SUPPORTING INFORMATION FOR

β-Hydroxysulfoxides as Chiral Cyclic Ketone Equivalents: Enantioselective Synthesis of Polysubstituted Cyclohexanones, Cyclohexenones and Cyclohexenediones

M. Carmen Carreño, Manuel Pérez-González, María Ribagorda, Álvaro Somoza and Antonio Urbano

Experimental Section

General: Melting points were obtained in open capillary tubes and are uncorrected. ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz, respectively. All reactions were monitored by thin layer chromatography that was performed on precoated sheets of silica gel 60, and flash column chromatography was done with silica gel 60 (230-400 mesh) of Merck. Eluting solvents are indicated in the text. The apparatus for inert atmosphere experiments was dried by flaming in a stream of dry argon. CH_2Cl_2 was dried over P_2O_5. Dry THF was distilled from sodium/benzophenone ketyl. CH_3CN was dried over 4Å molecular sieves. All other reagent quality solvents were used without purification. For routine workup, hydrolysis was carried out with water, extractions with CH_2Cl_2, and solvent drying with Na_2SO_4. The synthesis of derivatives **2a-d** and **13** has been previously described.[1]

General Procedure for *m*-CPBA Oxidations. Method A. *m*-CPBA (2 equiv) in CH_2Cl_2 (0.5 M) was added to a solution of sulfoxides **2a-d** (1 equiv) in CH_2Cl_2 (0.5 M) at 0 ºC. The mixture was stirred for 1-2 h and washed with saturated aqueous Na_2SO_3 and $NaHCO_3$. After workup, the residue was purified by crystallization.

[1] Carreño, M. C.; Pérez González, M.; Ribagorda, M.; Houk. K. N. *J. Org. Chem.* **1998**, *63*, 3687-3693.

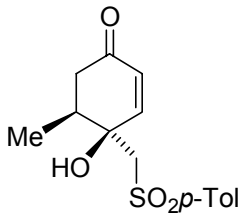
General Procedure for Reductions with $NaBH_4/CeCl_3$. Method B. To a solution of the corresponding carbonyl compound (1 equiv) in MeOH (0.5 M), $CeCl_3$ (3 equiv) and $NaBH_4$ (3 equiv) were sequentially added at –78 ºC. The reaction mixture was stirred for 2-3 h and treated with 5% HCl and saturated aqueous NaCl. After several extractions with AcOEt and workup, the residue was purified by flash chromatography.

General Procedure for Reductions with L-Selectride. Method C. To a solution of L-Selectride (1 M in THF, 3 equiv), a solution of the corresponding carbonyl compound (1 equiv) in THF (0.3 M) was added at –78 ºC. After stirring for 1-2 h, the mixture was sequentially treated with H_2O, MeOH, 5% NaOH and H_2O_2. After several extractions with AcOEt and workup, the residue was purified by flash chromatography.

General Procedure for TBDMS Protections. Method D. To a solution of the corresponding alcohols (1 equiv) in CH_2Cl_2 (0.5 M) at 0 ºC under argon, 2,6-lutidine (2.5 equiv) and TBDMSTf (1.5 equiv) were sequentially added. The reaction mixture was stirred for 4-5 h and treated with 5% HCl. After workup, the residue was purified by flash chromatography.

General Procedure for $MeSO_2$*p*Tol Elimination. Method E. To a solution of the corresponding β-hydroxy sulfone (1 equiv) in CH_3CN (0.1 M), Cs_2CO_3 (2 or 3 equiv) was added at rt. After the time indicated in each case (see Table 1 for reaction conditions), the mixture was filtered through celite and the solvent evaporated to afford a residue which was purified by flash chromatography.

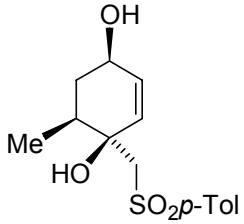
(4*S*,5*S*)-4-Hydroxy-5-methyl-4-[(*p*-tolylsulfonyl)methyl]-2-cyclohexenone (3a).



3a

Compound **3a** was obtained following method **A** from **2a**[1] (2.0 g, 6.9 mmol), in 90% yield as a white solid: mp 145-146 ºC (EtOAc/hexane); $[\alpha]_D^{20}$ = +21.2 (*c* 1, acetone); ^{1}H RMN δ 7.80 and 7.39 (AA'BB´ system, 4H), 7.06 (dd, 1H, *J* = 0.9 and 10.2 Hz), 5.96 (d, 1H, *J* = 10.2 Hz), 4.08 (broad s, 1H), 3.50 and 3.45 (AB system, 2H, *J* = 14.2 Hz), 2.62-2.37 (m, 3H), 2.47 (s, 3H), 1.09 (d, 3H, *J* = 6.6 Hz); ^{13}C RMN δ 197.8, 148.9, 145.6, 137.4, 130.2 (2C), 129.1, 127.6 (2C), 71.7, 62.7, 42.0, 38.3, 21.7, 14.5; FAB-MS *m/z* (rel intens) 295 ($[M + H]^+$, 51), 277 (77), 257 (66), 239 (54), 215 (60), 203 (76), 189 (94), 171 (100); HRMS (FAB) calcd for $C_{15}H_{19}O_4S$ $[M + H]^+$ 295.1004, found 295.1007.

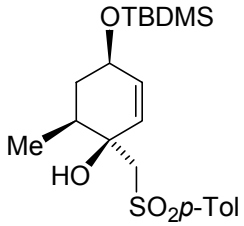
(1*S*,4*R*,6*S*)-6-Methyl-1-[(*p*-tolylsulfonyl)methyl]-2-cyclohexene-1,4-diol (4).



4

To a solution of DIBALH 1 M in hexanes (18.9 mL, 18.9 mmol) in THF (60 mL), a solution of **3a** (312 mg, 6.30 mmol) in THF (20 mL) was added dropwise under argon at –78 ºC. After 30 min at the same temperature, the excess of organoaluminum reagent was destroyed with methanol and the mixture was poured into an Erlenmeyer containing ethyl acetate and a saturated solution of potassium sodium tartrate and stirred vigorously for 30 min. The organic layer was washed with brine and dried over $MgSO_4$. After workup, compound **4** was obtained in 95% yield as a white solid: mp 118-119 ºC (EtOAc/hexane); $[\alpha]_D^{20}$ = +56.0 (*c* 1, acetone); ^{1}H RMN (CD_3OD) δ 7.76 and 7.40 (AA'BB´ system, 4H), 5.73 (dd, 1H, *J* = 2.0 and 10.2 Hz), 5.63 (dt, 1H, *J* = 10.2 and 1.6 Hz), 4.14 (m, 1H), 3.49 and 3.40 (AB system, 2H, *J* = 14.5 Hz), 2.43 (s, 3H), 2.13-2.00 (m, 1H), 1.70 (m, 1H), 1.48 (ddd, 1H, *J* = 10.1, 12.3, 12.6 Hz), 0.94 (d, 3H, *J* = 6.7 Hz); ^{13}C RMN (CD_3OD) δ 146.2, 139.4, 135.5, 132.2, 130.9 (2C), 129.1 (2C), 70.8, 68.1, 63.9, 36.8, 35.6, 21.5, 15.4. Anal. calcd. for $C_{15}H_{20}O_4S$: C, 60.79; H, 6.80; S, 10.82. Found C, 60.67; H, 6.48; S, 10.68.

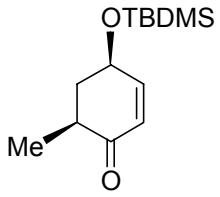
(1*S*,4*R*,6*S*)-4-[(*terc*-Butyldimethylsilyl)oxy)]-6-methyl-1-[(*p*-tolylsulfonyl)methyl]-2-cyclohexene-1-ol (5).



5

Compound **5** was obtained following method D from **4** (152 mg, 0.51 mmol), in 93% yield after flash chromatography (EtOAc/hexane 1:3), as a white solid: mp 145-147 ºC (ethyl ether/hexane); $[\alpha]_D^{20}$ = +47.0 (*c* 1, acetone); ^{1}H RMN δ 7.79 and 7.35 (AA'BB´ system, 4H), 5.94 (d, 1H, *J* = 10.2 Hz), 5.70 (dd, 1H, *J* = 3.2 and 10.2 Hz), 4.21 (m, 1H), 3.60 (s, 1H), 3.53 and 3.31 (AB system, 2H, *J* = 14.5 Hz), 2.44 (s, 3H), 2.32 (m, 1H), 1.89 (ddd, 1H, *J* = 5.4, 8.1, 13.5 Hz), 1.56 (ddd, 1H, *J* = 3.2, 5.3, 13.5 Hz), 1.00 (d, 3H, *J* = 7.0 Hz), 0.87 (s, 9H), 0.05 (s, 6H); ^{13}C RMN δ 144.9, 138.3, 131.9, 130.8, 129.9 (2C), 127.6 (2C), 71.6, 64.1, 63.8, 36.5, 34.5, 25.9, 25.8 (3C), 21.6, 18.2, 14.3, –4.5 (2C).

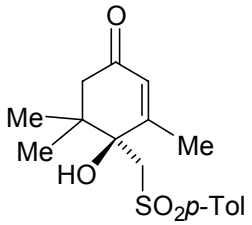
(4*R*,6*S*)-4-[(*terc*-Butyldimethylsilyl)oxy)]-6-methyl-2-cyclohexenone (6).



6

Compound **6** was obtained following method E from **5** (80 mg, 0.19 mmol), in 89% yield after flash chromatography (EtOAc/hexane 3:1), as a colorless oil: $[\alpha]_D^{20}$ = +67.0 (*c* 0.4, acetone); ^{1}H RMN δ 6.77 (dt, 1H, *J* = 10.1 and 2.0 Hz), 5.91 (dd, 1H, *J* = 2.4 and 10.1 Hz), 4.59 (m, 1H), 2.38 (m, 1H), 2.21 (m, 1H), 1.77 (dt, 1H, *J* = 10.5 and 12.5 Hz), 1.14 (d, 3H, *J* = 6.5 Hz), 0.91 (s, 9H), 0.12 (s, 6H); ^{13}C RMN δ 201.1, 154.1, 128.3, 68.1, 41.9, 40.2, 25.7 (3C), 18.1, 15.0, –3.5, –3.7; MS (EI): *m/z* (%) 183 ([M – C_4H_9]$^+$, 99), 165 (7), 139 (13), 113 (11), 85.9 (40), 84 (62), 75 (100); HRMS (EI) calcd for $C_9H_{15}O_2Si$ (M – C_4H_9)$^+$ 183.0841, found 183.0844.

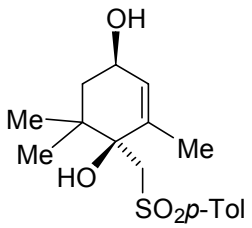
(4*S*)-4-Hydroxy-3,5,5-trimethyl-4-[(*p*-tolylsulfonyl)methyl]-2-cyclohexenone (3b).



3b

Compound **3b** was obtained following method **A** from **2b**[1] (2.40 g, 7.83 mmol), in 85 % yield as a white solid: mp 145-146 ºC (AcOEt/hexane); $[\alpha]_D^{20}$ = –25.4 (*c* 0.5, $CHCl_3$); ^{1}H RMN δ 7.79 and 7.39 (AA'BB´ system, 4H), 5.92 (broad s, 1H), 4.58 (s, 1H), 3.53 and 3.34 (AB system, 2H, *J* = 13.9 Hz), 2.47 (s, 3H), 2.26 (d, 3H, *J* = 1.2 Hz), 2.25 (s, 2H), 1.07 (s, 6H); ^{13}C RMN δ 196.2, 165.1, 145.5, 137.3, 130.1 (2C), 127.5(2C), 126.8, 77.1, 61.7, 48.9, 42.6, 23.6, 22.3, 21.6, 21.1; MS (EI): *m/z* (%) 322 (M$^+$, 0.2), 266 (8), 170 (18), 155 (18), 111 (100), 91 (67), 68 (34); HRMS (EI) calcd for $C_{17}H_{22}O_4S$ (M)$^+$ 322.1239, found 322.1233.

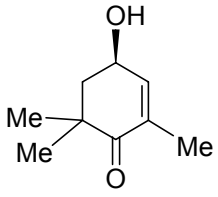
(1*S*,4*R*)-2,6,6-Trimethyl-1-[(*p*-tolylsulfonyl)methyl]-2-cyclohexene-1,4-diol (7).



