JOC The Journal of Organic Chemistry

J. Org. Chem., 1998, 63(14), 4732-4740, DOI:10.1021/jo9804700

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The Synthesis of (±)-Allocyathin B_2 and (+)-Erinacine A

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Supplementary Material

Methyl 2,4,5,6,7,7a-Hexahydro-7aα-methyl-4α-(3-methyl-3-butenyl)-3-(1-methylethyl)-1*H*-indene-5-carboxylate (15). To a solution of **13** (375 mg, 1.37 mmol) and 2-methyl-2-butene (11 mL) in *tert*-BuOH (14 mL) at 0 °C was added a solution of $NaClO_2$ (1.24 g, 13.7 mmol) and $NaH_2PO_4{\bullet}H_2O$ (13.7 mmol) in H_2O (5 mL). The resulting mixture was stirred at rt for 15 min, and quenched by addition of HOAc (1.2 mL). The solution was saturated with NaCl and extracted with EtOAc. The combined extracts were concentrated and excess HOAc was azeotropically removed under reduced pressure with heptane.

The crude acid was dissolved in ether (3 mL) and treated with a solution of CH_2N_2 in ether. Excess CH_2N_2 was quenched with HOAc. Crude ester **15** was taken up in ether (50 mL) which was washed with saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (49:1 hexane/EtOAc) to provide 396 mg (95%) of **15** as a 1:1 mixture of stereoisomers: ^{1}H NMR (both) 4.69 (br s, 0.5 × 1), 4.66 (br s, 0.5 × 1), 4.65 (br s, 0.5 × 1), 4.62 (br s, 0.5 × 1), 3.69 (s, 0.5 × 3), 3.63 (s, 0.5 × 3), 3.10 (br dd, 0.5 × 1, *J* = 8.3, 8.3), 3.03 (ddd, 0.5 × 1, *J* = 4.8, 4.8, 11.2), 2.71 (h, 1, *J* = 6.8), 2.58-2.52 (m, 0.5 × 1), 2.42 (ddd, 0.5 × 1, *J* = 3.4, 4.8, 12.7), 2.35-2.04 (m, 2), 2.00-1.35 (m, 9), 1.71 (br s, 0.5 × 3), 1.67 (br s, 0.5 × 3), 1.25-1.10 (m, 1), 1.08 (s, 0.5 × 3), 1.06 (s, 0.5 × 3), 0.97 (d, 3, *J* = 6.8), 0.96 (d, 0.5 × 3, *J* = 6.8), 0.95 (d, 0.5 × 3, *J* = 6.8); ^{13}C NMR (both) 175.3, 175.1, 146.2, 146.1, 142.4 (2 C), 137.1, 136.2, 109.6, 109.3, 51.4, 51.3, 48.0, 46.4, 46.1, 45.3, 41.9, 41.8, 41.1, 38.0, 36.6, 36.3, 36.0, 35.7, 33.4, 27.8, 27.5, 27.2, 26.44, 26.42, 25.1, 25.0, 22.60, 22.57, 21.7, 21.3, 20.9, 20.8, 20.5, 20.4; IR (neat) 3072, 1738, 1733, 1651.

Methyl 5β-Benzyloxymethyl-2,4,5,6,7,7a-hexahydro-7aα-methyl-4α-(3-methyl-3-butenyl)-3-(1-methylethyl)-1*H*-indene-5α-carboxylate (16). A solution of diisopropylamine (499 mg, 4.93 mmol) in THF (20 mL) and *n*-BuLi (1.97 mL of 2.5 M in hexane, 4.93 mmol) was stirred at 0 °C for 30 min and cooled to –78 °C. To the resulting solution was added a solution of **15** (1.00 g, 3.28 mmol) in THF at –78 °C. The solution was warmed to 0 °C over 2 h and recooled to –78 °C. A solution of BOMCl[19] (1.14 g of 90% pure, 6.56 mmol) in THF (5 mL) was added via a cannula. The reaction mixture was stirred 30 min at –78 °C, warmed to rt, and quenched by addition of saturated NH_4Cl. The resulting solution was taken up in ether, washed with H_2O and brine, and dried ($MgSO_4$). Removal of the solvent followed by flash chromatography on silica gel (49:1 hexane/EtOAc) gave 1.27 g (91%) of pure **16**: ^{1}H NMR 7.35-7.17 (m, 5), 4.64 (br s, 1), 4.60 (br s, 1), 4.47 (d, 1, J = 12.2), 4.39 (d, 1, J = 12.2), 3.69 (s, 3), 3.52 (d, 1, J = 9.1), 3.49 (d, 1, J = 9.1), 2.62 (h, 1, J = 6.8), 2.51 (dd, 1, J = 4.2, 11.7), 2.26 (ddd, 1, J = 7.5, 10.4, 15.5), 2.15-1.97 (m, 3), 1.89-1.55 (m, 4), 1.65 (br s, 3), 1.41-1.10 (m, 4), 1.08 (s, 3), 0.93 (d, 3, J = 6.8), 0.90 (d, 3, J = 6.8); ^{13}C NMR 176.6, 146.0, 144.3, 138.2, 135.1, 128.1, 127.7, 127.5, 109.4, 73.1, 72.2, 51.9, 51.5, 46.0, 42.4, 39.7, 36.3, 35.5, 28.4, 27.6, 26.2, 25.5, 22.6, 21.4, 20.6, 20.5; IR (neat) 1741, 1730, 1651. Anal. Calcd for $C_{28}H_{40}O_3$: C, 79.20; H, 9.49. Found: C, 78.98; H, 9.15.

5β-Benzyloxymethyl-2,4,5,6,7,7a-hexahydro-7aα-methyl-4α-(3-methyl-3-butenyl)-3-(1-methylethyl)-1*H*-indene-5α-methanol (17). To a solution of **16** (1.00 g, 2.35 mmol) in THF (20 mL) at 0 °C was added $LiAlH_4$ (100 mg, 2.64 mmol). After 30 min at 0 °C, the reaction mixture was quenched by sequential addition of H_2O (0.10 mL), 15% NaOH (0.10 mL), and H_2O (0.30 mL). The precipitated salt was removed by filtering through a thin layer of silica, which was then rinsed with ether. The solvent was removed to afford 0.92 g (99%) of **17**: ^{1}H NMR 7.39-7.22 (m, 5), 4.66 (br s, 1), 4.65 (br s, 1), 4.50 (d, 1, J = 11.7), 4.36 (d, 1, J = 11.7), 3.63 (dd, 1, J = 3.7, 11.0), 3.56 (d, 1, J = 8.7), 3.55 (dd, 1, J = 7.8, 11.0), 3.33 (d, 1, J = 8.7), 3.09-3.03 (m, 1), 2.77 (dd, 1, J = 4.4, 12.3), 2.72 (h, 1, J = 6.8), 2.31 (ddd, 1, J = 7.5, 10.3, 15.6), 2.16 (dd, 1, J = 8.2, 10.3), 2.00-1.66 (m, 3), 1.70 (br s, 3), 1.64-1.38 (m, 4), 1.30-1.17 (m, 3), 1.09 (s, 3), 0.95 (d, 3, J = 6.8), 0.92 (d, 3, J = 6.8); ^{13}C NMR 146.8, 143.6, 137.8, 136.0, 128.4, 127.7, 127.6, 109.1, 76.5, 73.7, 69.3, 46.6, 42.4, 41.8, 36.8, 36.2, 36.1, 27.6, 26.8, 26.3, 25.2, 24.0, 22.7, 21.3, 20.5; IR (neat) 3453, 1649. Anal. Calcd for $C_{27}H_{40}O_2$: C, 81.77; H, 10.17. Found: C, 81.54; H, 10.21.

2,4,5,6,7,7a-Hexahydro-5bα,7aα-methyl-4α-(3-methyl-3-butenyl)-3-(1-

methylethyl)-1*H*-indene-5β-methanol (19). To a solution of **17** (0.92 g, 2.32 mmol) and HMPA (1.25 g, 6.96 mmol) in DME (23 mL) at 0 °C was added *n*-BuLi (1.86 mL of 2.5 M in hexane, 4.64 mmol). The solution was stirred for 15 min at 0 °C. Bis(dimethylamino)phosphorochloridate (0.76 mL of 90% pure, 4.64 mmol) was added and the reaction mixture was stirred at 0 °C for 1 h and at rt for 4 h. The reaction was quenched by addition of a saturated $NaHCO_3$ solution. The aqueous solution was extracted with EtOAc. The combined EtOAc extracts were washed with brine, dried ($MgSO_4$) and concentrated to yield 1.49 g of crude **18**.

Crude **18** (1.49 g) was dissolved in ether (5 mL) and $EtNH_2$ (20 mL) and the solution was cooled to –78 °C. Li (161 mg, 23.2 mmol) was added in small pieces. The solution was stirred at –78 °C until the blue color of the reaction solution faded. Additional Li was added into the reaction mixture at 0 °C as needed to maintain a faint blue color until the reaction was complete as judged by TLC analysis. The mixture was diluted with ether, washed with H_2O and brine, dried ($MgSO_4$) and concentrated. Flash chromatography on silica gel (19:1 hexane/EtOAc) provided 495 mg (73% for two steps) of pure **19**: ^{1}H NMR 4.67 (br s, 1), 4.65 (br s, 1), 3.48 (d, 1, J = 10.8), 3.24 (d, 1, J = 10.8), 2.66 (h, 1, J = 6.8), 2.31 (ddd, 1, J = 7.6, 10.4, 15.5), 2.22 (dd, 1, J = 4.5, 10.3), 2.15 (ddd, 1, J = 1.2, 9.4, 15.5), 2.01 (m, 2), 1.71 (br s, 3), 1.70-1.32 (m, 6), 1.22 (br s, 1), 1.08 (s, 3), 1.06-0.84 (m, 2), 0.95 (s, 3), 0.95 (d, 3, J = 6.8), 0.93 (d, 3, J = 6.8); ^{13}C NMR 146.9, 142.9, 137.1, 109.1, 69.0, 46.2, 42.4, 40.2, 38.7, 37.4, 36.4, 27.7, 27.6, 27.3, 26.3, 25.3, 23.3, 22.7, 21.3, 20.6; IR (neat) 3361, 1649. Anal. Calcd for $C_{20}H_{34}O$: C, 82.69; H, 11.80. Found: C, 82.31; H, 11.82.

2,4,5,6,7,7a-Hexahydro-5α,7aα-dimethyl-4α-(3-methyl-3-butenyl)-3-(1-methylethyl)-1*H*-indene-5β-carboxaldehyde (14b). To a solution of oxalyl chloride (615 mg of 98% pure, 4.75 mmol) in CH_2Cl_2 (30 mL) at –78 °C was added a solution of DMSO (988 mg, 12.6 mmol) in CH_2Cl_2 (2 mL). The mixture was stirred for 30 min at –78 °C and a solution of **19** (460 mg, 1.58 mmol) in CH_2Cl_2 (4 mL) was added. Further stirring for 1 h at the same temperature was followed by addition of triethylamine (3.53 mL, 25.3 mmol). The reaction mixture was allowed to warm to rt. H_2O was added and the mixture was taken up in ether. The ether layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The crude residue was purified by flash chromatography (49:1 hexane/EtOAc) to provide 372 mg (82%) of pure **14b**: ^{1}H NMR 9.39 (s, 1), 4.69 (br s, 1), 4.67 (br s, 1), 2.87 (dd, 1, J = 5.1, 11.7), 2.76 (h, 1, J = 6.8), 2.29 (ddd, 1, J = 7.8, 10.0, 15.7), 2.14 (ddd, 1, J = 1.7, 9.3, 15.7), 2.07-1.82 (m, 2), 1.75-1.23 (series of m, 8), 1.72 (br s, 3), 1.09 (s, 3), 0.97 (s, 3), 0.97 (d, 6, J = 6.8); ^{13}C NMR 207.4, 146.5, 143.5, 135.7, 109.4, 50.4, 46.0, 41.7, 38.8, 38.4, 36.0, 27.54, 27.49, 27.3, 26.6, 25.1, 22.7, 21.3, 21.2, 20.8; IR (neat) 1728, 1651.

2,4,5,6,7,7a-Hexahydro-5α,7aα-dimethyl-3-(1-methylethyl)-4α-(3-oxobutyl)-1*H*-indene-5β-methanol (20). To a solution of **14b** (27 mg, 0.092 mmol) in H_2O (0.5 mL) and acetone (4 mL) was added KIO_4 (63 mg, 0.28 mmol) and OsO_4 (47 mg of 2.5% solution in *tert*-BuOH, 0.005 mmol). The mixture was stirred at rt for 24 h, and quenched by addition of a solution of 10% $Na_2S_2O_3$ (2 mL). The mixture was taken up in ether, washed with H_2O and brine, dried ($MgSO_4$) and concentrated. Flash chromatography of the residue on silica gel (4:1 hexane/EtOAc) provided 22 mg (82%) of pure **20**: ^{1}H NMR 3.47 (d, 1, J = 10.6), 3.23 (d, 1, J = 10.6), 2.55 (h, 1, J = 6.8), 2.45-2.12 (m, 5), 2.10 (s, 3), 1.88-1.32 (m, 9), 1.05 (s, 3), 0.97 (d, 3, J = 6.8), 0.97 (s, 3), 0.93 (d, 3, J =6.8); ^{13}C NMR 209.4, 143.6, 136.6, 68.8, 46.1, 42.3, 42.2, 39.2, 38.7, 37.2, 29.8, 27.6, 27.1, 26.3, 25.4, 23.1, 22.7, 21.3, 20.7; IR (neat) 3444, 1714. Anal. Calcd for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 77.90; H, 11.27.

2,4,5,6,7,7a-Hexahydro-5α,7aα-dimethyl-3-(1-methylethyl)-4α-(3-oxobutyl)-1*H*-indene-5β-carboxaldehyde (21). To a solution of oxalyl chloride (22 mg of 98% pure, 0.17 mmol) in CH_2Cl_2 (1 mL) at –78 °C was added dropwise a solution of DMSO (40 mg, 0.51 mmol) in CH_2Cl_2 (1 mL). The mixture was stirred for 30 min at –78 °C. A solution of **20** (10 mg, 0.034 mmol) in CH_2Cl_2 (1 mL) was added. The temperature was maintained at –78 °C for 1 h and Et_3N (0.14 mL, 1.02 mmol) was added. The resulting solution was warmed to rt, quenched with H_2O, and diluted with ether. The ether layer was washed with H_2O, and brine, dried ($MgSO_4$), and concentrated. The crude residue was purified by flash chromatography on silica gel (19:1 hexane/EtOAc) to afford 8 mg (81%) of pure **21**: ^{1}H NMR 9.36 (s, 1), 2.86 (dd, 1, J = 4.9, 12.6), 2.66 (h, 1, J = 6.8), 2.44 (ddd, 1. J = 5.6, 9.3, 15.5), 2.37 (dd, 1, J = 6.2, 9.3), 2.28 (ddd, 1, J = 7.9, 9.9, 15.5), 2.19-2.09 (m, 1), 2.13 (s, 3), 1.88-1.53 (m, 6), 1.47-1.23 (m, 2), 1.05 (s, 3), 0.99 (s, 3), 0.99 (d, 3, J = 6.8), 0.98 (d, 3, J = 6.8); ^{13}C NMR 208.9, 206.9, 144.1, 135.5, 50.5, 45.9, 41.7, 41.6, 38.4, 37.7, 29.9, 27.6, 27.3, 26.6, 25.2, 22.2, 21.2, 21.1, 20.9; IR (neat) 1722, 1716.

