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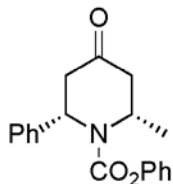
Organic Letters

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“Stereoselective Synthesis of Acyclic Amino Alcohols via von Braun Ring Opening of Chiral Piperidines”

- I. Experimental procedures and characterization data for **4-16**.
- II. ^1H and ^{13}C NMR spectra for **4-10** and **12-16**.
- III. ORTEP plots for **7** and **17**.

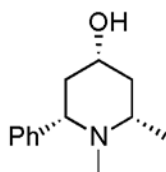
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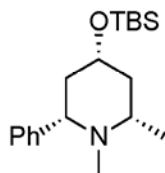
(2S*,6S*)-Phenyl 2-methyl-4-oxo-6-phenylpiperidine-1-carboxylate (4).

A mixture of dihydropyridone **3** (5.0 g, 7.0 mmol) and CuBr·Me₂S (7.0 g 34.1 mmol) was stirred at rt in THF (25 mL, 0.14 M) for 30 minutes. The solution was cooled to -78 °C, BF₃·OEt₂ (4.32 mL, 34.1 mmol) was added dropwise, and stirring was continued for 45 min. A 3.0 M solution of MeMgBr (11.4 mL, 34.08 mmol) in diethyl ether was added drop wise at -78 °C over a period of 2 h. After the addition was complete, the solution was allowed to stir at -78 °C for 9 h and then quenched with 1/1 saturated NH₄Cl/25% NH₄OH solution. The crude reaction mixture was extracted with Et₂O (3 x 70 mL). The combined organic extracts were washed with portions of H₂O (2 x 30 mL) and brine (30 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude oil was purified by radial PLC (5-30% EtOAc/hexanes) to give 3.28 g (62%) of the major isomer and 0.89 g (17%) of the impure minor isomer. The major isomer **4** was isolated as a clear oil: ¹H NMR (CDCl₃, 300 MHz) δ 1.24 (d, 3H, *J* = 6.9 Hz), 2.39 (dd, 1H, *J* = 5.7, 16.8 Hz), 2.74 (dd, 1H, *J* = 6.6, 16.5 Hz), 2.91 (dd, 1H, *J* = 6.6, 17.1 Hz), 3.16 (dd, 1H, *J* = 4.8, 17.1 Hz), 4.81 (septet, 1H, *J* = 6.6 Hz), 5.8 (t, 1H, *J* = 5.6 Hz), 7.05 (d, 2H, *J* = 7.8 Hz), 7.12-7.43 (m, 8H); ¹³C NMR (CDCl₃, 100 MHz) δ 23.0, 43.7, 45.7, 49.2, 54.8, 121.9, 125.8, 126.4, 127.8, 129.1, 129.6, 142.2, 151.4, 154.9, 207.4; IR (neat) 751, 948, 1029, 1074, 1163, 1206, 1270,

1323, 1337, 1353, 1393, 1454, 1495, 1594, 1714, 2916, 1974, 3032, 3063 cm^{-1} ;
HRMS calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_3$ ($\text{M}+\text{H}$) $^+$: 310.1443, found 310.1458.

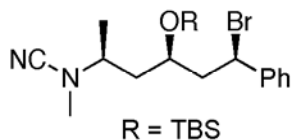


(2S*,4R*,6S*)-1,2-Dimethyl-6-(S)-phenylpiperidin-4-ol (5). To compound **4** (608 mg, 1.97 mmol) in THF (50 mL) was added portion wise LiAlH_4 (443 mg, 11.82 mmol). The reaction flask was fitted with a reflux condenser, and the mixture was refluxed for 6 h and monitored by TLC to observe the disappearance of starting material. Once complete, the reaction was cooled to 0 $^{\circ}\text{C}$ and 0.68 mL of water was added slowly drop wise, followed by the addition of 1.35 mL of aqueous 25% NaOH solution. Celite (13 g) was added and the mixture was allowed to warm to rt. After stirring for 1.5 h, the slurry was filtered through a pad of Celite, and the filtrate was concentrated under reduced pressure. The crude product was purified by radial PLC ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 4:1 (v/v)) to give 296 mg (73%) of **5** as a white solid, mp 82-84 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz) δ 1.77 (d, 3H, J = 4 Hz), 1.52 (q, 1H, J = 16.8 Hz), 1.62 (q, 1H, J = 16.4 Hz), 1.95 (s, 3H), 1.92-1.99 (m, 2H), 2.12-2.19 (m, 1H), 2.24 (br s, 1H), 7.20-7.3 (m, 5H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 21.6, 39.9, 44.2, 45.3, 58.3, 68.6, 69.3, 127.3, 127.7, 128.7, 144.7; IR (neat) 700, 757, 820, 967, 1026, 1085, 1138, 1178, 1232, 1304, 1372, 1453, 1493, 2777, 2845, 2936, 2970, 3334 cm^{-1} ; HRMS: ($\text{M}+\text{H}$) $^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{NO}$, 206.1545; found 206.1536.

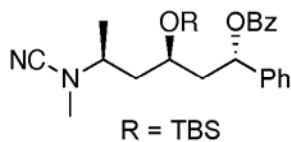


(2S*,4R*,6S*)-4-(*tert*-Butyldimethylsilyloxy)-1,2-dimethyl-6-phenylpiperidine

(6). To a solution of **5** (983 mg, 4.78 mmol) in 90 mL of CH₂Cl₂ was added imidazole (16.3 mg, 0.24 mmol), TEA (704 mg, 5.6 mmol), and TBSCl (2.17 g, 14.4 mmol). The mixture was allowed to stir at rt for 18 h. The reaction mixture was quenched with saturated NaHCO₃ (10 mL) and extracted with CH₂Cl₂ (3 x 60 mL). The extracts were combined, washed with H₂O (50 mL) and brine (2 x 50 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. The crude oil was purified by radial PLC (30% EtOAc/hexanes) to give 1.2 g (78%) of **6** as a clear oil. ¹H NMR (CDCl₃, 300 MHz) δ 0.05 (d, 6H, *J* = 7.5 Hz), 0.87 (s, 9H), 1.18 (d, 3H, *J* = 6.3 Hz), 1.53 (quart, 1H, *J* = 11.7 Hz), 1.70 (quart, 1H, *J* = 11.1 Hz), 1.87 (m, 2H), 1.90 (s, 3H), 2.11-2.17 (m, 1H), 2.95 (dd, 1H, *J* = 3, 12 Hz), 3.66-3.76 (m, 1H), 7.20-7.36 (m, 5H); ¹³C NMR (CDCl₃, 75 MHz) δ -4.13, 18.3, 21.7, 26.1, 40.1, 44.8, 45.8, 58.4, 69.5, 127.2, 127.8, 128.7, 145.1; IR (neat) 806, 957, 1005, 1054, 1103, 1254, 1360, 1379, 1457, 1469, 1603, 1650, 1746, 2671, 2778, 2858, 2888, 2934, 2935, 3029, 3064, 3423 cm⁻¹; HRMS: (M + H)⁺ calcd for formula +H, C₁₉H₁₃NOSi (M+H)⁺ 320.2410; found, 320.2413.

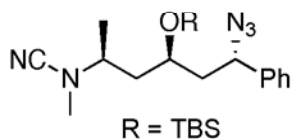


(2S*,4R*,6R*)-6-Bromo-4-(*tert*-butyldimethylsilyloxy)-N-isocyano-N-methyl-6-phenylhexan-2-amine (7). To piperidine **6** (120 mg, 0.38 mmol) in CH₂Cl₂ (8 mL) was added BrCN (0.63 mL, 1.8 mmol, 3.0 M in CH₂Cl₂), and the solution was warmed to reflux. The reaction progress was monitored by TLC analysis. After 3 h, the reaction was cooled and concentrated under reduced pressure to give a light yellow solid. The crude solid was recrystallized from hexanes to give **7** (158 mg, 98%) as a white crystalline solid, mp 94 °C; ¹H NMR (CDCl₃, 300 MHz) δ 0.1 (s, 6H), 0.9 (s, 9H), 1.21 (d, 3H, *J* = 8.8 Hz), 1.53 (m, 1H), 1.89 (m, 1H), 2.17 (m, 1H), 2.56 (m, 1H), 5.03 (dd, 1H, *J* = 5.1, 9.6 Hz), 7.26-7.40 (m, 5H); ¹³C NMR (CDCl₃, 75 MHz) δ -4.2, -3.7, 18.2, 36.9, 41.9, 47.7, 51.1, 54.5, 68.2, 117.3, 127.4, 128.8, 129.1, 142.1; IR (neat) 720, 836, 906, 925, 1005, 1071, 1158, 1253, 1298, 1361, 1388, 1457, 1472, 1496, 1508, 1560, 1655, 1685, 2209, 2362, 2857, 2896, 2930, 2954, 3032 cm⁻¹; HRMS: (M+H)⁺ calcd for C₂₀H₃₃BrN₂OSi: 425.1624; found, 425.1629.



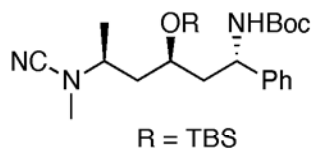
(1S*,3R*,5S*)-3-(*tert*-Butyldimethylsilyloxy)-5-(isocyano(methyl)amino)-1-phenylhexyl benzoate (8). To bromide **7** (16 mg, 0.04 mmol) in 0.5 mL of

DMPU was added sodium benzoate (7 mg, 0.05 mmol). The reaction mixture was stirred at rt for 22 h, then 2 mL of brine and 2 mL of Et₂O were added. The layers were separated, and the aqueous layer was extracted with Et₂O (3 X 3 mL). The combined organic extracts were washed with H₂O (2 X 3 mL) and brine (1 X 3 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. The crude product was purified by radial PLC (100% hexanes-60%-hexanes/EtOAc) to give **8** (13 mg, 77%) as a clear oil. ¹H NMR (CDCl₃, 300 MHz) δ -0.01 (d, 6H, *J* = 6 Hz), 0.89 (s, 9H), 1.24 (d, 3H, *J* = 6.6 Hz), 1.62 (m, 1H), 1.91(m, 1H), 2.04 (m, 1H), 2.24 (m, 1H), 2.24 (m, 1H), 2.76 (s, 3H), 3.12 (m, 1H), 3.88 (m, 1H), 5.99 (dd, 1H, *J* = 6.3, 1.8 Hz), 7.29-7.58 (m, 8H), 8.06 (dd, 2H, *J* = 0.6, 7.2 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ -4.2, 18.3, 26.1, 37.7, 42.8, 45.3, 54.6, 66.3, 74.1, 117.3, 126.7, 128.4, 128.6, 128.9, 129.8, 130.5, 133.3, 140.8, 165.9; IR (neat) 715, 774, 834, 1070, 1110, 1270, 1451, 1645, 1716, (bs) 2103, 2208, 3515 cm⁻¹; HRMS: (M+H)⁺ calcd for C₂₇H₃₈N₂O₃Si, 467.2730; found, 467.2745.



(2S*,4R*,6S*)-6-Azido-4-(*tert*-butyldimethylsilyloxy)-N-isocyano-N-methyl-6-phenylhexan-2-amine (9). Bromide **7** (81 mg, 0.19 mmol) was stirred in 3 mL of freshly distilled DMSO with NaN₃ (62 mg, 0.95 mmol) at room temperature for 17 h. Brine was added (3 mL), the layers were separated, and the aqueous layer

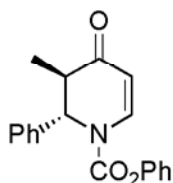
was extracted with Et₂O (3 X 3 mL). The combined organic extracts were washed with H₂O (3 X 3 mL) and brine (1 X 3 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by radial PLC (100% hexanes-50%-hexanes/EtOAc) to give 68 mg of **9** (93%) as a clear oil. ¹H NMR (CDCl₃, 300 MHz) δ 0.06 (d, 6H, *J* = 20 Hz), 0.9 (s, 9H), 1.22 (dd, 3H, *J* = 6.8 2.0 Hz), 1.56 (m, 1H), 1.84 (m, 1H), 2.77 (s, 3H), 3.02 (m, 1H), 3.85 (m, 1H), 4.59 (m, 1H), 7.32-7.41 (m, 5H); ¹³C NMR (CDCl₃, 75 MHz) δ -4.1, 18.2, 26.1, 37.3, 42.9, 44.7, 54.6, 62.9, 66.6, 117.3, 127.2, 128.7, 129.2, 139.8; IR (neat) 702, 775, 836, 1252, 2096, 2360, 2857, 2930, 2953 cm⁻¹; HRMS: (M+H)⁺ calcd for C₂₀H₃₃N₅OSi: 388.2533; found, 388.2541.



***tert*-Butyl-(1*S*,3*S*,5*S*)-3-(*tert*-butyldimethylsilyloxy)-5-**

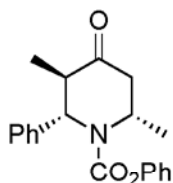
(isocyano(methyl)amino)-1-phenylhexylcarbamate (10**).** To azide **9** (45 mg, 0.12 mmol) in 3 mL of EtOAc was added Pearlman's catalyst (Pd(OH)₂) (7 mg, 0.05 mmol) and Boc₂O (31 mg, 0.14 mmol). The suspension was placed under a balloon atmosphere of hydrogen gas. The mixture was stirred at rt for 15 h, filtered through a Celite pad, and concentrated to give a yellow oil. Purification by radial PLC gave **10** (51 mg, 96%) as a white solid, mp 84 °C; ¹H NMR (CDCl₃, 300 MHz) δ 0.05 (d, 6H, *J* = 19.8 Hz); 0.92 (s, 9H); 1.21 (d, 3H, *J* = 6.3 Hz); 1.39

(s, 9H); 1.66 (m, 1H); 1.88 (m, 3H); 2.77 (s, 3H); 3.09 (bs, 1H); 3.82 (bs, 1H); 4.66 (bs, 1H); 5.50 (bs, 1H); 7.26-7.36 (m, 5H); ^{13}C NMR (CDCl_3 , 75 MHz) δ -4.8, -3.9, 18.2, 26.2, 28.6, 37.0, 41.5, 44.6, 54.6, 67.0, 117.3, 126.3, 127.5, 128.9, 204.4 ; IR (neat) 836, 1170, 1365, 1701, 2209, 2360, 2857, 2934, 2961 cm^{-1} ; HRMS: $(\text{M}+\text{H})^+$ calcd for 462.3152; found, 462.3128.



