

Article

Eucalyptol as a bio-based solvent for Buchwald-Hartwig reaction on O,S,N-Heterocycles

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Received: date; Accepted: date; Published: date

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1. Materials and Methods

1.1. General Methods

All reagents were purchased from commercial suppliers and were used without further purification. The reactions were monitored by thin-layer chromatography (TLC) analysis using silica gel (60 F254) plates. Compounds were visualized by UV irradiation. Flash column chromatography was performed on silica gel 60 (230 - 400 mesh, 0.040 - 0.063 mm). Melting points (mp [°C]) were taken on samples in open capillary tubes and are uncorrected. ¹H and ¹³C NMR spectra were recorded on a Bruker avance II spectrometer at 250 MHz (¹³C, 62.9 MHz) and on a Bruker avance III HD nanobay 400 MHz (¹³C 100.62 MHz). Chemical shifts are given in parts per million from tetramethylsilane (TMS) or deterred solvent (MeOH-*d*₄, Chloroform-*d*) as internal standard. The following abbreviations are used for the proton spectra multiplicities: b : broad, s: singlet, d: doublet, t: triplet, q: quartet, p: pentuplet, m: multiplet. Coupling constants (J) are reported in Hertz (Hz). Multiplicities were determined by the DEPT 135 sequence. High-resolution mass spectra (HRMS) were performed on a Maxis UHR-q-TOF mass spectrometer Bruker 4G with an electrospray ionisation (ESI) mode.

1.2. General procedure for synthesis of compounds (1a-f, 2a-e, 3a-f, 4a-c, 5a-c)

A mixture of bromo compound (50 mg), amino derivative (2 eq.), Pd(OAc)₂ (0.05 eq.), BINAP (0.1 eq.), Cs₂CO₃ (2 eq.) in Eucalyptol (2 mL) was stirred at 110 °C for time specified and mentioned in Figure 3,5,7 and 9. The reaction was followed by TLC. After completion the reaction was then cooled to room temperature and the mixture was concentrated under vacuum. The solid obtained was purified by flash chromatography using a mixture of AcOEt/petroleum ether.

N-phenyl-9H-fluoren-2-amine (1a) [47]

Gray solid (46 mg, 87 %), m.p. 129 – 131 °C. ¹H NMR (400 MHz, CDCl₃) δ 3.89 (s, 2H), 5.80 (s, 1H), 6.99 (t, J = 7.3 Hz, 1H), 7.13 (t, J = 8.5 Hz, 3H), 7.34 (tt, J = 20.5, 7.4 Hz, 5H), 7.54 (d, J = 7.4 Hz, 1H), 7.72 (dd, J = 11.1, 8.0 Hz, 2H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 37.0 (CH), 114.6 (CH), 117.2 (CH), 117.8 (2xCH), 119.0 (CH), 120.6 (CH), 120.9 (CH), 124.9 (CH), 125.6 (CH), 126.8 (CH), 129.4 (2xCH), 135.3 (C), 141.8 (C), 142.2 (C), 142.7 (C), 143.4 (C), 144.9 (C) ppm.

1-(9H-fluoren-2-yl)piperidine (1b) [48]

Yellow solid (38 mg, 75 %), m.p. 152 – 154 °C. ¹H NMR (400 MHz, CDCl₃) δ 1.61 (q, J = 5.9 Hz, 2H), 1.75 (p, J = 5.7 Hz, 4H), 3.18 – 3.26 (m, 4H), 3.85 (s, 2H), 6.98 (dd, J = 8.4, 2.2 Hz, 1H), 7.12 – 7.16 (m, 1H), 7.20 (td, J = 7.4, 0.9 Hz, 1H), 7.32 (t, J = 7.4 Hz, 1H), 7.48 (d, J = 7.4 Hz, 1H), 7.65 (t, J = 7.3 Hz, 2H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 24.4 (CH), 26.0 (2xCH), 37.1 (CH), 51.3 (2xCH), 113.3 (CH), 115.7 (CH), 118.8 (CH), 120.2 (CH), 124.7 (CH), 125.2 (CH), 126.6 (CH), 133.5 (C), 142.1 (C), 142.6 (C), 144.6 (C), 151.9 (C) ppm

N-(4-methoxyphenyl)-9H-fluoren-2-amine (1c)

Brown solid (35 mg, 60 %), m.p. 130 – 132 °C. ¹H NMR (400 MHz, CDCl₃) δ 3.83 (s, 5H), 5.57 (s, 1H), 6.90 (d, J = 8.8 Hz, 3H), 7.11 (s, 3H), 7.22 (t, J = 7.3 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 7.49 (d, J = 7.4 Hz, 1H), 7.65 (dd, J = 17.4, 7.9 Hz, 2H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 37.0 (CH), 55.6 (CH), 112.3 (C), 114.8 (2xCH), 115.0 (C), 118.8 (CH), 122.2 (2xCH), 120.6 (CH), 124.8 (2xCH), 125.3 (CH), 126.7 (2xCH), 135.9 (C), 142.0 (C), 142.5 (C), 145.0 (C), 155.3 (C) ppm. HRMS: calcd for C₂₀H₁₈NO [M+H]⁺ 288.1383, found 288.1379.

***N*-(4-(trifluoromethyl)phenyl)-9*H*-fluoren-2-amine (1d)**

Yellow solid (44 mg, 66 %), m.p. 117 – 119 °C. HRMS: calcd for C₂₀H₁₅F₃N [M+H]⁺ 326.1151, found 326.1150. ¹H NMR (400 MHz, CDCl₃) δ 3.89 (s, 2H), 5.97 (s, 1H), 7.06 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.37 (dd, *J* = 15.0, 7.5 Hz, 2H), 7.51 (dd, *J* = 16.3, 8.0 Hz, 3H), 7.72 (d, *J* = 2.9 Hz, 2H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 37.0 (CH), 115.3 (2xCH), 117.0 (CH), 119.4 (2xCH), 120.7 (CH), 121.3 (C), 123.3 (C), 125.0 (CH), 126.2 (CH), 126.8 (CH), 126.9 (2xCH), 137.2 (C), 140.0 (C), 141.4 (C), 142.9 (C), 144.9 (C), 147.1 (C) ppm. ¹⁹F NMR (376 MHz, CDCl₃) δ - 61.38 ppm.

***N*-(naphthalen-1-yl)-9*H*-fluoren-2-amine (1e) [49]**

Gray solid (55 mg, 88 %), m.p. 139 – 141 °C. ¹H NMR (400 MHz, CDCl₃) δ 3.88 (s, 2H), 6.07 (s, 1H), 7.05 – 7.11 (m, 1H), 7.22 (s, 1H), 7.29 (d, *J* = 6.8 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.46 (q, *J* = 6.9, 6.4 Hz, 2H), 7.50 – 7.59 (m, 3H), 7.63 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.70 – 7.76 (m, 2H), 7.91 – 7.96 (m, 1H), 8.10 (d, *J* = 8.0 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 37.0 (CH), 114.2 (CH), 115.8 (CH), 116.7 (CH), 118.9 (CH), 120.7 (CH), 121.8 (CH), 122.9 (CH), 124.8 (CH), 125.5 (CH), 125.7 (CH), 126.1 (CH), 126.2 (CH), 126.7 (CH), 127.7 (C), 128.6 (CH), 134.8 (C), 134.9 (C), 139.1 (C), 141.9 (C), 142.6 (C), 143.9 (C), 145.0 (C) ppm.

Methyl 2-((9*H*-fluoren-2-yl)amino)-5-ethylthiophene-3-carboxylate (1f)

Brown solid (35 mg, 49 %), m.p. 109 – 111 °C. ¹H NMR (400 MHz, CDCl₃) δ 1.30 (t, *J* = 7.5 Hz, 3H), 2.71 (q, *J* = 8.0, 7.5 Hz, 2H), 3.90 (d, *J* = 19.9 Hz, 5H), 6.82 (s, 1H), 7.27 – 7.32 (m, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.48 – 7.56 (m, 2H), 7.74 (t, *J* = 7.5 Hz, 2H), 9.90 (s, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 15.4 (CH), 23.0 (CH), 37.1 (CH), 51.1 (CH), 106.4 (C), 114.8 (CH), 117.3 (CH), 119.3 (CH), 120.3 (CH), 120.6 (CH), 124.9 (CH), 126.1 (CH), 126.8 (CH), 128.4 (C), 136.8 (C), 140.0 (C), 141.4 (C), 142.9 (C), 144.9 (C), 157.2 (C), 166.3 (C) ppm. HRMS: calcd for C₂₁H₂₀NO₂S [M+H]⁺ 350.1209, found 350.1203.

***N*-phenylbenzo[*d*][1,3]dioxol-5-amine (2a) [50]**

Red solid (41 mg, 77 %), m.p. 151 – 153 °C. ¹H NMR (400 MHz, CDCl₃) δ 5.47 (s, 1H), 5.94 (s, 2H), 6.58 (d, *J* = 8.2 Hz, 1H), 6.70 – 6.79 (m, 2H), 6.89 (d, *J* = 7.3 Hz, 1H), 6.96 (d, *J* = 8.1 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 2H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 101.1 (CH), 102.6 (CH), 108.6 (CH), 113.0 (CH), 116.4 (2xCH), 120.1 (CH), 129.4 (2xCH), 137.4 (C), 142.9 (C), 144.7 (C), 148.3 (C) ppm.

1-(benzo[*d*][1,3]dioxol-5-yl)piperidine (2b) [51]

Red oil (22 mg, 43 %). ¹H NMR (400 MHz, CDCl₃) δ 1.55 (q, *J* = 5.6 Hz, 2H), 1.67 – 1.75 (m, 4H), 2.98 – 3.03 (m, 4H), 5.88 (s, 2H), 6.39 (d, *J* = 7.8 Hz, 1H), 6.58 (s, 1H), 6.71 (d, *J* = 8.4 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 24.1 (CH), 26.0 (2xCH), 29.7 (C), 52.5 (2xCH), 100.5 (CH), 100.8 (CH), 108.1 (CH), 109.6 (CH), 141.3 (C), 148.1 (C) ppm.

***N*-(4-methoxyphenyl)benzo[*d*][1,3]dioxol-5-amine (2c) [50]**

Red oil (49 mg, 81%). ¹H NMR (400 MHz, CDCl₃) δ 3.78 (s, 3H), 5.90 (s, 2H), 6.42 (s, 1H), 6.56 (s, 1H), 6.69 (d, *J* = 8.3 Hz, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 2H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 55.6 (CH), 59.2 (CH), 100.2 (CH), 100.9 (CH), 108.6 (CH), 110.0 (C), 114.8 (2xCH), 120.6 (2xCH), 122.0 (C), 141.8 (C), 148.3 (C), 154.8 (C) ppm.

***N*-(4-(trifluoromethyl)phenyl)benzo[*d*][1,3]dioxol-5-amine (2d)**

Red oil (45 mg, 65%). ¹H NMR (400 MHz, CDCl₃) δ 6.35 – 6.37 (m, 2H), 7.03 – 7.16 (m, 3H), 7.32 (d, *J* = 8.5 Hz, 2H), 7.63 – 7.68 (m, 1H), 7.81 (d, *J* = 8.5 Hz, 2H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 148.0 (C), 147.0 (C), 144.2 (C), 133.2 (C), 126.6 (CH), 123.6 (C), 114.6 (CH), 113.3 (C), 110.9 (CH), 108.7 (CH),

104.5 (CH), 102.9 (CH), 101.6 (CH), 101.4 (CH) ppm. ^{19}F NMR (376 MHz, CDCl_3) δ -61.61 ppm. HRMS: calcd for $\text{C}_{14}\text{H}_{11}\text{F}_3\text{NO}_2$ $[\text{M}+\text{H}]^+$ 282.0736, found 282.0733.

***N*-(naphthalen-1-yl)benzo[*d*][1,3]dioxol-5-amine (2e)**

(Aurora Building Blocks, United States [CAS: 1511731-00-2]): red oil (61 mg, 93%). ^1H NMR (400 MHz, CDCl_3) δ 5.95 (s, 2H), 6.52 (dd, J = 8.2, 2.2 Hz, 1H), 6.67 (d, J = 2.2 Hz, 1H), 6.76 (d, J = 8.2 Hz, 1H), 7.18 (d, J = 6.8 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.46 – 7.54 (m, 3H), 7.86 (dd, J = 6.7, 2.6 Hz, 1H), 7.97 – 8.02 (m, 1H), ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 101.1 (CH), 102.1 (CH), 108.6 (CH), 112.3 (CH), 113.2 (CH), 121.3 (CH), 121.6 (CH), 125.5 (CH), 126.1 (CH), 126.1 (CH), 126.5 (C), 128.6 (CH), 134.7 (C), 138.8 (C), 140.3 (C), 142.6 (C), 148.3 (C) ppm.

2-methyl-*N*-phenylquinolin-6-amine (3a) [52]

White solid (44 mg, 84%), m.p. 165 – 167 °C. ^1H NMR (400 MHz, CDCl_3) δ 2.69 (s, 3H), 6.04 (s, 1H), 7.00 (t, J = 7.3 Hz, 1H), 7.18 (t, J = 8.2 Hz, 3H), 7.29 – 7.35 (m, 3H), 7.39 (d, J = 9.1 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 9.0 Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 25.0 (CH), 110.2 (CH), 118.6 (2xCH), 121.8 (CH), 122.4 (CH), 123.1 (CH), 127.6 (C), 129.5 (2xCH), 129.7 (CH), 134.7 (CH), 140.9 (C), 142.6 (C), 143.9 (C), 156.1 (C) ppm.

2-methyl-6-(piperidin-1-yl)quinoline (3b)

(Aurora Building Blocks, United States [CAS: 1266871-97-9]): yellow solid (47 mg, 92%), m.p. 91 – 93 °C. ^1H NMR (400 MHz, CDCl_3) δ 1.61 (q, J = 5.9 Hz, 2H), 1.71 – 1.78 (m, 4H), 2.67 (s, 3H), 3.22 – 3.27 (m, 4H), 6.99 (s, 1H), 7.16 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 9.3 Hz, 1H), 7.83 – 7.89 (m, 2H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 24.3 (CH), 25.0 (CH), 25.8 (2xCH), 50.8 (2xCH), 109.3 (CH), 122.0 (CH), 123.2 (CH), 127.5 (C), 129.0 (CH), 134.9 (CH), 143.2 (C), 149.7 (C), 155.6 (C) ppm.

***N*-(4-methoxyphenyl)-2-methylquinolin-6-amine (3c) [52]**

Yellow oil (60 mg, 99%). ^1H NMR (400 MHz, CDCl_3) δ 2.66 (s, 3H), 3.81 (s, 3H), 5.87 (s, 1H), 6.92 – 6.87 (m, 2H), 7.08 (d, J = 2.6 Hz, 1H), 7.12 – 7.17 (m, 3H), 7.26 (dd, J = 9.0, 2.6 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 9.0 Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 24.9 (CH), 55.6 (CH), 107.4 (CH), 114.8 (2xCH), 122.0 (CH), 122.3 (CH), 122.9 (2xCH), 127.8 (C), 129.6 (CH), 134.5 (CH), 135.2 (C), 142.9 (C), 143.4 (C), 155.4 (C), 155.7 (C) ppm.

2-methyl-*N*-(4-(trifluoromethyl)phenyl)quinolin-6-amine (3d)

Yellow solid (42 mg, 61%), m.p. 180 – 182 °C. ^1H NMR (400 MHz, CDCl_3) δ 2.74 (s, 3H), 6.34 (s, 1H), 7.22 (dd, J = 41.9, 8.8 Hz, 3H), 7.41 – 7.61 (m, 4H), 7.95 (dd, J = 24.4, 9.1 Hz, 2H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 157.3 (C), 146.3 (C), 144.6 (C), 138.8 (C), 135.0 (CH), 130.0 (CH), 127.4 (C), 126.8 (2xCH), 125.9 (C), 124.1 (CH), 123.2 (C), 122.6 (CH), 116.1 (2xCH), 113.6 (CH), 25.1 (CH) ppm. ^{19}F NMR (235 MHz, CDCl_3) δ -61.54 ppm. HRMS: calcd for $\text{C}_{17}\text{H}_{14}\text{F}_3\text{N}_2$ $[\text{M}+\text{H}]^+$ 303.1104, found 303.1102.

2-methyl-*N*-(naphthalen-1-yl)quinolin-6-amine (3e)

Yellow oil (63 mg, 98%). ^1H NMR (400 MHz, CDCl_3) δ 2.69 (s, 3H), 6.18 (s, 1H), 7.06 (d, J = 2.4 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H), 7.35 – 7.61 (m, 5H), 7.65 (t, J = 4.6 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.92 (dd, J = 16.5, 8.6 Hz, 2H), 8.04 (d, J = 8.3 Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 155.9 (C), 143.7 (C), 142.7 (C), 138.2 (C), 134.7 (CH), 129.7 (CH), 128.6 (CH), 128.3 (C), 126.3 (CH), 126.0 (CH), 124.0 (C), 122.7 (CH), 122.3 (CH), 122.0 (CH), 117.4 (CH), 109.9 (CH), 25.0 (CH) ppm. HRMS: calcd for $\text{C}_{20}\text{H}_{17}\text{N}_2$ $[\text{M}+\text{H}]^+$ 285.1386, found 285.1383.

Methyl 5-ethyl-2-((2-methylquinolin-6-yl)amino)thiophene-3-carboxylate (3f)

Yellow oil (73 mg, 99%). ¹H NMR (400 MHz, CDCl₃) δ 1.28 (t, *J* = 7.5 Hz, 3H), 2.70 (d, *J* = 6.1 Hz, 5H), 3.84 (s, 3H), 6.81 (s, 1H), 7.23 (d, *J* = 8.5 Hz, 1H), 7.48 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.61 (d, *J* = 2.0 Hz, 1H), 7.94 (d, *J* = 9.4 Hz, 2H), 10.04 (s, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 15.4 (CH), 23.0 (CH), 25.1 (CH), 51.2 (CH), 107.5 (C), 111.1 (CH), 120.3 (CH), 122.6 (CH), 123.1 (CH), 127.2 (C), 129.0 (C), 130.0 (CH), 135.2 (CH), 138.2 (C), 144.4 (C), 155.8 (C), 157.2 (C), 166.2 (C) ppm. HRMS: calcd for C₁₈H₁₉N₂O₂S [M+H]⁺ 327.1162, found 327.1161.

***N*,2-diphenylthieno[3,2-*b*]pyridin-3-amine (4a)**

Orange solid (32 mg, 62%), m.p. 137 – 139 °C. ¹H NMR (400 MHz, CDCl₃) δ 6.73 (s, 1H), 6.79 (t, *J* = 8.2 Hz, 3H), 7.09 (t, *J* = 7.9 Hz, 2H), 7.28 – 7.36 (m, 4H), 7.67 – 7.71 (m, 2H), 8.15 (dd, *J* = 8.1, 1.3 Hz, 1H), 8.67 (dd, *J* = 4.6, 1.3 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 116.2 (2xCH), 119.6 (CH), 120.0 (CH), 127.8 (2xCH), 128.1 (CH), 128.6 (2xCH), 128.7 (3xCH), 130.0 (C), 130.3 (CH), 131.5 (C), 133.6 (C), 143.4 (2xC), 146.7 (CH), 151.6 (C) ppm. HRMS: calcd for C₁₉H₁₅N₂S [M+H]⁺ 303.0950, found 303.0947.

2-phenyl-3-(piperidin-1-yl)thieno[3,2-*b*]pyridine (4b)

Orange solid (34 mg, 68%), m.p. 82 – 84 °C. ¹H NMR (400 MHz, CDCl₃) δ 1.58 – 1.63 (m, 2H), 1.70 (s, 4H), 3.28 – 3.32 (m, 4H), 7.18 (dd, *J* = 8.1, 4.6 Hz, 1H), 7.34 – 7.39 (m, 1H), 7.41 – 7.45 (m, 2H), 7.76 – 7.79 (m, 2H), 8.02 (dd, *J* = 8.1, 1.5 Hz, 1H), 8.67 (dd, *J* = 4.6, 1.5 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 24.4 (CH), 26.7 (2xCH), 52.5 (2xCH), 118.4 (CH), 128.1 (CH), 128.1 (2xCH), 129.4 (2xCH), 130.1 (CH), 131.4 (C), 132.9 (C), 134.7 (C), 141.8 (C), 146.3 (CH), 153.6 (C) ppm. HRMS: calcd for C₁₈H₁₉N₂S [M+H]⁺ 295.1263, found 295.1261.

***N*-(4-methoxyphenyl)-2-phenylthieno[3,2-*b*]pyridin-3-amine (4c)**

Orange oil (57 mg, 99%). ¹H NMR (400 MHz, CDCl₃) δ 3.72 (s, 3H), 6.64 – 6.68 (m, 2H), 6.72 – 6.77 (m, 3H), 7.24 – 7.34 (m, 4H), 7.63 – 7.66 (m, 2H), 8.13 (dd, *J* = 8.1, 1.3 Hz, 1H), 8.67 (dd, *J* = 4.6, 1.4 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 55.5 (CH), 114.1 (2xCH), 118.1 (2xCH), 119.6 (2xCH), 127.2 (C), 127.8 (2xCH), 128.5 (2xCH), 130.3 (CH), 130.9 (C), 131.6 (C), 133.7 (C), 136.8 (C), 146.5 (CH), 151.4 (C), 153.9 (C) ppm. HRMS: calcd for C₂₀H₁₇N₂OS [M+H]⁺ 333.1056, found 333.1059.

***N*,6-diphenylthieno[2,3-*b*]pyrazin-7-amine (5a)**

Orange solid (52 mg, 99%), m.p. 149 – 151 °C. ¹H NMR (400 MHz, CDCl₃) δ 6.40 (s, 1H), 6.74 (d, *J* = 8.0 Hz, 3H), 7.08 – 7.17 (m, 2H), 7.29 – 7.37 (m, 3H), 7.68 (d, *J* = 7.2 Hz, 2H), 8.50 (d, *J* = 2.3 Hz, 1H), 8.58 (d, *J* = 2.3 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 115.1 (CH), 116.0 (2xCH), 118.5 (CH), 120.3 (CH), 128.1 (2xCH), 128.9 (3xCH), 129.3 (CH), 132.5 (C), 132.9 (C), 140.9 (CH), 141.3 (CH), 143.5 (C), 146.2 (C), 146.4 (C), 154.0 (C) ppm. HRMS: calcd for C₁₈H₁₄N₃S [M+H]⁺ 304.0903, found 304.0899.