2,4,5,6,7,7a-Hexahydro-5α,7aα-dimethyl-3-(1-methylethyl)-4α-(3-oxobutyl)-1*H*-indene-5β-carboxylic Acid (22). A solution of **21** (12 mg, 0.041 mmol) and PDC (31 mg, 0.082 mmol) in DMF (1 mL) was stirred at rt for 20 h. The solution was diluted with ether, washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The crude residue was purified by flash chromatography on silica gel (3:2 hexane/EtOAc) to afford 11 mg (87%) of **22** which was crystallized from 1:1 hexane-ether: mp 155-157 °C; ^1H NMR 3.06 (dd, 1, J = 4.6, 12.6), 2.65 (h, 1, J = 6.8), 2.45-2.08 (m, 4), 2.12 (s, 3), 1.88-1.37 (series of m, 8), 1.24 (s, 3), 1.04 (s, 3), 0.97 (d, 3, J = 6.8), 0.91 (d, 3, J = 6.8); ^{13}C NMR 209.0, 183.1, 143.7, 135.7, 48.0, 46.0, 42.05, 41.98, 39.0, 38.9, 29.9, 28.1, 27.5, 26.6, 25.4, 25.2, 22.3, 20.98, 20.95; IR (CCl_4) 3524, 1719, 1698. Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.51; H, 9.87. Found: C, 74.76; H, 9.88.

(3aα,5aβ,6β,10aβ)-2,3,3a,4,5,5a,6,7,10,10a-Decahydro-3a,5a-dimethyl-1-(1-methylethyl)-6-(dimethyl-1,1-dimethylethylsilyloxy)-cyclohept[*e*]indene-8-methanol (26). To a solution of **23** (477 mg, 1.65 mmol) in DMF (2 mL) was added imidazole (225 mg, 3.31 mmol) and TBDMSCl (514 mg of 97% pure, 3.31 mmol). The mixture was stirred at rt for 1 d. The reaction mixture was taken up in ether and washed with saturated NH_4Cl and brine, dried ($MgSO_4$) and concentrated. Flash chromatography (99:1 hexane/EtOAc) of the crude residue provided 664 mg (100%) of the silyl ether as a clear oil: ^1H NMR 4.66 (br s, 1), 4.65 (br s, 1), 3.47 (d, 1, J = 9.7), 2.63 (h, 1, J = 6.8), 2.61 (dd, 1, J = 10.3, 14.1), 2.42-2.35 (m, 1), 2.33 (d, 1, J = 10.5), 2.25 (ddd, 1, J = 7.2, 10.1, 15.4), 2.19-2.09 (m, 3), 1.78-1.63 (m, 2), 1.56-1.36 (m, 5), 1.28-1.19 (m, 1), 0.97 (d, 3, J = 6.8), 0.96 (s, 3), 0.93 (d, 3, J = 6.8), 0.90 (s, 9), 0.77 (s, 3), 0.09 (s, 3), 0.04 (s, 3); ^{13}C NMR 149.2, 142.4, 139.2, 110.7, 80.3, 46.1, 43.4, 41.3, 41.0, 40.8, 39.3, 36.7, 30.9, 30.3, 27.7, 26.4, 26.0, 24.7, 21.4, 21.2, 19.2, 18.0, –3.7, –4.8; IR (CCl_4) 1639. Anal Calcd for $C_{26}H_{46}OSi$: C, 77.54; H, 11.51. Found: C, 77.52; H, 11.72.

To a solution of the above silyl ether (664 mg, 1.65 mmol) in *tert*-BuOH (8.0 mL) and H_2O

(2.0 mL) was added NMO (398 mg of 97% pure, 3.30 mmol) and OsO_4 (168 mg of 2.5% in *tert*-BuOH, 0.017 mmol). The mixture was stirred at rt for 1 d and was quenched by addition of a solution of 10% $Na_2S_2O_3$. After 30 min at rt the reaction mixture was extracted with EtOAc. The combined extracts were washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure to afford 715 mg of a crude 2:1 mixture of the epimeric diols that was used without further purification.

A solution of crude diols (715 mg) in CH_2Cl_2 (10 mL) and pyridine (4 mL) was treated with Ac_2O (0.31 mL, 3.30 mmol). The mixture was stirred at rt for 10 h, diluted with ether, washed with saturated $CuSO_4$, H_2O, and brine, dried ($MgSO_4$), and concentrated. The crude residue was purified by flash chromatography on silica gel (9:1 hexane/EtOAc) to give 635 mg (80% for 2 steps) of a 2:1 mixture of epimeric hydroxy acetates.

To a solution of the epimeric hydroxy acetates (600 mg, 1.25 mmol) in CH_2Cl_2 (20 mL) and Et_3N (2 mL) at –78 °C was added MsCl (0.50 mL, 6.25 mmol) dropwise. The mixture was kept at –20 °C for 2 h and at rt for 1 h. The solution was diluted with ether, washed with H_2O, dried ($MgSO_4$) and concentrated to give crude allylic acetate.

Crude allylic acetate was dissolved in MeOH (30 mL) and 10% NaOH (5 mL) was added. The resulting solution was heated to reflux for 1 h, diluted with ether, washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The crude residue was purified by flash chromatography on silica gel (9:1 hexane/EtOAc) to provide 356 mg (68%) of pure **26**: ^{1}H NMR 5.66 (br d, 1, J = 8.3), 4.05-3.92 (m, 2), 3.67 (dd, 1, J = 1.3, 10.7), 2.75-2.64 (m, 1), 2.58 (h, 1, J = 6.8), 2.54-2.45 (m, 1), 2.39 (d, 1, J = 11.7), 2.26 (ddd, 1, J = 7.3, 10.5, 15.5), 2.13 (dd, 1, J = 9.1, 15.5), 1.89 (d, 1, J = 17.1), 1.72-1.32 (m, 8), 0.98 (s, 3), 0.95 (d, 3, J = 6.8), 0.90 (d, 3, J = 6.8), 0.89 (s, 9), 0.79 (s, 3), 0.05 (s, 3), 0.04 (s, 3); ^{13}C NMR 141.1, 140.2, 138.2, 126.8, 78.5, 68.8, 46.1, 41.7, 41.5, 40.9, 36.6, 34.0, 32.3, 29.4, 27.7, 26.1, 25.9, 25.0, 21.4, 21.1, 18.0, 17.6, –4.1, –4.8; IR (neat) 3300, 1669.

(3aα,5aβ,6β,10aβ)-2,3,3a,4,5,5a,6,7,10,10a-Decahydro-3a,5a-dimethyl-1-(1-methylethyl)-6-(dimethyl-1,1-dimethylethylsilyloxy)-cyclohept[*e*]indene-8-carboxaldehyde (27). A reaction identical to that described above for the preparation of **26** was carried out using 300 mg (0.63 mmol) of a 2:1 epimeric mixture of hydroxy acetates. However, the crude **26**

obtained was oxidized directly by stirring in a slurry of CH_2Cl_2 (5.0 mL) and MnO_2 (644 mg of 85% pure, 6.30 mmol) for 15 h at rt. The reaction mixture was filtered through a thin layer of silica gel, and rinsed with CH_2Cl_2. The filtrate was concentrated and the crude residue was purified by flash chromatography on silica gel (49:1 hexane/EtOAc) to provide 164 mg (62% from the hydroxy acetates) of pure **27**: ^{1}H NMR 9.36 (s, 1), 6.71 (d, 1, J = 7.6), 3.53 (dd, 1, J = 4.7, 7.3), 2.88-2.74 (m, 1), 2.58-2.48 (m, 3), 2.43 (d, 1, J = 11.9), 2.27 (ddd, 1, J = 7.3, 10.5, 15.8), 2.15 (dd, 1, J = 9.1, 14.7), 2.04 (dd, 1, J = 7.8, 9.1), 1.68 (dd, 1, J = 7.0, 11.9), 1.65-1.36 (m, 5), 1.01 (s, 3), 0.94 (d, 3, J = 6.8), 0.91 (d, 3, J = 6.8), 0.88 (s, 9), 0.81 (s, 3), 0.02 (s, 3), 0.00 (s, 3); ^{13}C NMR 193.7, 154.9, 142.4, 141.3, 140.0, 78.2, 46.1, 41.6, 41.2, 40.5, 36.4, 33.8, 29.2, 28.3, 27.8, 26.2, 25.9, 25.1, 21.3, 21.1, 18.0, 17.5, –4.3, –4.9; IR (neat) 1690, 1643.

(3aα,5aβ,6β,10aβ)-8,9-epoxy-2,3,3a,4,5,5a,6,7,8,9,10,10a-Dodecahydro-3a,5a-dimethyl-1-(1-methylethyl)-6-(dimethyl-1,1-dimethylethylsilyloxy)-cyclohept[*e*]indene-8-methyl *t*-butyldimethylsilyl ether (28). To a solution of **26** (100 mg, 0.24 mmol) in CH_2Cl_2 (5.0 mL) at 0 °C were added $VO(acac)_2$ (3.2 mg, 0.012 mmol) and *tert*-BuOOH (32 µL, 0.29 mmol). The mixture was stirred at 0 °C for 2 h and was quenched by addition of a solution of 10% $Na_2S_2O_3$ (2.0 mL). The mixture was stirred at rt for 15 min, and was taken up in ether. The ether layer was washed with H_2O and brine and dried ($MgSO_4$). The solvent was removed providing 109 mg of epoxy alcohols as a 3:1 mixture of epimers, which were sensitive to silica gel purification: partial ^{1}H NMR (major) 3.29 (dd, 1, J = 2.1, 8.2), 2.57 (h, 1, J = 6.8), 1.86 (d, 1, J = 15.5), 0.96 (d, 3, J = 6.8), 0.93 (d, 3, J = 6.8), 0.91 (s, 3), 0.87 (s, 9), 0.74 (s, 3), 0.08 (s, 3), 0.04 (s, 3); ^{13}C NMR (major) 140.3, 140.1, 80.1, 76.6, 72.4, 65.1, 59.0, 46.1, 41.3, 36.4, 32.6, 29.4, 27.8, 27.7, 26.2, 25.9, 24.8, 21.4, 21.1, 18.0, –4.1, –4.7 (2 C were not assigned); IR (both, CCl_4) 3569.

To a solution of crude epoxy alcohols (109 mg, 0.24 mmol) in DMF (1.0 mL) were added imidazole (49 mg, 0.72 mmol) and TBDMSCl (112 mg, 0.72 mmol). The mixture was stirred at rt for 10 h. The solution was taken up in ether, washed with saturated NH_4Cl, H_2O, and brine, and dried ($MgSO_4$). Removal of the solvent gave 136 mg of crude **28** as a 3:1 mixture of epimers, which was used without further purification: partial ^{1}H NMR 3.56 (d, 1, J = 10.9), 3.51 (dd, 1, J = 1.5, 11.0), 3.45 (d, 1, J = 10.9), 3.07 (dd, 1, J = 2.3, 8.3), 2.61 (h, 1, J = 6.8), 2.39 (dd, 1, J = 11.0, 15.5), 1.91 (d, 1, J = 15.5), 0.92 (s, 3), 0.91 (s, 9), 0.88 (s, 9), 0.75 (s, 3), 0.09 (s, 3), 0.07 (s, 3), 0.05 (s, 3), 0.046 (s, 3); ^{13}C NMR (major) 140.6, 140.0, 80.3, 77.0, 72.6, 68.6, 60.6, 46.1, 41.3, 36.5, 32.6, 31.4, 29.3, 27.8, 26.2, 25.9, 25.8, 24.8, 21.4, 21.0, 18.2, 18.0, 17.2, –4.1, –4.6, –5.36, –5.41.

(3aα,5aβ,6β,10aβ)-2,3,3a,4,5,5a,6,7,10,10a-Decahydro-3a,5a-dimethyl-1-(1-methylethyl)-6-hydroxycyclohept[*e*]indene-8-methanol. To a solution of **26** (150 mg, 0.358 mmol) in THF (5 mL) was added a solution of 10% HCl (1.0 mL). The mixture was stirred at rt for 15 h and diluted with ether. The ether solution was washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated. The crude residue was purified by flash chromatography on silica gel (hexane:EtOAc, 4:1) to afford 98 mg (90%) of pure diol as a white solid: mp 140-142 °C; ^{1}H NMR 5.71 (br d, 1, J = 7.6), 4.00 (d, 1, J = 12.3), 3.97 (d, 1, J = 12.3), 3.74 (d, 1, J = 10.7), 2.73-2.47 (m, 3), 2.41 (d, 1, J = 11.7), 2.26 (ddd, 1, J = 7.1, 10.3, 16.0), 2.20-2.08 (m, 2), 1.91 (br s, 2), 1.74-1.40 (m, 6), 1.00 (s, 3), 0.95 (d, 3, J = 6.8), 0.91 (d, 3, J = 6.8), 0.84 (s, 3); ^{13}C NMR 140.7 (2 C), 137.9, 127.4, 77.6, 68.5, 46.1, 41.7, 41.54, 41.47, 40.4, 36.4, 33.6, 32.0, 29.1, 27.7, 26.1, 25.0, 21.4, 21.1; IR (KBr) 3321. Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 79.12; H, 10.72.

5-*epi*-Cyathin B_2 (29). To a solution of the above diol (17 mg, 0.056 mmol) in CH_2Cl_2 (2 mL) was added PDC (84 mg, 0.22 mmol). The mixture was stirred for 10 h at rt and diluted with ethyl acetate. The mixture was filtered through a thin layer of silica gel and rinsed with ethyl acetate. The solvent was removed and the crude residue was purified by flash chromatography on silica gel (9:1 hexane/EtOAc) to give 14 mg (82%) of pure **29** as a tan solid: mp 90-92 °C; ^{1}H NMR 9.37 (s, 1), 6.74 (ddd, 1, J = 2.5, 2.5, 7.6), 3.67 (br d, 1, J = 14.4), 3.41 (dd, 1, J = 14.4, 1.1), 2.96 (br d, 1, J = 12.0), 2.78-2.68 (m, 1), 2.61 (h, 1, J = 6.8), 2.33 (ddd, 1, J = 7.1, 10.3, 15.7), 2.31-2.17 (m, 2), 1.89 (ddd, 1, J = 4.7, 15, 15), 1.73 (ddd, 1, J = 1.4, 7.2, 12.1), 1.78-1.65 (m, 2), 1.55 (dd, 1, J = 10, 10), 1.41 (ddd, 1, J = 4.7, 14, 14), 1.11 (s, 3), 1.02 (s, 3), 1.00 (d, 3, J = 6.8), 0.96 (d, 3, J = 6.8); ^{13}C NMR 211.9, 192.1, 153.1, 143.7, 137.9, 137.2, 51.7, 46.0, 41.7, 39.2, 35.7, 34.9, 34.6, 28.1, 26.4, 25.2, 23.5, 22.3, 21.5, 21.1; IR (CCl_4) 2717, 1711, 1696, 1645.

