Room Temperature C-H Activation & Cross-Coupling of Aryl Ureas in Water**

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Supporting Information

General Information

For TLC analyses precoated Kieselgel 60 F_{254} plates (Merck, 0.25 mm thick) were used; for column chromatography Silica *Flash*® P60 (SiliCycle, 40-63 μm) was used. Reactions were monitored using a Hewlett-Packard HP6890 gas chromatograph. ^{1}H and ^{13}C NMR spectra were obtained using a Varian UNITY INOVA 400 MHz NMR spectrometer. High resolution mass analyses were obtained using a VG70 double-focusing magnetic sector instrument (VG Analytical) for EI and a PE Sciex QStar Pulsar quadrupole/TOF instrument (API) for ESI.

General procedure

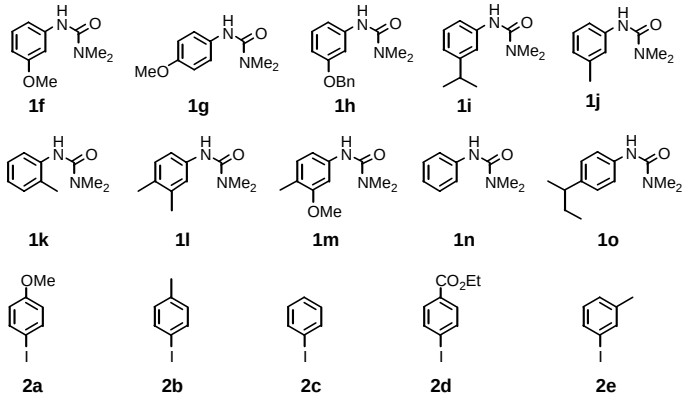


Figure 1. Starting materials.

Aryl urea **1** (0.25 mmol), aryl iodide **2** (0.5 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg) were sequentially added under air to a reaction tube equipped with a stir bar and a septum. An aqueous solution containing the surfactant (1.0 mL, 2 wt %), and 48 wt % HBF_4 (1.25 mmol, 0.16 mL) was added by syringe and the resulting mixture vigorously stirred for 20 h at amibient temperature. After this time, the contents of the flask were quenched with aqueous $NaHCO_3$ and extracted with EtOAc. The solution obtained was filtered through the plug of silica gel and anhydrous $MgSO_4$, and then concentrated by rotary evaporation. The residue was purified by flash chromatography, eluting with hexane/EtOAc to afford the product.

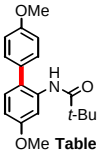
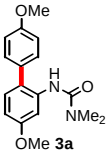


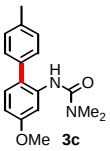
Table 1, run 3

Following the general procedure above, using **1c** (52 mg, 0.25 mmol), **2a** (117 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % HBF_4 solution (1.25 mmol, 0.16 mL), yielded the product (18 mg, 24%), ^{1}H NMR ($CDCl_3$) δ: 1.11 (s, 9H), 3.84 (s, 6H), 3.85 (s, 3H), 3.86 (s, 3H), 6.69 (dd, J = 2.6 and 8.5 Hz, 1H), 7.01 (d, J = 8.8 Hz, 2H), 7.10 (d, J = 8.5 Hz, 1H), 7.25 (d, J = 8.8 Hz, 2H), 7.57 (brs, 1H), 8.13 (d, 2.6 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 27.56, 40.06, 55.48, 55.57, 105.03, 110.70, 114.57, 123.93, 130.09, 130.66, 130.88, 136.45, 159.30, 159.60, 176.56; HRESIMS calcd. for $C_{17}H_{20}N_2O_3Na$ ($M+Na^+$): 336.1576; found 336.1577.



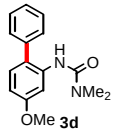
3a

Following the general procedure above, using **1f** (49 mg, 0.25 mmol), **2a** (117 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL), 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL) the product **3a** was obtained (57 mg, 76%); ^{1}H NMR ($CDCl_3$) δ: 2.81 (s, 6H), 3.84 (s, 6H), 6.60 (brs, 1H), 6.61 (dd, J = 2.6 and 8.3 Hz, 1H), 6.98 (d, J = 8.6 Hz, 2H), 7.05 (d, J = 8.3 Hz, 1H), 7.27 (d, J = 8.6 Hz, 2H), 7.92 (d, J = 2.6 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 36.34, 55.46, 55.52, 104.43, 109.32, 114.59, 123.23, 130.51, 130.67, 130.79, 137.64, 155.51, 159.13, 159.66; HRESIMS calcd for $C_{17}H_{20}N_2O_3Na$ ($M+Na^+$): 323.1372; found 323.1377.



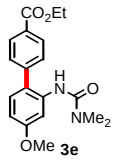
3c

Following the general procedure above, using **1f** (49 mg, 0.25 mmol), **2b** (109 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3c** was obtained (61 mg, 87%); ^{1}H NMR ($CDCl_3$) δ: 2.40 (s, 3H), 2.81 (s, 6H), 3.85 (s, 3H), 6.63 (dd, J = 2.7 and 8.5 Hz, 1H), 6.64 (brs, 1H), 7.02 (d, J = 8.5 Hz, 1H), 7.25 (brs, 4H), 7.94 (d, J = 2.7 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 21.33, 36.34, 55.50, 104.49, 109.36, 123.54, 129.49, 129.92, 130.46, 135.55, 137.44, 137.54, 155.53, 159.73; HRESIMS calcd. for $C_{17}H_{20}N_2O_2Na$ ($M+Na^+$): 307.1422; found 307.1418.



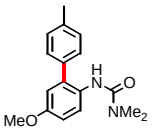
3d

Following the general procedure above, using **1f** (49 mg, 0.25 mmol), **2c** (102 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3d** was obtained (47 mg, 70%); ^{1}H NMR ($CDCl_3$) δ: 2.96 (s, 6H), 3.85 (s, 3H), 6.60 (brs, 1H), 6.63 (dd, J = 2.6 and 8.4 Hz, 1H), 7.08 (d, J = 8.6 Hz, 1H), 7.34-7.38 (m, 3H), 7.43-7.47 (m, 2H), 7.94 (d, J = 2.6 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 36.29, 55.52, 104.61, 109.42, 123.65, 127.72, 129.23, 129.64, 130.38, 137.49, 138.61, 155.49, 159.87; HRESIMS calcd. for $C_{16}H_{18}N_2O_2Na$ ($M+Na^+$): 293.1266; found 293.1270.



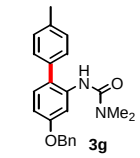
3e

Following the general procedure above, using **1f** (49 mg, 0.25 mmol), **2d** (138 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3e** was obtained (36 mg, 42%), ^{1}H NMR ($CDCl_3$) δ: 1.41 (t, J = 7.1 Hz, 3H), 2.82 (s, 6H), 3.84 (s, 3H), 4.39 (q, J = 7.1 Hz, 2H), 6.49 (brs, 1H), 6.65 (dd, J = 2.6 and 8.4 Hz, 1H), 7.08 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 2.6 Hz, 1H), 8.11 (d, J = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ: 14.48, 36.41, 55.56, 61.31, 105.40, 109.92, 122.89, 129.56, 129.63, 130.40, 130.46, 137.30, 143.51, 155.46, 160.29, 166.40; HRESIMS calcd. for $C_{19}H_{22}N_2O_4Na$ ($M+Na^+$): 365.1477; found 365.1478.



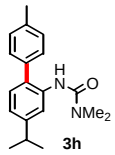
3f

Following the general procedure above, using **1g** (49 mg, 0.25 mmol), **2b** (109 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3f** was obtained (51 mg, 72%), ^{1}H NMR ($CDCl_3$) δ: 2.39 (s, 3H), 2.80 (s, 6H), 3.78 (s, 3H), 6.29 (brs, 1H), 6.75 (d, J = 3.0 Hz, 1H), 6.87 (dd, J = 3.0 and 9.0 Hz, 1H), 7.28 (brs, 4H), 7.93 (d, J = 9.0 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 21.35, 36.34, 55.65, 113.44, 115.31, 123.13, 129.11, 129.65, 129.76, 133.65, 135.81, 137.75, 155.42, 156.15; HRESIMS calcd. for $C_{17}H_{17}N_2O_2Na$ ($M+Na^+$): 307.1422; found 307.1420.



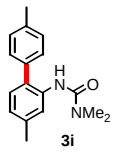
3g

Following the general procedure above, using **1h** (67 mg, 0.25 mmol), **2b** (109 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3g** was obtained (63 mg, 70%); ^1H NMR ($CDCl_3$) δ: 2.40 (s, 3H), 2.82 (s, 6H), 5.11 (s, 2H), 6.65 (brs, 1H), 6.70 (dd, J = 2.6 and 8.4 Hz, 1H), 7.08 (d, J = 8.4 Hz, 1H), 7.26 (brs, 4H), 7.32 (d, J = 7.2 Hz, 1H), 7.39 (t, J = 7.2 Hz, 2H), 7.47 (d, J = 7.2 Hz, 2H), 8.05 (d, J = 2.6 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 21.93, 36.93, 70.67, 106.07, 110.61, 124.41, 128.30, 128.53, 129.20, 130.03, 130.51, 131.09, 136.09, 137.87, 138.05, 138.10, 156.13, 159.52; HRESIMS calcd. for $C_{23}H_{24}N_2O_2Na$ ($M+Na^+$): 383.1735; found 383.1735.



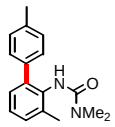
3h

Following the general procedure above, using **1i** (51 mg, 0.25 mmol), **2b** (109 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3h** was obtained (54 mg, 74%); ^1H NMR ($CDCl_3$) δ: 1.29 (t, J = 7.0 Hz, 6H), 2.40 (s, 3H), 2.82 (s, 6H), 2.95 (sept, J = 7.0 Hz, 1H), 6.57 (brs, 1H), 6.93 (dd, J = 1.7 and 8.7 Hz, 1H), 7.11 (d, J = 8.7 Hz, 1H), 7.26 (brs, 4H), 8.10 (d, J = 1.7 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 21.34, 24.10, 34.33, 36.37, 118.52, 120.71, 128.94, 129.33, 129.71, 135.82, 136.29, 137.51, 149.35, 155.79; HRESIMS calcd. for $C_{19}H_{24}N_2ONa$ ($M+Na^+$): 319.1786; found 319.1788.



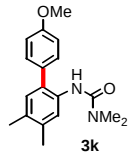
3i

Following the general procedure above, using **1j** (44 mg, 0.25 mmol), **2b** (109 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3i** was obtained (49 mg, 74%); ^1H NMR ($CDCl_3$) δ: 2.38 (s, 3H), 2.40 (s, 3H), 2.81 (s, 6H), 6.52 (brs, 1H), 6.88 (dd, J = 1.0 and 7.7 Hz, 1H), 7.07 (d, J = 7.7 Hz, 1H), 7.26 (brs, 4H), 8.02 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 21.34, 21.66, 36.33, 120.99, 123.51, 128.70, 129.33, 129.64, 135.78, 136.18, 137.53, 138.32, 155.74; HRESIMS calcd. for $C_{17}H_{20}N_2ONa$ ($M+Na^+$): 291.1473; found 291.1473.



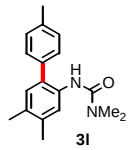
3j

Following the general procedure above, using **1k** (44 mg, 0.25 mmol), **2b** (109 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 solution (1.25 mmol, 0.16 mL), the product **3j** was obtained (48 mg, 72%); ^1H NMR ($CDCl_3$) δ: 2.32 (s, 3H), 2.39 (s, 3H), 2.85 (s, 6H), 5.71 (brs, 1H), 7.12 (dd, J = 1.8 and 7.5 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.20-7.26 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 18.88, 21.33, 36.60, 126.18, 127.71, 129.04, 129.22, 130.15, 134.53, 136.66, 136.96, 137.07, 138.53, 157.00; HRESIMS calcd. for $C_{17}H_{20}N_2ONa$ ($M+Na^+$): 291.1473; found 291.1476.



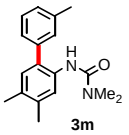
3k

Following the general procedure above, using **1l** (48 mg, 0.25 mmol), **2a** (117 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3k** was obtained (60 mg, 81%), ^1H NMR ($CDCl_3$) δ: 2.22 (s, 3H), 2.28 (s, 3H), 2.82 (s, 6H), 3.85 (s, 3H), 6.38 (brs, 1H), 6.95 (brs, 1H), 6.98 (dd, J = 8.8 Hz, 2H), 7.28 (d, J = 8.8 Hz, 2H), 7.91 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 19.79, 20.53, 36.92, 56.02, 115.01, 122.68, 129.58, 131.15, 131.50, 131.53, 131.60, 134.60, 137.13, 156.45, 159.68; HRESIMS calcd. for $C_{18}H_{22}N_2O_2Na$ ($M+Na^+$): 321.1579; found 321.1581.



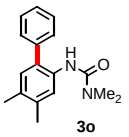
3l

Following the general procedure, using **1l** (48 mg, 0.25 mmol), **2b** (109 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3l** was isolated (54 mg, 76%), ^1H NMR ($CDCl_3$) δ: 2.22 (s, 3H), 2.29 (s, 3H), 2.39 (s, 3H), 2.81 (s, 6H), 6.42 (brs, 1H), 6.96 (s, 1H), 7.25 (brs, 4H), 7.92 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 19.21, 19.96, 21.33, 36.35, 122.16, 129.28, 129.76, 130.88, 130.99, 133.92, 135.88, 136.66, 137.37, 155.93; HRESIMS calcd. for $C_{18}H_{22}N_2ONa$ ($M+Na^+$): 305.1630; found 305.1631.



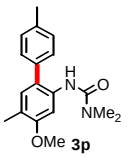
3m

Following the general procedure above, using **1l** (48 mg, 0.25 mmol), **2e** (109 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3m** was obtained (56 mg, 79%), ^1H NMR ($CDCl_3$) δ: 2.23 (s, 3H), 2.29 (s, 3H), 2.39 (s, 3H), 2.81 (s, 6H), 6.44 (brs, 1H), 6.96 (s, 1H), 7.15-7.17 (m, 3H), 7.33 (dd, J = 7.2 and 8.2 Hz, 1H), 7.94 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 19.21, 19.99, 21.57, 36.29, 122.00, 126.36, 128.37, 128.92, 129.37, 130.20, 130.71, 130.92, 133.90, 136.76, 138.84, 155.88; HRESIMS calcd. for $C_{18}H_{22}N_2ONa$ ($M+Na^+$): 305.1630; found 305.1627.



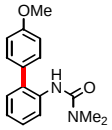
3o

Following the general procedure above, using **1l** (48 mg, 0.25 mmol), **2c** (102 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3o** was obtained (65 mg, 97%), ^1H NMR ($CDCl_3$) δ: 2.23 (s, 3H), 2.30 (s, 3H), 2.80 (s, 6H), 6.37 (brs, 1H), 6.98 (s, 1H), 7.34-7.38(m, 3H), 7.43-7.47 (m, 2H), 7.93 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 19.22, 19.99, 36.30, 122.29, 127.67, 129.07, 129.45, 130.78, 131.08, 133.87, 136.87, 138.94, 155.89; HRESIMS calcd. for $C_{17}H_{20}N_2ONa$ ($M+Na^+$): 291.1473; found 291.1473.



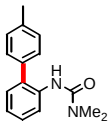
3p

Following the general procedure above, using **1m** (52 mg, 0.25 mmol), **2b** (109 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3p** was obtained (52 mg, 70%); ^1H NMR ($CDCl_3$) δ: 2.18 (s, 3H), 2.39 (s, 3H), 2.82 (s, 6H), 3.89 (s, 3H), 6.59 (brs, 1H), 6.94 (s, 1H), 7.24 (brs, 4H), 7.87 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 15.77, 21.33, 36.35, 55.62, 102.66, 120.50, 122.91, 129.44, 129.84, 131.49, 135.17, 135.73, 137.24, 155.76, 157.46; HRESIMS calcd. for $C_{18}H_{22}N_2O_2Na$ ($M+Na^+$): 321.1576; found 321.1576.



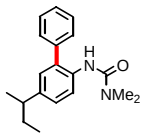
3r

Following the general procedure above, using **1n** (40 mg, 0.25 mmol), **2a** (117 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3r** was obtained (50 mg, 75%); ^{1}H NMR ($CDCl_3$) δ: 2.81 (s, 6H), 3.85 (s, 3H), 6.53 (brs, 1H), 7.00 (d, J = 8.6 Hz, 2H), 7.04 (dt, J = 1.0 and 7.5 Hz, 1H), 7.16 (dd, J = 1.6 and 7.5 Hz, 1H), 7.28-7.33 (m, 3H), 8.16 (d, J = 7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 36.34, 55.48, 114.58, 120.38, 122.62, 128.30, 129.91, 130.57, 130.87, 131.12, 136.61, 155.63, 159.34; HRESIMS calcd. for $C_{16}H_{18}N_2O_2Na$ ($M+Na^+$): 293.1266; found 293.1261.



3s

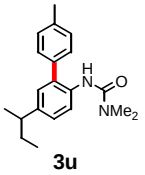
Following the general procedure above, using **1n** (40 mg, 0.25 mmol), **2b** (109 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3s** was obtained (44 mg, 70%); ^{1}H NMR ($CDCl_3$) δ: 2.40 (s, 3H), 2.80 (s, 6H), 6.55 (brs, 1H), 7.05 (t, J = 7.4 Hz, 1H), 7.17 (d, J = 7.4 Hz, 1H), 7.27 (brs, 4H), 7.31 (t, J = 8.3 Hz, 1H), 8.17 (d, J = 8.3 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 21.36, 36.33, 120.36, 122.61, 128.39, 129.25, 131.38, 135.75, 136.50, 137.74, 155.64; HRESIMS calcd. for $C_{16}H_{18}N_2ONa$ ($M+Na^+$): 277.1317; found 277.1313.



3t

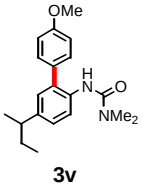
Following the general procedure above, using **1o** (55 mg, 0.25 mmol), **2c** (102 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3t** was obtained (53 mg, 71%); ^{1}H NMR ($CDCl_3$) δ: 0.83 (t, J = 7.5 Hz, 3H), 1.22 (t, J = 6.9 Hz, 3H), 1.56 (sept, J = 7.5 Hz, 2H), 2.54-2.62 (m, 1H), 2.79 (s, 6H), 6.42 (brs, 1H), 7.00 (d, J = 1.9

Hz, 1H), 7.15 (dd, J = 1.9 and 8.5 Hz, 1H), 7.35-7.40 (m, 3H), 7.44-7.48 (m, 2H), 8.02 (t, J = 8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 12.42, 22.03, 31.34, 36.30, 41.21, 120.89, 127.13, 127.81, 128.34, 129.10, 129.45, 131.64, 134.03, 139.24, 142.18, 155.83; HRESIMS calcd. for $C_{19}H_{24}N_2ONa$ ($M+Na^+$): 319.1786; found 319.1789.



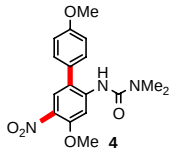
3u

Following the general procedure above, using **1o** (55 mg, 0.25 mmol), **2b** (64 mg, 0.30 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3u** was obtained (54 mg, 70%); ^{1}H NMR ($CDCl_3$) δ: 0.83 (t, J = 7.3 Hz, 3H), 1.22 (t, J = 7.0 Hz, 3H), 1.52-1.61 (m, 2H), 2.40 (s, 3H), 2.56 (sext, J = 7.0 Hz, 1H), 2.81 (s, 6H), 6.47 (brs, 1H), 6.99 (d, J = 2.2 Hz, 1H), 7.13 (dd, J = 2.2 and 8.4 Hz, 1H), 7.25-7.30 (m, 4H), 8.01 (d, J = 8.4 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 12.42, 21.35, 22.04, 31.34, 36.36, 41.21, 120.76, 126.93, 128.45, 129.29, 129.78, 131.50, 134.08, 136.19, 137.55, 142.10, 155.88; HRESIMS calcd. for $C_{20}H_{26}N_2ONa$ ($M+Na^+$): 333.1943; found 333.1946.



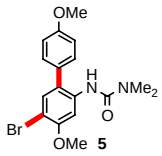
3v

Following the general procedure above, using **1o** (55 mg, 0.25 mmol), **2a** (117 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg), 2 wt % Brij 35 solution (1.0 mL) 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL), the product **3v** was obtained (58 mg, 71%); ^{1}H NMR ($CDCl_3$) δ: 0.83 (t, J = 7.4 Hz, 3H), 1.22 (t, J = 6.9 Hz, 3H), 1.54-1.61 (m, 2H), 2.55 (sext, J = 6.9 Hz, 1H), 2.81 (s, 6H), 3.85 (s, 3H), 6.43 (brs, 1H), 6.98 (brs, 1H), 7.00 (d, J = 8.4 Hz, 2H), 7.13 (dd, J = 2.1 and 8.4 Hz, 1H), 7.32 (d, J = 8.4 Hz, 2H), 8.01 (d, J = 8.4 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 12.42, 22.03, 31.33, 36.36, 41.20, 55.48, 114.48, 120.75, 126.84, 128.51, 130.60, 131.2,, 131.35, 134.20, 142.10, 155.84, 159.23; HRESIMS calcd. for $C_{20}H_{26}N_2O_2Na$ ($M+Na^+$): 349.1892; found 349.1896.



4

Aryl urea **1f** (49 mg, 0.25 mmol), **2a** (117 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg) were sequentially added under air to a reaction tube equipped with a stir bar and a septum. Brij 35 solution (2 wt %, 1 mL), and 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL) were added by syringe and vigorously stirred for 20 h. After the reaction, the mixture was extracted with EtOAc. The solution obtained was filtered through a plug of silica gel and anhydrous $MgSO_4$, and concentrated by rotary evaporation at 40-45 °C. The residue was purified by flash chromatography eluting with hexane/EtOAc to afford the product **4** (41 mg, 48%); ^{1}H NMR ($CDCl_3$) δ: 2.83 (s, 6H), 3.87 (s, 3H), 4.03 (s, 3H), 6.95 (brs, 1H), 7.03 (d, J = 8.7 Hz, 2H), 7.29 (d, J = 8.7 Hz, 2H), 7.88 (s, 1H), 8.36 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 36.36, 55.53, 56.75, 102.72, 115.08, 122.10, 127.74, 127.95, 130.74, 132.62, 143.17, 154.55, 154.65, 159.97; HRESIMS calcd. for $C_{17}H_{19}N_3O_5Na$ ($M+Na^+$): 368.1222; found 368.1222.



5

Aryl urea **1f** (49 mg, 0.25 mmol), **2a** (117 mg, 0.50 mmol), AgOAc (0.5 mmol, 83 mg), and $Pd(OAc)_2$ (0.025 mmol, 5.6 mg) were sequentially added under air to a reaction tube equipped with a stir bar and a septum. 2 wt % Brij 35 solution (1 mL), and 48 wt % aqueous HBF_4 (1.25 mmol, 0.16 mL) were added by syringe and vigorously stirred for 20 h. After the reaction, the mixture was extracted with EtOAc. The solution obtained was filtered through a plug of silica gel and anhydrous $MgSO_4$. Br_2 (19 uL, 0.37 mmol) was added to the solution and after stirring for 15 min at rt, Na_2SO_3 and $NaHCO_3$ solution were added to the reaction mixture. After extraction, the organic layers were combined and dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation. The residue was purified by flash chromatography eluting with hexane/EtOAc to afford the product **5** (66 mg, 70%); ^{1}H NMR ($CDCl_3$) δ: 2.82 (s, 6H), 3.85 (s, 3H), 3.94 (s, 3H), 6.28 (brs, 1H), 6.99 (d, J = 8.6 Hz, 2H), 7.26 (d, J = 8.6 Hz, 2H), 7.32 (s, 1H), 8.08 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 36.33, 55.49, 56.46, 103.65, 114.74, 124.21, 129.18, 130.69, 133.57, 137.17, 155.28, 155.48, 159.46; HRESIMS calcd. for $C_{17}H_{19}N_2O_3NaBr$ ($M+Na^+$): 401.0477; found 401.0473.

