Synthesis of the Left-hand Portion of Geldanamycin Using an Anti Glycolate Aldol Reaction

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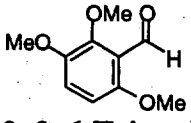
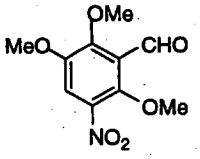
Supplementary Material

General Information. Air and water sensitive reactions were performed in flame-dried glassware under a nitrogen atmosphere. Air and moisture sensitive reagents were introduced via dry syringe and cannula. Methylene chloride, toluene, acetonitrile, triethylamine and pyridine were distilled from CaH_2. THF and diethyl ether were distilled from sodium benzophenone ketyl. DMF was stored over molecular sieves. Reagents were purchased from Aldrich and Lancaster. Flash chromatography was carried out using 60-230 mesh silica gel. Radial chromatography was performed using 1, 2, and 4 mm plates loaded with 230-400 mesh PF-254 gypsum bound silica. Analytical thin-layer chromatography was performed with Merck silica gel 60 F_{254}, 0.25 mm pre-coated TLC plates. TLC plates were visualized using UV_{254} and cerium molybdate with charring. All ^1H NMR spectra were obtained with either 300 or 500 MHz Varian spectrometers using TMS (0.0 ppm) or chloroform (7.26 ppm) as an internal reference. Signals are reported as m (multiplet), s (singlet), d (doublet), t (triplet), q (quartet), bs (broad singlet), ABq (AB quartet); and coupling constants are reported in hertz (Hz). ^{13}C NMR were obtained with either 75 or 125 MHZ Varian spectrometers using chloroform (77.2 ppm) as the internal standard. Infrared spectra were obtained on a Perkin Elmer FTIR instument. Mass spectral data (HRMS, CI, EI, FAB) were obtained from the Brigham Young University mass spectrometry facility. Optical rotations were obtained using the sodium D line. Combustion analysis was performed by M-H-W Laboratories, Phoenix, AZ.

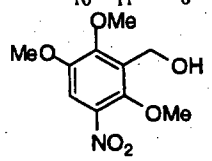


2, 3, 6-Trimethoxybenzaldehyde. A flame-dried 3-neck 1 L round bottom flask equipped with reflux condenser and a pressure equalized dropping funnel was charged with 1, 2, 4-trimethoxybenzene **5** (20.0 g, 119 mmol) and 400 mL of anhydrous Et_2O. The solution was then heated to reflux under a nitrogen atmosphere and *n*-BuLi (89.3 mL, 1.6 M hexanes) was *cautiously* added over 20 min via dropping funnel. The resulting milky solution was then refluxed for 2 h. After cooling to ambient temperature 37.0 mL (476 mmol) of dry DMF was slowly added over 15 min. The resulting bright yellow solution was then heated at reflux for an additional 2 h and then *cautiously* quenched upon cooling to ambient temperature with 120 mL of 6N HCl. After stirring for 1 h the aqueous layer was separated and extracted further with Et_2O (3 x 200mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. Flash chromatography (20% EtOAc/Hexanes) afforded the title compound, 15.8 g (68%) as a yellow oil. TLC R_f = 0.50 (50% EtOAc/Hexanes) ^1H NMR ($CDCl_3$, 300 MHz) δ 10.44 (s, 1H),

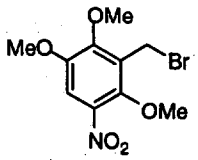
7.08 (d, J = 9.3 Hz, 1H), 6.64 (d, J = 9.0 Hz, 1H), 3.91 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 189.9, 155.0, 152.3, 147.0, 119.8, 119.3, 106.5, 62.2, 56.9, 56.4; IR (neat) 2938-2763, 1690, 1653, 1636, 1487, 1436; HRMS (EI^+) found 196.0725 M^+, calcd for $C_{10}H_{12}O_4$ 196.0736.



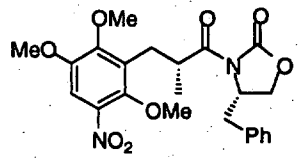
5-Nitro-2,3,6-trimethoxybenzaldehyde (6). A 1 L erlenmeyer flask was charged with 2,3,6-trimethoxybenzaldehyde (15.8 g, 80.6 mmol) and 80 mL glacial acetic acid and warmed to 60 °C. To the warm stirring solution, a premixed solution consisting of 42 mL of 70% HNO_3 and 160 mL glacial acetic acid was slowly added. The resulting orange-yellow solution was stirred for 0.5 h at that temperature and then allowed to cool to ambient temperature. Then 130 mL of cold H_2O was added with crystallization and the mixture was then stored in the freezer overnight. The resulting crystals were then vacuum filtered and washed thoroughly with ice cold H_2O (3 x 50 mL) to afford the title compound, 16.1g (83%) as light yellow crystals: TLC R_f= 0.20 (20% EtOAc/Hex); ^1H NMR ($CDCl_3$, 300 MHz) δ 10.38 (s, 1H), 7.63 (s, 1H), 4.05 (s, 3H), 3.97 (s, 3H), 3.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 188.3, 155.9, 148.9, 148.6, 139.1, 125.1, 113.0, 64.7, 62.4, 56.6; IR (thin film) 3000-2800, 1698, 1576, 1522, 1479, 1429, 1404, 1362, 1261 cm^{-1}; mp = 106-108 °C; HRMS (EI^+) found 241.0593 M^+, calcd for $C_{10}H_{11}NO_6$ 241.0586; Anal. calcd for $C_{10}H_{11}NO_6$: C, 49.80; H, 4.60. Found: C, 49.66; H, 4.49.



5-Nitro-2,3,6-trimethoxybenzyl alcohol. A 500 mL round bottom flask was charged with aldehyde **6** (8.20 g, 34.0 mmol) and 170 mL THF. To the stirred solution, at ambient temperature under a nitrogen atmosphere, was added $NaBH_4$ (1.29 g, 34.0 mmol). The resulting light orange mixture was stirred for 1 h before being diluted with 30 mL of H_2O and quenched to a bright yellow solution with 5 mL of 1M HCl. The solution was allowed to stir for 0.5 h and then diluted with 150 mL of Et_2O. The mixture was washed with 100 mL of 1 N HCl and the layers were separated, and the aqueous layer was extracted further (3 x 150 mL) with Et_2O. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. The crude light orange residue was directly filtered over a silica gel plug (50% EtoAc/hexanes) to afford the title compound 8.14 g (98%) as a light yellow crystalline solid. TLC R_f= 0.18 (30% EtOAc/hexanes); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.49 (s, 1H), 4.76 (bs, 2H), 4.01 (s, 3H), 3.94 (s, 3H), 3.91 (s, 3H), 2.41 (bs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.9, 148.6, 147.5, 138.6, 130.2, 108.8, 63.9, 61.8, 56.4, 55.2; IR (thin film) 3421, 2947, 1576, 1522, 1484, 1427, 1341, 1284, 1252 cm^{-1}; mp = 68-70 °C HRMS (CI^+) found 243.0738 M^+, calcd 243.0743 for $C_{10}H_{13}NO_6$; Anal. calcd for $C_{10}H_{13}NO_6$: C, 49.38; H, 5.39. Found: C, 49.55; H, 5.35.

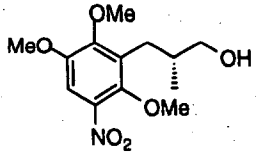


5-Nitro-2,3,6-trimethoxybenzyl bromide (7). A 250 mL round bottom flask was charged with 5-Nitro-2,3,6-trimethoxybenzyl alcohol (2.00 g, 8.23 mmol) and 20 mL of anhydrous Et_2O. Then the solution was stirred under a nitrogen atmosphere at ambient temperature and dry pyridine (0.014 mL, 0.165 mmol) was added followed by dropwise addition of phosphorous tribromide (0.31 mL, 3.29 mmol) over 5 min. The resulting light yellow solution, with visible off white precipitate, was stirred for 0.5 h and then diluted with 20 mL Et_2O and quenched with 20 mL H_2O. The solution was allowed to stir further for 10 min and then the layers were separated. The aqueous phase was extracted further with Et_2O (4 x 50 mL). The combined organic layers were washed with 100 mL of saturated $NaHCO_3$ solution. The organic layer was then dried over anhydrous $MgSO_4$ and concentrated. The residue was then filtered over a silica gel plug (30% EtOAc/hexanes) to afford the title compound, 2.35g (93 %) as a light yellow crystalline solid. The product may also be effectively recrystallized from EtOAc/hexanes. TLC R_f= 0.71 (30% EtOAc/ hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52 (s, 1H), 4.62 (s, 2H), 4.09 (s, 3H), 4.01 (s, 3H), 3.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.0, 148.6, 147.6, 138.2, 128.3, 109.5, 63.2, 61.5, 56.5, 21.4; mp = 100-102 °C; HRMS (CI$^+$) found 305.9972 $[M+H]^+$, calcd 305.9977 for $C_{10}H_{12}BrNO_5$; Anal. calcd for $C_{10}H_{12}BrNO_5$: C, 39.24; H, 3.95. Found: C, 39.45; H, 4.09.

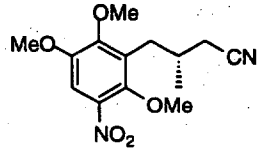


(4*S*)-4-Benzyl-3-[(2*R*)-2-methyl-3-(5-nito-2,3,6-trimethoxyphenyl)-propionyl]-oxazolidin-2-one (8). A flame dried 250 mL round bottom flask was charged with (4*S*)-4-benzyl-3-propionyl-oxazolidin-2-one (3.42 g, 14.7 mmol) and 65 mL of anhydrous THF. The solution was cooled to –78 °C under a nitrogen atmosphere and NaHMDS (16.1 mL, 1.0 M THF) was added dropwise. The resulting solution was stirred at –78 °C for 10 minutes and then bromide **7** (4.94 g, 16.1 mmol) was added slowly as a THF (10 mL) solution down the wall of the flask. The mixture was then allowed to stir for 3.5 h before being quenched at –78 °C by the careful addition of 10 mL of saturated NH_4Cl solution. Upon warming to ambient temperature the solution was diluted with 200 mL Et_2O and 150 mL of saturated NH_4Cl solution. Separation of the organic layer was followed by further extraction of the aqueous layer with Et_2O (4 x 200 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. The diastereoselectivty was >19:1 as determined by ^{1}H NMR of the crude reaction material. Flash chromatography (gradient 10-30% EtOAc/hexanes) afforded the title compound, 5.80 g (88%) as a light yellow foam. TLC R_f= 0.38 (30% EtOAc/hexanes); $[\alpha]_D^{25}$ = +18.6 ° (*c* 0.14 , $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42 (s, 1H), 7.36-7.24 (m's, 3H), 7.22-7.19 (m, 2H), 4.70-4.63 (m, 1H), 4.21-4.09 (m, 3H), 3.98 (s, 3H), 3.89 (s, 3H), 3.86 (s, 3H), 3.34 (dd, *J* = 3.0 Hz, 13.5 Hz, 1H), 3.14 (dd, *J* = 13.2 Hz, 6.3 Hz, 1H), 3.02 (dd, *J* = 7.8 Hz, 13.2 Hz, 1H), 2.73 (dd, *J* = 9.6 Hz, 13.5 Hz, 1H), 1.16 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.8, 153.2, 148.4, 148.1, 138.2, 135.7, 129.6, 129.1, 128.9, 127.4, 107.8, 66.2, 62.7, 61.2, 56.4, 55.7, 37.8, 37.6, 27.9, 17.5; IR (thin

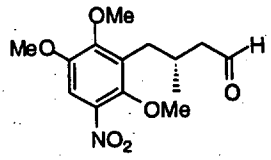
film) 3024, 2973, 2940, 2838, 1778, 1697, 1575, 1518, 1481, 1455, 1424, 1385, 1347, 1282, 1247, 1210 cm^{-1}; HRMS (CI^+) found 458.1682 M^+ , calcd 485.1689 for $C_{23}H_{26}N_2O_8$.



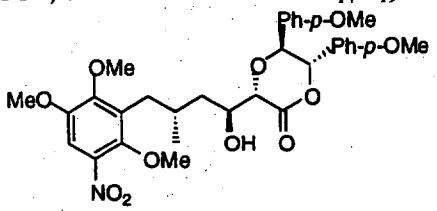
(2*R*)-2-Methyl-3-(5-nitro-2,3,6-trimethoxy-phenyl)-propan-1-ol. A 250 mL round bottom flask was charged with adduct **8** (2.35 g, 5.13 mmol), 65 mL Et_2O and 0.2 mL of H_2O. The resulting solution was then cooled to 0 °C under a nitrogen atmosphere and $LiBH_4$ (5.60 mL, 2.0 M THF) was slowly added. The resulting cloudy solution was stirred for 0.5 h at 0 °C and then quenched by careful addition of 30 mL of saturated NH_4Cl solution. The layers were separated and the aqueous layer was extracted further with CH_2Cl_2 (3 x 50 mL) and the combined organic layers were washed with brine (100 mL). The organic layer was separated, dried over anhydrous $MgSO_4$ and concentrated. Flash chromatography (gradient 30-40% EtoAC/hexanes) afforded title compound, 1.40 g (96%), as a light yellow sticky solid. TLC R_f = 0.19 (30% EtOAc/hexanes); $[\alpha]_D^{23}$ = -14.5 ° (*c* 0.20 , $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.41 (s, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.87 (s, 3H), 3.39 (app t, *J* = 5.1 Hz, 2H), 2.74 (dd, *J* = 12.9 Hz, 8.4 Hz, 1H), 2.63 (dd, *J* = 12.9 Hz, 6.3 Hz, 1H), 2.21 (app t, *J* = 6.0 Hz, 1H), 2.00-1.86 (m, 1H), 1.00 (d, *J* = 6.9 Hz, 3H) ; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.6, 148.6, 147.6, 138.6, 130.7, 107.2, 66.6, 62.8, 61.2, 56.3, 36.6, 27.9, 17.4; IR (thin film) 3417, 2942, 2871, 1575, 1519, 1480, 1424, 1339, 1282, 1245 cm^{-1}; HRMS (CI^+) found 286.1290 $[M+H]^+$, calcd 286.1289 for $C_{13}H_{20}NO_6$.



(3*R*)-3-Methyl-4-(5-nitro-2,3,6-trimethoxyphenyl)-butyronitrile (9). A flame-dried 100 mL round bottom flask was charged with (2*R*)-2-Methyl-3-(5-nitro-2,3,6-trimethoxy-phenyl)-propan-1-ol (4.30 g, 15.1 mmol) and 50 mL of anhydrous Et_2O and cooled to 0 °C under a nitrogen atmosphere. To the stirred solution was added triphenylphosphine (7.91 g, 30.2 mmol) and then DEAD (4.75 mL, 30.2 mmol) dropwise over a period of 15 min. The thick mixture, with a light yellow precipitate, was stirred for 10 min further before acetone cyanohydrin (1.6 mL, 17.5 mmol) was introduced dropwise as an anhydrous Et_2O solution (10 mL) with the disappearance of the precipitate. The resulting solution was allowed to warm to ambient temperature and stirred for 20 h. The solution was then filtered directly over a silica gel plug (eluting with 50% EtOAc/hexanes). Concentration was followed by flash chromatography (gradient 10-20% EtOAc/hexanes) to afford the title compound 3.60 g (81%) as a viscous yellow oil. TLC R_f = 0.39 (30% EtOAc/hexanes); $[\alpha]_D^{25}$ = -24.3 ° (*c* 0.14, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.44 (s, 1H), 3.96 (s, 3H), 3.91 (s, 3H), 3.86 (s, 3H), 2.76 (dd, *J* = 7.8, 12.6 Hz, 1H), 2.71 (dd, *J* = 6.9, 12.9 Hz, 1H), 2.30 (app d, *J* = 6.3 Hz, 2H), 2.26-2.13 (m, 1H), 1.11 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.6, 148.5, 147.7, 138.4, 129.1, 118.9, 107.7, 62.6, 61.1, 56.3, 31.6, 30.7, 24.3, 19.8; IR (neat) 2941, 1748, 1731, 1575, 1521, 1481, 1424, 1340, 1288, 1247 cm^{-1}; HRMS (CI^+) found 294.1212 M^+ , calcd 294.1216 for $C_{14}H_{18}N_2O_5$.

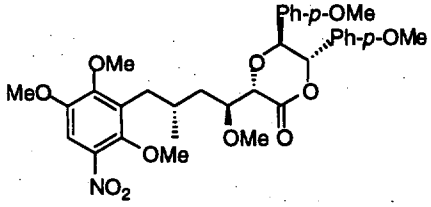


(3*R*)-3-Methyl-4-(5-nitro-2,3,6-trimethoxyphenyl)-butyraldehyde (3). A flame-dried 25 mL round bottom flask was charged with cyanide **9** (0.150 g, 0.510 mmol) and 6.5 mL of dry toluene. The solution was cooled to –78 °C under a nitrogen atmosphere and DIBAL (0.68 mL, 1.5 M toluene) was added slowly. The resulting reddish-orange solution was allowed to warm to ambient temperature over 1 h at which time 0.2 mL of acetone, 0.2 mL EtOAc, and 0.2 mL pH 7 phosphate buffer were added in sequence. The mixture was then stirred vigorously for 20 min and then anhydrous Na_2SO_4 was added maintaining the vigorous stirring for an additional 20 min. The resulting yellow solution was then filtered over a pad of silica gel and Na_2SO_4. Concentration and subsequent purification via radial chromatography (20% EtOAc/hexanes) afforded the title compound, upon concentration, 0.140 g (92%) as a light yellow viscous oil. TLC R_f = 0.41 (30% EtOAc/hexanes); $[\alpha]_D^{25}$ = -17.0 ° (*c* 1.0, $CHCl_3$) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.71 (app t, *J* = 2.0 Hz, 1H), 7.42 (s, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.84 (s, 3H), 2.67 (d, *J* = 6.6 Hz, 2H), 2.50-2.26 (m's, 3H), 0.98 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 202.6, 152.8, 148.5, 147.8, 138.4, 130.0, 107.4, 62.5, 61.0, 56.3, 50.4, 31.3, 29.0, 20.4; IR (neat) 2941, 1683, 1558, 1521, 1480, 1457, 1339, 1287, 1246 cm^{-1}; HRMS (CI$^+$) found 297.1209 M$^+$, calcd 297.1212 for $C_{14}H_{19}NO_6$.

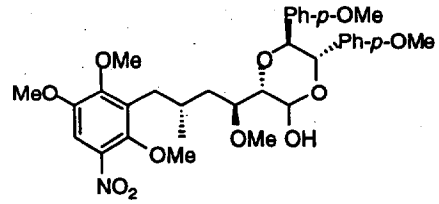


(3*S*, 5*S*, 6*S*)-3-[(1*S*, 3*R*)-1-Hydroxy-3-methyl-4-(5-nitro-2,3,6-trimethoxy-phenyl)-butyl]-5,6-bis-(4-methoxy-phenyl)-[1,4]dioxan-2-one (12). A flame-dried 100 mL round bottom flask was charged with oxypyrone **4** (0.233 g, 0.740 mmol) and 20 mL dry CH_2Cl_2. The solution was cooled to -78 °C under a nitrogen atmosphere and Et_3N (0.26 mL, 1.865 mmol) was added dropwise followed by *c*Hex_2BOTf (1.85 mL, 1.0 M hexane) which was also added dropwise over 5 min. The resulting solution was stirred at-78 °C for 3h at which time aldehyde **3** (0.264 g, 0.888 mmol) was added in 1 mL dry CH_2Cl_2 dropwise over 10 min. The resulting solution was stirred at -78 °C for 3 h at which time it was quenched at that same temperature by the addition of pH 7 buffer (2.5 mL), MeOH (2 mL) and 30% aqueous H_2O_2 (0.5 mL). The solution was stirred vigorously for 1 h and then warmed to ambient temperature were it was diluted with 50 mL Et_2O and 10 mL of dilute HCl. The aqueous layer was extracted with Et_2O (4 x 50 mL) and then the combined organic layers were washed with 30 mL of dilute $NaHCO_3$ solution. Drying of the organic solution with anhydrous $MgSO_4$ was followed by concentration and radial chromatography to afford the title compound 0.32 g (70%) and a minor stereoisomer 0.018g as a foamy yellow solid. The selectivity was found to be 15:1 (anti/anti) via ^{1}H NMR of the crude reaction material. TLC R_f = 0.69 (50% EtOAc/hexanes); $[\alpha]_D^{23}$ = -109.3 ° (*c* 0.80 , $CHCl_3$) ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37 (s, 1H), 6.99 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.78 (d, *J* = 9.0 Hz, 2H), 6.76 (d, *J* = 9.5 Hz, 2H), 5.36 (d, *J* = 9.5 Hz, 1H), 4.91 (d, *J* = 9.5 Hz, 1H), 4.54 (d, *J* = 5.0 Hz, 1H), 4.28-4.23 (m, 1H), 3.91 (s, 3H), 3.86 (s, 3H), 3.82 (s, 3H), 3.77 (s, 3H),

3.76 (s, 3H), 2.77 (br s, 1H), 2.68 (dd, J = 7.0, 12.5 Hz, 1H), 2.64 (dd, J = 7.0, 12.0 Hz, 1H), 2.15-2.07 (m, 1H), 1.72 (ddd, J = 4.5, 10.5, 13.7 Hz, 1H), 1.64 (ddd, J = 3.0, 9.5, 13.9 Hz, 1H), 0.95 (d, J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.1, 160.3, 160.0, 153.0, 148.5, 148.0, 138.5, 131.0, 129.0, 128.7, 128.1, 126.8, 114.0, 107.3, 85.2, 78.3, 76.7, 71.4, 62.6, 61.1, 56.3, 55.4, 40.4, 32.6, 30.3, 19.4; HRMS (FAB+) found 634.2256 [M+ Na^+]$^+$, calcd 634.2265 for $C_{32}H_{37}NO_{11}Na$.

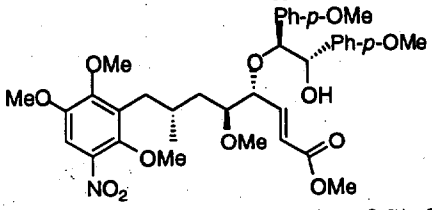


(3*S*, 5*S*, 6*S*)-3-[(1*S*, 3*R*)-1-Methoxy-3-methyl-4-(5-nitro-2,3,6-trimethoxy-phenyl)-butyl]-5,6-bis-(4-methoxy-phenyl)-[1,4]dioxan-2-one. A flame-dried 25 mL round bottom flask was charged with aldol adduct **12** (0.280 g, 0.458 mmol) and 6 mL of dry CH_2Cl_2. The solution was cooled to 0 °C under nitrogen atmosphere and proton sponge (0.196 g, 0.916 mmol) was added followed by Me_3OBF_4 (0.135 g, 0.916 mmol). The resulting heterogeneous light brown solution was then allowed to slowly warm to ambient temperature and was stirred for 8 h. The mixture was then filtered directly over a silica plug eluting with 50% EtOAc/hexanes and concentrated. Radial chromatography (20% EtOAc/hexanes) afforded the title compound, 0.260 g (91%), as a yellow foamy solid. TLC R_f = 0.73 (50% EtOAc/hexanes); $[\alpha]_D^{23}$ = -142.7 ° (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (s, 1H), 7.01 (d, J = 8.7 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 6.78 (d, J = 8.7 Hz, 2H), 6.74 (d, J = 8.9 Hz, 2H), 5.37 (d, J = 8.7 Hz, 1H), 4.98 (d, J = 8.7 Hz, 1H), 4.88 (d, J = 2.1 Hz, 1H), 3.95-3.88 (m, 1H), 3.91 (s, 3H), 3.85 (s, 6H), 3.77 (s, 3H), 3.75 (s, 3H), 3.44 (s, 3H), 2.70-2.59 (m, 2H), 2.11-1.98 (m, 1H), 1.90 (ddd, J = 5.0, 9.0, 13.8 Hz, 1H), 1.56 (ddd J = 4.80, 9.0, 13.5 Hz, 1H), 0.96 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.2, 160.0, 159.8, 153.8, 152.9, 148.5, 148.0, 138.4, 130.9, 128.9, 128.2, 127.4, 113.9, 107.2, 85.7, 82.8, 77.9, 74.3, 62.6, 61.0, 57.7, 56.2, 55.4, 38.0, 32.3, 30.6, 19.9; HRMS (FAB$^+$) found 648.2424 [M+ Na^+]$^+$, calcd 648.2421 for $C_{33}H_{39}NO_{11}Na$.

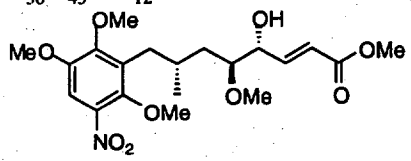


(3*S*, 5*S*, 6*S*)-3-[(1*S*, 3*R*)-1-Methoxy-3-methyl-4-(5-nitro-2,3,6-trimethoxy-phenyl)-butyl]-5,6-bis-(4-methoxy-phenyl)-[1,4]dioxan-2-ol (13). A flame-dried 100 mL round bottom flask was charged with adduct **12** (0.304 g, 0.486 mmol) and 15 mL of dry toluene. The solution was cooled to -78 °C under a nitrogen atmosphere and DIBAL (1.3 mL, 1.5 M toluene) was added dropwise over 15 min. The resulting red-orange solution was then allowed to stir at -78 °C for an additional 25 min before being quenched, at the same temperature, by the addition of 0.5 mL pH 7 buffer solution and 0.5 mL of MeOH. The solution turned bright yellow and was allowed to warm to ambient temperature. Then anhydrous $MgSO_4$ was added and the solution was vigorously stirred for 20 min. The crude solution was then filtered over celite and anhydrous Na_2SO_4 plug eluting with EtOAc. The residue was then concentrated and then purified via radial chromatography (gradient 20-30% EtOAc/hexanes) to afford the title compound, 0.255 g (84%) (9:1 mixture of anomers; from ^{1}H NMR), as a light yellow foamy solid. TLC R_f=0.13 (30%

EtOAc/hexanes); Major anomer ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.16 (s, 1H), 6.91 (d, J = 9.0 Hz, 2H), 6.84 (d, J = 9.0 Hz, 2H), 6.71 (d, J = 9.0 Hz, 2H), 6.68 (d, J = 9.0 Hz, 2H), 5.39 (d, J = 5.0 Hz, 1H), 4.94 (d, J = 10.0 Hz, 1H), 4.32 (d, J = 9.0 Hz, 1H), 4.06-4.02 (m, 1H), 3.84 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H), 3.74 (s, 6H), 3.50-3.46 (m, 1H), 3.47 (s, 3H), 3.11 (d, J = 4.5 Hz, 1H), 2.56 (d, J = 7.0 Hz, 2H), 2.14-2.10 (m, 1H), 1.68 (ddd, J = 2.0, 10.0, 15.0 Hz, 1H), 1.54 (ddd, J = 2.5, 7.0, 15.0 Hz, 1H), 1.04 (d, J = 6.5 Hz, 3H); HRMS (FAB$^+$) found 650.2575 [M+ Na$^+$]$^+$, calcd 650.2578 for $C_{33}H_{41}NO_{11}Na$.