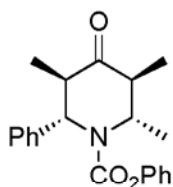
(2S*,3R*)-Phenyl 3-methyl-4-oxo-2-phenyl-3,4-dihydropyridine-1(2H)-carboxylate (11). A solution of dihydropyridone **3** (2.2 g, 7.48 mmol) in 100 mL of freshly distilled THF was cooled to $-78\text{ }^{\circ}\text{C}$. Drop wise addition of a THF solution of LiHMDS (1.0 M, 8.23 mL, 8.23 mmol) was performed at $-78\text{ }^{\circ}\text{C}$. The reaction was stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min. Iodomethane (1.4 mL, 22.4 mmol) was added in one portion and then the reaction mixture was allowed to warm to $-23\text{ }^{\circ}\text{C}$ and stirred for 8 h. The reaction was quenched with 30 mL of brine and allowed to warm to rt. The aqueous layer was extracted with Et_2O (3 X 50 mL). The combined organic extracts were washed with H_2O (2 X 25 mL) and brine (1 X 25 mL), dried over MgSO_4 , and concentrated to give a crude yellow oil which was purified using a Biotage purification system (silica gel, hexanes/ EtOAc , 7/3) to give compound **11** as a yellow oil (2.3 g, 99%). ^1H NMR (CDCl_3 , 300 MHz) δ

1.47 (d, 3H, $J = 7.2$ Hz), 2.87 (q, 1H, $J = 7.2$ Hz), 5.43 (d, 1H, $J = 4.2$ Hz), 5.51 (s, 1H), 7.07 (d, 2H, $J = 2.8$ Hz), 7.25-7.39 (m, 8H), 8.07 (dd, 1H, $J = 1.2$ Hz, $J = 8.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 18.7, 46.5, 63.22, 107.2, 121.5, 126.3, 126.7, 128.4, 129.0, 129.2, 129.8, 138.4, 141.3, 150.6, 196.7; IR (neat) 735, 905, 1198, 1265, 1329, 1611, 1677, 1743, 2975, 3065 cm^{-1} ; HRMS: $(\text{M}+\text{H})^+$ calcd for $\text{C}_{19}\text{H}_{17}\text{NO}_3$, 308.1287; found, 308.1296.



(2S*,3R*,6S*)-Phenyl 3,6-dimethyl-4-oxo-2-phenylpiperidine-1-carboxylate (12). A mixture of dihydropyridone **11** (3.93 g, 12.8 mmol) and $\text{CuBr}\cdot\text{Me}_2\text{S}$ (5.26 g, 265.6 mmol) in 300 mL of dry THF was stirred at rt for 30 min. The solution was cooled to -78°C and $\text{BF}_3\cdot\text{OEt}_2$ (2.06 g, 14.5 mmol) was added drop wise. After stirring for an additional 30 min at this temperature, a THF solution of MeMgBr (8.5 mL, 25.6 mmol) was added drop wise over 1 h via syringe pump. The mixture was allowed to stir at -78°C for 7 h upon which it was deemed by TLC analysis that the reaction was complete. The reaction mixture was quenched with 1/1 saturated $\text{NH}_4\text{Cl}/25\%\text{NH}_4\text{OH}$ solution (75 mL) and allowed to warm to room temperature. The aqueous layer was extracted with Et_2O (3 X 250 mL). The organic layers were combined, washed with water (2 X 150 mL) and brine (150 mL), dried over MgSO_4 and concentrated. The yellow oil was purified

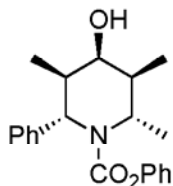
by radial PLC (hexanes/EtOAc) to give **12** (2.96 g, 72%) as a clear oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.25 (d, 3H, J = 6.6 Hz), 1.39 (d, 3H, J = 6.9 Hz), 2.34 (dd, 1H, J = 6.3 Hz, J = 17.4 Hz), 2.75 (dd, 1H, J = 6.9 Hz, J = 17.4 Hz), 3.19 (quin, 1H, J = 7.2 Hz), 4.72 (sextet, 1H, J = 6.6 Hz), 5.37 (d, 1H, J = 5.7 Hz), 6.95 (d, 2H, J = 7.8 Hz), 7.2 (t, 1H, J = 0.9 Hz), 7.27-7.43 (m, 7H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 15, 23.3, 44.3, 46.1, 48.6, 61.7, 121.8, 125.7, 127, 127.8, 129, 130, 142, 151; IR (neat) 1204, 1332, 1392, 1712, 2878, 2935, 2974 cm^{-1} ; HRMS: $(\text{M}+\text{H})^+$ calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_3$, 324.1600; found, 324.1624.



(2S*,3S*,5R*,6S*)-Phenyl 2,3,5-trimethyl-4-oxo-6-phenylpiperidine-1-

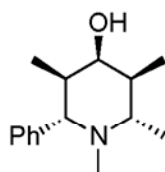
carboxylate (13). Substituted piperidone **12** (1.4 g, 4.3 mmol) was dissolved in 150 mL of dry THF and then cooled to $-78\text{ }^{\circ}\text{C}$. LiHMDS (1.0 M in THF, 4.75 mL, 4.75 mmol) was added drop wise. After 30 min, 20 mL of freshly distilled HMPA was added followed by MeI (1.83 g, 12.9 mmol). The reaction mixture was slowly warmed to rt, allowed to stir for 18 h, and then 100 mL of H_2O was added. The aqueous layer was extracted with Et_2O (3 X 125 mL). The combined organic extracts were washed with H_2O (2 X 100 mL) and brine (100 mL), dried over MgSO_4 , filtered, and concentrated under reduced pressure. The crude product was purified using a Biotage column (silica gel, 8/2, hexanes/EtOAc) to give 966 mg (67%) of **13** as a clear oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.18 (d, 3H, J = 6.6

Hz), 1.23 (d, 3H, $J = 7.2$ Hz), 1.49 (d, 3H, 6.6), 2.45 (quint, 1H, $J = 6.6$ Hz), 4.26 (quint, 1H, $J = 6.6$ Hz), 5.33 (d, 1H, $J = 5.4$ Hz), 6.95 (d, 2H, $J = 7.8$ Hz), 7.18-7.44 (m, 8H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 14.4, 14.9, 22.6, 45.5, 47.7, 55.2, 61.6, 112.1, 121.8, 125.7, 127.0, 127.8, 128.9, 129.2, 141.8, 151.3, 155.3, 204.9, 211.5; IR (neat) 738, 989, 1205, 1326, 1455, 1494, 1712, 2879, 2979 cm^{-1} ; HRMS: $(\text{M}+\text{H})^+$ calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_3$, 338.1756; found, 338.1776.



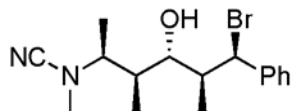
(2S*,3S*,4S*,5R*,6S*)-Phenyl 4-hydroxy-2,3,5-trimethyl-6-phenylpiperidine-1-carboxylate (14). A solution of piperidinone **13** (535 mg, 1.56 mmol) in dry THF (50 mL) was cooled to -78 $^{\circ}\text{C}$ and then L-Selectride (3.12 mL, 3.12 mmol) was added drop wise. The mixture was stirred for 10 h at -78 $^{\circ}\text{C}$, quenched with saturated aqueous NH_4Cl (25 mL), and allowed to warm to room temperature. The crude mixture was extracted with Et_2O (3 X 35 mL). The combined organic extracts were washed with water (2 X 25 mL) and brine (1 x 30 mL), dried over MgSO_4 , and concentrated to give an oil. Purification by column chromatography (silica gel, EtOAc /hexanes) gave 31 mg (74%) of **14** as a yellow oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.11 (d, 3H, $J = 6.9$ Hz), 1.22 (d, 3H, $J = 6.9$ Hz), 1.45 (d, 3H, $J = 6.6$ Hz), 1.79 (m, 1H), 2.06 (m, 1H), 3.74 (m, 1H), 3.99 (m, 1H), 4.80 (d, 1H, $J = 9.6$ Hz), 6.84 (d, 2H, $J = 7.2$ Hz), 7.08 (m, 1H,), 7.22-7.41 (m, 7H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 17.1, 17.7, 23.3, 40.9, 42.6, 53.4, 61.5, 72.9, 122.0,

125.2, 127.1, 128.1, 128.4, 129.3, 143.5; IR (neat) 750, 1207, 1346, 1695, 2879, 2932, 2968, 3464 cm^{-1} ; HRMS: $(\text{M}+\text{H})^+$ calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_3$, 340.1913; found, 340.1925.



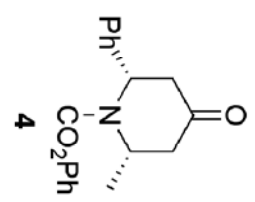
(2S*,3S*,4S*,5R*,6S*)-1,2,3,5-Tetramethyl-6-phenylpiperidin-4-ol (15). To piperidinol **14** (135 mg, 0.40 mmol) in 13 mL of dry THF was added LiAlH_4 (45 mg, 1.2 mmol) portion wise under an atmosphere of argon. The mixture was brought to a gentle reflux and stirred for 6 h, cooled to 0 °C, and slowly quenched with a 1 M solution of NaOH (0.6 mL). Celite was added (1 g) and the cloudy gray suspension was allowed to warm to rt and stirred for 1.5 h. The mixture was filtered through a pad of Celite, and the solids were washed with hot THF. The filtrate was concentrated to give a crude white solid which was triturated with CH_2Cl_2 and filtered through Celite. Concentration gave pure **15** (91.5 mg, 98%) as a white solid, mp 77-78 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 0.623 (d, 3H, J = 7.2 Hz), 1.07 (d, 3H, J = 6.9 Hz), 1.15 (d, 3H, J = 6.6 Hz), 1.43 (s, 1H), 1.75 (m, 1H), 1.92 (m, 1H), 1.99 (s, 3H), 2.28 (m, 1H), 3.07 (d, 1H, J = 10.5 Hz), 3.66 (s, 1H), 7.17-7.30 (m, 5H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 0.2, 16.1, 16.7, 18.1, 40.9, 41.9, 42.5, 59.2, 75.2, 122.0, 127.1, 128.5, 150.1; IR (neat) 735, 966, 1453, 1603,

2781, 2876, 2930, 2961, 3416 cm^{-1} ; HRMS: $(\text{M}+\text{H})^+$ calcd for $\text{C}_{15}\text{H}_{23}\text{NO}$, 234.1858; found, 234.1864.

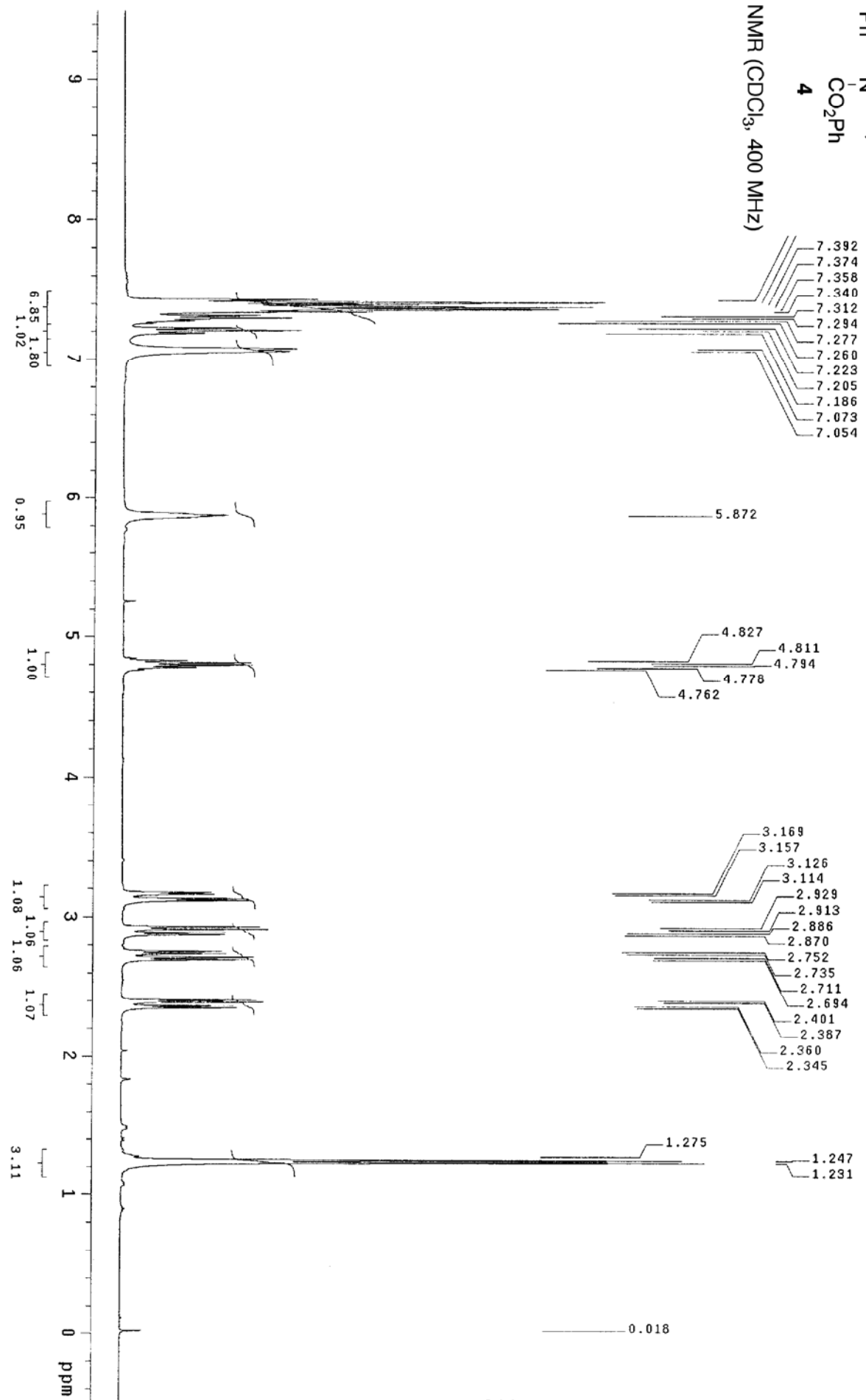


***N*-((2*S**,3*S**,4*S**,5*S**,6*R**)-6-Bromo-4-hydroxy-3,5-dimethyl-6-phenylhexan-2-yl)-*N*-methylcyanamide (**16**).** To **15** (93 mg, 0.4 mmol) in 10 mL of CH_2Cl_2 was added BrCN (0.67 mL, 2.0 mmol), and the reaction was stirred at rt for 3 h. The reaction was concentrated and the residue purified by radial PLC (silica gel, EtOAc /hexanes) to give 91 mg (67%) of compound **16** as a clear oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.02 (m, 6H), 1.25 (d, 3H, $J = 6.9$ Hz), 1.97 (m, 2H), 2.49 (bs, 1H), 2.78 (s, 3H), 3.20 (m, 1H), 3.5 (bs, 1H), 5.62 (d, 1H, $J = 3.6$ Hz), 7.26–7.44 (m, 5H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 12.8, 13.0, 14.5, 37.7, 38.0, 44.1, 57.0, 60.3, 118.1, 128.1, 128.5, 128.6, 140.9; IR (neat) 701, 1207, 1453, 1707, 2209, 2934, 2975, 3435 cm^{-1} ; HRMS: $(\text{M}+\text{H})$ calcd for $\text{C}_{16}\text{H}_{23}\text{BrN}_2\text{O}$, 339.1072; found, 339.1081.