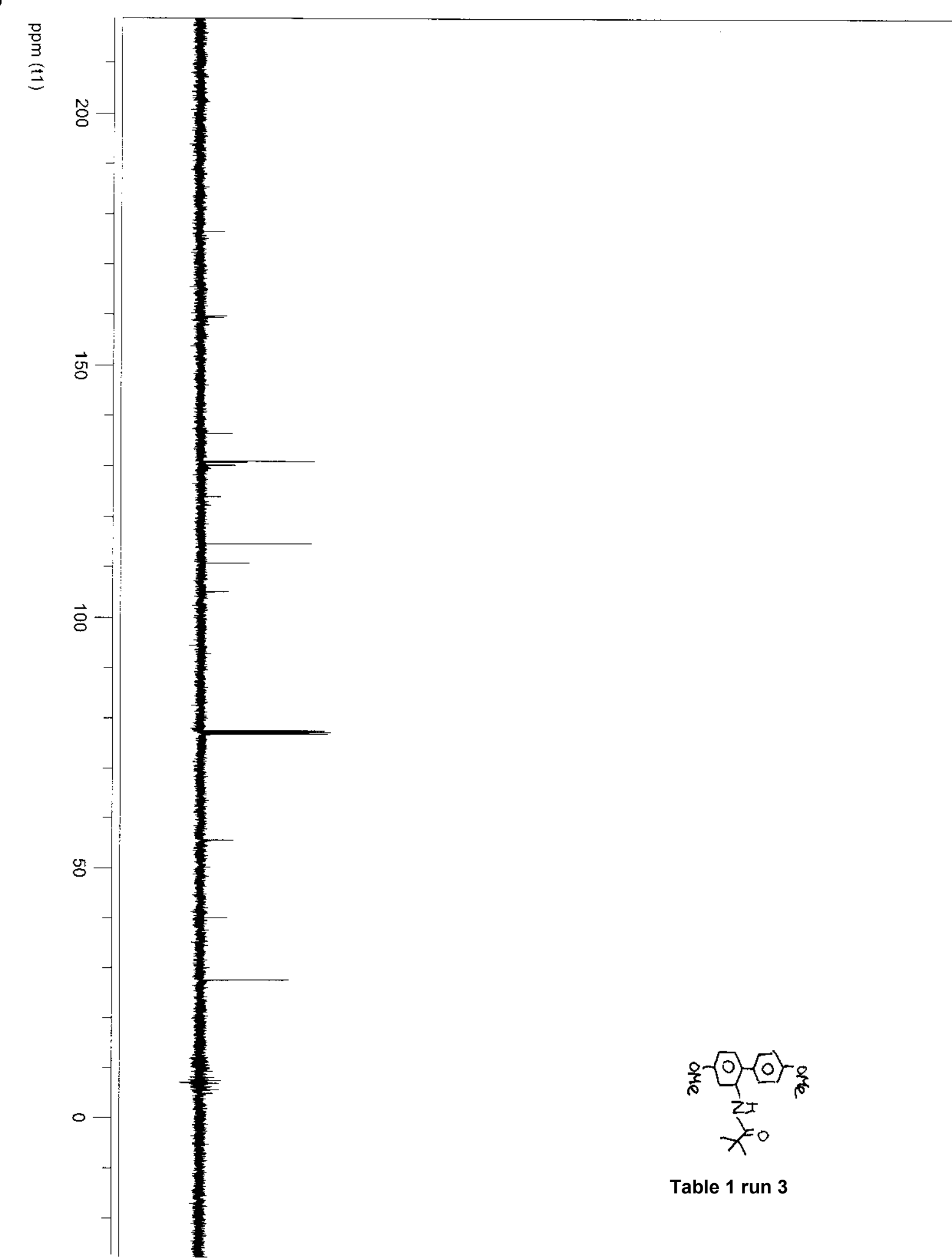


Table 1 run 3

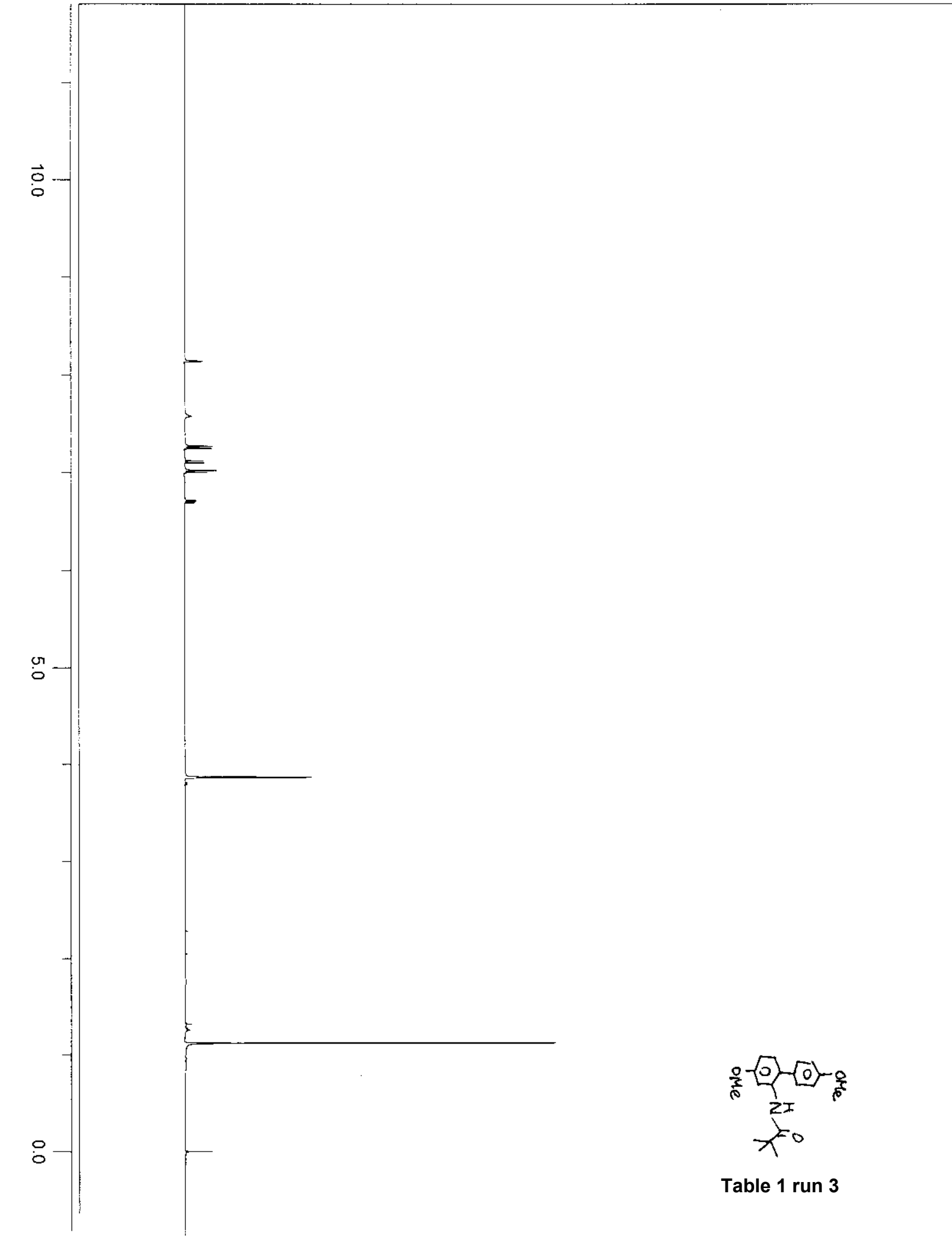
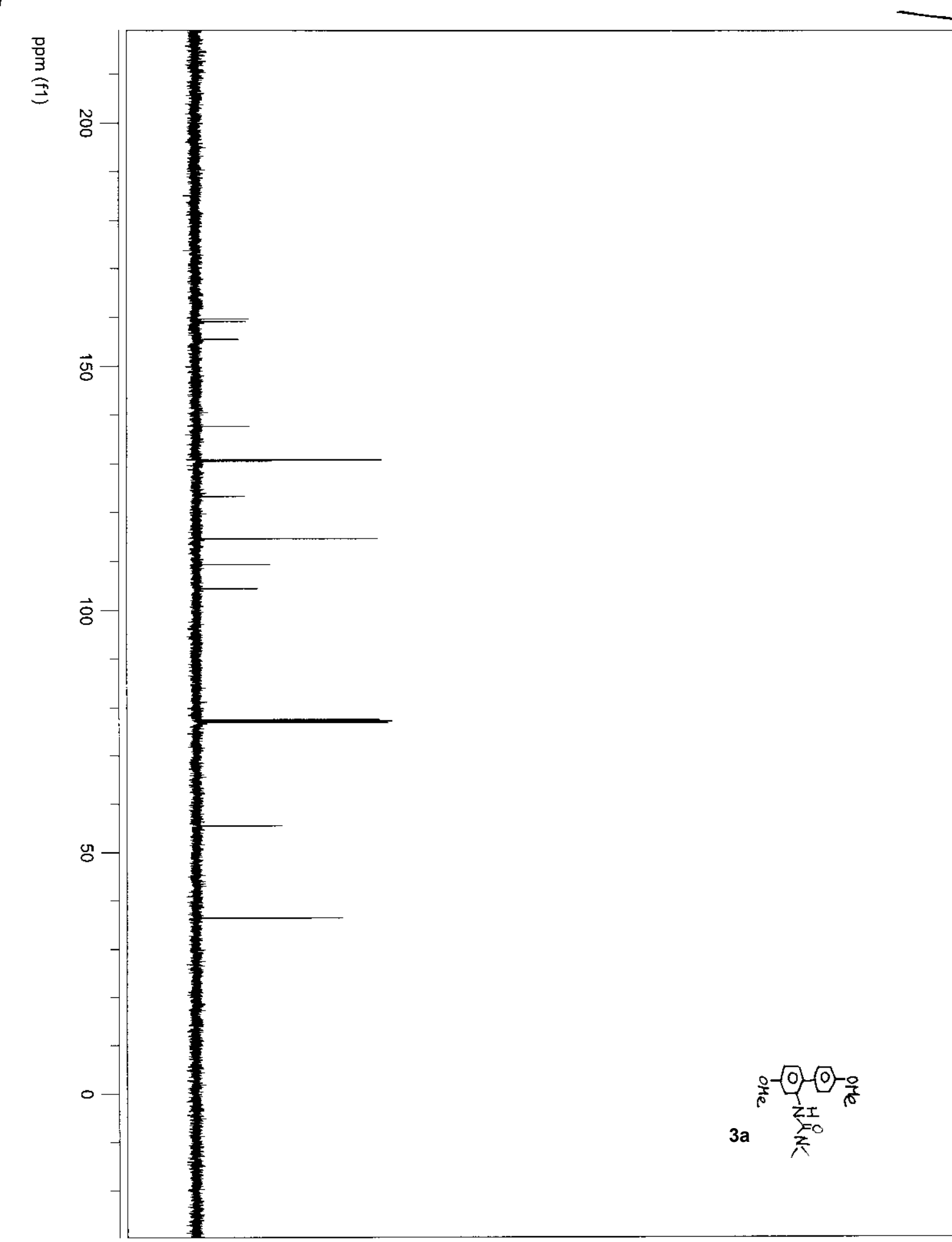


Table 1 run 3



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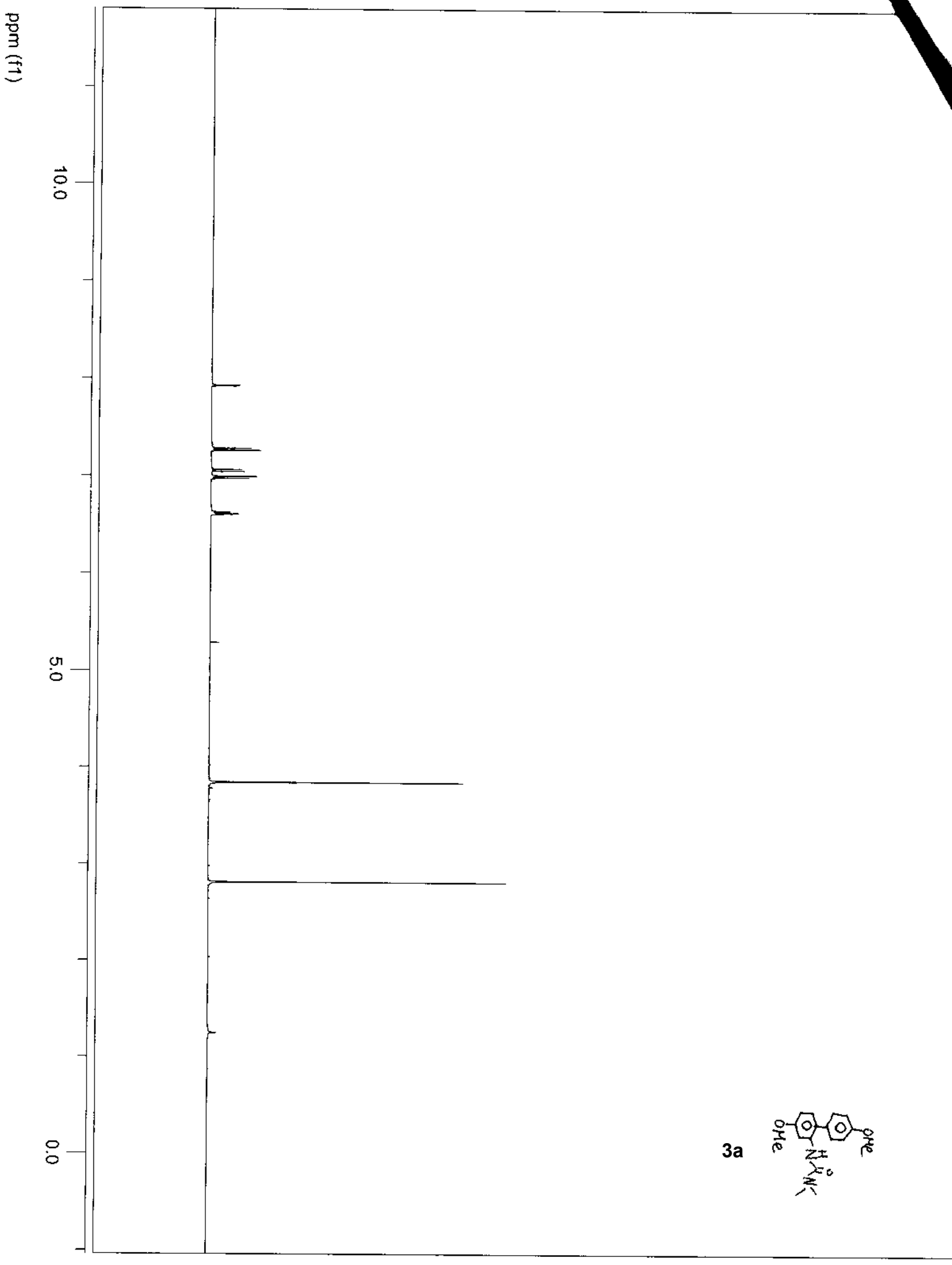

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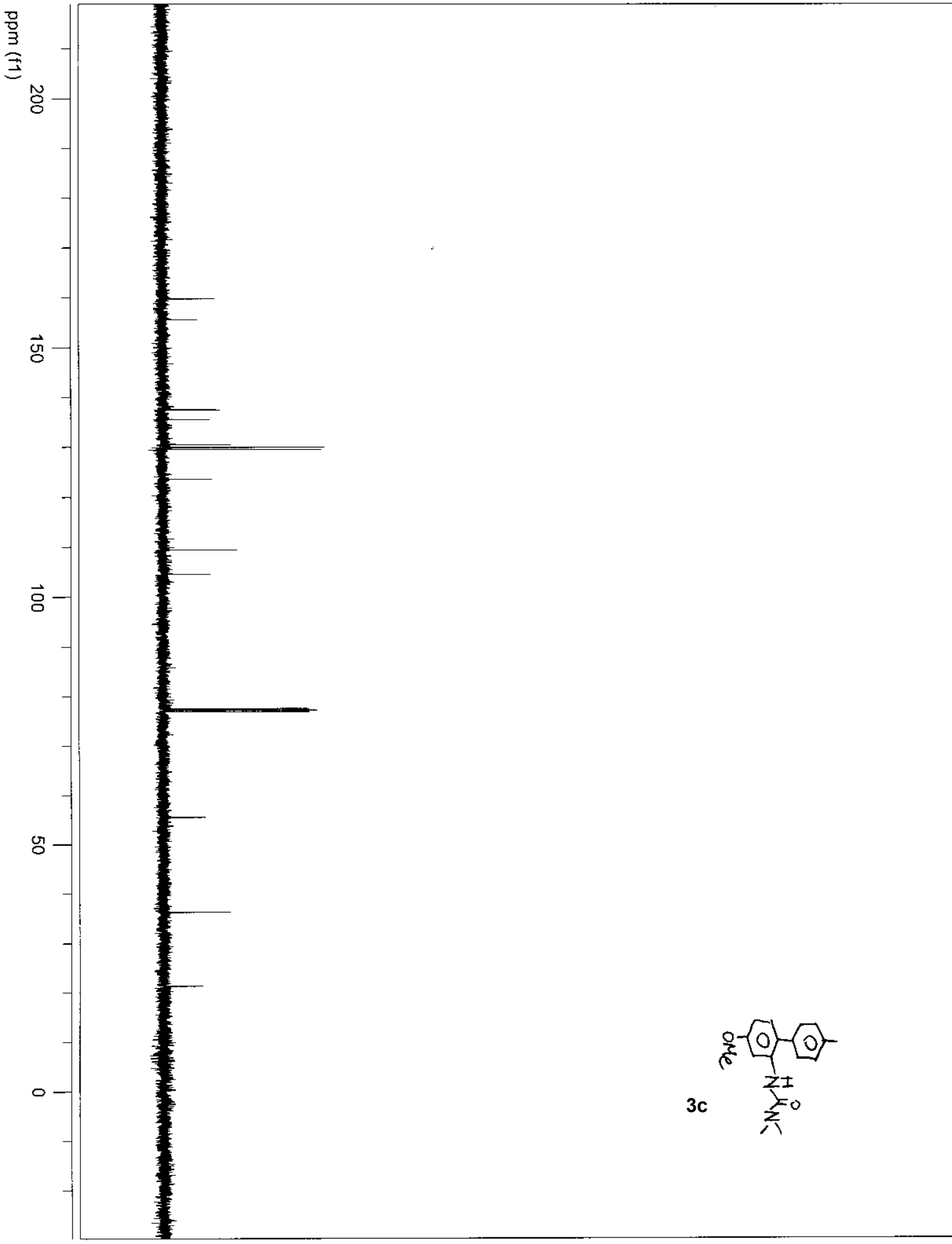

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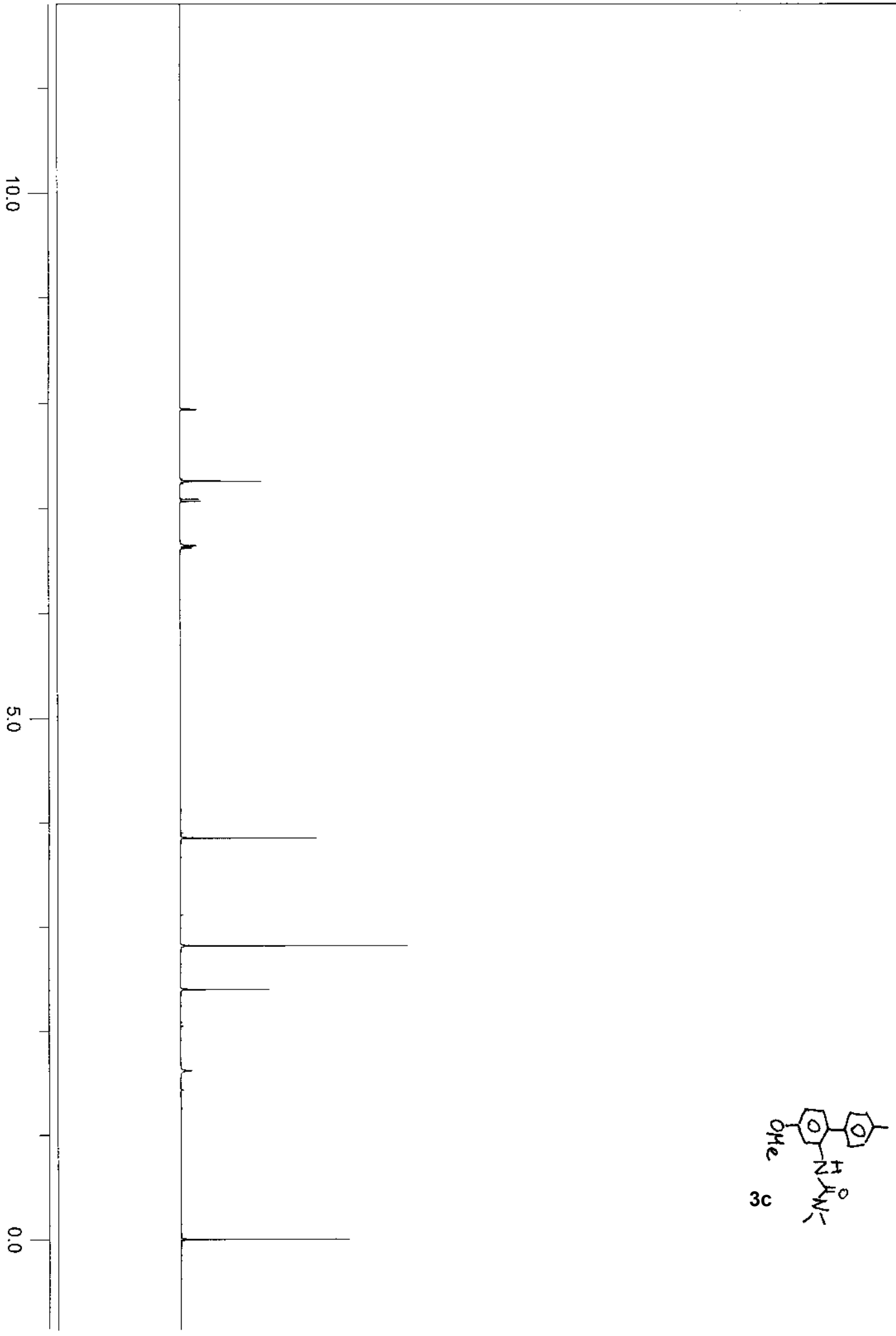