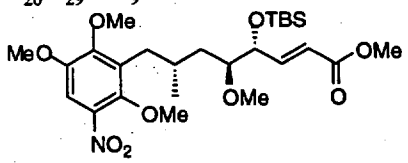


(2*E*, 4*R*, 5*S*, 7*R*)-4-[(1*S*, 2*S*)-2-Hydroxy-1,2-bis-(4-methoxy-phenyl)-ethoxy]-5-methoxy-7-methyl-8-(5-nitro-2,3,6-trimethoxy-phenyl)-oct-2-enoic acid methyl ester (14). A 50 mL round bottom flask was charged with lactol **13** (0.205 g, 0.327 mmol), 10 mL of dry CH_3CN, dry LiCl (0.027 g, 0.653 mmol), and methyl (triphenylphosphoranylidene) acetate (0.218 g, 0.653 mmol) was added portions. The resulting solution was heated at reflux under nitrogen atmosphere for 3.5 h at which time the solution was concentrated in vacuo. The crude residue was dissolved in CH_2Cl_2 and filtered directly over a silica gel plug (eluting with 50% EtOAc/hexanes). The residue was then purified via radial chromatography (30% EtOAc/hexanes) to afford the title compound, 0.207 g (93%) (>19:1, E/Z; from 1H NMR), as a light yellow foamy solid. TLC R_f = 0.57 (45% EtOAc/hexanes); $[\alpha]_D^{20}$ = -75.8 ° (*c* 1.1, $CHCl_3$); 1H NMR ($CDCl_3$, 300 MHz) 7.40 (s, 1H), 6.93 (d, J = 9.0 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 6.75-6.68 (m, 1H), 6.70 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.7 Hz, 2H), 5.91 (dd, J = 1.8, 15.6 Hz, 1H), 4.66 (d, J = 8.7 Hz, 1H), 4.38 (d, J = 8.4 Hz, 1H), 4.39-4.35 (m, 1H), 4.02 (d, J = 1.2 Hz, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.85 (s, 3H), 3.75 (s, 3H), 3.74 (s, 3H), 3.69 (s, 3H), 3.40 (s, 3H), 3.46-3.40 (m, 1H), 2.70 (dd, J = 5.7, 12.6 Hz, 1H), 2.57 (d, J = 8.7, 12.9 Hz, 1H), 2.10-1.97 (m, 1H), 1.80 (ddd, J = 4.2, 9.9, 14.7 Hz, 1H), 1.27-1.18 (m, 1H), 0.81 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.6, 159.4, 159.1, 152.9, 148.5, 148.0, 145.6, 138.4, 131.7, 131.0, 130.3, 129.0, 128.6, 122.2, 113.6, 113.4, 107.2, 88.0, 82.1, 78.9, 78.5, 62.6, 61.1, 58.3, 56.3, 55.3, 51.8, 37.2, 32.5, 30.6, 19.4;HRMS (FAB$^+$) found 706.2831 [M+ Na$^+$]$^+$, calcd 706.2840 for $C_{36}H_{45}NO_{12}Na$.

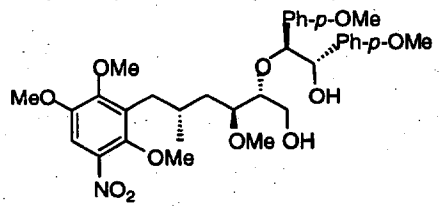


(4*R*, 5*S*, 7*R*)-4-Hydroxy-5-methoxy-7-methyl-8-(5-nitro-2,3,6-trimethoxy-phenyl)-oct-2-enoic acid methyl ester. A 25 mL round bottom flask was charged with enoate **14** (0.190 g, 0.278 mmol), 5 mL CH_3CN/H_2O 9:1 and cooled to 0 °C. To the solution was added in portion ceric ammonium nitrate (0.381 g, 0.695 mmol). The resulting orange-yellow solution was stirred for 0.5 h at which time it was diluted with 10 mL Et_2O and 10 mL H_2O. The layers were separated and the aqueous layer was extracted further with Et_2O (4 x 10 mL). The combined organic layers were then dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue was then purified via radial chromatography (30-50% EtOAc/hexanes) to afford the title compound, 0.111 g (93%), as a viscous yellow oil. TLC R_f = 0.16 (30% EtOAc/hexanes);

$[\alpha]_D^{23}$ = -7.20 ° (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.39 (s, 1H), 6.91 (dd, *J* = 4.5, 15.6 Hz, 1H), 6.15 (dd, *J* = 1.8, 15.6 Hz, 1H), 4.60-4.55 (m, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.83 (s, 3H), 3.76 (s, 3H), 3.44-3.36 (m, 1H), 3.41 (s, 3H), 2.66 (dd, *J* = 6.0, 12.6 Hz, 1H), 2.56 (dd, *J* = 3.6, 12.3 Hz, 1H), 2.08-1.94 (m, 1H), 1.63 (ddd, *J* = 4.5, 9.6, 14.4 Hz, 1H), 1.17 (ddd, *J* = 3.6, 9.3, 14.4 Hz, 1H), 1.14 (d, *J* = 3.6 Hz, 1H), 0.83 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.9, 152.8, 148.4, 147.9, 146.2, 138.3, 130.9, 121.4, 107.1, 81.5, 70.9, 62.5, 61.0, 57.9, 56.2, 51.7, 36.5, 32.3, 30.2, 19.3; HRMS (FAB^+) found 450.1740 $[M+ Na^+]^+$, calcd 450.1740 for $C_{20}H_{29}NO_9Na$.

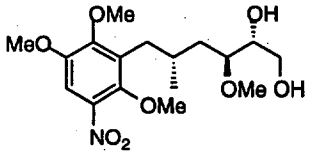


(4*R*, 5*S*, 7*R*)- 4-(*tert*-Butyl-dimethyl-silanyloxy)-5-methoxy-7-methyl-8-(5-nitro-2,3,6-trimethoxy-phenyl)-oct-2-enoic acid methyl ester (2). A 10 mL round bottom flask was charged with the preceding hydroxy-ester (0.110 g, 0.257 mmol) and 3 mL of dry CH_2Cl_2. The solution was stirred under a nitrogen atmosphere at ambient temperature and imidazole (0.070 g, 1.03 mmol) was added followed by TBSCl (0.078 g, 0.515 mmol). The resulting solution was stirred for 40 h at which time imidazole (0.017 g, 0.257 mmol) and TBSCl (0.039 g, 0.257 mmol) were again added. Stirring was continued for 8 h at which the solution was diluted with 10 mL CH_2Cl_2 and washed with 10 mL saturated NH_4Cl solution. The aqueous layer was extracted further with CH_2Cl_2 (3 x 10 mL). The combined organic layers were then dried over anhydrous $MgSO_4$ and concentrated. Radial chromatography (gradient 5-10% EtOAc/hexanes) afforded the title compound, 0.127 g (91%), as a viscous yellow oil. TLC R_f=0.26 (10% EtOAc/hexanes); $[\alpha]_D^{23}$ = -22.0 ° (*c* 2.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.36 (s, 1H), 6.93 (dd, *J* = 4.5, 15.6 HZ, 1H), 6.04 (dd, *J* = 1.8, 15.6 HZ, 1H), 4.36-4.33 (m, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.80 (s, 3H), 3.73 (s, 3H), 3.35 (s, 3H), 3.21 (dt, *J* = 2.7, 10.5 HZ, 1H), 2.62 (dd, *J* = 6.6, 12.9 HZ, 1H), 2.54 (dd, *J* = 8.1, 12.9 HZ, 1H), 2.06-1.92 (m, 1H), 1.51 (ddd, *J* = 3.9, 10.5, 14.4 HZ, 1H), 1.15 (ddd, *J* = 2.4, 9.9, 14.1 HZ, 1H), 0.87 (s, 9H), 0.82 (d, *J* = 6.6 HZ, 3H), 0.01 (s, 3H), -0.01 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.0, 152.9, 148.5, 148.4, 148.0, 138.3, 131.1, 121.2, 107.0, 82.8, 73.9, 62.4, 61.0, 58.8, 56.2, 51.7, 37.7, 32.6, 30.2, 25.9, 19.5, 18.3, -4.7, -4.8; HRMS (FAB^+) found 564.2623 $[M+ Na^+]^+$, calcd 564.2605 for $C_{26}H_{43}NO_9SiNa$.

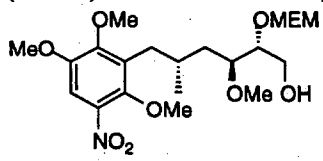


(2*R*, 3*S*, 5*R*)-2-[(1*S*, 2*S*)-2-Hydroxy-1,2-bis-(4-methoxy-phenyl)-ethoxy]-3-methoxy-5-methyl-6-(5-nitro-2,3,6-timethoxy-phenyl)-hexan-1-ol. A 50 mL round bottom flask was charged with aldol adduct **12** (0.260 g, 0.415 mmol), 8 mL of THF and 0.05 mL of MeOH. The solution was cooled to 0 °C under a nitrogen atmosphere and $LiBH_4$ (0.014 g; 0.620 mmol) was added. The resulting solution was allowed to slowly warm to ambient temperature and stir for 4 h at which time the solution was diluted with 20 mL Et_2O and quenched with 1 mL of saturated NH_4Cl solution. An additional 10 mL of NH_4Cl solution was added and the aqueous layer was further extracted with Et_2O (4 x 20 mL). The organic layers were combined and dried over anhydrous $MgSO_4$ concentration and radial chromatography afforded the title compound 0.260 g

(99%), as a light yellow foamy solid. TLC R_f = 0.23 (50% EtOAc / hexanes); $[\alpha]_D^{23}$ = -9.7 ° (*c* 0.70, $CHCl_3$) ^1H NMR ($CDCl_3$, 300 MHz) δ 7.41 (s, 1H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 2H), 6.74 (d, *J* = 8.7 Hz, 2H), 6.70 (d, *J* = 8.9 Hz, 2H), 4.65 (d, *J* = 8.7 Hz, 1H), 4.32 (d, *J* = 8.7 Hz, 1H), 4.24 (m, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.84 (s, 3H), 3.76 (s, 3H), 3.75-3.69 (m, 1H), 3.74 (s, 3H), 3.59-3.51 (m, 1H), 3.51-3.41 (m, 2H), 3.43 (s, 3H), 2.71 (dd, *J* = 6.0, 12.6 Hz, 1H), 2.60 (dd, *J* = 8.7, 12.6 Hz, 1H), 2.11-1.98 (m, 1H), 1.82 (ddd, *J* = 5.0, 9.3, 14.1 Hz, 1H), 1.72-1.62 (m, 1H), 1.45-1.25 (m, 1H), 0.86 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$,75 MHz) δ 159.4, 159.0, 152.8, 148.5, 147.9, 138.4, 131.8, 131.0, 130.9, 128.9, 128.5, 113.8, 113.3, 107.1, 88.2, 80.3, 80.0, 78.6, 62.8, 62.5, 61.0, 58.1, 56.2, 55.2, 37.8, 32.4, 30.6, 19.5; HRMS (FAB^+) found 652.2728 $[M+ Na^+]^+$, calcd 652.2734 for $C_{33}H_{43}NO_{11}Na$.

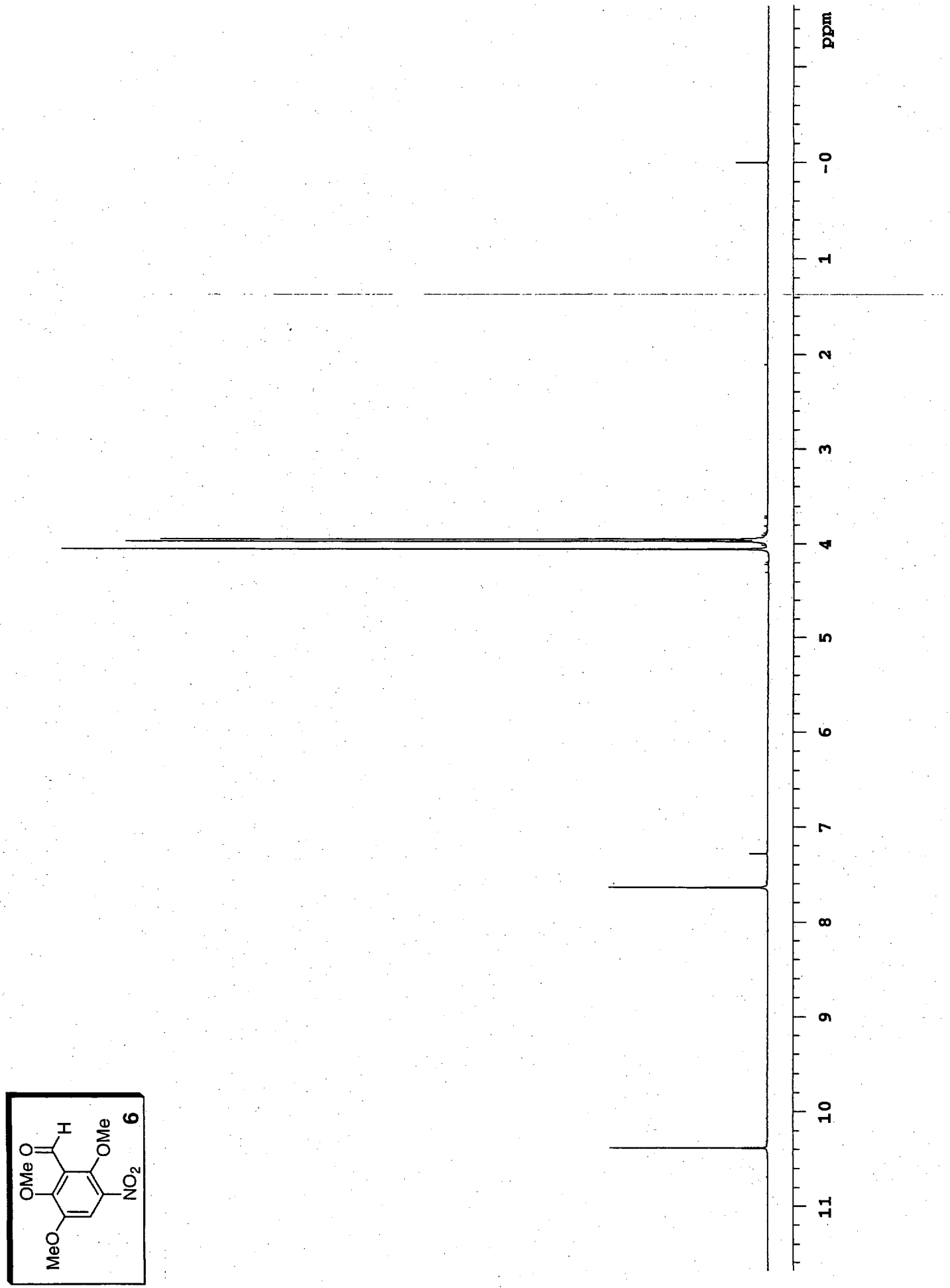


(2*R*, 3*S*, 5*R*)-3-Methoxy-5-methyl-6-(5-nitro-2,3,6-trimethoxy-phenyl)-hexan-1,2-diol (17). A 10 mL round bottom flask was charged with the preceding diol (0.091 g, 0.144 mmol) and CH_3CN / H_2O (10:1, 2 mL). The solution was cooled to 0 °C and ceric ammonium nitrate (0.198 g, 0.361 mmol) was added in portion over 3 min. The resulting light orange-yellow solution was then stirred at 0 °C for 30 min and diluted with 5 mL of Et_2O and 5 mL of H_2O. The layers were separated and the aqueous phase was extracted further with Et_2O (4 x 5 mL). The combined organic layers were dried over anhydrous $MgSO_4$. Concentration followed by radial chromatography provided the title compound 0.041 g (80%) as a viscous yellow oil. TLC R_f = 0.16 (50% EtOAc/hexanes); $[\alpha]_D^{25}$ = -17.6 ° (*c* 0.5, $CHCl_3$) ^1H NMR ($CDCl_3$, 300 MHz) δ 7.40 (s, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.84 (s, 3H), 3.68-3.56 (m, 1H), 3.59-3.15 (m, 2H), 3.45-3.38 (m, 1H), 3.40 (s, 3H), 2.96 (bs, 1H), 2.76 (bs, 1H), 2.67 (dd, *J* = 6.3, 12.6 Hz, 1H), 2.57 (dd, *J* = 8.4, 12.9 Hz, 1H), 2.07-1.97 (m, 1H), 1.62 (ddd, *J* = 4.8, 8.7, 13.8 Hz, 1H), 1.30 (ddd, *J* = 3.9, 9.0, 13.2 Hz, 1H), 0.88 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$,75 MHz) δ 152.8, 148.5, 147.9, 138.4, 130.9, 107.1, 81.3, 72.8, 63.5, 62.5, 61.0, 58.5, 56.3, 37.9, 32.3, 30.4, 19.8; HRMS (FAB^+) found 396.1652 $[M+ Na^+]^+$, calcd 396.1635 for $C_{17}H_{27}NO_8Na$.



(2*R* , 3*S* , 5*R*)-3-Methoxy-2-(2-methoxy-ethoxymethoxy)-5-methyl-6-(5-nitro-2,3,6-trimethoxy-phenyl)-hexan-1-ol (18). A 5 mL round bottom flask was charged with diol **17** (0.043 g, 0.115 mmol), 1 mL of dry CH_2Cl_2, *i*Pr_2NEt (0.1 mL), 4-DMAP (0.003 g, 0.0231 mmol) and TBSCl (0.19 g, 0.127 mmol). The resulting solution was stirred under a nitrogen atmosphere for 24 h and then an additional 0.019 g of TBSCl was added and stirring continued for 8 h. Then 0.1 mL of *i*Pr_2NEt was added followed by MEMCl (0.053 mL, 0.461 mmol) and the solution was allowed to stir for 10 h at which time it was diluted with 10 mL CH_2Cl_2 and 10 mL H_2O. The layers were separated and the aqueous phase was extracted further with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated. The crude material was then taken up in 1 mL THF and treated with a TBAF solution (0.5mL, 1.0 M THF). The resulting solution was allowed to stir for 3 h and then it was diluted with 10 mL of Et_2O and 10 mL of H_2O. The layers were separated and then the aqueous layer was

further extracted with Et_2O (4 x 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. Radial chromatography afforded the title compound 0.041 g (77%). TLC R_f = 0.19 (50% EtOAc/hexanes); $[\alpha]_D^{23}$ = +11.2 ° (*c* 1.3, $CHCl_3$) ^1H NMR ($CDCl_3$, 300 MHz) δ 7.38 (s, 1H), 4.81 (ABq, *J* = 7.2 Hz, 2H), 3.91 (s, 3H), 3.89 (s, 3H), 3.88-3.81 (m, 1H), 3.83 (s, 3H), 3.72-3.65 (m, 3H), 3.64-3.61 (m, 1H), 3.59-3.56 (m, 2H), 3.43-3.33 (m, 2H), 3.40 (s, 3H), 3.39 (s, 3H), 2.67 (dd, *J* = 6.3, 12.6 Hz, 1H), 2.56 (dd, *J* = 8.4, 12.6 Hz, 1H), 2.10-1.96 (m, 1H), 1.61 (ddd, *J* = 4.5, 9.6, 13.8 Hz, 1H), 1.29 (ddd, *J* = 3.3, 9.5, 13.3 Hz, 1H), 0.86 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$,75 MHz) δ 152.9, 148.5, 148.0, 138.4, 131.1, 107.1, 96.3, 83.3, 80.1, 71.8, 67.6, 62.7, 62.5, 61.0, 59.2, 58.6, 56.3, 38.8, 32.6, 30.4, 19.6; HRMS (FAB^+) found 484.2166 $[M+ Na^+]^+$, calcd 484.2159 for $C_{21}H_{35}NO_{10}Na$.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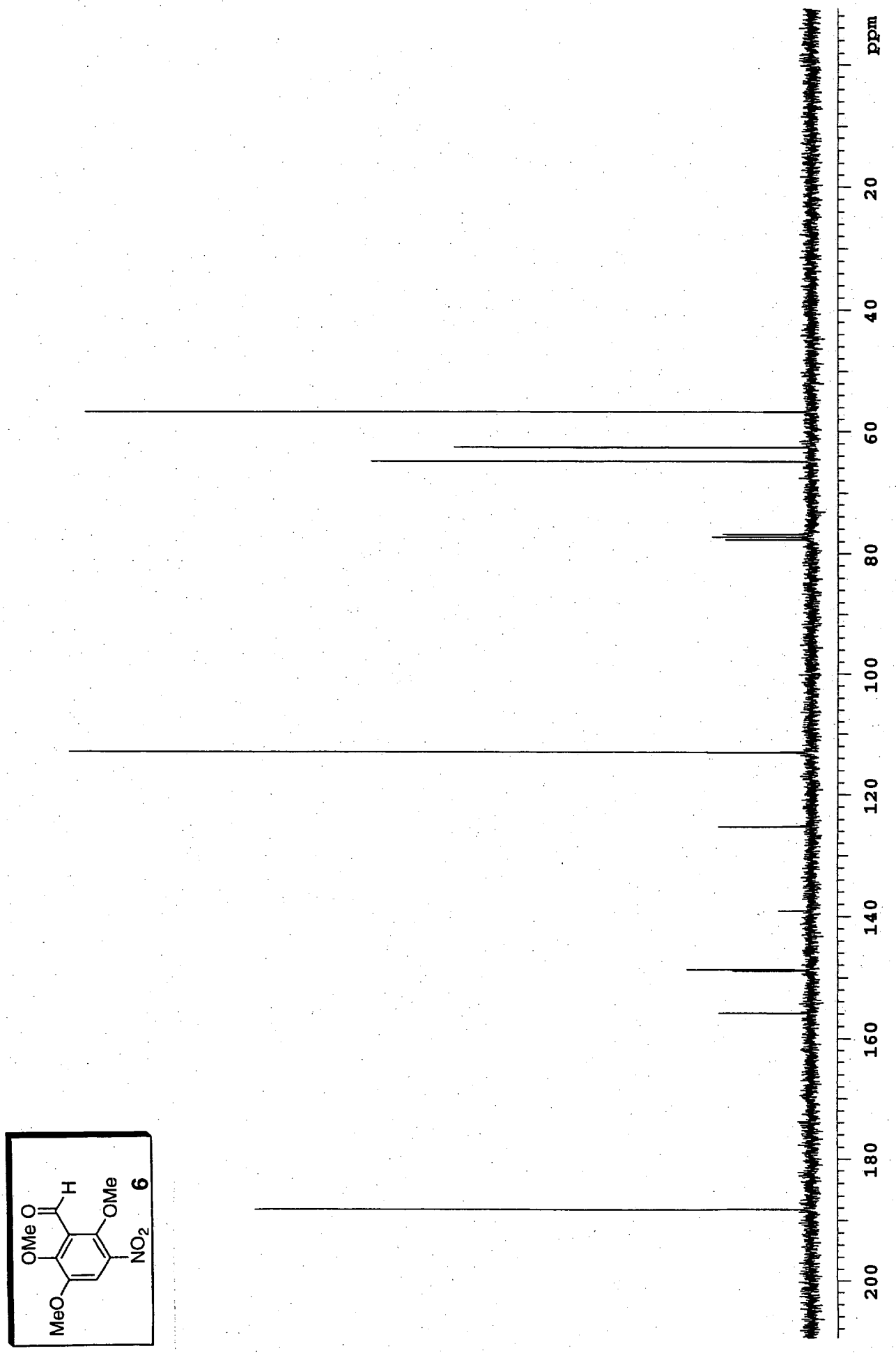
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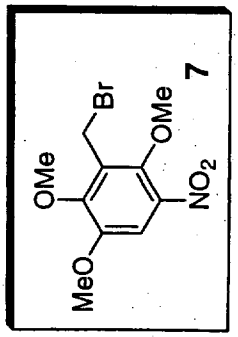

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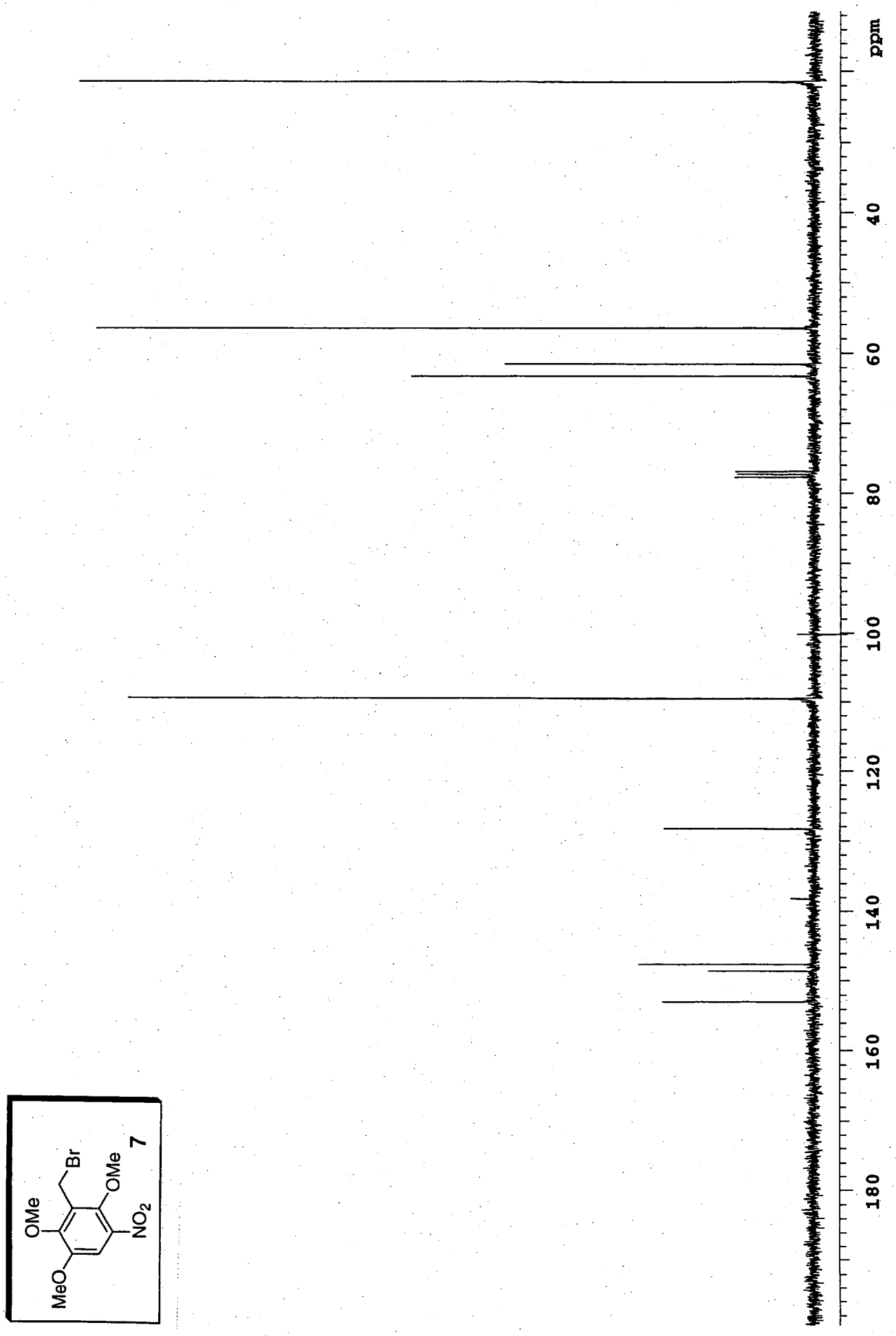

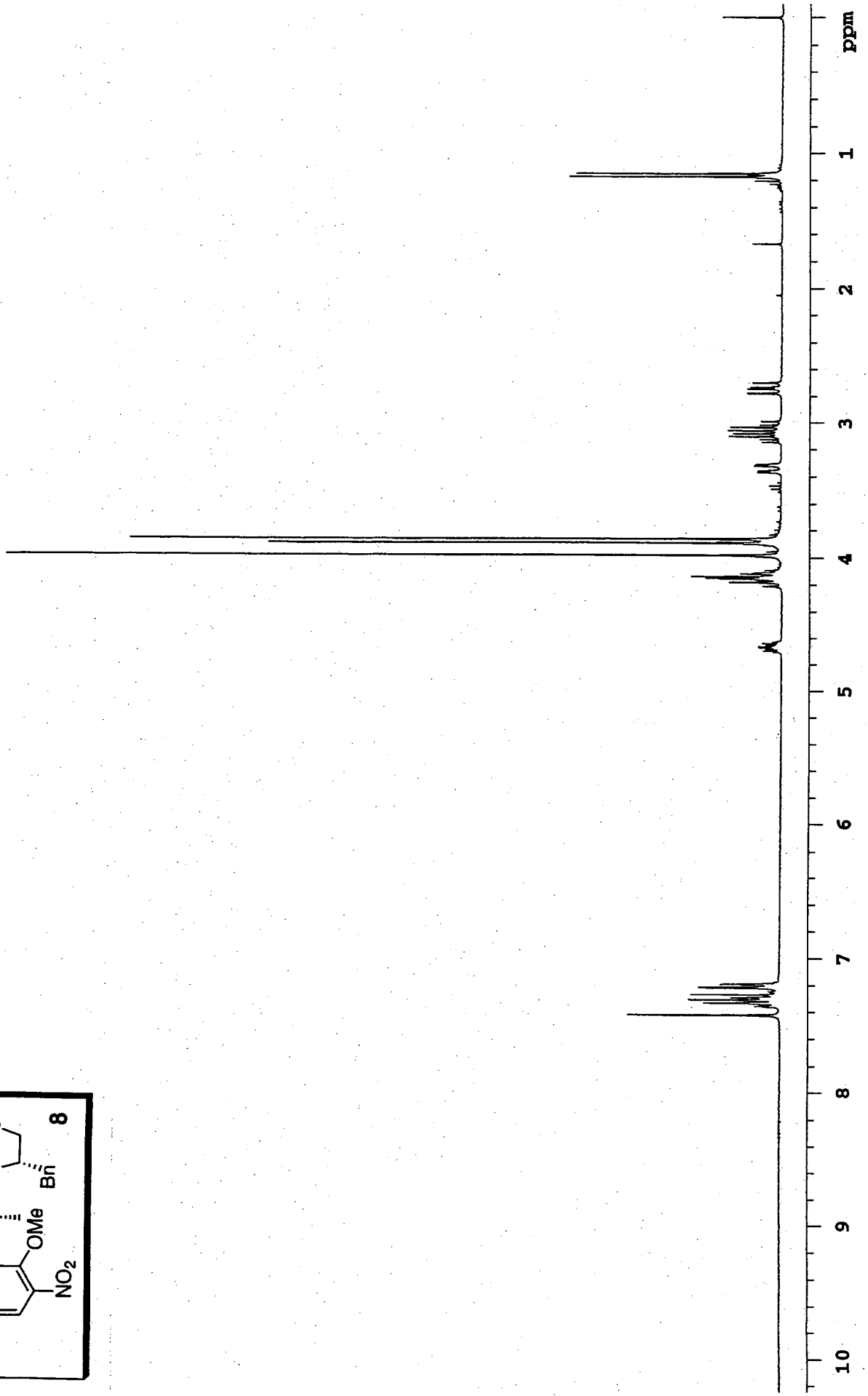
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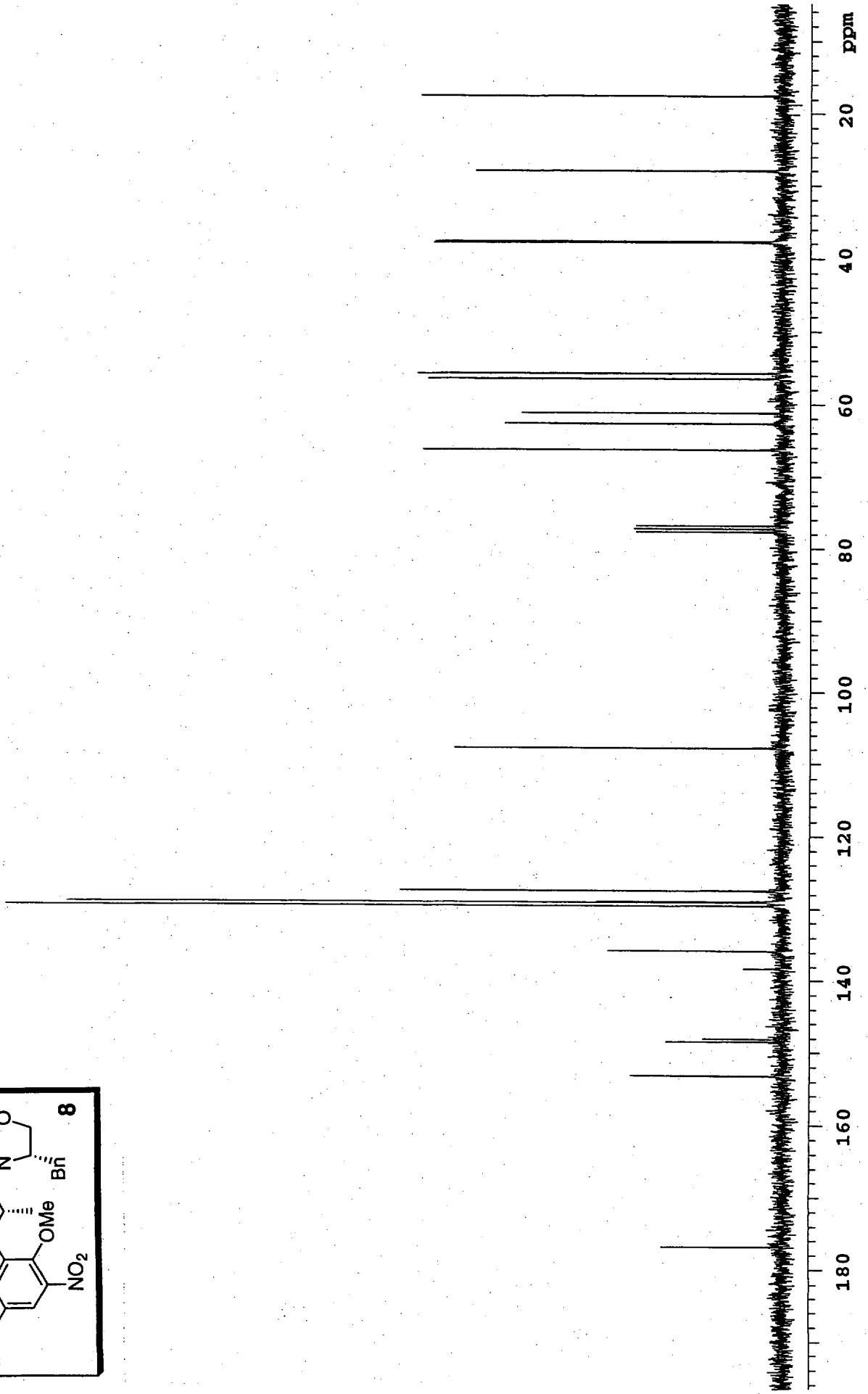
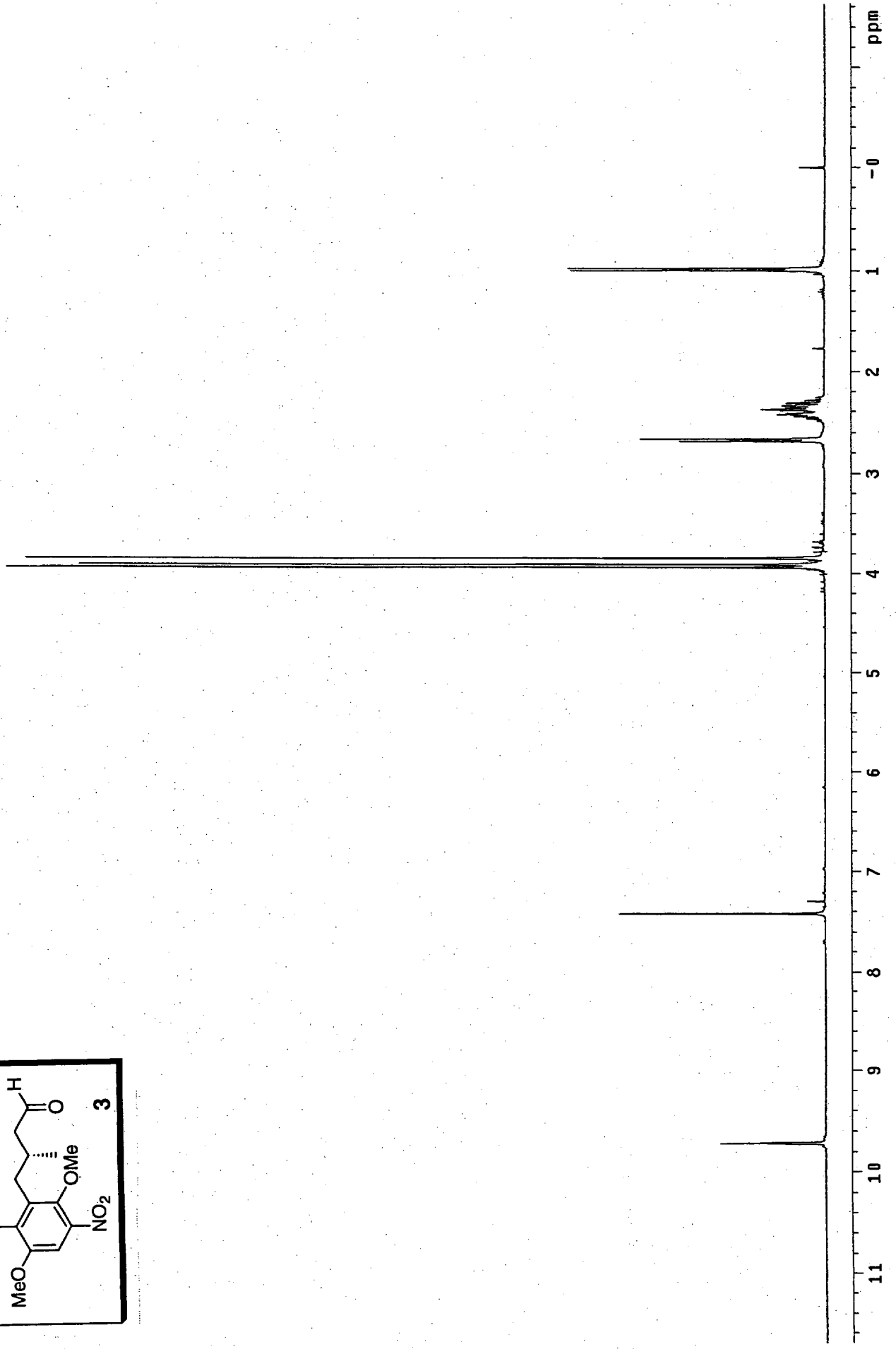
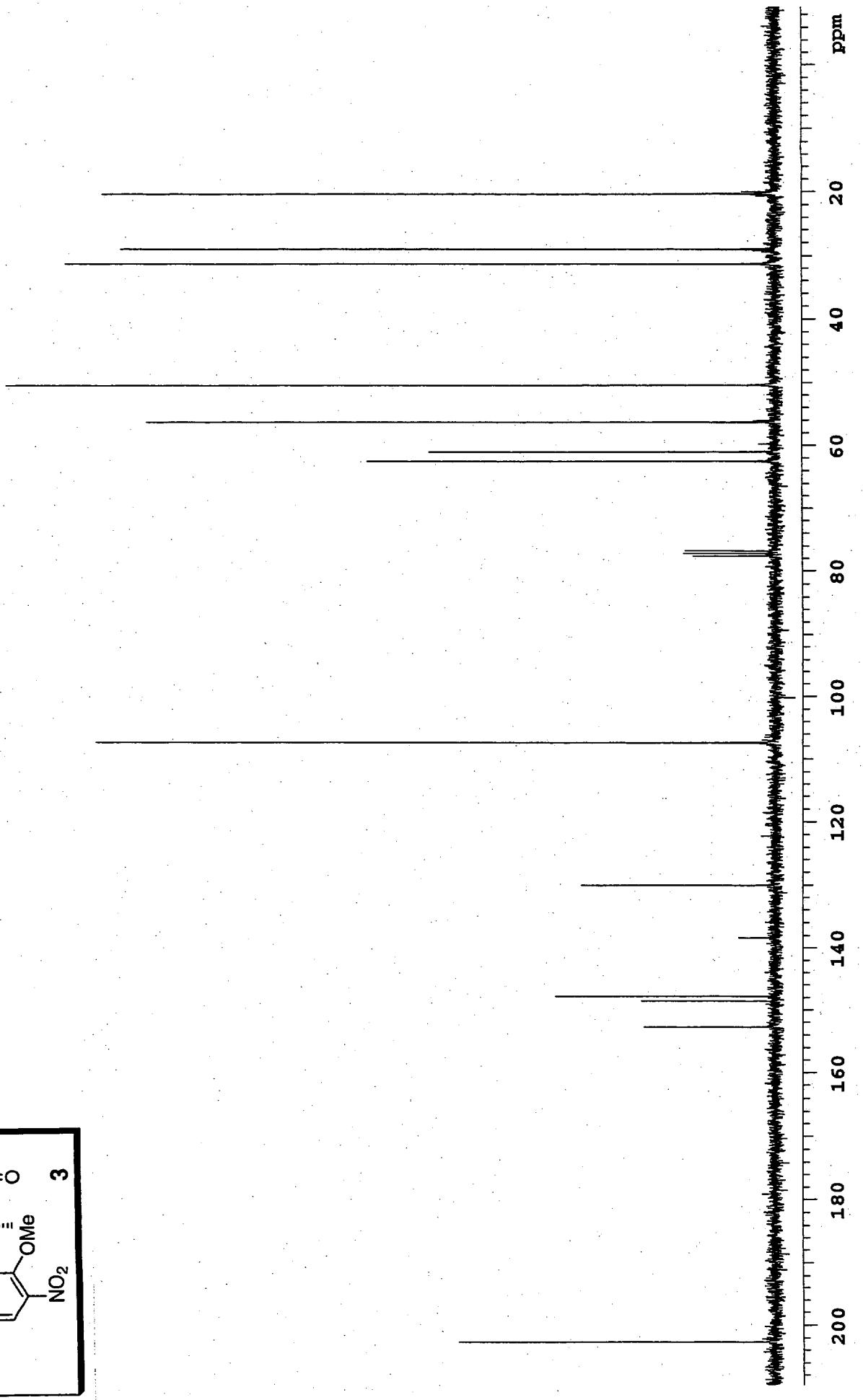
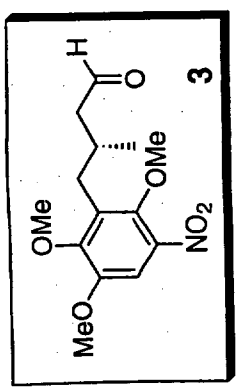
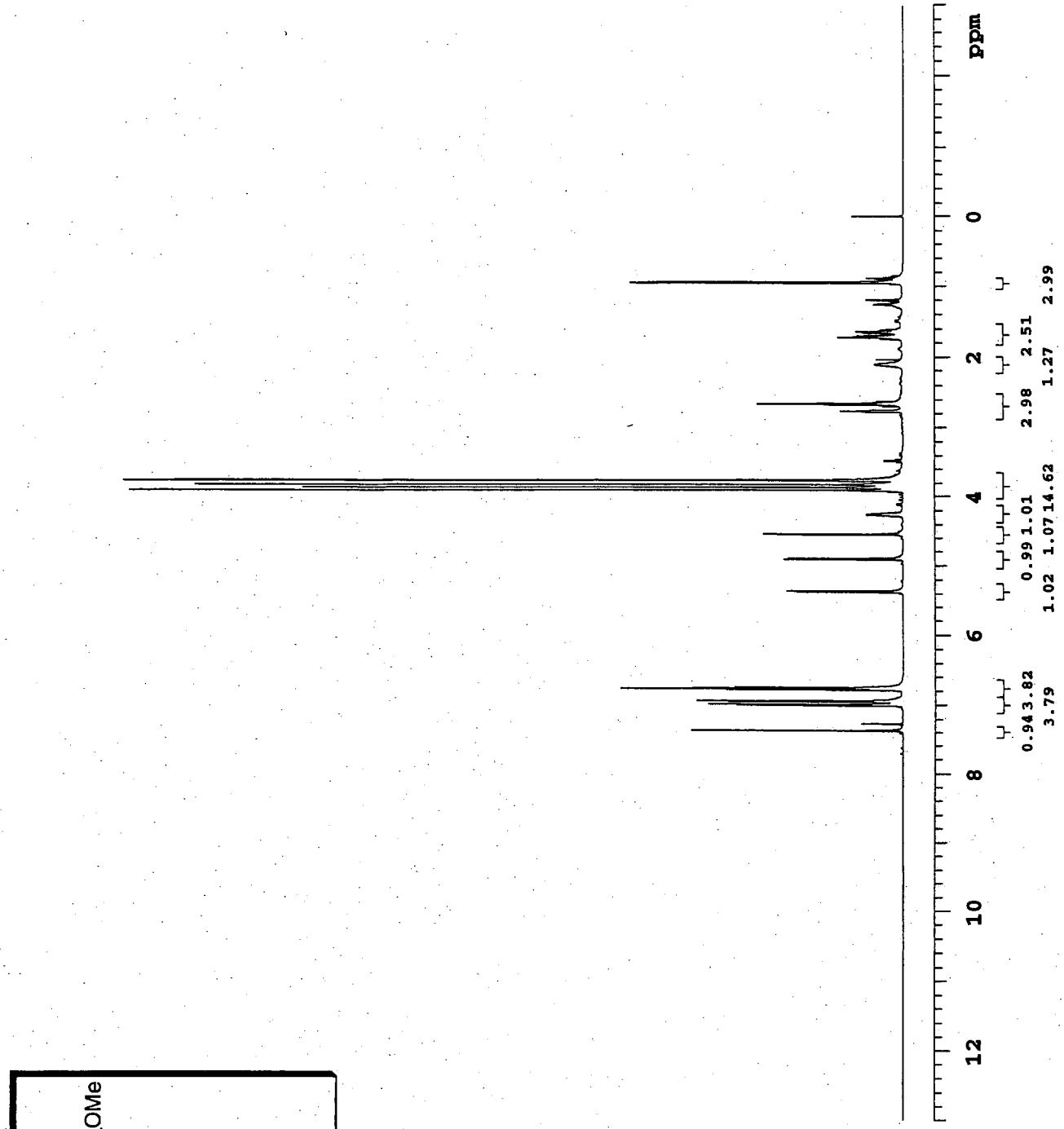
MeO

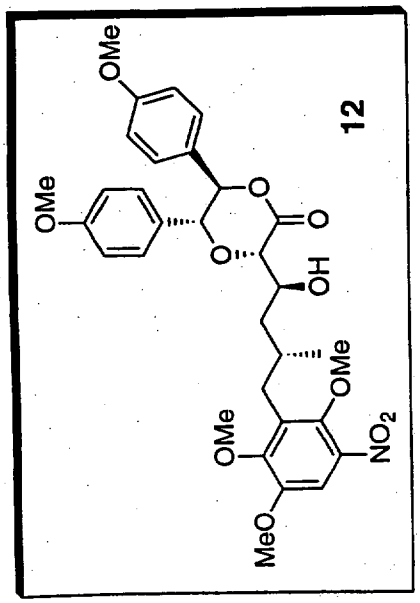


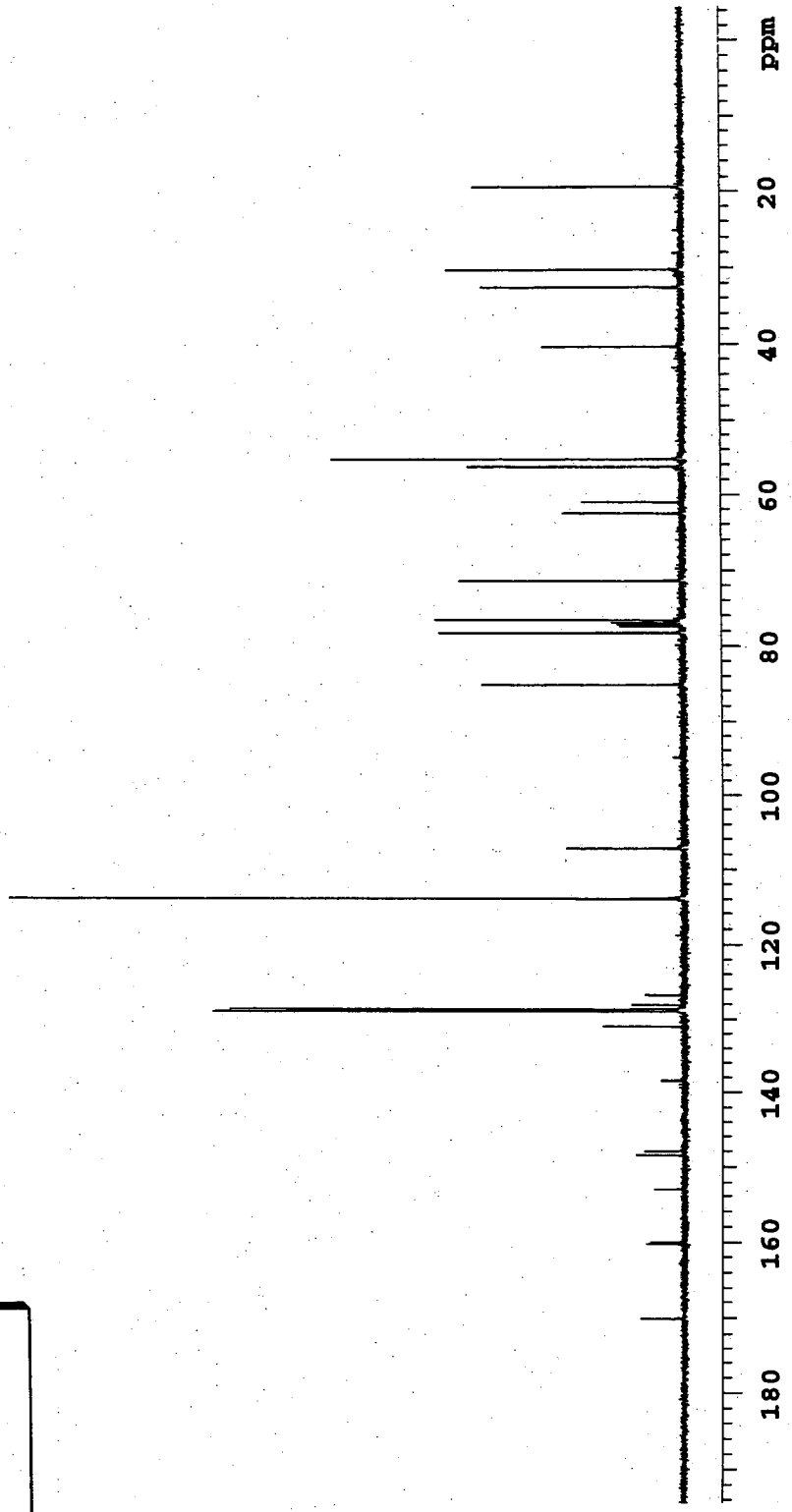




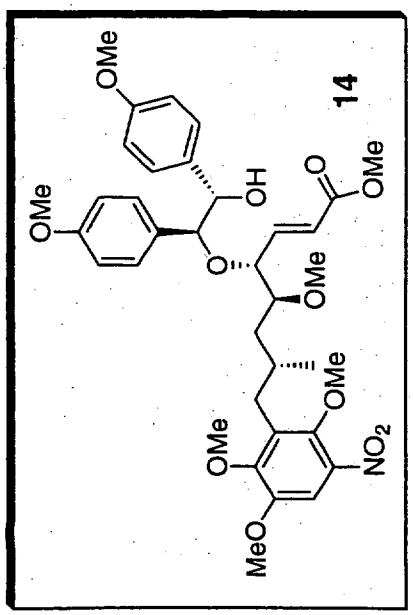


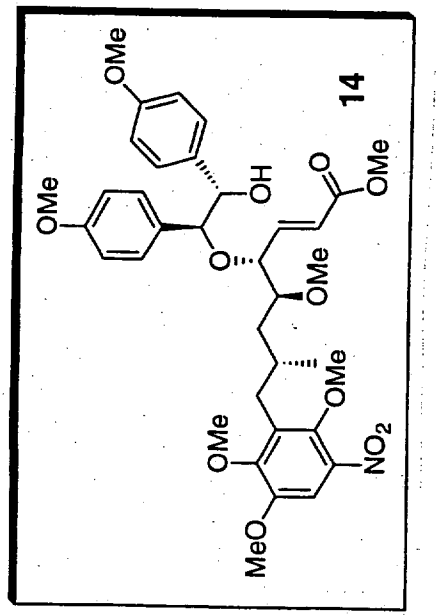


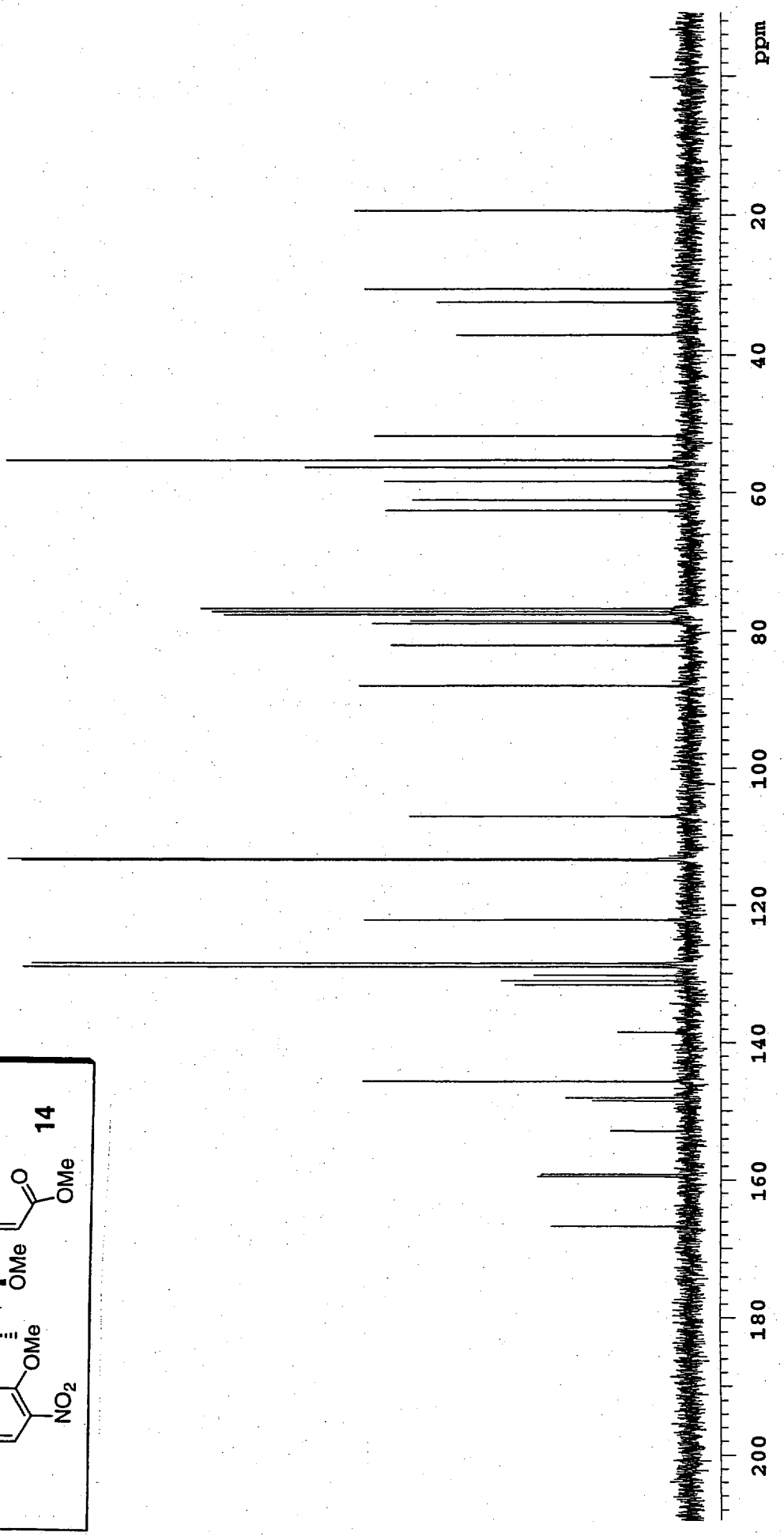




S20







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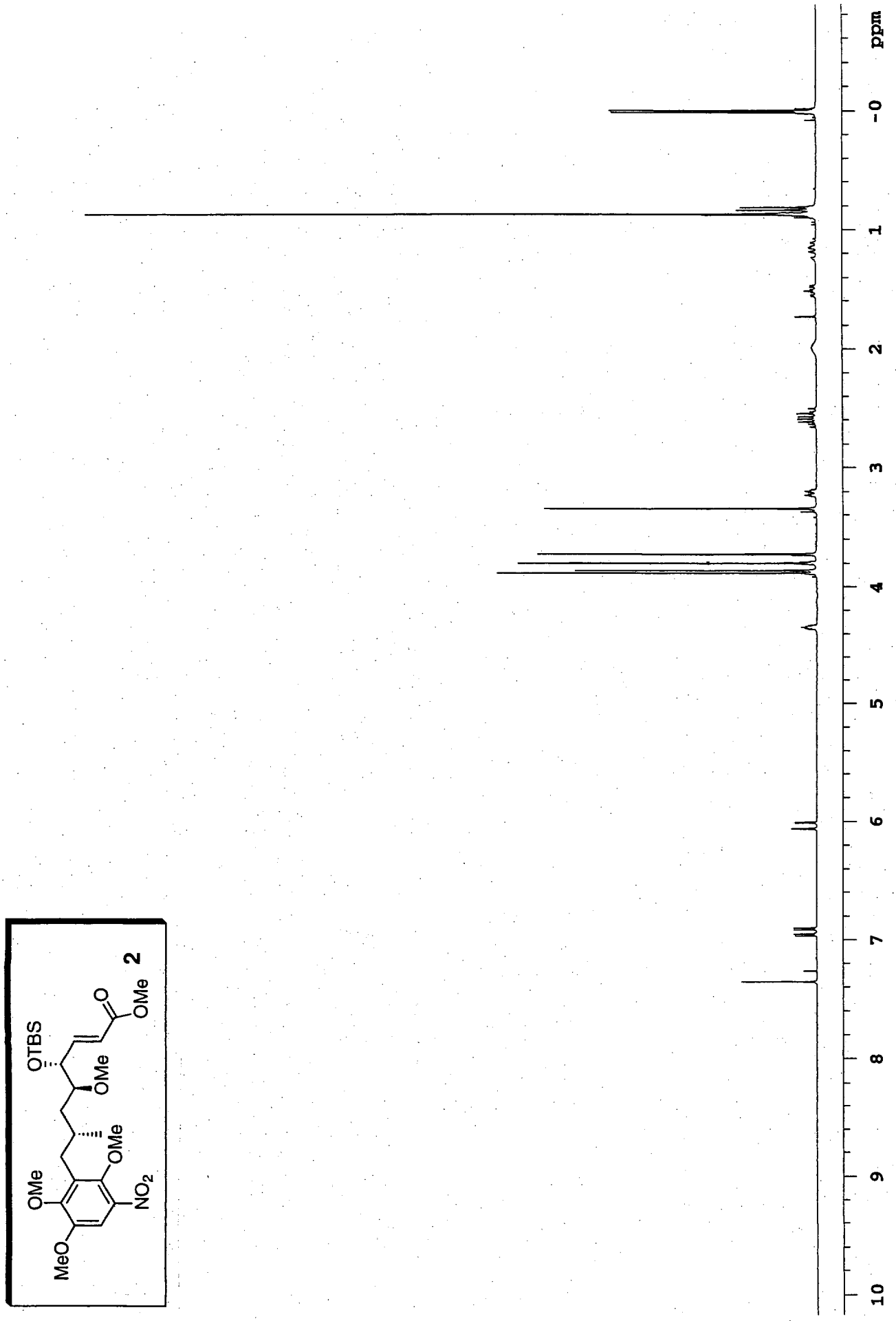