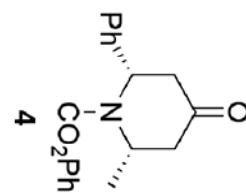
660 MAR



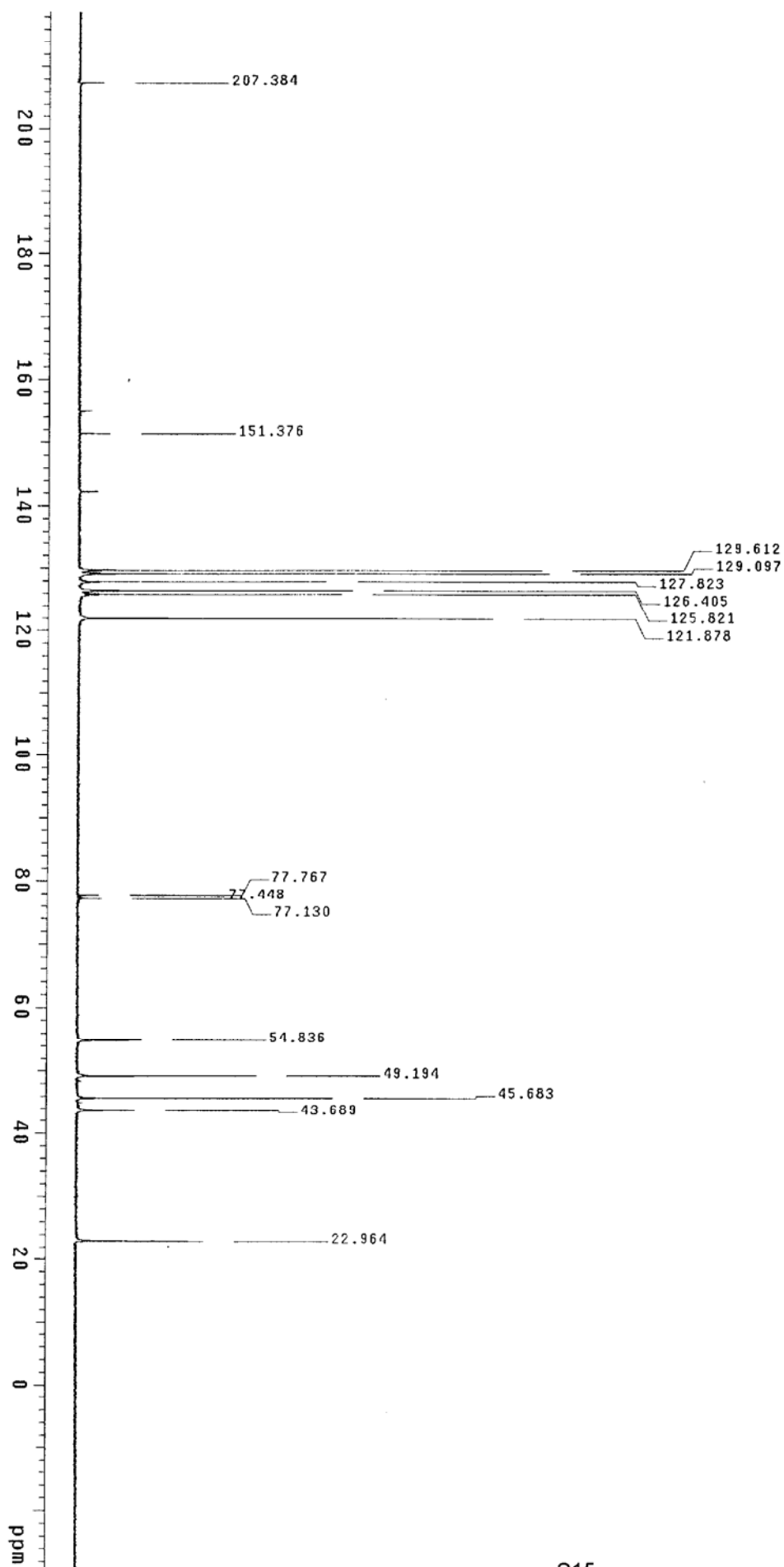
¹H NMR (CDCl₃, 400 MHz)

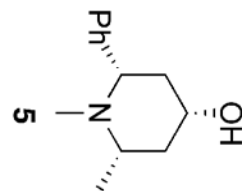


410 MHz

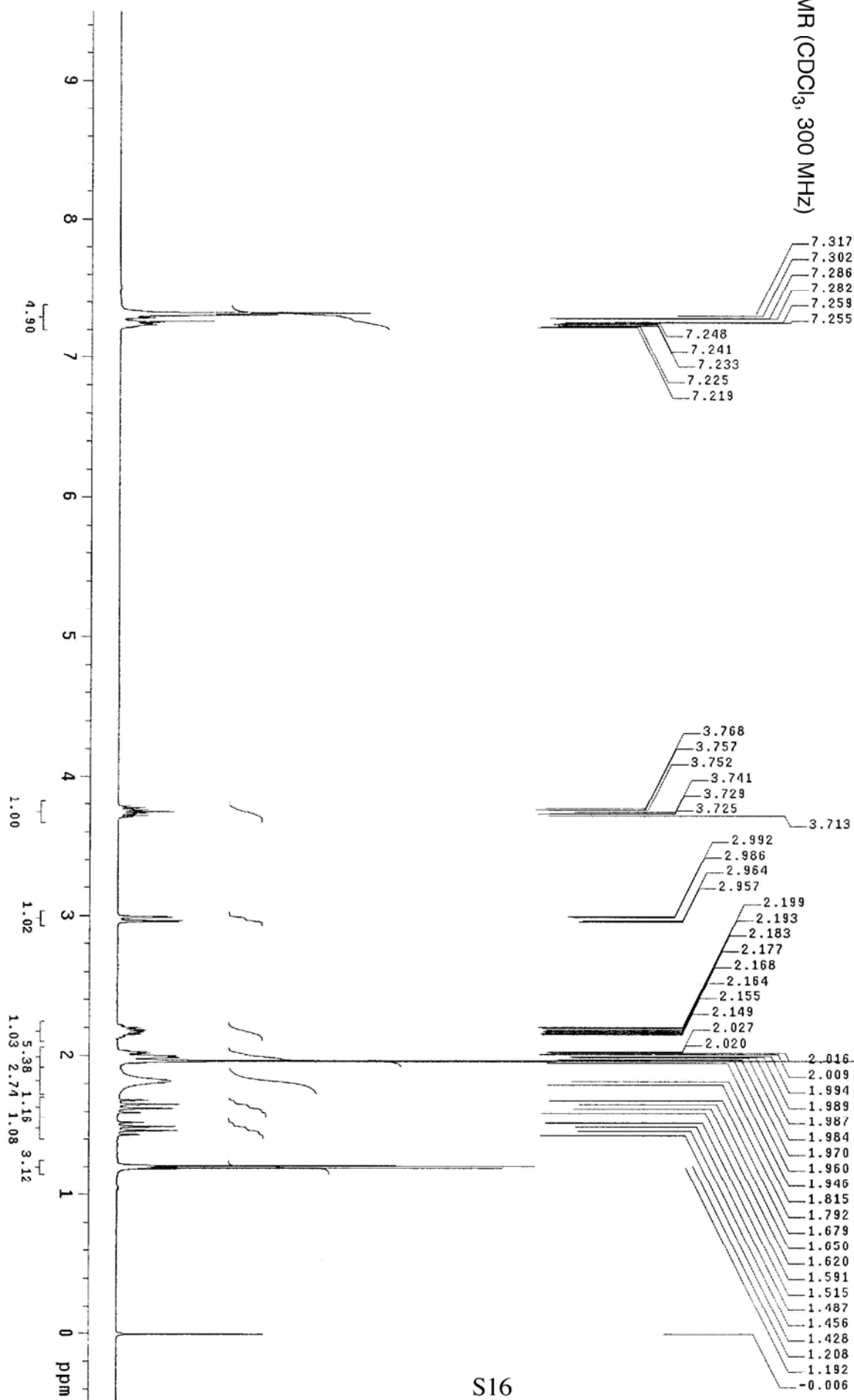


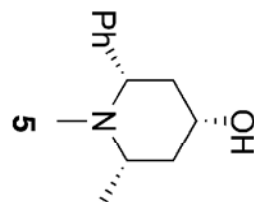
^{13}C NMR (CDCl_3 , 100 MHz)



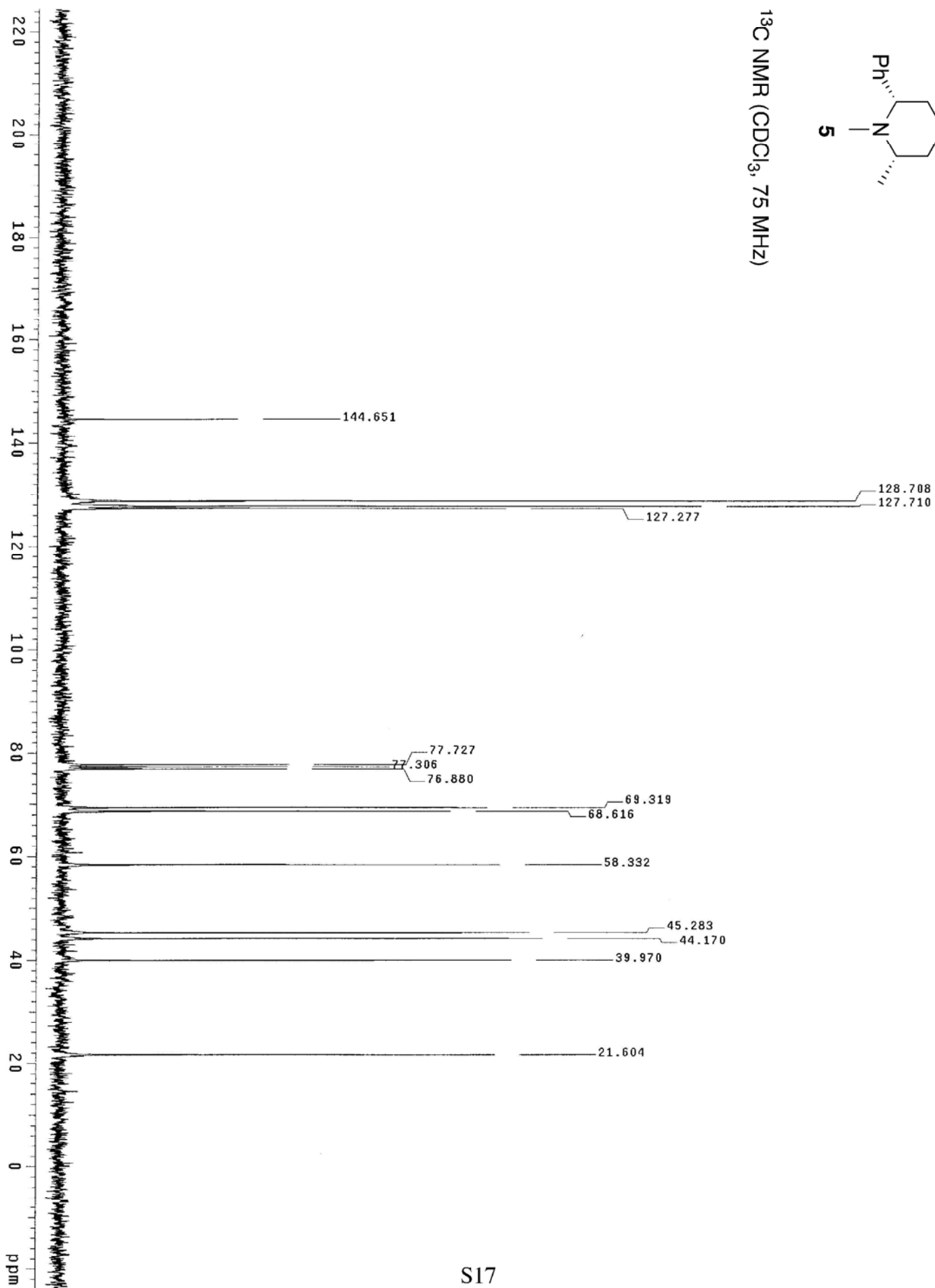


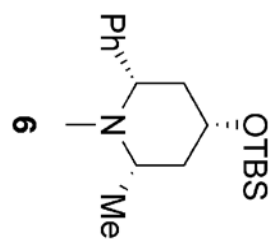
¹H NMR (CDCl₃, 300 MHz)



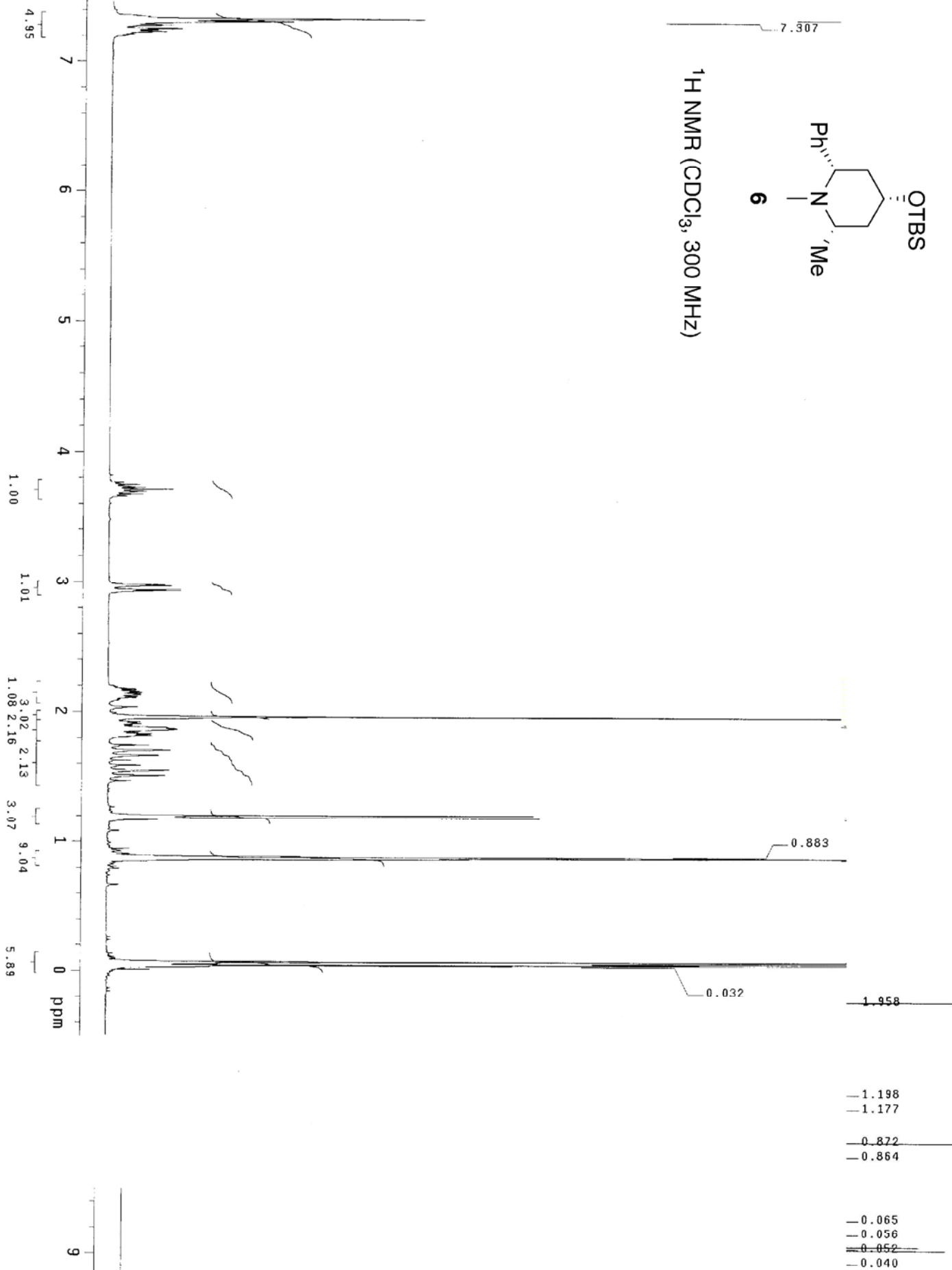


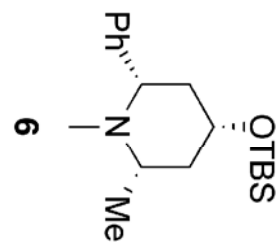
^{13}C NMR (CDCl_3 , 75 MHz)



