Supporting Information

Total Synthesis of Plukenetione A

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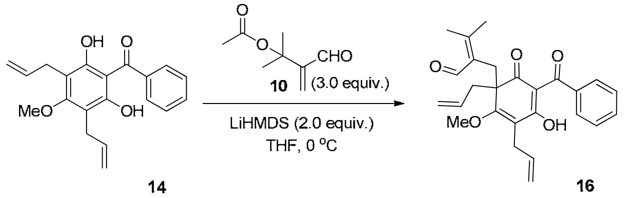
I. General Information

^1H NMR spectra were recorded at 300, 400, or 500 MHz at ambient temperature with $CDCl_3$ (Cambridge Isotope Laboratories, Inc.) as the solvent unless otherwise stated. ^{13}C NMR spectra were recorded at 75.0, 100, or 125 MHz at ambient temperature with $CDCl_3$ as the solvent unless otherwise stated. Chemical shifts are reported in parts per million relative to $CDCl_3$ (^1H, δ 7.24; ^{13}C, δ 77.0). Data for ^1H NMR are reported as follows: chemical shift, integration, multiplicity (app = apparent, 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 apparatus (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 (Scientific Absorbents, Inc.). Yields refer to chromatographically and spectroscopically pure materials unless otherwise stated. All other reagents were purchased from Sigma-Aldrich, Lancaster, Alfa Aesar, and Strem Chemicals. Methylene chloride, acetonitrile, and benzene were purified by passing through two packed columns of neutral alumina (Innovative Technology, Inc, Newburyport, MA). All 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. Spartan 08. (v1.2.0) wave function, Inc. for conformational search calculation.

II. Experimental Procedures and Compound Characterization



2-((1,3-Diallyl-5-benzoyl-4-hydroxy-2-methoxy-6-oxocyclohexa-2,4-dien-1-yl)methyl)-3-methylbut-2-enal 16. 3,5-Diallyl-2,6-dihydroxy-4-methoxyphenyl(phenyl)methanone **14**[S1] (360 mg, 1.11 mmol) was dissolved in THF (10 mL). After being stirred at room temperature for 3 minutes, the reaction mixture was cooled to 0°C. A solution of LiHMDS (2.0 equiv, 1 M in THF, 2.22 mmol) was added dropwise forming a dark orange solution. After 5 min, α-acetoxy enal **10**[S2] (3.0 equiv, 519 mg, 3.33 mmol) in 6 mL of benzene was added dropwise. The resulting mixture was stirred at 0 °C for 4 h. The reaction mixture was finally quenched with 1N HCl and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, decanted, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (7: 3 hexane/EtOAc) to afford 430 mg (1.02 mmol, 92 %) of **16** as an orange oil (1.6: 1 ratio of enol tautomers as determined by ^{1}H NMR analysis ($CDCl_3$)).

Major tautomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (1H, s), 7.45 (3H, m), 7.36 (2H, m), 5.99 (1H, m), 5.47 (1H, m), 5.25 (4H, m), 4.11 (3H, s), 3.28 (2H, m), 2.78 (2H, m), 2.65 (2H, m), 2.13 (3H, s), 1.83 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$) δ 196.7, 193.0, 190.8, 190.4, 176.0, 157.5, 138.9, 136.3, 133.6, 131.7, 130.8, 127.7 (2 carbon ovrlp), 127.3 (2 carbon ovrlp), 119.5, 117.9, 115.6, 112.1, 62.2, 59.3, 41.8, 35.7, 27.9, 24.4, 20.1.

Minor tautomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (1H, s), 7.45 (3H, m), 7.36 (2H, m), 5.85 (1H, m), 5.52 (1H, m), 5.25 (4H, m), 4.00 (3H, s), 3.14 (2H, m), 2.78 (2H, m), 2.65(2H, m), 2.07 (3H, s), 1.88 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 191.2, 190.0, 183.7, 167.8, 157.8, 138.4, 136.8, 132.7, 132.5, 131.6, 128.2 (2 carbon ovrlp), 127.6 (2 carbon ovrlp), 118.6, 114.7, 112.6, 107.7, 61.9,

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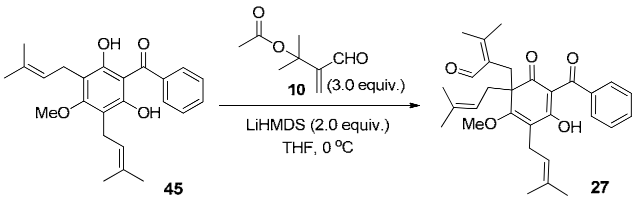
[S1] Mitasev, B.; Porco, J. A., Jr. *Org Lett.* **2009**, *11*, 2285.

[S2] Qi, J.; Porco, J. A., Jr. *J. Am. Chem. Soc.* **2007**, *129*, 12682.

54.3, 39.9, 34.9, 28.1, 24.1, 19.9.

IR ν_{mas} (film): 3300, 2919, 1674, 1594, 1450, 1218 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{26}H_{28}O_5$ 421.2015 found 421.2014 (M+H).



2-((5-Benzoyl-4-hydroxy-2-methoxy-1,3-*bis*(3-methylbut-2-en-1-yl)-6-oxocyclohexa-2,4-dien-1-yl)methyl)-3-methylbut-2-enal 27. To a stirred solution of (2,6-dihydroxy-4-methoxy-3,5-*bis*(3-methylbut-2-en-1-yl)phenyl)(phenyl) methanone **45**[S1] (117 mg, 0.39 mmol) in THF (10 mL) was added a solution of LiHMDS (2.0 equiv, 1 M in THF, 0.62 mmol) at 0°C leading to a dark orange solution. After 5 min, α-acetoxy enal **10** (3.0 equiv, 144 mg, 0.92 mmol) in 3 mL of benzene was added dropwise. The resulting mixture was stirred at 0 °C for 4 h, quenched with 1N HCl solution, and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, decanted, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (7:3 hexane/EtOAc) to afford 100 mg (0.210 mmol 70 %) of dearomatized product **27** as an orange oil (1.6: 1 ratio of enol tautomers as determined by ^{1}H NMR analysis ($CDCl_3$)).

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95 (1H, s), 7.43 (3H, m), 7.35 (2H, m), 5.07 (1H, t, *J* = 6.0, 6.0 Hz), 4.75 (1H, t, *J* = 6.3, 6.3 Hz), 4.04 (3H, s), 3.11 (2H, m), 2.61 (2H, m), 2.78 (2H, m), 2.11 (3H, s), 1.82 (3H, m), 1.71 (3H, s), 1.70 (3H, s), 1.62 (3H, s), 1.58 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 191.5, 188.8, 188.4, 174.2, 155.6, 137.9, 133.3, 130.7, 131.4, 130.5, 129.8, 126.9 (2 carbon ovrlp), 126.5 (2 carbon ovrlp), 121.7, 118.4, 114.5, 62.4, 59.5, 37.8, 36.3, 26.8, 25.4, 25.0, 24.0, 21.2, 19.2, 19.1.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (1H, s), 7.43 (3H, m), 7.35 (2H, m), 4.94 (1H, t, *J* = 6.0, 6.0 Hz), 4.79 (1H, t, *J* = 6.3, 6.3 Hz), 3.92 (3H, s), 3.11 (2H, m), 2.61 (2H, m), 2.78 (2H, m), 2.07 (3H, s), 1.88 (3H, m), 1.68 (3H, s), 1.64 (3H, s), 1.62 (3H, s), 1.60 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 189.9, 182.3, 188.1, 165.9, 155.4, 137.5, 134.0, 131.7,

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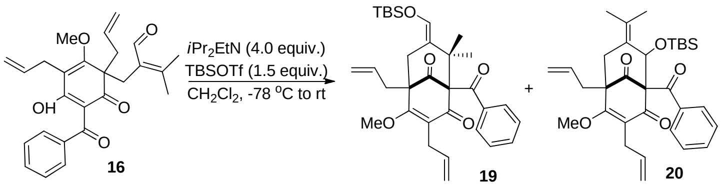
130.9, 130.6, 130.5, 127.3 (2 carbon ovrlp), 126.7 (2 carbon ovrlp), 122.0, 117.7, 112.2, 62.0, 54.6, 35.7, 35.6, 32.4, 26.7, 26.5, 24.2, 21.0, 19.2, 19.0.

IR ν_{mas} (film): 3502, 2923, 2853, 1669, 1515, 1260, 1096 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{30}H_{36}O_5Na$ 499.2499 found 499.2460 (M+Na).



19: 20 = 3 : 1

Bicyclo[3.3.1] nonane derivatives 19 and 20: To a stirred solution of aldehyde **16** (140 mg, 0.333 mmol) in CH_2Cl_2 (10 mL) was added *N*, *N*-diisopropylethylamine (4 equiv, 0.23 mL, 1.30 mmol) at -78 °C followed by dropwise addition of *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.5 equiv, 115 μL, 0.16 mmol). The reaction was gradually warmed to room temperature and stirred overnight (16 h). The reaction was diluted with ethyl acetate and quenched by addition of sat. NH_4Cl solution, the aqueous layer was extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, decanted, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (100:3 hexane/EtOAc) to afford 74 mg (0.139 mmol 43%) of **19** and 24 mg (0.045 mmol 13%) of **20** as colorless oils.

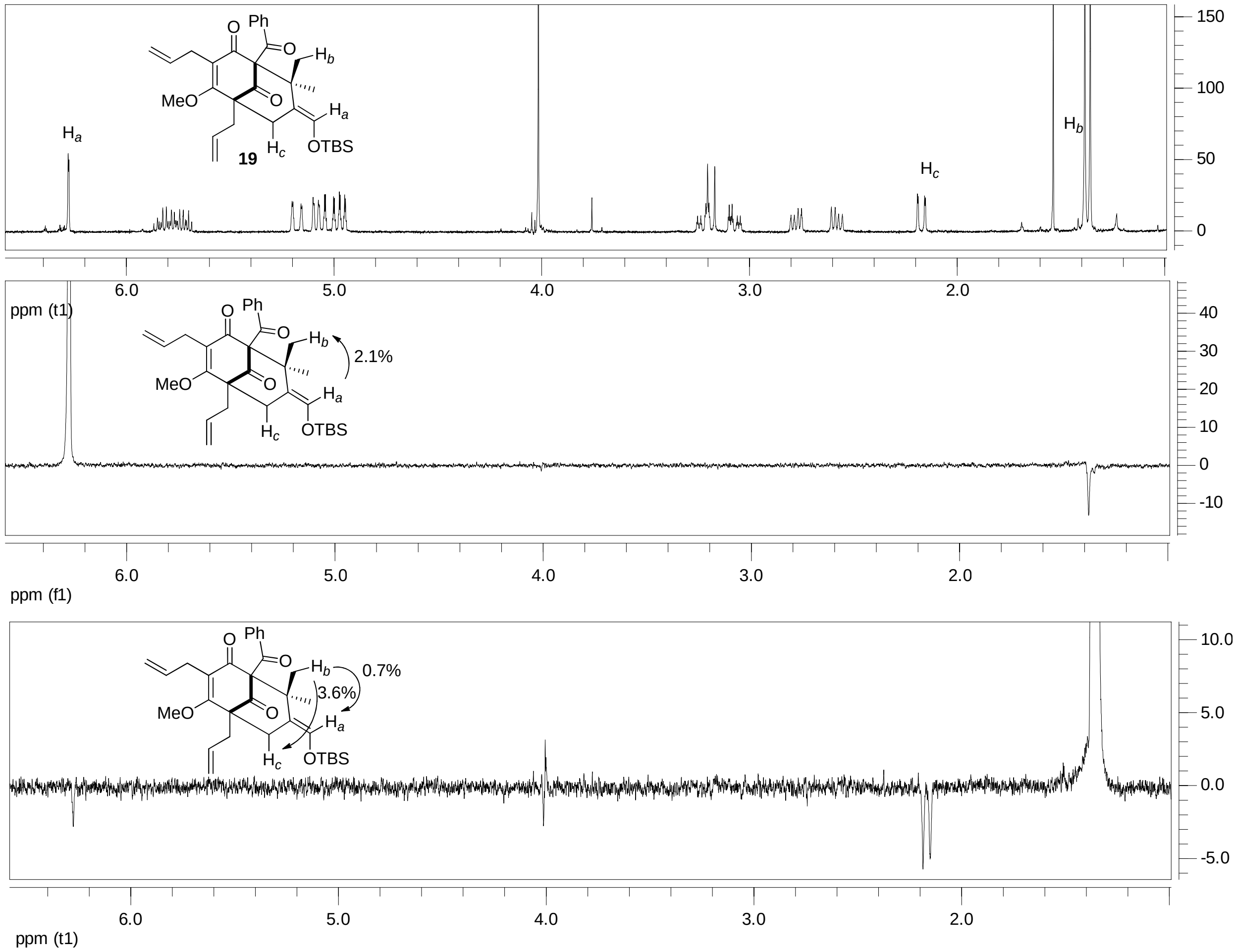
Silyl enol ether **19** : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (2H, d, *J* = 7.2 Hz), 7.35 (1H, d, *J* = 7.3 Hz), 7.21 (2H, d, *J* = 7.3 Hz), 6.27 (1H, s), 5.77 (2H, m), 5.05 (4H, m), 4.01 (3H, s), 3.20 (2H, m), 2.77 (1H, d, *J* = 14.0 Hz), 2.57 (1H, d, *J* = 14.0 Hz), 2.16 (1H, d, *J* = 14.0 Hz), 1.38 (3H, s), 1.36 (3H, s), 0.88 (9H, s), 0.10 (3H, s), 0.07 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$) δ 207.1, 194.5, 194.1, 173.4, 138.1, 136.5, 136.0, 134.1, 132.3, 128.8 (2 carbon ovrlp), 128.2 (2 carbon ovrlp), 123.3, 120.9, 118.9, 115.7, 78.7, 63.0, 59.5, 48.2, 35.4, 34.2, 28.2, 25.3 (3 carbon ovrlp), 23.6, 20.0, 17.8, -5.6, -6.0.

IR ν_{mas} (film): 2930, 2857, 1721, 1598, 1340, 1221 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{32}H_{42}O_5SiNa$ 557.2699 found 557.2719 (M+Na).

Key nOe data (400 MHz, $CDCl_3$) for silyl enol ether **19**



Silyl ether **20**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (2H, d, J = 8.3 Hz), 7.41 (1H, dd, J = 8.3, 8.3 Hz), 7.28 (2H, dd, J = 8.3, 8.3 Hz), 5.89 (2H, m), 5.68 (2H, m), 5.56 (1H, d, J = 2.0 Hz), 5.11 (2H, m), 4.98 (2H, m), 4.03 (3H, s), 3.15 (2H, m), 3.20 (2H, m), 2.65 (3H, m), 2.60 (1H, dd, J = 13.7, 2.0 Hz), 1.68 (3H, d, J = 1.68 Hz), 1.60 (3H, s), 0.75 (9H, s), 0.18 (3H, s), 0.04 (3H, s),.

^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 193.1, 192.6, 174.5, 136.9, 136.5, 135.5, 133.9, 133.4, 129.1 (2 carbon ovrlp), 129.0 (2 carbon ovrlp), 127.5, 122.8, 119.1, 116.4, 79.8, 74.8, 63.2, 60.3, 38.2, 35.4, 28.9, 25.9 (3 carbon ovrlp), 21.0, 20.8, 18.4, -4.8, -4.9.

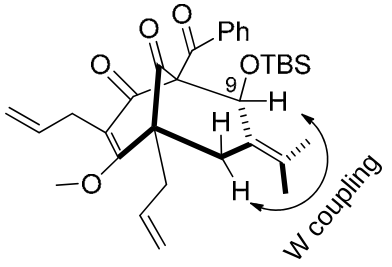
IR ν_{mas} (film): 2927, 2856, 1733, 1695, 1248, 1082 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{32}H_{42}O_5Si$ 535.2880 found 535.2902 (M+H).

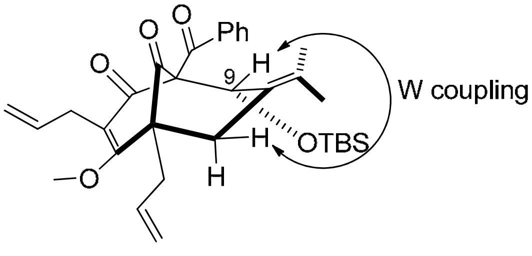
Assignment of the C9 stereocenter for silyl ether **20** was attempted. The proton at C9 has a unique W coupling (J = 2 Hz), which was thought be helpful for the assignment. However, calculations[S3]

[S3] Calculations performed using Spartan 08, v1.2.0. conformer search at the ground state, semi-empirical, AM1.

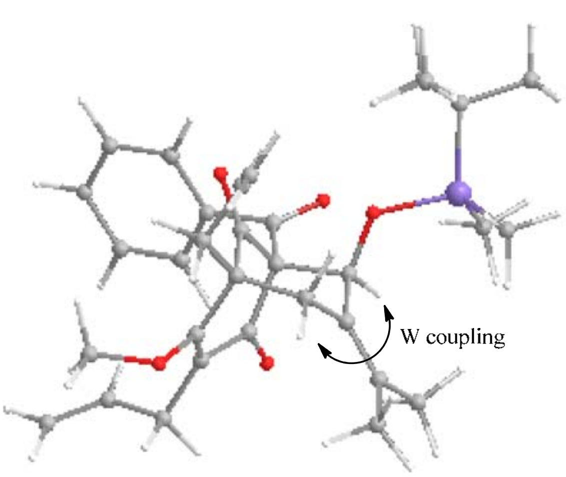
revealed that both **20-chair** and **20- boat** ground state conformers are likely to have W coupling. NOe experiments did not give conclusive information on the stereochemical assignment. Attempted desilylation of **20** led to decomposition. Accordingly, we were not able to assign the C9 stereocenter of silyl ether **20**.



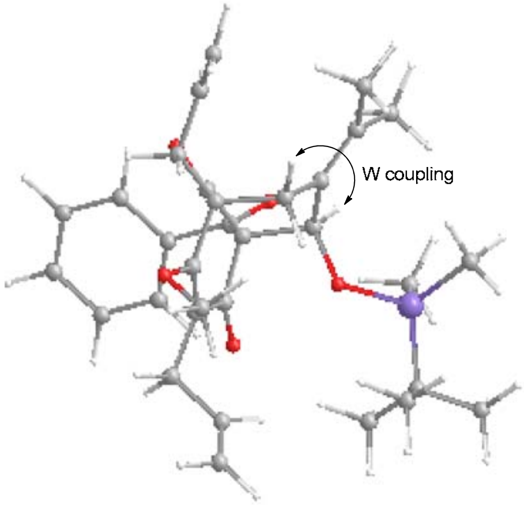
20- chair



20- boat

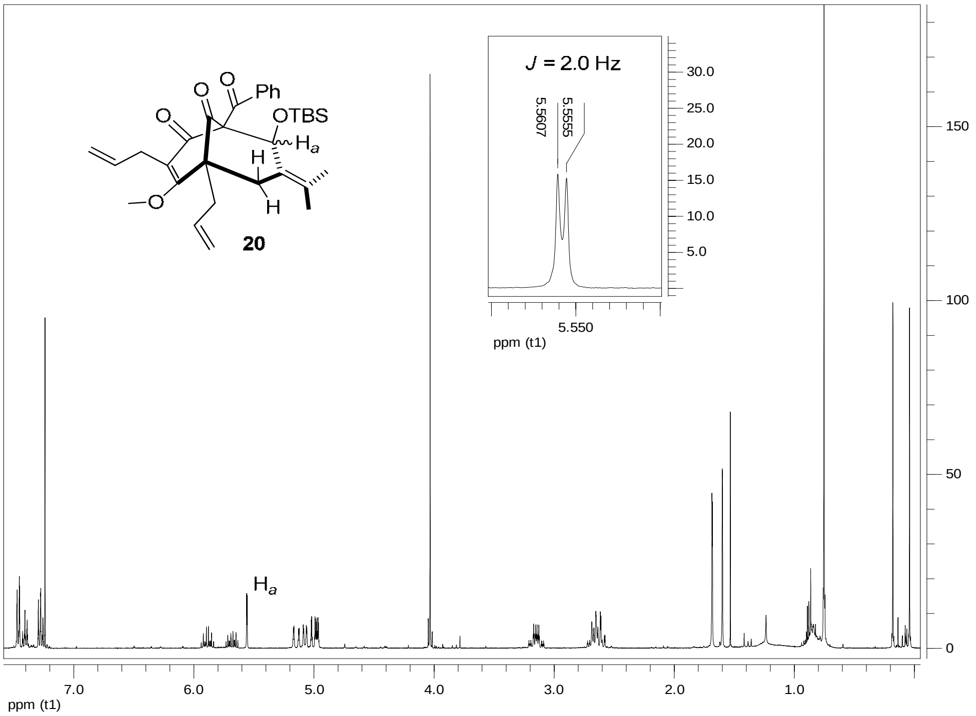


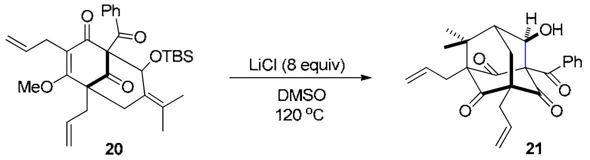
20 - chair



20- boat

^{1}H NMR (400 MHz, $CDCl_3$) for **20**





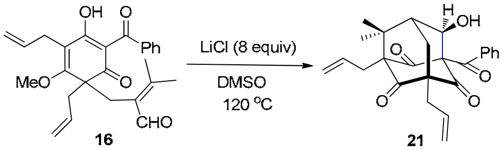
3,5-Diallyl-1-benzoyl-8-hydroxy-6,6-dimethyladamantane-2,4,9-trione 21. To silyl ether **20** (11.0 mg, 0.021 mmol) and LiCl (8.0 equiv, 7.0 mg, 0.16 mmol) was added DMSO (2.0 mL) at room temperature and the reaction mixture was heated for 2 h at 120 °C. The reaction was diluted with EtOAc and quenched with water and the organic layer washed two times with water. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (10: 1 hexane/EtOAc) to afford 4.2 mg (50 %) of adamantane **21** as a colorless film.

