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Asymmetric Synthesis of the Phytopathogen (+)-Fomannosin

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(-)-(1R,2S,3R)-3-(4-methoxybenzyloxy)-2-(tert-butyldimethylsilyloxy)-1-((tert-butyldiphenylsilyloxy)methyl)cyclobutanecarbaldehyde (4). A solution of **2** (2.637 g, 5.245 mmol) in CH_2Cl_2 (10 ml) was treated with imidazole (1.786 g, 26.23 mmol) and TBSCl (1.187 g, 7.868 mmol) at 0 ^oC. The reaction mixture was stirred at 0 ^oC for 15 min and then at rt for 9 h before being quenched with saturated $NaHCO_3$ solution. The mixture was diluted with ethyl acetate, washed with water and brine, dried, and concentrated. The residue was purified by silica gel chromatography (elution with hexanes/ethyl acetate 30:1) to give the TBS ether (2.940 g, 91%) as a colorless oil; IR (film, cm^{-1}) 1613, 1514, 1472; ^1H NMR (300 MHz, $CDCl_3$) δ 7.65 (m, 4 H), 7.40 (m, 6 H), 7.27 (m, 2 H), 6.86 (m, 2 H), 6.17 (dd, *J* = 17.8, 11.0 Hz, 1 H), 5.11 (dd, *J* = 11.0, 1.4 Hz, 1 H), 4.94 (dd, *J* = 17.8, 1.4 Hz, 1 H), 4.57 (d, *J* = 11.6 Hz, 1 H), 4.52 (dd, *J* = 5.2, 1.9 Hz, 1 H), 4.37 (d, *J* = 11.6 Hz, 1 H), 4.06 (dt, *J* = 6.8, 5.2 Hz, 1 H), 3.81 (s, 3 H), 3.55 (ABq, *J* = 10.3 Hz, Δν = 34.3 Hz, 2 H), 2.21 (ddd, *J* = 12.1, 6.9, 2.3 Hz, 1 H), 2.02 (dd, *J* = 12.1, 4.9 Hz, 1 H), 1.07 (s, 9 H), 0.91 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 139.3 (4 C), 135.7 (2 C), 133.4, 131.0, 129.7 (2 C), 129.1 (2 C), 127.7 (4 C), 114.1, 113.6 (2 C), 72.8, 72.1, 70.5, 67.1, 55.3, 49.7, 31.8, 26.9 (3 C), 25.9 (3 C), 19.4, 18.4, -4.6, -4.7; HRMS (ES) *m/z* $(M+Na)^+$ calcd 639.3296, obsd 639.3297; $[\alpha]_D^{24}$ +0.73 (*c* 1.1, $CHCl_3$).

Five drops of a 0.1% solution of Sudan III in dichloromethane were added to a solution of the TBS ether (0.219 g, 0.355 mmol) in dichloromethane (8 ml). The resulting red solution was cooled to -78 ^oC. A stream of O_3 was passed through the solution at -78 ^oC until the color disappeared. Triphenylphospine (0.140 g, 0.532 mmol) was added. The solution was allowed to warm slowly to rt and stirred at rt for 1 h. The solution was

concentrated. The residue was purified by silica gel chromatography (elution with hexanes/ethyl acetate 15:1) to give **4** (0.200 g, 91%) as a red oil; IR (film, cm^{-1}) 1714, 1514, 1249; ^1H NMR (300 MHz, $CDCl_3$) δ 10.10 (s, 1 H), 7.65-6.85 (series of m, 14 H), 3.84 (d, *J* = 10.9 Hz, 1 H), 3.81 (s, 3 H), 3.73 (d, *J* = 10.9 Hz, 1 H), 2.22 (dd, *J* = 13.2, 3.6 Hz, 1 H), 2.14 (ddd, *J* = 12.8, 6.1, 1.3 Hz, 1 H), 1.06 (s, 9 H), 0.87 (s, 9 H), 0.07 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.8, 159.1, 135.6 (4 C), 133.0, 133.0, 129.8, 129.2 (2 C), 129.2 (2 C), 127.8 (4 C), 113.7 (2 C), 74.2, 71.4, 70.8, 62.5, 59.4, 55.3, 26.9 (3 C), 26.5, 25.7 (3 C), 19.3, 18.1, -4.9, -5.0; HRMS (ES) *m/z* $(M+Na)^+$ calcd 641.3089, obsd 641.3091; $[\alpha]_D^{24}$ -30.4 (*c* 1.19, $CHCl_3$).

(-)-1-((1R,2S,3R)-3-(4-methoxybenzyloxy)-2-(tert-butyldimethylsilyloxy)-1-((tert-butyldiphenylsilyloxy)methyl)cyclobutyl)-3,3-dimethylhex-5-en-1-one (7). A solution of 5-iodo-4,4-dimethylpent-1-ene **5** (22.00 g, 98.23 mmol) in pentane (650 ml) was treated with *t*-BuLi (1.36 M in pentane, 144.5 ml, 196.5 mmol) at -78 °C under argon. The milky solution was stirred at -78 °C for 1 h. A solution of **4** (30.40 g, 49.12 mmol) in THF (490 ml) was added at -78 °C. The reaction mixture was stirred at -78 °C for 1 h and quenched with brine at -78 °C. The suspension was allowed to warm to rt and diluted with ether and water. The organic layer was washed with brine, dried and concentrated. The residue was purified by filtering through a short pad of silica gel, and eluting with hexanes/ethyl acetate (20:1) to give carbinol **6** (33.92 g, 96%) as a colorless oil; IR (film, cm^{-1}) 3532, 1614, 1514; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68-6.89 (series of m, 14 H), 5.86-5.78 (m, 1 H), 5.01-4.94 (m, 2 H), 4.71-4.67 (m, 2 H), 4.48 (d, *J* = 11.3 Hz, 1 H), 4.42 (d, *J* = 11.3 Hz, 1 H), 4.06 (dt, *J* = 5.9, 2.2 Hz, 1 H), 4.00 (d, *J* = 10.7 Hz, 1 H), 3.84 (s, 3 H), 3.59 (d, *J* = 10.7 Hz, 1 H), 3.23 (s, 1 H), 2.04-1.96 (m, 3 H), 1.45 (d, *J*

= 12.9 Hz, 1 H), 1.17-1.06 (m, 2 H), 1.10 (s, 9 H), 0.94 (s, 9 H), 0.91 (s, 3 H), 0.89 (s, 3 H), 0.14 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 136.0, 135.6 (4 C), 133.5, 133.4, 130.5, 129.6 (2 C), 129.1 (2 C), 127.7 (4 C), 116.6, 113.5 (2 C), 74.5, 70.8, 70.0, 69.7, 62.1, 55.2, 53.0, 47.1, 42.5, 32.9, 27.1, 27.1, 27.0 (3 C), 26.9, 25.8 (3 C), 19.3, 18.1, -4.6, -5.3; HRMS (ES) *m/z* $(M+Na)^+$ calcd 739.4184, obsd 739.4185; $[\alpha]_D^{24}$ -33.9 (*c* 1.07, $CHCl_3$).

A solution of **6** (107 mg, 0.149 mmol) in CH_2Cl_2 (5 ml) was treated with 4 Å MS (430 mg) and pyridinium dichromate (196 mg, 0.522 mmol). The suspension was stirred at rt for 24 h, treated with Celite, and diluted with ether. The mixture was filtered through a pad of silica gel and concentrated. The residue was purified by silica gel chromatography (elution with hexanes/ethyl acetate 20:1) to give **7** (89 mg, 83%) as a colorless oil; IR (film, cm^{-1}) 1707, 1514, 1249; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64-6.84 (series of m, 14 H), 5.88-5.69 (m, 1 H), 5.02-4.92 (m, 2 H), 4.43 (d, *J* = 5.9 Hz, 1 H), 4.37 (d, *J* = 5.9 Hz, 1 H), 4.32-4.29 (m, 1 H), 3.83-3.80 (m, 1 H), 3.82 (s, 3 H), 3.81 (d, *J* = 10.2 Hz, 1 H), 3.59 (d, *J* = 10.2 Hz, 1 H), 2.69-2.53 (m, 3 H), 2.12 (d, *J* = 7.5 Hz, 2 H), 2.02-1.96 (m, 1 H), 1.05 (s, 9 H), 0.99 (s, 6 H), 0.88 (s, 9 H), 0.03 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.9, 159.0, 135.7 (2 C), 135.7, 135.6 (2 C), 133.0, 130.6, 129.8 (2 C), 129.3 (4 C), 127.8 (2 C), 116.9, 113.5 (2 C), 73.5, 72.2, 69.8, 67.0, 59.5, 55.3, 51.4, 46.5, 45.1, 33.1, 30.0, 27.1, 26.9 (3 C), 25.9 (3 C), 19.3, 18.4, -4.7, -4.8; HRMS (ES) m/z $(M+Na)^+$ calcd 737.4028, obsd 737.4034; $[\alpha]_D^{23}$ -42.6 (*c* 1.14, $CHCl_3$).

(-)-1-(((1R,2S,3R)-2-(tert-butyldimethylsilyloxy)-3-((tert-butyldiphenylsilyloxy) methyl)-3-(4,4-dimethylhepta-1,6-dien-2-yl)cyclobutoxy)methyl)-4-methoxybenzene (8). A solution of ketone **7** (89.1 mg, 0.125 mmol) in pentane-toluene (1:1, 6 ml) was

treated with a solution of $TMSCH_2Li$ in pentane (0.75 M, 1.00 ml, 0.748 mmol) at -78 °C. The mixture was stirred at -78 °C for 2 h. The cooling bath was removed and the reaction mixture was immediately quenched with water. The mixture was extracted with ethyl acetate, washed with brine, dried, and concentrated. The crude product was taken into benzene (5 ml), treated with pTSA•H_2O (2.4 mg, 0.0125 mmol), and stirred at rt for 5 h. Three drops of triethylamine were added to quench the reaction. The mixture was concentrated. The residue was purified by silica gel chromatography (elution with hexanes/ethyl acetate 30:1) to give diene **8** (74.0 mg, 83%) as a colorless oil; IR (film, cm^{-1}) 1513, 1248, 1112, 1075; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68-6.84 (series of m, 14 H), 5.87-5.76 (m, 1 H), 5.08 (br s, 1 H), 5.02-4.92 (m, 2 H), 4.89 (d, *J* = 1.0 Hz, 1 H), 4.39 (s, 2 H), 4.39-4.35 (m, 1 H), 3.96-3.90 (m, 1 H), 3.82 (s, 3 H), 3.56 (s, 2 H), 2.34 (dd, *J* = 11.4, 7.1 Hz, 1 H), 2.28-2.18 (m, 2 H), 2.05-1.96 (m, 2 H), 1.82 (d, *J* = 15.2 Hz, 1 H), 1.60 (s, 9 H), 0.90 (s, 9 H) 0.85 (s, 3 H), 0.84 (s, 3 H), 0.04 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.5, 135.9, 135.7 (4 C) , 133.5, 133.4, 131.1, 129.6, 129.1 (2 C) 127.8, 127.7 (2 C), 127.7 (2 C), 116.7, 115.1, 113.6 (2 C), 75.3, 70.7, 69.8, 68.9, 55.2, 51.7, 47.6, 45.1, 44.5, 33.8, 27.5, 27.1, 26.9 (3 C), 26.0 (3 C), 19.3, 1.4, -4.4, -4.7; HRMS (ES) *m/z* $(M+Na)^+$ calcd 735.4235, obsd 735.4265; $[\alpha]_D^{23}$ -47.0 (*c* 1.26, $CHCl_3$).

(-)-(1S,2R,4R)-4-(4-methoxybenzyloxy)-2-(4,4-dimethylcyclopent-1-enyl)-2-(hydroxymethyl)cyclobutanol (9). A solution of the second-generation Grubbs catalyst (78.6 mg, 5mol%, 0.0925 mmol) in benzene (20 ml) was added dropwise into a refluxing solution of **8** (1.32 g, 1.85 mmol) in benzene (400 ml). The reaction mixture was refluxed for 6 h, filtered through a short pad of silica gel, washed with hexanes/ethyl acetate

(10:1), and concentrated. The residue was purified by silica gel chromatography (elution with hexanes/ethyl acetate 40:1) to give the cyclopentene (1.152 g, 91%) as a colorless oil; IR (film, cm^{-1}) 1514, 1248, 1112; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67-6.84 (series of m, 14 H), 5.32 (t, *J* = 1.9 Hz, 1 H), 4.49-4.47 (m, 1 H), 4.48 (d, *J* = 11.5 Hz, 1 H), 4.40 (d, *J* = 11.5 Hz, 1 H), 3.99 (dd, *J* = 12.0, 5.5 Hz, 1 H), 3.82 (s, 3 H), 3.62 (d, *J* = 10.1 Hz, 1 H), 3.49 (d, *J* = 10.1 Hz, 1 H), 2.24-2.11 (m, 6 H), 1.05 (s, 9 H), 1.04 (s, 3 H), 1.03 (s, 3 H), 0.89 (s, 9 H), 0.04 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 142.5, 135.7 (2 C), 135.7 (2 C), 133.6, 133.5, 131.1, 129.6 (2 C), 129.1 (2 C), 127.6 (4 C), 124.7, 113.5 (2 C), 73.3, 72.7, 70.0, 67.4, 55.2, 49.2, 48.9, 47.7, 38.1, 31.6, 30.0, 30.0, 26.9 (3 C), 26.0 (3 C), 19.3, 18.4, -4.9 (2 C); HRMS (ES) *m/z* $(M+Na)^+$ calcd 707.3922, obsd 707.3915; $[\alpha]_D^{22}$ -26.7 (*c* 0.70, $CHCl_3$).

A solution of the above cyclopentene (103 mg, 0.150 mmol) in THF (5 ml) was treated with TBAF (0.45 ml of 1.0 M in THF), stirred at rt overnight, and concentrated. The residue was chromatographed on silica gel (elutions with hexanes/ethyl acetate 2:1) to provide 38 mg (76%) of **9** as a waxy semi-solid; IR ($CHCl_3$, cm^{-1}) 3425, 1613, 1515, ^1H NMR (500 MHz, $CDCl_3$) δ 7.30-7.28 (m, 2 H), 6.91-6.89 (m, 2H), 5.53 (t, *J* = 1.9 Hz, 1 H), 4.46 (s, 2H), 4.13-4.11 (m, 2 H), 3.83 (s, 3 H), 3.64 (dd, *J* = 0.5, 10.7 Hz, 1 H), 3.62 (d, *J* = 10.7 Hz, 1 H), 2.30-2.16 (m, 6 H), 1.11 (s, 3 H), 1.10 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 142.0, 129.8, 129.6, 128.0, 113.9, 72.3, 71.6, 70.7, 66.3, 55.3, 48.4, 47.8, 47.5, 38.8, 32.5, 29.8, 29.7; HRMS (ES) *m/z* $(M+Na)^+$ calcd 355.1880, obsd 355.1876; $[\alpha]_D^{22}$ -43.7 (*c* 0.375, $CHCl_3$).

(+)-(1R,6R,7R,Z)-7-(4-methoxybenzyloxy)-1-(4,4-dimethylcyclopent-1-enyl)-6-hydroxy-5-(hydroxymethylene)-3-oxa-bicyclo[4.2.0]octan-4-one (12). A solution of

EDCI (46.1 mg, 0.240 mmol) in dry CH_2Cl_2 (2 ml) was added dropwise to a solution of **9** (72.6 mg, 0.218 mmol) and ethylsulfanylcarbonyl acetic acid (35.6 mg, 0.240 mmol) in 8 ml of the same solvent at -40 °C. The reaction mixture was stirred in the cold for 2 h, allowed to warm to rt, diluted with hexanes/ethyl acetate (2:1), filtered through a short pad of silica gel, and concentrated. Chromatography of the residue on silica gel (elution with hexanes/ethyl acetate 6:1) gave 70.4 mg of colorless oil.

The above material was dissolved in distilled DMSO, treated with IBX (213 mg, 0.761 mmol) in one portion, and stirred at rt for 3 h before being diluted with ether and water. The separated organic phase was washed with brine (2x), dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with hexanes/ethyl acetate 7:1) to afford a colorless oil (44 mg) shown by NMR to be a mixture of **10** and **11** (ca 5:4, 44% over 2 steps).

Triethylsilane (25.5 μL, 0.160 mmol) was added dropwise to a suspension of the above mixture (24.5 mg, 53.2 mmol) and 10% palladium on carbon (17 mg, 0.016 mmol) in 2 ml of CH_2Cl_2 at rt under argon. After being stirred for 1 h, the mixture was diluted with hexanes/ethyl acetate (2/1), filtered through a short pad of silica gel, and concentrated. Flash chromatographic purification (SiO_2, hexanes/ethyl acetate 1:1) afforded **12** (15.8 mg, 74%) as a colorless oil; IR (film, cm^{-1}) 3492, 1661, 1612; ^1H NMR (500 MHz, $CDCl_3$) δ 12.27 (d, J = 13.0 Hz, 1 H), 7.54 (d, J = 12.9 Hz, 1 H), 7.24 (d, J = 8.6 Hz, 2 H), 6.91 (d, J = 8.6 H, 2 H), 5.54 (t, J = 1.8 Hz, 1 H), 4.53 (d, J = 11.3 Hz, 1 H), 4.46 (d, J = 11.3 Hz, 1 H), 4.18 (d, J = 11.8 Hz, 1 H), 4.01 (d, J = 11.8 Hz), 3.91 (t, J = 5.8 Hz, 1 H), 3.84 (s, 3 H), 3.42 (s, 1 H), 2.24-2.14 (m, 6 H), 1.09 (s, 3 H), 1.08 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 166.7, 159.7, 139.8, 129.7, 129.6, 129.2, 127.8,

114.2, 114.1, 104.5, 78.8, 74.3, 72.5, 71.8, 55.3, 48.5, 47.3, 45.4, 38.8, 30.6, 24.7, 29.6; HRMS (ES) *m/z* $(M+Na)^+$ calcd 423.1778, obsd 423.1779; $[\alpha]_D^{22}$ +13.4 (*c* 0.79, $CHCl_3$).

(+)-(1R,5S,6S,7R)-7-(4-methoxybenzyloxy)-1-(4,4-dimethylcyclopent-1-enyl)-6-hydroxy-5-(hydroxymethyl)-3-oxa-bicyclo[4.2.0]octan-4-one (13) and (-)-(1R,5R,6S,7R)-7-(4-methoxybenzyloxy)-1-(4,4-dimethylcyclopent-1-enyl)-6-hydroxy-5-(hydroxymethyl)-3-oxa-bicyclo[4.2.0]octan-4-one (14). Sodium borohydride (11.3 mg, 0.300 mmol) and potassium dihydrogen phosphate (0.204 g, 1.498 mmol) were added simultaneously to a solution of **12** (0.120 g, 0.300 mmol) in methanol (15 ml) at 0 °C. The mixture was stirred at 0 °C for 40 min. Glacial acetic acid was then introduced through a pipet to bring the pH of the solution to around neutral as indicated by pH paper. Small portions of $NaBH_4$ were added at 0 °C, followed by the addition of glacial acetic acid to keep the pH neutral. This process of adding glacier acetic acid followed by $NaBH_4$ was repeated every 5 min until the starting material disappeared almost completely. The reaction mixture was quenched with saturated NH_4Cl solution, the methanol was evaporated, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried, and concentrated. The residue was purified by flash chromatography (silica gel, elution with hexane/ethyl acetate 4:1 to 3:2) to afford **13** (less polar) as a colorless oil (51.3 mg. 43%) and **14** (more polar) as a sticky oil (26.0 mg, 22%). For **13**: IR (film, cm^{-1}) 3472, 1737, 1414; ^1H NMR (500 MHz, $CDC1_3$) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.91, (d, *J* = 8.6 Hz, 2 H), 5.59 (t, *J* = 1.8 Hz, 1 H) 4.50 (d, *J* = 11.3 Hz 1 H), 4.44 (d, *J* = 11.3 Hz, 1 H), 4.38 (d, *J* = 11.9 Hz, 1 H). 4.07 (dd, *J* = 5.6, 11.8 Hz,1 H), 4.00 (dd, *J* = 4.9, 11.8 Hz, 1 H), 3.97 (d, *J* = 11.9 Hz,1 H), 3.92 (dd, *J* = 4.6, 7.5 Hz, 1 H), 3.83 (s, 3H), 3.52 (s, 1 H), 2.97 (t, *J* = 5.3 Hz, 1 H), 2.35-2.13 (m, 6 H), 1.114 (s, 3

H), 1.107 (s, 3H); ^{13}C NMR (125 MHz, $CDC1_3$) δ 173.7, 159.7, 139.1, 129.6 (2 C), 129.2, 128.7, 114.1 (2 C), 73.3, 71.8, 70.4, 58.3, 55.4, 49.0, 48.7, 47.5, 47.3, 39.1, 32.1, 29.81, 29.78, 29.73; HRMS (ES) *m/z* $(M+Na)^+$ calcd 425.1940, obsd 425.1937; $[\alpha]_D^{22}$ + 2.51 (*c* 0.66, $CHC1_3$).

For **14**: IR (film, cm $^{-1}$) 3496, 1742, 1611; ^{1}H NMR (500 MHz, $CDC1_3$) δ 7.25 (d, *J* = 8.5 Hz, 2 H), 6.91 (d, *J* = 8.5 Hz, 2 H), 5.64 (s, 1 H), 4.54 (d, *J* = 11.4 Hz, 1 H), 4.47 (d, *J* = 11.4 Hz, 1 H), 4.39 (d, *J* = 11.8 Hz, 1 H), 4.20-4.15 (m, 1 H), 4.13 (d, *J* = 11.8 Hz, 1 H), 4.02 (dd, *J* = 3.6, 7.2 Hz, 1 H), 3.88-3.82 (m, 1 H), 3.84 (s, 3 H), 3.20 (s, 1 H), 2.88 (dd, *J* = 5.2, 7.5 Hz, 1 H), 2.54 (dd, *J* = 5.0, 8.6 Hz, 1 H), 2.31-2.12 (m, 6 H), 1.10 (s, 3 H), 1.09 (s, 3 H); ^{13}C NMR (125 MHz, $CDC1_3$) δ 172.8, 159.6, 140.6, 129.4, 129.1, 128.1, 114.0, 76.2, 74.2, 71.7, 58.5, 55.3, 50.0, 48.9, 47.3, 46.7, 38.8, 32.2, 29.8, 29.7; HRMS (ES) *m/z* $(M +Na)^+$ calcd 425.1935, obsd 425.1929; $[\alpha]_D^{22}$ -2.1 (*c* 0.19, $CHC1_3$).

(+)-(1S,5S,6S,7R)-7-(4-methoxybenzyloxy)-5-((tert-butyldimethylsilyloxy) methyl)-1-((1R,2R)-1,2-dihydroxy-4,4-dimethylcyclopentyl)-6-hydroxy-3-oxa-bicyclo[4.2.0]octan-4-one (15). *tert*-Butydimethylsilyl triflate (0.583 ml. 2.53 mmol) was added dropwise in a solution of **13** (0.204 g. 0.507 mmol) and 2,6-lutidine (1.77 ml, 15.21 mmol) in 17 ml of dry CH_2Cl_2 at -78 ^{o}C under argon. The mixture was stirred at -78 ^{o}C for 5 min, saturated $NaHCO_3$ solution (10 ml) was added at -78 ^{o}C to quench the reaction, and the mixture was diluted with ether and allowed to warm to rt. The organic layer was washed with brine, dried, and concentrated. The residue was dried under vacuum to remove most of the 2,6-lutidine before being purified by flash chromatography (silica gel, elution with hexanes/ethyl acetate 9:1) to afford the monosilyl ether as a sticky oil that solidified in the refrigerator (0.233 g. 89%): IR (film,

cm $^{-1}$) 1757, 1514, 1250; ^{1}H NMR (500 MHz, $CDC1_3$) δ 7.23 (d. *J* = 8.5 Hz, 2 H), 6.87 (d. *J* = 8.5 Hz, 2 H), 5.53 (s, 1 H), 4.47 (d, *J* = 11.3 Hz, 1 H), 4.39 (d, *J* = 11.3 Hz, 1 H), 4.35 (d,. *J* = 11.9 Hz, 1 H), 4.15 (dd, *J* = 5.3, 10.3 Hz 1 H), 4.01 (dd, *J* = 5.3, 10.3 Hz, 1 H), 3.914 (s, 1 H), 3.912 (d, *J* = 11.8 Hz, 1 H), 3.85 (dd, *J* = 5.2, 7.0 Hz, 1 H), 3.81 (s, 3 H), 2.84 (t, *J* = 5.3 Hz, 1 H), 2.29-2.16 (m, 6 H), 1.09 (s, 3 H), 1.07 (s, 3 H), 0.90 (s, 9 H), 0.12 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (125 MHz, $CDC1_3$) δ 171.8, 159.5, 139.8, 129.8, 129.5 (2 C), 127.8, 114.0 (2 C), 77.6, 73.6, 71.2, 70.0, 59.2, 55.4, 49.3, 48.9, 47.3, 47.1, 39.0, 32.1, 29.8, 29.7, 26.0 (3 C), 18.4, -5.3, -5.4; HRMS (ES) *m/z* $(M+Na)^+$ calcd 539.2805, obsd 539.2820; $[\alpha]_D^{22}$ + 15.8 (*c* 0.76, $CHC1_3$).