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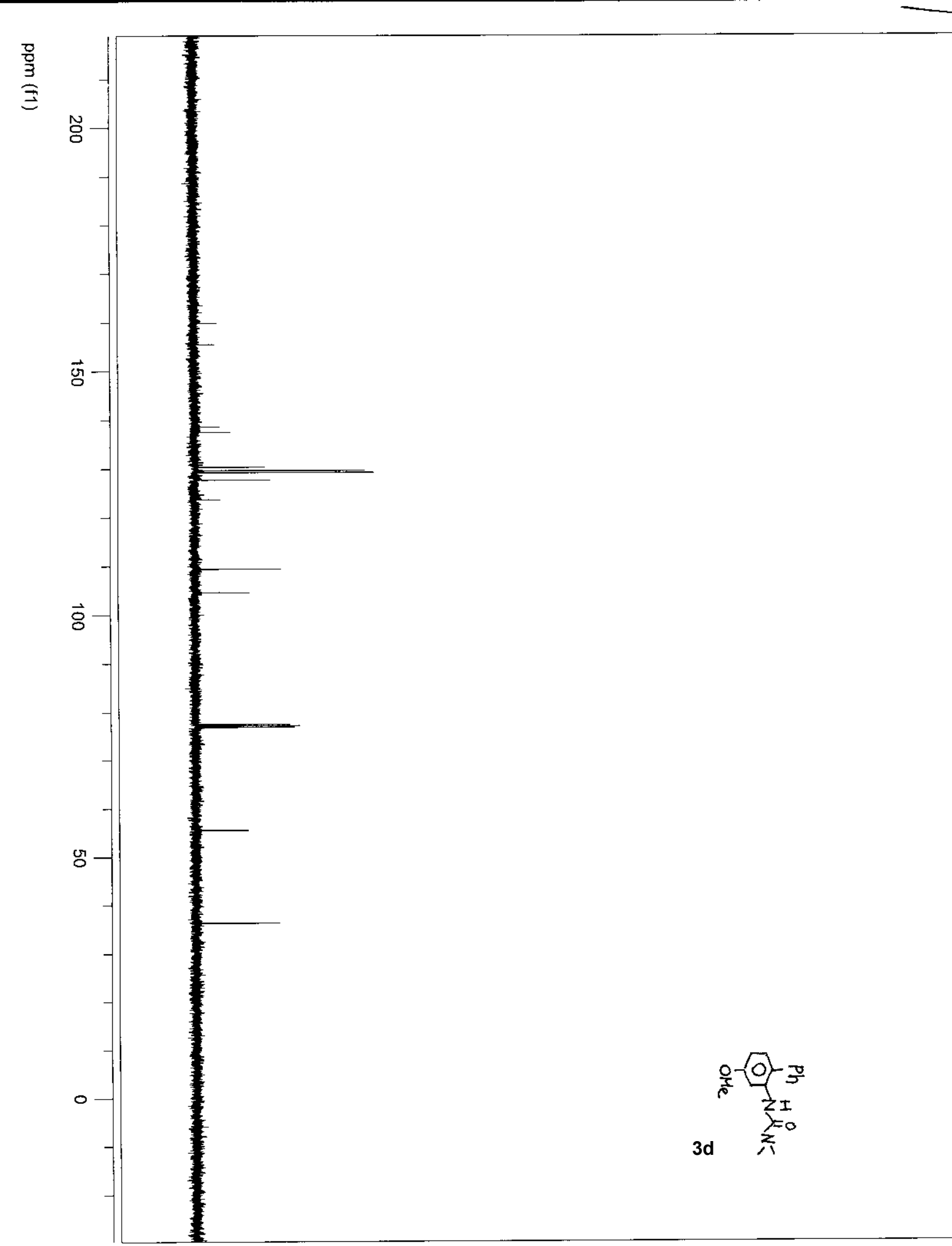

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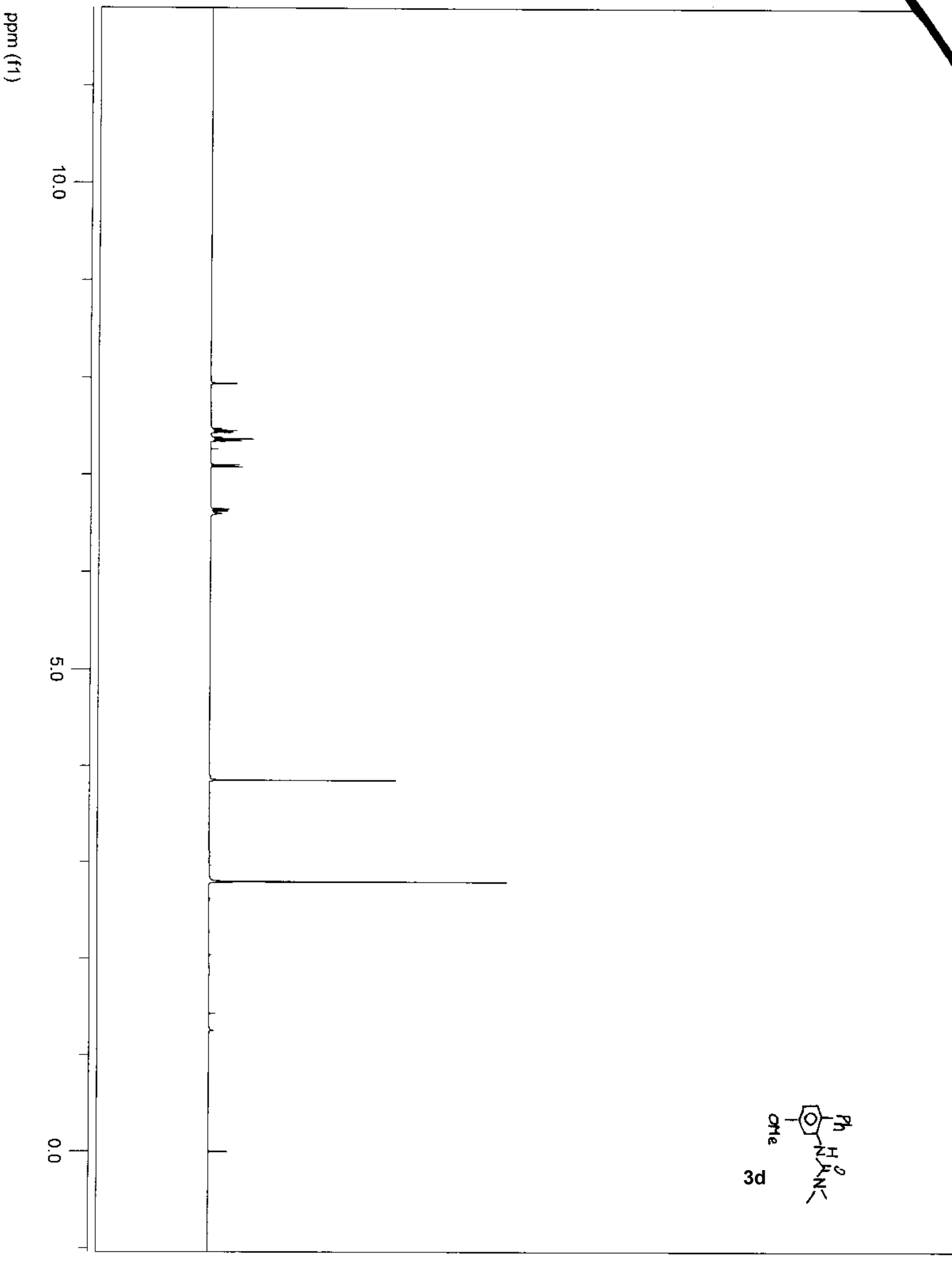
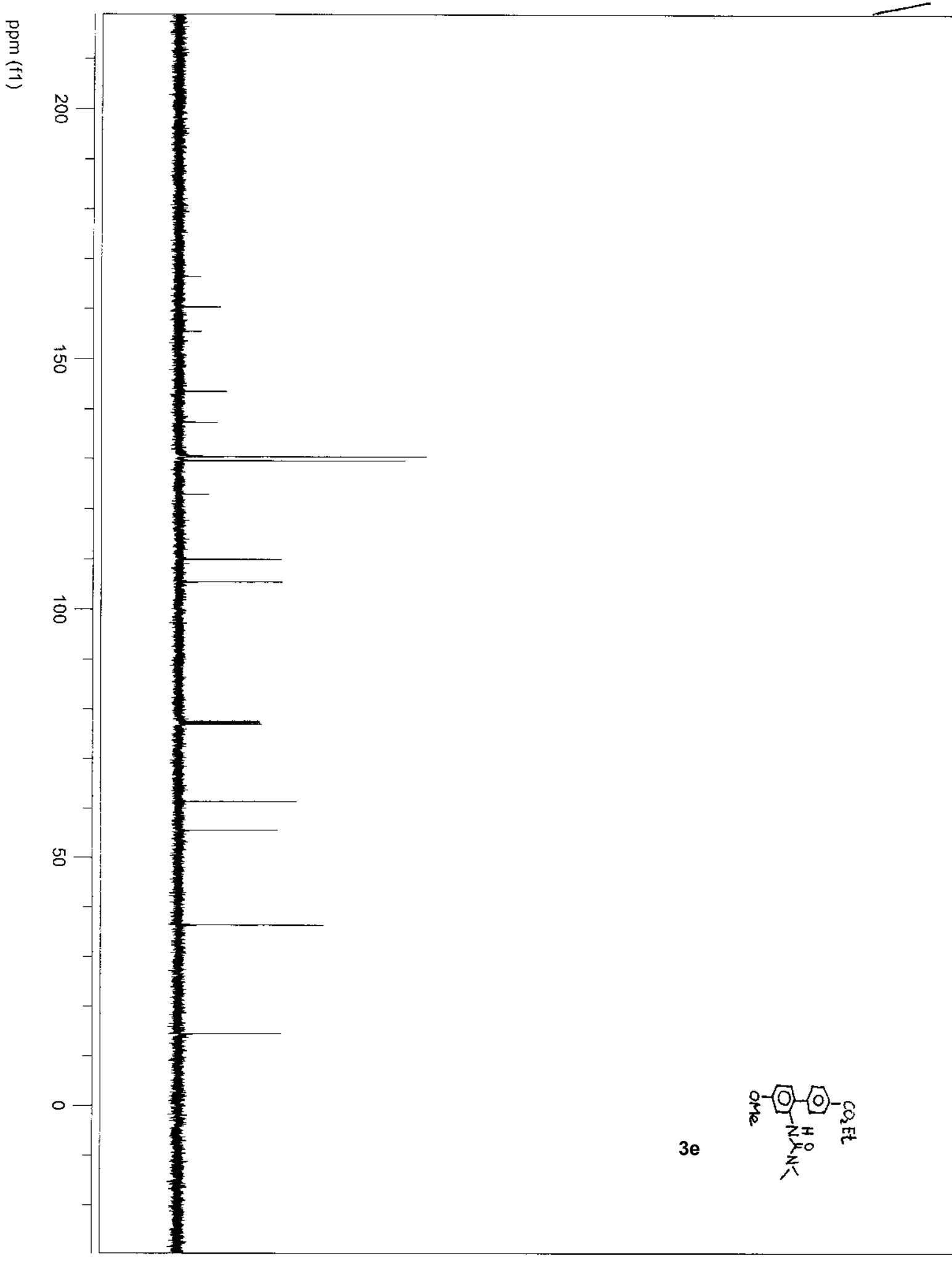


3d



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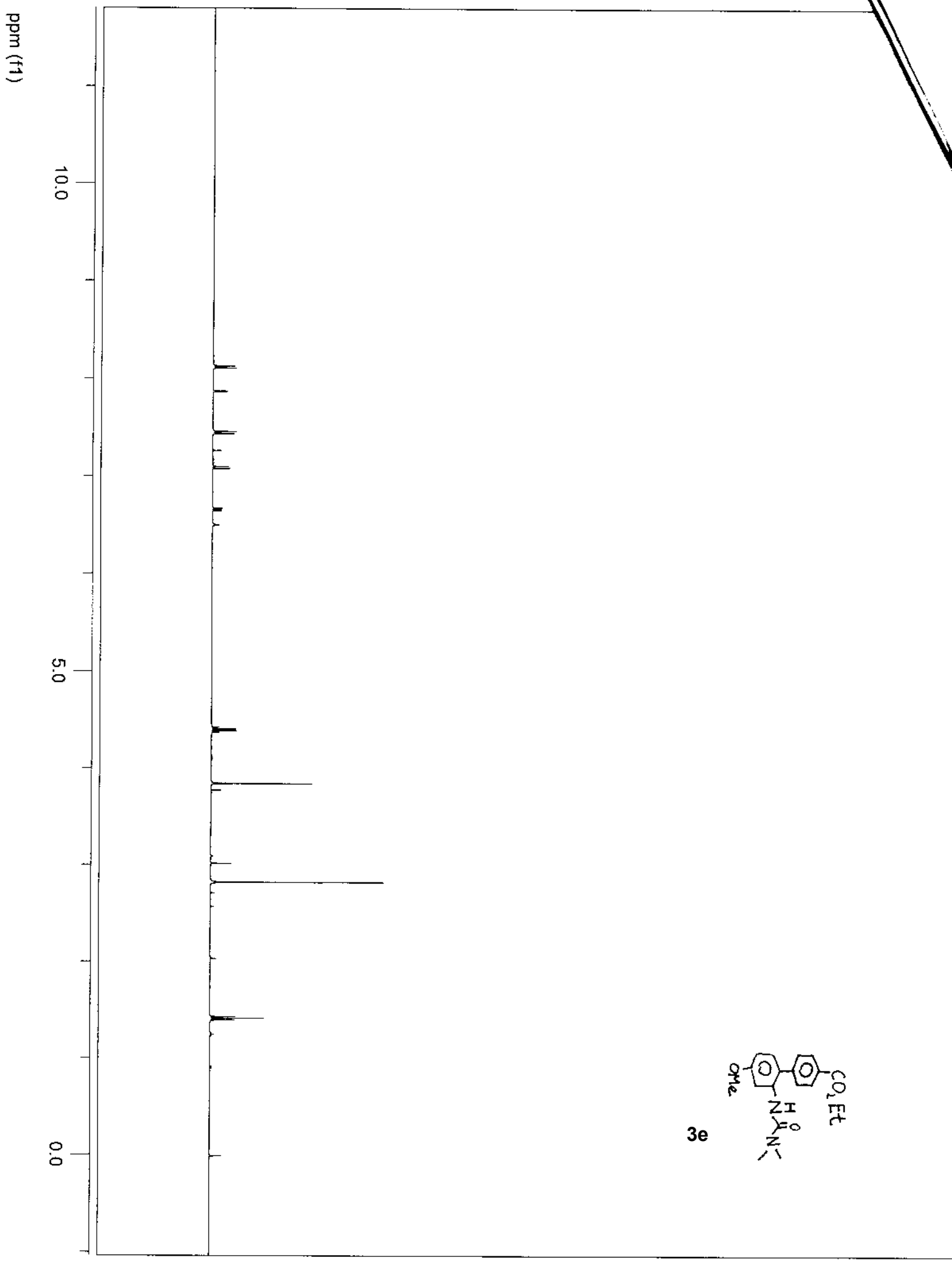

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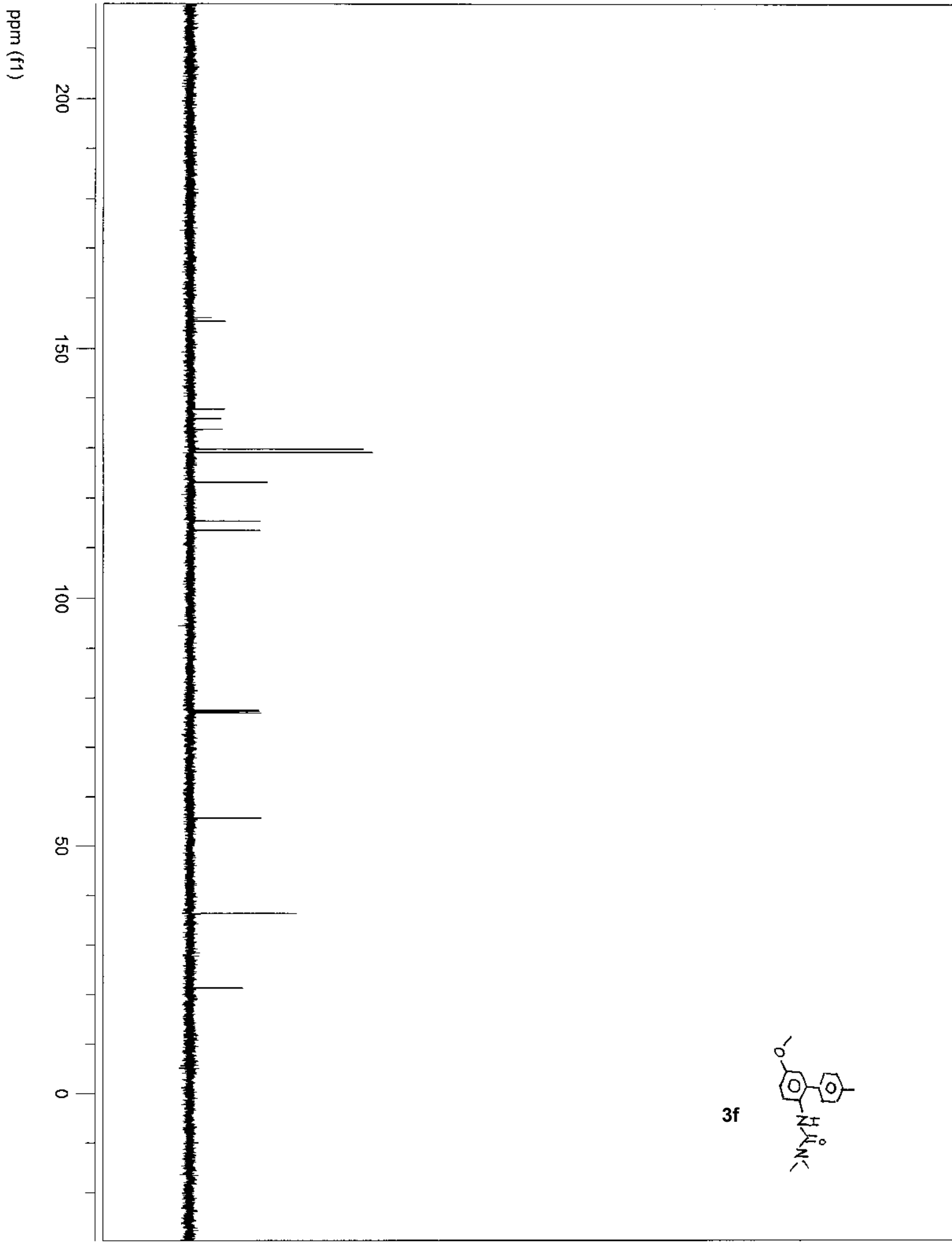