^{1}H NMR (400 MHz, $CDCl_3$) **21**: δ 7.50 (1H, dt, *J* = 7.1, 2.0, 2.0 Hz), 7.32 (4H, m), 5.89 (1H, m), 5.68 (1H, m), 5.20(1H, ddd, *J* = 5.7, 2.7, 2.5 Hz), 5.11 (4H, m), 4.16 (1H, d, *J* = 2.7 Hz), 2.78 (1H, dd, *J* = 13.4, 2.8 Hz), 2.56 (3H, m), 2.45 (1H, m), 2.42 (1H, ddd, *J* = 13.7, 2.6, 2.5 Hz), 2.13 (1H, ddd, *J* = 5.7, 2.8, 2.6 Hz), 1.17 (3H, s), 1.10 (3h, s).

^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 195.9, 194.9, 194.4, 132.6, 132.4, 131.9, 131.6, 128.5 (two carbon ovrlp), 127.1 (two carbon ovrlp), 118.4, 118.3, 82.6, 80.3, 75.7, 68.1, 49.7, 47.3, 40.0, 34.2, 29.3, 24.7, 24.0.

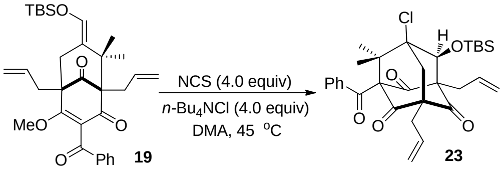
IR ν_{mas} (film): 35341, 3078, 2925, 2851, 1742, 1701, 1455, 1233 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{25}H_{26}O_5$ 407.1858 found 407.1853 (M+H).



3,5-Diallyl-1-benzoyl-8-hydroxy-6,6-dimethyladamantane-2,4,9-trione 21. To aldehyde **16** (20.0 mg, 0.048 mmol) and LiCl (8.0 equiv, 16.1 mg, 0.38 mmol) was added DMSO (4.0 mL) at room temperature and the reaction mixture was heated for 2 h at 120 °C. The reaction was diluted with EtOAc and quenched with water and the organic layer washed two times with water. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (10: 1 hexane/EtOAc) to afford 13.0 mg (65 %) of adamantane **21** as a colorless film.

(The spectral data for compound **21** obtained using this procedure were found to be identical to those provided on page S8)



1,3-Diallyl-5-benzoyl-8-((tert-butyldimethylsilyl)oxy)-7-chloro-6,6-dimethyladamantane-2,4,9-trione 23. To a stirred solution of silyl enol ether **19** (8.0 mg, 0.015 mmol) and tetra-*N*-butylammonium chloride (4.0 equiv, 17.0 mg, 0.06 mmol) in *N, N*-dimethylacetamide (1.2 mL) was slowly added *N*-chlorosuccinimide (4.0 equiv, 8.0 mg, 0.06 mmol) in *N, N*-dimethylacetamide (0.1 mL) at room temperature, and the reaction mixture heated to 45 °C for 1 h. The reaction mixture was finally quenched with water and aqueous layer extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, decanted, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (30:1 hexane/EtOAc) to afford 6.0 mg (72%) of **23** as a white film.

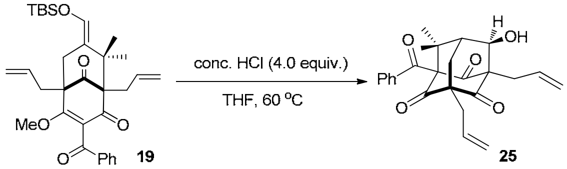
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (1H, m), 7.27 (2H, dd, J = 8.4, 8.4 Hz), 7.10 (2H, d, J = 8.4

Hz), 5.77 (2H, m), 5.17 (4H, m), 4.40 (1H, d, *J* = 2.5 Hz), 3.11 (1H, d, *J* = 13.1, Hz), 2.89 (1H, m), 2.59 (1H, m), 2.45 (3H, m), 1.59 (3H, s), 1.44 (3H, s), 0.94 (9H, s), 0.19 (3H, s), 0.18 (3H, s).

^{13}C NMR (75 MHz, $CDCl_3$) δ 199.6, 198.6, 196.8, 191.4, 134.5, 132.7, 132.1, 132.0, 129.1 (2 carbon ovrlp), 128.1(2 carbon ovrlp), 119.9, 119.8, 84.7, 80.7, 76.3, 75.4, 67.4, 54.2, 44.5, 32.9, 31.7, 26.2 (3 carbon ovrlp), 19.6, 19.3, 18.8, -3.1, -3.4.

IR ν_{mas} (film): 3075, 2938, 2863, 1636, 1591, 1508, 1453, 1422 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{31}H_{39}O_5SiCl$ 555.2334 found 555.2325 (M+H).



1,3-Diallyl-5-benzoyl-8-hydroxy-6,6-dimethyladamantane-2,4,9-trione 25. To a stirred solution of silyl enol ether **19** (40 mg, 0.075 mmol) in THF (2.4 mL) was slowly added concentrated HCl (4.0 equiv, 25.0 μL 0.30 mmol) and the resulting mixture heated to 60 °C for 14 h. The reaction mixture was finally quenched with water and aqueous layer extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, decanted, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (10:1 hexane/EtOAc) to afford 21.0 mg (0.052 mmol 69 %) of adamantane **25** as a white solid.

Adamantane **25**: m.p. 122 – 126 °C (petroleum ether)

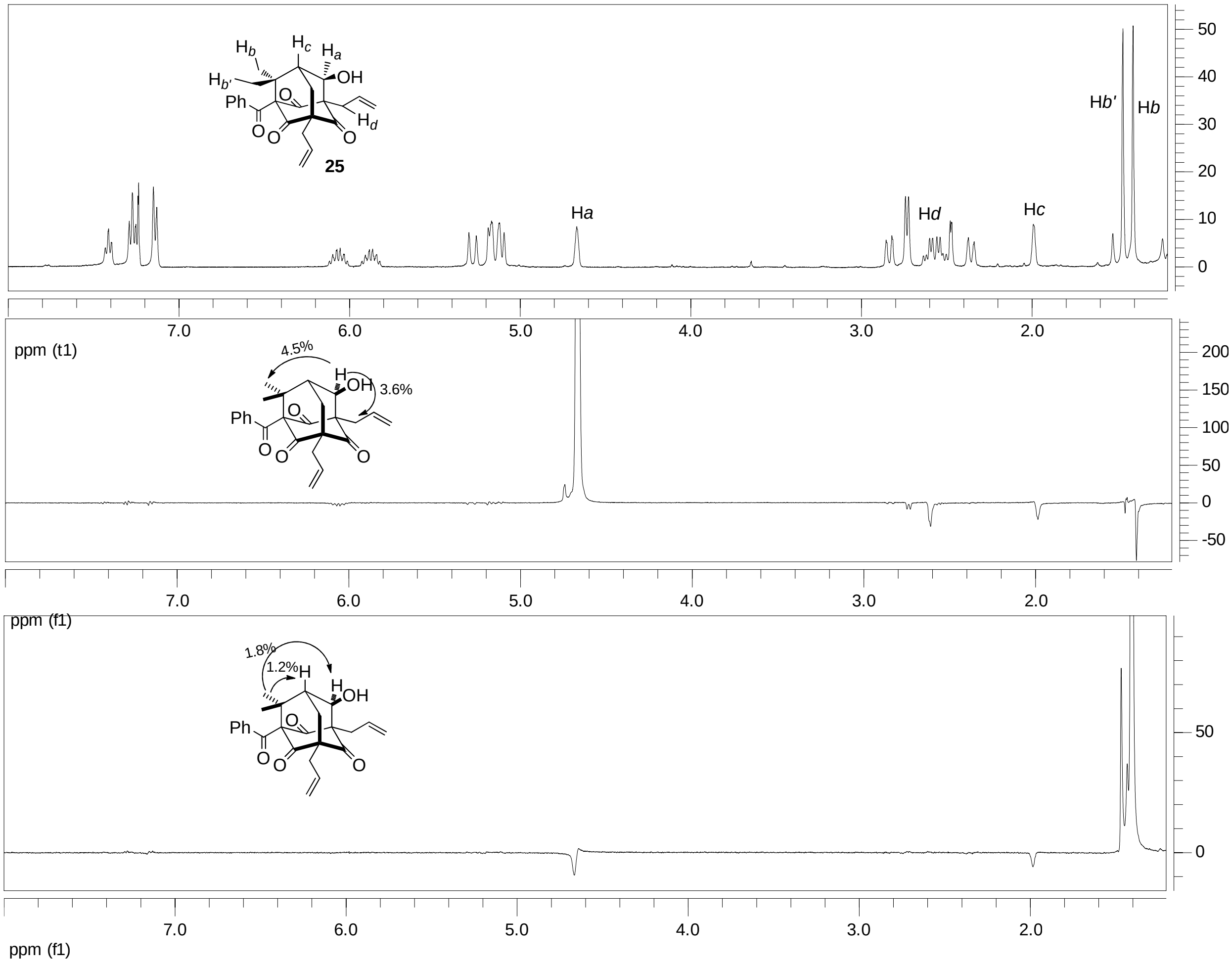
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (1H, t, *J* = 7.6 Hz), 7.27 (2H, dd, *J* = 7.6, 7.6 Hz), 7.13 (2H, d, *J* = 7.6 Hz), 6.02 (1H, m), 6.86 (1H, m), 5.16 (4H, m), 4.63 (1H, ddd, *J* = 2.8, 2.8, 2.0 Hz), 2.82 (1H, dd, *J* = 13.6, 2.8 Hz), 2.76 (1H, d, *J* = 4.0 Hz), 2.71 (1H, brs), 2.70 (1H, d, *J* = 4.0 Hz), 2.55 (2H, m), 2.33 (1H, dt, *J* = 13.6, 2.8, 2.8 Hz), 1.95 (1H, q, *J* = 2.8, 2.8, 2.8 Hz), 1.45 (3H, s), 1.38 (3H, s)

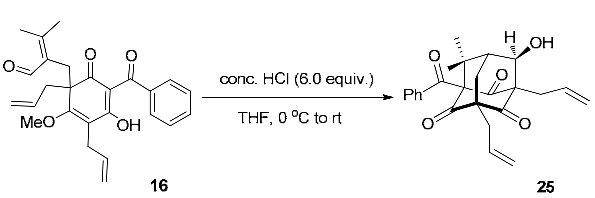
^{13}C NMR (100 MHz, $CDCl_3$) δ 201.9, 201.3, 199.7, 193.3, 135.1, 134.5, 133.0, 132.9, 129.2 (2 carbon ovrlp), 128.3 (2 carbon ovrlp), 119.8, 119.5, 81.2, 78.4, 74.7, 67.4, 50.7, 48.3, 38.0, 33.1, 30.7, 22.9, 22.7.

IR ν_{mas} (film): 3531, 3079, 2919, 1746, 1691, 1442, 1227 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{25}H_{26}O_5$ 407.1858 found 407.1863 (M+H).

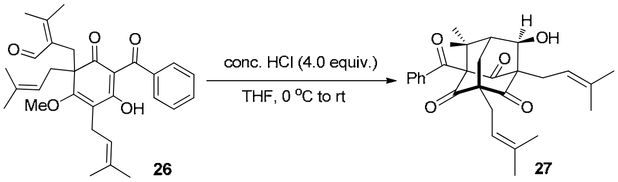
Key nOe data (400 MHz, $CDCl_3$) for adamantane **25**





1,3-Diallyl-5-benzoyl-8-hydroxy-6,6-dimethyladamantane-2,4,9-trione 25. To a stirred solution of aldehyde **16** (250 mg, 0.594 mmol) in THF (6 mL) was slowly added concentrated HCl (6.0 equiv, 243 *μ*L 2.97 mmol) at 0 °C and the reaction was gradually warmed to room temperature and stirred for 48 h. The reaction mixture was finally quenched with water and the aqueous layer extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, decanted, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (10:1 hexane/EtOAc) to afford 187 mg (0.46 mmol 75 %) of **25** as a white solid.

(The spectral data for compound **25** obtained using this procedure were found to be identical to those provided on page S10)



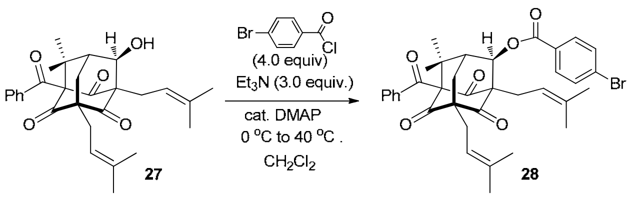
5-Benzoyl-8-hydroxy-6,6-dimethyl-1,3-*bis*(3-methylbut-2-en-1-yl)adamantane-2,4,9-trione 27. To a stirred solution of aldehyde **26** (50 mg, 0.105 mmol) in THF (1.1 mL) was slowly added concentrated HCl (4.0 equiv, 24.0 μL 0.420 mmol) at 0 °C and the reaction was gradually warmed to room temperature. The reaction mixture was stirred for 40 h. The reaction was quenched with water and aqueous layer extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, decanted, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (12:1 hexane/EtOAc) to afford 14.0 mg (0.03 mmol 30 %) of adamantane **27** as a white film.

Adamantane **27**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (1H, t, J = 7.5 Hz), 7.26 (2H, dd, J = 7.5, 7.5 Hz), 7.14 (2H, d, J = 7.5 Hz), 5.36 (1H, dd, J = 7.0, 1.5 Hz), 5.17 (1H, dd, J = 7.0, 1.5 Hz), 4.64 (1H, m), 2.84 (1H, dd, J = 13.5, 2.8 Hz), 2.72 (1H, m), 2.64 (1H, m), 2.53 (1H, d, J = 3.0 Hz), 2.51 (2H, d, J = 7.0 Hz), 2.35 (1H, ddd, J = 2.8, 2.5, 2.5 Hz), 1.72 (3H, s), 1.71 (3H, s), 1.68 (3H, s), 1.47 (3H, s), 1.41 (3H, s).

^{13}C NMR (75 MHz, $CDCl_3$) δ 202.3, 202.0, 200.0, 193.5, 136.7, 135.4, 135.3, 132.8, 129.3 (2 carbon ovrlp), 128.3 (2 carbon ovrlp), 119.2, 118.5, 81.2, 79.2, 74.9, 68.3, 50.7, 48.3, 38.0, 27.3, 25.8, 25.7, 24.8, 23.0, 22.8, 17.7, 17.6.

IR ν_{mas} (film): 3485, 2923, 2843, 1733, 1699, 1446, 1252 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{29}H_{34}O_5$ 463.2484 found 463.2502 (M+H).



5-Benzoyl-4,4-dimethyl-1,7-*bis*(3-methylbut-2-en-1-yl)-6,8,9-trioxoadamantan-2-yl 4-bromobenzoate 28. To a stirred solution of adamantane **27** (4.1 mg, 0.09 mmol), DMAP (0.09 equiv, 0.10 mg, 0.001 mmol) and 4-bromobenzoyl chloride (4.0 equiv, 7.8 mg, 0.035 mmol) in CH_2Cl_2 (0.20 mL) was added triethylamine (3.0 equiv, 3.7 μL, 0.027 mmol). The reaction was heated at 40°C for 1 h. The resulting mixture was quenched with sat. NH_4Cl solution and extracted twice with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by preparative thin layer chromatography (10: 1 hexane/EtOAc) to afford 2.0 mg (0.0031 mmol 35 %) of **28** as a white solid.

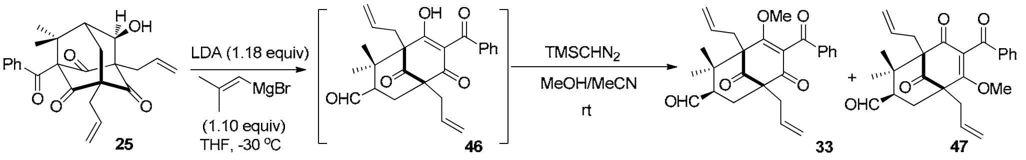
Adamantane **28**: m.p. = 140-145°C (petroleum ether)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (2H, d, J = 8.4 Hz), 7.61 (2H, d, J = 8.4 Hz), 7.43 (1H, d, J = 7.6 Hz), 7.29 (2H, dd, J = 7.6, 7.6 Hz), 7.18 (2H, d, J = 7.6 Hz), 5.82 (1H, dd, J = 3.7, 2.4 Hz), 5.22(1H, t, J = 7.0 Hz), 5.14 (1H, m), 2.73 (1H, d, J = 15.4 Hz), 2.64 (1H, dd, J = 13.7, 2.7 Hz), 2.55 (3H, m), 2.35 (1H, ddd, J = 13.7, 2.7, 2.4 Hz), 2.28 (1h, dt, J = 3.7, 2.7, 2.7 Hz), 1.69 (3H, s), 1.64 (3H, s), 1.57 (3H, s), 1.56 (3H, s), 1.48 (3H, s), 1.35 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 200.6, 198.1, 192.5, 163.5, 136.2, 135.6, 134.9, 132.6, 132.4 (two carbon ovrlp), 132.2 (two carbon ovrlp), 131.9 (two carbon ovrlp), 131.0 (two carbon ovrlp), 130.2, 129.2, 118.1, 117.1, 81.7, 79.1, 72.5, 68.3, 51.5, 46.0, 38.8, 27.5, 26.1, 25.9, 24.8, 23.2, 23.0, 18.1, 17.9.

IR ν_{mas} (film): 2923, 2847, 1788, 1712, 1573, 1260, 999, 741 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{36}H_{37}BrO_6$ 645.1852 found 645.1861 (M+H).



1,5-Diallyl-7-benzoyl-6-methoxy-4,4-dimethyl-8,9-dioxobicyclo[3.3.1]non-6-ene-3-carbaldehyde 33 and **1,5-diallyl-7-benzoyl-6-methoxy-2,2-dimethyl-8,9-**

dioxobicyclo[3.3.1]non-6-ene-3-carbaldehyde 47. To a stirred solution of adamantane **25** (20 mg, 0.0492 mmol) in THF (0.10 mL) was slowly added freshly prepared LDA (1.18 equiv, 0.05 M, 12.0 µL, 0.058 mmol) at -78 °C. After 10 minutes, 2-methyl-1-propenyl-magnesium bromide (1.10 equiv, 0.5 M in THF, 103.0 µL, 0.0517 mmol) was added dropwise. The reaction mixture was stirred at the same temperature for 1 h, gradually warmed to -50 °C, and stirred for 1 d. After this time, TLC analysis (3:1 hexane: EtOAc) indicated that starting material remained along with a new polar spot. The reaction was quenched with 1N HCl and aqueous layer extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo* to afford a yellow oil. To this stirred crude residue in acetonitrile (450 µL) was added MeOH (50 µL) at room temperature, followed by the slow addition of trimethylsilyldiazomethane (1.5 equiv, 2 M in hexane, 37.0 µL, 0.074 mmol). The resulting reaction mixture was stirred for 1 h and the reaction mixture was concentrated *in vacuo*. The residue was purified by preparative thin layer chromatography (6: 1 hexane/EtOAc) to afford 6.4 mg (31 %) of the inseparable isomers **33** and **47** as a colorless oil (1: 2 ratio of methyl enol ethers as determined by ^{1}H NMR analysis ($CDCl_3$)).

^{1}H NMR (400 MHz, $CDCl_3$) **33**: δ 9.80 (1H, s), 7.78 (2H, dd, *J* = 7.5, 7.5 Hz), 7.54 (1H, dd, *J* = 7.5, 7.5 Hz), 7.42 (2H, dd, *J* = 7.5, 7.5 Hz), 5.76 (1H, m), 5.66(1H, m), 5.06 (5H, m), 3.65 (3H, s), 3.06 (1H, dd, *J* = 13.2, 4.9 Hz),2.83 (1H, m), 2.54 (3H, m), 2.43 (2H, d, 8.0 Hz), 2.00 (1H, partial ovrlp), 1.93 (1H, partial ovrlp), 1.53 (3H, s), 0.88 (3H, s)

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 198.7, 192.2, 192.1, 170.3, 136.0, 132.7, 132.6, 132.0, 128.2 (two carbons ovrlp), 127.6 (two carbons ovrlp), 123.0, 118.2, 117.6, 65.4, 62.9, 61.6, 53.9, 46.3, 36.6, 35.6, 30.4, 25.4, 19.5.

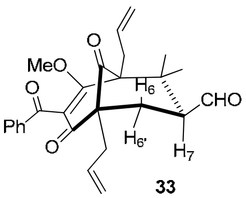
^{1}H NMR (400 MHz, $CDCl_3$) **47**: δ 9.83 (1H, s), 7.78 (2H, dd, *J* = 7.5, 7.5 Hz), 7.54 (1H, dd, *J* = 7.5, 7.5 Hz), 7.42 (2H, dd, *J* = 7.5, 7.5 Hz), 5.81 (1H, m), 5.54(1H, m), 5.06 (4H, m), 3.63 (3H, s,) 2.97 (1H, dd, *J* = 13.0, 4.5 Hz), 2.74 (1H, ddd, *J* = 14.0, 5.6, 1.5Hz), 2.54 (3H, m), 2.14 (1H, dd, *J* = 14.3, 4.5 Hz), 1.98 (1H, dd, *J* = 14.3, 13.0 Hz), 1.30 (3H, s), 0.83 (3H, s)

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 198.8, 192.5, 191.2, 170.0, 136.1, 132.5, 132.3, 132.2, 128.3 (two carbon ovrlp), 127.5 (two carbon ovrlp), 121.9, 118.8, 117.5, 71.0, 61.5, 56.8, 54.4, 46.4, 36.8, 35.5, 29.6, 23.9, 19.3.

IR ν_{mas} (film): 3075, 2919, 2854, 1730, 1664, 1558, 1336, 1214 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{26}H_{28}O_5$ 421.2015 found 421.2021 (M+H).

