An Efficient Oxidative Dearomatization-Radical Cyclization Approach to Symmetrically Substituted Bicyclic Guttiferone Natural Products.

Nicholas A. McGrath, Joshua R. Binner, Georgious Markopoulos, Matthew Brichacek and Jon T. Njardarson*

Department of Chemistry and Chemical Biology, Baker Laboratory, Cornell University
Ithaca, New York 14853-1301

Supporting Information

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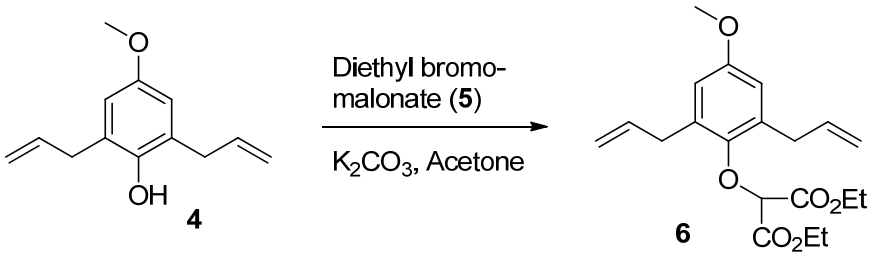
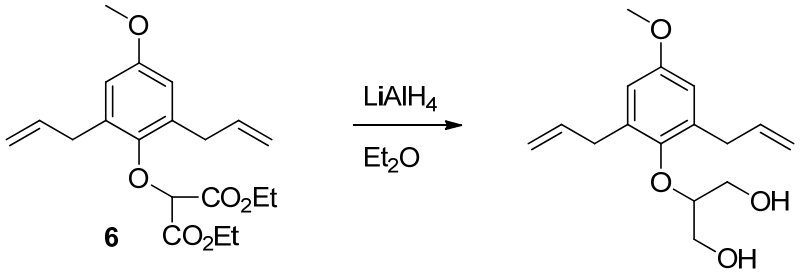
General Information: Commercial reagents were purchased and used without further purification. All glassware was flame dried and reactions were performed under a nitrogen atmosphere, unless otherwise stated. Toluene, dichloromethane, diethyl ether, and THF were dried over a column of alumina. Flash chromatography was done with MP Silitech 32-63D 60Å silica, and thin layer chromatography (TLC) was performed with EMD 250 μm silica gel 60-F_{254} plates. ^{1}H and ^{13}C NMR data was acquired on a Varian Inova 400, 500, or 600 (400, 500 or 600 MHz) spectrometer and referenced to residual protic solvent or TMS. IR spectroscopy was done on a Nicolet Avatar 370 OTGS spectrometer. High-resolution mass spectrometry was performed at the University of Illinois at Urbana-Champaign facility.



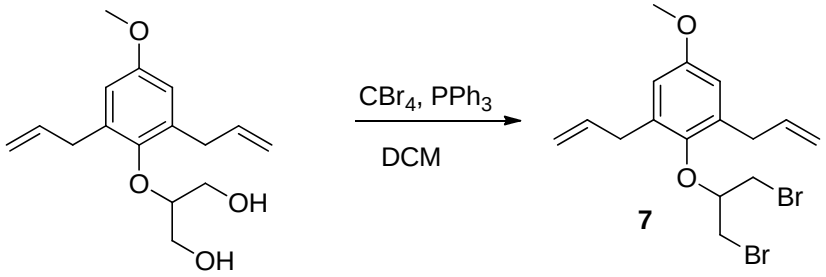
Starting phenol **4** (3.48 g, 17.03 mmol) was dissolved in dry acetone (34.8 ml) and anhydrous potassium carbonate (4.80 g, 34.74 mmol) was added. Diethyl bromomalonate (14.6 ml, 86.67 mmol) was then added and a reflux condenser was attached to the flask. The reaction was refluxed for 14 hours until starting material was consumed. The potassium carbonate was filtered off and the reaction was diluted with diethyl ether and subsequently washed with brine and dried over sodium sulfate. The solvent was removed and the residue was purified with silica gel chromatography to give the malonyl ether **6** (4.30 g, 70%).

FT-IR (thin film/NaCl) 2917, 1743, 1595, 1466, 1195, 1078, 915 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 6.54 (s, 2H), 5.89 (ddt, *J*=6.4, 10.2, 16.6, 2H), 5.07 – 4.98 (m, 4H), 4.75 (s, 1H), 4.32 – 4.15 (m, 4H), 3.70 (s, 3H), 3.38 (d, *J*=6.4, 4H), 1.27 – 1.23 (t, *J*=7.1, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 166.3, 156.3, 148.3, 136.9, 133.9, 116.5, 113.8, 81.9, 62.3, 55.5, 34.3, 14.1; **HRMS** (EI) m/z 362.1741 [calc'd for $C_{20}H_{26}O_6$ (M+) 362.1729].



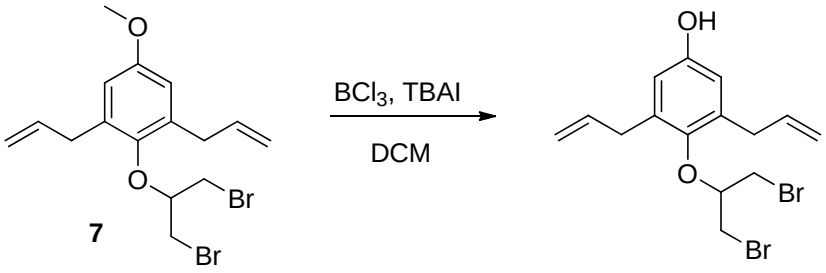
Lithium aluminum hydride (1.57 g, 41.3 mmol) was placed in a flask and ether (37 mL) was added slowly at room temperature. To this slurry was added drop-wise a solution of starting material **6** (3.74 g, 10.33 mmol) and ether (4 mL) over ten minutes and the reaction was allowed to stir an additional 2 hours. The reaction was quenched by slow addition of ethyl acetate followed by water and 1 molar HCl. The reaction was then diluted with ether and washed with brine. The ether was concentrated and the oil was purified with silica gel chromatography to give diol (2.68 g, 93%).

FT-IR (thin film/NaCl) 3406, 2938, 1602, 1466, 1323, 1197, 1050, 915 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 6.58 (s, 2H), 5.97 – 5.83 (m, 2H), 5.11 – 5.01 (m, 4H), 3.96 – 3.90 (m, 1H), 3.87 (dd, *J*=4.7, 11.6, 2H), 3.79 (dd, *J*=4.1, 11.4, 2H), 3.72 (s, 3H), 3.41 – 3.38 (m, 4H), 2.64 (bs, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 155.8, 146.8, 137.0, 134.1, 116.5, 113.9, 82.1, 62.3, 55.6, 34.5; **HRMS** (EI) m/z 278.1521 [calc'd for $C_{16}H_{22}O_4$ (M+) 278.1518].



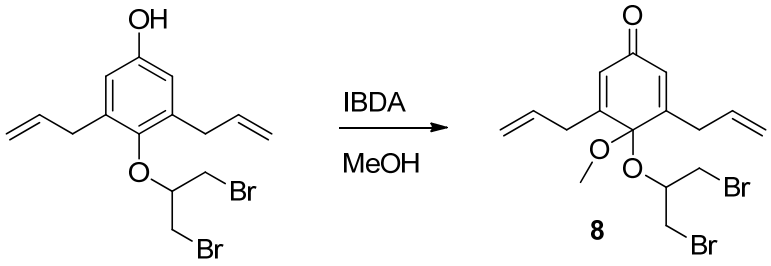
Starting diol (318 mg, 1.14 mmol) and triphenylphosphine (1.05 g, 4.00 mmol) were dissolved in dry dichloromethane (11.4 ml) at 0°C and carbon tetrabromide (1.33 g, 4.00 mmol) was then added. The ice bath was removed and the reaction was allowed to stir 12 hours to ensure completion. The reaction mixture was then concentrated and purified directly with silica gel chromatography to give pure dibromide **7** (427 mg, 92%).

FT-IR (thin film/NaCl) 2937, 1638, 1602, 1465, 1327, 1186, 1052, 915 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 6.59 (s, 2H), 6.00 – 5.84 (m, 2H), 5.20 – 4.97 (m, 4H), 4.23 – 4.19 (m, 1H), 3.74 (s, 3H), 3.73 (dd, *J*=3.7, 10.4, 2H), 3.64 (dd, *J*=3.7, 10.4, 2H), 3.42 – 3.39 (m, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 156.2, 145.8, 136.7, 134.2, 116.8, 114.1, 79.5, 55.6, 34.7, 32.4; **HRMS** (EI) m/z 401.98379 [calc'd for $C_{16}H_{20}O_2Br_2$ (M+) 401.98303].



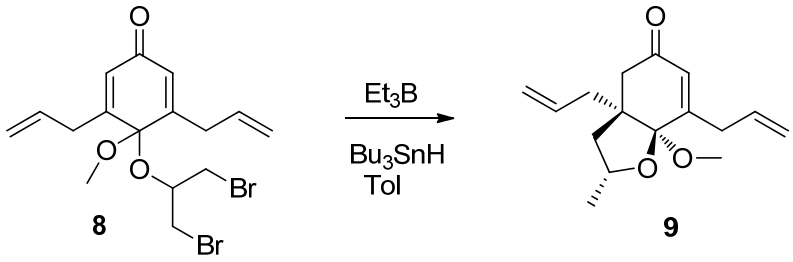
Dibromide **7** (19 mg, 0.048 mmol) was dissolved in dichloromethane (0.24 ml) and tetrabutylammonium iodide (20 mg, 0.053 mmol) was added. The reaction was cooled to -78°C and boron trichloride solution (0.058 ml, 1M, 0.058 mmol) was added slowly. The reaction was then placed in a -10°C bath and stirred two hours. When complete, the reaction was quenched with saturated sodium bicarbonate and extracted with dichloromethane. The organics were dried over sodium sulfate, concentrated and purified with silica gel chromatography to give phenol (15 mg, 80%).

FT-IR (thin film/NaCl) 3387, 2917, 1598, 1454, 1322, 916 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 6.53 (s, 2H), 6.00 – 5.82 (m, 2H), 5.18 – 5.02 (m, 4H), 4.22 – 4.19 (m, 1H), 3.72 (dd, *J*=6.2, 10.4, 2H), 3.63 (dd, *J*=6.2, 10.4, 2H), 3.40 – 3.36 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 152.2, 145.8, 136.6, 134.5, 116.9, 115.5, 79.5, 34.5, 32.3; **HRMS** (EI) m/z 387.9670 [calc'd for $C_{15}H_{18}O_2Br_2$ (M+) 387.9674].



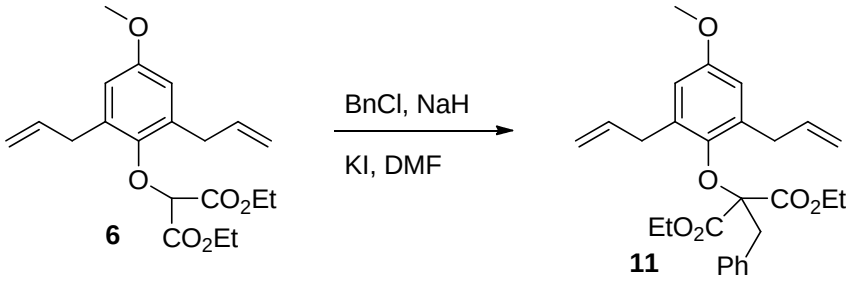
Dibromide phenol (1.00 g, 2.56 mmol) was dissolved in dry methanol (23 ml) and cooled to 0°C. Iodobenzene diacetate (0.908 g, 2.82 mmol) was added and the reaction turned bright yellow immediately. The reaction was concentrated and purified with a plug of silica gel to give pure dearomatized product **8** (1.01 g, 94%).

FT-IR (thin film/NaCl) 2977, 2944, 1675, 1640, 1427, 1294, 1102, 1061, 1037, 923 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 6.33 (s, 2H), 5.90 – 5.79 (m, 2H), 5.35 – 5.19 (m, 4H), 3.83 (tt, *J*=3.3, 6.5, 1H), 3.62 – 3.50 (m, 4H), 3.30 – 3.17 (m, 2H), 3.09 (s, 3H), 3.10 – 2.99 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 184.5, 157.2, 132.3, 130.5, 120.1, 98.4, 72.0, 51.6, 33.4, 33.0; **HRMS** (EI) m/z 417.9782 [calc'd for $C_{16}H_{20}O_3Br_2$ (M+) 417.9780].



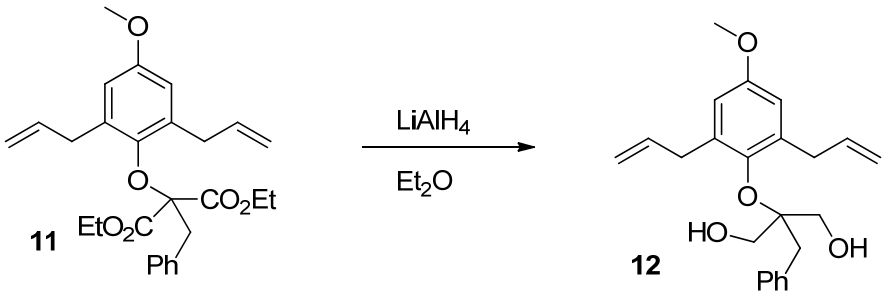
Starting material **8** (46 mg, 0.110 mmol) was dissolved in freshly distilled toluene (11 ml) and was cooled to -78° C. Tributyltin hydride (0.09 ml, 0.330 mmol) was added to the reaction followed by triethylborane (0.01 ml, 0.011 mmol). The reaction was allowed to stir 30 minutes and the bath was removed. After 30 additional minutes at room temperature, the reaction was concentrated and purified with silica gel chromatography to give mono cyclized product **9** (25 mg, 87%).

FT-IR (thin film/NaCl) 2970, 2935, 1678, 1262, 1122, 1026, 669 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 5.85 (s, 1H), 5.85 – 5.65 (m, 2H), 5.21 – 5.05 (m, 4H), 4.40 – 4.35 (m, 1H), 3.48 (s, 3H), 3.11 – 3.05 (m, 2H), 2.56 – 2.36 (m, 3H), 2.19 (dd, *J*=7.8, 13.9, 1H), 1.92 – 1.71 (m, 2H), 1.36 (d, *J*=6.2, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 198.1, 159.5, 133.9, 133.9, 127.2, 119.3, 118.8, 105.3, 75.2, 52.6, 52.3, 44.3, 43.2, 39.3, 35.3, 21.4; **HRMS** (EI) m/z 262.1566 [calc'd for $C_{16}H_{22}O_3$ (M+) 262.1569].



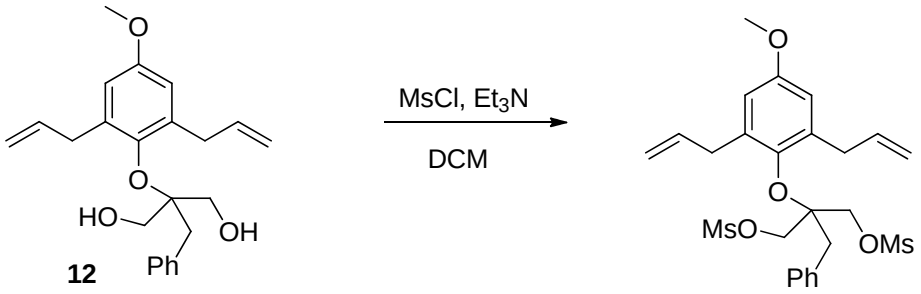
Potassium iodide (1.26 g, 7.62 mmol) and sodium hydride (0.112 g, 2.79 mmol) were mixed and dry DMF (25 ml) was added and cooled to -10°C. The starting material **6** (0.92 g, 2.54 mmol) was dissolved in dry DMF (2 ml) and added slowly to the slurry. After complete addition, benzyl chloride (0.44 ml, 3.81 mmol) was added and the bath was removed. After 4 hours the reaction was diluted with ether and washed with distilled water. The ethereal solution was dried over sodium sulfate, concentrated and purified with silica gel chromatography to give benzylated product **11** (0.98 g, 85%).

FT-IR (thin film/NaCl) 3073, 2981, 2838, 1741, 1602, 1463, 1247, 1195, 1055, 914, 700 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.21 – 7.05 (m, 5H), 6.52 (s, 2H), 5.97 – 5.79 (m, 2H), 5.14 – 5.00 (m, 4H), 4.05 – 3.94 (m, 4H), 3.73 (s, 3H), 3.49 (s, 2H), 3.42 (d, *J*=6.8, 4H), 1.06 (t, *J*=7.2, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 168.2, 156.5, 145.6, 136.8, 134.8, 130.5, 128.3, 128.1, 127.2, 116.7, 112.9, 88.6, 62.0, 55.5, 41.1, 35.4, 13.8; **HRMS** (EI) m/z 452.2198 [calc'd for $C_{27}H_{32}O_6$ (M+) 452.2199].



Lithium aluminum hydride (147 mg, 3.87 mmol) was added to a flask and dry ether (8.7 ml) was added carefully. Starting material **11** (875 mg, 1.94 mmol) was dissolved in ether (1 ml) and added drop-wise to the LAH solution over twenty minutes. The reaction was allowed to stir 1 hour and then quenched with ethyl acetate followed by water and 1 molar HCl. The product was extracted with ether, dried over sodium sulfate and concentrated to an oil. The oil was purified with silica gel chromatography to give pure diol **12** (700 mg, 98%).

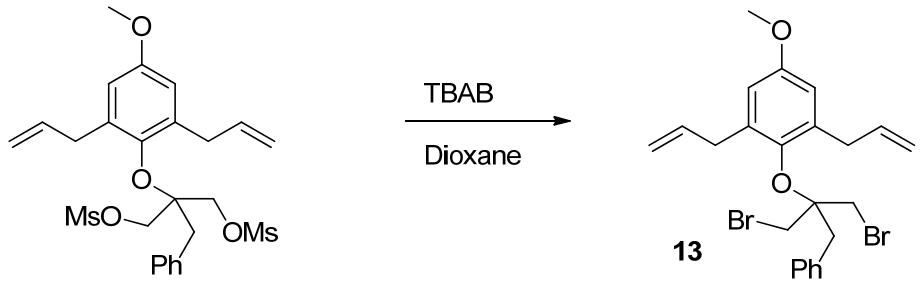
FT-IR (thin film/NaCl) 3460, 2938, 1638, 1602, 1461, 1320, 1197, 1052, 915 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.30 – 7.15 (m, 5H), 6.63 (s, 2H), 5.98 – 5.82 (m, 2H), 5.16 – 5.06 (m, 4H), 3.76 – 3.75 (m, 7H), 3.48 (d, *J*=6.4, 4H), 3.05 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 155.9, 145.3, 136.9, 136.5, 135.9, 130.7, 128.5, 128.3, 116.9, 113.9, 86.4, 65.0, 55.5, 39.1, 35.7; **HRMS** (EI) m/z 368.1987 [calc'd for $C_{23}H_{28}O_4$ (M+) 368.1988].



12

Starting diol **12** (75 mg, 0.20 mmol) was dissolved in dry dichloromethane at 0°C. Freshly distilled triethylamine (0.11 ml, 0.80 mmol) was added followed by drop-wise addition of methane sulfonyl chloride (0.04 ml, 0.44 mmol). The reaction was stirred ten minutes and then neutralized with saturated sodium bicarbonate and extracted with dichloromethane. The combined extracts were dried over sodium sulfate, concentrated and subjected to silica gel chromatography to yield bis-mesylate (81 mg, 76%).

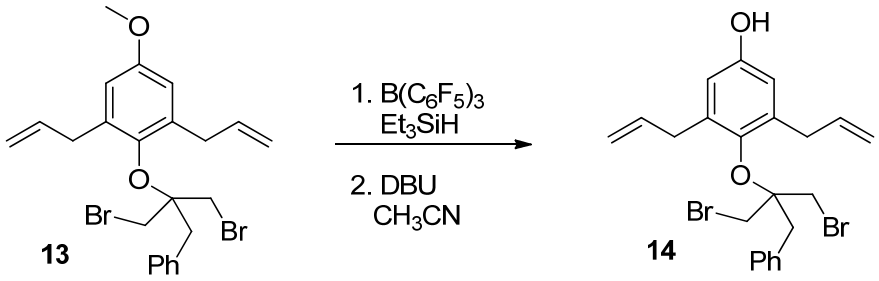
FT-IR (thin film/NaCl) 3028, 2938, 1639, 1602, 1464, 1367, 1343, 1175, 1053 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.42 – 7.13 (m, 5H), 6.63 (s, 2H), 5.89 – 5.82 (m, 2H), 5.18 – 5.09 (m, 4H), 4.37 (d, *J*=10.3, 2H), 4.31 (d, *J*=10.3, 2H) 3.76 (s, 3H), 3.40 (d, *J*=6.3, 4H), 3.02 (s, 2H), 2.88 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 156.4, 144.5, 136.6, 135.8, 134.1, 130.9, 128.8, 127.7, 117.4, 114.0, 81.8, 68.1, 55.7, 39.5, 37.5, 35.3; **HRMS** (ESI) m/z 547.1437 [calc'd for $C_{25}H_{32}O_8S_2Na$ (M+Na) 547.1436].



13

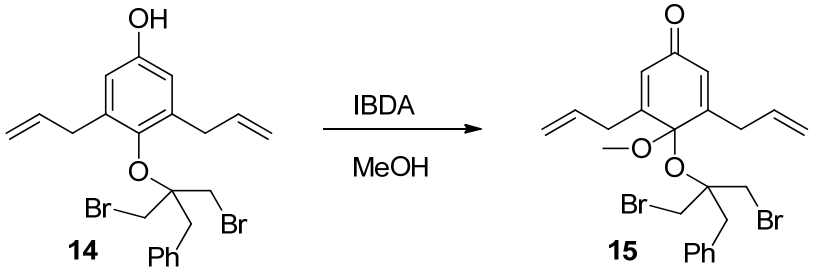
Starting material (80 mg, 0.15 mmol) and tetrabutyl ammonium bromide (500 mg, 1.5 mmol) were dissolved in dioxane (1.6 ml) and sealed tightly in a small vial. The reaction was heated at 130°C for 18 hours until TLC showed complete conversion. The solids were filtered and the solvent removed. The resulting residue was purified with silica gel chromatography to give dibromide **13** (65 mg, 86%).

FT-IR (thin film/NaCl) 3076, 2977, 2936, 1602, 1462, 1321, 1195, 1054, 997, 916 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.32 – 7.03 (m, 5H), 6.58 (s, 2H), 5.90 – 5.78 (m, 2H), 5.16 – 5.00 (m, 4H), 3.80 (s, 4H), 3.76 (s, 3H), 3.34 (d, *J*=6.5, 4H), 3.27 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 156.2, 145.1, 136.8, 135.9, 135.2, 131.1, 128.4, 127.3, 117.1, 113.6, 82.5, 55.6, 41.3, 37.4, 35.6; **HRMS** (ESI) m/z 515.0209 [calc'd for $C_{23}H_{26}Br_2O_2$ (M+Na) 515.0197].



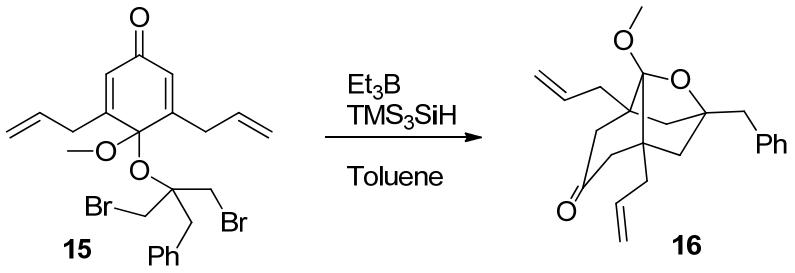
Starting material **13** (25 mg, 0.051 mmol) and tris(pentaflurobenzene) borane (2.6 mg, 0.005 mmol) were mixed at room temperature and 0.5 ml of a 10% solution of triethylsilane (0.09 ml, 0.56 mmol) in dichloromethane (4.91 ml) was added. The reaction was allowed to stir 36 hours for complete consumption of starting material. The TES group was then removed by addition of DBU (0.006 ml, 0.051 mmol) and 0.5 ml of acetonitrile and stirring 5 minutes. The reaction was treated with saturated ammonium chloride and extracted with dichloromethane. The organics were then dried over sodium sulfate, concentrated down and purified with silica gel to give free phenol **14** (18 mg, 75%).

FT-IR (thin film/NaCl) 3061, 2956, 2930, 1600, 1496, 1452, 1184, 996, 703 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.26 – 7.14 (m, 5H), 6.52 (s, 2H), 5.89 – 5.77 (m, 2H), 5.14 – 5.05 (m, 4H), 4.56 (bs, 1H), 3.79 (s, 4H), 3.31 (d, *J*=6.4, 4H), 3.27 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 152.2, 145.2, 136.6, 136.3, 135.2, 131.1, 128.4, 127.4, 117.2, 115.1, 82.6, 41.4, 37.4, 35.4; **HRMS** (EI) m/z 478.0139 [calc'd for $C_{22}H_{24}O_2Br_2$ (M+) 478.0143].



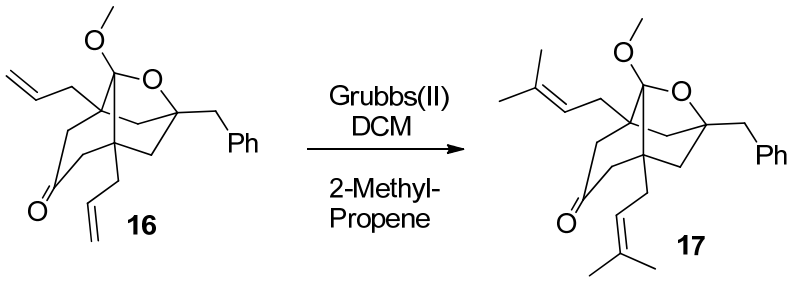
Starting phenol **14** (7.5 mg, 0.016 mmol) and anhydrous methanol (0.2 ml) were mixed at room temperature and iodobenzene diacetate (5 mg, 0.016 mmol) was added. The reaction was stirred five minutes and then the solvent was removed and the residue purified with silica gel chromatography to yield pure dearomatized bis-bromide **15** (6.0 mg, 75%).

FT-IR (thin film/NaCl) 2965, 1657, 1640, 1495, 1426, 1294, 1015, 922, 703 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.38 – 7.14 (m, 5H), 6.22 (s, 2H), 5.80 – 5.69 (m, 2H), 5.25 – 4.99 (m, 4H), 3.54 (aq, *J*=11.4, 4H), 3.24 (dd, *J*=18.2, 7.2, 2H), 3.22 (s, 2H), 2.92 (s, 3H), 2.90 (dd, *J*=18.2, 7.2, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 184.7, 159.5, 135.2, 132.8, 131.1, 129.9, 128.8, 127.8, 120.0, 97.6, 81.5, 50.7, 41.8, 37.8, 33.8; **HRMS** (DART) m/z 509.03447 [calc'd for $C_{23}H_{27}O_3Br_2$ (M+H) 509.03273].



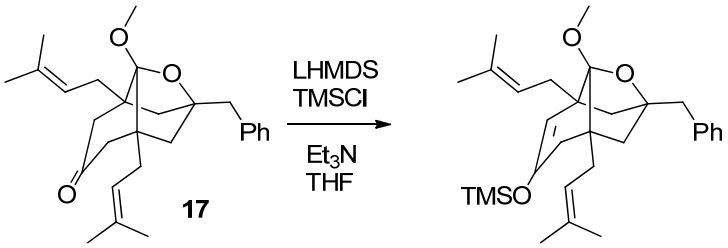
Starting material **15** (40 mg, 0.078 mmol) was dissolved in dry toluene (1.57 ml) at room temperature and tris(trimethylsilyl)silane (0.07 ml, 0.235 mmol) was added followed by triethyl borane (0.07 ml, 0.07 mmol). The reaction was purged with air and subsequently stirred for 4 hours. The reaction was loaded directly onto a silica gel column and purified to provide the cyclized product **16** (20 mg, 73%).