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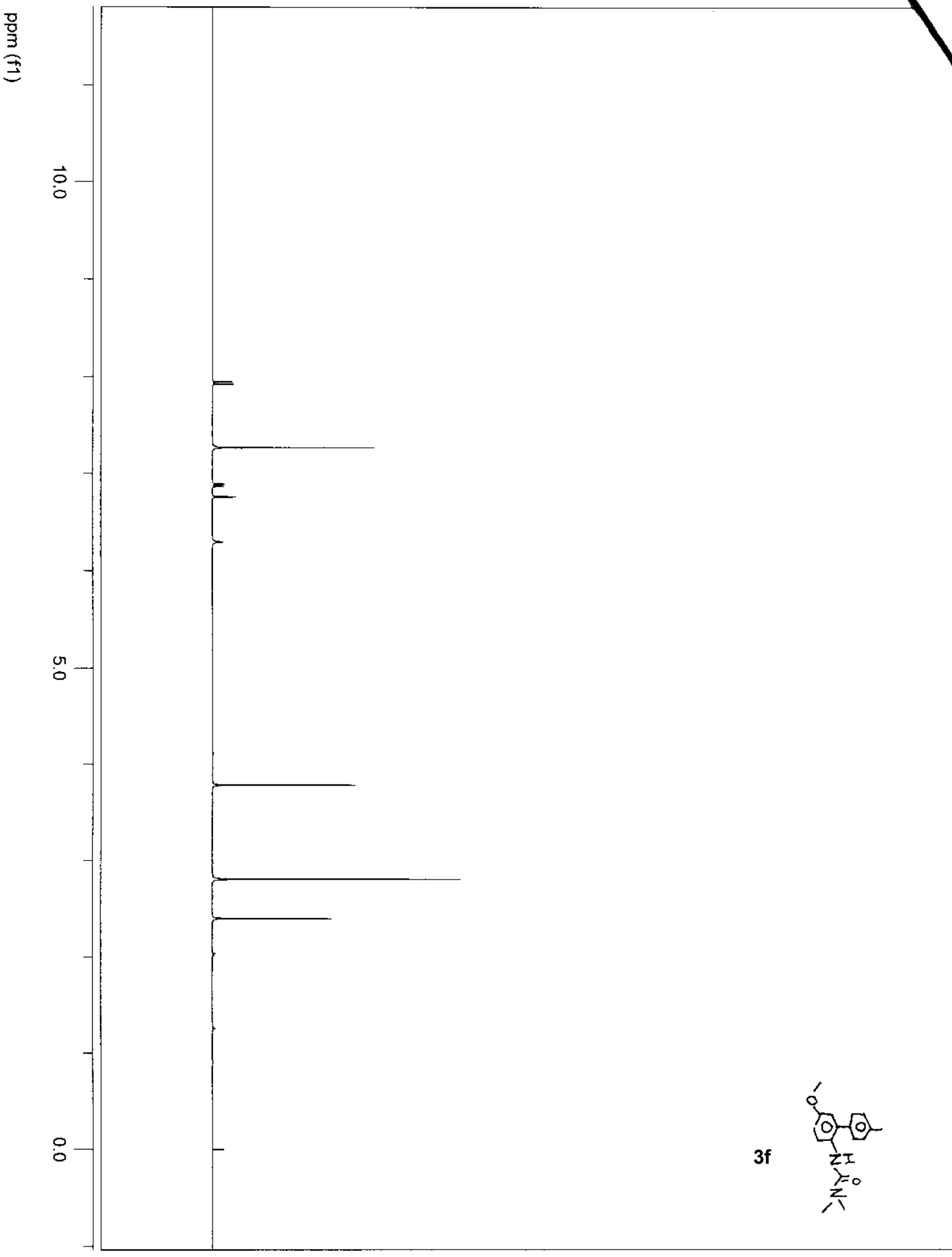
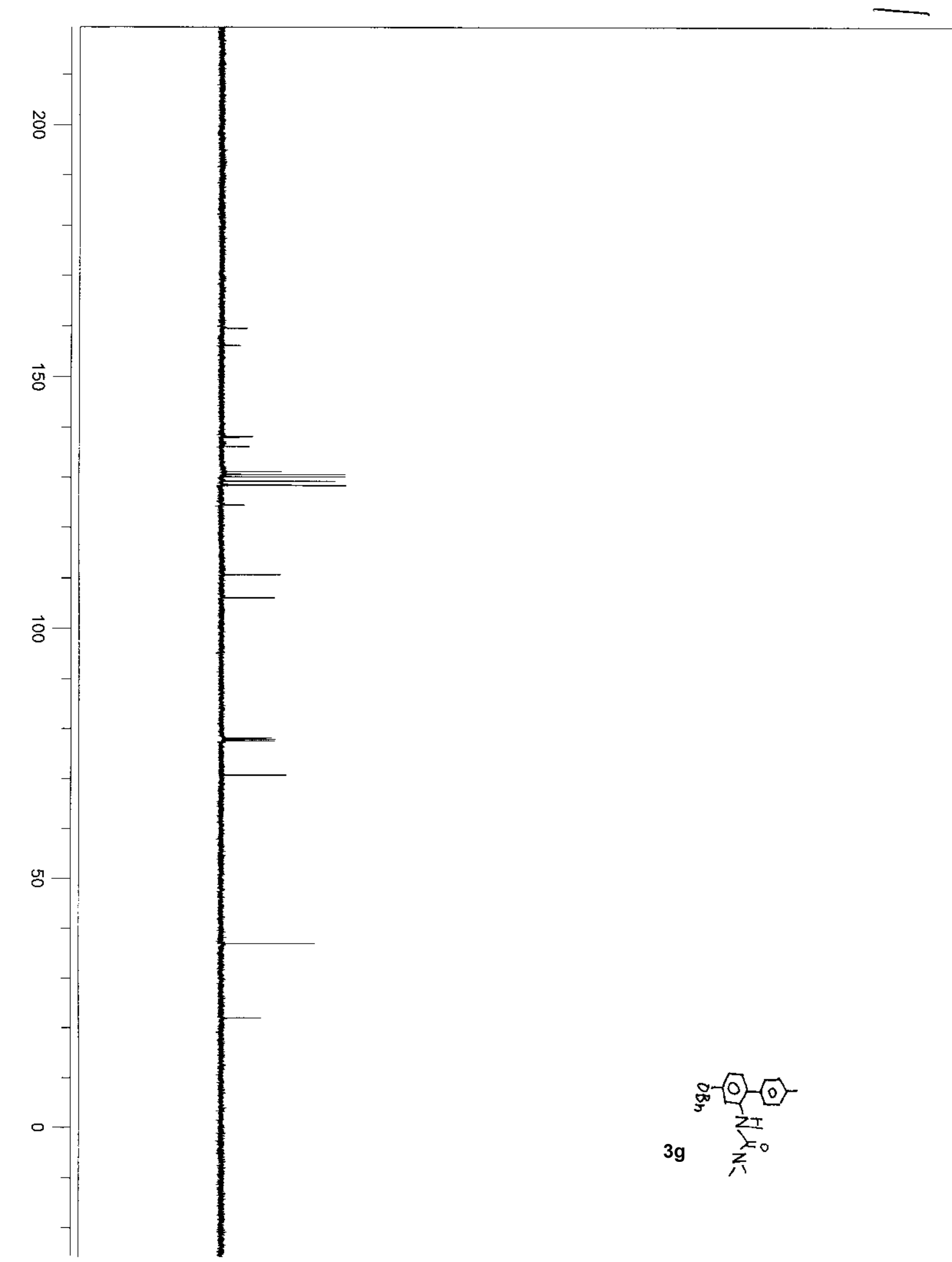
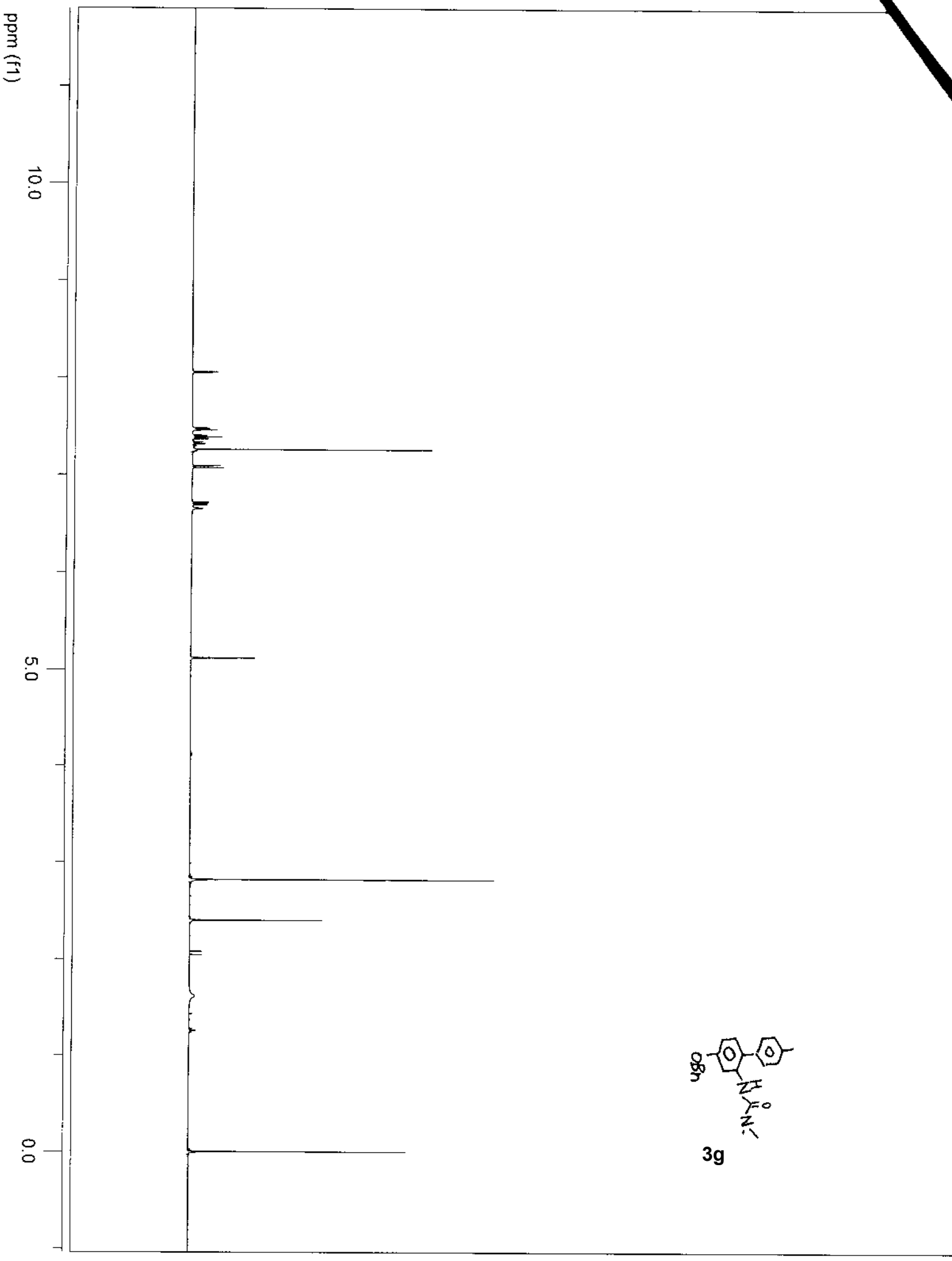


3f



3g



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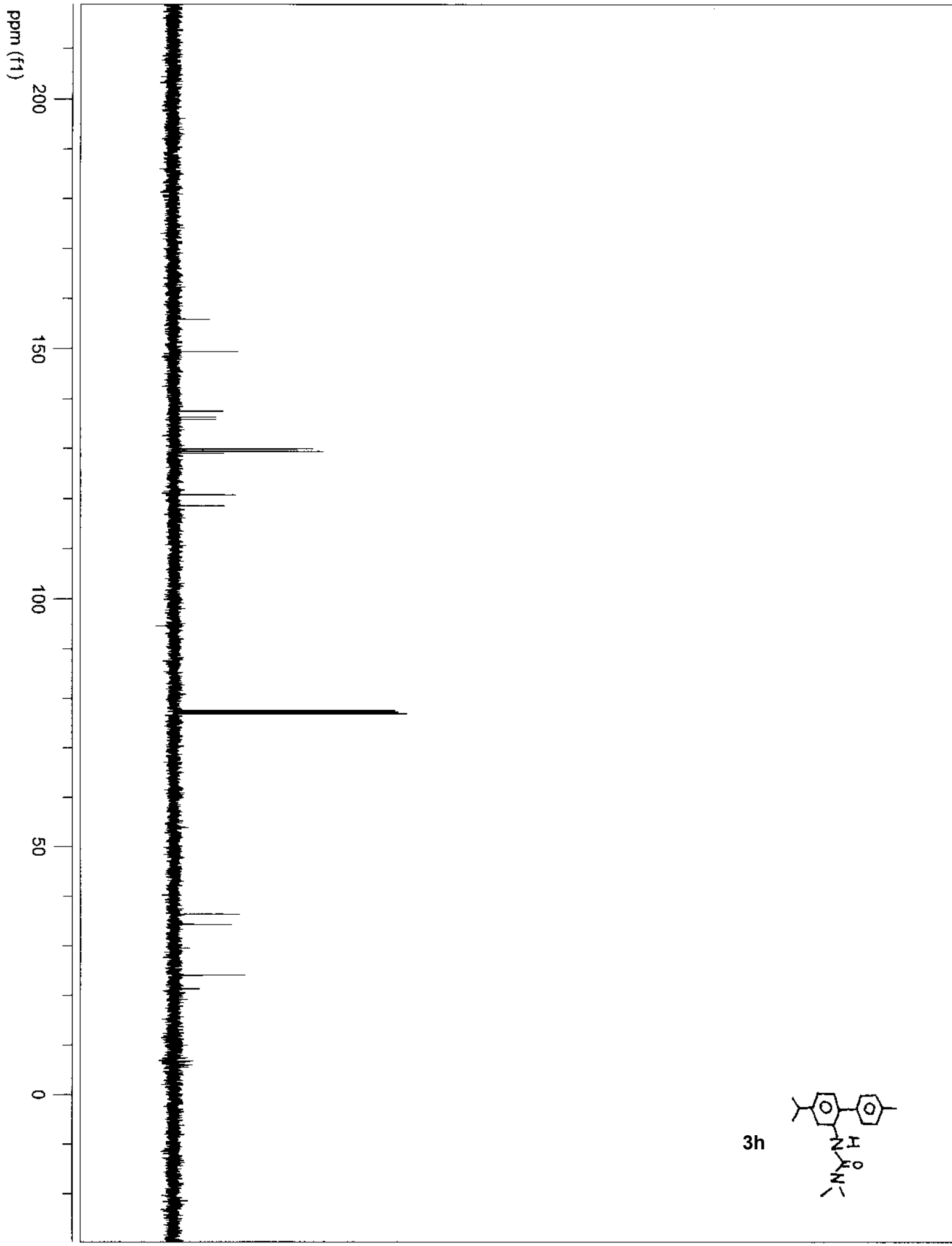

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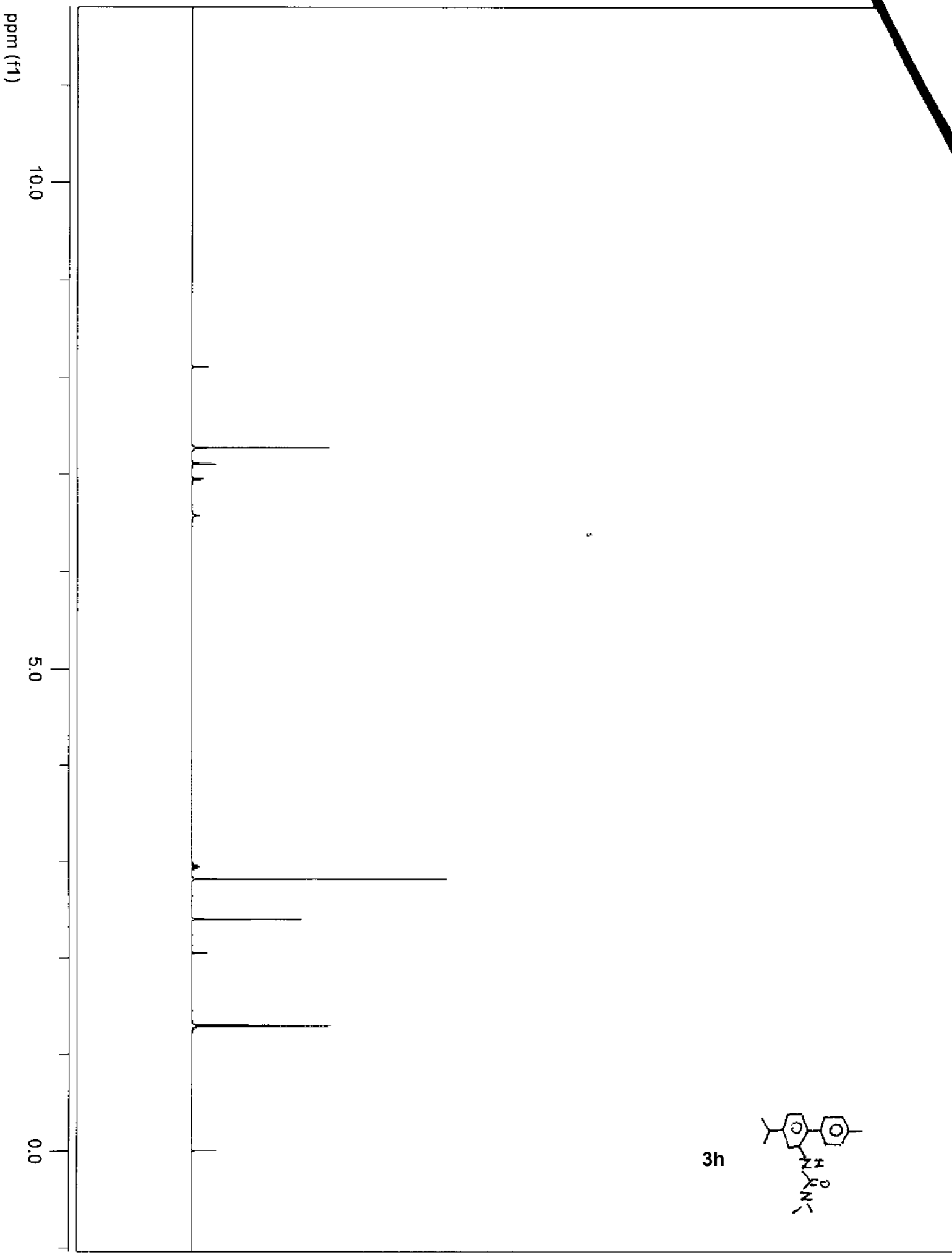
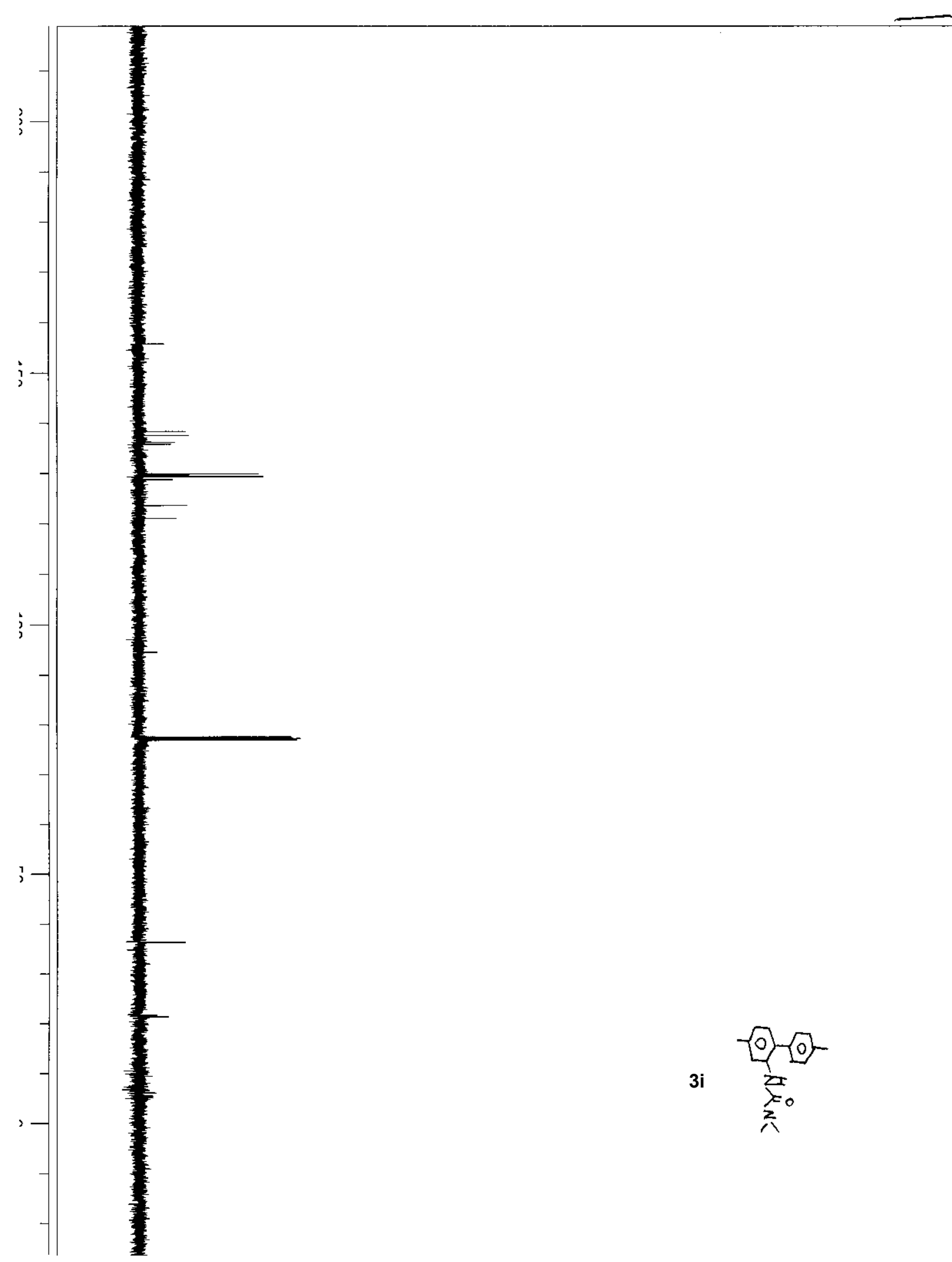
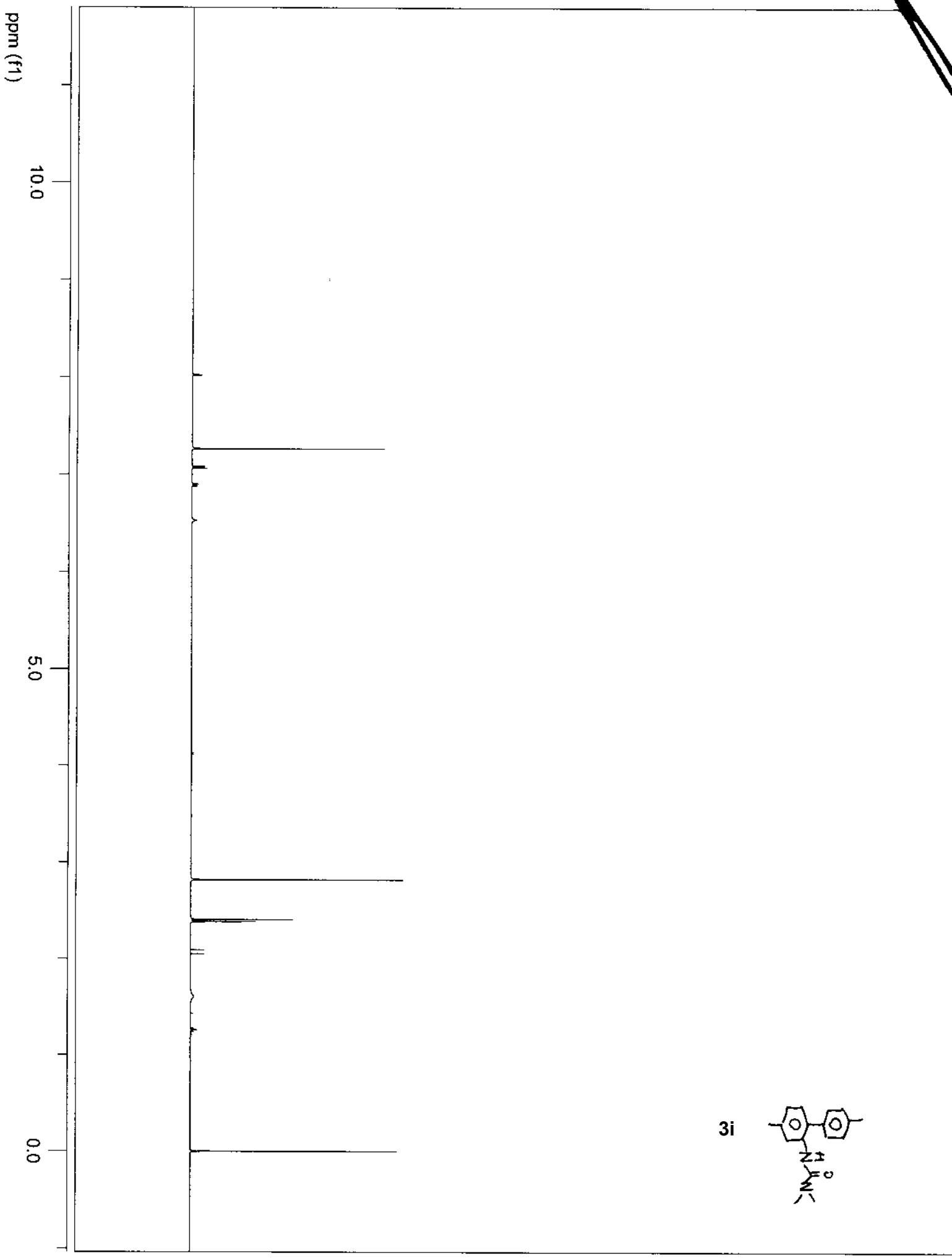


3h



3i



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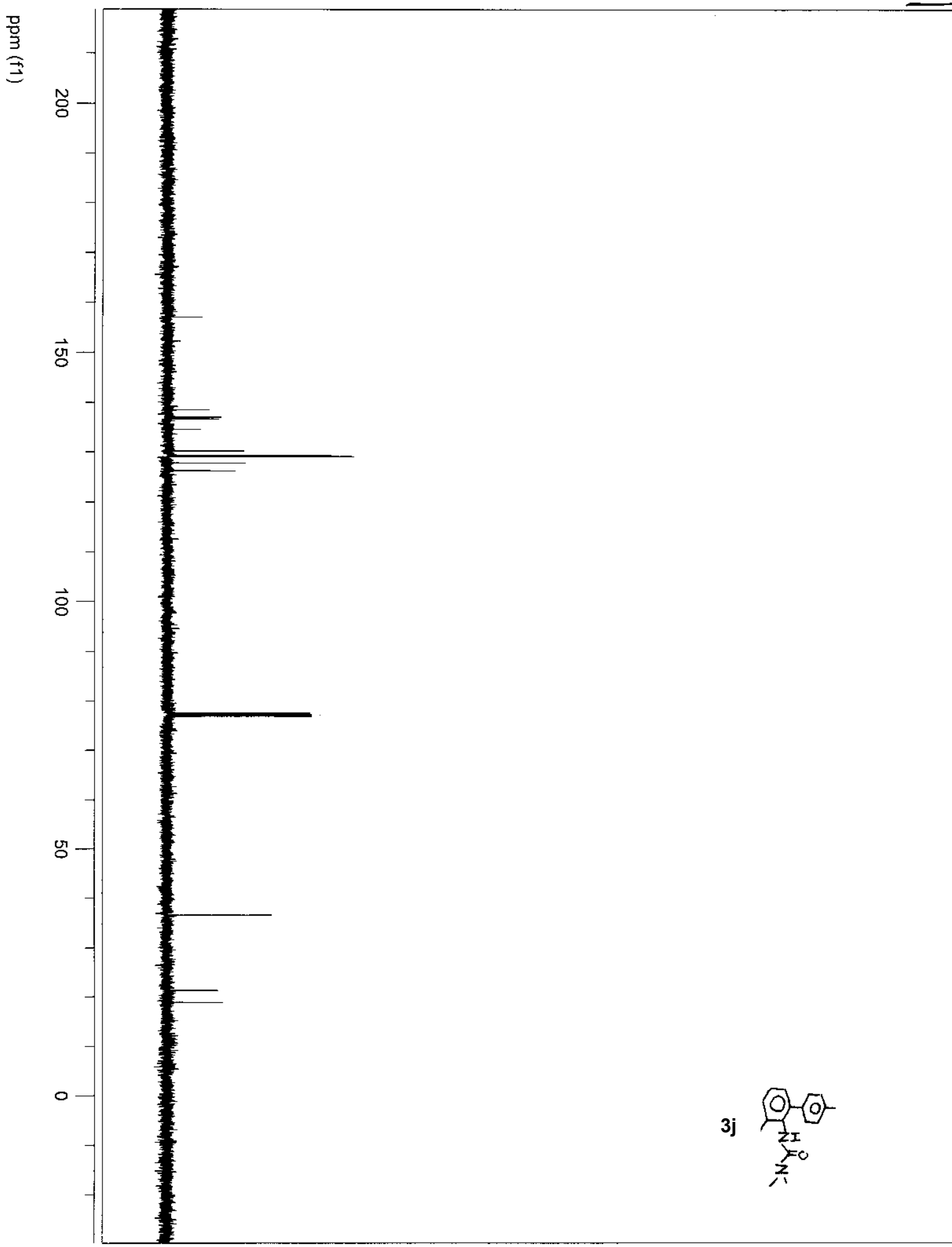