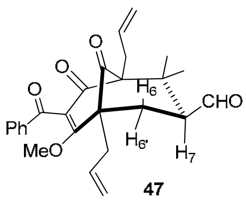
Coupling constant for stereochemistry determination of **33** and **47** in comparison to methyl clusianone.[S4]



33

$J_{7\text{-}6}$ = 13.2 Hz

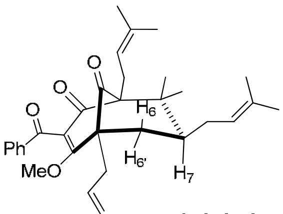
$J_{7\text{-}6'}$ = 4.9 Hz



47

$J_{7\text{-}6}$ = 13.0 Hz

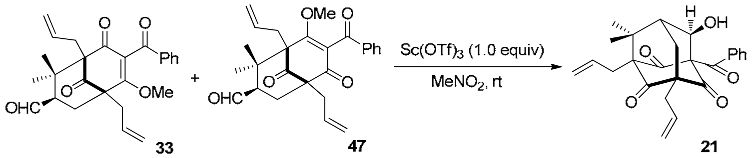
$J_{7\text{-}6'}$ = 4.5 Hz



methyl clusianone

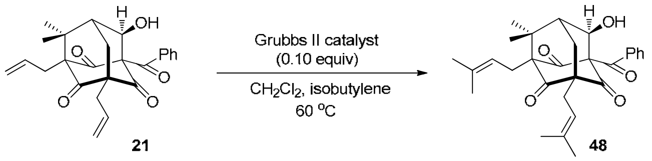
reported coupling constant $J_{7\text{-}6}$ = 13.5 Hz

$J_{7\text{-}6'}$ = 4.4 Hz



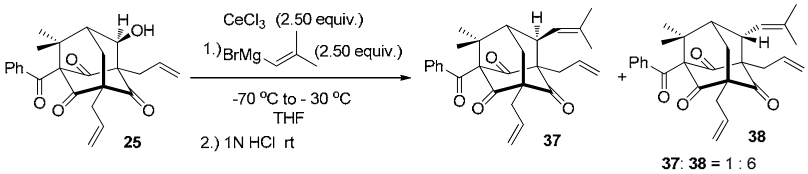
3,5-Diallyl-1-benzoyl-8-hydroxy-6,6-dimethyladamantane-2,4,9-trione 21. To a stirred solution of methyl ethers **33**, **47** (5.0 mg, 0.01 mmol) and $Sc(OTf)_3$ (1.0 equiv, 5.5 mg, 0.01 mmol) was added $MeNO_2$ (0.5 mL) at room temperature and the reaction mixture was stirred for 1 h. The reaction was quenched with sat. $NaHCO_3$ and the aqueous layer extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (10: 1 hexane/EtOAc) to afford 3.0 mg (62 %) of **21** as a colorless film.

(The spectral data for compound **21** obtained using this procedure were found to be identical to those provided on page S8)



1-benzoyl-8-hydroxy-6,6-dimethyl-3,5-bis(3-methylbut-2-en-1-yl)adamantane-2,4,9-trione 48. To a stirred solution of adamantane **21** (6.0 mg, 0.015 mmol) in CH_2Cl_2 (0.3 mL) in a high pressure safe seal tube at -78 °C was added isobutylene (71 equiv, 100 µL, 1.060 mmol) through a cannula, followed by Grubbs II reagent (0.10 equiv, 1.3 mg 0.0015 mmol). The tube was placed under vacuum and recharged with argon; this procedure was repeated twice and the tube was sealed. The reaction mixture was stirred for 2 h at 60 °C under shield protection and was cooled to room temperature. A needle was used to generate a hole on the seal in order to release pressure of the sealed tube. The reaction mixture was concentrated *in vacuo* and the residue purified by silica gel chromatography (8: 1 hexane/EtOAc) to afford 2.3 mg (34 %) of adamantane **48** as a colorless film.

Spectral data for **48** perfectly matched our previously reported data.[S2]



1,3-Diallyl-5-benzoyl-6,6-dimethyl-8-(2-methylprop-1-en-1-yl)adamantane-2,4,9-trione 37 and 38. $CeCl_3 \cdot 6H_2O$ was dehydrated according to the Dimitrov procedure[S5] prior to reaction. $CeCl_3$ (2.5 equiv, 60 mg, 0.246 mmol) was heated under high vacuum to 137 °C for 1 h. Argon was charged to the flask while still hot, and a stir bar was placed in the reaction flask quickly. The flask was heated under high vacuum for another 1 h with strong stirring, argon was charged to the flask again while the flask was still hot, and immediately cooled to 0 °C. THF (300 µL) was added to the reaction mixture and the resulting slurry was stirred at room temperature for 4 h (until a semi-transparent gel formed. The reaction mixture was cooled to 0 °C and adamantane **25** (40 mg, 0.098 mmol) in 150 µL of THF was added. The reaction mixture was stirred for 1 h. To the stirred reaction mixture was slowly added 2-methyl-1-propenyl-magnesium bromide (2.5 equiv, 0.5 M in THF, 491 µL, 0.246 mmol) at -70 °C. The resulting yellow mixture was stirred at the same temperature for 15 min, warmed to -30 °C, and the reaction stirred for 12 h. The reaction was finally quenched with 1N HCl and the aqueous layer extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (10:1

[S4] Rodeschini, V.; Ahmad, N.; Simpkins, N.S. *Org. Lett.* **2006**, *8*, 5283.
[S5] Dimitrov, V.; Kostova, K.; Genov, M. *Tetrahedron Lett.* **1996**, *37*, 6787.

hexane/EtOAc) to afford 39.0 mg (0.088 mmol 89 %) of an inseparable mixture of **37** and **38** as a white amorphous solid. (1: 6 ratio of adamantane stereoisomers **37** and **38** as determined by ^{1}H NMR analysis ($CDCl_3$))

Adamantane **38**: m.p. = 90-94°C (CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (1H, d, *J* = 8.0 Hz), 7.27 (2H, dd, *J* = 8.0, 8.0 Hz), 7.13 (1H, d, *J* = 8.0 Hz), 5.81 (2H, m), 5.15(4H, m), 5.04 (1H, t, *J* = 8.9 Hz), 3.35 (1H, d, *J* = 8.9 Hz), 2.63 (1H, dd, *J* = 13.7, 2.7 Hz), 2.58 (2H, d, *J* = 7.3 Hz), 2.43 (2H, d, *J* = 8.0 Hz), 2.18 (1H, dd, *J* = 13.7, 2.4 Hz), 1.87 (1H, dt, *J* = 2.7, 2.4 Hz), 1.55 (3H, s), 1.59 (3h, s), 1.43 (3H, s), 1.40 (3H, s)

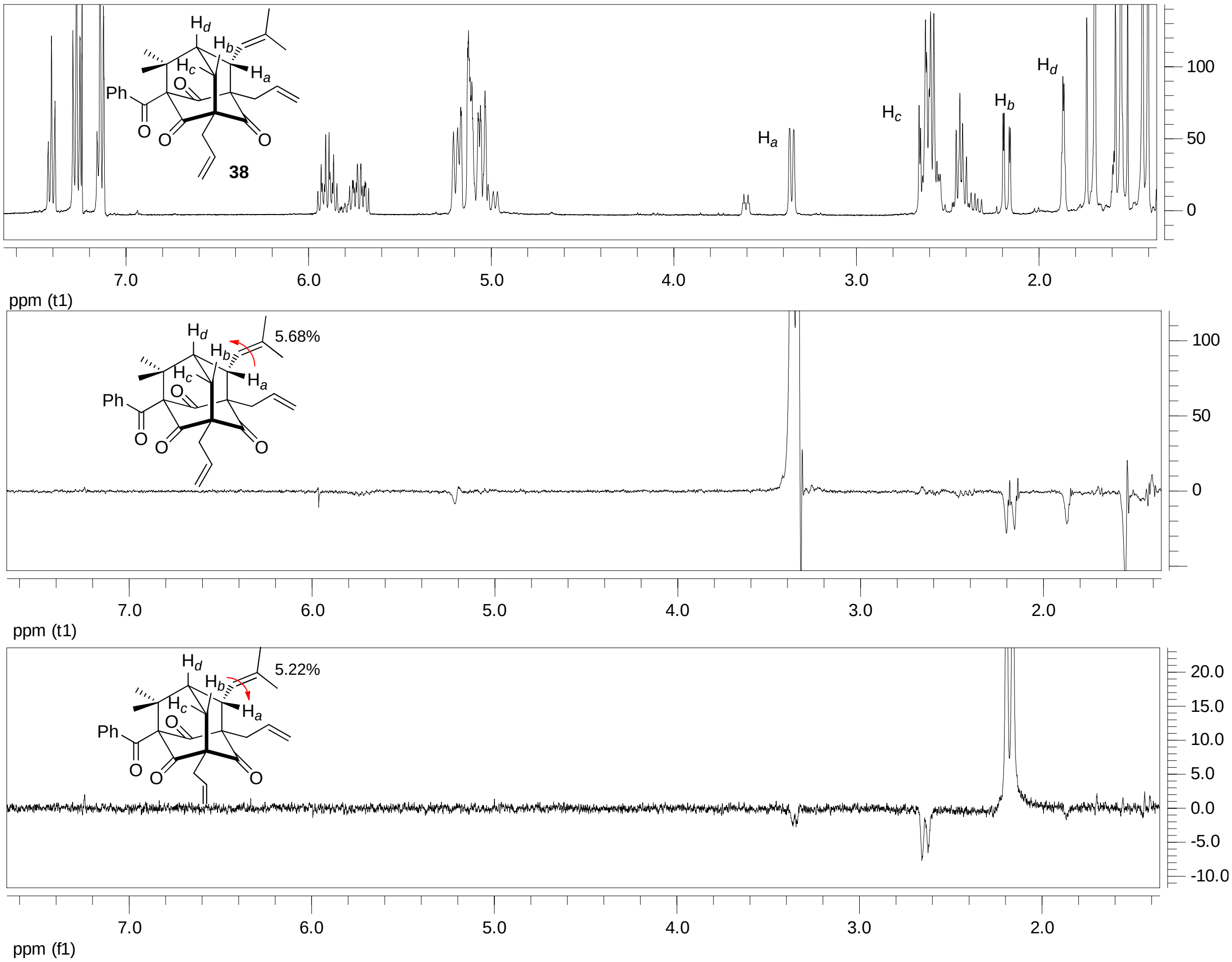
^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 202.0, 201.5, 193.0, 134.8, 134.5, 133.0, 132.4, 132.3, 128.9 (two carbon ovrlp), 128.0 (two carbon ovrlp), 121.4, 119.4, 119.3, 82.6, 70.9, 67.6, 57.7, 57.0, 48.1, 44.4, 33.5, 30.9, 25.9, 25.7, 25.4, 18.0.

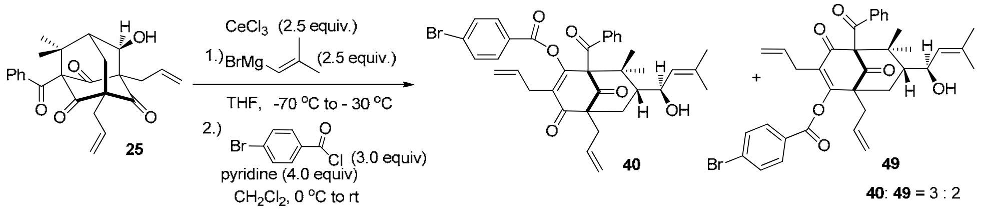
IR ν_{mas} (film): 2928, 2852, 1742, 1704, 1450, 1244 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{29}H_{32}O_4$ 445.2379 found 445.2376 (M+H).

Data for adamantane **37** are reported on page S23.

Key nOe data (300 MHz, $CDCl_3$) for adamantane **38**





3,5-Diallyl-1-benzoyl-7-1-hydroxy-3-methylbut-2-en-1-yl)-8,8-dimethyl-4,9-dioxobicyclo[3.3.1]non-2-en-2-yl 4-bromobenzoate 40 and **1,3-diallyl-5-benzoyl-7-(-1-hydroxy-3-methylbut-2-en-1-yl)-6,6-dimethyl-4,9-dioxobicyclo[3.3.1]non-2-en-2-yl 4-bromobenzoate 49.** $CeCl_3$ (2.5 equiv, 28 mg, 0.114 mmol) was heated under high vacuum to 137 °C for 1 h, argon was charged to the flask while still hot, and a stir bar was quickly placed in the reaction flask. The flask was heated under high vacuum for another 1 h with strong stirring, argon was charged to the flask again while the flask was still hot, and the flask was immediately cooled to 0 °C. THF (100 μL) was added to the reaction mixture and the resulting slurry was stirred at room temperature for 4 h until a semi-transparent gel formed. The reaction mixture was cooled to 0 °C, adamantane **25** (19 mg, 0.046 mmol) in 100 μL of THF was added, and the reaction mixture stirred for 1 h. To this stirred reaction mixture was slowly added 2-methyl-1-propenyl-magnesium bromide (2.5 equiv, 0.5 M in THF, 228.0 μL, 0.114 mmol) at -70 °C. The resulting yellow mixture was stirred at the same temperature for 15 min, warmed to -30 °C and the reaction stirred for 12 h. The reaction was quenched with pH 7 buffer and aqueous layer extracted three times with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo* to afford a yellow oil. To this stirred crude residue and 4-bromobenzoyl chloride (3.0 equiv, 40 mg, 0. 182 mmol) in CH_2Cl_2 (1.0 mL) was added pyridine (4.0 equiv, 18.0 μL, 0.23 mmol) at 0 °C. After 1 h, the reaction mixture was heated to 40 °C for 1 h. The reaction was finally quenched with water and the aqueous layer extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (6: 1 hexane\EtOAc) to afford **40** and **49** as white solids which were contaminated of 4-bromobenzoyl chloride. Further purification by preparative thin layer chromatography (10: 1 hexane/EtOAc) afforded 9.5 mg (0.015 mmol 32 %) of **40** and 6.8 mg (0.011 mmol 23%) of **49** as white solids.

Ester 40: m.p. 76-80 °C (petroleum ether)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (2H, d, *J* = 8.0 Hz), 7.47 (3H, m), 7.37 (2H, d, *J* = 8.3 Hz), 7.30 (2H, dd, *J* = 8.0, 8.0 Hz), 5.84 (1H, m), 5.56 (1H, m), 5.11 (3H, m), 4.82 (3H, m), 3.32 (1H, dd, *J* = 15.2, 6.2 Hz), 2.95 (1H, dd, *J* = 15.2, 7.8 Hz), 2.76 (1H, dd, *J* = 14.0, 2.5 Hz), 2.72 (1H, ovrlp), 2.60 (1H, dd, *J* = 13.7, 7.2 Hz), 2.12 (1H, dd, *J* = 14.0, 7.6 Hz), 1.69 (3H, s), 1.68 (1H, ovrlp), 1.66 (3H, s), 1.45 (3H, s), 1.36 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$) δ 207.4, 194.9, 193.0, 160.5, 158.4, 136.9, 134.0, 133.8, 132.6, 132.3, 132.1 (two carbon ovrlp), 131.6 (two carbon ovrlp), 130.5, 130.0, 129.7, 129.0 (two carbon ovrlp), 128.0 (two carbon ovrlp), 126.7, 119.2, 117.9, 71.5, 65.2, 64.2, 52.8, 51.1, 37.1, 35.2, 30.3, 28.0, 25.8, 22.7, 18.3.

IR ν_{mas} (film): 3535, 2928, 2852, 1754, 1660, 1590, 1429, 1210, 999, 754 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{36}H_{37}BrO_6Na$ 667.1671 found 667.1682 (M+Na).

Ester 49: m.p. 75-78 °C (petroleum ether)

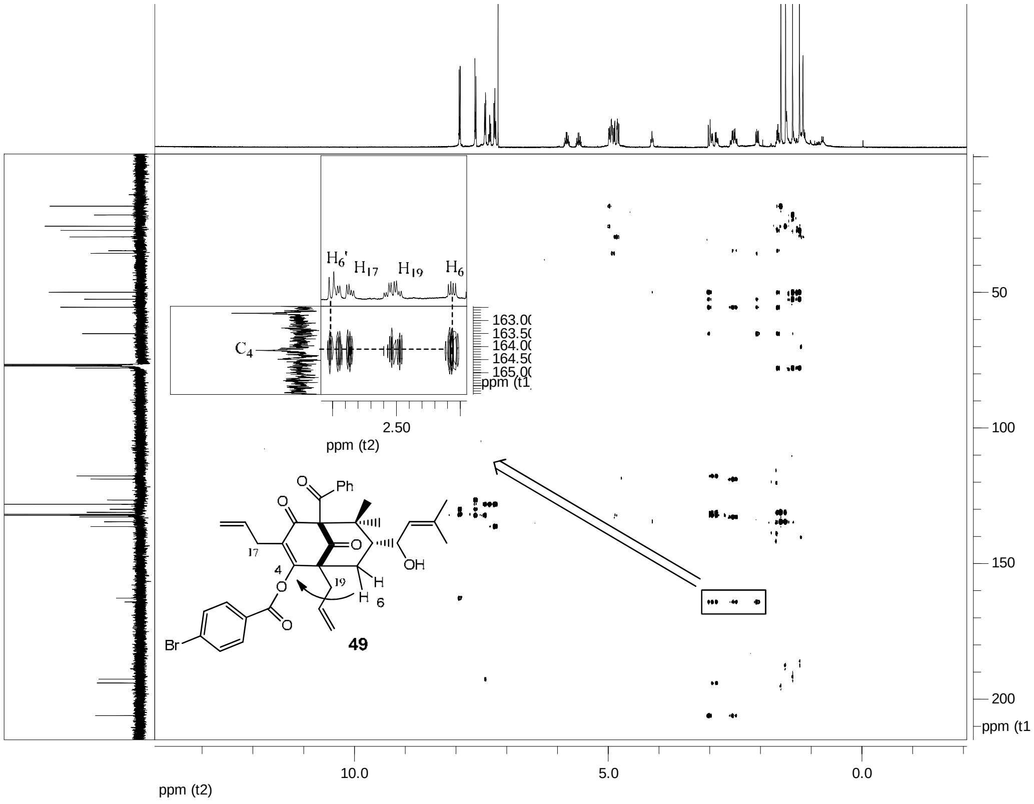
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (2H, d, J = 8.5 Hz), 7.68 (2H, d, J = 8.5 Hz), 7.50 (2H, d, J = 7.6 Hz), 7.40 (1H, dd, J = 7.6, 7.6 Hz), 7.30 (2H, d, J = 7.6, 7.6 Hz), 5.89 (1H, m), 5.65 (1H, m), 4.95 (5H, m), 4.21 (1H, t, 8.8, 8.4 Hz), 3.08 (1H, d, J = 14.7 Hz), 2.98 (2H, dd, J = 14.5, 7.0 Hz), 2.60 (2H, dd, 14.8, 6.8 Hz), 2.13 (1H, dd, J = 14.7, 7.6 Hz), 1.72 (1H, m), 1.67 (3H, s), 1.57 (3H, s), 1.43 (3H, s), 1.30 (3H, s).

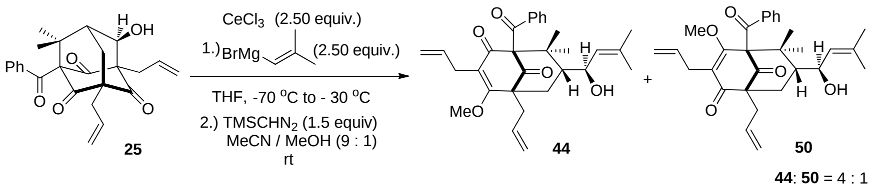
^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 194.2, 192.8, 164.2, 162.9, 136.5, 134.7, 133.0, 132.5, 132.4 (two carbon ovrlp), 132.3, 132.2, 132.0 (two carbon ovrlp), 131.3, 130.1, 128.3 (two carbon ovrlp), 128.2 (two carbon ovrlp), 126.7, 119.0, 117.6, 78.0, 65.4, 55.6, 52.7, 50.1, 35.7, 34.8, 29.7, 27.3, 25.8, 21.6, 18.4.

IR ν_{mas} (film): 3539, 2982, 2923, 1737, 1691, 1425, 1248, 1206, 999, 750 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{36}H_{37}BrO_6$ 645.1852 found 645.1878 (M+H).

Key HMBC correlations (100 MHz, $CDCl_3$) for ester **49**





3,5-diallyl-1-benzoyl-7-(-1-hydroxy-3-methylbut-2-en-1-yl)-4-methoxy-8,8-dimethylbicyclo[3.3.1]non-3-ene-2,9-dione 44 and **1,3-Diallyl-5-benzoyl-7-(-1-hydroxy-3-methylbut-2-en-1-yl)-4-methoxy-6,6-dimethylbicyclo[3.3.1]non-3-ene-2,9-dione 50**. CeCl$_3$ (2.5 equiv, 23 mg, 0.093 mmol) was heated under high vacuum to 137 °C for 1 h, argon was charged to the flask while it was still hot, and a stir bar was quickly placed in the reaction flask. The flask was heated under high vacuum for another 1 h with strong stirring, argon was charged to the flask again while the flask was still hot, and the flask immediately cooled to 0 °C. THF (100 μL) was added to the reaction mixture and the resulting slurry stirred at room temperature for 4 h until a semi-transparent gel formed. The reaction mixture was cooled to 0 °C and adamantane **25** (15.0 mg, 0.037 mmol) in 100 μL of THF was added. The reaction mixture was stirred for 1 h. To the stirred reaction mixture was slowly added 2-methyl-1-propenyl-magnesium bromide (2.5 equiv, 0.5 M in THF, 187.0 μL, 0.093 mmol) at -70 °C. The resulting yellow mixture was stirred at the same temperature for 15 min, warmed to -30 °C, and stirred for 12 h. The reaction was quenched with pH 7 buffer and the aqueous layer extracted three times with ethyl acetate. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated *in vacuo* to afford a yellow oil. To this stirred crude residue in acetonitrile (450 μL) was added MeOH (50 μL) at room temperature which was followed by slow addition of trimethylsilyldiazomethane (1.5 equiv, 2 M in hexane, 27.6 μL, 0.055 mmol). The resulting reaction mixture was stirred for 1 h and concentrated *in vacuo*. The residue was purified by preparative thin layer chromatography (6: 1 hexane/EtOAc) to afford 7.2 mg (40 %) of an inseparable mixture of **44** and **50** as white solids (4: 1 ratio of methyl enol ethers as determined by ^{1}H NMR analysis (CDCl$_3$)).

