Stereoselective Synthesis of the ABC Ring System of Norzoanthamine

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Supporting Information

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General Techniques

All reagents were commercially obtained (Aldrich, Acros) at highest commercial quality and used without further purification except where noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Organic solutions were concentrated by rotary evaporation below 45 °C at approximately 20 mmHg. All non-aqueous reactions were carried out under anhydrous conditions using flame-dried glassware within an argon atmosphere in dry, freshly distilled solvents, unless otherwise noted. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), toluene ($PhCH_3$) and benzene (PhH) were purified by passage through a bed of activated alumina.[1] *N*,*N*-diisopropylethylamine (DIPEA), diisopropylamine, pyridine, triethylamine (TEA) and boron trifluoride etherate were distilled from calcium hydride prior to use.[2] Dimethyl sulfoxide (DMSO) and dimethylformamide (DMF) were distilled from calcium hydride under reduced pressure (20 mmHg) and stored over 4Å molecular sieves until needed. Yields refer to chromatographically and spectroscopically (^{1}H NMR, ^{13}C NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as the visualizing agent and 10% ethanolic phosphomolybdic acid (PMA) or *p*-anisaldehyde solution and heat as developing agents. E. Merck silica gel (60, particle size 0.040-0.063 mm) was used for flash chromatography. Preparative thin-layer chromatography separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Varian Mercury 300, 400 and/or Unity 500 MHz instruments and calibrated using the residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. IR spectra were recorded on a Nicolet 320 Avatar FT-IR spectrometer and values are reported in cm^{-1} units. Optical rotations were recorded on a Jasco P-1010 polarimeter and values are reported as follows: $[\alpha]^{T}_{\lambda}$ (c: g/100ml, solvent). High resolution mass spectra (HRMS) were recorded on a VG 7070 HS mass spectrometer under chemical

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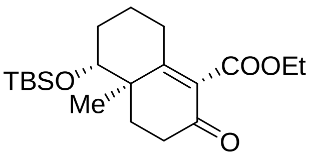
[1] . Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.

[2] . Perrin, D. D.; Armarego, W. L. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: Oxford, **1988**.

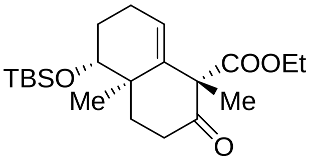
ionization (CI) conditions or on a VG ZAB-ZSE mass spectrometer under fast atom bombardment (FAB) conditions. X-ray data were recorded on a Bruker SMART APEX 3kW Sealed Tube X-ray diffraction system.



13

Ester 13: To a stirred solution of enone **8** (11.2 g, 44.7 mmol) in dry EtOH (180 mL) at -78 °C was added $NaBH_4$ (413 mg, 11.1 mmol) portionwise (4 x 100 mg) The reaction mixture was stirred at that temperature for 1 h and was quenched with glacial acetic acid (2 mL). After evaporation of EtOH under reduced pressure, the residue was extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were washed with brine (2 x 100 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography (silica, 40:60 ethyl acetate in hexanes) to give the corresponding C13 alcohol (10.39 g, 41.1 mmol 92%), as a white solid R_f = 0.25 (50% ethyl acetate in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.24 (2H, q, *J* = 7.0 Hz), 3.45 (1H, m), 2.51-2.00 (6H, m), 1.91-1.78 (3H, m), 1.72 (1H, m), 1.41 (1H, m), 1.90 (3H, t, *J* = 7.0 Hz), 1.20 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0, 166.9, 164.7, 131.9, 77.5, 61.3, 41.5, 33.3, 33.2, 29.8, 29.0, 22.7, 15.6, 14.2.

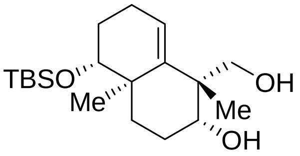
A solution of alcohol obtained in the above step (10.0 g, 39.63 mmol) and dry DMF (70 mL) was treated with ammonium nitrate (9.5 g, 118.9 mmol) and TBSCl (8.9 g, 59.4 mmol) at 0 °C. The mixture was warmed to 25 ^{0} °C and stirred overnight, and then quenched with a saturated solution of aqueous ammonium chloride (30 mL). The reaction mixture was extracted with ethyl acetate (2 x 150 mL). The combined organic extracts were washed with brine (2 x 100 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography (silica, 6:94 ethyl acetate in hexanes), to give **13** (13.07 g, 35.65 mmol, 90%). **13:** White solid: R_f = 0.47 (20% ethyl acetate in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27 (2H, q, *J* = 7.2 Hz), 3.44 (1H, dd, *J* = 4.8, 11.2 Hz), 2.50-2.40 (2H, m), 2.35-2.10 (2H, m), 2.10 (1H, m), 1.86 (1H, m), 1.80-1.66 (3H, m), 1.42 (1H, m), 1.31 (3H, t, *J* = 7.2 Hz), 1.21 (3H, s), 0.90 (9H, s), 0.06 (3H, s), 0.045 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 166.5, 164.0, 131.7, 78.1, 60.8, 41.7, 33.5, 33.2, 30.1, 28.7, 25.6, 25.5, 22.3, 17.8, 15.6, 14.0, -4.1, -5.0; HRMS calcd. for $C_{20}H_{34}O_4Si$ (M+ Na^+) 389.2124, found 389.2103.



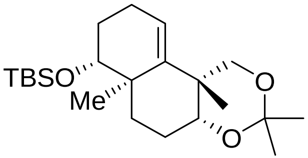
7

Ester 7: A solution of compound **13** (10.0 g, 27.28 mmol) was added to a suspension of potassium *tert*-butoxide (3.36 g, 30 mmol) in dry benzene (100 mL) at 0 °C. After stirring at 25 °C for 30 min it was cooled to 0 °C and treated with excess methyl iodide (5 mL, 80.31 mmol). After stirring for 12 h at 25 °C the reaction mixture was quenched with saturated solution of aqueous ammonium chloride (30 mL) and extracted with ethyl acetate (2 x 100 mL). The combined organic extracts were washed with brine (100 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography (silica, 4:96

ethyl acetate in hexanes) to give **7** (7.05 g, 18.7 mmol, 68%). **7:** White solid: R_f = 0.5 (20% ethyl acetate in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.52 (1H, t, *J* = 3.8 Hz), 4.20-4.06 (2H, m), 3.47 (1H, dd, *J* = 11.6, 3.6, Hz), 2.70 (1H, m), 2.42 (1H, m), 2.20-2.04 (3H, m), 1.78 (1H, m), 1.73-1.63 (3H, m), 1.43 (3H, s), 1.22 (3H t, *J* = 6.8 Hz), 1.08 (3H, s), 0.90 (9H, s), 0.07 (3H, s), 0.04 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.4, 172.6, 141.8, 123.6, 76.0, 61.4, 60.3, 39.9, 34.9, 32.7, 26.6, 25.9, 24.8, 22.7,18.3, 18.1, 14.0, -3.8, -4.7; HRMS calcd. for $C_{21}H_{36}O_4Si$ (M+ Na^+) 403.2281, found 403.2270.

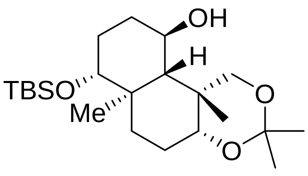


Alkene 14 Precursor: Lithium aluminum hydride (1.36 g, 36.8 mmol) was added to a stirred solution of compound **7** (7.0 g, 18.4 mmol) in dry tetrahydrofuran (100 mL) at 0 ^{o}C. The mixture was stirred at 0 ^{o}C for 2h and at 25 ^{o}C for 6h. After cooling to 0 ^{o}C, the reaction mixture was quenched with saturated solution of aqueous Na_2SO_4 (20 mL) and was extracted with ethyl acetate (3 x 100 mL), the combined organic extracts were washed with brine (2 x 50 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography (silica, 35:65 ethyl acetate in hexane) to give the corresponding diol (5.32 g, 15.6 mmol, 85%) as a white solid: R_f = 0.5 (70% ethyl acetate in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (1H, dd, *J* = 4.0, 3.6 Hz), 4.06 (1H, dd, *J* = 5.5, 10.6 Hz), 3.46 (1H, d, *J* = 10.8 Hz), 3.40-3.30 (2H, m), 2.37 (1H, dd, *J* = 5.6 Hz), 2.28 (1H, m), 2.17-2.14 (2H, m), 1.97-1.86 (2H, m), 1.81-1.75 (1H, m), 1.69-1.63 (2H, m), 1.57 (1H, m), 1.32 (3H, s), 1.07 (3H, s), 0.90 (9H, s), 0.06 (3H, s), 0.04 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 123.8, 78.6, 78.2, 67.5, 46.3, 39.2, 35.2, 27.4, 26.5, 26.0, 25.2, 21.9, 19.8, 18.2, -3.8, -4.6; HRMS calcd. for $C_{19}H_{36}O_3Si$ (M+ Na^+) 363.2331, found 363.2361.



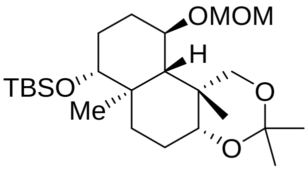
14

Alkene 14: A stirred solution of diol (5.0 g, 14.7 mmol) in CH_2Cl_2 (30 mL) was treated with excess 2,2-dimethoxy propane (10 mL, 81.32 mmol) and CSA (34 mg, 0.146 mmol) at 0 ^{o}C. After stirring for 30 min the reaction mixture was quenched with a saturated solution of sodium bicarbonate (10 mL) and extracted with CH_2Cl_2 (100 mL). The organic layer was washed with brine (30 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography (silica, 2:98 ethyl acetate in hexanes) to give **14** (5.3 g, 13.9 mmol, 95%). **14:** White solid; R_f = 0.8 (10% ethyl acetate in hexanes).^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (1H, t, *J* = 3.6 Hz), 3.92 (1H, d, *J* = 11.6 Hz), 3.67 (1H, t, *J* = 5.6 Hz), 3.39 (1H dd, *J* = 12.0, 3.6 Hz), 3.30 (1H, d, *J* = 11.6 Hz), 2.23-2.09 (2H, m), 1.91-1.73 (4H, m), 1.62 (1H, m), 1.42 (3H, s), 1.41 (3H, s), 1.26 (1H, m), 1.23 (3H, s), 1.12 (3H, s), 0.90 (9H, s), 0.06 (3H, s), 0.05 (3H, s), ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 121.0, 98.4, 77.3, 74.2, 68.8, 39.0, 38.9, 30.7, 26.9, 26.6, 26.3, 26.0, 24.8, 24.5, 23.7, 20.3, 18.2 -3.7, -4.6; HRMS calcd. for $C_{22}H_{40}O_3Si$ (M+ Na^+) 403.2644, found 403.2674.



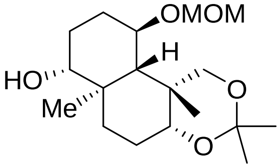
15

Alcohol 15: A stirred solution of compound **14** (6.0 g, 15.8 mmol) in dry THF (40 mL) at 0 °C was treated with 1 M BH3:THF solution (31.6 mL, 31.6 mmol). The mixture was kept at 0 °C for 6 h and then 25 °C overnight. A mixture of aqueous NaOH (3N, 42 mL) and H_2O_2 (30%, 42 mL) was added at 0 °C and the reaction was stirred for 6h. The reaction mixture was extracted with ethyl acetate (2 x 150 mL), the combined organic extracts were washed with brine (100 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by column chromatography (silica, 8:92 ethyl acetate in hexanes) to give **15** (3.39 g, 8.5 mmol, 54 %). **15:** White solid; R_f = 0.45 (30% ethyl acetate in hexanes). ^1H NMR (400 MHz, $CDCl_3$) d (4.02, 1H, d, *J* = 11.2 Hz), 3.84(1H, m), 3.63(1H, d, *J* = 11.2 Hz), 3.45(1H, dd, *J* = 6.0, 3.2 Hz), 3.19(1H, dd, *J* = 9.6, 5.0 Hz), 1.93 (1H, m), 1.80 (1H, m), 1.72-1.56 (5H, m), 1.43 (3H, s), 1.37 (3H, s), 1.33 (1H, m), 1.34 (3H, s), 1.21 (3H, s), 1.05 (1H, d, *J* = 10.8), 0.95 (1H, d, *J* = 6.0 Hz), 0.87 (9H, s), 0.05(3H, s), 0.03 (3H, s). ^{13}C NMR (100 M Hz, $CDCl_3$) δ 99.8, 80.2, 75.6, 68.5, 64.6, 52.7, 39.3, 38.4, 36.0, 32.9, 29.7, 28.6, 25.9, 25.3, 24.6, 23.0, 18.2, 15.9, -3.5, -4.7; HRMS calcd. for $C_{22}H_{42}O_4Si$ (M+ Na^+) 421.2750, found 421.2781.



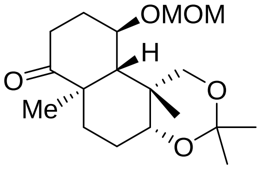
16

MOM protected Alcohol 16: A stirred solution of compound **15** (3 g, 7.53 mmol) in dry dichloromethane (30 mL) was treated at 0 °C with DIPEA (5.32 mL, 30.12 mmol) followed by MOMCl (1.71 mL, 22.59 mmol). After stirring at 25 °C for 24 h the reaction mixture was quenched with aqueous ammonium chloride and extracted with ethyl acetate (2 x 75 mL), the combined organic extracts were washed with brine (50 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by column chromatography (silica, 6:94 ethyl acetate in hexanes), to give **16** (2.99 g, 6.8 mmol, 90 %). **16:** Colorless liquid; R_f = 0.55 (30% ethyl acetate in hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 4.47 (1H, d, *J* = 6.8 Hz), 4.60 (1H, d, *J* = 6.8 Hz), 3.96 (1H, d, *J* = 11.2 Hz), 3.62 (1H, dt, *J* = 10.8, 4.4Hz), 3.47 (1H, d, *J* = 11.2 Hz), 3.43 (1H, m), 3.36 (3H, s), 3.18 (1H, dd, *J* = 10.8, 4.4 Hz), 2.17 (1H, m), 1.78 (1H, m), 1.71-1.46 (4H, m), 1.42 (3H, s), 1.40-1.25 (2H, m,) 1.36 (3H, s), 1.31 (3H, s), 1.21 (3H, s), 1.05 (1H, d, *J* = 10.8 Hz), 0.87 (9H, s), 0.04 (3H, s), 0.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.8, 96.1, 80.2, 76.3, 75.5, 64.5, 56.1, 51.6, 39.4., 38.5, 32.9, 32.0, 29.5, 28.1, 25.9, 25.1, 24.6, 22.8, 18.2, 16.0, -3.5, -4.8; HRMS calcd. for $C_{24}H_{46}O_5Si$ (M+ Na^+) 465.3012, found 465.3032.



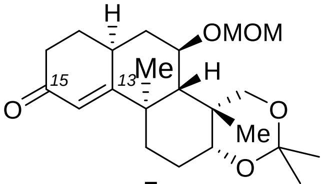
Ketone 6 Precursor: A stirred solution of compound **16** (2.9 g, 6.56 mmol) in anhydrous THF (15 mL) was treated at 0 °C with 1M TBAF in THF (13.10 mL, 13.10 mmol). The resulting mixture was heated at 50 °C for 48 h and then quenched with aqueous ammonium chloride and extracted with ethyl acetate (2 x 70 mL) the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by column chromatography (silica,

16:84 ethyl acetate in hexanes) to give the alcohol (2.04 g, 6.23 mmol, 95 %): R_f = 0.25 (30% ethyl acetate in hexane).