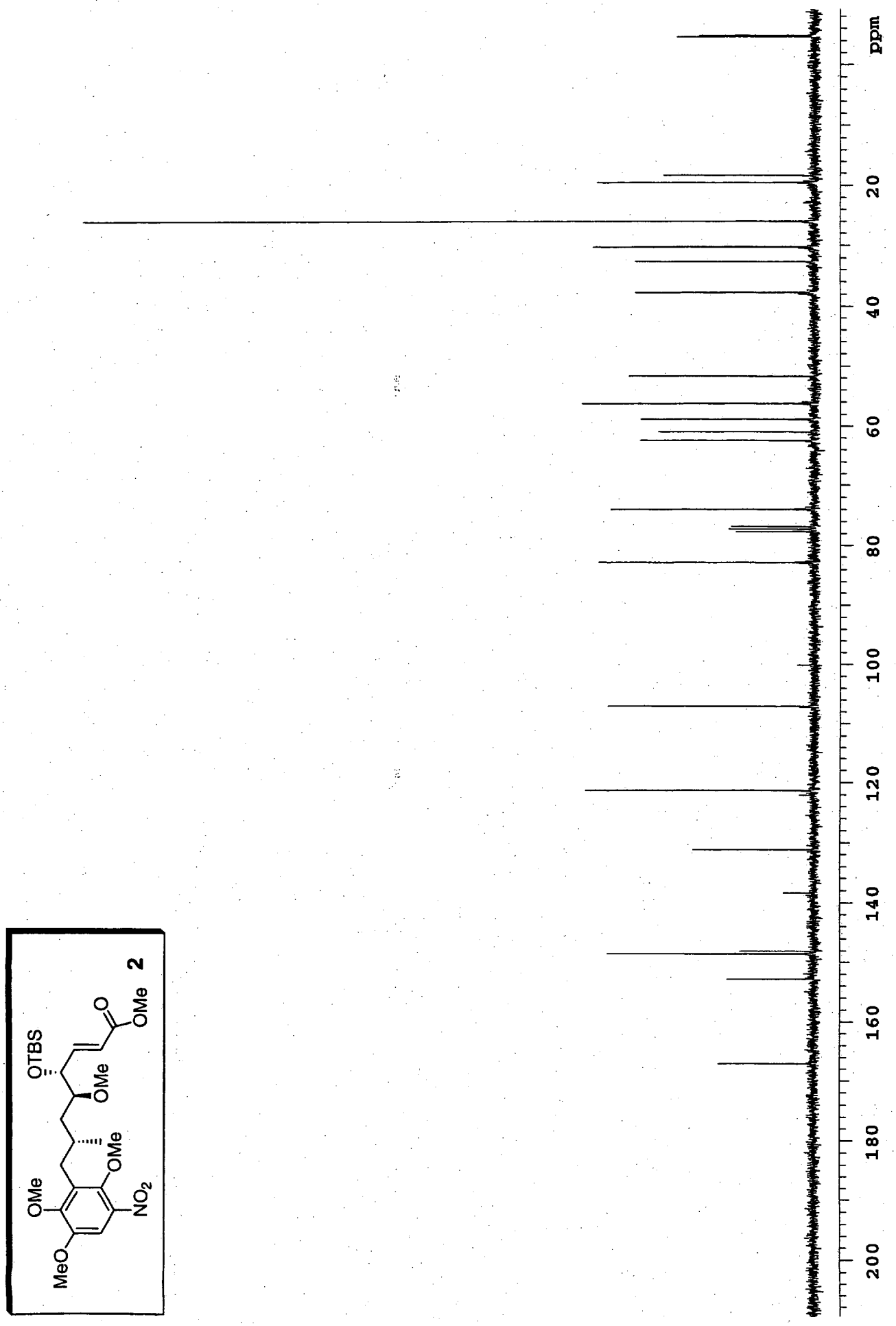

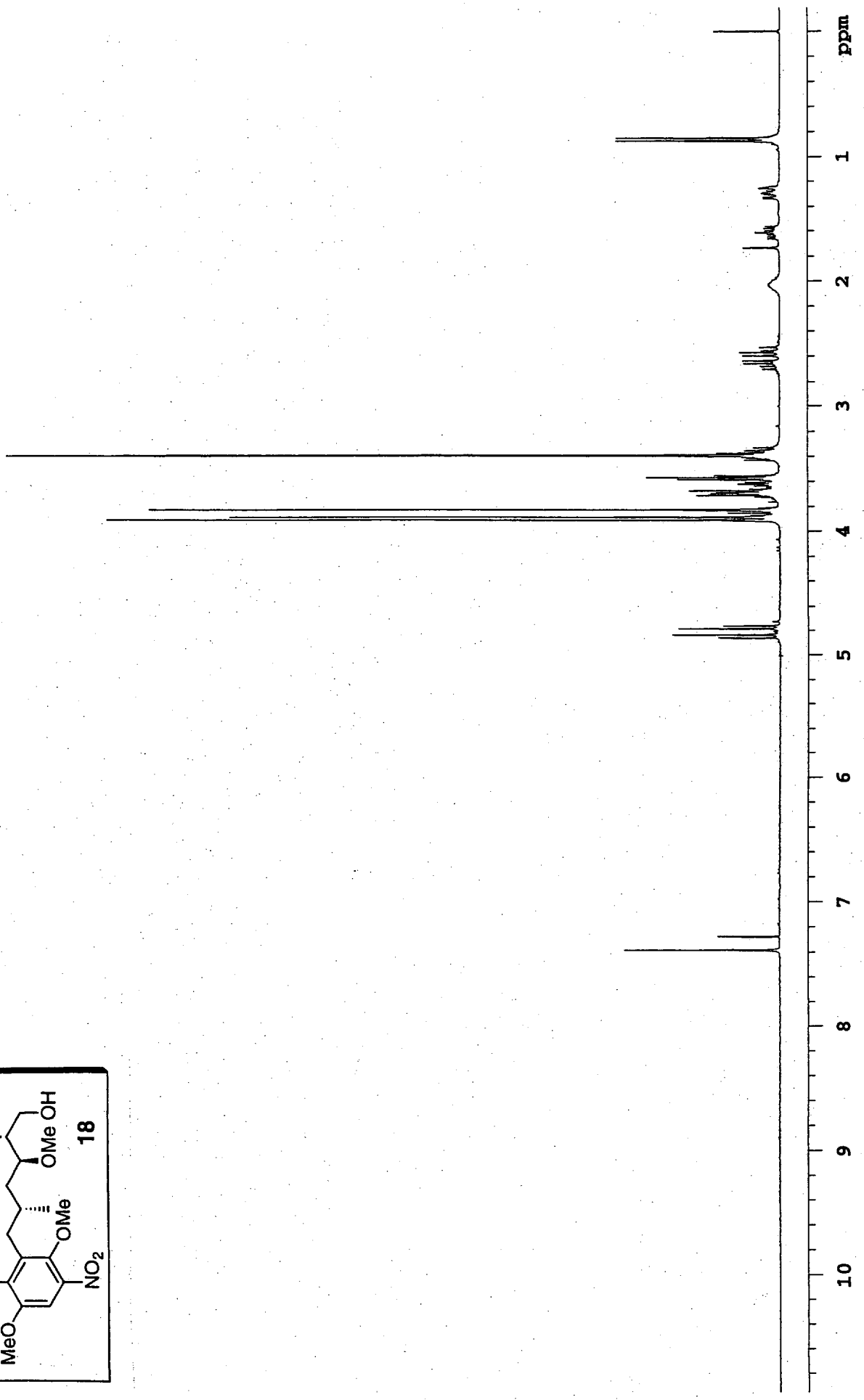

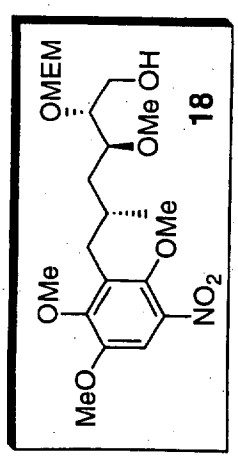

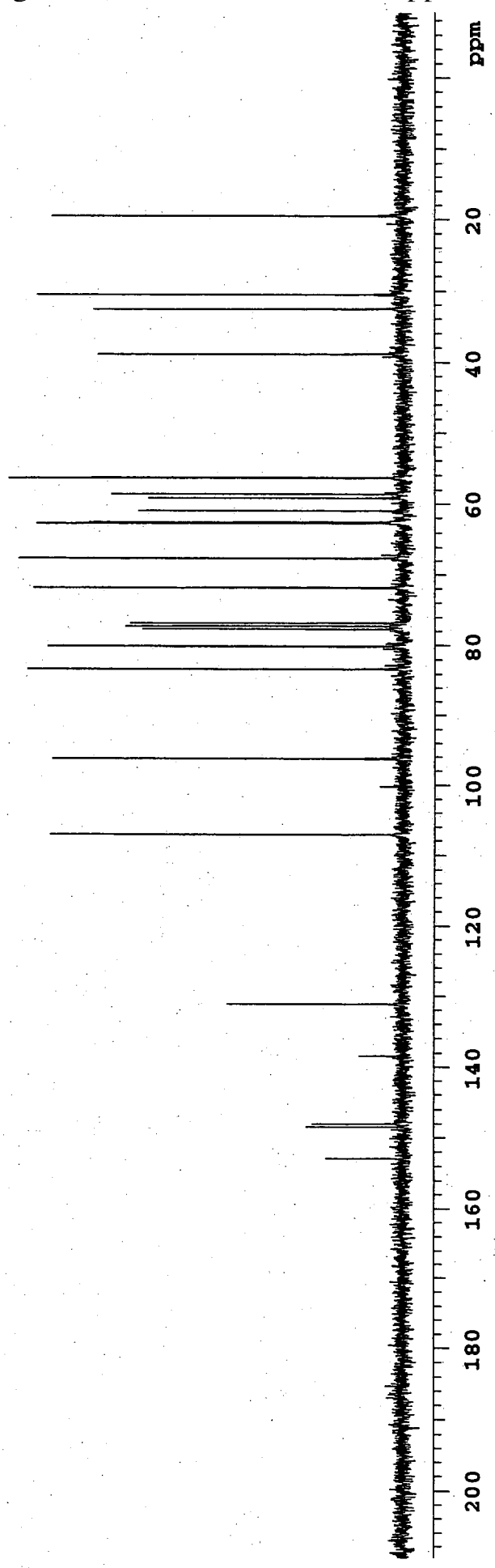

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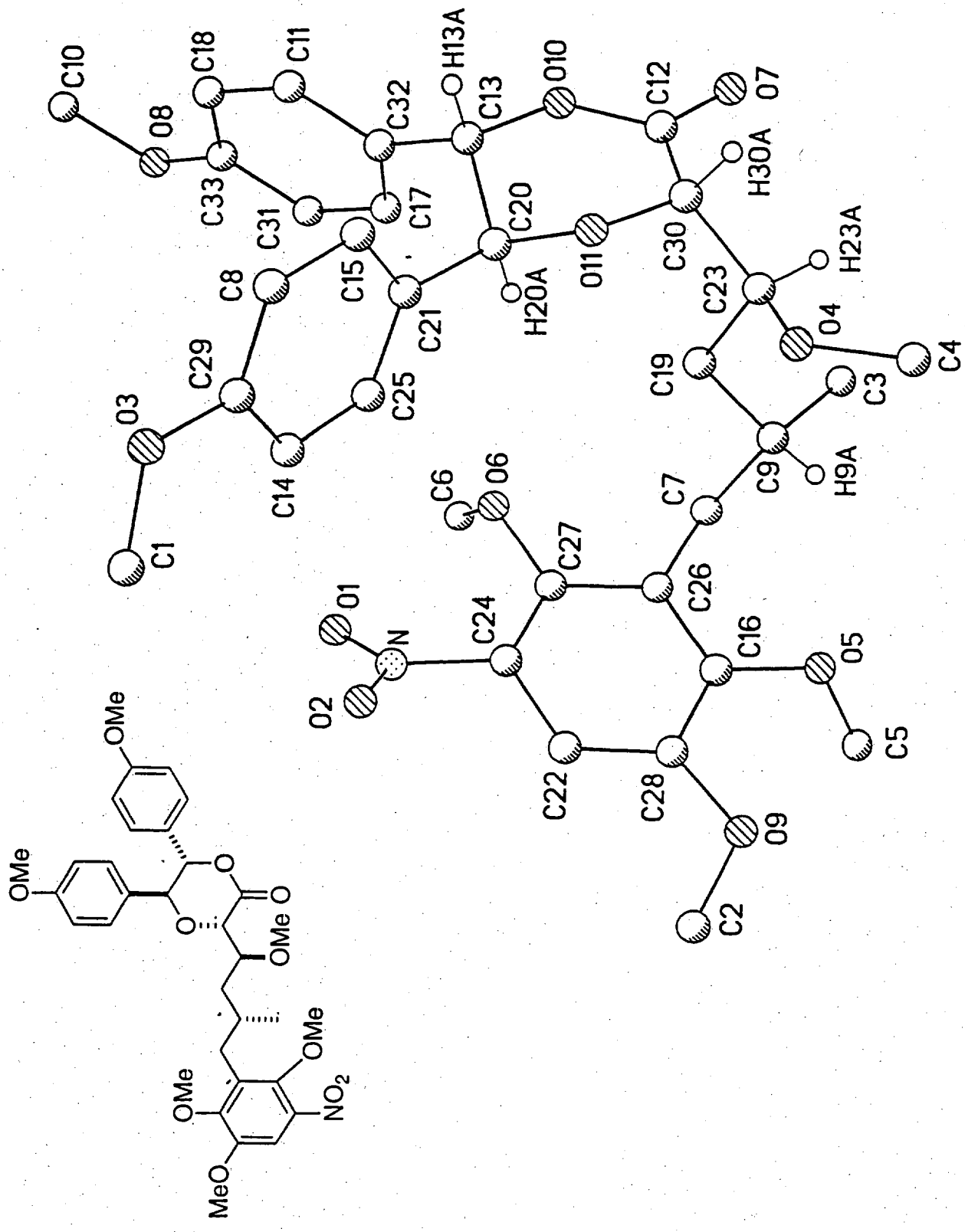

Table 1. Crystal data and structure refinement for 1.

Identification code	s115
Empirical formula	$C_{33}H_{39}NO_{11}$
Formula weight	625.65
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	a = 9.629(6) Å alpha = 90° b = 17.661(3) Å beta = 90° c = 19.081(3) Å gamma = 90°
Volume, Z	3245(2) $Å^3$, 4
Density (calculated)	1.281 Mg/m^3
Absorption coefficient	0.096 mm^{-1}
F(000)	1328
Crystal size	0.5 x 0.4 x 0.4 mm
Θ range for data collection	2.13 to 24.98°
Limiting indices	$0 \le h \le 11$, $0 \le k \le 21$, $-1 \le l \le 22$
Reflections collected	3415
Independent reflections	3385 (R_{int} = 0.0121)
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3383 / 0 / 428
Goodness-of-fit on F^2	1.055
Final R indices [I>2σ(I)]	R1 = 0.0505, wR2 = 0.0999
R indices (all data)	R1 = 0.1105, wR2 = 0.1291
Absolute structure parameter	-1(2)
Extinction coefficient	0.0016(5)
Largest diff. peak and hole	0.123 and -0.138 $eÅ^{-3}$

Table 2. Atomic coordinates [x 10^4] and equivalent isotropic displacement parameters [$Å^2$ x 10^3] for 1. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
O(1)	10571(4)	2998(2)	811(2)	87(1)
C(1)	10128(5)	3567(3)	538(3)	67(2)
O(2)	10057(4)	3586(2)	-168(2)	70(1)
C(3)	9617(5)	4278(3)	-528(3)	58(1)
C(4)	8604(5)	4709(3)	-80(2)	52(1)
O(5)	9255(4)	4882(2)	573(2)	61(1)
C(6)	9665(5)	4234(3)	964(3)	57(1)
C(7)	9035(5)	4034(3)	-1226(3)	52(1)
C(8)	9607(6)	4299(3)	-1841(3)	67(2)
C(9)	9088(6)	4085(3)	-2489(3)	69(2)
C(10)	7997(6)	3598(3)	-2524(3)	61(1)
O(10)	7435(4)	3337(2)	-3137(2)	86(1)
C(11)	8009(9)	3610(4)	-3780(3)	105(2)
C(12)	7398(5)	3323(3)	-1917(3)	61(1)
C(13)	7910(5)	3541(3)	-1277(3)	60(1)
C(14)	8116(5)	5447(3)	-388(3)	54(1)
C(15)	9023(6)	6020(3)	-584(3)	73(2)
C(16)	8520(7)	6702(3)	-821(3)	85(2)
C(17)	7120(6)	6834(3)	-868(3)	65(2)
O(17)	6722(5)	7532(2)	-1112(2)	92(1)
C(18)	5299(8)	7717(4)	-1046(5)	126(3)
C(19)	6210(6)	6271(3)	-689(3)	64(2)
C(20)	6713(5)	5590(3)	-460(3)	61(1)
C(21)	8599(5)	3996(3)	1517(3)	62(1)
O(21)	8413(5)	4634(2)	1971(2)	88(1)
C(22)	8624(7)	4502(4)	2687(3)	95(2)
C(23)	7209(5)	3755(3)	1221(3)	61(1)
C(24)	6248(5)	3364(3)	1734(3)	69(2)
C(25)	6796(8)	2587(3)	1966(5)	116(3)
C(26)	4803(5)	3278(3)	1412(3)	73(2)
C(27)	4026(5)	4011(3)	1346(3)	59(1)
C(28)	3892(5)	4387(3)	707(3)	62(1)
O(28)	4548(4)	4110(2)	124(2)	79(1)
C(29)	3768(7)	3571(5)	-278(4)	105(2)
C(30)	3226(6)	5080(4)	707(3)	68(2)
N(30)	3067(5)	5529(4)	53(4)	88(2)
O(30)	2945(6)	5198(3)	-497(3)	126(2)
O(31)	3063(7)	6208(3)	97(3)	147(3)
C(32)	2654(5)	5399(3)	1298(3)	67(2)
C(33)	2721(5)	5019(3)	1913(3)	64(1)
O(33)	2177(4)	5267(2)	2533(2)	87(1)
C(34)	1296(8)	5917(4)	2510(4)	114(3)