Methyl Ether **44**: m.p. 69-72 °C (CH$_2$Cl$_2$)

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.54 (2H, d, *J* = 7.3 Hz), 7.41 (1H, d, *J* = 7.3 Hz), 7.29 (2H, dd, *J* = 7.3, 7.3 Hz), 5.89 (2H, m), 5.06(4H, m), 5.02 (1H, d, *J* = 9.7 Hz), 4.41 (1H, td, *J* = 8.4, 8.4, 3.3 Hz), 3.35 (3H, s), 3.35 (1H, m, ovrlp), 3.09 (1H, ddt, *J* = 16.0, 6.4, 1.6 Hz), 2.76 (1H, d, *J* = 14.5 Hz), 2.63 (2H, m), 2.06 (1H, dd, *J* = 14.2, 7.6 Hz), 1.66 (3H, s), 1.66 (1H, m, ovrlp), 1.64 (3H, s), 1.43 (3H, s), 1.29 (3H, s).

^{13}C NMR (125 MHz, $CDCl_3$) δ 205.2, 193.6, 191.1, 169.1, 135.8, 134.4, 133.3, 132.9, 130.9, 130.8, 127.8, 127.0 (two carbon ovrlp), 126.9 (two carbon ovrlp), 119.7, 117.9, 73.3, 66.1, 64.1, 62.6, 53.6, 50.3, 38.2, 36.0, 32.9, 29.1, 24.4, 23.9, 19.5.

Methyl Ether **50**: m.p. 69-72 °C (CH_2Cl_2)

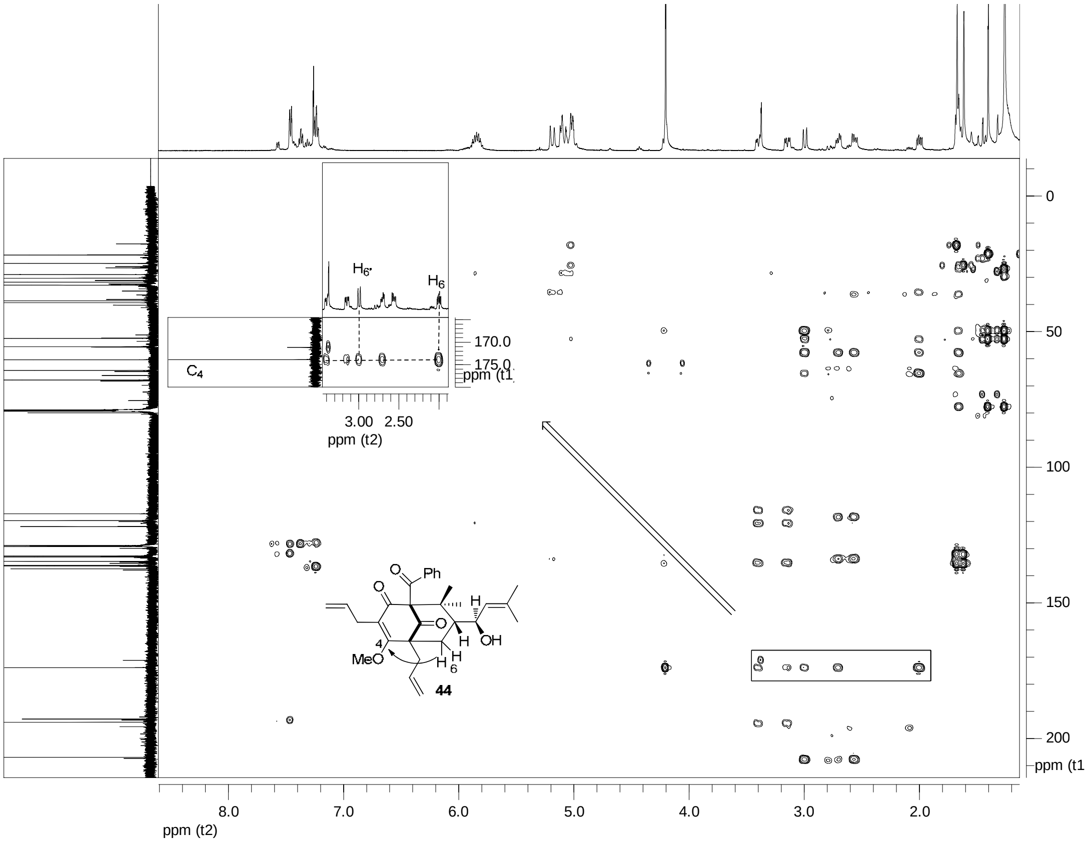
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (2H, d, *J* = 7.3 Hz), 7.35 (1H, d, *J* = 7.3 Hz), 7.12 (2H, dd, *J* = 7.3, 7.3 Hz), 5.82 (2H, m), 5.12(4H, m), 4.99 (1H, d, *J* = 8.8 Hz), 4.19 (1H, m, partial ovrlp), 4.18 (3H, s), 3.38 (1H, ddt, *J* = 15.6, 6.2, 1.6 Hz), 3.12 (1H, ddt, *J* = 15.6, 6.2, 1.6 Hz), 2.97 (1H, d, *J* = 14.3 Hz), 2.60 (2H, m), 1.98 (1H, dd, *J* = 14.3, 7.4 Hz), 1.65 (3H, s), 1.64 (1H, m, partial ovrlp), 1.59 (3H, s), 1.38 (3H, s), 1.24 (3H, s).

^{13}C NMR (125 MHz, $CDCl_3$) δ 204.8, 191.9, 190.7, 171.8, 135.3, 134.3, 134.0, 132.6, 131.0, 130.6, 127.1 (two carbon ovrlp), 126.7(two carbon ovrlp), 120.0, 117.6, 115.1, 77.8, 65.7, 62.2, 58.3, 53.5, 50.4, 37.3, 36.5, 30.8, 29.7, 26.9, 22.8, 19.7.

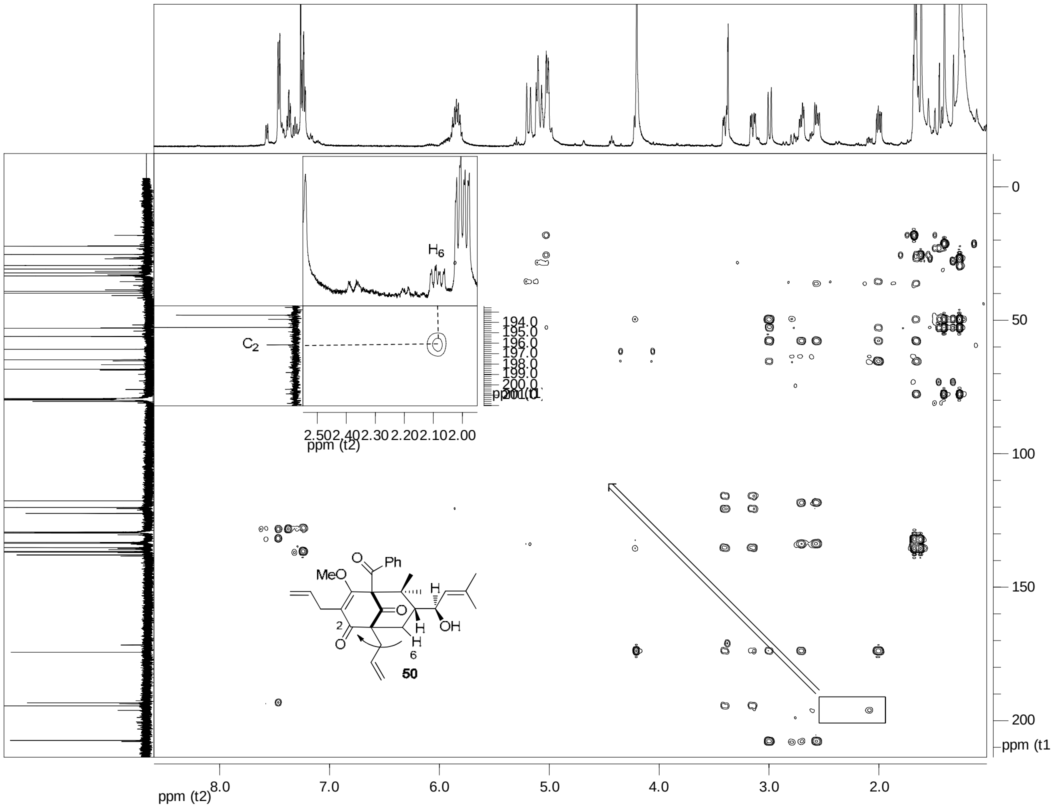
IR ν_{mas} (film): 3371, 2928, 2847, 1742, 1653, 1446, 1239 cm^{-1}.

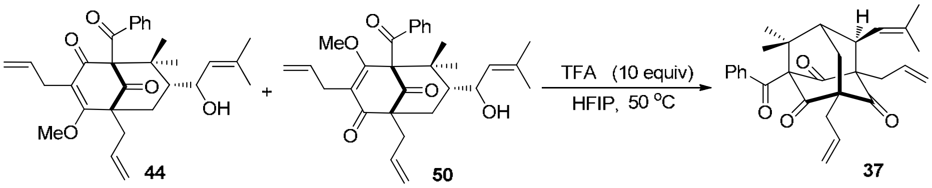
HRMS (ESI+) m/z calculated for $C_{30}H_{36}O_5$ 477.2641 found 477.2644 (M+H).

Key HMBC correlations (100 MHz, $CDCl_3$) for enol ether **44**



Key HMBC correlations (100 MHz, $CDCl_3$) for enol ether **50**





1,3-Diallyl-5-benzoyl-6,6-dimethyl-8-(2-methylprop-1-en-1-yl)adamantane-2,4,9-trione 37. To a stirred solution of **44** and **50** (8.6 mg, 0.018 mmol) in 1,1,1,3,3,3-hexafluoro-2-propanol (1.2 mL) was added trifluoroacetic acid (10 equiv, 14.00 μL, 0.182 mmol) at room temperature. The reaction mixture was heated to 50°C for 12 h. The crude mixture was concentrated *in vacuo* and the residue was purified by silica gel chromatography (30: 1 hexane/EtOAc) to afford 6.5 mg (0.014 mmol, 80 %) of **37** as a white, amorphous solid.

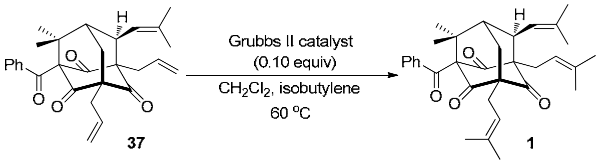
m.p. 90-94 °C (CH_2Cl_2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (1H, d, *J* = 8.1 Hz), 7.27 (2H, dd, *J* = 8.1, 8.1 Hz), 7.15 (1H, d, *J* = 8.1 Hz), 5.85 (2H, m), 5.06 (4H, m), 4.90 (1H, t, *J* = 8.8 Hz), 3.61 (1H, dt, *J* = 9.0, 2.3 Hz), 2.57 (3H, ovrlp), 2.38 (3H, ovrlp), 1.74 (3H, s), 1.59, (1H, partial ovrlp) 1.59 (3H, s), 1.52 (3H, s), 1.43 (3H, s)

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 200.3, 199.9, 191.5, 136.7, 134.0, 132.1, 132.0, 131.7, 128.5 (two carbon ovrlp), 128.0 (two carbon ovrlp), 118.8, 118.7, 118.5, 82.1, 71.7, 68.0, 55.3, 52.0, 49.0, 41.0, 33.9, 32.5, 26.6, 24.0, 23.5, 18.9.

IR ν_{mas} (film): 2953, 2923, 2843, 1742, 1695, 1438, 1227 cm^{-1}.

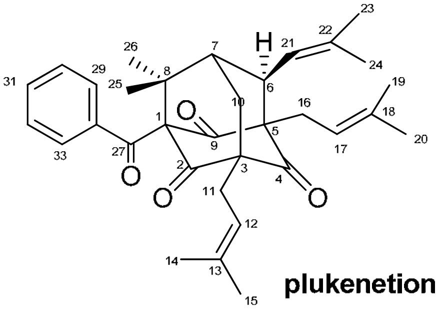
HRMS (ESI+) m/z calculated for $C_{29}H_{32}O_4$ 445.2379 found 445.2422 (M+H).



Plukenetione A 1. To a high pressure safe sealed tube was added adamantane **37** (8.0 mg, 0.018 mmol) in CH_2Cl_2 (0.3 mL). The tube was sealed and cooled to -78 °C and isobutylene (700 equiv, 680 μL, 7.199 mmol) was added using a cannula followed by Grubbs II catalyst (0.10 equiv, 1.5 mg 0.0018 mmol). The tube was evacuated using high vacuum and recharged with argon. This procedure was repeated twice and the tube was sealed. The reaction mixture was stirred at 60 °C under shield protection for 2h and was cooled to room temperature; a needle was used to generate a hole in the seal in order to release pressure of the sealed tube. The reaction mixture was concentrated *in vacuo* and the residue purified by silica gel chromatography (30: 1 hexane/EtOAc) to afford 7.0 mg (0.014 mmol, 74 %) of plukenetione A as a colorless film.

IR ν_{mas} (film): 2928, 2852, 1729, 1699, 1446, 1391, 1244 cm^{-1}.

HRMS (ESI+) m/z calculated for $C_{33}H_{40}O_4$ 501.3005 found 501.3028 (M+H).



plukenetione A

	^{1}H	
	Natural -1[S6]	**Synthetic 1 (this work)**
Positions	δ lit.[S7] ($J_{\text{H-H}}$ in Hz)	δ ($J_{\text{H-H}}$ in Hz)
6	3.63 (1H, 9.3,2.7,2.5)	3.63 (1H, ddd, 9.0, 2.6, 2.5)
7	1.58 (1H, ovrlp)	1.59 (1H, ovrlp)
10	2.45 (1H, 13.7, 2.7, 2.7) 2.47 (1H, 13.7, 2.7)	2.43(1H, dt, 13.5, 2.6, 2.6) 2.47(1H, dd, 13.5, 2.6)
11	2.52 (2H, 7.3)	2.53 (2H, d, 7.2)
12	5.19 (1H, 7.3, 1.5)	5.18 (1H, dd, 7.2, 1.4)
14	1.70 (3H, s)	1.71 (3H, s)
15	1.67 (3H, s)	1.68 (3H, s)
16	2.39 (2H, 7.1, 1.4)	2.40 (2H, dd, 7.2, 1.4)
17	5.08 (1H, 7.1, 1.4)	5.07 (1H, dd, 7.2, 1.4)
19	1.64 (3H, s)	1.64 (3H, s)
20	1.57 (3H, s)	1.58 (3H, s)
21	5.00 (1H, 9.3, 1.4)	5.00 (1H, dd, 9.0, 1.4)
23	1.75 (3H, s)	1.76 (3H, s)
24	1.59 (3H, s)	1.59 (3H, s)
25	1.45 (3H, s)	1.46 (3H, s)
26	1.54 (3H, s)	1.55 (3H, s)
29, 33	7.18 (2H, 8.3)	7.15 (2H, d, 8.1)
30, 32	7.27 (2H, 8.3, 8.3)	7.25 (2H, dd, 8.1,8.1)
31	7.41 (1H, 8.3)	7.39 (1H, d, 8.1)

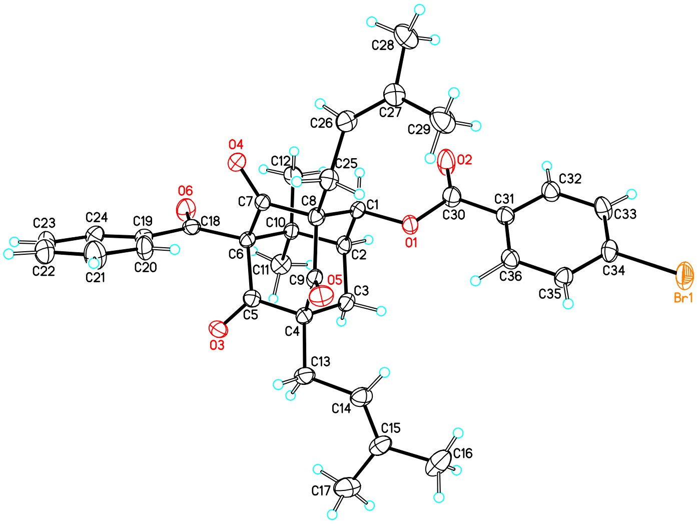
[S6] Chemical shifts are reported in parts per million relative to $CDCl_3$ (^{1}H, δ 7.24; ^{13}C, δ 77.0).

[S7] Henry, G. E.; Jacobs, H.; Sean Carrington, C. M.; McLean, S.; Reynolds, W. F. *Tetrahedron Lett.* **1996**, *37*, 8663.

	^{13}C	
	Natural -1[S7]	**Synthetic 1 (this work)**
Positions	δ lit. (J_{H-H} in Hz)	δ (J_{H-H} in Hz)
1	82.13	82.14
2	202.21	202.38
3	68.66	68.66
4	203.28	203.37
5	71.88	71.89
6	51.57	51.57
7	48.74	48.75
8	54.96	54.97
9	201.81	201.88
10	40.53	40.53
11	27.67	27.67
12	118.44	118.47
13	134.94	134.99
14	25.98	25.98
15	18.05	18.04
16	26.45	26.44
17	118.33	118.35
18	134.61	134.66
19	25.98	25.98
20	17.95	17.94
21	119.49	119.52
22	137.02	137.07
23	26.09	26.10
24	17.86	17.86
25	22.90	22.90
26	23.26	23.25
27	193.24	193.30
28	134.87	134.89
29, 33	129.11	129.15
30, 32	127.85	127.89
31	132.26	132.30

III. X-ray Crystallographic Data

X-ray crystallographic data for 28



Crystals of compound **28** suitable for x-ray analysis were obtained by slow evaporation from methanol, CH_2Cl_2, and EtOAc (8:1:1). Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (772040). 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 1. Crystal data and structure refinement for **28**.

Identification code	**28**	
Empirical formula	C36 H37 Br O6	
Formula weight	645.57	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pna2(1)	
Unit cell dimensions	a = 19.7588(9) Å	α= 90°.
	b = 7.7830(4) Å	β= 90°.
	c = 20.3595(10) Å	γ = 90°.
Volume	3130.9(3) Å^3	
Z	4	

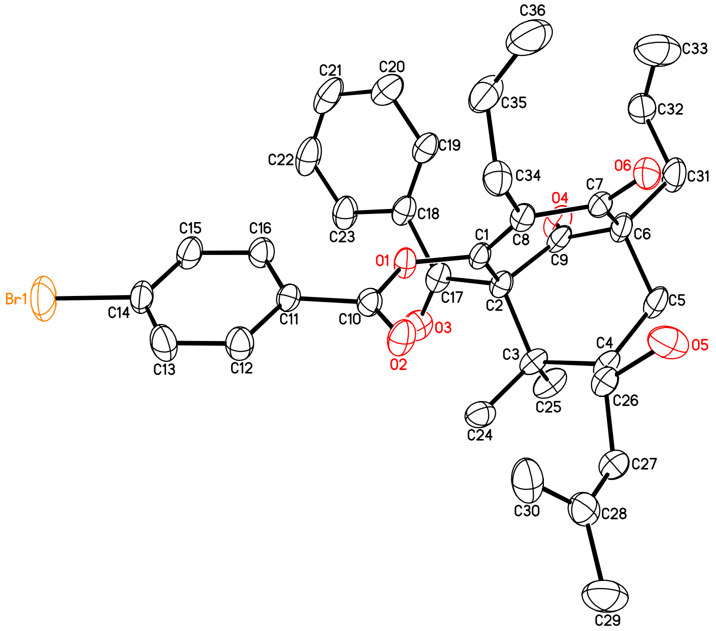
Density (calculated)	1.370 Mg/m^3
Absorption coefficient	1.358 mm^{-1}
F(000)	1344
Crystal size	0.40 x 0.25 x 0.20 mm^3
Theta range for data collection	2.00 to 28.39°.
Index ranges	-26<=h<=26, -10<=k<=8, -21<=l<=27
Reflections collected	19766
Independent reflections	6669 [R(int) = 0.0390]
Completeness to theta = 28.39°	98.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7729 and 0.6126
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6669 / 1 / 395
Goodness-of-fit on F^2	1.020
Final R indices [I>2sigma(I)]	R1 = 0.0363, wR2 = 0.0699
R indices (all data)	R1 = 0.0677, wR2 = 0.0791
Absolute structure parameter	0.568(5)
Largest diff. peak and hole	0.311 and -0.368 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **28**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	6562(1)	1358(1)	6703(1)	45(1)
O(1)	9631(1)	-1257(2)	7779(1)	27(1)
O(2)	9862(1)	-1278(2)	6700(1)	52(1)
O(3)	11454(1)	-275(2)	9847(1)	35(1)
O(4)	11250(1)	-4822(2)	8569(1)	29(1)
O(5)	9535(1)	-2391(2)	9415(1)	35(1)
O(6)	12669(1)	-2224(2)	8773(1)	38(1)
C(1)	10316(1)	-1768(3)	7916(1)	25(1)
C(2)	10748(1)	-185(3)	8060(1)	25(1)
C(3)	10424(1)	823(3)	8621(1)	28(1)
C(4)	10403(1)	-283(3)	9259(1)	25(1)
C(5)	11134(1)	-789(3)	9384(1)	26(1)
C(6)	11466(1)	-1893(3)	8850(1)	22(1)
C(7)	11026(1)	-3414(3)	8651(1)	22(1)
C(8)	10284(1)	-2971(3)	8516(1)	25(1)
C(9)	10017(1)	-1937(3)	9101(1)	24(1)
C(10)	11491(1)	-680(3)	8213(1)	24(1)
C(11)	11911(1)	922(3)	8352(1)	35(1)
C(12)	11796(1)	-1601(3)	7613(1)	31(1)
C(13)	10091(1)	685(3)	9833(1)	33(1)
C(14)	9420(1)	1495(3)	9662(1)	34(1)
C(15)	9179(1)	2946(3)	9890(1)	33(1)
C(16)	8500(1)	3620(4)	9690(2)	53(1)
C(17)	9554(2)	4043(4)	10377(2)	58(1)
C(18)	12164(1)	-2546(3)	9085(1)	28(1)
C(19)	12211(1)	-3588(3)	9700(1)	28(1)
C(20)	11660(1)	-4335(3)	10016(1)	35(1)
C(21)	11754(1)	-5343(4)	10563(1)	47(1)
C(22)	12393(1)	-5623(3)	10811(1)	45(1)
C(23)	12935(1)	-4842(3)	10514(1)	42(1)
C(24)	12851(1)	-3854(3)	9964(1)	35(1)
C(25)	9842(1)	-4578(3)	8406(1)	29(1)

C(26)	9940(1)	-5415(3)	7756(1)	31(1)
C(27)	9467(1)	-5725(3)	7310(1)	32(1)
C(28)	9654(1)	-6540(3)	6663(2)	45(1)
C(29)	8734(1)	-5271(4)	7381(1)	48(1)
C(30)	9471(1)	-1046(3)	7139(1)	32(1)
C(31)	8756(1)	-492(3)	7053(1)	27(1)
C(32)	8531(1)	-191(3)	6424(1)	32(1)
C(33)	7875(1)	393(3)	6314(1)	34(1)
C(34)	7464(1)	633(3)	6843(1)	30(1)
C(35)	7676(1)	327(3)	7482(1)	28(1)
C(36)	8329(1)	-235(3)	7586(1)	29(1)

X-ray crystallographic data for 40



Crystals of compound **40** suitable for x-ray analysis were obtained by slow evaporation from methanol, CH_2Cl_2, and EtOAc (8:1:1). Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (772041). 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 3. Crystal data and structure refinement for **40**.

