Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

NH_4I-Promoted Electrosynthesis of 2-Aminothiazole Derivatives from Ketone Compounds and NH_4SCN

Chaowei Zhang and Gaoqing Yuan*

Key Laboratory of Functional Molecular Engineering of Guangdong Province, School of Chemistry and Chemical Engineering, South China University of Technology
Guangzhou 510640, China
E-mail: gqyuan@scut.edu.cn

List of contents

1. General information

Unless otherwise stated, analytical grade commercial reagents and solvents were used as the received. Amines were bought from Alfa Aesar, Acros and Aldrich. Analytical thin layer chromatography (TLC) was performed by using commercially prepared 100–400 mesh silica gel plates (GF254) and visualization was effected at 254 nm. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 MHz NMR spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C), DMSO-d_6 was used as the solvent with TMS as the internal standard. Mass spectra were recorded on a Shimadzu GCMS-QP5050A spectrometer at an ionization voltage of 70 eV equipped with a DB-WAX capillary column (internal diameter: 0.25 mm, length: 30 m). HRMS analysis was performed in an Agilent 1290/Bruker maXis Impact high resolution mass spectrometer.

2. General procedure for the synthesis of 2-aminothiazole derivatives

In a typical procedure, ketones (1 mmol), NH_4SCN (1.2 mmol), NaOH (1 mmol), NH_4I (0.2 $mol \cdot L^{-1}$), CH_3CN (5.0 mL) were added to the undivided cell wich was equipped with a graphite plate as the anode and the cathode (5 mm × 10 mm × 2 mm). The anode and cathode were connecting to a DC regulated power supply. The electrosythesis was carried out with current 10 mA at room temperature for 20 h under magnetic stirring. After the electrolysis, the reaction mixture was decolorized with saturated aqueous $Na_2S_2O_3$ solution, and then washed with distilled water (50 mL) and extracted with ethyl acetate (15 mL × 3). The organic layer was dried over anhydrous $MgSO_4$ and concentrated in vacuum. The crude product was purified by column chromatography on silica gel with petroleum ether-ethyl acetate (*v/v*=4:1) as eluent to give pure desired product.

3. Gram-scale experiment

In a scale-up procedure, ketones (8.3 mmol), NH_4SCN (12 mmol), NaOH (5 mmol), NH_4I (0.2 mol·L^{-1}), CH_3CN (25.0 mL) were added to the undivided cell which was equipped with a graphite plate as the anode and the cathode (10 mm × 25 mm × 2 mm). The electrosythesis was carried out with current density 15 mA/cm^2 (i.e, *I*=37.5 mA) at room temperature for 48 h under magnetic stirring. The diagram of electrlytic device for the scale-up process is shown in Fig. 1s.

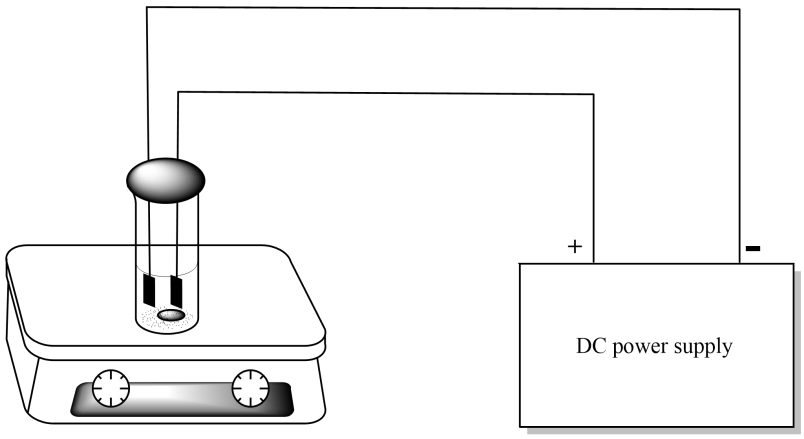
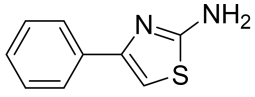


Fig. 1s The diagram of electrlytic device for the scale-up process.

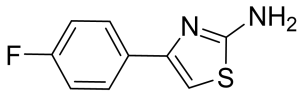
4. Characterization data of products

2-Amino-4-phenylthiazole(2a)[1]



100.2 mg as light-yellow solid, mp: 152–153 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.86–7.79 (m, 2H), 7.36 (dd, *J* = 8.4, 7.0 Hz, 2H), 7.30–7.21 (m, 1H), 7.13 (s, 2H), 6.98 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.8, 150.3, 135.4, 129.0, 127.7, 126.0, 102.0.

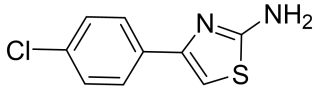
2-Amino-4-(4-fluorophenyl)thiazole(2b)[1]



115 mg as yellow solid, mp: 117–119 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.84 (dd, *J* = 8.8, 5.6 Hz, 2H), 7.18 (d, *J* = 8.9 Hz, 2H), 7.14 (d, *J* = 3.4 Hz, 2H), 6.93 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.9,

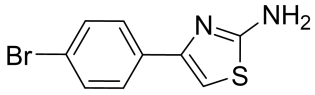
163.1 and 160.7 (d, *J* (C, F)=242.7 Hz)), 149.3, 132.0, 128.0 and 127.9 (d, *J* (C, F)=8.0 Hz)), 115.8 and 115.6 (d, *J* (C, F)=21.5 Hz)), 101.7.

4-(4-Chlorophenyl)-2-thiazolamine(2c) [2]



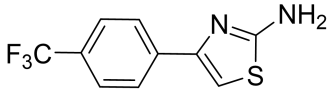
120 mg as yellow solid, mp: 175–176 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.81 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 7.15 (s, 2H), 7.01 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.9, 149.1, 134.2, 132.1, 128.9, 127.8, 102.7.

4-(4-Bromophenyl)-2-thiazolamine(2d) [1]



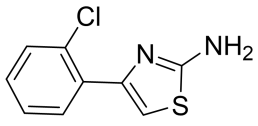
125 mg as yellow solid, mp: 180–182 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.75 (d, *J* = 8.6 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.12 (s, 2H), 7.05 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.9, 149.1, 134.6, 131.8, 128.0, 120.6, 102.8.

4-[4-(Trifluoromethyl)phenyl]-2-thiazolamine(2e)[3]



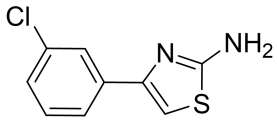
94 mg as yellow solid, mp: 147–148 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 8.00 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.21 (s, 2H), 7.20 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 169.0, 148.8, 139.0, 127.9 and 127.6 (d, *J* (C, F)=31.6 Hz)), 126.4 and 126.2 (d, *J* (C, F)=27.2 Hz)), 125.9 and 125.8 (d, *J* (C, F)=10.9 Hz)), 123.5, 104.7.

4-(2-Chlorophenyl)-2-thiazolamine(2f)[4]



80 mg as yellow solid, mp: 125–127 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.85 (d, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.36 (t, *J* = 8.2 Hz, 1H), 7.32–7.26 (m, 1H), 7.07 (s, 2H), 7.04 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 167.7, 146.8, 133.9, 131.6, 131.0, 130.8, 129.1, 127.5, 106.8.

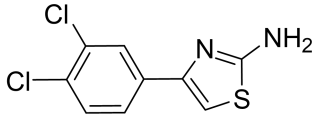
4-(3-Chlorophenyl)-2-thiazolamine(2g)[5]



101 mg as red solid, mp: 132–133 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.86 (t, *J* = 1.8 Hz, 1H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 7.16 (s, 1H), 7.14 (s, 2H). **^{13}C NMR** (100 MHz,

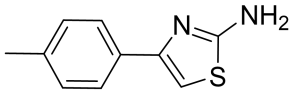
DMSO) δ (ppm) 168.8, 148.7, 137.4, 133.9, 130.8, 127.3, 125.7, 124.4, 103.6.

2-Amino-4-(3,4-dichlorophenyl)thiazole(2h)[2]



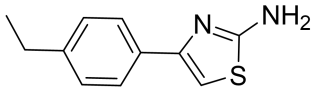
122 mg as yellow solid, mp: 193–194 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 8.01 (d, J = 2.0 Hz, 1H), 7.76 (dd, J = 8.4, 2.0 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.18 (s, 1H), 7.17 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 169.0, 147.7, 135.9, 131.8, 131.0, 129.8, 127.6, 125.9, 104.2.

2-Amino-4-(4-methylphenyl)thiazole(2i)[2]



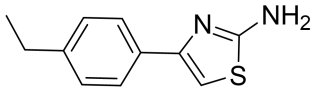
110 mg as yellow solid, mp: 134–135 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.70 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.07 (s, 2H), 6.89 (s, 1H), 2.29 (s, 3H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.6, 150.4, 136.8, 132.8, 129.5, 126.0, 101.0, 21.2.

4-(4-Ethylphenyl)-2-thiazolamine(2j)[2]



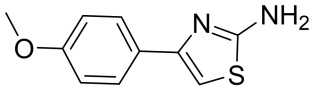
60 mg as yellow solid, mp: 142–143 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.71 (d, J = 8.2 Hz, 2H), 7.19 (d, J = 8.2 Hz, 2H), 7.04 (s, 2H), 6.90 (s, 1H), 2.59 (q, J = 7.6 Hz, 2H), 1.18 (t, J = 7.6 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.6, 150.5, 143.2, 133.0, 128.3, 126.0, 101.0, 28.4, 16.0.

4-[4-(1-Methylethyl)phenyl]-2-thiazolamine(2k)[1]



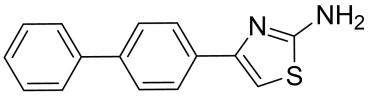
72 mg as yellow solid, mp: 166–167 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.72 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H), 7.08 (s, 2H), 6.89 (s, 1H), 2.86 (p, J = 6.9 Hz, 1H), 1.20 (d, J = 6.9 Hz, 6H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.6, 150.4, 147.8, 133.2, 126.8, 126.0, 101.0, 33.7, 24.3.

2-Amino-4-(4-methoxyphenyl)thiazole(2l)[1]



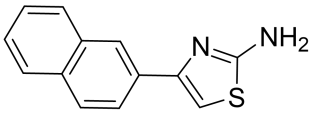
30 mg as yellow solid, mp: 206–207 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.73 (d, J = 8.8 Hz, 2H), 7.02 (s, 2H), 6.92 (d, J = 8.9 Hz, 2H), 6.82 (s, 1H), 3.77 (s, 3H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.6, 159.0, 150.2, 128.3, 127.3, 114.3, 99.2, 55.5.

4-[1,1′-Biphenyl]-4-yl-2-thiazolamine(2m)[1]



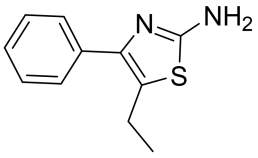
79 mg as yellow solid, mp: 205–207 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.90 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 4.9 Hz, 2H), 7.67 (d, J = 6.2 Hz, 2H), 7.46 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.3 Hz, 1H), 7.12 (s, 2H), 7.05 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.8, 150.0, 140.2, 139.2, 134.6, 129.4, 127.8, 127.2, 126.9, 126.6, 102.2.

2-Amino-4-(2-naphthyl)thiazole(2n)[1]



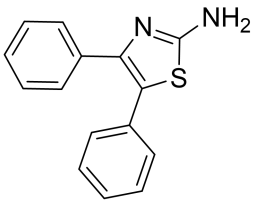
81 mg as yellow solid, mp: 153–155 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 8.36 (s, 1H), 8.00–7.85 (m, 4H), 7.53–7.43 (m, 2H), 7.18 (s, 2H), 7.15 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.8, 150.3, 133.7, 132.8, 128.6, 128.4, 128.0, 126.8, 126.3, 124.6, 124.5, 102.9.

5-Ethyl-4-phenyl-2-thiazolamine(2o)[6]



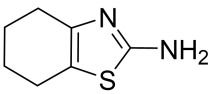
69 mg as yellow solid, mp: 68–70 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.51 (d, J = 7.1 Hz, 2H), 7.39 (t, J = 7.6 Hz, 2H), 7.28 (t, J = 7.3 Hz, 1H), 6.80 (s, 2H), 2.73 (q, J = 7.5 Hz, 2H), 1.18 (t, J = 7.5 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 165.1, 144.9, 136.1, 128.6, 128.4, 127.3, 123.4, 20.6, 17.1.

2-Amino-4,5-diphenylthiazole(2p)[7]



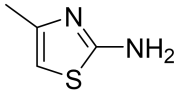
60 mg as light-yellow solid, mp: 183–185 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 7.42 (d, J = 2.1 Hz, 1H), 7.40 (d, J = 1.6 Hz, 1H), 7.31–7.20 (m, 8H), 7.19 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 145.4, 135.9, 133.3, 129.4, 129.2, 129.0, 128.5, 127.8, 127.5, 119.6.

4,5,6,7-Tetrahydro-2-benzothiazolamine(2q)[8]



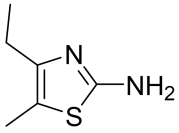
30 mg as brown solid, mp: 92–93 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 6.59 (s, 2H), 2.46 (t, J = 4.1 Hz, 2H), 2.37 (t, J = 4.2 Hz, 2H), 1.70 (p, J = 2.8 Hz, 4H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 165.8, 145.2, 114.9, 26.8, 23.7, 23.2, 23.0.

2-Amino-4-methylthiazole(2r)[1]



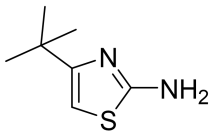
57 mg as yellow solid, mp: 43–44 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 6.80 (s, 2H), 6.07 (s, 1H), 2.06 (s, 3H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.5, 148.0, 100.8, 17.6.

4-Ethyl-5-methyl-2-thiazolamine(2s)



35 mg as yellow solid, mp: 70–72 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 6.55 (s, 2H), 2.32 (q, J = 7.5 Hz, 2H), 2.09 (s, 3H), 1.06 (t, J = 7.5 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 165.1, 148.4, 111.5, 21.9, 14.4, 10.8. **HRMS** (ESI) *m/z*: calcd for $C_6H_{11}N_2S$ $[M + H]^+$ 143.0637, found 143.0641.

4-(1,1-Dimethylethyl)-2-thiazolamine(2t)[9]



54 mg as orange solid, mp: 100–101 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm) 6.82 (s, 2H), 6.04 (s, 1H), 1.18 (s, 9H). **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 168.3, 161.8, 97.8, 34.6, 30.1.

5. Reference

[1] T. Keshari, R. Kapoorr and L. D. S. Yadav., *Tetrahedron Lett.*, 2015, **56**, 5623–5627.

[2] B. M. Reddy, P. M. K. Mohinuddin, G. T. Reddy and N. C. G. Reddy, *Cogent Chem.*, 2016, **2**, 1154237.

[3] R. Gawali, J. Trivedi, S. Bhansali, R. Bhosale, D. Sarkar and D. Mitra, *Eur. J. Med. Chem.*, 2018, **157**, 310–319.

[4] Q. Xu, L. Huang, J. Liu, L. Ma, T. Chen, J. Chen, F. Peng, D. Cao, Z. Yang, N. Qiu, J. Qiu, G. Wang, X. Liang, A. Peng, M. Xiang, Y. Wei and L. Chen, *Eur. J. Med. Chem.*, 2012, **52**, 70–81.

[5] C. Ma, Y. Miao, M. Zhao, P. Wu, J. Zhou, Z. Li, X. Xie and Wei Zhang, *Tetrahedron*, 2018, **74**, 3602–3607.

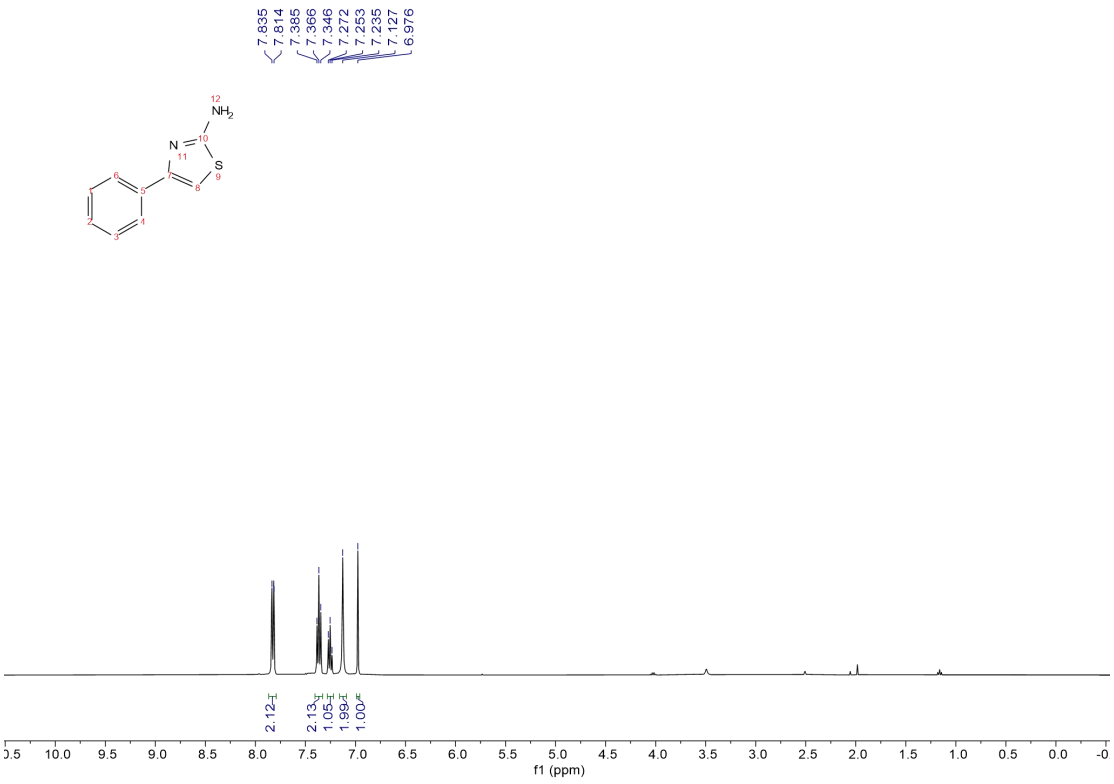
[6] Z. Zhang, Y. Luo, H. Du, J. Xu and P. Li, *Chem. Sci.*, 2019, **10**, 5156–5161.