7

Compound **7** was obtained following method C from **3b** (101 g, 0.31 mmol), in 71% yield as a colorless oil: $[\alpha]_D^{20}$ = +60.0 (*c* 1, acetone); ^{1}H RMN δ 7.79 and 7.35 (AA'BB´ system, 4H), 5.54 (broad s, 1H), 4.15 (m, 1H), 4.09 (s, 1H), 3.42 and 3.25 (AB system, 2H, *J* = 14.5 Hz), 2.44 (s, 3H), 1.94 (t, 3H, *J* = 1.1 Hz), 1.77 (dd, 1H, *J* = 6.8 and 14.9 Hz), 1.65 (ddd, 1H, *J* = 1.1, 4.4 and 14.9 Hz), 1.06 and 0.93 (2s, 6H); ^{13}C RMN δ 144.9, 139.2, 138.1, 129.9 (2C), 127.6 (2C), 127.2, 76.4, 63.9, 60.9, 42.3, 38.0, 23.7 (2C), 21.6, 19.6; FAB-MS *m/z* (rel intens) 323 ($[M - H]^+$, 31), 307 (100), 289 (72); HRMS (FAB) calcd for $C_{17}H_{23}O_4S$ $[M - H]^+$ 323.1317, found 323.1313.

(4*R*)-4-Hydroxy-2,6,6-trimethyl-2-cyclohexenone (9).

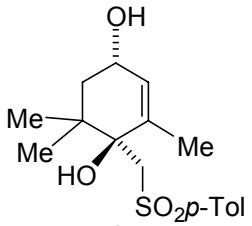


(+)-**9**

Compound (+)-**9** was obtained following method E from **7** (100 mg, 0.31 mmol), in 90% yield after flash chromatography (CH_2Cl_2/acetone 10:1), as a colorless oil: $[\alpha]_D^{20}$ = +48.0 (*c* 2, EtOH) [Lit[2] $[\alpha]_D^{20}$ = +52.7 (*c* 0.45, EtOH)]; ^{1}H RMN δ 6.61 (q, 1H, *J* = 1.7 Hz), 4.58 (m, 1H), 2.13 (ddd, 1H, *J* = 2.0, 5.0, 12.6 Hz), 1.82 (dd, 1H, *J* = 10.0 and 12.8 Hz), 1.77 (d, 1H, *J* = 1.7 Hz), 1.13 and 1.10 (2s, 6H); ^{13}C RMN δ 203.8, 146.1, 133.7, 64.9, 46.7, 41.9, 25.8, 24.4, 16.1; MS (EI): *m/z* (%) 154 (M^+, 5), 111 (14), 98 (87), 84 (100), 70 (45); HRMS (EI) calcd for $C_9H_{14}O_2$ $(M)^+$ 154.0994, found 154.0987.

[2] Kiyota, H.; Nakabayashi, M.; Oritani, T. *Tetrahedron: Asymmetry* **1999**, *10*, 3811-3817

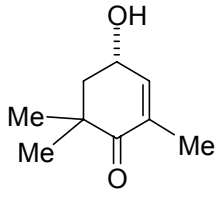
(1*S*,4*S*)-2,6,6-Trimethyl-1-[(*p*-tolylsulfonyl)methyl]-2-cyclohexene-1,4-diol (8).



8

Compound **8** was obtained following method B from **3b** (50 mg, 0.16 mmol), in 64% yield as a colorless oil: $[\alpha]_D^{20}$ = +17.0 (*c* 0.3, acetone); ^{1}H RMN δ 7.79 and 7.33 (AA'BB´ system, 4H), 5.62 (broad s, 1H), 4.09 (m, 1H), 3.40 and 3.24 (AB system, 2H, *J* = 14.5 Hz), 2.42 (s, 3H), 1.83 (broad s, 3H), 1.73-1.39 (m, 2H), 0.98 and 0.95 (2s, 6H); ^{13}C RMN δ 145.1, 140.4, 138.3, 130.1 (2C), 127.9 (2C), 127.0, 77.7, 65.4, 62.5, 43.8, 41.6, 24.7, 22.2, 21.8, 18.6.

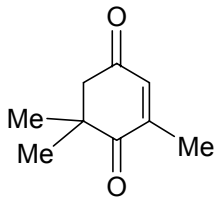
(4*S*)-4-Hydroxy-2,6,6-trimethyl-2-cyclohexenone (9).



(-)-**9**

Compound (-)-**9** was obtained following method E from **8** (27 mg, 0.08 mmol), in 93% yield after flash chromatography (CH_2Cl_2/hexane 12:1), as a colorless oil: $[\alpha]_D^{20}$ = –44.0 (*c* 0.2, EtOH) [Lit[2] $[\alpha]_D^{20}$ = –50.0 (*c* 0.1, EtOH)].

2,6,6-Trymethylcyclohexene-1,4-dione (10b).

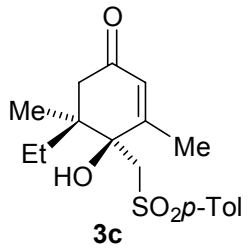


10b

Compound **10b**[3] was obtained following method E from **3b** (47 mg, 0.15 mmol), in 54% yield after flash chromatography (eluent EtOAc/hexane 1:15), as a colourless oil: ^{1}H-NMR δ 6.70 (broad s, 1H), 2.71 (s, 2H), 2.01 (s, 3H), 1.21 (s, 6H).

[3] This compound, also named 4-oxoisophorone, is commercially available.

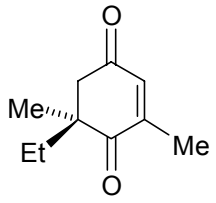
(4*R*,5*S*)-4-Hydroxy-5-ethyl-3,5-dimethyl-4-[(*p*-tolylsulfonyl)methyl]-2-cyclohexenone (3c).



3c

Compound **3c** was obtained following method A from **2c**[1] (99 mg, 0.31 mmol), in 95% yield as a white solid: mp 107-108 ºC (ethyl ether); $[\alpha]_D^{20}$ = –36.0 (*c* 0.9, $CHCl_3$); ^{1}H RMN δ 7.79 and 7.38 (AA'BB´ system, 4H), 5.93 (t, 1H, *J* = 1.4 Hz), 4.55 (broad s, 1H), 3.58 and 3.38 (AB system, 2H, *J* = 13.7 Hz), 2.47 (s, 3H), 2.45 and 2.04 (AB system, 2H, *J* = 18.6 Hz) 2.26 (d, 3H, *J* = 1.4 Hz), 1.74-1.43 (m, 2H), 0.99 (s, 3H), 0.79 (t, *J* = 7.5 Hz, 3H); ^{13}C RMN δ 196.1, 165.7, 145.4, 137.2, 130.0 (2C), 127.5 (2C), 127.1, 78.0, 61.9, 45.6, 44.2, 24.7, 21.5, 21.3, 19.3, 8.5; MS (EI): *m/z* (%) 336 (M^+, 0.14), 307 (1.6), 266 (10), 170 (10), 155 (2), 124 (8), 111 (100), 91 (46), 68 (20); HRMS (EI) calcd for $C_{18}H_{24}O_4S$ $(M)^+$ 336.1395, found 336.1386.

(6*S*)-6-Ethyl-2,6-dimethyl-2-cyclohexene-1,4-dione (10c).

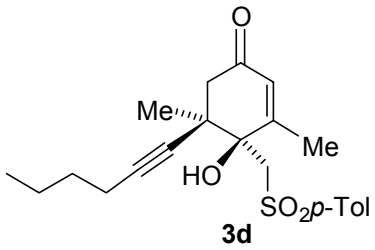


10c

Compound **10c**[4] was obtained following method E from **3c** (15 mg, 0.07 mmol), in 70% yield after flash chromatography (eluent EtOAc/hexane 1:10), as a yellowish oil: $[\alpha]_D^{20}$ = +0.6 (c 0.6, $CHCl_3$); ^{1}H-NMR δ 6.55 (bs, 1H), 2.78 (dd, *J* = 16.4 and 0.8 Hz, 1H), 2.65 (d, *J* = 16.4 Hz, 1H), 1.99 (d, *J* = 1.6 Hz, 3H), 1.79-1.51 (m, 2H), 1.19 (s, 3H), 0.82 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR δ 203.2, 198.1, 149.3, 137.0, 49.6, 48.7, 32.2, 23.2, 16.7; MS (EI): *m/z* (%) 166 (M^+, 56), 151 (15), 95 (76), 83 (37), 68 (77) 55 (100); HRMS (EI) calcd for $C_{10}H_{14}O_2$ $(M)^+$ 166.0994, found 166.0993.

[4] Racemic **10c**: Aponick, A.; Buzdygon, R. S.; Tomko, Jr., R. J.; Fazal, A. N.; Shughart, E. L.; McMaster, D. M.; Myers, M. C.; Pitcock, Jr., W. H.; Wigal, C. T. *J. Org. Chem.* **2002**, *67*, 242-244.

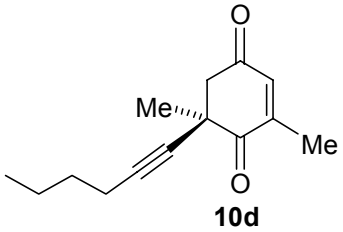
(4*R*,5*S*)-5-(1-Hexynyl)-4-hydroxy-3,5-dimethyl-4-[(*p*-tolylsulfonyl)methyl]-2-cyclohexenone (3d).



3d

Compound **3d** was obtained following method A from **2d**[1] (150 mg, 0.40 mmol), in 99% yield as a white solid: mp 86-87 ºC (ethyl ether); $[\alpha]_D^{20}$ = +15.0 (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.78 and 7.34 (AA´BB´ system, 4H), 5.91 (d, 1H, *J* = 1.4 Hz), 3.74 (broad s, 1H), 3.52 and 3.36 (AB system, 2H, *J* = 14.1 Hz), 2.71-2.46 (m, 2H), 2.43 (s, 3H), 2.19 (d, 3H, *J* = 1.4 Hz), 2.08 (t, 2H, *J* = 6.9 Hz), 1.43-1.22 (m, 4H), 1.32 (s, 3H), 0.84 (t, 3H, *J* = 7.3 Hz); ^{13}C RMN δ 195.2, 145.2, 137.5, 129.9 (2C), 127.8 (2C), 127.6, 85.1, 81.1, 75.8, 60.3, 47.8, 44.8, 30.6, 22.7, 21.6, 21.6, 20.9, 18.1, 13.4. Anal. calcd. for $C_{22}H_{28}O_4S$: C, 68.01; H, 7.26. Found C, 67.78; H, 7.43.

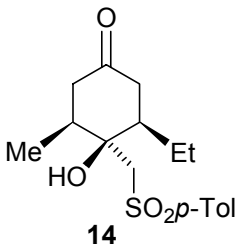
(6*R*)-6-(1-Hexynyl)-2,6-dimethyl-2-cyclohexene-1,4-dione (10d).



10d

Compound **10d** was obtained following method **E** from **3d** (42 mg, 0.108 mmol), in 68% yield after flash chromatography (EtOAc/hexane 1:10), as a yellowish oil: $[\alpha]_D^{20}$ = –3.0 (c 0.8, $CHCl_3$); ^{1}H-NMR δ 6.53 (q, *J* = 1.4 Hz, 1H), 2.97 (dd, *J* = 15.8 and 1.4 Hz , 1H), 2.76 (d, *J* = 15.8 Hz, 1H), 2.10 (t, *J* = 6.9 Hz, 2H), 2.04 (d, *J* = 1.4 Hz, 3H), 1.45 (s, 3H), 1.43-1.22 (m, 4H), 0.86 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR δ 196.3, 195.8, 149.4, 136.9, 85.3, 80.1, 51.3, 44.0, 30.5, 23.9, 21.7, 18.3, 17.1, 13.5; MS (EI): *m/z* (%) 218 (M^+, 13), 203 (20), 190 (32), 175 (32), 161 (30), 147 (25), 133 (17) , 96 (100), 68 (82); HRMS (EI) calcd for $C_{14}H_{18}O_2$ $(M)^+$ 218.1307, found 218.1304.

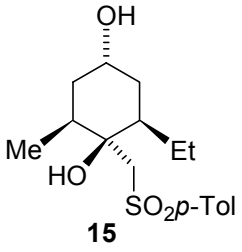
(3*R*,4*S*,5*S*)-3-Ethyl-4-hydroxy-5-methyl-4-[(*p*-tolylsulfonyl)methyl]-cyclohexanone (14).