6-phenyl-7-(piperidin-1-yl)thieno[2,3-*b*]pyrazine (5b)

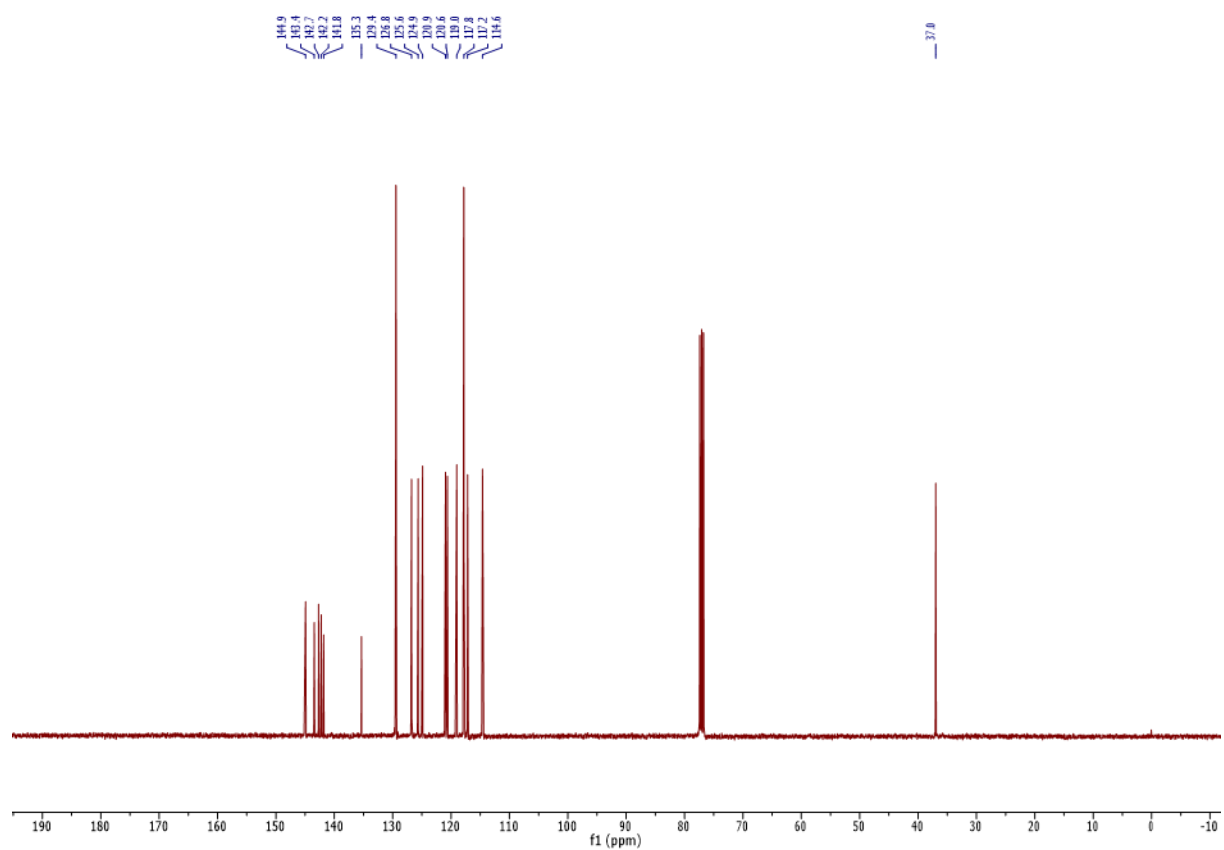
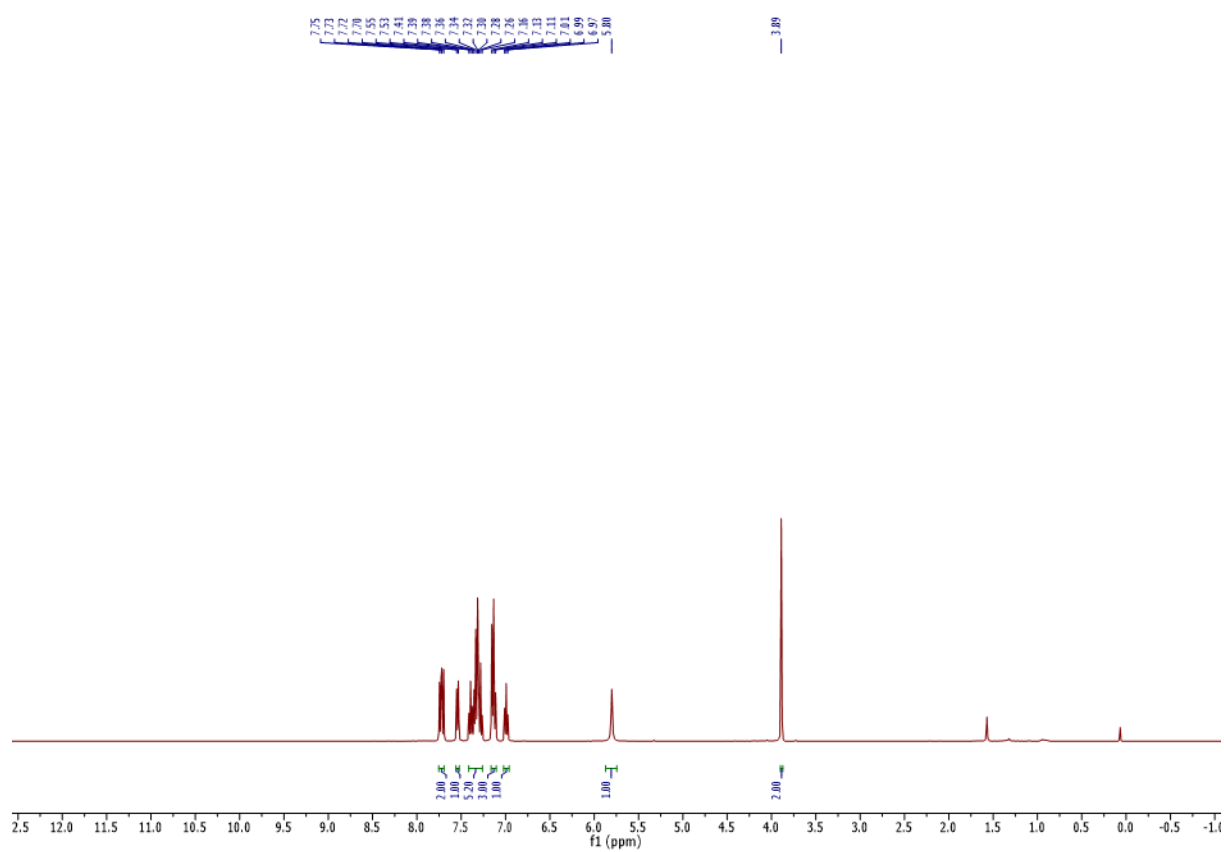
Yellow solid (47 mg, 93%), m.p. 128 – 130 °C. ¹H NMR (400 MHz, CDCl₃) δ 1.60 (t, *J* = 7.6 Hz, 2H), 1.67 (q, *J* = 5.3 Hz, 4H), 3.25 (d, *J* = 5.5 Hz, 4H), 7.37 – 7.47 (m, 3H), 7.78 – 7.81 (m, 2H), 8.41 (d, *J* = 2.4 Hz, 1H), 8.59 (d, *J* = 2.4 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 24.3 (CH), 26.6 (2xCH), 52.5 (2xCH), 128.3 (2xCH), 128.5 (CH), 129.3 (2xCH), 133.5 (C), 134.1 (C), 139.4 (C), 139.7 (CH), 140.6 (CH), 147.9 (C), 153.6 (C) ppm. HRMS: calcd for C₁₇H₁₈N₃S [M+H]⁺ 296.1216, found 296.1215.

***N*-(4-methoxyphenyl)-6-phenylthieno[2,3-*b*]pyrazin-7-amine (5c)**

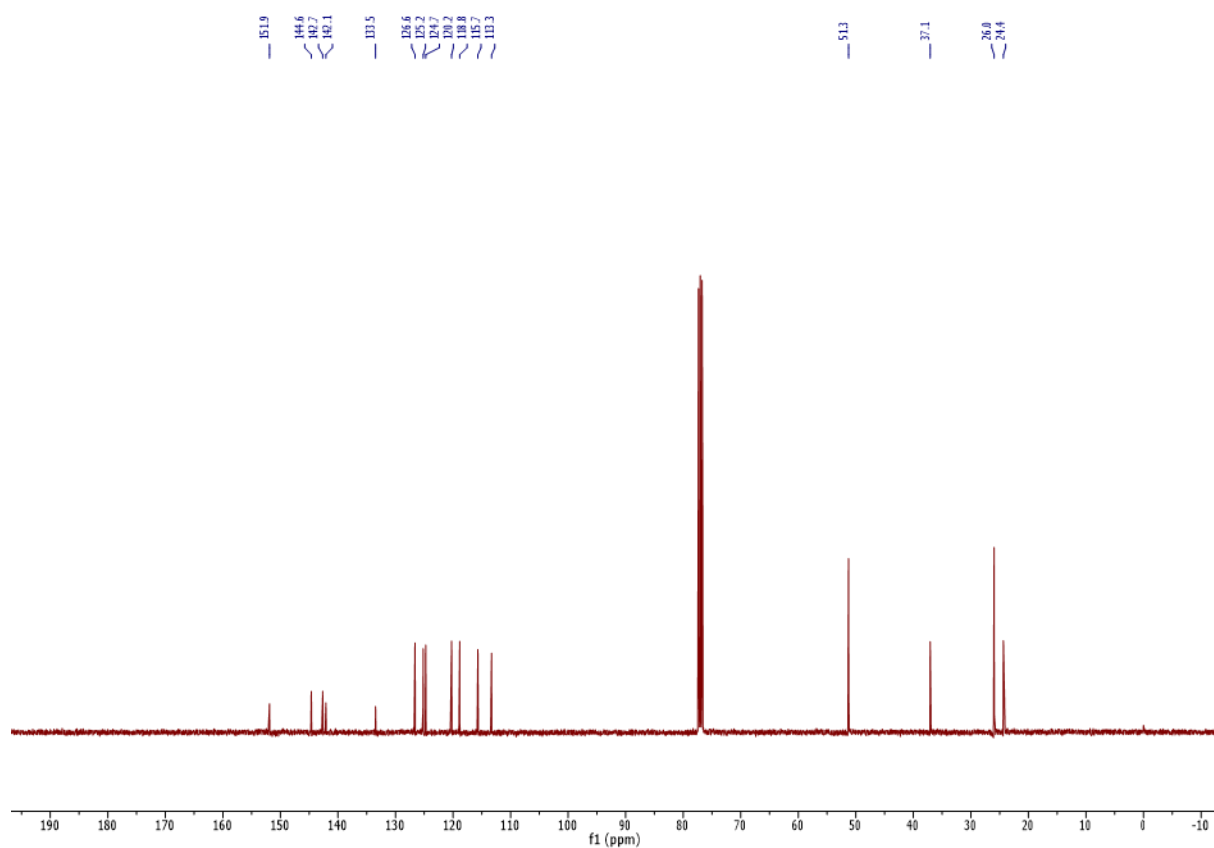
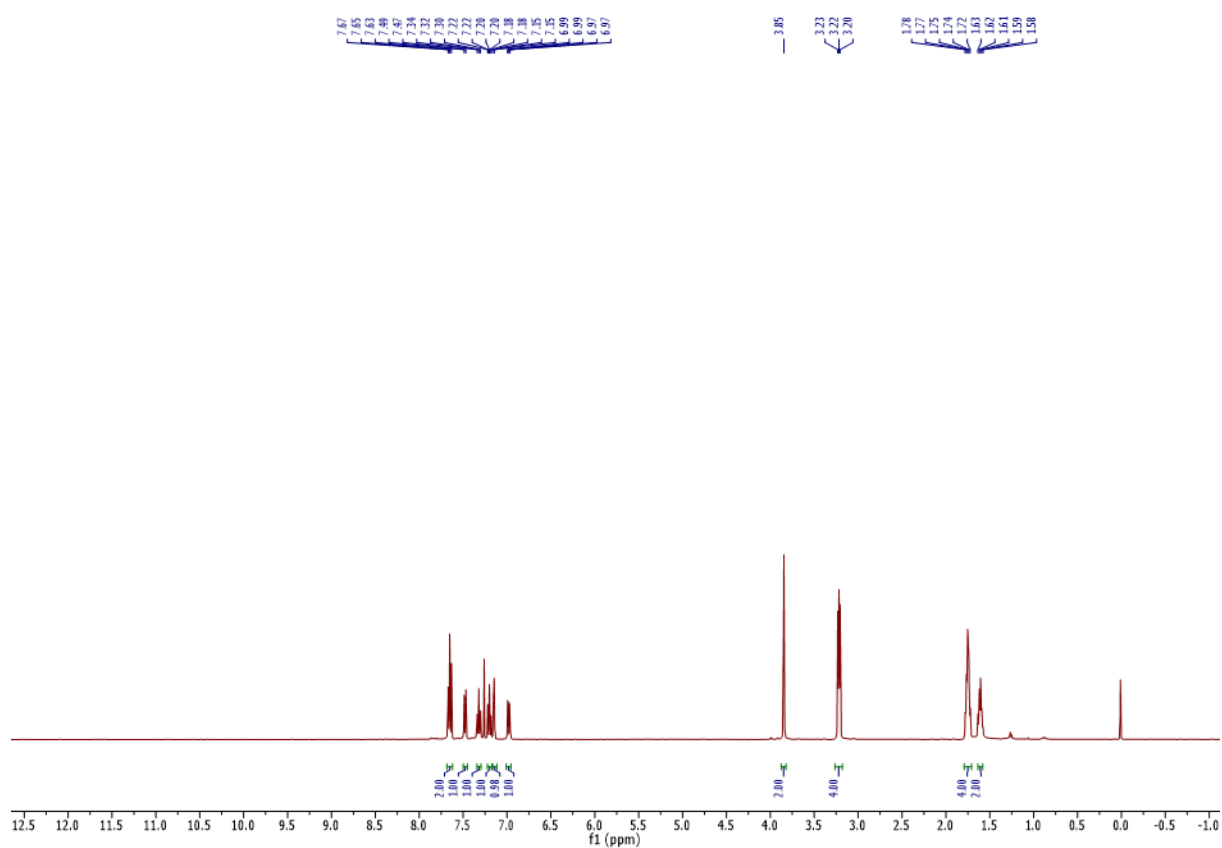
Orange solid (48 mg, 84%), m.p. 143 – 145 °C. ^1H NMR (400 MHz, CDCl_3) δ 3.71 (s, 3H), 6.39 (s, 1H), 6.65 – 6.74 (m, 4H), 7.27 – 7.35 (m, 3H), 7.61 – 7.66 (m, 2H), 8.50 (d, J = 2.4 Hz, 1H), 8.57 (d, J = 2.4 Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 55.5 (CH), 114.2 (2xCH), 118.0 (2xCH), 128.1 (2xCH), 128.5 (CH), 128.7 (2xCH), 128.8 (C), 129.5 (C), 133.0 (C), 136.7 (C), 140.9 (CH), 141.1 (CH), 145.9 (C), 154.1 (C), 154.1 (C) ppm. HRMS: calcd for $\text{C}_{19}\text{H}_{16}\text{N}_3\text{OS}$ $[\text{M}+\text{H}]^+$ 334.1009, found 334.1009.

1.3. ^1H NMR, ^{13}C NMR and ^{19}F NMR Spectra of all Products

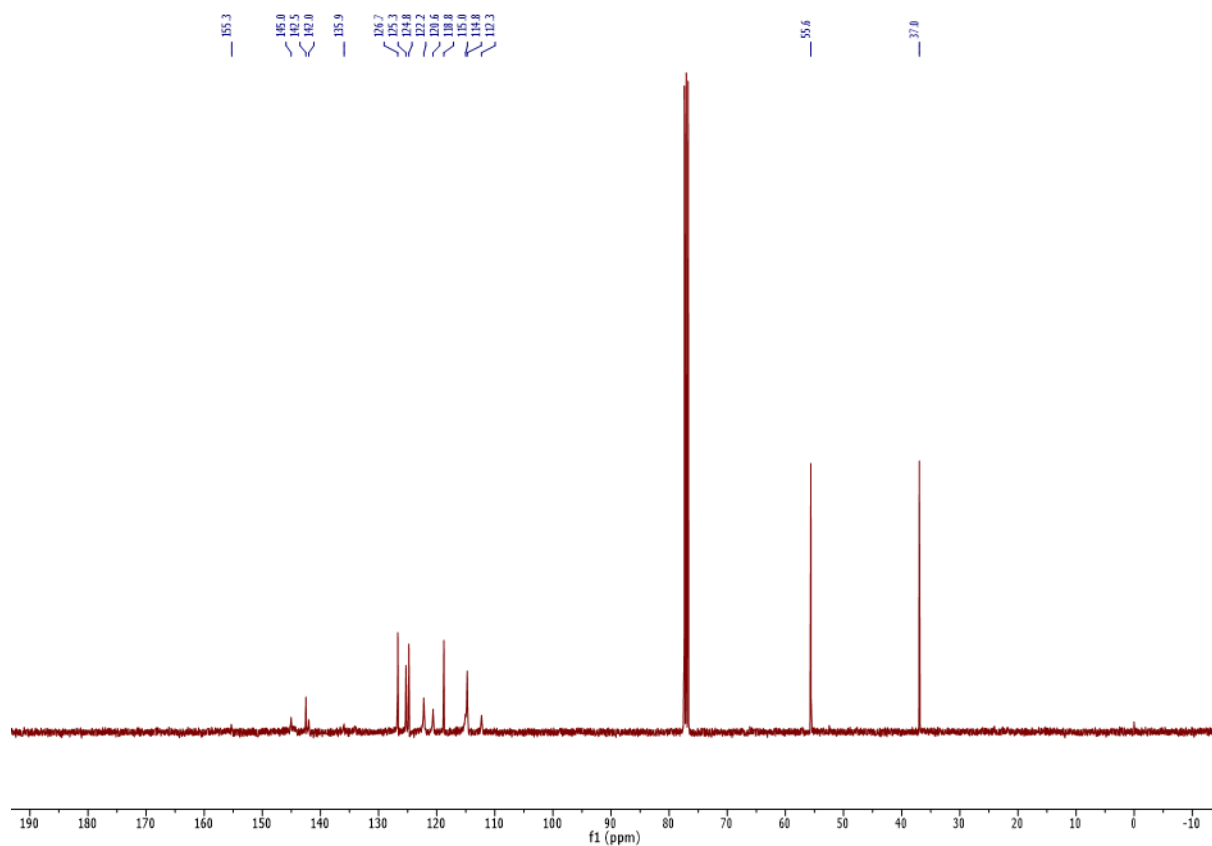
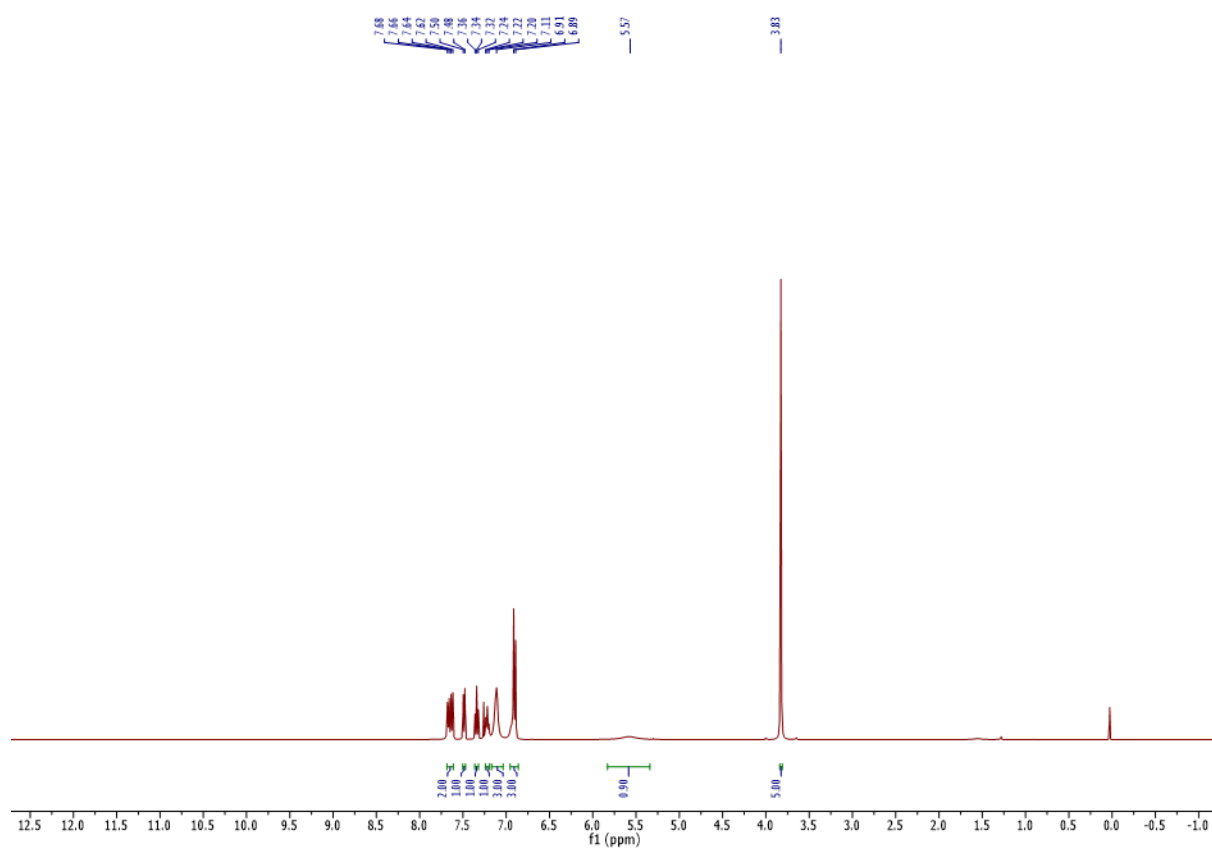
N-phenyl-9*H*-fluoren-2-amine (**1a**)