FT-IR (thin film/NaCl) 2952, 2892, 1672, 1455, 1244, 1083, 914 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.31 – 7.18 (m, 5H), 5.62 (dd, *J*=10.0, 16.0, 2H), 5.03 (d, *J*=10.0, 2H), 4.92 (d, *J*=16.0, 2H), 3.67 (s, 3H), 2.96 (s, 2H), 2.40 (d, *J*=13.3, 2H), 2.33 (dd, *J*=7.4, 13.7, 2H), 2.26 (d, *J*=13.3, 2H), 2.15 (dd, *J*=8.5, 13.7, 2H), 1.74 (d, *J*=11.5, 2H), 1.18 (d, *J*=11.5, 2H); **^{13}C NMR** (HSQC-AD/gHMBC-AD Derived 150 MHz, $CDCl_3$) δ = 211.0, 136.9, 133.6, 130.0, 128.2, 126.6, 118.8, 108.1, 79.4, 55.5, 51.1, 47.4, 44.5, 42.6, 42.3; **HRMS** (ESI) m/z 375.1935 [calc'd for $C_{23}H_{28}O_3$ (M+Na) 375.1936].



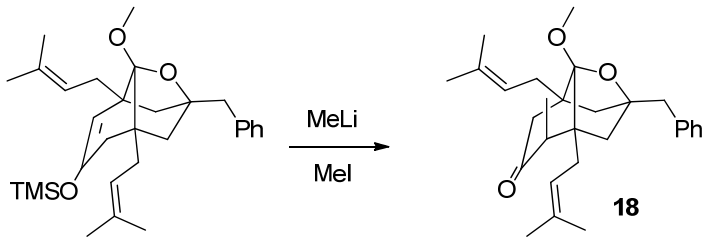
Starting material **16** (10 mg, 0.028 mmol) was dissolved in dry dichloromethane (2 ml) and to this was added Grubbs second generation catalyst (2.4 mg, 0.0028 mmol). Meanwhile, 2-methyl-propene (2 ml) was condensed into a pressure vessel at -78^{o}C and to this was added the starting material/Grubbs mixture. The pressure vessel was sealed and heated at 40^{o}C for 8 hours. The reaction was then removed from the bath and pressure was carefully allowed to escape. The remaining solution was filtered through a plug of silica gel with 30% ethyl acetate 70% hexanes to afford pure prenylated product **17** (10 mg, 87%).

FT-IR (thin film/NaCl) 2957, 2926, 2855, 1715, 1455, 1251, 1066, 841 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.25 – 7.18 (m, 5H), 4.98 (t, *J* = 7.6, 2H), 3.69 (s, 3H), 2.94 (s, 2H), 2.37 (d, *J* = 13.3, 2H), 2.29 (d, *J* = 13.3, 2H), 2.27 (dd, *J* = 7.5, 13.9, 2H), 2.13 (dd, *J* = 7.6, 13.9, 2H), 1.70 – 1.66 (m, 2H), 1.67 (s, 6H), 1.49 (s, 6H), 1.17 (d, *J* = 11.4, 2H); **^{13}C NMR** (HSQC-AD/gHMBC-AD Derived 150 MHz, $CDCl_3$) δ = 211.7, 136.7, 134.6, 129.9, 128.1, 126.5, 118.9, 108.3, 79.3, 55.2, 52.1, 46.8, 44.5, 42.3, 35.7, 26.0, 17.8; **HRMS** (EI) m/z 408.2662 [calc'd for $C_{27}H_{36}O_3$ (M+) 408.2665].



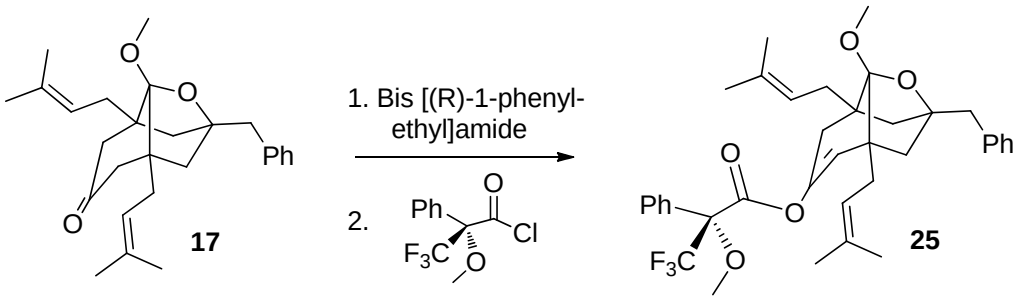
Starting ketone **17** (5 mg, 0.012 mmol) was dissolved in dry THF (0.25 mL) and cooled to 0°C under nitrogen. A solution of LHMDS (1M, 0.06 mmol, 0.06 mL) was added over the course of 2 minutes. The reaction was allowed to stir 10 additional minutes before a 3:1 mixture of TMSCl:Et_3N (0.06 mmol, 0.01 mL) was added and the reaction was allowed to warm to room temperature. After 30 minutes, the reaction was diluted with ether and washed with water. The combined organics were concentrated and purified with silica gel chromatography to give the TMS enol ether (5.0 mg, 85%).

FT-IR (thin film/NaCl) 2956, 2924, 2853, 1454, 1250, 1164, 1064, 1031, 841 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.25 – 7.16 (m, 5H), 5.15 (t, *J* = 7.4, 1H), 5.04 (t, *J* = 7.4, 1H), 4.92 (s, 1H), 3.58 (s, 3H), 2.95 – 2.92 (m, 2H), 2.31 – 2.02 (m, 6H), 1.78 (dd, *J* = 12.2, 2.9, 1H), 1.73 – 1.71 (m, 1H), 1.72 (s, 3H), 1.71 (s, 3H), 1.56 (s, 3H), 1.51 (s, 3H), 1.39 (d, *J* = 11.1, 1H), 1.32 (d, *J* = 12.2, 1H), 0.14 (s, 9H); **^{13}C NMR** (HSQC-AD/gHMBC-AD Derived 150 MHz, $CDCl_3$) δ = 146.6, 137.4, 133.9, 133.5, 130.1, 128.5, 128.1, 126.4, 125.7, 120.6, 119.9, 111.2, 108.6, 78.9, 54.2, 51.8, 47.7, 47.1, 45.1, 42.6, 37.7, 35.2, 34.6, 26.2, 26.1, 18.1, 18.0, 0.49; **HRMS** (EI) m/z 480.3050 [calc'd for $C_{30}H_{44}O_3Si$ (M+) 480.3060].



The TMS enol ether (2.0 mg, 0.0042 mmol) was dissolved in dry DME (0.1 mL) and cooled to 0°C under nitrogen. To this was added MeLi (0.04 mmol, 0.04 mL) and the reaction was allowed to stir for 5 minutes. Methyl iodide (0.04 mmol, 0.01 mL) was then added and the bath was removed. After 45 minutes at room temperature, the reaction was diluted with ether and washed with water. The combined organics were dried over sodium sulfate, concentrated and purified with silica gel chromatography to give the methylated product **18** (3.0 mg, 86%).

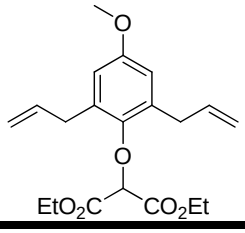
FT-IR (thin film/NaCl) 2917, 2849, 1735, 1559, 1365, 1275, 1222, 750 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.26 – 7.18 (m, 5H), 5.00 (t, *J* = 7.3, 1H), 4.89 (t, *J* = 7.3, 1H), 3.67 (s, 3H), 2.91 (s, 2H), 2.60 (d, *J* = 13.7, 1H), 2.47 (dd, *J* = 7.3, 14.0, 1H), 2.38 (q, *J* = 7.0, 1H), 2.28 (dd, *J* = 7.5, 13.7, 1H), 2.16 (d, *J* = 13.7, 1H), 2.16 – 2.04 (m, 2H), 1.73 – 1.63 (m, 2H), 1.68 (s, 3H), 1.67 (s, 3H), 1.50 (s, 3H), 1.48 (s, 3H), 1.23 – 1.10 (m, 2H), 1.13 (d, *J* = 7.0, 3H); **^{13}C NMR** (HSQC-AD/gHMBC-AD Derived 150 MHz, $CDCl_3$) δ = 216.2, 136.9, 134.5, 134.5, 130.0, 129.9, 128.4, 128.2, 126.5, 119.1, 118.1, 108.9, 79.4, 55.4, 53.1, 51.7, 50.1, 45.6, 45.1, 42.8, 42.5, 35.8, 30.7, 26.0, 26.0, 17.9, 17.9, 13.8; **HRMS** (EI) m/z 422.2832 [calc'd for $C_{28}H_{38}O_3$ (M+) 422.2821].



Representative Procedure

Bis [(R)-1-phenylethyl]amine (0.0294 mmol, 0.007 mL) was added to a reaction vial along with dry THF (0.2 mL). After cooling to -78°C, ^{n}BuLi (0.0284 mmol, 0.02 mL) was added and the reaction was allowed to stir 15 minutes. LiCl (0.5 eq, 0.2 mg) was added immediately following the ^{n}BuLi. At which time the starting ketone **17** (4 mg, 0.0098 mmol) was added drop-wise and allowed to stir 15 minutes. To this was added (S)-Mosher acid chloride (0.012 mmol, 0.002 mL) and the reaction was maintained at -78°C for 30 minutes. The bath was then removed and at room temperature the reaction was loaded directly on a silica gel plug and eluted with 30% ethyl acetate: 70% hexanes to give the respective Mosher ester **25** (5.0 mg, 83%, 10:1). The product ratios were simply determined by ^{19}F NMR peak integration. The two respective diastereomers have ^{19}F NMR shifts of -74.942 and -74.970 relative to an internal standard of hexafluorobenzene.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.00 (m, 10H), 5.49 (s, 1H), 5.15 – 5.06 (m, 1H), 5.03 – 4.94 (m, 1H), 3.61 (s, 3H), 3.57 (s, 3H), 3.01 – 2.89 (m, 2H), 2.39 – 2.08 (m, 6H), 1.85 – 1.65 (m, 2H), 1.71 (s, 3H), 1.70 (s, 3H), 1.51 (s, 6H), 1.48 – 1.40 (m, 2H).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O
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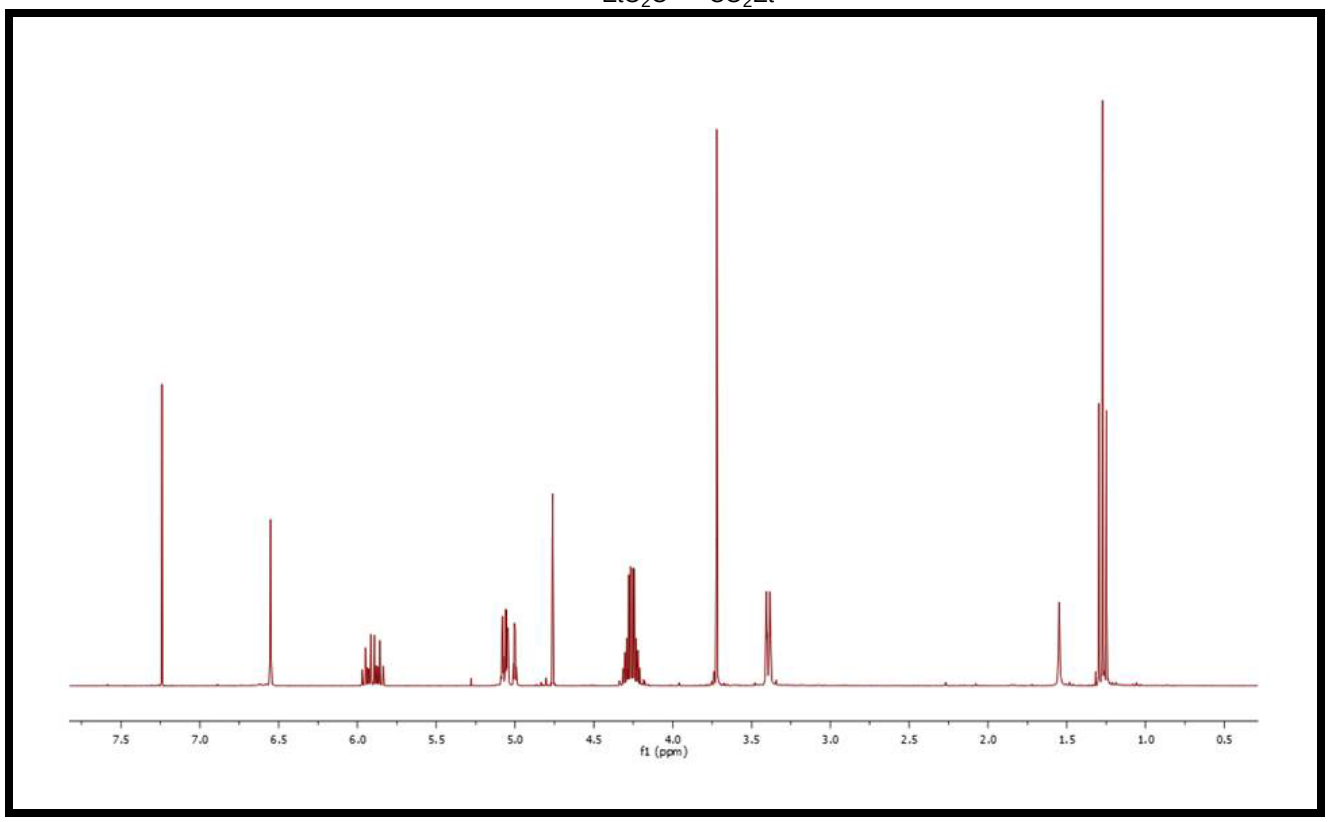
CO2Et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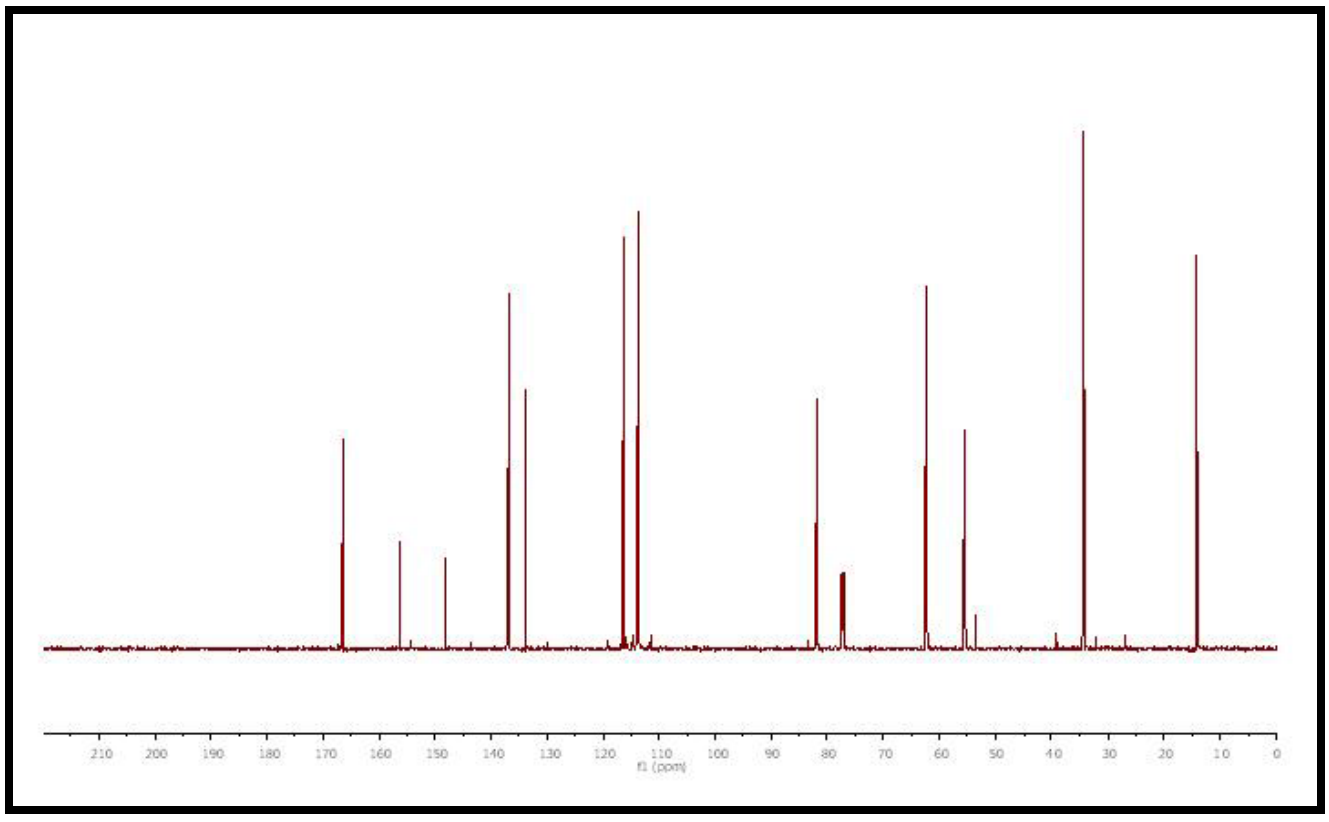
0.5
f1 (ppm)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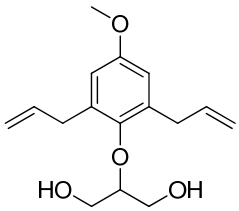
f1 (ppm)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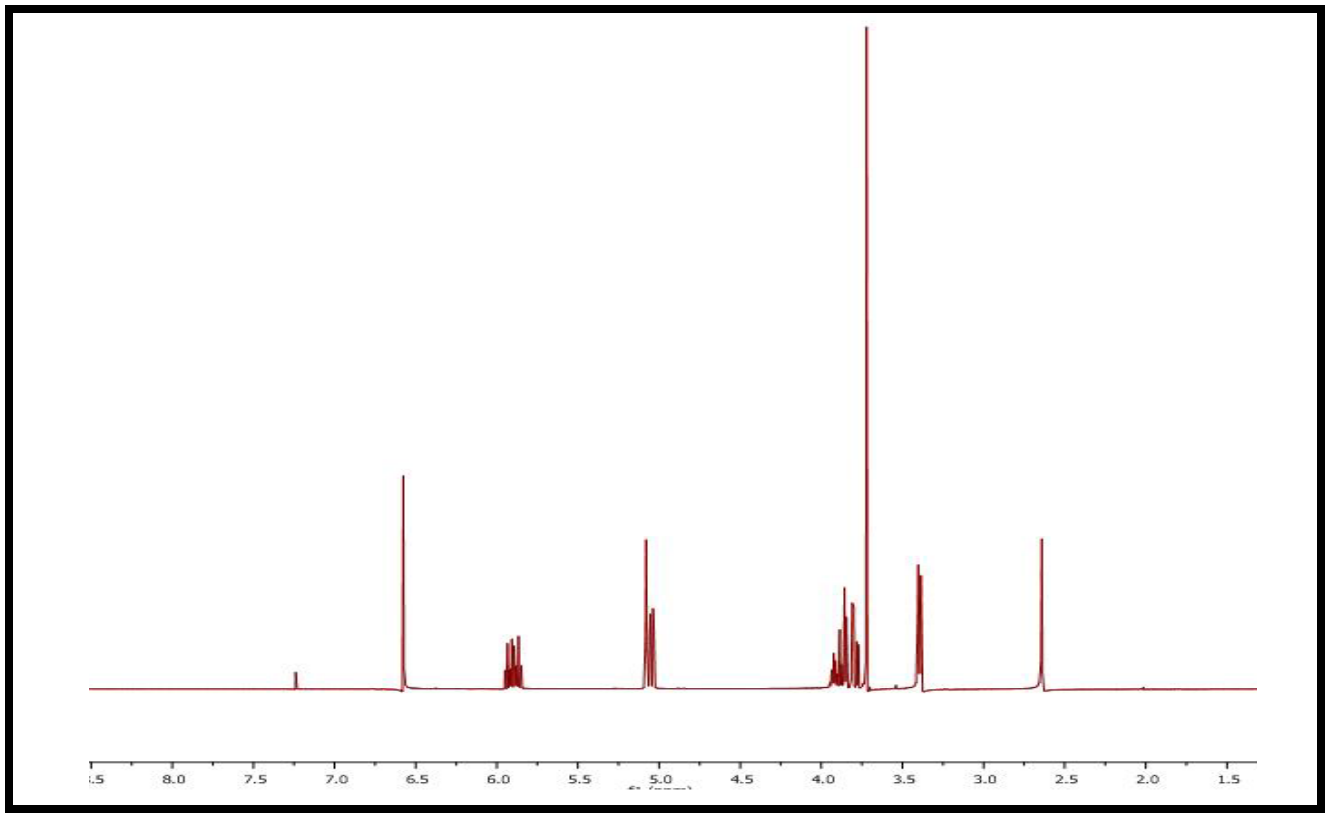
O
HO
OH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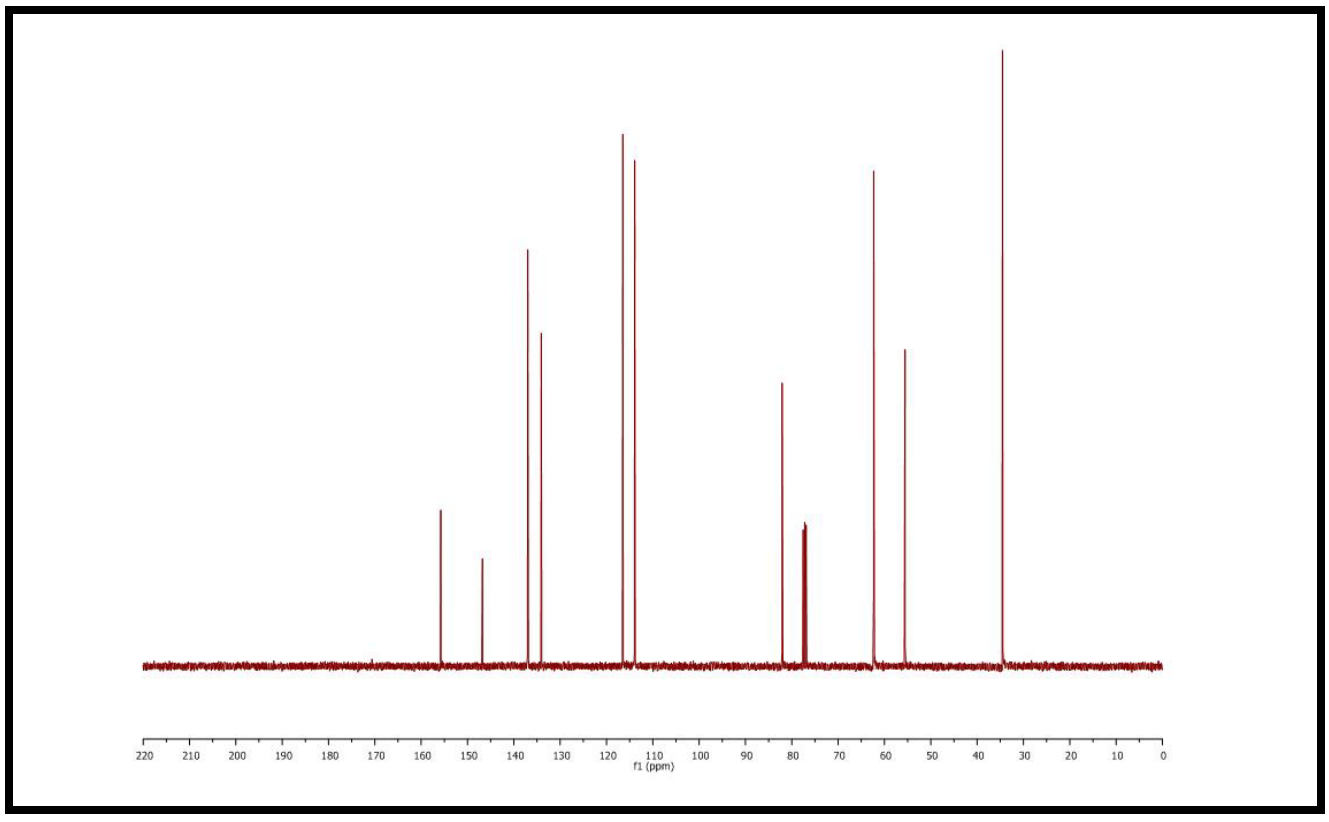
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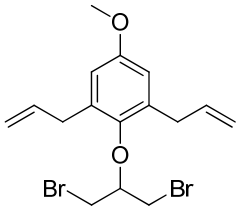
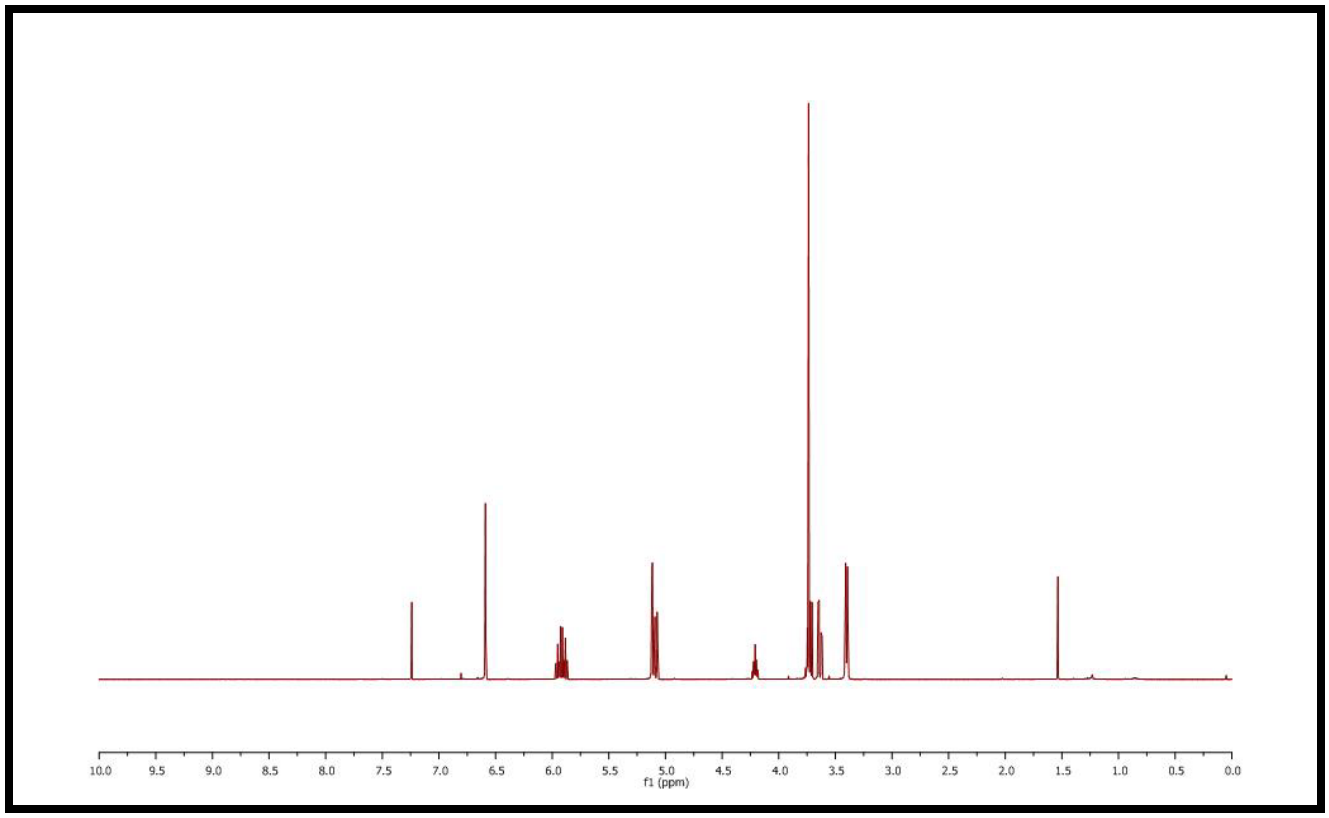
f1 (ppm)