14

Compound **14** was obtained following method A from **13**[1] (235 mg, 0.76 mmol), in 98% yield as a white solid: mp 147-148 ºC (ethyl ether); $[\alpha]_D^{20}$ = +9.0 (*c* 1, acetone); ^{1}H NMR δ 7.76 and 7.34 (AA´BB´ system, 4H), 3.44 and 3.38 (AB system, 2H, *J* = 14.4 Hz), 2.49-2.12 (m, 6H), 2.39 (s, 3H), 1.83-1,76 (m, 1H), 1.30-1.22 (m, 1H), 1.04 (d, 3H, *J* = 6.0 Hz), 0.85 (t, 3H, *J* = 7.3 Hz); ^{13}C RMN δ 210.2, 144.9, 138.0, 130.0 (2C), 127.6 (2C), 74.9, 59.4, 45.5, 44.8, 40.9, 39.3, 22.7, 21.6, 15.8, 11.3. Anal. calcd. for $C_{17}H_{24}O_4S$: C, 62.94; H, 7.46; S, 9.88. Found C, 63.06; H, 7.13; S, 9.71.

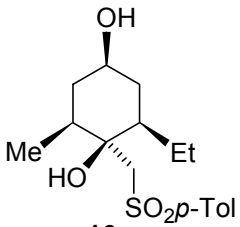
(1*S*,2*R*,4*S*,6*S*)-2-Ethyl-6-methyl-1-[(*p*-tolylsulfonyl)methyl]-cyclohexane-1,4-diol (15).



15

Compound **15** was obtained following method **C** from **14** (130 mg, 0.40 mmol), in 73 % yield after flash chromatography (EtOAc/hexane 1:1), as a white solid: mp 146-147 ºC; $[\alpha]_D^{20}$ = +3.0 (*c* 1, acetone); ^{1}H-RMN δ 7.80 and 7.33 (AA´BB´ system, 4H), 4.05 (m, 1H), 3.44 and 3.35 (AB system, 2H, *J* = 15.0 Hz), 2.43 (s, 3H), 2.43-2.32 (m, 1H), 2.09-1.97 (m, 1H), 1.86-1.38 (m, 5H), 1.22-1.05 (m, 1H), 0.90 (d, 3H, *J* = 7.5 Hz), 0.87 (t, 3H, *J* = 6.9 Hz); ^{13}C-RMN δ 144.6, 138.3, 129.9 (2C), 127.7 (2C), 75.9, 65.5, 60.3, 39.4, 36.8, 32.9, 32.6, 22.0, 21.6, 15.4, 11.9. Anal. calcd. for $C_{17}H_{26}O_4S$: C, 62.55; H, 8.03; S, 9.82; Found: C, 62.33; H, 7.81; S, 10.06.

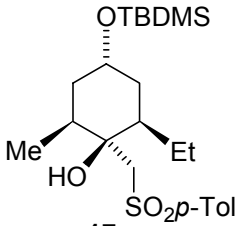
(1*S*,2*R*,4*R*,6*S*)-2-Ethyl-6-methyl-1-[(*p*-tolylsulfonyl)methyl]-cyclohexane-1,4-diol (16).



16

Compound **16** was obtained following method **B** from **14** (124mg, 0.38 mmol), in 75% yield after flash chromatography (EtOAc/hexane 1:1), as a white solid: mp 87-88 ºC (EtOAc/hexane); $[\alpha]_D^{20}$ = +3.8 (*c* 1, $CHCl_3$); ^{1}H-NMR δ 7.79 and 7.35 (AA´BB´ system, 4H), 3.77-3.67 (m, 1H), 3.39 and 3.30 (AB system, 2H, *J* = 14.5 Hz), 2.45 (s, 3H), 2.28-2.15 (m, 1H), 2.09-1.97 (m, 1H), 1.95-1.64 (m, 3H), 1.50-1.32 (m, 1H), 1.29-1.08 (m, 2H), 1.01 (d, 3H, *J* = 6.5 Hz), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C-RMN δ 144.9, 138.7, 130.1 (2C), 127.8 (2C), 75.5, 59.5, 43.7, 37.3, 35.1, 22.4, 21.8, 19.8, 15.8, 15.6, 12.0. Anal. calcd. for $C_{17}H_{26}O_4S$: C, 62.94; H, 7.46; S, 9.88. Found C, 63.06; H, 7.13; S, 9.71.

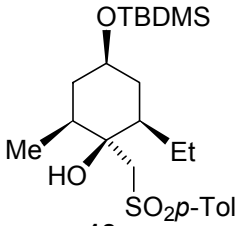
(1*S*,2*R*,4*S*,6*S*)-4-(*terc*-Butyldimethylsilyloxy)-2-ethyl-6-methyl-1-[(*p*-tolylsulfonyl)methyl]-cyclohexan-1-ol (17).



17

Compound **17** was obtained following method **D** from **15** (95 mg, 0.29 mmol), in 81% yield after flash chromatography (EtOAc/hexane 4:1), as a white solid: mp 121-122 ºC (EtOAc/hexane); $[\alpha]_D^{20}$ = +1.0 (*c* 1, acetone). ^{1}H-NMR δ 7.78 and 7.32 (AA´BB´ system, 4H), 4.05 (m, 1H), 3.42 and 3.35 (AB system, 2H, *J* = 14.5 Hz), 2.42 (s, 3H), 2.45-2.31 (m, 1H), 2.13-1.94 (m, 1H), 1.82-0.90 (m, 5H), 0.92-0.86 (m, 15H), 0.07 (s, 6H); ^{13}C-NMR δ 144.4, 138.4, 129.7 (2C), 127.9 (2C), 75.9, 65.9, 60.7, 39.7, 37.0, 33.2 (2C), 25.8 (3C), 21.8, 21.6, 15.9, 15.4, 11.9, –3.4 (2C). Anal. calcd. for $C_{23}H_{40}O_4SSi$: C, 62.68; H, 9.15; S, 7.27; Found: C, 62.57; H, 8.98; S, 7.33.

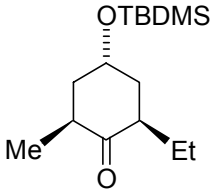
(1*S*,2*R*,4*R*,6*S*)-4-(*terc*-Butyldimethylsilyloxy)-2-ethyl-6-methyl-1-[(*p*-tolylsulfonyl)methyl]-cyclohexan-1-ol (18).



18

Compound **18** was obtained following method **D** from **16** (90 mg, -0.27 mmol), in 87% yield after flash chromatography (EtOAc/hexane 1:4), as a white solid: mp 121-122 ºC (EtOAc/hexane); $[\alpha]_D^{20}$ = +3.8 (*c* 0.8, $CHCl_3$). ^{1}H-NMR δ 7.75-7.32 (AA´BB´ system, 4H), 3.70-3.60 (m, 1H), 3.36 and 3.27 (AB, *J* = 14.5 Hz, 2H), 2.41 (s, 3H), 2.25-2.16 (m, 1H), 1.94-1.60 (m, 4H), 1.46-1.33 (m, 2H), 1.28-1.13 (m, 3H), 0.97 (d, *J* = 6.4 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 6H); ^{13}C-NMR δ 144.4, 138.4, 129.8 (2C), 127.3 (2C), 75.3, 69.6, 58.8, 43.2, 39.6, 36.8, 25.8 (3C), 25.5, 22.1, 21.5, 18.0, 15.6, 11.7, –3.7 (2C); FAB-MS *m/z* (rel intens) 441 ($[M + H]^+$, 100), 423 (47), 383 (32), 291 (74), 267 (62), 231 (41), 213 (43); HRMS (FAB) calcd for $C_{23}H_{41}O_4SiS$ $([M + H])^+$ 441.2516, found 441.2495.

(2*R*, 4*S*, 6*S*)-2-Ethyl-6-methyl-4-(*terc*-butyldimethylsilyloxy) -cyclohexanone (11).



11

Compound **11** was obtained following method **E** from **17** (50 mg, 0.11 mmol), in 60% yield after flash chromatography (hexane), as a colourless oil: $[\alpha]_D^{20}$ = –1.7 (c 1.1, $CHCl_3$); ^{1}H-NMR δ 4.13 (q, 1H, *J* = 2.8 Hz), 2.91 (sept, 1H, *J* = 6.5 Hz), 2.71 (sext, 1H, *J* = 6.1 Hz), 2.08 (m, 2H), 1.79 (sept, 1H, 6.5 Hz), 1.49 (m, 2H), 1.17 (m, 1H), 0.98 (d, 3H, *J* = 6.5 Hz), 0.92 (s, 9H), 0.87 (t, 3H, *J* = 7.7 Hz), 0.09 (s, 6H); ^{13}C-NMR δ 214.8, 66.0, 45.9, 44.5, 41.7, 39.5, 25.8 (3C), 21.6, 18.0, 14.1, 11.7, –3.4 (2C); MS (EI): *m/z* (%) 213 ($[M - C_4H_9]^+$, 70), 171 (100), 157 (82), 143 (9) 129 (32), 101 (11), 86 (46), 75 (92); HRMS (EI) calcd for $C_{11}H_{21}O_2Si$ $([M - C_4H_9])^+$ 213.1311, found 213.1309.

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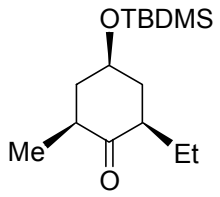
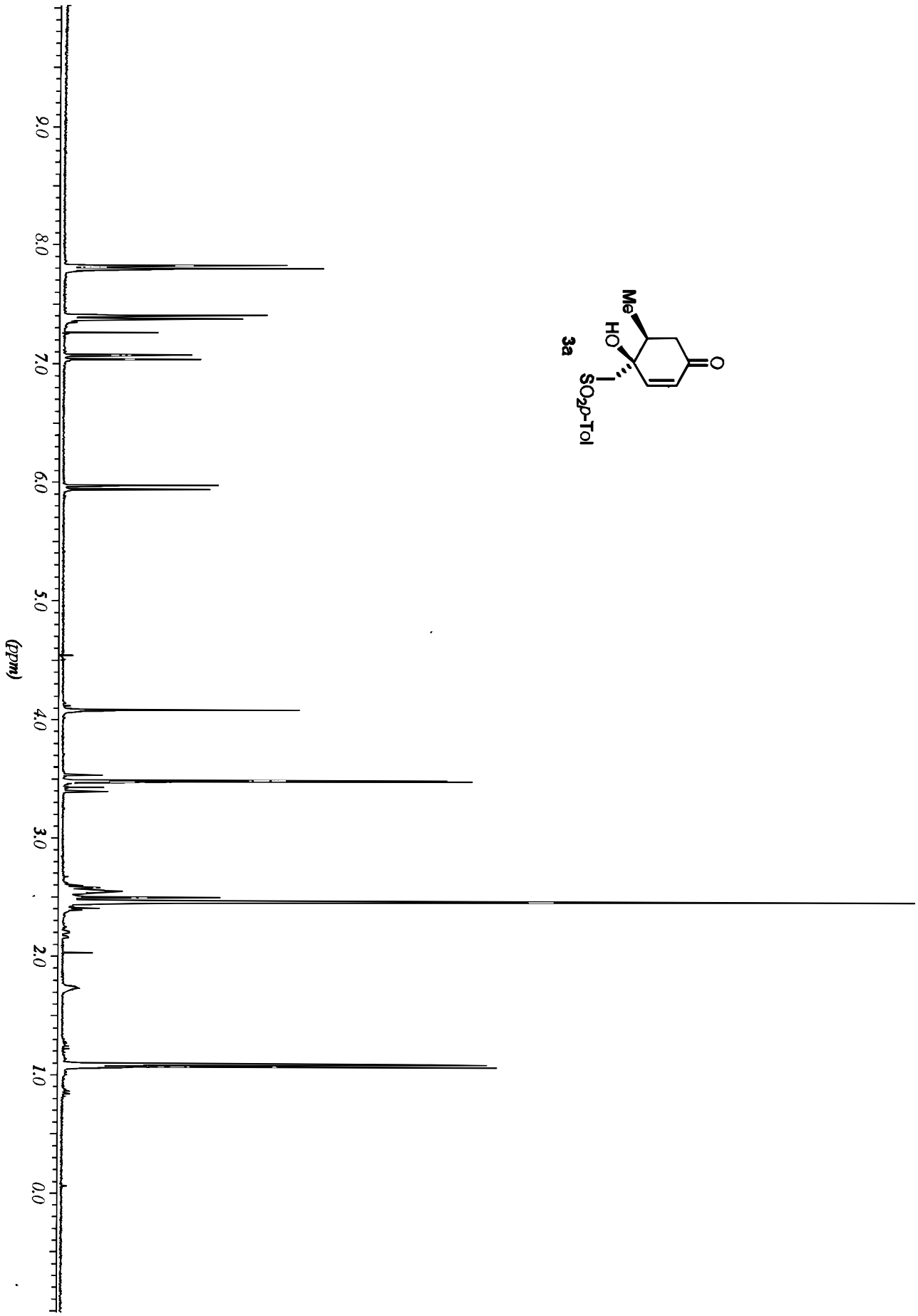
(2*R*, 4*R*, 6*S*)-2-Ethyl-6-methyl-4-(*terc*-butyldimethylsilyloxy) -cyclohexanone (12).