(3aα,5aβ,6β,10aβ)-2,3,3a,4,5,5a,6,7,8,10a-Decahydro-8-hydroxy-3a,5a-dimethyl-1-(1-methylethyl)-6-(dimethyl-1,1-dimethylethylsilyloxy)-cyclohept[*e*]ind-ene-8-methyl *t*-butyldimethylsilyl ether (30). To a yellow solution of diphenyl diselenide (96 mg, 0.30 mmol) in EtOH (2.0 mL) was added $NaBH_4$ in small portions until the yellow color disappeared.[23] To this freshly prepared solution of sodium phenylselenide was added a solution of crude **28** (86 mg, 0.15 mmol) in EtOH (1.0 mL). The mixture was heated at reflux for 36 h, cooled to 0 °C, and treated with 30% H_2O_2 (0.70 mL, 6.0 mmol). The solution was stirred at rt for 3 h, diluted with ether, washed with saturated $NaHCO_3$, and brine, and dried ($MgSO_4$). Removal of solvent and flash chromatography on silica gel (99:1 hexane/EtOAc) gave 42 mg (51%) of one isomer of **30** and 5 mg (6%) of a minor isomer.

Spectral data for the major isomer: ^{1}H NMR 5.29 (dd, 1, J = 4.7, 11.5), 5.23 (br d, 1, J = 11.5), 3.82 (d, 1, J = 10.0), 3.45 (d, 1, J = 9.5), 3.41 (d, 1, J = 9.5), 2.98-2.93 (m, 1), 2.52 (br s, 1), 2.48 (h, 1, J = 6.8), 2.29 (ddd, 1, J = 7.1, 10.2, 15.4), 2.26-2.11 (m, 2), 1.70 (dd, 1, J = 7.1, 12.0), 1.60-1.35 (m, 6), 1.05 (s, 3), 0.96 (d, 3, J = 6.8), 0. 91 (d, 3, J = 6.8), 0.91 (s, 9), 0.88 (s, 9), 0.73 (s, 3), 0.11 (s, 3), 0.08 (s, 3), 0.073 (s, 3), 0.068 (s, 3); ^{13}C NMR 141.8, 138.5, 132.3, 131.7, 75.5, 75.4, 70.2, 46.3, 42.4, 41.4, 39.9, 39.6, 36.2, 31.0, 27.8, 26.2, 26.0, 25.8, 25.7, 24.6, 21.4, 21.2, 18.1, 18.0, –3.9, –4.9, –5.4, –5.5; IR (CCl_4) 3571.

Spectral data for the minor isomer: ^{1}H NMR 5.71 (dd, 1, J = 4.7, 11.7), 5.31 (ddd, 1, J = 2.4, 2.4, 11.7), 3.83 (d, 1, J = 9.3), 3.40 (d, 1, J = 9.4), 3.36 (d, 1, J = 9.4), 2.50 (s, 1), 2.12-2.09 (m, 1), 2.09 (dd, 1, J = 9.6, 14.8), 1.81-1.70 (m, 2), 1.63-1.44 (m, 6), 1.29-1.21 (m, 2), 1.11 (s, 3), 1.06 (d, 3, J = 6.8), 1.05 (d, 3, J = 6.8), 0.92 (s, 3), 0.90 (s, 9), 0.88 (s, 9), 0.11 (s, 3), 0.07 (s, 3), 0.06 (s, 6); ^{13}C NMR 132.3, 129.2, 78.2, 75.4, 69.8, 43.6, 41.4, 40.1, 34.5, 31.5, 30.5, 28.2, 25.9, 25.8 (2C), 22.3, 21.9, 19.8, 19.0, 18.9, 18.2, 18.0, –3.9, –4.9, –5.4, –5.5 (2C were not observed); IR (CCl_4) 3559.

(3aα,5aβ,6β,10aβ)-2,3,3a,4,5,5a,6,7,8,10a-Decahydro-8-hydroxy-3a,5a-dimethyl-1-(1-methylethyl)-6-(dimethyl-1,1-dimethylethylsilyloxy)-cyclohept[*e*]ind-

ene-8-methanol (31). To a solution of **30** (30 mg, 0.055 mmol) in THF (2 mL) at 0 °C was added TBAF (0.27 mL of 1.0 M in THF, 0.27 mmol). The reaction mixture was stirred at rt for 1 h, diluted with ether, washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The crude residue was purified by flash chromatography on silica gel (4:1 hexane/EtOAc) to provide 22 mg (92%) of **31**: ^1H NMR 5.36 (dd, 1, *J* = 5.1, 11.4), 5.24 (ddd, 1, *J* = 2.3, 2.3, 11.4), 3.77 (d, 1, *J* = 9.7), 3.48 (d, 1, *J* = 9.5), 3.45 (d, 1, *J* = 9.5), 3.02-2.96 (m, 1), 2.44 (h, 1, *J* = 6.8), 2.32 (dd, 1, *J* = 10.0, 15.1), 2.25 (ddd, 1, *J* = 7.1, 10.3, 15.6), 2.16 (dd, 1, *J* = 9.1, 15.6), 1.70 (dd, 1, *J* = 7.3, 12.1), 1.68 (br s, 1), 1.61-1.34 (m, 5), 1.05 (s, 3), 0.95 (d, 3, *J* = 6.8), 0.90 (d, 3, *J* = 6.8), 0.88 (s, 9), 0.74 (s, 3), 0.12 (s, 3), 0.07 (s, 3); ^{13}C NMR 142.2, 138.1, 133.3, 130.9, 76.1, 75.3, 70.0, 46.3, 42.4, 41.4, 39.8, 39.6, 36.1, 31.0, 27.9, 26.3, 25.9, 24.7, 21.4, 21.2, 18.02, 17.99, –3.9, –4.9; IR (CCl_4) 3611.

(3aα,5aβ,6β,10aβ)-2,3,3a,4,5,5a,6,7,8,10a-Decahydro-3a,5a-dimethyl-1-(1-methylethyl)-6-(dimethyl-1,1-dimethylethylsilyloxy)-8-(dimethyl-1,1-dimethylethylsilyloxymethylene)-cyclohept[*e*]indene (32). To a solution of **30** (10 mg, 0.018 mmol) in CH_2Cl_2 (1 mL) and Et_3N (0.1 mL) at 0 °C was added MsCl (14 μL, 0.18 mmol). The mixture was stirred at 0 °C for 30 min and at rt for 1 h. The solution was diluted with ether, washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The crude residue was purified by flash chromatography on silica gel (99:1 hexane/EtOAc) to give 8 mg (84%) of **32** as a 2:1 mixture of *E*/*Z*-stereoisomers: partial ^1H NMR (major) 6.36 (br s, 1), 5.68 (dd, 1, *J* = 2.0, 11.2), 4.95 (dd, 1, *J* = 4.9, 11.2), 3.60 (dd, 1, *J* = 1.8, 9.3), 3.25 (br s, 1); (minor) 6.29 (br d, 1, *J* = 11.5), 6.07 (br s, 1), 5.10 (ddd, 1, *J* = 1.6, 5.0, 11.5), 3.59 (dd, 1, *J* = 1.7, 9.3), 3.32 (br s, 1); IR (both, CCl_4) 1632, 1598.

(3aα,5aβ,6β,10aβ)-2,3,3a,4,5,5a,6,7,8,10a-Decahydro-3a,5a-dimethyl-1-(1-methylethyl)-6-(dimethyl-1,1-dimethylethylsilyloxy)-cyclohept[*e*]inden-8-one (33). To a solution of **31** (17 mg, 0.039 mmol) at 0 °C was added Dess-Martin reagent (34 mg, 0.078 mmol).[25] The reaction mixture was stirred at rt for 2 h and quenched by addition of saturated $NaHCO_3$ (2 mL) and 10% $Na_2S_2O_3$ (2 mL). After stirring for 15 min, the reaction mixture was extracted with ether. The ether layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The crude residue was purified by flash chromatography on silica gel (95:5 hexane/EtOAc) to afford 14 mg (89%)

of pure **33**: ^{1}H NMR 6.13 (dd, 1, *J* = 4.1, 12.3), 5.87 (dd, 1, *J* = 2.5, 12.3), 3.71 (d, 1, *J* = 7.8), 3.40-3.33 (m, 1), 2.88 (dd, 1, *J* = 7.8, 17.6), 2.72 (d, 1, *J* = 17.6), 2.56 (h, 1, *J* = 6.8), 2.32 (ddd, 1, *J* = 7.4, 10.5, 15.7), 2.21 (dd, 1, *J* = 9.0, 15.7), 1.75 (ddd, 1, *J* = 1.4, 7.4, 12.1), 1.70-1.32 (m, 5), 1.02 (s, 3), 0.96 (d, 3, *J* = 6.8), 0.94 (d, 3, *J* = 6.8), 0.90 (s, 3), 0.87 (s, 9), 0.06 (s, 3), 0.04 (s, 3); ^{13}C NMR 201.4, 149.9, 142.5, 137.4, 130.3, 75.6, 47.7, 46.7, 43.1, 41.0, 40.4, 36.2, 30.3, 27.9, 26.3, 25.7, 24.5, 21.4, 21.2, 21.1, 18.0, –4.1, –5.0; IR (CCl_4) 1674.

Preparation of 35. To a solution of **33** (5.0 mg, 0.012 mmol) in CH_2Cl_2 (0.1 mL) at 0 °C were added sequentially 2,6-di-*tert*-butyl-4-methylpyridine (8.0 mg, 0.036 mmol) and triflic anhydride (6 μL, 0.036 mmol). The mixture was stirred at rt for 1 h and diluted with ether. The ether layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The crude residue was passed through a short column of silica gel, eluting with hexane. The enol triflate **34**, which coeluted with 2,6-di-*tert*-butyl-4-methylpyrindine, was used directly in the carbonylation reaction without further purification.

The crude enol triflate was dissolved in a solution of anhydrous MeOH (1.0 mL) and *N,N*-diisopropylethylamine (2 drops). The mixture was purged with CO for 5 min via a syringe and $Pd(OAc)_2$ (1 mg, 4.5 μmol) and $P(Ph)_3$ (2.5 mg, 9.5 μmol) were added. The resulting solution was stirred at rt for 10 h, while CO was bubbled through. The mixture was diluted with ether, washed with H_2O and brine, and dried ($MgSO_4$). Solvent removal and flash chromatography on silica gel (99:1 hexane/EtOAc) provided 4.0 mg (75% for 2 steps) of pure **35**: ^{1}H NMR 7.27-7.24 (m, 1), 5.31 (br s, 1), 3.71 (s, 3), 3.62 (dd, 1, *J* = 2.9, 4.9), 2.77 (dd, 1, *J* = 4.9, 19.0), 2.49 (dd, 1, *J* = 2.9, 19.0), 2.41 (d, 1, *J* = 15.4), 1.82 (dd, 1, *J* = 2.9, 15.4), 1.77-1.70 (m, 1), 1.63 (h, 1, *J* = 7.0), 1.59 (br s, 1), 1.39-1.16 (m, 4), 1.13 (s, 3), 1.05 (d, 3, *J* = 7.0), 0.98 (d, 3, *J* = 7.0), 0.97 (s, 3), 0.89 (s, 9), 0.07 (s, 3), 0.04 (s, 3); ^{13}C NMR 168.8, 152.6, 142.4, 126.1, 117.8, 77.4, 51.8, 44.2, 40.7, 35.6, 34.6, 33.1, 31.7, 30.9, 29.7, 28.6, 28.1, 25.9, 24.6, 24.0, 23.6, 22.0, 18.1, –4.1, –5.0; IR (CCl_4) 1709, 1654.

(3aα,5aβ,6β,10aβ)-2,3,3a,4,5,5a,6,10a-Octahydro-3a,5a-dimethyl-1-(1-methylethyl)-6-(dimethyl-1,1-dimethylethylsilyloxy)-8-trifluoromethylsulfonyloxy-cyclohept[*e*]indene (36). To a solution of KHMDS (90 μL of 0.5 M in toluene, 0.045 mmol) in

THF (0.5 mL) at –78 °C was added dropwise a solution of **33** (7 mg, 0.018 mmol) in THF (0.6 mL). The mixture was stirred for 15 min and was quenched by addition of *N*-phenyltrifluoromethanesulfonimide (16 mg, 0.045 mmol) as a powder. After warming to 0 °C over 15 min, the reaction mixture was diluted with ether, washed with saturated NH_4Cl, H_2O, and brine, and dried ($MgSO_4$). Removal of the solvent followed by flash chromatography on silica gel (hexane:EtOAc, 199:1) provided 7.8 mg (84%) of impure **36**: ^{1}H NMR 6.21 (dd, 1, J = 5.7, 10.6), 6.11 (dd, 1, J = 1.2, 4.9), 5.92 (d, 1, J = 10.6), 3.70 (d, 1, J = 4.9), 2.86-2.79 (m, 1), 2.44 (h, 1, J = 6.8), 2.30 (ddd, 1, J = 7.4, 10.2, 15.7), 2.18 (ddd, 1, J = 1.0, 9.2, 15.7), 1.73 (ddd, 1, J = 1.4, 7.4, 12.1), 1.60-1.31 (m, 5), 1.08 (s, 3), 0.92 (d, 3, J = 6.8), 0.90 (s, 9), 0.88 (s, 3), 0.87 (d, 3, J = 6.8), 0.02 (s, 6); ^{13}C NMR 146.1, 135.9, 130.6, 122.7, 120.8, 79.0, 46.3, 44.2, 40.9, 35.3, 30.7, 27.9, 26.0, 25.8, 24.1, 21.3, 21.1, 18.6, 18.0, –4.4, –5.1 (3 carbons not observed); IR (CCl_4) 1638, 1609.

Methyl (3aα,5aβ,10aβ)-2,3,3a,4,5,5a,10,10a-Octahydro-3a,5a-dimethyl-1-(1-methylethyl)-6-(dimethyl-1,1-dimethylethylsilyloxy)-cyclohept[*e*]indene-8-carboxylate (37). To a solution of crude **36** (7.3 mg, 0.014 mmol) in anhydrous MeOH (1.0 mL) was added *N,N*-diisopropylethylamine (2 drops). The solution was purged with CO for 5 min followed by addition of $Pd(OAc)_2$ (1.0 mg, 4.4×10^{-3} mmol) and $P(Ph)_3$ (2.3 mg, 8.8×10^{-3} mmol). The mixture was heated to reflux for 15 h, while CO was bubbled through. After being cooled to rt, the reaction solution was diluted with ether, washed with H_2O and brine, and dried ($MgSO_4$). Removal of solvent followed by flash chromatography on deactivated silica gel (hexane/EtOAc, 99:1) gave 5.1 mg (79%) of pure **37**: ^{1}H NMR 7.04 (dd, 1, J = 4.0, 8.9), 5.71 (s, 1), 3.75 (s, 3), 2.57 (h, 1, J = 6.8), 2.45 (dd, 1, J = 9.5, 9.5), 2.28 (ddd, 1, J = 7.5, 10.4, 15.5), 2.15 (dd, 1, J = 9.0, 15.5), 2.05 (dd, 1, J = 9.0, 13.9), 1.94-1.88 (m, 1), 1.69 (dd, 1, J = 7.5, 12.0), 1.60-1.40 (m, 5), 1.04 (s, 3), 1.03 (s, 3), 0.96 (s, 9), 0.94 (d, 3, J = 6.8), 0.93 (d, 3, J = 6.8), 0.26 (s, 3), 0.25 (s, 3); ^{13}C NMR 167.9, 140.5, 140.0, 139.2, 128.0, 101.4, 51.8, 46.5, 45.8, 44.6, 41.6, 36.4, 34.3, 29.1, 27.9, 26.2, 26.0, 25.9, 24.9, 24.6, 21.3, 21.1, 18.4, –4.3, –4.5; IR (CCl_4) 1717, 1608.

