Synthesis of (*S*,*R*,*R*,*S*,*R*,*S*) 4,6,8,10,16,18-Hexamethyldocosane from *Antitrogus parvulus* via Diastereoselective Hydrogenations

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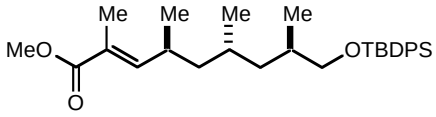
Supporting Information

General procedures: NMR spectra were recorded on a Varian Unity-500 and VXR-300 spectrometer. Optical rotations were measured on Jasco DIP-360 digital polarimeter. Flash chromatography was performed using silica gel (230–600 mesh). Thin layer chromatography was performed using glass plates coated with silica gel 60 F254 (E. Merck, Darmstadt, Germany). Toluene and THF were distilled over Na/benzophenone. Other solvents and reagents were used as received. General catalytic hydrogenation conditions: the corresponding alkene was dissolved in CH_2Cl_2 (1 M) and the Iridium catalyst (L-**2**) (1 mol% for small scale, 0.2 mol% for gram scale reactions, unless otherwise stated) was then added. The resulting solution was degassed by three cycles of freeze-pump-thaw and then transferred to a Parr Bomb. The bomb was flushed with hydrogen for 1 min without stirring. The mixture was then stirred at 700 rpm at 50 atm. After 4 h, the bomb was vented and the solvent evaporated. The crude product was passed through a silica plug (EtOAc/hexanes =3:7). The diastereomeric ratio of the crude material was then measured through chiral capillary GC analysis using β- or a γ-CD

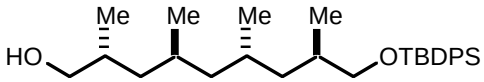
column (carrier gas: helium; column pressure: 29.71 Psi; gas flow rate: 2.1 mL/min; gradient temperature: 5 ^{o}C/min: 90 ^{o}C hold time: 30 min, 200 ^{o}C, 5 min). For compound **16**, the MS (ESI) data was collected by addition of LiCl solution (0.1 M in MeOH) to the sample solution.

Experimental Procedures



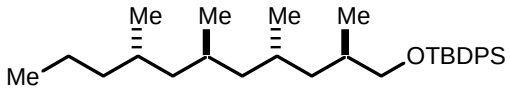
11

To a solution of alcohol **10** (137 mg, 0.332 mmol) in CH_2Cl_2 (5 mL) at 25 ^{o}C was added NMO (47 mg, 0.40 mmol), 4 Å MS (1.5 g) followed by TPAP (6.0 mg, 0.02 mmol). The reaction mixture was stirred for 30 min and then filtered through Celite, eluting with hexanes (25 mL). The filtrate was concentrated and the resulting residue was put on a high vacuum pump for 30 min., the resulting residue was dissolved in toluene (5 mL) at 25 ^{o}C without any further purification. To this solution was added the Wittig reagent 2-(triphenylphosphanylidene)propionic acid methyl ester (347 mg, 1.0 mmol) in one portion. The reaction mixture was then put in an oil bath (preheated to 80 ^{o}C) and stirred for 12 h. After being cooled to 25 ^{o}C, the reaction mixture was diluted with hexanes (15 mL) and filtered through Celite, the filtrate was then concentrated. Purification of the residue by flash chromatography on silica gel, eluting with EtOAc/hexanes (5:95) gave alkene **11** as a colorless oil (104 mg, 65% over 2 steps). $[\alpha]^{23}_{D}$ +32.6 (*c* 4.20, $CHCl_3$); IR (neat) 3066, 2959, 2860, 1717, 1646, 1468, 1424, 1274, 1108 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67-7.62 (m, 4H), 7.43-7.34 (m, 6H), 6.52 (d, *J* = 10.3 Hz, 1H), 3.72 (s, 3H), 3.48-3.38 (m, 4H), 2.61-2.49 (m, 1H), 1.81 (d, *J* = 1.2 Hz, 3H), 1.74-1.64 (m, 1H), 1.46-1.37 (m, 1H), 1.27-1.07 (m, 4H), 1.01 (s, 9H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 148.7, 135.6, 134.0, 129.5, 127.5, 125.5, 69.6, 51.7, 45.1, 40.4, 33.1, 30.7, 27.8, 26.9, 19.9, 19.3, 16.4, 12.5. HRMS (ESI): Exact mass calcd for $C_{30}H_{45}O_3Si$ $[M+H]^+$ 481.3138. Found 481.3140.



12

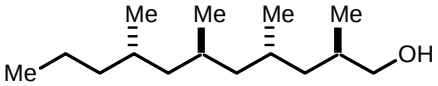
Hydrogenation of **11** (104 mg, 0.216 mmol) was carried out according to the general procedure using L-**2** (1 mol%, 3.6 mg, 0.02 mmol) in CH_2Cl_2 (0.3 mL). NMR of the crude product showed 100% conversion. GC analysis of the crude material showed *anti*:*syn* ratio in the newly formed stereocenter to be 20.0:1.00 ($t_{R(syn)}$ = 54.09 min, $t_{R(anti)}$ = 54.81 min). Without further purification, the reaction mixture was reduced to the more readily separable alcohol (DIBALH, THF, 0 ^oC, 30 min) and purification by column chromatography EtOAc/hexanes (2:98) gave alcohol **12** as a colorless oil (78 mg, 80% **;** GC analysis showed *anti:syn* >120:1.0). $[\alpha]^{23}_D$ +14.6 (*c* 2.22, $CHCl_3$); IR (neat) 3386 (br), 2955, 2908, 2852, 1468, 1424, 1377, 1088 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69-7.64 (m, 4H), 7.43-7.34 (m, 6H), 3.51-3.34 (m, 4H), 1.76-1.66 (m, 2H), 1.58-1.51 (m, 2H), 1.31 (t, *J* = 5.4 Hz, 1H), 1.21-0.96 (m, 6H), 1.04 (m, 9H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.77 (d, *J* = 6.4 Hz, 3H), 0.76 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6, 134.1, 129.4, 127.5, 69.4, 69.0, 46.4, 41.3, 41.2, 33.1, 27.1, 27.0, 26.8, 19.4, 19.3, 19.2, 16.8, 16.4. HRMS (ESI): Exact mass calcd for $C_{29}H_{47}O_2Si[M+H]^+$ 455.3345. Found 455.3350.



13

To a solution of alcohol **12** (777 mg, 1.71 mmol) in CH_2Cl_2 (13 mL) at 25 ^oC was added NMO (220 mg, 1.8 mmol), 4 Å MS (1.0 g) followed by TPAP (30 mg, 0.08 mmol). The reaction mixture was stirred for 30 min and then filtered through Celite, eluting with hexanes (45 mL). The filtrate was concentrated and the resulting residue was put on a high vacuum pump for 30 min. Without any further purification, the resulting residue was dissolved in THF (5 mL) and cooled to -78 ^oC. In a separate round bottom flask, ethyltriphenylphosphonium bromide (1.26 g, 3.4 mmol) suspension in THF (10 mL) cooled to -78 ^oC was added dropwise KHMDS (0.5 M in toluene, 6.8 mL, 3.4 mmol). Stirring was continued for 1 h before the crude aldehyde solution was added via a cannula. After 1 h, saturated NH_4Cl aqueous solution (10 mL) was added and the mixture was stirred and allowed to warm to 25 ^oC. The layers were then separated and the aqueous layer was extracted with Et_2O (3 × 15 mL). The combined

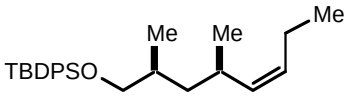
organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. The resulting residue was filtrated through a plug of silica eluting with EtOAc/hexanes (10:90), the filtrate was concentrated to leave a slightly yellow residue. The resulting residue was then dissolved in THF/MeOH(1/1, 10 mL) at 25 ^oC and Pd/C (10%, 150 mg) was added. The atmosphere above the solution was removed under vacuum and then replaced with hydrogen. Stirring was continued for 7 h and the reaction mixture was filtered through Celite. The filtrate was concentrated, the residue was purified though column chromatography, eluting with EtOAc/hexanes (10:90) gave the two-carbon homologated product **13** (607 mg, 76% over three steps) as a colorless oil. $[\alpha]^{23}_D$ +9.76 (*c* 1.20, $CHCl_3$); IR (neat) 2960, 2924, 2863, 1456, 1423, 1374, 1118 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68-7.65 (m, 4H), 7.43-7.34 (m, 6H), 3.47 (dd, *J* = 5.4, 9.8 Hz, 1H), 3.39 (dd, *J* = 6.8, 9.8 Hz, 1H), 1.79-1.67 (m, 1H), 1.58-1.40 (m, 4H), 1.35-1.07 (m, 5H), 1.05 (s, 9H), 1.01-0.96 (m, 4H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.85 (t, *J* = 6.8 Hz, 3H), 0.78 (d, *J* = 6.8 Hz, 3H), 0.76 (d, *J* = 6.8 Hz, 3H), 0.73 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6, 134.1, 129.5, 127.6, 69.5, 46.4, 45.5, 41.4, 40.2, 33.2, 29.7, 27.3, 27.2, 26.9, 20.1, 19.6, 19.5, 19.4, 19.3, 16.9, 14.4. HRMS (ESI): Exact mass calcd for $C_{31}H_{51}OSi[M+H]^+$ 467.3709. Found 467.3715.



14

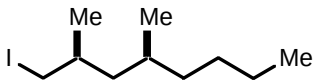
To a solution of compound **13** (192 mg, 0.41 mmol) in THF (1 mL) was added dropwise a solution of TBAF (1 M in THF, 0.8 mL, 0.8 mmol) at 25 ^oC. Stirring was continued for 1.5 h, then the reaction was diluted with EtOAc (5 mL) followed by NH_4Cl (2 mL of a saturated, aqueous solution). The organic layer was separated and the aqueous layer was extracted with ether (3 × 5 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash column chromatography, eluting with Et_2O/hexanes (10:90) gave alcohol **14** (79 mg, 84%) as a colorless oil. $[\alpha]^{23}_D$ +23.51 (*c* 1.20, $CHCl_3$); IR (neat) 3359 (br), 2920, 2880, 2852, 2825 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.49 (dd, *J* = 5.8, 10.3 Hz, 1H), 3.44 (dd, *J* = 6.8, 10.3 Hz, 1H), 1.74-1.70 (m, 1H), 1.64-1.46 (m, 4H), 1.34-1.01 (m, 9H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.90 (t, *J* = 6.5 Hz, 3H), 0.85 (d, *J* = 6.4 Hz, 3H), 0.83 (d, *J* = 6.8 Hz,

3H), 0.82 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 69.0, 46.5, 45.5, 41.3, 40.2, 33.2, 29.7, 27.3, 27.1, 20.1, 19.6, 19.5, 19.4, 16.4, 14.4. HRMS (ESI): Exact mass calcd for $C_{15}H_{33}O[M+H]^+$ 229.2531. Found 229.2529.



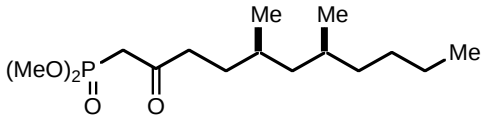
7

To a solution of oxalyl chloride (0.83 mL, 9.51 mmol) in CH_2Cl_2 (13 mL) cooled to -78 ^{o}C was added dropwise DMSO (1.12 mL, 15.7 mmol). After 5 min, a -78 ^{o}C solution of alcohol **6** (1.67 g, 4.53 mmol)[1] in CH_2Cl_2 (10 mL, 2× 1 mL for rinsing) was rapidly added via cannula. After 5 min, Et_3N (3.2 mL, 22.7 mmol) was introduced and the reaction mixture was allowed to warm to 0 ^{o}C before NH_4Cl (10 mL) was added followed by Et_2O (25 ml). The layers were separated, the organic layer was washed sequentially with H_2O (2 mL) and brine (3 mL). The organic extract was dried (Na_2SO_4) and concentrated *in vacuo*. The resulting residue was carried out to the next step without any further purification. In a separate round bottom flask, ^{n}propyltriphenylphosphonium bromide (2.62 g, 6.8 mmol) suspension in THF (15 mL) cooled to -78 ^{o}C was added dropwise KHMDS (0.5 M in toluene, 13.5 mL, 6.75 mmol). Stirring was continued for 1 h before the crude aldehyde in THF solution (1.5 mL, 2× 0.5 mL for rinsing) was cannulated. After 1 h, saturated NH_4Cl aqueous solution (20 mL) was added and the mixture was stirred and allowed to warm to 25 ^{o}C. The layers were then separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* Purification by flash column chromatography, eluting with EtOAc/hexanes (10:90) gave *Z*-alkene **7** (1.49 g, 83% over two steps) as a colorless oil. $[\alpha]^{23}_D$ +2.78 (*c* 1.05, $CHCl_3$); IR (neat) 3074, 2961, 2860, 1461, 1389, 1108 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (m, 4H), 7.38 (m, 6H), 5.30 (td, *J* = 7.2, 10.8 Hz, 1H), 5.03 (dd, *J* = 9.9, 10.8 Hz, 1H), 3.45 (m, 2H), 2.54 (m, 1H), 2.04 (m, 2H), 1.65 (m, 1H), 1.38 (m, 1H), 1.06 (s, 9H), 0.93 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6, 135.5, 134.1, 130.1, 129.4, 127.5, 69.4, 41.2, 33.6, 29.1, 26.8, 22.2, 20.8, 19.3, 16.6, 14.6. HRMS (ESI): Exact mass calcd for $C_{26}H_{39}OSi[M+H]^+$ 395.2770. Found 395.2770.