C(35)	3411(5)	4326(3)	1937(3)	63(1)
O(35)	3633(4)	3961(2)	2570(2)	92(1)
C(36)	2466(8)	3672(4)	2925(4)	115(3)

Table 3. Bond lengths [Å] and angles [°] for 1.

O(1)-C(1)	1.210(6)	C(1)-O(2)	1.349(7)
C(1)-C(6)	1.498(7)	O(2)-C(3)	1.465(6)
C(3)-C(4)	1.502(6)	C(3)-C(7)	1.508(7)
C(4)-O(5)	1.429(5)	C(4)-C(14)	1.506(7)
O(5)-C(6)	1.423(5)	C(6)-C(21)	1.532(7)
C(7)-C(8)	1.379(6)	C(7)-C(13)	1.394(6)
C(8)-C(9)	1.386(7)	C(9)-C(10)	1.359(7)
C(10)-O(10)	1.368(6)	C(10)-C(12)	1.383(7)
O(10)-C(11)	1.429(7)	C(12)-C(13)	1.371(7)
C(14)-C(20)	1.381(7)	C(14)-C(15)	1.386(7)
C(15)-C(16)	1.375(7)	C(16)-C(17)	1.371(8)
C(17)-C(19)	1.367(7)	C(17)-O(17)	1.374(6)
O(17)-C(18)	1.415(8)	C(19)-C(20)	1.369(7)
C(21)-O(21)	1.432(6)	C(21)-C(23)	1.514(7)
O(21)-C(22)	1.400(6)	C(23)-C(24)	1.514(6)
C(24)-C(26)	1.529(7)	C(24)-C(25)	1.535(7)
C(26)-C(27)	1.501(7)	C(27)-C(35)	1.389(7)
C(27)-C(28)	1.394(7)	C(28)-O(28)	1.369(6)
C(28)-C(30)	1.383(8)	O(28)-C(29)	1.435(7)
C(30)-C(32)	1.375(8)	C(30)-N(30)	1.486(7)
N(30)-O(31)	1.202(7)	N(30)-O(30)	1.207(7)
C(32)-C(33)	1.353(7)	C(33)-O(33)	1.365(6)
C(33)-C(35)	1.393(7)	O(33)-C(34)	1.428(7)
C(35)-O(35)	1.386(6)	O(35)-C(36)	1.408(7)

O(1)-C(1)-O(2)	117.9(6)	O(1)-C(1)-C(6)	121.6(6)
O(2)-C(1)-C(6)	120.5(5)	C(1)-O(2)-C(3)	120.2(4)
O(2)-C(3)-C(4)	110.1(4)	O(2)-C(3)-C(7)	106.4(4)
C(4)-C(3)-C(7)	114.0(4)	O(5)-C(4)-C(3)	108.7(4)
O(5)-C(4)-C(14)	106.9(4)	C(3)-C(4)-C(14)	114.8(4)
C(6)-O(5)-C(4)	114.0(3)	O(5)-C(6)-C(1)	115.6(4)
O(5)-C(6)-C(21)	113.3(4)	C(1)-C(6)-C(21)	111.0(4)
C(8)-C(7)-C(13)	117.5(5)	C(8)-C(7)-C(3)	120.5(4)
C(13)-C(7)-C(3)	122.0(5)	C(7)-C(8)-C(9)	121.6(5)
C(10)-C(9)-C(8)	119.6(5)	C(9)-C(10)-O(10)	124.1(5)
C(9)-C(10)-C(12)	120.2(5)	O(10)-C(10)-C(12)	115.7(5)
C(10)-O(10)-C(11)	117.9(4)	C(13)-C(12)-C(10)	119.8(5)
C(12)-C(13)-C(7)	121.2(5)	C(20)-C(14)-C(15)	117.2(5)
C(20)-C(14)-C(4)	120.1(4)	C(15)-C(14)-C(4)	122.7(4)
C(16)-C(15)-C(14)	120.4(5)	C(17)-C(16)-C(15)	121.1(5)
C(19)-C(17)-C(16)	119.4(5)	C(19)-C(17)-O(17)	123.9(5)
C(16)-C(17)-O(17)	116.6(5)	C(17)-O(17)-C(18)	116.5(5)
C(17)-C(19)-C(20)	119.4(5)	C(19)-C(20)-C(14)	122.6(5)
O(21)-C(21)-C(23)	109.7(4)	O(21)-C(21)-C(6)	106.6(4)
C(23)-C(21)-C(6)	114.4(4)	C(22)-O(21)-C(21)	116.2(5)
C(21)-C(23)-C(24)	115.3(5)	C(23)-C(24)-C(26)	110.0(4)
C(23)-C(24)-C(25)	112.5(5)	C(26)-C(24)-C(25)	109.9(5)
C(27)-C(26)-C(24)	113.7(4)	C(35)-C(27)-C(28)	118.6(5)
C(35)-C(27)-C(26)	119.4(5)	C(28)-C(27)-C(26)	122.0(5)
O(28)-C(28)-C(30)	122.0(5)	O(28)-C(28)-C(27)	119.9(5)
C(30)-C(28)-C(27)	117.7(5)	C(28)-O(28)-C(29)	115.4(4)
C(32)-C(30)-C(28)	123.2(5)	C(32)-C(30)-N(30)	115.4(6)
C(28)-C(30)-N(30)	121.4(6)	O(31)-N(30)-O(30)	123.0(7)
O(31)-N(30)-C(30)	118.2(7)	O(30)-N(30)-C(30)	118.8(6)
C(33)-C(32)-C(30)	119.4(5)	C(32)-C(33)-O(33)	125.1(5)

C(32)-C(33)-C(35)	119.0(6)	O(33)-C(33)-C(35)	115.9(6)
C(33)-O(33)-C(34)	117.3(5)	O(35)-C(35)-C(27)	117.0(5)
O(35)-C(35)-C(33)	120.7(5)	C(27)-C(35)-C(33)	122.0(5)
C(35)-O(35)-C(36)	117.7(5)		