Osmium tetraoxide (13.1 mg, 0.0516 mmol) was added in one portion to a solution of the above compound in a mixture of THF and pyridine (4:1, 1.5 ml) at 0 ^{o}C. The reaction mixture was stirred at rt for 35 min before a large excess of H_2S gas was introduced at 0 ^{o}C. After further admixture with ethyl acetate, saturated $NaHSO_3$ solution, and a small amount of water, the organic layer was washed with brine, dried, and filtered through a short pad of Celite. The filtrate was concentrated. The residue was purified by flash chromatography (silica gel, elution with hexanes/EtOAc 4:1 with 1% ethanol) to afford **15** as a colorless sticky oil; (20.6 mg. 76%); IR (film, cm^{-1}) 3431, 1743, 1514, 1250; ^{1}H NMR (500 MHz, $CDC1_3$) δ 7.24 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 5.18 (s, 1 H), 4.58 (d, *J* = 11.3 Hz, 1 H), 4.54 (d, *J* = 12.2 Hz, 1 H), 4.44 (d, *J* = 11.3 Hz, 1 H), 4.36 (d, *J* = 12.2 Hz, 1 H), 4.25-4.22 (m, 2 H), 4.07 (dd, *J* = 9.3, 10.9 Hz, 1 H), 3.81-3.78 (m, 4 H), 3.23 (s, 1 H), 2.95 (dd, *J* = 4.3, 9.2 Hz, 1 H), 2.81 (d, *J* = 8.4 Hz, 1 H), 2.25 (d, *J* = 15.0 Hz, 1 H), 2.07-2.06 (m, 2 H), 1.82 (d, *J* = 15.0 Hz, 1 H), 1.78 (dd, *J* = 7.0, 12.1 Hz, 1 H), 1.70 (d, *J* = 10.9 Hz, 1 H), 1.13 (s, 3 H), 1.00 (s, 3 H), 0.90 (s,

9 H), 0.14 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (125 MHz, $CDC1_3$) δ 170.9, 159.6, 129.6, 129.4 (2 C), 114.0 (2 C), 82.0, 78.8, 75.1, 73.3, 71.3, 69.4, 60.4, 55.4, 51.5, 50.7, 48.3, 46.9, 33.1, 32.1, 31.0, 28.9, 25.9 (3 C), 18.2, -5.4, -5.6; HRMS (ES) *m/z* $(M+Na)^+$ calcd 573.2860, obsd 573.2879; $[\alpha]_D^{22}$ +56.0 (*c* 1.02, $CHC1_3$).

(+)-(1R,5S,6S,7R)-7-(4-methoxybenzyloxy)-5-((tert-butyldimethylsilyloxy) methyl)-6-hydroxy-1-((R)-1-hydroxy-4,4-dimethyl-2-oxocyclopentyl)-3-oxa-bicyclo[4.2.0]octan-4-one (16). Dimethyl sulfoxide (65.4 μl, 0.921 mmol) was added dropwise to a solution of oxalyl chloride (31.6 μl, 0.368 mmol) in 2 ml of dry CH_2Cl_2 at -78 ^oC under argon. After 30 min at -78 ^oC, a solution of **15** (50.7 mg, 0.0921 mmol) in 1.3 ml of CH_2Cl_2 was added dropwise at -78 ^oC. After one hour in the cold, triethylamine (0.129 ml, 0.921 mmol) was introduced dropwise at -78^o C. After 10 min, the reaction mixture was allowed to warm to rt and diluted with ethyl acetate and a small amount of water. The mixture was washed with brine (2x), dried, and concentrated. The residue was purified by flash chromatography (silica gel, elution with hexane/ethyl acetate 4:1 containing 1% ethanol) to afford **16** (39.6 mg, 79%) as a white foam; IR (film, cm^{-1}) 3299, 1753, 1515, 1464; ^{1}H NMR (500 MHz, $CDC1_3$) δ 7.25 (d, *J* = 8.4 Hz, 2 H) 6.88 (d, *J* = 8.4 Hz, 2 H), 5.78 (s, 1 H), 4.63 (d, *J* = 10.5 Hz, 1 H), 4.39 (d, *J* = 11.8 Hz, 1 H), 4.27 (d, *J* = 10.5 Hz, 1H) 4.22 (d, *J* = 11.8 Hz, 1 H), 4.15 (dd, *J* = 5.5, 10.6 Hz, 1 H), 4.01 (dd, *J* = 4.7, 10.7 Hz, 1 H), 3.92 (dd, *J* = 5.3, 8.9 Hz, 1 H), 3.81 (s, 3 H), 3.22 (s, 1 H), 2.76 (t, *J* = 5.0 Hz, 1 H), 2.39 (dd, *J* = 5.3, 14.8 Hz, 1 H), 2.25 (dd, *J* = 9.0, 14.8 Hz, 1 H), 1.93 (d, *J* = 14.7 Hz 1 H), 1.85 (d, *J* = 13.8 Hz, 1 H), 1.77 (d, *J* = 13.8 Hz, 1 H), 1.20 (s, 3 H), 1.11 (s, 3 H), 0.91 (s, 9 H), 0.12 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (125 MHz, CDC_3) δ 170.5, 159.9, 130.0 (2 C), 128.2, 119.1, 114.2 (2 C), 86.8, 86.3, 71.8, 71.7, 68.9, 58.4,

55.4, 50.5, 49.6, 48.7, 36.8, 32.6, 31.8, 29.3, 26.0 (3C) 18.5, -5.2, -5.3; HRMS (ES) *m/z* $(M + Na)^+$ calcd 571.2703, obsd 571.2697; $[\alpha]_D^{22}$ +72.7 (*c* 0.88, $CHCl_3$).

(1R,5S,6S,7R)-7-(4-methoxybenzyloxy)-5-((tert-butyldimethylsilyloxy) methyl)-1-(4,4-dimethyl-2-oxocyclopentyl)-6-hydroxy-3-oxa-bicyclo[4.2.0]octan-4-one (17). Samarium diiodide (0.1 M in THF, 0.766 ml, 0.0766 mmol) was rapidly added dropwise to a solution of **16** (13.6 mg, 0.0255 mmol) in a mixture of THF and *tert*-butanol (4:1, 0.5 ml) at rt under argon. The solution was stirred for 15 min before being exposed to air to quench the reaction. The mixture was diluted with ethyl acetate and poured into saturated $NaHCO_3$ solution. The separated organic layer was washed with brine, dried, and concentrated. The residue was purified by flash chromatography (silica gel, elution with hexane/ethyl acetate 6:1) to deliver **17** as a colorless viscous oil (8.4 mg, 64%) constituted of a pair of diastereomers; IR (film, cm^{-1}) 3438, 1754, 1514; ^1H NMR (500 MHz, $CDC1_3$) δ 7.25 (d, *J* = 8.3 Hz, 4 H), 6.86 (d, *J* = 8.3 Hz, 4 H), 5.68 (s, 1 H), 5.03 (d, *J* = 11.4 Hz, 1 H), 4.85 (s, 1 H), 4.64 (d, *J* = 10.7 Hz, 1 H), 4.52 (d, *J* = 11.0 Hz, 1 H), 4.50 (d, *J* = 10.6 Hz, 1H), 4.37-4.32 (m, 4 H), 4.26 (dd, *J* = 11.2, 19.4 Hz, 1 H), 4.21-4.11 (m, 6 H), 4.11-3.99 (m, 5 H), 3.89-3.86 (m, 2 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.75 (d, *J* = 5.7 Hz, 1 H), 3.74 (d, *J* = 5.8 Hz, 1 H), 3.12 (dd, *J* = 8.7, 12.8 Hz, 1 H), 3.07 (t, *J* = 5.5 Hz, 1 H), 2.99 (dd, *J* = 4.5, 8.1 Hz, 1 H), 2.75 (dd, *J* = 4.1, 6.2 Hz, 1 H), 2.66 (dd, *J* = 7.1, 12.5 Hz, 1 H), 2.54 (dd, *J* = 8.9, 14.2 Hz, 1 H), 2.39-2.33 (m, 3 H), 2.25-2.15 (m, 6 H), 2,15-2.02 (m, 6 H), 1.97-1.91 (m, 4 H), 1.19 (s, 3 H), 1.09 (s, 3 H), 1.08 (s, 3 H), 1.03 (s, 3 H), 0.91 (s, 9 H), 0.87 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H), 1.10 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (125 MHz, $CDC1_3$) δ 171.9, 171.6, 170.9, 159.5, 130.0, 129.8, 129.7, 129.5, 124.5, 114.2, 114.0, 113.9, 78.7, 73.4, 72.6, 71.2, 71.0, 70.2, 68.4, 60.1,

59.5, 55.4, 54.2, 49.9, 49.7, 49.3, 45.7, 44.2, 39.1, 34.1, 34.0, 33.2, 30.1, 29.9, 27.7, 27.6, 26.1, 26.0, 25.9, 18.6, 18.4, 18.2, -5.2, -5.3, -5.4, -5.5; HRMS (ES) *m/z* $(M+Na)^+$ calcd 555.2754, obsd 555.2767.

(+)-(1R,5S,6S,7R)-5-((tert-butyldimethylsilyloxy)methyl)-1-((R)-4,4-dimethyl-2-oxocyclopentyl)-6,7-dihydroxy-3-oxa-bicyclo[4.2.0]octan-4-one (18). Trifluoroacetic acid (0.5 ml) was added rapidly dropwise to a solution of **17** (53.0 mg, 0.100 mmol) in 5 ml of dry CH_2Cl_2 at rt under argon. After 8 min, saturated $NaHCO_3$ solution was quickly introduced to quench the reaction. The mixture was diluted with CH_2Cl_2, the aqueous layer was back-extracted with ethyl acetate, and the combined organic phases were washed with brine, dried, and concentrated. The residue was purified by flash chromatography (silica gel, elution with hexanes/ethyl acetate 6:1 with 0.5% ethanol) to afford **18** (20.7 mg, 50%) as a white solid and its C-9 epimer (3.4 mg, 8%) as a thick oil.

For the C-9 epimer: IR (film, cm^{-1}) 3415, 1736, 1463; ^1H NMR (500 MHz, $CDCl_3$) δ 5.29 (s, 1 H), 5.02 (d, *J* = 11.5 Hz, 1 H), 4.18 (dd, *J* = 3.9, 10.8 Hz, 1 H), 4.04 (dd, *J* = 8.7, 10.8 Hz, 1 H), 3.92-3.88 (m, 2 H), 3.13 (dd, *J* = 3.9, 8.7 Hz, 1 H), 2.91 (d, *J* = 7.6 Hz, 1 H), 2.35-2.30 (m, 3 H), 2.13-2.05 (m, 2 H), 1.99 (dd, *J* = 5.5, 13.8 Hz, 1 H), 1.94-1.90 (m, 1 H), 1.24 (s, 3 H), 1.04 (s, 3 H), 0.88 (s, 9 H), 0.12 (s, 3 H), 0.20 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.1, 171.2, 78.5, 70.7, 66.6, 60.5, 53.4, 49.0, 47.2, 44.4, 42.3, 36.9, 34.1, 30.0, 27.6, 25.8 (3 C), 18.1, -5.58, -5.63; HRMS (ES) *m/z* $(M+Na)^+$ calcd 435.2179, obsd 435.2175; $[\alpha]_D^{22}$ +6.1 (*c* 0.37, $CHCl_3$).

For **18**: IR (film, cm^{-1}) 3415, 1753, 1463; ^1H NMR (500 MHz, $CDCl_3$) δ 4.72 (s, 1 H), 4.22-4.17 (m, 2 H), 4.09 (dd, *J* = 7.6, 10.7 Hz, 1 H), 4.00 (d, *J* = 11.6 Hz, 1 H), 3.91-

3.86 (m, 1 H), 3.05 (dd, *J* = 4.1, 7.4 Hz, 1 H), 3.00 (d, *J* = 9.0 Hz, 1 H), 2.73 (dd, *J* = 8.3, 12.6 Hz, 1 H), 2.40 (dd, *J* = 5.5, 13.6 Hz, 1 H), 2.33 (dd, *J* = 8.1, 13.6 Hz, 1 H), 2.21 (s, 2 H), 1.87 (dd, *J* = 8.3, 12.0 Hz, 1 H), 1.65 (t, *J* = 12.5 Hz, 1 H), 1.20 (s, 3 H), 1.07 (s, 3 H), 0.89 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.8, 171.2, 76.7, 69.4, 66.6, 60.0, 53.9, 49.3, 48.2, 44.4, 40.1, 35.6, 33.9, 30.0, 27.9, 25.9 (3 C), 18.2, -5.5, -5.6; HRMS (ES) *m/z* $(M+Na)^+$ calcd 435.2179, obsd 435.2177; $[\alpha]_D^{22}$ +120.9 (*c* 0.34, $CHCl_3$).

(+)-(1S,7R)-5-((tert-butyldimethylsilyloxy)methyl)-1-((S)-4,4-dimethyl-2-oxocyclopentyl)-7-hydroxy-3-oxa-bicyclo[4.2.0]oct-5-en-4-one (19) and (+)-(1S,7R)-5-((tert-butyldimethylsilyloxy)methyl)-1-((R)-4,4-dimethyl-2-oxocyclopentyl)-7-hydroxy-3-oxa-bicyclo[4.2.0]oct-5-en-4-one (20). Thionyl chloride (1.08 μl, 0.015 mmol) was added slowly to a solution of **18** (5.1 mg, 0.012 mmol) and triethylamine (5.17 μl, 0.037 mmol) in 0.6 ml of dry CH_2Cl_2 at 0 °C under argon. After 20 min at this temperature, the solution was poured into a mixture of ethyl acetate, water and a small amount of triethylamine. The organic layer was washed with brine, dried, and concentrated. The solid residue was immediately taken up in 1.0 ml of dry CH_2Cl_2 and cooled to 0 °C. DBU (5.6 μl, 0.037 mmol) was added at 0 °C under argon. After 30 min at 0 °C, the mixture was loaded directly onto a silica gel column, eluted with hexanes/ethyl acetate (3:1, with 1% ethanol) to afford **19** (1.7 mg, 35%) and **20** (1.5 mg, 31%), both as white solids.

For **19**: IR (film, cm^{-1}) 3456, 1725, 1463; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.09 (dt, *J* = 2.4, 6.7 Hz, 1 H), 4.57 (d, *J* = 14.6 Hz, 1 H), 4.39 (d, *J* = 14.6 MHz, 1 H), 4.24 (d, *J* = 10.8 Hz, 1 H), 4.25 (d, *J* = 10.8 Hz, 1 H), 3.38 (d, *J* = 7.3 Hz, 1 H), 3.33 (dd, *J* = 8.3, 13.1

Hz, 1 H), 2.35 (dd, *J* = 6.6, 13.4 Hz, 1 H), 2.31 (d, *J* = 20.1 Hz, 1 H), 2.15 (dd, *J* = 2.7, 13.4 Hz, 1 H), 2.08 (d, *J* = 19.0 Hz, 1 H), 2.06-2.02 (m, 1 H), 1.71 (t, *J* = 12.8 Hz, 1 H), 1.22 (s, 3 H), 1.12 (s, 3 H), 0.92 (s, 9 H), 0.13 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 221.1, 163.5, 125.2, 76.0, 70.6, 59.8, 54.4, 53.3, 44.8, 40.1, 38.5, 33.4, 30.1, 27.9, 26.1 (3 C), 18.5, -5.3, -5.4; HRMS (ES) *m/z* $(M+Na)^+$ calcd 417.2073, obsd 417.2089; $[\alpha]_D^{22}$ +22.4 (*c* 0.36, $CHCl_3$).

For **20**: IR (film, cm^{-1}) 3410, 1728, 1694; 1H NMR (500 MHz, $CDCl_3$) δ 5.13 (d, *J* = 6.3 Hz, 1 H), 4.83 (d, *J* = 10.5 Hz, 1 H), 4.65 (dd, *J* = 1.0, 15.8 Hz, 1 H), 4.37 (d, *J* = 15.8 Hz, 1 H), 4.17 (d, *J* = 10.5 Hz, 1 H), 3.12 (dd, *J* = 8.5, 12.6 Hz, 1 H), 2.34 (dd, *J* = 6.7, 13.5 Hz, 1 H), 2.29 (d, *J* = 2.2 Hz, 1 H), 2.22-2.15 (m, 2 H), 2.07 (d, *J* = 18.3 Hz, 1 H), 2.02 (dd, *J* = 2.6, 13.4 Hz, 1 H), 1.92 (ddd, *J* = 2.4, 8.4, 12.8 Hz, 1 H), 1.25 (s, 3 H), 1.08 (s, 3 H), 0.93 (s, 9 H), 0.13 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 218.6, 163.7, 156.9, 125.7, 76.3, 69.9, 61.1, 54.2, 49.1, 44.3, 40.1, 35.8, 33.7, 30.0, 27.8, 26.1 (3 C), 18.5, -5.3, -5.4; HRMS (ES) *m/z* $(M+Na)^+$ calcd 417.2073, obsd 417.2087; $[\alpha]_D^{22}$ +100.8 (*c* 0.19, $CHCl_3$).

Equilibration of 19 and 20. A solution of compound **20** (2.6 mg, 6.6 μmol) in dichloromethane (0.6 ml) was treated with DBU (3.0 μl, 19.8 μmol) at rt. After 45 min at rt, the mixture was loaded directly onto a silica gel column and eluted with hexanes/ethyl acetate (3.5:1, with 1% ethanol) to afford **19** (1.4 mg, 54%) and **20** (1.2 mg, 46%).

(S)-5-((tert-butyldimethylsilyloxy)methyl)-1-((R)-4,4-dimethyl-2-oxocyclopentyl)-3-oxa-bicyclo[4.2.0]octa-5,7-dien-4-one (21). Triflic anhydride (6.4 μl, 0.038 mmol) was added slowly to a solution of **19** (1.5 mg, 3.80 μmol) and pyridine (6.1 μl, 0.076 mmol) in dry dichloromethane (0.8 ml) at 0 °C under argon. After 15 min at 0

^{o}C, isopropyl alcohol (2.9 µl, 0.038 mmol) was added. After 20 min at 0 °C, DBU (5.7 µl, 0.028 mmol) was added dropwise at 0 ^{o}C. After another 5 min, the reaction mixture was loaded onto a silica gel column, eluted with hexanes/ethyl acetate/dichloromethane (5:1:1) to afford a slightly yellow solid, which was used directly for the next step.

The above triflate was taken up in 0.2 ml of benzene. DBU (1.7 µl in 30 µl of benzene, 11.4 µmol) was added at rt. After 2 h at rt, the mixture was loaded onto a silica gel column, eluted with hexanes/ethyl acetate/dichloromethane (6:1:1 with 0.5% triethylamine) to afford **21** (less polar, 0.5 mg, 35% over 2steps) and its C-9 epimer (more polar, 0.3 mg, 21%) both as colorless oils;

For **21**: ^{1}H NMR (500 MHz, C_6D_6) δ 6.71 (d, *J* = 2.2 Hz, 1 H), 6.16 (d, *J* = 2.3 Hz, 1 H), 5.02 (d, *J* = 10.0 Hz, 1 H), 4.86 (d, *J* = 15.3 Hz, 1 H), 4.59 (d, *J* = 15.4 Hz, 1 H), 3.97 (d, *J* = 10.1 Hz, 1 H), 3.18 (dd, *J* = 9.4, 11.4 Hz, 1 H), 1.93 (d, *J* = 17.8 Hz, 1 H), 1.68 (d, *J* = 18.1 Hz, 1H), 1.53-1.49 (m, 2H), 1.03 (s, 9H), 0.83 (s, 3H), 0.63 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H); HRMS (ES) *m/z* $(M+Na)^{+}$ calcd 399.1968, obsd 399.1986.

(+)-Fomannosin (1). Tetrabutylammonium fluoride (4.0 µl, 1.0 M in THF, 4.0 µmol) was added dropwise to a solution of **21** (0.5 mg, 1.33 µmol) in tetrahydrofuran (0.5 ml) at 0 ^{o}C under argon. After 20 min at 0 ^{o}C, the reaction mixture was filtered through a short pad of silica gel, washing with ethyl acetate/dichloromethane (2/1, with 0.5% triethylamine). The filtrate was concentrated. The residue was purified by preparative thin layer chromatography (silica gel, ethyl acetate/dichloromethane 1/1 with 0.5% triethylamine) to afford (+)-**1** (0.3 mg, 86%) as a colorless oil; IR (film, cm^{-1}) 3580, 1724, 1709, 1461, 1408; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (d, *J* = 2.4 Hz, *H*-6, 1 H), 6.69 (d, *J* = 2.4 Hz, *H*-5, 1 H), 4.90 (d, *J* = 10.2 Hz, *H*-8, 1 H), 4.42 (dd, *J* = 5.2, 13.8 Hz,

H-1, 1 H), 4.35 (dd, *J* = 6.0, 13.8 Hz, *H*-1, 1 H), 4.28 (d, *J* = 10.2 Hz, *H*-8, 1 H), 3.18 (dd, *J* = 8.9, 12.4 Hz, *H*-9, 1 H), 2.37-2.35 (m, OH, 1H), 2.22 (d, *J* = 18.5 Hz, *H*-12, 1 H), 1.95 (d, *J* = 18.5 Hz, *H*-12, 1 H), 1.73 (ddd, *J* = 2.4, 8.7, 12.6 Hz, *H*-10, 1 H), 1.57 (*H*-10, 1 H, overlap with H_2O peak), 1.16 (s, 3 H), 1.10 (s, 3 H); ^{13}C NMR* (150 MHz, CD_2Cl_2) δ 218.37 (*C*-13), 165.72 (*C*-3), 154.85 (*C*-4), 147.96 (*C*-5), 139.53 (*C*-6), 73.50 (*C*-8), 58.52 (*C*-1), 53.61 (*C*-12), 52.79 (*C*-7), 46.60 (*C*-9), 38.39 (*C*-10), 32.94 (*C*-11), 29.65 (*CH*$_3$), 27.89 (*CH*$_3$); HRMS (ES) *m/z* $(M+Na)^+$ calcd 285.1103, obsd 285.1119; $[\alpha]_D^{22}$ + 160 (*c* 0.02, $CHCl_3$).

*Due to small quantities of material, ^{13}C data was extrapolated from HSQC and HMBC data.

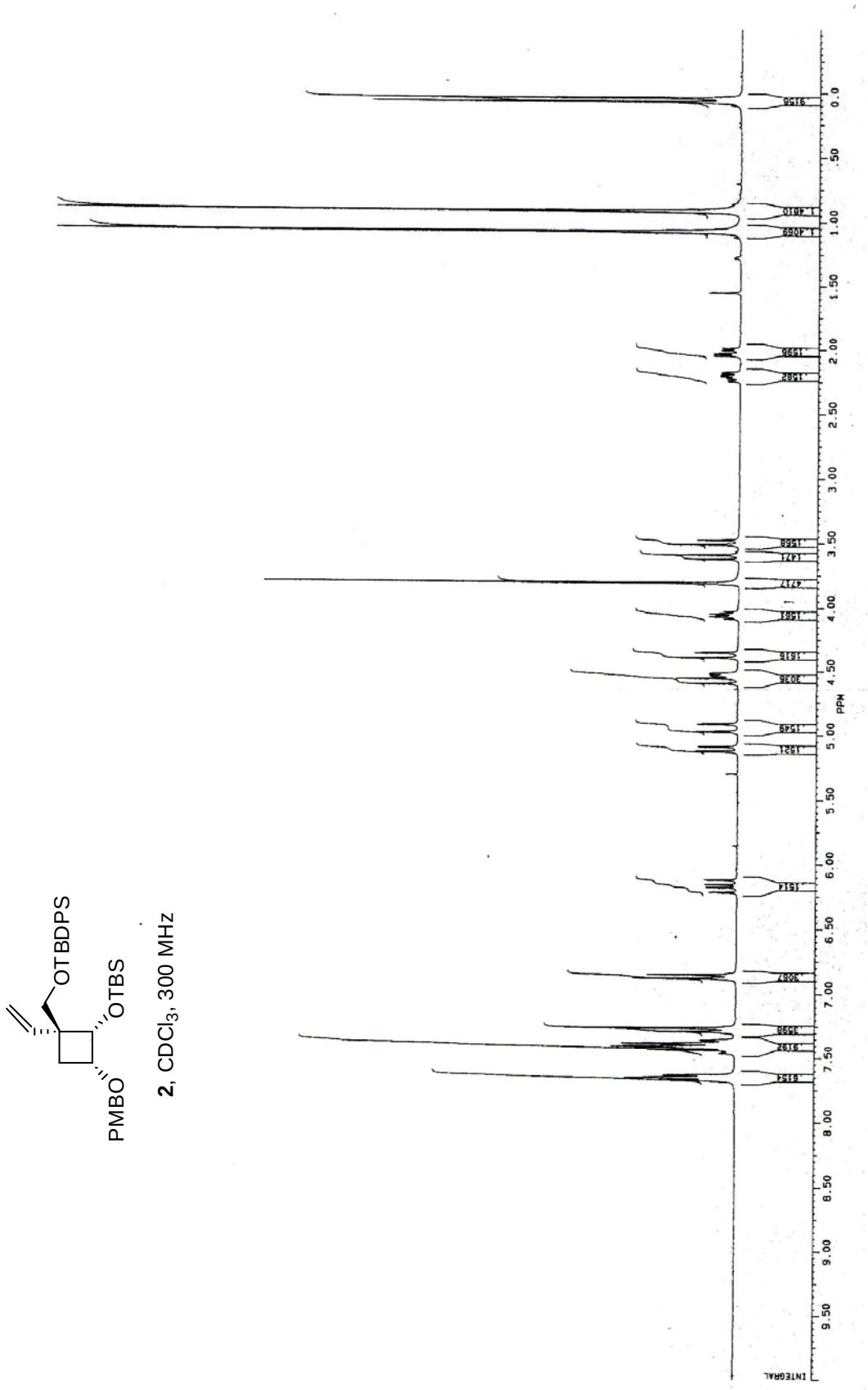
	Natural ($CDCl_3$, 270 MHz)[4]	Synthetic ($CDCl_3$, 500 MHz)	Synthetic (C_6D_6, 500 MHz)
	^{1}H NMR, δ (mult, *J*)	^{1}H NMR, δ (mult, *J*)	^{1}H NMR, δ (mult, *J*)
H-6	6.90 (d, *J* = 2.4 Hz)	6.89 (d, *J* = 2.4 Hz)	6.12 (d, *J* = 2.3 Hz)
H-5	6.70 (d, *J* = 2.4 Hz)	6.69 (d, *J* = 2.4 Hz)	5.91 (d, *J* = 2.3 Hz)
H-8a	4.91 (d, *J* = 10.1 Hz)	4.90 (d, *J* = 10.2 Hz)	4.85 (d, *J* = 10.1 Hz)
H-1a	4.43 (d, *J* = 13.7 Hz)	4.42 (dd, *J* = 5.2, 13.8 Hz)	4.28 (dd, *J* = 4.1, 14.3 Hz)
H-1b	4.35 (d, *J* = 13.7 Hz)	4.35 (dd, *J* = 6.0, 13.8 Hz)	4.30 (dd, *J* = 5.7, 14.3 Hz)
H-8b	4.29 (d, *J* = 10.1 Hz)	4.28 (d, *J* = 10.2 Hz)	3.76 (d, *J* = 10.1 Hz)
H-9	3.18 (dd, *J* = 9.0, 12.1 Hz)	3.18 (dd, *J* = 8.9, 12.4 Hz)	3.00 (dd, *J* = 8.9, 10.9 Hz)
OH	2.64 (s)	2.37-2.35 (m)	1.77-1.76 (m)
H-12a	2.23 (d, *J* = 18.3 Hz)	2.22 (d, *J* = 18.5 Hz)	1.79 (d, *J* = 18.2 Hz)
H-12b	1.95 (d, *J* = 18.3 Hz)	1.95 (d, *J* = 18.5 Hz)	1.52 (d, *J* = 18.2 Hz)
H-10a	1.74 (ddd, *J* = 2.4, 9.0, 12.8 Hz)	1.73 (ddd, *J* = 2.4, 8.7, 12.6 Hz)	1.32 (ddd, *J* = 2.3, 8.9, 12.7 Hz)
H-10b	1.57 (dd, *J* = 12.1, 12.8 Hz)	Overlap with H_2O peak	1.18 (t, *J* = 12.3 Hz)
CH_3	1.16 (s)	1.16 (s)	0.71 (s)
CH_3	1.10 (s)	1.10 (s)	0.50 (s)