9

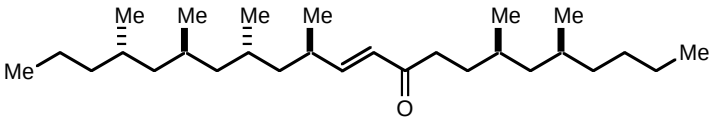
To a solution of silyl ether **8** (1.96 g, 4.95 mmol) in THF (25 mL) was added dropwise a solution of TBAF (1 M in THF, 6.4 mL, 6.4 mmol) at 25 ^{o}C. Stirring was continued for 2 h and then the reaction was diluted with EtOAc (30 mL) followed by NH_4Cl (10 mL of a saturated, aqueous solution). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo.* Purification by flash column chromatography, eluting with Et_2O/hexanes (10:90) gave a colorless oil, NMR analysis showed considerable amount of silyl impurities. Without further attempts for the purification, this material was dissolved in CH_2Cl_2 (5 mL) and used in the next step. To a separate flask charged with PPh_3 (2.6 g, 9.90 mmol), imidazole (1.0 g, 14.6 mmol) and CH_2Cl_2 (10 mL) was added I_2 (2.51 g, 9.90 mmol) at 0 ^{o}C. After 10 min the previous alcohol solution was transferred via cannula into this mixture and stirring was continued for additional 20 min. After concentration the residue was put on silica gel column and flushed with hexanes to give iodide **9** (1.14 g, 86% over two steps) as a colorless oil. $[\alpha]^{23}_{D}$ +4.70 (*c* 1.1, $CHCl_3$); IR (neat) 2953, 2925, 2866, 1457, 1367, 1194 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.25 (dd, *J* = 4.1, 9.6 Hz, 1H), 3.13 (dd, *J* = 6.0, 9.6 Hz, 1H), 1.48 (m, 2H), 1.27 (m, 6H), 0.97 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.0, 36.6, 31.8, 29.9, 29.0, 22.9, 21.3, 19.8, 18.3, 14.1. MS (GCMS/CI): calcd for $C_{10}H_{22}I$ $[M+H]^{+}$ 269.0. Found 269.1.



3

Sodium hydride (187 mg, 60% suspension in mineral oil, 4.67 mmol) in a round bottom flask under nitrogen atmosphere was washed with dry hexanes (3 × 0.5 mL). Then THF (6 mL) was charged into this flask and the mixture was cooled to 0 ^{o}C. To this solution was added dropwise dimethyl (2-oxopropyl)-phosphonate (776 mg, 4.67 mmol). After 30 min, *n*-BuLi (2.33 mL, 2.0 M in cyclohexanes, 4.66 mmol) was introduced dropwise into this white suspension; this gave a yellow solution. After 30 min, iodide **9** (1.14 g, 4.24 mmol) in THF (2 mL) was added dropwise via cannula. Stirring was continued for 1 h and then the reaction mixture was diluted with ether (10 mL) followed by NH_4Cl (10 mL of a saturated, aqueous solution). The organic

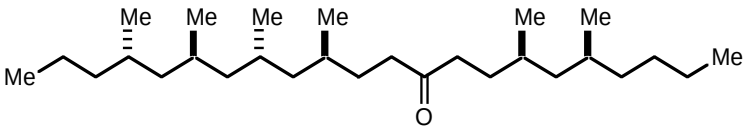
layer was separated and the aqueous layer was extracted with ether (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash column chromatography, eluting with EtOAc/hexanes (1:1) gave phosphonate **3** (1.02 g, 79%) as a colorless oil. $[\alpha]^{23}_D$ -0.61 (*c* 1.31, $CHCl_3$); IR (neat) 2953, 2920, 2860, 1714, 1456, 1392, 1271, 1180, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.74 (d, $J_{(H-P)}$ = 11.1 Hz, 6H), 3.05 (d, $J_{(H-P)}$ = 22.5 Hz, 2H), 2.60-2.53 (m, 2H), 1.62-1.58 (m, 1H), 1.47-1.44 (m, 2H), 1.42-1.11 (m, 7H), 0.99-0.90 (m, 2H), 0.88-0.78 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.1, 52.9(d, $J_{(C-P)}$ = 6.8 Hz), 44.8, 42.02, 41.7(d, $J_{(C-P)}$ = 1.4 Hz), 40.3, 36.4, 29.9, 29.8, 29.4, 29.0, 22.9, 20.1, 19.8, 14.1. HRMS (ESI): Exact mass calcd for $C_{15}H_{32}O_4P[M+H]^+$ 307.3859. Found 307.3857.



15

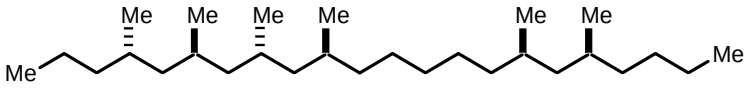
To a solution of alcohol **14** (60.7 mg, 0.266 mmol) in CH_2Cl_2 (3 mL) at 25 ^oC was added NMO (46 mg, 0.392 mmol), 4 Å MS (300 mg) followed by TPAP (5 mg, 0.013 mmol). The reaction mixture was stirred for 30 min and then filtered through a short plug of silica, eluting with ether (5 mL). The filtrate was concentrated and gave a colorless oil. Without further purification, the resulting residue was dissolved in THF (1 mL). To a separate round bottom flask charged with activated $Ba(OH)_2$ (85 mg, 0.266 mmol) was added a solution of phosphonate **3** (81 mg, 0.266 mmol) in wet THF (2 mL, THF:H_2O 40:1) at 25 ^oC. After 10 min, the previous aldehyde solution was added dropwise into the white suspension via cannula. Stirring was continued for 5 min, and then the reaction mixture was concentrated *in vacuo*. Purification of the resulting residue by flash column chromatography on silica gel, eluting with EtOAc/hexanes (5:95) gave *α,β*-unsaturated ketone **15** (92.5 mg, 86% over two steps) as a colorless oil. $[\alpha]^{23}_D$ -19.8 (*c* 1.01, $CHCl_3$); IR (neat) 2959, 2927, 2970, 1694, 1676, 1631, 1464, 1379 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.67 (dd, *J* = 7.8, 15.9 Hz, 1H), 6.00 (d, *J* = 15.9 Hz, 1H), 2.53-2.36 (m, 2H), 1.68-1.40 (m, 6H), 1.36-1.14 (m, 12H), 1.09-0.92 (m, 10H), 0.88-0.72 (m, 22H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.4, 152.9, 128.1, 45.7, 45.3, 44.9, 44.4, 40.1, 37.8, 36.5,

34.1, 31.0, 29.9, 29.8, 29.6, 29.1, 27.6, 27.2, 23.0, 20.1, 20.0 (two), 19.8, 19.6, 19.5, 19.3, 14.4, 14.1. HRMS (ESI): Exact mass calcd for $C_{28}H_{54}LiO[M+Li]^+$ 413.4335. Found 413.4339.



16

The enone **15** (81.3 mg, 0.20 mmol) was dissolved in THF/MeOH (2 mL, v:v 1:1), palladium on carbon (10%, 21 mg) was then added carefully. The atmosphere above the solution was removed under vacuum and the replaced with hydrogen. Stirring was continued for 4 h. After filtration through Celite and concentration of the filtrate, the residue was purified though column chromatography, eluting with EtOAc/hexanes (5:95) to give ketone **16** (80.2 mg, 98%) as a colorless oil. $[\alpha]^{23}_D$ +11.6 (*c* 2.20, $CHCl_3$); IR (neat) 2963, 2910, 2875, 1714, 1469, 1383 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.47-2.27 (m, 4H), 1.64-1.37 (m, 8H), 1.31-1.10 (m, 12H), 1.08-0.91 (m, 8H), 0.88-0.74 (m, 24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.1, 46.5, 45.5, 45.1, 44.8, 40.5, 40.3, 40.1, 36.5, 31.6, 30.5, 29.9, 29.8, 29.7, 29.6, 29.1, 27.2 (two coincident signals), 23.0, 20.2, 20.1, 20.0, 19.6, 19.5, 19.4, 19.3, 14.4, 14.2. HRMS (ESI): Exact mass calcd for $C_{28}H_{56}LiO$ $[M+Li]^+$ 415.6846. Found 415.6851.



1

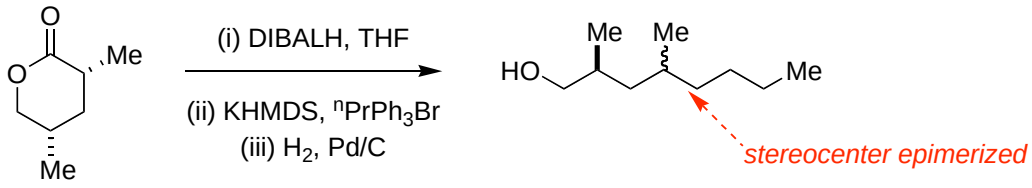
To a solution of ketone **16** (68 mg, 0.16 mmol) and $TsNHNH_2$ (45 mg, 0.241 mmol) in dry DMF/sulfolane (1 mL, 1/1) was added *p*-toluenesulfonic acid monohydrate (4.0 mg, 0.021 mmol) and the reaction mixture was heated to 100 ^oC. Then $NaBH_3CN$ (40 mg, 0.63 mmol) was added and the reaction temperature was raised to 110 ^oC and

continued for 2 h. After cooling to 25 ^{o}C, water (2 mL) then hexanes (2 mL) were added to the reaction mixture with vigorous stirring. The organic layer was separated and the aqueous layer was extracted with hexanes (3 × 1 mL). The organic layers were combined and washed with saturated $NaHCO_3$ solution (2 mL) then dried (Na_2SO_4). After concentration, the residue was purified through column chromatography, eluting with hexanes to give saturated hydrocarbon **1** (59 mg, 94%) as a colorless oil. $[\alpha]^{23}_{D}$ +12.1 (*c* 0.80, $CHCl_3$), natural material: $[\alpha]^{20}_{D}$ +10.7 (*c* 0.44, $CHCl_3$)[2]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.58-1.52 (m, 2H), 1.48-1.42 (m, 4H), 1.32-1.15 (m, 17H), 1.09-0.95 (m, 10H), 0.91-0.84 (m, 7H), 0.82-0.76 (m, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 46.52, 45.54, 45.52, 45.20, 40.21, 37.87, 36.86, 36.55, 30.36, 29.98, 29.95, 29.95, 29.69, 29.17, 27.26, 27.26, 27.06, 26.94, 23.07, 20.29, 20.29, 20.08, 19.64, 19.58, 19.55, 19.53, 14.39, 14.19. Full MS(EI, 70 ev) attached on page S32.

Table S1 comparison of ^{13}C NMR of natural and synthetic **1**

atom number	natural **1** (δc)[3]	synthetic **1** (δc)
C1	14.39	14.39
C2	20.08	20.08
C3	40.22	40.21
C4	29.71	29.69
C5	45.56	45.54
C6	27.29	27.26
C7	46.53	46.52
C8	27.29	27.26
C9	45.54	45.52
C10	30.00	29.98
C11	37.88	37.88
C12	26.94	26.94
C13	30.36	30.36
C14	27.07	27.06
C15	36.88	36.86
C16	29.98	29.95
C17	45.22	45.20
C18	29.98	29.95
C19	36.57	36.55
C20	29.17	29.17
C21	23.07	23.07
C22	14.18	14.19
Me-4,10	19.65, 19.59	19.64, 19.58
Me-6,8	19.55, 19.56	19.55, 19.53
Me-16,18	20.30, 20.30	20.29, 20.29

Our epimerization problem encountered during the synthesis of compound **3** was shown in the following reaction:



(dr >140:1)

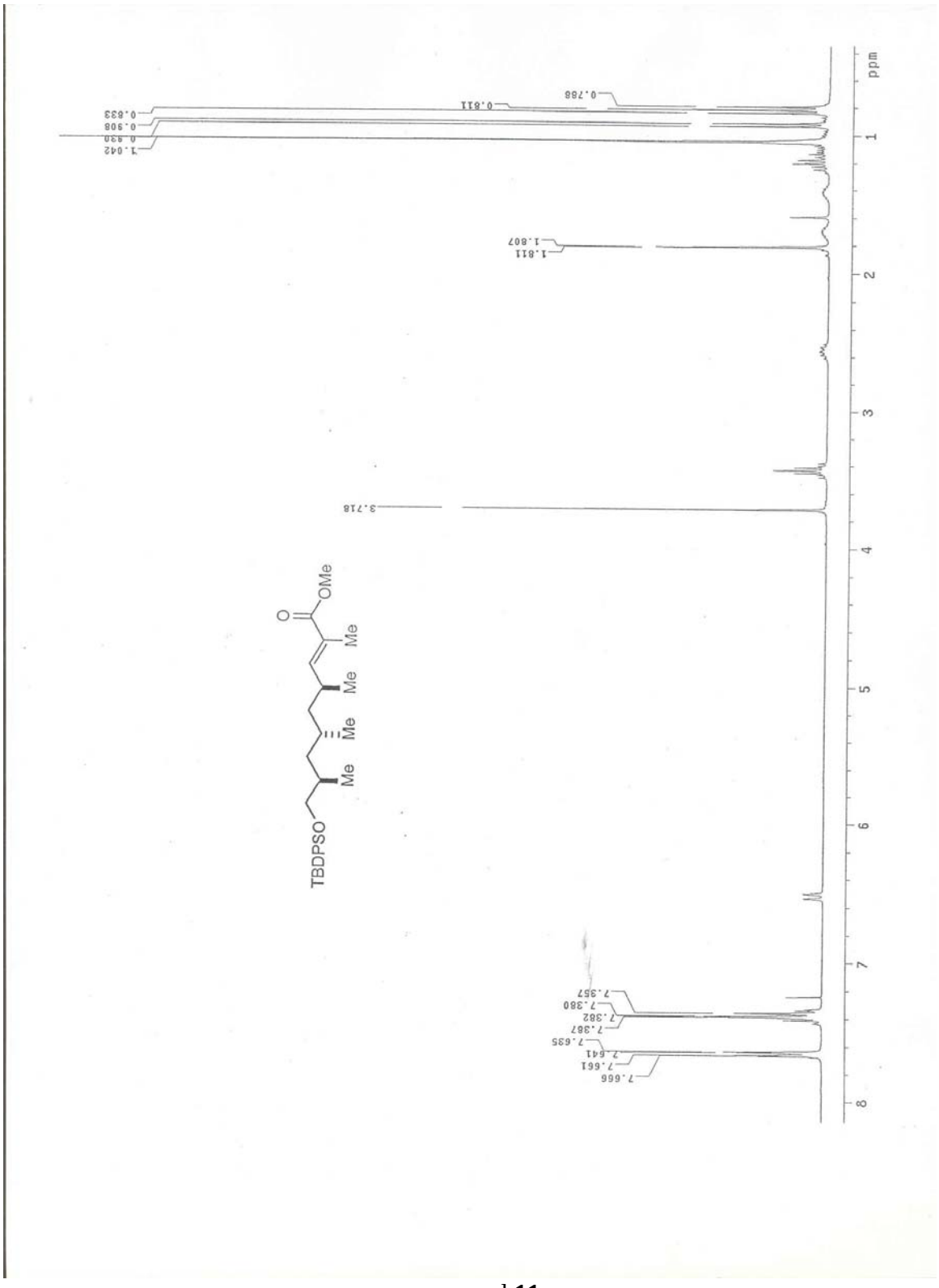
17

(dr ~ 8:1)

