Supporting Information for:

Stereocontrolled Synthesis and Pharmacological Evaluation of *cis*-2,6-Diphenethyl-1-azabicyclo[2.2.2]octanes as Lobelane Analogues

Guangrong Zheng, Linda P. Dwoskin, Agripina G. Deaciuc, Peter A. Crooks[*]

College of Pharmacy, University of Kentucky, Lexington, Ky 40536-0082, USA

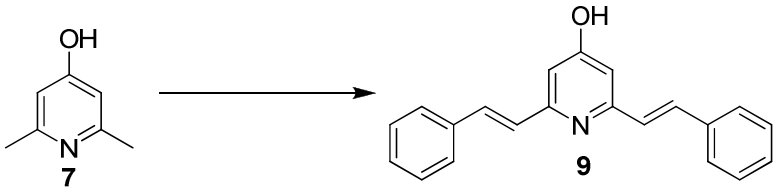
pcrooks@email.uky.edu

Table of Contents

General methods:

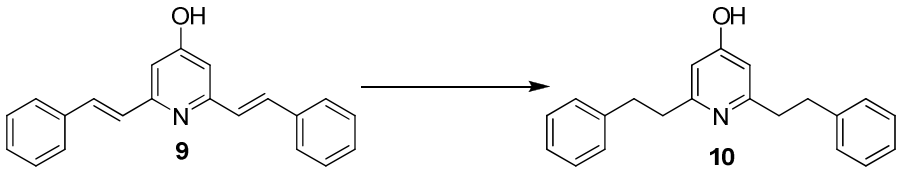
Reagents obtained from commercial sources were used without further purification. If dry and air-free conditions were required, reactions were performed in oven-dried glassware (130 ºC) under a positive pressure of argon. Flash column chromatography was carried out using 32-63 µM, 60 Å silica gel. TLC analysis was carried out on glass plates pre-coated with silica gel 60 F_{254}. Melting points were determined on a melting point apparatus and are uncorrected. NMR spectroscopic data were recorded in $CDCl_3$ on a 300 MHz instrument, and are reported in ppm relative to TMS as internal standard unless otherwise mentioned. High resolution electron impact ionization mass spectra were recorded at 70eV at a resolution of greater than 10000.

Synthesis of 2,6-distyrylpyridin-4-ol (9).



A mixture of compound **7** (1.04g, 8.44 mmol), benzaldehyde (1.97g, 18.58 mmol) and Ac_2O (10 mL) was charged with argon and heated under reflux. Benzaldehyde (450 mg, 4.22 mmol) was added to the reaction mixture every 3 days. After reflux for 12 days, the mixture was allowed to cool to room temperature, 95% EtOH (40 mL) was added and the resulting solution was stirred at room temperature for 3 days. The precipitated solid was filtered and recrystalized twice from benzene to afford **9** (1.08 g, 38%) as a pale yellow crystalline solid: mp >300 °C; ^{1}H NMR (300 MHz, DMSO-d6) δ 6.84 (s, 2H), 7.18-7.46 (m, 8H), 7.62-7.78 (m, 6H), 10.64 (s, 1H); ^{13}C NMR (300 MHz, DMSO-d6) δ 108.8, 127.0, 128.1, 128.4, 128.7, 131.7, 136.3, 155.8, 164.7; MS (EI) *m/z* 299 (M^+), 298 (100), 282, 254, 220, 115, 91, 77, 51; HRMS calcd for $C_{21}H_{17}NO$ (M^+) *m/z* 299.1310, found 299.1309.

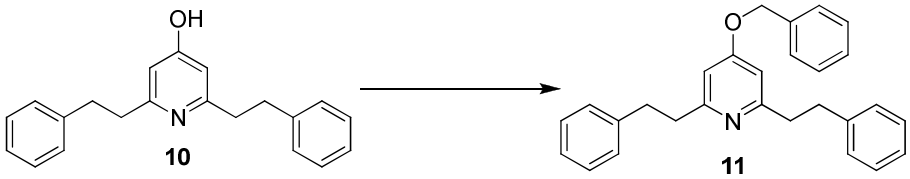
Synthesis of 2,6-diphenethylpyridin-4-ol (10).



To a solution of compound **9** (2.50 g, 8.35 mmol) in MeOH (80 mL) was added Pd/C (10 %, 250 mg). The mixture was hydrogenated on a Parr hydrogenation apparatus (45 psi) for 24 h. The catalyst was removed by filtration through a Celite pad. The filter cake was rinsed with MeOH, and the combined organic portion was concentrated under reduced pressure. The crude product was chromatographed on silica (CH_2Cl_2/MeOH 20:1) to afford **10** (2.52 g, 100%) as a white crystalline solid: mp 214-215 °C; ^{1}H NMR (300 MHz) δ 3.01 (q, A of AA′BB′ system, 4H), 3.27 (q, B of AA′BB′ system, 4H), 7.07 (s, 2H), 7.12-7.25 (m, 10H); ^{13}C NMR (75 MHz) δ 34.8, 35.6, 111.9, 126.9, 128.6, 128.8,

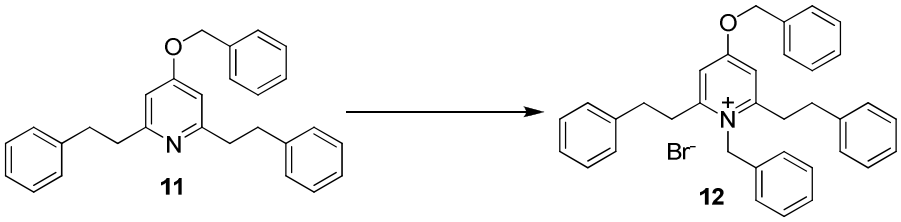
138.8, 156.9, 171.6; MS (EI) *m/z* 303 (M^+), 302 (100), 226, 211, 172, 135, 91; HRMS calcd for $C_{21}H_{21}NO$ (M^+) *m/z* 303.1623, found 303.1621.

Synthesis of 4-benzyloxy-2,6-diphenethylpyridine (11).



A mixture of compound **10** (1.72 g, 5.67 mmol), benzyl bromide (1.16 g, 6.80 mmol) and K_2CO_3 (1.56 g, 11.34 mmol) in DMF (30 mL) was heated at 80 °C overnight. Water (100 mL) was added to the cooled reaction mixture, which was then extracted with Et_2O (40 mL × 3). The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was chromatographed on silica (hexanes/EtOAc 10:1) to afford **11** (1.95 g, 87%) as a white crystalline solid: mp 79-80 °C; ^{1}H NMR (300 MHz) δ 3.03 (s, 8H), 4.95 (s, 2H), 6.49 (s, 2H), 7.13-7.40 (m, 15H); ^{13}C NMR (75 MHz) δ 36.3, 40.5, 69.7, 107.2, 126.0, 127.6, 128.3, 128.4, 128.6, 128.7, 136.1, 141.7, 162.4, 165.4; MS (EI) *m/z* 393 (M^+) (100), 316, 302, 274, 182, 91, 77, 65; HRMS calcd for $C_{28}H_{27}NO$ (M^+) *m/z* 393.2092, found 393.2092.

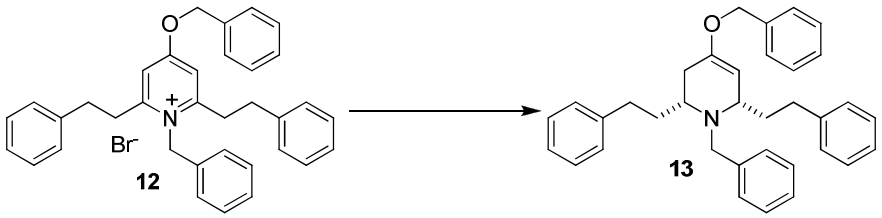
Synthesis of *N*-benzyl-4-benzyloxy-2,6-diphenethylpyridinium bromide (12).



A mixture of compound **11** (149 mg, 0.38 mmol) and benzyl bromide (1.30 g, 7.60 mmol) in acetonitrile (5 mL) was heated under reflux for 4 days. Solvent was removed under reduced pressure and the resulting residue was washed several times with a mixture of diethyl ether and hexanes (1:4). The crude product was chromatographed on silica, eluted with hexanes/EtOAc (8:1) to recover compound **11** (67 mg) and then eluted with

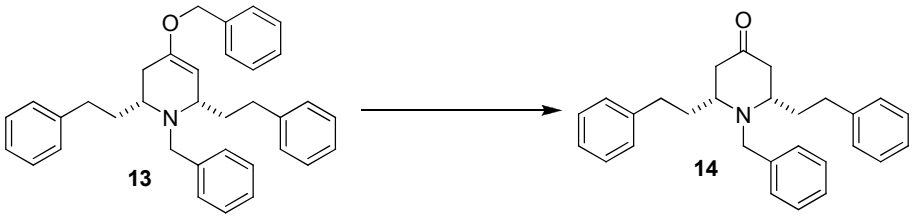
CH_2Cl_2/MeOH (10:1) to afford **12** (76 g, 36%) as a pale yellow gum: ^{1}H NMR (300 MHz) δ 3.05 (t, J = 7.5 Hz, 4H), 3.36 (t, J = 7.5 Hz, 4H), 5.40 (s, 2H), 5.74 (s, 2H), 6.86 (t, J = 3.6 Hz, 2H), 7.08-7.52 (m, 20H); ^{13}C NMR (75 MHz) δ 34.5, 35.6, 54.3, 73.3, 113.8, 125.2, 127.0, 128.5, 128.6, 128.9, 129.2, 129.8, 132.9, 133.8, 138.5, 159.8, 169.2.

Synthesis of *cis*-*N*-benzyl-4-benzyloxy-2,6-diphenethyl-1,2,5,6-tetrahydropyridine (13).



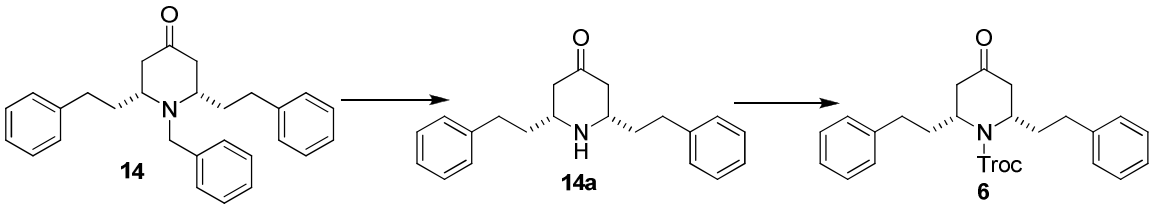
To a solution of compound **12** (166 mg, 0.29 mmol) in ethanol (5 mL) was added $NaBH_4$ (45 mg, 1.18 mmol). The reaction mixture was stirred at room temperature for 30 min. The reaction was then quenched by slowly adding acetone (1 mL) and solvents were removed under reduced pressure. The residue was taken up into water and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was chromatographed on silica (hexanes/EtOAc 8:1) to afford **13** (127 mg, 89%) as a pale yellow oil: ^{1}H NMR (300 MHz) δ 1.50-1.66 (m, 1H), 1.68-1.87 (m, 2H), 1.92-2.08 (m, 2H), 2.12-2.88 (m, 2H), 2.63-2.83 (m, 2H), 2.86-3.02 (m, 1H), 3.05-3.25 (m, 2H), 3.35 (d, J = 13.8 Hz, 1H), 3.84 (d, J = 13.8 Hz, 1H), 4.56 (d, J = 3.6 Hz, 1H), 4.75 (s, 2H), 6.93-6.98 (m, 2H), 7.06-7.43 (m, 18H); ^{13}C NMR (75 MHz) δ 29.9, 33.2, 33.4, 34.5, 37.3, 49.8, 51.4, 56.4, 68.7, 96.7, 125.5, 125.9, 126.8, 127.7, 127.9, 128.3, 128.46, 128.49, 128.6, 129.2, 137.5, 140.9, 142.6, 143.1, 152.6; MS (EI) *m/z* 487 (M^+), 382 (100), 340, 278, 224, 91, 77, 65; HRMS calcd for $C_{35}H_{37}NO$ (M^+) m/z 487.2874, found 487.2878.

Synthesis of *cis*-*N*-benzyl-2,6-diphenethyl piperidin-4-one (14).



To a solution of compound **13** (127 mg, 0.26 mmol) in CH_2Cl_2 (5 mL) was added trifluoroacetic acid (1 mL) and water (0.2 mL). The mixture was stirred at room temperature overnight before being neutralized with saturated aqueous K_2CO_3 and diluted with water (10 mL). The aqueous phase was extracted with CH_2Cl_2 (20 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was chromatographed on silica (CH_2Cl_2/MeOH 30:1) to afford **14** (67 mg, 96%) as a pale yellow oil: ^{1}H NMR (300 MHz) δ 1.60-1.76 (m, 2H), 1.84-2.00 (m, 2H), 2.24 (ddd, J = 14.1, 6.9, 1.2 Hz, 2H), 2.46-2.64 (m, 4H), 2.76 (ddd, J = 15.6, 9.9, 5.4 Hz, 2H), 3.22-3.34 (m, 2H), 3.65 (d, J = 13.8 Hz, 1H), 4.11 (d, J = 14.1 Hz, 1H), 7.02-7.50 (m, 15H); ^{13}C NMR (75 MHz) δ 32.8, 35.1, 42.8, 49.3, 56.0, 126.0, 127.3, 128.4, 128.5, 128.66, 128.69, 139.6, 141.8, 209.3; MS (EI) *m/z* 397 (M^+), 292, 132, 91 (100), 77, 65; HRMS calcd for $C_{16}H_{16}{}^{35}Cl_3NO_3$ (M^+) m/z 397.2405, found 397.2403.

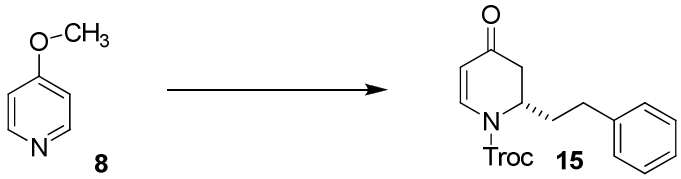
Synthesis of *cis*-*N*-[(2,2,2-trichloroethoxy)carbonyl]-2,6-diphenethyl piperidin-4-one (6)



To a solution of compound **14** (67 mg, 0.17 mmol) in ethanol (10 mL) and 2N HCl (1 mL) was added Pd/C (10%, 10 mg). The mixture was hydrogenated using a balloon for 2 h. The catalyst was removed by filtration through a Celite pad. The filter cake was rinsed with methanol, and the combined organic portion was concentrated under reduced pressure to afford **14a** as an HCl salt, which was used for the next reaction without

further purification. A small amount of **14a** (free base) was purified by silica column chromatography (CH_2Cl_2/MeOH 30:1): ^{1}H NMR (300 MHz) δ 1.72-1.90 (m, 4H), 2.10 (dd, J = 14.1, 12.0 Hz, 2H), 2.40 (dd, J = 13.8, 2.1 Hz, 2H), 2.67 (t, J = 7.8 Hz, 4H), 2.74-2.86 (m, 2H), 7.10-7.40 (m, 10H); ^{13}C NMR (75 MHz) δ 32.4, 38.7, 48.9, 56.2, 126.2, 128.4, 128.6, 141.4, 209.0; MS (EI) m/z 307 (M^+), 202 (100), 160, 91, 77, 65; HRMS calcd for $C_{21}H_{25}NO$ (M^+) *m/z* 307.1936, found 307.1940. To a solution containing **14a**·HCl in CH_2Cl_2 (10 mL), DIPEA (77 mg, 0.60 mmol) and DMPA (2 mg) was added drop-wise TrocCl (72 mg, 0.34 mmol). After stirring at room temperature for 24 h, the mixture was diluted with CH_2Cl_2 (20 mL) and washed subsequently with 0.1N HCl, saturated $NaHCO_3$, water and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was chromatographed on silica (hexanes/EtOAc 4:1) to afford **6** (75 mg, 91%) as a colorless oil: ^{1}H NMR (300 MHz) δ 1.80-1.97 (m, 2H), 2.02-2.20 (m, 2H), 2.49 (dd, J = 15.3, 3.3 Hz, 2H), 2.56-2.76 (m, 4H), 2.78 (dd, J = 15.3, 7.5 Hz, 2H), 4.63-4.92 (m, 4H), 7.05-7.37 (m, 10H); ^{13}C NMR (75 MHz) δ 33.3, 38.7, 41.7, 52.0, 75.4, 95.6, 126.4, 128.4, 128.7, 140.5, 153.6, 206.4; MS (EI) m/z 481/483/485 (M^+), 446/448, 376/378/380, 272/274/276, 174, 117 (100), 91; HRMS calcd for $C_{24}H_{26}{}^{35}Cl_3NO_3$ (M^+) *m/z* 481.0978, found 481.0977.

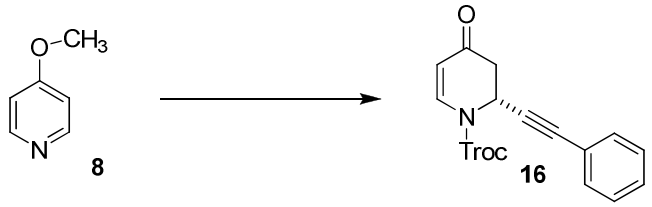
Synthesis of 1-(2,2,2-trichloroethoxy)carbonyl-2-phenethyl-4-oxo-1,2,3,4-tetrahydropyridine (15).



To a solution of 4-methoxypyridine (**8**) (2.73 g, 25.00 mmol) in THF (80 mL) at −20 °C was added drop-wise TrocCl (5.30 g, 25.00 mmol). The resulting white slurry was stirred at this temperature for 30 min, and then phenethyl magnesium chloride (1.0 M, 37.5 mL, 37.5 mmol) was added slowly over 20 min. The reaction mixture was stirred continuously at −20 °C for 2 h, aqueous HCl (10%, 40 mL) was then added and the resulting mixture was stirred for 30 min at room temperature. The aqueous layer was extracted with EtOAc (3 × 80 mL), the combined organic layers were washed with water

and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (hexanes/EtOAc 5:1) to afford **15** (4.70 g, 78%) as a white crystalline solid: mp 83-84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.87-2.16 (m, 2H), 2.53-2.81 (m, 3H), 2.88 (dd, *J* = 16.5, 6.3 Hz, 1H), 4.62-4.77 (m, 1H), 4.76-5.00 (br s, 2H), 5.45 (d, *J* = 8.1 Hz, 1H), 7.05-7.37 (m, 5H), 7.76 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.1, 39.8, 53.9, 76.0, 94.6, 108.8, 126.4, 128.3, 128.6, 140.2, 141.0, 151.3, 192.5; MS (EI) *m/z* 375/377/379 (M^+), 340/342, 317/319/321, 271/273/275, 243/245/247, 140, 91 (100), 77, 68; HRMS calcd for $C_{16}H_{16}{}^{35}Cl_3NO_3$ (M^+) m/z 375.0195, found 375.0192.

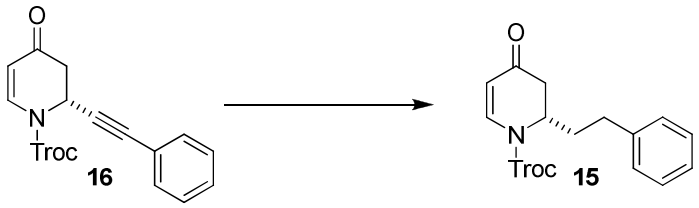
Synthesis of 1-(2,2,2-trichloroethoxy)carbonyl-2-phenethynyl-4-oxo-1,2,3,4-tetrahydropyridine (16).



To a solution of 4-methoxypyridine (**8**) (1.09 g, 10.00 mmol) in CH_2Cl_2 (30 mL) at room temperature under an argon atmosphere was added TrocCl (2.54 g, 12.00 mmol) drop-wise, and the resulting mixture was stirred for 30 min. Phenylacetylene (1.53 g, 15.00 mmol), CuI (286 mg, 1.50 mmol) and DIPEA (1.94 g, 15.00 mmol) was then added to the mixture and the reaction was stirred continuously at room temperature for 1 h. Aqueous HCl (10%, 20 mL) was then added and the resulting mixture was stirred for 30 min at room temperature. The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL), the combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silic gel column chromatography (hexanes/EtOAc 8:1) to afford **16** (2.62 g, 70%) as a white crystalline solid: mp 123-124 °C; ^{1}H NMR (300 MHz) δ 2.79 (dt, J = 16.5, 1.5 Hz, 1H) 2.99 (dd, J = 16.5, 6.3 Hz, 1H), 4.85-5.07 (AB q, 2H), 5.58 (d, J = 8.4 Hz, 1H), 5.67 (dt, J = 6.3, 1.5 Hz, 1H), 7.23-7.42 (m, 5H), 7.81 (d, J = 8.7 Hz, 1H); ^{13}C NMR (75 MHz) δ 41.8, 46.5, 76.3, 84.0, 84.9, 94.5, 109.4, 121.6, 128.4, 129.1, 132.1, 140.3, 150.9, 191.0; MS (EI)

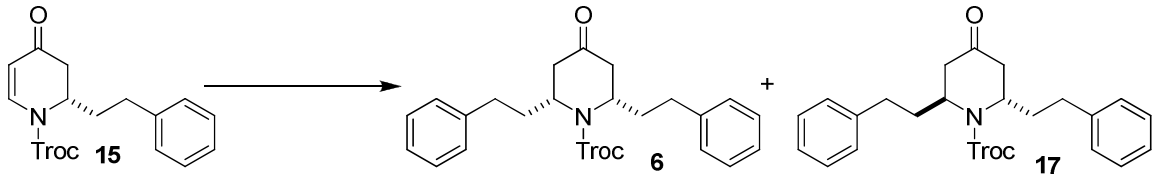
m/z 371/373/375 (M^+), 340/342, 294, 168, 154, 128 (100), 115, 96, 77; HRMS calcd for $C_{16}H_{12}{}^{35}Cl_3NO_3$ (M^+) *m/z* 370.9882, found 370.9884.