O
O
Br
Br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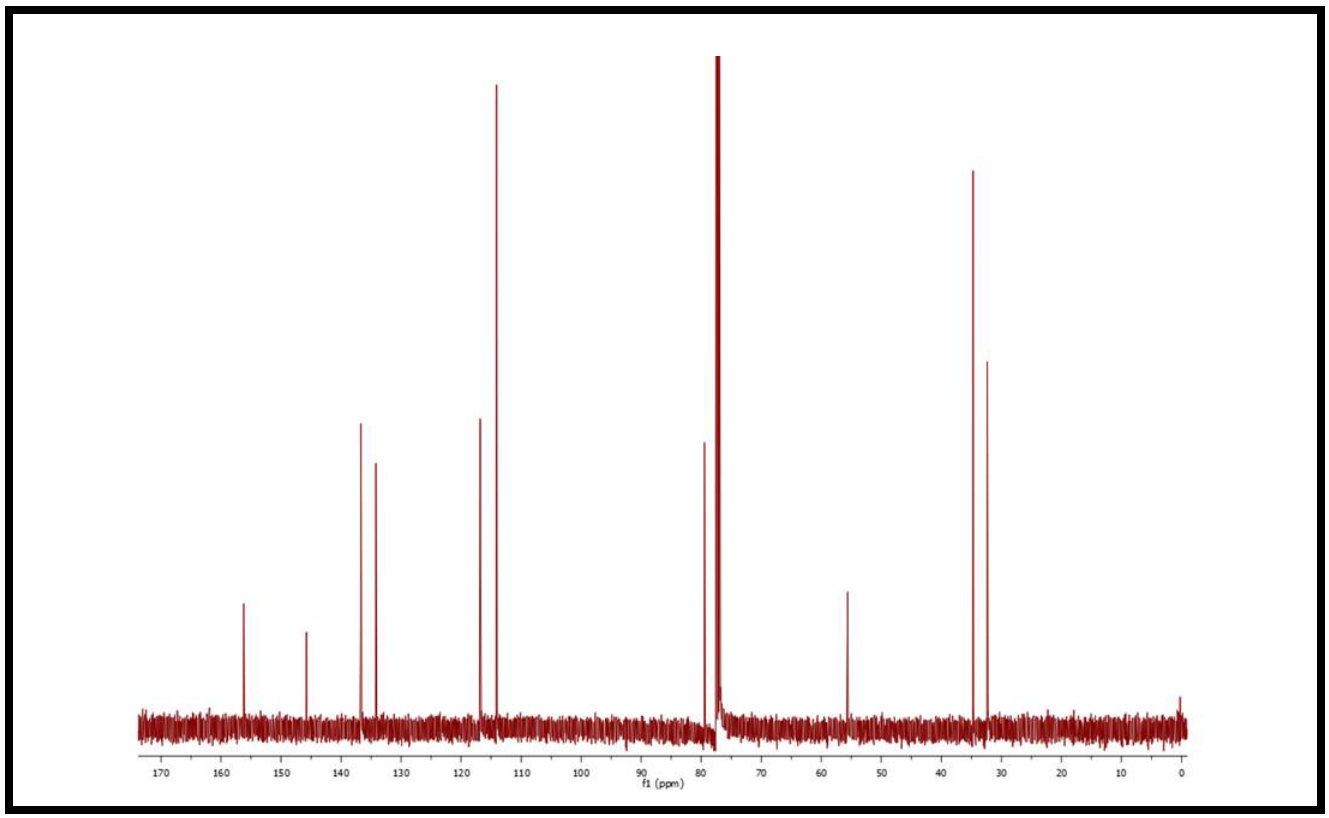
0.0
f1 (ppm)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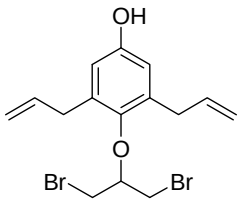
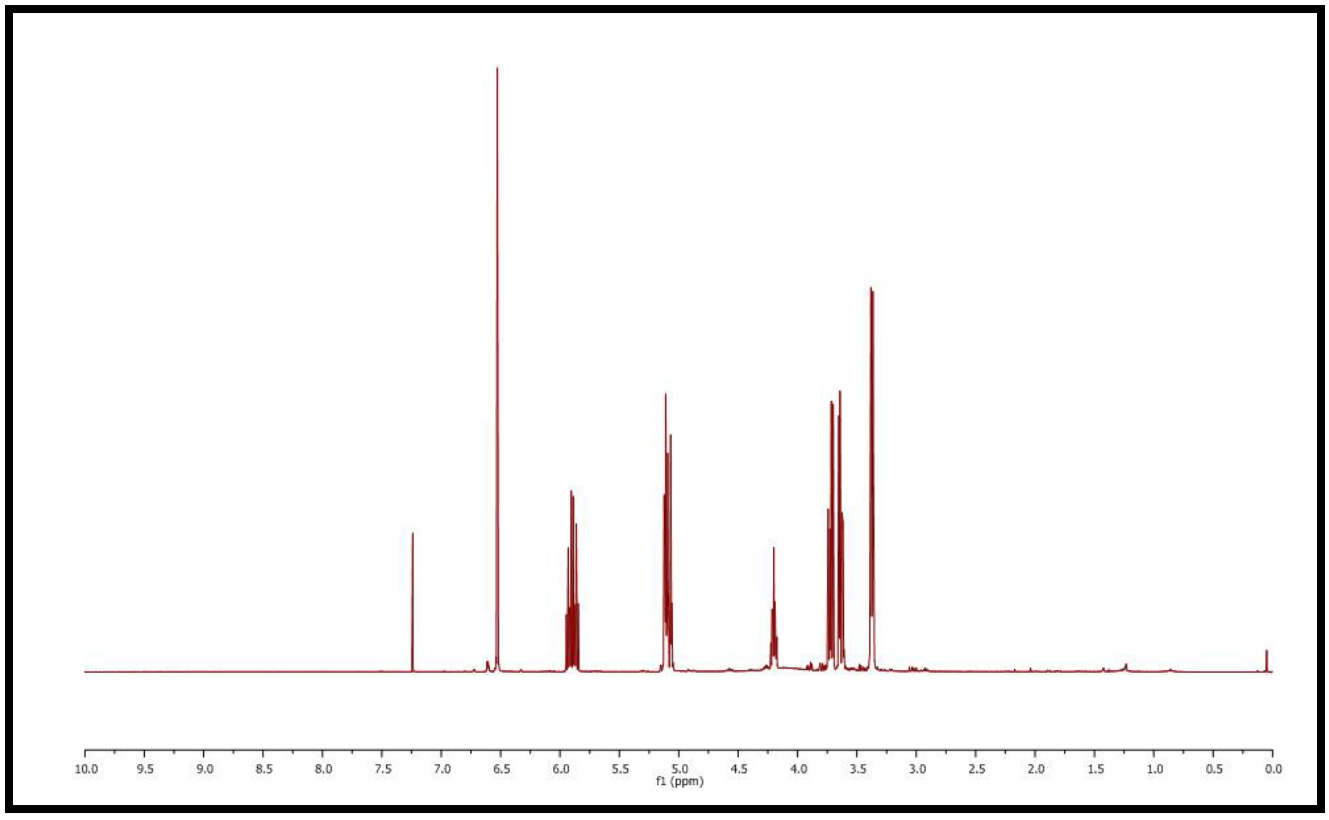

OH
O
Br
Br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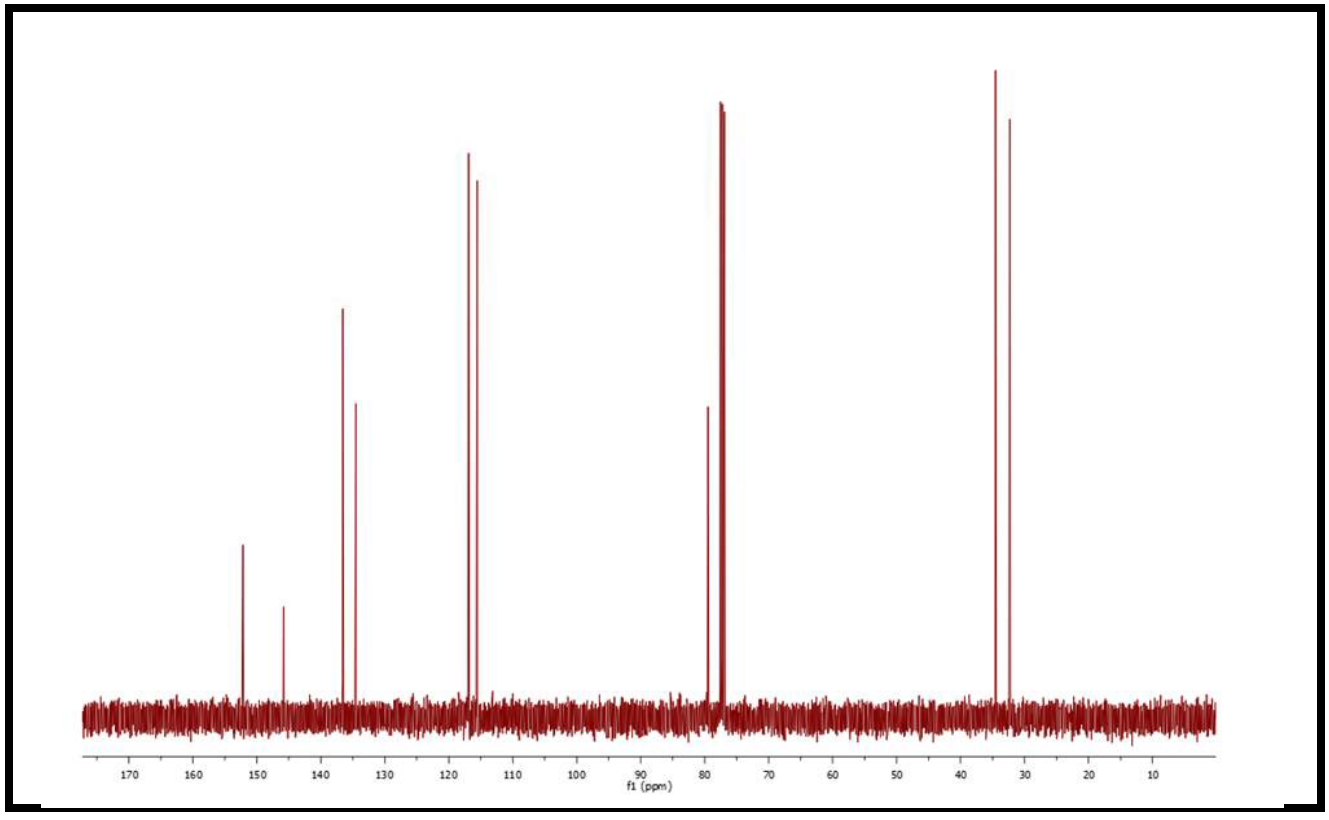
0.0
f1 (ppm)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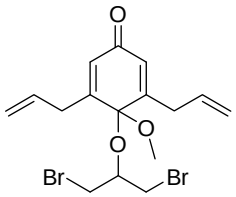
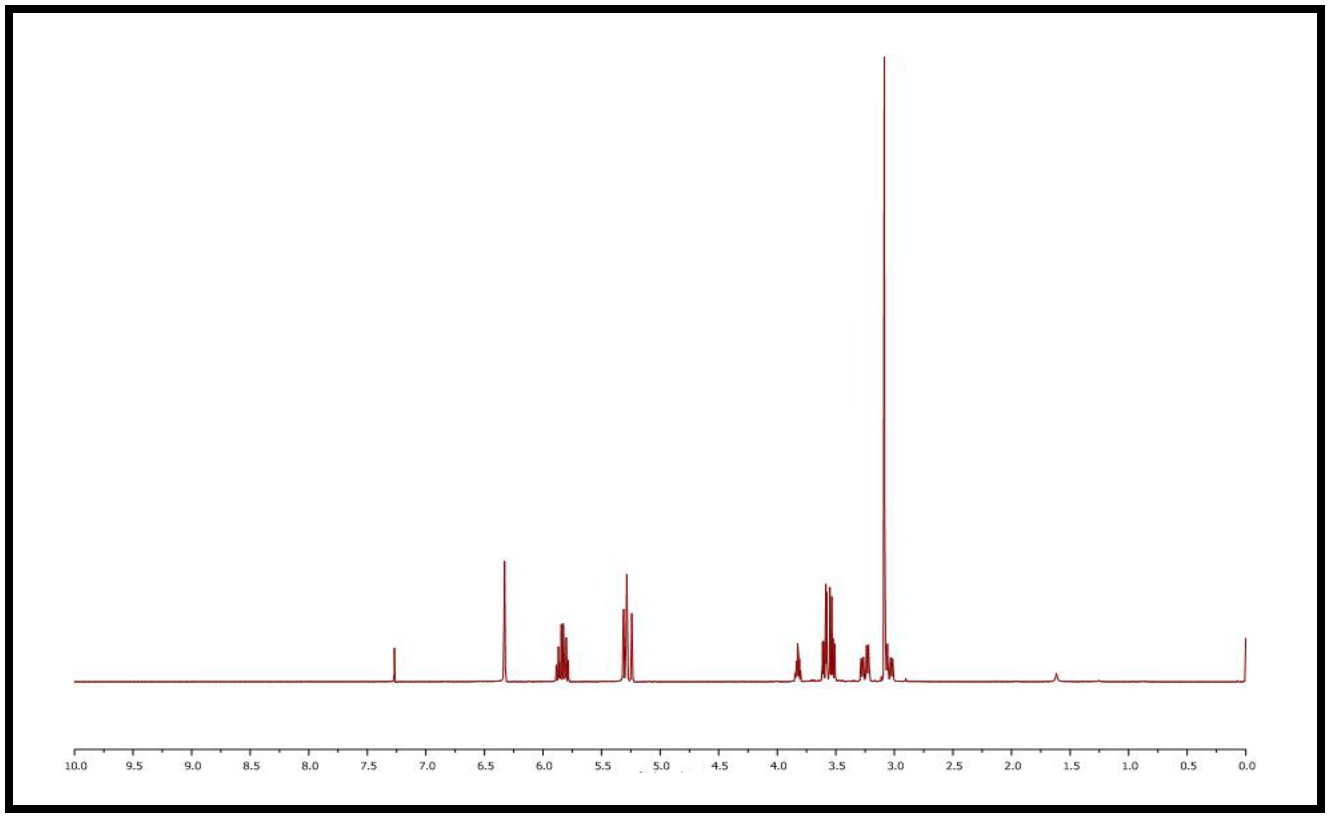
20
10
f1 (ppm)


O
O
O
Br
Br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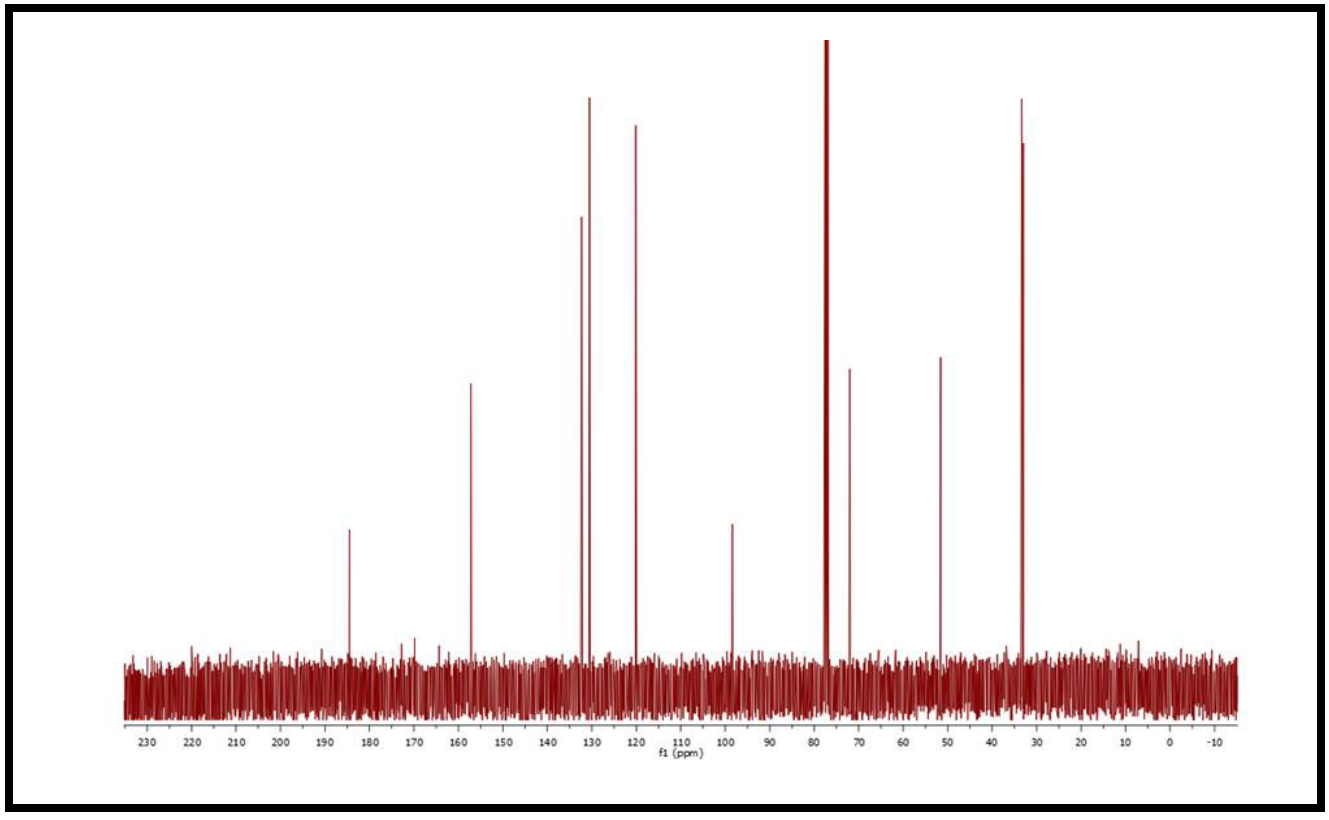
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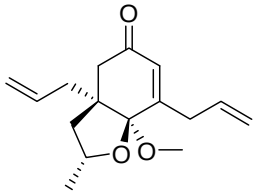
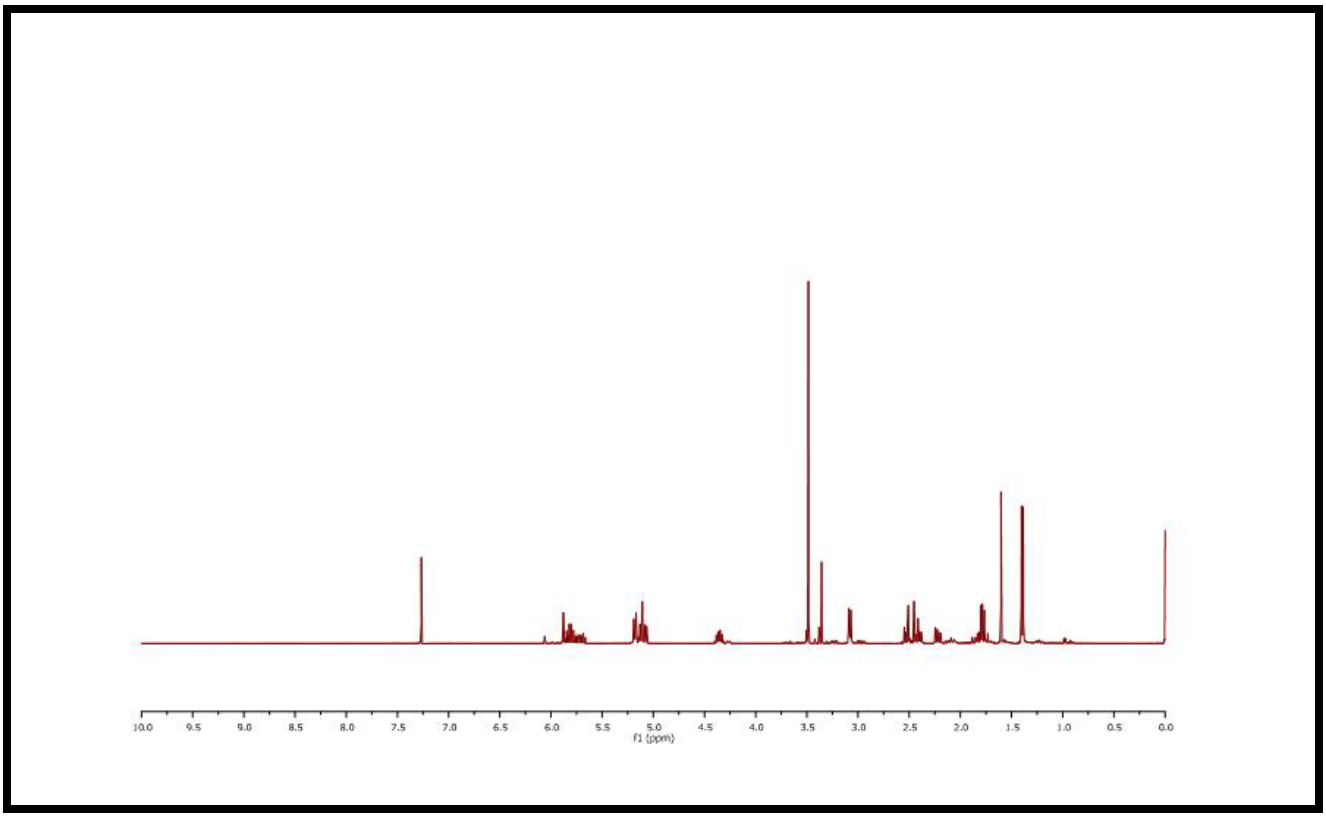
f1 (ppm)


O
O
O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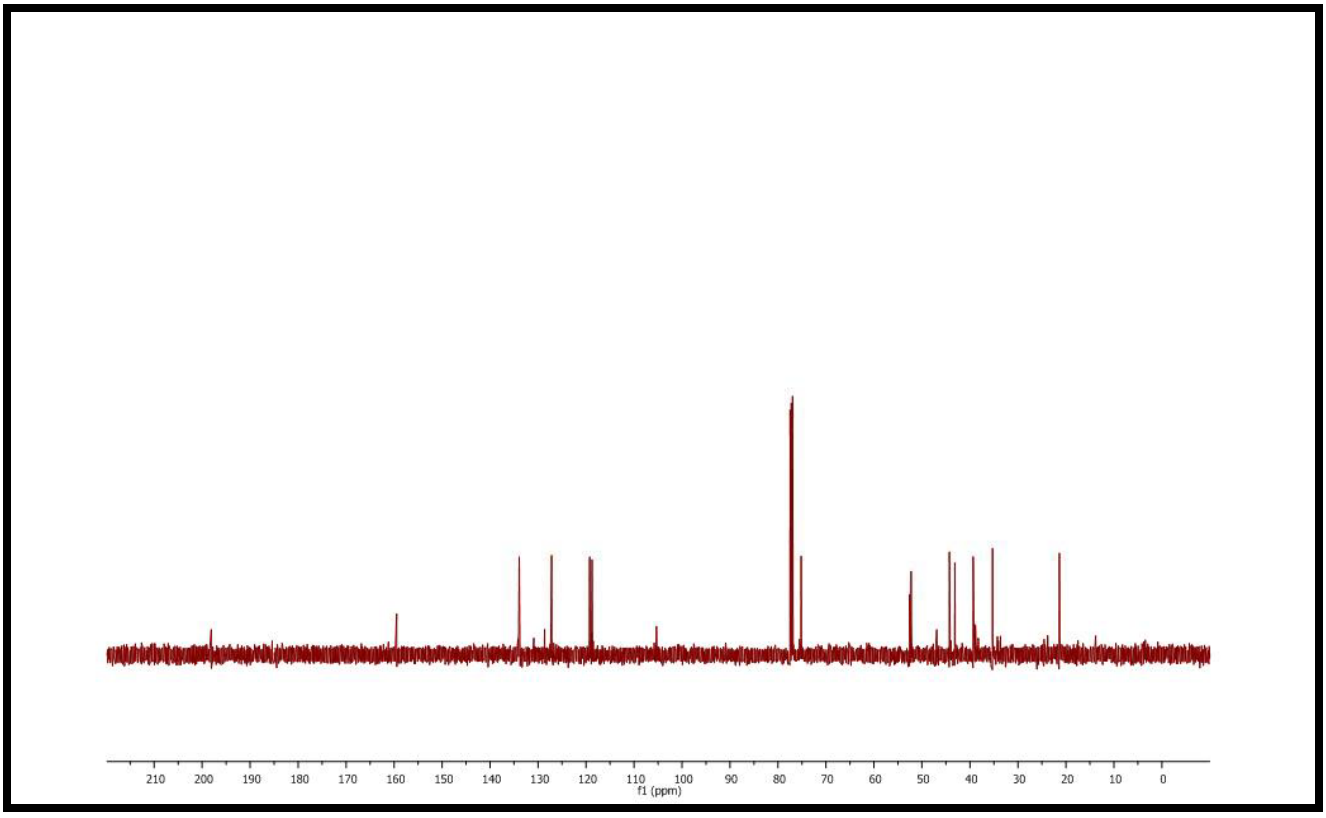
f1 (ppm)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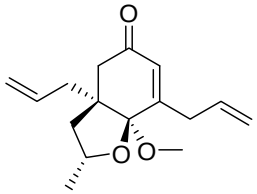
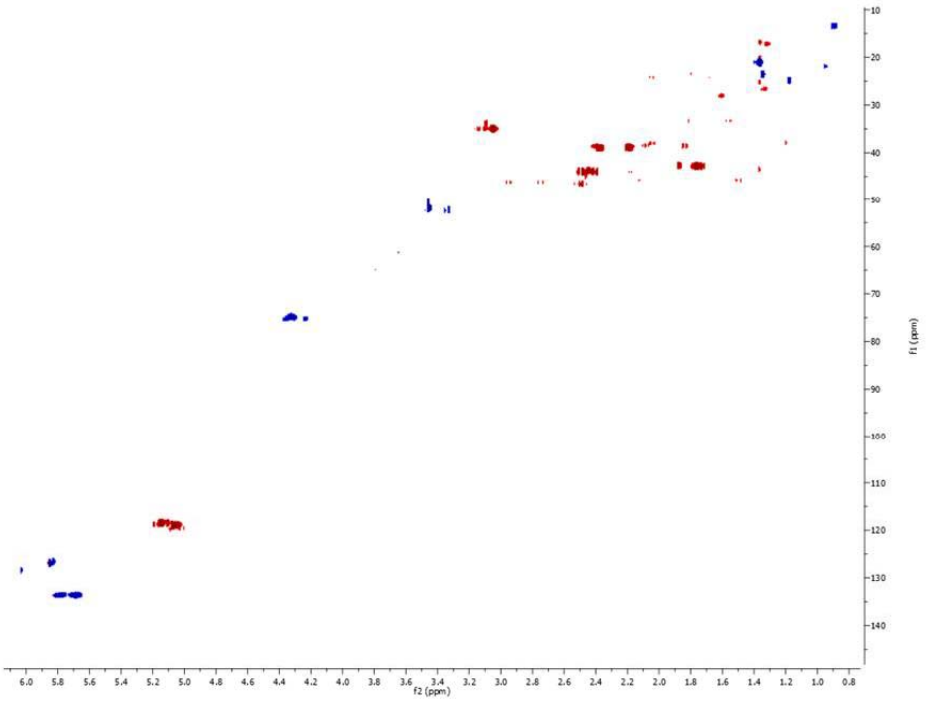
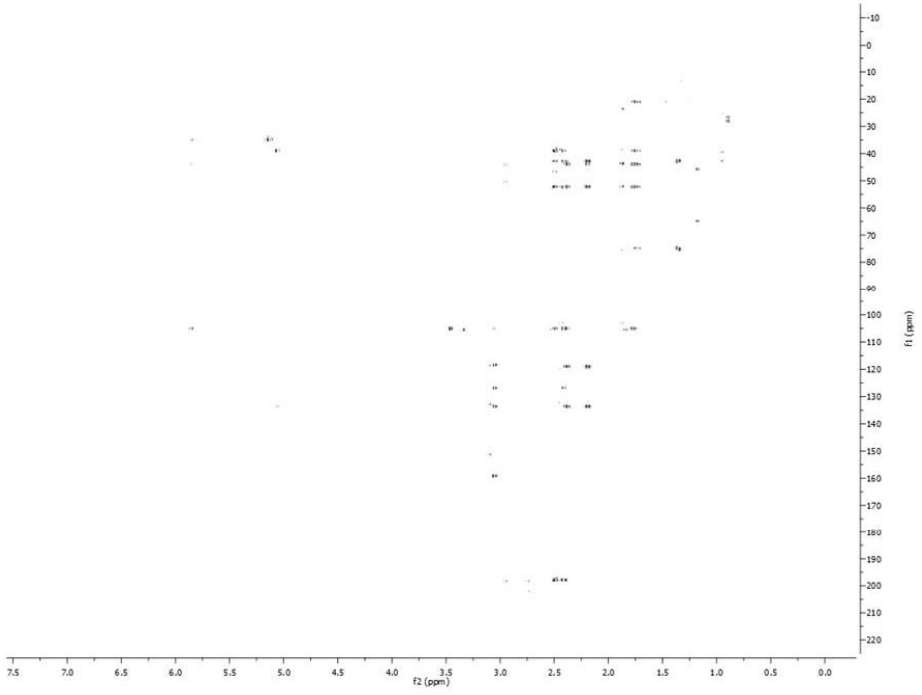
f1 (ppm)



