

## SUPPORTING INFORMATION

### **Studies on the Synthesis of Landomycin A. Synthesis of the Originally Assigned Structure of the Aglycone, Landomycinone, and Revision of Structure**

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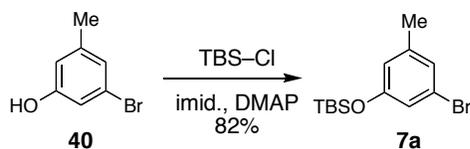
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## General Experimental

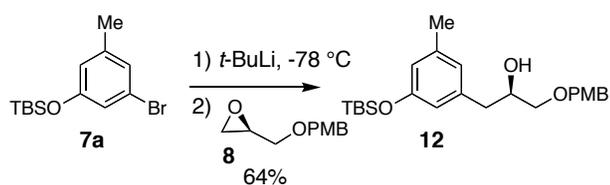
Unless otherwise noted, all reactions were performed in flame-dried or oven-dried (120°C) glassware with magnetic stirring under atmospheres of dry nitrogen or argon. Diethyl ether, THF, methylene chloride, and toluene were purified by passage through a solvent column composed of activated alumina (A-1) (HPLC grade solvents). 2,6-Lutidine and diisopropylethylamine were dried by distillation over calcium hydride. Acetone was dried by distillation from anhydrous powdered calcium sulfate. Methanol was dried by distillation from magnesium methoxide. *N,N*-Dimethylformamide and chloroform were dried over activated 4Å molecular sieves. All extraction and chromatography solvents were reagent grade and used without purification. Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F254 (250 μm silica gel) glass plates and visualized with aqueous KMnO<sub>4</sub> solution. Flash column chromatography was performed using Kieselgel 60 (230-400 mesh) silica gel.<sup>1</sup>

<sup>1</sup>H NMR spectra were recorded on commercial 300 MHz, 400 MHz, or 500 MHz spectrometers. <sup>13</sup>C NMR spectra were recorded on commercial 400 (100 MHz) or 500 (125 MHz) spectrometers. The proton signal of residual CHCl<sub>3</sub> (δ 7.24) was used as an internal reference for <sup>1</sup>H spectra in CDCl<sub>3</sub>, while the chemical shifts for <sup>13</sup>C spectra are reported relative to the δ 77.0 resonance of CDCl<sub>3</sub>. Optical rotations were measured on a polarimeter using a quartz cell with a 1 mL capacity and a 10 cm cell path length. Melting points were determined on a hot stage melting point apparatus and are uncorrected. Mass spectra were recorded at the University of Michigan Mass Spectrometry Laboratory. Infrared (IR) spectra were recorded as thin films on a NaCl plates. HPLC purifications were performed using an HPLC system composed of two pumps connected to an axial compression column packed with 60 Å irregular silica gel. Samples were loaded with a 2 mL injector and detected by using a combination of a UV detector (254 nm) or a RI detector. Single crystal X-ray diffraction analysis was performed by Dr. Jeff Kampf using a low temperature device at the University of Michigan

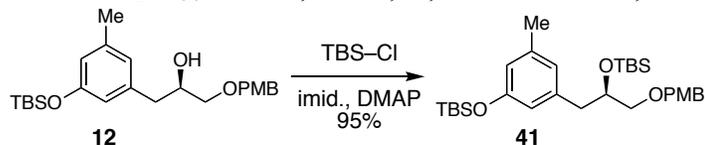


**(3-Bromo-5-methyl-phenoxy)-tert-butyldimethylsilane (7a).** The known phenol **40**<sup>2</sup> (26.3 g, 140 mmol, containing ca. 5% of the corresponding aryl iodide) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (250 mL) and chilled to 0 °C before addition of imidazole (16.3 g, 280 mmol), DMAP (catalytic),

and TBS–Cl (27.4 g, 182 mmol). The mixture was allowed to warm slowly to 23 °C over the course of 18 h. At this point, saturated aqueous ammonium chloride was added. The organic phase was separated and rinsed with saturated sodium bicarbonate solution and brine before being dried over sodium sulfate. The drying agent was filtered and the filtrate concentrated under reduced pressure to give **7a** (37.9 g, 82% yield) as a yellow oil. This material was used directly in the next step: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  6.95 (s, 1H), 6.82 (s, 1H), 6.56 (s, 1H), 2.28 (s, 3H), 1.00 (s, 9H), 0.21 (s, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  156.2, 140.9, 131.2, 125.2, 122.0, 120.4, 119.7, 25.6, -4.5; IR (thin film from CCl<sub>4</sub> on NaCl):  $\nu$  3054, 1598, 1566, 1422, 1265, 1160, 1020, 896, 845, 783, 750, 705 cm<sup>-1</sup>; HRMS calcd for C<sub>13</sub>H<sub>21</sub>BrOSi [M<sup>+</sup>] 300.0545, found 300.0545 m/z.

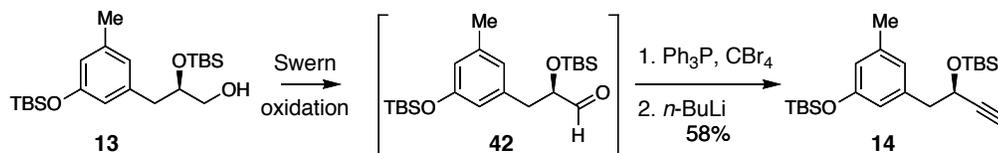


**(+)-1-[3-(*tert*-Butyldimethylsilyloxy)-5-methylphenyl]-3-(4-methoxybenzyloxy)propan-2-ol (**12**)** A solution of aryl bromide **7a** (1.5 g, 4.55 mmol) in Et<sub>2</sub>O (39 mL) was added slowly (over 0.5 h) *via* a Teflon canula to a –78 °C solution of *t*-BuLi (10.1 mmol, 7.15 mL of a 1.4M solution in pentanes). This mixture was stirred for 1 h at –78 °C before addition of epoxide **8** (1.14 g, 5.85 mmol) *via* syringe as a neat oil. The reaction mixture was allowed to warm to 23 °C and stirred for 14 h. The reaction was quenched by addition of saturated ammonium chloride solution and extracted with ethyl acetate. The organic phase was separated and rinsed with saturated sodium bicarbonate solution and brine before being dried over sodium sulfate. The filtrate was concentrated under reduced pressure to yield the crude product as a yellow oil. The crude material was purified by flash chromatography (using 30 to 50% ethyl ether-hexanes as the mobile phase) to give **12** (1.22 g, 64% yield):  $[\alpha]_D^{25.4} = +8.8$  (*c* 12.6, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) 7.25 (d, *J*=8.5 Hz, 2H), 6.87 (d, *J*=8.8 Hz, 2H), 6.61 (s, 1H), 6.52 (s, 1H), 6.50 (s, 1H), 4.46 (s, 2H), 4.00 (m, 1H), 3.79 (s, 3H), 3.45 (dd, *J*=3.3, 6.0, 1H), 3.35 (dd, *J*=6.8, 2.5, 1H), 2.69 (sept, *J*=6.9 Hz, 2H), 2.32 (d, *J*=3.0 Hz, 1H), 2.25 (s, 3H), 0.99 (s, 9H), 0.19 (s, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) 159.2, 155.5, 139.2, 139.0, 130.0, 129.3, 123.2, 123.1, 118.2, 118.8, 118.0, 117.9, 113.7, 113.7, 73.2, 72.9, 72.9, 71.2, 55.1, 39.7, 25.6, 21.2, 18.1, -4.5; IR (thin film from CDCl<sub>3</sub> on NaCl)  $\nu$  3460b, 2954, 2930, 2858, 1720, 1609, 1592, 1513, 1463, 1361, 1319, 1303, 1250, 1160, 1100, 1037, 839, 781 cm<sup>-1</sup>; HRMS calcd for C<sub>24</sub>H<sub>36</sub>O<sub>4</sub>Si [M+Na]<sup>+</sup> 439.2281, found 439.2286 m/z; *Anal.* calcd for C<sub>24</sub>H<sub>36</sub>O<sub>4</sub>Si: C, 69.19; H, 8.71. Found C, 68.98; H, 8.69.





65.7, 40.4, 25.8, 25.7, 21.3, 18.1, -4.4, -4.8; IR (thin film from CDCl<sub>3</sub> on NaCl)  $\square$  3693, 3584, 3054, 1593, 1421, 1265, 1160, 896, 740, 705 cm<sup>-1</sup>; HRMS calcd for C<sub>22</sub>H<sub>42</sub>O<sub>3</sub>Si<sub>2</sub>Na [M+Na]<sup>+</sup> 433.2570 m/z, found 433.2548. *Anal.* Calcd for C<sub>22</sub>H<sub>42</sub>O<sub>3</sub>Si<sub>2</sub>: C, 64.33; H, 10.31. Found C, 64.35; H, 10.07.



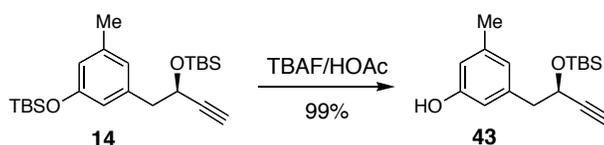
**(+)-3-(*tert*-Butyldimethylsilyloxy)-4-[3-*tert*-butyldimethylsilyloxy-5-methyl-phenyl]**

**butyne (14).** To a solution of DMSO (0.27 g, 3.4 mmol, 0.24 mL) in 10 mL of CH<sub>2</sub>Cl<sub>2</sub> at -78 °C was added oxalyl chloride (0.39 g, 3.1 mmol, 0.27 mL) as a neat liquid. This mixture was stirred at -78 °C for 0.5 h, then a CH<sub>2</sub>Cl<sub>2</sub> (5 mL) solution of the primary alcohol **13** (0.64 g, 1.55 mmol) was added contemporaneously with triethylamine (0.63 g, 6.2 mmol, 0.87 mL) as a neat liquid. This mixture was stirred for 15 min at -78 °C, then the reaction was warmed to 0 °C and allowed to stir for an additional 15 min. Pentanes were then added to precipitate the amine salts. The resulting heterogeneous mixture was filtered through a sintered glass frit. The filtrate was concentrated under reduced pressure, and the resulting yellow oil was again treated with pentanes to precipitate any remaining amine salts. Again the mixture was filtered and the filtrate was concentrated under reduced pressure to give crude aldehyde **42** as a pale yellow oil. This material was used directly in the next step due to its instability to flash chromatographic purification: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\square$  9.65 (d, *J*=1.4 Hz, 1H), 6.64 (s, 1H), 6.54 (s, 1H), 6.52 (s, 1H), 4.12 (ddd, *J*=8.8, 3.9, 1.4 Hz, 1H), 2.91 (dd, *J*=13.4, 3.9 Hz, 1H), 2.70 (dd, *J*=13.4, 9.0 Hz, 1H), 2.28 (s, 3H), 1.00 (s, 9H), 0.87 (s, 9H), 0.20 (s, 6H), -0.07 (s, 3H), -0.18 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\square$  203.6, 155.5, 139.0, 137.8, 124.0, 119.0, 118.4, 79.0, 39.0, 25.7, 21.3, 18.1, -4.4, -4.5, -5.1, -5.4

A 0 °C solution of CBr<sub>4</sub> (1.03 g, 3.1 mmol, freshly sublimed) in CH<sub>2</sub>Cl<sub>2</sub> (5mL) was treated with triphenylphosphine (1.63 g, 6.2 mmol) added as a solid. To this red solution was added a CH<sub>2</sub>Cl<sub>2</sub> (5 mL) solution of crude aldehyde **42** from the previous experiment. The reaction was stirred for 5 min, then was quenched by addition to a saturated aqueous sodium bicarbonate solution. The resulting heterogeneous mixture was transferred to a separatory funnel and diluted with ethyl acetate. The organic solution was separated, dried over sodium sulfate and concentrated under reduced pressure to give a wet, yellow solid. The solid was dissolved in pentanes and filtered through a sintered glass funnel to give a yellow solution. Pentane was added to this solution to further precipitate any remaining solids, which were again filtered by passing the mixture through a sintered glass funnel. The resulting yellow filtrate was concentrated under reduced pressure and passed through a short plug of silica gel with 30% ethyl acetate-hexanes as

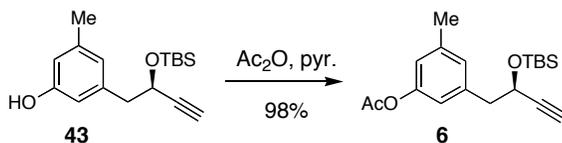
eluent to remove any remaining triphenylphosphine oxide. The filtrate was concentrated to give the crude dibromoolefin as a yellow oil. This material was taken directly to the next step:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.59 (s, 1H), 6.49 (s, 1H), 6.46 (s, 1H), 6.40 (d,  $J=8.1\text{Hz}$ , 1H), 4.39 (td,  $J=8.1, 4.6\text{ Hz}$ , 1H), 2.68 (dd,  $J=13.2, 4.4\text{ Hz}$ , 1H), 2.62 (dd,  $J=13.2, 7.8\text{ Hz}$ , 1H), 2.24 (s, 3H), 0.96 (s, 9H), 0.80 (s, 9H), 0.16 (s, 6H), -0.10 (s, 3H), -0.17 (s, 3H)

The crude dibromoolefin from the previous step was dissolved in THF (10 mL) and cooled to  $-78\text{ }^\circ\text{C}$ .  $n\text{-BuLi}$  (3.41 mmol, 1.6 mL) was added and the solution immediately turned dark red in color. After being stirred for fifteen minutes at  $-78\text{ }^\circ\text{C}$ , the reaction was quenched with a saturated, aqueous ammonium chloride solution. After being warmed to  $23\text{ }^\circ\text{C}$ , the mixture was extracted with ethyl acetate. The organic extracts were rinsed with saturated sodium bicarbonate solution and brine before being dried over  $\text{Na}_2\text{SO}_4$ . Concentration of the filtrate under reduced pressure provided the crude alkyne as a yellow oil. Subsequent purification of this material by careful flash chromatography using silica gel (6% EtOAc/hexanes) gave pure **14** as a pale yellow oil (0.37 g, 0.89 mmol, 58% yield over three steps):  $[\alpha]_{\text{D}}^{26.4} = +23.5$  ( $c$  14.4,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.62 (s, 1H), 6.51 (bs, 2H), 4.41 (m, 1H), 2.85 (d,  $J=2.4\text{ Hz}$ , 1H), 2.84 (d,  $J=4.1\text{ Hz}$ , 1H), 2.38 (d,  $J=1.2\text{ Hz}$ , 1H), 2.24 (s, 3H), 0.96 (s, 9H), 0.83 (s, 9H), 0.16 (s, 6H), -0.03 (s, 3H), -0.07 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  155.5, 139.0, 138.7, 124.1, 119.2, 118.7, 85.4, 72.7, 64.3, 45.2, 25.9, 21.5, 18.4, -4.2, -4.8, -5.1; IR (thin film from  $\text{CDCl}_3$  on NaCl)  $\nu$  3312, 2957, 2930, 2886, 2858, 1594, 1471, 1462, 1313, 1252, 1161, 1090, 1045, 838, 778  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{23}\text{H}_{40}\text{O}_2\text{Si}_2\text{Na}$   $[\text{M}+\text{Na}]^+$  427.2465  $m/z$ , found 427.2455. *Anal.* Calcd for  $\text{C}_{23}\text{H}_{40}\text{O}_2\text{Si}_2$ : C, 68.25; H, 9.96. Found C, 67.98; H, 9.89.