Table 1. Comparison of ^{1}H NMR Data for Natural and Synthetic Fomannosin

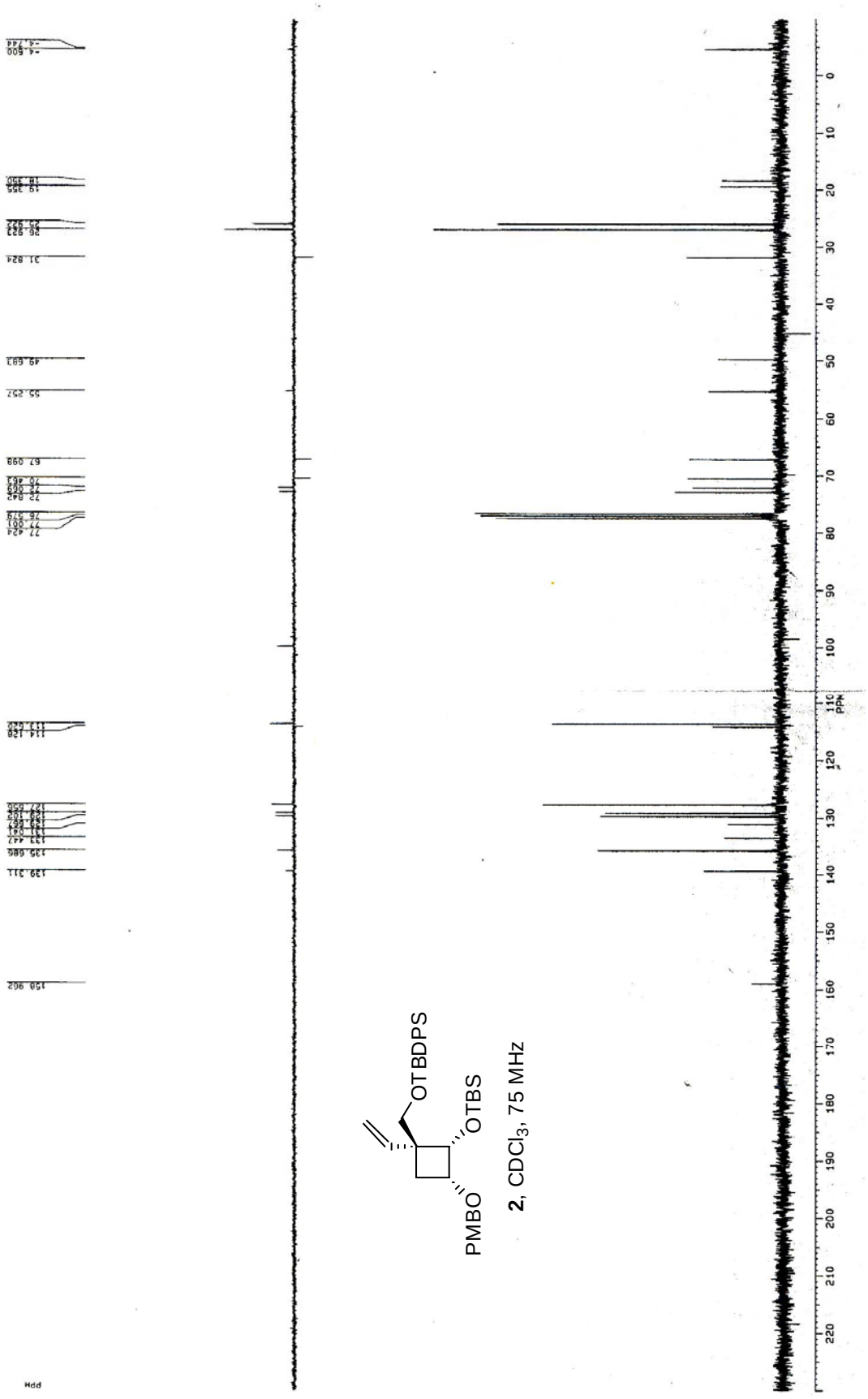
	Natural ($CDCl_3$, δ)[2, 5]	Synthetic (CD_2Cl_2, δ)*
C-13	219.10	218.37
C-3	166.15	165.72
C-4	155.05	154.85
C-5	146.76	147.96
C-6	139.93	139.53
C-2	114.09	-
C-8	73.95	73.50
C-1	58.56	58.52
C-12	53.58	53.61
C-7	52.77	52.79
C-9	46.70	46.60
C-10	38.41	38.39
C-11	33.86	32.94
CH_3	29.90	29.65
CH_3	28.34	27.89

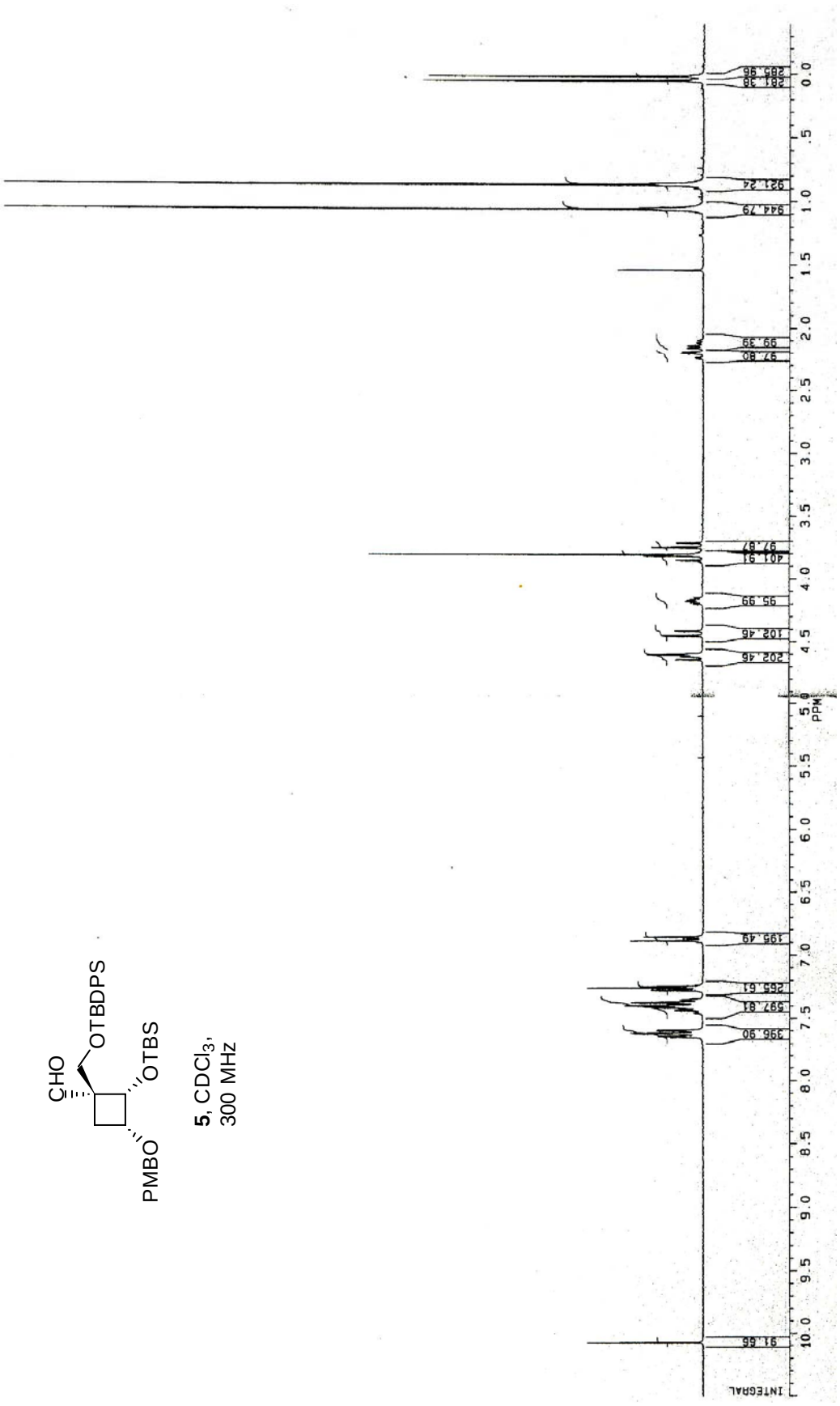
Table 2. Comparison of ^{13}C NMR Data for Synthetic and Natural Fomannosin

* Due to limited sample, the ^{13}C data were obtained through HSQC and HMBC experiments.