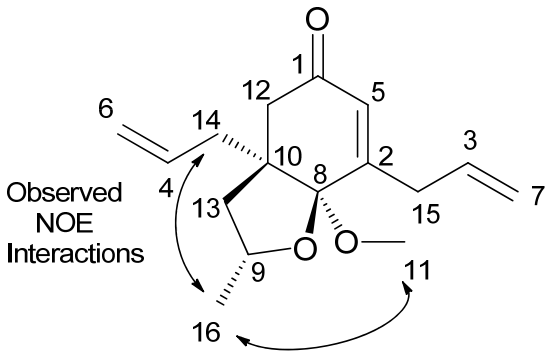
HSQCAD



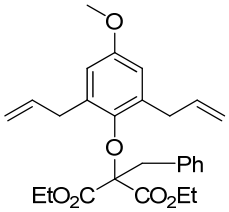
gHMBCAD

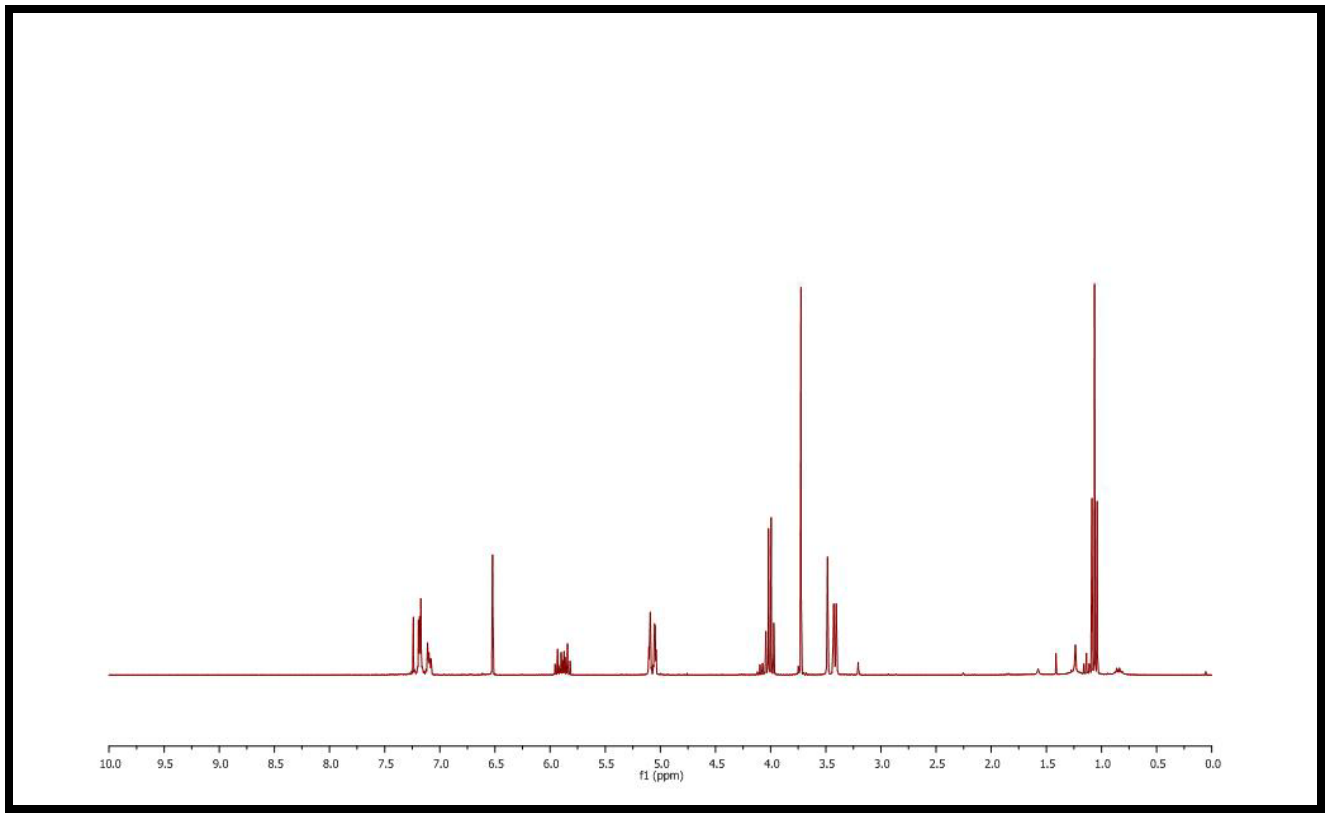


C	^{13}C (δ ppm)	HSQC-AD ^{1}H (δ ppm)	gHMBC-AD (^{1}H-Correlations)
1	198.1	---	2.49, 2.42
2	159.5	---	3.05
3	133.9	5.80	3.05
4	133.9	5.69	5.06, 2.38, 2.19
5	127.1	5.85	3.05, 2.42
6	119.3	5.04, 5.06	2.38, 2.19
7	118.8	5.12, 5.16	3.05
8	105.3	---	5.85, 3.46, 3.05, 2.49, 2.38. 1.75
9	75.2	4.33	1.87, 1.75, 1.36
10	52.6	---	2.49, 2.42, 2.38, 2.19, 1.87, 1.75
11	52.3	3.46	----
12	44.3	2.49, 2.42	5.85, 2.38, 2.19, 1.87, 1.75
13	43.2	1.87, 1.75	2.49, 2.42, 2.19, 1.36
14	39.3	2.38, 2.19	5.69, 5.06, 2.49, 2.42, 1.75
15	35.3	3.05	5.85, 5.16
16	21.4	1.36	1.75



The NOE interactions that are most relevant to determining the stereochemical outcome of the reaction are indicated above. The protons on the methoxy group have a correlation to the resulting methyl group which in turn correlate to the CH2 of the allyl group indicating that all three groups are positioned on the same side of the fused bicylic system.


O
O
Ph
EtO2C
CO2Et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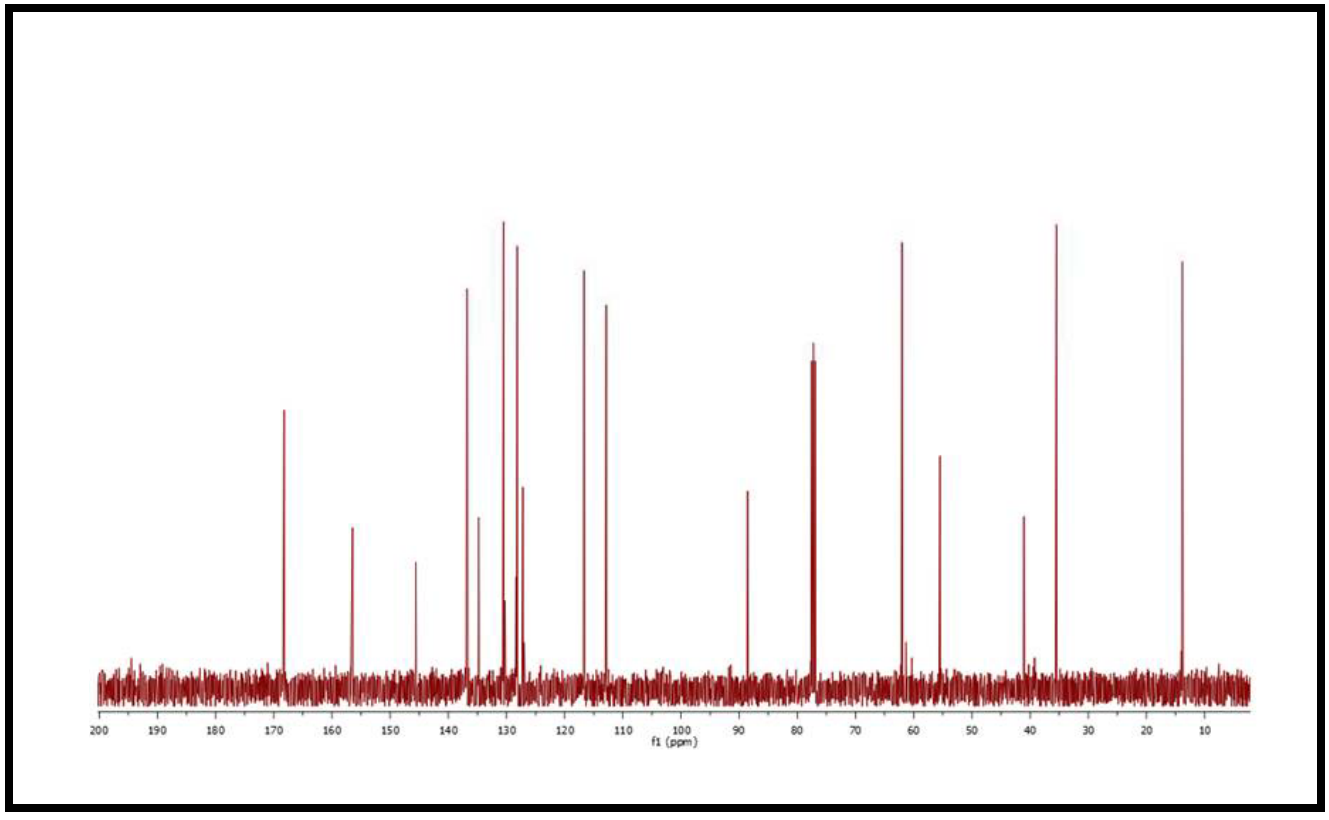
f1 (ppm)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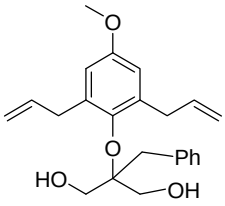
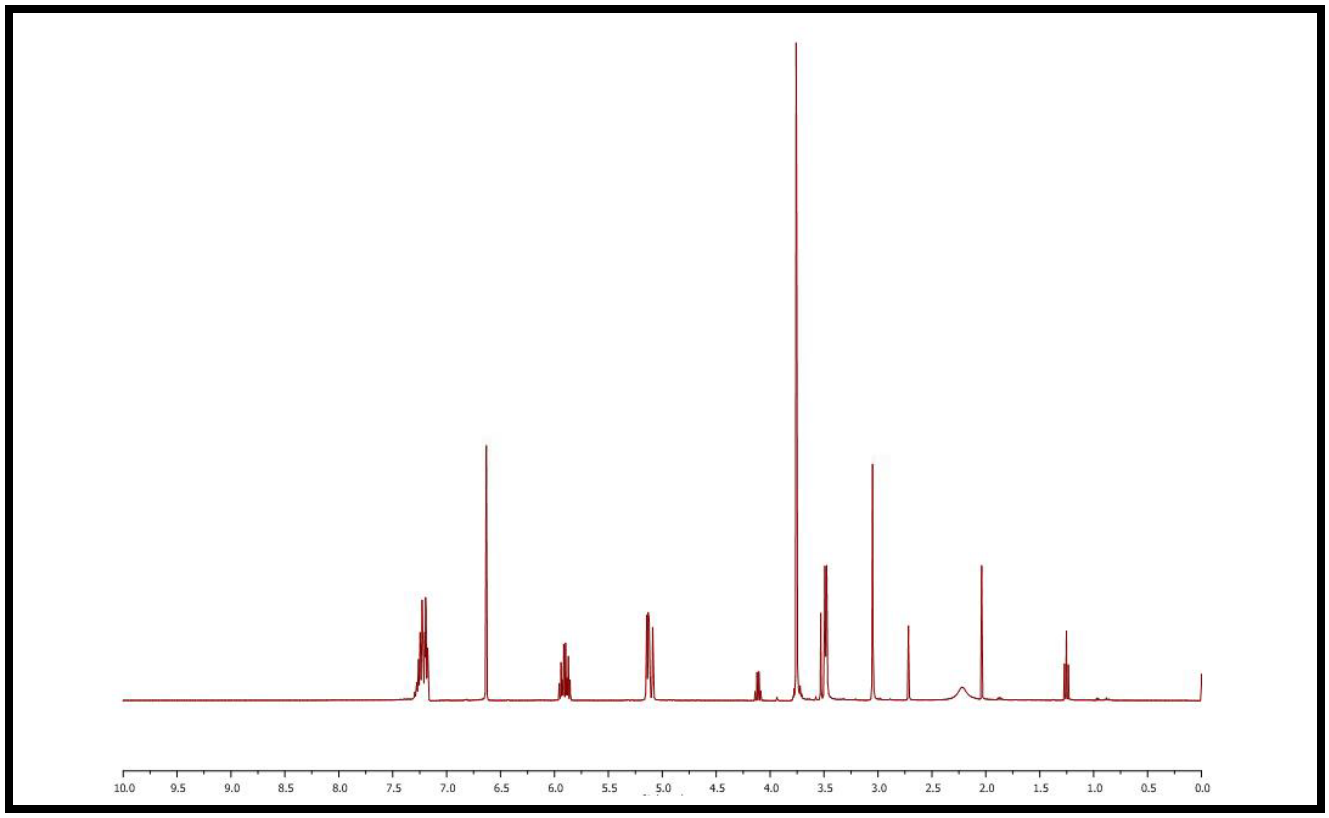
f1 (ppm)


O
O
Ph
HO
OH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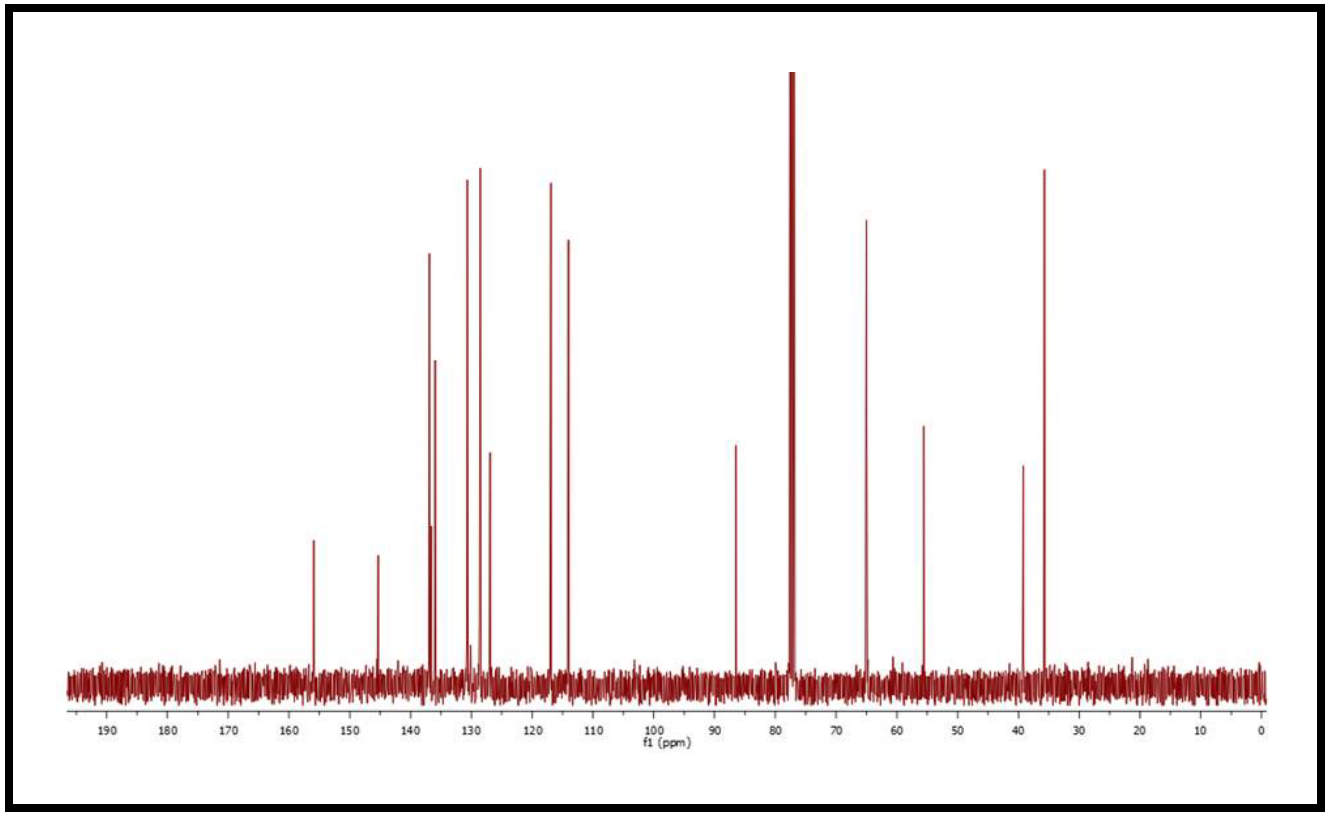
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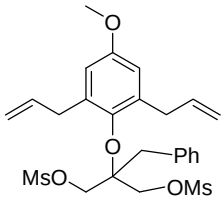
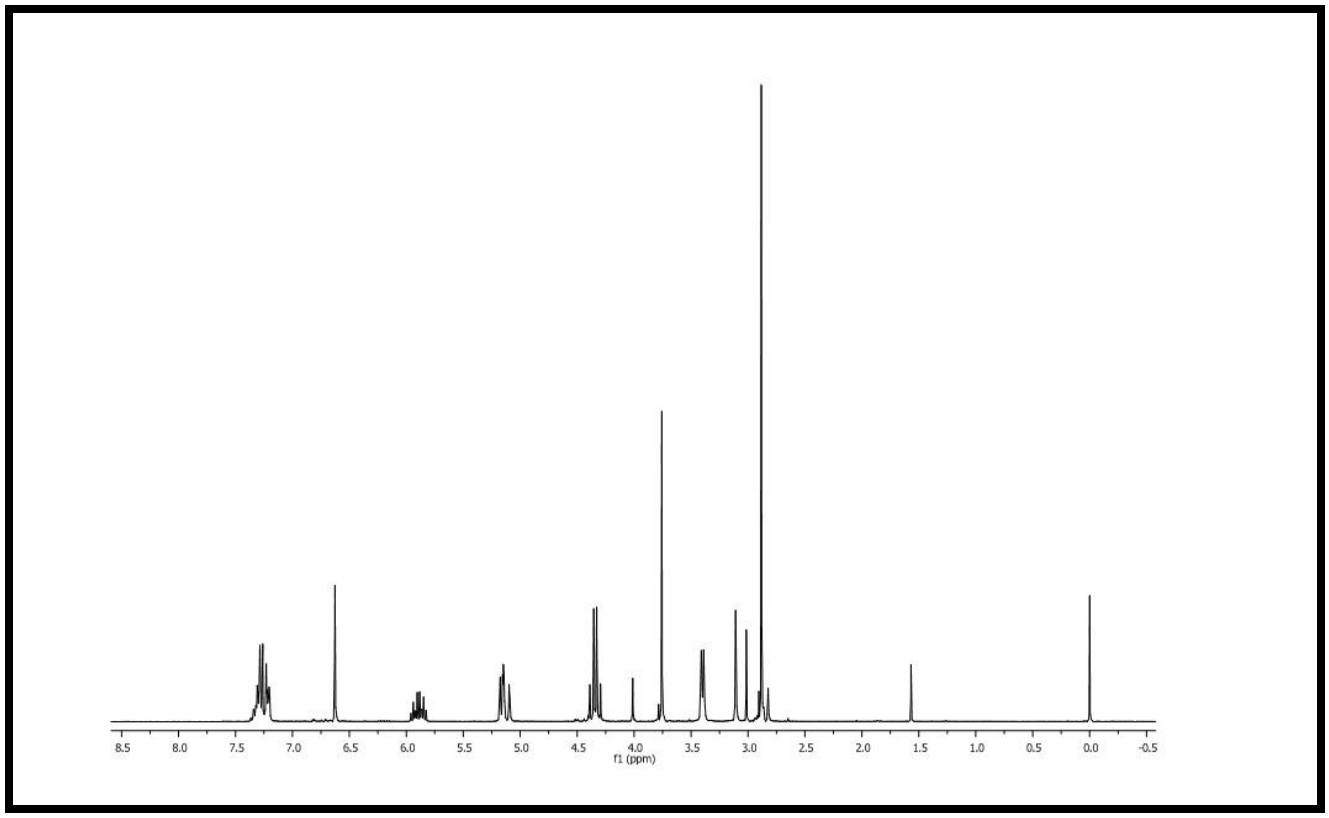
f1 (ppm)


O
O
Ph
MsO
OMs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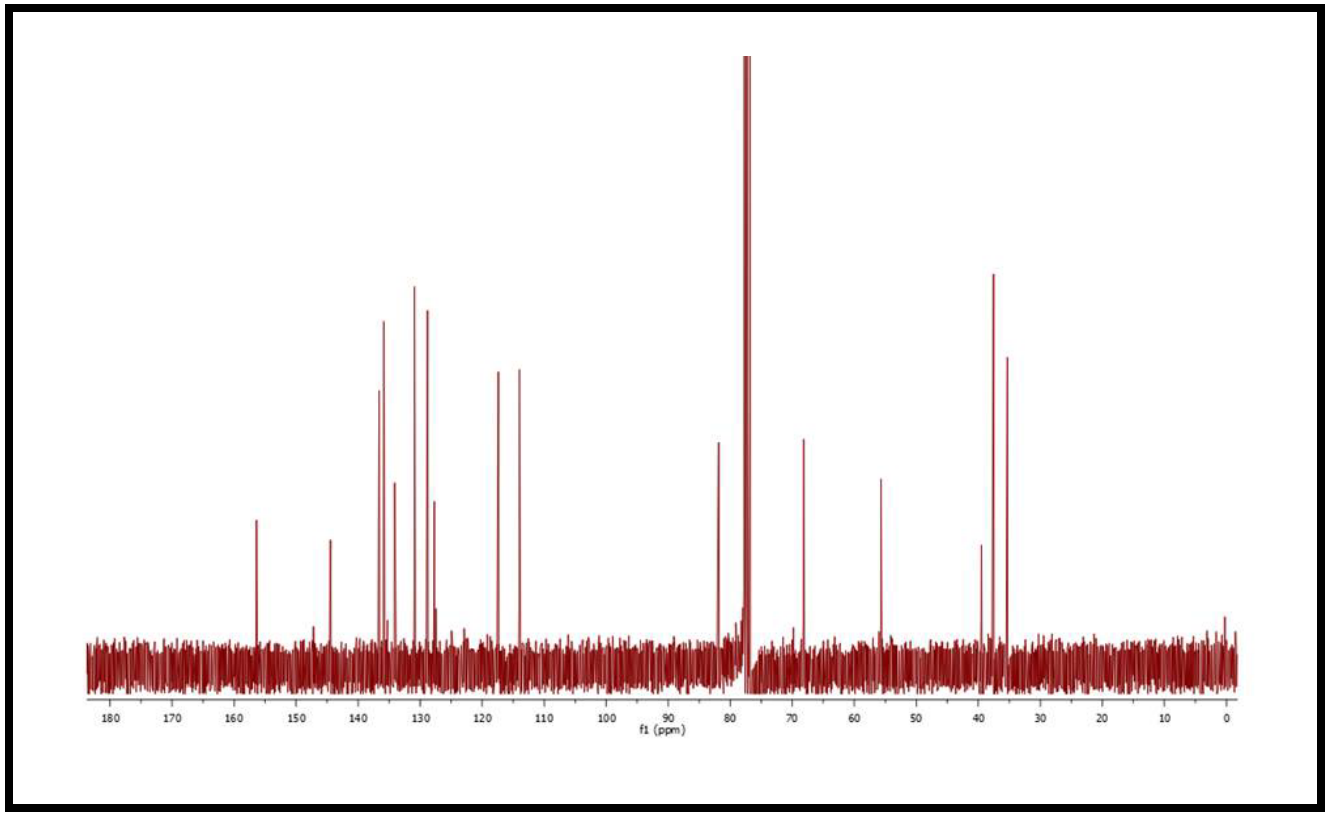
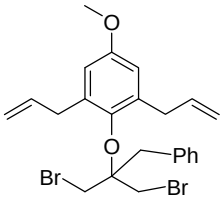
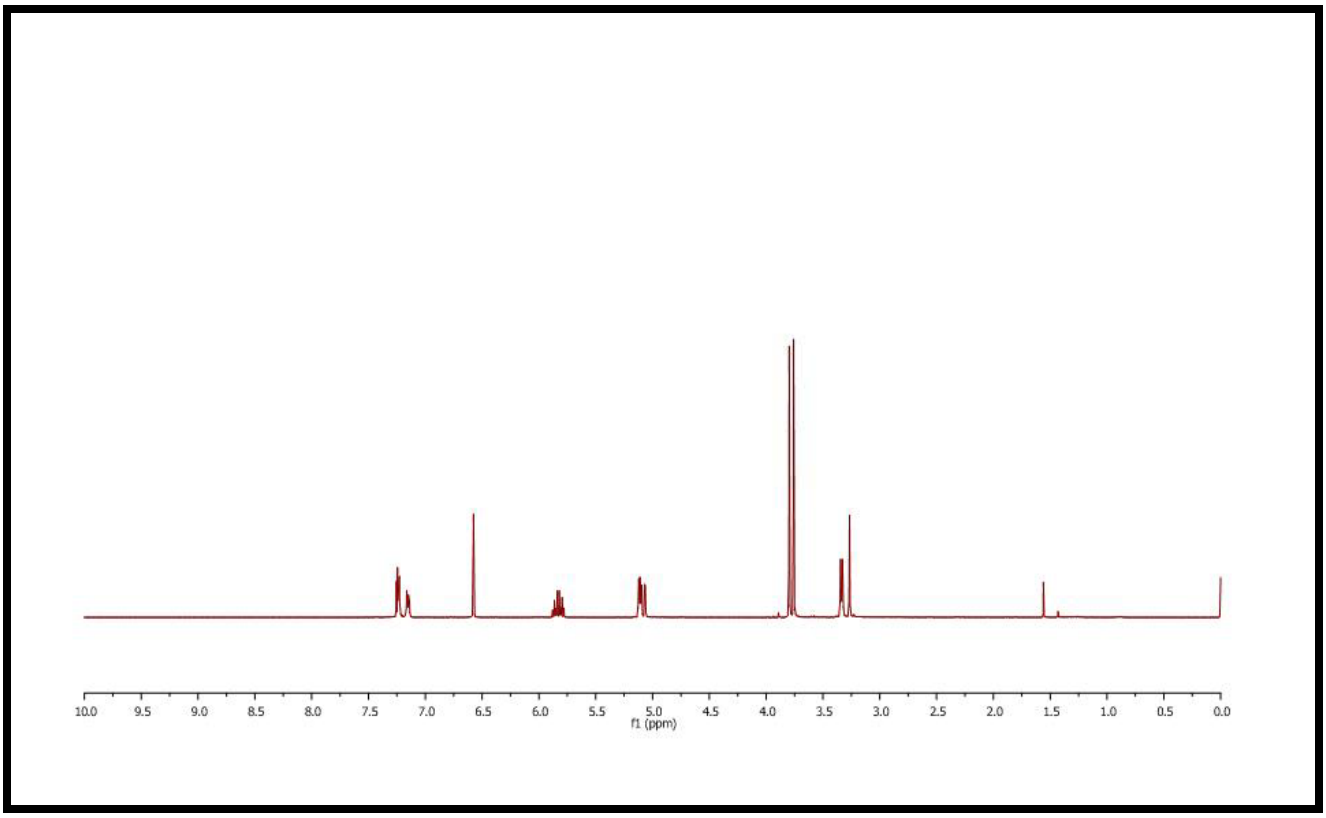
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
Ph
Br
Br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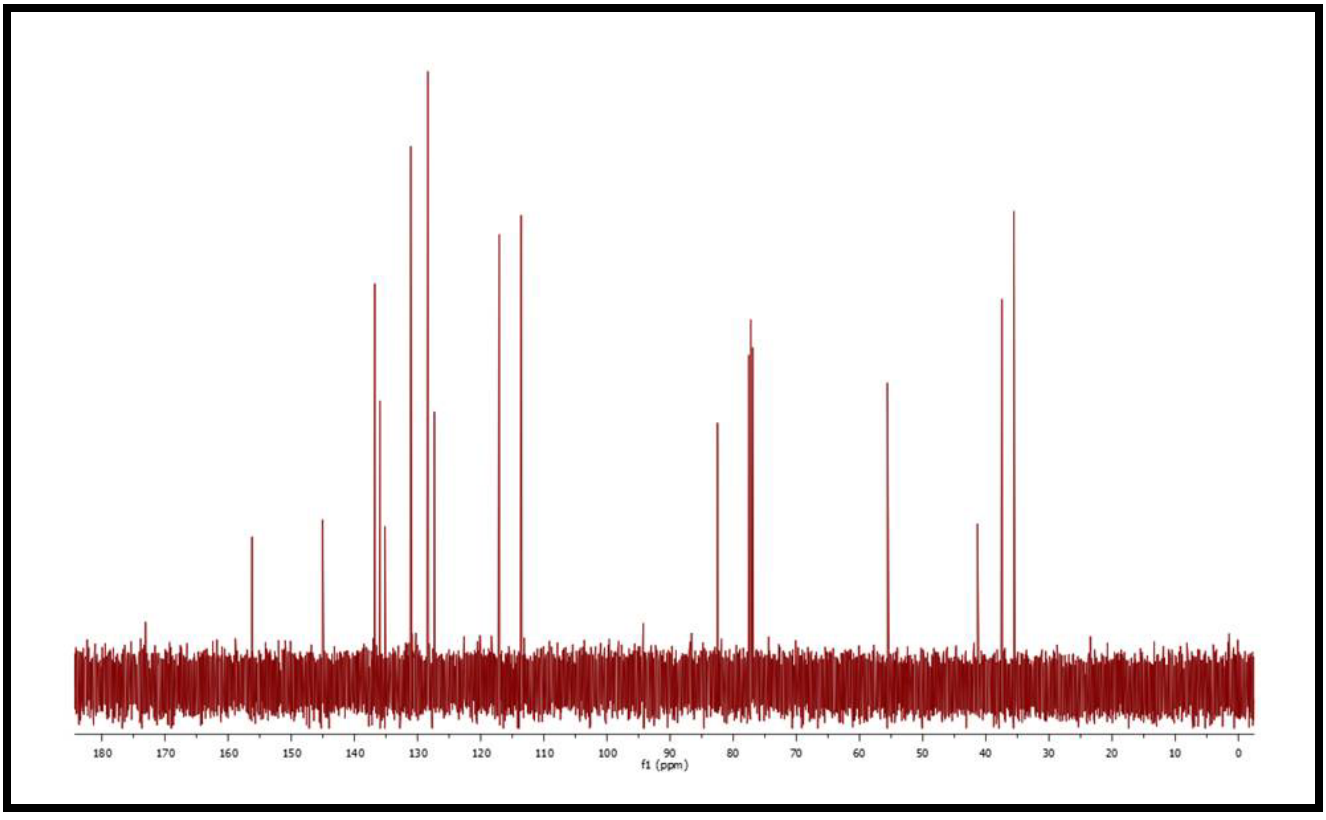
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


