Electronic Supplementary Material (ESI) for Green Chemistry

SUPPORTING INFORMATION

Application of a recyclable fluorous oxime in the convenient syntheses of 3-amino-1,2-benzisoxazoles and 4-amino-1*H*-2,3-benzoxazines

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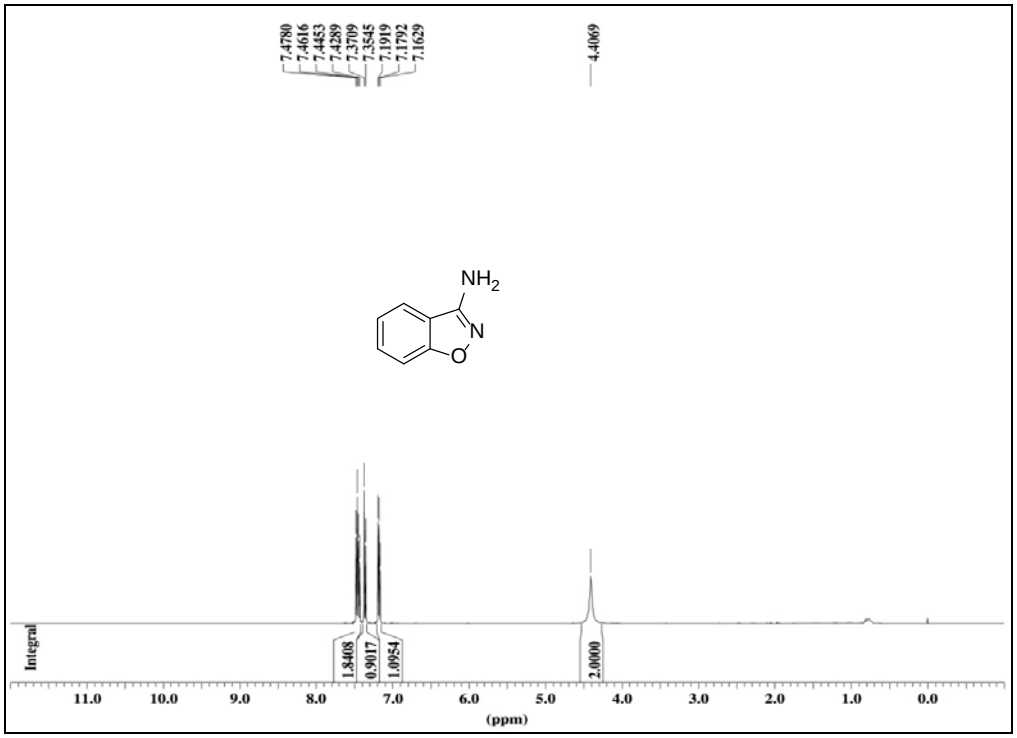
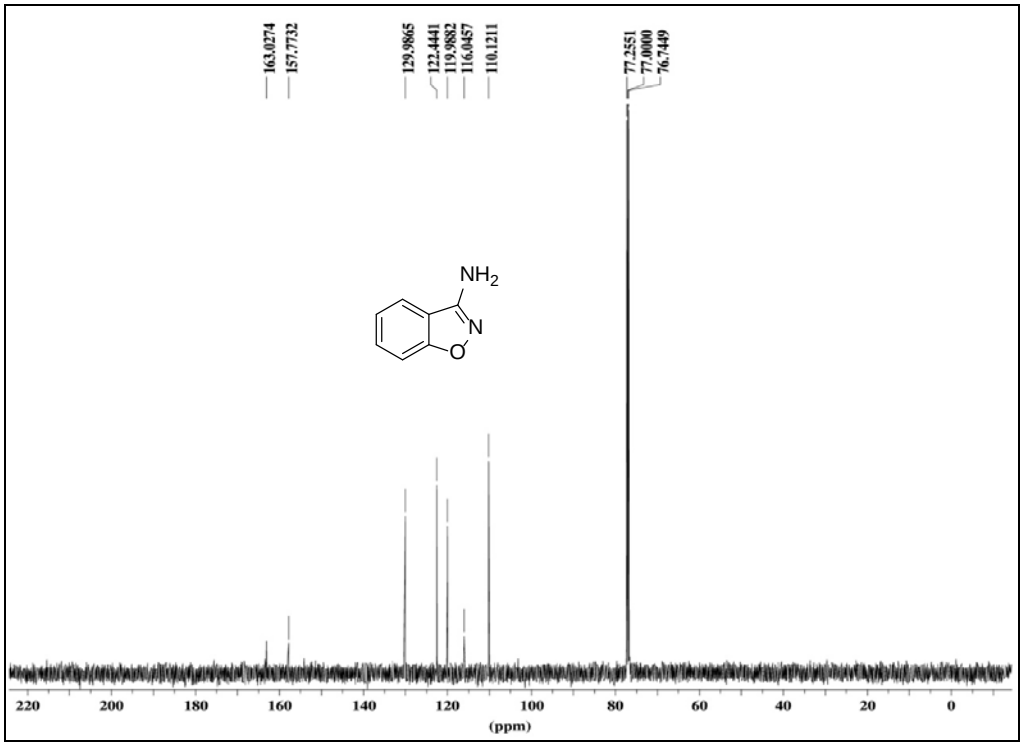
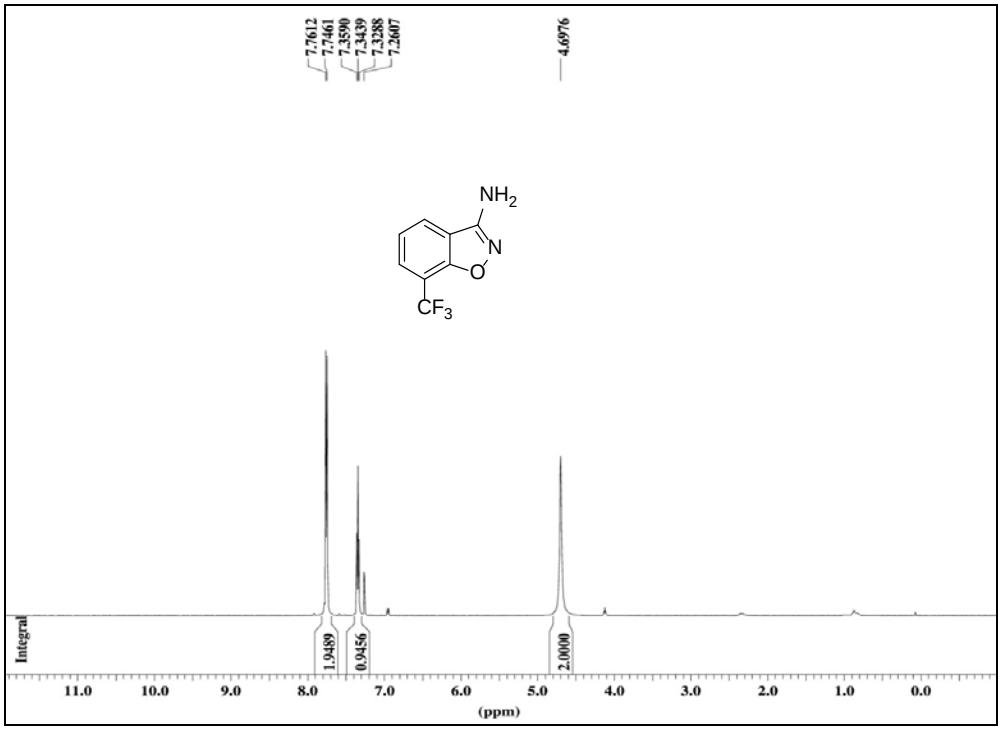
NMR and mass spectrometry characterization data of compounds **2** and **3**

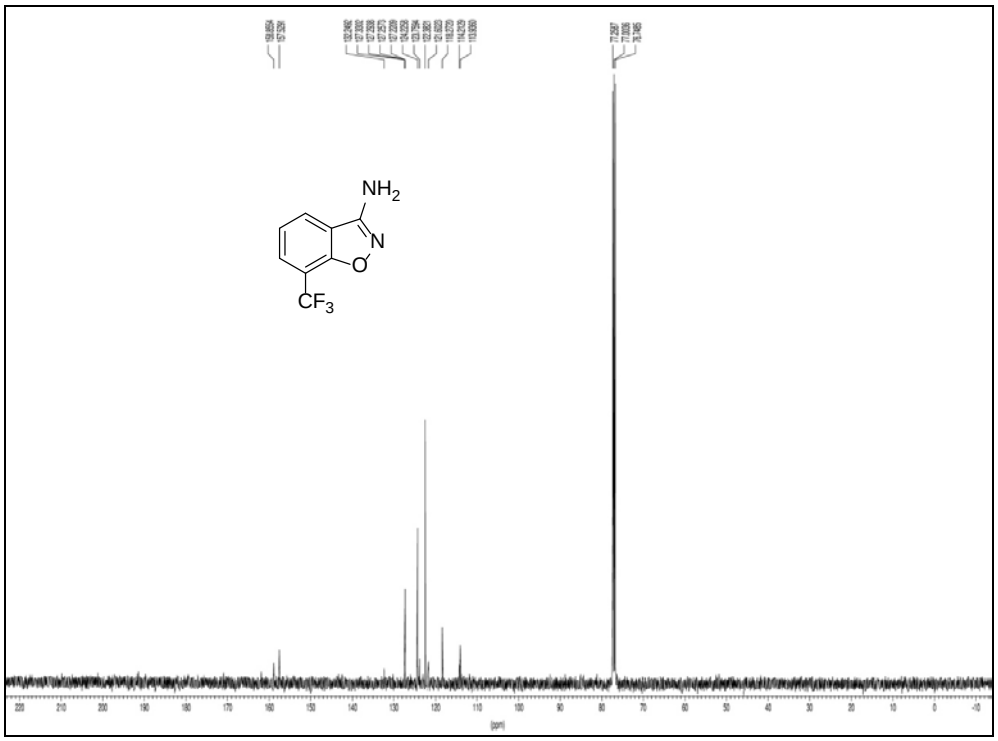
3-Amino-1,2-benzisoxazole (**2a**). Yellow solid. Mp: 109-110 ºC (lit.[1] mp 111 ºC). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 16.2, 7.7 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.20 – 7.15 (m, 1H), 4.41 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.0, 157.8, 130.0, 122.4, 120.0, 116.1, 110.1. HRMS (EI): calcd for $C_7H_6O_1N_2$ 134.0480, found 134.047



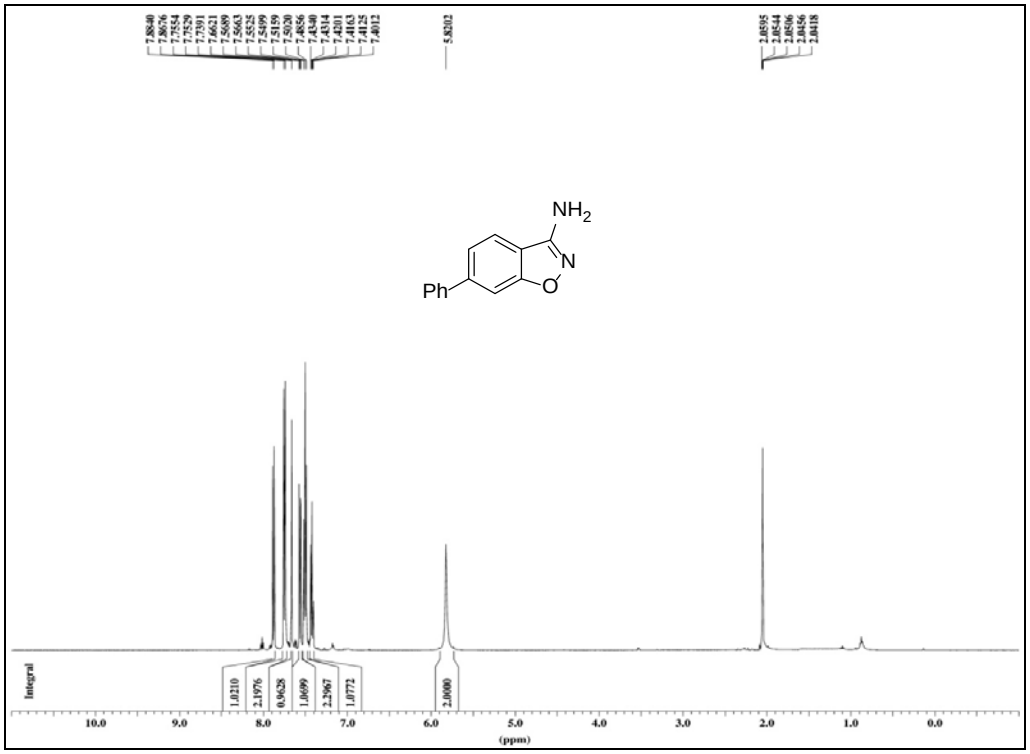


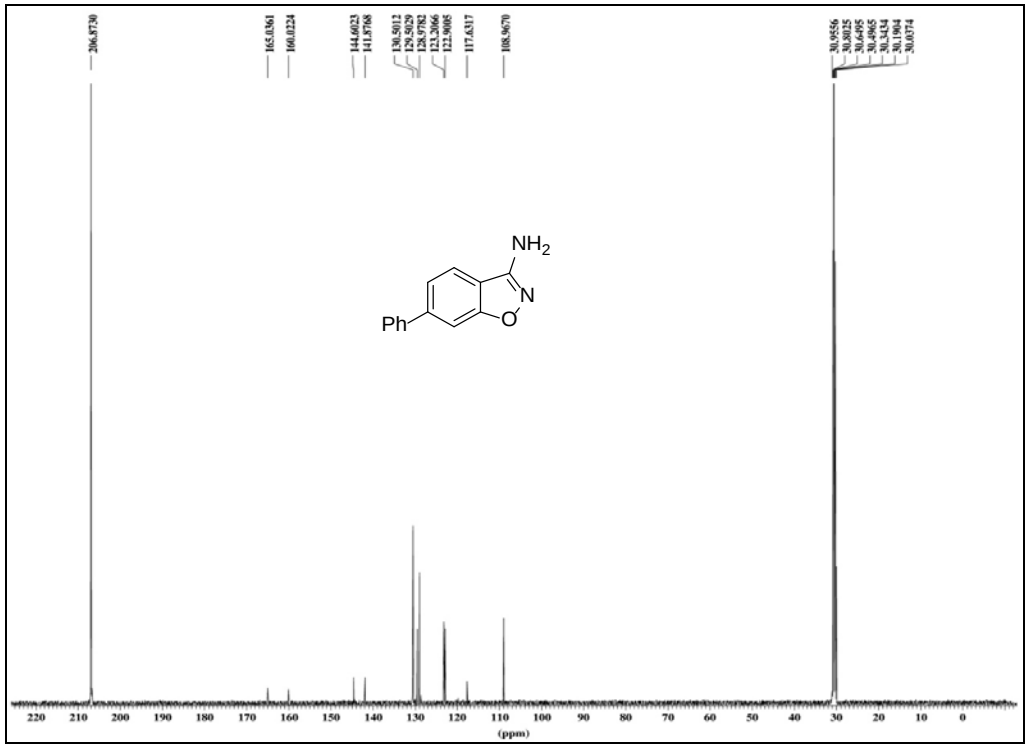
7-Trifluoromethyl-3-amino-1,2-benzisoxazole (**2b**). White solid. Mp: 110-112 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.7 Hz, 1H), 4.70 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 157.5, 132.3, 127.3 (q, *J* = 4.6 Hz), 122.7 (q, *J* = 270 Hz), 122.4, 118.3, 114.1 (q, *J* = 34.6 Hz). HRMS (EI): calcd for $C_8H_5O_1N_2F_3$ 202.0354, found 202.0360.