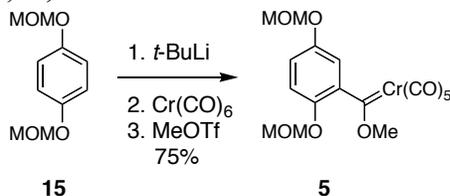


**(+)-3-[2-*tert*-Butyldimethylsilyloxy]-but-3-ynyl]-5-methylphenol (43).** A  $0\text{ }^\circ\text{C}$  solution of alkyne **14** (362 mg, 0.9 mmol) in THF (3 mL) was treated with glacial acetic acid (52  $\mu\text{L}$ , 0.9 mmol) and TBAF (1.1 mmol, 1.1 mL of a 1M solution in THF), added simultaneously. The reaction was complete after 2 h, as determined by TLC analysis (10% ethyl acetate / hexanes). The reaction was worked up by addition of saturated, aqueous sodium bicarbonate solution and the mixture was extracted with ethyl acetate. The organic phase was rinsed with brine before being dried over sodium sulfate. The organic solution was then concentrated under reduced pressure to yield the crude phenol **43** as a yellow oil. Purification of this material by flash chromatography (30%  $\text{Et}_2\text{O}$  / hexanes) gave **43** (265 mg, 0.9 mmol, 99% yield) as a pale yellow oil:  $[\alpha]_{\text{D}}^{25.0} = +28.6$  ( $c$  14.3,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.58 (s, 1H), 6.48 (s, 2H), 4.41 (dt,  $J=5.2, 2.2\text{ Hz}$ , 1H), 2.84 (d,  $J=1.5\text{ Hz}$ , 1H), 2.82 (d,  $J=2.9\text{ Hz}$ , 1H), 2.37 (d,  $J=2.2$ , 1H), 2.23 (s, 3H), 0.81 (s,

9H), -0.04 (s, 3H), -0.09 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\square$  155.2, 139.3, 138.9, 123.3, 114.4, 113.9, 85.0, 72.8, 64.1, 44.9, 25.7, 21.2, 18.2, -5.1, -5.3; IR (thin film from  $\text{CDCl}_3$  on NaCl)  $\square$  3309, 2955, 2929, 2885, 2857, 1619, 1597, 1471, 1463, 1302, 1252, 1152, 1088, 1039, 838, 778  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{17}\text{H}_{26}\text{O}_2\text{SiNa}$   $[\text{M}+\text{Na}]^+$  313.1600, found 313.1601  $m/z$ . *Anal.* Calcd for  $\text{C}_{17}\text{H}_{26}\text{O}_2\text{Si}$ : C, 70.29; H, 9.02. Found C, 70.34; H, 9.16.

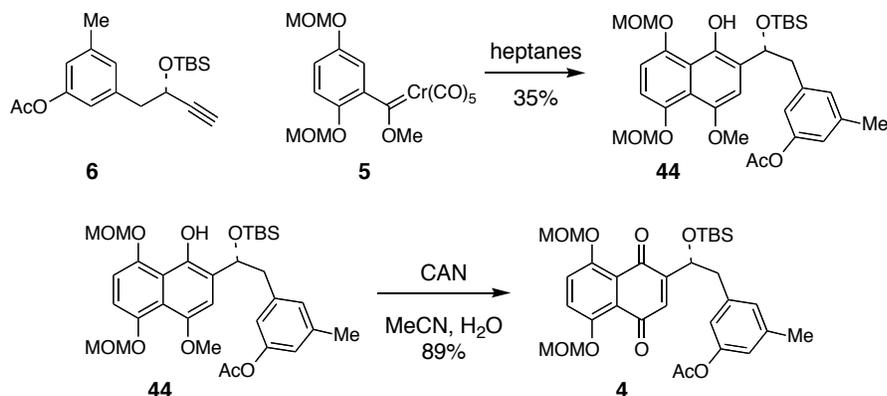


**(+)-3-(*tert*-Butyldimethylsilyloxy)-4-[3-acetoxy-5-methyl-phenyl]-butyne (6).** A  $0^\circ\text{C}$  solution of phenol **43** (250 mg, 0.86 mmol) in pyridine (2 mL) was treated with acetic anhydride (0.88 g, 8.6 mmol, 0.81 mL). The solution was allowed to slowly warm to  $23^\circ\text{C}$  and stirred for 18 h. The reaction was then worked up by addition of a saturated aqueous ammonium chloride solution and extracted with ethyl acetate. The organic solution was rinsed with 1M HCl (3x20 mL) and saturated, aqueous copper sulfate solution to remove any remaining pyridine. The organic solution was then rinsed with saturated, aqueous sodium bicarbonate, and brine before being dried over sodium sulfate. The dry solution was filtered and concentrated under reduced pressure to give the crude product as a light yellow oil. Purification of this material by flash chromatography (5% EtOAc-hexanes) gave pure **6** (280 mg, 0.84 mmol, 98% yield) as a colorless oil:  $[\alpha]_{\text{D}}^{25.8} = +32.5$  ( $c$  7.8,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\square$  6.94 (s, 1H), 6.79 (s, 2H), 4.48 (m, 1H), 2.94 (m, 2H), 2.44 (s, 1H), 2.34 (s, 3H), 2.29 (s, 3H), 0.87 (s, 9H), 0.02 (s, 3H), -0.04 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\square$  169.5, 150.4, 139.0, 138.8, 128.4, 120.4, 119.9, 84.9, 63.8, 44.7, 25.6, 21.2, 21.1, 18.1, -5.1, -5.4; IR (thin film from  $\text{CDCl}_3$  on NaCl)  $\square$  3307, 2957, 2930, 2886, 2858, 2254, 1764, 1370, 1264, 1218, 1137, 1088, 908, 839, 733, 650  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{19}\text{H}_{28}\text{O}_3\text{SiNH}_4^+$   $[\text{M}+\text{NH}_4]^+$  350.2151, found 350.2135  $m/z$ . *Anal.* Calcd for  $\text{C}_{19}\text{H}_{28}\text{O}_3\text{Si}$ : C, 68.63; H, 8.49. Found C, 68.41; H, 8.40.



**Chromium Pentacarbonyl[(2,5-di-methoxymethoxy)-methoxymethylene] (5).** A  $-78^\circ\text{C}$  solution of protected hydroquinone **15** (3.0 g, 15.1 mmol) in THF (50 mL) was treated with *t*-BuLi (11.9 mL of a 1.4 M solution in pentanes, 16.6 mmol), added by syringe. The reaction mixture was allowed to warm to  $0^\circ\text{C}$  and stir for 0.5 h before  $\text{Cr}(\text{CO})_6$  was added as a solid. The reaction was allowed to warm to  $23^\circ\text{C}$  and stirred for 0.5 h at  $23^\circ\text{C}$ . THF was removed *in vacuo*

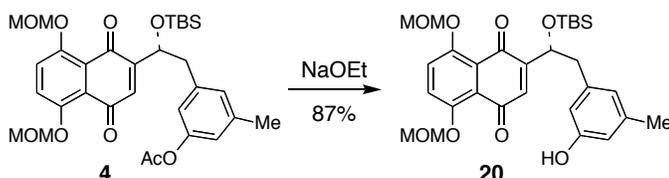
and the red residue was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (15 mL). MeOTf was added as a neat liquid and the reaction was allowed to stir for 0.5 h. The reaction mixture was concentrated under reduced pressure and the crude was purified by column chromatography using 20% EtOAc/hexanes as the mobile phase. Pure carbene **5** (4.78 g, 11.3 mmol, 75% yield) was obtained as a cherry red oil: IR (thin film from CDCl<sub>3</sub> on NaCl) 2956, 2904, 2828, 2064, 2018, 1989, 1933, 1852, 1487, 1442, 1152, 993, 651cm<sup>-1</sup>; HRMS calcd for C<sub>17</sub>H<sub>16</sub>CrO<sub>10</sub> [M] 432.0149, found 432.0139 m/z. *Anal.* Calcd for C<sub>17</sub>H<sub>16</sub>CrO<sub>10</sub>: C, 47.23; H, 3.73. Found C, 47.29; H, 3.69.



**(+)-2-[1-(*tert*-Butyldimethylsilyloxy)-2-(3-acetoxy-5-methyl-phenyl)-ethyl]-4-methoxy-5,8-dimethoxymethoxy-[1,4]naphthoquinone (4).** A 5-mL reaction vial was flame dried and charged with alkyne **6** (209 mg, 0.63 mmol) and carbene **5** (271 mg, 0.63 mmol). Dry heptanes (200  $\mu$ L) were added and the solution was purged of oxygen by bubbling argon gas through it for fifteen minutes. A microcondenser was affixed under positive pressure of argon, and the reaction was heated to 57  $^{\circ}$ C. After being heated for 14 h, the reaction was allow to cool to 23  $^{\circ}$ C before the condenser was removed. The reaction mixture was diluted with ethyl acetate before and then was stirred open to the air for 15 min to assure oxidation of the intermediate chromium arene complex. The organic solution was then rinsed with saturated, aqueous bicarbonate solution to give a red solution which was dried over sodium sulfate. The organic filtrate was concentrated under reduced pressure to give a red oil which was purified by column chromatography (20% ethyl acetate-hexanes), giving the unstable hydroquinone **44** (130 mg, 0.21 mmol, 35% yield) as a brown oil. This material was used immediately in the following step:  $[\alpha]_D^{25.5} = +31.2$  (*c* 19.6, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  9.57 (s, 1H), 7.11 (s, 1H), 7.66 (d, *J*=8.5 Hz, 1H), 6.96 (s, 1H), 6.92 (d, *J*=8.5, 1H), 6.82 (s, 1H), 6.73 (s, 1H), 5.38 (m, 2H), 5.32 (d, *J*=8.8 Hz, 1H), 5.13 (m, 2H), 3.85 (s, 3H), 3.59 (s, 3H), 3.57 (s, 3H), 3.03 (dd, *J*=10.7, 2.5 Hz, 1H), 2.67 (dd, *J*=9.0, 4.2 Hz, 1H), 2.30 (s, 3H), 2.25 (s, 3H), 0.80 (s, 9H), -0.32 (s, 3H), -0.33 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  169.6, 150.4, 149.7, 149.0, 148.7, 143.0, 141.2, 138.6, 128.8, 128.7, 126.7, 120.1, 120.0, 119.7, 117.5, 114.6, 108.9, 108.3, 108.3, 97.8, 96.5, 70.1, 57.3, 56.8, 56.4, 56.3, 44.9, 25.7, 21.2, 21.1, 18.1, -5.3, -5.8; IR (thin film from CDCl<sub>3</sub> on NaCl) 3379, 2953, 2928, 2898, 2855, 1765,

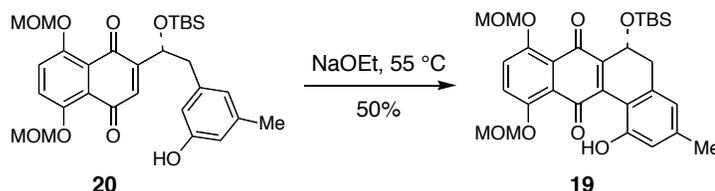
1610, 1593, 1518, 1471, 1448, 1401, 1378, 1247, 1211, 1154, 1086, 1051, 1024, 966, 837, 778  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{32}\text{H}_{44}\text{O}_9\text{SiNa}$   $[\text{M}+\text{Na}]^+$  623.2652, found 623.2651  $\text{m/z}$ .

A 0 °C solution of the unstable phenol **44** (110 mg, 0.18 mmol) in acetonitrile (2 mL) was added to a 0 °C solution of ceric ammonium nitrate (247 mg, 0.45 mmol) in water (2 mL) contained within a 25-mL separatory funnel. The mixture was shaken for five minutes before being extracted with methylene chloride (3 x 10 mL). The organic solution was rinsed with a saturated, aqueous sodium bicarbonate and then was dried over sodium sulfate. The dry, filtered solution was concentrated under reduced pressure and the resulting red oil was purified by flash chromatography (20% ethyl acetate-hexanes) to give pure quinone **4** (95 mg, 0.16 mmol, 89% yield) as a red oil:  $[\alpha]_{\text{D}}^{25.5} = +60.3$  ( $c$  19.6,  $\text{CHCl}_3$ )  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.48, 7.45 (AB system,  $J=9.6$ , 6 Hz, 2H), 6.94 (s, 1H), 6.84 (s, 1H), 6.79 (s, 1H), 6.72 (s, 1H), 5.28 (s, 3H), 5.24 (s, 3H), 4.97 (d,  $J=7.7$  Hz, 1H), 3.54 (s, 3H), 3.52 (s, 3H), 3.01 (dd,  $J=9.0$ , 2.2 Hz, 1H), 2.50 (dd,  $J=8.8$ , 4.4 Hz, 1H), 2.27 (s, 3H), 2.23 (s, 3H), 0.77 (s, 9H), -0.28 (s, 3H), -0.42 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  184.7, 184.4, 169.4, 152.4, 151.8, 150.5, 139.8, 138.9, 134.1, 134.1, 128.6, 125.5, 124.5, 122.4, 122.3, 120.2, 120.1, 120.0, 96.1, 96.0, 95.8, 69.6, 69.5, 56.6, 56.5, 56.5, 44.5, 25.7, 21.1, 21.0, 18.0, -5.3, -5.9; IR (thin film from  $\text{CDCl}_3$  on NaCl)  $\nu$  2955, 2930, 2901, 2856, 2829, 1766, 1658, 1636, 1617, 1587, 1565, 1471, 1442, 1401, 1369, 1332, 1252, 1210, 1153, 1138, 1084, 1001, 954, 838, 778, 733  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{31}\text{H}_{40}\text{O}_9\text{SiNa}$   $[\text{M}+\text{Na}]^+$  607.2339, found 607.2341  $\text{m/z}$ . *Anal.* Calcd for  $\text{C}_{31}\text{H}_{40}\text{O}_9\text{Si}$ : C, 63.68; H, 6.90. Found C, 63.66; H, 7.12.