180
170
160
150
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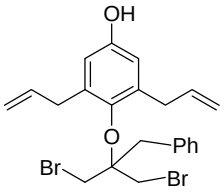
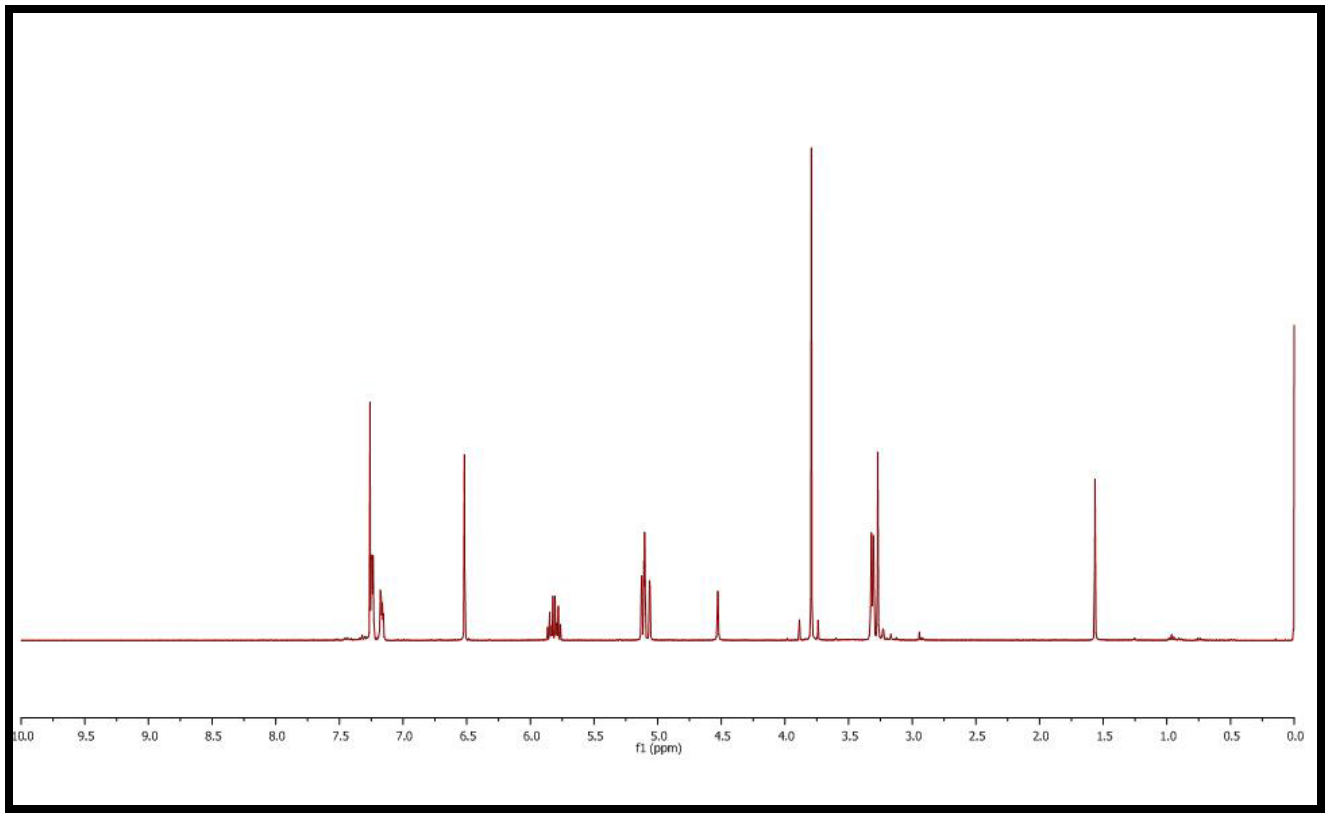
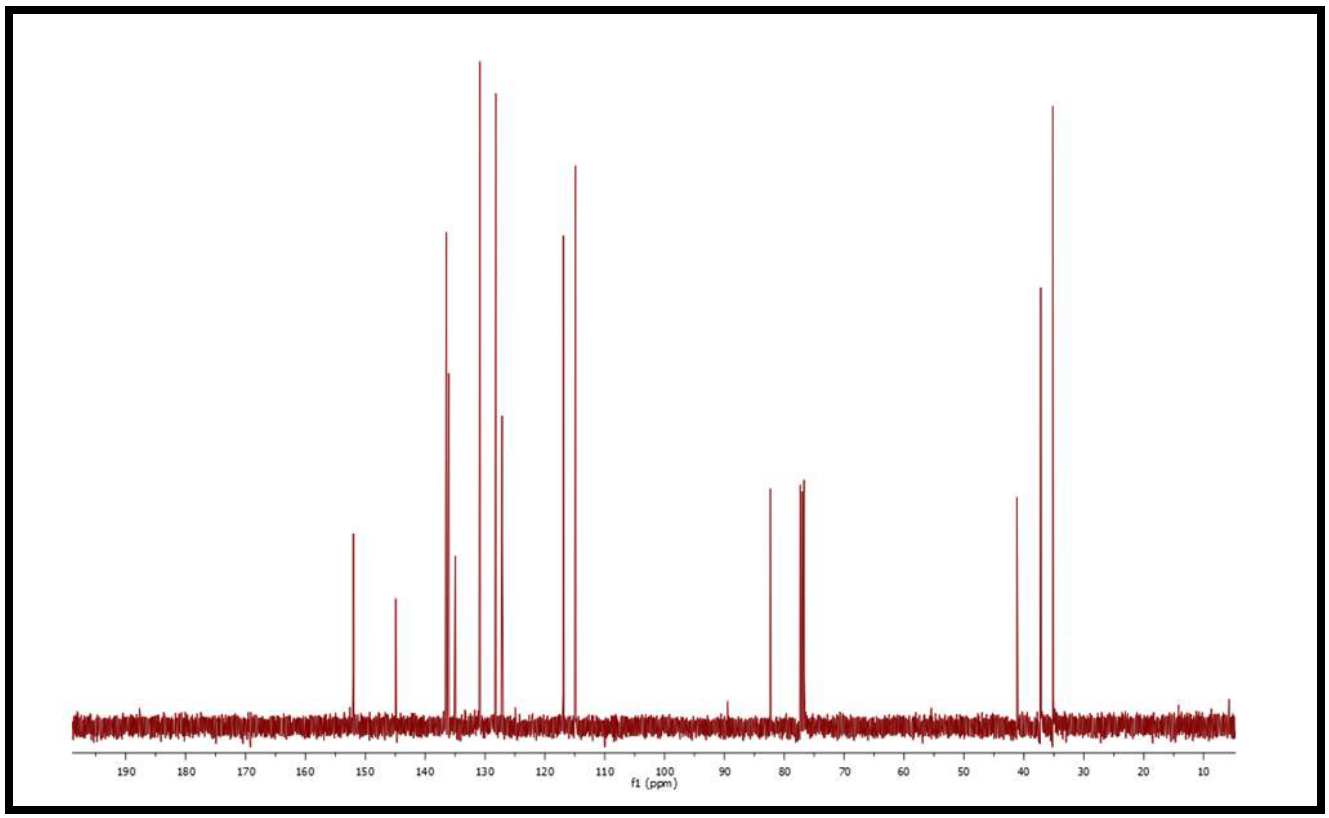
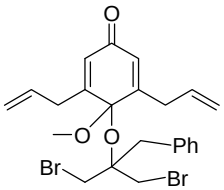
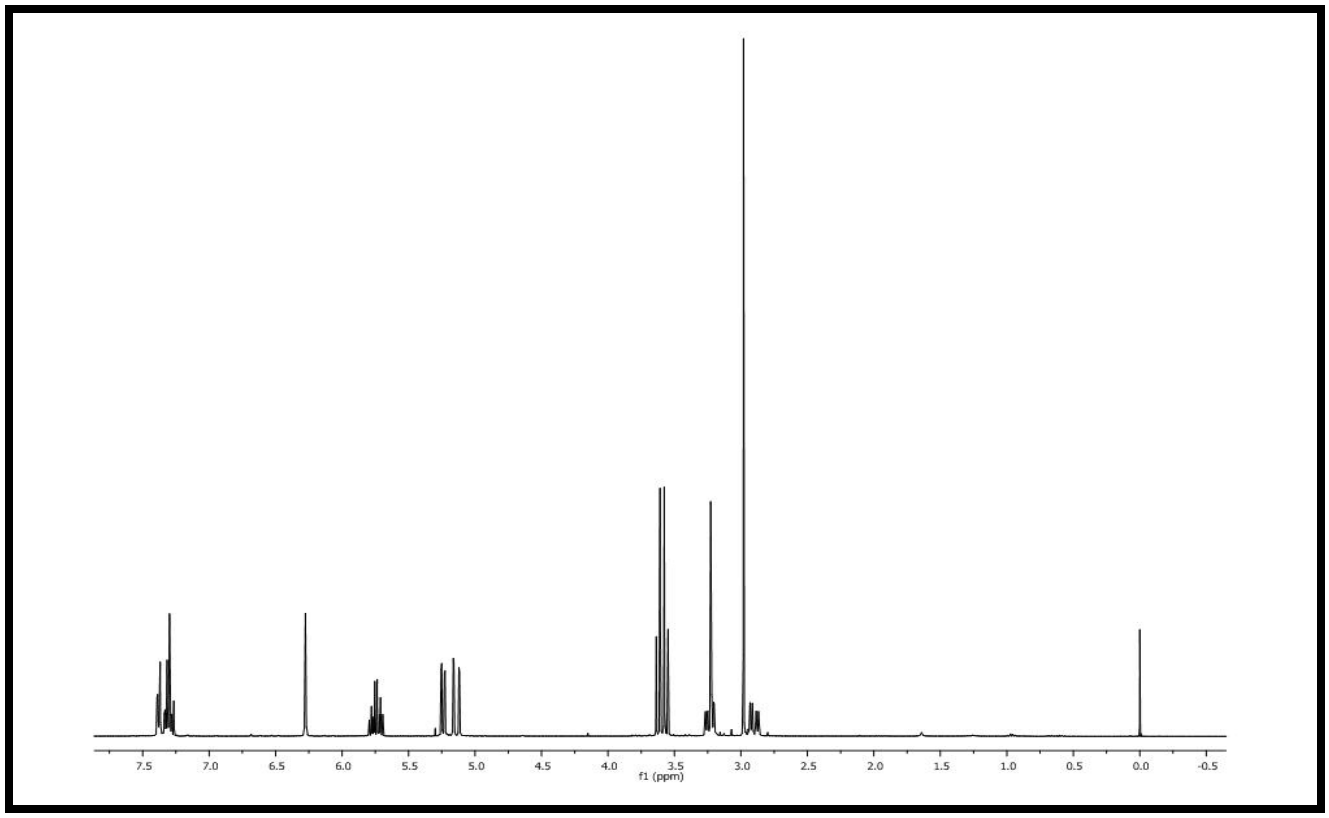
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

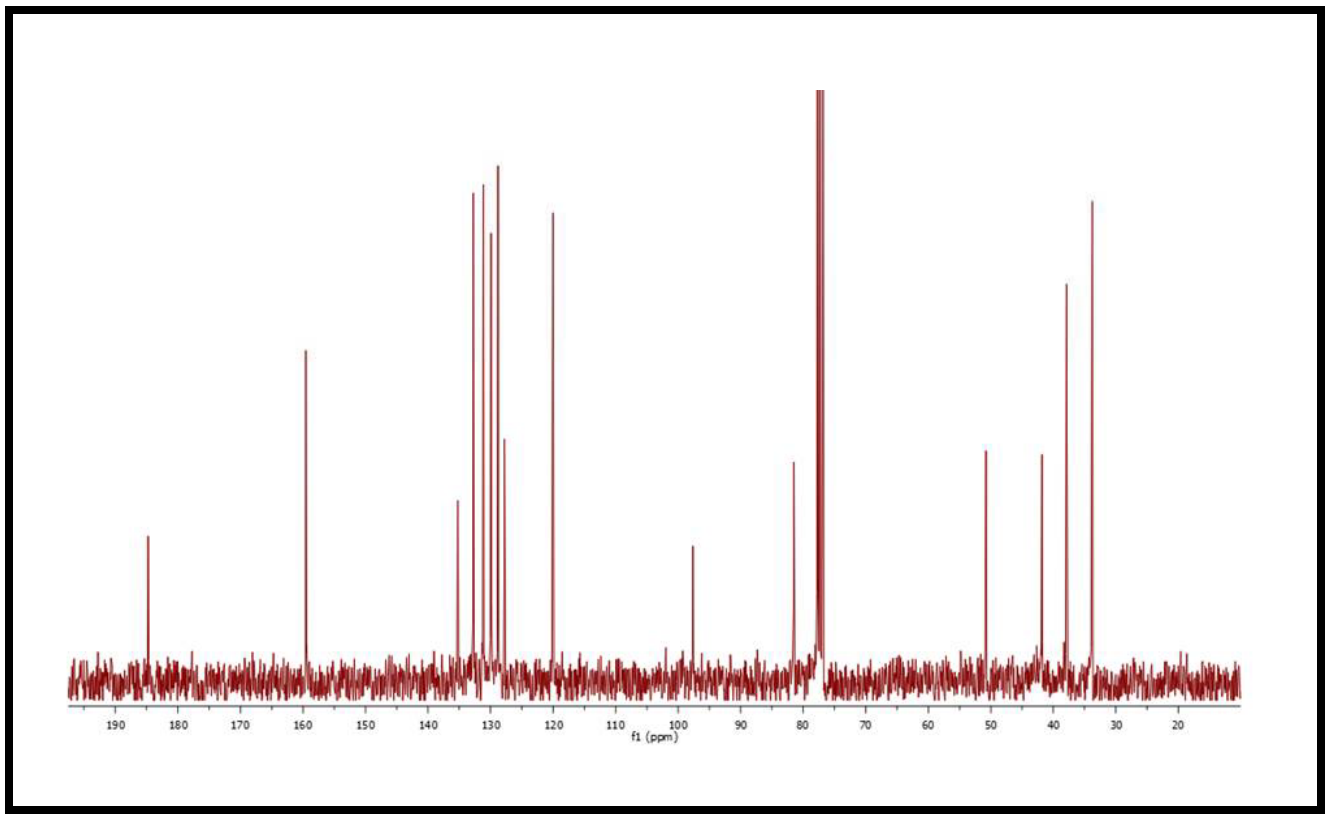

OH
O
Ph
Br
Br

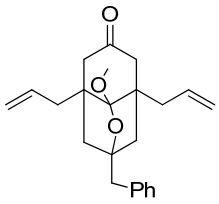

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

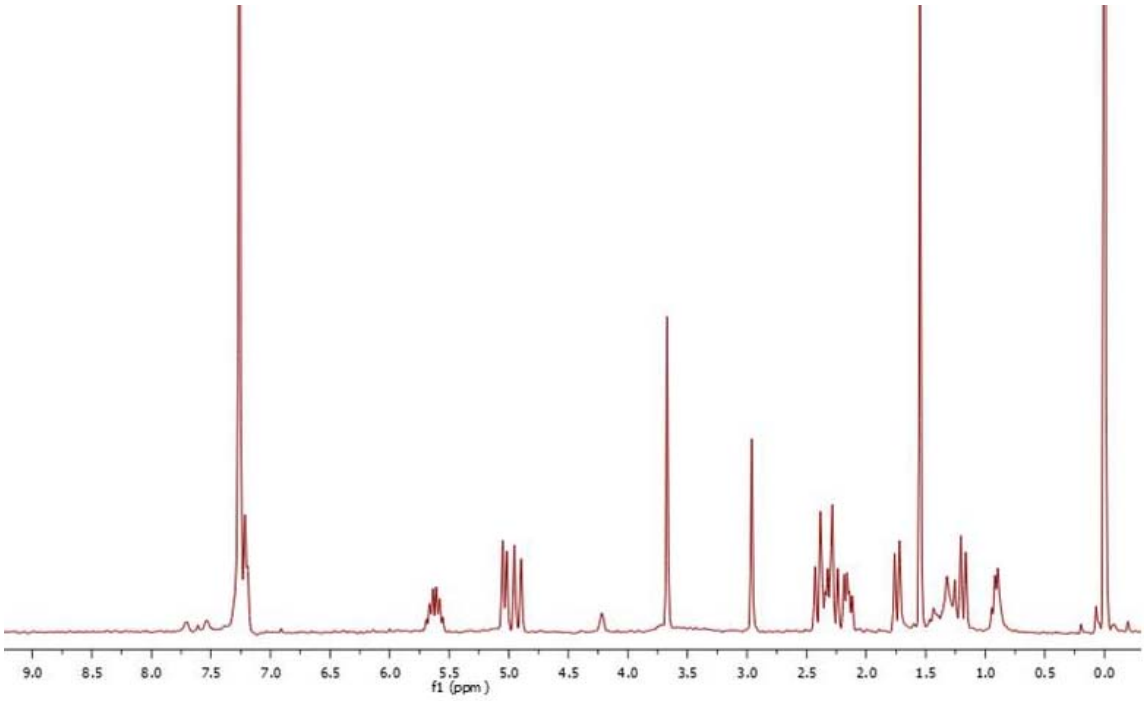

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O
O
O
Ph
Br
Br

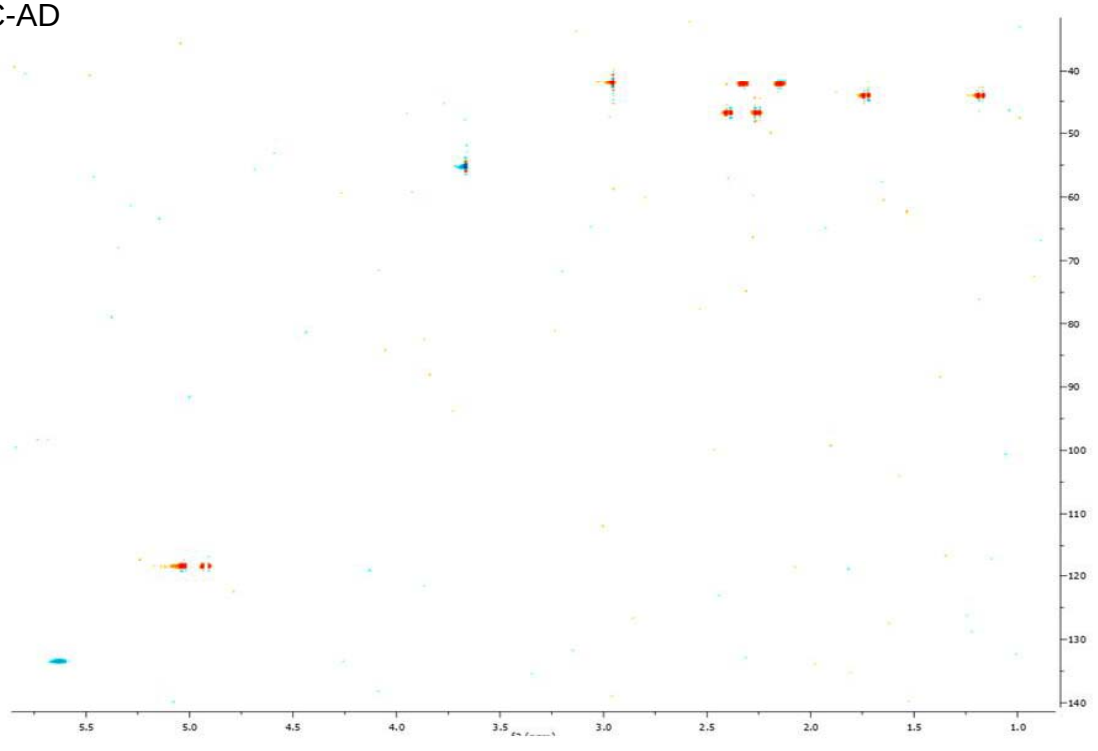

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

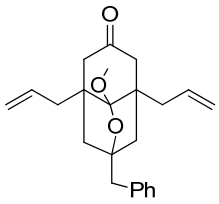

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


O
O
O
Ph

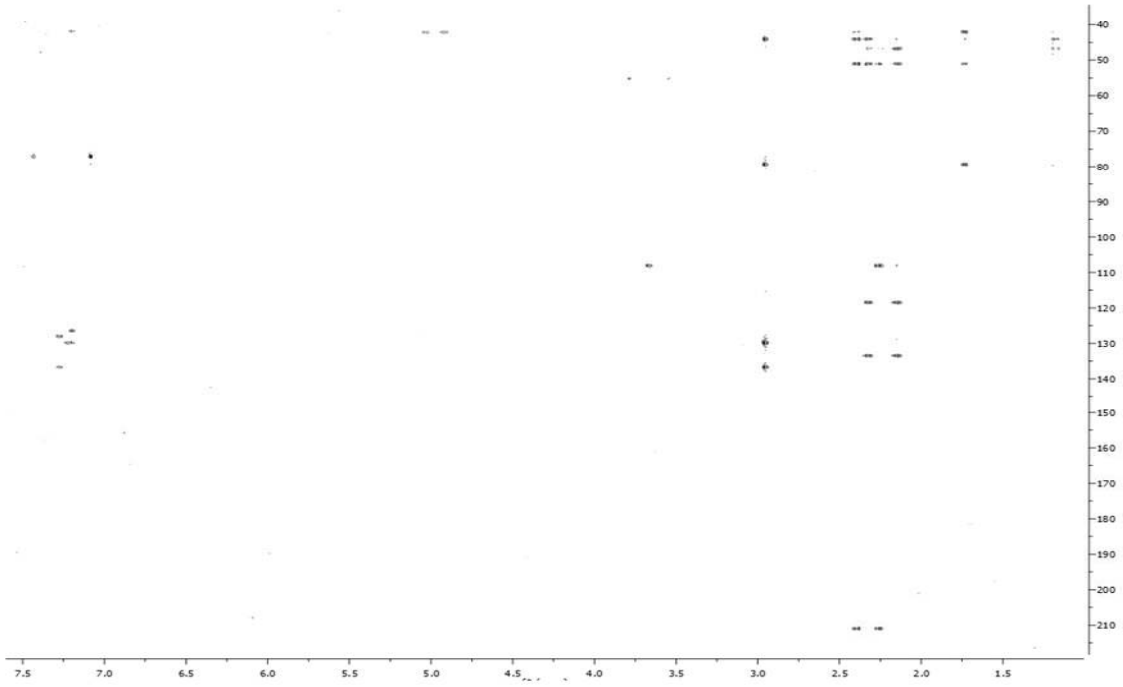

9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

HSQC-AD

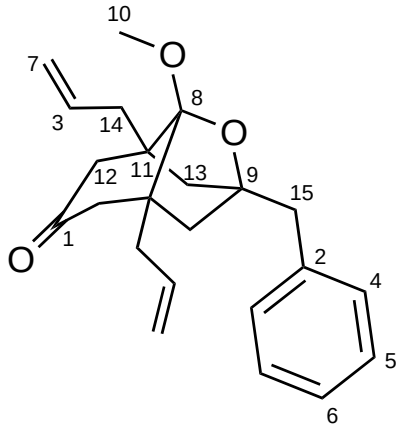

40
50
60
70
80
90
100
110
120
130
140
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

