaginary Mode -290.2293 cm $^{-1}$

Zero-point correction= 0.534541 (Hartree/Particle)
Thermal correction to Energy= 0.571464
Thermal correction to Enthalpy= 0.572408
Thermal correction to Gibbs Free Energy= 0.463836
Sum of electronic and zero-point Energies= -2039.389112
Sum of electronic and thermal Energies= -2039.352190
Sum of electronic and thermal Enthalpies= -2039.351246
Sum of electronic and thermal Free Energies= -2039.459818

Transition State TS-B (manuscript, Figure 4) **B3LYP/6-31G(d)**

Charge = 1 Multiplicity = 1

C,	0,	-0.0371480929,	0.0023558343,	0.0612358167
C,	0,	0.0365357792,	0.0685783708,	1.4267946363
O,	0,	2.3697500472,	0.0224275864,	-0.106933921
C,	0,	1.3295284289,	-0.017096525,	2.0759622424
C,	0,	1.1592120417,	-0.2059412285,	-0.7045548408
C,	0,	2.4812157893,	-0.0339959409,	1.2620914071
C,	0,	1.5018953229,	-0.0347132272,	3.4821634252
H,	0,	4.6227772442,	-0.0692807323,	1.1344937533
C,	0,	2.7834060584,	-0.0859974248,	4.0268153043
H,	0,	2.8913421024,	-0.1072872468,	5.1055464589
C,	0,	3.8971474417,	-0.0993417833,	3.1839590274
H,	0,	4.8906273091,	-0.1332192337,	3.6203011721
C,	0,	3.7638974005,	-0.0692123367,	1.7956767825
O,	0,	0.4338998741,	-0.0164040863,	4.3173995938
O,	0,	-1.076922914,	0.2345420416,	2.1485388858
Si,	0,	-1.1590396452,	0.3409222923,	3.8596075388
C,	0,	-2.2946683447,	-1.0129688703,	4.4864040604
H,	0,	-2.20790184,	-0.9816928389,	5.5837226096
C,	0,	-1.8479287101,	-2.4118736023,	4.0158535351
H,	0,	-1.9193089849,	-2.505869131,	2.9255239494
H,	0,	-2.4932509047,	-3.1828730018,	4.4530397315
H,	0,	-0.8172715827,	-2.6350265352,	4.3124016727
C,	0,	-3.7689686149,	-0.7372088528,	4.1167763845
H,	0,	-3.9152039574,	-0.7292445388,	3.0299434954

H,	0,	-4.1282703359,	0.2198131269,	4.5118442402
H,	0,	-4.4149821891,	-1.5224635458,	4.5267982
C,	0,	-1.5922451085,	2.1042460931,	4.335918961
H,	0,	-2.5932328468,	2.2907689642,	3.9170647434
C,	0,	-1.6801438867,	2.258539157,	5.8707895566
H,	0,	-1.9638411133,	3.2847552677,	6.1323009301
H,	0,	-0.715291494,	2.0542391718,	6.3497858387
H,	0,	-2.4253442085,	1.5897750495,	6.3164652404
C,	0,	-0.6217126058,	3.1344684165,	3.723185062
H,	0,	-0.9300243205,	4.1518459466,	3.9917904177
H,	0,	-0.5948936883,	3.077850602,	2.6291771391
H,	0,	0.3994547127,	2.9954403913,	4.0976415208
C,	0,	1.1074351081,	0.2612551466,	-2.1459593113
O,	0,	0.1012372555,	0.1423879427,	-2.8159520205
O,	0,	2.2670074899,	0.7611965347,	-2.5633344943
C,	0,	2.2920316486,	1.2391624751,	-3.9289041856
H,	0,	3.2965739943,	1.6332711668,	-4.0739922587
H,	0,	1.5430259718,	2.0217661073,	-4.0653019376
H,	0,	2.09215271,	0.4169057027,	-4.6194583029
C,	0,	2.1728908384,	-2.4758178746,	-2.1057296636
C,	0,	1.4409855104,	-2.8564287376,	-3.2111296754
C,	0,	0.0867492967,	-2.8753191704,	-2.793862029
O,	0,	-0.0133440207,	-2.5460810418,	-1.5041445065
C,	0,	1.2638251171,	-2.1795625523,	-1.0481567707
H,	0,	1.4304714187,	-2.4572653454,	-0.0129246892
H,	0,	-0.9832392213,	0.0589358831,	-0.4599700571
H,	0,	3.2463724328,	-2.351672944,	-2.0432126989
H,	0,	1.7969394378,	-3.0935216985,	-4.2025224969
O,	0,	-1.0144494366,	-3.1444719869,	-3.3961729729
Si,	0,	-1.44969969,	-3.2527433135,	-5.1059371754
C,	0,	-3.3065170249,	-3.0865656939,	-5.0354202729

H,	0,	-3.7522369404,	-3.8673222185,	-4.4095555807
H,	0,	-3.739871649,	-3.1758268304,	-6.0387655212
H,	0,	-3.6036026836,	-2.1141783718,	-4.6281082501
C,	0,	-0.8689794355,	-4.9349419288,	-5.6897779774
H,	0,	-1.146313208,	-5.0829741099,	-6.7408104128
H,	0,	-1.3341913631,	-5.7400028757,	-5.1103912584
H,	0,	0.2183839382,	-5.0530346766,	-5.6209202848
C,	0,	-0.6024032707,	-1.8165346588,	-5.9657505857
H,	0,	-1.0884439994,	-1.6274203632,	-6.9306379538
H,	0,	0.4568646613,	-2.0079479901,	-6.1700345079
H,	0,	-0.6772608371,	-0.9002765911,	-5.3690554205

E(RB+HF-LYP) = -2039.91878310

Imaginary Frequency -278.3615 cm^{-1}

Zero-point correction= 0.533949 (Hartree/Particle)

Thermal correction to Energy= 0.571197

Thermal correction to Enthalpy= 0.572141

Thermal correction to Gibbs Free Energy= 0.461335

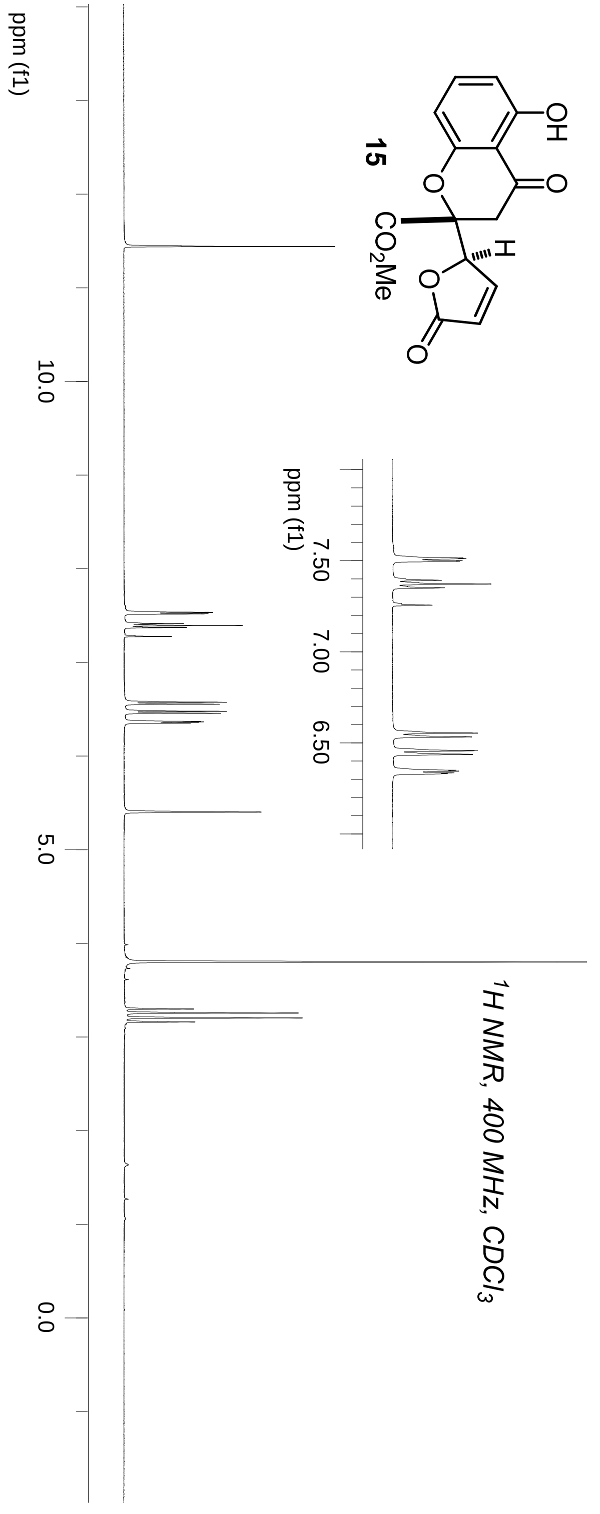
Sum of electronic and zero-point Energies= -2039.384834