[7] M. Walter, Y. von Coburg, K. Isensee, K. Sander, X. Ligneau, J.-C. Camelin, J.-C. Schwartz and H. Stark, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 5879–5882.

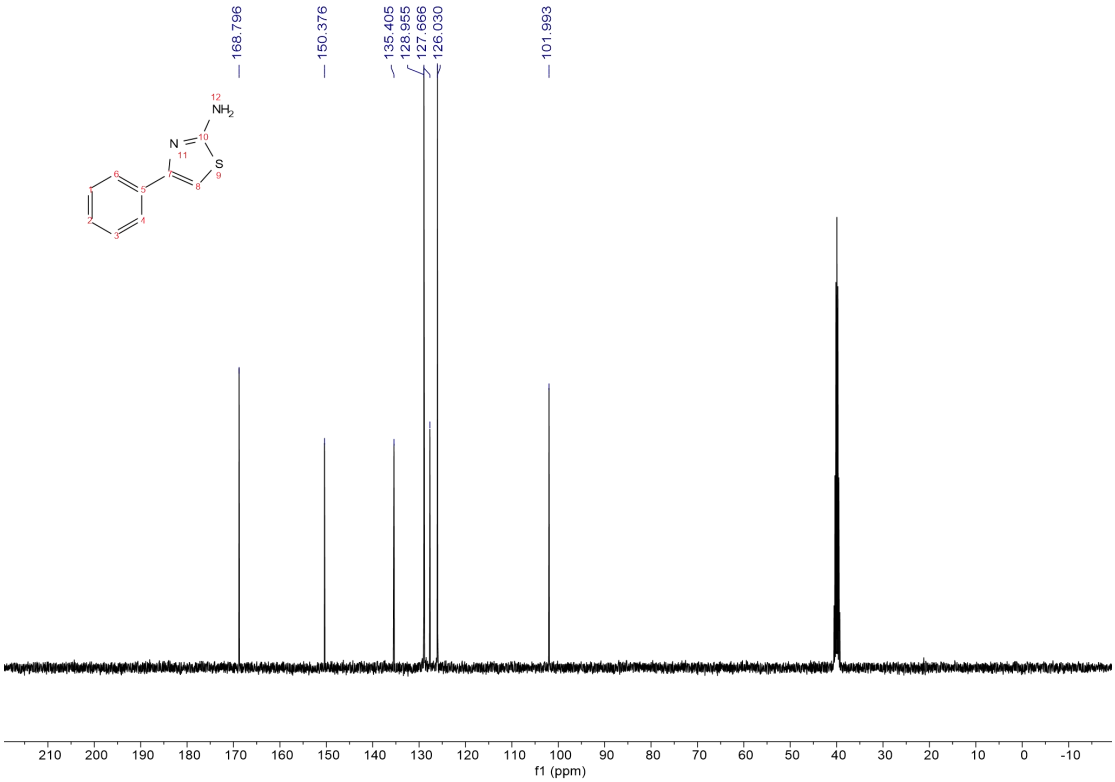
[8] N.-Y. Wang, Y. Xu, W.-Q. Zuo, K.-J. Xiao, L. Liu, X.-X. Zeng, X.-Y. You, L.-D. Zhang, C. Gao, Z.-H. Liu, T.-H. Ye, Y. Xia, Y. Xiong, X.-J. Song, Q. Lei, C.-T. Peng, H. Tang, S.-Y. Yang and Y.-Q. Wei, *J. Med. Chem.*, 2015, **58**, 2764–2778.

[9] B. H. Babu, K. Vijay, K. B. M. Krishna, N. Sharmila and M. B. Ramana, *J. Chem. Sci.*, 2016, **128**, 1475–1478.

