One- Pot Synthesis of Pyrrolo[1,2-*a*]quinoxaline Derivatives via Iron-promoted Aryl Nitro Reduction and Aerobic Oxidation of alcohols

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Supporting information

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General information

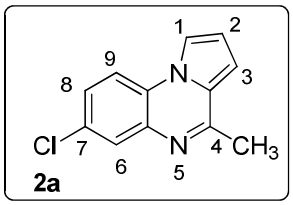
All commercially available compounds were used as received without further purification. Silica gel 0.063-0.2 mm (70-230 mesh) was used for all column chromatography. NMR spectra were recorded on a Jeol NMR LA400 spectrometer in chloroform-d or DMSO-d_6 at 400 MHz for ^{1}H NMR spectra and 100 MHz MHz for ^{13}C NMR spectra. Chemical shifts were reported in ppm and multiplicities were described as follows: bs, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants 'J' were reported in Hz. IR spectra were recorded on a Perkin Elmer spectrum 100 FT-IR ATR spectrometer. Absorptions are given in wavenumbers (cm^{-1}). Melting points were determined on a Kofler melting point apparatus. Mass spectra were measured with a Micro mass Q-TOF spectrometer.

Experimental Section:

Synthesis of pyrrolo[1,2-*a*]quinoxalines **2a-o**:

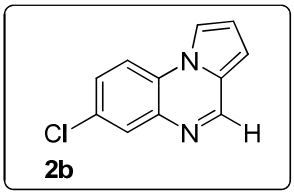
General procedure for the preparation of 4-substituted pyrrolo[1,2-*a*]quinoxalines **2a-o**:

To a solution of 1-(2-nitrophenyl)pyrrole derivative **1** (1 equiv, 2.25 mmol) in alcohol (15 mL) was added iron powder (9 equiv, 20.25 mmol). Hydrochloric acid solution (12 M, 11 equiv, 2 mL) was added slowly via syringe at room temperature. After the addition was complete, the mixture was stirred at reflux for 48 hours, cooled to room temperature and then was quenched with saturated aqueous solution of $NaHCO_3$. The resulting mixture was then extracted with EtOAc (3 times). The combined organic layers were washed with brine, dried on $MgSO_4$, filtered and evaporated. Products were purified by column chromatography with petroleum ether/ethyl acetate to yield the desired products.



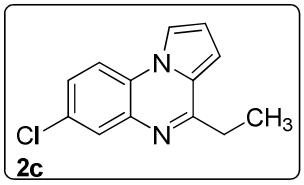
2a

7-Chloro-4-methylpyrrolo[1,2-*a*]quinoxaline (**2a**)
Prepared following the general procedure using 1-(4-chloro-2-nitrophenyl)pyrrole **1a** (500 mg, 2.25 mmol), iron powder (1.13 g, 20.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in ethanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2 to 7/3) afforded **2a** (389 mg, 80 %) as a white solid. Mp = 176 °C ; IR (neat, cm^{-1}) 3097, 1579, 1481, 1413, 811, 738 ; ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 2.30 Hz, 1H), 7.87 (dd, *J* = 2.60, 1.10 Hz, 1H), 7.76 (d, *J* = 8.70 Hz, 1H), 7.43 (dd, *J* = 8.70, 2.30 Hz, 1H), 6.92 (dd, *J* = 4.00, 1.10 Hz, 1H), 6.87 (dd, *J* = 4.00, 2.60 Hz, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4 (C), 137.3 (C), 130.7 (C), 129.3 (CH), 127.5 (CH), 126.7 (C), 126.5 (C), 115.3 (CH), 115.1 (CH), 114.4 (CH), 107.6 (CH), 22.4 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{12}H_{10}N_2Cl$ 217.0533, found 217.0523.



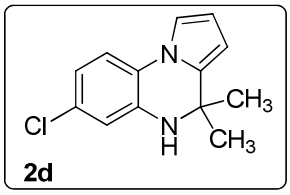
2b

7-Chloropyrrolo[1,2-*a*]quinoxaline (**2b**)
Prepared following the general procedure using 1-(4-chloro-2-nitrophenyl)pyrrole **1a** (500 mg, 2.25 mmol), iron powder (1.13 g, 20.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in methanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2 to 7/3) afforded **2b** (182 mg, 40 %) as a beige solid. Mp = 174 °C ; IR (neat, cm^{-1}) 3094, 1583, 1483, 1334, 816, 742 ; ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.94 (d, *J* = 2.30 Hz, 1H), 7.90 (dd, *J* = 2.60, 1.10 Hz, 1H), 7.80 (d, *J* = 8.80 Hz, 1H), 7.48 (dd, *J* = 8.80, 2.30 Hz, 1H), 6.93 (dd, *J* = 4.00, 1.10 Hz, 1H), 6.90 (dd, *J* = 4.00, 2.60 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9 (CH), 136.9 (C), 130.42 (C), 129.6 (CH), 127.9 (CH), 126.7 (C), 126.3 (C), 115.1 (CH), 114.6 (CH), 114.5 (CH), 108.0 (CH) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{11}H_8N_2Cl$ 203.0385, found 203.0376.



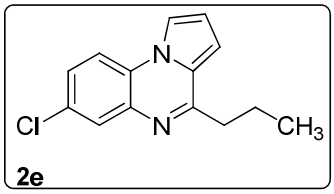
7-Chloro-4-ethylpyrrolo[1,2-*a*]quinoxaline (**2c**)

Prepared following the general procedure using 1-(4-chloro-2-nitrophenyl)pyrrole **1a** (500 mg, 2.25 mmol), iron powder (1,13 g, 20.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in *n*-propanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 7/3) afforded **2c** (290 mg, 56 %) as a yellow solid. Mp = 113 °C ; IR (neat, cm^{-1}) 3106, 2967, 1577, 1483, 1422, 805, 729 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 2.30 Hz, 1H), 7.87 (dd, *J* = 2.60, 1.10 Hz, 1H), 7.75 (d, *J* = 8.70 Hz, 1H), 7.42 (dd, *J* = 8.70, 2.30 Hz, 1H), 6.93 (dd, *J* = 4.00, 1.10 Hz, 1H), 6.86 (dd, *J* = 4.00, 2.60 Hz, 1H), 3.04 (q, *J* = 7.60 Hz, 2H), 1.44 (t, *J* = 7.60 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7 (C), 137.1 (C), 130.2 (C), 128.9 (CH), 126.9 (CH), 125.9 (C), 125.6 (C), 114.8 (CH), 114.4 (CH), 113.8 (CH), 106.7 (CH), 28.8 (CH_2), 12.3 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{13}H_{12}N_2Cl$ 231.0689, found 231.0695.



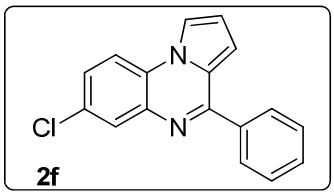
7-Chloro-4,4-dimethyl-4,5-dihydropyrrolo[1,2-*a*]quinoxaline (**2d**)

Prepared following the general procedure using 1-(4-chloro-2-nitrophenyl)pyrrole **1a** (500 mg, 2.25 mmol), iron powder (1.13 g, 20.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in isopropanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2) afforded **2d** (320 mg, 61 %) as a brown solid. Mp = 84 °C ; IR (neat, cm^{-1}) 3323, 2963, 1608, 1517, 1336, 783, 703 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.40 Hz, 1H), 7.07 (dd, *J* = 3.20, 1.60 Hz, 1H), 6.76 (dd, *J* = 8.40, 2.20 Hz, 1H), 6.70 (d, *J* = 2.20 Hz, 1H), 6.28 (dd, *J* = 3.60, 3.20 Hz, 1H), 5.99 (dd, *J* = 3.60, 1.60 Hz, 1H), 3.76 (s, 1H), 1.50 (s, 6H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6 (C), 134.5 (C), 129.7 (C), 124.0 (C), 118.8 (CH), 115.6 (CH), 115.4 (CH), 114.1 (CH), 110.4 (CH), 102.4 (CH), 51.6 (C), 29.6 ($2XCH_3$) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{13}H_{14}N_2Cl$ 233.0846, found 233.0856.



7-Chloro-4-propylpyrrolo[1,2-*a*]quinoxaline (**2e**)

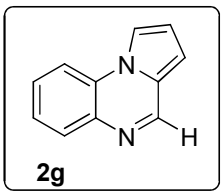
Prepared following the general procedure using 1-(4-chloro-2-nitrophenyl)pyrrole **1a** (500 mg, 2.25 mmol), iron powder (1.13 g, 20.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in *n*-butanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2 to 7/3) afforded **2e** (320 mg, 58 %) as a yellow solid. Mp = 72 °C ; IR (neat, cm^{-1}) 3143, 2967, 1578, 1481, 1420, 803, 716 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 2.40 Hz, 1H), 7.86 (dd, *J* = 2.60, 1.20 Hz, 1H), 7.74 (d, *J* = 8.80 Hz, 1H), 7.41 (dd, *J* = 8.80, 2.40 Hz, 1H), 6.93 (dd, *J* = 4.00, 1.20 Hz, 1H), 6.85 (dd, *J* = 4.00, 2.60 Hz, 1H), 2.98 (t, *J* = 7.60 Hz, 2H), 1.92 (sex, 2H), 1.07 (t, *J* = 7.60 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8 (C), 137.1 (C), 130.3 (C), 129.0 (CH), 126.9 (CH), 126.1 (C), 126.0 (C), 114.9 (CH), 114.6 (CH), 113.9 (CH), 107.0 (CH), 37.8 (CH_2), 21.8 (CH_2), 14.3 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{14}H_{14}N_2Cl$ 245.0845, found 245.0848.



2f

7-Chloro-4-phenylpyrrolo[1,2-*a*]quinoxaline (**2f**)[1]

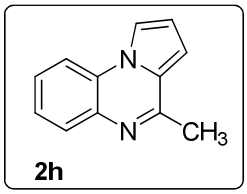
Prepared following the general procedure using 1-(4-chloro-2-nitrophenyl)pyrrole **1a** (500 mg, 2.25 mmol), iron powder (1.13 g, 20.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in benzyl alcohol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 9/1 to 8/2) afforded **2f** (340 mg, 54 %) as a yellow solid. Mp = 152 °C ; IR (neat, cm^{-1}) 3142, 2922, 1573, 1475, 1369, 804, 691 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 2.30 Hz, 1H), 7.99-7.90 (m, 3H), 7.82 (d, *J* = 8.80 Hz, 1H), 7.55-7.50 (m, 3H), 7.48 (dd, *J* = 8.80, 2.30 Hz, 1H), 7.03 (dd, *J* = 4.00, 1.10 Hz, 1H), 6.92 (dd, *J* = 4.00, 2.60 Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0 (C), 138.6 (C), 137.8 (C), 130.9 (C), 130.7 (CH), 130.1 (CH), 129.2 (CH), 129.2 (CH), 128.0 (CH), 126.3 (C), 125.8 (C), 115.5 (CH), 115.3 (CH), 114.9 (CH), 109.9 (CH) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{17}H_{12}N_2Cl$ 279.0689, found 279.0691.



2g

Pyrrolo[1,2-*a*]quinoxaline (**2g**)[2]

Prepared following the general procedure using 1-(2-nitrophenyl)pyrrole **1b** (500 mg, 2.66 mmol), iron powder (1.34 g, 23.94 mmol), hydrochloric acid solution 12 M (2.36 mL, 29.26 mmol) in methanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2 to 7/3) afforded **2g** (182 mg, 31 %) as a beige solid. Spectral data are in accordance with literature data.



2h

4-Methylpyrrolo[1,2-*a*]quinoxaline (**2h**)[3]

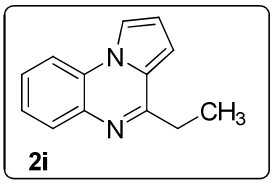
Prepared following the general procedure using 1-(2-nitrophenyl)pyrrole **1b** (500 mg, 2.66 mmol), iron powder (1.34 g, 23.94 mmol), hydrochloric acid solution 12 M (2.36 mL, 29.26 mmol) in ethanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2 to 7/3) afforded **2h** (390 mg, 81 %) as a beige solid. Mp = 132 °C ; IR (neat, cm^{-1}) 3099, 1611, 1529, 1480, 1415, 1361, 1042, 759, 729 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.86 (m, 2H), 7.81 (dd, *J* = 8.00, 1.60 Hz, 1H), 7.44 (m, 2H), 6.89 (dd, *J* = 4.00, 1.60 Hz, 1H), 6.84 (dd, *J* = 4.00, 2.60 Hz, 1H), 2.73 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.87 (C), 136.11 (C), 129.45 (CH), 127.48 (C), 127.10 (CH), 126.45 (C), 125.29 (CH), 114.38

[1] Guillon, J.; Dallemagne, P.; Pfeiffer, B.; Renard, P.; Manechez, D.; Kervran, A.; Rault, S. *Eur. J. Med. Chem.* **1998**, *33*, 293–308.

[2] Reeves, J. T.; Fandrick, D. R.; Tan, Z.; Song, J. J.; Lee, H.; Yee, N. K.; Senanayake, C. H. *J. Org. Chem.* **2010**, *75*, 992–994.

[3] Guillon, J.; Forfar, I.; Mamani-Matsuda, M.; Desplat, V.; Saliège, M.; Thiolat, D.; Massip, S.; Tabourier, A.; Léger, J.-M.; Dufaure, B.; Haumont, G.; Jarry, C.; Mossalayi, D. *Bioorg. Med. Chem.* **2007**, *15*, 194–210.

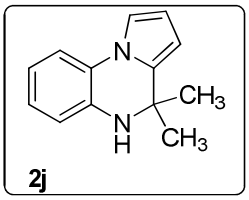
(CH), 113.81 (CH), 113.66 (CH), 106.65 (CH), 22.06 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{12}H_{11}N_2$ 183.0922, found 183.0925.



2i

4-Ethylpyrrolo[1,2-*a*]quinoxaline (**2i**)

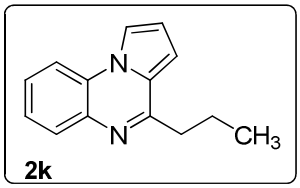
Prepared following the general procedure using 1-(2-nitrophenyl)pyrrole **1b** (500 mg, 2.66 mmol), iron powder (1.34 g, 23.94 mmol), concentrated hydrochloric acid solution 12 M (2.36 mL, 29.26 mmol) in *n*-propanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 7/3) afforded **2i** (291 mg, 56 %) as a beige solid. Mp = 70 °C ; IR (neat, cm^{-1}) 3106, 2965, 1613, 1527, 1481, 1423, 750, 729 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 7.80, 1.60 Hz, 1H), 7.90 (dd, *J* = 2.60, 1.10 Hz, 1H), 7.82 (dd, *J* = 7.80, 1.60 Hz, 1H), 7.44 (m, 2H), 6.90 (dd, *J* = 4.00, 1.10 Hz, 1H), 6.83 dd, *J* = 4.00, 2.60 Hz, 1H), 3.06 (q, *J* = 7.60 Hz, 2H), 1.46 (t, *J* = 7.60 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6 (C), 136.2 (C), 129.6 (CH), 127.4 (C), 127.1 (CH), 125.8 (C), 125.2 (CH), 114.3 (CH), 113.8 (CH), 113.6 (CH), 106.3 (CH), 29.0 (CH_2), 12.7 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{13}H_{13}N_2$ 197.1078, found 197.1079.



2j

4,4-Dimethyl-4,5-dihydropyrrolo[1,2-*a*]quinoxaline (**2j**)

Prepared following the general procedure using 1-(2-nitrophenyl)pyrrole **1b** (500 mg, 2.66 mmol), iron powder (1.34 g, 23.94 mmol), hydrochloric acid solution 12 M (2.36 mL, 29.26 mmol) in isopropanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 7/3) afforded **2j** (316 mg, 60 %) as a beige solid. Mp = 92 °C ; IR (neat, cm^{-1}) 3376, 2962, 1610, 1509, 1332, 745 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 7.90, 1.30 Hz, 1H), 7.12 (dd, *J* = 2.90, 1.60 Hz, 1H), 6.95 (td, *J* = 7.60, 1.30 Hz, 1H), 6.80 (td, *J* = 7.60, 1.30 Hz, 1H), 6.71 (dd, *J* = 7.90, 1.30 Hz, 1H), 6.28 (t, *J* = 3.60, 1H), 5.99 (dd, *J* = 3.60, 1.60 Hz, 1H), 3.73 (s, 1H), 1.50 (s, 6H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.3 (C), 134.6 (C), 125.2 (C), 124.6 (CH), 119.0 (CH), 115.6 (CH), 114.5 (CH), 113.8 (CH), 109.8 (CH), 101.8 (CH), 51.2 (C), 29.3 (2XCH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{13}H_{15}N_2$ 199.1235, found 199.1235.

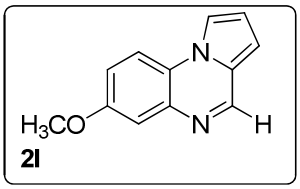


2k

4-Propylpyrrolo[1,2-*a*]quinoxaline (**2k**)[3]

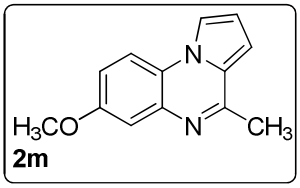
Prepared following the general procedure using 1-(2-nitrophenyl)pyrrole **1b** (500 mg, 2.66 mmol), iron powder (1.34 g, 23.94 mmol), hydrochloric acid solution 12 M (2.36 mL, 29.26 mmol) in *n*-butanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 7/3) afforded **2k** (279 mg, 50 %) as a beige solid. Mp <50 °C ; IR (neat, cm^{-1}) 3095, 2962,1610,1480, 1092, 746, 724 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 7.60, 1.60 Hz, 1H), 7.86 (dd, *J* = 2.40, 1.10 Hz, 1H), 7.78 (dd, *J* = 7.60, 1.60 Hz, 1H), 7.46 – 7.37 (m, 2H), 6.89 (dd, *J* = 4.00, 1.10 Hz, 1H), 6.82 (dd, *J* = 4.00, 2.40 Hz, 1H), 3.01 (t, *J* = 7.40 Hz, 2H),

1.93 (sex, 2H), 1.07 (t, J = 7.40 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4 (C), 135.9 (C), 129.3 (CH), 127.2 (C), 126.8 (CH), 126.0 (C), 125.0 (CH), 114.0 (CH), 113.5 (CH), 113.3 (CH), 106.2 (CH), 37.7 (CH_2), 21.8 (CH_2), 14.1 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{14}H_{15}N_2$ 211.1235, found 211.1238.



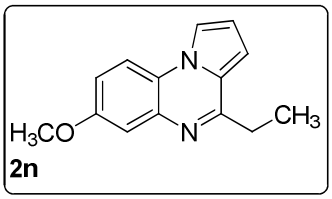
7-Methoxypyrrolo[1,2-*a*]quinoxaline (**2l**)

Prepared following the general procedure using 1-(4-methoxy-2-nitrophenyl)pyrrole **1c** (490 mg, 2.25 mmol), iron powder (1.13 g, 20,.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in methanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2) afforded **2l** (90 mg, 20 %) as a brown solid. Mp = 102 °C ; IR (neat, cm^{-1}) 3095, 1599, 1489, 1243, 840, 732 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 7.87 (dd, J = 2.40, 1.10 Hz, 1H), 7.79 (d, J = 9.00 Hz, 1H), 7.44 (d, J = 2.90 Hz, 1H), 7.14 (dd, J = 9.00, 2.90 Hz, 1H), 6.89 (dd, J = 4.00, 1.10 Hz, 1H), 6.85 (dd, J = 4.00, 2.40 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1 (C), 146.1 (CH), 136.9 (C), 126.2 (C), 122.3 (C), 116.8 (CH), 114.7 (CH), 113.8 (CH), 113.7 (CH), 111.4 (CH), 107.1 (CH), 55.6 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{12}H_{11}N_2O$ 199.0871, found 199.0870.



7-Methoxy-4-methylpyrrolo[1,2-*a*]quinoxaline (**2m**)[3]

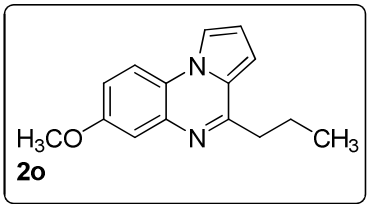
Prepared following the general procedure using 1-(4-methoxy-2-nitrophenyl)pyrrole **1c** (245 mg, 1.12 mmol), iron powder (565 mg, 10.12 mmol), hydrochloric acid solution 12 M (1 mL, 12.38 mmol) in ethanol (8 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2) afforded **2m** (165 mg, 69 %) as an orange solid. Mp = 88 °C ; IR (neat, cm^{-1}) 3086, 1617, 1594, 1489, 1246, 799, 714 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, J = 2.40, 1.10 Hz, 1H), 7.70 (d, J = 9.00 Hz, 1H), 7.37 (d, J = 2.80 Hz, 1H), 7.06 (dd, J = 9.00, 2.80 Hz, 1H), 6.85 (dd, J = 4.00, 1.10 Hz, 1H), 6.80 (dd, J = 4.00, 2.40 Hz, 1H), 3.90 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1 (C), 154.0 (C), 137.0 (C), 126.0 (C), 121.6 (C), 115.9 (CH), 114.5 (CH), 113.9 (CH), 113.1 (CH), 110.6 (CH), 106.2 (CH), 55.6 (CH_3), 21.9 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{13}H_{13}N_2O$ 213.1027, found 213.1027.



7-Methoxy-4-ethylpyrrolo[1,2-*a*]quinoxaline (**2n**)

Prepared following the general procedure using 1-(4-methoxy-2-nitrophenyl)pyrrole **1c** (490 mg, 2.25 mmol), iron powder (1.13 g, 20.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in *n*-propanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2) afforded **2n** (240 mg, 47 %) as a yellow solid. Mp = 74 °C ; IR (neat, cm^{-1}) 3100, 2962, 1615, 1596, 1489, 1240, 710 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 2.60, 1.10 Hz, 1H), 7.72 (d, J = 9.00 Hz, 1H), 7.41 (d, J = 2.80 Hz, 1H), 7.08 (dd, J = 9.00,

2.80 Hz, 1H), 6.88 (dd, *J* = 4.00, 1.10 Hz, 1H), 6.81 (dd, *J* = 4.00, 2.60 Hz, 1H), 3.91 (s, 3H), 3.04 (q, *J* = 7.60 Hz, 2H), 1.45 (t, *J* = 7.60 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.87 (C), 157.10 (C), 137.13 (C), 125.40 (C), 121.58 (C), 116.00 (CH), 114.54 (CH), 113.79 (CH), 113.09 (CH), 110.73 (CH), 105.80 (CH), 55.62 (CH_3), 28.92 (CH_2), 12.60 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{14}H_{15}N_2O$ 227.1184, found 227.1185.

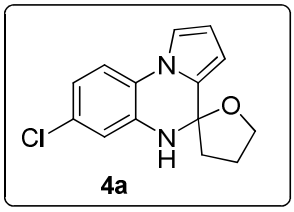


2o

7-Methoxy-4-propylpyrrolo[1,2-*a*]quinoxaline (**2o**)[3]

Prepared following the general procedure using 1-(4-methoxy-2-nitrophenyl)pyrrole **1c** (245 mg, 1.12 mmol), iron powder (565 mg, 10.12 mmol), hydrochloric acid solution 12 M (1 mL, 12.38 mmol) in *n*-butanol (8 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2) afforded **2o** (120 mg, 44 %) as an orange solid. Mp = 68 °C ; IR (neat, cm^{-1}) 3132, 2960, 1620, 1583, 1482, 1275, 1157, 723 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 dd, , *J* = 2.40, 1.10 Hz, 1H), 7.74 (d, *J* = 9.00 Hz, 1H), 7.41 (d, *J* = 2.80 Hz, 1H), 7.09 (dd, *J* = 9.00, 2.80 Hz, 1H), 6.89 (dd, *J* = 4.00, 1.10 Hz, 1H), 6.81 (dd, *J* = 4.00, 2.40 Hz 1H), 3.91 (s, 3H), 2.95 (t, *J* = 7.30 Hz, 2H), 1.93 (sex, 2H), 1.08 (t, *J* = 7.30 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9 (C), 157.1 (C), 137.1 (C), 125.9 (C), 121.6 (C), 116.0 (CH), 114.5 (CH), 113.8 (CH), 113.1 (CH), 110.7 (CH), 106.0 (CH), 55.6 (CH_3), 37.8 (CH_2), 22.0 (CH_2), 14.2 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{15}H_{17}N_2O$ 241.1341, found 241.1340.