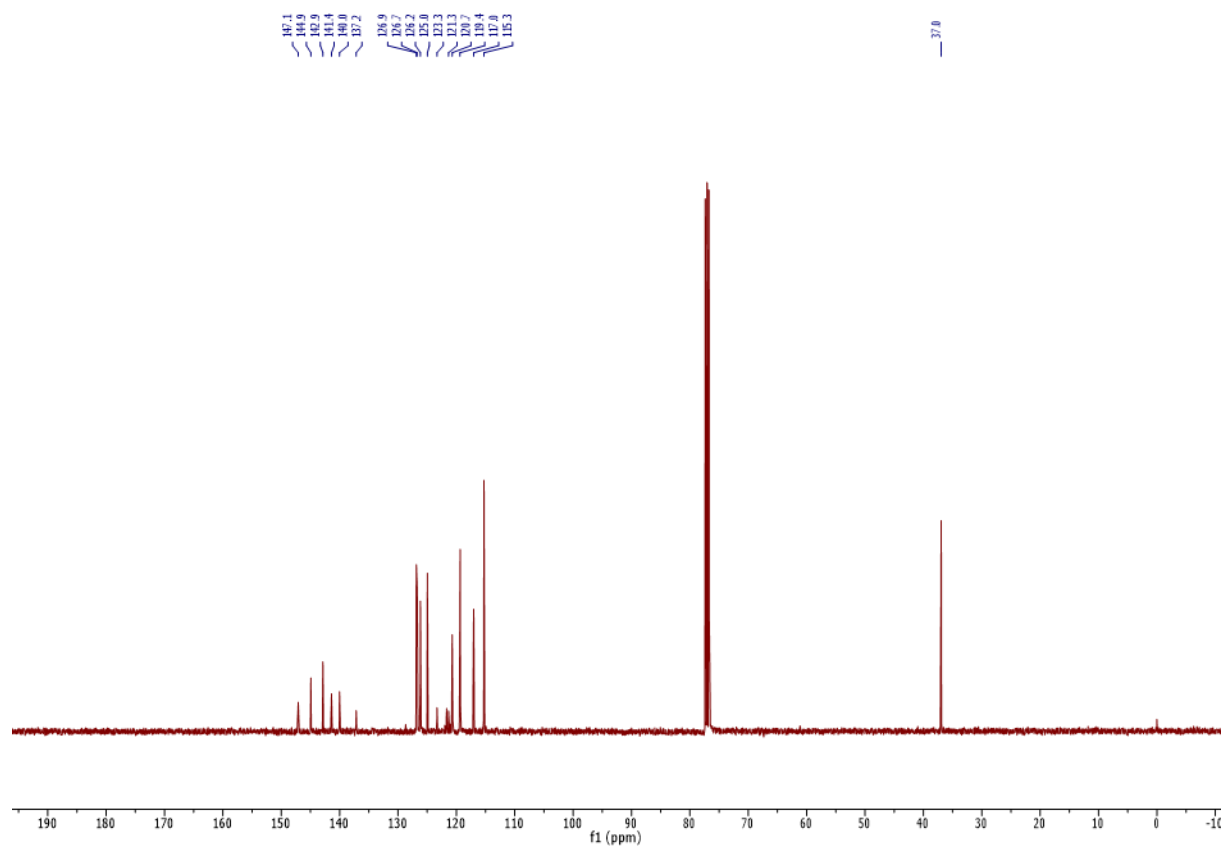
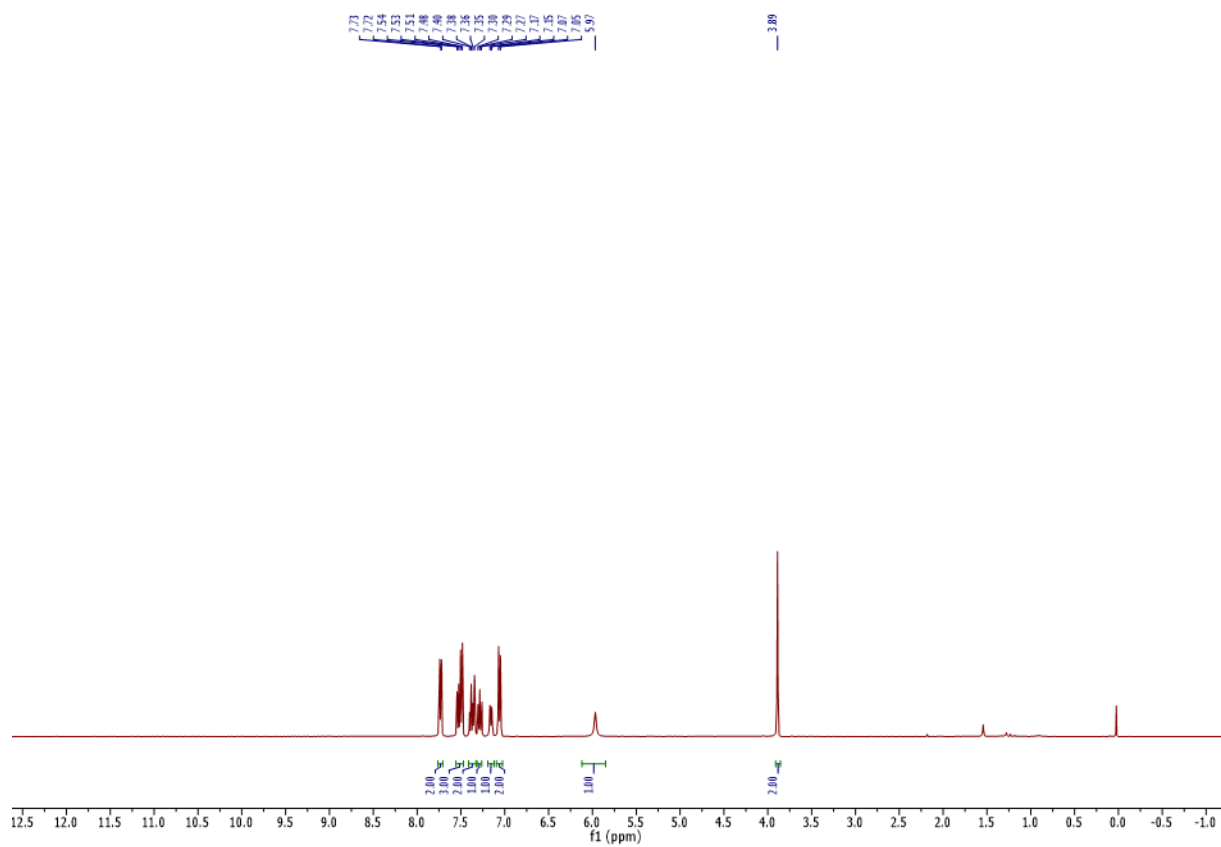
1-(9*H*-fluoren-2-yl)piperidine (**1b**)

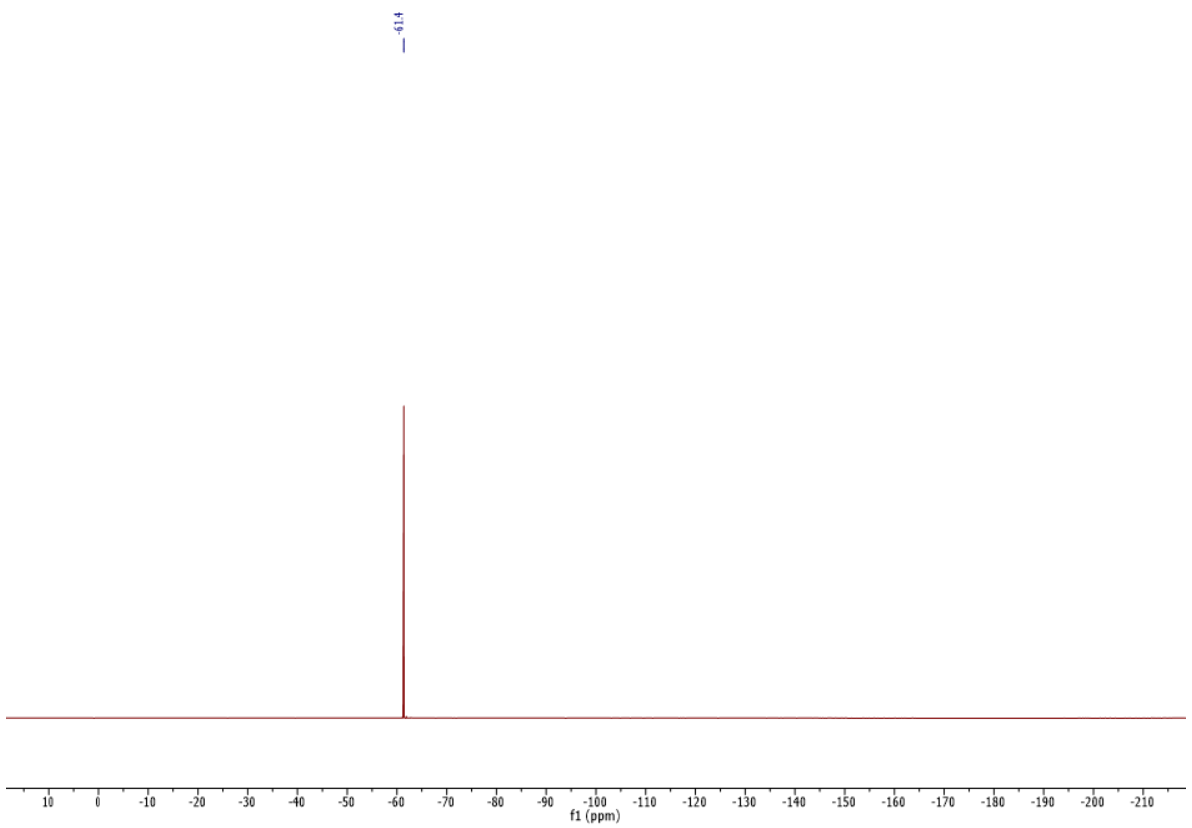


N-(4-methoxyphenyl)-9*H*-fluoren-2-amine (**1c**)

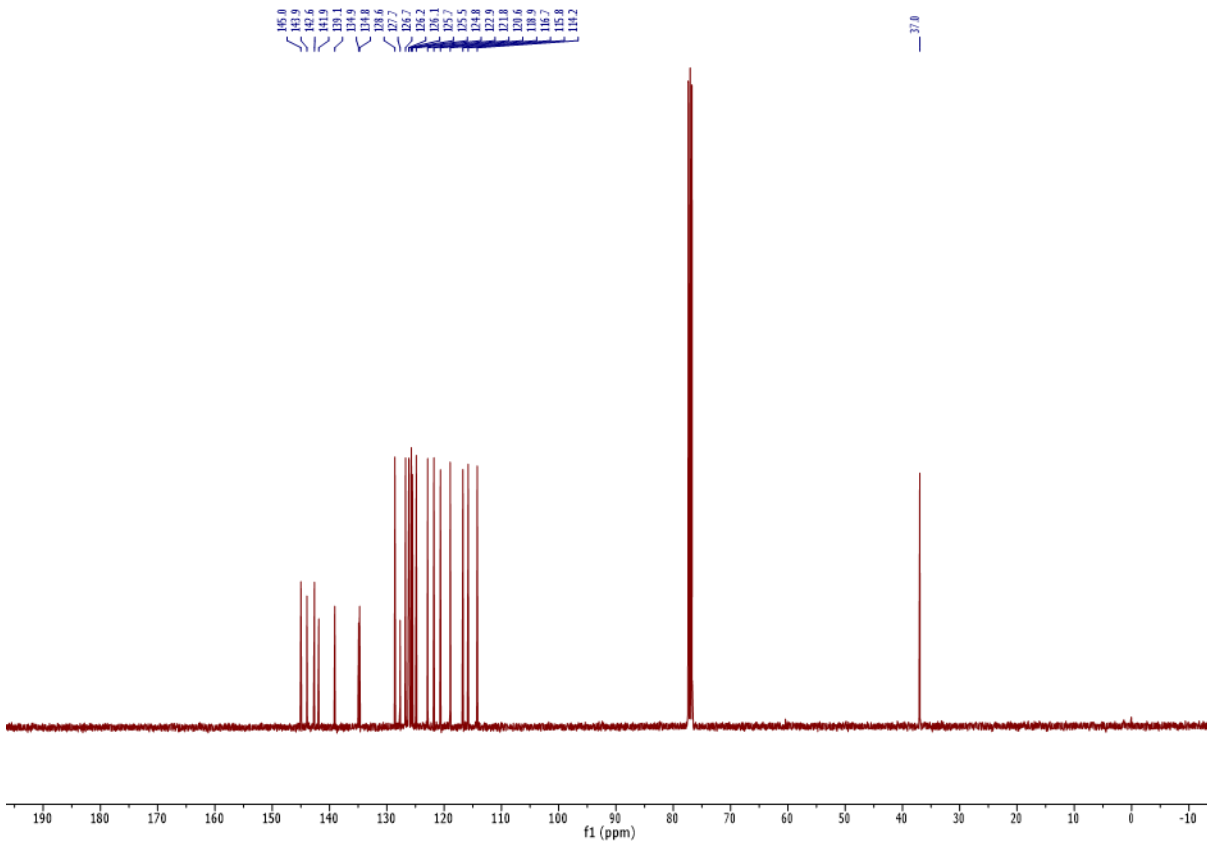
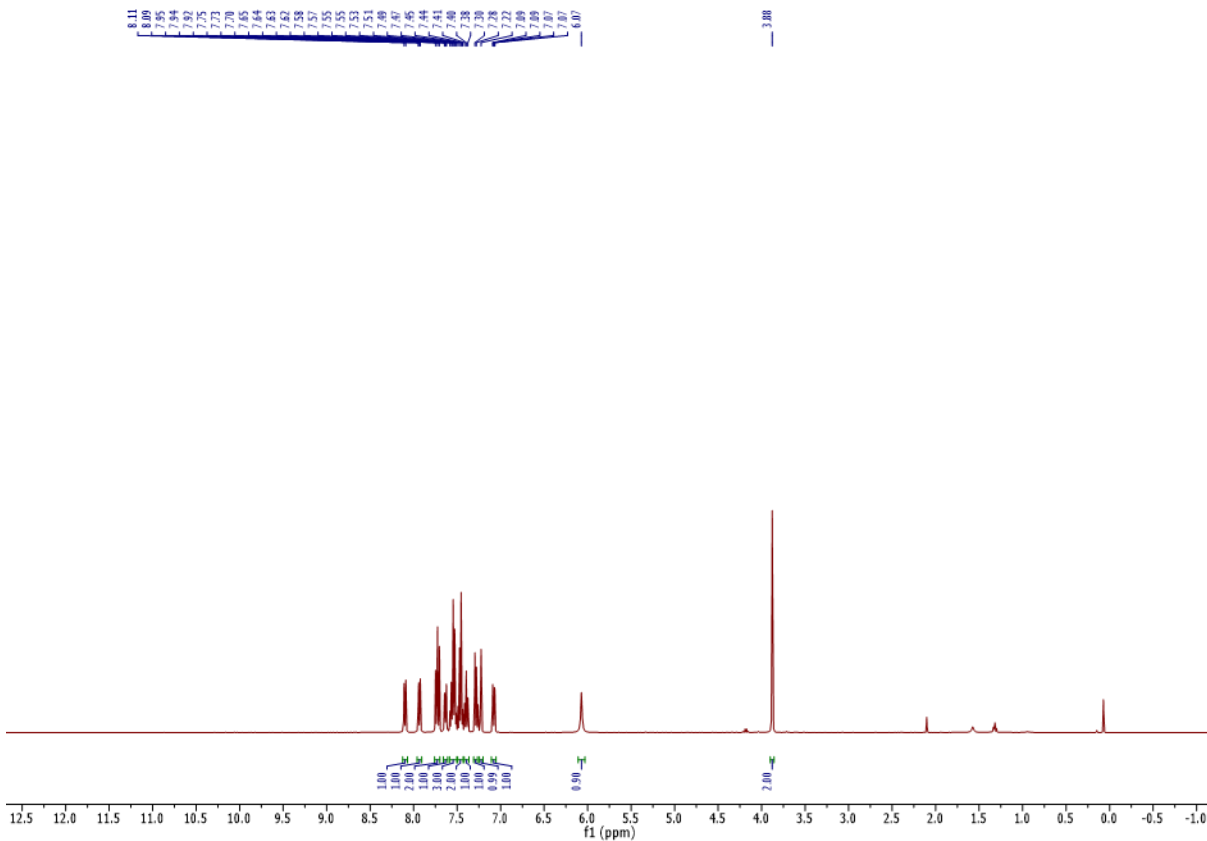


N-(4-(trifluoromethyl)phenyl)-9*H*-fluoren-2-amine (**1d**)

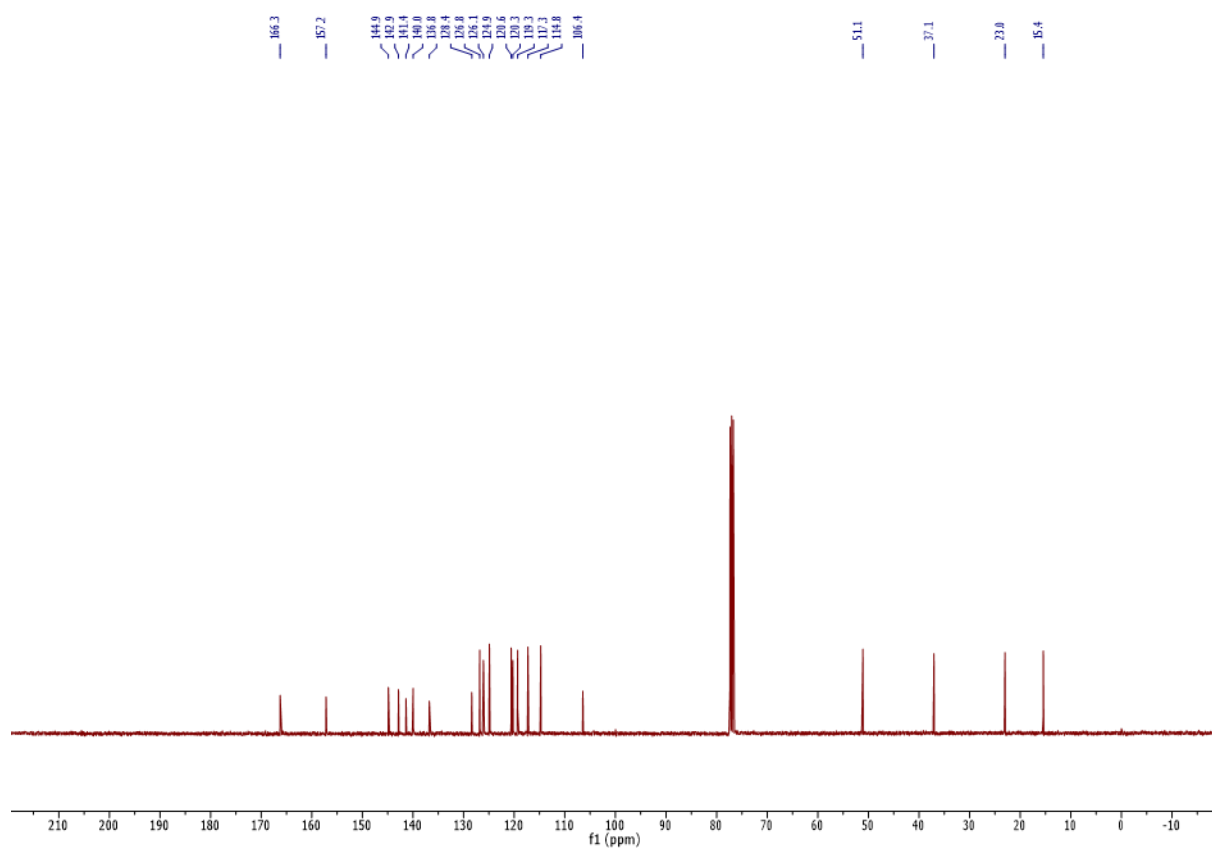
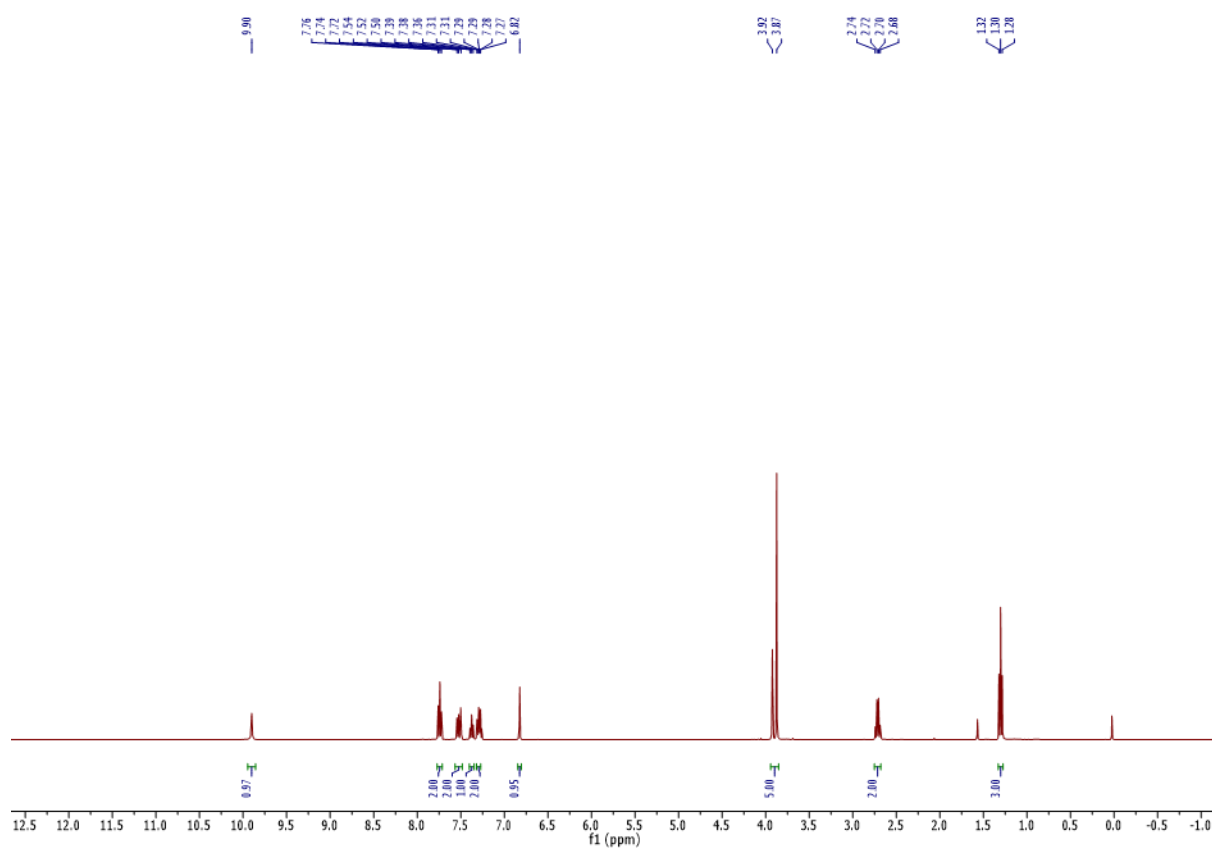