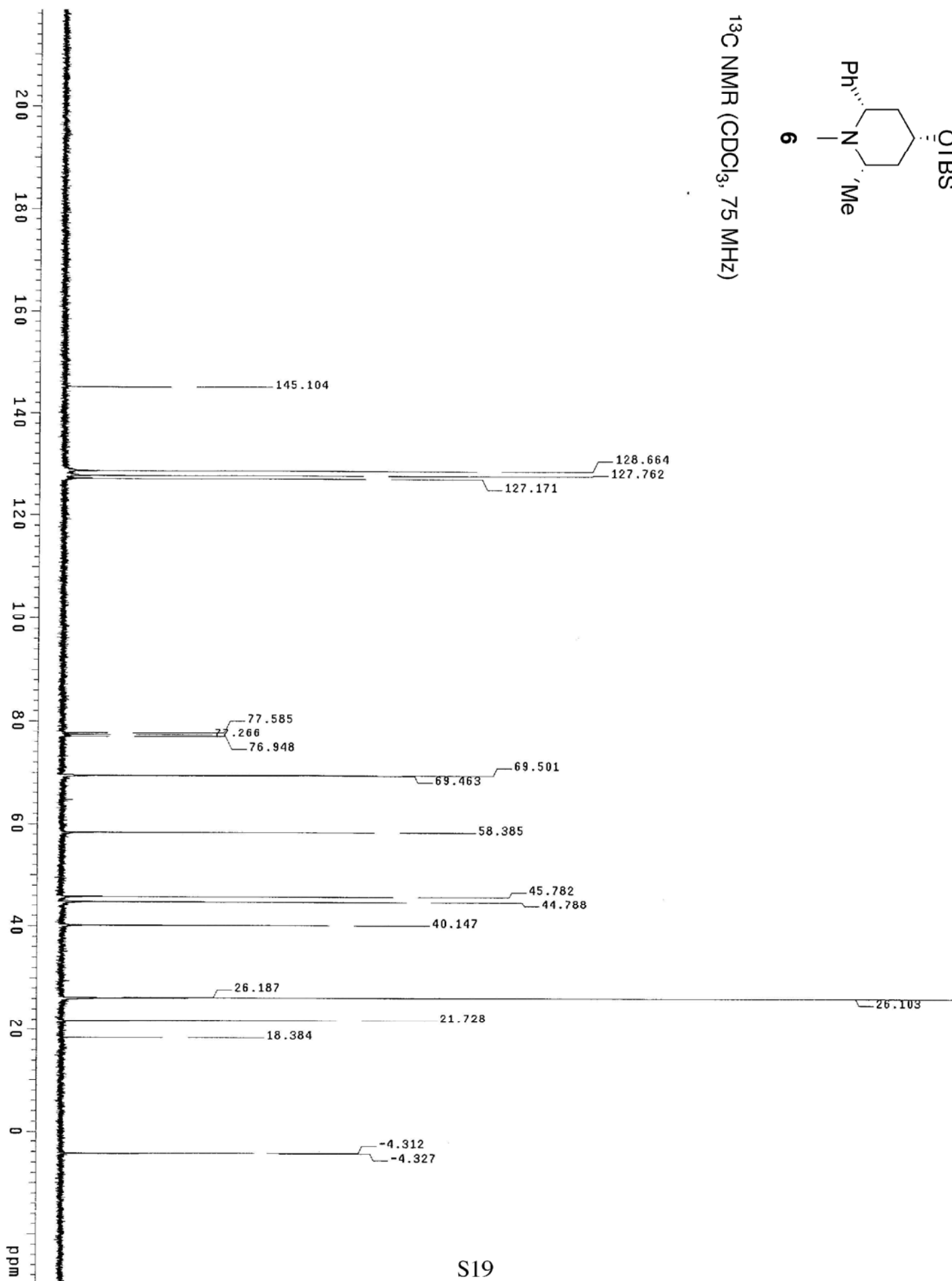


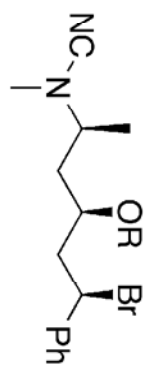
^1H NMR (CDCl_3 , 300 MHz)





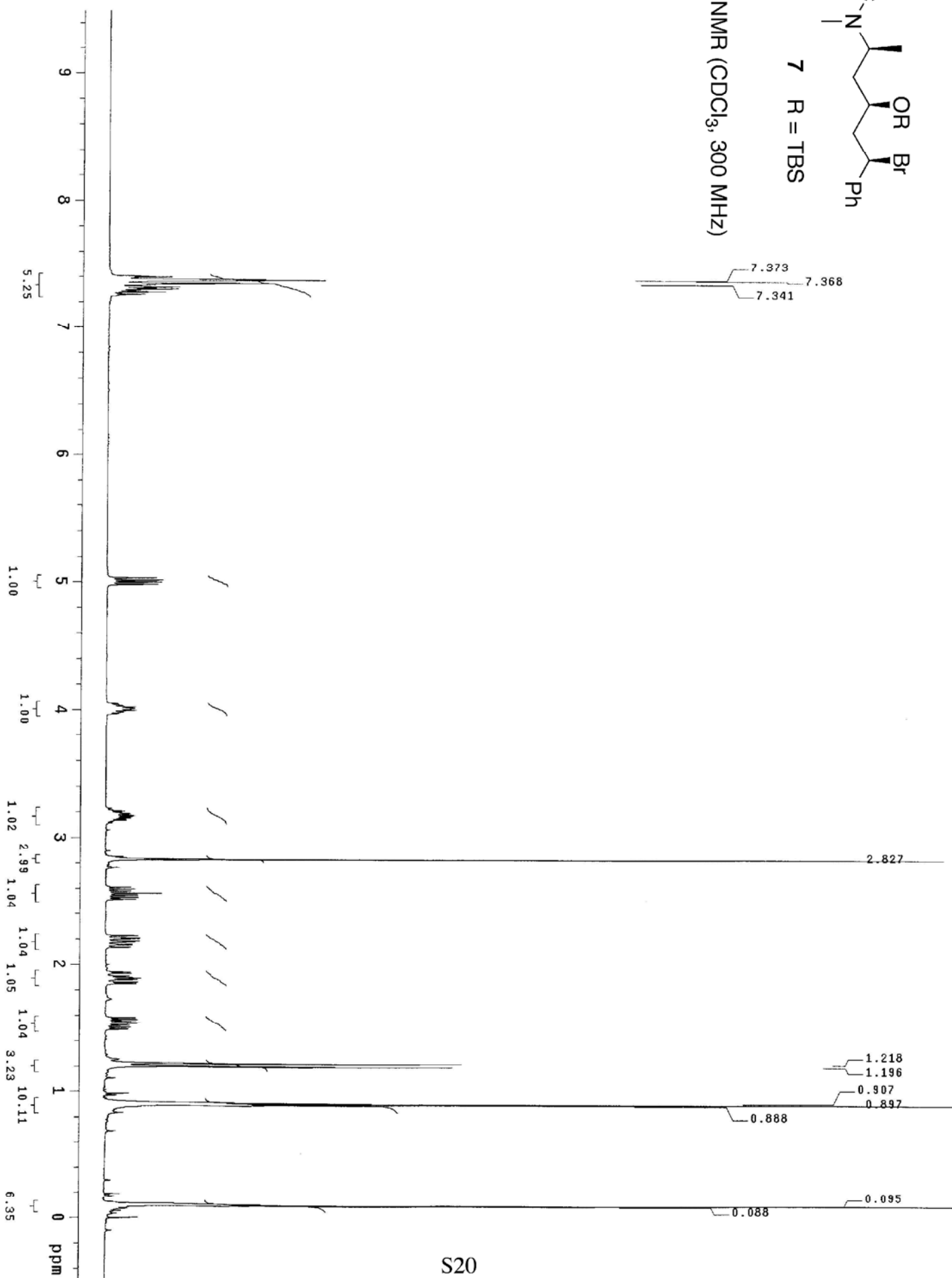
^{13}C NMR (CDCl_3 , 75 MHz)

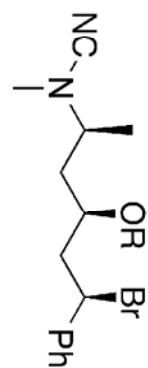




7 R = TBS

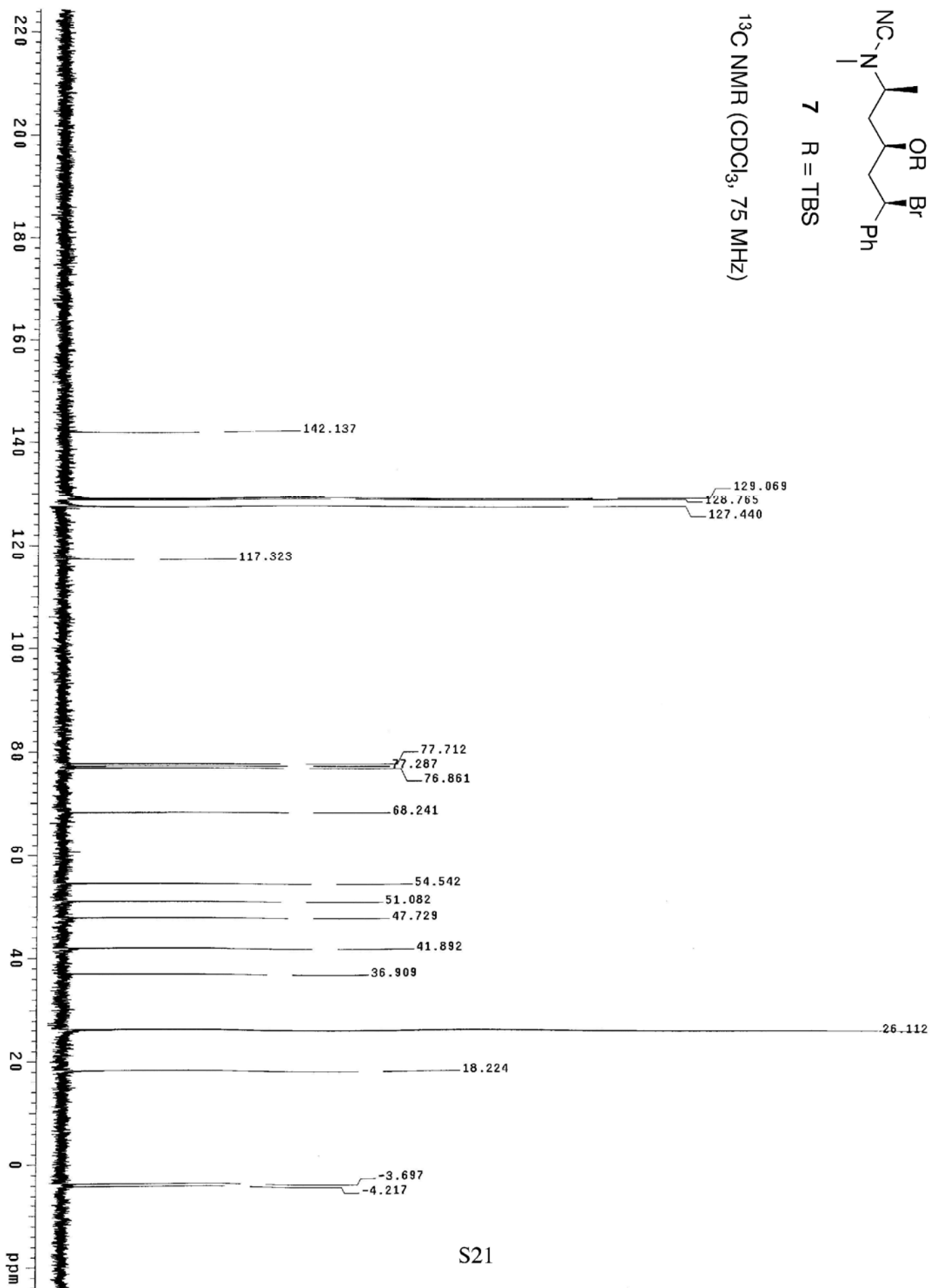
^1H NMR (CDCl_3 , 300 MHz)





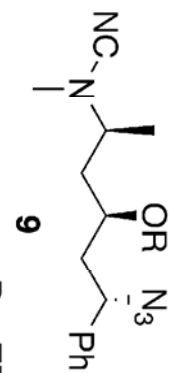
7 R = TBS

¹³C NMR (CDCl₃, 75 MHz)



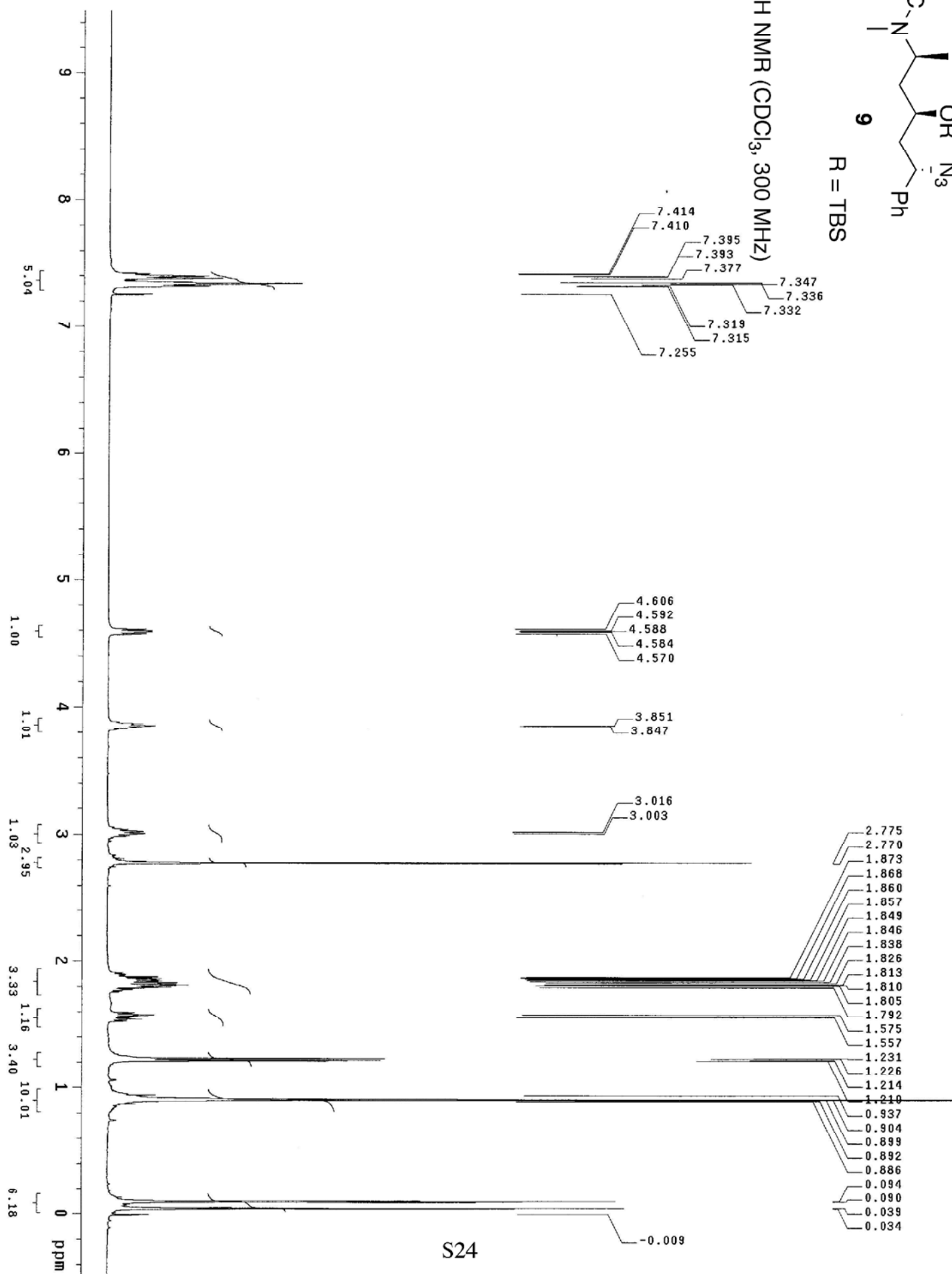
¹H NMR (CDCl₃, 300 MHz)