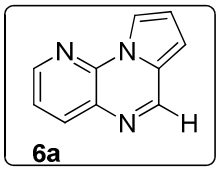
Synthesis of spirocyclic pyrrolo[1,2-*a*]quinoxaline **4a**



4a

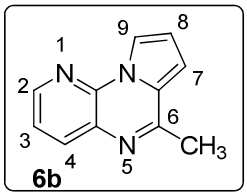
7'-Chloro-4,5-dihydro-3*H*,5'*H*-spiro[furan-2,4'-pyrrolo[1,2-*a*]quinoxaline] (**4a**)
To a solution of 1-(4-chloro-2-nitrophenyl)pyrrole **1a** (500 mg, 2.25 mmol, 1 equiv) in tetrahydrofuran (15 mL) was added ethanol (0.40 mL, 6.75 mmol, 3 equiv) and iron powder (1.13 g, 20.25 mmol, 9 equiv). Hydrochloric acid solution 12 M (2 mL, 24.75 mmol, 11 equiv) was added slowly via syringe at room temperature. The mixture was continued to stir for 48 hours and then was quenched with a solution of saturated aqueous $NaHCO_3$. The resulting mixture was then extracted with EtOAc (3 times). The combined organic layers were washed with brine, dried on $MgSO_4$, filtered and evaporated. Products were purified by column chromatography with petroleum ether/ethyl acetate (8/2) afforded **4a** (400 mg, 68 %) as a white solid. Mp = 122 °C ; IR (neat, cm^{-1}) 3189, 3112, 2860, 1579, 1485, 1425, 1050, 806, 737 ; ^{1}H NMR (400 MHz, $CDCl_3$+D_2O) δ 7.92 – 7.87 (m, 2H), 7.76 (d, *J* = 8.80 Hz, 1H), 7.44 (dd, *J* = 8.80, 2.30 Hz, 1H), 6.98 (dd, *J* = 4.00, 1.20 Hz, 1H), 6.88 (dd, *J* = 4.00, 2.7 Hz, 1H), 3.84 – 3.77 (m, 2H), 3.26 – 3.19 (m, 2H), 2.20 – 2.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1 (C), 136.2 (C), 130.4 (C), 128.6 (CH), 127.3 (CH), 125.8 (C), 125.8 (C), 115.0 (CH), 114.8 (CH), 114.2 (CH), 107.4 (CH), 62.5 (CH_2), 32.54 (CH_2), 29.44 (CH_2) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{14}H_{14}N_2OCl$ 261.0795, found 261.0798.

Synthesis of 6-substituted pyrido[3,2-*e*]pyrrolo[1,2-*a*]pyrazines **6a-f**



6a

Pyrido[3,2-*e*]pyrrolo[1,2-*a*]pyrazine (**6a**)[4]
Prepared following the same general procedure using nitro-3(pyrrolyl-1)-2 pyridine **5** (213 mg, 1.12 mmol), iron powder (565 mg, 10.12 mmol), hydrochloric acid solution 12 M (1 mL, 12.38 mmol) in methanol (8 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2) afforded **6a** (50 mg, 25 %) as a brown solid. Mp = 94 °C ; IR (neat, cm^{-1}) 3141, 1604, 1534, 1467 1340, 734 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.55 (dd, *J* = 4.50, 1.50 Hz, 1H), 8.39 (d, *J* = 1.60 Hz, 1H), 8.25 (dd, *J* = 8.00, 1.50 Hz, 1H), 7.45 (dd, *J* = 8.00, 4.50 Hz, 1H), 6.99 (dd, *J* = 3.90, 1.60 Hz, 1H), 6.93 (dd, *J* = 3.90, 2.70 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0 (CH), 146.6 (CH), 139.9 (C), 137.5 (CH), 130.8 (C), 128.0 (C), 121.5 (CH), 115.6 (CH), 114.5 (CH), 108.9 (CH) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{10}H_8N_3$ 170.0718, found 170.0717.

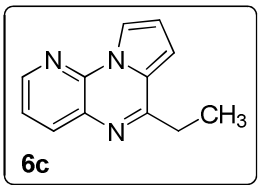


6b

6-Methylpyrido[3,2-*e*]pyrrolo[1,2-*a*]pyrazine (**6b**)

[4] Lancelot, J.-C.; Rault, S.; Laduree, D.; Robba, M. *Chem.Pharm. Bull.* **1985**, *33*, 2798–2802.

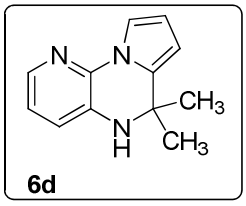
Prepared following the general procedure using nitro-3(pyrrolyl-1)-2 pyridine **5** (426 mg, 2.25 mmol), iron powder (1.13 g, 20.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in ethanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2) afforded **6b** (260 mg, 63 %) as a beige solid. Mp = 82 °C ; IR (neat, cm^{-1}) 3147, 3063, 1597, 1530, 1473, 1416, 803, 733 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (dd, *J* = 4.50, 1.50 Hz, 1H), 8.36 (dd, *J* = 2.70, 1.30 Hz, 1H), 8.17 (dd, *J* = 8.00, 1.50 Hz, 1H), 7.42 (dd, *J* = 8.00, 4.50 Hz, 1H), 6.96 (dd, *J* = 3.90, 1.30 Hz, 1H), 6.89 (dd, *J* = 3.90, 2.70 Hz, 1H), 2.74 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8 (C), 146.2 (CH), 139.5 (C), 136.5 (CH), 130.7 (C), 127.6 (C), 121.4 (CH), 115.5 (CH), 114.0 (CH), 108.0 (CH), 21.7 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{11}H_{10}N_3$ 184.0874, found 184.00876.



6c

6-Ethylpyrido[3,2-*e*]pyrrolo[1,2-*a*]pyrazine (**6c**)

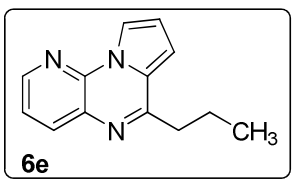
Prepared following the general procedure using nitro-3(pyrrolyl-1)-2 pyridine **5** (426 mg, 2.25 mmol), iron powder (1.13 g, 20.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in *n*-propanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2) afforded **6c** (220 mg, 50 %) as a yellow solid. Mp = 62 °C ; IR (neat, cm^{-1}) 3107, 2981, 1596, 1527, 1460, 1421, 740 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (dd, *J* = 4.50, 1.50 Hz, 1H), 8.36 (dd, *J* = 2.70, 1.10 Hz, 1H), 8.20 (dd, *J* = 8.00, 1.50 Hz, 1H), 7.44 – 7.38 (m, 1H), 7.00 – 6.94 (dd, , *J* = 4.00, 1.10 Hz 1H), 6.90 – 6.84 (m, 1H), 3.06 (q, *J* = 7.60 Hz, 2H), 1.46 (t, *J* = 7.60 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5 (C), 146.1 (CH), 139.6 (C), 136.7 (CH), 130.9 (C), 127.1 (C), 121.4 (CH), 115.4 (CH), 113.9 (CH), 107.6 (CH), 28.7 (CH_2), 12.4 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{12}H_{12}N_3$ 198.1031, found 198.1030.



6d

Dihydro-5,6-dimethyl-6,6-pyrido[3,2-*e*]pyrrolo[1,2-*a*]pyrazine (**6d**)[4]

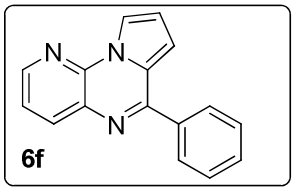
Prepared following the general procedure using nitro-3(pyrrolyl-1)-2 pyridine **5** (213 mg, 1.12 mmol), iron powder (565 mg, 10.12 mmol), hydrochloric acid solution 12 M (1 mL, 12.38 mmol) in isopropanol (8 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2) afforded **6d** (30 mg, 12 %) as a white solid. Mp = 94 °C ; IR (neat, cm^{-1}) 3313, 2967, 1589, 1479, 1458, 1279, 791, 720 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 4.50 Hz, 1H), 7.61 – 7.55 (m, 1H), 6.97 – 6.92 (m, 1H), 6.91 – 6.85 (m, 1H), 6.30 (m, 1H), 6.02 (dd, *J* = 3.90, 1.5O Hz, 1H), 3.72 (s, 1H), 1.53 (s, 6H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0 (C), 137.4 (CH), 134.3 (C), 130.6 (C), 121.3 (CH), 120.3 (CH), 114.7 (CH), 110.3 (CH), 103.2 (CH), 51.4 (C), 29.9 (2XCH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{12}H_{14}N_3$ 200.1188, found 200.1190.



6e

6-Propylpyrido[3,2-*e*]pyrrolo[1,2-*a*]pyrazine (**6e**)

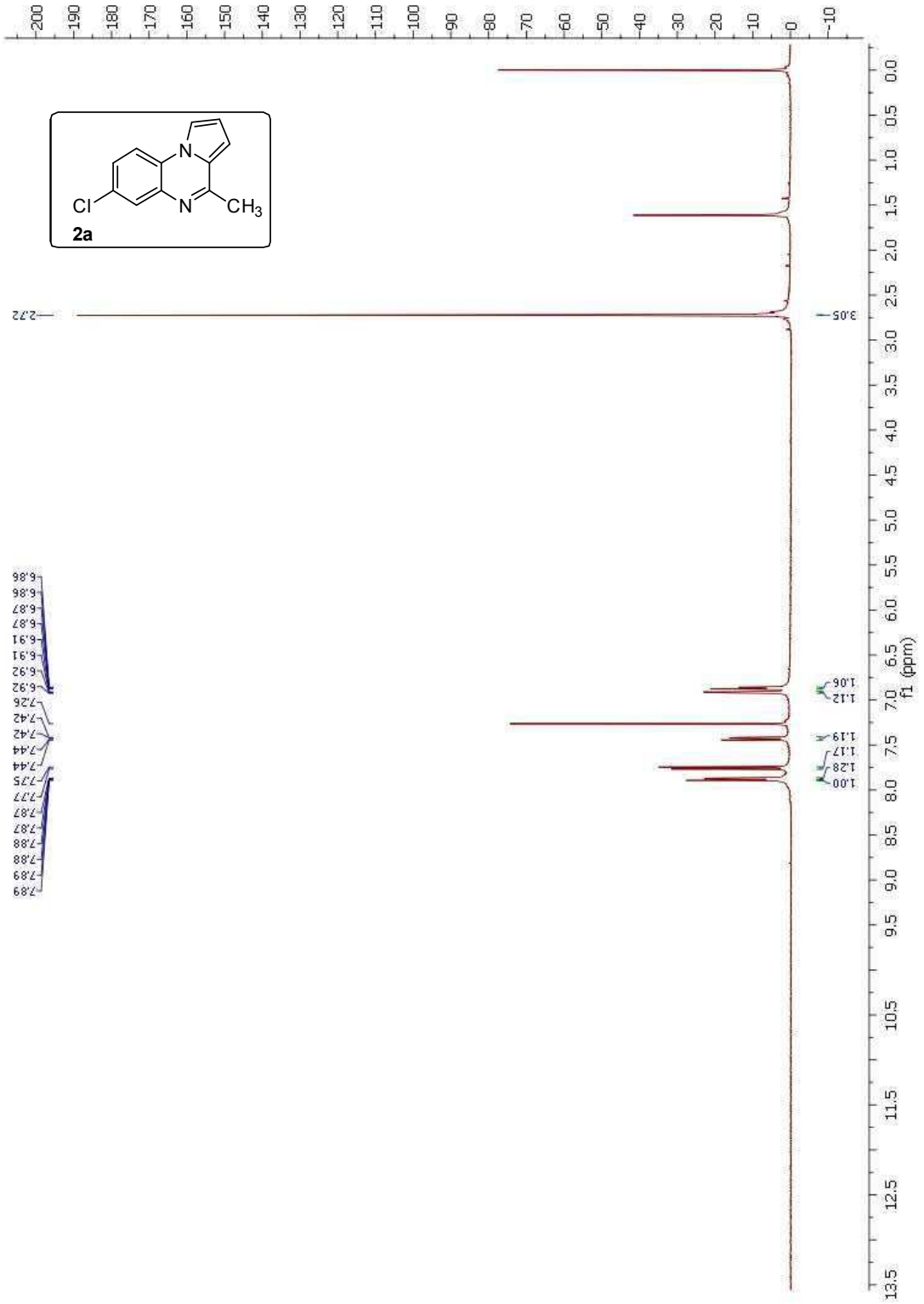
Prepared following the general procedure using nitro-3(pyrrolyl-1)-2 pyridine **5** (426 mg, 2.25 mmol), iron powder (1.13 g, 20.25 mmol), hydrochloric acid solution 12 M (2 mL, 24.75 mmol) in *n*-butanol (15 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 9/1) afforded **6e** (155 mg, 33 %) as a yellow solid. Mp = <50 °C ; IR (neat, cm^{-1}) 3144, 2954, 1595, 1528, 1471, 1423, 738 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (dd, *J* = 4.50, 1.50 Hz, 1H), 8.37 (dd, *J* = 2.70, 1.30 Hz, 1H), 8.19 (dd, *J* = 8.00, 1.50 Hz, 1H), 7.41 (dd, *J* = 8.00, 4.50 Hz, 1H), 6.98 (dd, *J* = 3.90, 1.30 Hz, 1H), 6.88 (dd, *J* = 3.90, 2.70 Hz, 1H), 3.04 – 2.96 (m, 2H), 1.99 – 1.87 (m, 2H), 1.08 (t, *J* = 7.40 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6 (C), 146.1 (CH), 139.5 (C), 136.6 (CH), 130.9 (C), 127.5 (C), 121.4 (CH), 115.4 (CH), 113.9 (CH), 107.8 (CH), 37.5 (CH_2), 21.8 (CH_2), 14.1 (CH_3) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{13}H_{14}N_3$ 212.1188, found 212.1189.

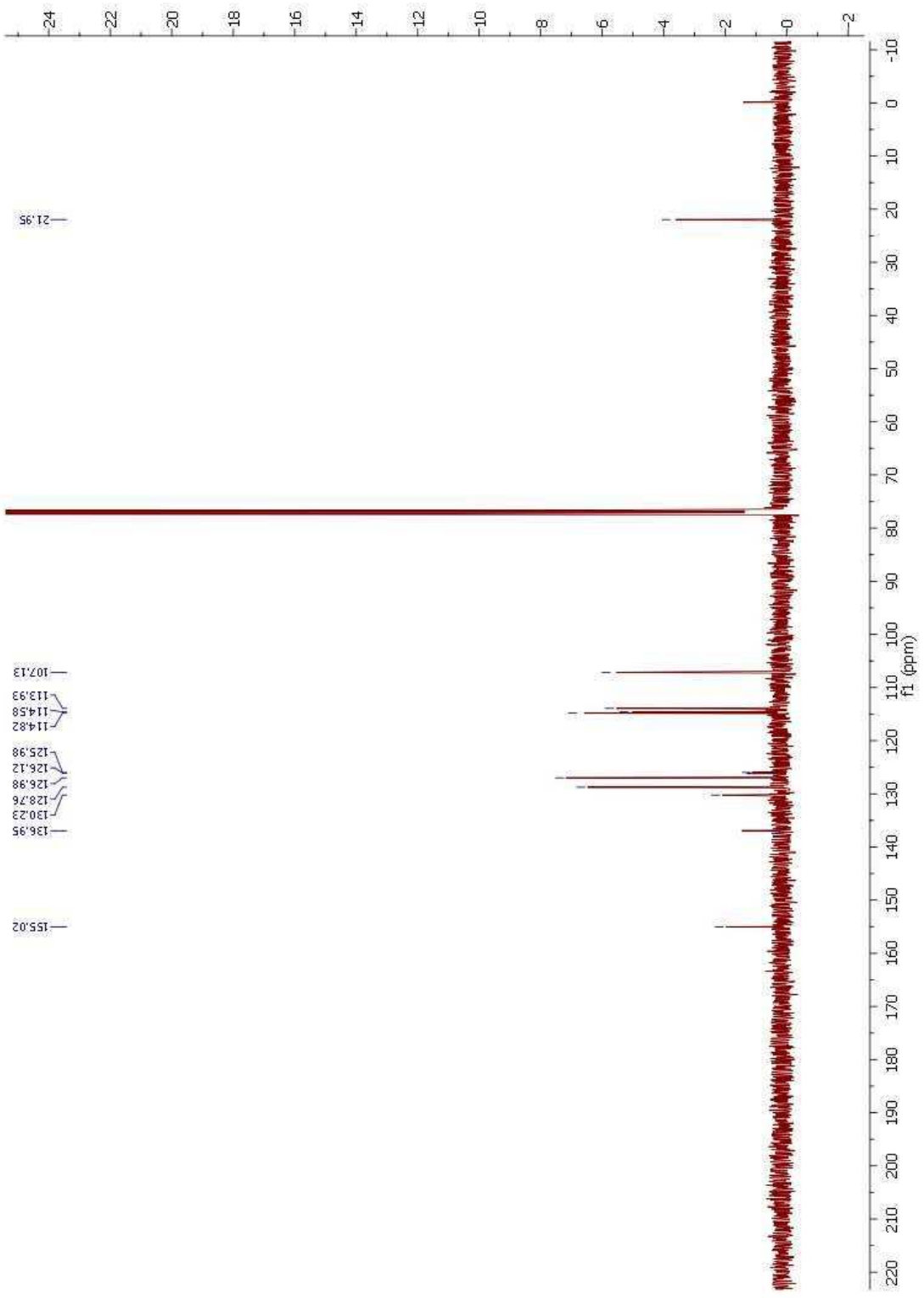


6-Phenylpyrido[3,2-*e*]pyrrolo[1,2-*a*]pyrazine (**6f**)

Prepared following the general procedure using nitro-3(pyrrolyl-1)-2 pyridine **5** (213 mg, 1.12 mmol), iron powder (565 mg, 10.12 mmol), hydrochloric acid solution 12 M (1 mL, 12.38 mmol) in benzyl alcohol (8 mL) for 48 hours. Column chromatography (petroleum ether/ethyl acetate: 8/2) afforded **6f** (150 mg, 54 %) as a white solid. Mp = 150 °C ; IR (neat, cm^{-1}) 3147, 3063, 1597, 1530, 1465, 1416, 733 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (dd, *J* = 4.50, 1.50 Hz, 1H), 8.48 (dd, *J* = 2.70, 1.30 Hz, 1H), 8.32 (dd, *J* = 8.00, 1.50 Hz, 1H), 8.05 – 7.98 (m, 2H), 7.60 – 7.52 (m, 3H), 7.46 (dd, *J* = 8.00, 4.50 Hz, 1H), 7.07 (dd, *J* = 4.00, 1.30 Hz, 1H), 6.94 (dd, *J* = 4.00, 2.70 Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2 (C), 146.6 (CH), 137.9 (C), 137.3 (CH), 131.0 (C), 130.1 (CH), 128.6 (CH), 128.5 (CH), 127.0 (C), 126.8 (C), 121.6 (CH), 115.9 (CH), 114.4 (CH), 110.2 (CH) ; HRMS (ESI) m/z [M+H]+ calcd for $C_{16}H_{12}N_3$ 246.1031, found 246.1032.

NMR spectra

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114.58
114.82
125.98
126.12
126.98
128.76
130.23
136.95
155.02
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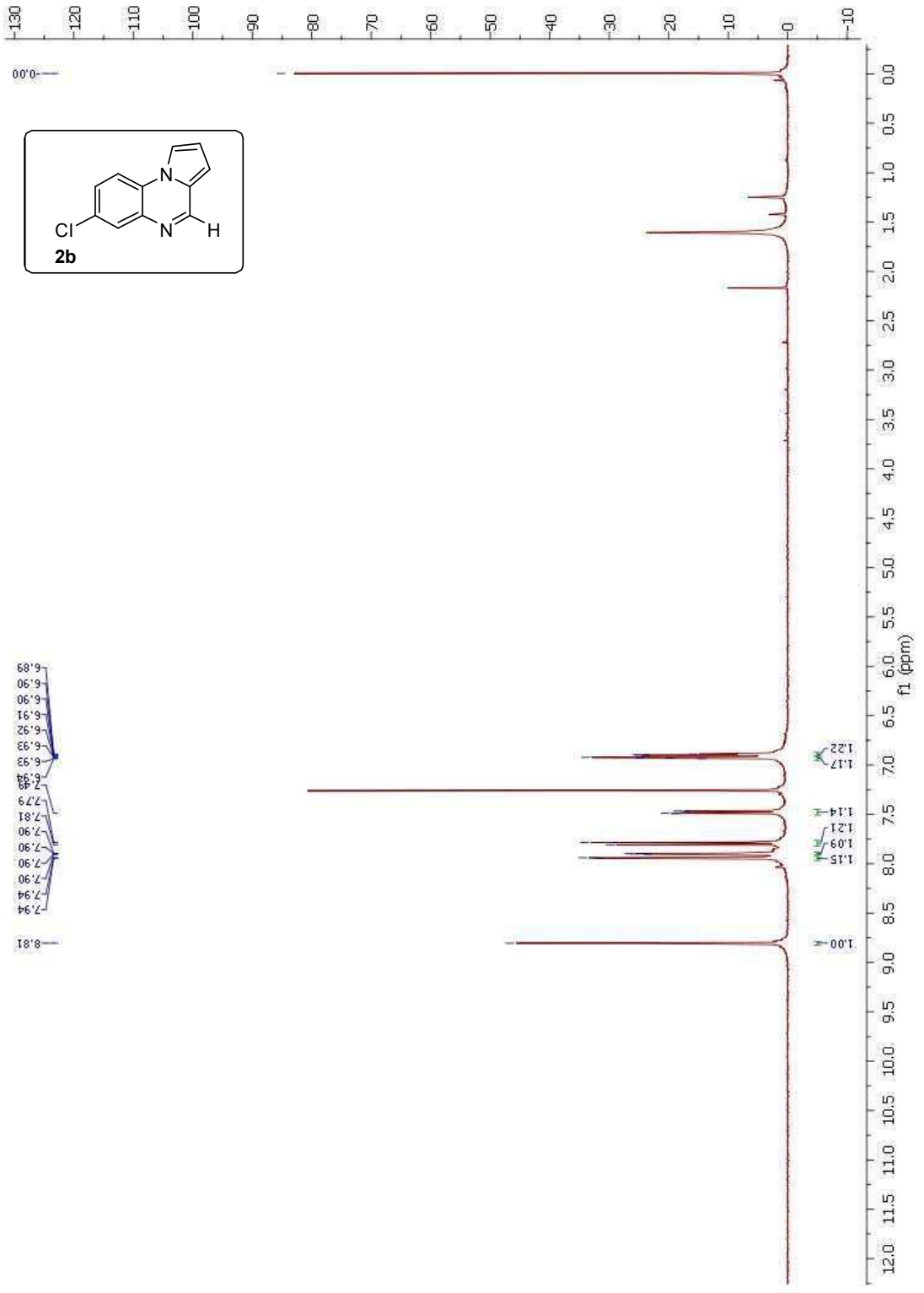
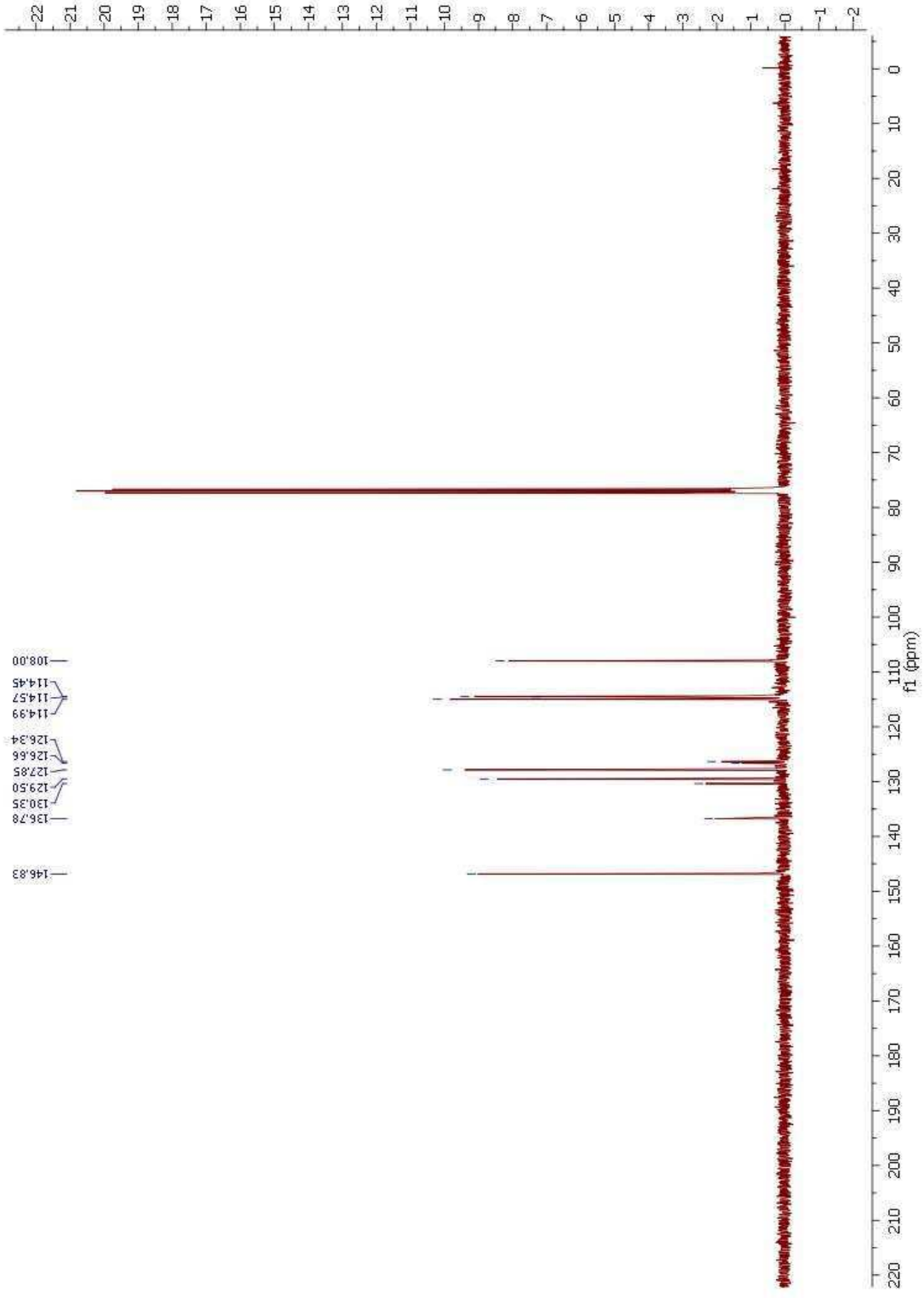

Cl
N
N
H
2b
f1 (ppm)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114.99
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126.66
127.85
129.50
130.35
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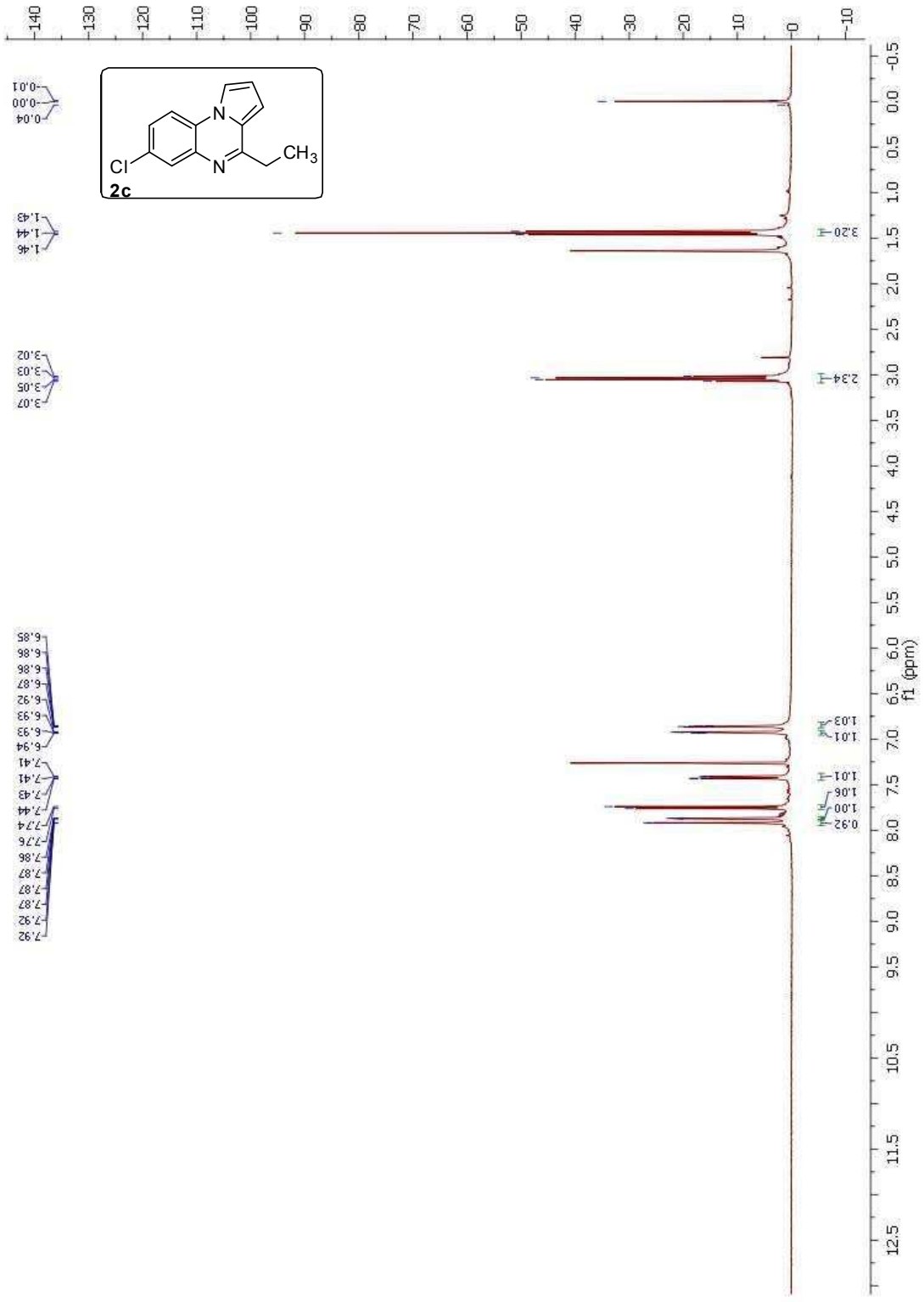
f1 (ppm)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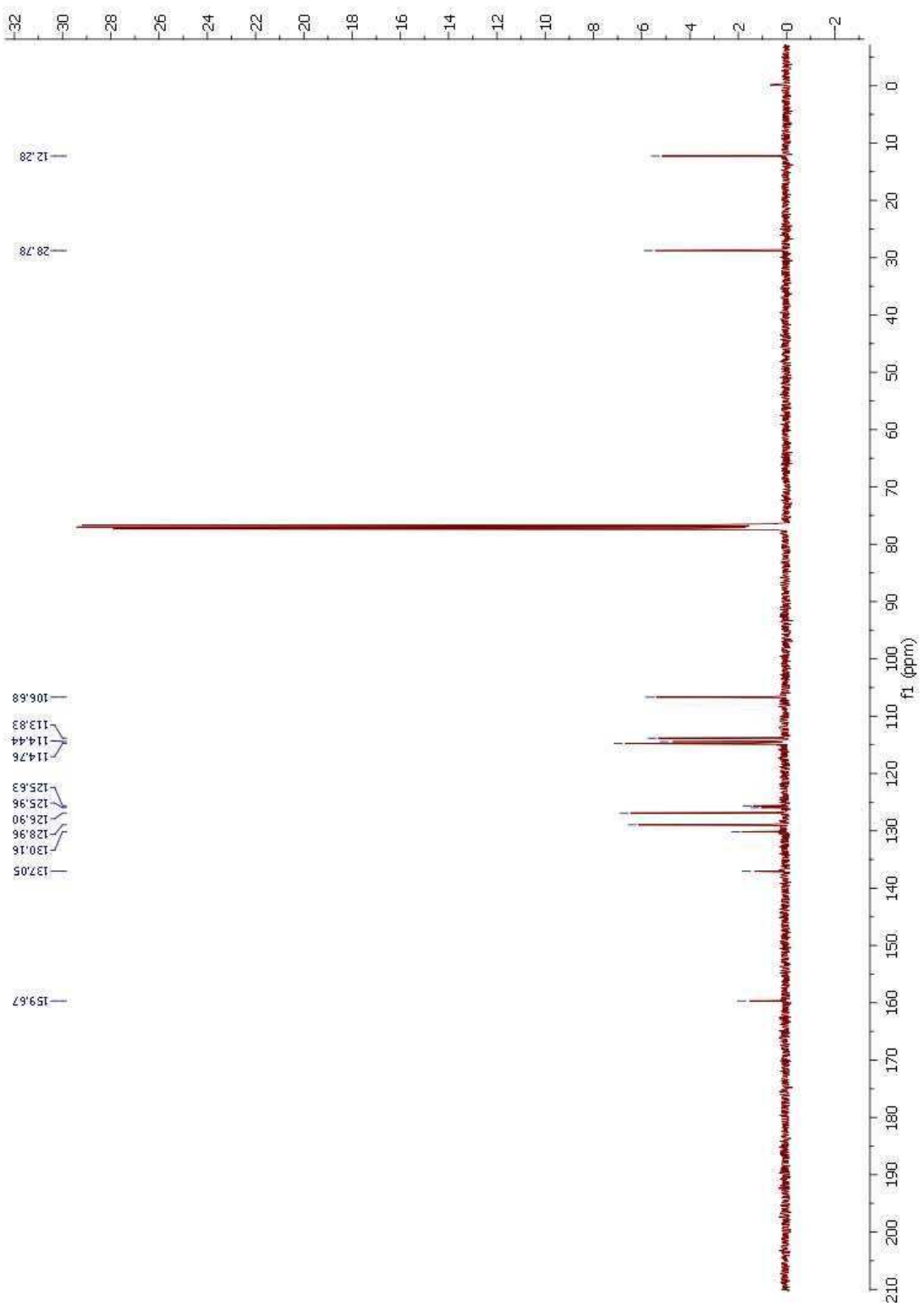
N
CH3
2c
f1 (ppm)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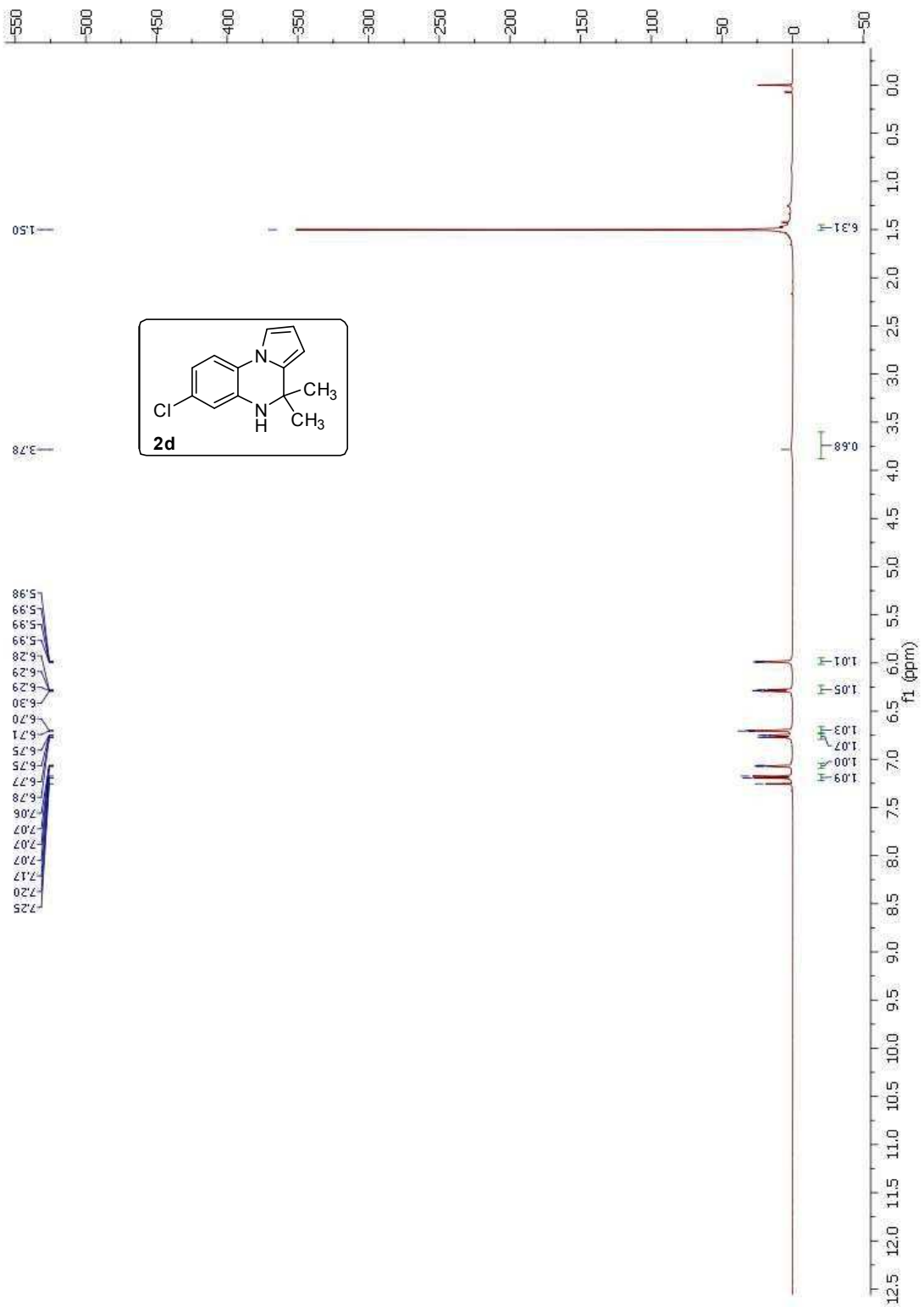
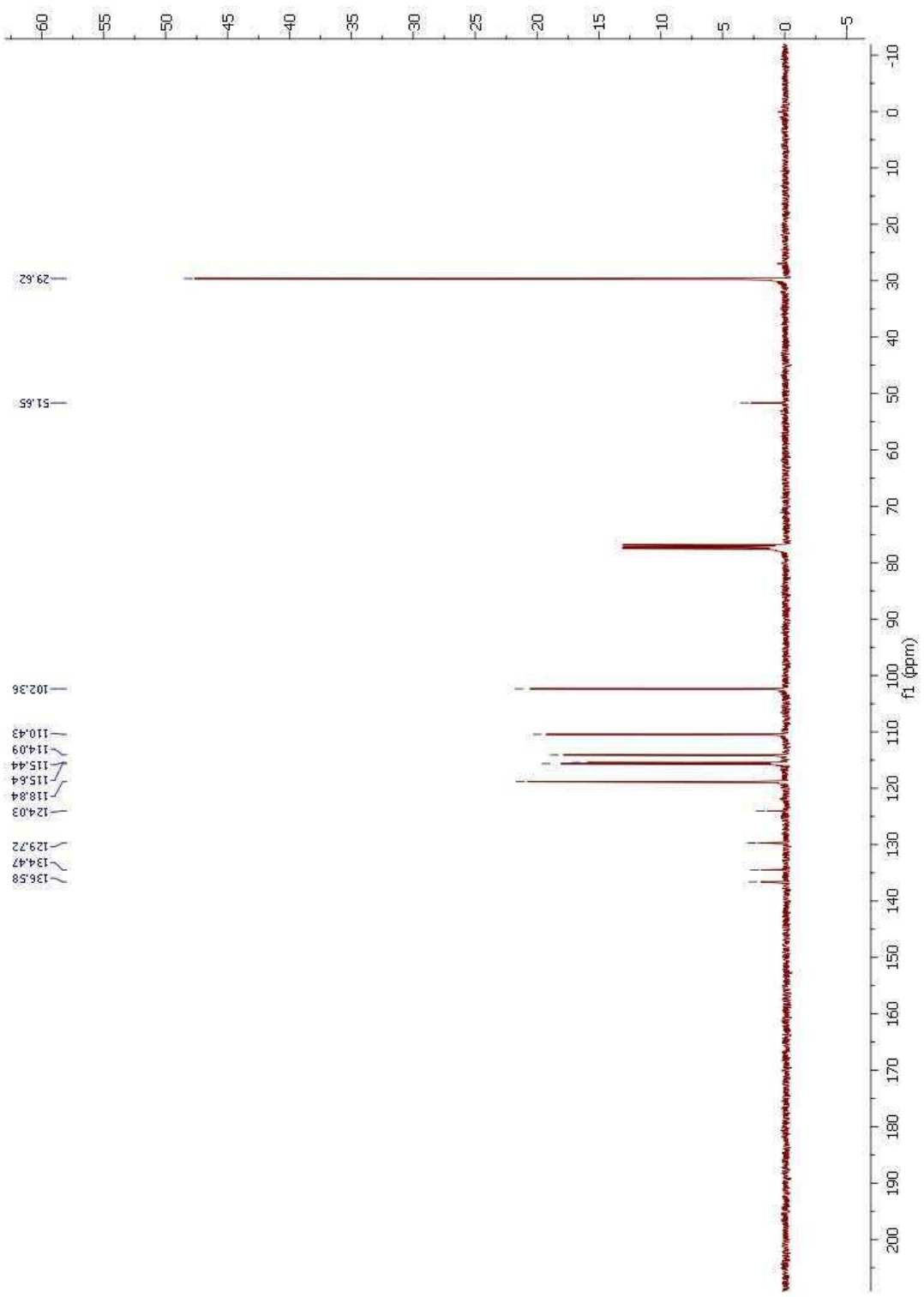
12.28
f1 (ppm)


Cl
N
H
CH3
CH3
2d
f1 (ppm)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129.72
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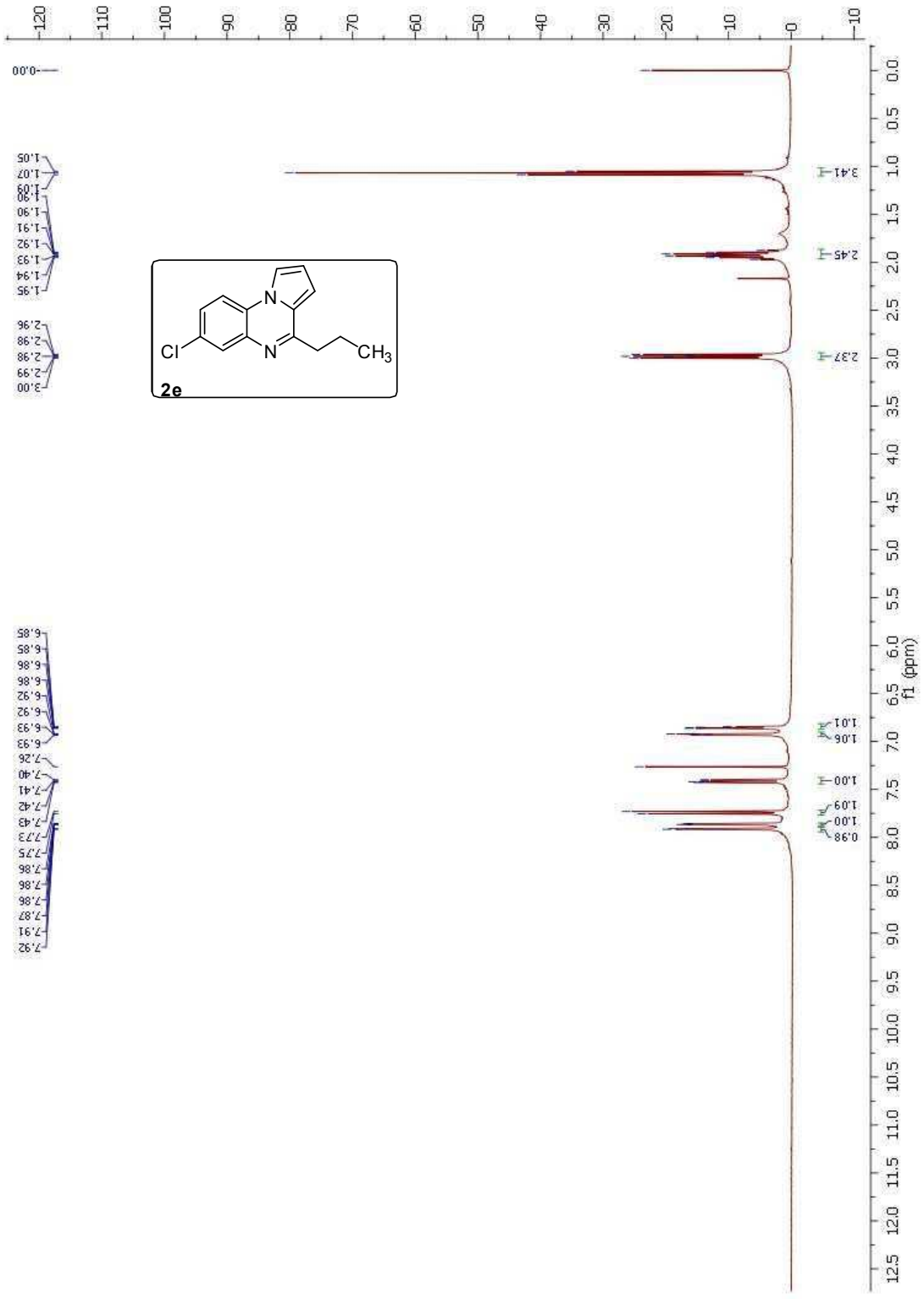
136.58
f1 (ppm)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N
N
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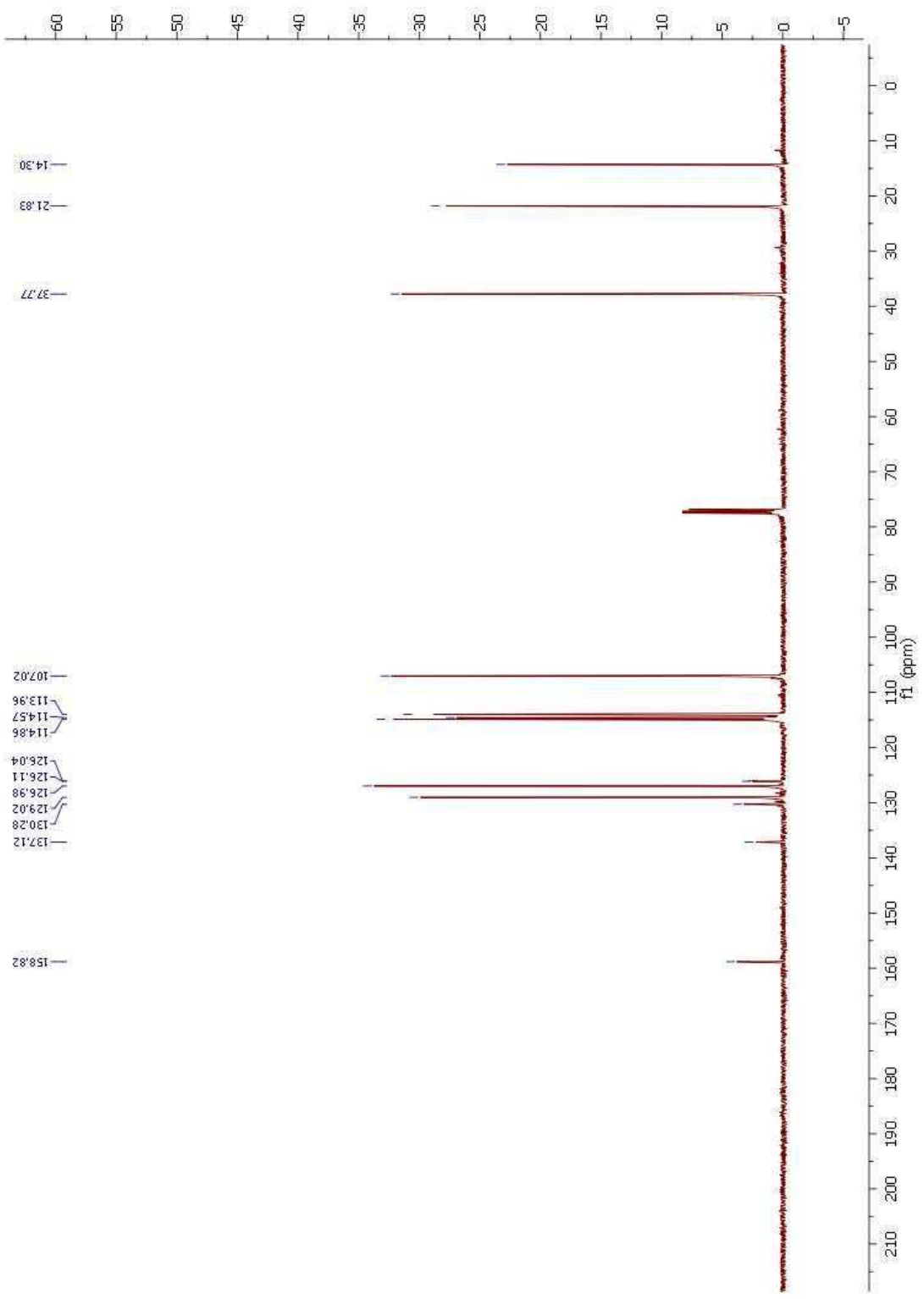
f1 (ppm)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113.96
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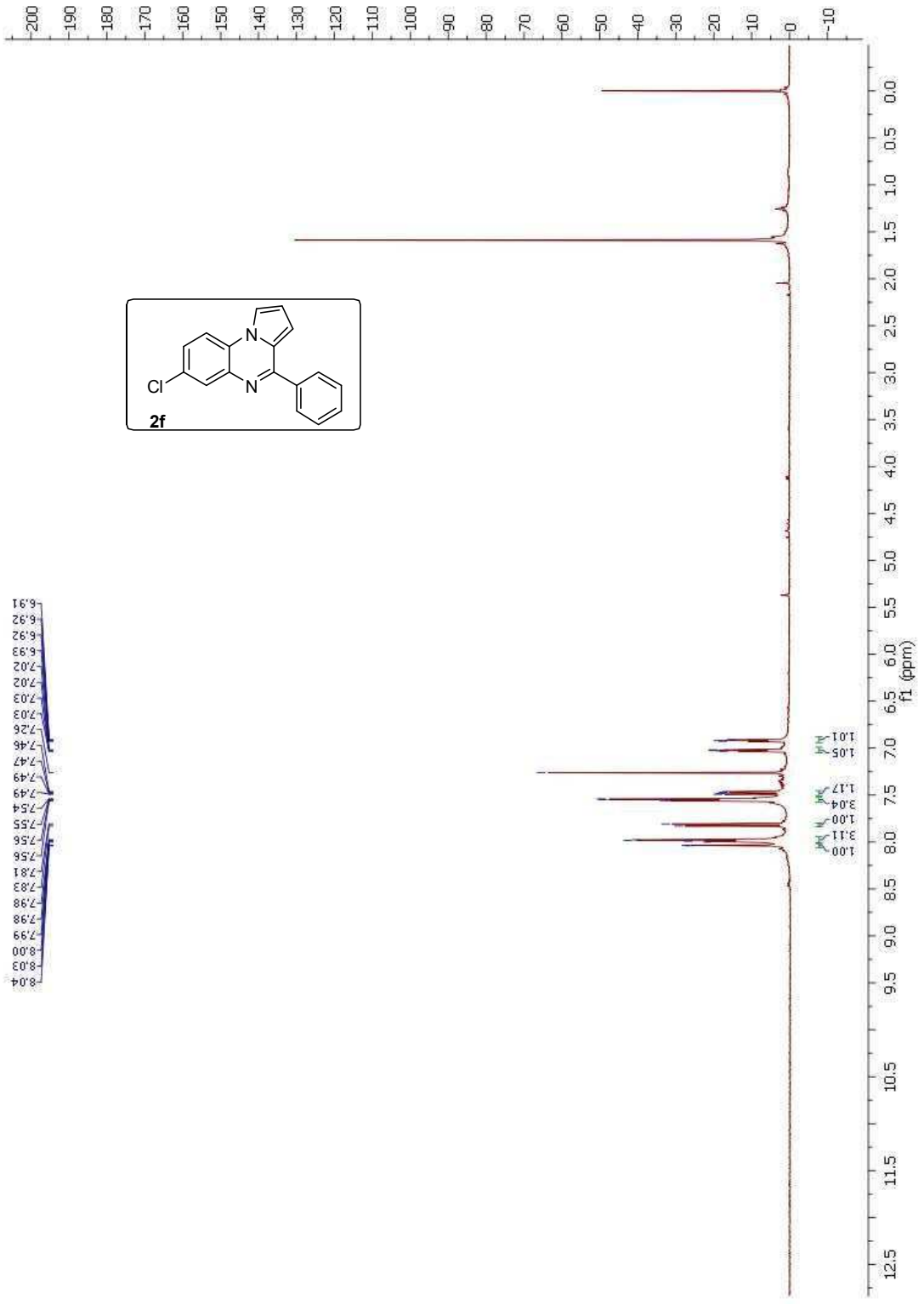
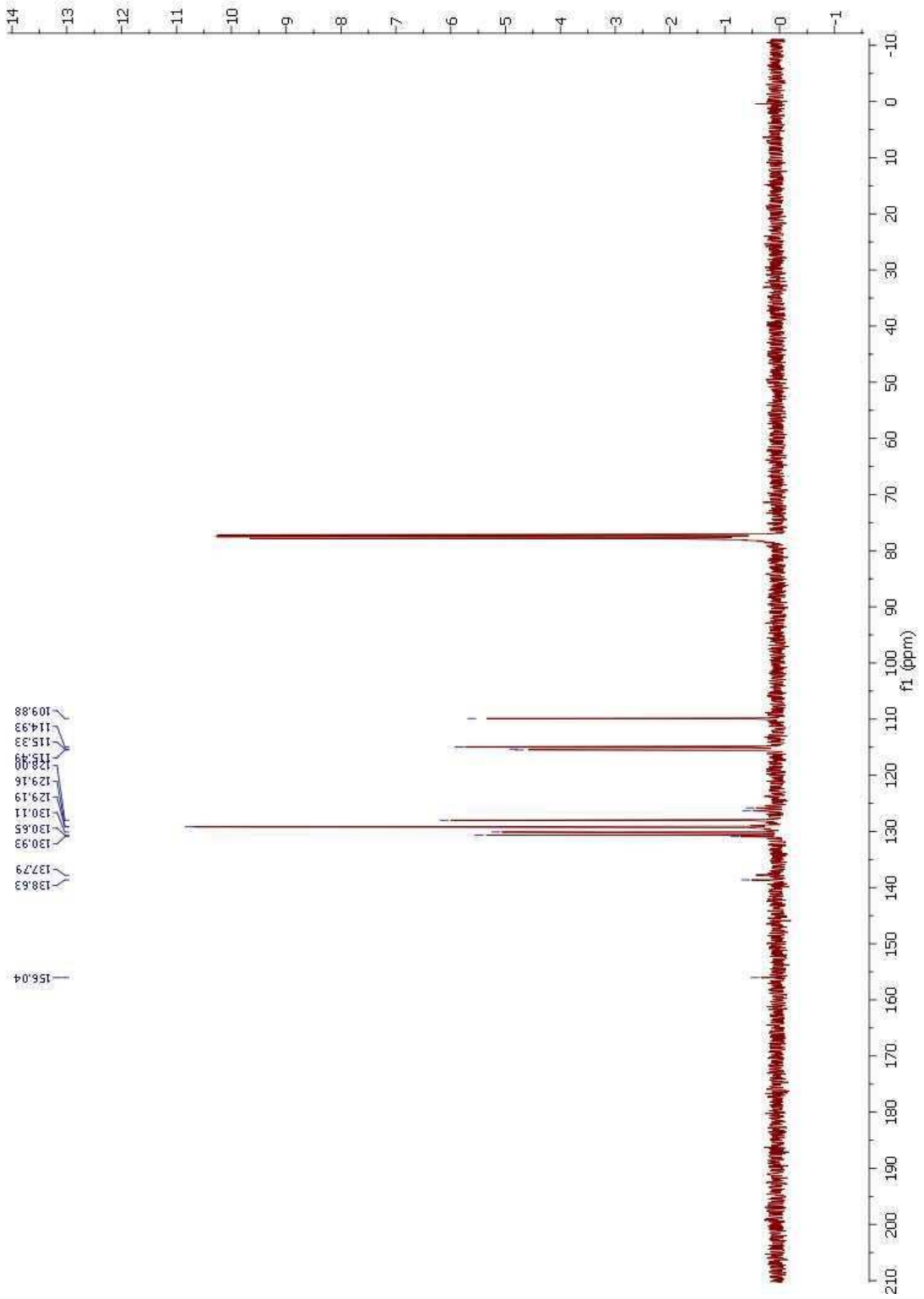
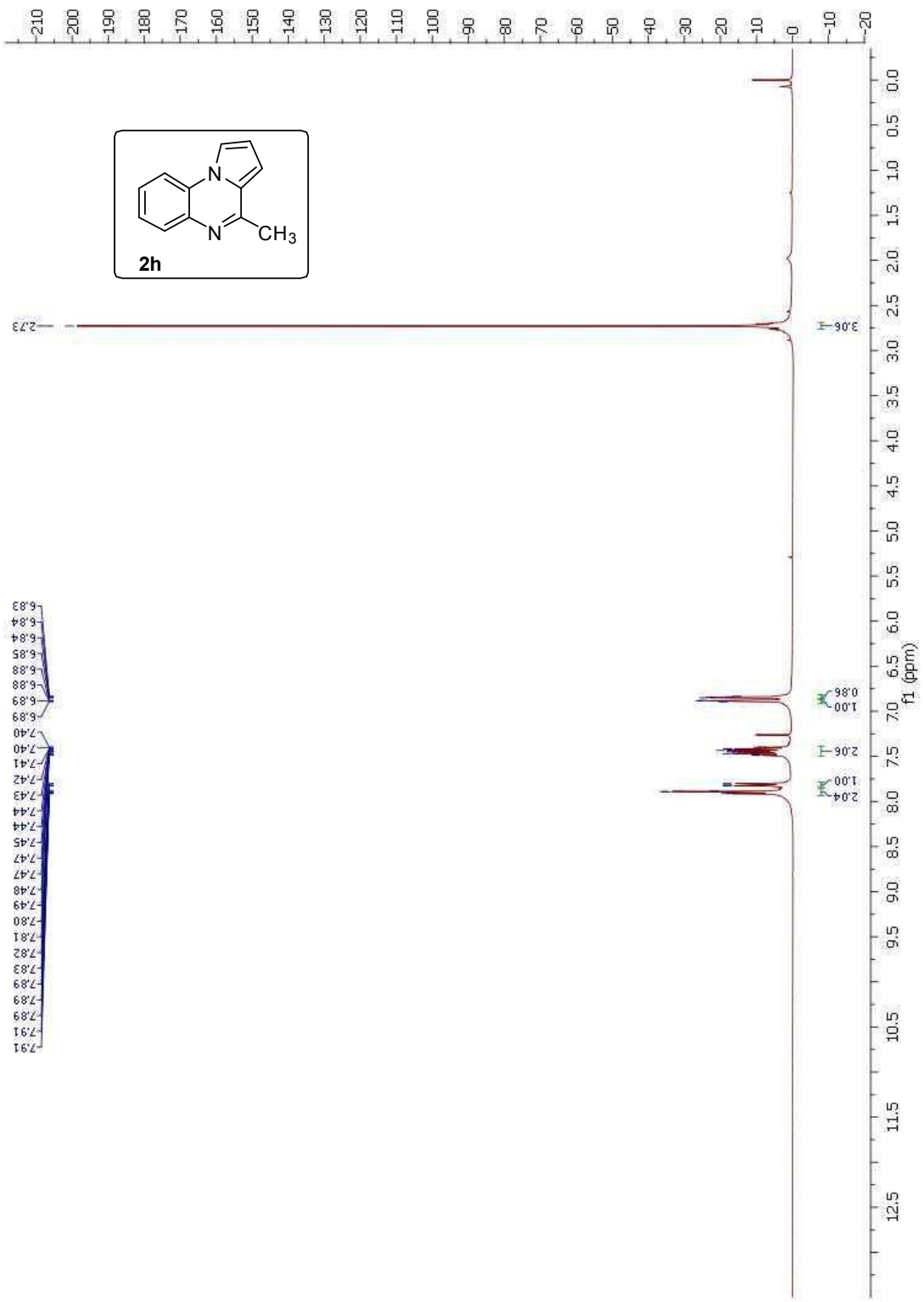
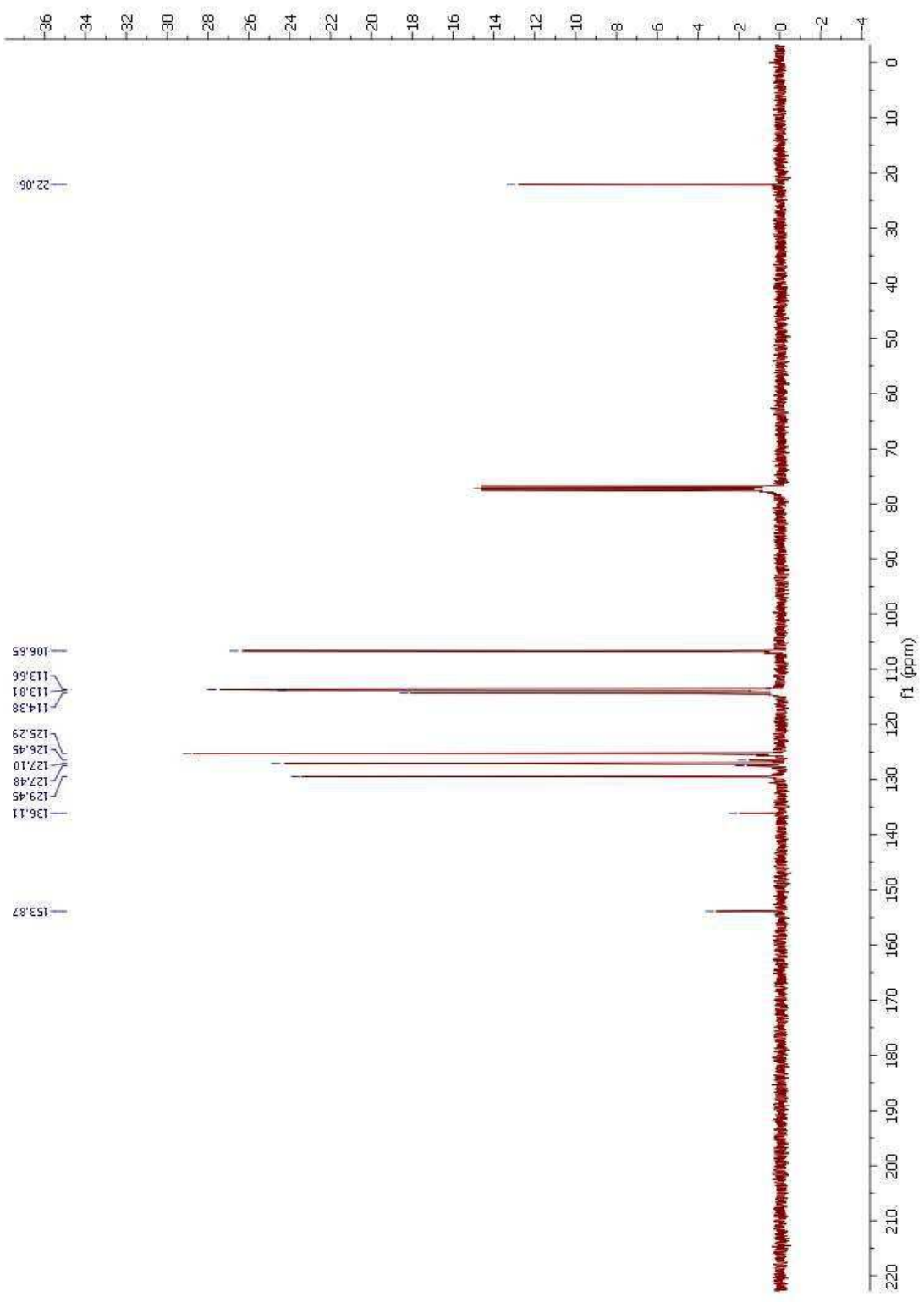
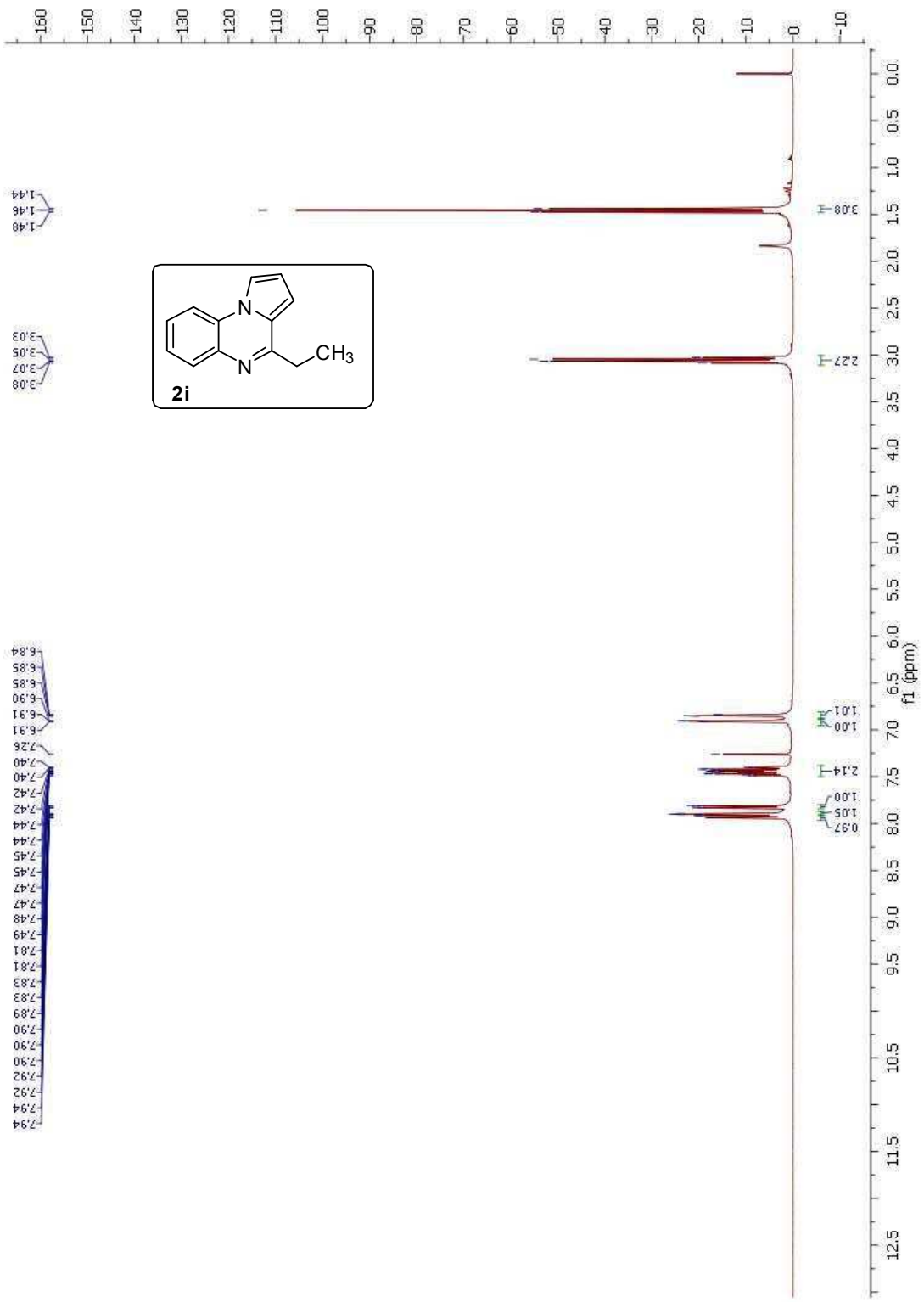
126.04
126.11
126.98
129.02
130.28
137.12
158.82
f1 (ppm)

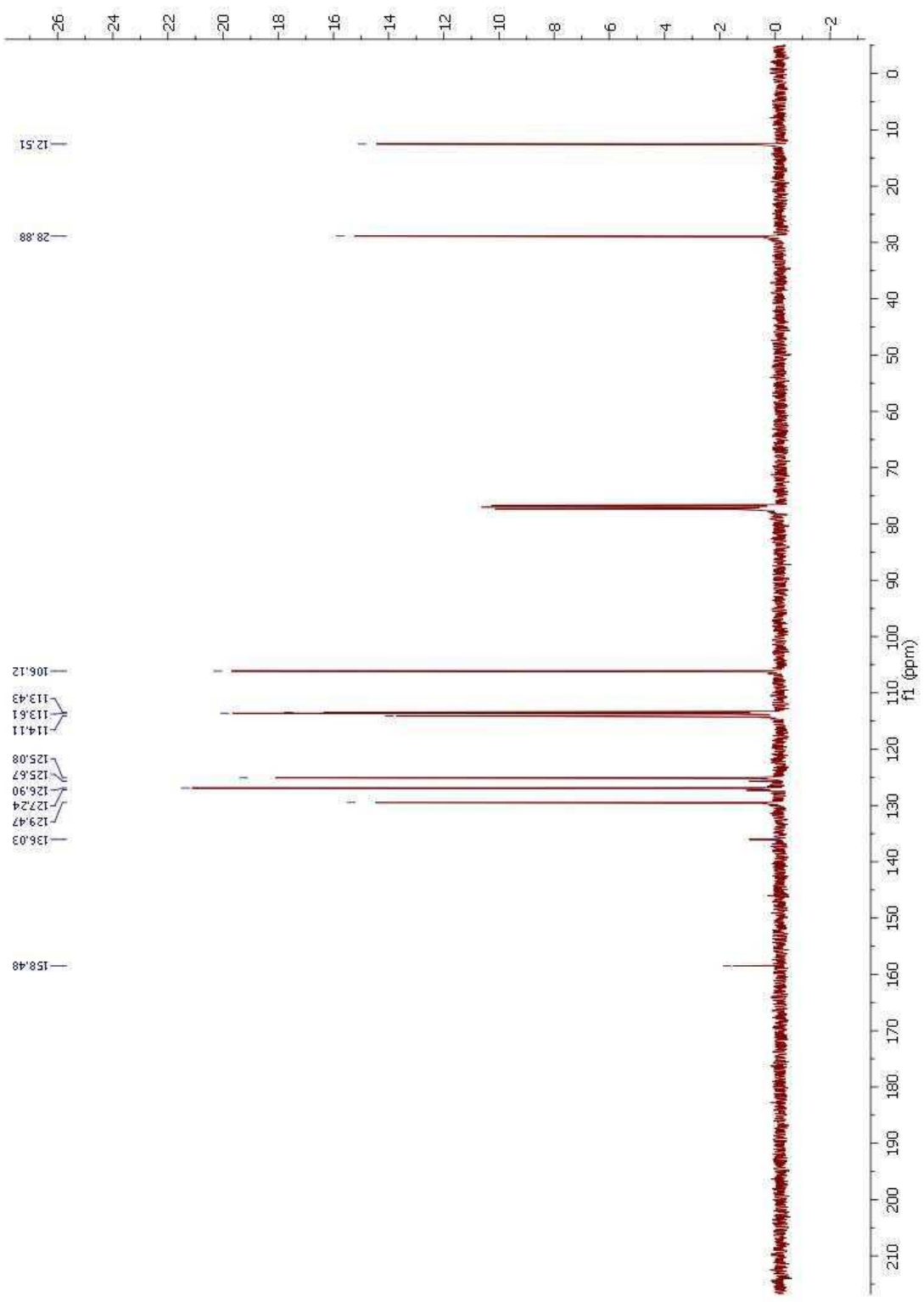

Cl
N
N
2f
f1 (ppm)

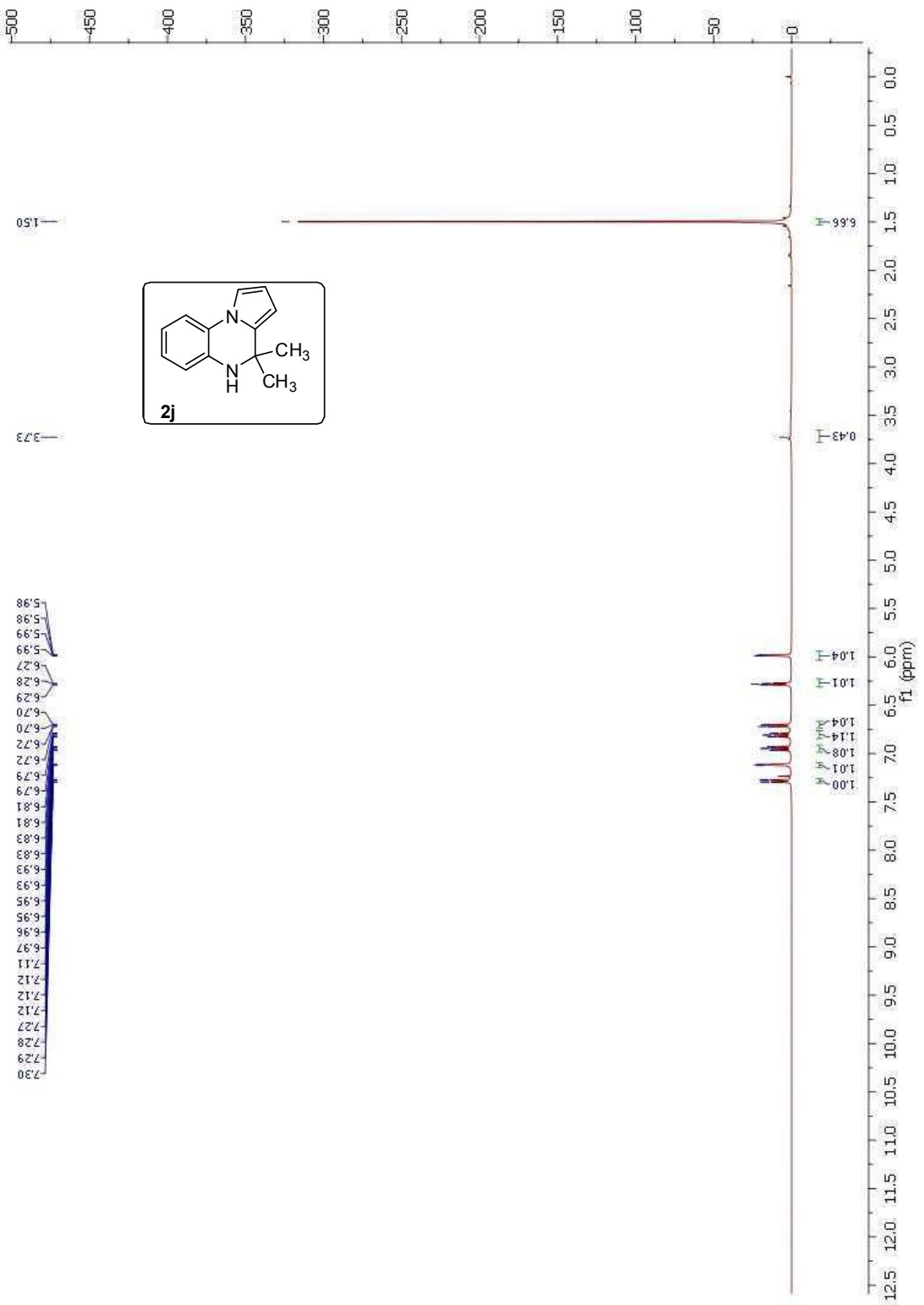

156.04
138.63
137.79
130.93
130.65
130.11
129.19
129.16
128.00
115.49
115.33
114.93
109.88
f1 (ppm)

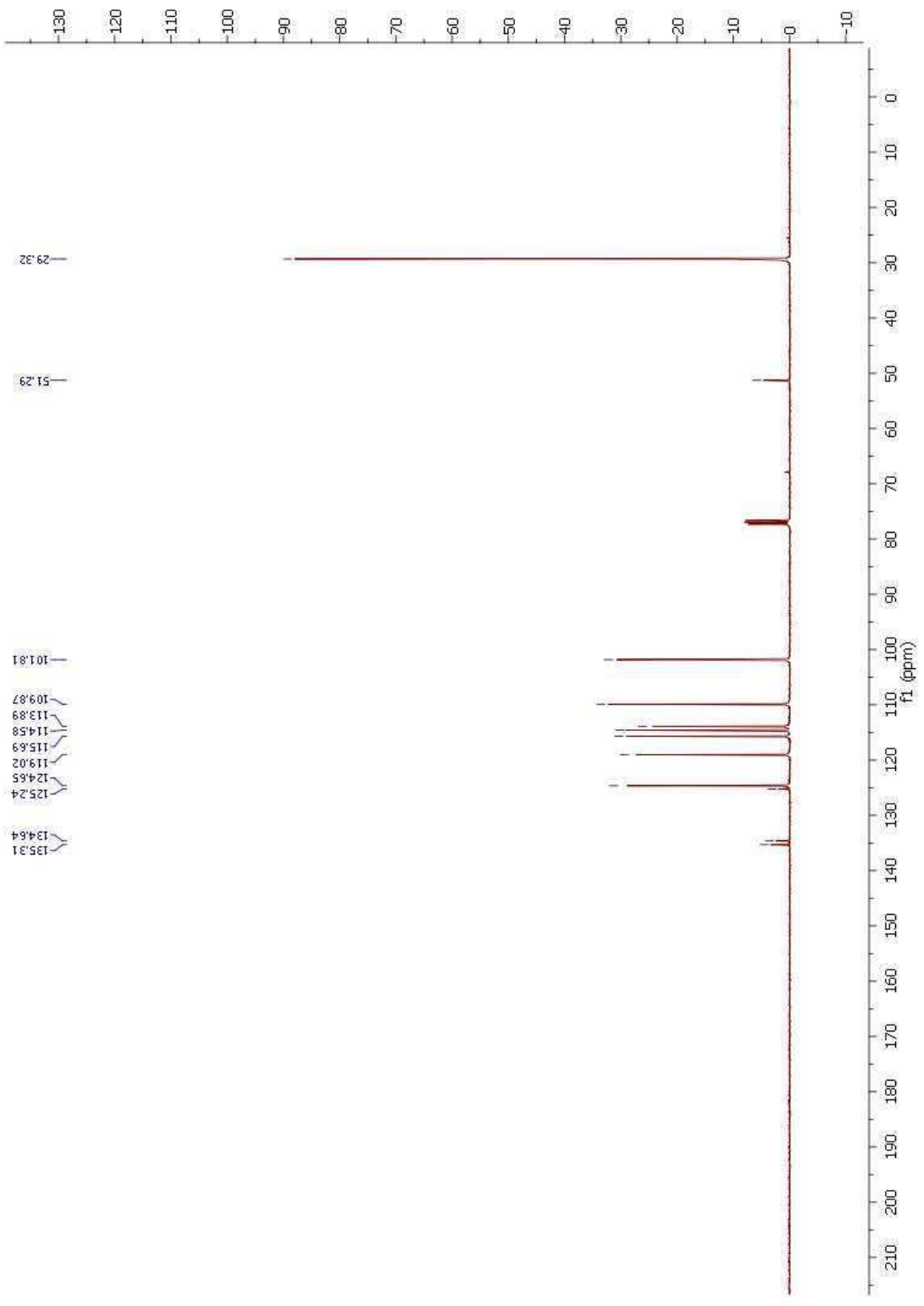

N
N
CH3
2h
f1 (ppm)

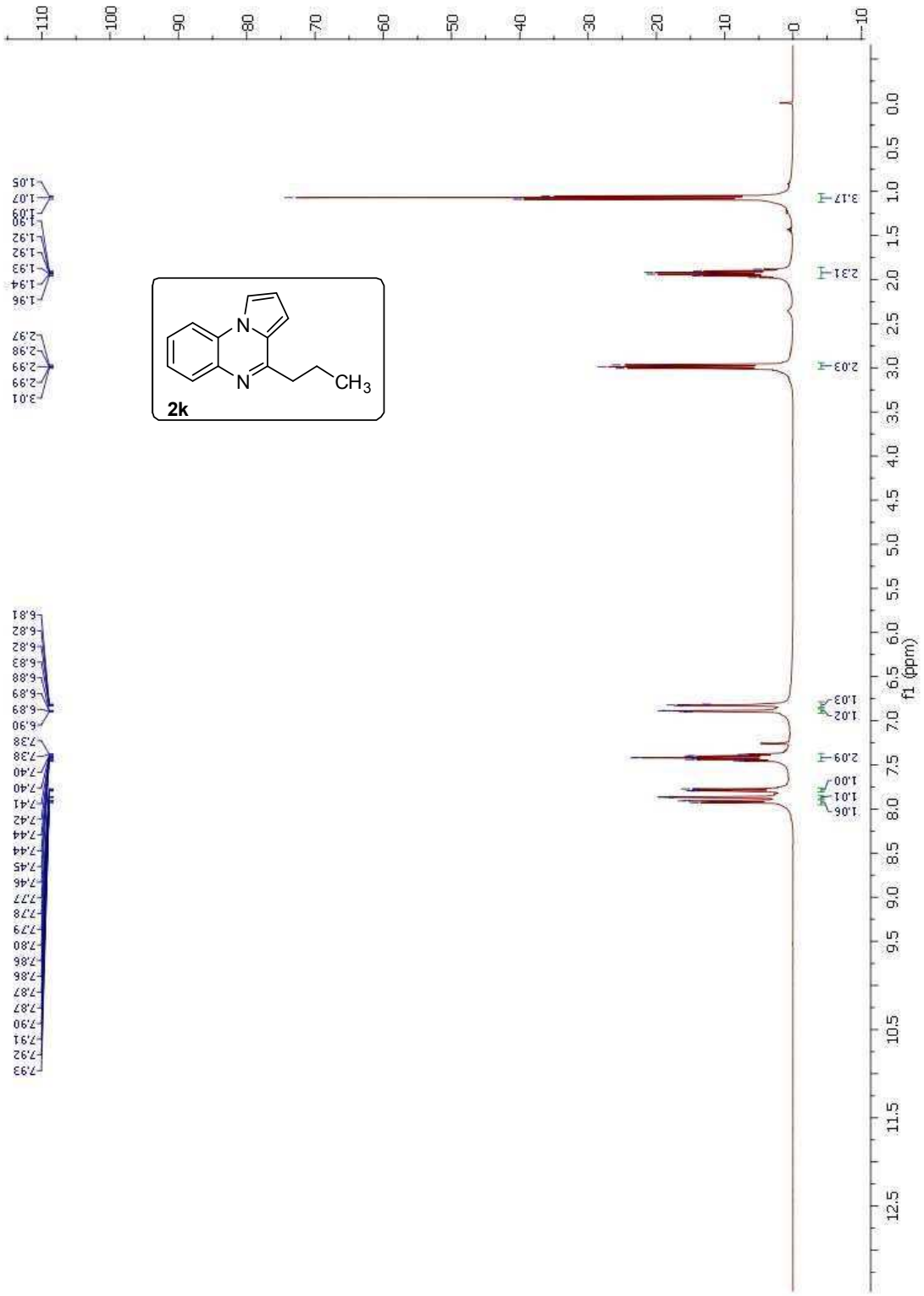

22.06
106.65
113.66
113.81
114.38
125.29
126.45
127.10
127.48
129.45
136.11
153.87
f1 (ppm)

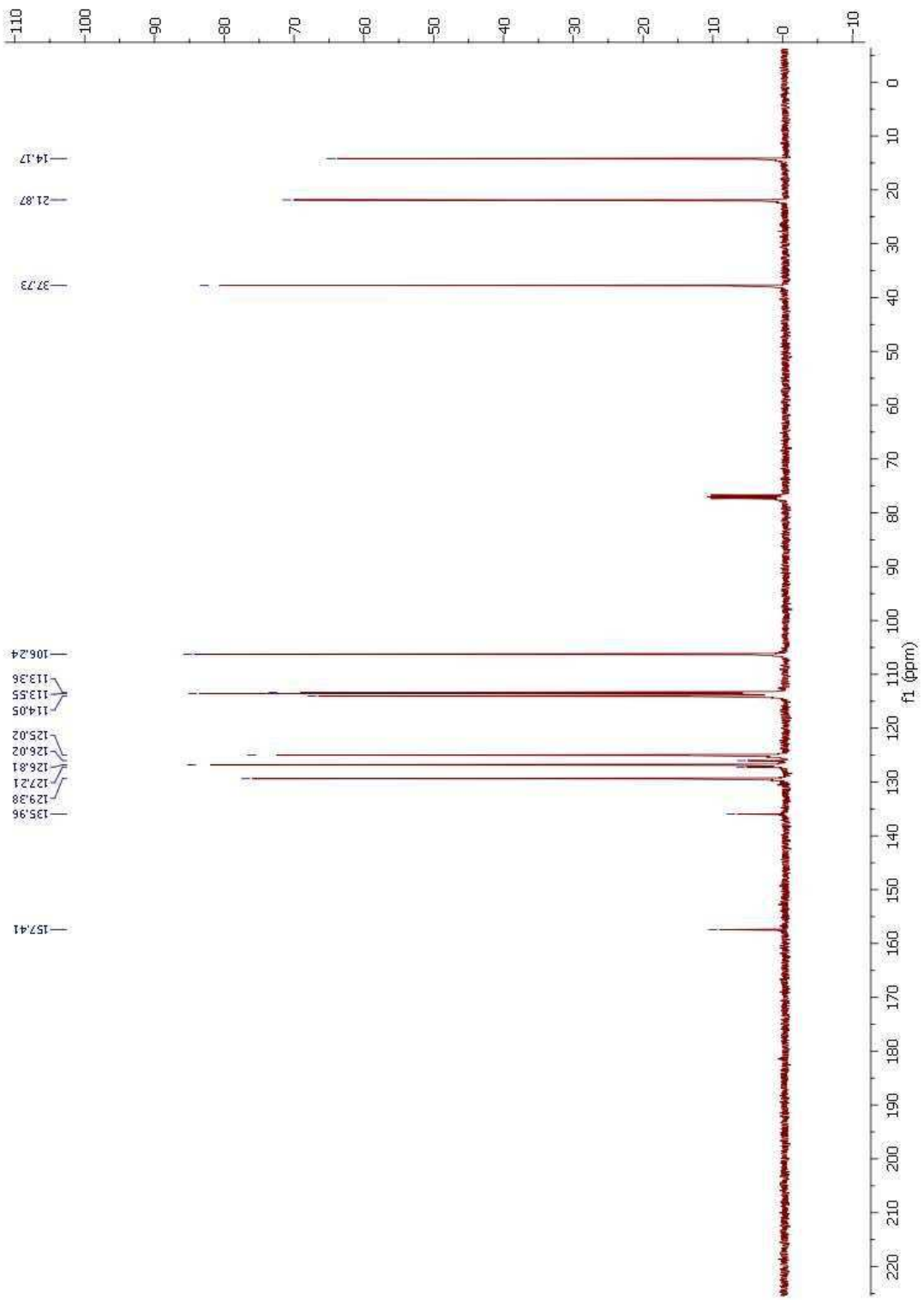

2i
f1 (ppm)

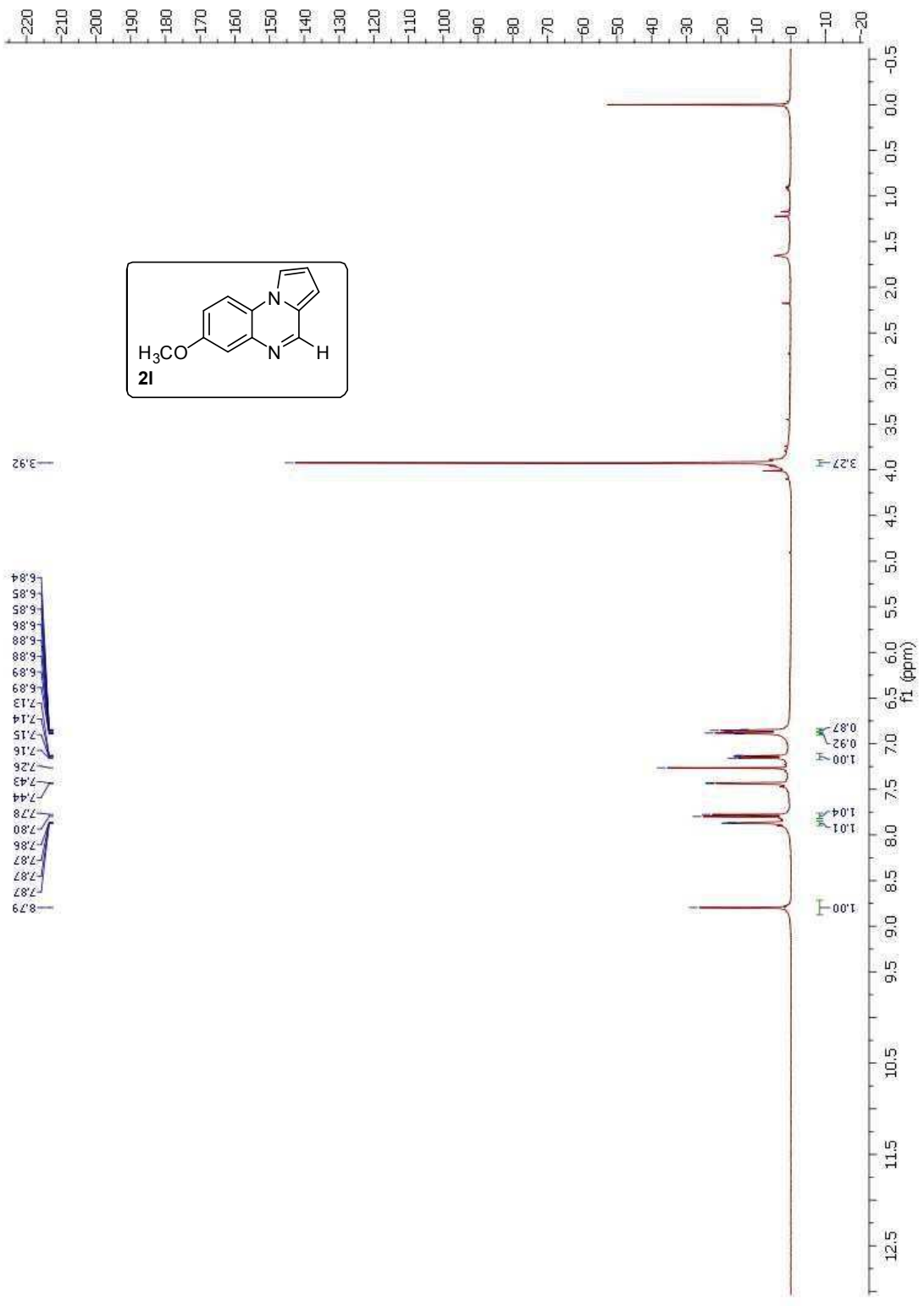

12.51
28.88
106.12
113.43
113.61
114.11
125.08
125.67
126.90
127.24
129.47
136.03
158.48
f1 (ppm)

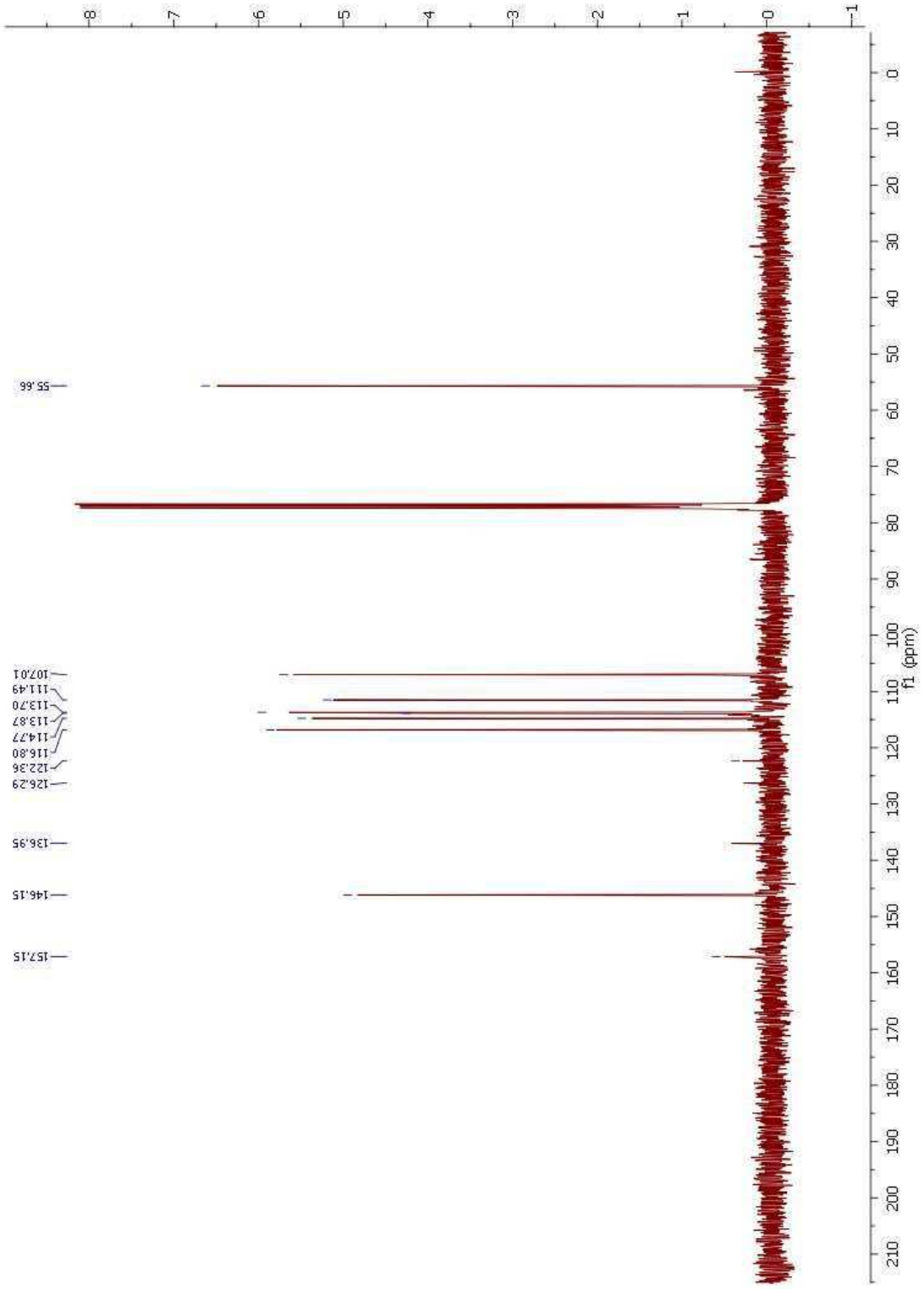

2j
f1 (ppm)

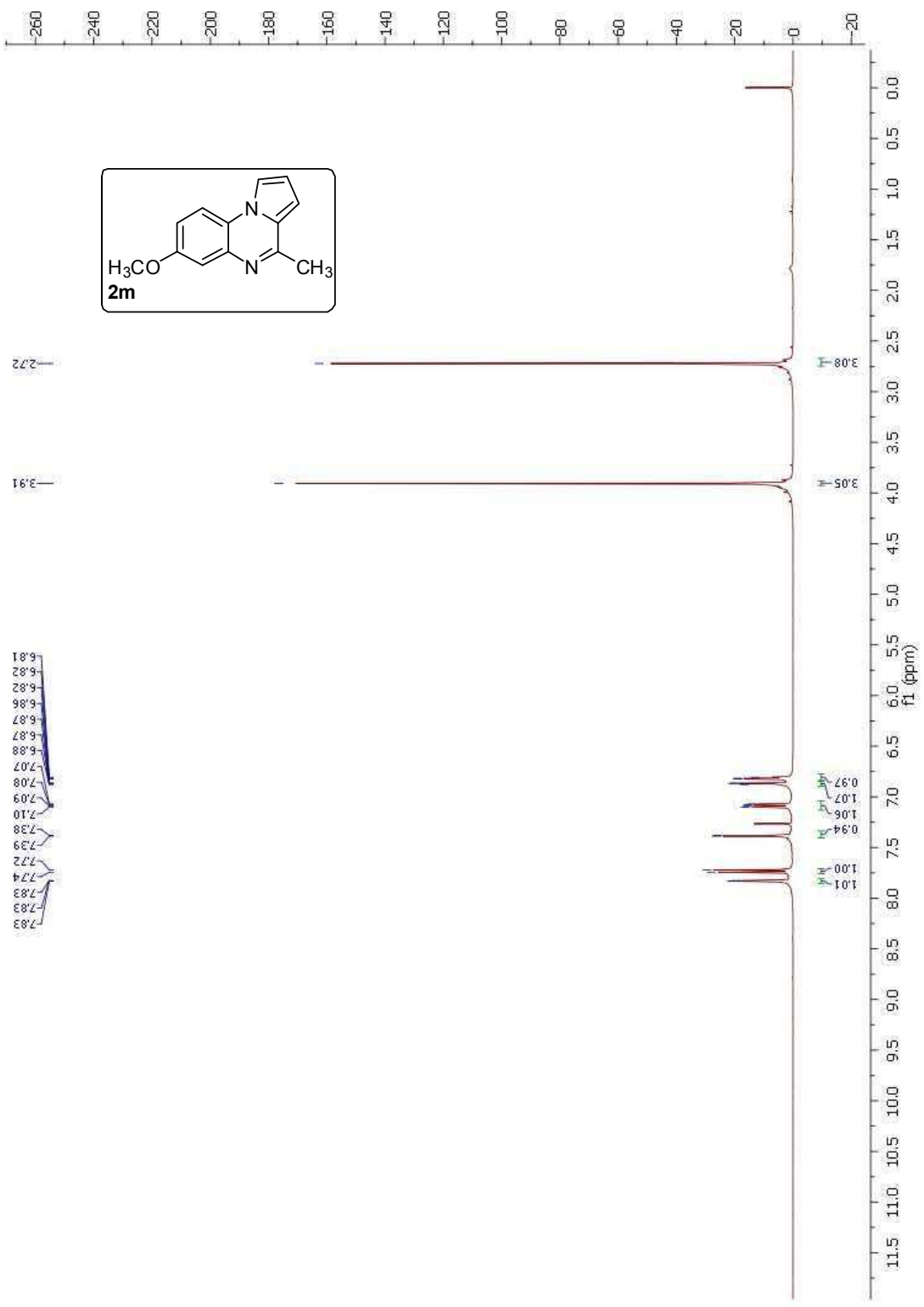

29.32
51.29
101.81
109.87
113.89
114.58
115.69
119.02
124.65
125.24
134.64
135.31
f1 (ppm)

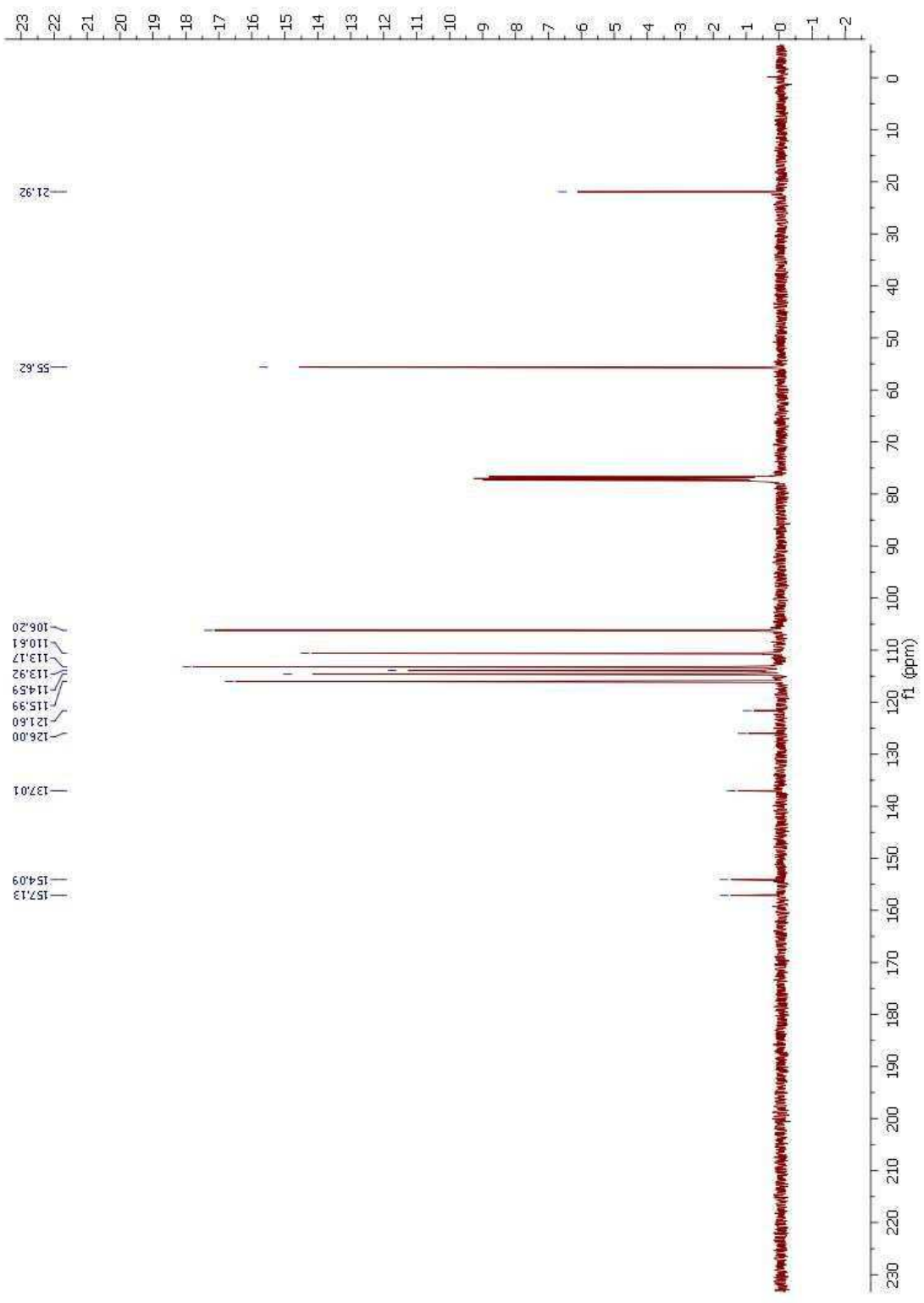

2k
N
N
CH3
f1 (ppm)

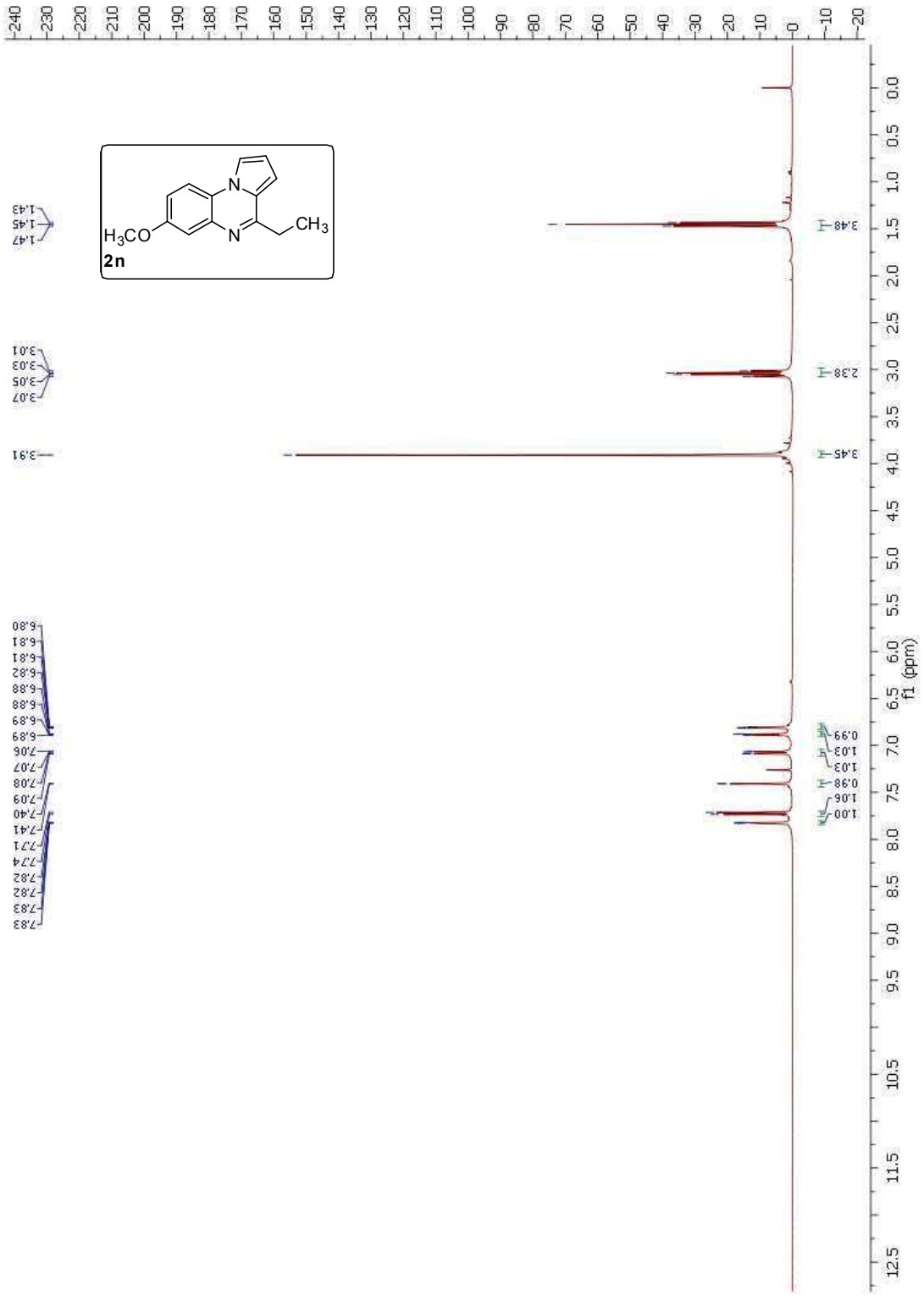

14.17
21.87
37.73
106.24
113.36
113.55
114.05
125.02
126.02
126.81
127.21
129.38
135.96
157.41
f1 (ppm)

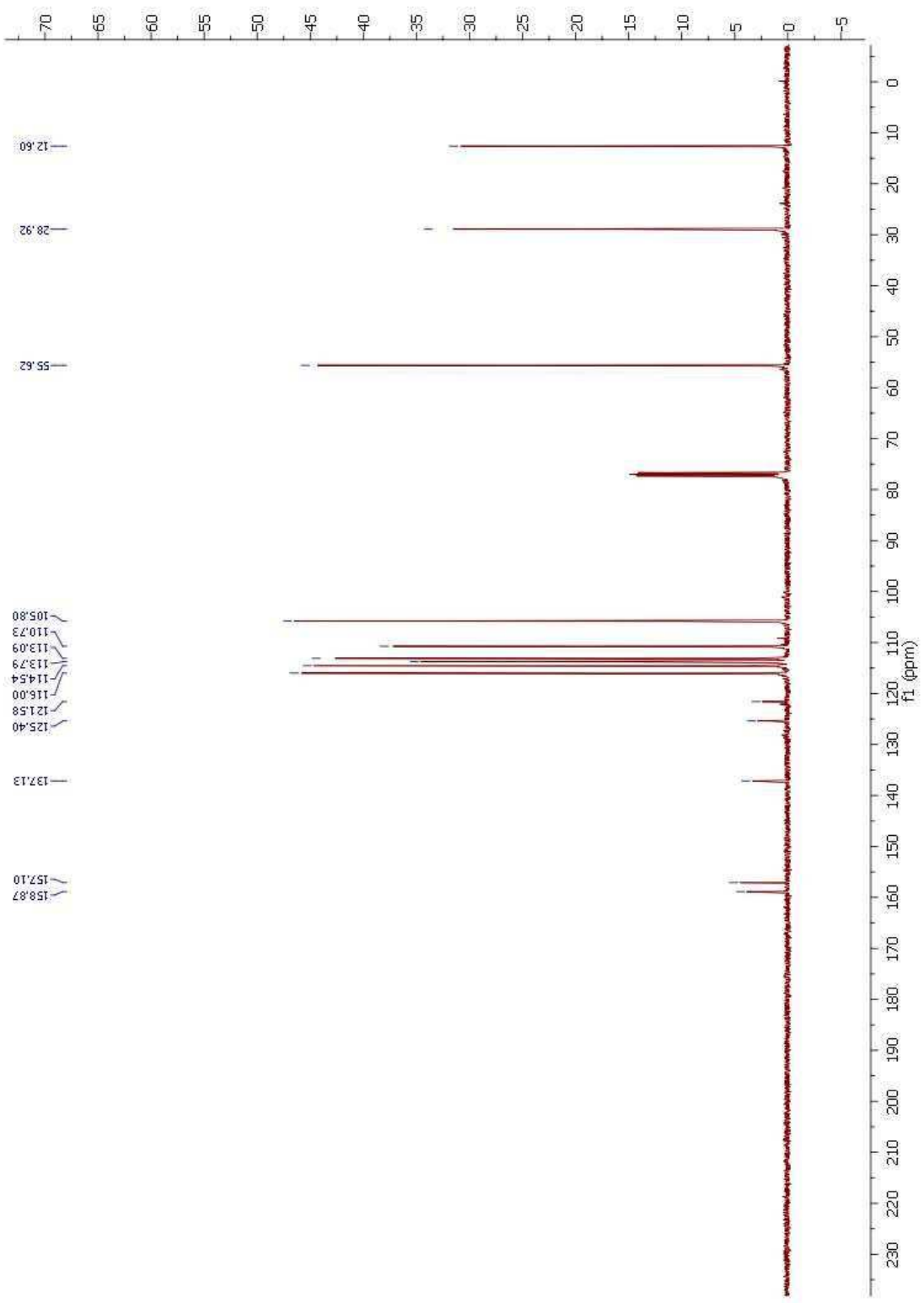

H3CO
N
N
H
2l
f1 (ppm)

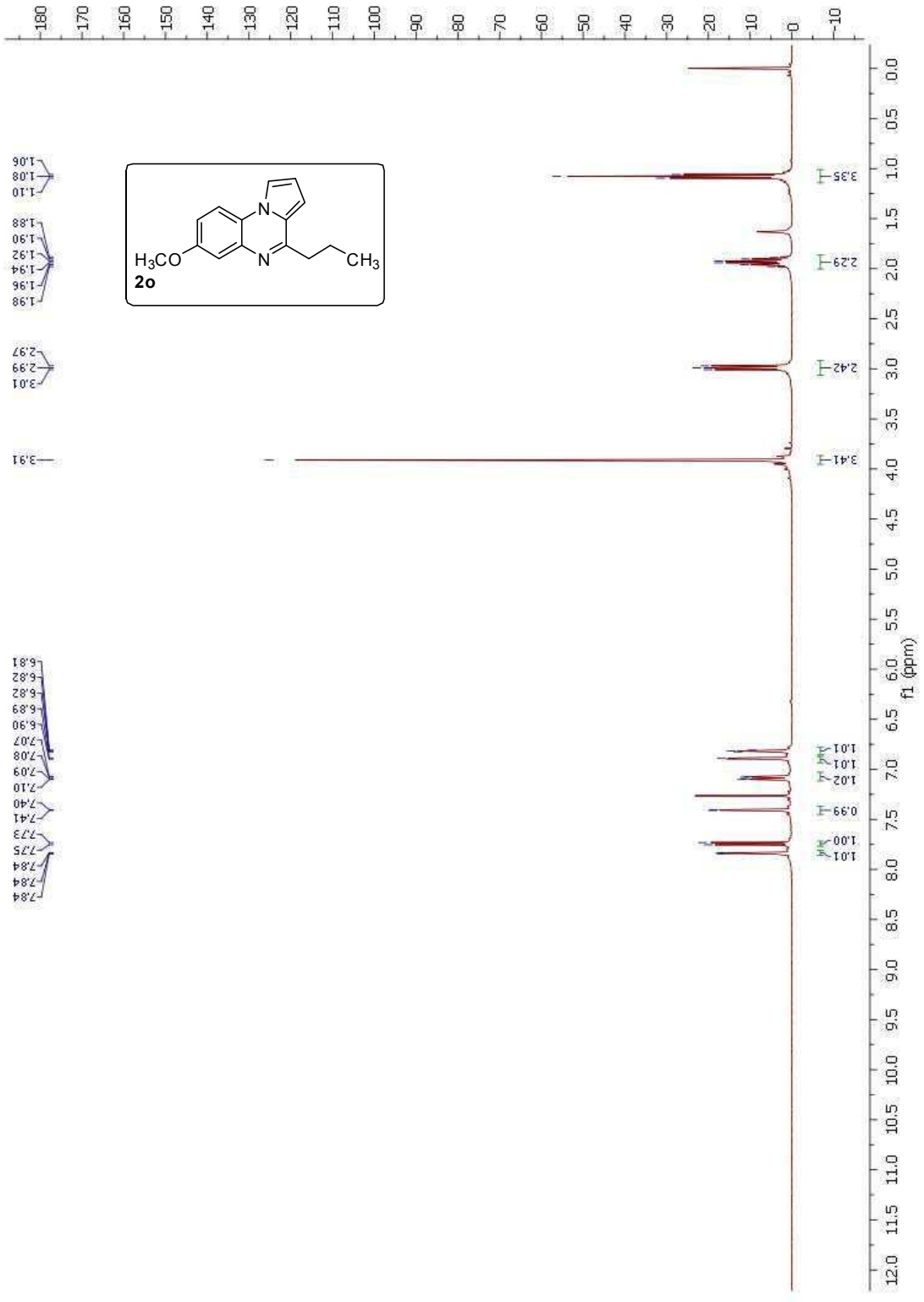

55.66
107.01
111.49
113.70
113.87
114.77
116.80
122.36
126.29
136.95
146.15
157.15
f1 (ppm)

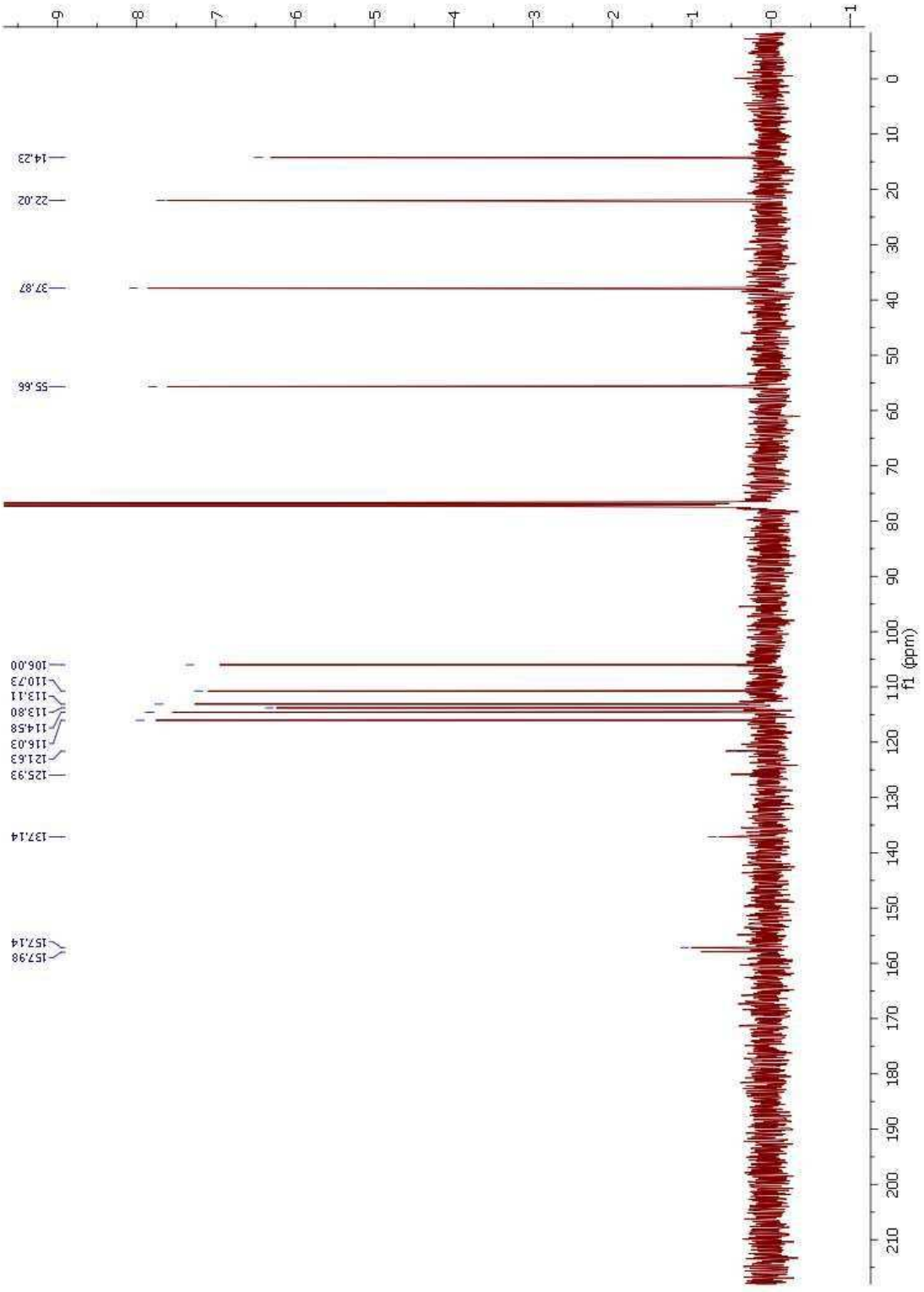

H3CO
CH3
N
N
2m
f1 (ppm)

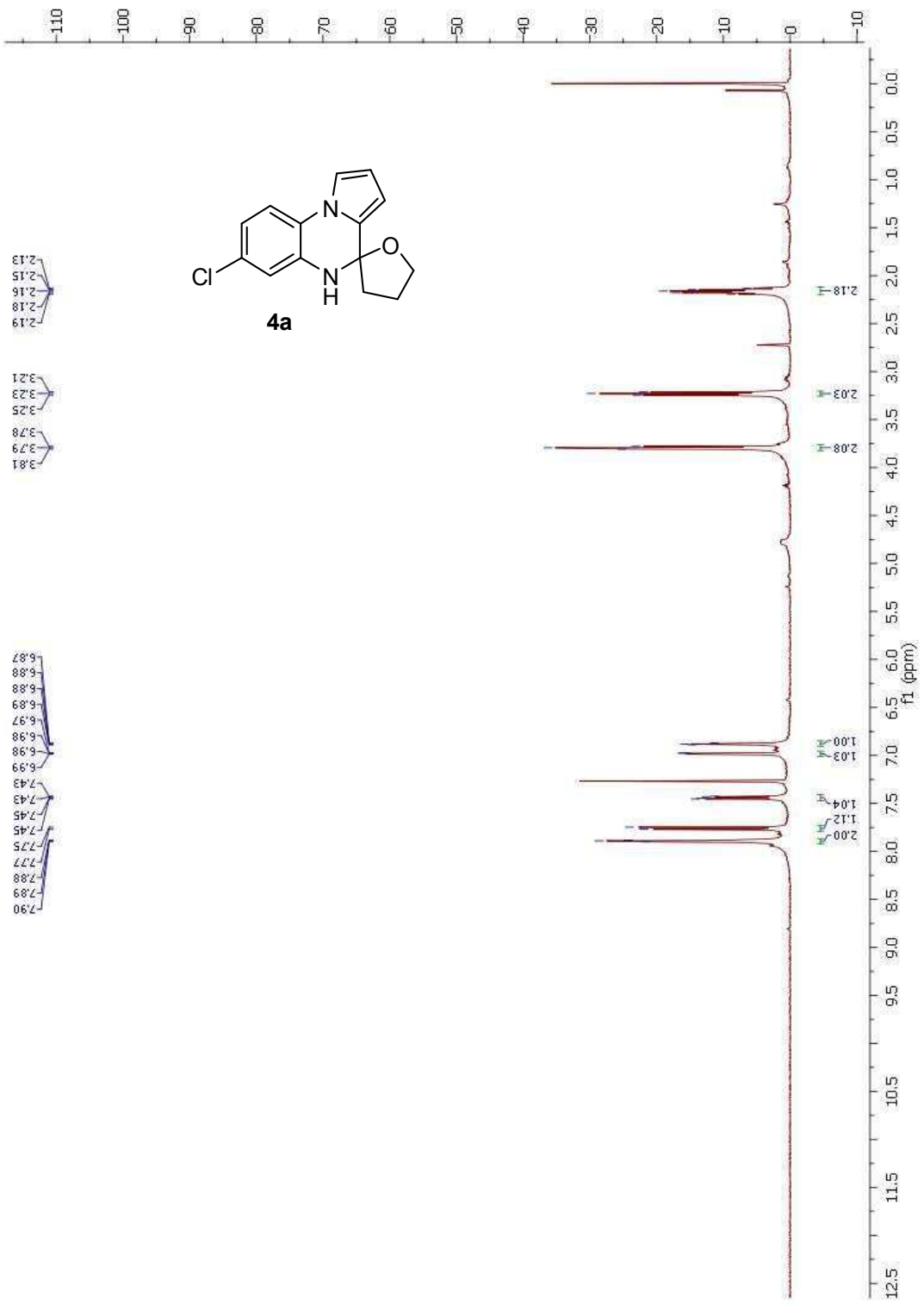

21.92
55.62
106.20
110.61
113.17
113.92
114.59
115.99
121.60
126.00
137.01
154.09
157.13
f1 (ppm)

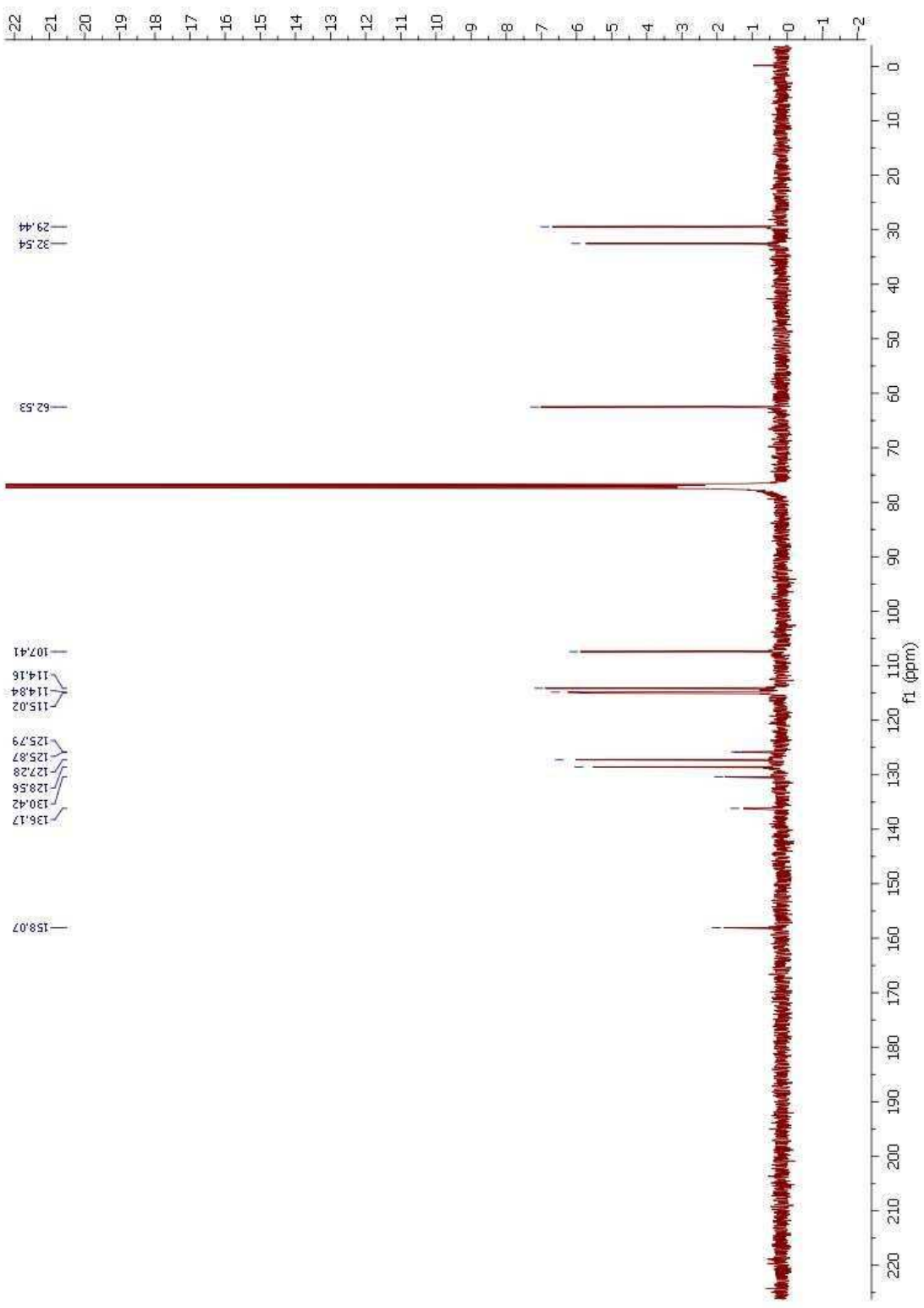

H3CO
CH3
2n
f1 (ppm)

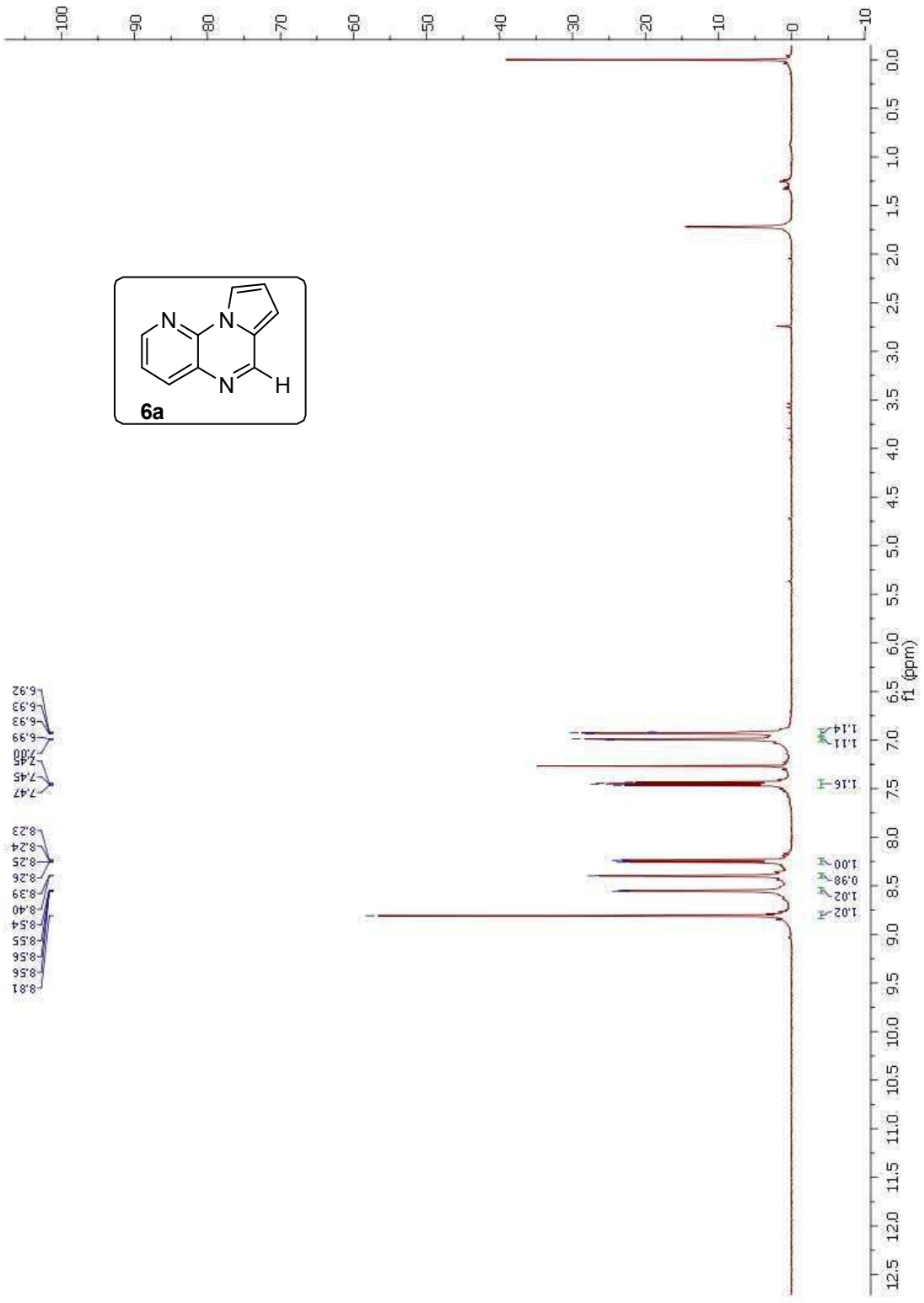

12.60
28.92
55.62
105.80
110.73
113.09
113.79
114.54
116.00
121.58
125.40
137.13
157.10
158.87
f1 (ppm)

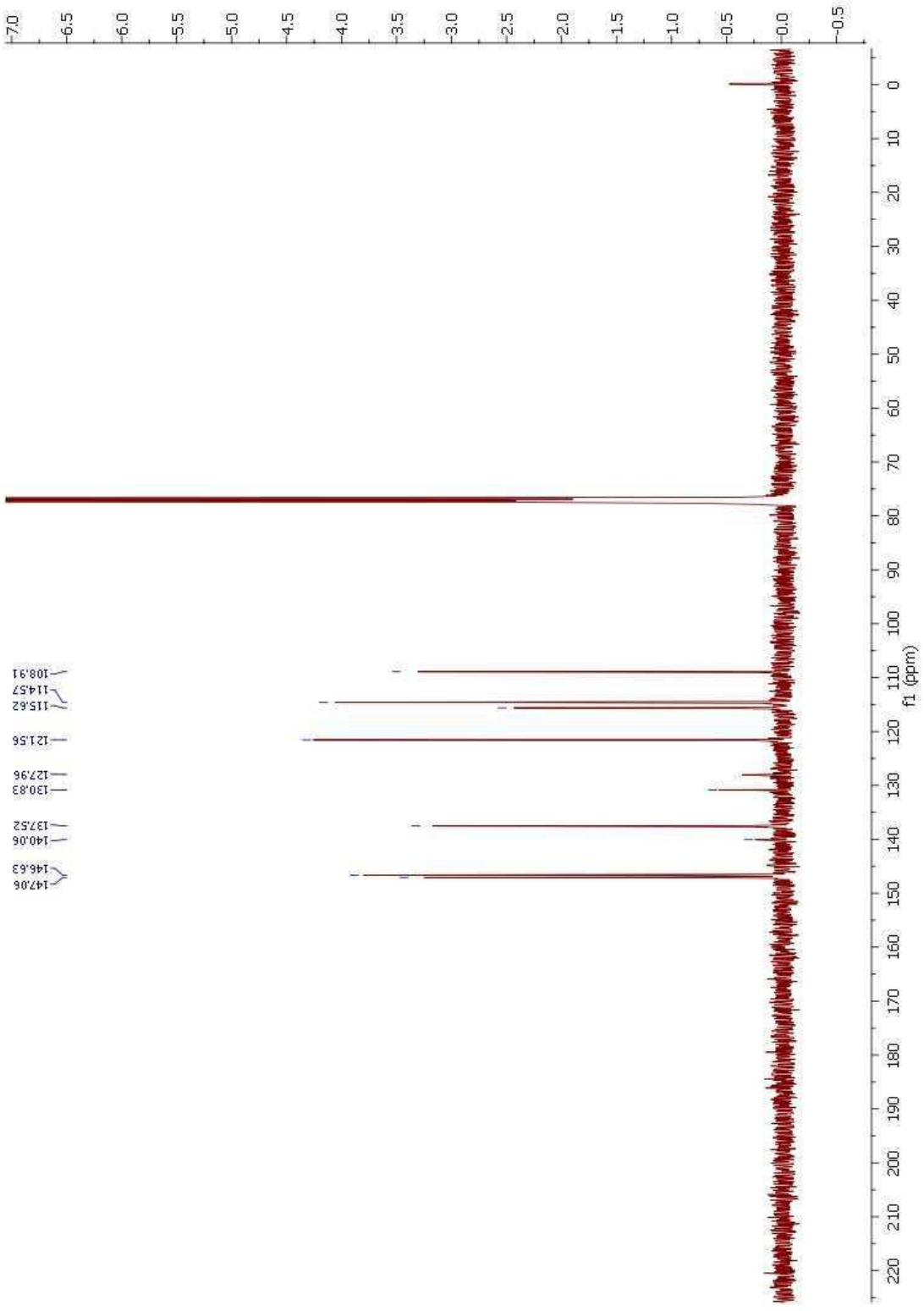

H3CO
N
N
CH3
2o
f1 (ppm)

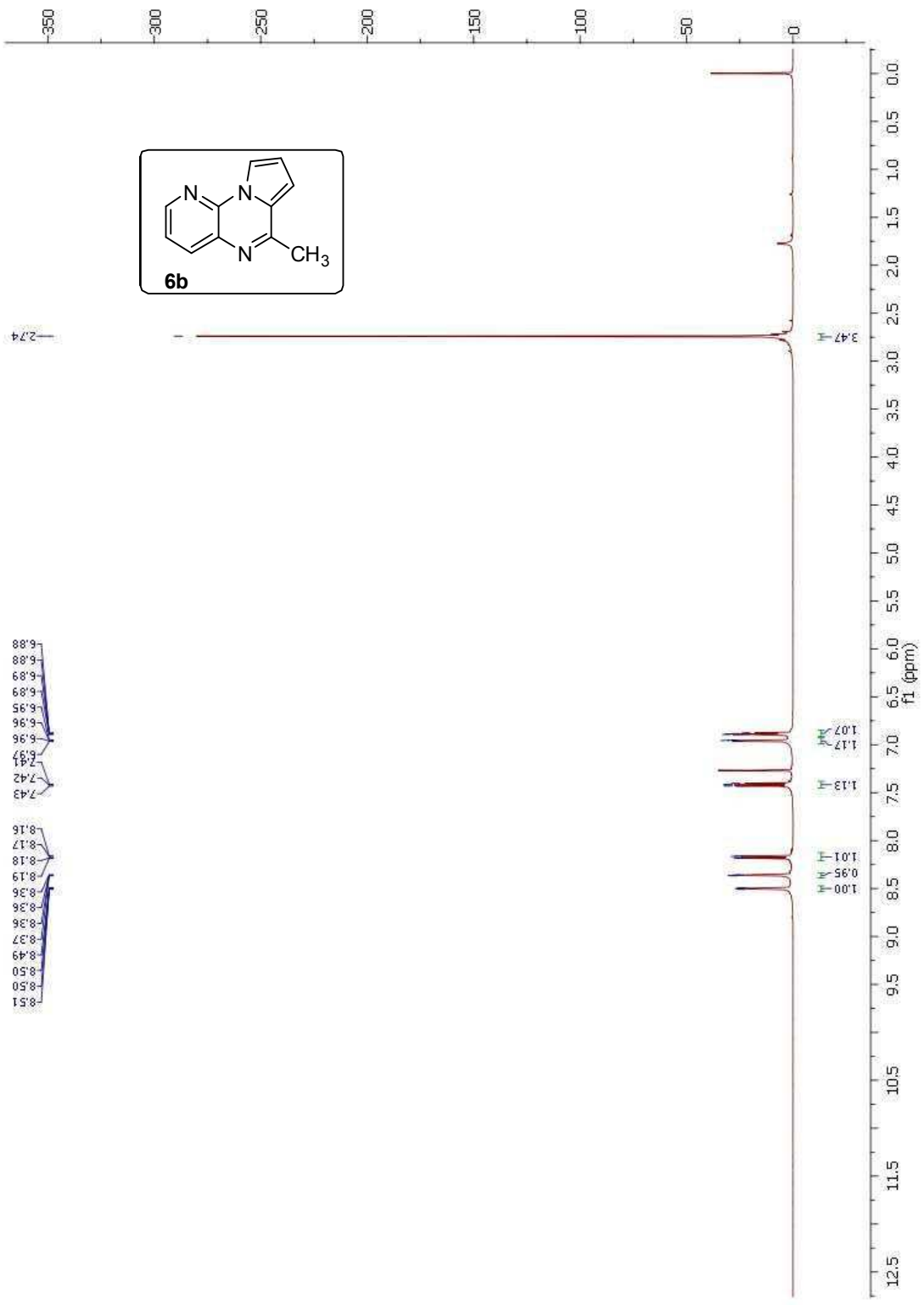

14.23
22.02
37.87
55.66
106.00
110.73
113.11
113.80
114.58
116.03
121.63
125.93
137.14
157.98
157.14
f1 (ppm)

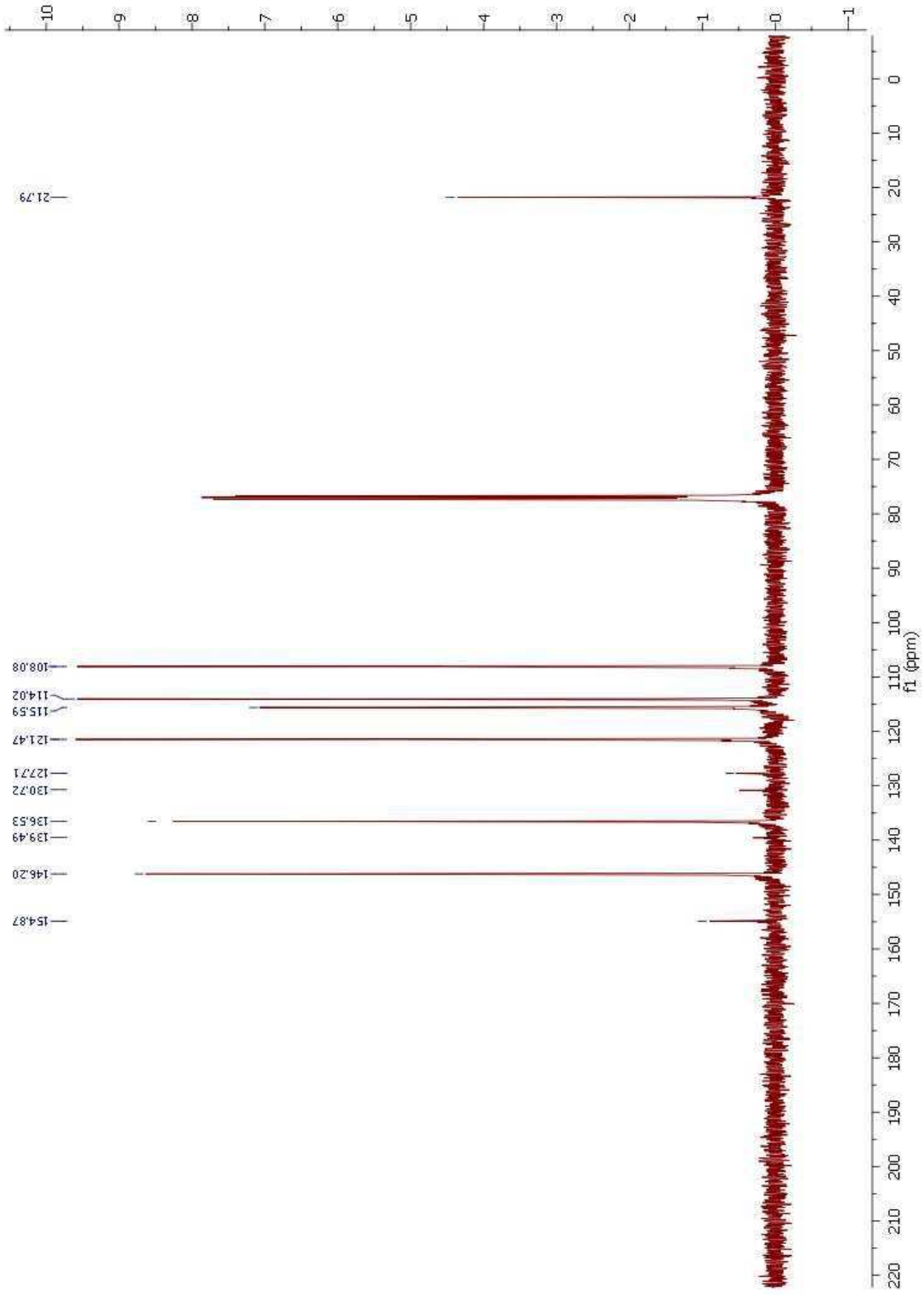

Cl
N
O
N
H
4a
f1 (ppm)

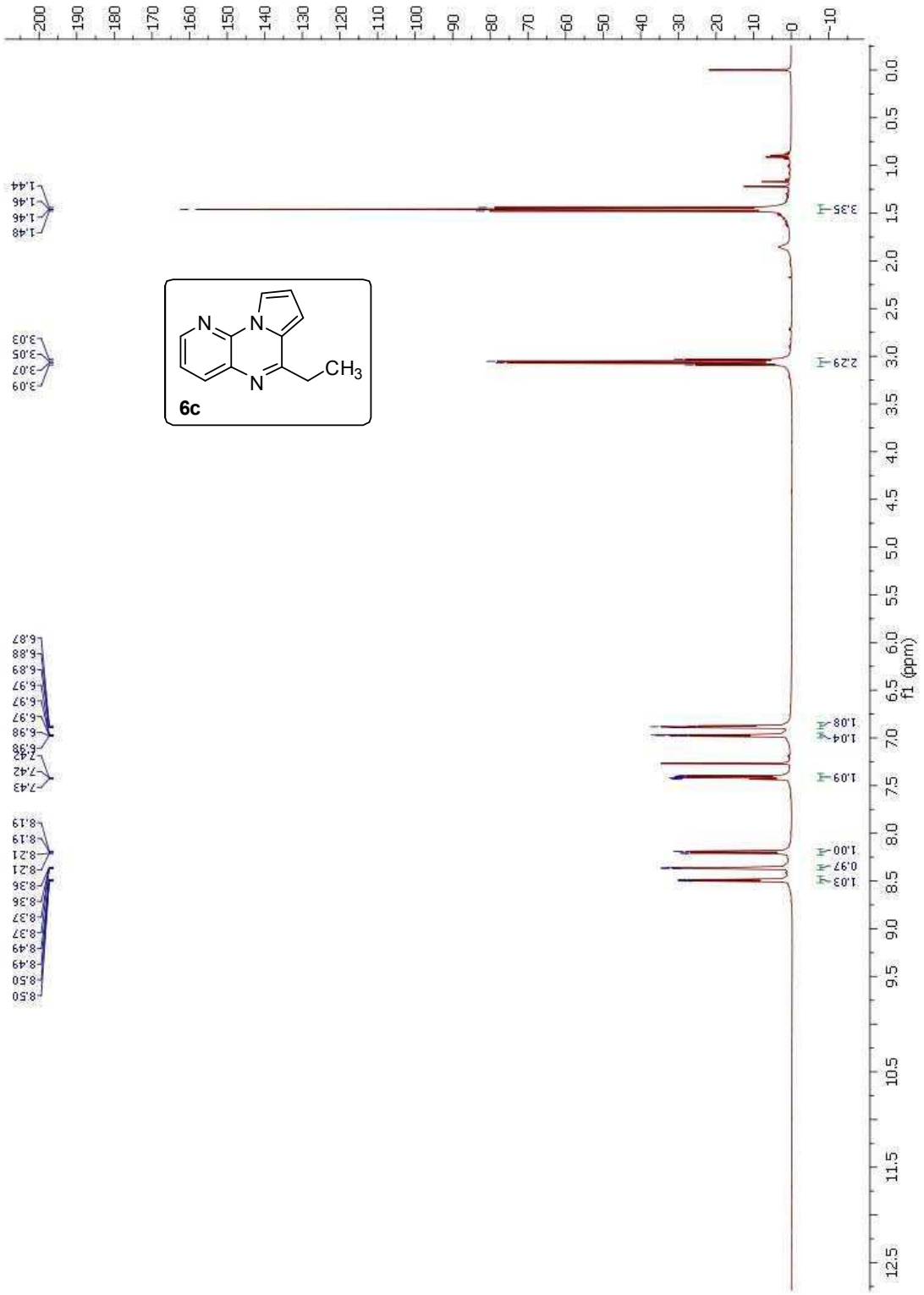

158.07
136.17
130.42
128.56
127.28
125.87
125.79
115.02
114.84
114.16
107.41
62.53
32.54
29.44
f1 (ppm)

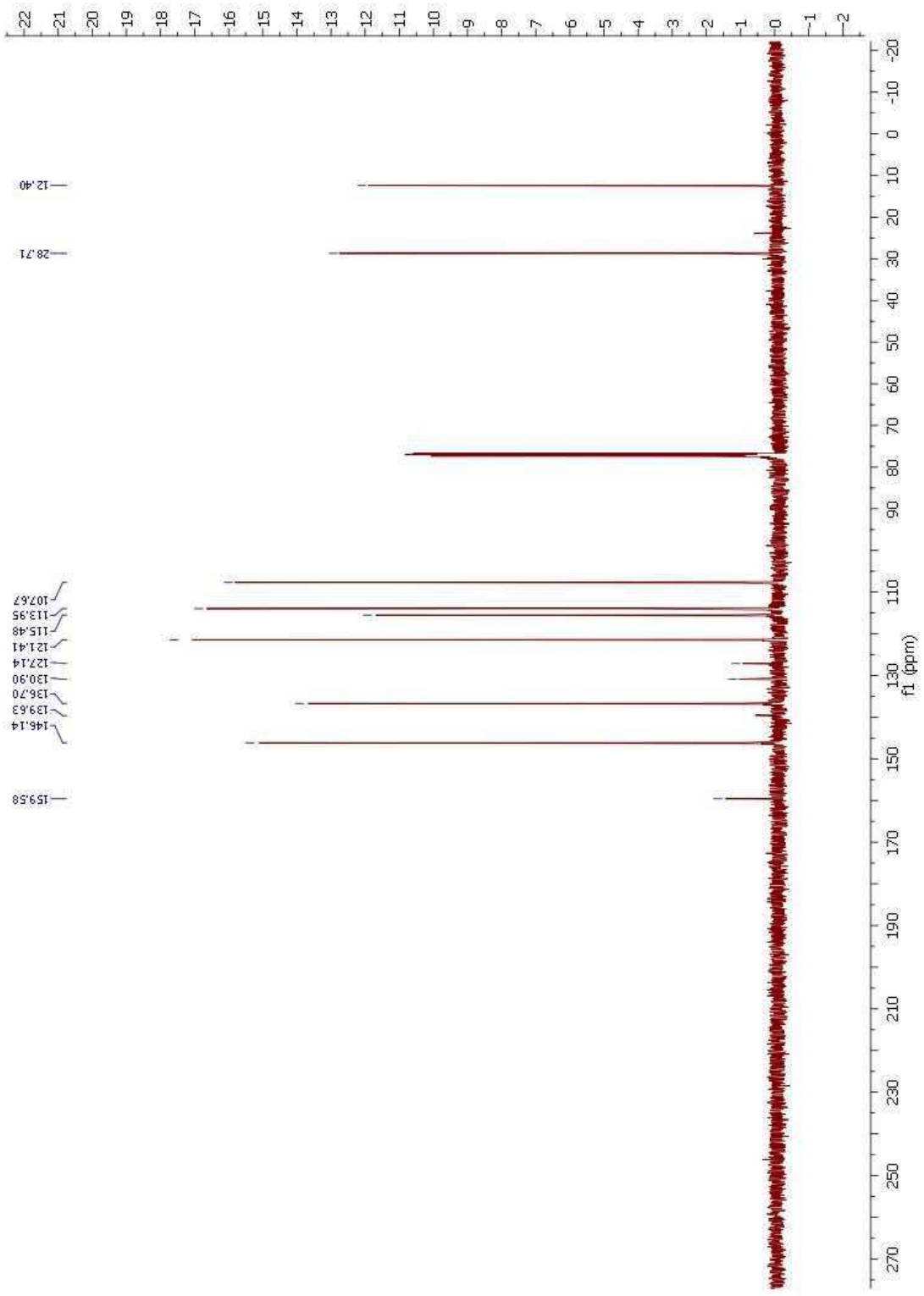

N
N
N
H
6a
f1 (ppm)

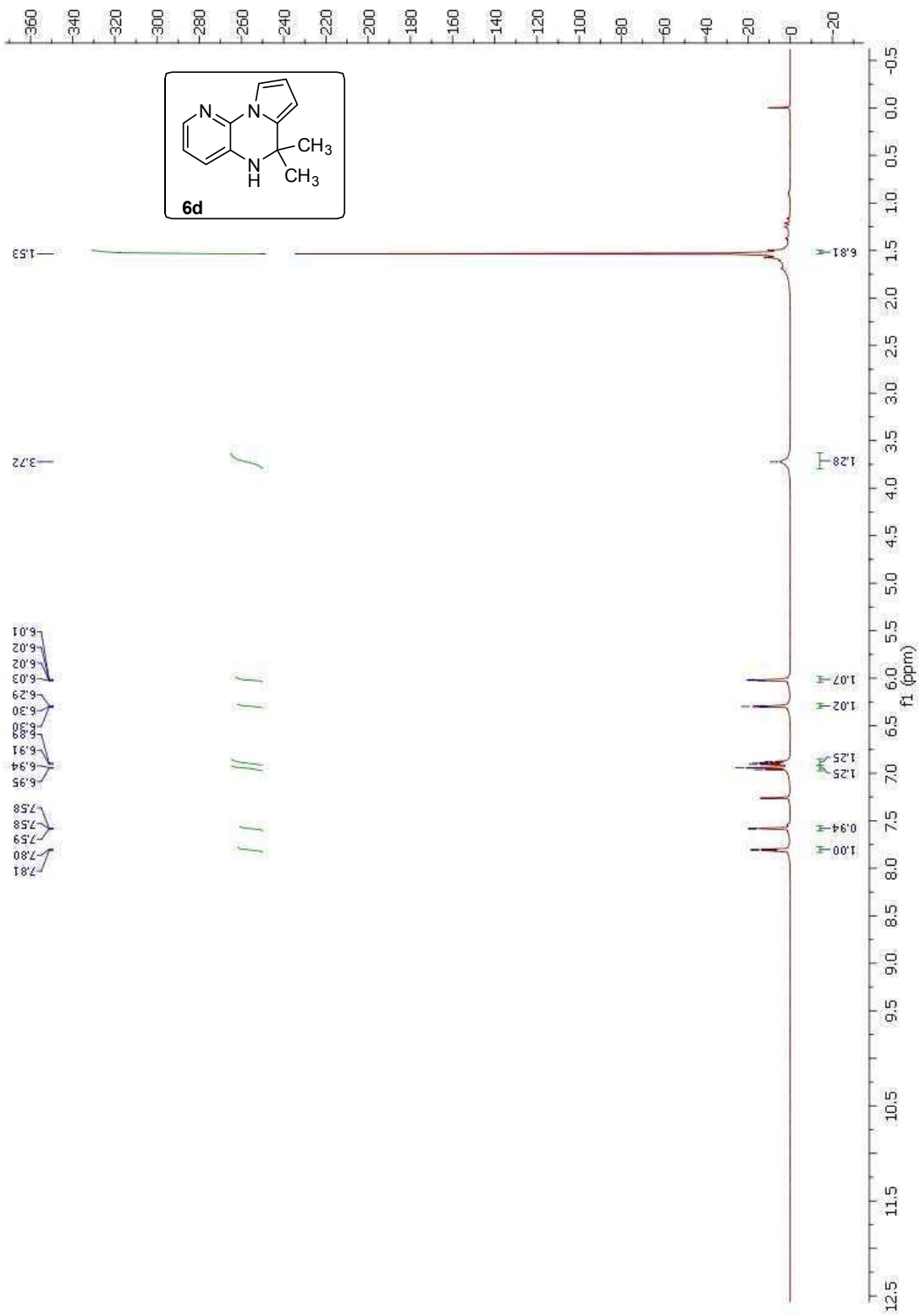

147.06
146.63
140.06
137.52
130.83
127.96
121.56
115.62
114.57
108.91
f1 (ppm)

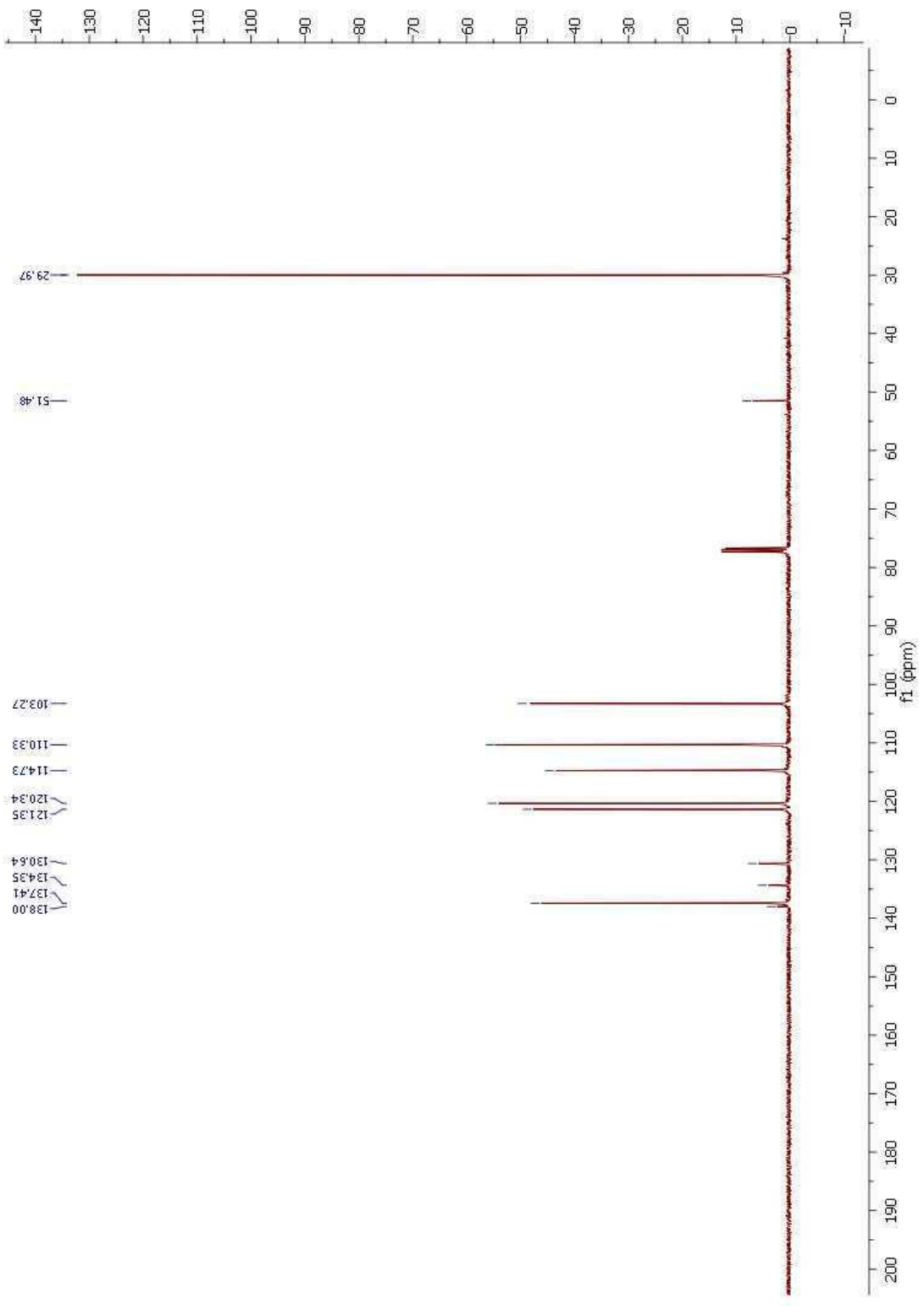

N
N
N
CH3
6b
f1 (ppm)

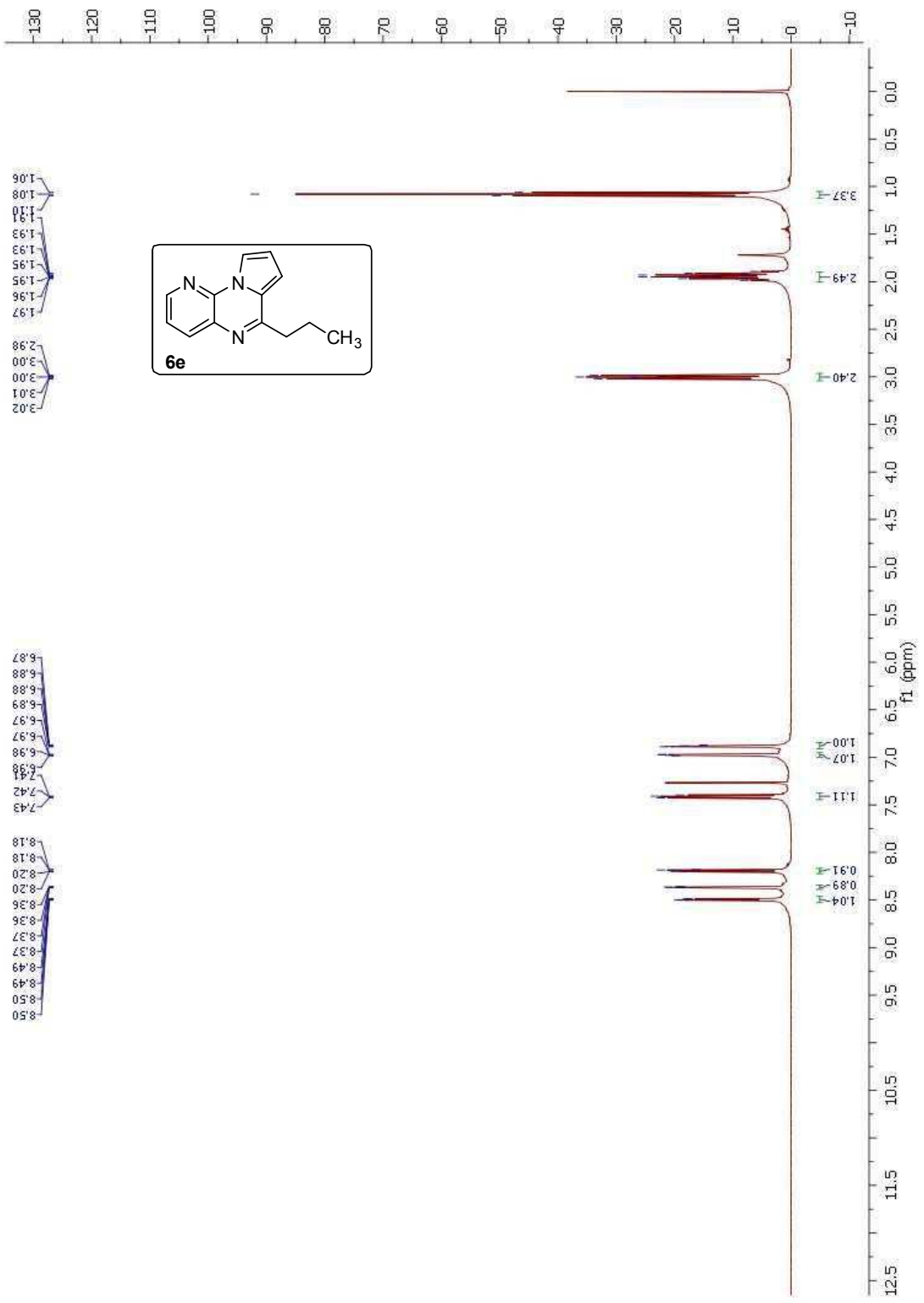

21.79
108.08
114.02
115.59
121.47
127.71
130.72
136.53
139.49
146.20
154.87
f1 (ppm)

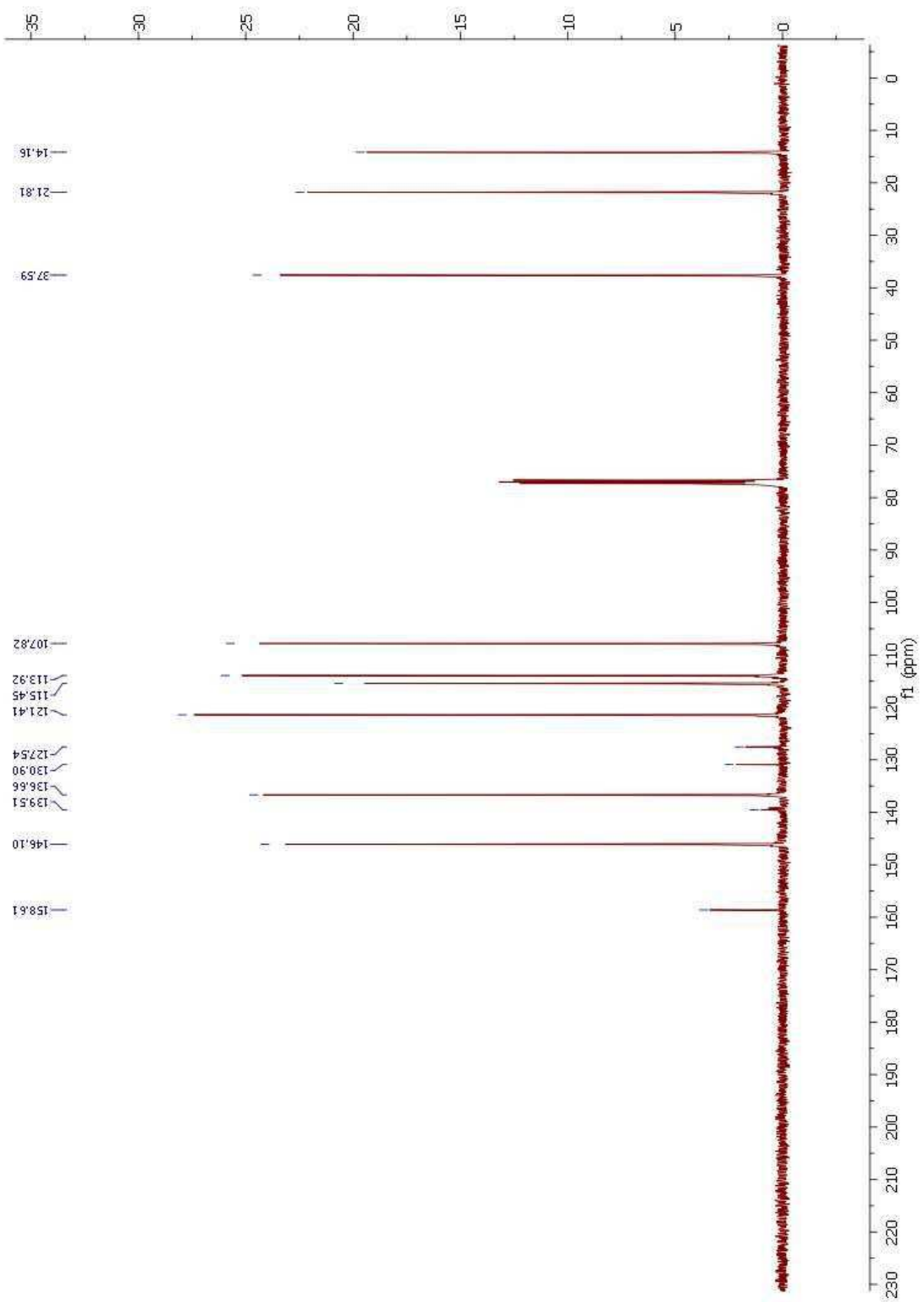

6c
f1 (ppm)

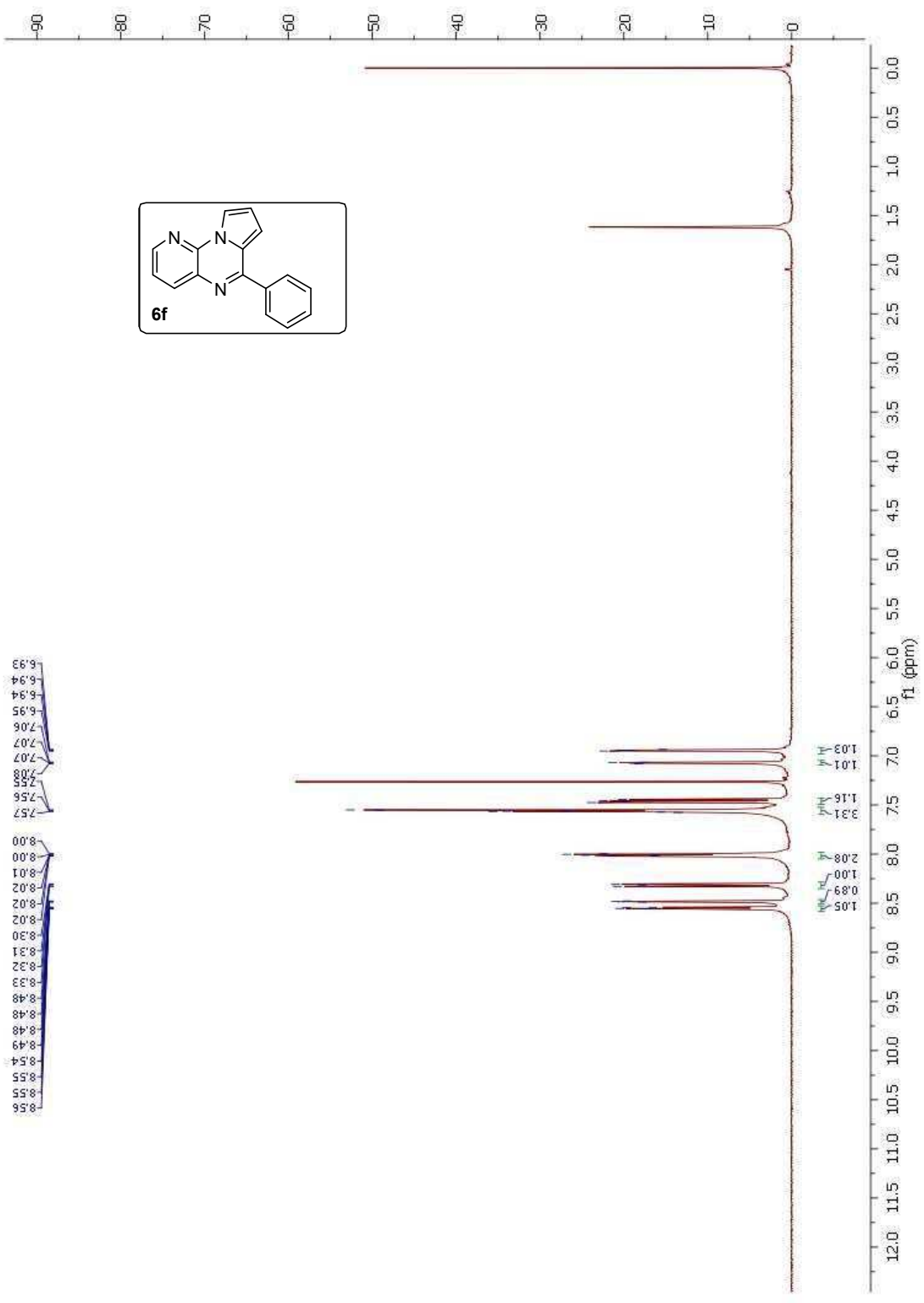

12.40
28.71
107.67
113.95
115.48
121.41
127.14
130.90
136.70
139.63
146.14
159.58
f1 (ppm)

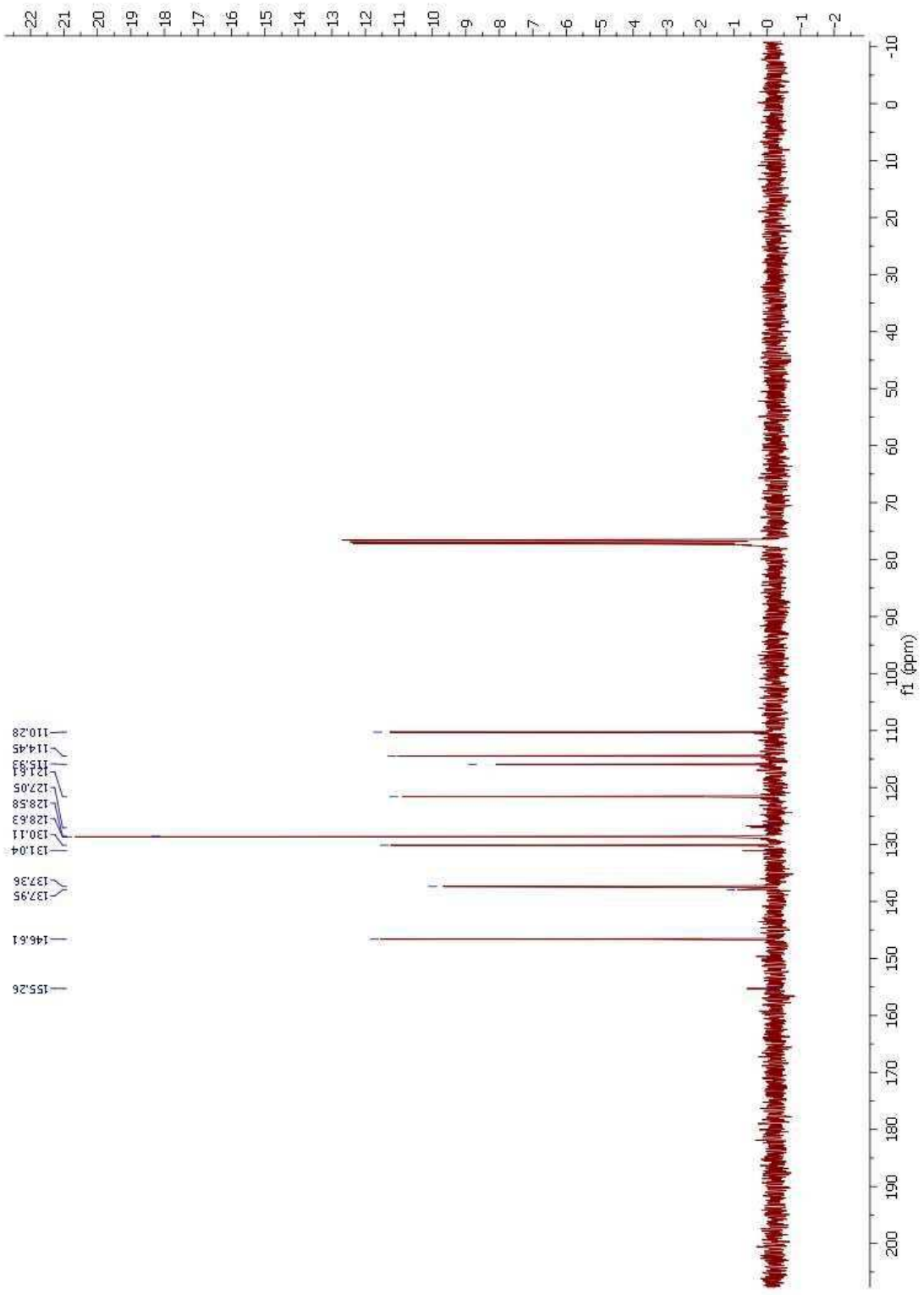

6d
f1 (ppm)


29.97
51.48
103.27
110.33
114.73
120.34
121.35
130.64
134.35
137.41
138.00
f1 (ppm)


6e
f1 (ppm)


14.16
21.81
37.59
107.82
113.92
115.45
121.41
127.54
130.90
136.66
139.51
146.10
158.61
f1 (ppm)


6f
f1 (ppm)


110,28
114,45
115,53
121,61
127,05
128,58
128,63
130,11
131,04
137,36
137,95
146,61
155,26
f1 (ppm)