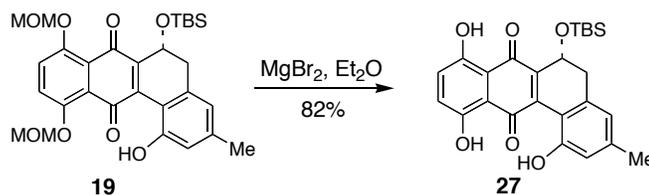


**(+)-2-[1-(*tert*-Butyldimethylsilyloxy)-2-(3-hydroxy-5-methyl-phenyl)-ethyl]-4-methoxy-5,8-dimethoxymethoxy-[1,4]naphthoquinone (20).** To a 0 °C solution of quinone **4** (90 mg, 0.15 mmol) in freshly distilled ethanol (200  $\mu\text{L}$ ) was added a 1M solution of sodium ethoxide in ethanol (200  $\mu\text{L}$ ) by syringe. After 2 h the reaction was complete as determined by TLC analysis (4 %  $\text{MeOH}-\text{CH}_2\text{Cl}_2$ ). The reaction was worked up by addition of a saturated, aqueous ammonium chloride solution and extracted with methylene chloride. The organic solution was rinsed with saturated, aqueous sodium bicarbonate, dried over sodium sulfate, and concentrated under reduced pressure. The crude red oil was purified by column chromatography (20 to 50% ethyl acetate-hexanes) to give pure **20** (70 mg, 0.13 mmol, 87% yield):  $[\alpha]_{\text{D}}^{25.5} = +56.6$  ( $c$  20.7,  $\text{CHCl}_3$ )  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  7.48 (AB system,  $J=9.6$ , 2.7 Hz, 2H), 6.88 (s, 1H), 6.65 (s, 1H), 6.56 (s, 1H), 6.54 (s, 1H), 5.70 (s, 1H), 5.30 (s, 3H), 5.28 (s, 3H), 5.04 (d,  $J=7.0$ , 1H), 3.54 (s, 3H), 3.53 (s, 3H), 2.99 (dd,  $J=10.4$ , 2.8 Hz, 1H), 2.52 (dd,  $J=8.3$ , 4.6 Hz, 1H), 2.21 (s, 3H), 0.82 (s, 9H), -0.19 (s, 3H), -0.30 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  184.9, 184.5, 155.8,

152.9, 152.4, 151.9, 139.5, 139.0, 134.2, 134.0, 125.2, 125.1, 124.6, 124.5, 123.2, 123.0, 122.2, 122.1, 114.2, 114.1, 114.0, 113.9, 96.1, 96.0, 95.8, 95.7, 95.5, 95.4, 69.7, 69.4, 56.8, 56.6, 56.4, 44.6, 44.5, 25.7, 21.2, 21.0, 18.0, -5.2, -5.4, -5.7, -5.9; IR (thin film from CDCl<sub>3</sub> on NaCl) 3417, 2955, 2929, 2856, 2830, 1654, 1618, 1597, 1564, 1471, 1402, 1334, 1300, 1253, 1212, 1197, 1153, 1085, 997, 952, 923, 838, 778, 733 cm<sup>-1</sup>; HRMS calcd for C<sub>29</sub>H<sub>38</sub>O<sub>8</sub>SiNa [M+Na]<sup>+</sup> 565.2234, found 565.2230 m/z.

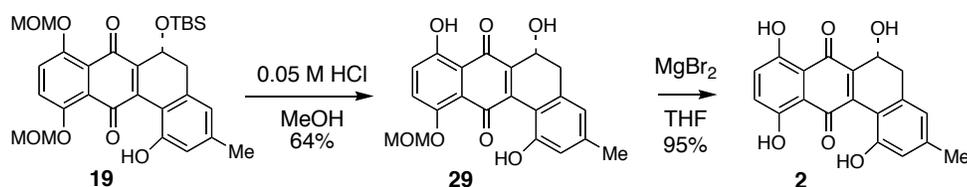


**(+)-6-(tert-butyl-dimethyl-silyloxy)-1-hydroxy-8,11-dimethoxymethoxy-3-methyl-5,6-dihydro-benzo[a]anthracene-7,12-dione (19)**. Phenolic quinone **20** (65 mg, 0.12 mmol) was dissolved in freshly distilled ethanol (300  $\mu$ L) and 240  $\mu$ L of a 0.05 M solution of sodium ethoxide in ethanol was then added. A spatula tip of activated, powdered 4 Å molecular sieves were added to the vial and it was sealed under a blanket of argon via Teflon septum. The vial was heated to 55 °C for 17 h and then the reaction was quenched by addition of saturated, aqueous ammonium chloride solution. The mixture was extracted with methylene chloride, dried over sodium sulfate, and concentrated under reduced pressure to give crude product as a red oil. Purification of this material was effected *via* preparative thin layer chromatography (500  $\mu$ m plate w/ 70% ethyl ether-hexanes) gave recovered phenol **20** (20 mg, 0.04 mmol, 31% yield) and desired product **19** (30 mg, 0.06 mmol, 50% yield):  $[\alpha]_{D}^{23.7} = +166.1$  (*c* 5.6, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.27 (s, 1H), 7.48 (AB system, *J*=9.6, 7.3 Hz, 2H), 6.75 (s, 1H), 6.68 (s, 1H), 5.26-5.36 (m, 5H), 3.56 (s, 3H), 3.54 (s, 3H), 2.96 (dd, *J*=6.1, 2.4 Hz, 1H), 2.84 (dd, *J*=12.5, 3.6 Hz, 1H), 2.32 (s, 3H), 0.72 (s, 9H), 0.15 (s, 3H), -0.02 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  190.1, 182.4, 154.9, 151.5, 151.1, 142.7, 141.1, 140.7, 137.6, 125.0, 124.2, 123.8, 123.3, 121.9, 118.8, 113.5, 95.8, 95.7, 59.3, 56.6, 56.4, 38.0, 25.6, 21.2, 17.9, -4.5, -5.0; IR (thin film from CDCl<sub>3</sub> on NaCl) 3405, 2953, 2928, 2855, 1650, 1615, 1586, 1571, 1473, 1411, 1331, 1300, 1256, 1217, 1152, 1083, 1041, 1006, 926, 837, 779 cm<sup>-1</sup>; HRMS calcd for C<sub>29</sub>H<sub>36</sub>O<sub>8</sub>SiNa [M+Na]<sup>+</sup> 563.2089, found 563.2095 m/z.



**(+)-6-(tert-Butyldimethylsilyloxy)-1,8,11-Tetrahydroxy-3-methyl-5,6-dihydro-**

**benzo[*a*]anthracene-7,12-dione (27).** To a 0 °C solution of **19** (21 mg, 0.04 mmol) in diethyl ether (2 mL) was added MgBr<sub>2</sub>•OEt<sub>2</sub> (10 mg) as a white solid. The ice bath was removed and the mixture was warmed to 23 °C. The mixture was stirred for 35 min, at which point the reaction was deemed complete according to TLC analysis (4% MeOH-CH<sub>2</sub>Cl<sub>2</sub>). A saturated solution of sodium bicarbonate was added and the resulting mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was separated and dried over sodium sulfate. After filtration, the filtrate was concentrated under reduced pressure to give a red oil as crude product. Purification of this material by preparative TLC using a 500 μm silica plate with 3% MeOH/CH<sub>2</sub>Cl<sub>2</sub> as the mobile phase gave **27** (15 mg, 0.033 mmol, 82% yield):  $[\alpha]_{633}^{25.2} = +367$  (*c* 0.9, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  13.06 (s, 1H), 12.79 (s, 1H), 9.10 (s, 1H), 7.33 (d, *J*=9.6 Hz, 1H), 7.25 (d, *J*=9.6 Hz, 1H), 6.80 (s, 1H), 6.68 (s, 1H), 5.26 (t, *J*=3 Hz, 1H), 2.96 (dd, *J*=15.7, 2.5 Hz, 1H), 2.79 (dd, *J*=15.7, 3.0 Hz, 1H), 2.31 (s, 3H), 0.66 (s, 9H), 0.12 (s, 3H), -0.04 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  162.2, 155.3, 144.0, 143.4, 141.0, 137.9, 132.3, 130.6, 123.7, 119.7, 112.6, 59.3, 38.0, 25.5, 21.2, 17.8, -4.5, -4.9; HRMS calcd for C<sub>25</sub>H<sub>28</sub>O<sub>6</sub>Si [M]<sup>+</sup> 453.1733, found 453.1750 m/z.



**(+)-1,6,8,11-Tetrahydroxy-3-methyl-5-6-dihydrobenzo- [*a*]anthracene-7,12-dione (2).**

Protected quinone **19** (285 mg, 0.53 mmol) was dissolved in 2 mL of 0.05 M HCl in MeOH which had been chilled to 0 °C. The reaction was carefully monitored by TLC (4% MeOH/CH<sub>2</sub>Cl<sub>2</sub>) until complete loss of starting material was observed after 65 min. The reaction was promptly quenched with saturated, aqueous sodium bicarbonate and the mixture was extracted with methylene chloride. The organic solution was dried over sodium sulfate, filtered and concentrated under reduced pressure to give a red oil as crude product. This material was purified by column chromatography using 1% MeOH-CH<sub>2</sub>Cl<sub>2</sub> as the mobile phase. The major product is the mono-MOM protected aglycone **29** (130 mg, 0.34 mmol, 64% yield); di-MOM protected **28** and elimination product **30** were recovered as a mixture in 25% yield.

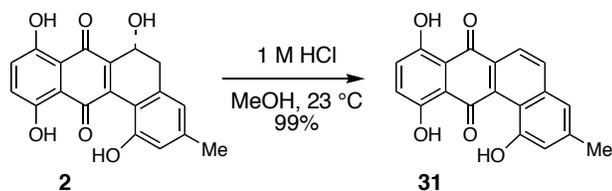
**Data for 29:**  $[\alpha]_{633}^{26.1} = +260$  (*c* 0.7, CHCl<sub>3</sub>); mp 161 °C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  12.48 (s, 1H), 8.51 (s, 1H), 7.50 (d, *J*=9.5 Hz, 1H), 7.25 (d, *J*=9.5 Hz, 1H), 6.71 (s, 1H), 6.70 (s, 1H), 5.28 (s, 2H), 5.17 (t, *J*=4.0 Hz, 1H), 3.53 (s, 3H), 3.08 (dd, *J*=16.0, 4.0 Hz, 1H), 2.91 (dd, *J*=16.0, 5.5 Hz, 1H), 2.29 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  188.4, 187.9, 157.2, 155.6, 152.1, 144.2, 143.9, 140.0, 137.0, 127.8, 127.3, 123.9, 119.9, 114.0, 113.9, 95.8, 74.6, 60.4, 56.7, 36.5, 21.3; HRMS calcd for C<sub>21</sub>H<sub>18</sub>O<sub>7</sub> [M+Na]<sup>+</sup> 405.0950, found 405.0944 m/z.

**Partial Data for 28:** <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.95 (d, *J*=2.7 Hz, 1H), 7.50 (d, *J*=9.0 Hz, 1H), 7.46 (d, *J*=9.0 Hz, 1H), 6.74 (s, 1H), 6.71 (s, 1H), 5.31-5.24 (m, 5H), 5.11 (d, *J*=4.2 Hz,

1H), 3.53 (s, 3H), 3.52 (s, 3H), 3.06 (dd,  $J=16.0, 5.5$  Hz, 1H), 2.93 (dd,  $J=15.5, 4.9$  Hz, 1H), 2.81 (d,  $J=3.6$  Hz, 1H), 2.29 (s, 3H).

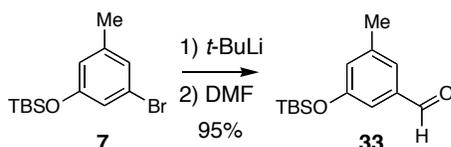
**Data for 30:**  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.66 (s, 1H), 8.84 (d,  $J=8.8$  Hz, 1H), 8.82 (d,  $J=8.6$  Hz, 1H), 7.47 (s, 2H), 7.26 (s, 1H), 7.10 (s, 1H), 5.32 (s, 2H), 5.30 (s, 2H), 3.56 (s, 3H), 3.55 (s, 3H), 2.48 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  192.3, 154.4, 151.4, 151.3, 141.1, 138.1, 135.7, 134.8, 126.7, 124.6, 124.4, 122.4, 122.0, 121.3, 119.4, 118.2, 96.1, 96.0, 56.6, 21.4; IR (thin film from  $\text{CDCl}_3$  on NaCl) 2956, 2829, 1667, 1621, 1591, 1568, 1472, 1416, 1329, 1255, 1226, 1152, 1080, 990, 960, 922; HRMS calcd for  $\text{C}_{23}\text{H}_{22}\text{O}_7$   $[\text{M}+\text{Na}]^+$  431.1107, found 431.1109 m/z.

