Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

$Bi(OTf)_3$-catalyzed C-H Bond Functionalization of Azaarenes for the Facile Access to Oxindoles Featuring Quaternary Carbon Centers

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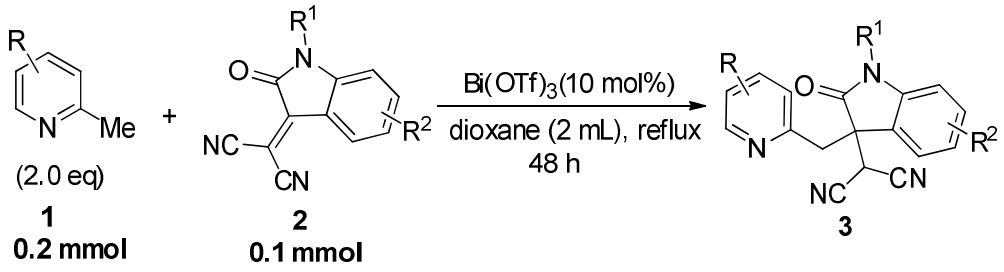
Part I: Experimental section

General information:

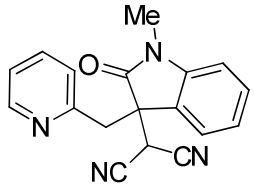
Commercially available materials purchased from Alfa Aesar or Aldrich was used as received. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker AV400 (400 MHz) or Bruker AV500 (500 MHz) spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker AV400 (100 MHz) or Bruker AV500 (125 MHz) spectrometer. High resolution mass spectral analysis (HRMS) was performed on Waters Q-TOF Premier mass spectrometer. Analytical thin-layer chromatography (TLC) was carried out on Merck 60 F254 pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp.

General procedure for the catalytic reactions (Table 1-3):



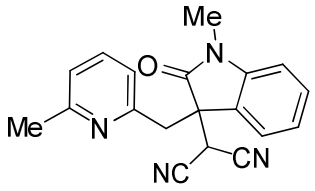
To a dry Schlenk tube equipped with a magnetic stir bar, was added azaarenes **1** (0.2 mmol), isatylidene malononitriles **2** (0.1 mmol), $Bi(OTf)_3$ (0.01 mmol). Freshly distilled dioxane (2 mL) was added and the reaction mixture was then stirred at reflux temperature till **2** was completely consumed (monitored by TLC). The mixture was concentrated under reduced pressure. The resulting crude residue was purified *via* column chromatography on silica gel (5:1 hexanes/EtOAc) to afford the desired products **3**.

Characterization of products (3):



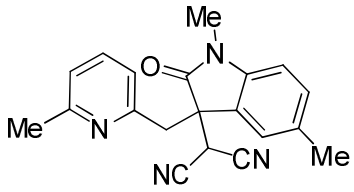
3a

2-(1-methyl-2-oxo-3-(pyridin-2-ylmethyl)indolin-3-yl)malononitrile (3a): Pale yellow solid, yield: 25.2 mg (83%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.43 (d, *J* = 4.5 Hz, 1 H), 7.52-7.49 (m, 1 H), 7.36-7.33 (m, 2 H), 7.12-7.06 (m, 2 H), 6.95 (d, *J* = 7.5 Hz, 1 H), 6.83 (d, *J* = 8.0 Hz, 1 H), 5.06 (s, 1 H), 3.51 (d, *J* = 14.0 Hz, 1 H), 3.45 (d, *J* = 14.0 Hz, 1 H), 3.22 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.6, 154.5, 149.1, 143.7, 136.4, 130.4, 125.2, 124.3, 124.2, 123.4, 122.4, 111.2, 110.1, 108.9, 52.0, 41.4, 29.9, 26.7; HRMS (ESI) calcd for $C_{18}H_{15}N_4O$ $(M+H)^+$: 303.1246 , Found: 303.1255.



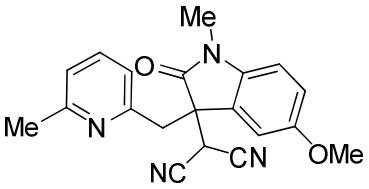
3b

2-(1-methyl-3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (3b): Oil, yield: 25.5 mg (81%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41-7.30 (m, 3 H), 7.07-7.03 (m, 1 H), 6.94 (d, *J* = 7.6 Hz, 1 H), 6.85 (d, *J* = 7.6 Hz, 1 H), 6.77 (d, *J* = 7.6 Hz, 1 H), 5.00 (s, 1 H), 3.49 (d, *J* = 14.4 Hz, 1 H), 3.42 (d, *J* = 14.4 Hz, 1 H), 3.25 (s, 3 H), 2.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 157.6, 153.6, 143.9, 136.6, 130.3, 125.4, 124.1, 123.2, 121.7, 120.9, 111.2, 110.2, 108.7, 51.8, 41.0, 30.0, 26.6, 24.3; HRMS (ESI) calcd for $C_{19}H_{17}N_4O$ $(M+H)^+$: 317.1402, Found: 317.1398.



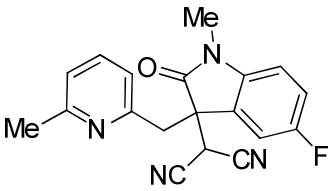
3c

2-(1,5-dimethyl-3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (3c): White solid, yield: 24.5 mg (74%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (t, *J* = 8.0 Hz, 1 H), 7.15-7.12 (m, 2 H), 6.94 (d, *J* = 7.6 Hz, 1 H), 6.77 (d, *J* = 7.6 Hz, 1 H), 6.73 (d, *J* = 8.0 Hz, 1 H), 4.95 (s, 1 H), 3.43 (s, 2 H), 3.22 (s, 3 H), 2.40 (s, 3 H), 2.30 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 157.6, 153.7, 141.5, 136.6, 132.9, 130.6, 125.5, 124.8, 121.7, 120.9, 111.3, 110.3, 108.5, 51.8, 41.1, 30.1, 26.6, 24.3, 21.1; HRMS (ESI) calcd for $C_{20}H_{19}N_4O$ $(M+H)^+$: 331.1559, Found: 331.1559.



3d

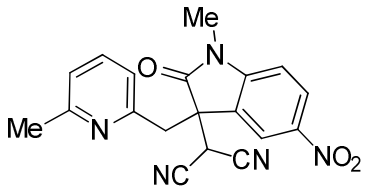
2-(5-methoxy-1-methyl-3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (3d): Colorless solid, yield: 24.9 mg (72%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41 (t, *J* = 7.6 Hz, 1 H), 6.95 (d, *J* = 7.6 Hz, 1 H), 6.92-6.91 (m, 1 H), 6.87-6.85 (m, 1 H), 6.80-6.76 (m, 2 H), 5.02 (s, 1 H), 3.74 (s, 3 H), 3.48 (d, *J* = 14.8 Hz, 1 H), 3.40 (d, *J* = 14.4 Hz, 1 H), 3.23 (s, 3 H), 2.41 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 157.7, 156.2, 153.7, 137.3, 136.7, 126.6, 121.7, 121.0, 114.8, 111.4, 111.1, 110.2, 109.2, 55.8, 52.0, 40.9, 30.0, 26.7, 24.3; HRMS (ESI) calcd for $C_{20}H_{19}N_4O_2$ $(M+H)^+$: 347.1508, Found: 347.1512.



3e

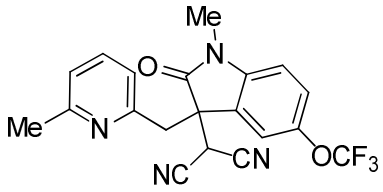
2-(5-fluoro-1-methyl-3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (3e): Colorless oil, yield: 28.2 mg (84%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42 (t, *J* = 7.6 Hz, 1 H), 7.10-7.03 (m, 2 H), 6.95 (d, *J* = 7.6 Hz, 1 H), 6.82-6.78 (m, 2 H), 4.99 (s, 1 H), 3.51 (d, *J* = 14.8 Hz, 1 H), 3.43 (d, *J* = 14.8 Hz, 1 H), 3.25 (s, 3 H), 2.38 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 159.1 (d, *J* = 241.0 Hz), 157.7, 153.2,

140.1 (d, J = 2.0 Hz), 136.8, 126.9 (d, J = 8.0 Hz), 121.9, 120.9, 116.7 (d, J = 23.0 Hz), 112.5 (d, J = 26.0 Hz), 110.9, 109.9, 109.3 (d, J = 8.0 Hz), 52.0 (d, J = 2.0 Hz), 40.8, 30.0, 26.8, 24.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.6; HRMS (ESI) calcd for $C_{19}H_{16}N_4OF$ $(M+H)^+$: 335.1308, Found: 335.1309.



3f

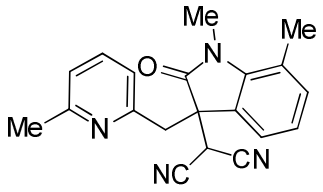
2-(1-methyl-3-((6-methylpyridin-2-yl)methyl)-5-nitro-2-oxoindolin-3-yl)malononitrile (3f): Yellow solid, yield: 31.3 mg (87%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.33 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1 H), 8.23 (d, J = 2.0 Hz, 1 H), 7.44 (t, J = 8.0 Hz, 1 H), 7.00 (d, J = 8.8 Hz, 1 H), 6.95 (d, J = 7.6 Hz, 1 H), 6.88 (d, J = 7.6 Hz, 1 H), 4.92 (s, 1 H), 3.68 (d, J = 15.2 Hz, 1 H), 3.55 (d, J = 15.2 Hz, 1 H), 3.38 (s, 3 H), 2.32 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 157.6, 152.6, 149.9, 143.6, 137.1, 127.3, 126.4, 122.0, 120.7, 120.2, 110.3, 109.5, 108.3, 51.3, 40.4, 30.0, 27.1, 24.2; HRMS (ESI) calcd for $C_{19}H_{16}N_5O_3$ $(M+H)^+$: 362.1253, Found: 362.1245.



3g

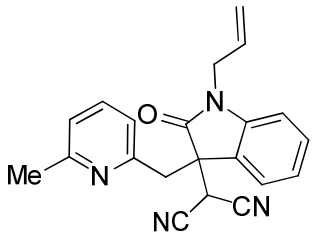
2-(1-methyl-3-((6-methylpyridin-2-yl)methyl)-2-oxo-5-(trifluoromethoxy)indolin-3-yl)malononitrile (3g): White solid, yield: 36.9 mg (92%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41 (t, J = 7.6 Hz, 1 H), 7.23-7.18 (m, 2 H), 6.96 (d, J = 7.6 Hz, 1 H), 6.85 (d, J = 8.4 Hz, 1 H), 6.80 (d, J = 7.6 Hz, 1 H), 5.01 (s, 1 H), 3.54 (d, J = 14.8 Hz, 1 H), 3.41 (d, J = 14.4 Hz, 1 H), 3.26 (s, 3 H), 2.38 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 157.8, 153.1, 144.8, 142.7, 136.8, 126.7, 123.4, 121.9, 120.9, 120.4 (q, J = 255.8 Hz), 118.5, 110.7,

109.9, 109.2, 51.9, 40.8, 29.8, 26.8, 24.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.5; HRMS (ESI) calcd for $C_{20}H_{16}N_4O_2F_3$ $(M+H)^+$: 401.1225, Found: 401.1231.



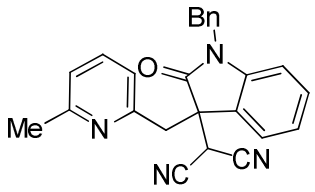
3h

2-(1,7-dimethyl-3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (3h): Yellow solid, yield: 21.6 mg (65%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40 (t, *J* = 7.6 Hz, 1 H), 7.12 (d, *J* = 7.2 Hz, 1 H), 7.06 (d, *J* = 7.6 Hz, 1 H), 6.97-6.90 (m, 2 H), 6.75 (d, *J* = 7.6 Hz, 1 H), 5.01 (s, 1 H), 3.52 (s, 3 H), 3.43 (d, *J* = 14.8 Hz, 1 H), 3.38 (d, *J* = 14.4 Hz, 1 H), 2.54 (s, 3 H), 2.43 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 157.6, 153.7, 141.6, 136.6, 134.0, 126.1, 123.1, 121.8, 121.7, 121.0, 120.4, 111.3, 110.4, 51.2, 41.3, 30.2, 30.0, 24.4, 19.0; HRMS (ESI) calcd for $C_{20}H_{19}N_4O$ $(M+H)^+$: 331.1559, Found: 331.1554.



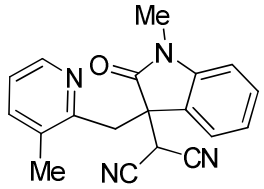
3i

2-(1-allyl-3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (3i): Oil, yield: 33.2 mg (97%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40-7.26 (m, 3 H), 7.15-7.01 (m, 1 H), 6.95 (d, *J* = 8.0 Hz, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 6.76 (d, *J* = 7.6 Hz, 1 H), 5.81-5.71 (m, 1 H), 5.22-5.18 (m, 2 H), 5.04 (s, 1H), 4.48-4.42 (m, 1H), 4.27-4.20 (m, 1H), 3.50 (d, *J* = 14.4 Hz, 1 H), 3.41 (d, *J* = 14.0 Hz, 1 H), 2.40 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 157.8, 153.6, 143.0, 136.6, 130.5, 130.2, 125.4, 124.2, 123.2, 121.8, 121.1, 118.2, 111.1, 110.5, 109.7, 51.9, 42.9, 41.4, 30.0, 24.3; HRMS (ESI) calcd for $C_{21}H_{19}N_4O$ $(M+H)^+$: 343.1559, Found: 343.1562.



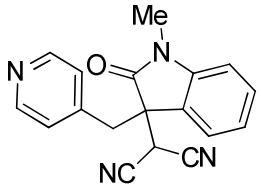
3j

2-(1-benzyl-3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (3j): Yellow solid, yield: 34.8 mg (89%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39-7.35 (m, 2 H), 7.29-7.20 (m, 6 H), 7.04 (td, J_1 = 0.8 Hz, J_2 = 7.6 Hz, 1 H), 6.97 (d, J = 8.0 Hz, 1 H), 6.75 (d, J = 7.6 Hz, 1 H), 6.70 (d, J = 8.0 Hz, 1 H), 5.10 (s, 1 H), 5.00 (d, J = 15.6 Hz, 1 H), 4.81 (d, J = 15.6 Hz, 1 H), 3.53 (d, J = 14.0 Hz, 1 H), 3.43 (d, J = 14.4 Hz, 1 H), 2.40 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 157.9, 153.5, 143.0, 136.7, 134.7, 130.2, 128.8, 127.8, 127.2, 125.4, 124.3, 123.3, 121.9, 121.2, 111.2, 110.4, 109.9, 52.0, 44.4, 41.6, 30.0, 24.3; HRMS (ESI) calcd for $C_{25}H_{21}N_4O$ $(M+H)^+$: 393.1715, Found: 393.1720.



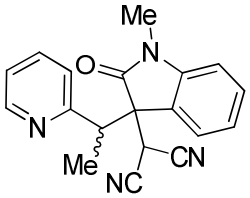
3k

2-(1-methyl-3-((3-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (3k): Colorless oil, yield: 20.8 mg (66%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.24 (d, J = 4.4 Hz, 1 H), 7.38-7.34 (m, 2 H), 7.29 (d, J = 7.2 Hz, 1 H), 7.05-7.00 (m, 2 H), 6.91 (d, J = 7.6 Hz, 1 H), 5.30 (s, 1 H), 3.61 (d, J = 15.6 Hz, 1 H), 3.33 (d, J = 16.0 Hz, 1 H), 3.31 (s, 3 H), 2.15 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 153.2, 146.2, 144.1, 137.9, 132.0, 130.3, 126.0, 123.9, 123.2, 122.3, 111.3, 110.3, 108.9, 51.3, 37.2, 29.8, 26.7, 18.8; HRMS (ESI) calcd for $C_{19}H_{17}N_4O$ $(M+H)^+$: 317.1402, Found: 317.1399.



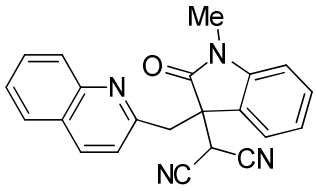
3l

2-(1-methyl-2-oxo-3-(pyridin-4-ylmethyl)indolin-3-yl)malononitrile (3l): Colorless oil, yield: 21.2 mg (70%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.31-8.30 (m, 2 H), 7.73 (d, J = 7.6 Hz, 1 H), 7.39 (td, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1 H), 7.27-7.25 (m, 1 H), 6.76-6.75 (m, 2 H), 6.72 (d, J = 8.0 Hz, 1 H), 4.39 (s, 1 H), 3.40 (d, J = 12.8 Hz, 1 H), 3.29 (d, J = 12.8 Hz, 1 H), 3.01 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 149.5, 143.6, 141.7, 131.1, 124.7, 123.93, 123.90, 123.7, 110.6, 109.42, 109.36, 53.4, 39.9, 30.3, 26.5; HRMS (ESI) calcd for $C_{18}H_{15}N_4O$ $(M+H)^+$: 303.1246, Found: 303.1240.



3m

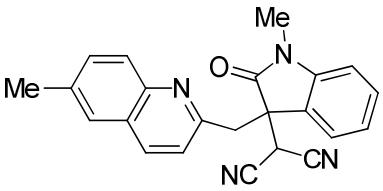
2-(1-methyl-2-oxo-3-(1-(pyridin-2-yl)ethyl)indolin-3-yl)malononitrile (3m): Colorless oil, yield: 17.2 mg (54%, dr = 2.5:1.0); (The major one) ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.52 (d, J = 4.0 Hz, 1 H), 7.57 (td, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1 H), 7.34-7.23 (m, 2 H), 7.18-7.15 (m, 1 H), 7.07-7.04 (m, 2 H), 6.80 (d, J = 7.5 Hz, 1 H), 4.98 (s, 1 H), 3.90-3.83 (m, 1 H), 3.25 (s, 3 H), 1.30 (d, J = 7.0 Hz, 3 H); (mixture) ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 172.5, 159.3, 158.4, 148.8, 148.6, 144.1, 143.9, 136.7, 136.4, 130.5, 130.3, 125.9, 125.2, 124.5, 124.0, 123.8, 123.5, 123.3, 123.2, 122.7, 122.6, 110.9, 110.3, 109.0, 108.7, 55.5, 54.9, 45.2, 44.6, 29.6, 29.2, 26.6, 26.5, 15.1, 14.2; HRMS (ESI) calcd for $C_{19}H_{17}N_4O$ $(M+H)^+$: 317.1402, Found: 317.1394.



3n

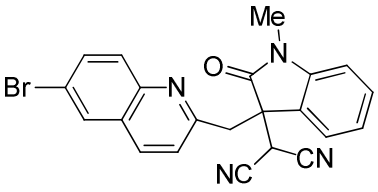
2-(1-methyl-2-oxo-3-(quinolin-2-ylmethyl)indolin-3-yl)malononitrile (3n): Colorless oil, yield: 21.2 mg (60%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00 (d, J = 8.4 Hz, 1 H), 7.85 (d, J = 8.4 Hz, 1 H), 7.74 (d, J = 8.0 Hz, 1 H), 7.67 (t, J = 7.6 Hz, 1 H), 7.50 (t, J = 7.2 Hz, 1 H), 7.42 (d, J = 7.6 Hz, 1 H), 7.32 (t, J = 8.0 Hz, 1 H), 7.11 (d, J = 8.4 Hz, 1 H), 7.04 (t,

J = 7.6 Hz, 1 H), 6.86 (d, *J* = 8.0 Hz, 1 H), 5.12 (s, 1 H), 3.77 (d, *J* = 15.2 Hz, 1 H), 3.65 (d, *J* = 14.8 Hz, 1 H), 3.29 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 154.8, 147.2, 144.1, 136.5, 130.4, 129.7, 128.9, 127.5, 126.9, 126.6, 125.5, 124.1, 123.3, 121.8, 111.1, 110.1, 108.9, 51.7, 41.5, 30.2, 26.8; HRMS (ESI) calcd for $C_{22}H_{17}N_4O$ $(M+H)^+$: 353.1402, Found: 353.1405.



3o

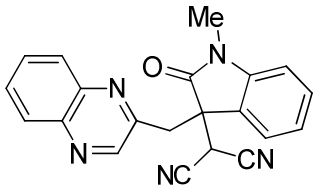
2-(1-methyl-3-((6-methylquinolin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (3o): Colorless solid, yield: 20.3 mg (55%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.90 (d, *J* = 8.4 Hz, 1 H), 7.75 (d, *J* = 9.2 Hz, 1 H), 7.50-7.49 (m, 2 H), 7.39 (d, *J* = 7.2 Hz, 1 H), 7.31 (td, J_1 = 0.8 Hz, J_2 = 7.6 Hz, 1 H), 7.06-7.00 (m, 2 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 5.16 (s, 1 H), 3.74 (d, *J* = 14.8 Hz, 1 H), 3.60 (d, *J* = 14.8 Hz, 1 H), 3.28 (s, 3 H), 2.50 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 153.8, 145.9, 144.0, 136.5, 135.8, 132.0, 130.4, 128.6, 126.9, 126.4, 125.5, 124.2, 123.3, 121.9, 111.2, 110.2, 108.9, 51.8, 41.4, 30.1, 26.7, 21.5; HRMS (ESI) calcd for $C_{23}H_{19}N_4O$ $(M+H)^+$: 367.1559, Found: 367.1548.



3p

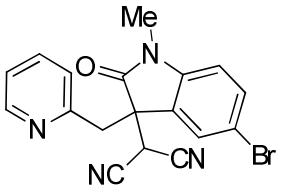
2-(3-((6-bromoquinolin-2-yl)methyl)-1-methyl-2-oxoindolin-3-yl)malononitrile (3p): White solid, yield: 23.4 mg (54%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91-7.89 (m, 2 H), 7.74-7.68 (m,2 H), 7.44 (d, *J* = 7.6 Hz, 1 H), 7.33 (t, *J* = 7.6 Hz, 1 H), 7.12 (d, *J* = 8.8 Hz, 1 H), 7.06 (t, *J* = 7.6 Hz, 1 H), 6.85 (d, *J* = 8.0 Hz, 1 H), 4.97 (s, 1 H), 3.73 (d, *J* = 14.8 Hz, 1 H), 3.66 (d, *J* = 14.8 Hz, 1 H), 3.27 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 155.3, 145.8, 144.0, 135.5, 133.3, 130.6, 130.5, 129.6, 127.9, 125.3, 124.0, 123.4, 122.7,

120.5, 111.1, 110.0, 108.9, 51.8, 41.6, 30.3, 26.8; HRMS (ESI) calcd for $C_{22}H_{16}N_4OBr$ $(M+H)^+$: 431.0507, Found: 431.0493.



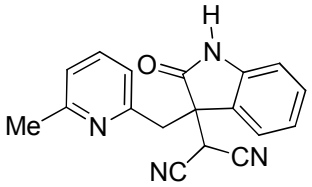
3q

2-(1-methyl-2-oxo-3-(quinoxalin-2-ylmethyl)indolin-3-yl)malononitrile (3q): Oil, yield: 15.8 mg (45%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1 H), 8.04-8.01 (m, 1 H), 7.87-7.84 (m, 1 H), 7.74-7.71 (m, 2 H), 7.53 (d, J = 7.2 Hz, 1 H), 7.35 (td, J_1 = 0.8 Hz, J_2 = 8.0 Hz, 1 H), 7.11 (t, J = 7.6 Hz, 1 H), 6.85 (d, J = 7.6 Hz, 1 H), 4.83 (s, 1 H), 3.80 (d, J = 15.2 Hz, 1 H), 3.76 (d, J = 15.2 Hz, 1 H), 3.27 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 149.7, 145.3, 143.9, 141.5, 141.3, 130.8, 130.4, 130.0, 129.3, 128.9, 124.7, 123.9, 123.7, 110.9, 109.7, 109.1, 51.7, 39.1, 30.4, 26.8; HRMS (ESI) calcd for $C_{21}H_{16}N_5O$ $(M+H)^+$: 354.1355, Found: 354.1360.