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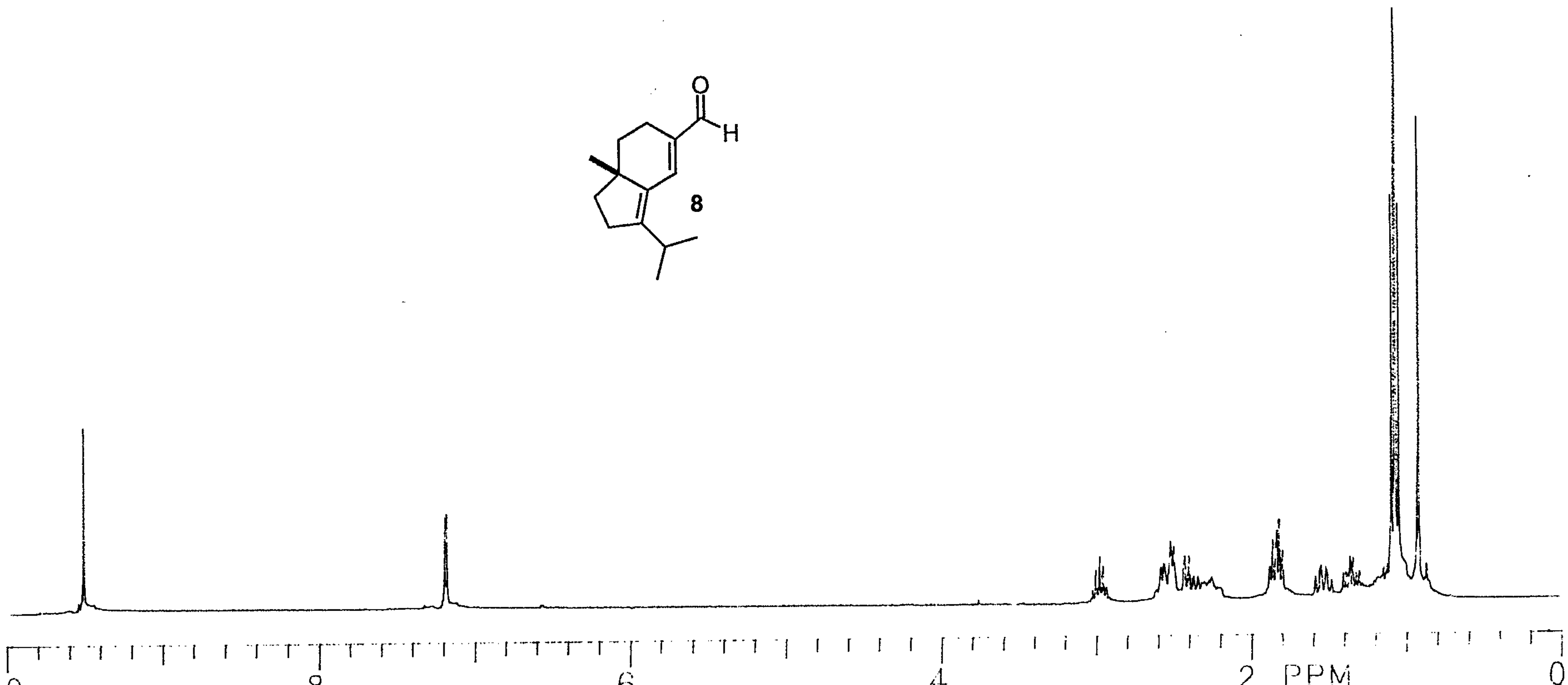

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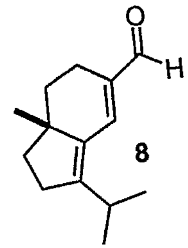

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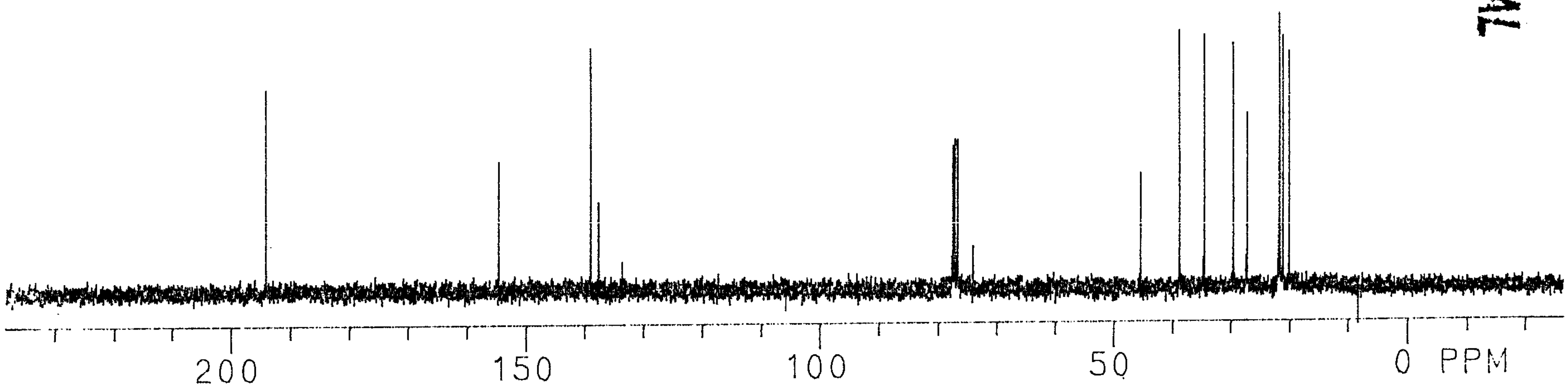

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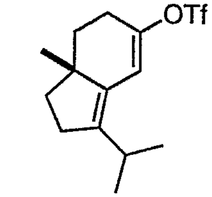

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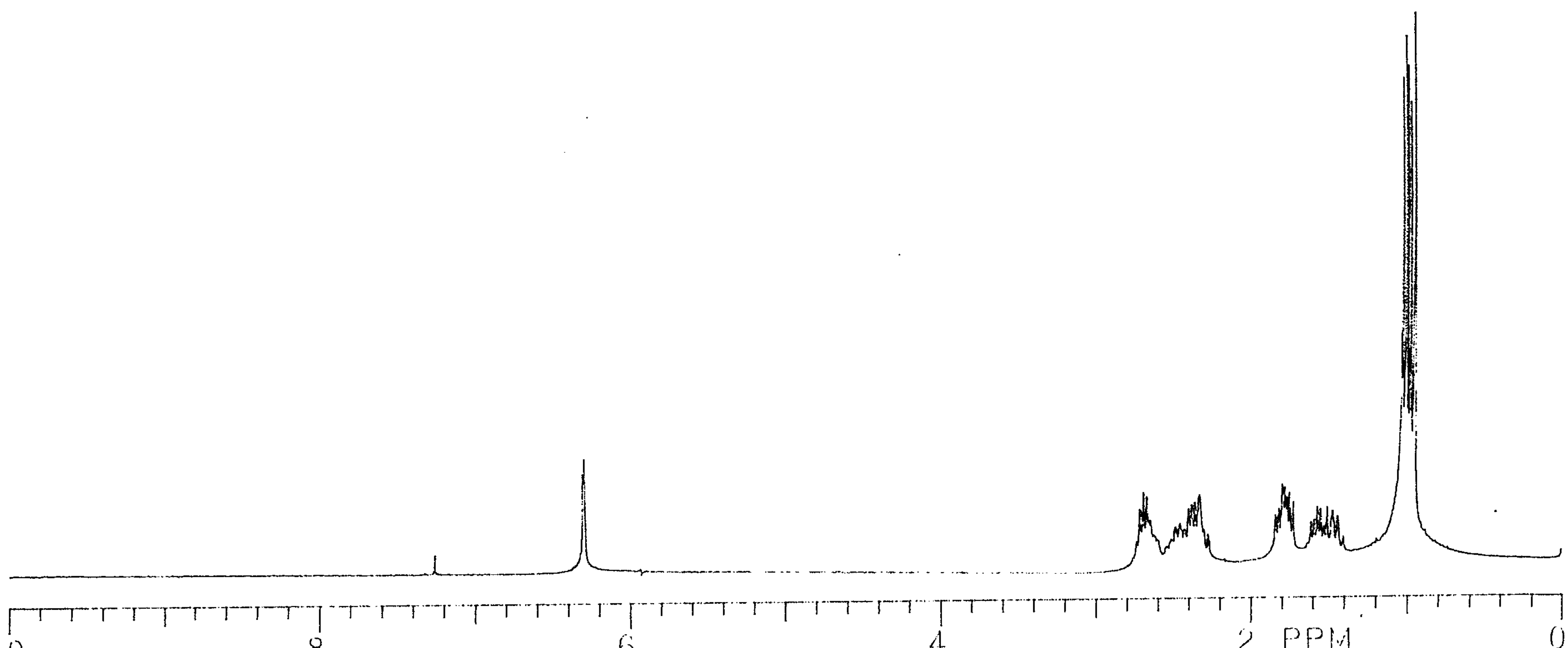

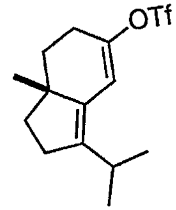

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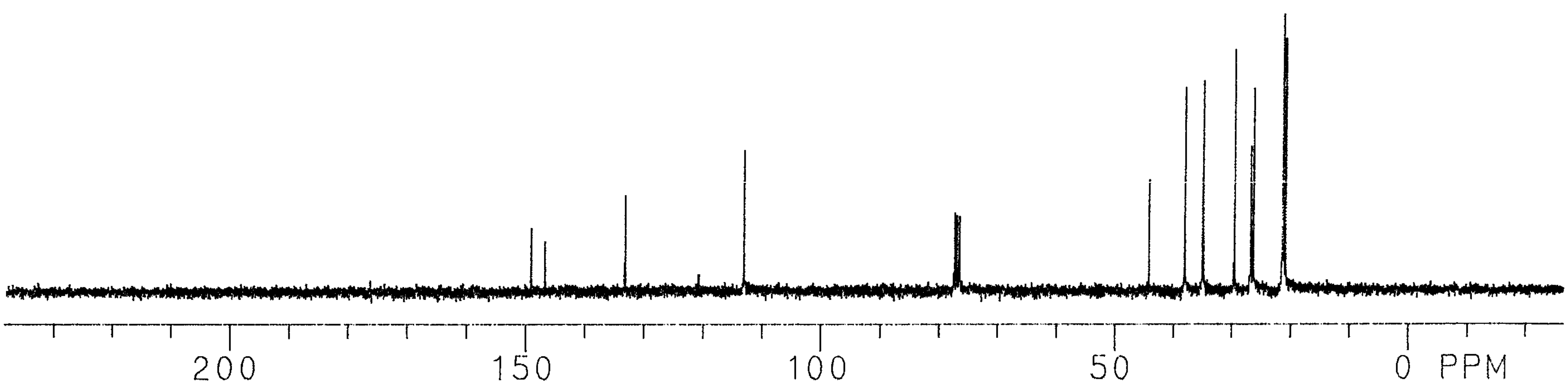

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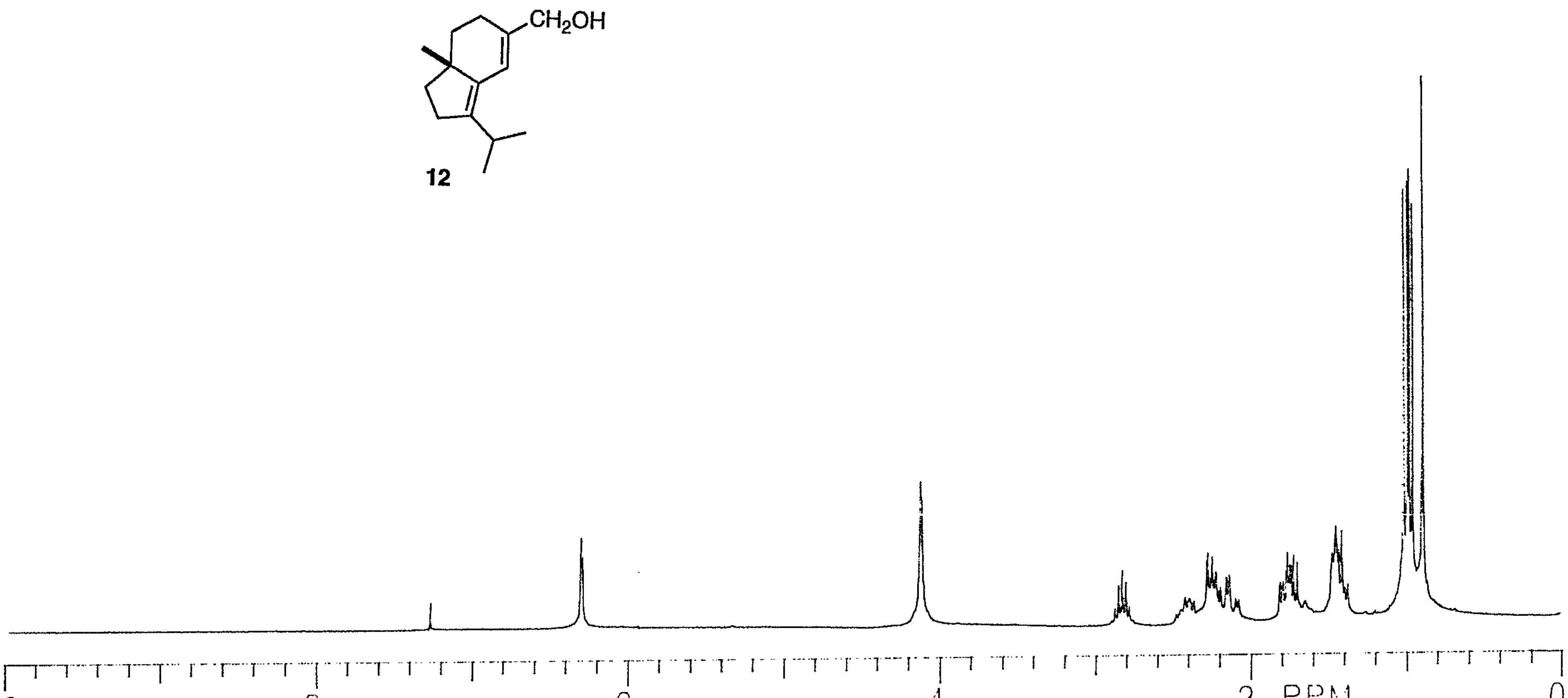

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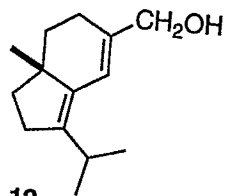