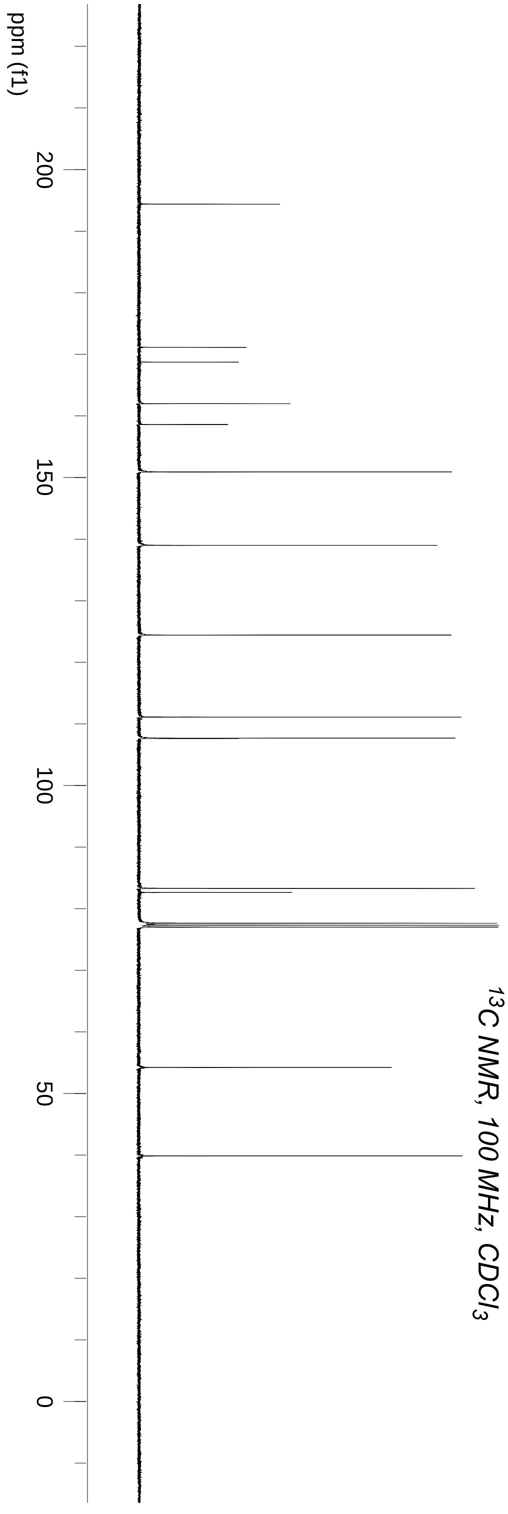
Sum of electronic and thermal Energies= -2039.347586

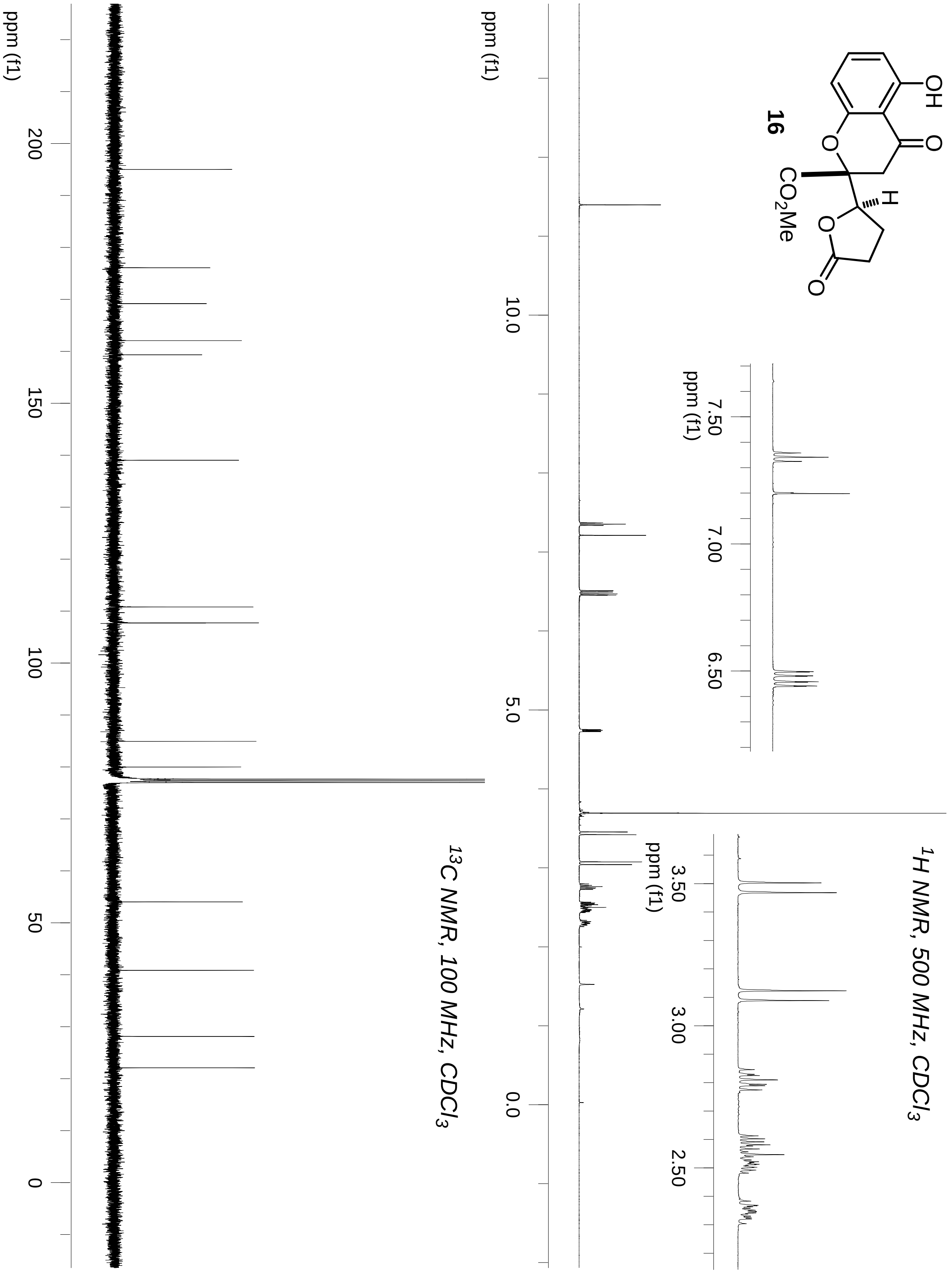
Sum of electronic and thermal Enthalpies= -2039.346642