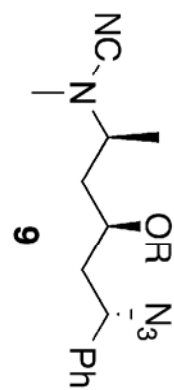




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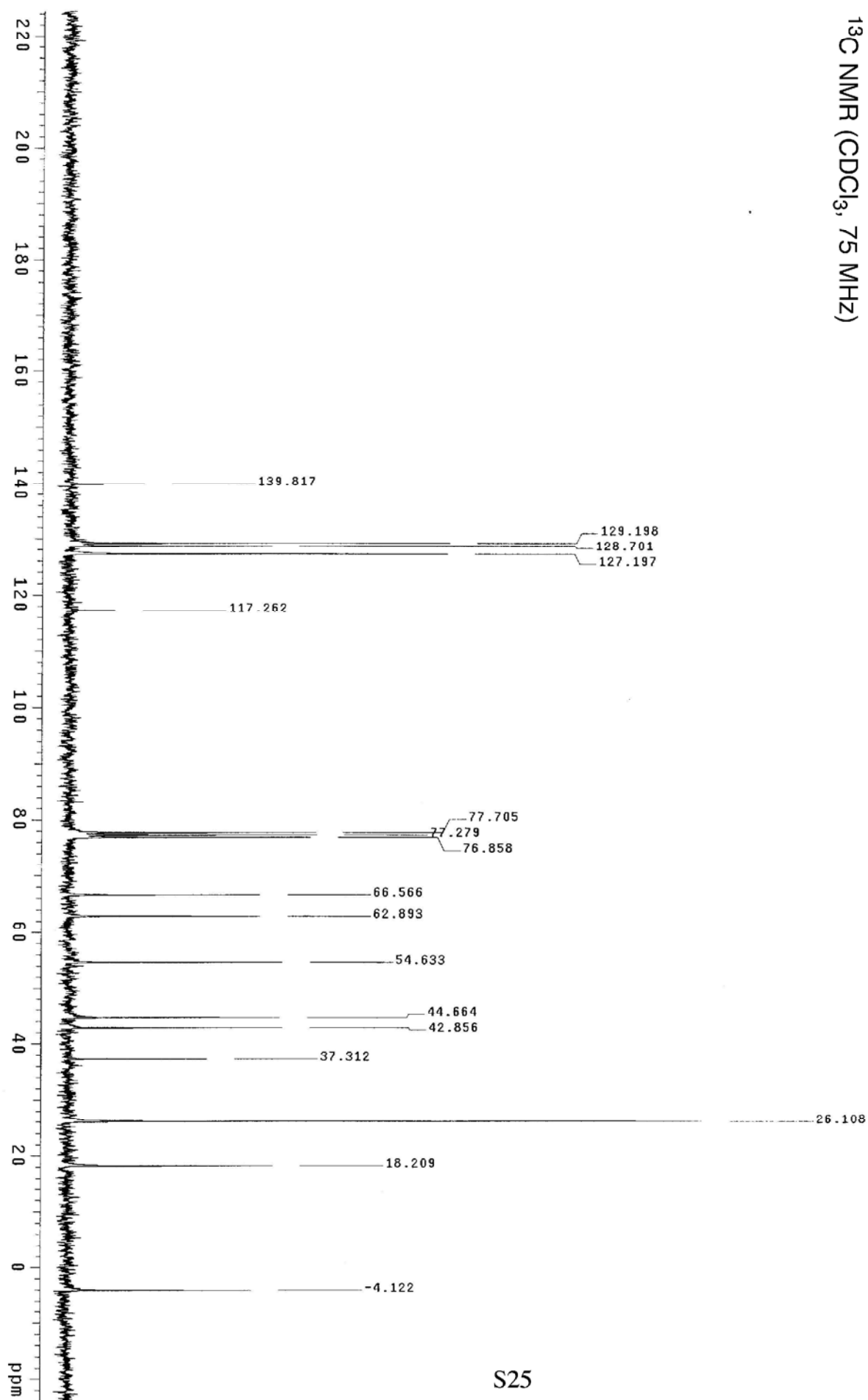
¹H NMR (CDCl₃, 300 MHz)

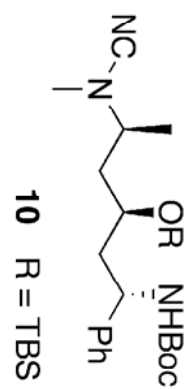




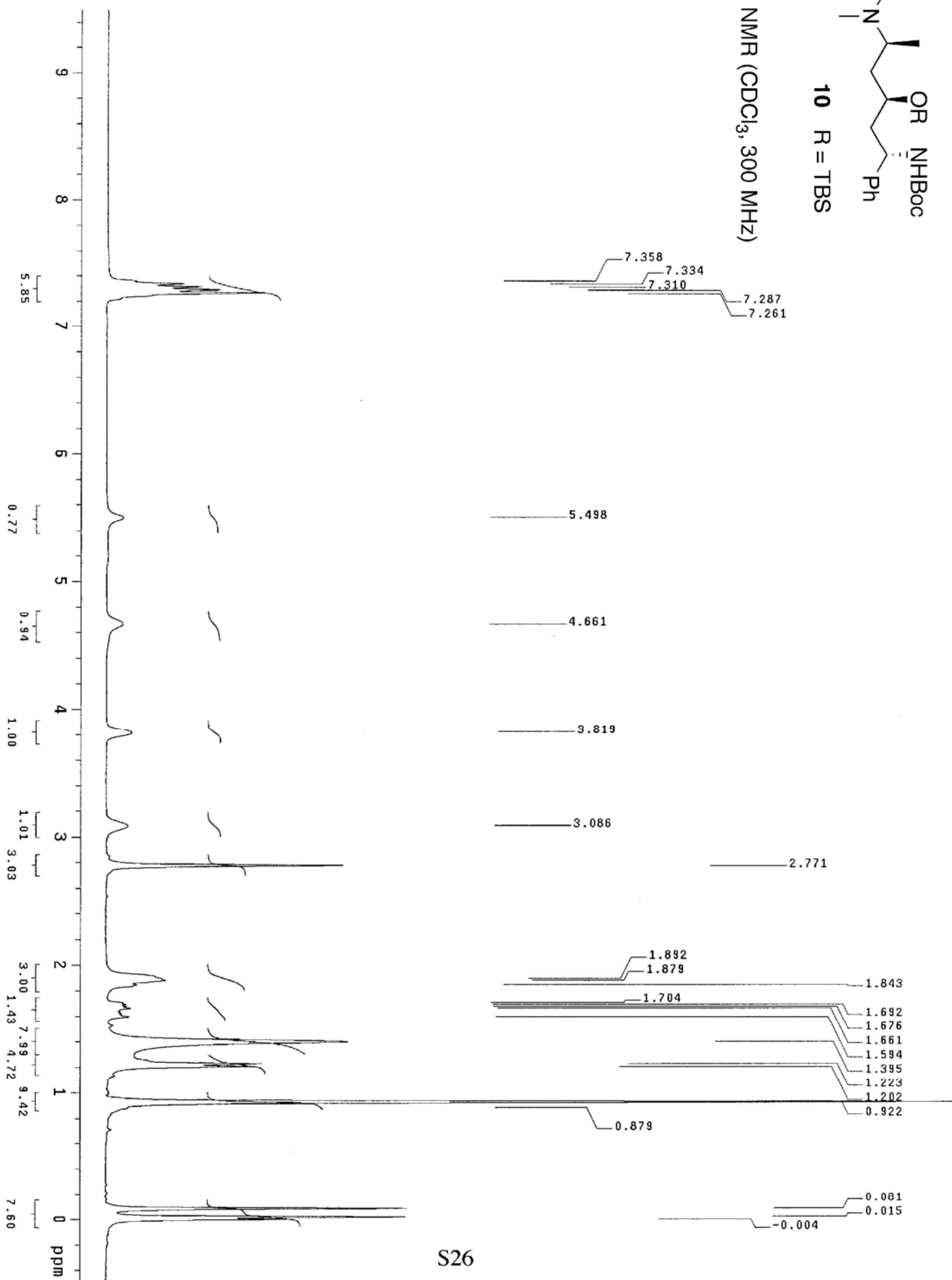
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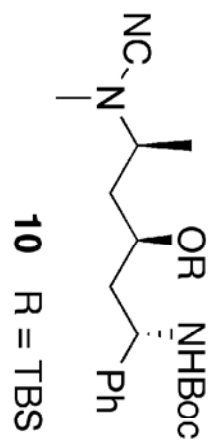
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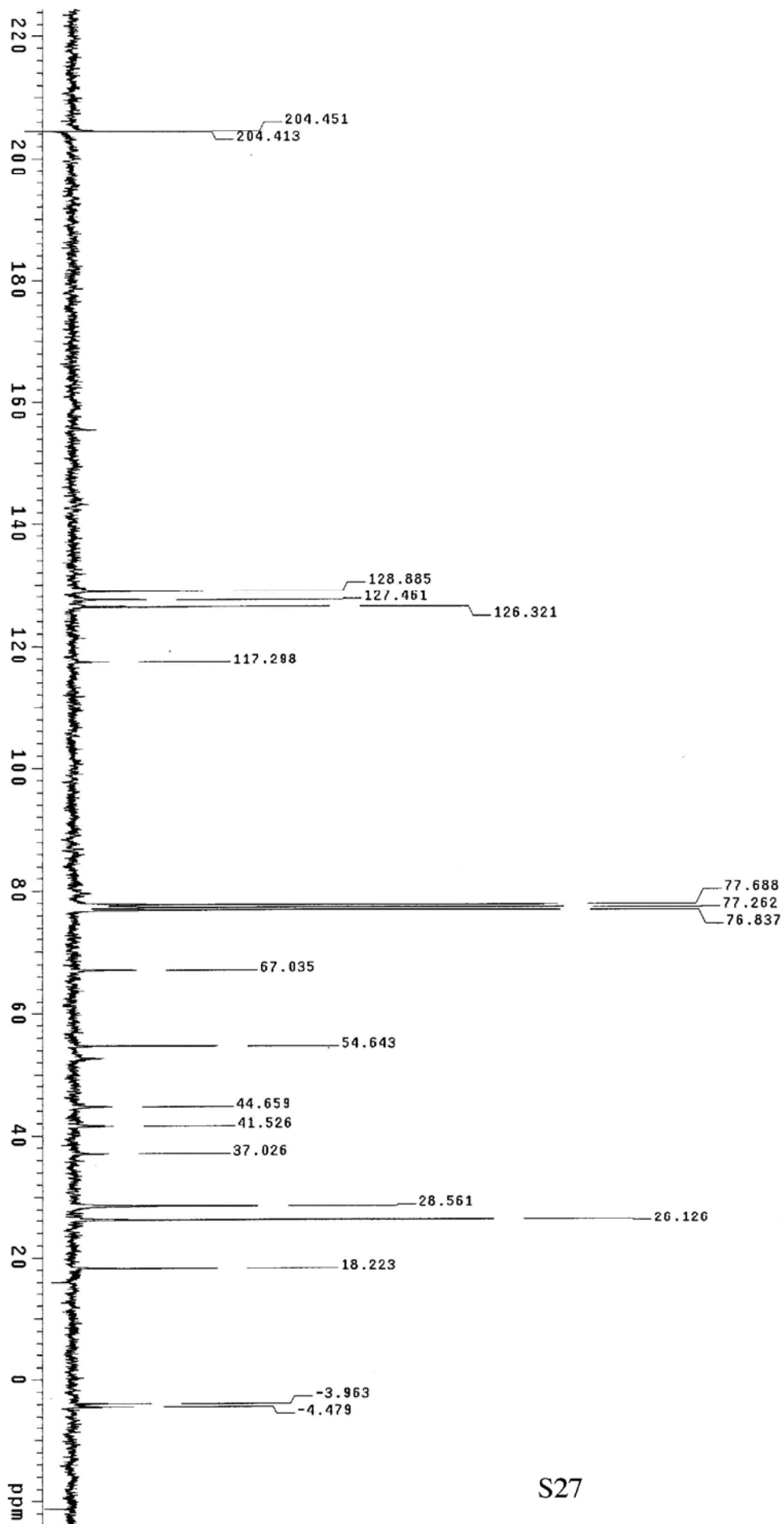


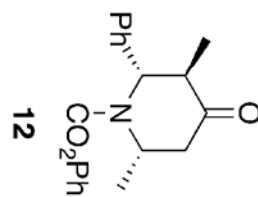
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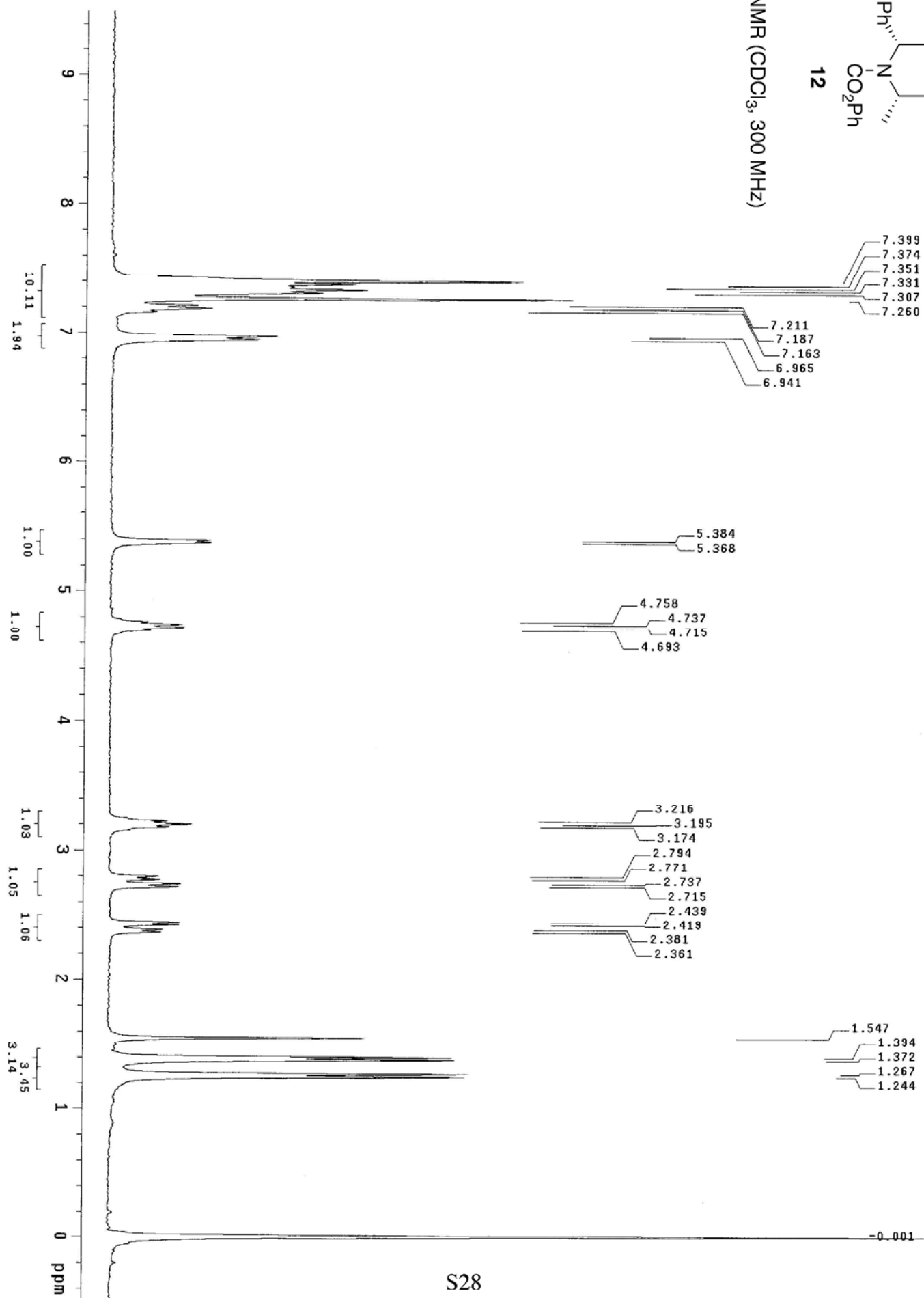