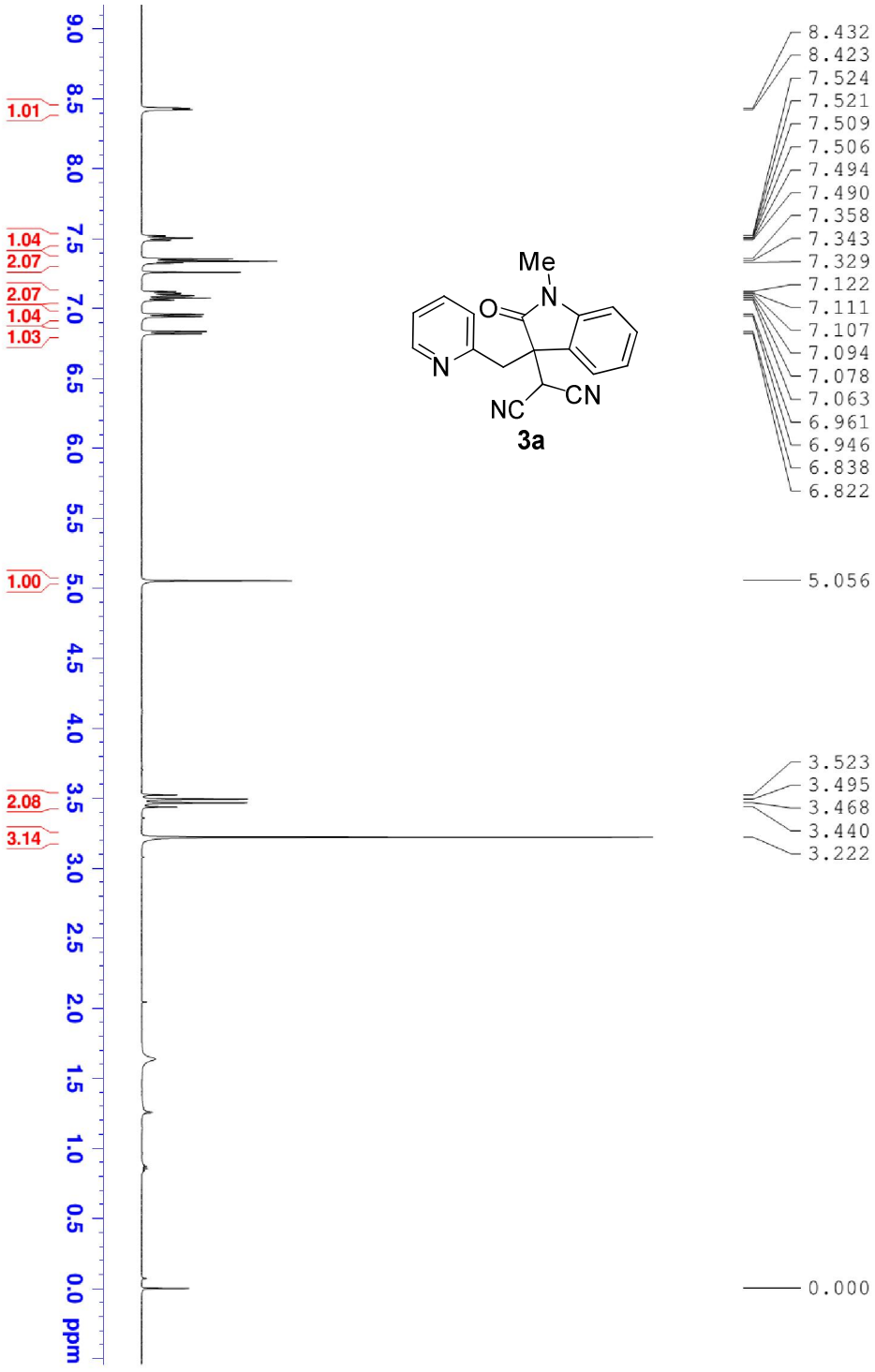
3r

2-(5-bromo-1-methyl-2-oxo-3-(pyridin-2-ylmethyl)indolin-3-yl)malononitrile (3r): Colorless oil, yield: 32.4 mg (85%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 4.4 Hz, 1 H), 7.55 (td, J = 7.6, 1.6 Hz, 1 H), 7.50-7.44 (m, 2 H), 7.14 (dd, J = 6.8, 4.8 Hz, 1 H), 6.99 (d, J = 7.6 Hz, 1 H), 6.73 (d, J = 8.4 Hz, 1 H), 5.07 (s, 1 H), 3.52 (d, J = 14.8 Hz, 1 H), 3.45 (d, J = 14.8 Hz, 1 H), 3.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 154.0, 149.1, 142.9, 136.6, 133.3, 127.4, 127.2, 124.2, 122.5, 115.9, 110.8, 110.3, 109.8, 51.9, 41.1, 29.8, 26.8; HRMS (ESI) calcd for $C_{18}H_{14}N_4OBr$ $(M+H)^+$: 381.0351, Found: 381.0344.



5

2-(3-((6-methylpyridin-2-yl)methyl)-2-oxoindolin-3-yl)malononitrile (5): Colorless solid, yield: 26.8 mg (89%); ^{1}H NMR ($(CD_3)_2CO$, 400 MHz) δ 9.88 (s, 1 H), 7.51-7.47 (m, 1 H), 7.28-7.24 (m, 1 H), 7.19-7.17 (m, 1 H), 7.04-7.02 (m, 1 H), 6.98-6.92 (m, 3 H), 5.53 (s, 1 H), 3.57 (d, *J* = 14.4 Hz, 1 H), 3.46 (d, *J* = 14.4 Hz, 1 H), 2.38 (s, 3 H); ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ 176.2, 158.5, 155.4, 143.6, 137.6, 130.8, 127.4, 125.5, 122.9, 122.3, 122.0, 113.0, 112.4, 111.0, 52.8, 41.6, 30.8, 24.2; HRMS (ESI) calcd for $C_{18}H_{15}N_4O$ $(M+H)^+$: 303.1246, Found: 303.1243.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1.5
1.0
0.5
0.0
ppm
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1.04
2.07
2.07
1.04
1.03
1.00
2.08
3.14
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8.423
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6.838
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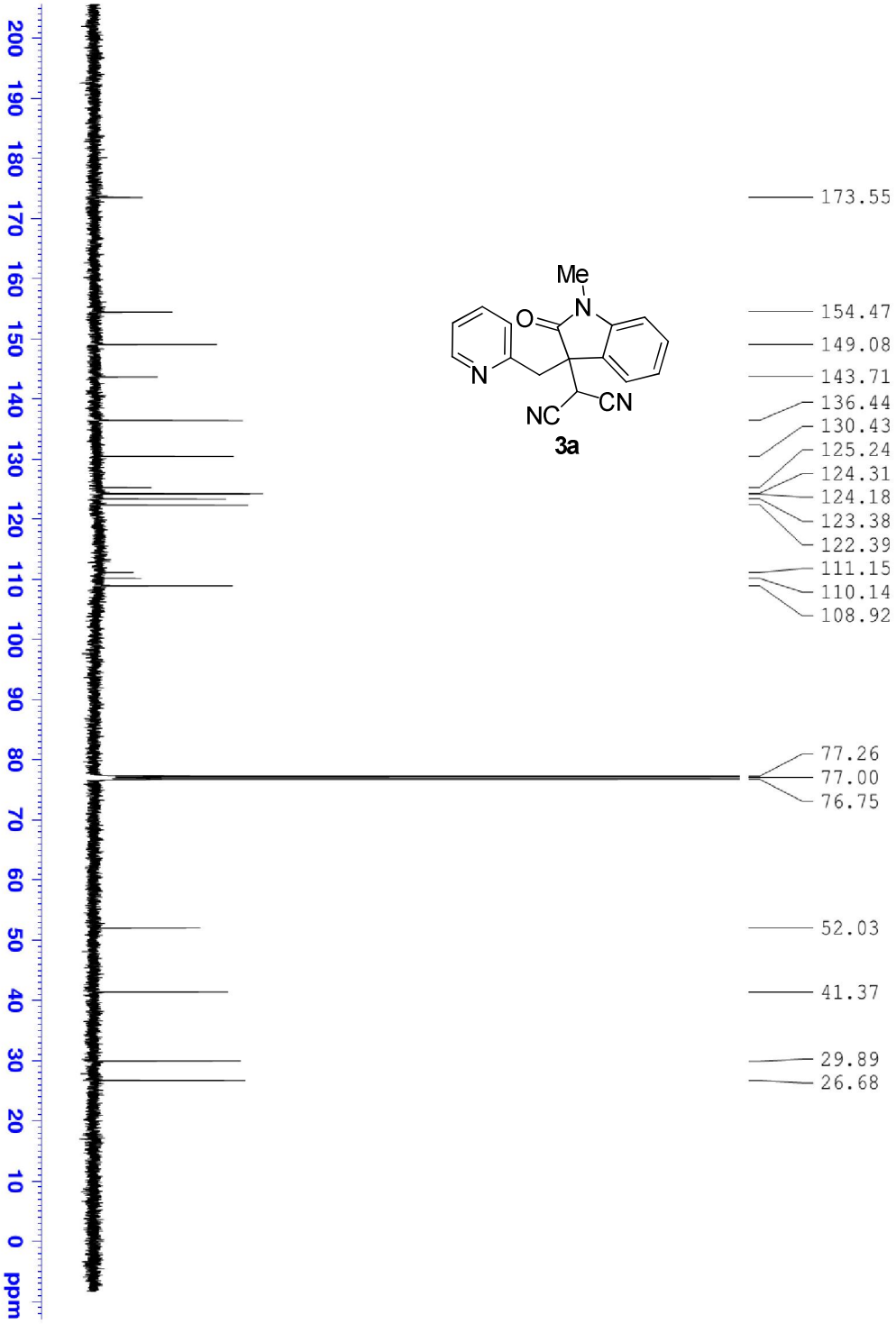
CN
3a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CN
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124.18
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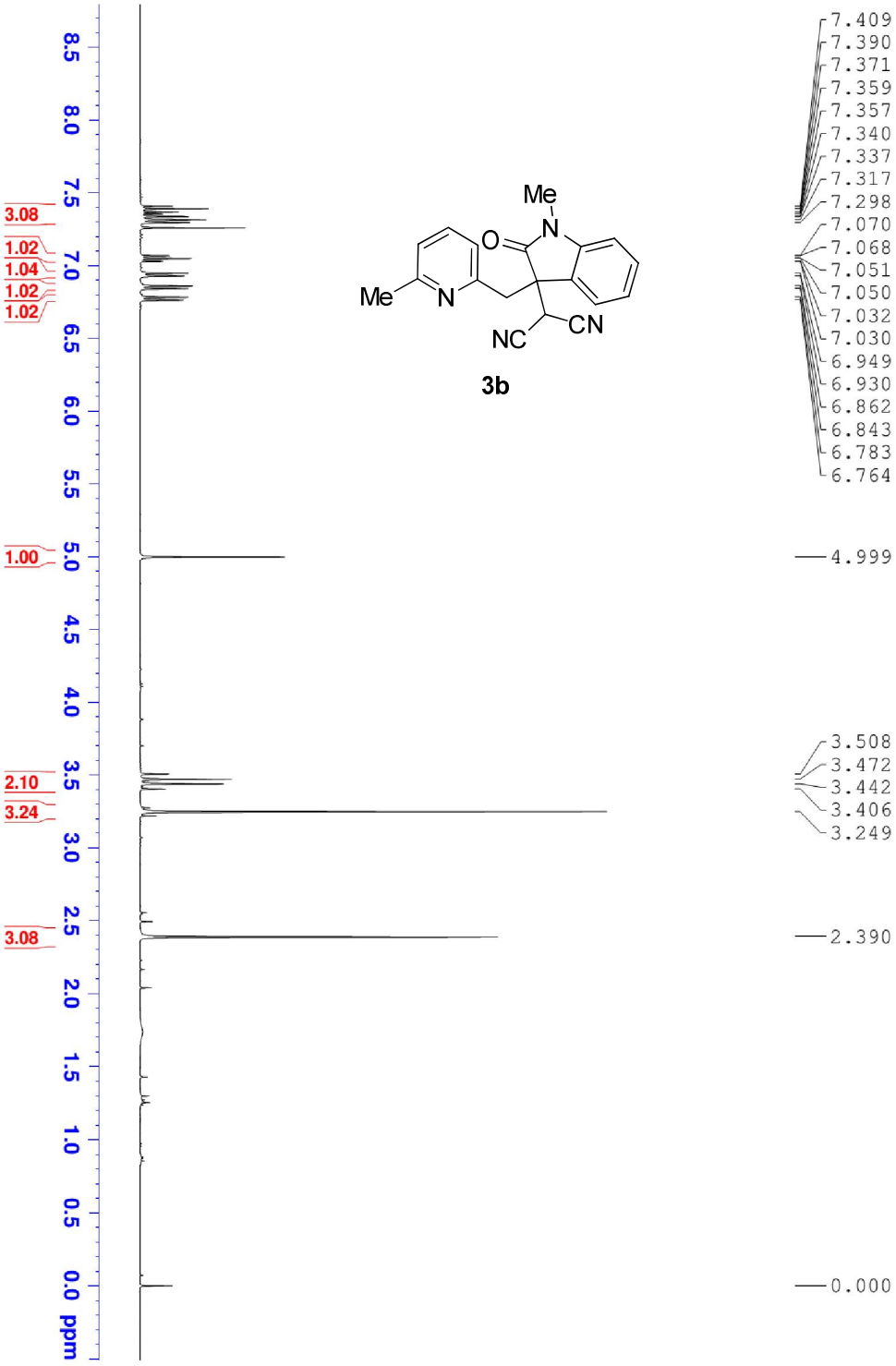
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7.317
7.298
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7.032
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6.783
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3.472
3.442
3.406
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3.08
1.02
1.04
1.02
1.02
1.00
2.10
3.24
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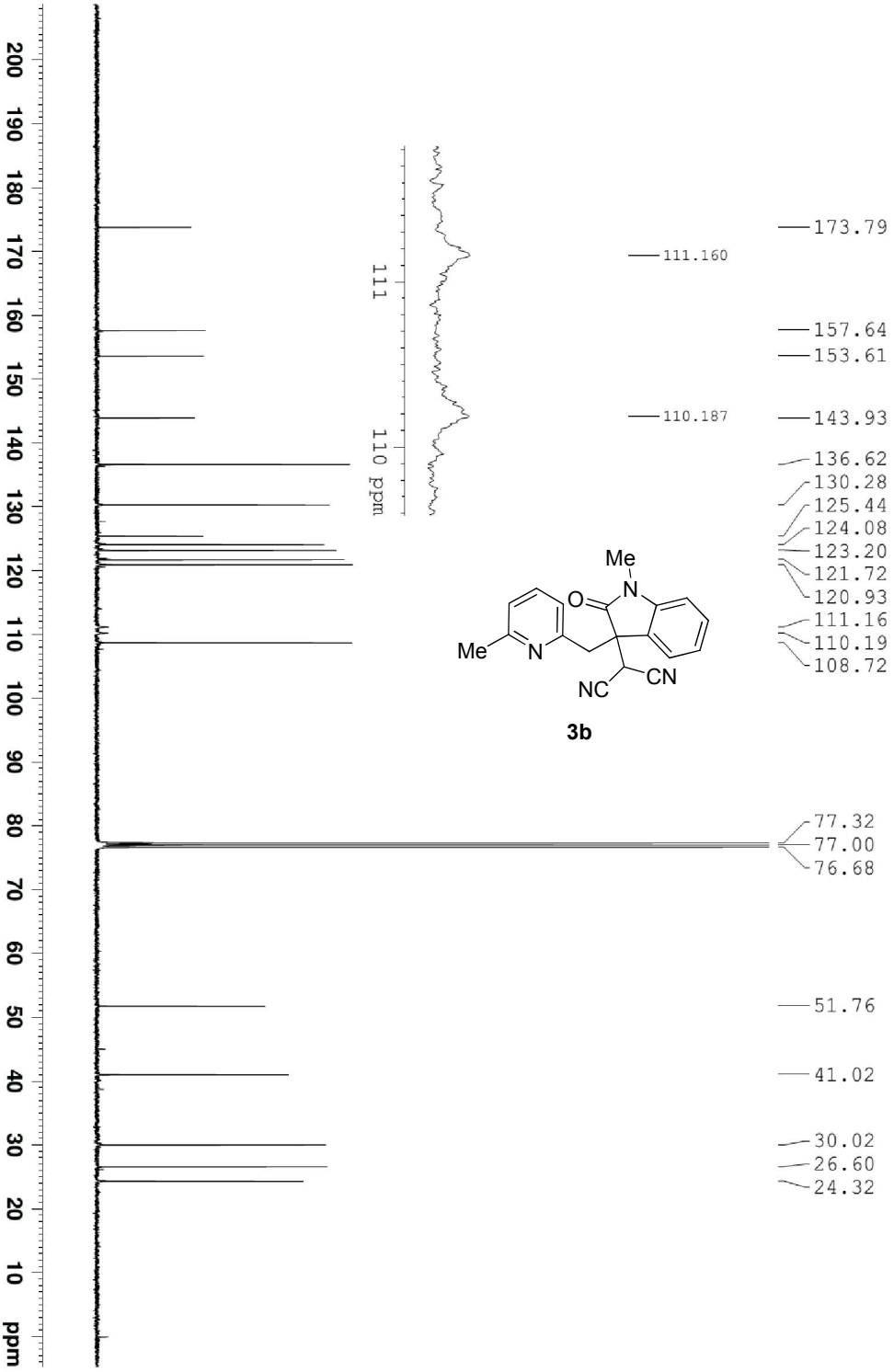
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123.20
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120.93
111.16
110.19
108.72
77.32
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41.02
30.02
26.60
24.32
Me
N
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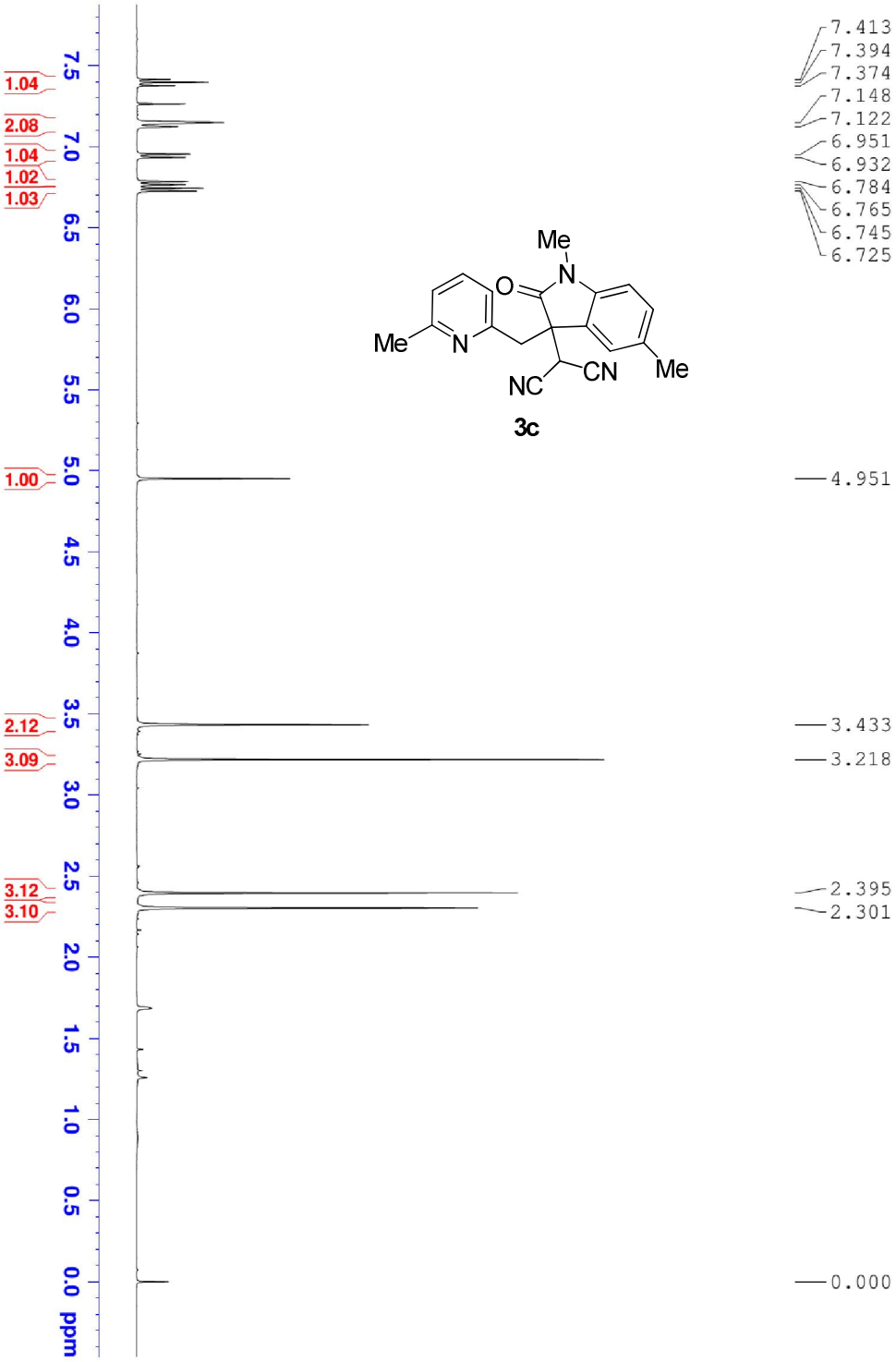
Me
N
NC
CN

3b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3.218
2.395
2.301
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2.08
1.04
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Me
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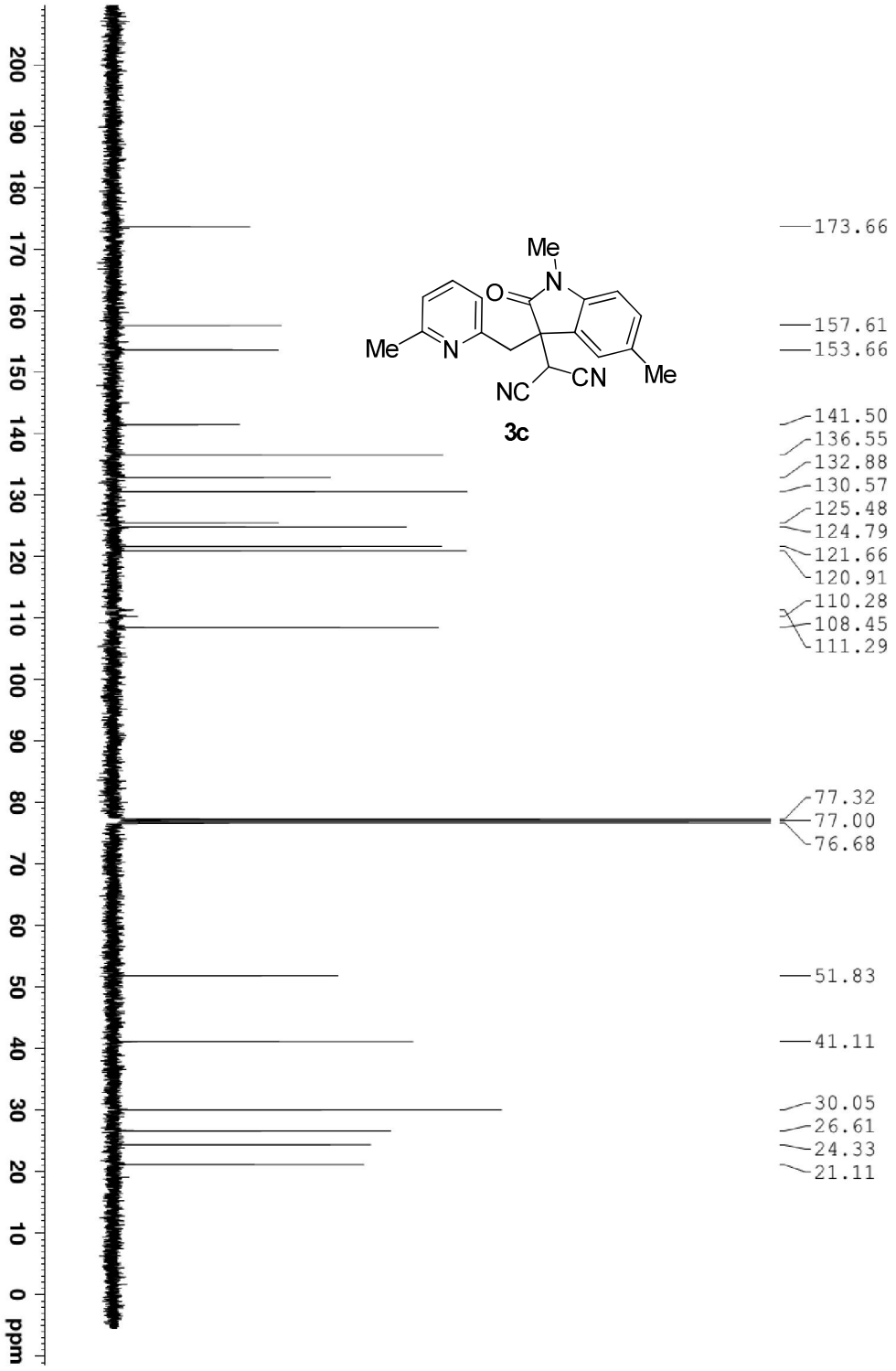
CN
Me
3c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77.00
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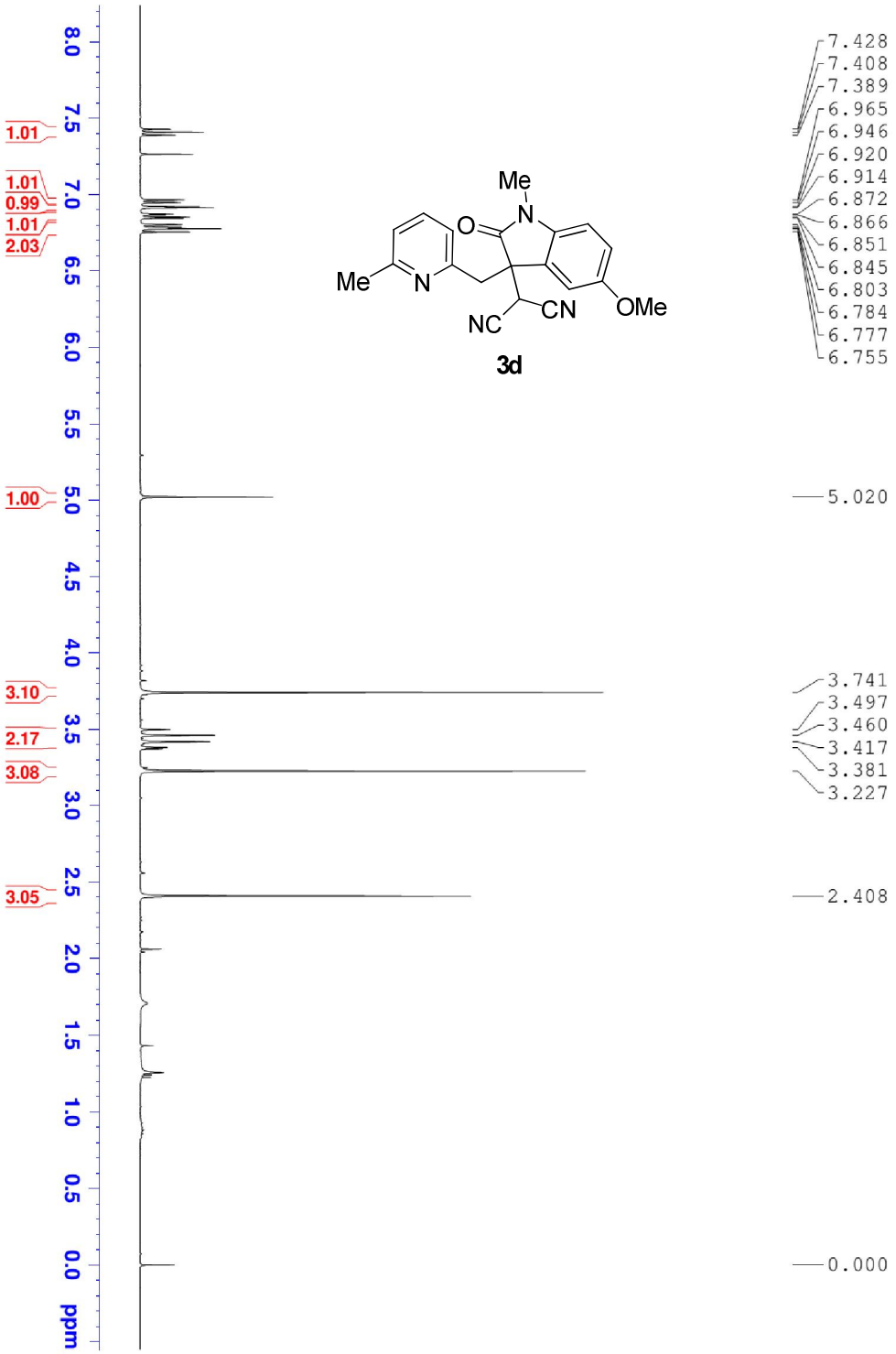
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6.845
6.803
6.784
6.777
6.755
5.020
3.741
3.497
3.460
3.417
3.381
3.227
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1.01
0.99
1.01
2.03
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3.08
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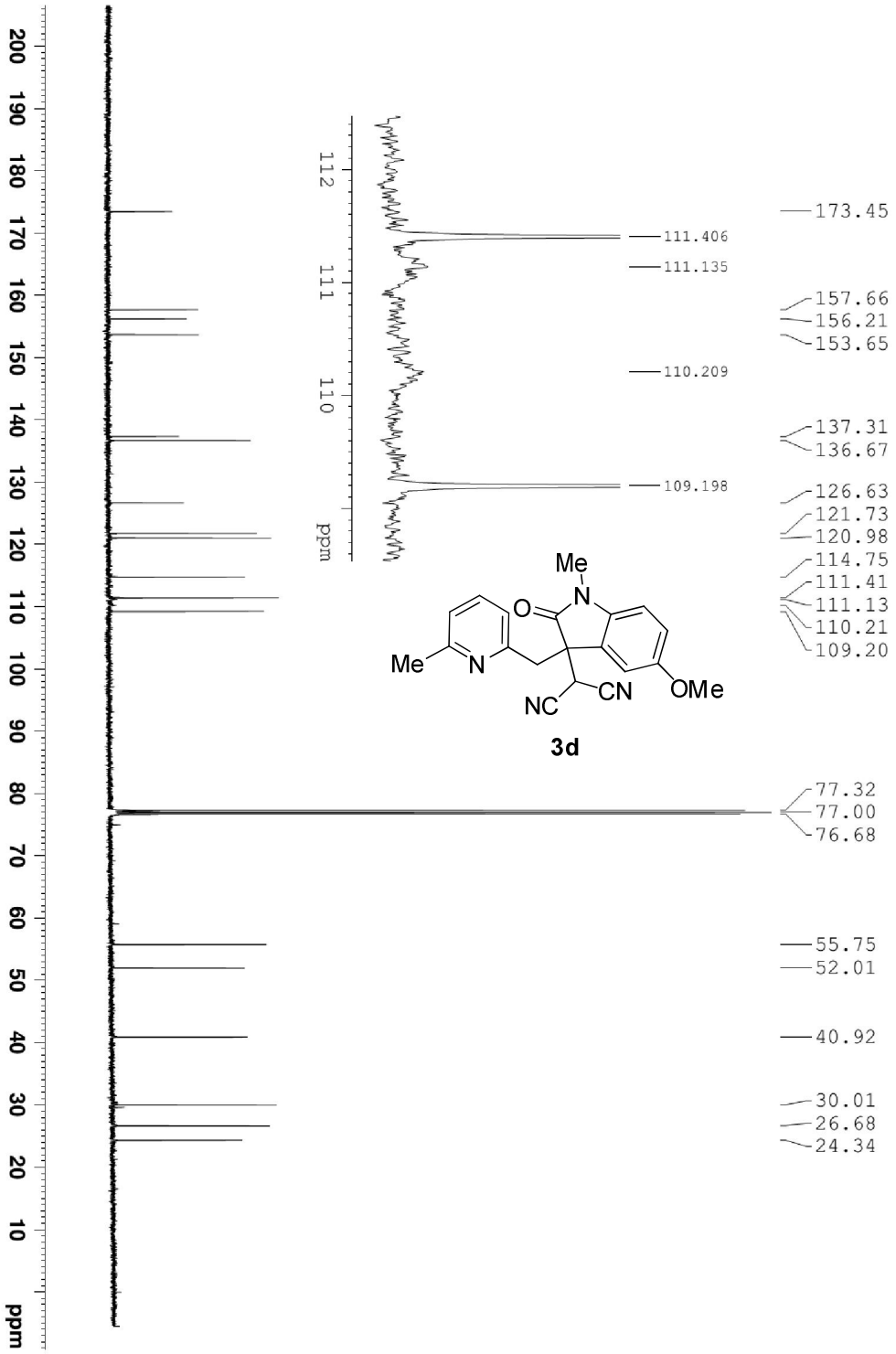
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110.21
109.20
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76.68
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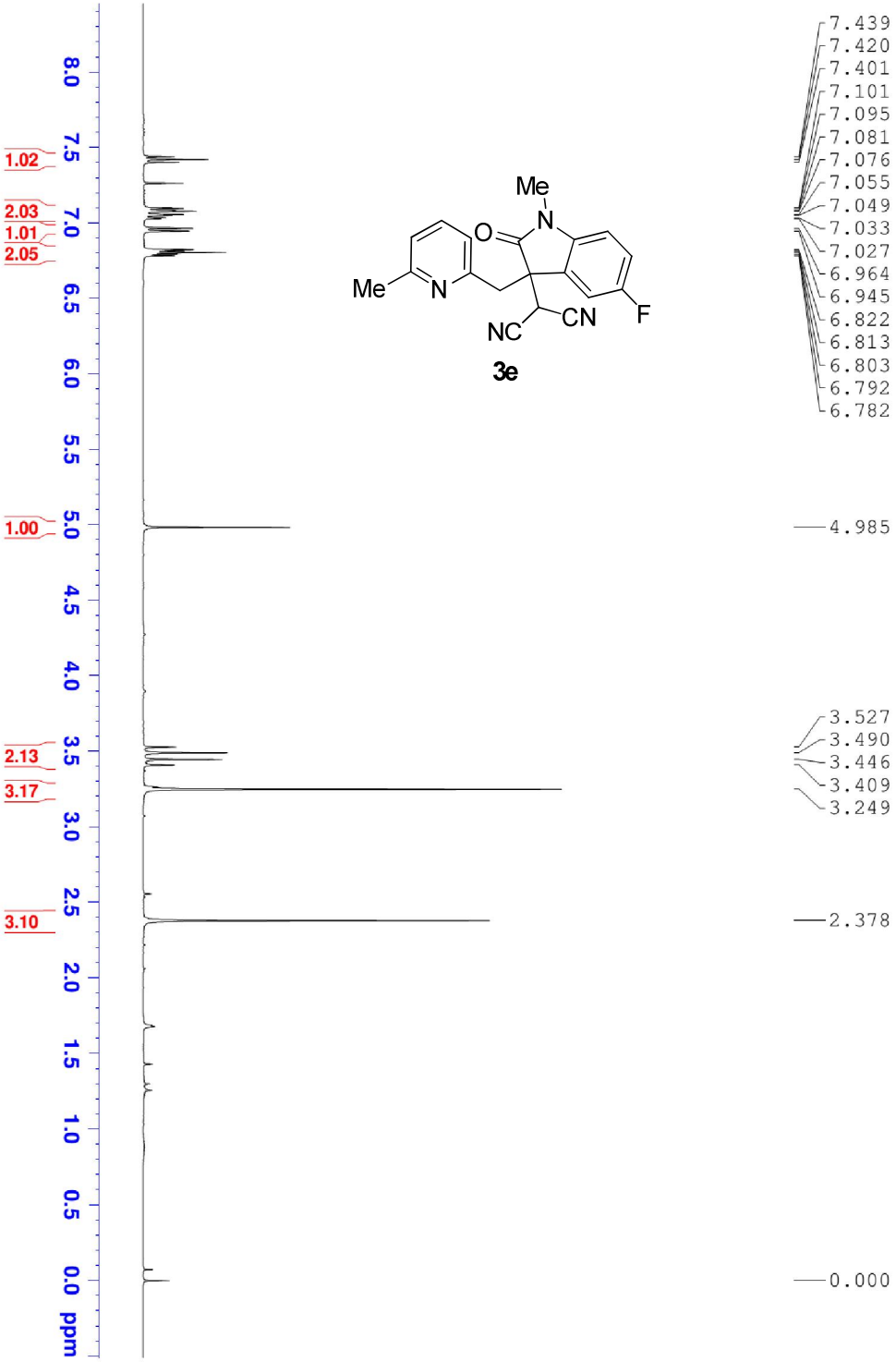
OMe
3d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Me
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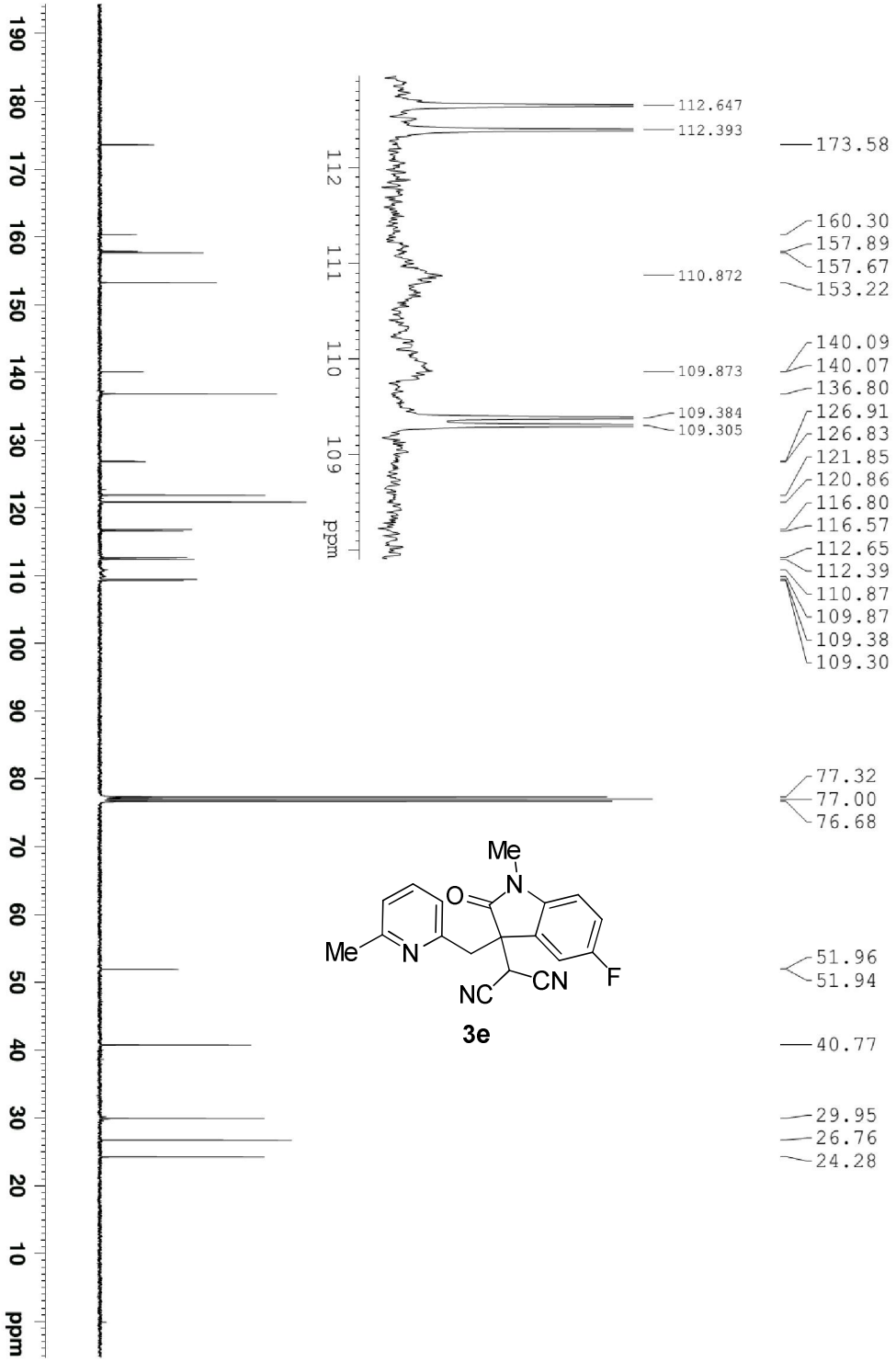
NC
CN
F

3e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140.07
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121.85
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112.39
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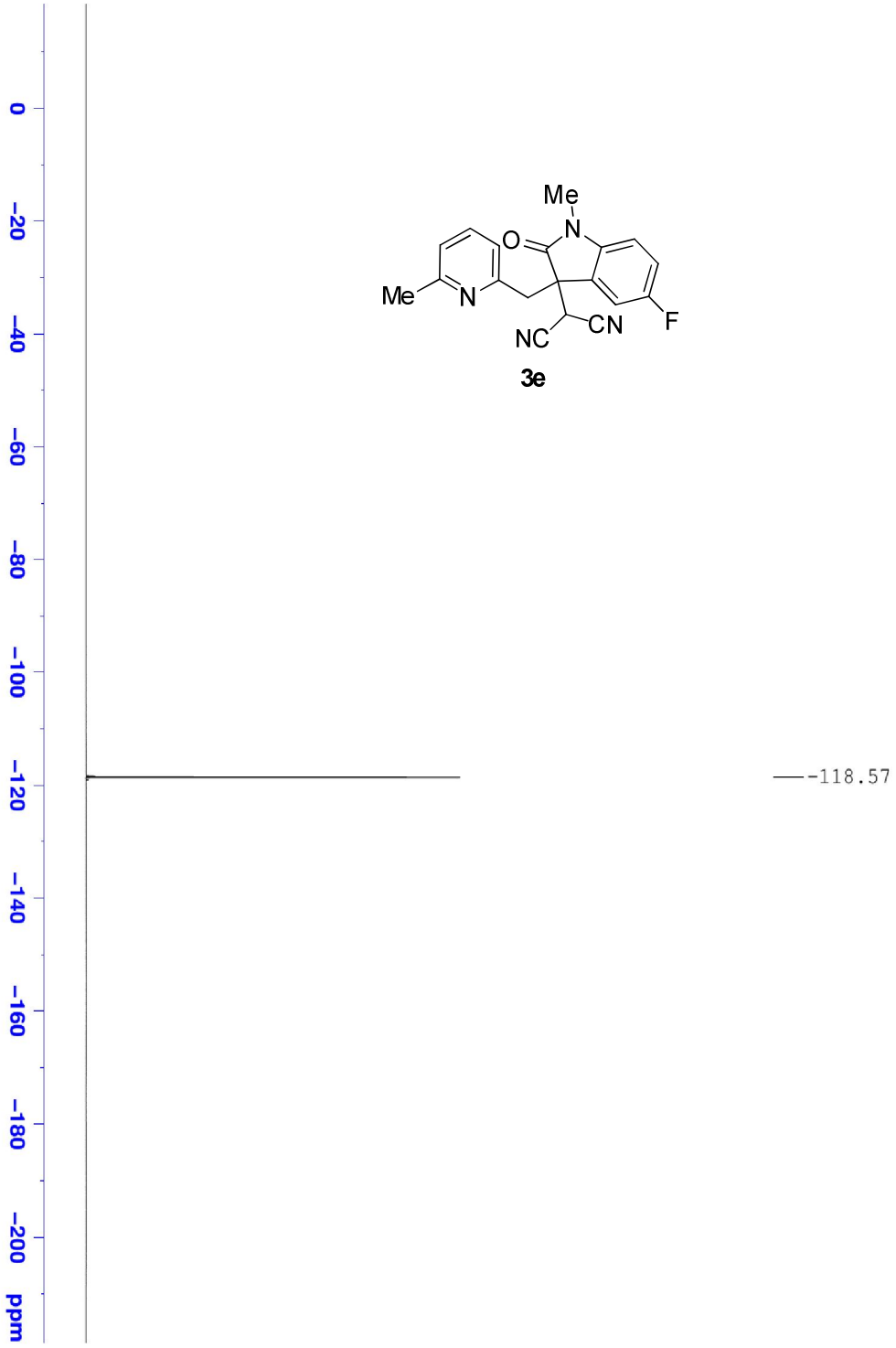
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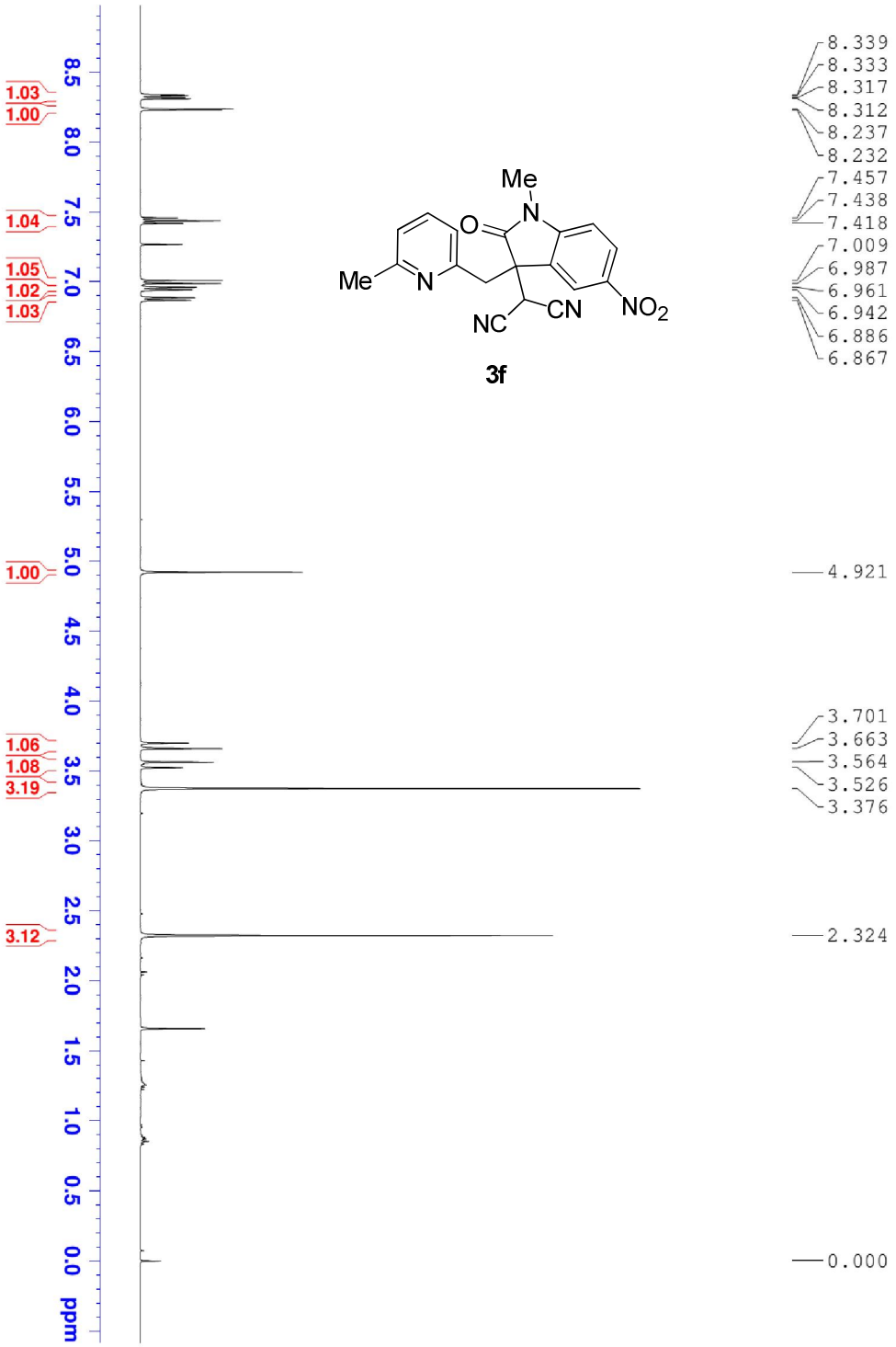
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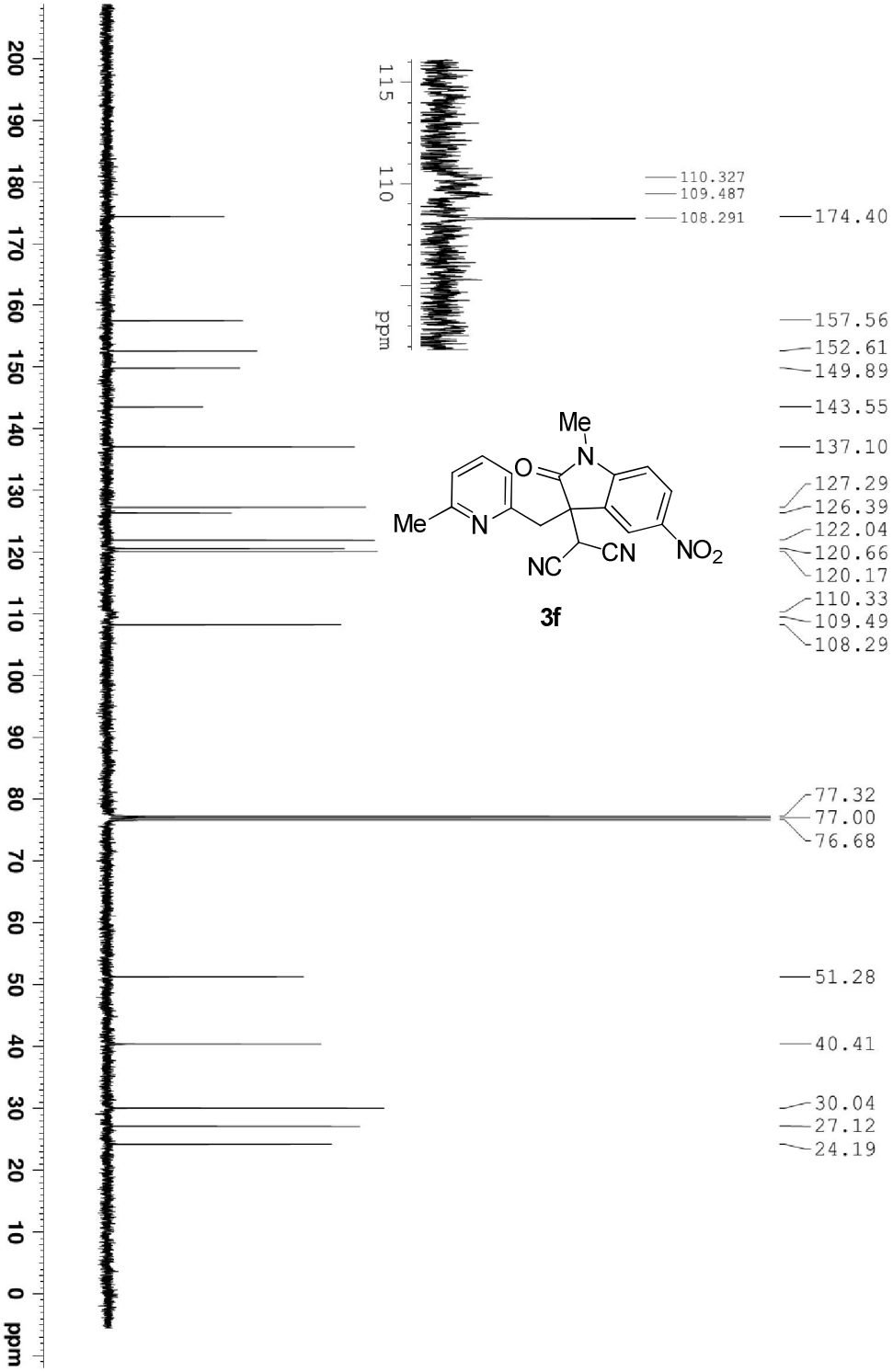
3f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126.39
122.04
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120.17
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108.29
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77.00
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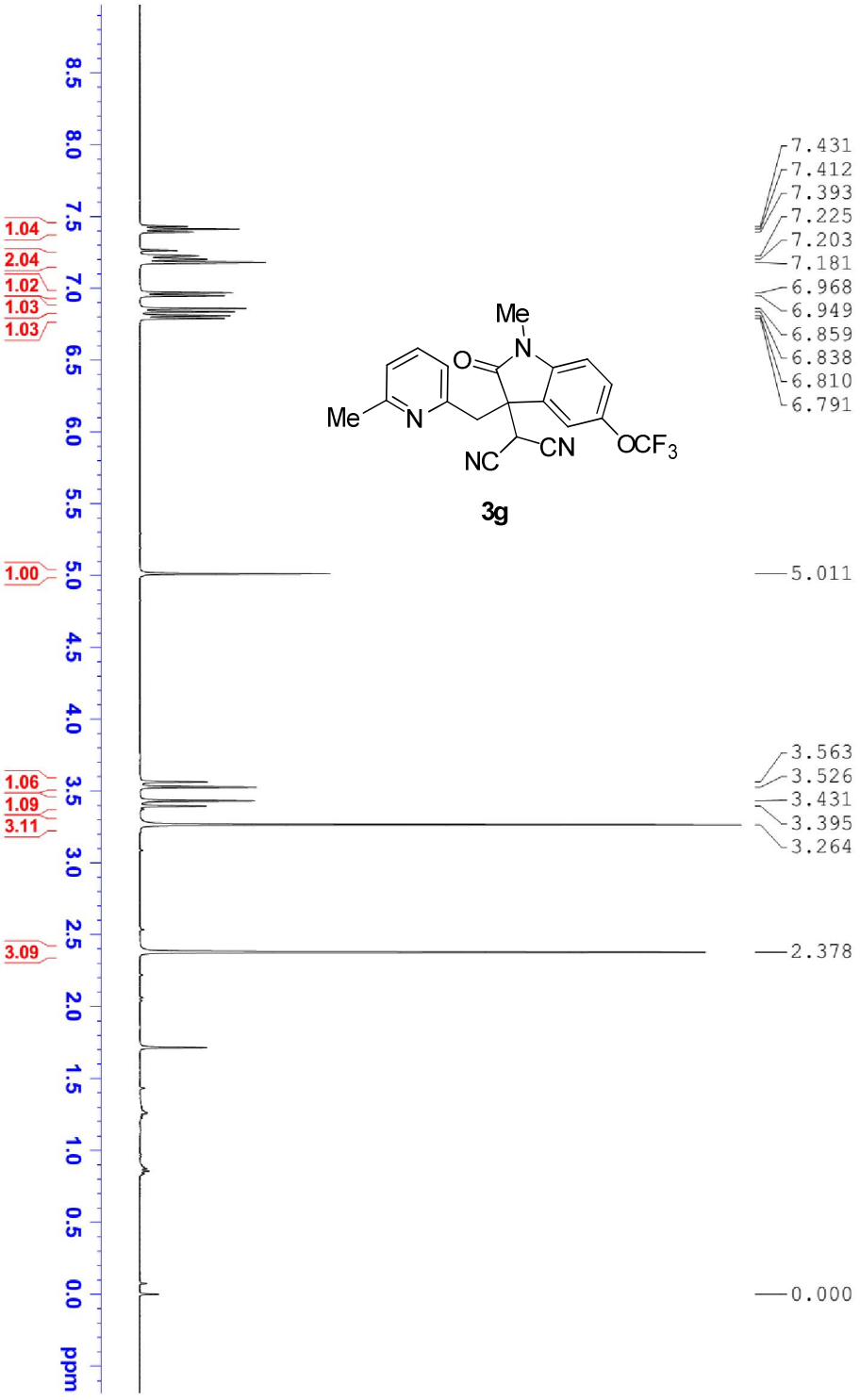
3f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1.06
1.09
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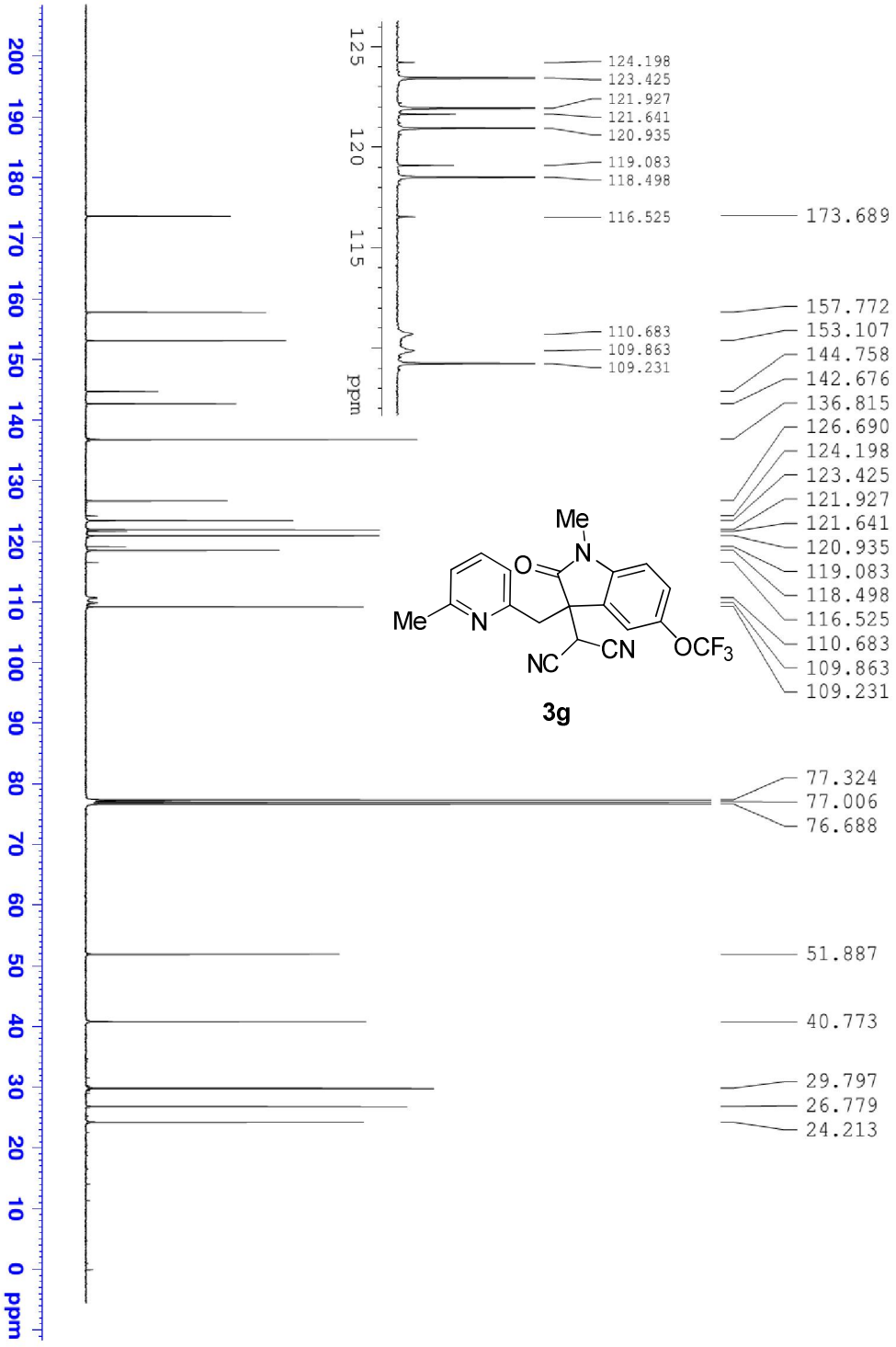
OCF3

3g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118.498
116.525
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109.231
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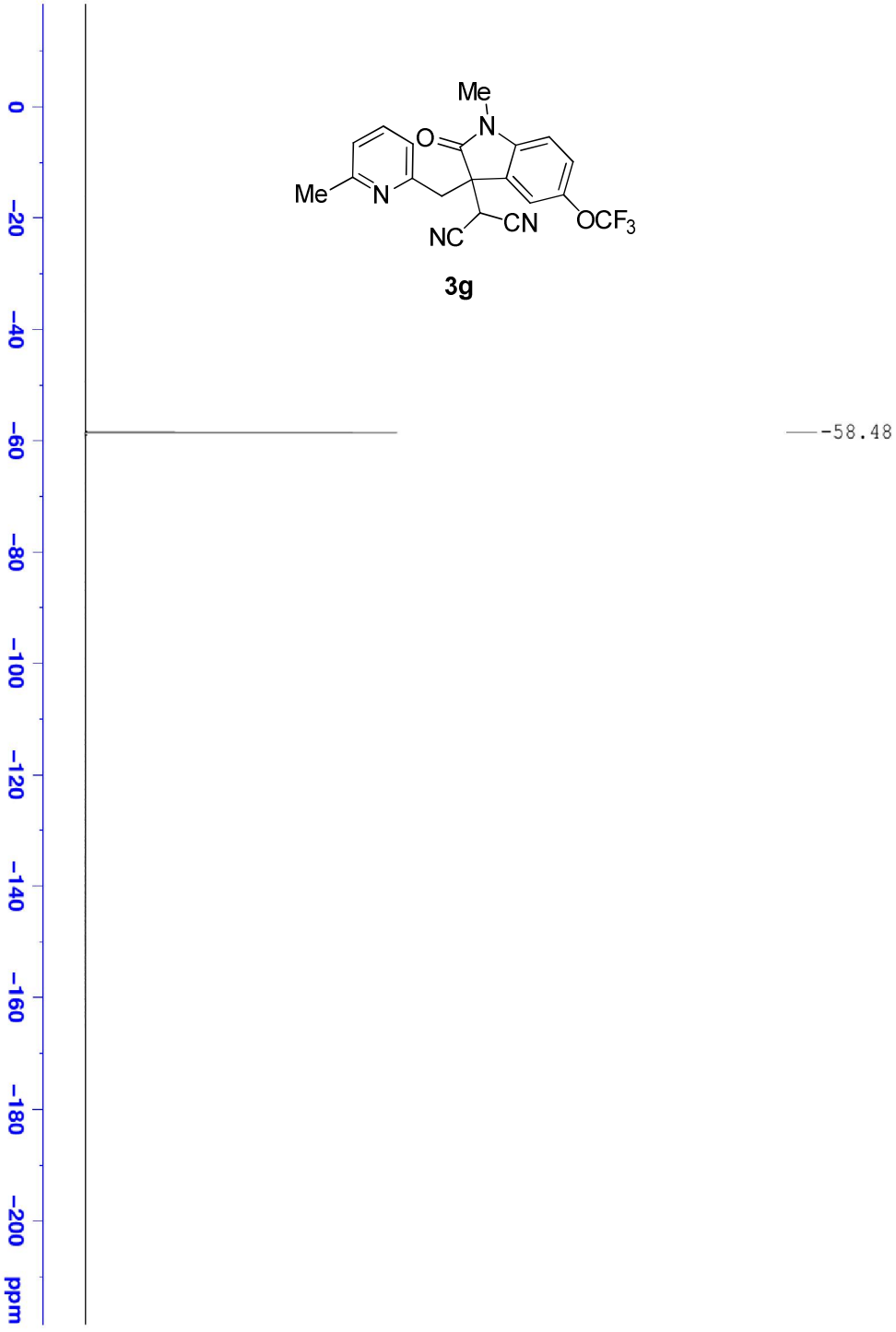
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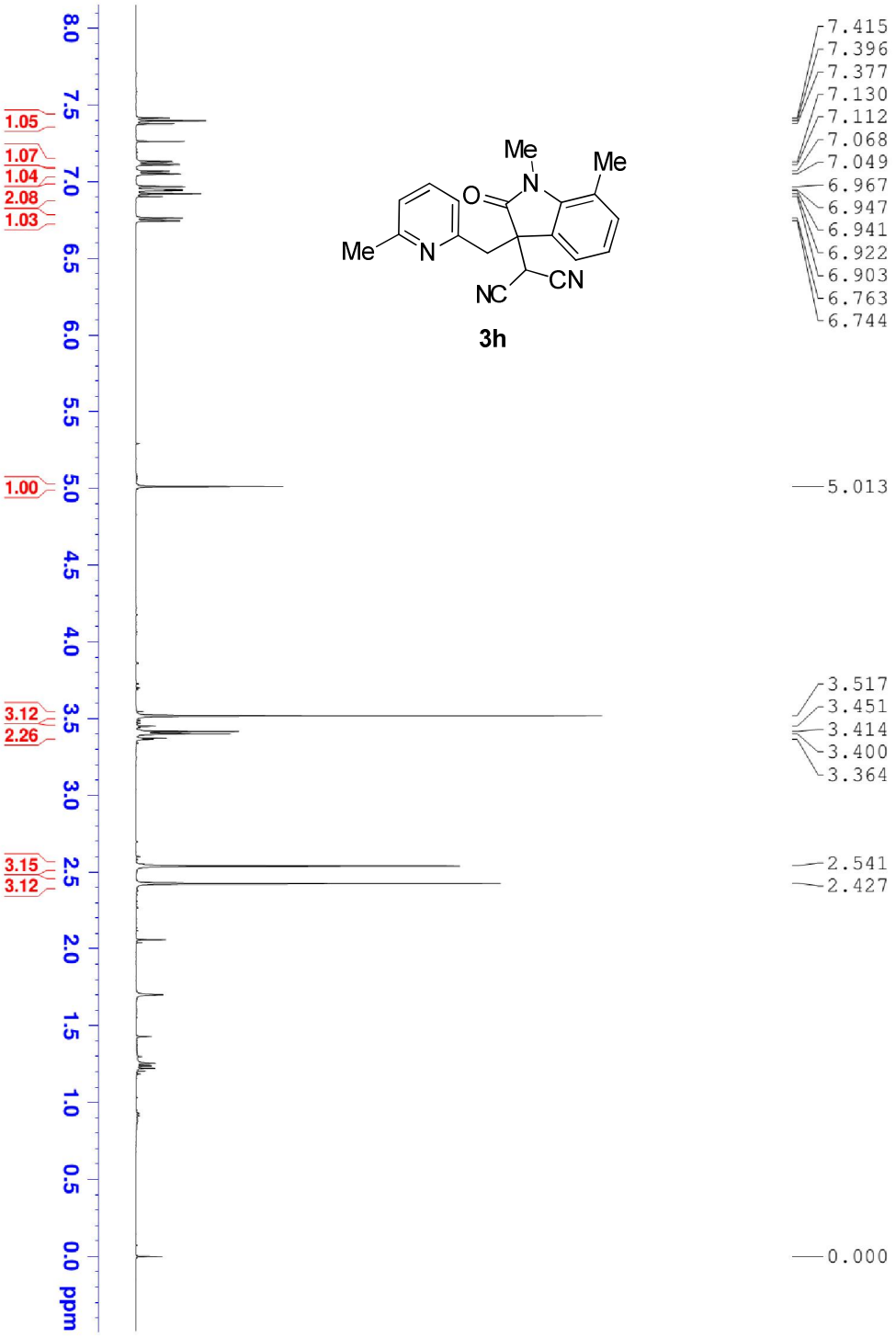
ppm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6.763
6.744
5.013
3.517
3.451
3.414
3.400
3.364
2.541
2.427
0.000
1.05
1.07
1.04
2.08
1.03
1.00
3.12
2.26
3.15
3.12
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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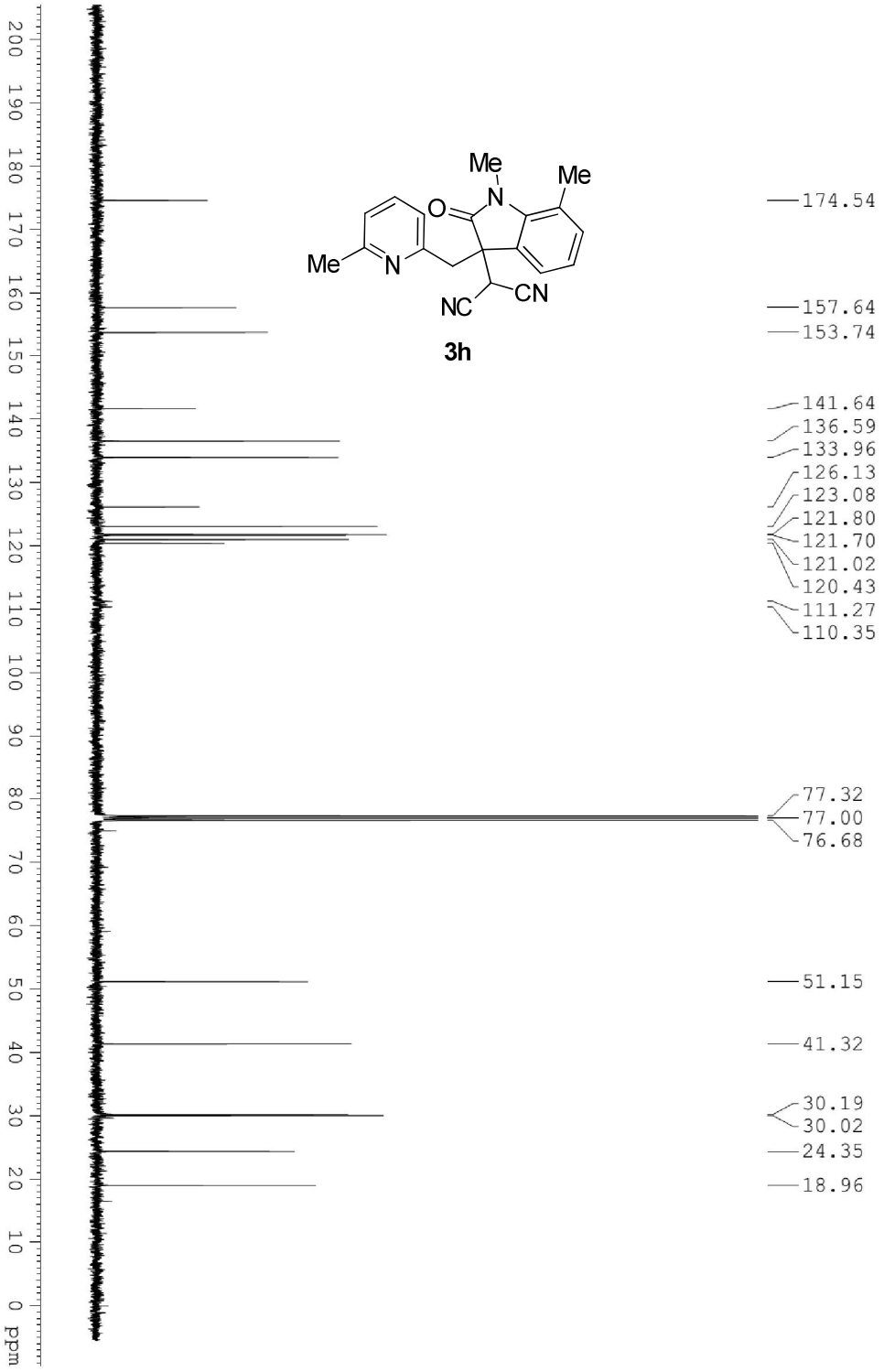
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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Me
O
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Me
N
NC
CN
3h
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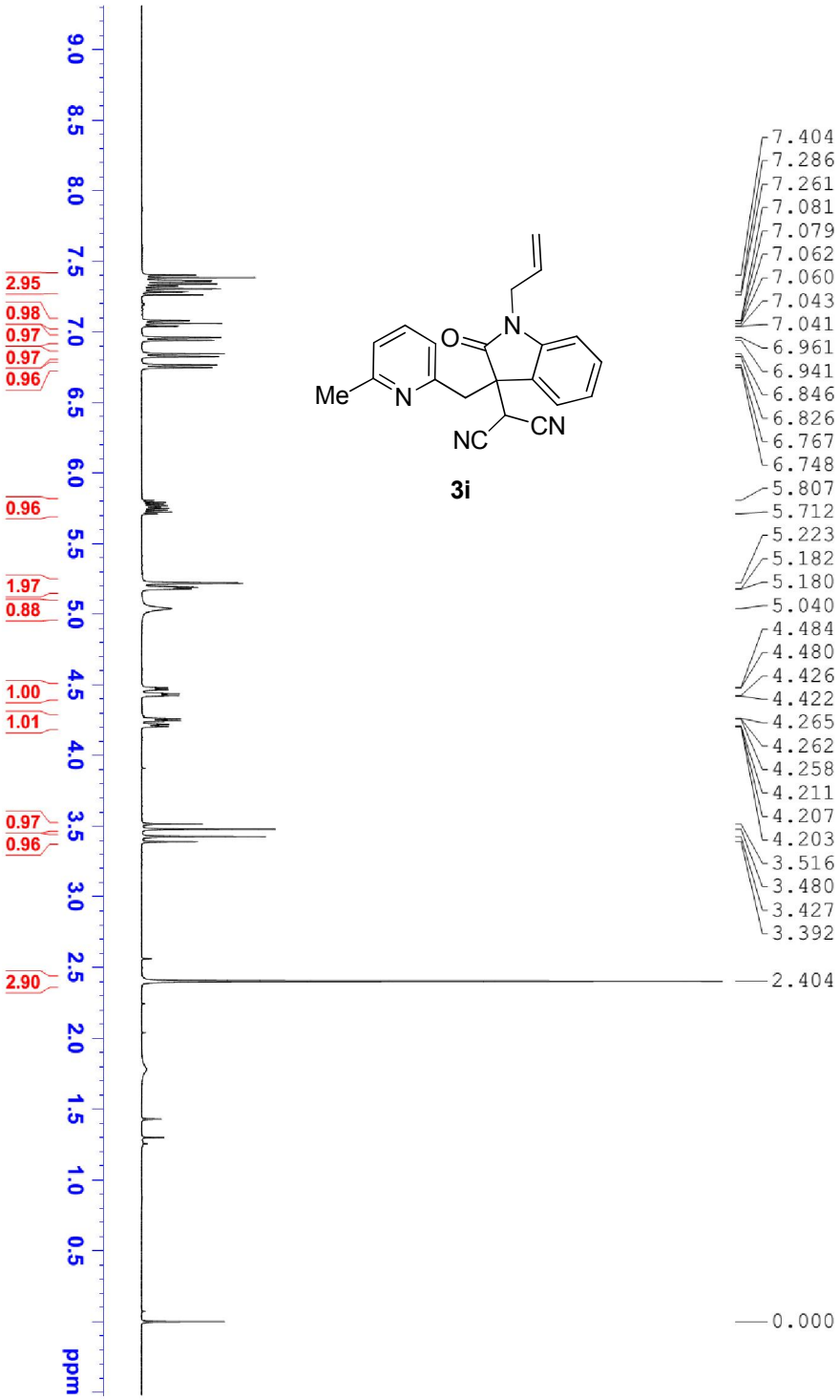
153.74
141.64
136.59
133.96
126.13
123.08
121.80
121.70
121.02
120.43
111.27
110.35
77.32
77.00
76.68
51.15
41.32
30.19
30.02
24.35
18.96
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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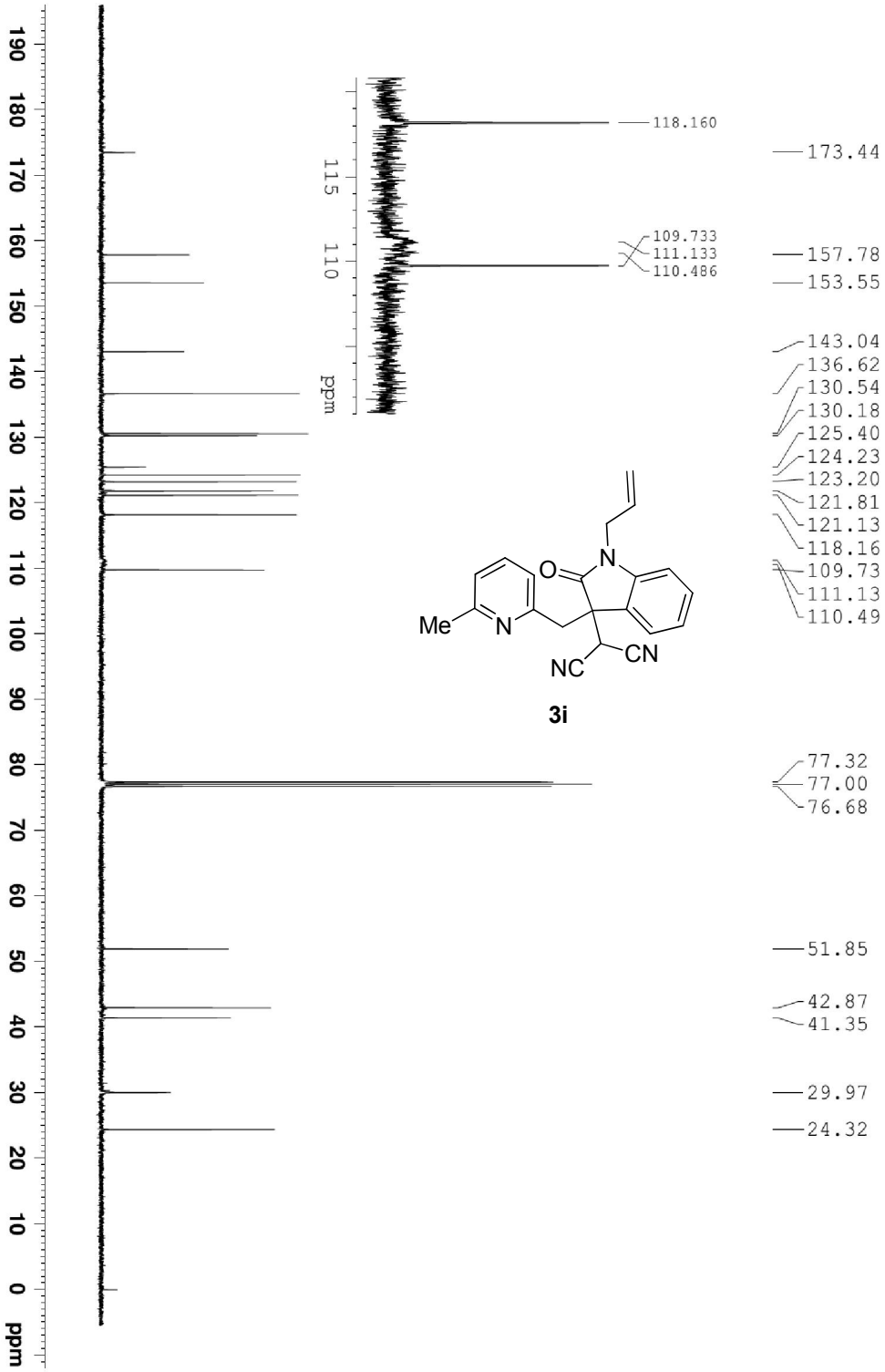
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.95
0.98
0.97
0.97
0.96
0.96
1.97
0.88
1.00
1.01
0.97
0.96
2.90
Me
N
O
N
NC
CN
7.404
7.286
7.261
7.081
7.079
7.062
7.060
7.043
7.041
6.961
6.941
6.846
6.826
6.767
6.748
5.807
5.712
5.223
5.182
5.180
5.040
4.484
4.480
4.426
4.422
4.265
4.262
4.258
4.211
4.207
4.203
3.516
3.480
3.427
3.392
2.404
0.000

3i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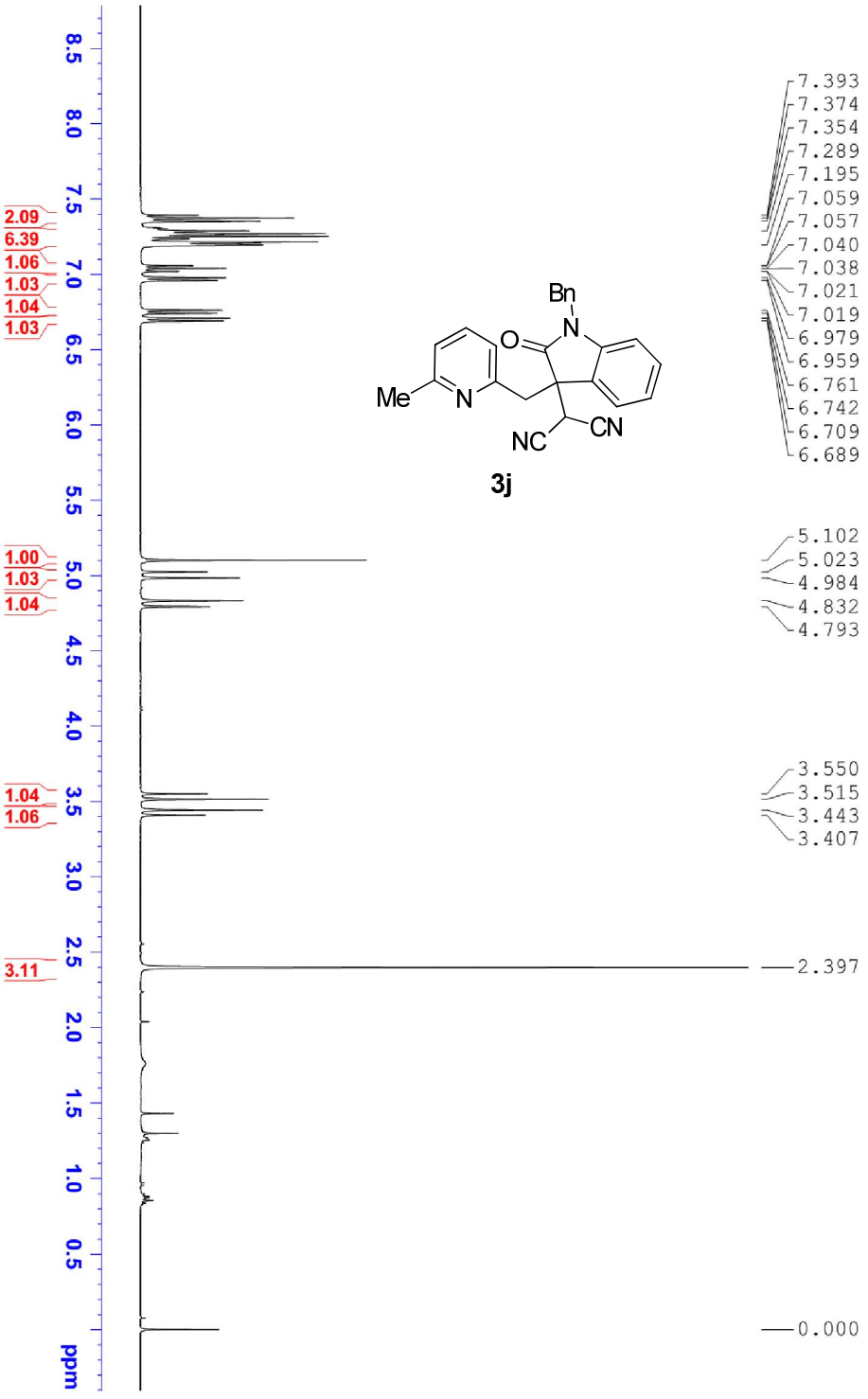
153.55
143.04
136.62
130.54
130.18
125.40
124.23
123.20
121.81
121.13
118.16
109.73
111.13
110.49
77.32
77.00
76.68
51.85
42.87
41.35
29.97
24.32
ppm
Me
N
O
N
NC
CN
3i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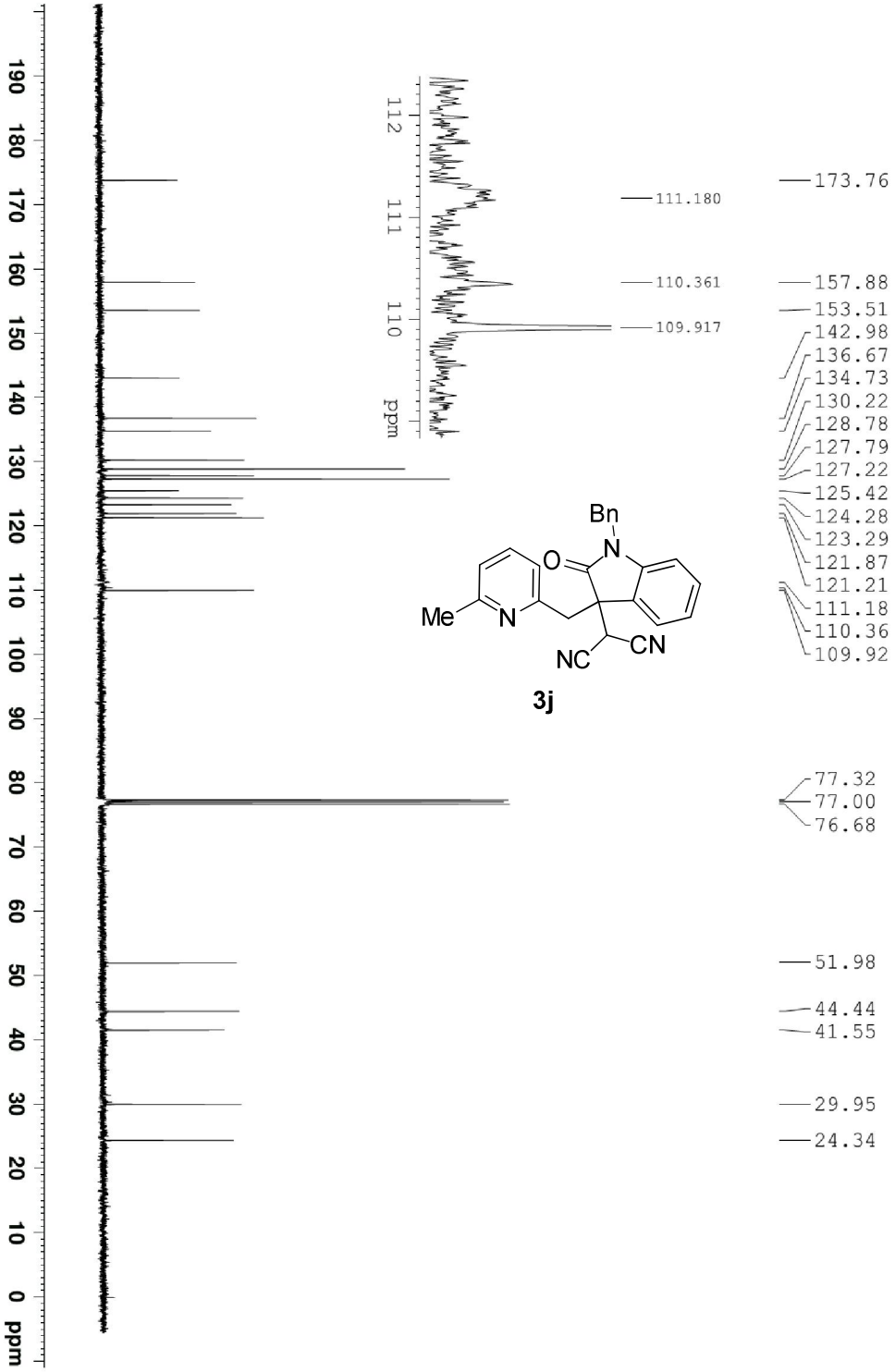
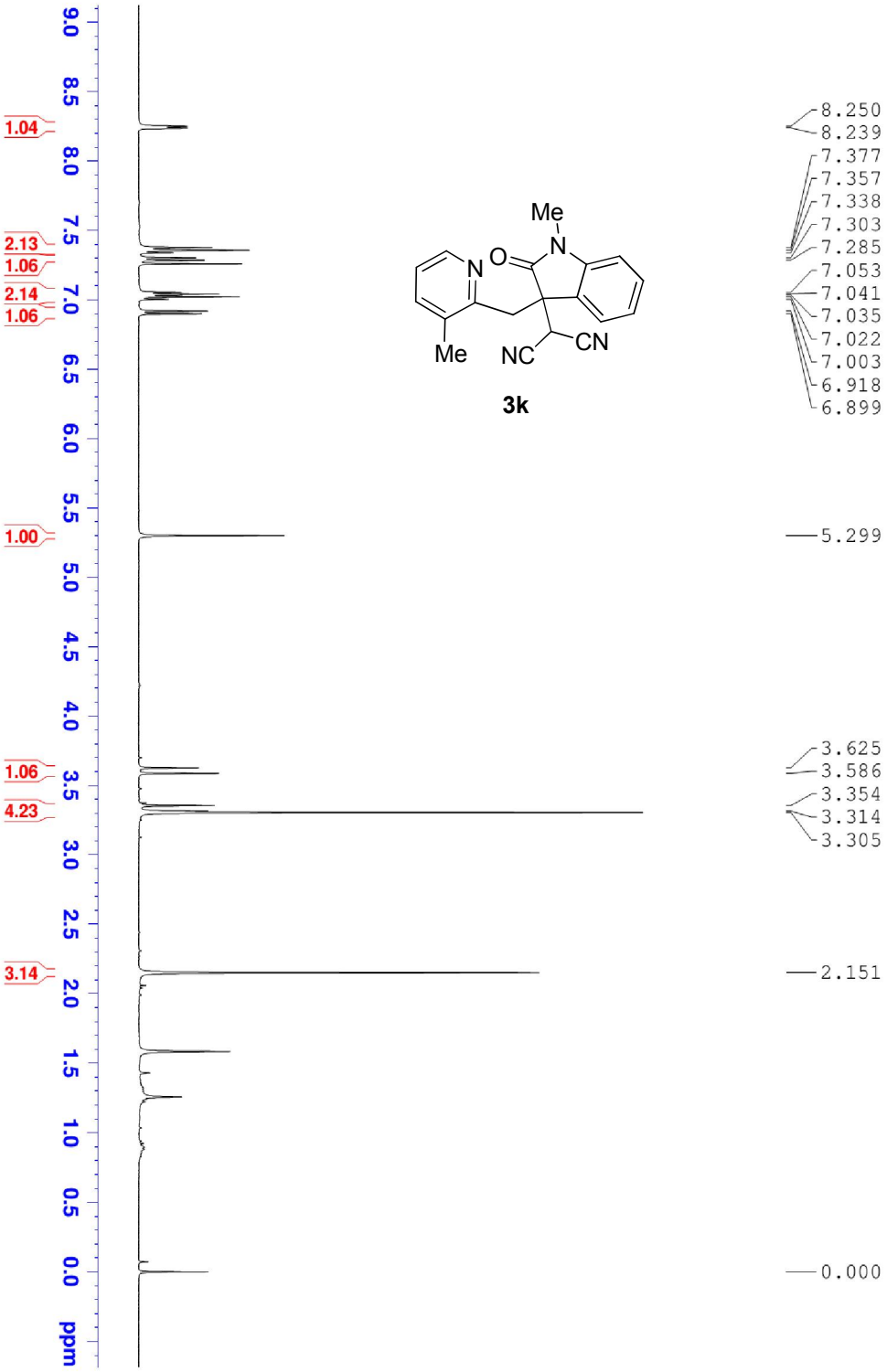
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.09
6.39
1.06
1.03
1.04
1.03
1.00
1.03
1.04
1.04
1.06
3.11
7.393
7.374
7.354
7.289
7.195
7.059
7.057
7.040
7.038
7.021
7.019
6.979
6.959
6.761
6.742
6.709
6.689
5.102
5.023
4.984
4.832
4.793
3.550
3.515
3.443
3.407
2.397
0.000
Bn
N
O
Me
N
NC
CN
3j


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
112 111 110 ppm
111.180
110.361
109.917
173.76
157.88
153.51
142.98
136.67
134.73
130.22
128.78
127.79
127.22
125.42
124.28
123.29
121.87
121.21
111.18
110.36
109.92
77.32
77.00
76.68
51.98
44.44
41.55
29.95
24.34
Bn
N
O
Me
N
NC
CN
3j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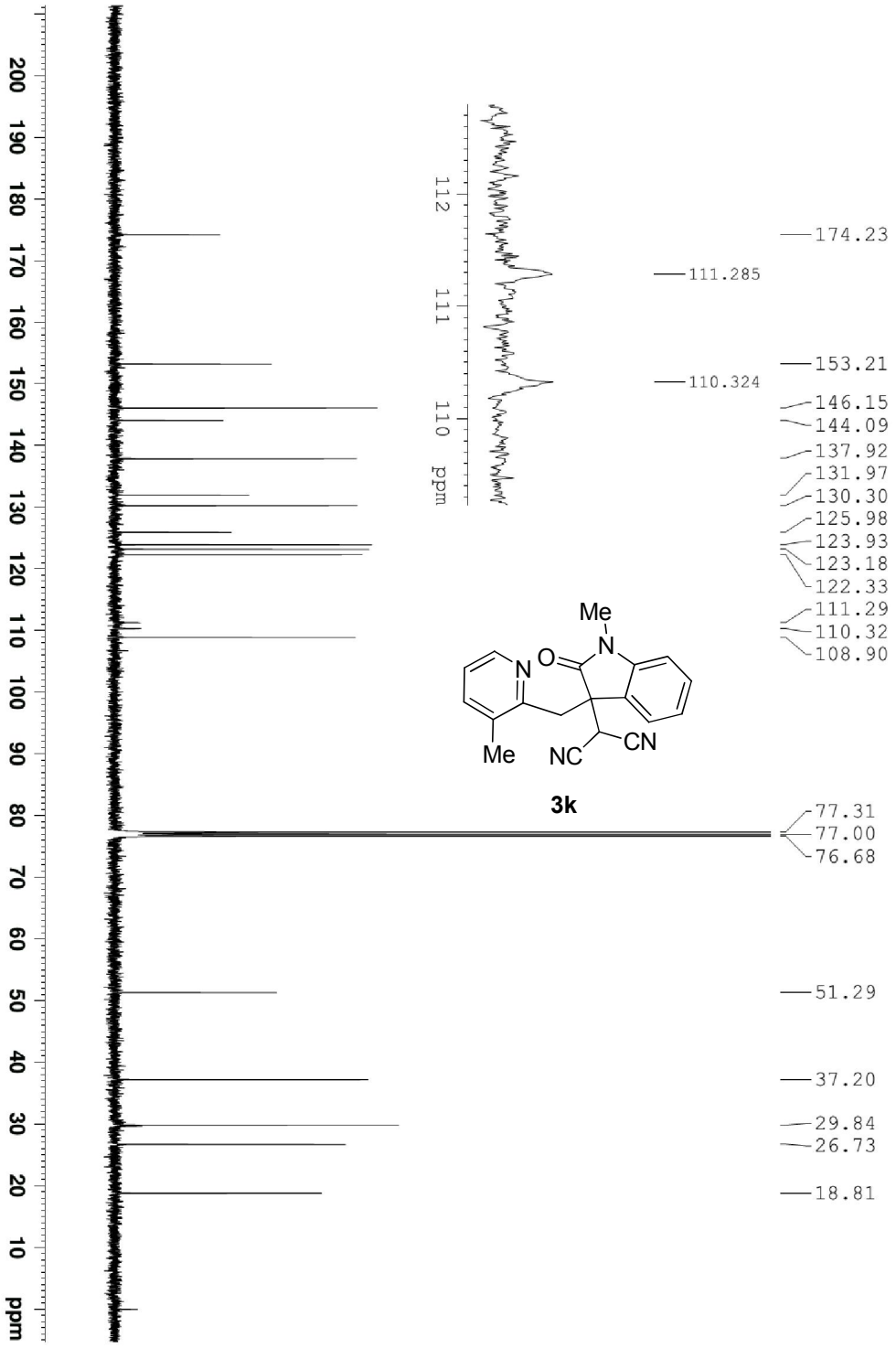
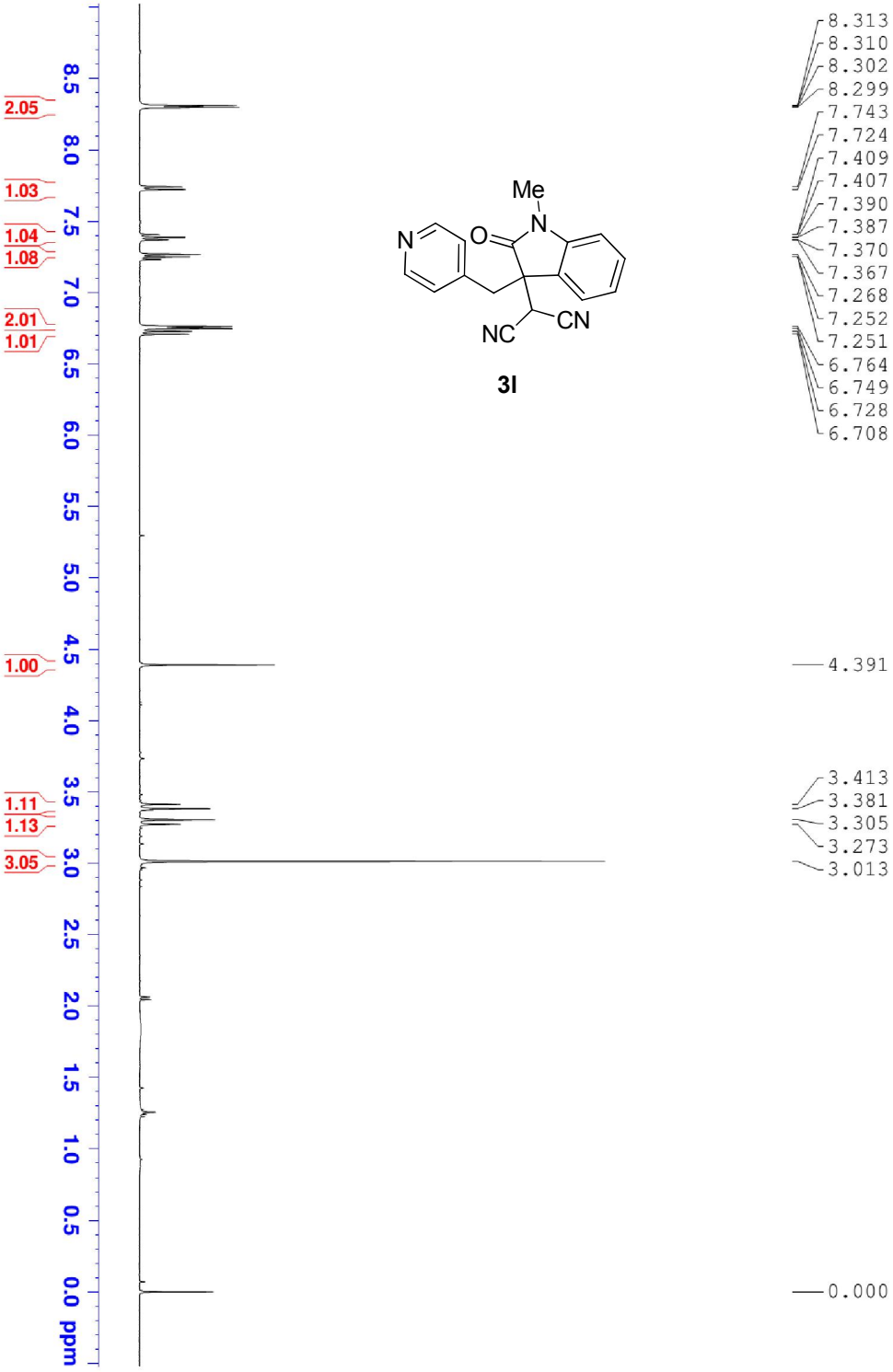
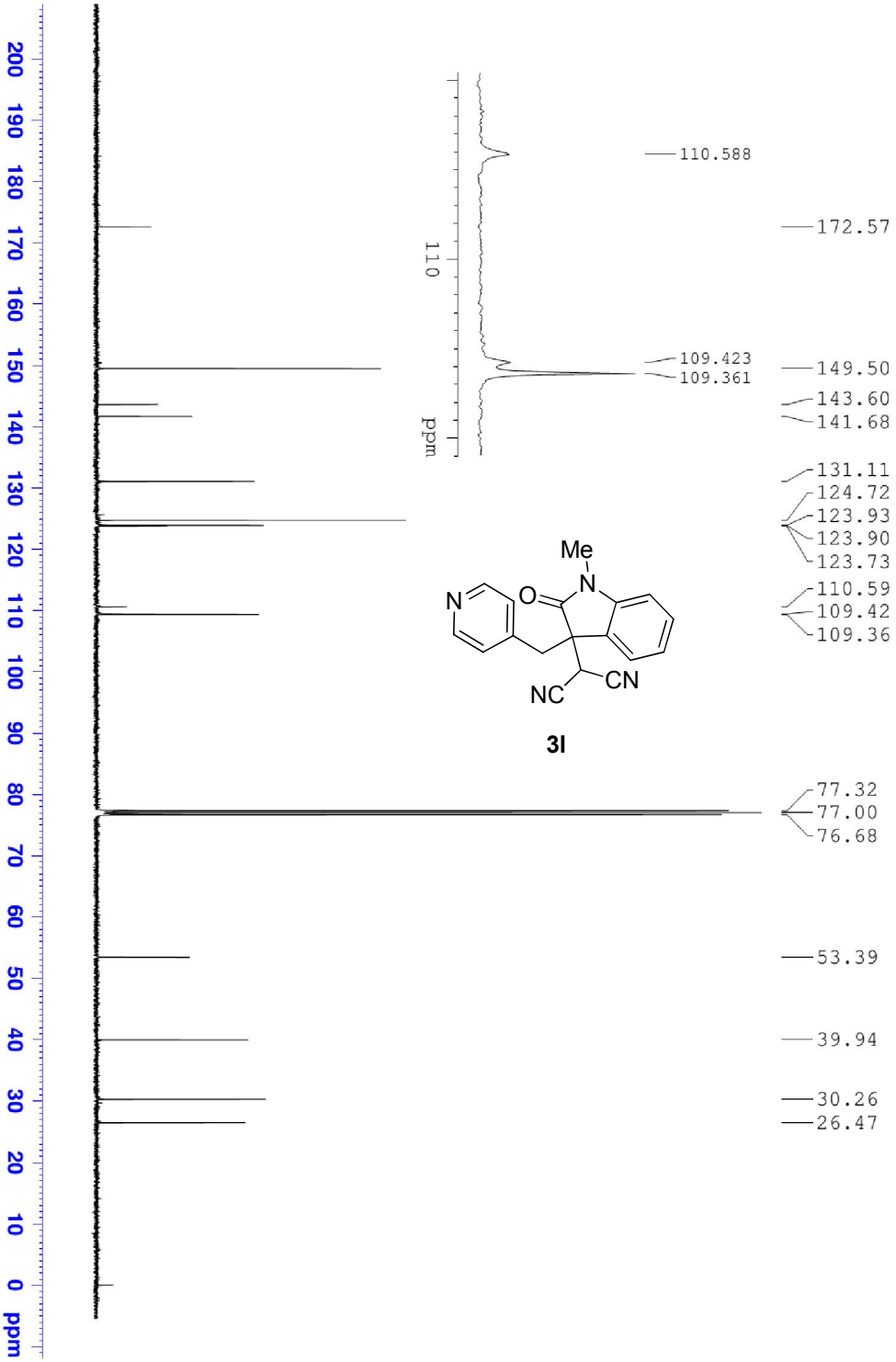
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.04
2.13
1.06
2.14
1.06
1.00
1.06
4.23
3.14
Me
N
O
N
Me
NC
CN
3k
8.250
8.239
7.377
7.357
7.338
7.303
7.285
7.053
7.041
7.035
7.022
7.003
6.918
6.899
5.299
3.625
3.586
3.354
3.314
3.305
2.151
0.000


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
112 111 110 ppm
111.285
110.324
174.23
153.21
146.15
144.09
137.92
131.97
130.30
125.98
123.93
123.18
122.33
111.29
110.32
108.90
77.31
77.00
76.68
51.29
37.20
29.84
26.73
18.81
Me
N
O
N
Me
NC
CN

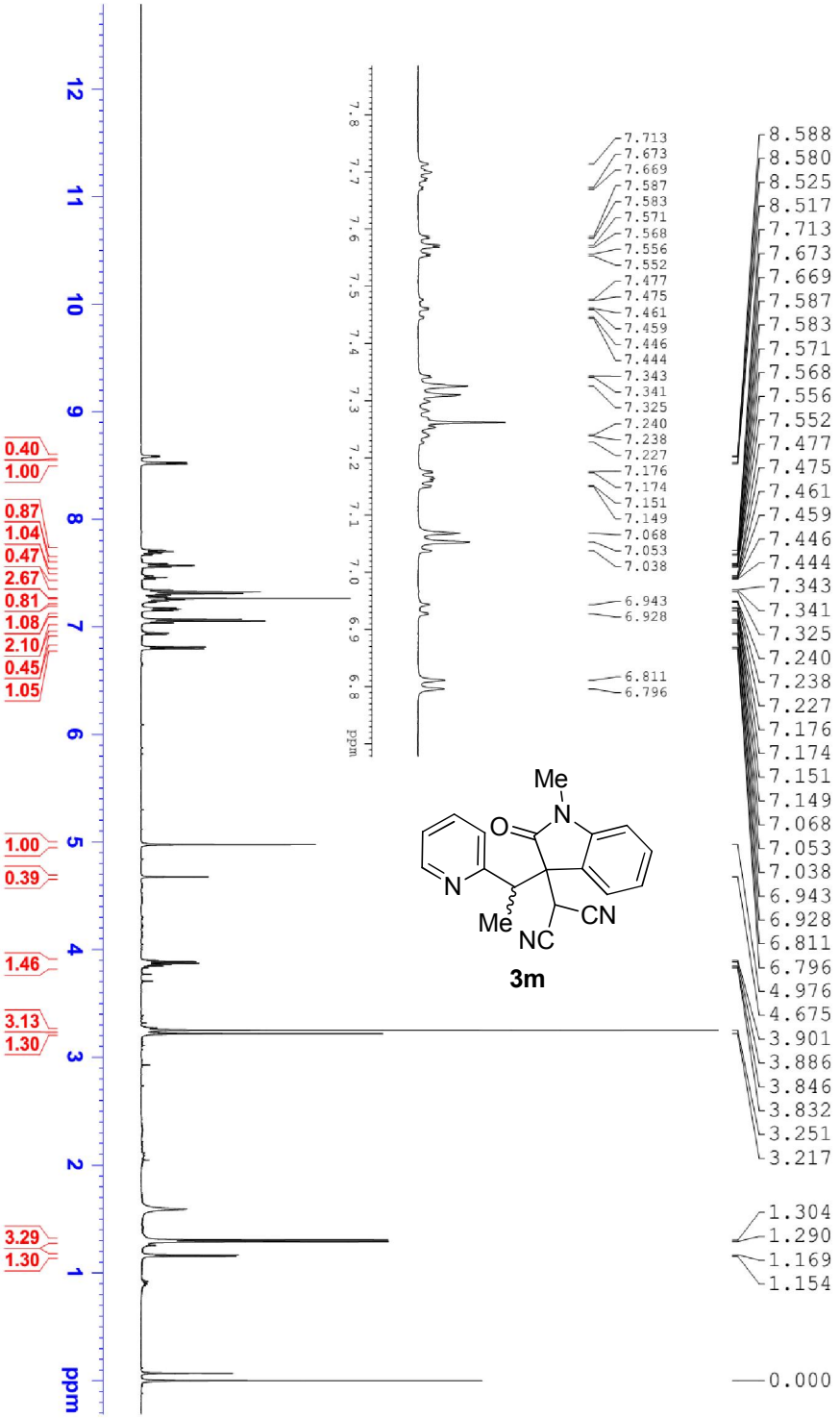
3k

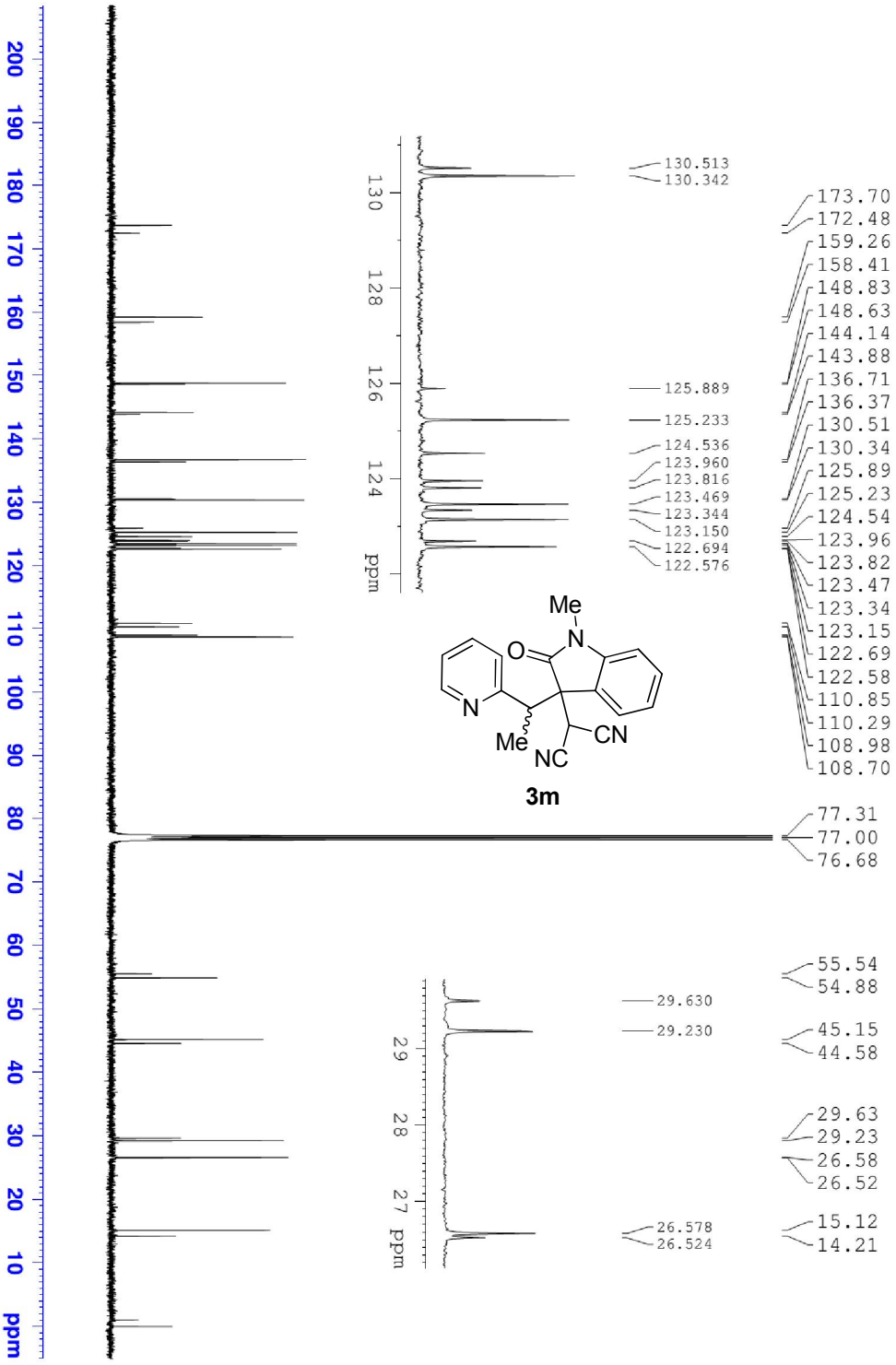

8.313
8.310
8.302
8.299
7.743
7.724
7.409
7.407
7.390
7.387
7.370
7.367
7.268
7.252
7.251
6.764
6.749
6.728
6.708
4.391
3.413
3.381
3.305
3.273
3.013
0.000
2.05
1.03
1.04
1.08
2.01
1.01
1.00
1.11
1.13
3.05
Me
N
O
N
NC
CN
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

3l


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
110
ppm
110.588
109.423
109.361
172.57
149.50
143.60
141.68
131.11
124.72
123.93
123.90
123.73
110.59
109.42
109.36
77.32
77.00
76.68
53.39
39.94
30.26
26.47
Me
N
O
N
NC
CN

3l


0.40
1.00
0.87
1.04
0.47
2.67
0.81
1.08
2.10
0.45
1.05
1.00
0.39
1.46
3.13
1.30
3.29
1.30
ppm
7.713
7.673
7.669
7.587
7.583
7.571
7.568
7.556
7.552
7.477
7.475
7.461
7.459
7.446
7.444
7.343
7.341
7.325
7.240
7.238
7.227
7.176
7.174
7.151
7.149
7.068
7.053
7.038
6.943
6.928
6.811
6.796
8.588
8.580
8.525
8.517
4.976
4.675
3.901
3.886
3.846
3.832
3.251
3.217
1.304
1.290
1.169
1.154
0.000
Me
N
O
N
Me
NC
CN
3m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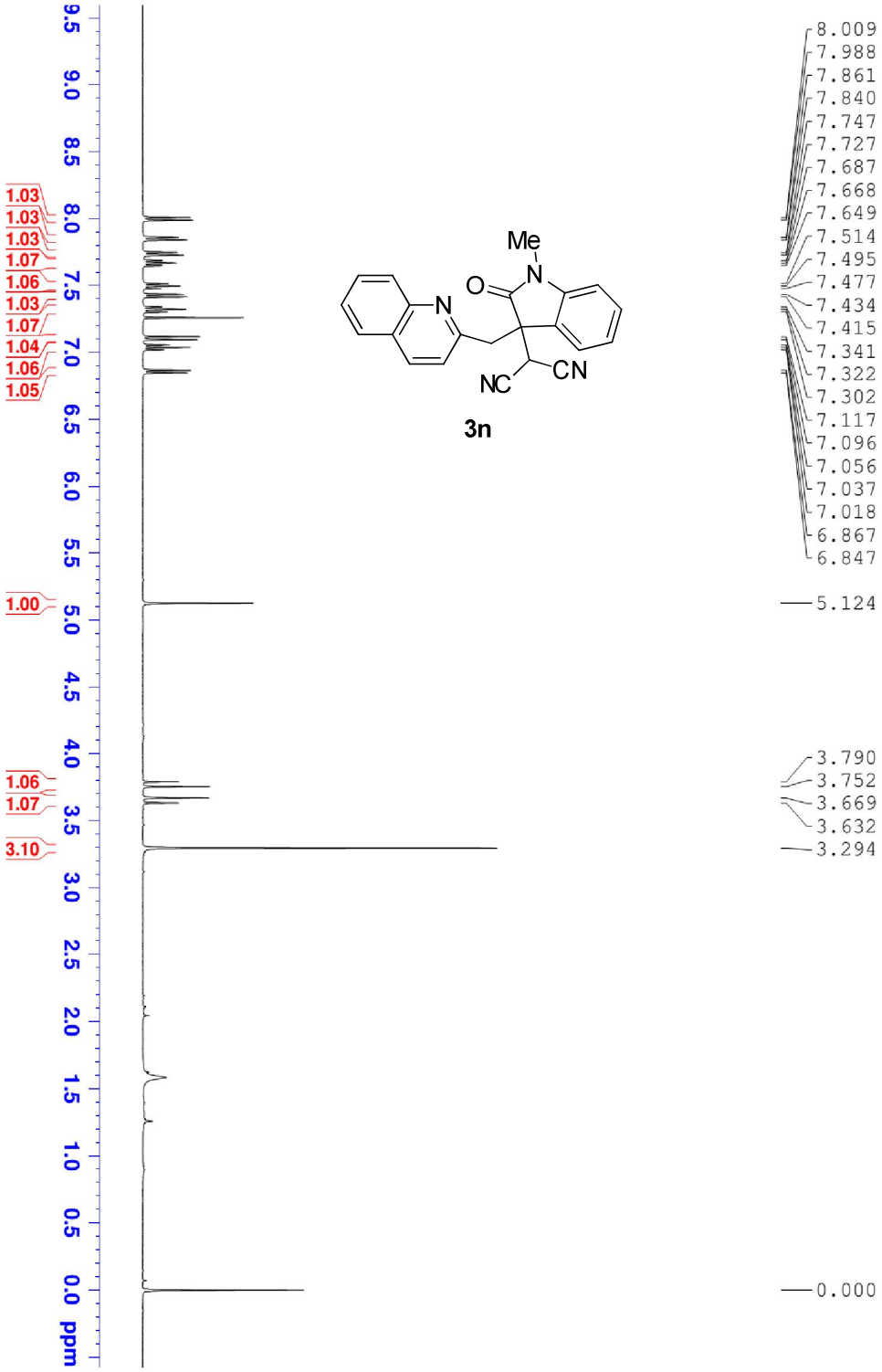
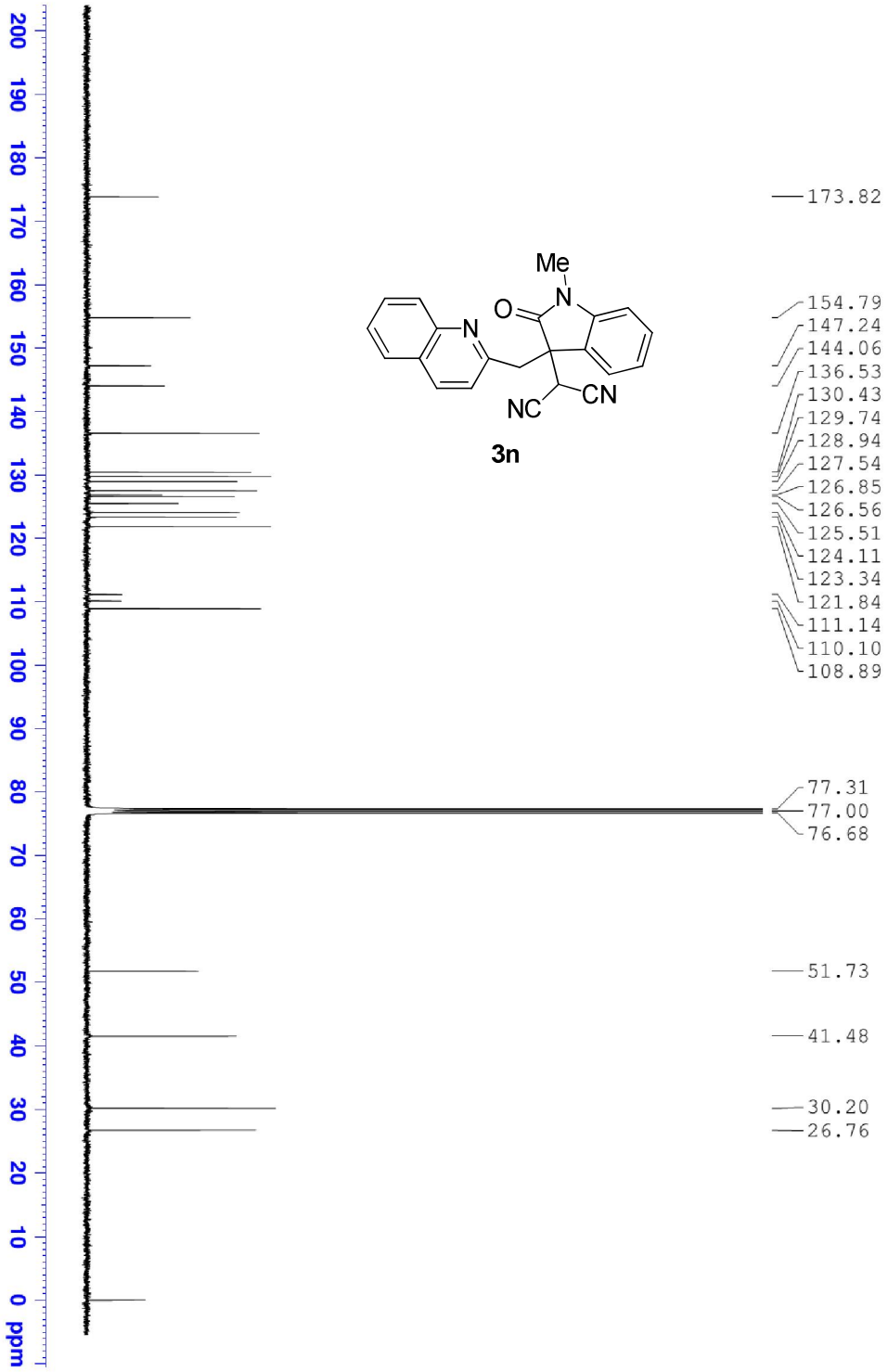
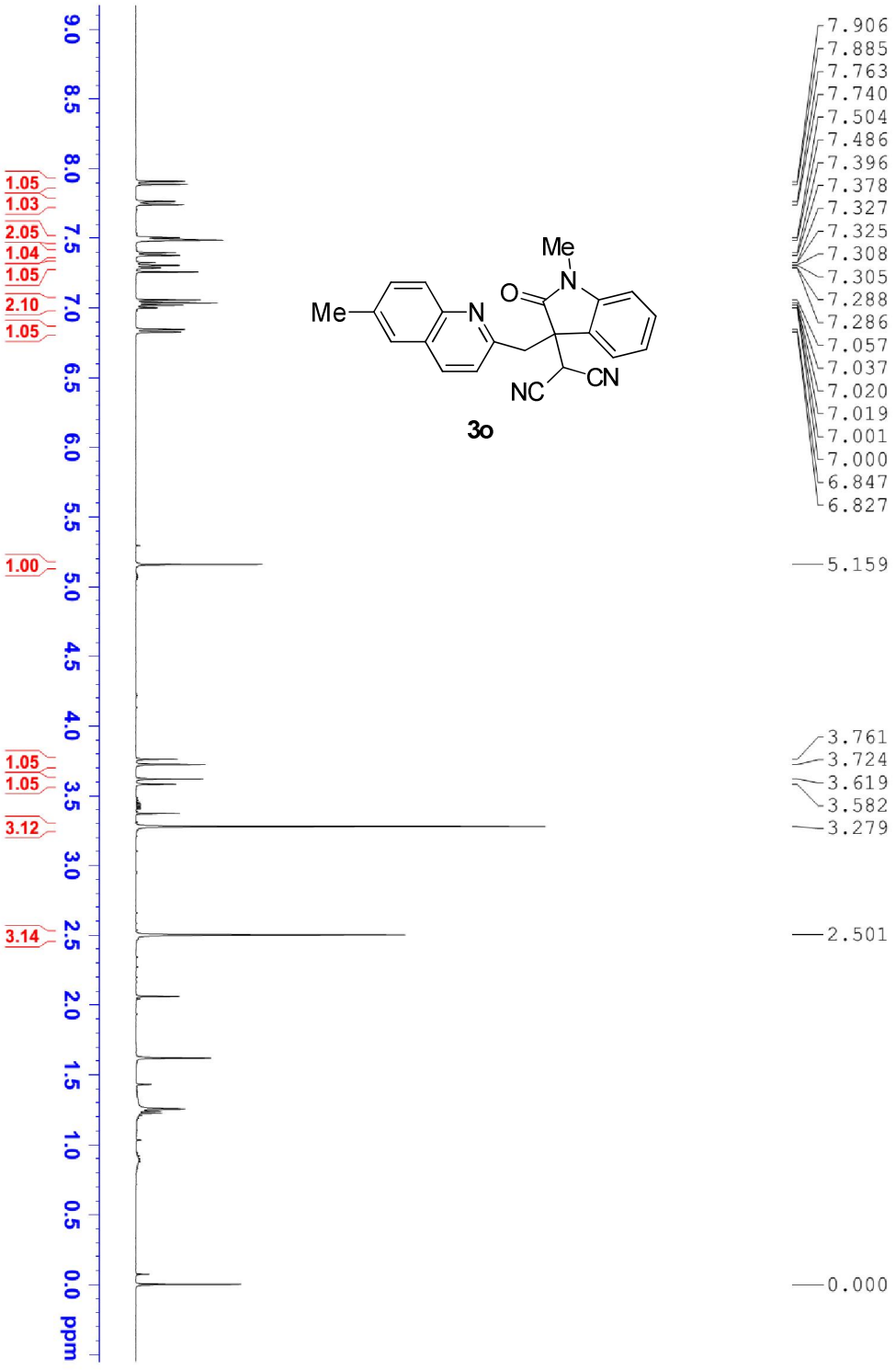
130.342
125.889
125.233
124.536
123.960
123.816
123.469
123.344
123.150
122.694
122.576
173.70
172.48
159.26
158.41
148.83
148.63
144.14
143.88
136.71
136.37
130.51
130.34
125.89
125.23
124.54
123.96
123.82
123.47
123.34
123.15
122.69
122.58
110.85
110.29
108.98
108.70
77.31
77.00
76.68
55.54
54.88
45.15
44.58
29.63
29.23
26.58
26.52
15.12
14.21
29.630
29.230
26.578
26.524
Me
N
O
N
Me
NC
CN
3m


Me
N
O
N
NC
CN
3n
8.009
7.988
7.861
7.840
7.747
7.727
7.687
7.668
7.649
7.514
7.495
7.477
7.434
7.415
7.341
7.322
7.302
7.117
7.096
7.056
7.037
7.018
6.867
6.847
5.124
3.790
3.752
3.669
3.632
3.294
0.000
1.03
1.03
1.03
1.07
1.06
1.03
1.07
1.04
1.06
1.05
1.00
1.06
1.07
3.10
ppm


Me
N
O
N
NC
CN
3n
173.82
154.79
147.24
144.06
136.53
130.43
129.74
128.94
127.54
126.85
126.56
125.51
124.11
123.34
121.84
111.14
110.10
108.89
77.31
77.00
76.68
51.73
41.48
30.20
26.76
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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8.0
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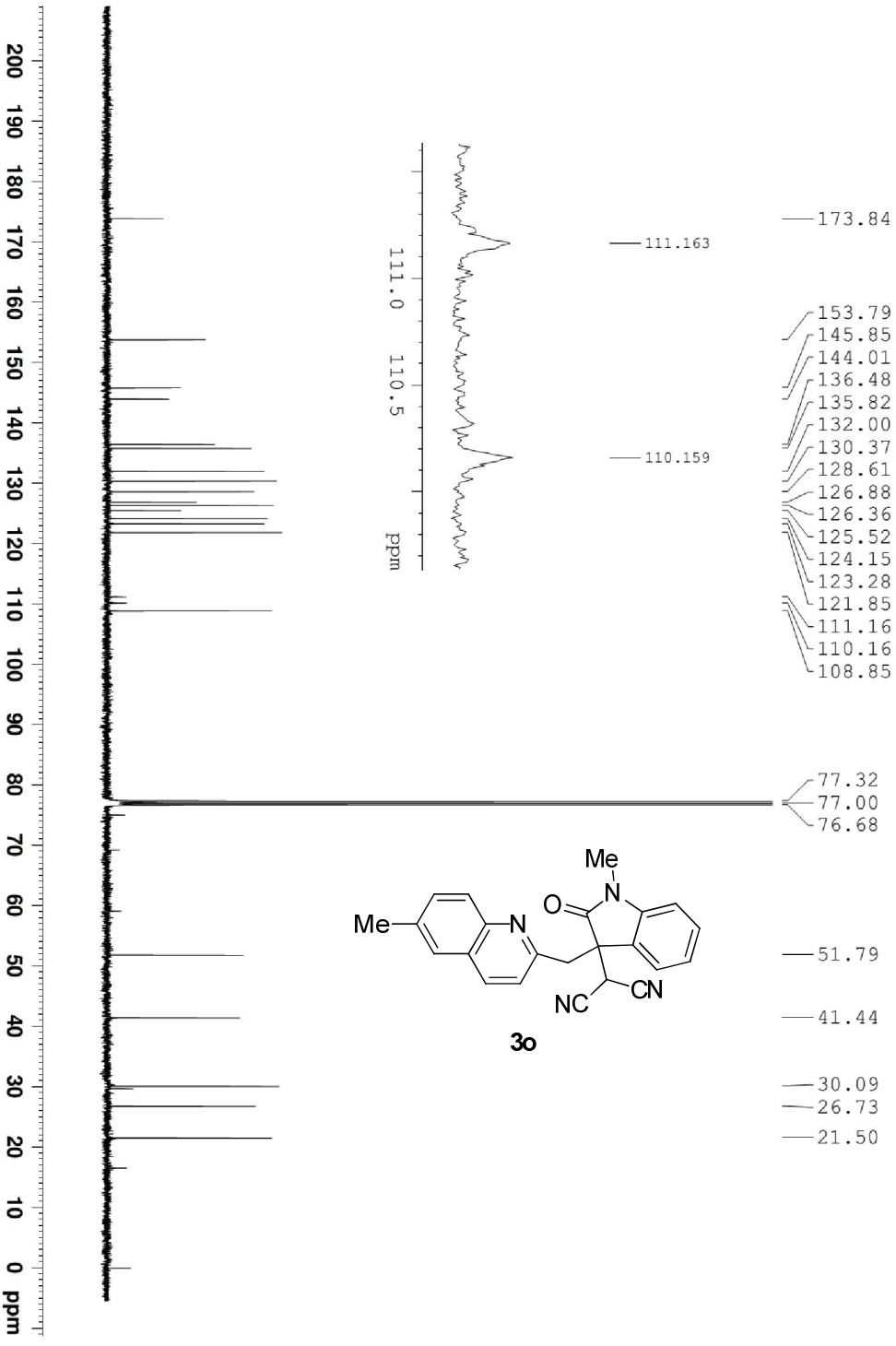
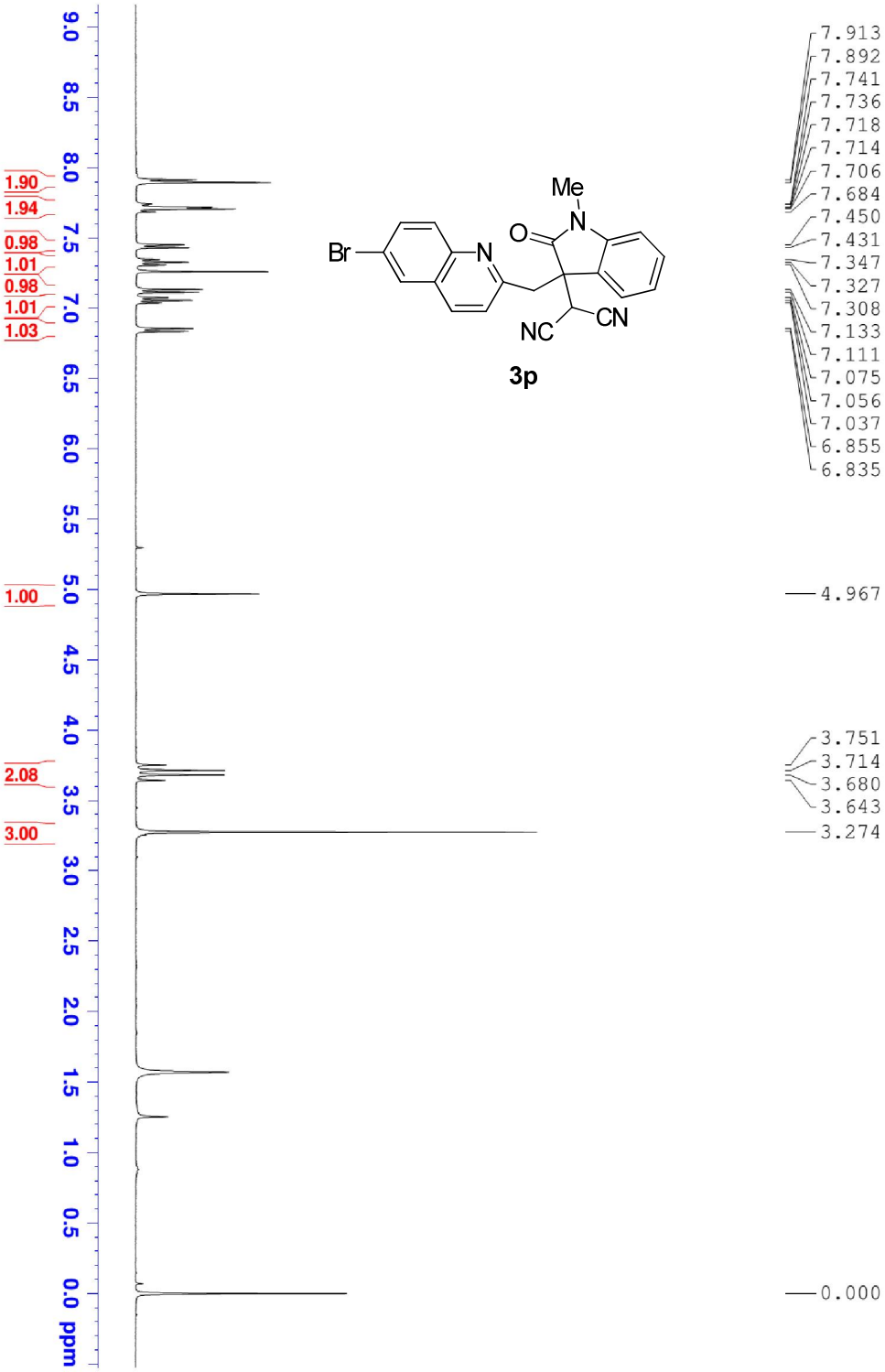
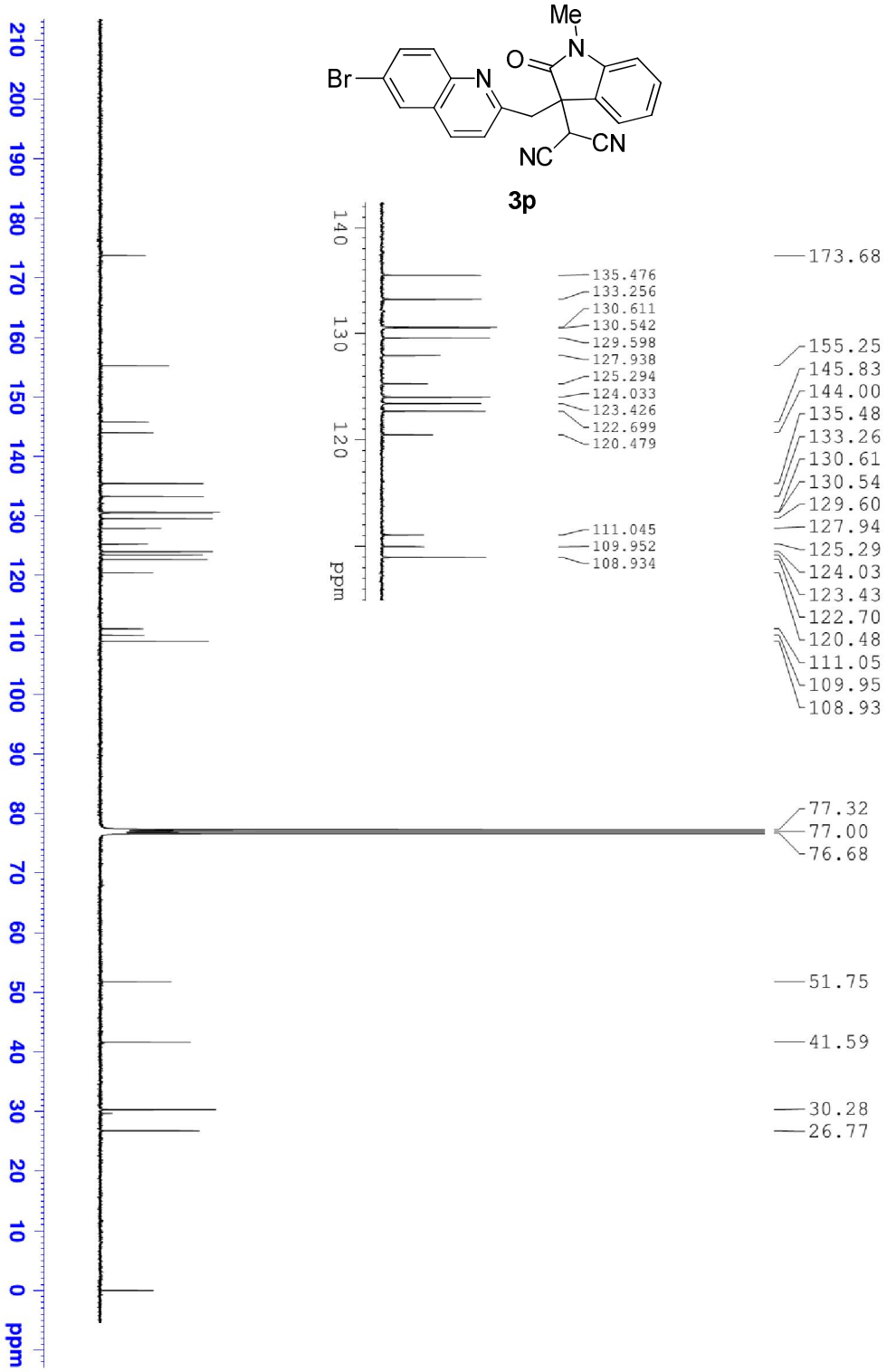
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.05
1.03
2.05
1.04
1.05
2.10
1.05
1.00
1.05
1.05
3.12
3.14
Me
N
O
Me
N
NC
CN
7.906
7.885
7.763
7.740
7.504
7.486
7.396
7.378
7.327
7.325
7.308
7.305
7.288
7.286
7.057
7.037
7.020
7.019
7.001
7.000
6.847
6.827
5.159
3.761
3.724
3.619
3.582
3.279
2.501
0.000

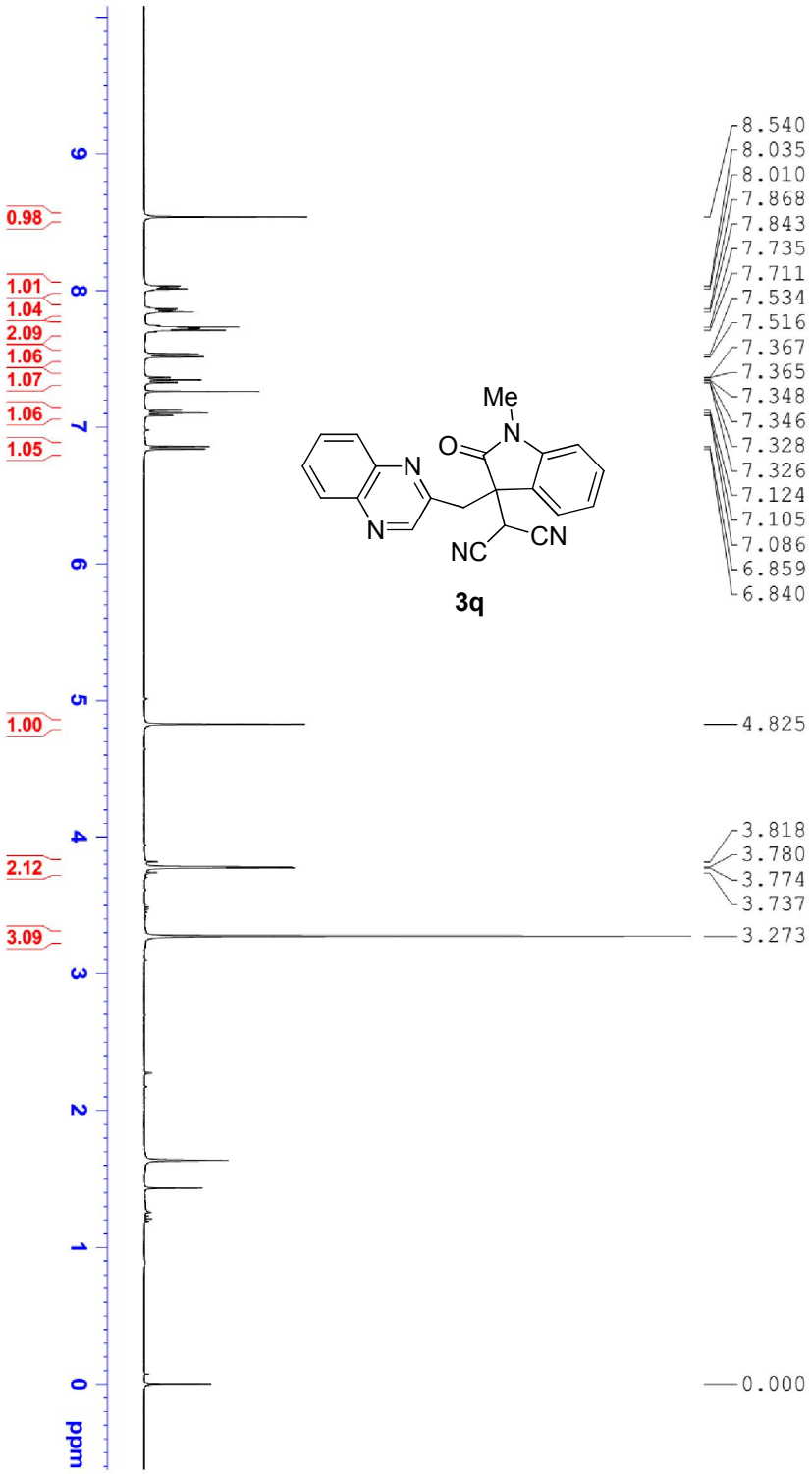
3o


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
111.0 110.5 ppm
111.163
110.159
173.84
153.79
145.85
144.01
136.48
135.82
132.00
130.37
128.61
126.88
126.36
125.52
124.15
123.28
121.85
111.16
110.16
108.85
77.32
77.00
76.68
51.79
41.44
30.09
26.73
21.50
Me
N
O
Me
N
NC
CN