Sum of electronic and thermal Free Energies= -2039.457448

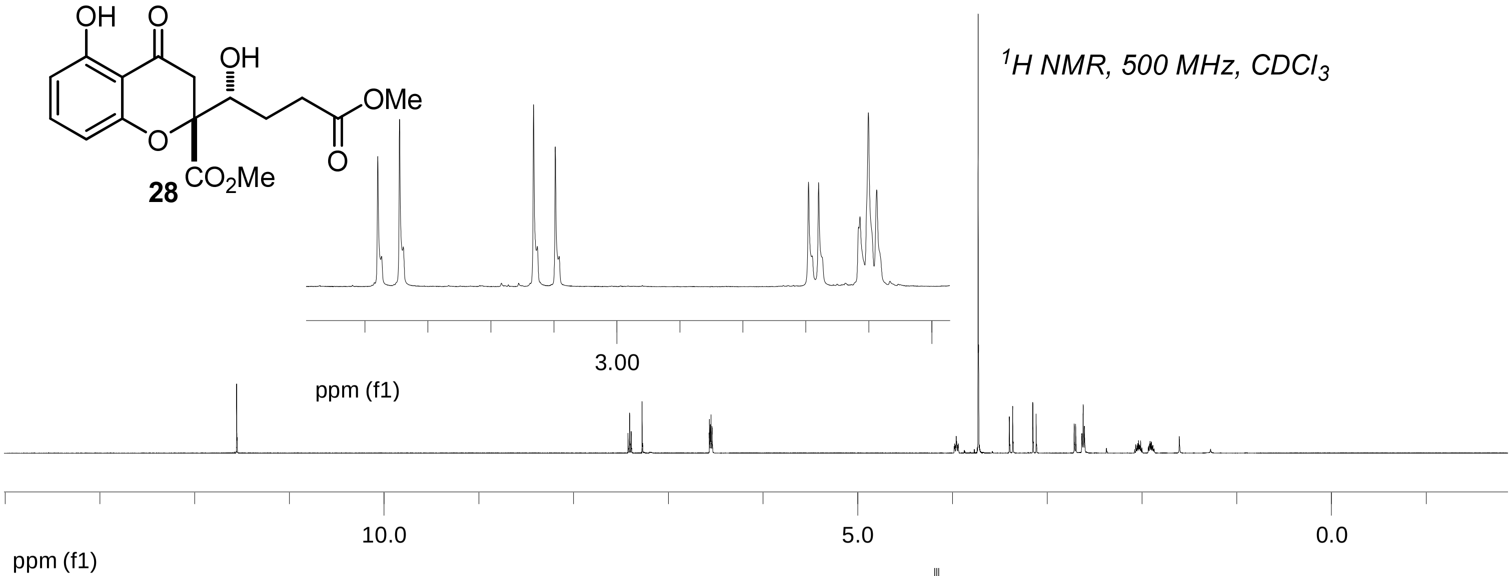
VII. Select NMR Spectra


15

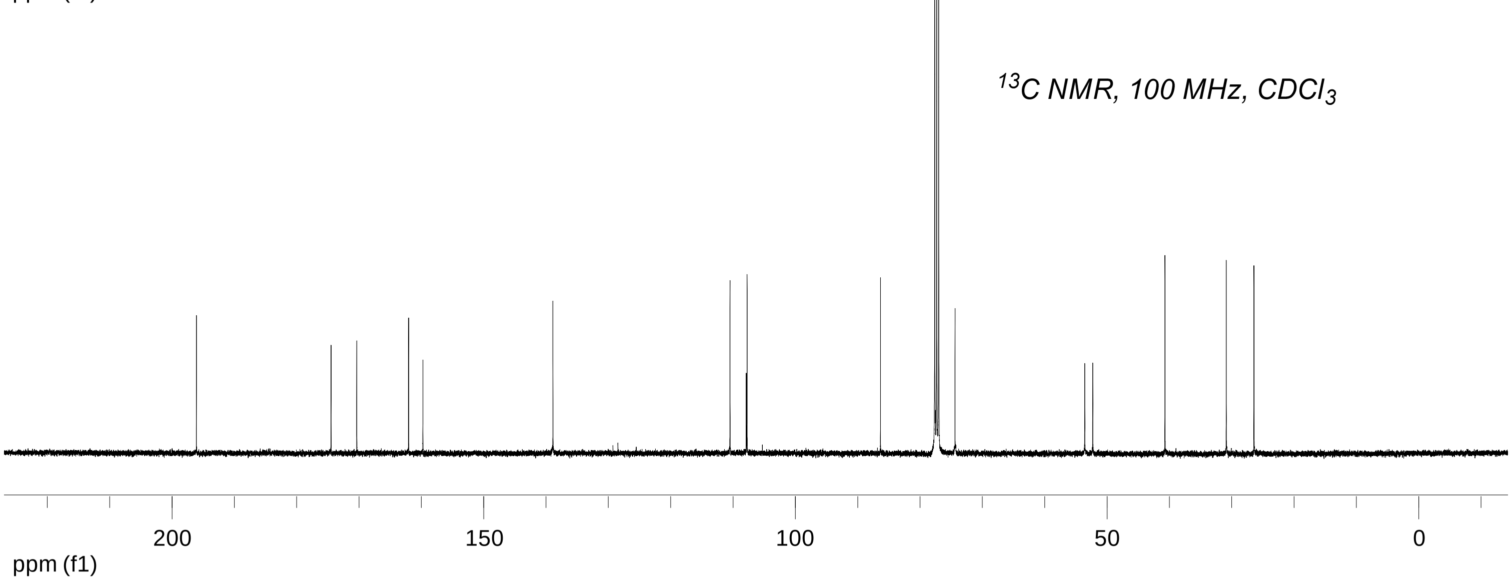



16

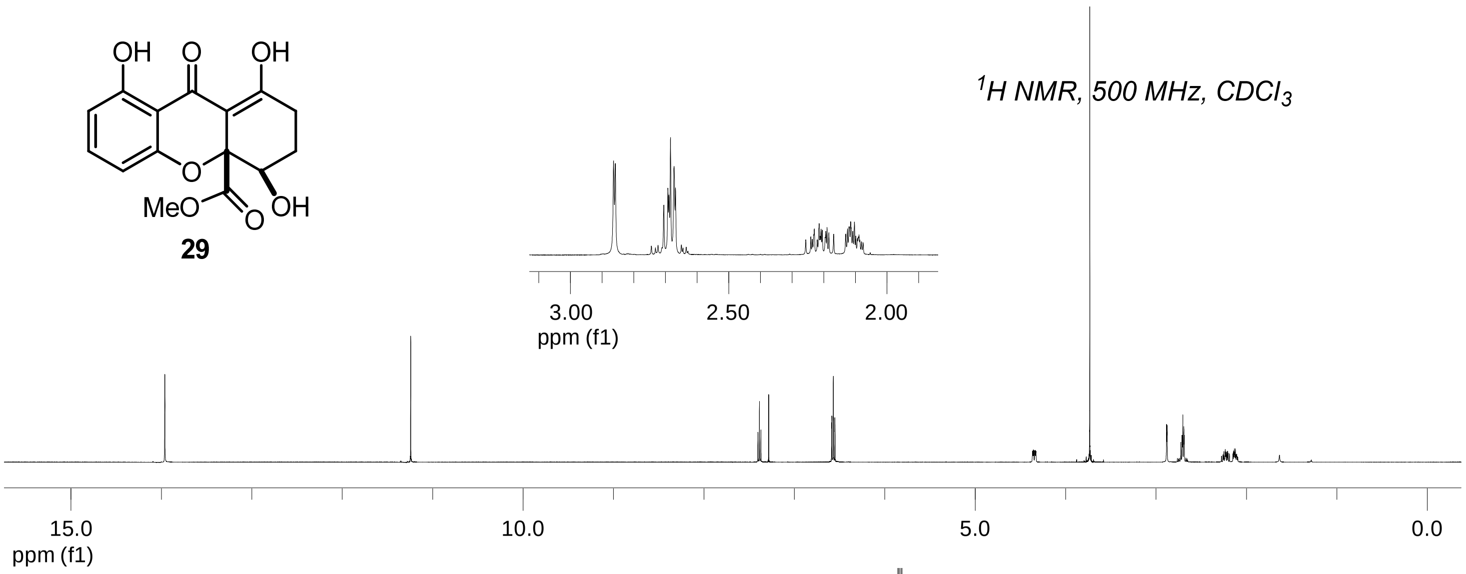
OH
O
O
H
O
O
CO2Me
1H NMR, 500 MHz, CDCl3
7.50
7.00
6.50
ppm (f1)
3.50
3.00
2.50
ppm (f1)
10.0
5.0
0.0
ppm (f1)
13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)


28

^{1}H NMR, 500 MHz, $CDCl_3$

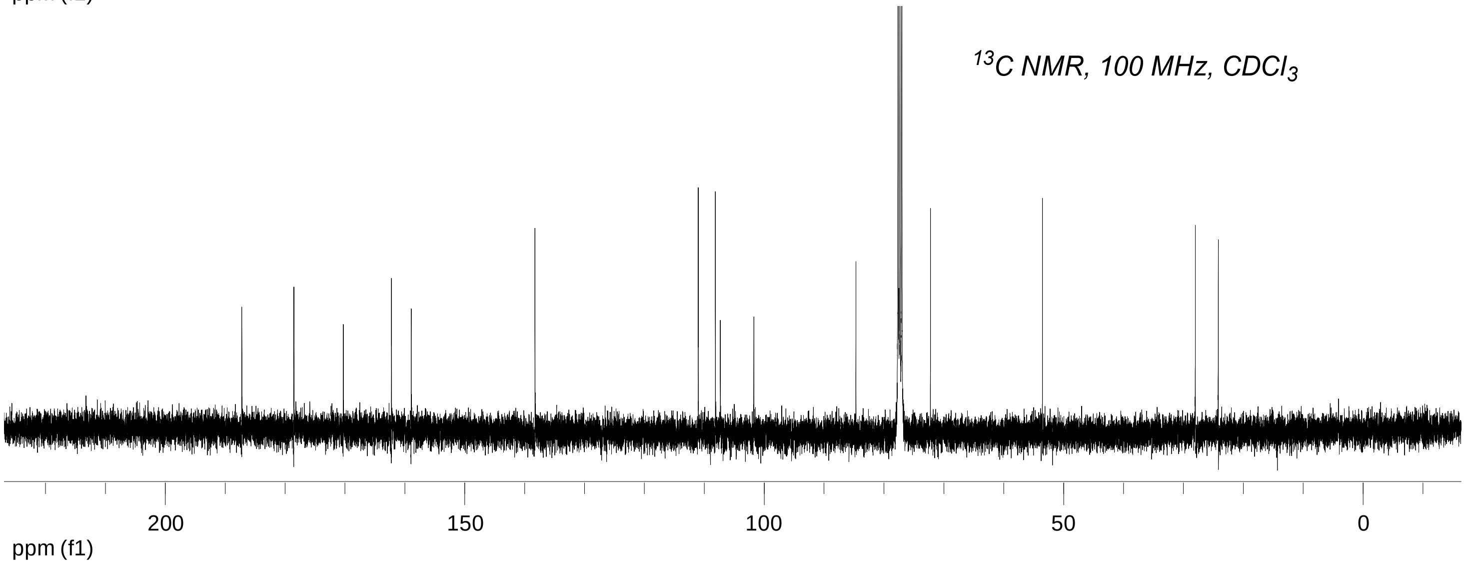


^{13}C NMR, 100 MHz, $CDCl_3$

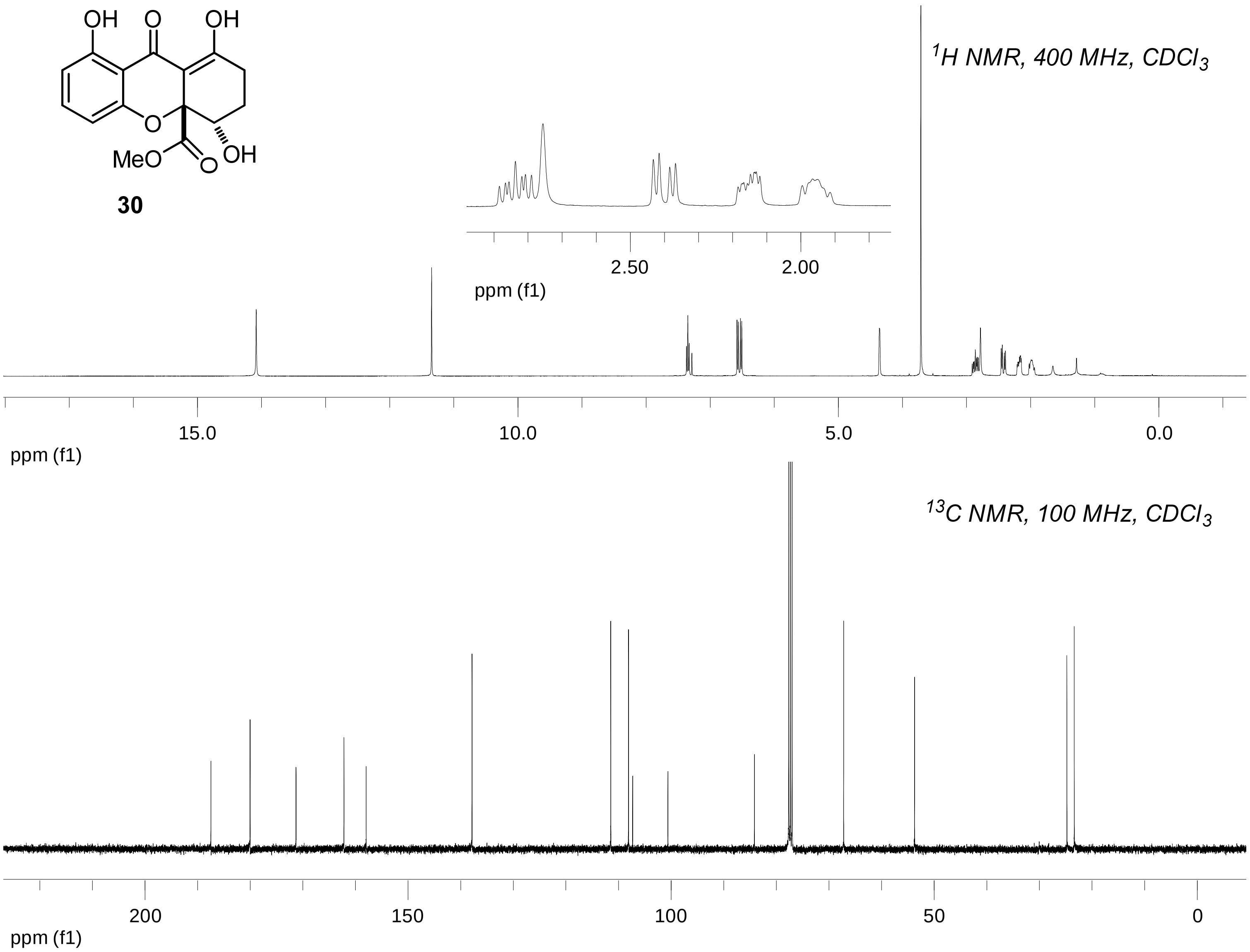


29

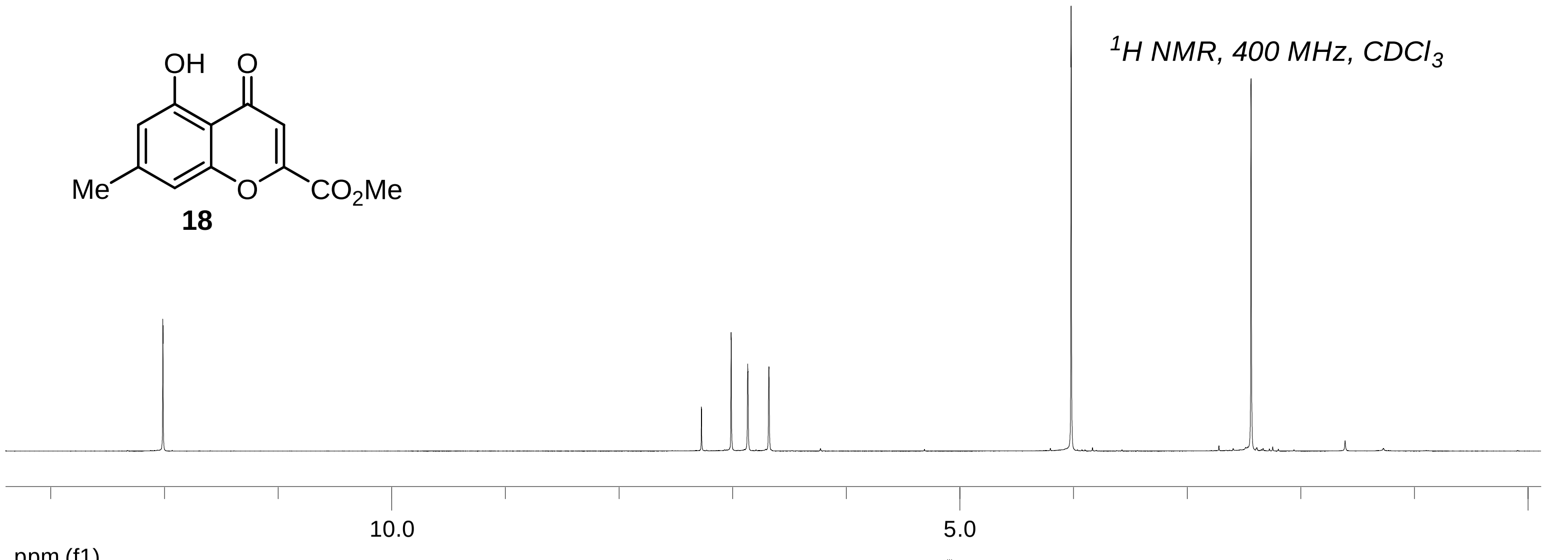
^1H NMR, 500 MHz, $CDCl_3$

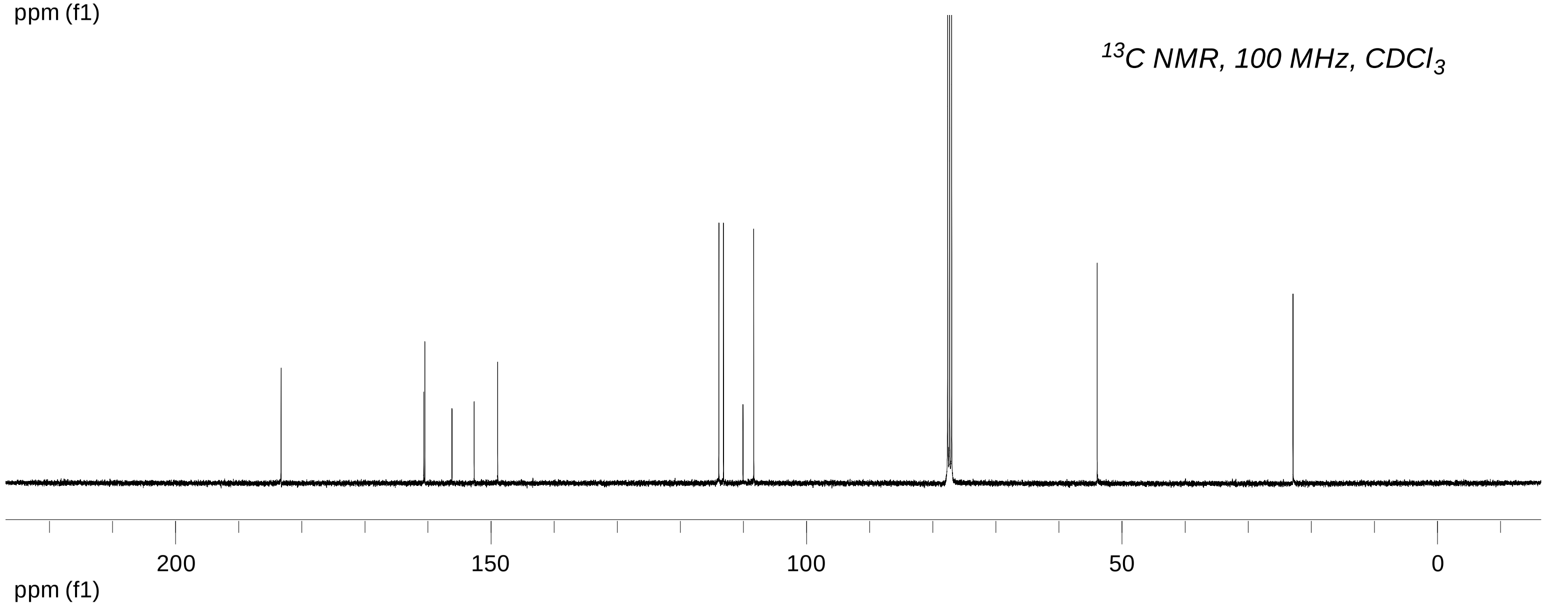