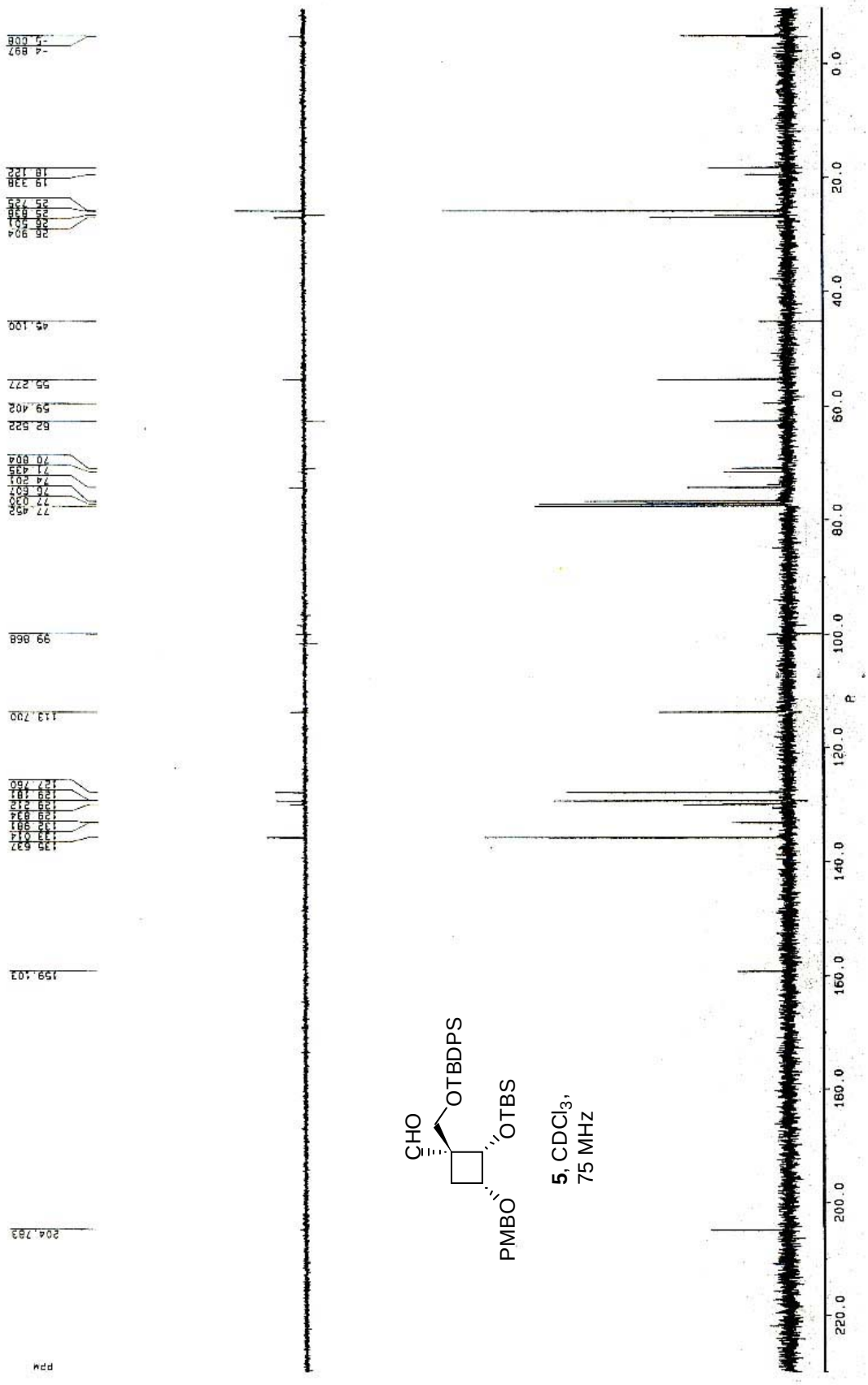


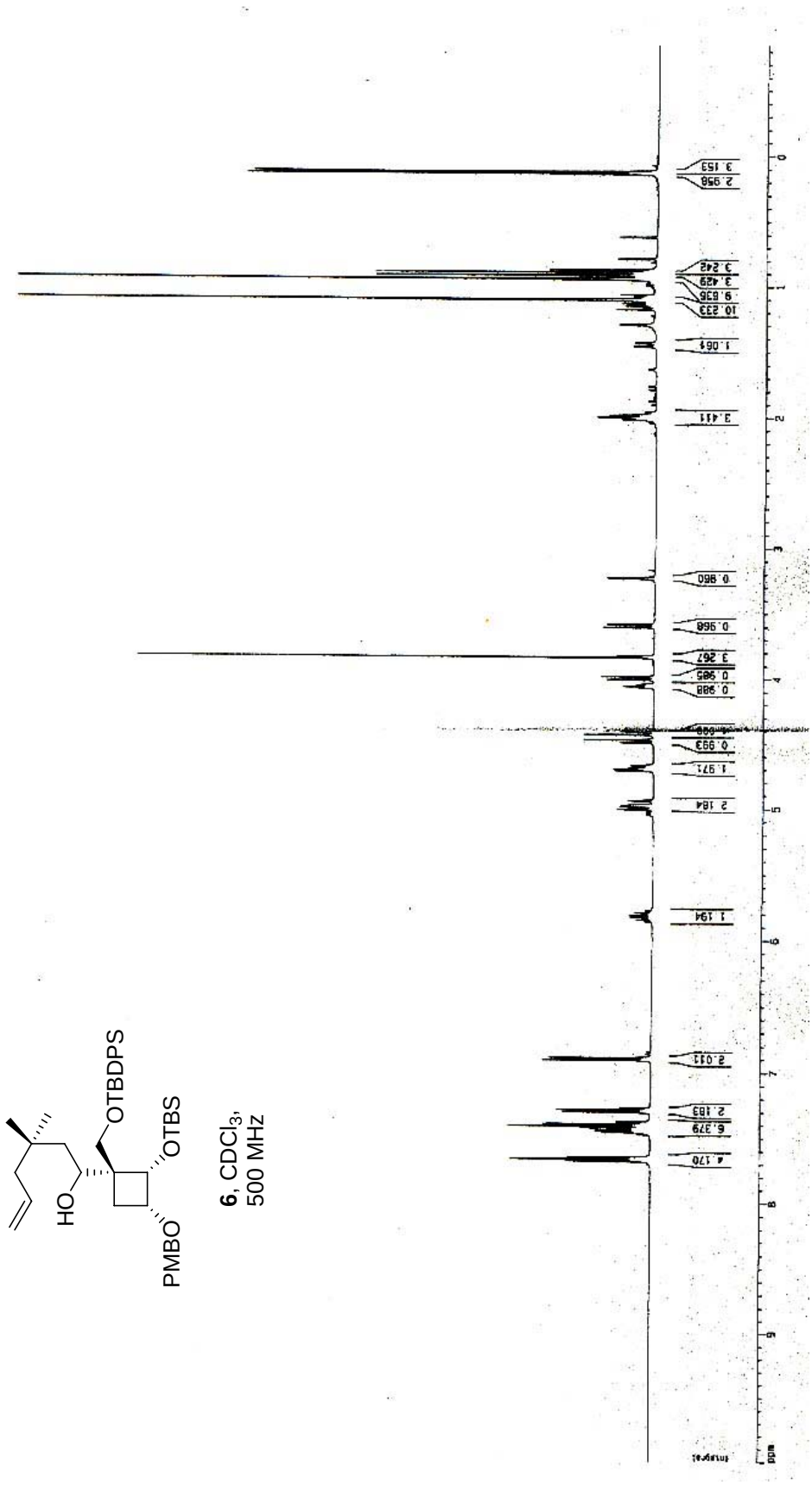
2, $CDCl_3$, 300 MHz


OTBDPS
OTBS
PMBO
2, CDCl3, 75 MHz
PPM

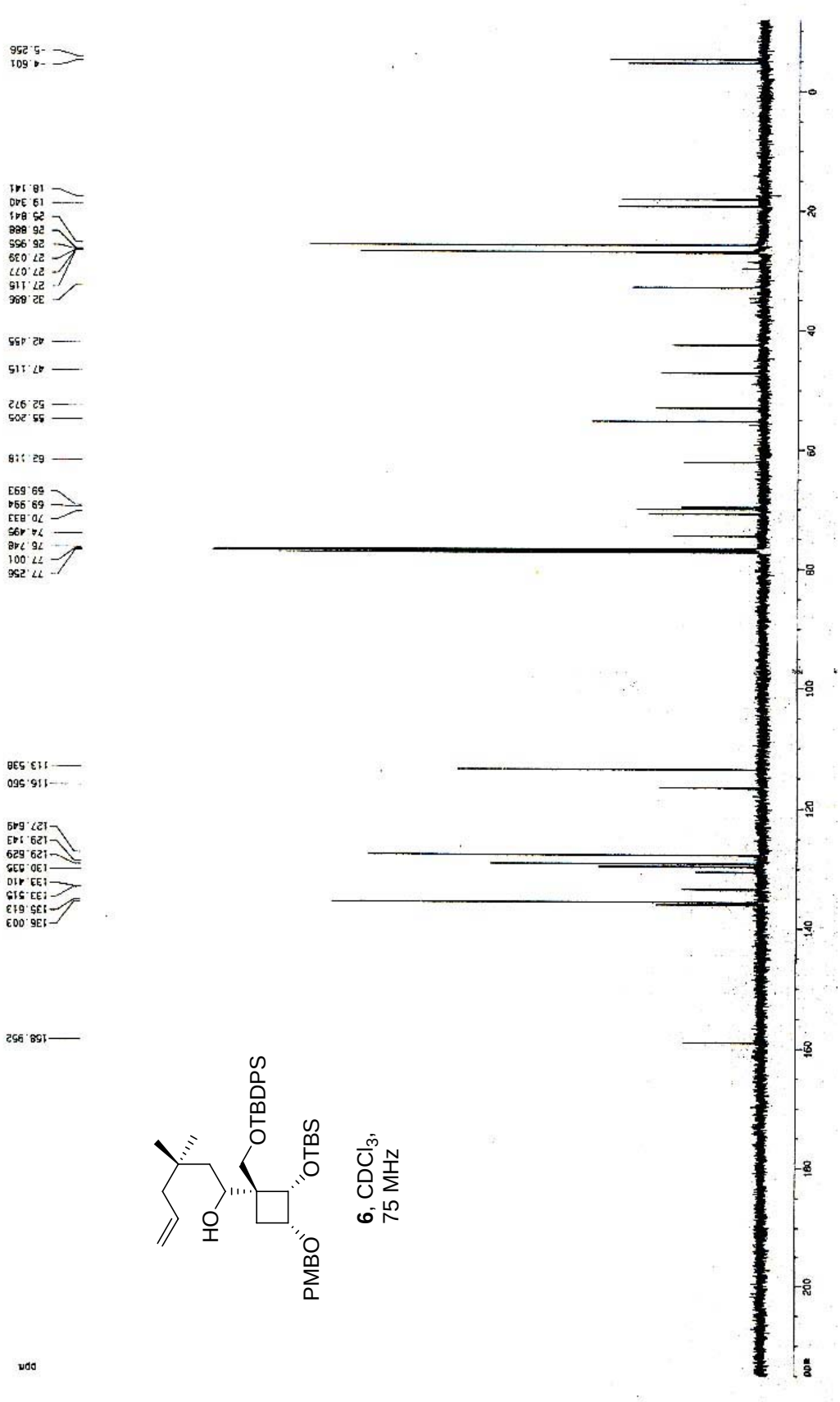


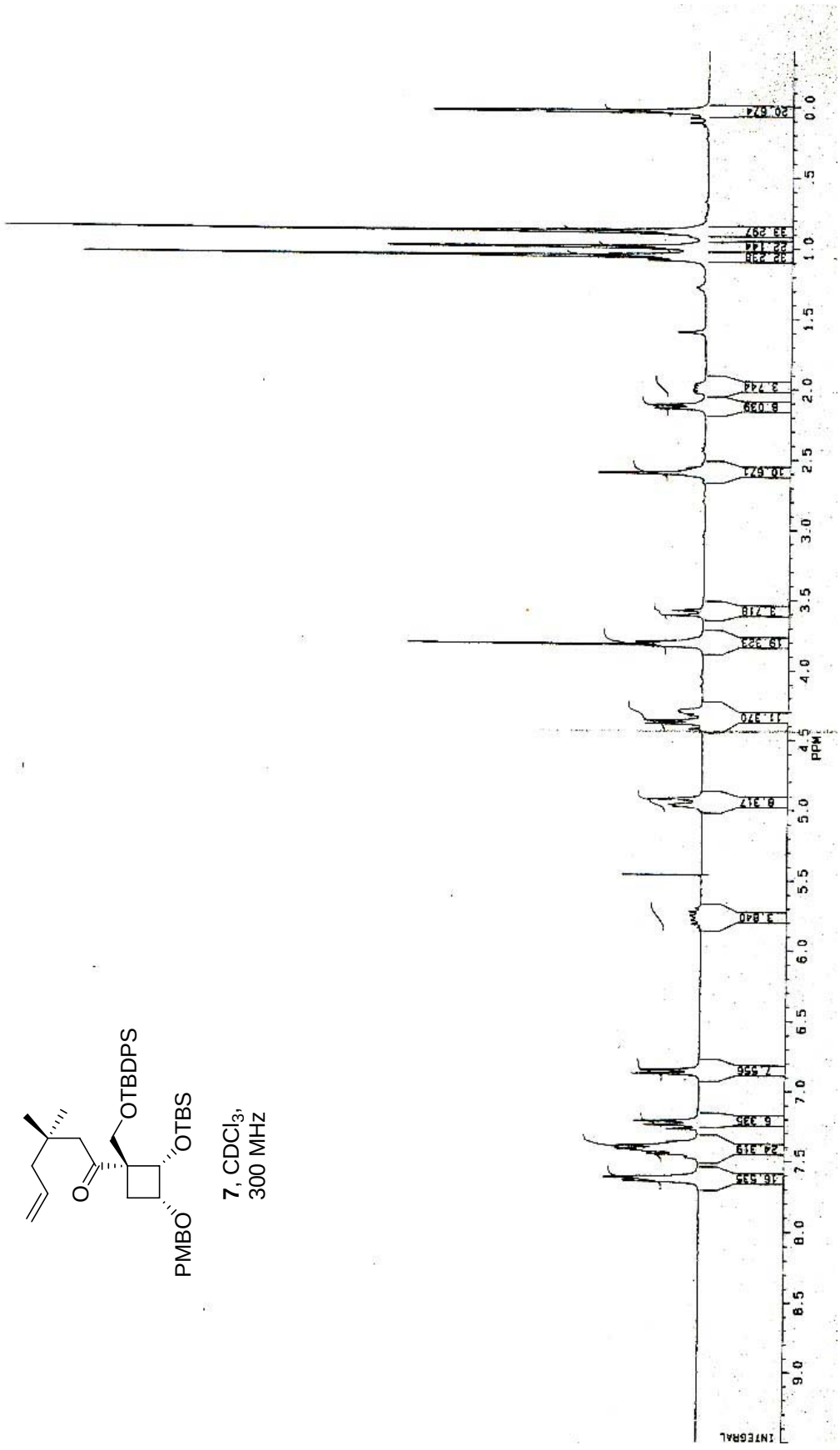
5, $CDCl_3$, 300 MHz

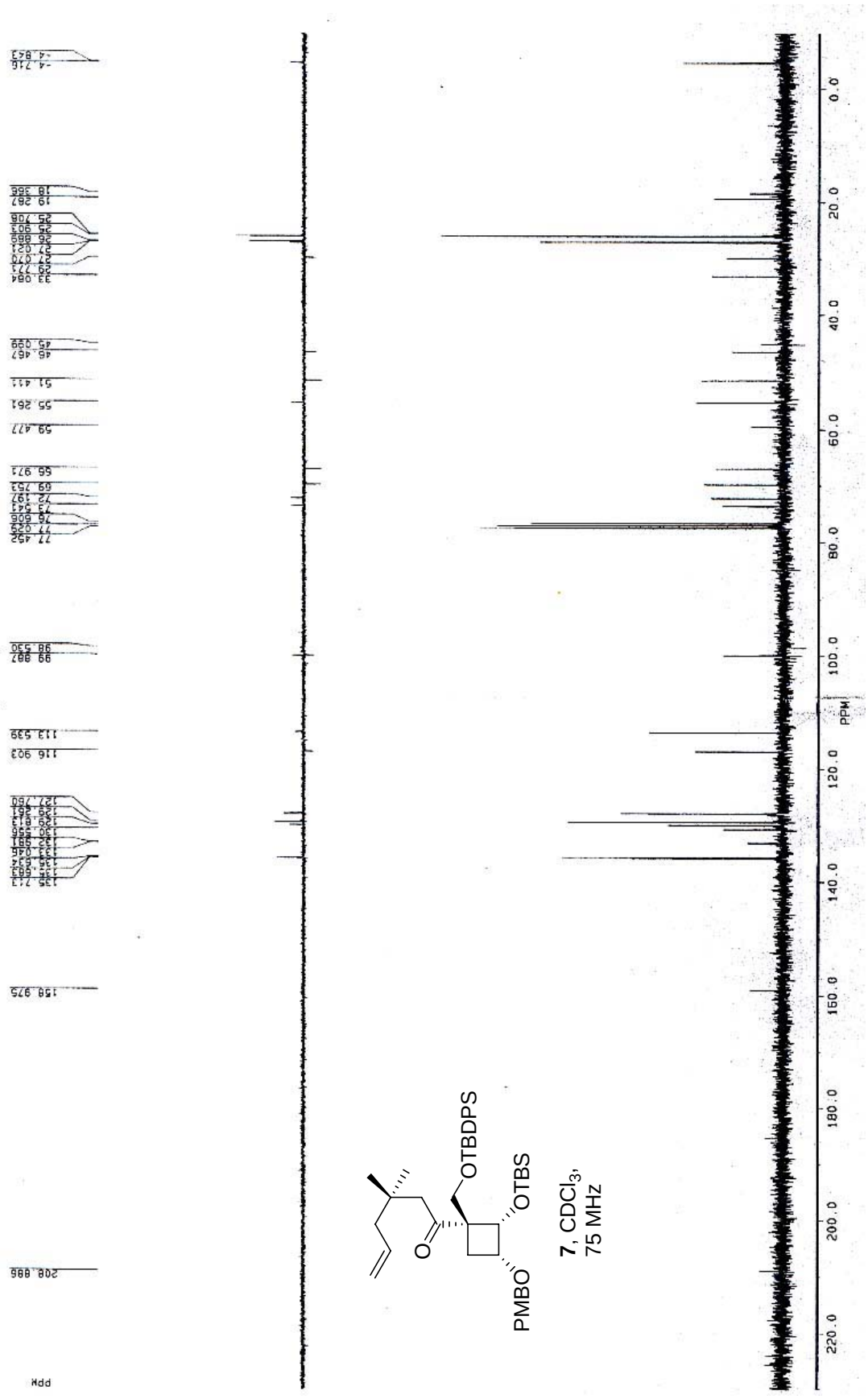

CHO
OTBDPS
OTBS
PMBO
5, $CDCl_3$,
75 MHz

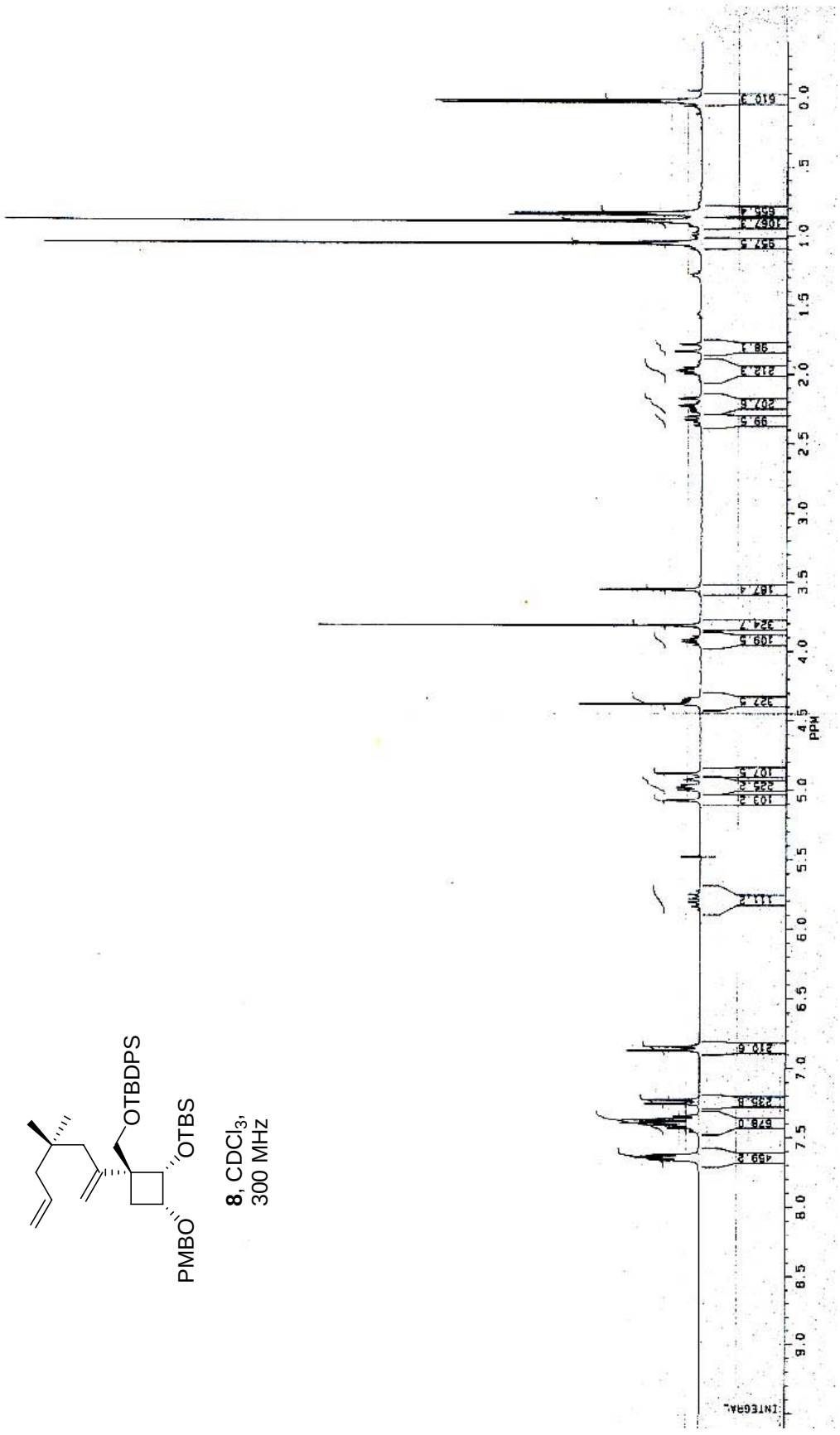


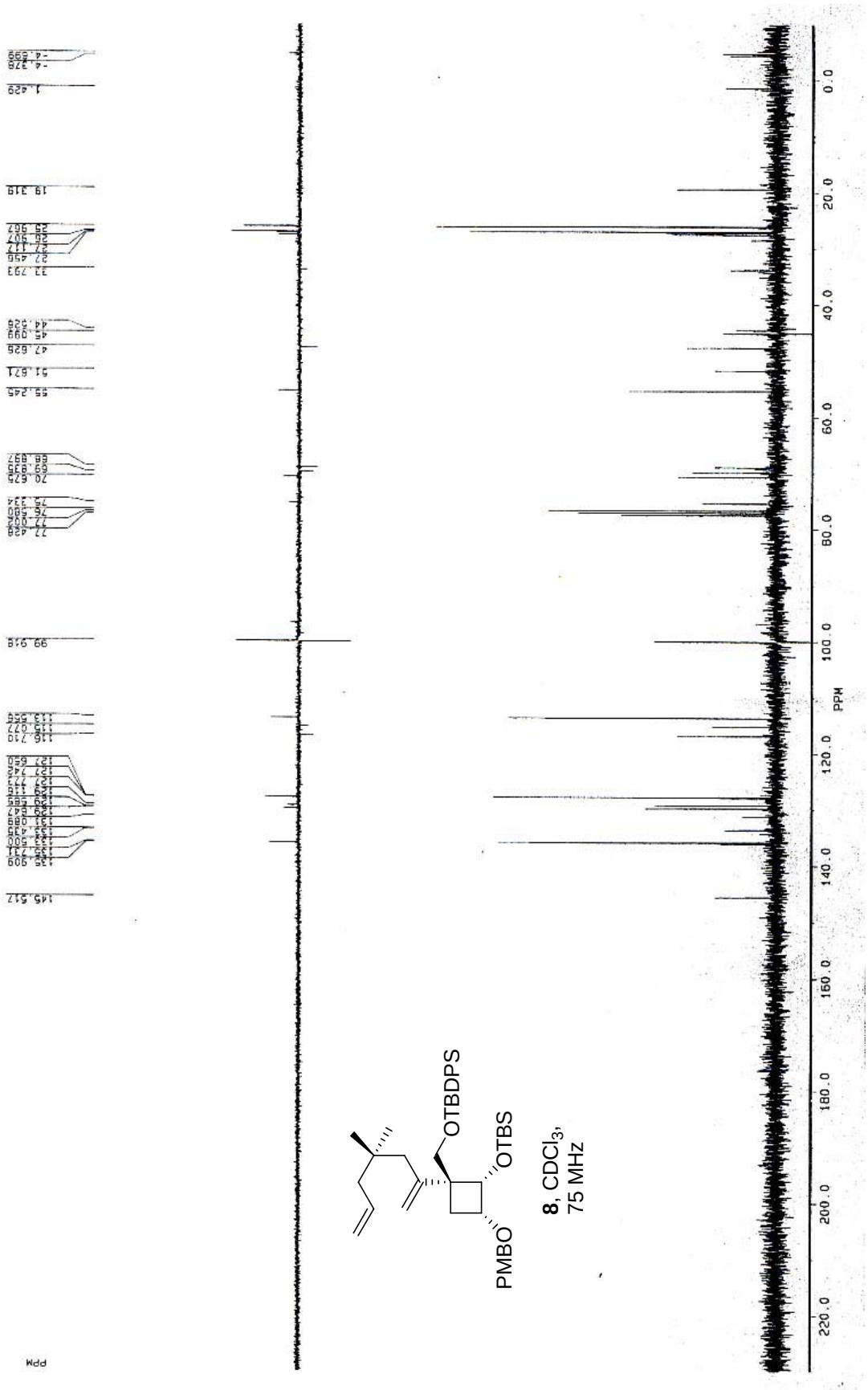
6, $CDCl_3$, 500 MHz

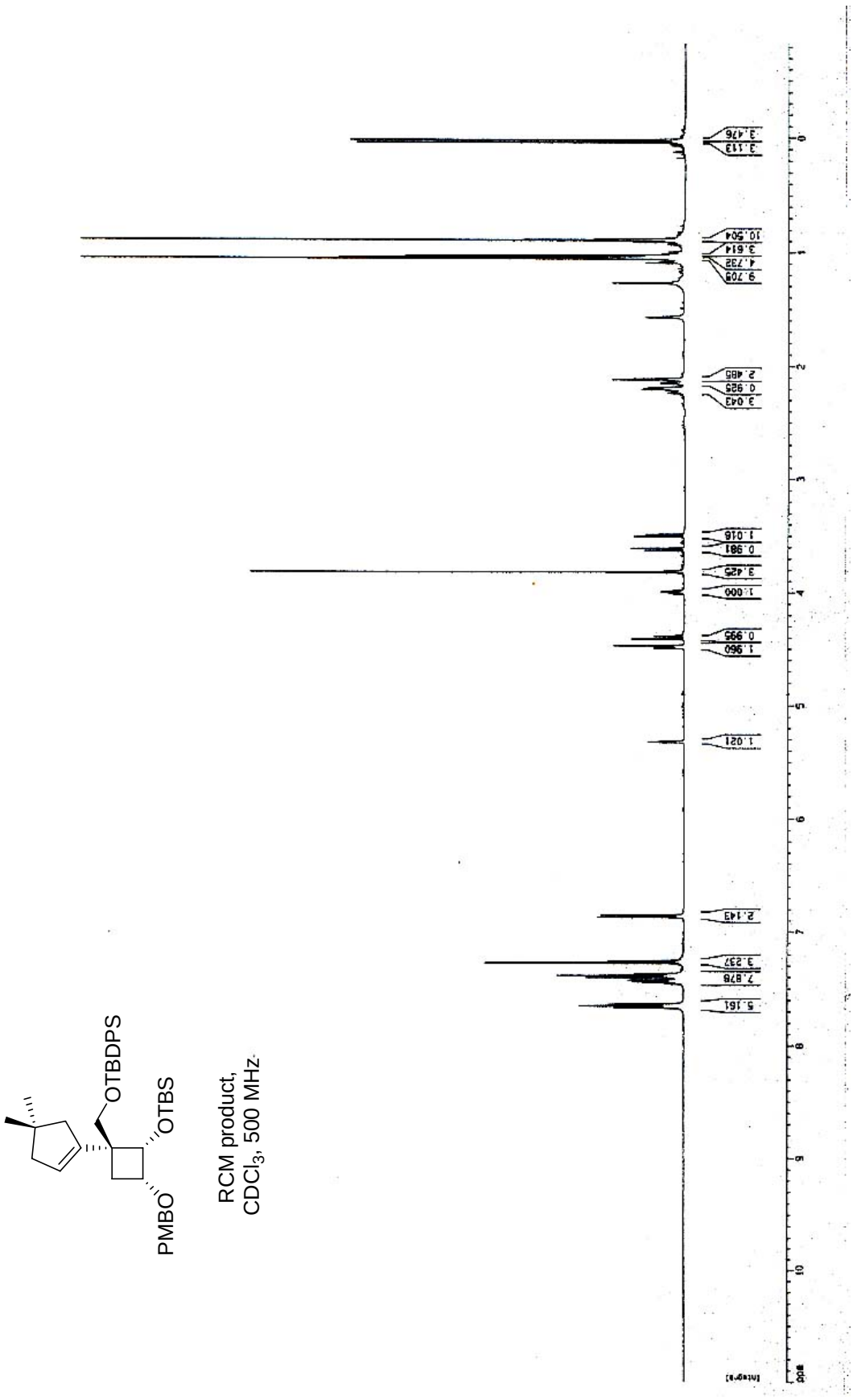

-5.256
-4.501
18.141
19.340
25.841
26.888
26.955
27.039
27.077
27.116
32.896
42.455
47.115
52.972
55.205
62.118
69.693
69.994
70.833
74.495
76.748
77.001
77.256
113.538
116.560
127.649
129.143
129.629
130.035
133.410
133.515
135.613
136.003
158.952
ppm
OTBDPS
OTBS
PMBO
HO
6, $CDCl_3$,
75 MHz