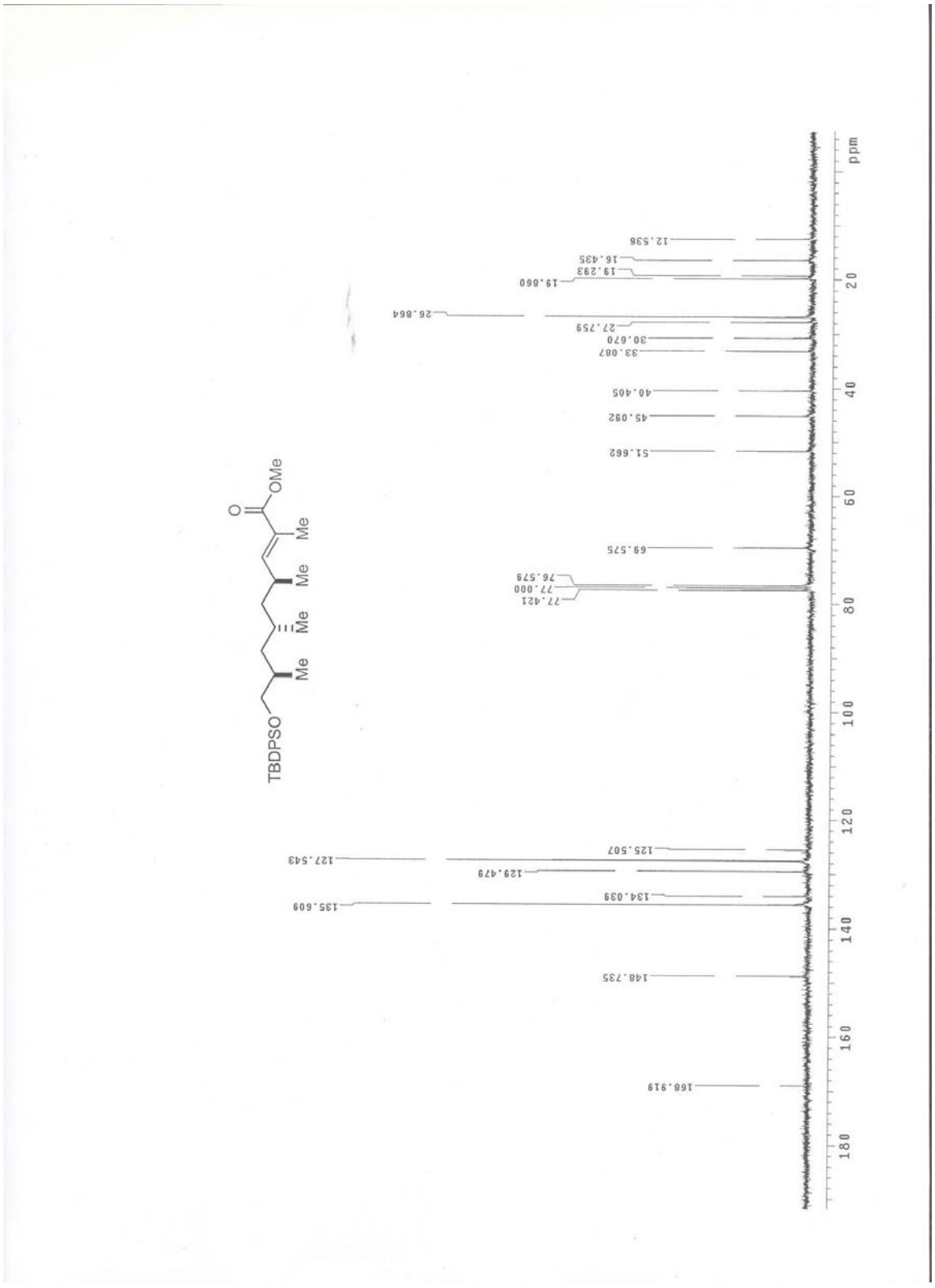
18

References

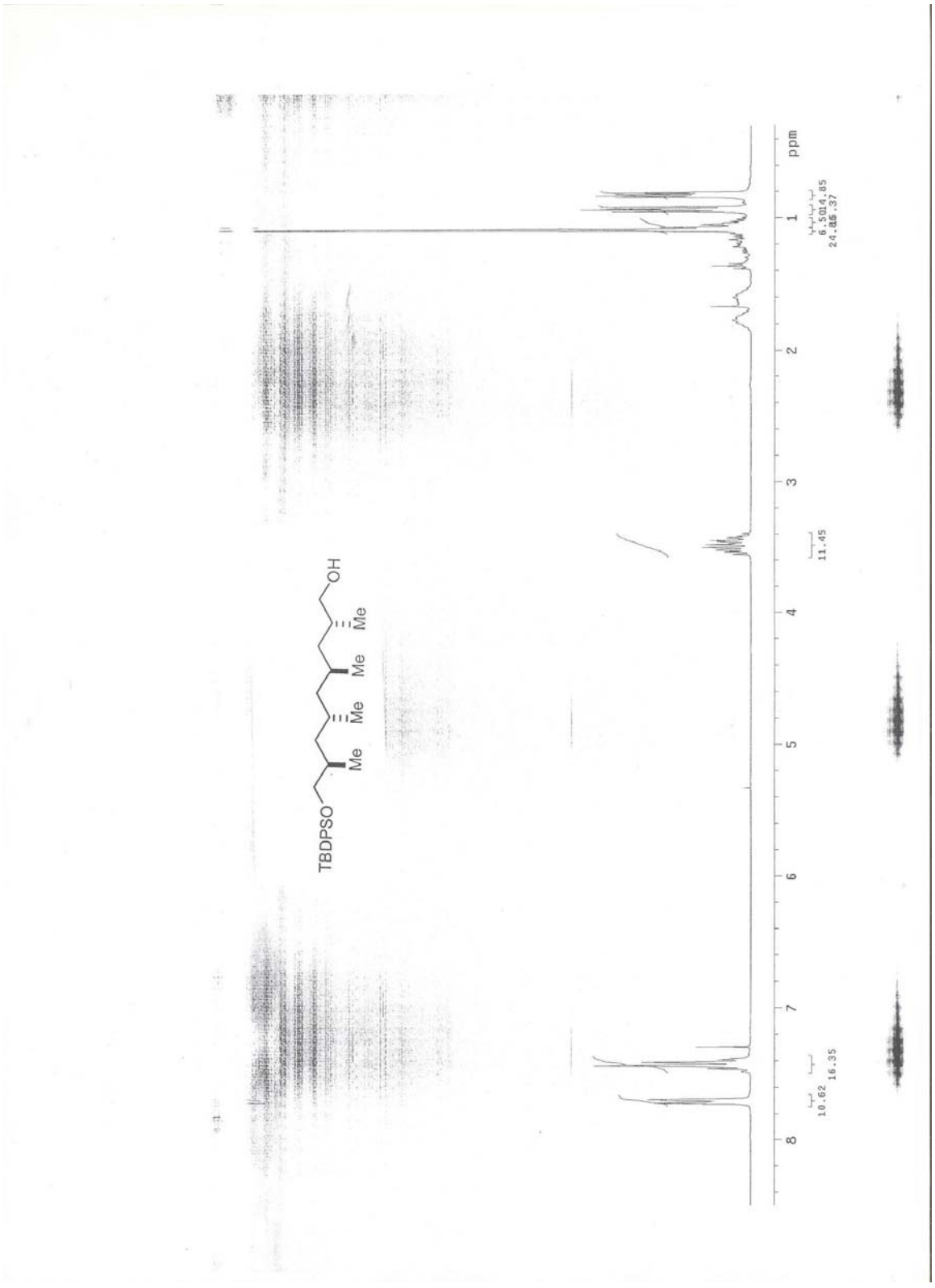
1. The synthesis of ent-**6** was described in: Zhou, J.; Burgess, K. *Angew. Chem. Int. Ed*. **2007**, 46, 1129-1131.
2. Herber, C.; Breit, B. *Angew. Chem. Int. Ed*. **2005**, *44*, 5267-5269.
3. Chow, S.; Fletcher, M. T.; Lambert, L. K.; Gallagher, O. P.; Moore, C. J.; Cribb, B. W.; Allsopp, P. G.; Kitching, W. *J. Org. Chem*. **2005**, *70*, 1808-1827.


ppm
1
2
3
4
5
6
7
8
0.788
0.811
0.833
0.908
0.930
1.042
1.807
1.811
3.718
7.357
7.380
7.382
7.387
7.635
7.641
7.661
7.666
OMe
O
Me
Me
Me
Me
TBDPSO

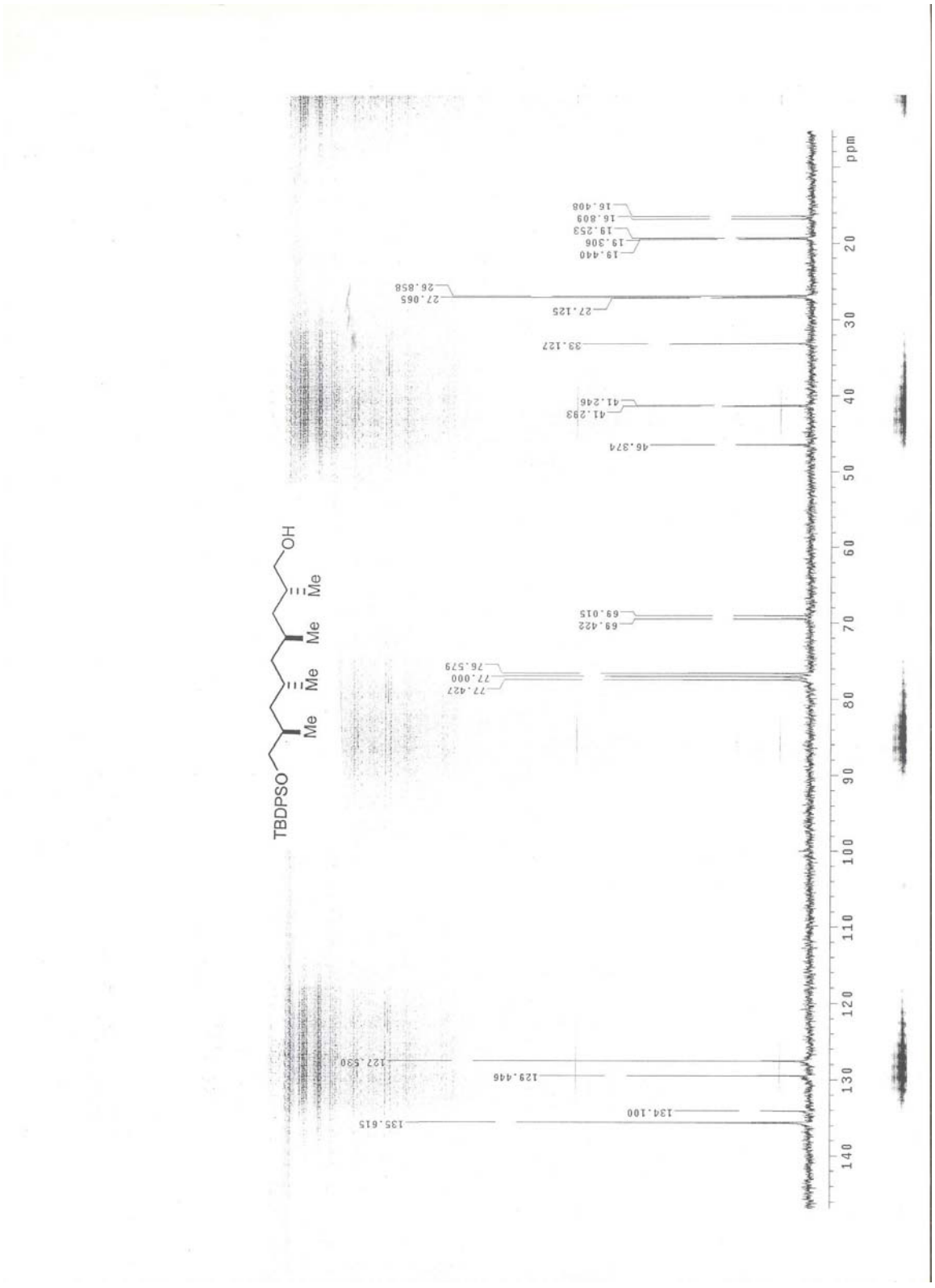
compound **11**


TBDPSO
Me
Me
Me
Me
O
OMe
ppm
12.536
16.435
19.293
19.660
26.864
27.759
30.670
33.087
40.405
45.092
51.662
69.575
76.579
77.000
77.421
125.507
127.543
129.479
134.039
135.609
148.735
168.919