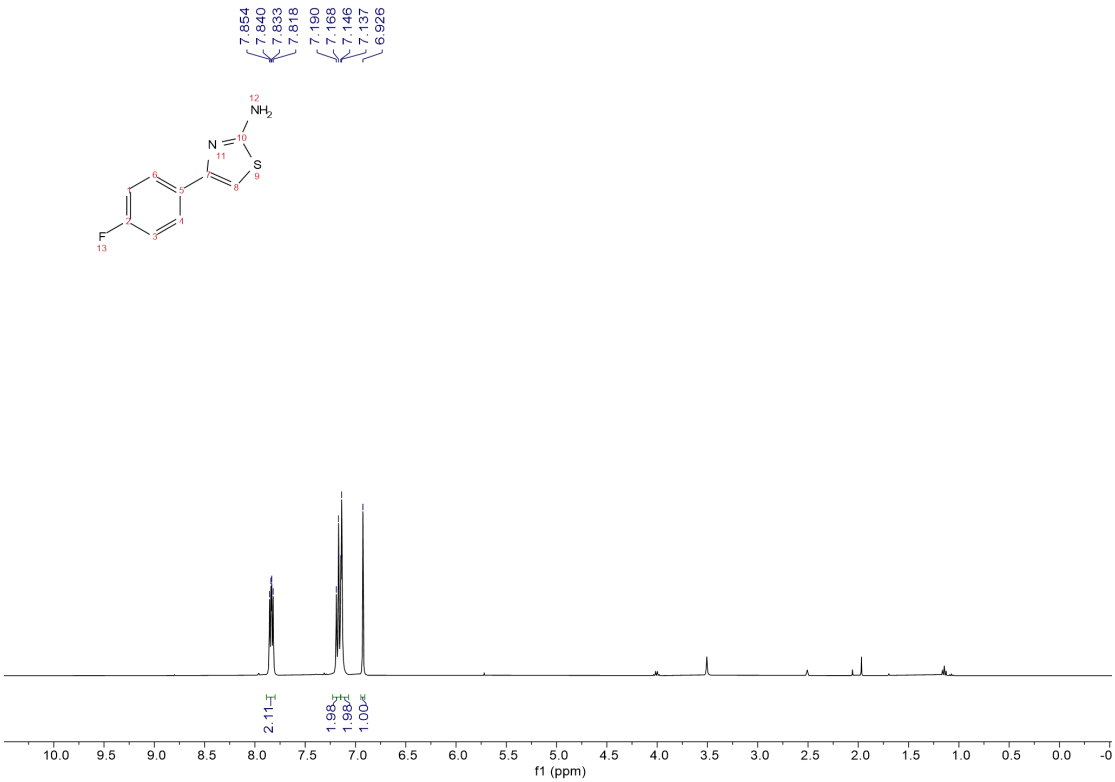
6. NMR spectra of products



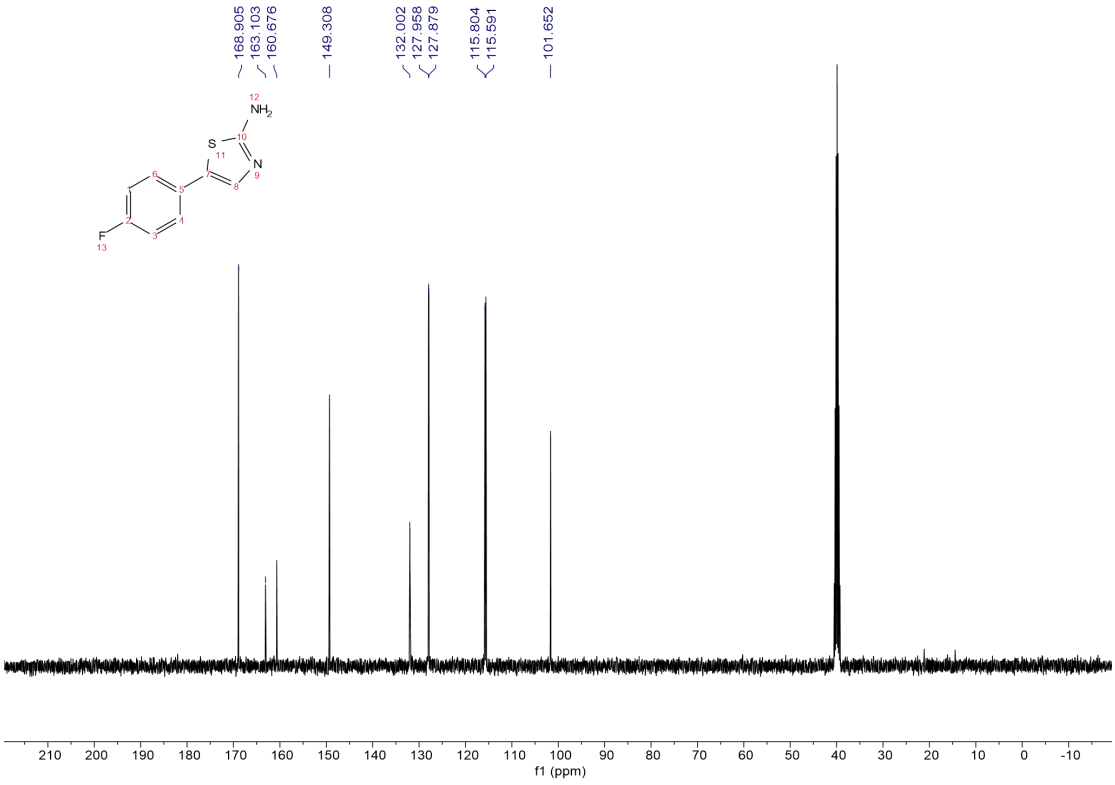
^{1}H NMR of **2a**



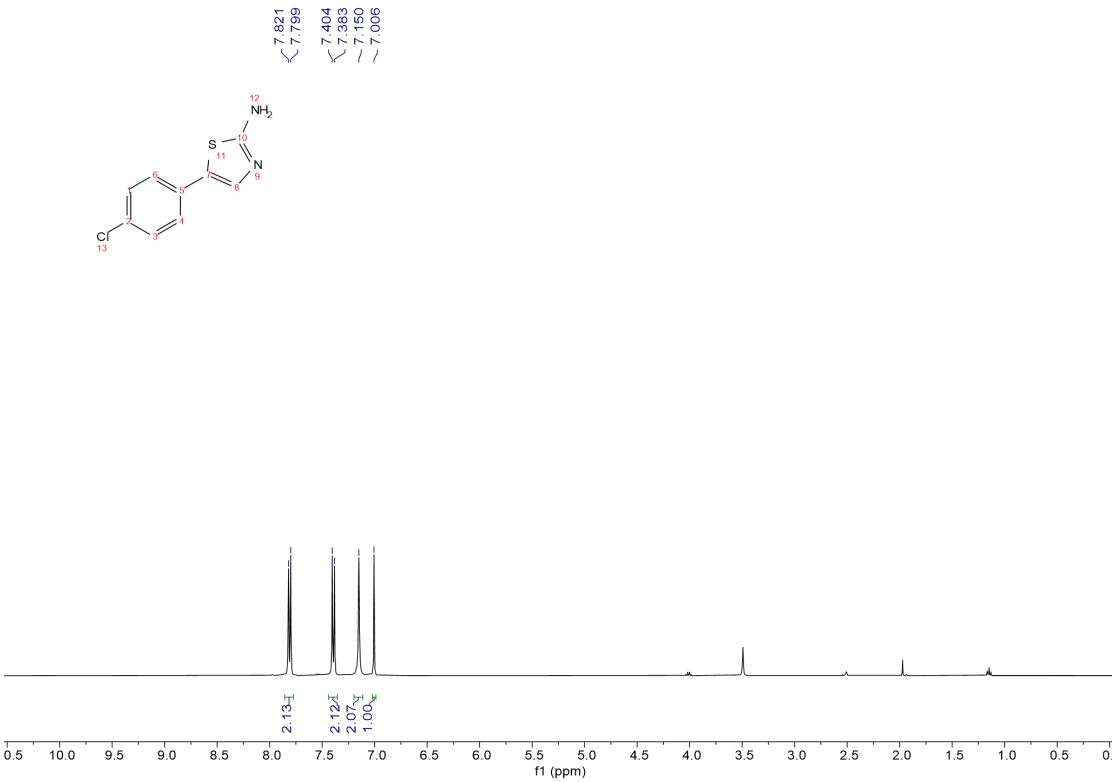
^{13}C NMR of **2a**



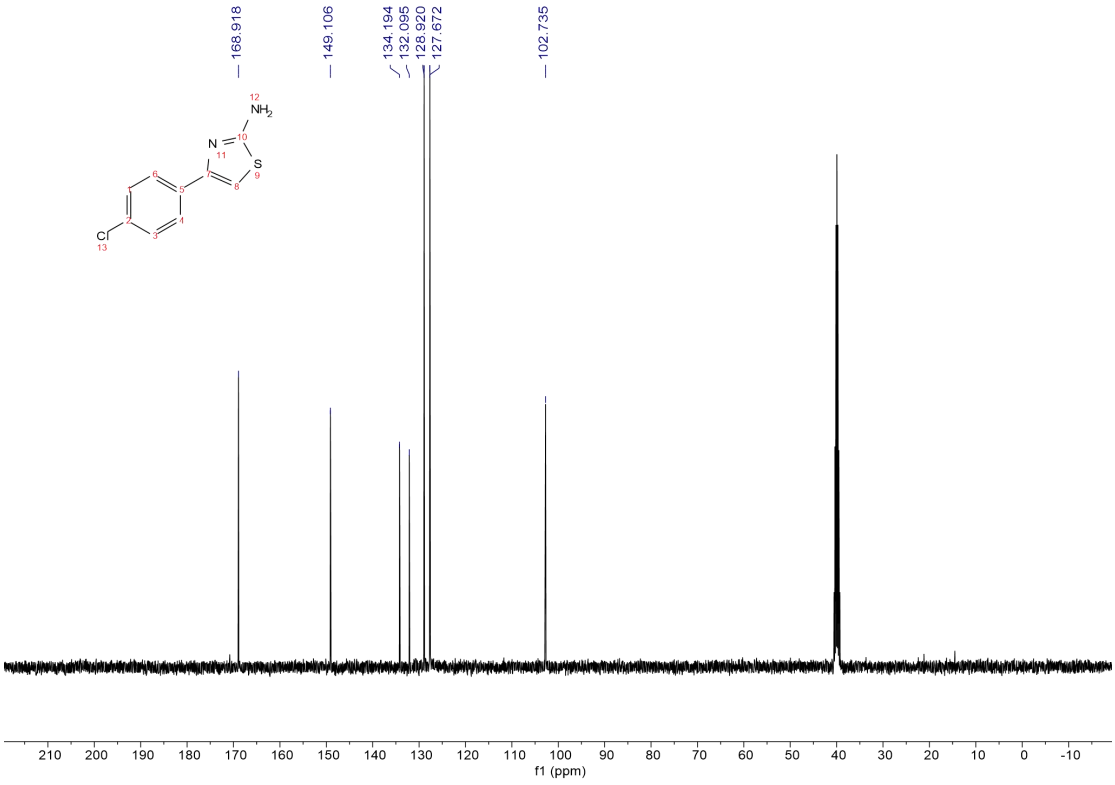
^{1}H NMR of **2b**



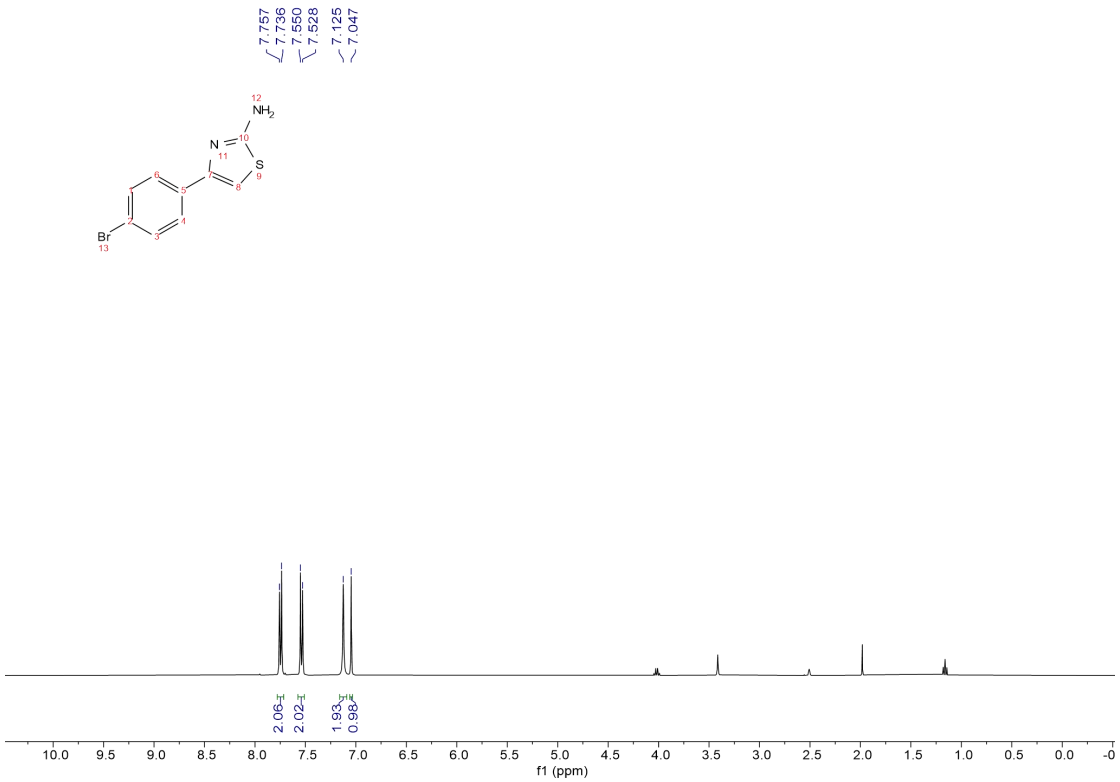
^{13}C NMR of **2b**



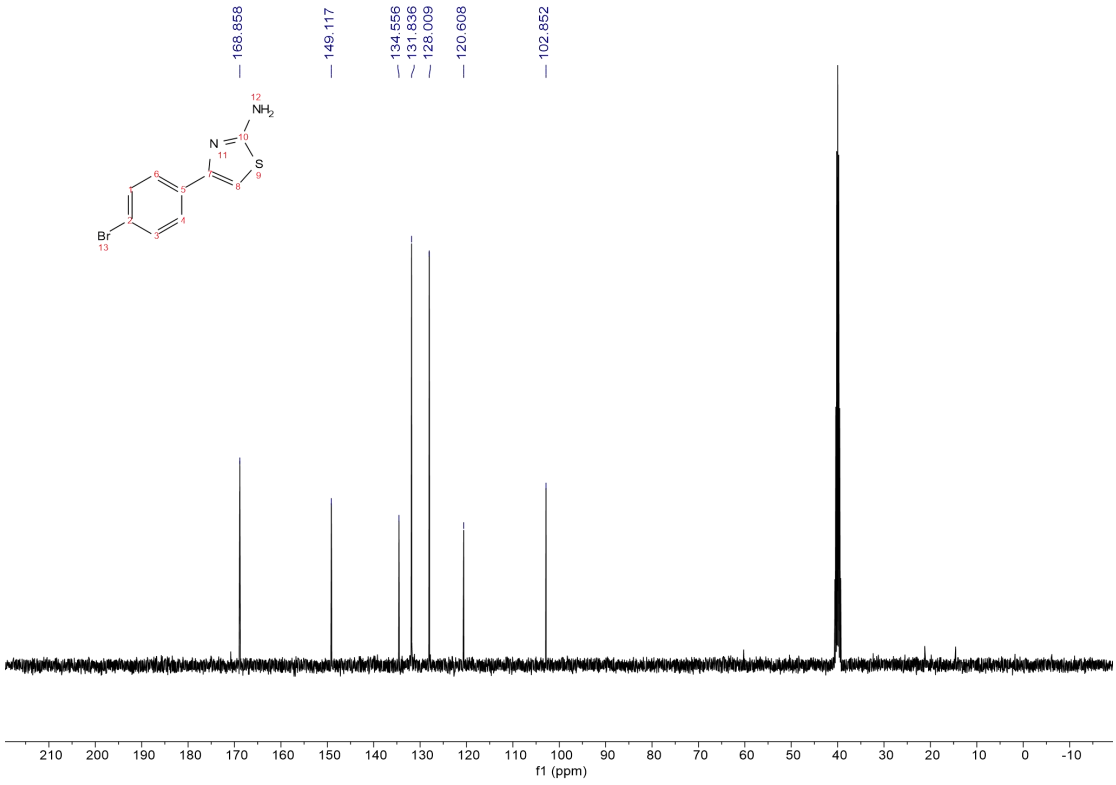
^{1}H NMR of **2c**