12

Compound **12** was obtained following method **E** from **18** (80 mg, 0.18 mmol), in 89% yield after flash chromatography (EtOAc/hexane 1:10), as a colouress oil: $[\alpha]_D^{20} = -4.5$ (c 1.1, $CHCl_3$); ^{1}H-NMR δ 4.15 (m, 1H), 2.42 (m, 1H), 2.17 (m, 1H), 1.78 (m, 1H), 1.51-1.34 (m, 2H), 1.28-1.17 (m, 2H), 0.99 (d, 3H, *J* = 6.5 Hz), 0.88 (t, 3H, *J* = 7.3 Hz), 0.89 (s, 9H), 0.09 (s, 6H); ^{13}C-NMR δ 212.7, 69.1, 48.4, 44.9, 42.3, 41.9, 25.8 (3C), 21.9, 18.1, 14.3, 11.7, –3.6 (2C); MS (EI): *m/z* (%) 213 ($[M - C_4H_9]^+$, 65), 171 (100), 157 (85), 129 (27), 75 (67); HRMS (EI) calcd for $C_{11}H_{21}O_2Si$ ($[M - C_4H_9]$)$^+$ 213.1279, found 213.1320.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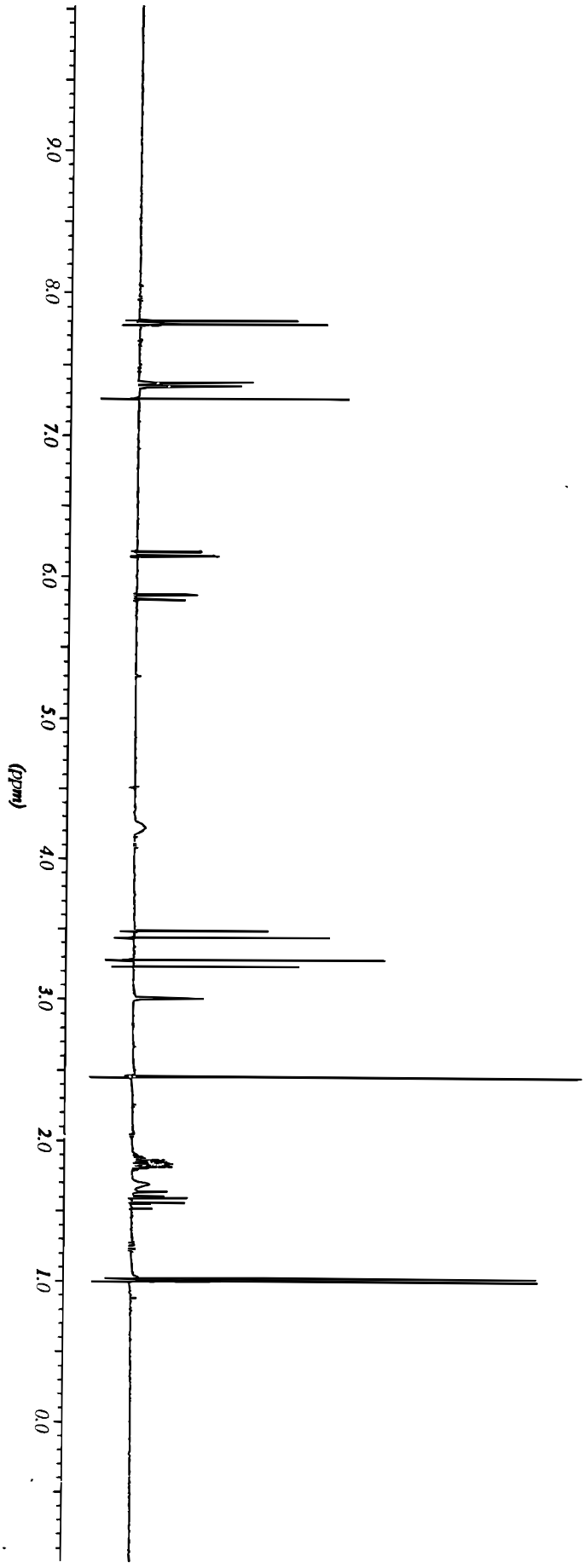
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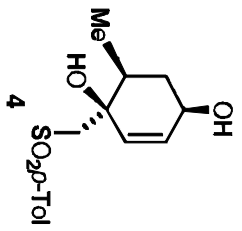
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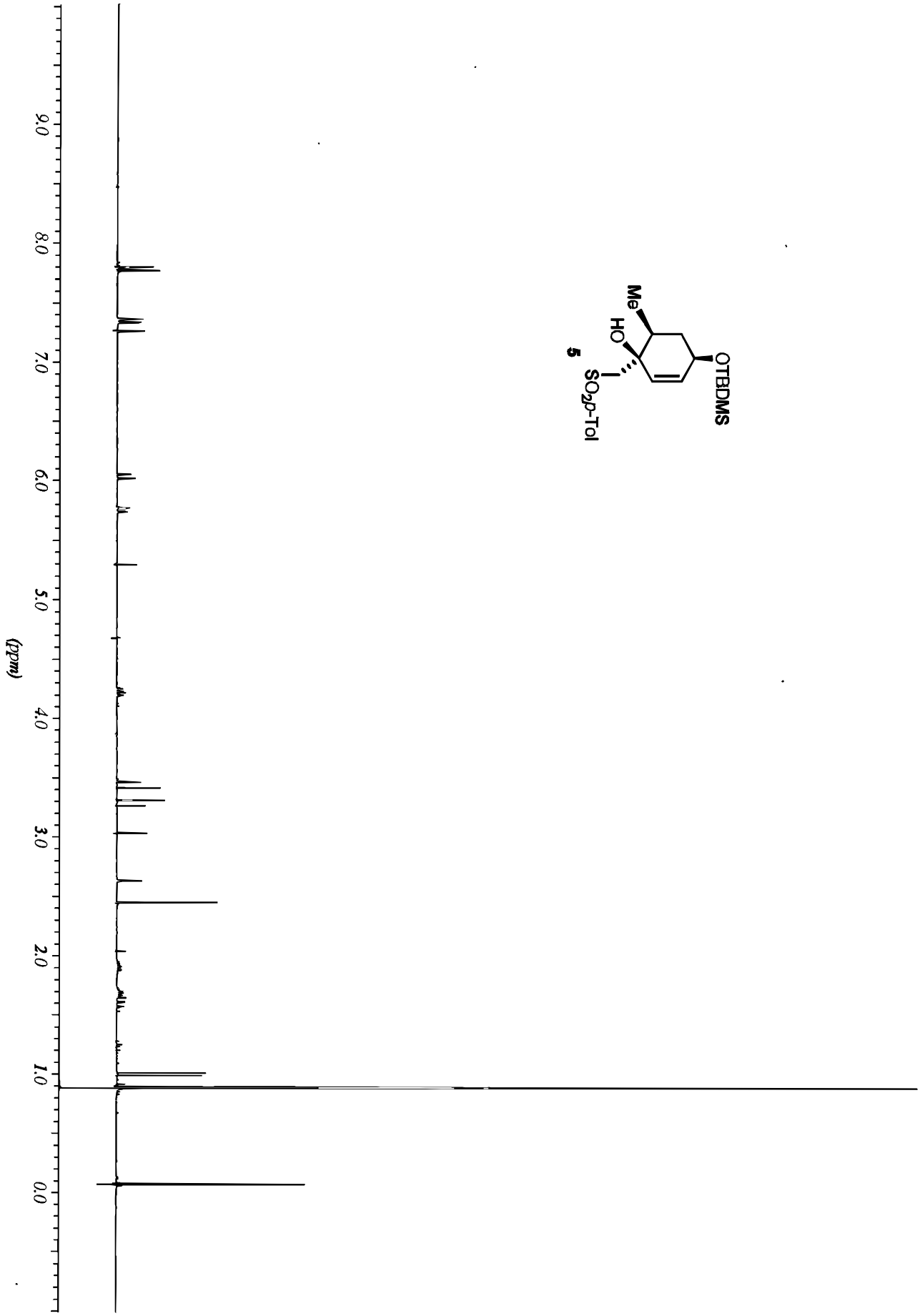

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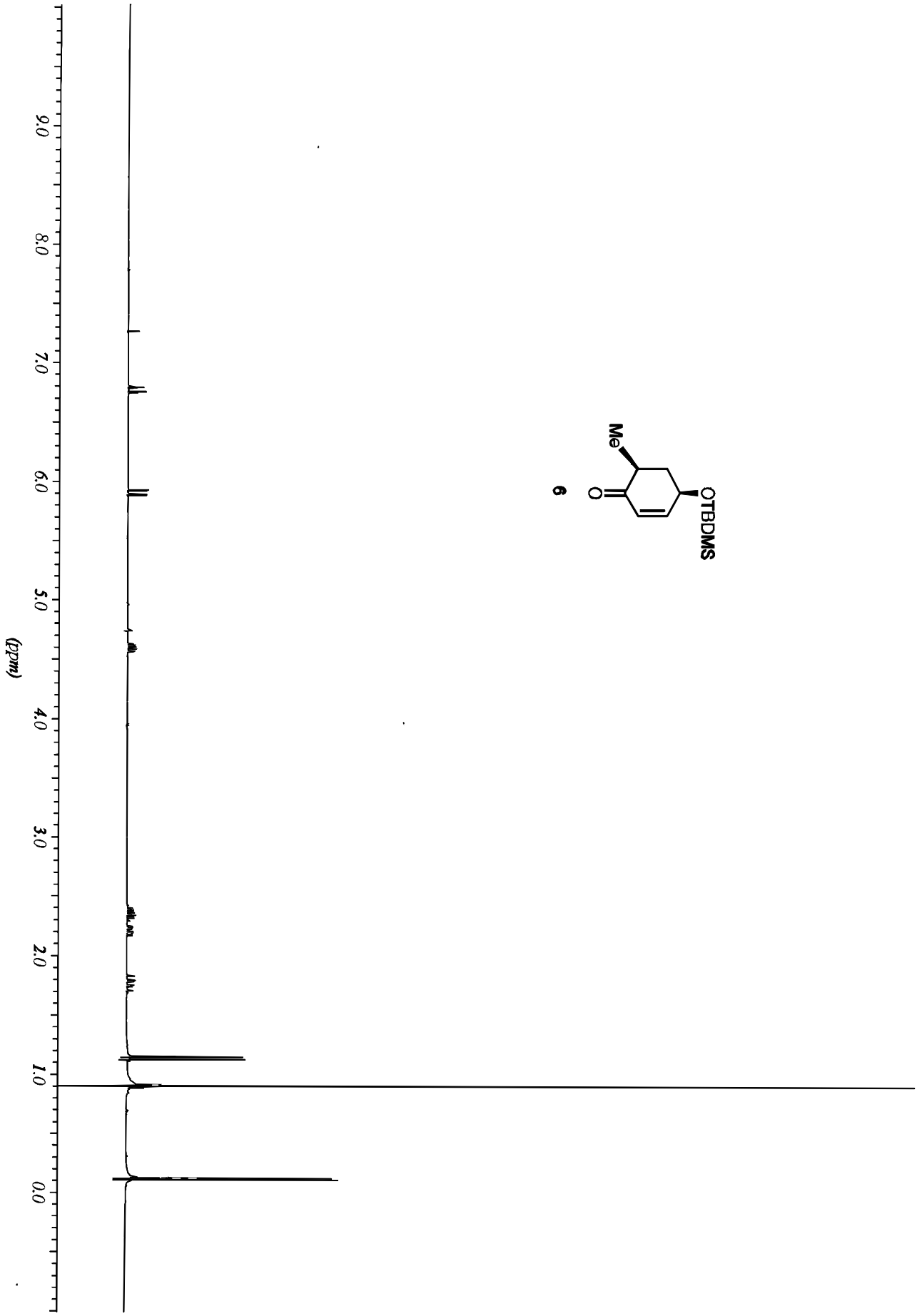
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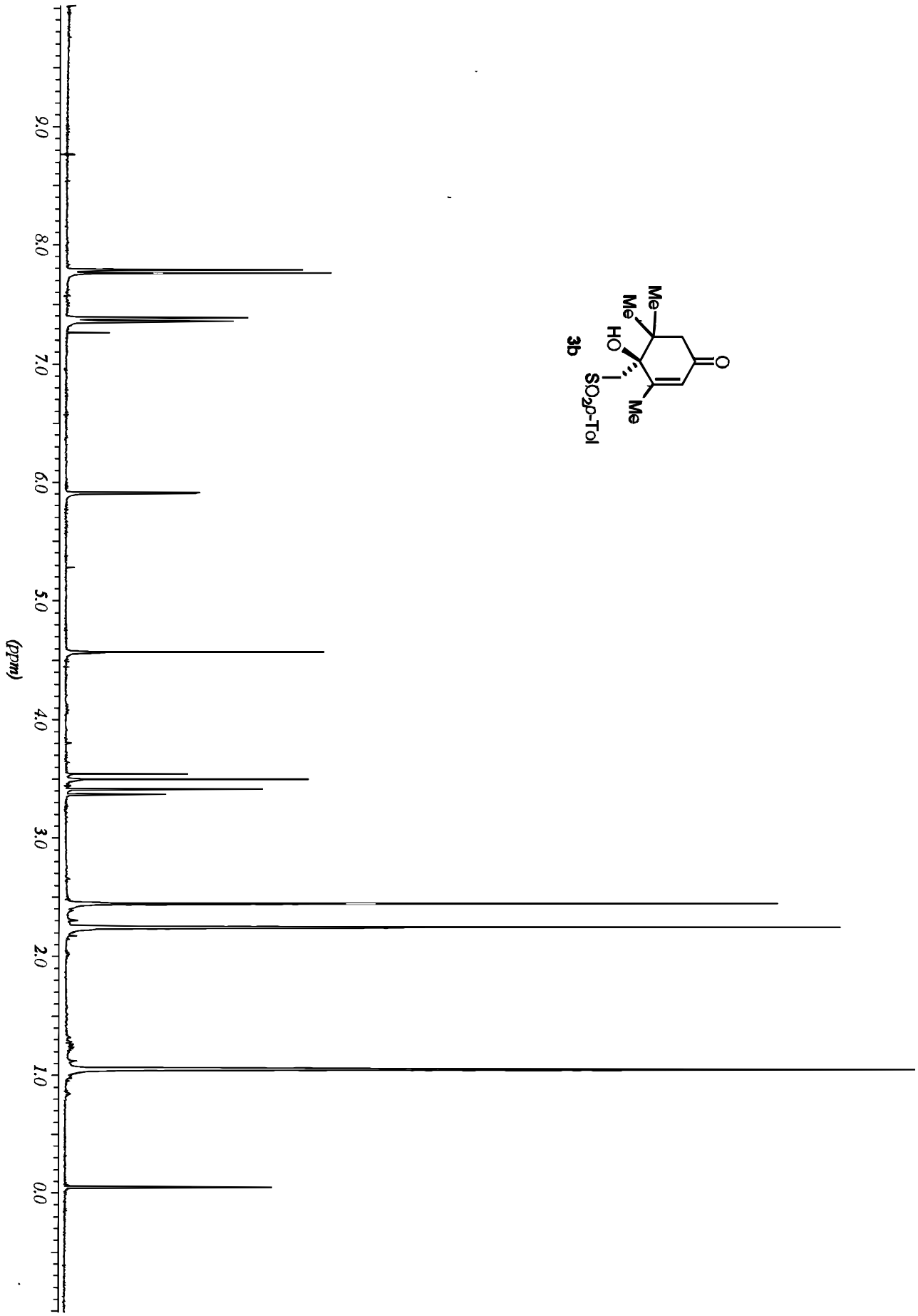
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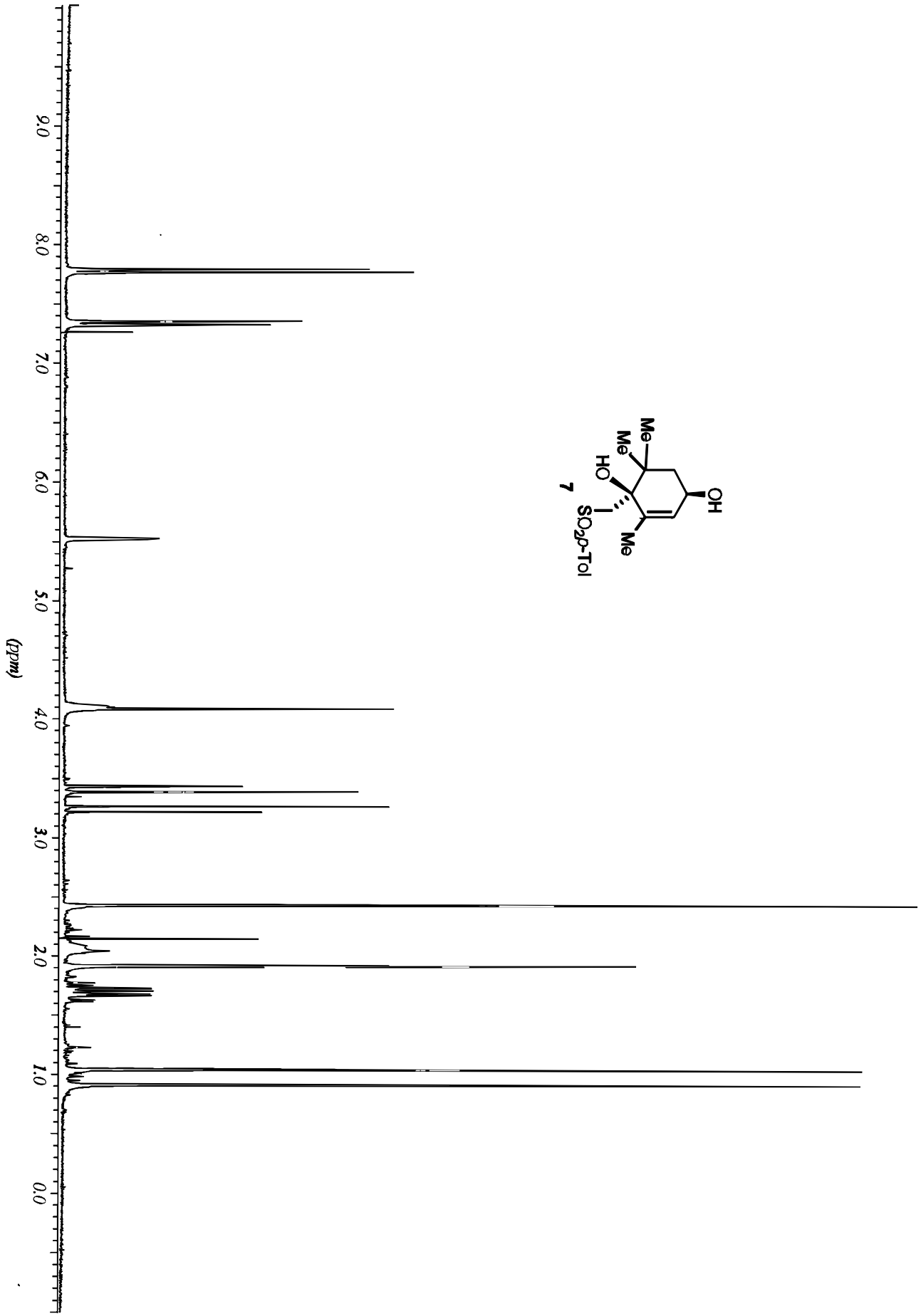
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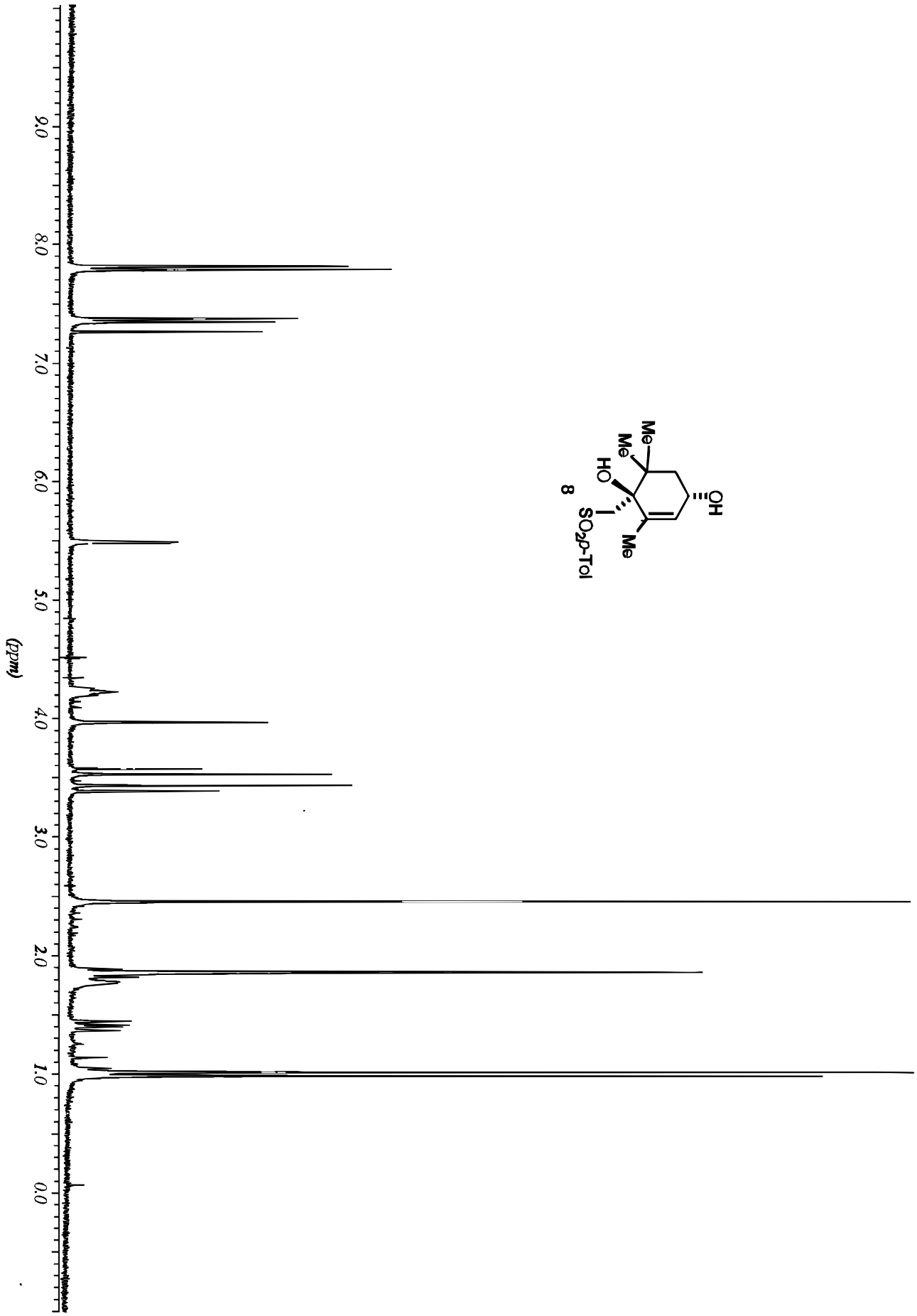

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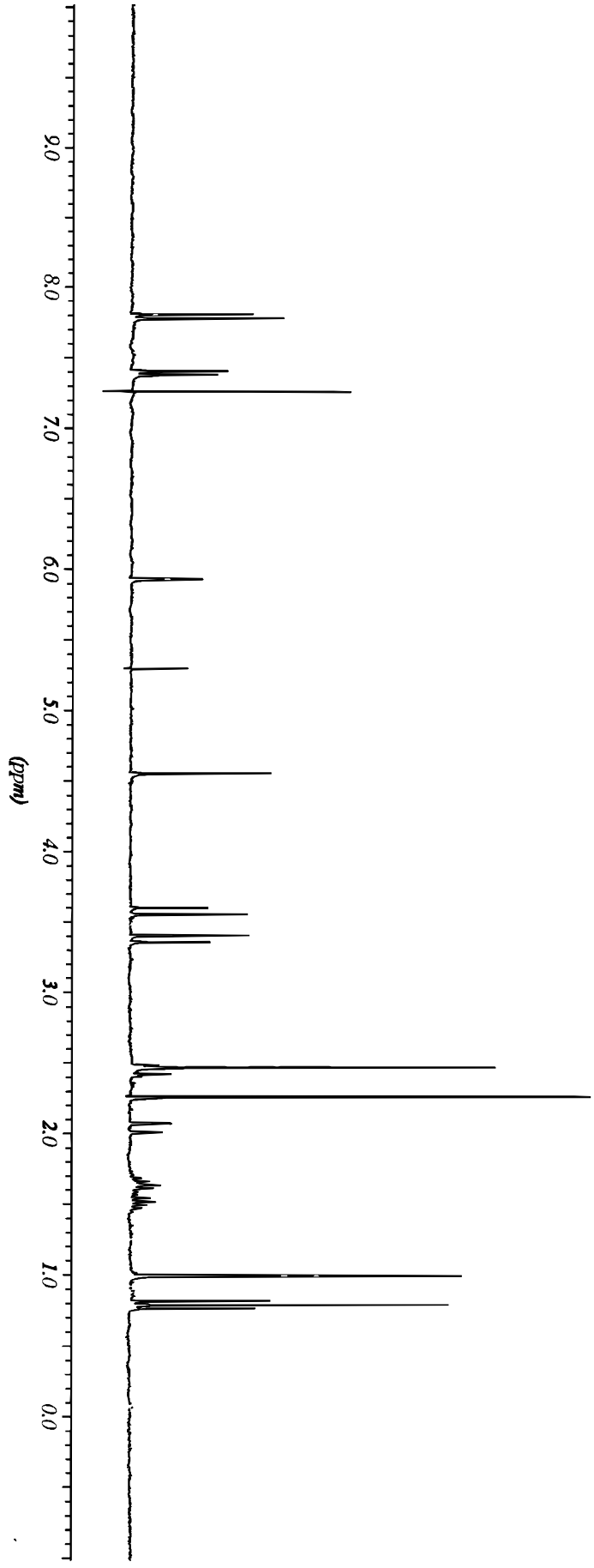

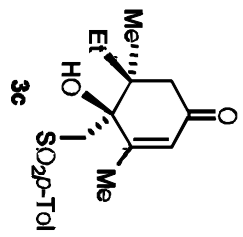

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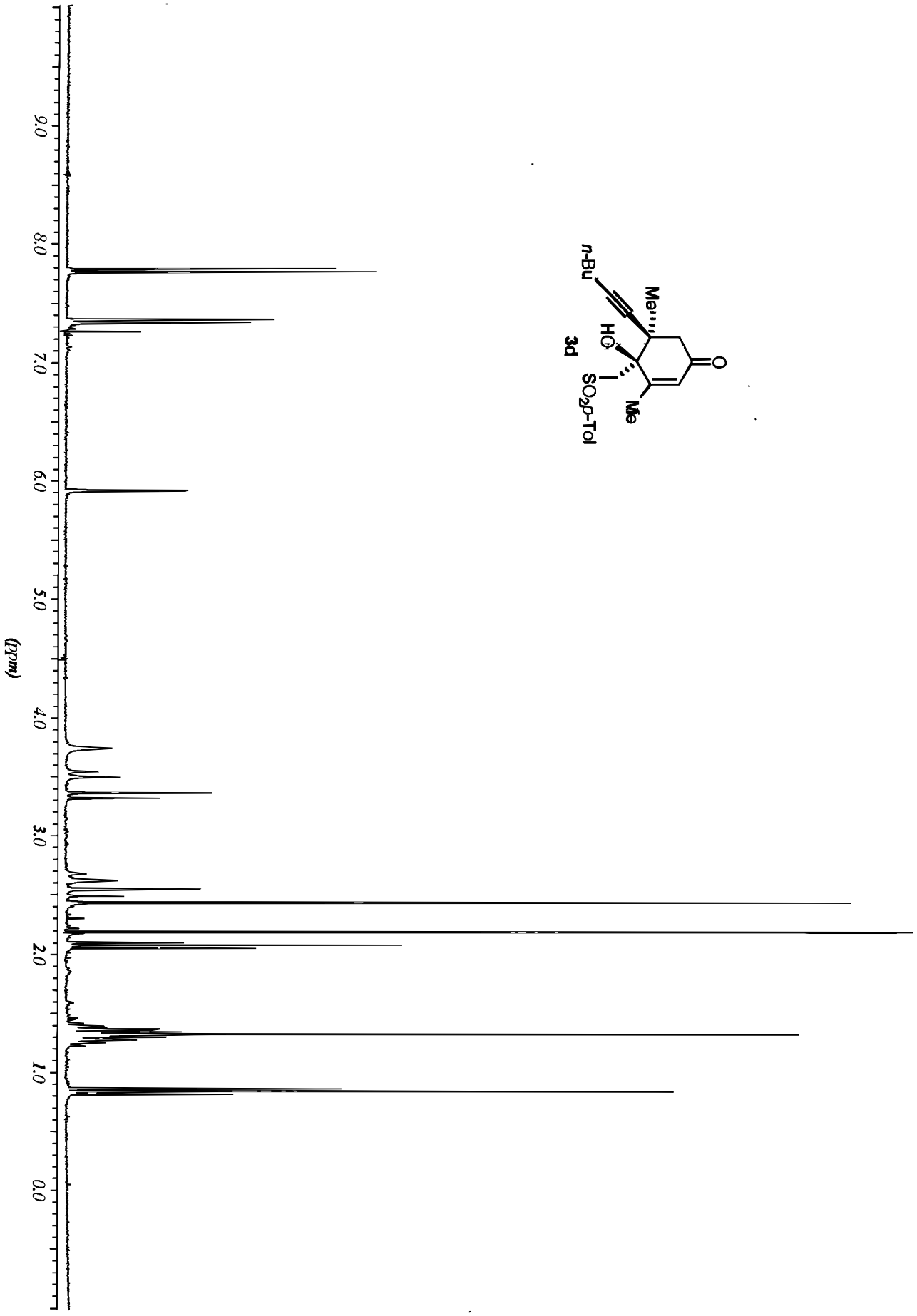
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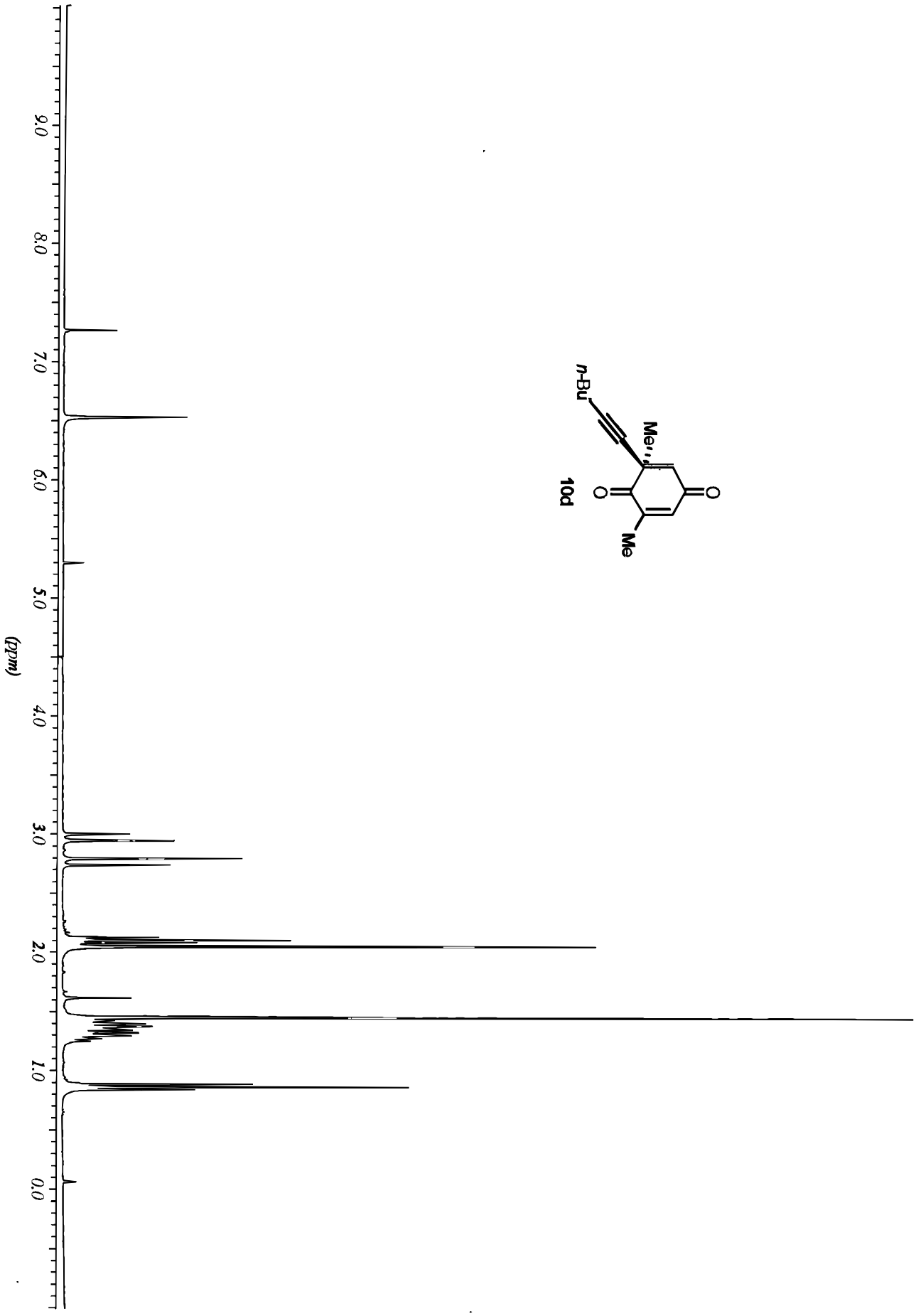
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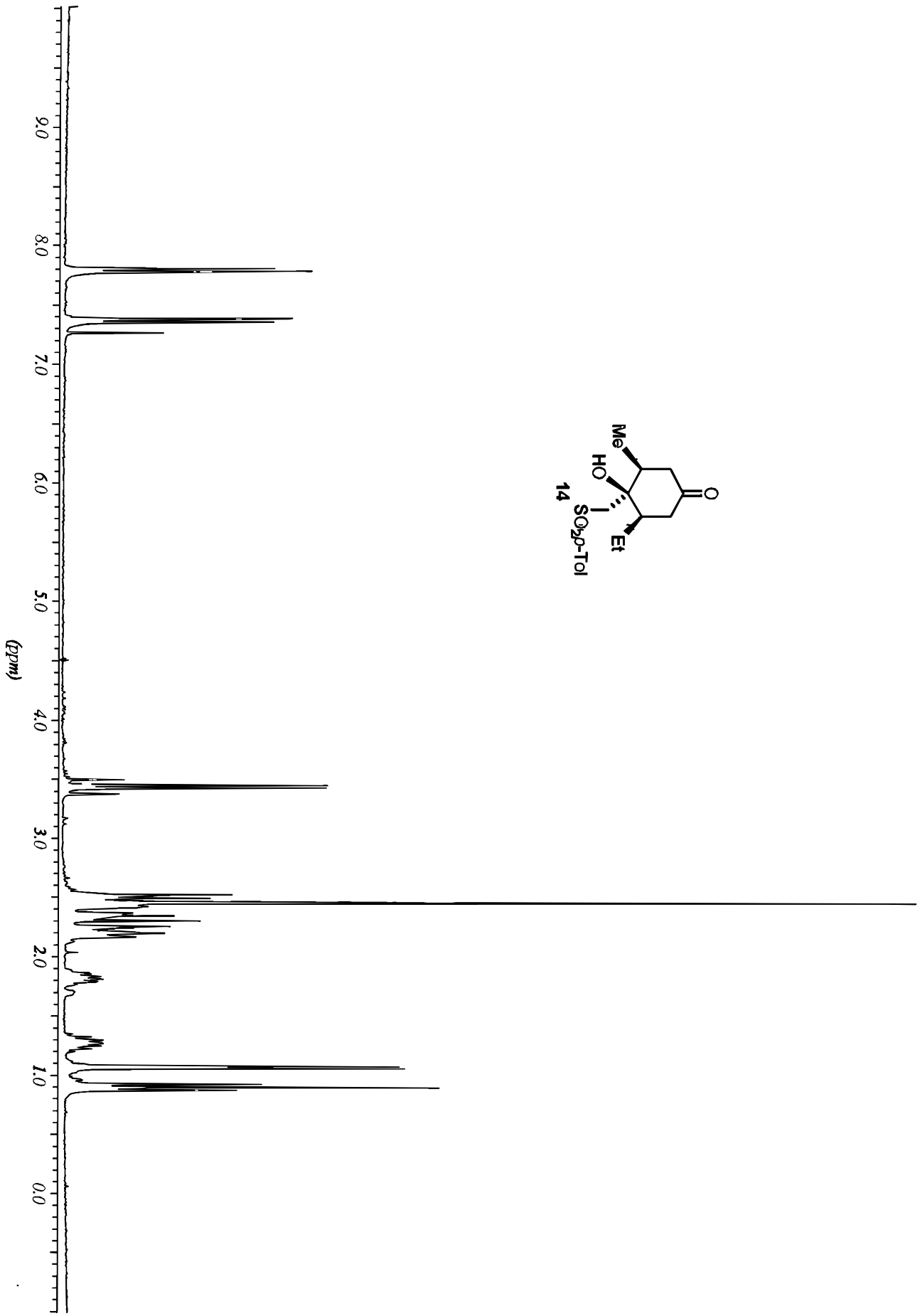
O
O
Me
10d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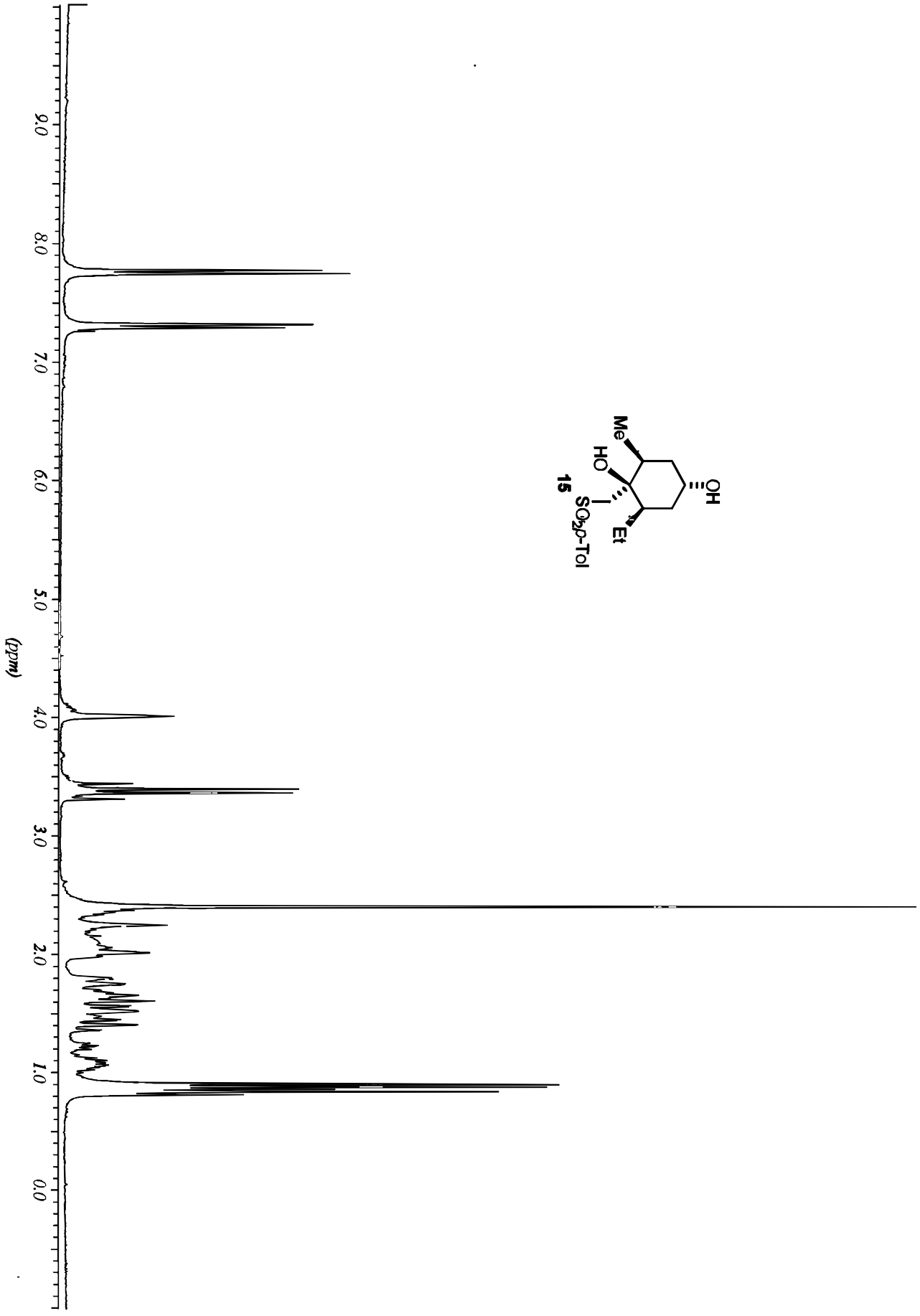

