Reaction of arynes, *N*-heteroaromatics and nitriles

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Electronic Supplementary Information (ESI)

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Experimental section:

General procedure for the reaction of arynes, *N*-heteroaromatics and nitriles:

A 25 mL round-bottomed side-arm flask containing CsF (2.00 mmol) was evacuated and purged with nitrogen gas three times. To the flask were then added benzyne precursor (**1**) (1.00 mmol), isoquinoline (1.00 mmol) and CH_3CN (3.0 ml) via syringes. The reaction mixture was allowed to stir at 50 °C for 8 h. At the end of the reaction, the reaction mixture was diluted with CH_2Cl_2, filtered through Celite and silica gel, and the filtrate was concentrated. The crude residue was purified through a silica gel column using hexane and ethyl acetate as eluent to give pure **4**. Products **4i-k** and **4o-r** were synthesized according to similar procedures by using quinolines (**2b-c**) and pyridine derivatives (**2d-g**) as the nucleophilic reagents, respectively. For the synthesis of products **4l-n**, similar procedures were also followed, but in these cases 1.0 ml of the corresponding substituted acetonitriles **3c-e** were used as solvent as well as the reactant.

Spectral data and copy of ^1H and ^{13}C NMR spectra of all compounds are listed below. For products **4l-n**, diastereomers were observed in *ca.* 1:1 ratios. In the **4l** and **4m** cases, we were able to isolate one pure diastereoisomeric form using column chromatography. The spectral data and the copy of ^1H and ^{13}C NMR spectra of these compounds **4l** and **4m** were provided. In addition, the copy of ^1H NMR spectra of 1:1 diastereoisomeric mixture of these compounds also provided.

(2-Phenyl-1,2-dihydro-1-isoquinolinyl)methyl cyanide (4a): Pale yellow viscous oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.35 (t, *J* = 7.0 Hz, 2 H), 7.28 - 7.25 (m, 1 H), 7.20 (t, *J* = 5.0 Hz, 2 H), 7.12 (d, *J* = 8.0 Hz, 1 H), 7.07 (d, *J* = 8.0 Hz, 2 H), 7.02 (t, *J* = 8.0 Hz, 1 H), 6.56 (d, *J* = 7.5 Hz, 1 H), 5.96 (d, *J* = 7.0 Hz, 1 H), 5.39 (t, *J* = 7.0 Hz, 1 H), 2.82 (dd, *J* = 16.5, 8.0 Hz, 1 H), 2.69 (dd, *J* = 16.5, 4.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.2, 130.8, 129.7, 128.6, 127.8, 127.5, 126.4, 126.3, 123.9,

122.2, 117.8, 116.5, 105.8, 57.0, 20.9; HRMS: calcd for $C_{17}H_{14}N_2$ 246.1157, found 246.1156.

(2-Phenyl-1,2-dihydro-1-isoquinolinyl)methyl cyanide-d_3 (4b): Pale yellow viscous oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 – 7.33 (m, 2 H), 7.28 - 7.25 (m, 1 H), 7.20 - 7.18 (m, 2 H), 7.12 (d, *J* = 8.0 Hz, 1 H), 7.06 (d, *J* = 8.5 Hz, 1 H), 7.03 (t, *J* = 7.0 Hz, 1 H), 6.56 (dd, *J* = 7.0, 1.5 Hz, 1 H), 5.96 (d, *J* = 7.0 Hz, 1 H), 5.38 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.1, 130.8, 129.7, 129.6, 128.6, 127.8, 127.4, 126.4, 126.3, 123.9, 122.1, 117.8, 116.4, 105.7, 56.9; HRMS: calcd for $C_{17}H_{12}D_3N_2$ 249.1345, found 249.1344.

[2-(3,4-Dimethylphenyl)-1,2-dihydro-1-isoquinolinyl]methyl cyanide (4c): Pale yellow viscous oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.10 – 7.08 (m, 3 H), 7.02 – 7.00 (m, 2 H), 6.77 – 6.73 (m, 2 H), 6.46 (dd, *J* = 7.2, 1.2 Hz, 1 H), 5.81 (d, *J* = 7.2 Hz, 1 H), 5.27 (t, *J* = 1.2 Hz, 1 H), 2.72 (dd, *J* = 16.2, 8.4 Hz, 1 H), 2.59 (dd, *J* = 16.2, 5.4 Hz, 1 H), 2.19 (s, 3 H), 2.13(s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 142.3, 137.9, 130.9, 130.6, 128.5, 128.3, 127.2, 126.2, 126.1, 123.7, 118.2, 117.9, 114.2, 104.7, 57.3, 20.8, 20.1, 18.8; HRMS: calcd for $C_{19}H_{18}N_2$ 274.1470, found 274.1470.

[2-(2,3-Dihydro-1*H*-5-indenyl)-1,2-dihydro-1-isoquinolinyl]methyl cyanide (4d): Pale yellow viscous oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.10 – 7.01 (m, 5 H), 6.88 (d, *J* = 1.8 Hz, 1 H), 6.78 (d, *J* = 8.4 Hz, 1 H), 6.45 (d, *J* = 7.2 Hz, 1 H), 5.81 (d, *J* = 7.2 Hz, 1 H), 5.28 (t, *J* = 1.2 Hz, 1 H), 2.83 – 2.73 (m, 4 H), 2.71 (dd, *J* = 16.2, 8.4 Hz, 1 H), 2.61 (dd, *J* = 16.2, 4.8 Hz, 1 H), 2.01 – 1.99 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 145.9, 143.1, 138.3, 130.9, 128.5, 128.4, 127.2, 126.2, 126.1, 125.1, 123.7, 117.9, 115.2, 113.2, 104.7, 57.6, 33.1, 32.0, 25.7, 20.1; HRMS: calcd for $C_{20}H_{18}N_2$ 286.1470, found 286.1469.

[2-(1,3-Benzodioxol-5-yl)-1,2-dihydro-1-isoquinolinyl]methyl cyanide (4e): Pale yellow viscous oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26 – 7.23 (m, 1 H), 7.18 –

7.14 (m, 2 H), 7.10 (d, *J* = 7.8 Hz, 1 H), 6.76 (d, *J* = 8.6 Hz, 1 H), 6.65 (d, *J* = 2.4 Hz, 1 H), 6.56 (dd, *J* = 8.4, 2.4 Hz, 1 H), 6.42 (dd, *J* = 7.4, 1.8 Hz, 1 H), 5.94 – 5.88 (m, 3 H), 5.27 – 5.25 (m, 1 H), 2.74 - 2.66 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 148.7, 143.4, 139.9, 130.8, 128.7, 128.6, 127.1, 126.2, 126.1, 123.8, 117.9, 110.4, 108.5, 104.9, 101.4, 100.2, 58.4, 21.0; HRMS: calcd for $C_{18}H_{14}N_2O_2$ 290.1055, found 290.1055.

[2-(3,4-Difluorophenyl)-1,2-dihydro-1-isoquinolinyl]methyl cyanide (4f): Pale yellow viscous oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (t, *J* = 7.0 Hz, 1 H), 7.20 (t, *J* = 8.0 Hz, 1 H), 7.17 - 7.10 (m, 3 H), 6.89 – 6.85 (m, 1 H), 6.80 – 6.77 (m, 1 H), 6.44 (dd, *J* = 7.0, 1.5 Hz, 1 H), 6.01 (d, *J* = 7.5 Hz, 1 H), 5.29 (t, *J* = 6.5 Hz, 1 H), 2.75 – 2.66 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.8 (d), 149.8 (d), 146.9 (d), 145.0 (d), 141.4 (d), 130.3, 128.8, 127.4, 127.1, 126.8, 126.1, 124.2, 118.0, 117.9, 117.63, 111.9 (q), 107.1, 106.3, 106.1, 57.6, 21.18; HRMS: calcd for $C_{17}H_{12}F_2N_2$ 282.0969, found 282.0965.

[2-(5,8-Dihydro-2-naphthalenyl)-1,2-dihydro-1-isoquinolinyl]methyl cyanide (4g): Pale yellow viscous oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.5 Hz, 1 H), 7.76 (dd, *J* = 7.5, 2.0 Hz, 1 H), 7.46 (t, *J* = 8.0 Hz, 1 H), 7.37 – 7.32 (m, 3 H), 7.30 – 7.21 (m, 1 H), 7.25 – 7.19 (m, 3 H), 7.15 (d, *J* = 7.5 Hz, 1 H), 6.68 (d, *J* = 7.5 Hz, 1 H), 6.03 (d, *J* = 8.0 Hz, 1 H), 5.53 (t, *J* = 4.5 Hz, 1 H), 2.87 (dd, *J* = 17.0, 8.0 Hz, 1 H), 2.78 (dd, *J* = 16.0, 5.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.7, 134.2, 130.7, 129.7, 129.4, 128.7, 127.9, 127.6, 127.4, 126.9, 126.5, 126.3, 124.4, 123.9, 117.9, 117.4, 112.2, 106.2, 57.2, 20.9; HRMS: calcd for $C_{21}H_{16}N_2$ 296.1313, found 296.1313.

[2-(3-Methoxyphenyl)-1,2-dihydro-1-isoquinolinyl]methyl cyanide (4h): Pale yellow viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 – 7.18 (m, 4 H), 7.10 (d, *J* = 7.6 Hz, 1 H), 6.66 (d, *J* = 8.0 Hz, 1 H), 6.58 (s, 1 H), 6.54 (t, *J* = 7.6 Hz, 2 H), 5.97 (d,

J = 7.2 Hz, 1 H), 5.37 (t, *J* = 7.2 Hz, 1 H), 3.81 (s, 3 H), 2.80 (dd, *J* = 16.4, 8.0 Hz, 1 H), 2.67 (dd, *J* = 17.2, 5.6 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.9, 145.5, 130.7, 130.4, 128.7, 127.7, 127.6, 126.4, 126.3, 123.9, 117.8, 108.8, 107.1, 105.9, 103.3, 57.0, 55.4, 20.9; HRMS: calcd for $C_{18}H_{16}N_2O$ 276.1263, found 276.1261.

(1-Phenyl-1,2-dihydro-2-quinolinyl)methyl cyanide (4i): Pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 - 7.16 (m, 4 H), 7.16 - 7.03 (m, 3 H), 6.83 – 6.76 (m, 1 H), 6.65 (d, *J* = 9.0 Hz, 1 H), 5.86 (dd, *J* = 9.6, 5.4 Hz, 1 H), 4.80 (dd, *J* = 12.0, 6.0 Hz, 1 H), 2.60 – 2.52 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 146.2, 140.5, 129.7, 128.8, 127.4, 127.2, 124.7, 124.2, 123.3, 121.6, 120.3, 118.0, 117.5, 56.9, 23.6; HRMS: calcd for $C_{17}H_{14}N_2$ 246.1157, found 246.1155.

2-(1,2-dihydro-1-(3,4-dimethylphenyl)quinolin-2-yl)acetonitrile (4j): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, *J* = 8.0 Hz, 1 H), 7.07 – 7.00 (m, 4 H), 6.99 (t, *J* = 7.2 Hz, 1 H), 6.80 – 6.76 (m, 2 H), 5.86 (dd, *J* = 9.6, 5.4 Hz, 1 H), 4.82 – 4.79 (m, 1 H), 2.65 – 2.52 (m, 2 H), 2.28 (s, 3 H), 2.27 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.2, 141.6, 138.3, 133.9, 130.9, 128.8, 127.3, 126.7, 122.9, 122.2, 121.0, 119.3, 117.5, 116.6, 57.3, 24.0, 19.9, 19.2; HRMS: calcd for $C_{19}H_{18}N_2$ 274.1470, found 274.1475.

2-(1,2-dihydro-6-methoxy-1-phenylquinolin-2-yl)acetonitrile (4k): Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 - 7.26 (m, 2 H), 7.17 (d, *J* = 8.4 Hz, 2 H), 7.05 (t, *J* = 7.2 Hz, 1 H), 6.92 (d, *J* = 6.8 Hz, 1 H), 6.74 (s, 1 H), 6.71 (d, *J* = 8.0 Hz, 1 H), 6.30 (d, *J* = 9.6 Hz, 1 H), 5.92 (dd, *J* = 9.2, 5.6 Hz, 1 H), 4.75 (q, *J* = 5.6 Hz, 1 H), 3.77 (s, 3 H), 2.55 (d, *J* = 7.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 147.8, 132.9, 129.4, 126.9, 125.6, 123.2, 123.1, 121.9, 121.8, 117.7, 115.1, 111.4, 56.8, 55.6, 22.8; HRMS: calcd for $C_{18}H_{16}N_2O$ 276.1263, found 276.1267.

1-(2-Phenyl-1,2-dihydro-1-isoquinolinyl)ethyl cyanide (4l) (one pure diastereoisomeric form)**:** Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 - 7.25

(m, 4 H), 7.21 - 7.04 (m, 5 H), 6.66 (d, *J* = 7.2 Hz, 1 H), 5.98 (d, *J* = 7.2 Hz, 1 H), 5.19 (t, *J* = 7.2 Hz, 1 H), 3.16 (q, *J* = 15.2, 7.6 Hz, 1 H), 1.16 (d, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.2, 131.8, 128.7, 128.1, 127.5, 127.1, 126.4, 126.0, 123.5, 122.3, 117.5, 116.6, 105.5, 57.0, 20.5, 11.5; HRMS: calcd for $C_{18}H_{16}N_2$ 260.1313, found 260.1311.

(2-Phenyl-1,2-dihydro-1-isoquinolinyl)methyl cyanide (4m) (one pure diastereoisomeric form)**:** Pale yellow viscous oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (t, *J* = 7.0 Hz, 2 H), 7.25 (t, *J* = 6.0 Hz, 2 H), 7.19 (t, *J* = 8.5 Hz, 2 H), 7.15 (d, *J* = 7.5 Hz, 2 H), 7.08 (d, *J* = 7.0 Hz, 1 H), 7.04 (t, *J* = 7.0 Hz, 1 H), 6.92 (d, *J* = 8.0 Hz, 2 H), 6.82 (t, *J* = 7.5 Hz, 1 H), 6.65 (d, *J* = 7.0 Hz, 1 H), 6.28 (d, *J* = 7.5 Hz, 1 H), 6.02 (d, *J* = 17.0 Hz, 1 H), 5.43 (dd, *J* = 8.5, 1.5 Hz, 1 H), 4.21 (d, *J* = 9.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.1, 132.4, 131.1, 129.4, 128.9, 128.6, 128.5, 128.3, 128.2, 128.1, 127.4, 125.3, 124.96, 123.5, 122.4, 120.5, 117.8, 107.2, 65.1, 39.9; HRMS: calcd for $C_{23}H_{18}N_2$ 322.1470, found 322.1471.

(2-Phenyl-1,2-dihydro-1-isoquinolinyl)(2-thienyl)methyl cyanide (4n) (1:1 diastereoisomeric mixture form)**:** Pale yellow viscous oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (t, *J* = 8.0 Hz, 2 H), 7.32 (t, *J* = 8.0 Hz, 2 H), 7.24 (m, 4 H), 7.17 – 7.11 (m, 2 H), 7.04 (d, *J* = 12.0 Hz, 2 H), 6.97 (t, *J* = 8.5 Hz, 2 H), 6.89 (t, *J* = 7.0 Hz, 1 H), 6.85 (t, *J* = 5.0 Hz, 1 H), 6.67 (d, *J* = 17.0 Hz, 2 H), 6.63 (dd, *J* = 8.0, 2.0 Hz, 2 H), 6.52 (d, *J* = 8.5 Hz, 1 H), 6.50 (d, *J* = 7.5 Hz, 1 H), 6.20 (d, *J* = 7.0, 1.5 Hz, 1 H), 6.07 (d, *J* = 7.0 Hz, 1 H), 5.60 (d, *J* = 8.5 Hz, 1 H), 5.29 (d, *J* = 7.5 Hz, 1 H), 4.50 (d, *J* = 8.5 Hz, 1 H), 4.45 (d, *J* = 9.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.96, 134.2, 133.9, 130.9, 130.8, 129.4, 129.0, 128.8, 128.1, 128.0, 127.8, 127.2, 126.9, 126.2, 125.9, 125.1, 123.9, 123.6, 122.5, 122.1, 118.9, 117.9, 117.1, 116.91, 107.9, 107.1, 65.6, 65.4, 34.9, 34.9; HRMS: calcd for $C_{21}H_{16}N_2S$ 328.1034, found 328.1032.

(1-Phenyl-1,2-dihydro-2-pyridinyl)methyl cyanide (4o) : Pale yellow oil; ^{1}H

NMR (500 MHz, $CDCl_3$): δ 7.32 (dd, *J* = 9.0, 2.5 Hz, 2 H), 7.05 - 7.01 (t, *J* = 8.5 Hz, 3 H), 6.47 (d, *J* = 7.5 Hz, 1 H), 6.19 (dd, *J* = 9.5, 5.5 Hz, 1 H), 5.50 – 5.41 (m, 2 H), 4.96 – 4.92 (m, 1 H), 2.70 (dd, *J* = 16.0, 7.5 Hz, 1 H), 2.52 (dd, *J* = 16.5, 5.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.5, 129.6, 128.2, 124.7, 122.5, 117.8, 116.8, 113.1, 103.9, 52.9, 19.7; HRMS: calcd for $C_{13}H_{12}N_2$ 196.1000, found 196.0999.

(1,4-Diphenyl-1,2-dihydro-2-pyridinyl)methyl cyanide (4p): Pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.48 - 7.46 (m, 2 H), 7.38 - 7.34 (m, 4 H), 7.33 - 7.31 (m, 1 H), 7.09 – 7.04 (m, 3 H), 6.64 (d, *J* = 8.5 Hz, 1 H), 5.82 (dd, *J* = 8.0, 2.5 Hz, 1 H), 5.11 (dd, *J* = 7.5, 1.5 Hz, 1 H), 5.02 (dd, *J* = 3.0, 1.5 Hz, 1 H), 2.84 (dd, *J* = 16.5, 7.5 Hz, 1 H), 2.62 (dd, *J* = 16.5, 5.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.1, 138.4, 136.9, 129.6, 128.9, 128.5, 127.9, 126.1, 122.62, 117.7, 116.7, 108.6, 104.5, 53.4, 19.7; HRMS: calcd for $C_{19}H_{16}N_2$ 272.1313, found 272.1313.

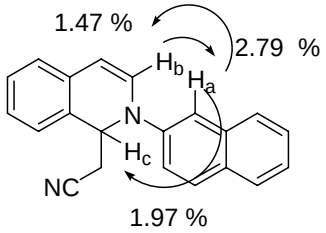
(1,5-Diphenyl-1,2-dihydro-2-pyridinyl)methyl cyanide (4q): Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.09 (m, 10 H), 6.91 (s, 1 H), 6.75 (d, *J* = 8.0 Hz, 1 H), 6.73 (dd, *J* = 5.2, 1.2 Hz, 1 H), 5.95 – 5.05 (m, 1 H), 2.79 (dd, *J* = 16.8, 8.0 Hz, 1 H), 2.70 (dd, *J* = 16.2, 4.5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.8, 137.9, 129.9, 129.0, 127.5, 126.3, 125.9, 125.5, 124.3, 123.3, 119.2, 117.6, 114.3, 53.3, 20.9; HRMS: calcd for $C_{19}H_{16}N_2$ 272.1313, found 272.1312.

(1,3-Diphenyl-1,2-dihydro-2-pyridinyl)methyl cyanide (4q'): Pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.41 – 7.31 (m, 7 H), 7.23 - 7.21 (m, 2 H), 7.07 (t, *J* = 7.0 Hz, 1 H), 6.58 – 6.55 (m, 2 H), 5.67 (t, *J* = 6.0 Hz, 1 H), 5.56 – 5.54 (m, 1 H), 2.90 (dd, *J* = 17.0, 8.0 Hz, 1 H), 2.48 (dd, *J* = 17.0, 4.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.9, 137.2, 129.5, 128.90, 127.7, 127.2, 124.7, 123.5, 123.1, 119.9, 118.6, 118.1, 105.7, 55.7, 18.6; HRMS: calcd for $C_{19}H_{16}N_2$ 272.1313, found 272.1313.

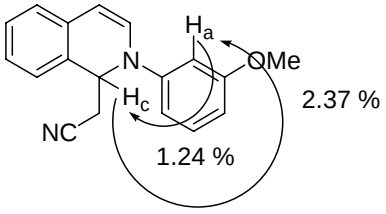
(1,6-Diphenyl-1,2-dihydro-2-pyridinyl)methyl cyanide (4r): Pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.52 (d, *J* = 8.0 Hz, 2 H), 7.22 (t, *J* = 7.5 Hz, 2 H),

7.19 – 7.16 (m, 1 H), 7.13 (d, *J* = 8.5 Hz, 2 H), 7.08 (d, *J* = 9.0 Hz, 2 H), 6.92 (t, *J* = 7.5 Hz, 1 H), 6.30 (dd, *J* = 9.0, 5.5 Hz, 1 H), 6.12 (d, *J* = 4.5 Hz, 1 H), 5.40 (dd, *J* = 9.0, 7.0 Hz, 1 H), 4.81 – 4.77 (m, 1 H), 2.80 (dd, *J* = 17.0, 9.5 Hz, 1 H), 2.46 (dd, *J* = 16.5, 4.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.4, 139.9, 136.9, 128.8, 128.4, 128.2, 127.6, 124.9, 123.4, 123.3, 118.5, 115.6, 109.2, 58.4, 20.9; HRMS: calcd for $C_{19}H_{16}N_2$ 272.1313, found 272.1315.