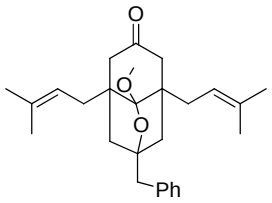

O
O
O
Ph

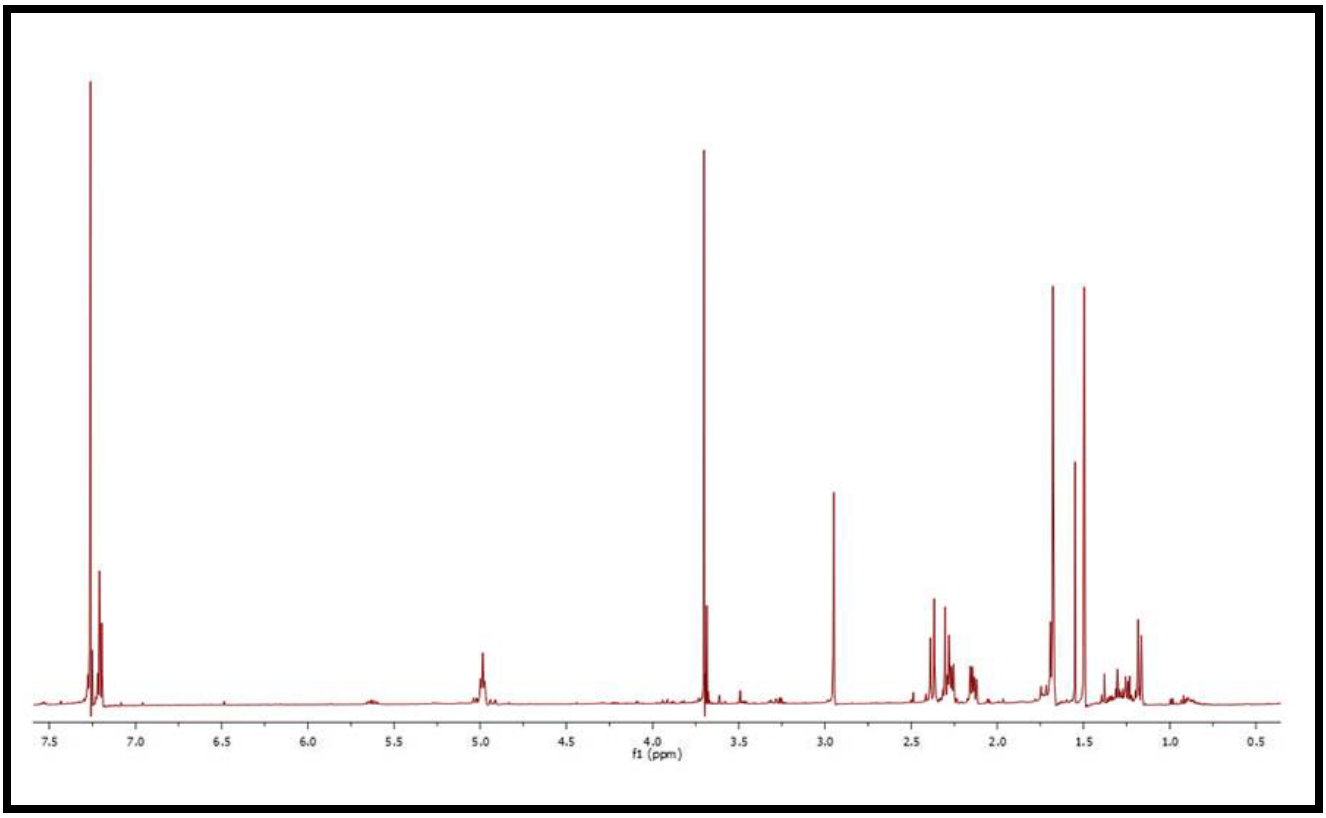
gHMBC-AD


40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

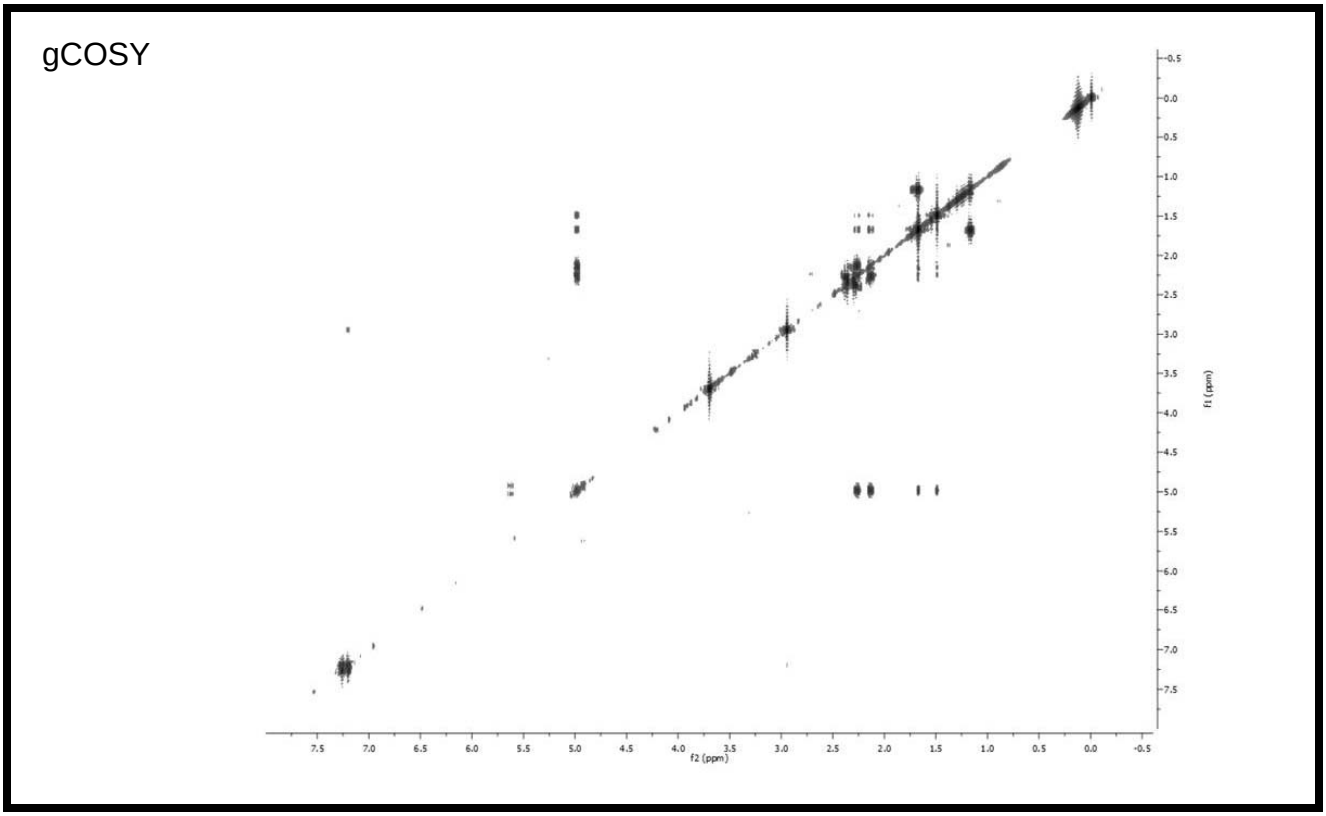
C	^{13}C (δ ppm)	HSQC-AD (δ ppm)	gHMBC-AD (^{1}H-Correlations)
1	211.0	-----	2.40, 2.26
2	136.9	-----	7.28, 2.96
3	133.6	5.62	2.33, 2.15
4	130.0	7.21	7.24, 7.21, 2.96
5	128.2	7.28	7.28, 7.21
6	126.6	7.24	7.21
7	118.8	5.03, 4.92	2.33, 2.15
8	108.1	-----	3.67, 2.26, 2.15, 1.19
9	79.4	-----	2.96, 1.74, 1.19
10	55.5	3.67	-----
11	51.1	-----	2.40, 2.33, 2.26, 2.15, 1.74, 1.19
12	47.4	2.40, 2.26	2.33, 2.15, 1.19
13	44.5	1.74, 1.19	2.96, 2.40, 2.33, 2.26, 2.15, 1.74, 1.19
14	42.6	2.33, 2.15	5.62, 5.03, 4.92, 2.40, 1.19
15	42.3	2.96	7.21, 1.74

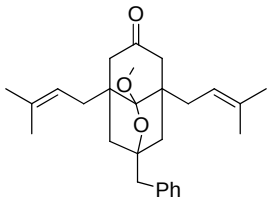



O
O
O
Ph

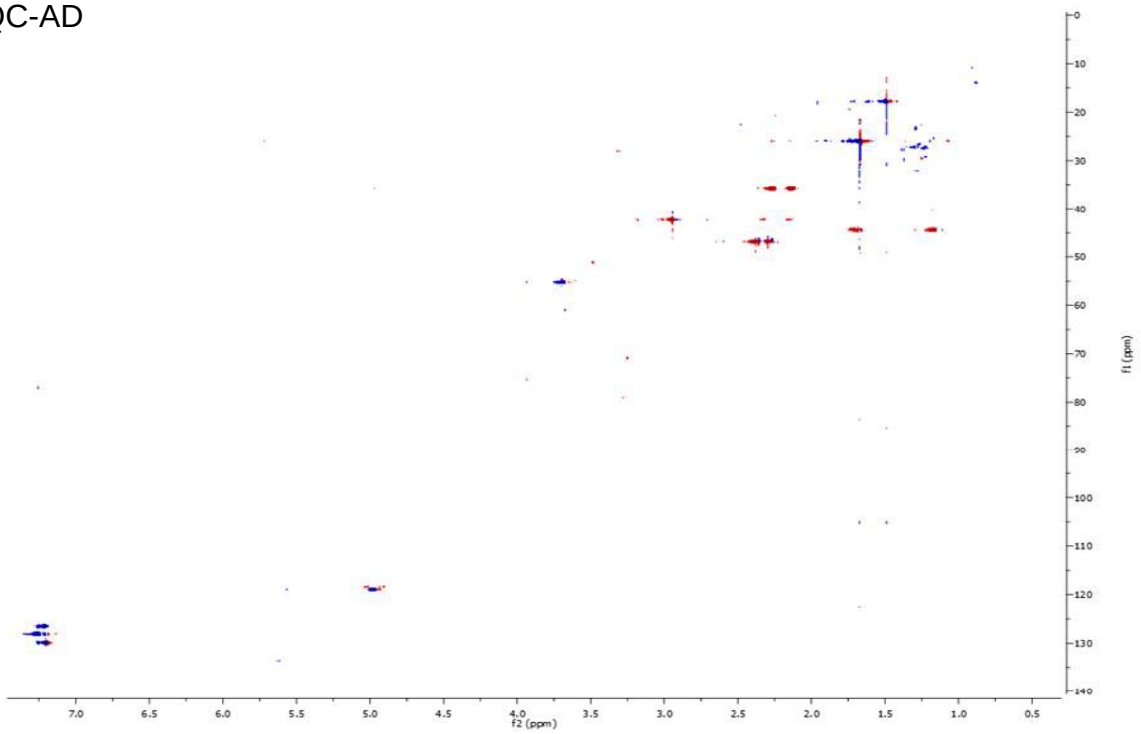

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

gCOSY

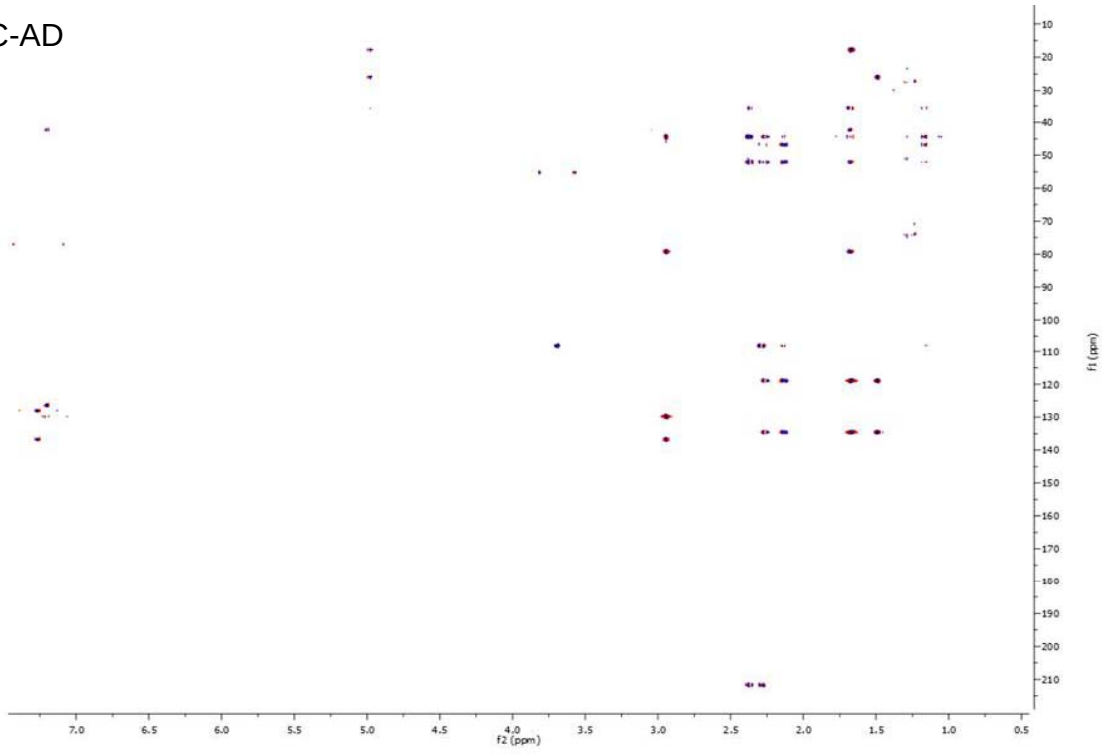

f2 (ppm)
f1 (ppm)



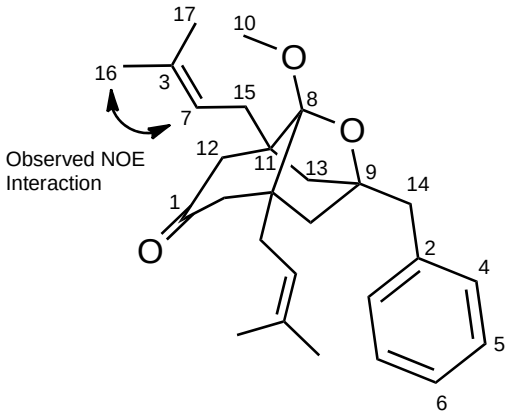
HSQC-AD



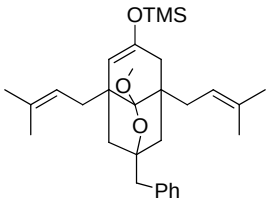
gHMBC-AD

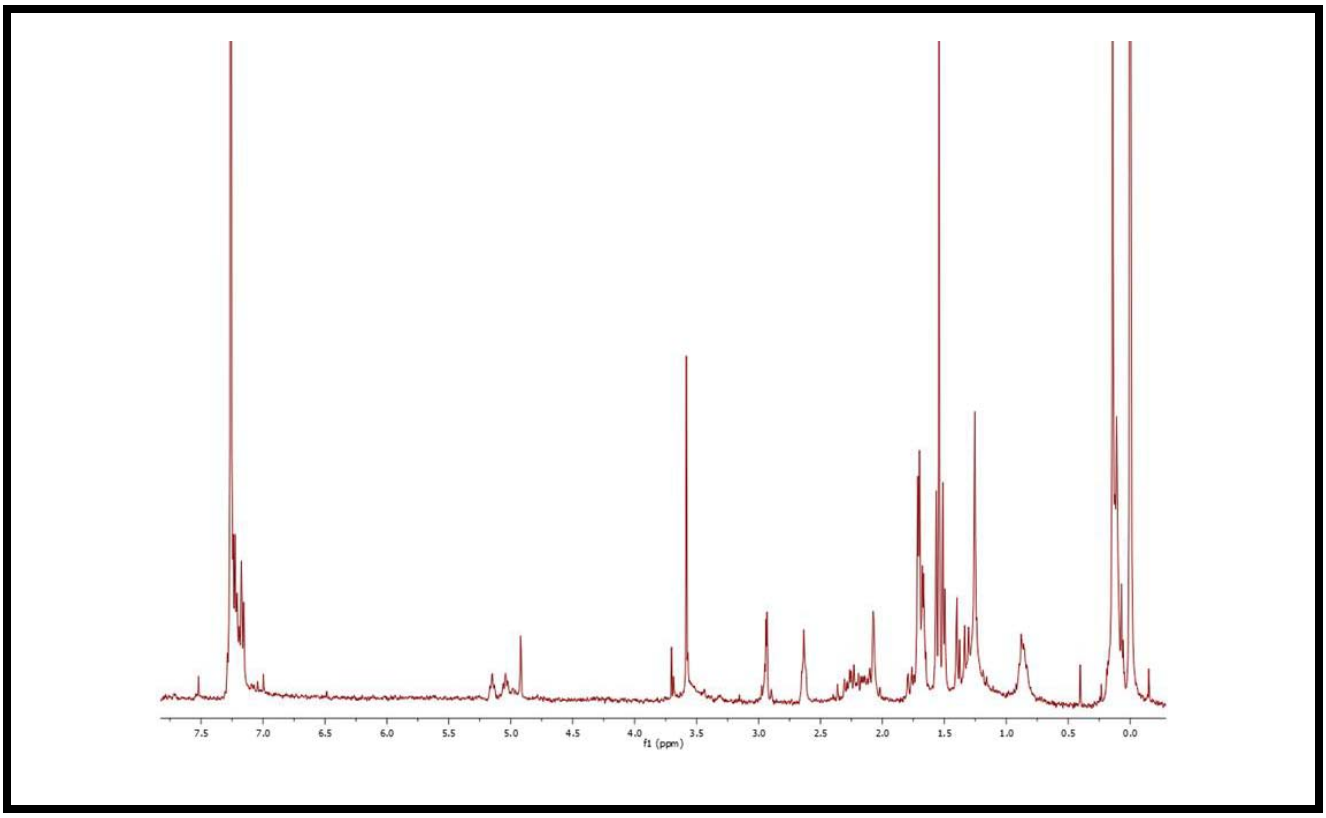


C	^{13}C (δ ppm)	HSQC-AD ^{1}H (δ ppm)	gHMBC-AD (^{1}H-Correlations)
1	211.7	-----	2.37, 2.29
2	136.7	-----	7.22, 2.94
3	134.6	-----	2.27, 2.13, 1.67, 1.49
4	129.9	7.22	2.94
5	128.1	7.23	7.22
6	126.5	7.22	7.22
7	118.9	4.98	2.27, 2.13, 1.67, 1.49
8	108.3	-----	2.29, 2.13, 1.67, 1.17
9	79.3	-----	2.94, 1.67
10	55.2	3.69	-----
11	52.1	-----	2.37, 2.27, 2.13, 1.67, 1.17
12	46.8	2.37, 2.29	2.13, 1.17
13	44.5	1.67, 1.17	2.94, 2.37, 2.27, 1.17
14	42.3	2.94	1.67
15	35.7	2.27, 2.13	2.37, 1.67
16	26.0	1.67	4.98, 1.49
17	17.8	1.49	4.98, 1.67

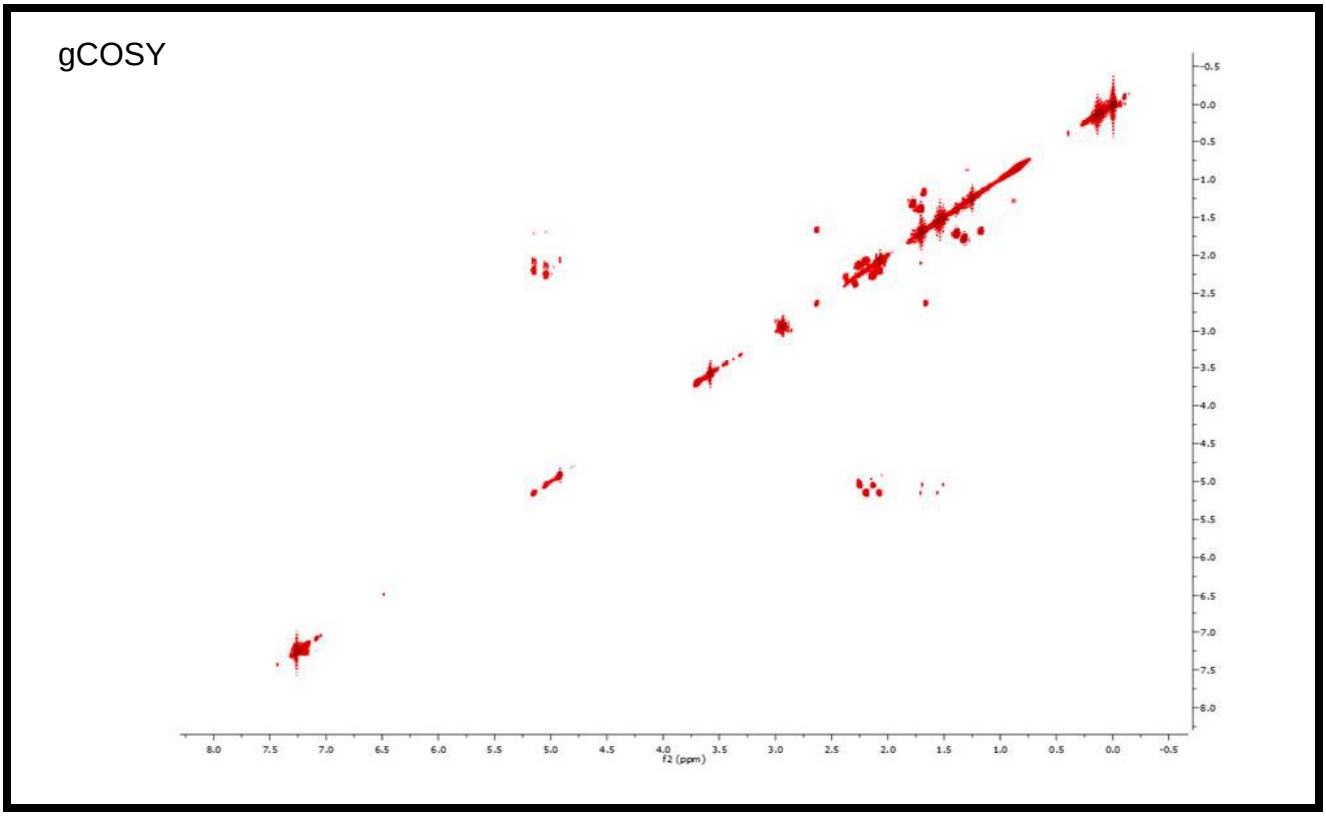


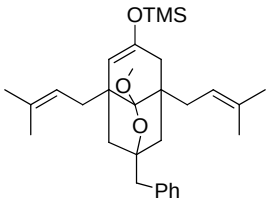
The methyl groups on the prenyl chains were assigned by the existence of a NOE interaction between methyl group (16) and the vinyl proton (7).


OTMS
O
O
Ph

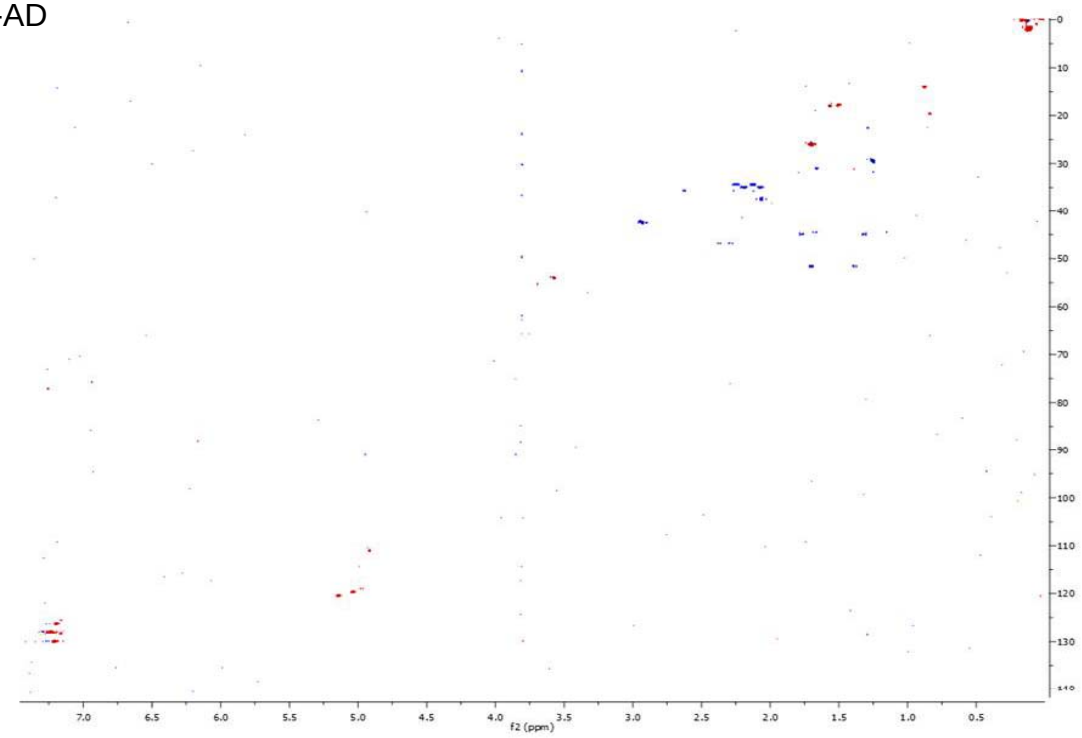

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

gCOSY

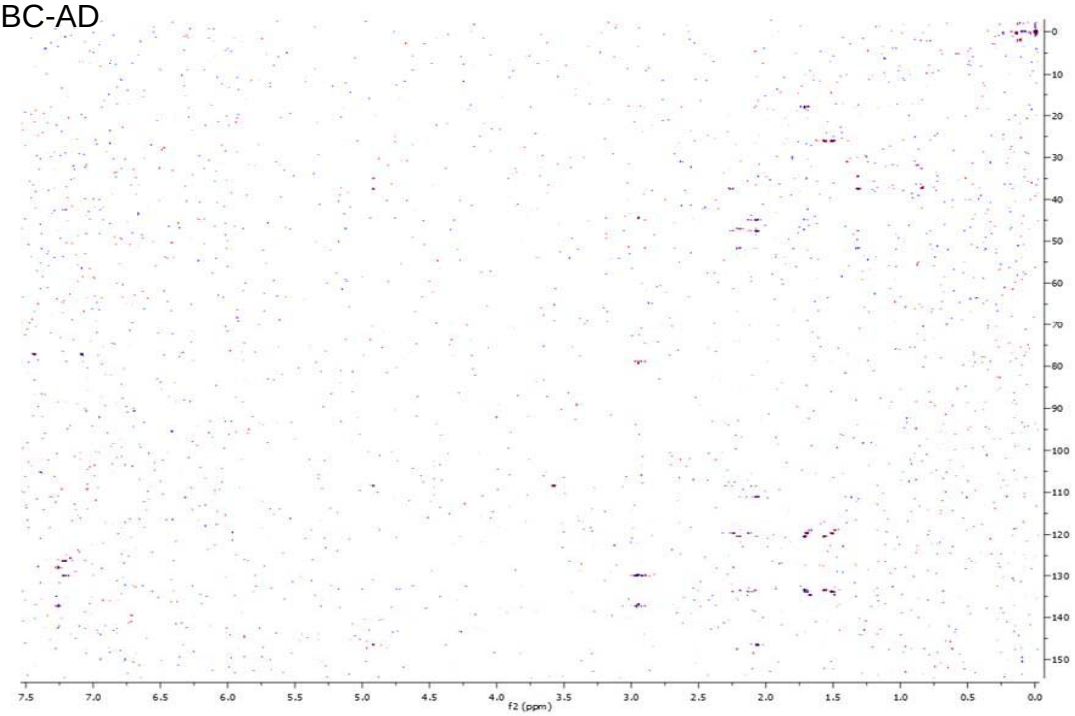

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)