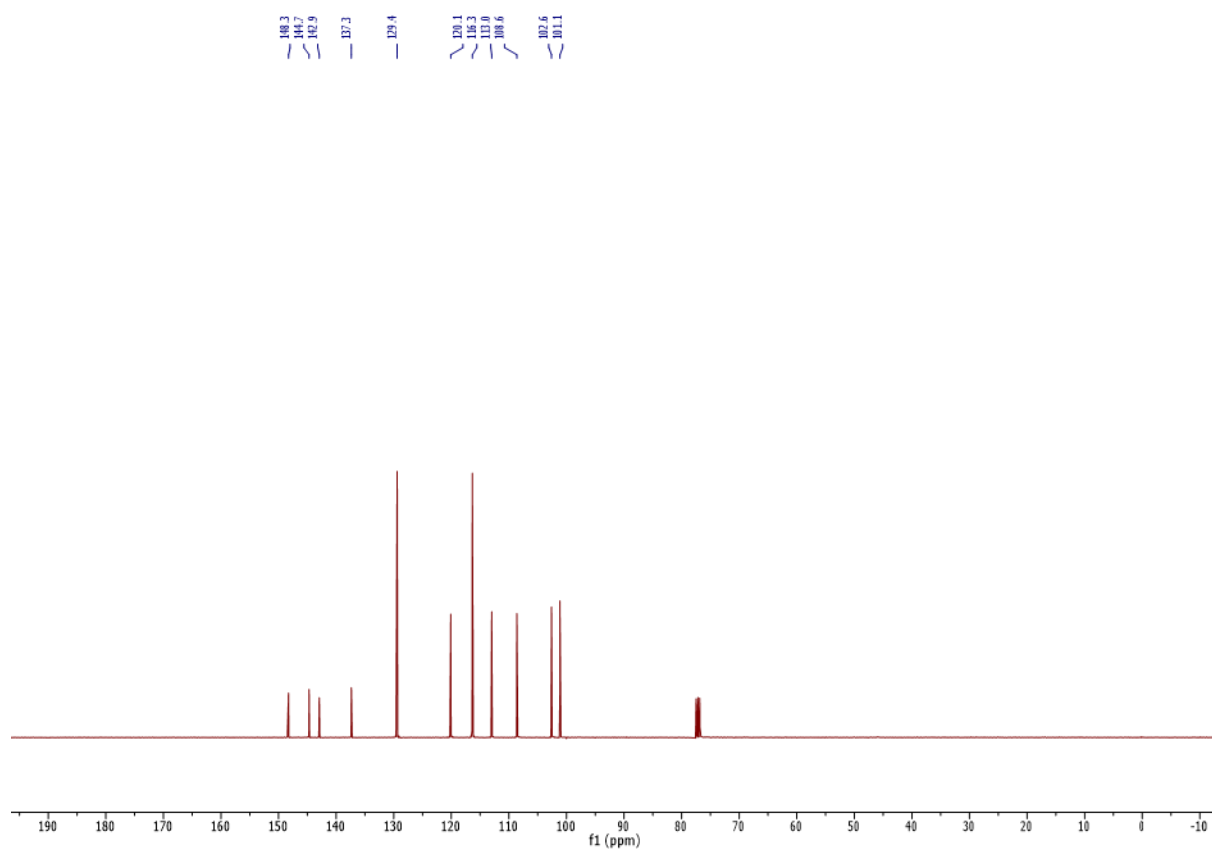
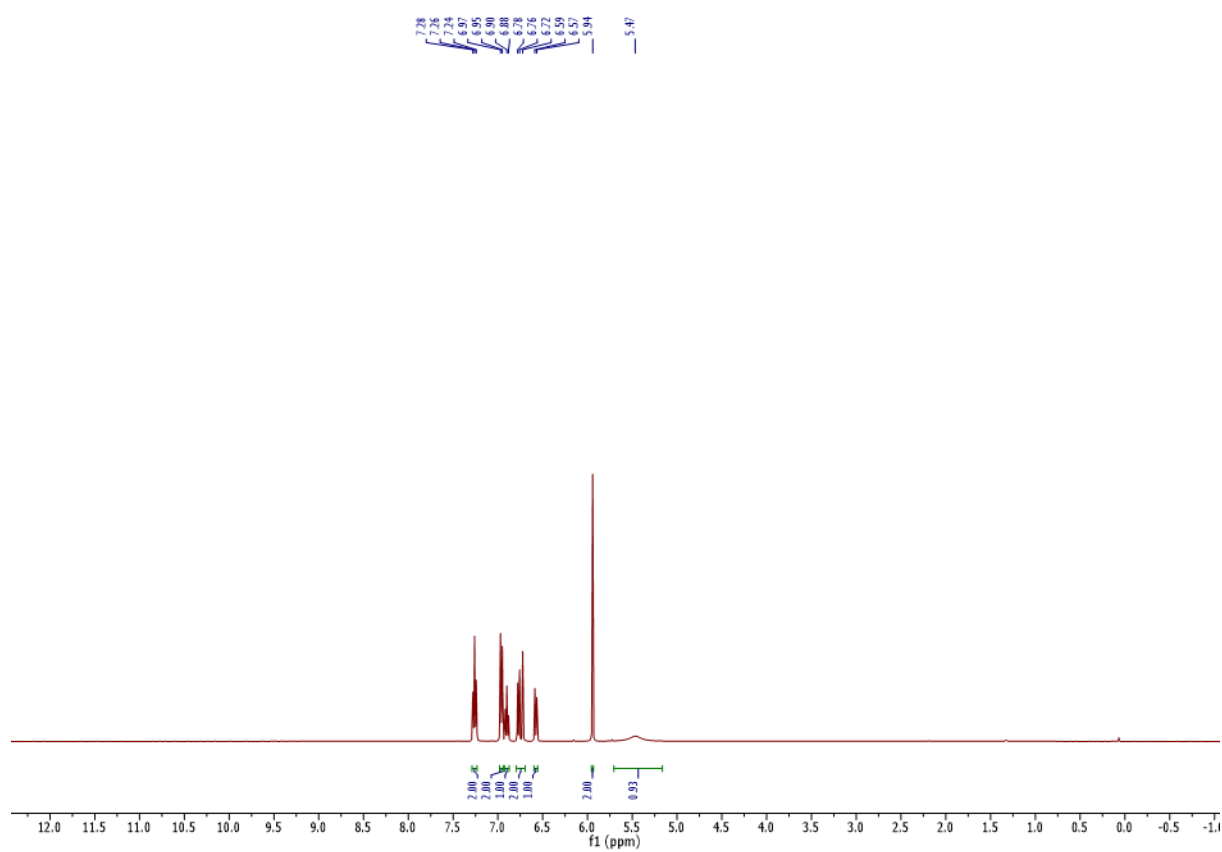
N-(naphthalen-1-yl)-9*H*-fluoren-2-amine (**1e**)



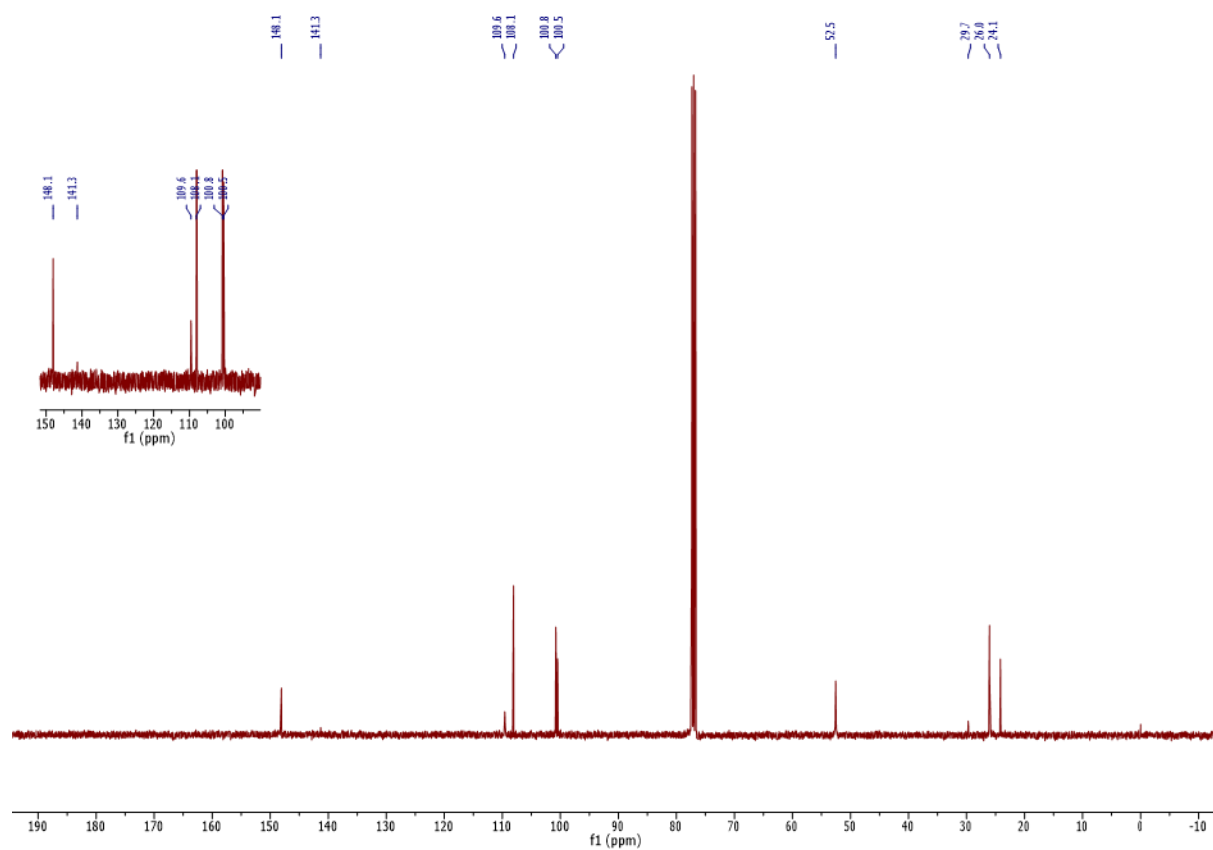
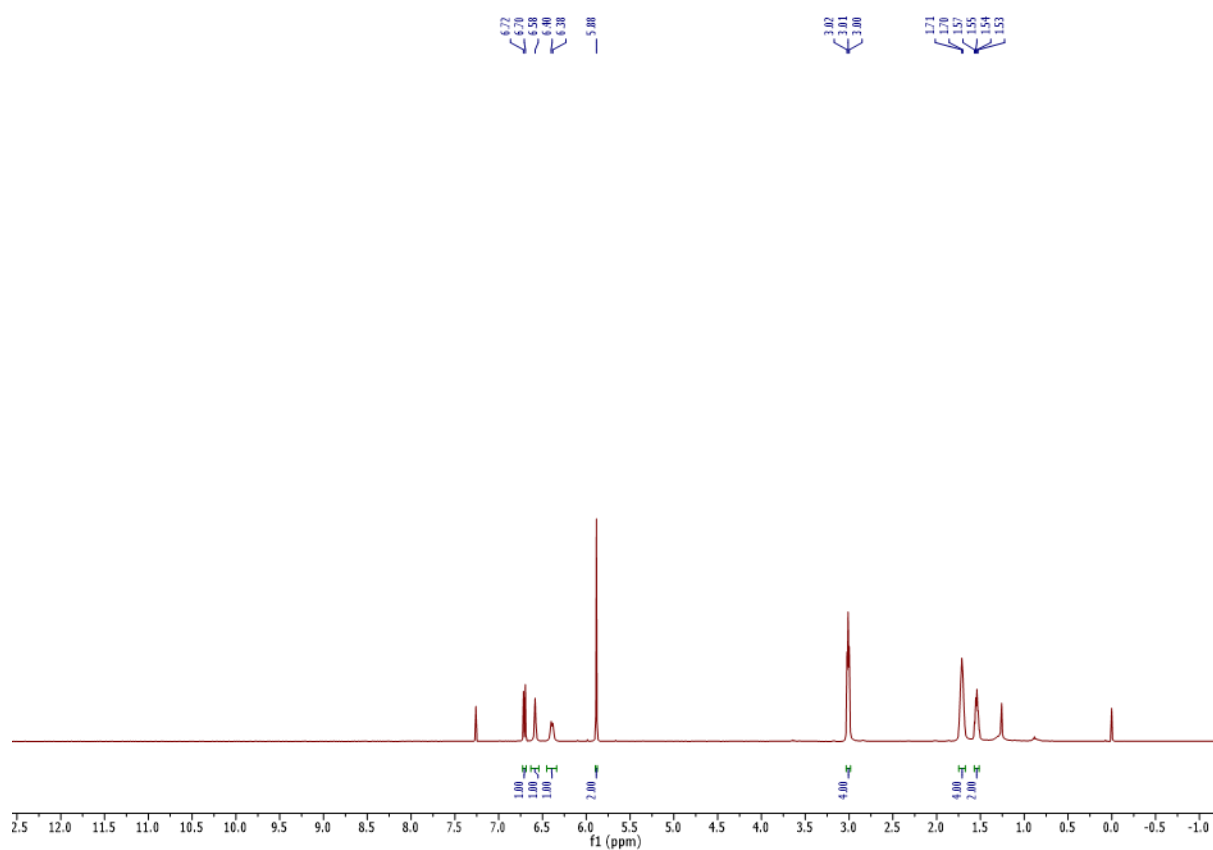
methyl 2-((9*H*-fluoren-2-yl)amino)-5-ethylthiophene-3-carboxylate (**1f**)



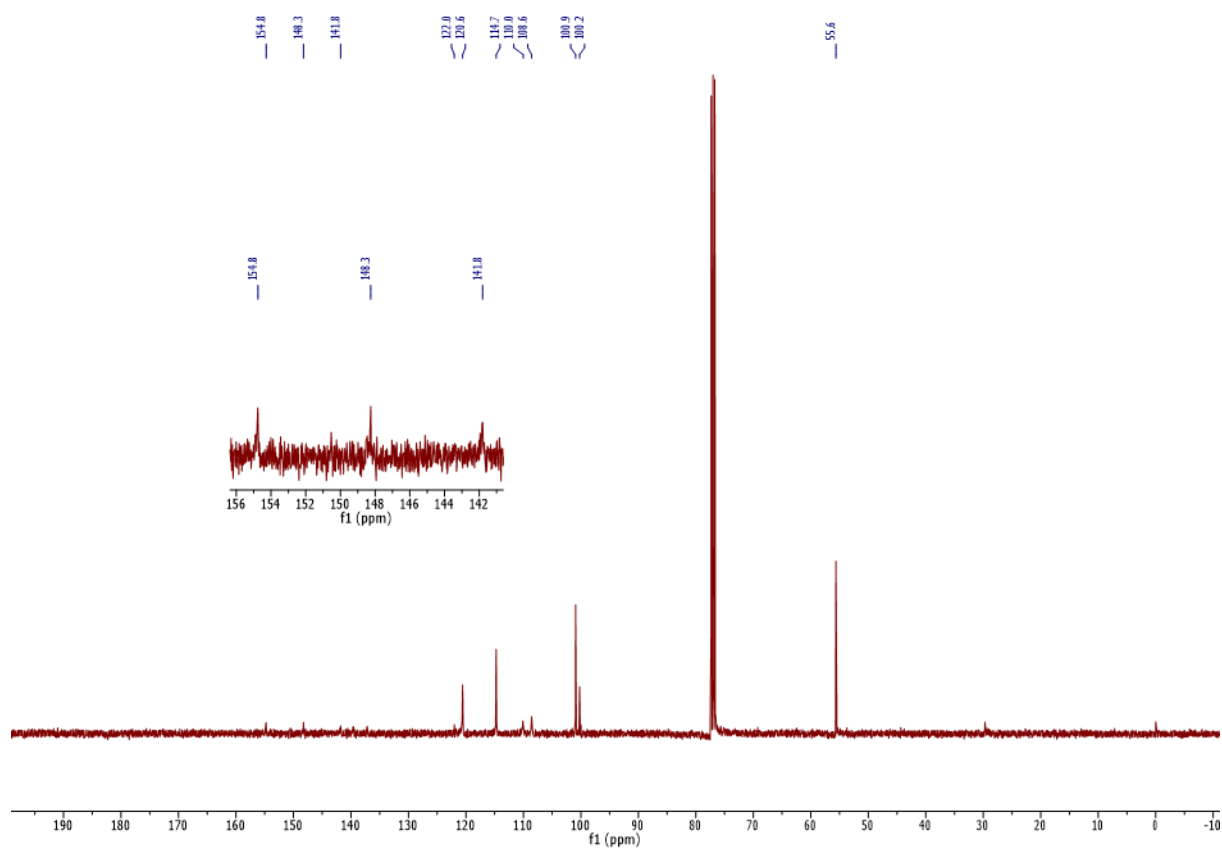
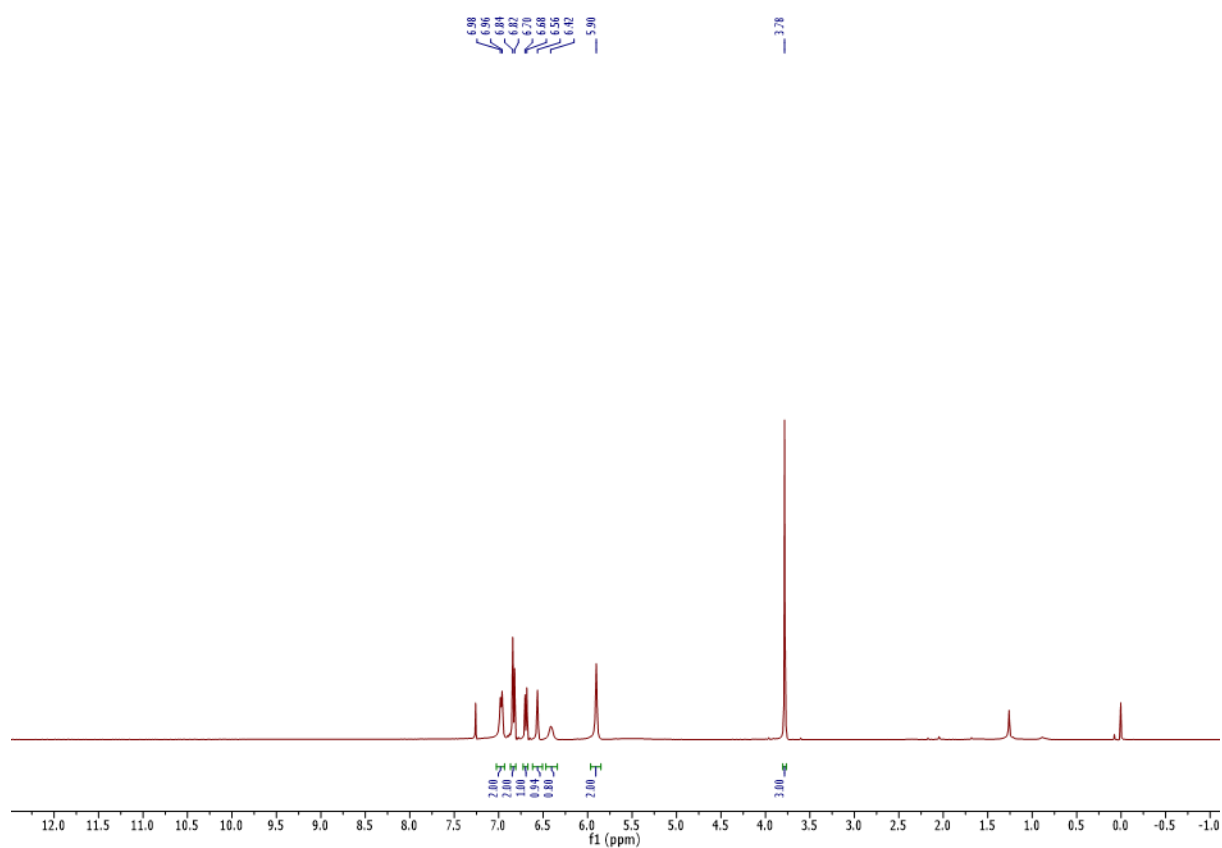
N-phenylbenzo[*d*][1,3]dioxol-5-amine (**2a**)



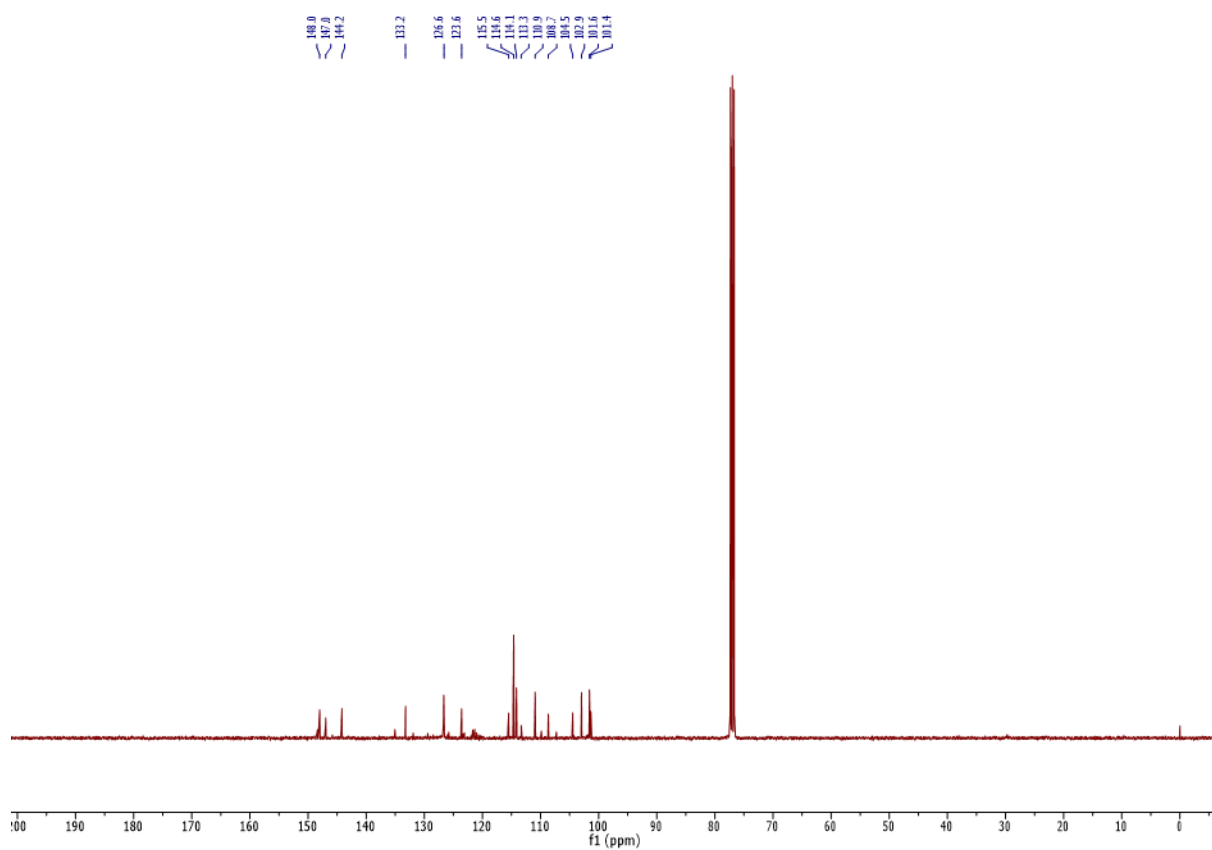
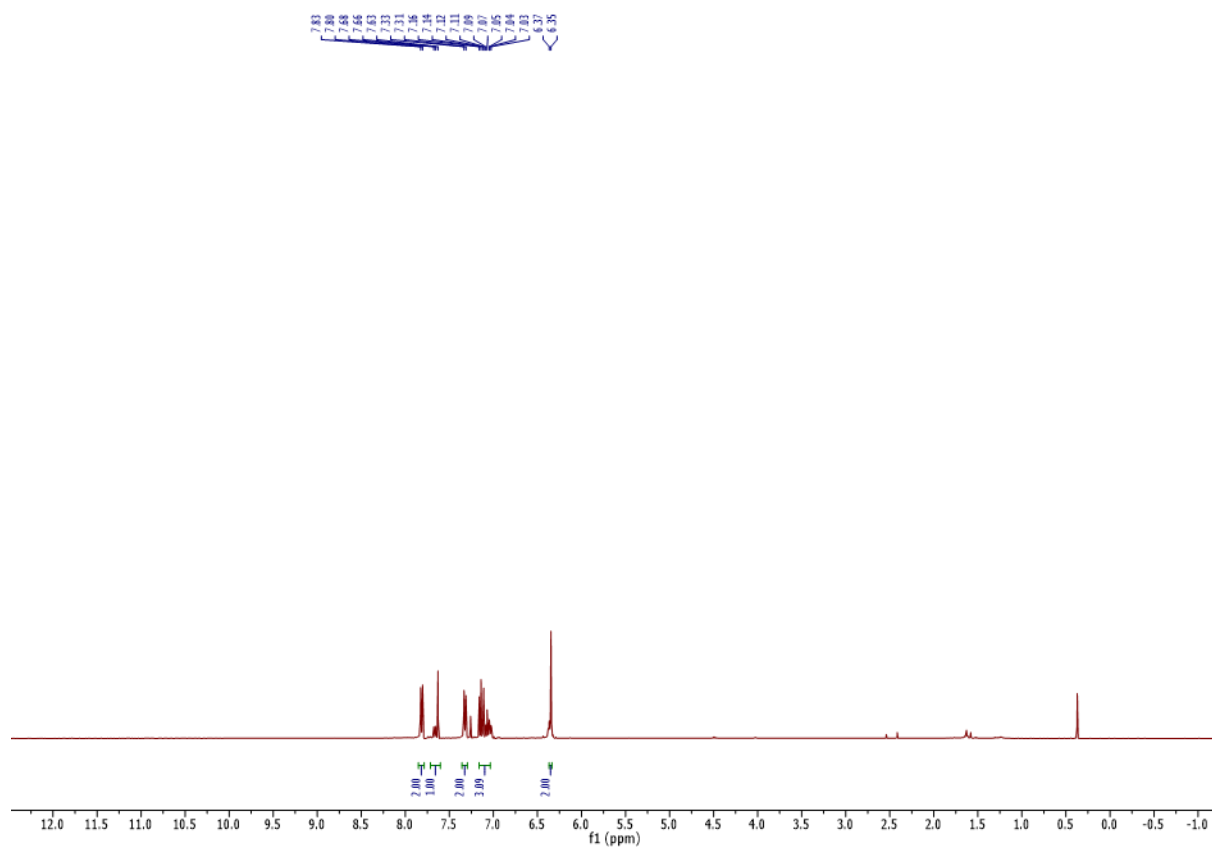
1-(benzo[d][1,3]dioxol-5-yl)piperidine (**2b**)

