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Direct Alkylation of Indoles and Amines by *tert*-Enamides: Facile Access to Pharmaceutically Active 2-Oxo-1-pyrrolidine Analogues

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Table of Contents

Experimental

General experimental

Melting points were recorded on an Electrothermal digital melting point apparatus and were uncorrected. IR spectra were recorded on a Varian FT-1000 spectrophotometer using KBr optics. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian INOVA 300 or 400 MHz (^{1}H NMR) and 75 or 100 MHz (^{13}C NMR) spectrumeter using $CDCl_3$ or DMSO-d_6 as solvent and TMS as internal standard. High resolution mass spectra were obtained using GCT-TOF instrument with EI or ESI source. X-ray diffraction data were recorded on a Rigaku Mercury CCD area detector with graphite monochromated Mo Kα radiation.

General procedure for the alkylation of indoles, anilines and thiols with enamide:

Nucleophile (1.0 mmol), I_2 (0.5 mol %) and enamide (2.5 mmol) were added into a flask. Then the mixture was vigorously stirred at room temperature, until nucleophile was completely consumed as indicated by TLC analysis. After the completion of reaction, the residue was directly purified by flash column chromatography with ethyl acetate and petroleum ether as eluents to afford pure product.

Characterization of compounds of Markovnikov Addition

1-(1-(1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3aa):[1] (207 mg, 91%). White solid. m.p. 165–167 °C. IR (KBr): ν = 3243, 3165, 3107, 2972, 2876, 1659, 1490, 1440, 1288, 1198, 751 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ = 1.52 (d, J = 7.0 Hz, 3H), 1.62–1.73 (m, 1H), 1.78–1.88 (m, 1H), 2.18–2.34 (m, 2H), 2.67–2.73 (m, 1H), 3.22–3.27 (m, 1H), 5.53 (q, J = 6.9 Hz, 1H), 6.97 (t, J = 7.4 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 7.32 (s, 1H), 7.37 (d, J = 8.1 Hz, 1H), 7.42 (d, J = 7.9 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.8, 137.0, 126.9, 122.8, 122.6, 120.3, 119.9, 116.4, 111.6, 43.1, 42.7, 32.2, 18.2, 17.1 ppm. HRMS: Calcd for $C_{14}H_{16}N_2O$: $[M]^+$ 228.1263; Found, 228.1266.

1-(1-(1-methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ab):[1] (227 mg, 94%). Yellow oil. IR (KBr): ν = 3056, 2971, 2890, 1673, 1468, 1280, 1213, 1095, 745 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.58 (d, J = 7.2 Hz, 3H), 1.78–193 (m, 2H), 2.40–2.46 (m, 2H), 2.85–2.93 (m, 1H), 3.23–3.31 (m, 1H), 3.77 (s, 3H), 5.73–5.80 (q, J = 6.9 Hz, 1H, CH), 6.97 (s, 1H), 7.07–7.12 (m, 1H), 7.21–7.30 (m, 2H), 7.61 (d, J = 8.1 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.4, 137.4, 127.1, 127.0, 122.3, 119.9, 114.7, 109.5, 42.8, 42.5, 33.1, 32.0, 18.0, 17.0 ppm. HRMS: Calcd for $C_{15}H_{18}N_2O$: $[M]^+$ 242.1419; Found, 242.1418.

1-(1-(2-methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ac):[1] (227 mg, 94%). White solid. m.p. 176–177 °C. IR (KBr): ν = 3317, 2974, 2933, 2876, 1656, 1491, 1435, 1287, 1198, 1051, 749 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.72 (d, J = 6.9 Hz, 3H), 1.82–2.00 (m, 2H), 2.32–2.41 (m, 2H), 2.48 (s, 3H), 3.11–3.19 (m, 1H), 3.53–3.61 (m, 1H), 5.71–5.78 (q, J = 7.2 Hz, 1H), 7.05–7.12 (m, 2H), 7.27 (t, J = 1.8 Hz, 1H), 7.70 (d, J = 7.5 Hz, 1H), 8.07 (br s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.3, 135.6, 133.9, 128.3, 121.3, 119.9, 119.6, 111.0, 110.8, 44.0, 44.0, 31.9, 18.1, 18.0, 13.0 ppm. HRMS: Calcd for $C_{15}H_{18}N_2O$: $[M]^+$ 242.1419; Found, 242.1420.

1-(1-(2-phenyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ad):[1] (288 mg, 95%). White solid. m.p. 166–167 °C. IR (KBr): ν = 3398, 3165, 2930, 2895, 1660, 1442, 1288, 1204, 778cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.62 (d, J = 6.9 Hz, 3H), 1.79–2.00 (m, 2H), 2.36–2.43 (m, 2H), 3.24–3.31 (m, 1H), 3.58–3.66 (m,1H), 5.68–5.75 (q, J = 7.2 Hz, 1H), 7.16–7.23 (m, 2H), 7.39–7.49 (m, 6H), 7.84 (d, J = 7.8 Hz, 1H), 8.21 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.3, 737.3,

136.3, 133.0, 129.5, 129.1, 128.8, 128.3, 122.5, 121.0, 120.3, 111.7, 111.5, 45.3, 44.9, 32.0, 18.7, 18.3 ppm. HRMS: Calcd for $C_{20}H_{20}N_2O$: $[M]^+$ 304.1576; Found, 304.1577.

1-(1-(4-phenoxy-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ae):[1] (297 mg, 89%). White solid. m.p. 215–216 °C. IR (KBr): ν = 3160, 2930, 2870, 1650, 1510, 1443, 1352, 1288, 1230, 1099, 737 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.58 (d, J = 6.9 Hz, 3H), 1.77–1.89 (m, 2H), 2.21–2.38 (m, 2H), 3.00–3.08 (m, 1H), 3.19–3.27 (m, 1H), 5.25 (s, 2H), 5.84–5.89 (q, J = 6.6 Hz, 1H), 6.45 (d, J = 7.5 Hz, 1H), 6.92–7.04 (m, 3H), 7.23–7.42 (m, 5H), 8.29 (br s, 1H) ppm. ^{13}C NMR (75 MHz, DMSO-d 6): δ = 173.4, 153.2, 138.9, 138.5, 129.0, 128.1, 127.8, 122.7, 122.4, 117.1, 116.0, 105.6, 101.2, 69.3, 44.8, 43.9, 32.0, 19.3, 18.3 ppm. HRMS: Calcd for $C_{21}H_{22}N_2O_2$: $[M]^+$ 334.1681; Found, 334.1678.

1-(1-(5-methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3af):[1] (222 mg, 92%). White solid. m.p. 173–174 °C. IR (KBr): ν = 3154, 2928, 2890, 1652, 1490, 1441, 1290, 792 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.58 (d, J = 6.9 Hz, 3H), 1.77–1.91 (m, 2H), 2.42–2.46 (m, 5H), 2.88–2.90 (m, 1H), 3.27–3.28 (m, 1H), 5.71–5.79 (q, J = 6.6 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 7.09 (s, 1H), 7.24–7.27 (m, 1H), 7.39 (s, 1H), 8.26 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.7, 135.3, 129.5, 127.1, 124.4, 122.8, 119.3, 115.8, 111.3, 43.2, 42.8, 32.2, 22.0, 18.2, 17.2 ppm. HRMS: Calcd for $C_{15}H_{18}N_2O$: $[M]^+$ 242.1419; Found, 242.1420.

1-(1-(5-bromo-1*H*-indol-3-yl) ethyl)pyrrolidin-2-one (3ag):[1] (266 mg, 87%). White solid. m.p. 154–156 °C. IR (KBr): ν = 3157, 3080, 2982, 1650, 1439, 1288, 1194, 885, 790 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.58 (d, J = 7.2 Hz, 3H), 1.79–1.98 (m, 2H), 2.45 (t, J = 8.1 Hz, 2H), 2.82–2.90 (m, 1H), 3.24–3.31 (m, 1H), 5.76–5.74 (q, J = 6.9 Hz, 1H), 7.14–7.31 (m, 3H), 7.74 (s, 1H), 8.25 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9, 135.7, 128.6, 125.7, 123.9, 122.3, 116.1, 113.6, 113.2, 43.0, 42.7, 32.2, 18.2, 17.2 ppm. HRMS: Calcd for $C_{14}H_{15}BrN_2O$: $[M]^+$ 308.0347(^{81}Br); Found, 308.0343.

1-(1-(5-nitro-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ah): (177 mg, 65%). Yellow solid. m.p. 241–242 °C. IR (KBr): ν = 3379, 2968, 1660, 1522, 1295 cm^{-1}. ^1H NMR (400 MHz, DMSO–d_6): δ = 1.54 (d, J = 6.8 Hz, 3H), 1.70–1.74 (m, 1H), 1.86–1.90 (m, 1H), 2.20–2.36 (m, 2H), 2.70–2.76 (m, 1H), 3.27–3.34 (m, 1H), 5.56–5.61 (m, 1H), 7.54 (d, J = 9.2 Hz, 1H), 7.64 (s,

1H), 8.00 (d, J = 8.4 Hz, 1H), 8.45 (s, 1H) ppm. ^{13}C NMR (100 MHz, DMSO–d_6): δ = 173.1, 140.5, 139.6, 127.2, 125.4, 117.6, 116.8, 115.7, 112.0, 41.4, 41.3, 31.0, 17.3, 16.7 ppm. HRMS: Calcd for $C_{14}H_{15}N_3O_3$: $[M]^+$ 273.1113; Found, 273.1112.

1-(1-(6-methyl-1*H*-indol-3-yl)ethyl)azepan-2-one (3ai): (232 mg, 96%). White solid. m.p. 135–136 °C. IR (KBr): ν = 3213, 3100, 2980, 2879, 1662,1610, 1493, 1440, 1289, 1119 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.57 (d, J = 7.0 Hz, 3H), 1.74–1.81 (m, 1H), 1.87–1.93 (m, 1H), 2.41–2.46 (m, 5H), 2.84–2.89 (m, 1H), 3.23–3.29 (m, 1H), 5.73–5.78 (q, J = 7.0 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 7.04 (s, 1H), 7.16 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 8.36 (br s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.50, 137.19, 132.19, 124.40, 121.84, 121.59, 119.07, 115.64, 111.38, 42.91, 42.39, 31.94, 21.80, 17.83, 16.80 ppm. HRMS: Calcd for $C_{15}H_{18}N_2O$: $[M]^+$ 242.1419; Found, 242.1416.

1-(1-(7-methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3aj):[1] (232 mg, 96%). White solid. m.p. 166–168 °C. IR (KBr): ν = 3222, 3113, 2971, 2933, 2873, 1650, 1614, 1498, 1444, 1298, 1201, 1123, 788 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.59 (d, J = 6.9 Hz, 3H), 1.78–1.91 (m, 2H), 2.40–2.46 (m, 2H), 2.49 (s, 3H), 2.83–2.91 (m, 1H), 3.23–3.31 (m, 1H), 5.74–5.80 (q, J = 6.6 Hz, 1H), 7.02–7.06 (m, 2H), 7.13(s, 1H), 7.46–7.49 (m, 1H), 8.11 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.7, 136.6, 126.4, 123.2, 122.4, 120.9, 120.4, 117.5, 116.7, 43.2, 42.7, 32.2, 18.2, 17.1, 17.1 ppm. HRMS: Calcd for $C_{15}H_{18}N_2O$: $[M]^+$ 242.1419; found, 242.1417.

1, 1'-(1,1'-(1H-pyrrole-2,5-diyl)bis(ethane-1,1-diyl))dipyrrolidin-2-one (3ak): (187 mg, 63%). Gray powder. m.p. 136–139 °C. IR (KBr): ν = 3197, 2975, 1689, 1664, 1439, 1289, 844 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.34 (d, J = 7.0 Hz, 6H), 1.79–1.88 (m, 4H), 2.22 (t, J = 8.0 Hz, 4H), 2.80–2.86 (m, 2H), 3.18–3.24 (m, 2H), 5.12 (q, J = 6.9 Hz, 2H), 5.83 (d, J = 2.2 Hz, 2H), 10.58 (br s, 1H, NH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 173.0, 131.0, 105.1, 43.5, 42.1, 31.1, 17.5, 16.6 ppm. HRMS: Calcd for $C_{16}H_{23}N_3O_2$: $[M]^+$ 289.1790; Found, 289.1795.

1-(1-(2,4,6-trimethoxyphenyl)ethyl)pyrrolidin-2-one (3al):[1] (251 mg, 90%). White solid. m.p. 94–96 °C. IR (KBr): ν = 3063, 2968, 2890, 1673, 1468, 1280, 1220, 1095 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (d, J = 7.3 Hz, 3H), 1.84–1.96 (m, 2H), 2.30–2.35 (m, 2H), 3.23–3.28 (m, 1H), 3.51–3.56 (m, 1H), 3.81 (s, 9H), 5.84 (q, J = 7.3 Hz, 1H), 6.12 (s, 2H) ppm. ^{13}C NMR (100

MHz, $CDCl_3$): δ = 174.2, 160.5, 160.0, 109.8, 91.1, 55.9, 55.4, 44.6, 42.6, 31.7, 18.3, 17.4 ppm. HRMS: Calcd for $C_{15}H_{21}NO_4$: $[M]^+$ 279.1471; Found, 279.1476.

1-(1-(1*H*-indol-3-yl)ethyl)azepan-2-one (3ba):[1] (243mg, 95%). White solid. m.p. 125–126 °C. IR (KBr): ν = 3482, 3182, 2930, 1607, 1483, 1178, 744 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.12–1.32 (m, 3H), 1.52 (d, *J* = 6.9 Hz, 3H), 1.57–1.70 (m, 3H), 2.59–2.62 (m, 2H), 3.01–3.19 (m, 2H), 6.26–6.33 (q, *J* = 6.9 Hz, 1H), 7.07–7.22 (m, 3H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 8.26(br s, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-*d6*): δ = 173.8, 136.4, 126.4, 123.5, 121.2, 118.7, 118.5, 115.2, 111.4, 43.9, 41.8, 37.0, 29.2, 28.6, 23.0, 17.0 ppm. HRMS: Calcd. for $C_{16}H_{20}N_2O$: $[M]^+$ 256.1576; Found, 256.1577.

1-(1-(2-methyl-1*H*-indol-3-yl)ethyl)azepan-2-one (3bc):[1] (178 mg, 66%). White solid. m.p. 151–153 °C. IR (KBr): ν = 3261, 2970, 2934, 2855, 1610, 1442, 1183, 745 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.05–1.41 (m, 4H), 1.58 (s, 2H), 1.70 (d, *J* = 7.2 Hz, 3H), 2.46 (s, 3H), 2.54–2.57 (m, 2H), 3.18–3.36 (m, 2H), 6.18–6.26 (q, *J* = 6.9 Hz, 1H), 7.05–7.14 (m, 2H), 7.29 (s, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 8.03 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 135.5, 134.2, 129.0, 121.2, 120.0, 119.4, 110.9, 110.9, 47.3, 44.6, 38.1, 30.4, 29.5, 24.0, 18.5, 13.3 ppm. HRMS: Calcd for $C_{17}H_{22}N_2O$: $[M]^+$ 270.1732; Found, 270.1732.

1-(1-(5-methyl-1*H*-indol-3-yl)ethyl)azepan-2-one (3bf):[1] (237mg, 88%). White solid. m.p. 75–76 °C. IR (KBr): ν = 3464, 3184, 3159, 2932, 1585, 1486, 1446, 1174 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.12–1.30 (m, 3H), 1.50 (d, *J* = 6.9 Hz, 3H), 1.57–1.72 (m, 3H), 2.42 (s, 3H), 2.59–2.63 (m, 2H), 3.01–3.19 (m, 2H), 6.21-6.28 (q, *J* = 6.9 Hz, 1H), 7.01–7.10 (m, 2H), 7.23–7.26 (m, 1H), 7.35 (s, 1H), 8.13 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.0, 135.3, 129.2, 127.3, 124.3, 123.3, 119.6, 116.3, 111.2, 45.6, 43.3, 38.2, 30.5, 29.3, 23.8, 21.9, 17.6 ppm. HRMS: Calcd for $C_{17}H_{22}N_2O$; $[M]^+$ 270.1732: Found, 270.1732.

1-(1-(5-bromo-1*H*-indol-3-yl)ethyl)azepan-2-one (3bg):[1] (217mg, 65%). White solid. m.p. 73–74 °C. IR (KBr): ν = 3484, 3006, 2973, 2934, 1584, 1486, 1377, 1113 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.07–1.35 (m, 3H), 1.50 (d, *J* = 6.9 Hz, 3H), 1.57–1.71 (m, 3H), 2.60–2.64 (m, 2H), 3.00–3.17 (m, 2H), 6.19–6.26 (q, *J* = 6.9 Hz, 1H), 7.14 (s, 1H), 7.21–7.37 (m, 2H), 7.71 (s, 1H), 8.32 (br s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.0, 136.9, 127.1, 123.1, 123.0,

122.7, 120.1, 117.1, 117.1, 111.6, 45.4, 43.4, 38.2, 30.5, 29.4, 23.9, 17.5 ppm HRMS: Calcd for $C_{16}H_{19}BrN_2O$: $[M]^+$ 336.0660(^{81}Br); Found, 336.0645.

***N*-(1-(1*H*-indol-3-yl)ethyl)-*N*-methylacetamide (3ca):**[2] (134mg, 62%). White solid. m.p. 95–98 °C. IR (KBr): ν = 3243, 3050, 2957, 1650, 1497, 1456 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, including isomer): δ = 1.51 (d, J = 6.9 Hz, 3H), 1.65 (d, J = 6.5 Hz, 1H), 2.15 (s, 3H), 2.40 (s, 1H), 2.62 (s, 3H), 2.64 (s, 1H), 5.33 (q, J = 6.6 Hz, 0.35 H), 6.33 (q, J = 6.9 Hz, 1H), 7.05–7.19 (m, 4H), 7.35–7.44 (m, 1.7H), 7.57 (d, J = 7.9 Hz, 1H), 8.17 (s, 1H), 8.90 (s, 0.35H) ppm. ^{13}C NMR (75 MHz, DMSO–d_6, including isomer): δ = 169.2, 169.0, 136.6, 136.5, 126.3, 126.0, 123.6, 123.6, 121.4, 121.3, 118.9, 118.7, 118.6, 118.4, 114.9, 114.6, 111.7, 111.5, 49.8, 43.5, 29.1, 26.7, 22.2, 21.8, 17.9, 16.5 ppm. HRMS: Calcd for $C_{13}H_{16}N_2O$: $[M]^+$ 216.1263; Found, 216.1268.

1-(1-(3, 4-dihydroquinolin-1(2*H*)-yl)ethyl)pyrrolidin-2-one (5aa): (51 mg, 21%). Colorless oil. IR (KBr): ν = 2981, 2939, 1677, 1499, 1316, 1186 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (d, J = 6.7 Hz, 3H), 1.91–1.98 (m, 4H), 2.35–2.40 (m, 2H), 2.78 (t, J = 5.8 Hz, 2H), 3.13–3.18 (m, 1H), 3.34–3.38 (m, 2H), 3.44–3.47 (m, 1H), 6.87 (q, J = 6.6 Hz, 1H), 6.63-6.68 (m, 2H), 6.98 (d, J = 6.9 Hz, 1H), 7.08 (t, J = 7.7 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.5, 143.8, 129.3, 127.8, 122.7, 117.1, 111.6, 61.3, 43.2, 42.4, 31.2, 28.5, 22.4, 18.0, 16.8 ppm. HRMS: Calcd for $C_{15}H_{21}N_2O$: $[M+H]^+$ 245.1654; Foud, 245.1660.

1-(1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)ethyl)pyrrolidin-2-one (5ab): (122 mg, 53%). White solid. m.p. 57–58°C. IR (KBr): ν = 3451, 2972, 1685, 1422, 1268, 1241, 1049, 752 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.84–1.87 (m, 1H), 1.99–2.04 (m, 1H), 2.12 (d, J = 6.7 Hz, 3H), 2.27–2.36 (m, 1H), 2.42–2.48 (m, 1H), 3.08–3.14 (m, 1H), 3.60–3.66 (m, 1H), 7.00 (q, J = 6.6 Hz, 1H), 7.39 (t, J = 7.3 Hz, 1H), 7.54-7.47 (m, 1H), 7.83 (d, J = 8.1 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.2, 145.9, 132.5, 127.9, 124.5, 119.7, 110.5, 60.0, 41.9, 31.0, 17.7, 17.1 ppm. HRMS: Calcd for $C_{12}H_{14}N_4O$: $[M]^+$ 230.1168; Found, 230.1168.

1-(1-(phenylamino)ethyl)pyrrolidin-2-one (5ac): (90mg, 44%). White solid; m.p.124–125°C. IR (KBr): ν = 3311, 3053, 2934, 1661, 1496, 1280, 1168 cm^{-1} ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (d, J = 6.4 Hz, 3H), 1.84–1.91 (m, 2H), 2.39 (t, J = 8.1 Hz, 2H), 3.17–3.23 (m, 1H), 3.27–3.33 (m, 1H), 3.95 (s, 1H, NH), 5.69 (q, J = 6.0 Hz, 1H), 6.64 (d, J = 8.2 Hz, 2H), 6.76 (t, J = 7.3 Hz, 1H), 7.18 (d, J = 7.8 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.0, 145.1, 129.6, 118.5, 113.3,

57.1, 41.0, 31.9, 19.5, 17.9 ppm. HRMS: Calcd for $C_{12}H_{16}N_2O$: $[M]^+$ 204.1263; Found, 204.1262.

4-(1-(2-oxopyrrolidin-1-yl)ethylamino)benzonitrile (5ad): (213mg, 93%). White solid; m.p. 185–186 °C. IR (KBr): ν = 3305, 2983, 2218, 1664, 1612, 1531, 1285, 1161 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.48 (d, J = 6.4 Hz, 3H), 1.88–2.05 (m, 2H), 2.39–2.44 (m, 2H), 3.15–3.21 (m, 1H), 3.30–3.36 (m, 1H), 4.51 (br s, 1H, NH), 5.70–5.75 (m, 1H), 6.67 (d, J = 8.6 Hz, 2H), 7.44 (d, J = 8.6 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.97, 148.93, 133.83, 120.30, 113.17, 99.97, 56.39, 40.86, 31.60, 19.08, 17.82 ppm. HRMS: Calcd for $C_{13}H_{15}N_3O$: $[M]^+$ 229.1215; Found, 229.1213.

ethyl 4-(1-(2-oxopyrrolidin-1-yl)ethylamino)benzoate (5ae): (240mg, 87%). White solid; m.p. 91–92°C. IR (KBr): ν = 3503, 2977, 1708, 1439, 1281, 1103, 844, 770 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.36 (t, J = 7.1 Hz, 3H), 1.47 (d, J = 6.3 Hz, 3H), 1.86–1.99 (m, 2H), 2.40 (t, J = 8.0 Hz, 2H), 3.14–3.20 (m, 1H), 3.29–3.34 (m, 1H), 4.31 (q, J = 7.1 Hz, 2H), 5.75 (q, J = 6.2 Hz, 1H), 6.64 (d, J = 8.5 Hz, 2H), 7.88 (d, J = 8.5 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 173.6, 165.7, 150.4, 130.9, 117.7, 111.8, 59.7, 55.6, 40.3, 18.5, 17.4, 14.3 ppm. HRMS: Calcd for $C_{15}H_{20}N_2O_3$: $[M]^+$ 276.1474; Found, 276.1473.

1-(1-(4-acetylphenylamino) ethyl)pyrrolidin-2-one (5af): (233mg, 95%). White solid; m.p. 152–153°C. IR (KBr): ν = 3221, 2968, 1746, 1678, 1445, 1162 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.48 (d, J = 6.4 Hz, 3H), 1.90–1.95 (m, 2H), 2.39–2.43 (m, 2H), 2.50 (s, 3H, CH_3), 3.51–3.21(m, 1H), 3.30–3.36 (m, 1H), 4.49 (br s, 1H, NH), 5.75–5.78 (m, 1H, CH), 6.65 (d, J = 8.7 Hz, 2H), 7.83 (d, J = 8.7 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.8, 175.1, 149.3, 131.0, 128.2, 112.6, 56.7, 41.0, 31.8, 26.3, 19.5, 18.0 ppm. HRMS: Calcd for $C_{14}H_{18}N_2O_2$: $[M]^+$ 246.1368; Found, 246.1385.