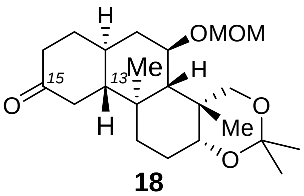
6

Ketone 6: To a stirred solution of the corresponding alcohol (2.0 g, 6.0 mmol) in dry CH_2Cl_2:DMSO (4:1) (15 mL) at 0 ^oC was added IBX (4.6.g, 12.0 mmol). The resulting mixture was stirred at 25 ^oC for 24 h and then quenched with aqueous sodium thiosulfate (15 mL) and extracted with CH_2Cl_2 (2 x 70 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by column chromatography (silica,16:84 ethyl acetate in hexanes), to give **6** (1.99 g, 5.82 mmol, 97 %). **6:** White solid; R_f = 0.5 (30% ethyl acetate in hexanes); IR (film) ?$_{max}$ 2936, 1710, 1037; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.67 (1H, d, *J* = 6.8 Hz), 4.64 (1H, d, *J* = 6.8 Hz) 4.08 (1H, ddd, *J* = 10.4, 10.0, 4.4 Hz), 3.99 (1H, d, *J* = 11.2 Hz), 3.53 (1H, d, *J*= 11.2Hz), 3.45 (1H, m), 3.38 (3H, s), 2.68 (1H, m), 2.48-2.41 (2H, m), 2.3 1 (1H, m), 1.78 (1H, m), 1.66-1.57 (2H, m), 1.54 (1H, d, *J* =10.8 Hz), 1.51 (3H, s), 1.39 (3H, s), 1.35 (3H, s), 1.33 (1H, m), 1.26 (3H, s); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 212.7, 100.23, 96.4, 75.2, 74.3, 64.7, 56.3, 50.81, 47.25, 39.7, 35.0, 32.1, 27.4, 25.3, 24.4, 24.3, 24.0, 22.2; HRMS calcd. for $C_{18}H_{30}O_5$ (M+ Na^+) 349.1991, found 349.1984.



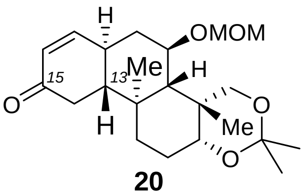
5

Enone 5: A solution of **6** (1.5g, 4.6 mmol) in dry toluene (15 mL) and dry THF (5 mL), was treated at 0 ^oC with 60% NaH (258 mg, 6.44 mmol) added portion wise. After stirring for 15 min excess HCOOMe (3mL, 48.66 mmol) was added to the reaction mixture. After stirring at 0 ^oC for 2 h then at 25 ^oC for 12 h the reaction mixture was quenched with a saturated solution of aqueous ammonium chloride (10 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were washed with brine (20 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by column chromatography to give **17** (1.4 g, 4.0 mmol, 89%), which was used in the next step. Compound **17** (1.4 g, 4.0 mmol) was treated with methyl vinyl ketone (1.38 mL, 16.6 mmol) and Et_3N (1.28 mL, 9.2 mmol) at 0 ^oC. After stirring for 4 h, the reaction mixture was poured into water and extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were washed with water and brine, then dried over $MgSO_4$. Removal of the solvent in vacuo gave a residue, which was dissolved in dry MeOH (5 mL) under argon at 0 ^oC and treated with a solution of NaOMe in methanol (23 mL, 1 M). After stirring at 0 ^oC for 4 h, the reaction mixture was allowed to warm to 25 ^oC and stirred overnight. Then the reaction mixture was quenched with water (10 mL), methanol was removed under reduced pressure and the residue was extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography (silica, 35:65.ethyl acetate in hexanes) to give **5** (1.05 g, 2.8 mmol, 72 %). **5:** White solid R_f = 0.45 (50% ethyl acetate in hexanes); IR (film) ?$_{max}$ 2937, 1662; 1H NMR (400 MHz, $CDCl_3$) δ 5.92 (1H, s), 4.76 (1H, d, *J* = 6.8 Hz), 4.72 (1H, d, *J* = 6.8 Hz) 4.14 (1H, m), 4.03 (1H, d, *J* = 11.6 Hz), 3.61 (1H, d, *J* = 11.6, Hz), 3.45 (1H, m), 3.41 (3H, s), 2.70 (1H, m), 2.53 (1H, dd, *J* = 14.0, 3.6 Hz), 2.39 (1H, m), 2.08-1.99 (3H, m), 1.90-1.72 (3H, m), 1.69 (3H, s), 1.64 (3H, s), 1.61 (1H, m), 1.48 (1H, d, *J* = 10.8 Hz), 1.39 (3H, s), 1.38 (3H, s), 1.26 (1H, m). ^{13}C NMR (100 M Hz, CDCl$_3$) δ 200.1, 170.6, 124.0, 99.7, 96.4, 75.3, 73.4, 69.5, 64.2, 56.2, 53.2, 48.4, 41.2, 39.2, 38.6, 33.2, 32.4, 29.0, 26.6, 25.4, 25.2, 23.5; HRMS calcd. for $C_{22}H_{34}O_5$ (M+ Na$^+$) 401.2304, found 401.2334.



18

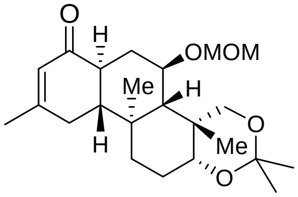
Ketone 18: A solution of **5** (500 mg, 1.32 mmol) in dry THF (3 mL) and dry EtOH (0.2 mL) was added drop wise to liq. NH$_3$ (8 mL) at -78 ^{o}C under argon. The resulting solution was treated with lithium (184 mg, 26.4 mmol) portion wise (4 x 46, mg) over 1 h. After stirring for 4 h solid ammonium chloride was added and the mixture was warmed slowly to 25 ^{o}C allowing the excess ammonia to be evaporated. The resulting mixture was diluted with water (5 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried over MgS0$_4$, concentrated under reduced pressure and purified by flash chromatography (silica, 22:78 ethyl acetate in hexanes) to give **18** (449 mg, 1.18 mmol, 90 %). **18:** White solid; R$_f$ = 0.5 (50% ethyl acetate in hexanes); IR (film) ?$_{max}$ 2918, 1665, 1034; 1H NMR (400 MHz, CDCl$_3$) δ 4.72 (1H, d, *J* = 6.8 Hz), 4.65 (1H, d, *J* = 6.8 Hz), 3.95 (1H, d, *J* =11.6Hz), 3.73 (1H, dt, *J* = 11.2, 4.0 Hz), 3.52 (1H, d, *J* = 11.6 Hz), 3.46 (1H, dd, *J* = 4.8, 3.2 Hz), 3.39 (3H, s), 2.40-2.27 (4H, m), 2.09 (1H, t, *J* = 13.6 Hz), 2.0 (1H, m), 1.83-1.64 (3H, m), 1.51 (1H, m), 1.38-1.25 (3H, m), 1.40 (3H, s), 1.36 (3H, s), 1.30 (3H, s), 1.25 (3H, s).1.21-1.03 (3H, m); ^{13}CNMR (100 MHz, CDCl$_3$) δ 212.3, 100.1, 96.3, 76.2, 74.6, 64.7, 56.2, 55.7, 53.8, 41.4, 41.2, 40.94, 38.7, 37.0, 34.7, 33.6, 32.8, 28.4, 24.5, 24.5, 22.5, 17.5; HRMS calcd. for $C_{22}H_{37}O_5$ (M+ Na$^+$) 404.2539, found 404.2509.



20

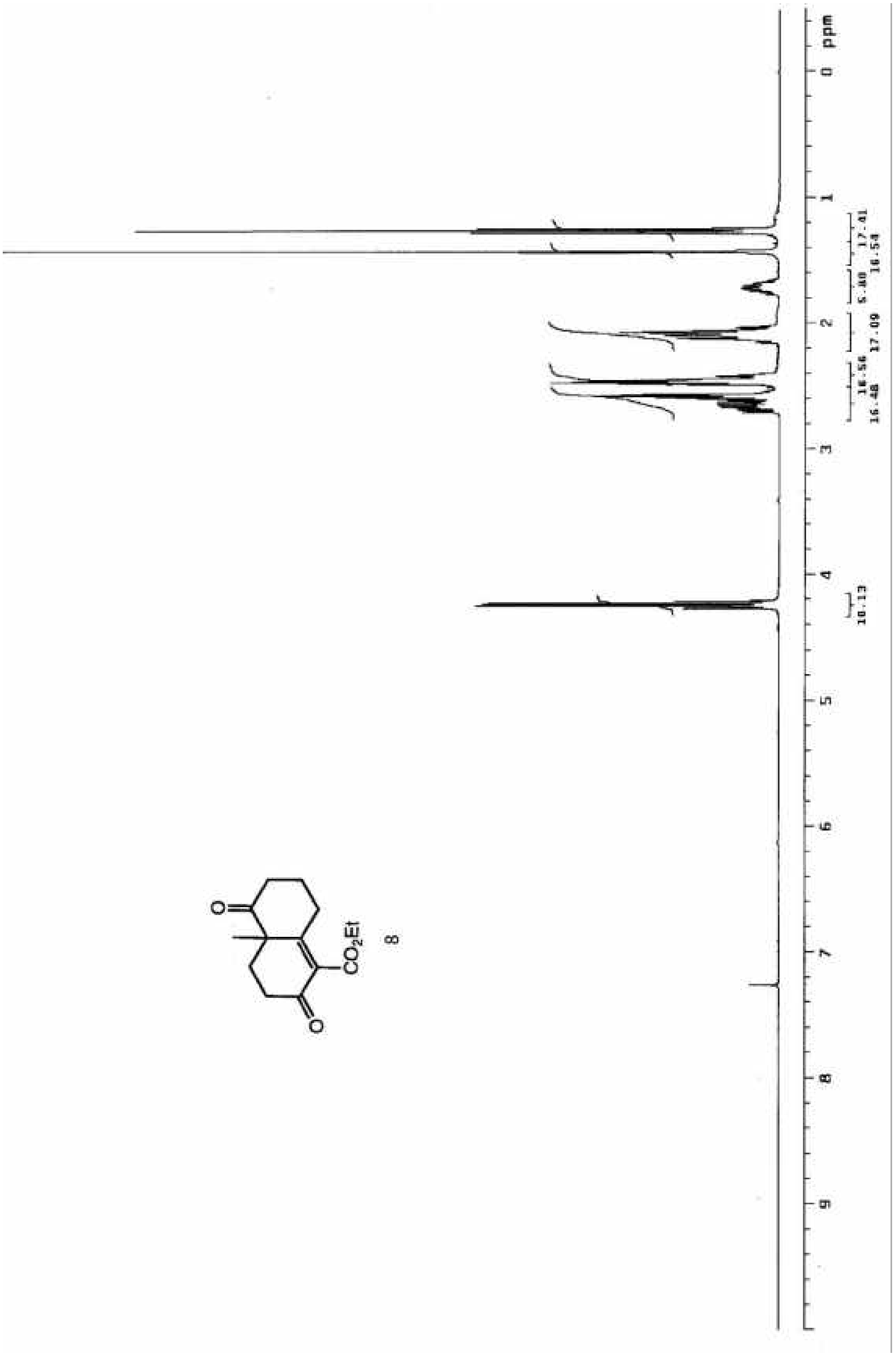
Enone 20: A solution of **18** (400 mg, 1.05 mmol) in dry THF (4 mL) was treated with 1 M NaHMDS in THF (1.5 mL), drop wise at -78 ^{o}C under argon. The mixture was stirred for 30 min and then treated with a solution of PhSeCl (401 mg, 2.1 mmol) in THF (2 mL). After stirring for 1 h the reaction mixture was quenched with saturated solution of aqueous ammonium chloride (2 mL) and extracted with ethyl acetate (2 x 8 mL), the combined organic extracts were washed with brine (3 mL), and dried over MgSO$_4$, concentrated under reduced pressure and purified by flash chromatography (silica, 12:88 ethyl acetate in hexanes) to give the selenide (417 mg, 0.78 mmol 75%) This selenide was dissolved in THF:H$_2$O (2:1) (4 mL) and treated with NaIO$_4$ (333 mg, 1.56 mmol) at 0 ^{o}C and stirred for 2 h at room temperature. Then the reaction mixture was diluted with water (2 mL) and extracted with ethyl acetate (2 x 10 mL). The combined organic extracts were washed with water (5 mL) and brine (5 mL), dried over MgS0$_4$, concentrated under reduced pressure and purified by flash chromatography (silica, 20:80 ethyl acetate in hexanes) to give **20** (265 mg, 0.70 mmol, 90%). **20:** White solid; R$_f$ = 0.5 (50% ethyl acetate in hexane); IR (film) ?$_{max}$ 2937, 1682, 1038; 1H NMR (400 MHz, CDCl$_3$) δ 6.67 (1H, dd, *J*

= 9.6, 1.6 Hz), 5.95(1H, dd, *J* = 9.6, 2, Hz), 4.76 (1H, d, *J* = 6.8 Hz), 4.64 (1H, d, *J* = 6.8 Hz), 3.92 (1H, d, *J* = 11.2 Hz), 3.78 (1H, ddd, *J* = 10.8, 10.4, 4.4 Hz), 3.51-3.47 (2H, m), 3.40 (3H s), 2.54-2.38 (2H, m), 2.14 (1H, dd, *J* = 16.0, 14.4 Hz), 1.85-1.66 (3H, m), 1.62-1.48 (2H ,m), 1.43-1.21 (3H, m), 1.40 (3H, s), 1.36 (3H, s), 1.30 (3H, s), 1.29 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 154.1, 128.5, 100.3, 96.5, 76.6, 74.4, 64.6, 56.2, 53.8, 53.6, 39.7, 38.9, 38.6, 36.5, 35.8, 32.2, 28.3, 24.4, 24.3, 22.2, 18.3; HRMS calcd. for $C_{22}H_{34}O_5$ (M+ Na$^+$) 401.2298, found 401.2307.



4

Enone 4: To a solution of **20** (200 mg, 0.52 mmol) in dry ether (4 mL) at 0 ^{o}C was added MeLi (1.04 mL, 1 M in ether). The mixture was stirred for 30 min and was quenched with a saturated solution of aqueous ammonium chloride (2 mL) and extracted with ethyl acetate (2 x 5 mL), the combined organic extracts were washed with brine (4 mL), dried over $MgSO_4$, and purified by flash chromatography to give the tertiary alcohol (182 mg, 0.46 mmol, 90%). This alcohol (182 mg, 0.46 mmol) was dissolved in anhydrous dichloromethane (3 mL), containing MS 3A (40 mg) and treated with PCC (198 mg, 0.92 mmol) at 0 ^{o}C. After stirring for 2 h the reaction mixture was filtered through silica gel, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (22:78 ethyl acetate in hexanes) to give **4** (148 mg, 0.35 mmol, 78%). **4:** White solid; R_f = 0.45 (45% ethyl acetate in hexanes); IR (film) $?_{max}$ 2925, 1666; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (1H, s), 4.77 (1H, d, *J* = 6.8 Hz), 4.64 (1H, d, *J* = 6.8Hz), 3.95 (1H d, *J*= 11.6 Hz), 3.73 (1H, ddd, *J* = 11.2, 10.4, 4.4 Hz), 3.59 (1H, d, *J* = 11.6 Hz), 3.47 (1H, dd, *J* = 5.2, 3.2 Hz), 3.42 (3H, s), 2.77 (1H, m), 2.26-2.13 (3H, m), 1.96 (3H, s), 1.89-1.51 (6H, m), 1.41 (3H, s), 1.37 (3H, s), 1.32 (3H, s), 1.27 (3H, s), 1.22 (1H, m); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 200.1, 161.4, 125.3, 100.0, 95.7, 75.6, 74.8, 64.6, 56.6, 53.9, 52.0, 43.8, 38.6, 37.0, 34.0, 33.0, 31.2, 29.8, 28.7, 24.7, 24.6, 22.7, 18.1; HRMS calcd. for $C_{23}H_{36}O_5$ (M+ Na$^+$) 415.2455, found 415.2468.