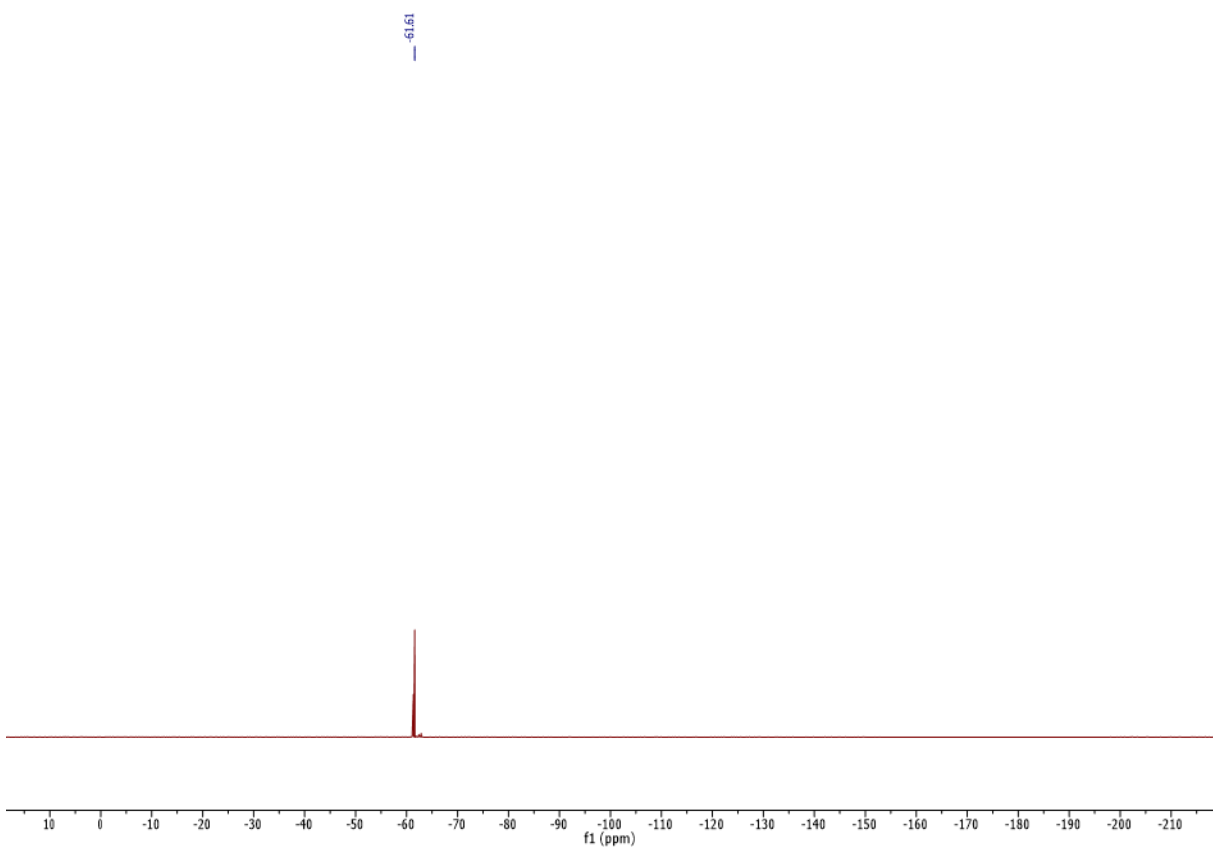


N-(4-methoxyphenyl)benzo[*d*][1,3]dioxol-5-amine (**2c**)

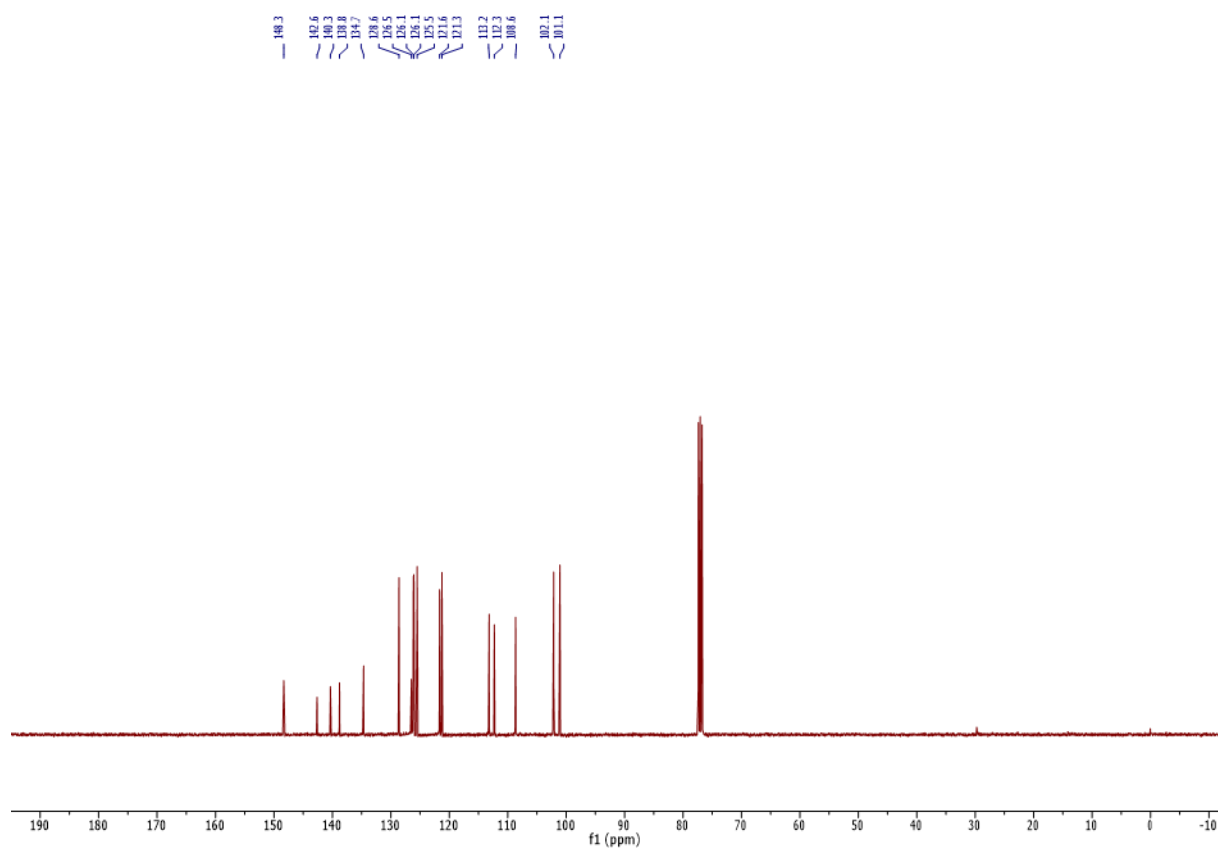
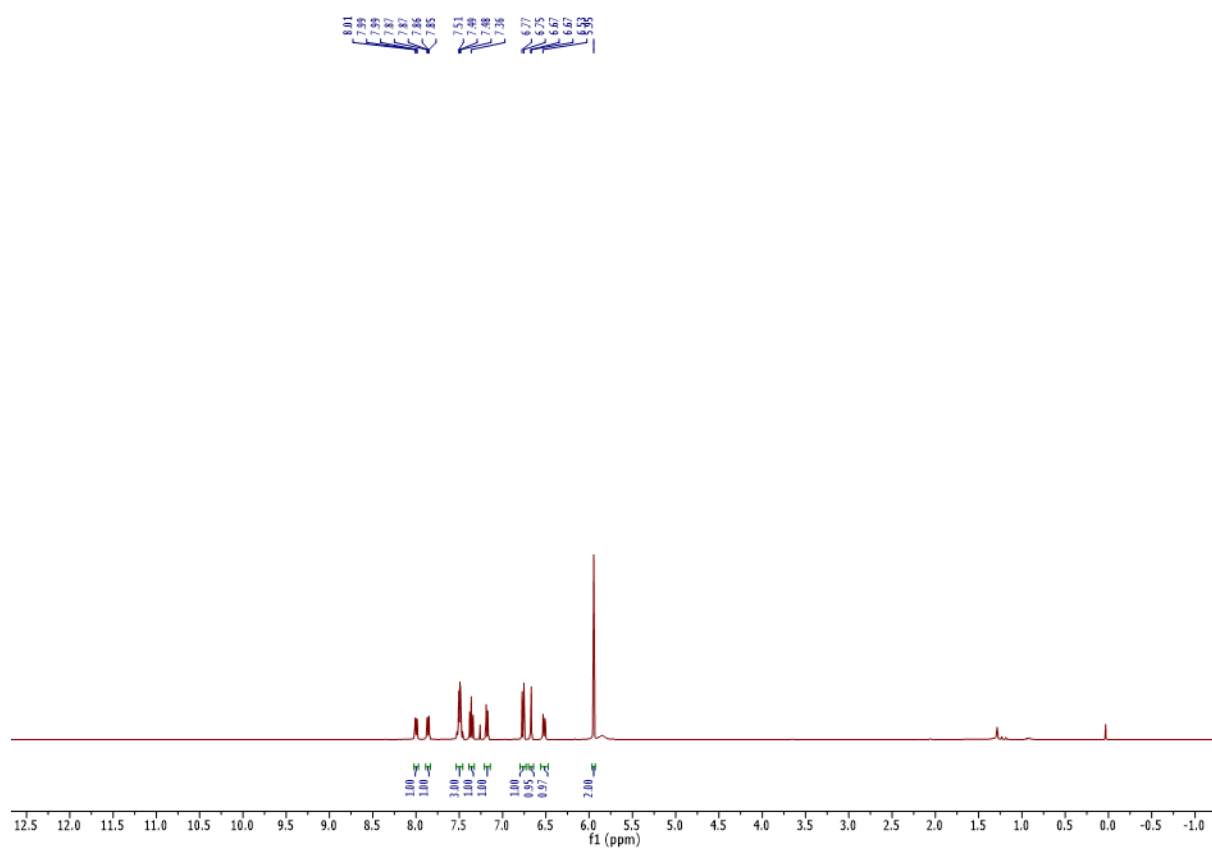


N-(4-(trifluoromethyl)phenyl)benzo[*d*][1,3]dioxol-5-amine (**2d**)

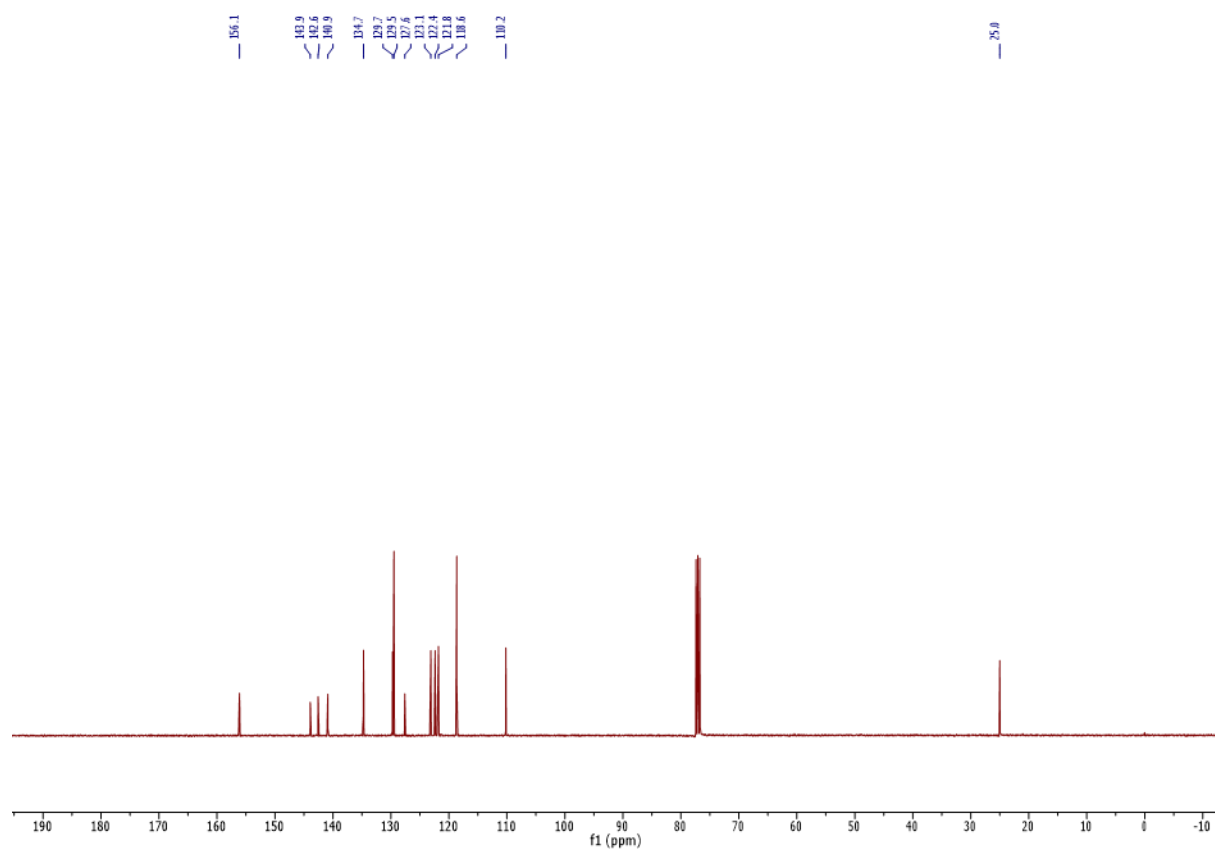
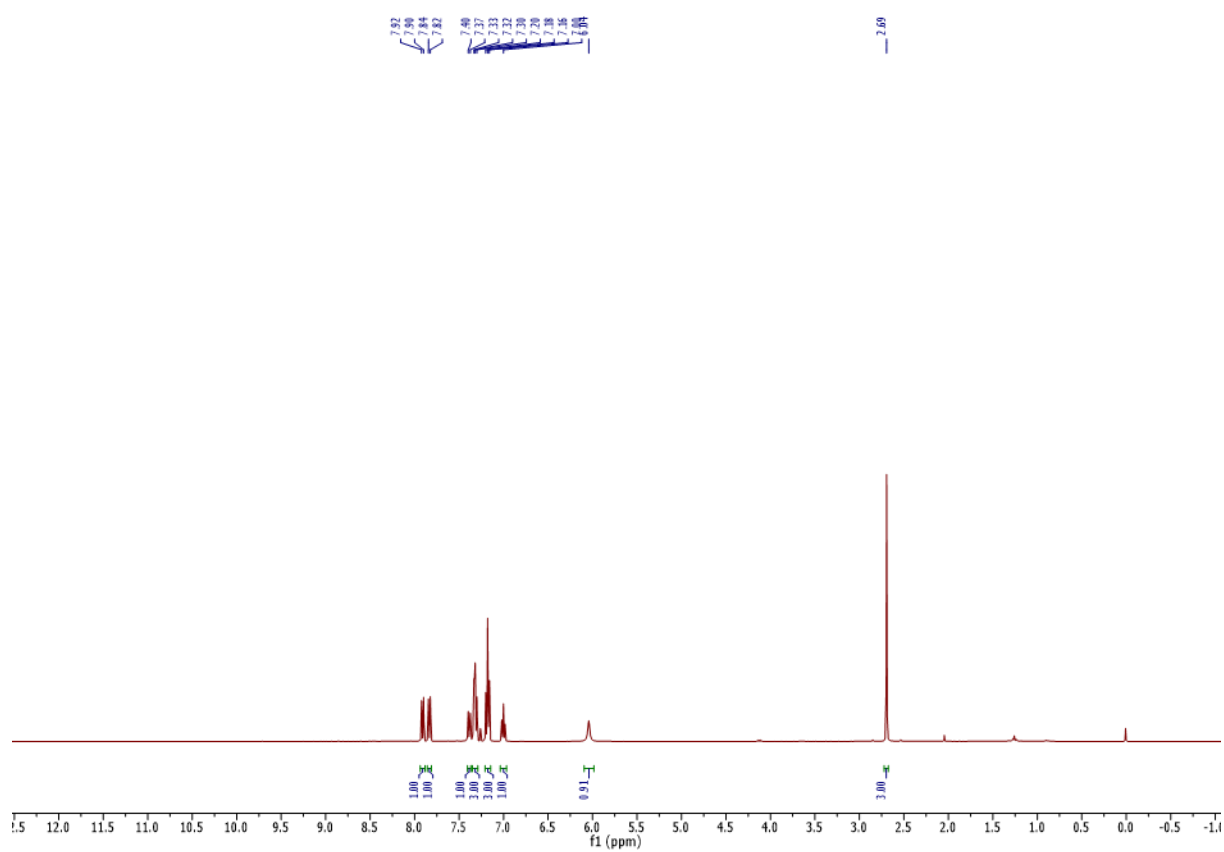




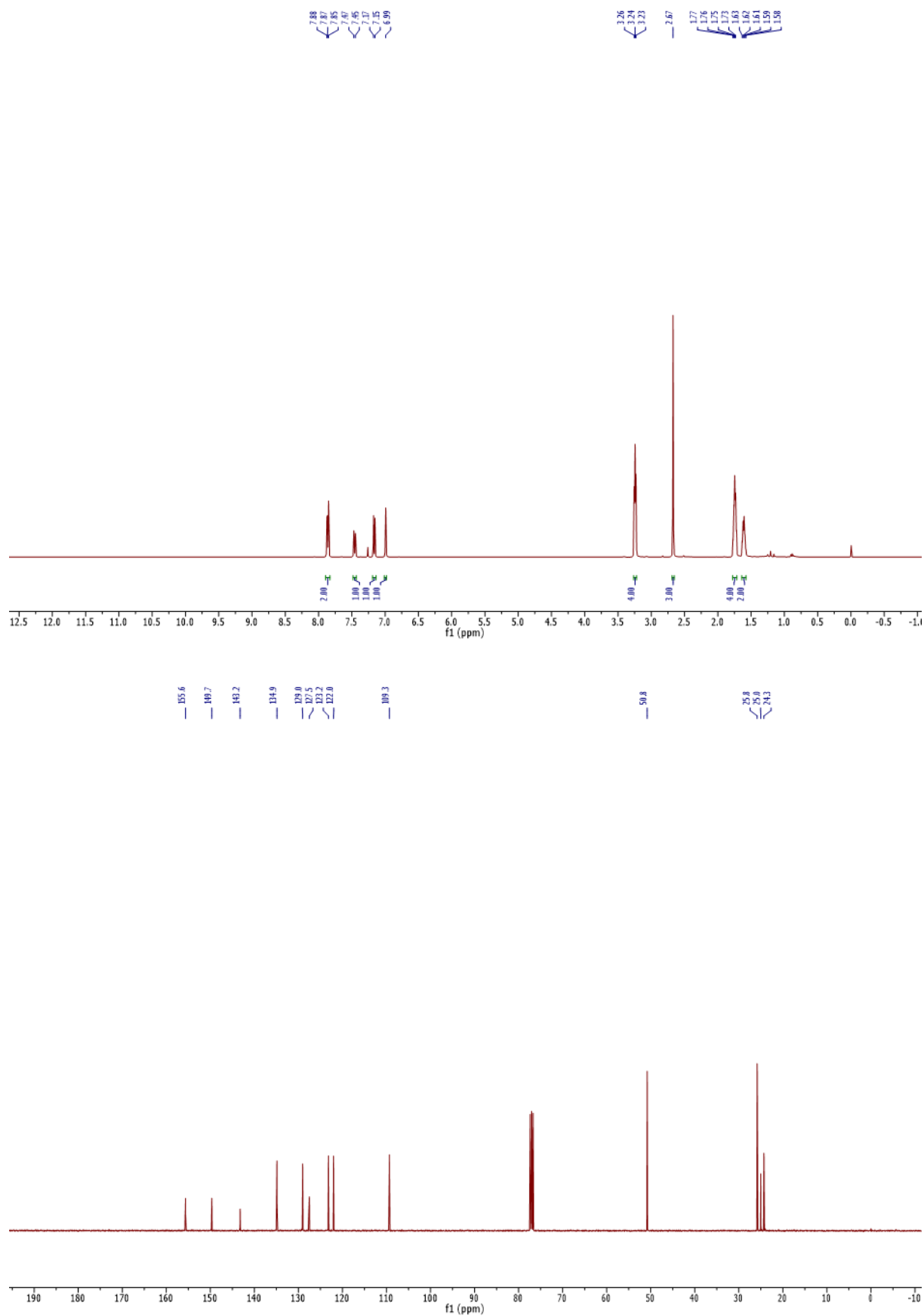
N-(naphthalen-1-yl)benzo[*d*][1,3]dioxol-5-amine (**2e**)



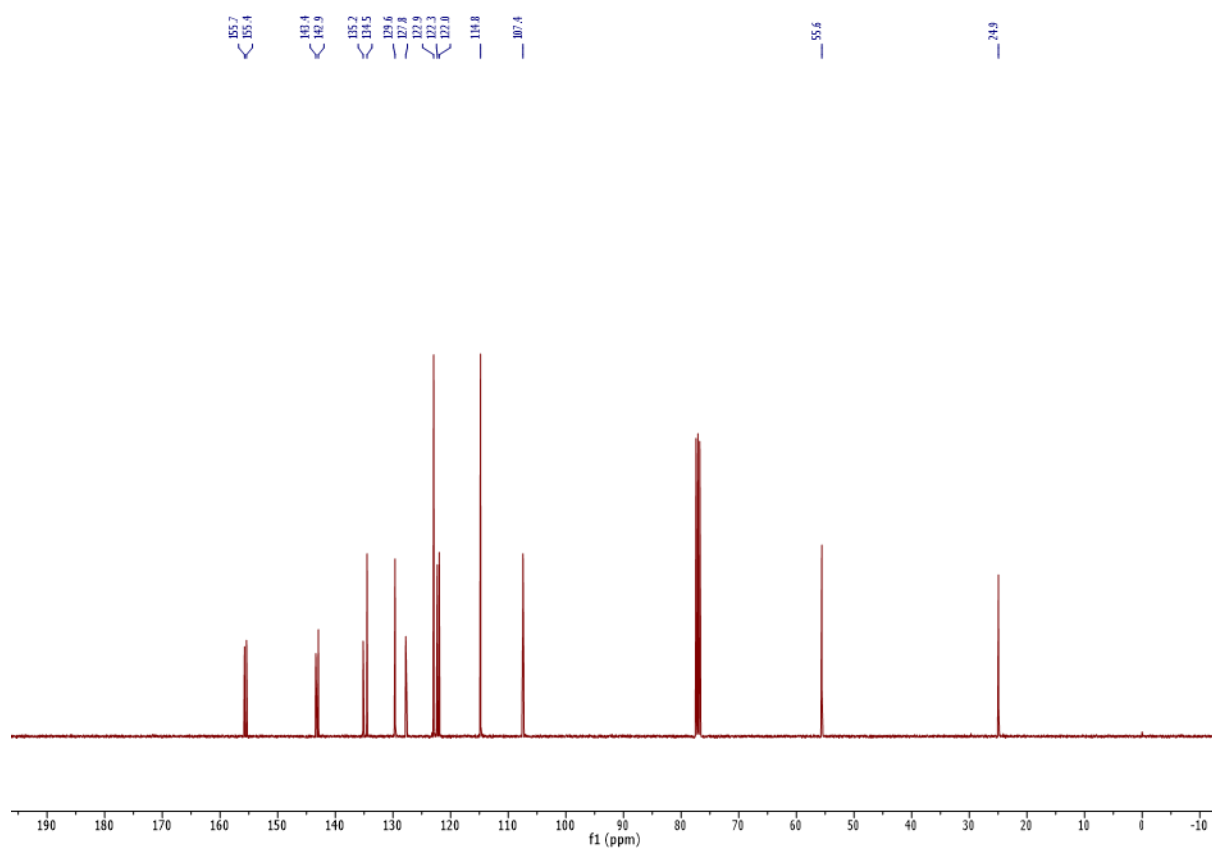
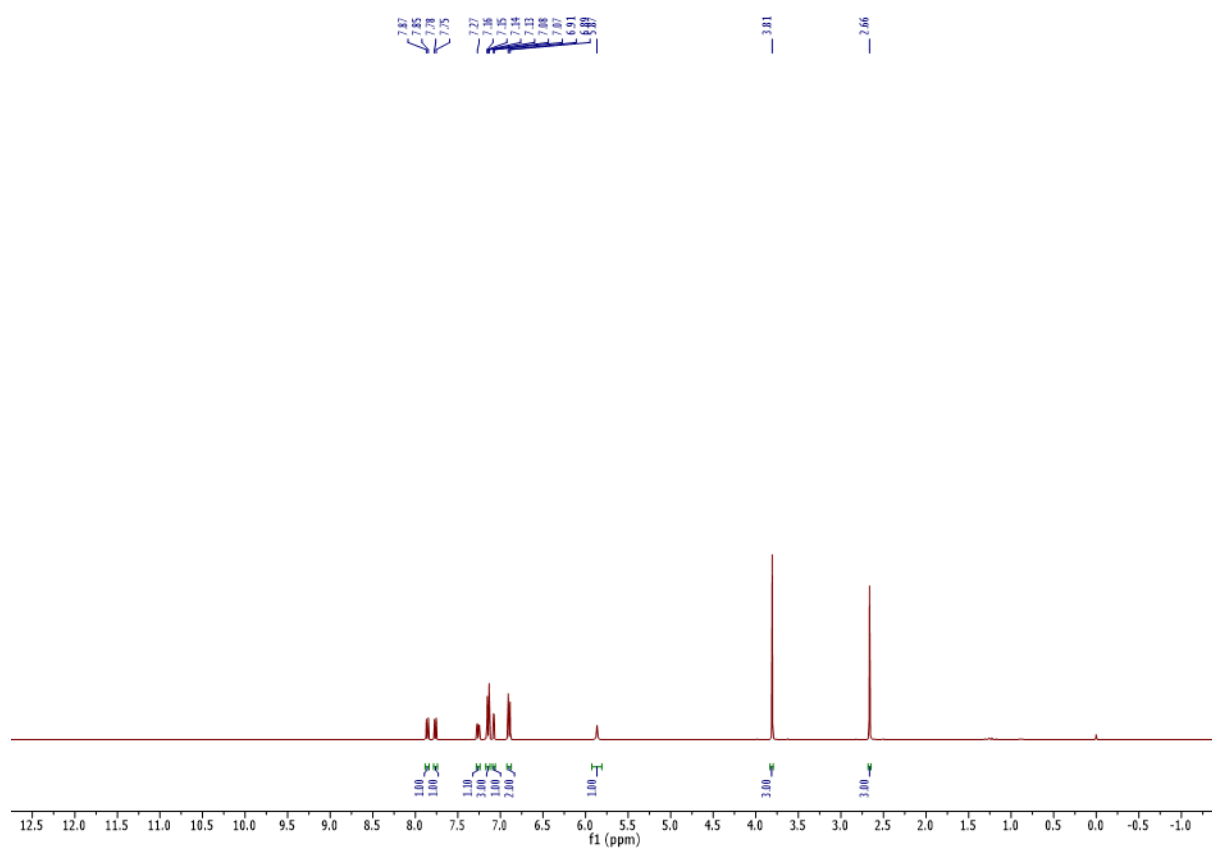
2-methyl-N-phenylquinolin-6-amine (**3a**)



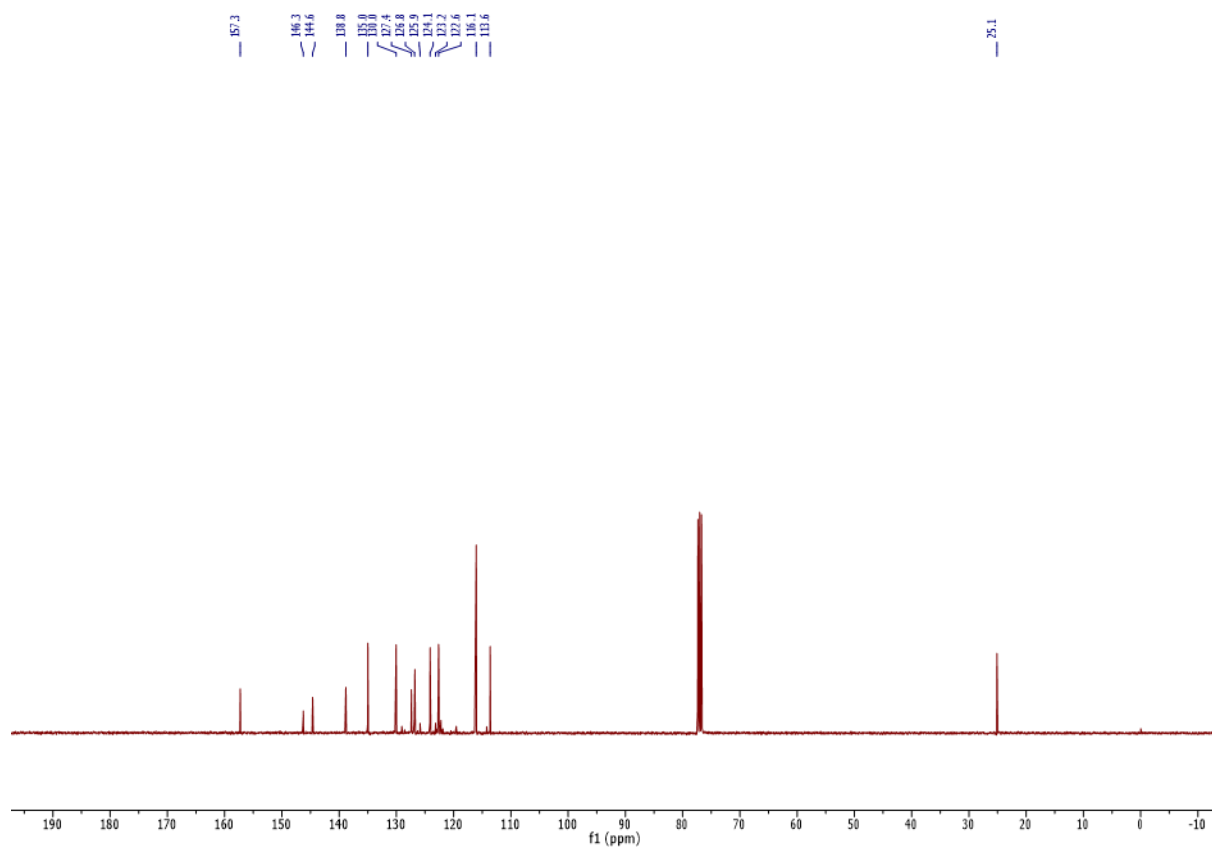
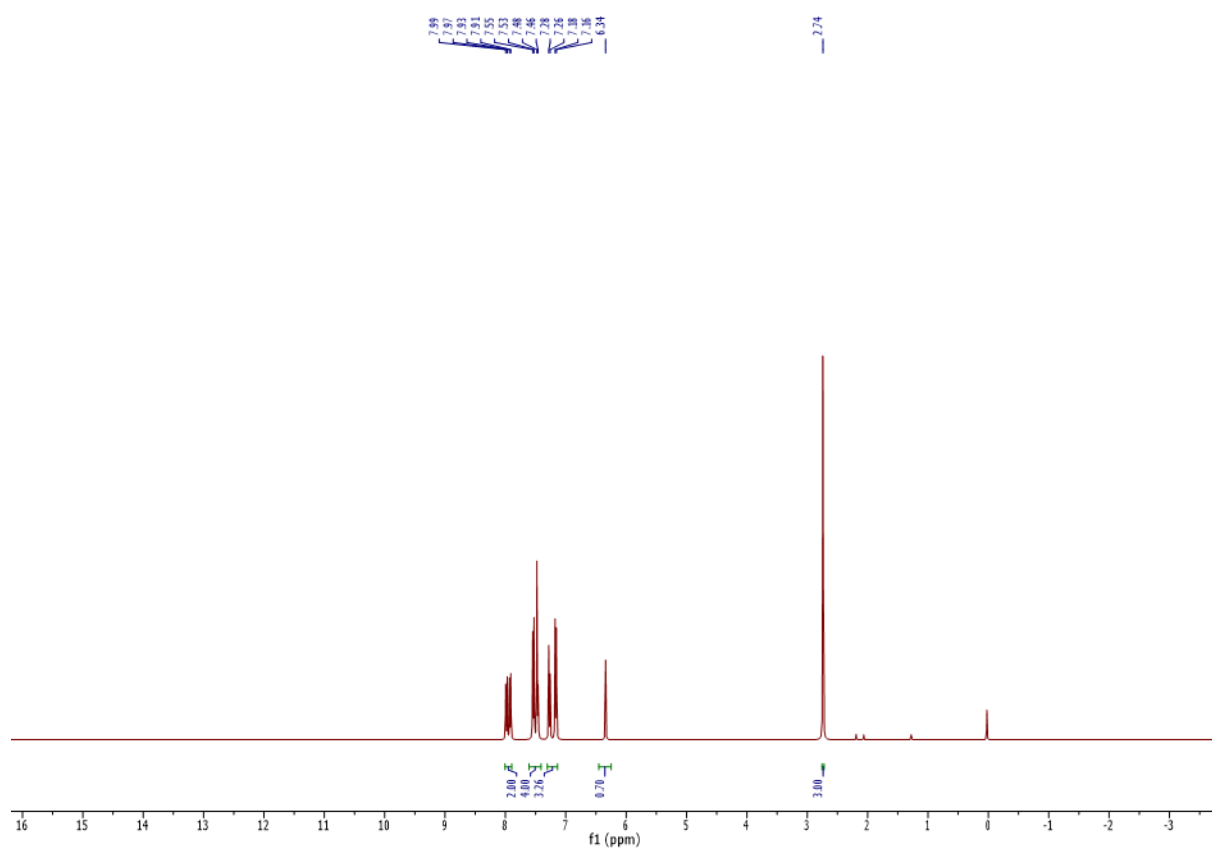
2-methyl-6-(piperidin-1-yl)quinoline (**3b**)

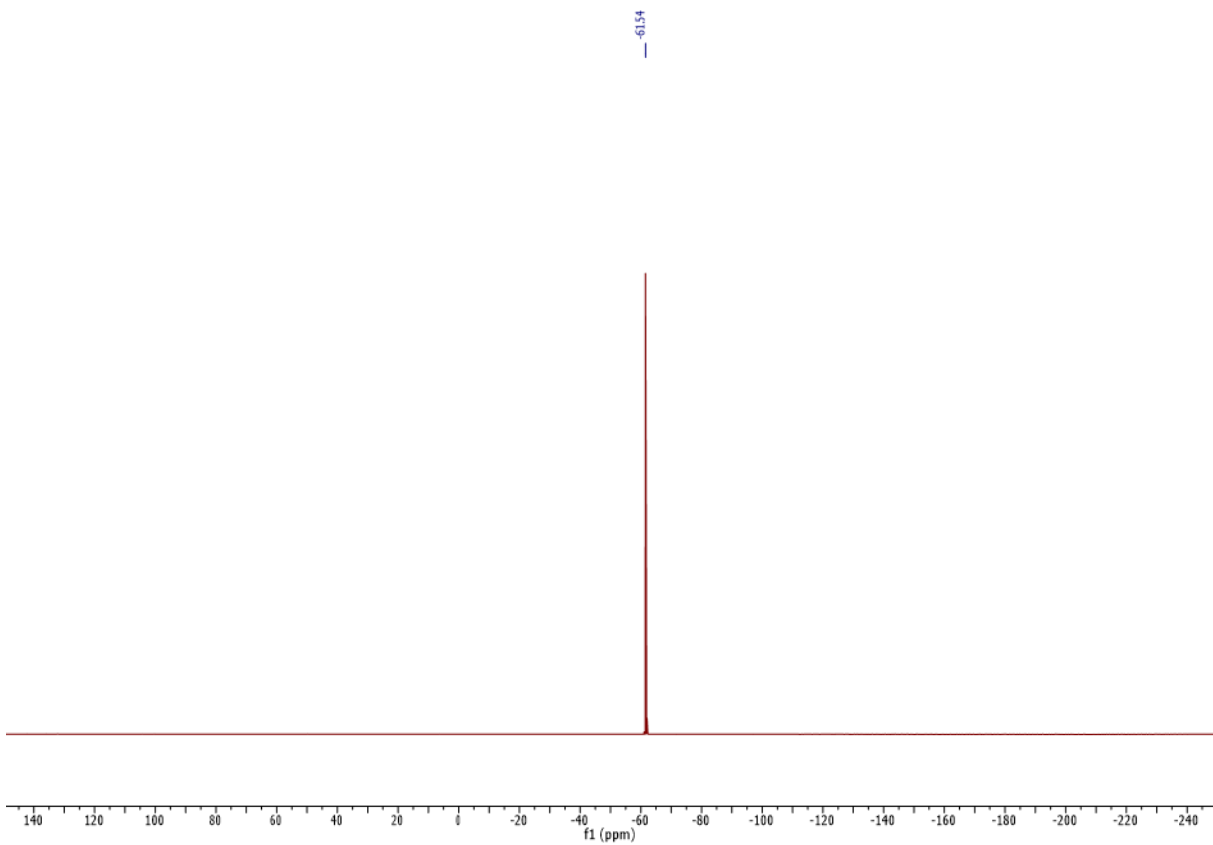


N-(4-methoxyphenyl)-2-methylquinolin-6-amine (**3c**)

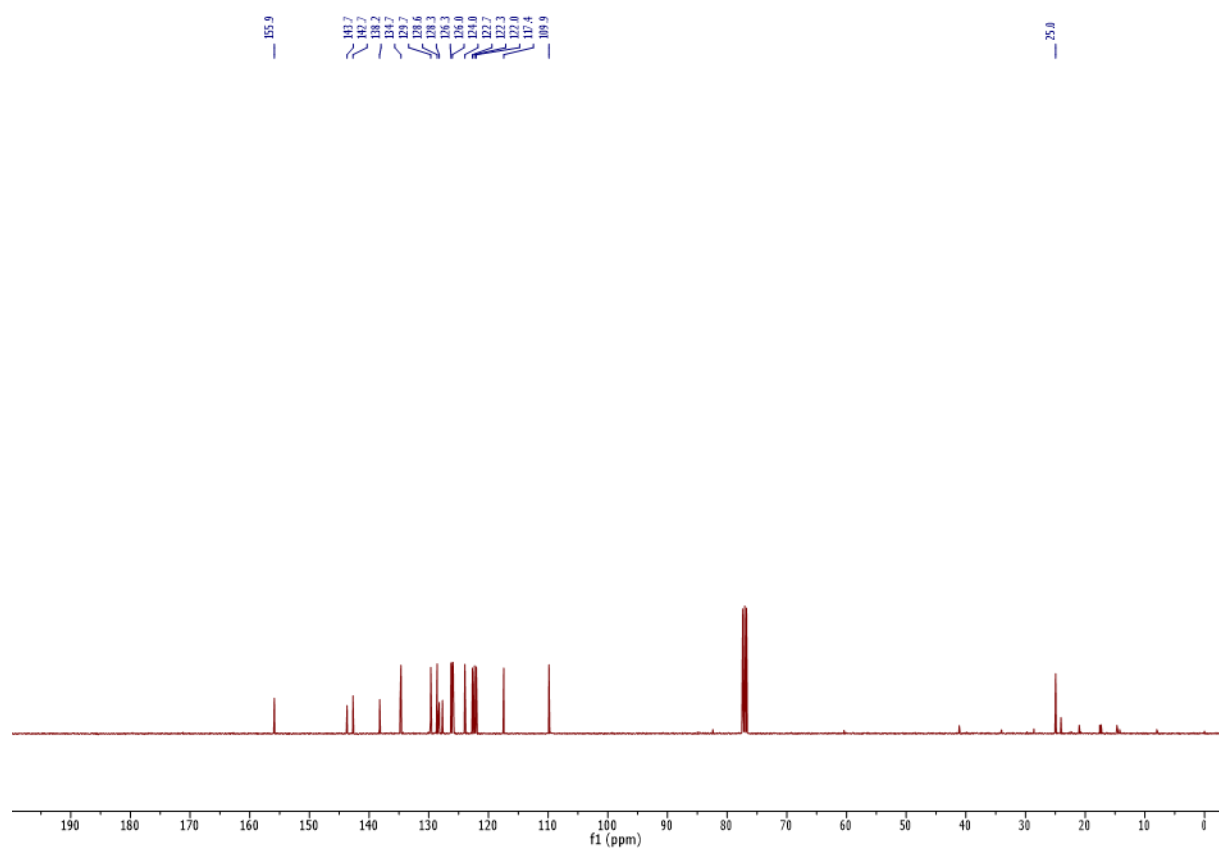
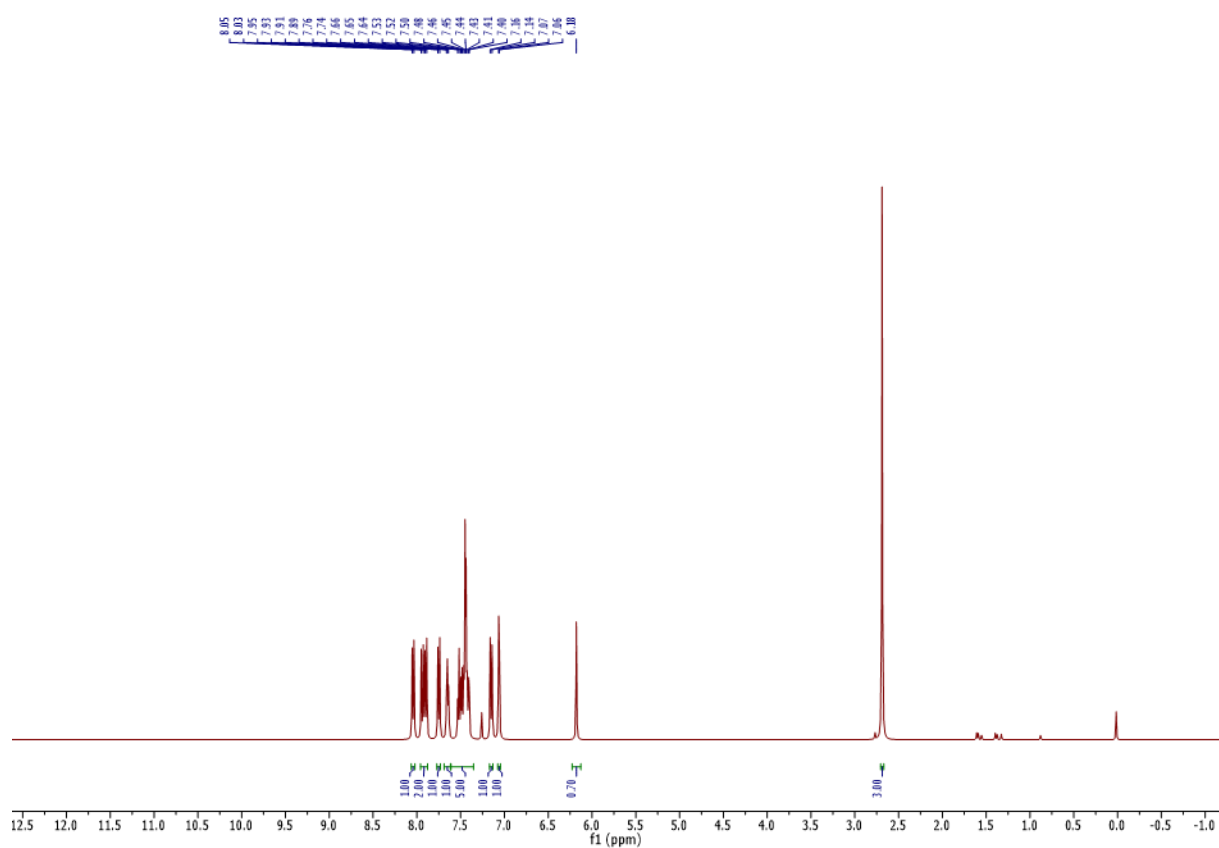


2-methyl-*N*-(4-(trifluoromethyl)phenyl)quinolin-6-amine (**3d**)

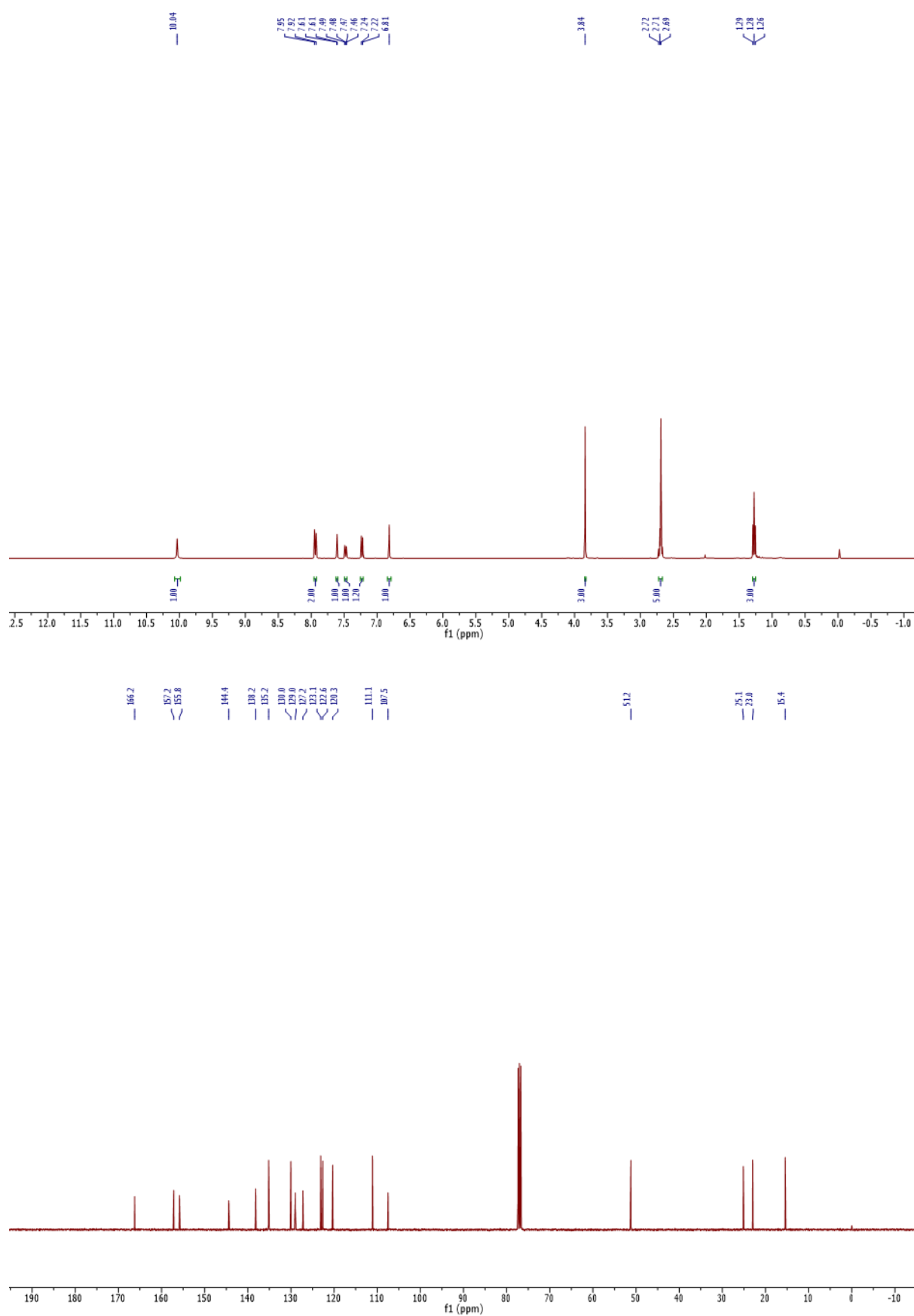




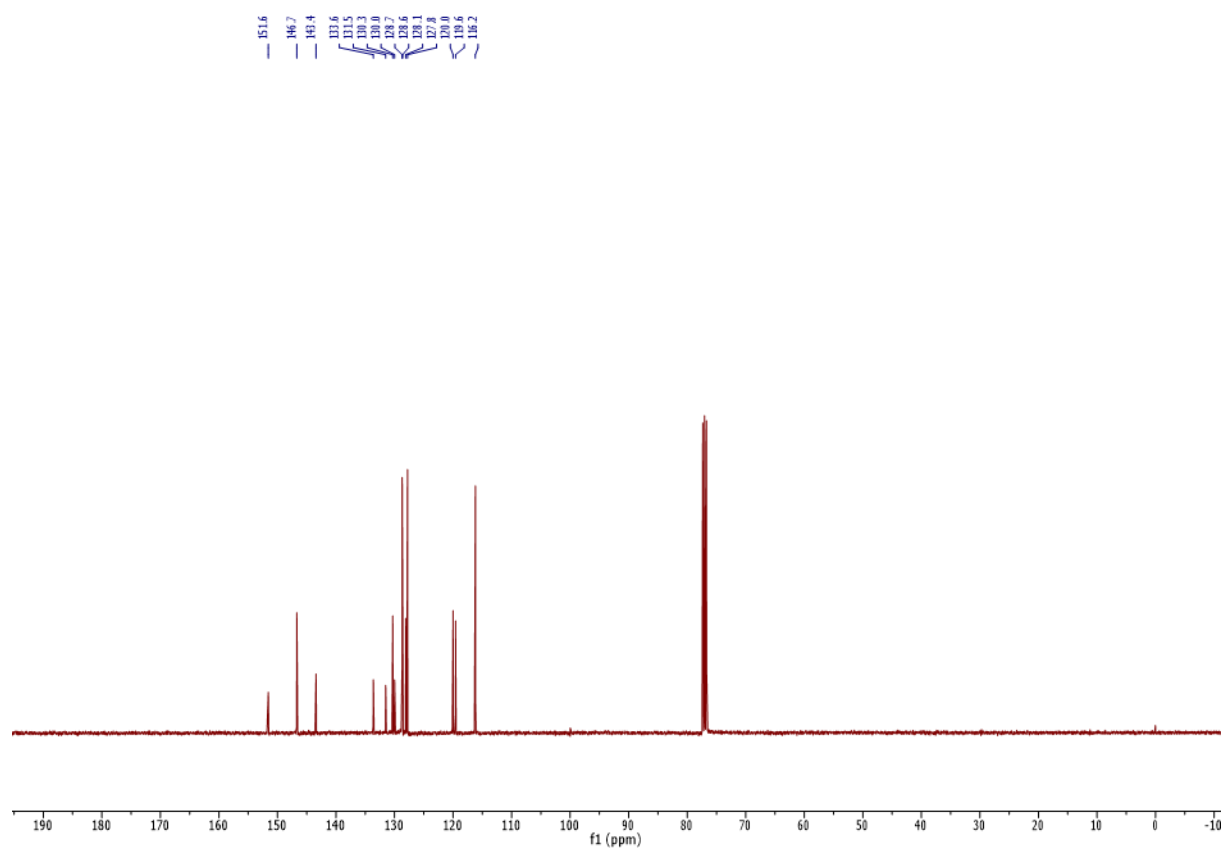
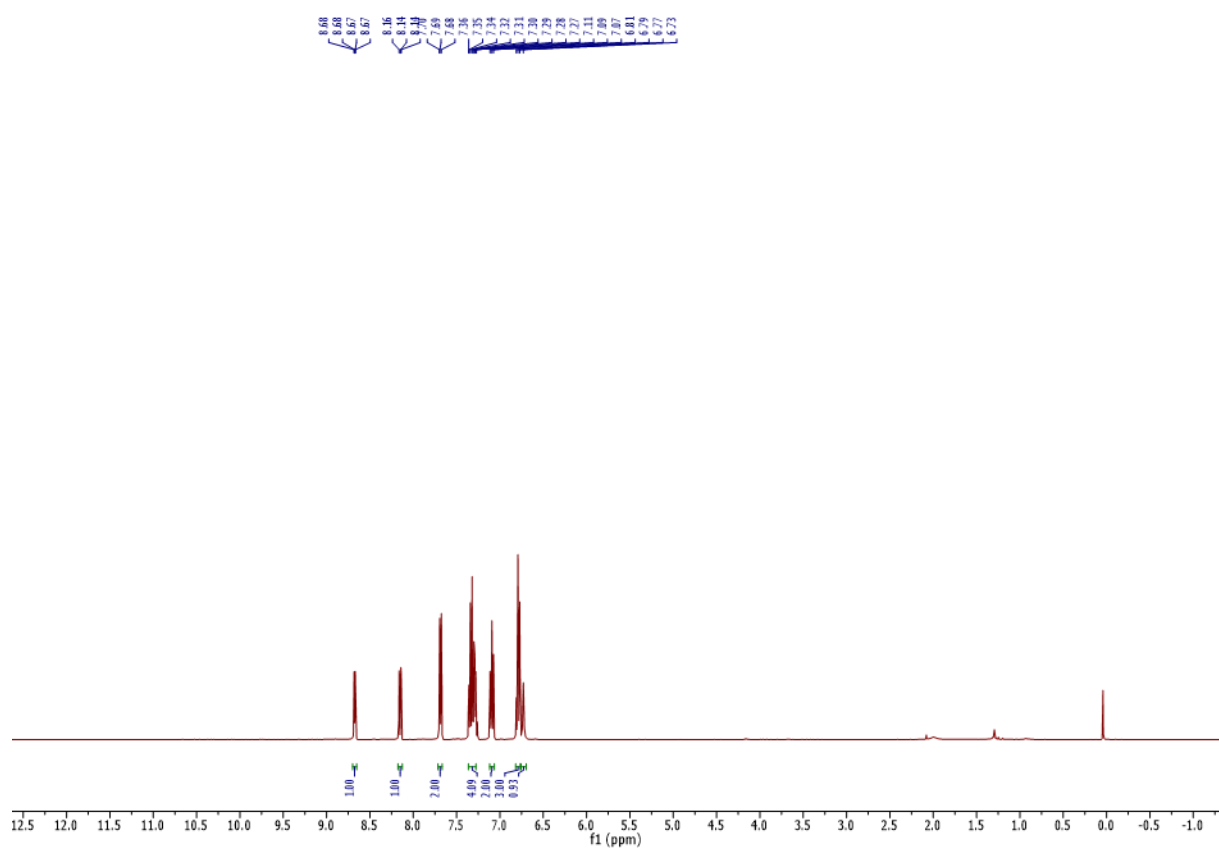
2-methyl-N-(naphthalen-1-yl)quinolin-6-amine (**3e**)



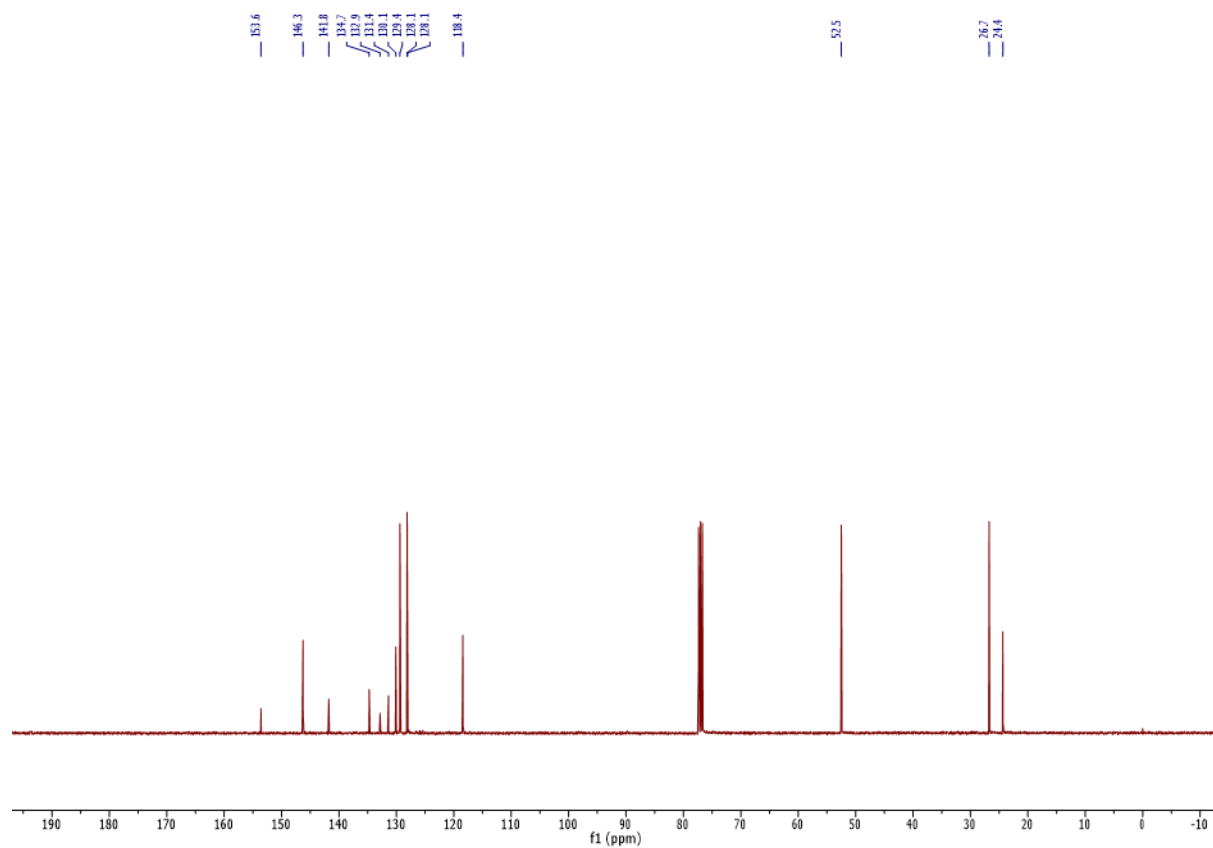
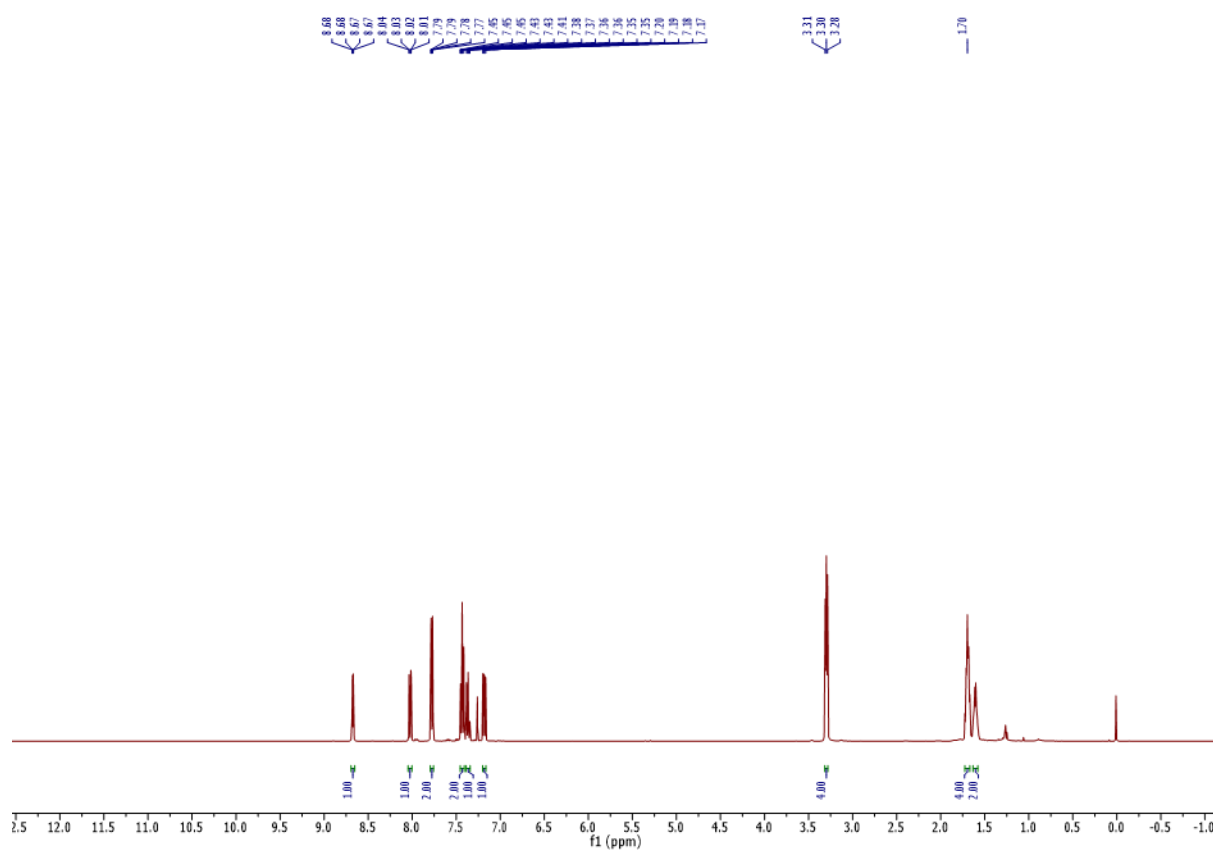
methyl 5-ethyl-2-((2-methylquinolin-6-yl)amino)thiophene-3-carboxylate (**3f**)



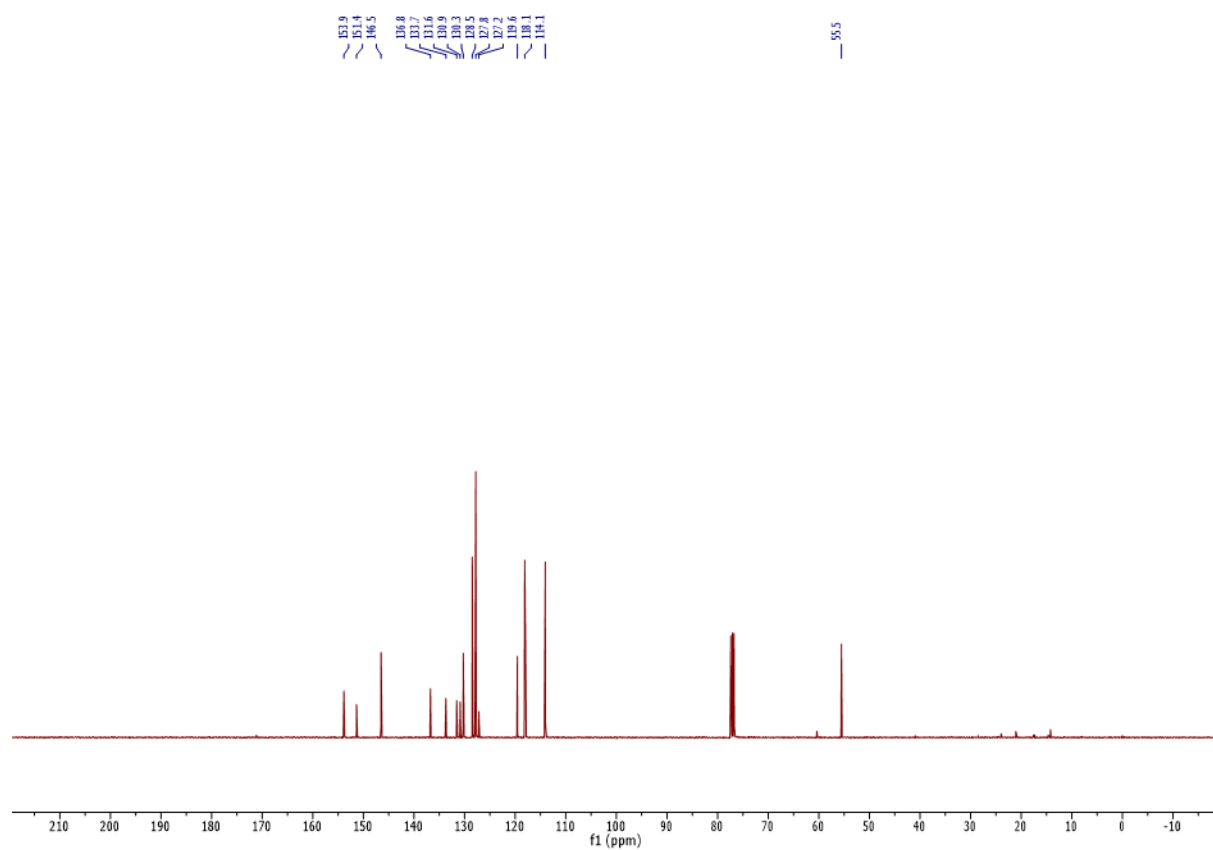
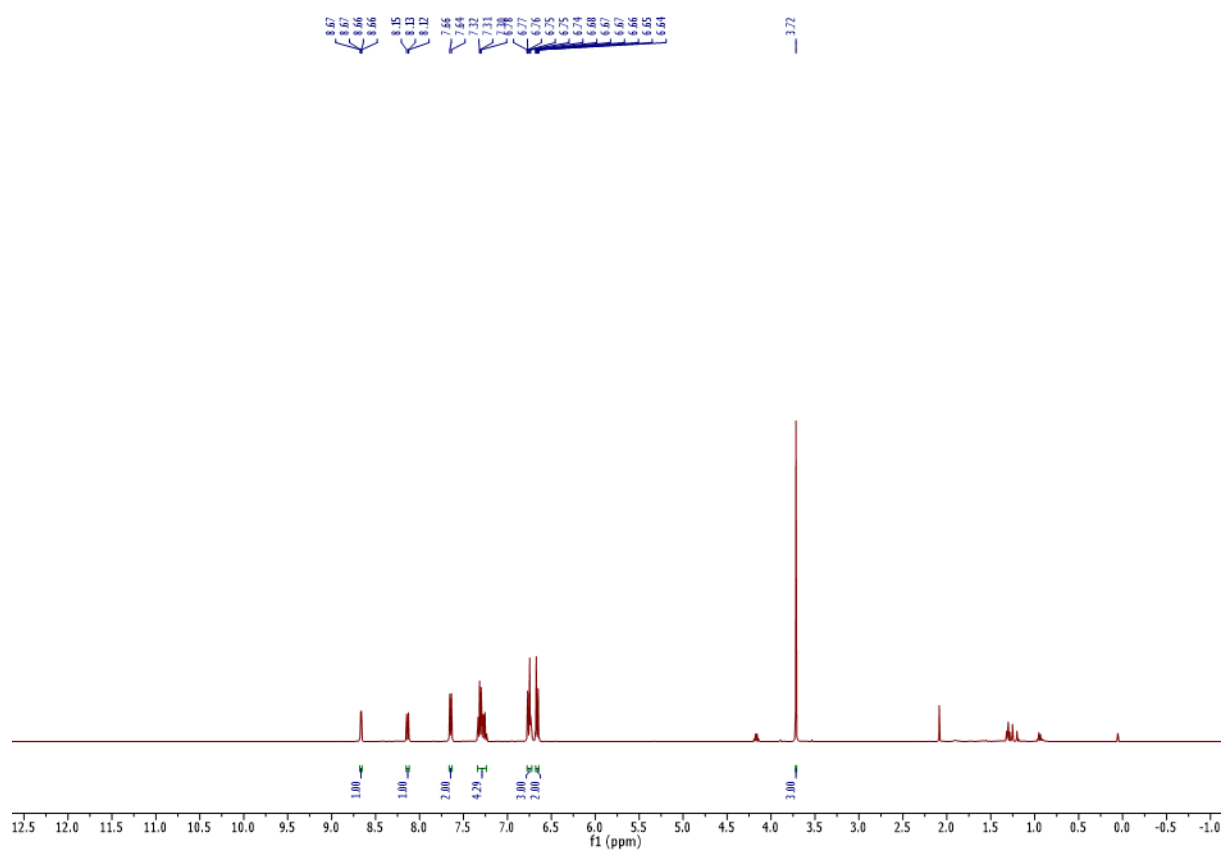
N,2-diphenylthieno[3,2-*b*]pyridin-3-amine (**4a**)