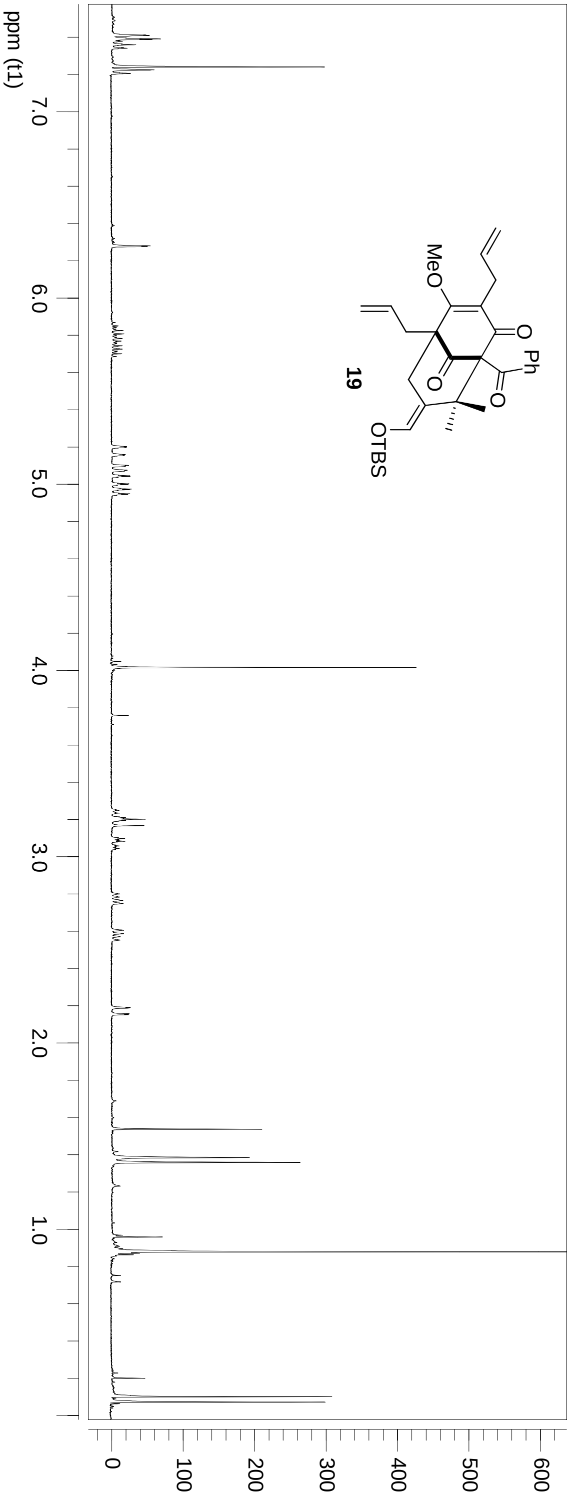
Identification code	**40**	
Empirical formula	C36 H37 Br O6	
Formula weight	645.57	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 16.1664(6) Å	α= 90°.
	b = 22.2456(9) Å	β= 91.709(2)°.
	c = 8.7124(4) Å	γ = 90°.
Volume	3131.9(2) $Å^3$	
Z	4	
Density (calculated)	1.369 Mg/m^3	
Absorption coefficient	1.358 mm^{-1}	
F(000)	1344	
Crystal size	0.30 x 0.20 x 0.10 mm^3	
Theta range for data collection	1.56 to 26.37°.	
Index ranges	-20<=h<=20, -25<=k<=27, -10<=l<=10	
Reflections collected	31778	
Independent reflections	6391 [R(int) = 0.0424]	
Completeness to theta = 26.37°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8762 and 0.6861	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6391 / 0 / 499	
Goodness-of-fit on F^2	1.007	
Final R indices [I>2sigma(I)]	R1 = 0.0414, wR2 = 0.0968	
R indices (all data)	R1 = 0.0734, wR2 = 0.1122	
Largest diff. peak and hole	0.866 and -0.864 e.$Å^{-3}$	

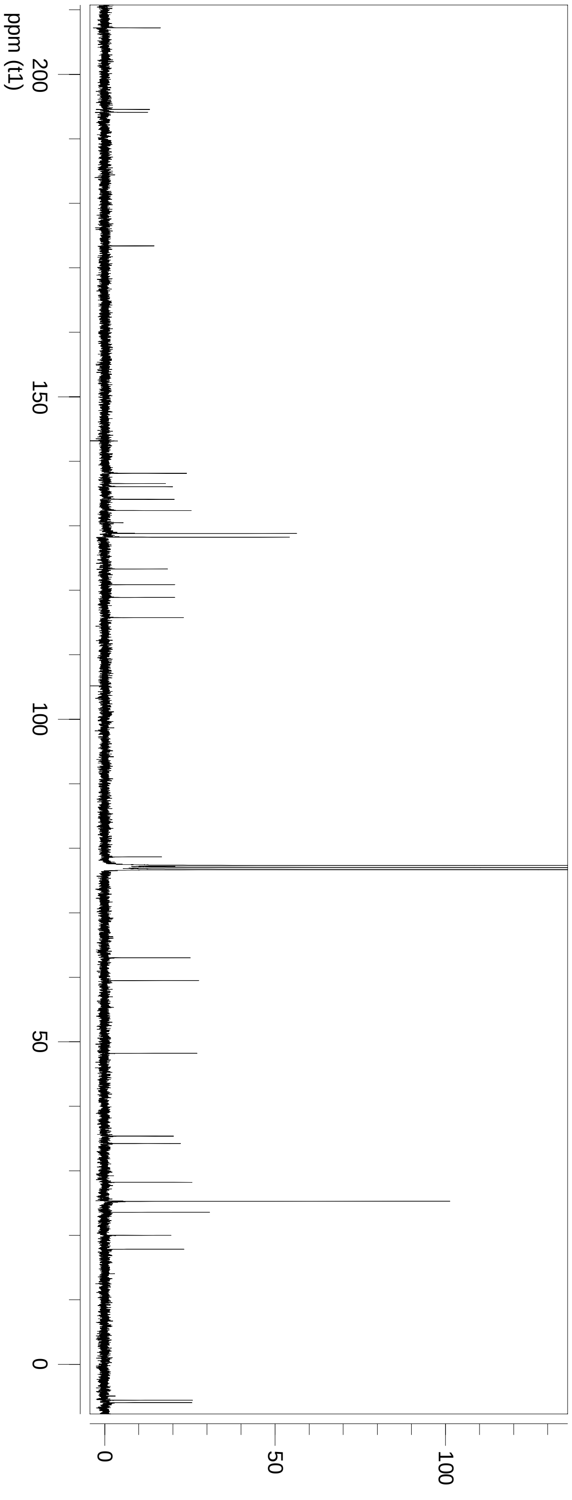
Table 4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **40**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

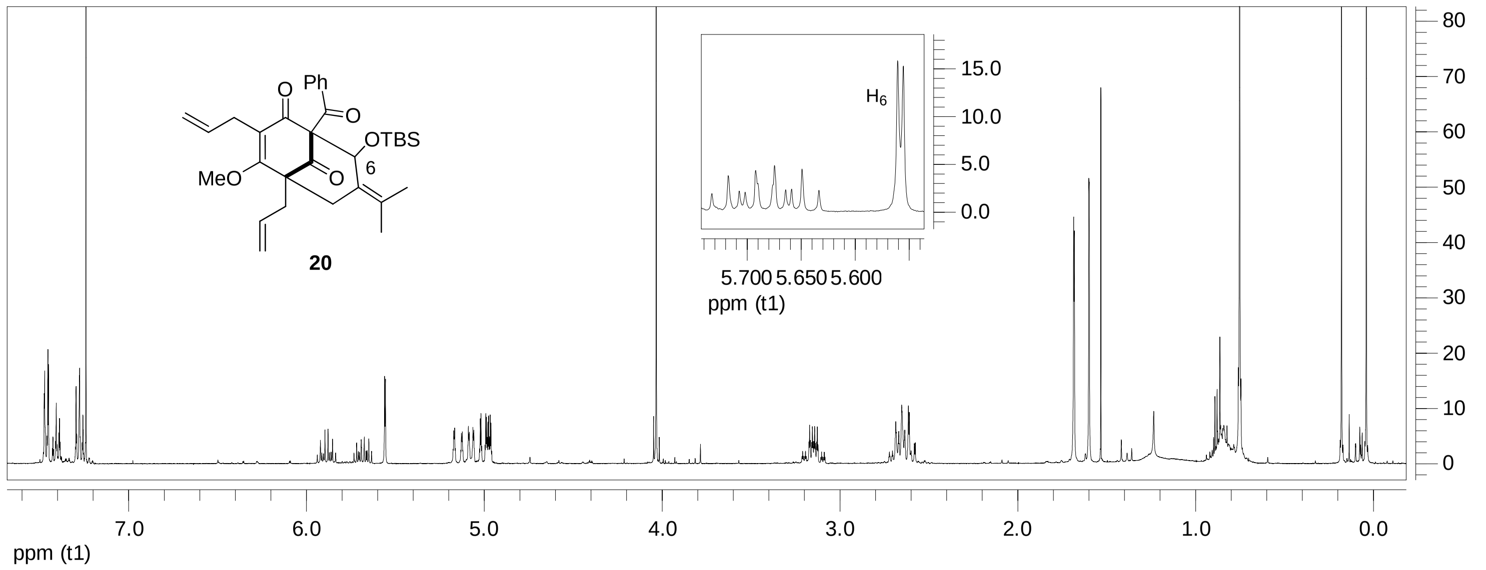
	x	y	z	U(eq)
Br(1)	3882(1)	2601(1)	2866(1)	71(1)
O(1)	6935(1)	4045(1)	-645(2)	31(1)
O(2)	7745(1)	3710(1)	1340(2)	40(1)
O(3)	6636(1)	3264(1)	-3852(2)	46(1)
O(4)	7401(1)	4585(1)	-5452(2)	45(1)
O(5)	10004(1)	4491(1)	-1154(3)	53(1)
O(6)	8882(1)	5564(1)	-1641(2)	43(1)
C(1)	7539(1)	4329(1)	-1489(3)	28(1)
C(2)	7579(1)	4054(1)	-3078(3)	30(1)
C(3)	8327(1)	3585(1)	-3214(3)	33(1)
C(4)	9184(1)	3910(1)	-2972(3)	33(1)
C(5)	9232(2)	4498(1)	-3885(3)	39(1)
C(6)	8489(1)	4935(1)	-3743(3)	36(1)
C(7)	8464(1)	5139(1)	-2070(3)	33(1)
C(8)	7922(1)	4825(1)	-995(3)	31(1)
C(9)	7762(1)	4554(1)	-4217(3)	35(1)
C(10)	7077(1)	3756(1)	731(3)	30(1)
C(11)	6288(1)	3504(1)	1263(2)	28(1)
C(12)	6315(2)	3126(1)	2515(3)	40(1)
C(13)	5599(2)	2863(1)	3019(3)	47(1)
C(14)	4865(2)	2981(1)	2244(3)	39(1)
C(15)	4823(2)	3365(1)	1018(3)	42(1)
C(16)	5536(2)	3628(1)	522(3)	38(1)
C(17)	6710(1)	3784(1)	-3502(3)	35(1)
C(18)	5952(1)	4173(1)	-3410(3)	35(1)
C(19)	5949(2)	4784(1)	-3136(3)	38(1)
C(20)	5213(2)	5092(2)	-2981(3)	49(1)
C(21)	4470(2)	4788(2)	-3098(3)	56(1)
C(22)	4461(2)	4183(2)	-3378(3)	57(1)
C(23)	5195(2)	3874(2)	-3545(3)	46(1)
C(24)	8238(2)	3072(1)	-2066(3)	40(1)
C(25)	8323(2)	3311(1)	-4837(3)	46(1)

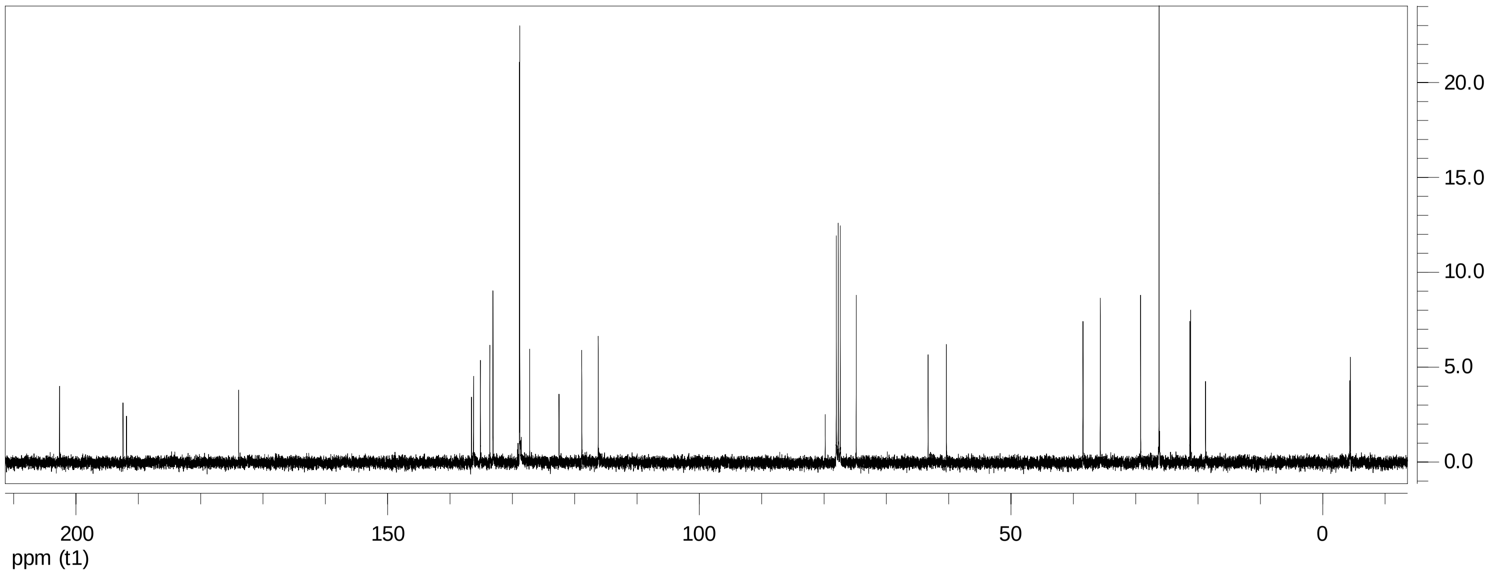
C(26)	9541(1)	3945(1)	-1297(3)	34(1)
C(27)	10104(2)	3430(1)	-933(3)	36(1)
C(28)	10234(2)	3159(1)	407(3)	43(1)
C(29)	10879(2)	2671(2)	579(4)	66(1)
C(30)	9792(2)	3309(2)	1831(3)	56(1)
C(31)	8597(2)	5475(2)	-4812(4)	50(1)
C(32)	7850(5)	5851(5)	-4998(10)	42(2)
C(32')	7994(9)	6034(7)	-4410(20)	46(3)
C(33)	7835(5)	6374(4)	-4405(16)	80(3)
C(33')	7646(7)	6340(5)	-5500(20)	67(4)
C(34)	7806(2)	5123(1)	534(3)	41(1)
C(35)	7242(2)	5655(2)	364(4)	55(1)
C(36)	7474(3)	6203(2)	539(6)	86(1)