Partially deprotected quinone **29** was transferred to a 5 mL conical vial. THF (100  $\mu\text{L}$ ) was added by syringe, and the resulting solution was chilled to 0  $^\circ\text{C}$ .  $\text{MgBr}_2$  (50  $\mu\text{L}$  of a 0.22M THF solution, prepared immediately before following the method of Vedejs<sup>3</sup>) was then added. The stirred reaction mixture was judged to be complete by TLC analysis (5% MeOH/ $\text{CH}_2\text{Cl}_2$ ) after 0.5 h. The reaction mixture was added to an aqueous solution of sodium bicarbonate and this mixture was extracted with  $\text{CH}_2\text{Cl}_2$ . The organic phase was dried over sodium sulfate and filtered to remove the drying agent. The filtrate was concentrated under reduced pressure to give a purple solid. This material was purified by using multiple preparative TLC plates (500  $\mu\text{m}$ ) with a 5% MeOH/ $\text{CH}_2\text{Cl}_2$  mobile phase. In this way, **2** (100 mg, 95% yield) was recovered as a poorly soluble purple solid. Recrystallization of this material by the vapor diffusion method using a  $\text{CH}_2\text{Cl}_2$  solution of **2** in a closed atmosphere saturated in heptanes yielded crystals suitable for X-ray diffraction:  $[\alpha]_{\text{D}}^{25.4} = +802$  ( $c$  0.07,  $\text{CHCl}_3$ ); mp= 210  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  12.86 (s, 1H), 12.76 (s, 1H), 9.00 (s, 1H), 7.34 (d,  $J=9.3$ Hz, 1H), 7.29 (d,  $J=9.3$ Hz, 1H), 6.81 (s, 1H), 6.76 (s, 1H), 5.21 (ad,  $J=4.1$ Hz, 1H), 3.10 (dd,  $J=15.6, 4.6$ Hz, 1H), 2.92 (dd,  $J=15.6, 4.1$ Hz, 1H), 2.63 (d,  $J=5.2$ Hz, 1H), 2.32 (s, 3H);  $^1\text{H}$  NMR (500 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  7.27 (s, 2H), 6.71 (s, 1H), 6.63 (s, 1H), 5.15 (s, 1H), 2.99 (ad,  $J=17.8$ hz, 1H), 2.84 (ad,  $J=17.8$ Hz, 1H), 2.29(s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , partial)  $\delta$  132.5, 131.0, 123.9, 120.5, 112.4, 110.9, 61.1, 36.6, 21.2; IR (thin film from  $\text{CDCl}_3$  on NaCl)  $\delta$  3457, 3215, 2561, 1623, 1589, 1560, 1455, 1411, 1358, 1298, 1252, 1217, 1184, 1143  $\text{cm}^{-1}$ ; UV ( $\epsilon_{\text{max}}$ ) 495, 287, 258, 222 nM; HRMS calcd for  $\text{C}_{19}\text{H}_{14}\text{O}_6$   $[\text{M}]^+$  338.0790, found 338.0774 m/z.

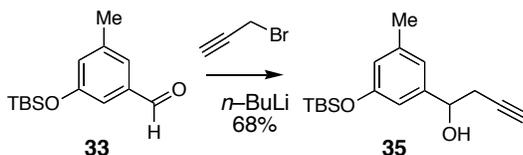


**1,8,11-Hydroxy-3-methyl-benzo[a]anthracene-7,12-dione (31—Synthetic Anhydro-landomycinone).** A 15-mL round bottom flask was charged with **2** (30 mg) and HCl (5 mL of a 1

M solution in MeOH). The reaction was complete according to TLC analysis (1:1 EtOAc/hexanes) after 2 h. The reaction mixture was transferred into a solution of saturated sodium bicarbonate and the resulting mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was separated and dried over sodium sulfate. The drying agent was removed by filtration and the filtrate was concentrated under reduced pressure to give the known compound<sup>4</sup> **31** (27 mg, 99% yield) as a red crust: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  12.98 (s, 1H), 12.49 (s, 1H), 11.06 (s, 1H), 8.36 (d, J=8.8 Hz, 1H), 8.21 (d, J=8.8 Hz, 1H), 7.37 (d, J=9.3 Hz, 1H), 7.36 (s, 1H), 7.17 (s, 1H), 7.35 (d, J=9.3 Hz, 1H), 2.51 (s, 3H); IR (thin film from CDCl<sub>3</sub> on NaCl)  $\nu$  3400, 2960, 2920, 1607, 1584, 1554, 1500 cm<sup>-1</sup>.

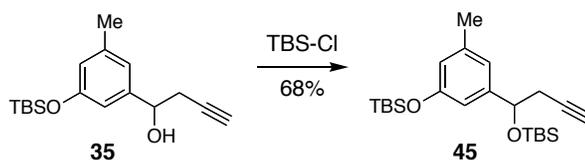


**3-(tert-Butyldimethylsilyloxy)-5-methyl-benzaldehyde (33).** To a  $-78$  °C solution of *t*-BuLi (13.2 mmol, 9.4 mL of 1.41M solution in pentanes) was added a solution of aryl bromide **7** (6 mmol, 2 g) in THF (10 mL). The mixture was stirred 1 h at  $-78$  °C, then dry DMF was added as a neat liquid, and the temperature was raised to  $0$  °C. After being stirred for 30 min at  $0$  °C, the reaction was quenched with a saturated aqueous solution of ammonium chloride. The biphasic mixture was extracted with ethyl acetate, rinsed with a saturated, aqueous solution of bicarbonate, and then dried over sodium sulfate. After filtration, the organic phase was concentrated under reduced pressure to yield a slightly yellow oil. The crude product was purified by column chromatography with 10% EtOAc/hexanes used as the mobile phase giving **33** (1.42g, 95% yield): <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  9.89 (s, 1H), 7.26 (s, 1H), 7.10 (s, 1H), 6.90 (s, 1H), 2.36 (s, 3H), 0.97 (s, 9H), 0.19 (s, 6H); <sup>13</sup>C NMR (100 MHz)  $\delta$  192.25, 156.22, 140.34, 137.74, 127.24, 124.19, 117.16, 25.58, 21.11, 18.13, -4.47; IR (thin film from CDCl<sub>3</sub> on NaCl)  $\nu$  2956, 2930, 2886, 2859, 2724, 1702, 1592, 1462, 1387, 1316, 1254, 1165, 838, 782 cm<sup>-1</sup>; HRMS calcd for C<sub>14</sub>H<sub>22</sub>O<sub>2</sub>Si [M]<sup>+</sup> 250.1389, found 250.1387 m/z.

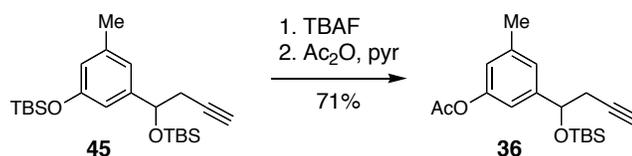


**1-[3-(tert-Butyldimethylsilyloxy)-5-methyl-phenyl]-but-3-yn-1-ol (35).** A solution of *n*-BuLi (3.24 mmol, 1.33 mL of a 2.1M solution in hexanes), TMEDA (1.39 mmol, 0.19 mL), Et<sub>2</sub>O (6.3 mL), and hexanes (3.8 mL) was cooled to  $-78$  °C. Propargyl bromide (2.19 mmol, 0.25 mL of an 80% solution in toluene) was added. The mixture was stirred for 2 minutes at  $-78$  °C, then a solution of aldehyde **33** (0.37 g, 1.46 mmol) in THF (3 mL) was added. The reaction mixture was

stirred for 30 min at  $-78\text{ }^{\circ}\text{C}$ , then the cooling bath was removed and the solution was allowed to warm to  $23\text{ }^{\circ}\text{C}$  and stirred for another 30 min. The reaction was then worked up by addition of a saturated, aqueous solution of ammonium chloride. The resulting mixture was extracted with ethyl acetate and rinsed with a saturated, aqueous solution of sodium bicarbonate before being dried over sodium sulfate. The organic phase was then decanted from the drying agent and concentrated under reduced pressure to give the crude product as a yellow oil. Purification of this material was affected by HPLC (20 % EtOAc/hexanes) to give **35** (276 mg, 0.95 mmol, 68 % yield):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.81 (s, 1H), 6.69 (s, 1H), 6.61 (s, 1H), 4.79 (t,  $J=6.3$  Hz, 1H), 2.64-2.61 (m, 2H), 2.31 (s, 3H), 2.09-2.08 (m, 1H), 1.00 (s, 9H), 0.21 (s, 6H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  155.48, 143.84, 139.34, 120.20, 119.34, 114.47, 80.76, 72.06, 72.04, 70.70, 29.23, 25.58, 21.31, 18.06, -4.50; IR (thin film from  $\text{CDCl}_3$  on NaCl) 3350, 3313, 2956, 2930, 2886, 2858, 1956, 1596, 1471, 1461, 1312, 1254, 1161, 1037, 838,  $781\text{ cm}^{-1}$ ; HRMS calcd for  $\text{C}_{17}\text{H}_{26}\text{O}_2\text{Si}[\text{M}+\text{Na}^++\text{MeOH}]^+$  345.1862, found 345.1866 m/z.

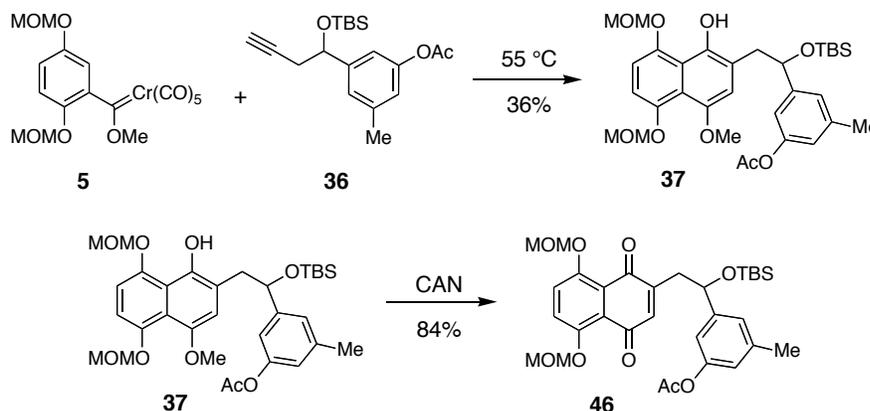


**1-(*tert*-Butyldimethylsilanyloxy)-3-[1-(*tert*-butyl-dimethyl-silanyloxy)-but-3-ynyl]-5-methylbenzene (45).** A solution of alcohol **35** (276 mg, 0.95 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) was treated with imidazole (168 mg, 3 mmol), TBS-Cl (300 mg, 2 mmol), and DMAP (10 mg). The reaction was stirred for 16 h at  $23\text{ }^{\circ}\text{C}$  before a saturated solution of ammonium chloride was added. The reaction mixture was extracted with EtOAc, and the organic layer was separated and dried over sodium sulfate. The mixture was filtered and the filtrate was concentrated under reduced pressure. The resulting yellow oil was purified by column chromatography using 10% EtOAc/hexanes as the mobile phase. Alkyne **45** (256 mg, 0.63 mmol, 68% yield) was isolated as a clear, colorless oil:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.70 (s, 1H), 6.63 (s, 1H), 6.53 (s, 1H), 4.69 (dd,  $J=7.3, 5.6$  Hz, 1H), 2.51 (ddd,  $J=16.6, 7.3, 2.7$  Hz, 1H), 2.42 (ddd,  $J=16.6, 5.6, 2.7$  Hz, 1H), 2.26 (s, 3H), 1.93 (t,  $J=2.6$  Hz, 1H), 0.96 (s, 9H), 0.87 (s, 9H), 0.16 (s, 3H), 0.15 (s, 3H), 0.05 (s, 3H), -0.08 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  155.23, 145.26, 138.83, 119.85, 119.56, 119.53, 114.49, 114.46, 81.78, 73.48, 73.46, 69.63, 30.86, 25.75, 25.69, 25.58, 21.31, 18.15, 18.07, -4.51, -4.81, -5.06; IR (thin film from  $\text{CDCl}_3$  on NaCl)  $\delta$  3314s, 2956, 2930, 2886, 2858, 1596, 1471, 1461, 1361, 1310, 1253, 1161,  $1096\text{ cm}^{-1}$ ; HRMS calcd for  $\text{C}_{22}\text{H}_{40}\text{O}_2\text{Si}_2[\text{M}+\text{Na}]^+$  427.2465, found 427.2456 m/z.



**1-Acetoxy-3-[1-(*tert*-butyl-dimethyl-silyloxy)-but-3-ynyl]-5-methyl-benzene (36).**

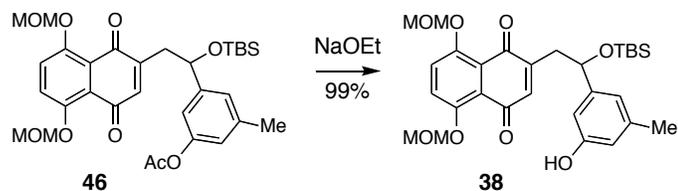
Alkyne **45** (256 mg, 0.63 mmol) was dissolved in THF (4 mL) and chilled to 0 °C. TBAF (0.63 mL of a 1 M solution in THF) was added, followed by HOAc (37  $\mu$ L, 0.63 mmol). The reaction was warmed to 23 °C, and stirred for 0.5 h. TLC analysis (10% EtOAc/hexanes) showed complete consumption of starting alkyne. A saturated, solution of ammonium chloride was added, and the resulting mixture was extracted with EtOAc. The organic layer was separated and dried over sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure to give a pale yellow oil which was dissolved in pyridine (5 mL). To this solution was added Ac<sub>2</sub>O (0.63 mL, 6.63 mmol). The mixture was stirred for 16 h, then a saturated solution of ammonium chloride was added, and the resulting mixture was extracted with EtOAc. The organic layer was separated and rinsed with an ammonium chloride solution (3 X 50 mL), saturated copper sulfate solution (2 X 30 mL), and brine (1 X 30 mL), and then was dried over sodium sulfate. The resulting mixture was filtered and the filtrate was concentrated under reduced pressure to give crude **36**. This material was purified by column chromatography using 5% EtOAc/hexanes, yielding pure **36** (148 mg, 0.45 mmol, 71% yield over 2 steps): <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.00 (s, 1H), 6.89 (s, 1H), 6.79 (s, 1H), 4.76 (dd, *J*=7.1, 5.6 Hz, 1H), 2.54 (ddd, *J*=16.8, 7.3, 2.7 Hz, 1H), 2.45 (ddd, *J*=16.8, 5.6, 2.7 Hz, 1H), 2.33 (s, 3H), 2.25 (s, 3H), 1.96 (t, *J*=2.7 Hz, 1H), 0.88 (s, 9H), 0.07 (s, 3H), -0.06 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) 169.28, 150.43, 145.43, 139.08, 123.93, 123.91, 121.21, 121.22, 121.09, 116.10, 116.08, 81.37, 73.23, 73.20, 70.03, 30.84, 25.70, 21.31, 21.05, 18.17, -4.81, -5.02; IR (thin film from CDCl<sub>3</sub> on NaCl) 3311s, 2955, 2930, 2886, 2857, 1770, 1617, 1596, 1471, 1463, 1367, 1288, 1252, 1207, 1135, 1099, 933, 837, 778 cm<sup>-1</sup>; HRMS calcd for C<sub>19</sub>H<sub>28</sub>O<sub>3</sub>Si [M+Na]<sup>+</sup> 355.1705, found 355.1701 m/z.



**2-[2-(*tert*-Butyl-dimethyl-silyloxy)-2-(3-acetoxy-5-methyl-phenyl)-ethyl]-5,8-**

**dimethoxymethoxy-[1,4]naphthoquinone (46).** A 5 mL reaction vial was flame dried and charged with alkyne **36** (45 mg, 0.14 mmol), carbene **5** (59 mg, 0.14 mmol), and THF (50  $\mu$ L). The solution was purged of oxygen by bubbling argon gas through it for 15 min. A microcondenser was affixed under positive pressure of argon, and the reaction was heated to 54  $^{\circ}$ C. After being heated for 14 h, the reaction was allowed to cool to 23  $^{\circ}$ C before the condenser was removed and the reaction mixture was diluted with diethyl ether. The mixture was stirred open to the air for 15 min to assure oxidation of the intermediate arene chromium(tricarbonyl) complex. The organic solution was then rinsed with saturated, aqueous bicarbonate solution to give a red solution, which was dried over sodium sulfate. The organic was concentrated under reduced pressure to give crude **37** which was purified by column chromatography (10% ethyl acetate / hexanes). In this way, naphthalene **37** (28 mg, 36% yield) was obtained as a red oil. This material was used directly in the subsequent oxidation step:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.55 (s, 1H), 6.99 (s, 1H), 6.97 (d,  $J=8.5\text{Hz}$ , 1H), 6.94 (s, 1H), 6.89 (d,  $J=8.5\text{Hz}$ , 1H), 6.74 (s, 1H), 6.61 (s, 1H), 5.37 (s, 2H), 5.09 (s, 2H), 5.02 (dd,  $J=8.6, 4.1\text{ Hz}$ , 1 H), 3.77 (s, 3H), 3.56 (s, 6H), 3.07 (dd,  $J=12.9, 4.2\text{ Hz}$ , 1H), 2.85 (dd,  $J=12.9, 8.8\text{ Hz}$ , 1H), 2.29 (s, 3H), 2.25 (s, 3H), 0.75 (s, 9H), -0.28 (s, 3H), -0.34 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  169.48, 150.51, 149.33, 148.82, 147.92, 147.61, 145.93, 138.84, 124.06, 120.51, 120.41, 120.14, 118.65, 117.57, 115.97, 114.87, 114.75, 108.74, 98.02, 96.38, 73.68, 57.52, 56.78, 56.37, 43.04, 25.73, 21.33, 21.15, 18.06, -5.17, -5.41; IR (thin film from  $\text{CDCl}_3$  on NaCl) 3387, 2953, 2929, 2897, 2855, 1953, 1879, 1768, 1611, 1595, 1495, 1448, 1402, 1376, 1250, 1208, 1154, 1084, 1049, 1013,  $971\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{32}\text{H}_{44}\text{O}_9\text{Si}[\text{M}+\text{Na}]^+$  623.2652, found 623.2662 m/z.

A 0  $^{\circ}$ C solution of hydroquinone **37** (65 mg, 0.11 mmol) in MeCN (2 mL) was added to a 0  $^{\circ}$ C solution of ceric ammonium nitrate (148 mg, 0.27 mmol) in water (2 mL) contained within a 25 mL separatory funnel. The mixture was shaken for 5 min before being extracted with methylene chloride (3 x 10 mL). The organic solution was rinsed with a saturated, aqueous sodium bicarbonate and then was dried over sodium sulfate. The dry, filtered solution was concentrated under reduced pressure and the resulting red oil was purified by flash chromatography (20% ethyl acetate / hexanes) to give pure quinone **46** as a red oil (53 mg, 0.09 mmol, 84% yield):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.47 (d,  $J=9.3\text{ Hz}$ , 1H), 7.44 (d,  $J=9.3\text{ Hz}$ , 1H), 7.06 (s, 1H), 6.93 (s, 1H), 6.76 (s, 1H), 6.64 (s, 1H), 5.27 (d,  $J=2.2\text{ Hz}$ , 2H), 5.24 (d,  $J=1.0\text{ Hz}$ , 2H), 4.88 (dd,  $J=9.5, 3.0\text{ Hz}$ , 1H), 3.54 (s, 3H), 3.51 (s, 3H), 2.94 (dd,  $J=12.7, 2.9\text{ Hz}$ , 1H), 2.49 (dd,  $J=12.7, 9.7\text{ Hz}$ , 1H), 2.32 (s, 3H), 2.26 (s, 3H), 2.15 (s, 3H); 0.77 (s, 9H), -0.20 (s, 3H), -0.25 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  184.97, 184.32, 169.39, 152.34, 151.69, 150.60, 146.84, 146.48, 139.32, 137.78, 125.28, 124.48, 123.82, 122.54, 122.42, 120.98, 115.89, 96.13, 95.83, 72.80, 56.50, 42.06, 25.83, 25.68, 21.31, 21.11, 18.00, -4.86, -5.09; IR (thin film from  $\text{CDCl}_3$  on NaCl)  $\delta$  2955, 2929, 2856, 1769, 1659, 1471, 1252, 1206, 1153, 1083, 1000, 961, 836,  $778\text{ cm}^{-1}$ ; HRMS calcd for  $\text{C}_{31}\text{H}_{40}\text{O}_9\text{Si}[\text{M}+\text{Na}]^+$  607.2339, found 607.2343 m/z.

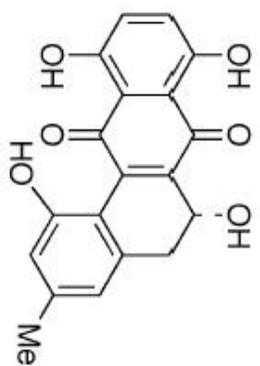


**2-[2-(*tert*-Butyldimethylsilyloxy)-2-(3-hydroxy-5-methyl-phenyl)-ethyl]-5,8-dimethoxymethoxy-[1,4]naphthoquinone (38).** Quinone **46** (23 mg, 0.04 mmol) was dissolved in freshly distilled ethanol (200  $\mu$ L) and chilled to 0  $^{\circ}$ C. To this solution was added a 1M solution of sodium ethoxide in ethanol (200  $\mu$ L) by syringe. The reaction was complete after 2 h as determined by TLC analysis (4% MeOH / CH<sub>2</sub>Cl<sub>2</sub>). The reaction was worked up by addition of a saturated, aqueous ammonium chloride solution and extracted with methylene chloride. The organic solution was rinsed with saturated, aqueous sodium bicarbonate and dried over sodium sulfate before being concentrated under reduced pressure. The crude red oil was purified by column chromatography (20 to 50% ethyl acetate / hexanes) to give pure **38** (19 mg, 0.04 mmol, 99% yield): <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.47 (d, *J*=9.3 Hz, 1H), 7.44 (d, *J*=9.3 Hz, 1H), 6.74 (s, 1H), 6.67 (s, 1H), 6.62 (s, 1H), 6.51 (s, 2H), 5.27 (d, *J*=1.9 Hz, 2H), 5.24 (s, 2H), 4.95 (s, 1H), 4.83 (dd, *J*=9.3, 3.7 Hz, 1H), 3.53 (s, 3H), 3.52 (s, 3H), 2.91 (dd, *J*=12.8, 3.4 Hz, 1H), 2.54 (dd, *J*=12.8, 9.3 Hz, 1H), 2.25 (s, 3H), 0.78 (s, 9H), -0.18 (s, 3H), -0.24 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  185.0, 184.4, 155.5, 152.3, 151.7, 147.1, 146.6, 139.5, 137.7, 125.2, 124.5, 122.5, 118.9, 114.9, 109.6, 96.1, 95.9, 73.0, 56.6, 41.9, 25.7, 21.3, 18.0, -4.8, -5.0; IR (thin film from CDCl<sub>3</sub> on NaCl)  $\nu$  3406, 2928, 2856, 1654, 1598, 1565, 1470, 1401, 1325, 1255, 1223, 1198, 1153, 1085, 997, 957, 836, 777, 732 cm<sup>-1</sup>; HRMS calcd for C<sub>29</sub>H<sub>38</sub>O<sub>9</sub>Si [M+Na]<sup>+</sup> 565.2234, found 565.2239 m/z.

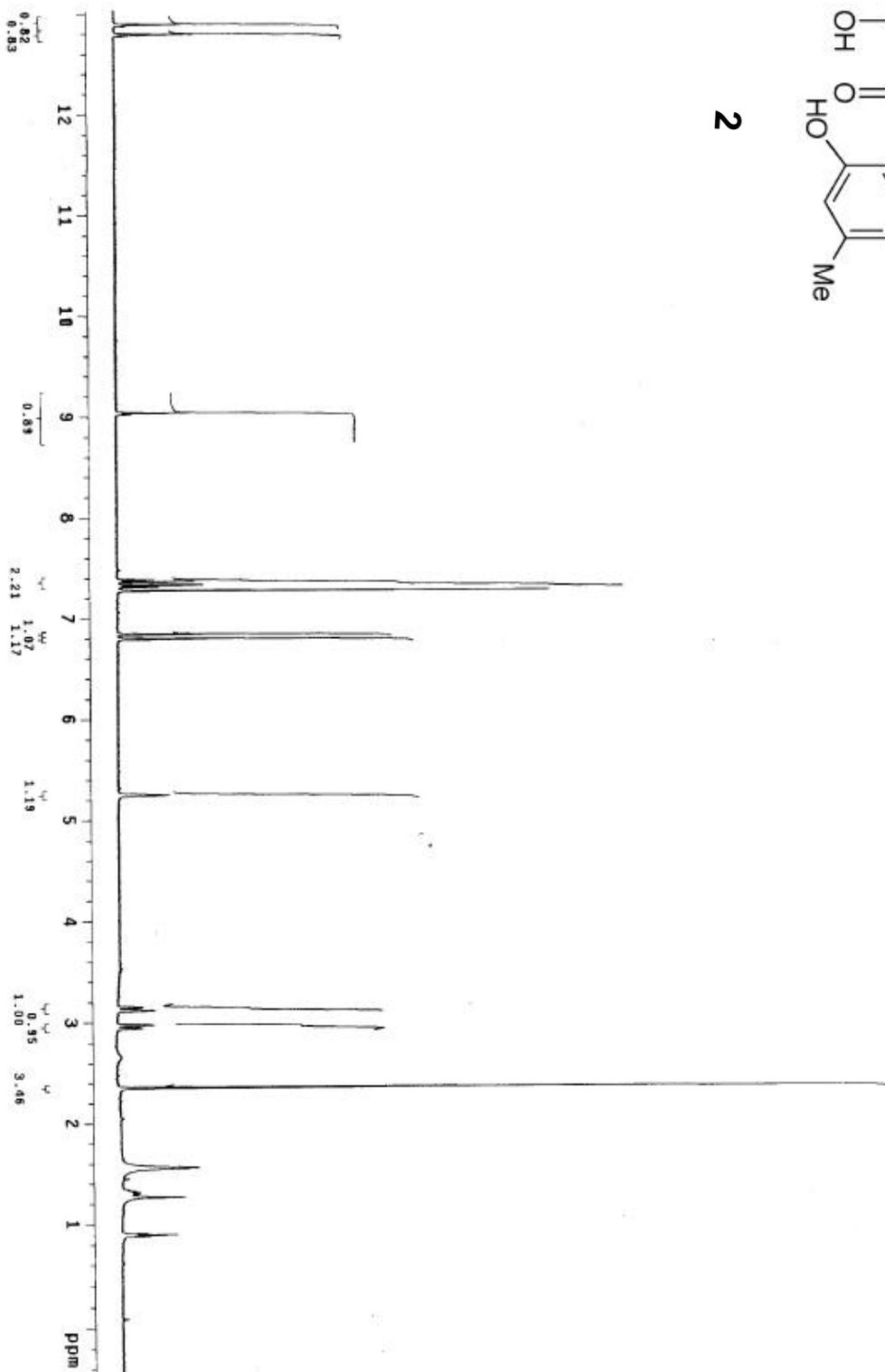
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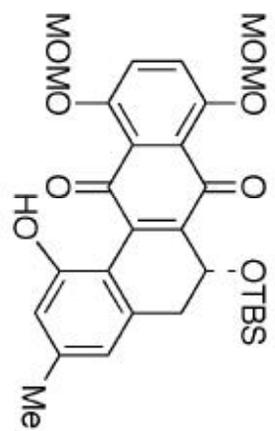
- (1) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.
- (2) Brittain, J. M.; De la Mare, P. B. D.; Newman, P. A. *J. Chem Soc., Perkin Trans. II* **1981**, 32-41.
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NMR Spectra:

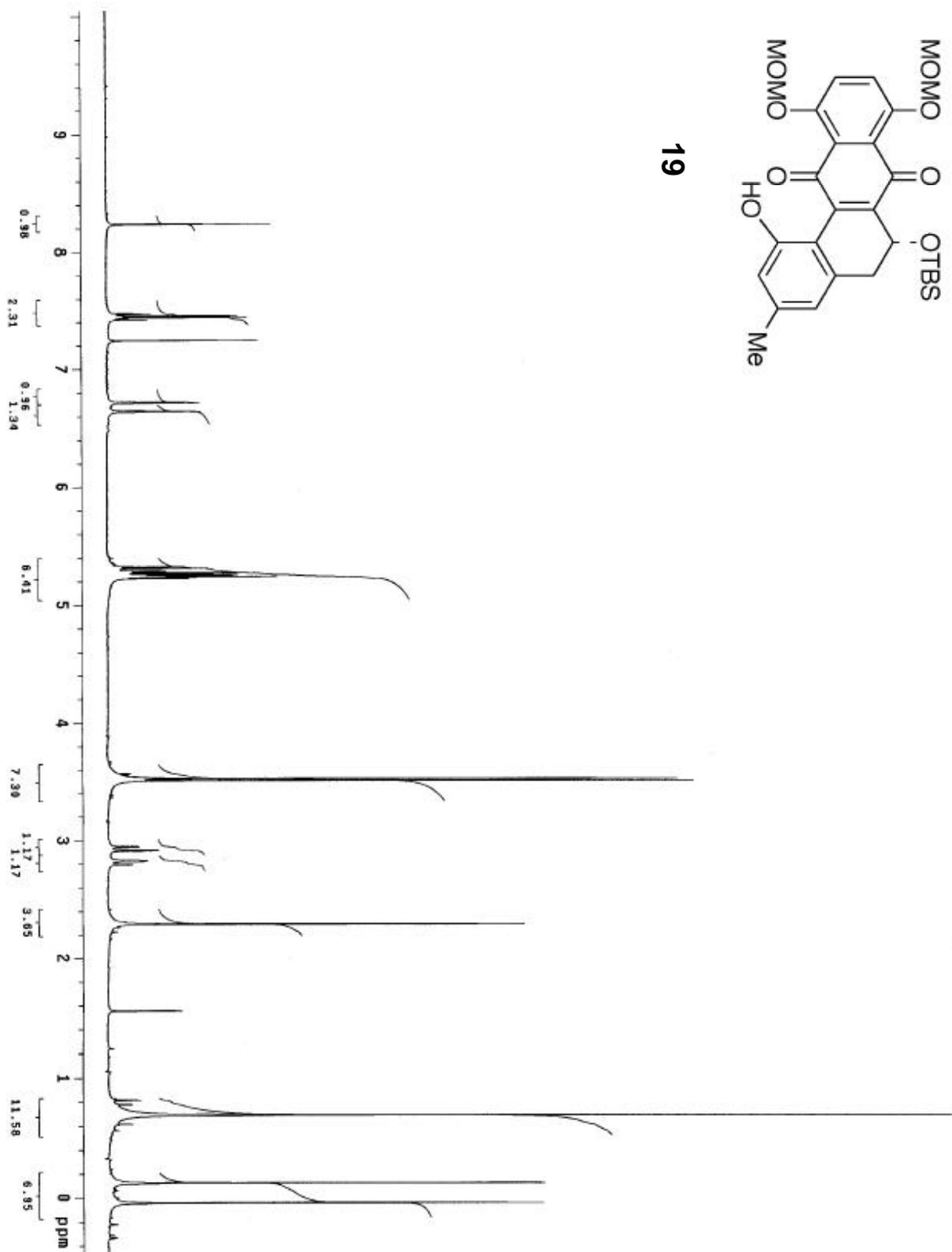


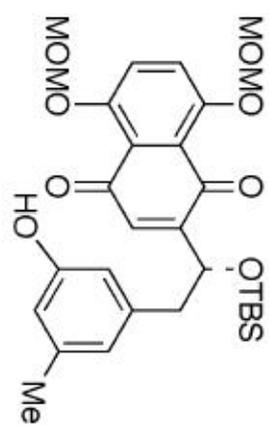
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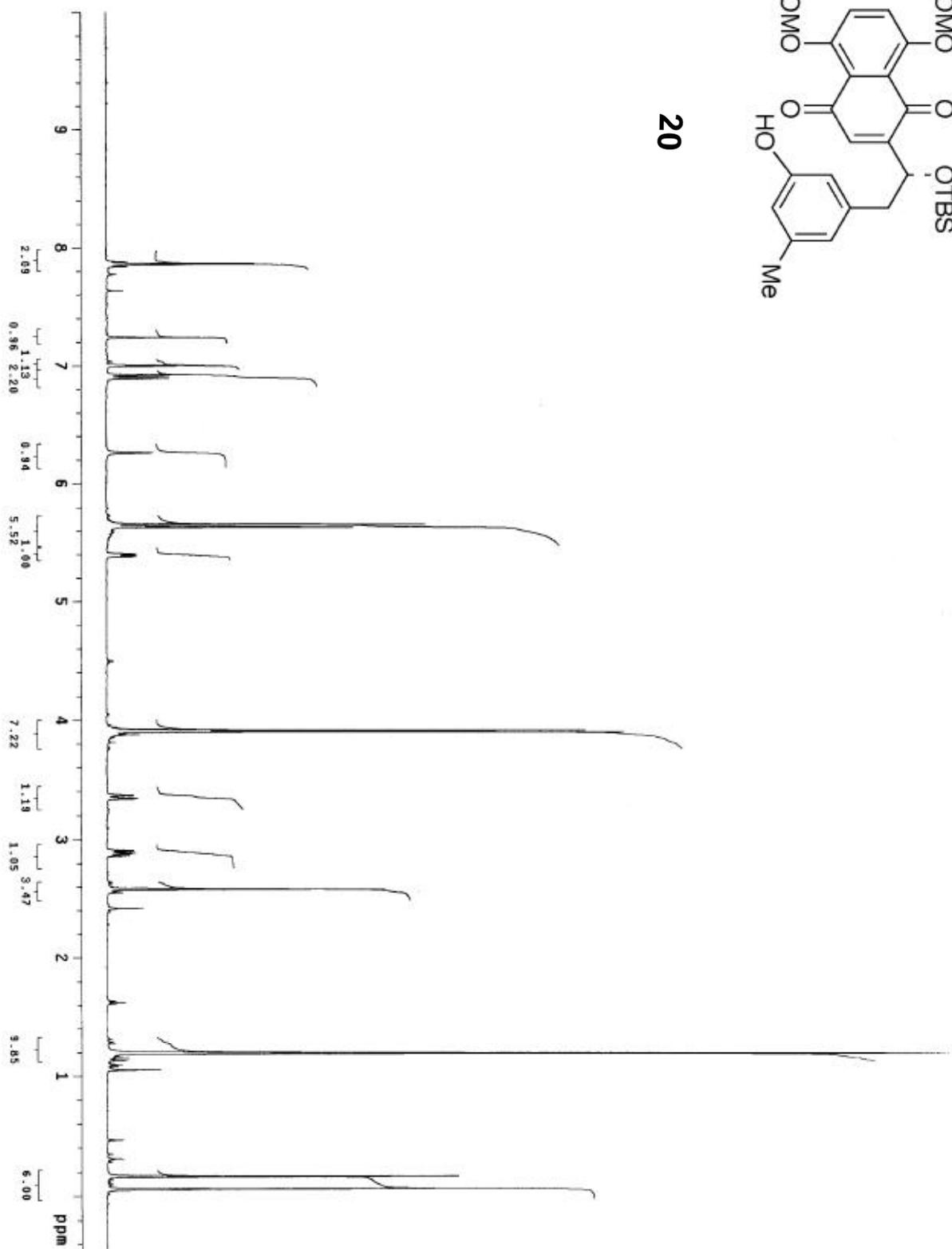


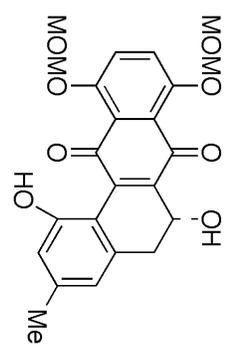
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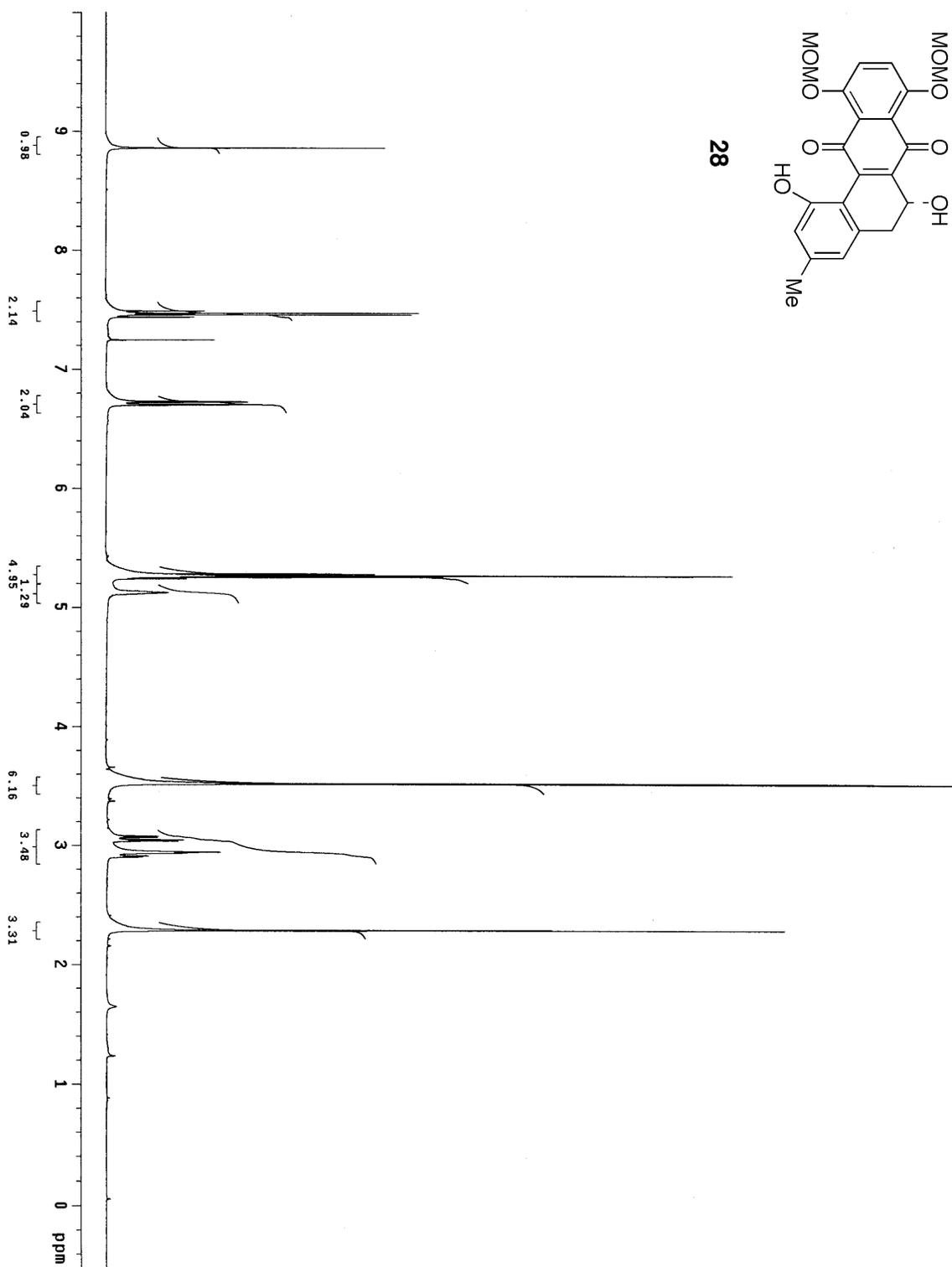


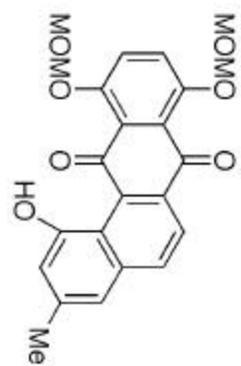
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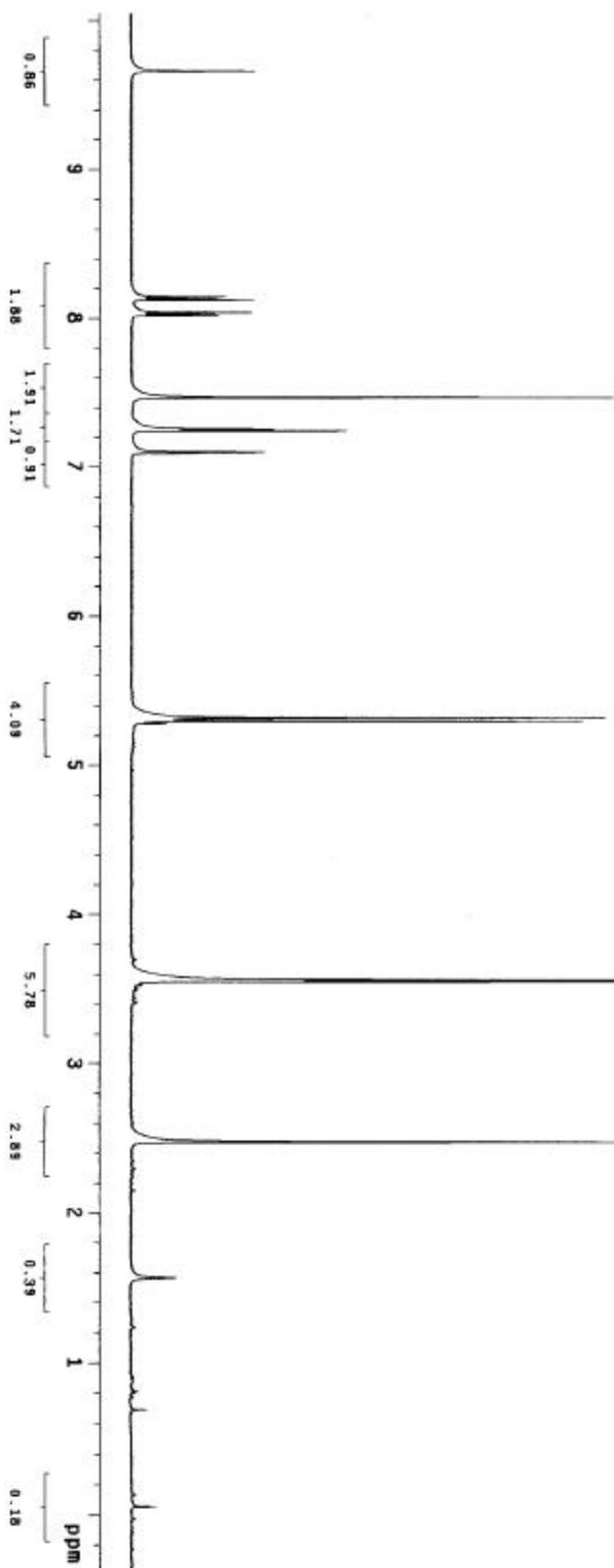


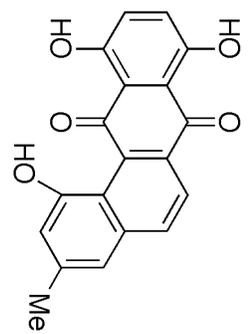
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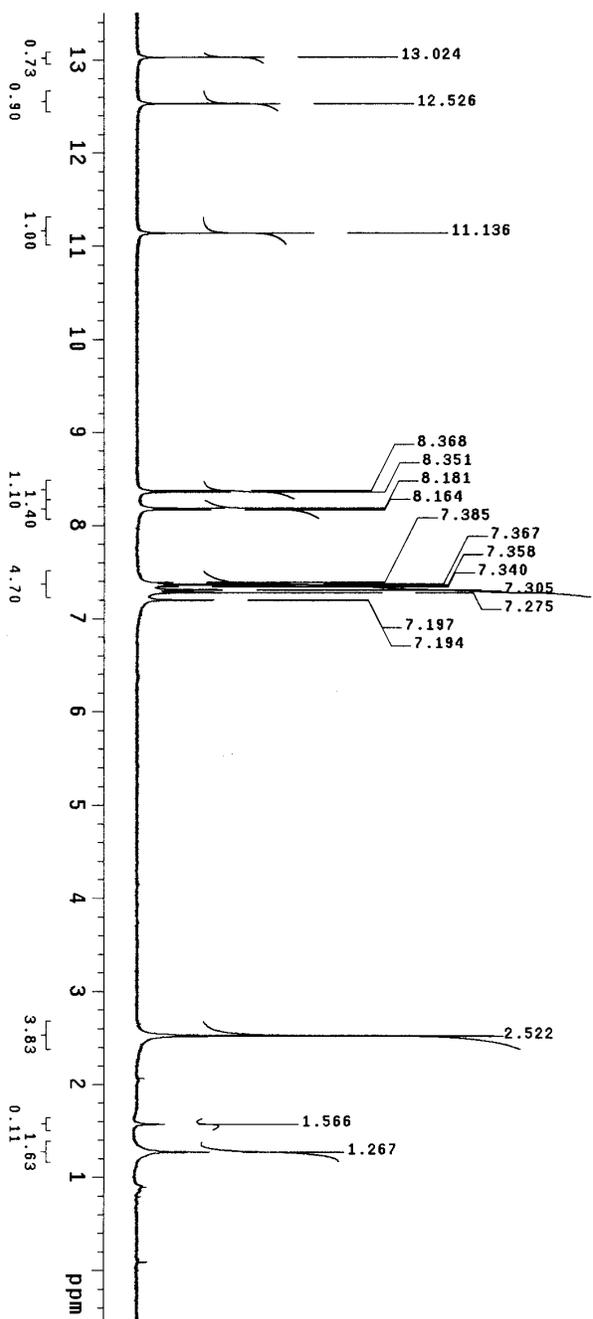


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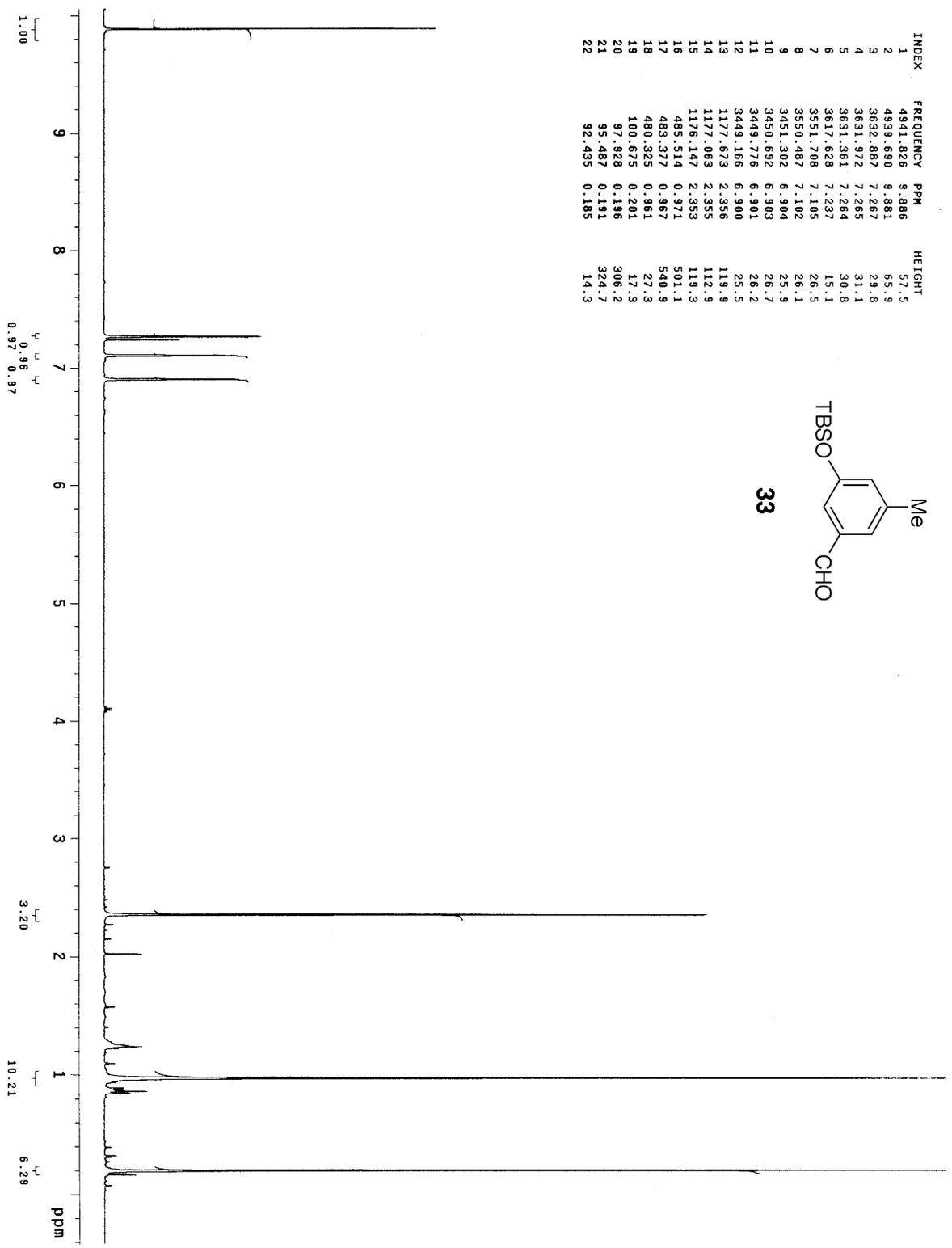
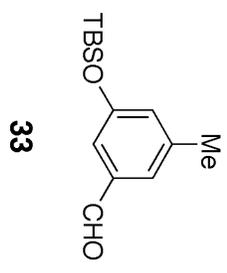


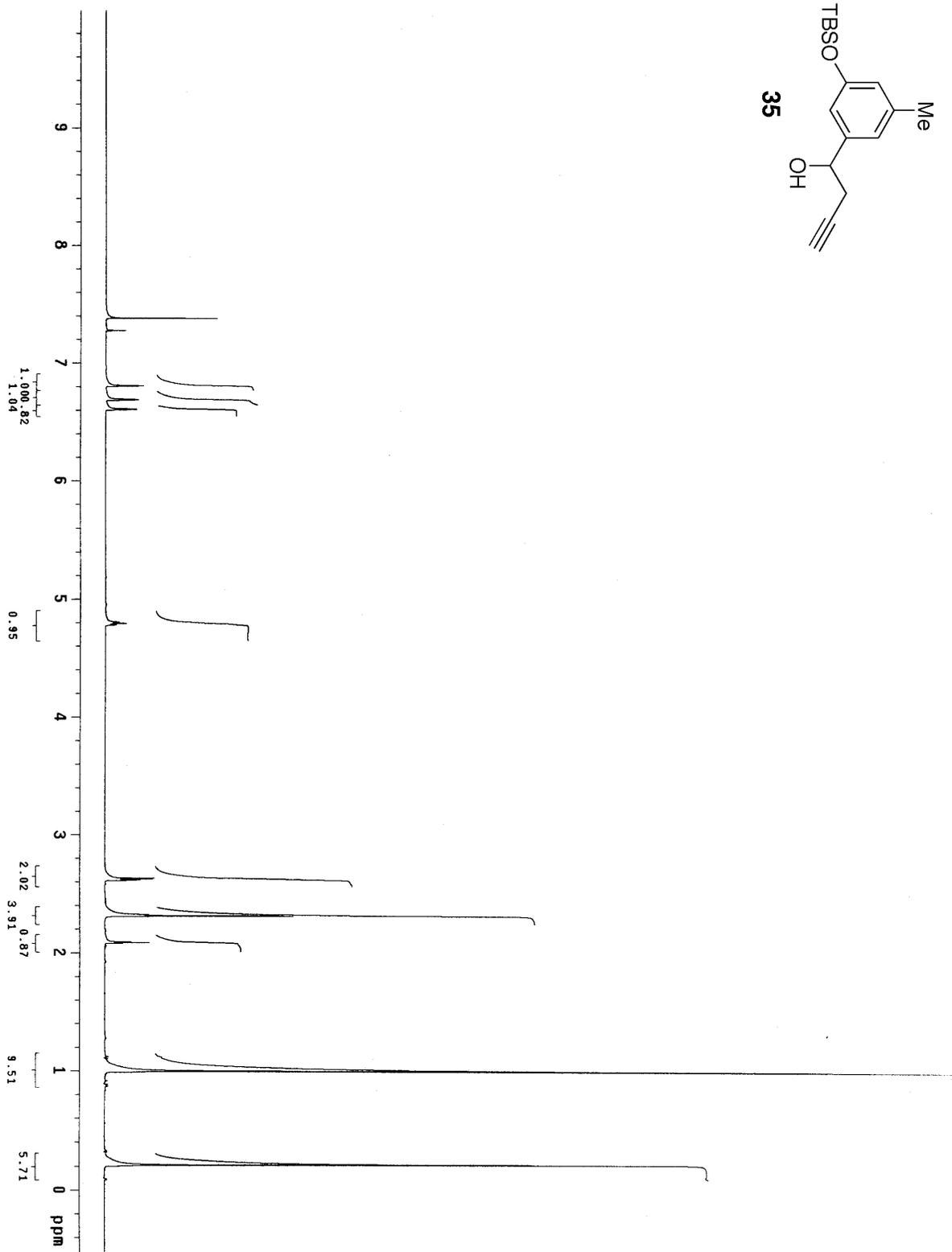
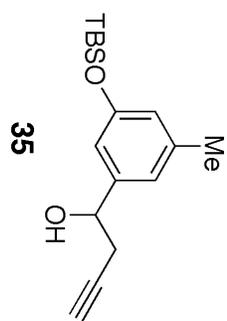


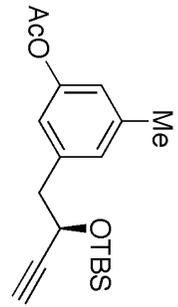
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4	3631.972	7.265	31.1
5	3631.361	7.264	30.8
6	3617.628	7.237	15.1
7	3551.708	7.105	26.5
8	3550.487	7.102	26.1
9	3451.302	6.904	25.9
10	3450.692	6.903	26.7
11	3449.776	6.901	26.2
12	3449.166	6.900	25.5
13	1177.673	2.356	113.9
14	1177.063	2.355	112.9
15	1176.147	2.353	119.3
16	485.514	0.971	501.1
17	483.377	0.967	540.9
18	480.325	0.961	27.3
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20	97.928	0.196	306.2
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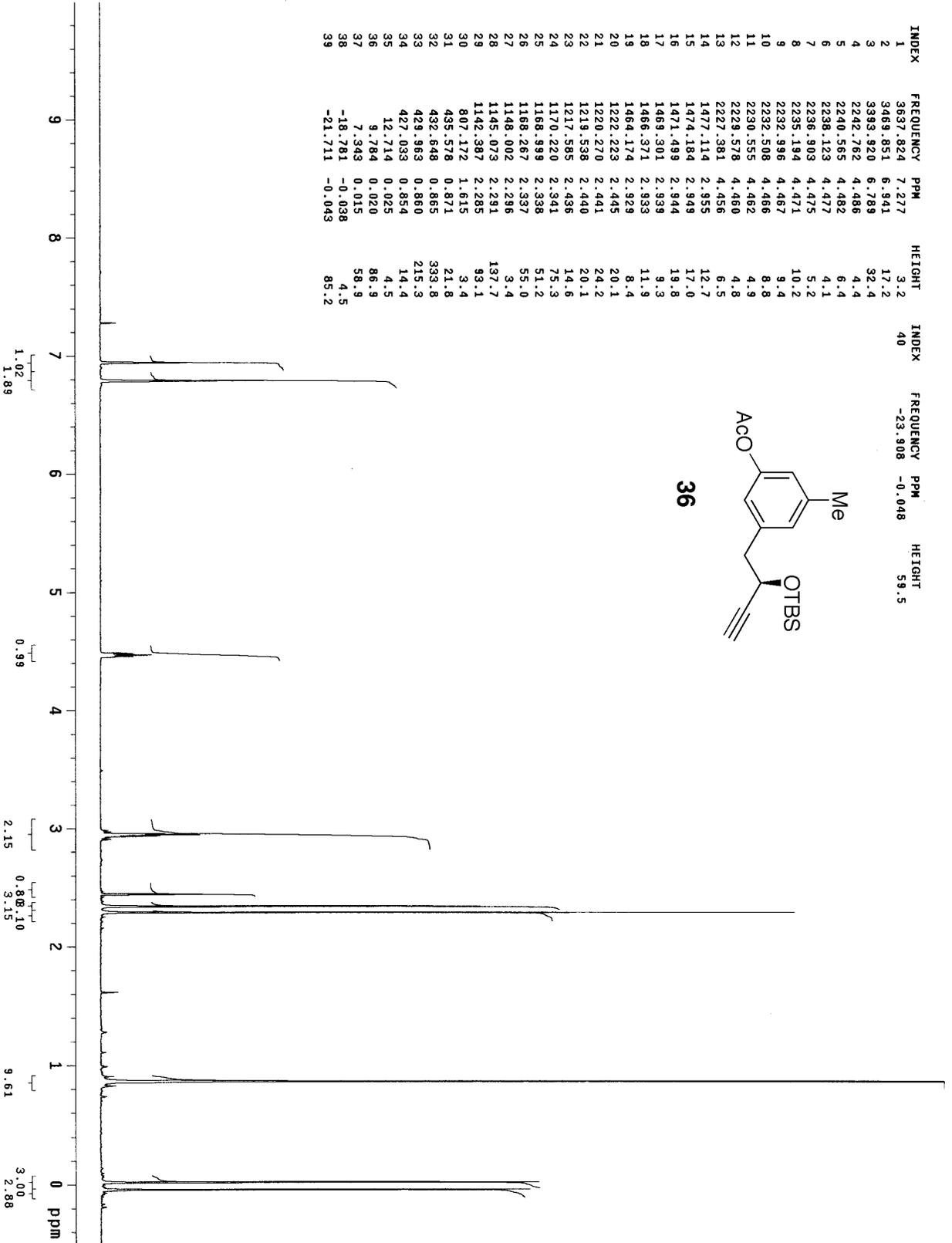


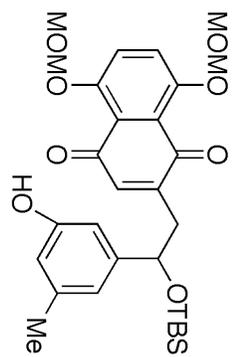




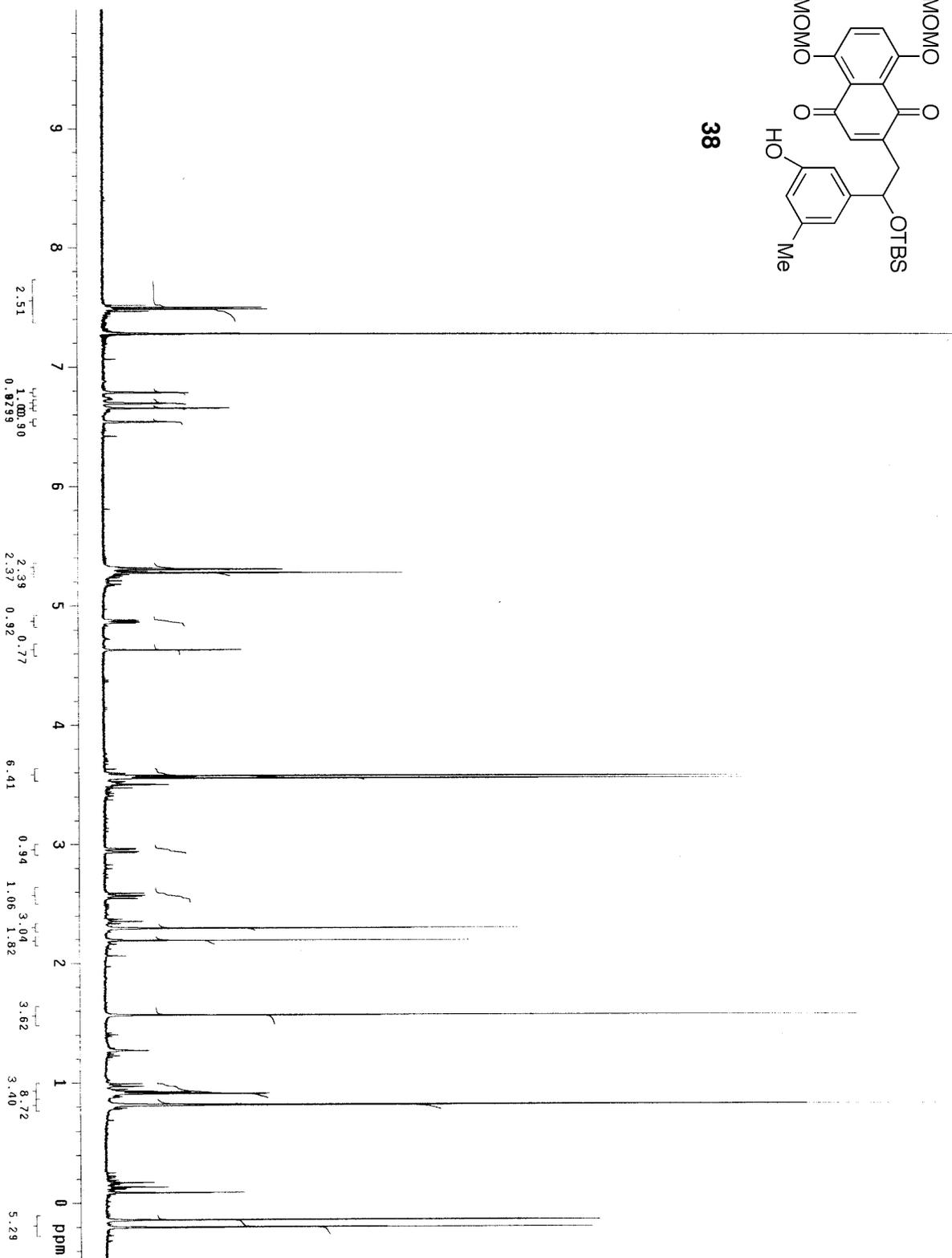
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5	2240.565	4.482
6	2238.123	4.477
7	2236.903	4.475
8	2235.194	4.471
9	2232.996	4.467
10	2232.508	4.466
11	2230.555	4.462
12	2229.578	4.460
13	2227.381	4.456
14	1477.114	2.955
15	1474.184	2.949
16	1471.499	2.944
17	1469.301	2.939
18	1466.371	2.933
19	1464.174	2.929
20	1222.223	2.445
21	1220.270	2.441
22	1219.538	2.440
23	1217.585	2.436
24	1170.220	2.341
25	1168.999	2.338
26	1168.267	2.337
27	1148.002	2.296
28	1145.073	2.291
29	1142.387	2.285
30	807.172	1.615
31	435.578	0.871
32	432.648	0.865
33	429.963	0.860
34	427.033	0.854
35	12.714	0.025
36	9.784	0.020
37	7.343	0.015
38	-18.781	-0.038
39	-21.711	-0.043

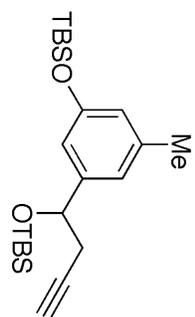
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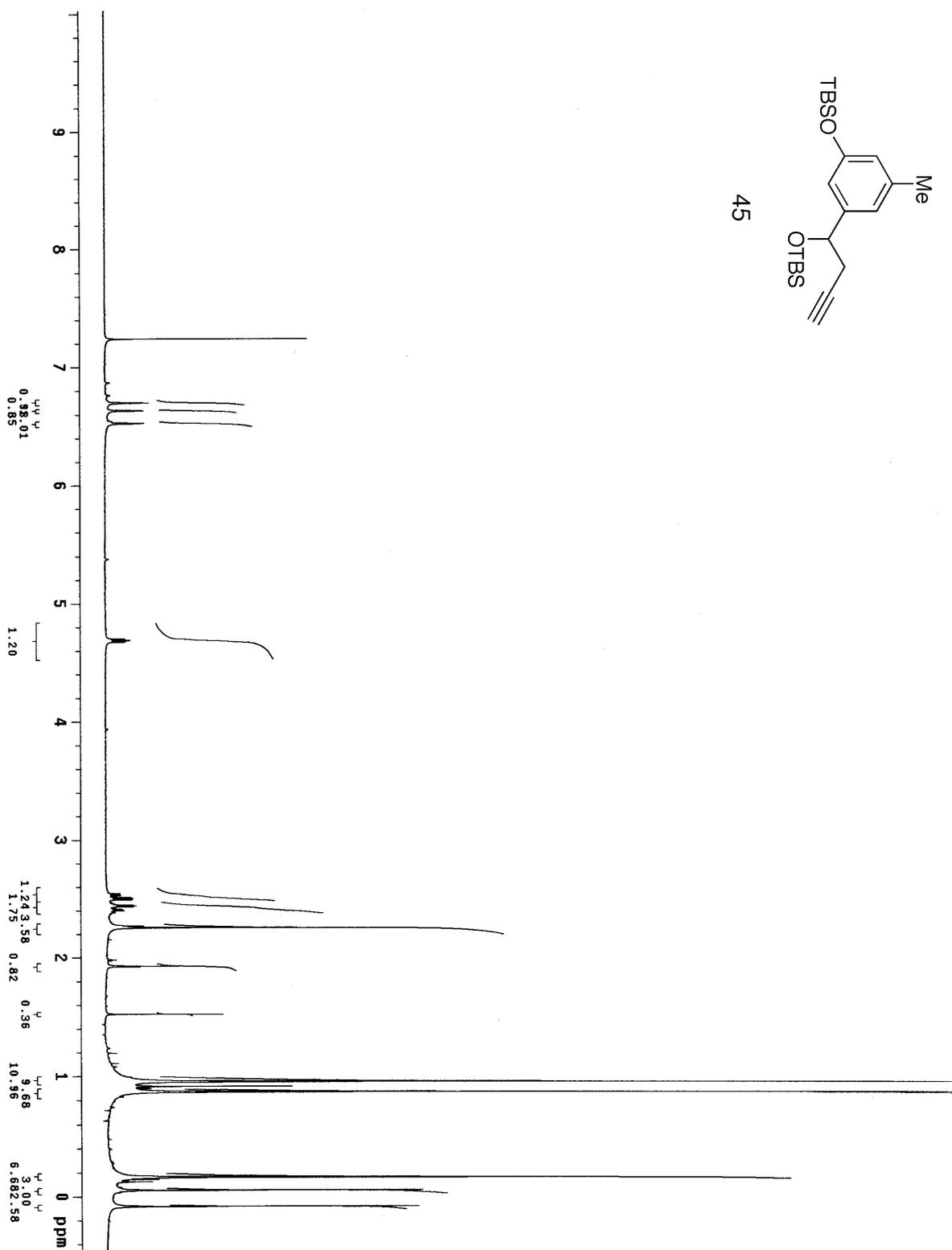


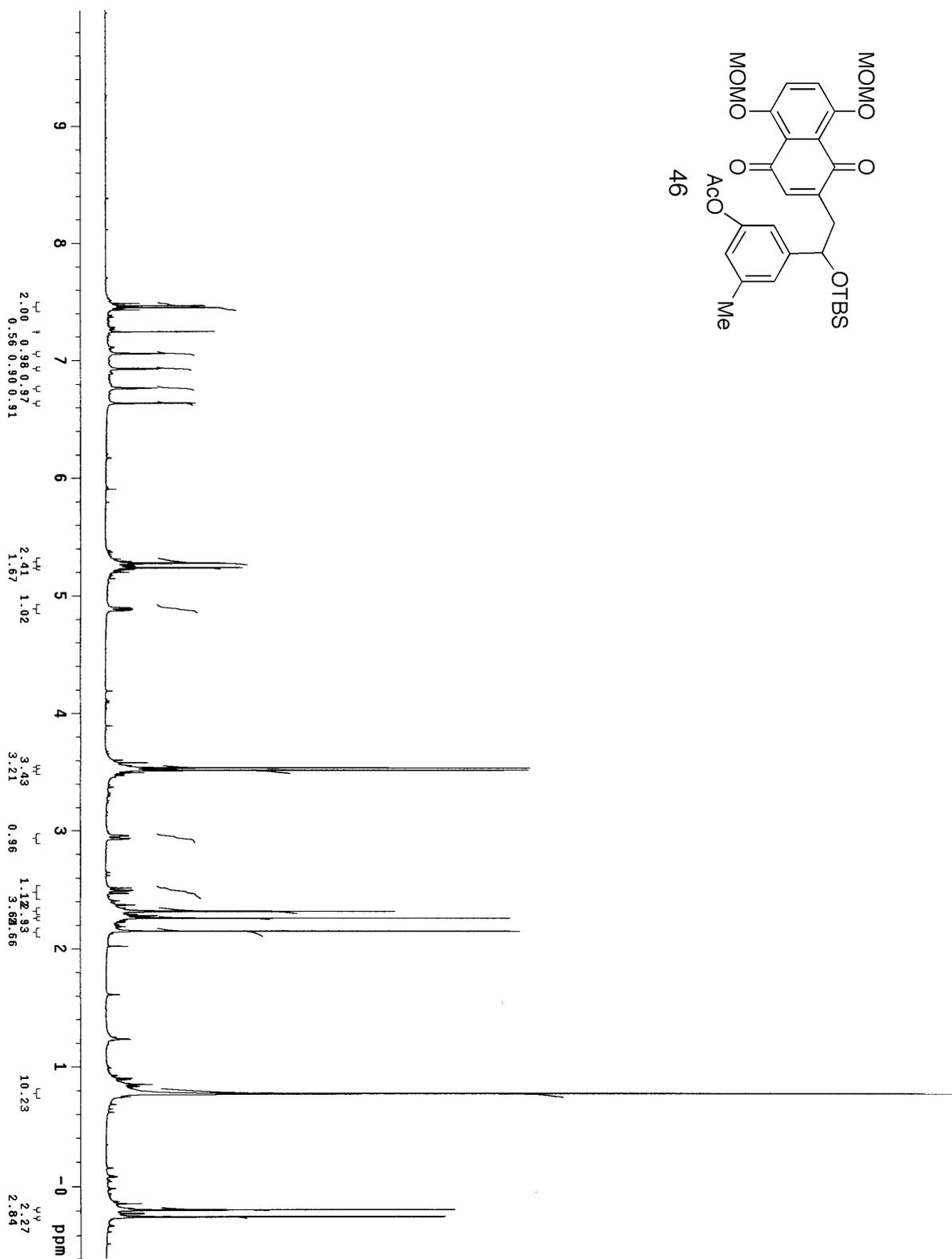
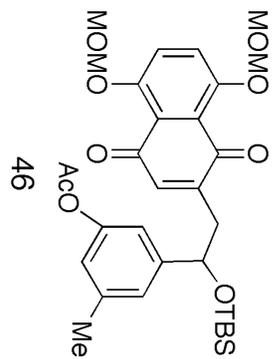
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