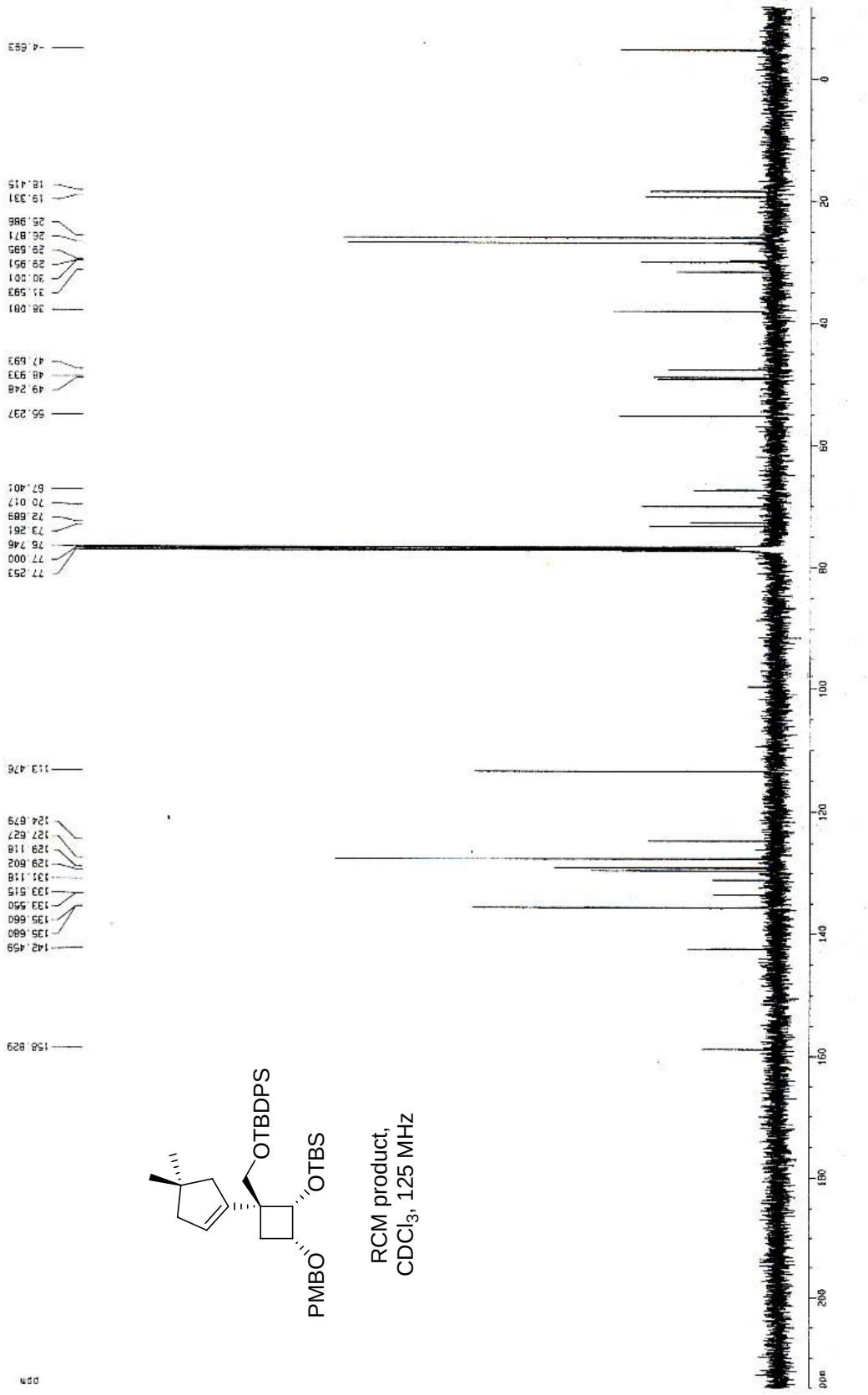

OTBDPS
OTBS
PMBO
O
7, $CDCl_3$,
300 MHz
PPM
INTEGRAL

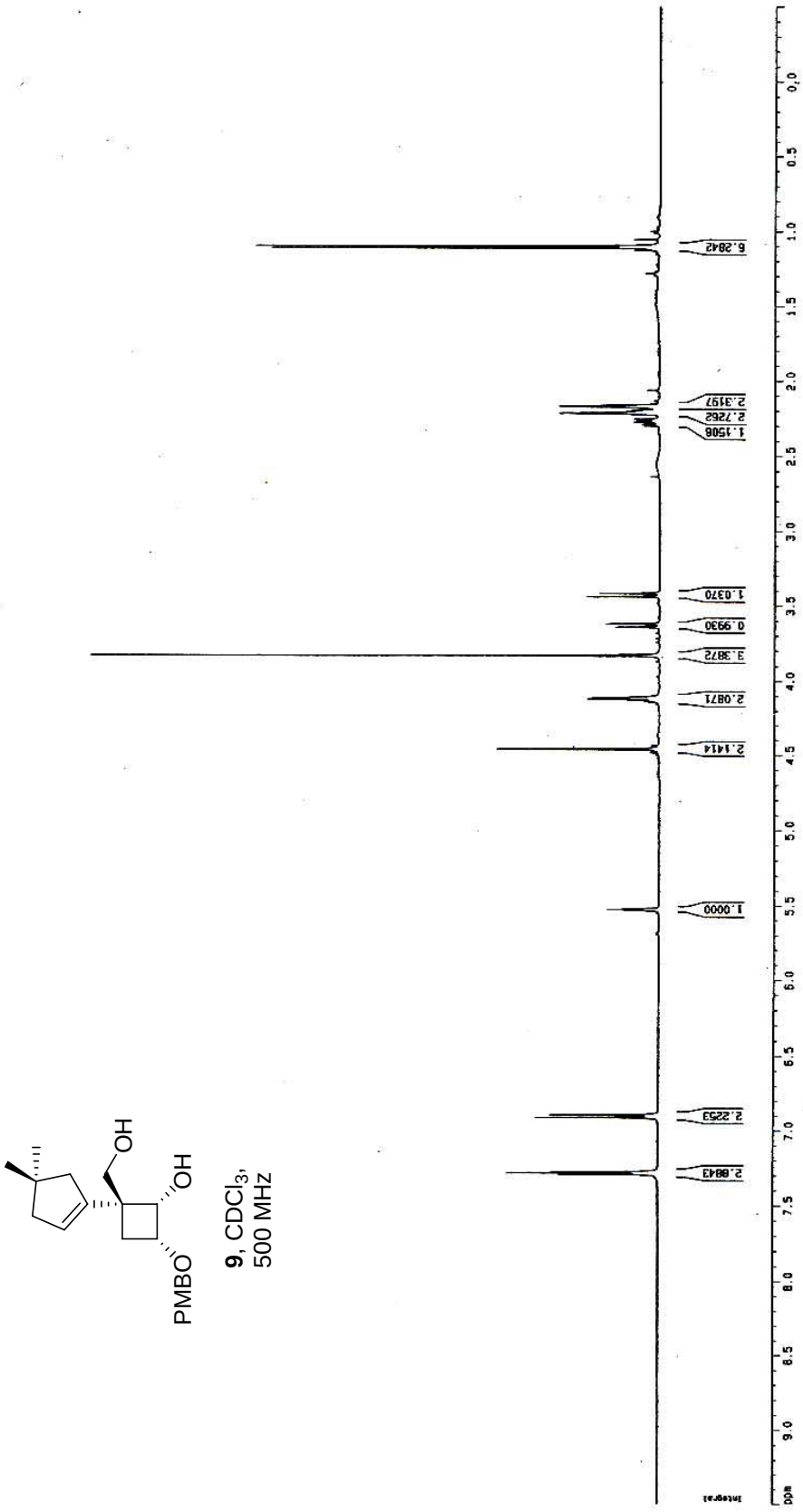

OTBDPS
OTBS
PMBO
O
7, $CDCl_3$,
75 MHz
PPM

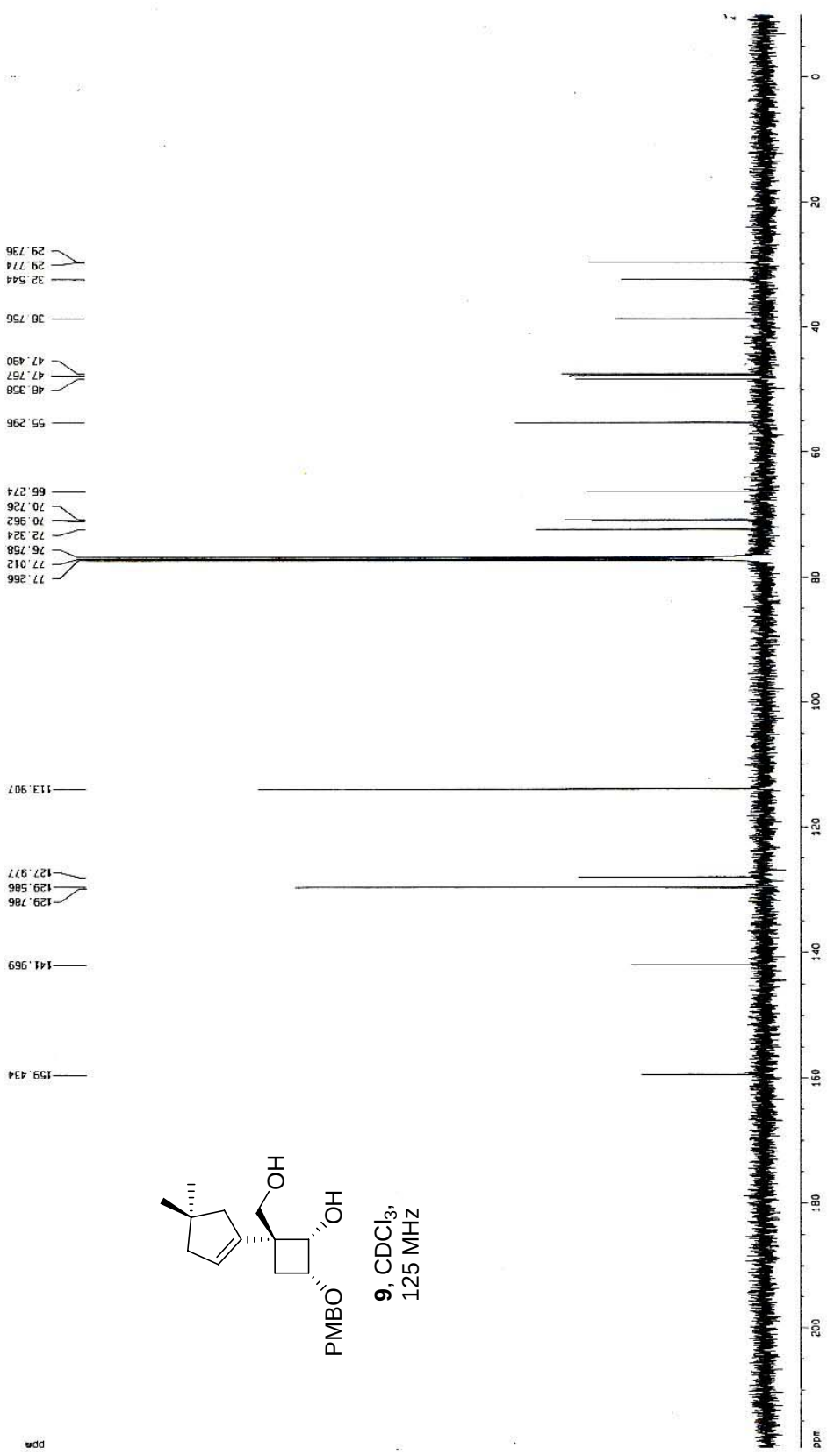

OTBDPS
OTBS
PMBO
8, $CDCl_3$,
300 MHz
PPM

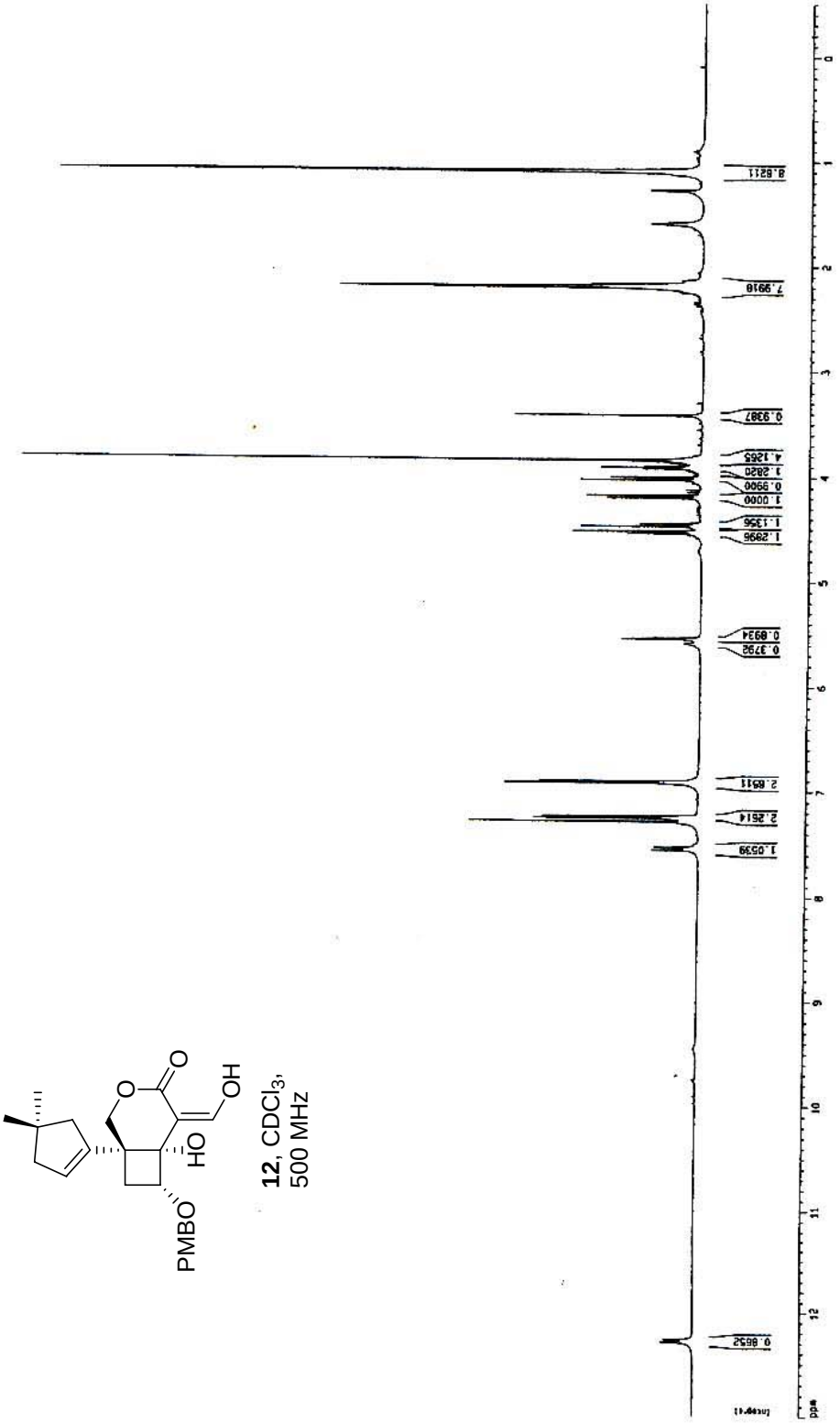

OTBDPS
OTBS
PMBO
8, $CDCl_3$,
75 MHz
PPM

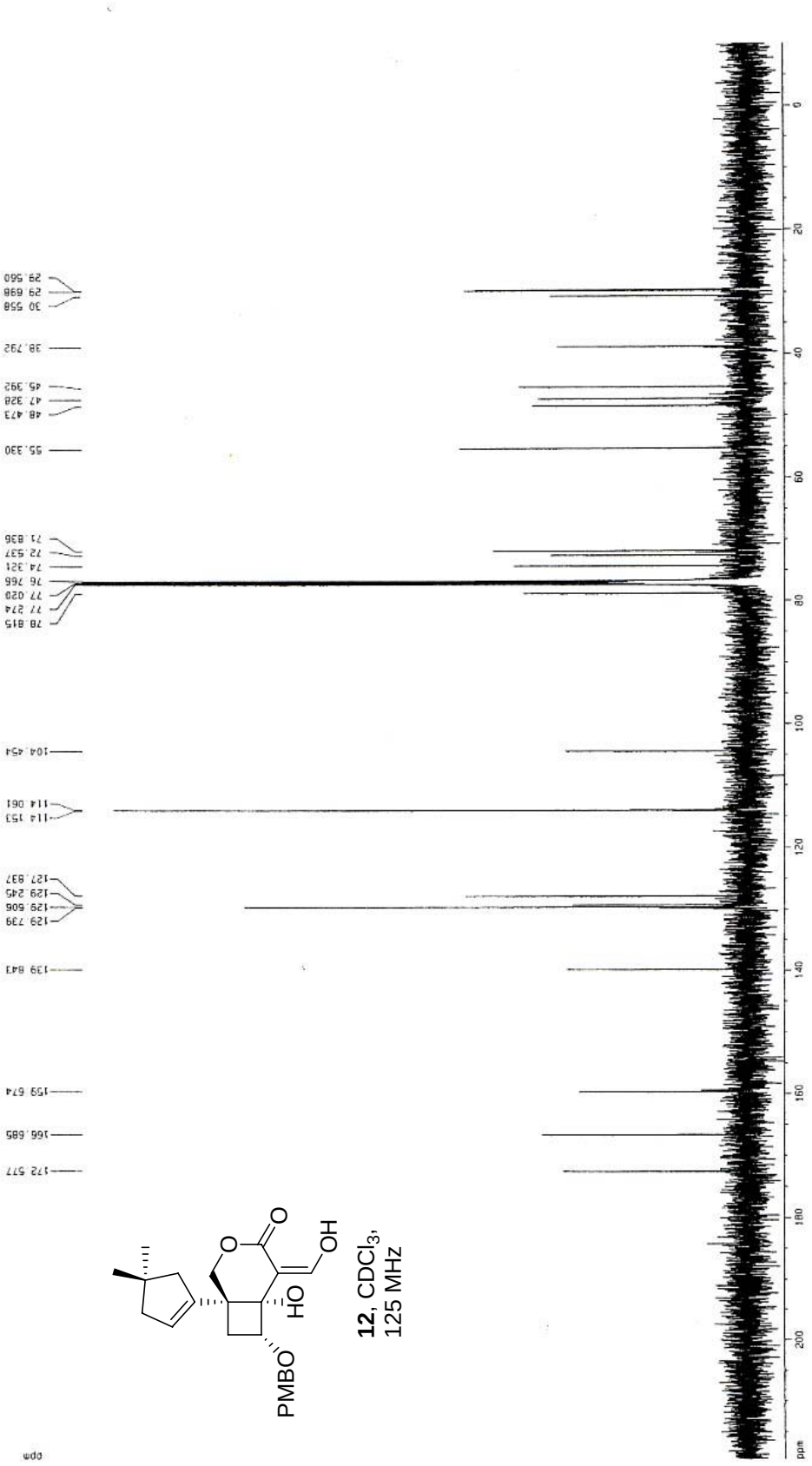

OTBDPS
OTBS
PMBO
RCM product,
CDCl3, 500 MHz

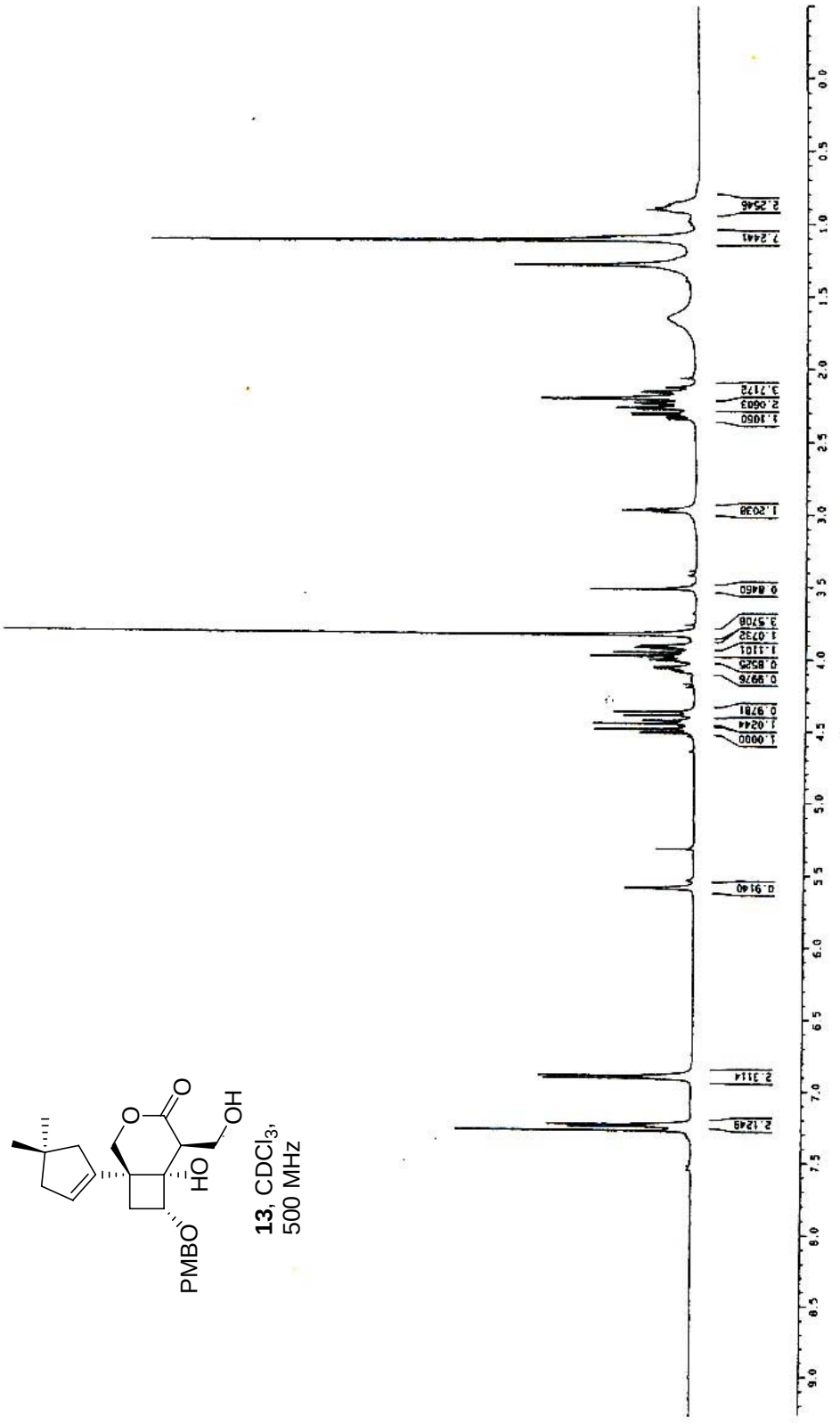

OTBDPS
OTBS
PMBO
RCM product,
CDCl3, 125 MHz

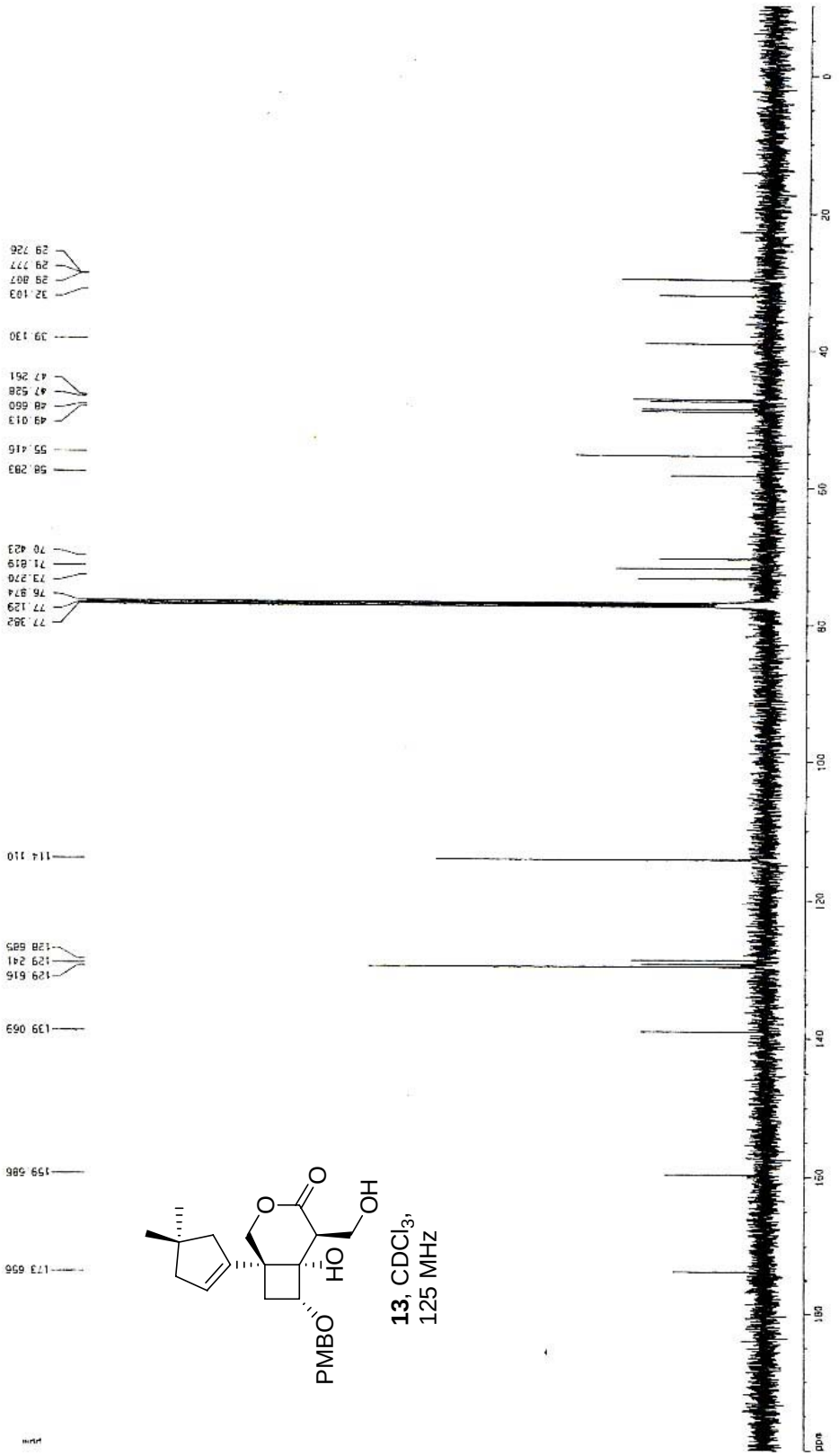

OH
OH
PMBO
9, $CDCl_3$,
500 MHz
6.2842
2.3197
2.2662
1.1508
1.0370
0.9930
3.3872
2.0871
2.1414
1.0000
2.2253
2.8843
ppm

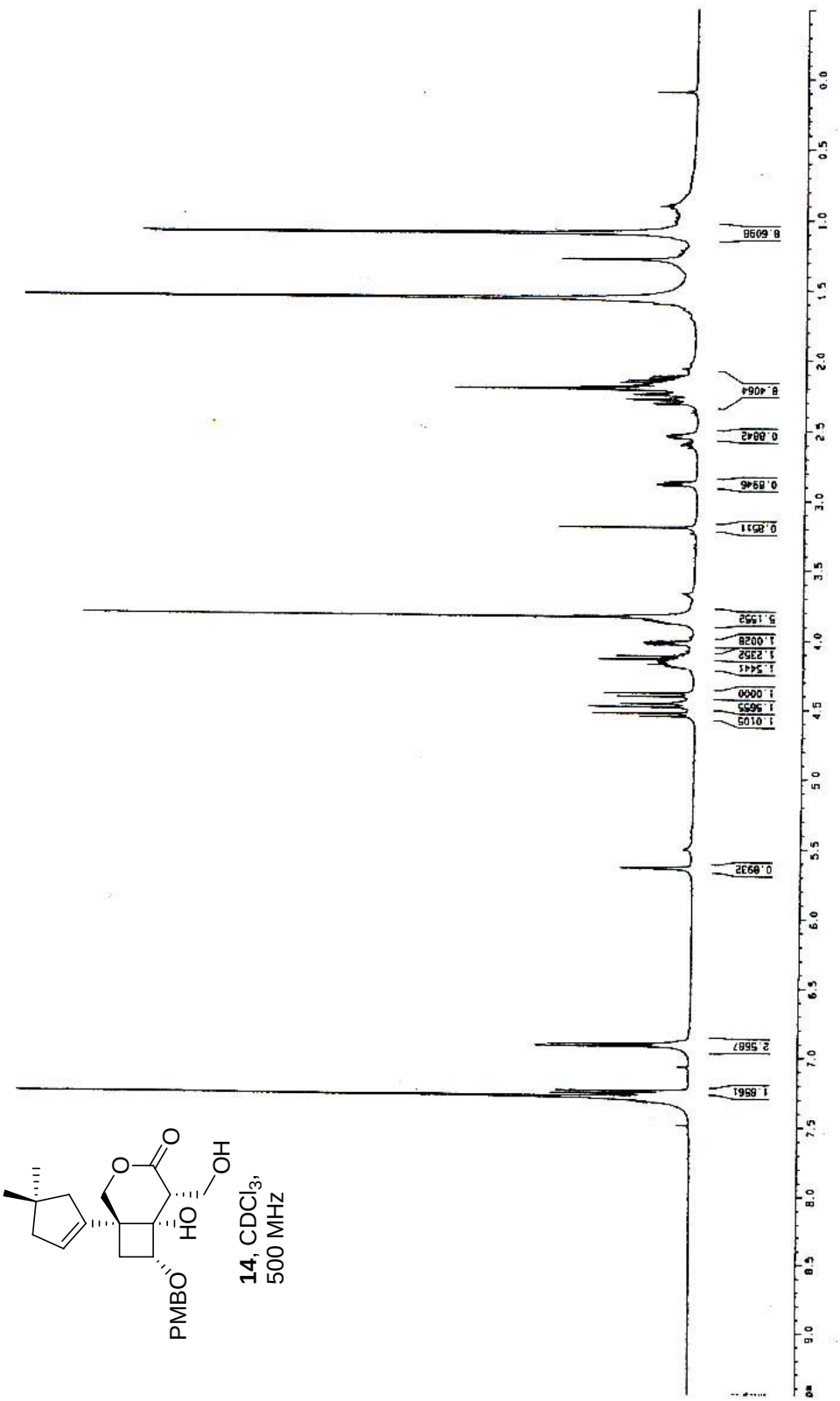

29.736
29.774
32.544
38.756
47.490
47.767
48.358
55.296
66.274
70.726
70.962
72.324
76.758
77.012
77.266
113.907
127.977
129.586
129.786
141.969
159.434
ppm
OH
OH
PMBO
9, $CDCl_3$,
125 MHz

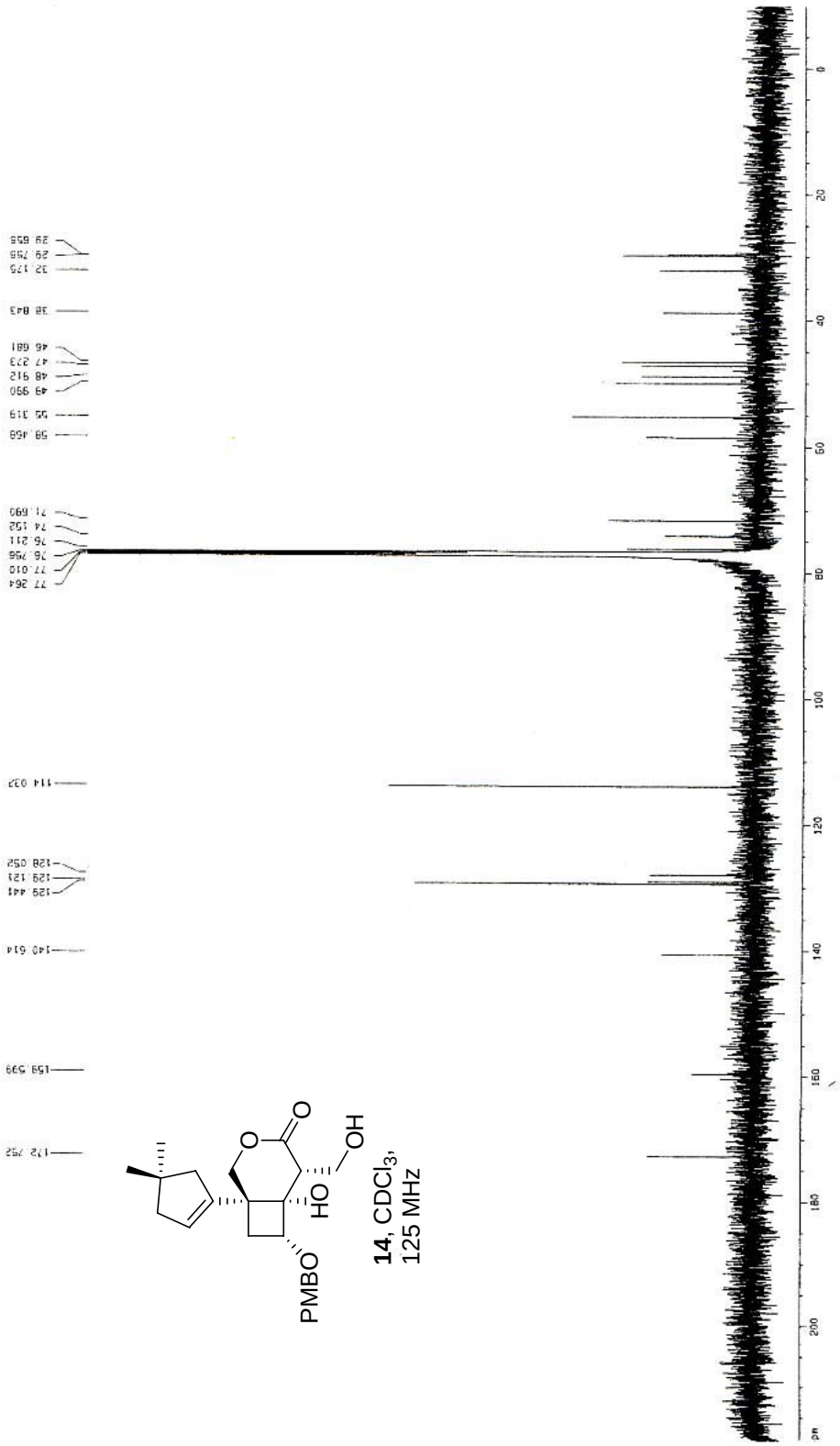

PMBO
HO
OH
O
O
12, $CDCl_3$,
500 MHz
8.8211
7.9818
0.9387
4.1265
3.2820
0.9900
1.0000
1.1356
1.2996
0.8934
0.3792
2.8511
2.2514
1.0539
0.8652
ppm