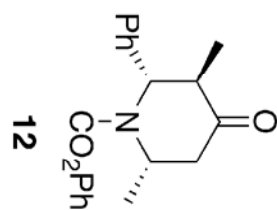
^{13}C NMR (CDCl_3 , 75 MHz)



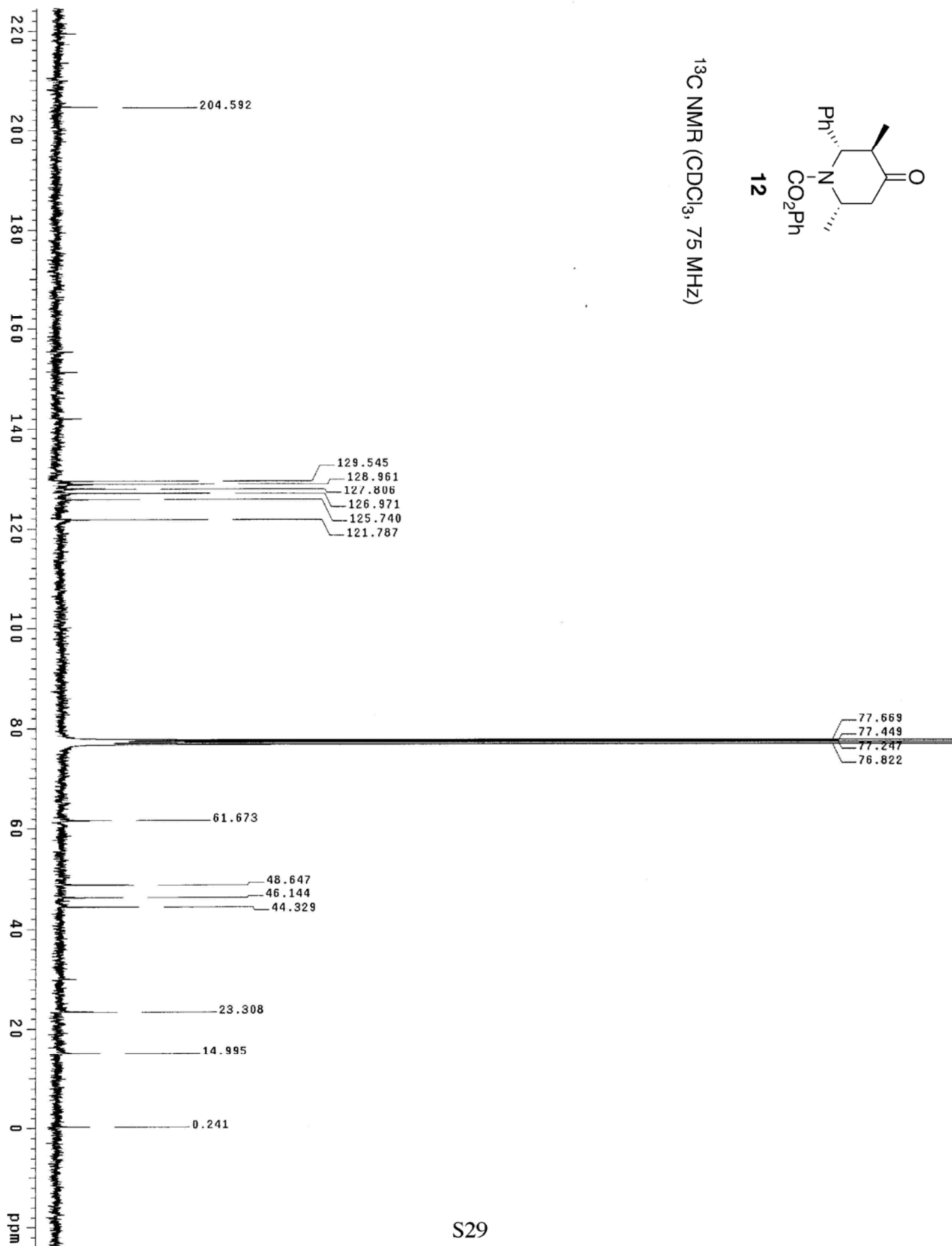


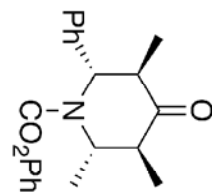
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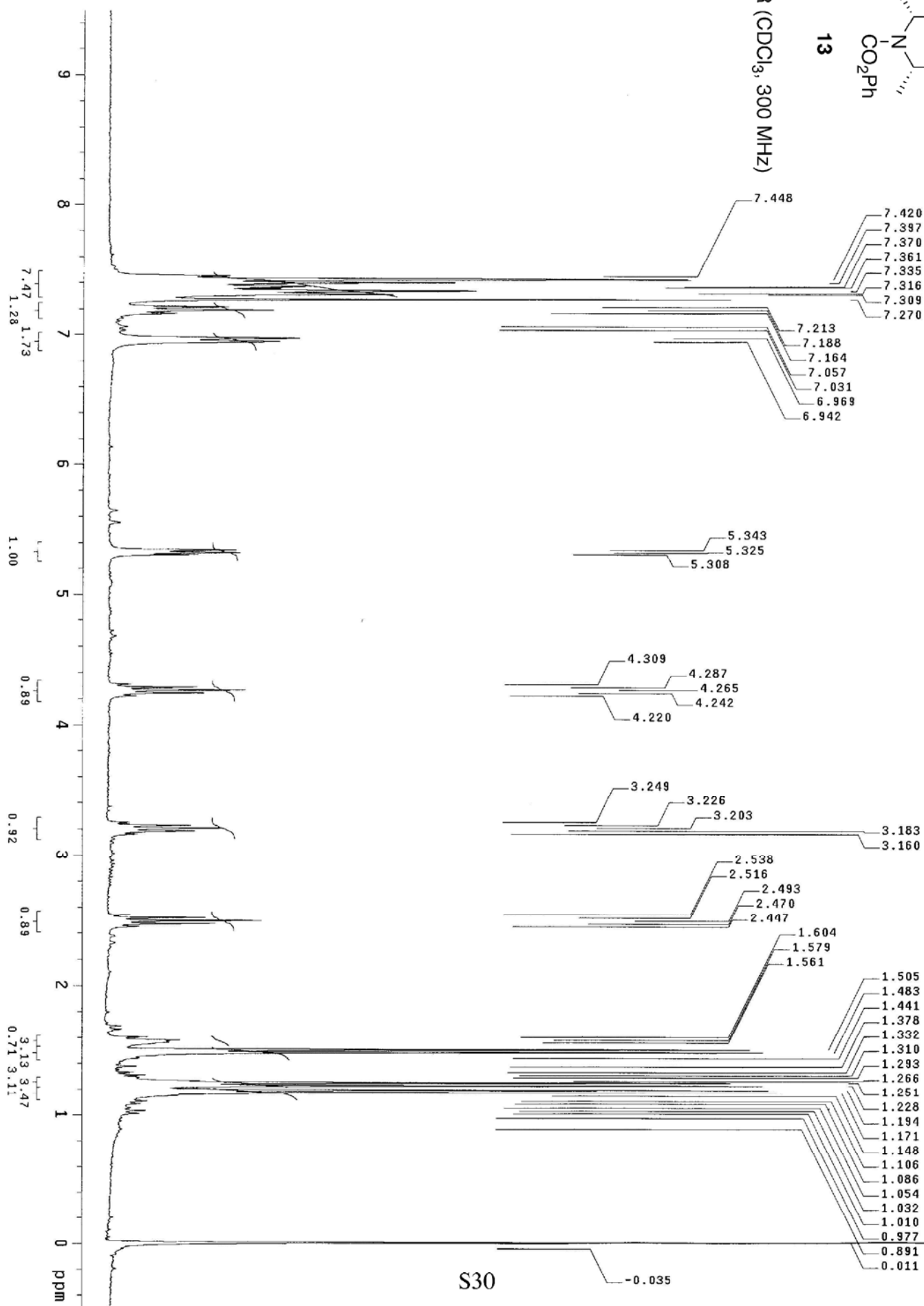
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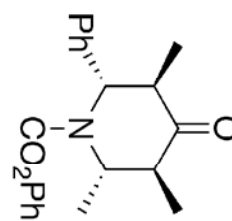




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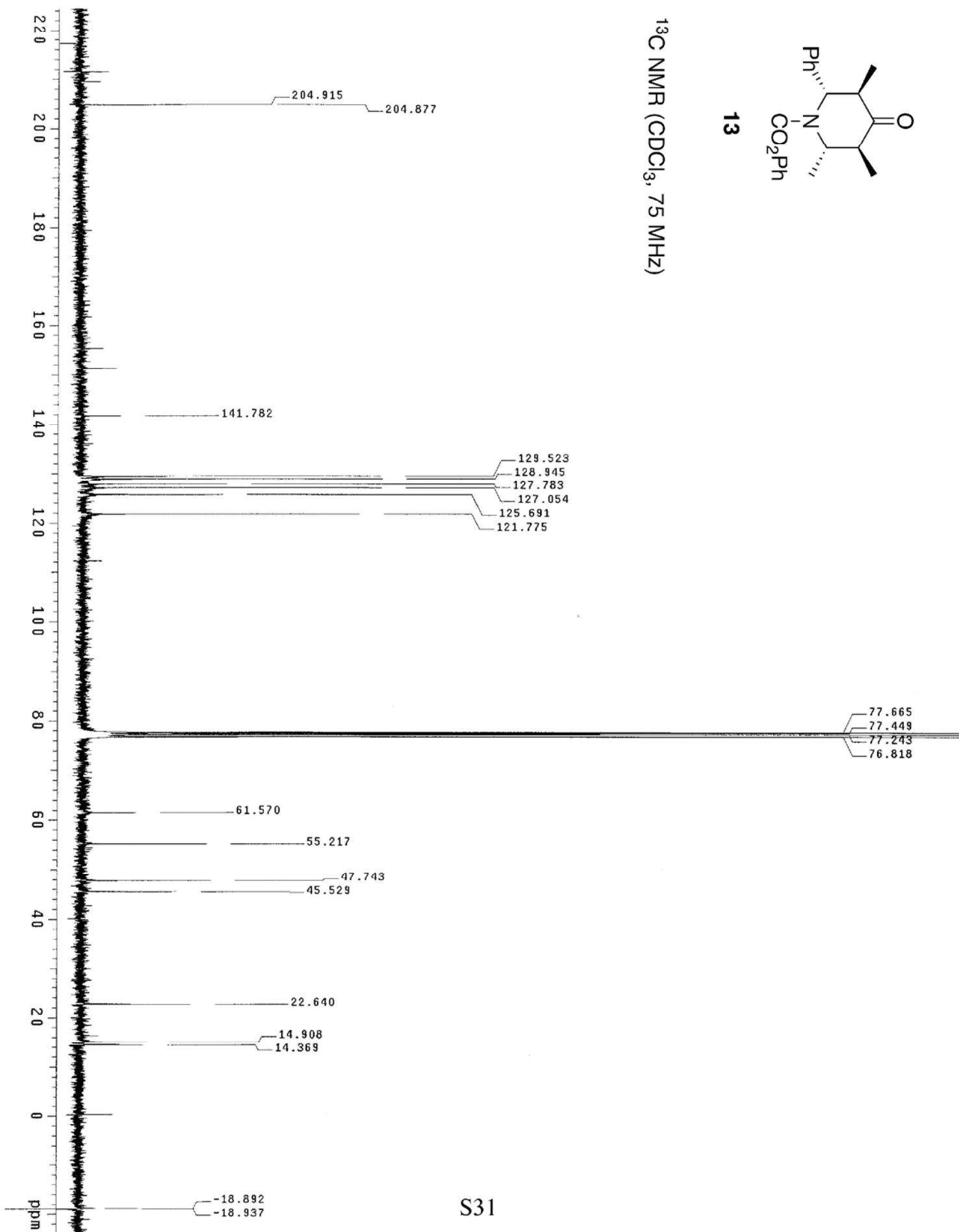
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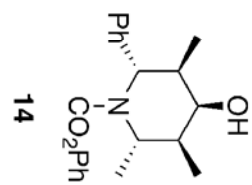