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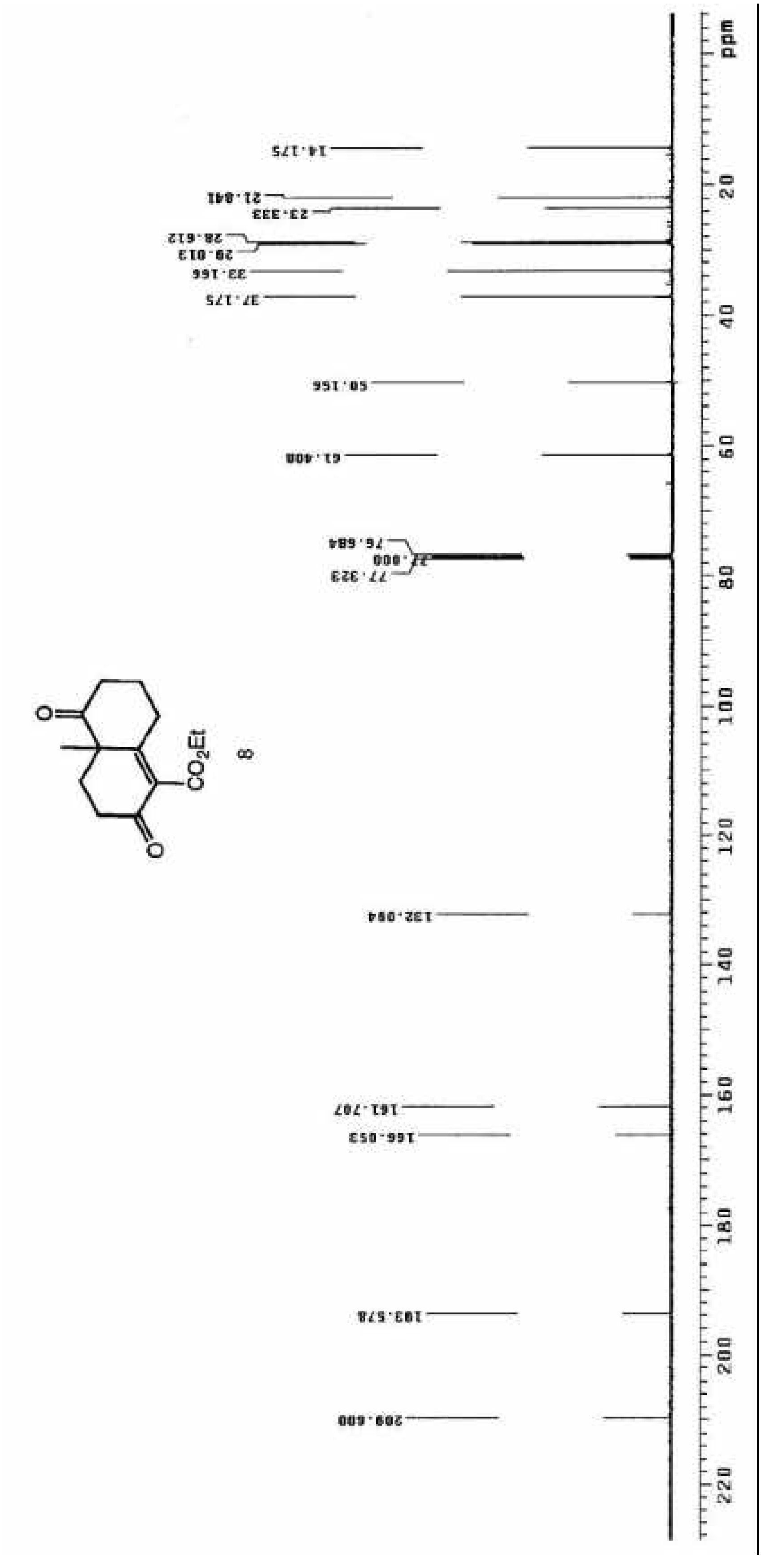

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200
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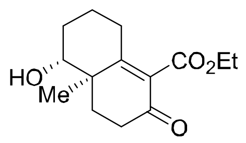
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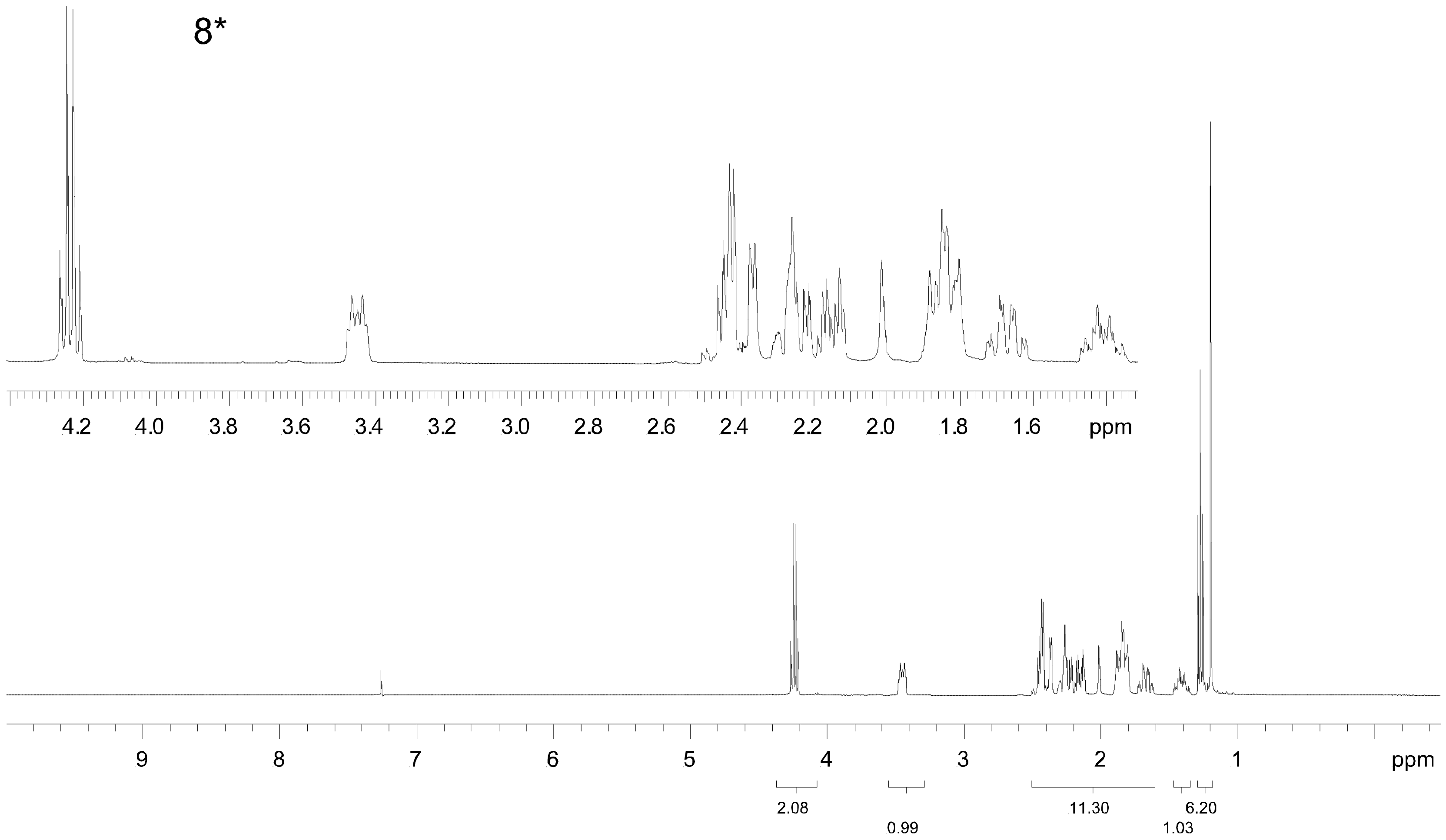
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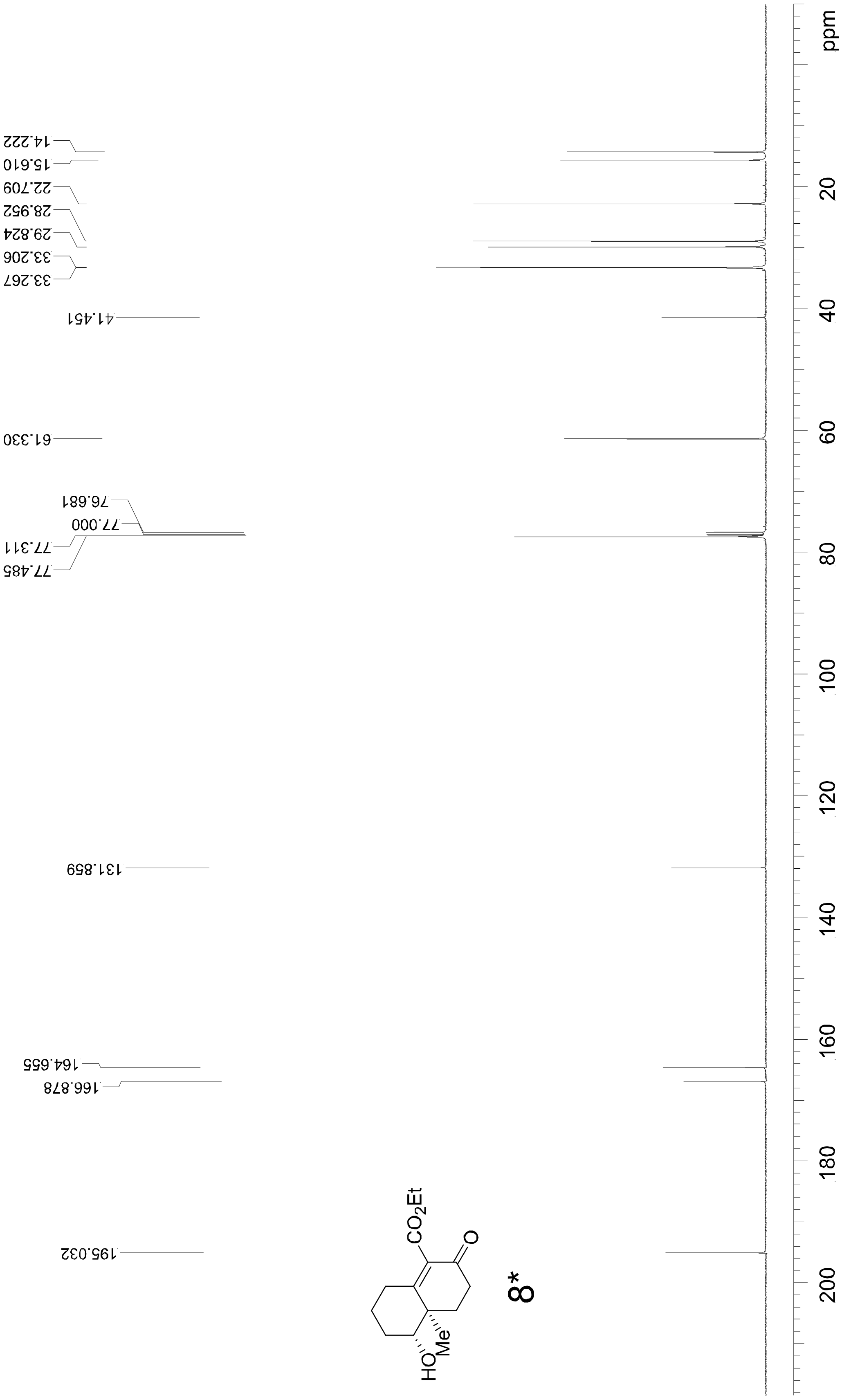
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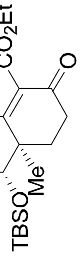
200

8*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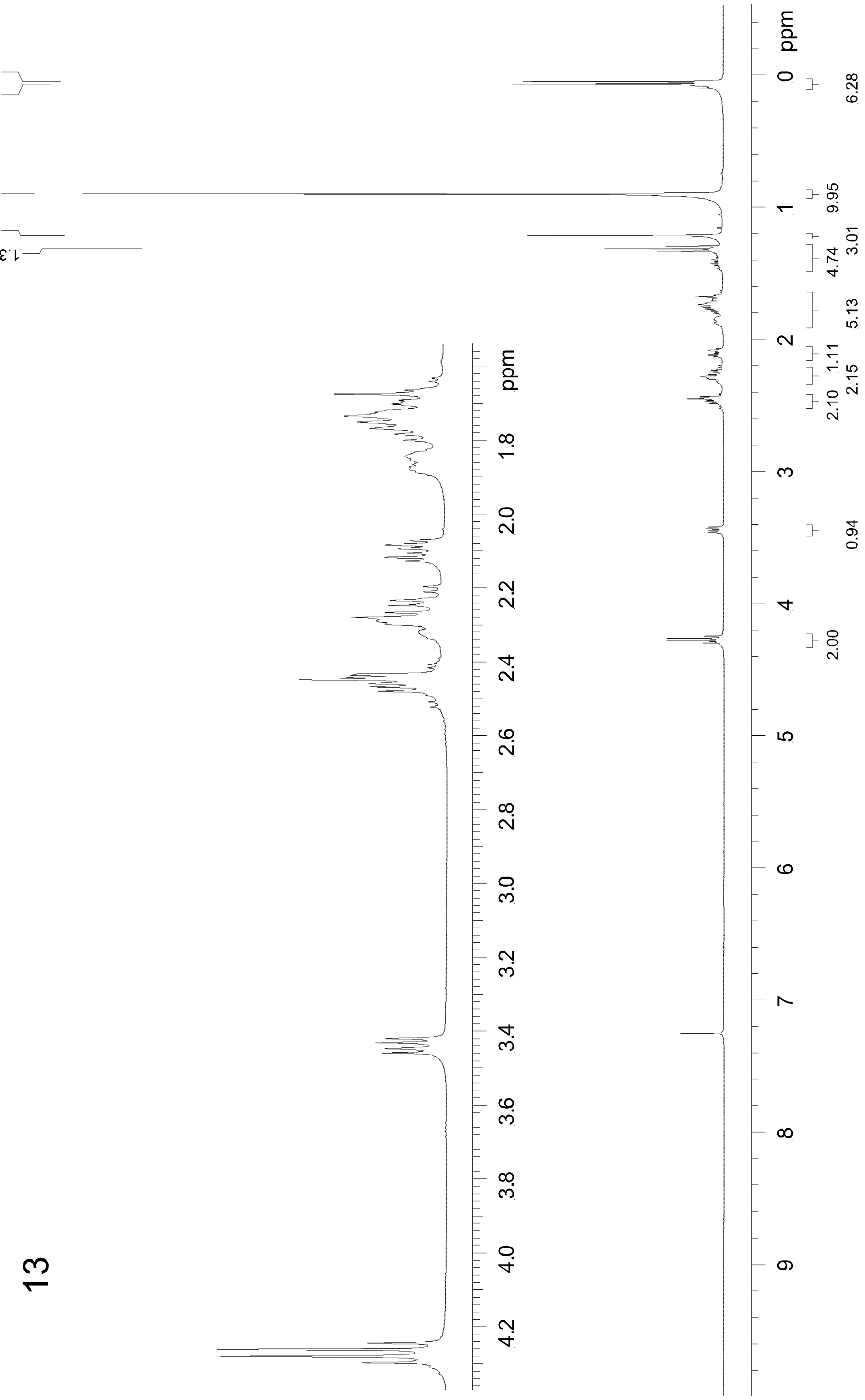
CO$_2$Et
O

13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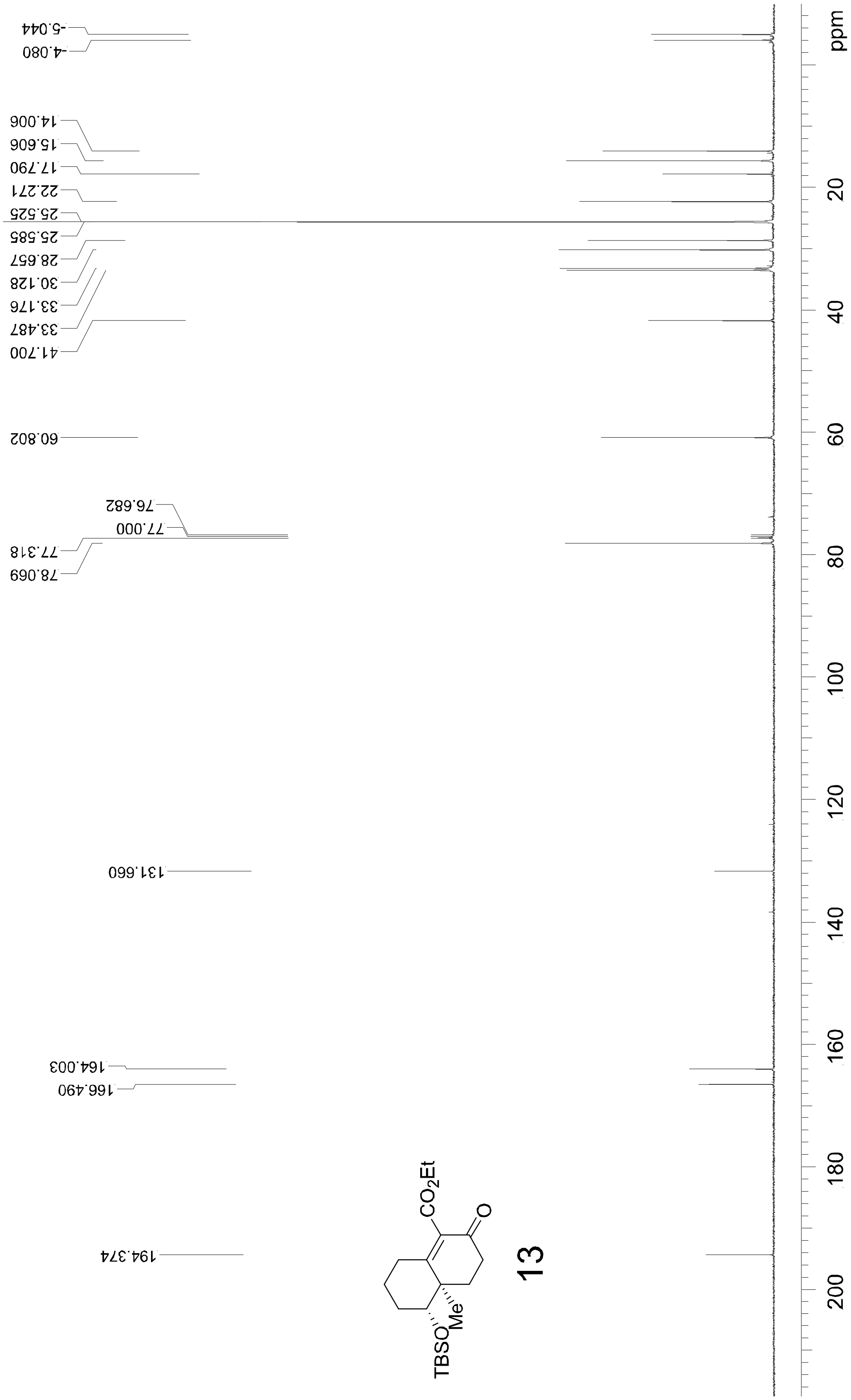
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TBSO
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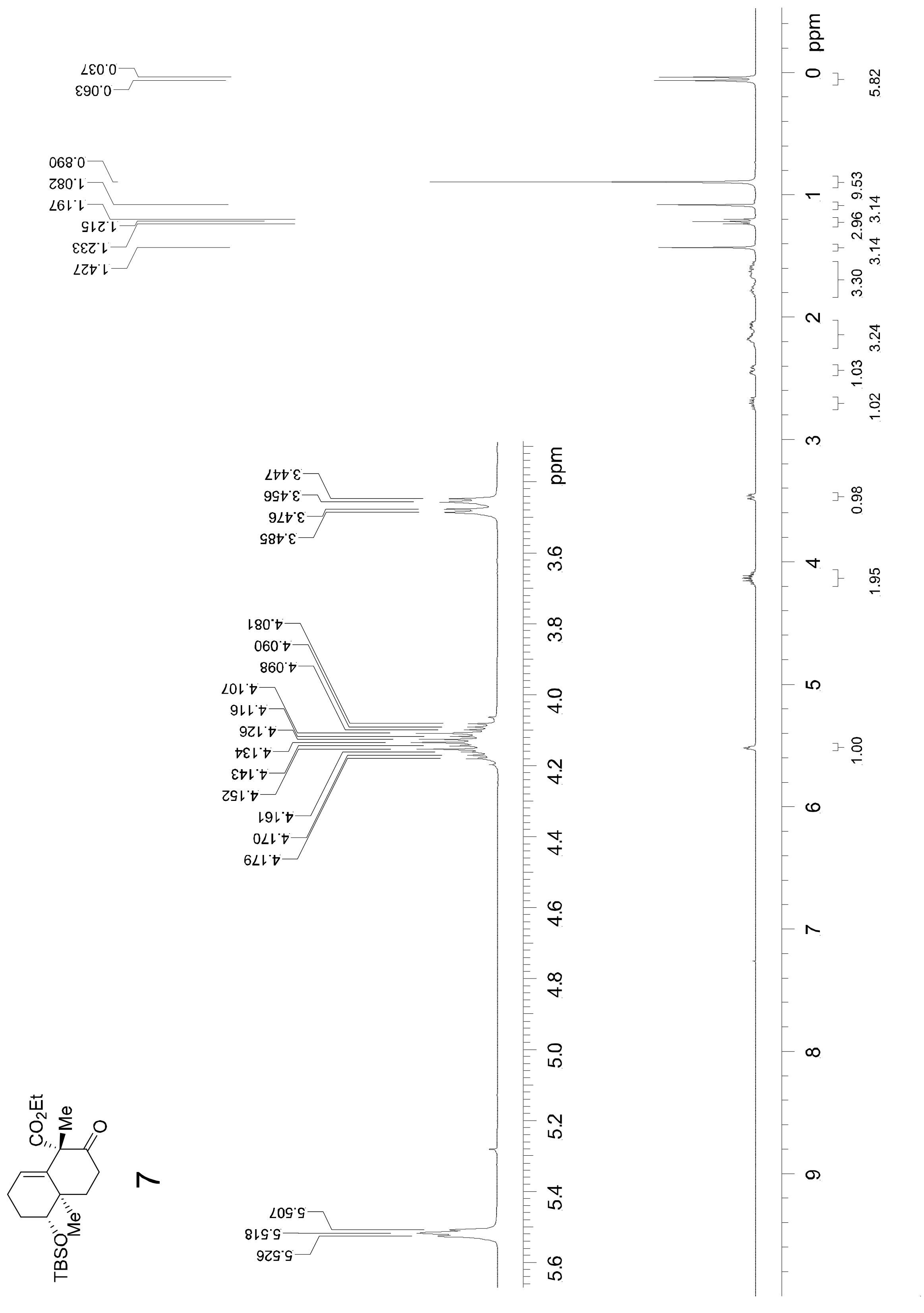
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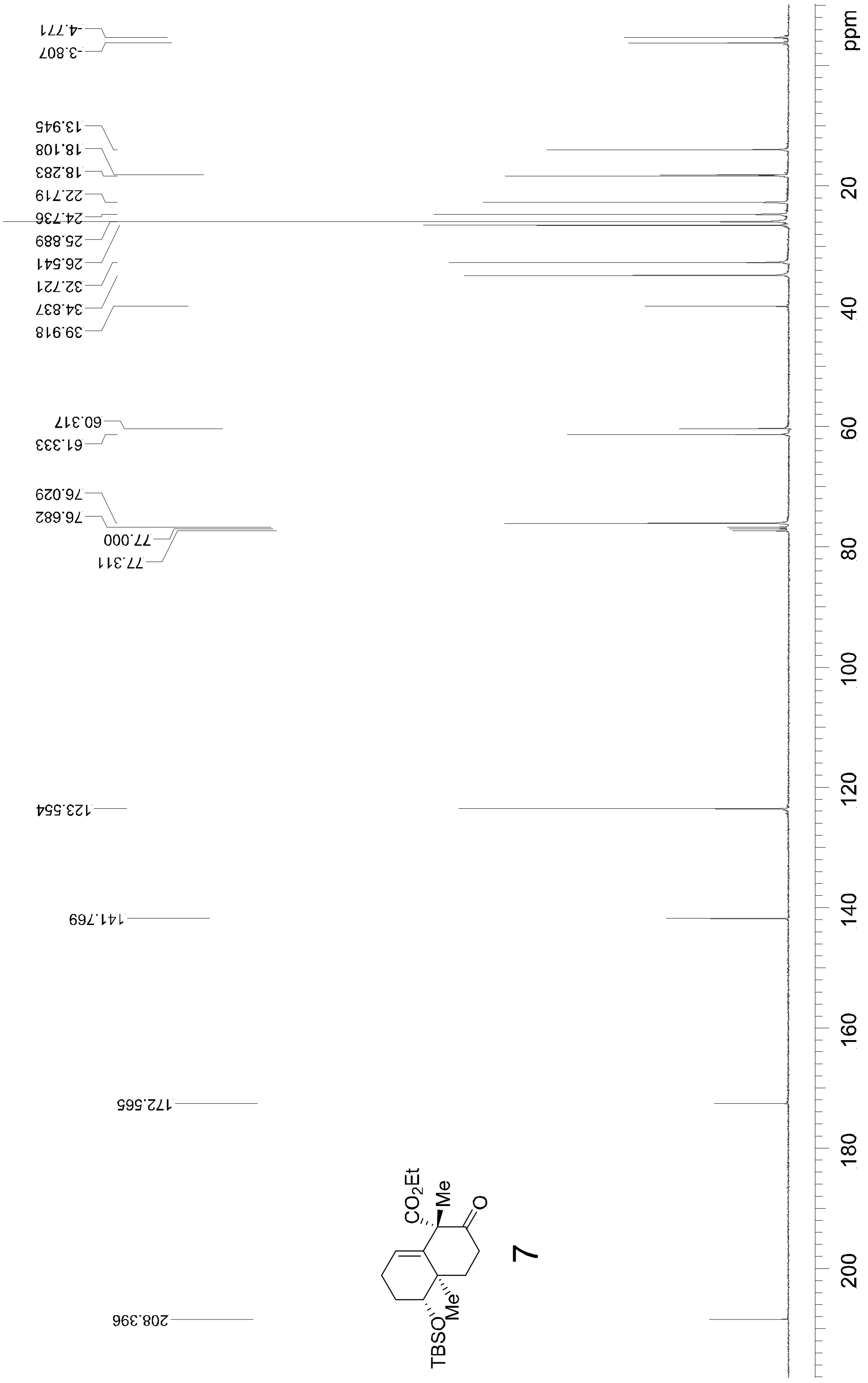

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TBSO
Me
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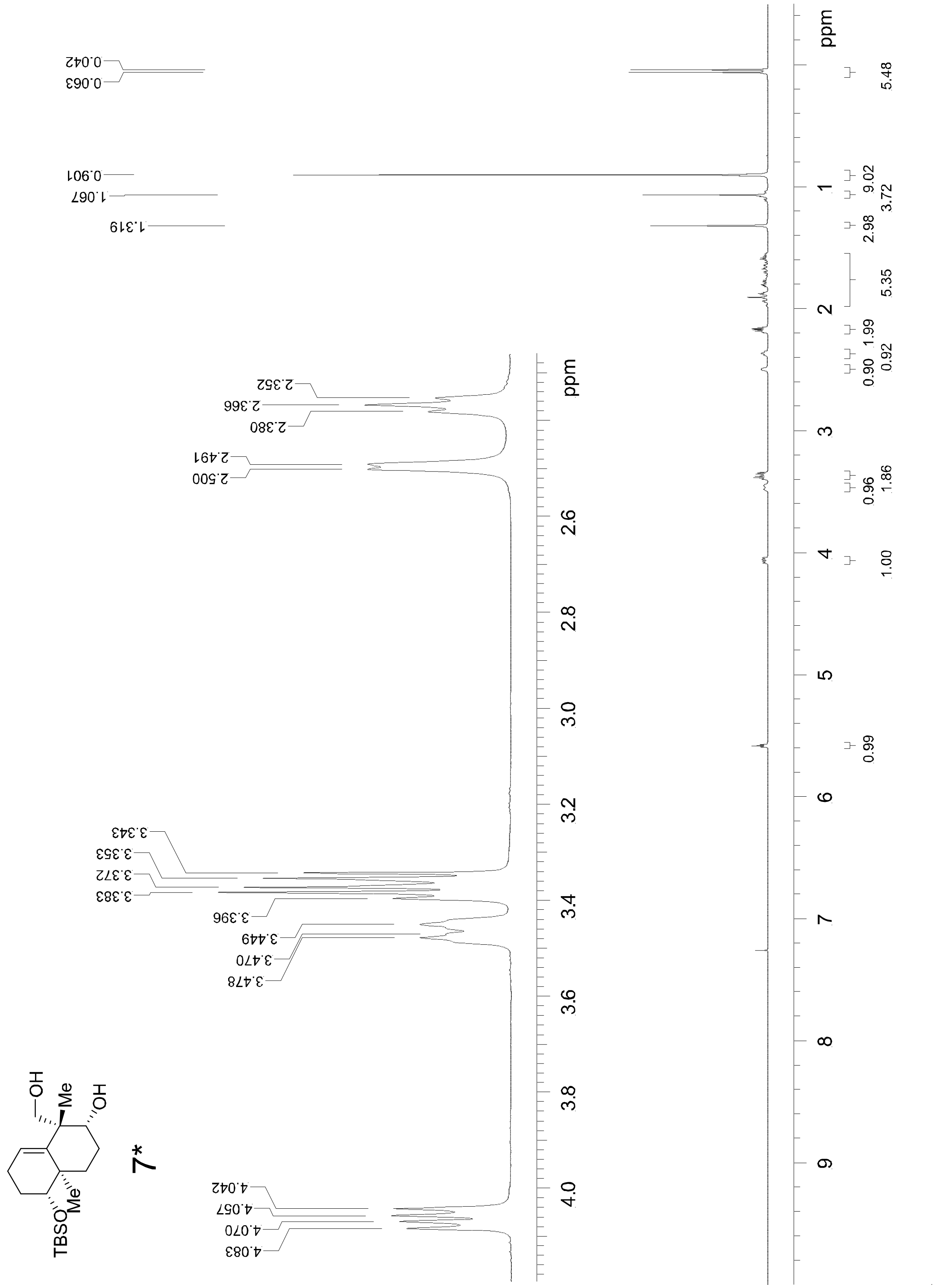