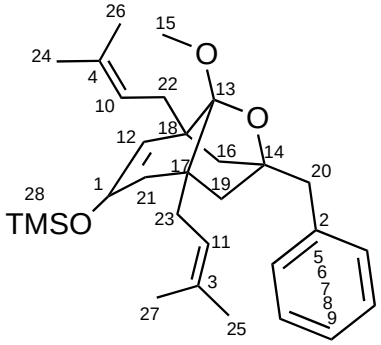
HSQC-AD

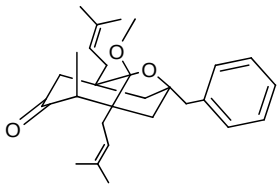


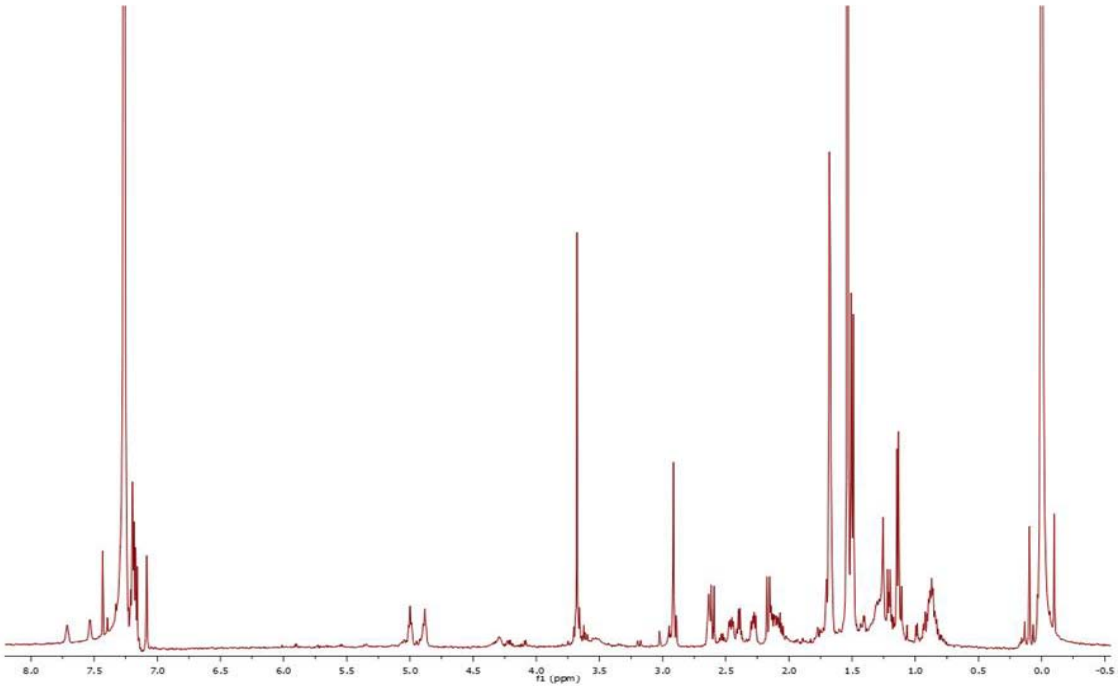
gHMBC-AD



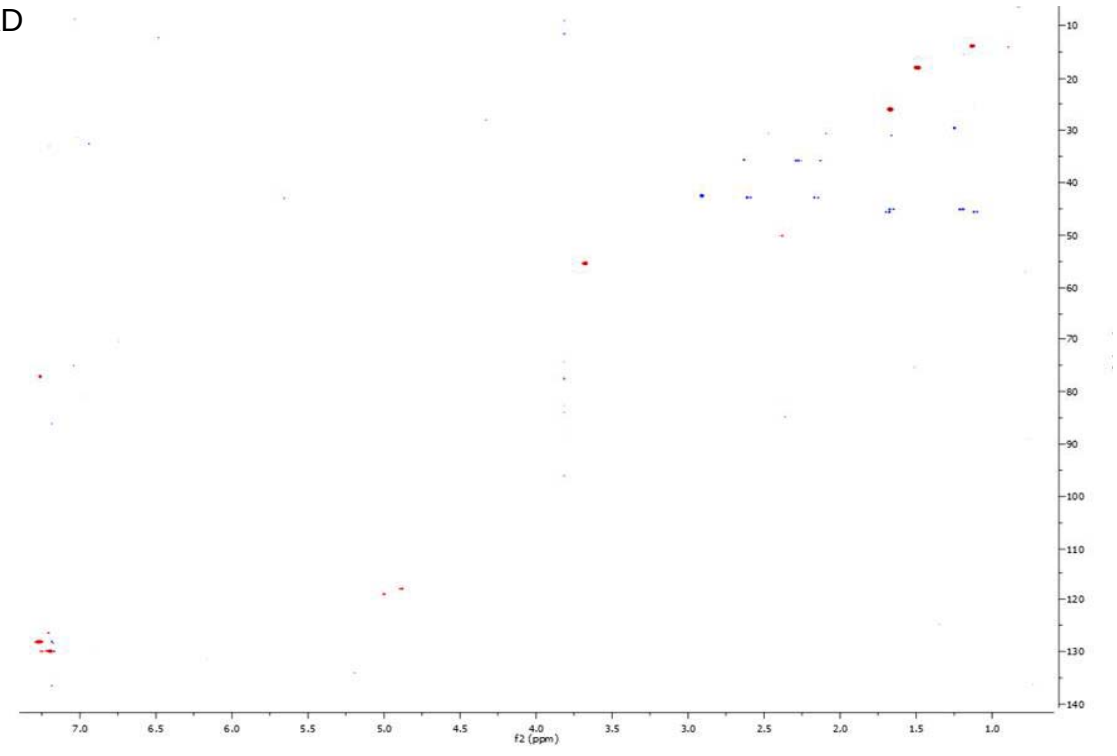
C	^{13}C (δ ppm)	HSQC-AD ^{1}H (δ ppm)	gHMBC-AD (^{1}H-Correlations)
1	146.6	-----	4.92, 2.07
2	137.4	-----	7.25, 2.94, 2.93
3	133.9	-----	2.25, 2.13, 1.71, 1.51
4	133.5	-----	2.20, 2.07, 1.72, 1.56
5	130.1	7.21	7.20, 2.94, 2.93
6	128.5	7.17	7.25
7	128.1	7.25	-----
8	126.4	7.20	7.21
9	125.7	7.16	-----
10	120.6	5.15	2.20, 2.07, 1.72, 1.56
11	119.9	5.04	2.25, 2.13, 1.71, 1.51
12	111.2	4.92	2.07, 1.39
13	108.6	-----	4.92, 3.58, 2.07, 1.39
14	78.9	-----	2.94, 2.93
15	54.2	3.58	-----
16	51.8	1.71, 1.39	2.20
17	47.7	-----	2.25, 2.07
18	47.1	-----	2.20, 2.07
19	45.1	1.78, 1.32	2.94, 2.07
20	42.6	2.94, 2.93	7.21
21	37.7	2.07	4.92
22	35.2	2.20, 2.07	4.92
23	34.6	2.25, 2.13	2.07, 1.78, 1.32
24	26.2	1.72	1.56
25	26.1	1.71	1.51
26	18.1	1.56	1.72
27	18.0	1.51	1.71
28	0.49	0.14	-----

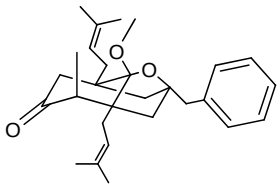



O
O
O

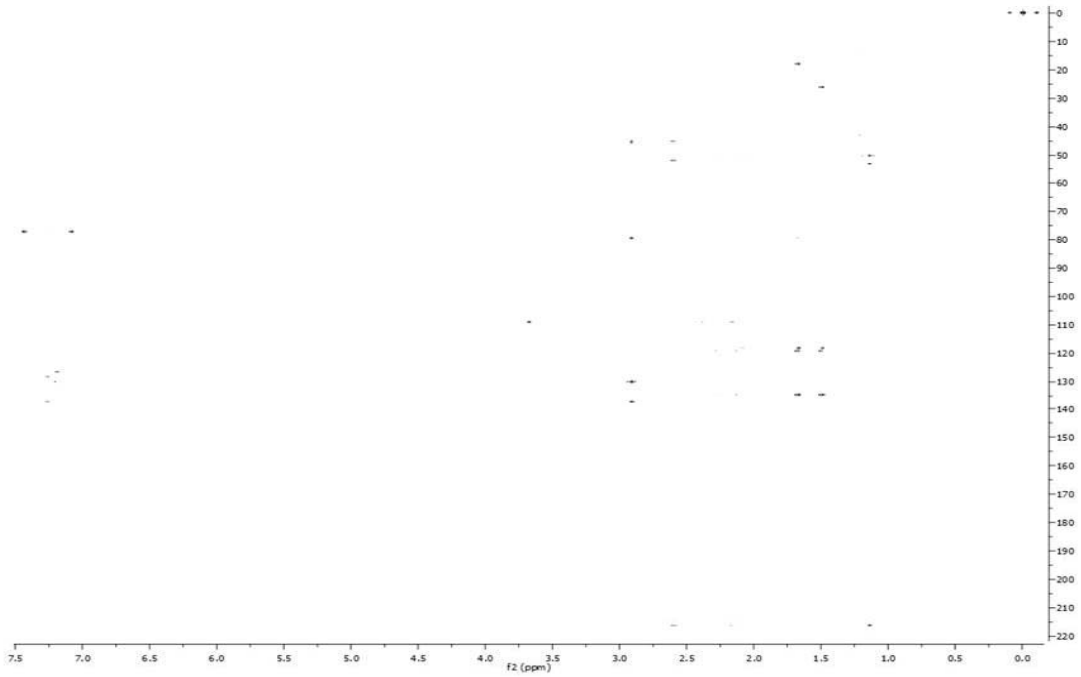

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

HSQC-AD

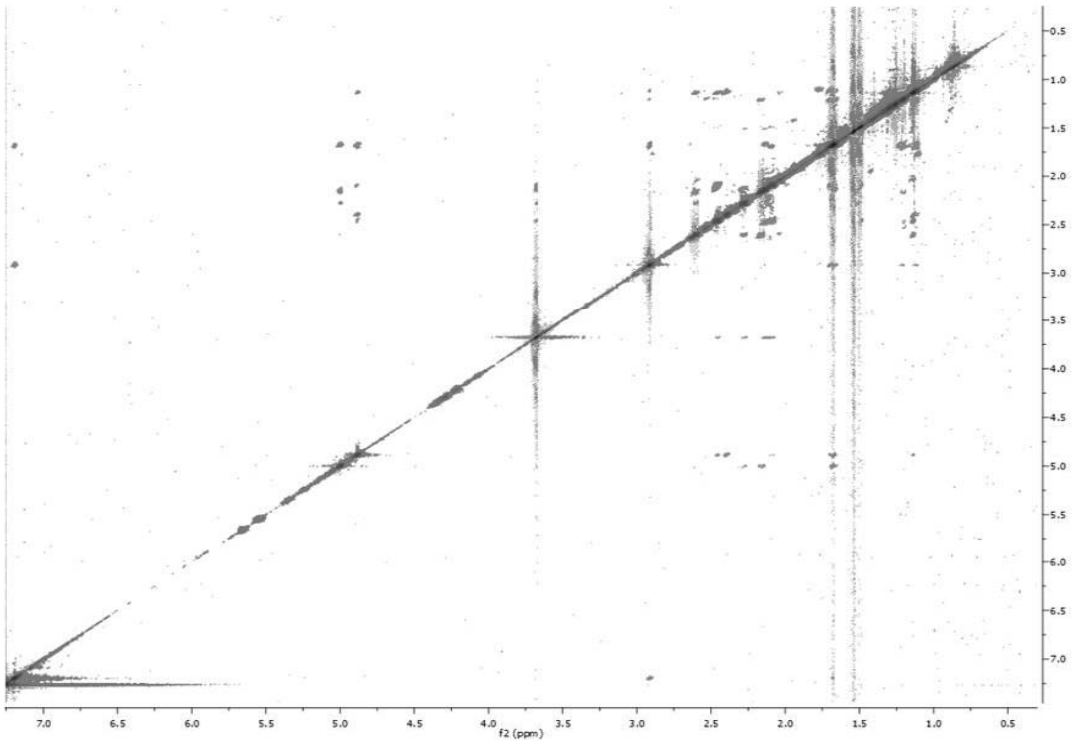

10
20
30
40
50
60
70
80
90
100
110
120
130
140
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)



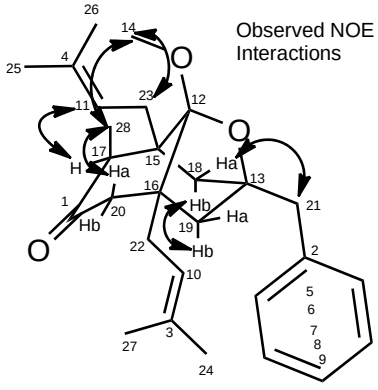
gHMBC-AD



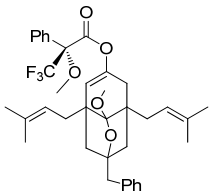
NOESY

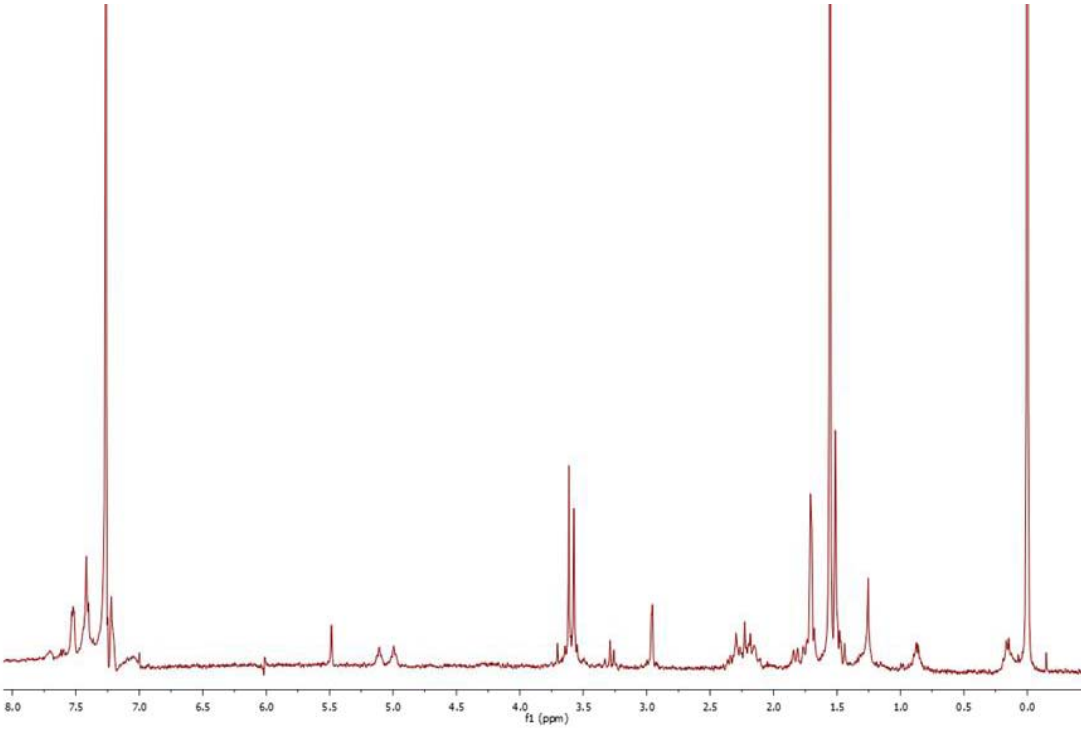


C	^{13}C (δ ppm)	HSQC-AD ^{1}H (δ ppm)	gHMBC-AD (^{1}H-Correlations)
1	216.2	-----	2.60, 2.38, 2.16, 1.13
2	136.9	-----	7.26, 2.91
3	134.5	-----	1.68, 1.67, 1.50, 1.48
4	134.5	-----	1.68, 1.67, 1.50, 1.48
5	130.0	7.25	2.91
6	129.9	7.20	7.21, 2.91
7	128.4	7.18	7.25
8	128.2	7.26	7.25
9	126.5	7.21	7.20, 7.18
10	119.1	5.00	2.28, 2.13, 1.68, 1.50
11	118.1	4.89	2.47, 2.09, 1.67, 1.48
12	108.9	-----	3.67, 2.38, 2.16
13	79.4	-----	2.91, 1.66
14	55.4	3.67	-----
15	53.1	-----	1.13
16	51.7	-----	2.60, 2.28, 2.13
17	50.1	2.38	1.13, 1.11
18	45.6	(a)1.69, (b)1.11	2.91
19	45.1	(a)1.66, (b)1.20	2.91, 2.60, 2.28
20	42.8	(a)2.60, (b)2.16	2.13, 1.20
21	42.5	2.91	1.66
22	35.8	2.28, 2.13	2.60
23	30.7	2.47, 2.09	1.11
24	26.0	1.68	1.50, 1.48
25	26.0	1.67	1.50, 1.48
26	17.9	1.48	1.68, 1.67
27	17.9	1.50	1.68, 1.67
28	13.8	1.13	2.38

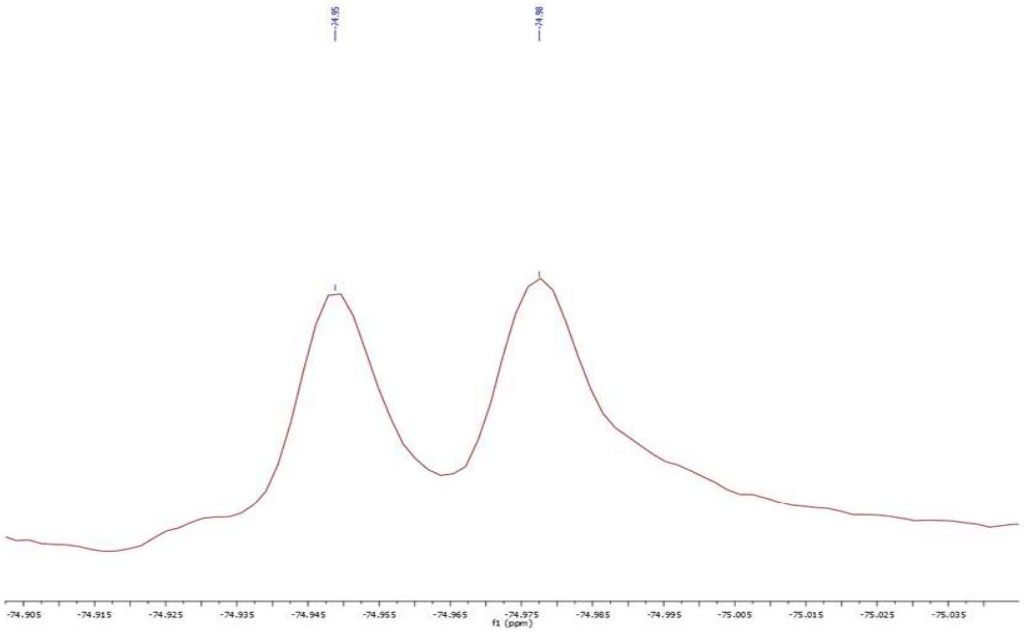


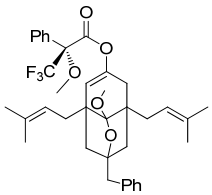
The NOE interactions that are most relevant to determining the stereochemical outcome of the experiment are indicated. The protons on the methoxy group have a correlation to the new methyl group (28) and the axial proton across the ring. In addition the protons on the other side of the bicyclic system (18, 19) were assigned by the relevant NOE interactions depicted.



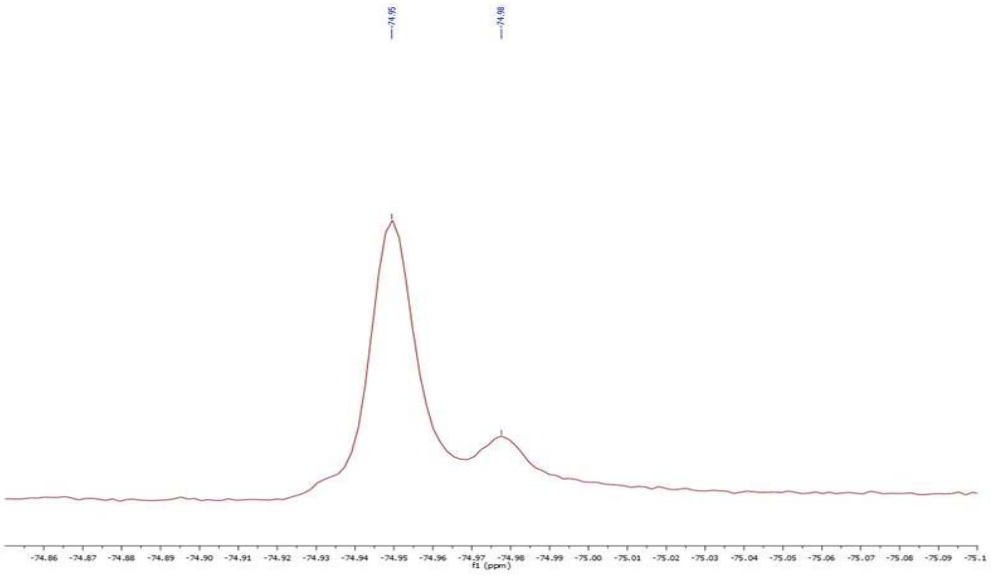


LHMDS Product Ratio

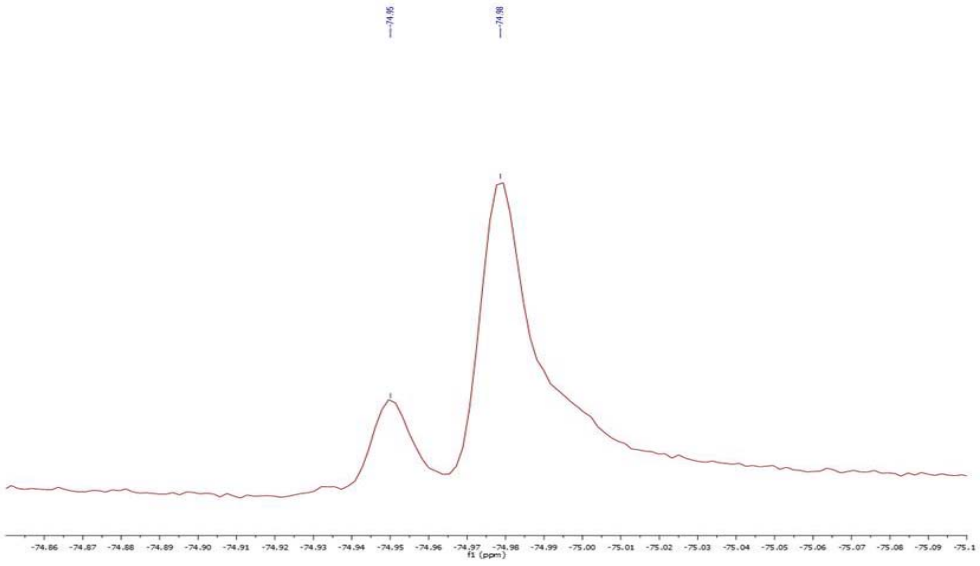




Bis [(R)-1-phenylethyl]amine Best Product Ratio



Bis [(S)-1-phenylethyl]amine Best Product Ratio



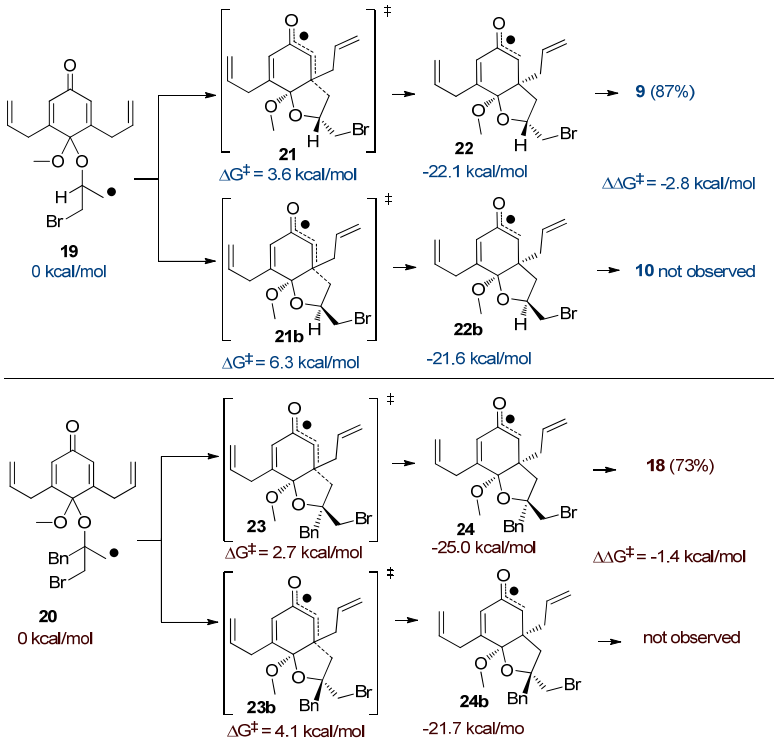
DFT Calculations

Coordinates and calculated energies

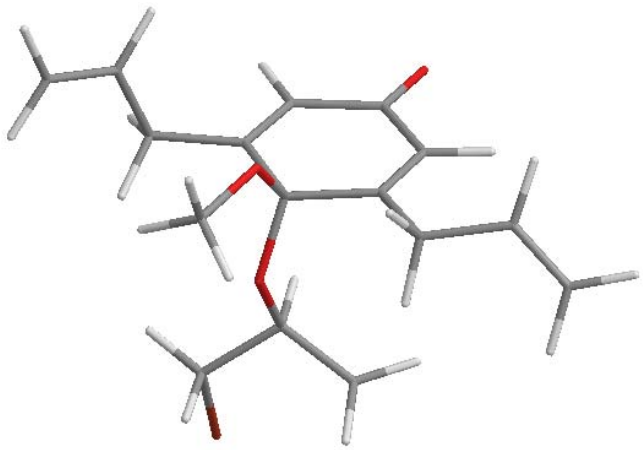
DFT calculations were performed with the program Gaussian03[1] by using the WebMO interface (WebMO, version 9.1.002p; www.webmo.net) for importing and constructing models. Transition states were verified by following the reaction coordinate forward and reverse (IRC).