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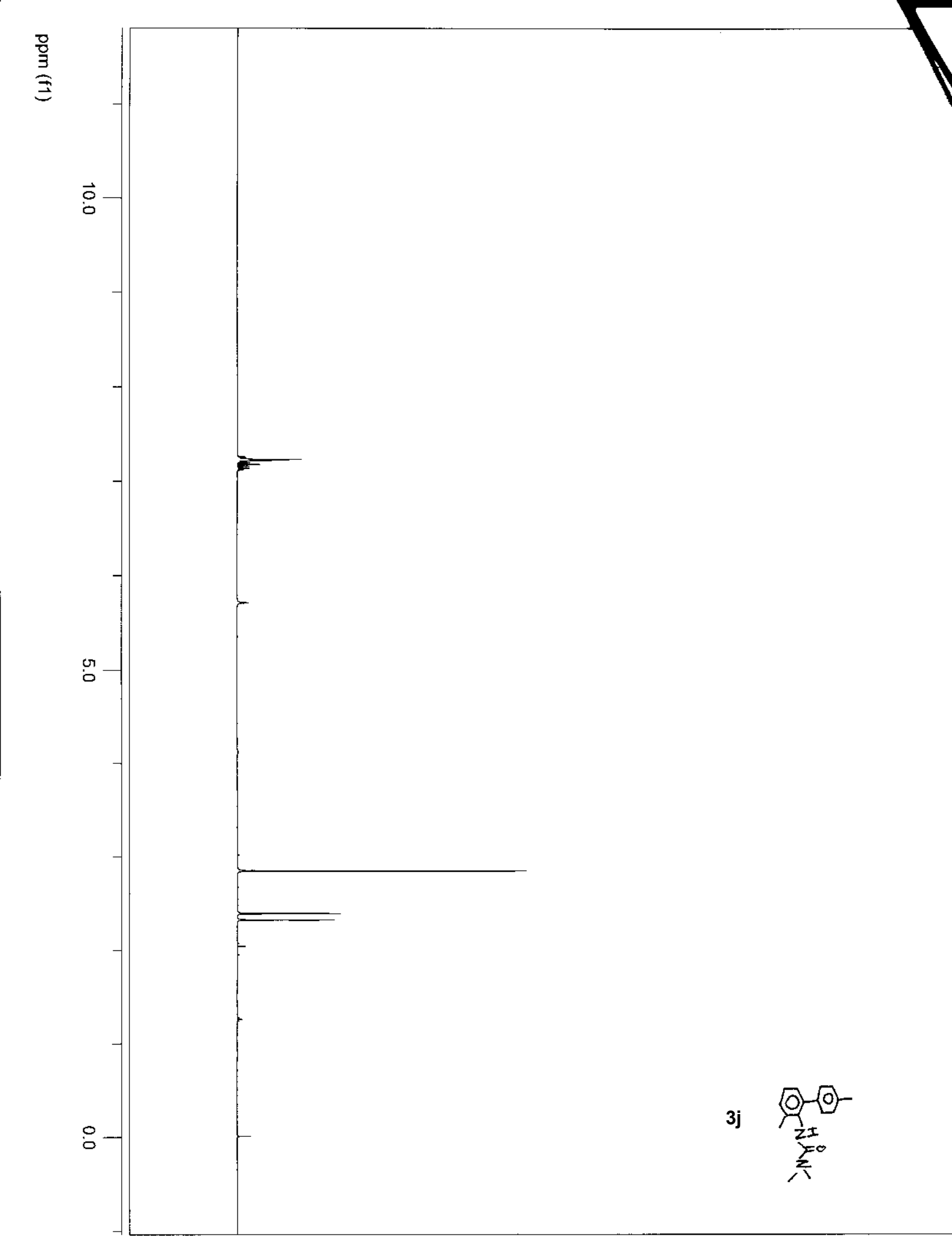

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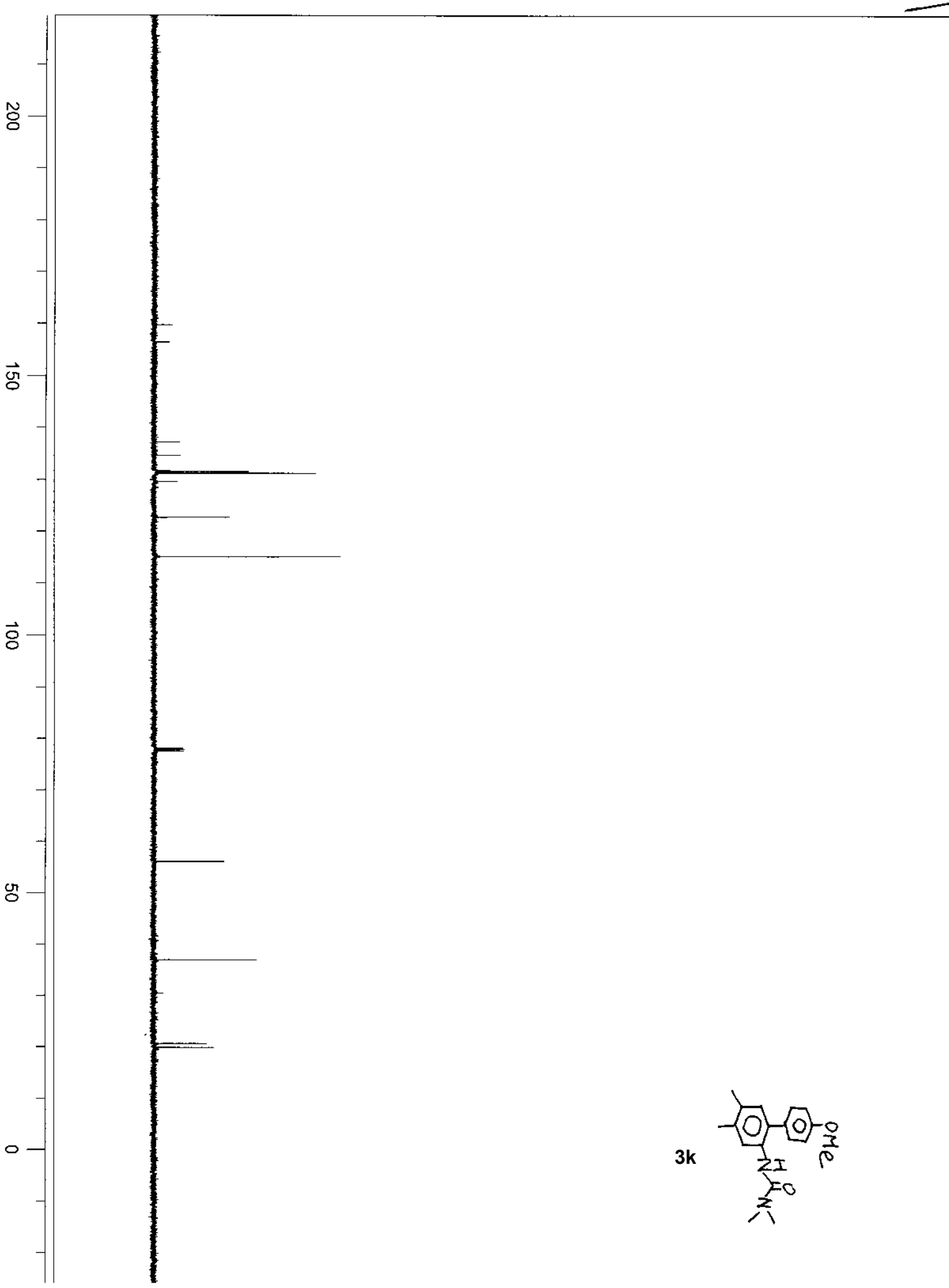

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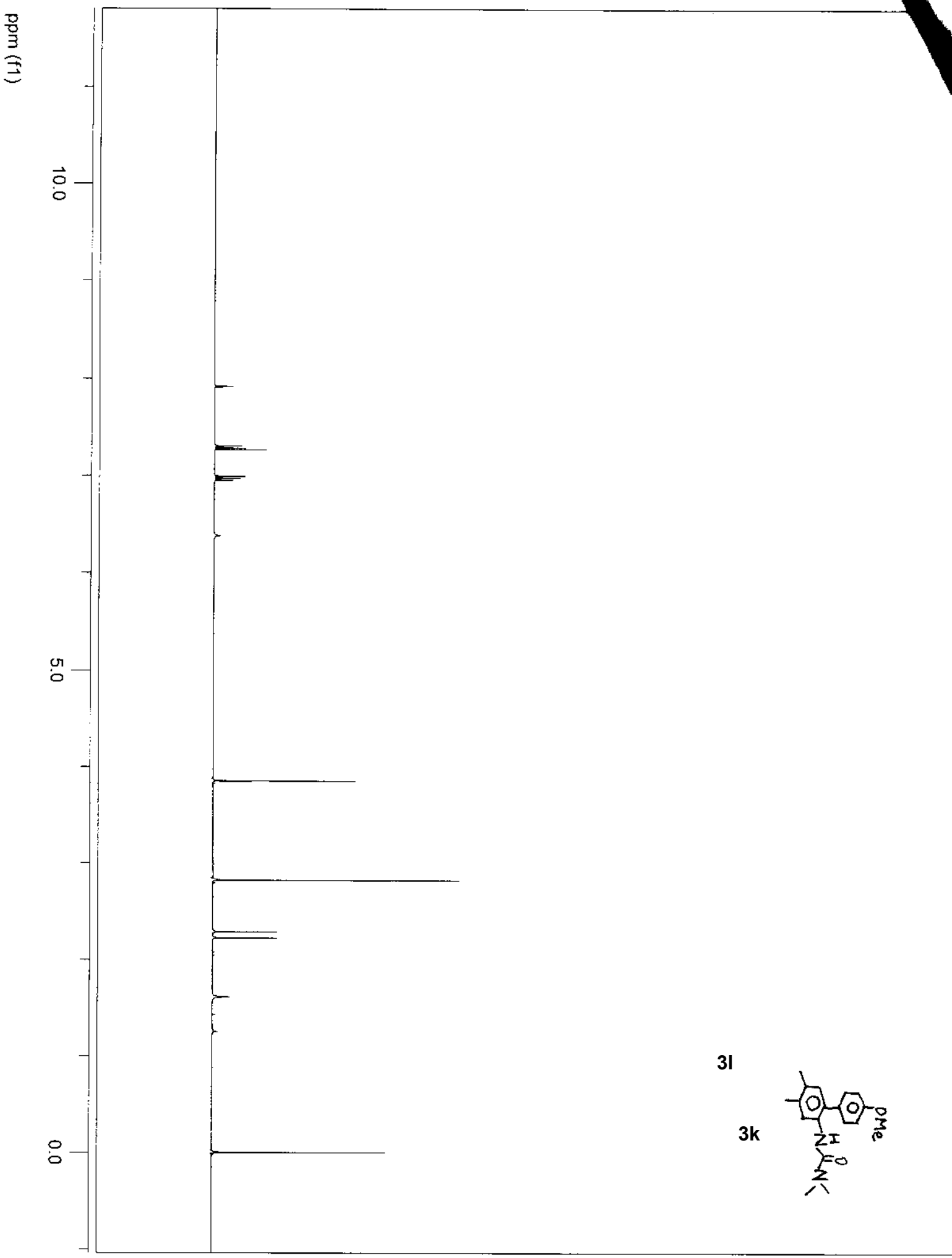
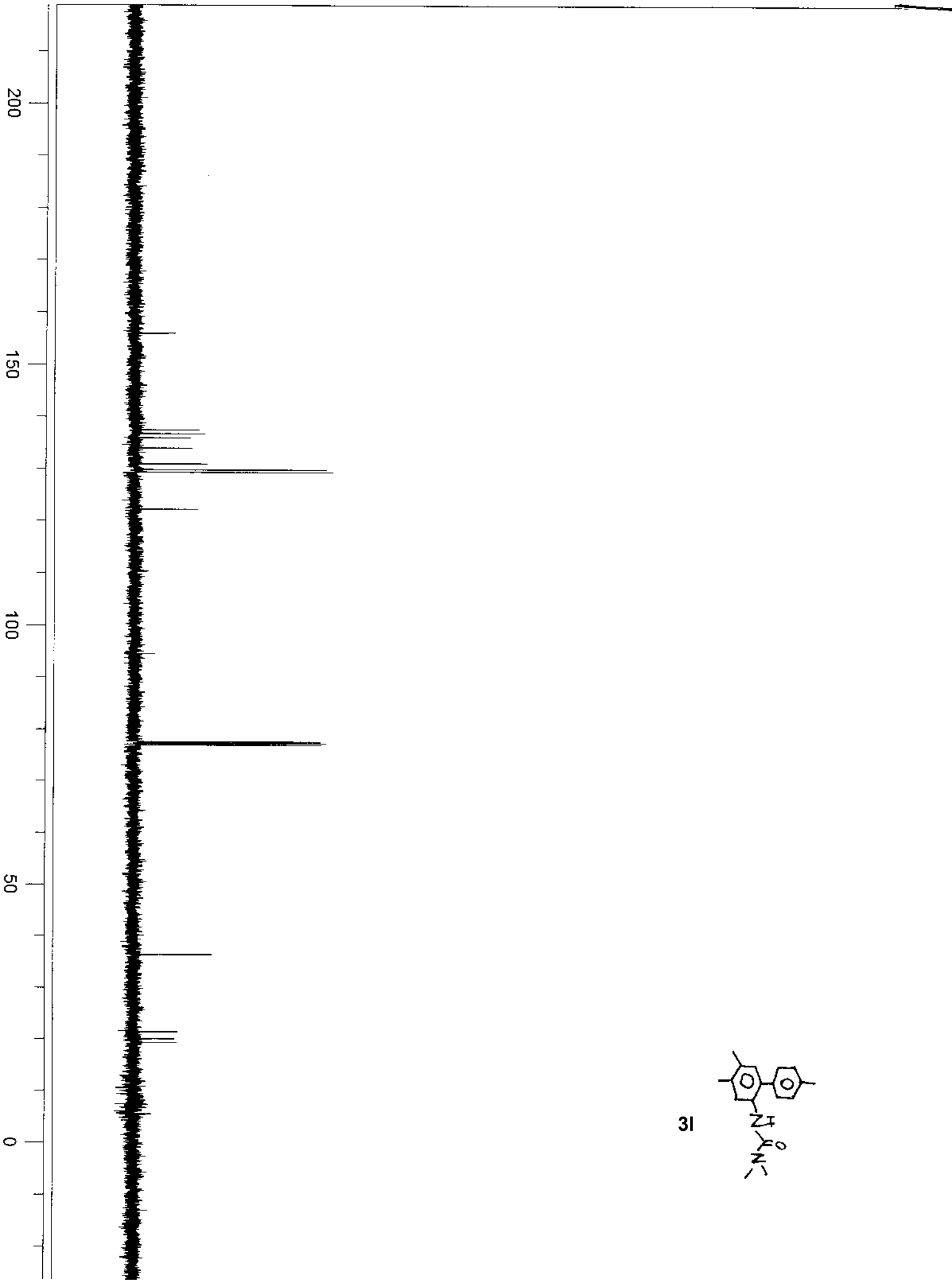


3l

3k



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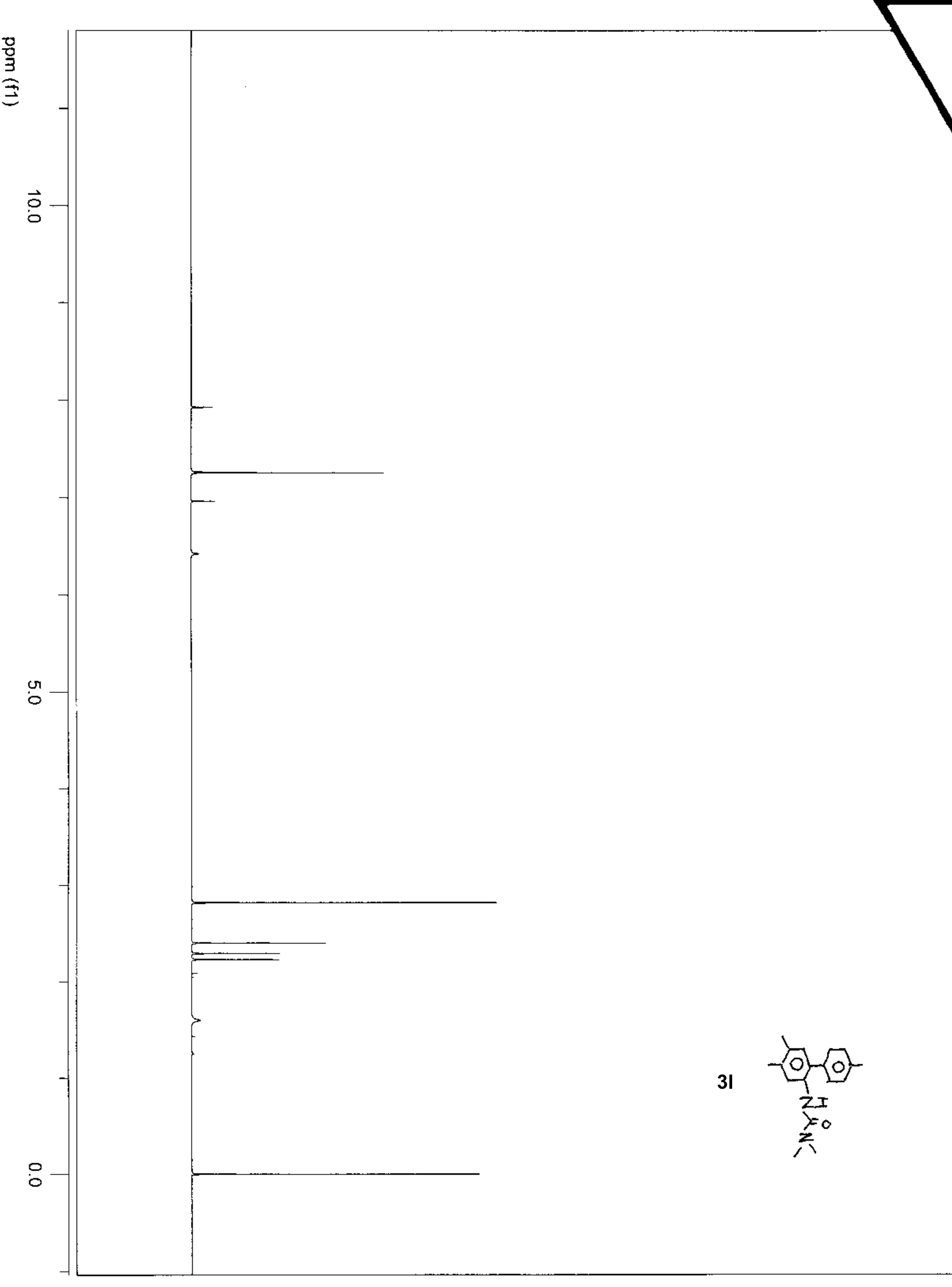
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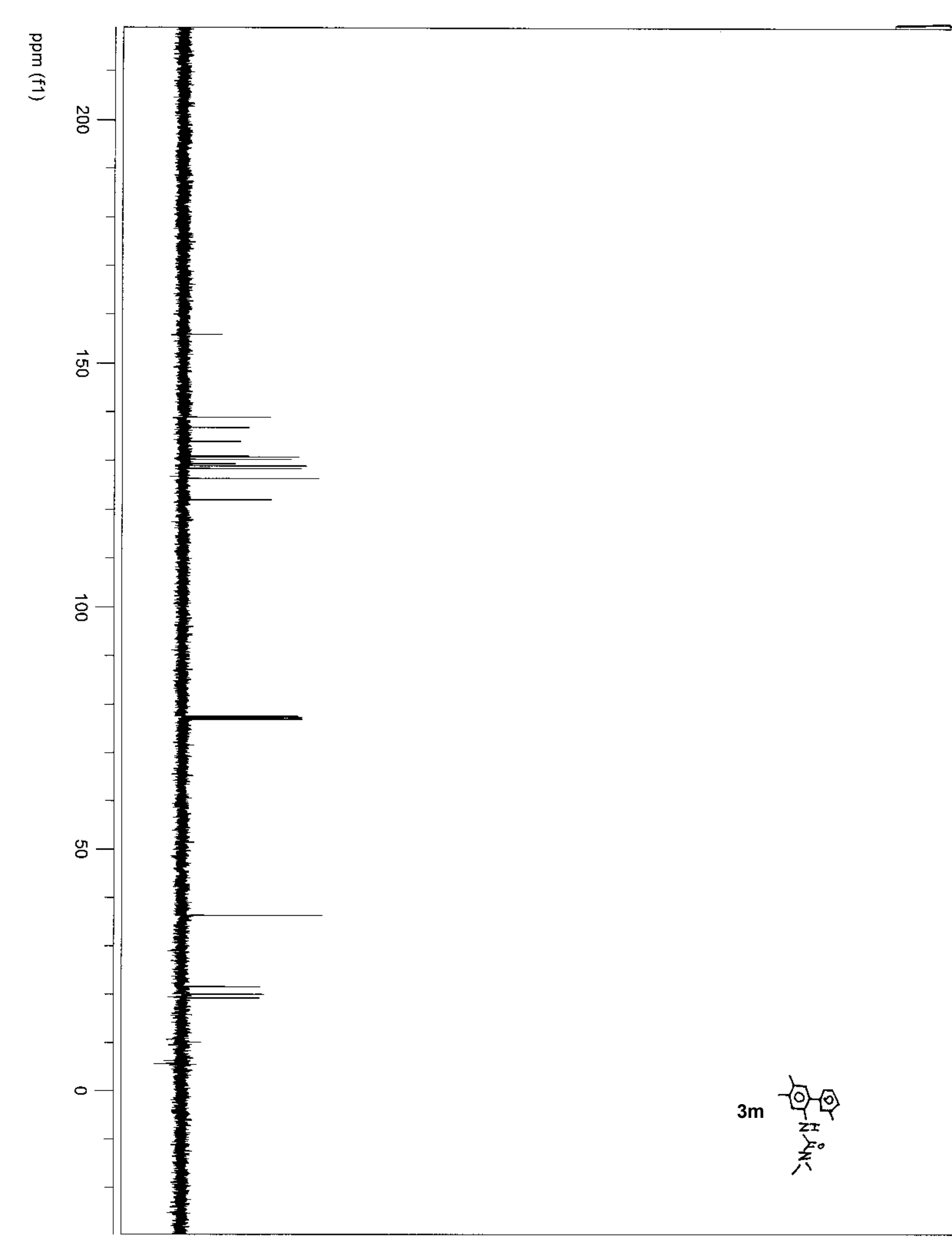
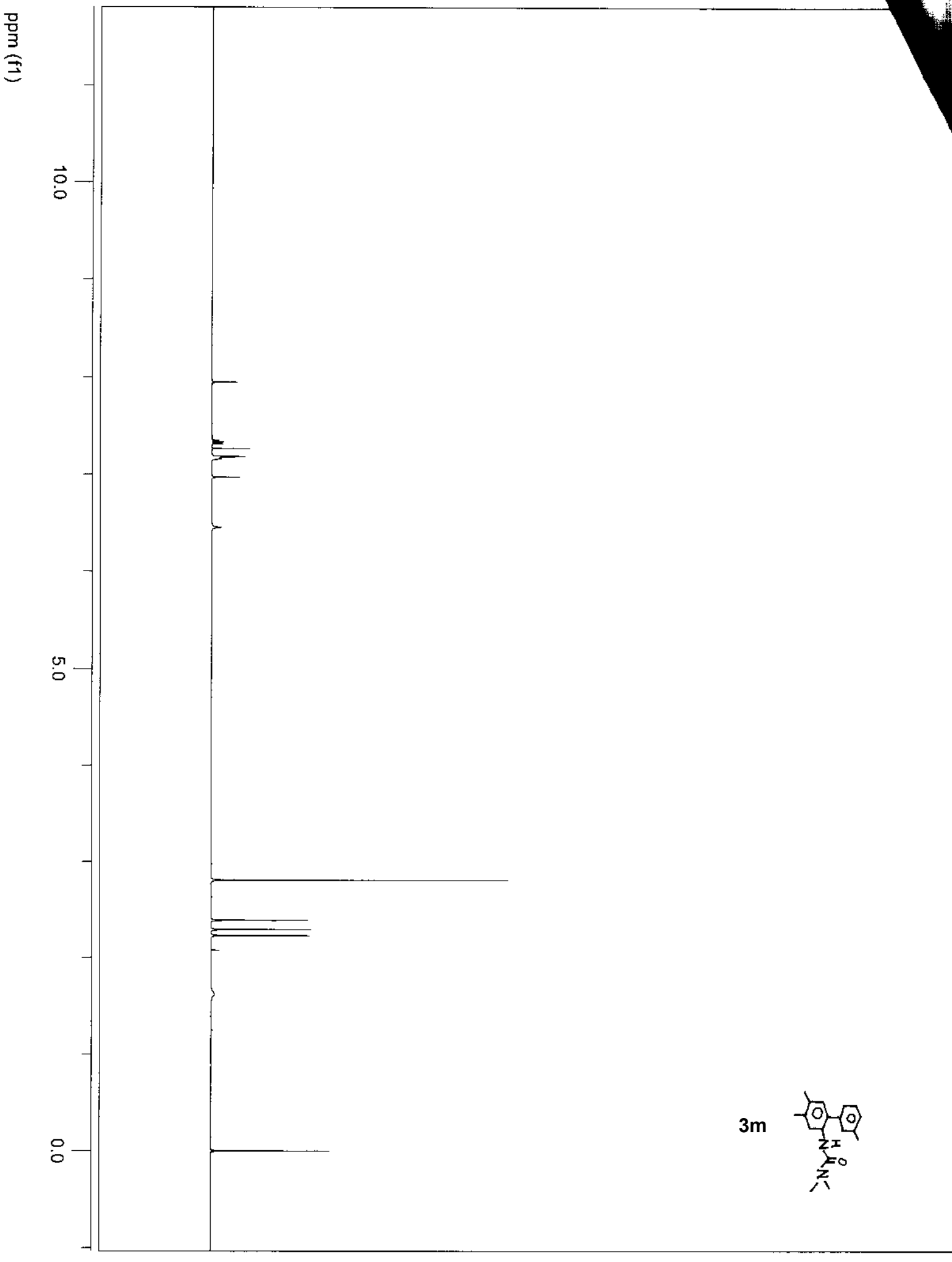
5.0
0.0
3l