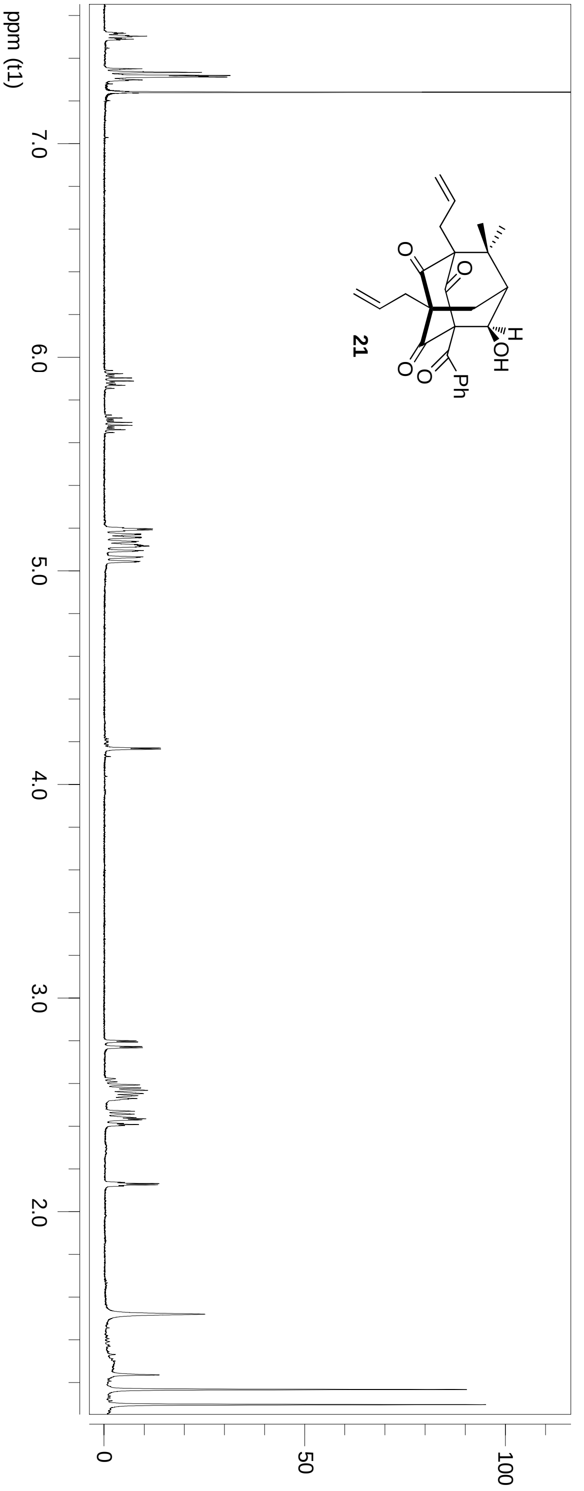
IV. Select Spectra



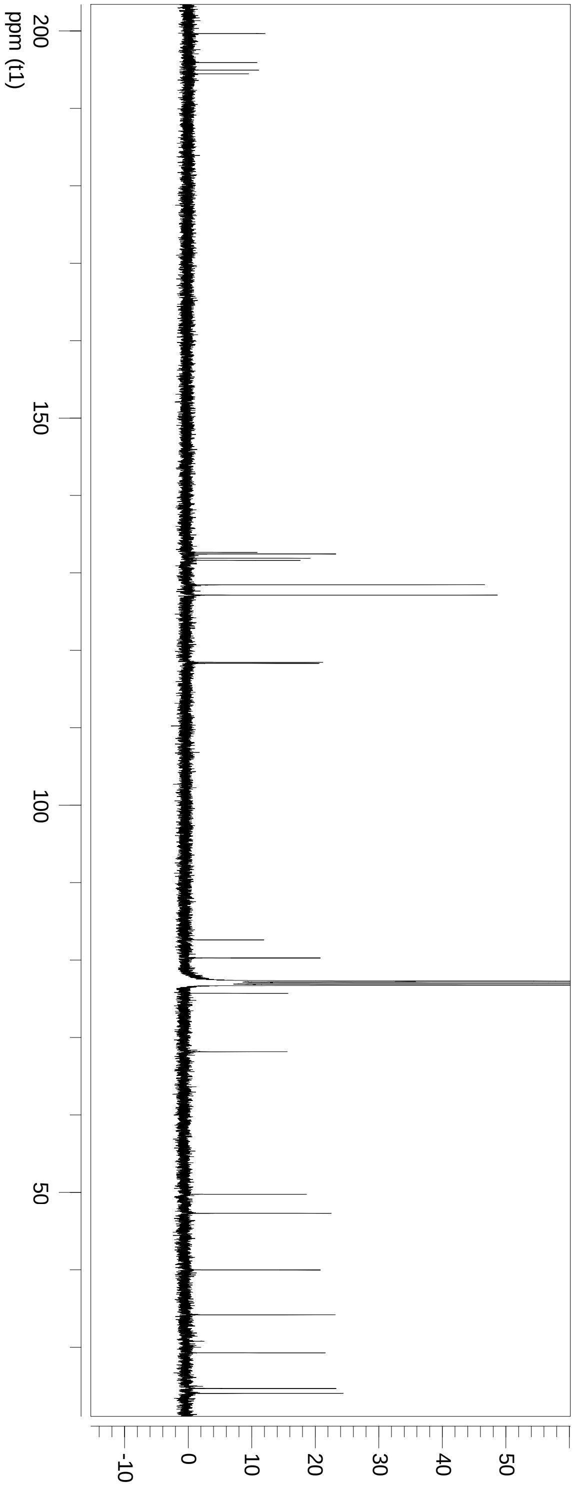


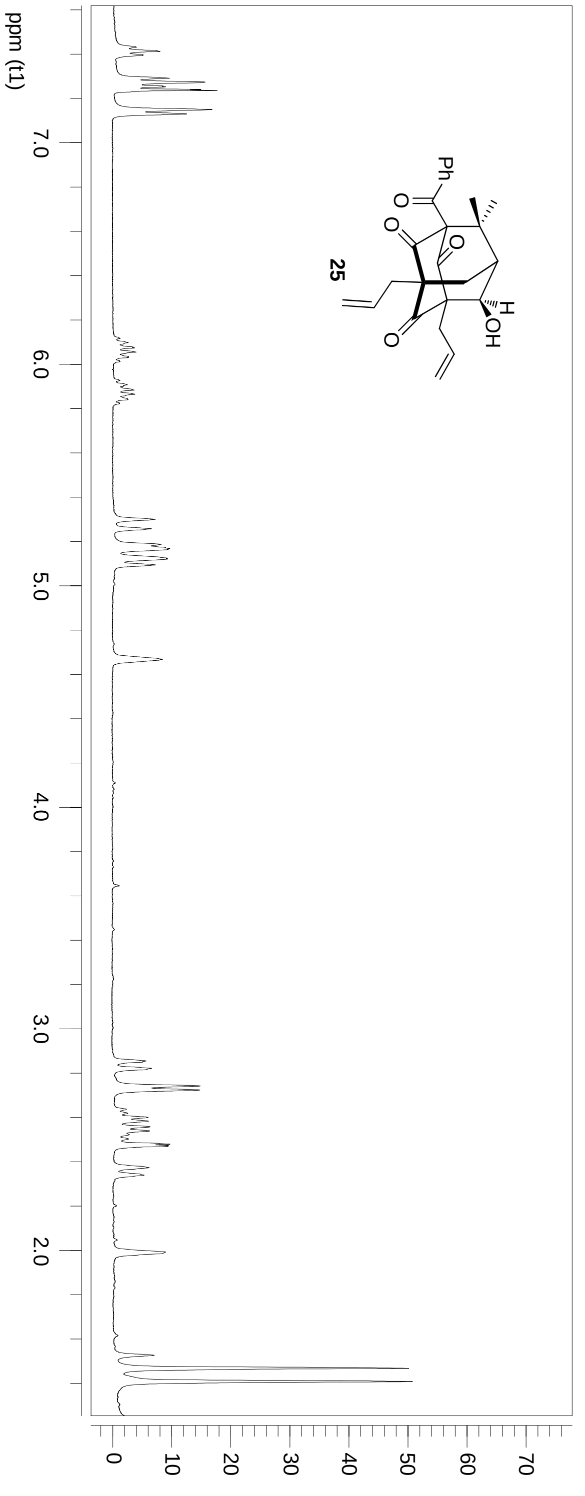

O
Ph
O
OTBS
6
MeO
O
20
H$_6$
5.700 5.650 5.600
ppm (t1)
15.0
10.0
5.0
0.0
80
70
60
50
40
30
20
10
0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


20.0
15.0
10.0
5.0
0.0
200
150
100
50
0
ppm (t1)

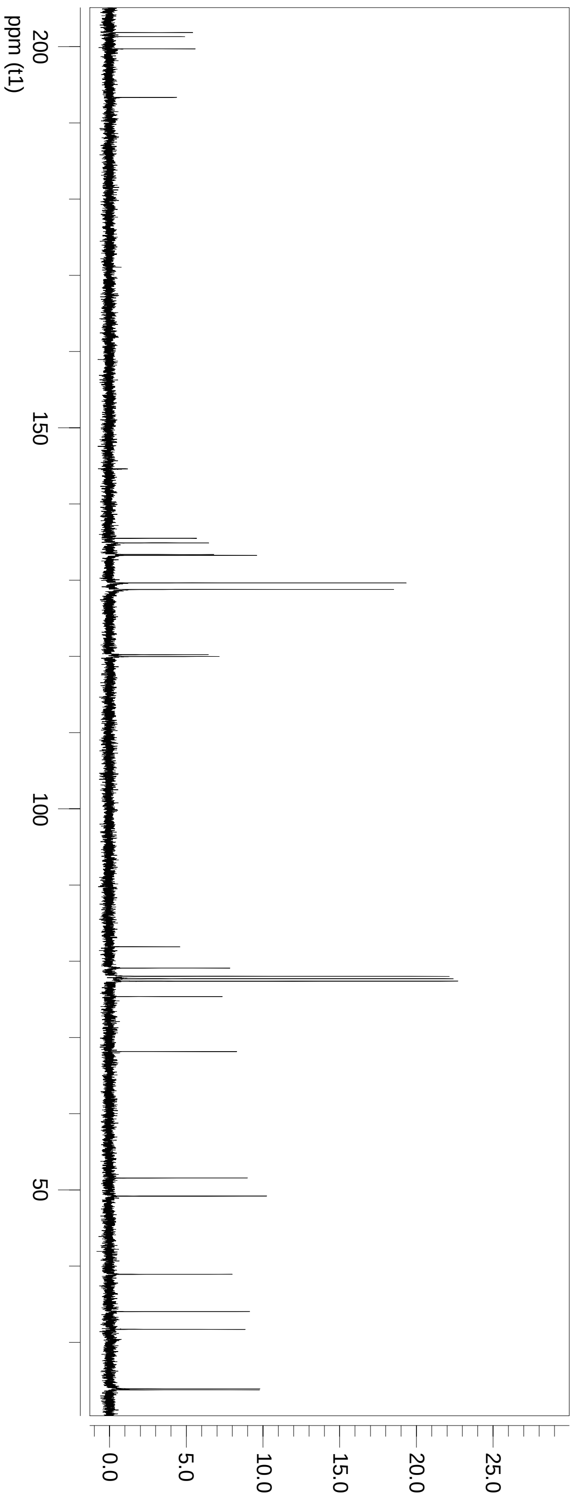

ppm (t1)
7.0
6.0
5.0
4.0
3.0
2.0
0
50
100
O
O
O
O
H
OH
Ph

21

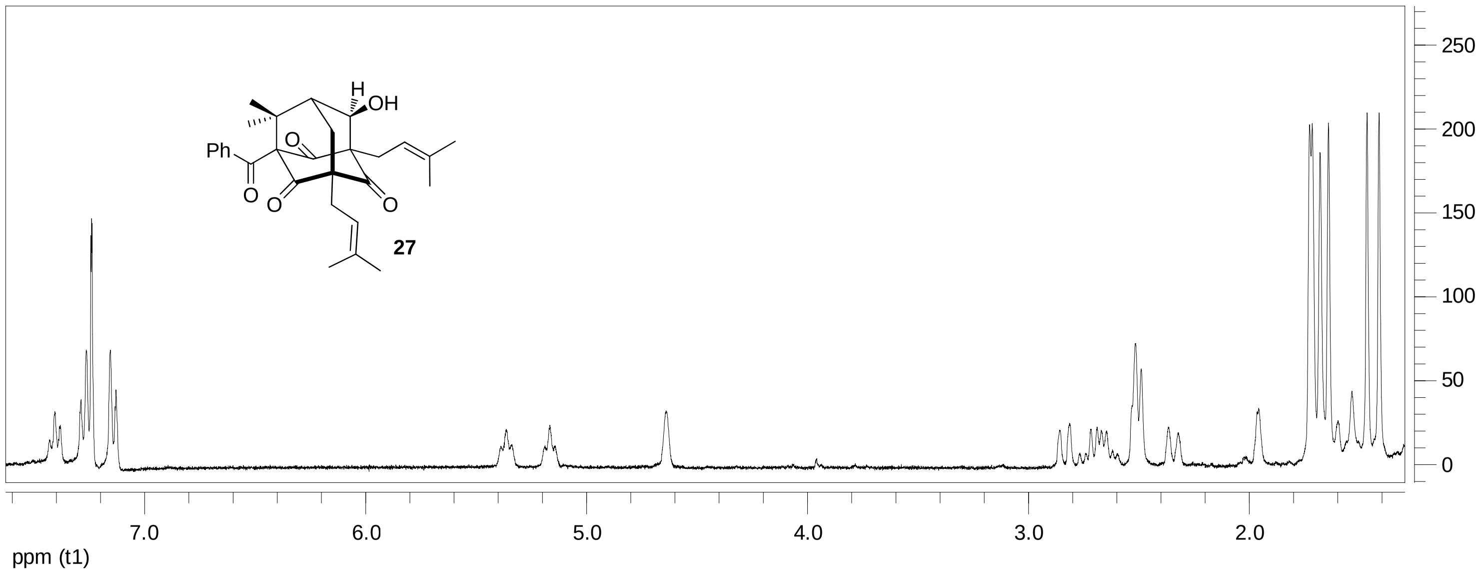

ppm (t1)
200
150
100
50
-10
0
10
20
30
40
50


25

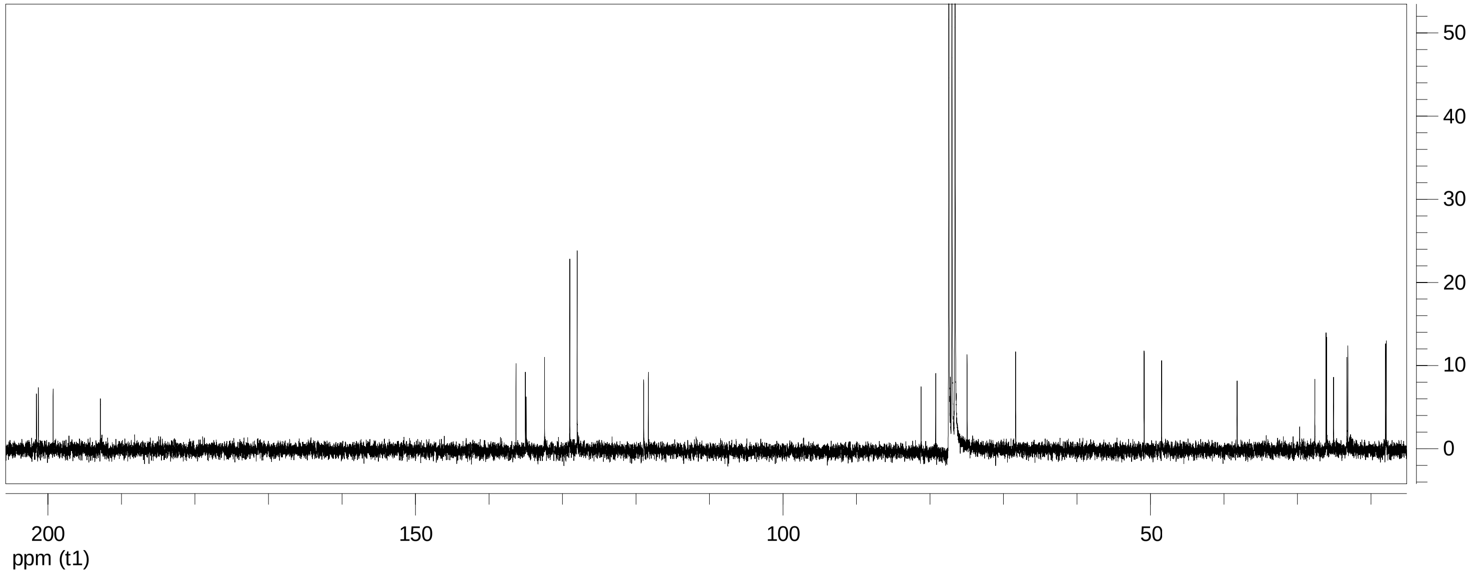
Ph
O
O
O
O
H
OH
ppm (t1)
7.0
6.0
5.0
4.0
3.0
2.0
0
10
20
30
40
50
60
70



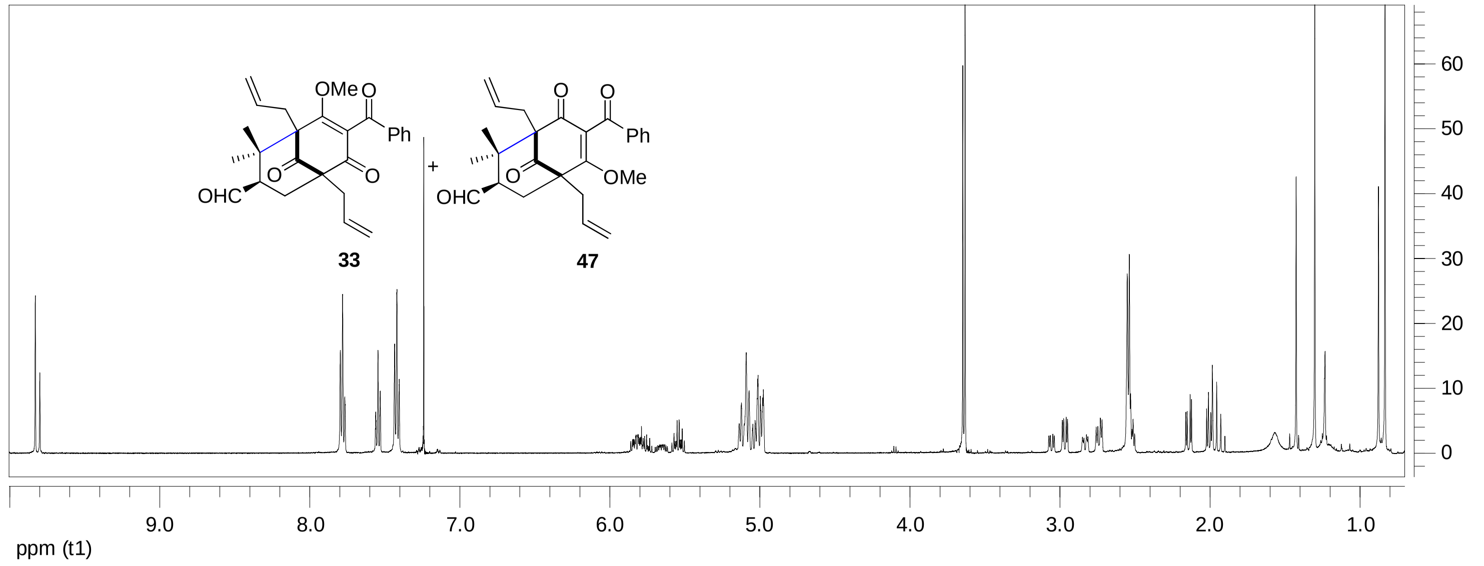
ppm (t1)
200
150
100
50
0.0
5.0
10.0
15.0
20.0
25.0

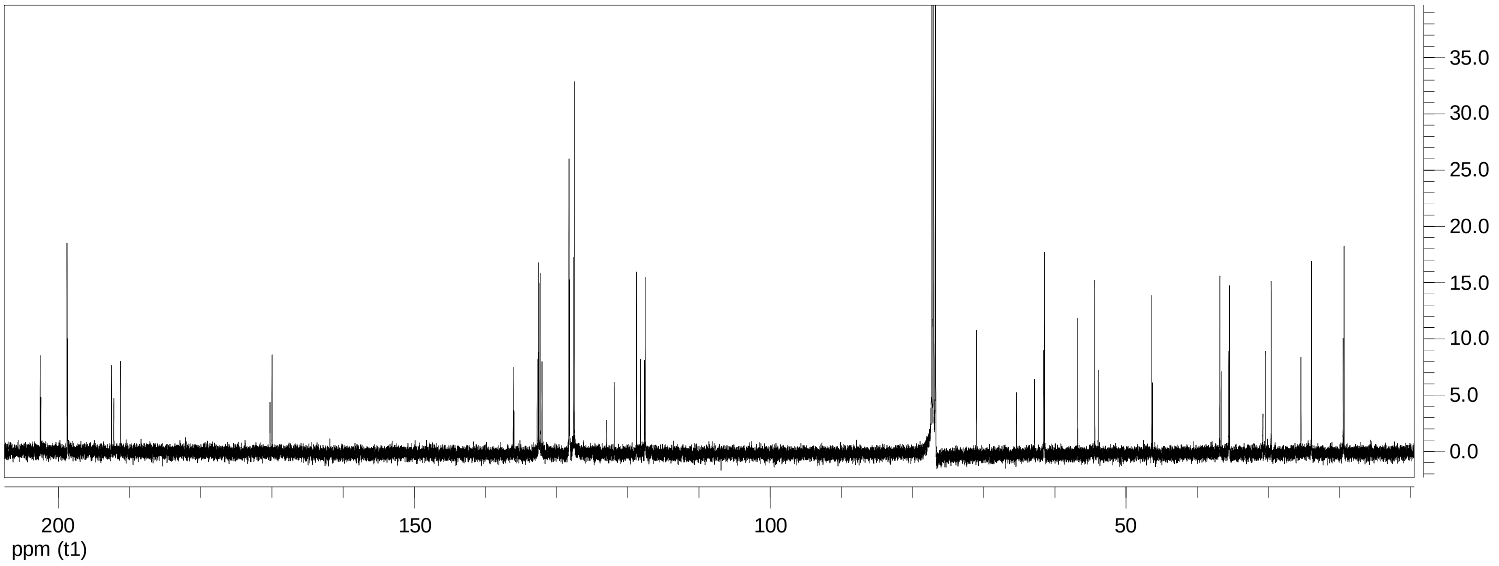

27

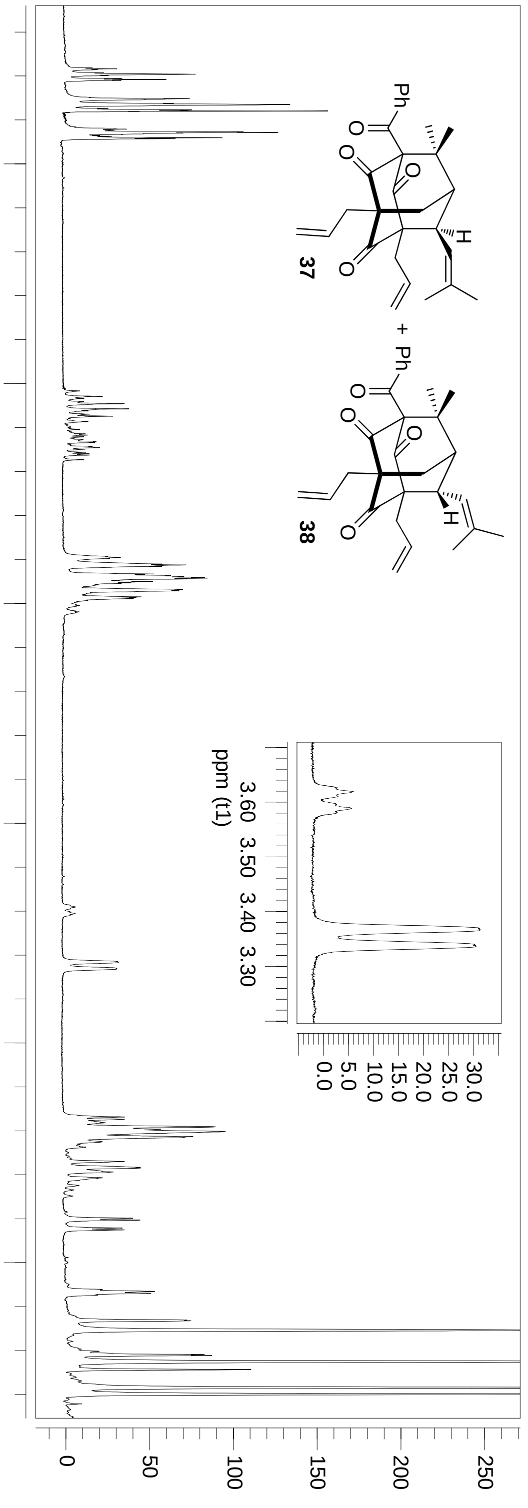
Ph
O
O
O
O
H
OH
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)
250
200
150
100
50
0



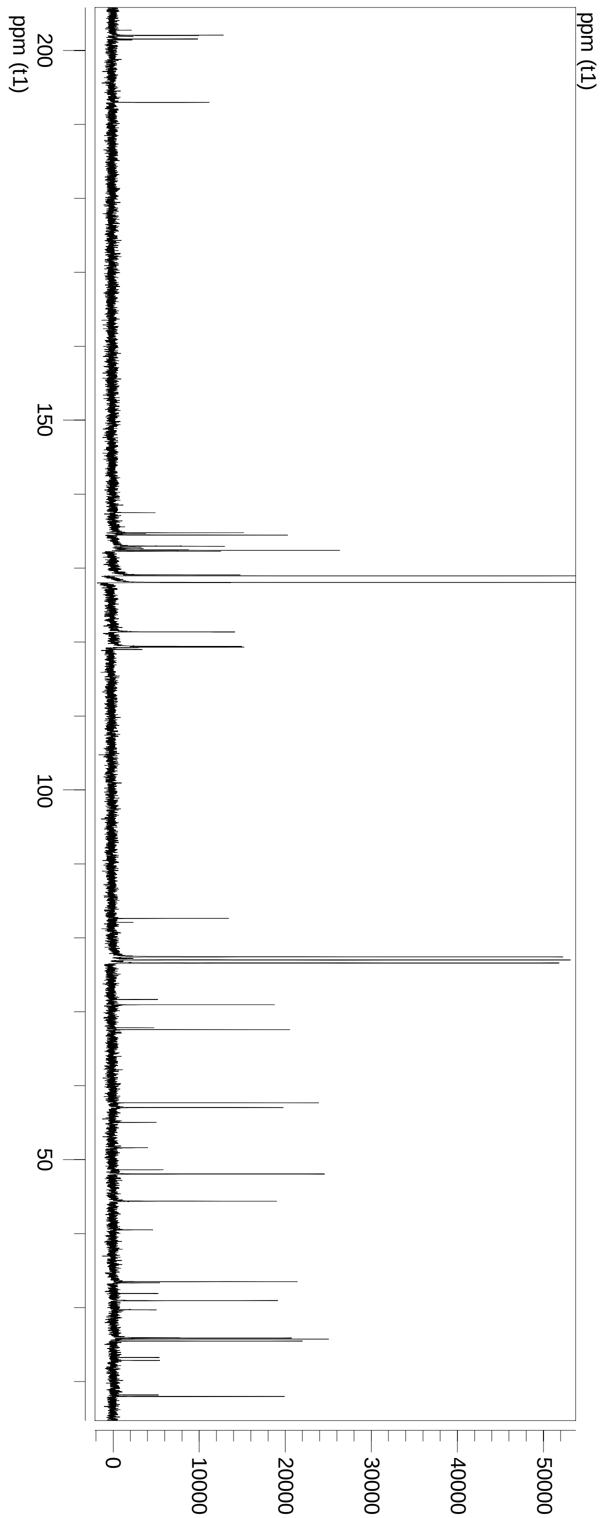
200
150
100
50
ppm (t1)
50
40
30
20
10
0


OMe
O
Ph
O
O
OHC
33
+
O
O
Ph
O
OMe
OHC
47
60
50
40
30
20
10
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

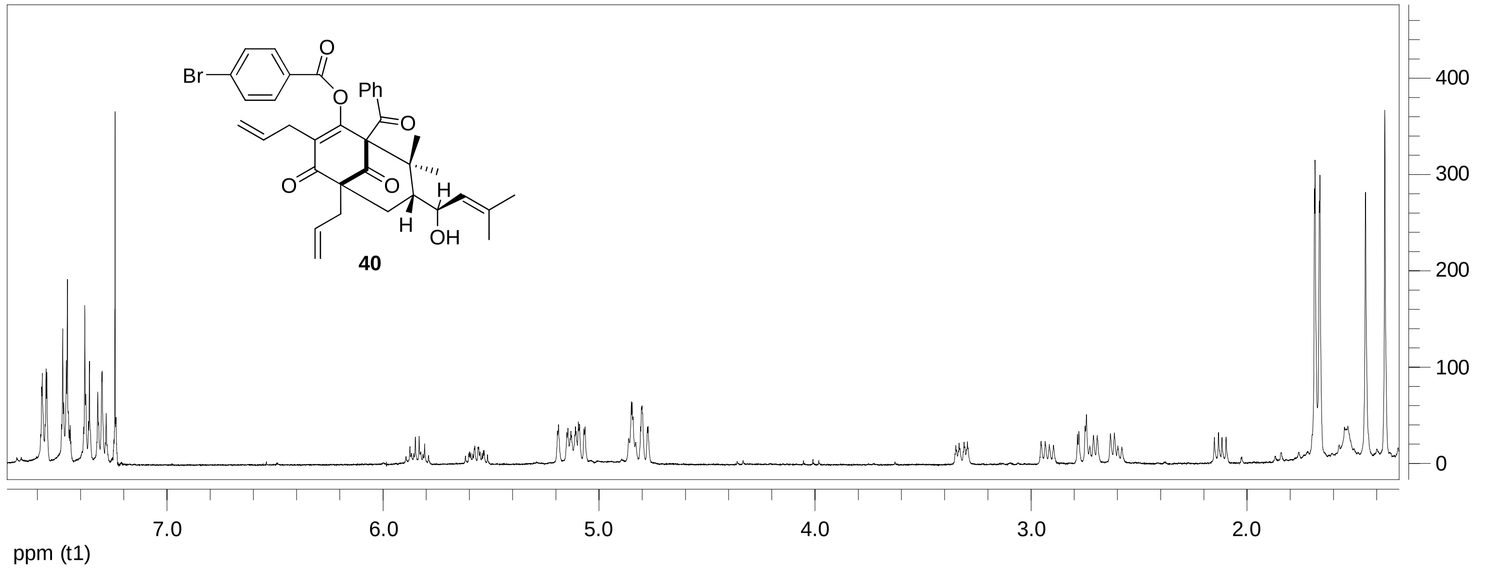

35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
200
150
100
50
ppm (t1)



Ph
O
O
O
O
H
37
+
Ph
O
O
O
O
H
38
3.60
3.50
3.40
3.30
ppm (t1)
30.0
25.0
20.0
15.0
10.0
5.0
0.0
ppm (t1)
7.0
6.0
5.0
4.0
3.0
2.0
0
50
100
150
200
250

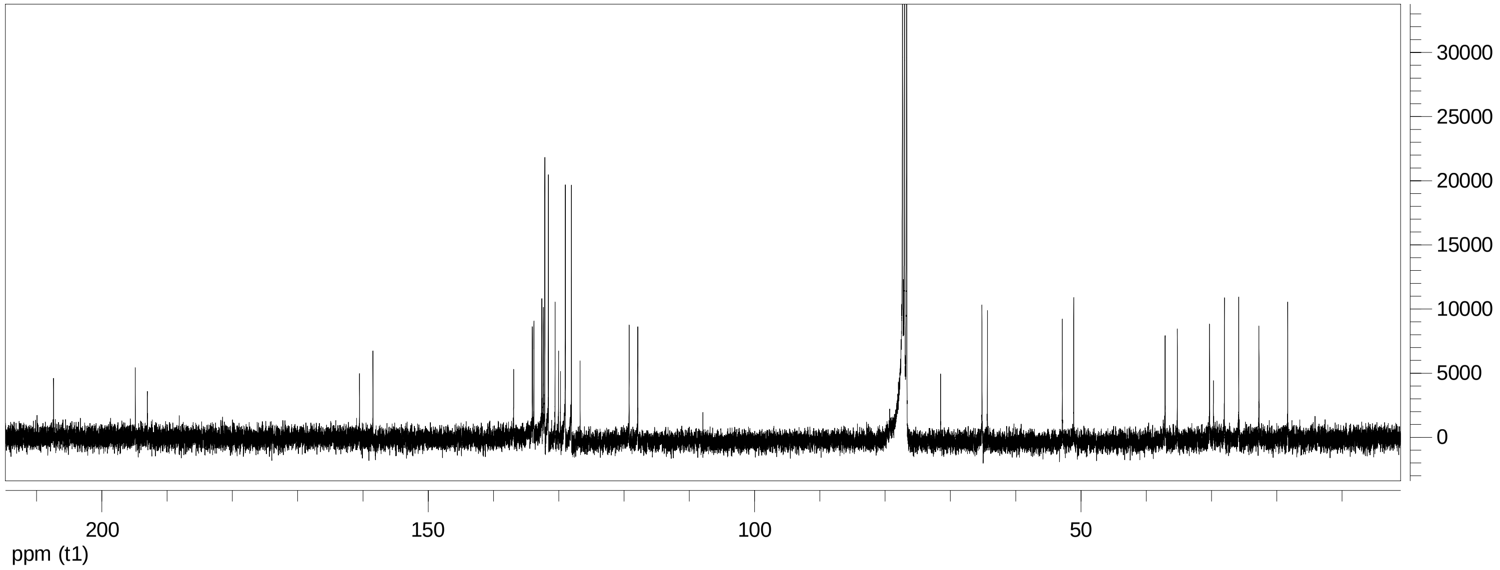


ppm (t1)
200
150
100
50
0
10000
20000
30000
40000
50000

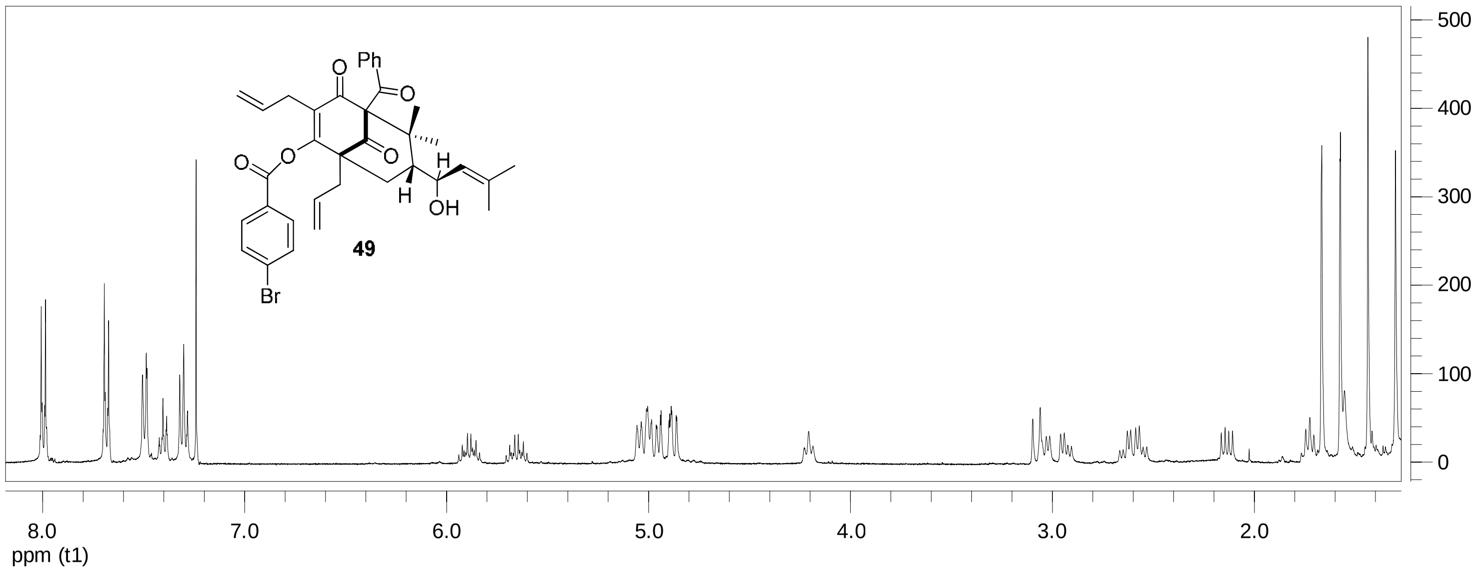


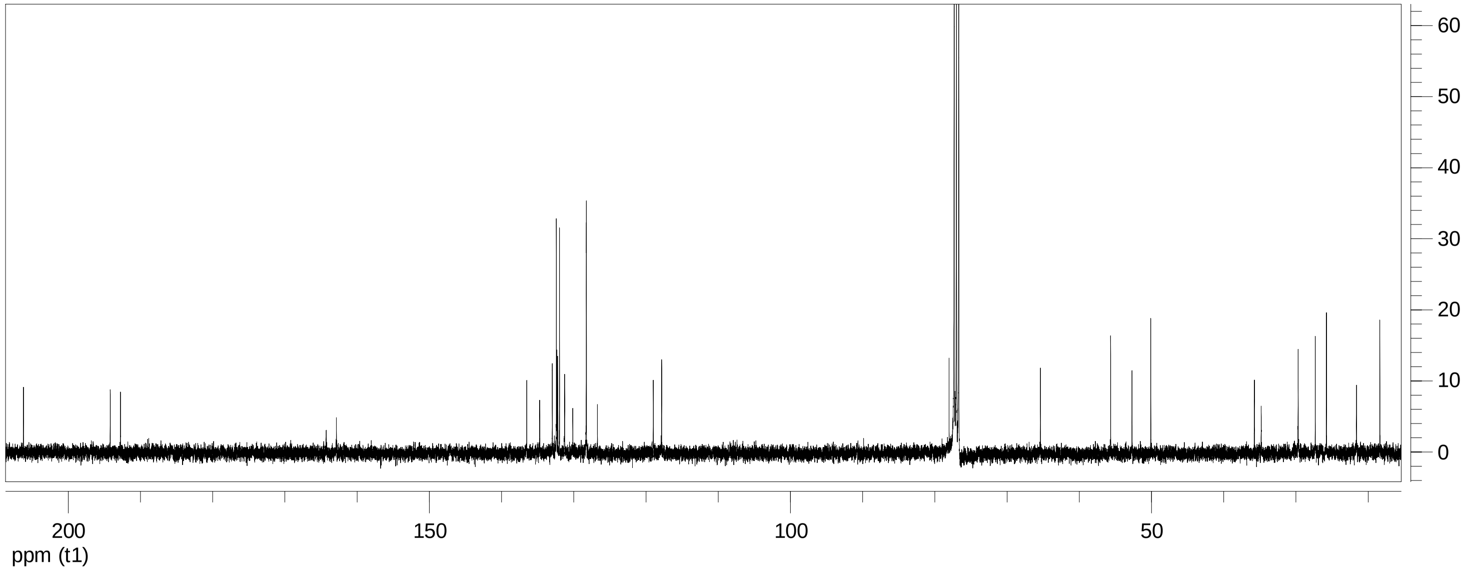
Br
O
O
Ph
O
O
O
H
H
OH
400
300
200
100
0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

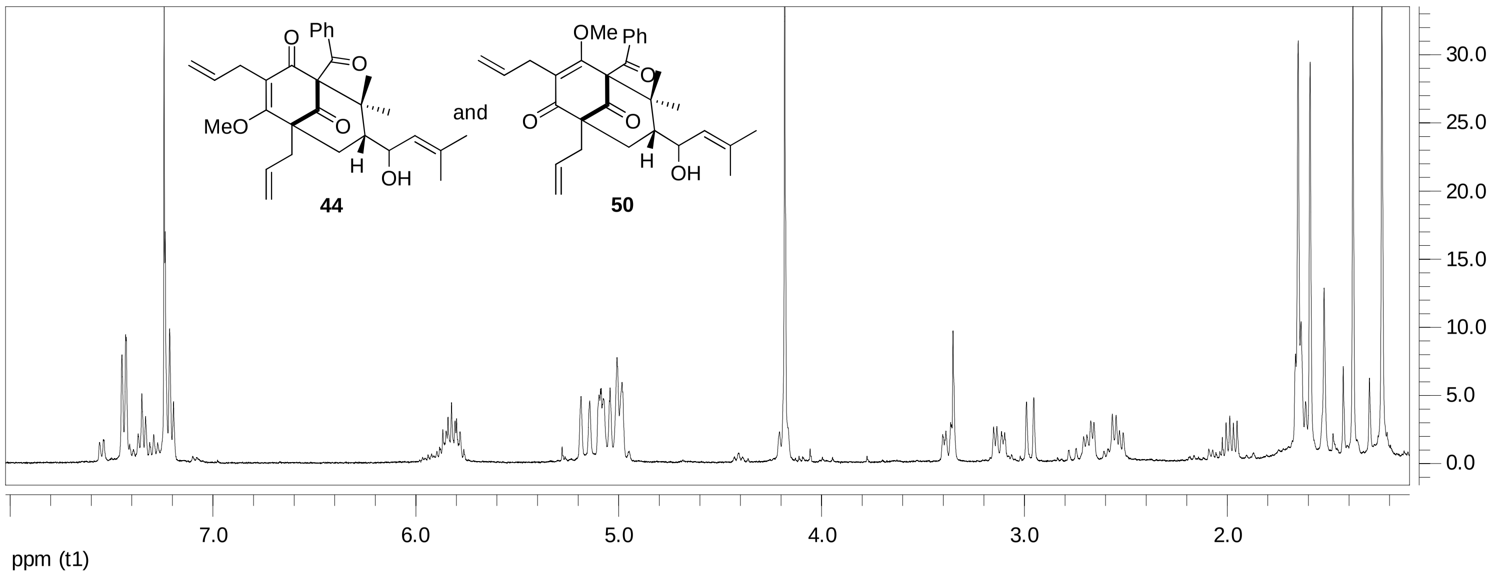
40

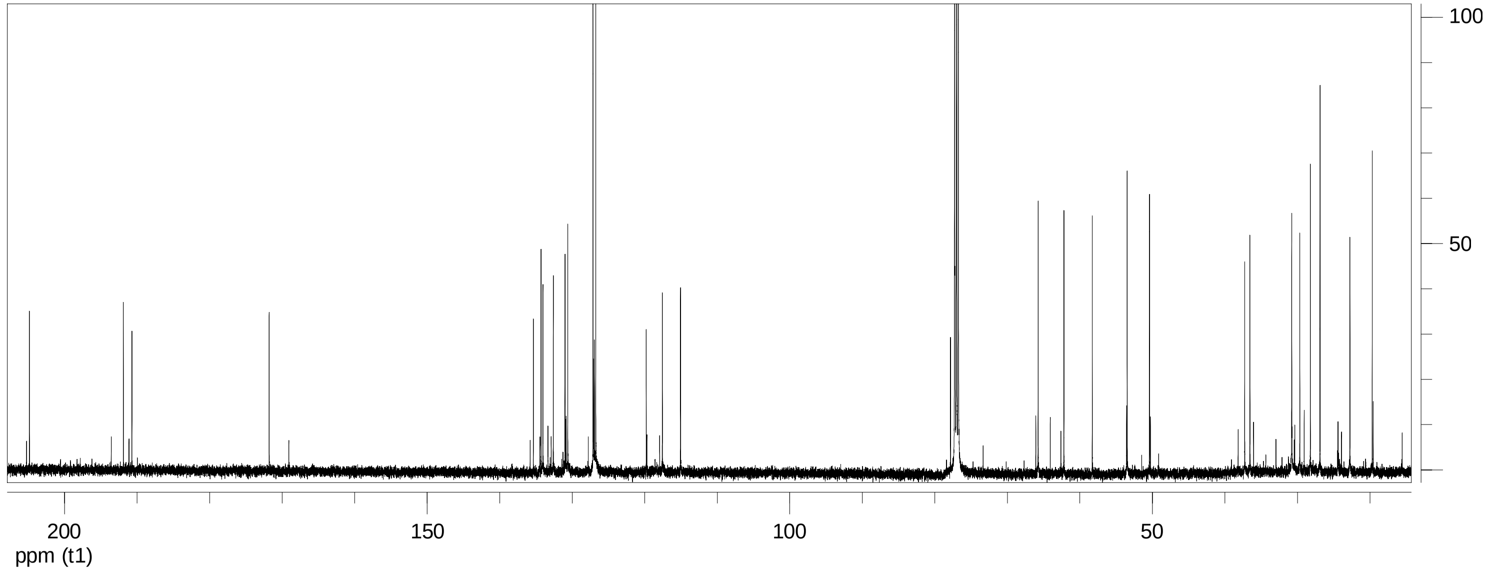


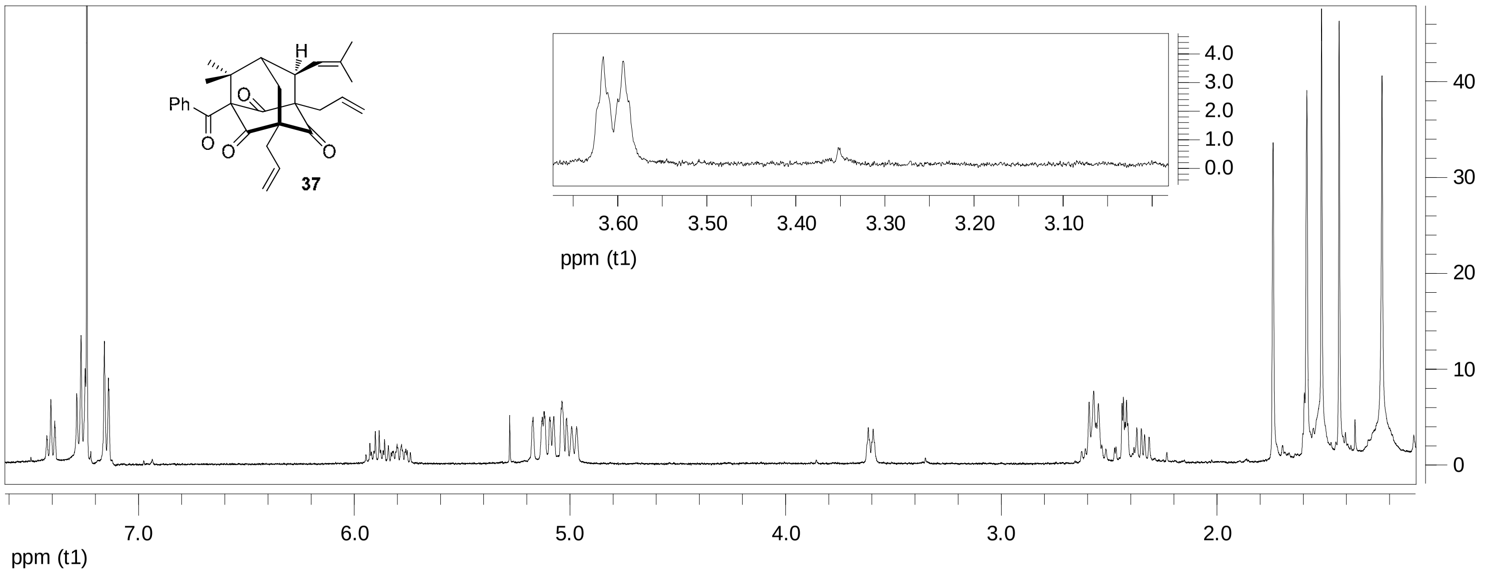
30000
25000
20000
15000
10000
5000
0
200
150
100
50
ppm (t1)