1-(1-(4-nitrophenylamino)ethyl)pyrrolidin-2-one (5ag): (239 mg, 96%). Yellow solid; m.p. 204–205°C. IR (KBr): ν = 3271, 3072, 2928, 1665, 1484, 1323, 1161, 832 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.51 (d, J = 6.4 Hz, 3H), 1.90–2.05 (m, 2H), 2.40–2.45 (m, 2H), 3.16–3.22 (m, 1H), 3.32–3.38 (m, 1H), 4.77 (d, J = 6.9 Hz, 1H), 5.75–5.81 (m, 1H, CH), 6.67 (d, J = 9.0 Hz, 2H), 8.09 (d, J = 9.0 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.15, 150.75, 126.53, 112.45, 56.69, 41.02, 31.62, 19.31, 17.98 ppm. HRMS: Calcd for $C_{12}H_{15}N_3O_3$: $[M]^+$ 249.1113; Found, 249.1108.

1-(1-(3-nitrophenylamino)ethyl)pyrrolidin-2-one (5ah): (201mg, 81%). Yellow solid; m.p.

89–90°C. IR (KBr): ν = 3297, 3094, 2979, 1663, 1572, 1339, 1156, 735 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (d, J = 6.3 Hz, 3H), 1.90–2.20 (m, 2H), 2.39–2.44 (m, 2H), 3.20–3.24 (m, 1H), 3.32–3.38 (m, 1H), 4.44 (br s, 1H), 5.74 (q, J = 6.2 Hz, 1H), 6.99 (d, J = 6.2 Hz, 1H), 7.31 (t, J = 8.1 Hz, 1H), 7.56 (s, 1H), 7.57 (d, J = 7.9 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.2, 149.3, 146.3, 130.3, 118.6, 112.8, 108.2, 56.9, 41.0, 31.7, 19.2, 17.9 ppm. HRMS: Calcd for $C_{12}H_{15}N_3O_3$: $[M]^+$ 249.1113; Found, 249.1108.

1-(1-(2-nitrophenylamino)ethyl)pyrrolidin-2-one (5ai): (202 mg, 81%). Yellow solid; m.p. 89–91°C. IR (KBr): ν = 3361, 3091, 2976, 1687, 1504, 1421, 1041, 753 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.57 (d, J = 6.3 Hz, 3H), 1.91–2.04 (m, 2H), 2.40–2.46 (m, 2H), 3.17–3.23 (m, 1H), 3.36-3.42 (m, 1H), 5.86–5.92 (m, 1H), 6.67 (t, J = 7.7 Hz, 1H), 7.04 (d, J = 8.6 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 8.09–8.19 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.8, 142.8, 136.7, 132.5, 126.6, 117.0, 115.3, 55.9, 40.7, 39.5, 19.3, 17.8 ppm. HRMS: Calcd for $C_{12}H_{15}N_3O_3$: $[M]^+$ 249.1113; Found, 249.1108.

1-(1-((4-chlorophenyl)amino)ethyl)pyrrolidin-2-one (5aj): (155 mg, 65%). White solid; m. p. 162–164°C. IR (KBr): ν = 3302, 3105, 2981, 1602, 1493, 1428, 1258, 1160, 820 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.44 (d, J = 6.4 Hz, 3H), 1.85–2.06 (m, 2H), 2.39 (t, J = 8.2 Hz, 2H), 3.12–3.20 (m, 1H), 3.25-3.33 (m, 1H), 5.65 (q, J = 6.3 Hz, 1H), 6.57 (d, J = 8.8 Hz, 2H), 7.12 (d, J = 8.8 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.1, 143.7, 129.4, 123.2, 114.5, 57.1, 40.9, 31.8, 19.5, 17.9 ppm. HRMS: Calcd for $C_{12}H_{15}ClN_2O$: $[M]^+$ 238.0873; Found, 238.0874.

1-(1-(2-iodophenylamino)ethyl)pyrrolidin-2-one (5ak): (155 mg, 47%). Pale yellow oil. IR (KBr): ν = 3231, 3067, 2978, 1680, 1498, 1418, 1121cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 (d, J = 6.4 Hz, 3H), 1.83–1.98 (m, 2H), 2.36–2.41 (m, 2H), 3.08–3.13 (m, 1H), 3.29–3.35 (m, 1H), 4.41 (br s, 1H), 5.75–5.79 (m, 1H, CH), 6.50 (t, J = 8.0 Hz, 1H), 6.70 (d, J = 8.2 Hz, 1H), 7.20 (t, J = 7.7 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.93, 144.24, 139.00, 129.90, 120.06, 112.43, 85.17, 56.96, 40.66, 31.69, 19.40, 17.78 ppm. HRMS: Calcd for $C_{12}H_{15}IN_2O$: $[M]^+$ 330.0229; Found: 330.0232.

1-(1-(p-tolylamino)ethyl)pyrrolidin-2-one (5al): (81mg, 37%). White solid; m.p. 147–148 °C. IR (KBr): ν = 3317, 3054, 2937, 1661, 1497, 1280, 1160 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (d, J = 6.4 Hz, 3H), 1.82–1.96 (m, 2H), 2.23 (s, 3H), 2.38 (t, J = 8.0 Hz, 2H), 3.16–3.22 (m, 1H), 3.26–3.31 (m, 1H), 3.87 (br s, 1H), 5.66 (q, J = 6.4 Hz, 1H), 6.56 (d, J = 8.4 Hz, 2H,), 6.98 (d,

J = 8.4 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9, 142.8, 130.0, 127.6, 113.3, 57.3, 41.0, 31.9, 20.5, 19.5, 17.9 ppm. HRMS: Calcd for $C_{13}H_{18}N_2O$: $[M]^+$ 218.1419; Found, 218.1417.

4-methyl-*N*-(1-(2-oxopyrrolidin-1-yl)ethyl)benzenesulfonamide (5an): (245 mg, 87%). White solid. m.p. 113–115°C. IR (KBr): ν = 3466, 3087, 1662, 1446, 1322, 1147, 1023, 878, 664 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 1.17 (d, *J* = 6.6 Hz, 3H), 1.59–2.03 (m, 2H), 1.95–2.03 (m, 1H), 2.38 (s, 3H), 2.74–2.78 (m, 1H), 2.97–3.03 (m, 1H), 3.34–3.37 (m, 1H), 5.39–5.42 (m, 1H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 7.8 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-*d6*): δ = 172.6, 142.8, 138.1, 129.3, 126.4, 56.4, 56.3, 30.4, 21.0, 18.9, 16.6 ppm. HRMS: Calcd for $C_{13}H_{18}N_2O_3S$: $[M]^+$ 282.1038; Found, 282.1039.

4-(1-(2-oxoazepan-1-yl)ethylamino)benzonitrile (5bd): (244 mg, 95%). White solid; m.p. 196–197 °C. IR (KBr): ν = 3294, 3163, 2931, 2215, 1612, 1536, 1340, 1164, 1142, 817 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (d, *J* = 6.4 Hz, 3H), 1.54–1.70 (m, 6H), 2.46–2.59 (m, 2H), 3.16–3.28 (m, 2H), 4.58 (br s, 1H), 6.15–6.20 (m, 1H, CH), 6.63 (d, *J* = 8.7 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.10, 149.14, 133.86, 120.39, 113.27, 99.98, 58.38, 41.57, 37.96, 30.07, 29.04, 23.47, 19.51 ppm. HRMS: Calcd for $C_{15}H_{19}N_3O$: $[M]^+$ 257.1528; Found, 257.1512.

1-(1-(3-nitrophenylamino)ethyl)azepan-2-one (5bh): (191 mg, 69%). Yellow solid; m.p. 115–117°C. IR (KBr): ν = 3288, 3063, 2936, 1623, 1530, 1339, 1151, 982cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.26 (m, 1H), 1.41 (d, *J* = 6.2 Hz, 3H), 1.54–1.68 (m, 5H), 2.49–2.56 (m, 2H), 3.20–3.30 (m, 2H), 4.64 (br s, 1H), 6.16–6.18 (m, 1H), 6.49 (d, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 8.2 Hz, 1H), 7.46 (s, 1H), 7.55 (d, *J* = 7.6 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.3, 149.3, 146.6, 130.2, 118.7, 112.7, 108.1, 59.0, 41.6, 38.0, 30.1, 29.1, 23.5, 19.6 ppm. HRMS: Calcd for $C_{14}H_{19}N_3O_3$: $[M]^+$ 277.1426; Found, 277.1426.

1-(1-(naphthalen-2-ylthio)ethyl)pyrrolidin-2-one (6a): (190 mg, 70%). White solid. 62–63°C. IR (KBr): ν = 2961, 1681, 1399, 1266, 1047, 644 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54 (d, *J* = 6.9 Hz, 3H), 1.72–1.80 (m, 1H), 1.86–1.94 (m, 1H), 1.98–2.06 (m, 1H), 2.21–2.39 (m, 1H), 3.32–3.38 (m, 1H), 3,56–3.62 (m, 1H), 6.31 (q, *J* = 6.9 Hz, 1H), 7.44–7.49 (m, 3H), 7.74–7.79 (m, 3H), 7.85 (s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170, 129.1, 127.8, 126.0, 124.0, 123.0, 122.0, 121.7, 49.6, 37.0, 26.7, 17.7, 13.3 ppm. HRMS: Calcd for $C_{16}H_{17}NOS$: $[M]^+$ 271.1031; Found, 271.1029.

2-(1-(naphthalen-2-ylthio)ethyl)cycloheptanone (6b): (254mg, 85%). Colorless oil. IR (KBr): ν = 2854, 1640, 1448, 1131, 1023, 823, 739 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35–1.40 (m, 1H), 1.47–1.58 (m, 8H), 2.33–2.43 (m, 2H), 3.32–3.36 (m, 1H), 3.44–3.50 (m, 1H), 6.65 (q, J = 6.8 Hz, 1H), 7.41–7.47 (m, 3H), 7.72–7.78 (m, 4H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.0, 133.8, 132.0, 131.9, 128.5, 128.3, 127.8, 127.7, 127.5, 126.6, 125.9, 55.8, 42.9, 37.6, 30.0, 29.2, 23.3, 19.4, 19.2 ppm. HRMS: Calcd for $C_{18}H_{21}NOS$: $[M]^+$ 299.1344; Found, 299.1344.

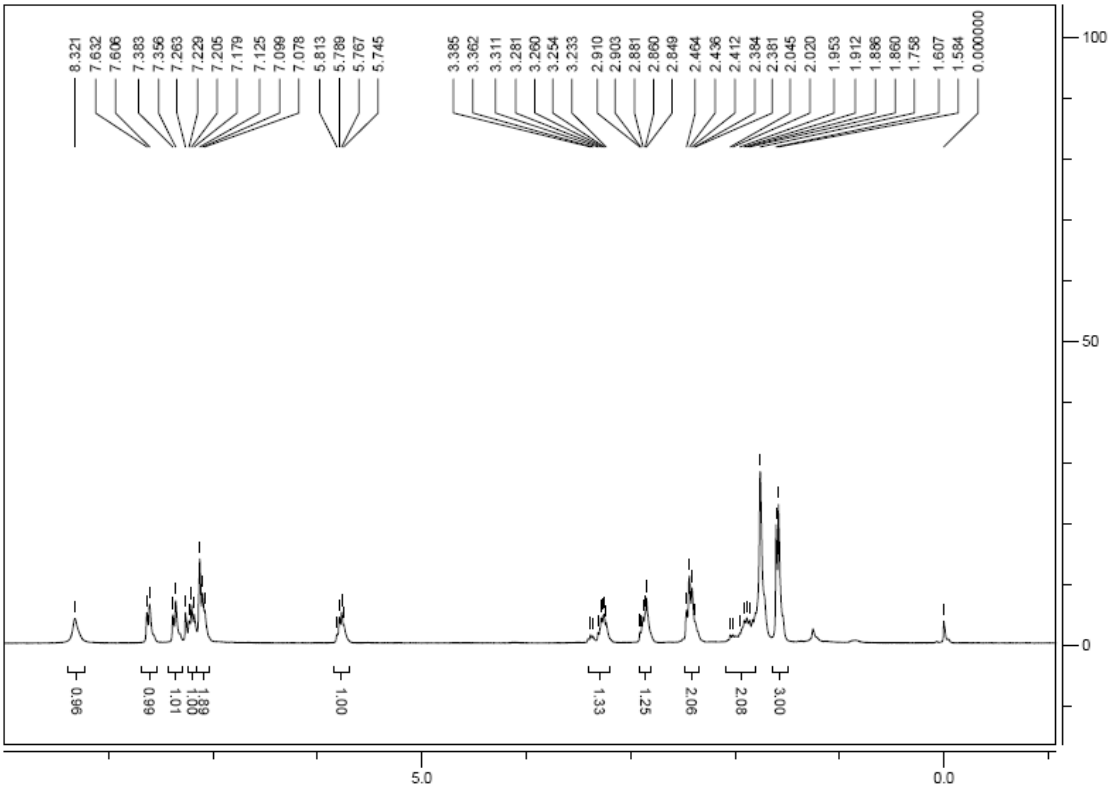
Reference:

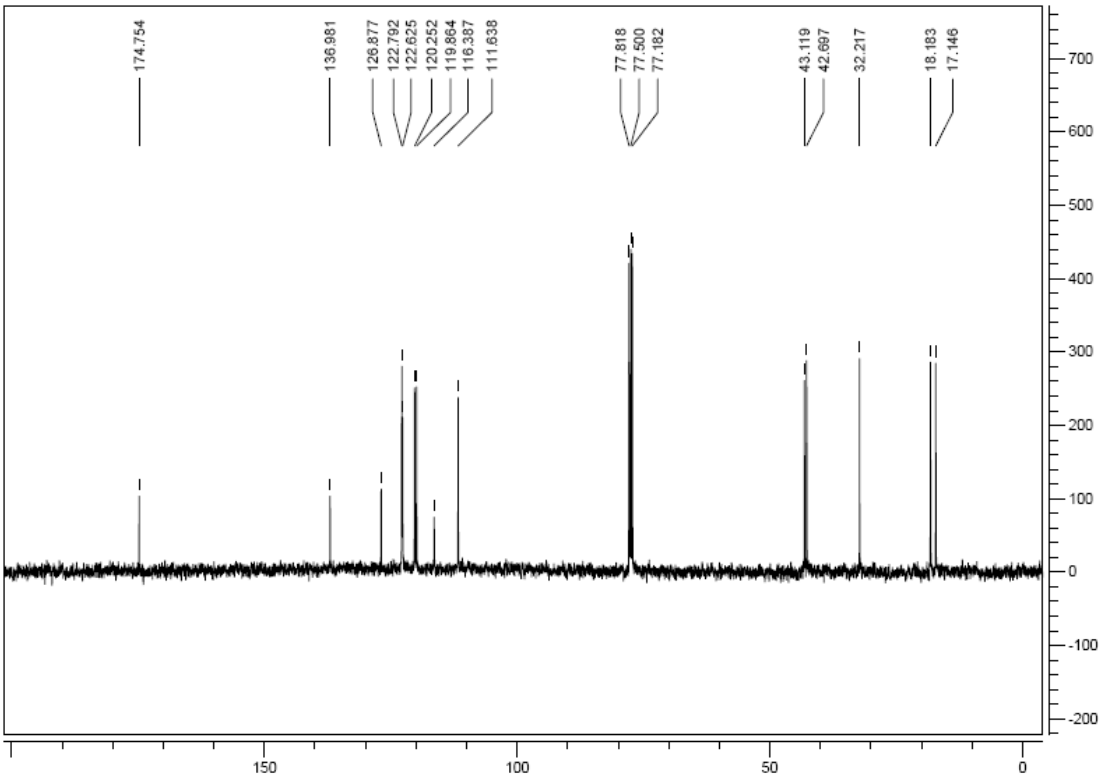
(1) R. Jiang, X.-J. Wu, X. Zhu, X.-P. Xu, S.-J. Ji, *Eur. J. Org. Chem.*, 2010, 5946–5950.

(2) T. M. Niu, L. H. Huang, T. X. Wu, Y. H. Zhang, *Org. Biomol. Chem.,* 2011, **9**, 273-277.

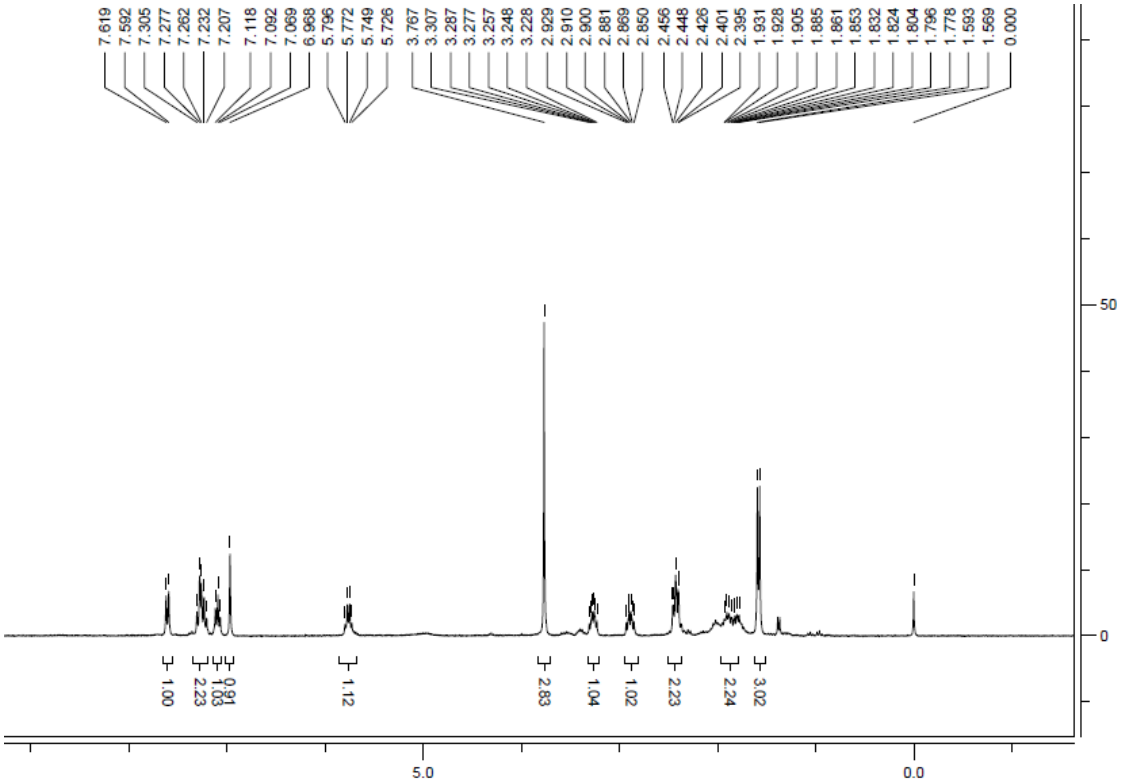
The ^1H NMR and ^{13}C NMR charts

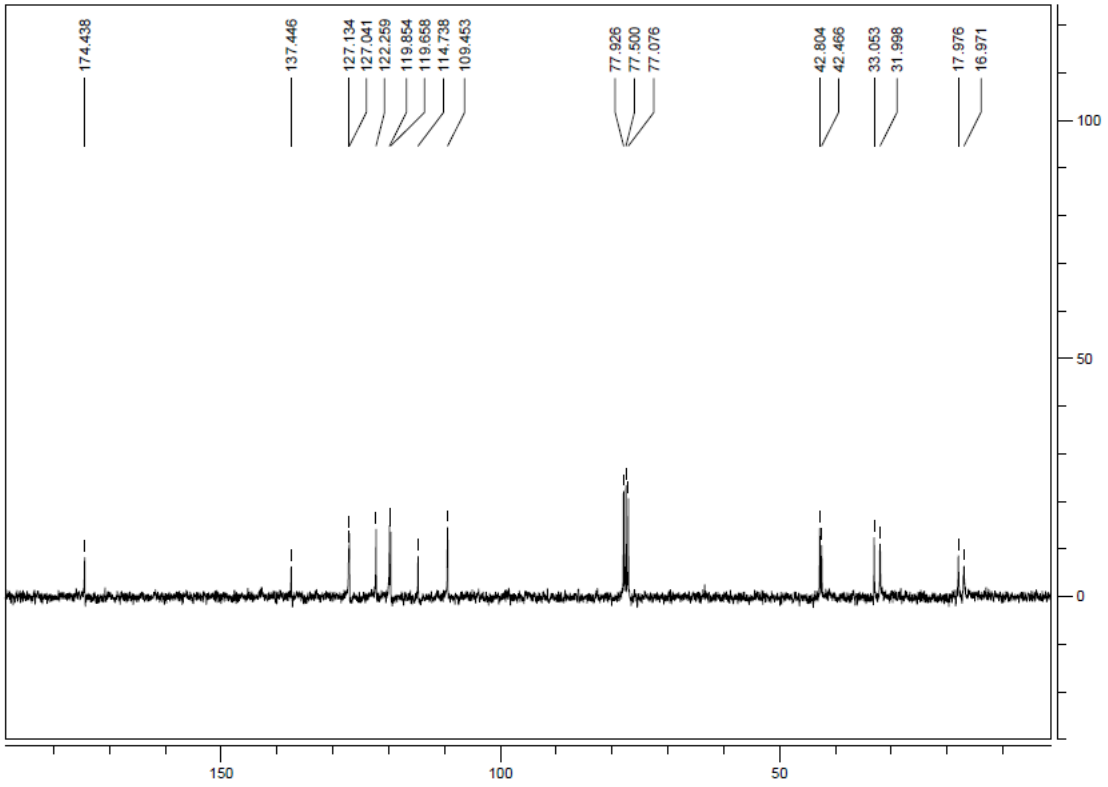
1-(1-(1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3aa):