Synthesis of compound 15 from compound 16.



To a solution of compound **16** (980 mg, 2.63 mmol) in EtOAc (20 mL) was added Pd/C (10 %, 90 mg). The mixture was hydrogenated using a balloon for 24 h. The catalyst was removed by filtration through a Celite pad. The filter cake was rinsed with EtOAc, and the combined organic portion was concentrated under reduced pressure. The crude product was chromatographed on silica (hexanes/EtOAc 8:1) to afford **15** (936 g, 94%) as a white crystalline solid.

Synthesis of *cis*-*N*-[(2,2,2-trichloroethoxy)carbonyl]-2,6-diphenethyl piperidin-4-one (6) and *trans*-*N*-[(2,2,2-trichloroethoxy)carbonyl]-2,6-diphenethyl piperidin-4-one (17).

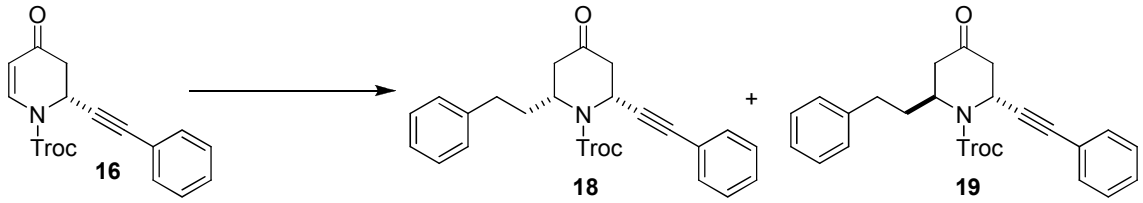


General method: To a suspension of $CuBr{\cdot}SMe_2$ (206 mg, 1.00 mmol) in THF (5 mL) at -78 °C was added subsequently phenethyl magnesium chloride (1.0 M, 1.0 mL, 1.00 mmol), TMSCl (272 mg, 2.50 mmol) or $BF_3{\cdot}Et_2O$ (142 mg, 1.00 mmol), The resulting mixture was stirred at -78 °C for 5 min and then a solution of **15** (186 mg, 0.5 mmol) in THF (3 mL) was added dropwise. The reaction was stirred at -78 °C for 2 h, quenched with 10 mL of aqueous 1 N HCl solution, diluted with H_2O (10 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The

crude product was purified by column chromatography (hexanes/EtOAc 8:1) to afford **6** and **17**.

Compound **17**: white crystalline solid, mp 123-124 °C; ^{1}H NMR (300 MHz) δ 1.62-1.77 (m, 2H), 2.18-2.35 (m, 2H), 2.54-2.70 (m, 6H), 2.77 (dd, J = 18.0, 4.8 Hz, 2H), 4.31 (ddd, J = 9.6, 6.0, 3.0 Hz, 2H), 4.74 (A of AB, 1H), 4.89 (B of AB, 1H), 7.05-7.36 (m, 10H); ^{13}C NMR (75 MHz) δ 33.3, 38.7, 41.7, 52.0, 75.4, 95.6, 126.4, 128.4, 128.7, 140.5, 153.6, 206.4; MS (EI) m/z 481/483/485 (M^+), 446/448, 376/378/380, 272/274/276, 117 (100), 91; HRMS calcd for $C_{24}H_{26}{}^{35}Cl_3NO_3$ (M^+) *m/z* 481.0978, found 481.0976.

Synthesis of *cis*-*N*-[(2,2,2-trichloroethoxy)carbonyl]-2-phenethynyl-6-phenethyl piperidin-4-one (18) and *trans*-*N*-[(2,2,2-trichloroethoxy)carbonyl]-2-phenethynyl-6-phenethyl piperidin-4-one (19).

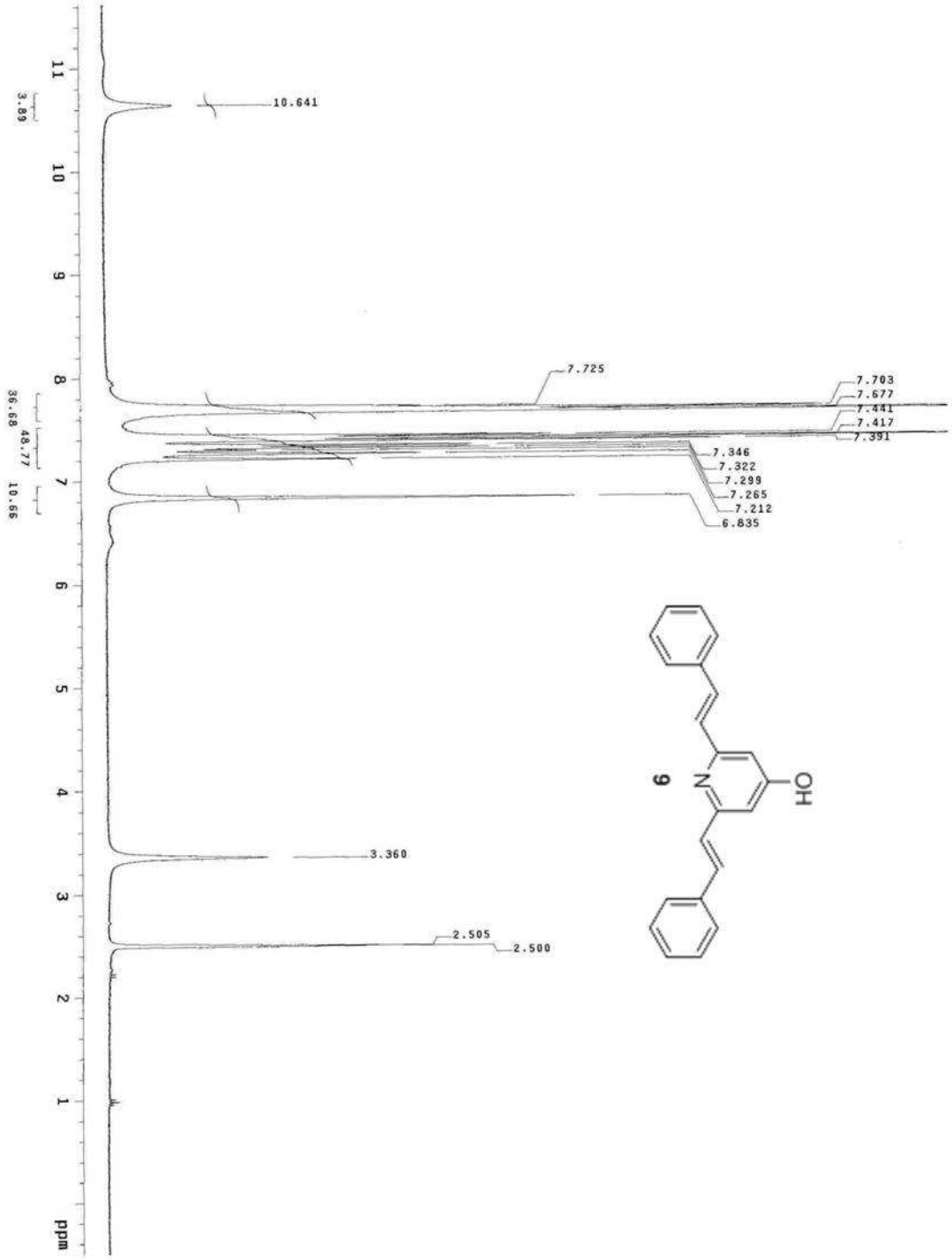


Compounds **18** and **19** were synthesized according to the general method described for compounds **6** and **17**.

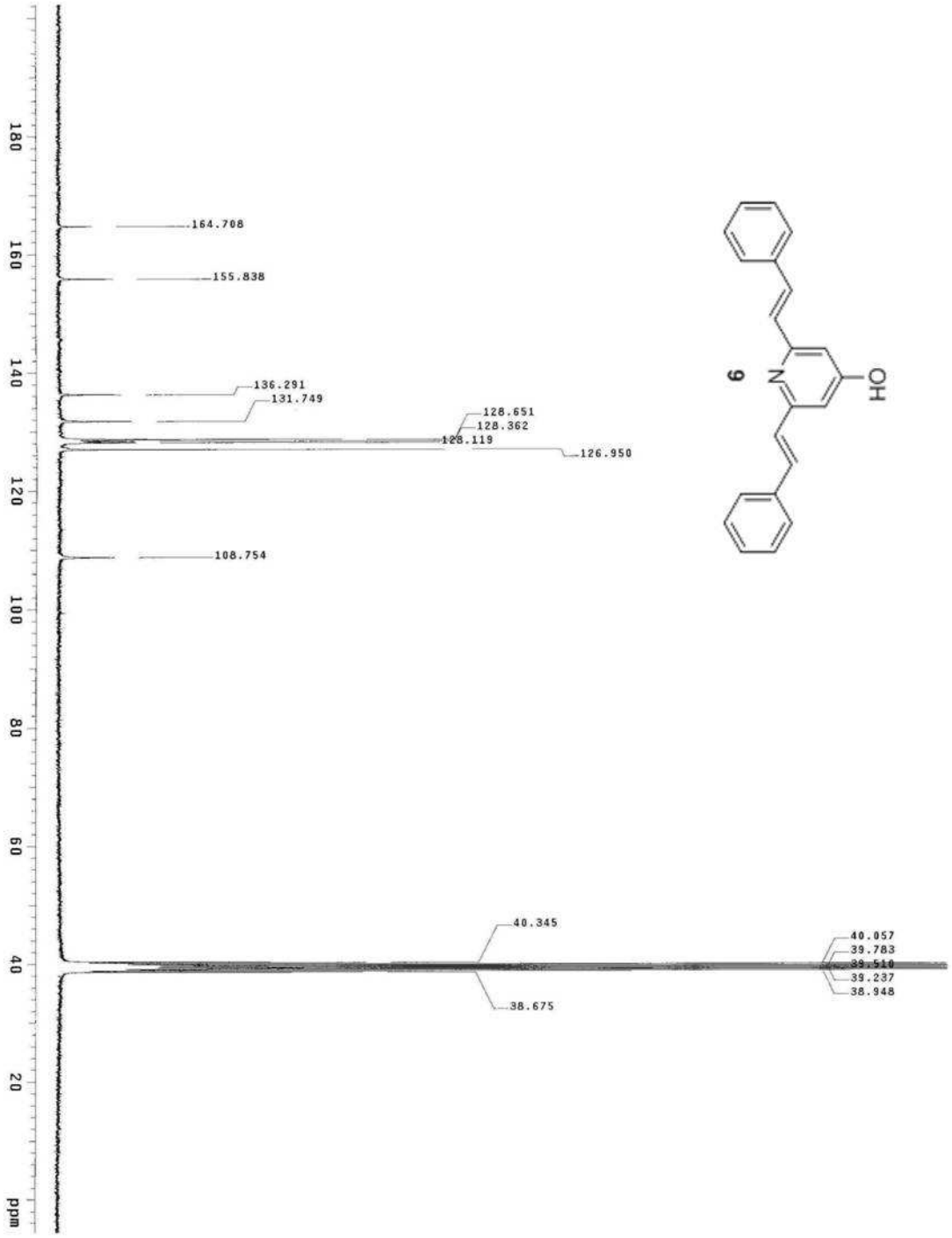
Compound **18**: colorless oil; ^{1}H NMR (300 MHz) δ 2.01-2.22 (br s, 1H), 2.43-2.60 (m, 1H), 2.65-2.97 (m, 6H), 4.70-4.94 (m, 3H), 5.86-5.98 (br d, J = 8.4 Hz, 1H), 7.05-7.38 (m, 10H); ^{13}C NMR (75 MHz) δ 32.9, 37.4, 44.2, 44.5, 45.7, 54.1, 75.7, 85.5, 87.2, 95.3, 121.9, 126.1, 128.3, 128.4, 128.44, 128.9, 131.7, 140.9, 153.5, 204.9 ppm; MS (EI) *m/z* 477/479/451, 441, 372/374/376, 346 (100), 330/332/334, 267, 155, 128, 91, 71, 57; HRMS calcd for $C_{24}H_{22}Cl_3NO_3$ (M^+) *m/z* 477.0665, found 477.0664.

Compound **19**: white crystalline solid, mp 119-120 °C; ^{1}H NMR (300 MHz) δ 1.60-1.75 (m, 1H), 2.18-2.37 (br, 1H), 2.58-2.96 (m, 5H), 3.43 (dd, J = 16.5, 5.4 Hz, 1H), 4.37-4.47 (m, 1H), 4.77 (A of AB, 1H), 4.96 (B of AB, 1H), 5.39 (dd, J = 5.4, 2.7 Hz, 1H), 7.12-7.43 (m, 10H) ppm; ^{13}C NMR (75 MHz) δ 32.9, 38.7, 41.5, 43.9, 44.1, 52.4, 75.6, 84.5, 87.9, 95.5, 122.0, 126.4, 128.4, 128.44, 128.7, 128.9, 131.9, 140.5, 153.6, 205.1 ppm; MS (EI) *m/z* 477/479/451, 373/375/377, 346 (100), 330/332/334, 155, 128, 91, 77; HRMS calcd for $C_{24}H_{22}Cl_3NO_3$ (M^+) *m/z* 477.0665, found 477.0665.

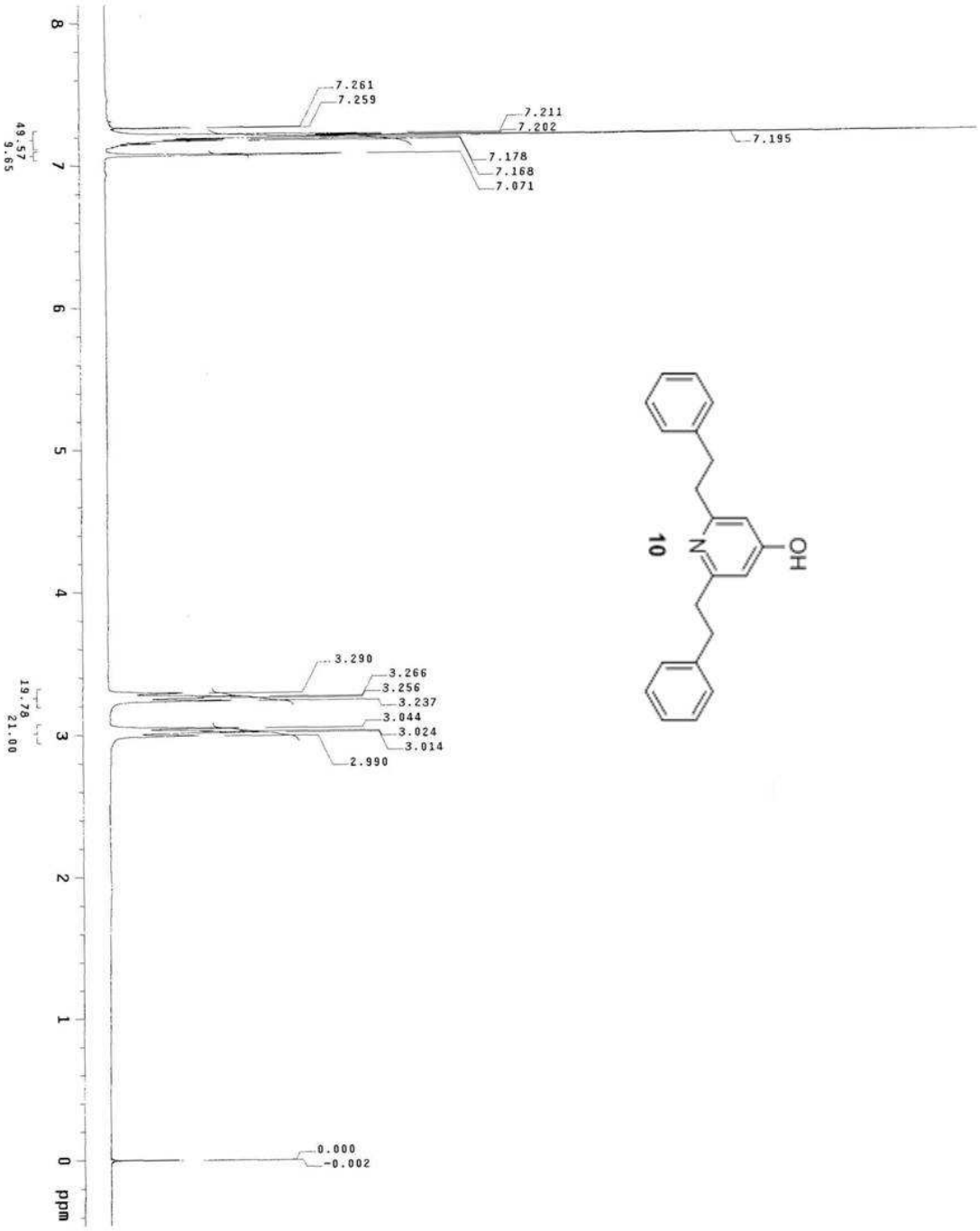
^{1}H NMR spectrum of compound **9** (DMSO-d6, 300 MHz)



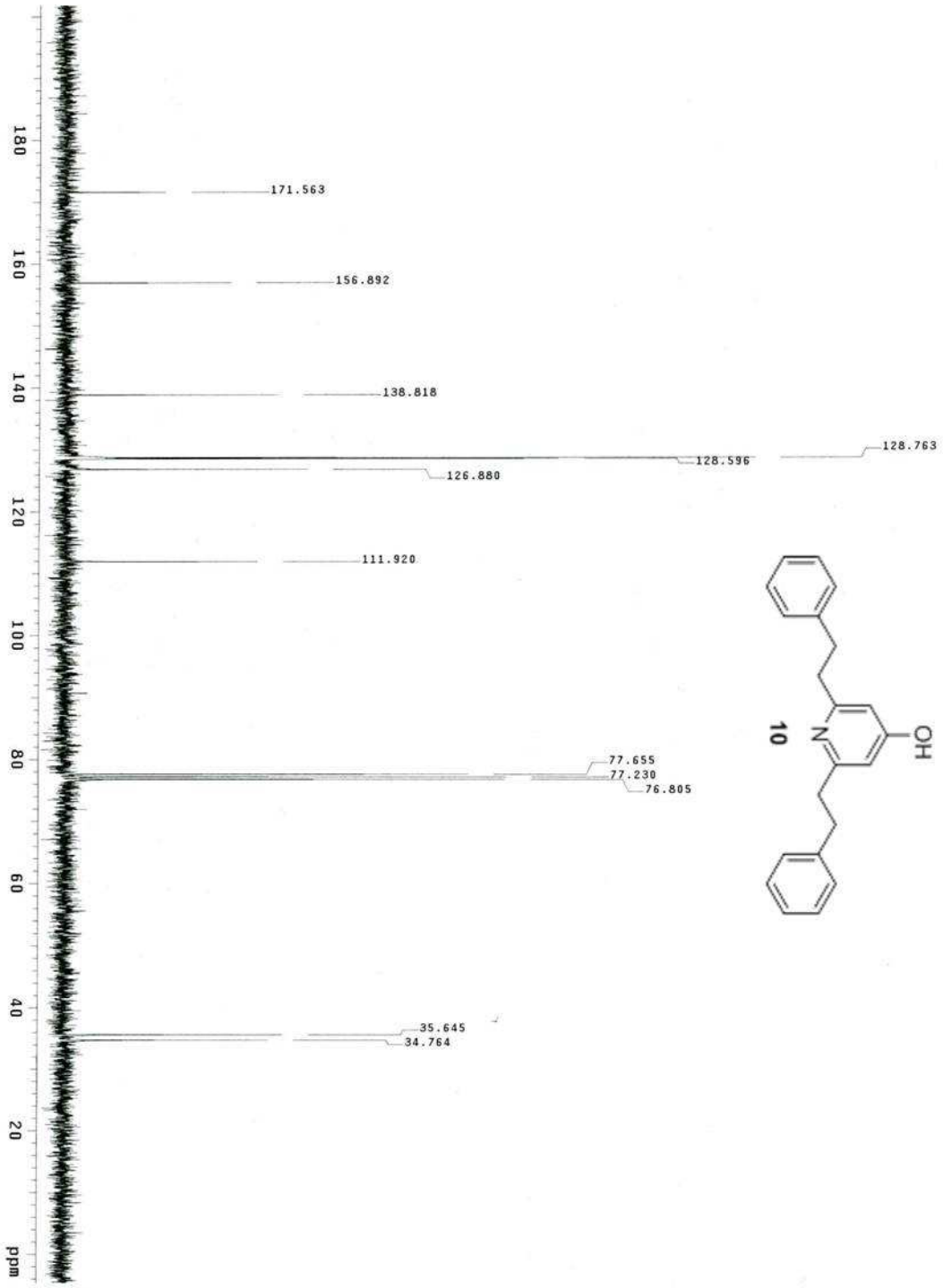
^{13}C NMR spectrum of compound **9** (DMSO-d6, 75 MHz)



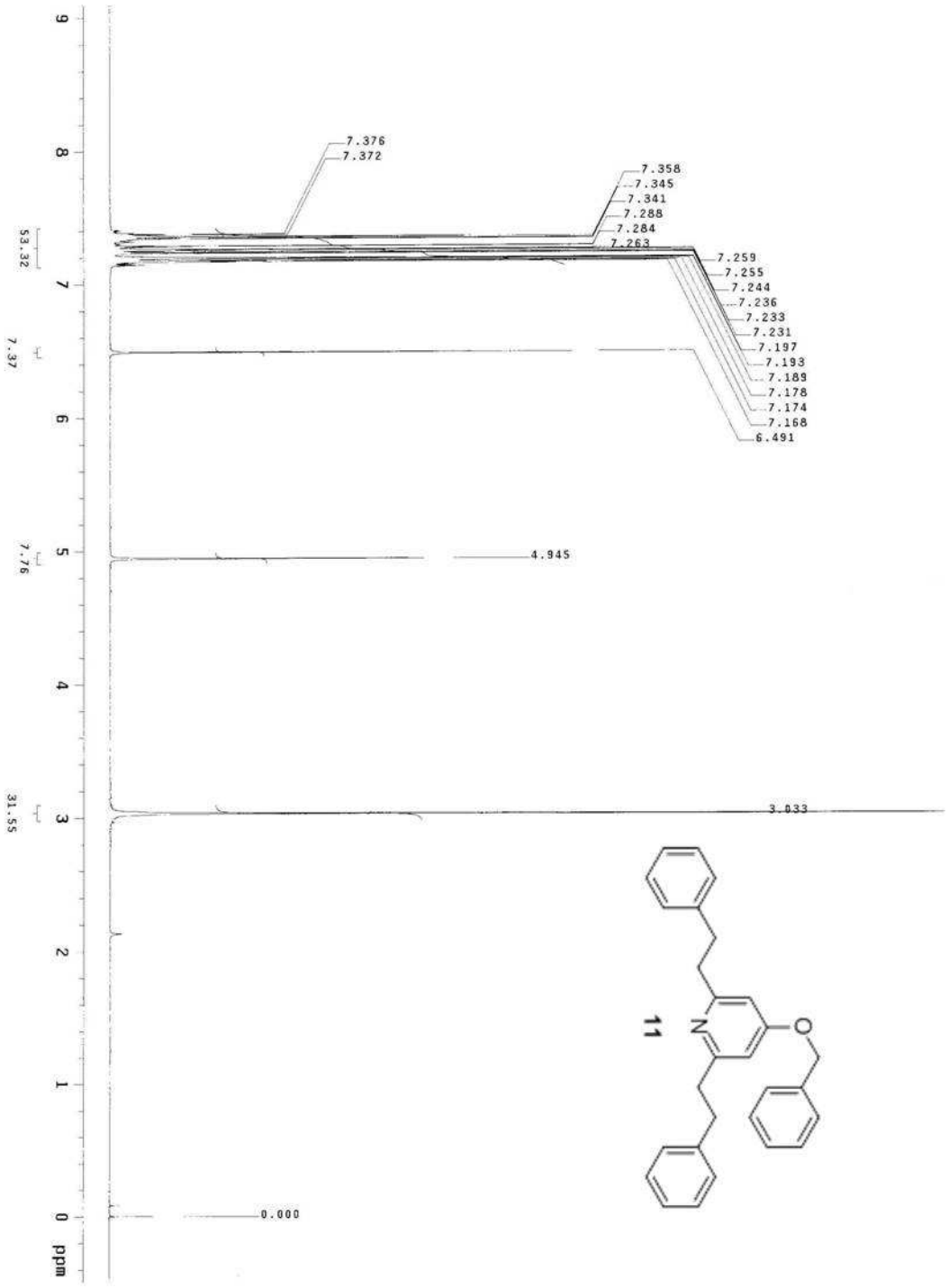
^{1}H NMR spectrum of compound **10** ($CDCl_3$, 300 MHz)



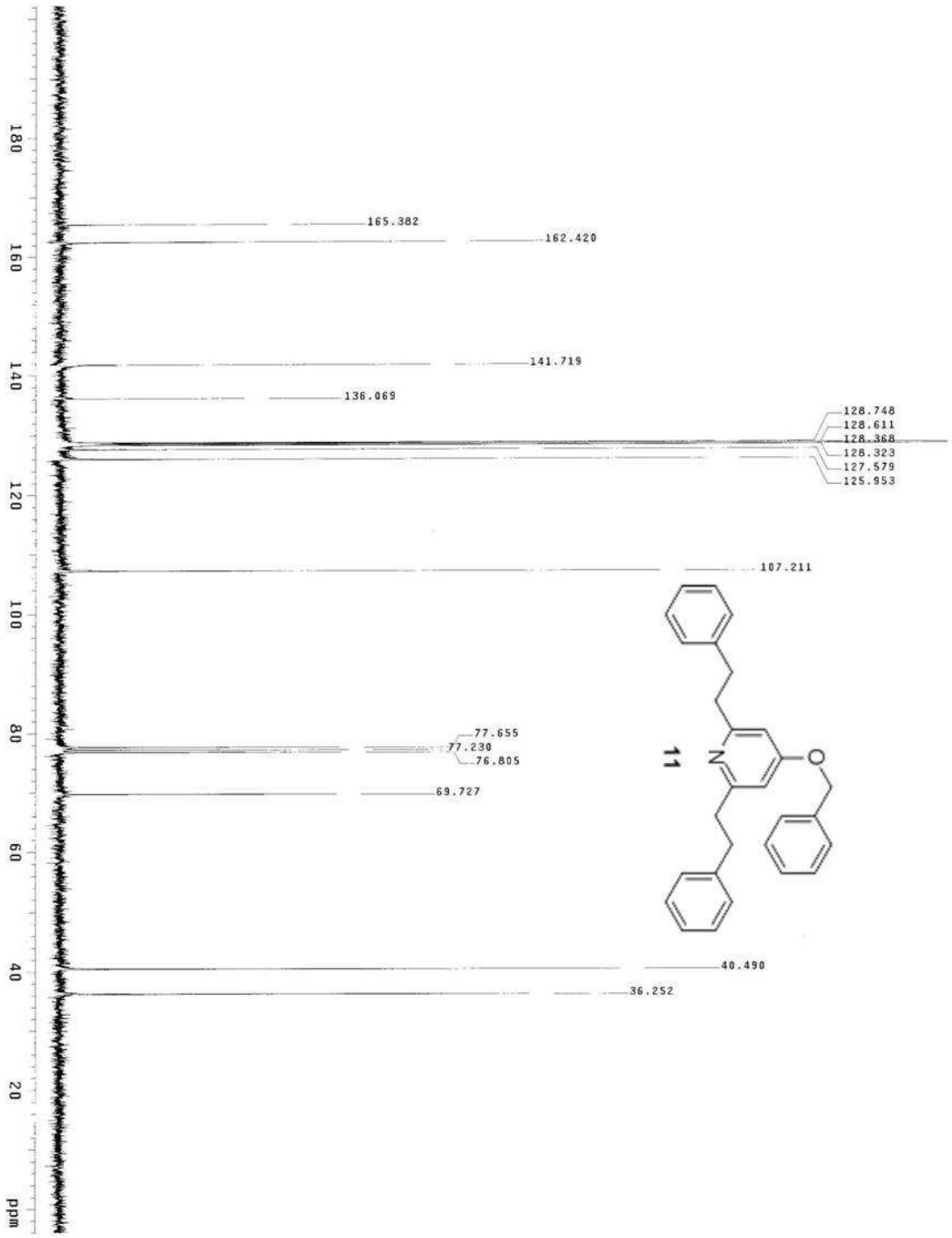
^{13}C NMR spectrum of compound **10** ($CDCl_3$, 75 MHz)



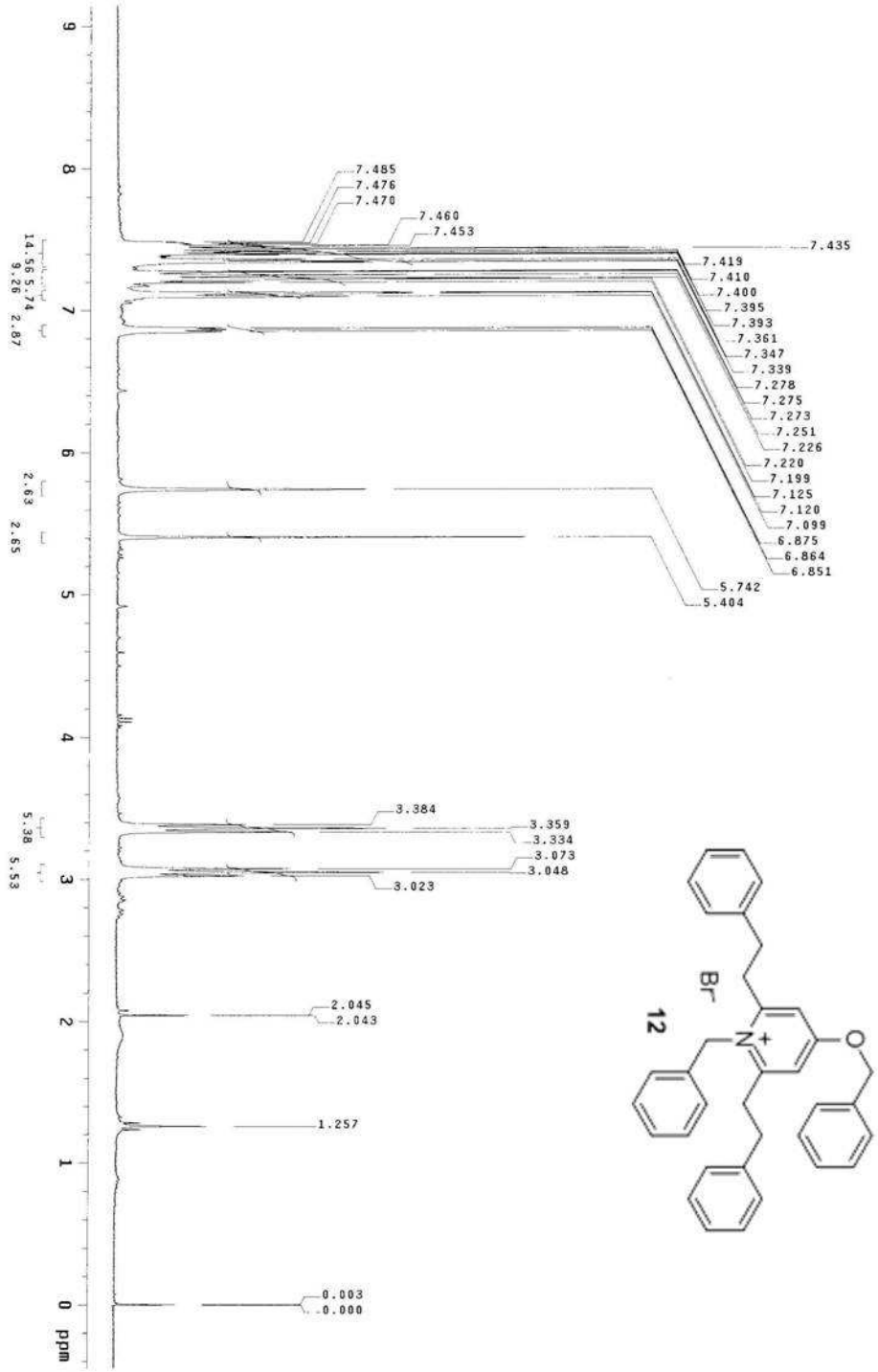
^{1}H NMR spectrum of compound **11** ($CDCl_3$, 300 MHz)



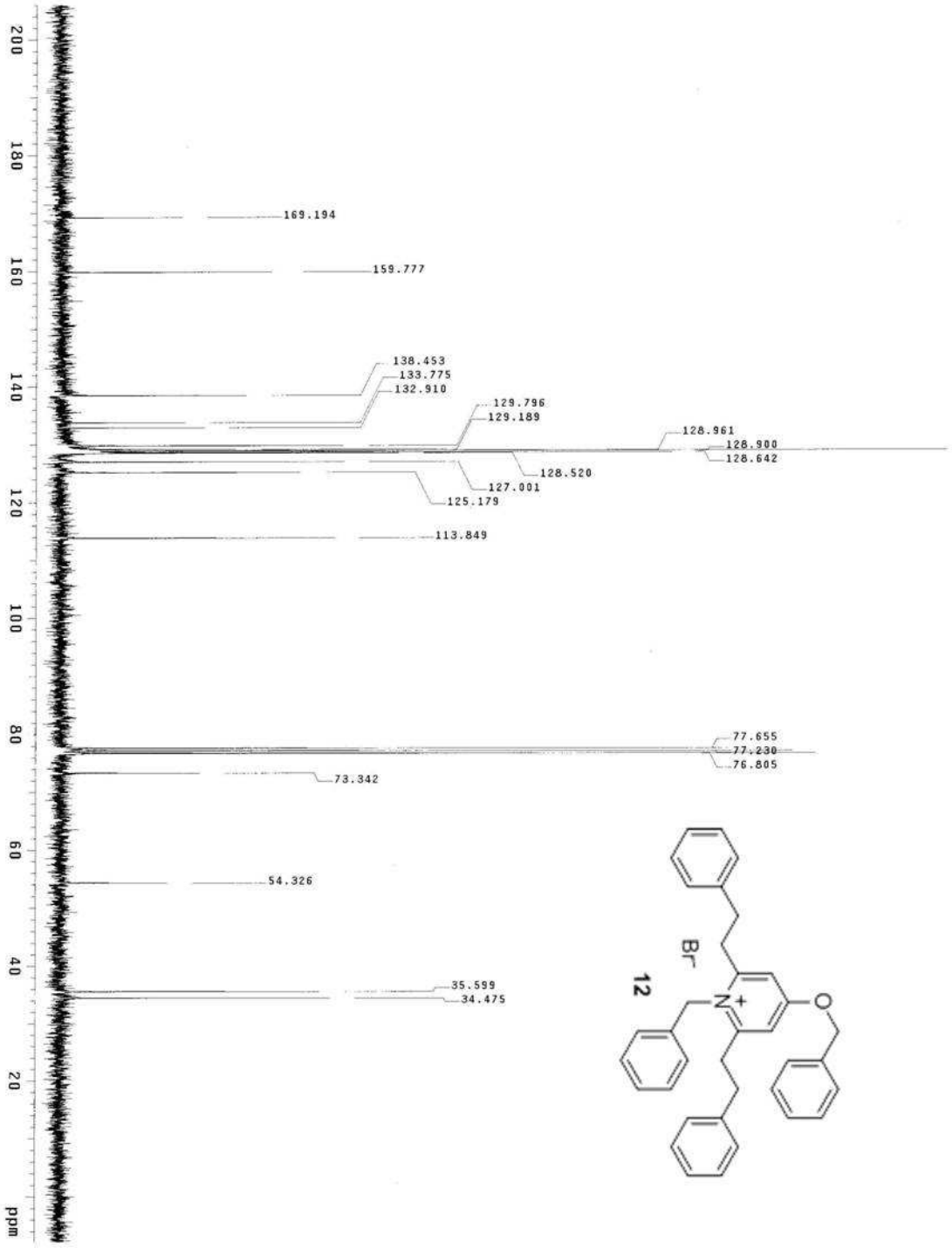
^{13}C NMR spectrum of compound **11** ($CDCl_3$, 75 MHz)



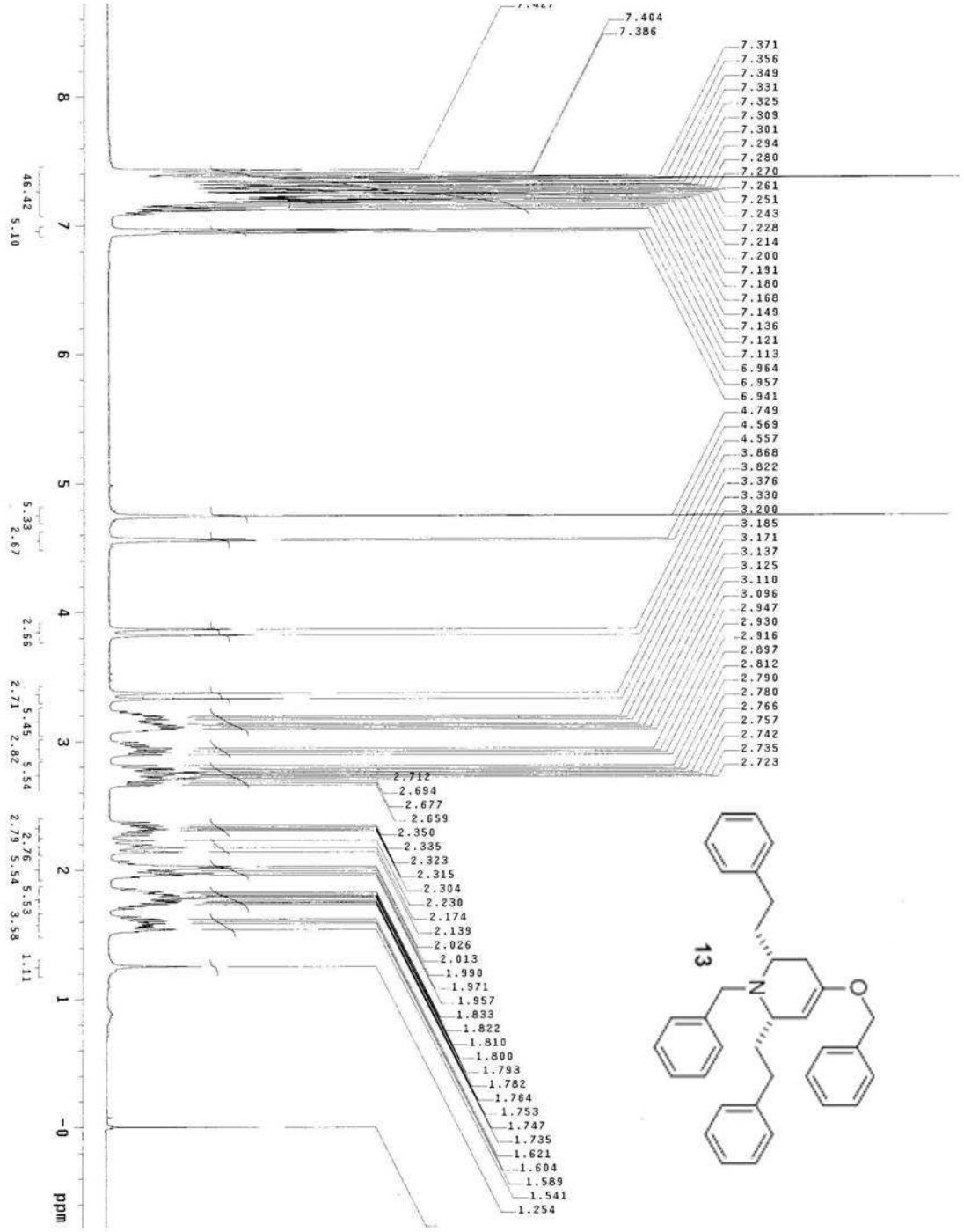
^{1}H NMR spectrum of compound **12** ($CDCl_3$, 300 MHz)



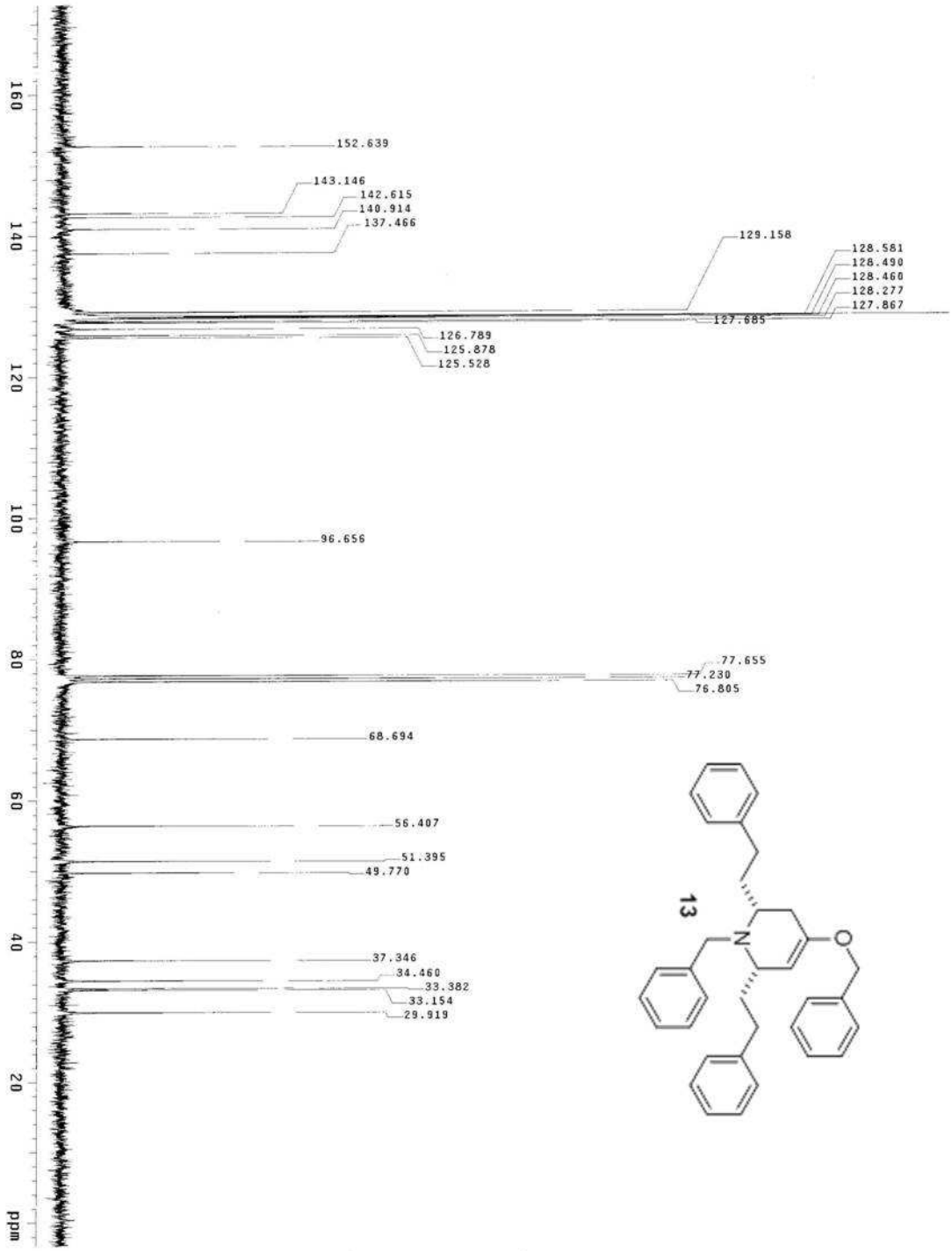
^{13}C NMR spectrum of compound **12** ($CDCl_3$, 75 MHz)