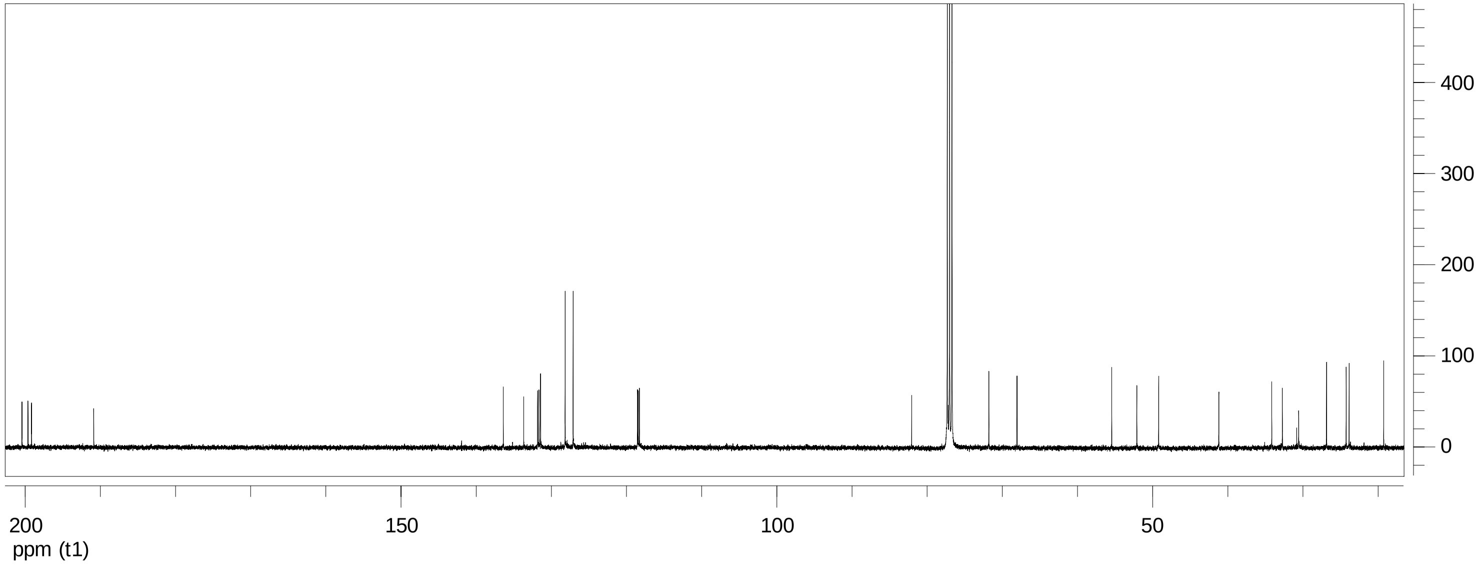

Ph
O
O
O
O
O
H
H
OH
Br
49
500
400
300
200
100
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

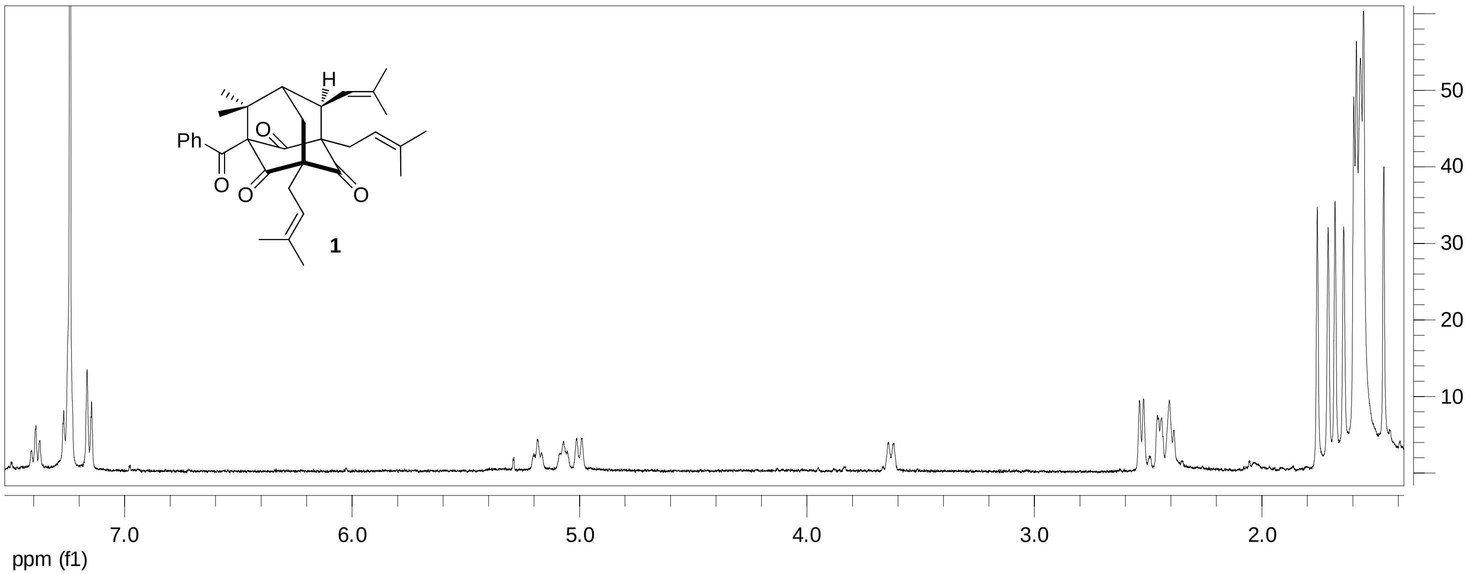

60
50
40
30
20
10
0
200
150
100
50
ppm (t1)

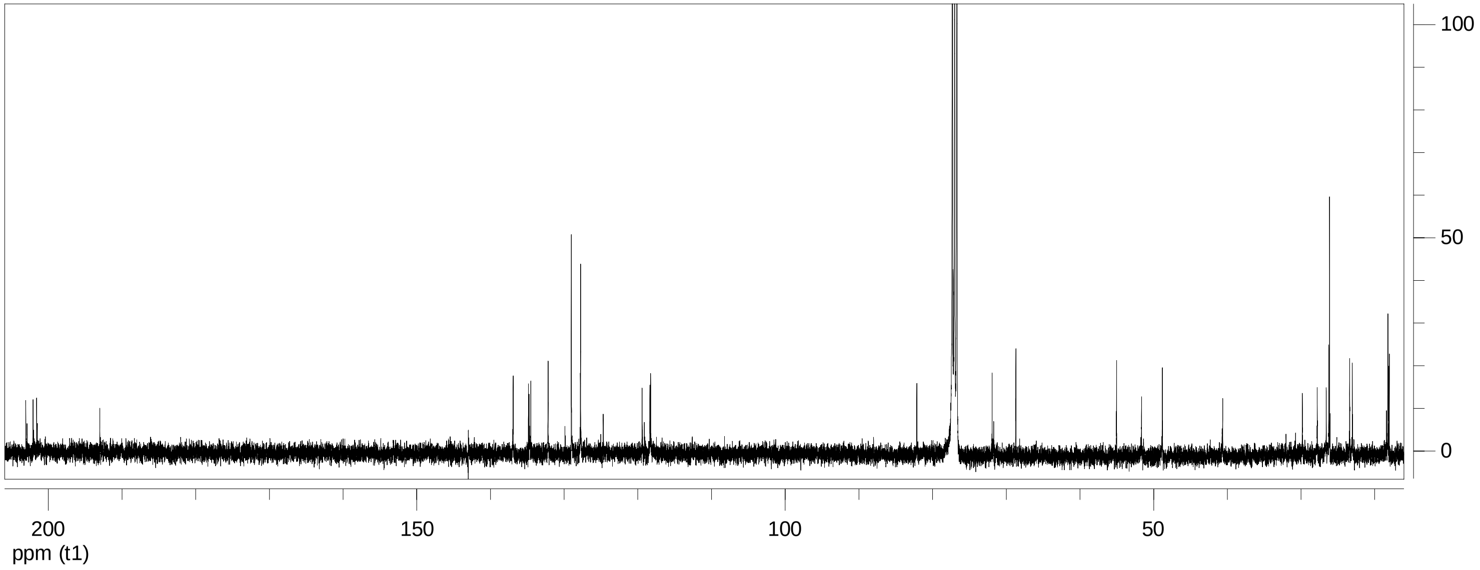

Ph
O
O
MeO
O
H
OH
44
and
OMe
Ph
O
O
O
H
OH
50
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)
30.0
25.0
20.0
15.0
10.0
5.0
0.0


200
150
100
50
ppm (t1)
100
50

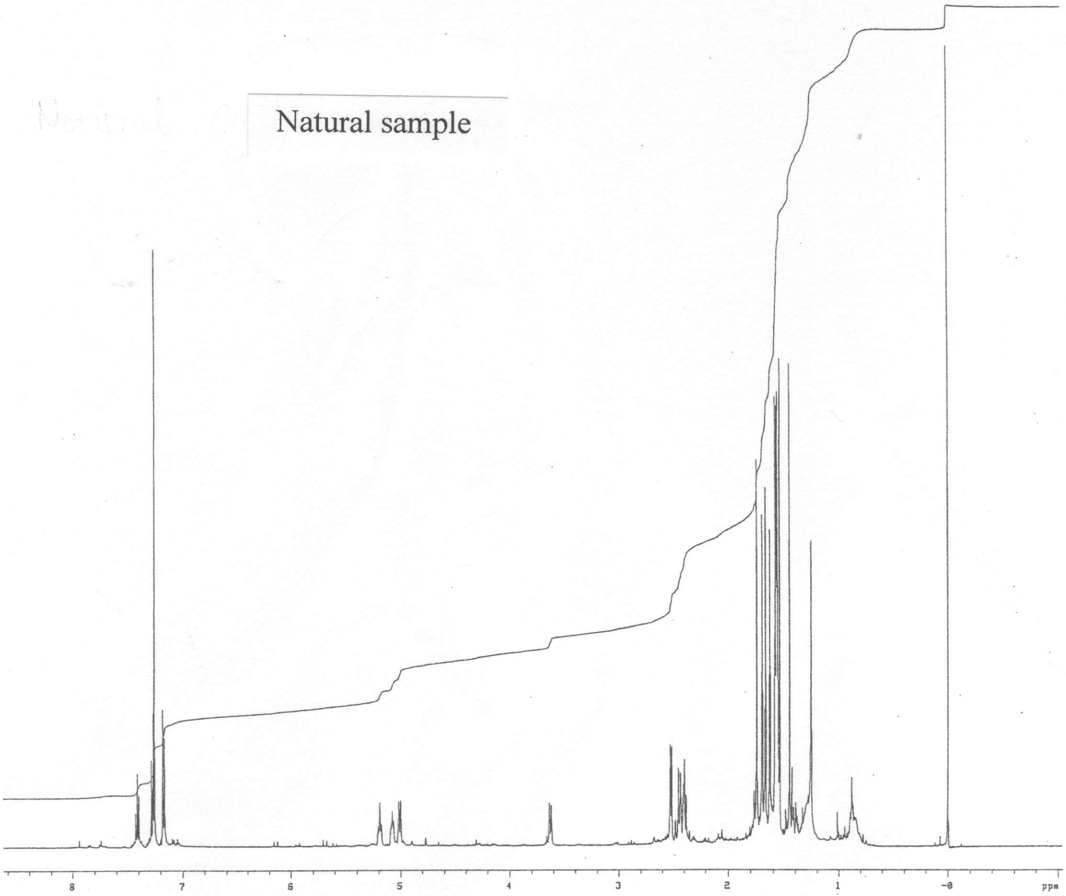

37
Ph
O
O
O
O
H
3.60
3.50
3.40
3.30
3.20
3.10
ppm (t1)
4.0
3.0
2.0
1.0
0.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)
0
10
20
30
40


200
150
100
50
ppm (t1)
0
100
200
300
400

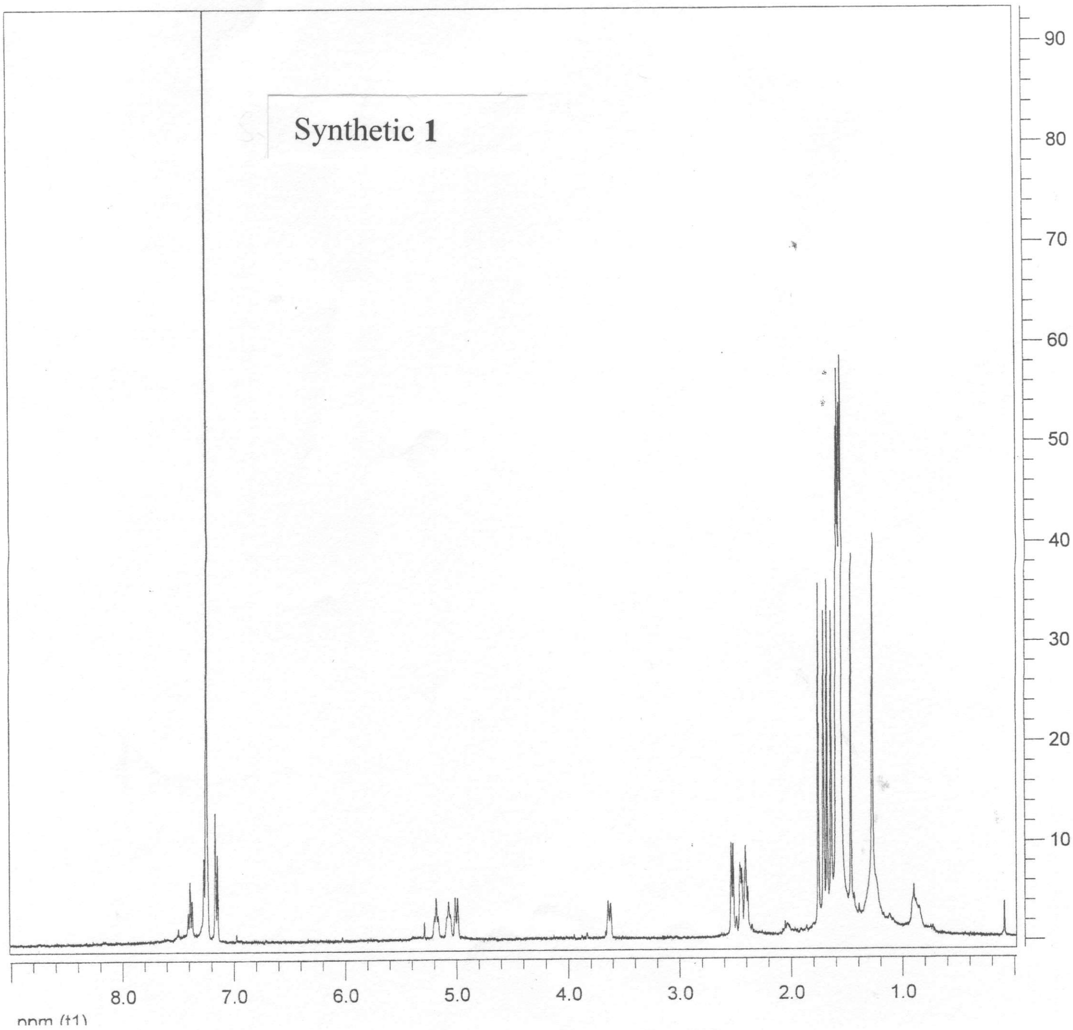

Ph
O
O
O
O
H
1
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)
10
20
30
40
50


200
150
100
50
ppm (t1)
0
50
100

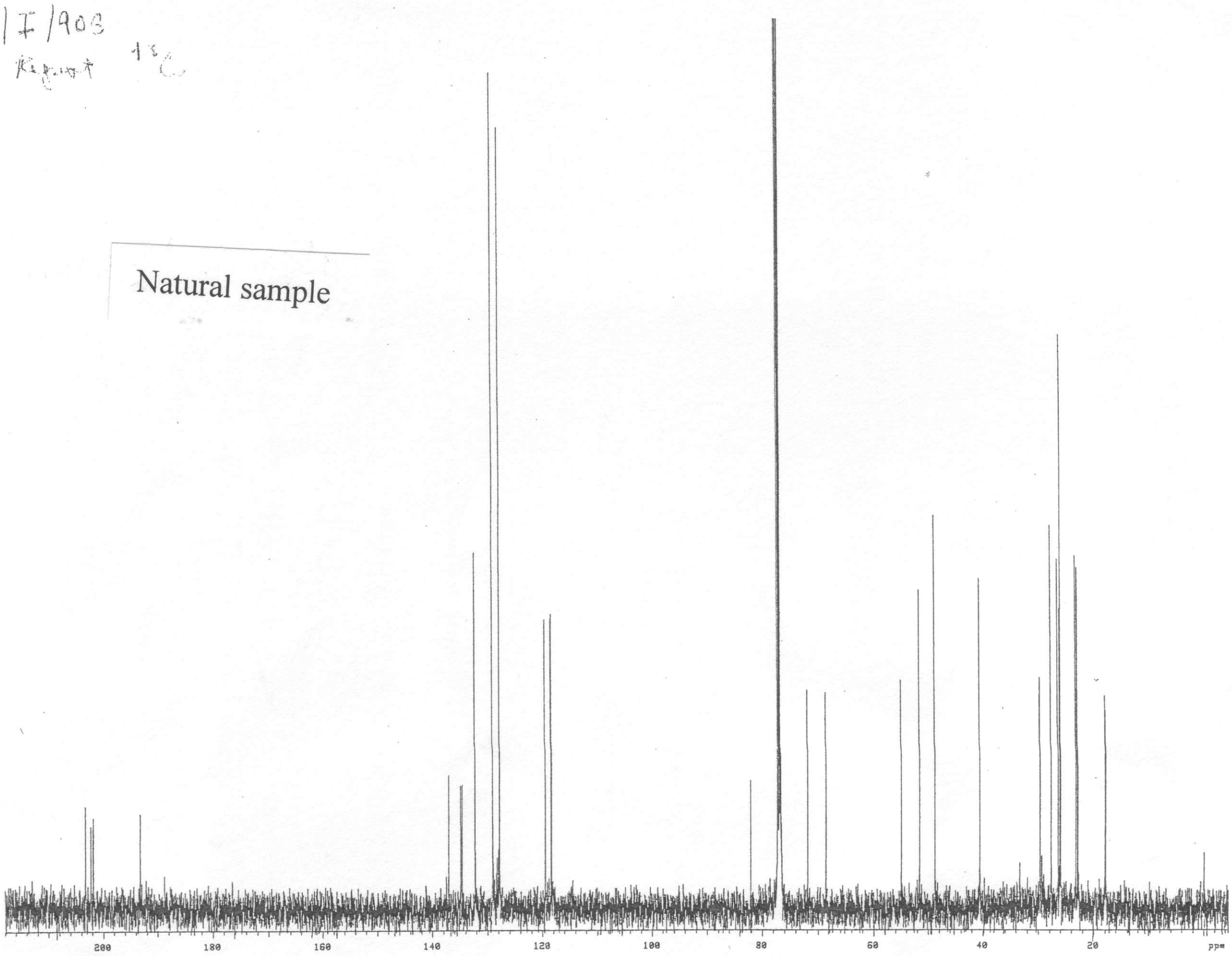
GH/I/90B ¹H



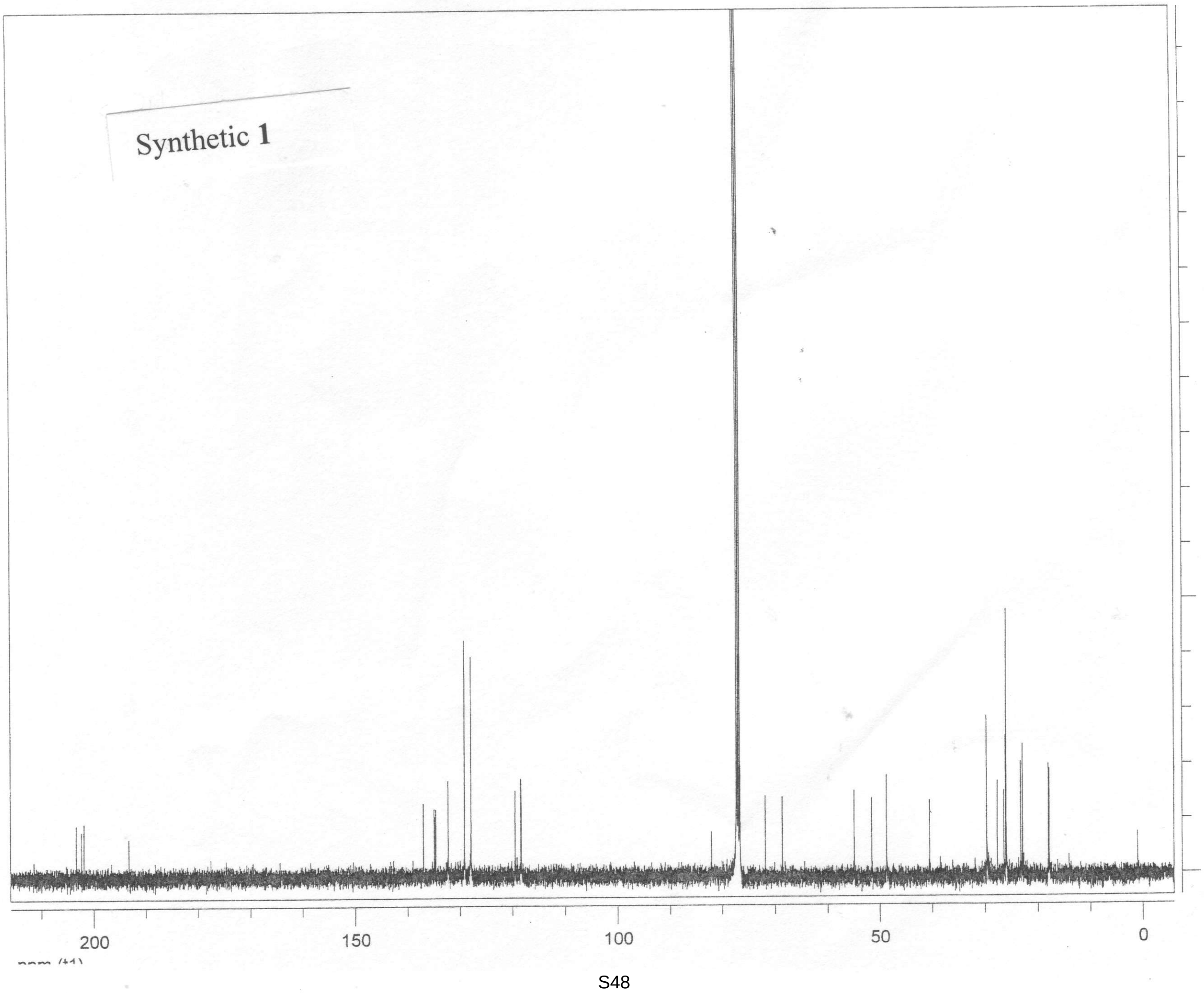
GH/I/9.



GH/II/90B
Repeat ^{13}C


Natural sample

GH/II/90B


Synthetic **1**