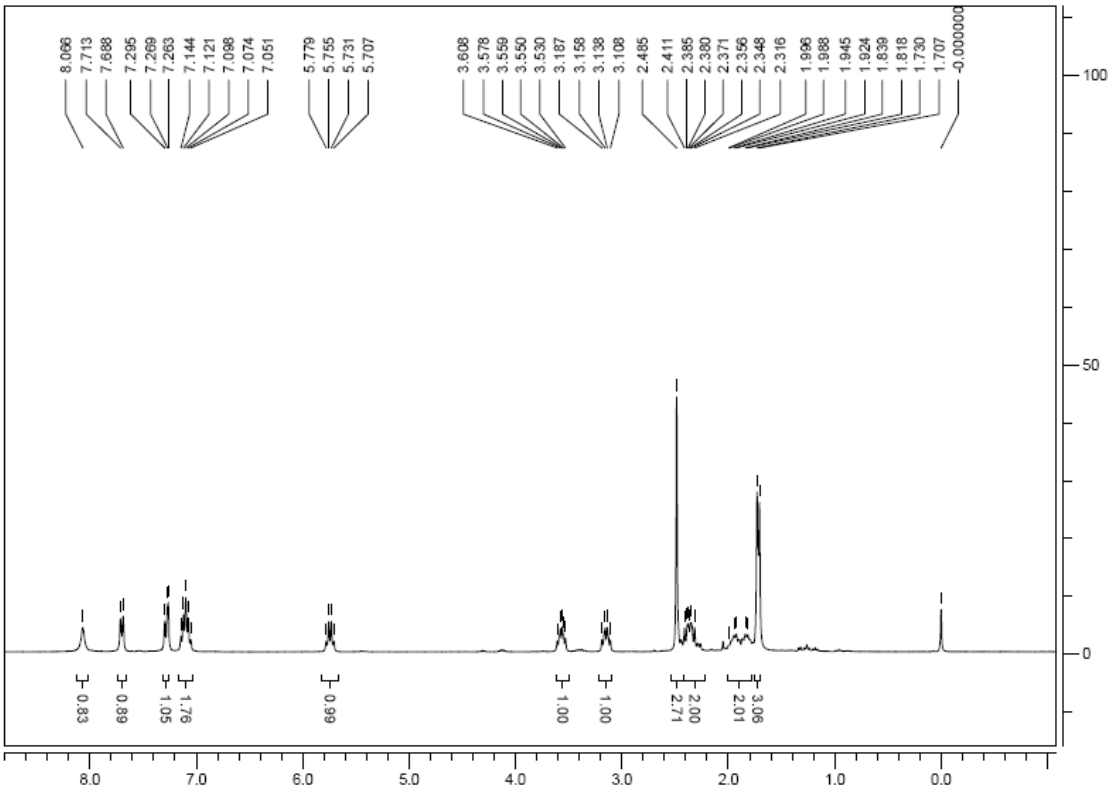


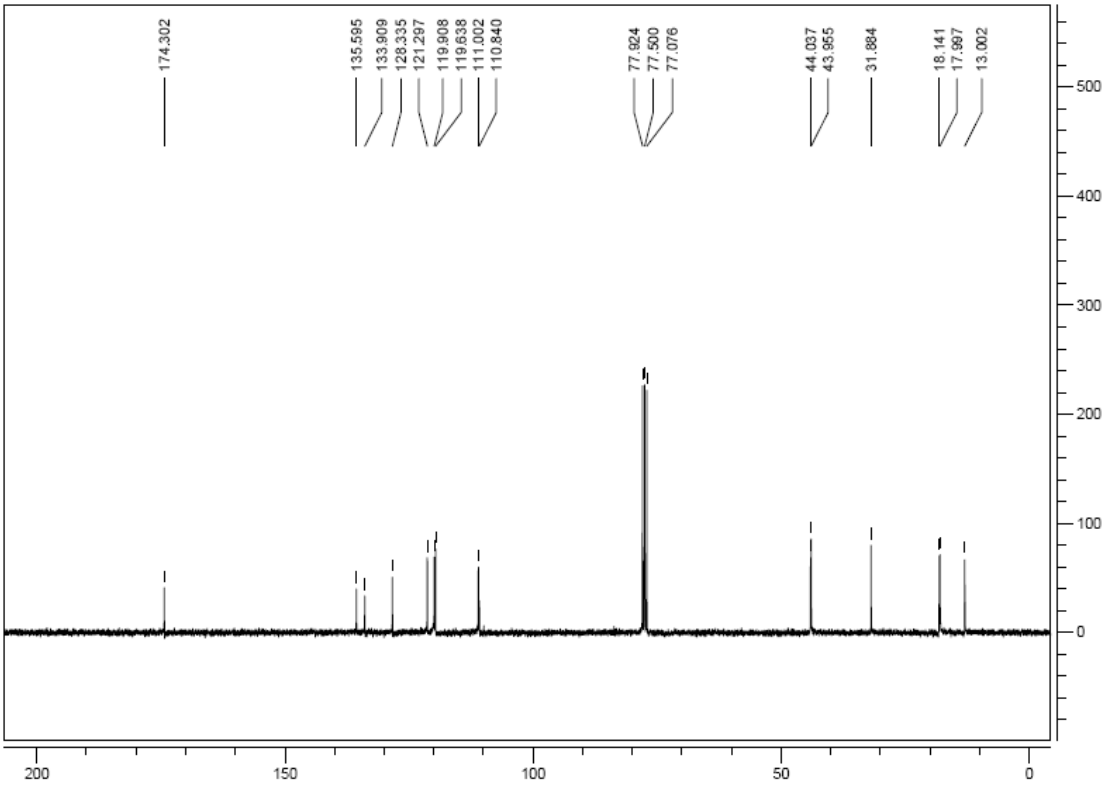
1-(1-(1-methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ab):



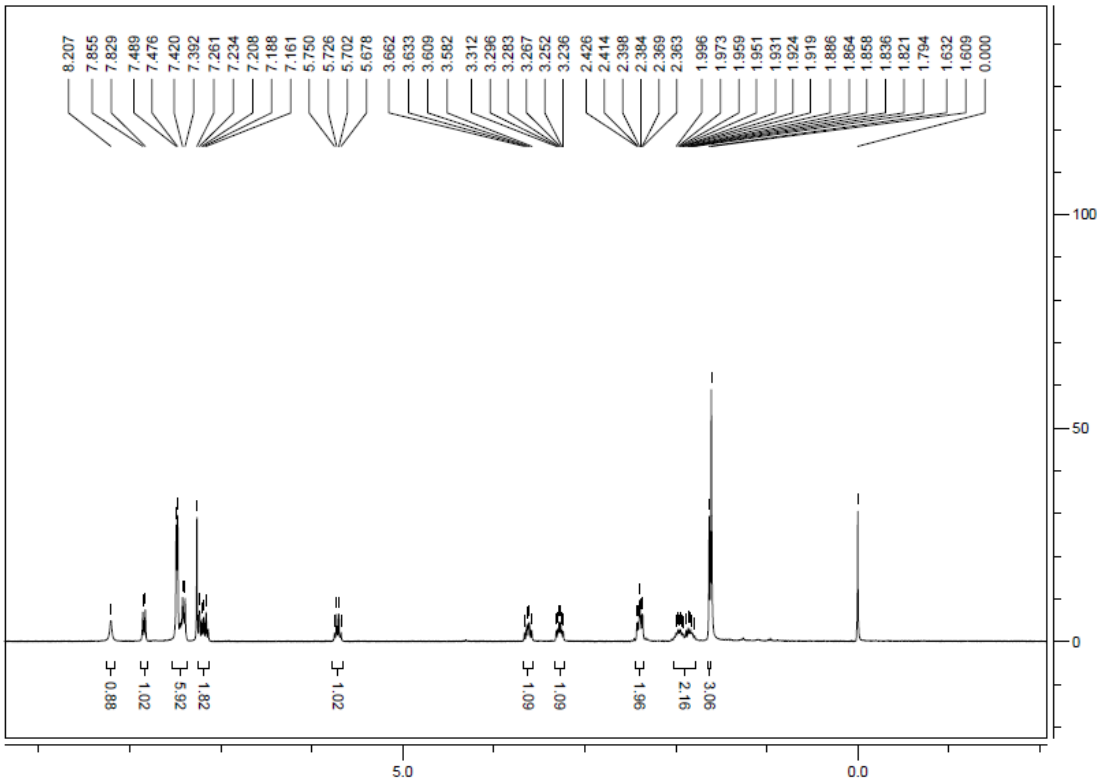


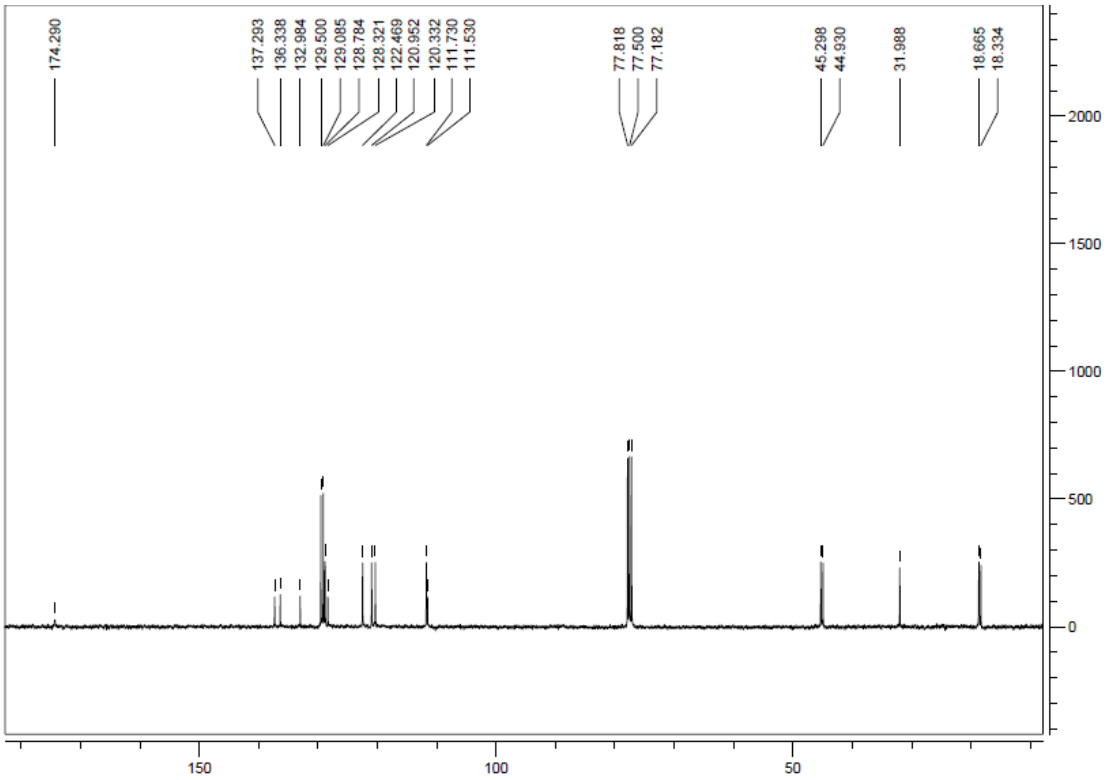
1-(1-(2-methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ac):



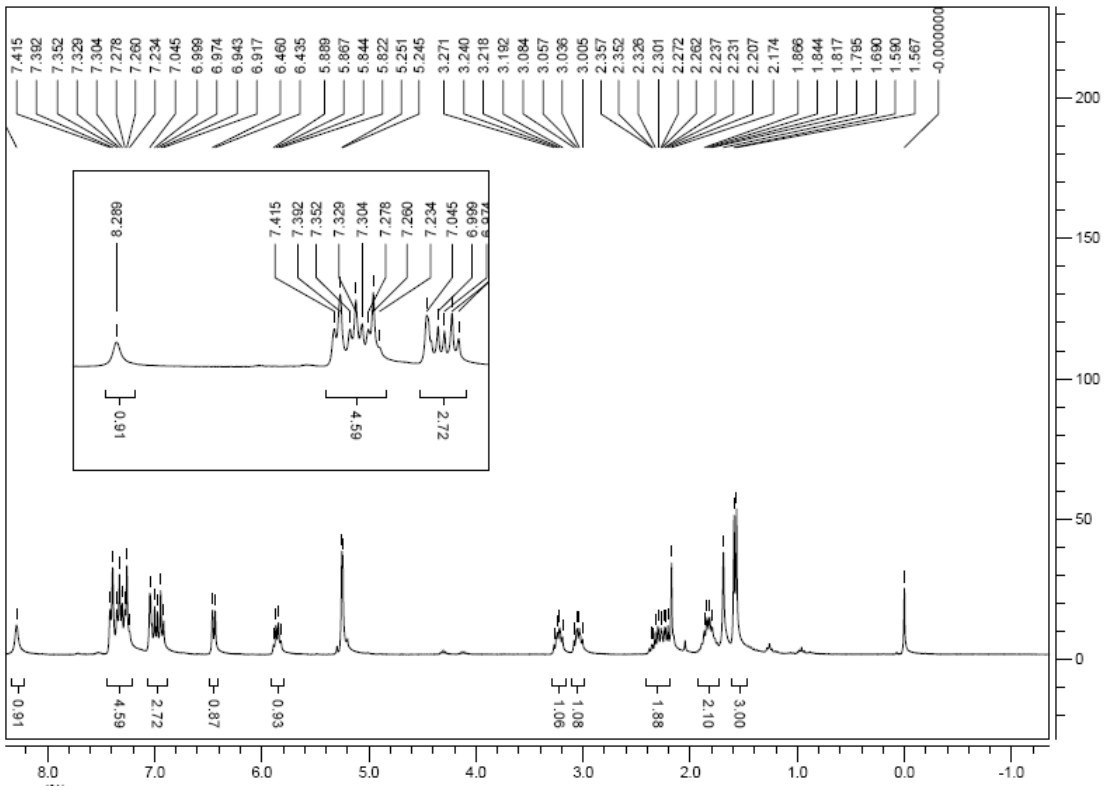


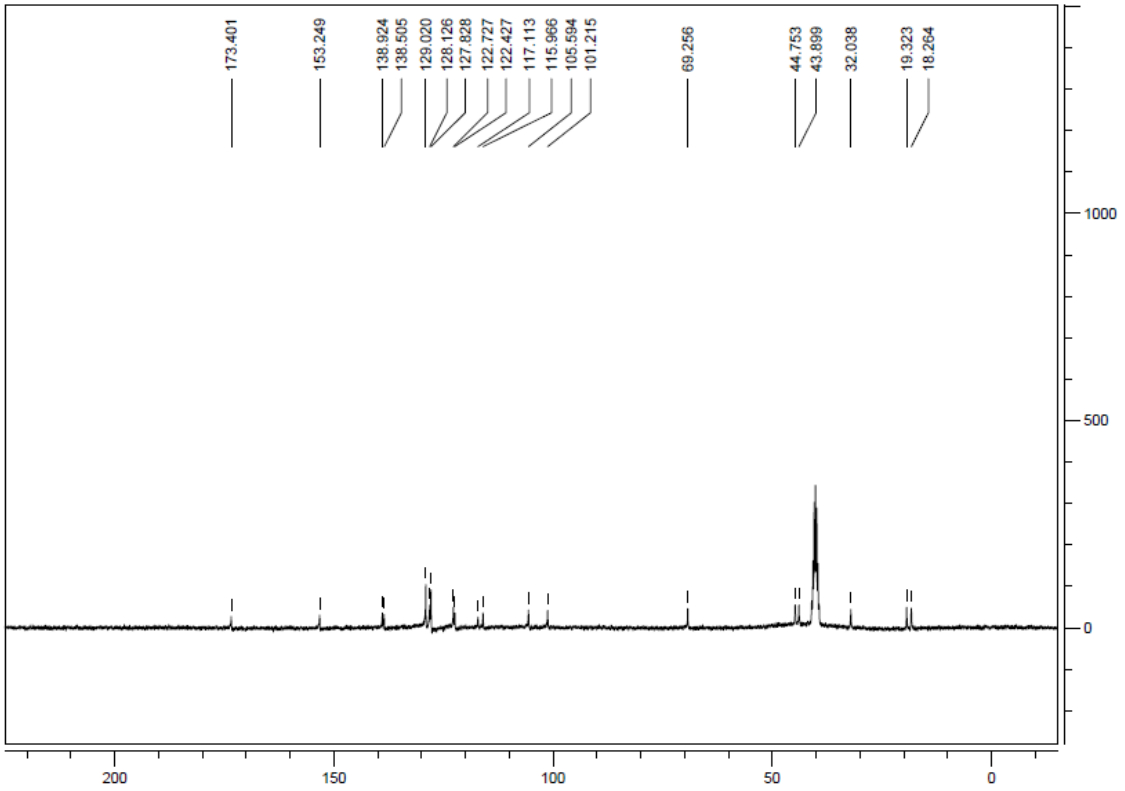
1-(1-(2-phenyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ad):



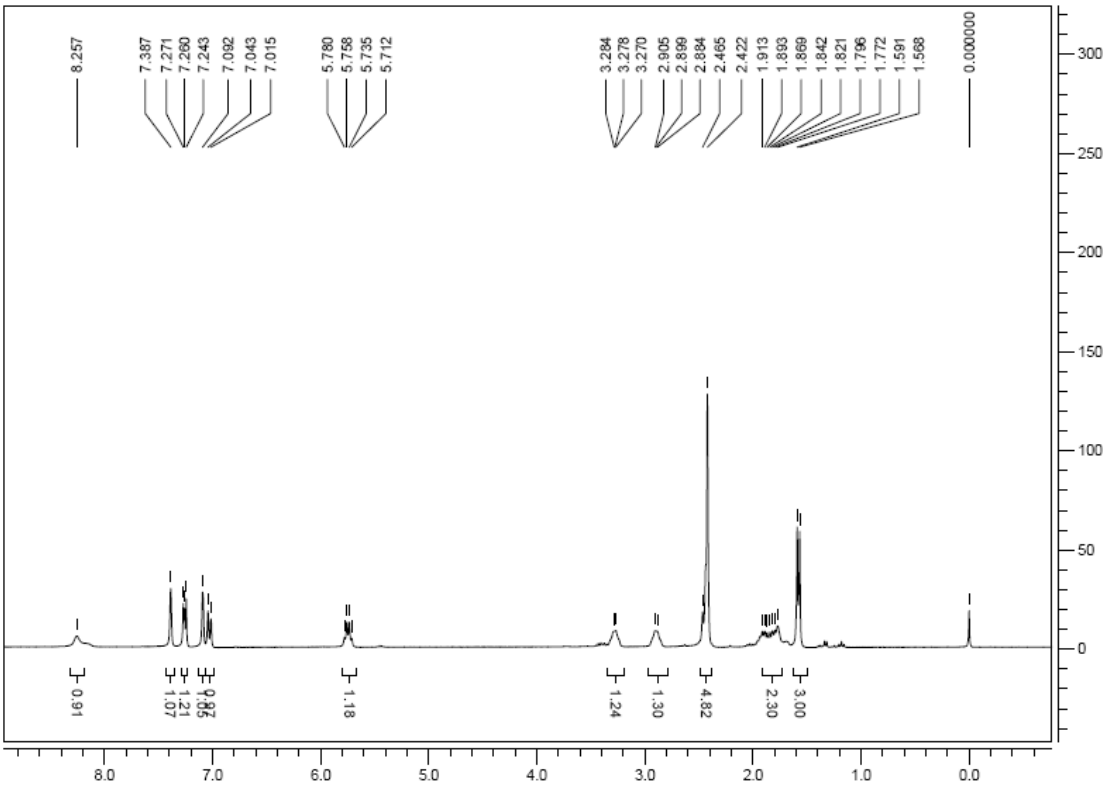


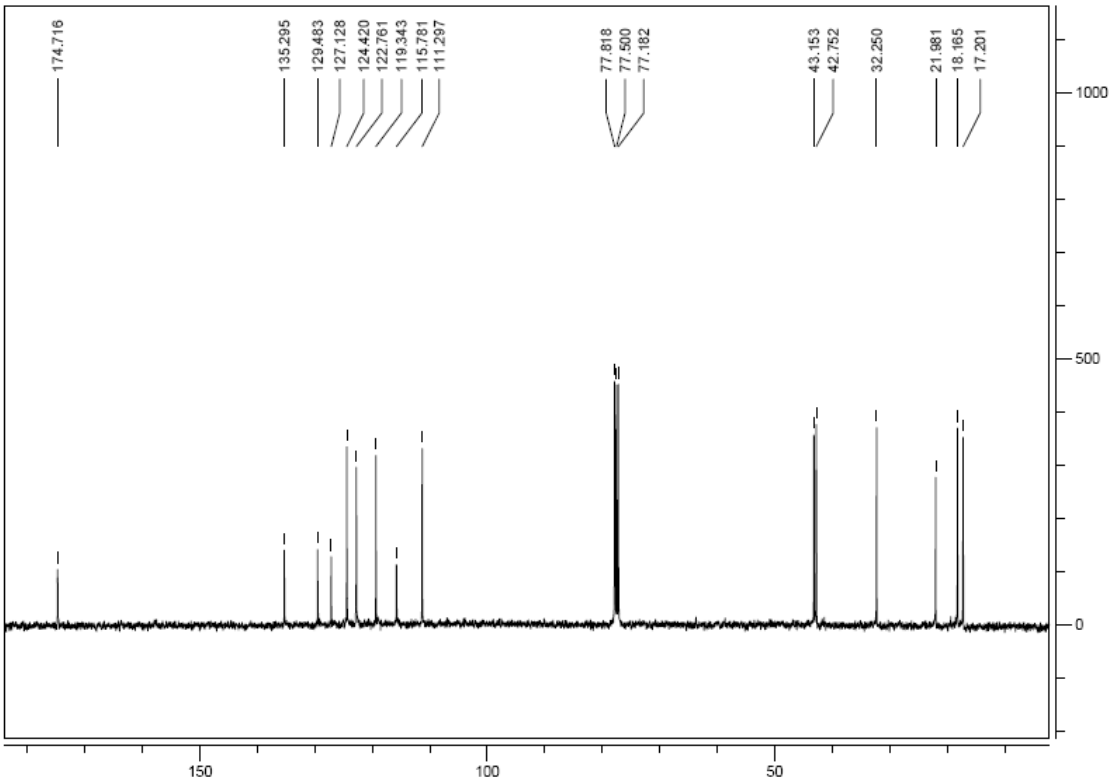
1-(1-(4-phenoxy-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ae):



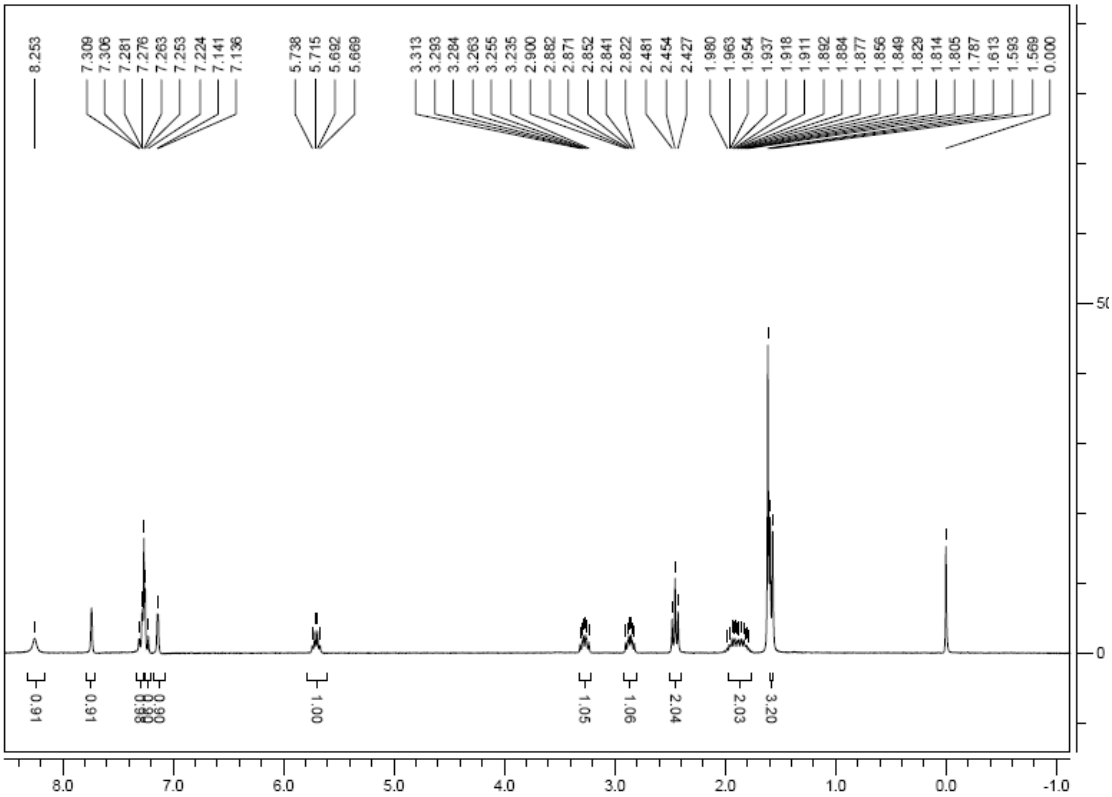


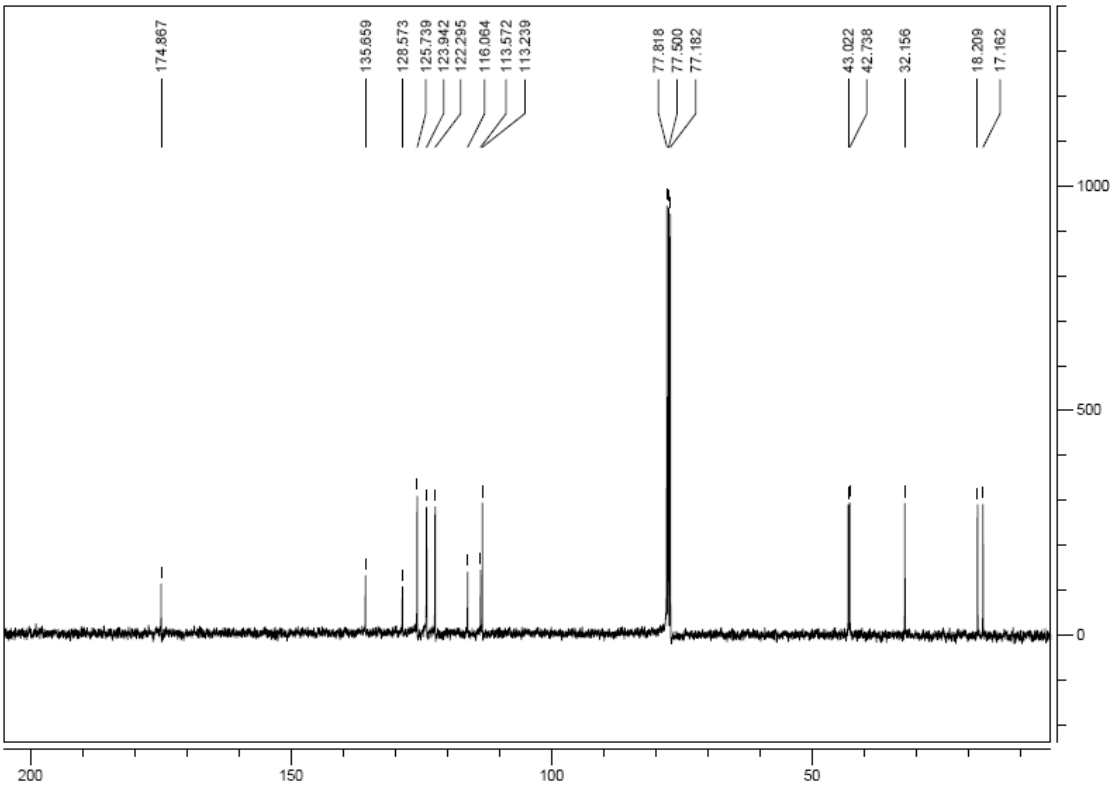
1-(1-(5-methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3af):



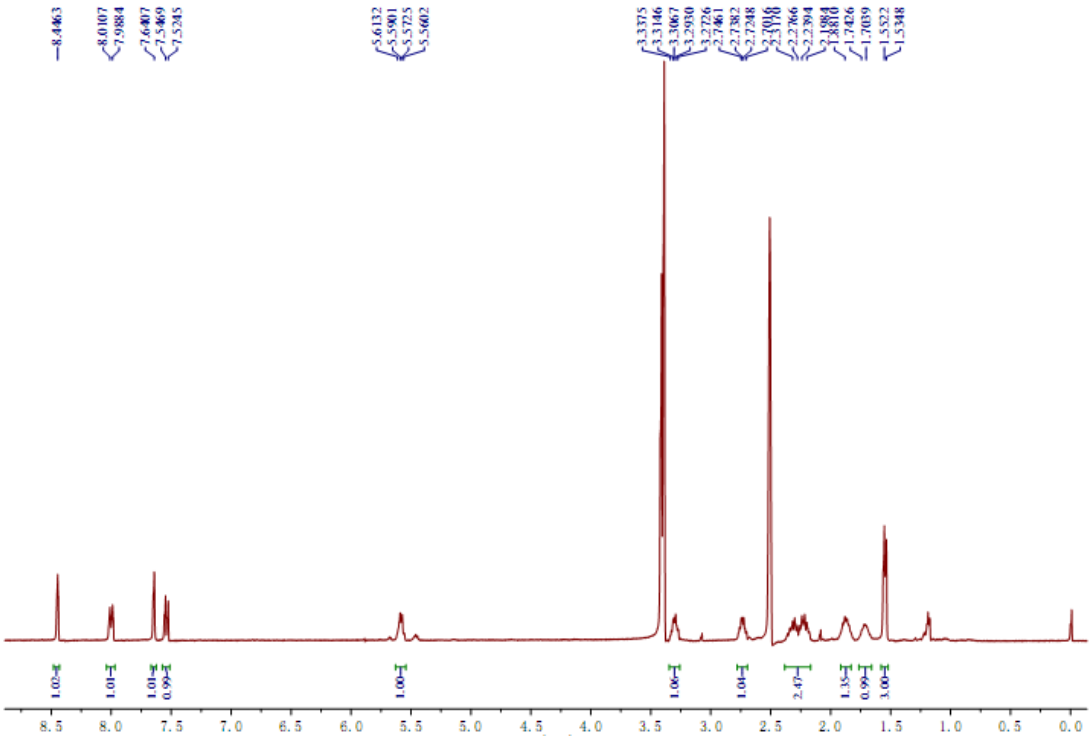


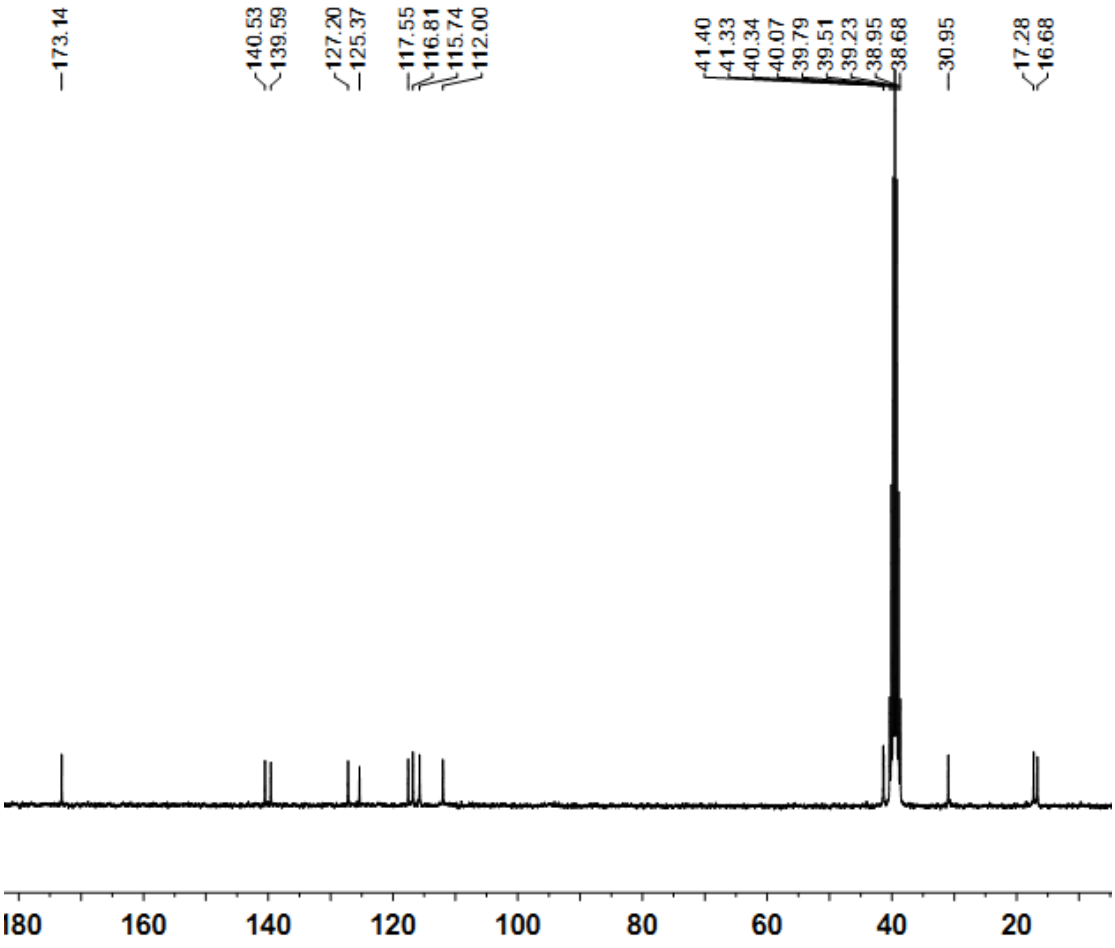
1-(1-(5-bromo-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ag):



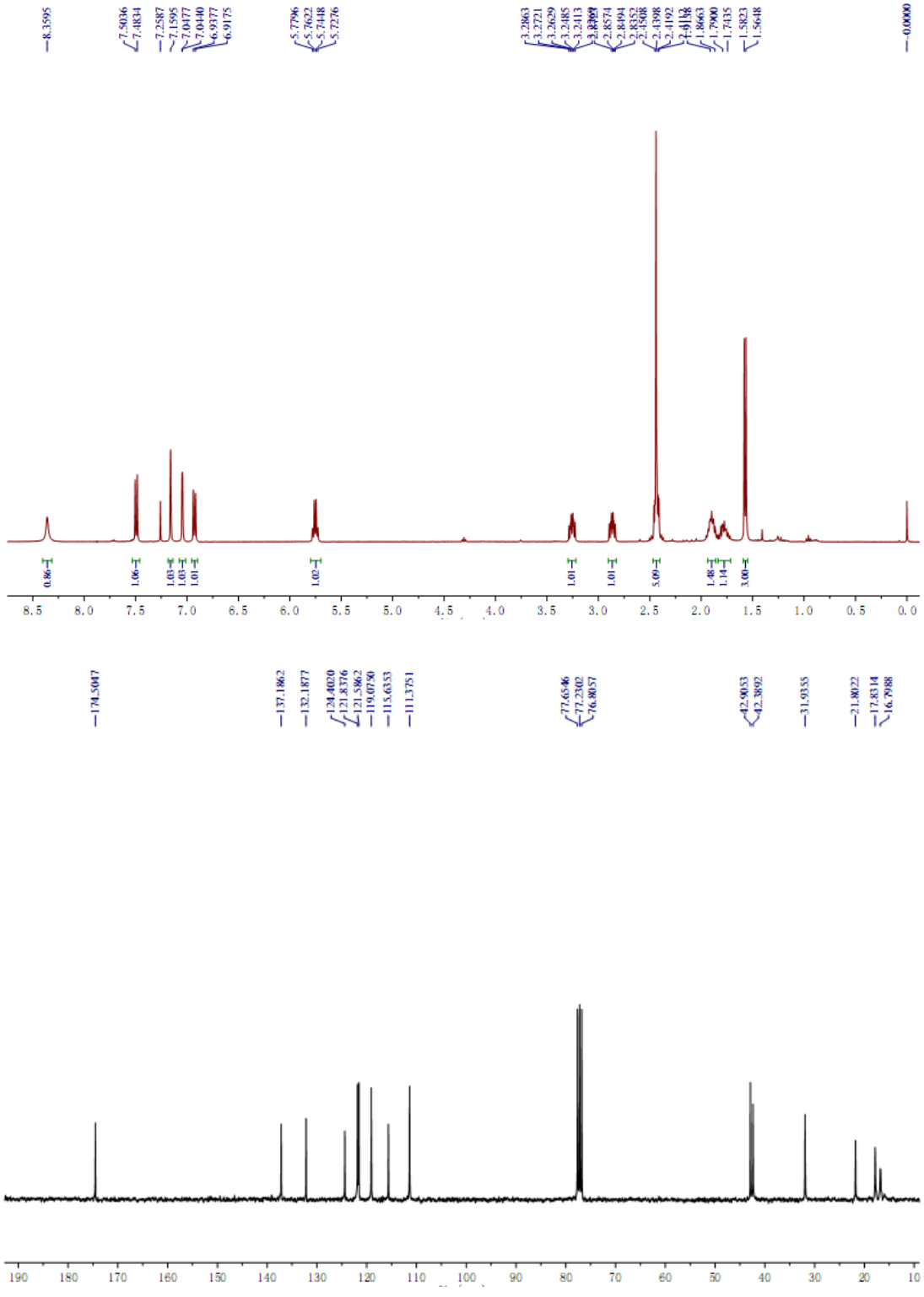


1-(1-(5-nitro-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ah):

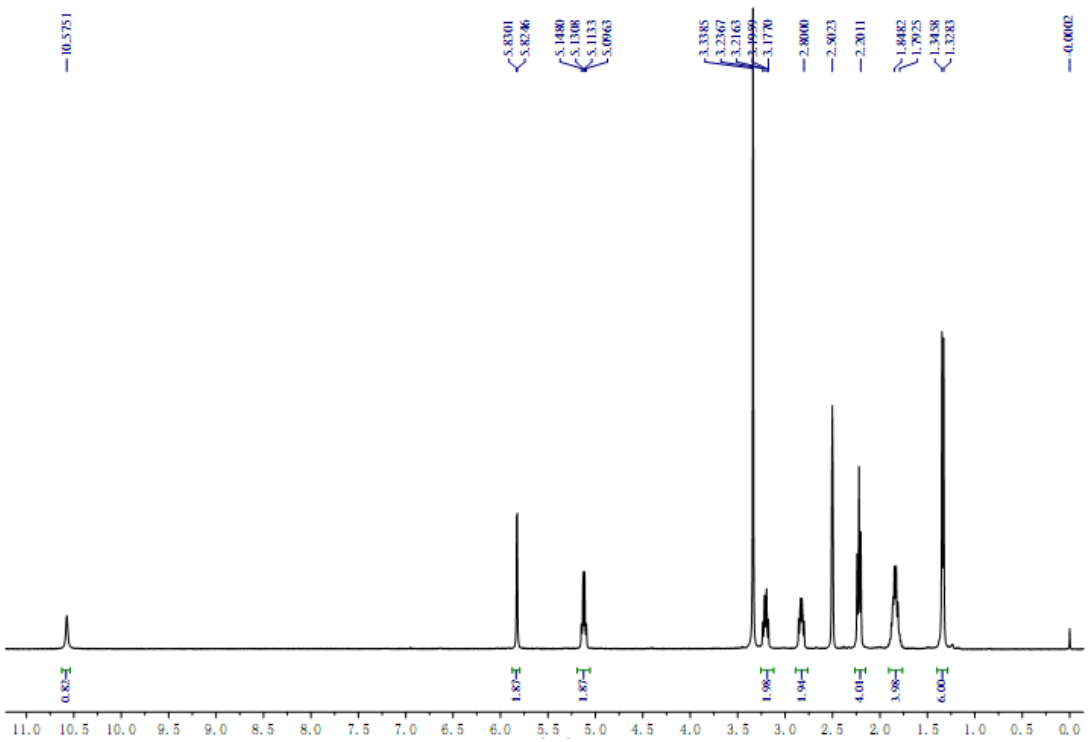


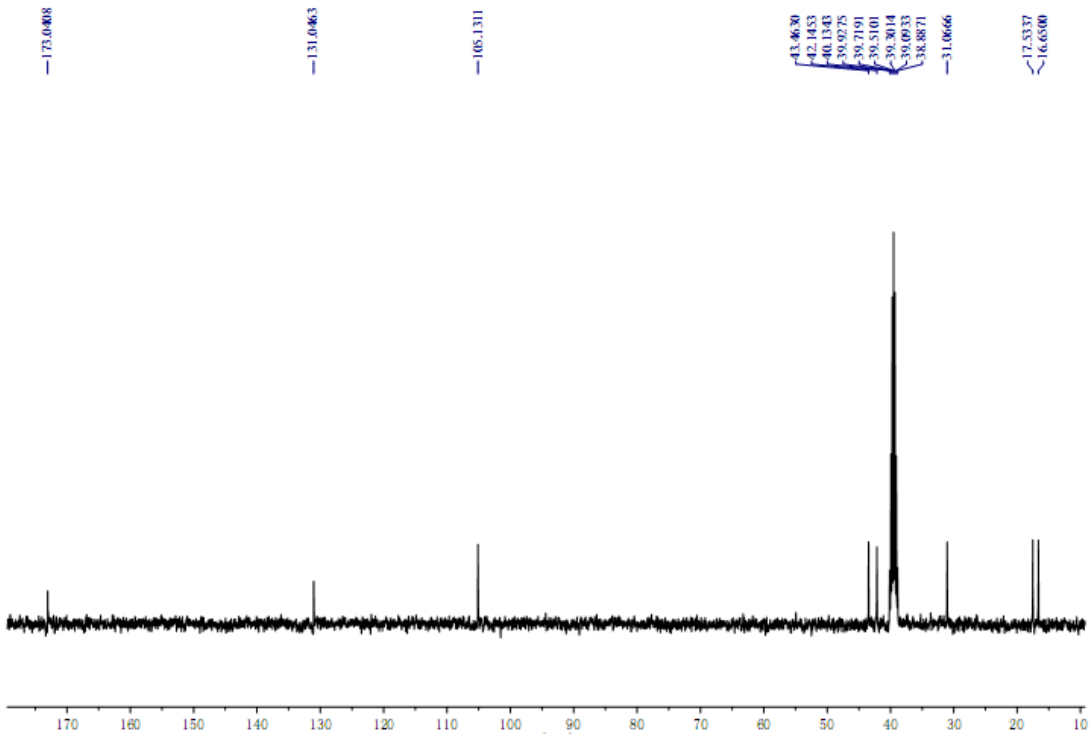


1-(1-(6-methyl-1*H*-indol-3-yl)ethyl)azepan-2-one (3ai):

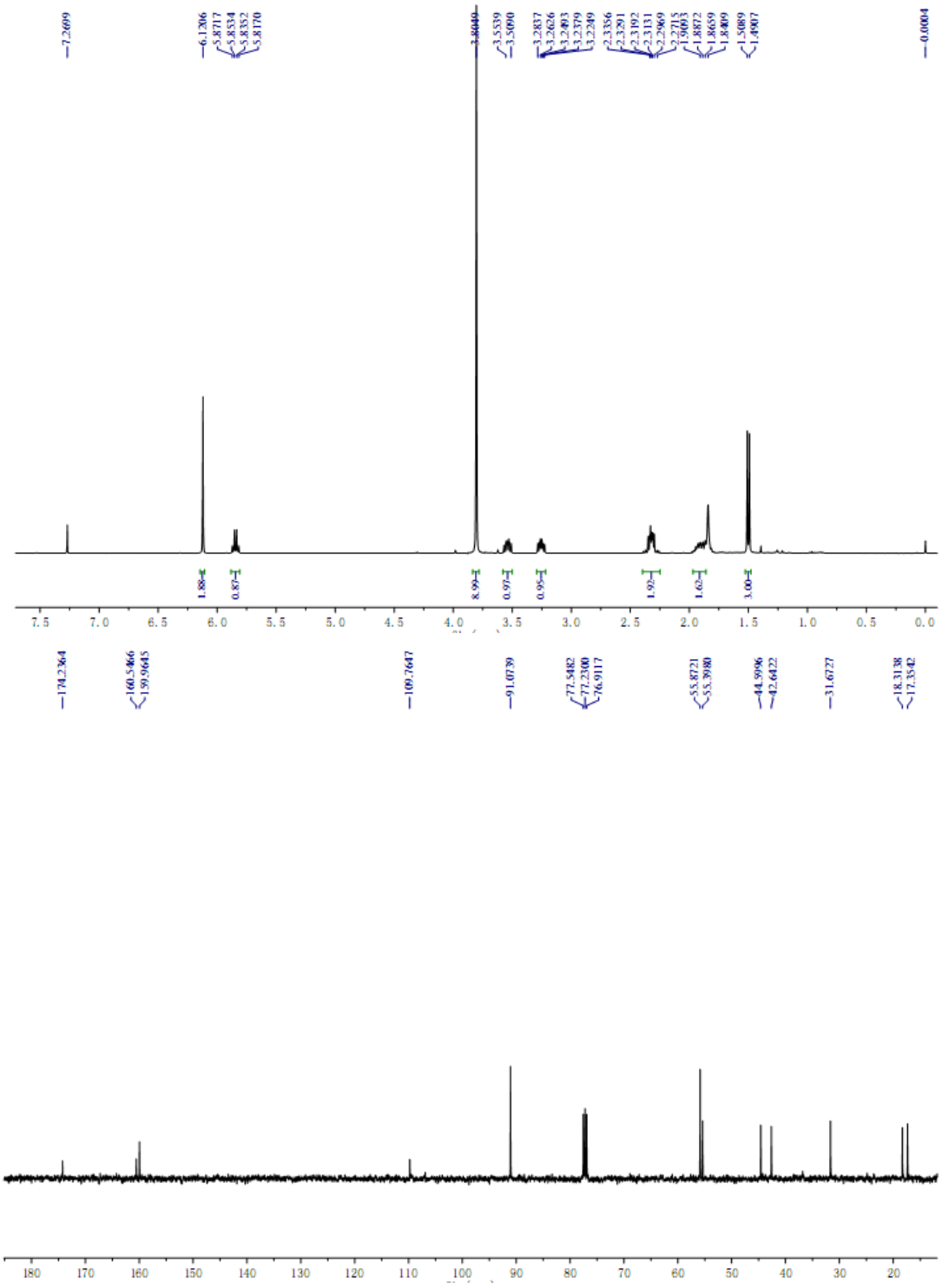


1, 1'-(1,1'-(1H-pyrrole-2,5-diyl)bis(ethane-1,1-diyl))dipyrrolidin-2-one (3ak):

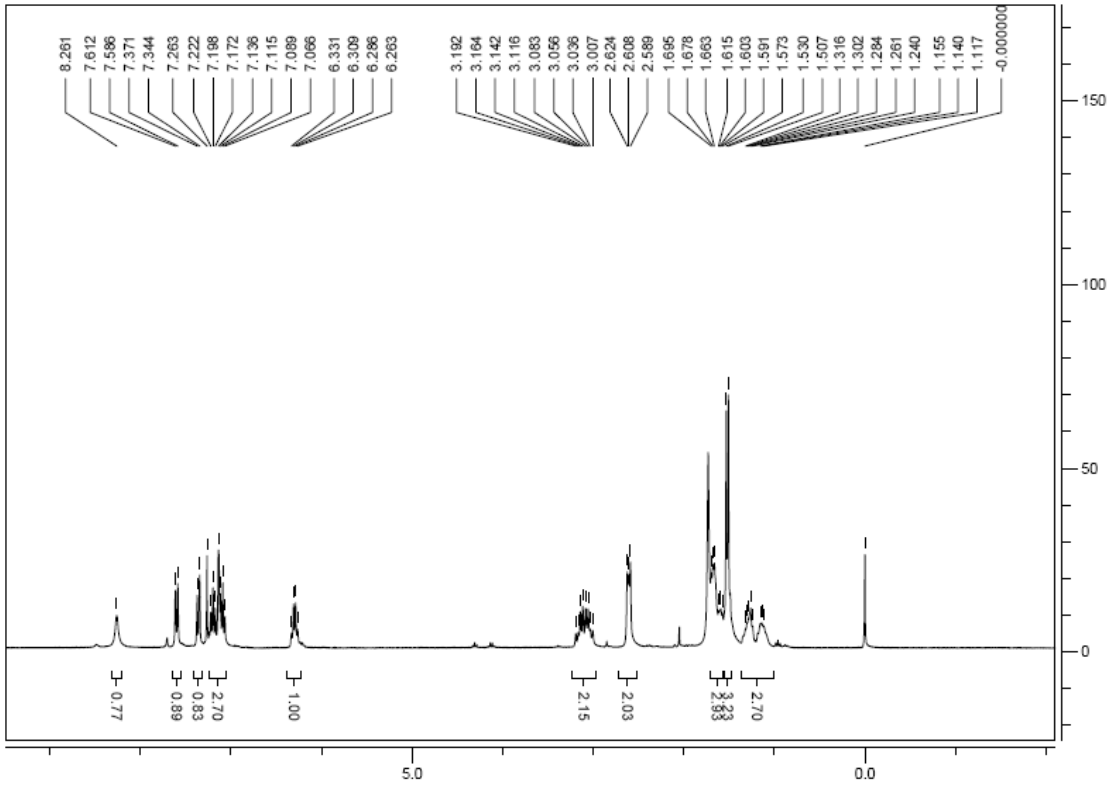


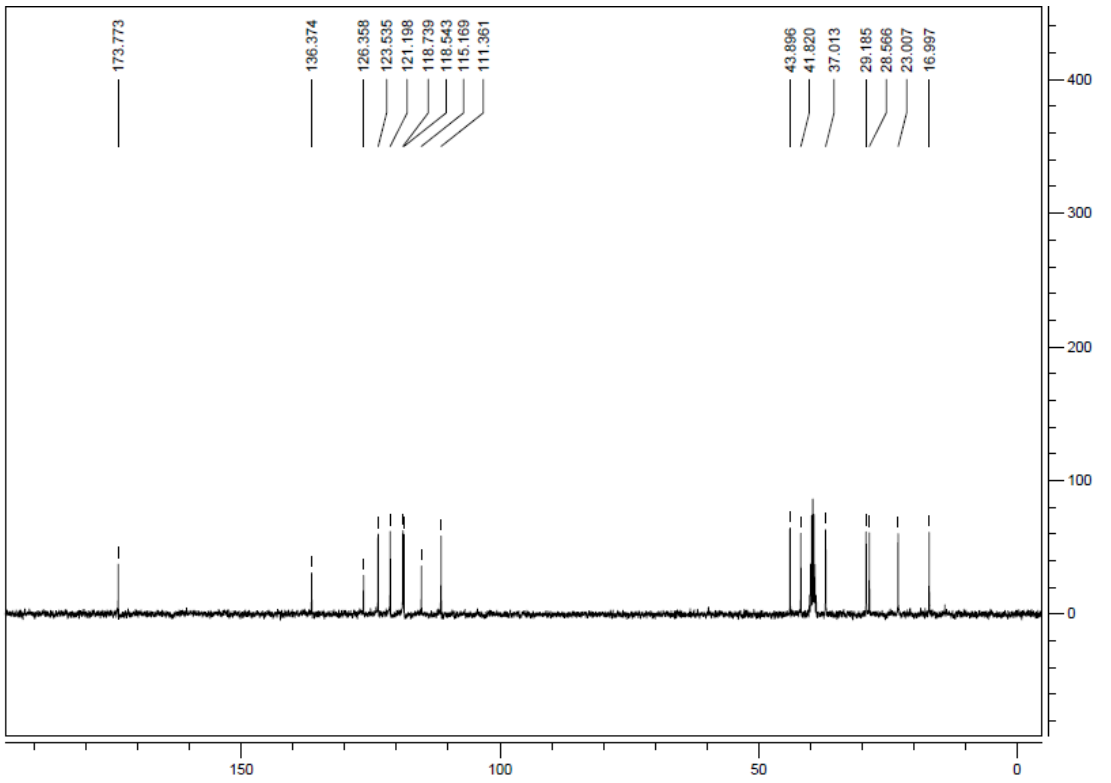


1-(1-(2,4,6-trimethoxyphenyl)ethyl)pyrrolidin-2-one (3al):

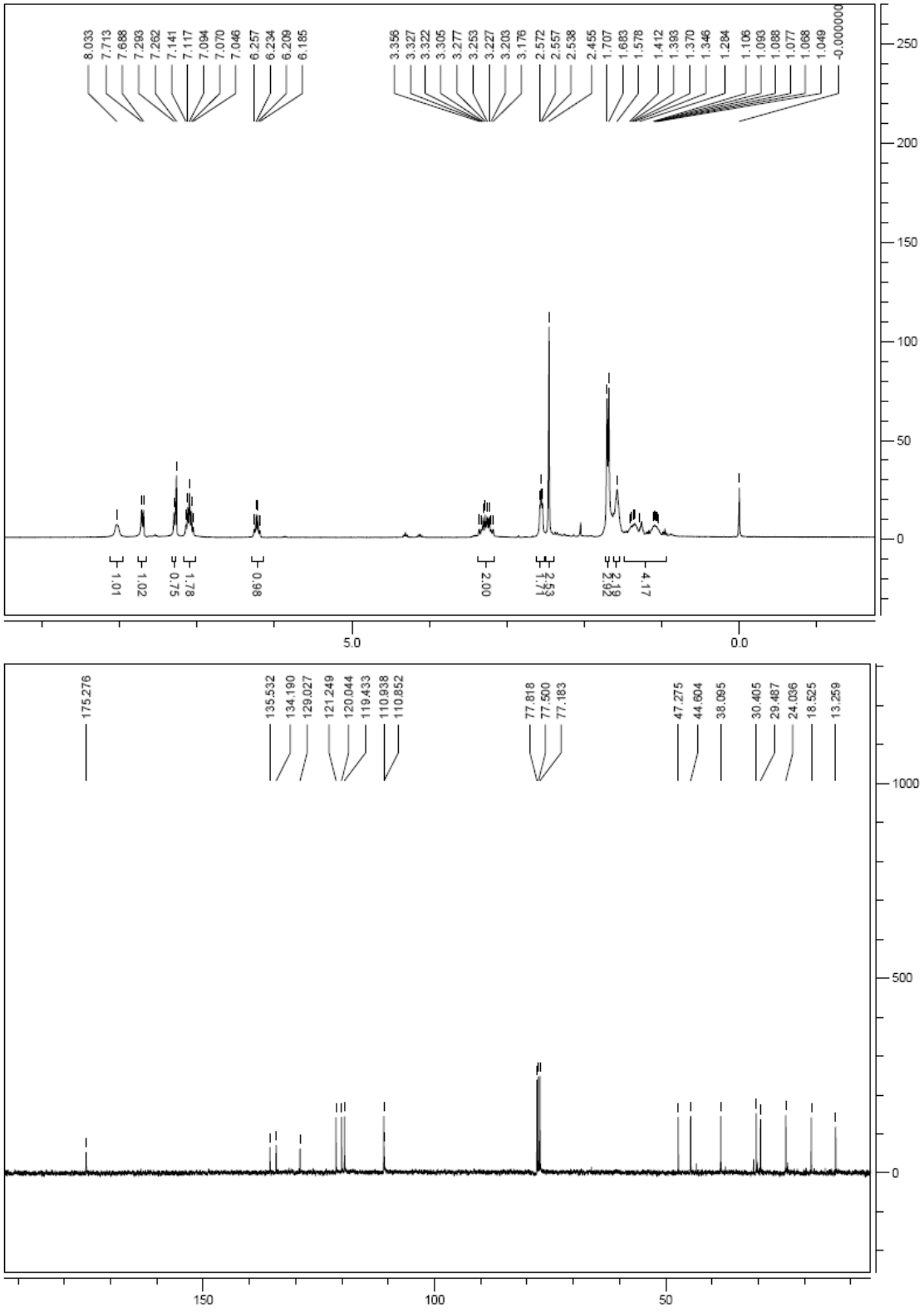


1-(1-(1*H*-indol-3-yl)ethyl)azepan-2-one (3ba):

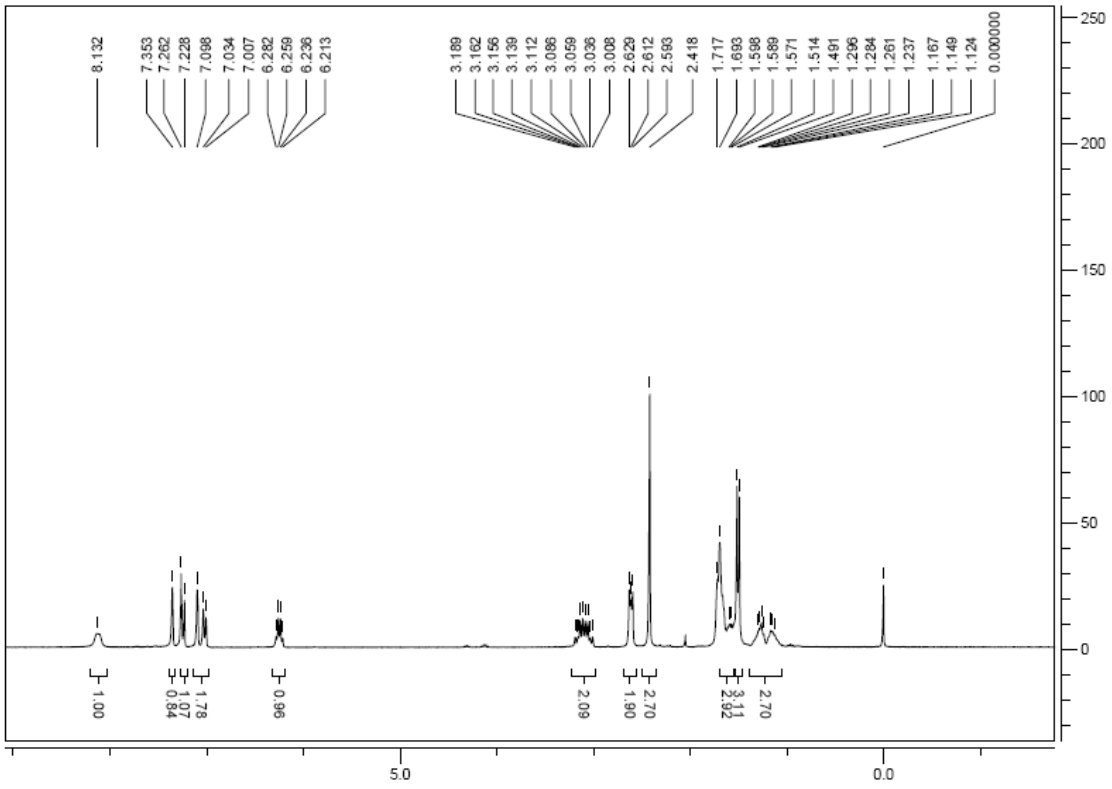


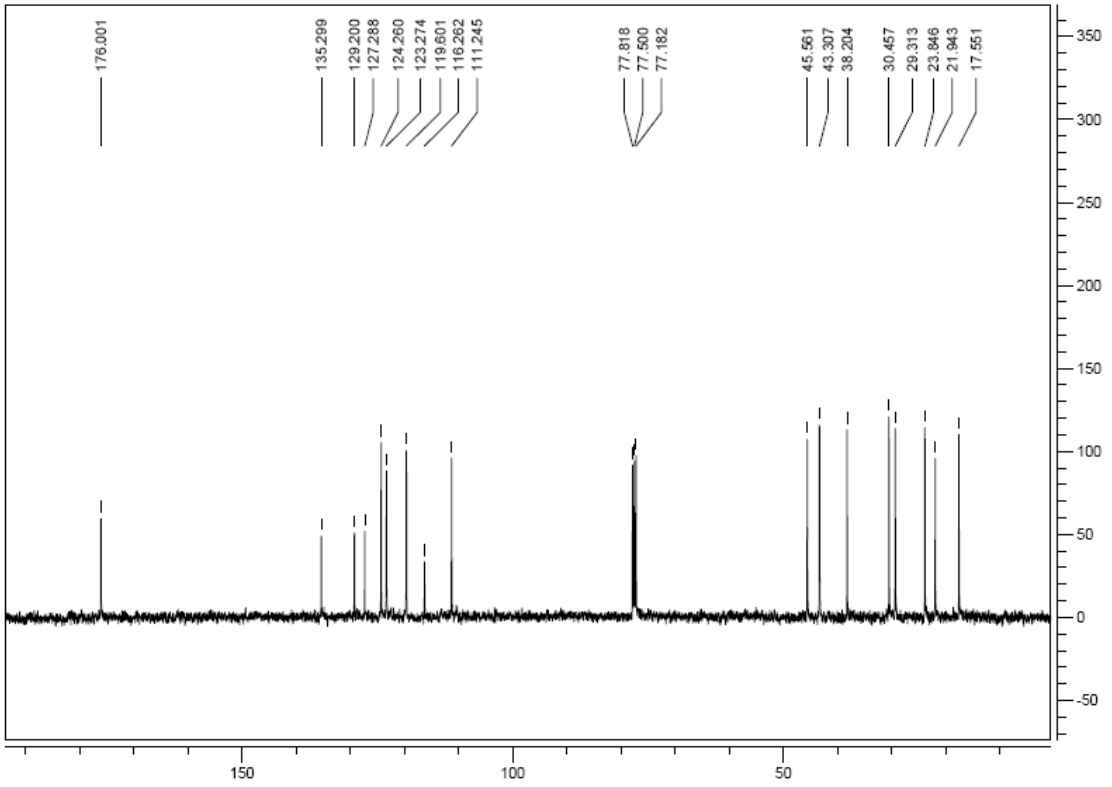


1-(1-(2-methyl-1*H*-indol-3-yl)ethyl)azepan-2-one (3bc):

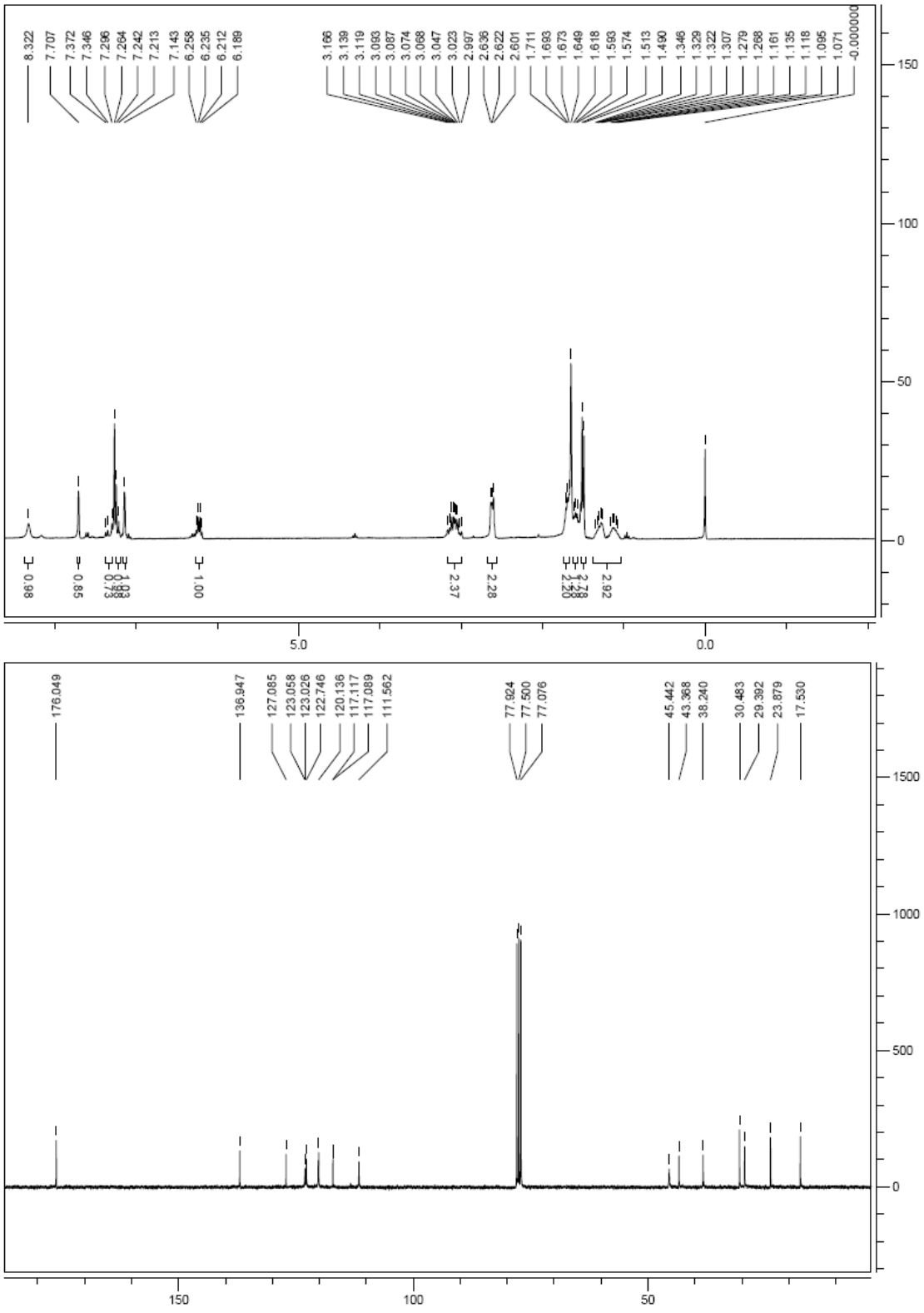


1-(1-(5-methyl-1*H*-indol-3-yl)ethyl)azepan-2-one (3bf):

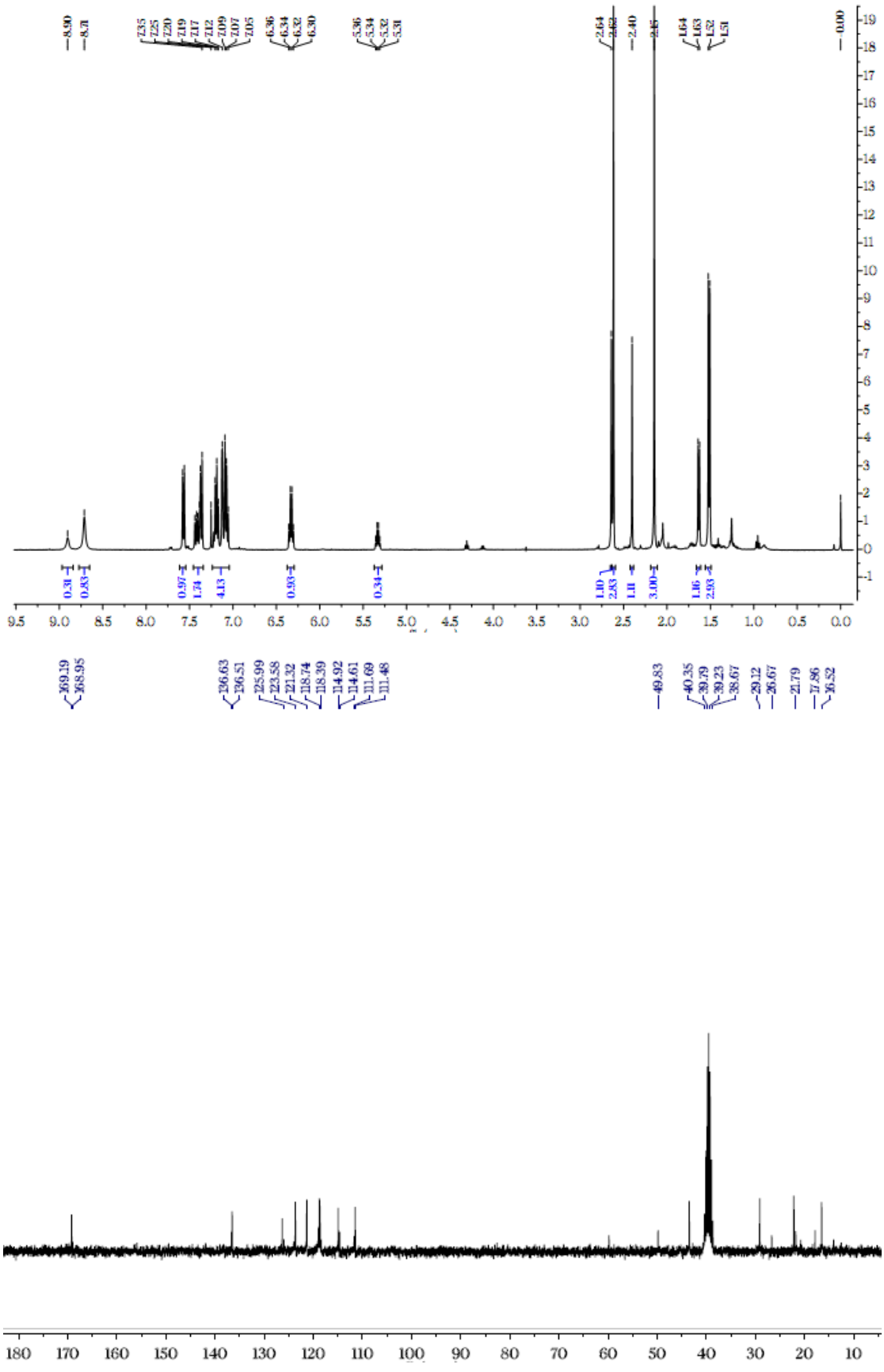




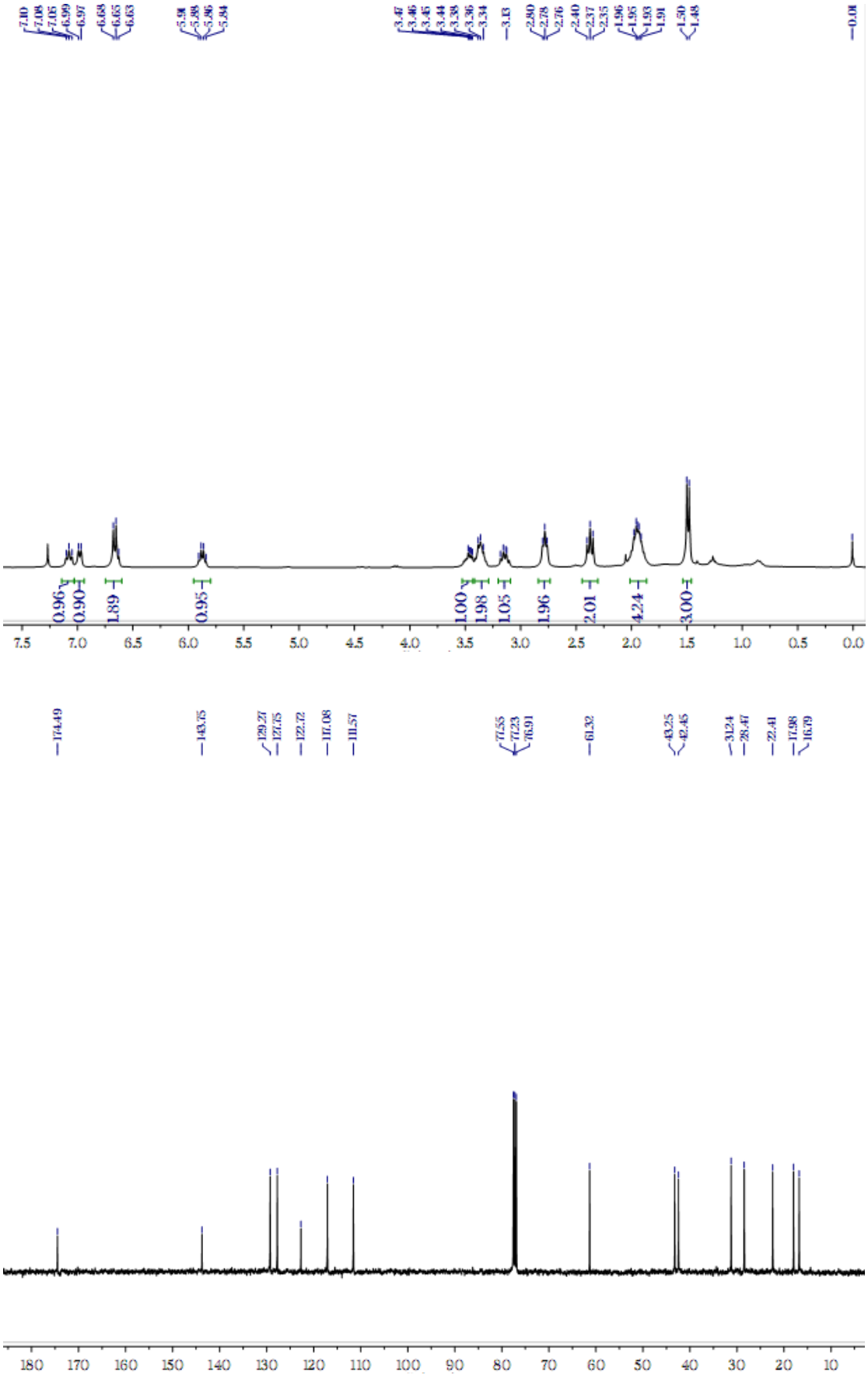
1-(1-(5-bromo-1*H*-indol-3-yl)ethyl)azepan-2-one (3bg):