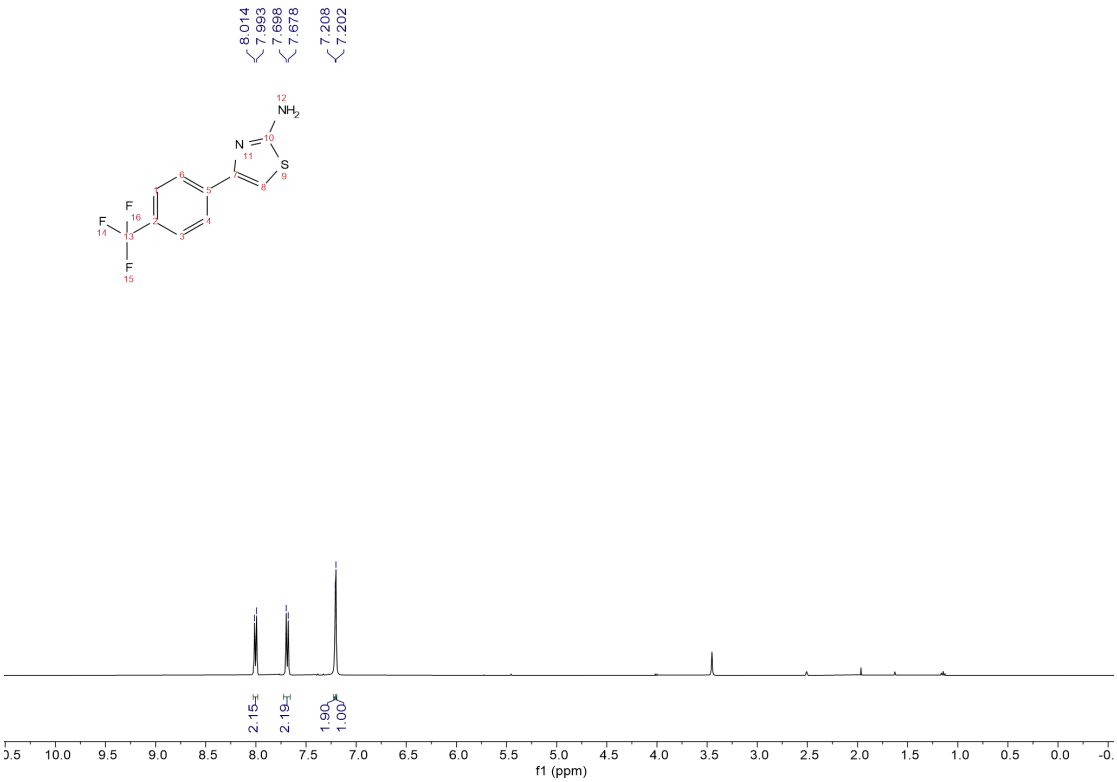
^{13}C NMR of **2c**



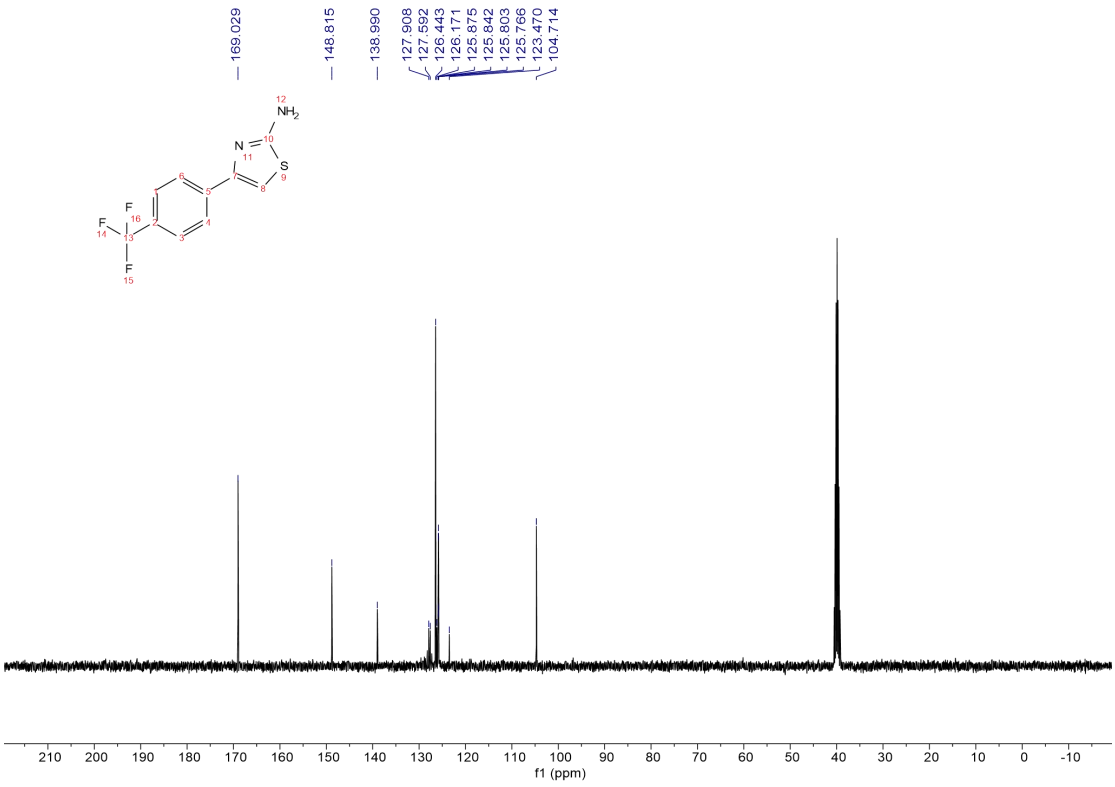
^{1}H NMR of **2d**



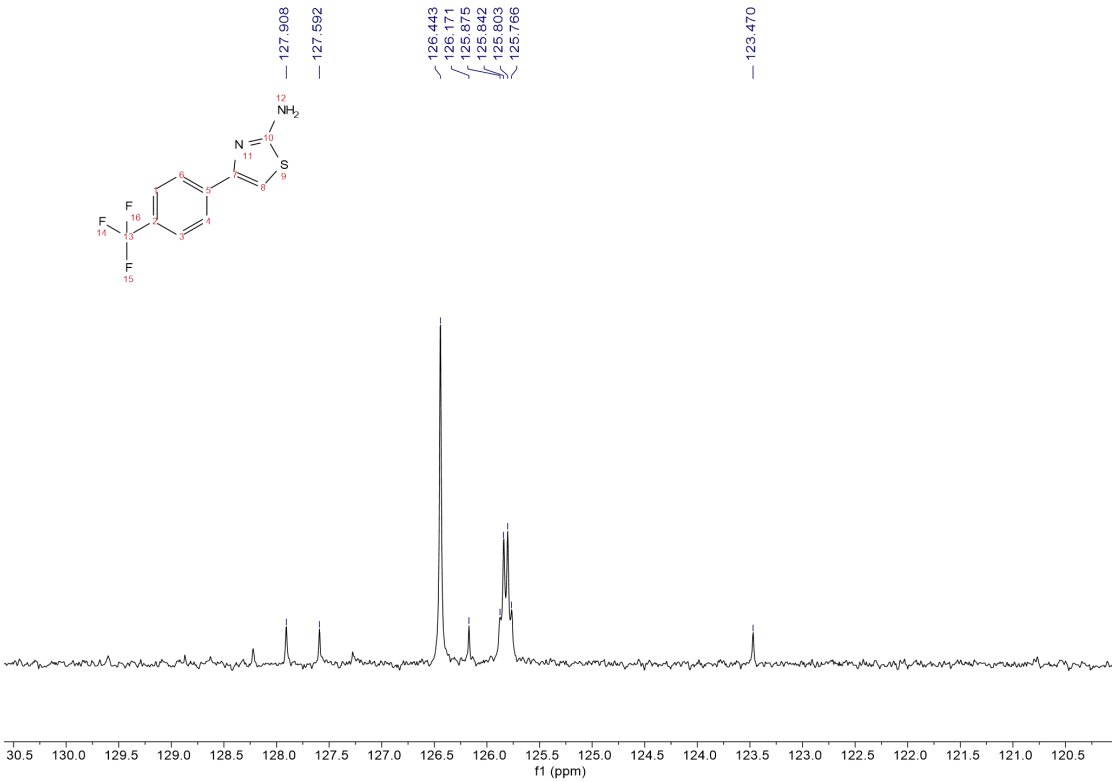
^{13}C NMR of **2d**



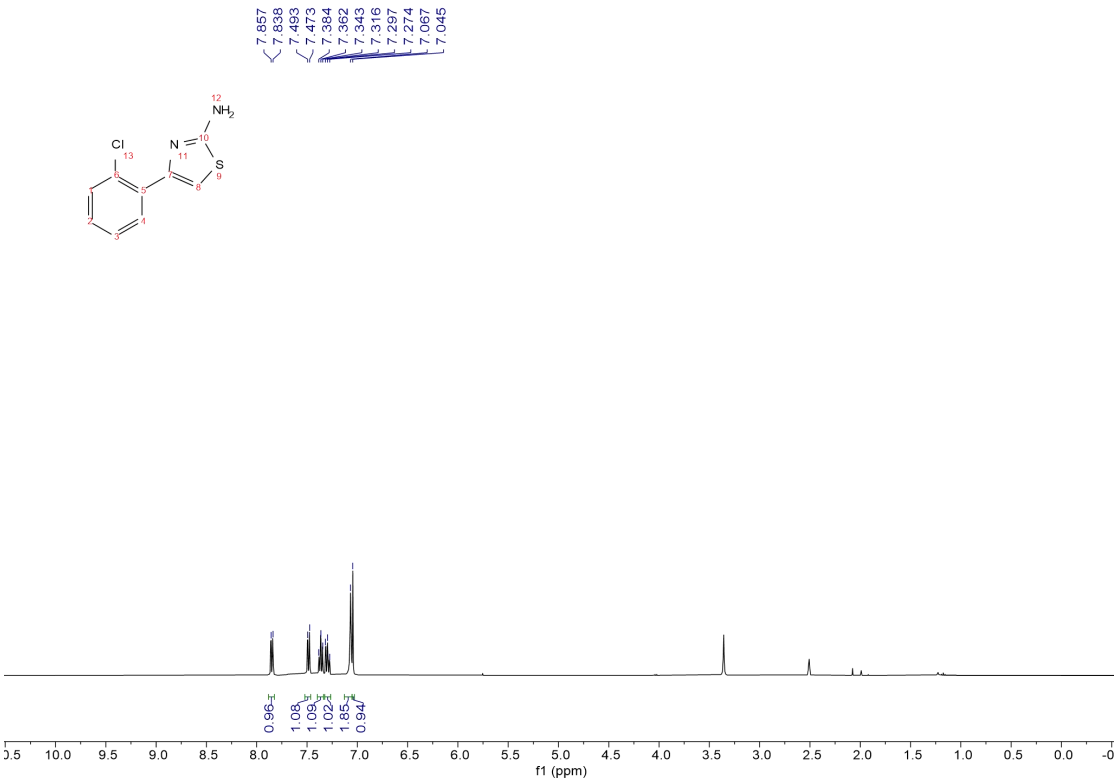
^{1}H NMR of **2e**



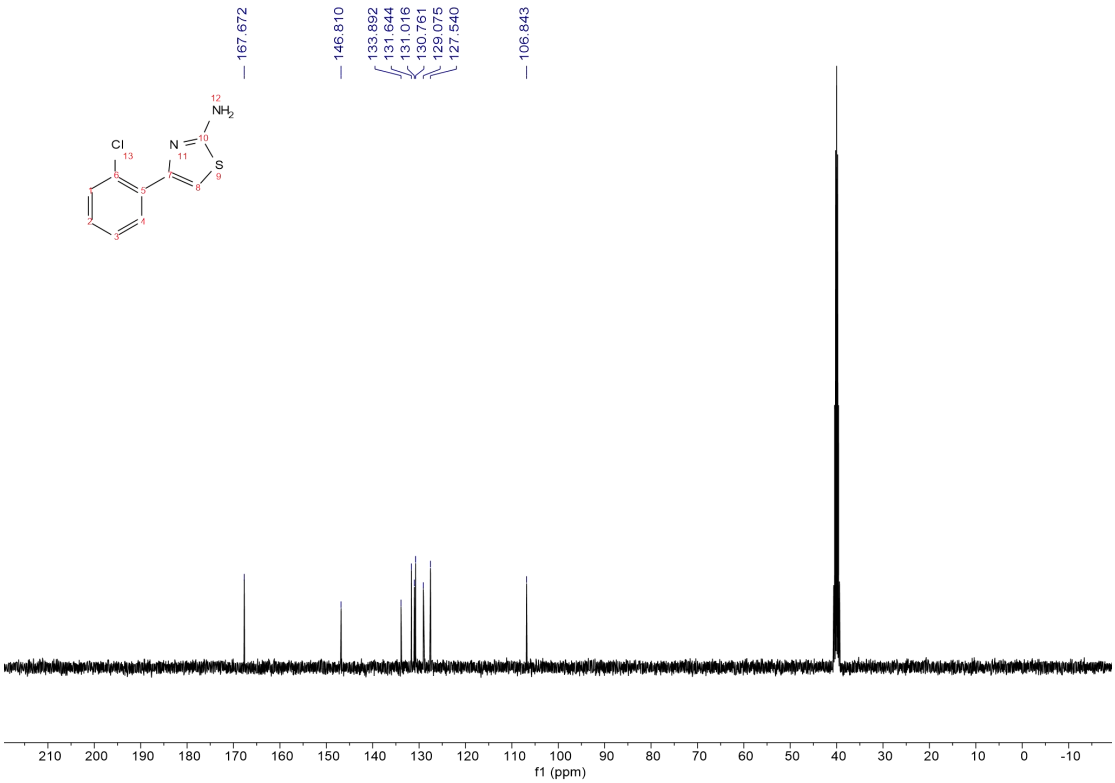
^{13}C NMR of **2e**



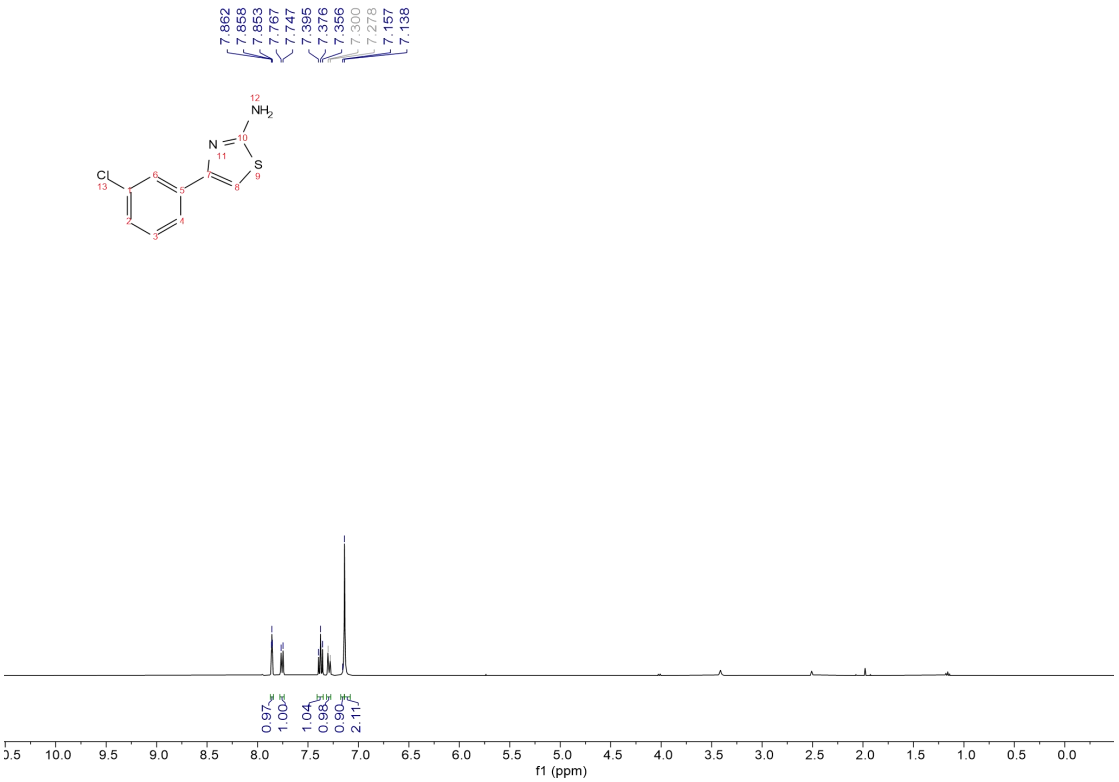
^{13}C NMR of **2e** (enlarged part)



