Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

An Efficient Metal Free Synthesis of 2- aminobenzothiozoles - A Greener Approach

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General information

All reactions were carried out with oven-dried glassware under aerobic conditions. The reactions were carried out in commercial solvents without degassing them prior to the reactions. All the anilines and the bases were commercially available and were used as received without further purification. Aryl isothiocyanates were prepared according to the procedures available in the literature. The compounds were purified by flash chromatography using Biotage Selekt autocolumn on a pre-packed pre-packed 25-gram KP-Sil BiotageϴSNAP. All the compounds were characterized by HRMS, ^{1}HNMR and ^{13}CNMR. Melting points were measured with a Polmon AUTO-MELT MP98 apparatus and are uncorrected. Thin layer chromatography (TLC) was done using Silica Gel 60 F_{254} plates (0.25 mm thick), purchased from Merck. LC-MS data was recorded on an Agilent Technologies 1200 LC system coupled with Agilent Technologies 5975C mass spectrometer using HP-column (4.6 mm × 50 mm, 5µ) purchased from Agilent Technologies. HPLC analyses were carried out in Shimadzu Prominence systems using Chiralpak IG 250mm*4.6mm, 5µ columns. ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ or DMSO-d6 using 300 MHz and 400 MHz Bruker NMR spectrometer. All the chemical shift values reported in the 1H NMR spectra are in parts per million (ppm) on the δ scale from an internal standard of residual $CDCl_3$ (7.26 ppm) or the central peak of DMSO-d^6 (2.50 ppm).

The data are reported as follows:

Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet), integration, and coupling constant in Hertz (Hz). Chemical shifts in ^{13}C NMR spectra are reported in ppm on the δ scale from the central peak of residual $CDCl_3$ (77.16 ppm) or the central peak of DMSO-d^6 (39.52 ppm).

Procedure for synthesis of isothiocyanate compounds

All the manipulations were carried out in oven-dried glassware under air. A stirred solution of aniline (10g, 0.062 mol) in DCM (200 mL) was cooled to 0 ℃ and trimethylamine (17.1 mL, 0.1241 mol) was added dropwise. This was followed by the addition of thiosphosgene (9.43 mL, 0.1241 mol). The solution was then stirred at room temperature for an hour until the disappearance of the starting material by TLC. On completion of the reaction, the reaction mass was quenched using 1.5N HCl solution and extracted from the aqueous layer using DCM (2×100ml). The

combined organic layers were washed with water (1×100 mL) and brine (1×100 mL) sequentially. The combined organic layers were then dried over anhydrous sodium sulphate and concentrated under reduced pressure at 45 ℃. The crude product was purified by a flash column using silica gel (60-120 mesh).

Optimization of reaction conditions for synthesis of benzothiazoles

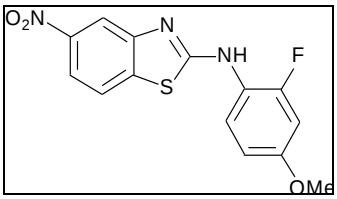
Table 1: Optimization of Equiv. of isothiocyanate substrate

Entry	Equiv. of isothiocyanate	Yield
1	1.00	67%
2	1.25	67%
3	1.50	98%
4	2.00	85%

Procedure for preparation of benzothiazoles

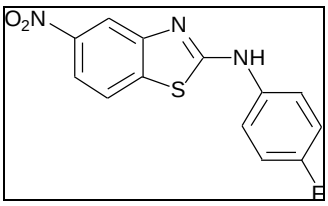
All the manipulations were carried out in an oven-dried glassware under air. 0.5 g (0.0032 mol) of the electron deficient 2-flouroaniline/ 2- chloroaniline was transferred into 25 mL Round bottomed flask and 0.71 g (0.0048 mol) of aromatic isothiocyanate was added to the flask. This was followed by the addition of 5 mL of 2-butanol and 1.1 g (0.008 mol) potassium carbonate. The reaction mixture was stirred at 80 ℃ for 16 hours. The progress of the reaction was monitored by TLC for the disappearance of the starting material. On completion of the reaction, the reaction mass was diluted with water and extracted using ethyl acetate (2×100 mL). The combined ethyl acetate layers were once again washed with water (1×100 mL) and brine (1×100 mL) sequentially, dried over anhydrous sodium sulphate and concentrated under reduced pressure at 45 ℃. The crude product was purified by a flash column on using Biotage Selekt autocolumn using pre-packed 25-gram KP-Sil Biotage® SNAP. All the compounds were characterized by ^{1}H NMR, ^{13}C NMR and HRMS,

***N*-(2-Fluoro-4-methoxyphenyl)-5-nitro-1,3-benzothiazol-2-amine (3a)**



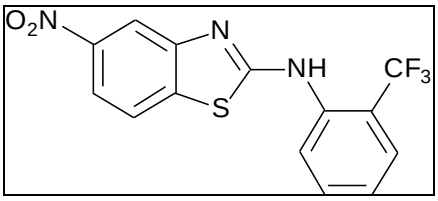
Pale yellow solid; (Yield = 90%), ^{1}H NMR (300 MHz, DMSO): δ 10.37 (s, 1H), 8.22 (s, 1H), 8.14–7.93 (m, 3H), 6.99 (dd, *J* = 12.8, 2.5 Hz, 1H), 6.90-6.81 (m, 1H), 3.79 (s, 3H).^{13}C NMR (101 MHz, DMSO): *δ* 166.1, 157.0, 156.9, 155.7 and 153.2(d,$^{1}J_{C\text{-}F}$ = 246 Hz), 152.2, 146.2, 138.5, 124.7, 121.8, 120.4 and 120.3 (d,$^{2}J_{C\text{-}F}$ = 16 Hz), 116.4, 112.8, 110.1, 110.0, 102.2 and 102.0(d, $^{2}J_{C\text{-}F}$ = 23.2 Hz), 55.7HRMS (ESI) m/z calcd for $(C_{14}H_{10}FN_3O_3S)^+$ $(M+H)^+$ 320.0460, found 320.0480. mp: 213.8- 221.2 ℃.

N-(4-Fluorophenyl)-5-nitro-1,3-benzothiazol-2-amine (3b)



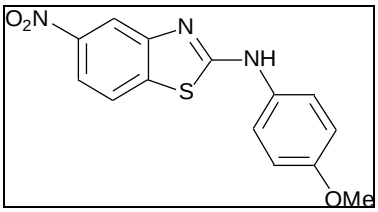
Pale yellow solid; (Yield=65%) ^{1}H NMR (400 MHz, DMSO): *δ* 10.83 (s, 1H), 8.26 (d, *J* = 2.2 Hz, 1H), 8.06 (d, *J* = 8.6 Hz, 1H), 7.98 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.83–7.75 (m, 2H), 7.27–7.17 (m, 2H). ^{13}C NMR (101 MHz, DMSO164.1, 159.3 and 156.1 (d, $^{1}J_{C\text{-}F}$ = 240.93 Hz), 152.3, 146.1, 138.0, 136.5, 121.6, 120.3 and 120.2 (d, $^{3}J_{C\text{-}F}$ = 7.6 Hz), 119.9, 116.6, 115.7 and 115.4(d, $^{2}J_{C\text{-}F}$ = 22.87 Hz), 112.9. HRMS (ESI) m/z calcd for $(C_{13}H_8N_3O_2S)^+$ $(M+H)^+$ 290.0355 found 290.0355. mp: 255.5- 261.0 ℃.

5-Nitro-*N*-[2-(trifluoromethyl)phenyl]-1,3-benzothiazol-2-amine (3c)



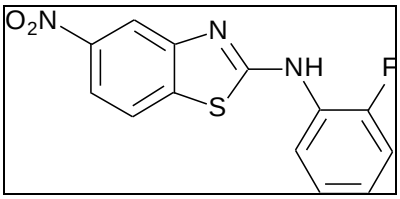
Off- white solid; (Yield=84%) ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.48 (d, *J* = 2.1 Hz, 1H), 8.19 (d, *J* = 8.2 Hz, 1H), 8.09 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.79–7.64 (m, 3H), 7.36 (t, *J* = 7.7 Hz, 1H).^{13}C NMR (101 MHz, DMSO): *δ* 146.2,133.7,127.7,126.8,126.7,126.6,124.7,126.7,125.0, 124.3,122.3, 122.1, 116.5.HRMS (ESI) m/z calcd for $(C_{14}H_8F_3N_3O_2S)^+$ $(M+H)^+$ 340.0289 found 340.0323.. mp: 157.4-158.8 ℃.

***N*-(4-Methoxyphenyl)-5-nitro-1,3-benzothiazol-2-amine (3d)**



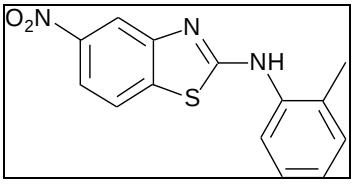
Pale yellow solid; (Yield=85%) ^{1}H NMR (400 MHz, DMSO): δ 10.62 (s, 1H), 8.22 (d, *J* = 2.1 Hz, 1H), 8.03 (d, *J* = 8.7 Hz, 1H), 7.96 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.65 (d, *J* = 9.1 Hz, 2H), 6.96 (d, *J* = 9.1 Hz, 2H), 3.73 (s, 3H).^{13}C NMR (75 MHz, DMSO): δ 164.6, 155.3, 152.6, 146.2, 138.0, 133.2, 121.6, 120.3, 116.3, 114.3, 112.6, 55.2. HRMS (ESI) m/z calcd for $(C_{14}H_{11}N_3O_3S)^+$ $(M+H)^+$ 302.0555 found 302.0555. mp: 254.0-265.4 ℃.

***N*-(2-Fluorophenyl)-5-nitro-1,3-benzothiazol-2-amine (3e)**



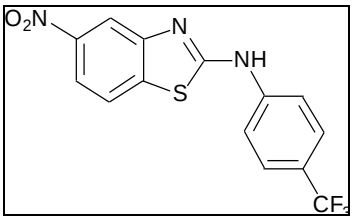
Pale yellow solid (Yield=87%) ^{1}H NMR (300 MHz, DMSO): *δ* 10.66 (s, 1H), 8.49 (t, *J* = 8.2 Hz, 1H), 8.32 (d, *J* = 2.2 Hz, 1H), 8.12 (d, *J* = 8.7 Hz, 1H), 8.03 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.39 – 7.23 (m, 2H), 7.21–7.11 (m, 1H). ^{13}C NMR (101 MHz, DMSO): δ 164.7, 153.7 and 151.9(d,$^{1}J_{C\text{-}F}$ = 190 Hz), 151.3, 146.1, 138.5 , 127.8 and 127.7(d,$^{3}J_{C\text{-}F}$ = 3.8 Hz), 124.7, 124.7, 124.2 and 124.2 (d, $^{3}J_{C\text{-}F}$ = 8.07 Hz), 121.9, 116.8, 115.5 and 115.3 (d, $^{2}J_{C\text{-}F}$ = 20 Hz), 113.3 HRMS (ESI) m/z calcd for $(C_{13}H_8FN_3O_2S)^+$ $(M+H)^+$ 290.0355 found 290.0355. mp: 224.1- 234.1 ℃.

N-(2-Methylphenyl)-5-nitro-1,3-benzothiazol-2-amine (3f)



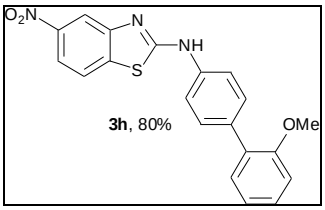
Pale yellow solid (Yield=80%) ^{1}H NMR (300 MHz, DMSO): *δ* 10.09 (s, 1H), 8.19 (d, *J* = 1.8 Hz, 1H), 8.08-7.91 (m, 2H) 7.80 (d, *J* = 7.9 Hz, 1H), 7.29 (dd, *J* = 11.4, 7.5 Hz, 2H), 7.16 (t, *J* = 7.5 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (75 MHz, DMSO): *δ* 167.1, 152.4, 146.1, 138.3, 138.0, 131.3, 130.8, 126.6, 125.50, 123.8, 121.7, 116.1, 112.5, 17.8. HRMS (ESI) m/z calcd for $(C_{14}H_{11}N_3O_2S)^+$ $(M+H)^+$ 286.0606 found 286.0616. mp: 195.5-208.9 ℃.

5-Nitro-N-[4-(trifluoromethyl)phenyl]-1,3-benzothiazol-2-amine (3g)



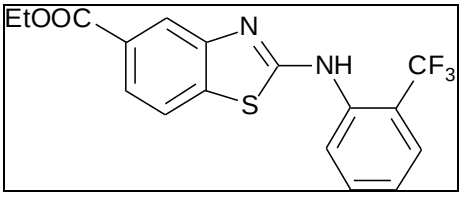
Pale yellow solid; (Yield=82%) ^{1}H NMR (400 MHz, MeOD): δ 8.41 (d, J = 2.2 Hz, 1H), 8.03 (dd, J = 8.7, 2.2 Hz, 1H), 7.96 (d, J = 8.7 Hz, 2H), 7.90 (d, J = 8.7 Hz, 1H), 7.63 (d, J = 8.7 Hz, 2H).^{13}C NMR (101 MHz, DMSO): δ ^{13}C NMR (101 MHz, DMSO): δ 163.8, 152.0, 146.2, 143.5, 138.3, 125.4 (q,$^{1}J_{C\text{-}F}$ = 272 Hz), 122.6, 122.3, 122.1, 118.0, 117.2, 113.6. HRMS (ESI) m/z calcd for $(C_{14}H_8F_3N_3O_2S)^+$ $(M+H)^+$ 340.0323 found 340.0323. mp: 172.4- 183.9 ℃.

***N*-(2'-Methoxy[1,1'-biphenyl]-4-yl)-5-nitro-1,3-benzothiazol-2-amine (3h)**



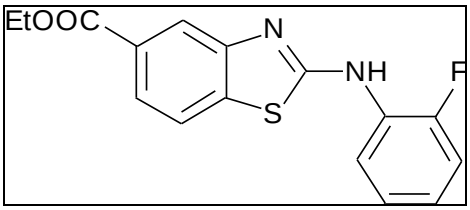
Pale yellow solid; (Yield= 80%) ^{1}H NMR (400 MHz, DMSO): δ 10.87 (s, 1H), 8.30 (d, J = 2.3 Hz, 1H), 8.08 (d, J = 8.7 Hz, 1H), 8.00 (dd, J = 8.7, 2.3 Hz, 1H), 7.80 (d, J = 8.7 Hz, 2H), 7.55–7.47 (m, 2H), 7.35–7.26 (m, 2H), 7.08 (d, J = 7.9 Hz, 1H), 7.05–6.97 (m, 1H), 3.76 (s, 3H). ^{13}C NMR (101 MHz, DMSO): δ 164.0, 156.1, 152.5, 146.2, 138.8, 138.1, 132.6, 130.2, 129.9, 129.3, 128.6, 121.8, 120.8, 117.9, 116.7, 113.1, 111.7, 55.4. HRMS (ESI) m/z calcd for $(C_{20}H_{15}N_3O_3S)^+$ $(M+H)^+$ 378.0834 found 378.0834. mp: 255.5- 261.0 ℃.

Ethyl 2-[2-(trifluoromethyl)anilino]-1,3-benzothiazole-5-carboxylate (3j)



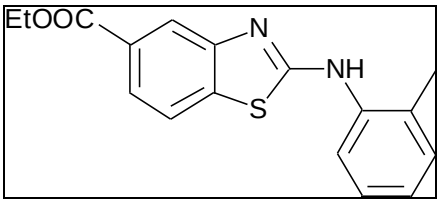
Off- white solid; (Yield= 80%) ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, J = 1.3 Hz, 1H), 8.25 (d, J = 8.3 Hz, 1H), 7.91 (dd, J = 8.3, 1.6 Hz, 1H), 7.69 (d, J = 8.3 Hz, 2H), 7.64 (t, J = 7.7 Hz, 1H), 7.29 (t, J = 7.7 Hz, 1H), 4.41 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H).^{13}C NMR (75 MHz, DMSO): δ 165.6, 133.6, 126.6 (q,$^{1}J_{C\text{-}F}$ = 272 Hz), 122.3, 121.6, 60.6, 14.0. HRMS (ESI) m/z calcd for $(C_{17}H_{13}F_3N_2O_2S)^+$ $(M+H)^+$ 367.0683 found 367.0683. mp: 146.2- 151.0 ℃

Ethyl 2-(2-fluoroanilino)-1,3-benzothiazole-5-carboxylate (3k)



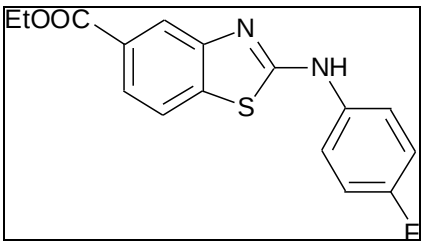
Off- white solid;(Yield= 70%) 1H NMR (400 MHz, DMSO): δ 10.45 (s, 1H), 8.51 (t, J = 8.2 Hz, 1H), 8.07 (s, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.73 (dd, J = 8.2, 1.6 Hz, 1H), 7.34–7.20 (m, 2H), 7.15–7.06 (m, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.32 (t, J = 7.1 Hz, 3H).13C NMR (75 MHz, DMSO): δ 165.7, 163.2, 154.0 and 151.6 (d, 1JC-F = 247 Hz), 150.8, 136.0, 128.1, 127.7, 124.6, 123.8 and 123.7(d, 3JC-F = 7 Hz), 122.7, 121.6, 121.2, 119.4, 115.4, and 115.1 (d, 2JC-F = 18.9 Hz), 60.6, 14.1.HRMS (ESI) m/z calcd for (C16H13FN2O2S)+ (M+H)+ 317.0715 found 317.0717. mp: 155.7- 165.6 ℃.

Ethyl 2-(2-methylanilino)-1,3-benzothiazole-5-carboxylate (3l)



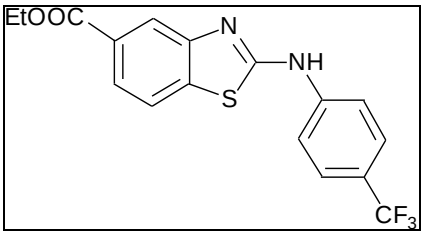
Off white solid; (Yield= 80%) ; ^{1}H NMR (300 MHz, DMSO): *δ* 9.85 (s, 1H), 7.97 (s, 1H), 7.87 (dd, *J* = 14.2, 8.0 Hz, 2H), 7.74–7.64 (m, 1H), 7.26 (t, *J* = 8.0 Hz, 2H), 7.12 (t, *J* = 6.9 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 2.29 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (75 MHz, DMSO): *δ* 167.1, 152.4, 146.1, 138.3, 138.0, 131.3, 130.8, 126.6, 125.50, 123.8, 121.7, 116.1, 112.5, 17.8. HRMS (ESI) m/z calcd for $(C_{17}H_{16}N_2O_2S)^+$ $(M+H)^+$ 313.0966 found 313.0980. mp: 187.7-191.2 ℃

Ethyl 2-(4-fluoroanilino)-1,3-benzothiazole-5-carboxylate (3m)



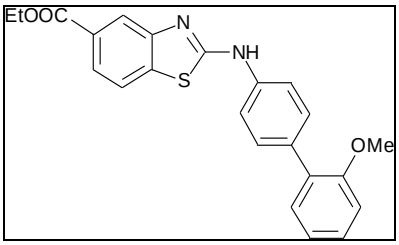
Off- white solid; (Yield= 70%); ^{1}H NMR (400 MHz, DMSO): *δ* 10.66 (s, 1H), 8.06 (d, *J* = 1.3 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.83 – 7.76 (m, 2H), 7.72 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.20 (t, *J* = 8.9 Hz, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$): *δ* 171.0, 167.9, 164.0 and 161.6 (d, $^{1}J_{C\text{-}F}$ = 247 Hz), 157.4, 142.0, 140.8, 133.0, 127.9, 126.5, 124.9 and 124. 8 (d, $^{3}J_{C\text{-}F}$ = 7.6 Hz), 120.9 and 120.7 (d, $^{2}J_{C\text{-}F}$ = 23 Hz), 66.0, 19.4.HRMS (ESI) m/z calcd for $(C_{16}H_{13}FN_2O_2S)^+$ $(M+H)^+$ 317.0715 found 317.0715. mp: 228.2- 240.6 ℃.

Ethyl 2-[4-(trifluoromethyl)anilino]-1,3-benzothiazole-5-carboxylate (3o)



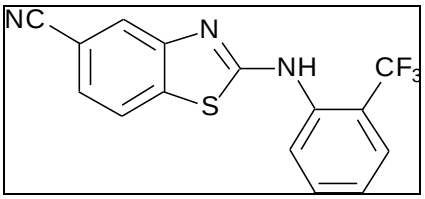
Off- white solid; (yield= 75%); ^{1}H NMR (300 MHz, DMSO): δ 11.05 (s, 1H), 8.17 (s, 1H), 8.01 (d, J = 8.2 Hz, 3H), 7.86 – 7.68 (m, 3H), 4.34 (q, J = 7.0 Hz, 2H), 1.36 (t, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, DMSO): δ 165.7, 162.1, 151.7, 143.6, 135.6, 127.8, 124.6 (q, $^{1}J_{C\text{-}F}$ = 225 Hz), 122.7, 122.3, 121.9, 121.4, 119.7, 117.7, 60.7, 14.1. HRMS (ESI) m/z calcd for $(C_{17}H_{13}F_3N_2O_2S)^+$ $(M+H)^+$ 367.0683 found 367.0683. mp: 196.3- 207.9 ℃.

Ethyl 2-[(2'-methoxy[1,1'-biphenyl]-4-yl)amino]-1,3-benzothiazole-5-carboxylate (3p)



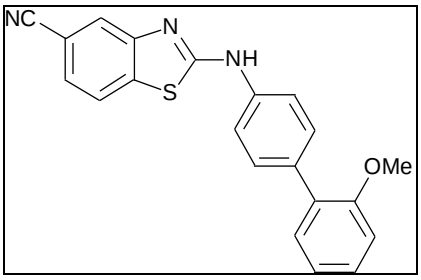
Off- white solid; (Yield= 85%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.58 (q, J = 8.5 Hz, 4H), 7.34 (t, J = 7.3 Hz, 2H), 7.11–6.96 (m, 2H), 4.40 (q, J = 7.1 Hz, 2H), 3.84 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H).^{13}C NMR (101 MHz, DMSO): δ 165.8, 162.6, 156.1, 152.3, 139.1, 135.7, 132.2, 130.1, 129.9, 129.4, 128.5, 127.8, 122.7, 121.3, 120.8, 119.3, 117.6, 111.7, 60.7, 55.5, 14.1. HRMS (ESI) m/z calcd for $(C_{23}H_{20}N_2O_3S)^+$ $(M+H)^+$ 405.1228 found 405.1228. mp: 248.7- 261.3 ℃.

2-[2-(Trifluoromethyl)anilino]-1,3-benzothiazole-5-carbonitrile (3q)



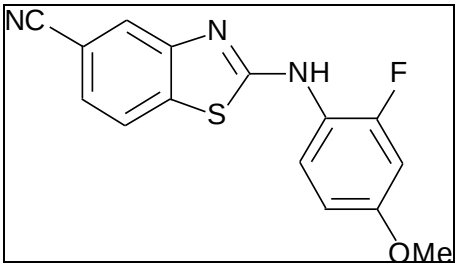
Off- white solid;(Yield= i) 75%, ii) 50%) ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16(d, J= 8 Hz, 1H), 7.92(s, 1H), 7.46 (d, J = 4Hz, 4H), 7.45 (d, J = 4Hz, 1H), 7.35(t, J = 8Hz, 1H) (s, H), 7.86(s,), 7.77(d, J = Hz, H), 7.73(s,), 7.49 (d, J= Hz, H). ^{13}C NMR (101 MHz, DMSO): δ 183.4, 137.0, 133.7, 132.6, 132.3, 127.2 (q, $^{1}J_{C\text{-}F}$ = 242 Hz), 125.9, 125.6, 124.9, 122.7, 122.3, 122.2, 119.2, 108.3HRMS(ESI) m/z calcd for $(C_{15}H_8F_3N_3S)^+$ $(M+H)^+$ 320.0425 found 320.0425. mp: 156.4 - 169.1 ℃.

2-[(2'-Methoxy[1,1'-biphenyl]-4-yl)amino]-1,3-benzothiazole-5-carbonitrile (3r)



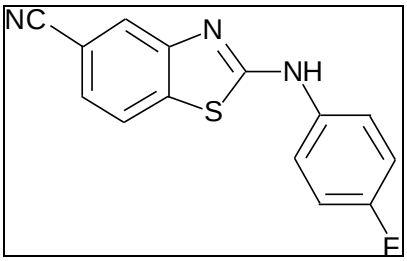
Pale yellow solid; (Yield i) 70%, ii) 0%) ; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 1.1 Hz, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.65–7.60 (m, 2H), 7.57–7.52 (m, 2H), 7.41 (dd, J = 8.1, 1.5 Hz, 1H), 7.38–7.32 (m, 2H), 7.09–6.99 (m, 2H), 3.85 (s, 3H). ^{13}C NMR (75 MHz, DMSO): δ 163.3, 156.14, 152.3, 138.8, 136.0, 132.5 130.13 129.8, 129.34, 128.5, 125.1, 122.4, 122.04, 120.8, 119.2, 117.8, 111.7, 108.4, 55.5. HRMS (ESI) m/z calcd for $(C_{21}H_{15}F_3N_3OS)^+$ $(M+H)^+$ 358.0969 found 358.0970. mp: 256.8 – 263.5 ℃.

2-(2-Fluoro-4-methoxyanilino)-1,3-benzothiazole-5-carbonitrile (3s)



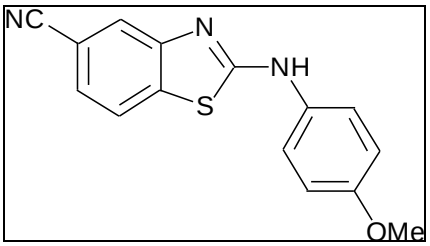
Off- white solid; (Yield= 75%) ^{1}H NMR (300 MHz, DMSO): δ 10.28 (s, 1H), 8.02 (dd, J = 14.9, 8.6 Hz, 2H), 7.92 (s, 1H), 7.51 (d, J = 8.0 Hz, 1H), 6.99 (d, J = 12.2 Hz, 1H), 6.85 (d, J = 8.6 Hz, 1H), 3.78 (s, 3H).^{13}C NMR (101 MHz, DMSO): δ 165.4, 157.0 and 156.9 (d, $^{3}J_{C\text{-}F}$ = 11.98 Hz), 155.8 and 153.3 (d, $^{1}J_{C\text{-}F}$ = 247 Hz), 152.1, 136.4, 124.9 and 124.8 (d, $^{3}J_{C\text{-}F}$ = 8 Hz), 121.8, 120.4, 120.3, 119.3, 110.1 and 110.1 (d, $^{3}J_{C\text{-}F}$ = 2.2 Hz), 108.2, 102.3 and 102.0 (d, $^{2}J_{C\text{-}F}$ = 25.29 Hz), 55.8.HRMS (ESI) m/z calcd for $(C_{15}H_{10}FN_3OS)^+$ $(M+H)^+$ 300.0562 found 300.0562. mp: 178.3–189.2 ℃.

2-(4-Fluoroanilino)-1,3-benzothiazole-5-carbonitrile (3t)



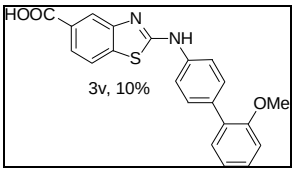
Off- white solid; (Yield= 65%) ^{1}H NMR (400 MHz, DMSO): δ 10.75 (s, 1H), 7.99 (dd, J = 14.7, 4.8 Hz, 2H), 7.81–7.73 (m, 2H), 7.53 (dd, J = 8.1, 1.6 Hz, 1H), 7.21 (t, J = 8.9 Hz, 2H). ^{13}C NMR (75 MHz, DMSO): δ 163.4, 159.3 and 156.1 (d, $^{1}J_{C\text{-}F}$ = 225 Hz), 152.1, 136.5, 135.9, 125.1, 122.4, 121.9, 119.9 and 119.9 (d, $^{3}J_{C\text{-}F}$ = 7 Hz), 119.6 and 119.2 (d, $^{2}J_{C\text{-}F}$ = 23 Hz), 115.7 and 115.4 (d, $^{2}J_{C\text{-}F}$ = 22 Hz), 108.3.HRMS (ESI) m/z calcd for $(C_{14}H_8FN_3S)^+$ $(M+H)^+$ 270.0456 found 270.0456. mp: 282.2- 240.6 ℃.

2-(4-Methoxyanilino)-1,3-benzothiazole-5-carbonitrile (3u)



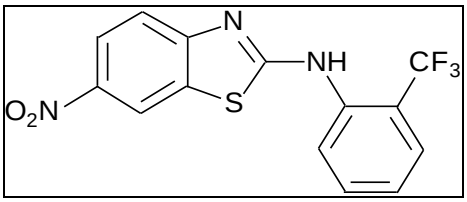
Off- white solid; (Yield= 65%); ^{1}H NMR (400 MHz, DMSO): δ 10.53 (s, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 1.3 Hz, 1H), 7.63 (d, J = 9.0 Hz, 2H), 7.49 (dd, J = 8.1, 1.3 Hz, 1H), 6.95 (d, J = 9.0 Hz, 2H), 3.73 (s, 3H).^{13}C NMR (75 MHz, DMSO): δ 163.8, 155.2, 152.4, 135.9, 133.3, 124.7, 122.3, 121.6, 120.2, 119.2, 114.2, 108.2, 55.2. HRMS (ESI) m/z calcd for $(C_{15}H_{11}N_3OS)^+$ $(M+H)^+$ 282.0656 found 282.0656. mp: 187.1 - 202.3 ℃.

2-[(2'-Methoxy[1,1'-biphenyl]-4-yl)amino]-1,3-benzothiazole-5-carboxylic acid (3v)



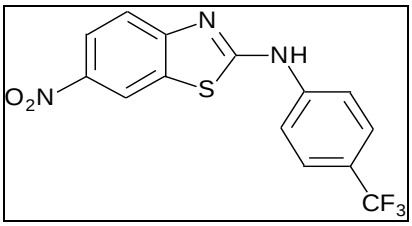
Off-white Solid; (Yield= 10%); ^{1}H NMR (400 MHz, DMSO): δ 12.89 (s, 1H), 10.67 (s, 1H), 8.06 (d, J = 1.2 Hz, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.79 (d, J = 8.6 Hz, 2H), 7.71 (dd, J = 8.2, 1.6 Hz, 1H), 7.48 (d, J = 8.6 Hz, 2H), 7.33-7.25 (m, 2H), 7.08 (d, J = 7.9 Hz, 1H), 7.00 (t, J = 7.4 Hz, 1H), 3.76 (s, 3H). ^{13}C NMR (75 MHz, DMSO): δ 169.1, 161.8, 156.2, 151.9, 139.5, 134.5, 132.6, 131.8, 130.1, 129.8, 129.5, 128.4, 123.4, 120.8, 120.0, 119.8, 117.4, 111.8, 55.5. HRMS (ESI) m/z calcd for $(C_{21}H_{16}N_2O_3S)^+$ $(M+H)^+$ 377.0915 found 377.0915. mp- 220. 6- 270.8 ℃.

6-Nitro-N-[2-(trifluoromethyl)phenyl]-1,3-benzothiazol-2-amine (3w)



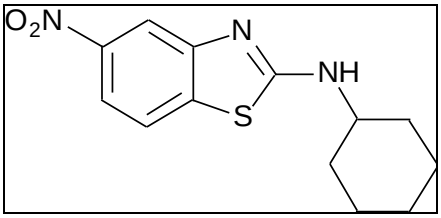
Brown solid; (Yield= 70%) ^{1}H NMR (300 MHz, DMSO): δ 10.81 (s, 1H), 8.75 (s, 1H), 8.14 (dd, J = 8.9, 2.4 Hz, 1H), 7.89–7.67 (m, 2H), 7.54-7.40 (m, 2H). ^{13}C NMR (101 MHz, DMSO): δ 167.9, 162.3, 154.8, 141.5, 139.4, 133.8, 126.7, 126.7, 126.6, 126.4, 124.6 (q, $^{1}J_{C\text{-}F}$ = 273 Hz), 123.5, 118.1, 116.6.HRMS (ESI) m/z calcd for $(C_{14}H_8F_3N_3O_2S)^+$ $(M+H)^+$ 340.0323 found 340.0323. mp: 166.4 - 177.1 ℃.

6-Nitro-N-[4-(trifluoromethyl)phenyl]-1,3-benzothiazol-2-amine (3y)



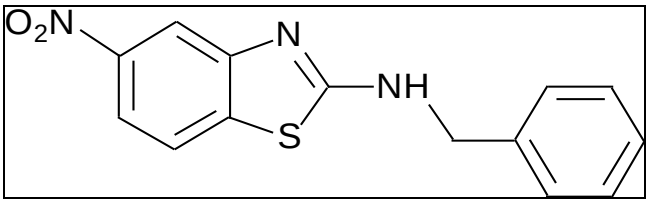
Pale yellow solid; (Yield= 50%) ^{1}H NMR (300 MHz, DMSO): δ 11.35 (s, 1H), 8.91 (s, 1H), 8.22 (d, J = 8.6 Hz, 1H), 8.01 (d, J = 8.6 Hz, 2H), 7.78 (d, J = 8.6, 2.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO): δ 167.9, 162.3, 154.8, 141.5, 139.4, 133.8, 127.7, 126.7, 126.4, 123.6 (q, $^{1}J_{C\text{-}F}$ = 282 Hz) , 118.1, 116.6.sHRMS (ESI) m/z calcd for $(C_{15}H_{12}F_3N_3O_2S)^+$ $(M+H)^+$ 340.0323 found 340.0323. mp: 227.3 - 237.6 ℃

***N*-Cyclohexyl-5-nitro-1,3-benzothiazol-2-amine (3aa)**



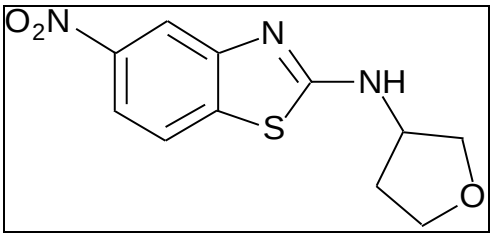
White solid; (Yield= 65%) ^{1}H NMR (400 MHz, DMSO): δ 8.40 (d, J = 7.4 Hz, 1H), 8.04 (d, J = 2.3 Hz, 1H), 7.90 (d, J = 8.6 Hz, 1H), 7.83 (dd, J = 8.6, 2.3 Hz, 1H), 3.72 (s, 1H), 2.05–1.88 (m, 2H), 1.75–1.65 (m, 2H), 1.61–1.49 (m, 1H), 1.40–1.09 (m, 6H).^{13}C NMR (101 MHz, $CDCl_3$): δ 168.4, 153.1, 147.0, 137.9, 120.7, 116.2, 113.4, 77.4, 55.1, 33.2, 33.0, 25.5, 25.4, 24.8. HRMS (ESI) m/z calcd for $(C_{13}H_{15}N_3O_2S)^+$ $(M+H)^+$ 278.0919 found 278.0919. mp: 253.9- 280.0℃

***N*-Benzyl-5-nitro-1,3-benzothiazol-2-amine (3ab)**



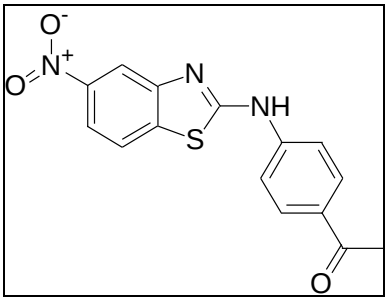
Pale yellow solid; (Yield=70%); ^{1}H NMR (400 MHz, DMSO): δ 8.92 (t, J = 5.6 Hz, 1H), 8.07 (d, J = 2.1 Hz, 1H), 7.94 (d, J = 8.6 Hz, 1H), 7.86 (dd, J = 8.6, 2.3 Hz, 1H), 7.40–7.30 (m, 4H), 7.29–7.23 (m, 1H), 4.61 (d, J = 5.6 Hz, 2H).^{13}C NMR (75 MHz, DMSO): δ 168.5, 152.8, 146.1, 138.6, 138.3, 128.4, 128.2, 127.5, 127.2, 121.6, 115.5, 111.8, 47.3. HRMS (ESI) m/z calcd for $(C_{14}H_{11}N_3O_2S)^+$ $(M+H)^+$ 286.0606 found 286.0606. mp: 169.7 - 179.0℃.

5-Nitro-N-(oxolan-3-yl)-1,3-benzothiazol-2-amine (3ac)



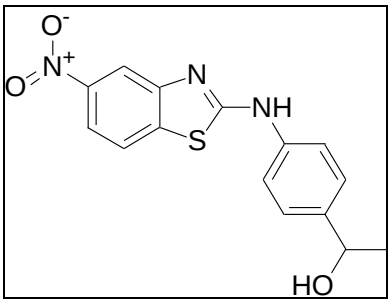
Off- white solid; (Yield= 83%); ^{1}H NMR (400 MHz, DMSO): δ 8.69 (d, J = 6.2 Hz, 1H), 8.08 (d, J = 2.2 Hz, 1H), 7.94 (d, J = 8.6 Hz, 1H), 7.87 (dd, J = 8.6, 2.2 Hz, 1H), 4.45 (s, 1H), 3.83 (dt, J = 14.3, 7.0 Hz, 2H), 3.72 (td, J = 8.3, 5.3 Hz, 1H), 3.66 (dd, J = 9.2, 3.0 Hz, 1H), 2.28–2.16 (m, 1H), 1.93–1.81 (m, 1H).^{13}C NMR (75 MHz, DMSO): δ 167.6, 152.8, 146.1, 1386, 121.6, 115.6, 111.8, 72.4, 66.3, 54.6, 32.1. HRMS (ESI) m/z calcd for $(C_{11}H_{11}N_3O_3S)^+$ $(M+H)^+$ 266.0555 found 266.0555. mp: 175.0 - 183.8℃

1-{4-[(5-Nitro-1,3-benzothiazol-2-yl)amino]phenyl}ethan-1-one (3ae)



Yellow Solid; (Yield= 80%) ^{1}H NMR (400 MHz, DMSO): δ 11.24 (s, 1H), 8.37 (d, J = 2.2 Hz, 1H), 8.13 (d, J = 8.7 Hz, 1H), 8.04 (dd, J = 8.7, 2.2 Hz, 1H), 7.99 (d, J = 8.7 Hz, 2H), 7.91 (d, J = 8.7 Hz, 2H), 2.53 (s, 3H). ^{13}C NMR (75 MHz, DMSO): δ 196.2, 163.6, 152.,0 146.3, 144.0, 138.1, 131.0, 129.8, 122.0, 117.3, 117.2, 113.6, 26.3. HRMS (ESI) m/z calcd for $(C_{15}H_{11}N_3O_3S)^+$ $(M+H)^+$ 314.0555 found 314.0555. mp: 220.7-254.3℃.

1-{4-[(5-Nitro-1,3-benzothiazol-2-yl)amino]phenyl}ethan-1-ol (6)



Yellow Solid; (Yield=78%) ^{1}H NMR (300 MHz, DMSO): δ 10.75 (s, 1H), 8.29 (s, 1H), 8.12–7.96 (m, 2H), 7.70 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.3 Hz, 2H), 5.10 (d, J = 4.2 Hz, 1H), 4.76–4.65 (m, 1H), 1.33 (t, J = 5.4 Hz, 4H), 1.22 (s, 1H). ^{13}C NMR (75 MHz, DMSO): δ 164.3, 152.5, 146.2, 142.1, 138.4, 138.0, 126.0, 121.7, 118.2, 116.6, 112.9, 67.7, 25.84. HRMS (ESI) m/z calcd for $(C_{15}H_{13}N_3O_3S)^+$ $(M+H)^+$ 316.0711found 316.0711. mp: 197.8- 215.5 ℃.

Specific Optical Rotation: $[A]_D^T$ for 1-{4-[(5-nitro-1,3-benzothiazol-2-yl)amino]phenyl}ethan-1-ol at 20 ℃ at 598 nm at a concentration of 10mg/ mL (DMSO) was found to be -22.4.

Scale-up reaction

To an oven dried 25 mL round bottom flask, 2g 2-fluoro-5-nitroaniline, 3.2g 1-isothiocyanato-4-methoxybenzene and 4.4g potassium carbonate were added followed by 20 mL 2- butanol. The reaction mixture was allowed to stir at 80 ℃ for 16 hours. The progress of the reaction was monitored by TLC for the disappearance of the starting material.

On completion of the reaction, the reaction mass was diluted with water and extracted using ethyl acetate (2×100ml). The combined ethyl acetate layers were once again washed with water (1×100ml) and brine(1×100ml) sequentially, dried over anhydrous sodium sulphate and concentrated under reduced pressure at 45 ℃.

The crude product was purified by a flash column on using Biotage Selekt

General procedure for reduction of 1-{4-[(5-nitro-2,3-dihydro-1,3-benzothiazol-2-yl)amino]phenyl}propan-2-one and subsequent enzymatic resolution of 1-{4-[(5-nitro-2,3-dihydro-1,3-benzothiazol-2-yl)amino]phenyl}propan-2-ol-

All the manipulations were carried out in oven-dried glassware under air. 0.5 g (1.5mmol) of 1-{4-[(5-nitro-2,3-dihydro-1,3-benzothiazol-2-yl)amino]phenyl}propan-2-one was weighed into a

25ml round bottomed flask and 90mg (2.3mmol) of sodium borohydride was charged into the flask following the addition of 8:2 DCM: MEOH (5ml) . The mixture was stirred at 0 ℃ for 3 hours.

The progress of the reaction was monitored by TLC for the disappearance of the starting material.

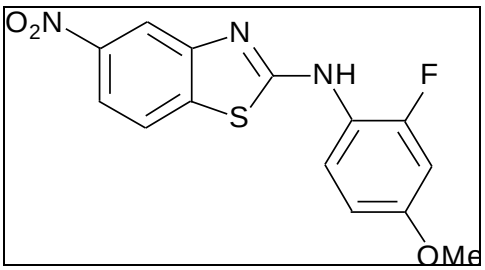
On completion of the reaction, the reaction mixture was diluted with water and extracted into THF (2*25ml). The organic layers were combined, dried over anhydrous sodium sulphate and concentrated under reduced pressure at 45 ℃.

The crude product was purified by a flash column on using Biotage Selekt autocolumn using packed pre-packed 25-gram KP-Sil BiotageϴSNAP. The final compound was characterized by HRMS, ^{1}HNMR and ^{13}CNMR.

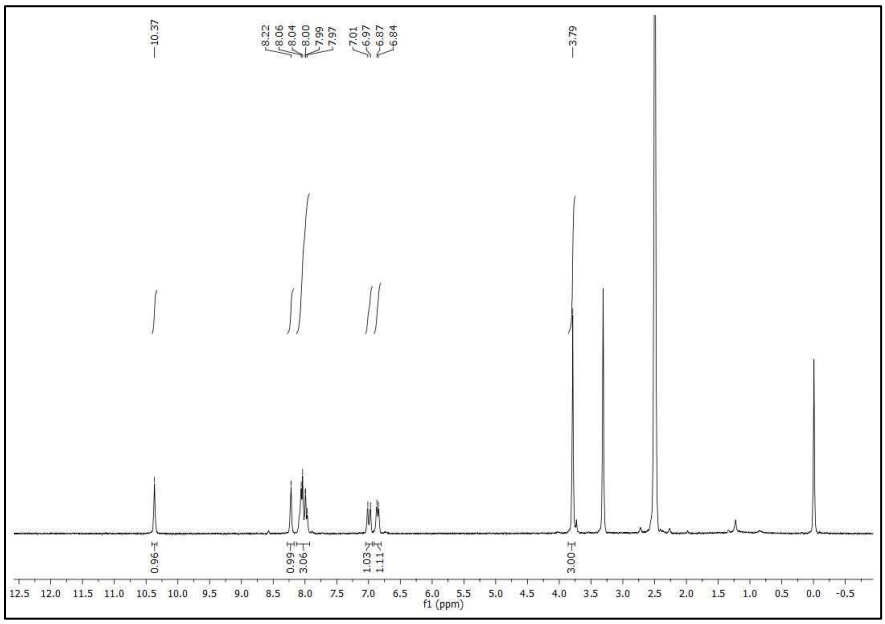
The purified 1-{4-[(5-nitro-2,3-dihydro-1,3-benzothiazol-2-yl)amino]phenyl}propan-2-ol (0.25g, 0.79mmol) was charged into a 25ml round bottomed flask and 0.07ml (0.79mmol) followed by 10 wt% Novozym- 435 beads and 2.5ml THF. The reaction mixture was stirred at RT for 24h. The resolution of the alcohol was monitored by chiral HPLC.

Analytical data of products

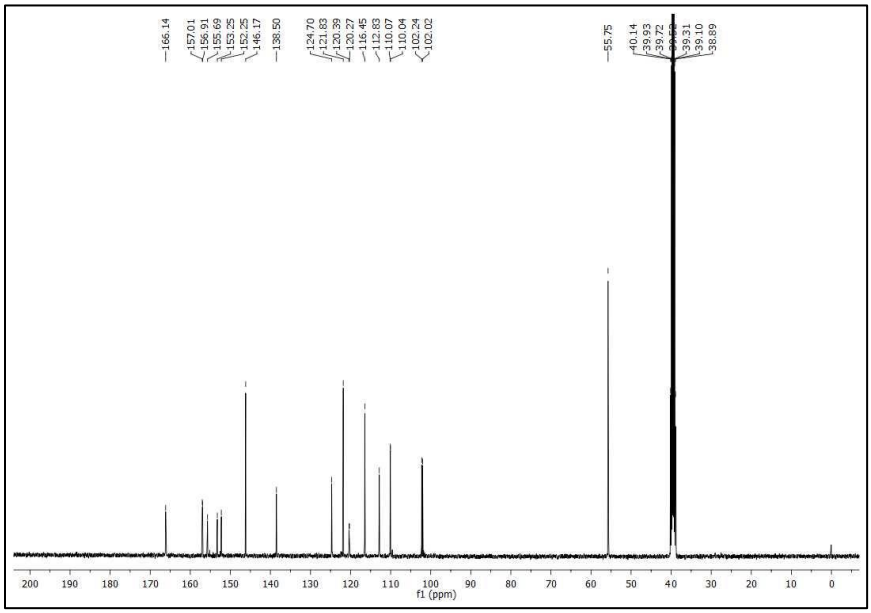
***N*-(2-fluoro-4-methoxyphenyl)-5-nitro-1,3-benzothiazol-2-amine (3a)**



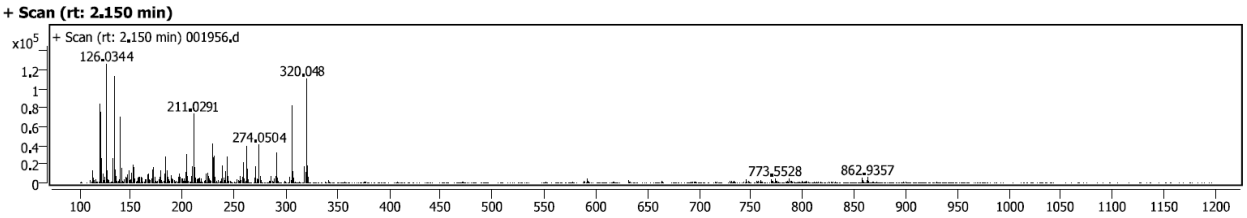
^{1}H NMR



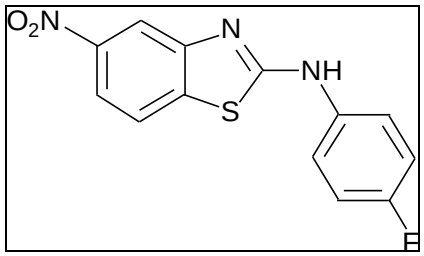
^{13} CNMR



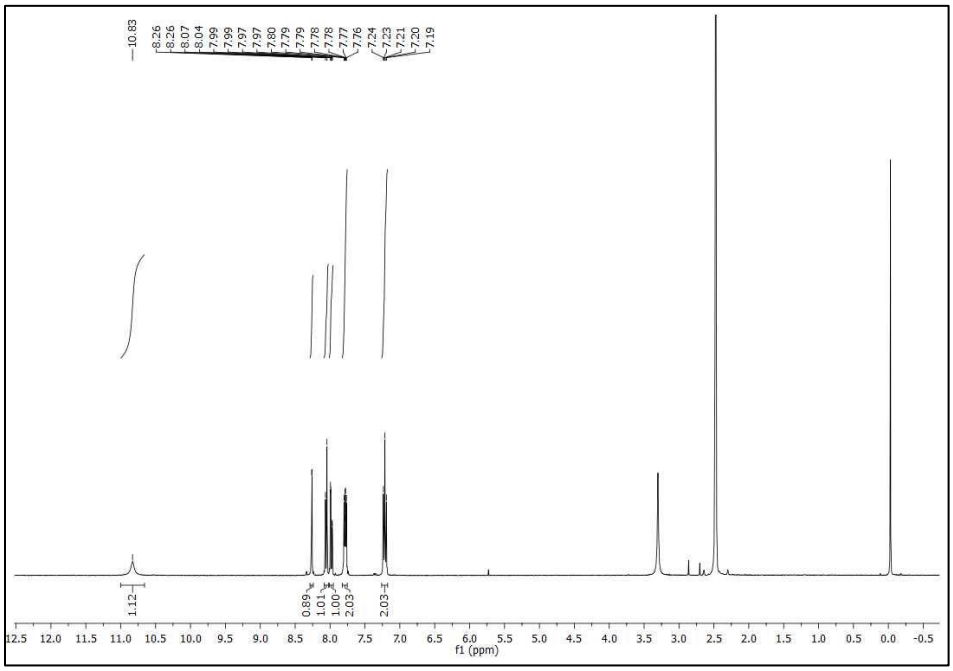
HRMS



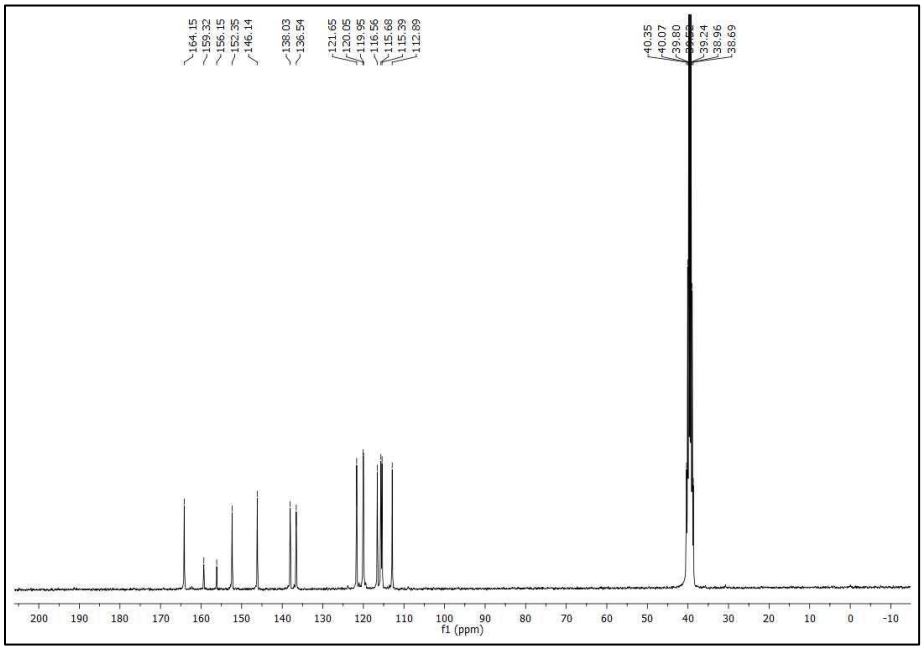
N-(4-fluorophenyl)-5-nitro-1,3-benzothiazol-2-amine (3b)



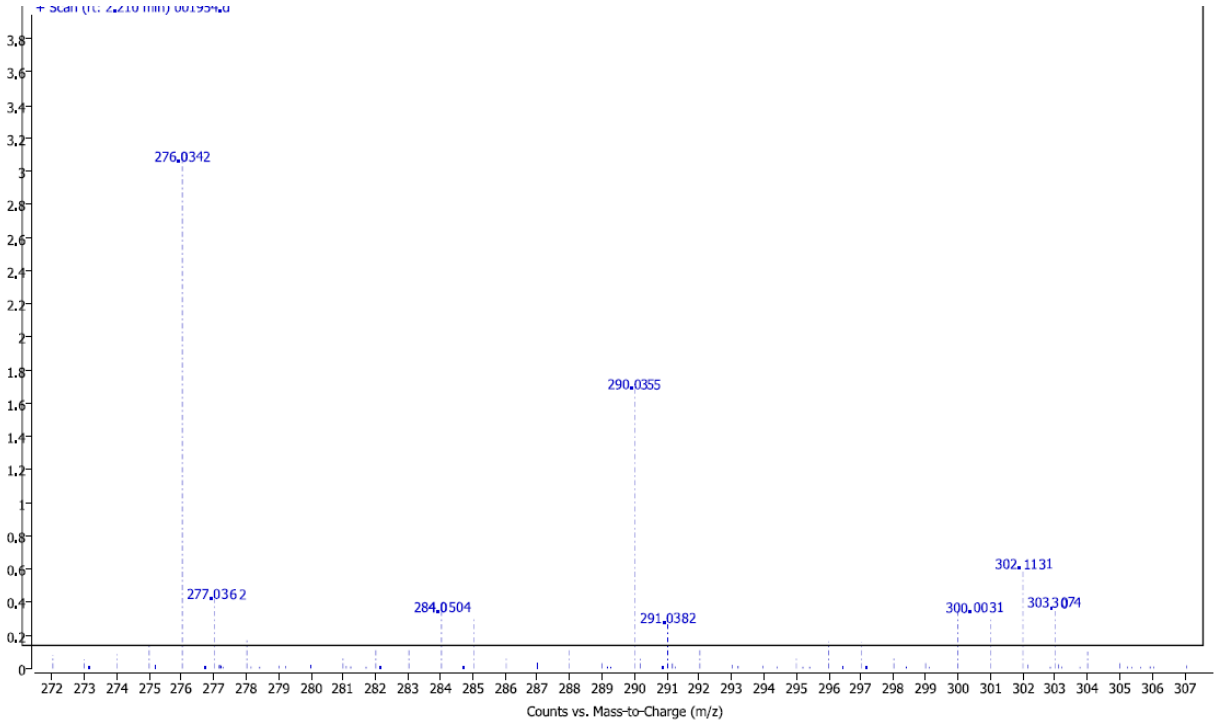
^{1}H NMR



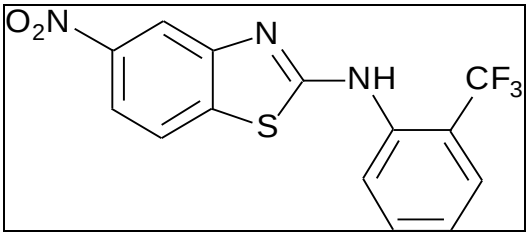
^{13}C NMR


164.15
159.32
156.15
152.35
146.14
138.03
136.54
121.65
120.05
119.95
116.56
115.68
115.39
112.89
40.35
40.07
39.80
39.24
38.96
38.69
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

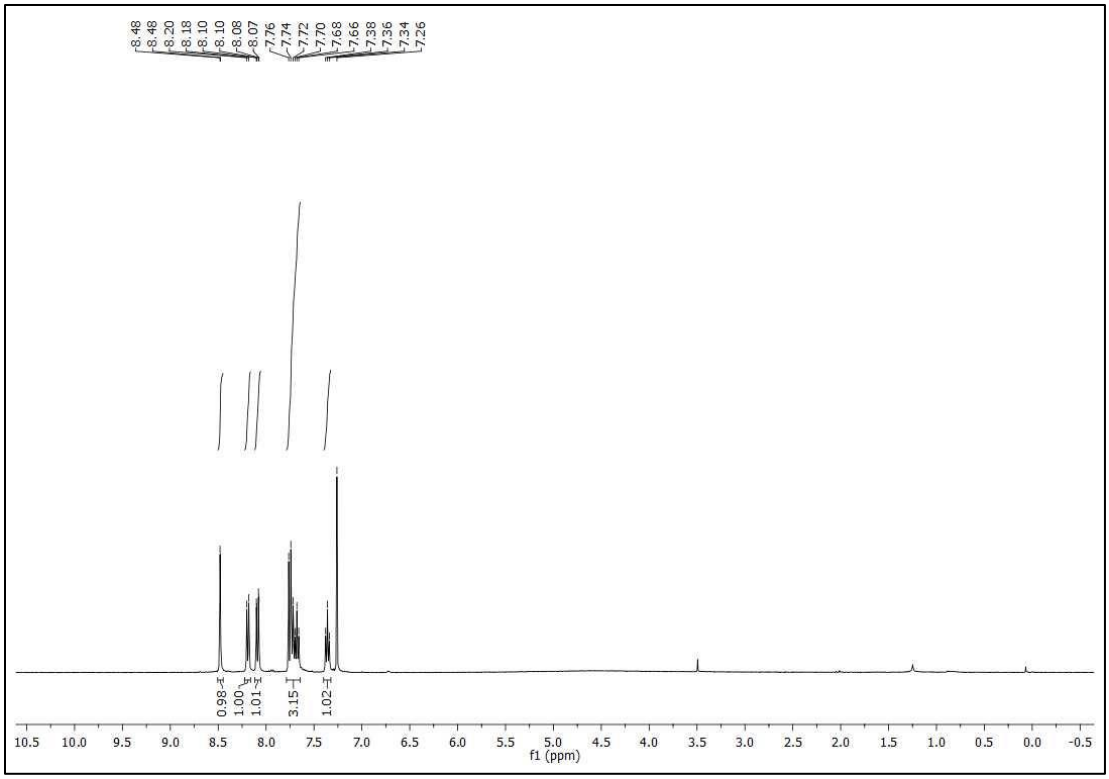
HRMS



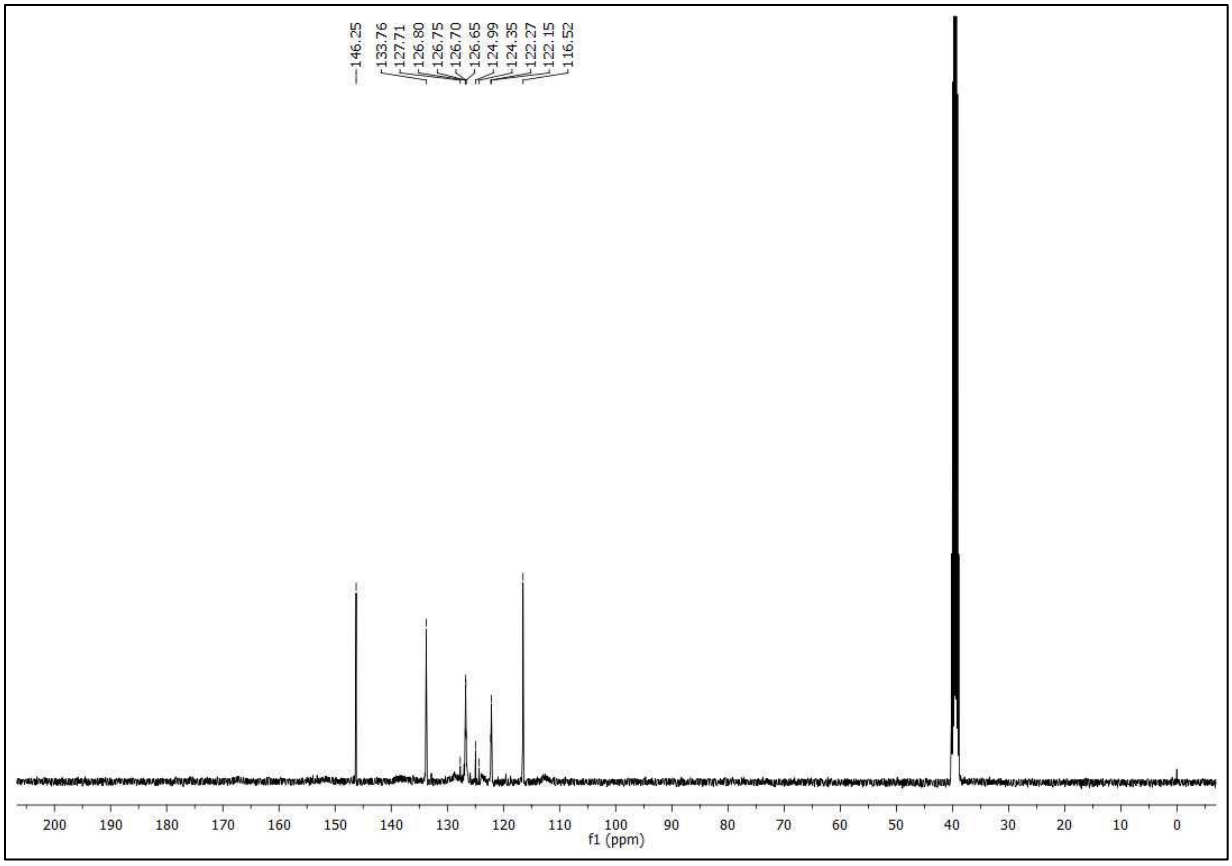
5-nitro-*N*-[2-(trifluoromethyl)phenyl]-1,3-benzothiazol-2-amine (3c)



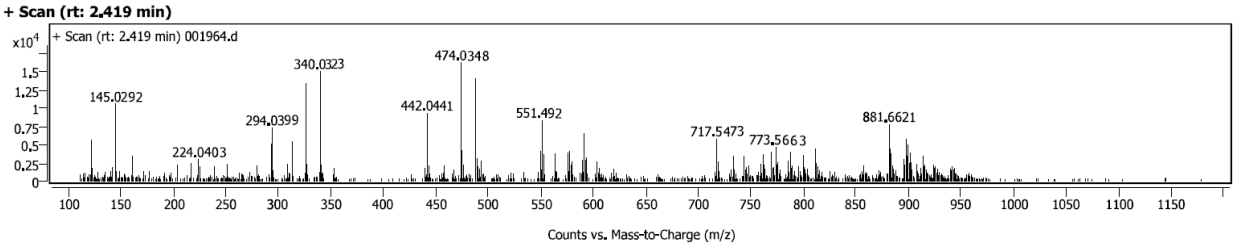
^{1}H NMR


8.48
8.48
8.20
8.18
8.10
8.10
8.08
8.07
7.76
7.74
7.72
7.70
7.68
7.66
7.38
7.36
7.34
7.26
0.98
1.00
1.01
3.15
1.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

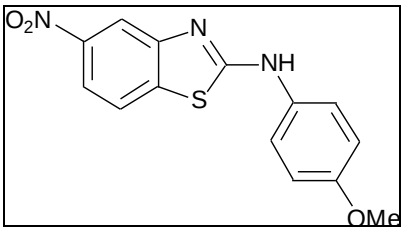
^{13}C NMR



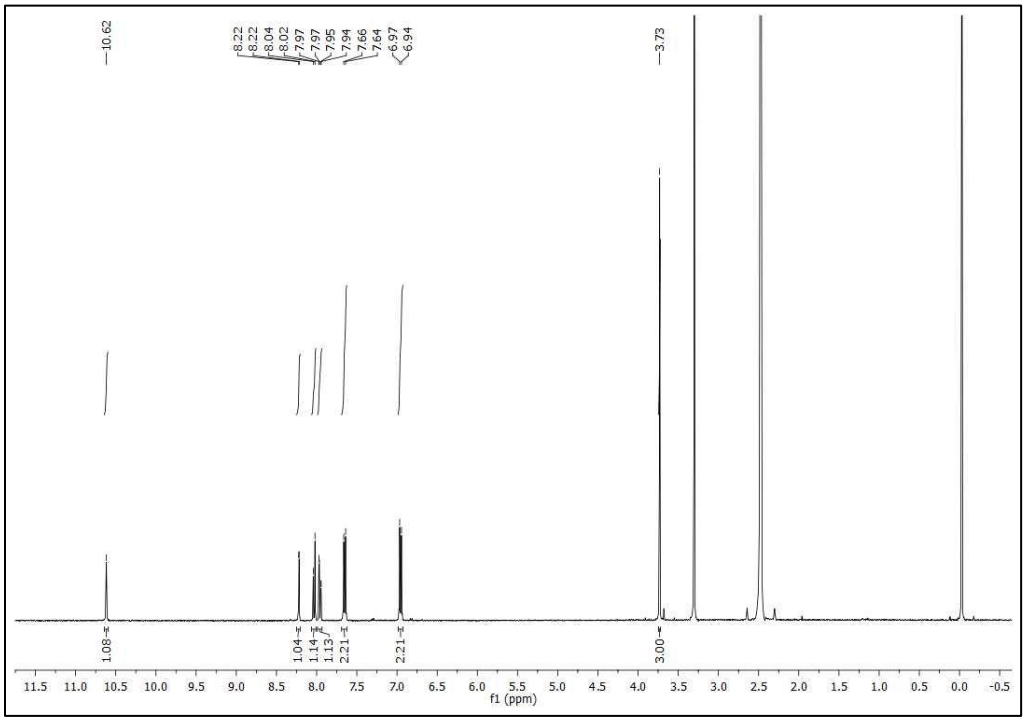
HRMS



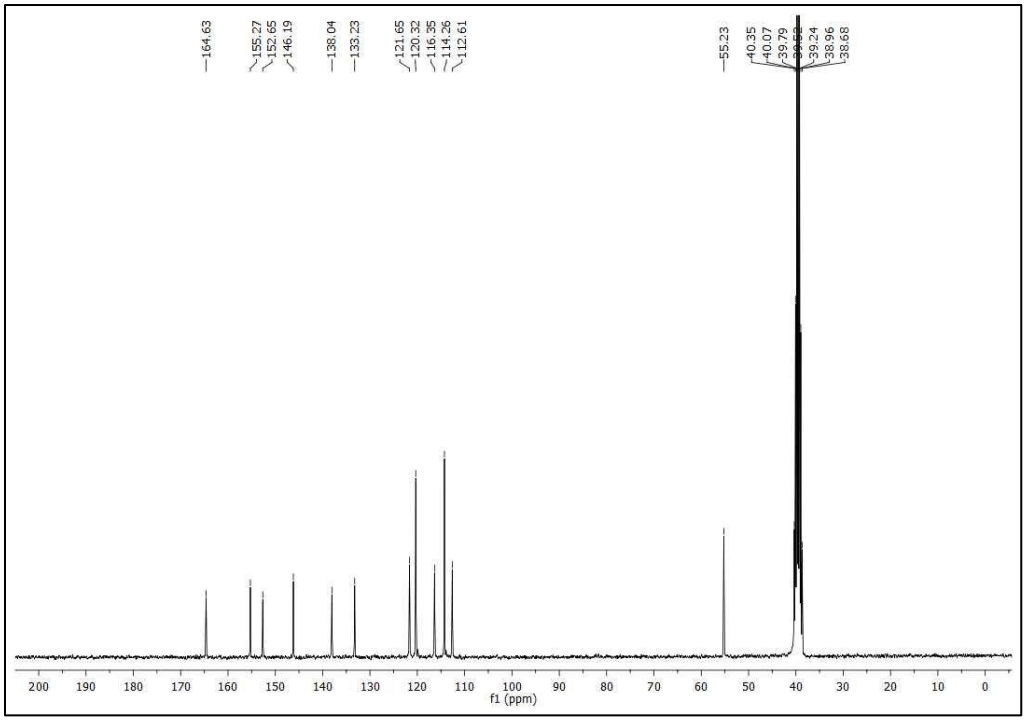
_N_-(4-methoxyphenyl)-5-nitro-1,3-benzothiazol-2-amine (3d)



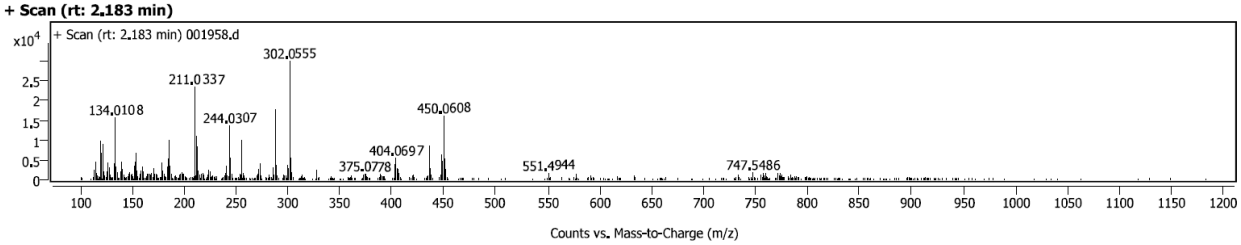
^{1}H NMR



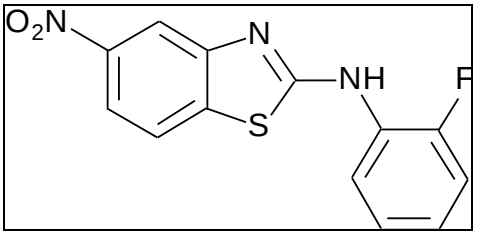
^{13}C NMR



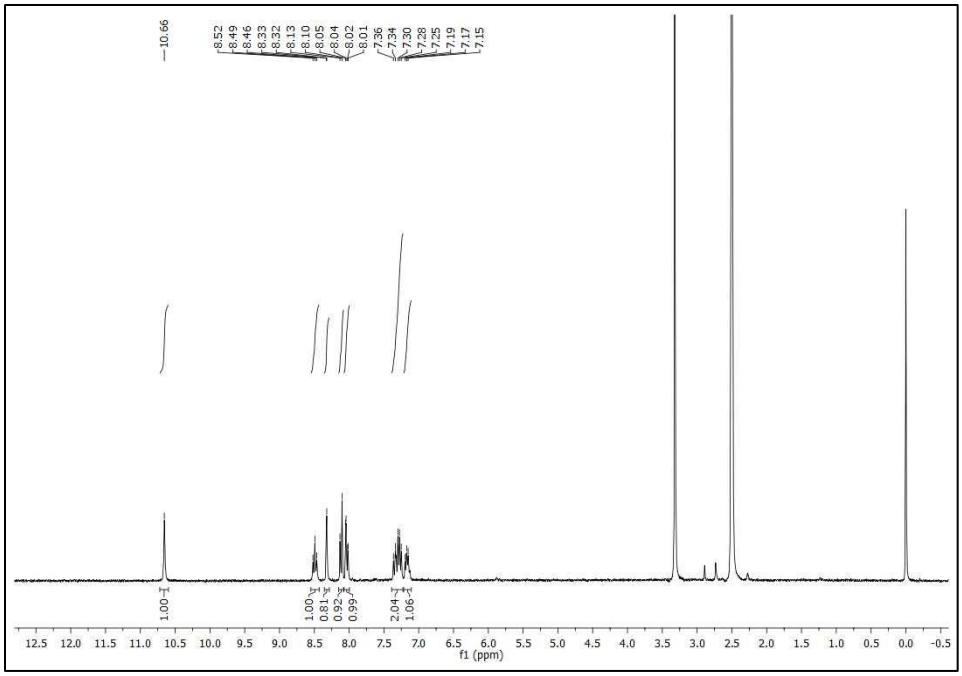
HRMS



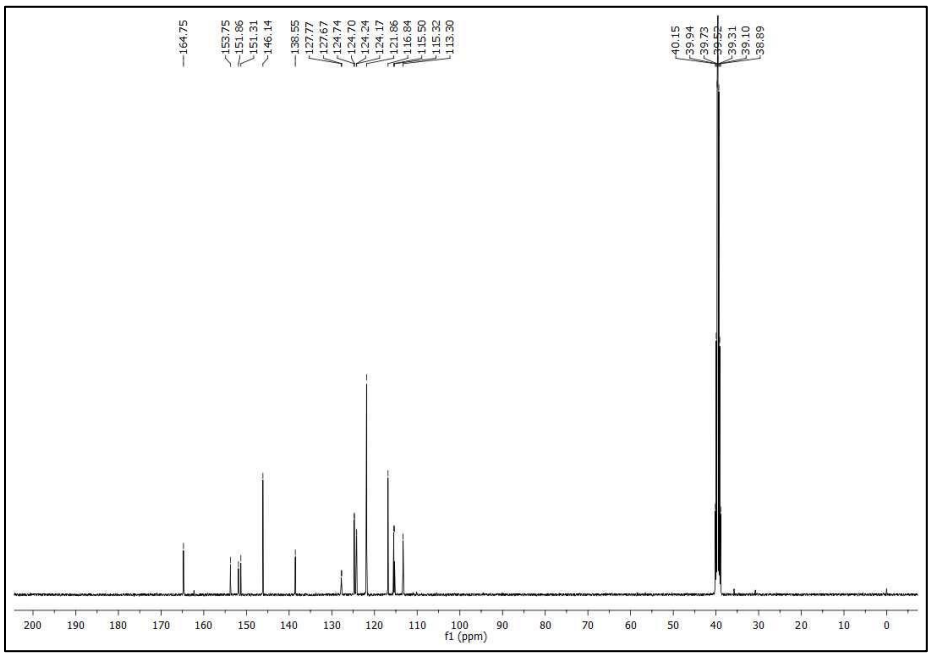
N-(2-fluorophenyl)-5-nitro-1,3-benzothiazol-2-amine (3e)



^{1}H NMR


10.66
8.52
8.49
8.46
8.33
8.32
8.13
8.10
8.05
8.04
8.02
8.01
7.36
7.34
7.30
7.28
7.25
7.19
7.17
7.15
1.00
1.00
0.81
0.92
0.99
2.04
1.06
f1 (ppm)

^{13}C NMR


164.75
153.75
151.86
151.31
146.14
138.55
127.77
127.67
124.74
124.70
124.24
124.17
121.86
116.84
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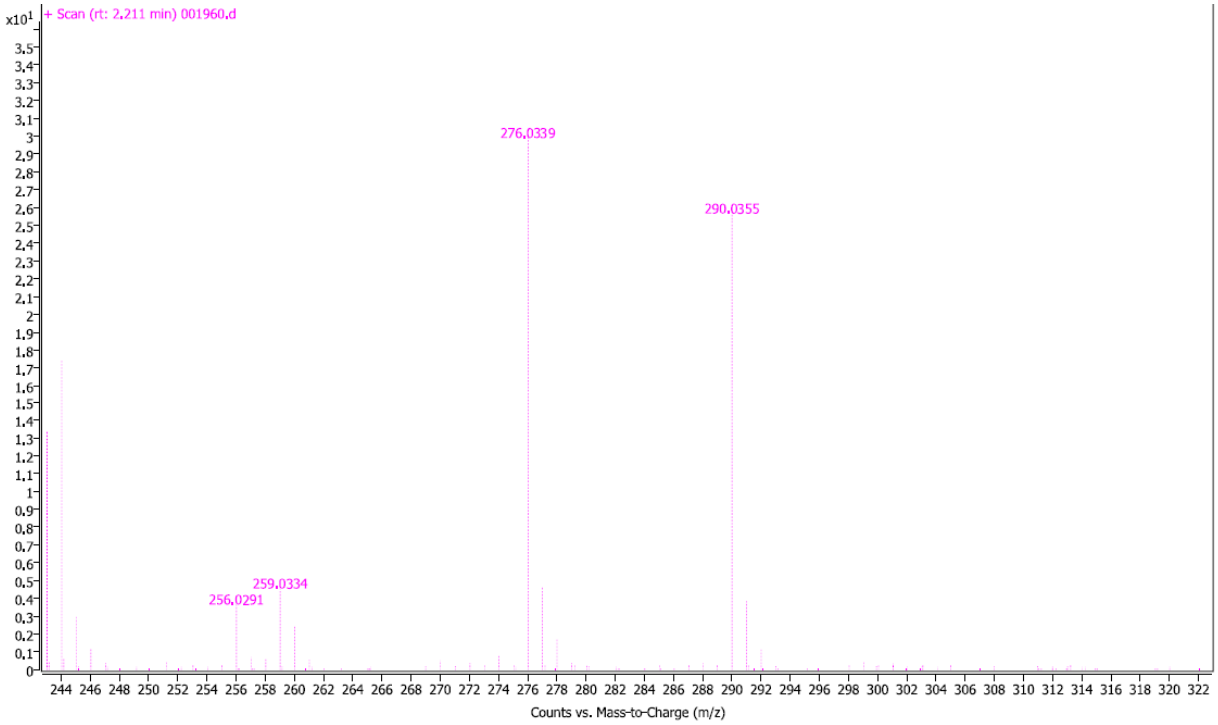
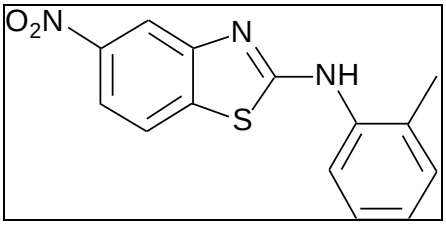
39.52
39.31
39.10
38.89
f1 (ppm)

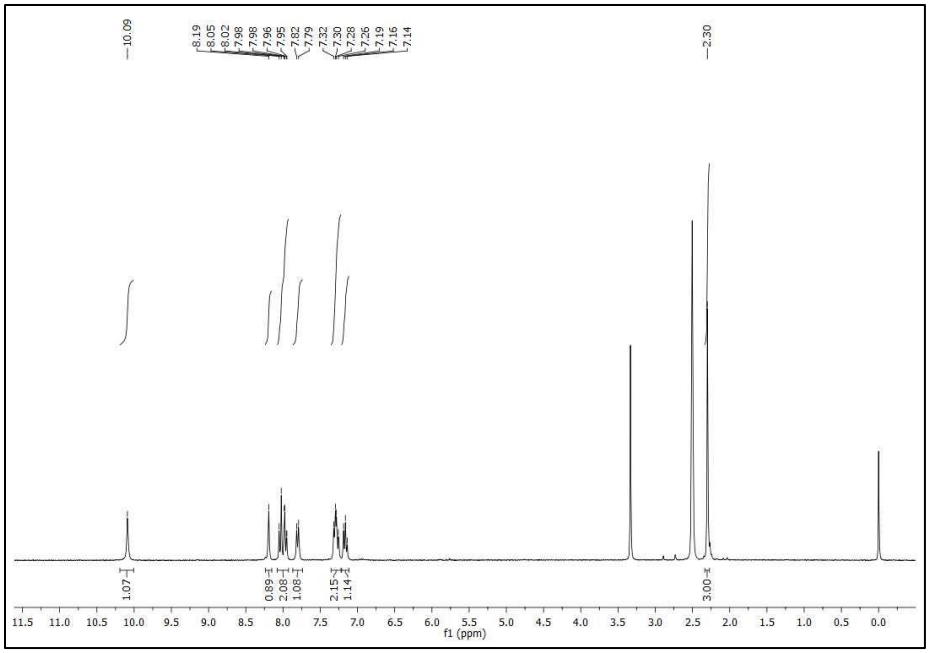
HRMS



N-(2-methylphenyl)-5-nitro-1,3-benzothiazol-2-amine (3f)



^{1}H NMR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8.19
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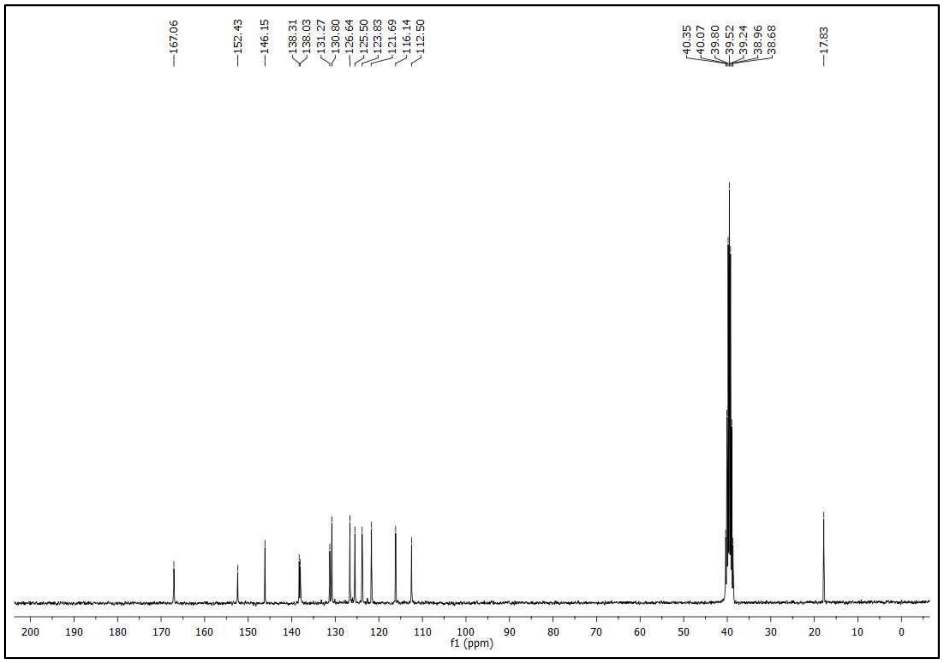
8.02
7.98
7.98
7.96
7.95
7.82
7.79
7.32
7.30
7.28
7.26
7.19
7.16
7.14
2.30
1.07
0.89
2.08
1.08
2.15
1.14
3.00
f1 (ppm)

^{13}C NMR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146.15
138.31
138.03
131.27
130.80
126.64
125.50
123.83
121.69
116.14
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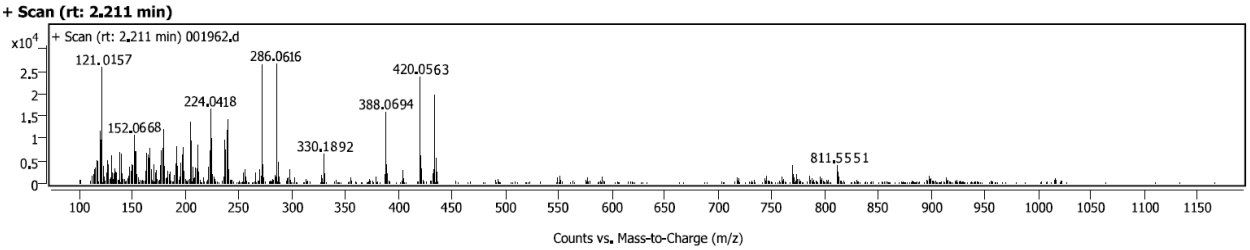
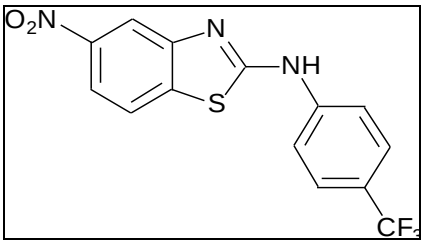
39.52
39.24
38.96
38.68
17.83
f1 (ppm)

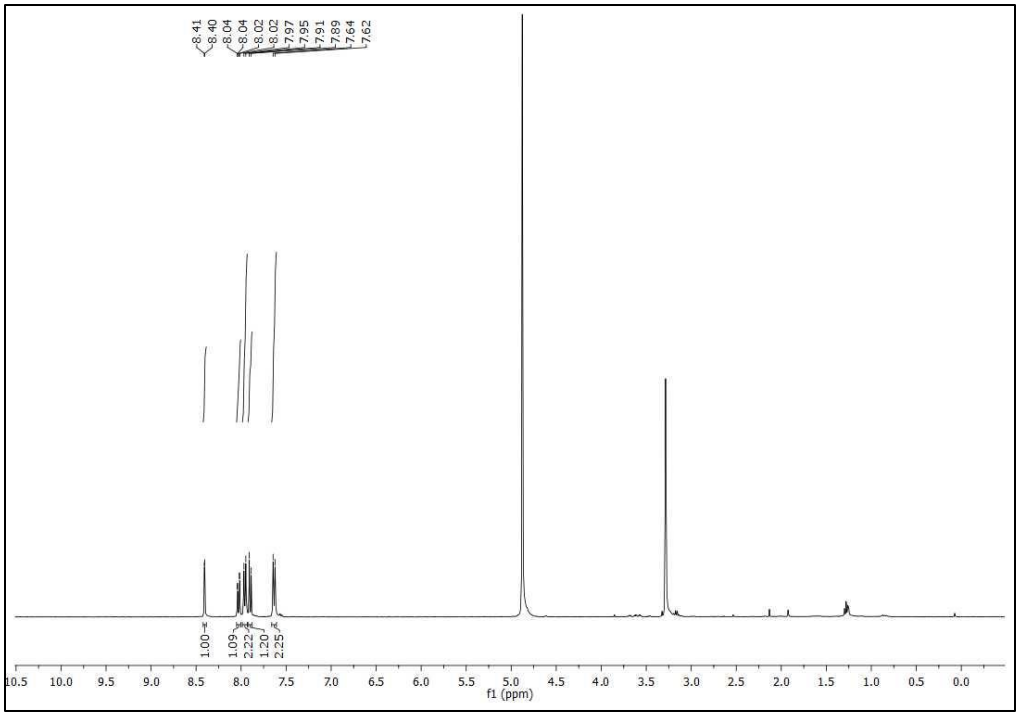
HRMS



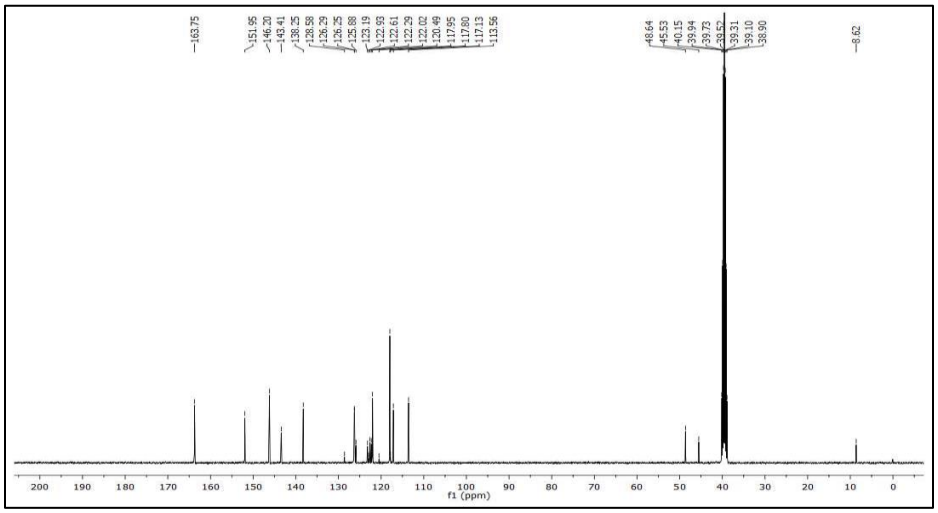
5-Nitro-N-[4-(trifluoromethyl)phenyl]-1,3-benzothiazol-2-amine (3g)



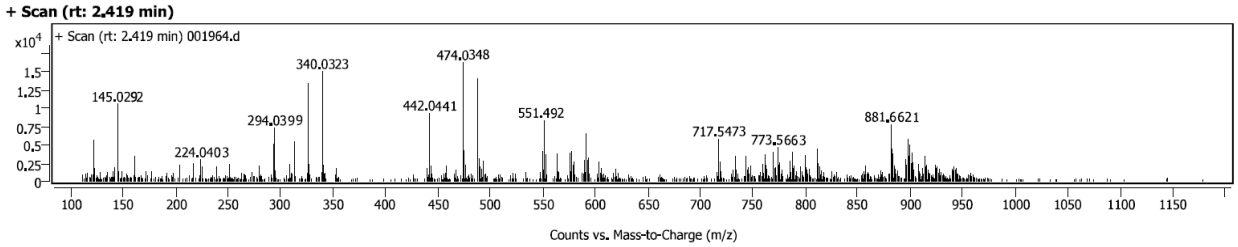
^{1}H NMR


8.41
8.40
8.04
8.04
8.02
8.02
7.97
7.95
7.91
7.89
7.64
7.62
1.00
1.09
2.22
1.20
2.25
f1 (ppm)

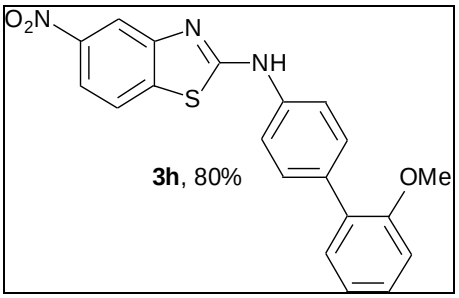
^{13}C NMR


163.75
151.95
146.20
143.41
138.25
128.58
126.29
126.25
125.88
123.19
122.93
122.61
122.29
122.02
120.49
117.95
117.80
117.13
113.56
48.64
45.53
40.15
39.94
39.73
39.52
39.31
39.10
38.90
8.62
f1 (ppm)

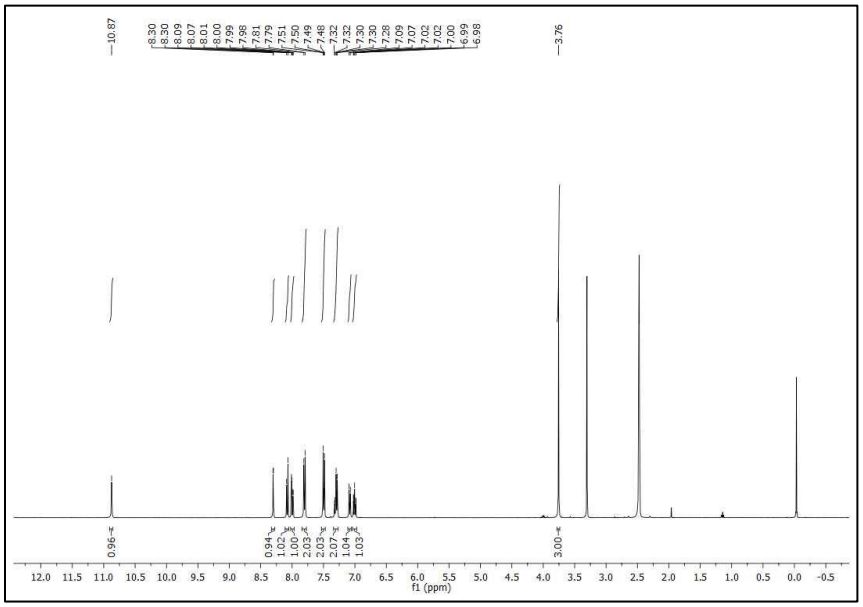
HRMS



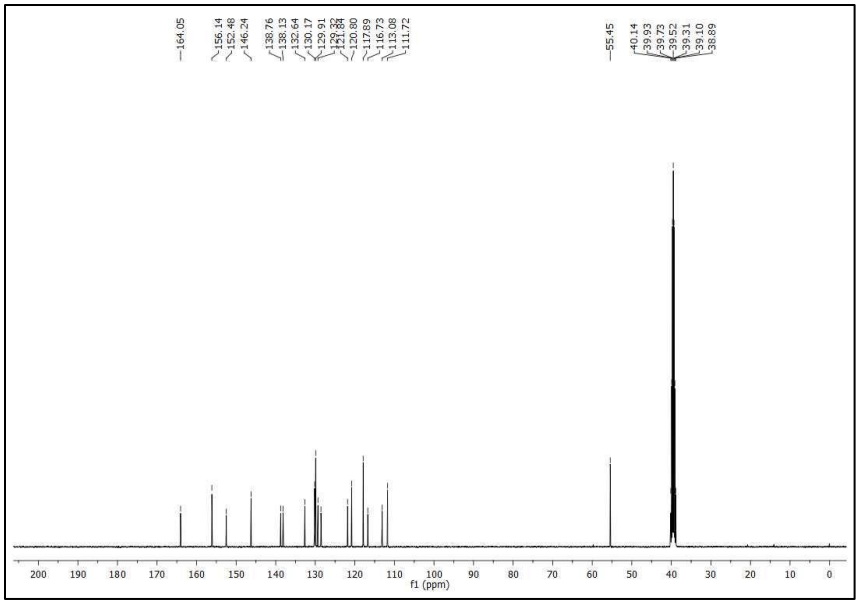
N-(2'-methoxy[1,1'-biphenyl]-4-yl)-5-nitro-1,3-benzothiazol-2-amine (3h)



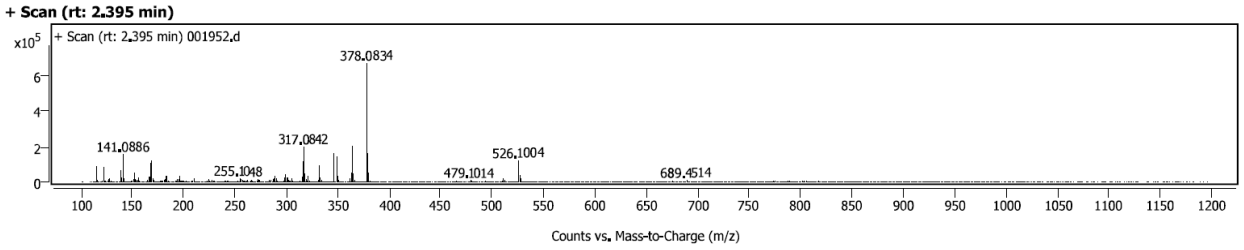
^{1}H NMR



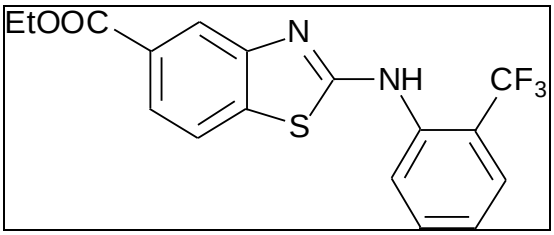
^{13}C.NMR



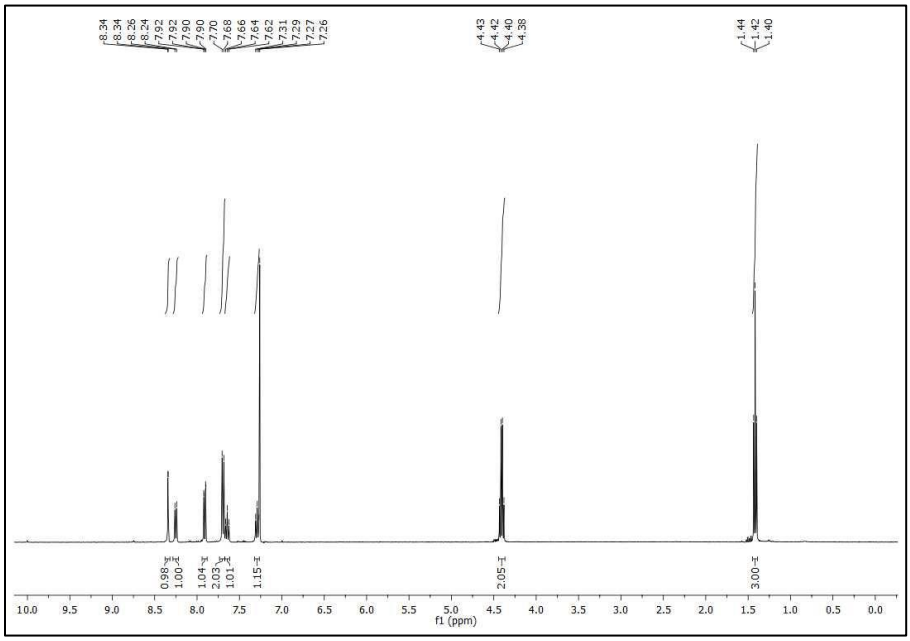
HRMS



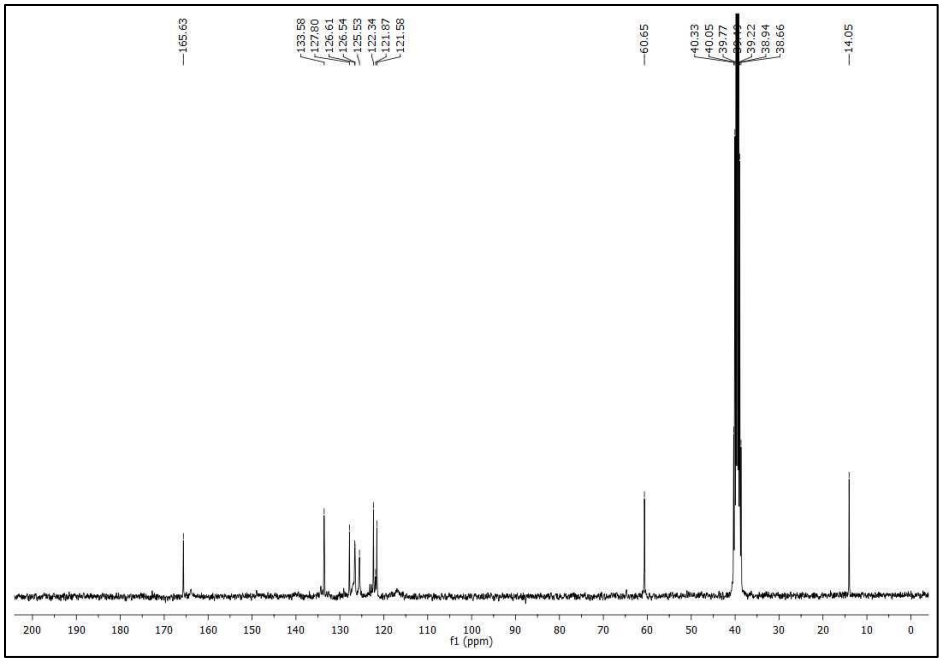
ethyl 2-[2-(trifluoromethyl)anilino]-1,3-benzothiazole-5-carboxylate (3j)



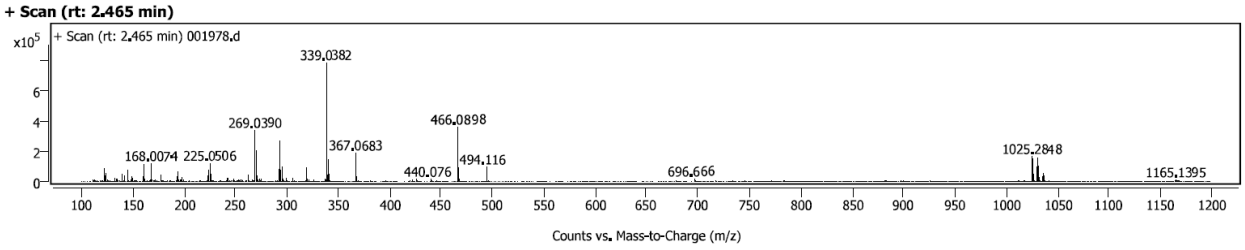
^{1}H.NMR



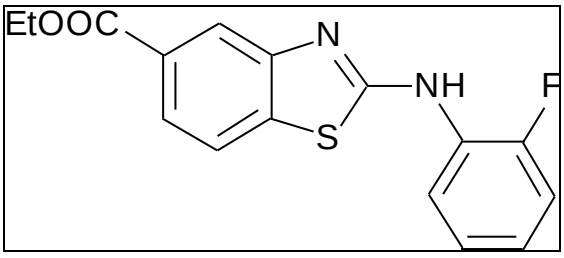
^{13}C.NMR



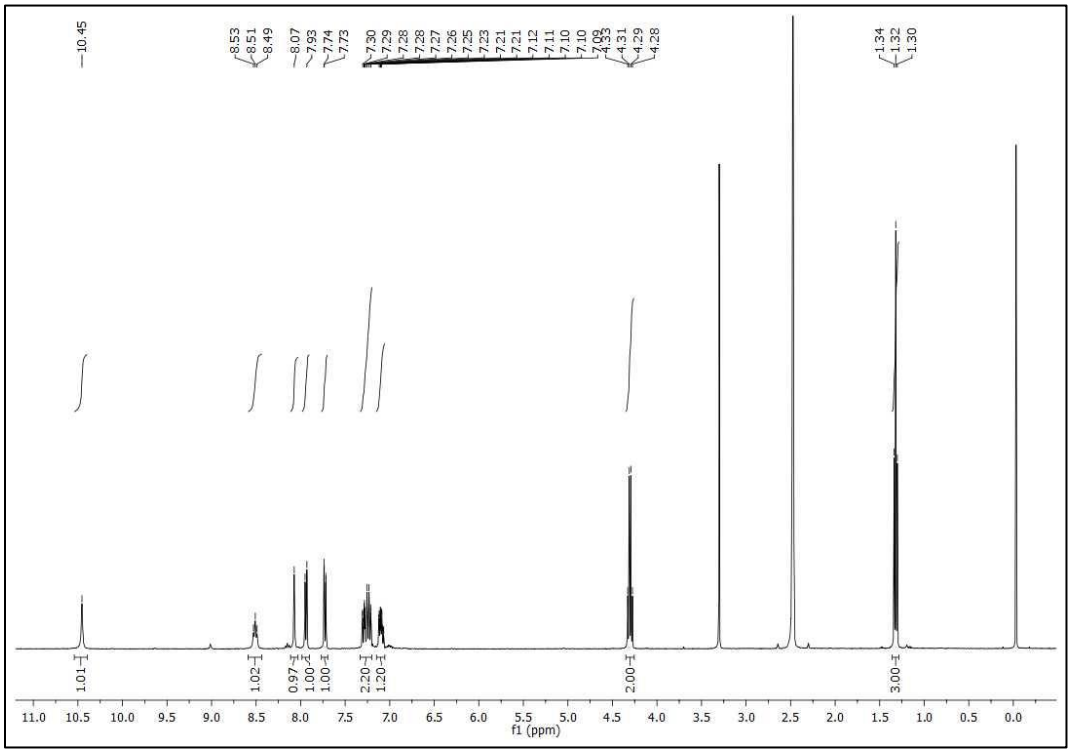
HRMS



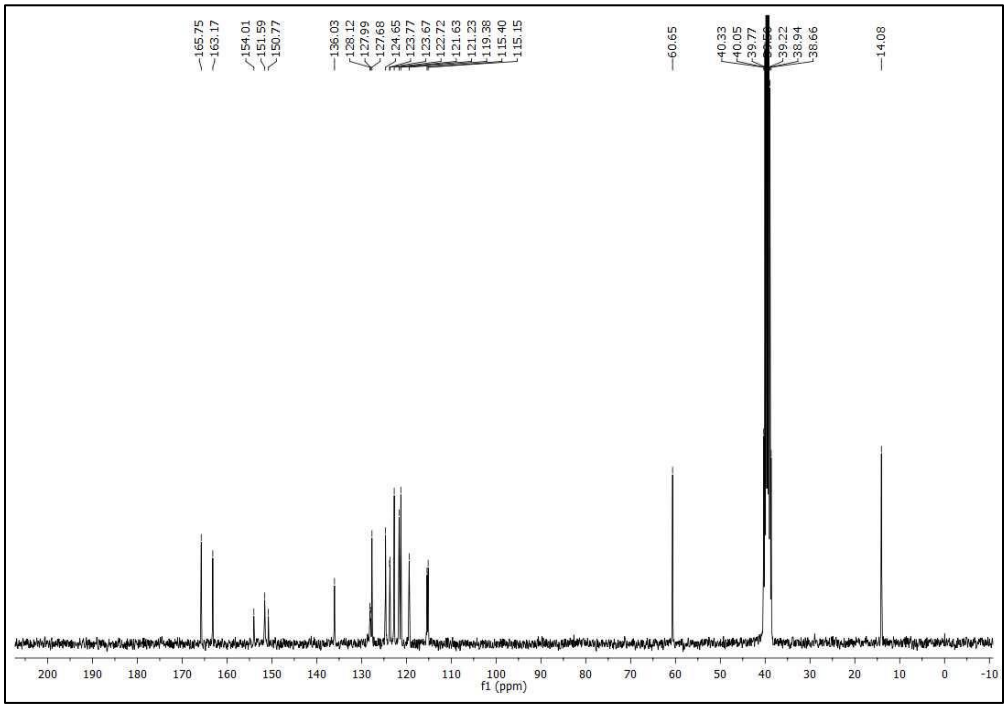
ethyl 2-(2-fluoroanilino)-1,3-benzothiazole-5-carboxylate (3k)



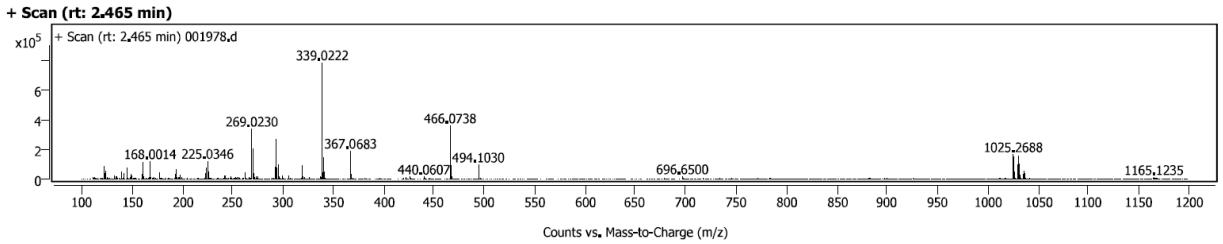
^{1}H.NMR



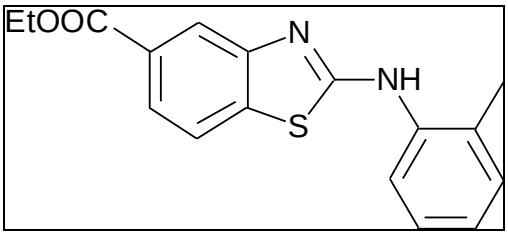
^{13}C.NMR



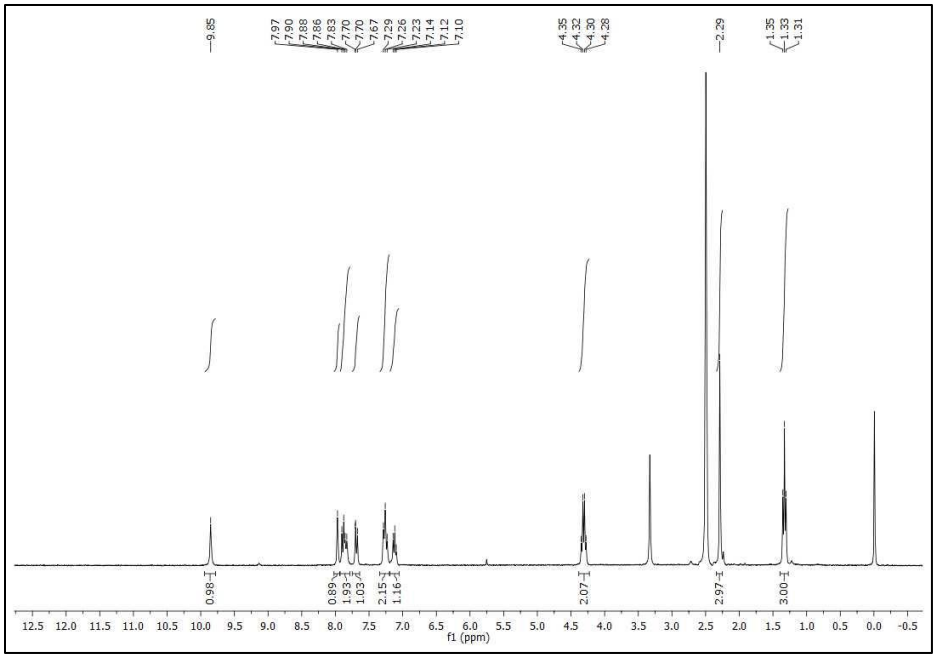
HRMS



ethyl 2-(2-methylanilino)-1,3-benzothiazole-5-carboxylate (3l)



^{1}H NMR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7.97
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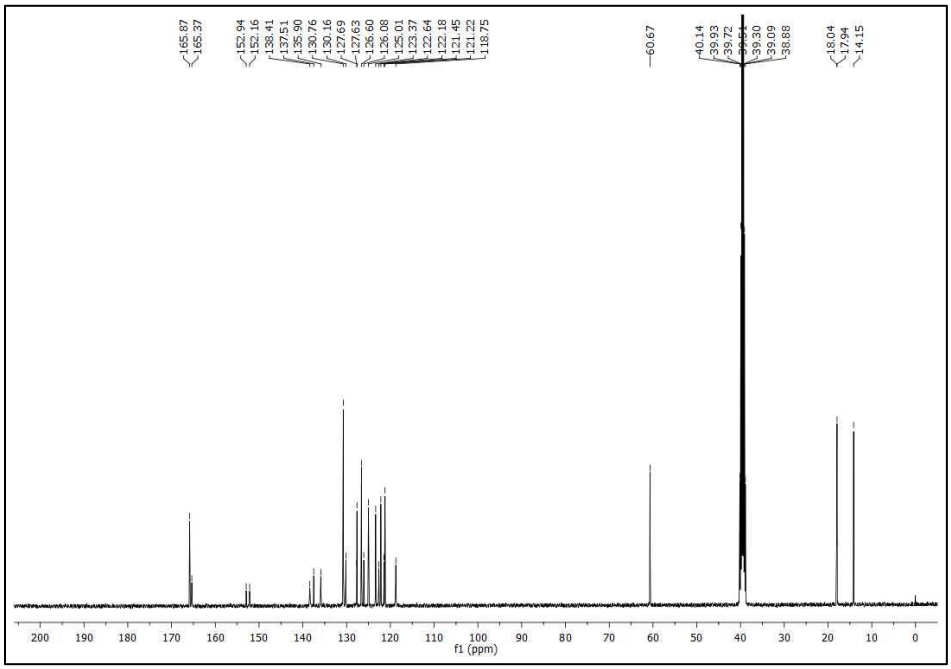
7.88
7.86
7.83
7.70
7.70
7.67
7.29
7.26
7.23
7.14
7.12
7.10
4.35
4.32
4.30
4.28
2.29
1.35
1.33
1.31
0.98
0.89
1.93
1.03
2.15
1.16
2.07
2.97
3.00
f1 (ppm)

^{13}C NMR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130.76
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127.63
126.60
126.08
125.01
123.37
122.64
122.18
121.45
121.22
118.75
60.67
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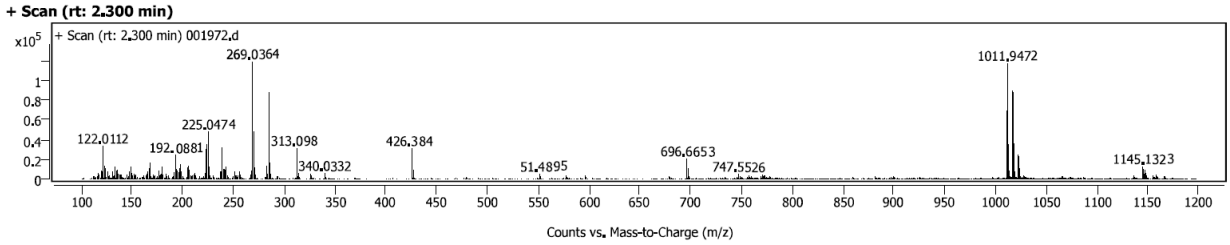
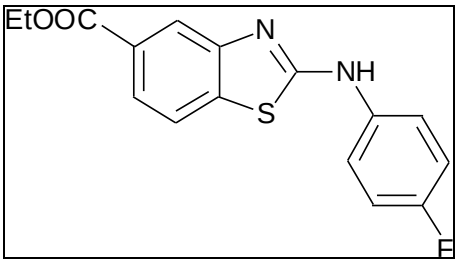
39.51
39.30
39.09
38.88
18.04
17.94
14.15
f1 (ppm)

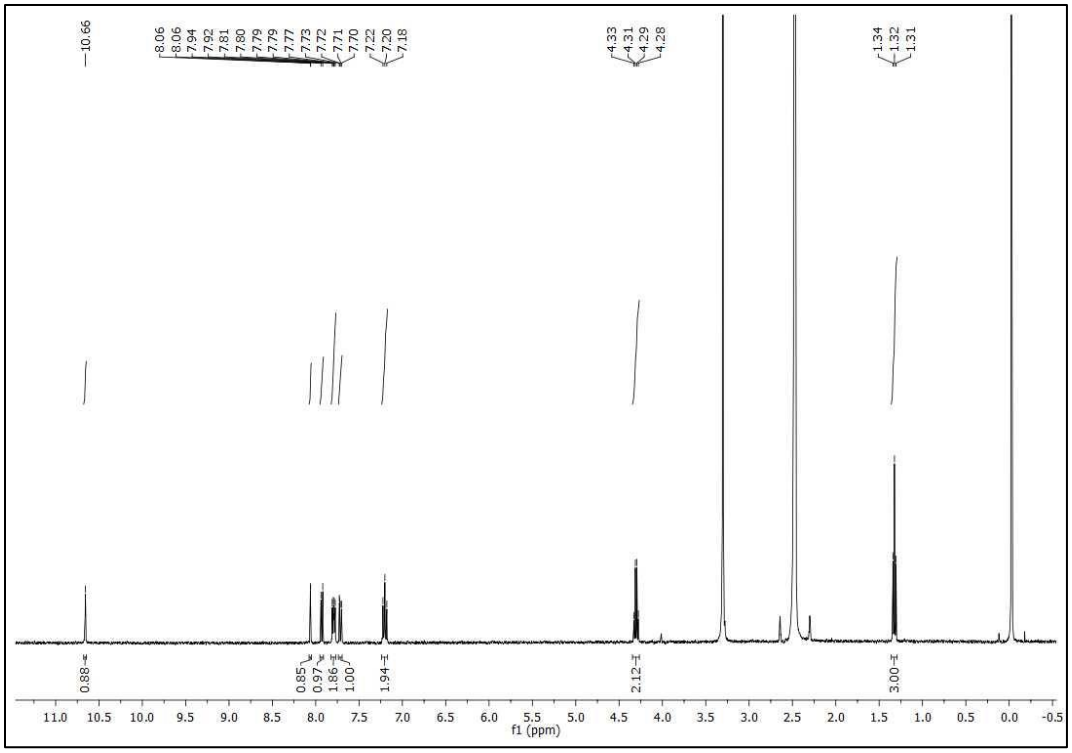
HRMS



ethyl 2-(4-fluoroanilino)-1,3-benzothiazole-5-carboxylate (3m)



^{1}H NMR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8.06
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7.81
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7.70
7.22
7.20
7.18
4.33
4.31
4.29
4.28
1.34
1.32
1.31
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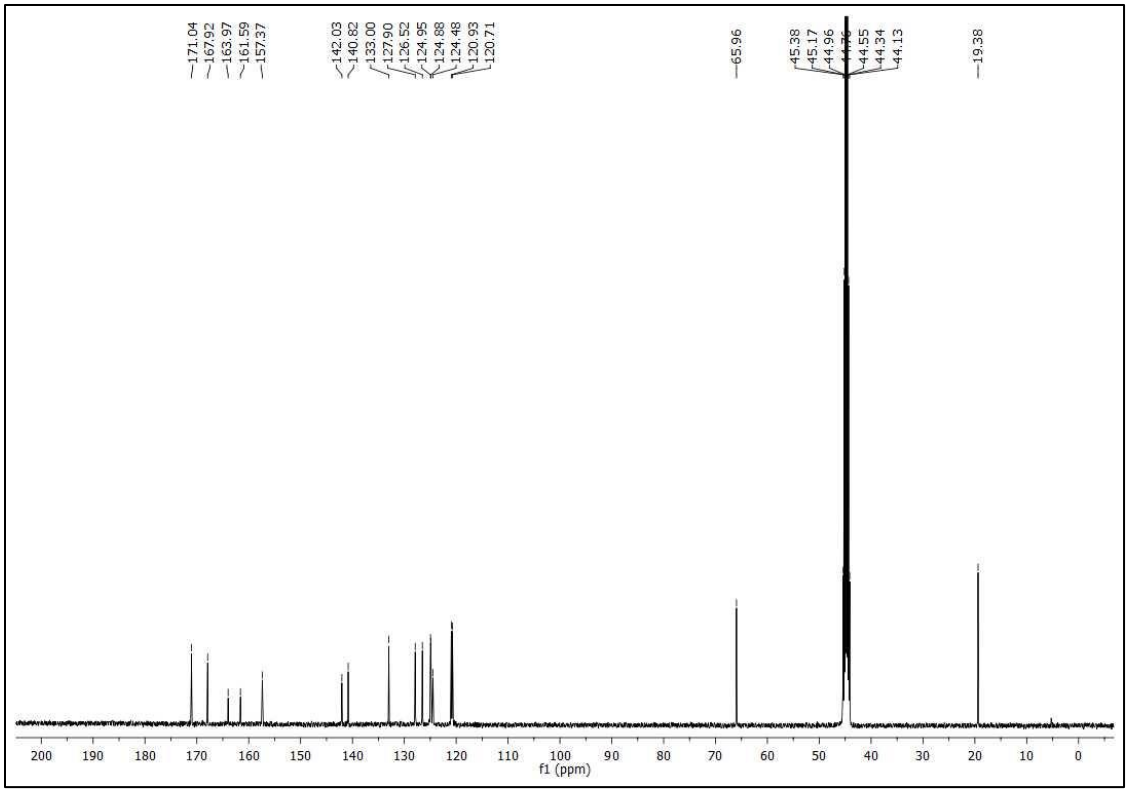
0.85
0.97
1.86
1.00
1.94
2.12
3.00
f1 (ppm)

^{13}C NMR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124.95
124.88
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120.93
120.71
65.96
45.38
45.17
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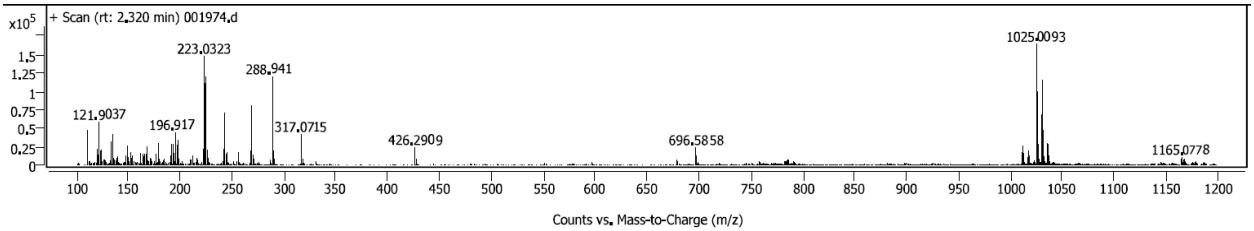
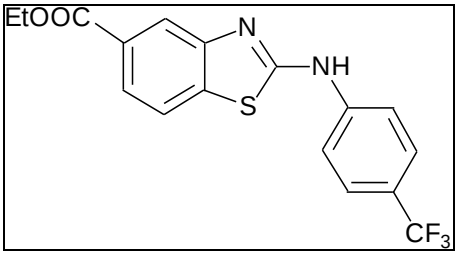
44.55
44.34
44.13
19.38
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

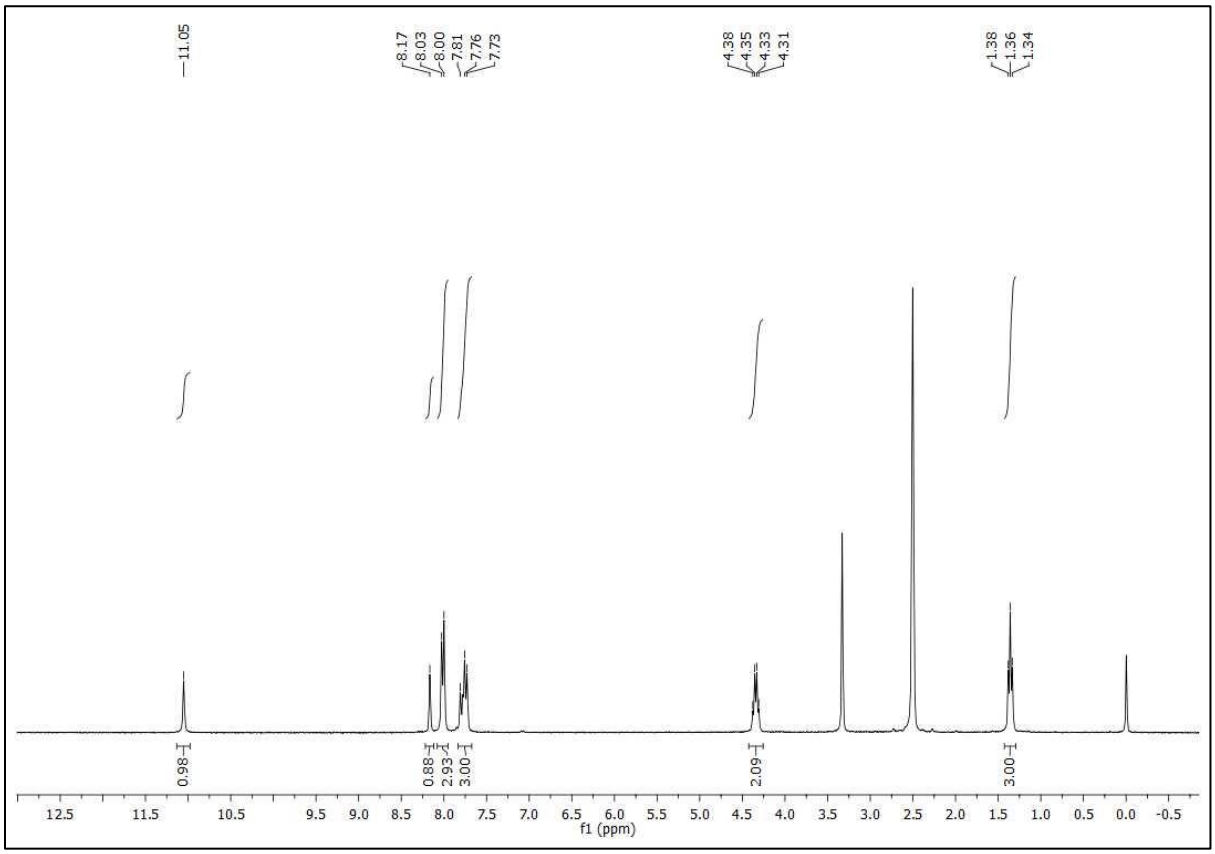
HRMS



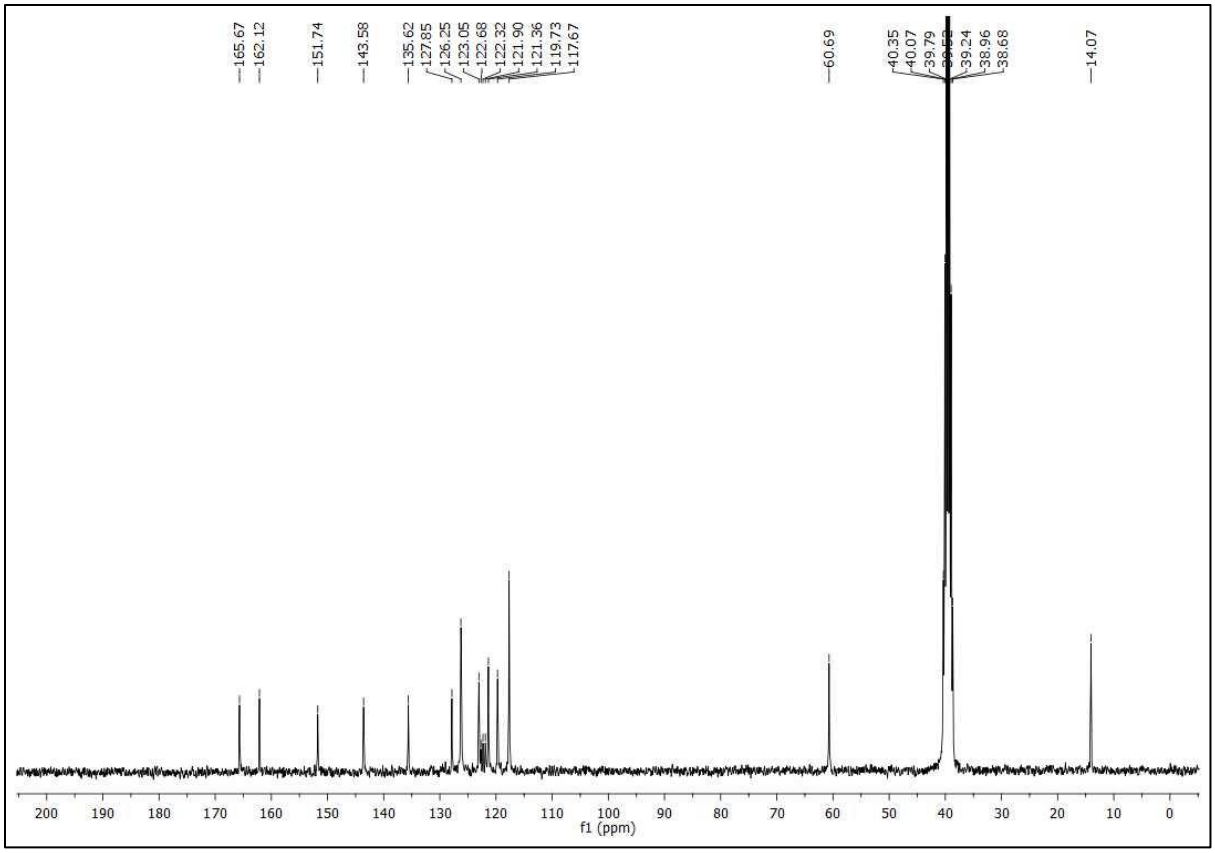
ethyl 2-[4-(trifluoromethyl)anilino]-1,3-benzothiazole-5-carboxylate (3o)



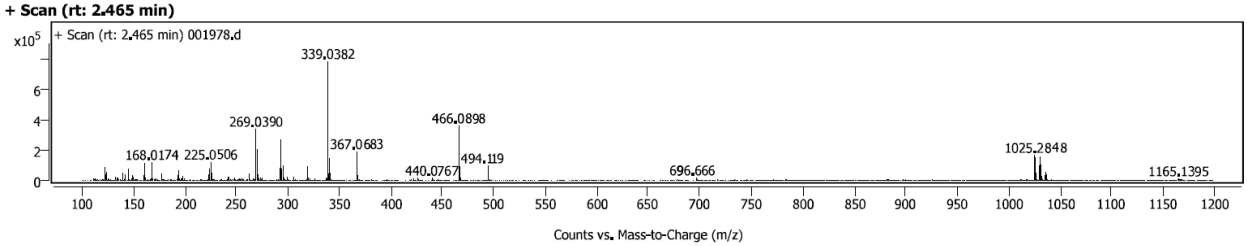
^{1}H NMR



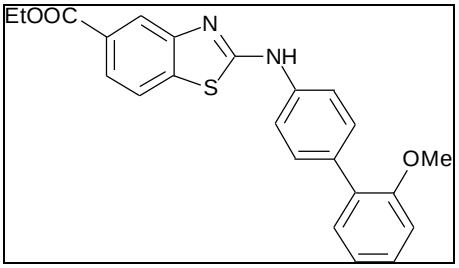
^{13}C NMR



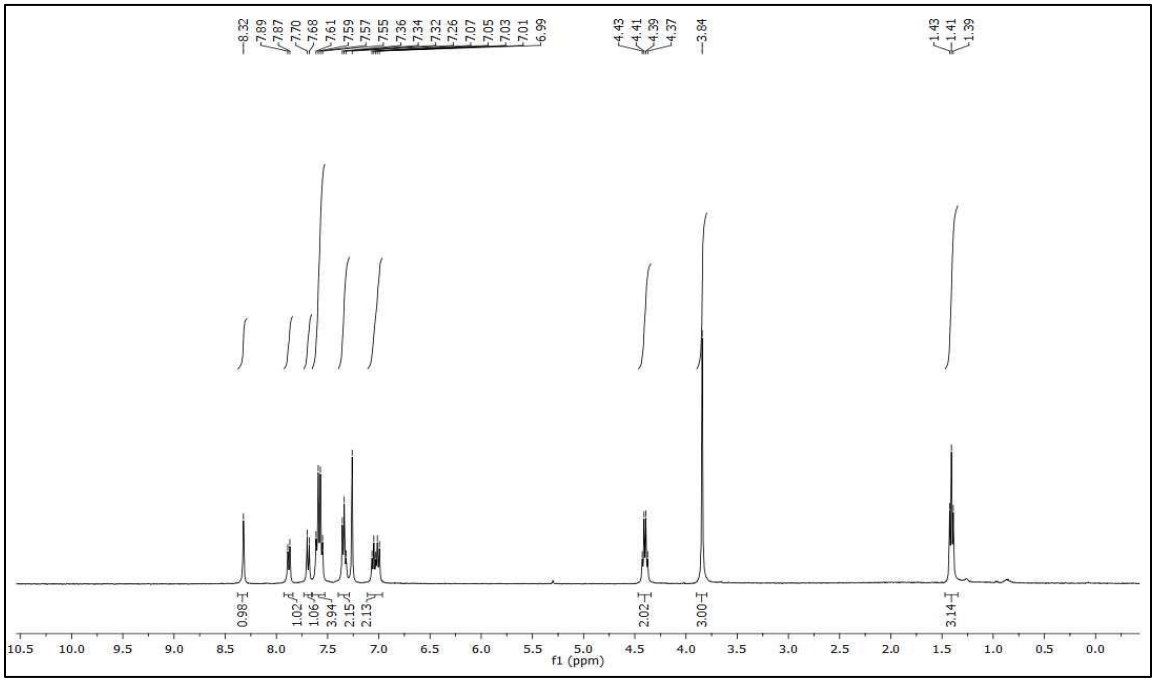
HRMS



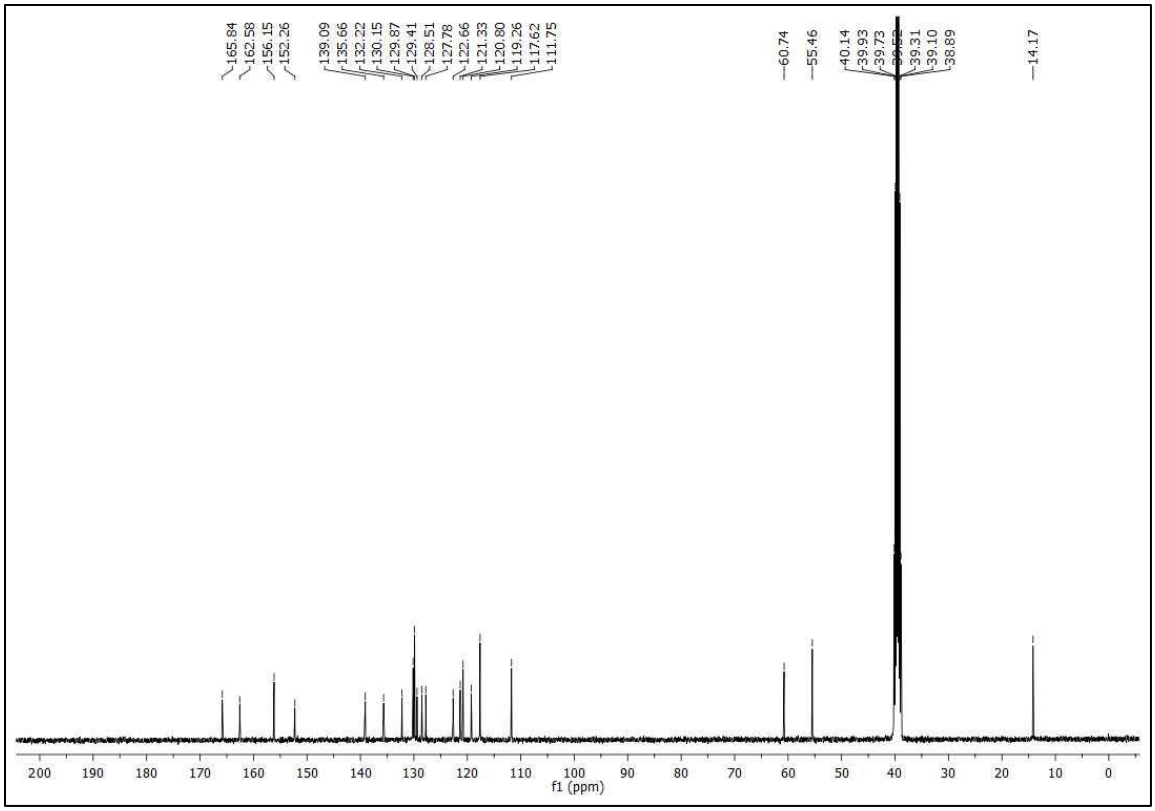
ethyl 2-[(2'-methoxy[1,1'-biphenyl]-4-yl)amino]-1,3-benzothiazole-5-carboxylate (3p)



^{1}H NMR



^{13}C NMR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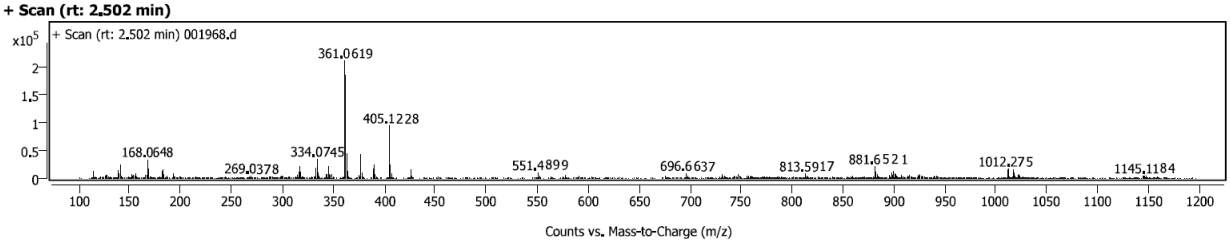
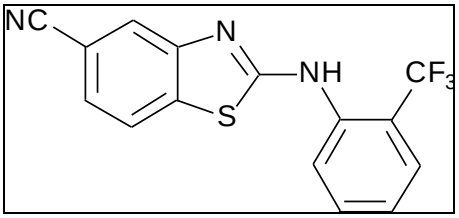
55.46
40.14
39.93
39.73
39.52
39.31
39.10
38.89
14.17
f1 (ppm)

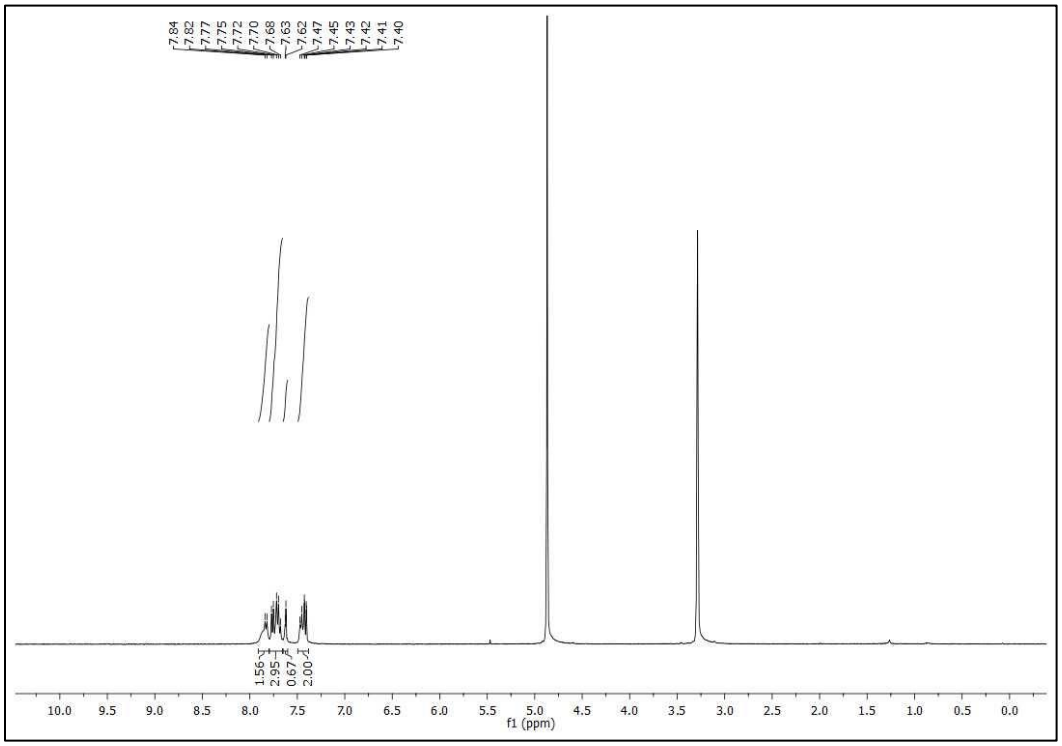
HRMS


+ Scan (rt: 2.502 min)
+ Scan (rt: 2.502 min) 001968.d
x10^5
361.0619
405.1228
168.0648
334.0745
269.0378
551.4899
696.6637
813.5917
881.6521
1012.275
1145.1184
Counts vs. Mass-to-Charge (m/z)

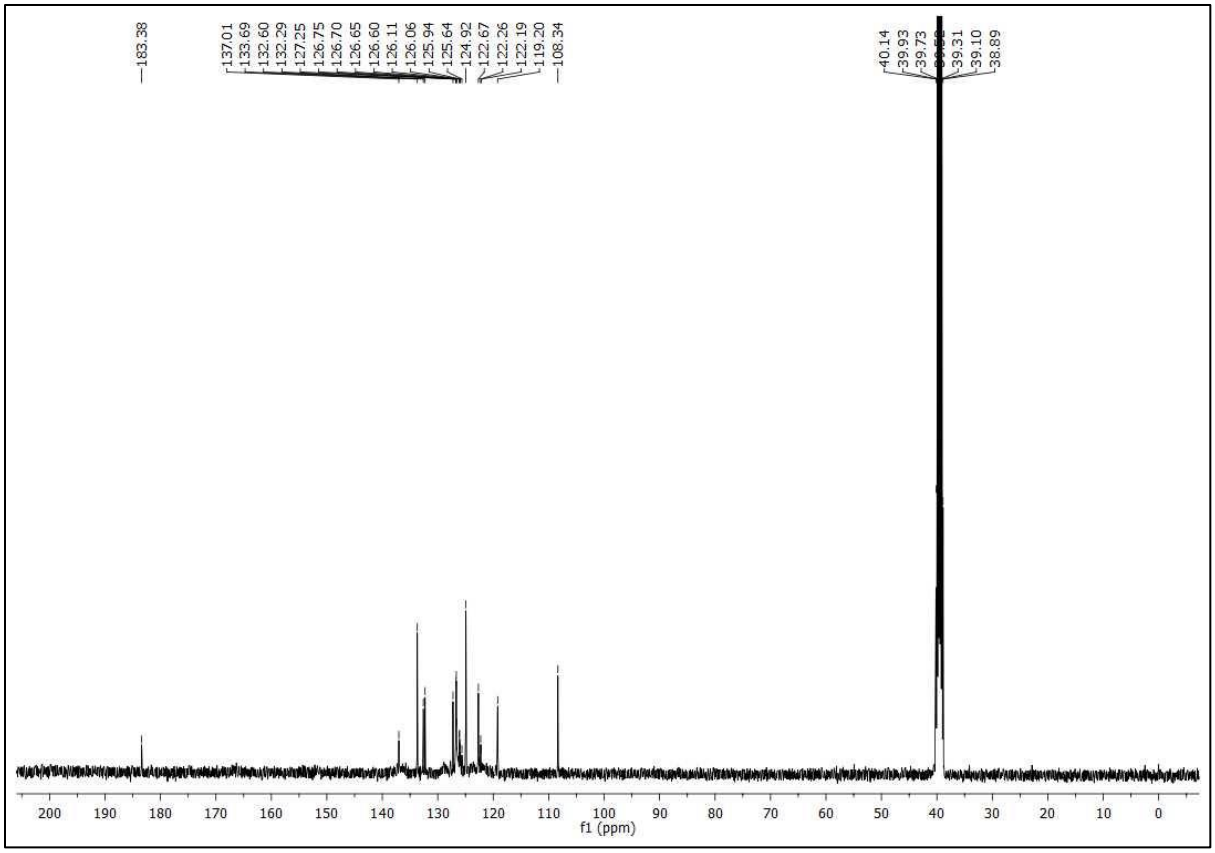
2-[2-(trifluoromethyl)anilino]-1,3-benzothiazole-5-carbonitrile (3q)



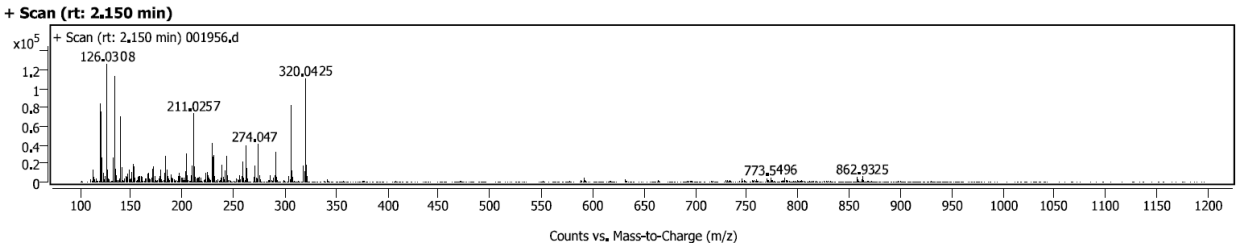
^{1}H NMR



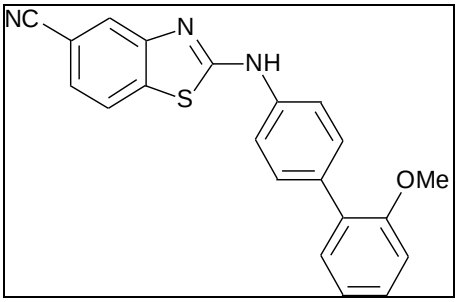
^{13}C NMR


183.38
137.01
133.69
132.60
132.29
127.25
126.75
126.70
126.65
126.60
126.11
126.06
125.94
125.64
124.92
122.67
122.26
122.19
119.20
108.34
40.14
39.93
39.73
39.52
39.31
39.10
38.89
f1 (ppm)

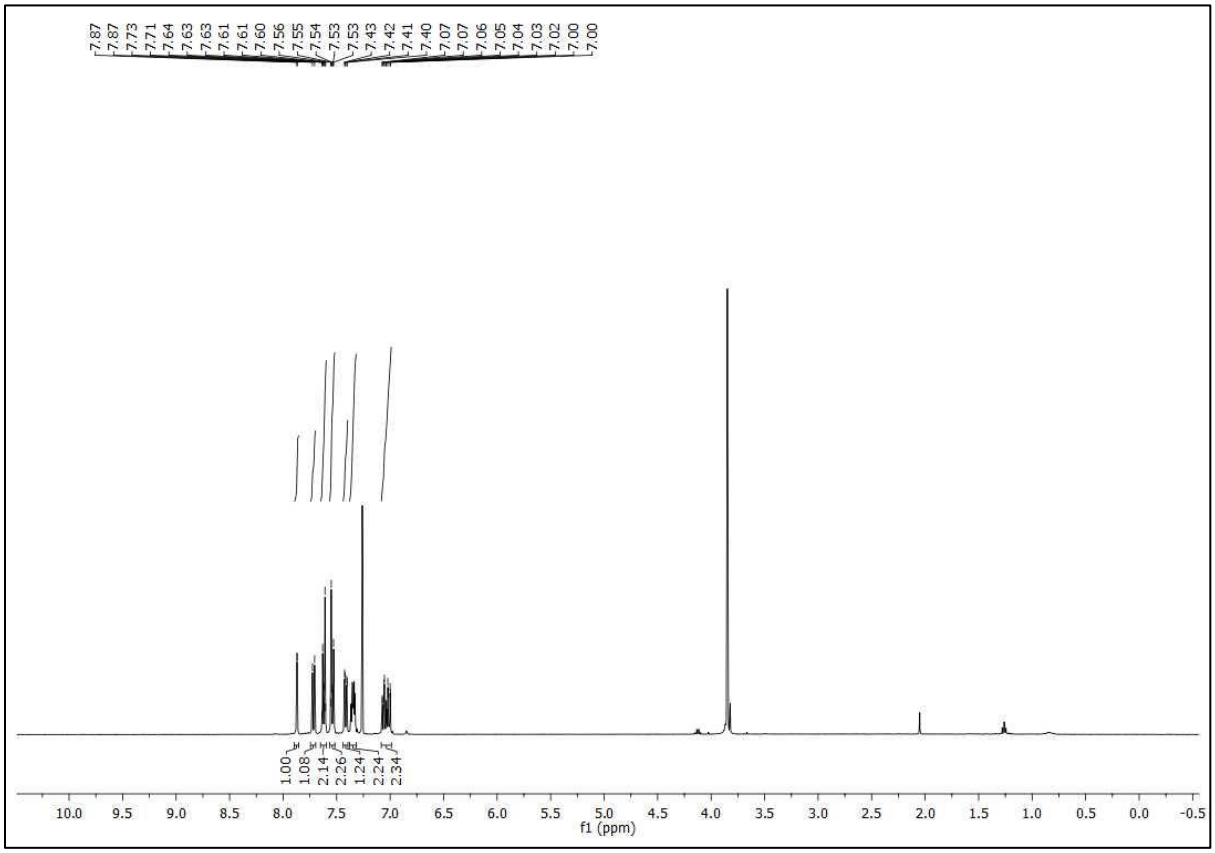
HRMS


+ Scan (rt: 2.150 min)
+ Scan (rt: 2.150 min) 001956.d
x10^5
126.0308
320.0425
211.0257
274.047
773.5496
862.9325
Counts vs. Mass-to-Charge (m/z)

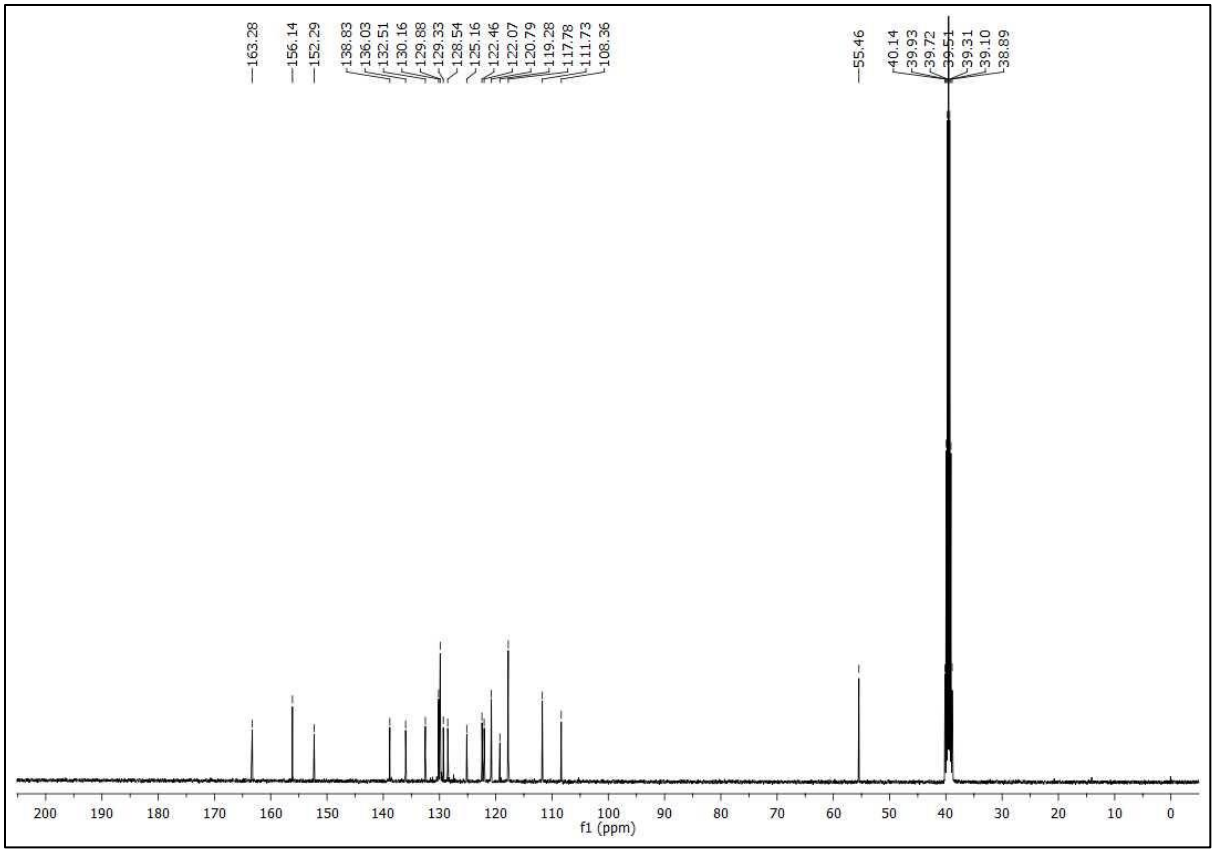
2-[(2'-methoxy[1,1'-biphenyl]-4-yl)amino]-1,3-benzothiazole-5-carbonitrile (3r)



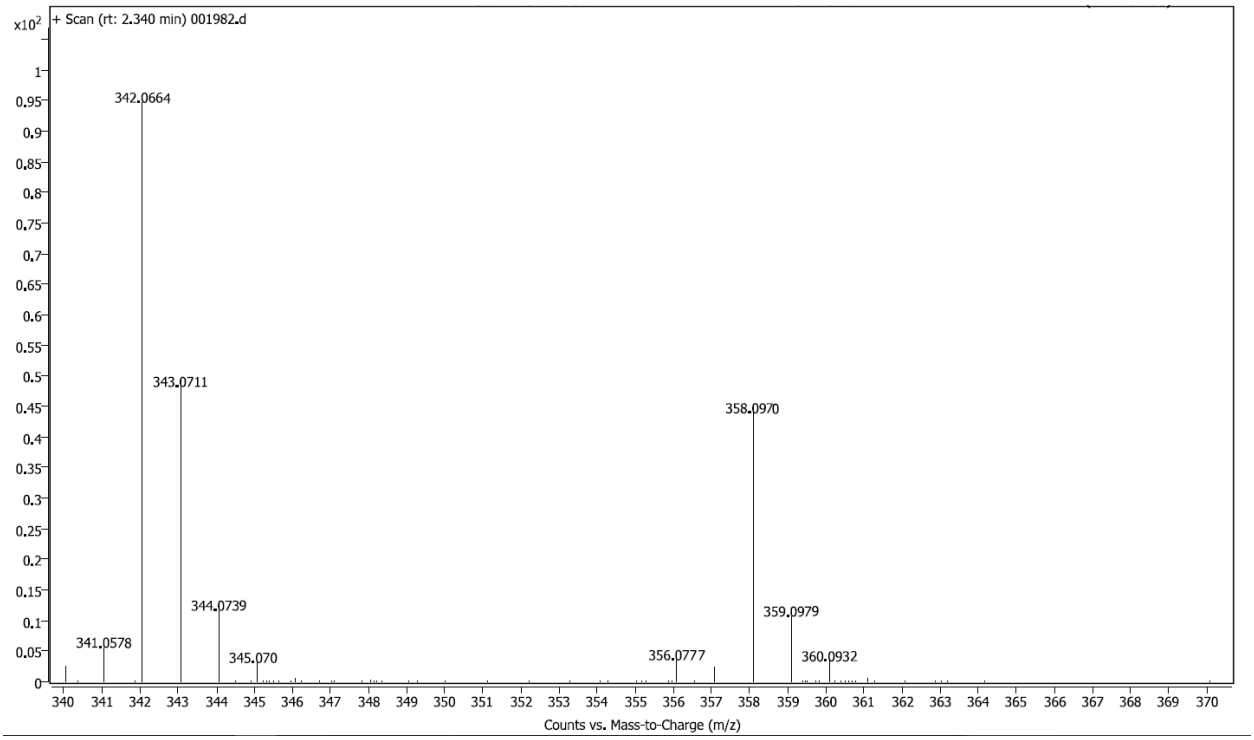
^{1}H NMR



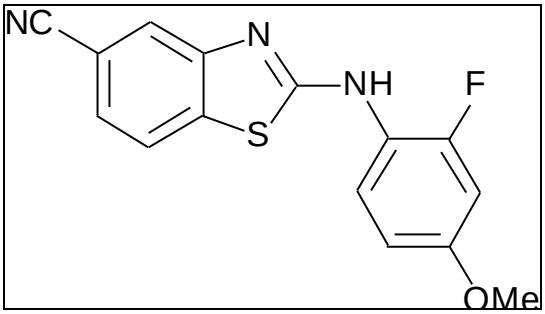
^{13}C NMR


163.28
156.14
152.29
138.83
136.03
132.51
130.16
129.88
129.33
128.54
125.16
122.46
122.07
120.79
119.28
117.78
111.73
108.36
55.46
40.14
39.93
39.72
39.51
39.31
39.10
38.89
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

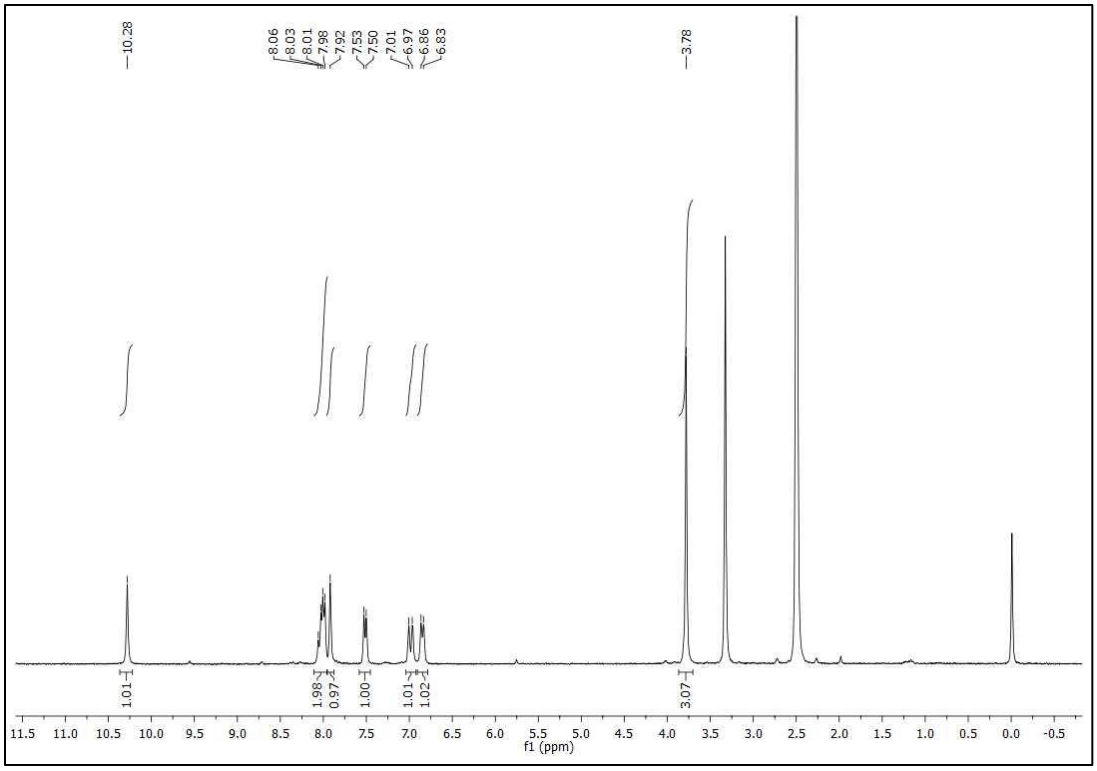
HRMS



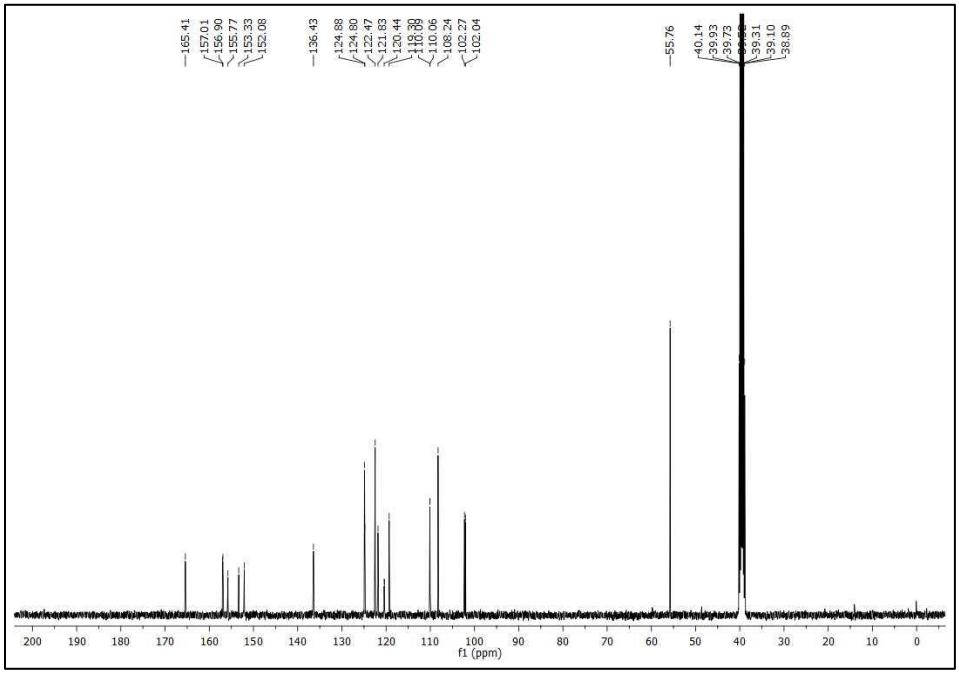
2-(2-fluoro-4-methoxyanilino)-1,3-benzothiazole-5-carbonitrile (3s)



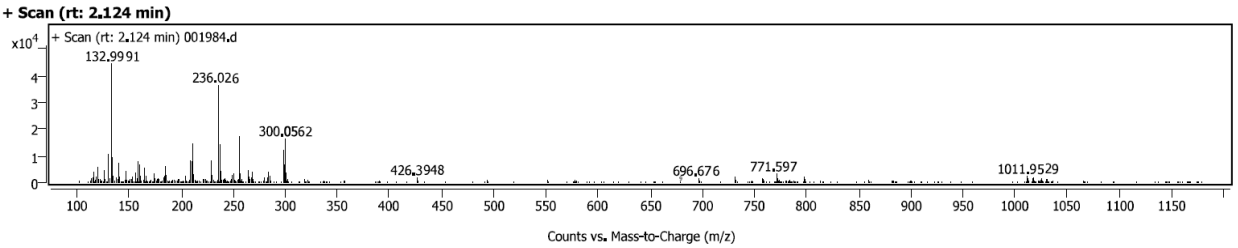
^{1}H NMR


10.28
8.06
8.03
8.01
7.98
7.92
7.53
7.50
7.01
6.97
6.86
6.83
3.78
1.01
1.98
0.97
1.00
1.01
1.02
3.07
f1 (ppm)

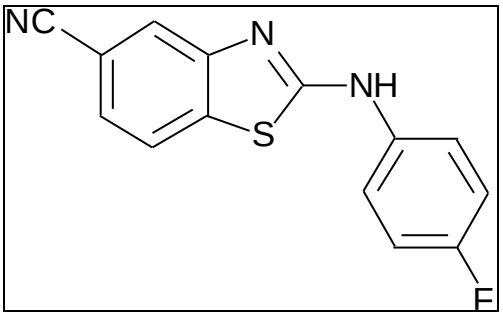
^{13}C NMR


165.41
157.01
156.90
155.77
153.33
152.08
136.43
124.88
124.80
122.47
121.83
120.44
110.30
110.08
110.06
108.24
102.27
102.04
55.76
40.14
39.93
39.73
39.31
39.10
38.89
f1 (ppm)

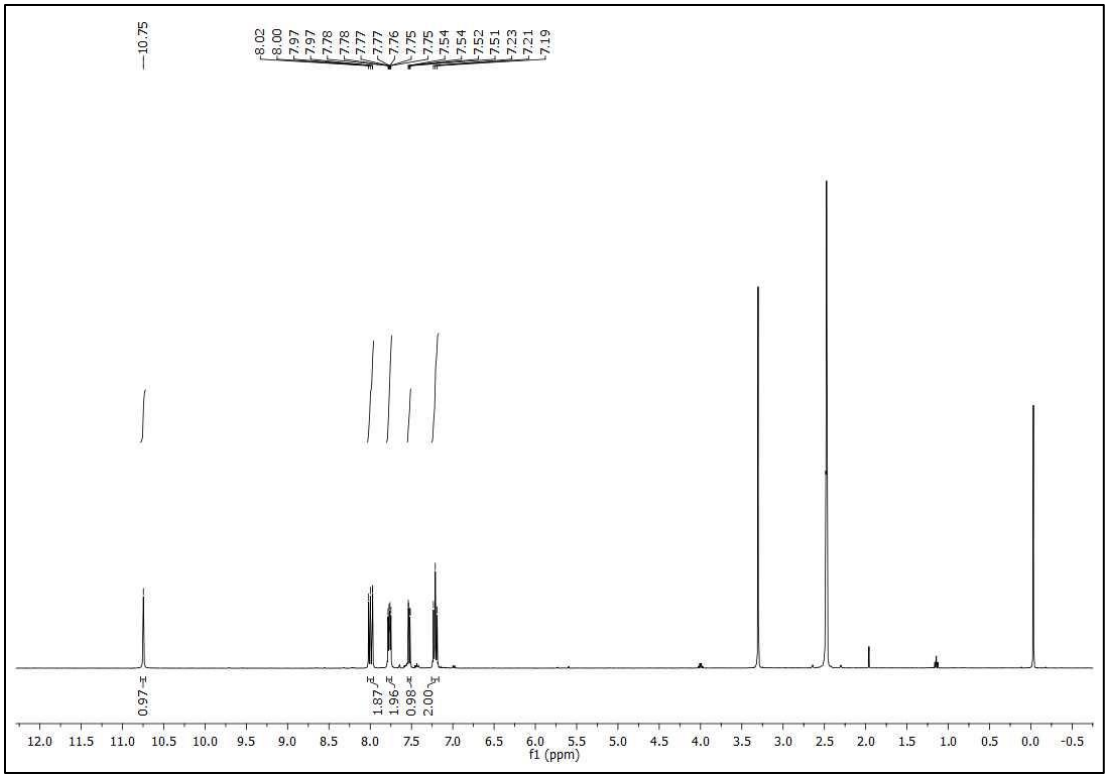
HRMS



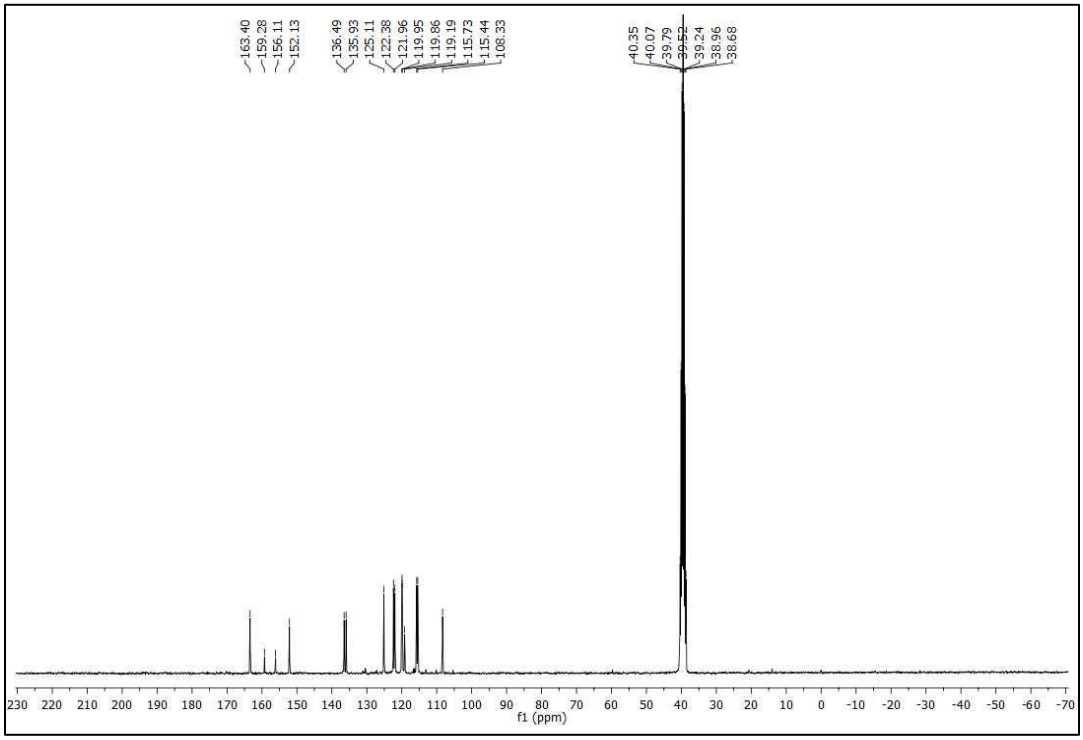
2-(4-fluoroanilino)-1,3-benzothiazole-5-carbonitrile (3t)



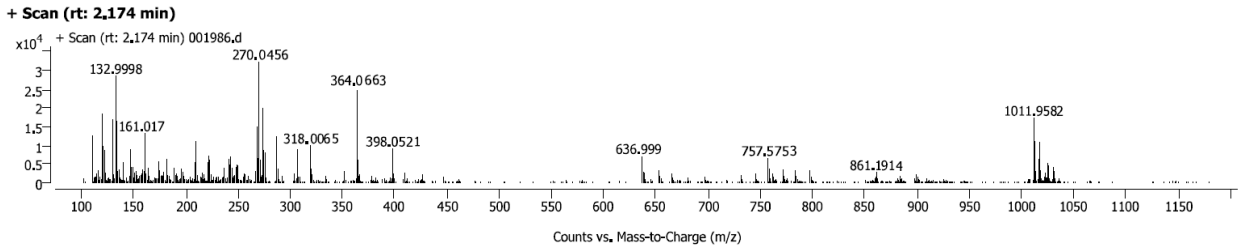
^{1}H NMR


10.75
8.02
8.00
7.97
7.97
7.78
7.78
7.77
7.77
7.76
7.75
7.75
7.54
7.54
7.52
7.51
7.23
7.21
7.19
0.97
1.87
1.96
0.98
2.00
f1 (ppm)

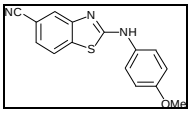
^{13}C NMR


163.40
159.28
156.11
152.13
136.49
135.93
125.11
122.38
121.96
119.95
119.86
119.19
115.73
115.44
108.33
40.35
40.07
39.79
39.52
39.24
38.96
38.68
f1 (ppm)

HRMS

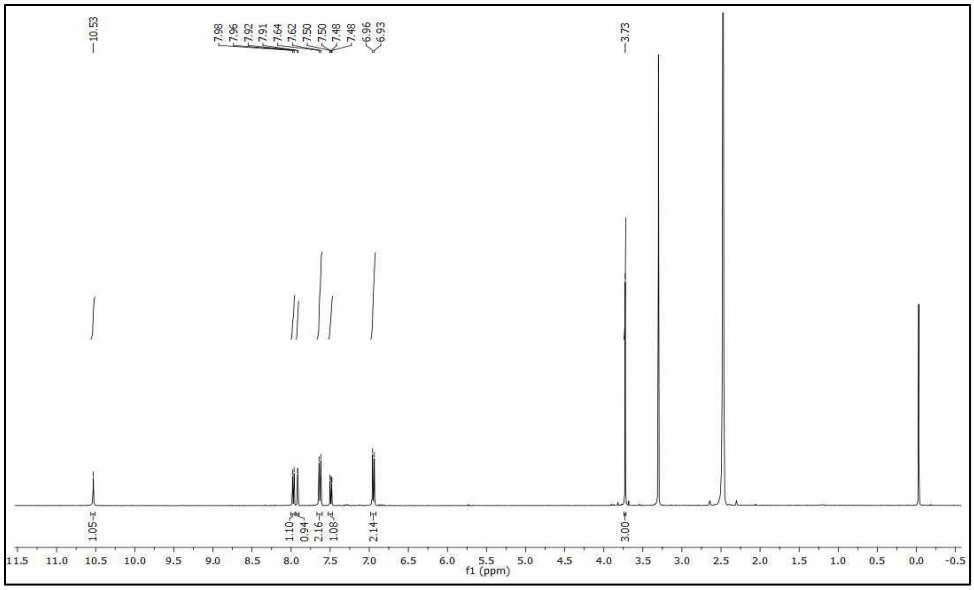


2-(4-methoxyanilino)-1,3-benzothiazole-5-carbonitrile (3u)

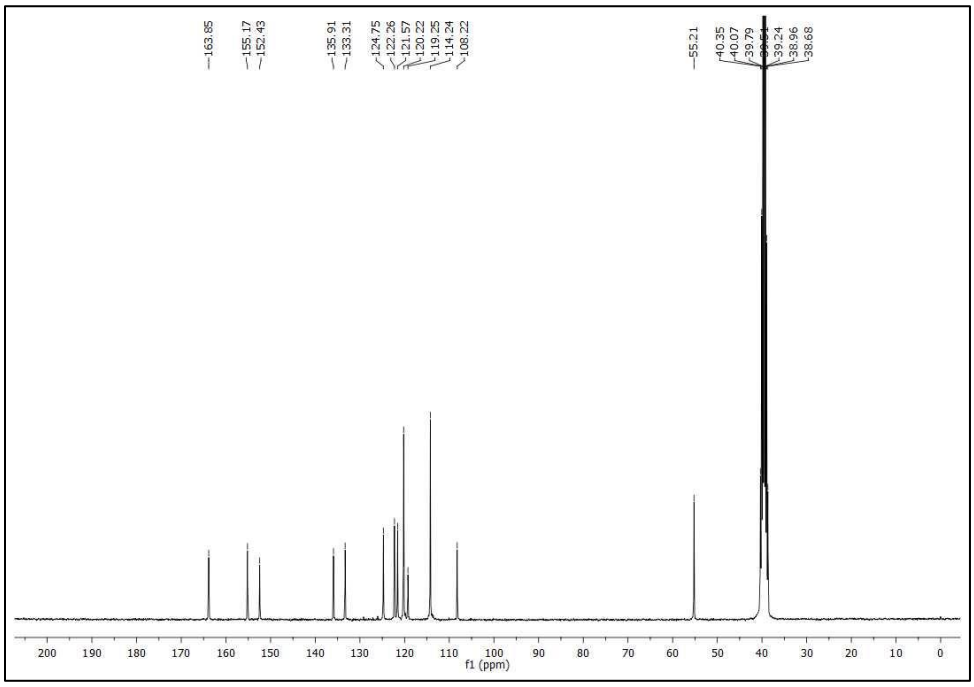


1

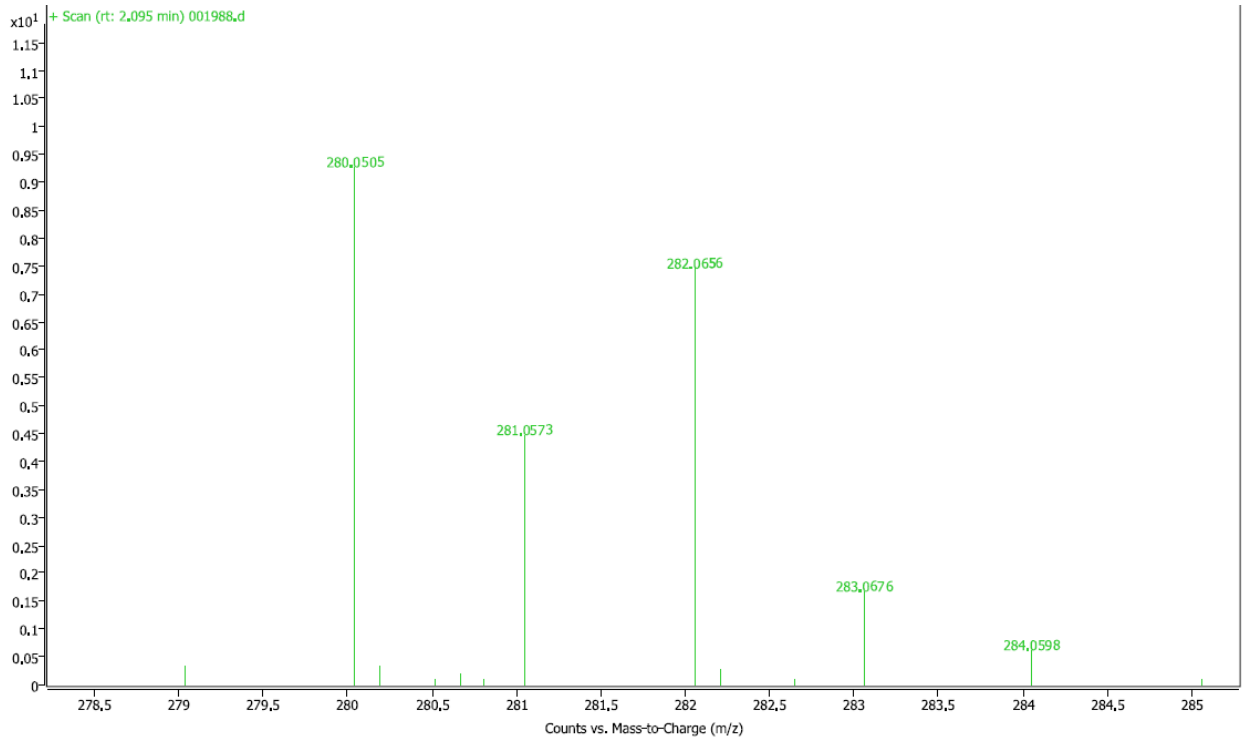
^{1}H NMR


10.53
7.98
7.96
7.92
7.91
7.64
7.62
7.50
7.50
7.48
6.96
6.93
3.73
1.05
1.10
0.94
2.16
1.08
2.14
3.00
f1 (ppm)

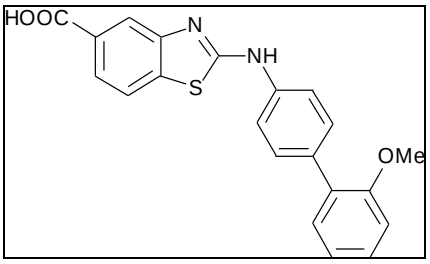
^{13}C NMR


163.85
155.17
152.43
135.91
133.31
124.75
122.26
121.57
120.22
119.25
114.24
108.22
55.21
40.35
40.07
39.79
39.51
39.24
38.96
38.68
f1 (ppm)

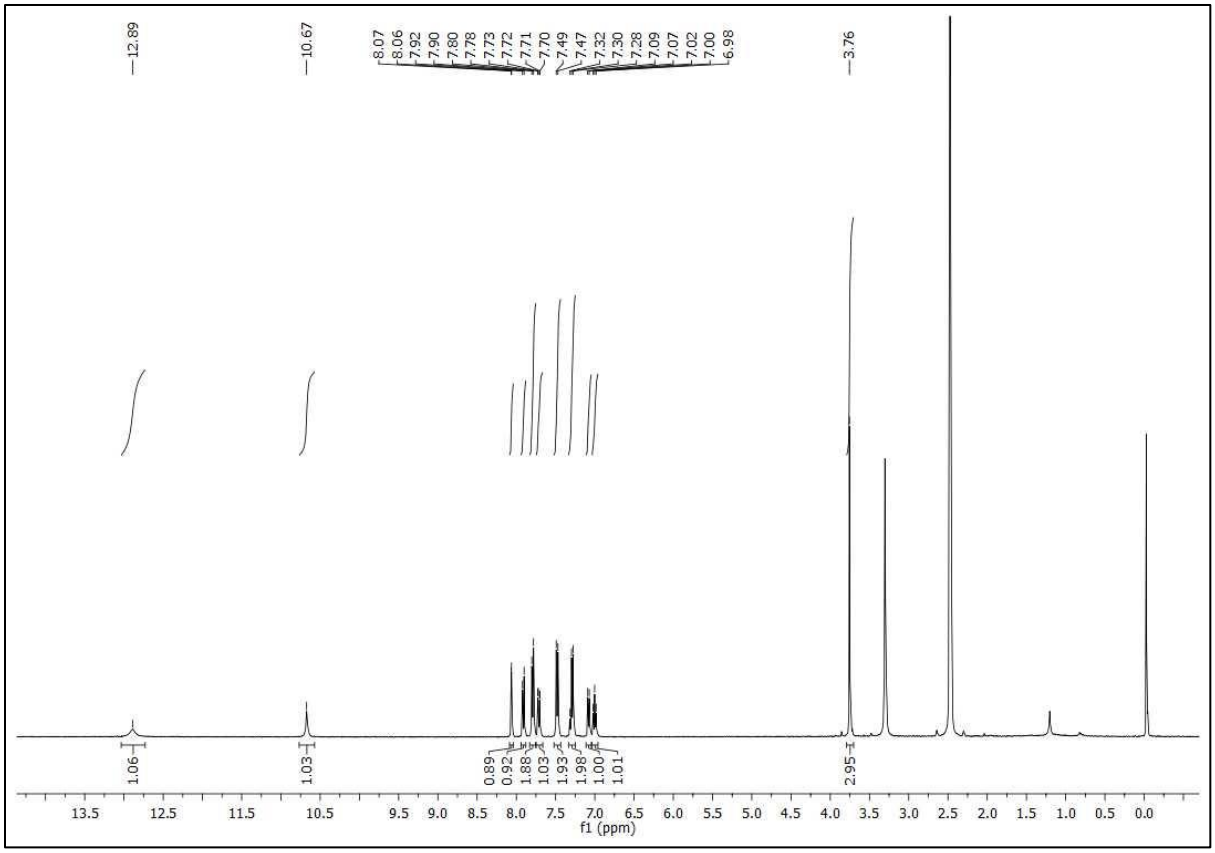
HRMS



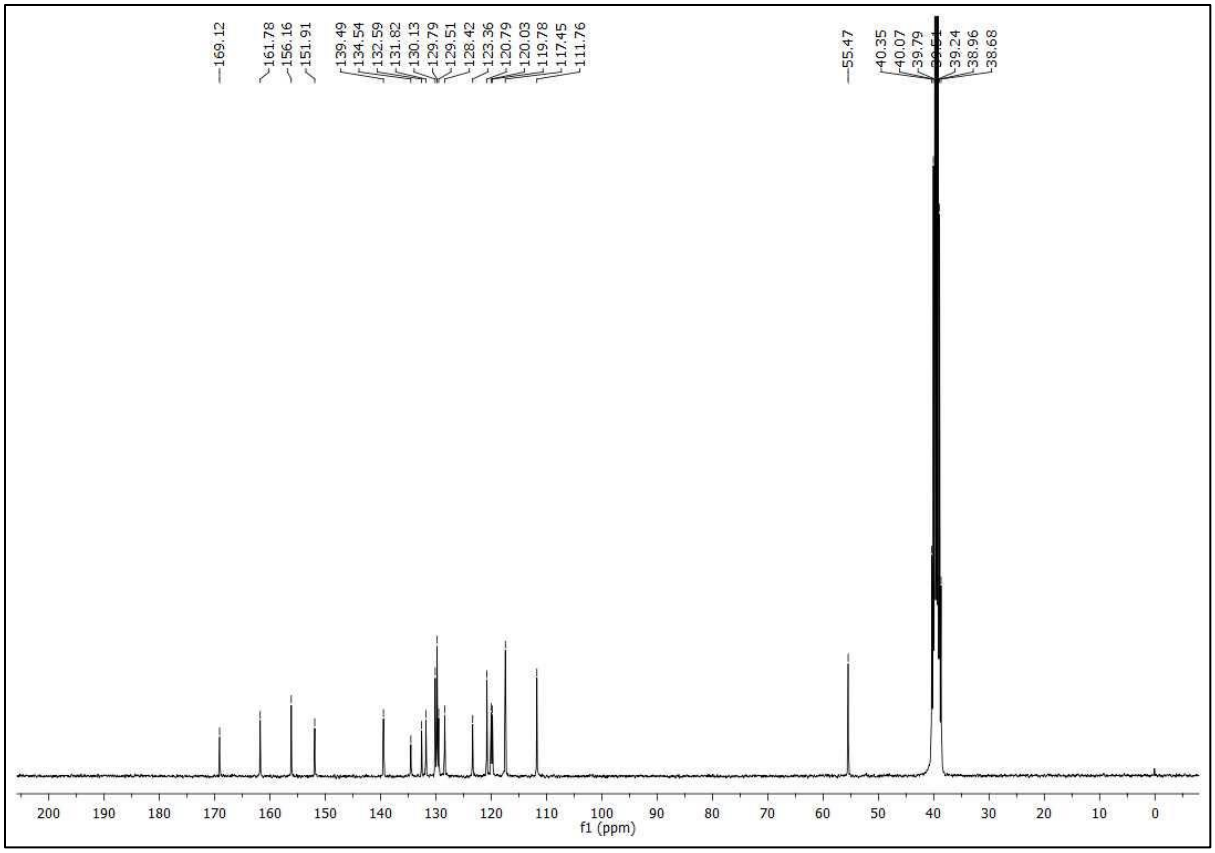
2-[(2'-methoxy[1,1'-biphenyl]-4-yl)amino]-1,3-benzothiazole-5-carboxylic acid (3v)



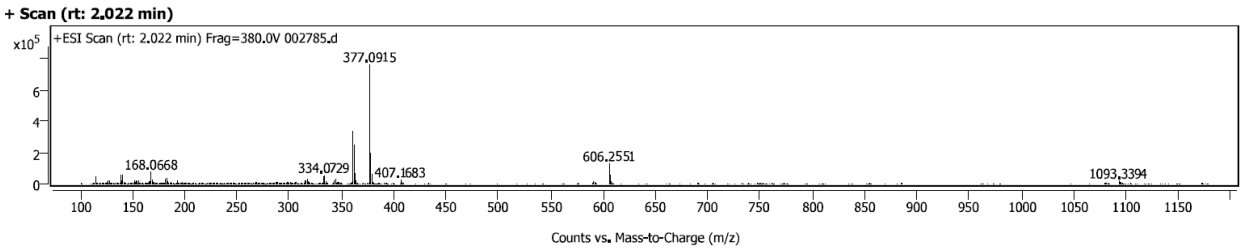
^{1}H NMR


12.89
10.67
8.07
8.06
7.92
7.90
7.80
7.78
7.73
7.72
7.71
7.70
7.49
7.47
7.32
7.30
7.28
7.09
7.07
7.02
7.00
6.98
3.76
1.06
1.03
0.89
0.92
1.88
1.03
1.93
1.98
1.00
1.01
2.95
f1 (ppm)

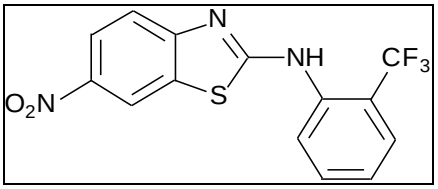
^{13}C NMR



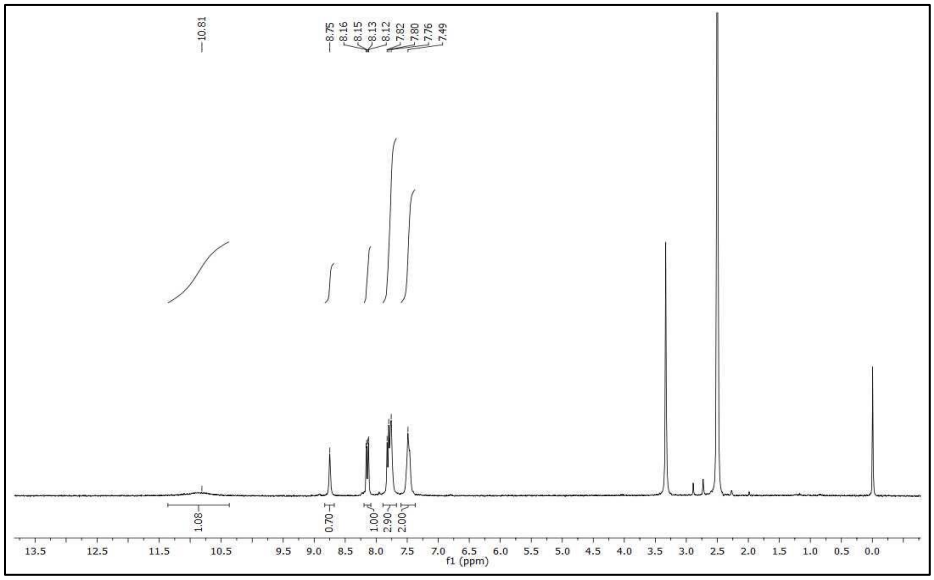
HRMS



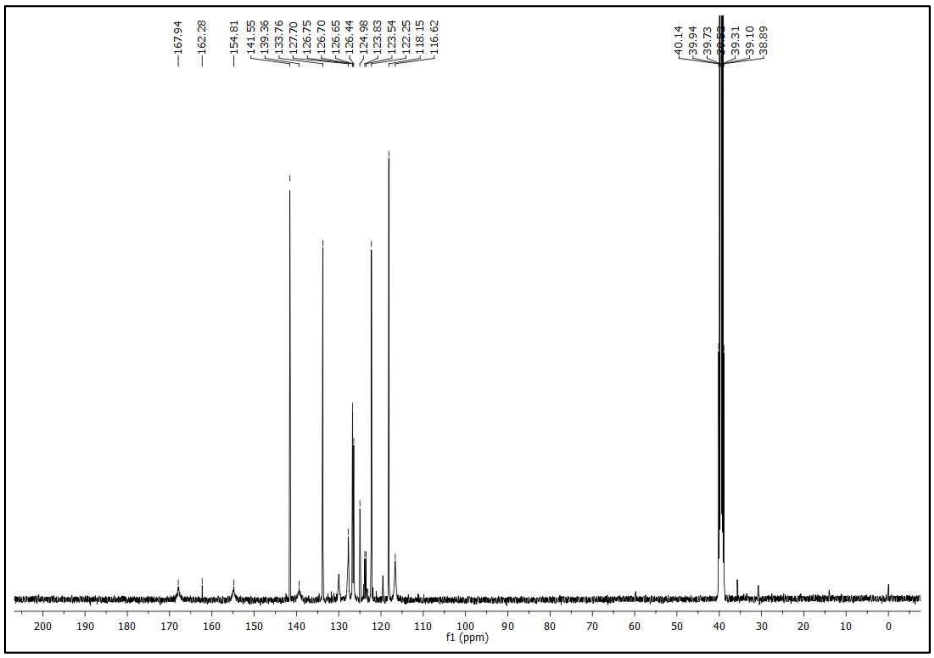
6-nitro-N-[2-(trifluoromethyl)phenyl]-1,3-benzothiazol-2-amine (3w)

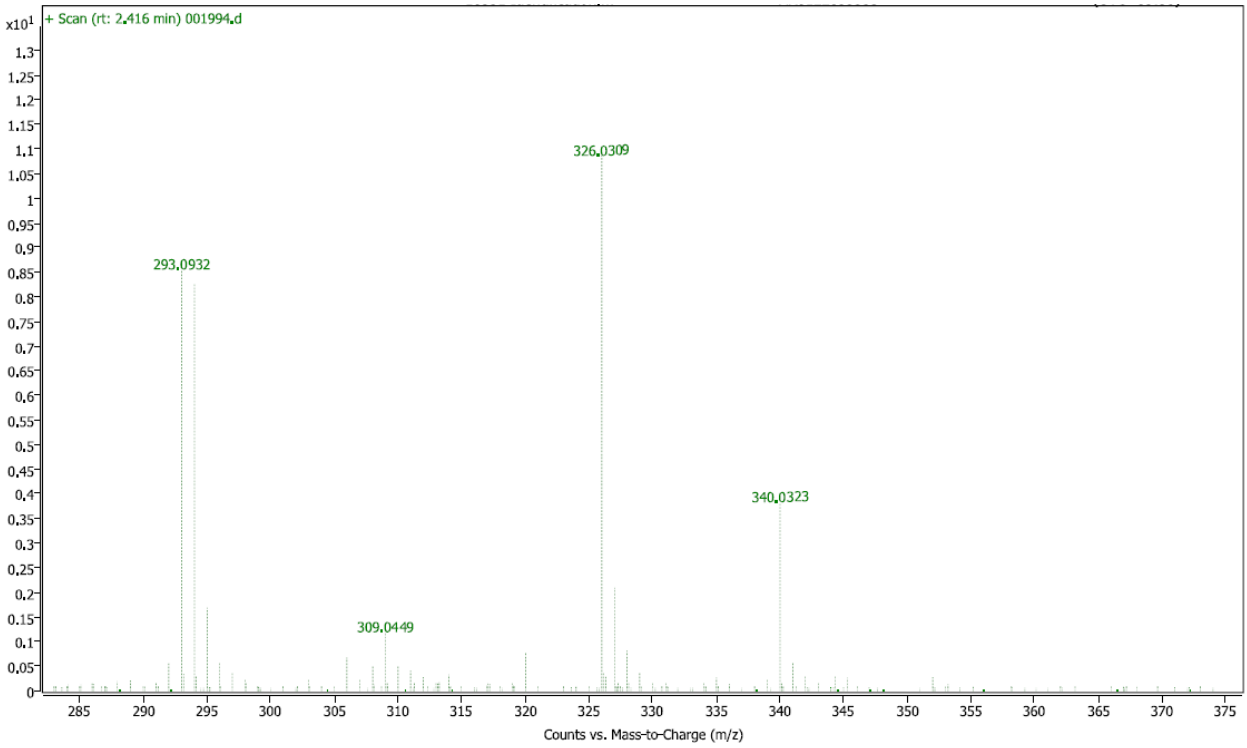


^{1}H NMR

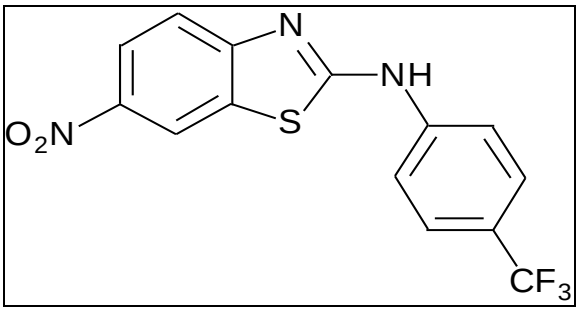


^{13}C NMR



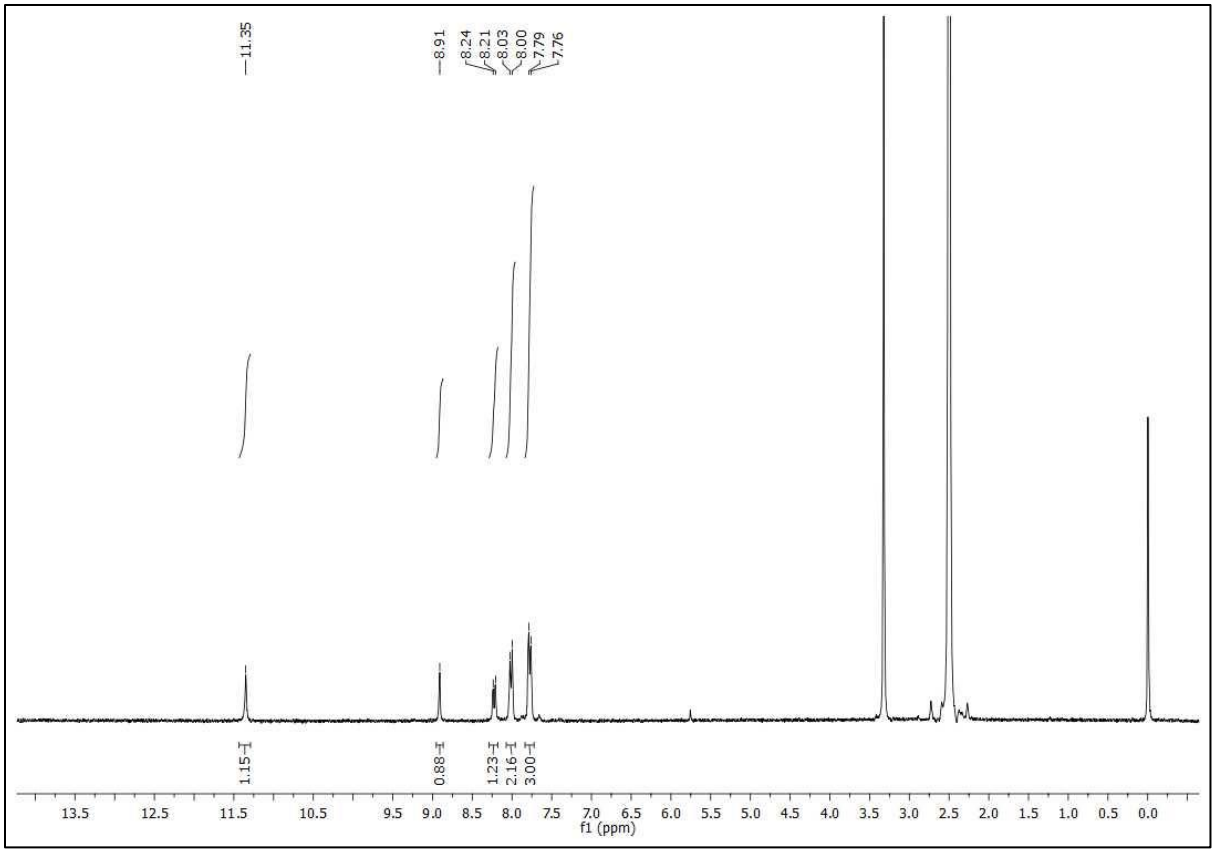


6-nitro-N-[4-(trifluoromethyl)phenyl]-1,3-benzothiazol-2-amine (3y)

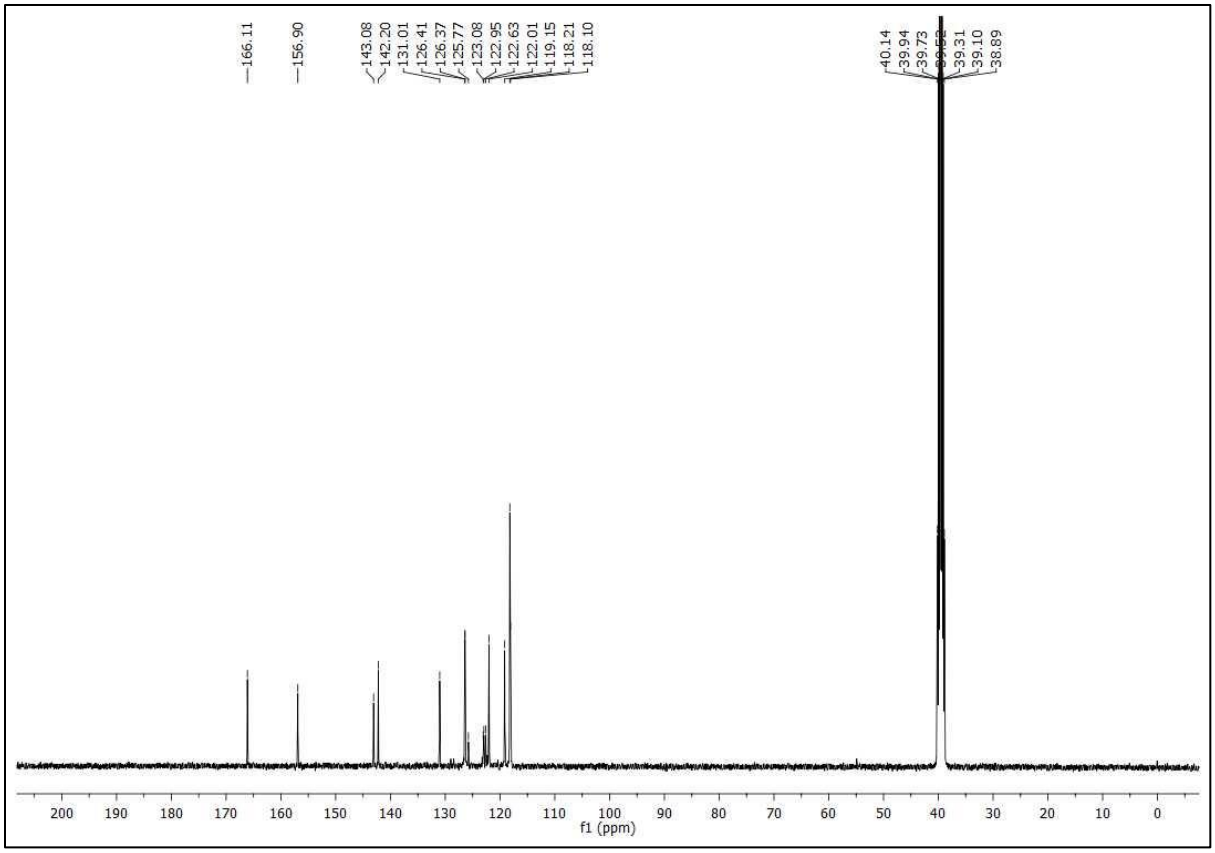


Pale yellow solid; 50%

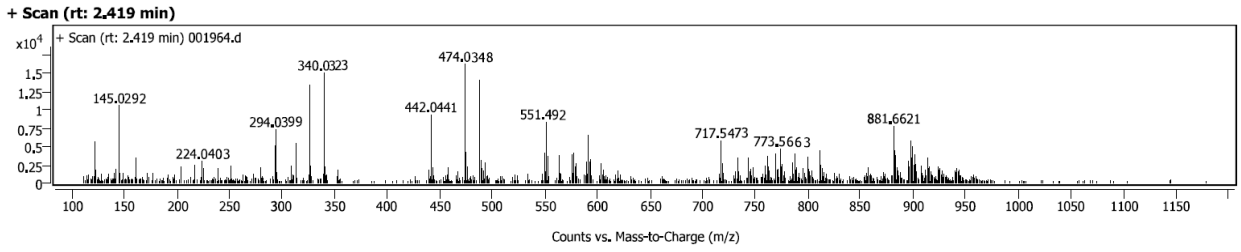
^{1}H NMR


11.35
8.91
8.24
8.21
8.03
8.00
7.79
7.76
1.15
0.88
1.23
2.16
3.00
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

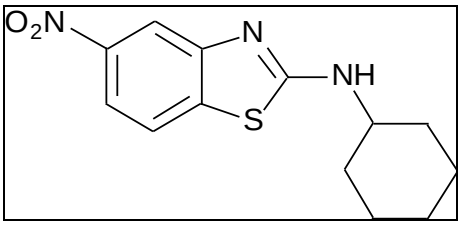
^{13}C NMR



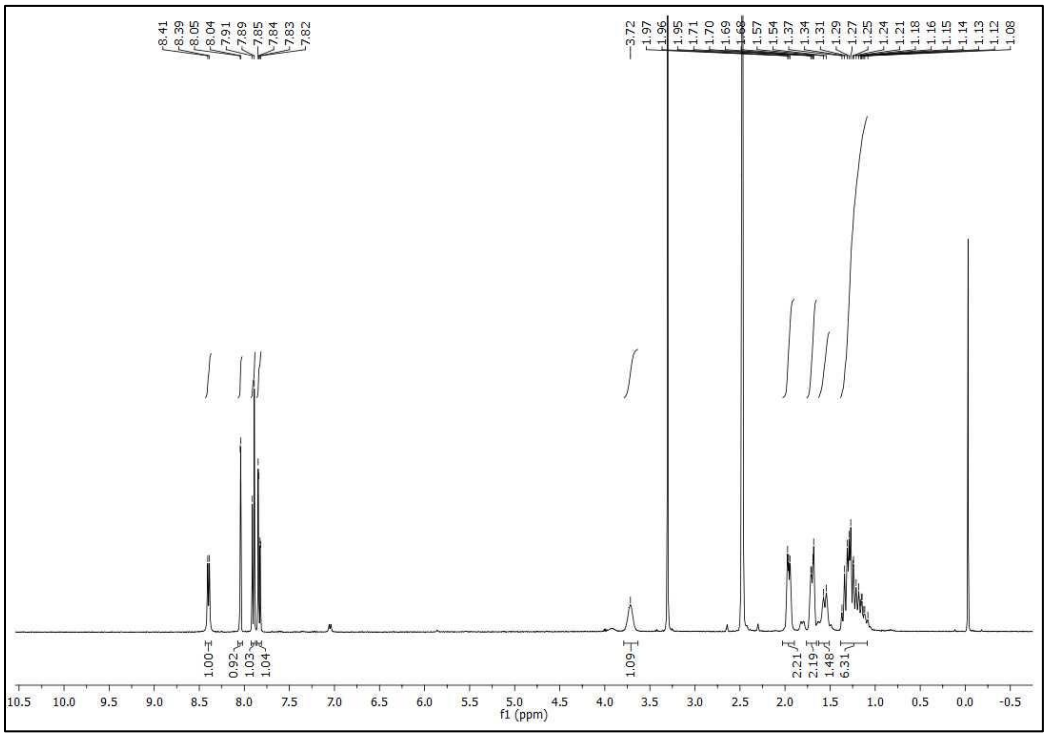
HRMS



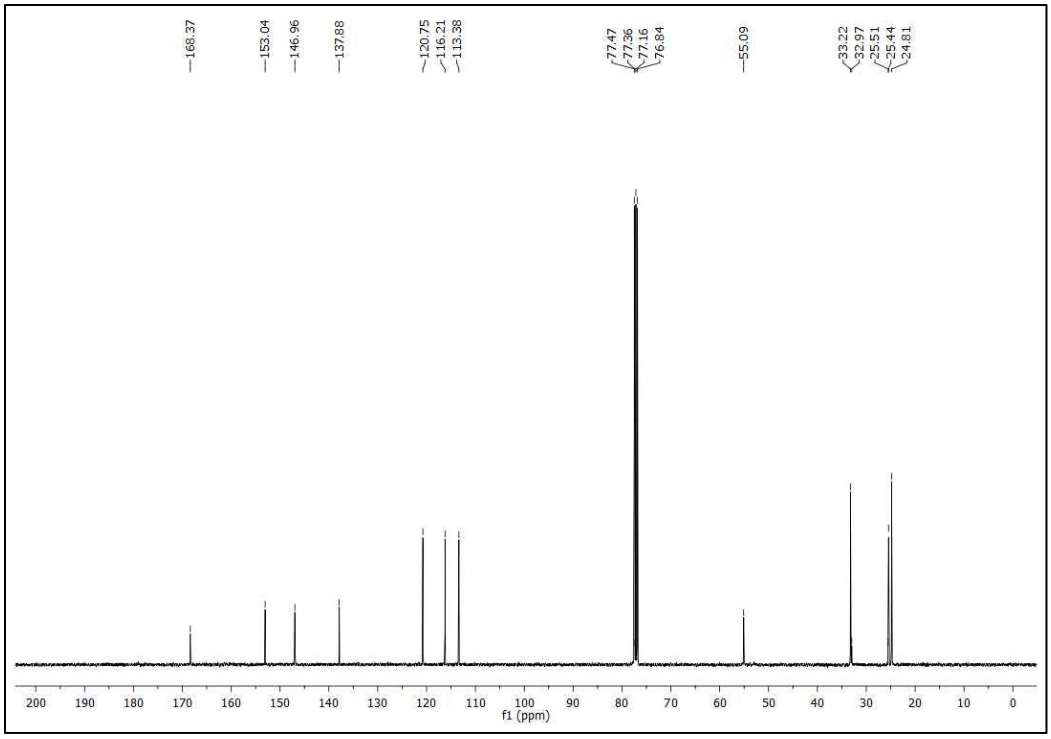
_N_-cyclohexyl-5-nitro-1,3-benzothiazol-2-amine (3aa)



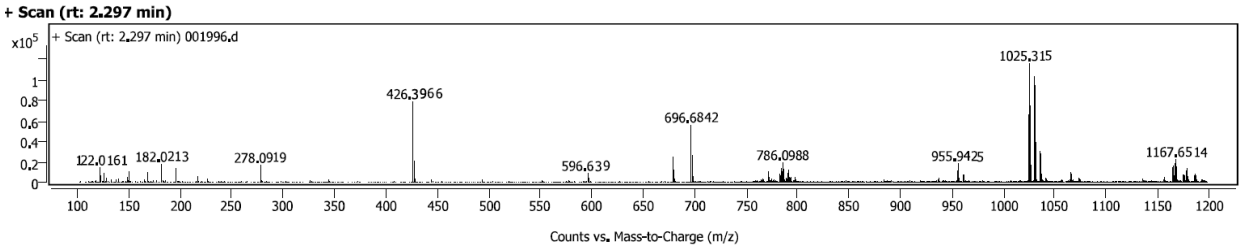
^{1}HNMR



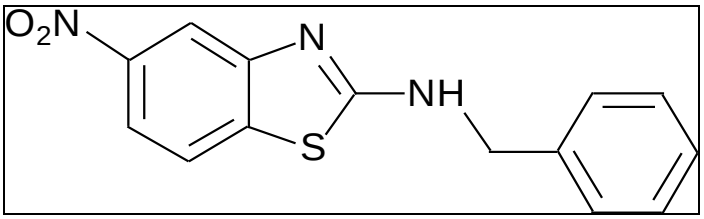
^{13}C NMR



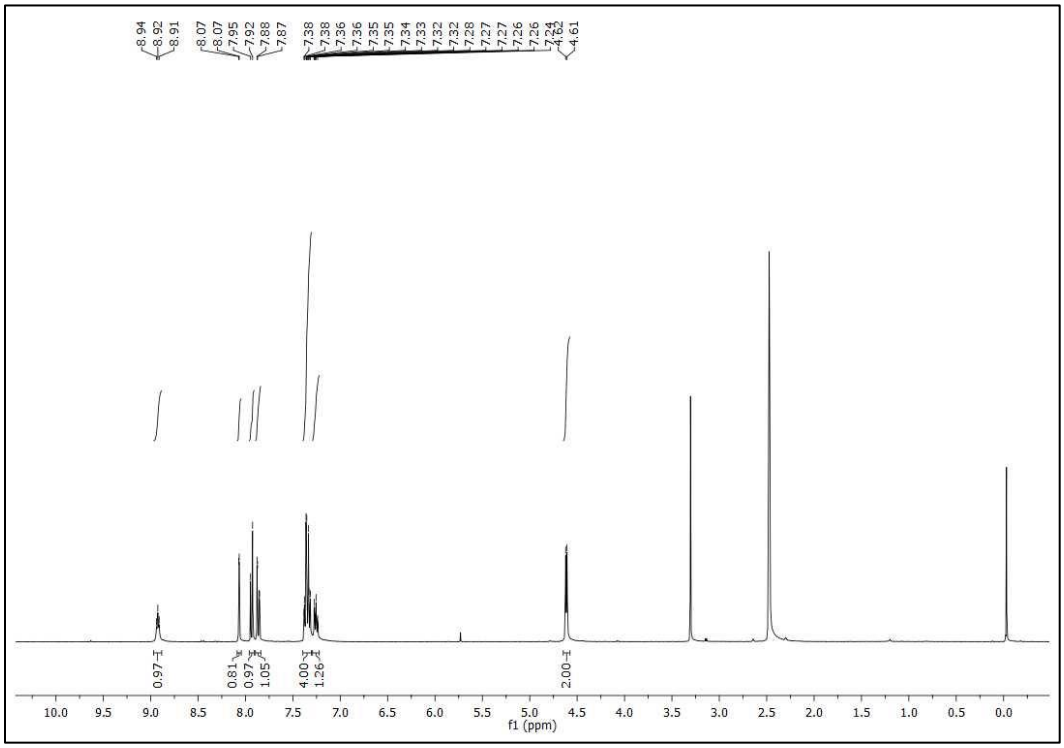
HRMS



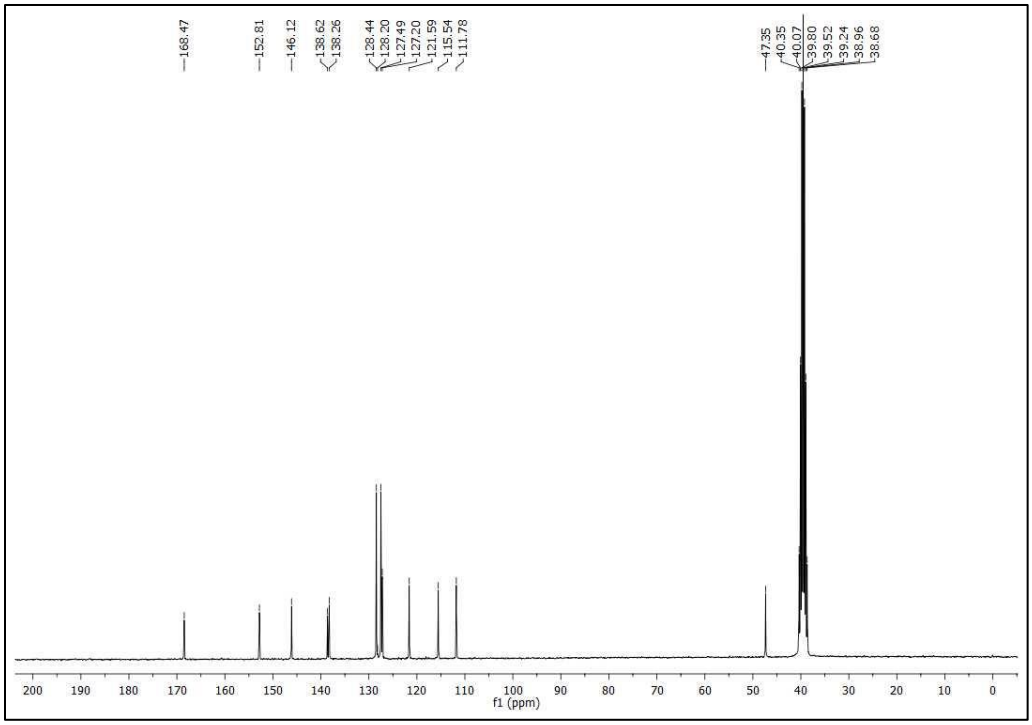
_N_-benzyl-5-nitro-1,3-benzothiazol-2-amine (3ab)



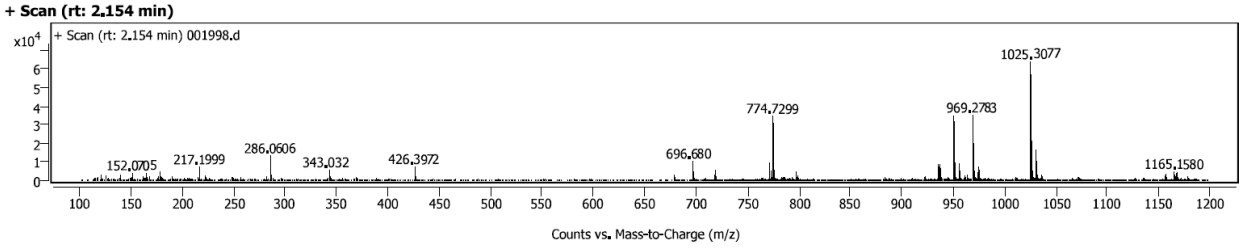
^{1}H NMR



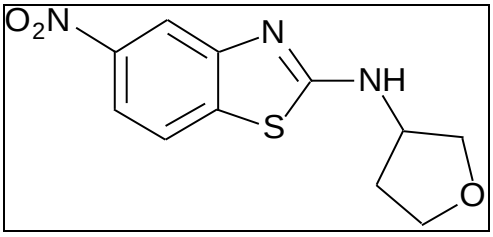
^{13}C NMR


168.47
152.81
146.12
138.62
138.26
128.44
128.20
127.49
127.20
121.59
115.54
111.78
47.35
40.35
40.07
39.80
39.52
39.24
38.96
38.68
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

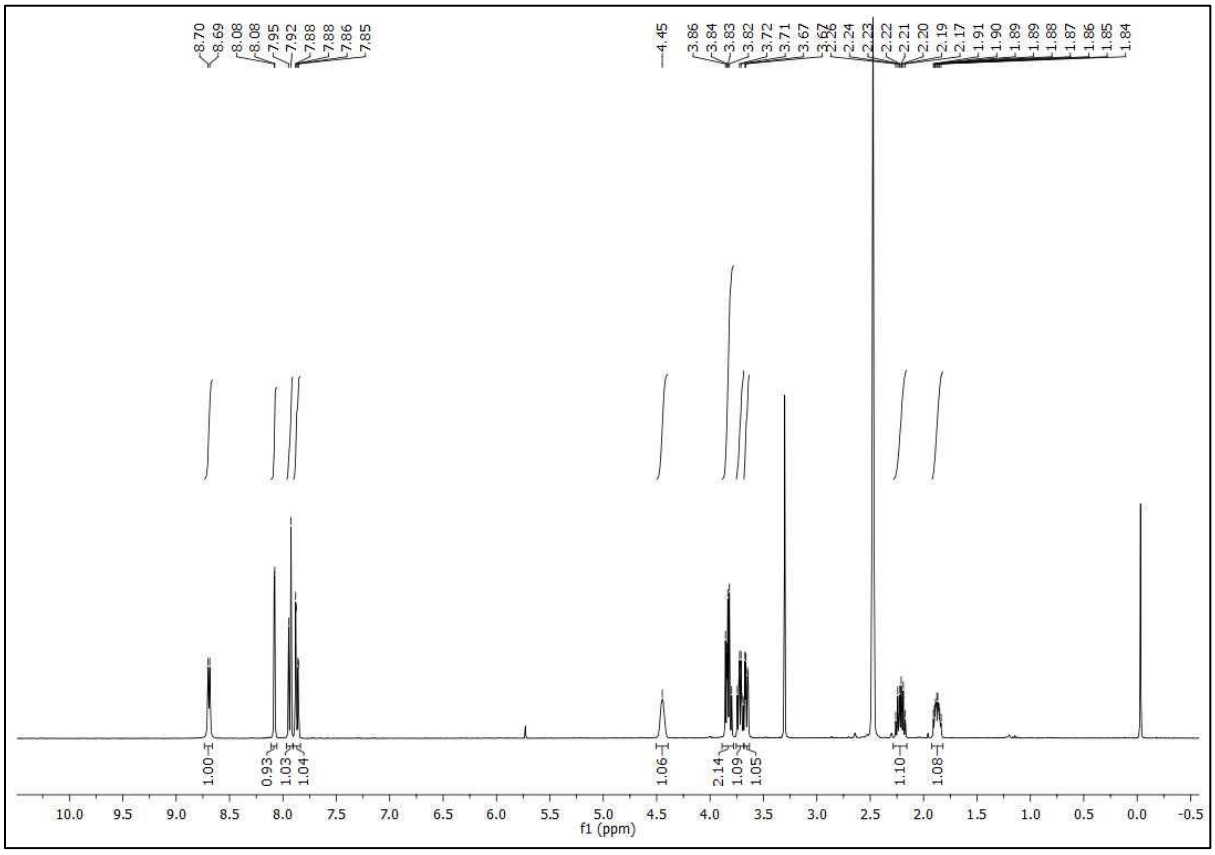
HRMS


+ Scan (rt: 2.154 min)
+ Scan (rt: 2.154 min) 001998.d
x10^4
6
5
4
3
2
1
0
1025.3077
774.7299
969.2783
152.0705
217.1999
286.0606
343.032
426.3972
696.680
1165.1580
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000 1050 1100 1150 1200
Counts vs. Mass-to-Charge (m/z)

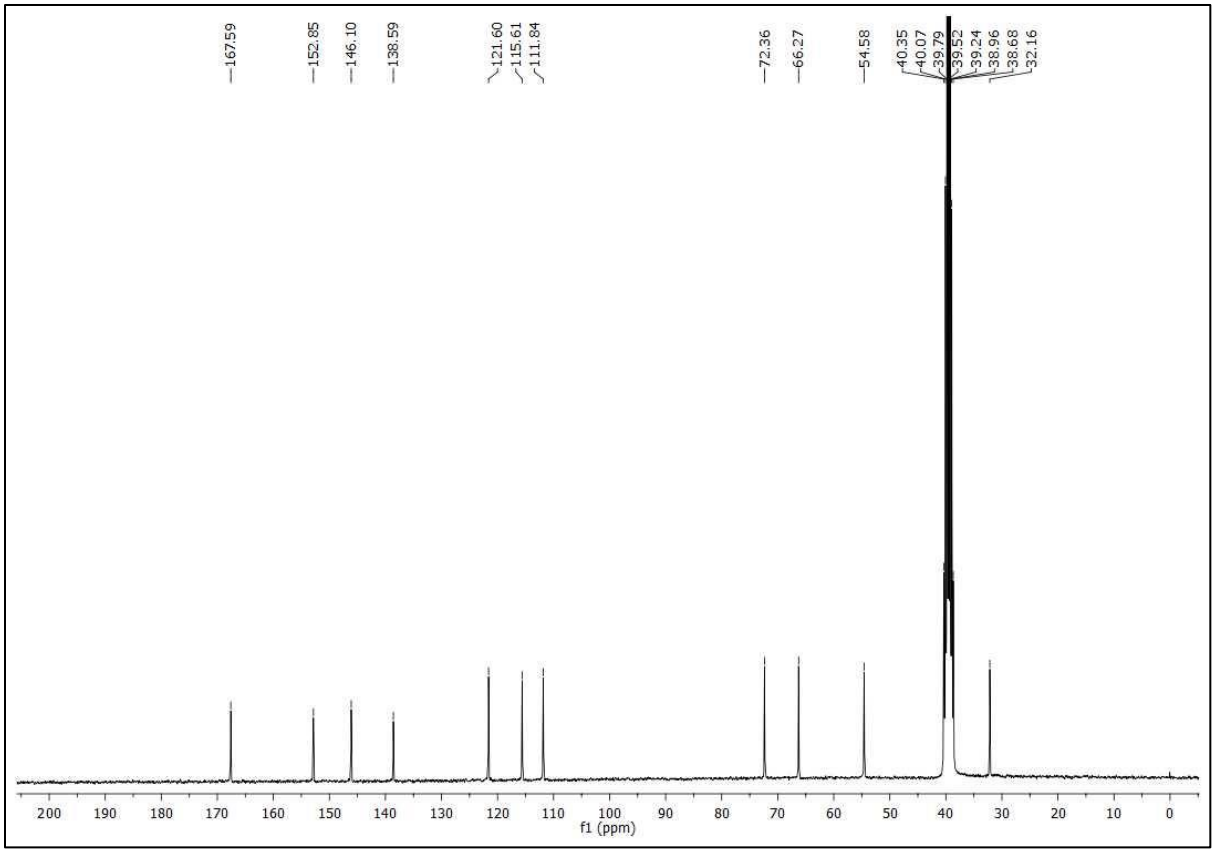
5-nitro-N-(oxolan-3-yl)-1,3-benzothiazol-2-amine (3ac)



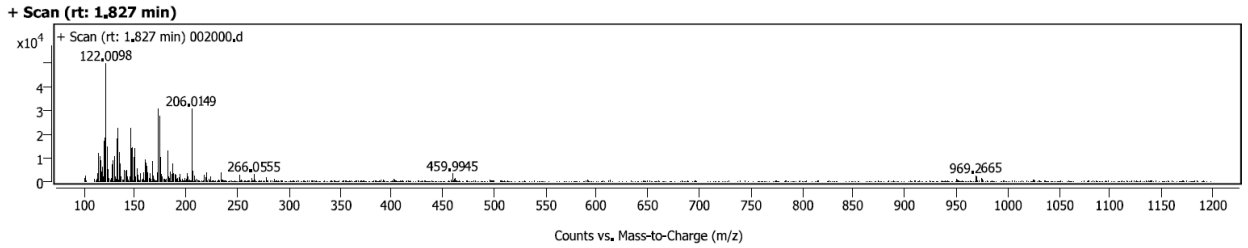
^{1}H NMR



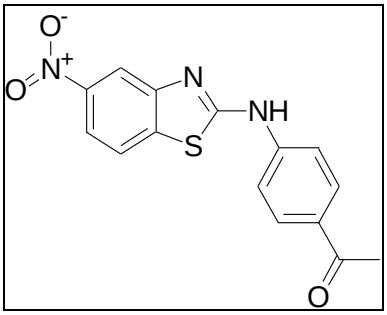
^{13}C NMR



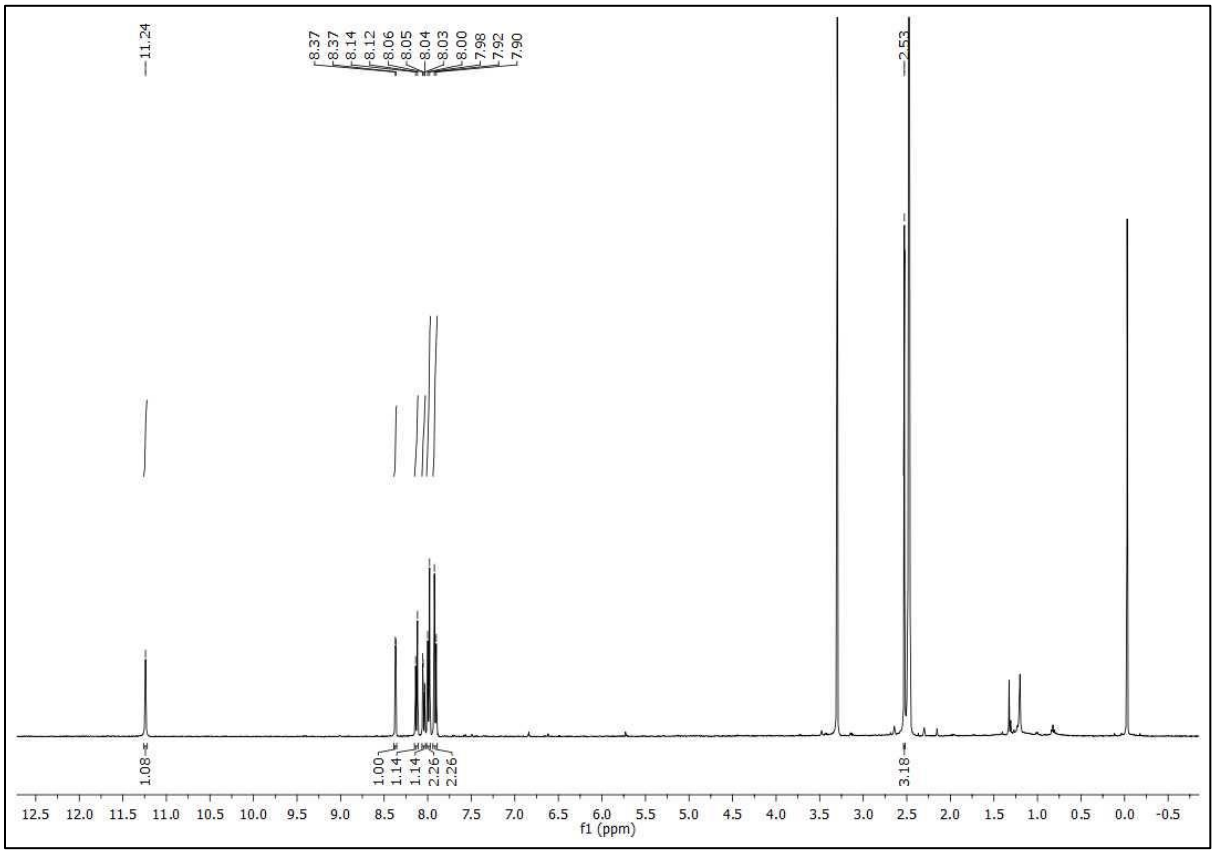
HRMS



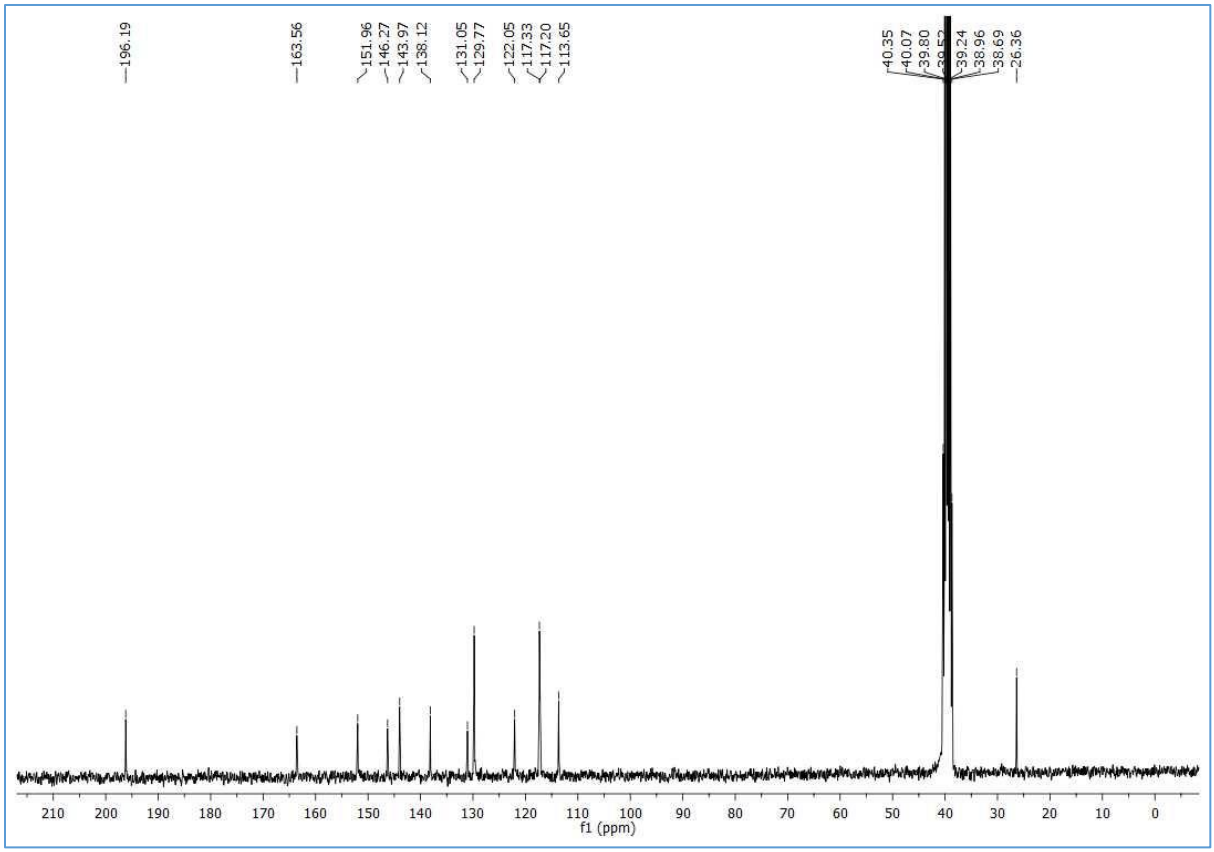
1-{4-[(5-nitro-1,3-benzothiazol-2-yl)amino]phenyl}ethan-1-one (3ae)



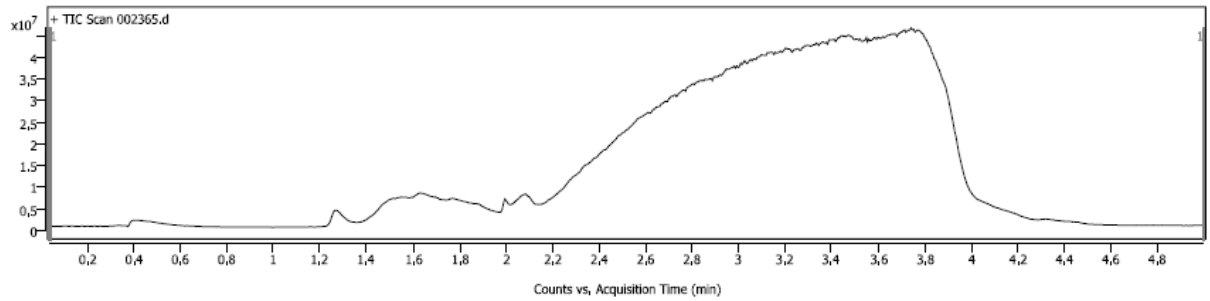
[1]HNMR

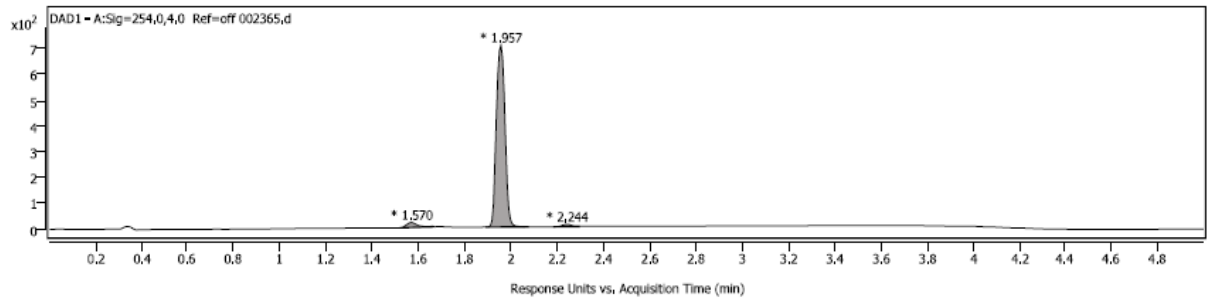


[13] CNMR


196.19
163.56
151.96
146.27
143.97
138.12
131.05
129.77
122.05
117.33
117.20
113.65
40.35
40.07
39.80
39.24
38.96
38.69
26.36
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

HRMS



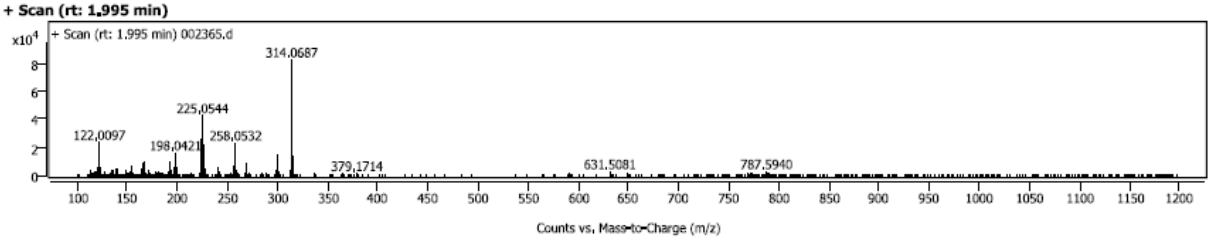


Chromatogram Peaks

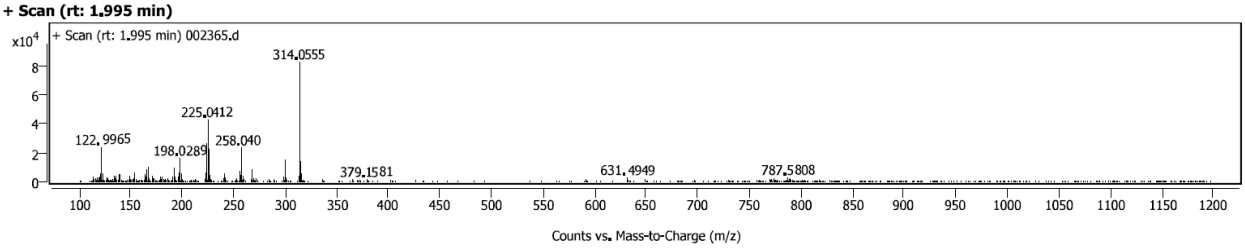
Peak	Start	RT	End	Height	Area	Area Sum %
1	1.517	1.570	1.664	19	60	3.13
2	1.890	1.957	2.077	706	1827	95.65
3	2.184	2.244	2.297	9	23	1.22

Sample Spectra

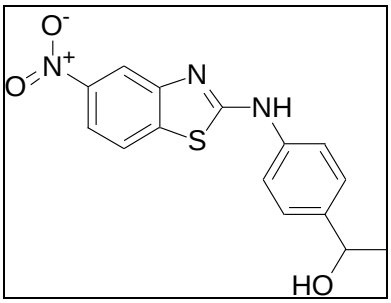
+ Scan (rt: 1.995 min)



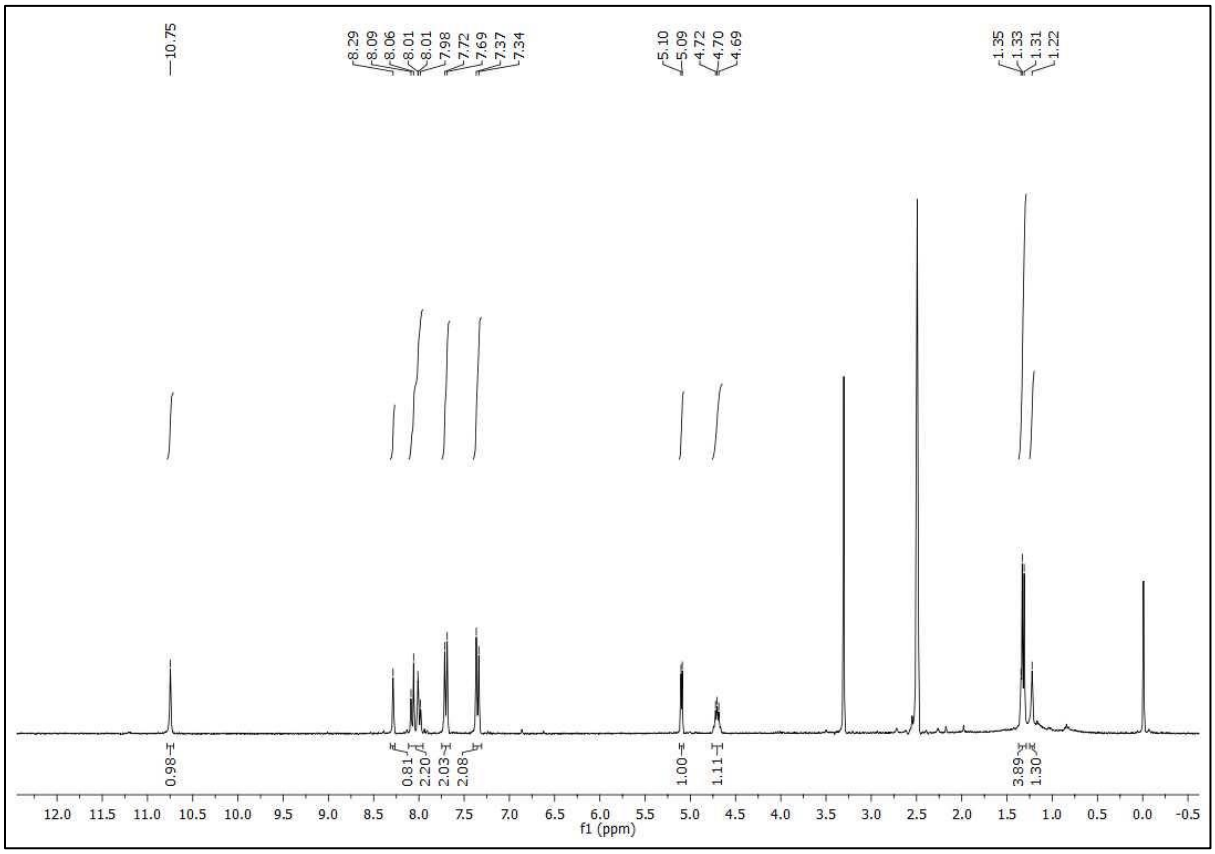
+ Scan (rt: 1.995 min)



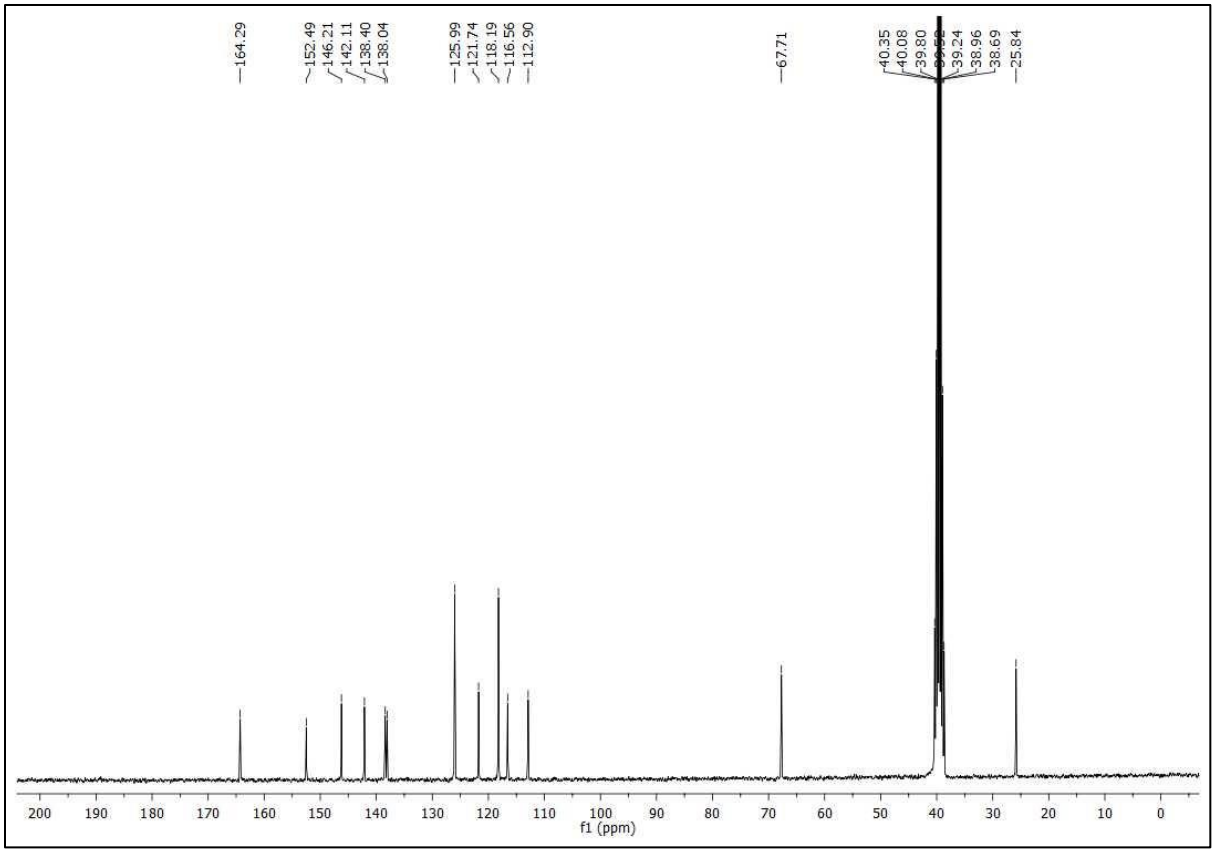
1-{4-[(5-nitro-1,3-benzothiazol-2-yl)amino]phenyl}ethan-1-ol (4)



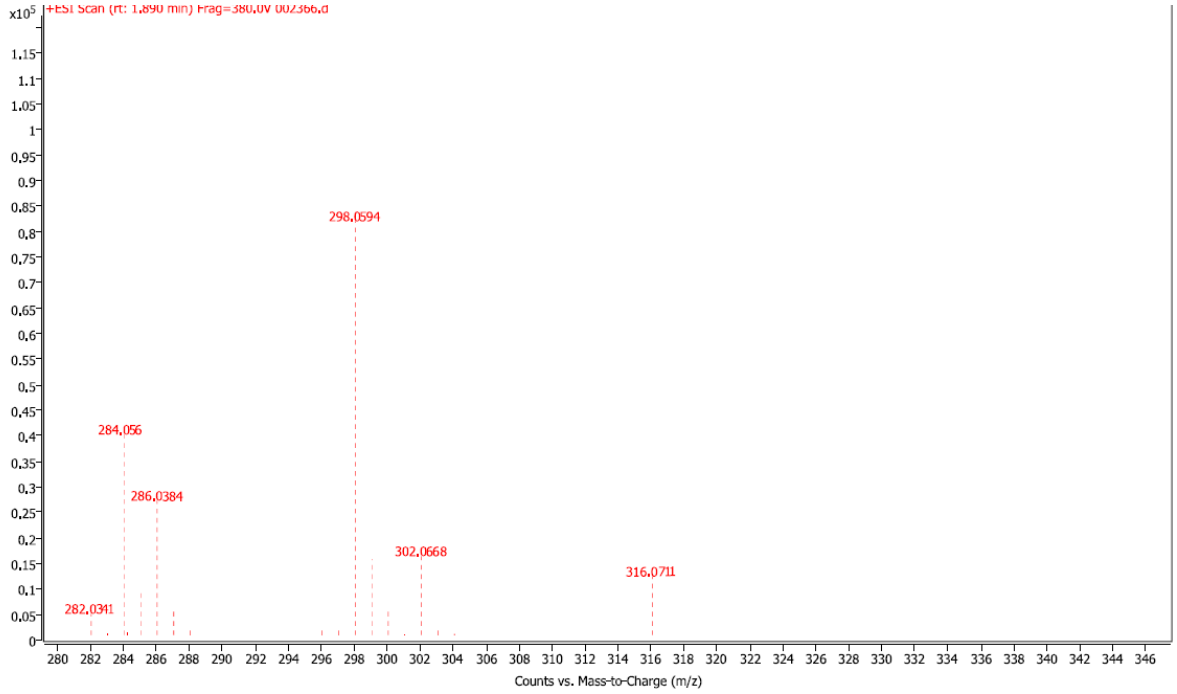
^{1}H NMR



^{13}C NMR

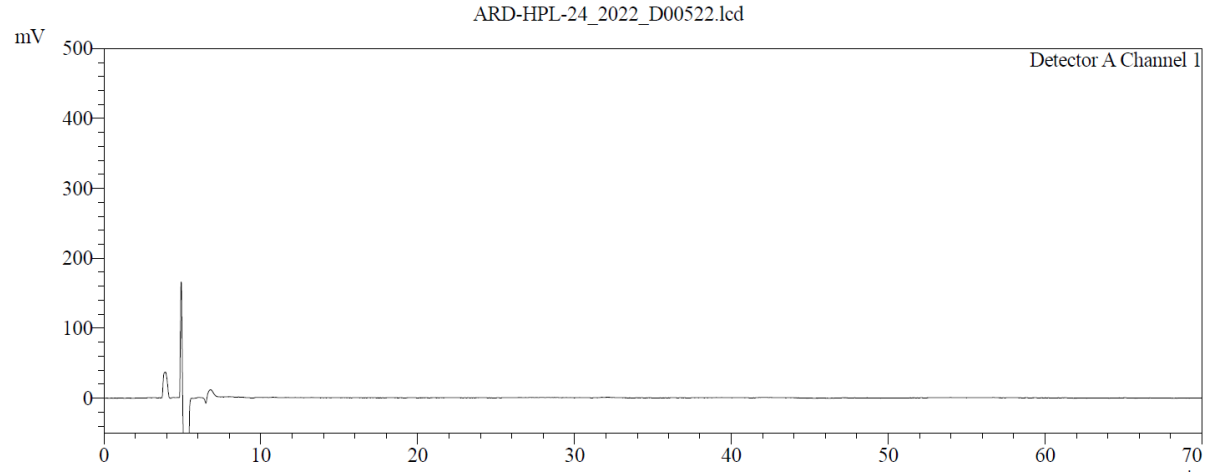

164.29
152.49
146.21
142.11
138.40
138.04
125.99
121.74
118.19
116.56
112.90
67.71
40.35
40.08
39.80
39.24
38.96
38.69
25.84
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

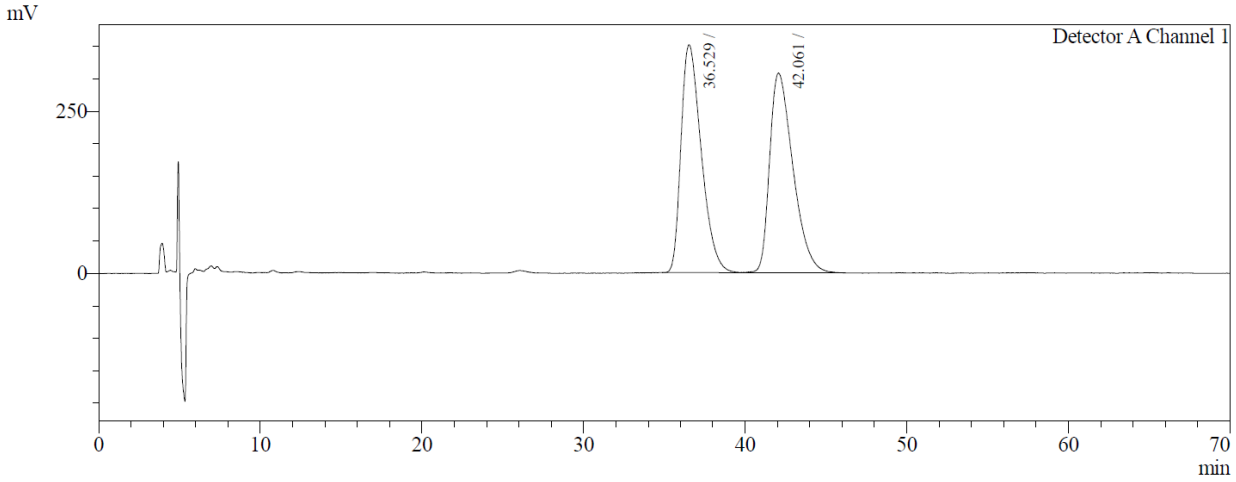
HRMS



HPLC of Racemic 1-{4-[(5-nitro-1,3-benzothiazol-2-yl)amino]phenyl}ethan-1-ol (4)

HPLC condition: Chiralpak AD-H 250mm*4.6mm,5µ , n-hexane /Ethanlol (0.1% diethylamine) = 85:15 , Diluent: Methanol, Injection volume= 10 µL, flow rate = 1.0 mL /min, 210nm UV detector, Run time- 70 min, column temperature = 30 °C.





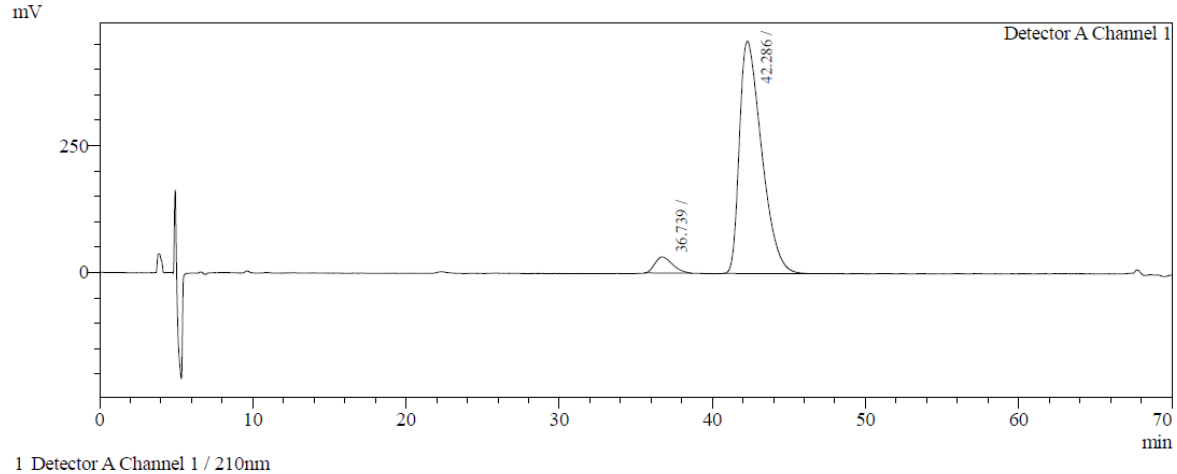
1 Detector A Channel 1 / 210nm

Peak Table

Detector A Channel 1 210nm

Peak#	Ret. Time (min	RRT	Height	Area	Area%	Name
1	36.529	0.868	351478	30620407	49.771	
2	42.061	1.000	307922	30902594	50.229	
Total			659400	61523002	100.000	

HPLC of resolved 1-{4-[(5-nitro-1,3-benzothiazol-2-yl)amino]phenyl}ethan-1-ol (6)



1 Detector A Channel 1 / 210nm

Peak Table

Detector A Channel 1 210nm

Peak#	Ret. Time (min	RRT	Height	Area	Area%	Name
1	36.739	0.869	31639	2518482	5.177	
2	42.286	1.000	457936	46130496	94.823	
Total			489575	48648978	100.000	

Reference

S. Vendeville, P. Raboisson, D. McGowan, *U.S Pat.*, 20220119385Al, 2022.