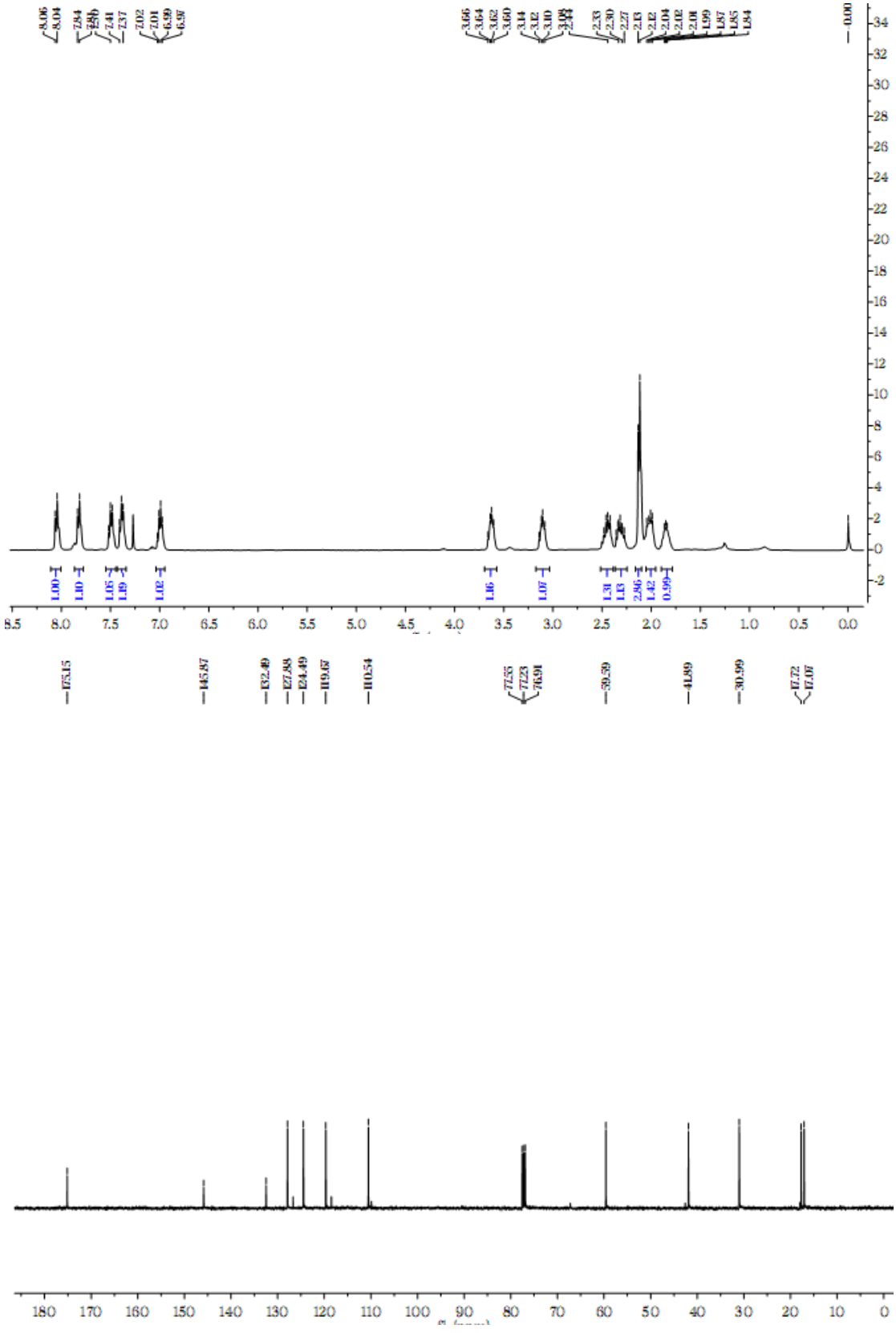
_N_-(1-(1_H_-indol-3-yl)ethyl)-_N_-methylacetamide (3ca):



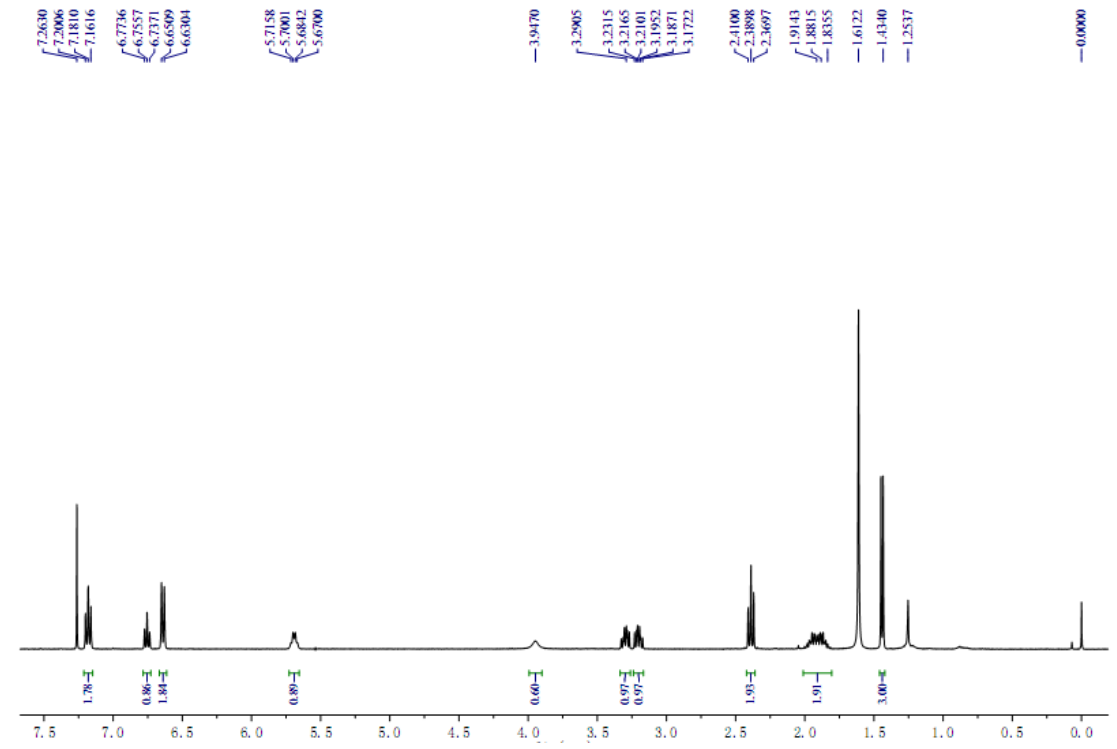
1-(1-(3,4-dihydroquinolin-1(2H)-yl)ethyl)pyrrolidin-2-one (5aa):

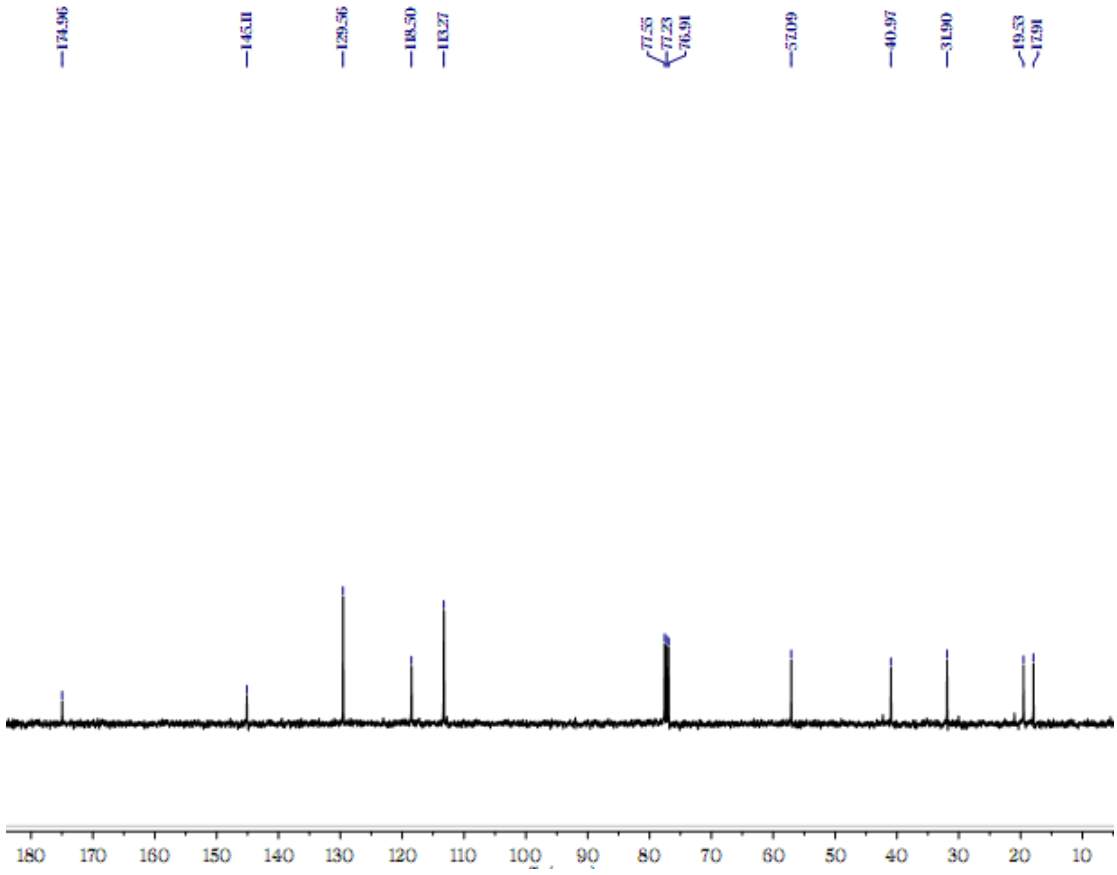


1-(1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)ethyl)pyrrolidin-2-one (5ab):

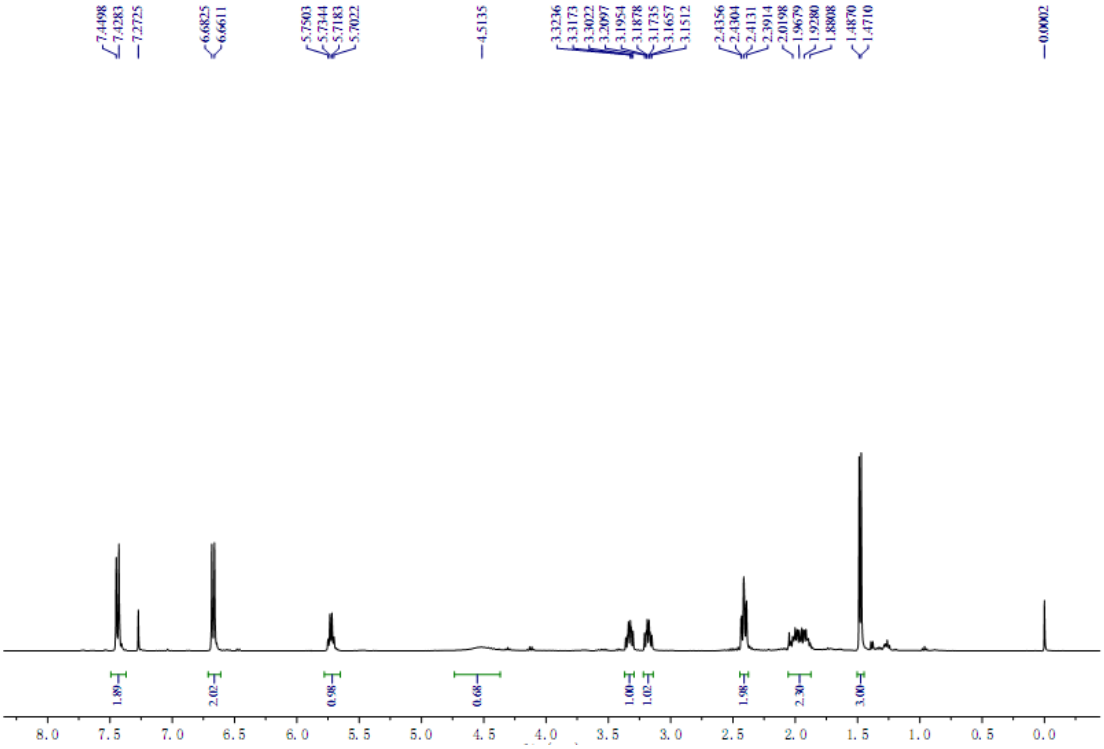


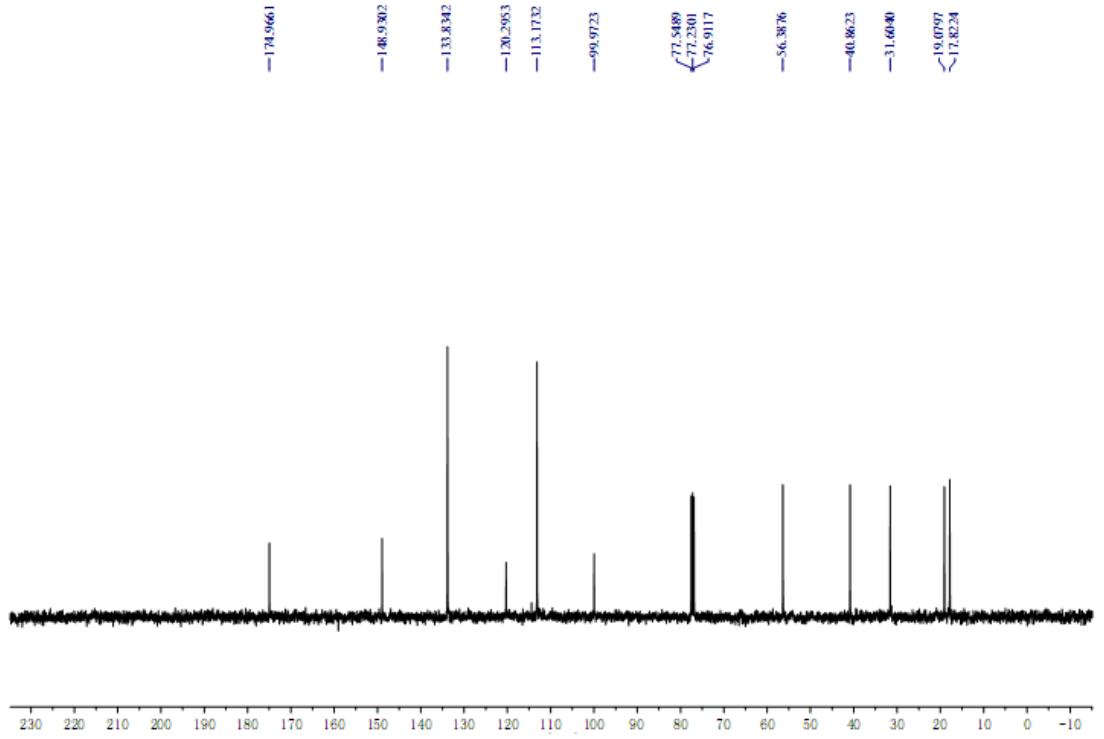
1-(1-(phenylamino)ethyl)pyrrolidin-2-one (5ac):



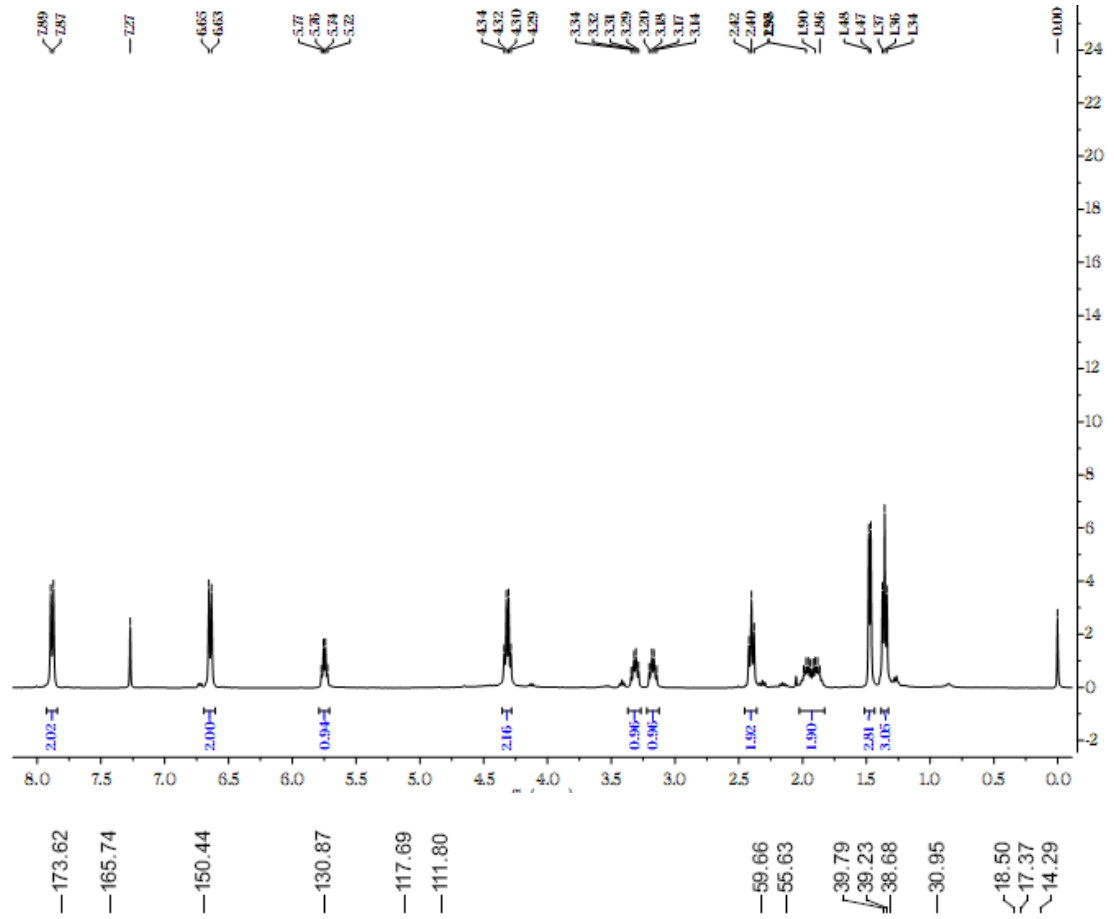


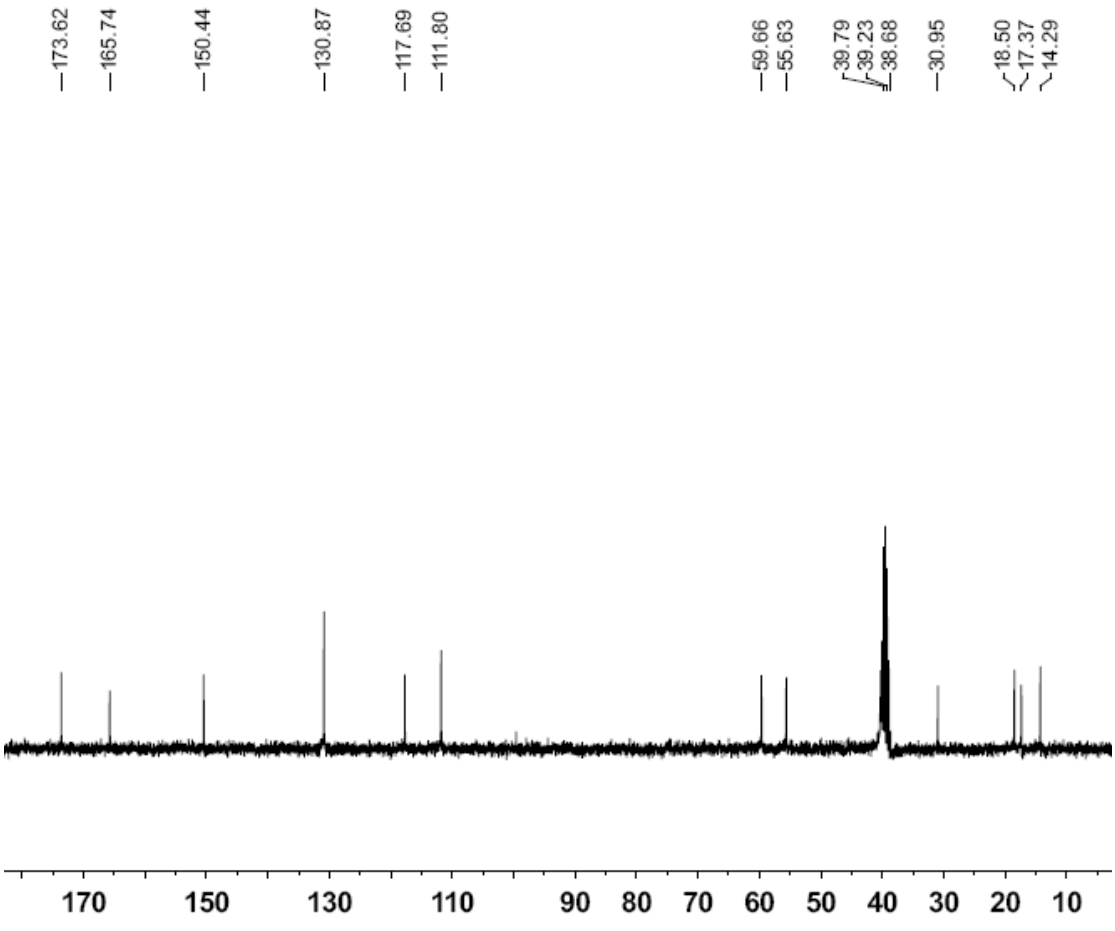
4-(1-(2-oxopyrrolidin-1-yl)ethylamino)benzonitrile (5ad):



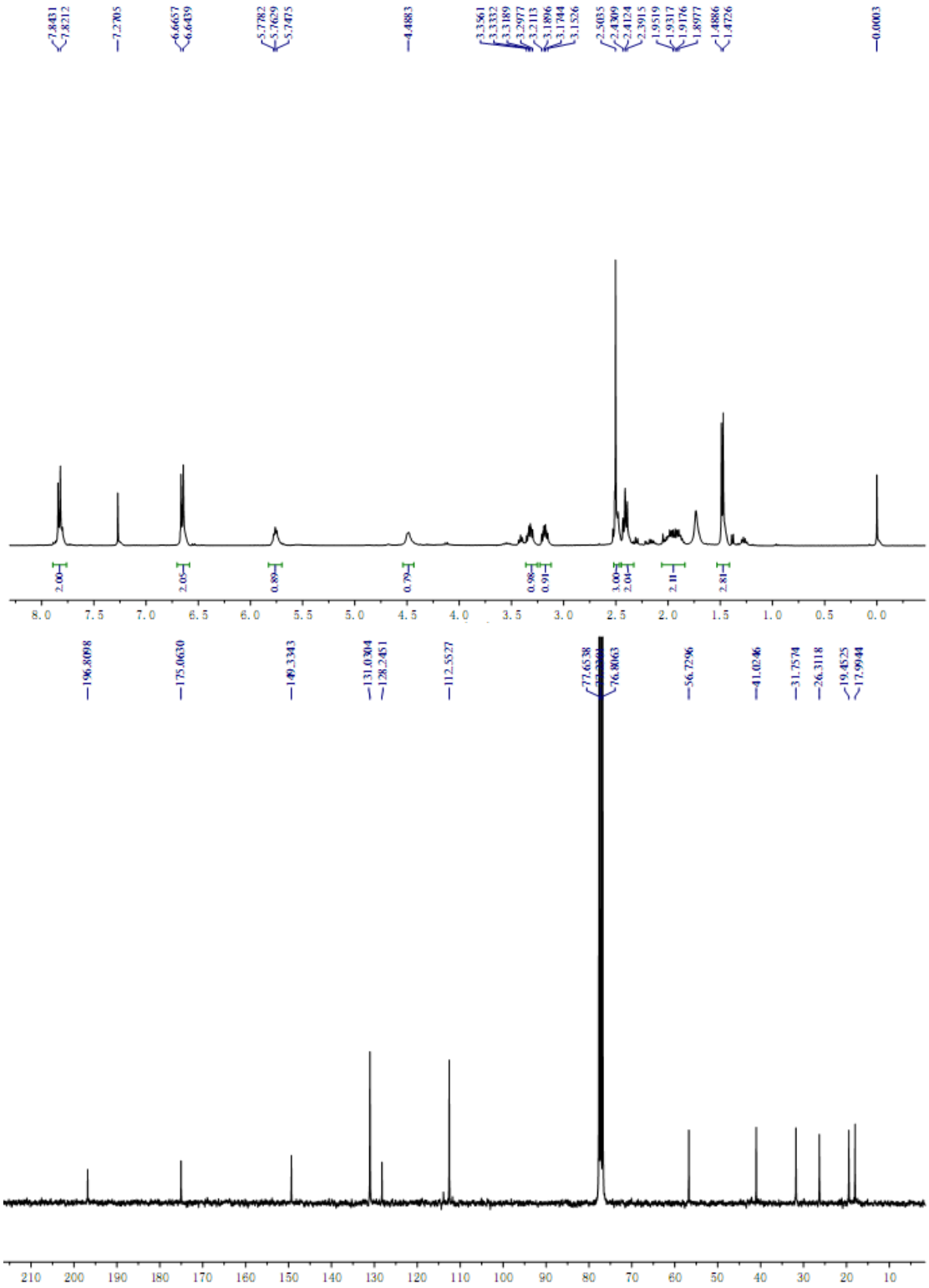


Ethyl 4-(1-(2-oxopyrrolidin-1-yl)ethylamino)benzoate (5ae):