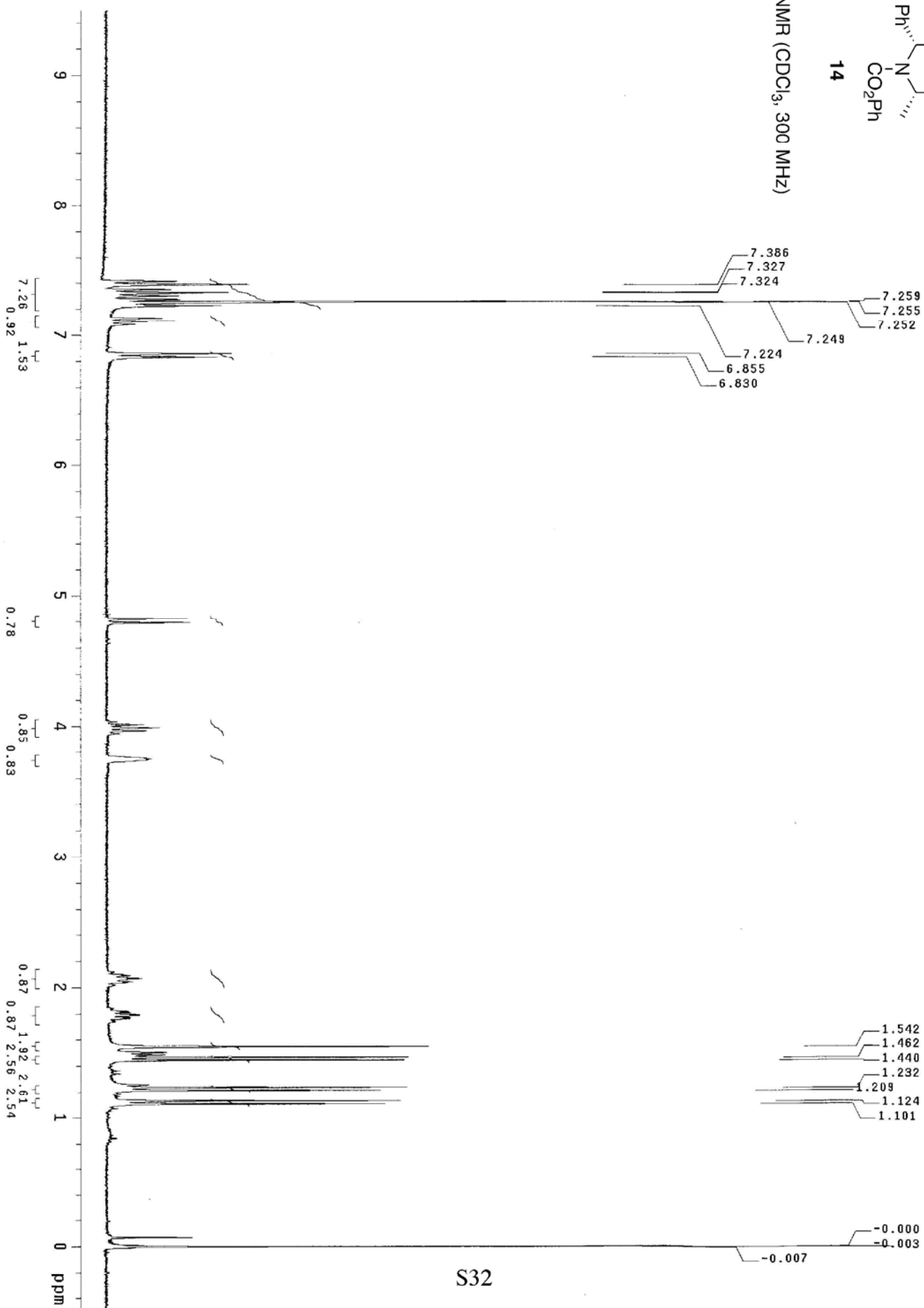
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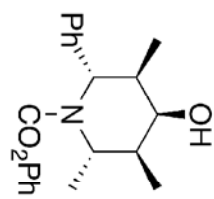
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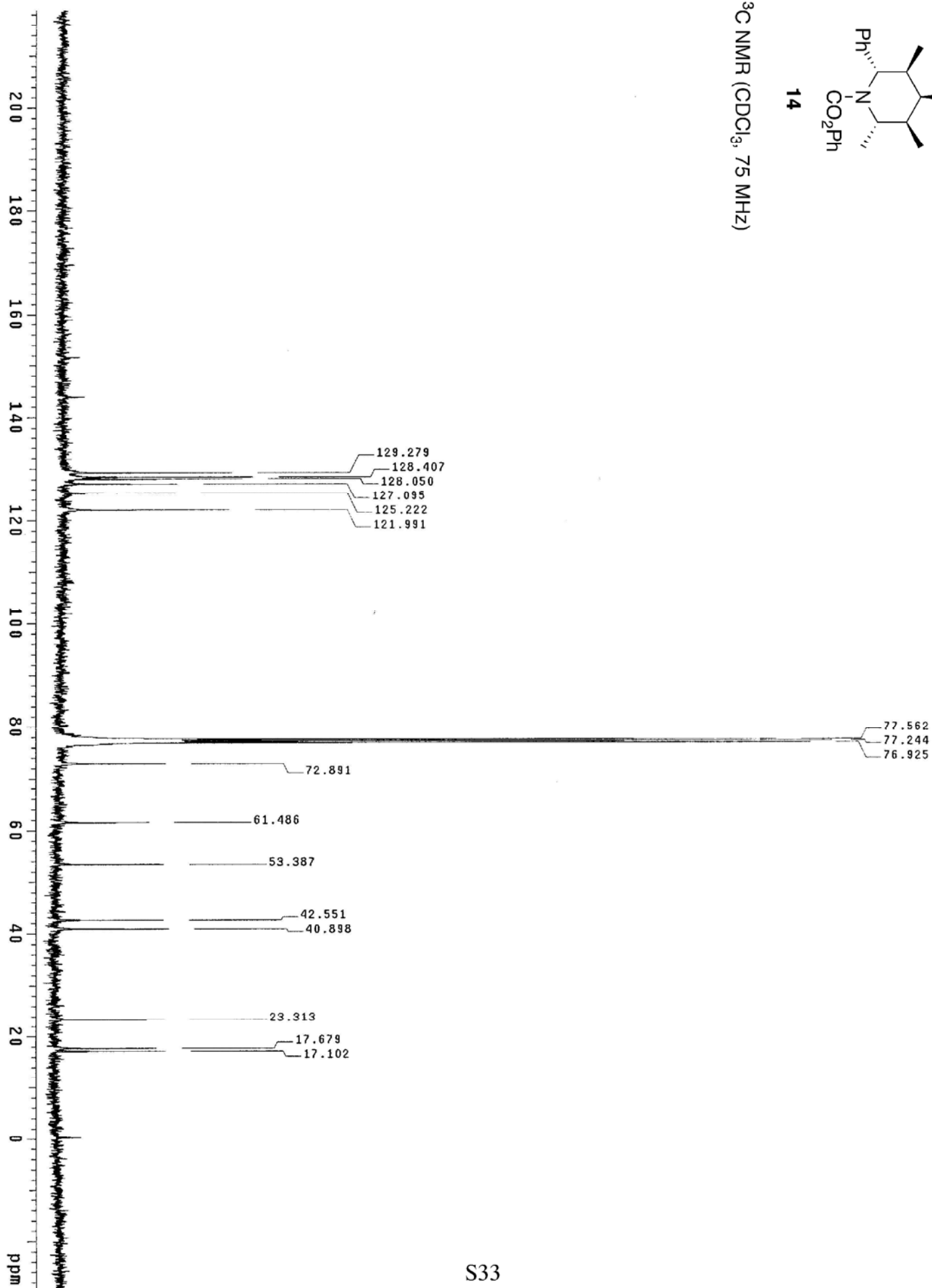


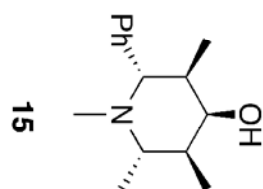
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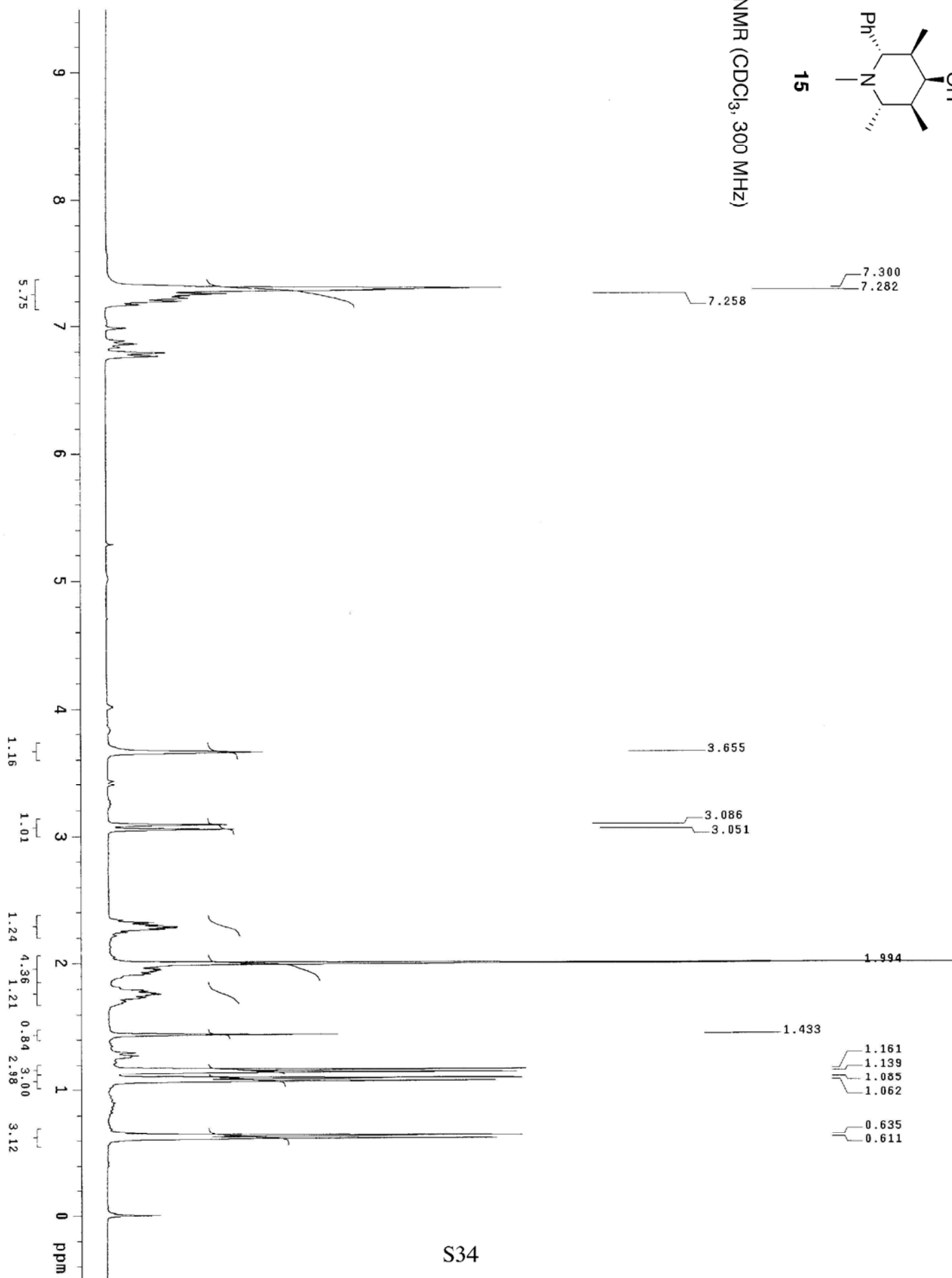


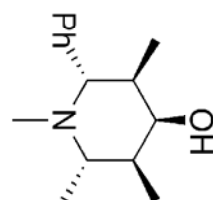
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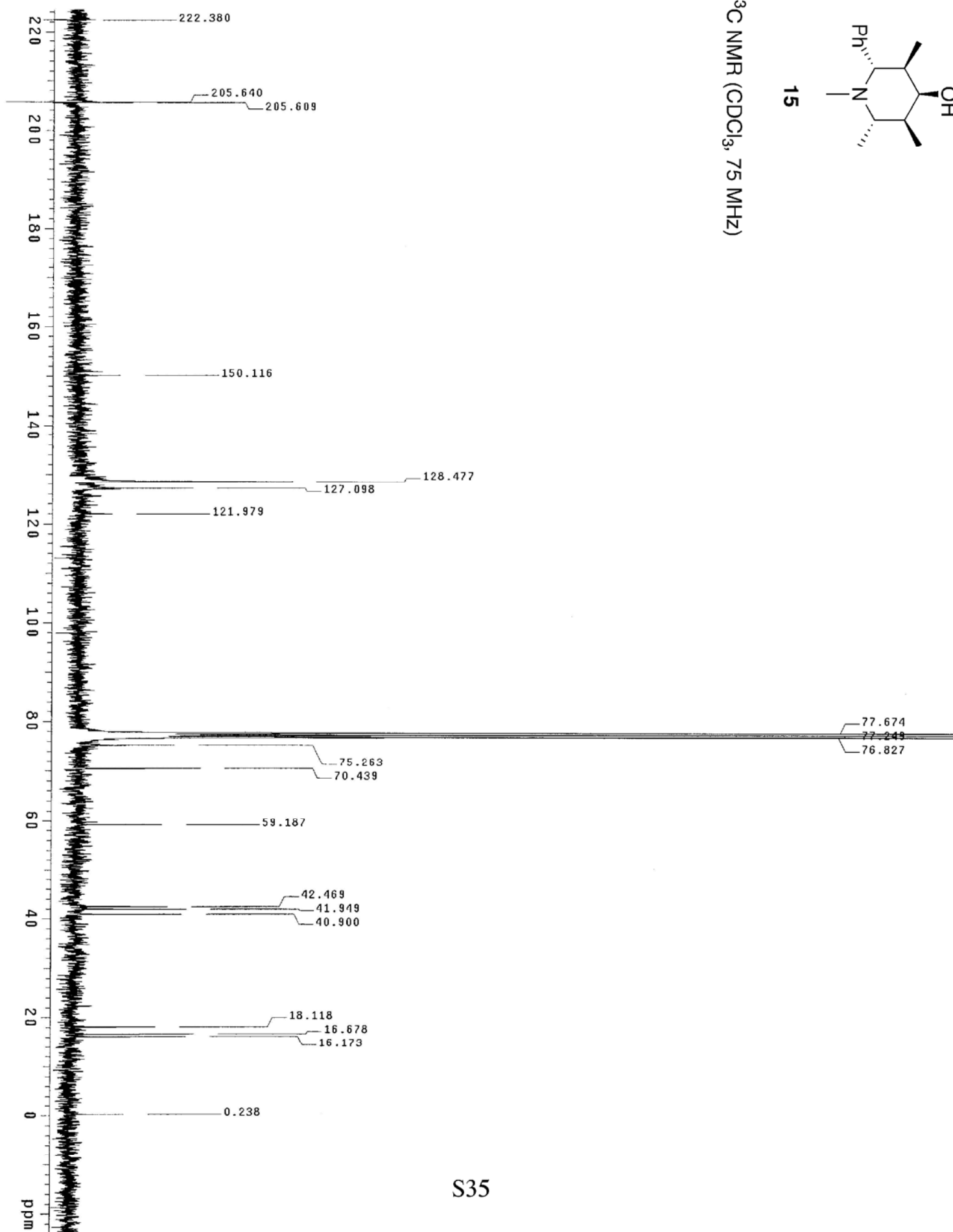
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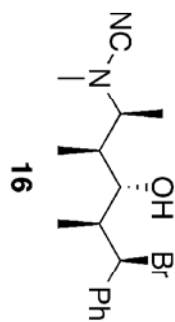