The regiochemistry of compounds **4g** and **4h** was established by ^{1}H NMR NOE experiments. For example, selective irradiation of the H_a proton at δ 7.35 in **4g** caused 1.47% enhancement of the H_b proton of the isoquinoline ring at δ 6.68 as well as 1.97 % enhancement in H_c proton. Selective irradiation of the H_b proton at δ 6.68 caused 2.79% enhancement of the H_a proton at δ 7.35. Similar result was obtained for **4h** as shown below. These NOE results strongly confirm the structures of **4g** and **4h.**



4g



4h

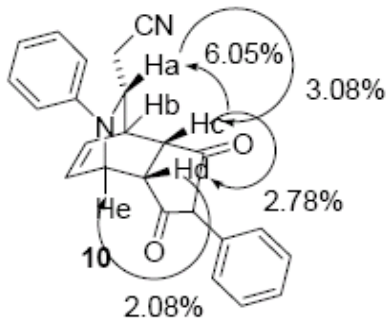
Procedure for cycloaddition reaction of 1,2-dihydropyridine (4o) with *N*-phenyl-maleimide (9):

A 25 mL round-bottomed side-arm flask containing *N*-phenyl-maleimide (**9**) (1.00 mmol) was evacuated and purged with nitrogen gas three times. To the flask were then added (1-Phenyl-1,2-dihydro-2-pyridinyl)methyl cyanide (**4o**) (1.00 mmol) and toluene (3.0 mL) via syringe. The reaction mixture was allowed to stir at 80 °C for 6 h. The crude residue was purified through a silica gel column using hexane and ethyl acetate as eluent to give pure **10**.

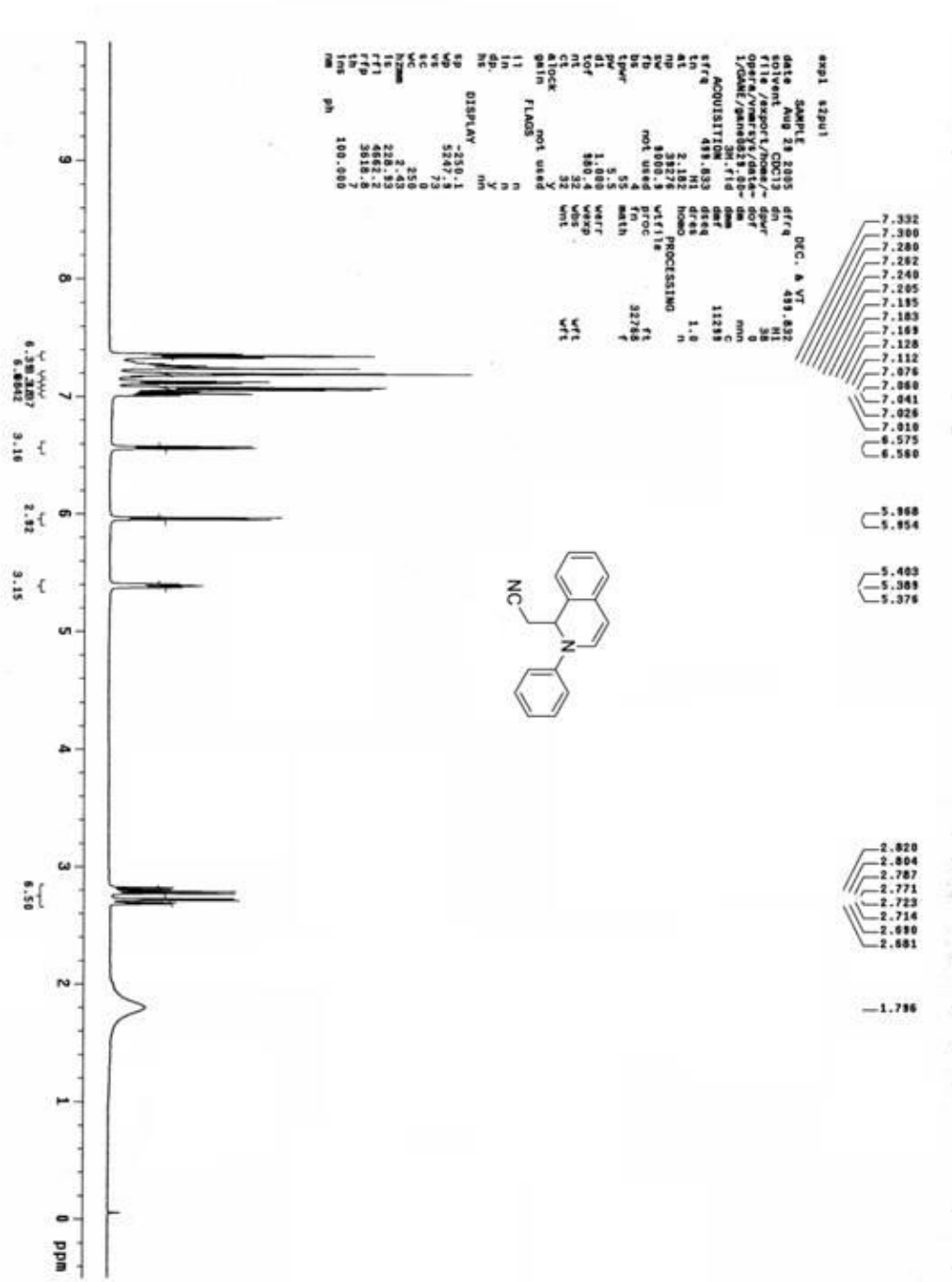
Compound 10:

Pale yellow viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.31 (m, 5 H), 7.19 (d, *J* = 6.0 Hz, 2 H), 6.99 – 6.87 (m, 3 H), 6.75 (t, *J* = 8.0 Hz, 1 H), 6.51 (t, *J* = 7.2 Hz, 1 H), 5.05 (t, *J* = 9.0 Hz, 1 H, *He*), 3.81 (m, 2 H, *Ha and Hb*), 3.43 (dd, *J* = 8.0, 4.0 Hz, 1 H, *Hd*), 3.10 (dd, *J* = 8.0, 2.4 Hz, 1 H, *Hc*), 2.73 (dd, *J* = 17.6, 3.2 Hz, 1 H), 2.33 (dd, *J* = 10.0, 3.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.9, 175.2, 144.6, 133.3, 131.4, 130.5, 129.9, 129.0, 128.7, 126.2, 119.5, 116.8, 113.8, 55.9, 48.9, 41.8, 40.9, 36.2, 21.7; HRMS (EI): calcd for $C_{23}H_{19}N_3O_2$ 369.1477, found 369.1475.

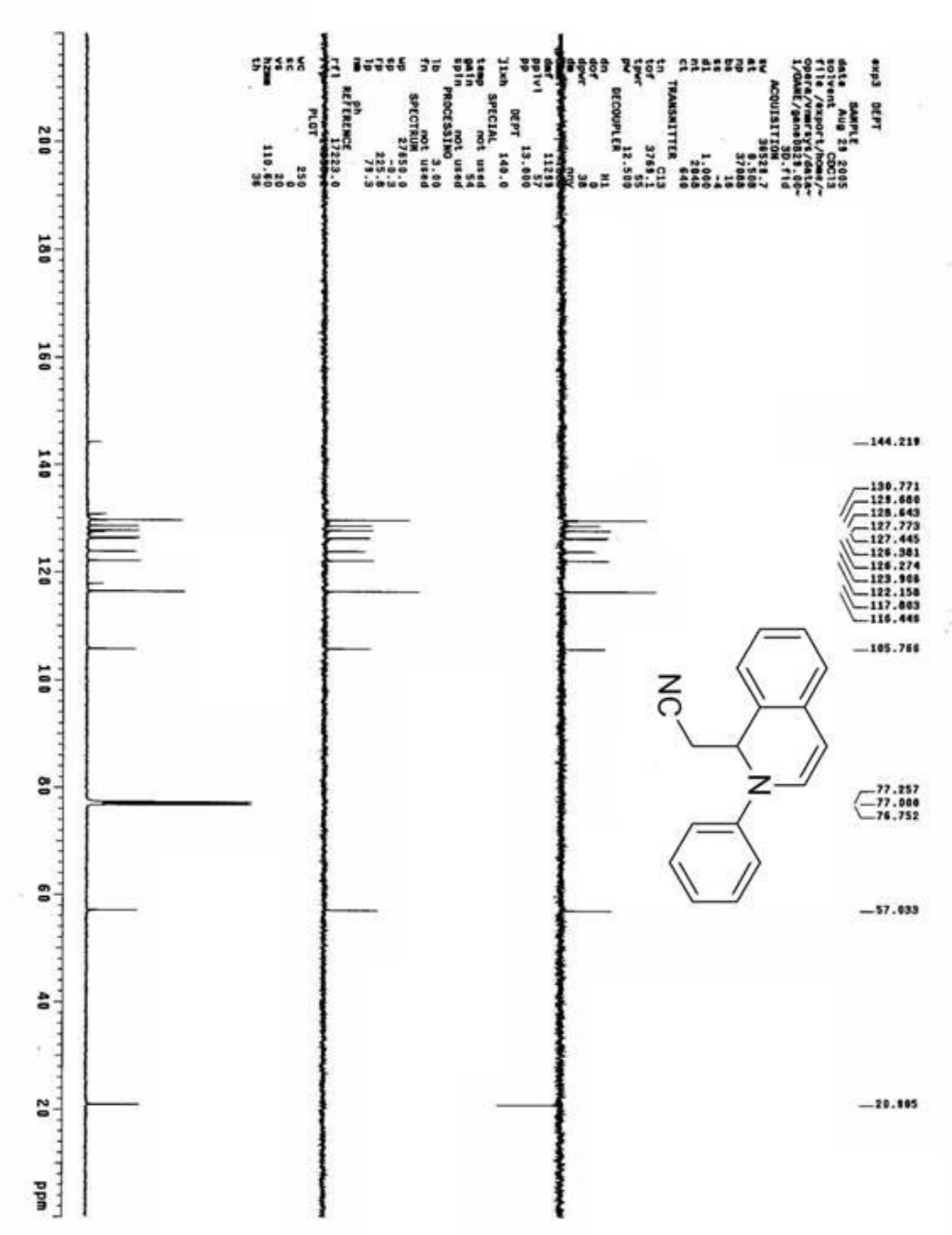
Chemical shifts of protons Ha-e in compound **10** were assigned by homo-decoupling experiments, while the stereochemistry of compound **10** was determined by NOE experiments. For example, selective irradiation of Ha at δ 3.81 in **10** caused 3.08% enhancement of Hc at δ 3.10. Selective irradiation of Hc at δ 3.10 caused 6.05% enhancement of the Ha and Hb at δ 3.81 as well as 2.78% enhancement of Hd at δ 3.43. Selective irradiation of Hd at δ 3.43 caused 2.08% enhancement of He at δ 5.05 as well as 2.42% enhancement of Hc at δ 3.10.



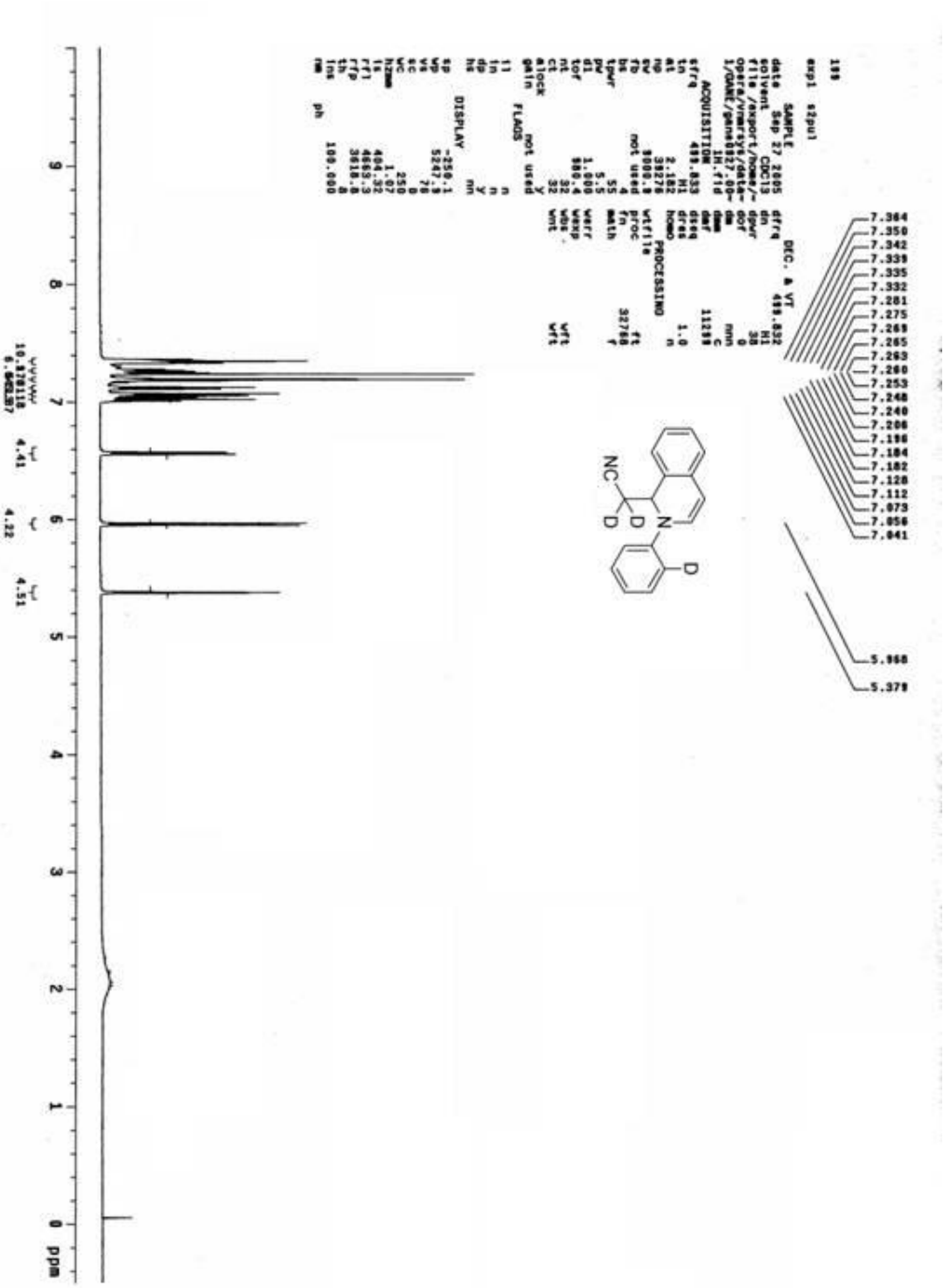
^{1}H NMR spectrum of compound **4a**:



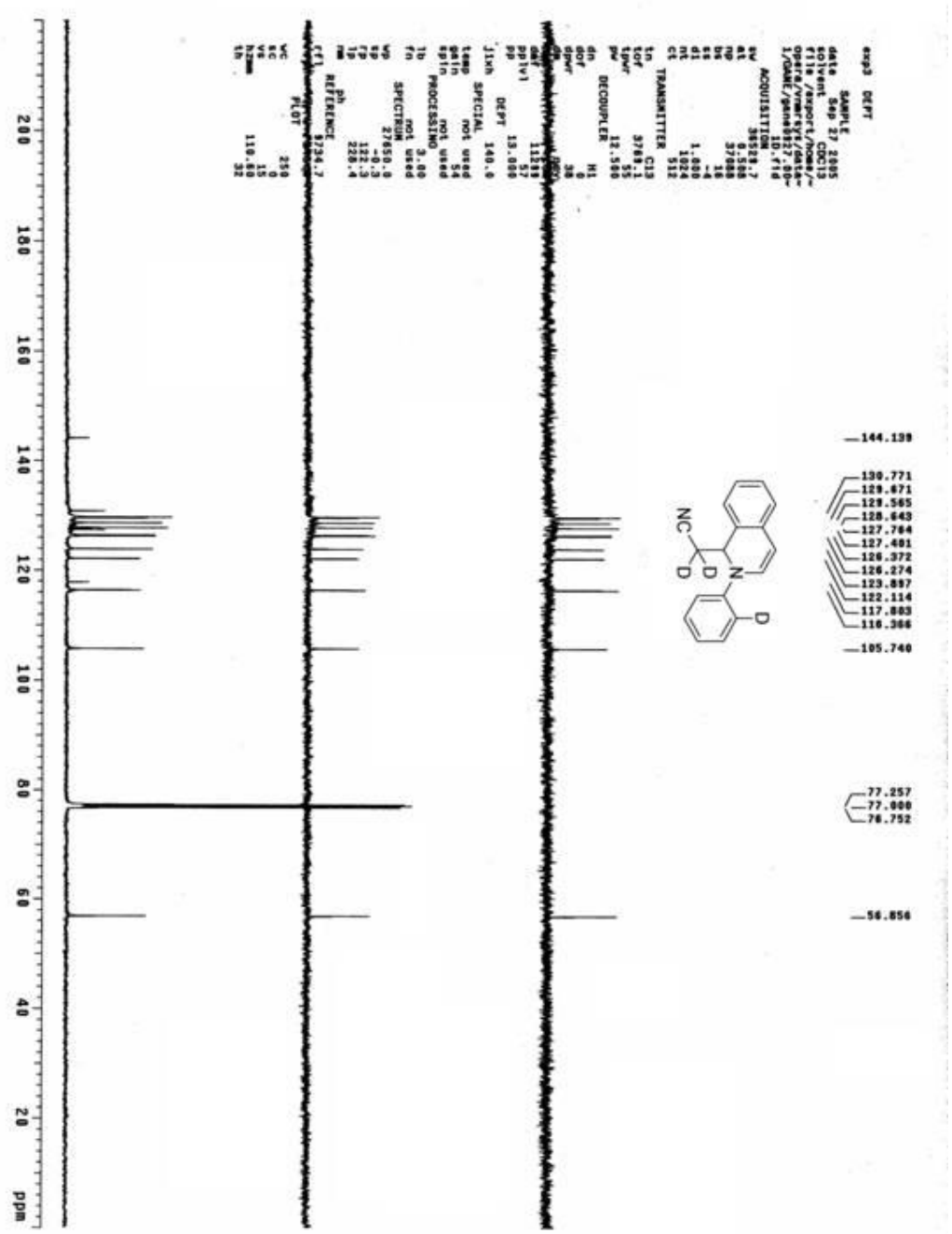
^{13}C NMR spectrum of compound **4a**:



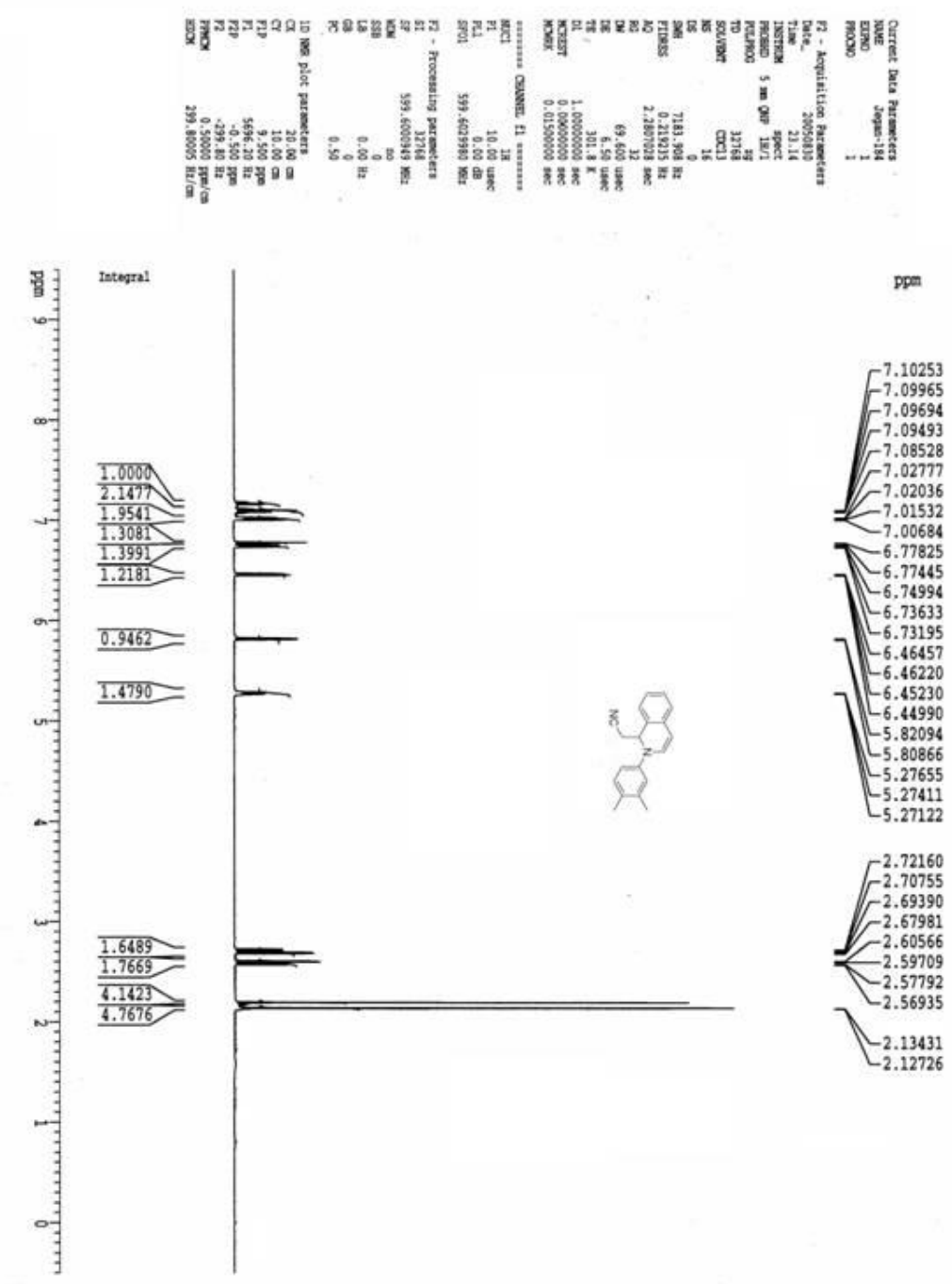
^{1}H NMR spectrum of compound **4b**:



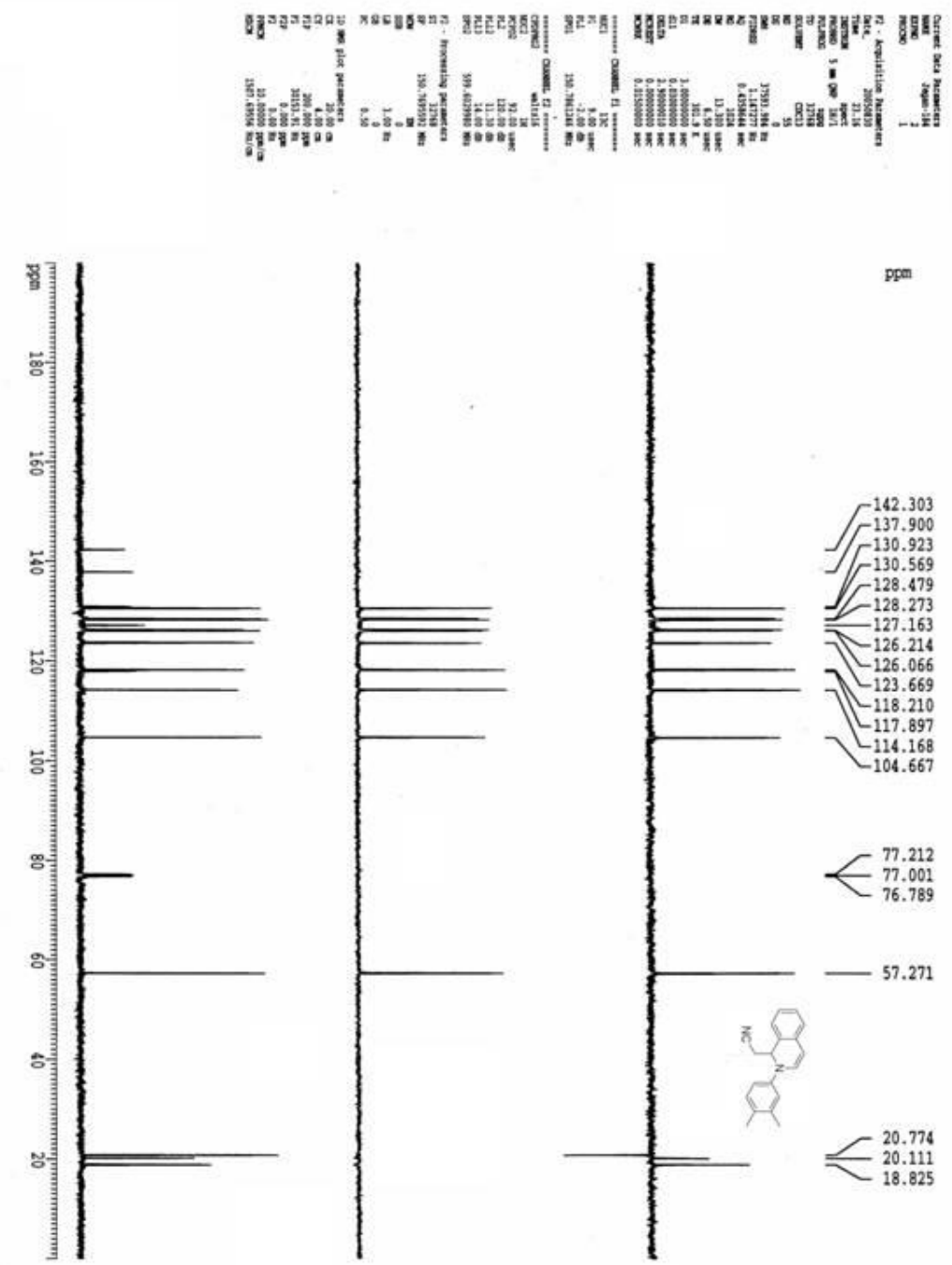
^{13}C NMR spectrum of compound **4b**:



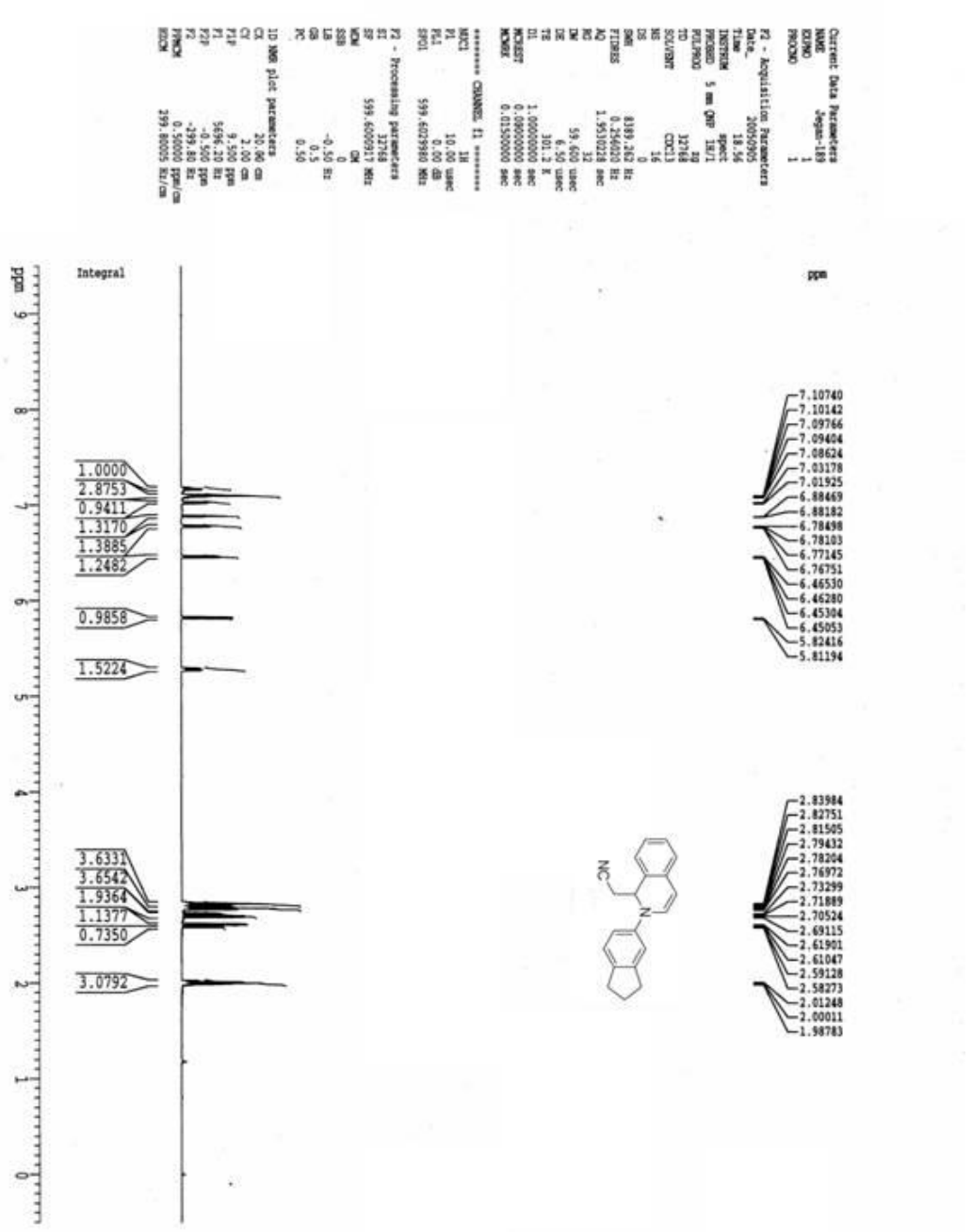
^{1}H NMR spectrum of compound **4c**:



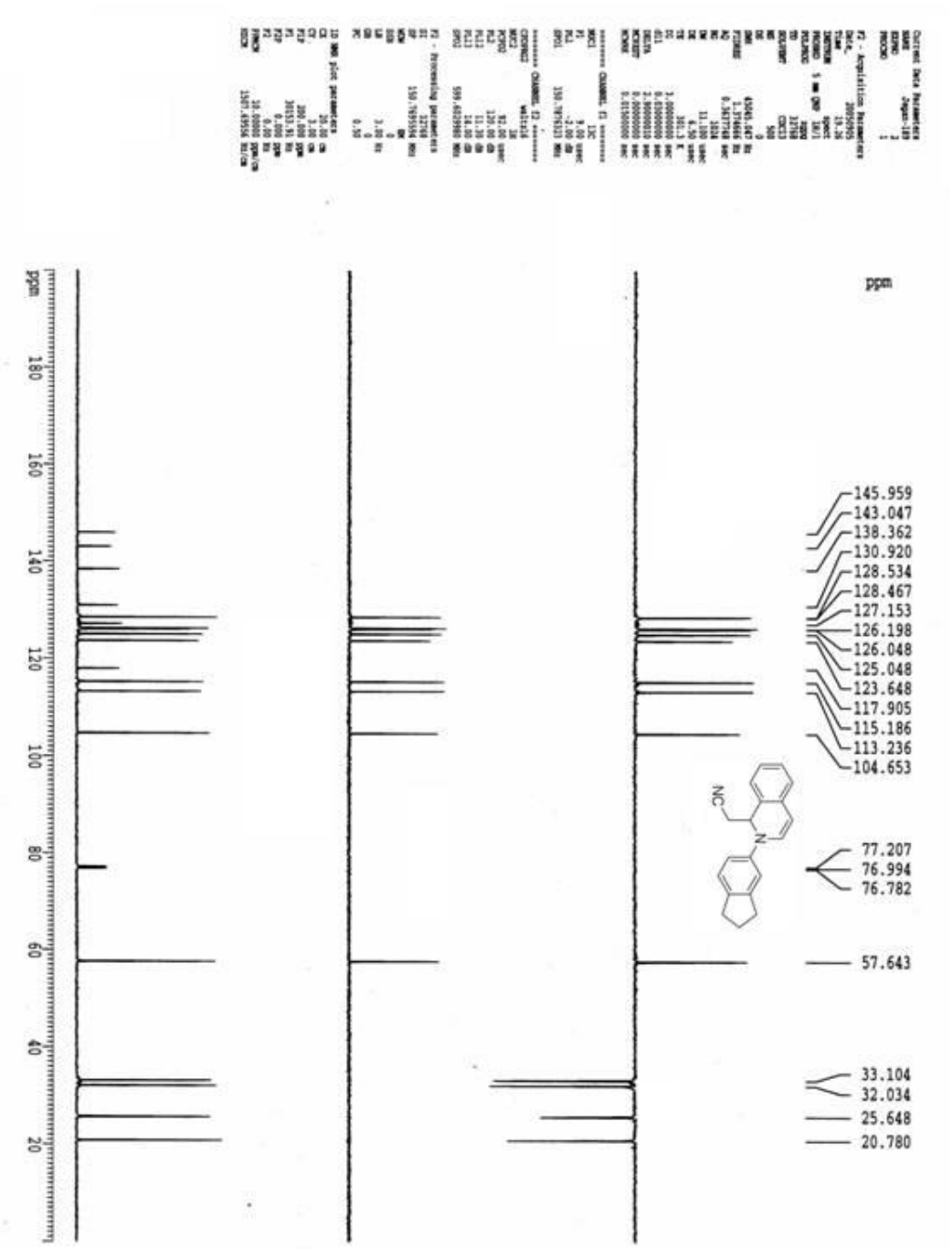
^{13}C NMR spectrum of compound **4c**:



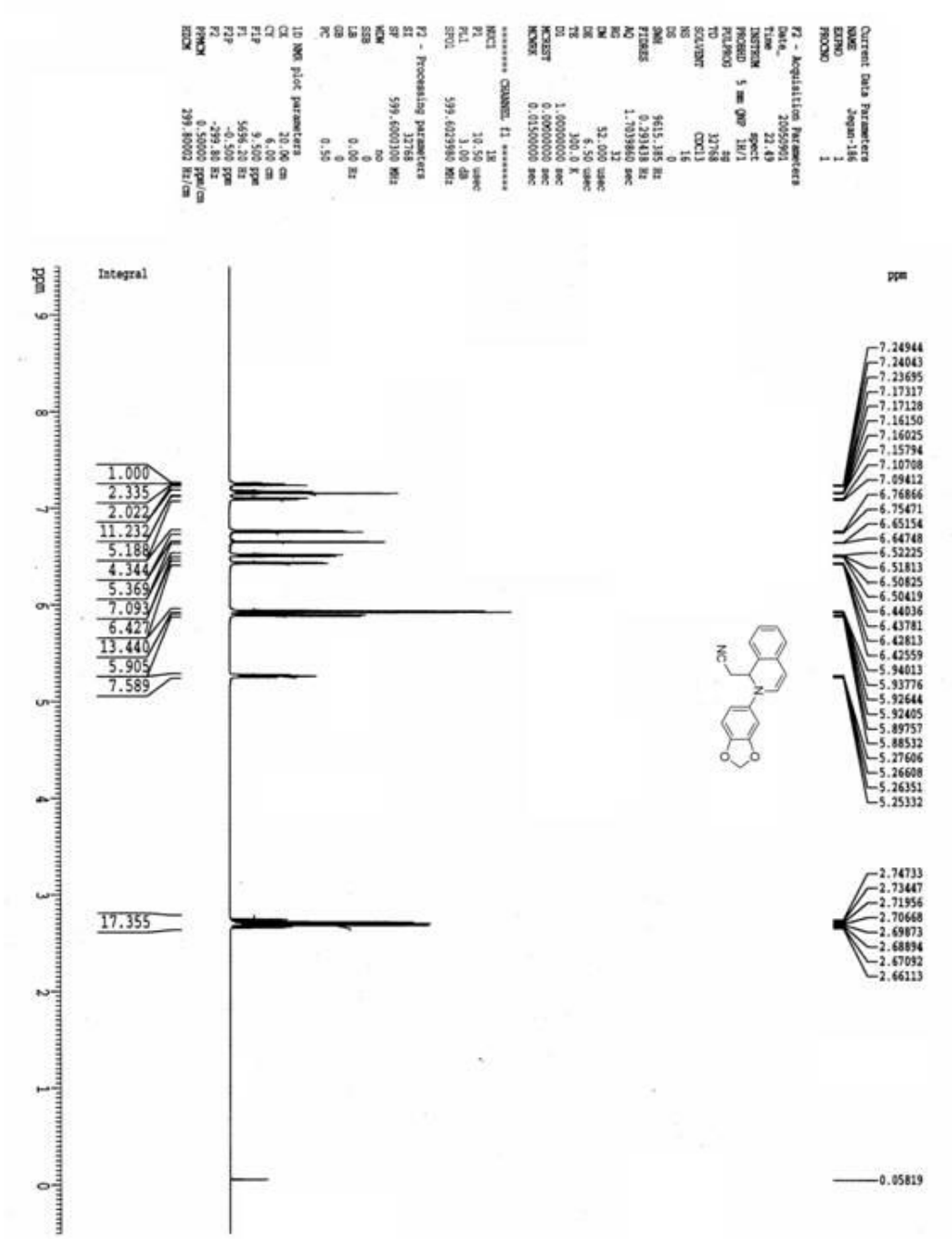
^{1}H NMR spectrum of compound **4d**:



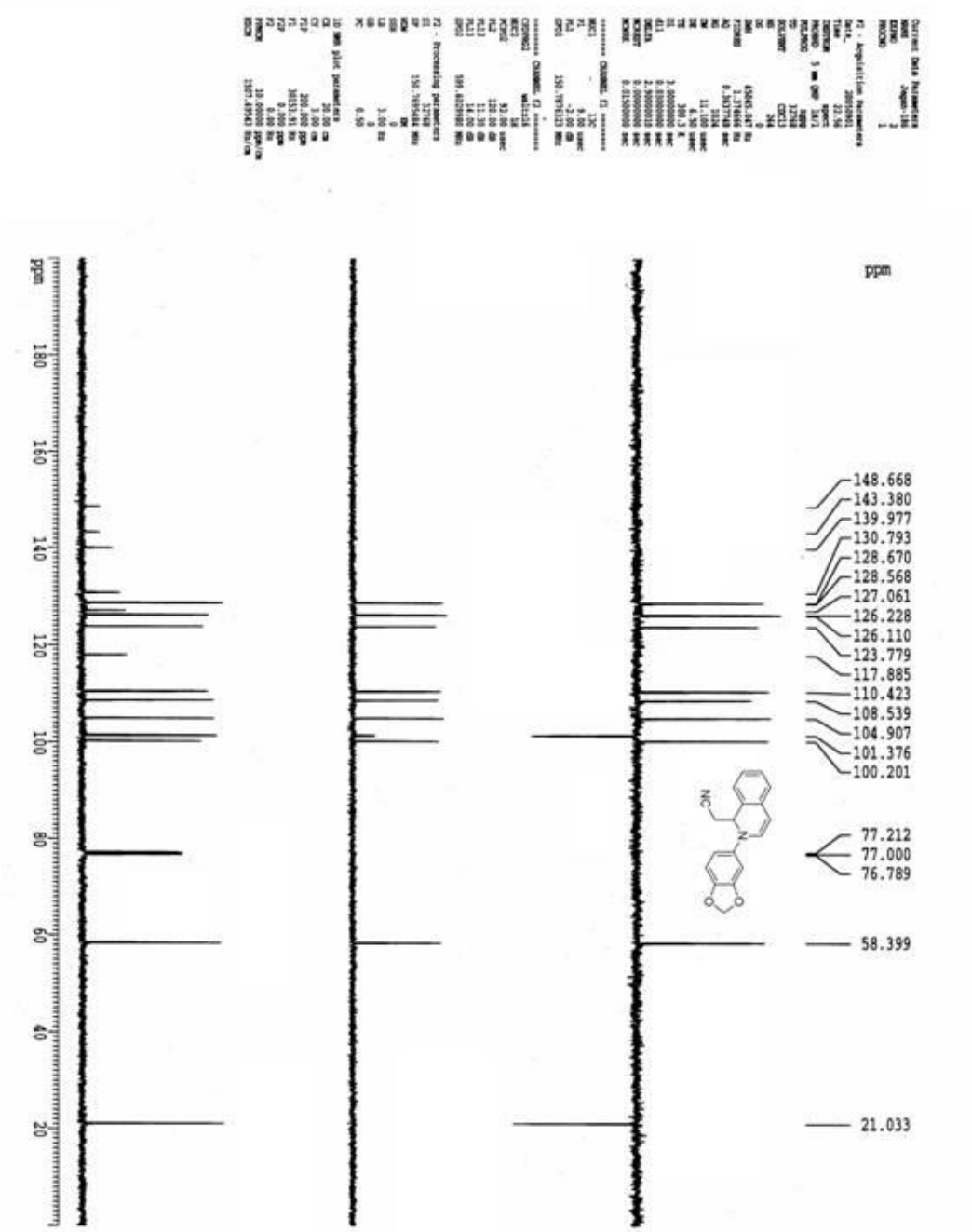
^{13}C NMR spectrum of compound **4d**:



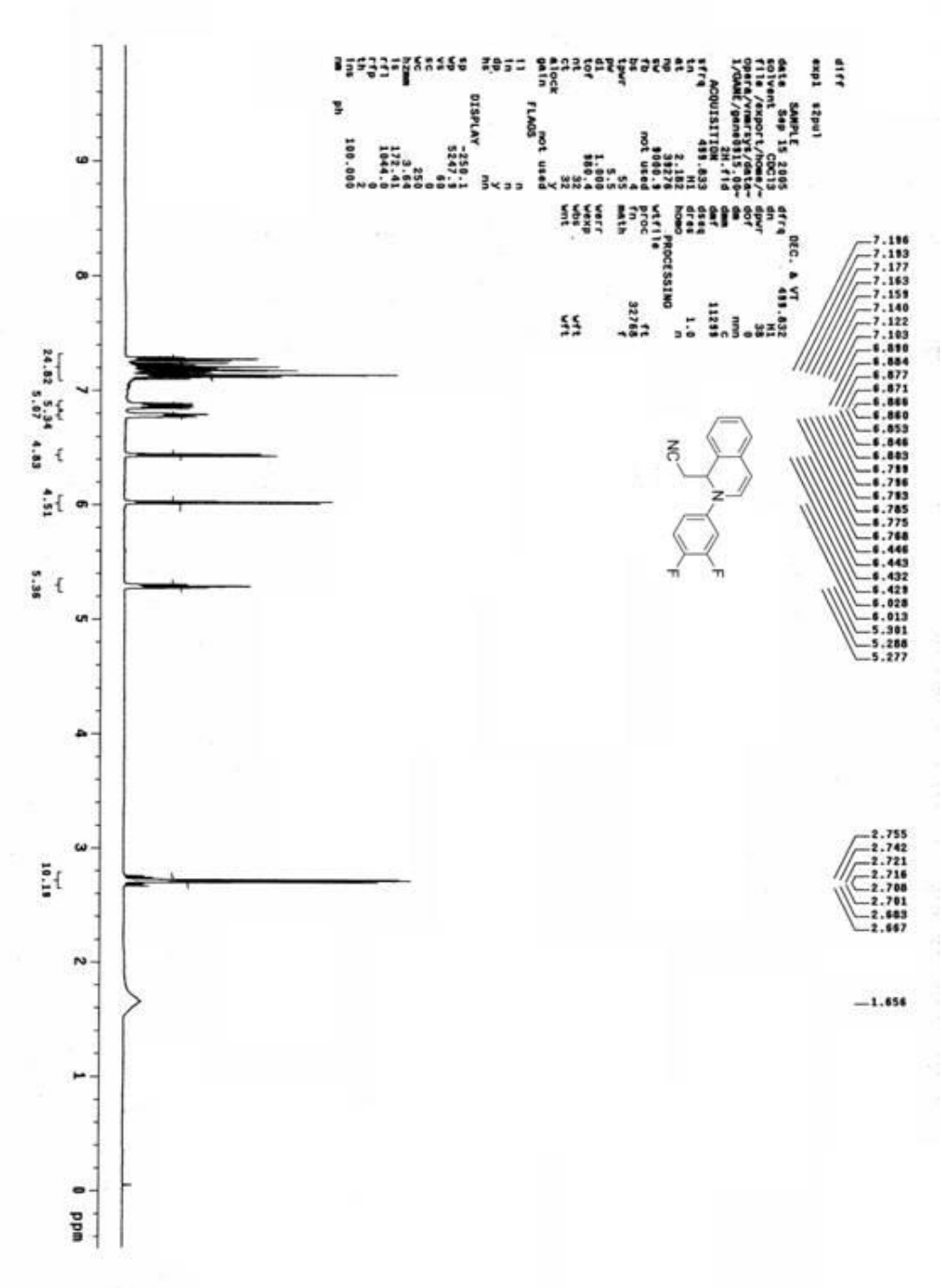
^{1}H NMR spectrum of compound **4e**:



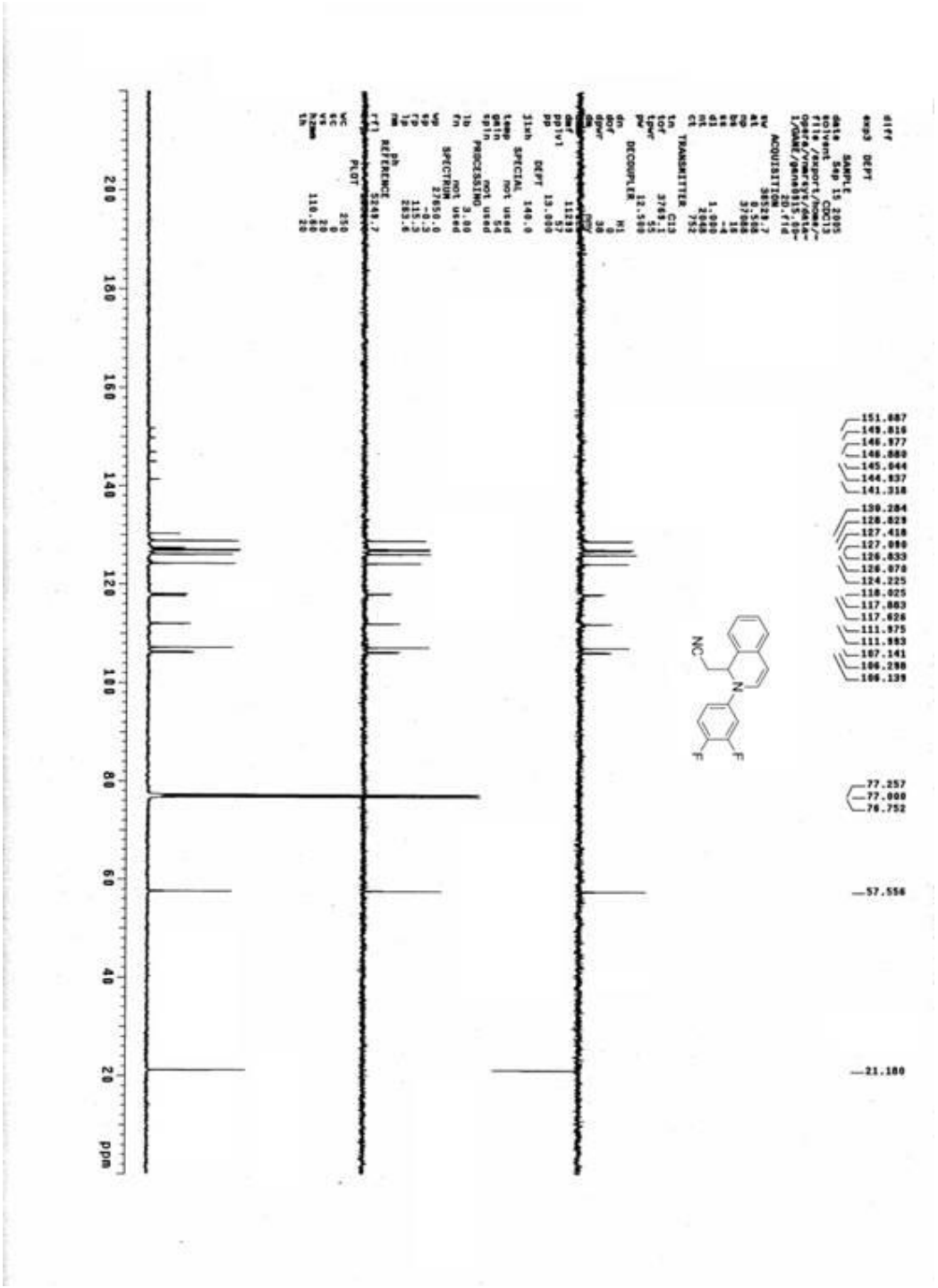
^{13}C NMR spectrum of compound **4e**:



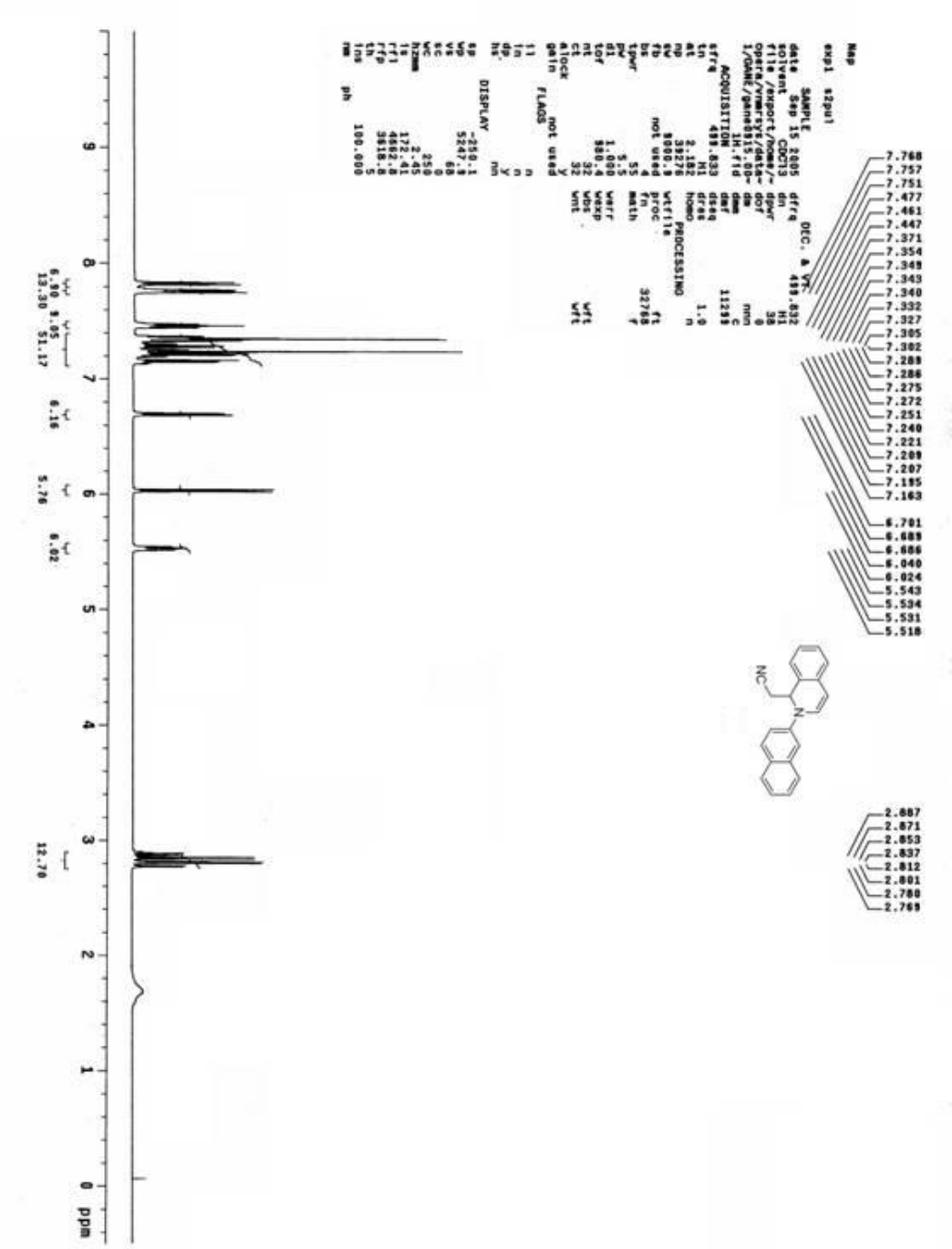
^{1}H NMR spectrum of compound **4f**:



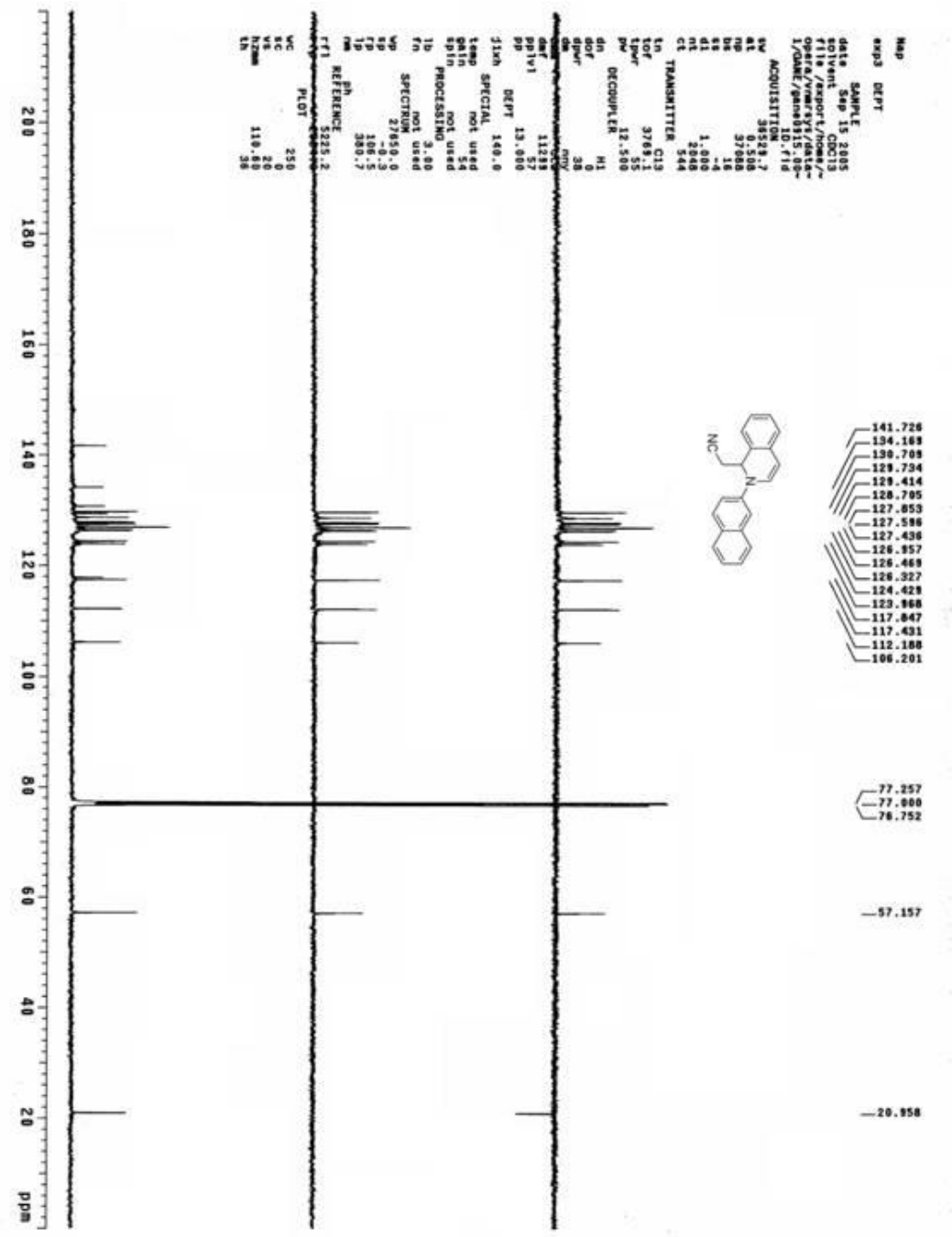
^{13}C NMR spectrum of compound **4f**:



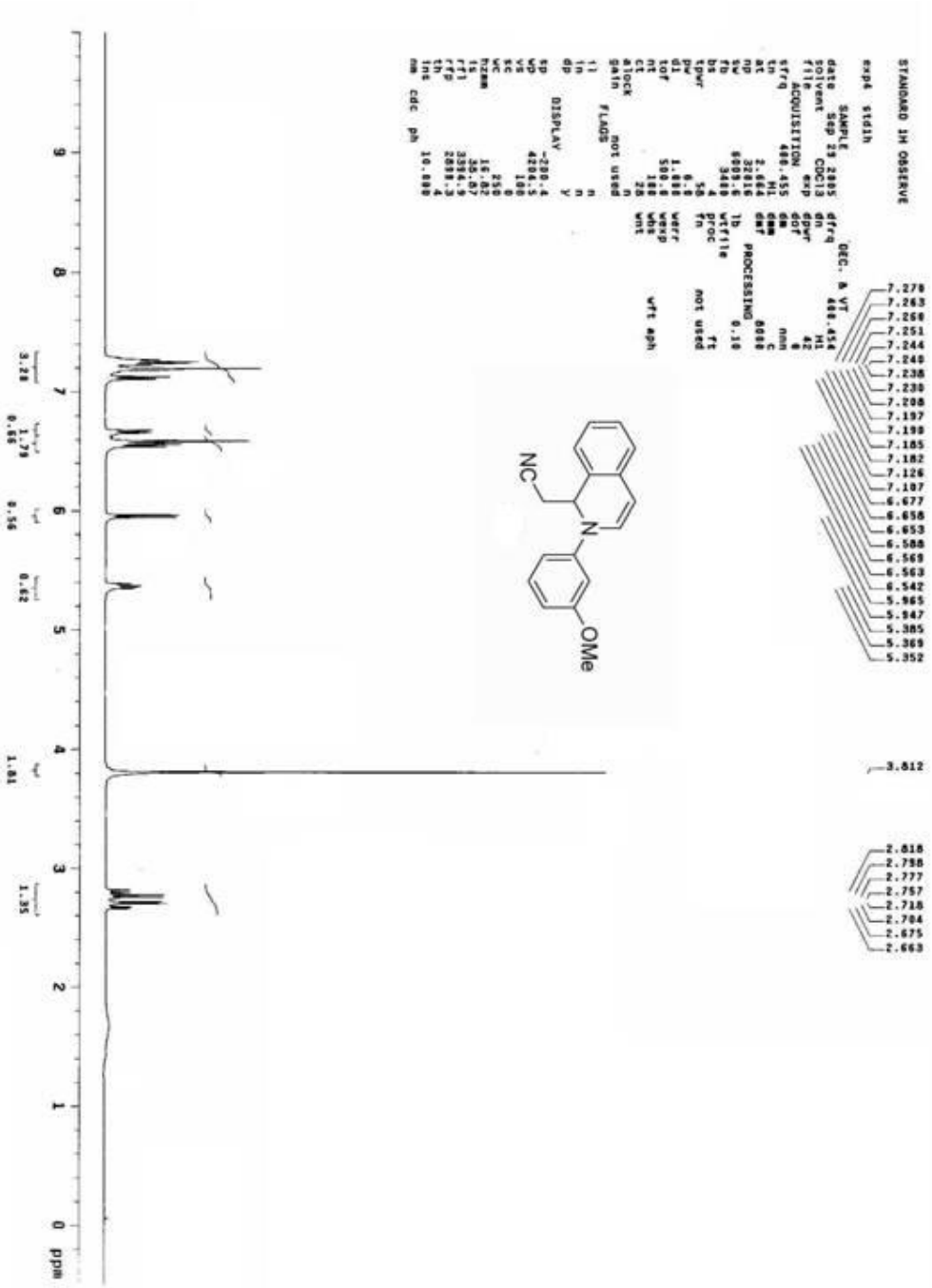
^{1}H NMR spectrum of compound **4g**:



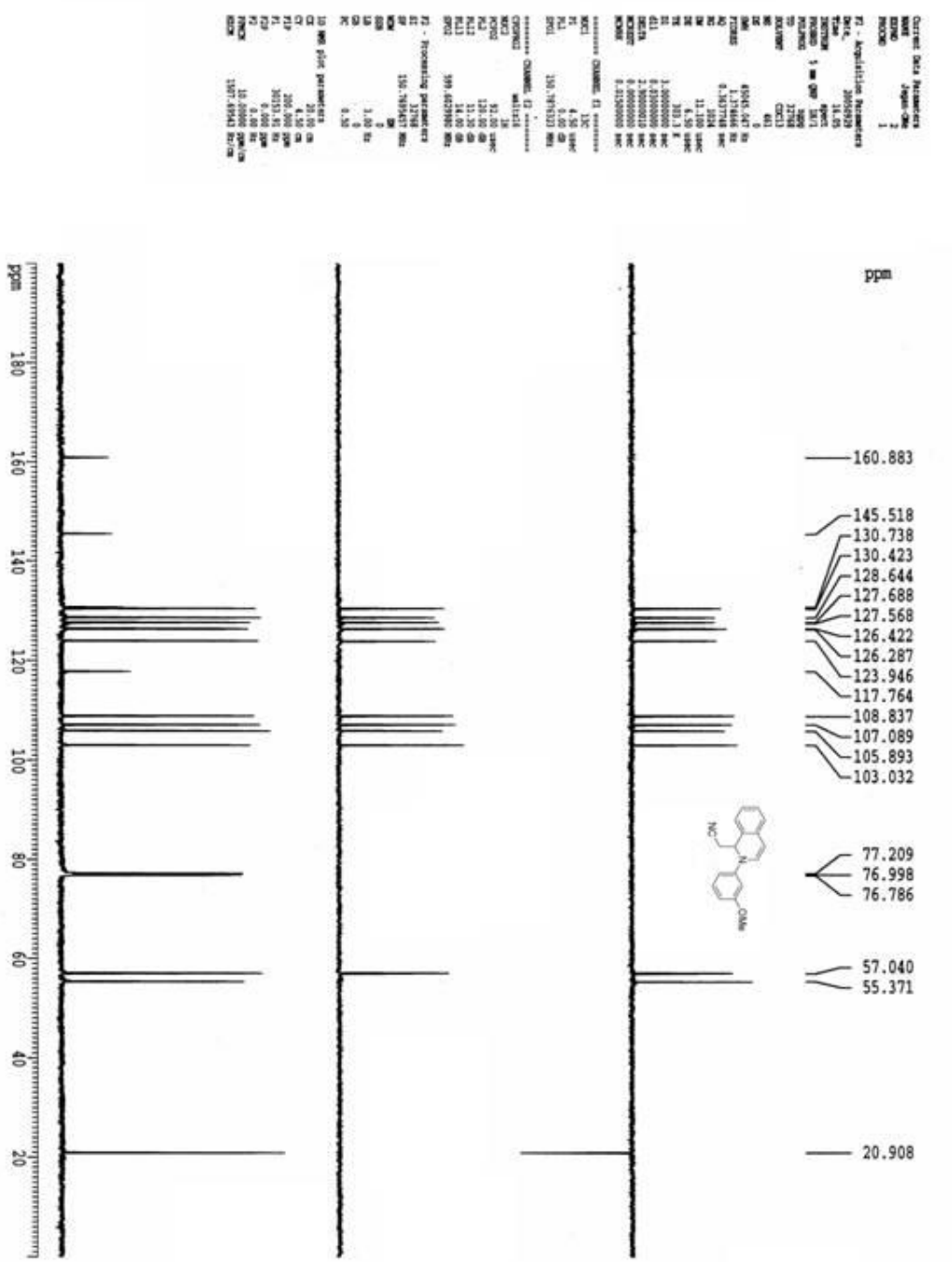
^{13}C NMR spectrum of compound **4g**:



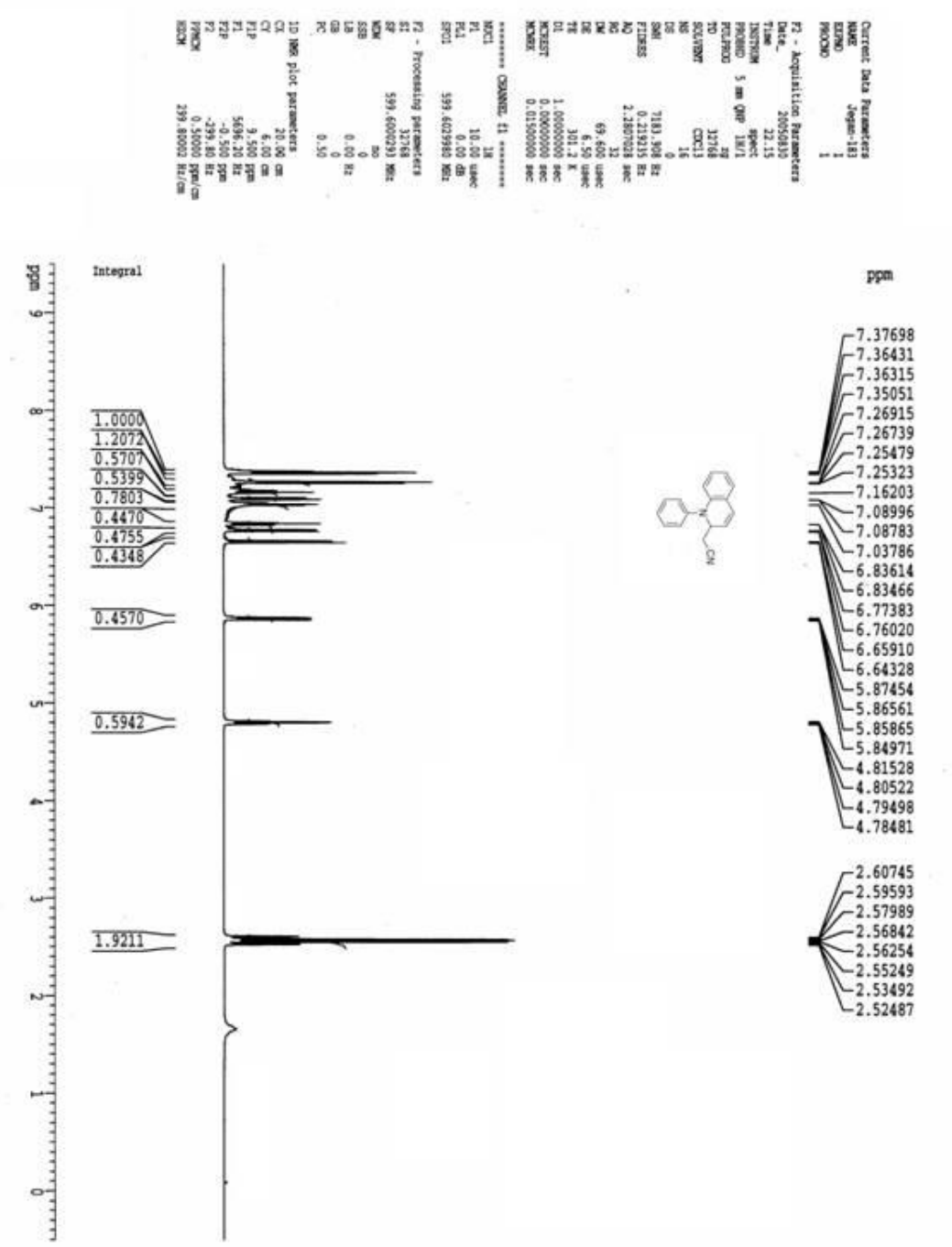
^{1}H NMR spectrum of compound **4h**:



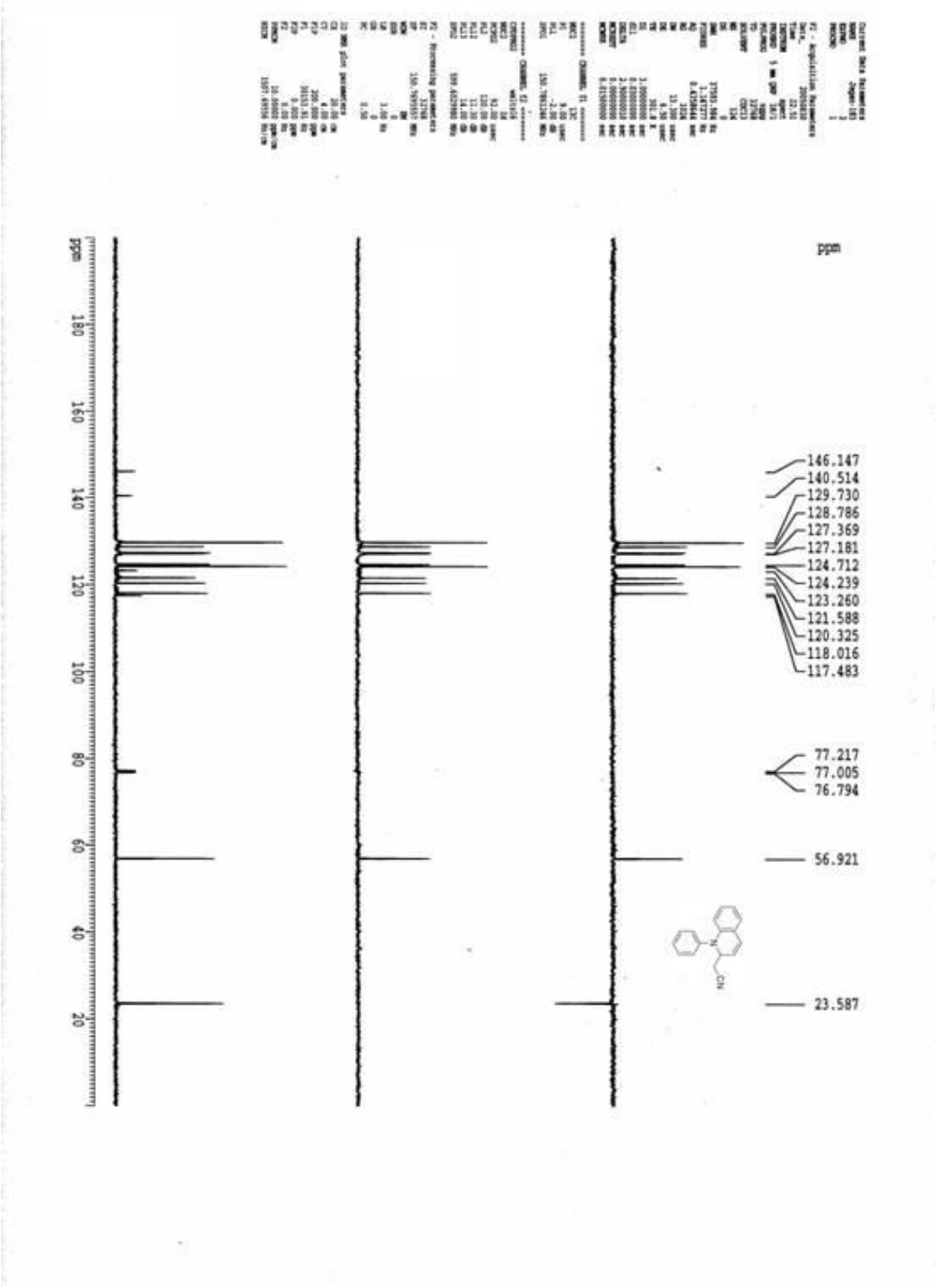
^{13}C NMR spectrum of compound **4h**:



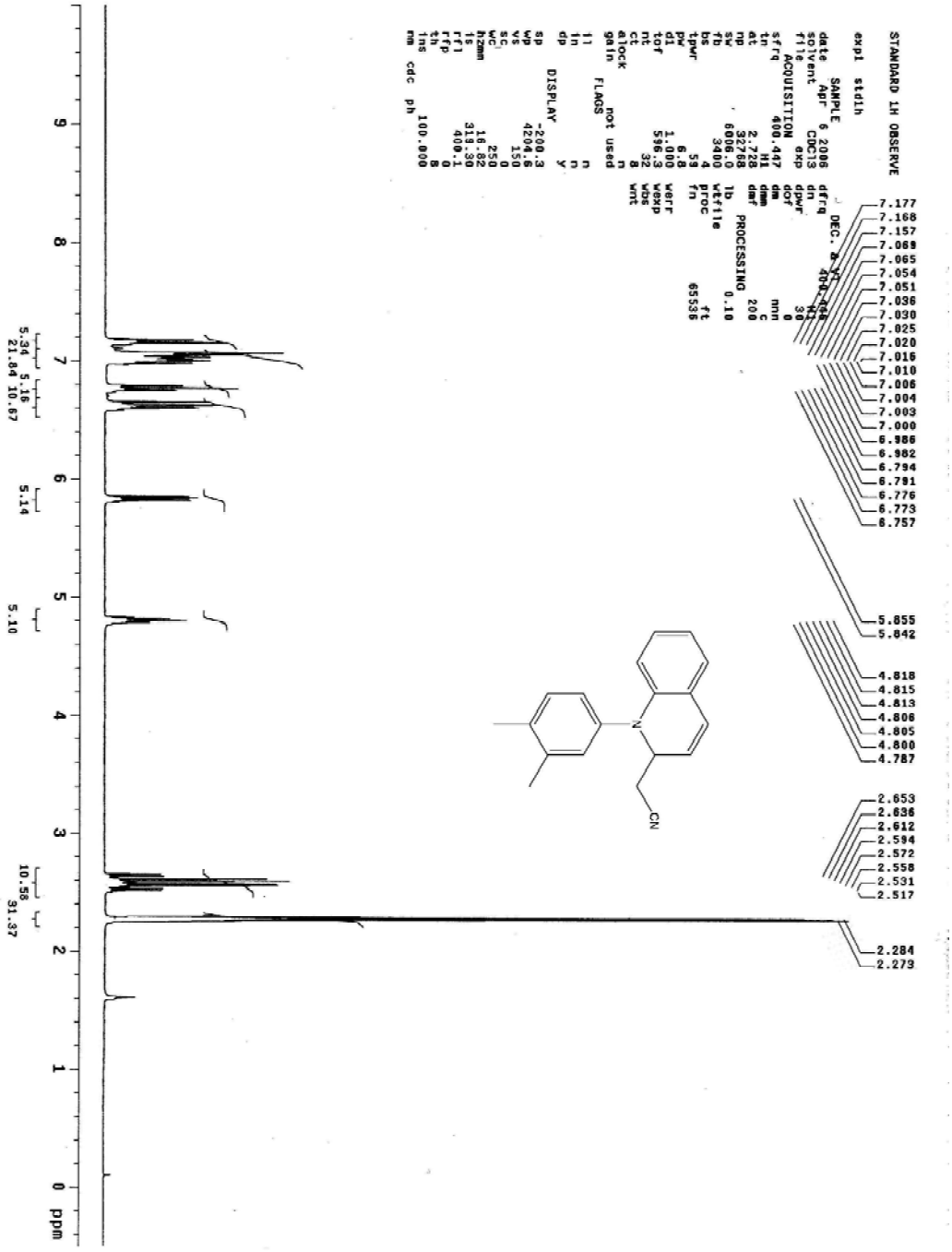
^{1}H NMR spectrum of compound **4i**:



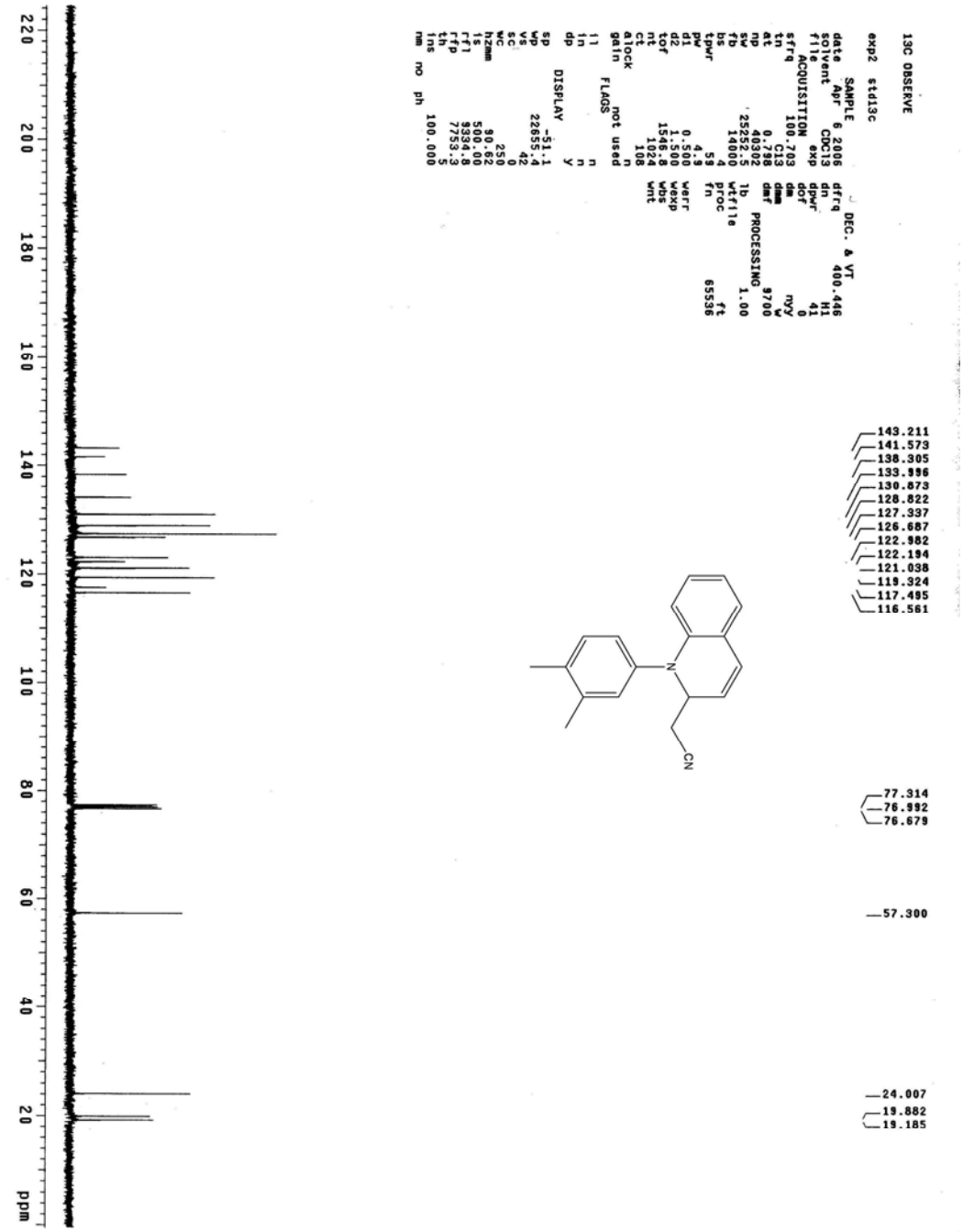
^{13}C NMR spectrum of compound **4i**:



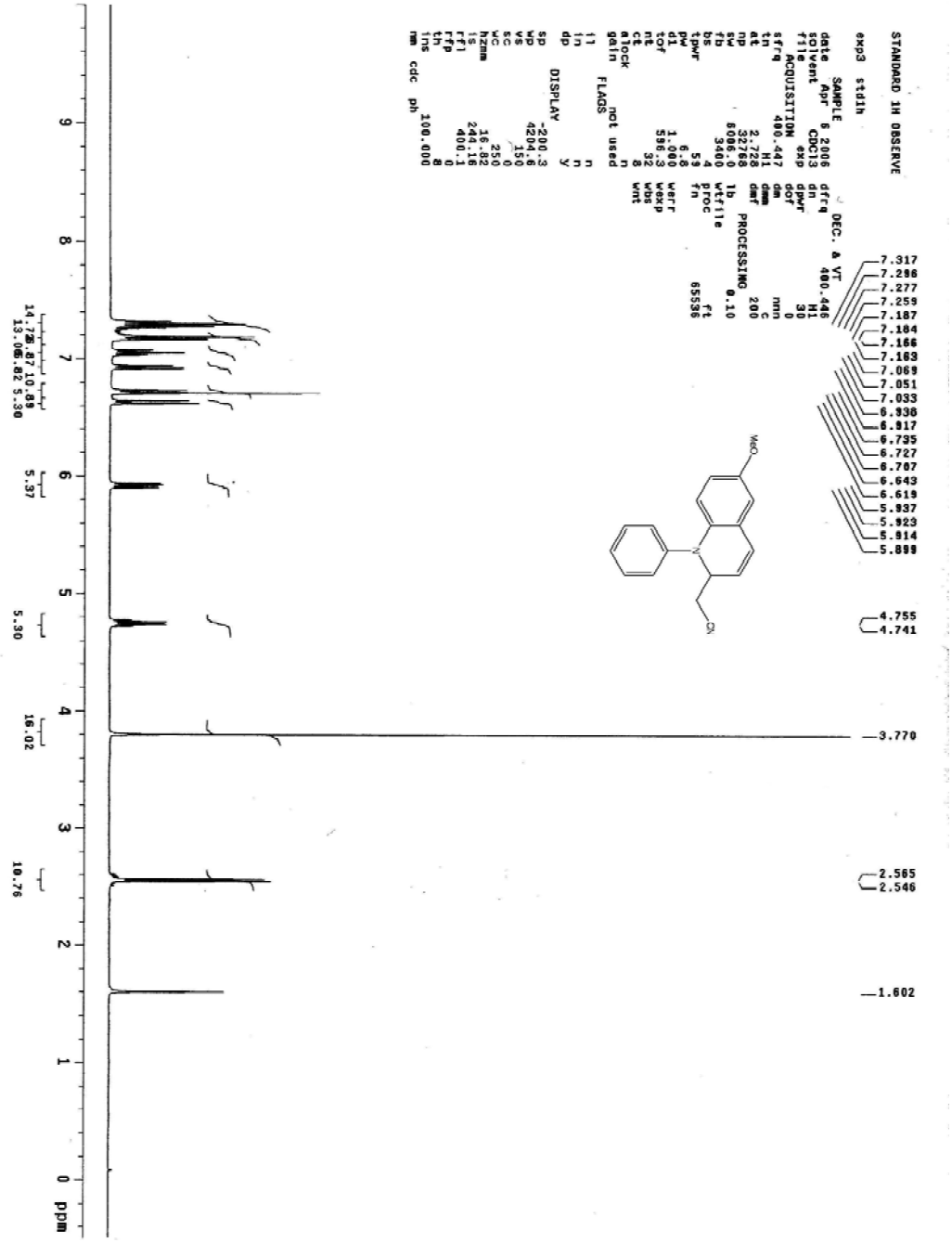
^{1}H NMR spectrum of compound **4j**:



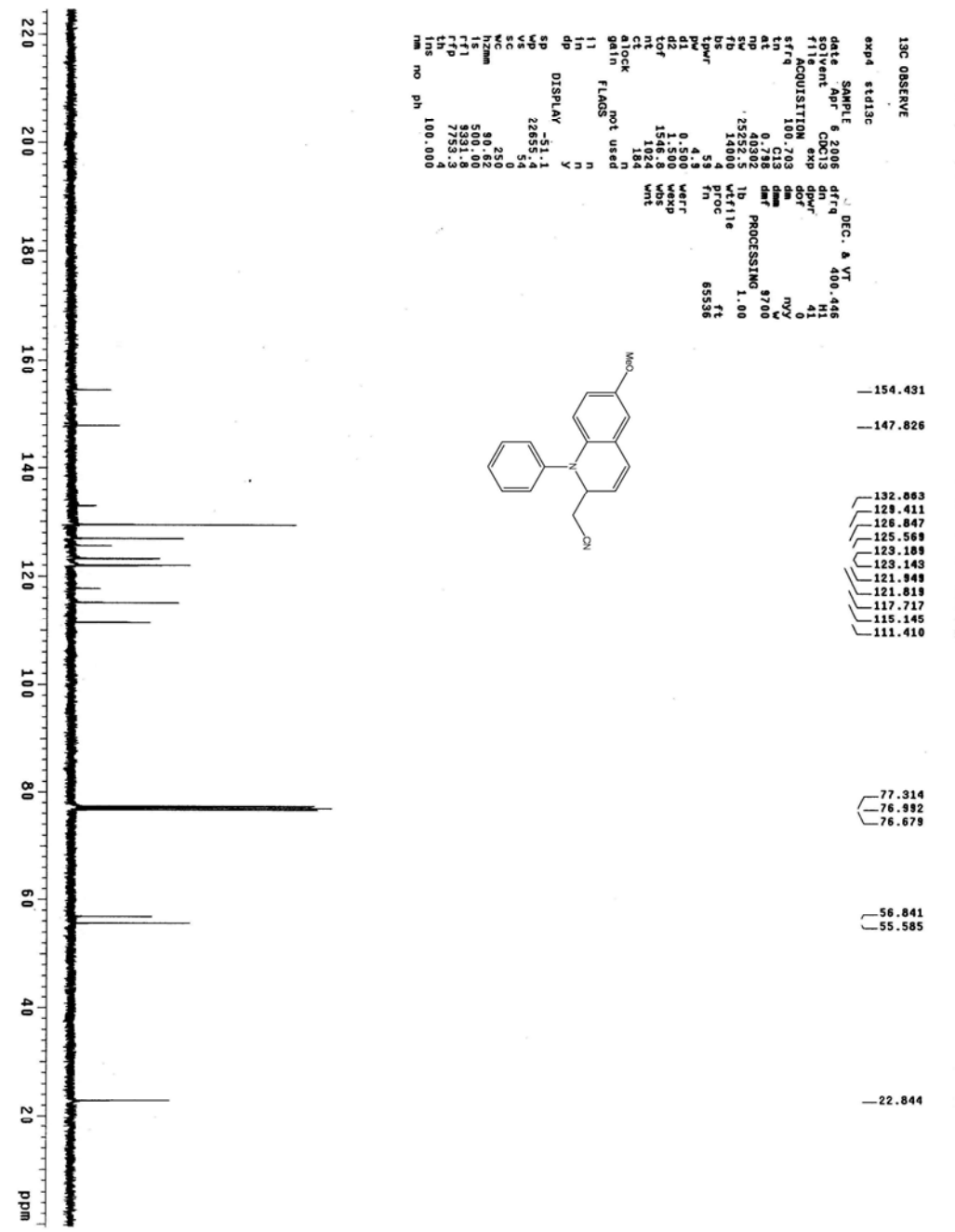
^{13}C NMR spectrum of compound **4j**:



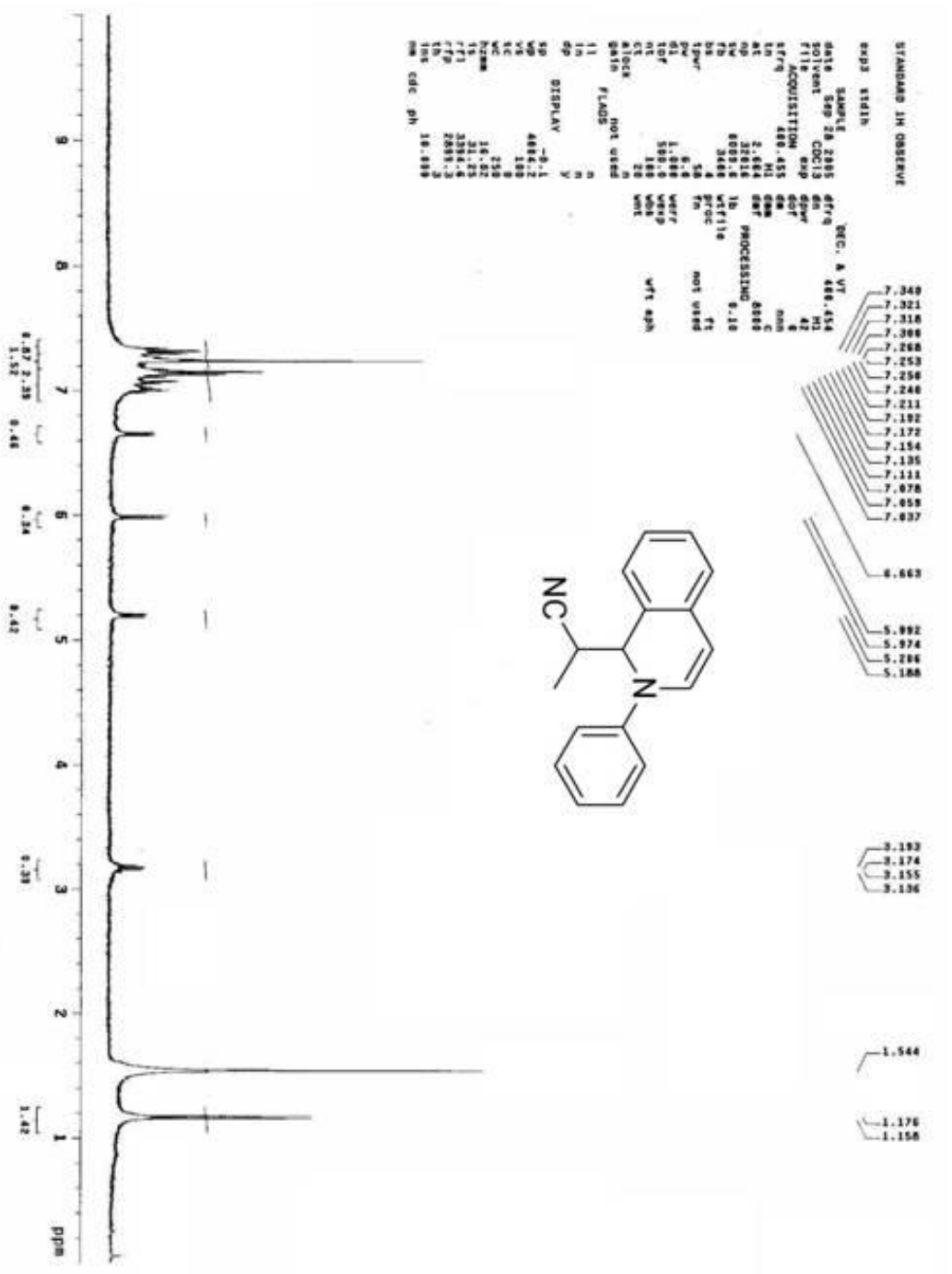
^{1}H NMR spectrum of compound **4k**:



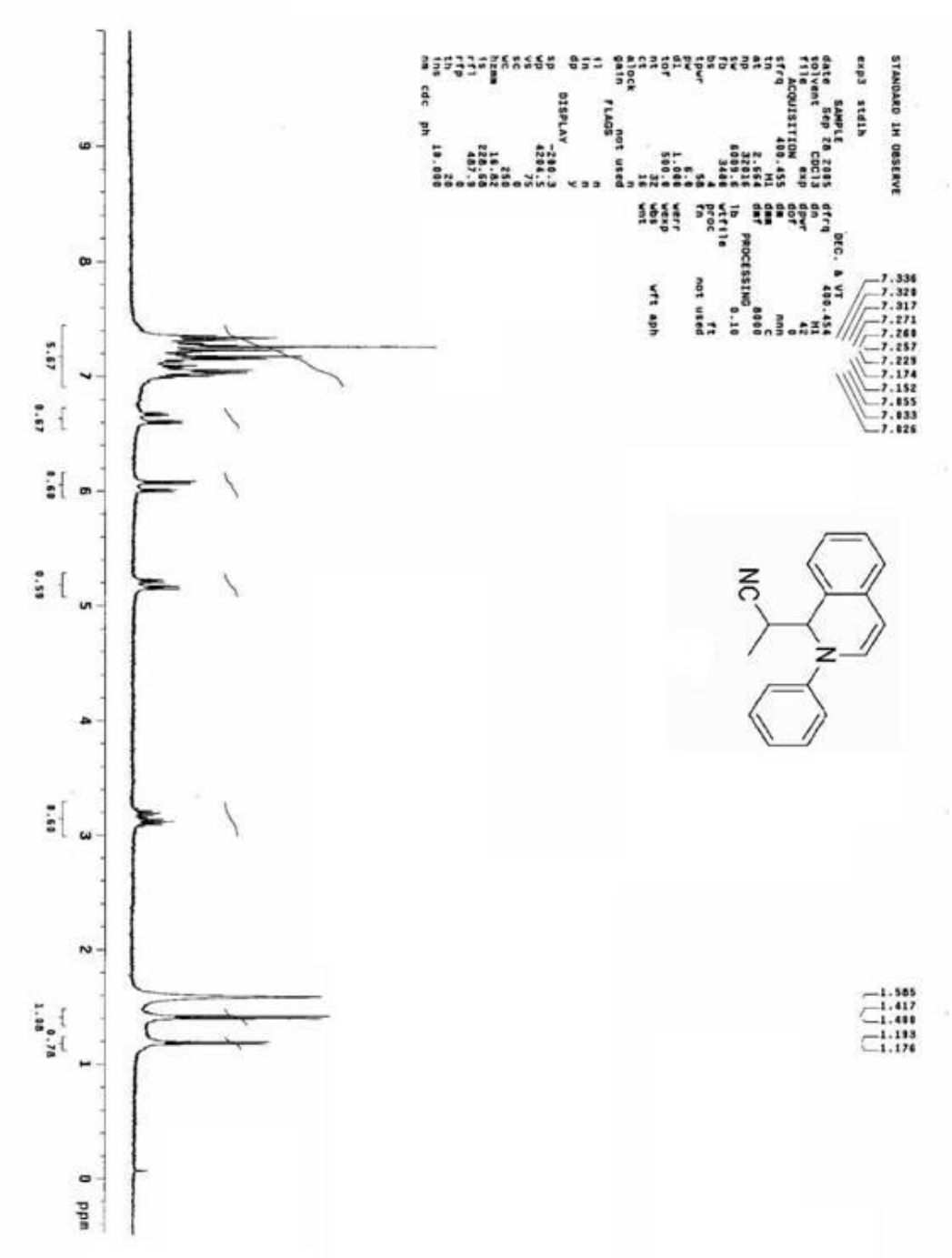
^{13}C NMR spectrum of compound **4k**:



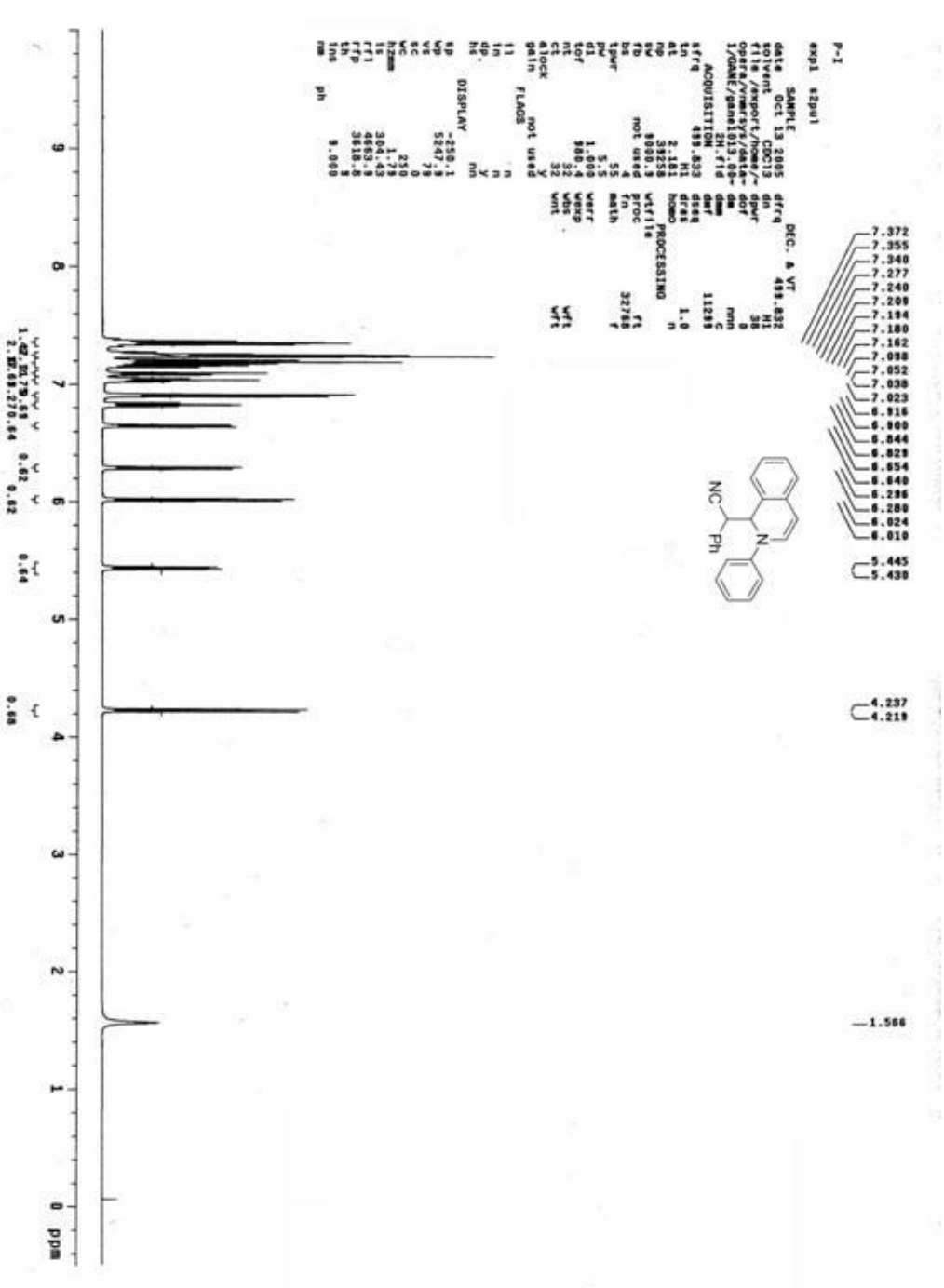
^{1}H NMR spectrum of compound **4l** (one pure diastereoisomeric form):



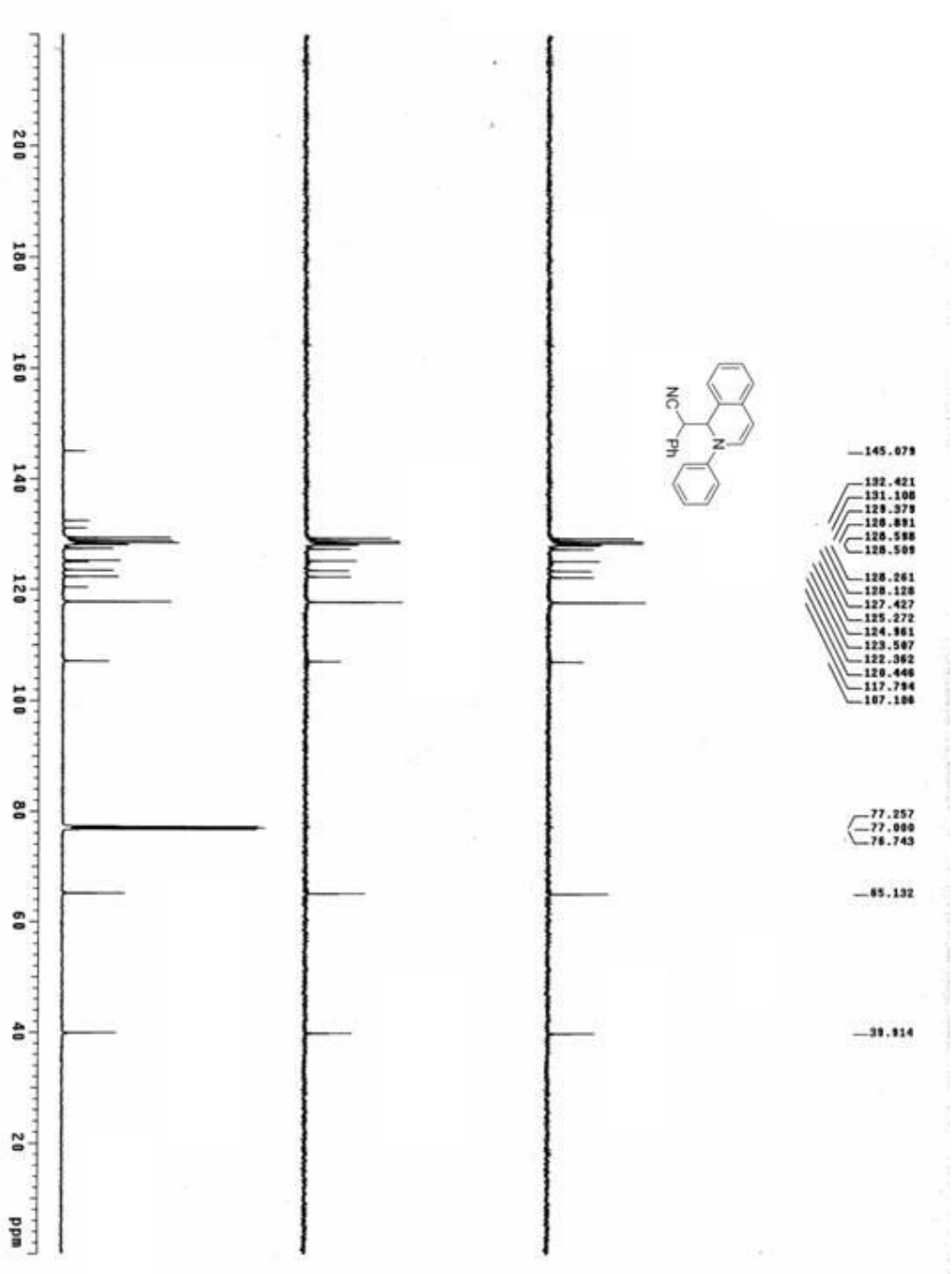
^{1}H NMR spectrum of compound **4l** (1:1 diastereoisomeric mixture form):



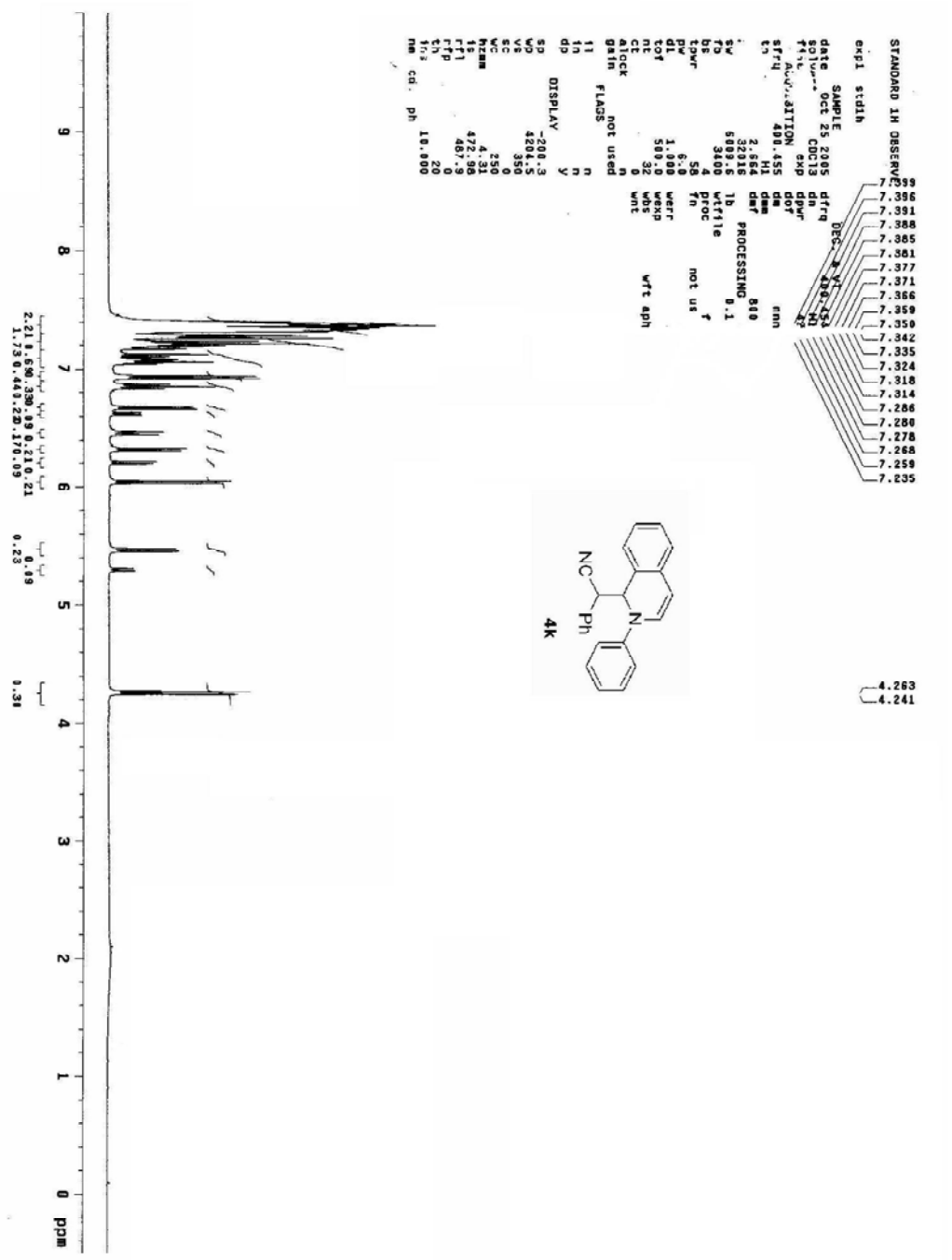
^{1}H NMR spectrum of compound **4m** (one pure diastereoisomeric form):



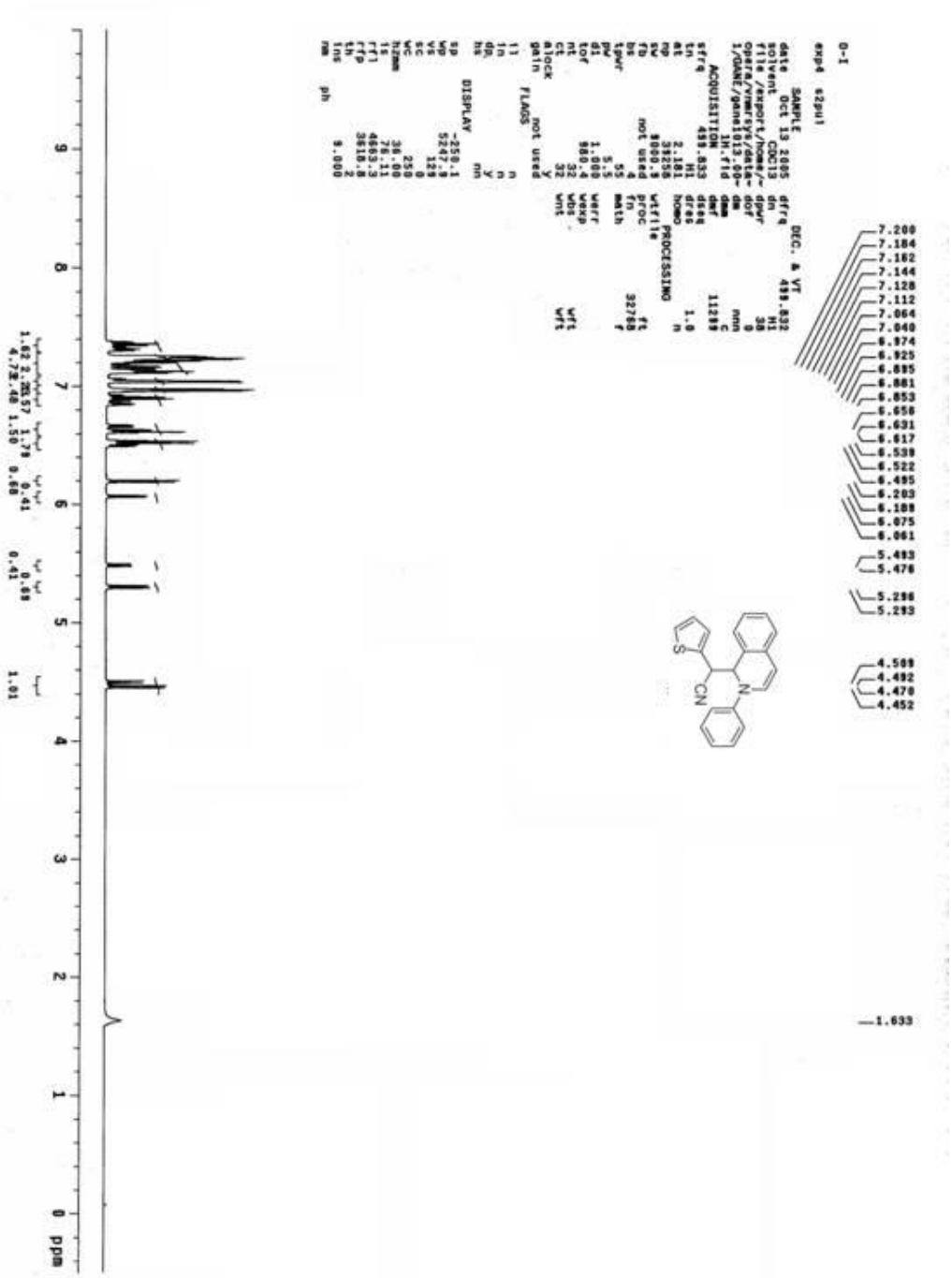
^{13}C NMR spectrum of compound **4m** (one pure diasteroisomeric form):