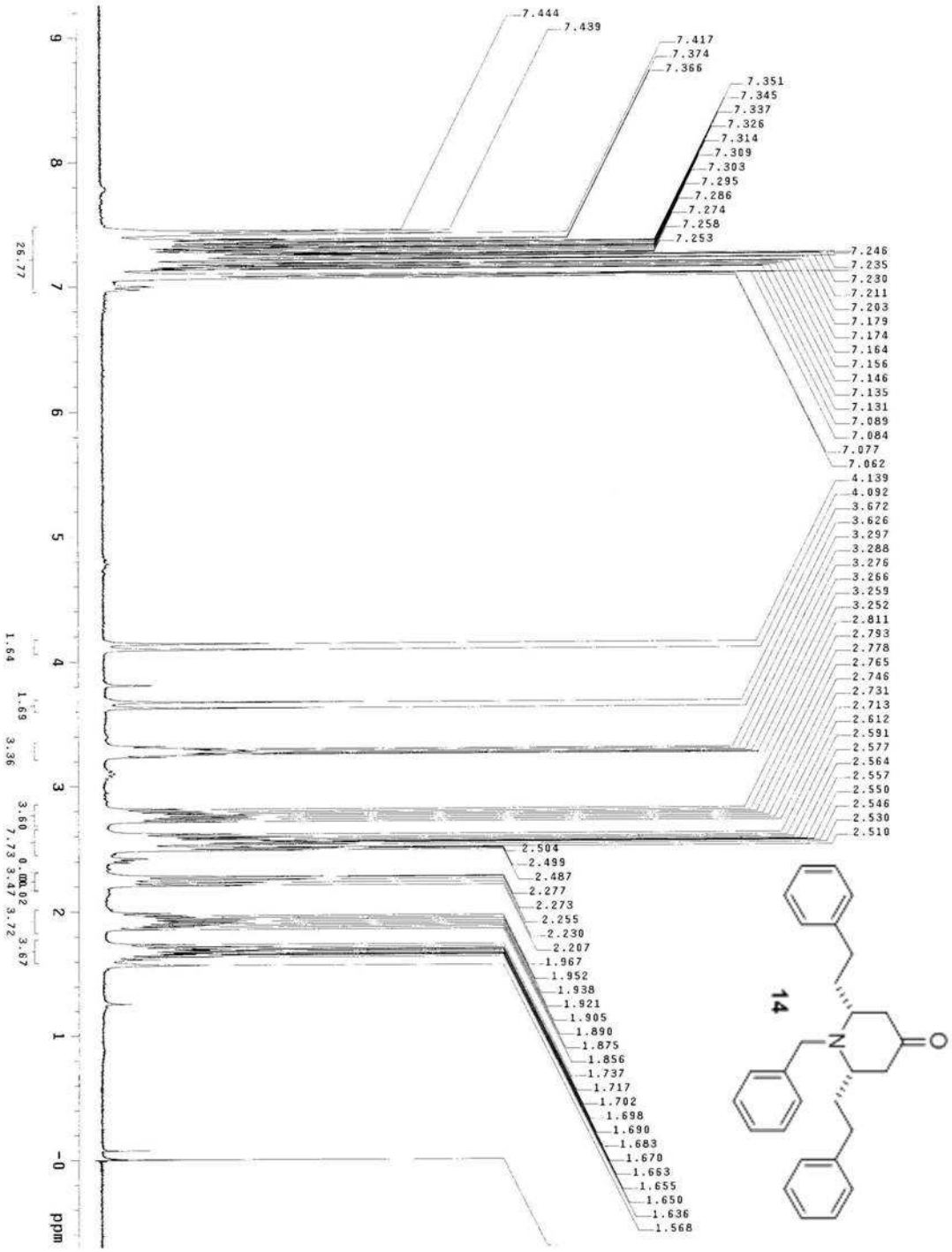
^{1}H NMR spectrum of compound **13** ($CDCl_3$, 300 MHz)



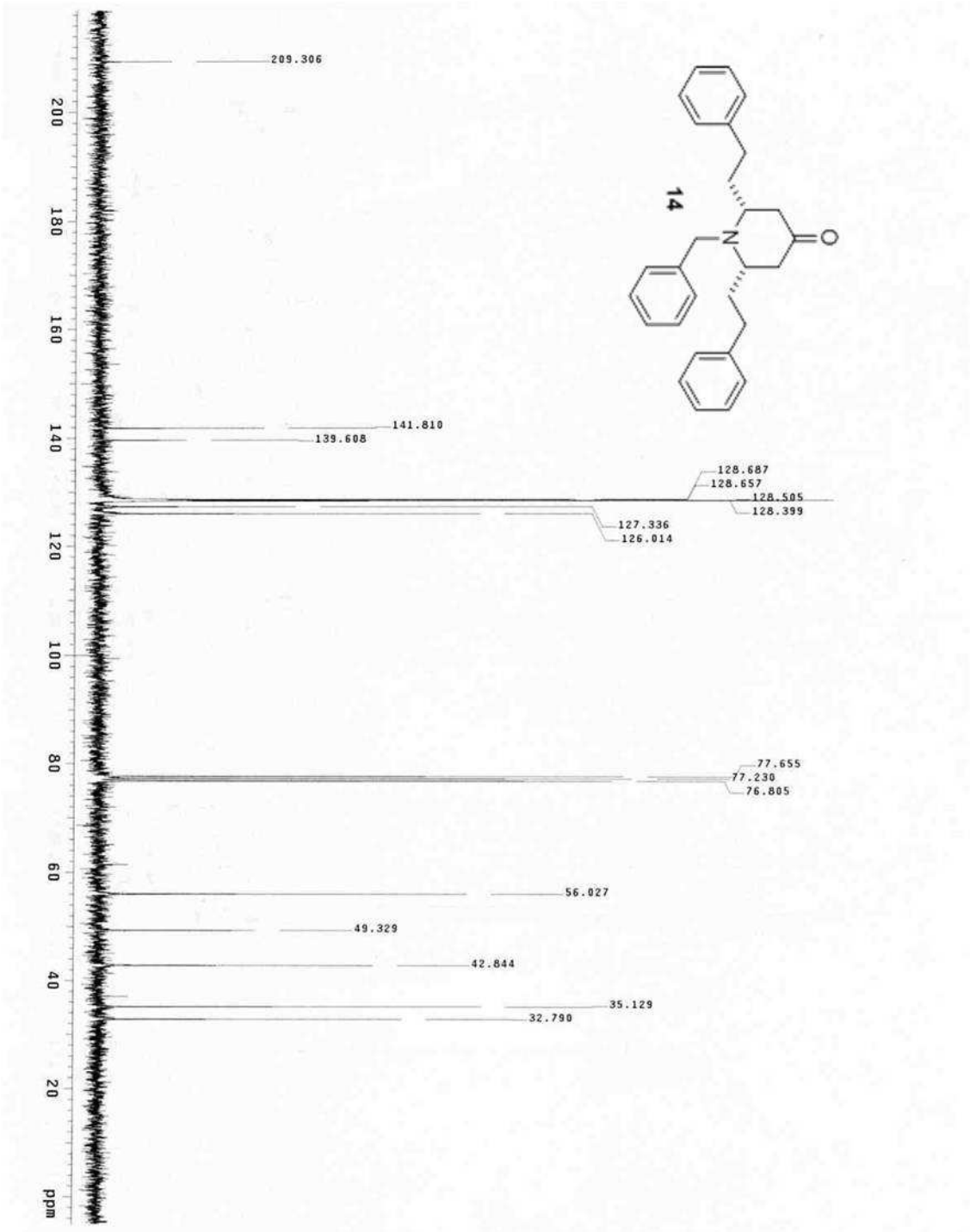
^{13}C NMR spectrum of compound **13** ($CDCl_3$, 75 MHz)



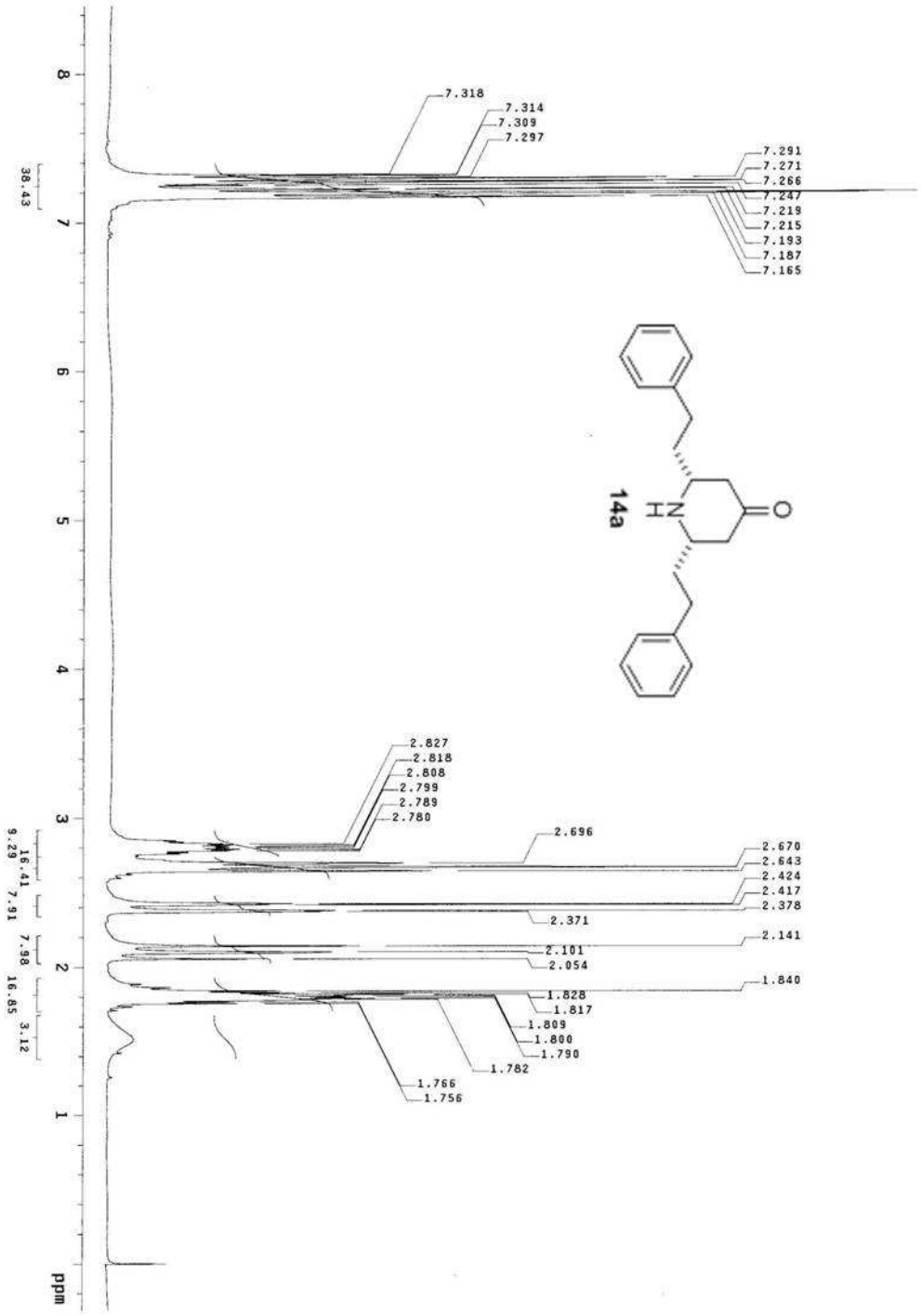
^{1}H NMR spectrum of compound **14** ($CDCl_3$, 300 MHz)



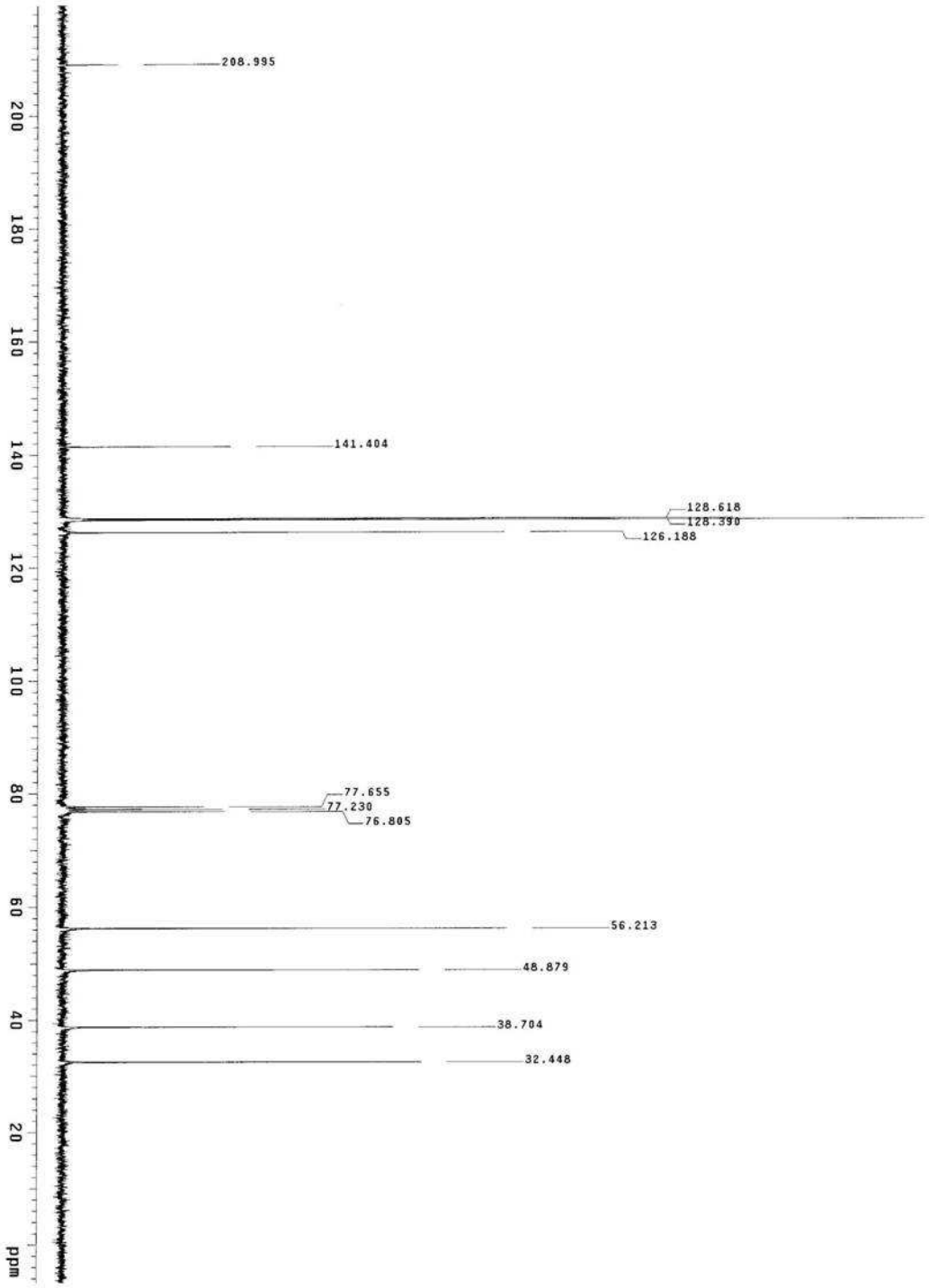
^{13}C NMR spectrum of compound **14** ($CDCl_3$, 75 MHz)



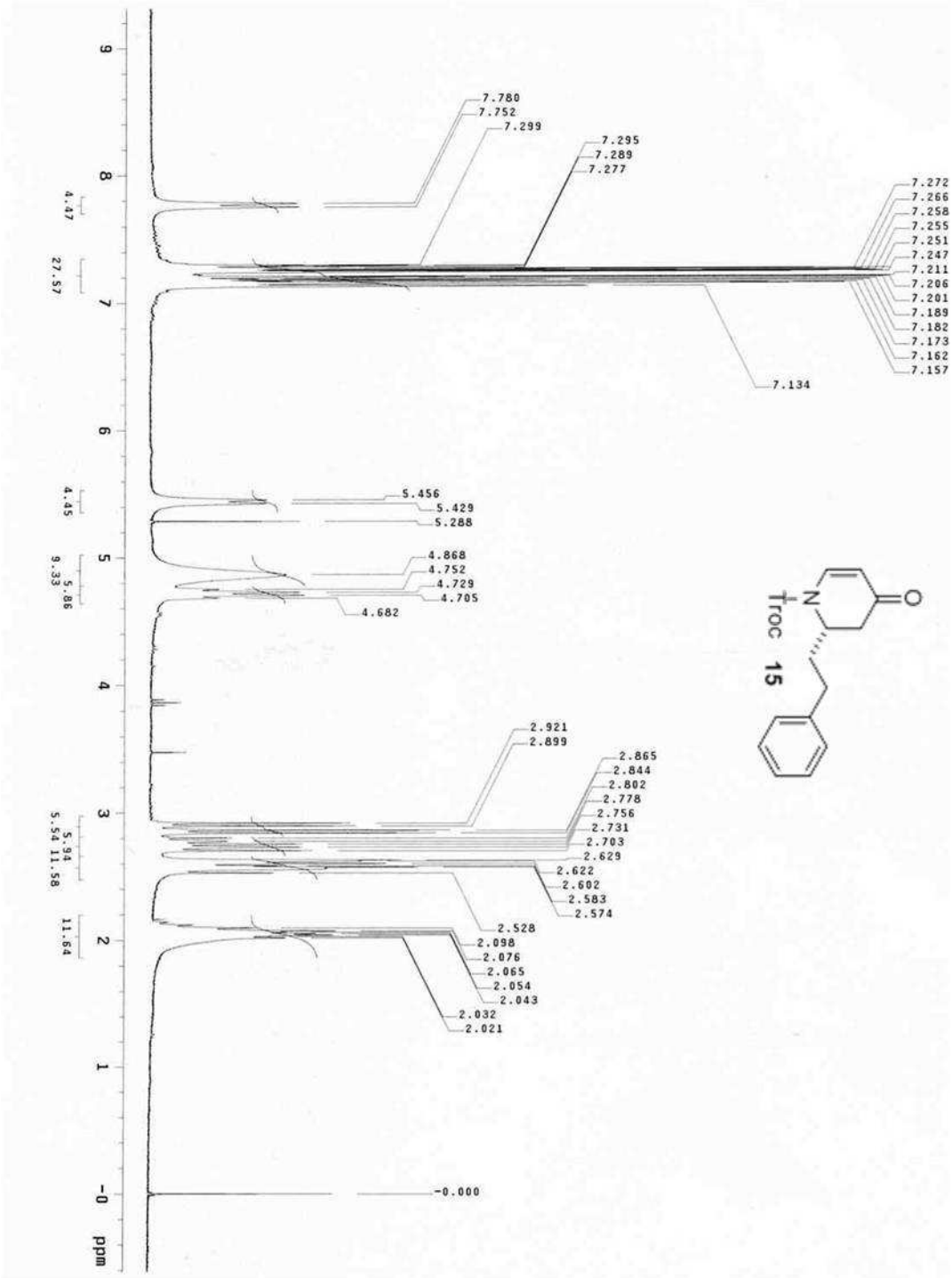
^{1}H NMR spectrum of compound **14a** ($CDCl_3$, 300 MHz)



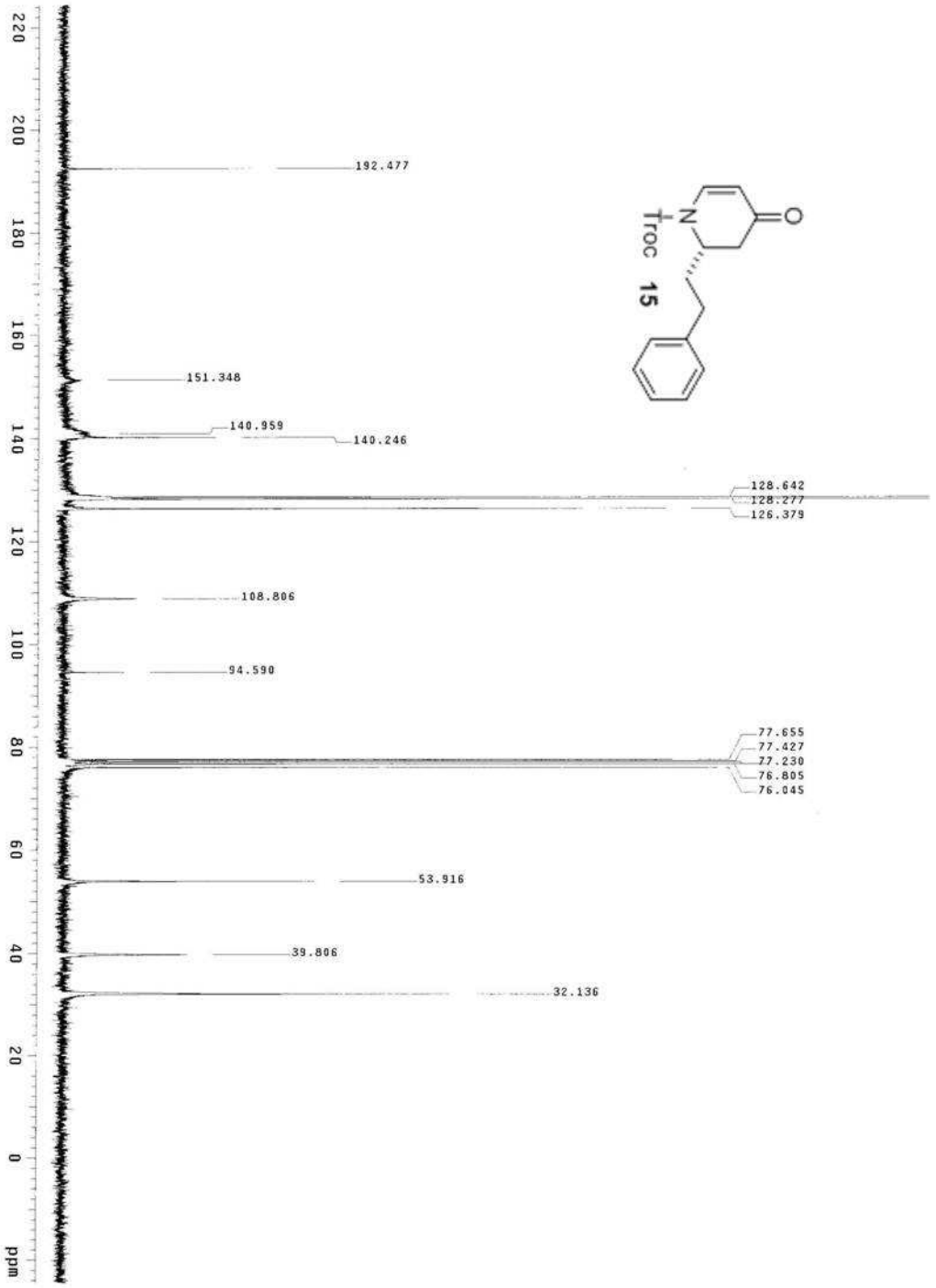
^{13}C NMR spectrum of compound **14a** ($CDCl_3$, 75 MHz)



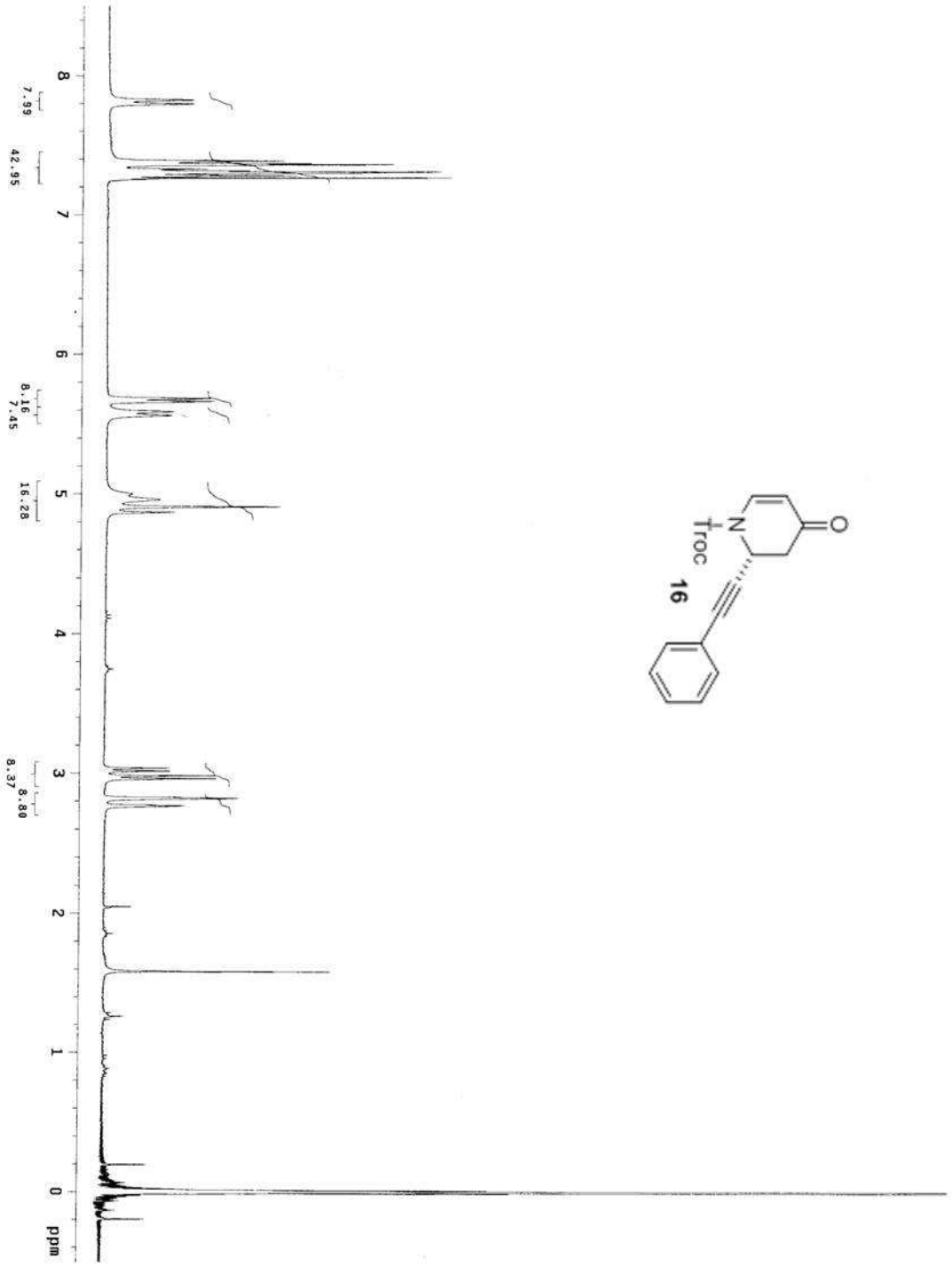
^{1}H NMR spectrum of compound **15** ($CDCl_3$, 300 MHz)



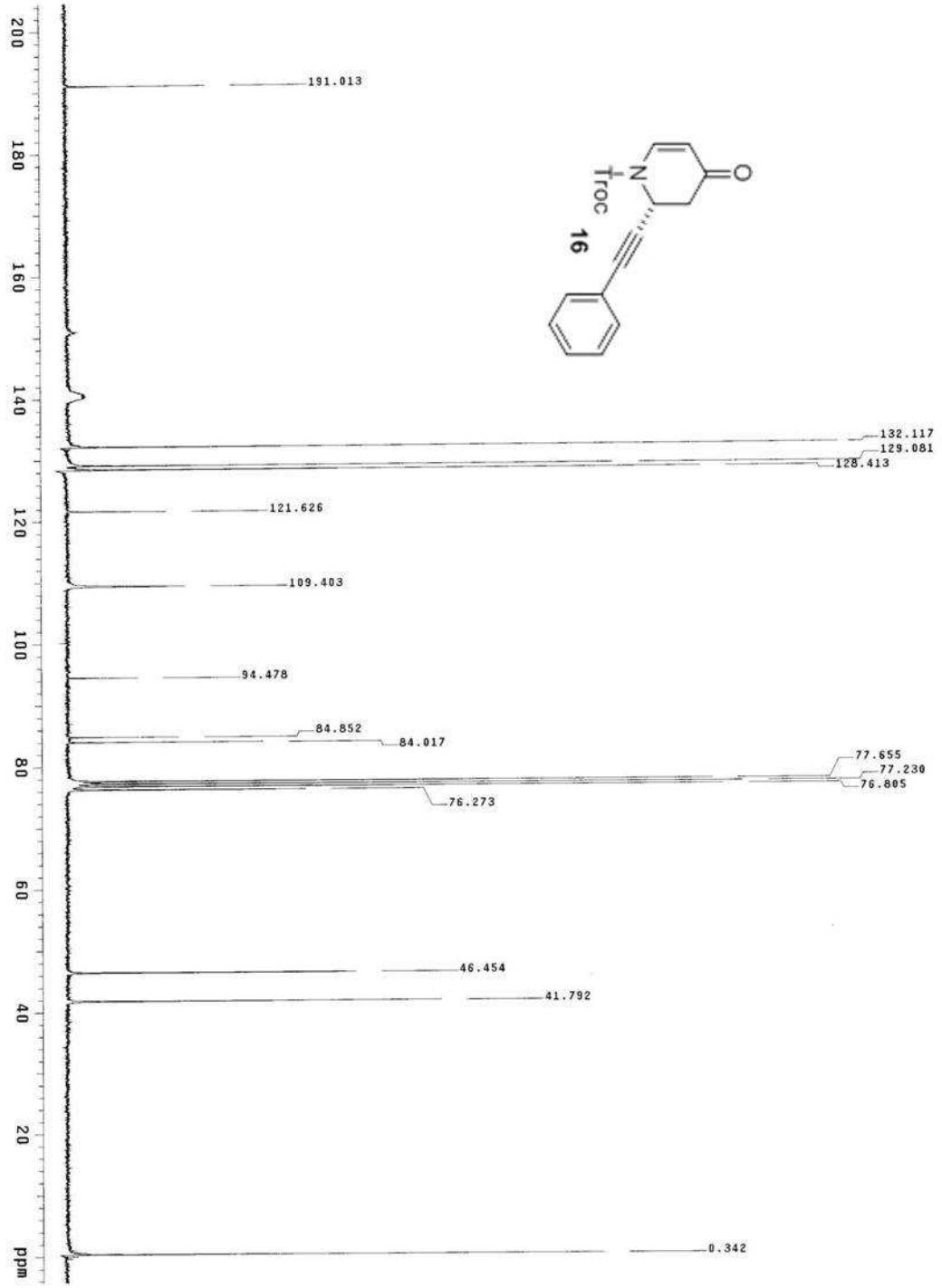
^{13}C NMR spectrum of compound **15** ($CDCl_3$, 75 MHz)



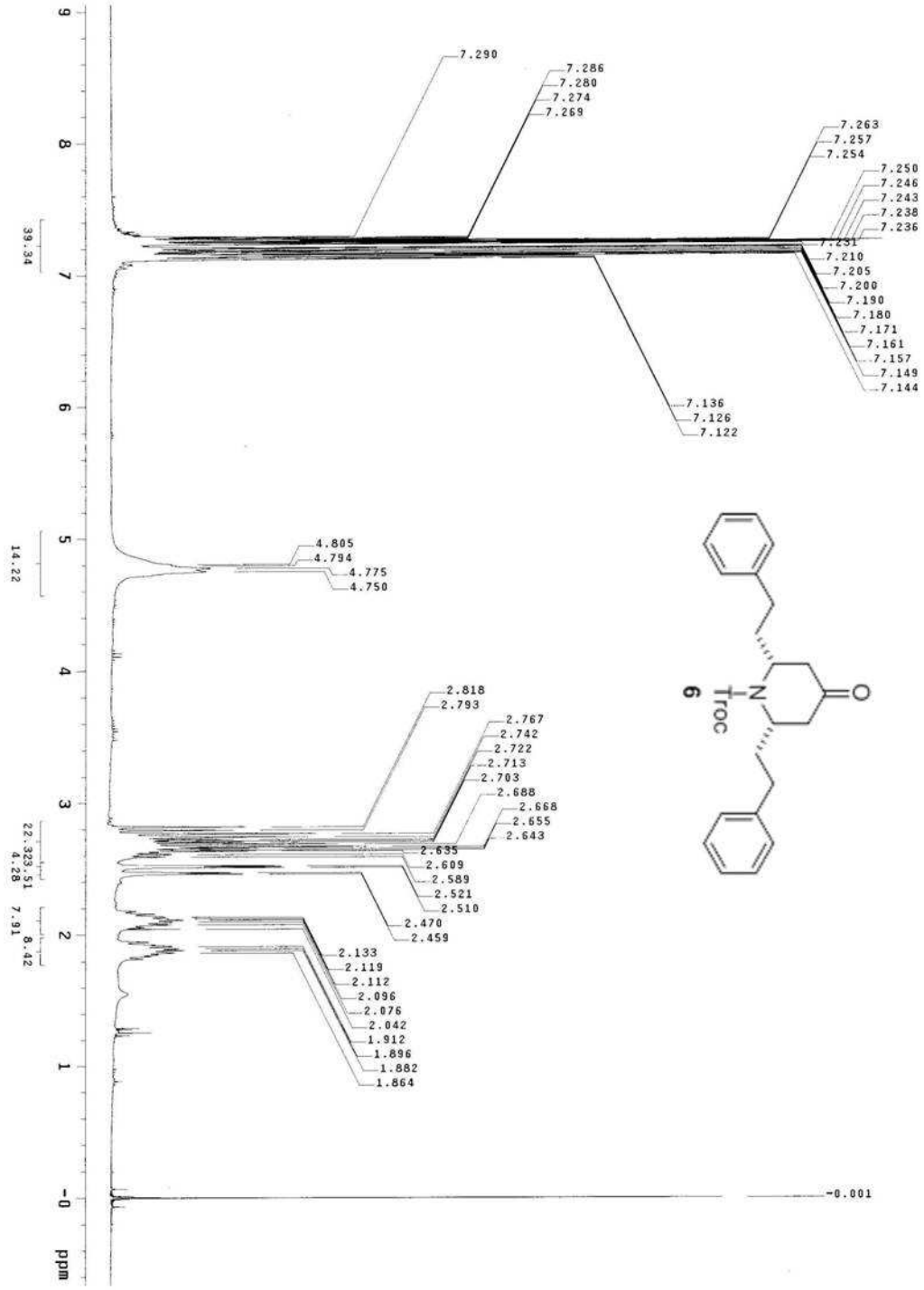
^{1}H NMR spectrum of compound **16** ($CDCl_3$, 300 MHz)



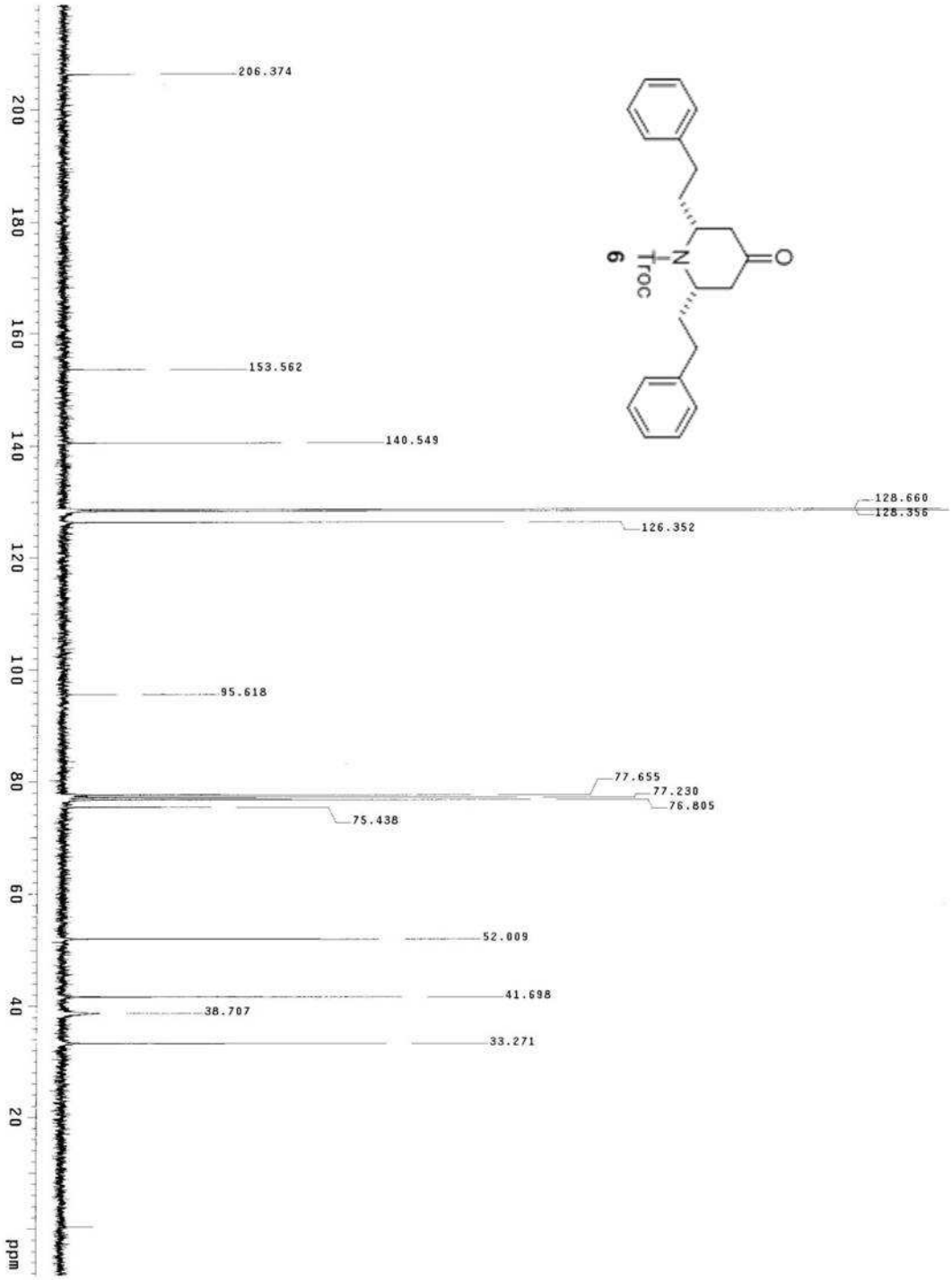
^{13}C NMR spectrum of compound **16** ($CDCl_3$, 75 MHz)



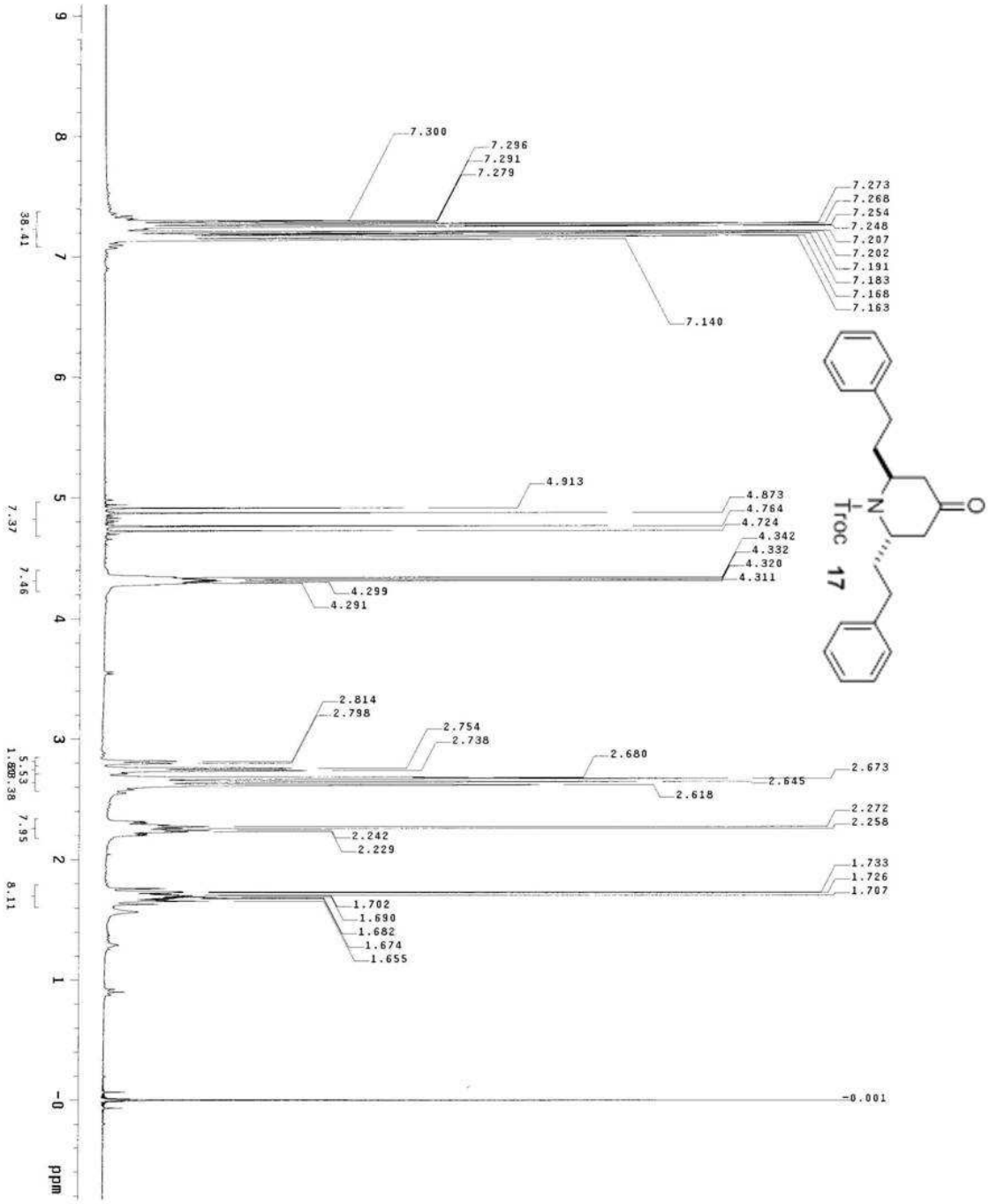
^{1}H NMR spectrum of compound **6** ($CDCl_3$, 300 MHz)