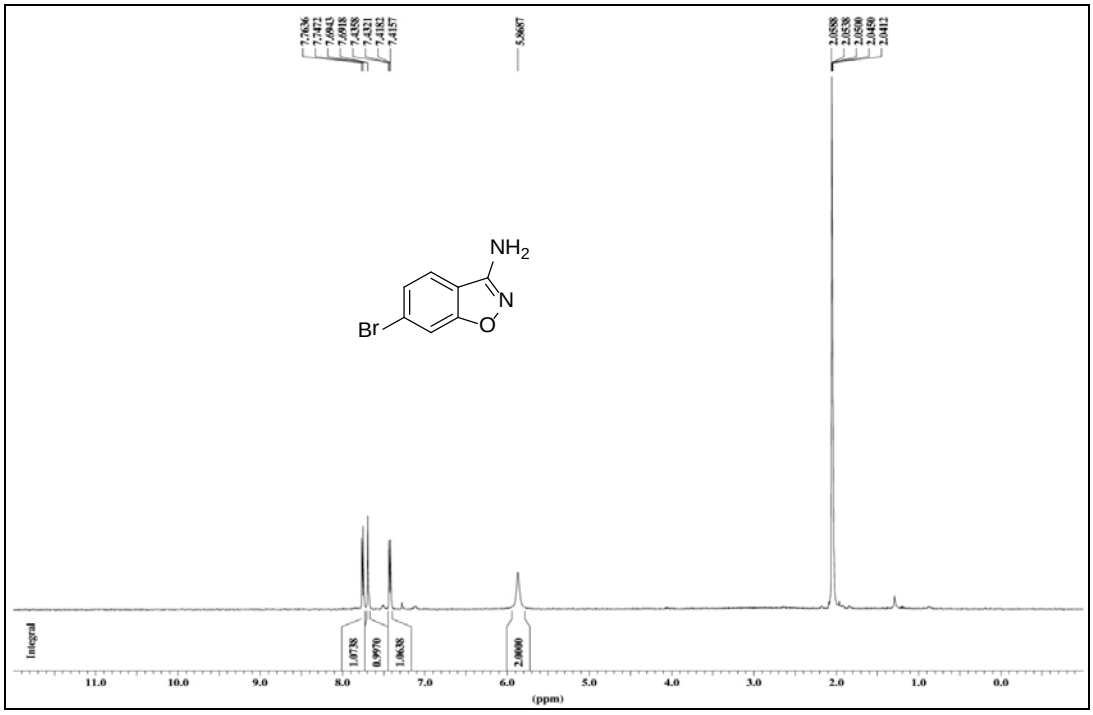


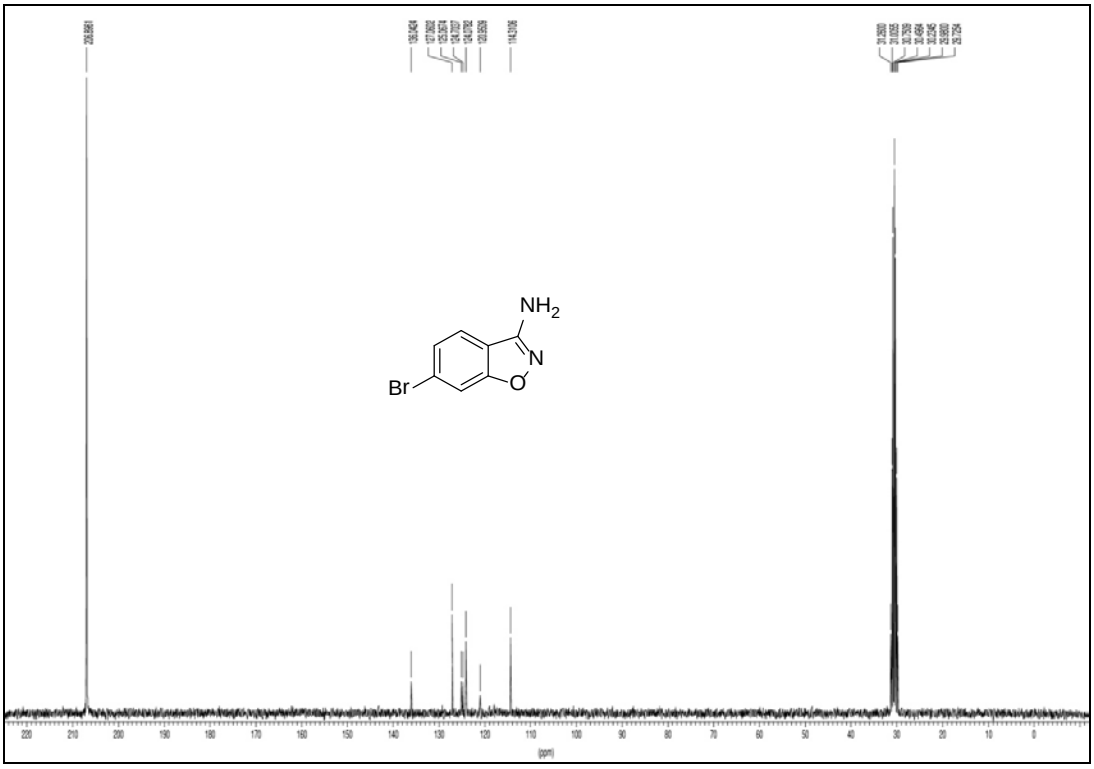
6-Phenyl-3-amino-1,2-benzisoxazole (**2c**). Brown solid. Mp: 184-186 ºC. ^{1}H NMR (500 MHz, Acetone) δ 7.88 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 7.1 Hz, 2H), 7.66 (s, 1H), 7.56 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.45 – 7.36 (m, 1H), 5.82 (s, 2H). ^{13}C NMR (125 MHz, Acetone) δ 165.0, 160.0, 144.6, 141.9, 130.5, 129.5, 129.0, 123.2, 122.9, 117.6, 109.0. HRMS (EI): calcd for $C_{13}H_{10}O_1N_2$ 210.0793, found 210.0790.



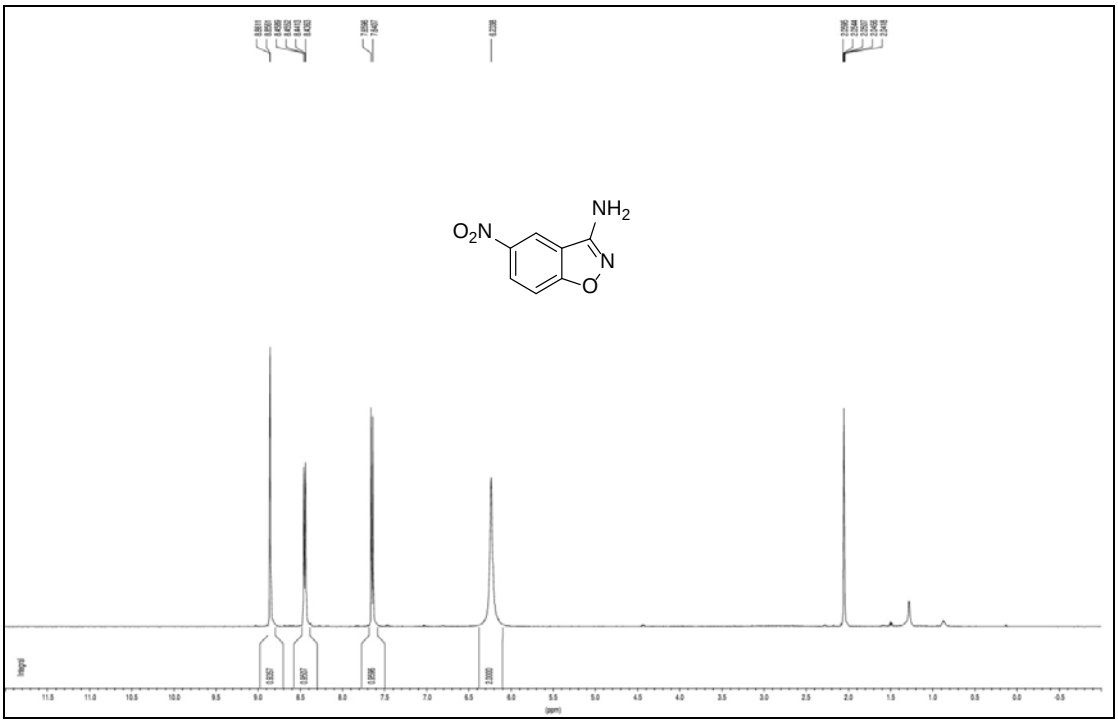


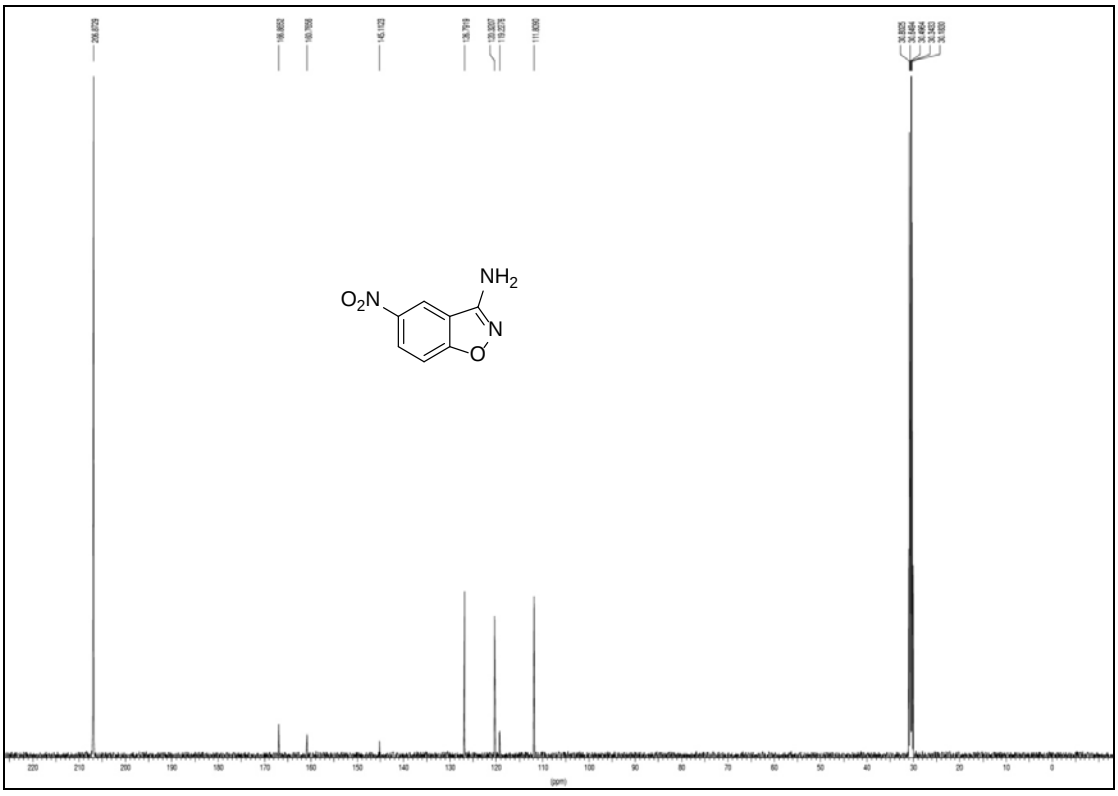
6-Bromo-3-amino-1,2-benzisoxazole (**2d**). Brown solid. Mp: 128-129 ºC. ^{1}H NMR (500 MHz, Acetone) δ 7.76 (d, *J* = 8.3 Hz, 1H), 7.69 (d, *J* = 1.4 Hz, 1H), 7.43 (dd, *J* = 8.3, 1.5 Hz, 1H), 5.87 (s, 2H). ^{13}C NMR (75 MHz, Acetone) δ 136.0, 127.1, 125.1, 124.7, 124.1, 121.0, 114.3. HRMS (EI): calcd for $C_7H_5O_1N_2{}^{79}Br_1$ 211.9585, found 211.9582; calcd for $C_7H_5O_1N_2{}^{81}Br_1$ 213.9565, found 213.9565.



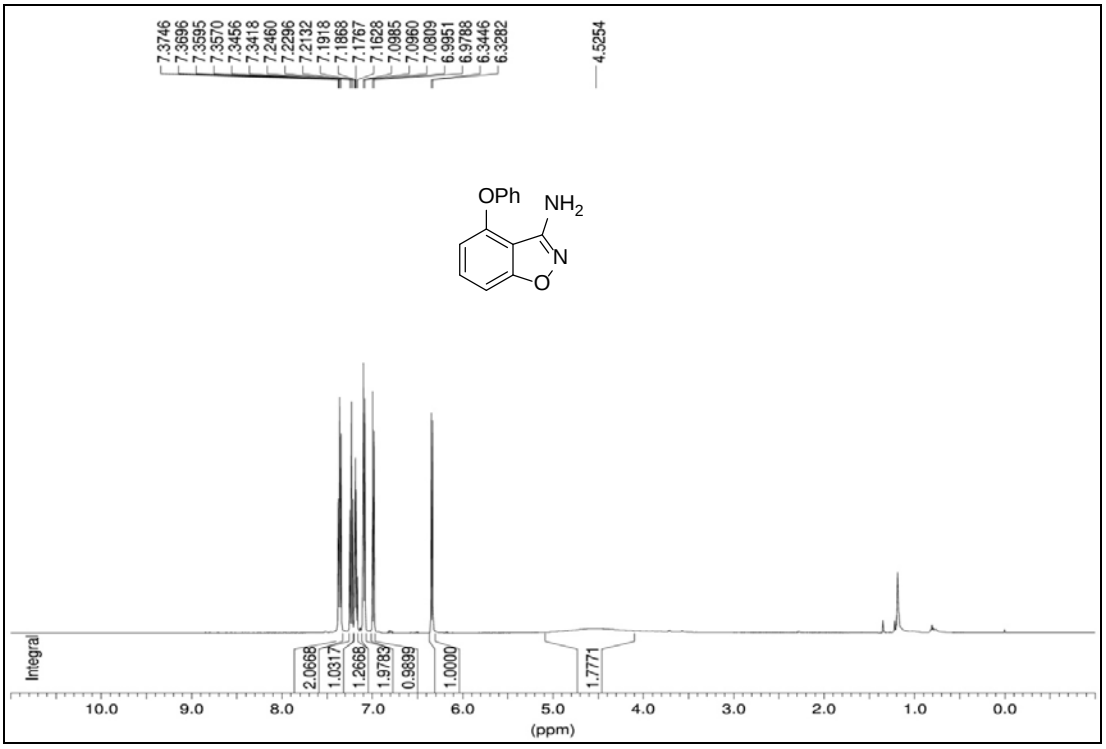


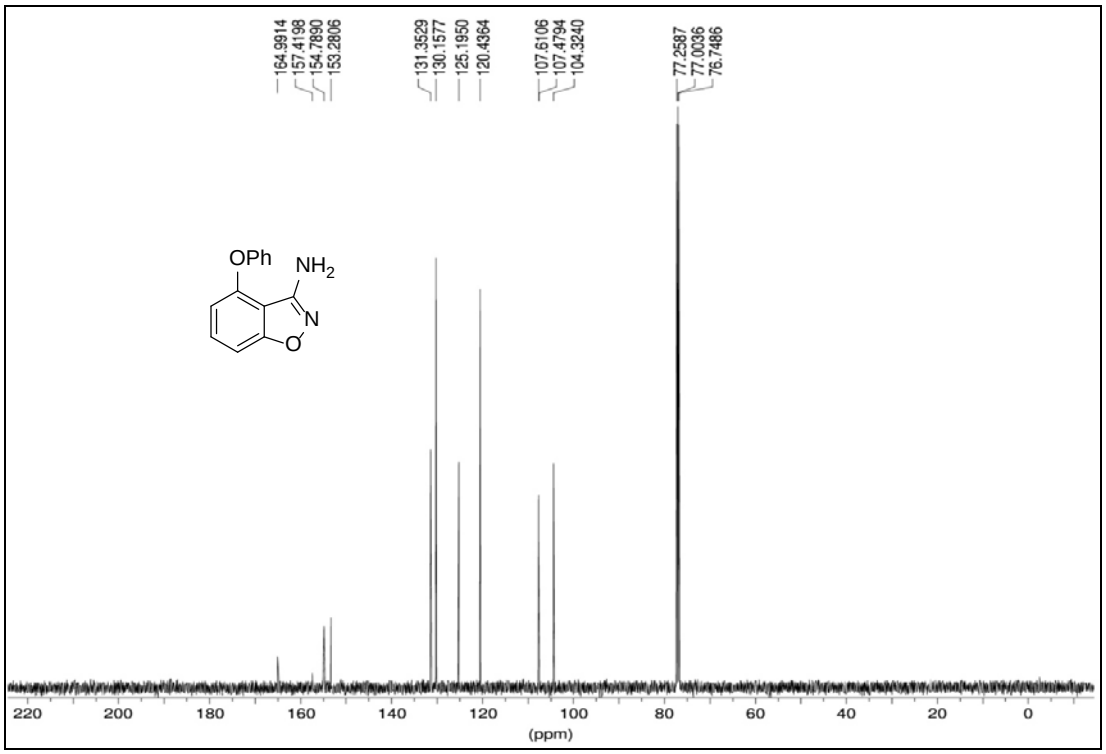
5-Nitro-3-amino-1,2-benzisoxazole (**2e**). Yellow solid. Mp: 208-210 ºC (lit.[2] mp 208 ºC). ^{1}H NMR (500 MHz, Acetone) δ 8.86 (d, *J* = 2.2 Hz, 1H), 8.45 (dd, *J* = 9.1, 2.2 Hz, 1H), 7.65 (d, *J* = 9.1 Hz, 1H), 6.23 (s, 2H). ^{13}C NMR (125 MHz, Acetone) δ 166.9, 160.8, 145.1, 126.8, 120.3, 119.2, 111.8. HRMS (EI): calcd for $C_7H_5O_3N_3$ 179.0331, found 179.0326.



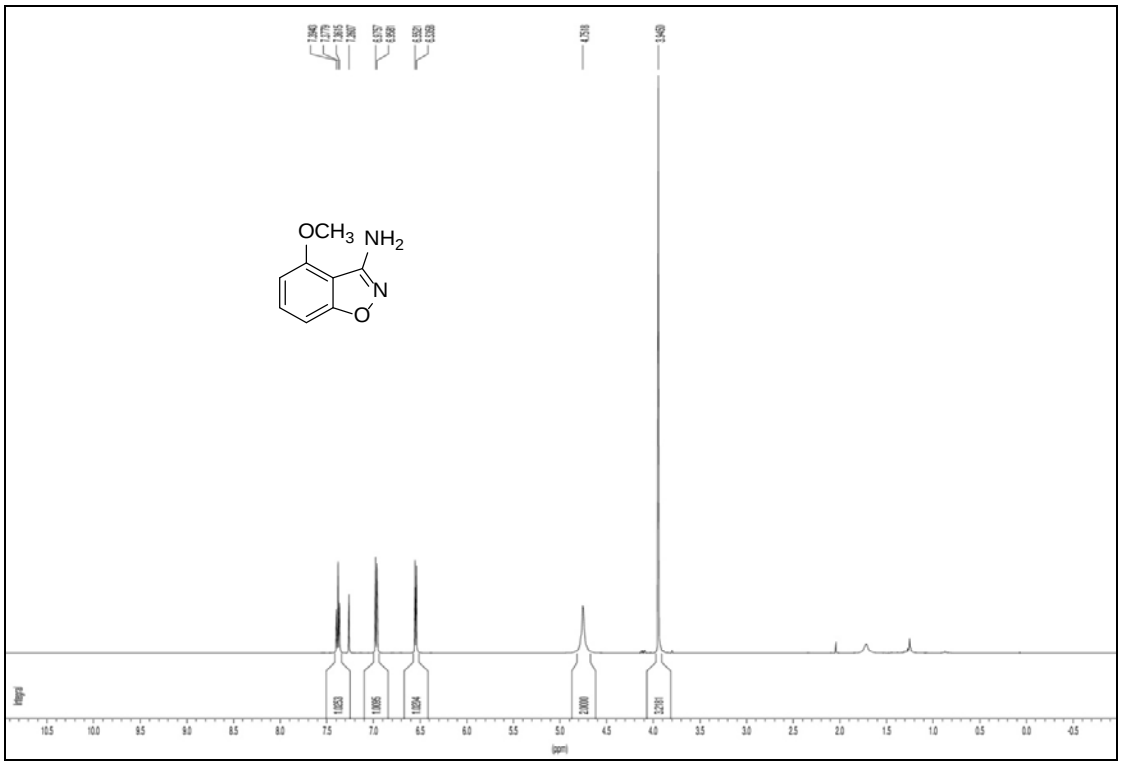


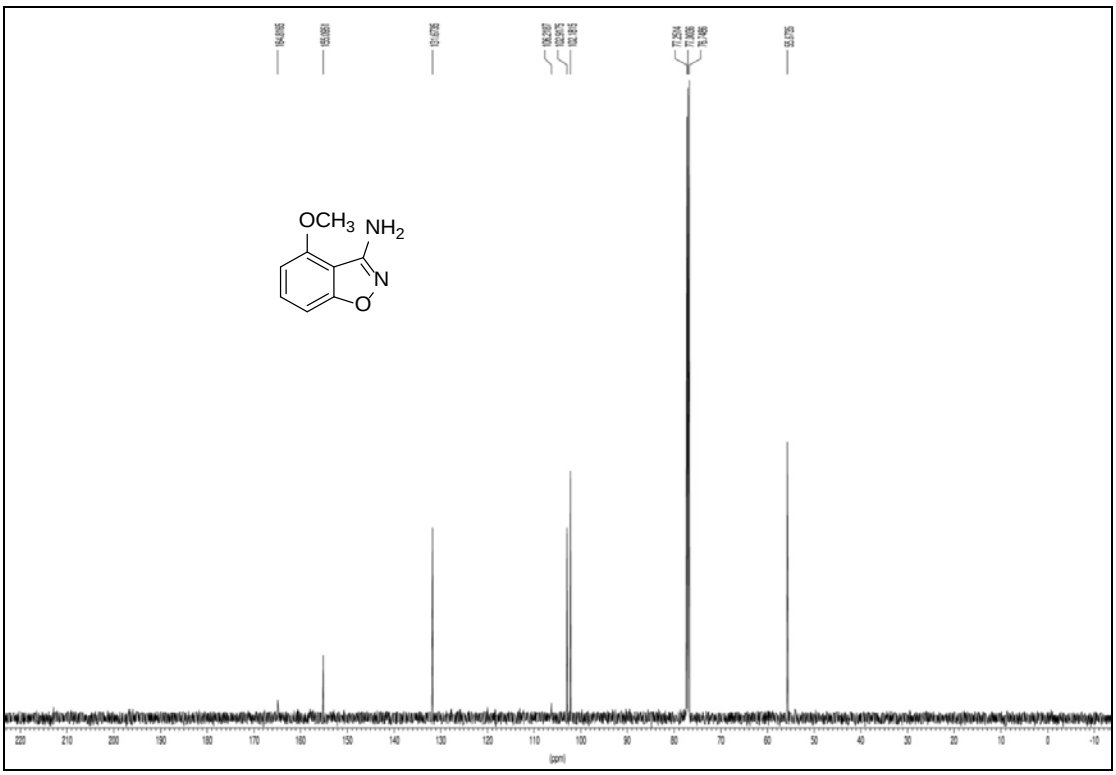
4-Phenoxy-3-amino-1,2-benzisoxazole (**2f**). White solid. Mp: 132-133 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.32 (m, 2H), 7.23 (t, *J* = 8.2 Hz, 1H), 7.18 (dd, *J* = 9.9, 5.0 Hz, 1H), 7.14 – 7.05 (m, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.34 (d, *J* = 8.0 Hz, 1H), 4.53 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 157.4, 154.8, 153.3, 131.4, 130.2, 125.2, 120.4, 107.6, 107.5, 104.3. HRMS (EI): calcd for $C_{13}H_{10}O_2N_2$ 226.0742, found 226.0739.



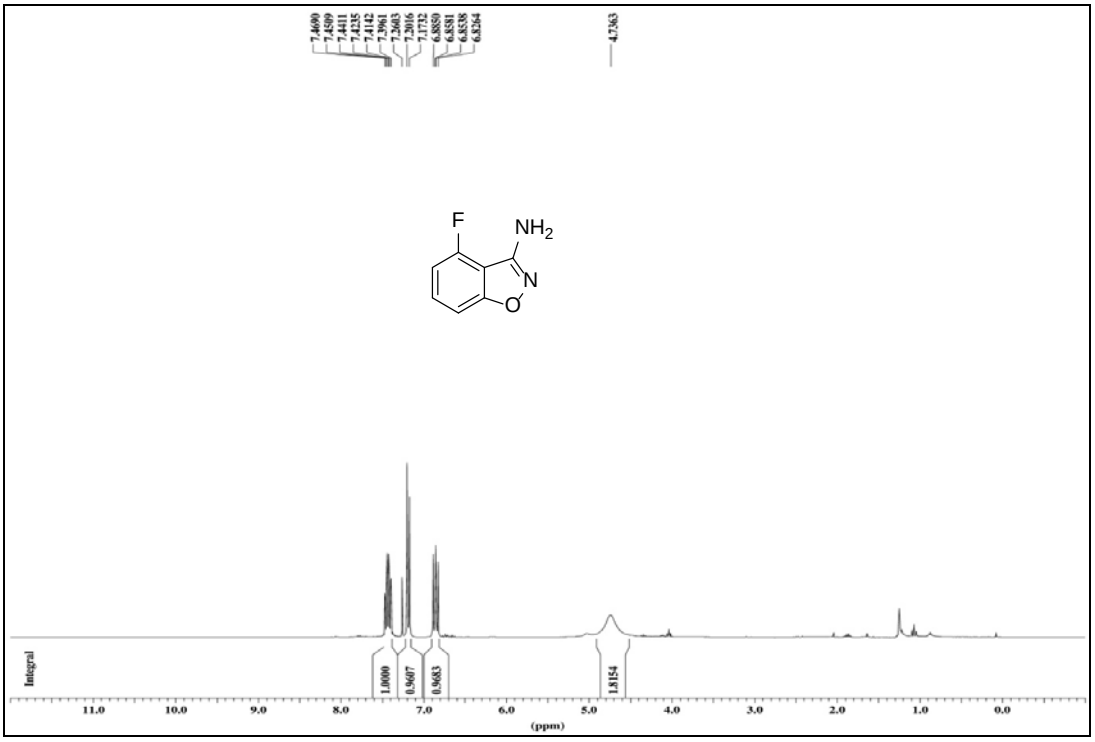


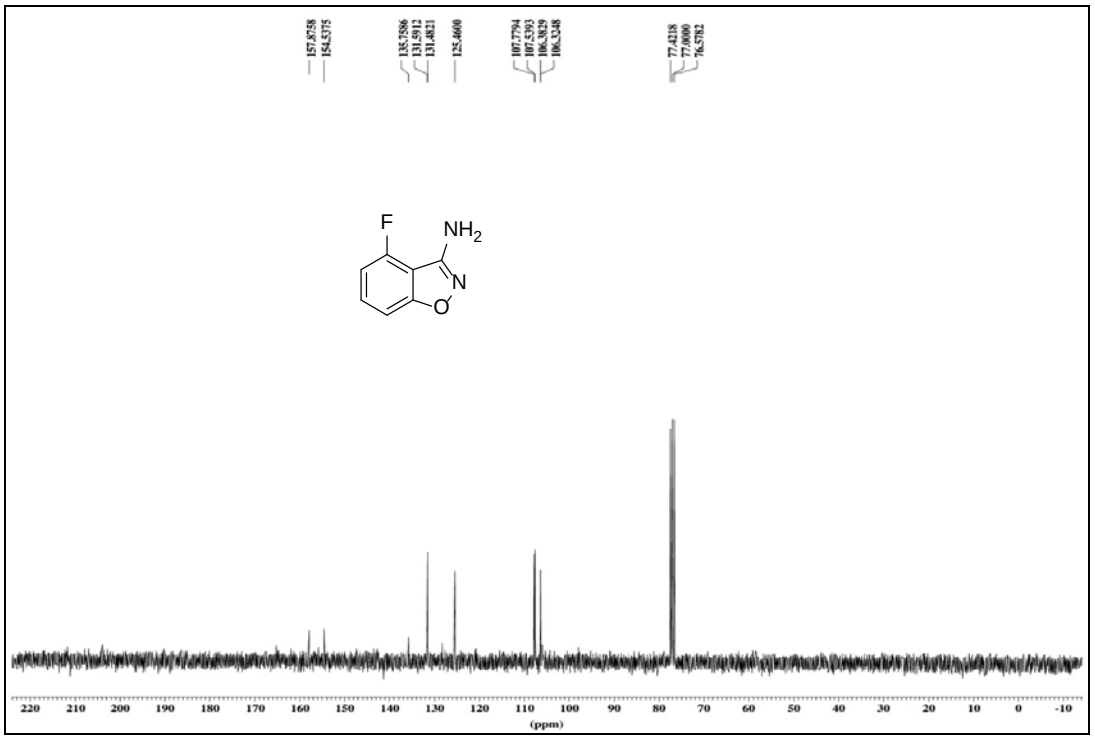
4-Methoxy-3-amino-1,2-benzisoxazole (**2g**). White solid. Mp: 141-142 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, *J* = 8.2 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.54 (d, *J* = 7.9 Hz, 1H), 4.75 (s, 2H), 3.94 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.8, 155.1, 131.7, 106.2, 102.9, 102.2, 55.7. HRMS (EI): calcd for $C_8H_8O_2N_2$ 164.0586, found 164.0587.



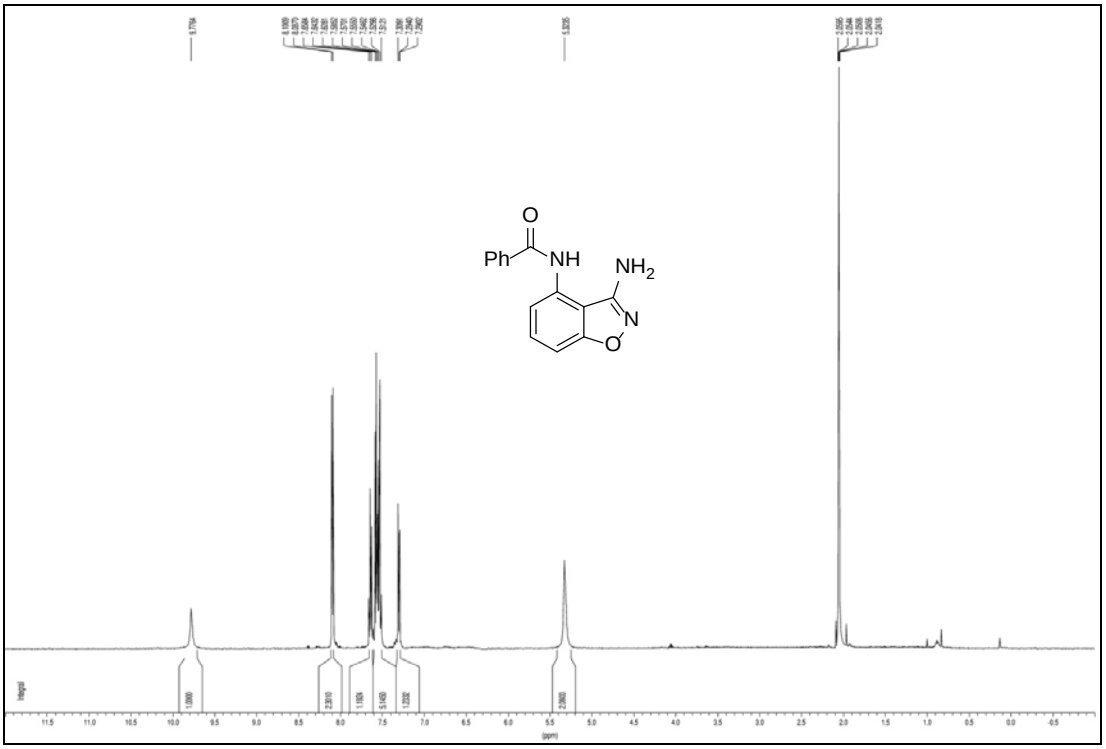


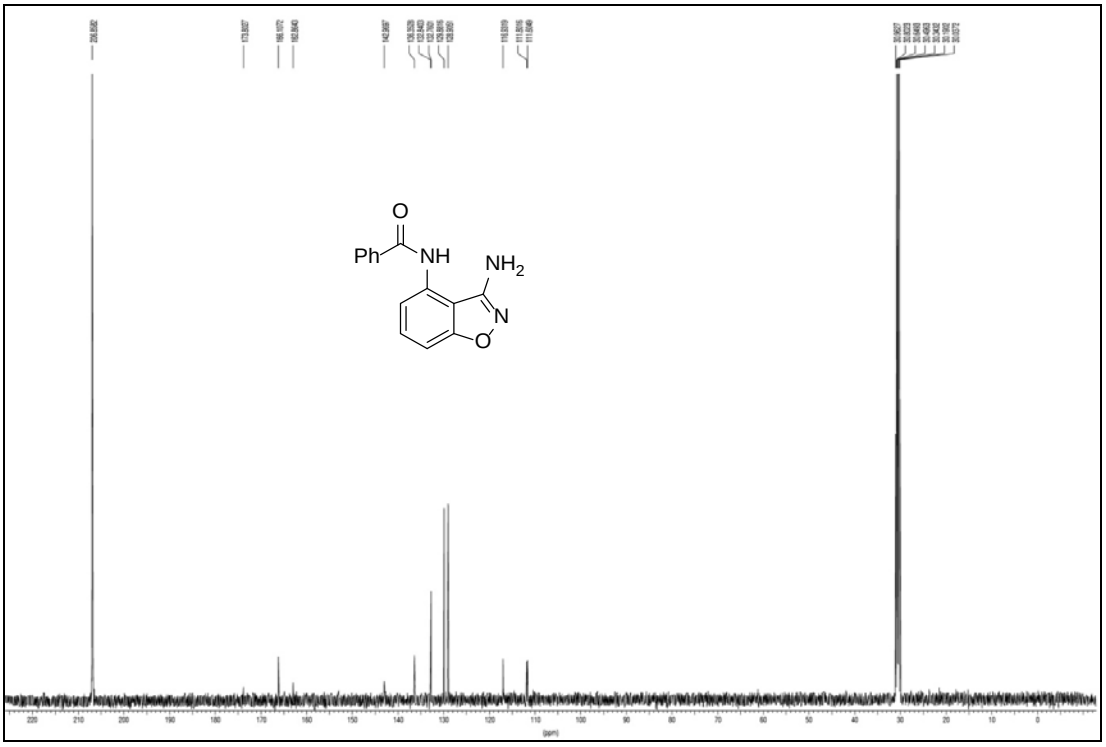
4-Fluoro-3-amino-1,2-benzisoxazole (**2h**). Brown solid. Mp: 42-43 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (td, *J* = 8.2, 5.4 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 1H), 6.86 (dd, *J* = 9.5, 8.1 Hz, 1H), 4.73 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2 (d, *J* = 250 Hz), 135.8, 131.5 (d, *J* = 8.2 Hz), 128.1, 125.5, 107.7 (d, *J* = 18 Hz), 106.4 (d, *J* = 4.4 Hz). HRMS (EI): calcd for $C_7H_5O_1N_2F_1$ 152.0386, found 152.0383.



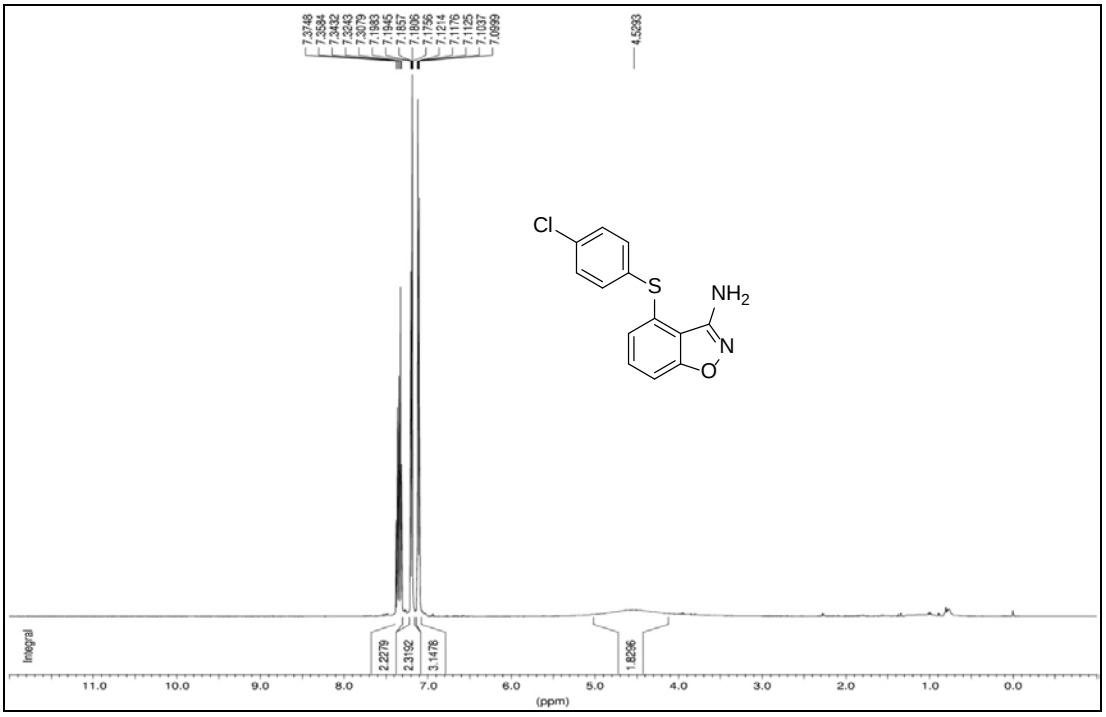


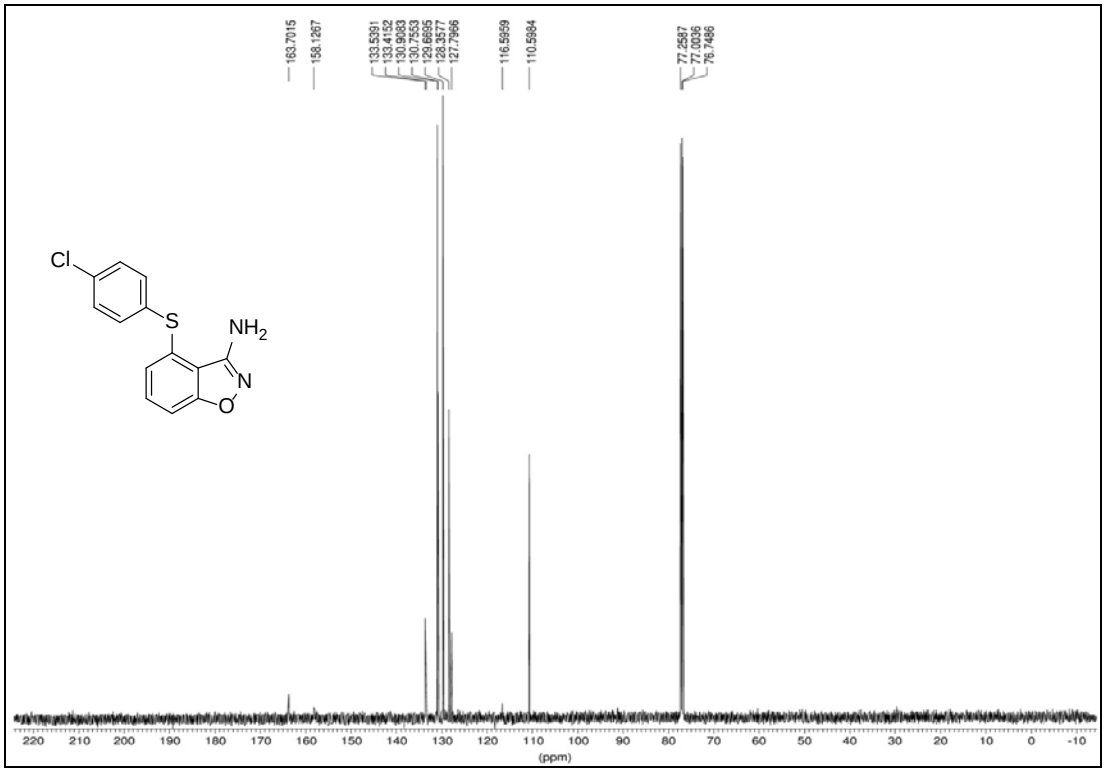
4-Benzamide-3-amino-1,2-benzisoxazole (**2i**). Brown solid. Mp: 164-165 ºC. ^{1}H NMR (500 MHz, Acetone) δ 9.78 (s, 1H), 8.09 (d, *J* = 7.3 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.59 – 7.50 (m, 5H), 7.30 (dd, *J* = 7.5, 1.4 Hz, 1H), 5.32 (s, 2H). ^{13}C NMR (125 MHz, Acetone) δ 173.8, 166.1, 162.9, 143.0, 136.4, 132.8, 132.8, 129.9, 128.9, 116.9, 111.8, 111.6. HRMS (EI): calcd for $C_{14}H_{11}O_2N_3$ 253.0851, found 253.0854.



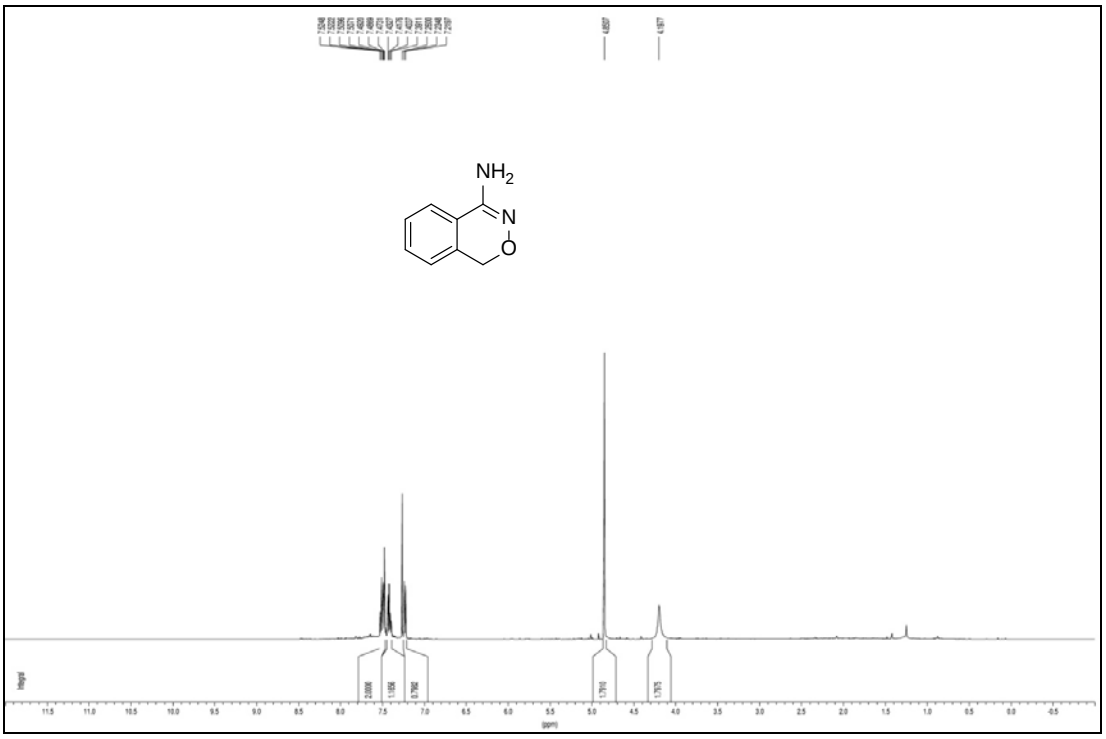


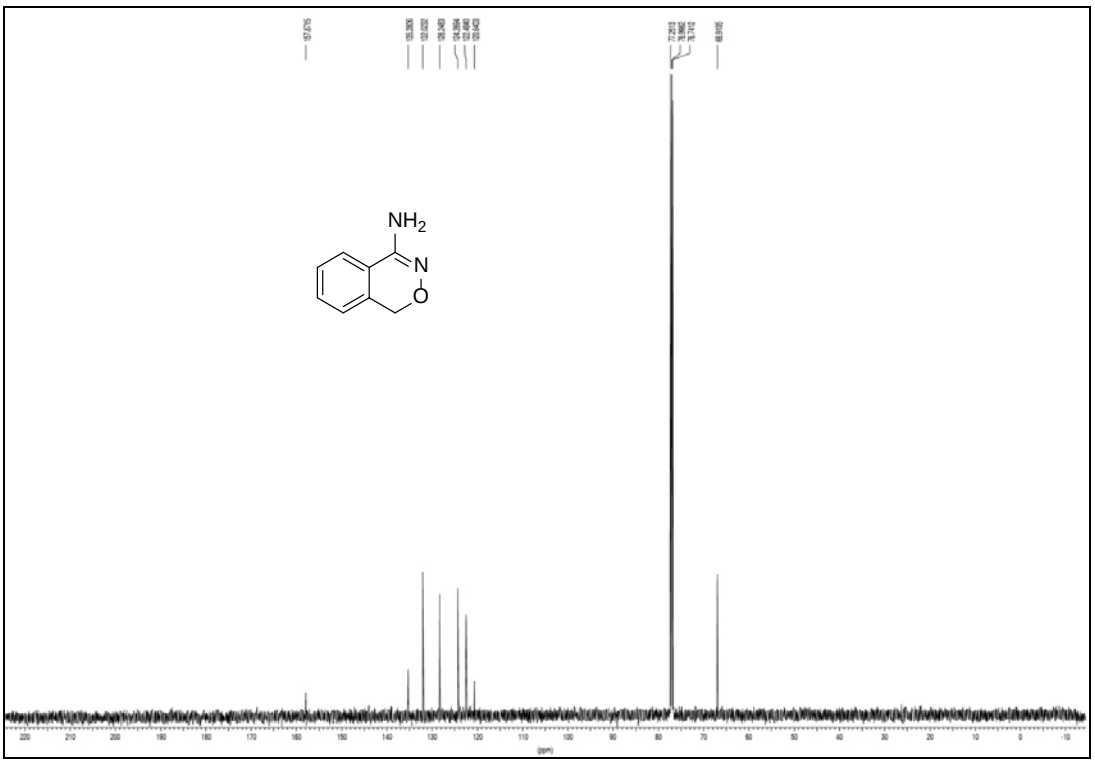
4-(4-Chlorophenylthio)-3-amino-1,2-benzisoxazole (**2j**). White solid. Mp: 133-134 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 2H), 7.21 – 7.17 (m, 2H), 7.13 – 7.08 (m, 3H), 4.53 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.7, 158.1, 133.5, 133.4, 130.9, 130.8, 129.7, 128.4, 127.8, 116.6, 110.6. HRMS (EI): calcd for $C_{13}H_9O_1N_2{}^{35}Cl_1{}^{32}S_1$ 276.0124, found 276.0118.



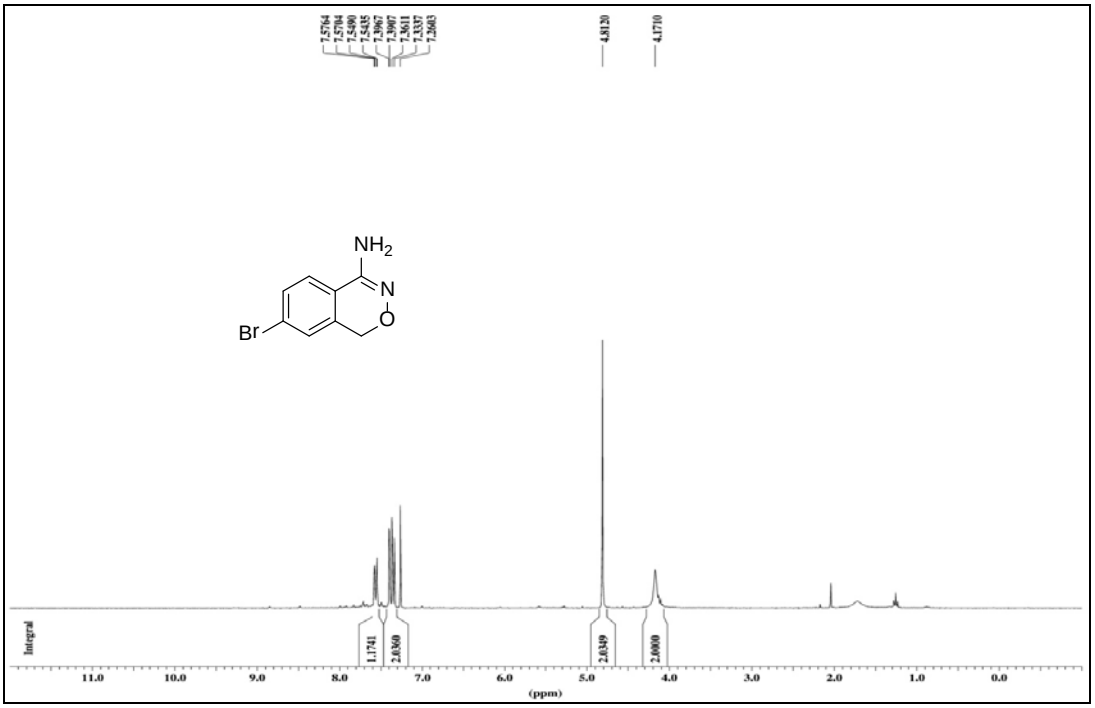


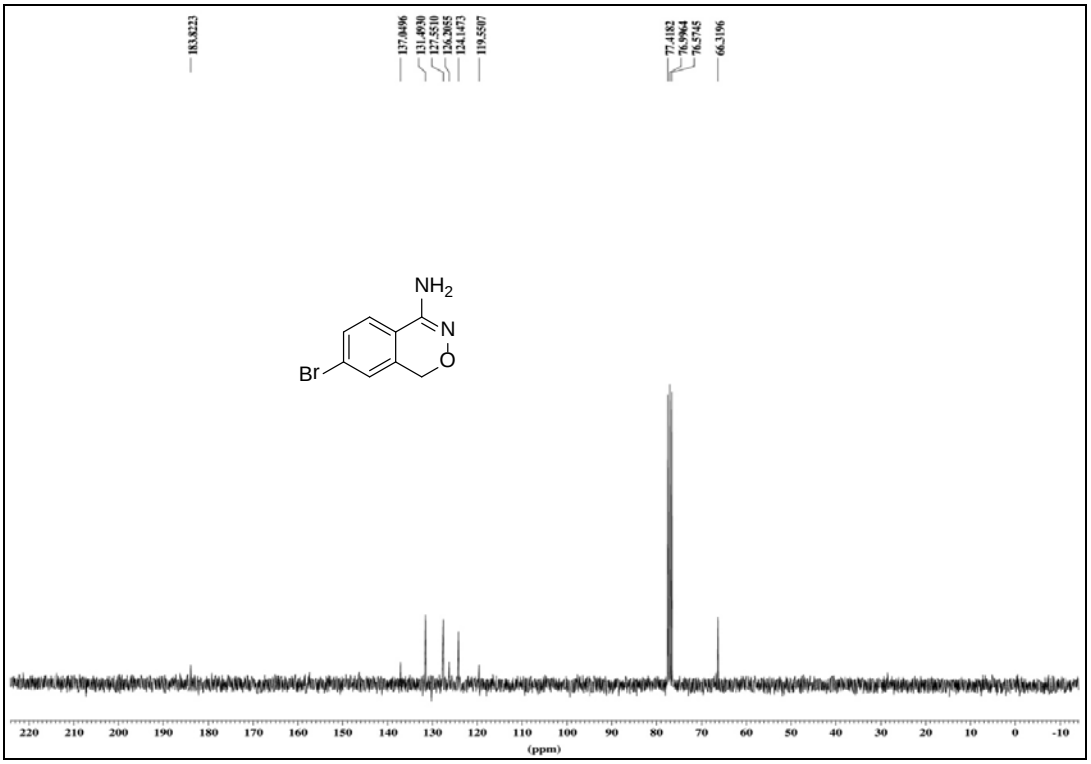
4-Amino-1H-2,3-benzoxazines (**3a**). Yellow solid. Mp: 137-139 ºC (lit.[3] mp 136-139 ºC). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.49 (m, 2H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 7.5 Hz, 1H), 4.88 (s, 2H), 4.22 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9, 135.3, 132.0, 128.2, 124.3, 122.5, 120.6, 66.9. HRMS (EI): calcd for $C_8H_8O_1N_2$ 148.0637, found 148.0637.



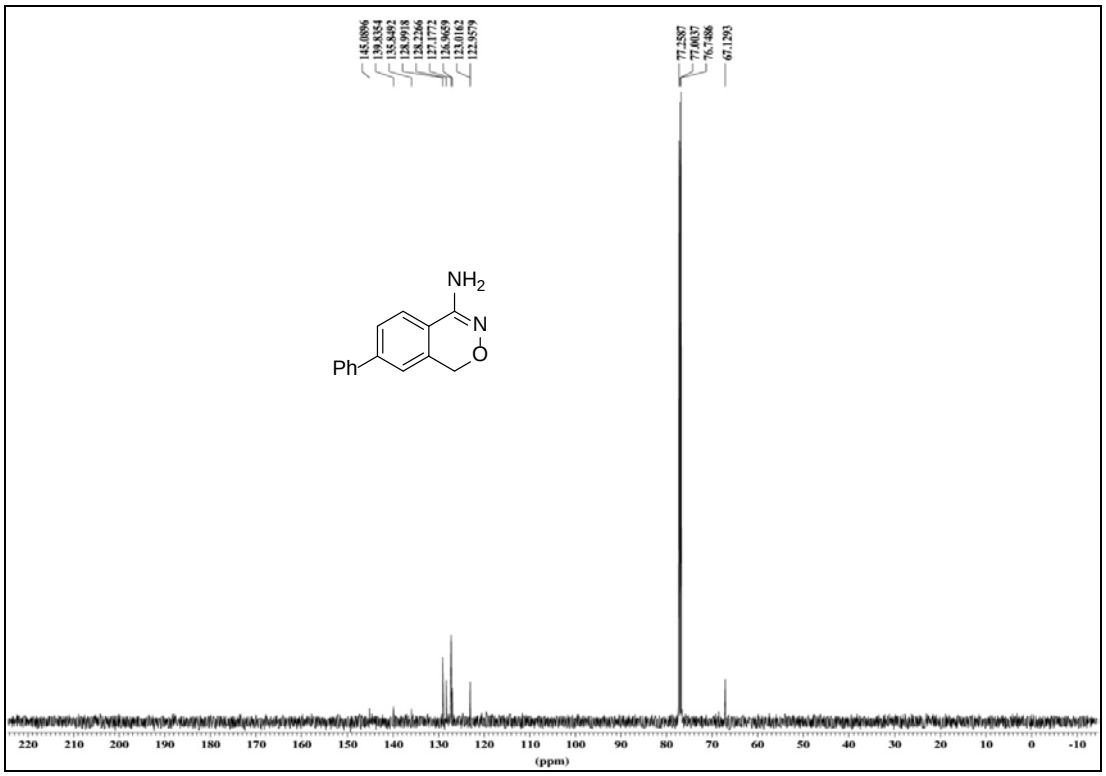


7-Bromo-4-amino-1H-2,3-benzoxazines (**3b**). Brown solid. Mp: 171-172 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.37 (dd, *J* = 13.9, 5.0 Hz, 2H), 4.81 (s, 2H), 4.17 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.8, 137.0, 131.5, 127.6, 126.2, 124.1, 119.6, 66.3. HRMS (EI): calcd for $C_8H_7O_1N_2{}^{79}Br_1$ 225.9742, found 225.9740; calcd for $C_8H_7O_1N_2{}^{81}Br_1$ 227.9721, found 227.9724.

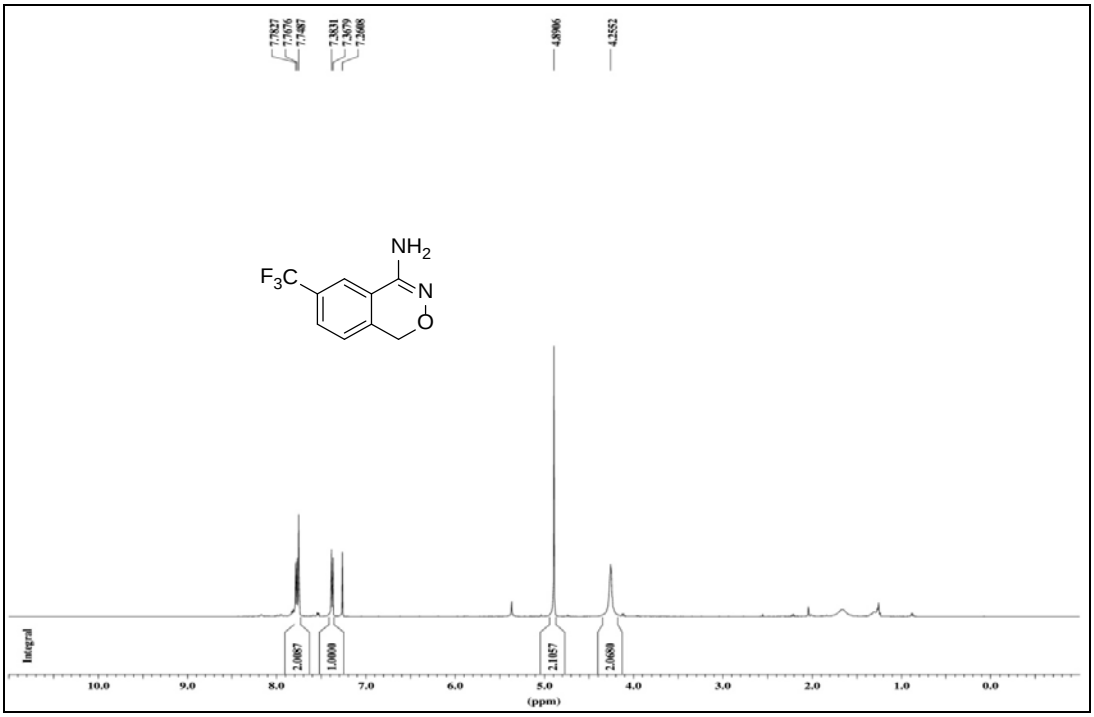


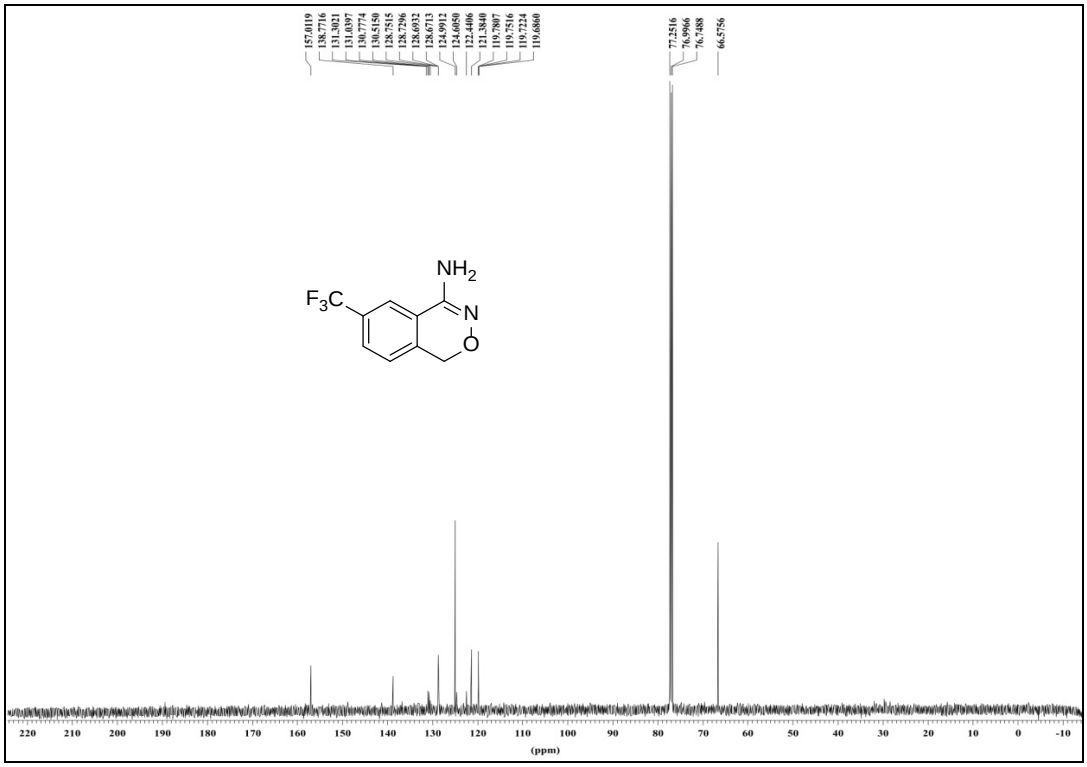


7-Phenyl-4-amino-1H-2,3-benzoxazines (**3c**). Yellow solid. Mp: 183-185 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 – 7.58 (m, 3H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.47 (dd, *J* = 14.2, 6.2 Hz, 3H), 7.40 (t, *J* = 7.3 Hz, 1H), 4.92 (s, 2H), 4.18 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.1, 139.8, 135.8, 129.0, 128.2, 127.2, 127.0, 123.0 (2), 67.1. HRMS (EI): calcd for $C_{14}H_{12}O_1N_2$ 224.0950, found 224.0952.

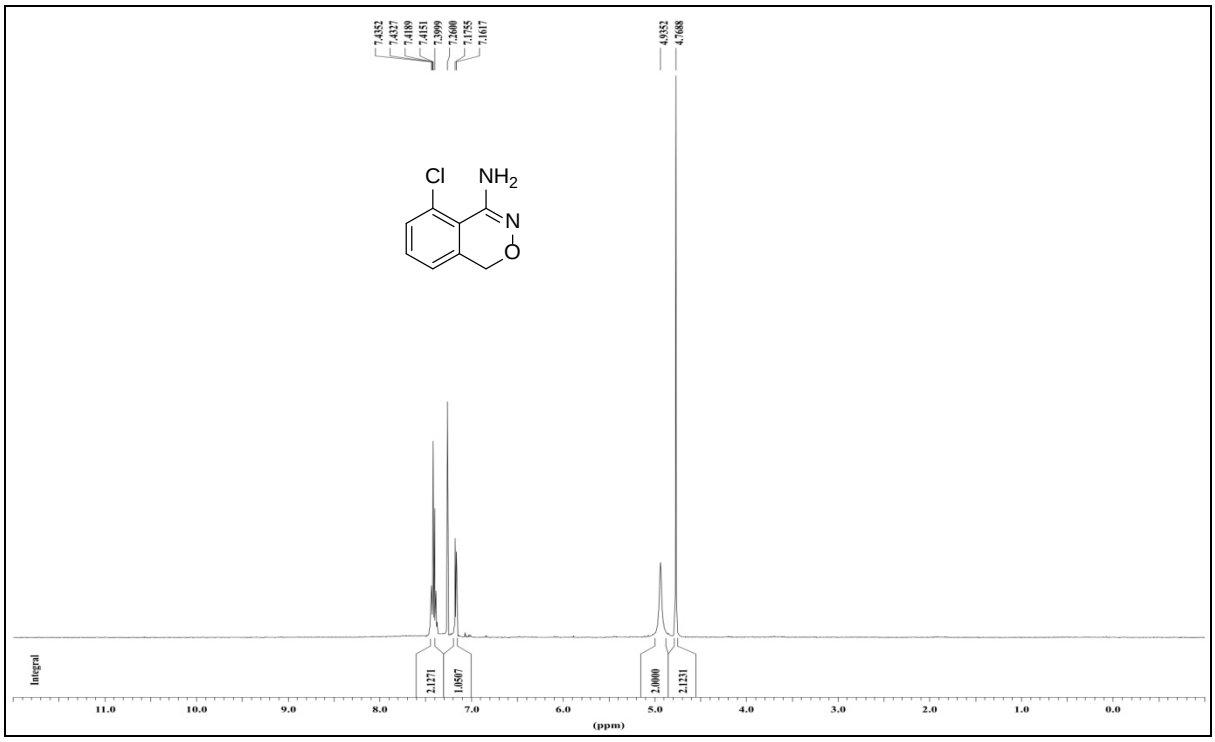


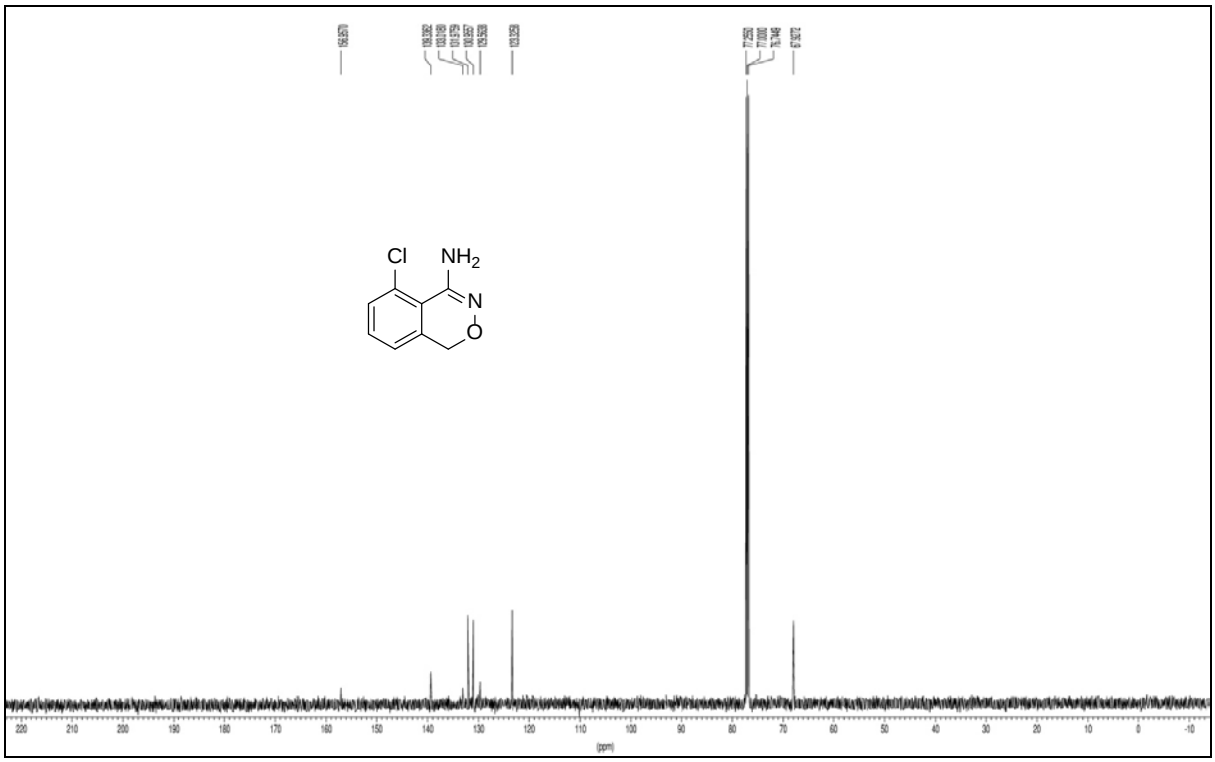
6-Trifluoromethyl-4-amino-1H-2,3-benzoxazines (**3d**). Brown solid. Mp: 162-163 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.70 (m, 2H), 7.37 (d, *J* = 7.8 Hz, 1H), 4.89 (s, 2H), 4.25 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 138.8, 130.9 (q, *J* = 32.8 Hz), 128.7 (q, *J* = 3.3 Hz), 125.0, 123.5 (d, *J* = 271 Hz), 121.4, 119.7 (q, *J* = 3.9 Hz), 66.6. HRMS (EI): calcd for $C_9H_7O_1N_2F_3$ 216.0510, found 216.0515.





5-Chloro-4-amino-1H-2,3-benzoxazines (**3e**). Brown solid. Mp: 123-124 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.40 (m, 2H), 7.17 (d, *J* = 6.9 Hz, 1H), 4.94 (s, 2H), 4.77 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 139.3, 133.0, 132.0, 131.0, 129.6, 123.3, 67.9. HRMS (EI): calcd for $C_8H_7O_1N_2{}^{35}Cl_1$ 182.0247, found 182.0245.



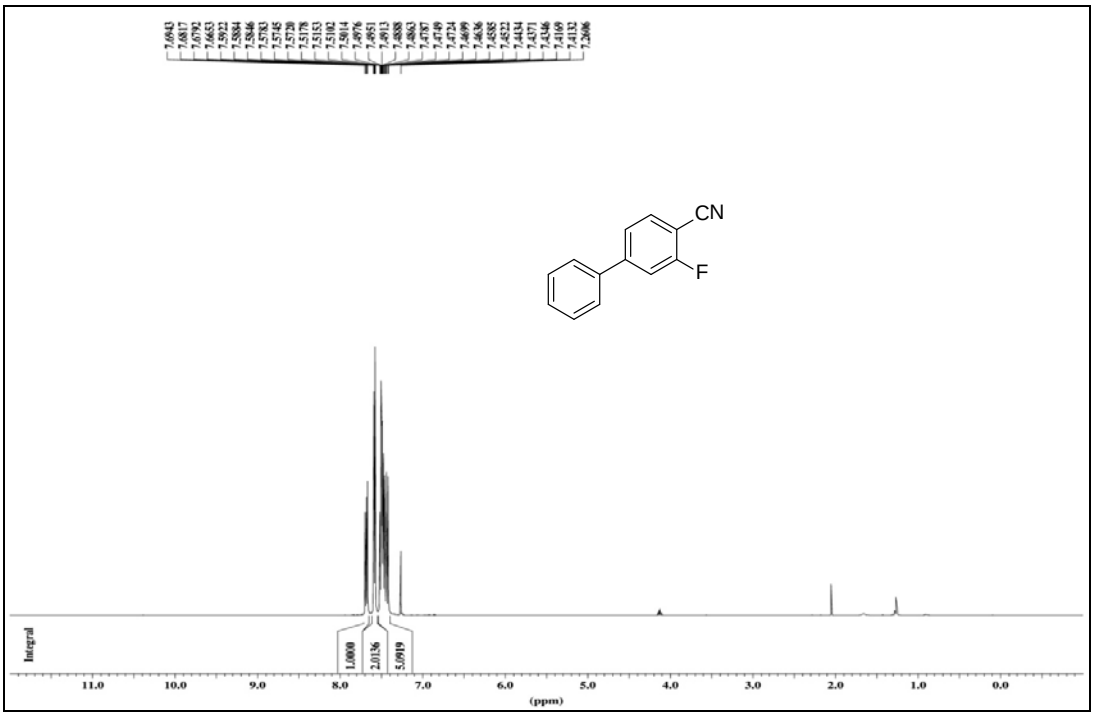


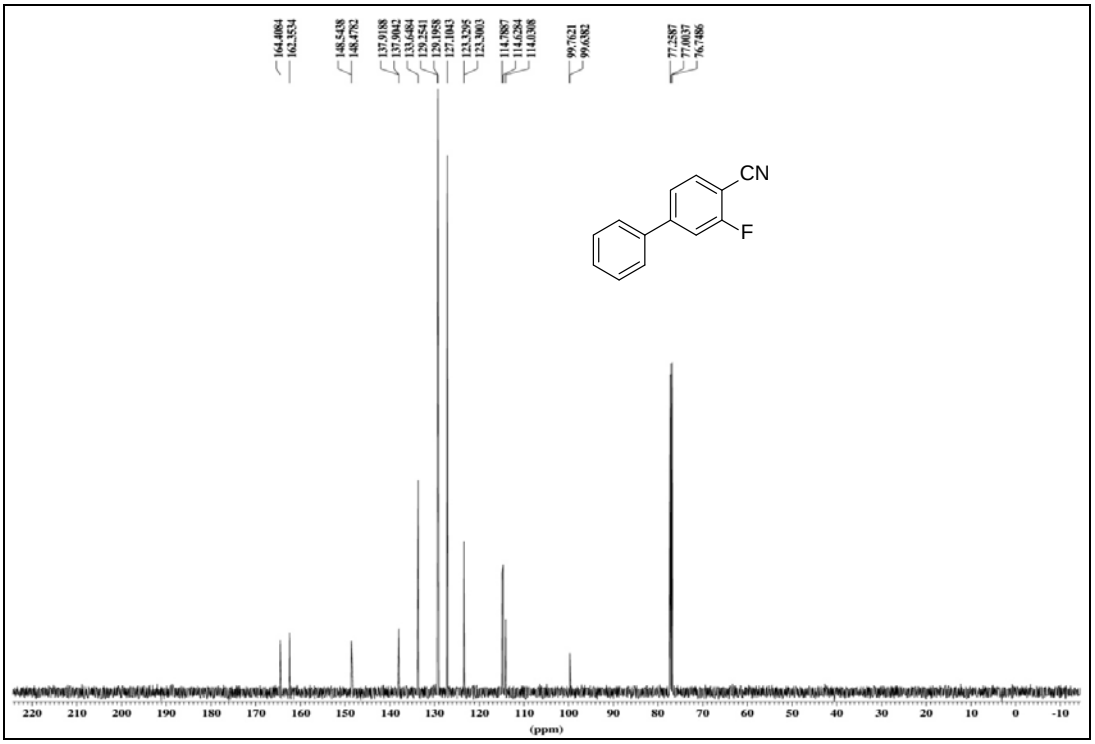
NMR and mass spectrometry characterization data of intermediate **6a**

Aryloxime intermediate (**6a**). White solid. Mp: 88-89 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.5 Hz, 1H), 7.59 – 7.51 (m, 6H), 7.06 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 4.16 – 4.06 (m, 4H), 2.41 – 2.26 (m, 4H), 2.18 – 2.09 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 161.3, 160.4, 159.8, 134.2, 133.1, 132.0, 130.6, 128.5, 124.3, 122.1, 116.0, 115.3, 114.3, 114.0, 99.8, 66.5, 66.4, 28.1-27.8 (m), 20.6. HRMS (ESI): calcd for $C_{42}H_{24}F_{34}N_2O_3Na$ 1273.1136, found 1273.1140.

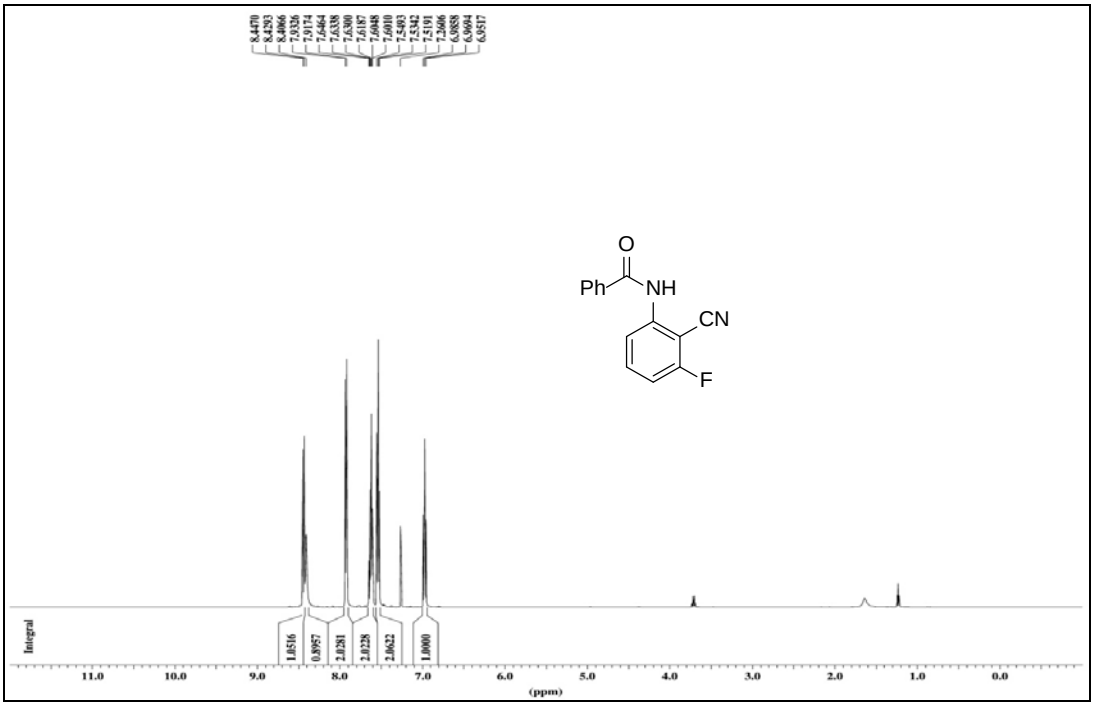
NMR and mass spectrometry characterization data of starting material **5c, 5i** and **7b-7e**

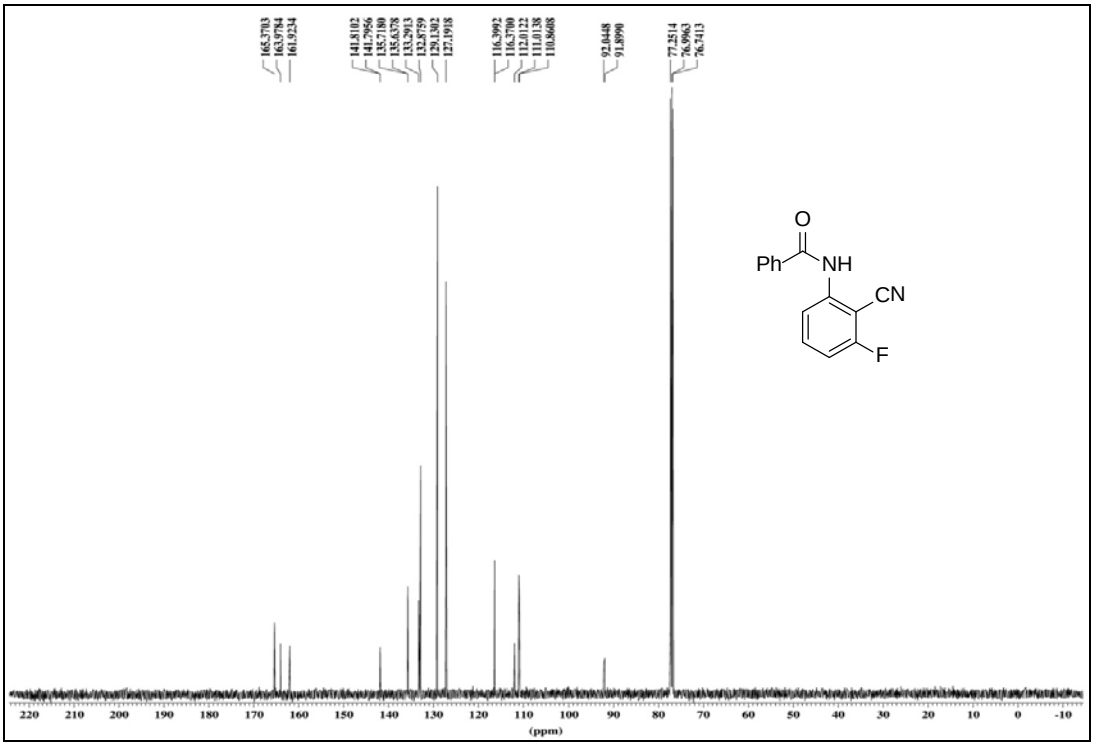
3-Fluorobiphenyl-4-carbonitrile (**5c**). White solid. Mp: 81-82 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 8.0, 6.7 Hz, 1H), 7.60 – 7.56 (m, 2H), 7.52 – 7.41 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.4 (d, *J* = 257 Hz), 148.5 (d, *J* = 8.2 Hz), 137.9 (d, *J* = 1.8 Hz), 133.6, 129.3, 129.2, 127.1, 123.3 (d, *J* = 3.7 Hz), 114.7 (d, *J* = 20.0 Hz), 114.0, 99.7 (d, *J* = 15.5 Hz). HRMS (EI): calcd for $C_{13}H_8N_1F_1$ 197.0641, found 197.0641.



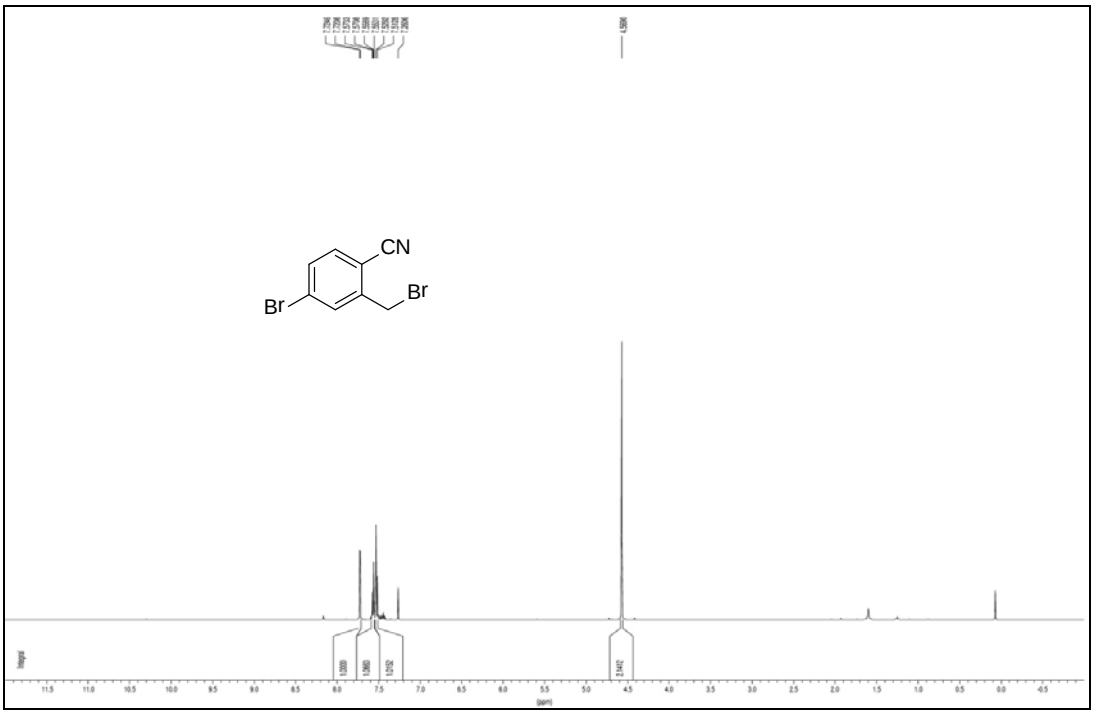


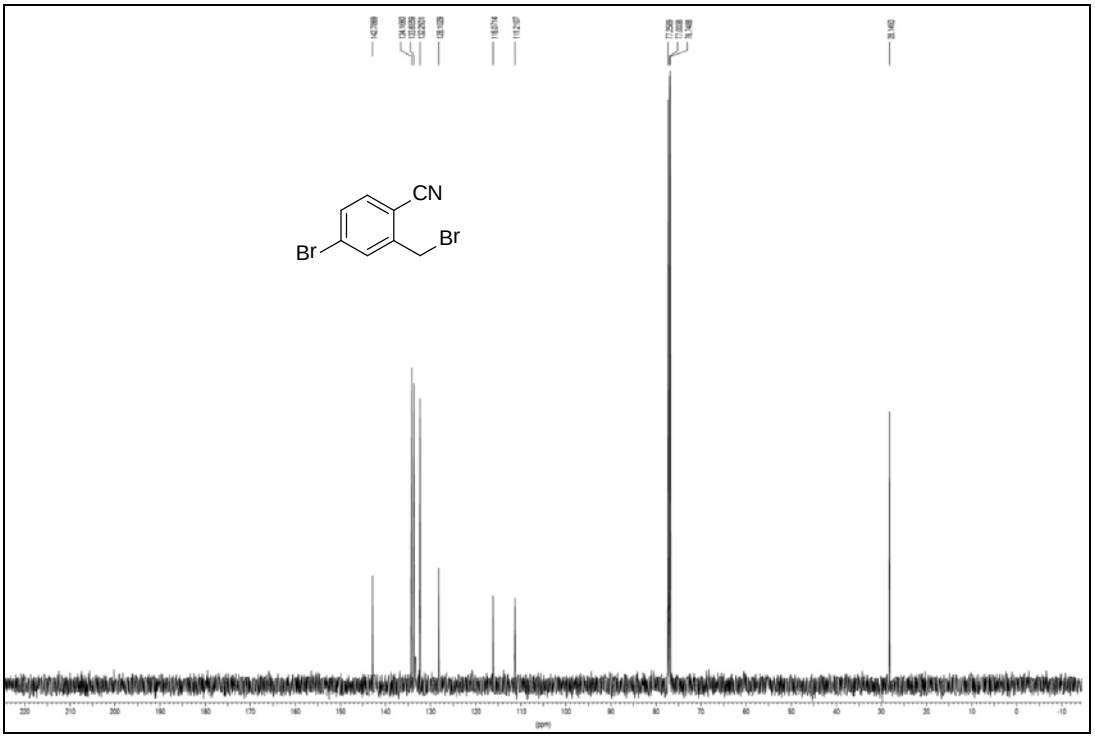
N-(2-cyano-3-fluorophenyl)benzamide (**5i**). White solid. Mp: 175-176 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.5 Hz, 1H), 8.41 (s, 1H), 7.92 (d, *J* = 7.5 Hz, 2H), 7.62 (td, *J* = 8.5, 4.0 Hz, 2H), 7.53 (t, *J* = 7.7 Hz, 2H), 6.97 (t, *J* = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 163.0 (d, *J* = 257 Hz), 141.8 (d, *J* = 1.8 Hz), 135.7 (d, *J* = 10 Hz), 133.3, 132.9, 129.1, 127.2, 116.4 (d, *J* = 3.7 Hz), 112.0, 110.9 (d, *J* = 19.1 Hz), 92.0 (d, *J* = 18.3 Hz). HRMS (EI): calcd for $C_{14}H_9O_1N_2F_1$ 240.0699, found 240.0699.



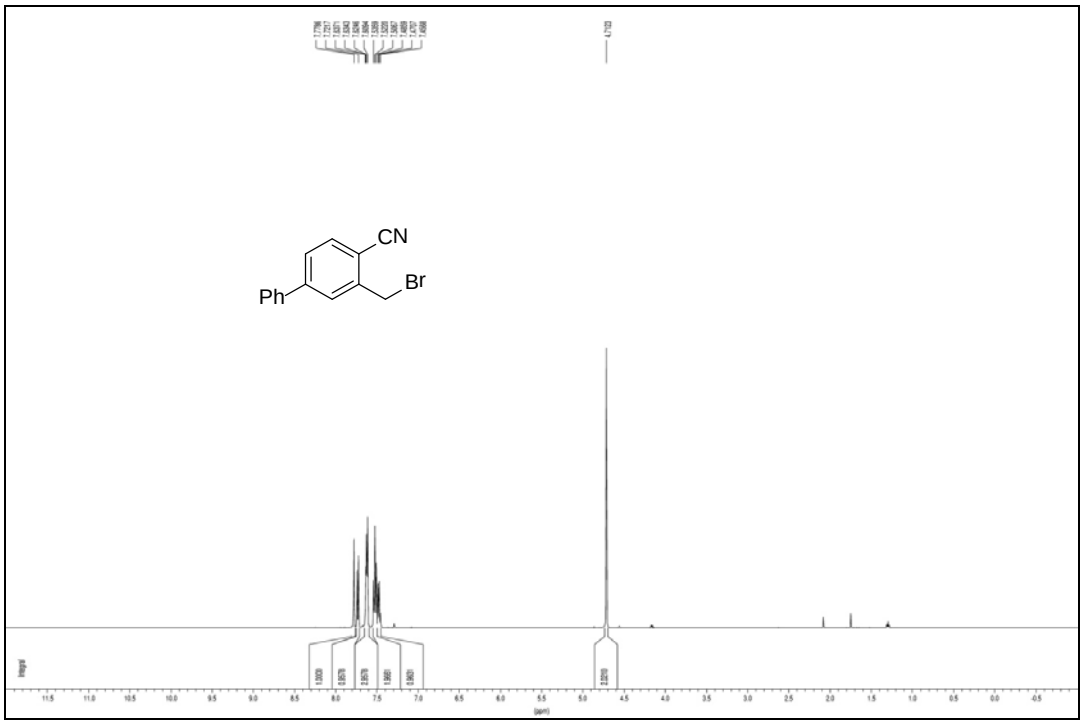


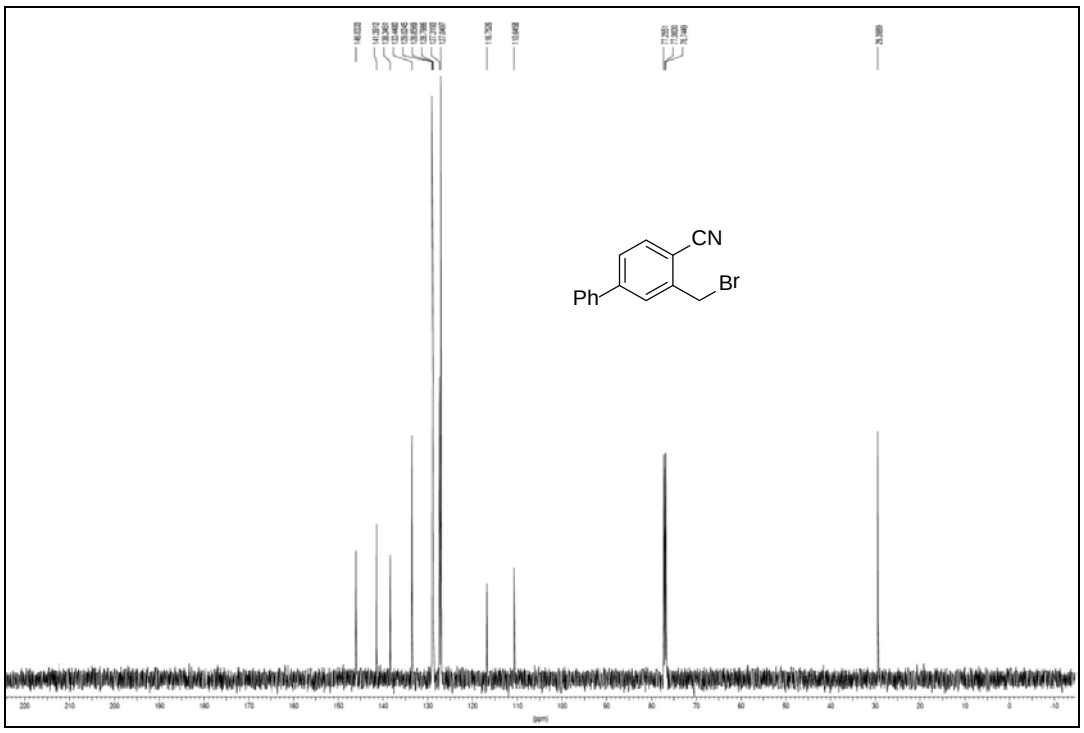
4-Bromo-2-(bromomethyl)benzonitrile (**7b**). White solid. Mp: 85-86 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 1.8 Hz, 1H), 7.56 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 4.57 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 134.2, 133.7, 132.3, 128.1, 116.1, 111.2, 28.2. HRMS (EI): calcd for $C_8H_5N_1{}^{79}Br_2$ 272.8789, found 272.8784; calcd for $C_8H_5N_1{}^{79}Br_1{}^{81}Br_1$ 274.8768, found 274.8763; calcd for $C_8H_5N_1{}^{81}Br_2$ 276.8748, found 276.8747.



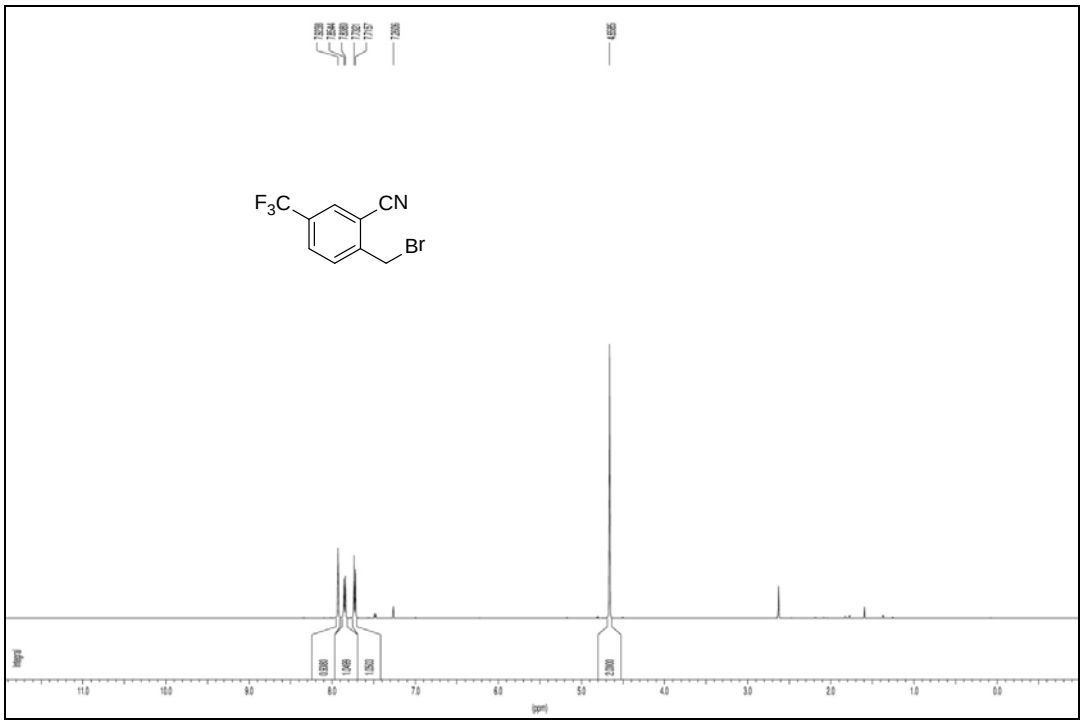


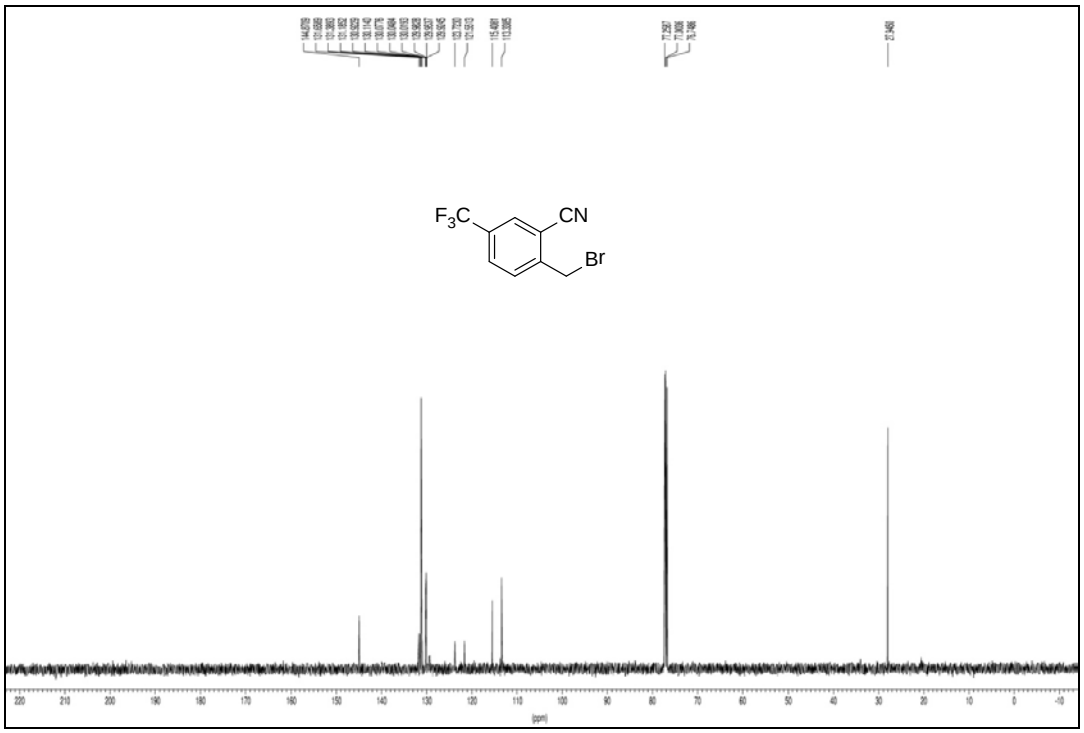
3-(Bromomethyl)biphenyl-4-carbonitrile (**7c**). White solid. Mp: 77-79 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.60 (dd, *J* = 9.2, 4.5 Hz, 3H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.45 (d, *J* = 7.2 Hz, 1H), 4.68 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.0, 141.4, 138.4, 133.5, 129.0, 128.9, 128.8, 127.3, 127.1, 116.8, 110.7, 29.4. HRMS (EI): calcd for $C_{14}H_{10}N_1{}^{79}Br_1$ 270.9997, found 270.9997; calcd for $C_{14}H_{10}N_1{}^{81}Br_1$ 272.9976, found 272.9975.



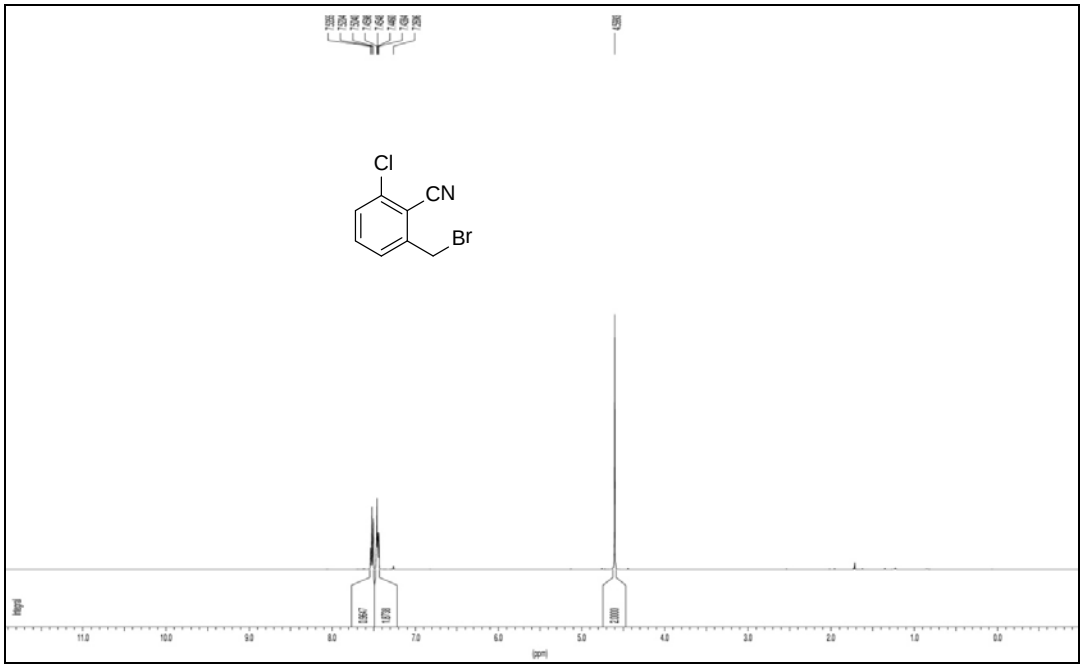


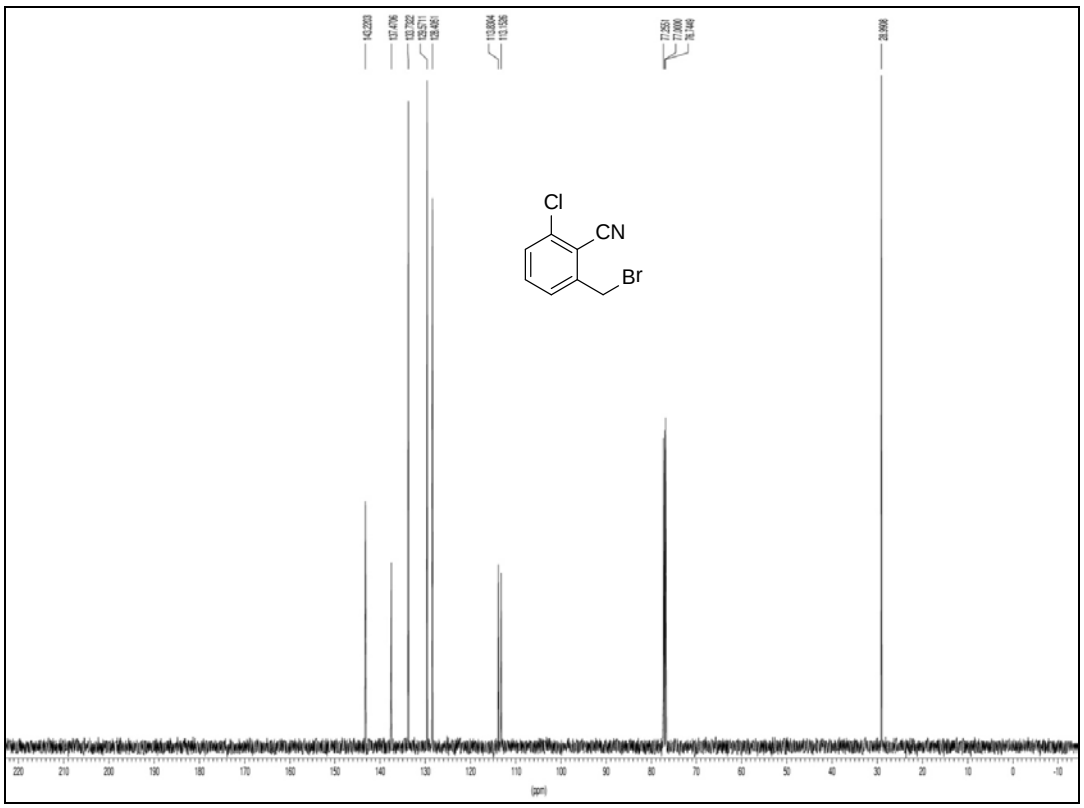
2-(Bromomethyl)-5-(trifluoromethyl)benzonitrile (**7d**). Pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 4.66 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 131.3 (q, *J* = 30.8 Hz), 130.1 (q, *J* = 4.6 Hz), 130.0 (q, *J* = 4.0 Hz), 129.2, 122.6 (q, *J* = 270 Hz), 115.4, 113.3, 27.9. HRMS (EI): calcd for $C_9H_4N_1{}^{79}Br_1F_3$ 261.9479, found 261.9488; calcd for $C_9H_4N_1{}^{81}Br_1F_3$ 263.9459, found 263.9467.





2-(Bromomethyl)-6-chlorobenzonitrile (**7e**). White solid. Mp: 82-84 ºC (lit.[4] mp 83 ºC). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (t, *J* = 7.9 Hz, 1H), 7.45 (dd, *J* = 7.5, 3.3 Hz, 2H), 4.60 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 137.7, 133.9, 129.8, 128.6, 114.0, 113.4, 29.2. HRMS (EI): calcd for $C_8H_5N_1{}^{79}Br_1{}^{35}Cl_1$ 228.9294, found 228.9294; calcd for $C_8H_5N_1{}^{81}Br_1{}^{35}Cl_1$ 230.9273, found 230.9267.





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2) H. Böshagen, *Deutsches Patentamt*, 1962, DE 1129488.
3) G. Pifferi, P. Consonni and E. Testa, *Farmaco, Edizione Scientifica*, 1968, **23**, 554.
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