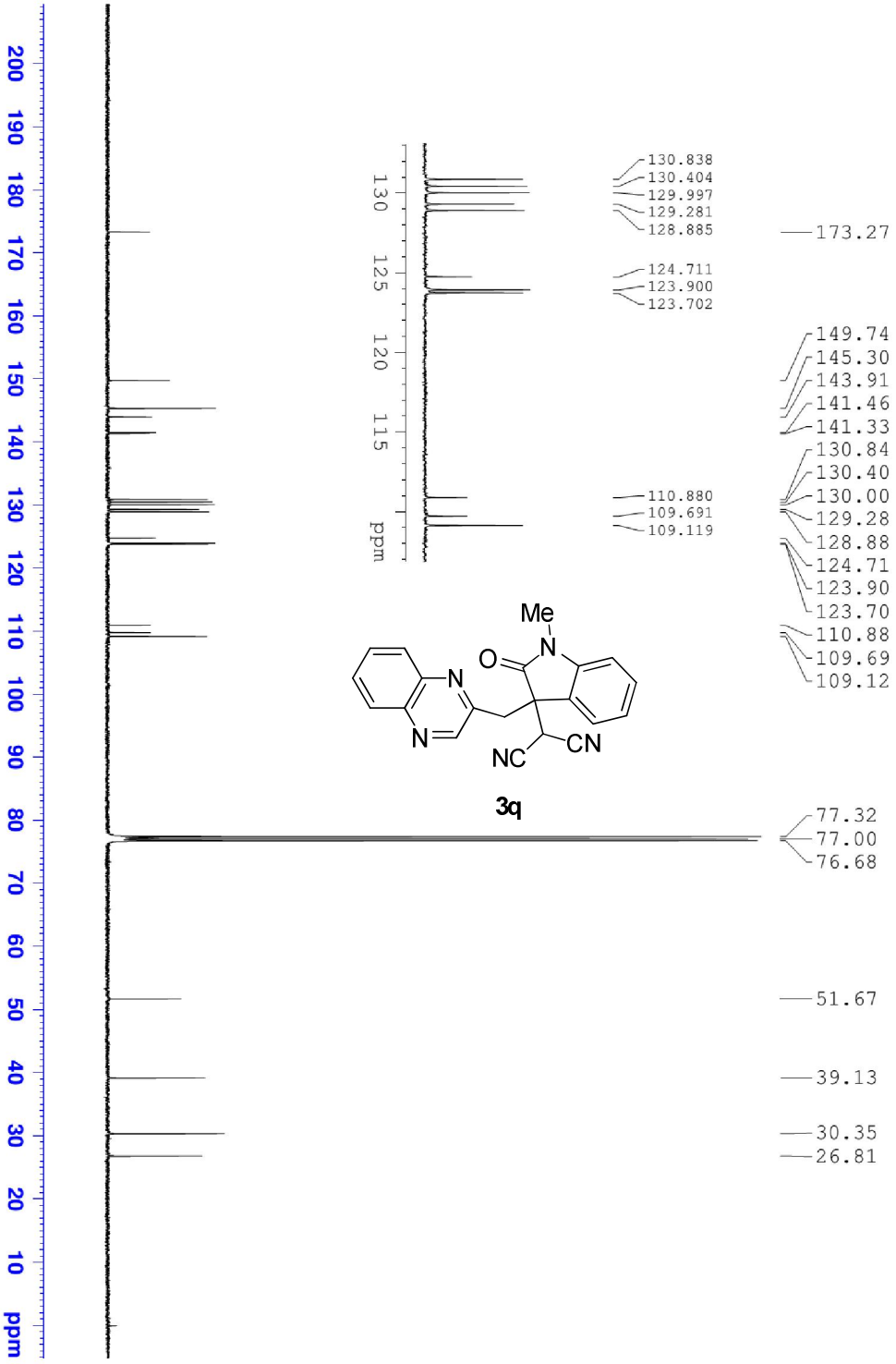
3o

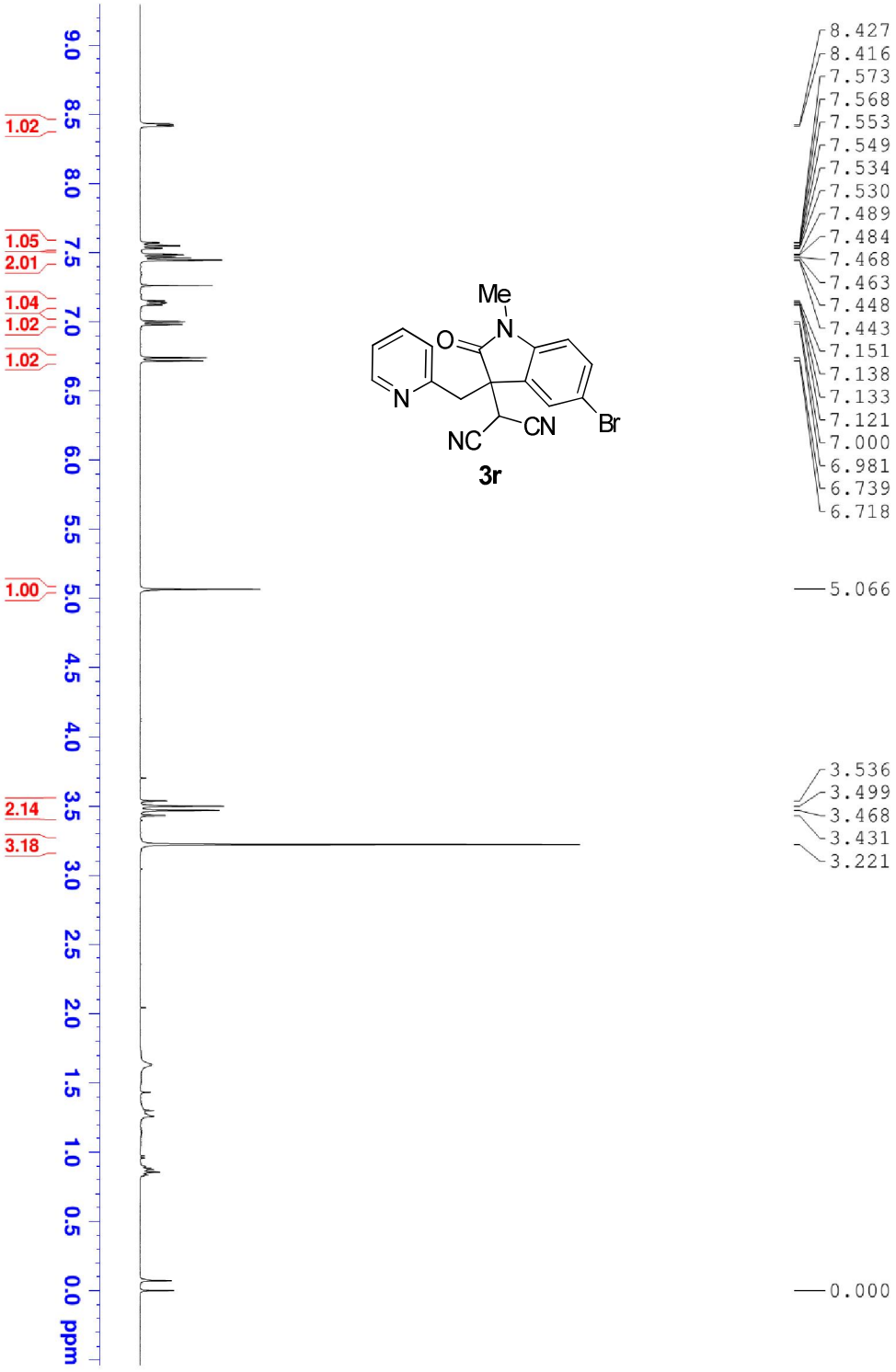

Me
N
O
Br
N
NC
CN
3p
7.913
7.892
7.741
7.736
7.718
7.714
7.706
7.684
7.450
7.431
7.347
7.327
7.308
7.133
7.111
7.075
7.056
7.037
6.855
6.835
4.967
3.751
3.714
3.680
3.643
3.274
0.000
1.90
1.94
0.98
1.01
0.98
1.01
1.03
1.00
2.08
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm


Me
N
O
Br
N
NC
CN
3p
140
130
120
ppm
135.476
133.256
130.611
130.542
129.598
127.938
125.294
124.033
123.426
122.699
120.479
111.045
109.952
108.934
173.68
155.25
145.83
144.00
135.48
133.26
130.61
130.54
129.60
127.94
125.29
124.03
123.43
122.70
120.48
111.05
109.95
108.93
77.32
77.00
76.68
51.75
41.59
30.28
26.77
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.540
8.035
8.010
7.868
7.843
7.735
7.711
7.534
7.516
7.367
7.365
7.348
7.346
7.328
7.326
7.124
7.105
7.086
6.859
6.840
4.825
3.818
3.780
3.774
3.737
3.273
0.000
0.98
1.01
1.04
2.09
1.06
1.07
1.06
1.05
1.00
2.12
3.09
ppm
Me
N
O
N
N
NC
CN

3q


130.838
130.404
129.997
129.281
128.885
124.711
123.900
123.702
110.880
109.691
109.119
173.27
149.74
145.30
143.91
141.46
141.33
130.84
130.40
130.00
129.28
128.88
124.71
123.90
123.70
110.88
109.69
109.12
77.32
77.00
76.68
51.67
39.13
30.35
26.81
Me
O
N
N
N
NC
CN
3q


9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.02
1.05
2.01
1.04
1.02
1.02
1.00
2.14
3.18
Me
N
O
N
NC
CN
Br
3r
8.427
8.416
7.573
7.568
7.553
7.549
7.534
7.530
7.489
7.484
7.468
7.463
7.448
7.443
7.151
7.138
7.133
7.121
7.000
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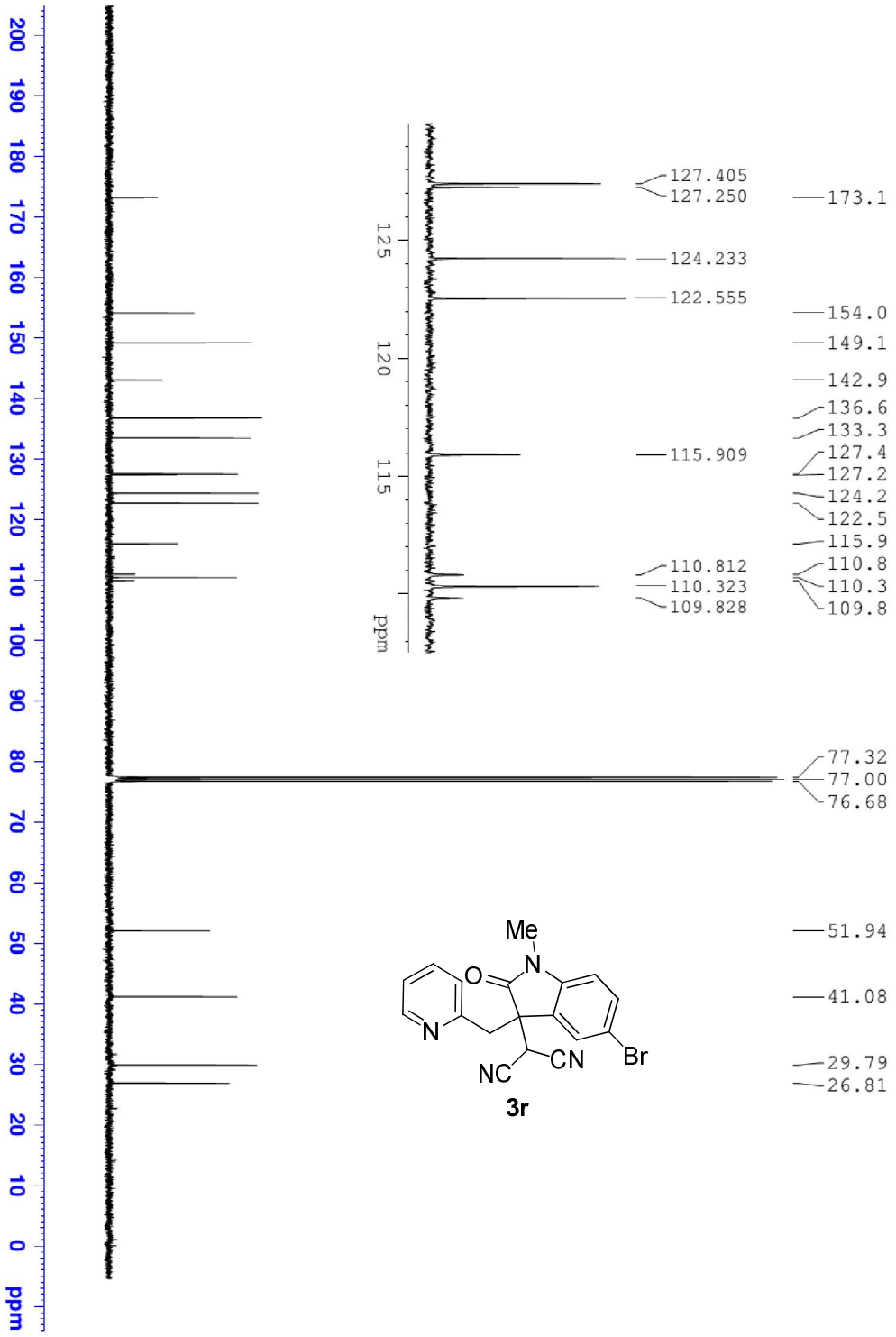
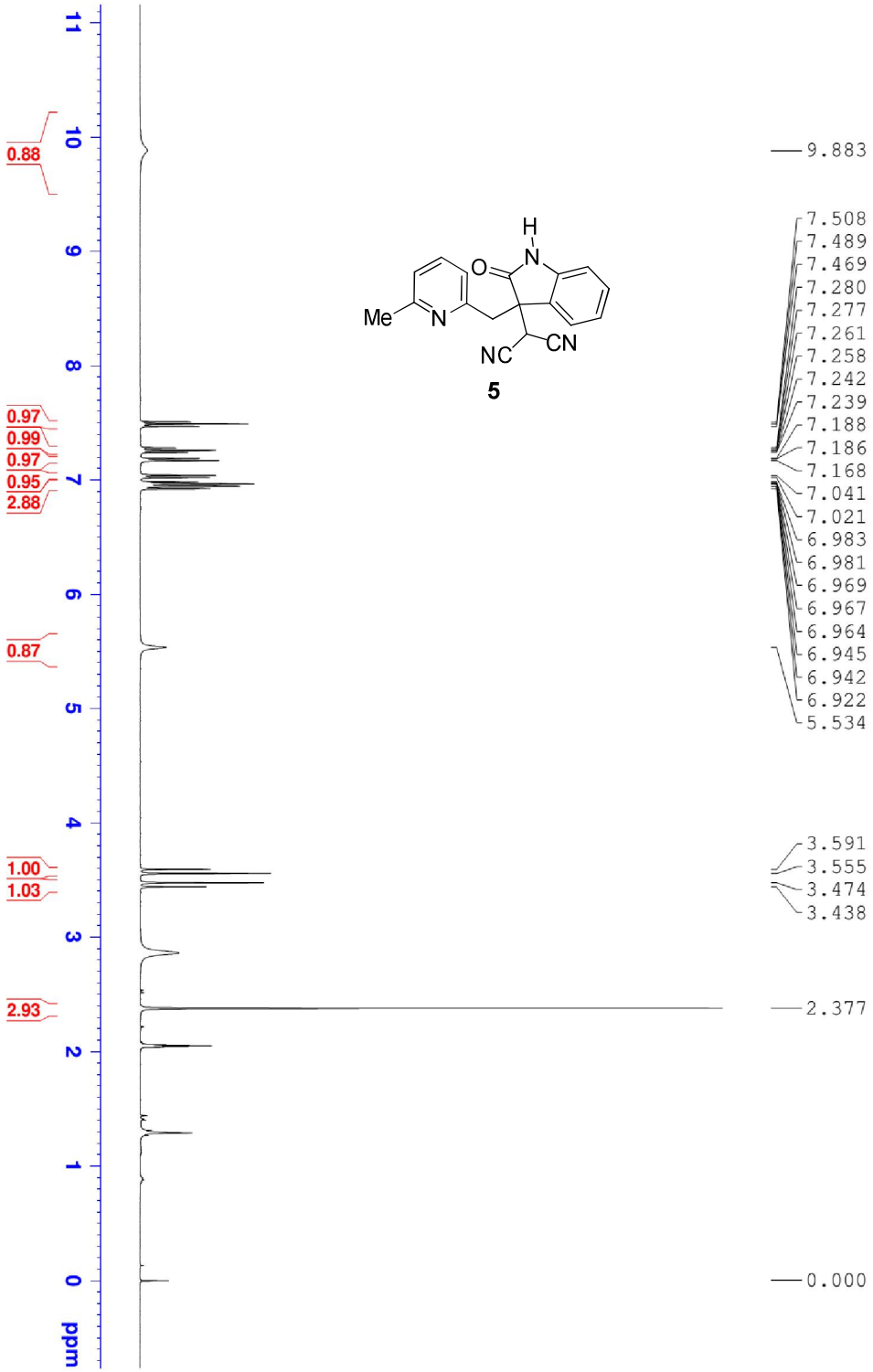
6.739
6.718
5.066
3.536
3.499
3.468
3.431
3.221
0.000


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
125 120 115 ppm
127.405
127.250
124.233
122.555
115.909
110.812
110.323
109.828
173.1
154.0
149.1
142.9
136.6
133.3
127.4
127.2
124.2
122.5
115.9
110.8
110.3
109.8
77.32
77.00
76.68
51.94
41.08
29.79
26.81
Me
N
O
N
NC
CN
Br

3r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NC
CN
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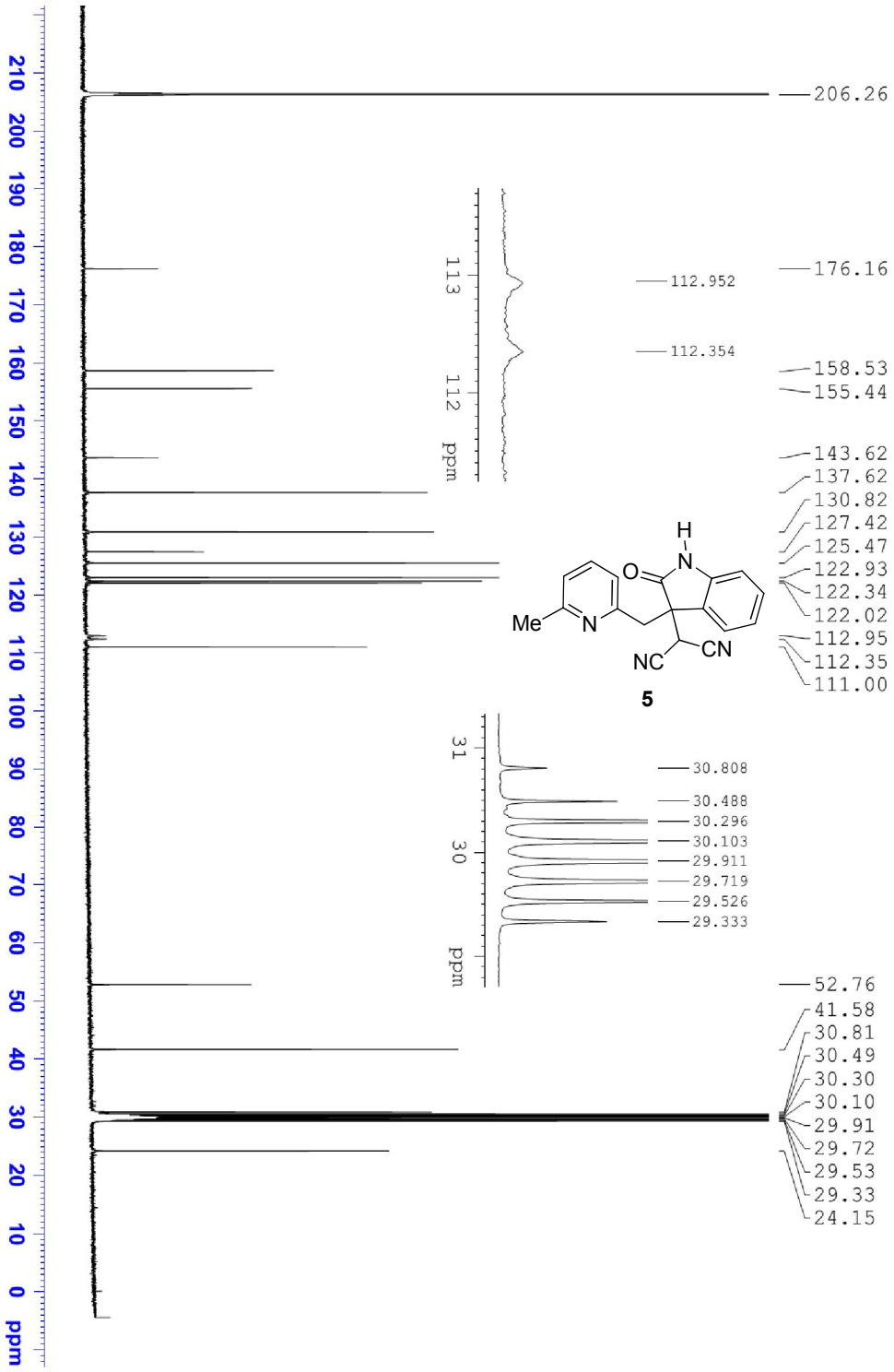
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