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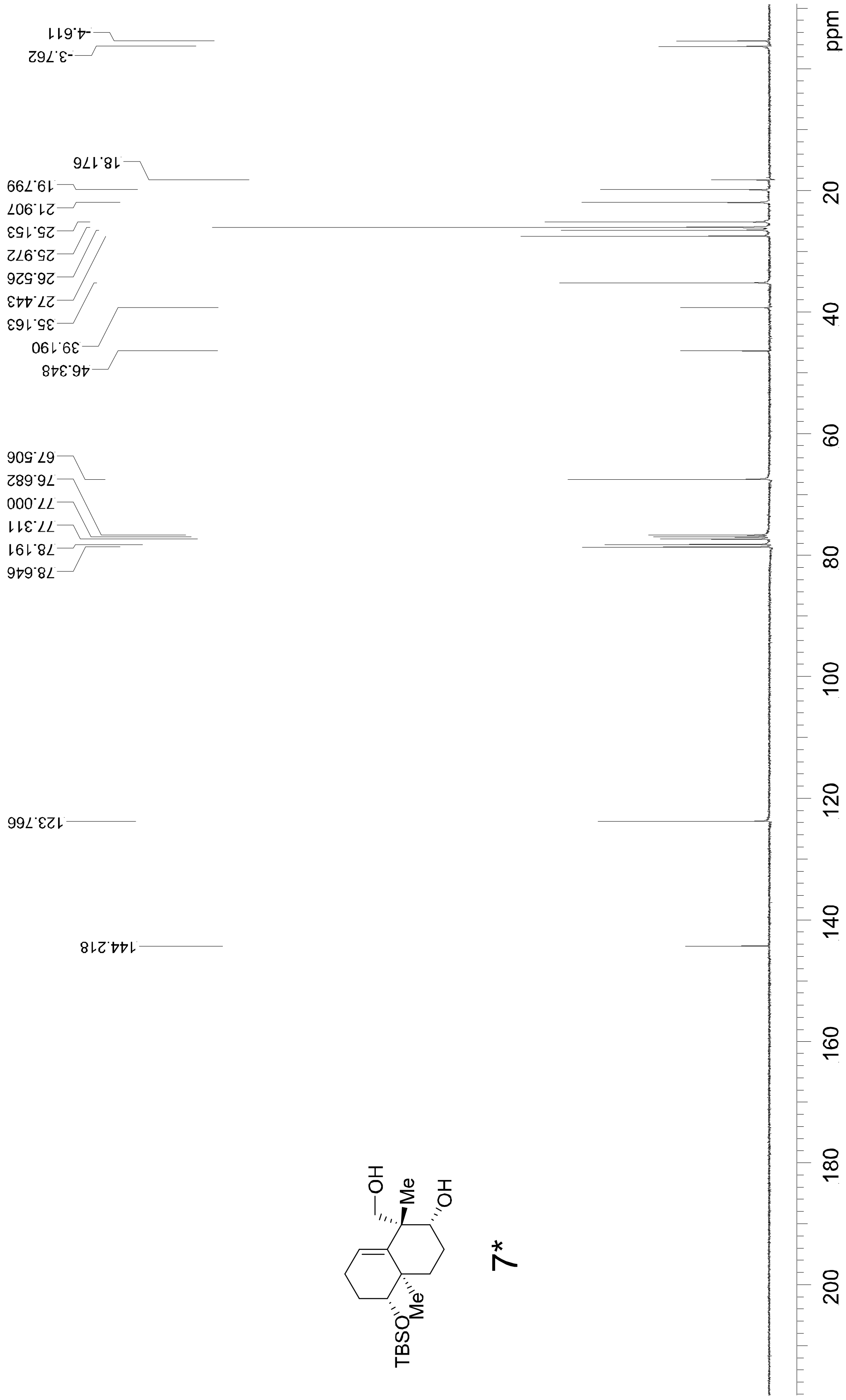
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TBSO
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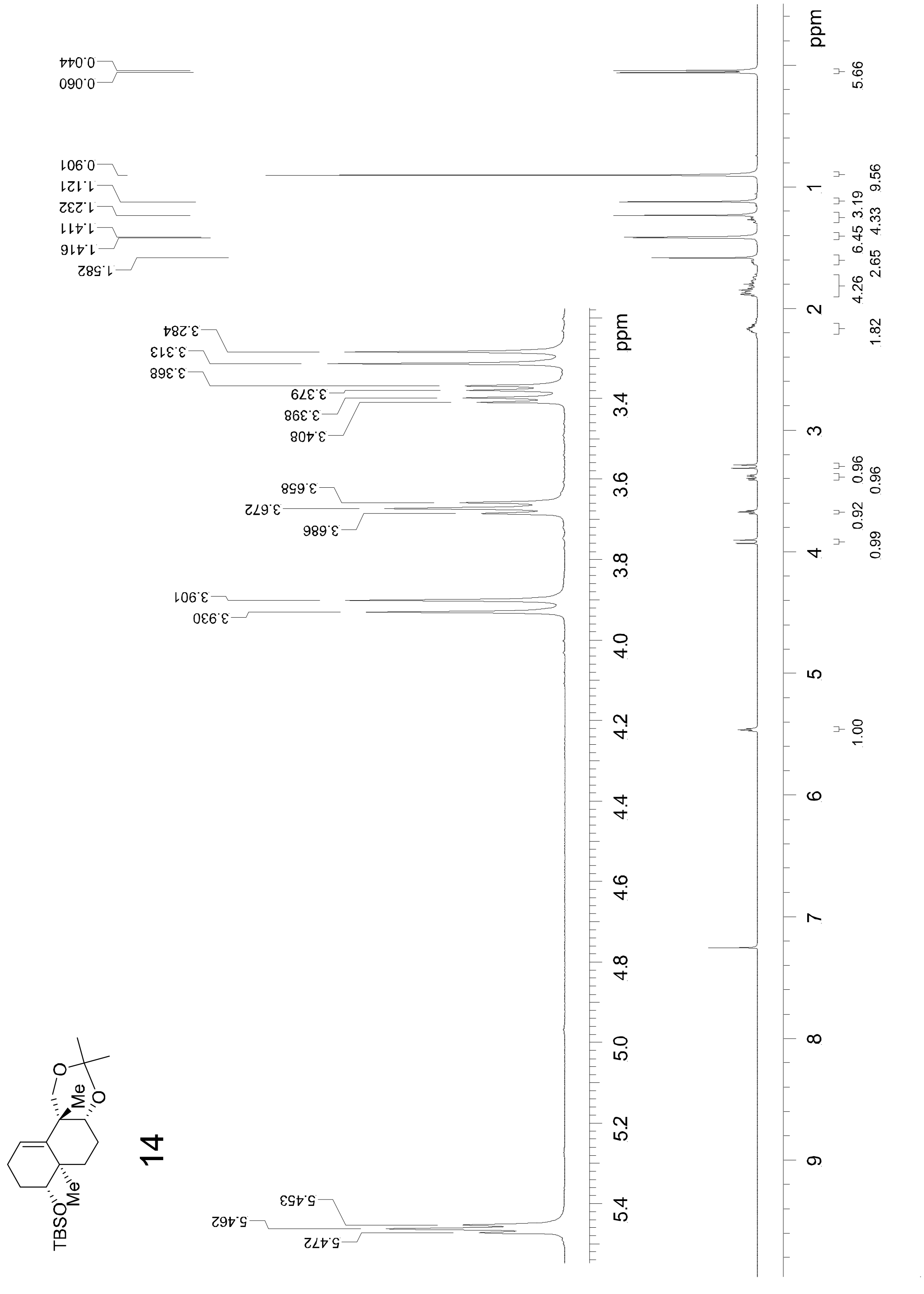
7*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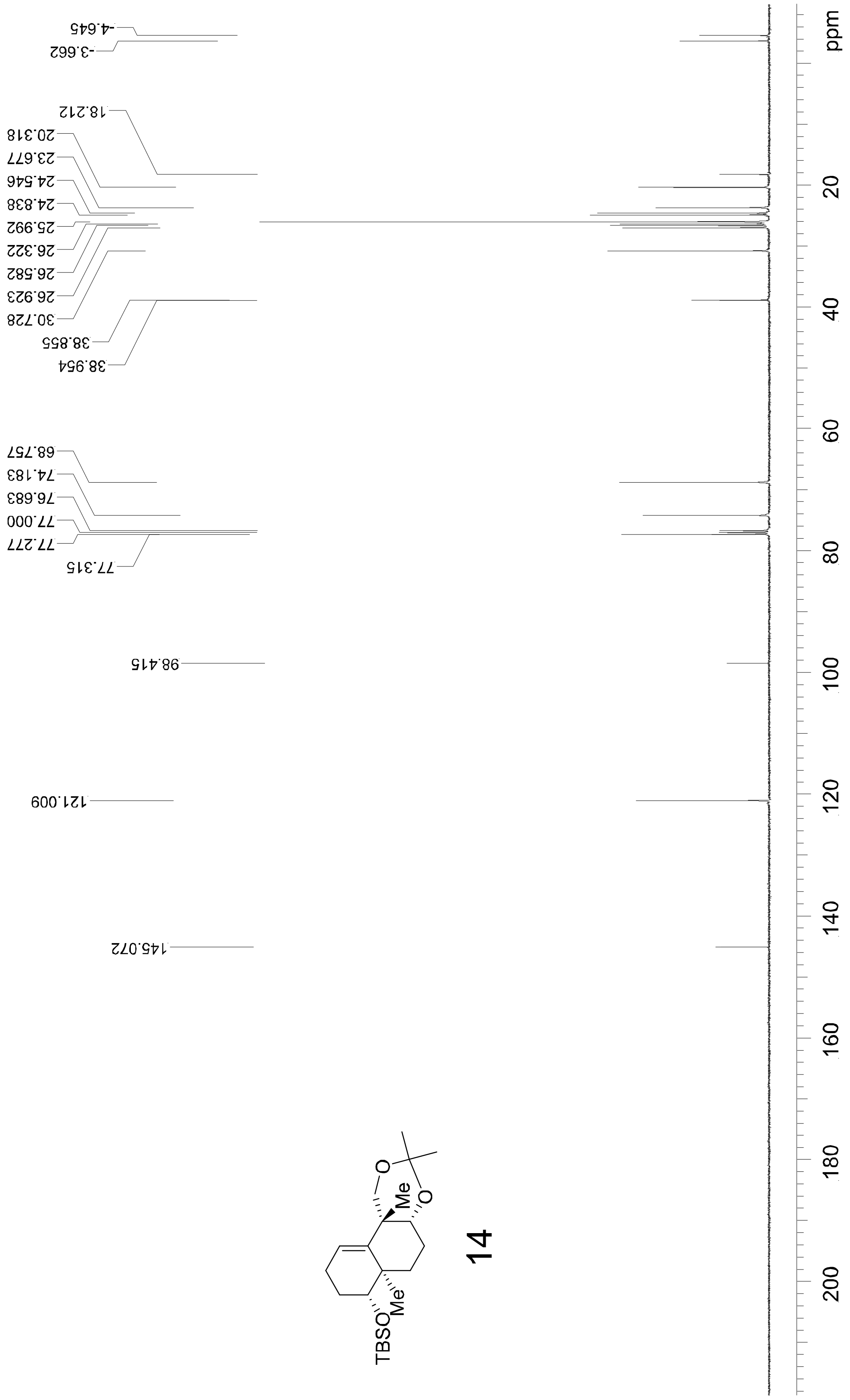
14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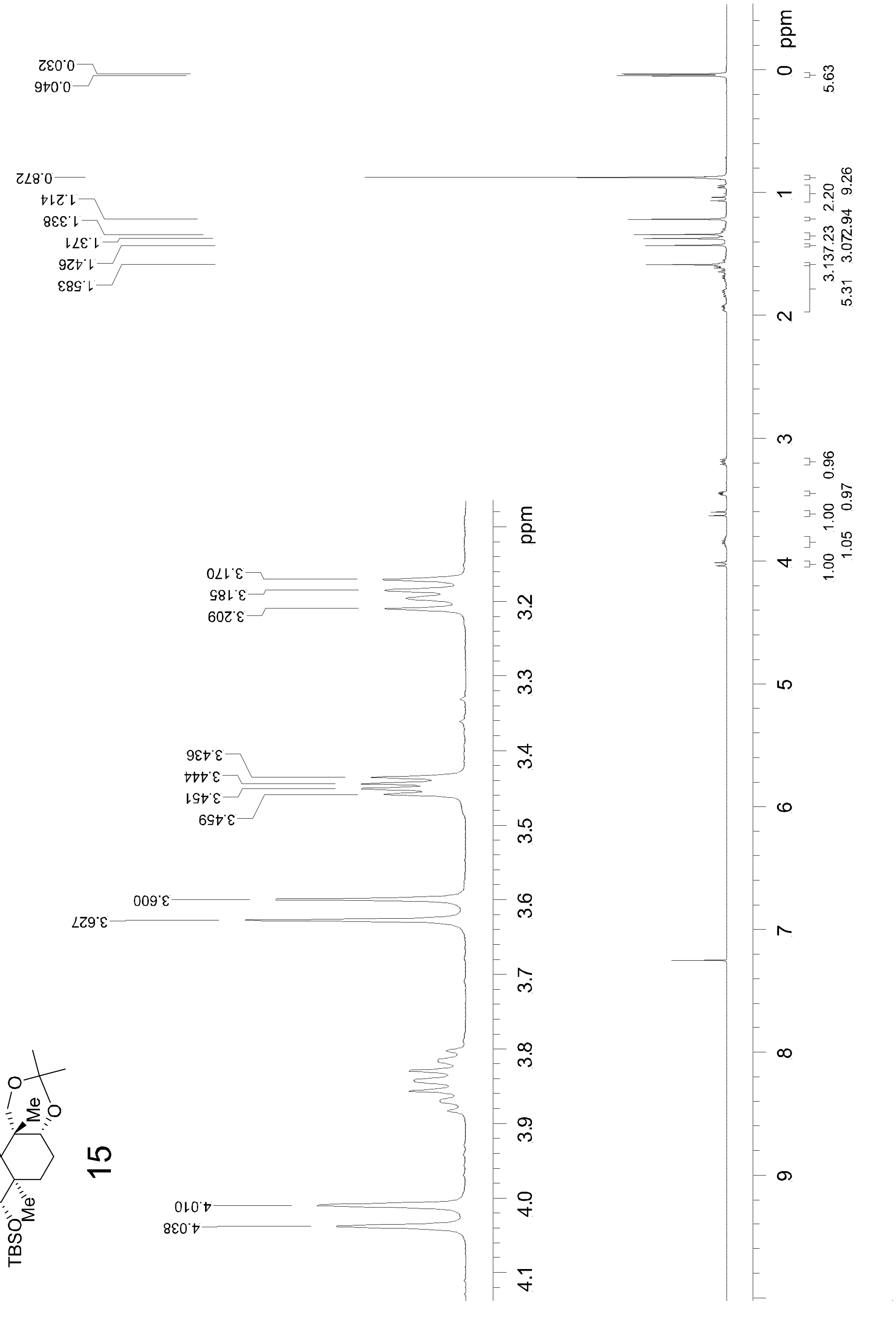
14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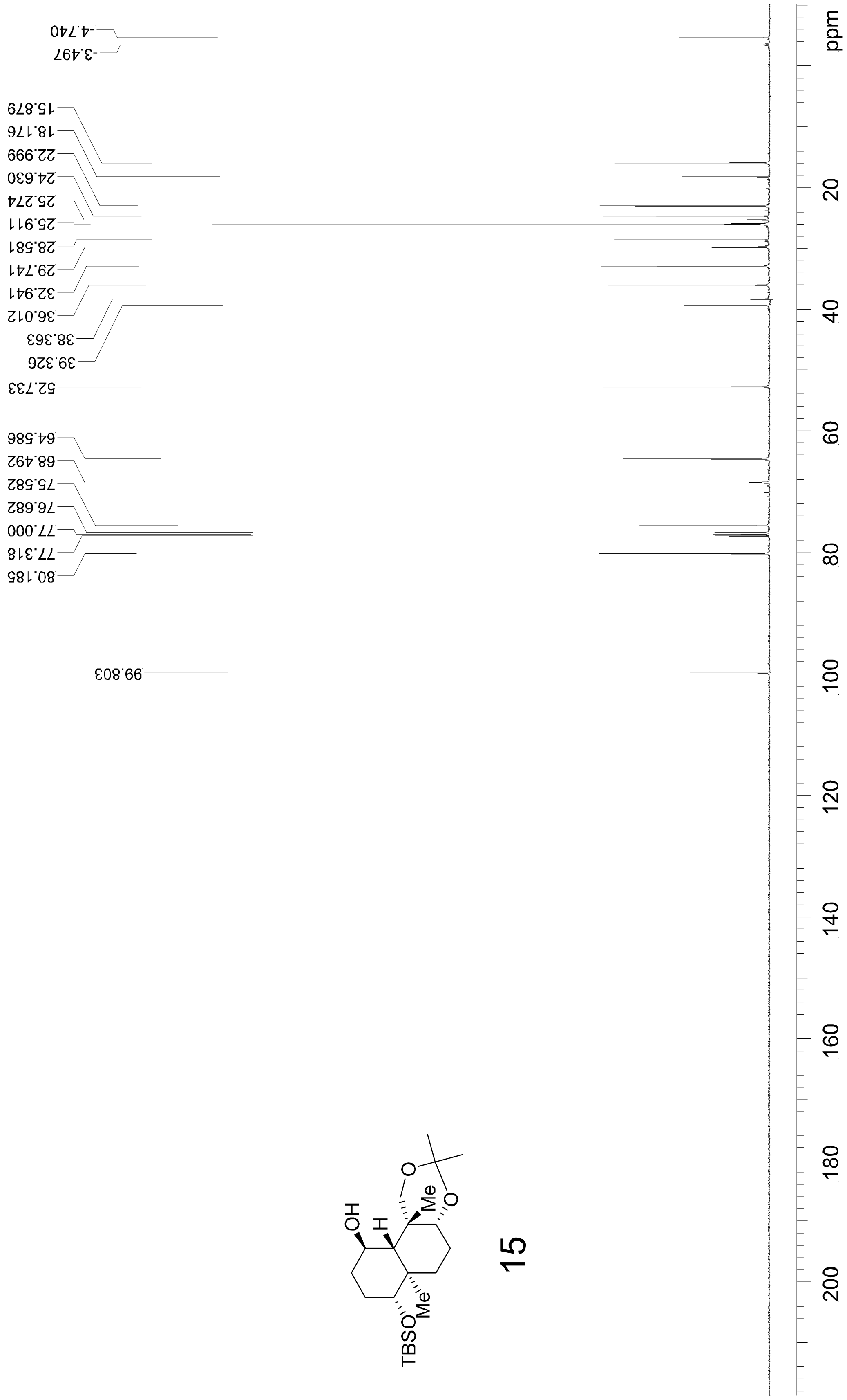
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TBSO
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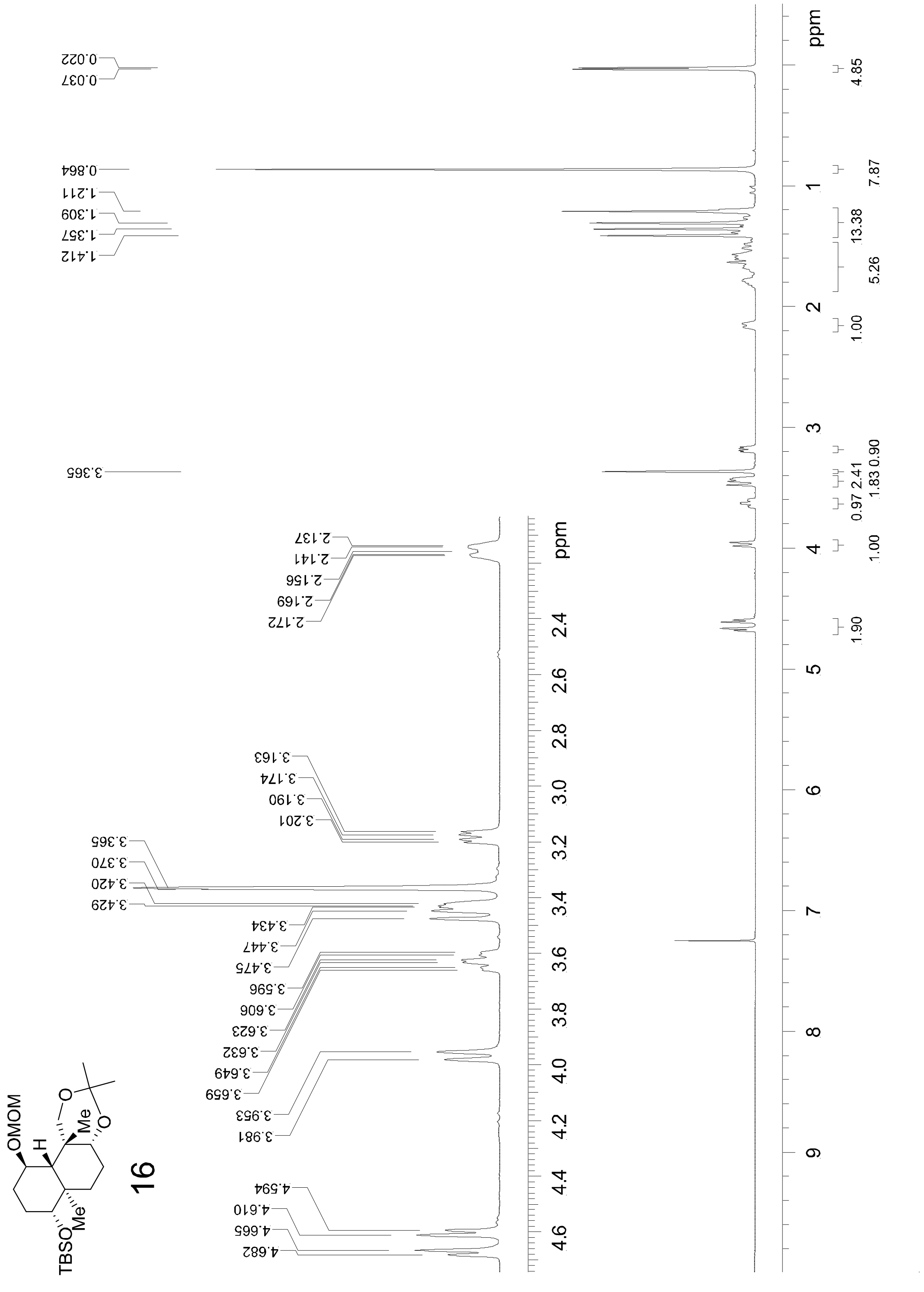
15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7
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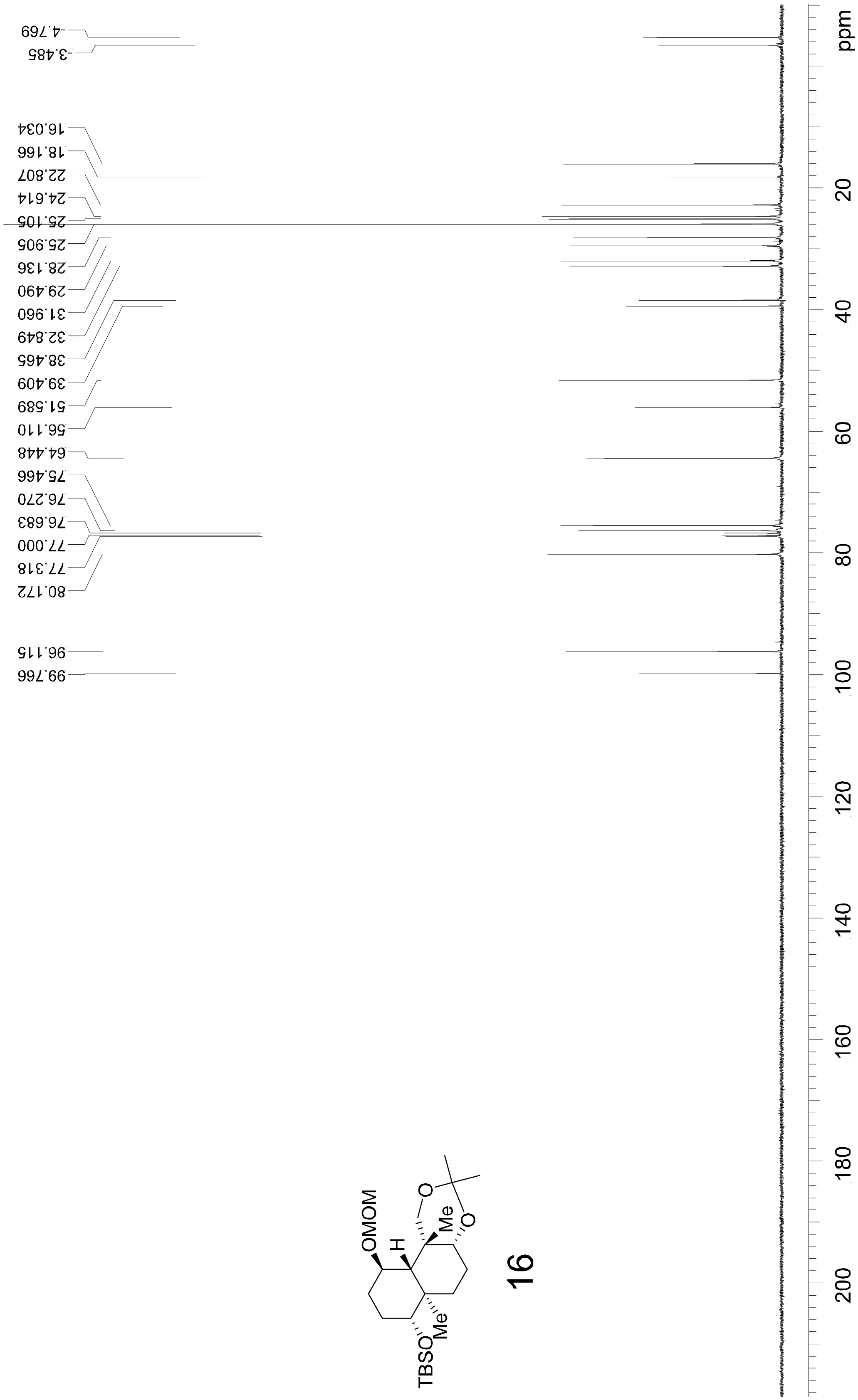
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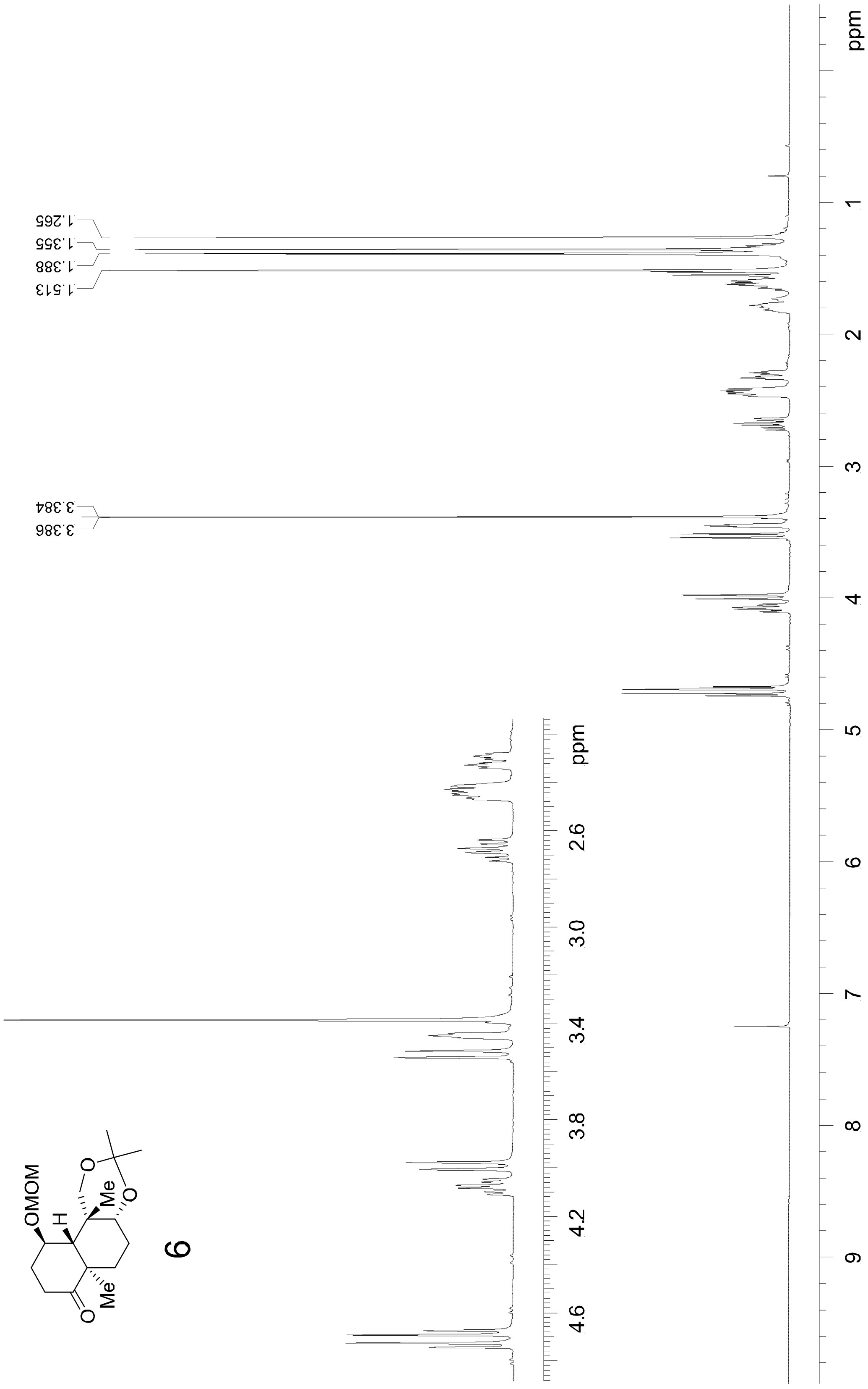
TBSO
Me

16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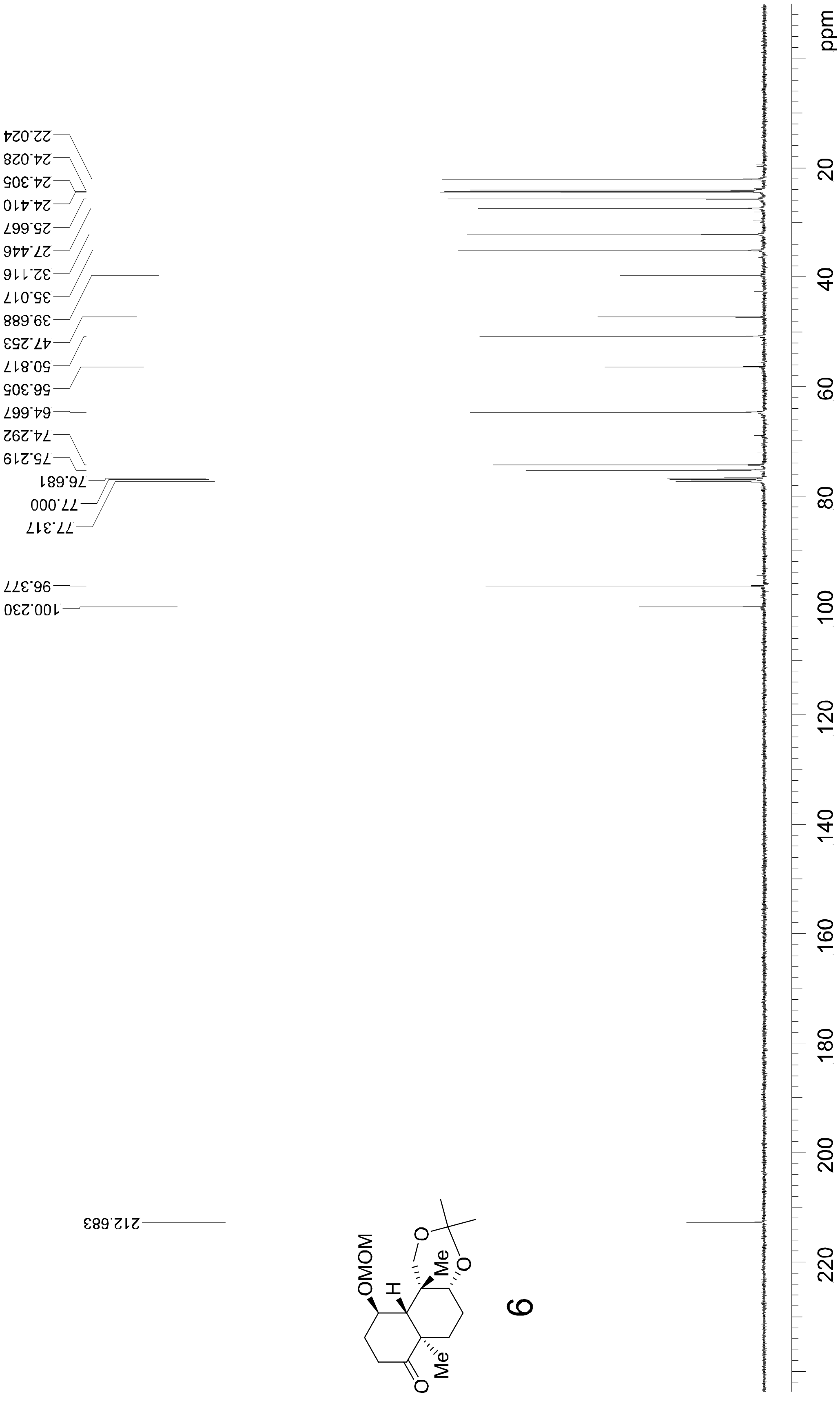
4.6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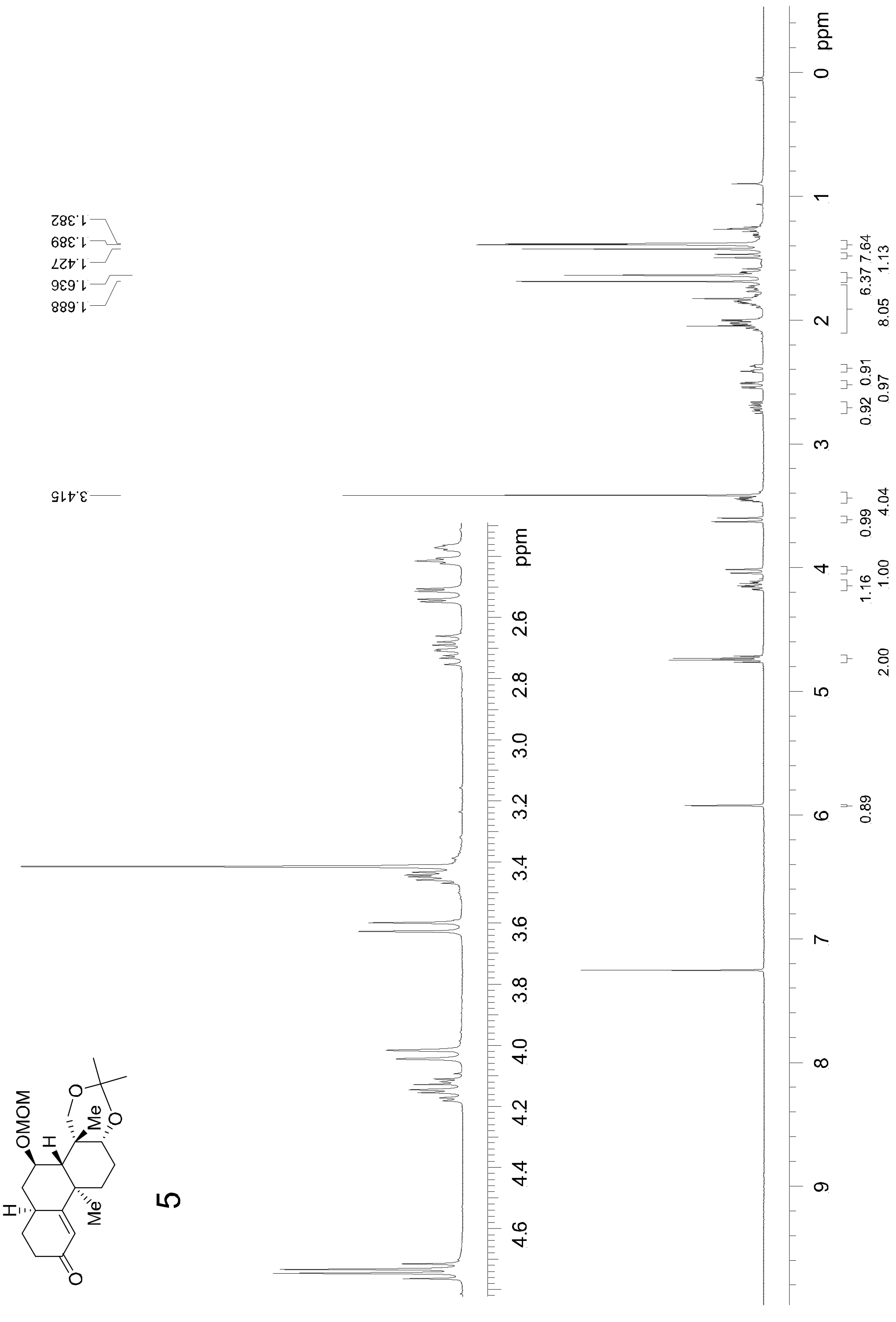
6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0.97
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7.64
1.13
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7
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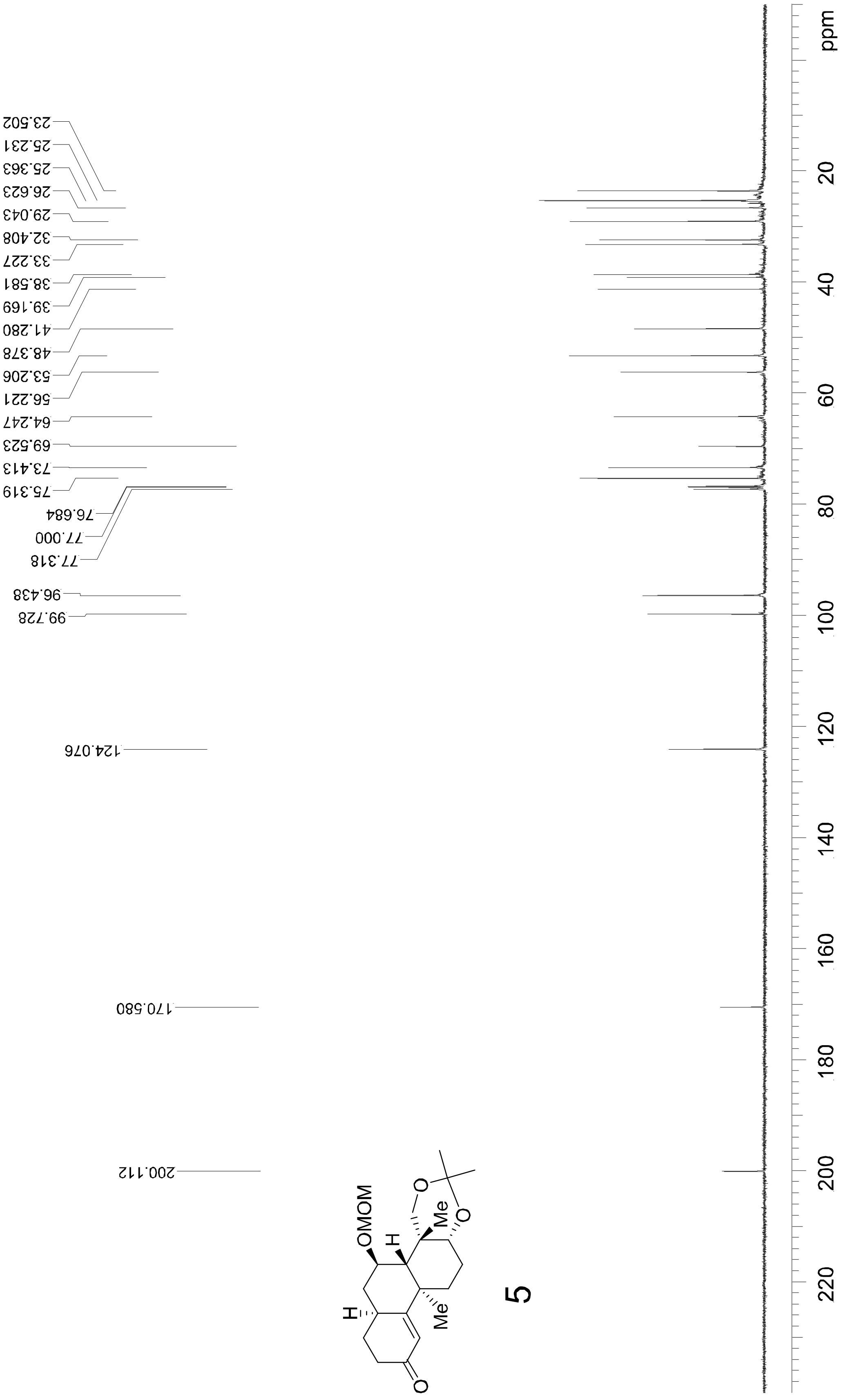
5



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96.438
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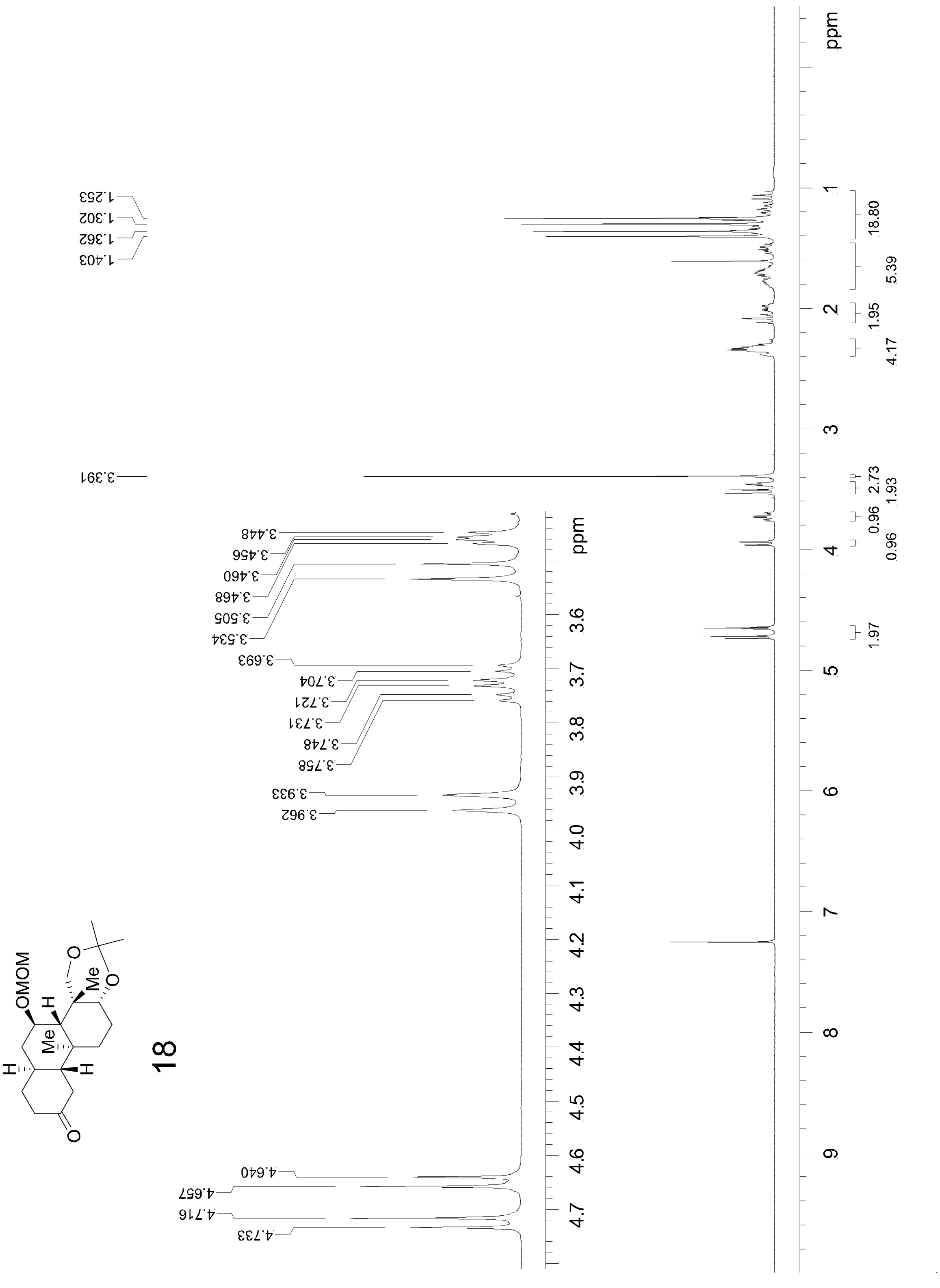
5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7
6
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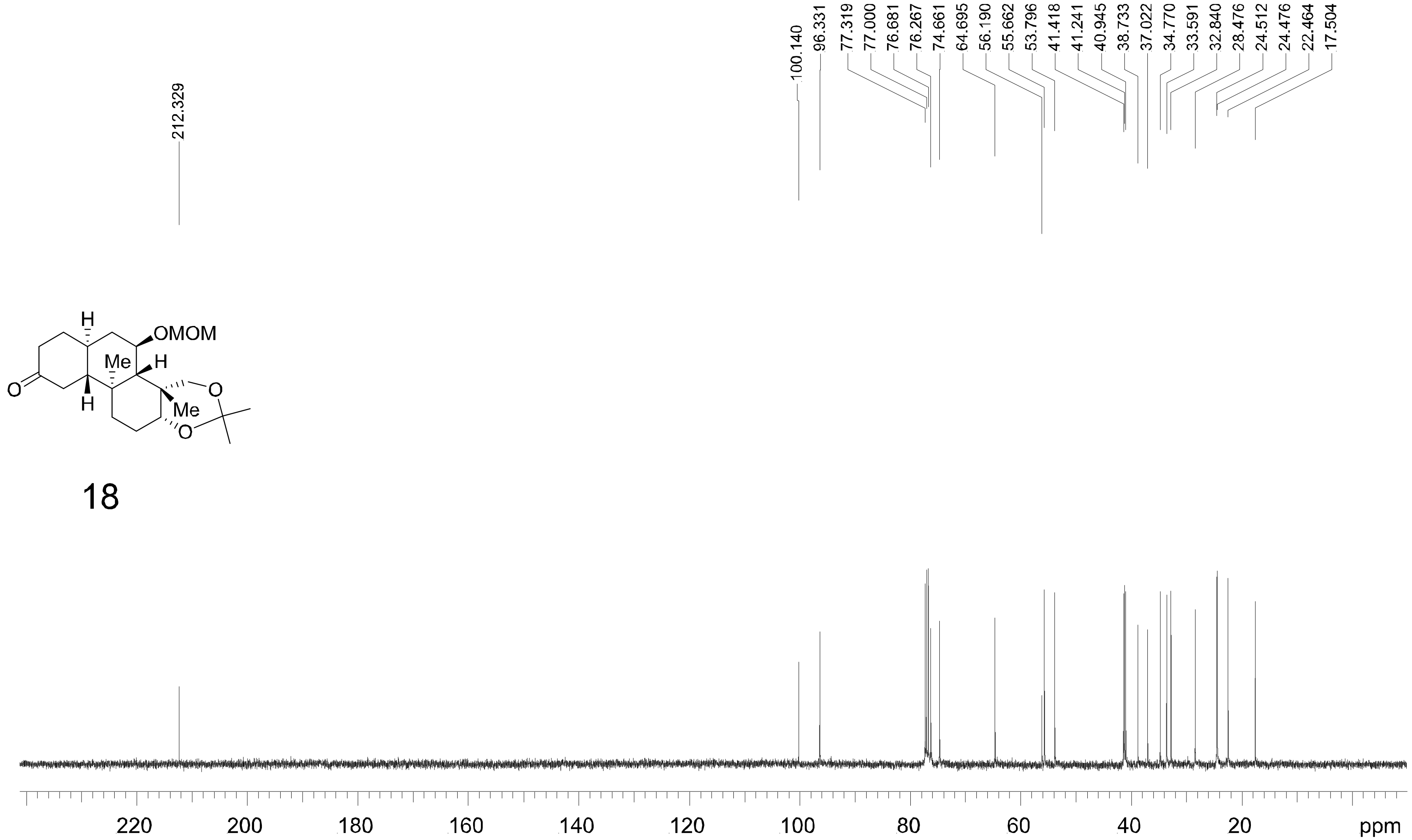
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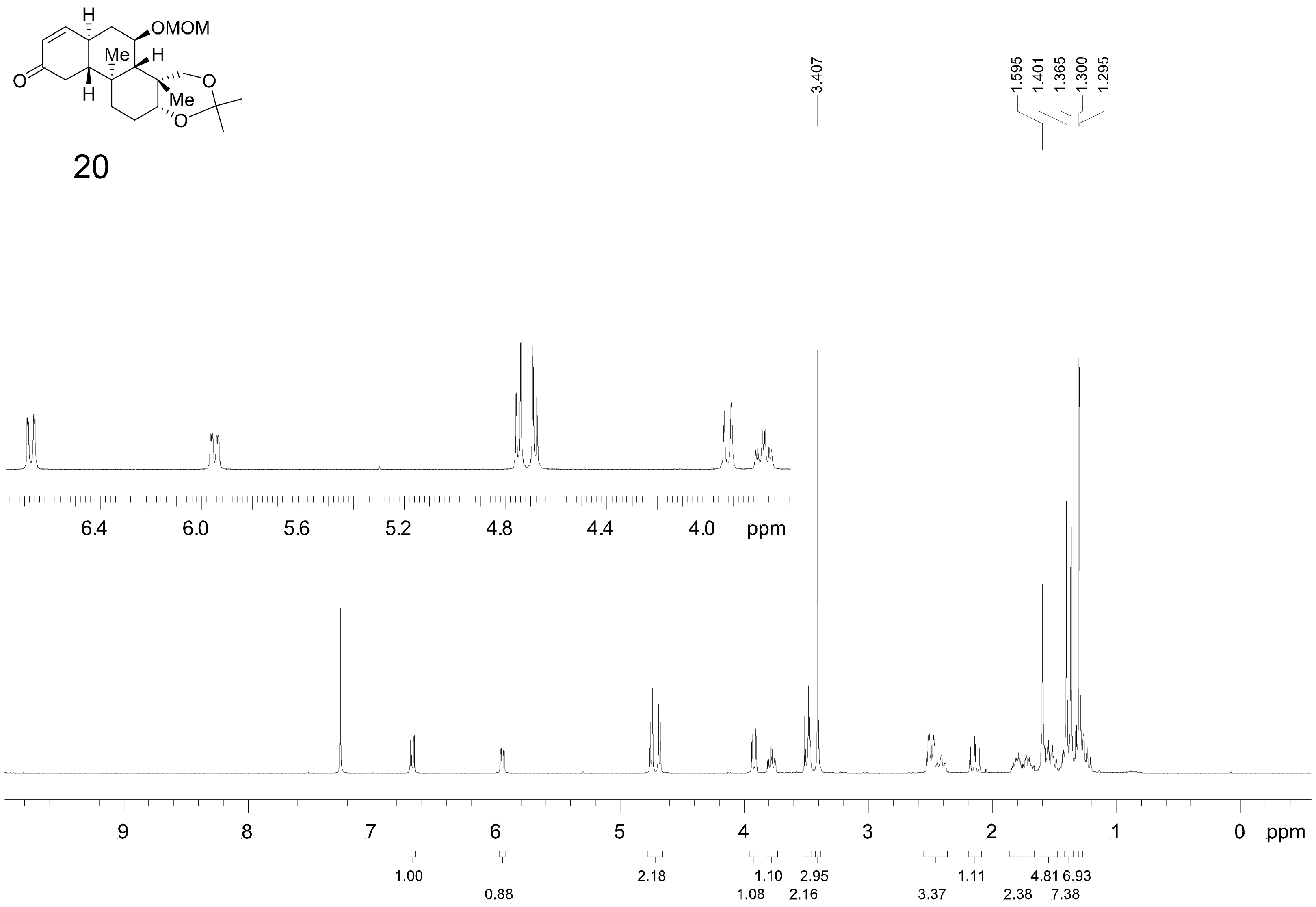
18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6
5
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3
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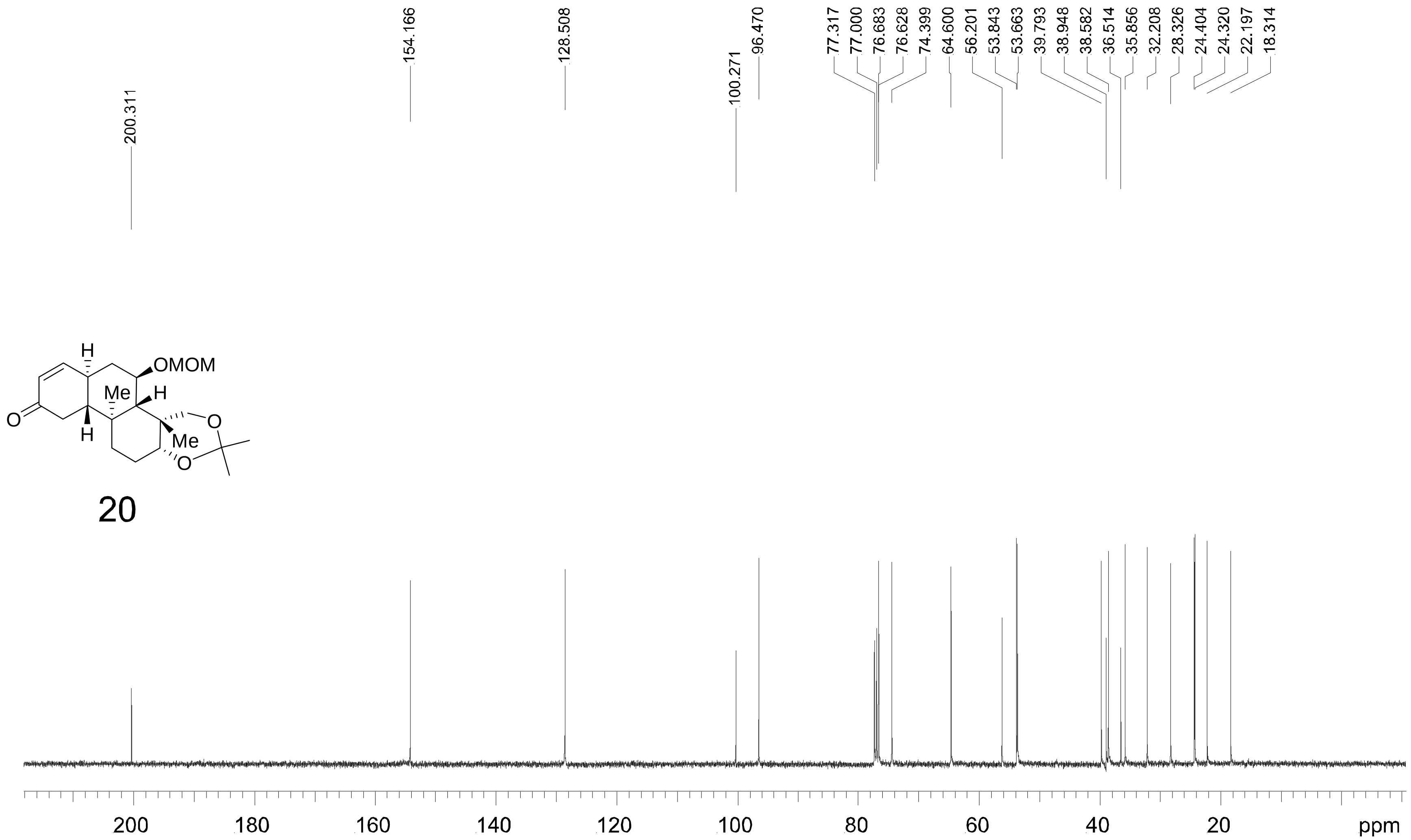

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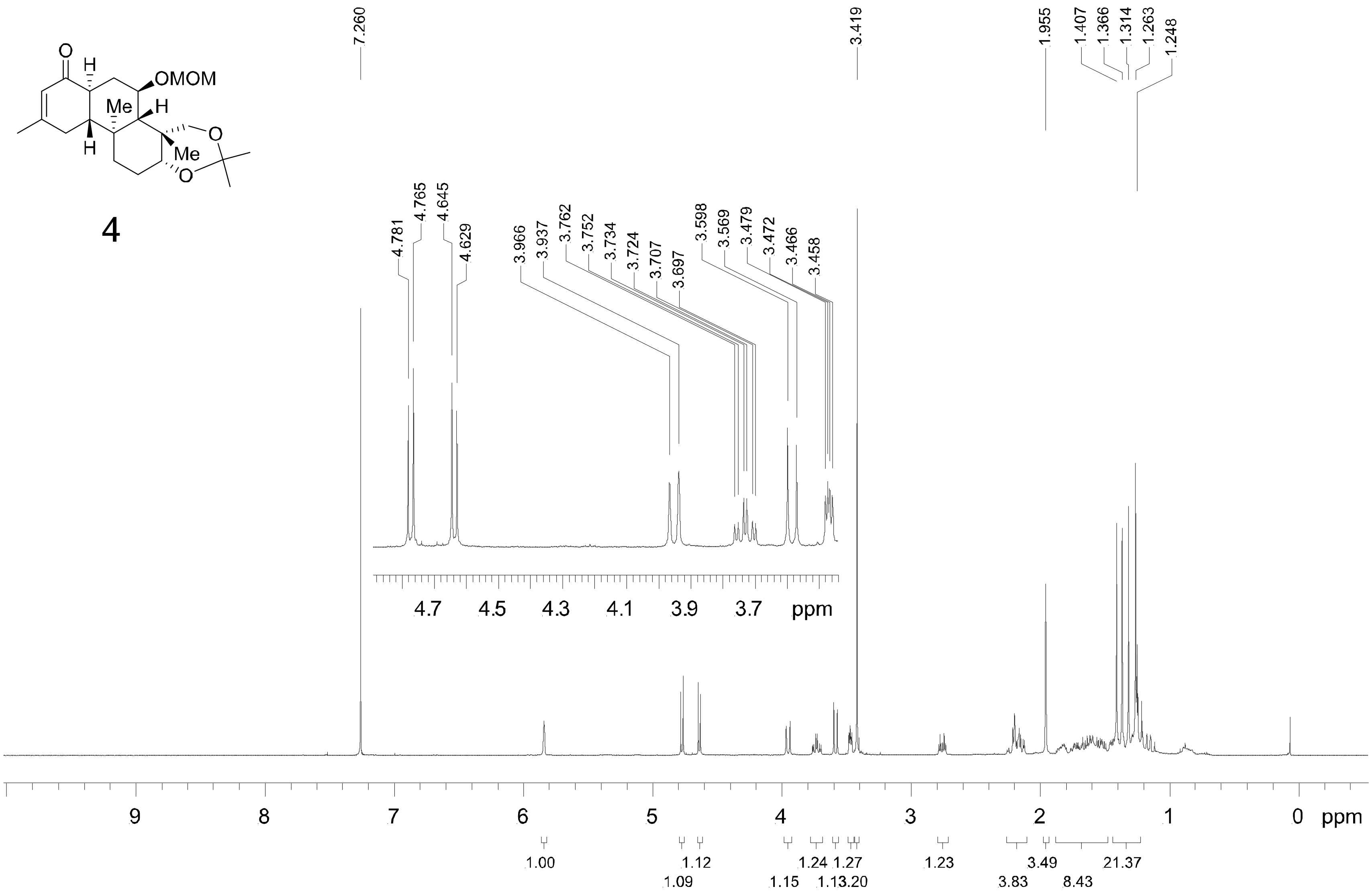

4

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Me
O
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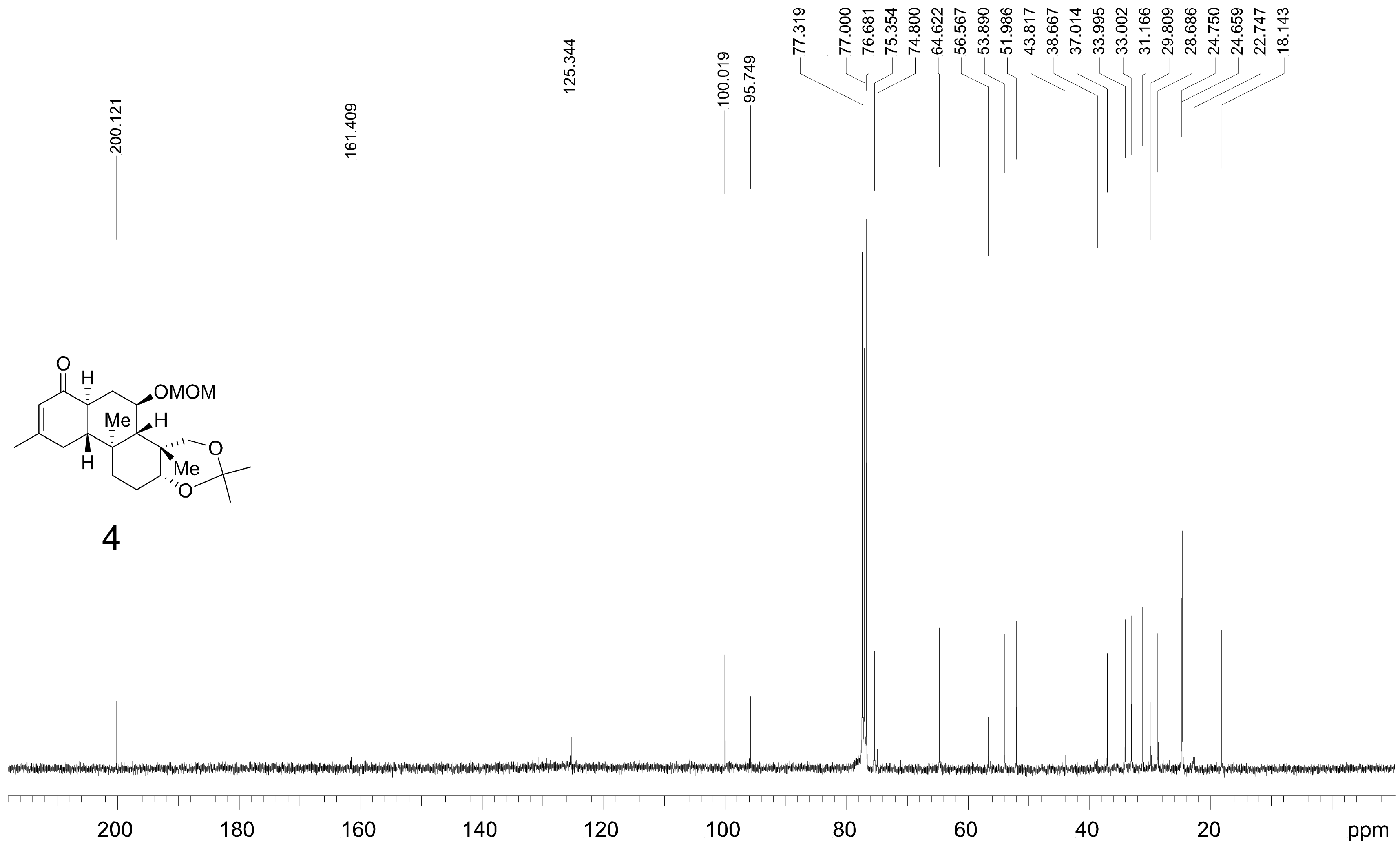

4

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ppm