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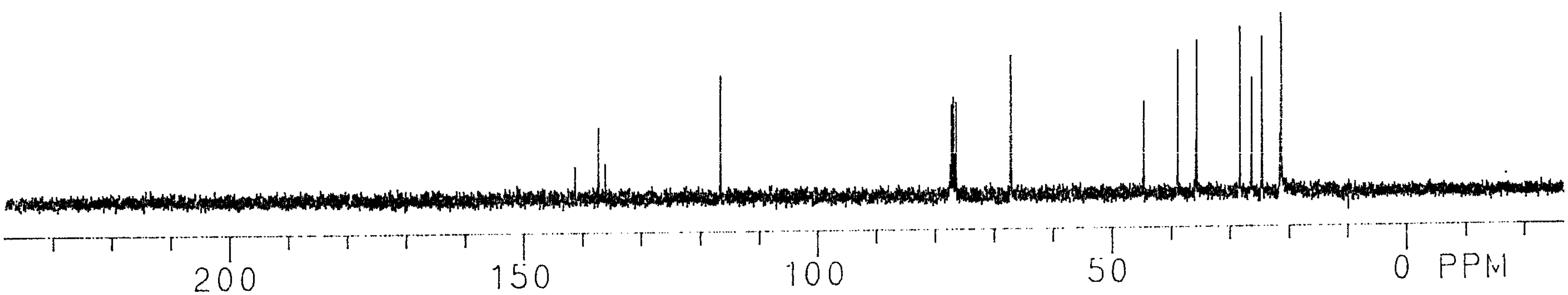

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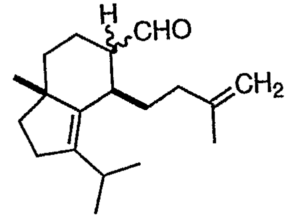

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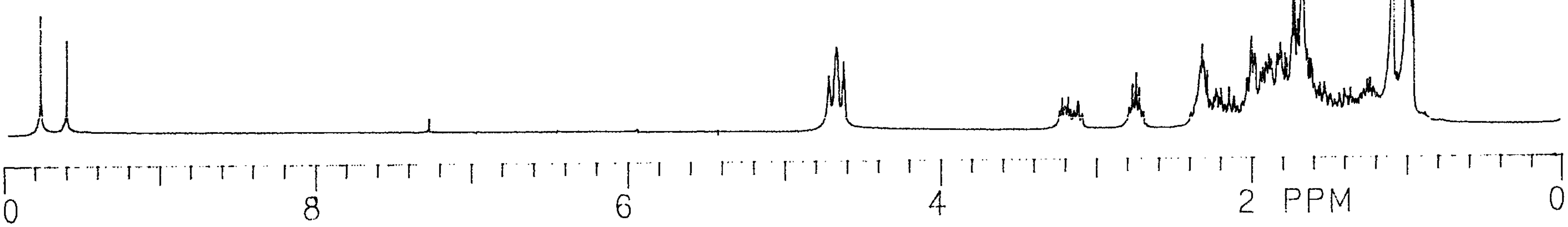

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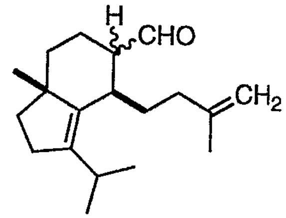

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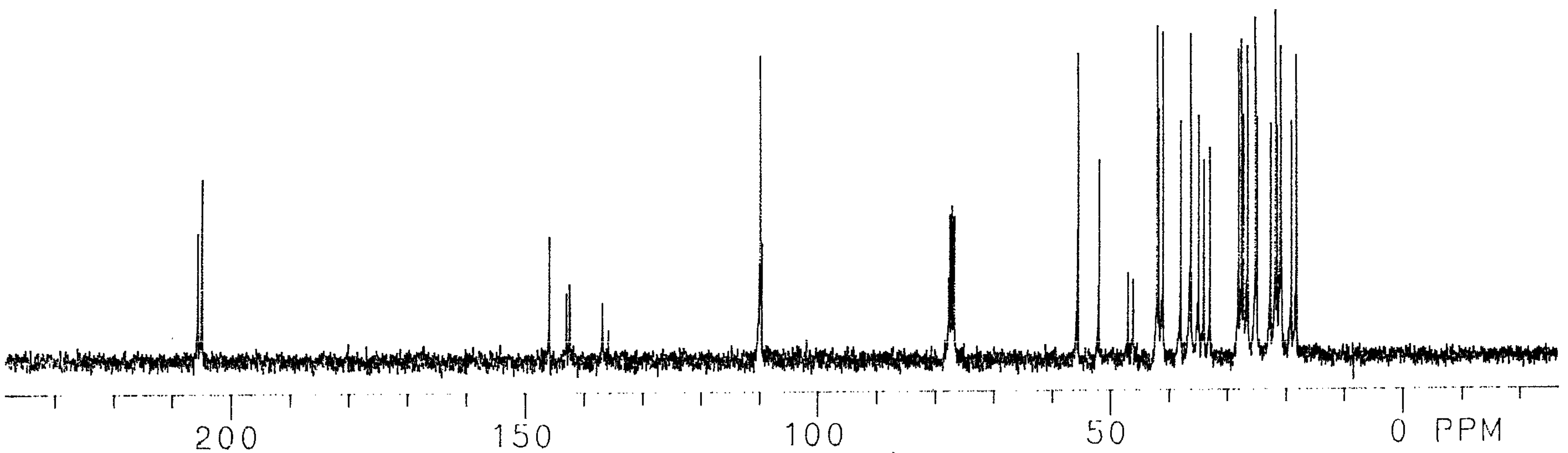

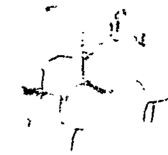

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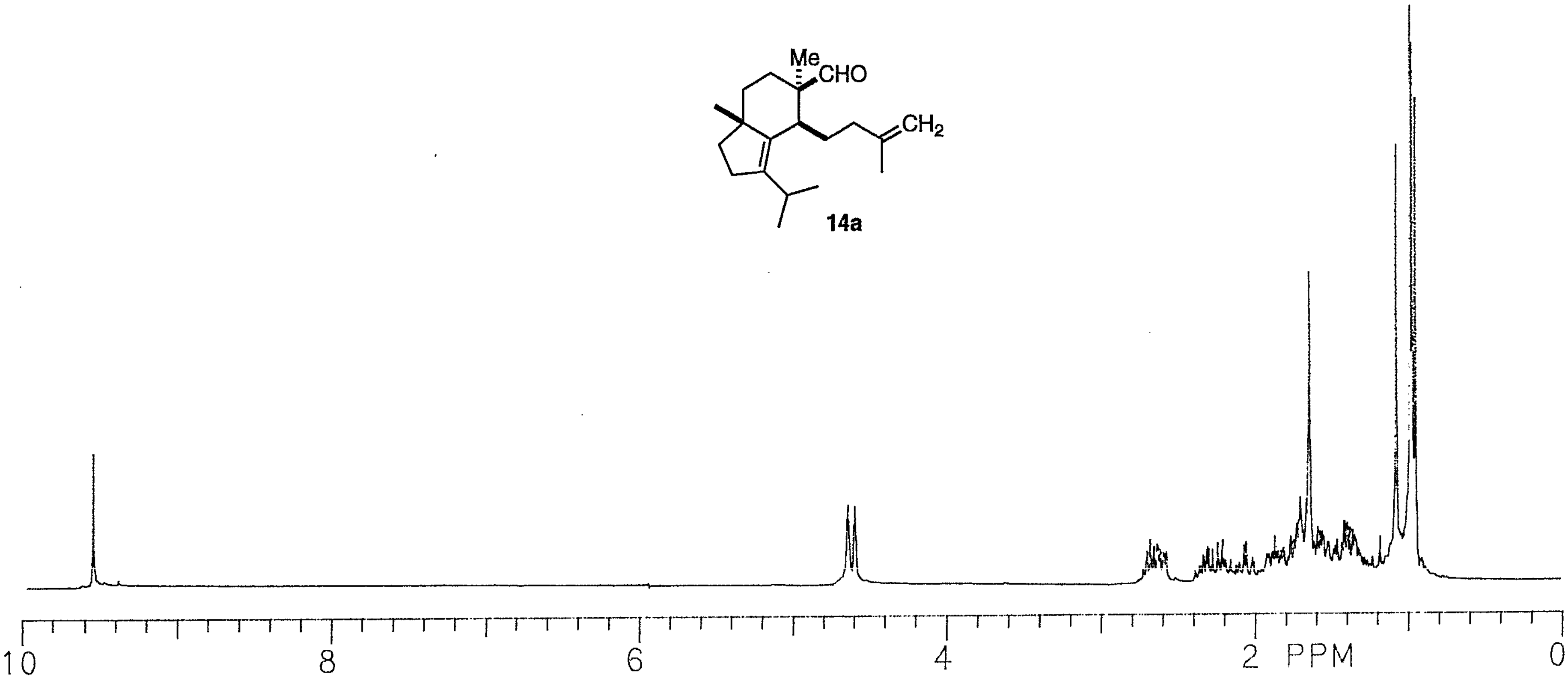

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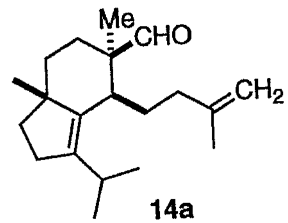

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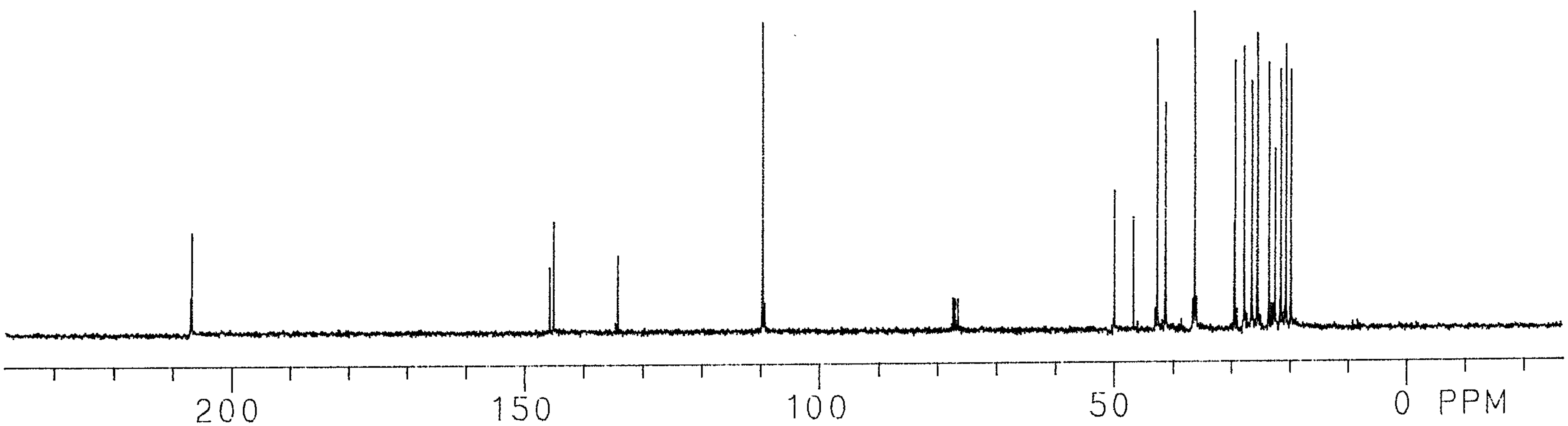

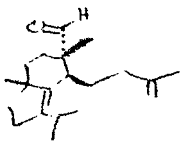

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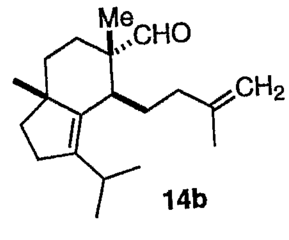

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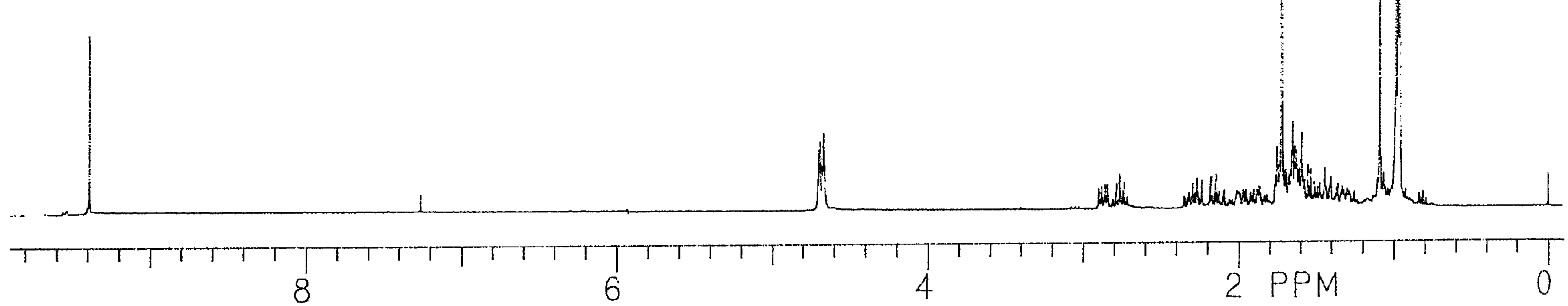

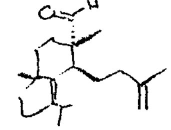

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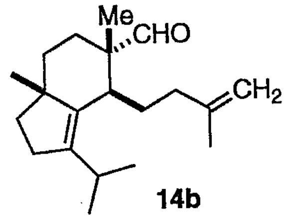

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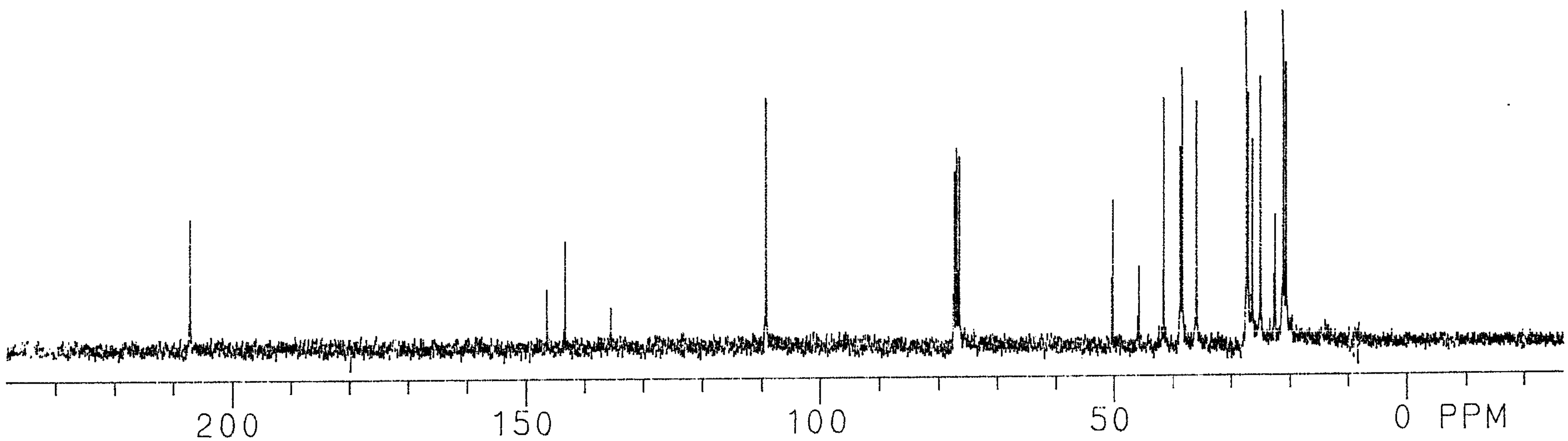