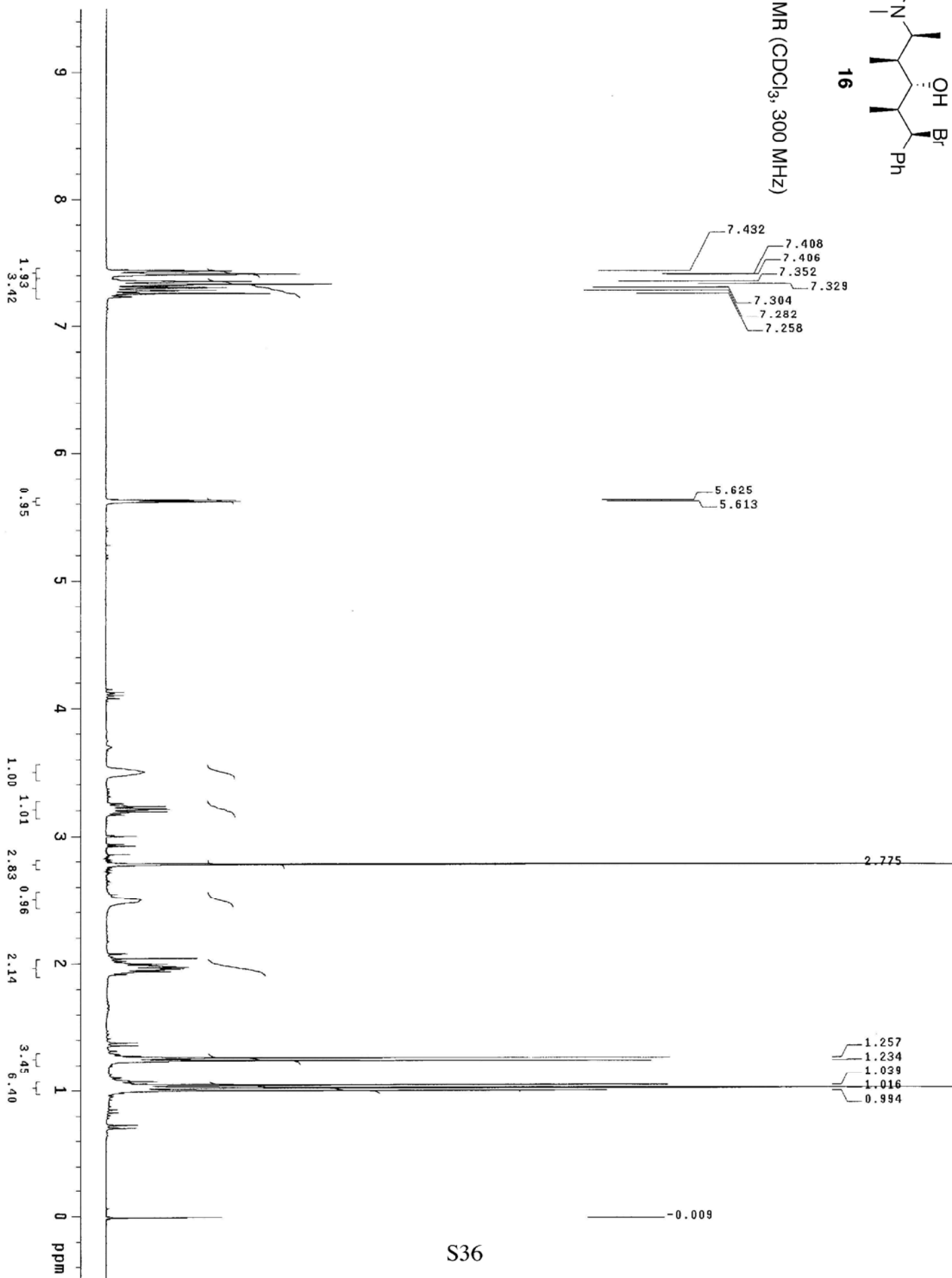
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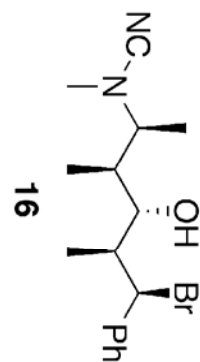
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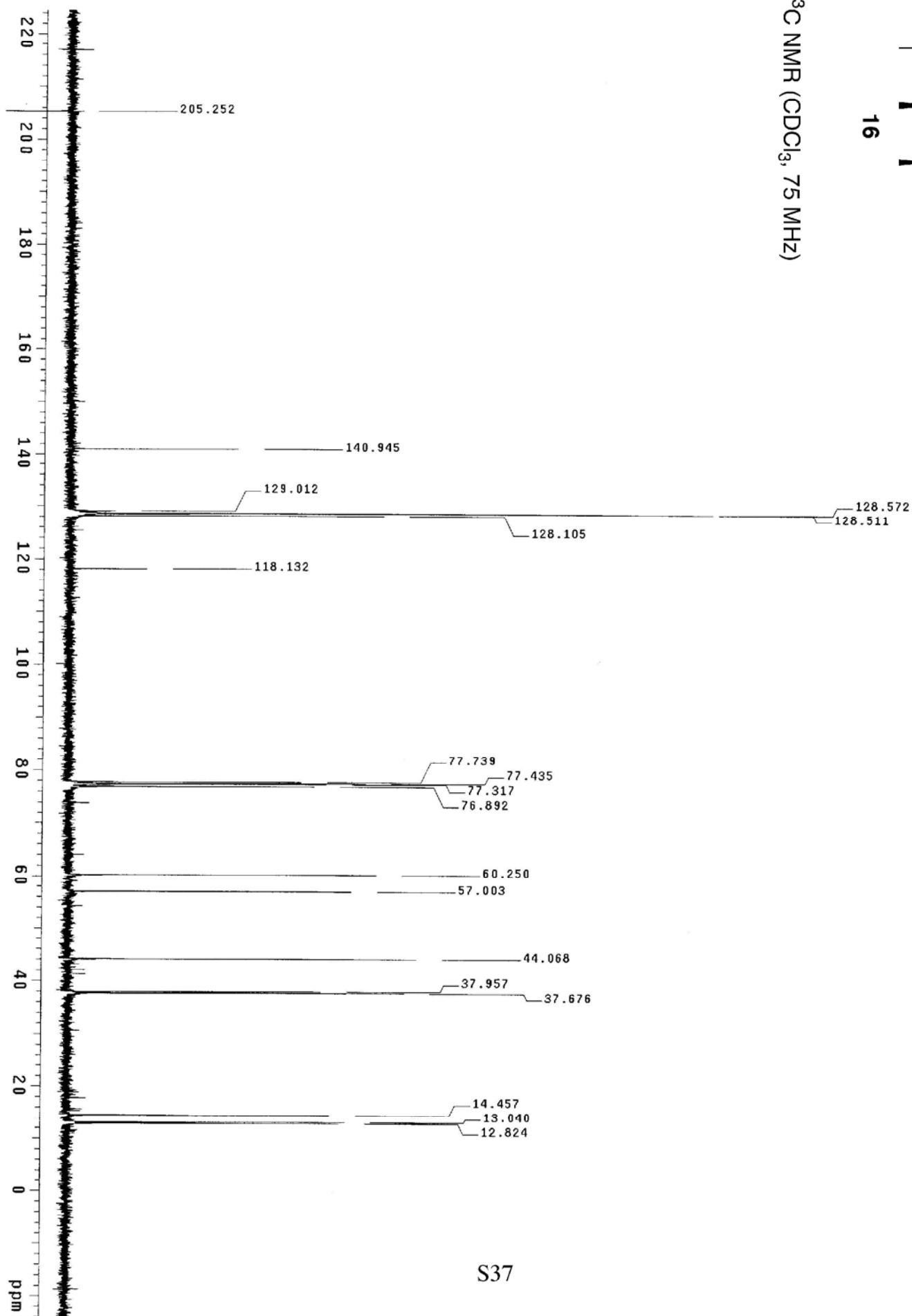


^1H NMR (CDCl_3 , 300 MHz)

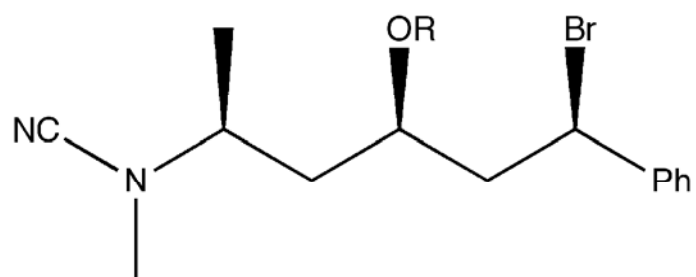
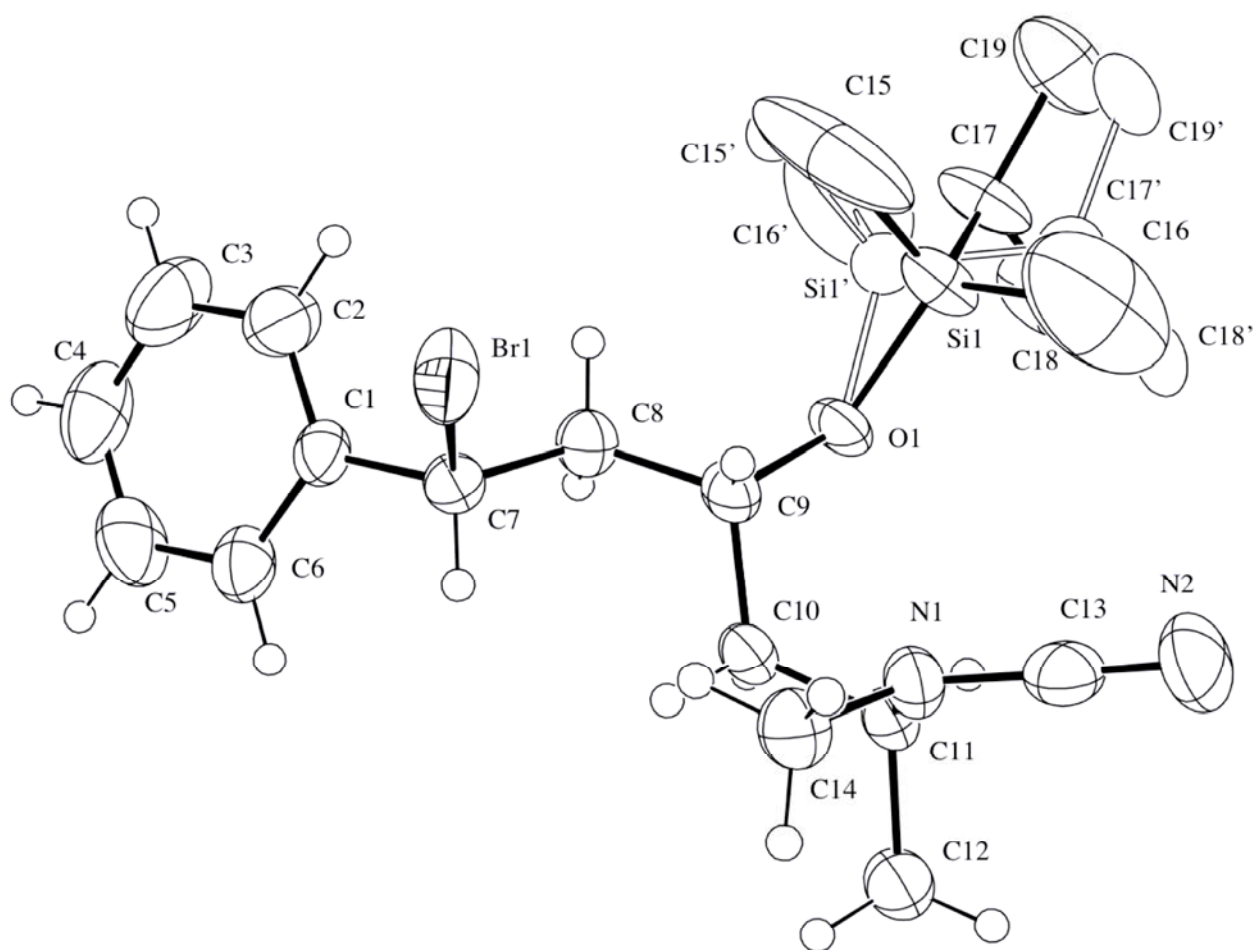




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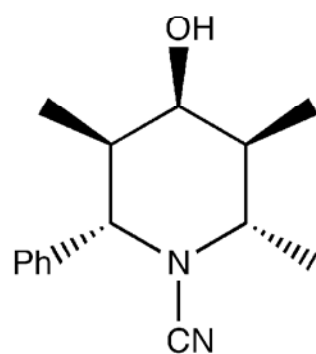
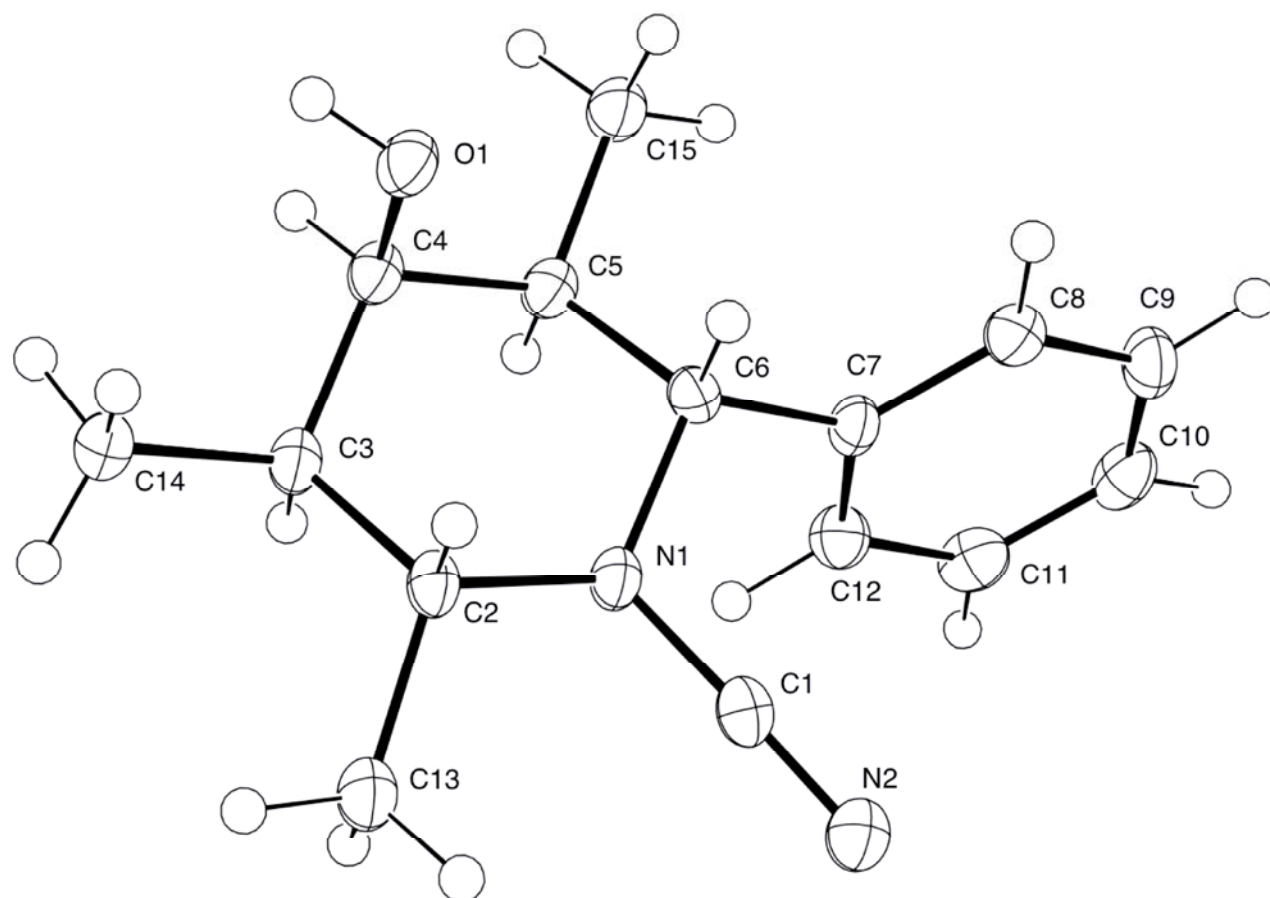


X-ray (ORTEP) of Bromide 7



7 R = TBS

X-ray (ORTEP) of Piperidine **17**



Note: Enantiomer shown in ORTEP

17
(minor)