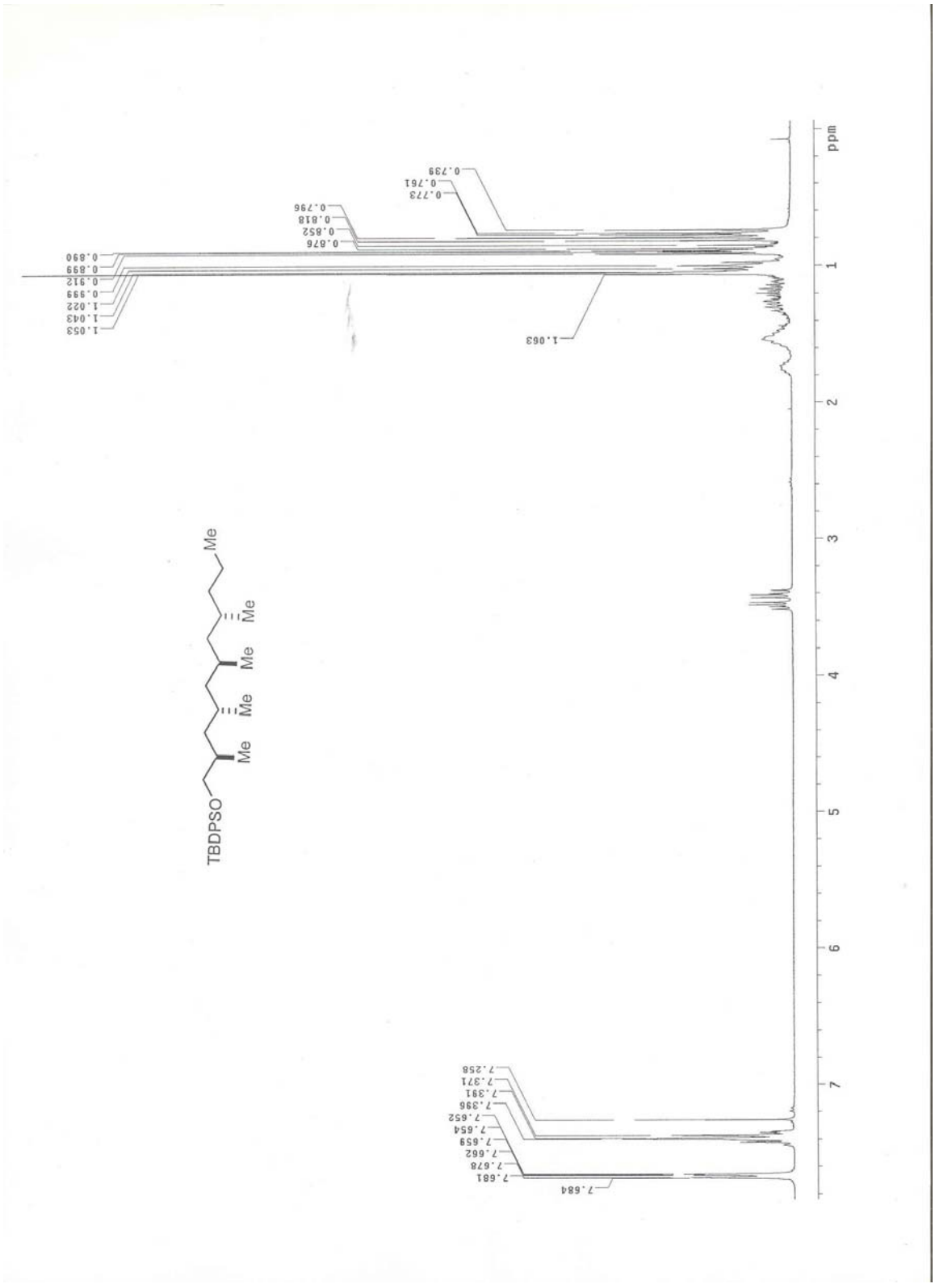
compound **11**


TBDPSO
Me
Me
Me
Me
Me
OH
ppm
1
2
3
4
5
6
7
8
6.50
14.85
24.85
37
11.45
10.62
16.35

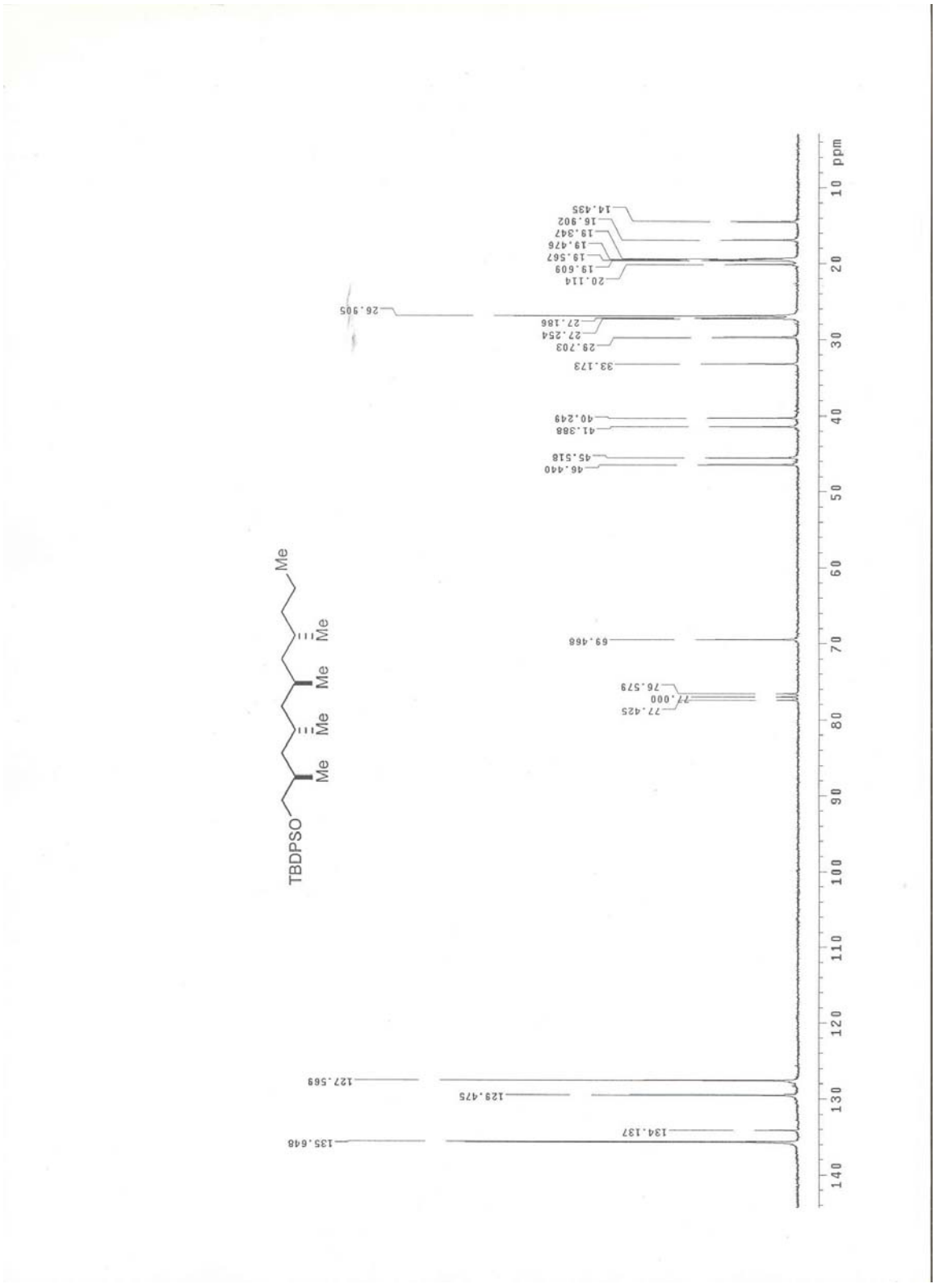
compound **12**


OH
Me
Me
Me
Me
Me
TBDPSO
16.408
16.809
19.253
19.306
19.440
26.858
27.065
27.125
33.127
41.246
41.293
46.374
69.015
69.422
76.579
77.000
77.427
127.530
129.446
134.100
135.615
ppm

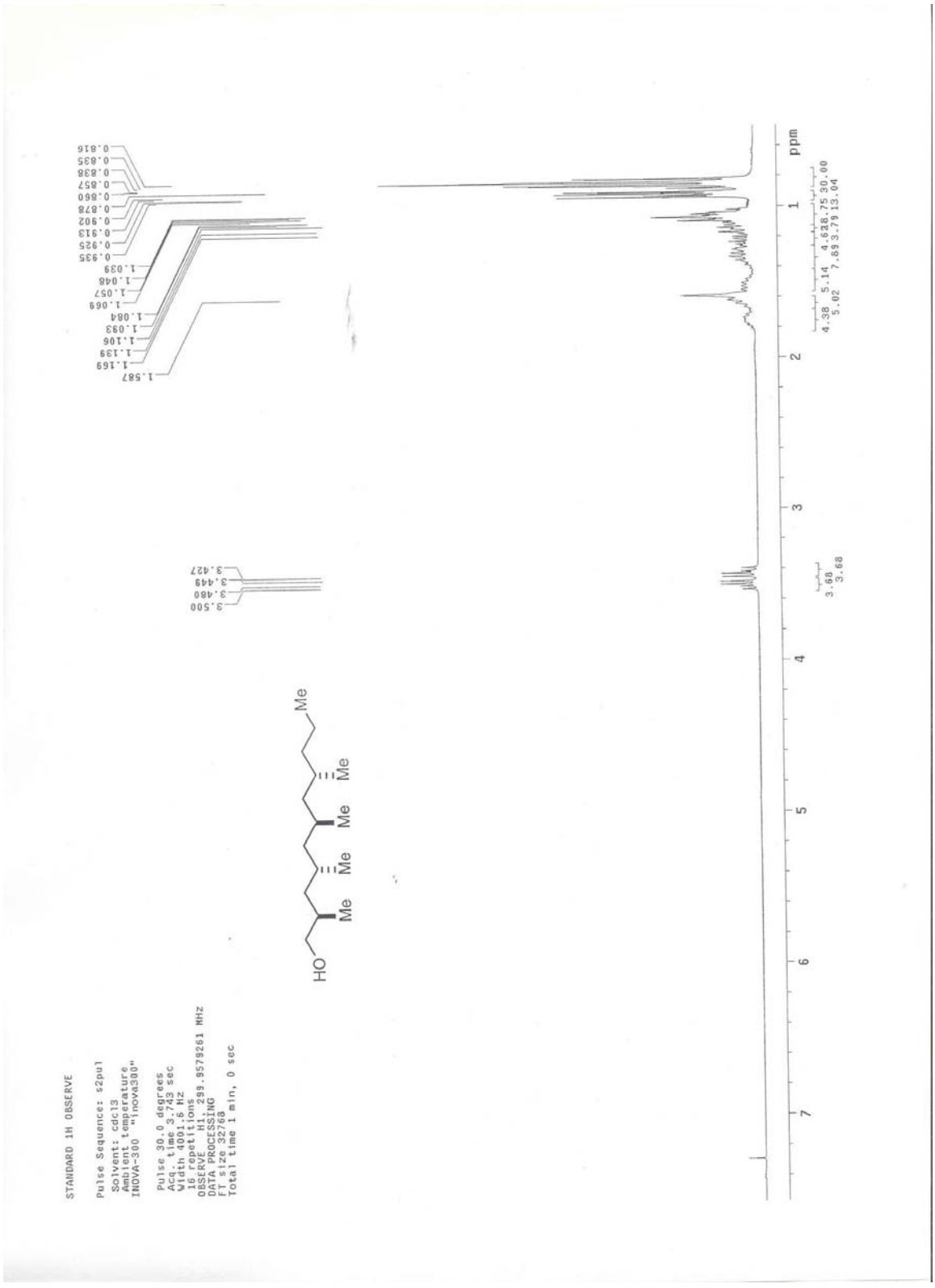
compound **12**


TBDPSO
Me
Me
Me
Me
Me
Me
ppm
0.739
0.761
0.773
0.796
0.818
0.852
0.876
0.890
0.899
0.912
0.999
1.022
1.043
1.053
1.063
7.256
7.371
7.391
7.396
7.652
7.654
7.659
7.662
7.678
7.681
7.684

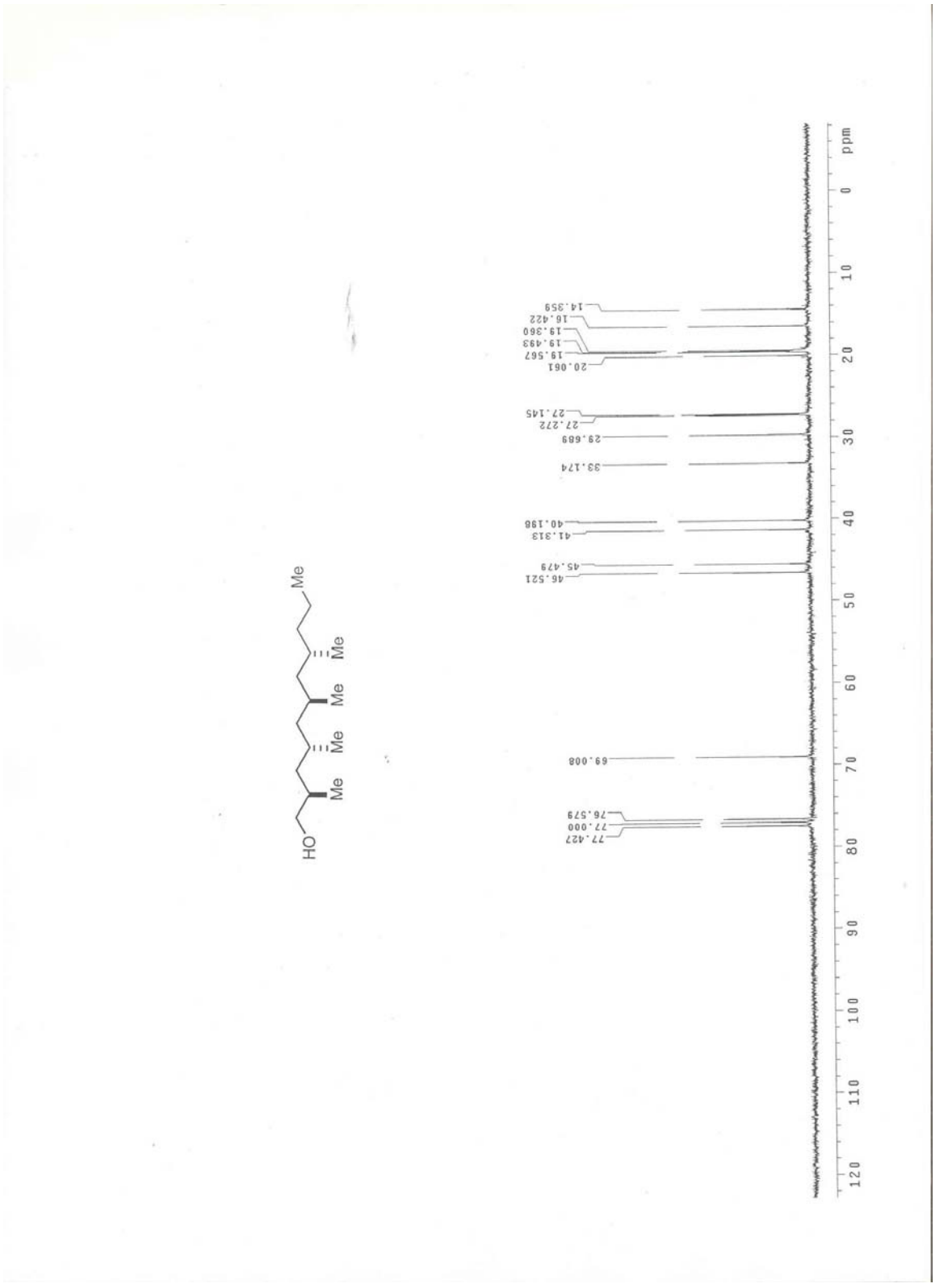
compound **13**


TBDPSO
Me
Me
Me
Me
Me
Me
14.435
16.902
19.347
19.476
19.567
19.609
20.114
26.905
27.186
27.254
29.703
33.173
40.249
41.388
45.516
46.440
69.466
76.579
77.000
77.425
127.569
129.475
134.137
135.646
10
20
30
40
50
60
70
80
90
100
110
120
130
140
ppm

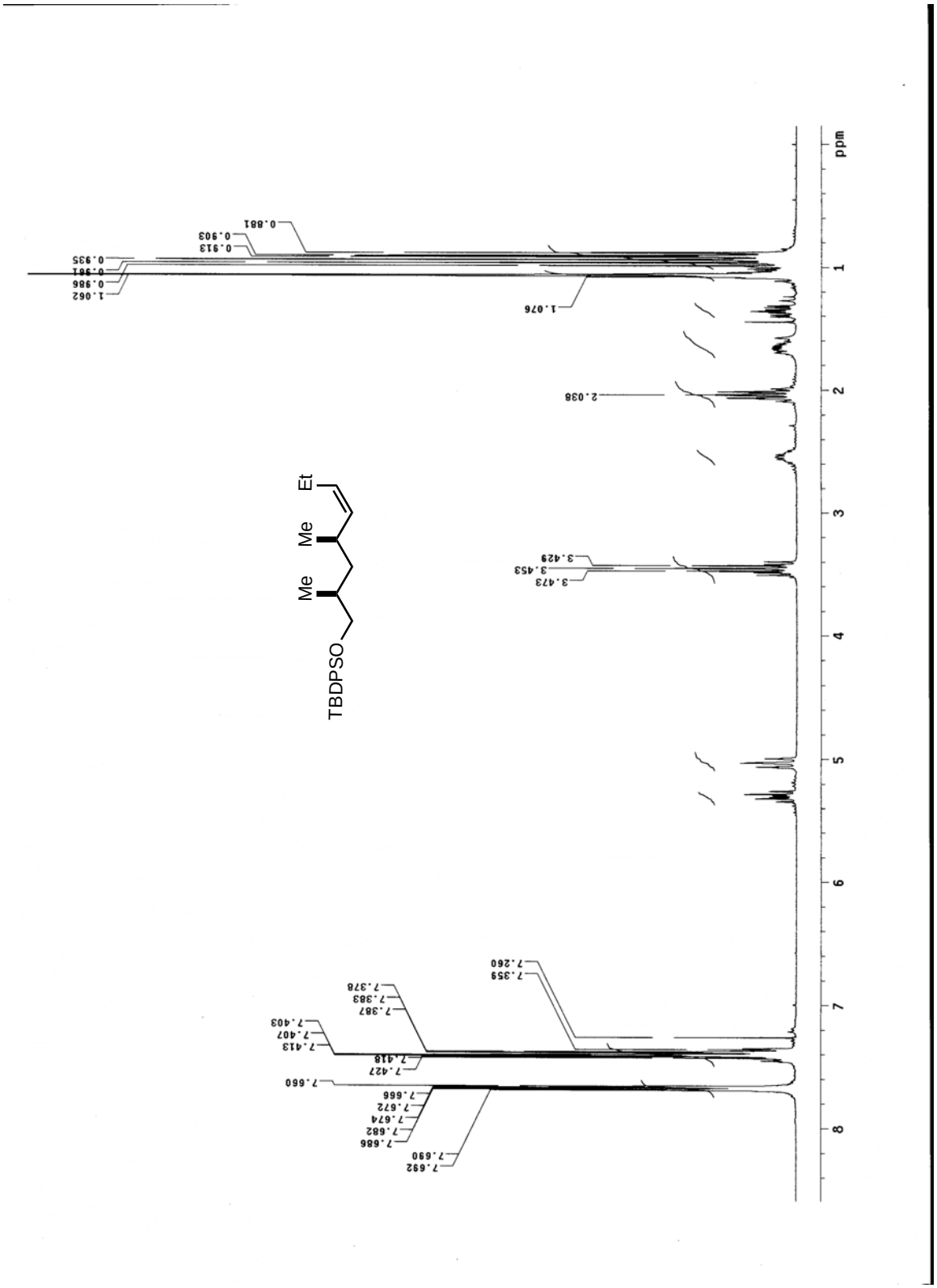
compound **13**


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
INOVA-300 "inova300"
Pulse 30.0 degrees
Acq. time 3.743 sec
Width 4001.6 HZ
16 repetitions
OBSERVE H1, 299.9579261 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 0 sec
HO
Me
Me
Me
Me
Me
Me
ppm
0.816
0.835
0.838
0.857
0.860
0.878
0.902
0.913
0.925
0.935
1.039
1.048
1.057
1.069
1.084
1.093
1.106
1.139
1.169
1.587
3.500
3.480
3.449
3.427
3.68
3.68
4.38
5.14
4.628.75 30.00
5.02
7.69 3.79 13.04

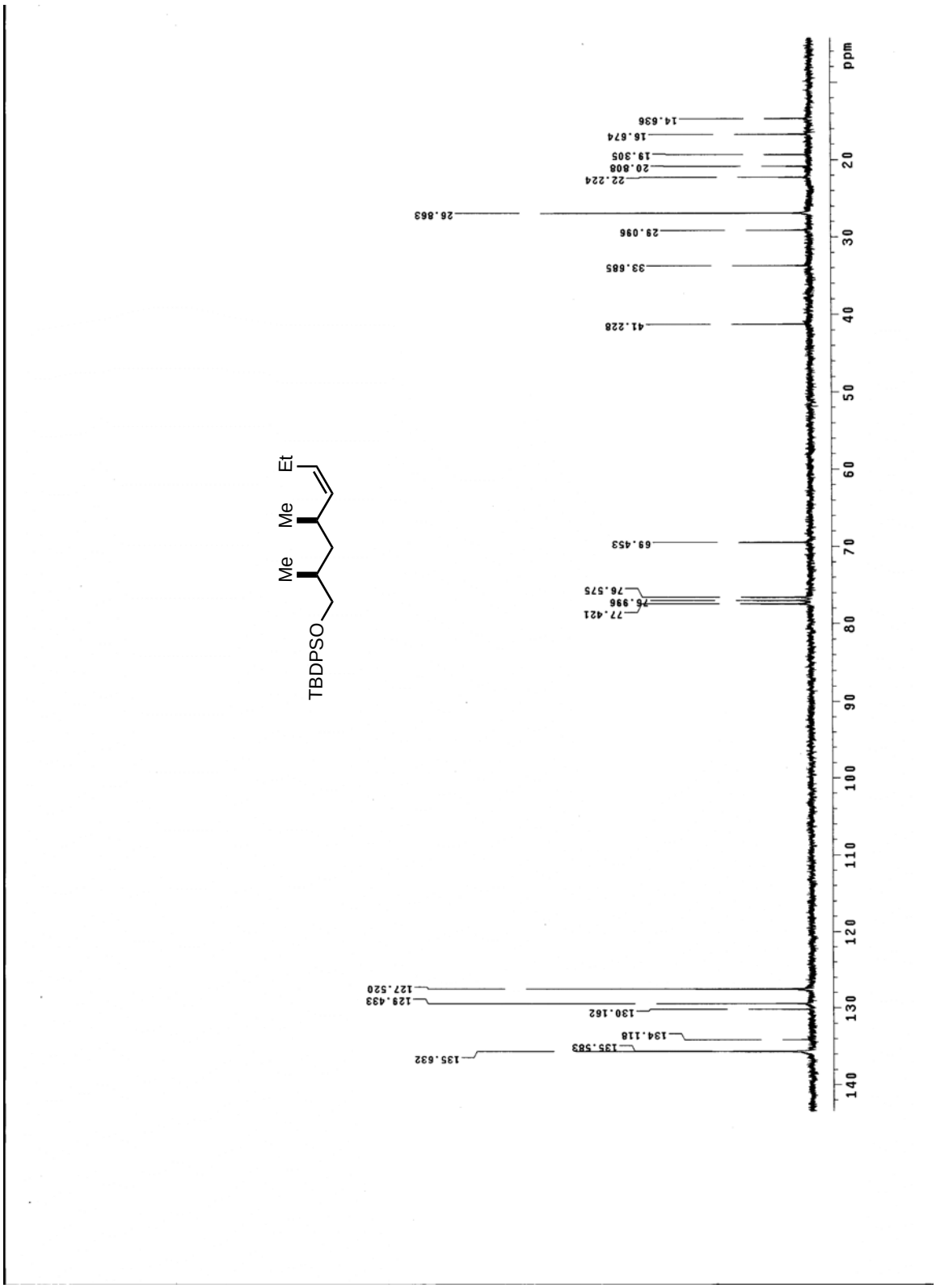
compound **14**


Me
Me
Me
Me
Me
HO
14.359
16.422
19.360
19.493
19.567
20.061
27.145
27.272
29.689
33.174
40.198
41.313
45.479
46.521
69.008
76.579
77.000
77.427
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120

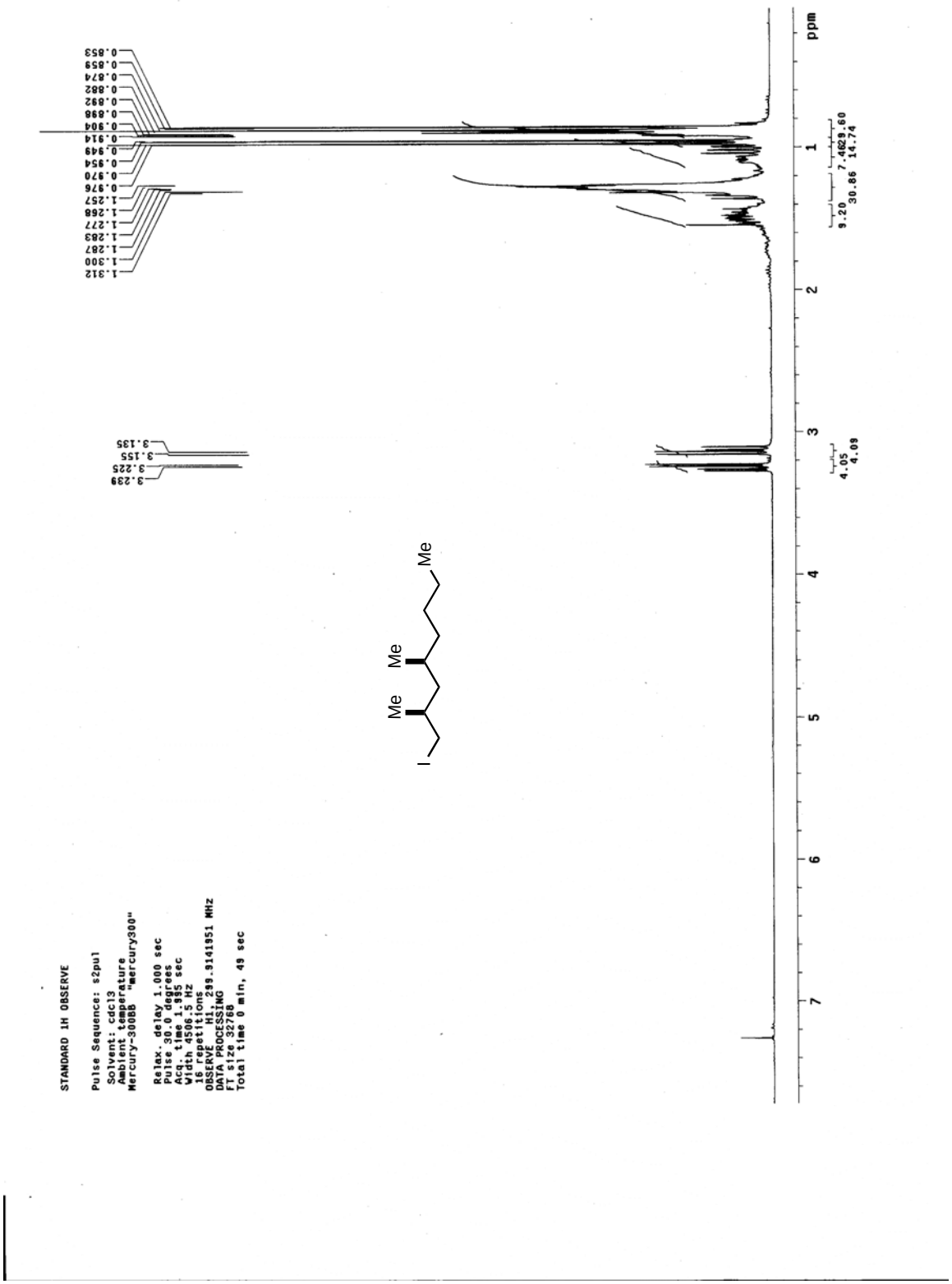
compound **14**


TBDPSO
Me
Me
Et
0.881
0.913
0.903
0.935
0.941
0.986
1.062
1.076
2.038
3.429
3.453
3.473
7.260
7.359
7.378
7.383
7.387
7.403
7.407
7.413
7.418
7.427
7.660
7.666
7.672
7.674
7.682
7.686
7.690
7.692
ppm

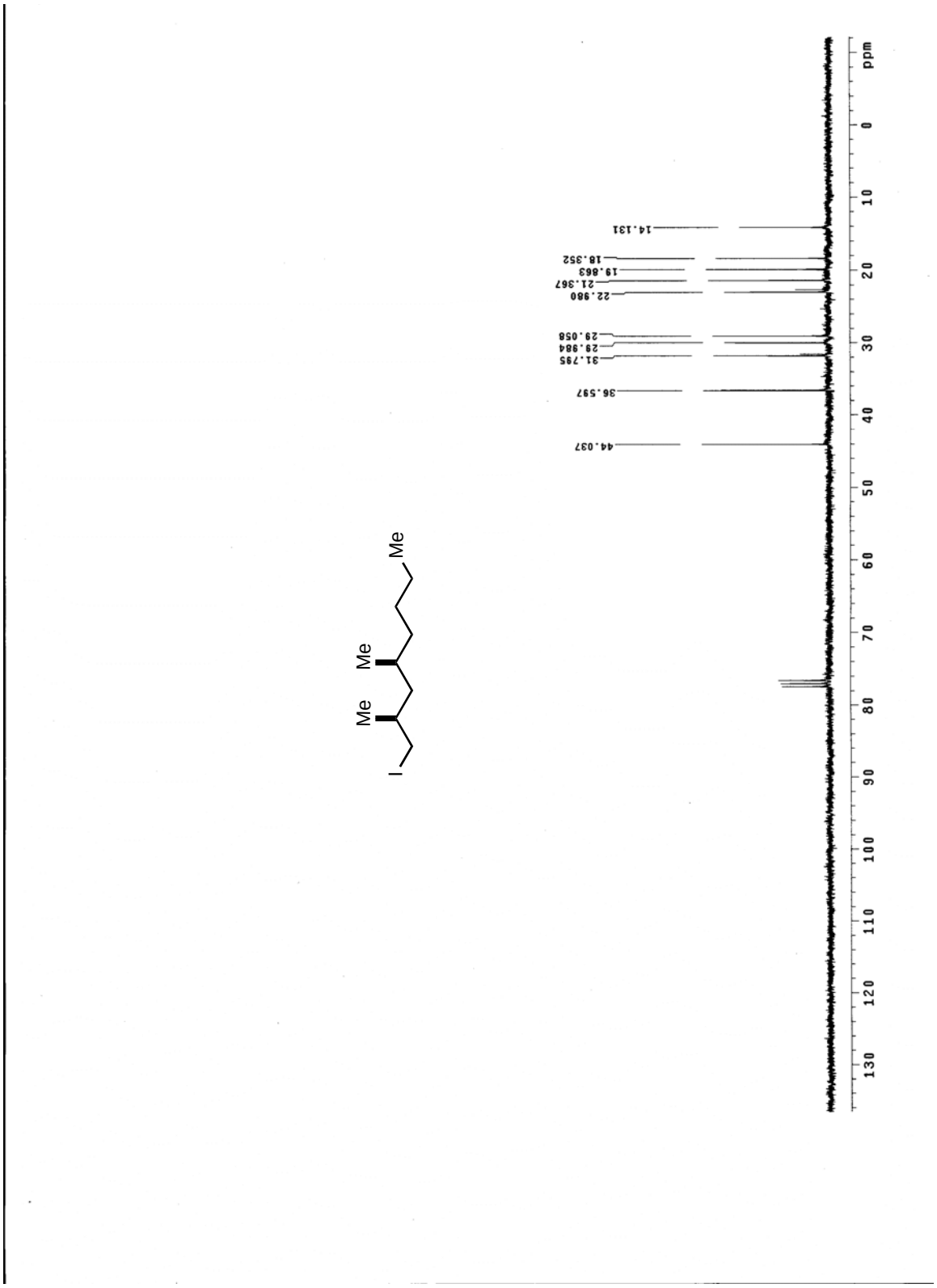
compound **7**


TBDPSO
Me
Me
Et
14.636
16.674
19.305
20.808
22.224
26.863
29.096
33.685
41.228
69.453
76.575
76.996
77.421
127.520
129.433
130.162
134.118
135.583
135.632
ppm

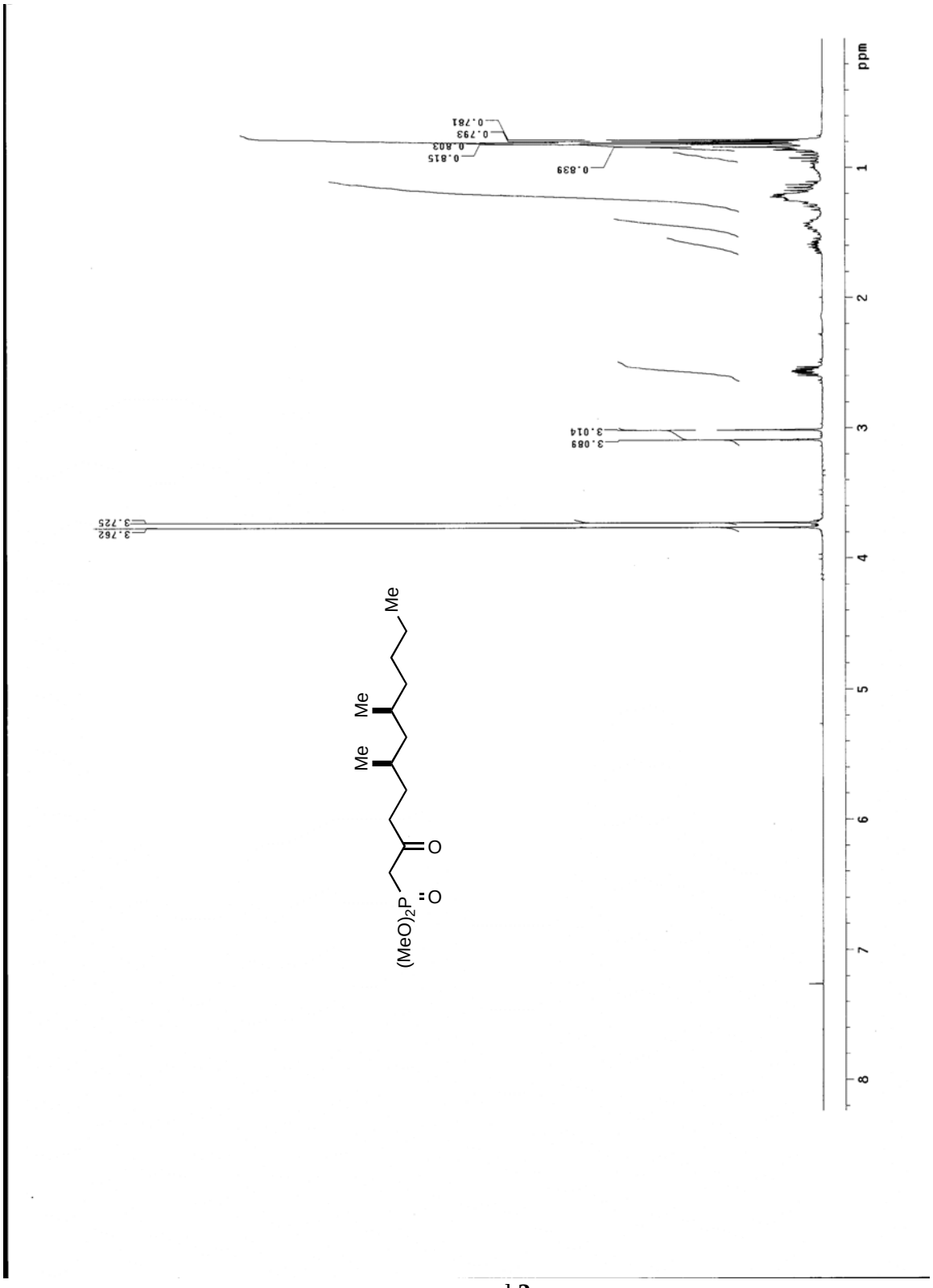
compound **7**


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Mercury-300BB "mercury300"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
16 repetitions
OBSERVE H1, 299.91441951 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 49 sec
Me
Me
Me
I
ppm

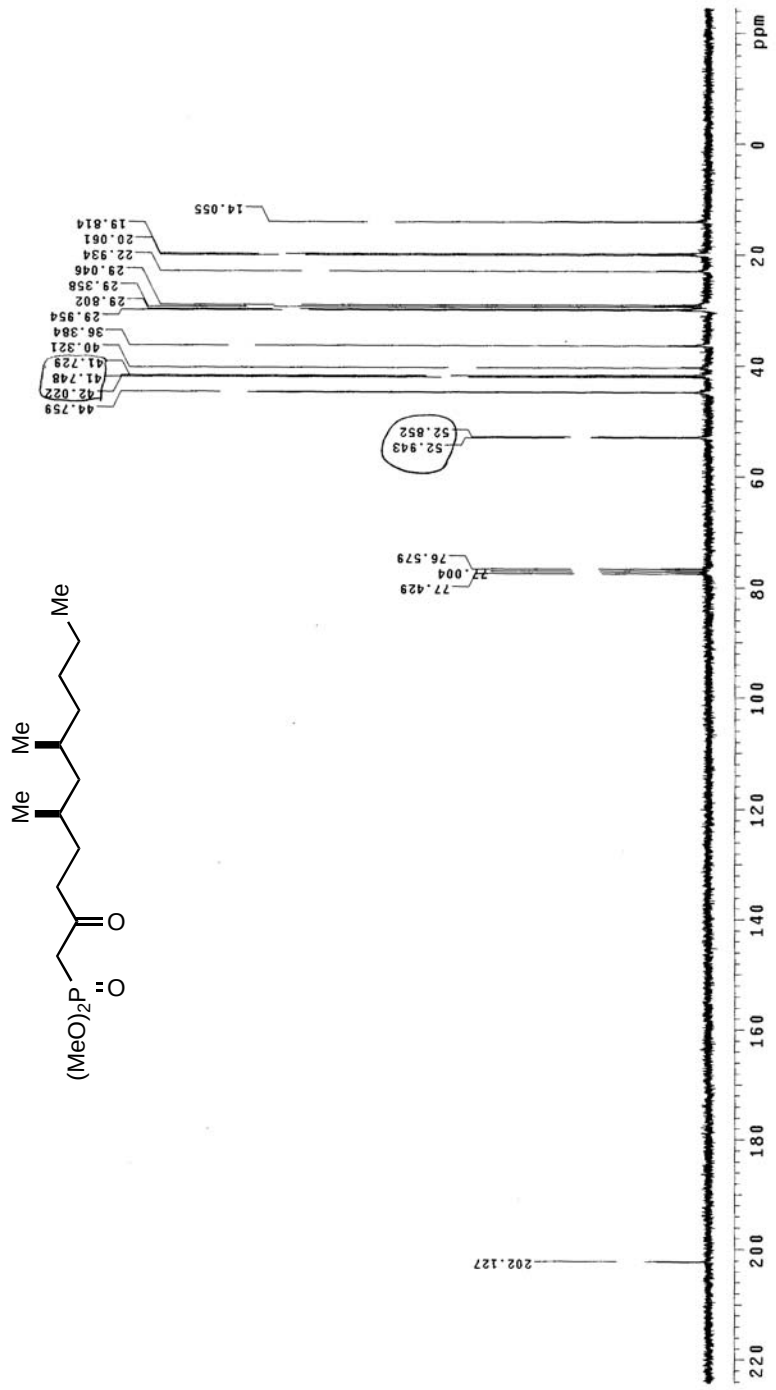
compound **9**


Me
Me
Me
I
14.131
18.352
19.863
21.367
22.980
29.058
29.884
31.795
36.597
44.037
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130