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

Structure	Method	Basis Set	Coorected Energy (hartree)	Corrected Energy (kcal/mol)	Relative Energy (kcal/mol)	Frequency (cm^{-1})
19	UB3LYP	6-31G(d)	-3418.68	-2153769	0	
21	UB3LYP	6-31G(d)	-3418.67	-2153765	3.6	-376.28
22	UB3LYP	6-31G(d)	-3418.72	-2153791	-22.1	
21b	UB3LYP	6-31G(d)	-3418.67	-2153762	6.3	-315.96
22b	UB3LYP	6-31G(d)	-3418.71	-2153790	-21.6	
20	UB3LYP	6-31G(d)	-3688.94	-2324032	0	
23	UB3LYP	6-31G(d)	-3688.94	-2324029	2.7	-267.35
24	UB3LYP	6-31G(d)	-3688.98	-2324057	-25.0	
23b	UB3LYP	6-31G(d)	-3688.93	-2324028	4.1	-313.73
24b	UB3LYP	6-31G(d)	-3688.97	-2324054	-21.7	



19



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C	0.73175400	2.34538000	0.88207400
C	-0.37496900	3.31587700	0.52283300
C	-0.27863500	4.26258100	-0.41034900
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H	0.61437100	4.38028500	-1.02138200
H	-1.28384400	3.23361700	1.11788300
H	1.47938000	2.33392600	0.08072000
H	1.23858300	2.71711300	1.78369000
H	0.25579300	1.17803700	3.29411800
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H	-1.21204600	-2.67271100	1.92643200
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C	-1.80801100	-3.45505300	-0.45055100
C	-1.40877500	-4.69601900	-0.73030000
H	-2.01179500	-5.56245600	-0.47285900
H	-0.46470200	-4.89395600	-1.23439100
H	-2.76208300	-3.30361000	0.05533200
H	-1.65650100	-1.57639700	-1.46178300
H	-0.14752000	-2.46439300	-1.38217200
O	-0.89248000	0.64131600	-0.89524100
C	-0.42794300	1.10543300	-2.16326700
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H	0.35956100	1.85911700	-2.07145700
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O	1.23090800	-0.22898000	-0.70451800
C	2.32651500	-0.89326200	0.00303700
C	2.41211900	-2.33318900	-0.36716600
H	2.85102300	-2.62450900	-1.31654000
H	1.95964900	-3.09812700	0.25241400
C	3.55839500	-0.09317600	-0.41686600
Br	5.17238300	-0.79138200	0.47830500
H	3.47626400	0.95292900	-0.12705500
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21

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C	1.47904200	-0.31016500	-2.13248300
C	1.72037600	-1.78107600	-2.38331000
C	2.73690300	-2.25917100	-3.10135500
H	2.86984700	-3.32592800	-3.26024500
H	3.47556400	-1.60497000	-3.56126100
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H	3.50216200	-0.24376500	-0.30712800
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H	-2.62158800	-0.52121100	-0.71952900
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Br	-2.73507700	3.50042700	0.25257500
H	-0.58059000	4.43284100	-0.63398800
H	-1.29694600	3.27143500	-1.79514800
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H	1.22607200	2.34417400	-2.00699100
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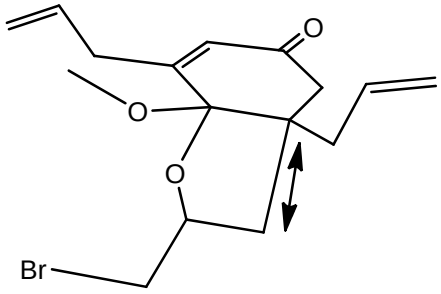
H	0.03750000	2.50292300	0.85218700



22

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C	-0.66731300	-1.42254700	0.03721900
C	-1.82952200	-1.62361000	-0.99217300
C	-3.01621500	-0.71644700	-0.81080300
C	-4.23670600	-1.12644100	-0.46394200
H	-5.06466800	-0.43078100	-0.35772500
H	-4.45782800	-2.17485400	-0.27236700
H	-2.83520900	0.34104800	-0.99527900
H	-1.40333400	-1.47177700	-1.98964500
H	-2.15159500	-2.67041000	-0.92318200
C	0.54941600	-2.30813900	-0.33230900
C	1.70118000	-1.60489300	0.39040100
O	1.36545800	-0.20722000	0.34597800
C	3.05513400	-1.83701700	-0.24953500
Br	4.51064000	-0.96710800	0.76341700
H	3.30128600	-2.89943000	-0.26793600
H	3.10100000	-1.42089600	-1.25580200
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O	-2.02599100	-1.12970200	3.48740600
H	-1.61473900	1.33803400	2.80320000
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C	1.13543900	2.91096000	1.08444500
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H	2.85876500	4.06507900	0.66917200
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H	0.64452600	1.49548100	-2.89174800
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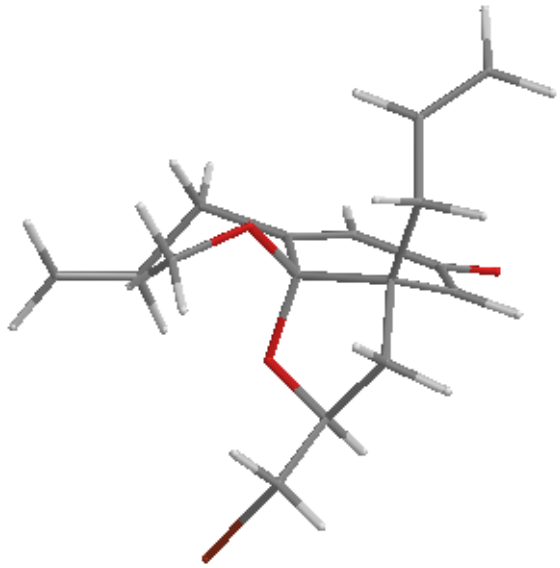

21b

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C	1.39314800	-0.11740700	-2.15386100
C	2.73330200	-0.38904800	-2.77971400
C	3.34935900	0.42288800	-3.63916100
H	4.30813400	0.16665000	-4.08177900
H	2.91464600	1.37479500	-3.93814400
H	3.20525300	-1.33285200	-2.50444700
H	0.68773400	-0.90977100	-2.43982200
H	0.97061100	0.81606400	-2.54790100
H	3.49134700	0.07890400	-0.37138200
O	3.53424600	0.21447100	2.22420100
H	1.22216600	-0.06993100	3.30432300
C	-1.28133700	-0.49045600	2.22957900
C	-1.28903400	-0.44684500	3.73371100
C	-2.15812900	0.25360100	4.46375000
H	-2.14137100	0.23041600	5.54980900
H	-2.92998400	0.86899300	4.00458300
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H	-1.40641600	-1.53185900	1.89941000
H	-2.15840700	0.04477600	1.85337400
O	-0.68583000	-1.17263800	-0.44686900
C	-2.00626600	-1.04609700	-0.97535800
H	-2.21193900	-2.00133200	-1.46446700
H	-2.75445100	-0.89005700	-0.18625800
H	-2.08205100	-0.23243700	-1.70047100
O	-0.57799600	1.17442200	-0.56239100
C	-1.31351000	2.05882800	0.29329000
C	-1.53418600	3.33141000	-0.51953700
Br	-2.62479600	2.97769500	-2.13983700
H	-2.08654800	4.07531800	0.05277000
H	-0.58952700	3.74070100	-0.87623300
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H	0.45042000	2.75731300	1.44234600
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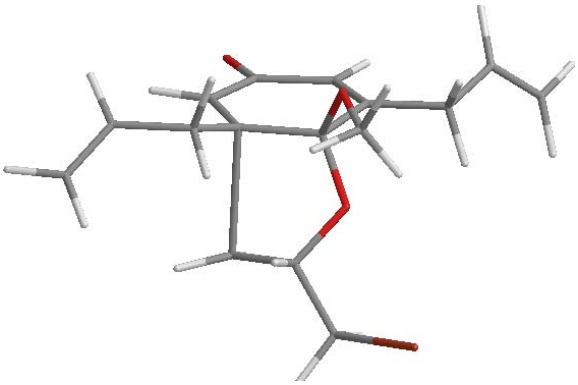

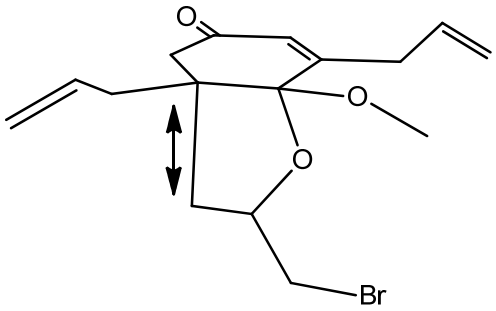

22b

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C	-0.53959400	-1.45394500	-0.21320400
C	-1.94498400	-1.53925500	-0.90065800
C	-3.07961400	-0.90282800	-0.14544700
C	-4.10739200	-1.56943500	0.38128500
H	-4.91107300	-1.06002700	0.90595600
H	-4.18655800	-2.65255600	0.30872100
H	-3.03783700	0.18122900	-0.05296900
H	-1.84642400	-1.05939400	-1.88033200
H	-2.16419100	-2.60118900	-1.06956500
C	0.55200300	-2.01960800	-1.15979400
C	1.84319100	-1.29035300	-0.73533700
O	1.41261800	-0.12329300	-0.01280100
C	2.73717900	-2.13781500	0.15704600
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H	3.07650600	-3.03363800	-0.36455700
H	2.42236900	-0.96105900	-1.60594200
H	0.30578400	-1.77075700	-2.19674700
H	0.63659600	-3.10893100	-1.09036300
H	-0.64120300	-3.29901900	1.04647400
O	-0.86427000	-2.26001500	3.39982700
H	-0.91821900	0.33534100	3.35768100
C	-0.30001400	2.16091400	1.46683800
C	1.11030400	2.70300900	1.59314800
C	1.54203200	3.83330000	1.03256600
H	2.55291700	4.19755500	1.19359700
H	0.90039600	4.44306600	0.39882300
H	1.78424200	2.12051200	2.22008200
H	-0.85636300	2.43509500	2.37397400
H	-0.80941900	2.64073400	0.62374900
O	-0.47841100	0.78206400	-1.09126500
C	0.45249200	1.60118500	-1.79889400
H	-0.15876700	2.22379100	-2.45754800
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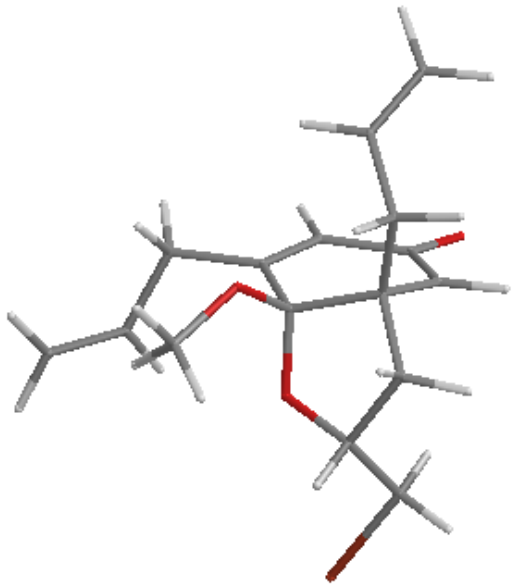
H	1.13497500	1.00164600	-2.41508800



20

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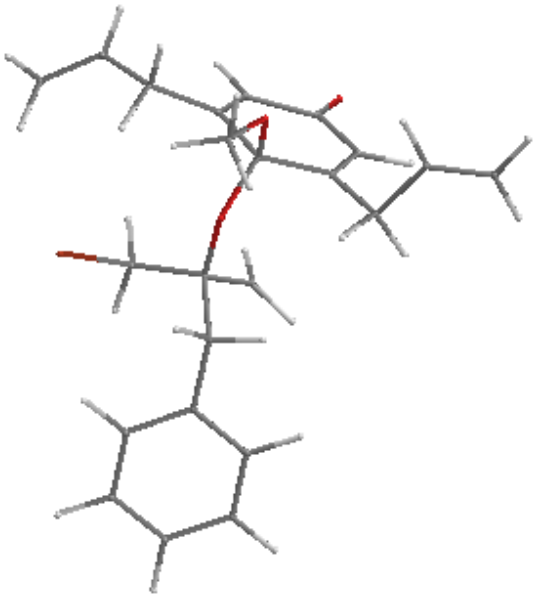
C	-0.92138200	0.96294900	2.11951700
C	-0.39061400	1.17520100	0.90363900
C	-0.20178000	2.55106300	0.29458600
C	-0.29140800	3.71150300	1.25009000
C	0.72112700	4.54252300	1.50438100
H	0.61460500	5.37917200	2.18982900
H	1.69219300	4.41514200	1.02959100
H	-1.25272500	3.87532200	1.73720900
H	0.75637600	2.58560200	-0.23219800
H	-0.97289400	2.65288800	-0.48486300
H	-1.18468100	1.78360600	2.78010100
O	-1.72622900	-0.54388400	3.75309300
H	-1.29232500	-2.49975600	2.09962300
C	-0.14389800	-2.55532200	-0.38871500
C	-1.41470800	-3.02852000	-1.05596200
C	-1.89476700	-4.26896700	-0.96874900
H	-2.81414900	-4.56036600	-1.46936400
H	-1.38737100	-5.04322300	-0.39616700
H	-1.94876100	-2.27243900	-1.62827300
H	0.29442100	-3.38377500	0.18059100
H	0.58856600	-2.26202800	-1.14961000
O	-0.73655200	0.14180700	-1.21827700
C	-0.05367700	0.48040800	-2.42968800
H	-0.85365700	0.68286200	-3.14635700
H	0.57980900	1.36480200	-2.32358700
H	0.56107600	-0.34782900	-2.79815800
O	1.37750000	0.04667100	-0.36947900
C	2.50998600	-0.13224500	0.54639600
C	2.19536500	-0.89894500	1.78824000
H	1.73163000	-0.41544300	2.63970700
H	2.48094300	-1.93901100	1.88641100
C	3.01312500	1.24867500	0.99973400
Br	3.46122400	2.46325100	-0.50719200
H	2.26071700	1.77861200	1.58281400
H	3.93335300	1.15504900	1.57430200
C	3.53899600	-0.88174100	-0.34735600
C	4.87928900	-1.19595800	0.28735100
C	5.12842400	-2.46276300	0.83501600
C	6.36021200	-2.76893000	1.41502900
C	7.37250600	-1.80930500	1.45335300
C	7.14399700	-0.54714900	0.90250400
C	5.91119600	-0.24447900	0.32313700
H	5.74730000	0.73835700	-0.11126800
H	7.92960500	0.20385600	0.91584300
H	8.33422200	-2.04564600	1.90059000
H	6.53018500	-3.75907800	1.82968800
H	4.35371700	-3.22545600	0.79227300
H	3.67446600	-0.27550800	-1.24795500
H	3.05320000	-1.81202900	-0.65896900



23

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C	1.16960300	0.00000000	2.23354300
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C	2.47082300	-0.40953500	0.12903800
C	1.37378800	-0.25782400	-0.63260900
C	1.40134200	-0.26110800	-2.15019200
C	2.66976000	-0.77537900	-2.77949700
C	2.74071700	-1.90157900	-3.49109000
H	3.67287200	-2.23626800	-3.93863000
H	1.86481600	-2.52774600	-3.64958400
H	3.56656400	-0.17080700	-2.64314800
H	0.54684200	-0.83447000	-2.52198900
H	1.22901400	0.77799700	-2.47229000
H	3.44535600	-0.60066600	-0.31033700
O	3.50006100	-0.37001100	2.25860200
H	1.18169500	0.15371300	3.30958700
C	-1.30177700	0.42704800	2.20958300
C	-1.27412800	1.87159900	2.65136100
C	-1.47991500	2.27784900	3.90432800
H	-1.45444700	3.33035800	4.17336800
H	-1.68461700	1.57588700	4.71076100
H	-1.06363800	2.59538800	1.86687000
H	-1.48739800	-0.20976200	3.08188900
H	-2.13200700	0.27128200	1.51110400
O	-0.40694700	1.32035700	-0.36460800
C	-1.41641000	1.50015100	-1.36125500
H	-1.48942300	2.58354900	-1.48483600
H	-1.14666800	1.04409700	-2.31906800
H	-2.38456200	1.10286100	-1.04252600
O	-0.97529700	-0.89406500	-0.52230100
C	-1.05995700	-2.25146400	0.00278200
C	-0.40254200	-2.37197500	1.34716600
H	0.62639700	-2.70898000	1.41048500
H	-1.01157000	-2.52876300	2.22990200
C	-0.32084800	-3.20656000	-0.95002000
Br	-1.00007600	-3.14539200	-2.81357800
H	0.73665600	-2.95516300	-1.02234700
H	-0.43911400	-4.24196100	-0.63392000
C	-2.58911400	-2.52525100	0.06295000
C	-3.00714900	-3.89326700	0.56497200
C	-3.38465800	-4.07440500	1.90365700
C	-3.77505800	-5.32634500	2.38099500
C	-3.79958500	-6.42526400	1.52151500
C	-3.43855700	-6.25889000	0.18334000
C	-3.04916000	-5.00555700	-0.29075000
H	-2.77999200	-4.88601500	-1.33706000
H	-3.46642900	-7.10534200	-0.49789200
H	-4.10607500	-7.40088100	1.88891200
H	-4.06646300	-5.44013200	3.42184400
H	-3.39005500	-3.22035600	2.57786700
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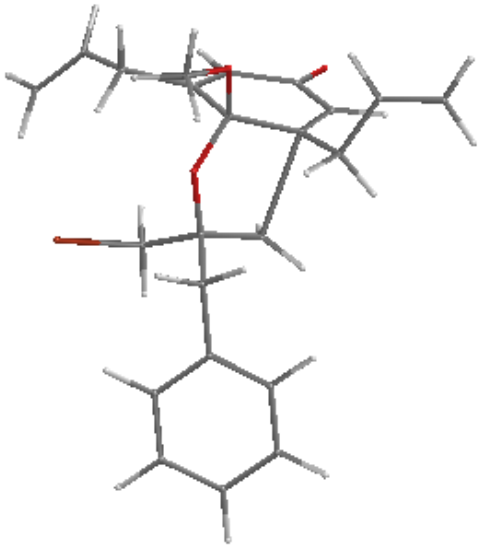
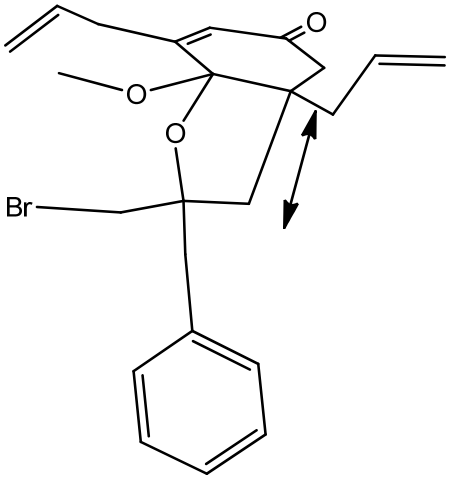
H	-3.01643700	-1.75244600	0.70962800





24

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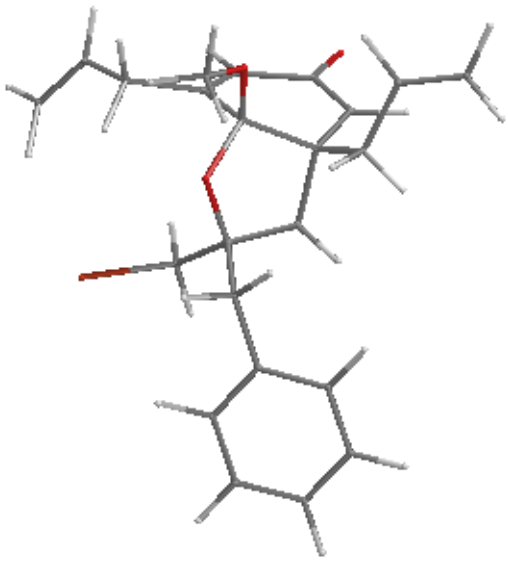
C	0.69887900	-1.09135400	0.81884100
C	0.73557100	-2.45763800	0.15767000
C	1.24170700	-3.58708500	1.01470000
C	0.47137100	-4.58771700	1.44444400
H	0.86800500	-5.39386600	2.05597900
H	-0.58833200	-4.63114900	1.19861300
H	2.29925500	-3.57077200	1.27914600
H	-0.26994800	-2.69465000	-0.20660800
H	1.36518500	-2.36590300	-0.74152800
H	1.77908800	-1.58846000	2.57549600
O	1.98122500	0.76232200	3.63216500
H	0.64048500	2.57605700	2.34675300
C	-0.53462700	2.53253300	-0.09610700
C	0.74906200	3.24691100	-0.43490400
C	0.96838800	4.54017600	-0.19142000
H	1.90422000	5.02126600	-0.46286000
H	0.22013400	5.17190900	0.28481200
H	1.51921600	2.64544900	-0.91089700
H	-1.20599400	3.23987700	0.40725100
H	-1.04147600	2.22037100	-1.01854700
O	0.85254900	0.30924500	-1.08891500
C	0.44799900	-0.03676100	-2.41392500
H	1.28818000	0.25549000	-3.04834000
H	0.26665900	-1.11110500	-2.52379400
H	-0.45033200	0.50473300	-2.72751500
O	-1.24371000	-0.47656600	-0.50037200
C	-2.32354300	-0.21636200	0.41391700
C	-1.77351600	0.85538900	1.39902900
H	-1.65660700	0.43374100	2.40228200
H	-2.44881800	1.70884000	1.49214200
C	-2.64029000	-1.48415100	1.21825700
Br	-3.14580300	-3.02850900	0.08451400
H	-1.76953800	-1.82029800	1.77919200
H	-3.48114900	-1.32298000	1.89251700
C	-3.50933100	0.26304200	-0.46129800
C	-4.78131600	0.63214000	0.27631800
C	-5.06977000	1.97228900	0.57276500
C	-6.23743400	2.32626200	1.25097600
C	-7.14412900	1.34078700	1.64262900
C	-6.87678700	0.00325300	1.34456900
C	-5.70916500	-0.34712500	0.66593700
H	-5.51533400	-1.39021900	0.42928600
H	-7.58226200	-0.77116700	1.63418300
H	-8.05549400	1.61304200	2.16798400
H	-6.44065400	3.37206500	1.46592600
H	-4.37974100	2.75047300	0.25310700
H	-3.70742500	-0.53474700	-1.18481800
H	-3.15173500	1.12675800	-1.03110000



23b

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C	1.40207300	-0.03449200	-0.63913600
C	1.43738800	0.27506300	-2.13451900
C	2.74464200	0.02550900	-2.83653000
C	2.89043600	-0.76673100	-3.89967200
H	3.85187400	-0.89499500	-4.38910600
H	2.05106200	-1.30872500	-4.33205500
H	3.61348400	0.56258600	-2.45828800
H	0.63687400	-0.26823500	-2.64639000
H	1.18271800	1.34230200	-2.22473900
H	3.50841500	0.14989800	-0.28741900
O	3.50643900	0.02871300	2.28206100
H	1.12809700	0.01968700	3.32555000
C	-1.36600700	0.07245400	2.19303400
C	-1.65851600	1.44879000	2.74394700
C	-1.96435300	1.70375500	4.01604200
H	-2.17309900	2.71304000	4.36052700
H	-2.02294000	0.91390900	4.76260000
H	-1.60109900	2.26094700	2.02142000
H	-1.41758700	-0.66083700	3.00687000
H	-2.13220300	-0.20590300	1.46085700
O	-0.63419100	1.23160400	-0.34774500
C	-1.63877200	1.25799300	-1.36823900
H	-2.06731700	2.26108800	-1.30447700
H	-1.21699500	1.11591000	-2.36998600
H	-2.41483700	0.50797300	-1.20358600
O	-0.82387800	-1.04130200	-0.50147300
C	-0.30340500	-2.39988100	-0.57333900
C	1.17930300	-2.40508400	-0.81429900
H	1.56961500	-2.41384000	-1.82663600
H	1.83850800	-2.80362300	-0.05224500
C	-0.98310900	-2.99246500	-1.81389900
Br	-2.96434700	-2.91014200	-1.73316800
H	-0.71732400	-2.42566000	-2.70516800
H	-0.73472900	-4.04434400	-1.94097700
C	-0.69361200	-3.14165000	0.73775900
C	-0.32913300	-4.61205100	0.80235800
C	0.84395800	-5.03023700	1.44738300
C	1.18546700	-6.38176000	1.51634500
C	0.35281100	-7.34368100	0.94319000
C	-0.82452000	-6.94392500	0.30797300
C	-1.16336000	-5.59203300	0.24064400
H	-2.08713500	-5.29021700	-0.24715200
H	-1.48656800	-7.68624200	-0.13032100
H	0.61425400	-8.39697400	0.99891900
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H	1.48939200	-4.29096900	1.91690300
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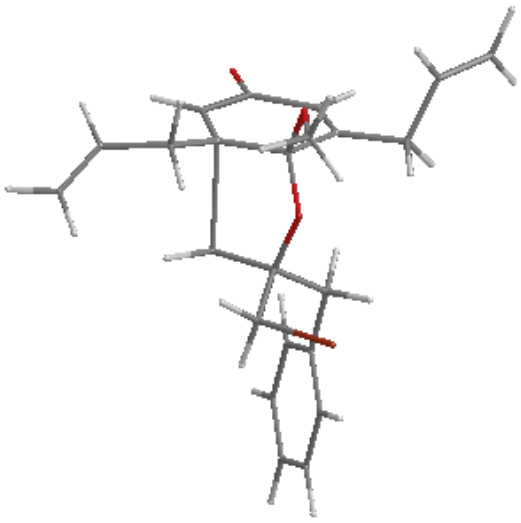
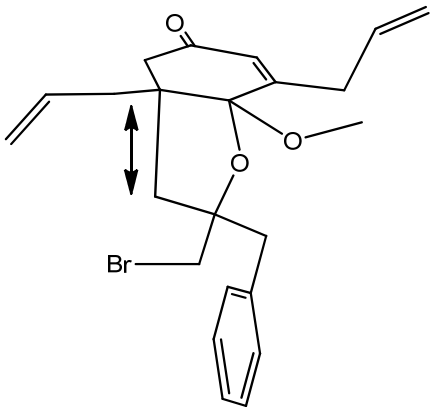
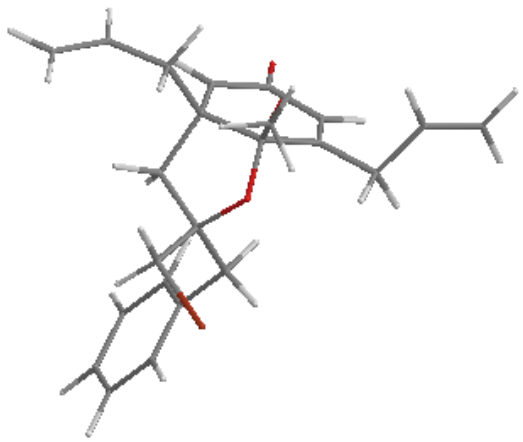




24b



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C	0.50808400	2.69464300	-1.19137300
C	-0.01377900	2.57797500	0.14122600
C	-0.43149100	1.30194000	0.80016400
C	0.13775000	1.24835700	2.26061700
C	-0.26227300	2.39918600	3.14296800
C	-1.02799900	2.28759800	4.23069100
H	-1.27203700	3.14646600	4.84997500
H	-1.42747500	1.32804300	4.55461000
H	0.12911200	3.38159700	2.88013200
H	-0.20034900	0.31671800	2.72609500
H	1.22938500	1.19122600	2.19059400
H	-0.17353700	3.51308500	0.67005500
O	0.75674700	3.80765200	-1.69176400
H	1.11292300	1.55996500	-2.94894800
C	0.78170800	-1.03794700	-2.23103600
C	2.26054600	-1.32472500	-2.34610300
C	2.91763800	-1.45401800	-3.49873900
H	3.98344400	-1.66423600	-3.52697900
H	2.41565100	-1.35902400	-4.45981800
H	2.79251200	-1.41702300	-1.40074200
H	0.35576900	-0.92924800	-3.23573700
H	0.26911000	-1.88412400	-1.76006300
O	1.06753800	-0.70193900	0.62524700
C	0.78761600	-1.89903100	1.35276800
H	1.76583100	-2.26409300	1.67427300
H	0.16655000	-1.71938900	2.23853300
H	0.29596400	-2.65238000	0.73178200
O	-1.14539900	-0.83746500	-0.02343800
C	-2.37553800	-0.10491100	0.10504700
C	-1.99826900	1.21199800	0.83012300
H	-2.34237400	1.21350100	1.86934300
H	-2.47365700	2.06859200	0.34783400
C	-3.28617500	-0.92924000	1.01275900
Br	-3.69581900	-2.72776700	0.29150300
H	-2.80522800	-1.11435700	1.97236300
H	-4.24875600	-0.44028900	1.15760200
C	-2.96009400	0.11884000	-1.31776900
C	-4.26694100	0.88310000	-1.39183700
C	-4.27585700	2.25575300	-1.68097200
C	-5.47343900	2.96990600	-1.75015600
C	-6.68890300	2.31918000	-1.53606900
C	-6.69701000	0.95047300	-1.25955100
C	-5.49871000	0.23922100	-1.19030800
H	-5.51526900	-0.82830600	-0.98461400
H	-7.63935700	0.43150200	-1.10423100
H	-7.62299800	2.87150000	-1.59335600
H	-5.45497000	4.03200400	-1.97984200
H	-3.33526300	2.76844200	-1.87133800
H	-3.07246900	-0.87134300	-1.77085500
H	-2.19492100	0.64820700	-1.89453300