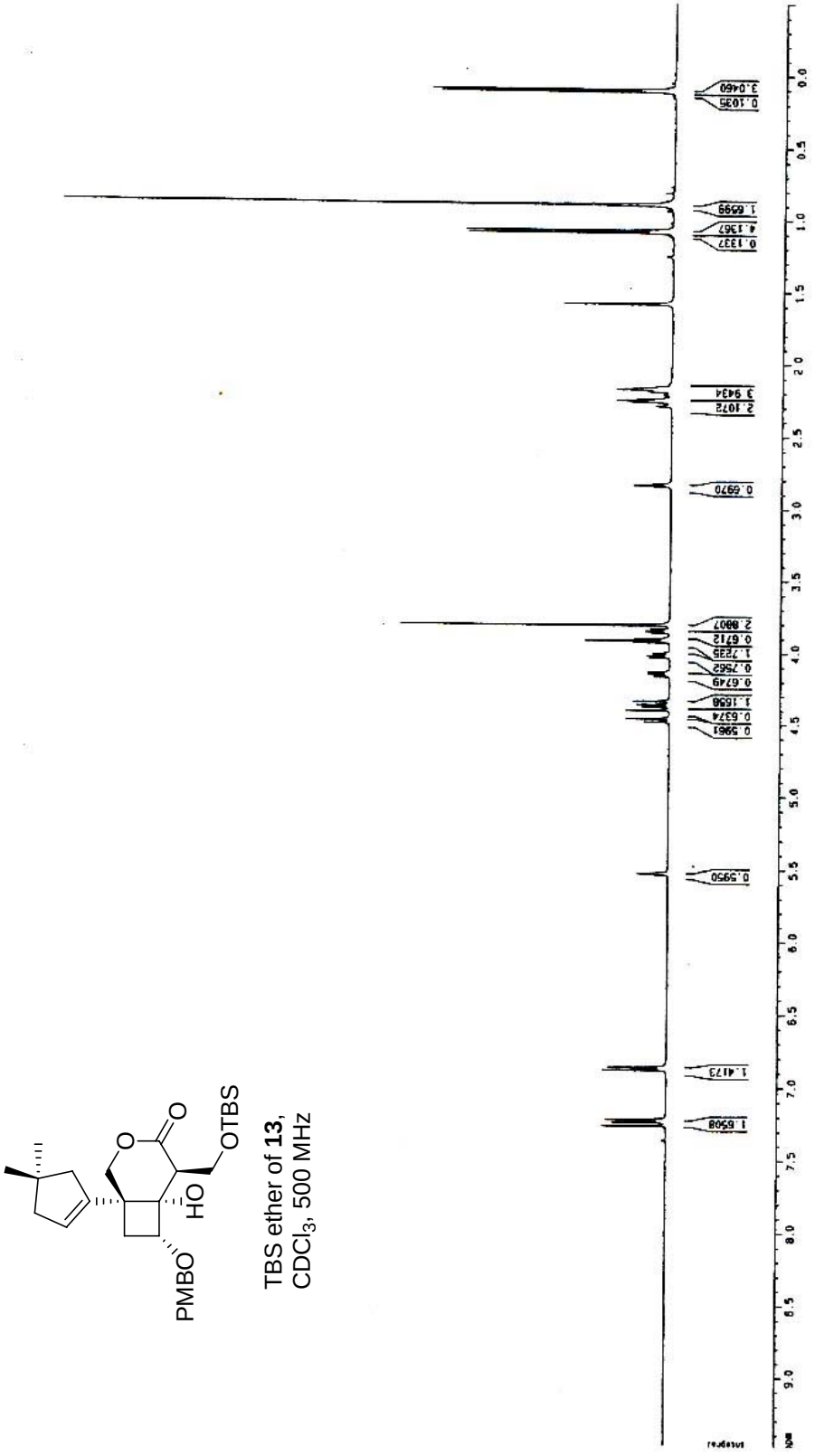

29.560
29.698
30.558
38.792
45.392
47.328
48.473
55.330
71.836
72.537
74.321
76.766
77.020
77.274
78.815
104.454
114.061
114.153
127.837
129.245
129.606
129.739
139.843
159.674
166.685
172.577
ppm
PMBO
HO
OH
O
O
12, CDCl3,
125 MHz


PMBO
HO
OH
O
O
13, $CDCl_3$,
500 MHz

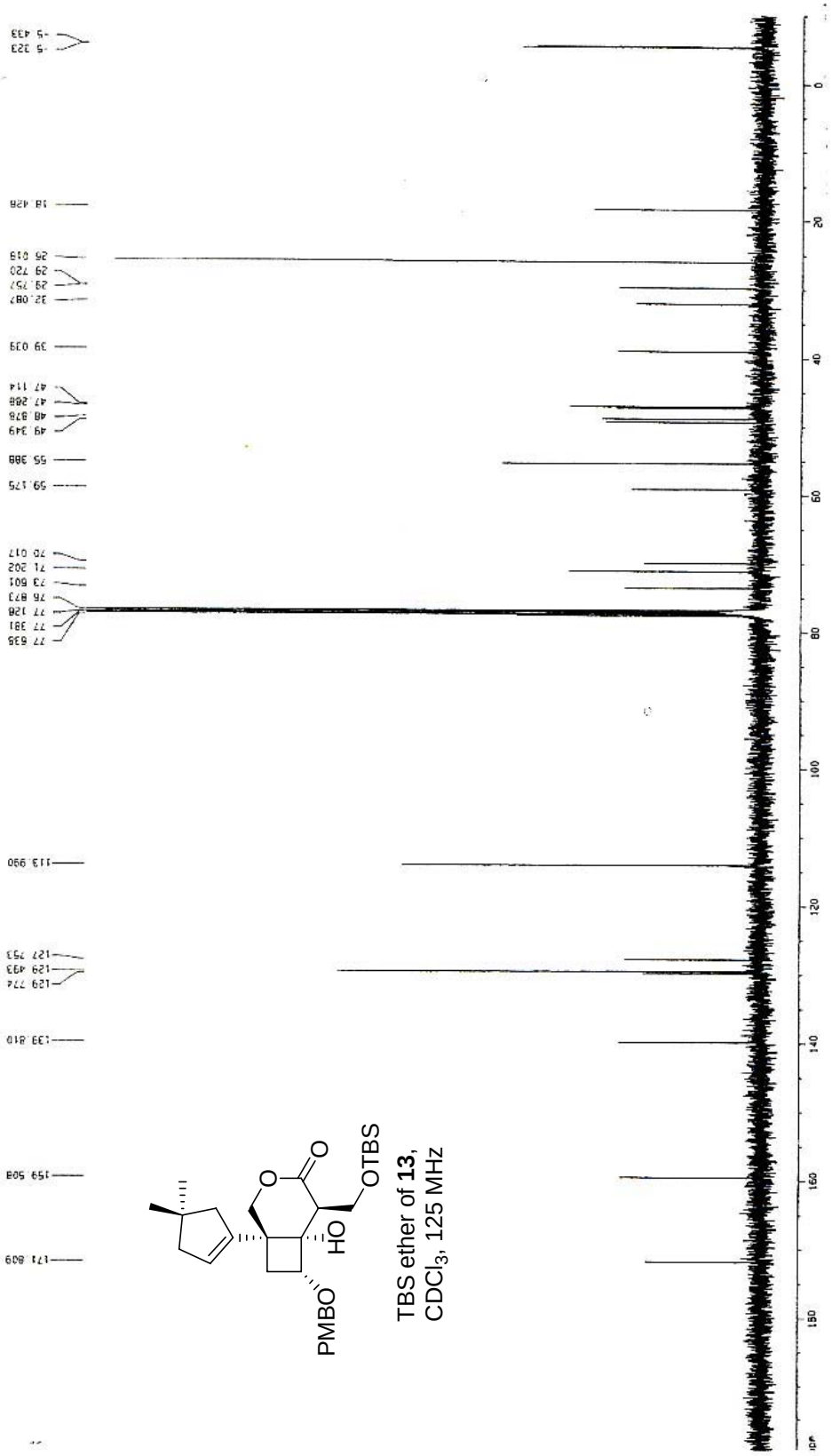

29.726
29.777
29.807
32.103
39.130
47.261
47.528
48.660
49.013
55.416
58.283
70.423
71.819
73.270
76.974
77.129
77.382
114.110
128.685
129.241
129.616
139.069
159.686
173.656
PMBO
HO
OH
O
O
13, $CDCl_3$,
125 MHz
ppm

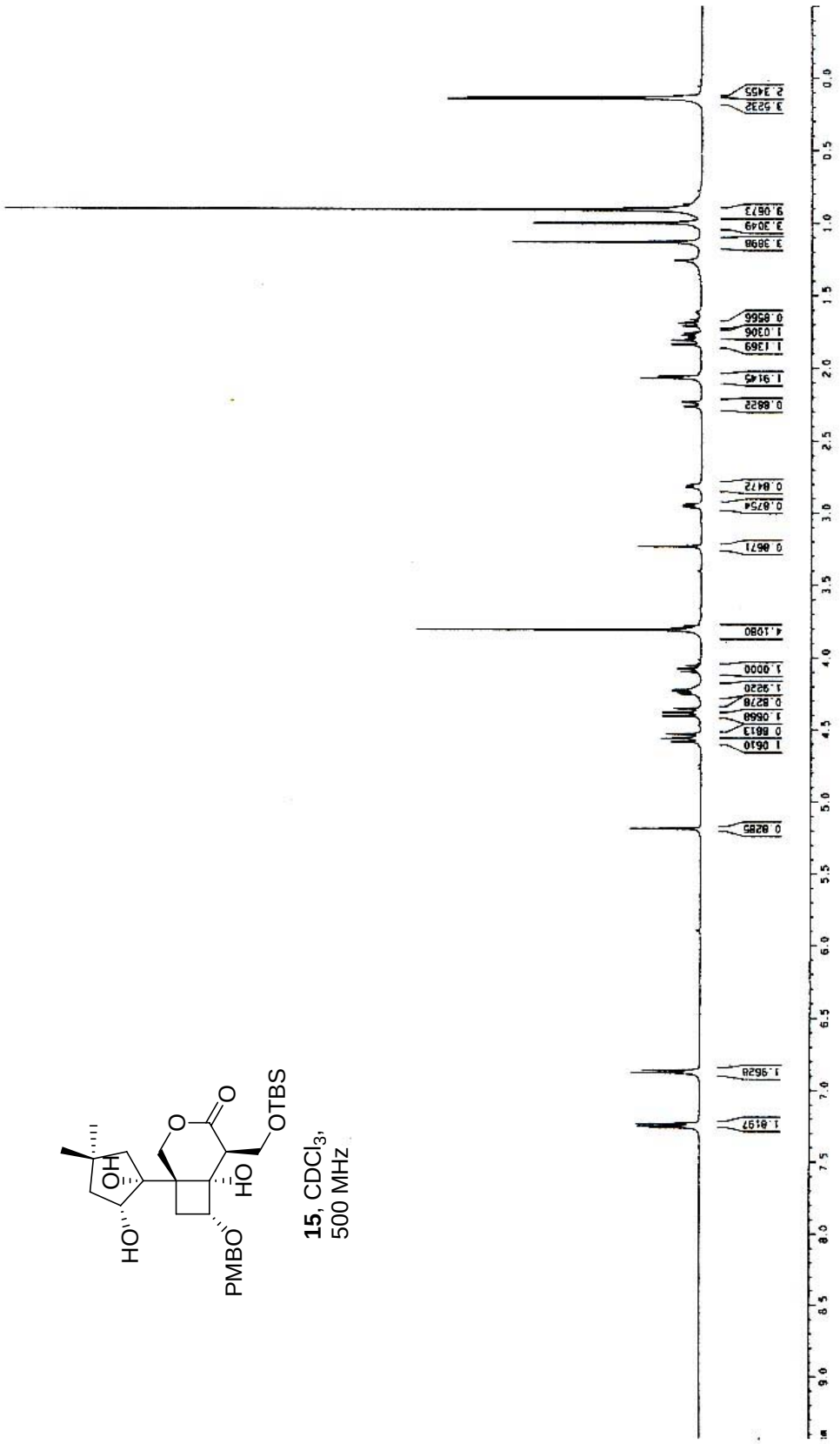

PMBO
HO
OH
O
O
14, $CDCl_3$,
500 MHz


PMBO
HO
OH
O
O
14, $CDCl_3$,
125 MHz

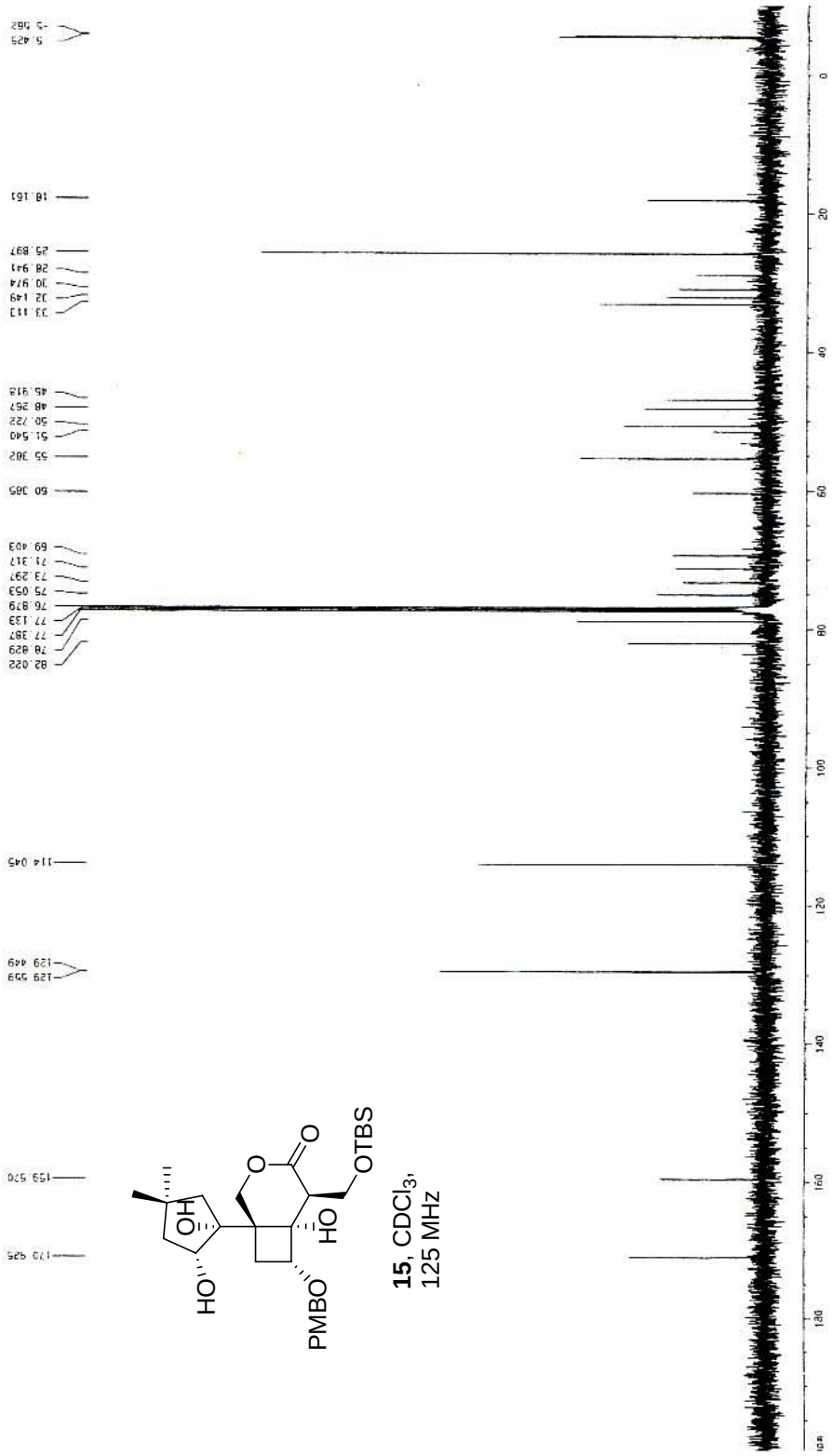


TBS ether of **13**,
$CDCl_3$, 500 MHz

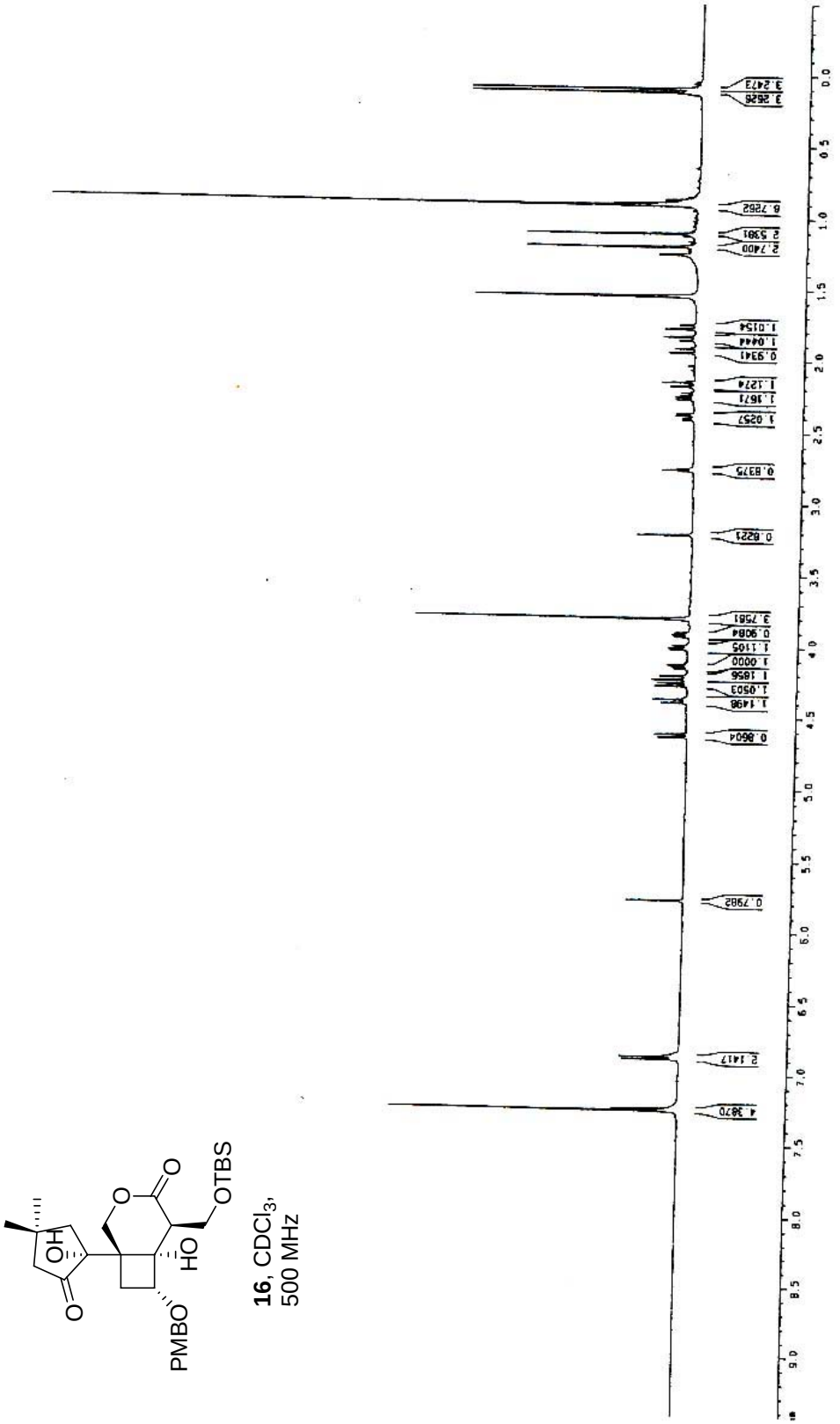

-5.433
-5.323
18.428
25.018
29.720
29.757
32.087
39.039
47.114
47.288
48.878
49.349
55.388
59.175
70.017
71.202
73.601
76.873
77.128
77.381
77.638
113.990
127.753
129.433
129.774
133.810
159.508
173.809
PMBO
HO
OTBS
O
O
TBS ether of **13**,
$CDCl_3$, 125 MHz



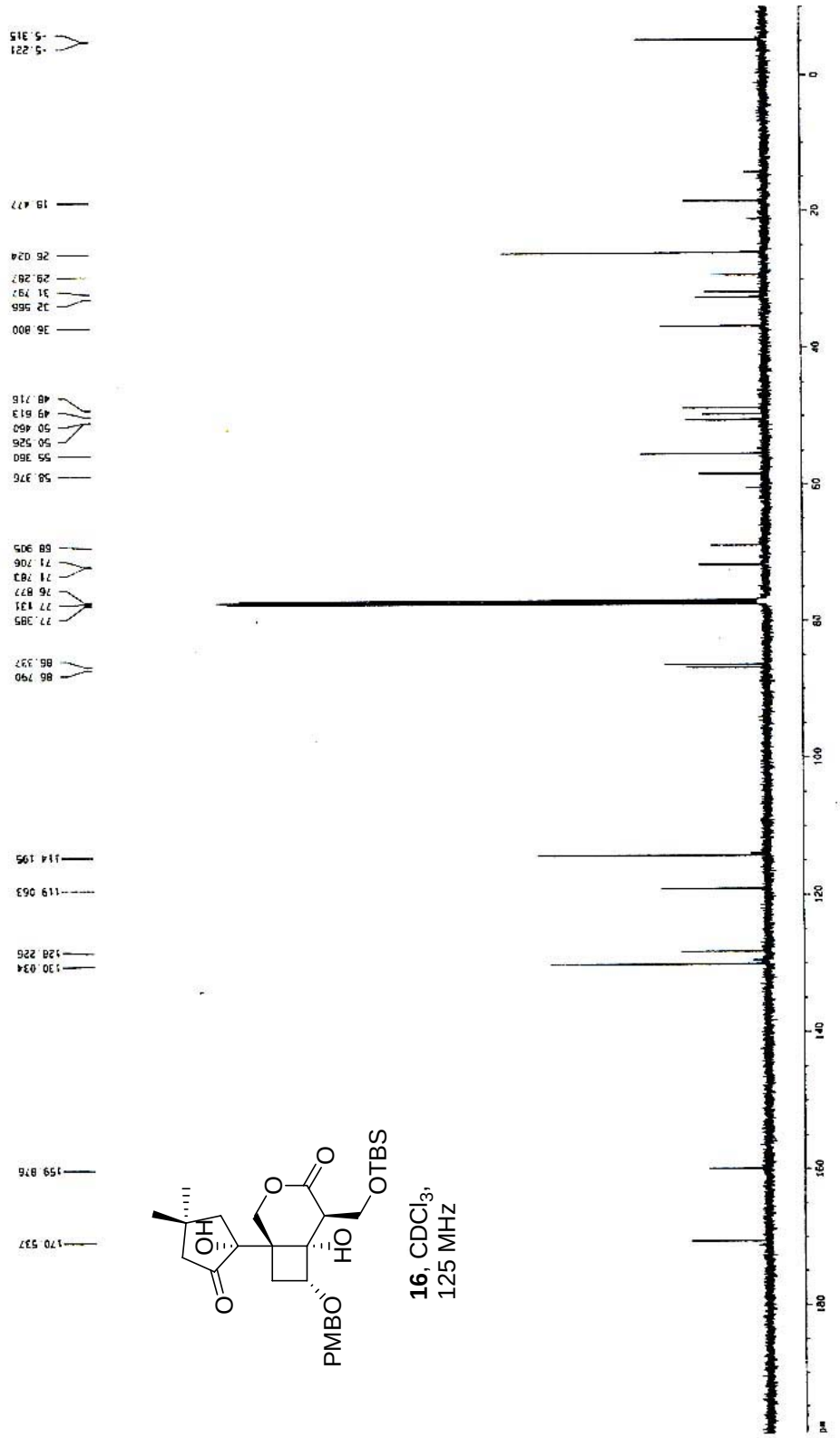
15, $CDCl_3$,
500 MHz

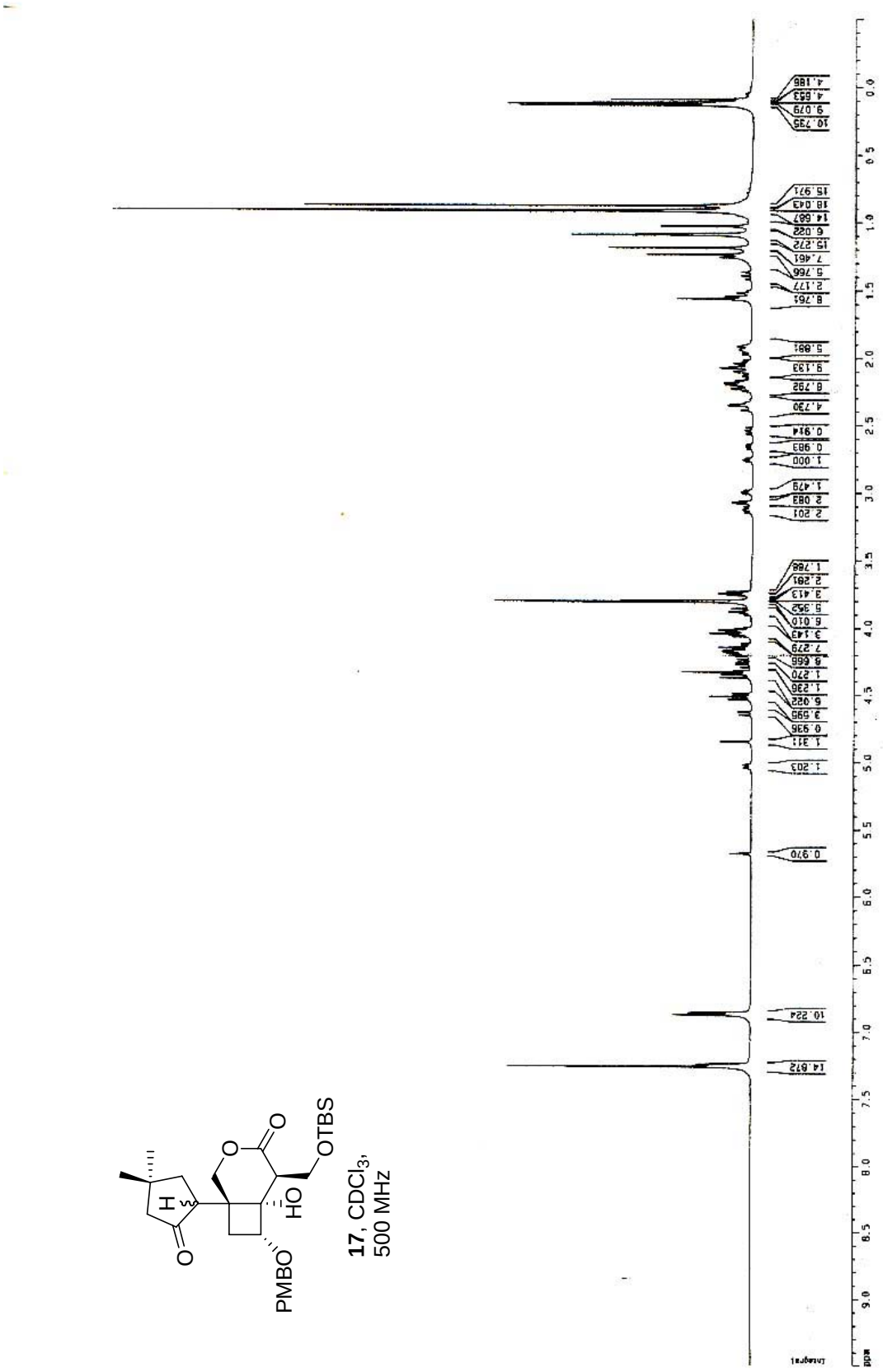


15, $CDCl_3$, 125 MHz

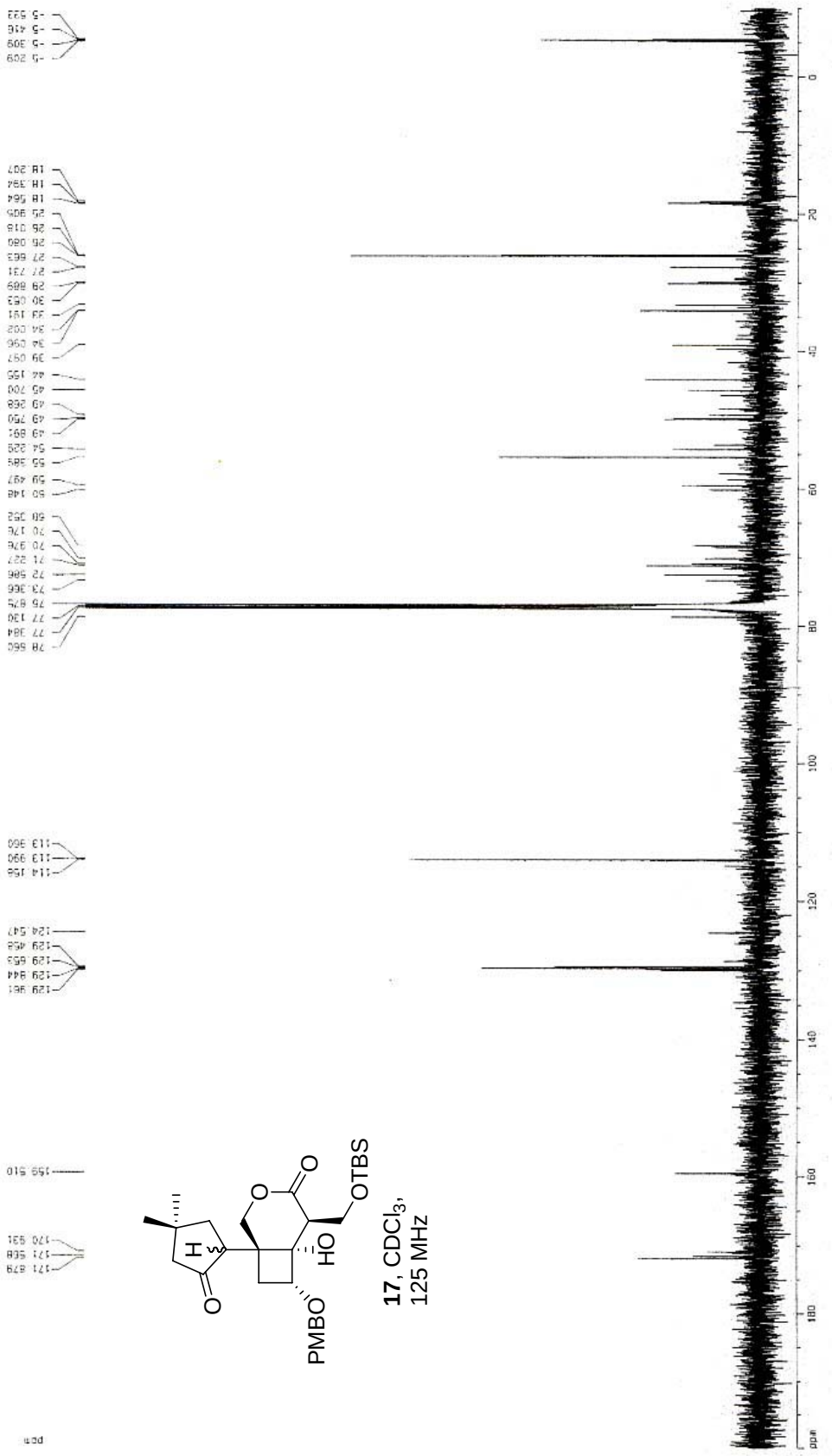


16, $CDCl_3$,
500 MHz

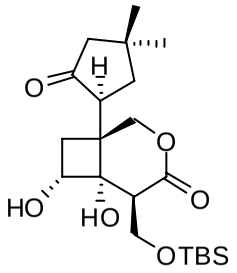

-5.315
-5.221
19.477
26.024
29.287
31.797
32.566
36.800
48.716
49.613
50.460
50.926
55.360
58.376
68.905
71.706
71.783
76.877
77.131
77.385
86.337
86.790
114.195
119.063
128.226
130.034
159.876
170.537
OH
O
O
O
HO
OTBS
PMBO
16, $CDCl_3$,
125 MHz