ppm (f1)
200
150
100
50
0
3m



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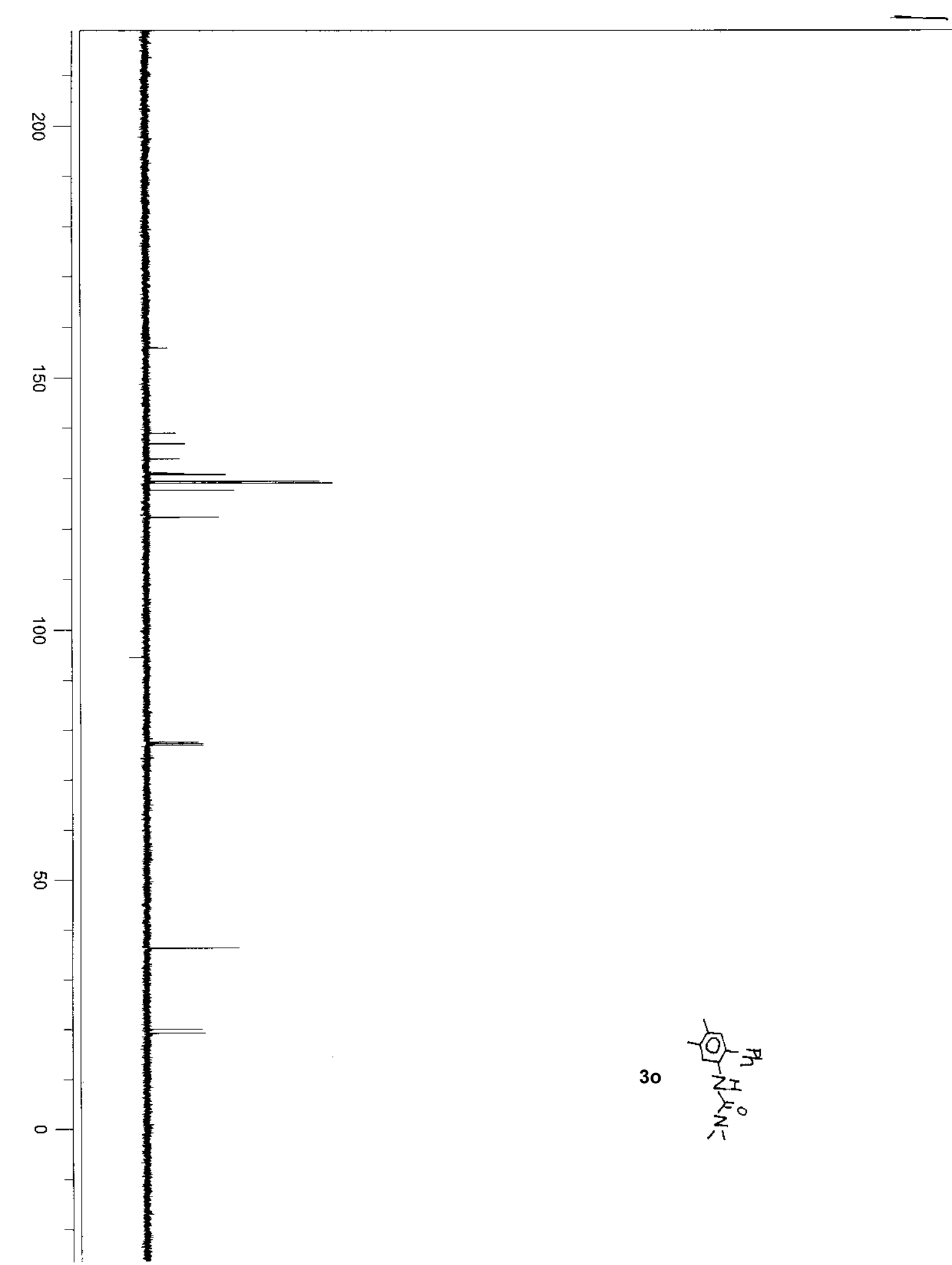

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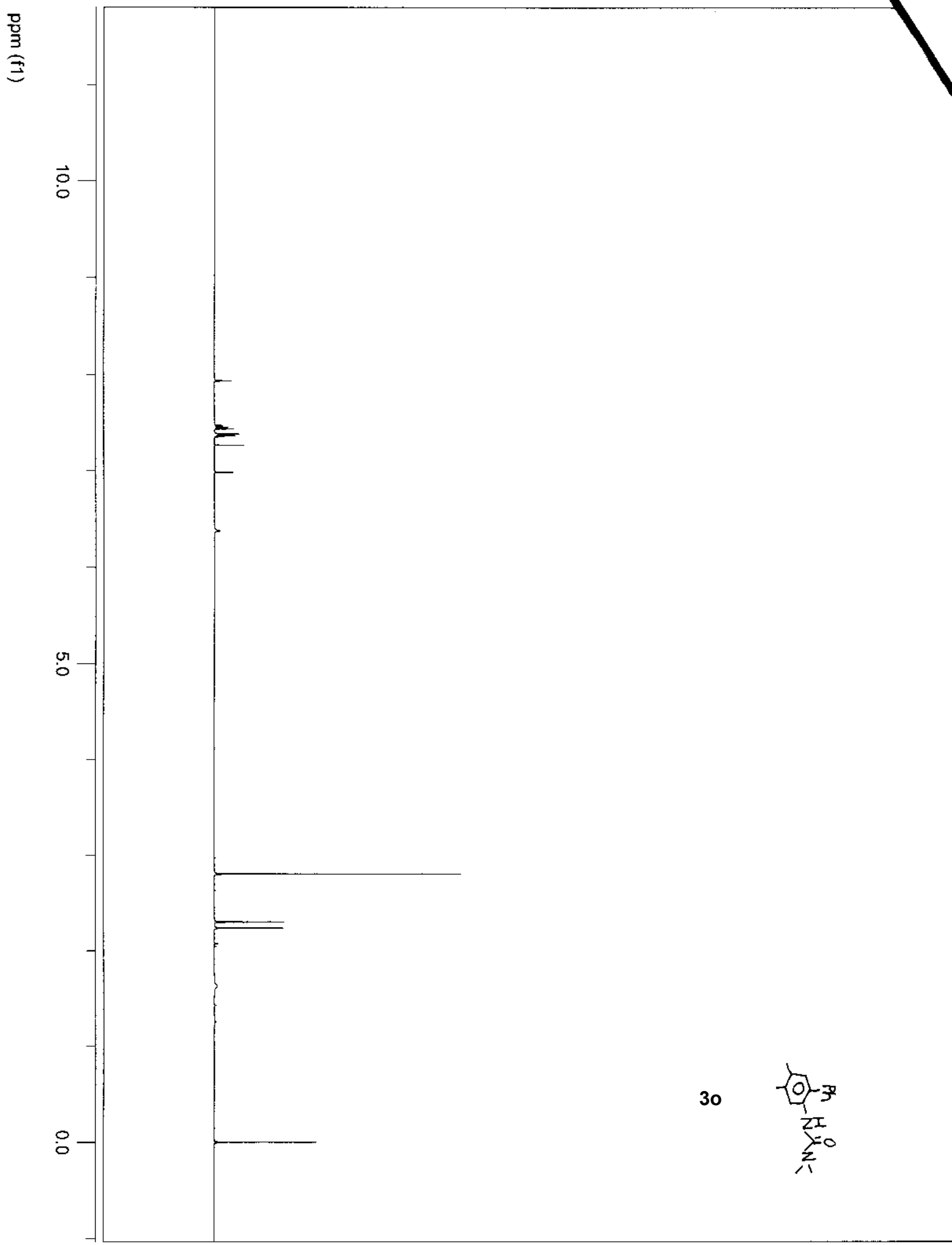
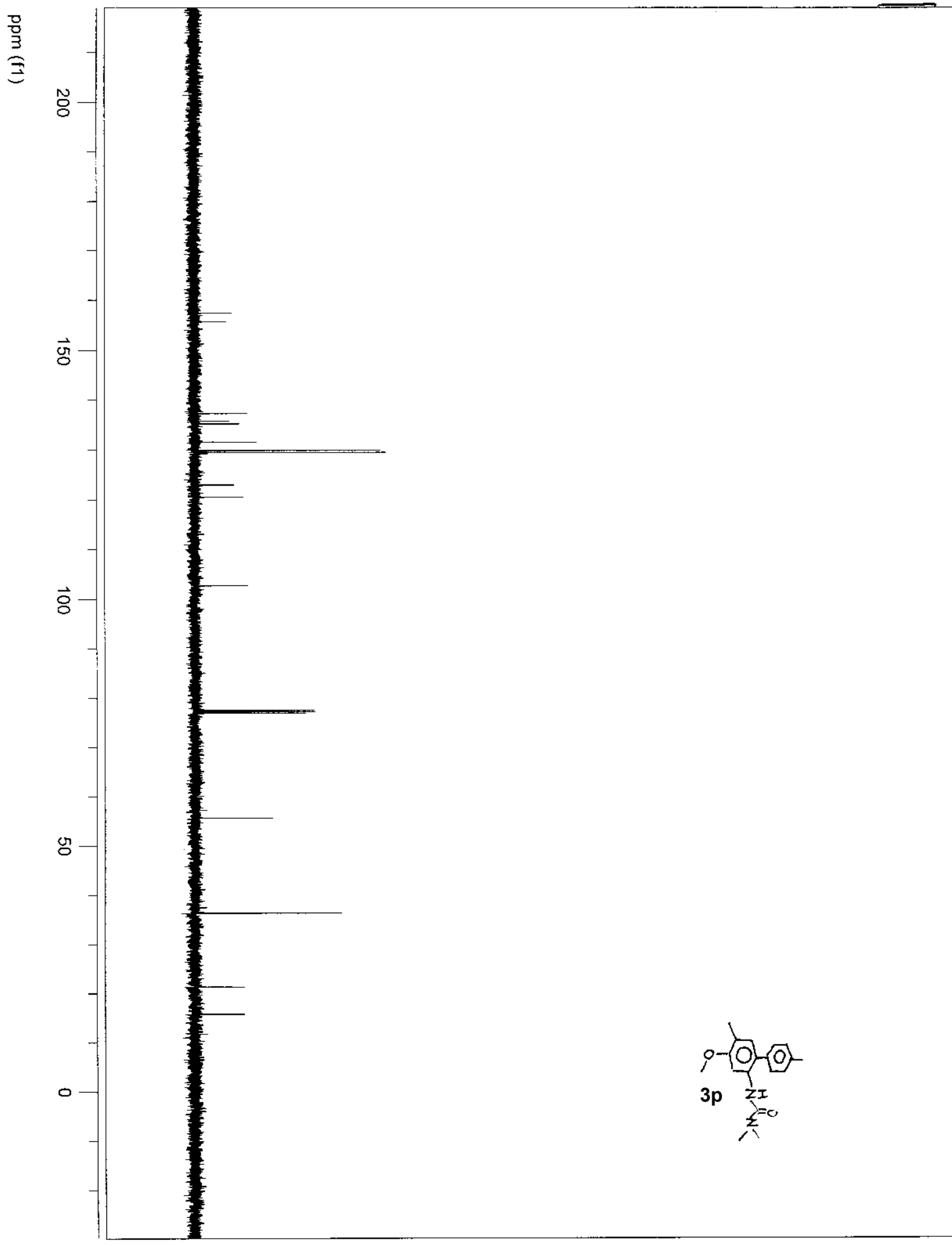
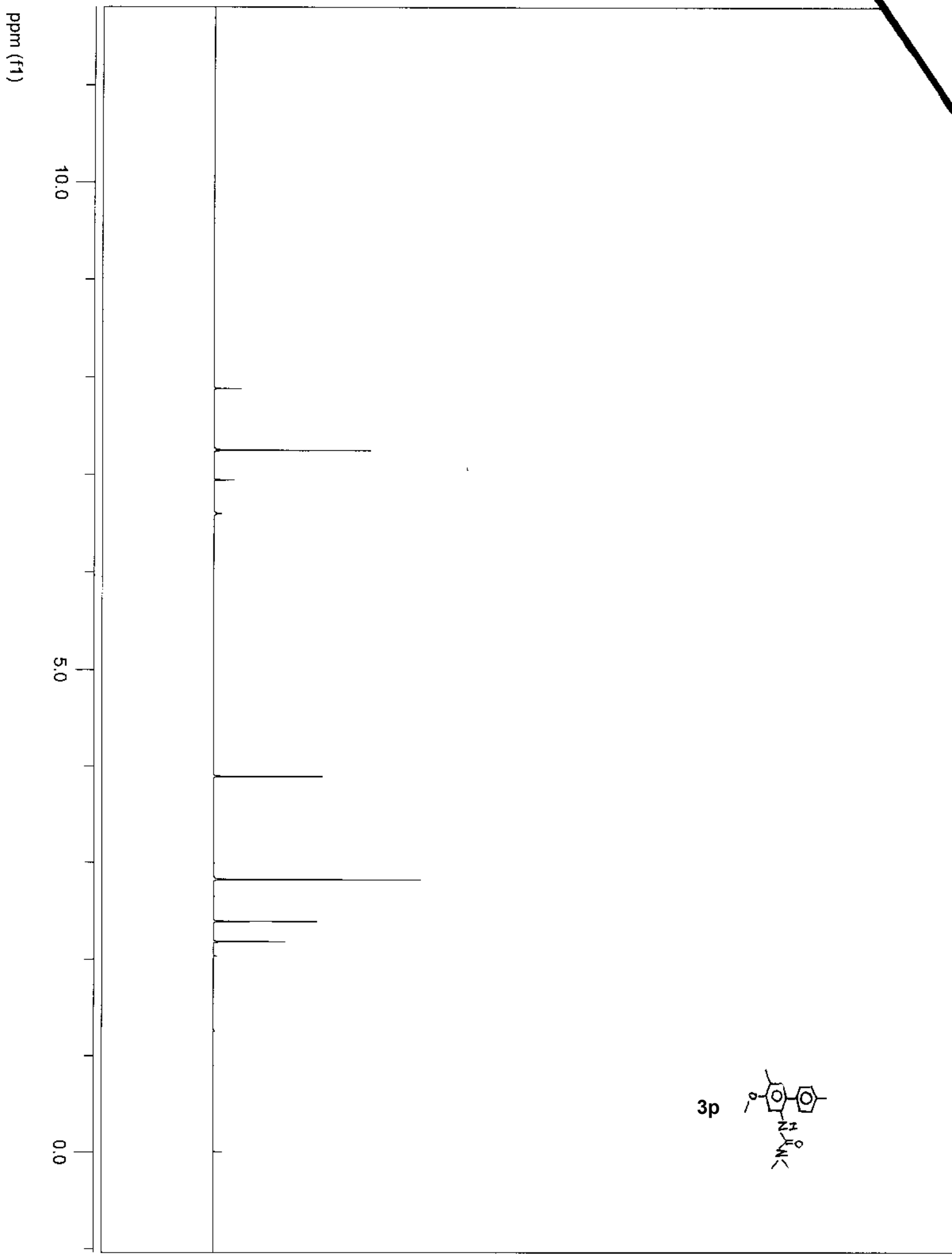


3o



3p



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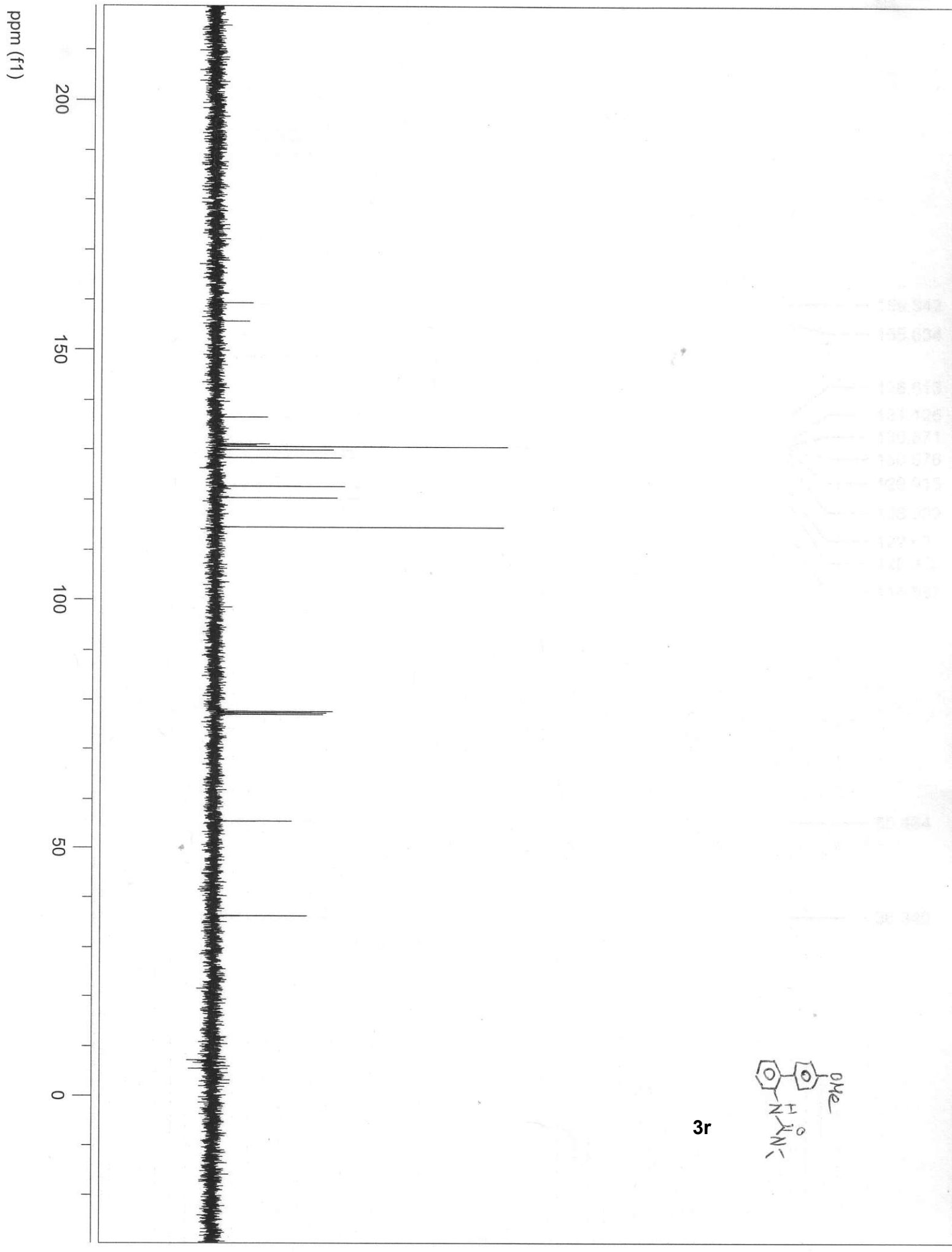