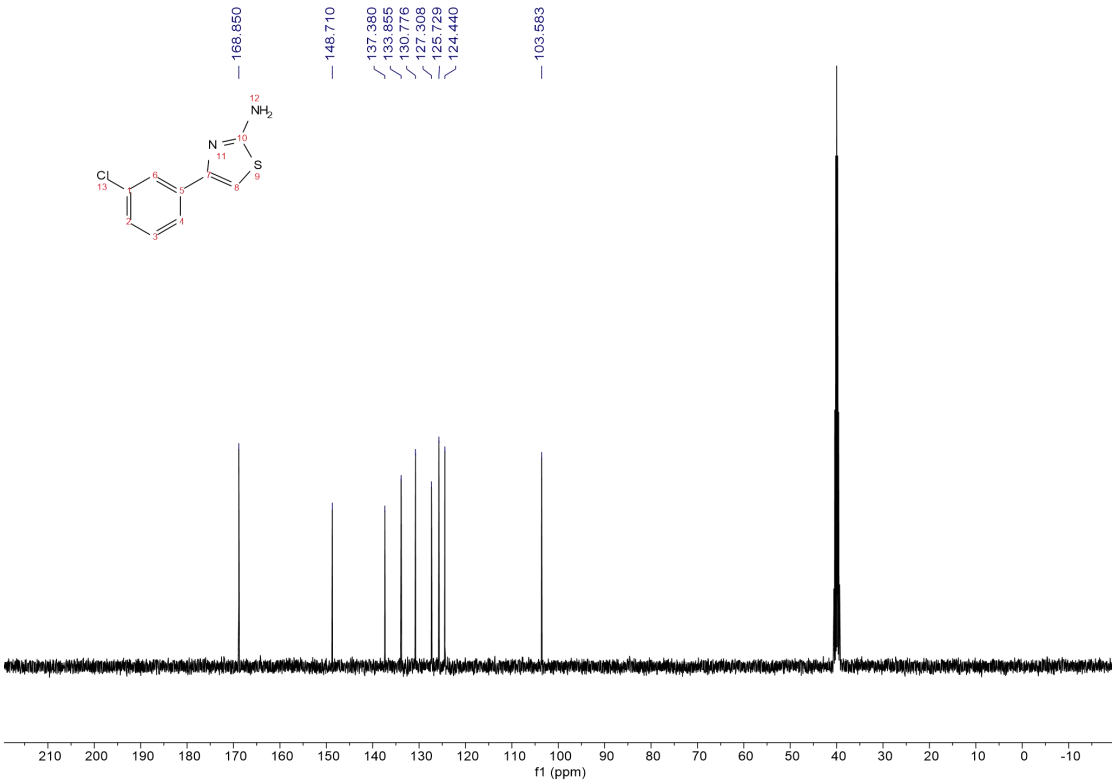
^{1}H NMR of **2f**



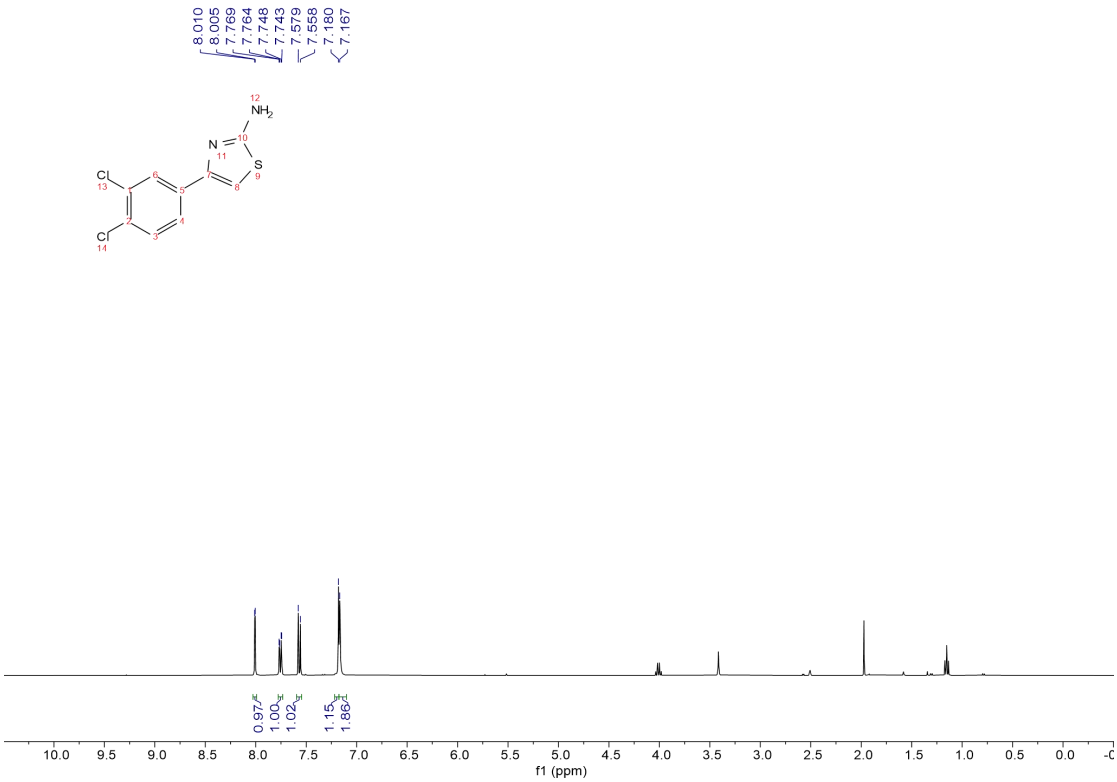
^{13}C NMR of **2f**



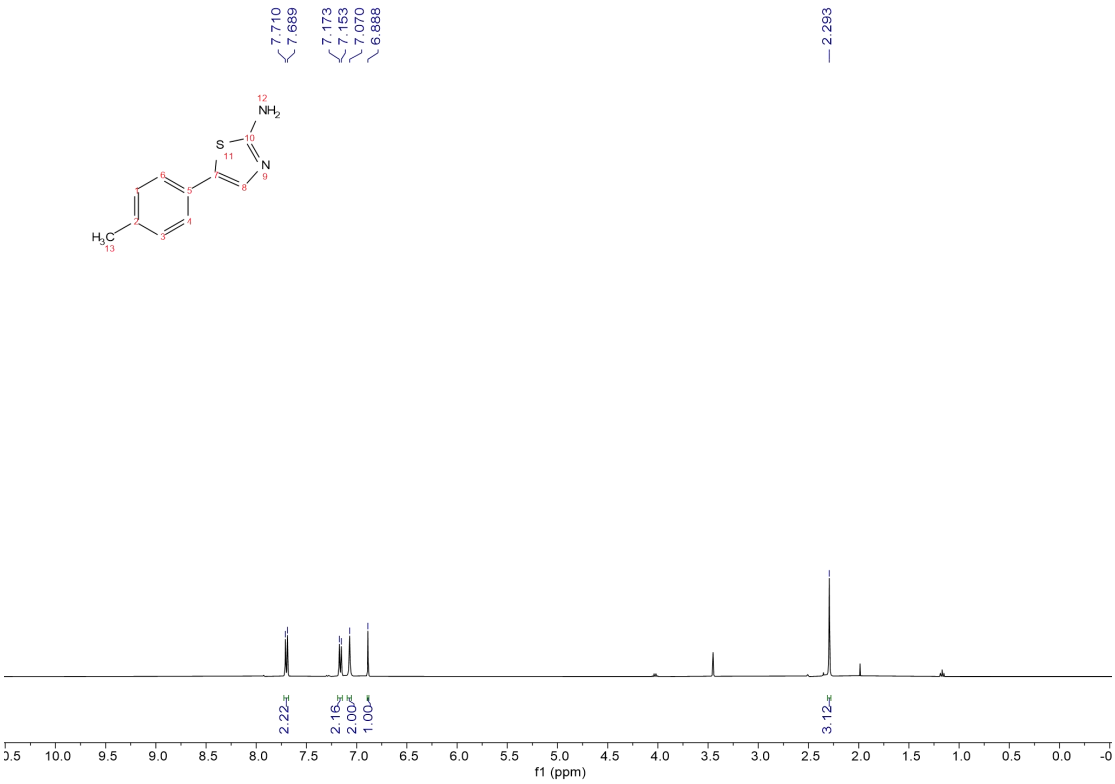
^{1}H NMR of **2g**



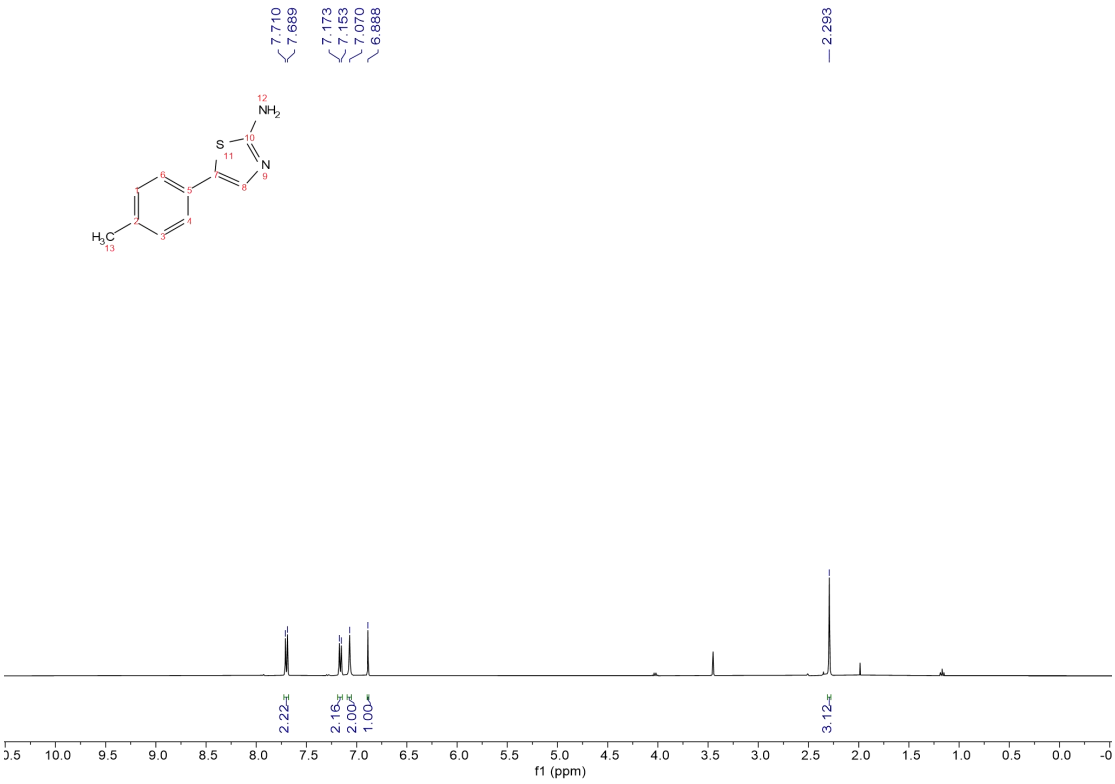
^{13}C NMR of **2g**



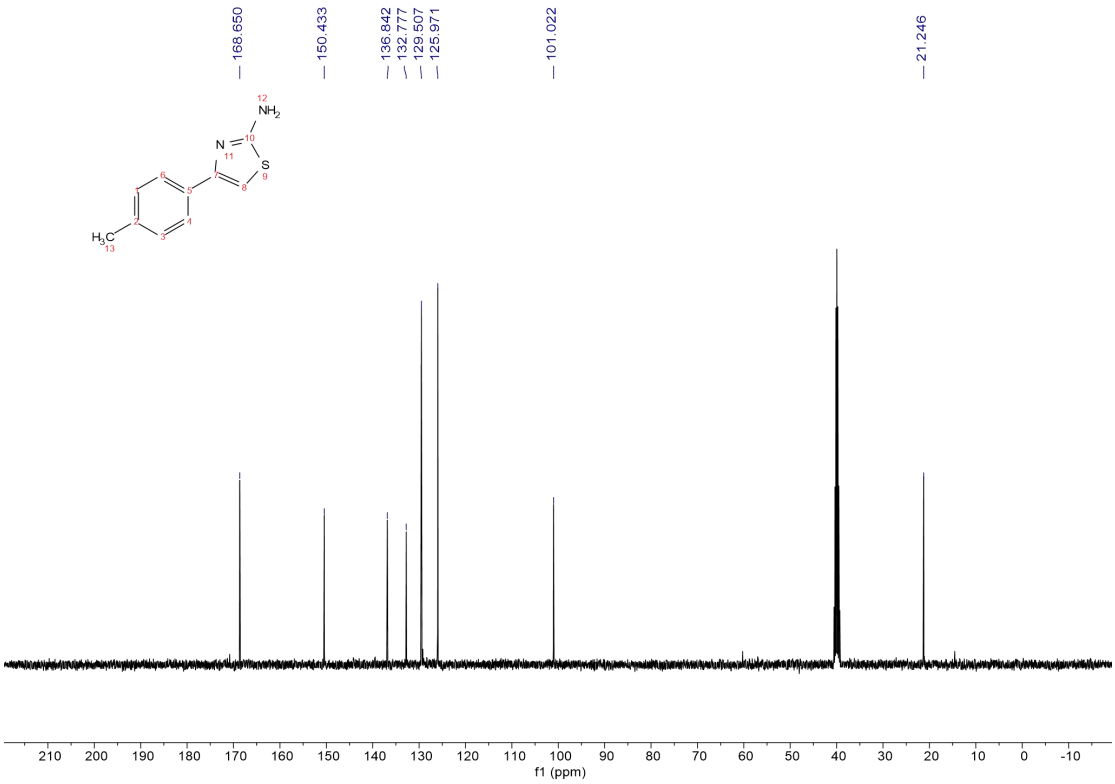
^{1}H NMR of **2h**



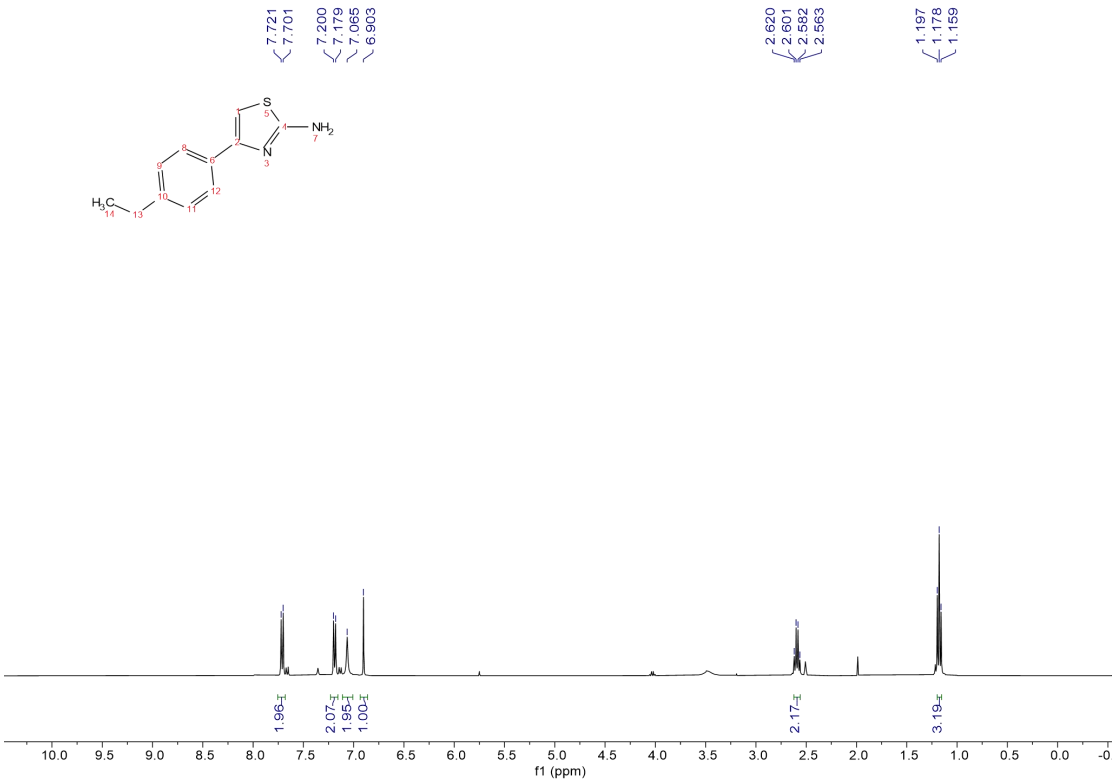
^{13}C NMR of **2h**



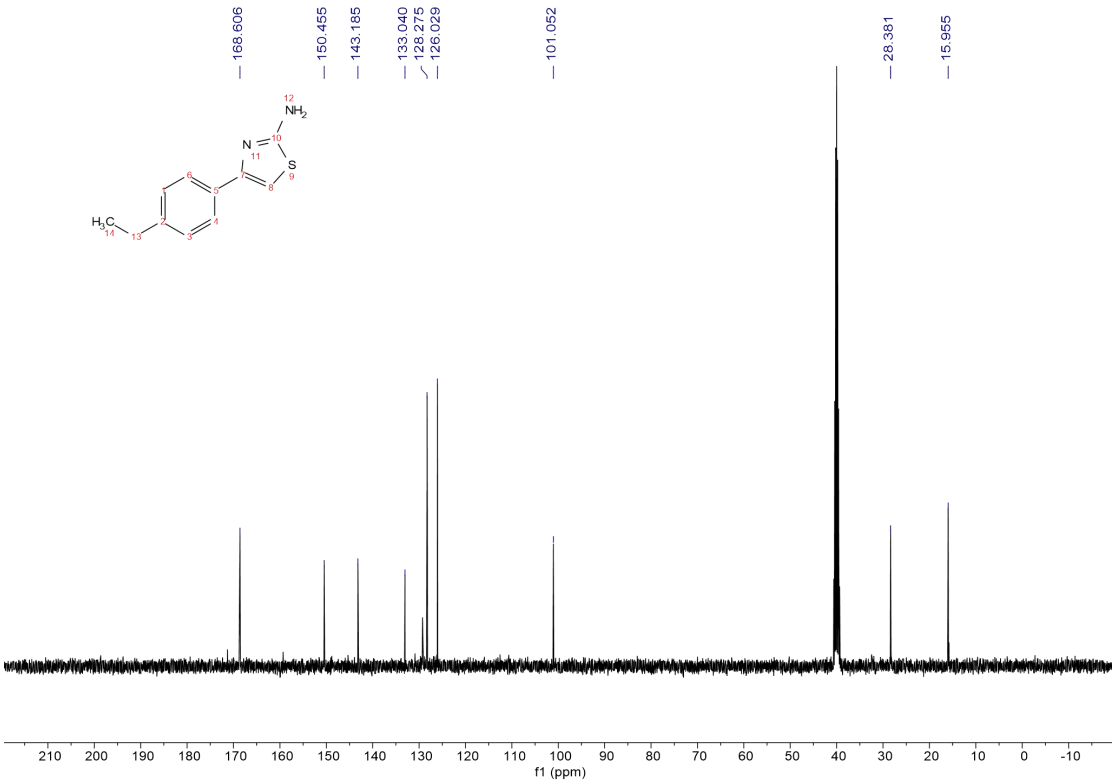
^{1}H NMR of **2i**



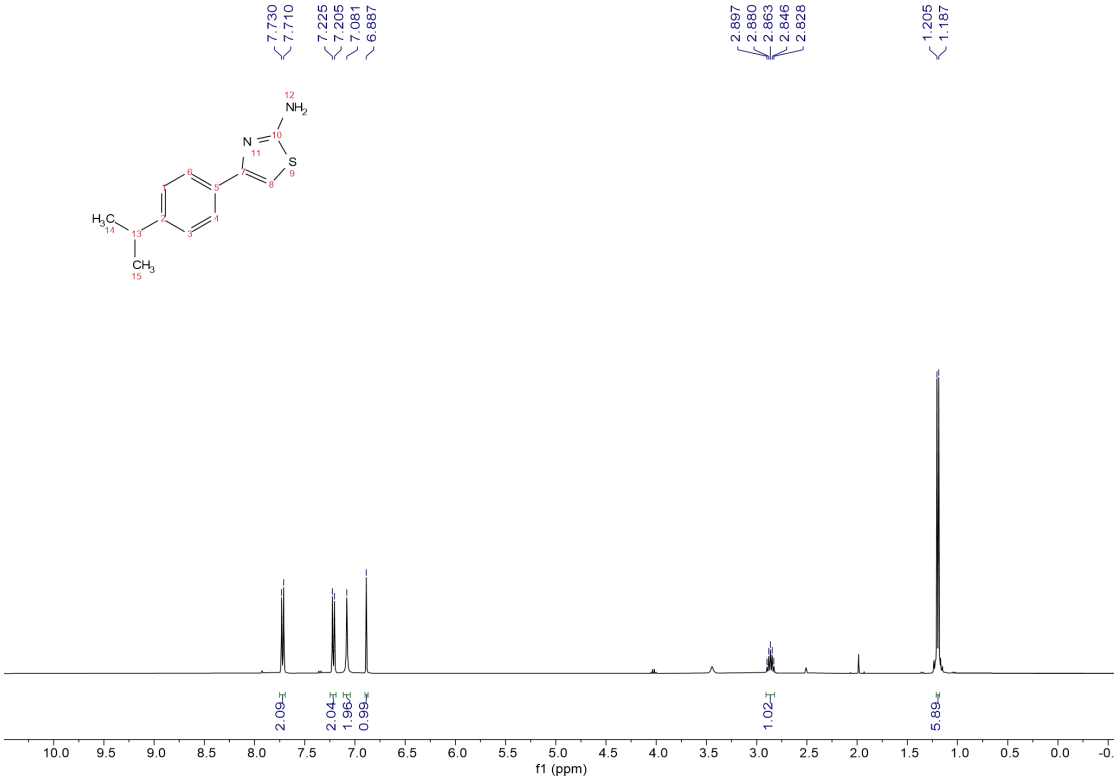
^{13}C NMR of **2i**



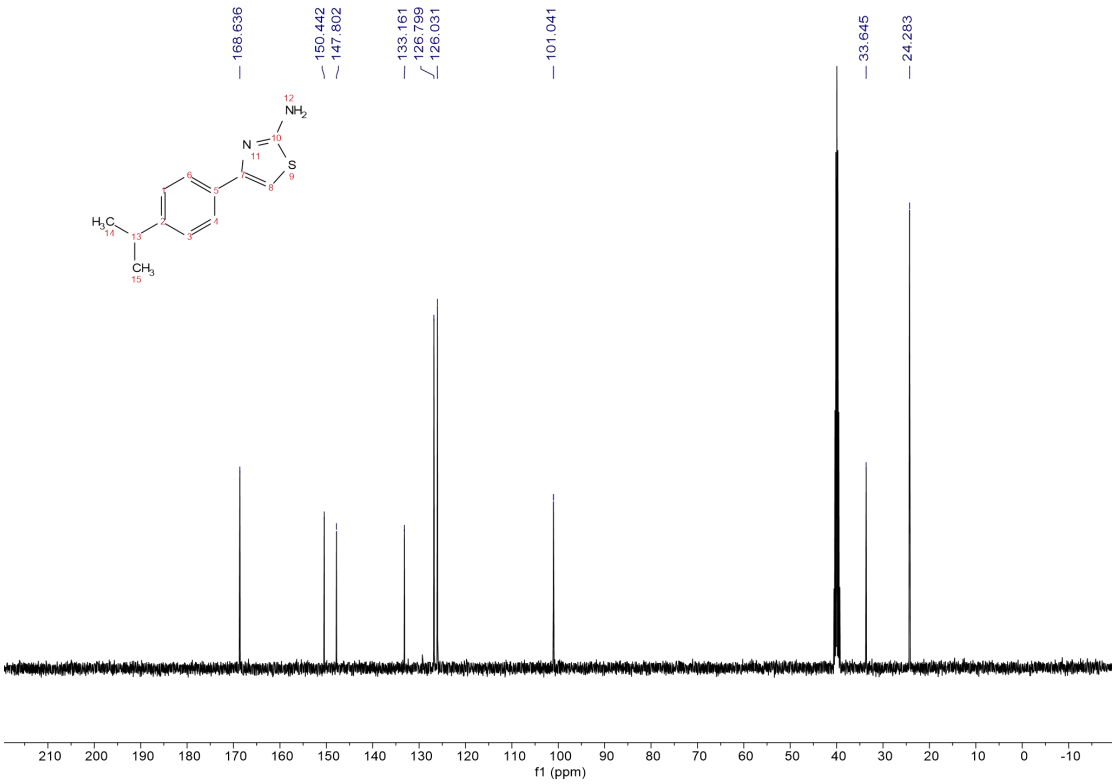