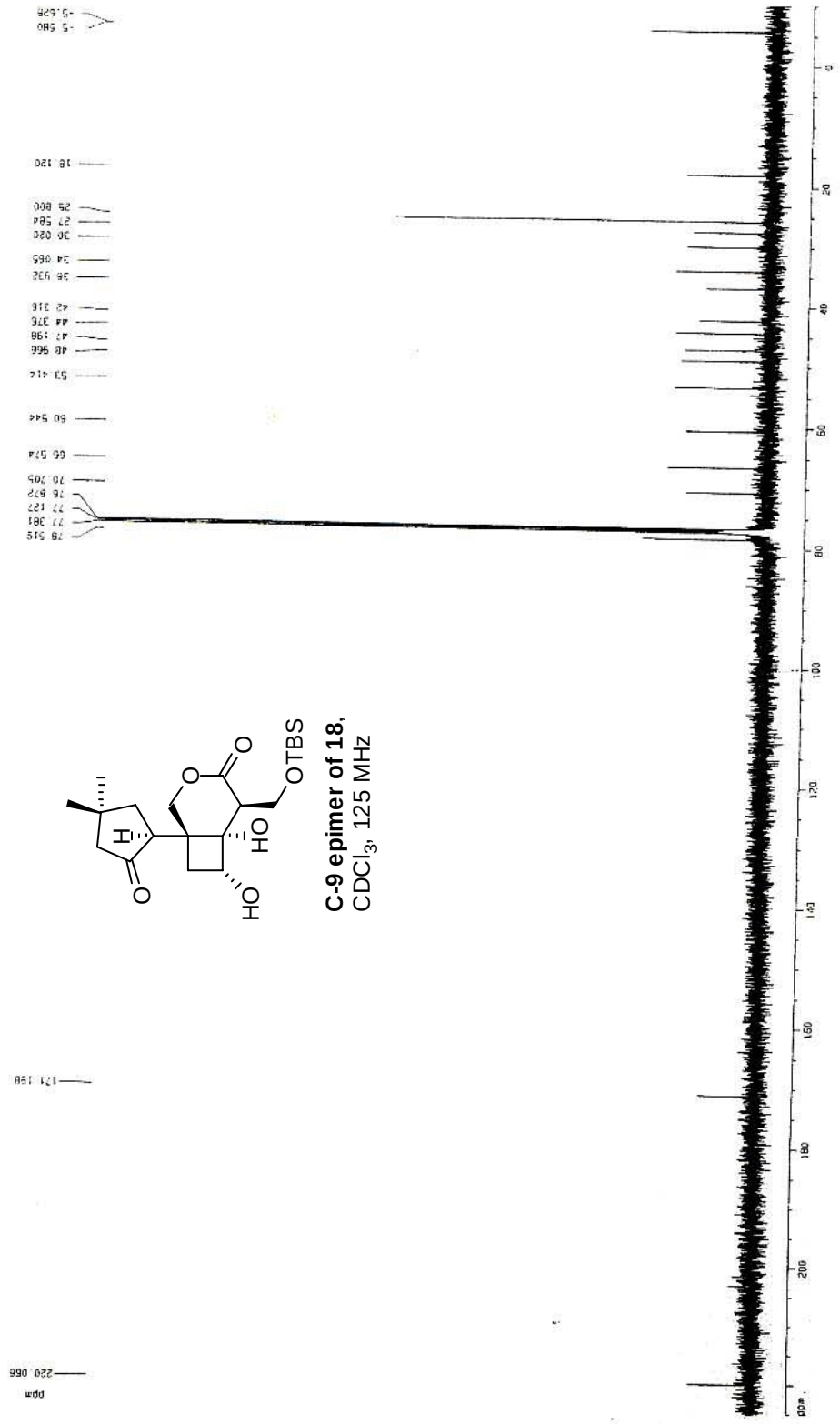
17, $CDCl_3$,
500 MHz



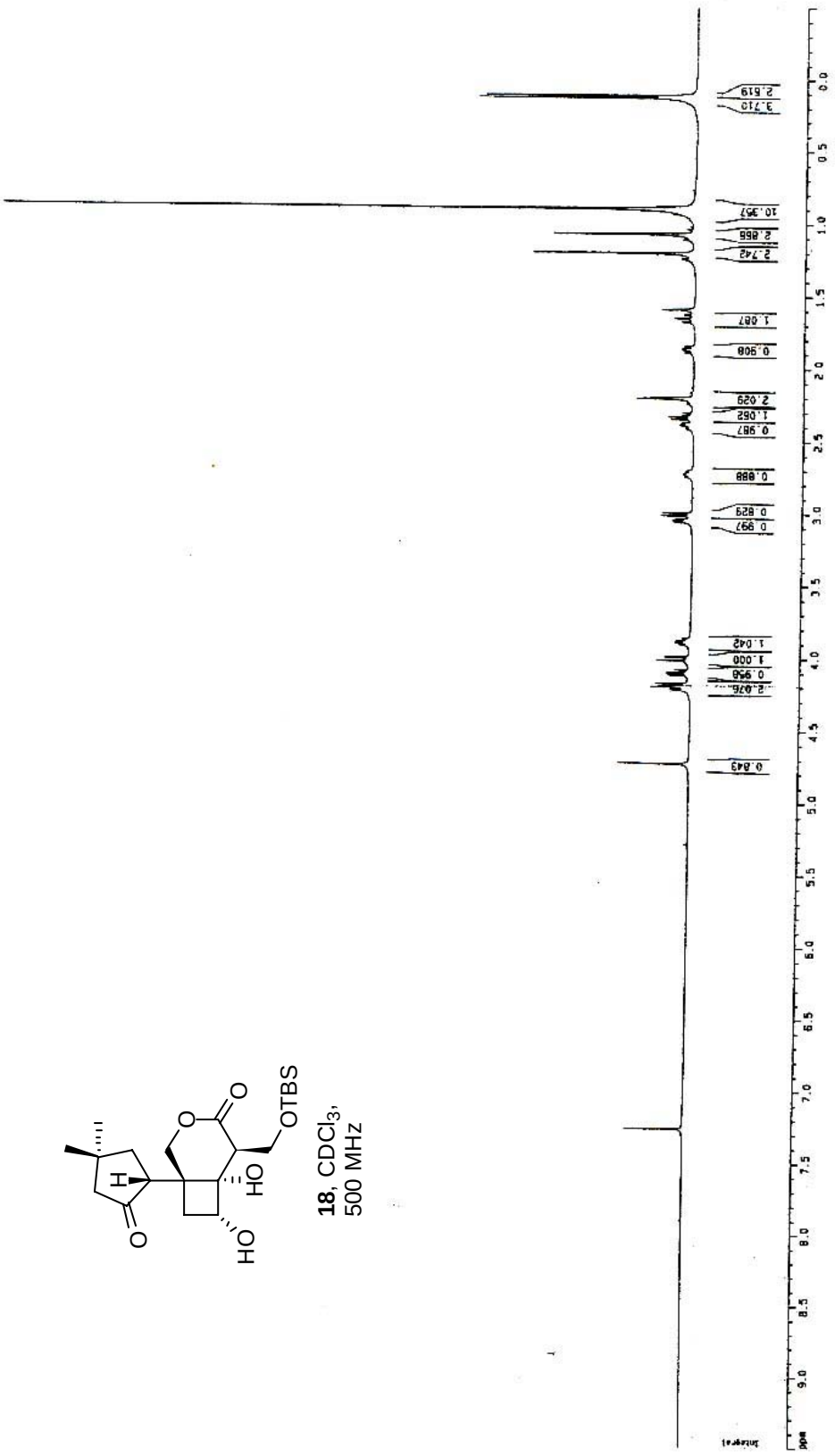
17, $CDCl_3$, 125 MHz



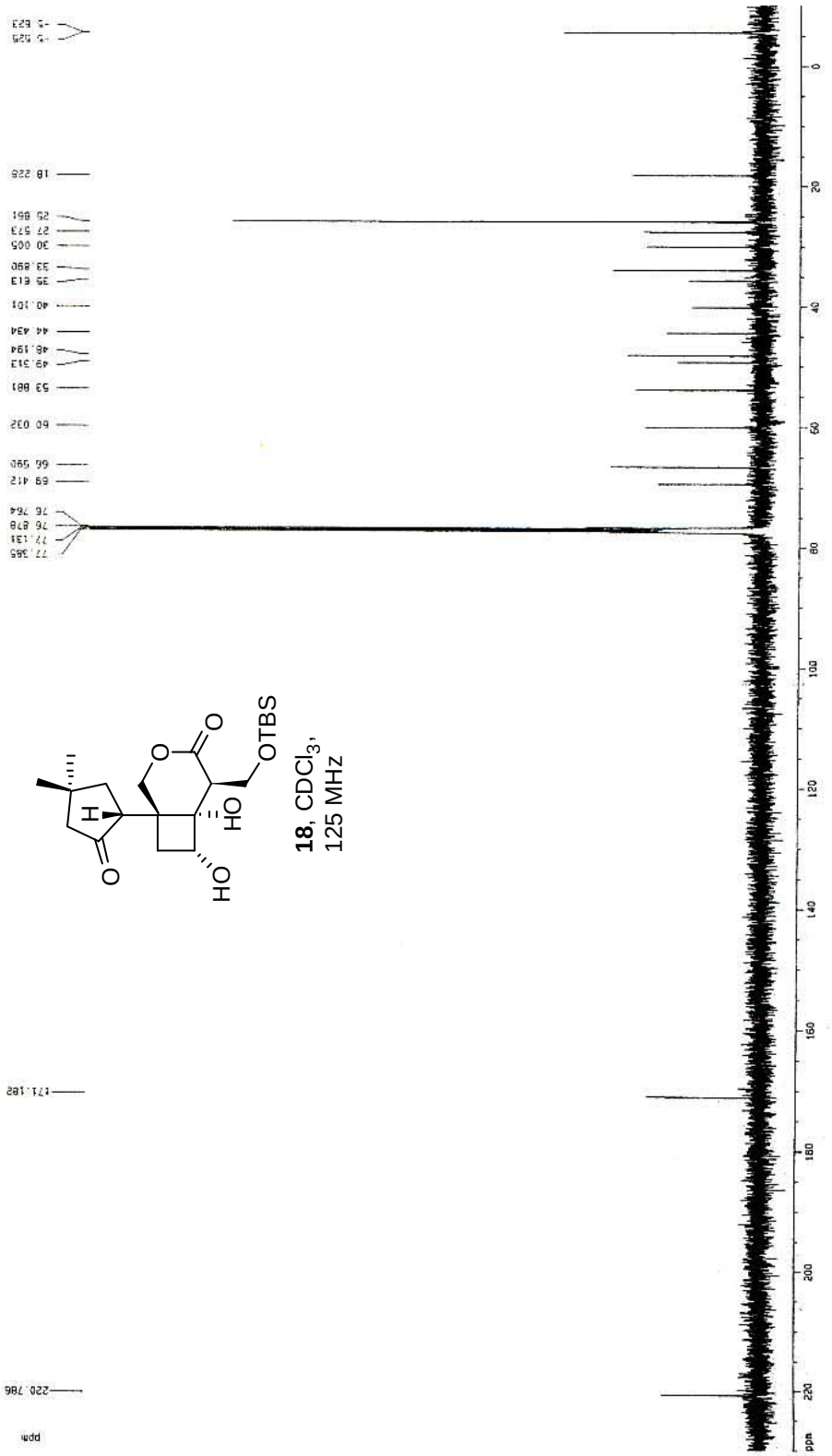
C-9 epimer of 18,
$CDCl_3$, 500 MHz

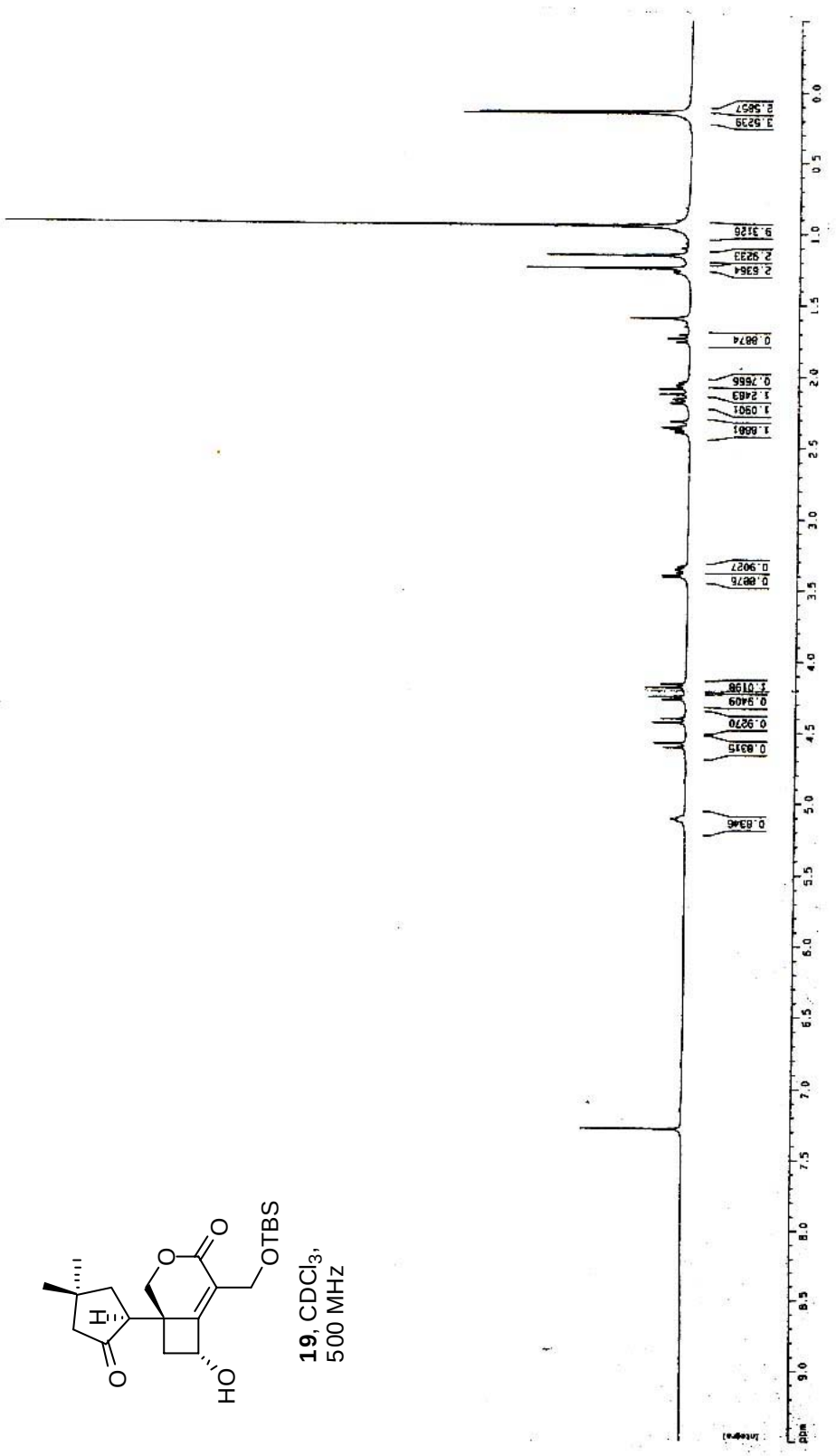


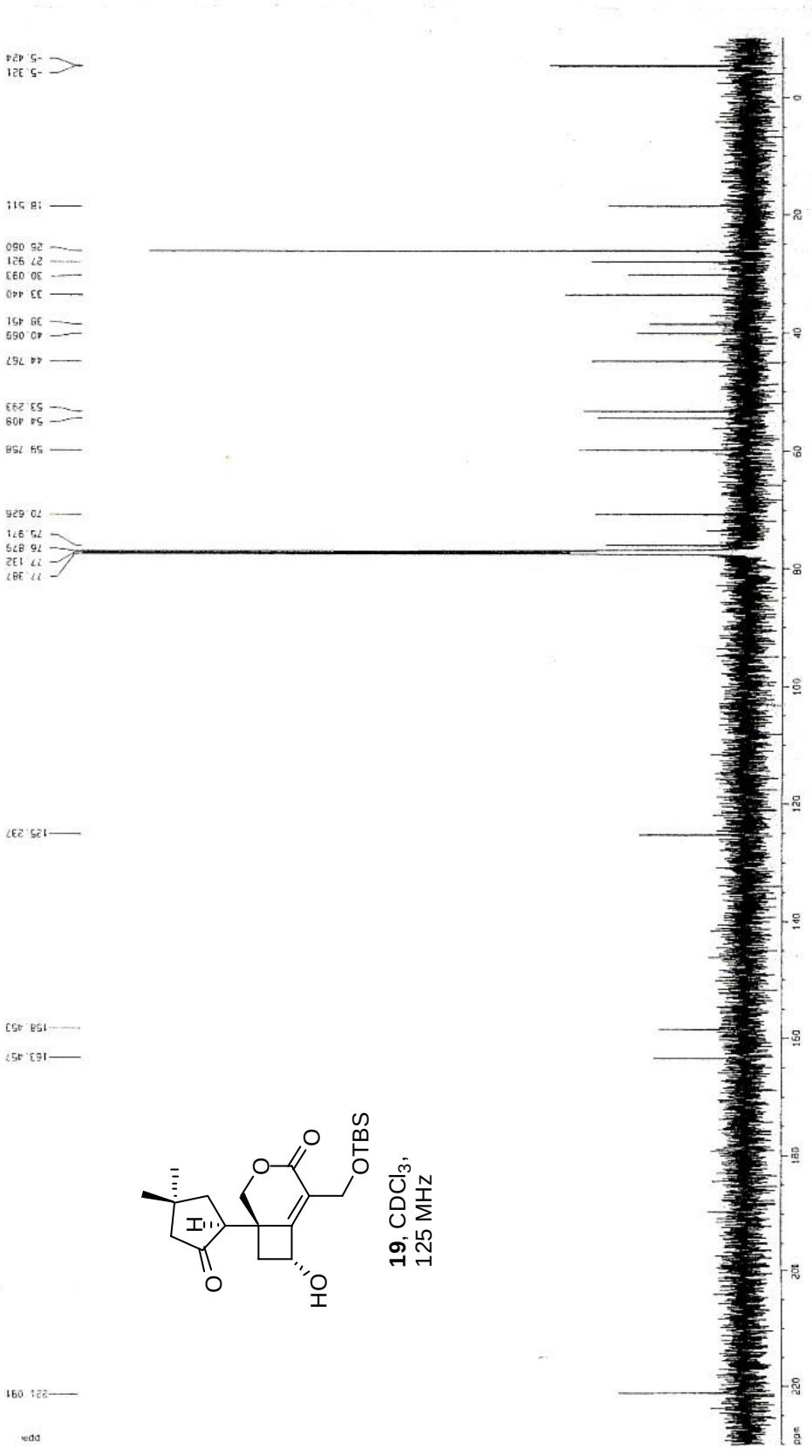
C-9 epimer of 18, $CDCl_3$, 125 MHz



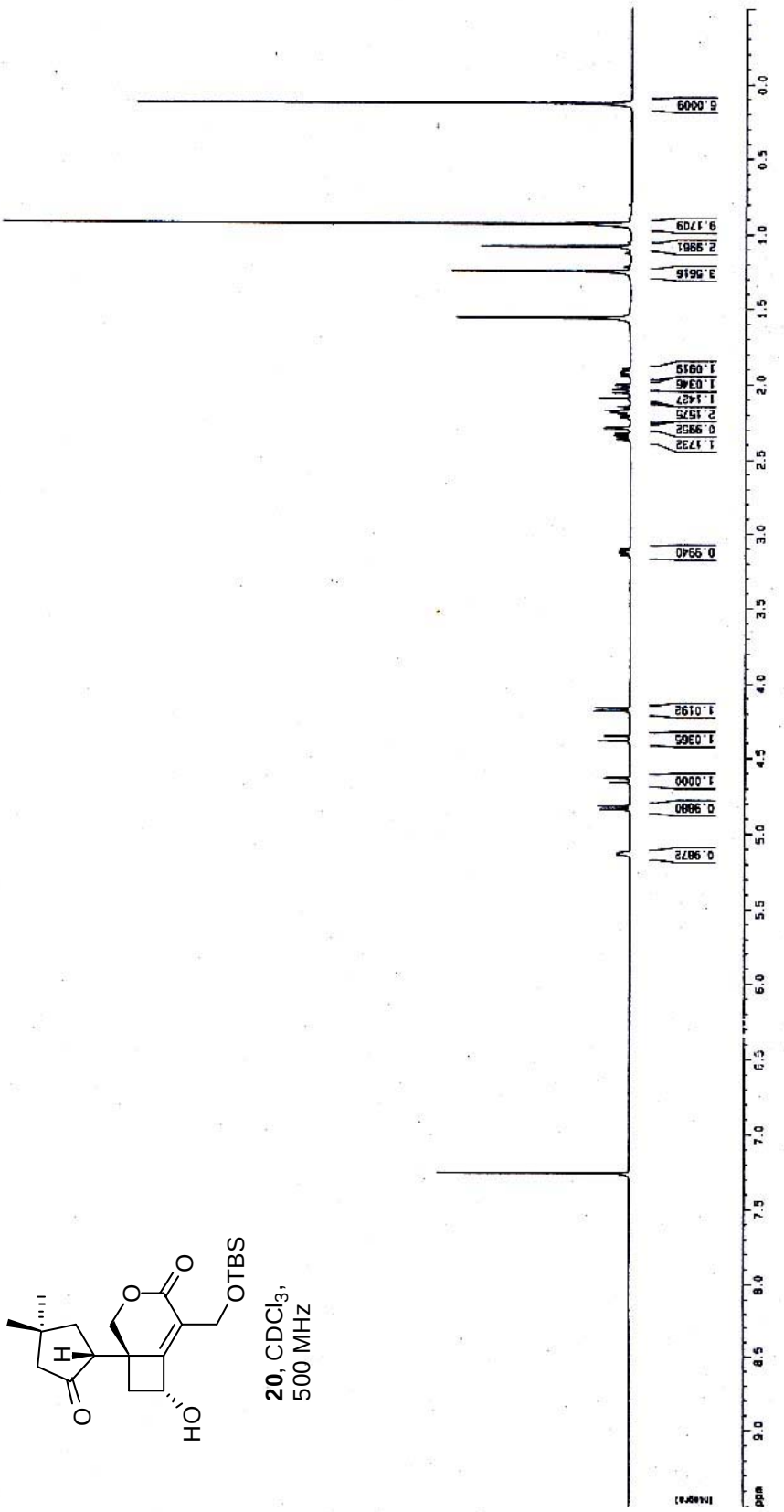
18, $CDCl_3$, 500 MHz


OTBS
HO
HO
O
O
O
H
18, CDCl3,
125 MHz
ppm

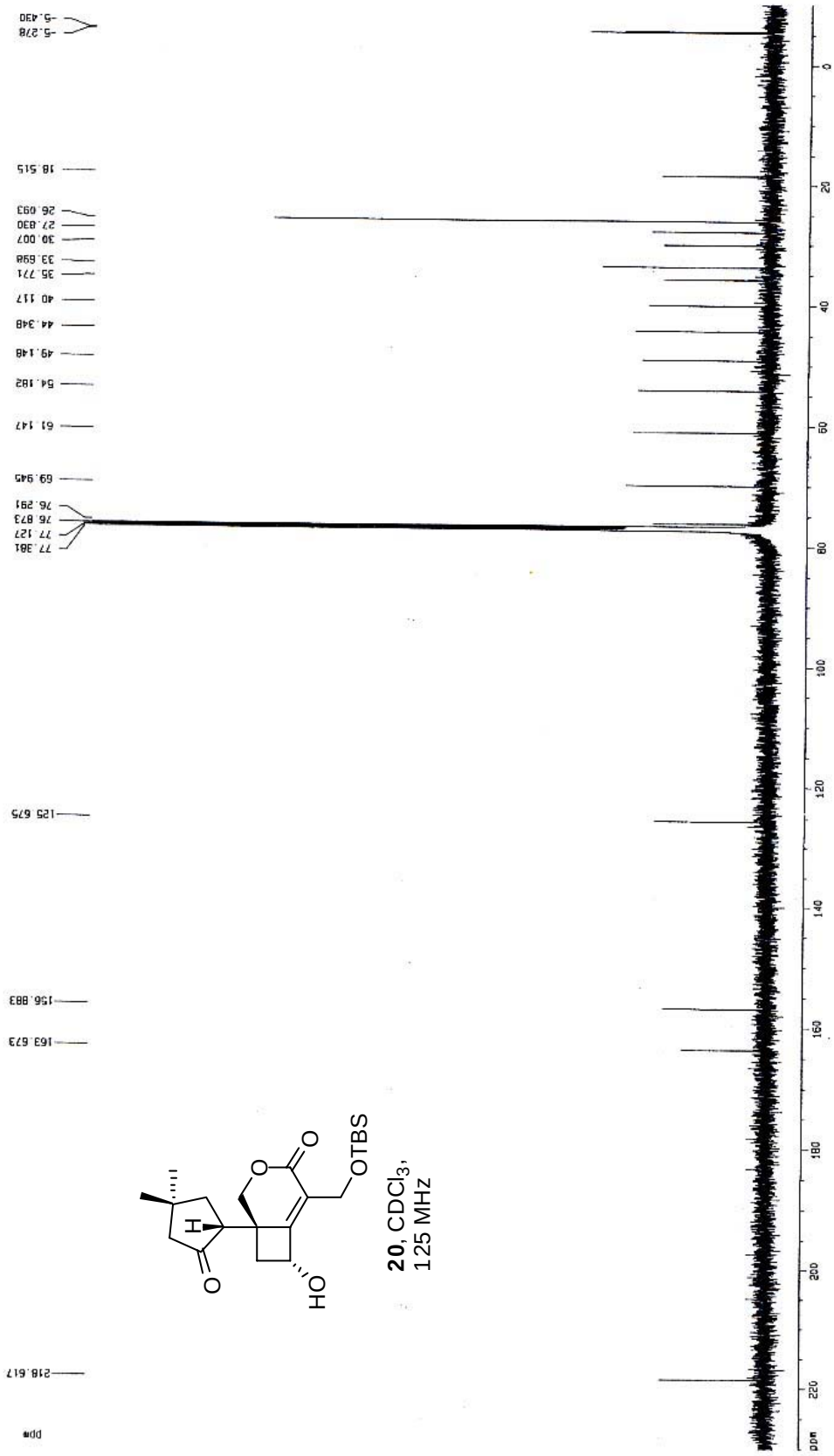

OTBS
HO
O
O
O
H
19, $CDCl_3$,
500 MHz



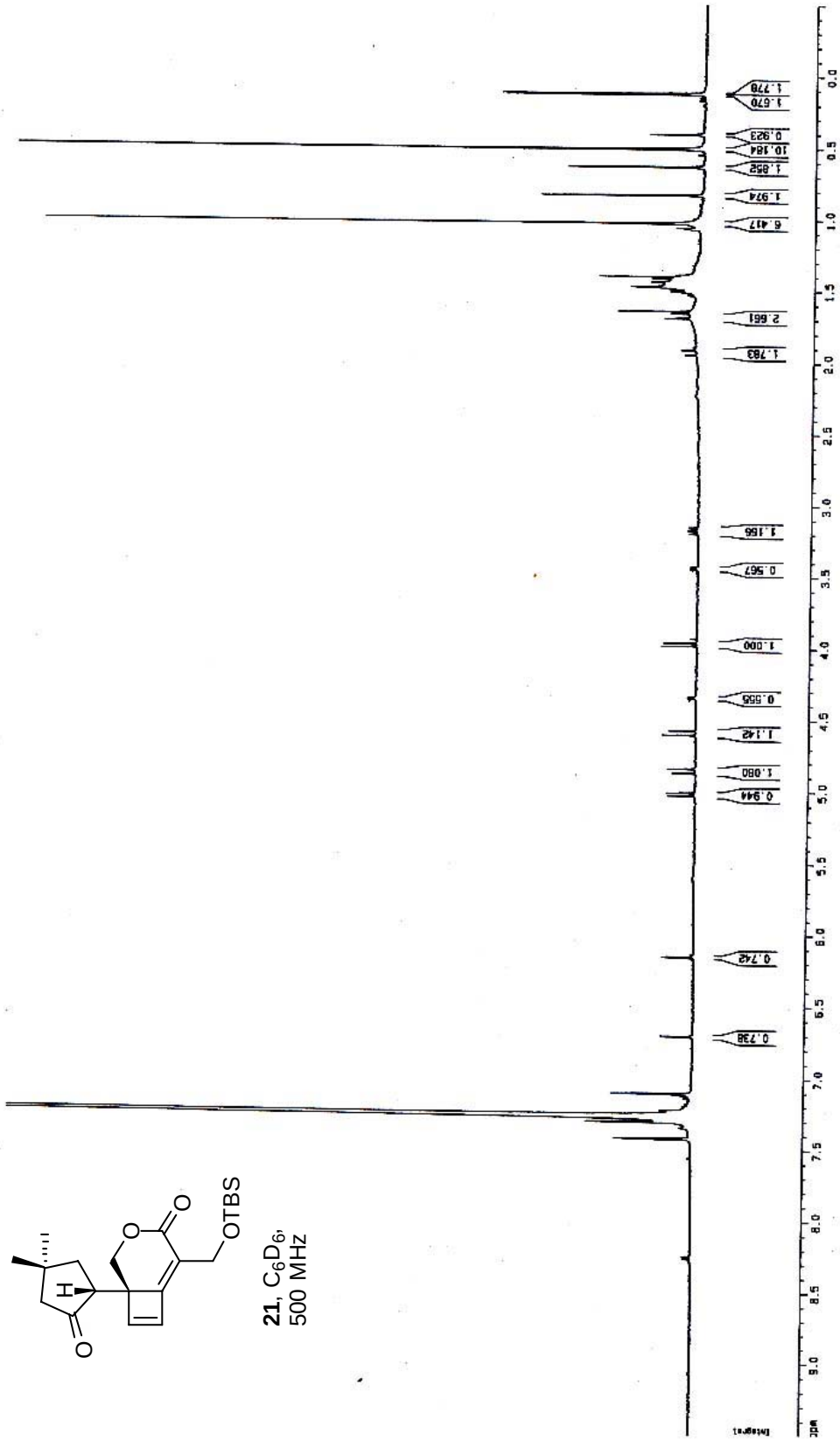
19, $CDCl_3$, 125 MHz

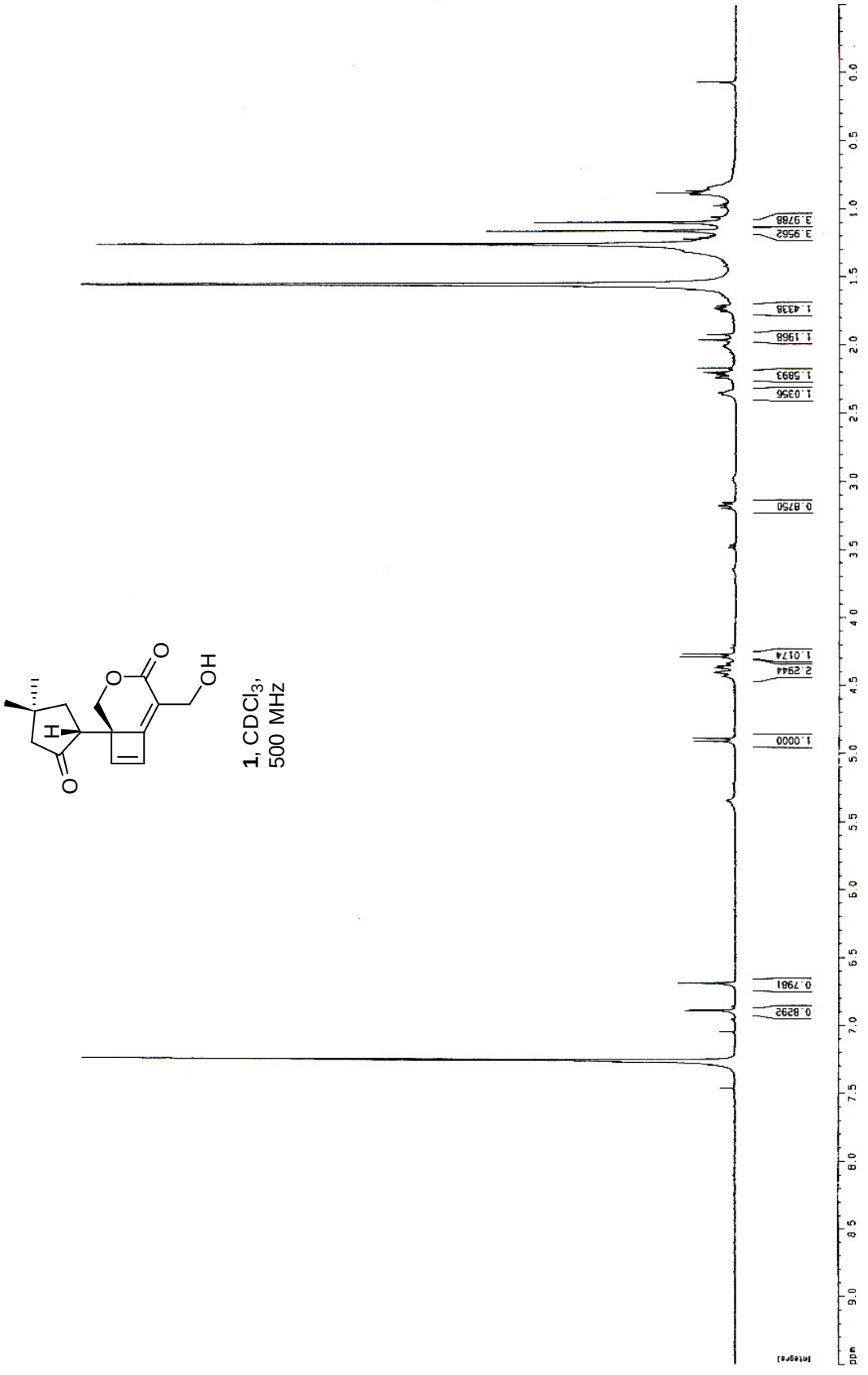


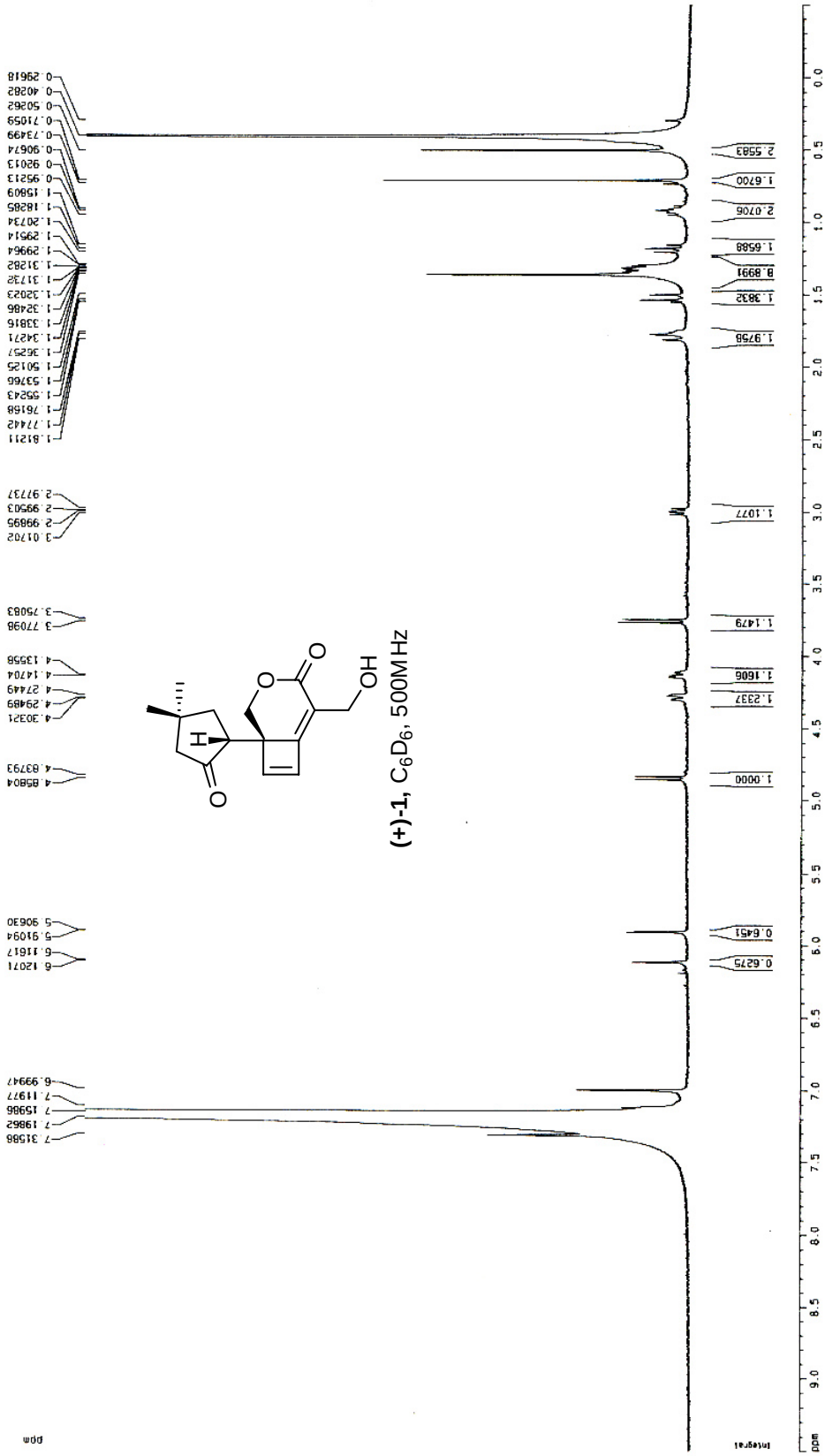
20, $CDCl_3$, 500 MHz

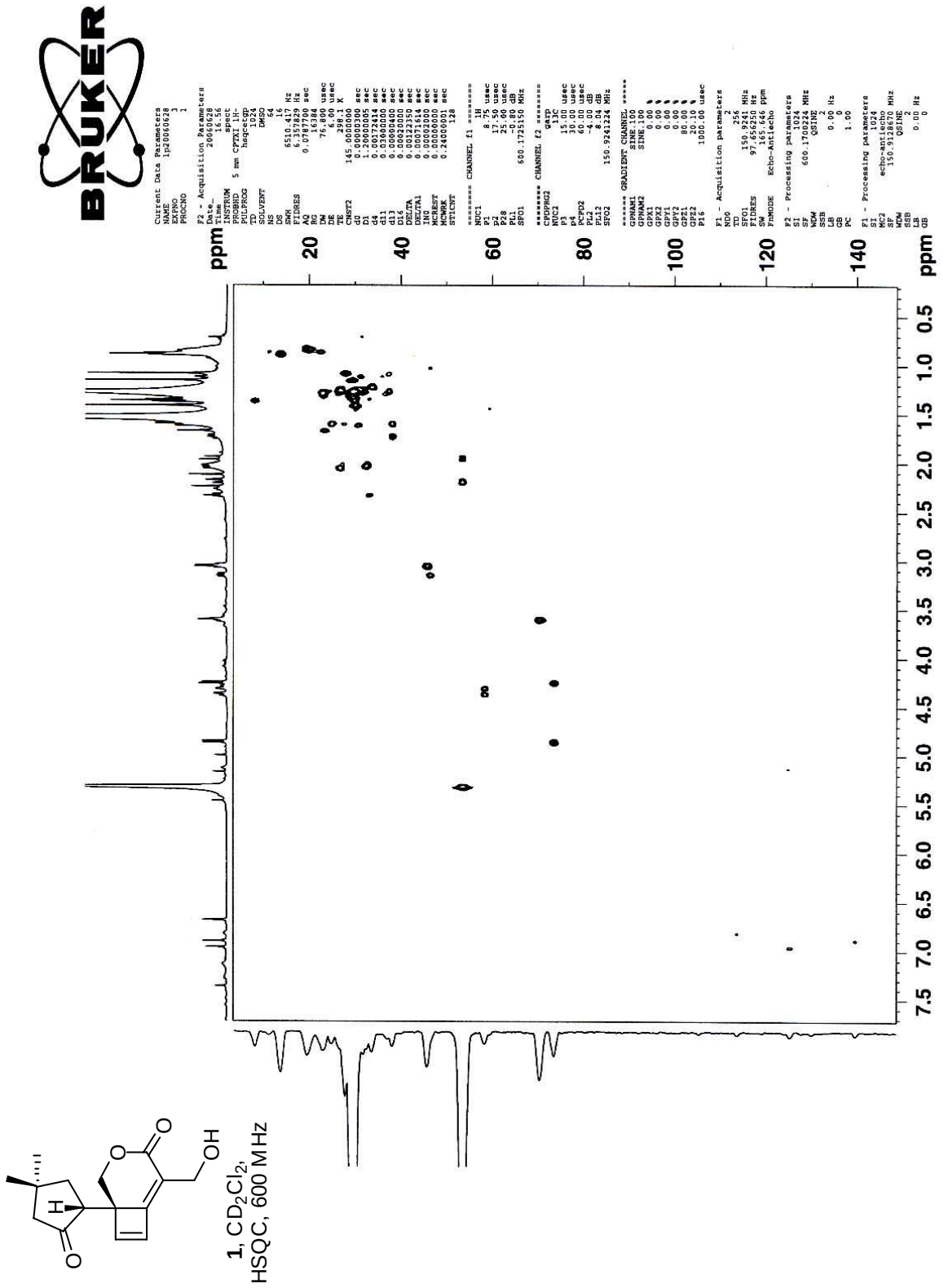


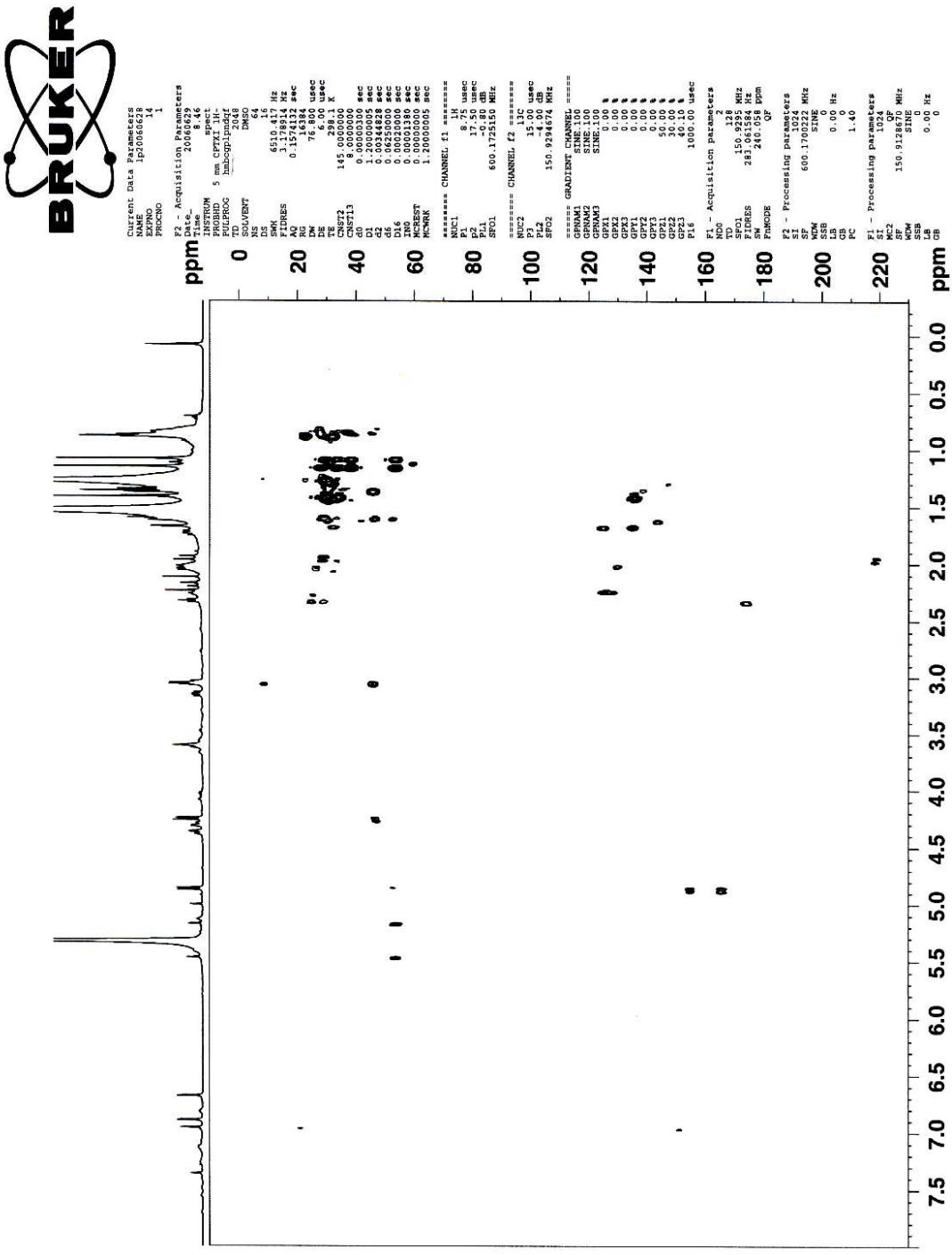
20, $CDCl_3$, 125 MHz


OTBS
O
O
O
H
21, C6D6,
500 MHz
1.778
3.670
0.923
10.184
1.852
1.974
6.417
2.661
1.783
3.166
0.567
1.000
0.555
1.142
1.080
0.944
0.742
0.738


O
O
OH
H
O
1, $CDCl_3$,
500 MHz
3.9788
3.9562
1.4338
1.1968
1.5893
1.0356
0.8750
1.0174
2.2944
1.0000
0.7981
0.8292
ppm


(+)-1, C6D6, 500MHz
OH
O
O
H
ppm
integral


1, CD_2Cl_2,
HSQC, 600 MHz
ppm
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
20 40 60 80 100 120 140



1, CD_2Cl_2,
HMBC, 600 MHz