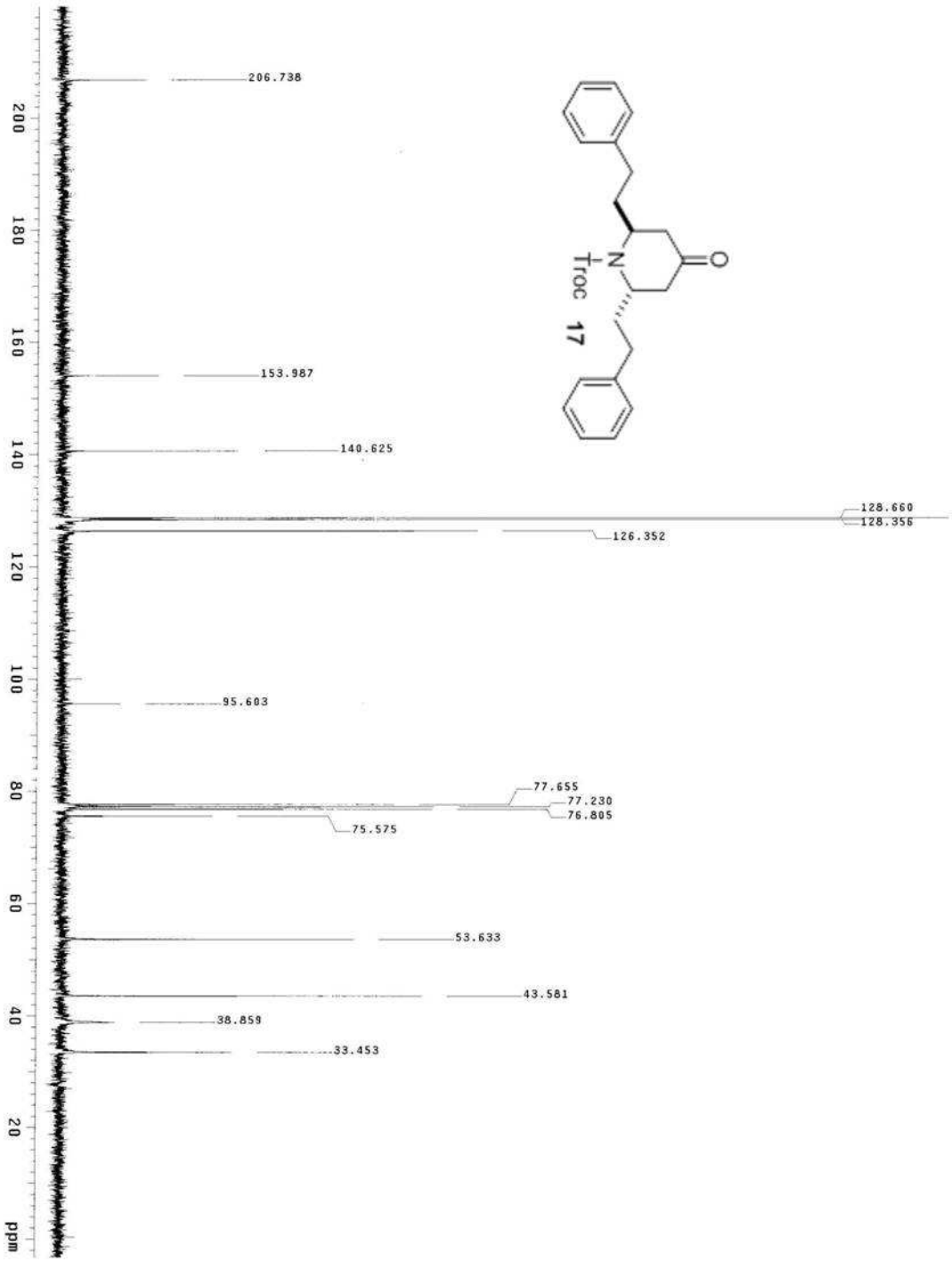
^{13}C NMR spectrum of compound **17** ($CDCl_3$, 75 MHz)



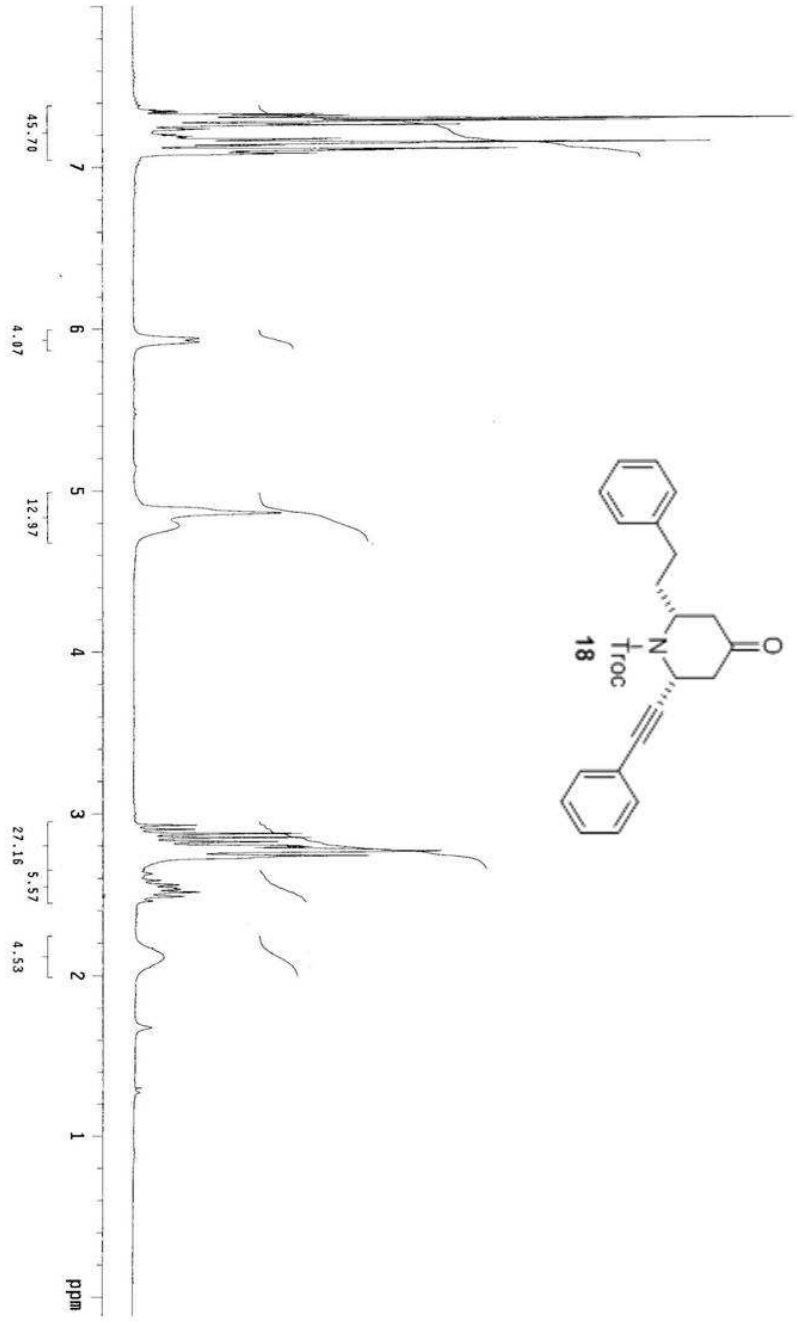
^{1}H NMR spectrum of compound **17** ($CDCl_3$, 300 MHz)



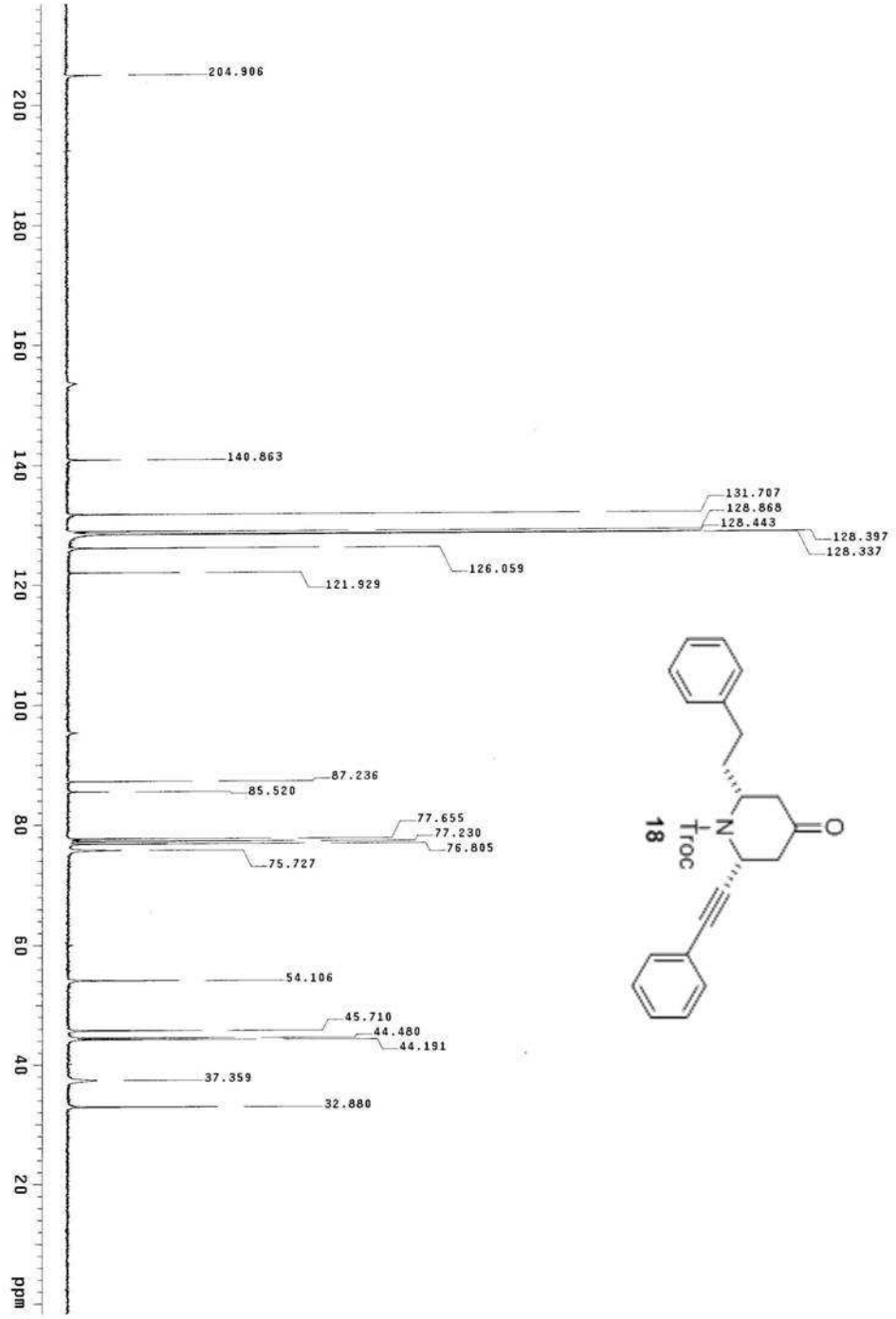
^{13}C NMR spectrum of compound **17** ($CDCl_3$, 75 MHz)



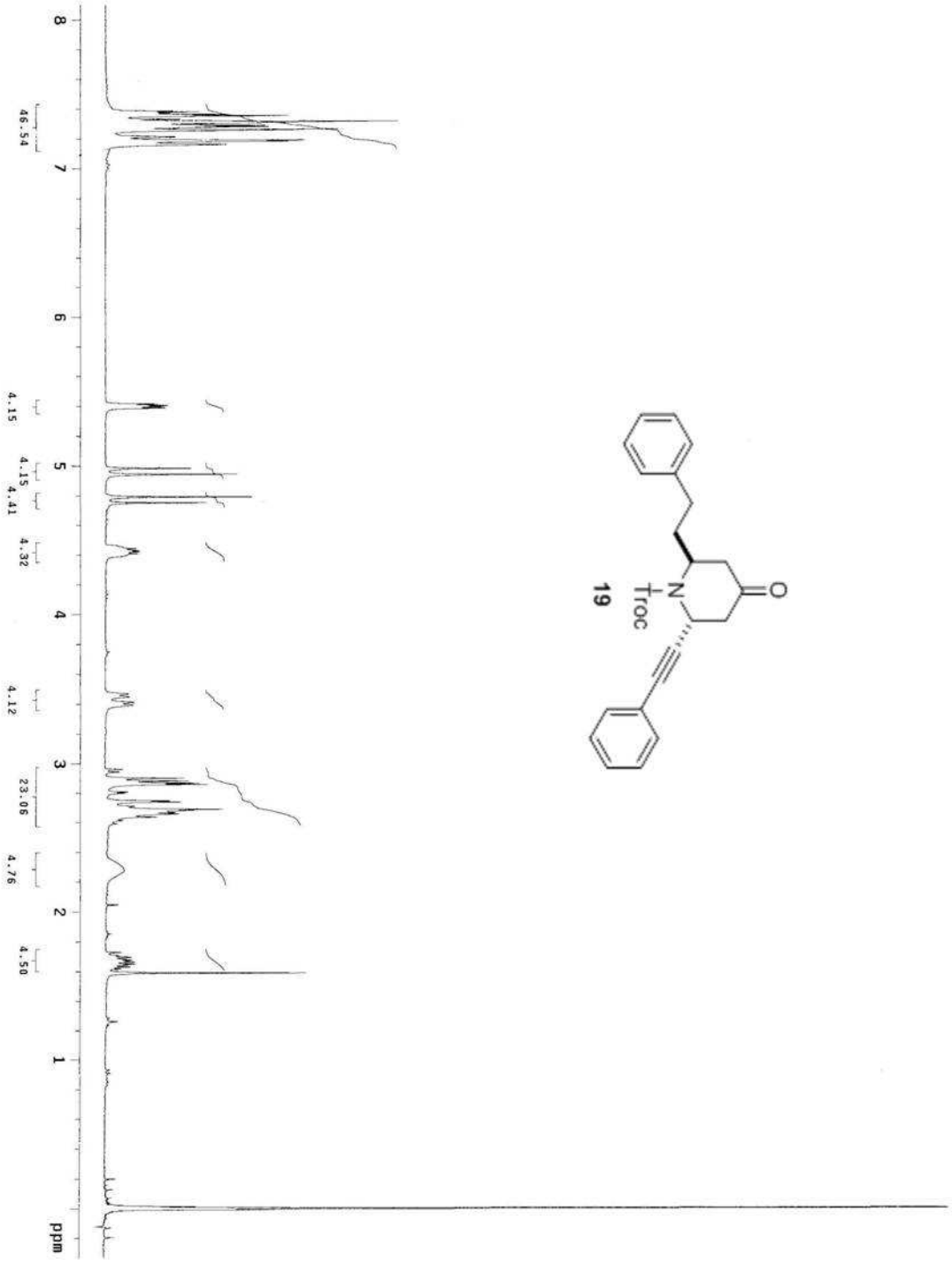
^{1}H NMR spectrum of compound **18** ($CDCl_3$, 300 MHz)



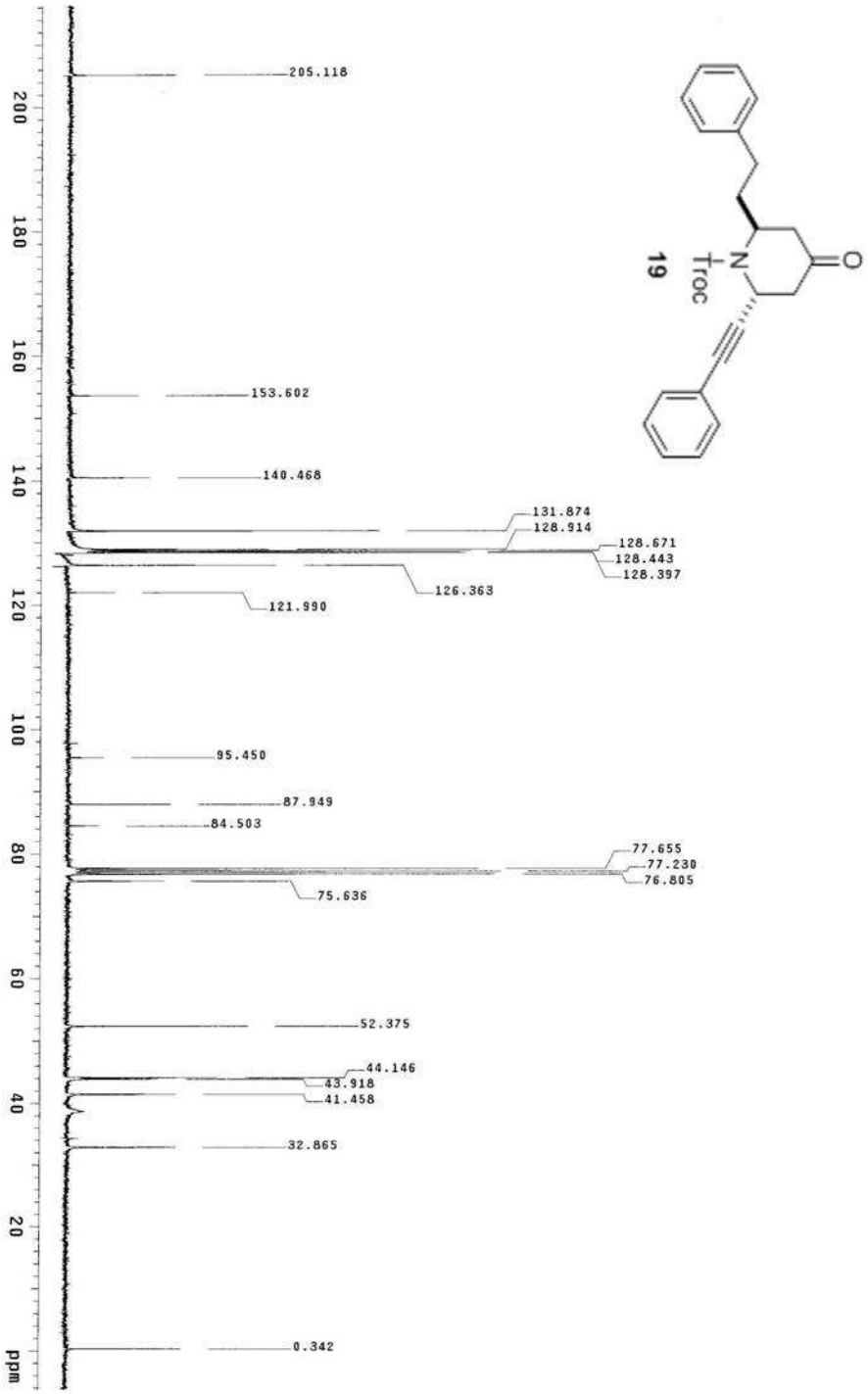
^{13}C NMR spectrum of compound **18** ($CDCl_3$, 75 MHz)



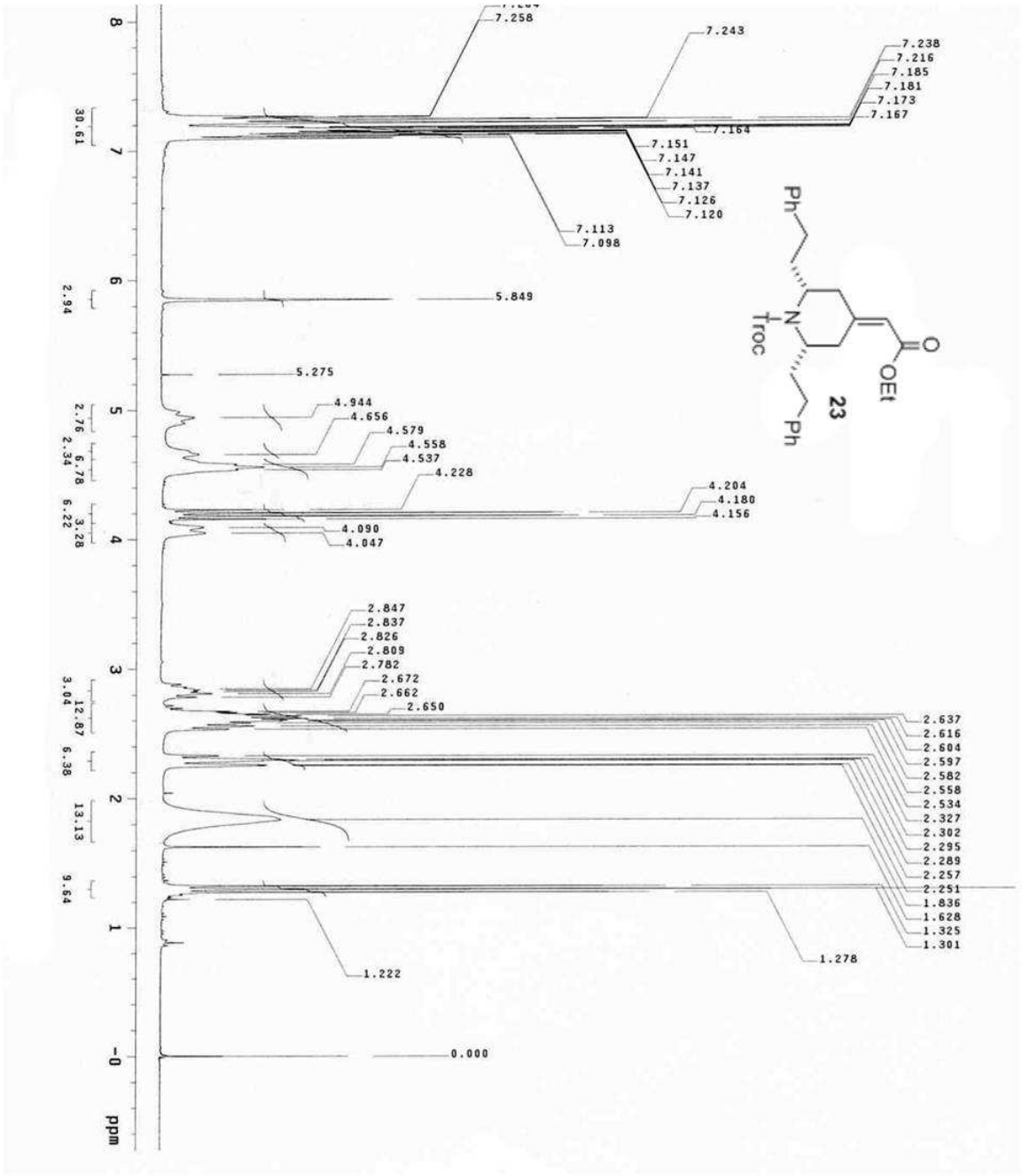
^{1}H NMR spectrum of compound **19** ($CDCl_3$, 300 MHz)



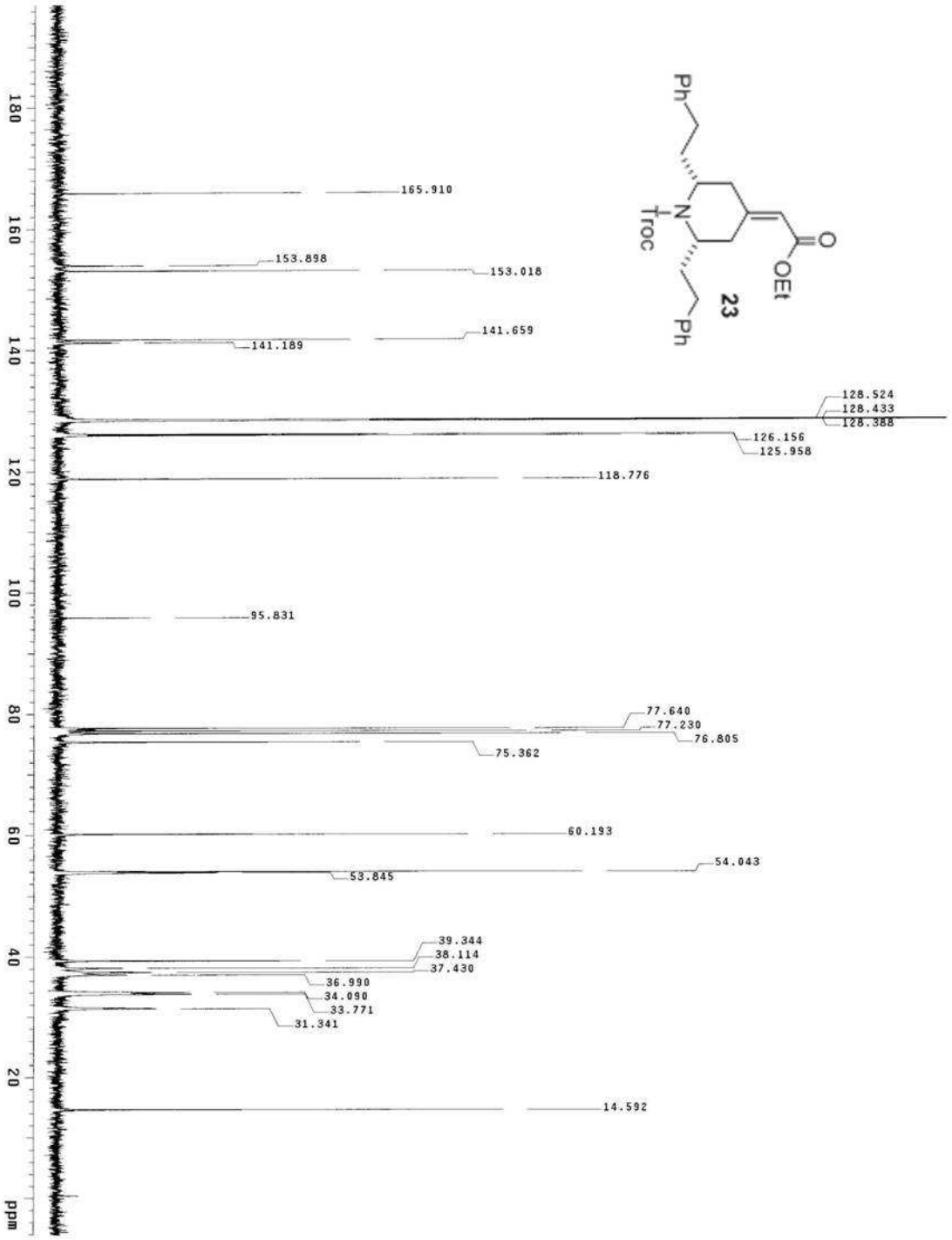
^{13}C NMR spectrum of compound **19** ($CDCl_3$, 75 MHz)



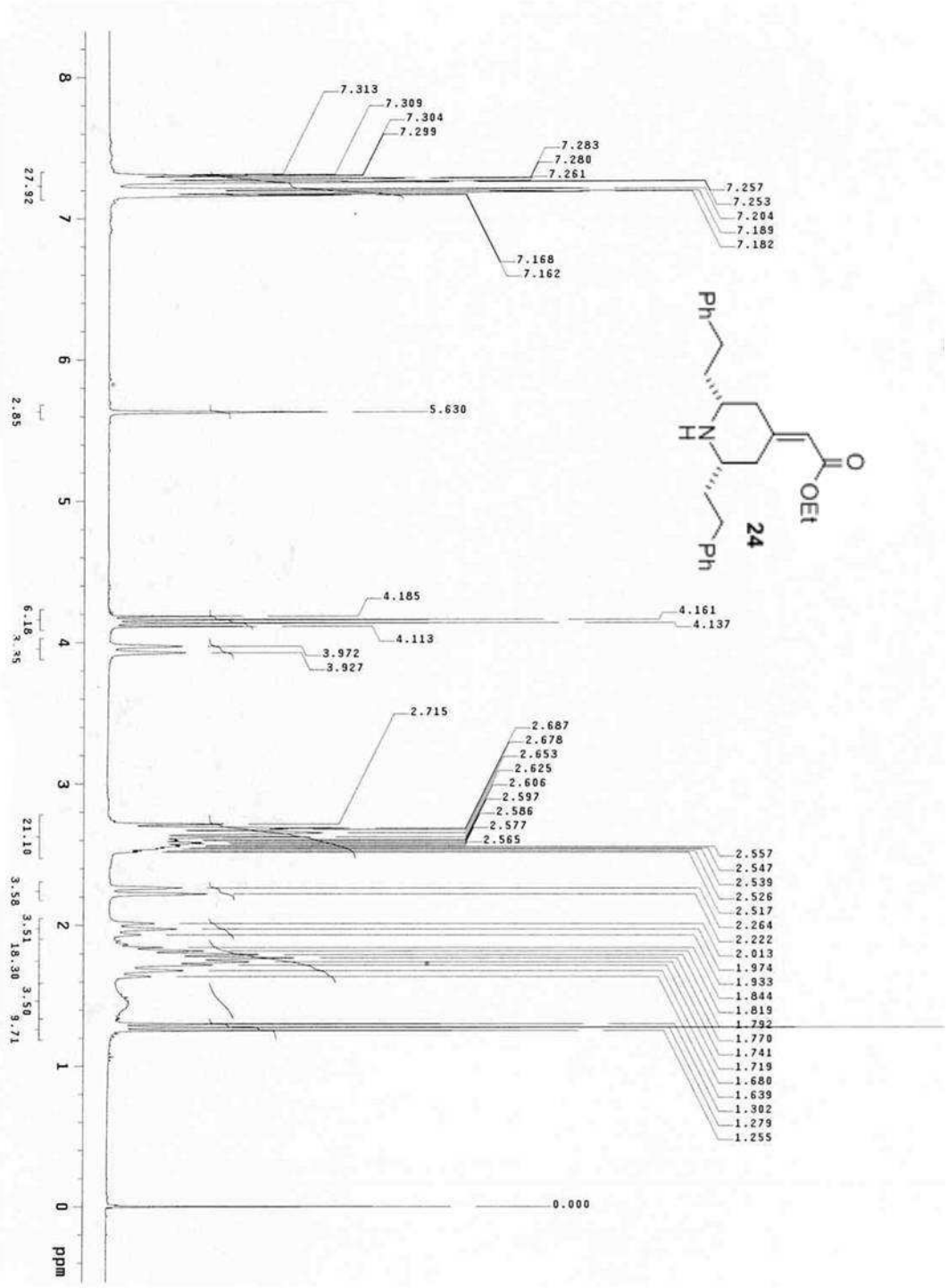
^{1}H NMR spectrum of compound **23** ($CDCl_3$, 300 MHz)



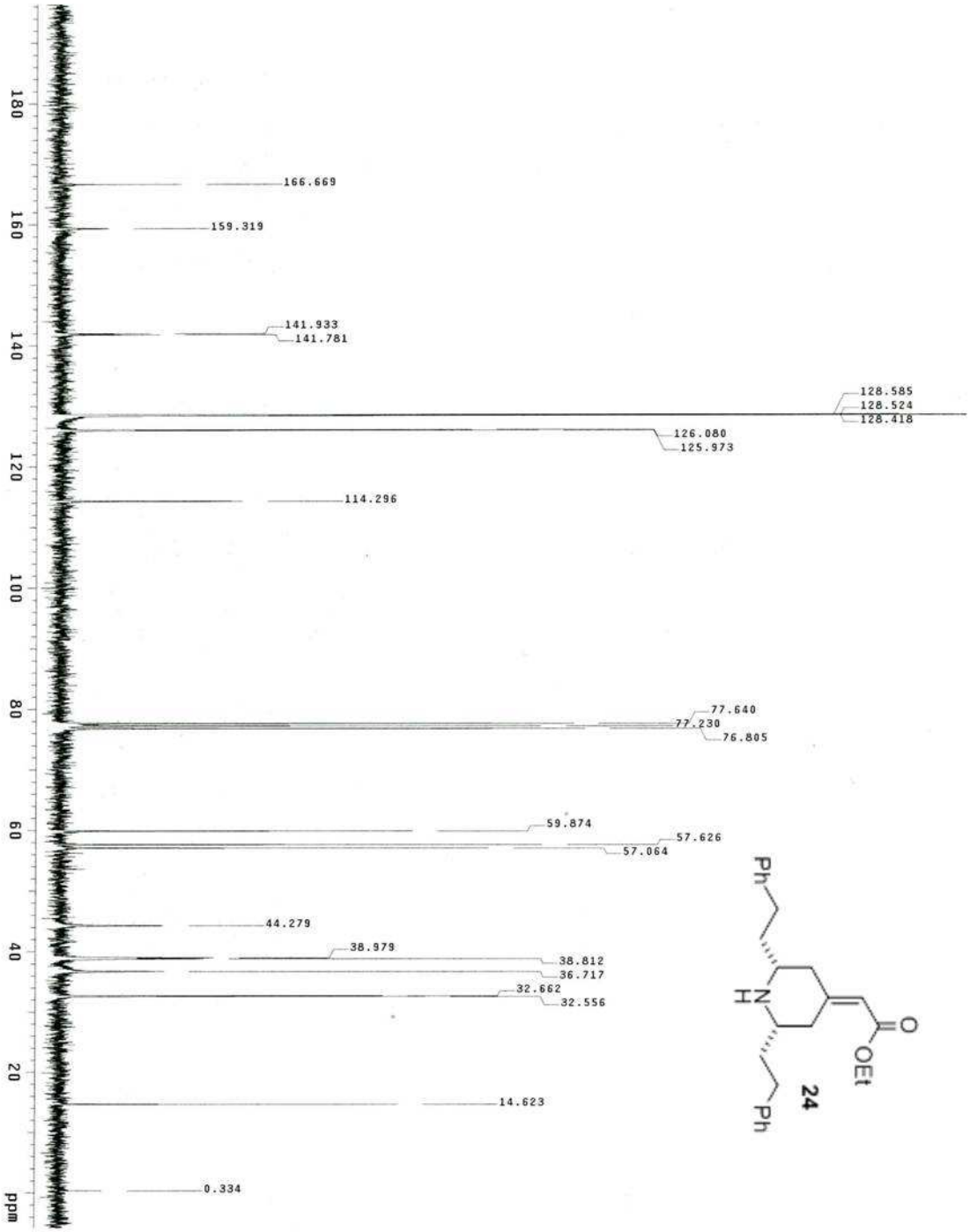
^{13}C NMR spectrum of compound **23** ($CDCl_3$, 75 MHz)



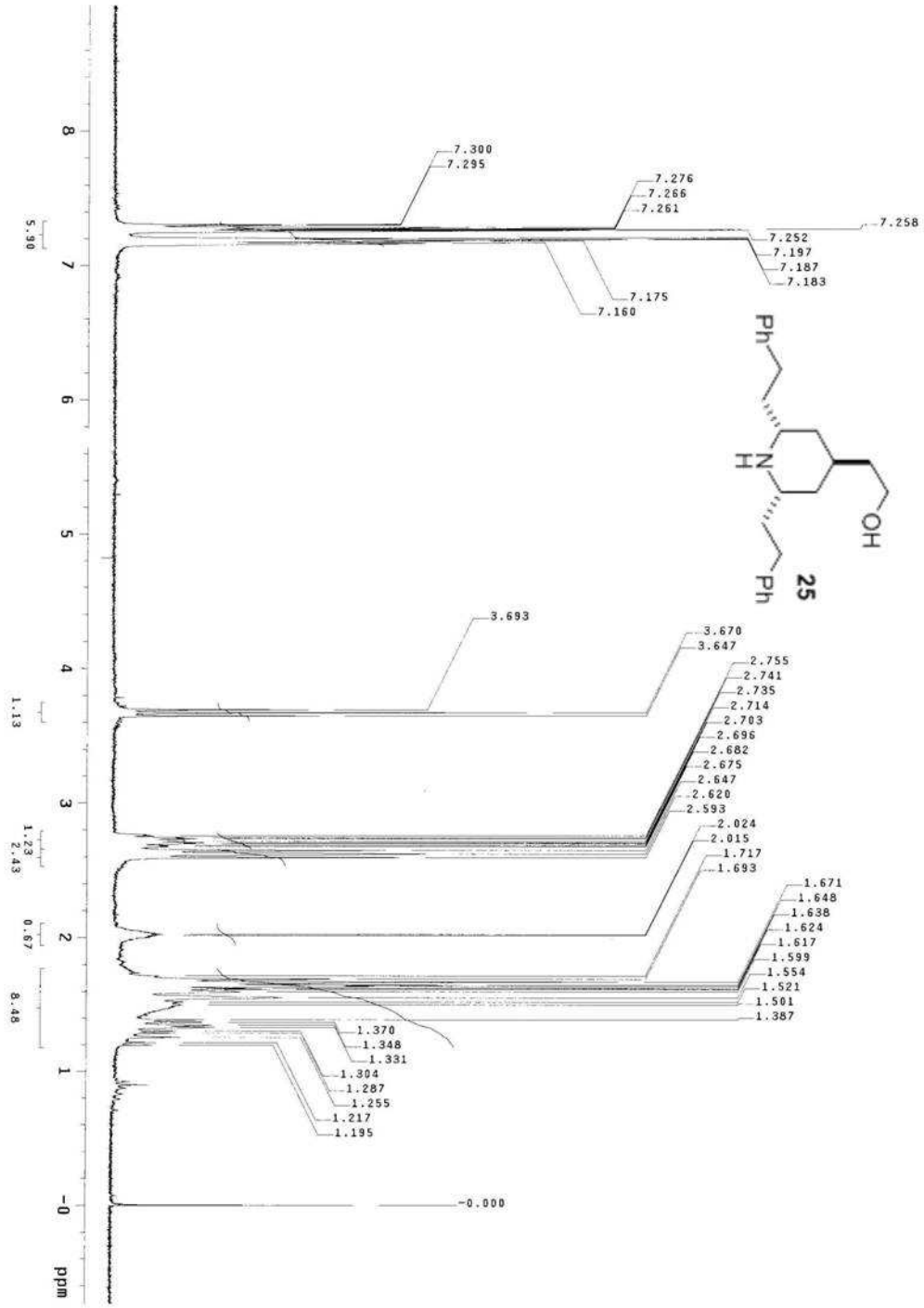
^{1}H NMR spectrum of compound **24** ($CDCl_3$, 300 MHz)



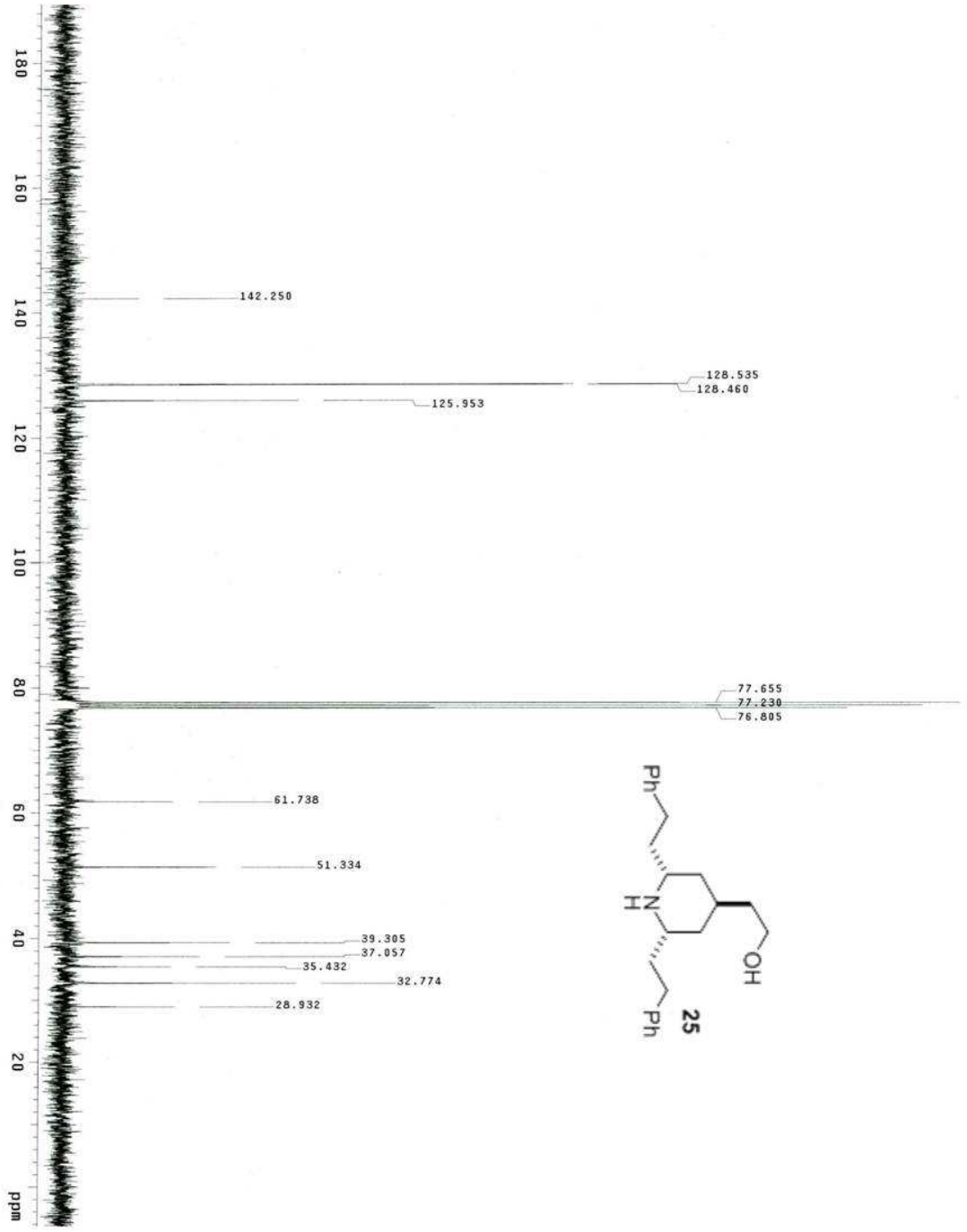
^{13}C NMR spectrum of compound **24** ($CDCl_3$, 75 MHz)



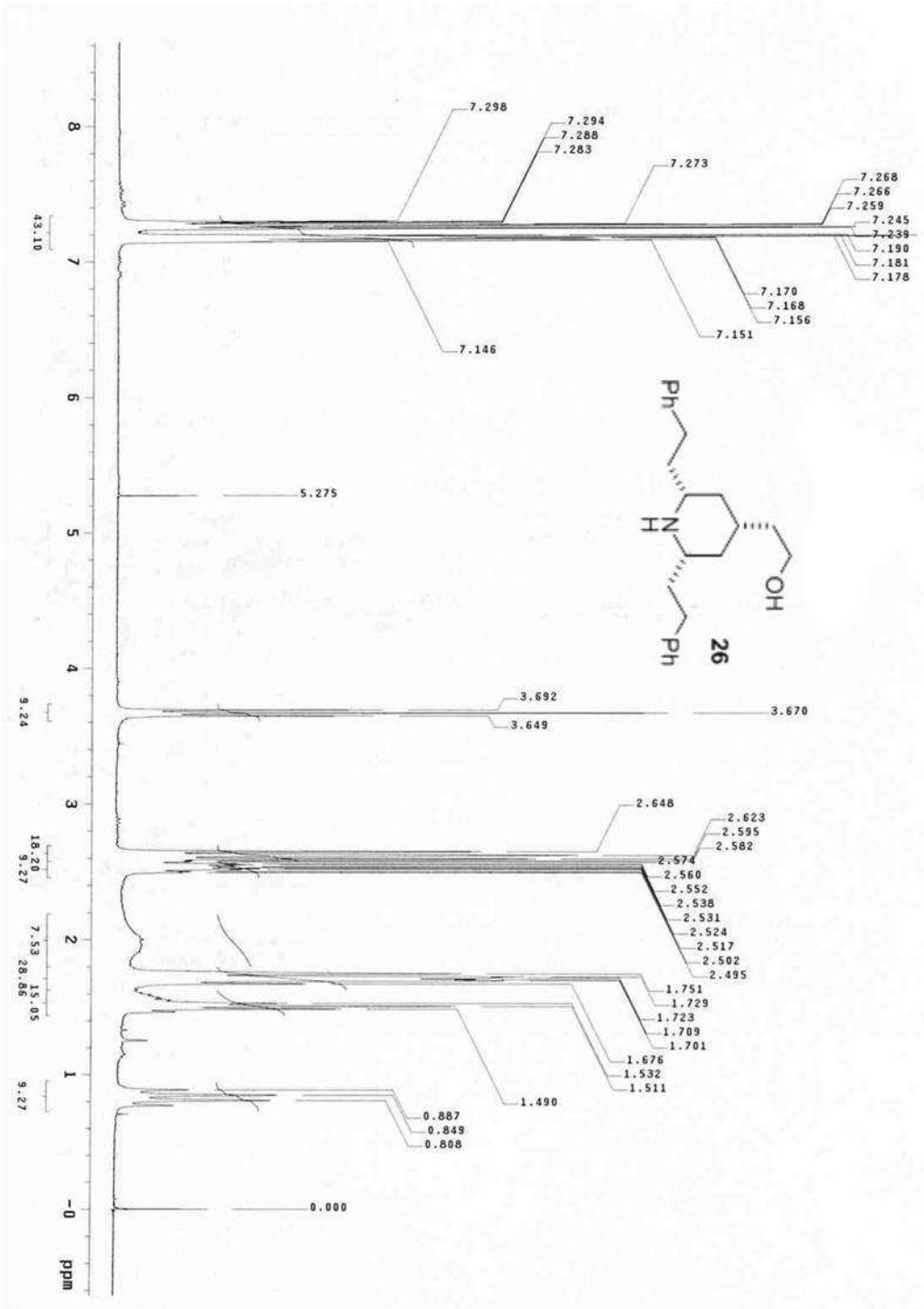
^{1}H NMR spectrum of compound **25** ($CDCl_3$, 300 MHz)



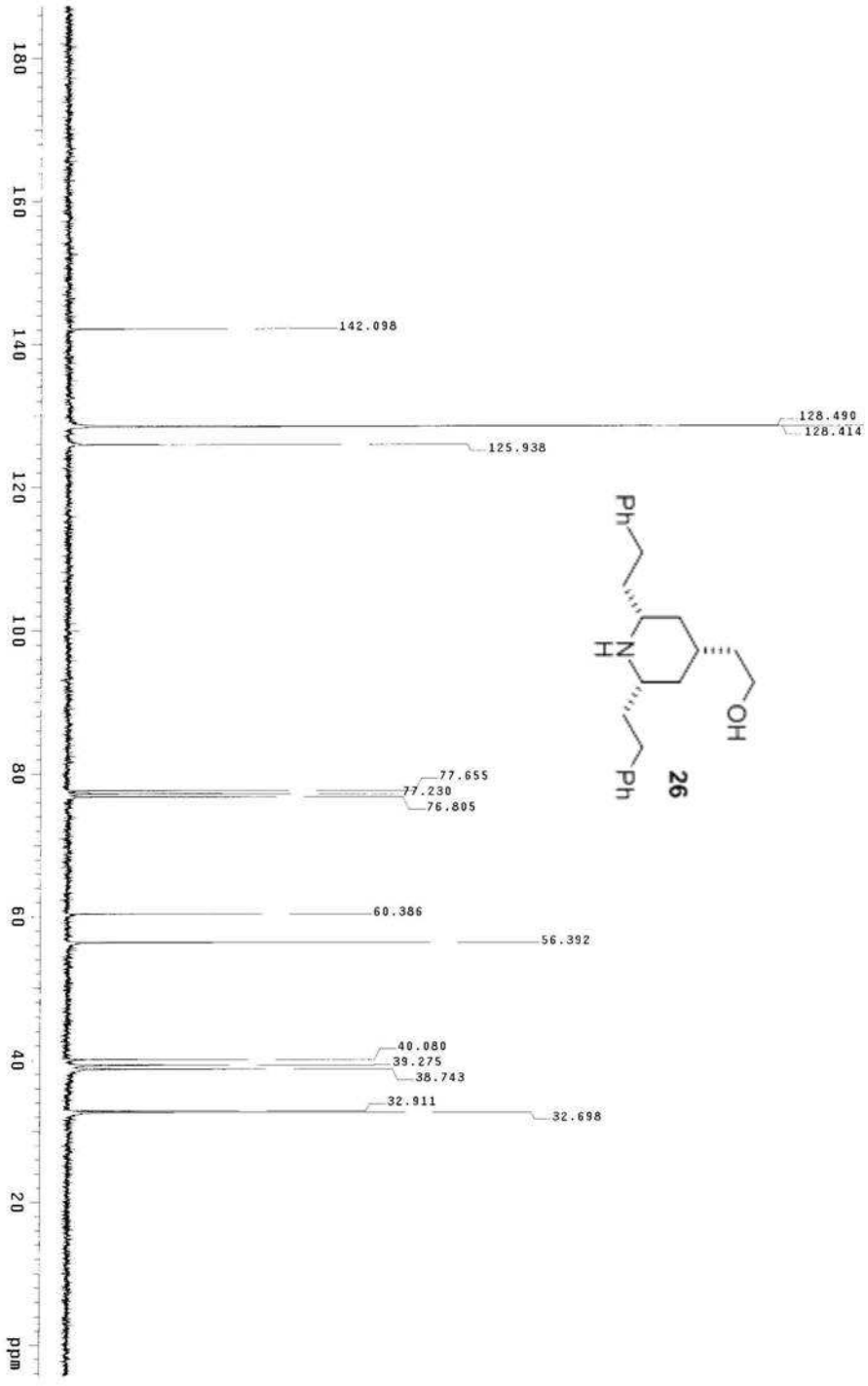
^{13}C NMR spectrum of compound **25** ($CDCl_3$, 75 MHz)



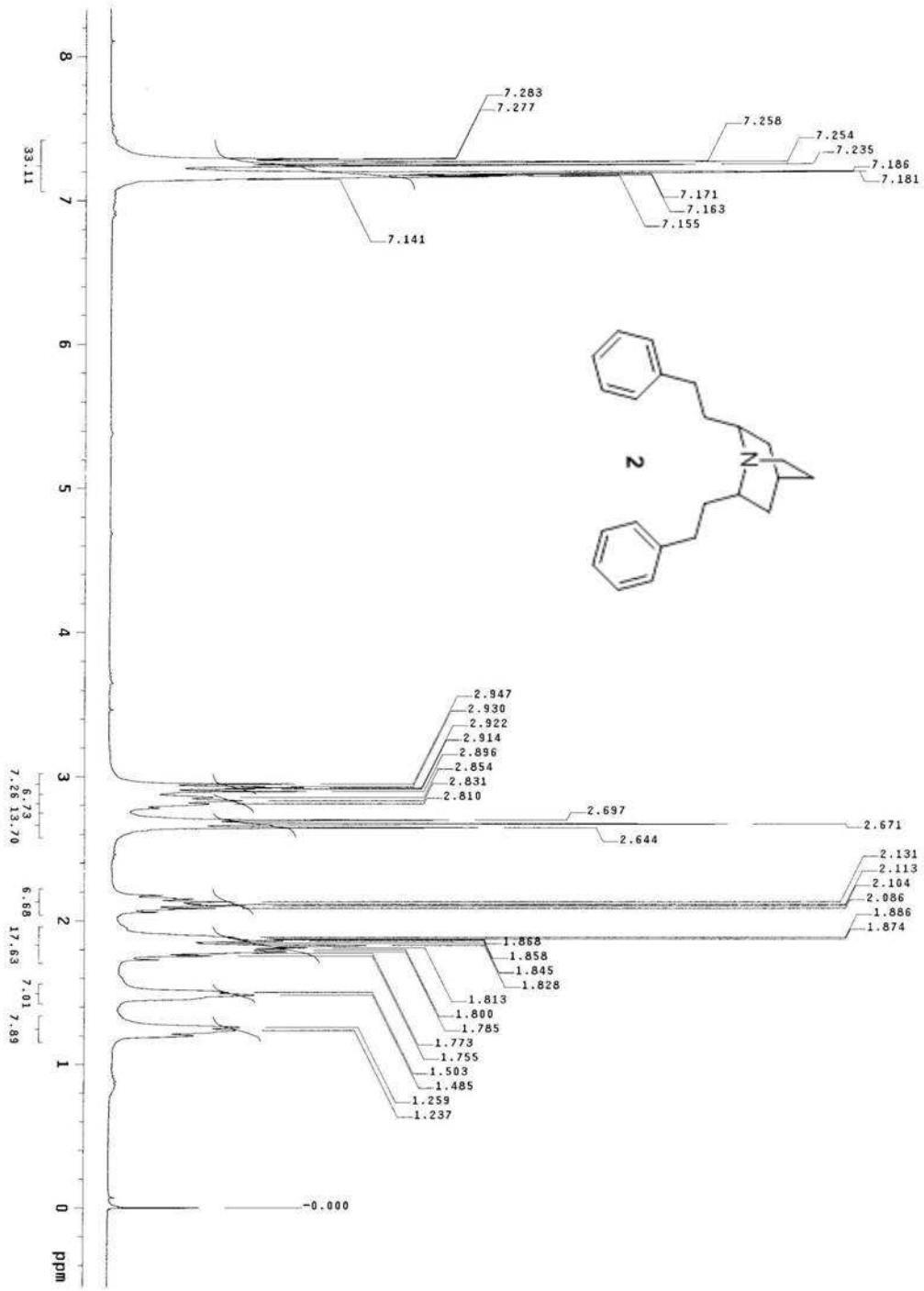
^{1}H NMR spectrum of compound **26** ($CDCl_3$, 300 MHz)



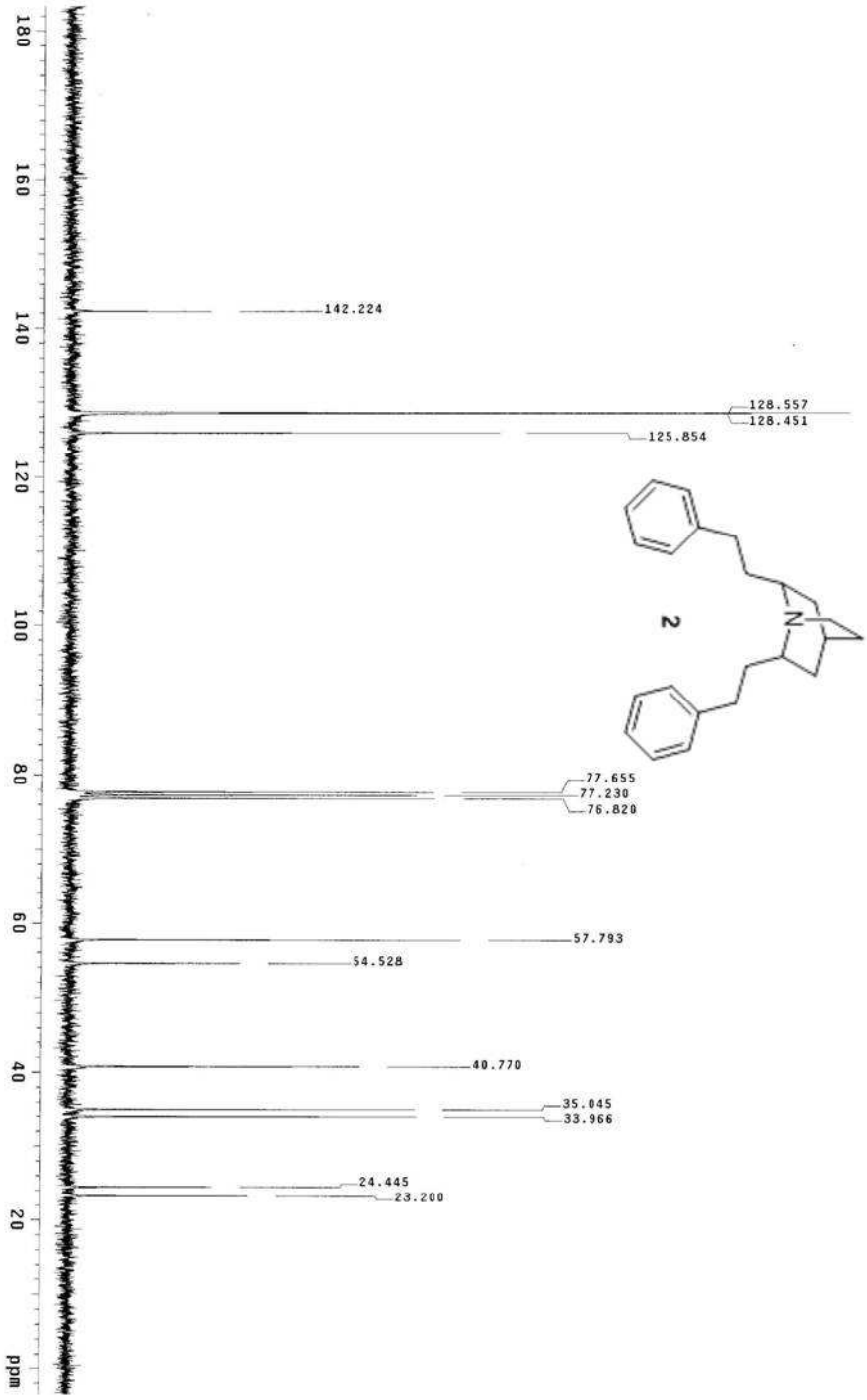
^{13}C NMR spectrum of compound **26** ($CDCl_3$, 75 MHz)



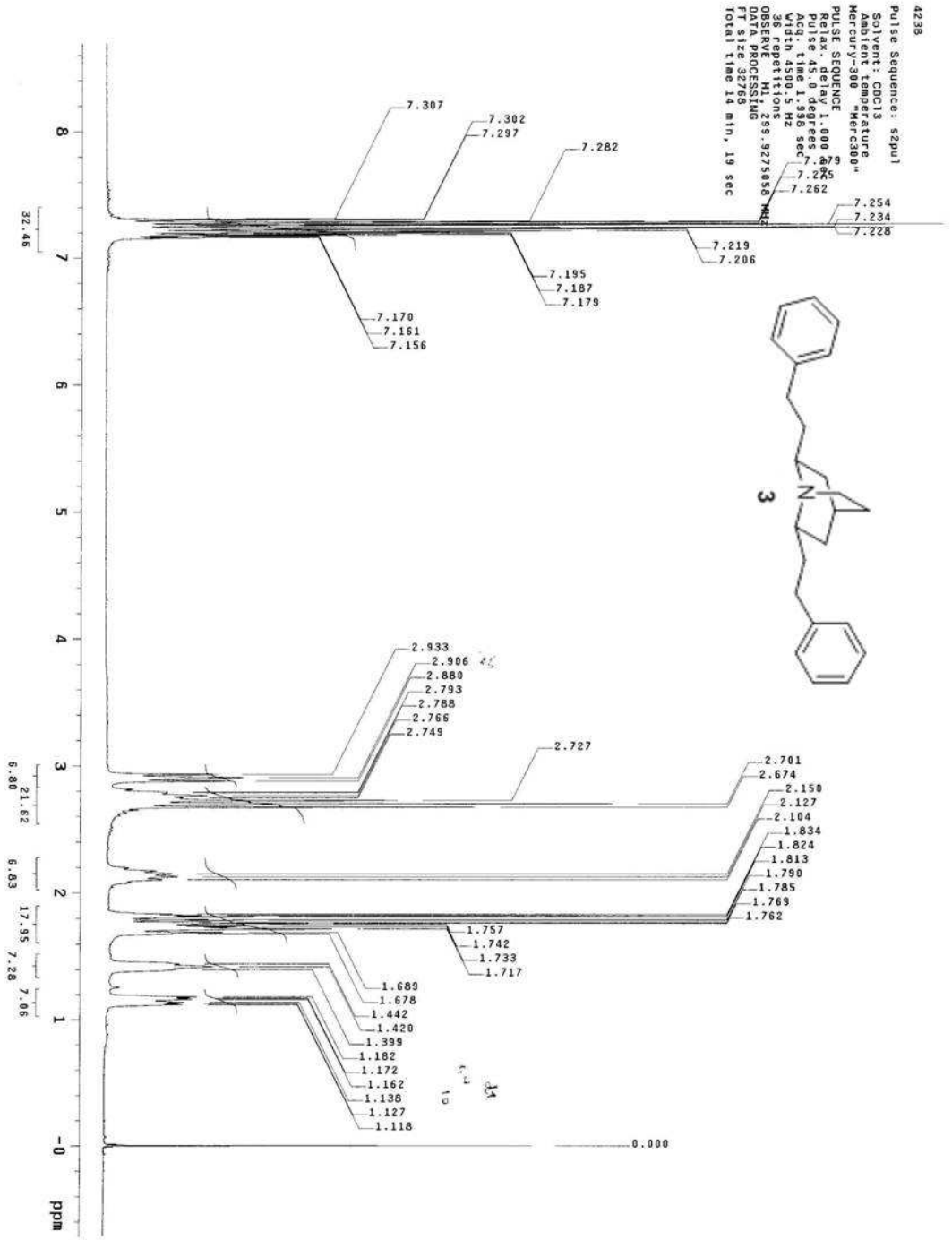
^{1}H NMR spectrum of compound **2** ($CDCl_3$, 300 MHz)



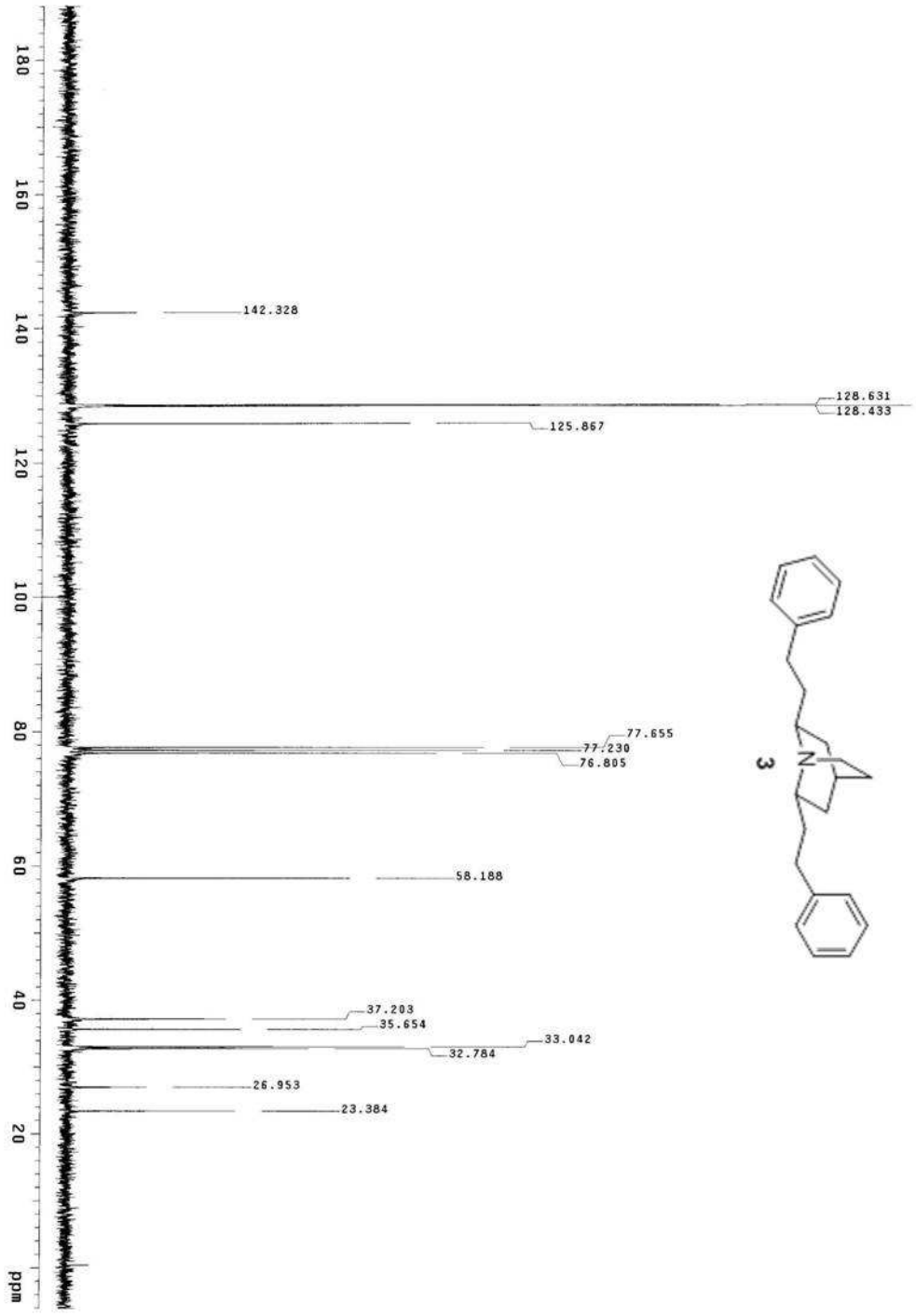
^{13}C NMR spectrum of compound **2** ($CDCl_3$, 75 MHz)



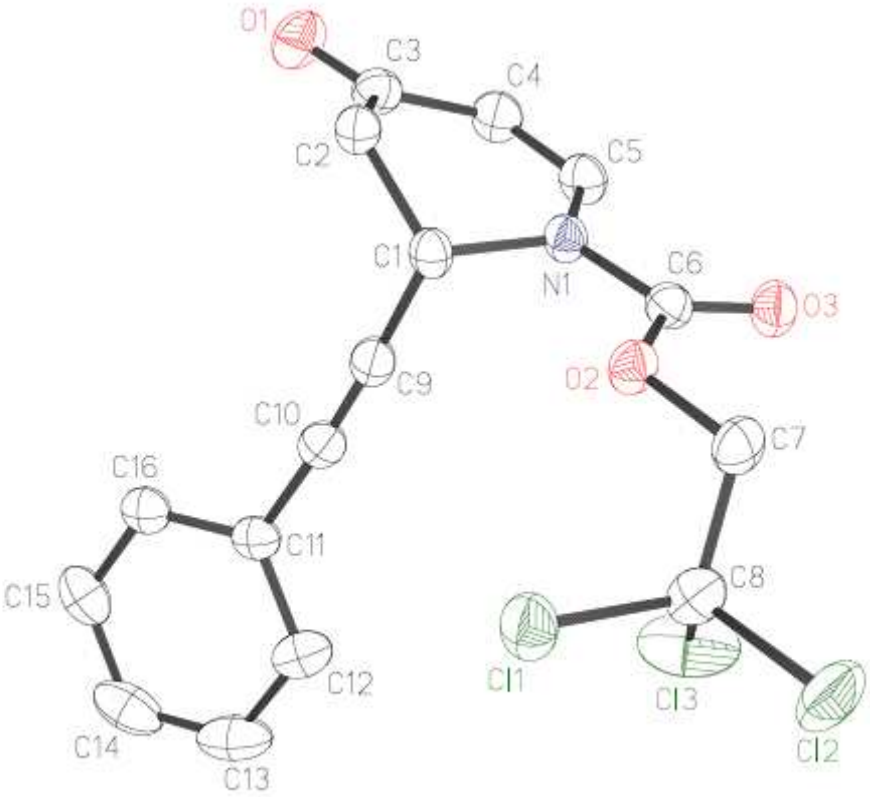
^{1}H NMR spectrum of compound **3** ($CDCl_3$, 300 MHz)



^{13}C NMR spectrum of compound **3** ($CDCl_3$, 75 MHz)



X-ray structure of compound **16**



X-ray structure of compound **17**