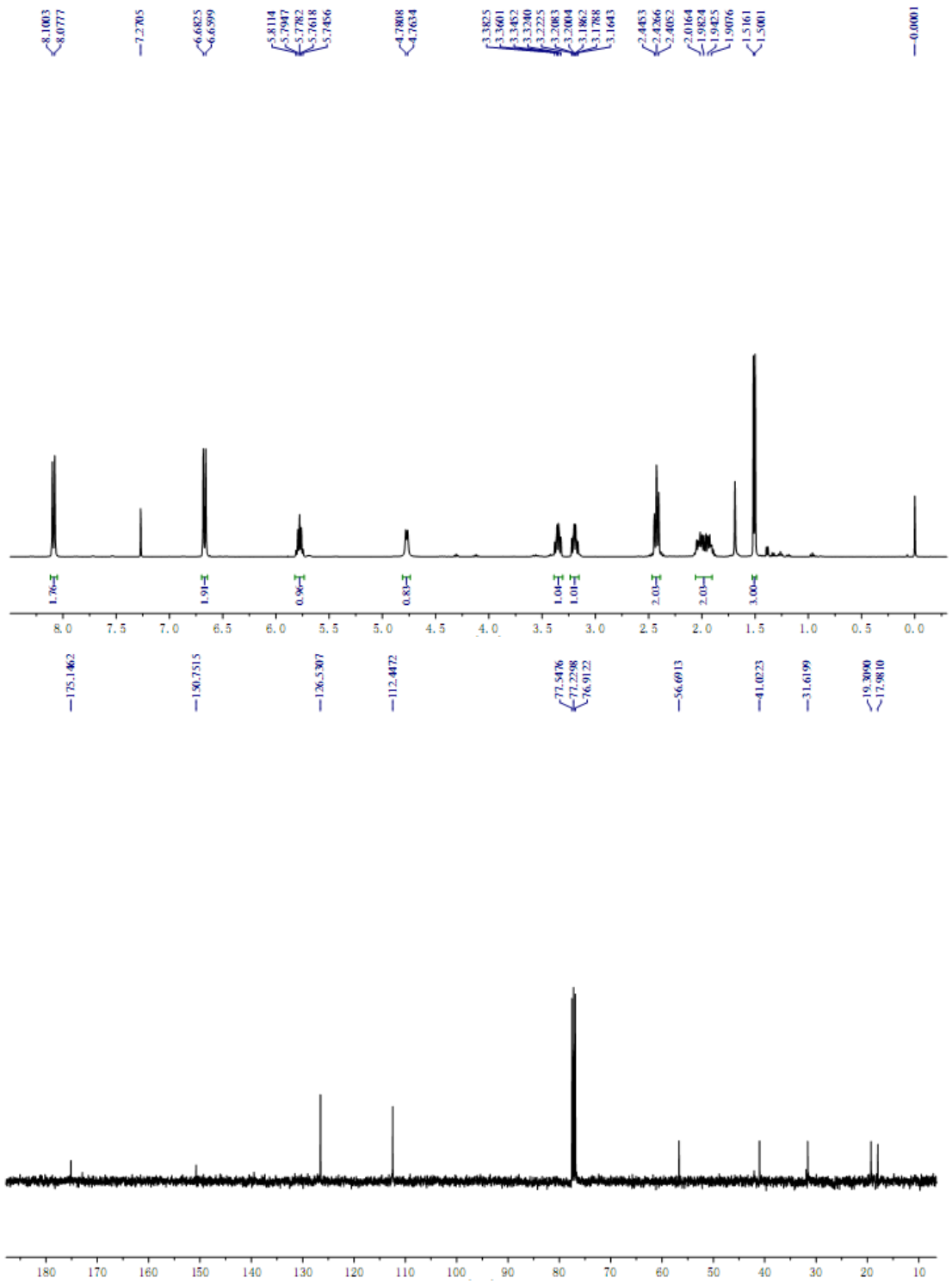




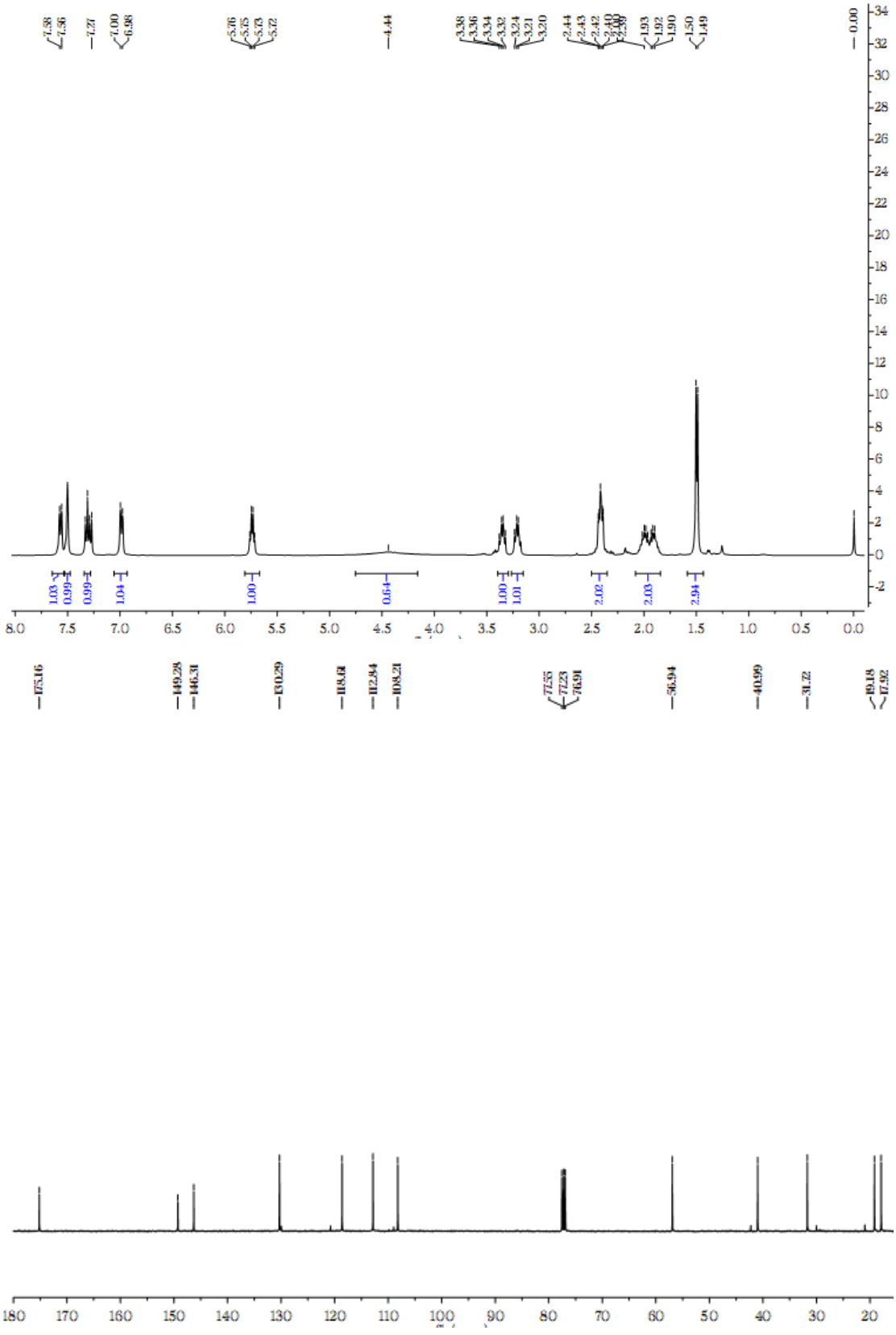
1-(1-(4-acetylphenylamino)ethyl)pyrrolidin-2-one (5af):



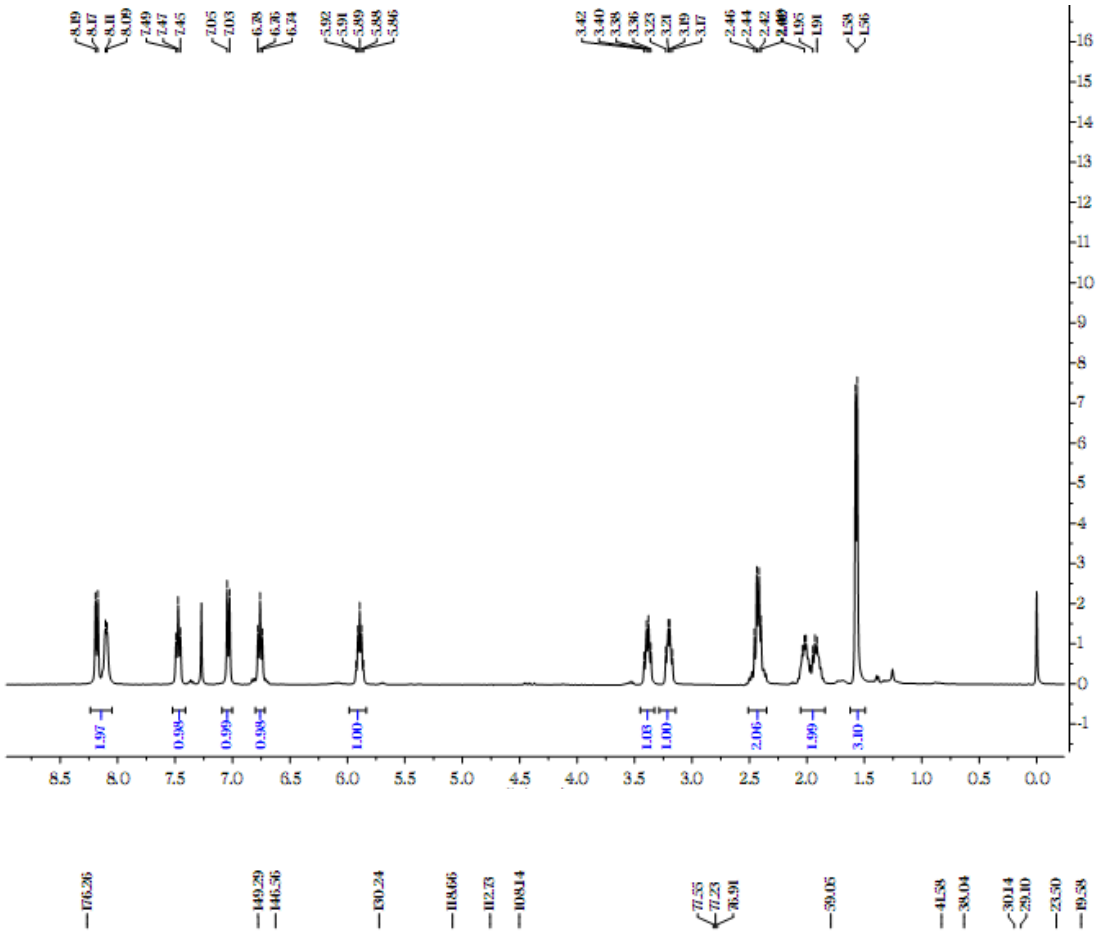
1-(1-(4-nitrophenylamino)ethyl)pyrrolidin-2-one (5ag):

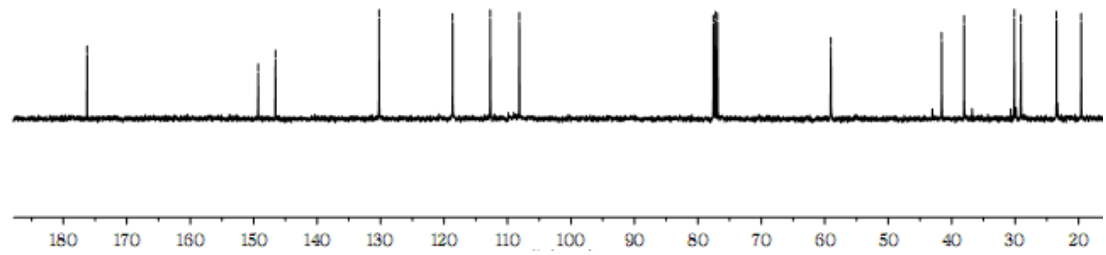


1-(1-(3-nitrophenylamino)ethyl)pyrrolidin-2-one (5ah):

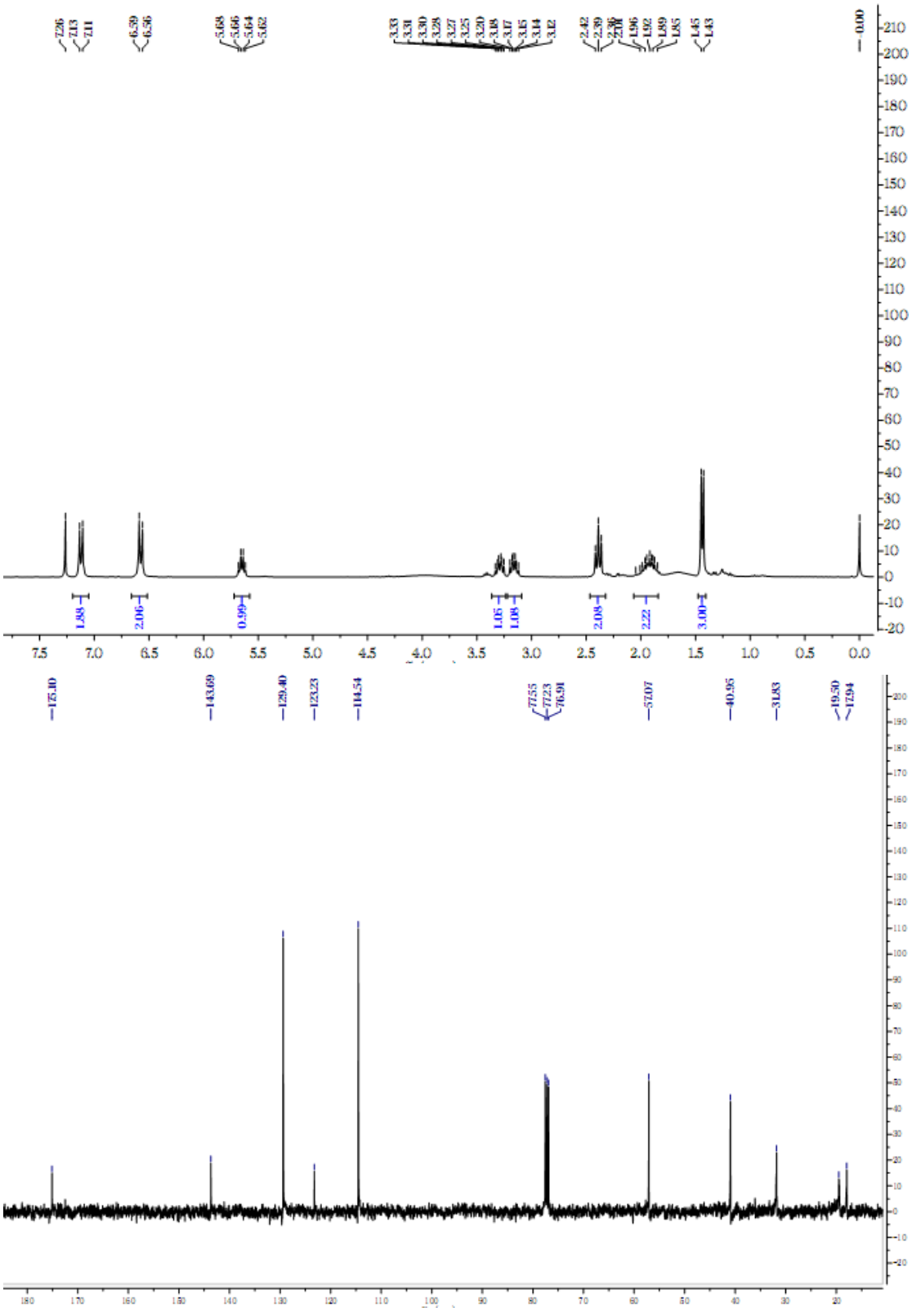


1-(1-(2-nitrophenylamino)ethyl)pyrrolidin-2-one (5ai):

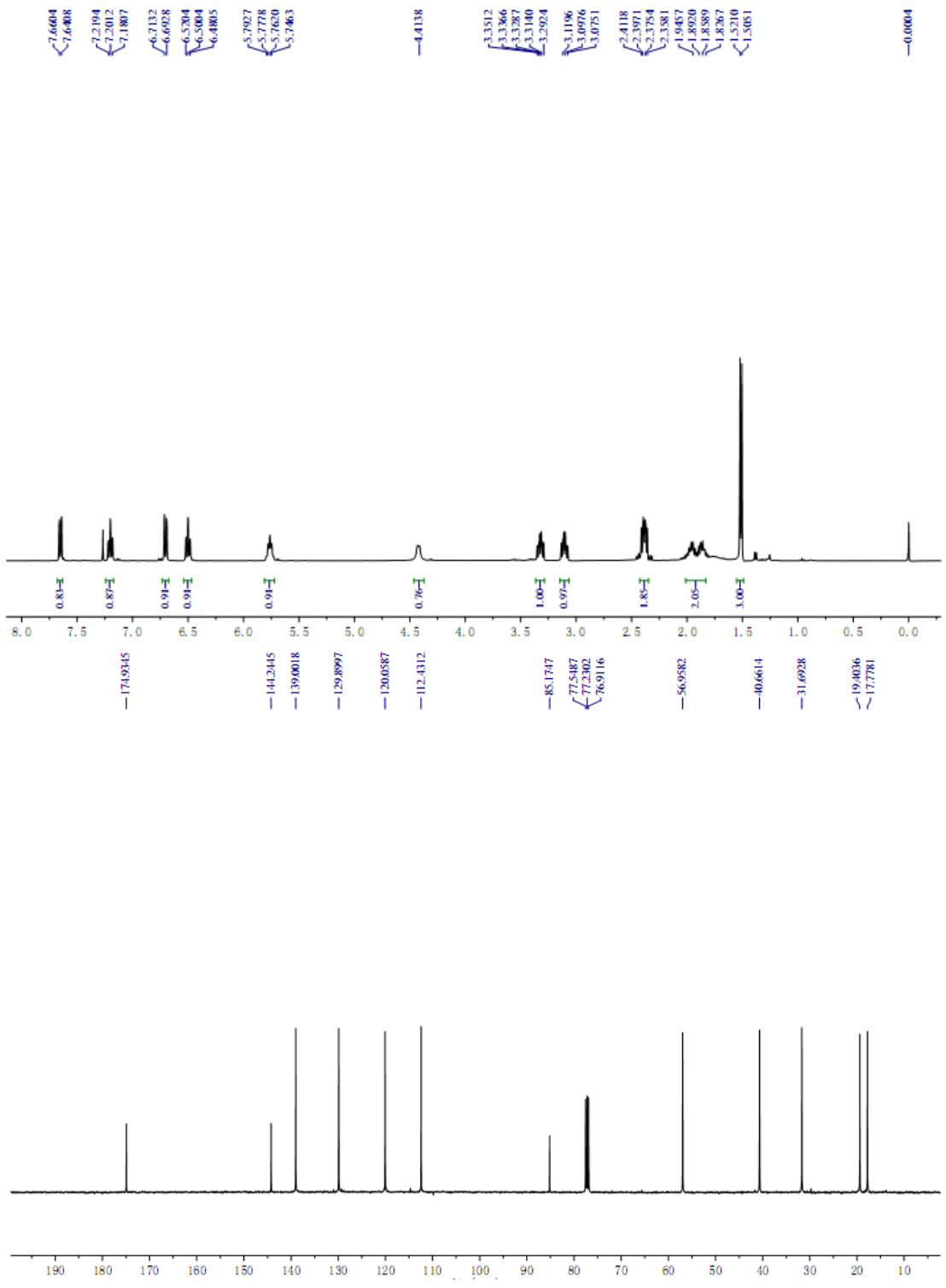




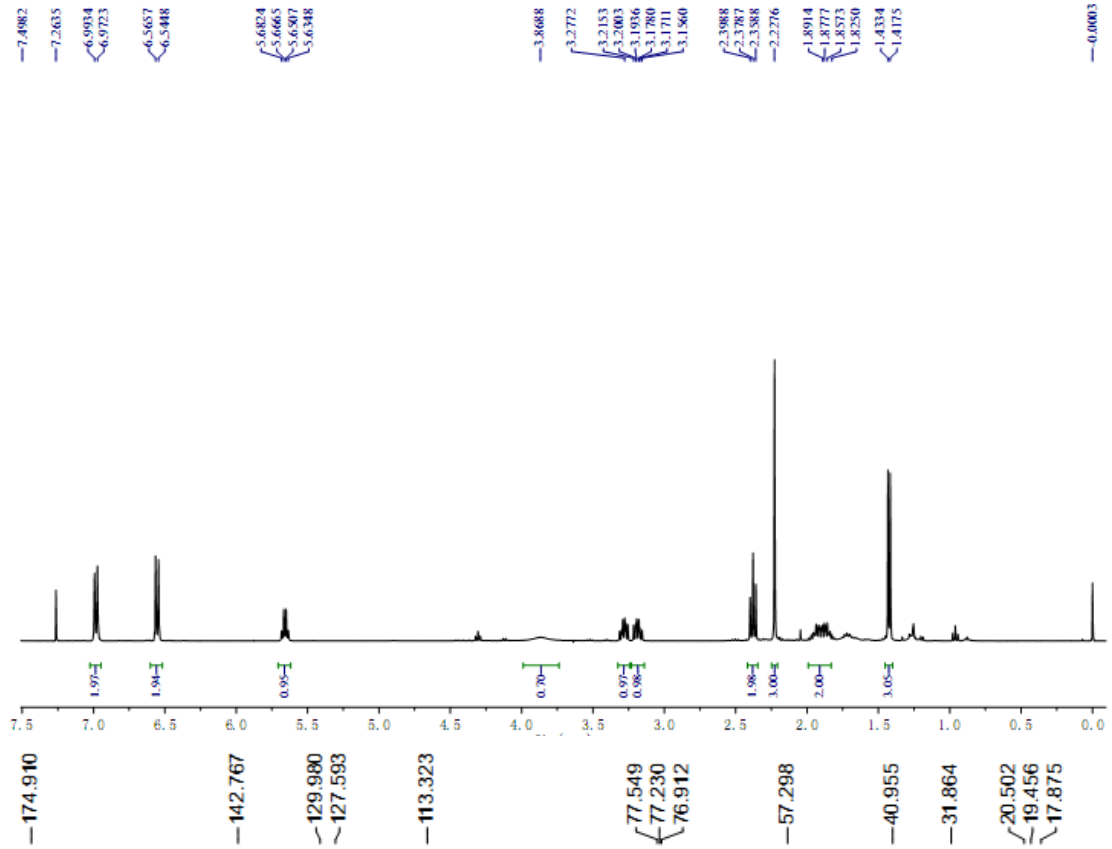
1-(1-((4-chlorophenyl)amino)ethyl)pyrrolidin-2-one (5aj):

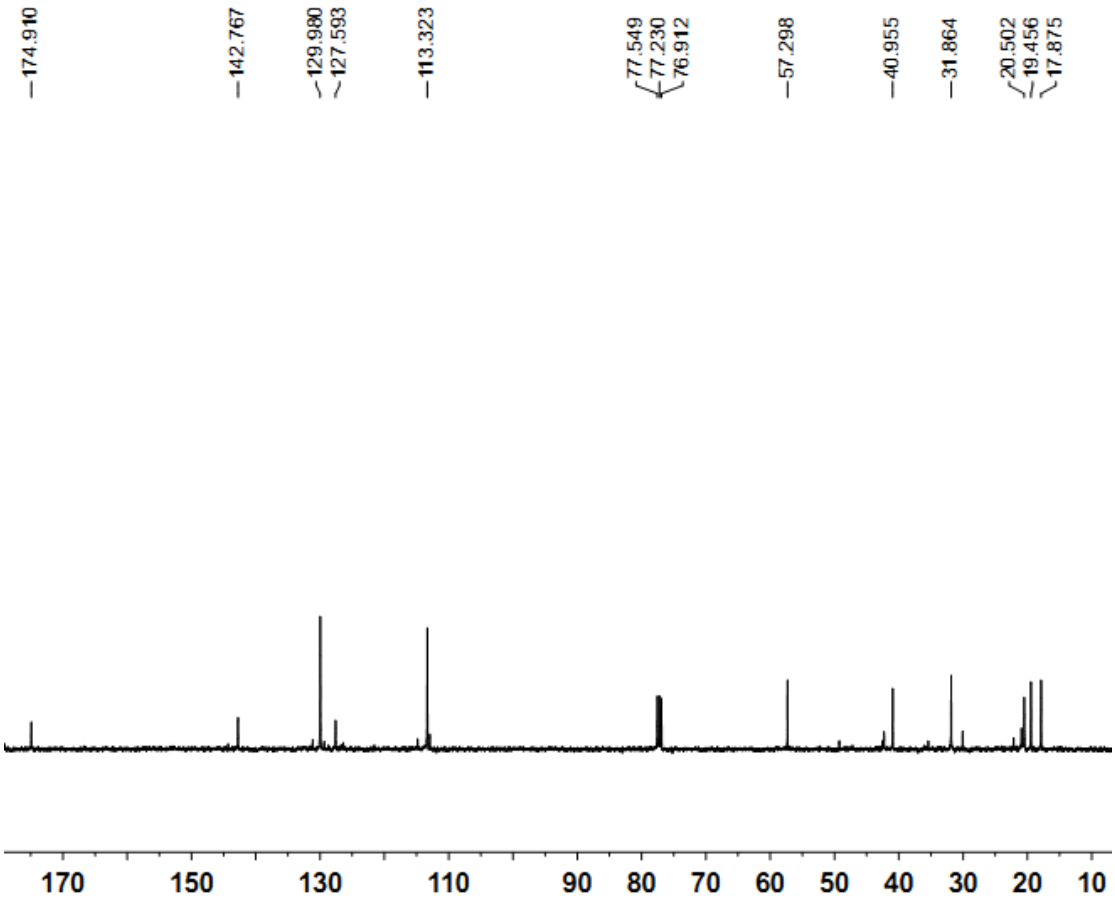


1-(1-(2-iodophenylamino)ethyl)pyrrolidin-2-one (5ak):