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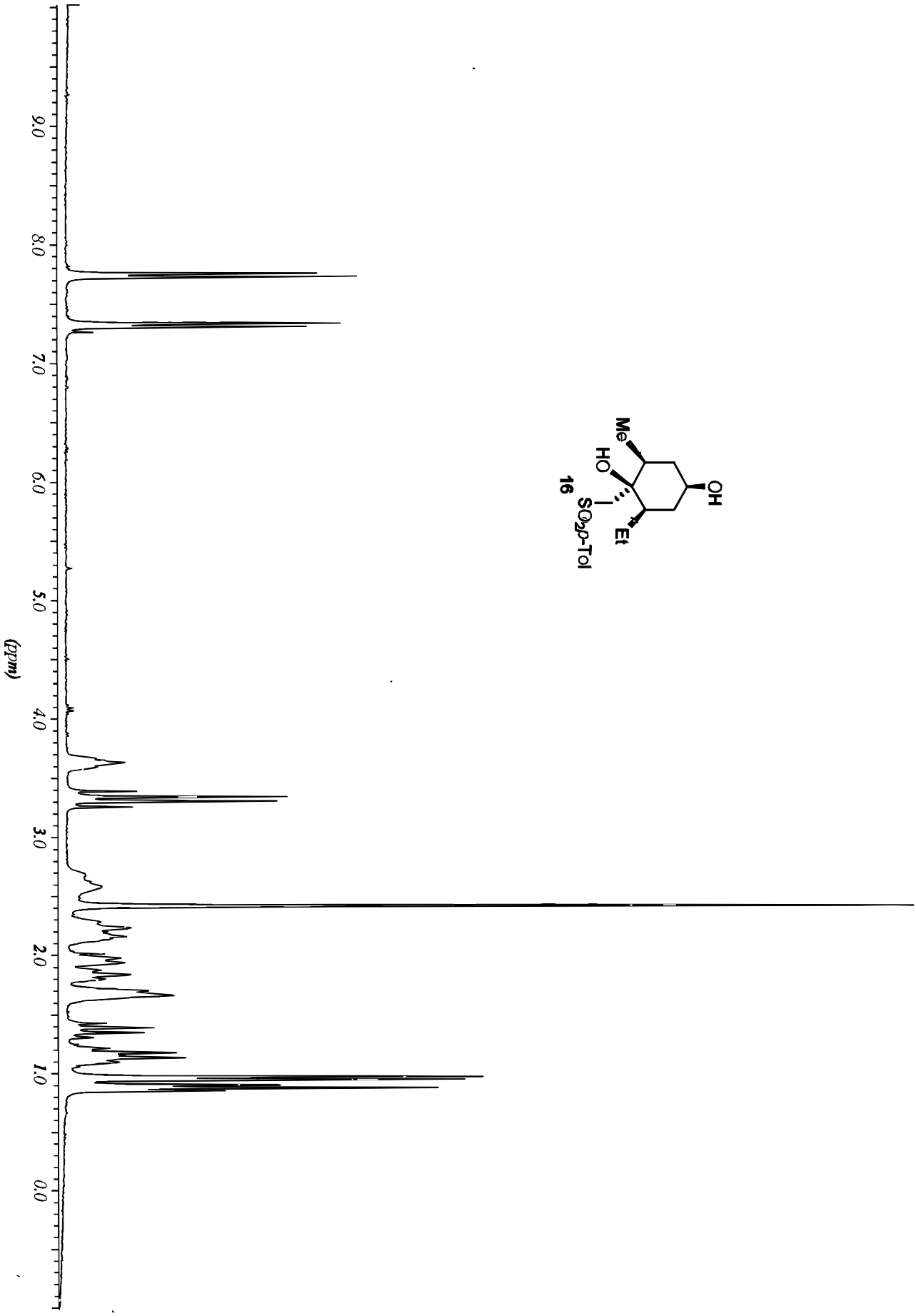
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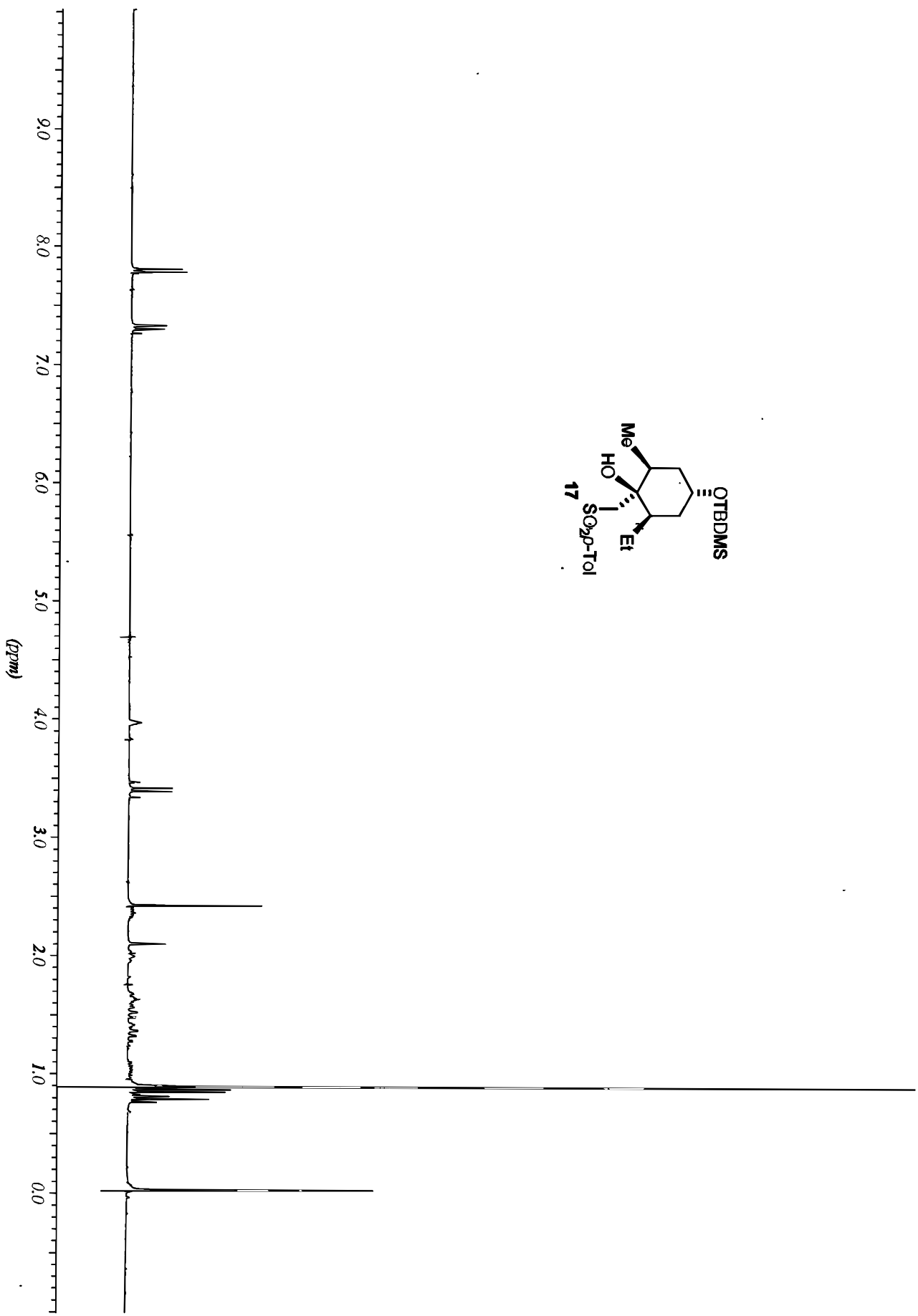
HO
Et
OH
SO2p-Tol
16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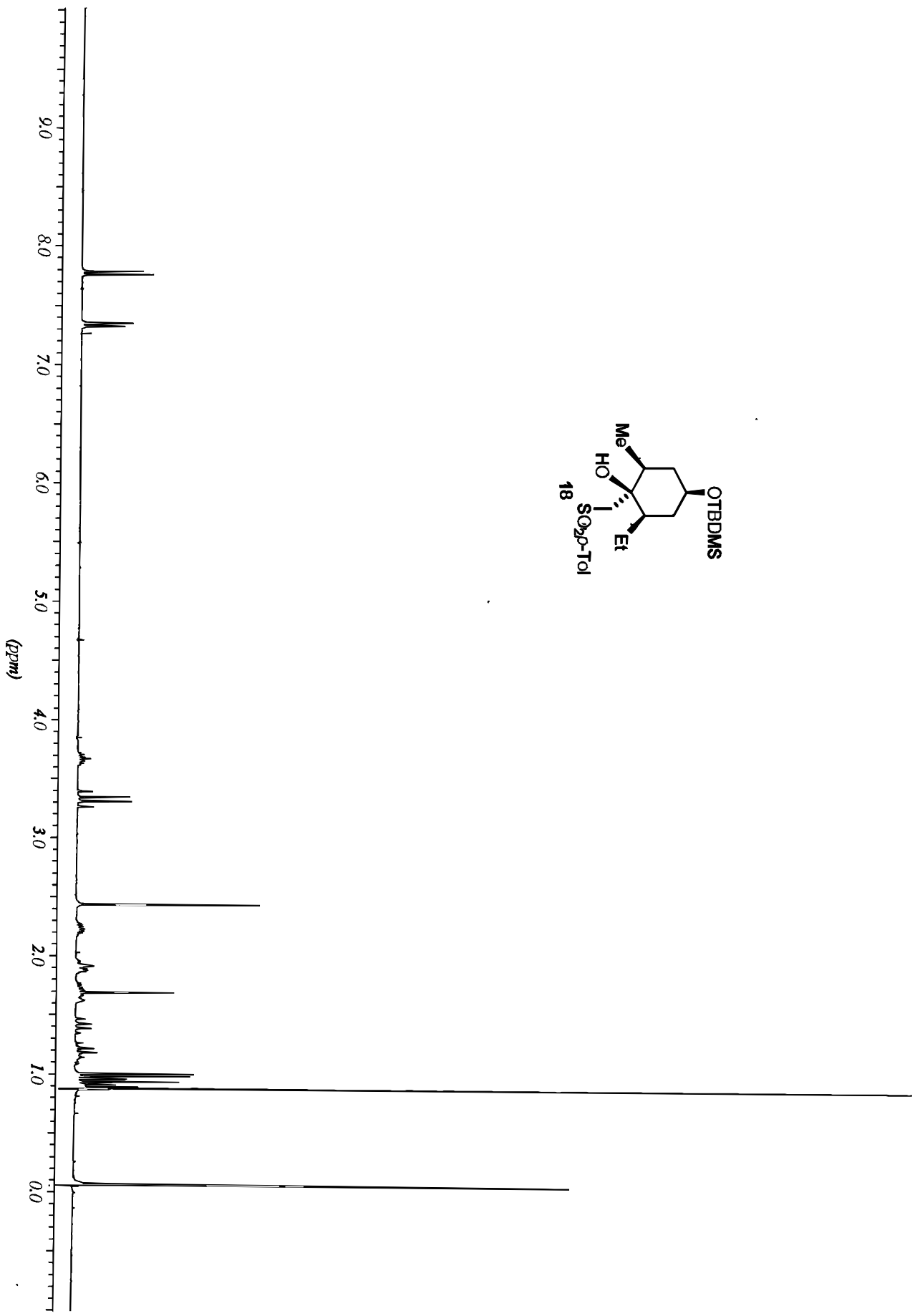
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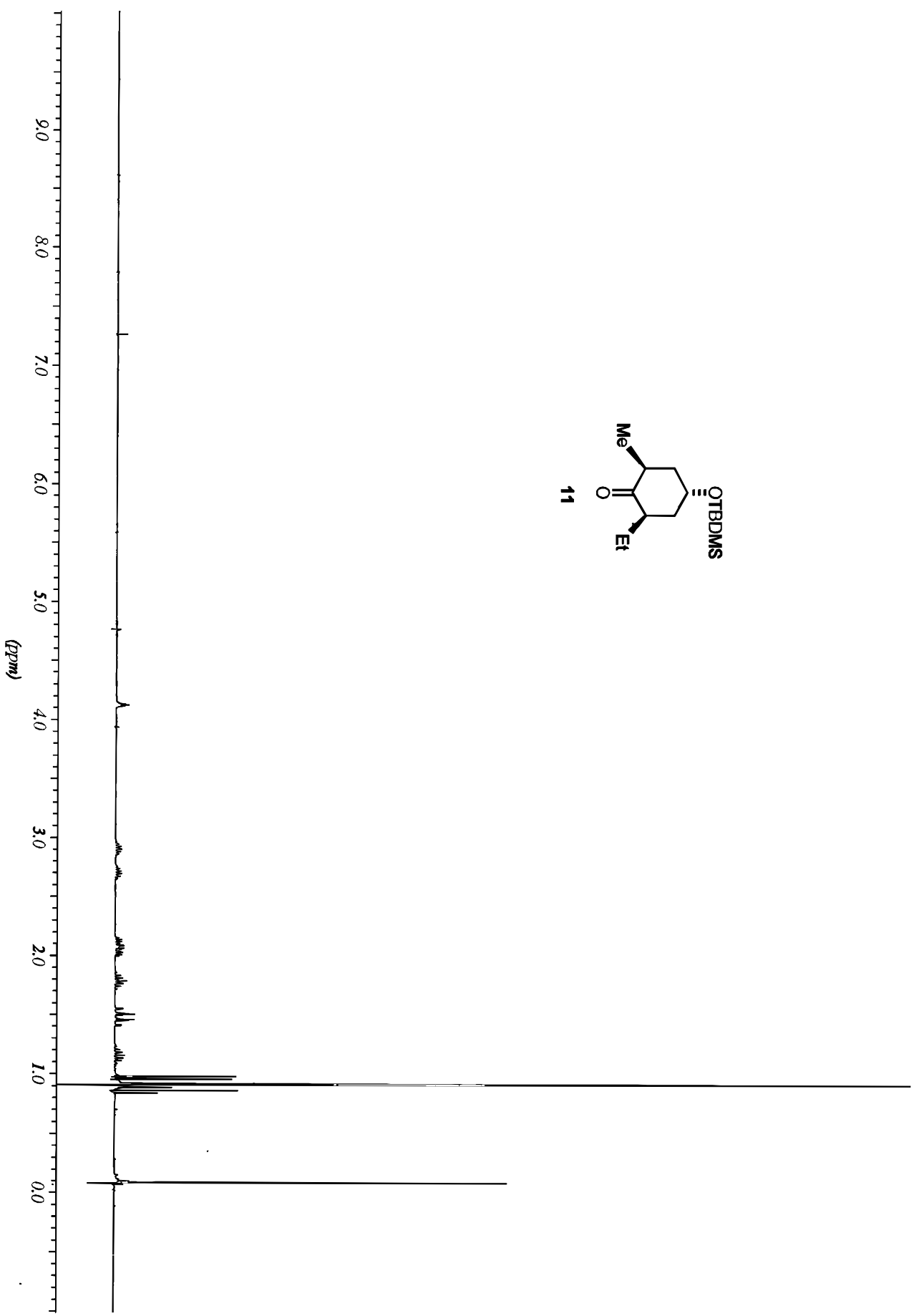
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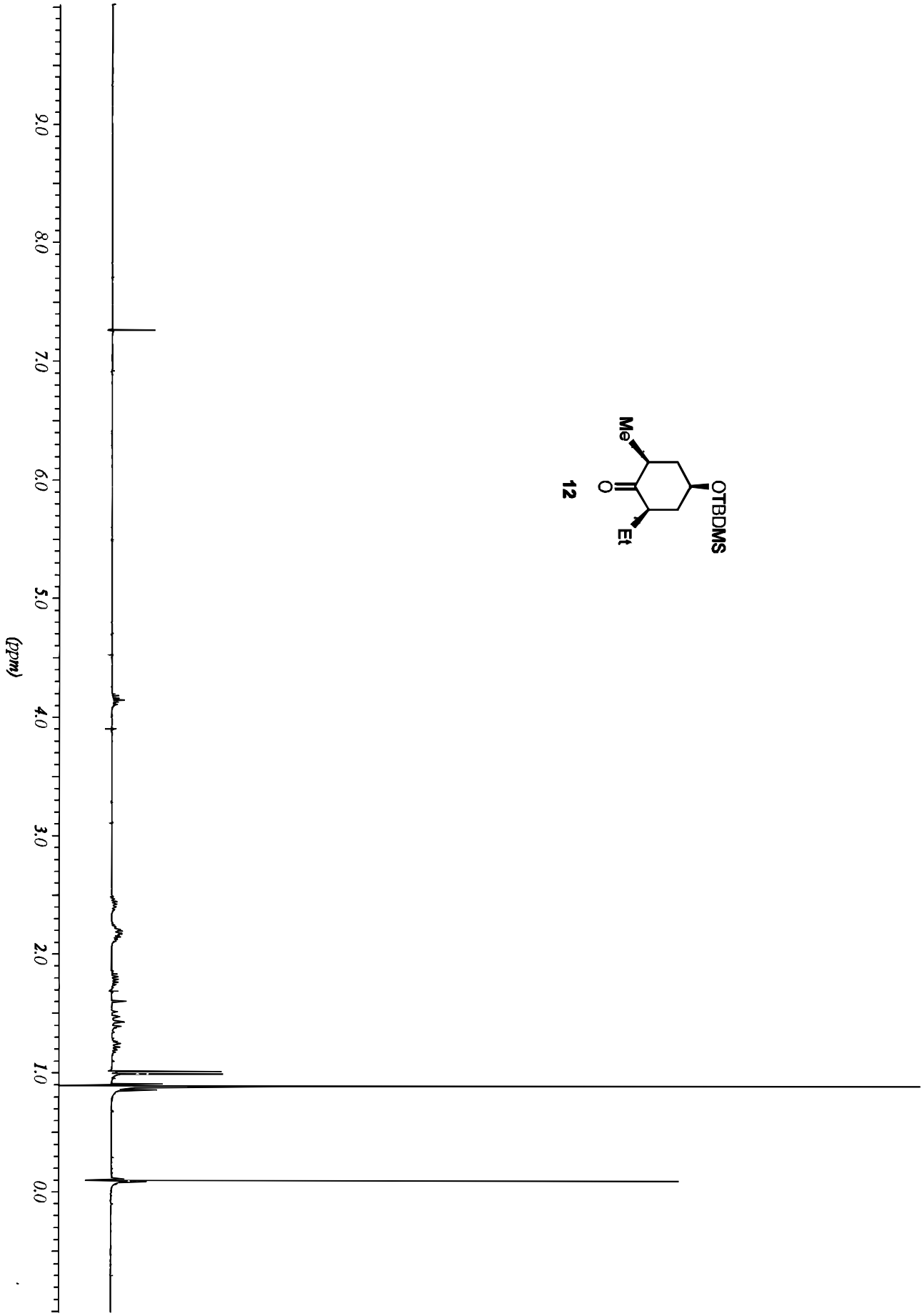
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Et
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12