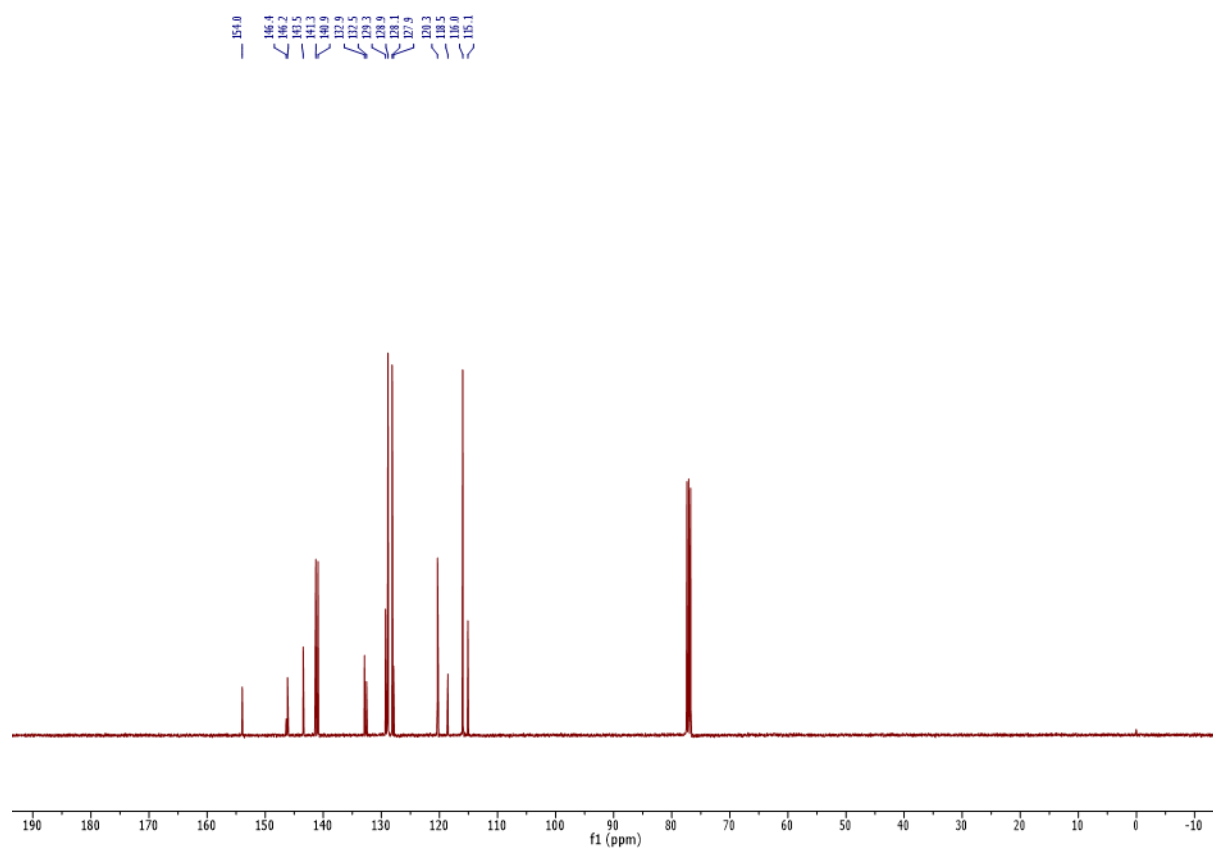
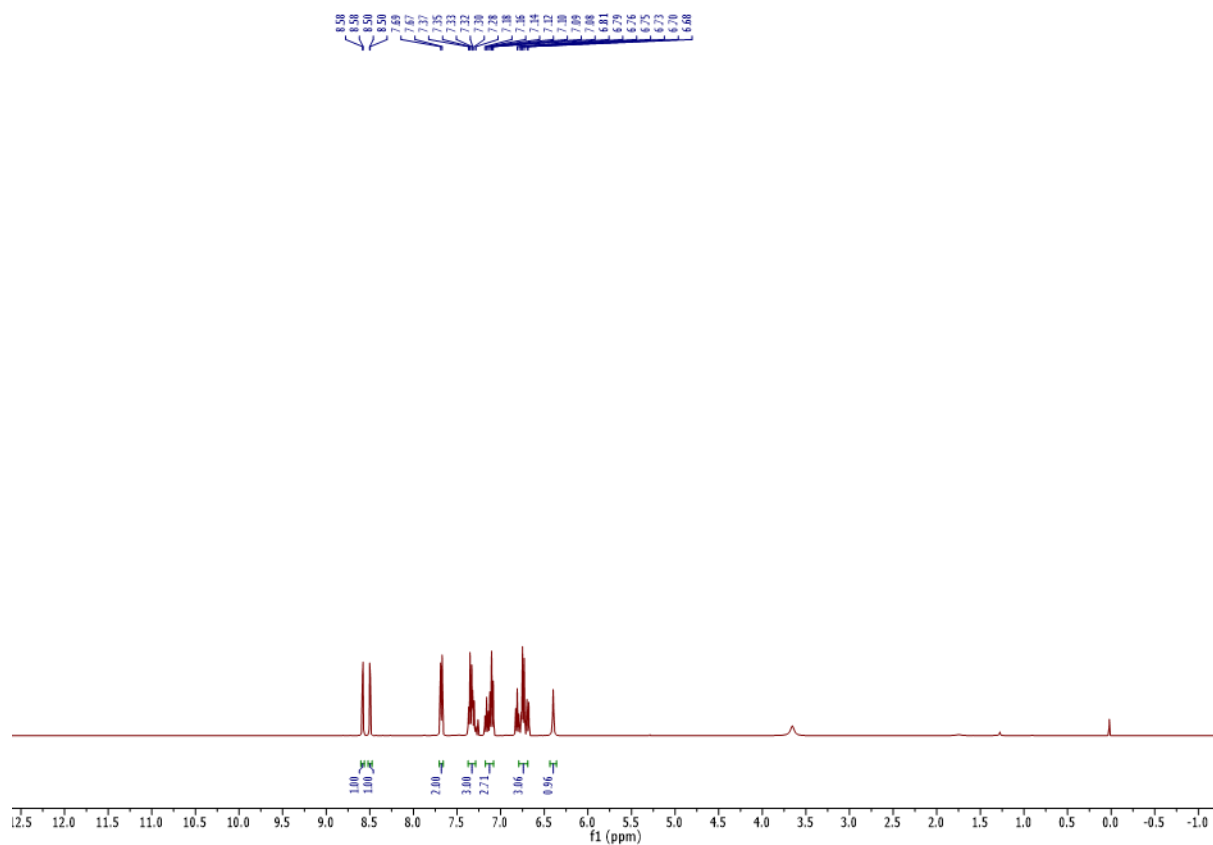
2-phenyl-3-(piperidin-1-yl)thieno[3,2-*b*]pyridine (**4b**)



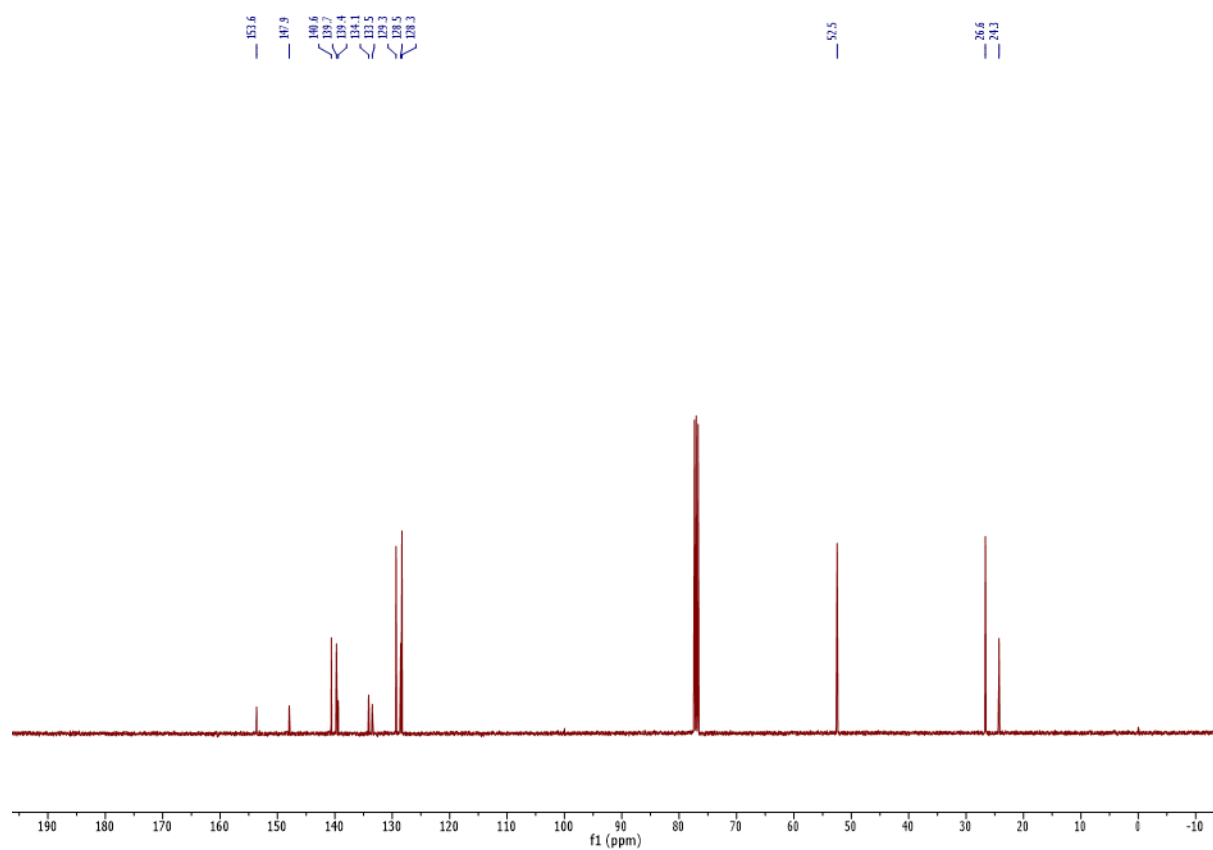
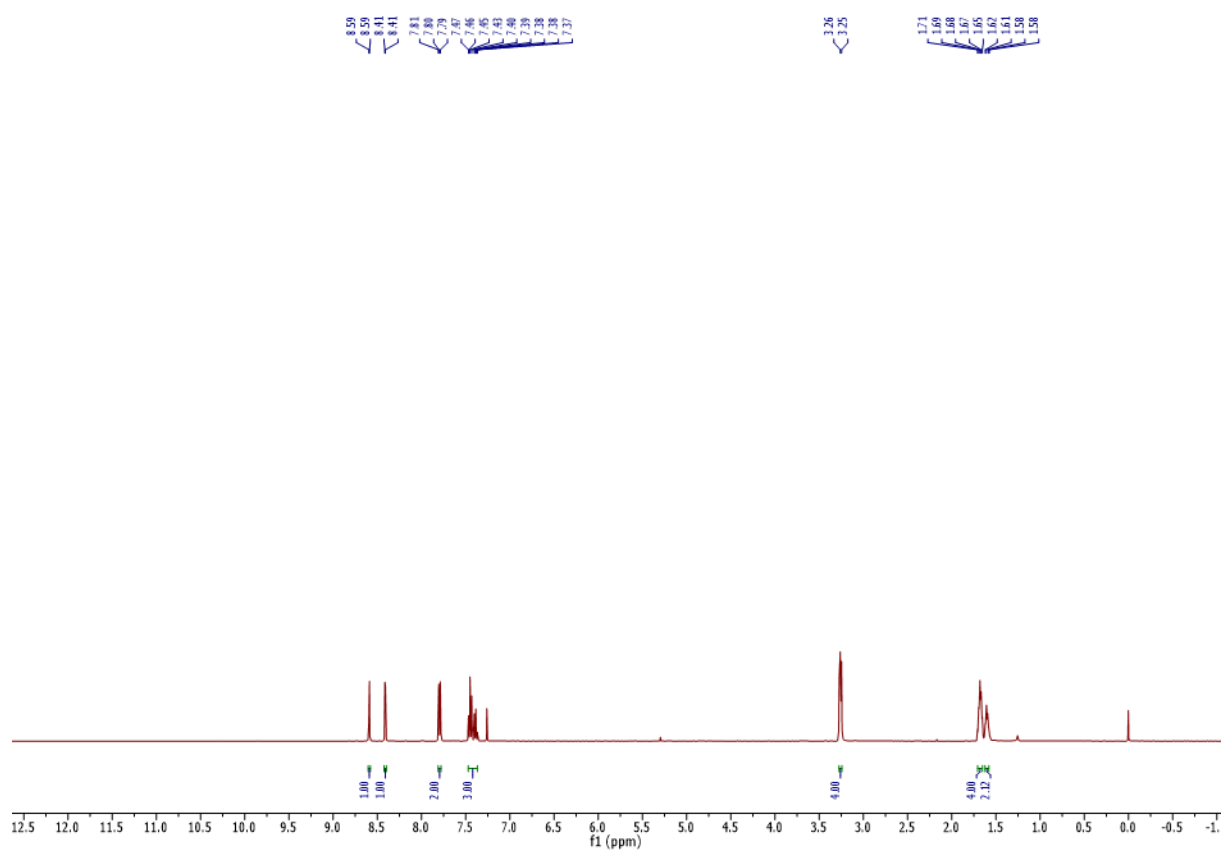
N-(4-methoxyphenyl)-2-phenylthieno[3,2-*b*]pyridin-3-amine (**4c**)



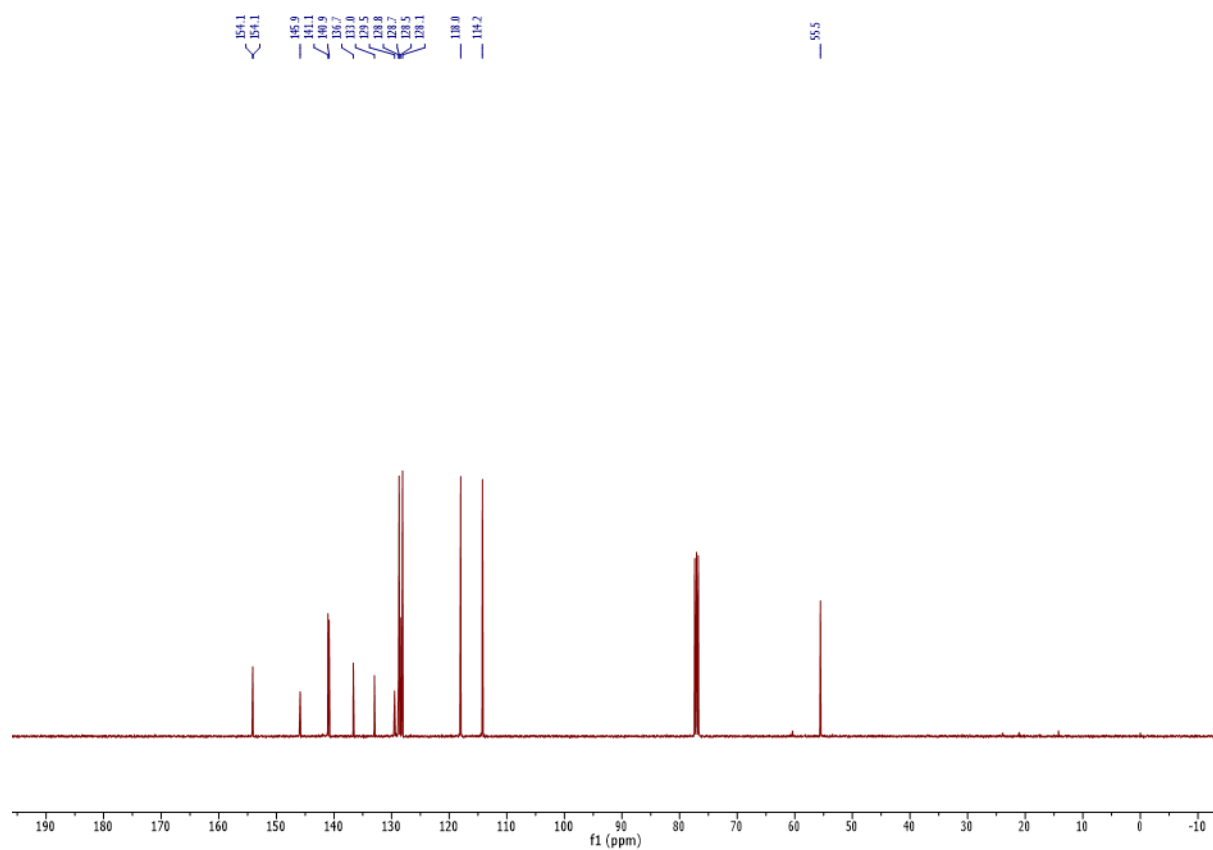
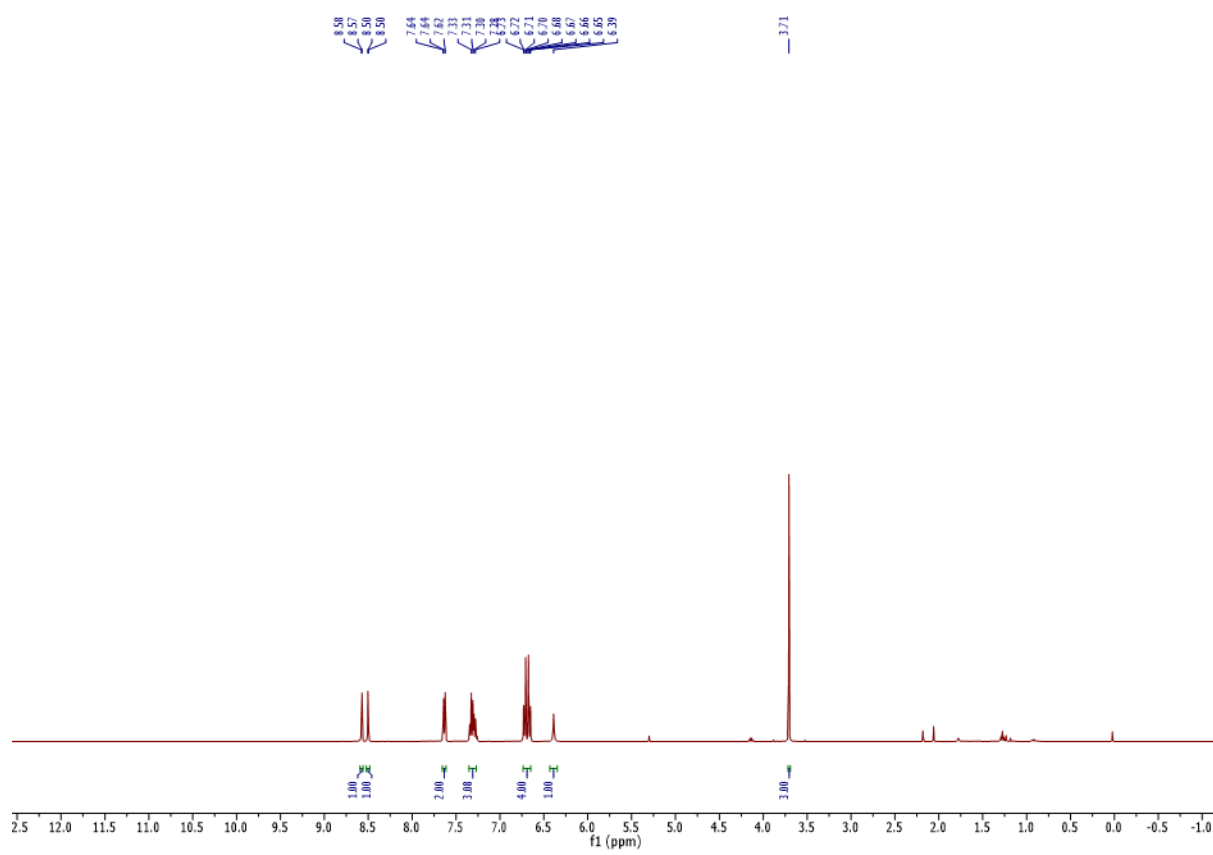
N,6-diphenylthieno[2,3-*b*]pyrazin-7-amine (**5a**)



6-phenyl-7-(piperidin-1-yl)thieno[2,3-*b*]pyrazine (**5b**)



N-(4-methoxyphenyl)-6-phenylthieno[2,3-*b*]pyrazin-7-amine (**5c**)



1.4. References

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