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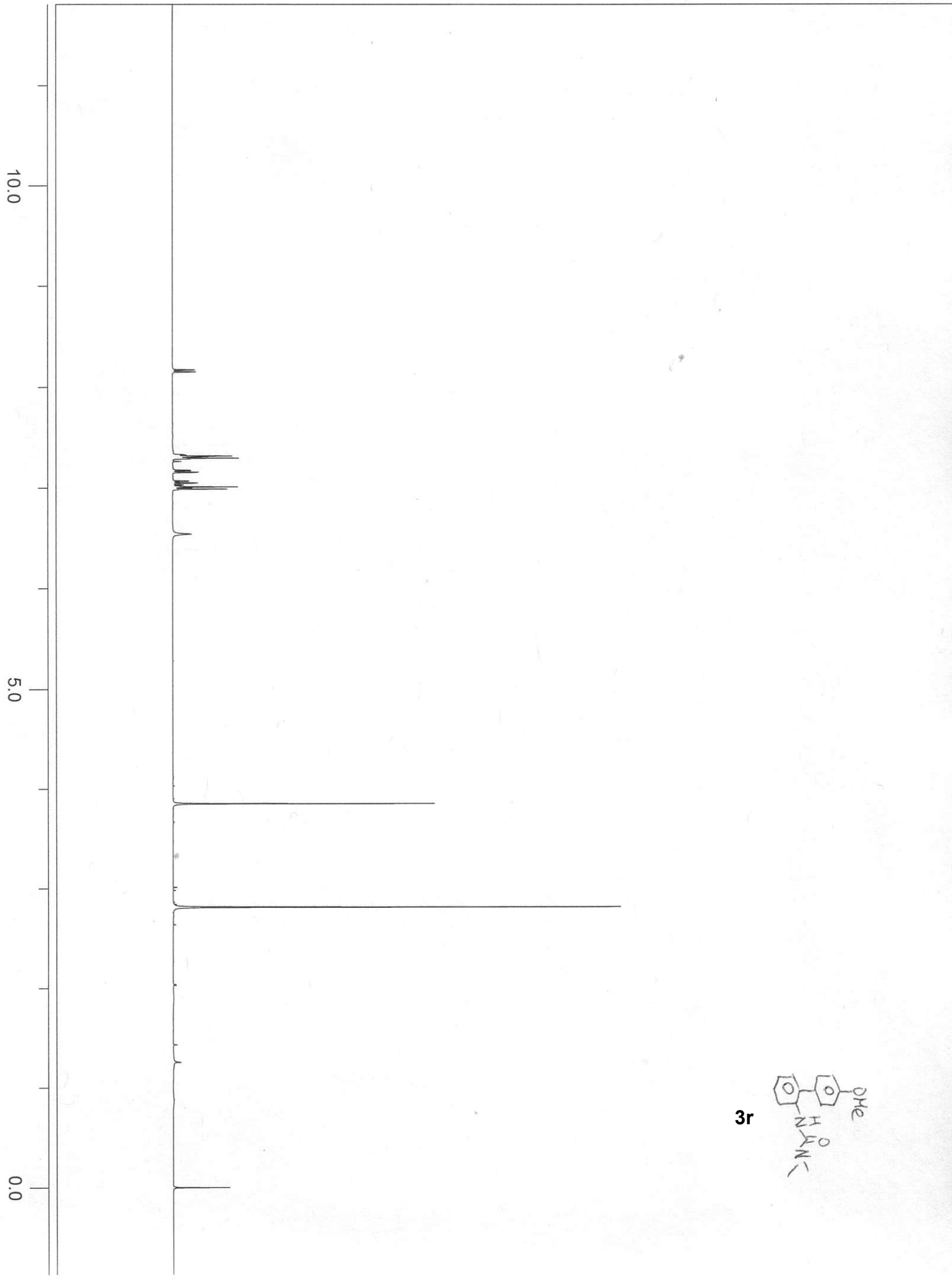

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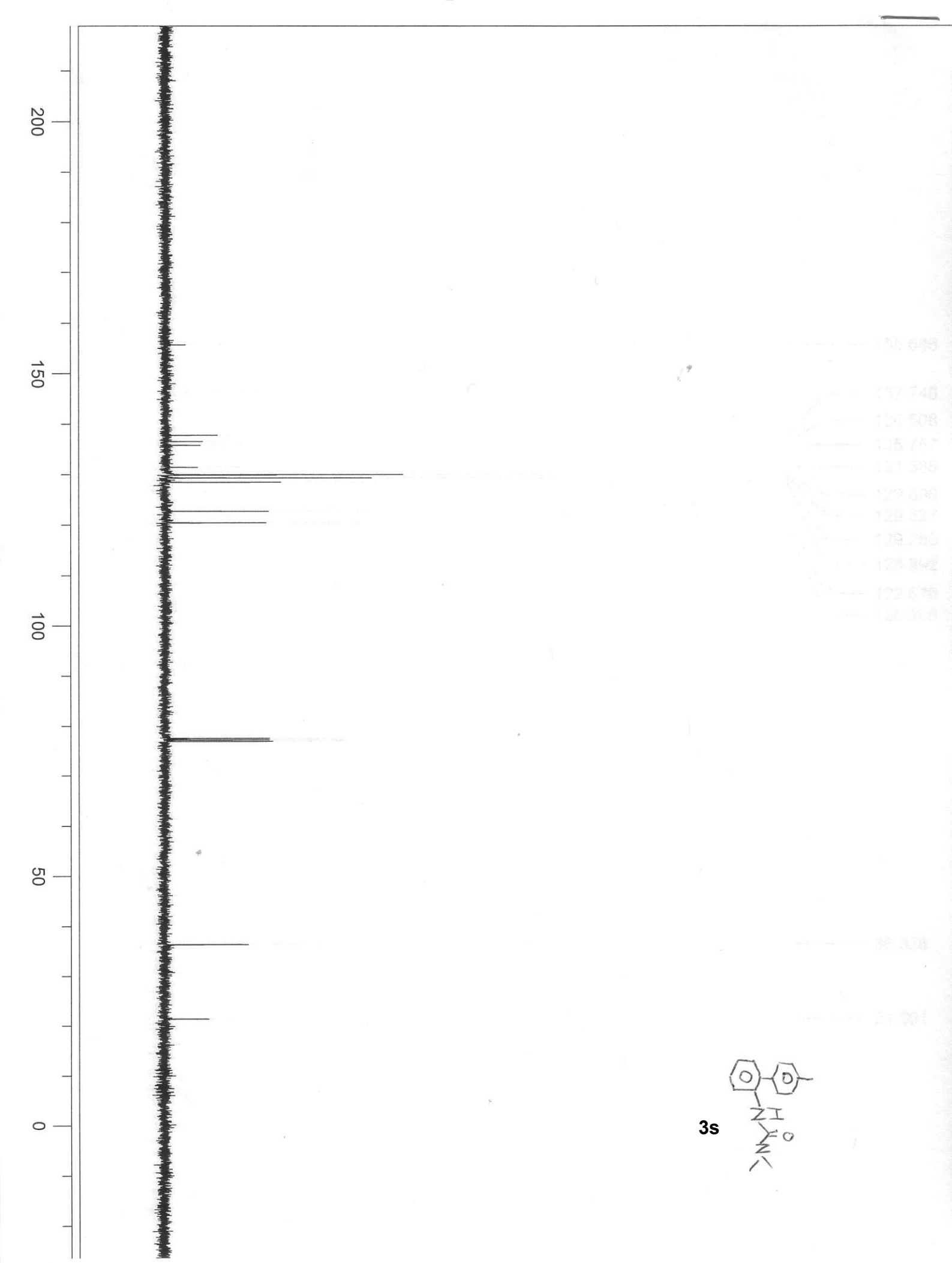
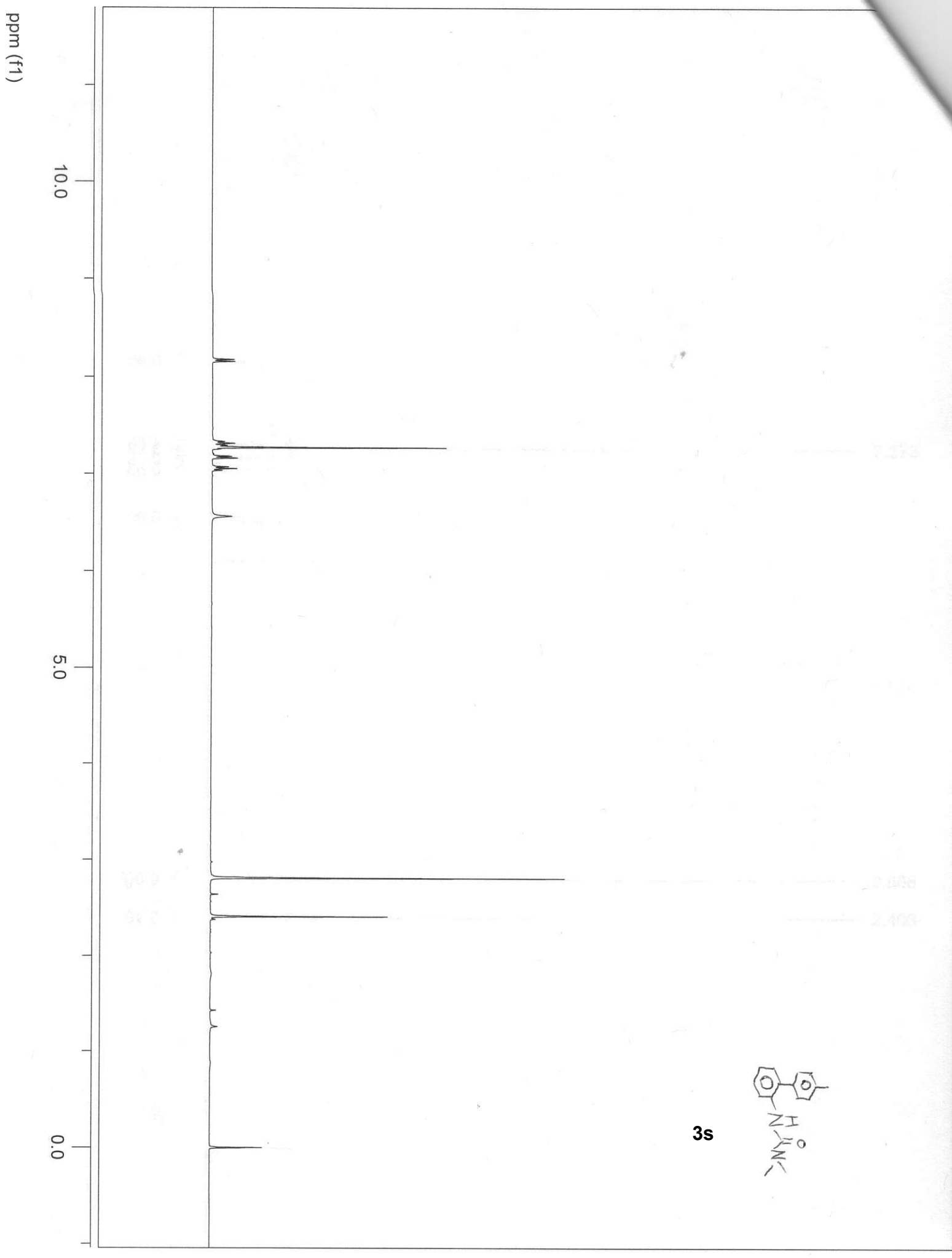
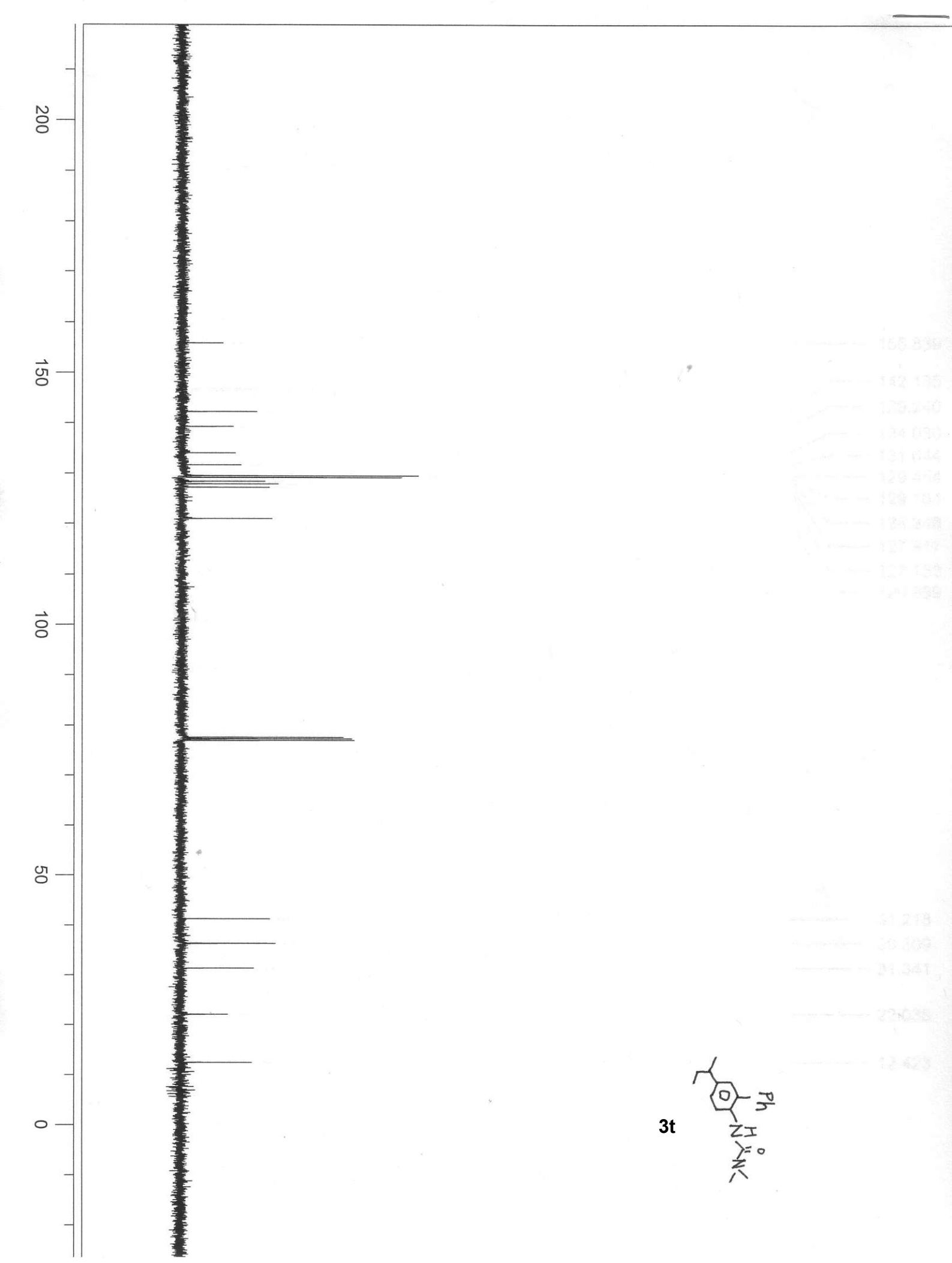


3s



3s



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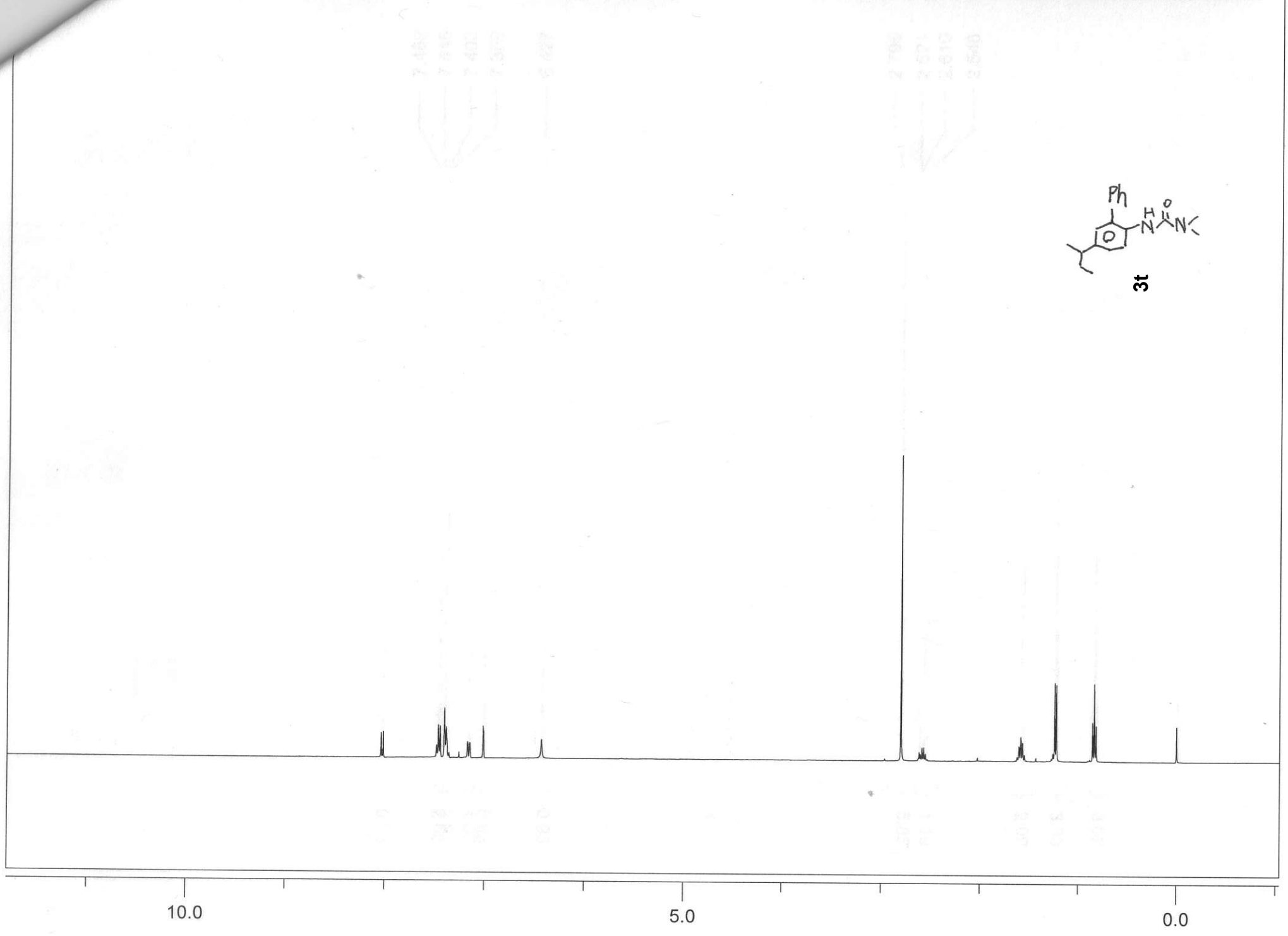

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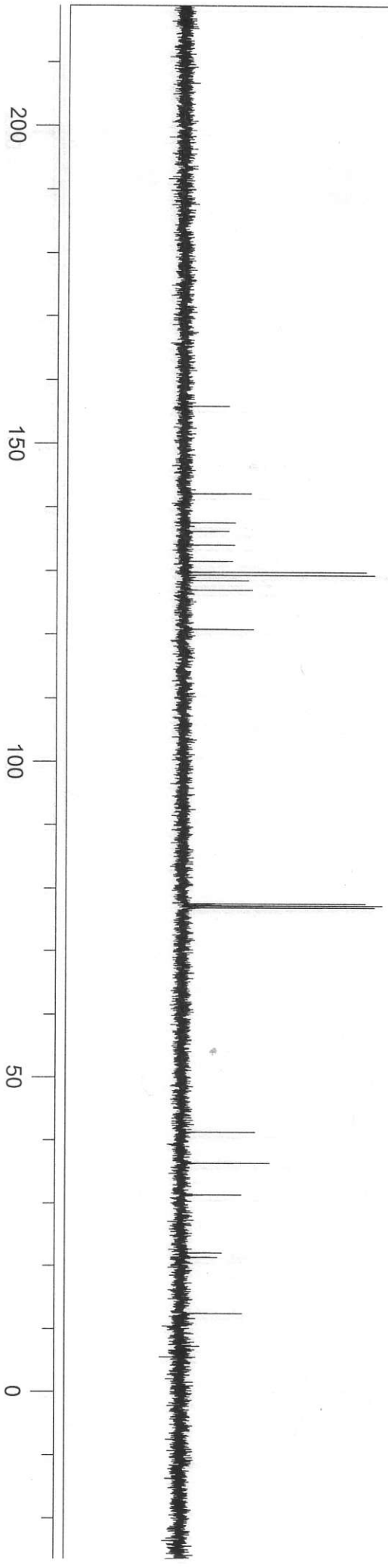

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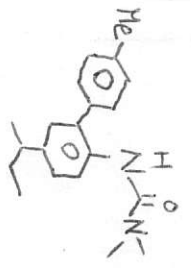

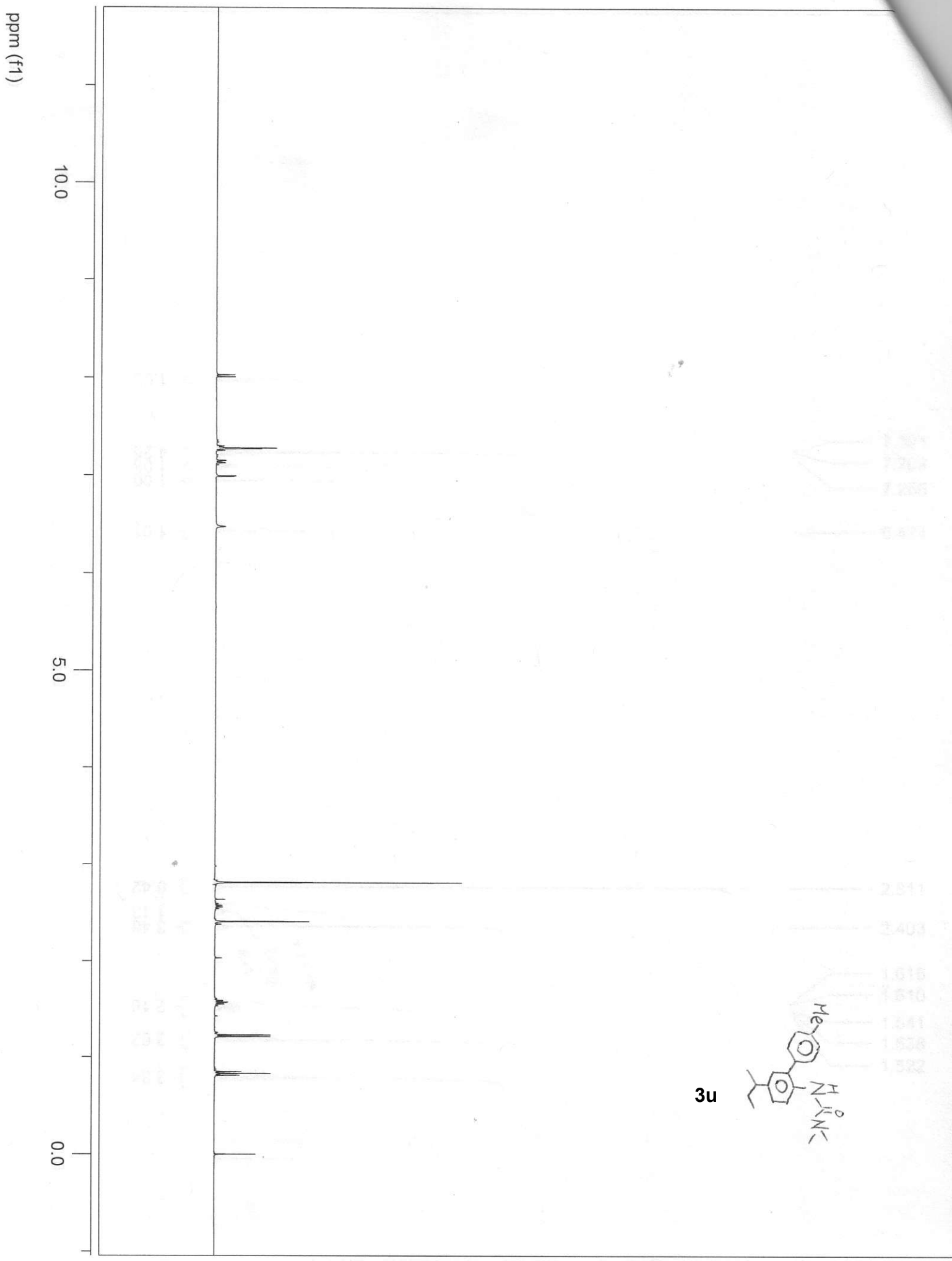

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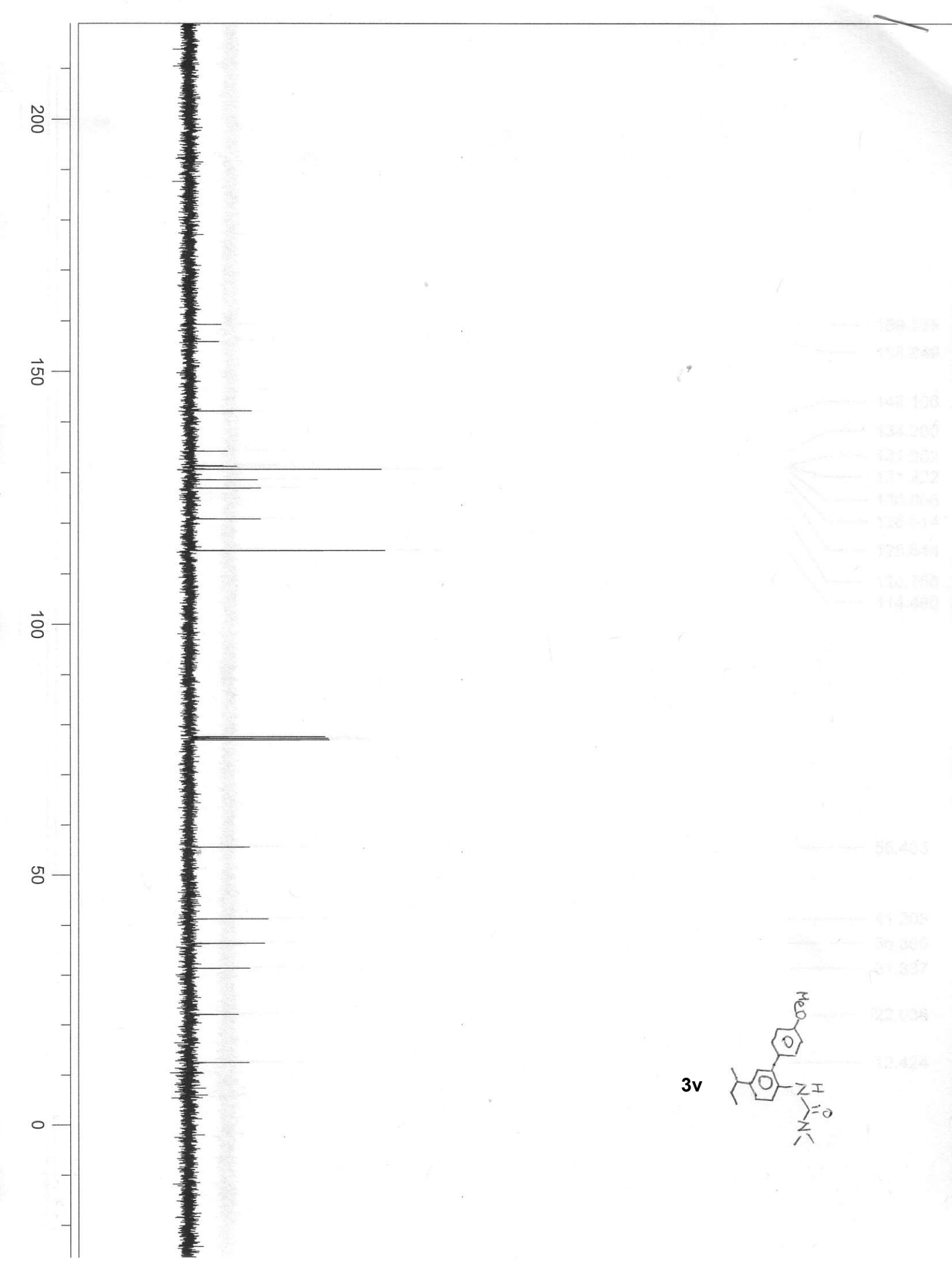

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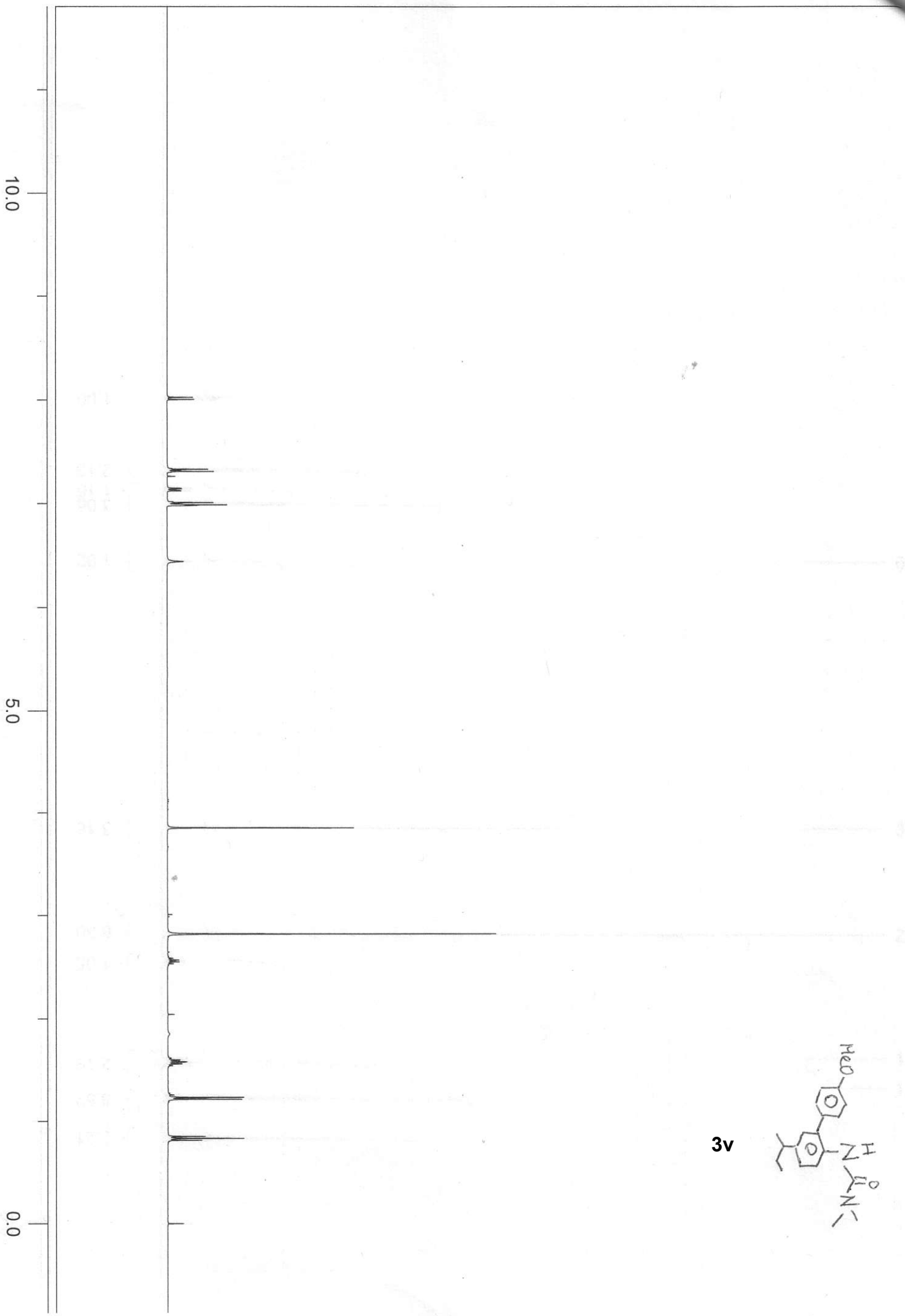

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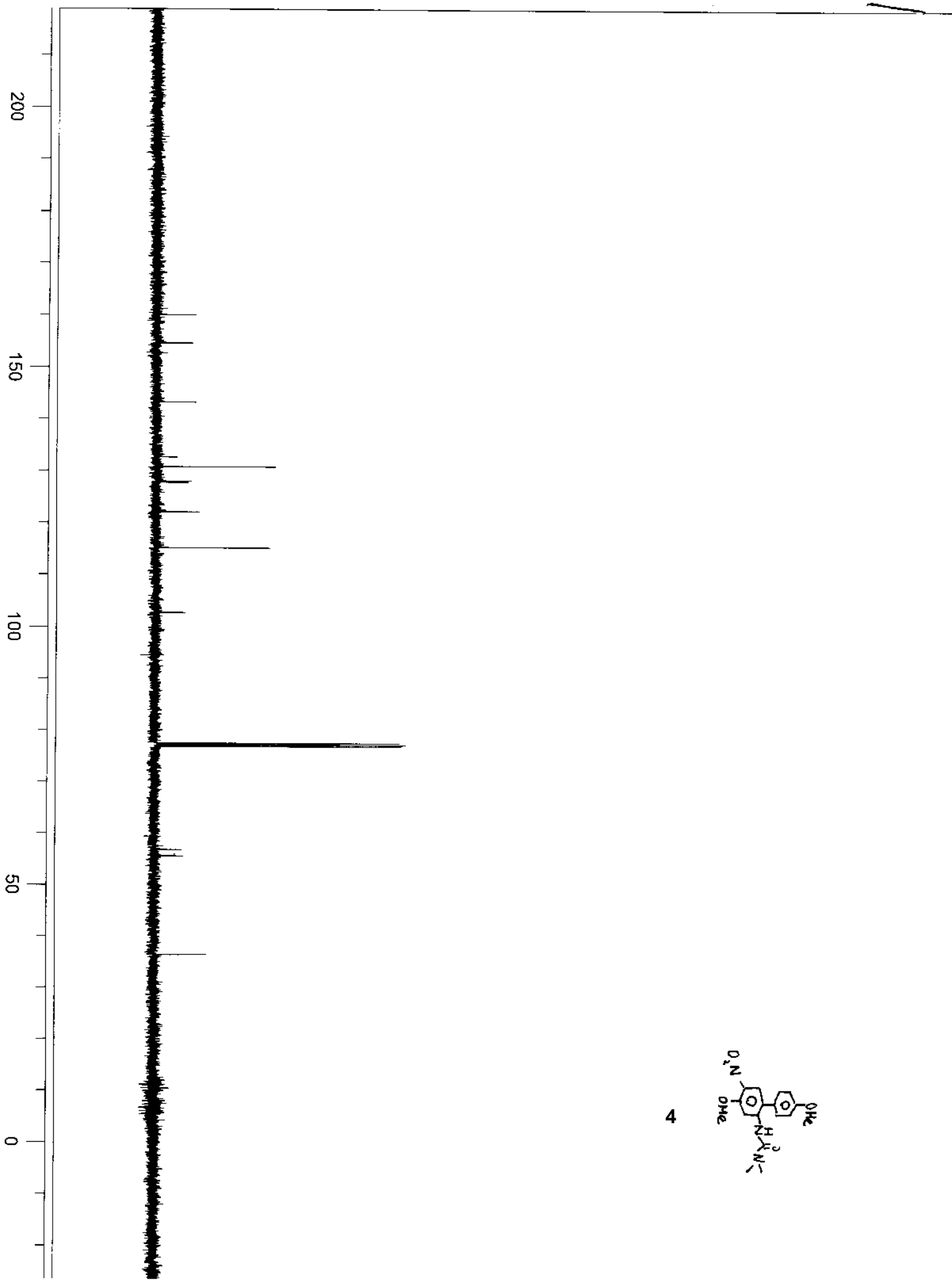

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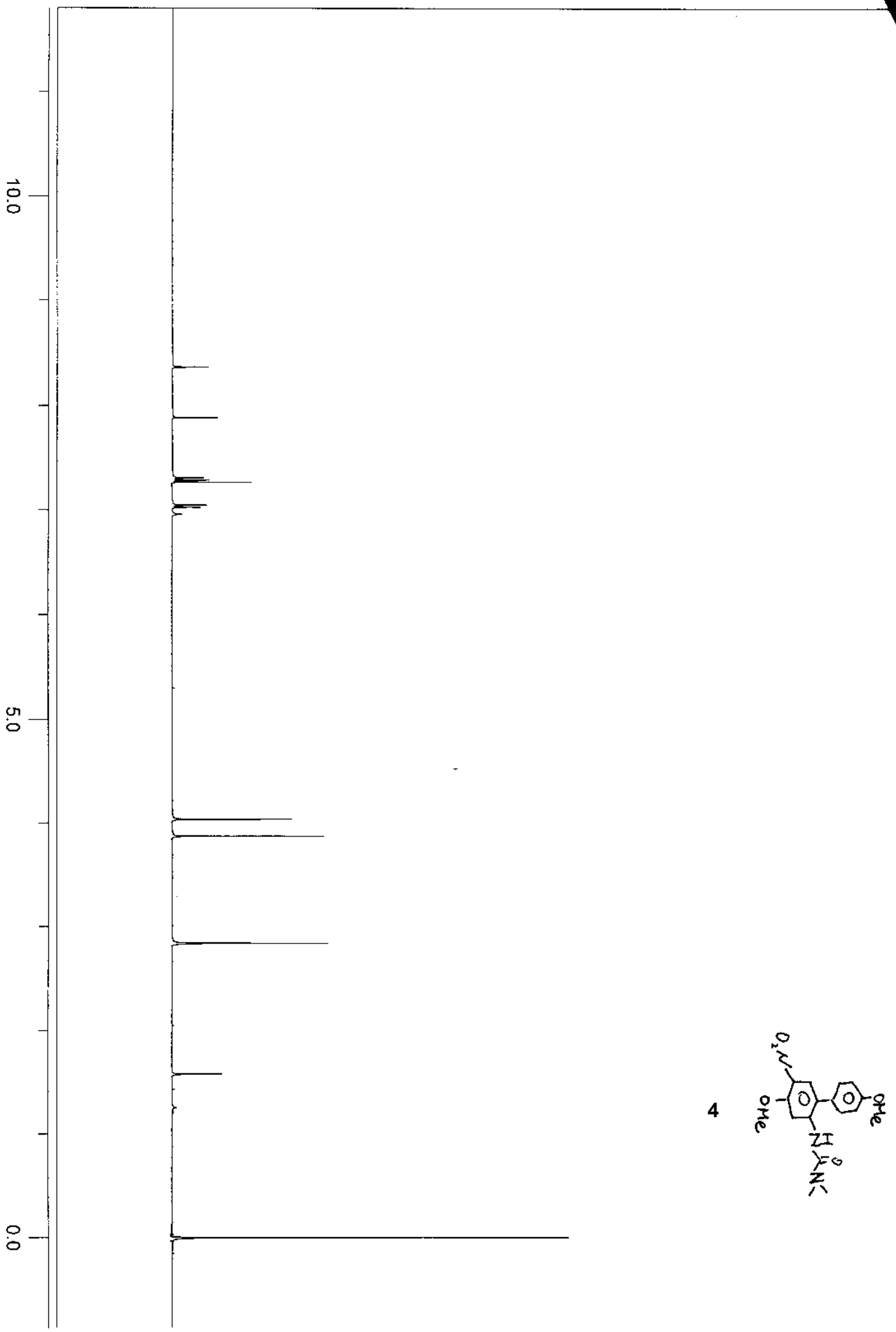

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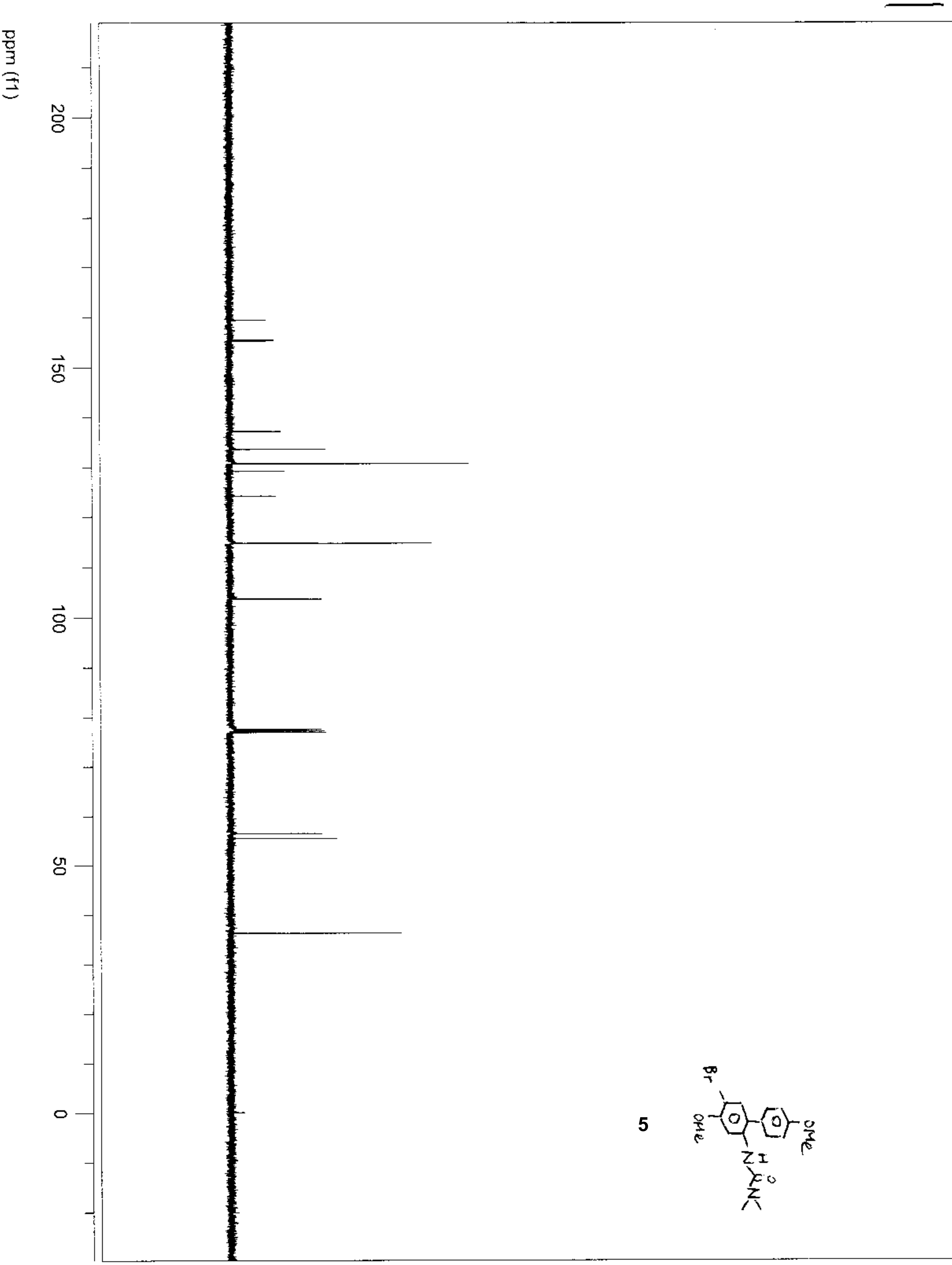
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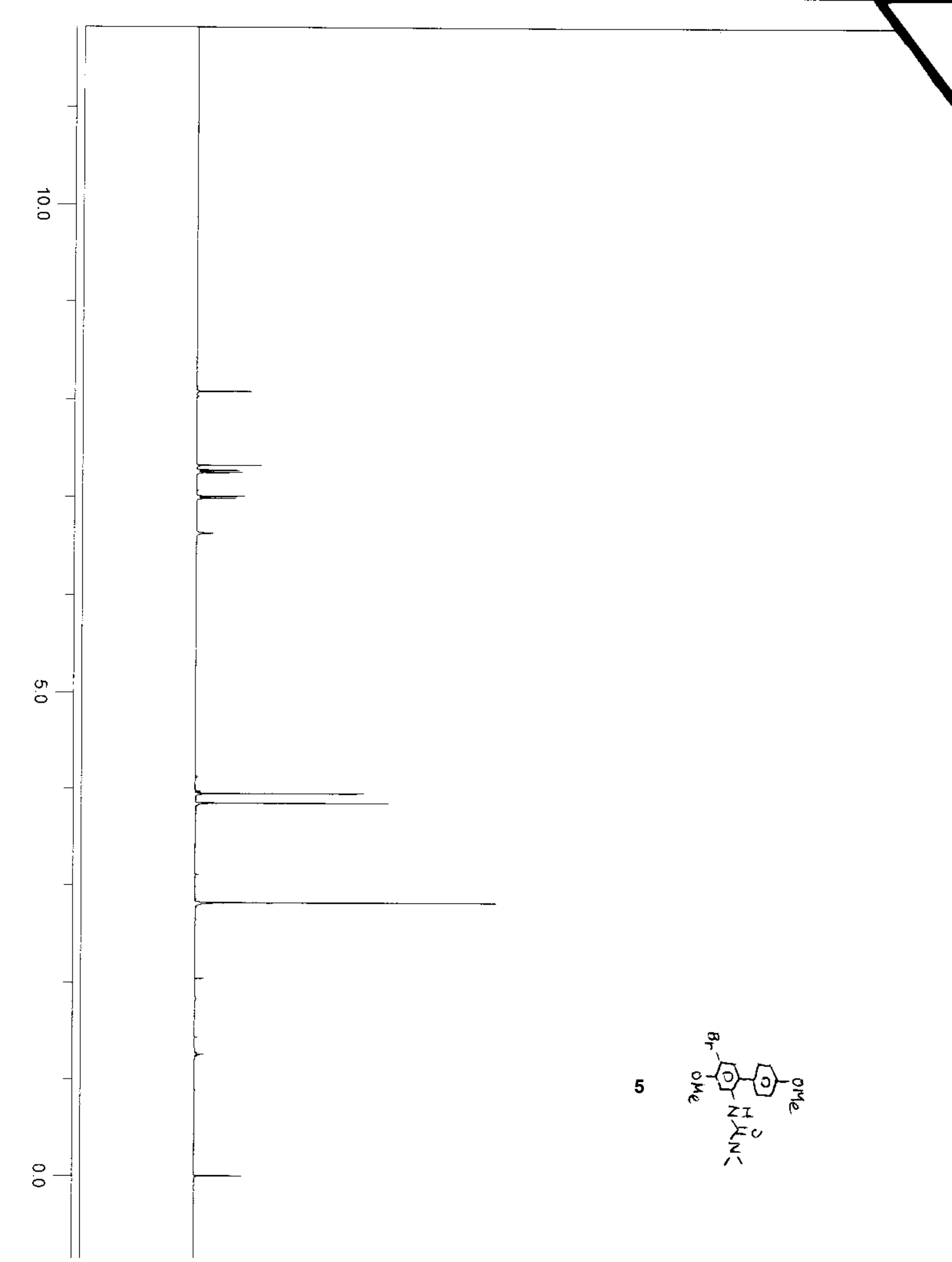

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