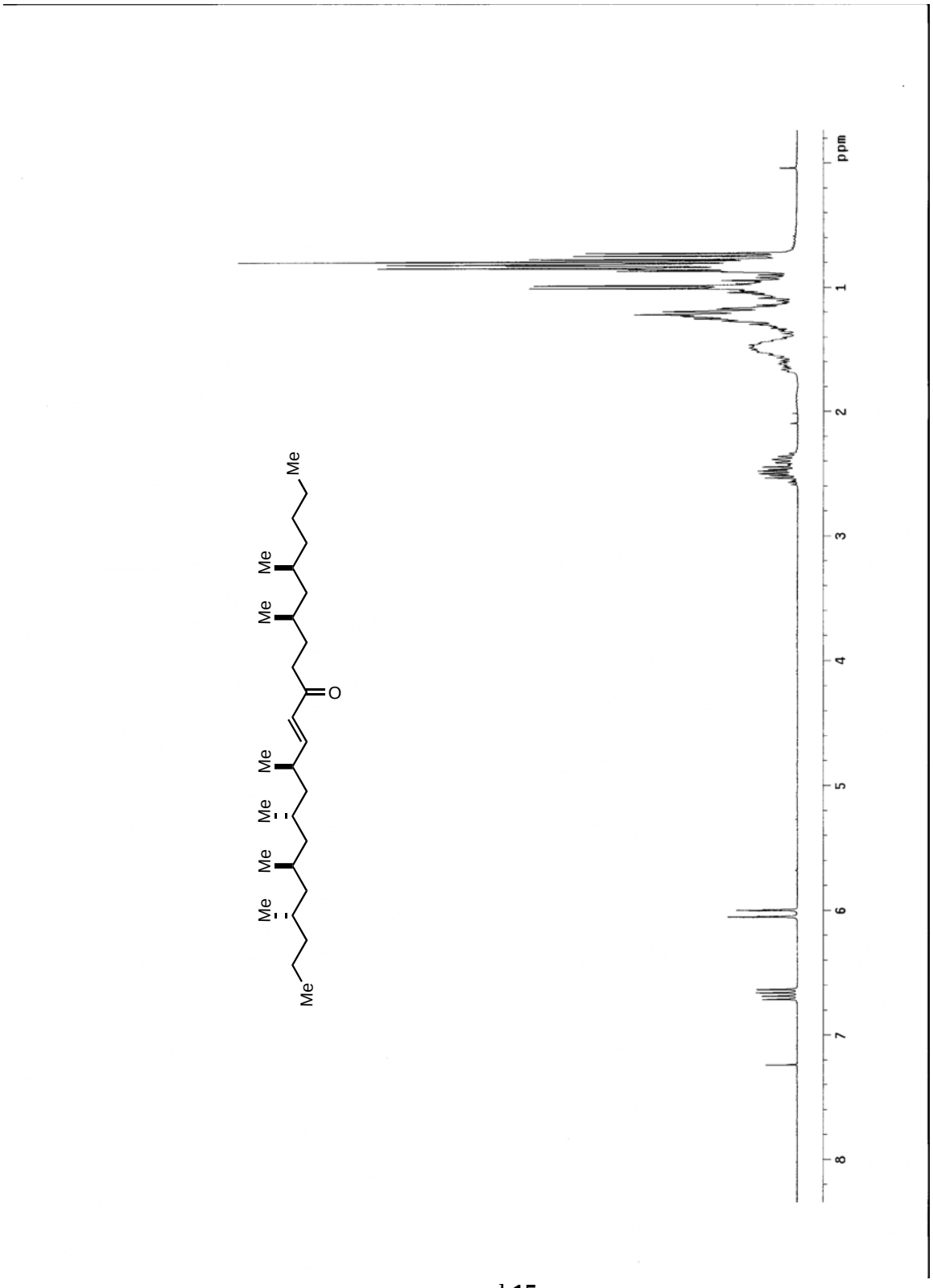
compound **9**


ppm
1
2
3
4
5
6
7
8
0.781
0.793
0.803
0.815
0.839
3.014
3.089
3.725
3.762
Me
Me
Me
O
O
(MeO)2P

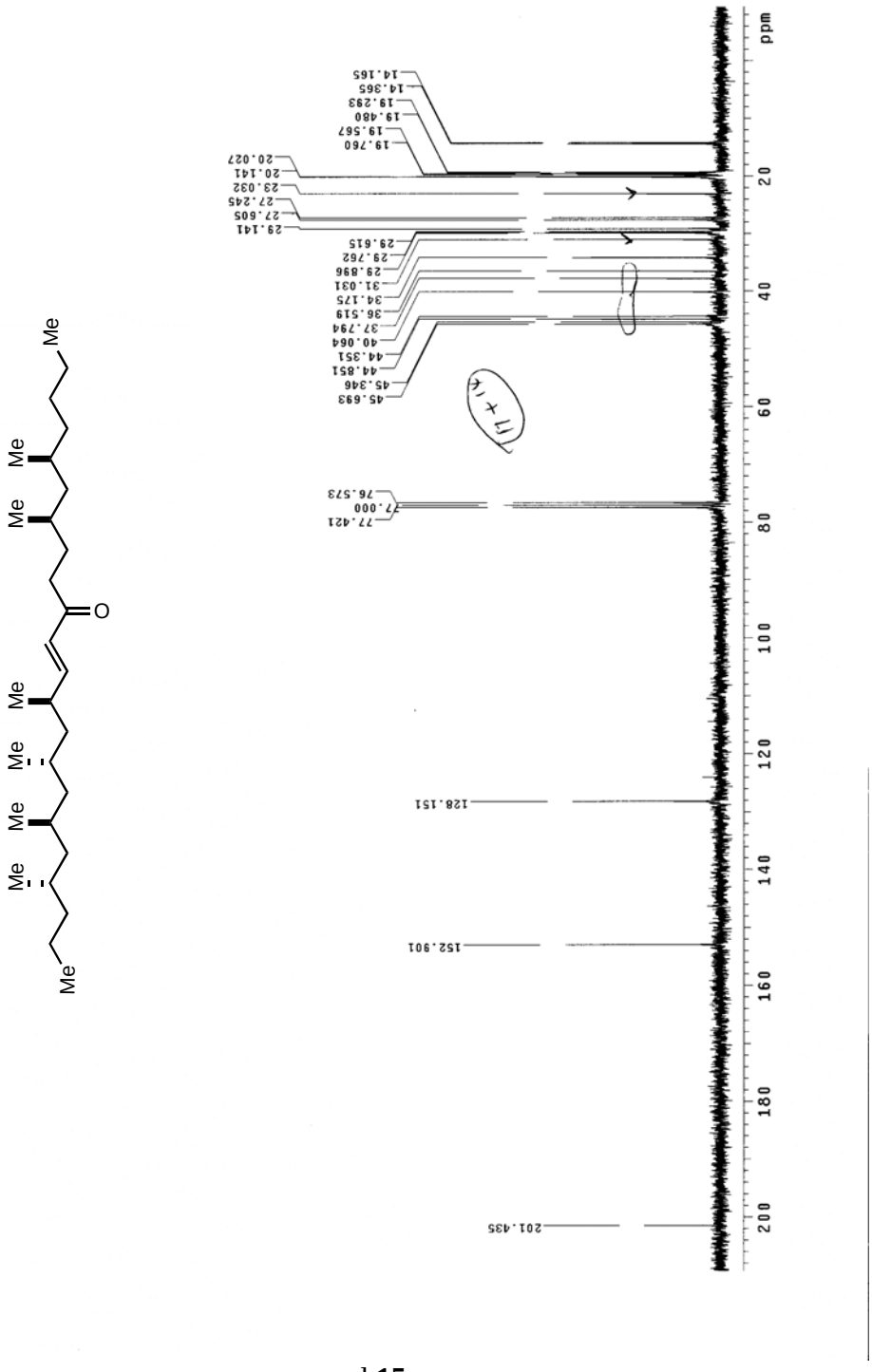
compound **3**


14.055
19.814
20.061
22.934
29.046
29.358
29.802
29.954
36.384
40.321
41.729
41.748
42.022
44.759
52.852
52.943
76.579
77.004
77.429
202.127
ppm
0
20
40
60
80
100
120
140
160
180
200
220
Me
Me
Me
O
O
(MeO)2P

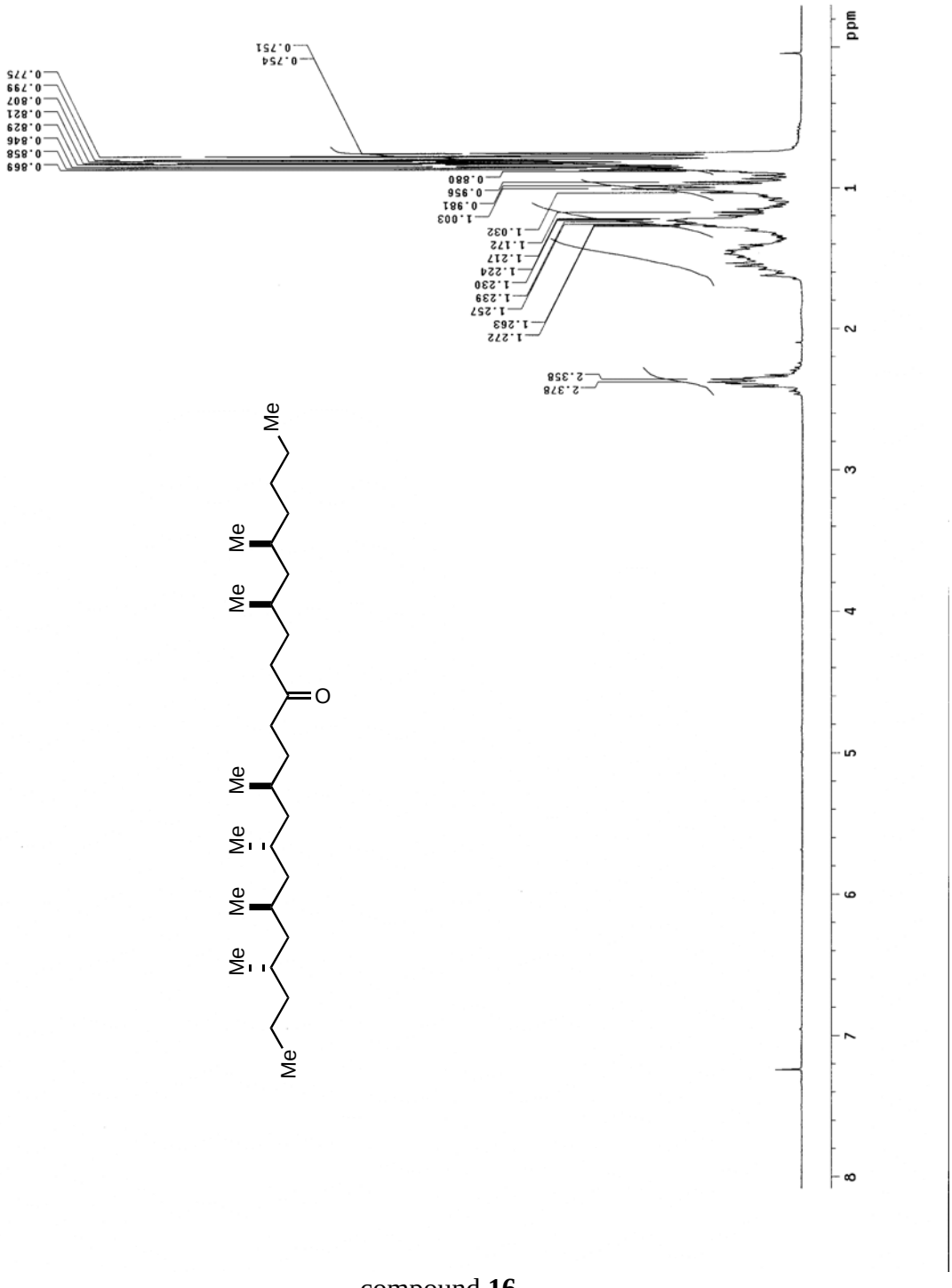
compound **3**



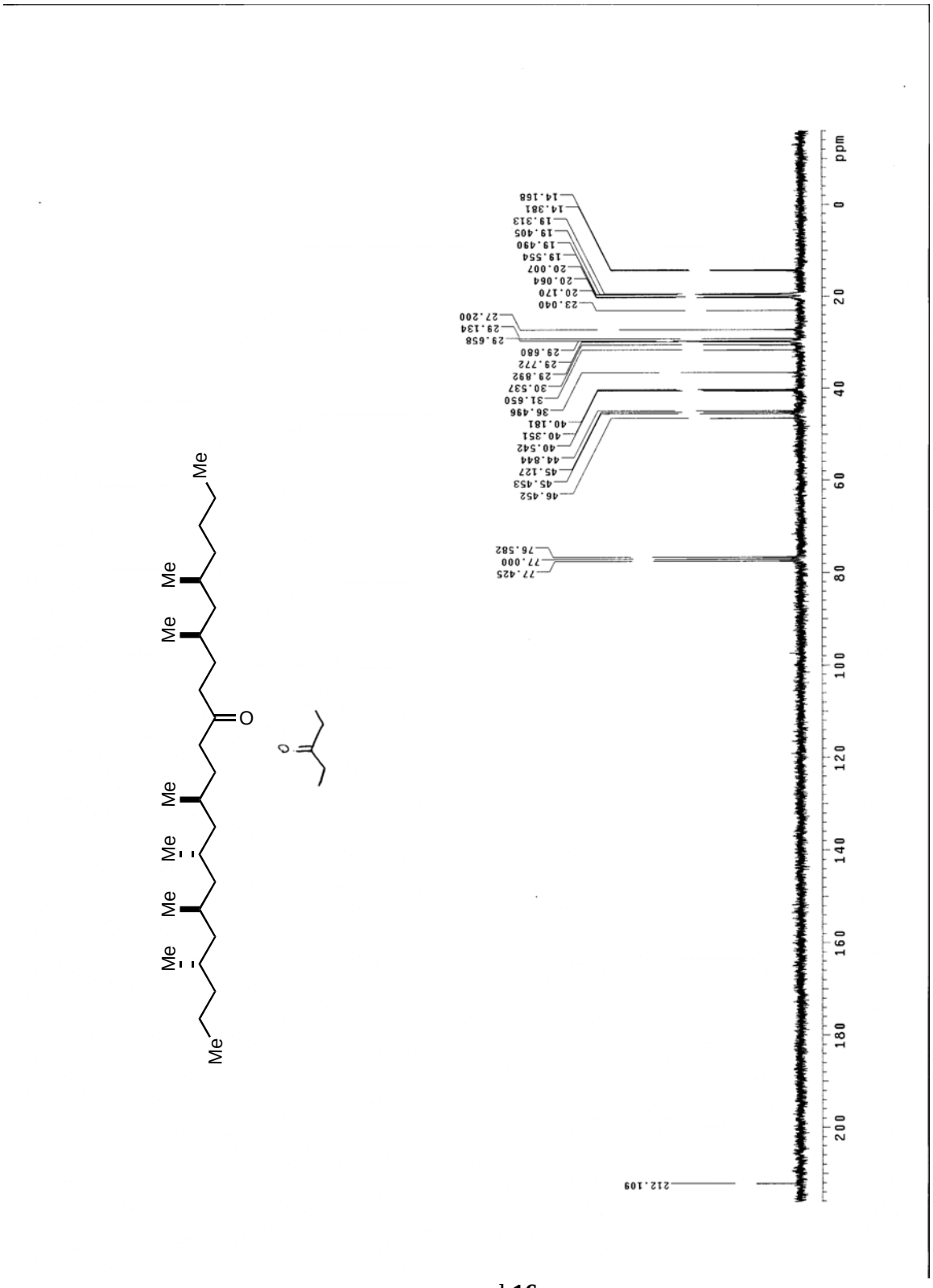
compound **15**


Me
Me
Me
O
Me
Me
Me
Me
Me
ppm
14.165
14.365
19.293
19.480
19.567
19.760
20.027
20.141
23.032
27.245
27.605
29.141
29.615
29.762
29.896
31.031
34.175
36.519
37.794
40.064
44.351
44.851
45.346
45.693
77.421
77.000
76.573
128.151
152.901
201.435

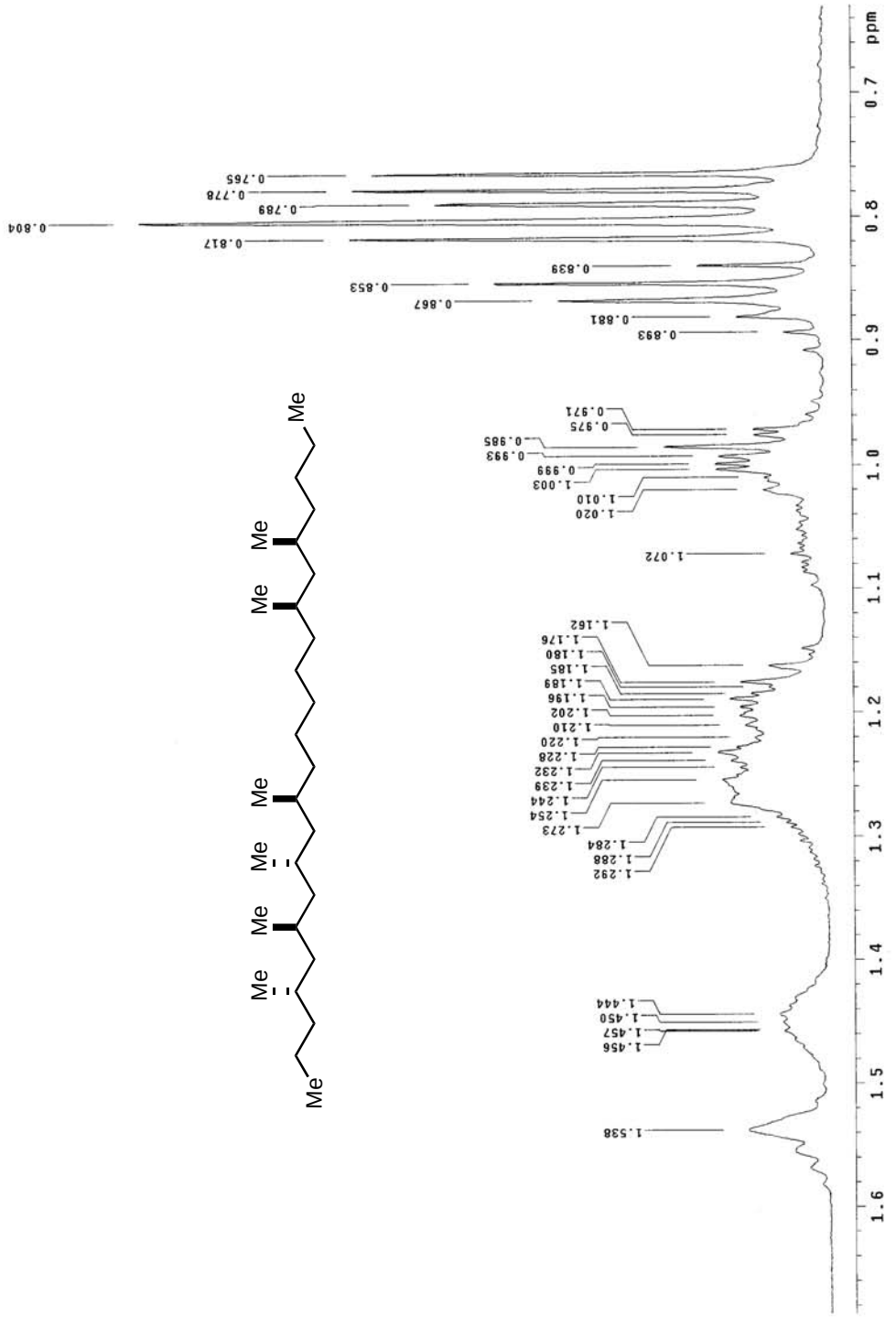
compound **15**


0.751
0.754
0.775
0.799
0.807
0.821
0.829
0.846
0.858
0.869
0.880
0.956
0.981
1.003
1.032
1.172
1.217
1.224
1.230
1.239
1.257
1.263
1.272
2.358
2.378
ppm
1
2
3
4
5
6
7
8
Me
Me
Me
Me
Me
Me
Me
Me
O

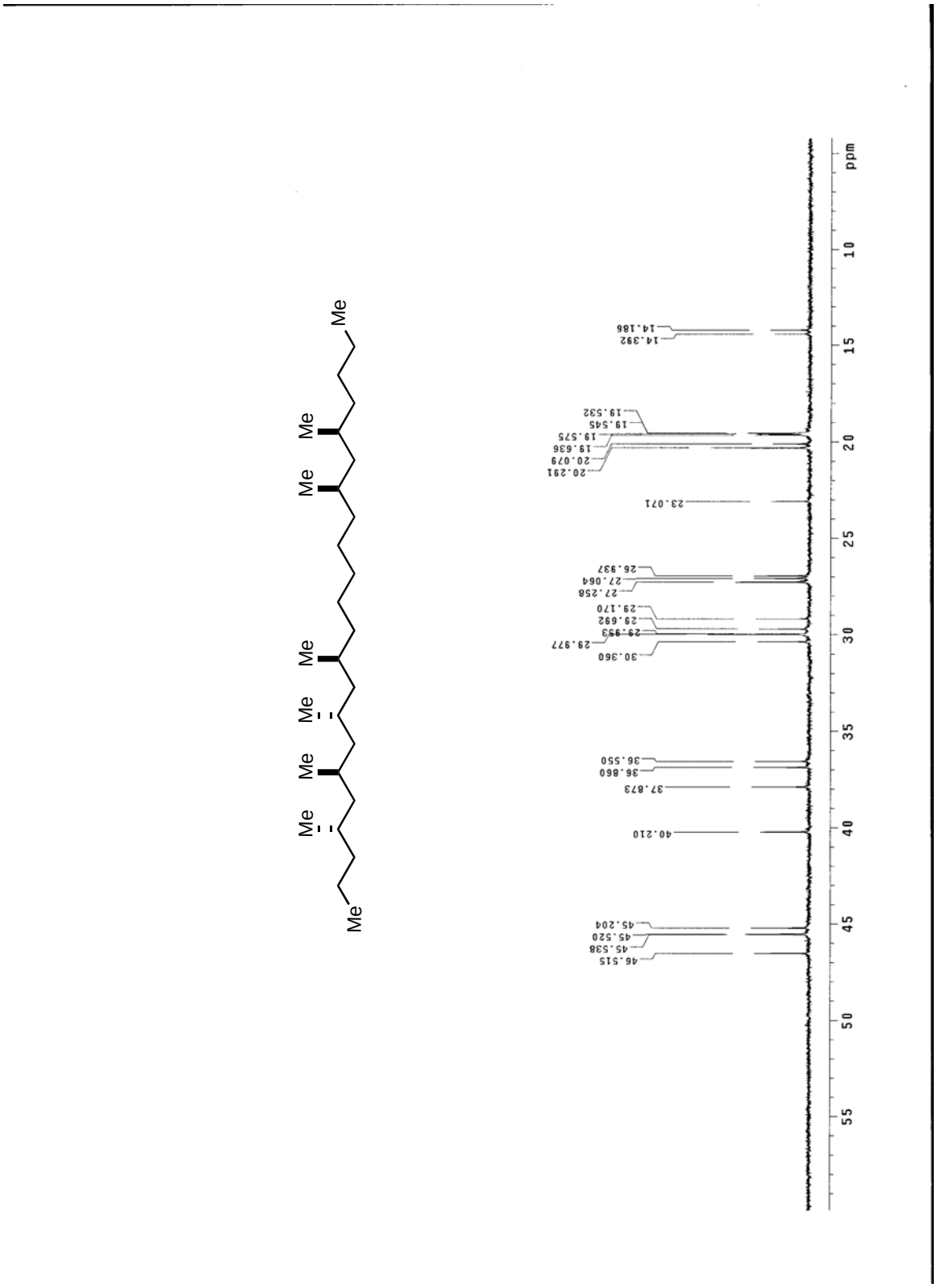
compound **16**


Me
Me
Me
O
Me
Me
Me
Me
O
14.168
14.381
19.313
19.405
19.490
19.554
20.007
20.064
20.170
23.040
27.200
29.134
29.658
29.680
29.772
29.892
30.537
31.650
36.496
40.181
40.351
40.542
44.844
45.127
45.453
46.452
76.582
77.000
77.425
212.109
ppm
0
20
40
60
80
100
120
140
160
180
200

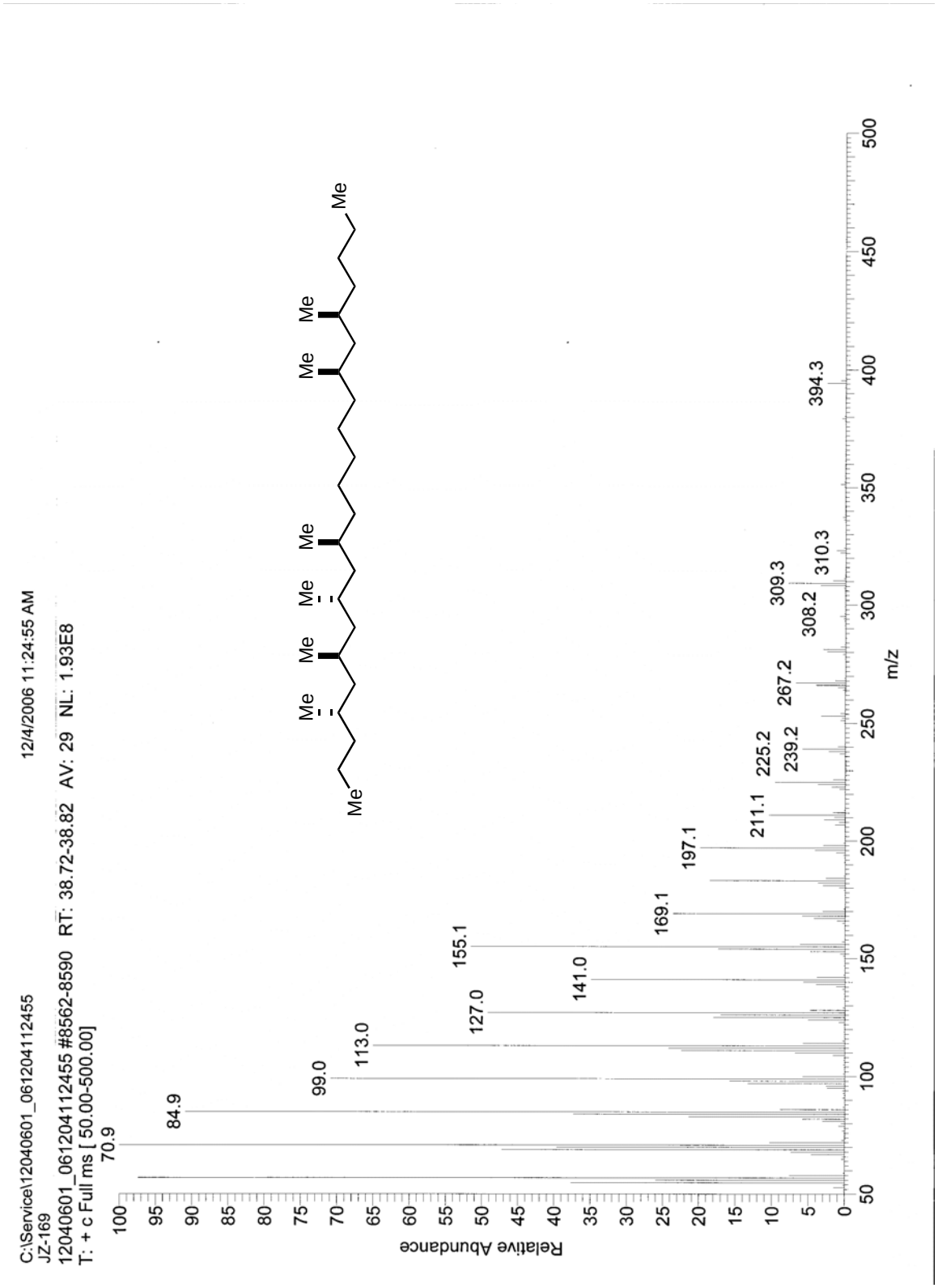
compound **16**


Me
Me
Me
Me
Me
Me
Me
0.765
0.778
0.789
0.804
0.817
0.839
0.853
0.867
0.881
0.893
0.971
0.975
0.985
0.993
0.999
1.003
1.010
1.020
1.072
1.162
1.176
1.180
1.185
1.189
1.196
1.202
1.210
1.220
1.228
1.232
1.239
1.244
1.254
1.273
1.284
1.288
1.292
1.444
1.450
1.457
1.456
1.538
ppm
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6

compound **1**


Me
Me
Me
Me
Me
Me
Me
Me
14.186
14.392
19.532
19.545
19.575
19.636
20.079
20.291
23.071
26.937
27.064
27.256
29.170
29.692
29.953
29.977
30.360
36.550
36.860
37.873
40.210
45.204
45.520
45.538
46.515
ppm
10
15
20
25
30
35
40
45
50
55

compound **1**


C:\Service\12040601_061204112455
JZ-169
12040601_061204112455 #8562-8590 RT: 38.72-38.82 AV: 29 NL: 1.93E8
T: + c Full ms [50.00-500.00]
12/4/2006 11:24:55 AM
Relative Abundance
m/z
Me
Me
Me
Me
Me
Me
Me
Me
70.9
84.9
99.0
113.0
127.0
141.0
155.1
169.1
197.1
211.1
225.2
239.2
267.2
308.2
309.3
310.3
394.3

compound **1**