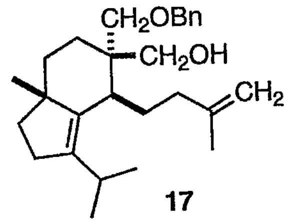

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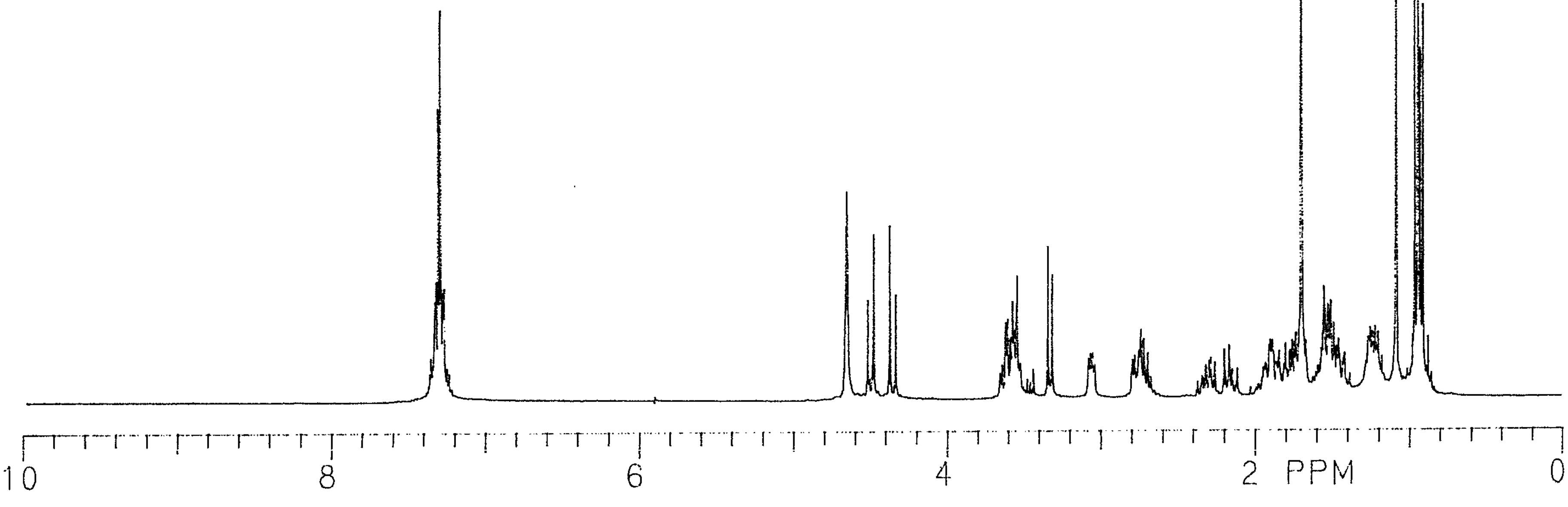

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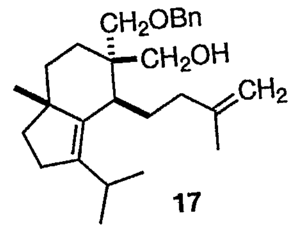

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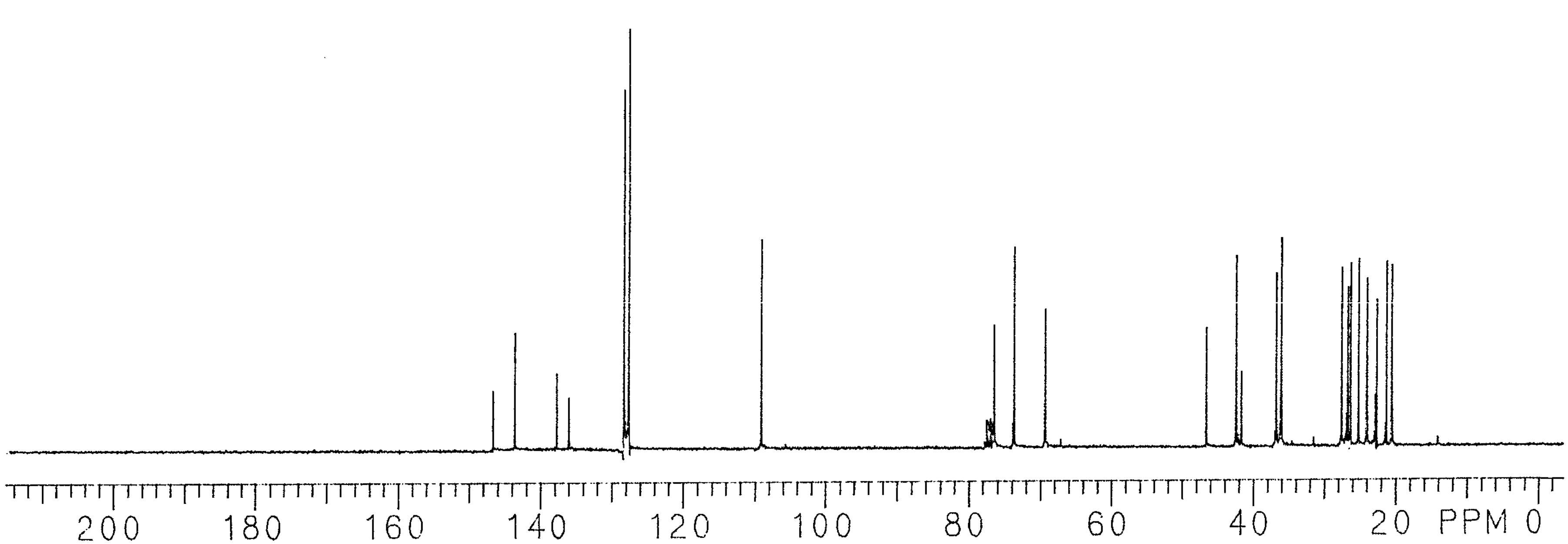

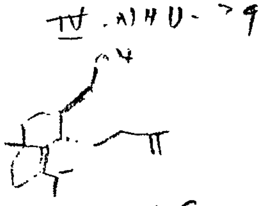

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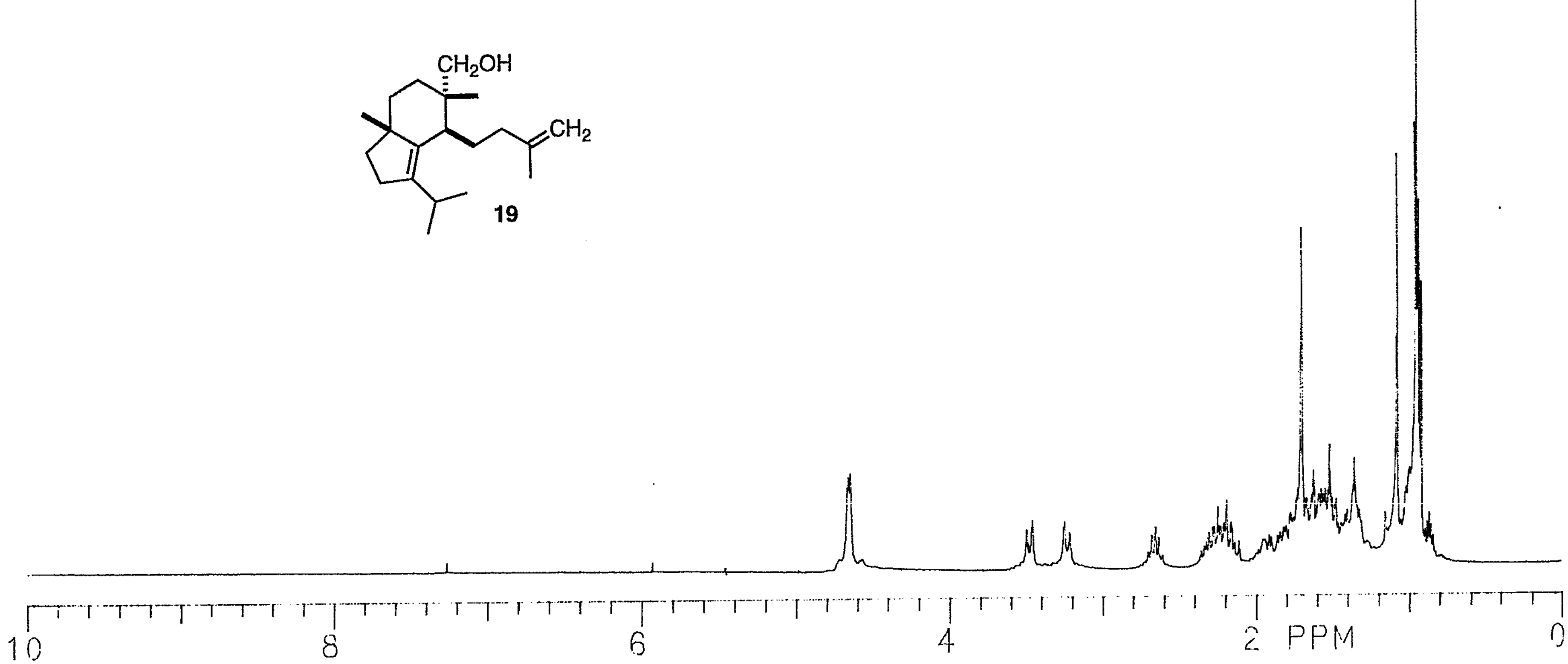

IV . MNU-79 .

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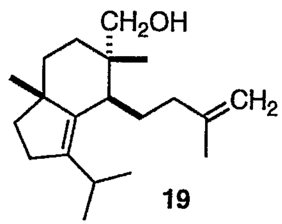

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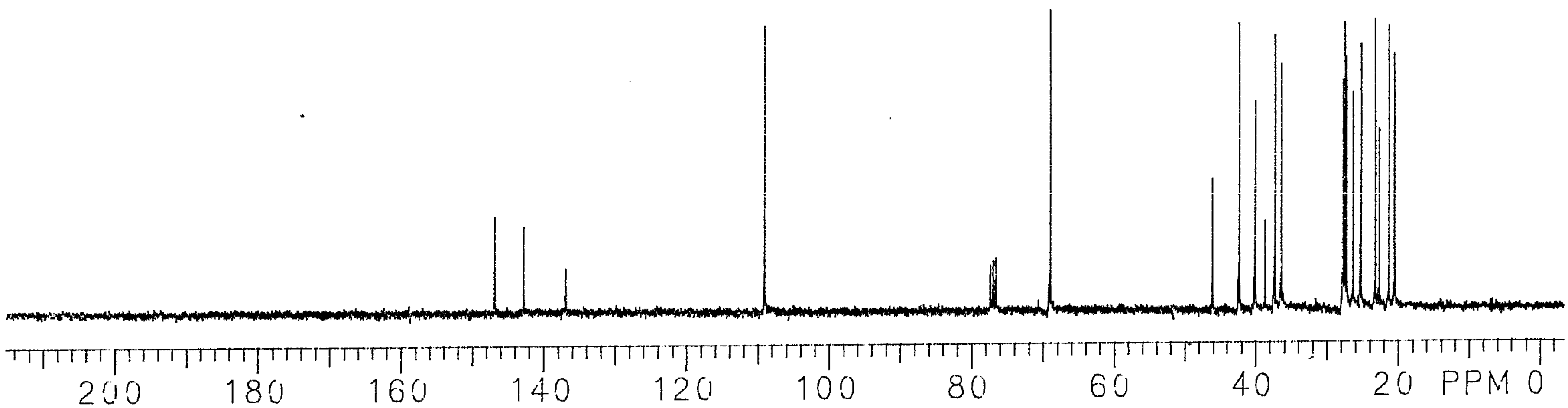

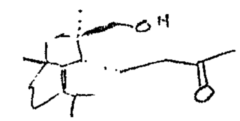

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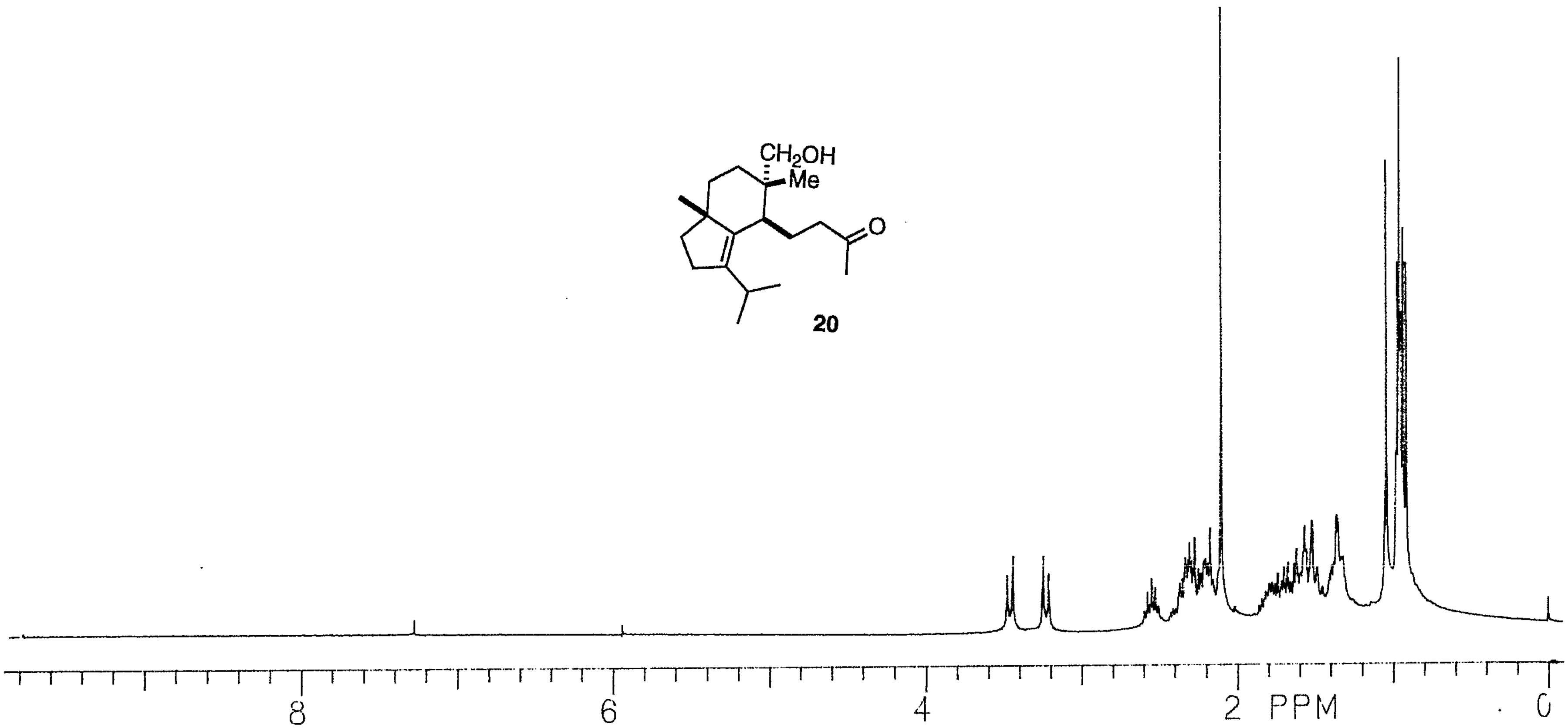

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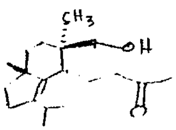

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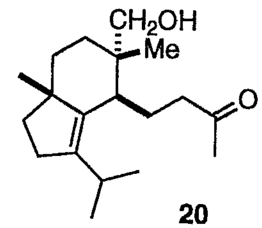

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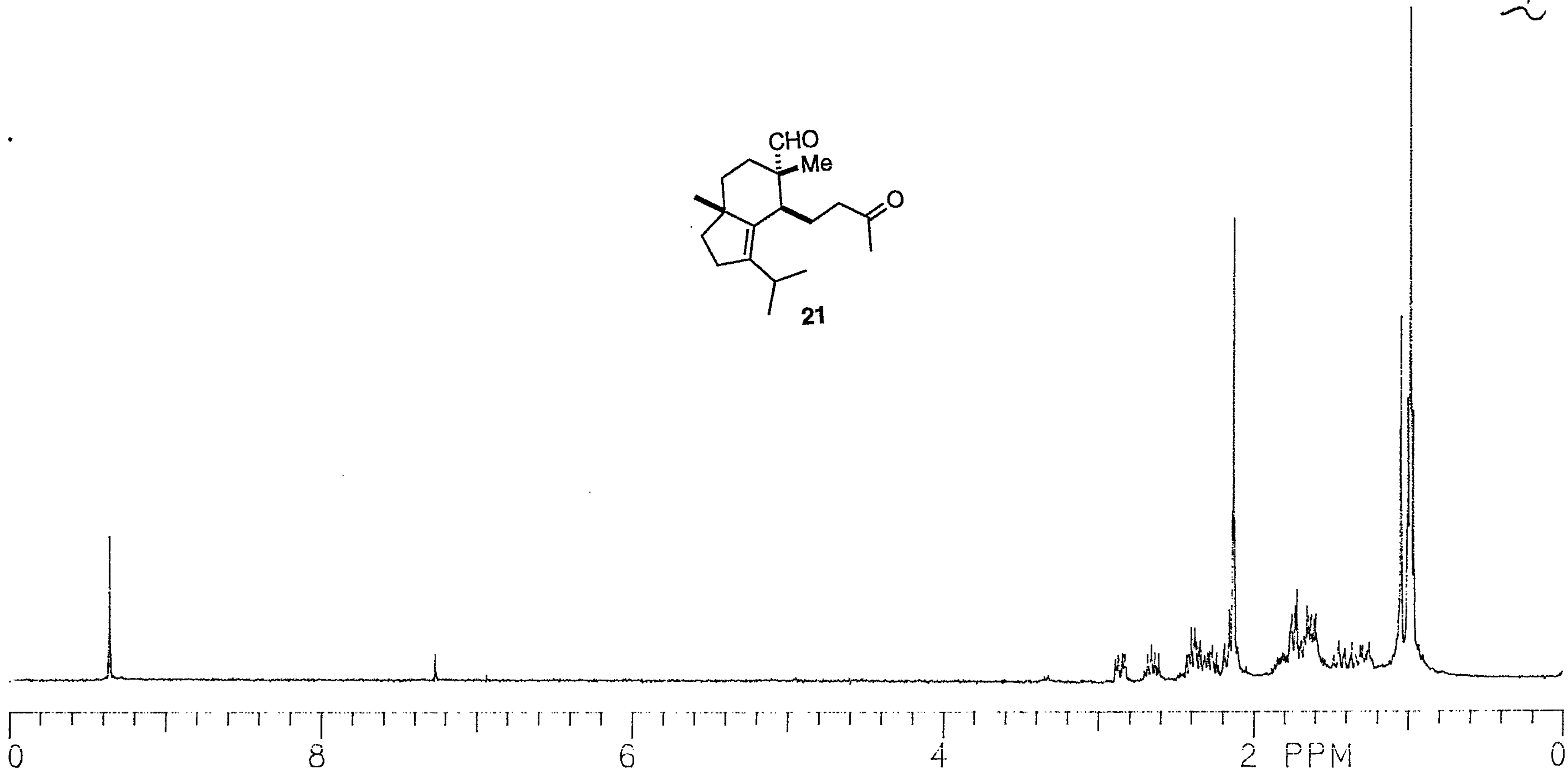

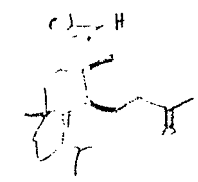

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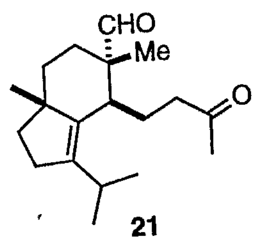

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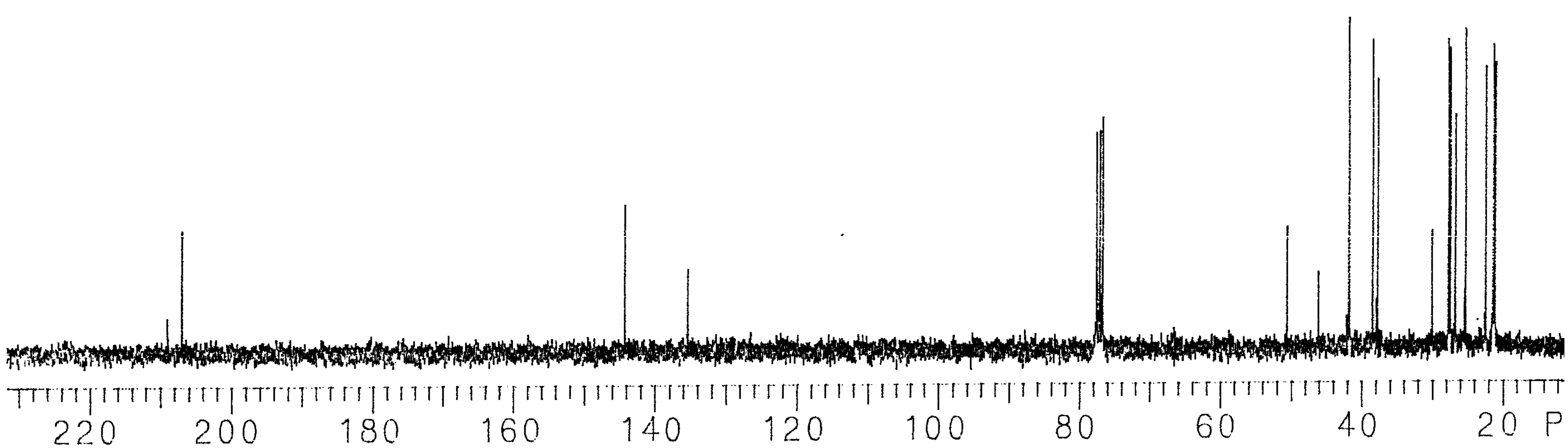
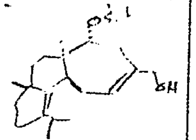


JH-XIII-139



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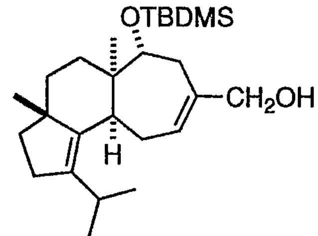

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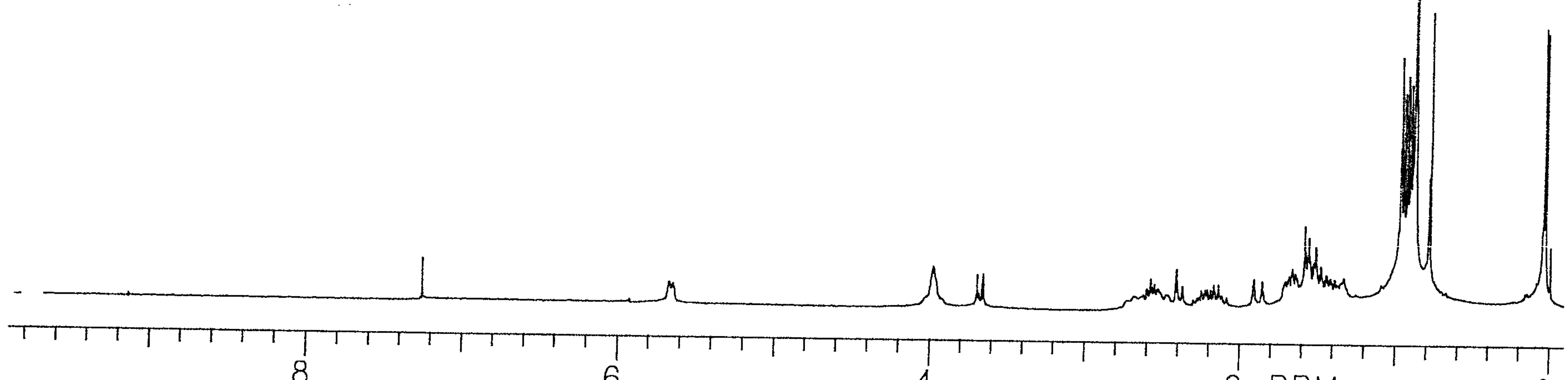

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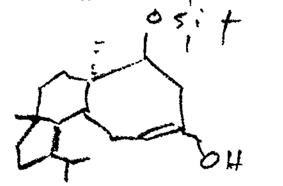

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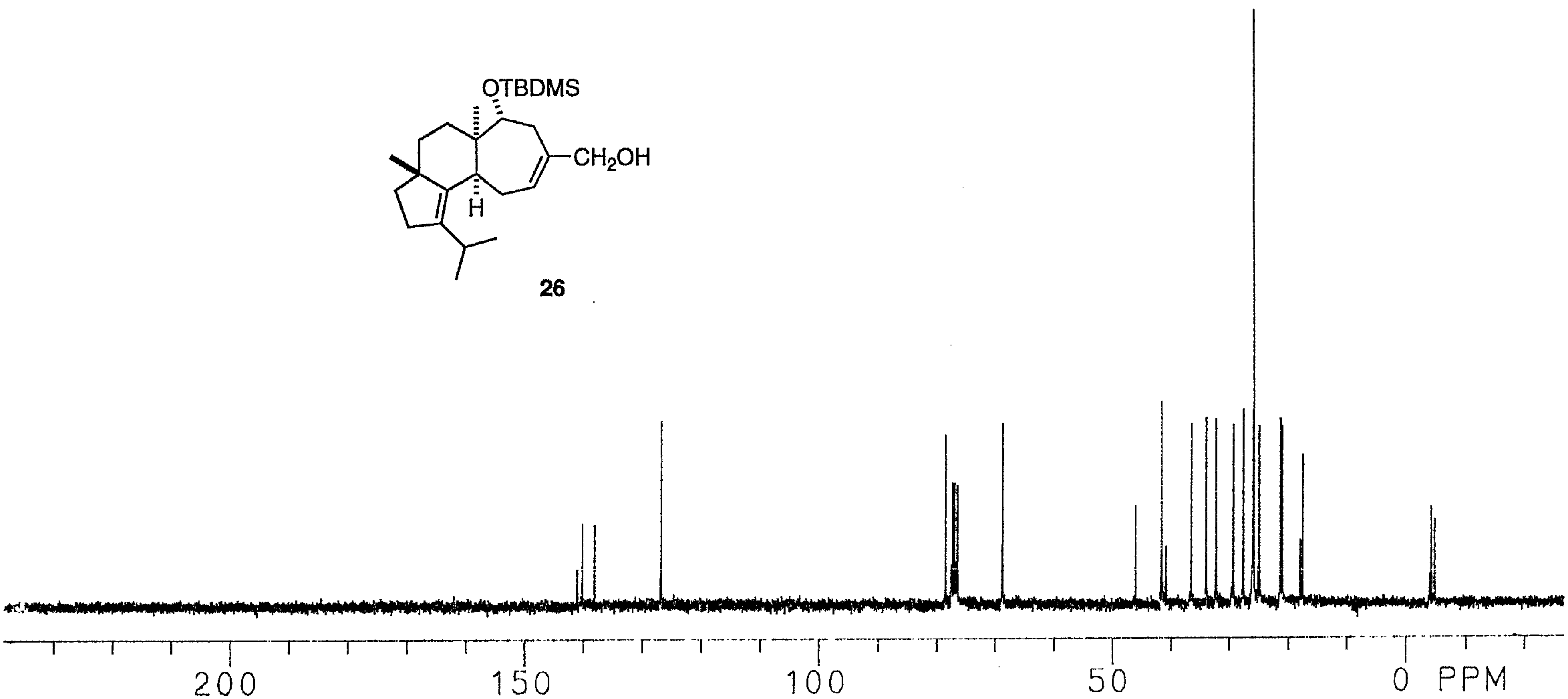
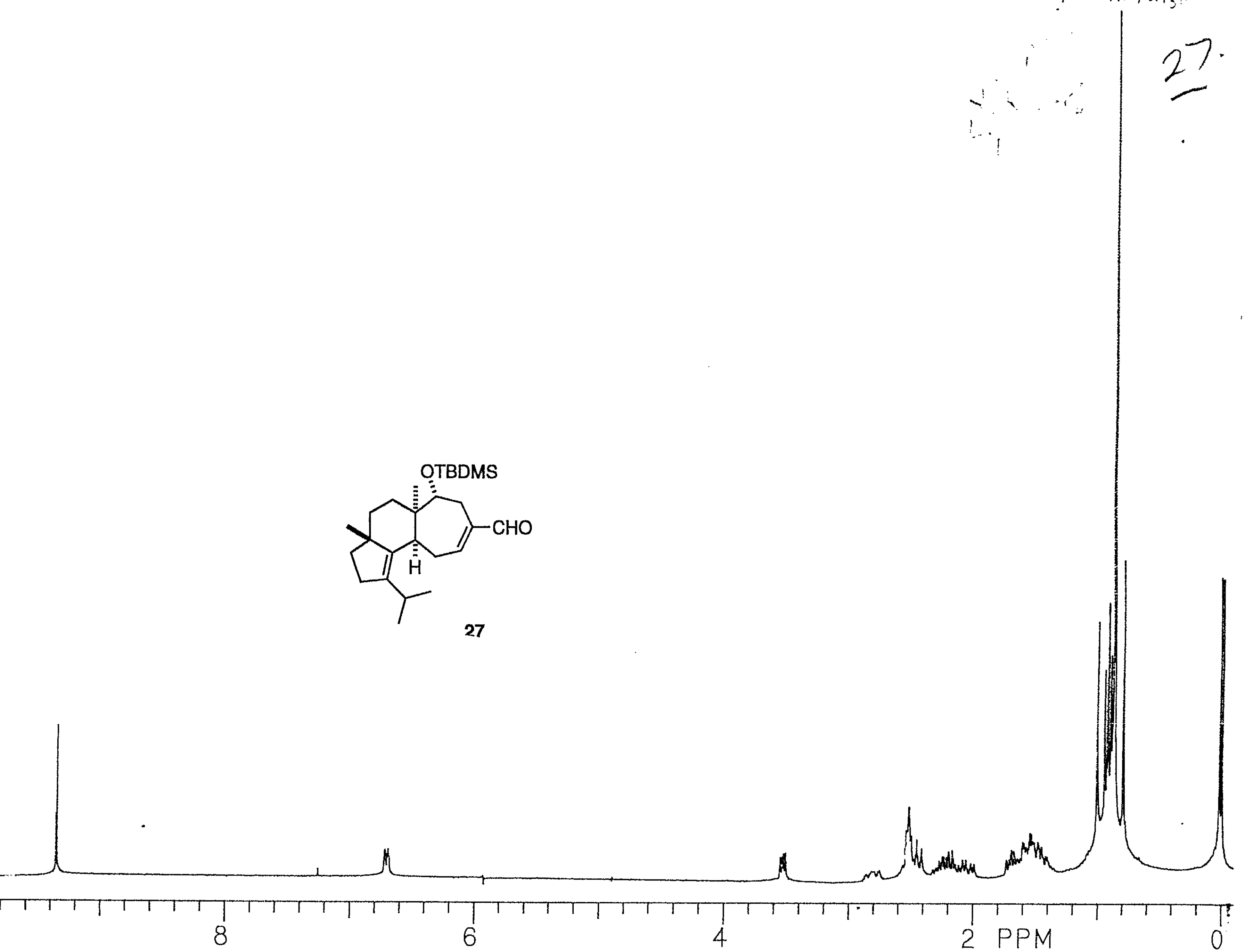
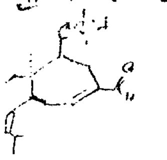