^{1}H NMR of **2j**



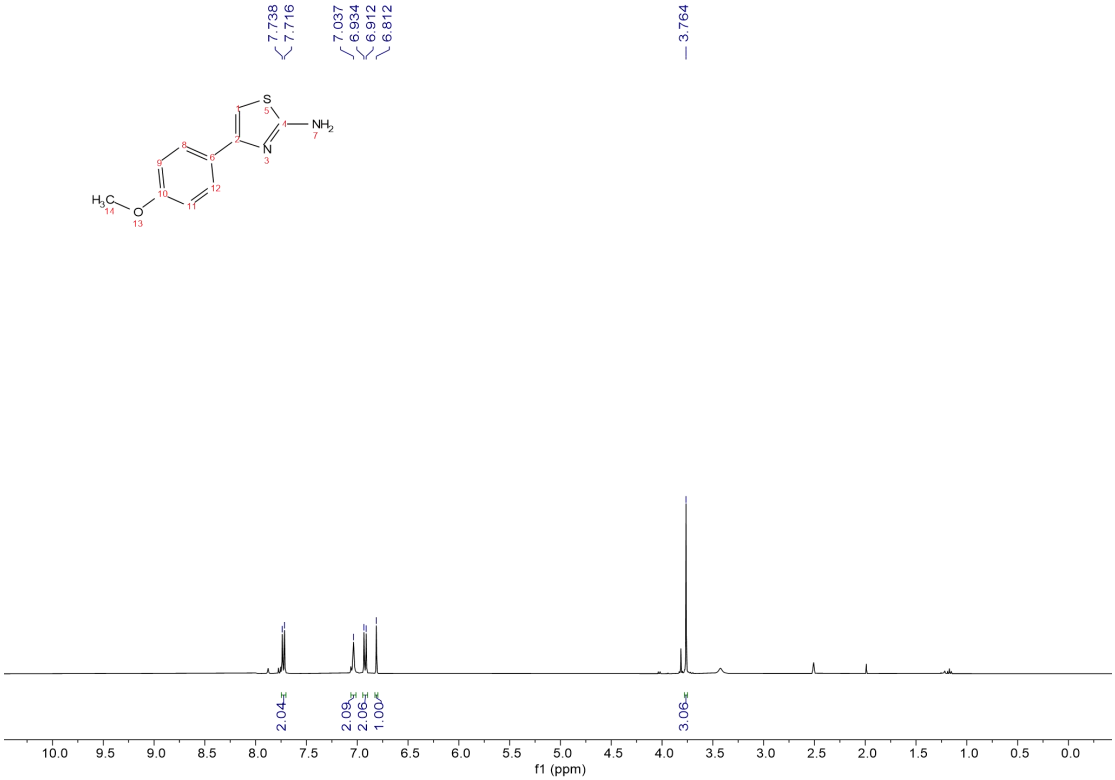
^{13}C NMR of **2j**



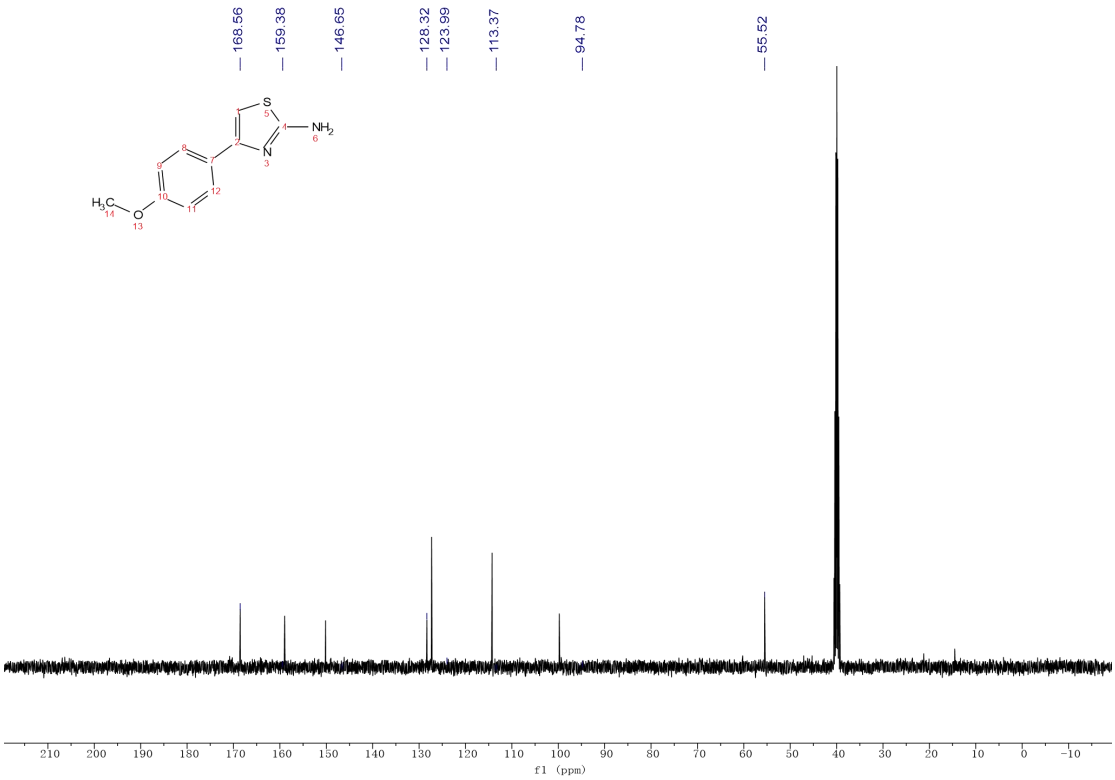
^{1}H NMR of **2k**



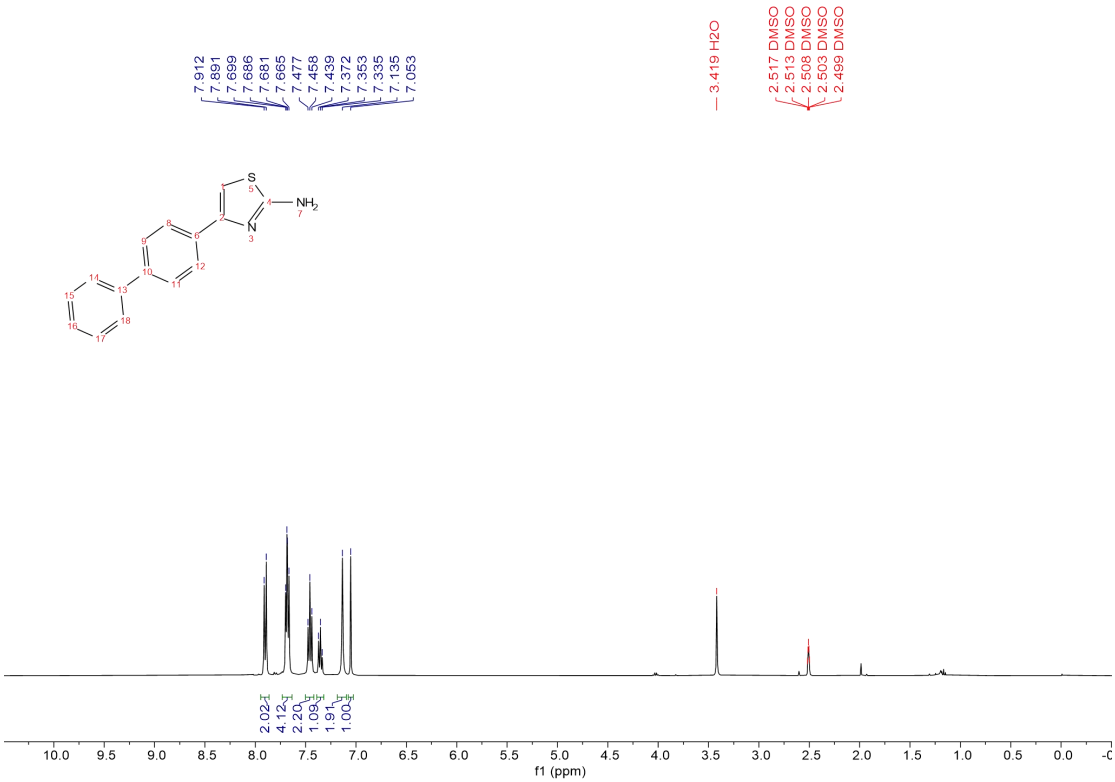
^{13}C NMR of **2k**



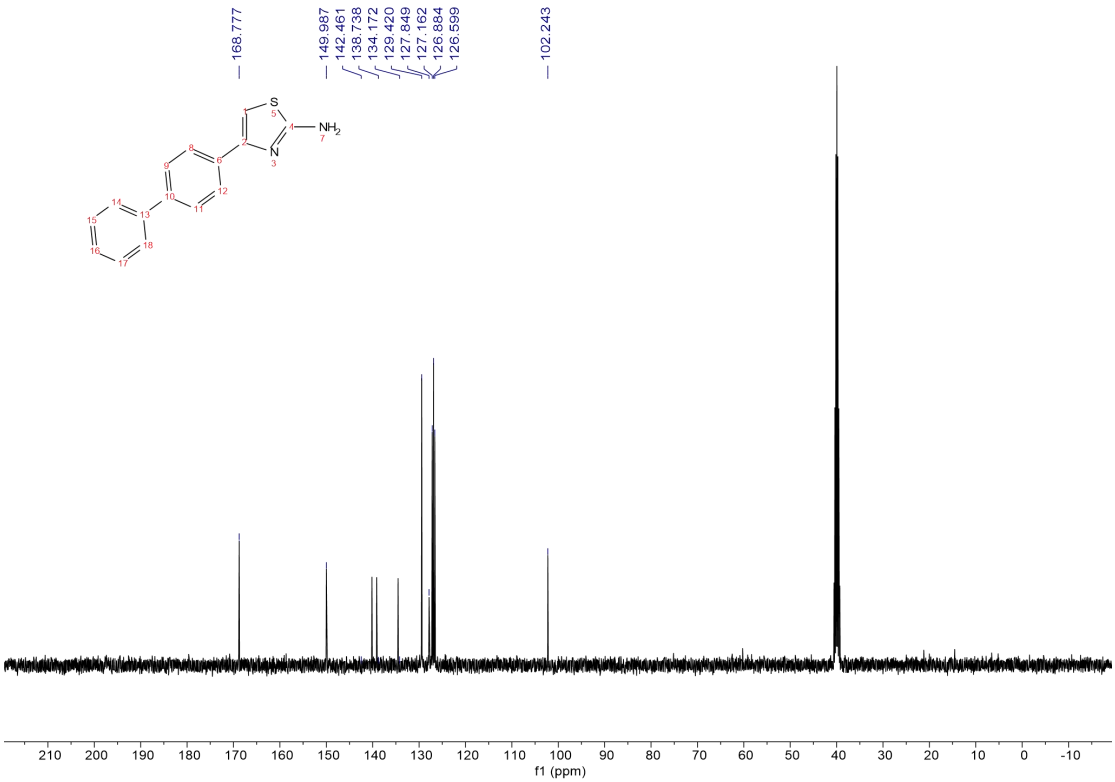
^{1}H NMR of **2l**



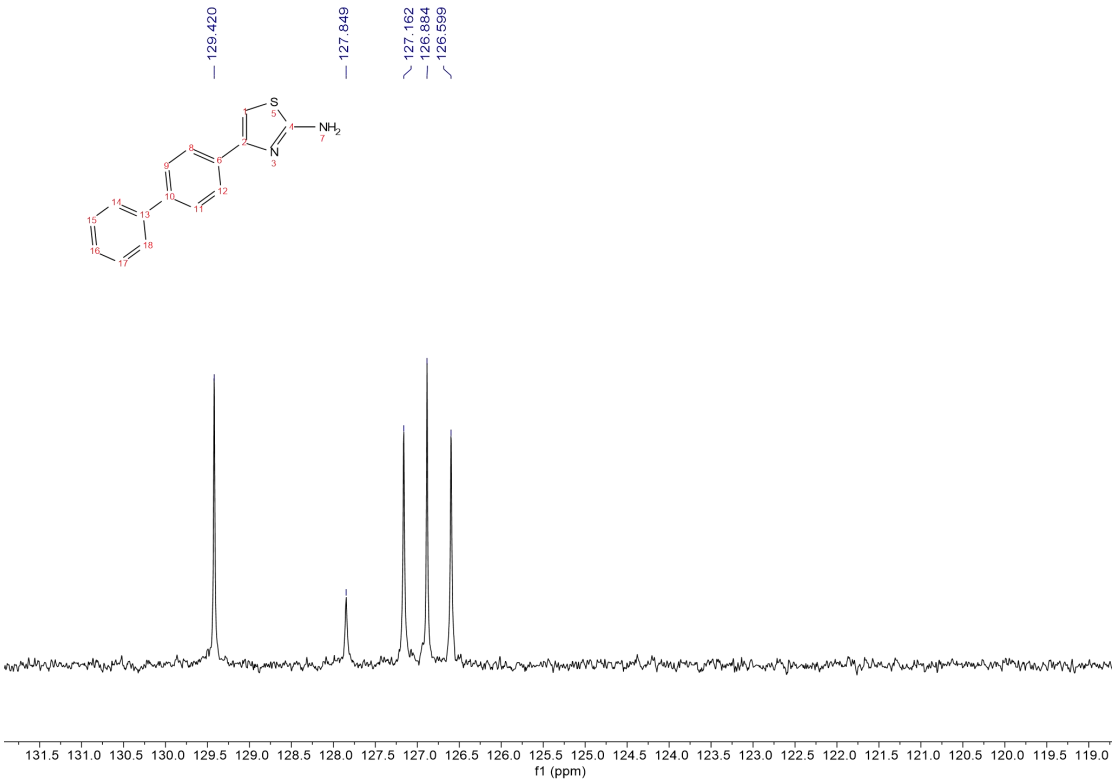
^{13}C NMR of **2l**



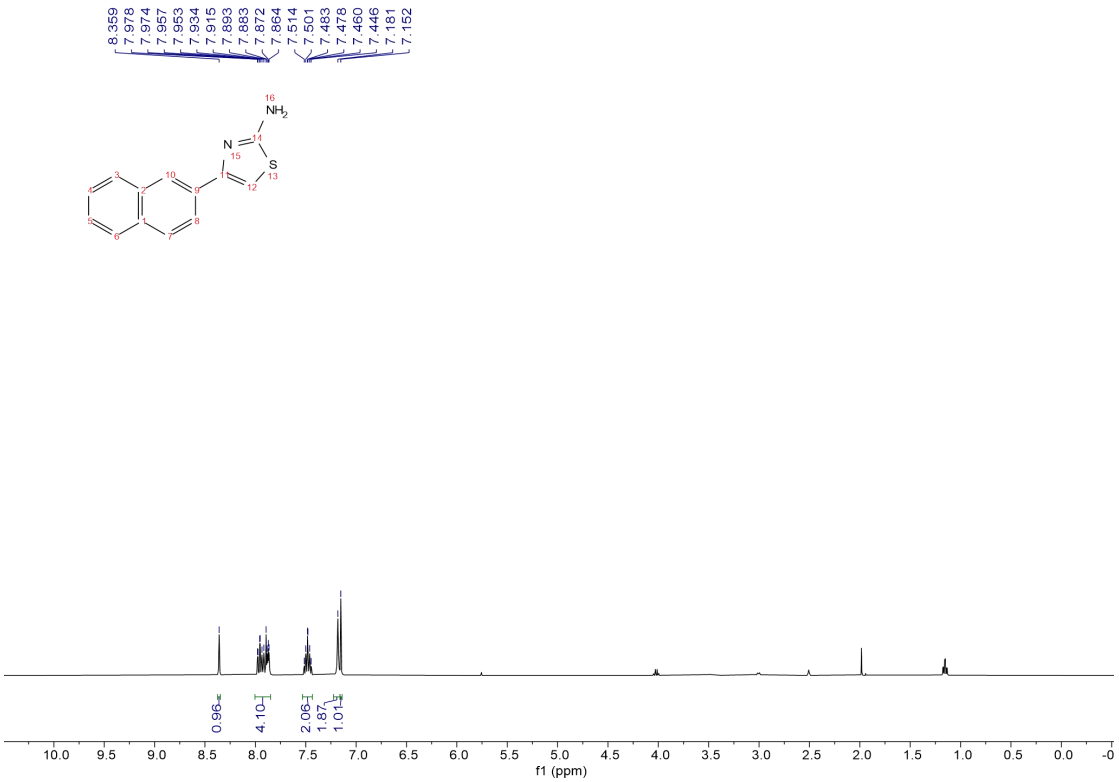
^{1}H NMR of **2m**



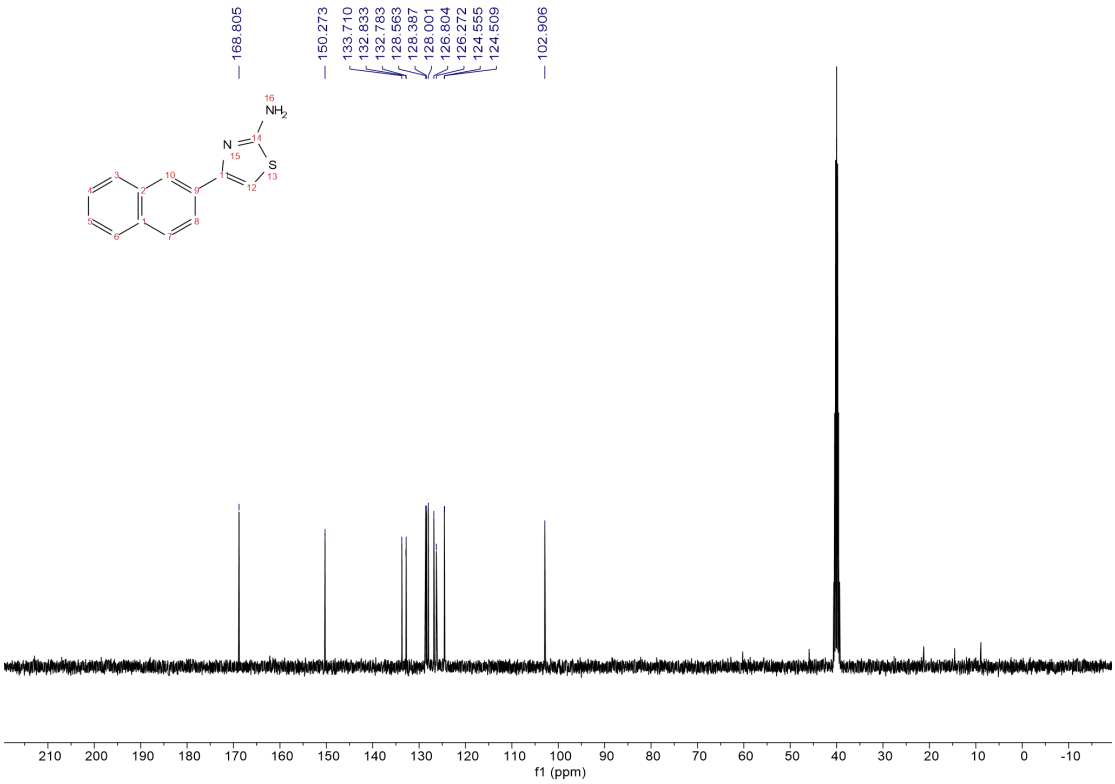
^{13}C NMR of **2m**



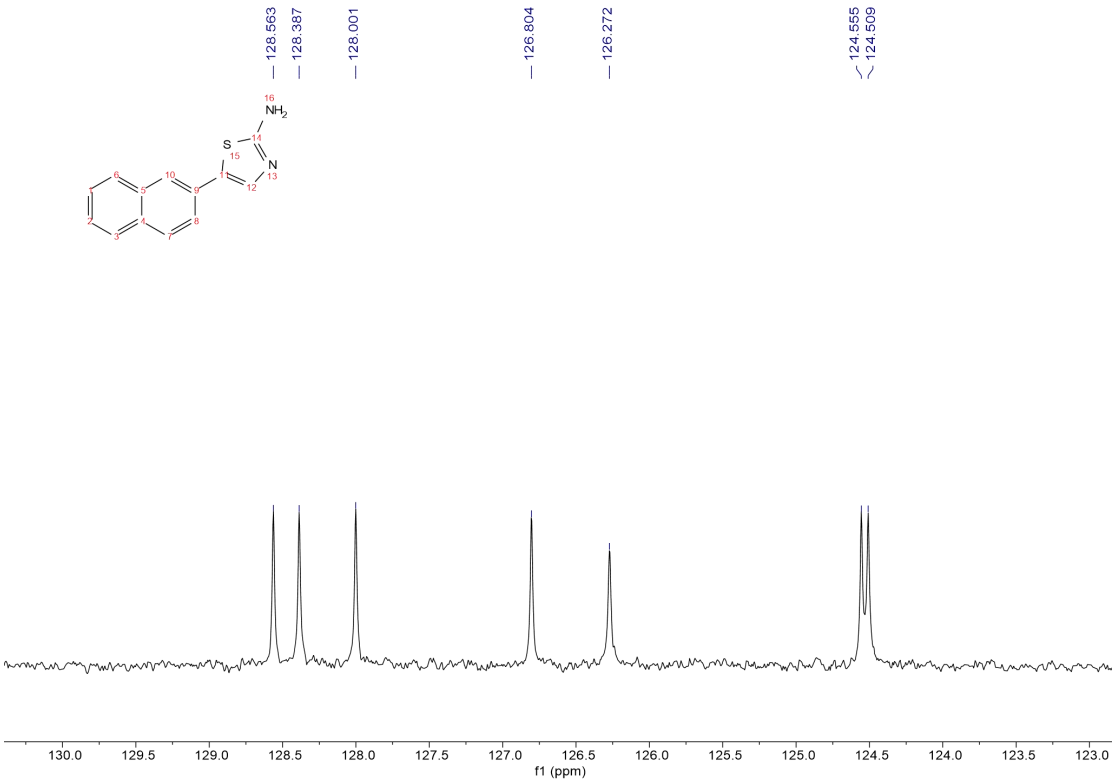
^{13}C NMR of **2m** (enlarged part)



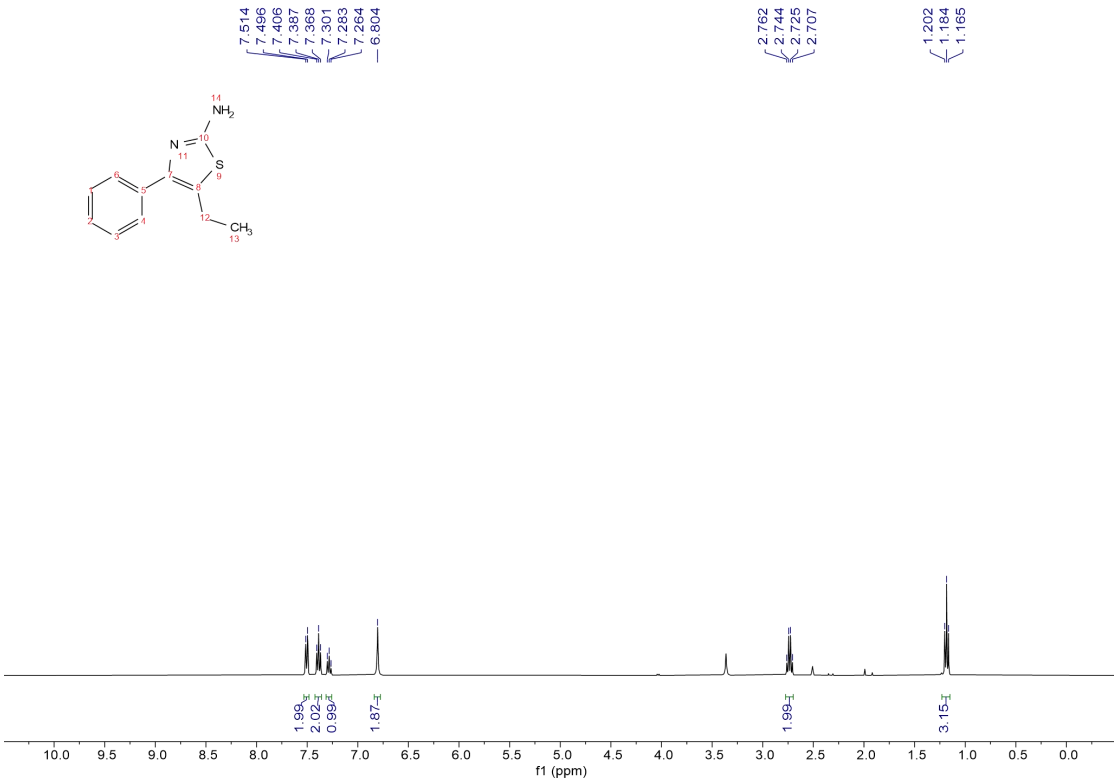
^{1}H NMR of **2n**



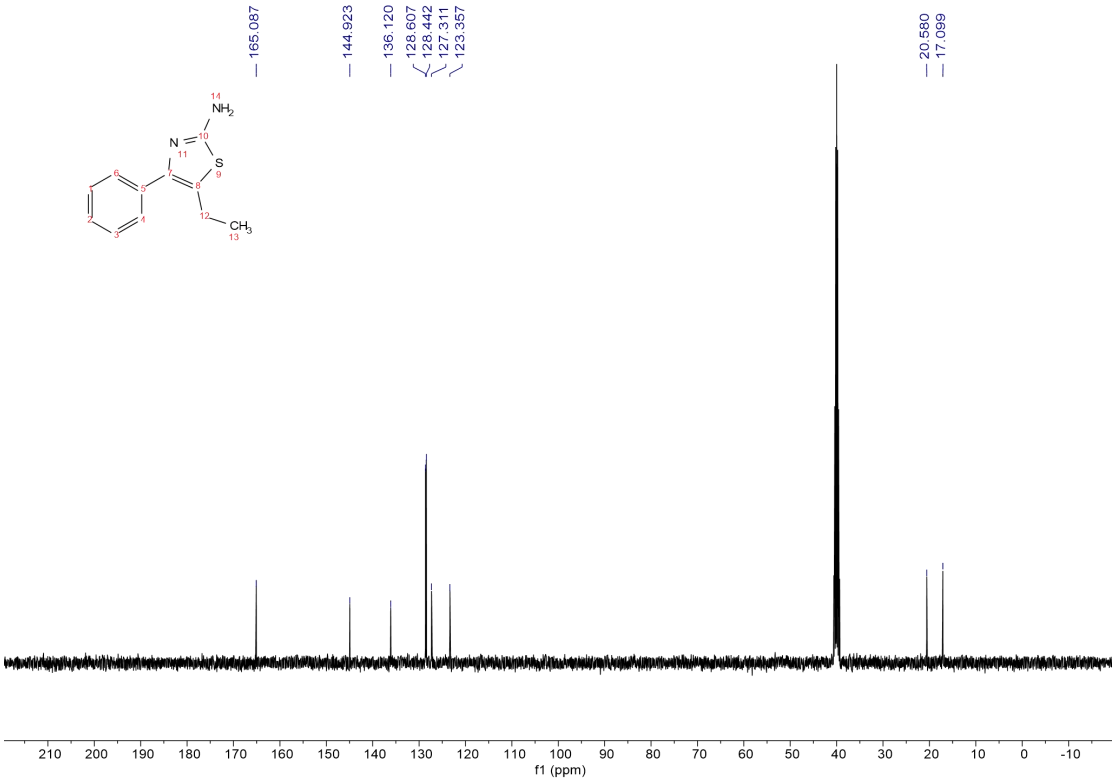
^{13}C NMR of **2n**



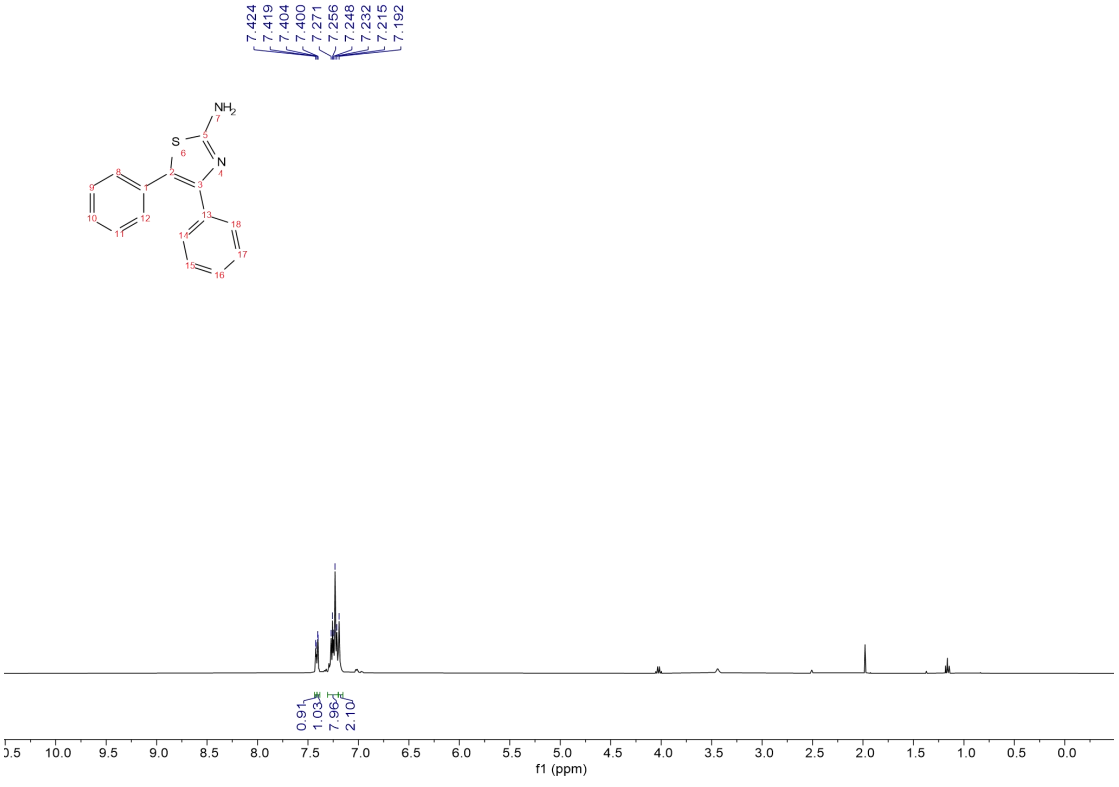
^{13}C NMR of **2n** (enlarged part)



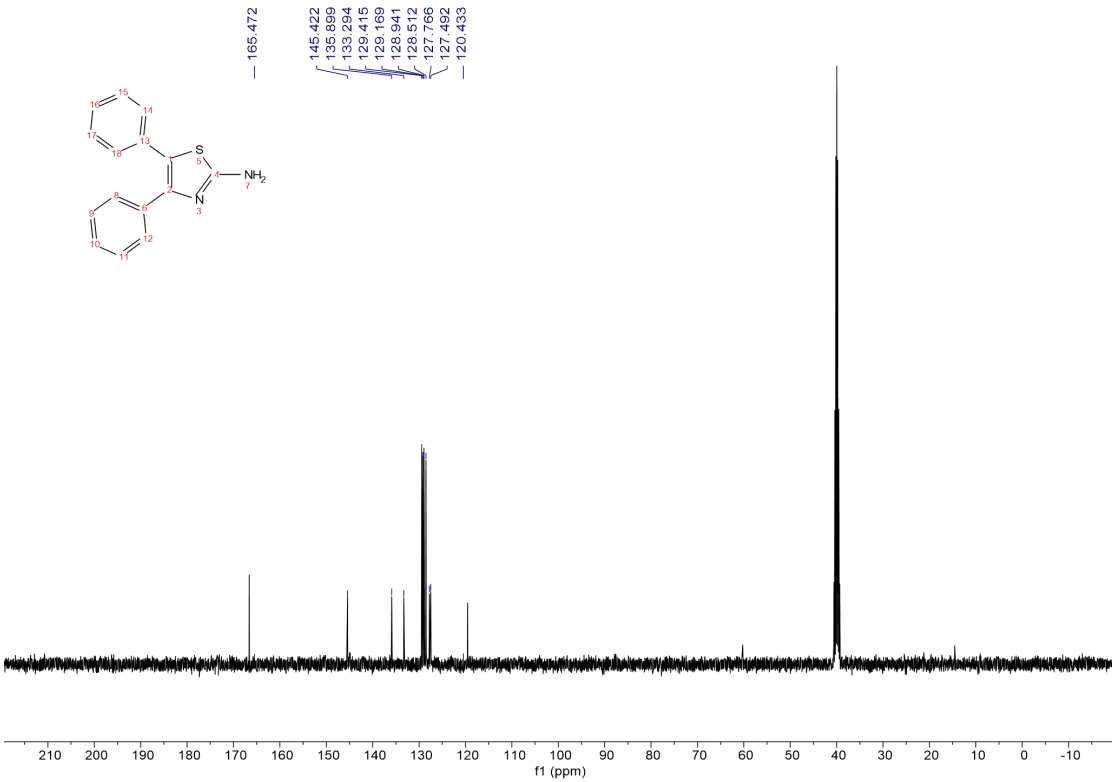
^{1}H NMR of **2o**



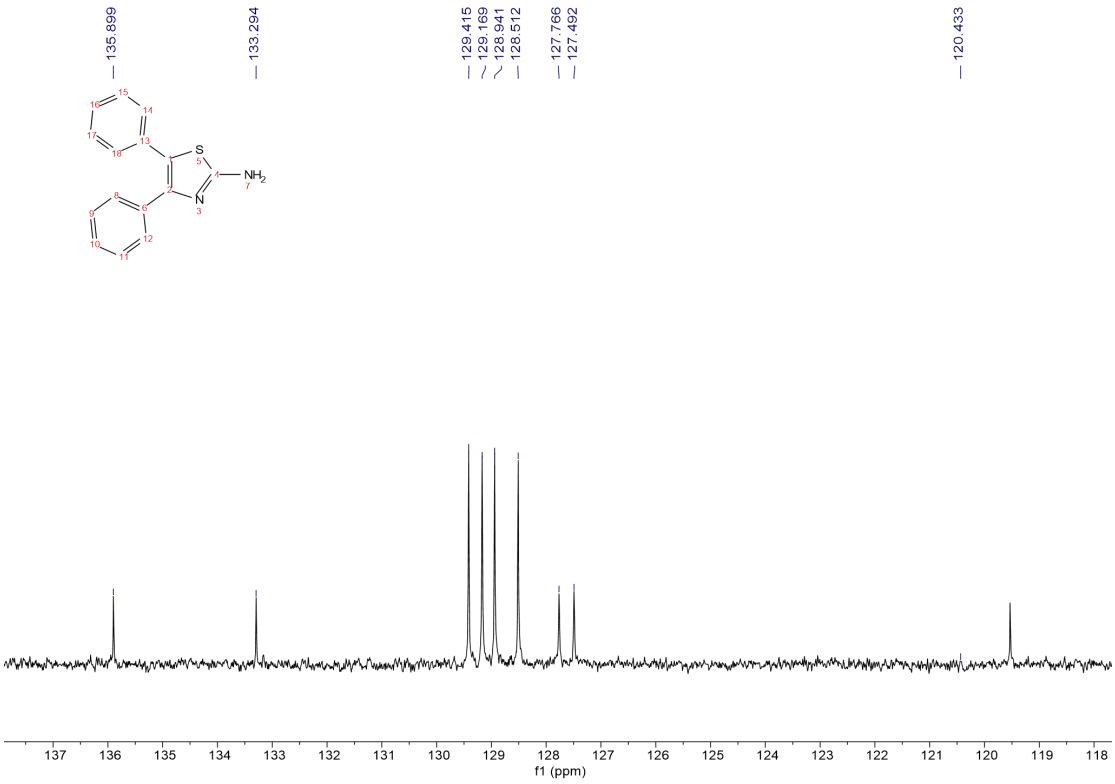
^{13}C NMR of **2o**



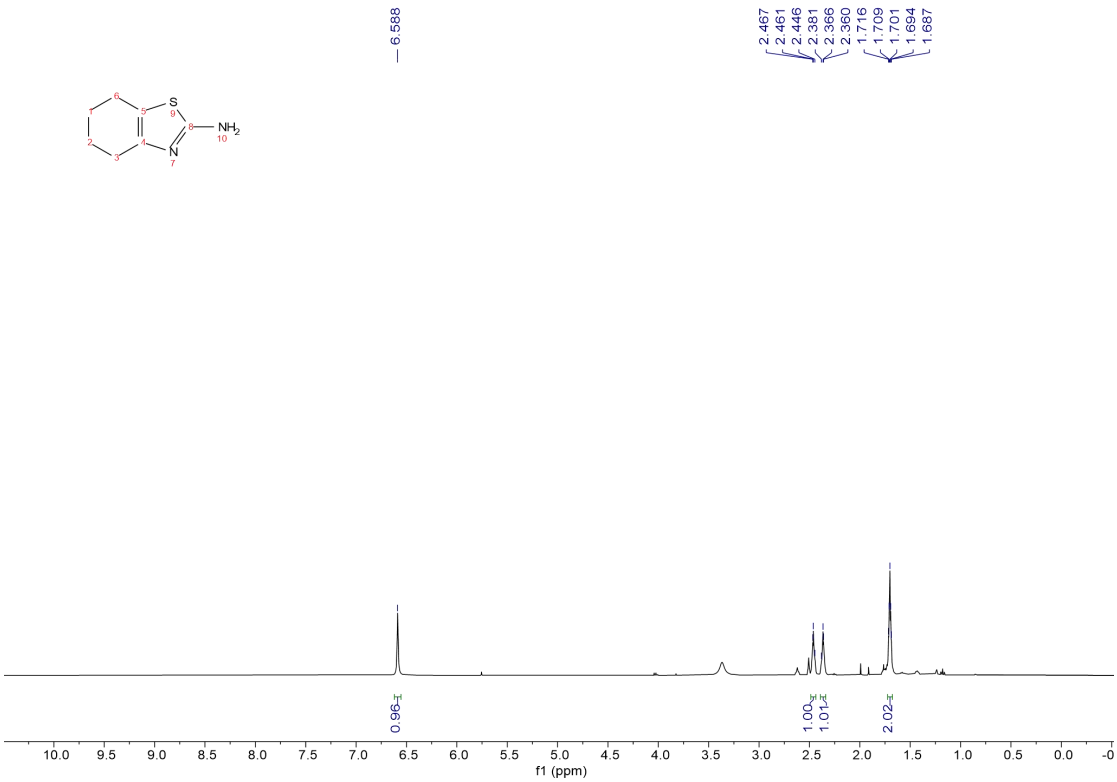
^{1}H NMR of **2p**



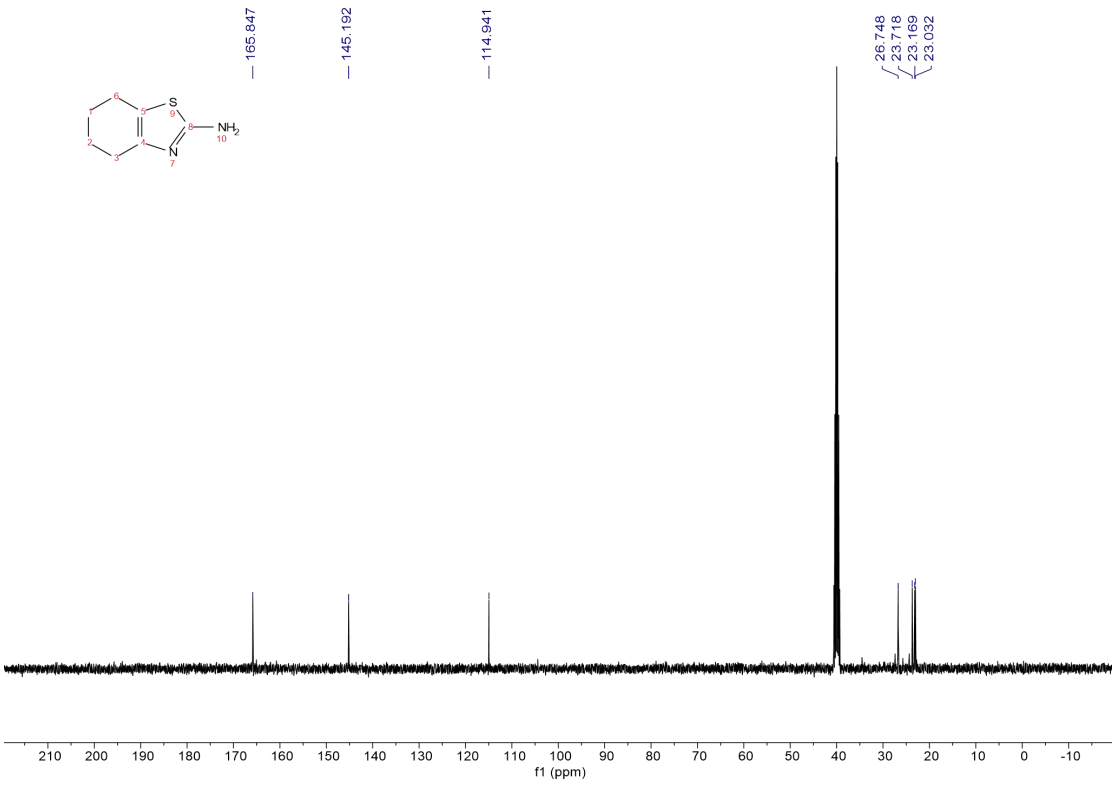
^{13}C NMR of **2p**



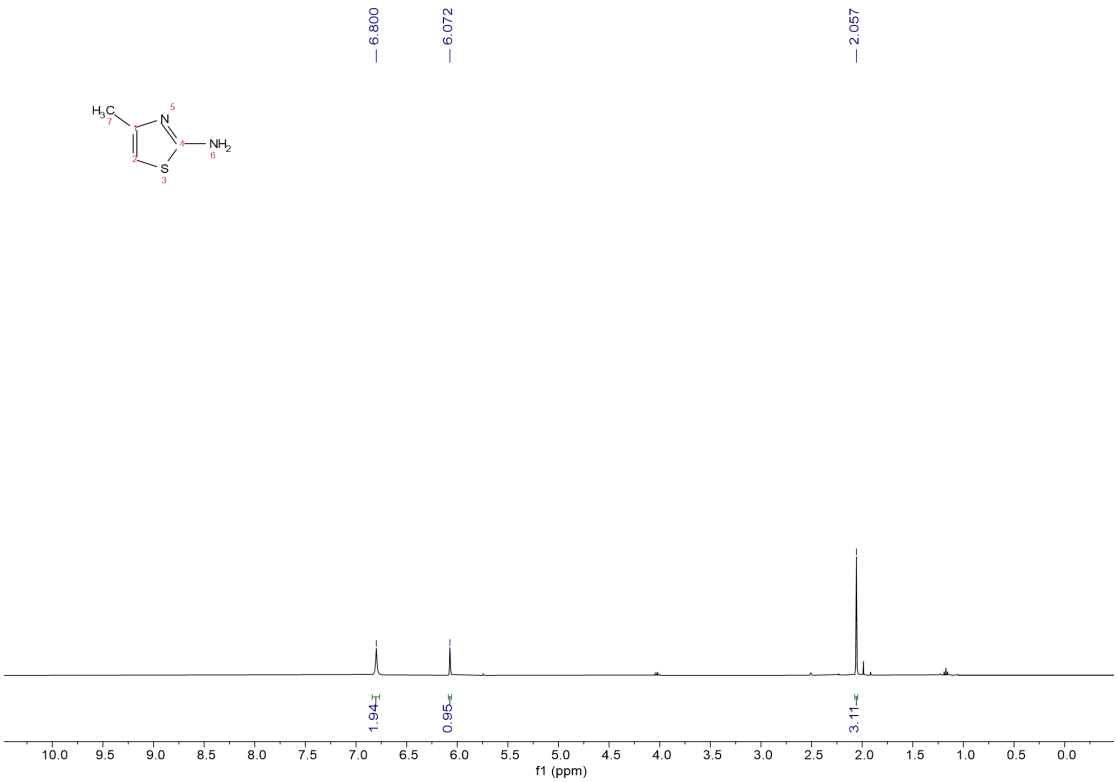
^{13}C NMR of **2p** (enlarged part)



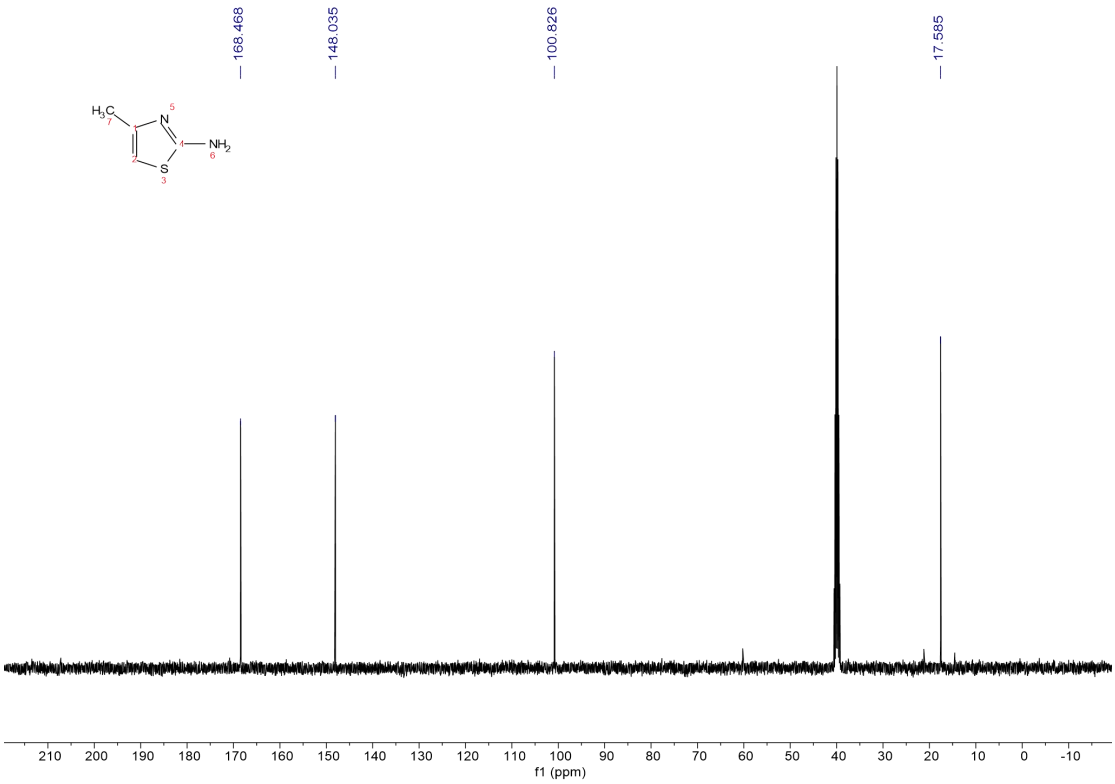
^{1}H NMR of **2q**



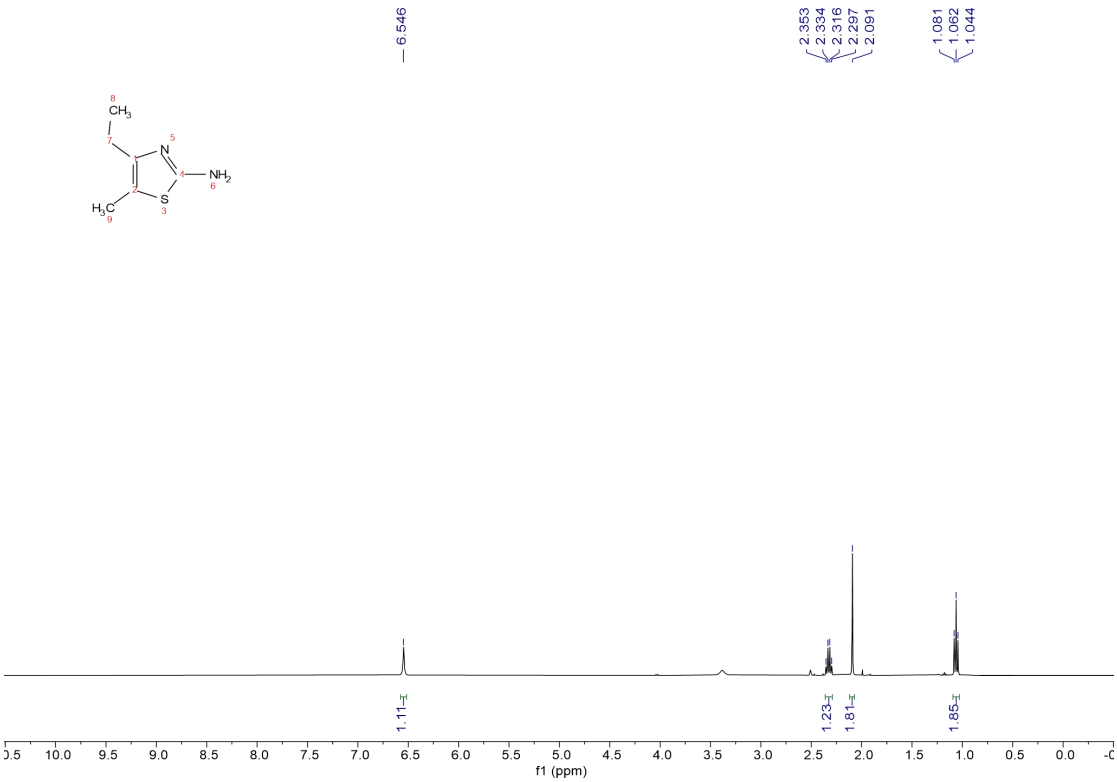
^{13}C NMR of **2q**



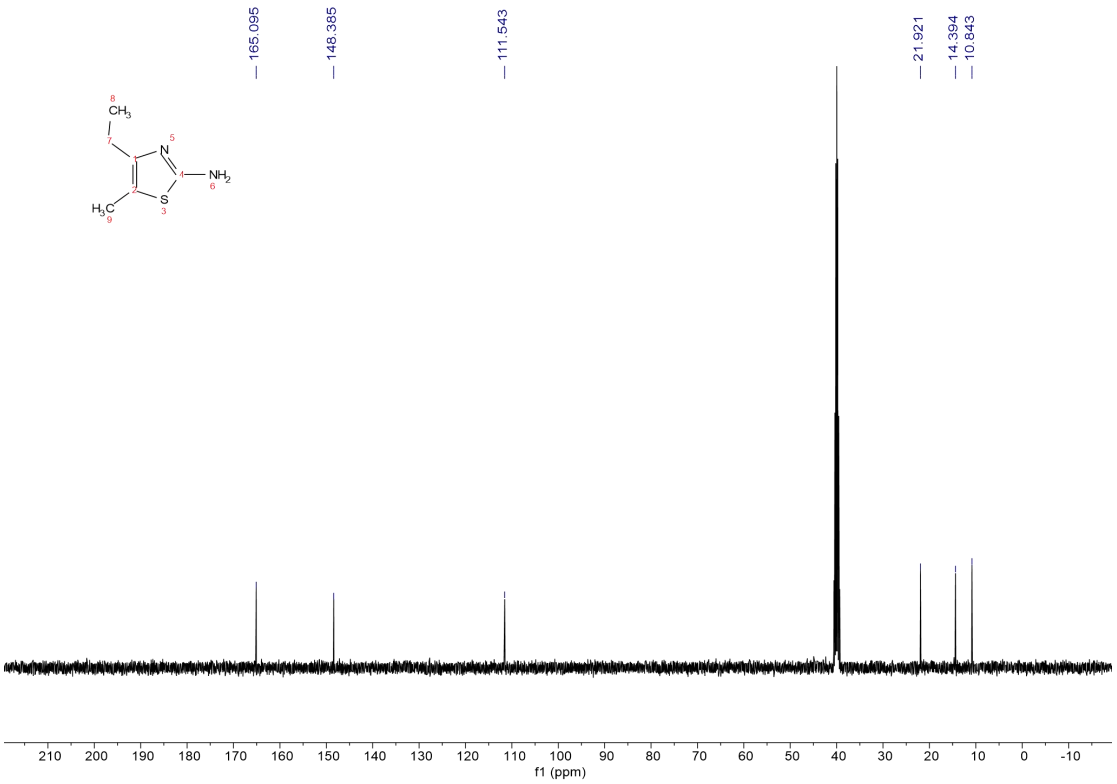
^{1}H NMR of **2r**



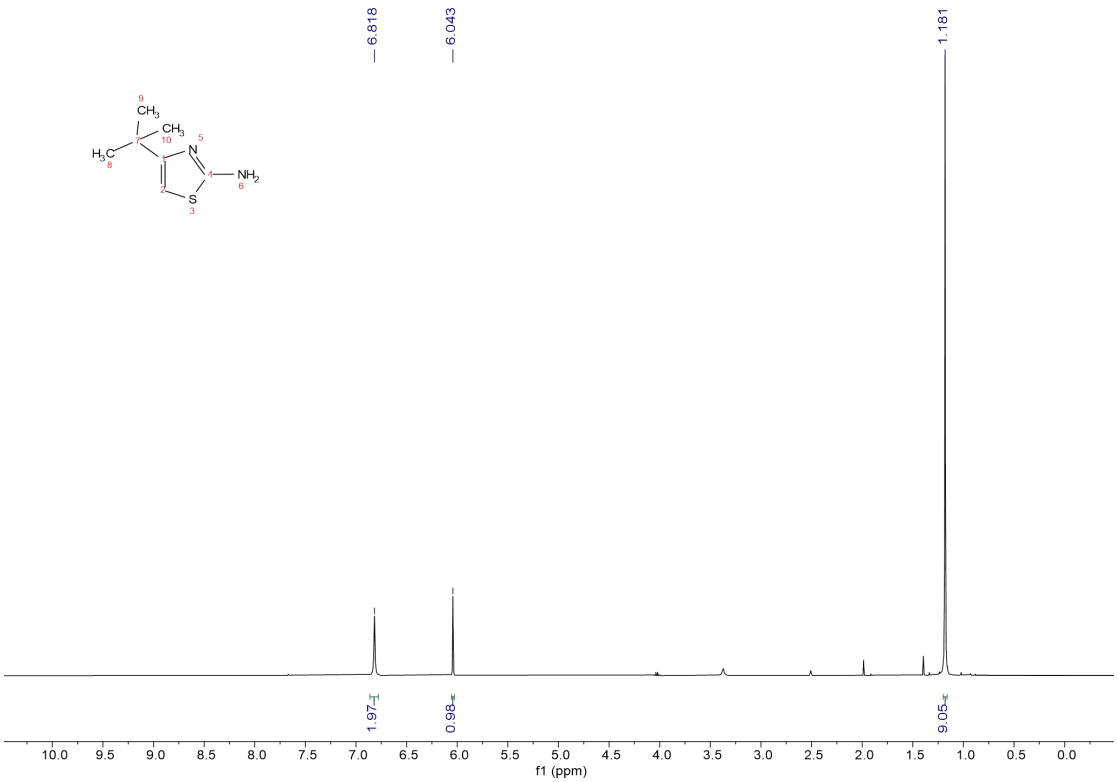
^{13}C NMR of **2r**



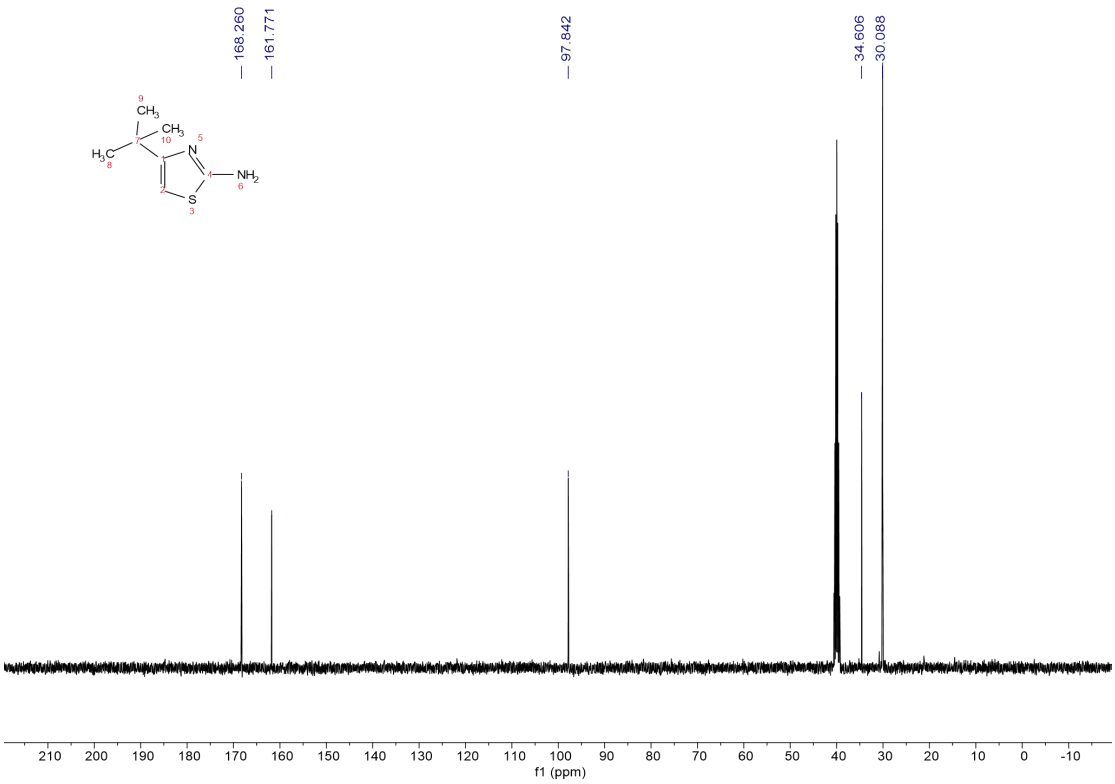
^{1}H NMR of **2s**



^{13}C NMR of **2s**



^{1}H NMR of **2t**



^{13}C NMR of **2t**