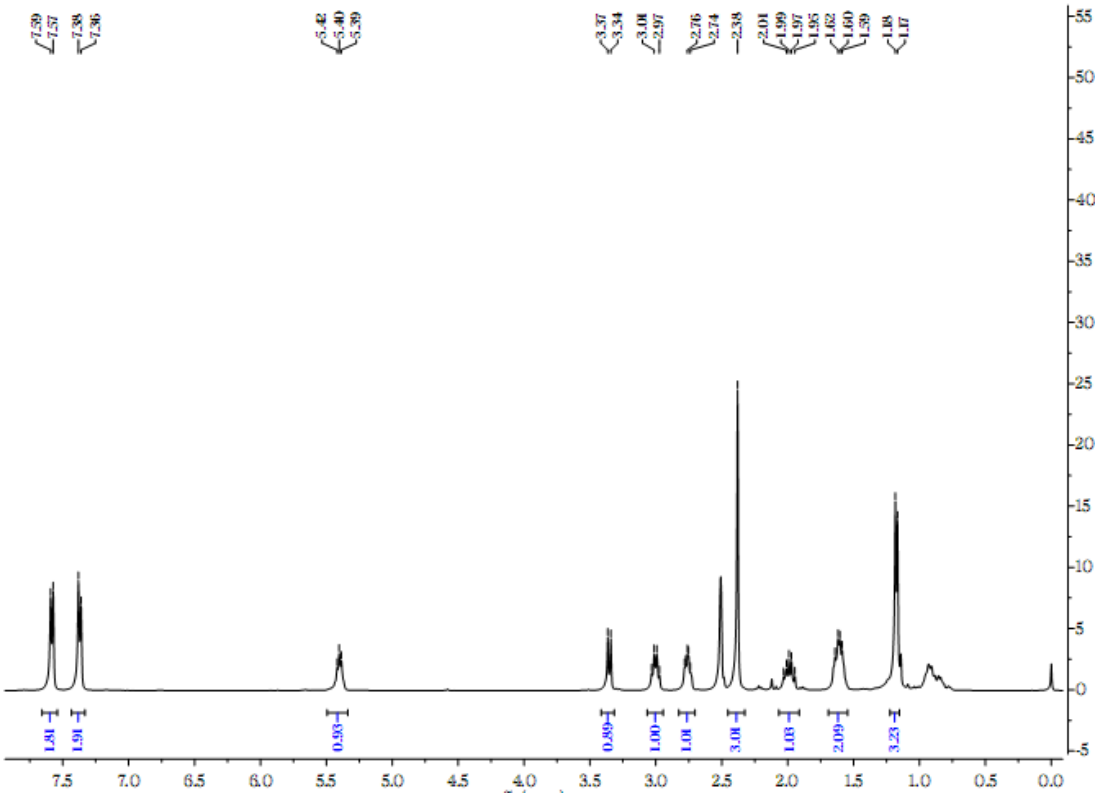


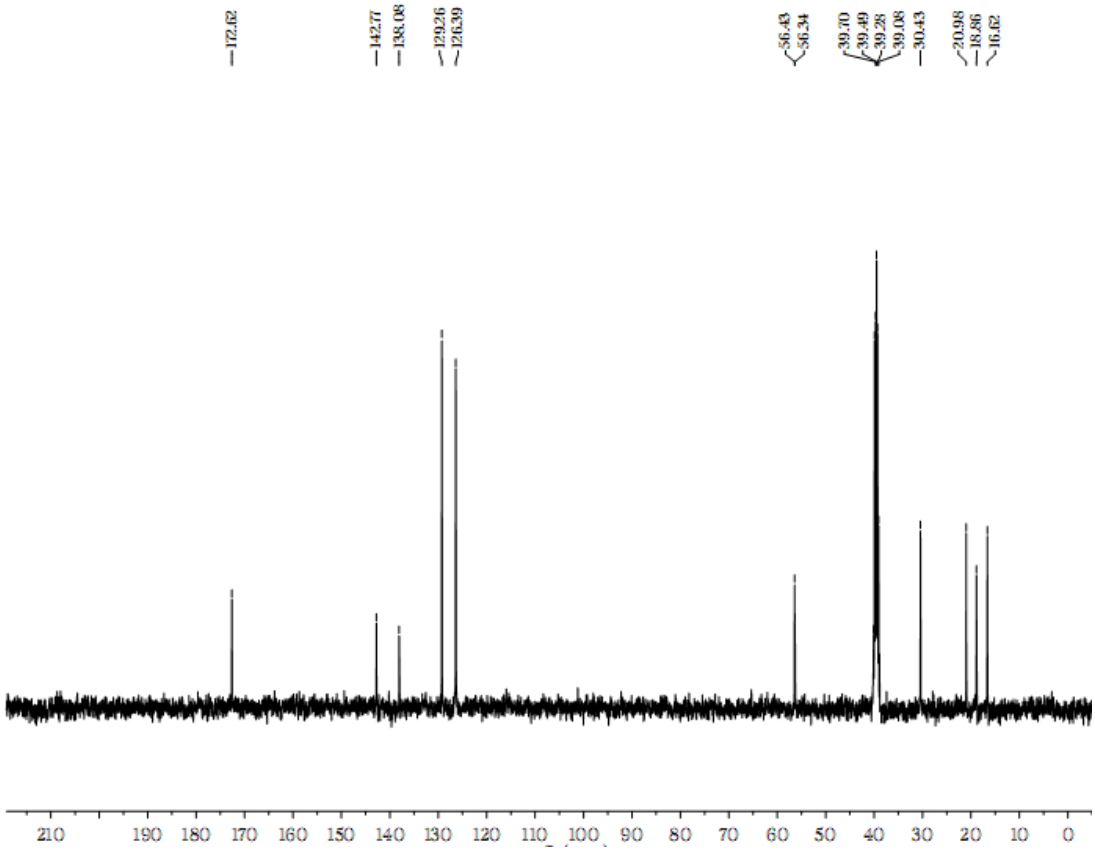
1-(1-(p-tolylamino)ethyl)pyrrolidin-2-one (5al):



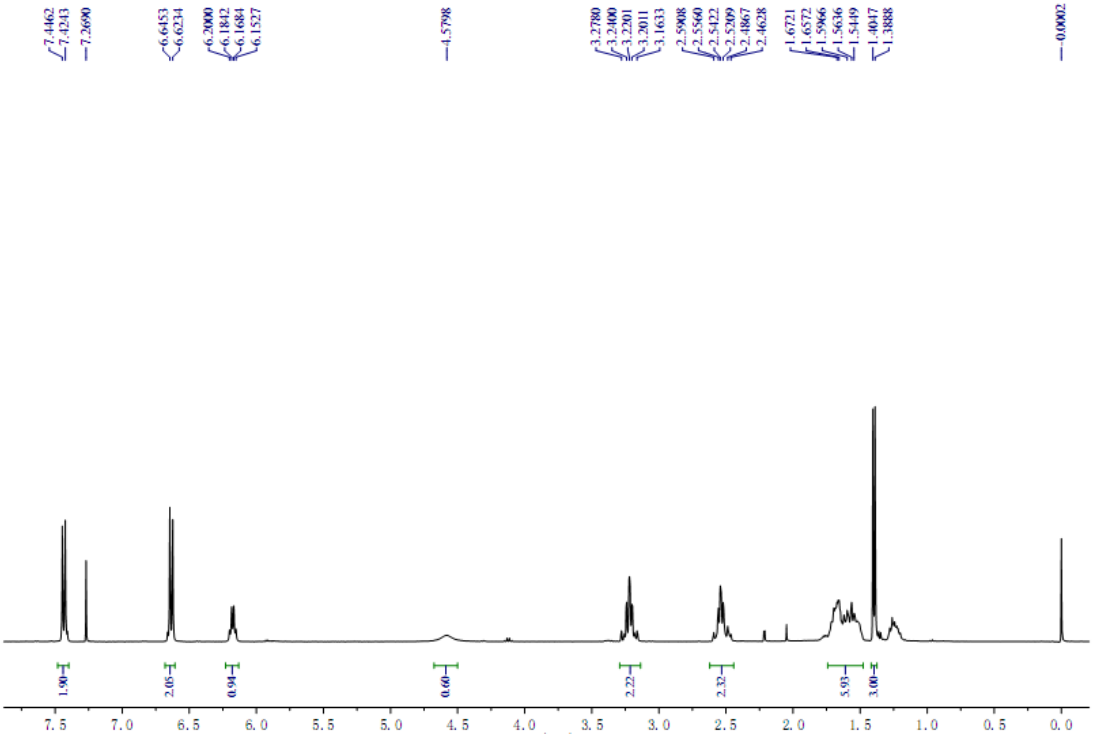


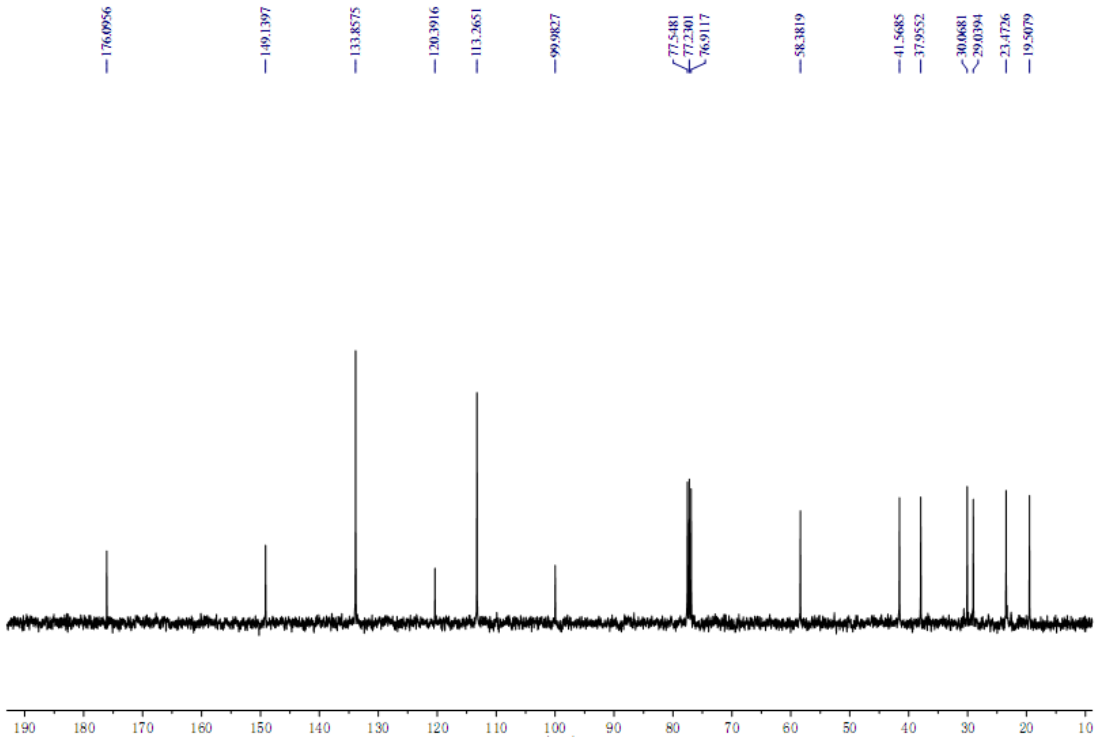
4-methyl-*N*-(1-(2-oxopyrrolidin-1-yl)ethyl)benzenesulfonamide (5an):



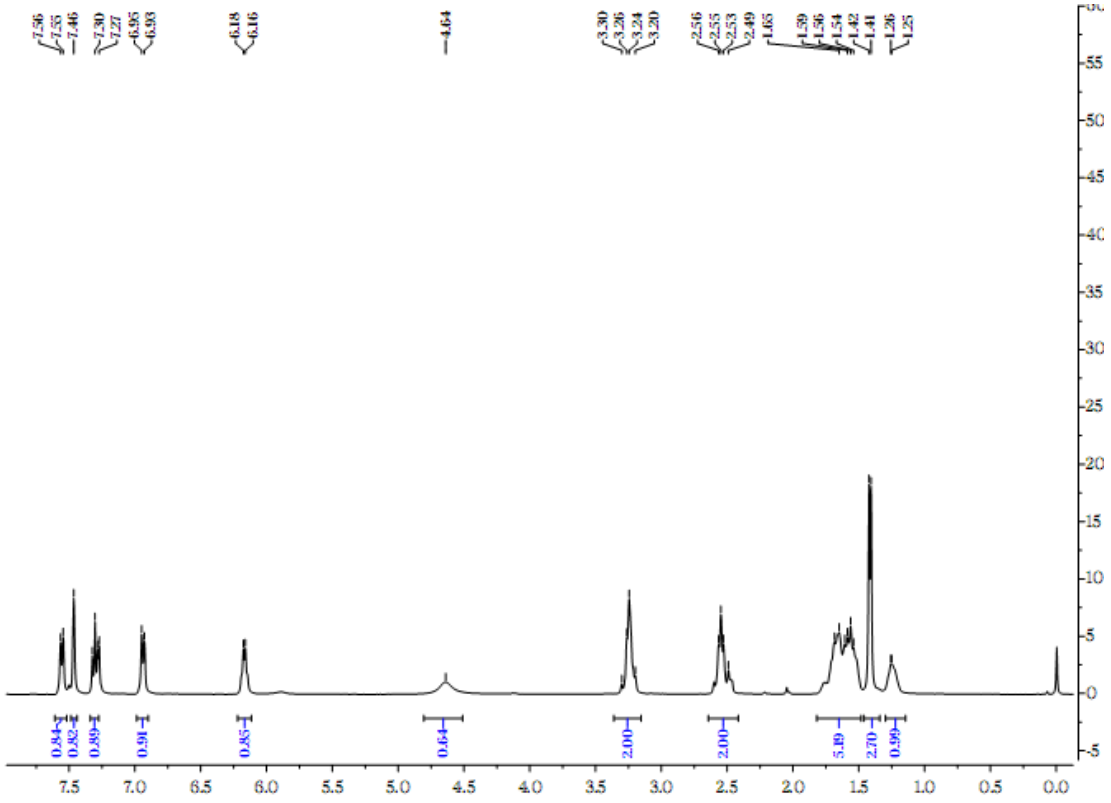


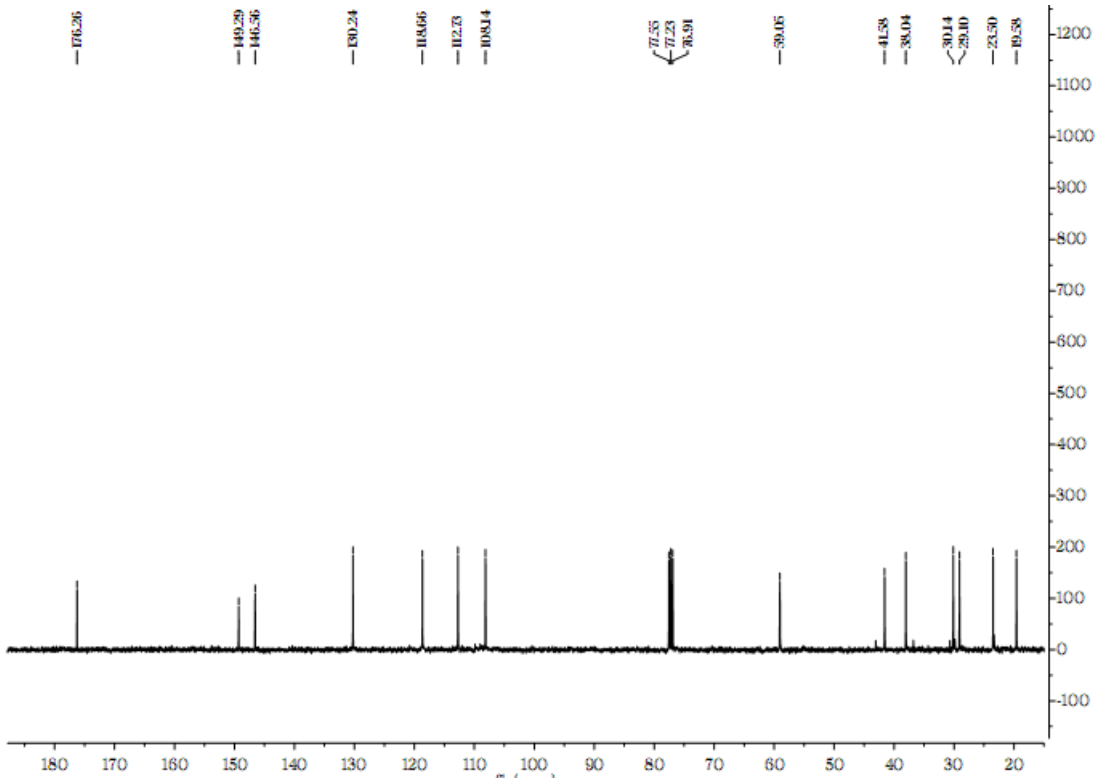
4-(1-(2-oxoazepan-1-yl)ethylamino)benzonitrile (5bd):



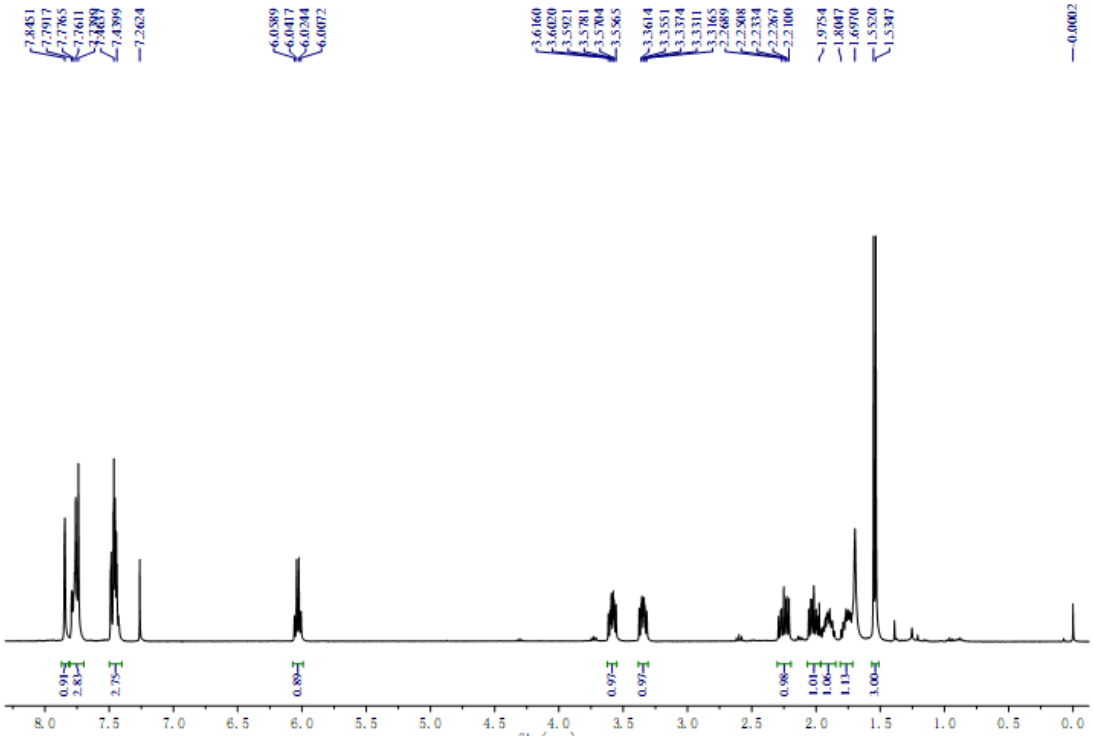


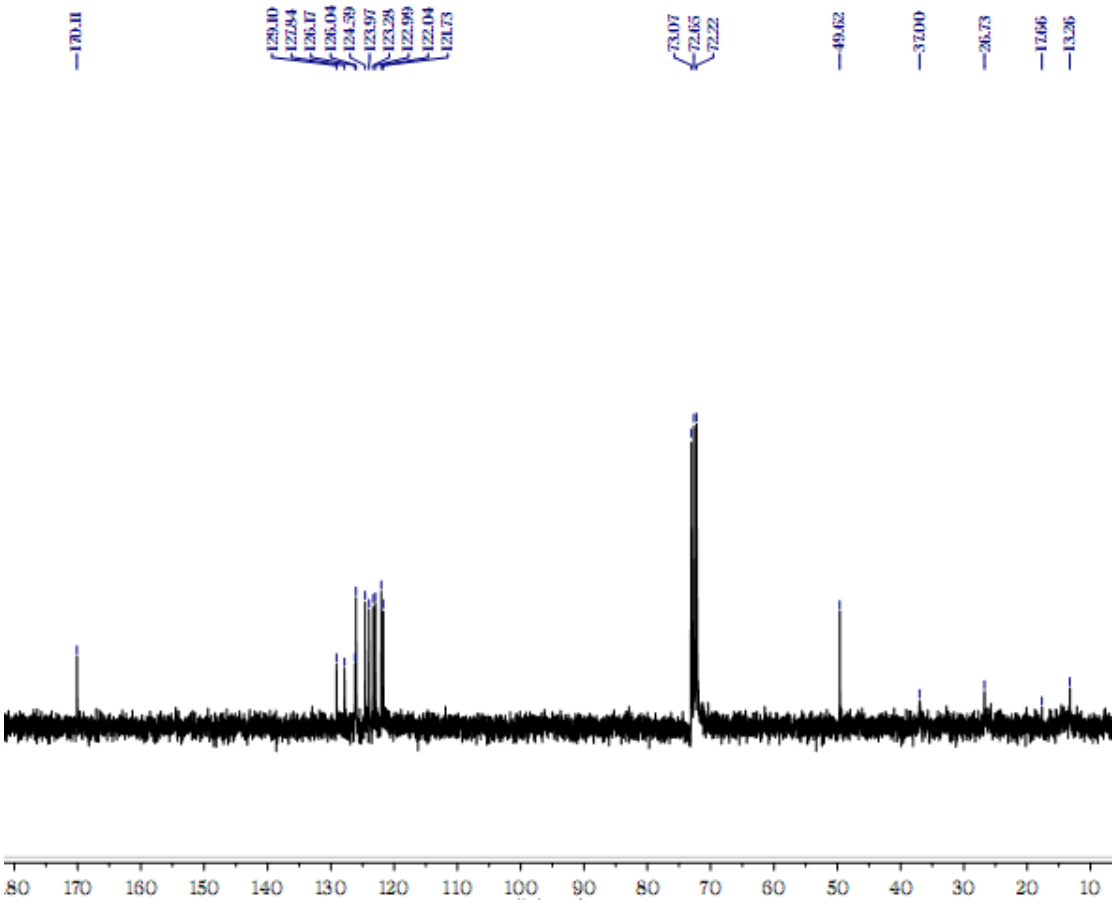
1-(1-(3-nitrophenylamino)ethyl)azepan-2-one (5bh):





1-(1-(naphthalen-2-ylthio)ethyl)pyrrolidin-2-one (6a):





2-(1-(naphthalen-2-ylthio)ethyl)cycloheptanone (6b):