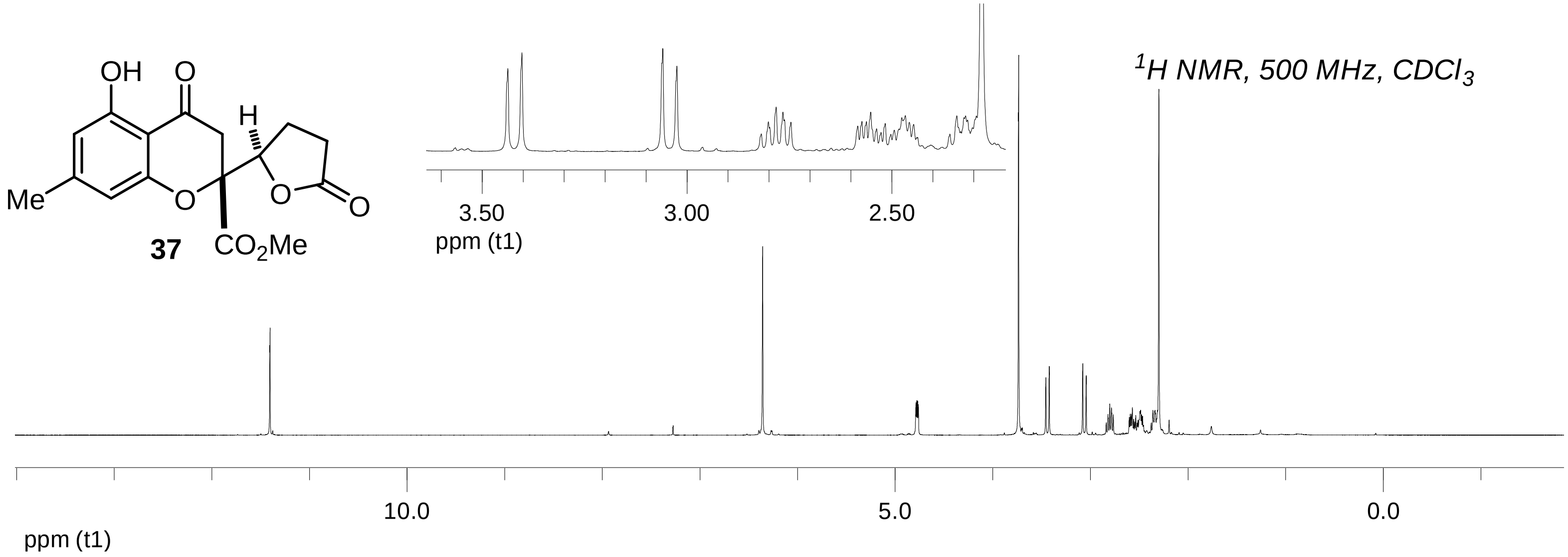
^{13}C NMR, 100 MHz, $CDCl_3$


OH
O
OH
O
MeO
O
OH
30
^{1}H NMR, 400 MHz, CDCl$_3$
2.50
2.00
ppm (f1)
15.0
10.0
5.0
0.0
ppm (f1)
^{13}C NMR, 100 MHz, CDCl$_3$
200
150
100
50
0
ppm (f1)

18

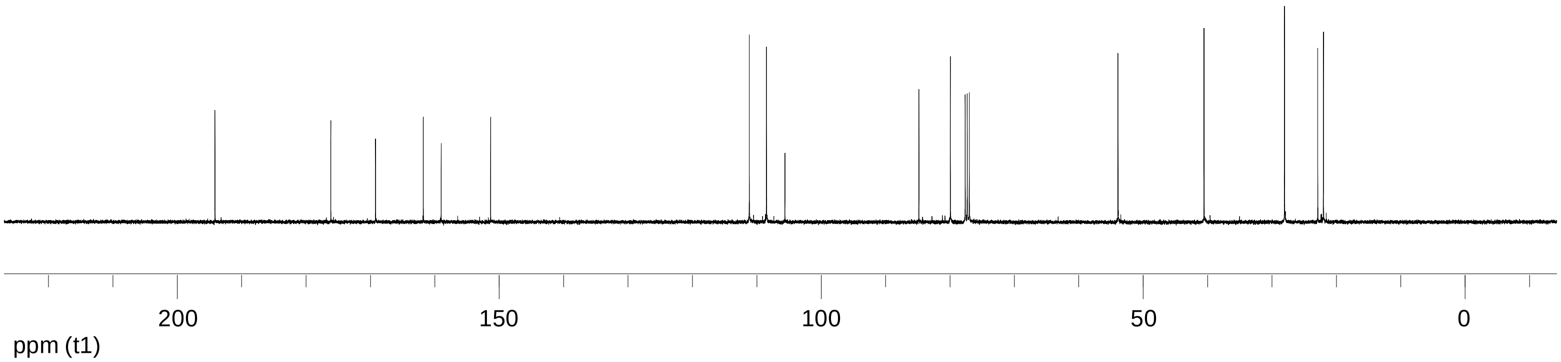

^{1}H NMR, 400 MHz, $CDCl_3$


^{13}C NMR, 100 MHz, $CDCl_3$

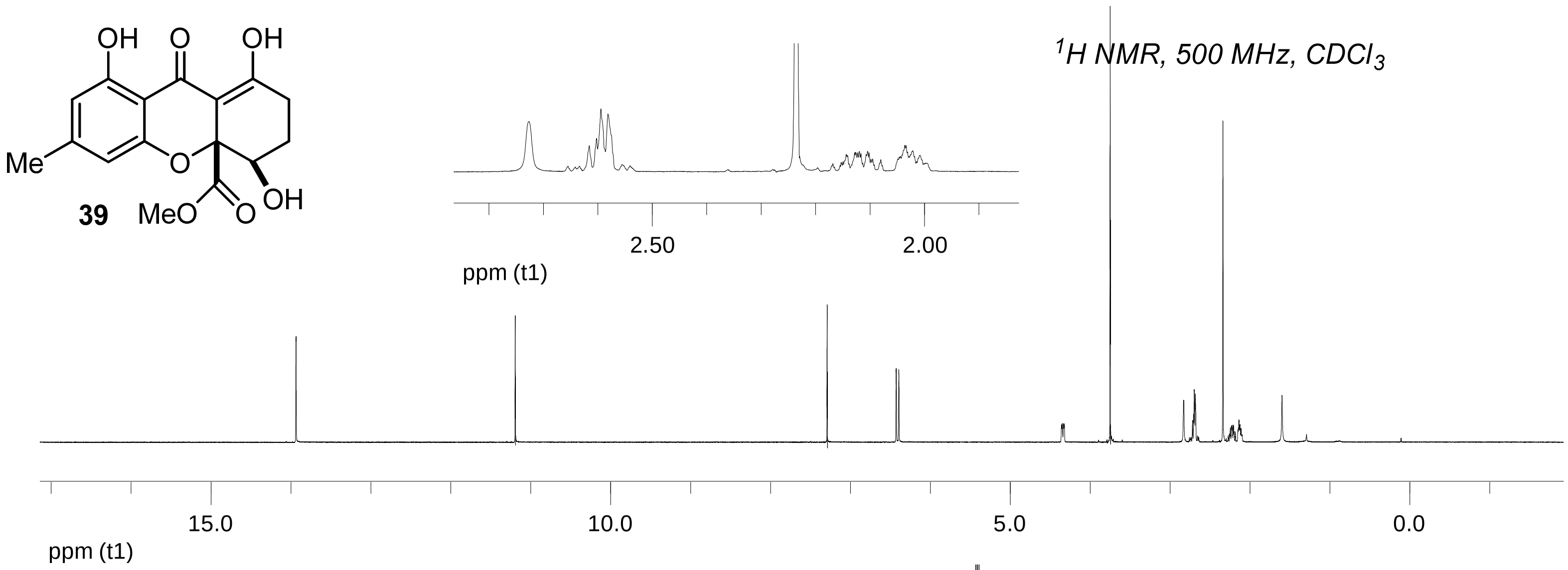


37

^{1}*H NMR, 500 MHz, CDCl$_3$*

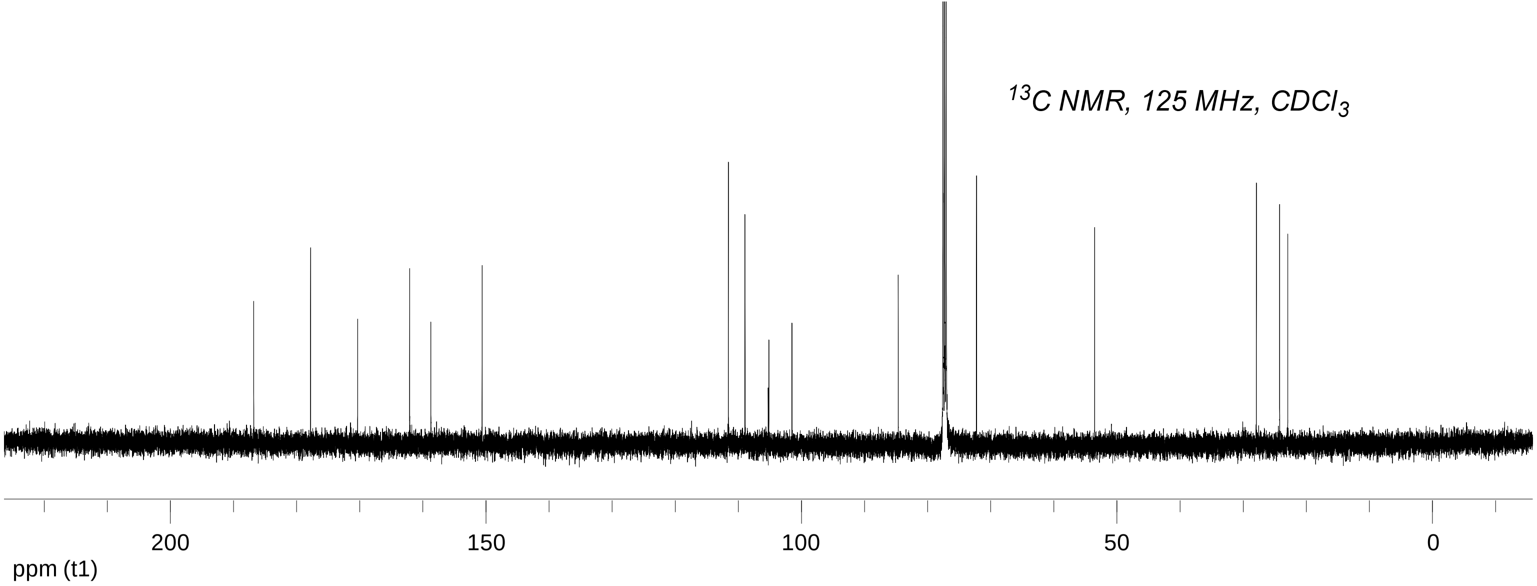


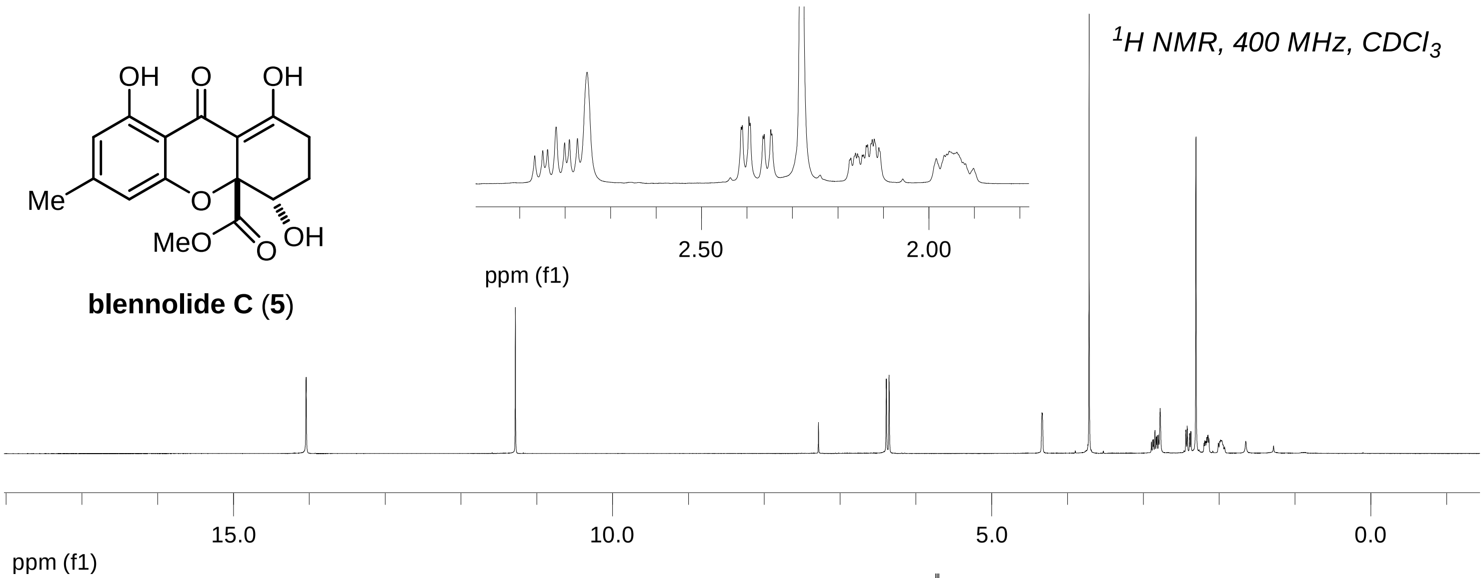
^{13}*C NMR, 100 MHz, CDCl$_3$*


OH
O
OH
Me
O
MeO
O
OH

39

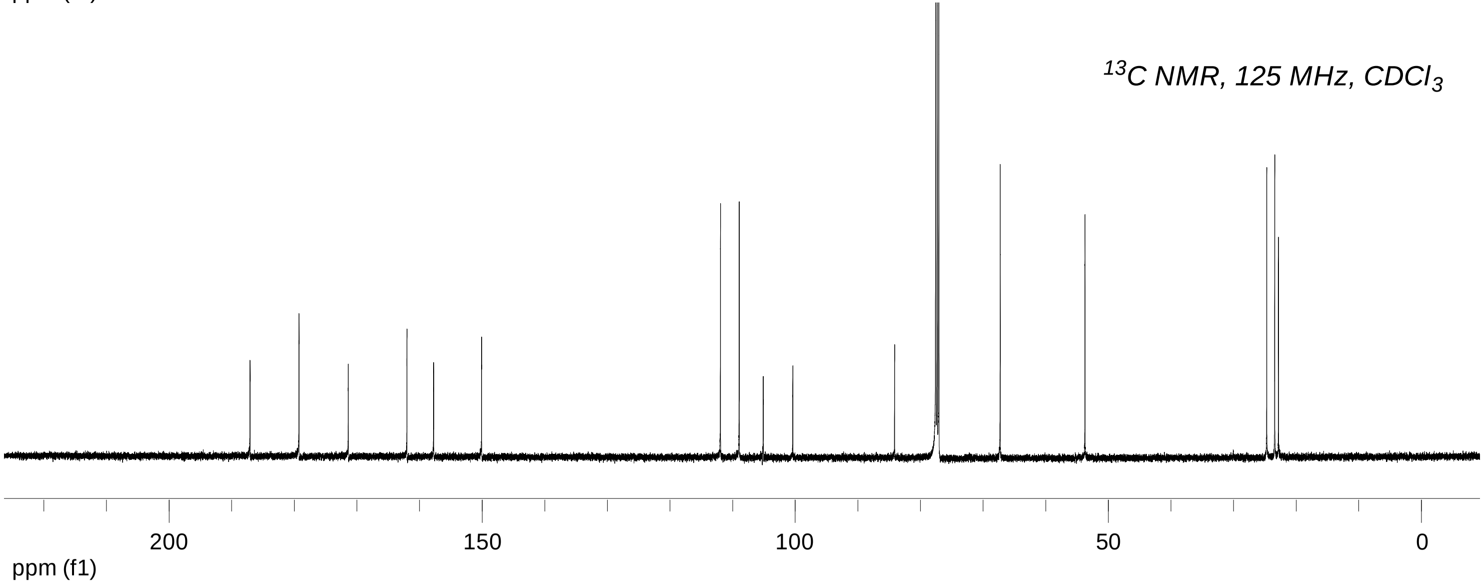
1H NMR, 500 MHz, CDCl3
2.50
2.00
ppm (t1)
15.0
10.0
5.0
0.0
ppm (t1)


13C NMR, 125 MHz, CDCl3
200
150
100
50
0
ppm (t1)

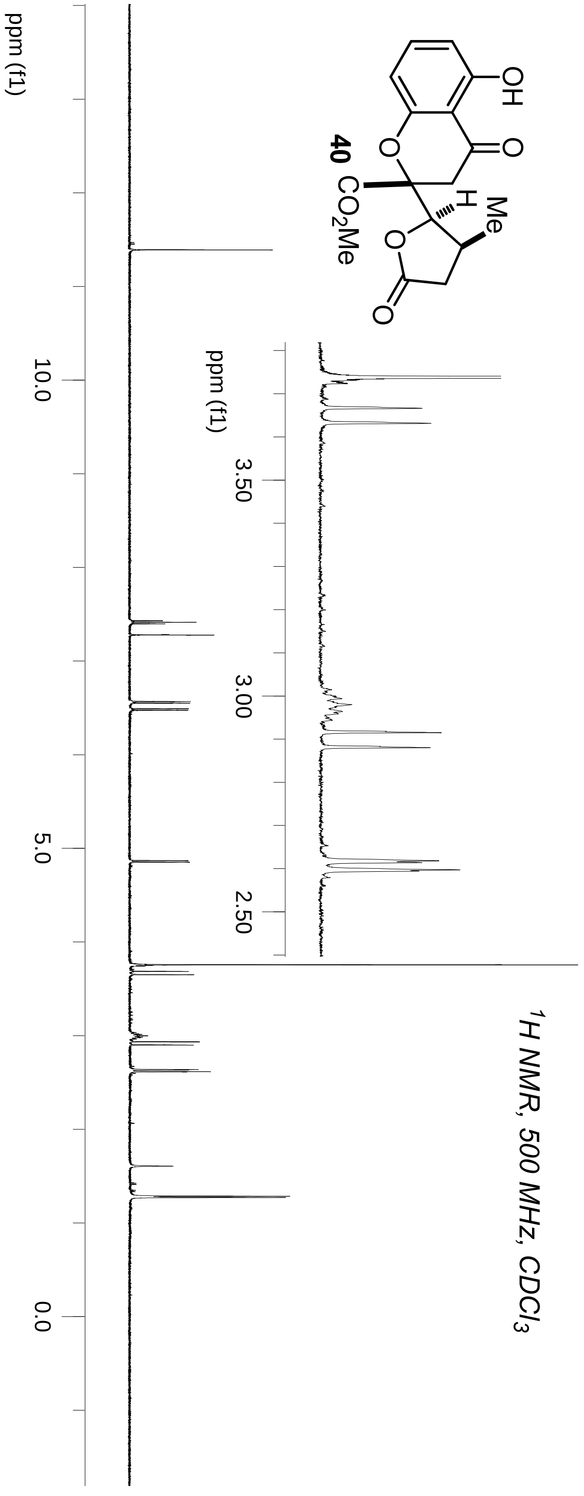


blennolide C (**5**)

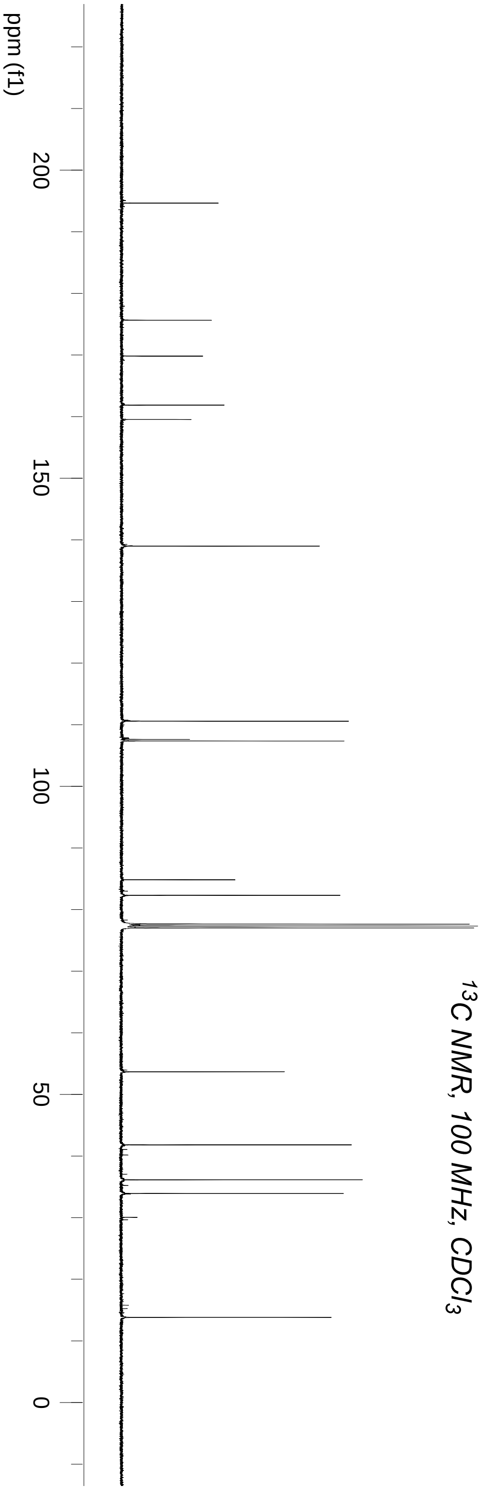
^{1}H NMR, 400 MHz, CDCl$_3$



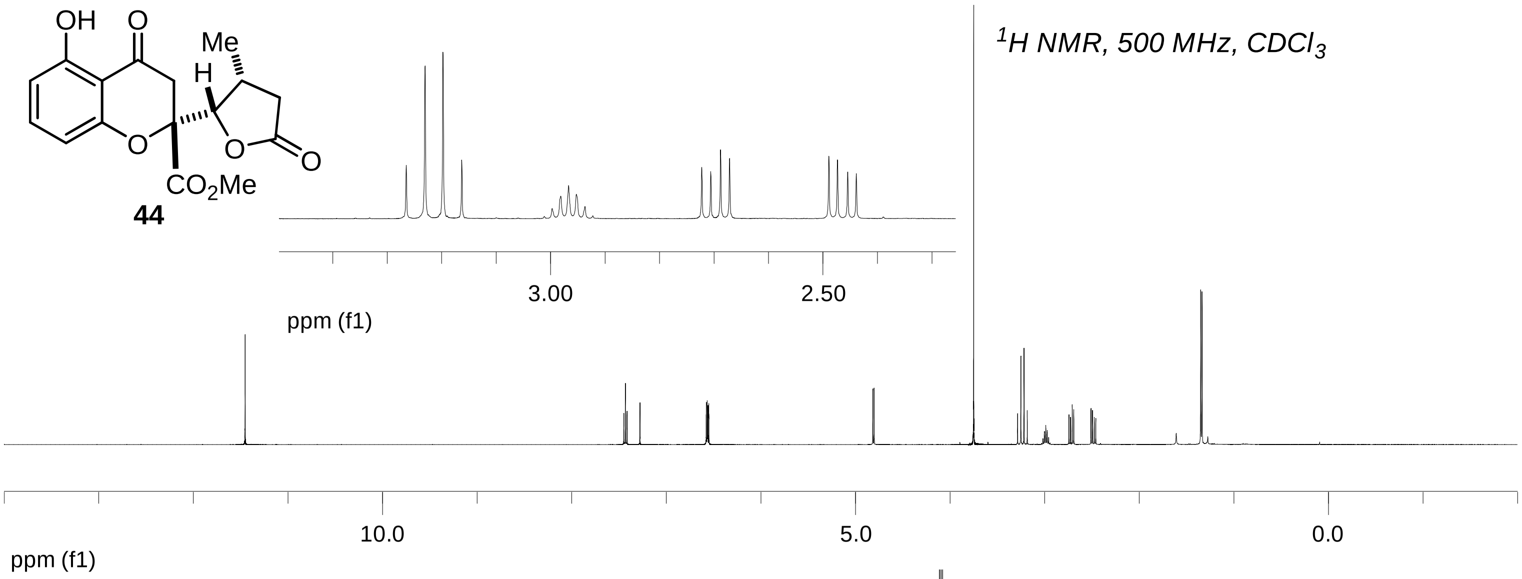
^{13}C NMR, 125 MHz, CDCl$_3$



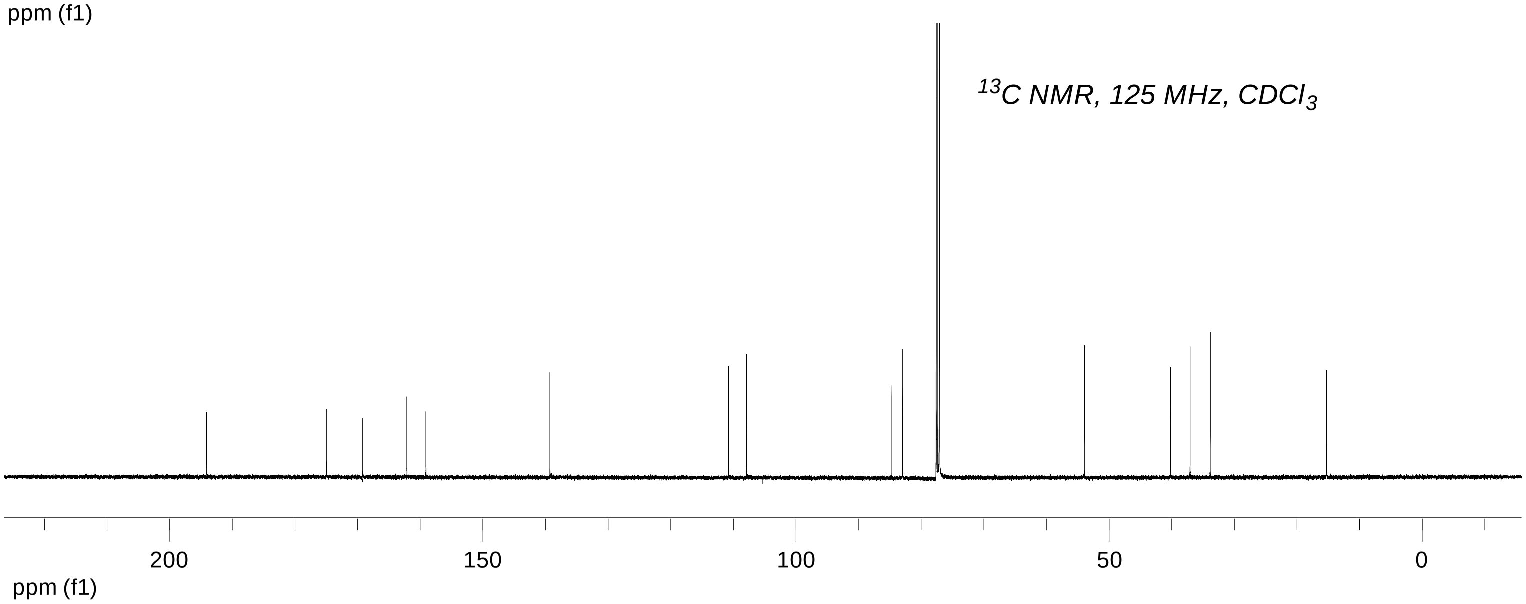
^{1}H NMR, 500 MHz, $CDCl_3$



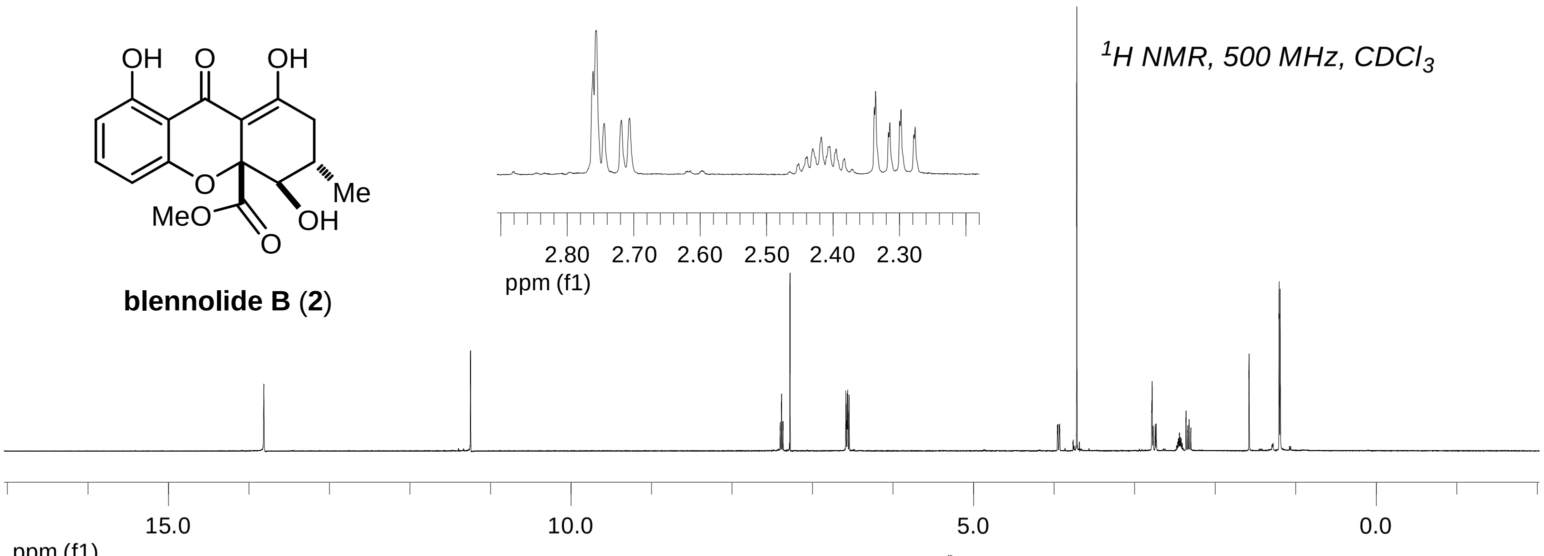
^{13}C NMR, 100 MHz, $CDCl_3$

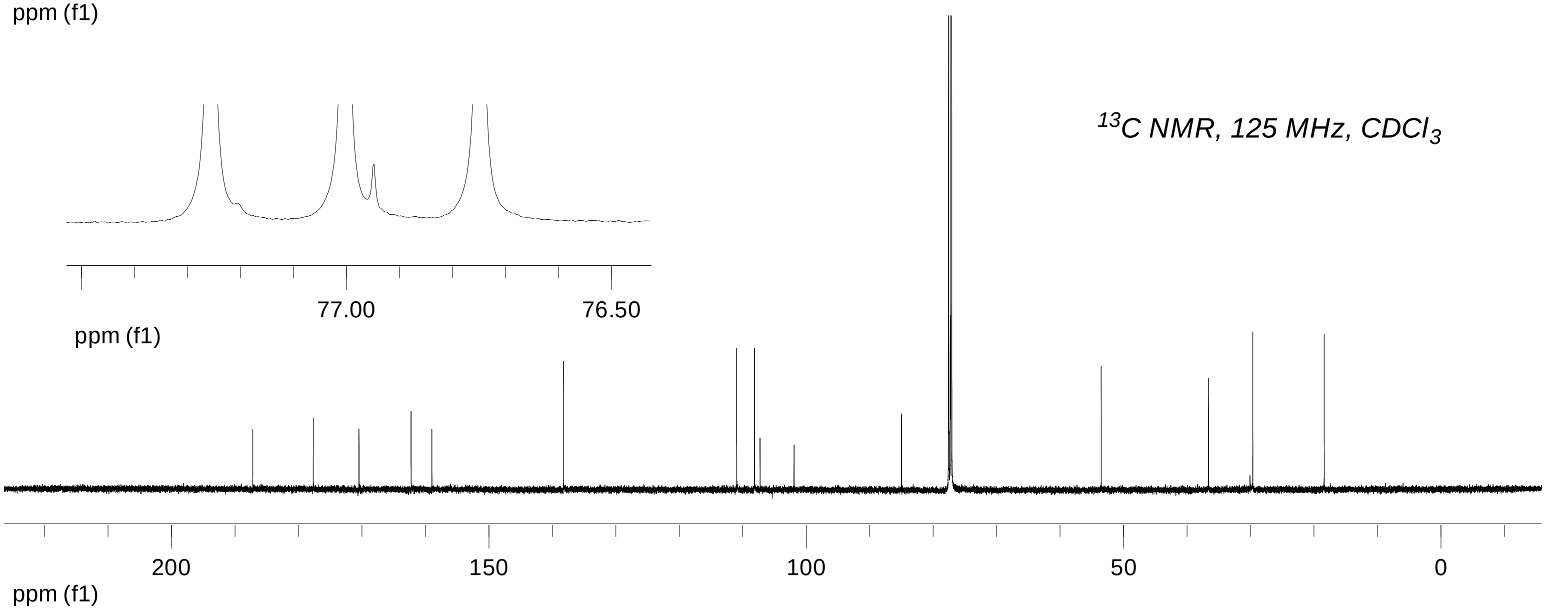

44

^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$


blennolide B (**2**)



VIII. Complete Ref. 5a

(5) (a) Parish, C. A.; Smith, S. K.; Calati, K.; Zink, D.; Wilson, K.; Roemer, T.; Jiang, B.; Xu, D.; Bill, G.; Platas, G.; Peláez, F.; Díez, M. T.; Tsou, N.; McKeown, A. E.; Ball, R. G.; Powles, M. A.; Yeung, L.; Liberator, P.; Harris, G. *J. Am. Chem. Soc.* **2008**, *130*, 7060.