27
OTBDMS
CHO
H
27
8
6
4
2 PPM
0

III - NHO - 134 -



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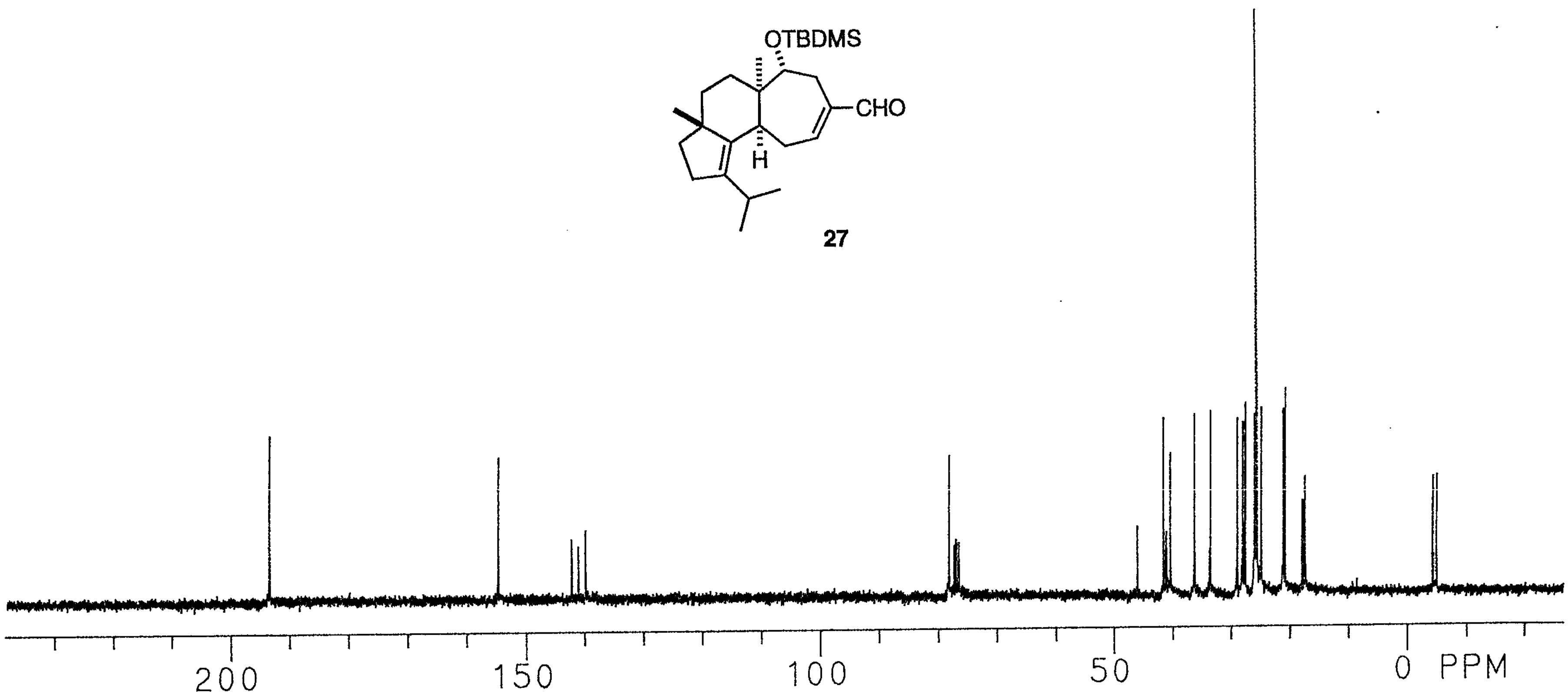

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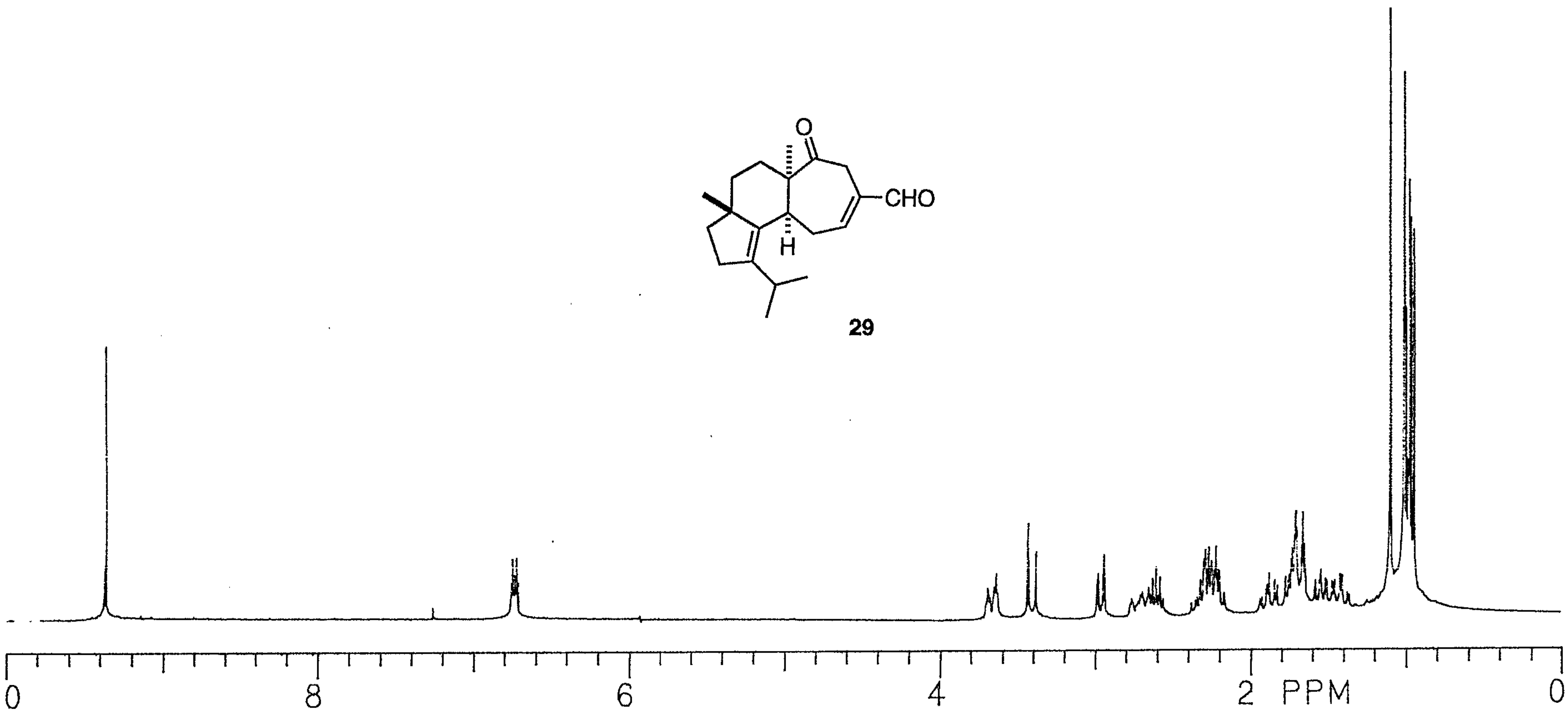

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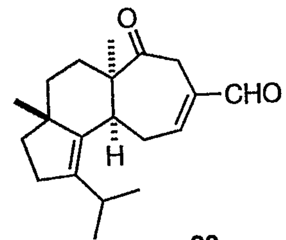

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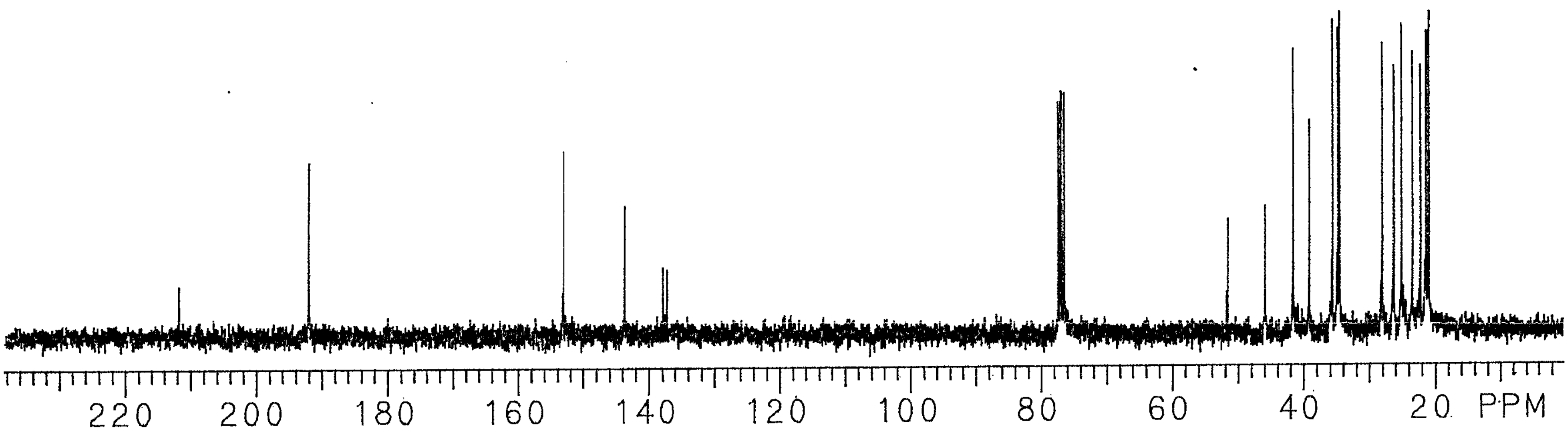

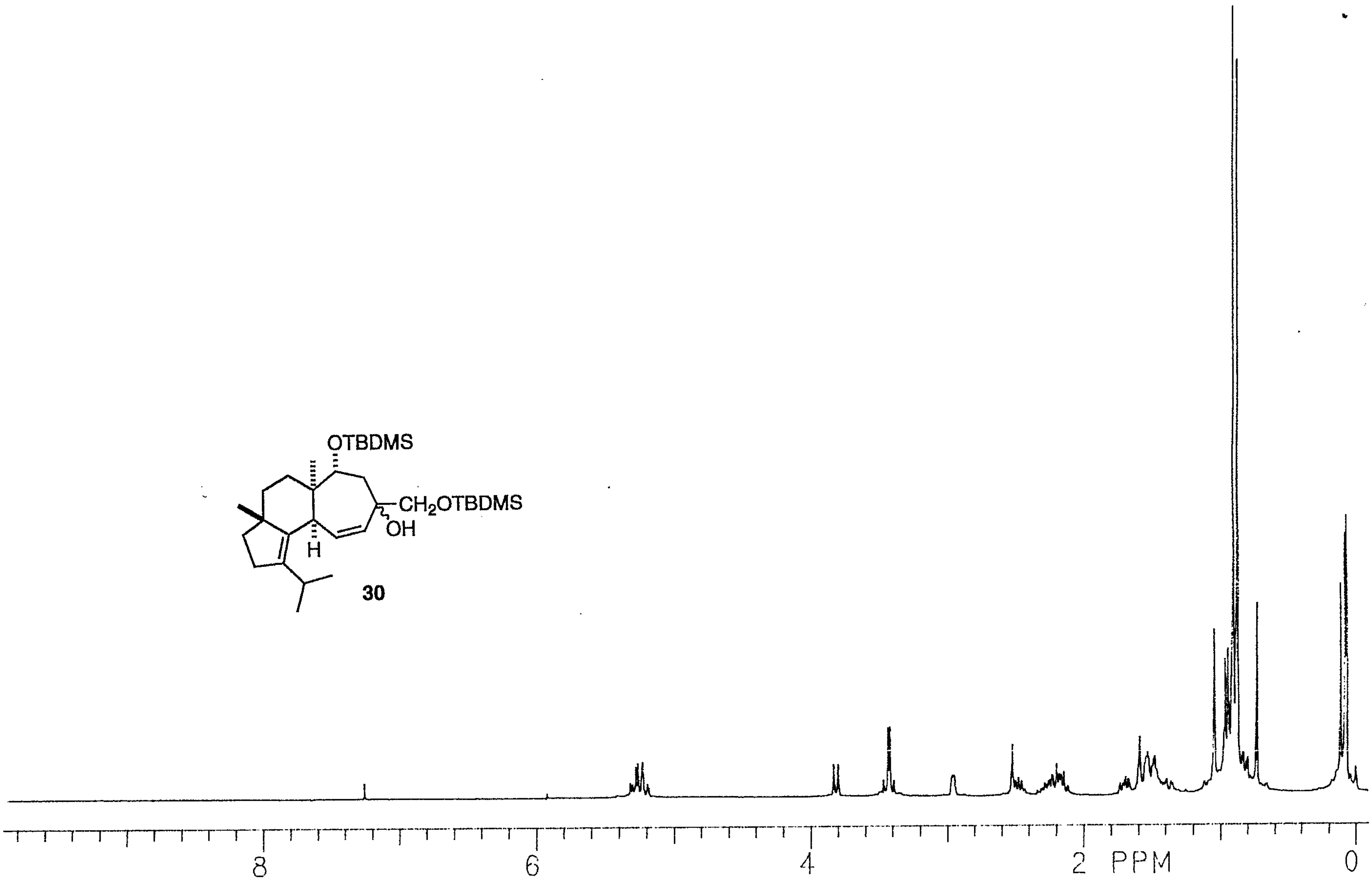
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CH2OTBDMS
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8
6
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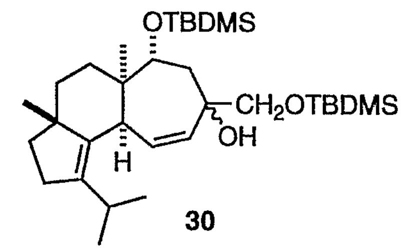

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