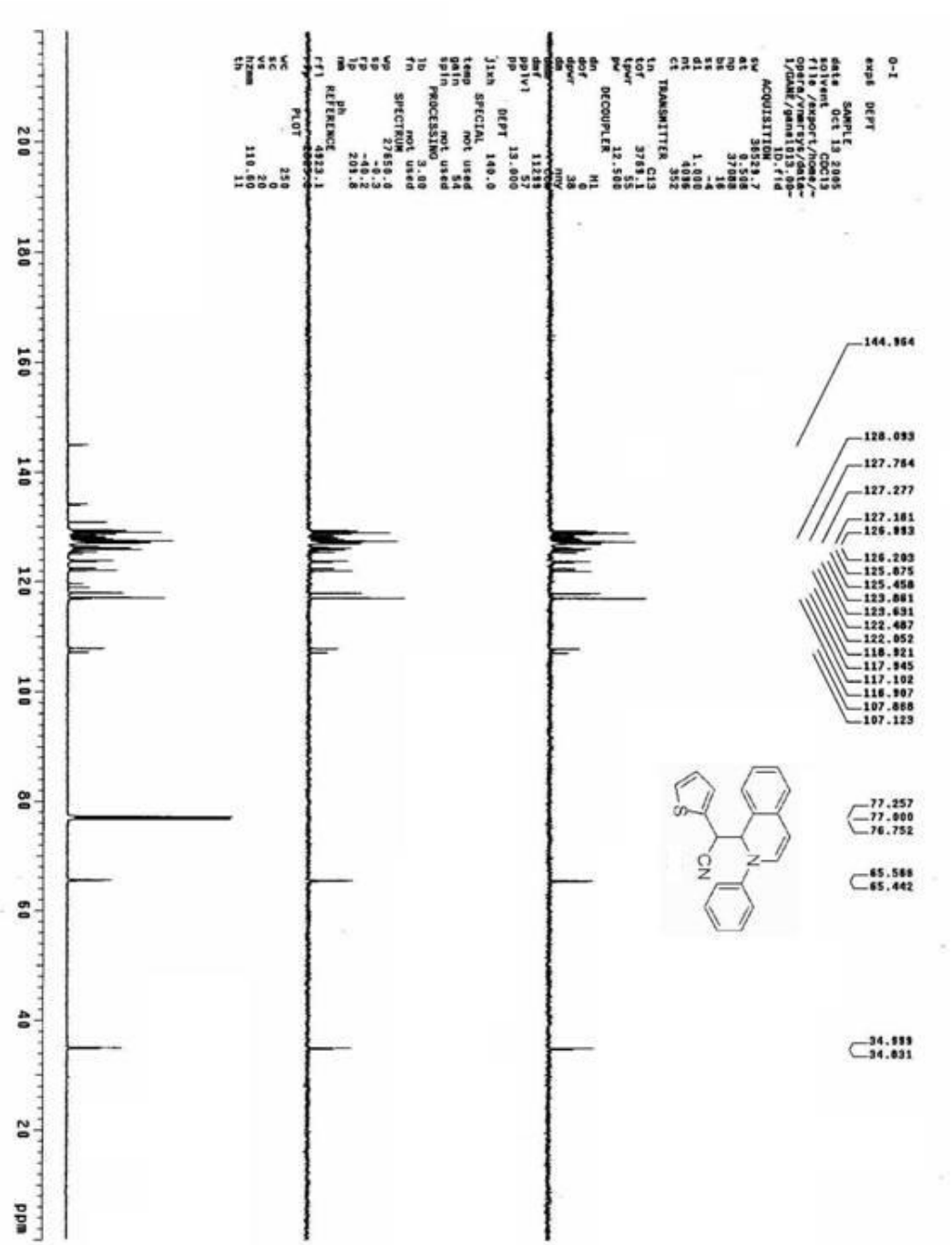
^{1}H NMR spectrum of compound **4m** (1:1 diastereoisomeric mixture form):



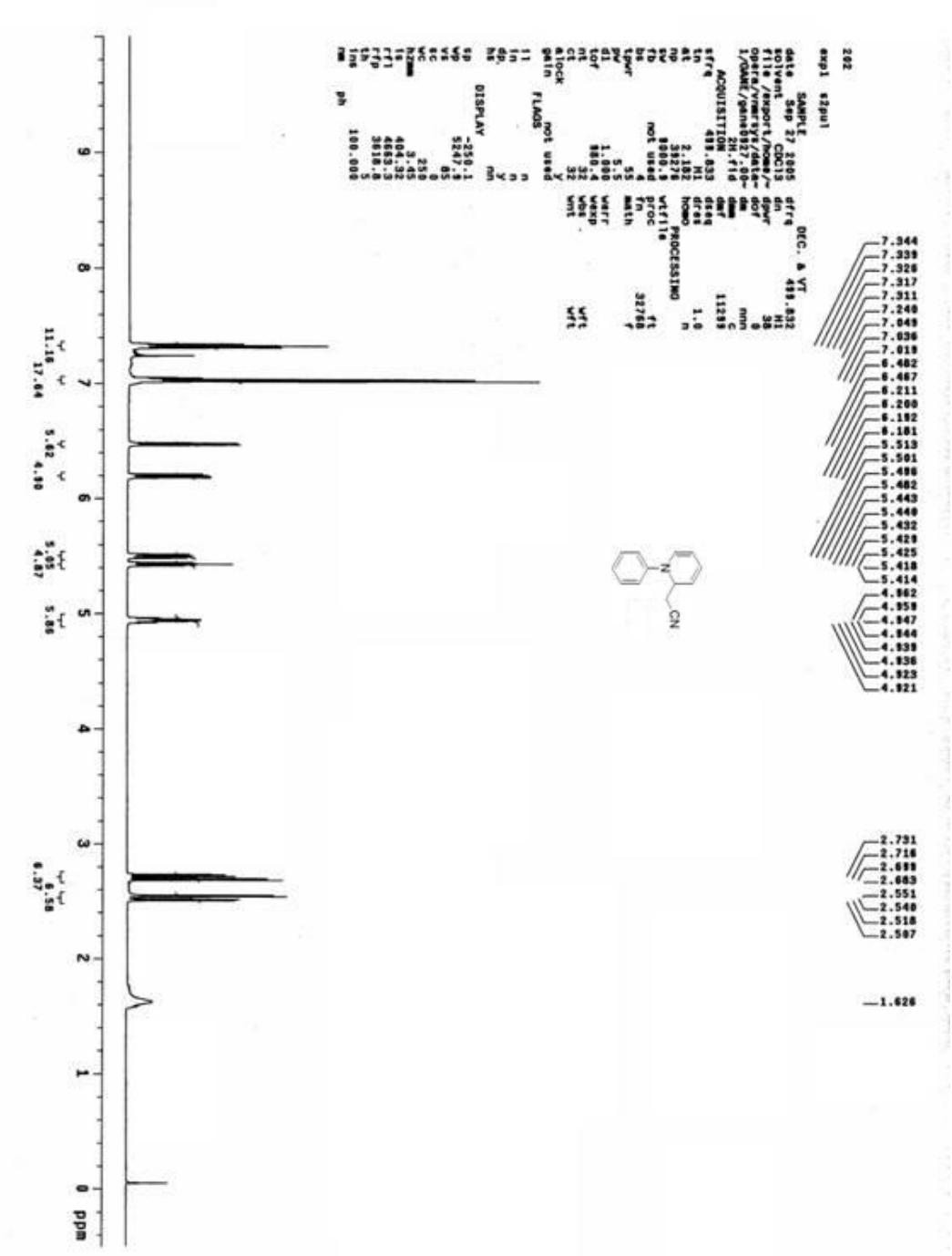
^{1}H NMR spectrum of compound **4n** (1:1 diastereoisomeric mixture form):



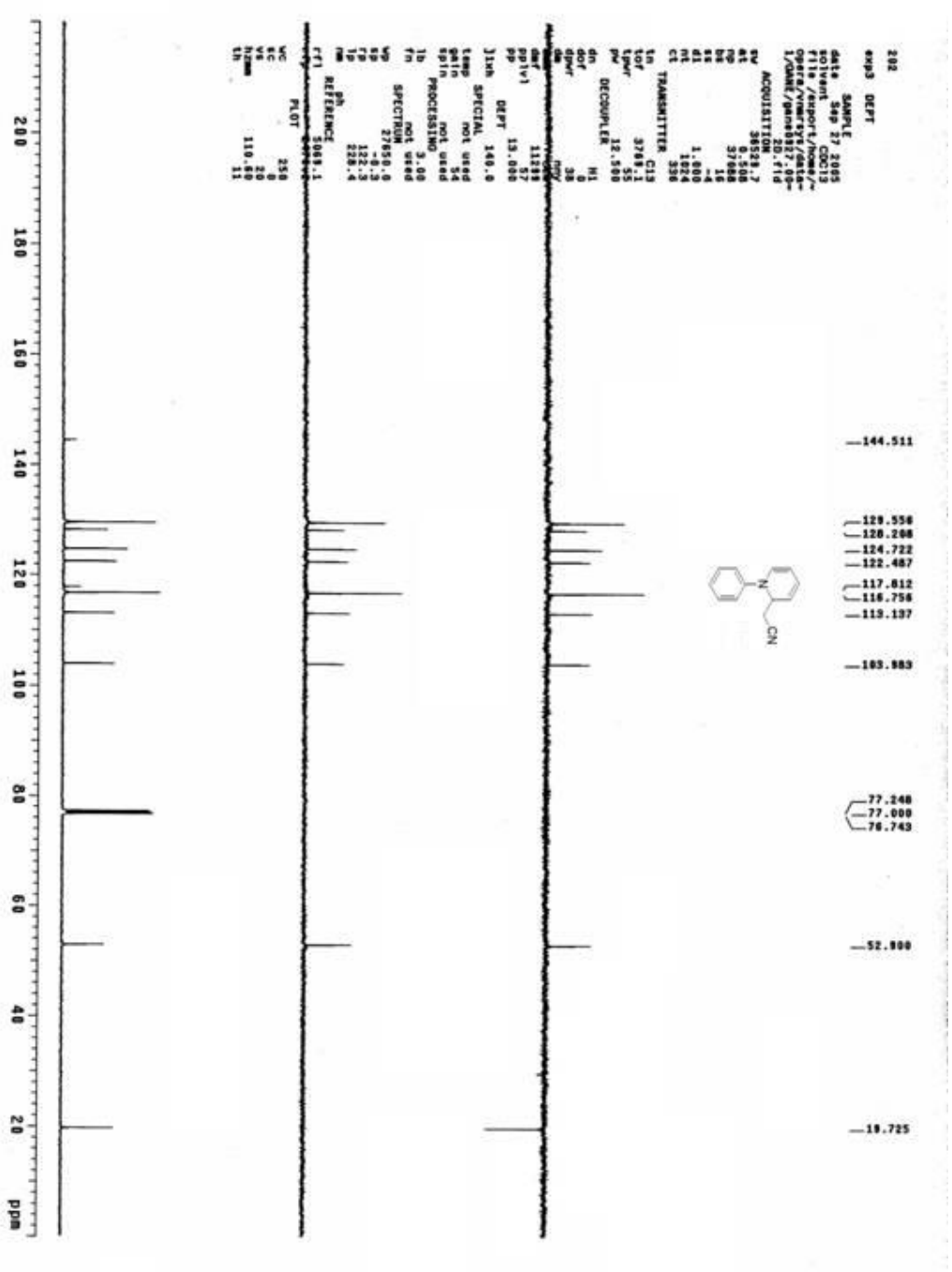
^{13}C NMR spectrum of compound **4n** (1:1 diastereoisomeric mixture form):



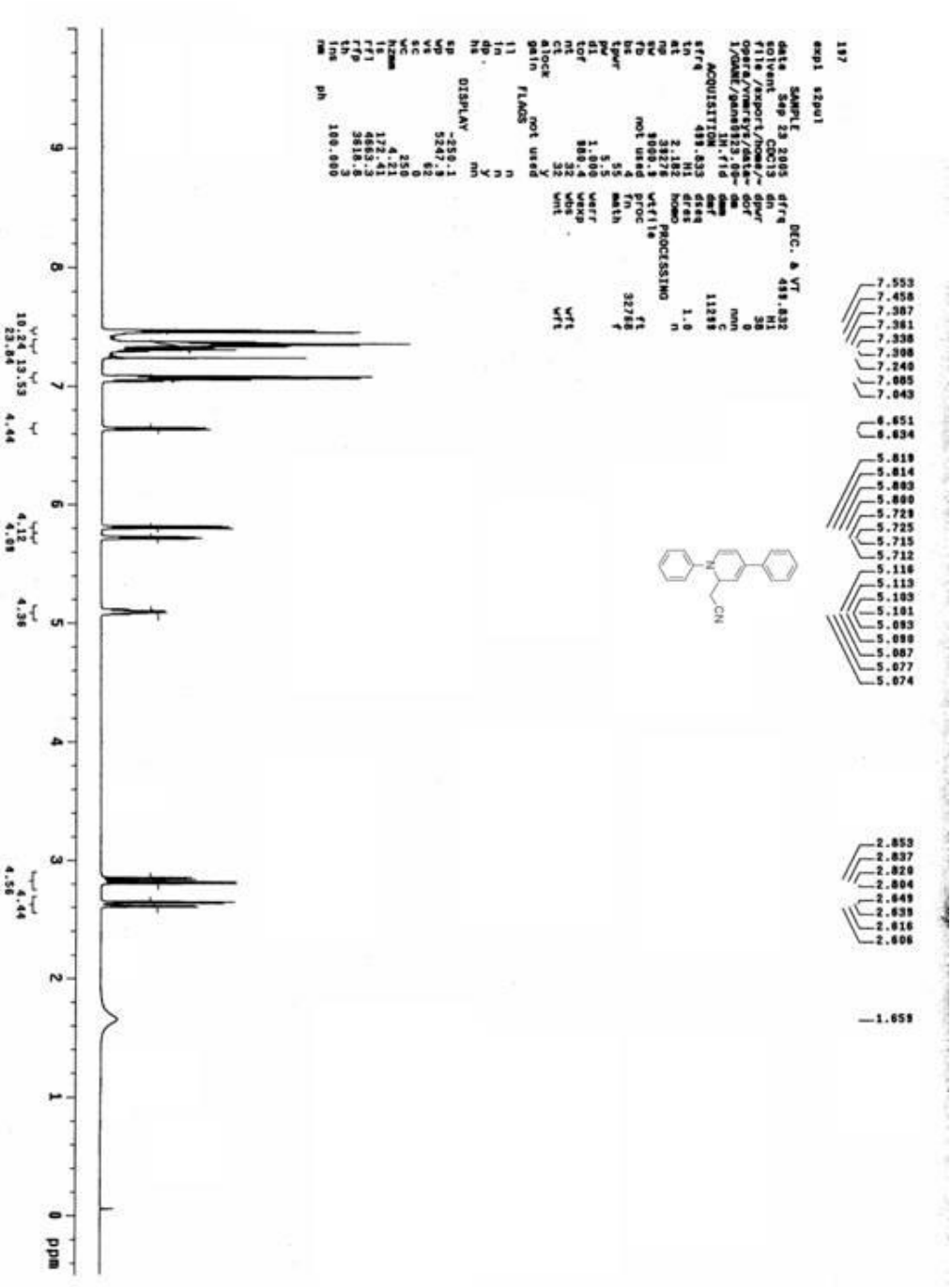
^{1}H NMR spectrum of compound **4o**:



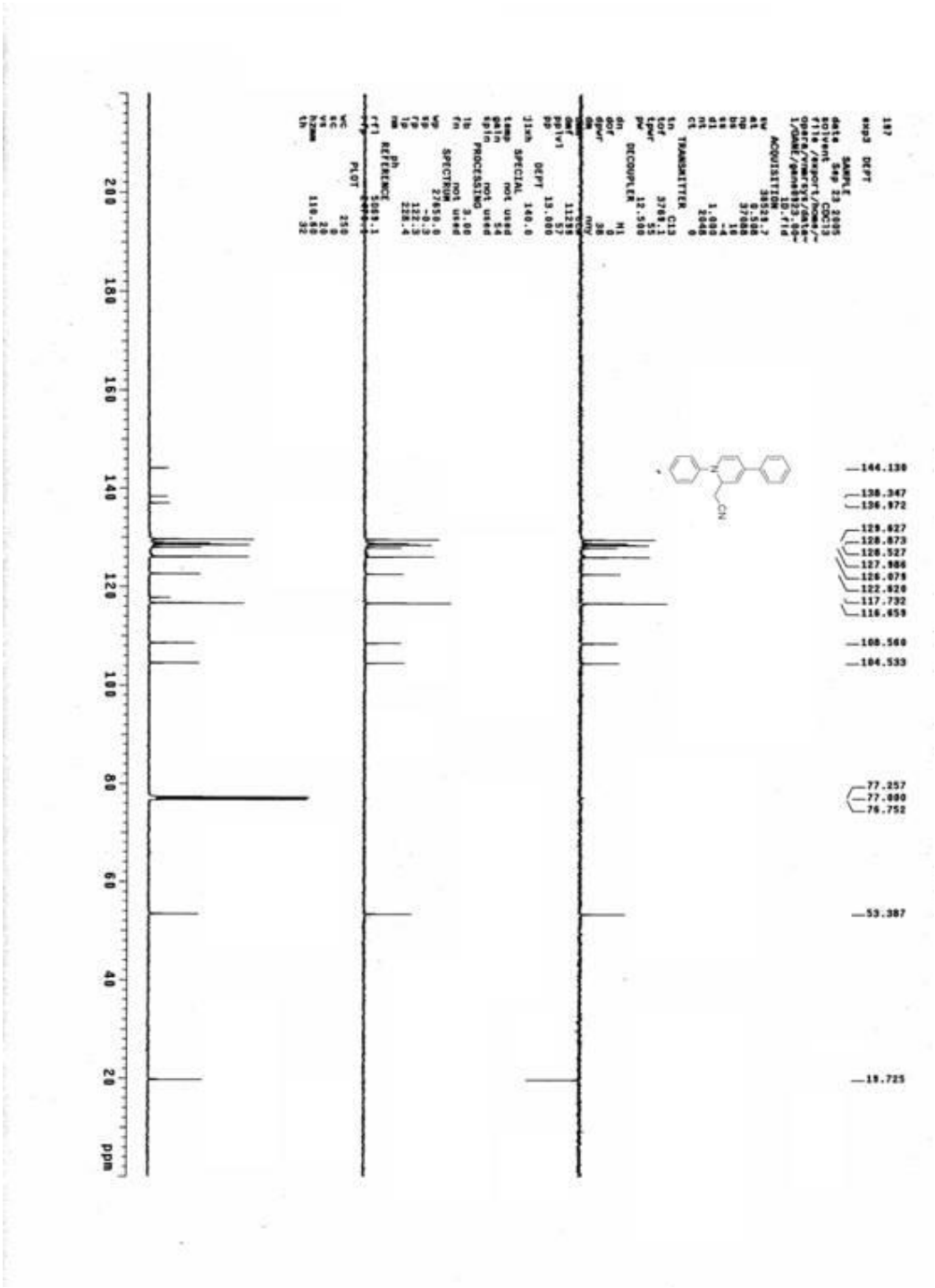
^{13}C NMR spectrum of compound **4o**:



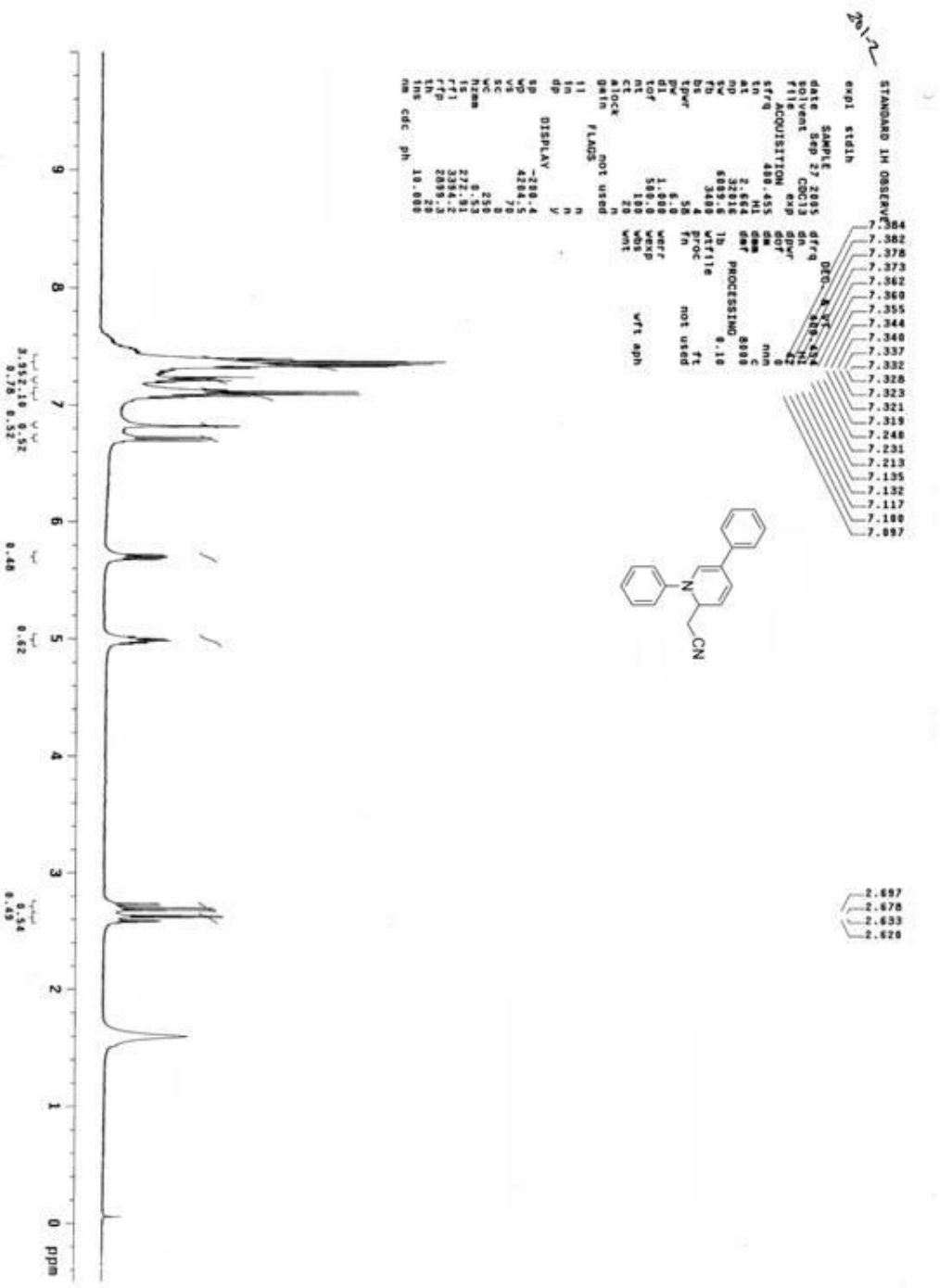
^{1}H NMR spectrum of compound **4p**:



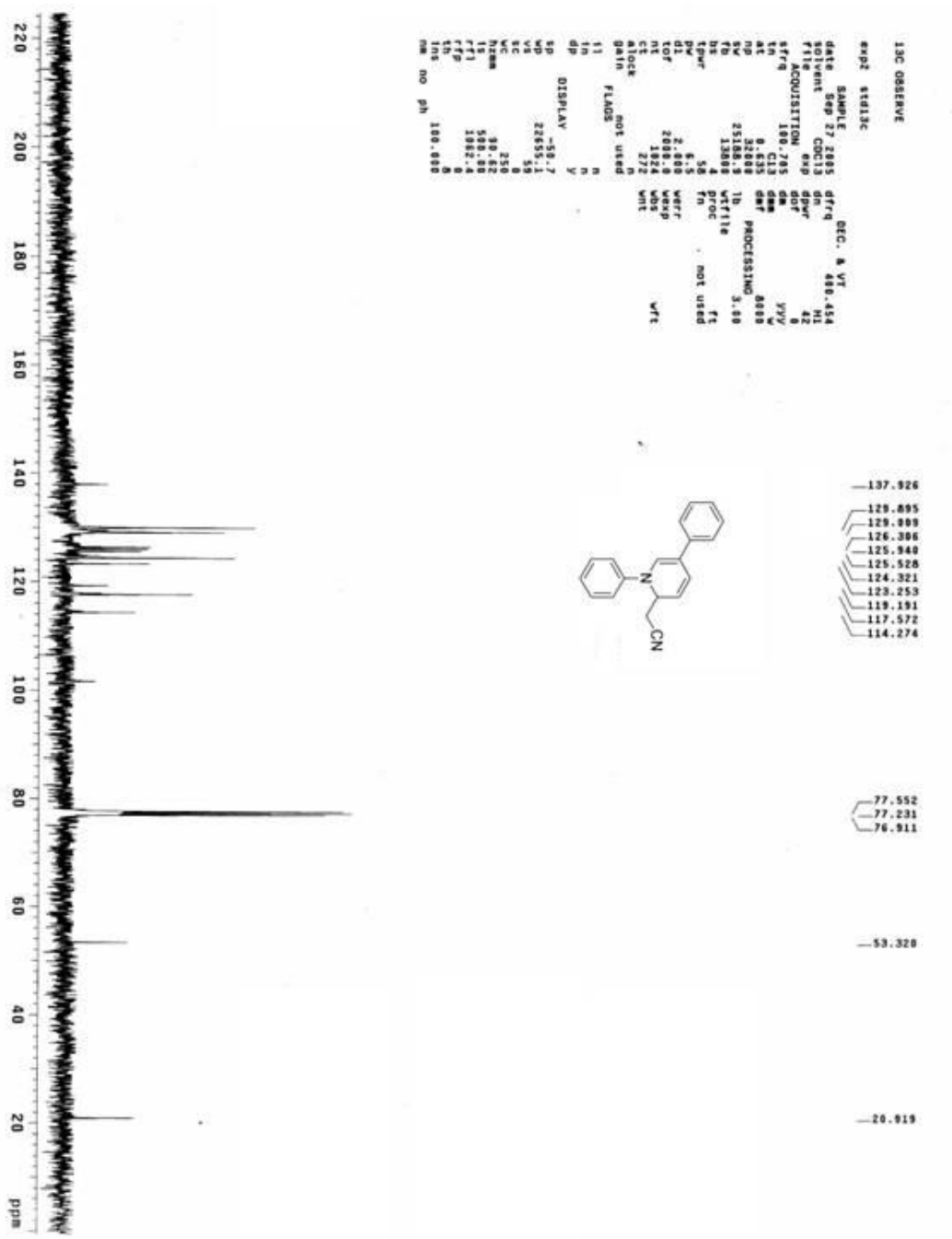
^{13}C NMR spectrum of compound **4p**:



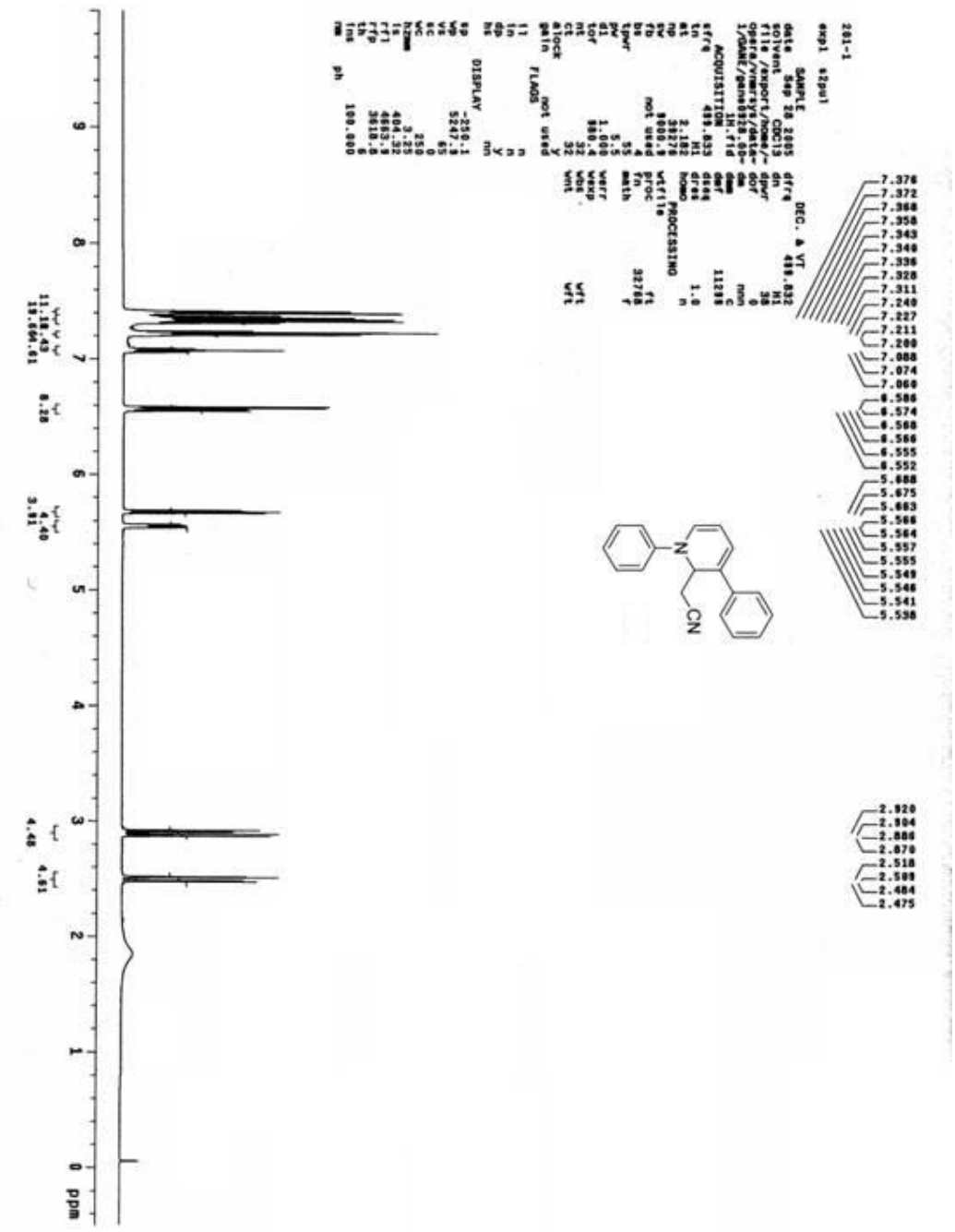
^{1}H NMR spectrum of compound **4q**:



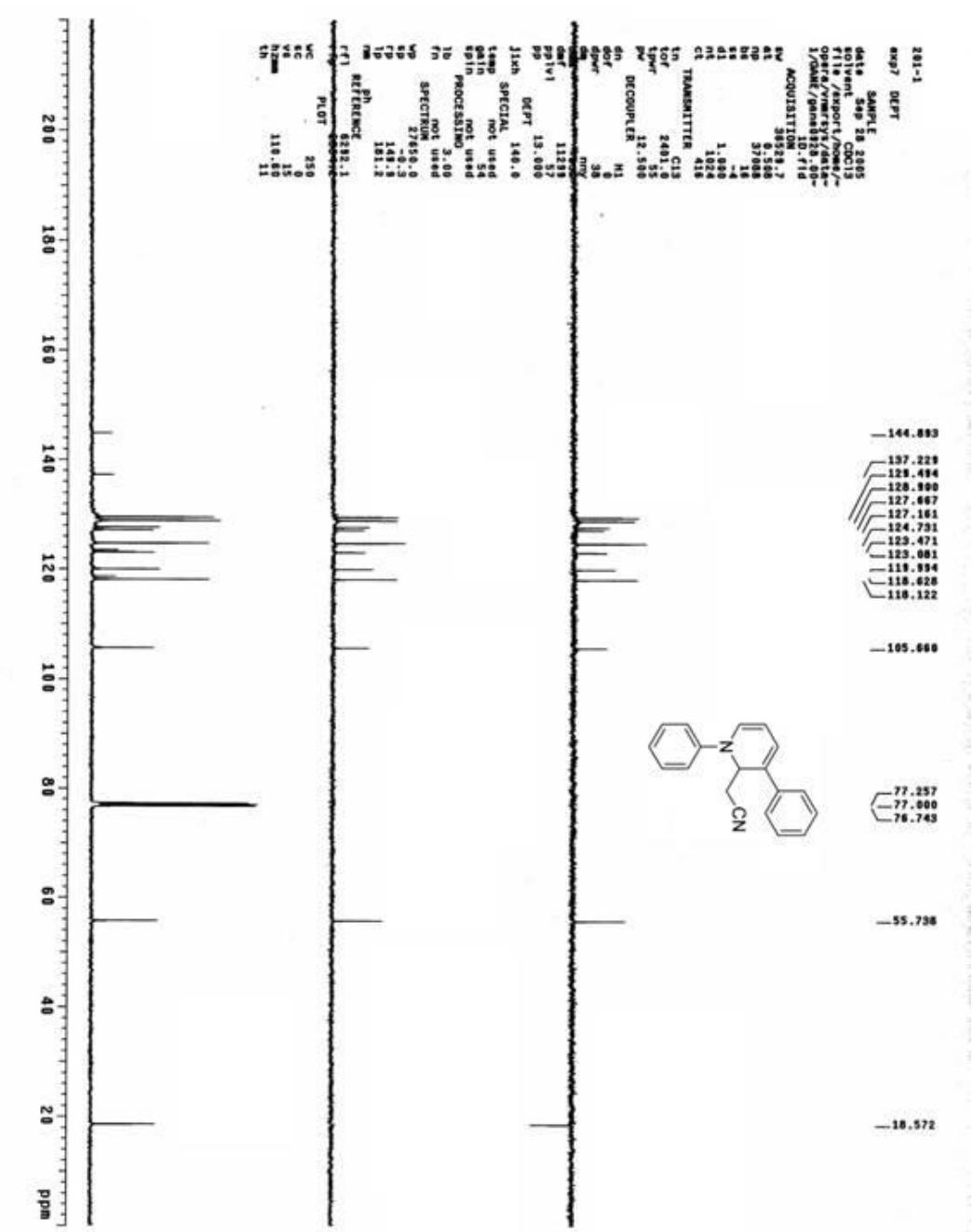
^{13}C NMR spectrum of compound **4q**:



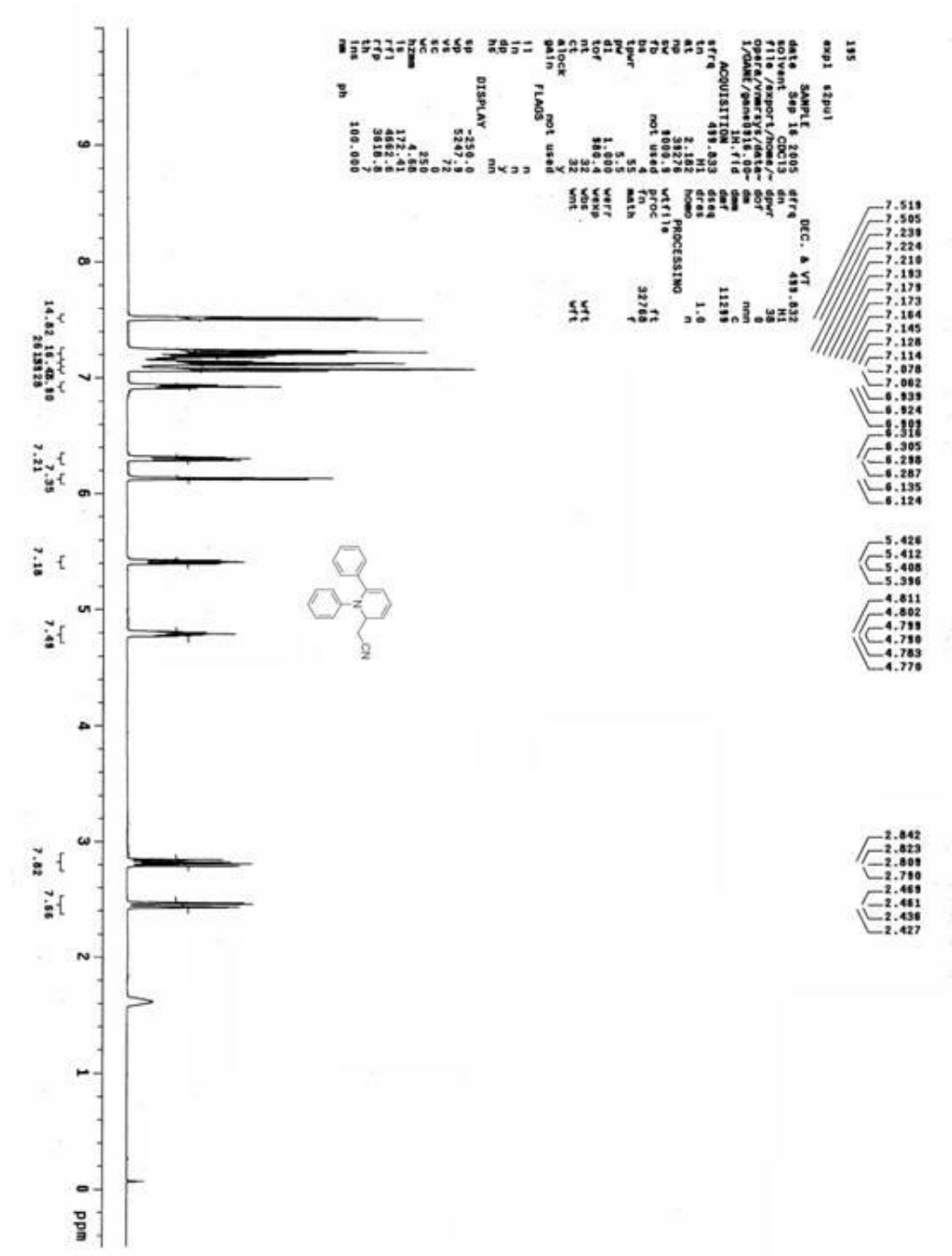
^{1}H NMR spectrum of compound **4q'**:



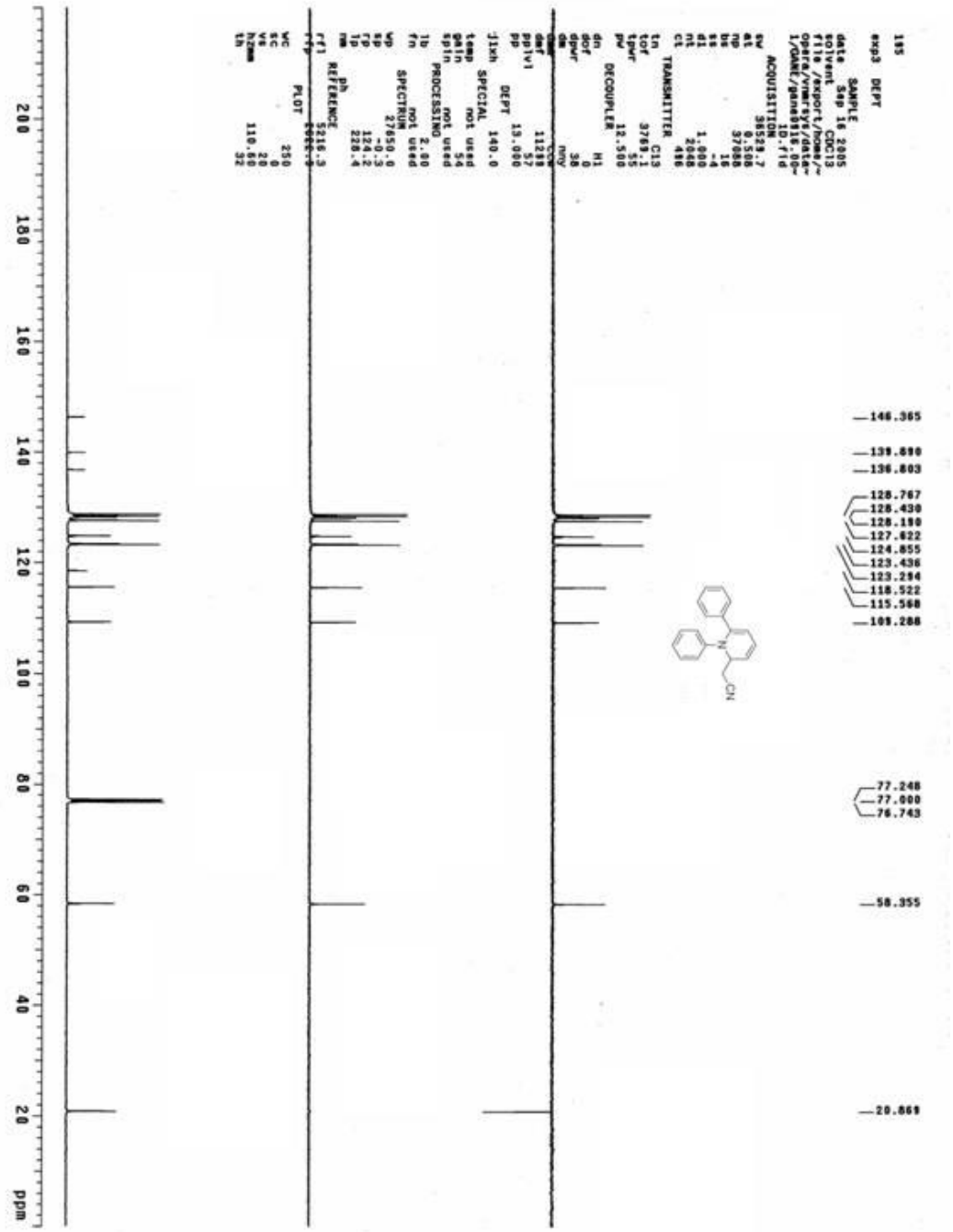
^{13}C NMR spectrum of compound **4q'**:



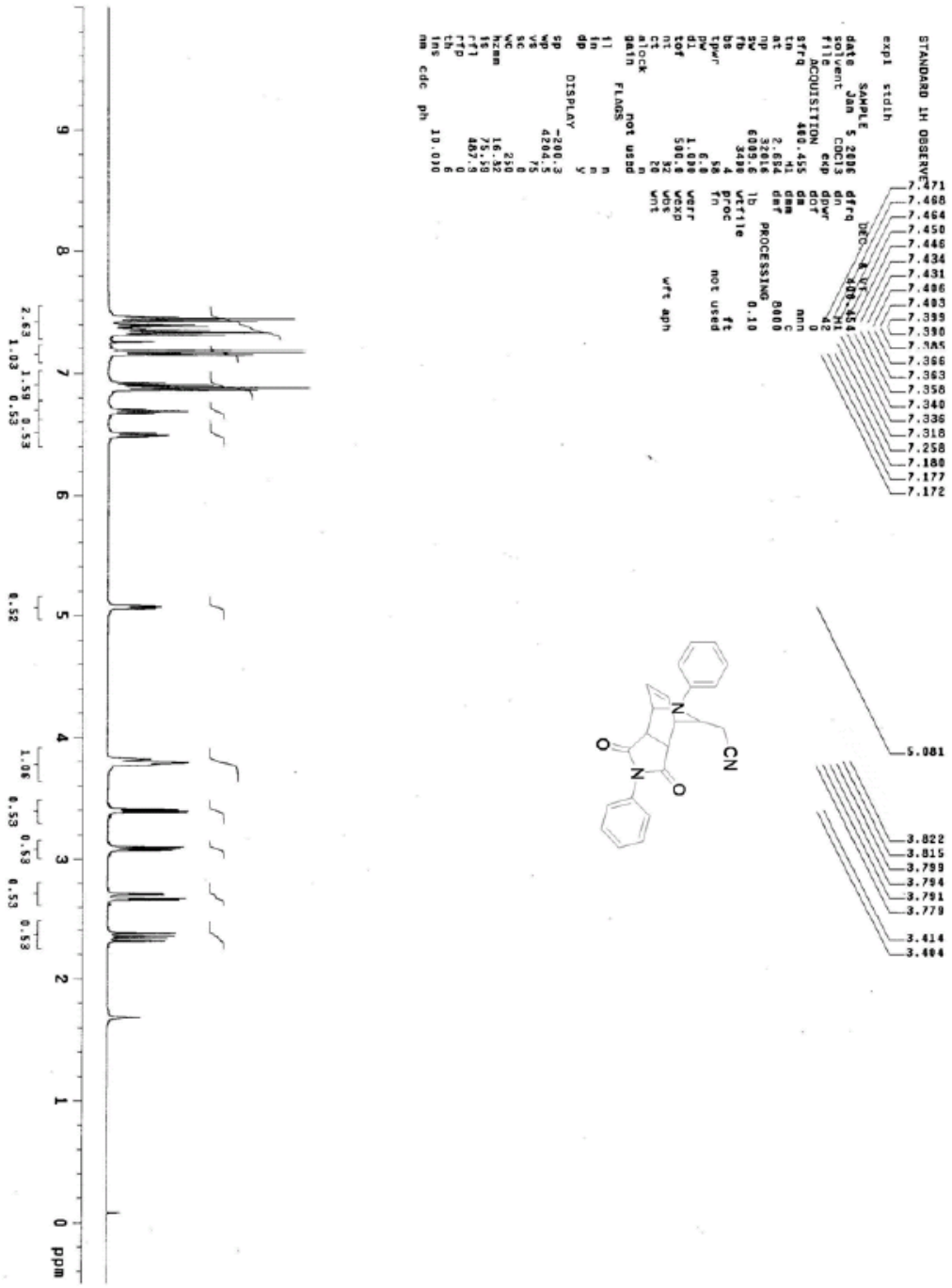
^{1}H NMR spectrum of compound **4r**:



^{13}C NMR spectrum of compound **4r**:



^{1}H NMR spectrum of compound **10**:



^{13}C NMR spectrum of compound **10**: