

Synthesis of Dihydrothiophenes or Spirocyclic Compounds by Domino Reactions of 1,3-Thiazolidinedione

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Supporting Information

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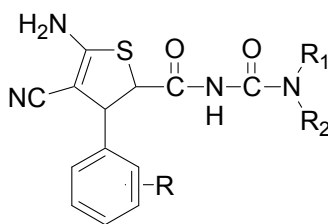
General Experimental Methods and

Characterization of compounds **9-67**

X-Ray Crystallographic Data **CIF in separate file.**

Crystallographic data (**1e**: CCDC 710889; **2a**: CCDC 710890; **2b**: CCDC 710891; **3b**: CCDC 710893; **3g**: CCDC 710892; **4d**: CCDC 710894; **5f**: CCDC 710895; **6b**: CCDC 710896; **7b**: CCDC 711371; **7c**: CCDC 7111257; **7h**: CCDC 711258.) have been deposited at the Cambridge Crystallographic Database Centre and is available on request from the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or [www:http//www.ccdc.cam.ac.uk](http://www.ccdc.cam.ac.uk)).

Scheme 1 Synthetic dihydrothiophene ureidoformamides **2a-2g**, **3a-3j**, **4a-4g** and **5a-5h**



2a-2g: R₁, R₂ = CH₃, R = H, 4-CH₃, 4-OCH₃, 4-F, 4-Cl, 4-Br, 3-NO₂

3a-3j: R₁, R₂ = (CH₂)₂, R = H; 4-CH₃; 4-CH(CH₃)₂; 4-OCH₃; 4-OH; 4-OH-3-OCH₃; 4-F; 4-Cl; 4-Br; 3-NO₂

4a-4g: R₁, R₂ = (CH₂CH₂)₂O, R = H; 4-CH₃; 4-OCH₃; 4-F; 4-Cl; 4-Br; 3-NO₂

5a-5h: R₁ = H, R₂ = CH₂Ph; R = H; 4-CH₃; 4-CH(CH₃)₂; 4-OCH₃; 4-F; 4-Cl; 4-Br; 3-NO₂

SCHEME 2. Formation mechanism for dihydrothiophene and spirocyclohexano-1,3-thiazole

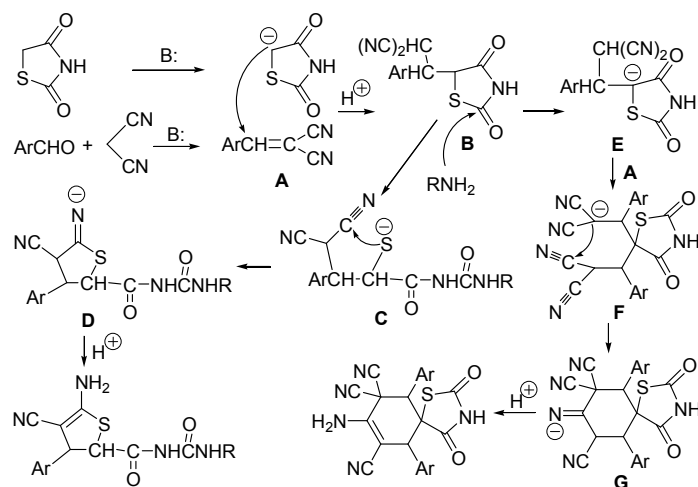


TABLE 1. The results of one-pot four-component reactions

Reaction scheme: $\text{Ar-CHO} + \text{NC-CH}_2\text{-CN} + \text{Cyclic Amine} + \text{Cyclic Thiourea} \xrightarrow[\text{RT}]{\text{CH}_3\text{CN}}$ Product

Entry	Compd	Ar	Yield (%)
1	1a	Ph	41
2	1b	<i>p</i> -CH ₃ C ₆ H ₄	31
3	1c	<i>p</i> - <i>i</i> -PrC ₆ H ₄	45
4	1d	<i>p</i> -HOC ₆ H ₄	32
5	1e	<i>p</i> -CH ₃ OC ₆ H ₄	48
6	1f	4-HO-3-CH ₃ OC ₆ H ₄	56
7	1g	<i>p</i> -FC ₆ H ₄	43
8	1h	<i>p</i> -ClC ₆ H ₄	35
9	1i	<i>p</i> -BrC ₆ H ₄	49
10	1j	<i>p</i> -NO ₂ C ₆ H ₄	27
11	1k	<i>m</i> -NO ₂ C ₆ H ₄	46

TABLE 2. The results of the four-component reactions with Et₂NH

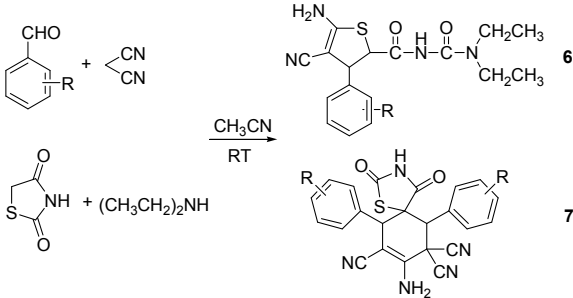
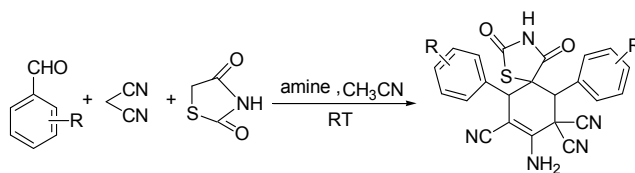
					
Entry	Ar	Compd	Yield (%)	Compd	Yield(%)
1	Ph	6a	34	7a	-
2	<i>p</i> -CH ₃ C ₆ H ₄	6b	11	7b	30
3	<i>p</i> - <i>i</i> -PrC ₆ H ₄	6c	10	7c	25
4	<i>p</i> -HOC ₆ H ₄	6d	35	7d	-
5	<i>p</i> -CH ₃ OC ₆ H ₄	6e	49	7e	-
6	4-HO-3-CH ₃ OC ₆ H ₄	6f	41	7f	-
7	<i>p</i> -FC ₆ H ₄	6g	27	7g	-
8	<i>m</i> -NO ₂ C ₆ H ₄	6h	45	7h	-
9	<i>p</i> -ClC ₆ H ₄	6i	-	7i	14
10	<i>p</i> -BrC ₆ H ₄	6j	-	7j	31

TABLE 3. Amine-catalyzed formation of spirocyclohexano-1,3-thiazole



Entry	amine	Ar	compd	Yield (%)
1	(iPr) ₂ NH	Ph	7a	35
2	DABCO	Ph	7a	30
3	DABCO	<i>p</i> -CH ₃ C ₆ H ₄	7b	29
4	(iPr) ₂ NH	<i>p</i> - <i>i</i> -PrC ₆ H ₄	7c	26
5	DABCO	<i>p</i> - <i>i</i> -PrC ₆ H ₄	7c	30
6	(iPr) ₂ NH	<i>p</i> -CH ₃ OC ₆ H ₄	7e	39
7	DABCO	<i>p</i> -CH ₃ OC ₆ H ₄	7e	42
8	DABCO	<i>p</i> -FC ₆ H ₄	7g	28
9	(iPr) ₂ NH	<i>p</i> -ClC ₆ H ₄	7i	25
10	DABCO	<i>p</i> -ClC ₆ H ₄	7i	48
11	(iPr) ₂ NH	<i>p</i> -BrC ₆ H ₄	7j	31
12	DABCO	<i>p</i> -BrC ₆ H ₄	7j	55

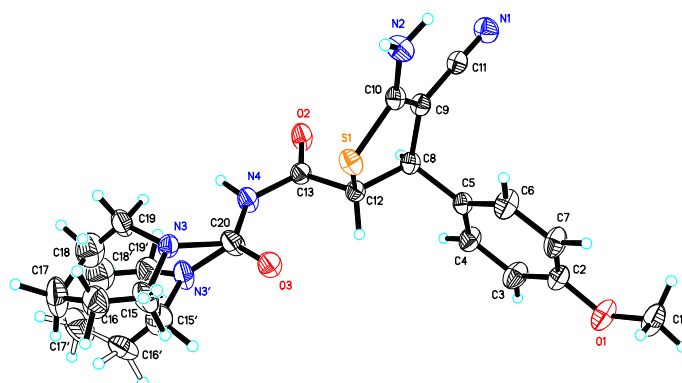


Figure S1 Crystal structure of the compound **1e**

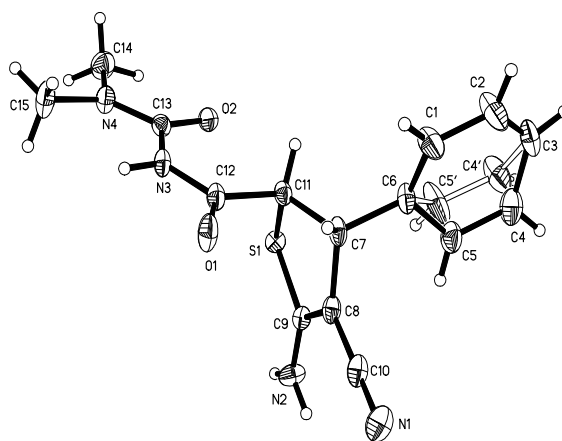


Figure S2 Crystal structure of the compound **2a**

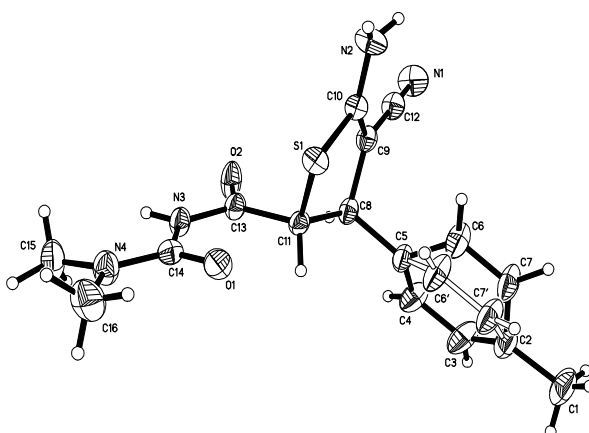


Figure S3 Crystal structure of the compound **2b**

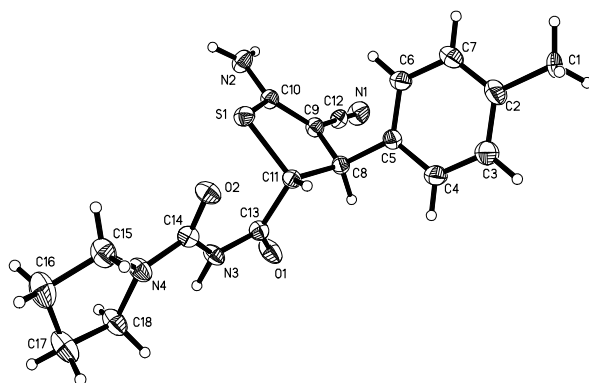


Figure S4 Crystal structure of the compound **3b**

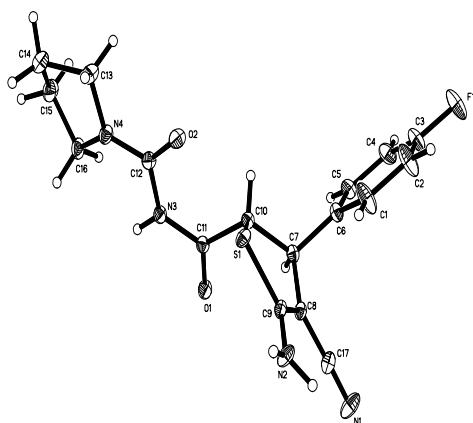


Figure S5 Crystal structure of the compound **3g**

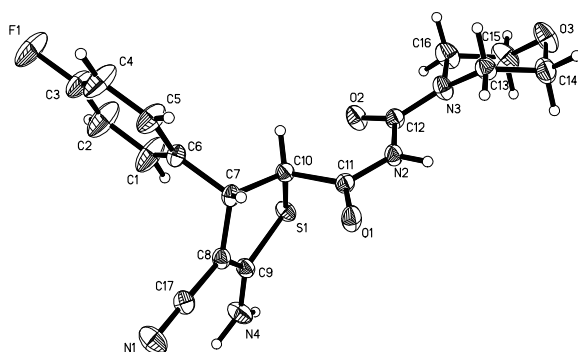


Figure S6 Crystal structure of the compound **4d**

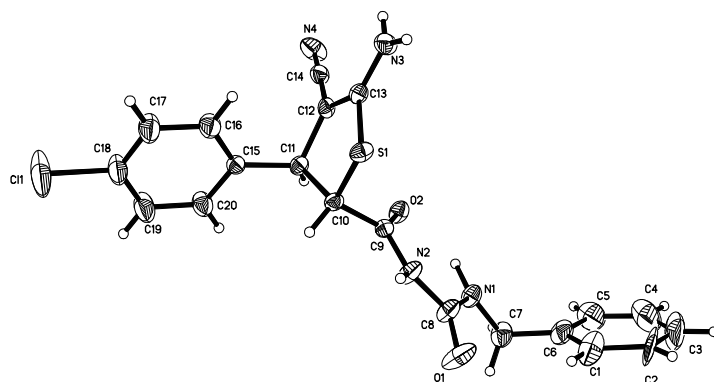


Figure S7 Crystal structure of the compound **5f**

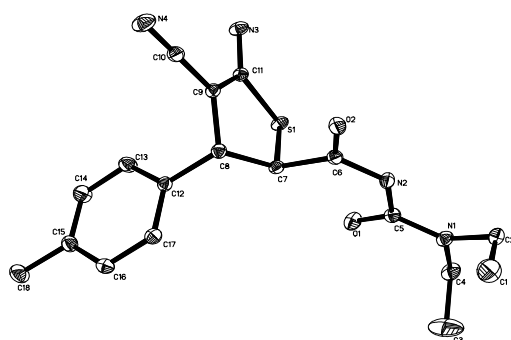


Figure S8 Crystal structure of the compound **6b**

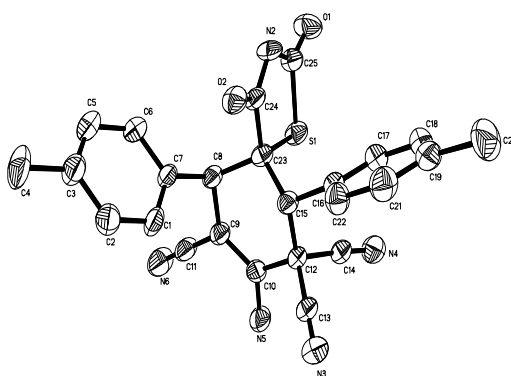


Figure S9 Crystal structure of the compound **7b**

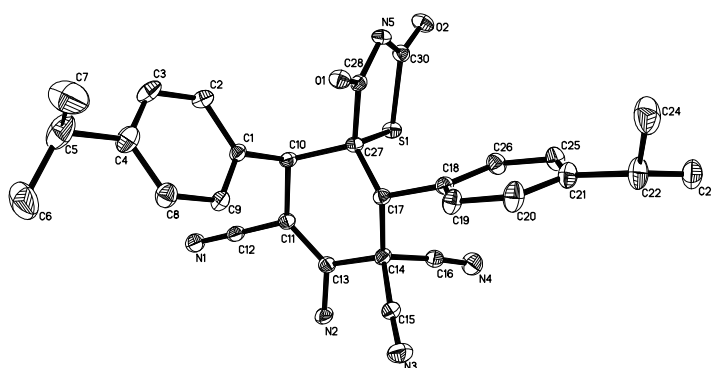


Figure S10 Crystal structure of the compound **7c**

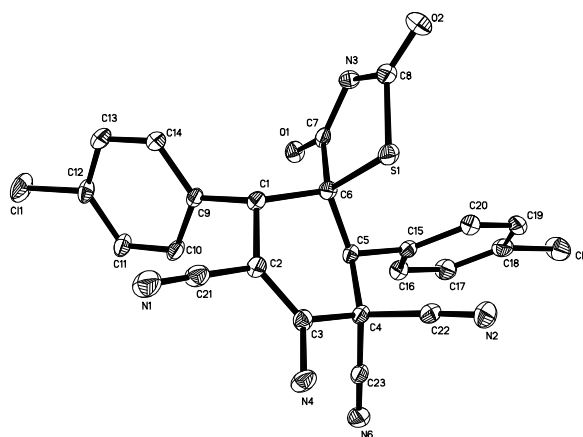
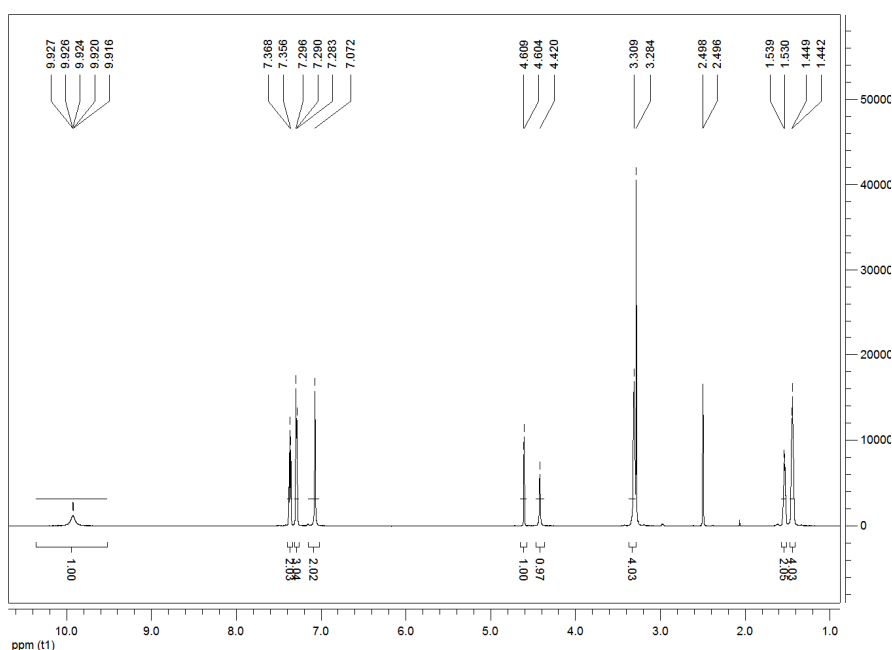


Figure S11 Crystal structure of the compound **7i**

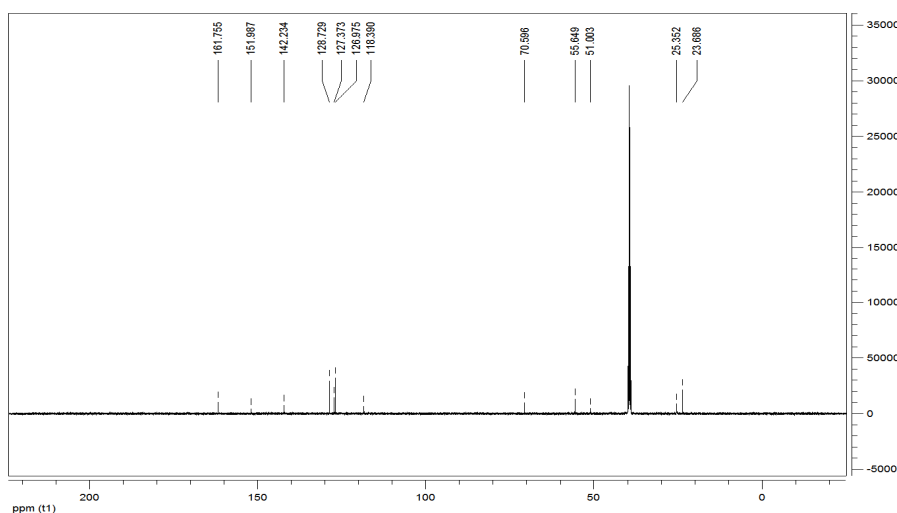
1. Typical preparation procedure of dihydrothiophenes by one-pot four-component reaction of 1,3-thiazolidinedione, benzaldehyde, malononitrile and piperidine: A mixture of benzaldehyde (4.0 mmol, 0.424g), malononitrile (4.0 mmol, 0.264 g) and piperidine (4.0 mmol, 0.350 g) in acetonitrile (5mL) was stirred at room temperature for two minutes. Then 1,3-thiazolidinedione (4.0mmol) was added and the reaction was stirred at room temperature for additional 48 hours. The resulting precipitate was collected by filtration and washed with acetonitrile. The crude product was recrystallized with a mixture of acetonitrile and N,N-dimethylformamide to give the pure product **1a**:

The same reaction procedure was carried out by using other aromatic aldehydes and other amine to substitute piperidine to give products **1b-1k**, **2a-2g**, **3a-3j**, **4a-4g**, **5a-5h**.

1a: white solid, 41%, m.p. 220~222 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 9.93 (s, 1H, NH), 7.38~7.36 (m, 2H, ArH), 7.30~7.28 (m, 3H, ArH), 7.07 (s, 2H, NH_2), 4.60 (d, $J = 3\text{ Hz}$, 1H, CH), 4.20 (s, 1H, CH), 3.33~3.29 (m, 4H, NCH_2), 1.57~1.51 (m, 2H, CH_2), 1.45~1.44 (m, 4H, CH_2); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 161.8, 152.0, 142.2, 128.7, 127.4, 127.0, 118.4, 70.6, 55.6, 51.0, 25.4, 23.7; IR(KBr) ν : 3667, 3399, 3306, 3194, 2942, 2855, 2195, 1686, 1654, 1587, 1491, 1449, 1246, 1137, 1025, 998, 751 cm^{-1} ; MS(m/z): 355.53 ($[\text{M}-1]^+$) 100%; Anal Calcd for $\text{C}_{18}\text{H}_{20}\text{N}_4\text{O}_2\text{S}$: C 60.65, H 5.66, N 15.72; Found: C 60.83, H 5.38, N 15.54.



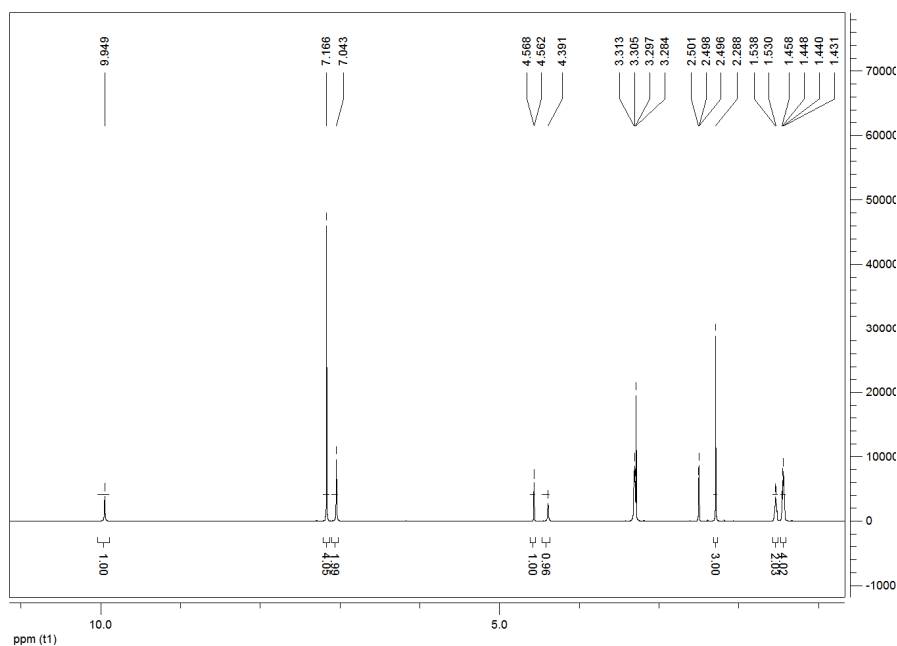
^1H NMR of **1a** (600 MHz, $\text{DMSO}-d_6$)



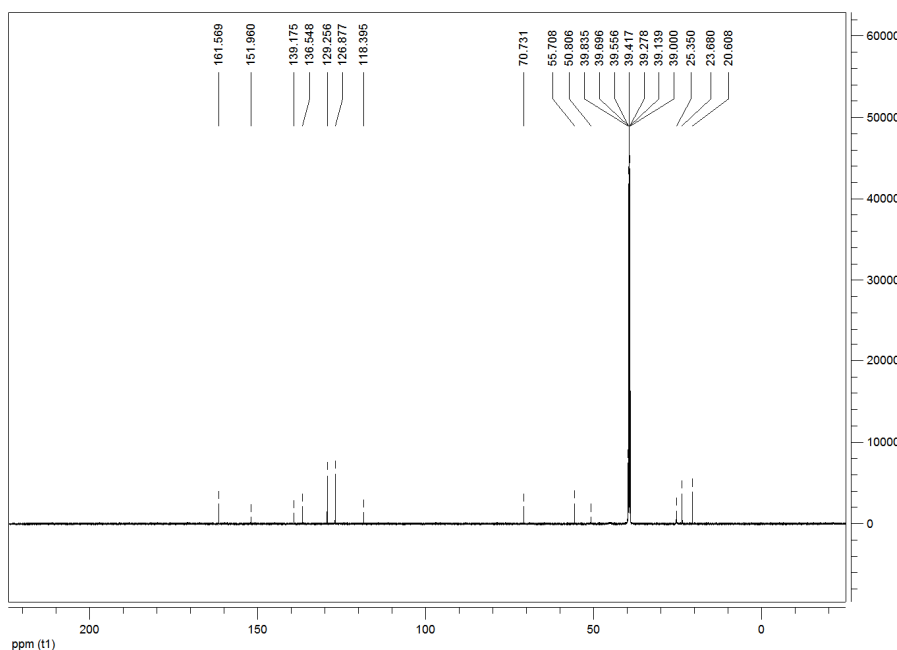
^{13}C NMR of **1a** (150 MHz, $\text{DMSO}-d_6$)

1b: white solid, 31%, m.p. 202~204 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 9.95 (s, 1H, NH), 7.17 (s, 4H, ArH), 7.04 (s, 2H, NH_2), 4.56 (d, $J = 3.6\text{ Hz}$, 1H, CH), 4.39 (s, 1H, CH), 3.31~3.30 (m,

4H, 2CH₂), 2.29 (s, 3H, CH₃), 1.54–1.52 (m, 2H, CH₂), 1.46–1.43 (m, 4H, 2CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 161.6, 152.0, 139.2, 136.6, 129.3, 126.9, 118.4, 70.7, 55.7, 50.8, 25.4, 23.7, 20.6; IR(KBr) ν: 3409, 3287, 3220, 3022, 2924, 2859, 2175, 1681, 1625, 1580, 1474, 1346, 1245, 1201, 1120, 1021, 994, 955, 879, 851, 811, 773, 740; MS(*m/z*): 369.33 ([M-1]⁺) 100%; Anal Calcd for C₁₉H₂₂N₄O₂S: C 61.60, H 5.99, N 15.12; Found: C 61.49, H 5.71, N 14.83.



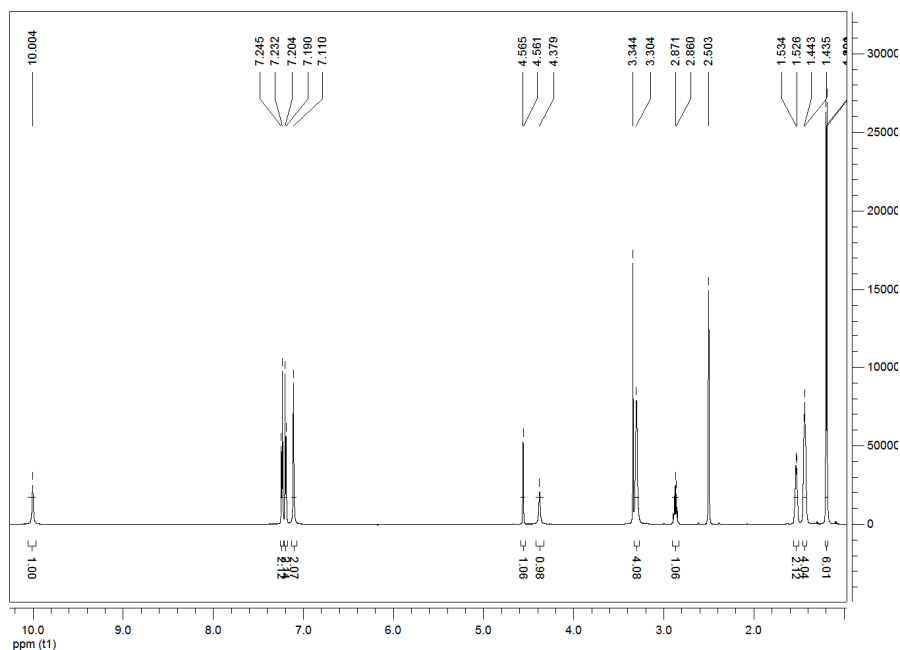
¹H NMR of **1b** (600 MHz, DMSO-*d*₆)



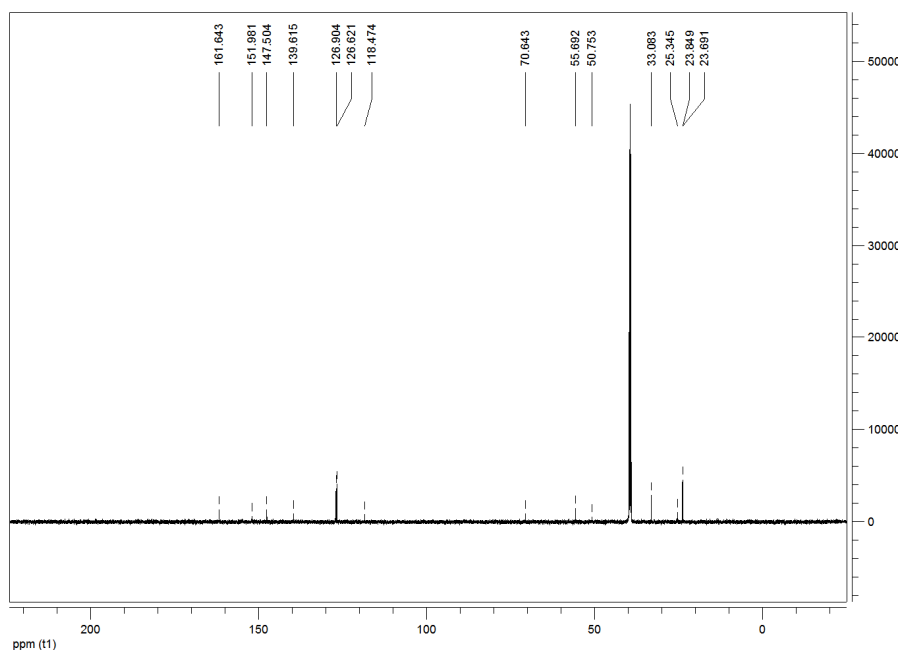
¹³C NMR of **1b** (150 MHz, DMSO-*d*₆)

1c: white solid, 45%, m.p. 214–216 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 10.00 (s, 1H, NH), 7.24 (d, *J* = 7.8 Hz, 2H, ArH), 7.20 (d, *J* = 7.8 Hz, 2H, ArH), 7.11 (s, 2H, NH₂), 4.56 (s, 1H, CH),

4.38 (s, 1H, CH), 3.33~3.27 (m, 4H, CH₂), 2.90~2.84 (m, 1H, CH), 1.53 (m, 2H, CH₂), 1.44 (m, 4H, CH₂); ¹³CNMR (150 MHz, DMSO-*d*₆) δ: 161.6, 152.0, 147.5, 139.6, 126.9, 126.6, 118.5, 70.6, 55.7, 50.8, 33.1, 25.3, 23.8, 23.7; IR(KBr) ν: 3401, 3308, 3194, 2953, 2195, 1688, 1654, 1588, 1496, 1380, 1248, 1137, 1059, 1023, 893, 822, 740; MS(*m/z*): 397.40 ([M-1]⁺) 100%. Anal Calcd for C₂₁H₂₆N₄O₂S: C 63.29, H 6.58, N 14.06; Found: C 63.64, H 6.76, N 13.82.



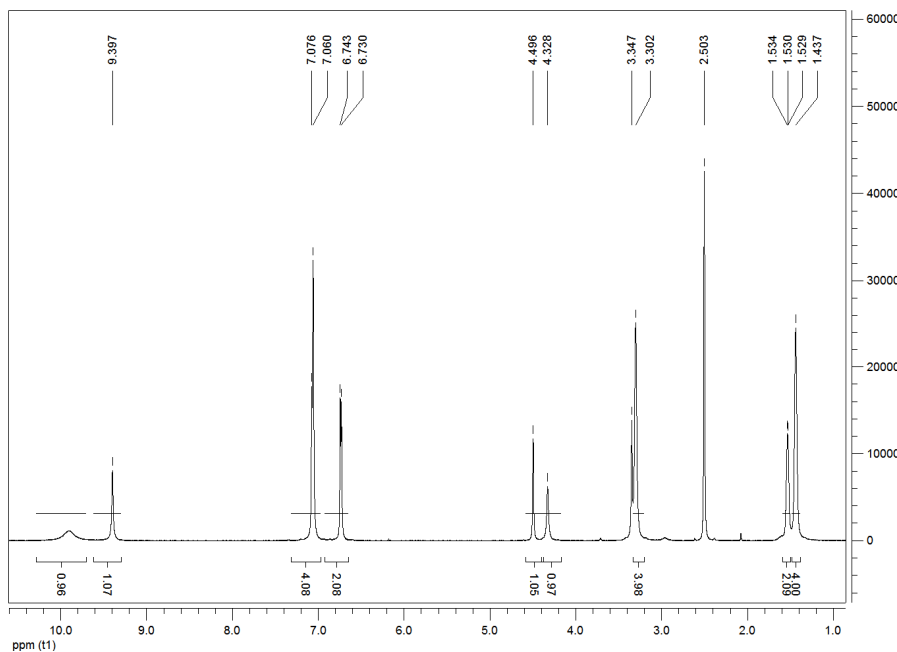
¹H NMR of **1c** (600 MHz, DMSO-*d*₆)



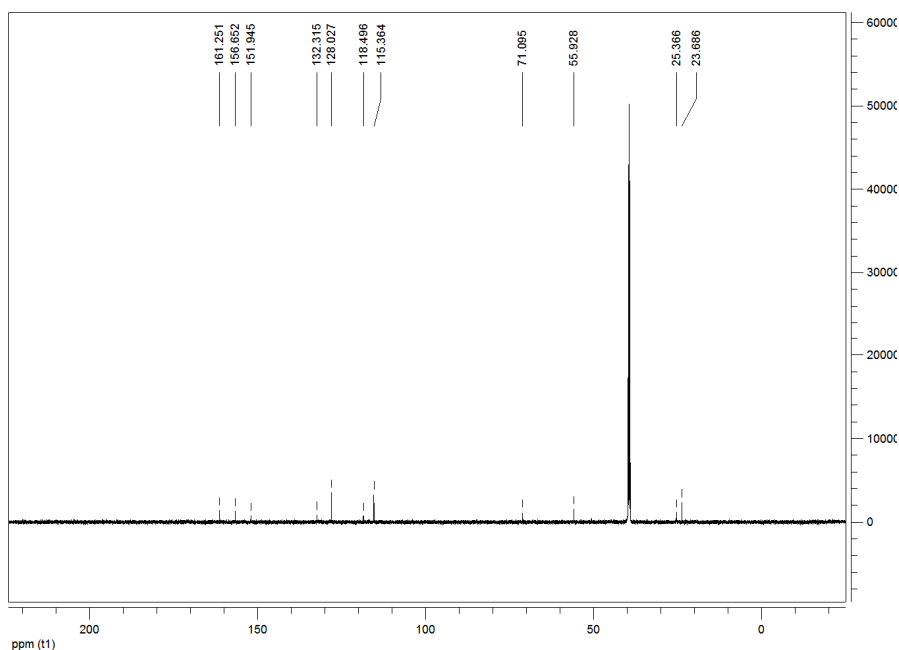
¹³C NMR of **1c** (150 MHz, DMSO-*d*₆)

1d: grey solid, 32%, m.p. 230~233 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.94 (brs, 1H, NH), 9.39 (s, 1H, OH), 7.07 (d, *J* = 9.6 Hz, 4H, ArH), 6.74 (d, *J* = 7.8 Hz, 2H, NH₂), 4.50 (s, 1H, CH),

4.33 (s, 1H, CH), 3.27~3.32 (m, 4H, 2CH₂), 1.50~1.58 (m, 2H, CH₂), 1.39~1.48 (m, 4H, CH₂);
¹³CNMR (150 MHz, DMSO-*d*₆) δ: 161.3, 156.7, 151.9, 132.3, 128.0, 118.5, 115.4, 71.1, 55.9, 25.4, 23.7; IR(KBr) ν: 3400, 3304, 3197, 3014, 2942, 2857, 2193, 1887, 1648, 1586, 1510, 1446, 1377, 1253, 1142, 1023, 1000, 955, 892, 725, 650, 604, 549, 512; MS(*m/z*): 371.40 ([M-1]⁺) 36.0%; Anal Calcd for C₁₈H₂₀N₄O₃S: C 58.05, H 5.41, N 15.04; Found: C 58.27, H 5.72, N 14.86.



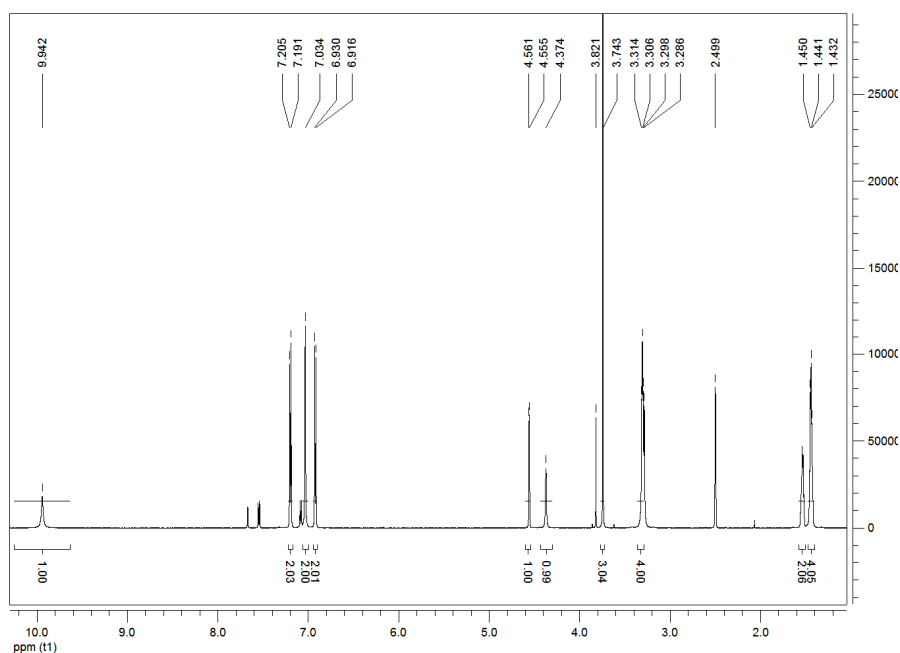
¹H NMR of **1d** (600 MHz, DMSO-*d*₆)



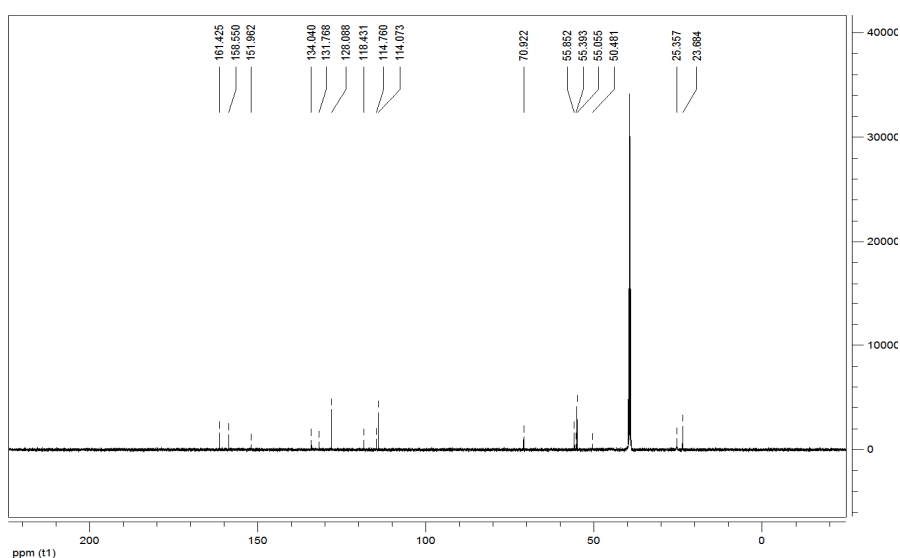
¹³C NMR of **1d** (150 MHz, DMSO-*d*₆)

1e: light yellow solid, 48%, m.p. 210~212 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.94 (s, 1H, NH), 7.20 (d, *J* = 8.4 Hz, 2H, ArH), 7.03 (s, 2H, NH₂), 6.92 (d, *J* = 8.4 Hz, 2H, ArH), 4.56 (d, *J* = 3.6

Hz, 1H, CH), 4.37 (s, 1H, CH), 3.74 (s, 3H, OCH₃), 3.31–3.29 (m, 4H, CH₂), 1.56–1.52 (m, 2H, CH₂), 1.45–1.43 (m, 4H, 2CH₂); ¹³CNMR (150 MHz, DMSO-*d*₆) δ : 161.4, 158.6, 152.0, 134.0, 131.8, 128.1, 118.4, 114.8, 114.1, 70.9, 55.8, 55.4, 55.1, 50.5, 25.4, 23.7; IR(KBr) ν : 3403, 3309, 3220, 3011, 2929, 2858, 2175, 1735, 1682, 1582, 1510, 1472, 1344, 1248, 1178, 1148, 1119, 1029, 954, 886, 775, 743; MS(*m/z*): 385.53 ([M-1]⁺) 100%; Anal Calcd for C₁₉H₂₂N₄O₃S: C 59.05, H 5.74, N 14.50; Found: C 58.74, H 6.11, N 14.22.



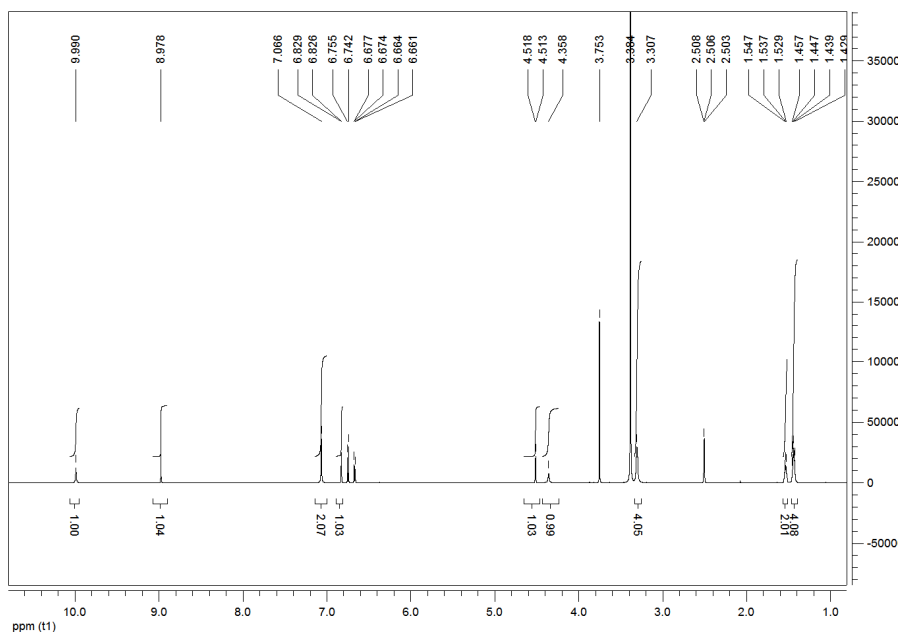
¹H NMR of **1e** (600 MHz, DMSO-*d*₆)



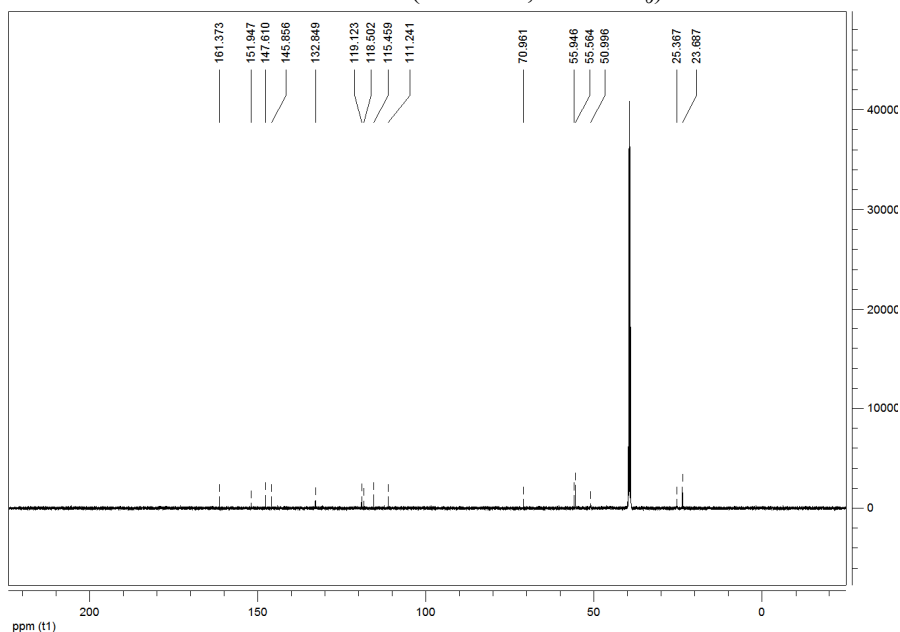
¹³C NMR of **1e** (150 MHz, DMSO-*d*₆)

1f: light yellow solid, 56%, m.p. 209~211 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ : 9.93 (s, 1H, NH), 8.89 (s, 1H, OH), 7.00 (s, 2H, NH₂), 6.82 (d, *J* = 1.8 Hz, 1H, ArH), 6.75 (d, *J* = 8.4 Hz, 1H,

ArH), 6.68–6.66 (m, 1H, ArH), 4.52 (d, $J = 3$ Hz, 1H, CH), 4.37 (s, 1H, CH), 3.75 (s, 3H, OCH₃), 3.33–3.29 (m, 4H, 2CH₂), 1.54–1.53 (m, 2H, CH₂), 1.46–1.44 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ : 161.4, 151.9, 147.6, 145.8, 132.8, 119.1, 118.5, 115.5, 110.2, 70.9, 55.9, 55.6, 51.0, 25.4, 23.7; IR(KBr) ν : 3373, 3313, 3222, 2941, 2855, 2179, 1694, 1667, 1638, 1573, 1510, 1469, 1357, 1313, 1269, 1239, 1205, 1146, 1026, 950, 856, 824, 743; MS(m/z): 401.27 ([M-1]⁺) 100%; Anal Calcd for C₁₉H₂₂N₄O₄S: C 56.70, H 5.51, N 13.92; Found: C 56.89, H 5.73, N 13.54.



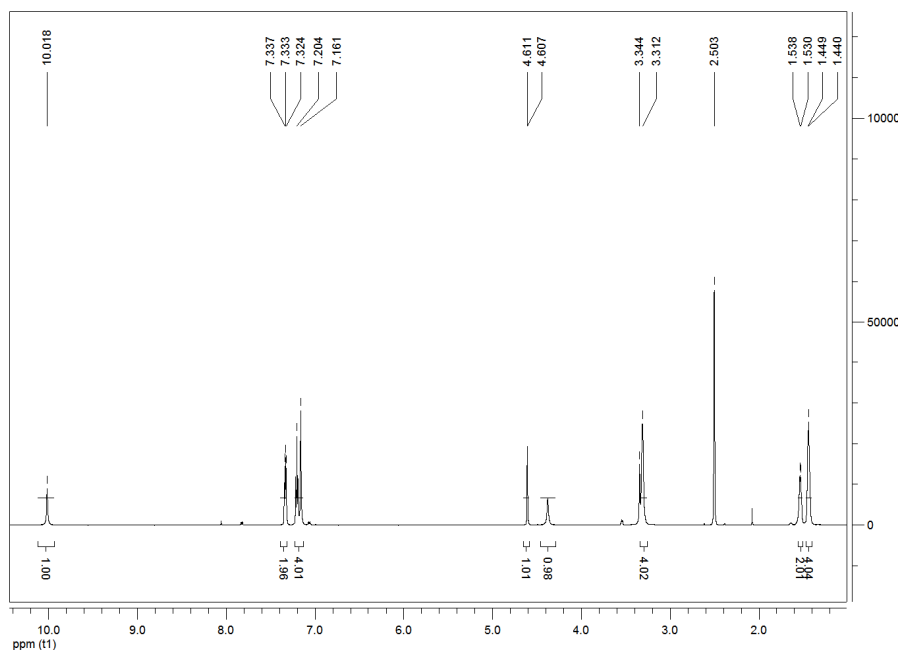
¹H NMR of **1f** (600 MHz, DMSO-*d*₆)



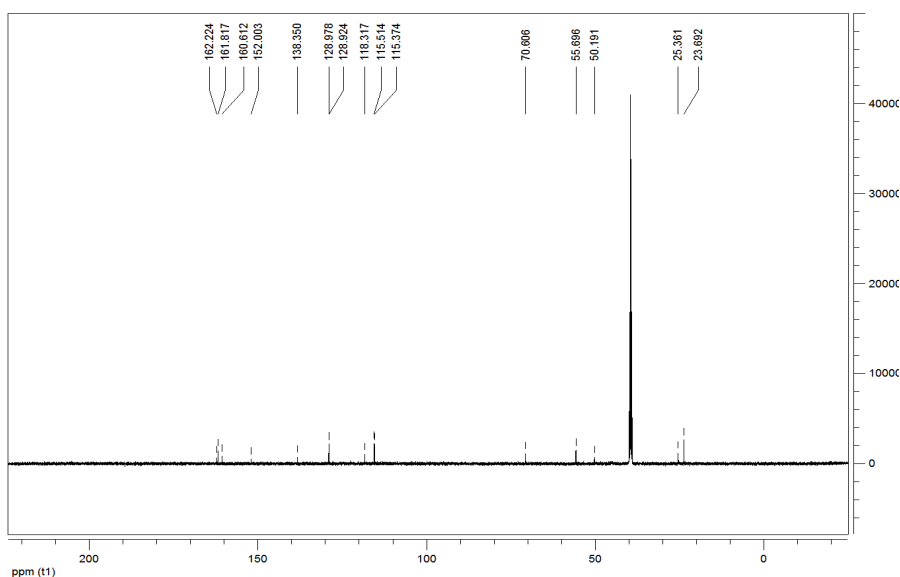
¹³C NMR of **1f** (150 MHz, DMSO-*d*₆)

1g: yellow solid, 43%, m.p. 220–222 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ : 10.02 (s, 1H, NH), 7.35–7.32 (m, 2H, ArH), 7.20 (t, $J = 8.4$ Hz, 2H, ArH), 7.16 (s, 2H, NH₂), 4.61 (s, 1H, CH), 4.38 (s,

1H, CH), 3.32~3.30 (m, 4H, 2CH₂), 1.54~1.53 (m, 2H, CH₂), 1.45~1.44 (m, 4H, 2CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 162.2, 161.8, 160.6, 152.0, 138.4, 129.0, 128.9, 118.3, 115.5, 115.4, 70.6, 55.7, 50.2, 25.4, 23.7; IR(KBr) ν: 3398, 3305, 3195, 3009, 2938, 2853, 2193, 1689, 1655, 1581, 1507, 1448, 1380, 1243, 1136, 1093, 1022, 997, 892, 825, 740; MS(*m/z*): 373.27 ([M-1]⁺) 100%; Anal Calcd for C₁₈H₁₉FN₄O₂S: C 57.74, H 5.11, N 14.96; Found: C 57.92, H 5.41, N 14.68.



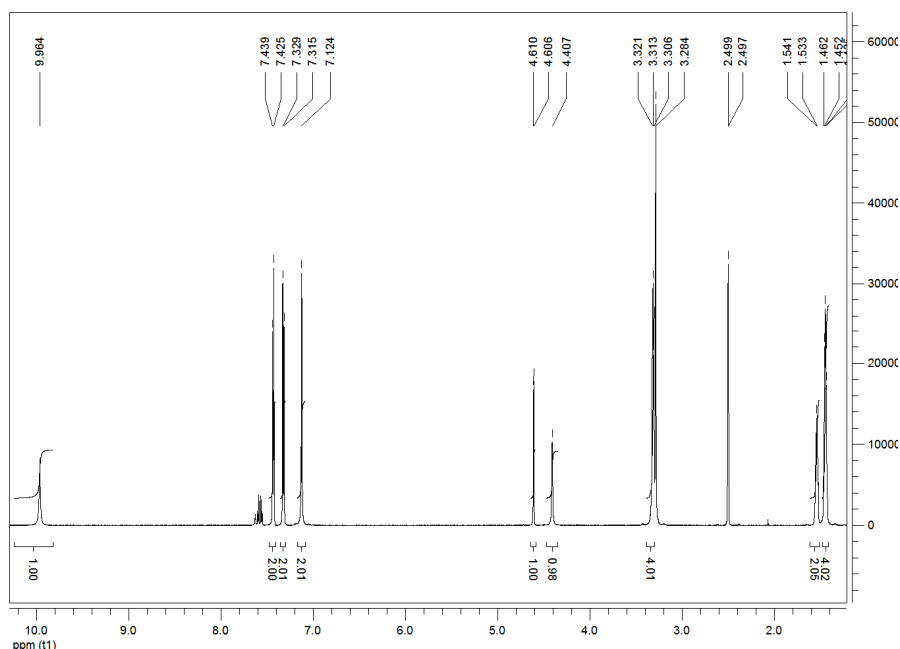
¹H NMR of **1g** (600 MHz, DMSO-*d*₆)



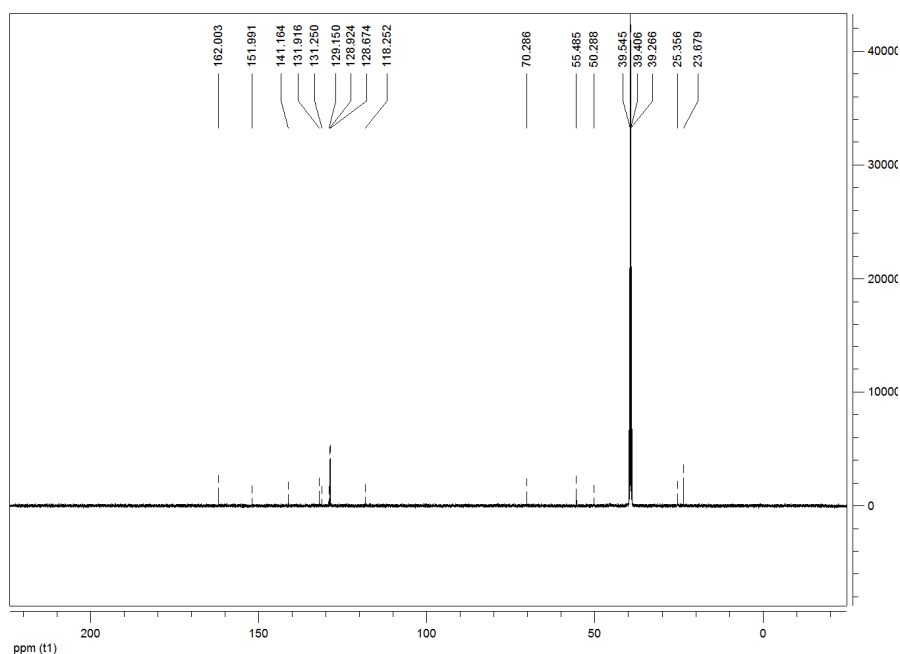
¹³C NMR of **1g** (150 MHz, DMSO-*d*₆)

1h: white solid, 35%, m.p. 299~301; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.96 (s, 1H, NH), 7.43 (d, *J* = 8.4Hz, 2H, ArH), 7.32 (d, *J* = 8.4Hz, 2H, ArH), 7.12 (s, 2H, NH₂), 4.61 (s, 1H, CH), 4.41 (s, 1H, CH), 3.32~3.31 (m, 4H, CH₂), 1.54~1.53 (m, 2H, CH₂), 1.45~1.44 (m, 4H, CH₂); ¹³C

NMR (150 MHz, DMSO- d_6) δ : 162.0, 152.0, 141.2, 131.9, 131.3, 129.2, 128.9, 128.7, 118.3, 70.3, 55.5, 50.3, 25.4, 23.7; IR(KBr) ν : 3404, 3308, 3221, 2929, 2858, 2175, 1677, 1625, 1578, 1478, 1406, 1344, 1243, 1092, 1018, 817, 741; MS(m/z): 389.33 ($[M-1]^+$) 100%, 391.27($[M-1]^+$) 44%; Anal Calcd for C₁₈H₁₉ClN₄O₂S: C 55.31, H 4.90, N 14.33; Found: C 55.09, H 5.38, N 14.16.



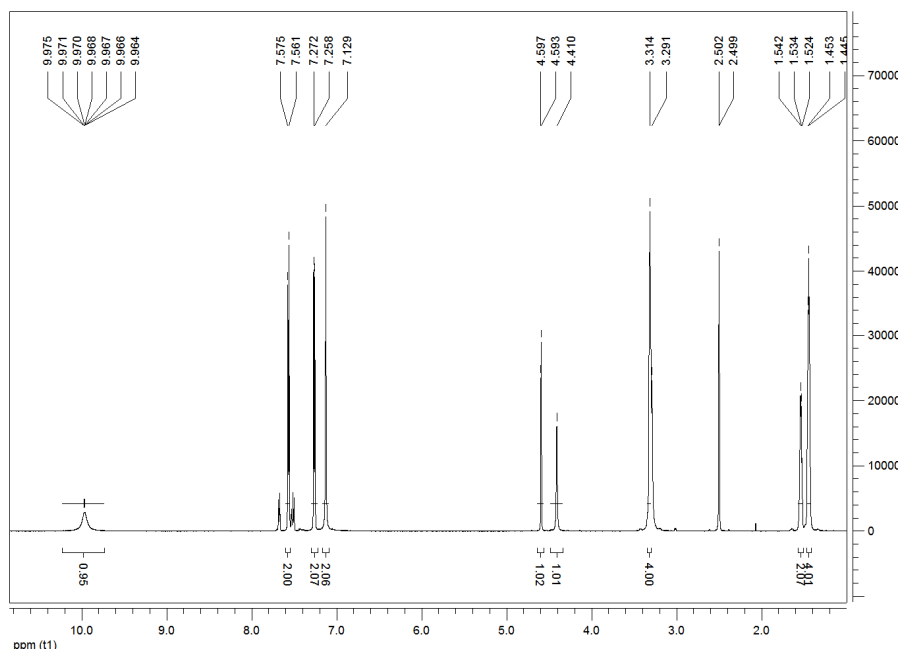
¹H NMR of **1h** (600 MHz, DMSO- d_6)



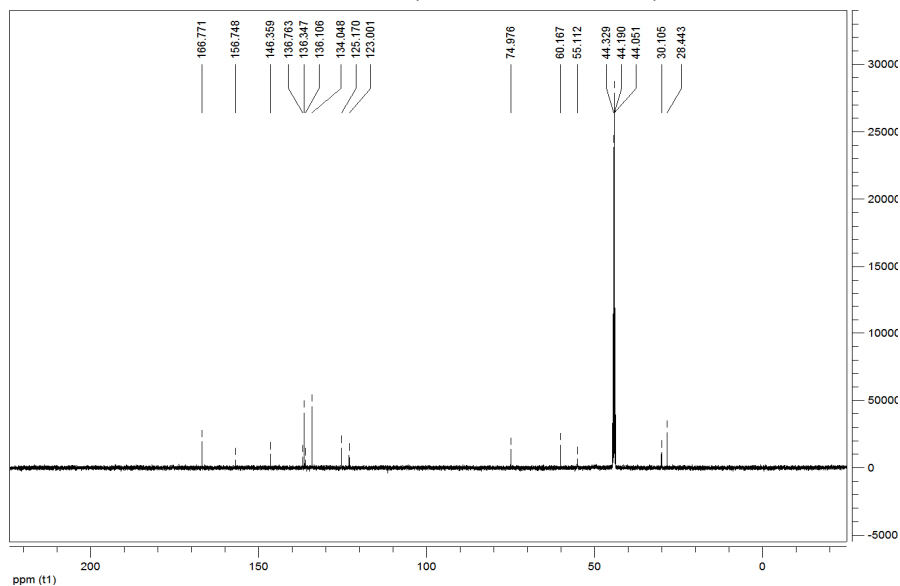
¹³C NMR of **1h** (150 MHz, DMSO- d_6)

1i: light yellow, 49%, m.p. 220~222 °C; ¹H NMR (600 MHz, DMSO- d_6) δ : 9.97(s, 1H, NH), 7.57 (d, J = 8.4Hz, 2H, ArH), 7.27 (d, J = 8.4Hz, 2H, ArH), 7.13 (s, 2H, NH₂), 4.60 (s, 1H, CH), 4.10 (s, 1H, CH), 3.3~3.30 (m, 4H, CH₂), 1.54~1.52 (m, 2H, CH₂), 1.45~1.44 (m, 4H, 2CH₂); ¹³C

NMR (150 MHz, DMSO- d_6) δ : 161.8, 151.7, 141.4, 131.8, 131.3, 131.1, 129.0, 120.2, 118.0, 70.0, 55.1, 50.1, 25.1, 23.4; IR(KBr) ν : 3404, 3301, 3221, 2927, 2858, 2173, 1723, 1678, 1625, 1578, 1479, 1405, 1346, 1243, 1202, 1073, 1012, 955, 889, 815, 740, 695; MS(m/z): 433.33 ($[M-1]^+$) 100%; Anal Calcd for $C_{18}H_{19}BrN_4O_2S$: C 49.66, H 4.40, N 12.87; Found: C 49.47, H 4.73, N 12.55.



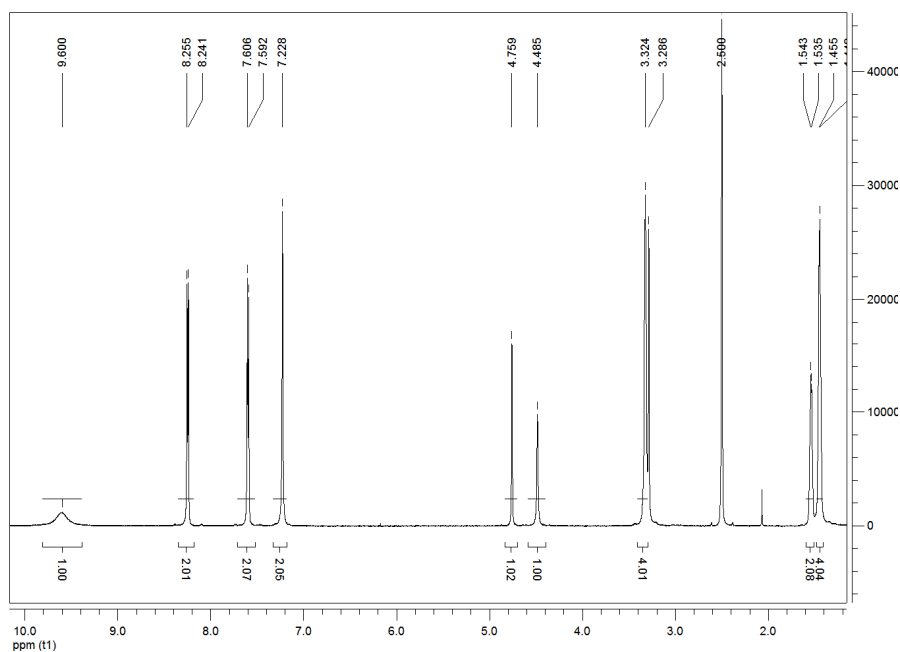
^1H NMR of **1i** (600 MHz, DMSO- d_6)



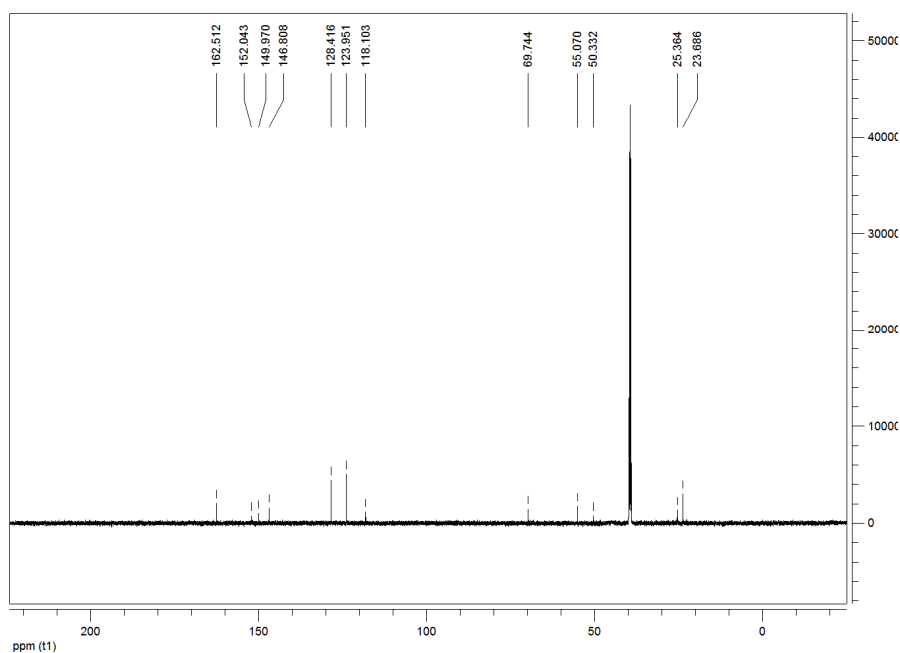
^{13}C NMR of **1i** (150 MHz, DMSO- d_6)

1j: grey solid, 27%, m.p. 209~211 $^\circ\text{C}$; ^1H NMR (600 MHz, DMSO- d_6) δ : 9.60 (s, 1H, NH), 8.25 (d, $J=8.4\text{Hz}$, 2H, ArH), 7.60(d, $J=8.4\text{Hz}$, 2H, ArH), 7.23 (s, 2H, NH_2), 4.76 (s, 1H, CH), 4.48 (s, 1H, CH), 3.33~3.31 (m, 4H, 2CH_2), 1.54~1.53 (m, 2H, CH_2), 1.46~1.45 (m, 4H, CH_2); ^{13}C NMR (150 MHz, DMSO- d_6) δ : 162.5, 152.0, 150.0, 146.8, 128.4, 124.0, 118.1, 69.7, 55.1, 50.3, 25.4,

23.7; IR(KBr) ν : 3420, 3331, 3232, 2950, 2859, 2177, 1668, 1573, 1521, 1475, 1347, 1240, 1137, 1109, 997, 896, 852, 741, 695; MS(m/z): 400.13 ($[M-1]^+$) 100%; Anal Calcd for $C_{18}H_{19}N_5O_4S$: C 53.85, H 4.77, N 15.94; Found: C 53.37, H 4.90, N 15.67.



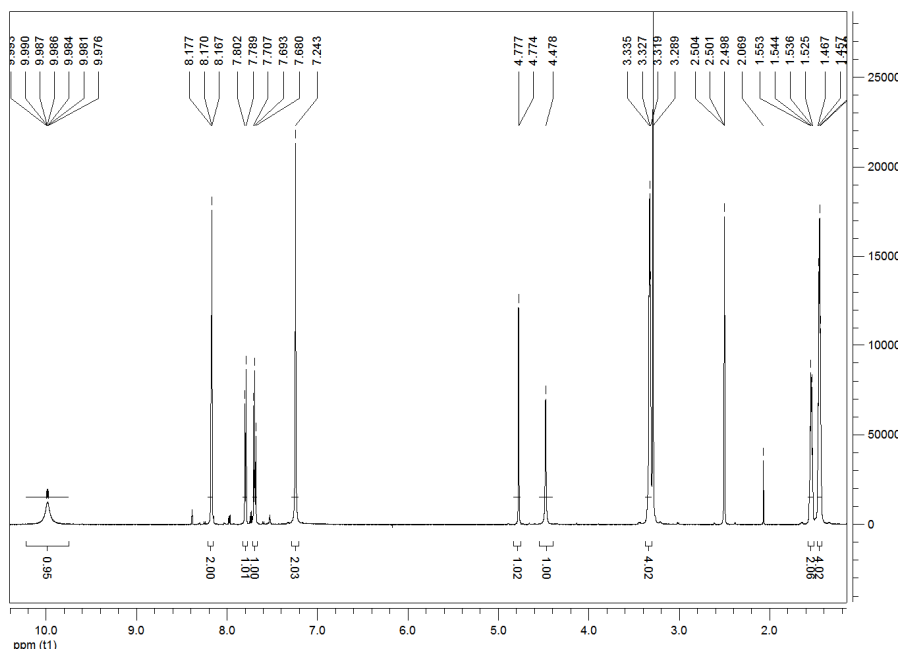
^1H NMR of **1j** (600 MHz, $\text{DMSO-}d_6$)



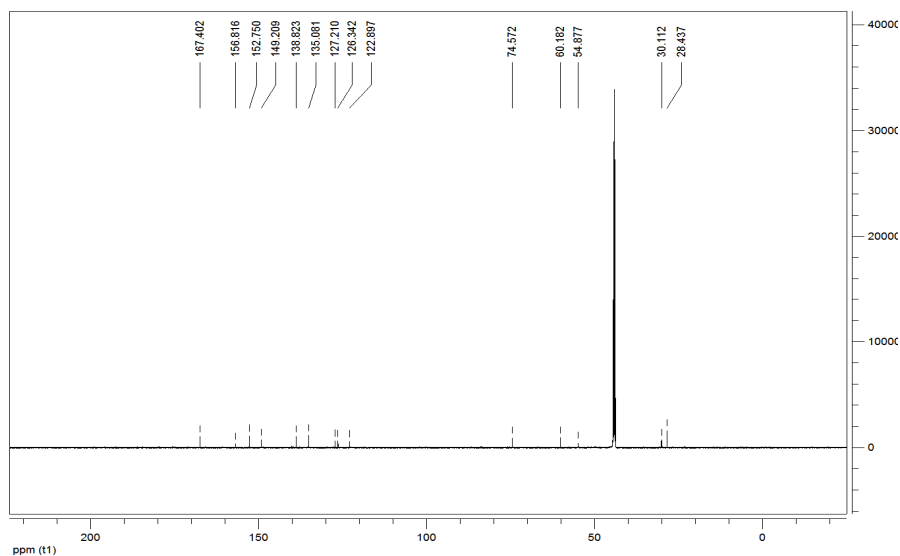
^{13}C NMR of **1j** (150 MHz, $\text{DMSO-}d_6$)

1k: light yellow solid, 46%, m.p. 231~233 °C; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ : 10.06~9.91 (brs, 1H, NH), 8.18~8.17 (m, 2H, ArH), 7.80~7.79 (d, $J=7.8$ Hz, 1H, ArH), 7.71~7.68 (m, 1H, ArH), 7.24 (s, 2H, NH_2), 4.78 (s, 1H, CH), 4.48 (s, 1H, CH), 3.33~3.32 (m, 4H, 2CH_2), 1.55~1.53 (m, 2H, CH_2), 1.47~1.44 (m, 4H, 2CH_2); ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ : 162.4, 151.8, 147.8,

144.2, 133.8, 130.1, 122.2, 121.3, 117.9, 69.6, 55.2, 49.9, 25.1, 23.4; IR(KBr) ν : 3406, 3317, 3233, 3204, 3087, 2940, 2856, 2180, 1694, 1667, 1574, 1529, 1481, 1356, 1254, 1207, 1170, 1139, 1093, 995, 933, 872, 814, 739, 691; MS(m/z): 400.33 ($[M-1]^+$) 100%; Anal Calcd for $C_{18}H_{19}N_5O_4S$: C 53.85, H 4.77, N 15.94; Found: C 53.69, H 5.12, N 15.50.



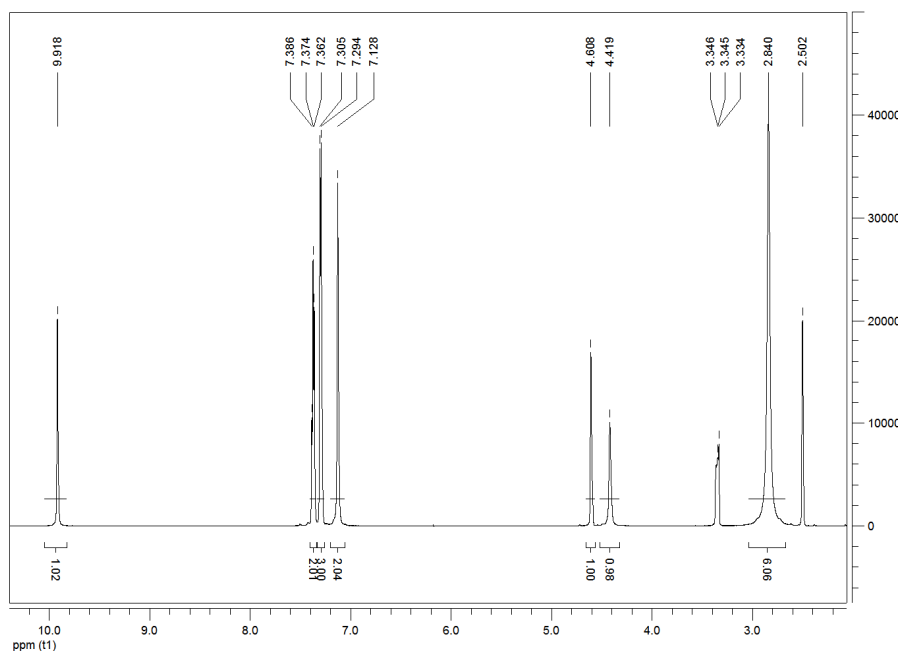
^1H NMR of **1k** (600 MHz, $\text{DMSO}-d_6$)



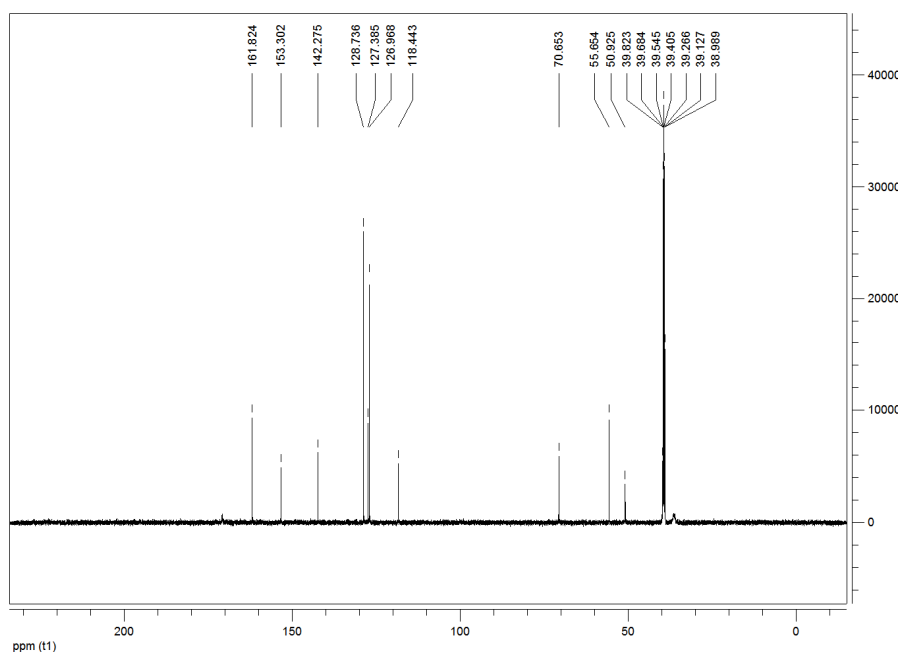
^{13}C NMR of **1k** (150 MHz, $\text{DMSO}-d_6$)

2a: white solid, 32.7%, m.p. 198~200 $^\circ\text{C}$; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 9.92 (s, 1H, NH), 7.39~7.36(t, $J = 7.2\text{Hz}$, 2H, ArH), 7.30 (d, $J = 6.6\text{Hz}$, 3H, ArH), 7.13 (s, 2H, NH_2), 4.61 (s, 1H, CH), 4.42 (s, 1H, CH), 2.84 (s, 6H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 161.8, 153.3, 142.3, 128.7, 127.4, 127.0, 118.4, 70.7, 55.7, 51.0; IR(KBr) ν : 3390, 3317, 3277, 3218, 3061, 3030, 2989,

2928, 2175, 2126, 1684, 1627, 1579, 1494, 1453, 1408, 1327, 1255, 1210, 1197, 1166, 1120, 1066, 1039, 1006, 924, 883, 827, 750; MS(m/z): 315.53 ($[M-1]^+$, 100%); Anal Calcd for $C_{15}H_{16}N_4O_2S$: C 56.94, H 5.10, N 17.71; Found: C 56.76, H 5.42, N 17.46.



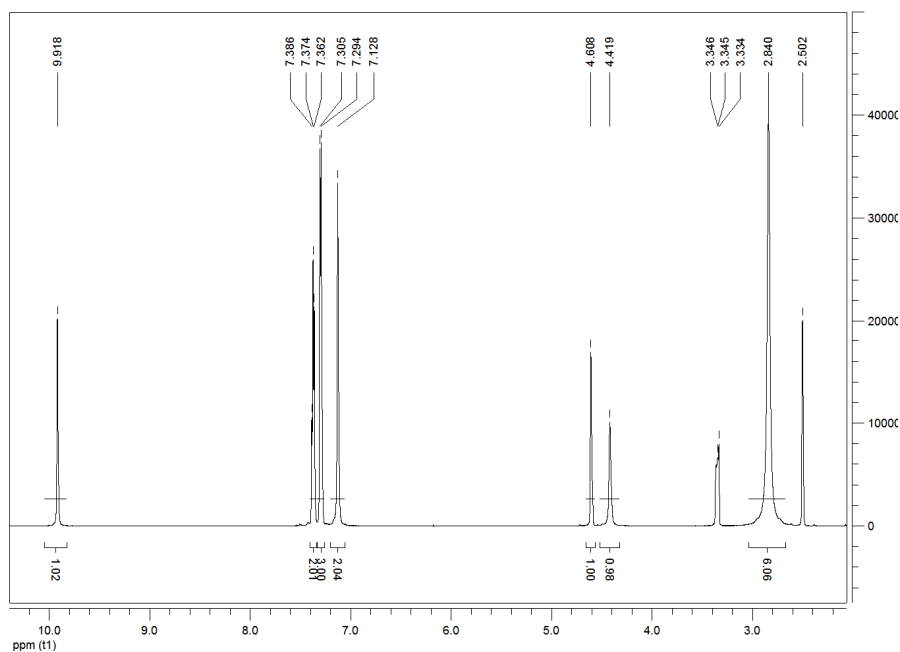
^1H NMR of **2a** (600 MHz, $\text{DMSO}-d_6$)



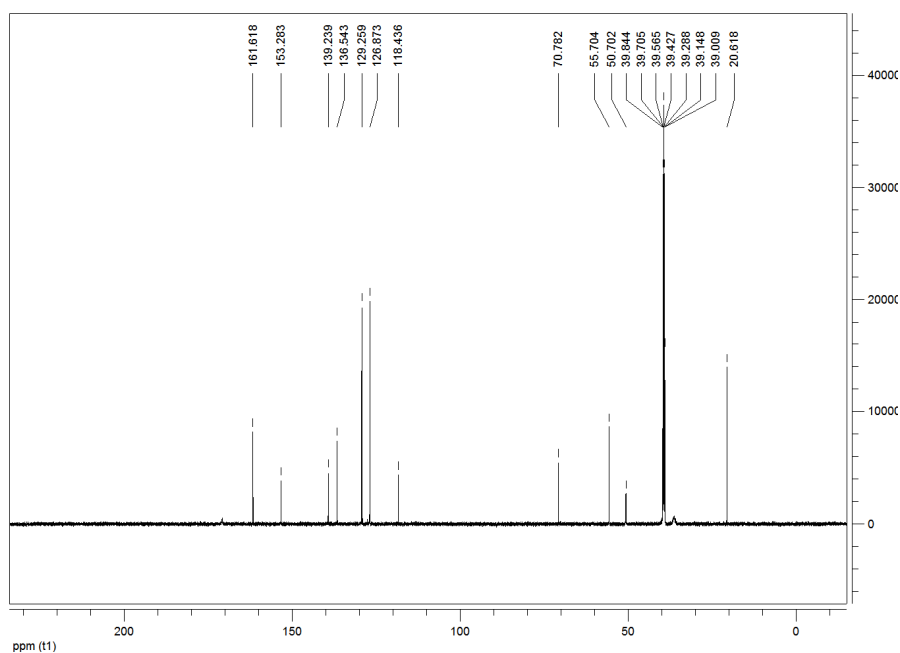
^{13}C NMR of **2a** (150 MHz, $\text{DMSO}-d_6$)

2b: light yellow solid, 41.5%, m.p. 205~208 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 9.91 (s, 1H, NH), 7.17 (s, 4H, ArH), 7.09 (s, 2H, NH_2), 4.57 (s, 1H, CH), 4.38 (s, 1H, CH), 2.84 (s, 6H, CH_3), 2.29 (s, 3H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 161.6, 153.3, 139.2, 136.5, 129.3, 126.9, 118.4, 70.8, 55.7, 50.7, 20.6; IR(KBr) ν : 3387, 3318, 3260, 3210, 3006, 2925, 2178, 1688, 1632,

1581, 1493, 1401, 1347, 1324, 1297, 1257, 1201, 1167, 1066, 1040, 1019, 917, 886, 813, 786, 753;
 MS(*m/z*): 329.60 ([*M*-1]⁺) 100%; Anal Calcd for C₁₆H₁₈N₄O₂S: C 58.16, H 5.49, N 16.96; Found:
 C 57.85, H 5.79, N 16.70.



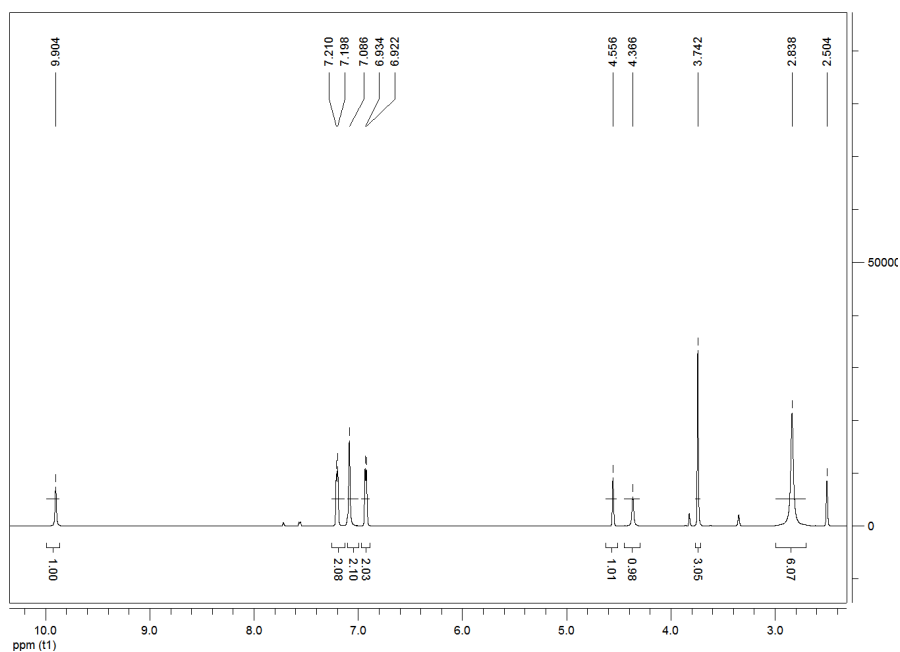
¹H NMR of **2b** (600 MHz, DMSO-*d*₆)



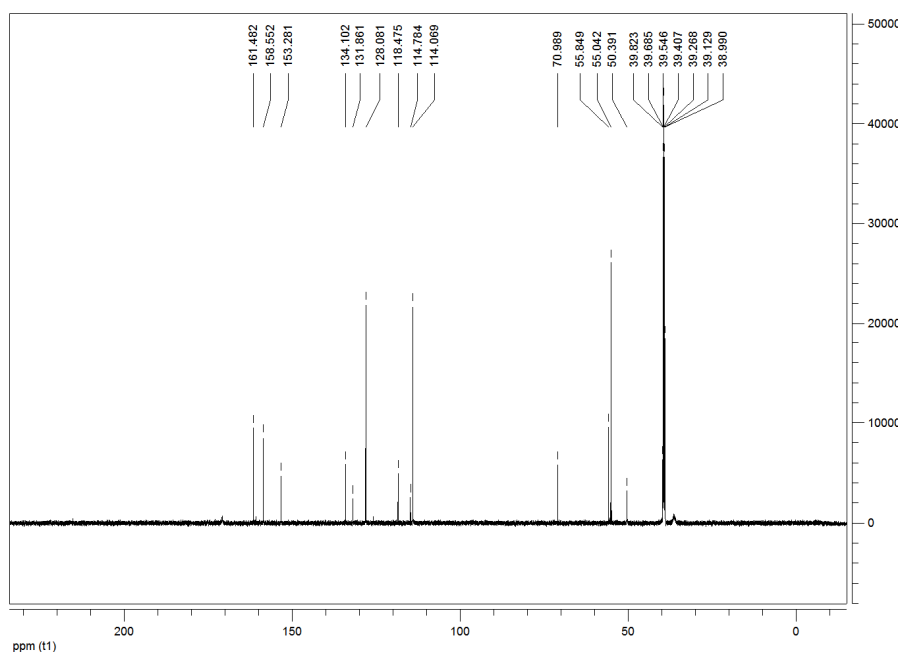
¹³C NMR of **2b** (150 MHz, DMSO-*d*₆)

2c: white solid, 36.2%, m.p. 198~201 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.90 (s, 1H, NH), 7.20 (d, *J* = 7.2 Hz, 2H, ArH), 7.09 (s, 2H, NH₂), 6.93 (d, *J* = 7.2 Hz, 2H, ArH), 4.56 (s, 1H, CH), 4.37 (s, 1H, CH), 3.74 (s, 3H, OCH₃), 2.84 (s, 6H, CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 161.5, 158.6, 153.3, 134.1, 131.9, 128.1, 118.5, 114.8, 114.1, 71.0, 55.8, 55.4, 55.0, 50.4; IR (KBr) ν: 3382,

3316, 3277, 3208, 2931, 2836, 2180, 1687, 1633, 1584, 1510, 1348, 1325, 1303, 1249, 1203, 1177, 1111, 1064, 1035, 891, 829, 771, 753; MS (m/z): 345.40 ([M-1]⁺, 100%); Anal Calcd for C₁₆H₁₈N₄O₃S: C 55.48, H 5.24, N 16.17; Found: C 55.56, H 5.60, N 15.87.



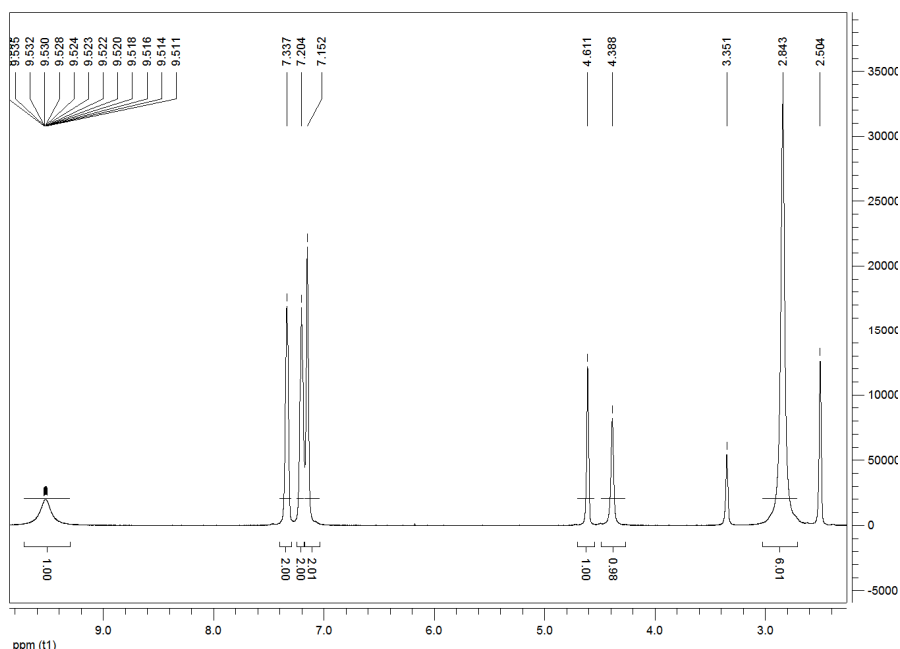
¹H NMR of **2c** (600 MHz, DMSO-*d*₆)



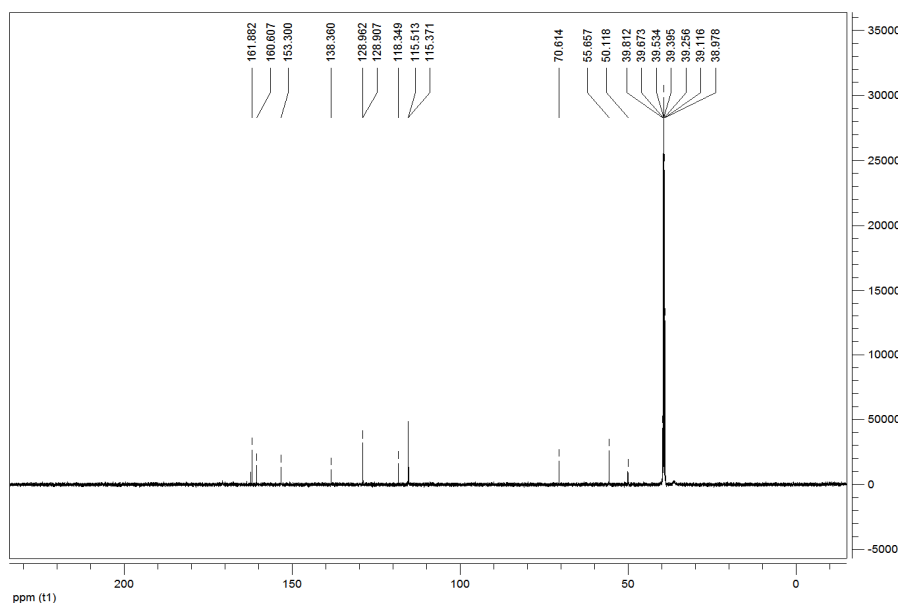
¹³C NMR of **2c** (150 MHz, DMSO-*d*₆)

2d: white solid, 16.4%, m.p. 195~197 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.71~9.35 (brs, 1H, NH), 7.39~7.29 (m, 2H, ArH), 7.25~7.17 (m, 2H, ArH), 7.15 (s, 2H, NH₂), 4.61 (s, 1H, CH), 4.39 (s, 1H, CH), 2.84 (s, 6H, CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 162.2, 161.9, 160.6, 153.3,

138.4, 129.0, 128.9, 118.3, 115.5, 115.4, 70.6, 55.7, 50.1; IR(KBr) ν : 3383, 3315, 3278, 3202, 2932, 2182, 1687, 1630, 1581, 1505, 1344, 1314, 1254, 1211, 1159, 1095, 1064, 1039, 1012, 918, 884, 849, 826, 790, 753; MS (m/z): 333.53 ($[M-1]^+$, 100%); Anal Calcd for $C_{15}H_{15}FN_4O_2S$: C 53.88, H 4.52, N 16.76; Found: C 53.65, H 4.77, N 16.38.



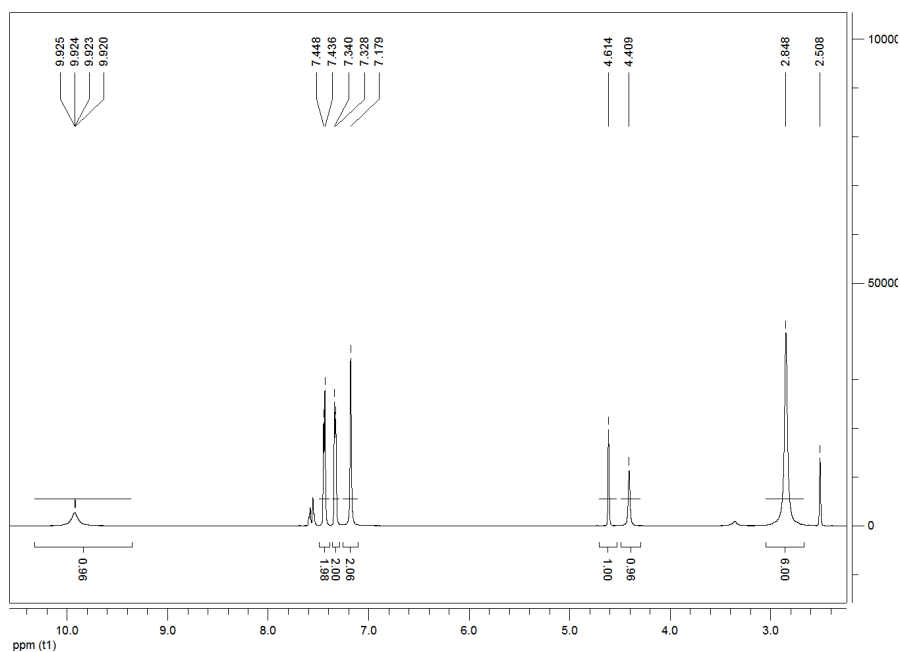
^1H NMR of **2d** (600 MHz, $\text{DMSO}-d_6$)



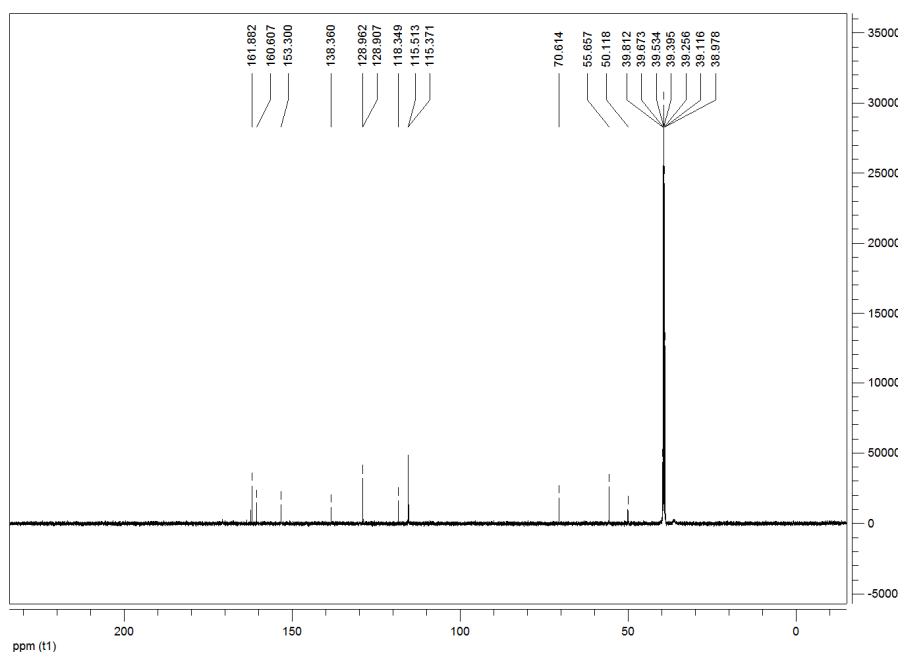
^{13}C NMR of **2d** (150 MHz, $\text{DMSO}-d_6$)

2e: light yellow solid, 47.5%, m.p. 207~209 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 10.13~9.77 (brs, 1H, NH), 7.44 (d, $J = 7.2\text{Hz}$, 2H, ArH), 7.33 (d, $J = 7.2\text{Hz}$, 2H, ArH), 7.18 (s, 2H, NH_2), 4.61 (s, 1H, CH), 4.41 (s, 1H, CH), 2.85 (s, 6H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 162.1, 153.3, 141.2, 131.9, 131.0, 129.0, 128.9, 128.7, 118.3, 70.3, 55.5, 50.2; IR(KBr) ν : 3374, 3315, 3267,

3206, 2930, 2179, 1687, 1631, 1579, 1491, 1407, 1346, 1317, 1289, 1253, 1204, 1168, 1091, 1066, 1041, 1014, 918, 890, 820, 782; MS(m/z): 349.40 ($[M-1]^+$, 100%); Anal Calcd for $C_{15}H_{15}ClN_4O_2S$: C 51.35, H 4.31, N 15.97; Found: C 51.09, H 4.58, N 15.61.



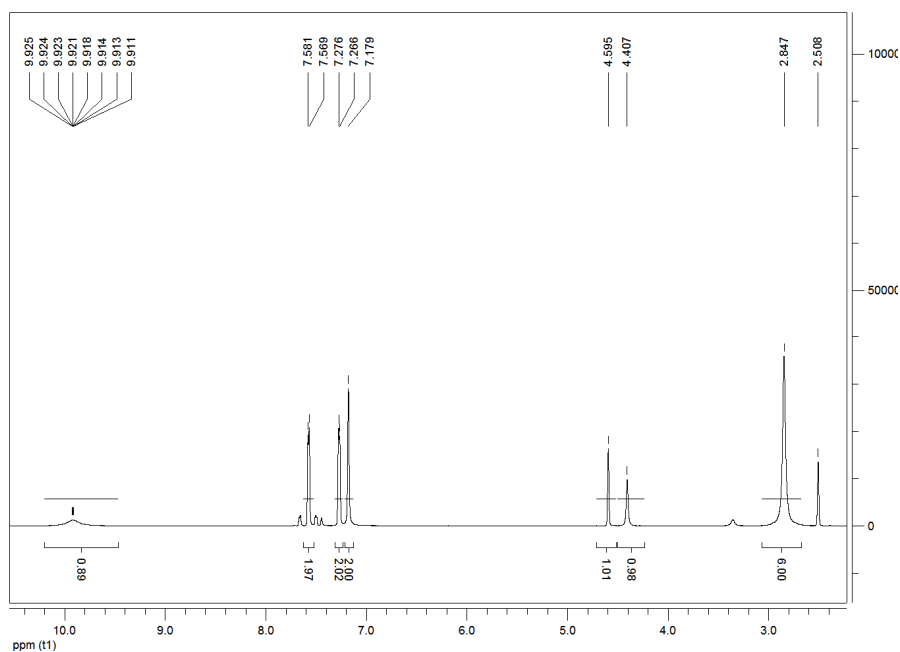
1H NMR of **2e** (600 MHz, $DMSO-d_6$)



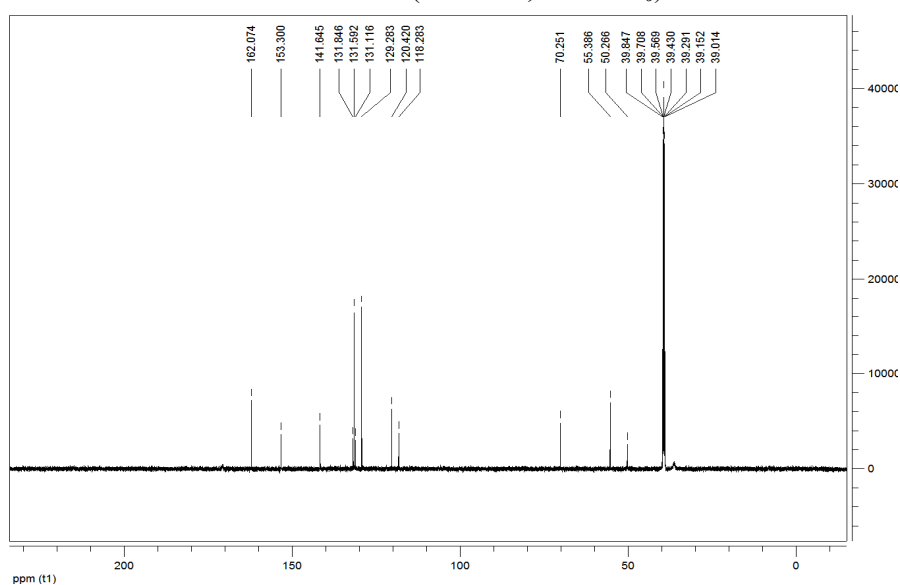
^{13}C NMR of **2e** (150 MHz, $DMSO-d_6$)

2f: light yellow solid, 36.2%, m.p. 218~220 °C; 1H NMR (600 MHz, $DMSO-d_6$) δ : 10.21~9.47 (brs, 1H, NH), 7.58(d, $J = 7.2$ Hz, 2H, ArH), 7.27(d, $J = 6.0$ Hz, 2H, ArH), 7.18 (s, 2H, NH_2), 4.60 (s, 1H, CH), 4.41 (s, 1H, CH), 2.85 (s, 6H, CH_3); ^{13}C NMR (150 MHz, $DMSO-d_6$) δ : 162.1, 153.3, 141.6, 131.8, 131.6, 131.1, 129.3, 120.4, 118.3, 70.3, 55.4, 50.3; IR(KBr) ν : 3375, 3315, 3265,

3209, 2928, 2176, 1686, 1631, 1578, 1489, 1405, 1346, 1317, 1289, 1254, 1203, 1168, 1070, 1041, 1011, 918, 889, 840, 817, 781, 752; MS(m/z): 393.33([M-1]⁺, 100%); 395.33 ([M-1]⁺, 100%); Anal Calcd for C₁₅H₁₅BrN₄O₂S: C 45.58, H 3.82, N 14.17; Found: C 45.51, H 4.03, N 13.89.



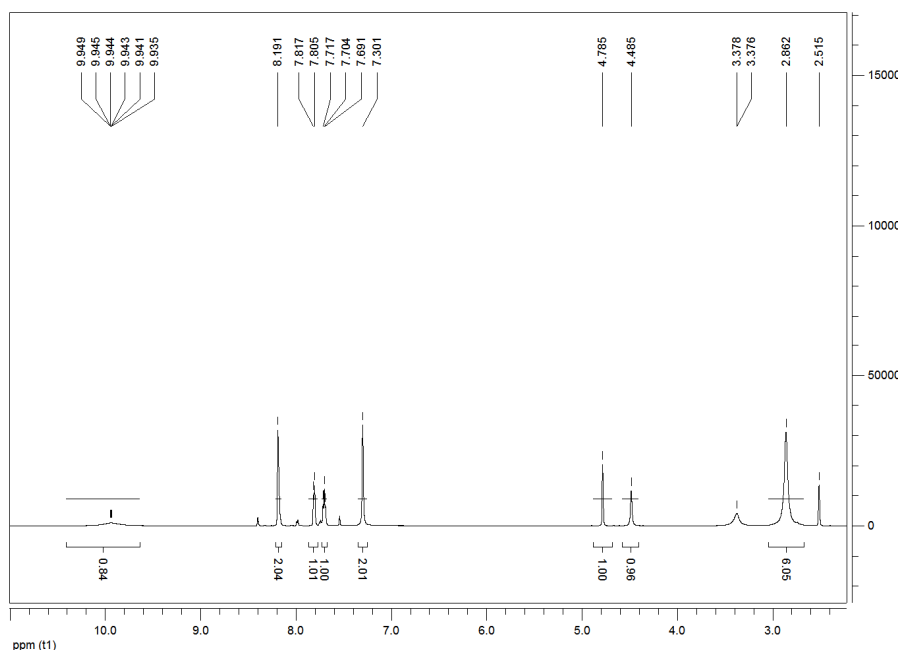
¹H NMR of **2f** (600 MHz, DMSO-*d*₆)



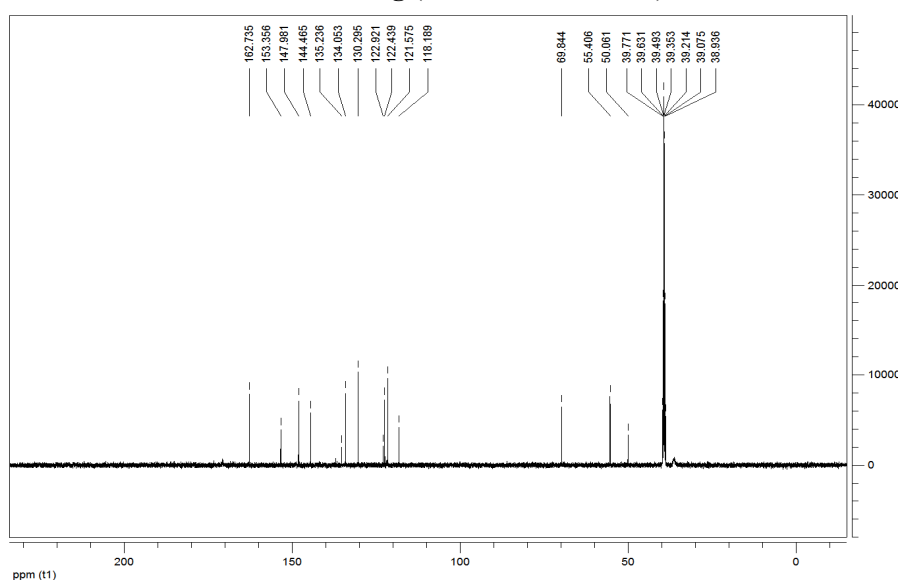
¹³C NMR of **2f** (150 MHz, DMSO-*d*₆)

2g: yellow solid, 26.5%, m.p. 188~190 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 10.30~9.58 (brs, 1H, NH), 8.19(s, 2H, ArH), 7.81 (d, *J* = 7.2Hz, 1H, ArH), 7.70 (t, *J* = 7.8Hz, 1H, ArH), 7.30 (s, 2H, NH), 4.78 (s, 1H, CH), 4.48 (s, 1H, CH); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 170.7, 170.6, 170.6, 162.7, 153.4, 148.1, 148.0, 144.5, 137.0, 135.2, 134.1, 130.3, 123.0, 122.5, 122.4, 121.7, 121.6, 118.2, 69.8, 55.4, 50.1; IR(KBr) ν: 3392, 3324, 3280, 3210, 3072, 2996, 2912, 2178, 1672, 1573,

1530, 1489, 1451, 1405, 1341, 1303, 1256, 1200, 1162, 1091, 1065, 1038, 1015, 948, 905, 881, 808, 775, 753; MS (m/z): 360.53 ($[M-1]^+$, 100%); Anal Calcd for $C_{15}H_{15}N_5O_4S$: C 49.85, H 4.18, N 19.38; Found: C 49.93, H 4.58, N 18.87.



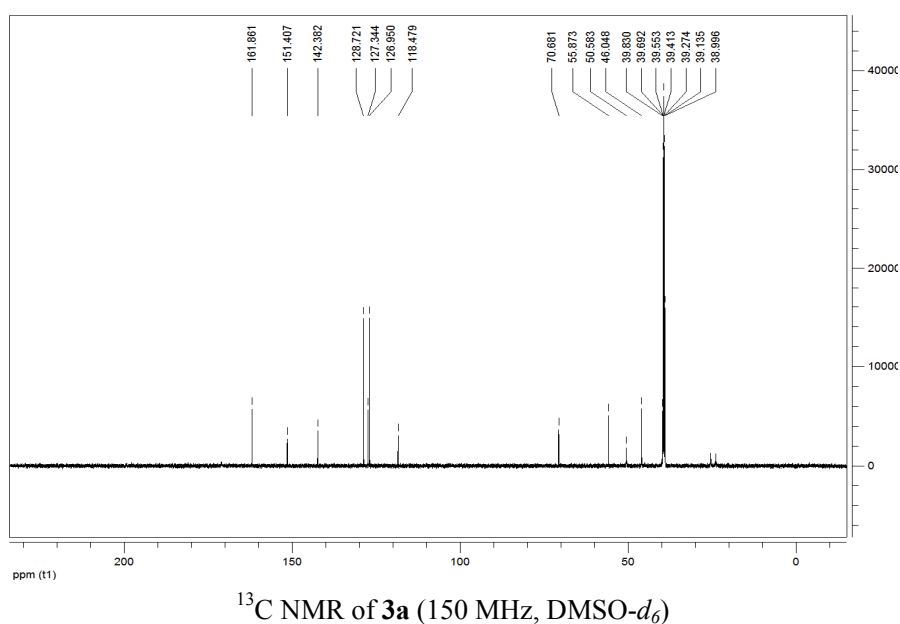
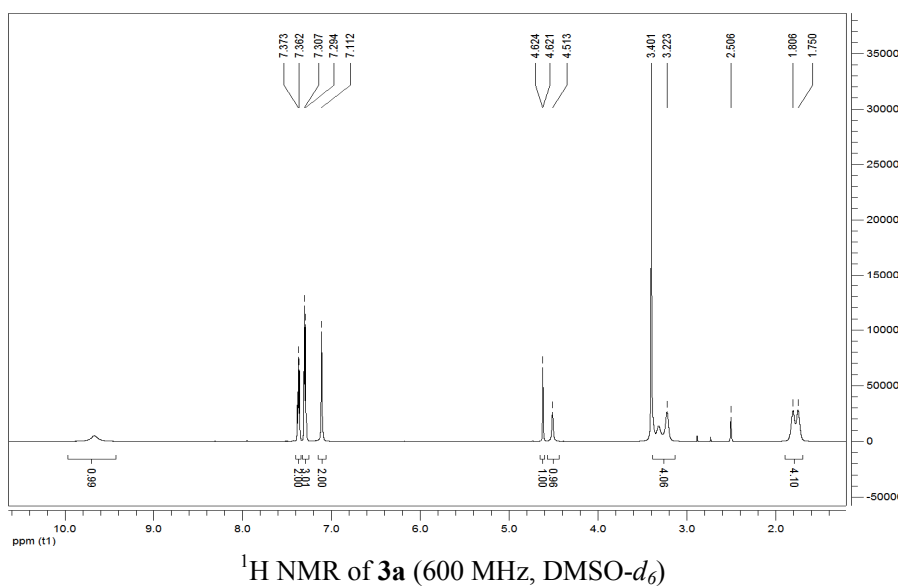
^1H NMR of **2g** (600 MHz, $\text{DMSO-}d_6$)



^{13}C NMR of **2g** (150 MHz, $\text{DMSO-}d_6$)

3a: white solid, 34.7%, m.p. 197~198 °C; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ : 9.87~9.53 (brs, 1H, NH), 7.39~7.36 (m, 2H, ArH), 7.31~7.28 (m, 3H, ArH), 7.11 (s, 2H, NH_2), 4.60 (d, $J = 1.8\text{ Hz}$, 1H, CH), 4.51 (s, 1H, CH), 3.32~3.22 (m, 4H, CH_2), 1.81~1.25 (m, 4H, CH_2); ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ : 161.9, 151.4, 142.4, 128.7, 127.3, 127.0, 118.5, 70.7, 55.9, 50.6, 46.0, 25.5, 24.0; IR(KBr) ν : 3406, 3312, 3067, 3030, 2954, 2868, 2177, 1698, 1672, 1638, 1570, 1494, 1469, 1359,

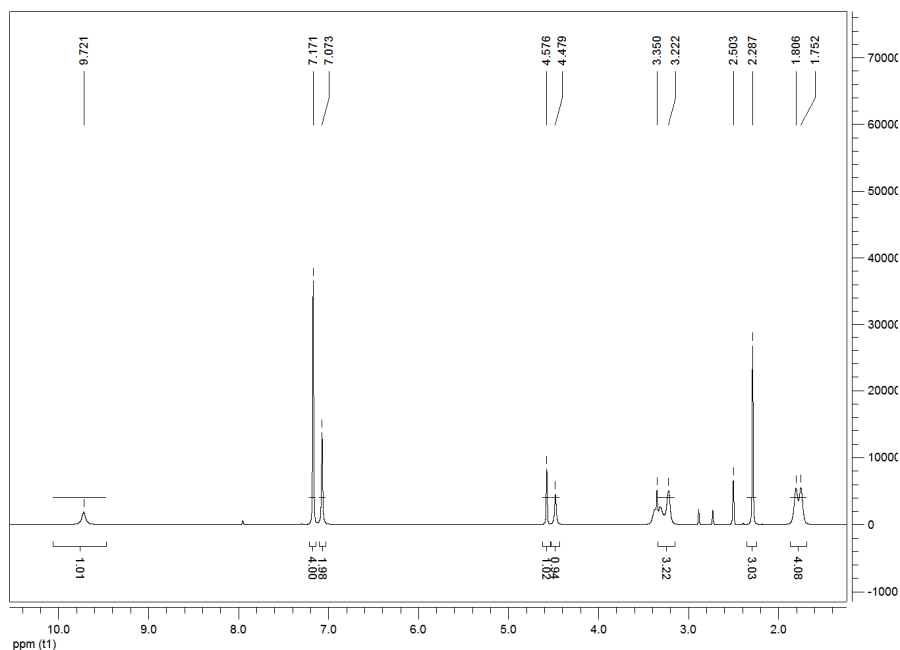
1336, 1301, 1261, 1228, 1189, 1162, 1077, 1026, 1002, 909, 889, 845, 813, 784, 767; MS(*m/z*): 341.27 ([*M*-1]⁺) 100%; Anal Calcd for C₁₇H₁₈N₄O₂S: C 59.63, H 5.30, N 16.36; Found: C 59.54, H 5.56, N 16.02.



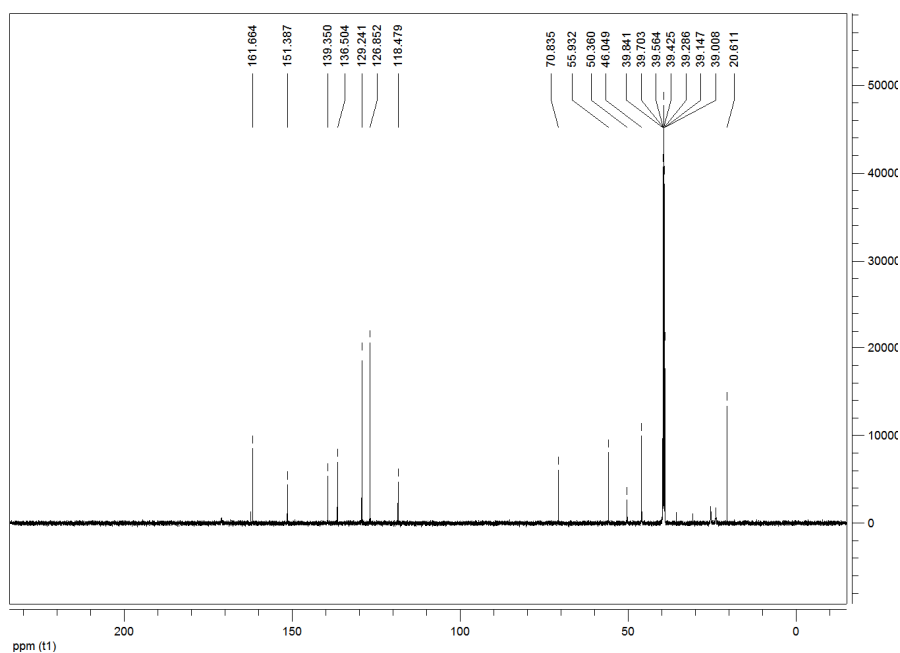
3b: light yellow solid, 32.4%, m.p. 204~207 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.79~9.66 (brs, 1H, NH), 7.17 (s, 4H, ArH), 7.07 (s, 2H, NH₂), 4.58 (s, 1H, CH), 4.48 (s, 1H, CH), 3.37~3.22 (m, 4H, CH₂), 2.29 (s, 3H, CH₃), 1.81~1.75 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 162.3, 161.7, 151.4, 139.4, 136.5, 129.2, 126.9, 118.5, 70.8, 55.9, 50.4, 46.0, 35.7, 30.7, 25.5, 24.0, 20.6; IR(KBr) ν: 3387, 3319, 3214, 2953, 2878, 2176, 1686, 1627, 1580, 1482, 1386, 1353, 1296,

1254, 1231, 1205, 1186, 1115, 1022, 914, 880, 845, 808, 784, 752; MS(*m/z*): 355.67 ([*M*-1]⁺) 100%;

Anal Calcd for C₁₈H₂₀N₄O₂S: C 60.65, H 5.66, N 15.72; Found: C 60.32, H 5.90, N 15.49.



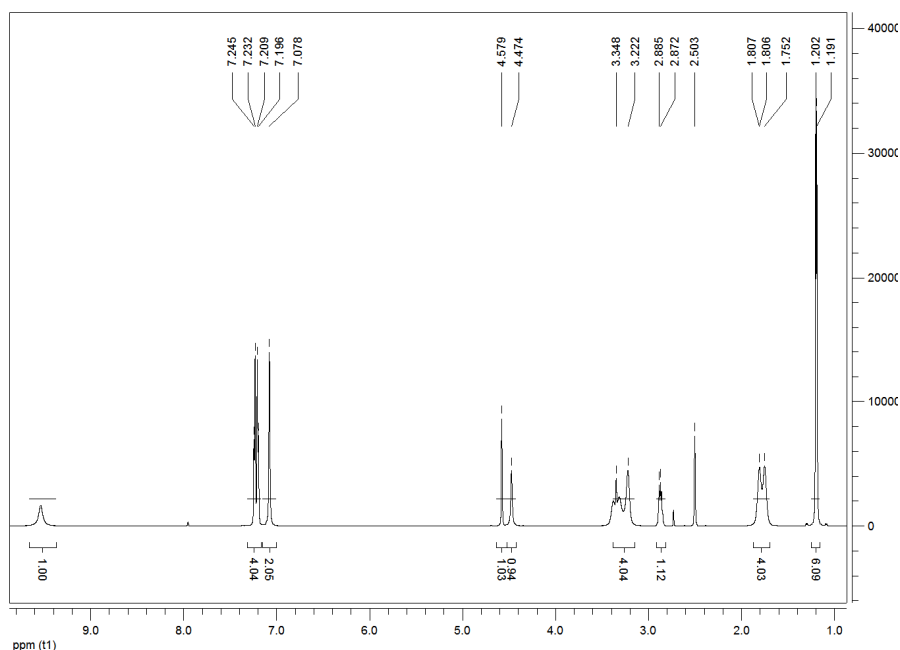
¹H NMR of **3b** (600 MHz, DMSO-*d*₆)



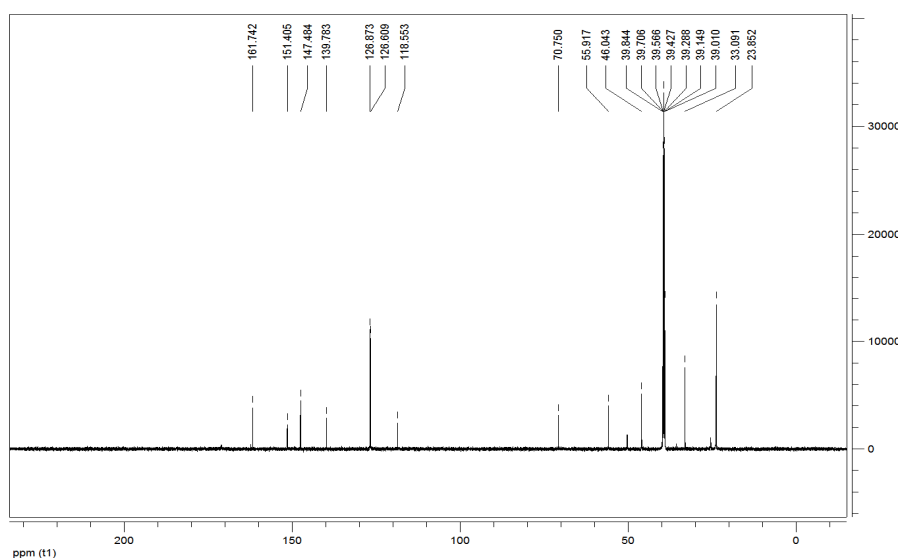
¹³C NMR of **3b** (150 MHz, DMSO-*d*₆)

3c: light yellow solid, 41.3%, m.p. 210~213 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.54 (brs, 1H, NH), 7.24 (d, *J* = 7.8 Hz, 2H, ArH), 7.20 (d, *J* = 7.8 Hz, 2H, ArH), 7.08 (s, 2H, NH₂), 4.58 (s, 1H, CH), 4.47 (s, 1H, CH), 3.38~3.22 (m, 4H, CH₂), 2.88~2.85 (m, 1H, CH), 1.81~1.75 (m, 4H, CH₂), 1.20 (d, *J* = 6.6 Hz, 6H, CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 161.7, 151.4, 147.5, 139.8, 126.9, 126.6, 118.6, 70.8, 55.9, 50.3, 46.0, 33.1, 25.5, 24.0, 23.9; IR(KBr) ν: 3396, 3265, 3192,

2958, 2881, 2196, 1690, 1656, 1590, 1464, 1365, 1288, 1265, 1215, 1178, 1112, 1054, 1016, 917, 889, 824, 772; MS(*m/z*): 383.67 ([*M*-1]⁺) 100%; Anal Calcd for C₂₀H₂₄N₄O₂S: C 62.48, H 6.29, N 14.57; Found: C 62.27, H 6.48, N 14.22.



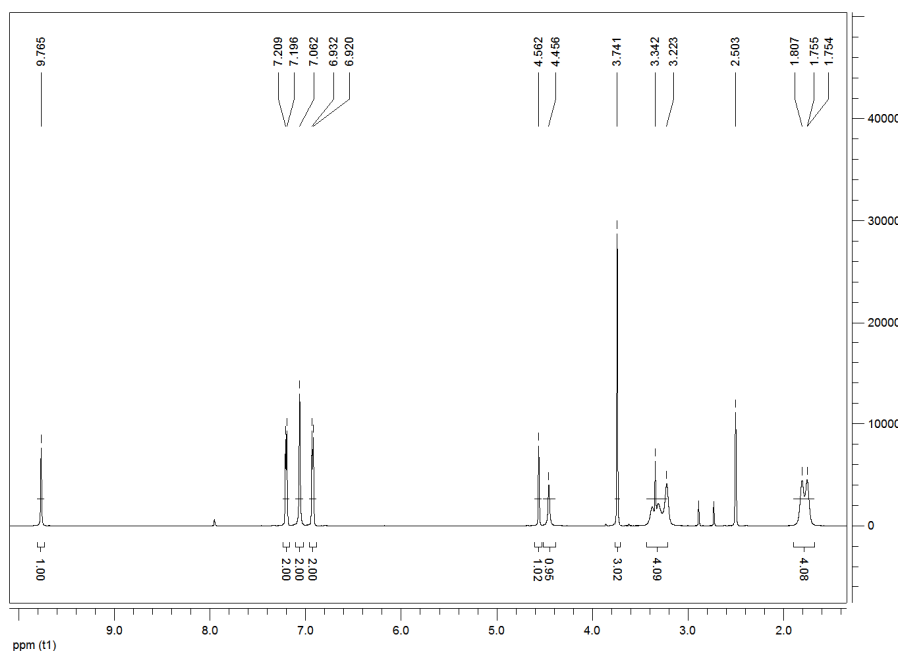
¹H NMR of **3c** (600 MHz, DMSO-*d*₆)



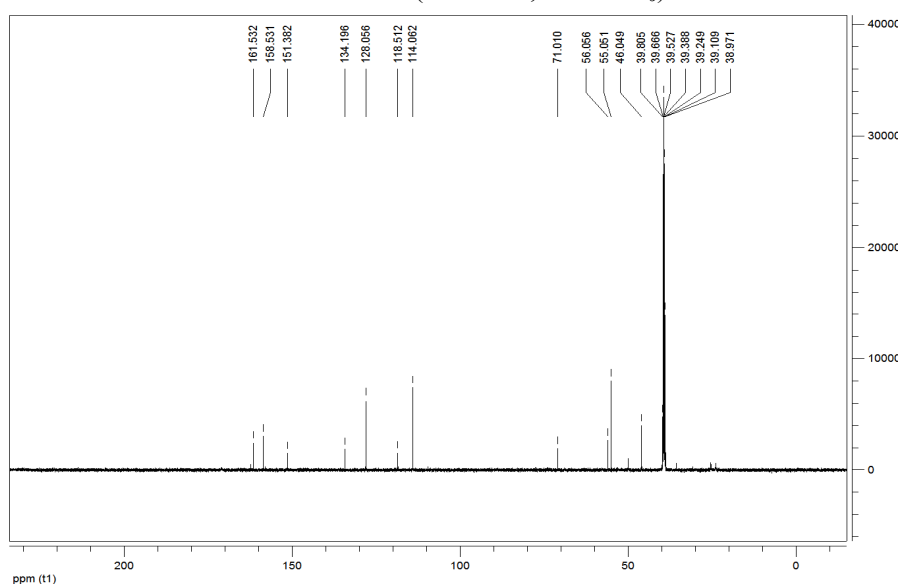
¹³C NMR of **3c** (150 MHz, DMSO-*d*₆)

3d: light yellow solid, 46.0%, m.p. 218~220 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.76 (s, 1H, NH), 7.20 (d, *J* = 7.8 Hz, 2H, ArH), 7.06 (s, 2H, NH₂), 6.93 (d, *J* = 7.2 Hz, 2H, ArH), 4.56 (s, 1H, CH), 4.46 (s, 1H, CH), 3.74 (s, 3H, OCH₃), 3.37~3.22 (m, 4H, CH₂), 1.81~1.75 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 161.5, 158.5, 151.4, 134.2, 128.1, 118.5, 114.1, 71.0, 56.1, 55.1, 50.0, 46.0, 35.8, 25.5, 24.0; IR(KBr) ν: 3394, 3315, 3255, 3218, 3074, 2951, 2928, 2875, 2836,

2177, 1684, 1625, 1582, 1511, 1461, 1390, 1344, 1304, 1249, 1213, 1178, 1114, 1034, 1012, 911, 880, 826, 802, 780, 753; MS(*m/z*): 371.40 ([M-1]⁺) 100%; Anal Calcd for C₁₇H₁₈N₄O₂S: C 58.05, H 5.41, N 15.04; Found: C 58.30, H 5.82, N 14.79.



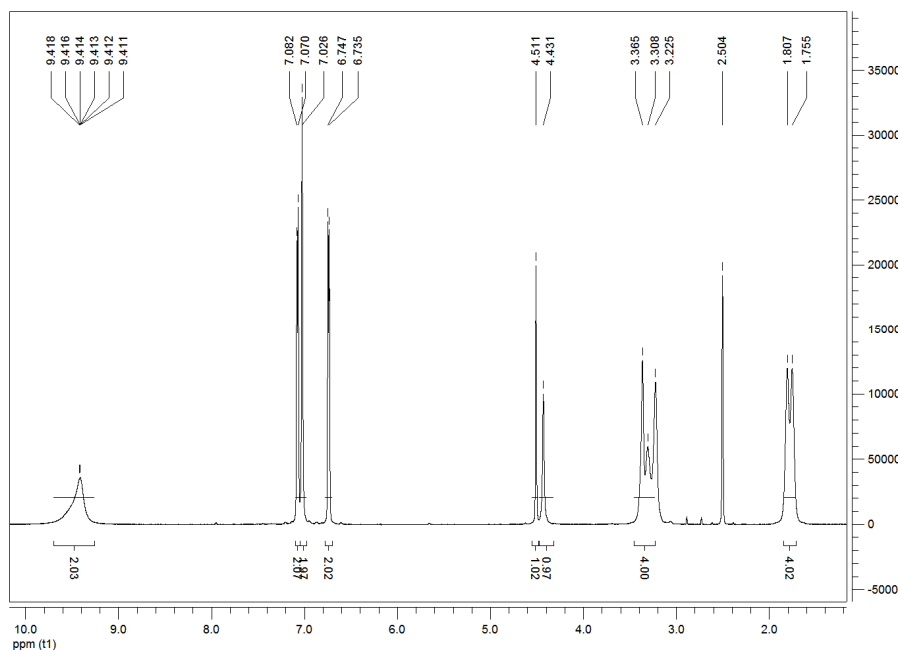
¹H NMR of **3d** (600 MHz, DMSO-*d*₆)



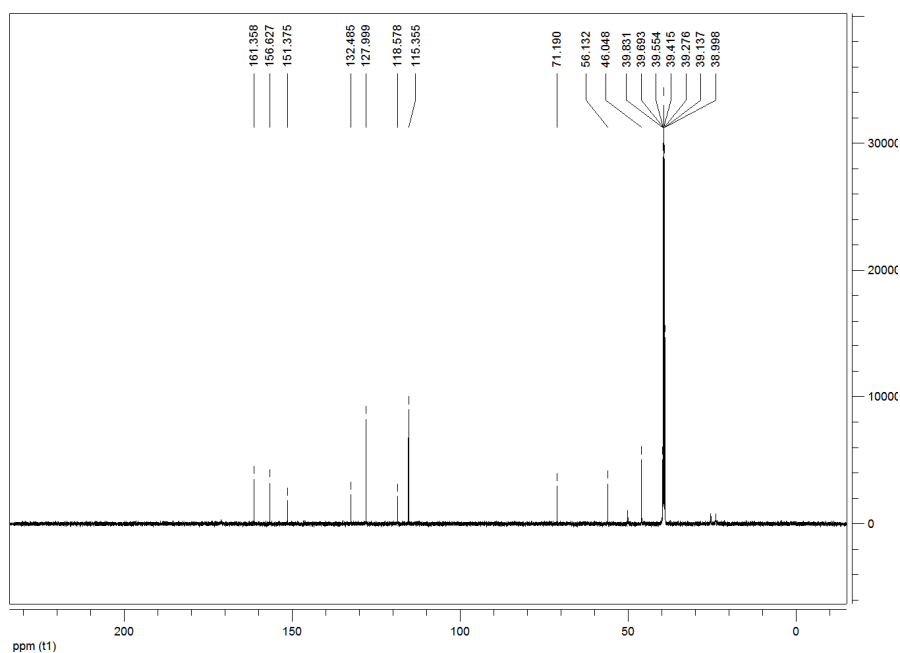
¹³C NMR of **3d** (150 MHz, DMSO-*d*₆)

3e: grey solid, 33.0%, m.p. 216~219 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.91~9.14 (m, 2H, NH, OH), 7.08 (d, *J* = 7.2 Hz, 2H, ArH), 7.03 (s, 2H, NH₂), 6.74 (d, *J* = 7.2 Hz, 2H, ArH), 4.51 (s, 1H, CH), 4.43 (s, 1H, CH), 3.36~3.22 (m, 4H, CH₂), 1.78 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 161.4, 156.6, 151.4, 132.5, 128.0, 118.6, 115.4, 71.2, 56.1, 50.1, 46.0, 25.5, 24.0; IR(KBr) ν: 3394, 3297, 3191, 2979, 2885, 2195, 1657, 1587, 1511, 1479, 1373, 1266, 1224, 1808,

1100, 1014, 915, 877, 818; MS(*m/z*): 357.40 ([*M*-1]⁺) 100%; Anal Calcd for C₁₇H₁₈N₄O₃S: C 56.97, H 5.06, N 15.63; Found: C 56.77, H 5.34, N 15.26.



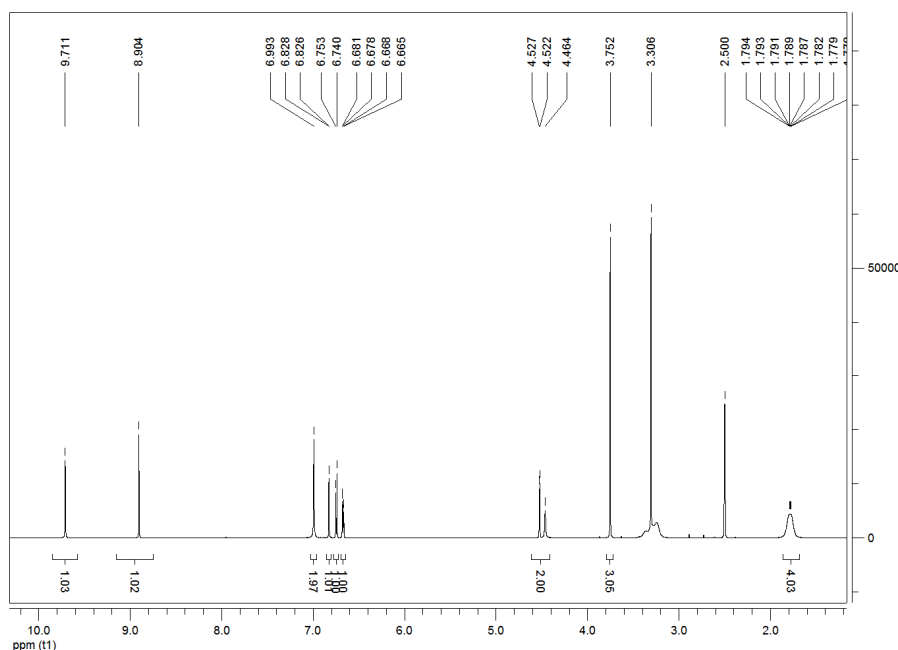
¹H NMR of **3e** (600 MHz, DMSO-*d*₆)



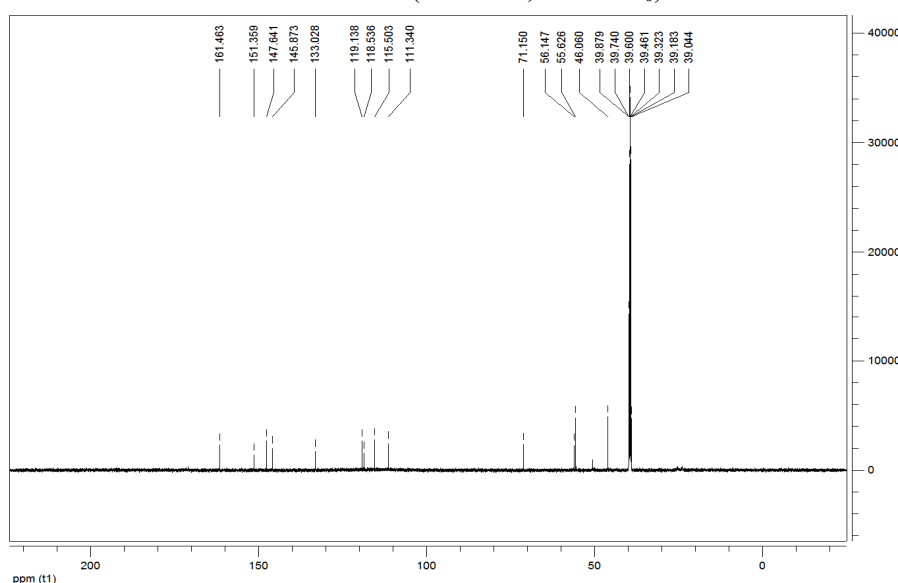
¹³C NMR of **3e** (150 MHz, DMSO-*d*₆)

3f: white solid, 30.5%, m.p. 204~206 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.71 (s, 1H, NH), 8.90(s, 1H, OH), 6.99 (s, 2H, NH₂), 6.83(d, *J* = 1.2Hz, 1H, ArH), 6.75 (d, *J* = 7.8Hz, 1H, ArH), 6.67~6.68(m, 1H, ArH), 4.52 (d, *J* = 3.0Hz, 1H, CH), 4.46 (s, 1H, CH), 3.75(s, 3H, OCH₃), 3.36~3.24 (m, 4H, CH₂), 1.79~1.78 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 161.5, 151.4, 147.6, 145.9, 133.0, 119.1, 118.5, 115.5, 111.3, 71.2, 55.6, 46.1; IR(KBr) ν: 3506, 3425, 3333,

3232, 2976, 2880, 2179, 1670, 1635, 1576, 1513, 1351, 1310, 1257, 1225, 1198, 1030, 875, 812, 780, 749; MS(*m/z*): 387.53([*M*-1]⁺) 100%; Anal Calcd for C₁₈H₂₀N₄O₄S: C 55.66, H 5.19, N 14.42; Found: C 55.37, H 5.49, N 14.27.



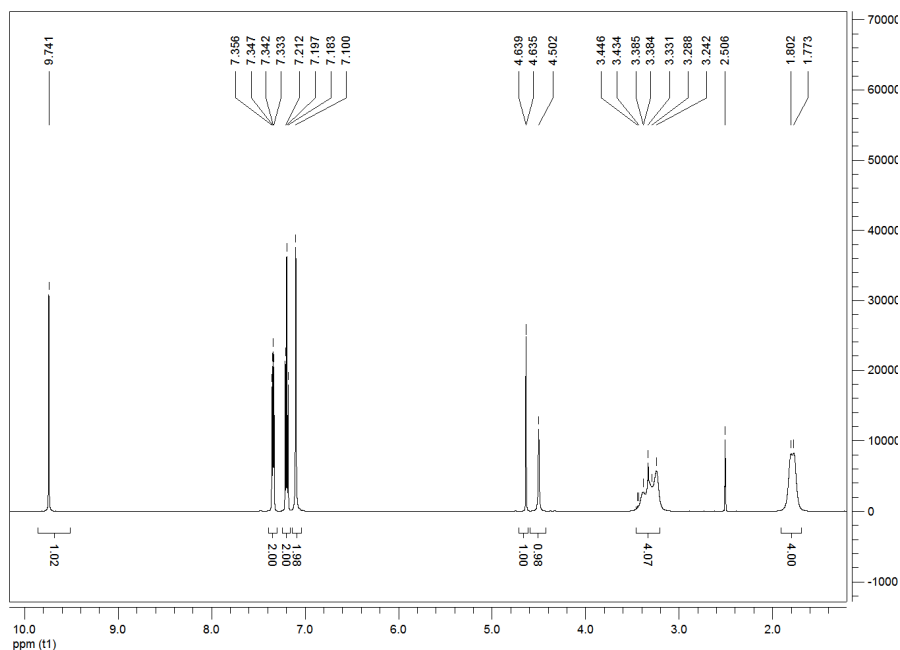
¹H NMR of **3f** (600 MHz, DMSO-*d*₆)



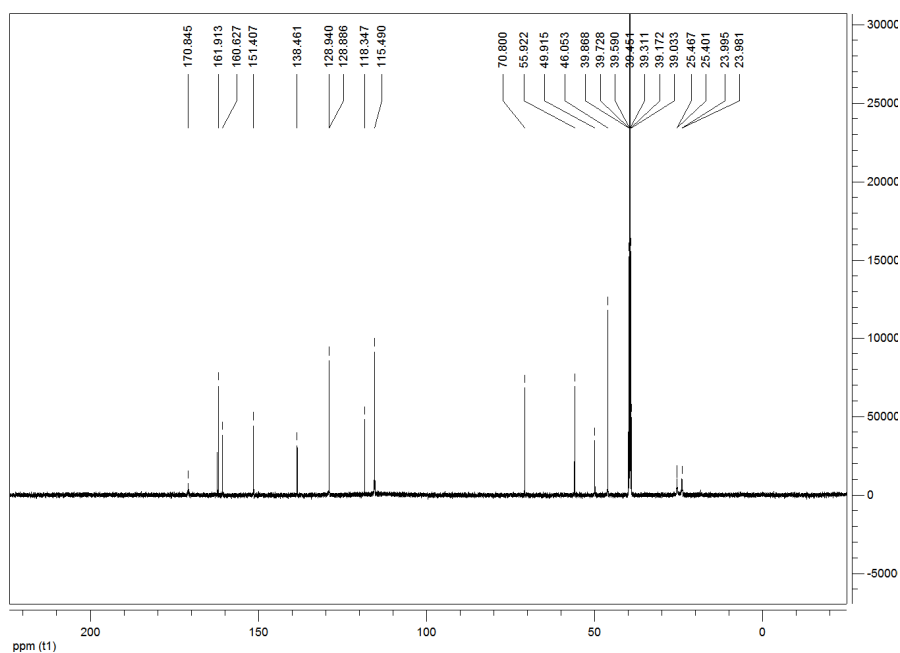
¹³C NMR of **3f** (150 MHz, DMSO-*d*₆)

3g: yellow solid, 33.9%, m.p. 205~207 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.74 (s, 1H, NH), 7.36~7.33(m, 2H, ArH), 7.20 (t, *J* = 8.4Hz, 2H, ArH), 7.10 (s, 2H, NH₂), 4.64 (d, *J* = 2.4Hz, 1H, CH), 4.50 (s, 1H, CH), 3.45~3.24 (m, 4H, CH₂), 1.95~1.65 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ:161.9, 160.6, 151.4, 138.5, 128.9, 128.8, 118.3, 115.5, 70.8, 55.9, 49.9, 46.1; IR(KBr) ν: 3403, 3194, 3066, 2975, 2880, 2187, 1689, 1663, 1581, 1508, 1361, 1257, 1226, 885, 819;

MS(*m/z*): 359.60([M-1]⁺) 100%; Anal Calcd for C₁₇H₁₇FN₄O₂S: C 56.65, H 4.75, N 15.55; Found: C 56.48, H 5.03, N 15.22.



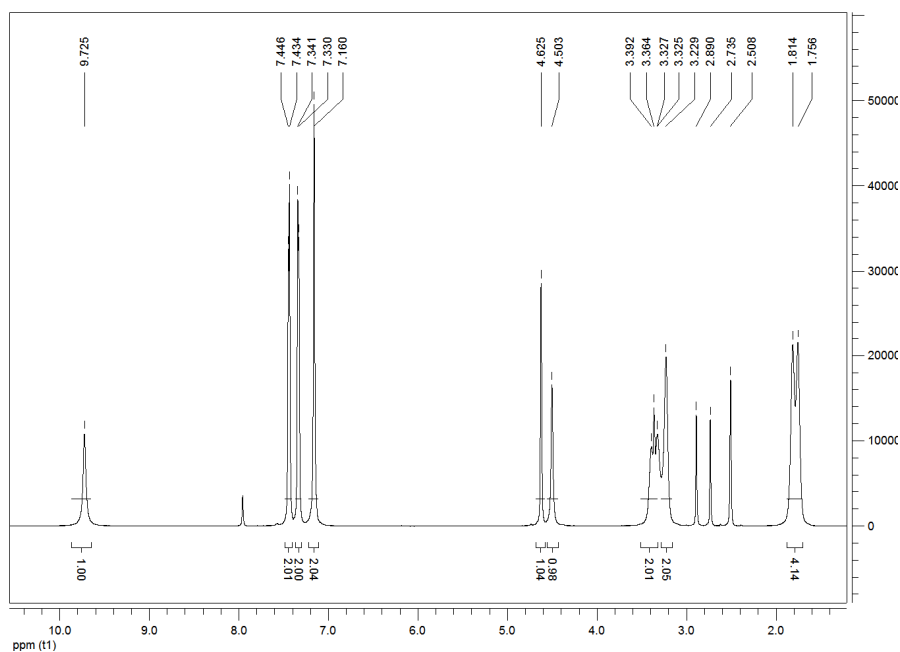
¹H NMR of **3g** (600 MHz, DMSO-*d*₆)



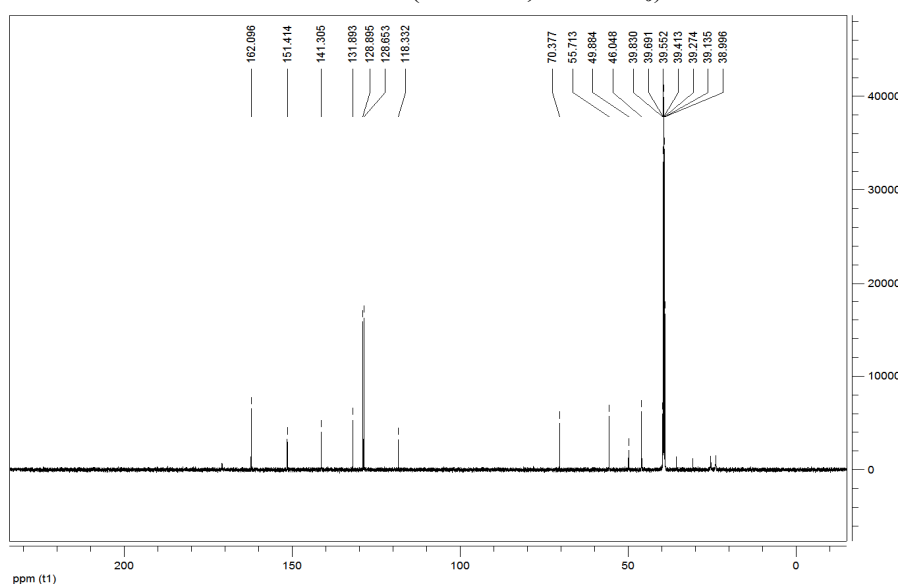
¹³C NMR of **3g** (150 MHz, DMSO-*d*₆)

3h: light yellow solid, 40.7%, m.p. 216~218□; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.72 (s, 1H, NH), 7.44 (d, *J* = 7.2Hz, 2H, ArH), 7.34 (d, *J* = 6.6Hz, 2H, ArH), 7.16 (s, 2H, NH₂), 4.62 (s, 1H, CH), 4.50 (s, 1H, CH), 3.39~3.23 (m, 4H, CH₂), 1.81~1.76 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 162.3, 162.1, 151.4, 141.3, 131.9, 128.9, 128.7, 118.3, 70.4, 55.7, 49.9, 46.0, 35.8, 30.7, 25.6, 25.5, 24.0; IR(KBr) ν: 3390, 3314, 3257, 3215, 2952, 2879, 2176, 1685, 1626, 1577,

1488, 1390, 1342, 1288, 1251, 1232, 1211, 1189, 1161, 1089, 1013, 914, 881, 846, 817, 781, 752;
 MS(*m/z*): 375.47 ($[M-1]^+$) 100%; 377.27 ($[M-1]^+$) 52%; Anal Calcd for $C_{17}H_{17}ClN_4O_2S$: C 54.18,
 H 4.55, N 14.87; Found: C 53.77, H 4.74, N 14.90.



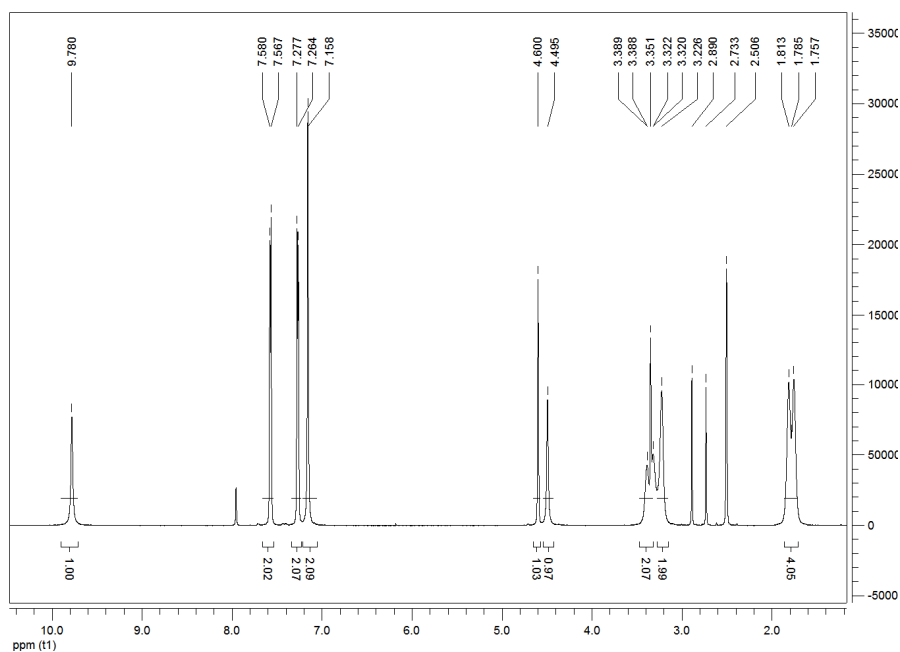
^1H NMR of **3h** (600 MHz, $\text{DMSO}-d_6$)



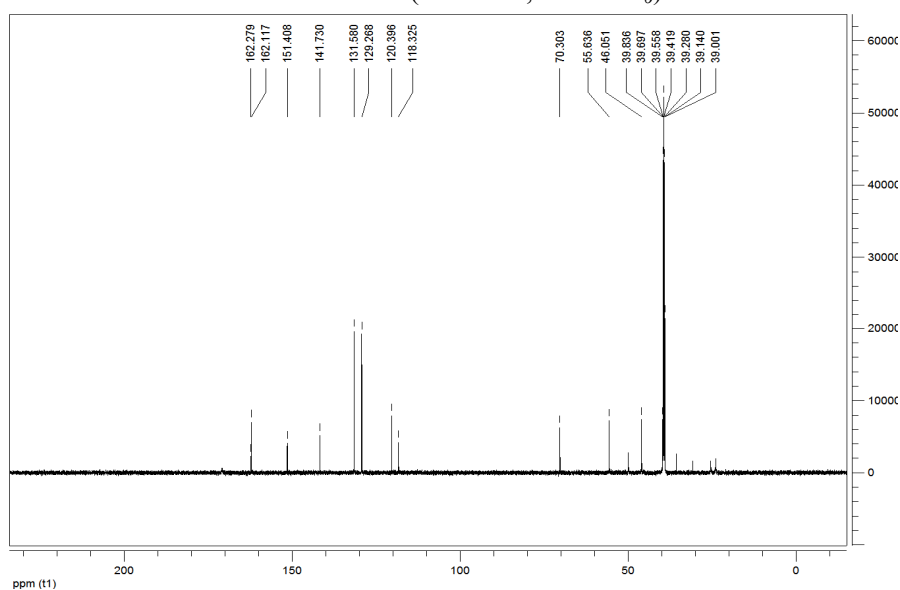
^{13}C NMR of **3h** (150 MHz, $\text{DMSO}-d_6$)

3i: light yellow solid, 36.2%, m.p. 220~222 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 9.78 (s, 1H, NH), 7.57 (d, $J = 7.8\text{Hz}$, 2H, ArH), 7.27 (d, $J = 7.8\text{Hz}$, 2H, ArH), 7.16 (s, 2H, NH₂), 4.60 (s, 1H, CH), 4.49 (s, 1H, CH), 3.39~3.22 (m, 4H, CH₂), 1.81~1.76 (m, 4H, CH₂); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 162.3, 162.1, 151.4, 141.7, 131.6, 129.3, 120.4, 118.3, 70.3, 55.6, 50.0, 25.5, 24.0; IR(KBr) ν : 3380, 3315, 3254, 3211, 2952, 2877, 2175, 1684, 1627, 1577, 1485, 1384, 1314, 1288,

1251, 1232, 1208, 1189, 1070, 1009, 912, 879, 844, 813, 781, 751; MS(*m/z*): 419.27 ([M-1]⁺) 100% ; 421.20 ([M-1]⁺) 100%; Anal Calcd for C₁₇H₁₇BrN₄O₂S: C 48.46, H 4.07, N 13.30; Found: C 48.29, H 4.23, N 13.05.



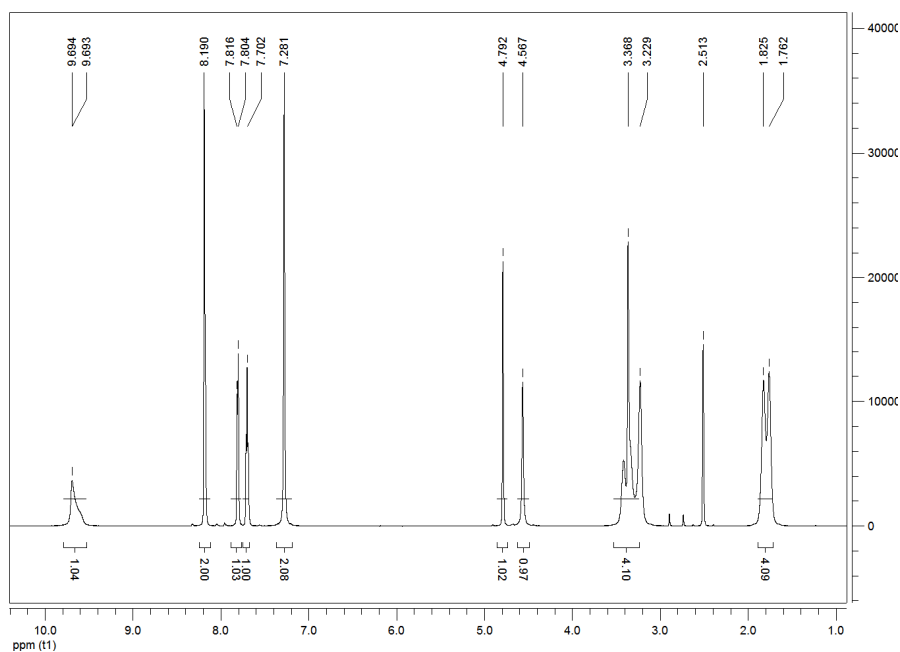
¹H NMR of **3i** (600 MHz, DMSO-*d*₆)



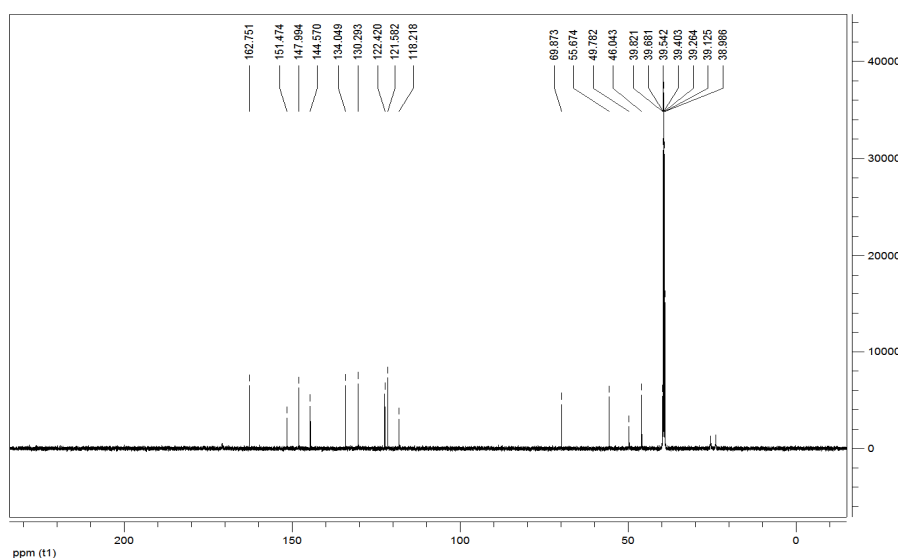
¹³C NMR of **3i** (150 MHz, DMSO-*d*₆)

3j: yellow solid, 34.1%, m.p. 216~219 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.75~9.50 (s, 1H, NH), 8.19(s, 1H, ArH), 7.81 (d, *J* = 7.2Hz, 2H, ArH), 7.71~7.69 (m, 1H, ArH), 7.28 (s, 2H, NH₂), 4.79 (s, 1H, CH), 4.57 (s, 1H, CH), 3.42~3.23 (m, 4H, CH₂), 1.83~1.76 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 162.8, 151.5, 148.0, 144.6, 134.0, 130.3, 122.4, 121.6, 118.2, 69.9, 55.7, 49.8, 46.0, 25.5, 24.0, 23.9; IR(KBr) ν: 3394, 3312, 3232, 3202, 3089, 3066, 2975, 2951, 2871,

2512, 2183, 2134, 1698, 1576, 1526, 1465, 1356, 1266, 1207, 1189, 1106, 1088, 1024, 934, 911, 876, 845, 814, 754; MS(*m/z*): 386.73([M-1]⁺) 100%; Anal Calcd for C₁₇H₁₇N₅O₄S: C 52.70, H 4.42, N 18.08; Found: C 52.87, H 4.75, N 17.73.



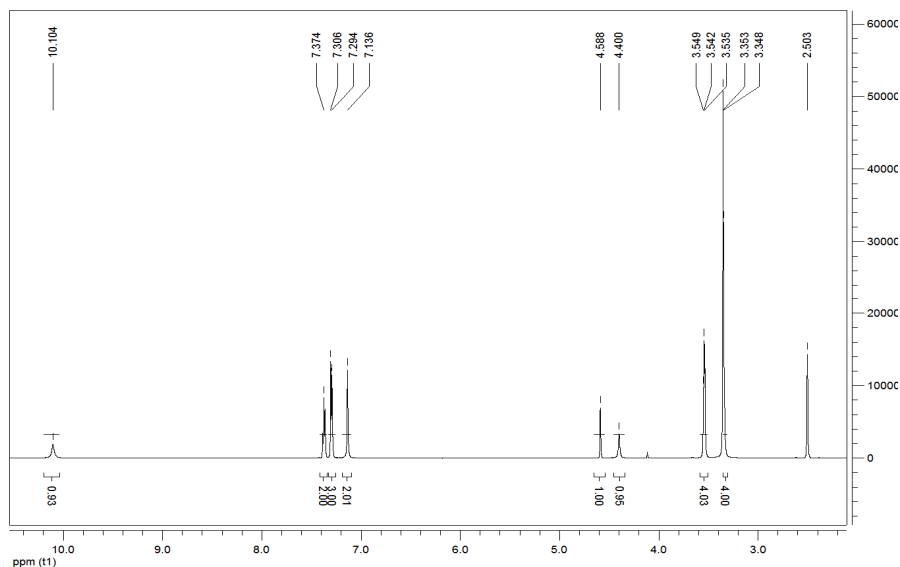
¹H NMR of **3j** (600 MHz, DMSO-*d*₆)



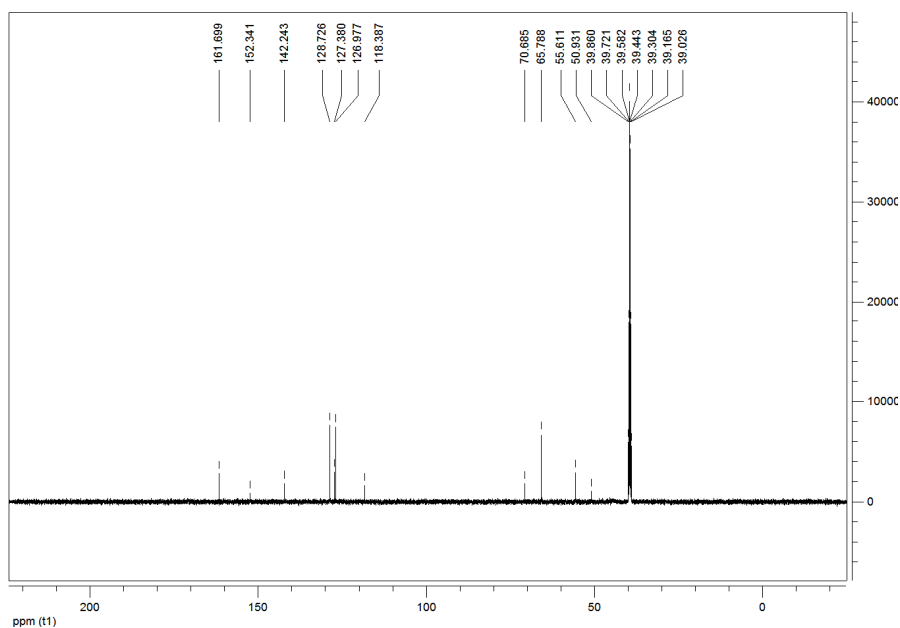
¹³C NMR of **3j** (150 MHz, DMSO-*d*₆)

4a: grey solid, 35.8%, m.p. 197~198°; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 10.10 (s, 1H, NH), 7.37 (t, *J* = 7.2Hz, 2H, ArH), 7.31~7.29 (m, 3H, ArH), 7.14 (s, 2H, NH₂), 4.59 (s, 1H, CH), 4.40 (s, 1H, CH), 3.55~3.54 (m, 4H, CH₂), 3.36~3.35 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 161.7, 152.3, 142.2, 128.7, 127.4, 127.0, 118.4, 70.7, 65.8, 55.6, 50.9; IR(KBr) ν: 3325, 3207, 2978, 2903, 2862, 2178, 1698, 1669, 1573, 1495, 1459, 1359, 1304, 1237, 1202, 1114, 1071, 1005,

933, 891, 869, 842, 745; MS(*m/z*): 357.40 ([*M*-1]⁺) 100%; Anal Calcd for C₁₇H₁₈N₄O₃S: C 56.97, H 5.06, N 15.63; Found: C 56.78, H 5.45, N 15.34.



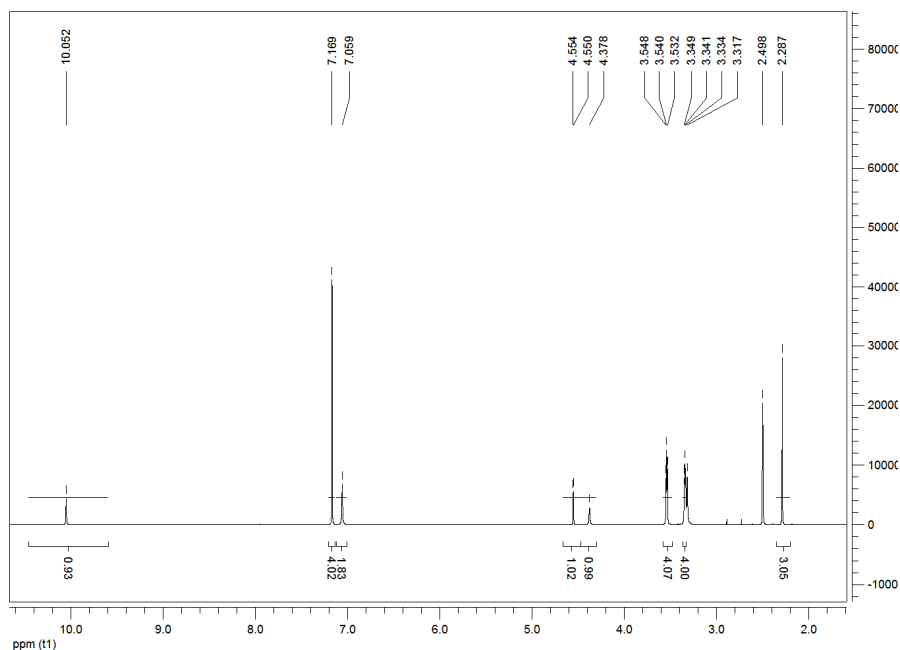
¹H NMR of **4a** (600 MHz, DMSO-*d*₆)



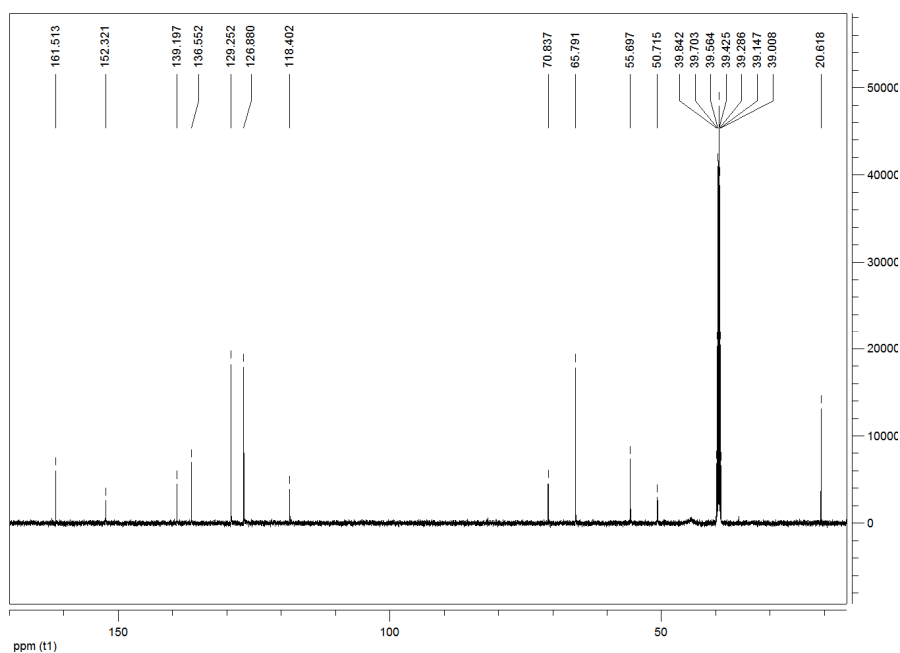
¹³C NMR of **4a** (150 MHz, DMSO-*d*₆)

4b: grey solid, 41.0%, m.p. 203~205 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 10.04 (s, 1H, NH), 7.17 (s, 4H, ArH), 7.04 (s, 2H, NH₂), 4.55 (d, *J* = 2.4 Hz, 1H, CH), 4.38 (s, 1H, CH), 3.55~3.53 (m, 4H, CH₂), 3.35~3.34 (m, 4H, CH₂), 2.29 (s, 3H, CH₃), ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 161.5, 152.3, 139.2, 136.6, 129.3, 126.9, 118.4, 70.8, 65.8, 55.7, 50.7, 20.6; IR(KBr) ν: 3418, 3307, 3230, 3198, 2984, 2924, 2864, 2183, 1711, 1663, 1637, 1593, 1519, 1456, 1434, 1345, 1307, 1275, 1245,

1180, 1106, 1067, 1020, 983, 875, 832, 806, 758 ; MS(*m/z*): 371.47 ([*M*-1]⁺) 100%; Anal Calcd for C₁₈H₂₀N₄O₃S: C 58.05, H 5.41, N 15.04; Found: C 58.35, H 5.27, N 14.67.



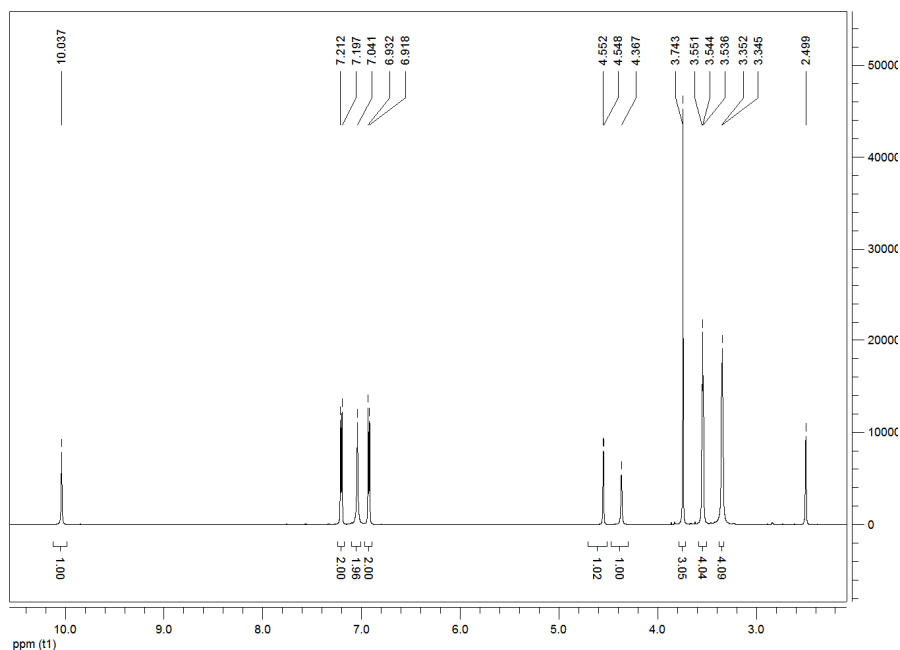
¹H NMR of **4b** (600 MHz, DMSO-*d*₆)



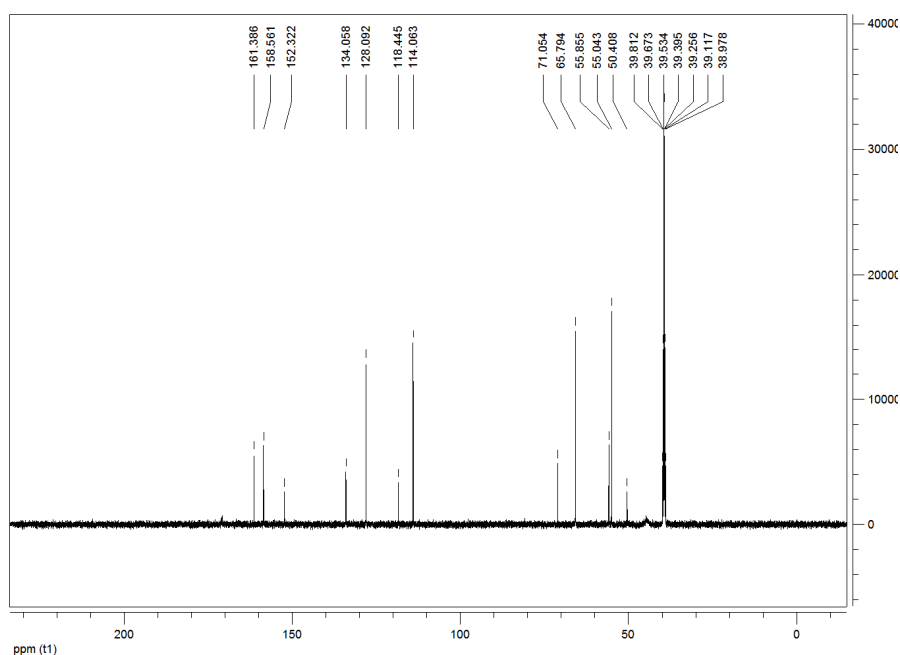
¹³C NMR of **4b** (150 MHz, DMSO-*d*₆)

4c: white solid, 21.4%, m.p. 198~201 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 10.04 (s, 1H, NH), 7.20 (d, *J* = 9 Hz, 2H, ArH), 7.04 (s, 2H, NH₂), 6.92 (d, *J* = 8.4 Hz, 2H, ArH), 4.55 (d, *J* = 2.4 Hz, 1H, CH), 4.37 (s, 1H, CH), 3.74 (s, 3H, OCH₃), 3.55~3.54 (m, 4H, CH₂), 3.35~3.34 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 161.4, 158.6, 152.3, 134.1, 128.1, 118.4, 114.1, 71.1, 65.8, 55.9, 55.0, 50.4; IR(KBr) ν: 3427, 3336, 3279, 2859, 2171, 1689, 1670, 1626, 1578, 1512, 1346, 1243,

1209, 1180, 1120, 1034, 1012, 877, 834, 750; MS(*m/z*): 387.67 ([*M*-1]⁺) 100%; Anal Calcd for C₁₈H₂₀N₄O₄S: C 55.66, H 5.19, N 14.42; Found: C 55.38, H 5.52, N 14.05.



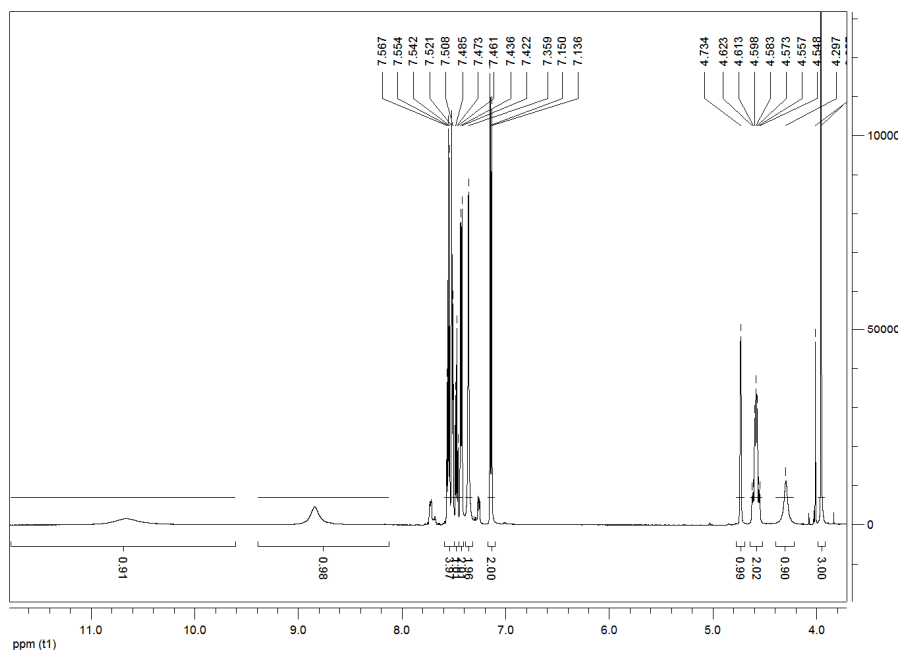
¹H NMR of **4c** (600 MHz, DMSO-*d*₆)



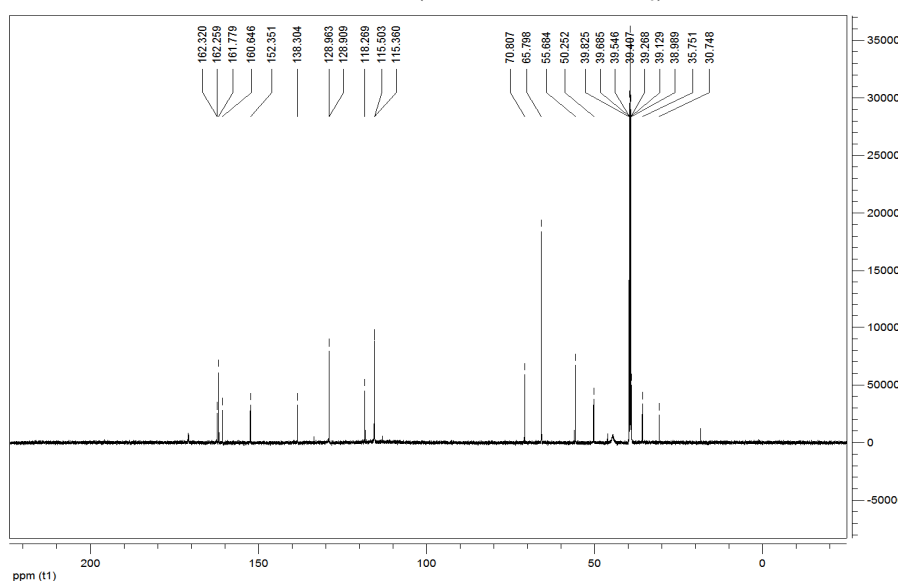
¹³C NMR of **4c** (150 MHz, DMSO-*d*₆)

4d: light yellow solid, 61.8%, m.p. 204~207°; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 10.07 (s, 1H, NH), 7.36~7.33 (m, 2H, ArH), 7.21~7.18 (m, 2H, ArH), 7.13 (s, 2H, NH₂), 4.62 (s, *J* = 1.8 Hz, 1H, CH), 4.40 (s, 1H, CH), 3.55~3.54 (m, 4H, CH₂), 3.37~3.35 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 162.3, 162.2, 161.8, 160.6, 152.4, 138.3, 129.0, 128.9, 118.3, 115.5, 115.4, 70.8, 65.8, 55.7, 50.3, 35.8, 30.7; IR(KBr) ν: 3380, 3326, 3211, 2974, 2922, 2864, 2176, 1698, 1667, 1569,

1507, 1461, 1360, 1240, 1208, 1159, 1010, 935, 872, 833, 790, 750; MS(*m/z*): 375.67 ([*M*-1]⁺) 100%; Anal Calcd for C₁₇H₁₇FN₄O₃S: C 54.25, H 4.55, N 14.88; Found: C 54.42, H 4.37, N 14.53.



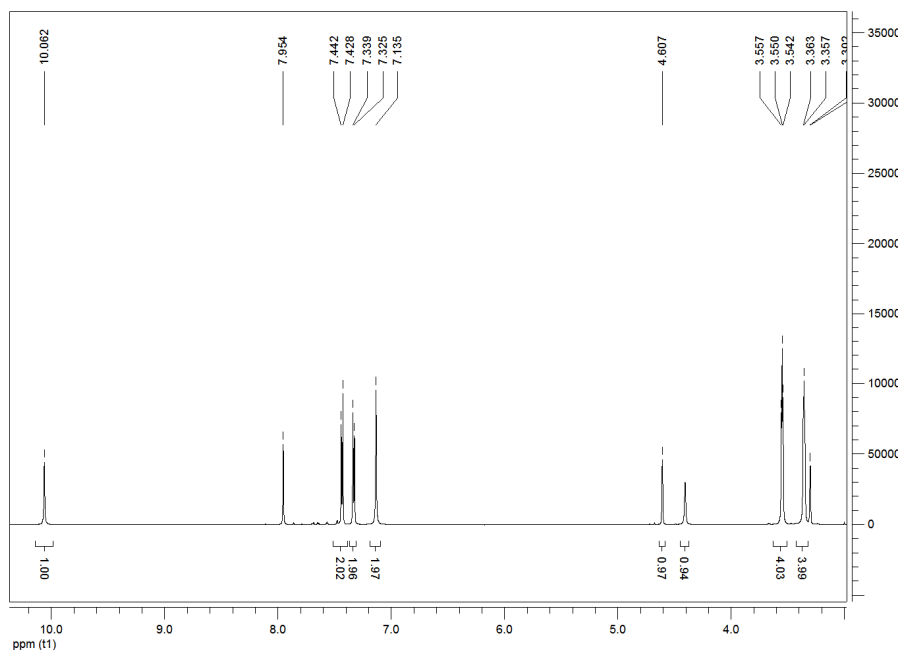
¹H NMR of **4d** (600 MHz, DMSO-*d*₆)



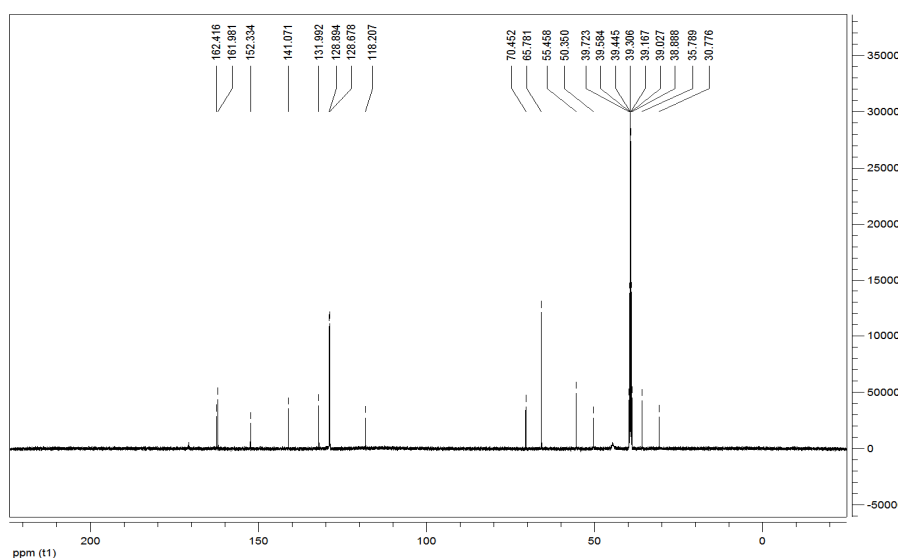
¹³C NMR of **4d** (150 MHz, DMSO-*d*₆)

4e: light yellow solid, 32.1%, m.p. 200~203 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 10.06 (s, 1H, NH), 7.43 (d, *J* = 8.4 Hz, 2H, ArH), 7.33 (d, *J* = 8.4 Hz, 2H, ArH), 7.14 (s, 2H, NH₂), 4.61 (s, 1H, CH), 4.40 (s, 1H, CH), 3.56~3.54 (m, 4H, CH₂), 3.36~3.35 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 162.4, 162.0, 152.3, 141.1, 132.0, 128.9, 128.7, 118.2, 70.5, 65.8, 55.5, 50.4, 35.8, 30.8; IR(KBr) ν: 3428, 3228, 3226, 2984, 2925, 2862, 2177, 1707, 1666, 1633, 1575, 1223, 1492, 1458, 1351, 1244, 1185, 1118, 1014, 984, 875, 843, 743; MS(*m/z*): 391.60 ([*M*-1]⁺) 100%,

393.47([M-1]⁺) 70%; Anal Calcd for C₁₇H₁₇ClN₄O₃S: C 51.97, H 4.36, N 14.26; Found: C 51.65 H 4.66, N 14.01.



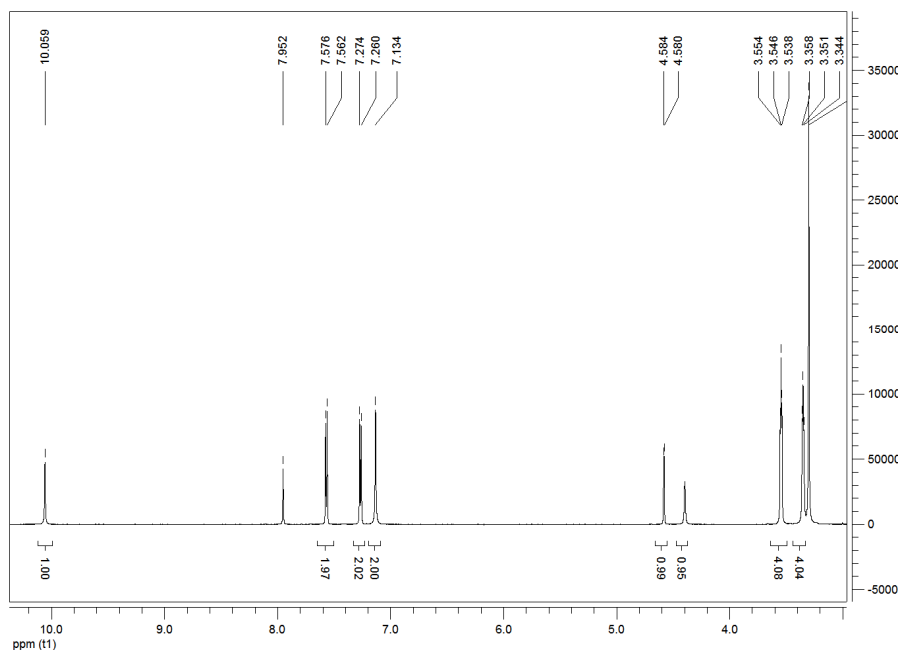
¹H NMR of **4e** (600 MHz, DMSO-*d*₆)



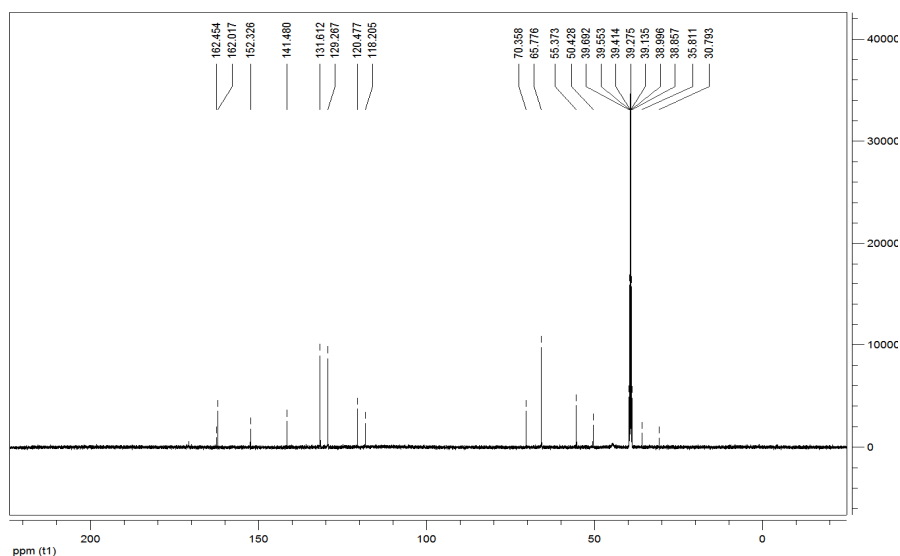
¹³C NMR of **4e** (150 MHz, DMSO-*d*₆)

4f: light yellow solid, 47.6%, m.p. 194~198°; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 10.06 (s, 1H, NH), 7.57 (d, *J* = 8.4Hz, 2H, ArH), 7.27 (d, *J* = 8.4Hz, 2H, ArH), 7.13 (s, 2H, NH₂), 4.58 (d, *J* = 2.4Hz, 1H, CH), 4.40 (s, 1H, CH), 3.55~3.54 (m, 4H, CH₂), 3.36~3.34 (m, 4H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 162.5, 162.0, 152.3, 141.5, 131.6, 129.3, 120.5, 118.2, 70.4, 65.8, 55.4, 50.4, 35.8, 30.8; IR(KBr) ν: 3419, 3335, 3284, 3226, 2921, 2860, 2170, 1687, 16668, 1630, 1573, 1490, 1408, 1351, 1244, 1205, 1120, 1071, 1012, 876, 816, 743; MS(*m/z*): 435.20 ([M-1]⁺) 100%;

437.20 ($[M-1]^+$) 100%; Anal Calcd for $C_{17}H_{17}BrN_4O_3S$: C 46.69, H 3.92, N 12.81; Found: C 46.27, H 3.66, N 12.40.



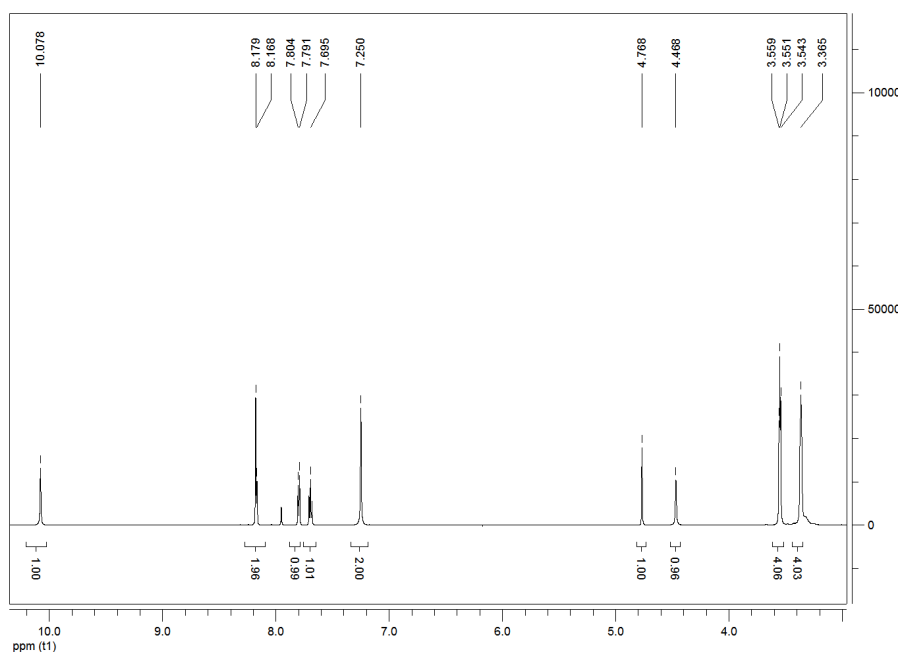
^1H NMR of **4f** (600 MHz, $\text{DMSO}-d_6$)



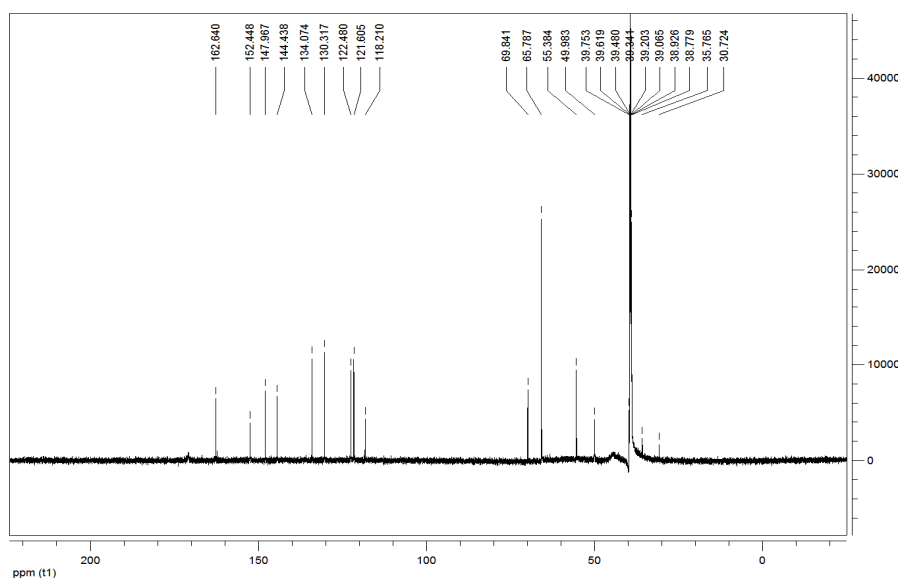
^{13}C NMR of **4f** (150 MHz, $\text{DMSO}-d_6$)

4g: light yellow solid, 32.0%, m.p. 210~213 $^\circ$; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 10.08 (s, 1H, NH), 7.57(m, 2H, ArH), 7.80 (d, $J = 7.8\text{Hz}$, 1H, ArH), 7.69 (m, 1H, ArH), 7.25(s, 2H, NH_2), 4.77 (s, 1H, CH), 4.47 (s, 1H, CH), 3.56~3.54 (m, 4H, CH_2), 3.37~3.35 (m, 4H, CH_2); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 162.6, 152.4, 148.0, 144.4, 134.1, 130.3, 122.5, 121.6, 118.2, 69.8, 65.8, 55.4, 50.0, 35.8, 30.7; IR(KBr) ν : 3374, 3326, 3205, 2988, 2901, 2866, 2176, 1703, 1664, 1569, 1528, 1499, 1462, 1356, 1263, 1238, 1211, 1115, 1007, 938, 870, 842, 820, 801; MS(m/z): 402.67 ($[M-1]^+$)

100%; Anal Calcd for C₁₇H₁₇N₅O₅S: C 50.61, H 4.25, N 17.88; Found: C 50.39, H 4.72, N 17.34.



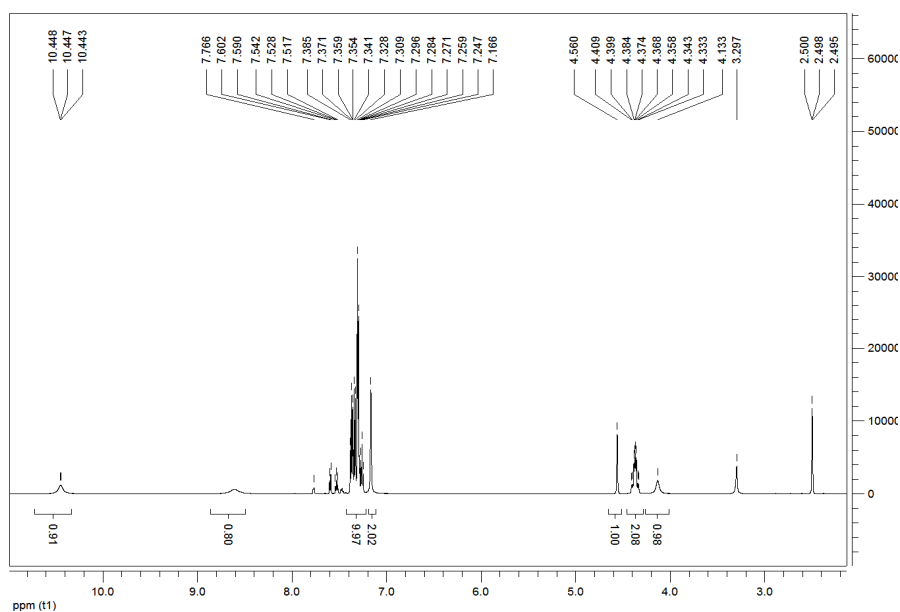
¹H NMR of **4g** (600 MHz, DMSO-*d*₆)



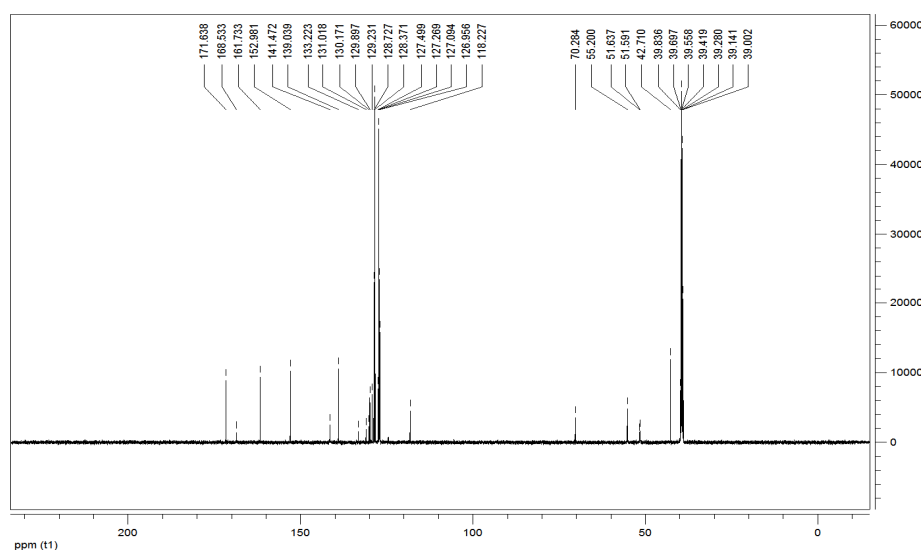
¹³C NMR of **4g** (150 MHz, DMSO-*d*₆)

5a: white solid, 40.3%, m.p. 201~203 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 10.50~10.35 (brs, 1H, NH), 8.71~ 8.49 (brs, 1H, NH), 7.38~7.25 (m, 10H, ArH), 7.17 (s, 2H, NH₂), 4.56 (s, 1H, CH), 4.41~4.33 (m, 2H, CH₂), 4.19~4.07 (brs, 1H, CH); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 171.6, 168.5, 161.7, 153.0, 141.5, 139.0, 133.2, 131.0, 130.2, 129.9, 129.2, 128.7, 128.4, 127.5, 127.3, 127.1, 127.0, 118.2, 70.3, 55.2, 51.6, 51.6, 42.7; IR(KBr) ν: 3441, 3320, 3221, 3153, 3062, 3031, 2969, 2177, 1702, 1684, 1619, 1576, 1494, 1451, 1349, 1257, 1186, 1079, 1026, 979, 879; MS (m/z): 377.40 ([M-1]⁺, 100%); Anal Calcd for C₂₀H₁₈N₄O₂S: C 63.47, H 4.79, N 14.80; Found: C 63.20, H

4.83, N 14.27.

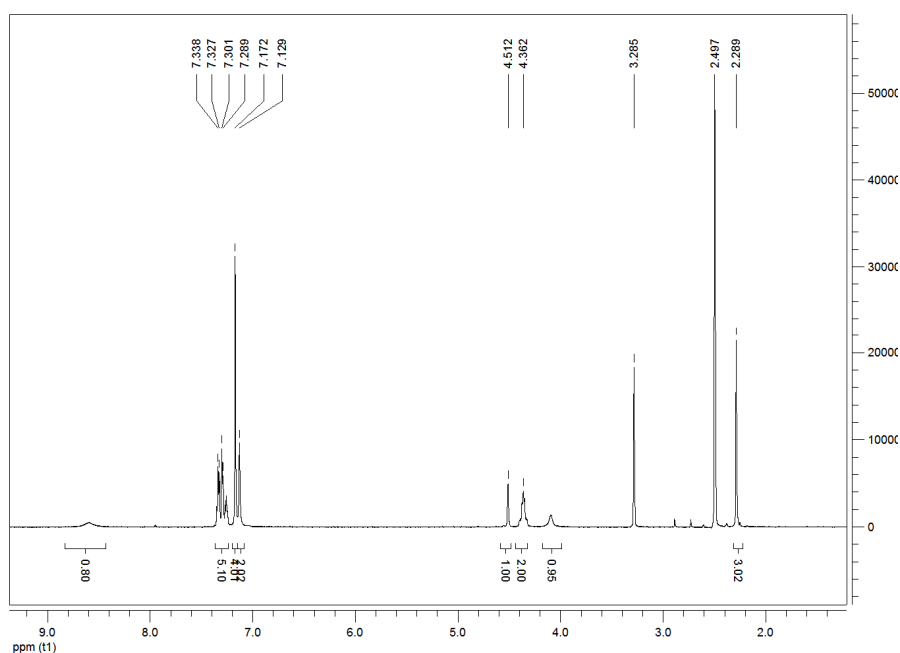


^1H NMR of **5a** (600 MHz, $\text{DMSO-}d_6$)

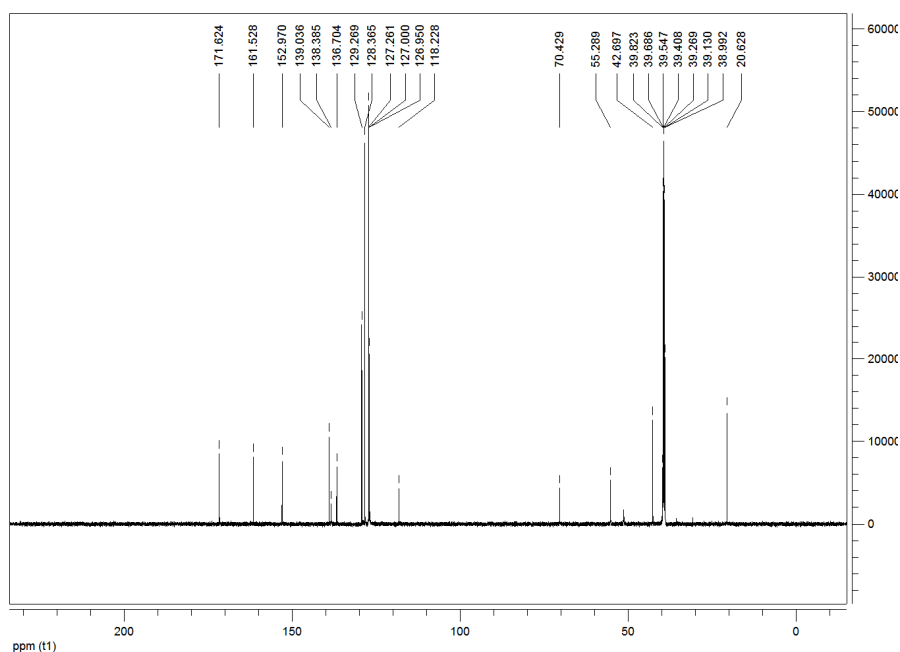


^{13}C NMR of **5a** (150 MHz, $\text{DMSO-}d_6$)

5b: grey solid, 52.2%, m.p. 204~207 $^{\circ}\text{C}$; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ : 8.82~8.43 (brs, 1H, NH), 7.35~7.25 (m, 5H, ArH), 7.17 (s, 4H, ArH), 7.13 (s, 2H, NH_2), 4.51 (s, 1H, CH), 4.38~4.35 (m, 2H, CH_2), 4.16~4.03 (brs, 1H, CH), 2.29 (s, 3H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ : 171.6, 161.5, 153.0, 139.0, 138.4, 136.7, 129.3, 128.4, 127.3, 127.0, 127.0, 118.2, 70.4, 55.3, 51.4, 42.7, 20.6; IR(KBr) ν : 3401, 3340, 3180, 2971, 2208, 1962, 1642, 1582, 1541, 1452, 1455, 1354, 1254, 1201, 1108, 1029, 979, 871, 793; MS (m/z): 391.60 ($[\text{M}-1]^+$, 100%), Anal Calcd for $\text{C}_{21}\text{H}_{20}\text{N}_4\text{O}_2\text{S}$: C 64.27, H 5.14, N 14.28; Found: C 63.85, H 5.46, N 14.03.



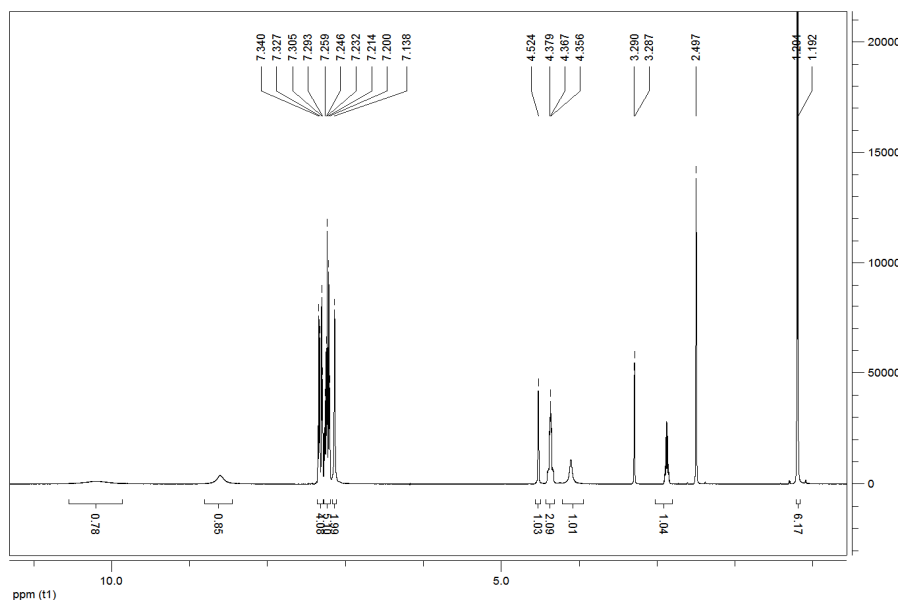
^1H NMR of **5b** (600 MHz, $\text{DMSO}-d_6$)



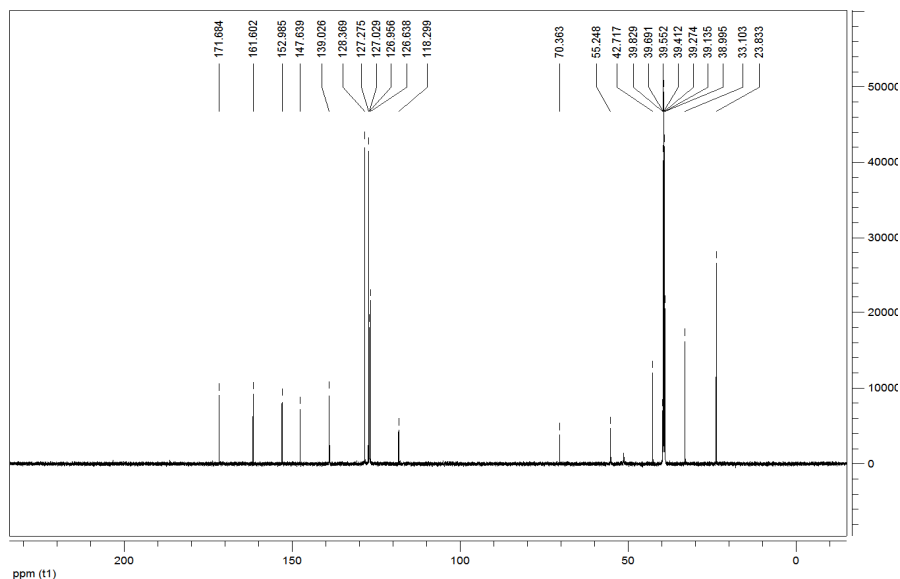
^{13}C NMR of **5b** (150 MHz, $\text{DMSO}-d_6$)

5c: white solid, 43.2%, m.p. 211~212 $^{\circ}\text{C}$; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 10.58~9.86 (brs, 1H, NH), 8.80~8.46 (brs, 1H, NH), 7.35~7.33 (m, 2H, ArH), 7.30 (d, $J = 7.2\text{Hz}$, 2H, ArH), 7.26~7.21 (brs, 5H, ArH), 7.14 (s, 2H, NH_2), 4.52 (s, 1H, CH), 4.40~4.33 (m, 2H, CH_2), 4.18~4.04 (brs, 1H, CH), 2.90~2.85 (m, 1H, CH), 1.20 (d, $J = 7.2\text{Hz}$, 6H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 171.7, 161.6, 153.0, 147.6, 139.0, 138.8, 128.4, 127.3, 127.0, 127.0, 126.6, 118.3, 70.4, 55.2, 51.3, 42.7, 33.1, 23.8; IR(KBr) ν : 3443, 3350, 3296, 3177, 2963, 2373, 2205, 1699, 1636, 1588, 1544, 1518, 1458, 1427, 1351, 1272, 1200, 1050, 977, 829, 791, 755; MS (m/z):

419.60 ($[M-1]^+$, 100%) Anal Calcd for $C_{23}H_{24}N_4O_2S$: C 65.69, H 5.75, N 13.32; Found: C 65.45, H 5.90, N 12.87.



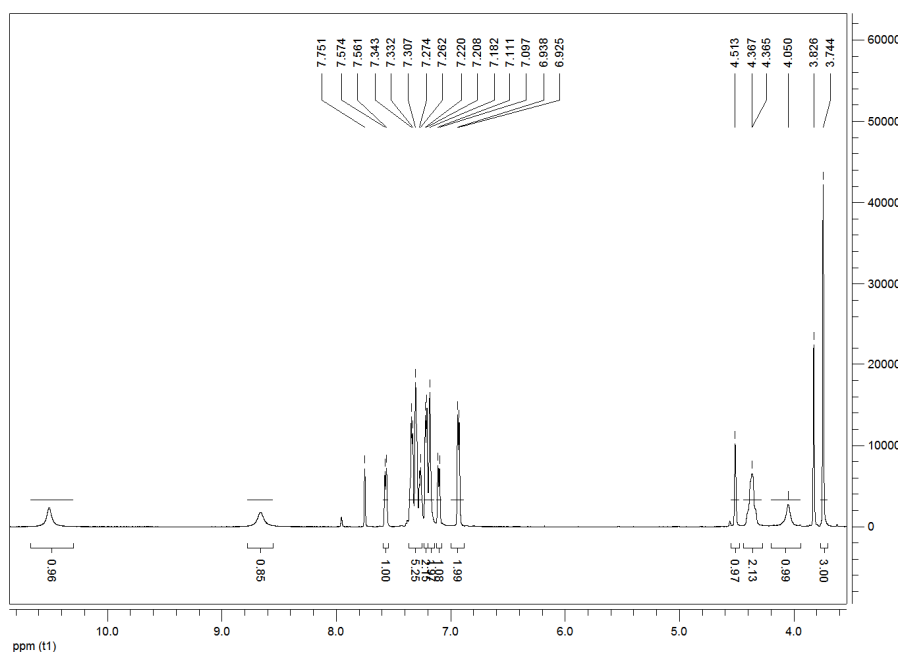
1H NMR of **5c** (600 MHz, $DMSO-d_6$)



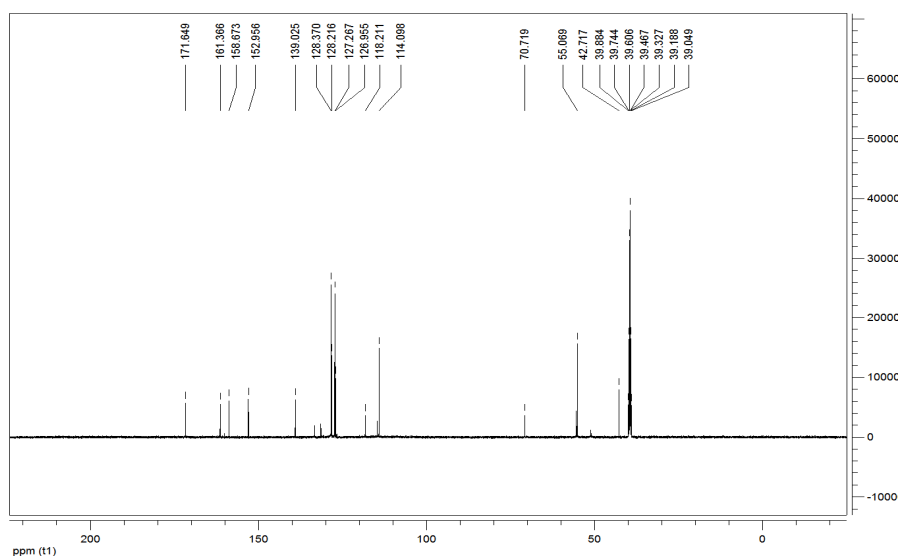
^{13}C NMR of **5c** (150 MHz, $DMSO-d_6$)

5d: light yellow solid, 59.0%, m.p. 198~200 $^{\circ}C$; 1H NMR (600 MHz, $DMSO-d_6$) δ : 11.01~9.86 (brs, 1H, NH), 9.17~8.59 (brs, 1H, NH), 7.57~7.51 (m, 4H, ArH), 7.49~7.46 (m, 1H, ArH), 7.44~7.42 (d, J = 8.4Hz, 2H, ArH), 7.36 (s, 2H, NH_2), 4.73 (s, 1H, CH), 4.62~4.55 (m, 2H, CH_2), 4.38~4.24 (brs, 1H, CH), 3.96 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, $DMSO-d_6$) δ : 171.6, 161.4, 158.7, 153.0, 139.0, 128.4, 128.2, 127.3, 127.0, 118.2, 114.1, 70.7, 55.0, 42.7; IR(KBr) ν : 3448, 3322, 3227, 3162, 2967, 2840, 2174, 1693, 1623, 1582, 1554, 1510, 1355, 1313, 1254, 1183, 1114, 1030, 981, 883, 828, 799, 763; MS (m/z): 407.47 ($[M-1]^+$, 100%); Anal Calcd for $C_{21}H_{20}N_4O_3S$: C

61.75, H 4.94, N 13.72; Found: C 61.50, H 5.27, N 13.44.

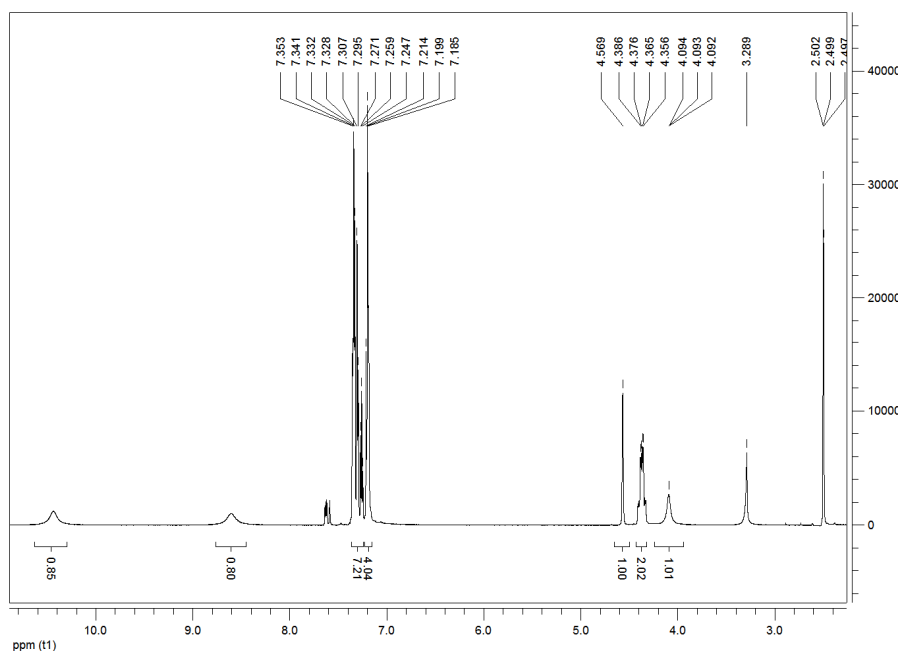


^1H NMR of **5d** (600 MHz, $\text{DMSO}-d_6$)

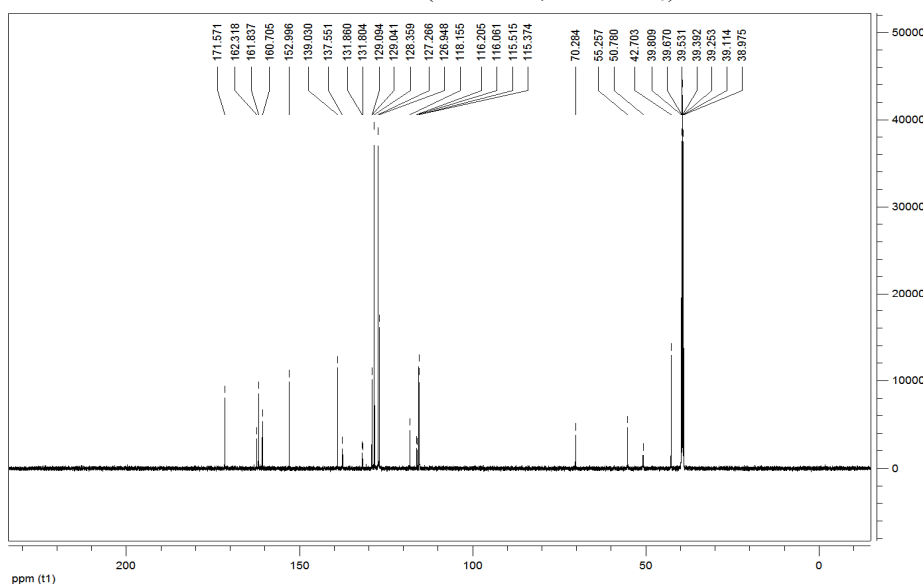


^{13}C NMR of **5d** (150 MHz, $\text{DMSO}-d_6$)

5e: white solid, 42.9%, m.p. 210~212 $^{\circ}\text{C}$; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 10.60~10.30 (brs, 1H, NH), 8.78~8.44 (brs, 1H, NH), 7.35~7.33 (m, 4H, ArH), 4.57(s, 1H, CH), 4.41~4.33 (m, 2H, CH_2), 4.15~ 4.03 (brs, 1H, CH); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 171.6, 162.3, 161.8, 160.7, 153.0, 139.0, 137.6, 131.9, 131.8, 129.1, 129.0, 128.4, 127.3, 127.0, 118.2, 116.2, 116.1, 115.5, 115.4, 70.3, 55.3, 50.8, 42.7; IR(KBr) ν : 3422, 3324, 3222, 3155, 2969, 2373, 2177, 1703, 1684, 1618, 1578, 1504, 11353, 1310, 1232, 1188, 1101, 980, 835, 809, 765; MS (m/z): 395.67 ($[\text{M}-1]^+$, 100%); Anal Calcd for $\text{C}_{20}\text{H}_{17}\text{FN}_4\text{O}_2\text{S}$: C 60.59, H 4.32, N 14.13; Found: C 60.53, H 4.76, N 13.88.

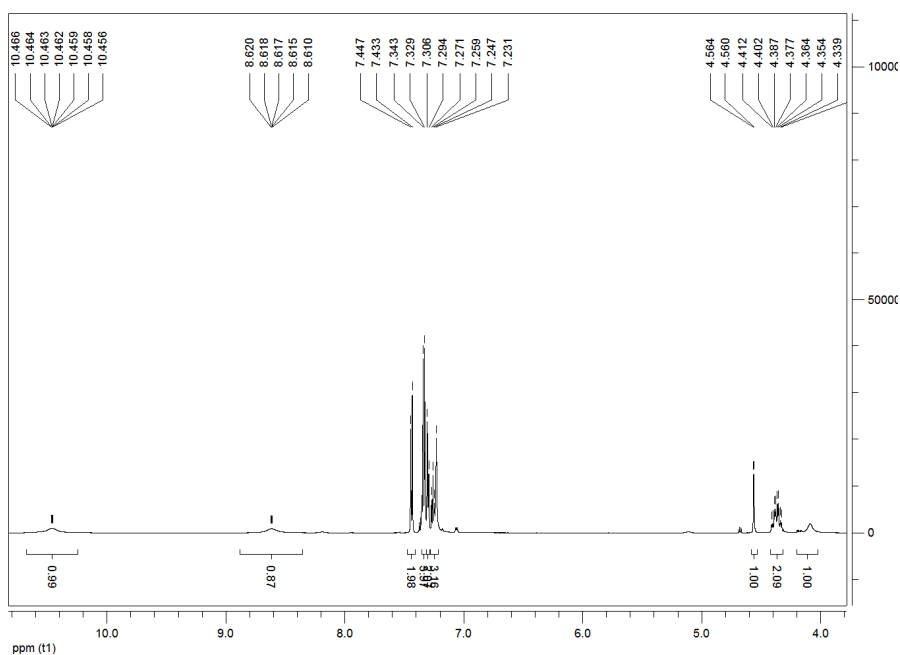


^1H NMR of **5e** (600 MHz, $\text{DMSO}-d_6$)

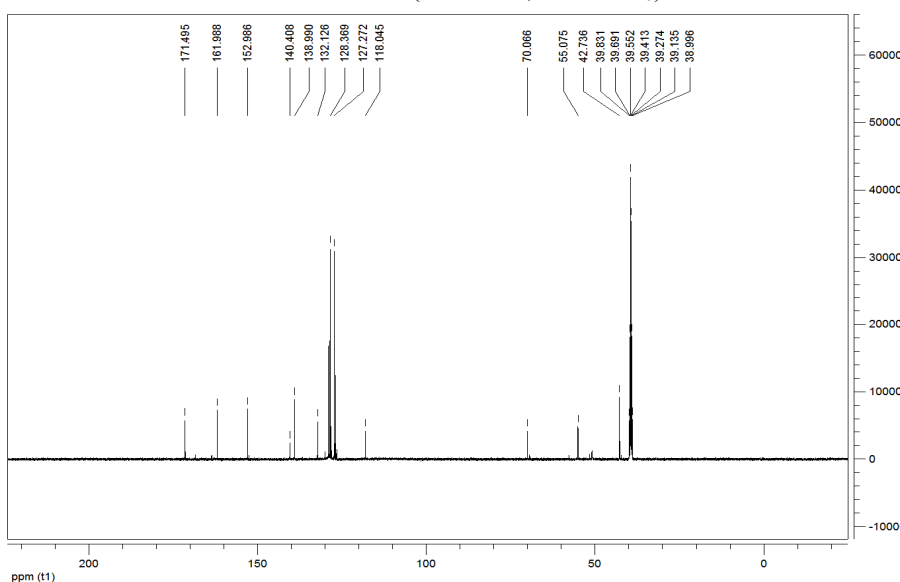


^{13}C NMR of **5e** (150 MHz, $\text{DMSO}-d_6$)

5f: white solid, 66.9%, m.p. 211~213 $^{\circ}\text{C}$; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 10.63~10.28 (brs, 1H, NH), 8.77~8.43 (brs, 1H, NH), 7.45~7.43 (m, 2H, ArH), 7.36~7.33 (m, 4H, ArH), 7.30 (d, J = 7.2 Hz, ArH), 7.27~7.23 (m, ArH, NH_2), 4.56 (s, 1H, CH), 4.41~4.33 (m, 2H, CH_2), 4.20~4.03 (brs, 1H, CH); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 171.5, 162.0, 153.0, 140.4, 139.0, 132.1, 128.4, 127.2, 118.0, 70.2, 55.1, 42.7; IR(KBr) ν : 3449, 3316, 3193, 2969, 2373, 2340, 2194, 1690, 1638, 1582, 1554, 1489, 1361, 1307, 1247, 1190, 1089, 1012, 978, 820, 783; MS (m/z): 411.20 ($[\text{M}-1]^+$, 100%); 413.20 ($[\text{M}-1]^+$, 47%); Anal Calcd for $\text{C}_{20}\text{H}_{17}\text{ClN}_4\text{O}_2\text{S}$: C 58.18, H 4.15, N 13.57; Found: C 57.92, H 4.46, N 13.25.

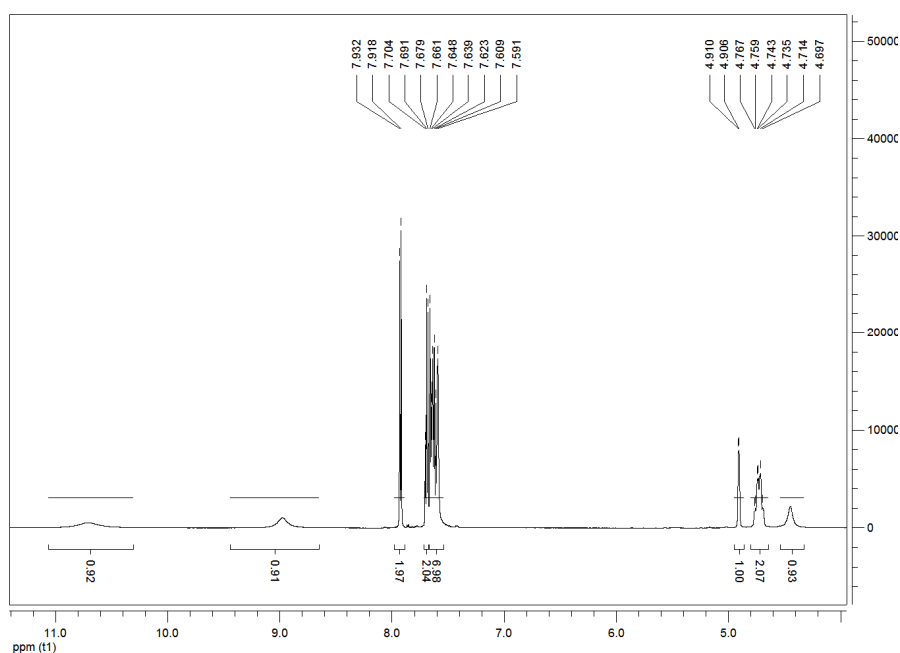


^1H NMR of **5f** (600 MHz, $\text{DMSO-}d_6$)

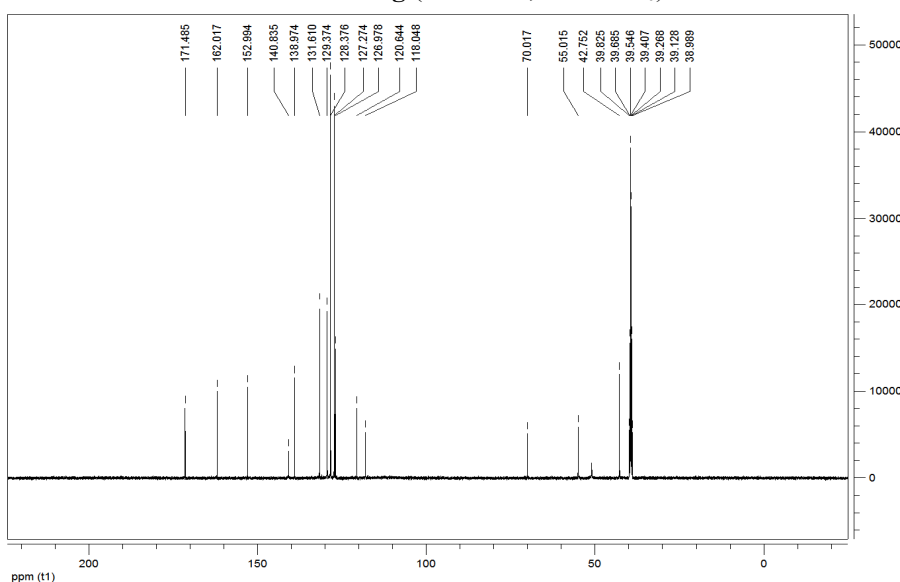


^{13}C NMR of **5f** (150 MHz, $\text{DMSO-}d_6$)

5g: light yellow solid, 57.4%, m.p. 218~220 $^{\circ}\text{C}$; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ : 11.02~10.32 (brs, 1H, NH), 9.12~8.82 (brs, 1H, NH), 7.92 (d, $J = 8.4\text{Hz}$, 2H, ArH), 7.70~7.68 (m, 2H, ArH), 7.66~7.59 (m, 7H, ArH, NH_2), 4.91 (s, 1H, CH), 4.77~4.70 (m, 2H, CH_2), 4.52~4.37 (brs, 1H, CH); ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ : 171.5, 162.0, 153.0, 140.8, 139.0, 131.6, 129.4, 128.4, 127.3, 127.0, 120.6, 118.0, 70.0, 55.0, 42.8; IR(KBr) ν : 3448, 3316, 3192, 2971, 2373, 2193, 1691, 1638, 1582, 1556, 1488, 1405, 1360, 1246, 1190, 1074, 1009, 979, 818, 782; MS (m/z): 455.00 ($[\text{M}-1]^+$, 100%); 457.07 ($[\text{M}-1]^+$, 100%); Anal Calcd for $\text{C}_{20}\text{H}_{17}\text{BrN}_4\text{O}_2\text{S}$: C 52.52, H 3.75, N 12.25; Found: C 52.45, H 3.93, N 11.79.



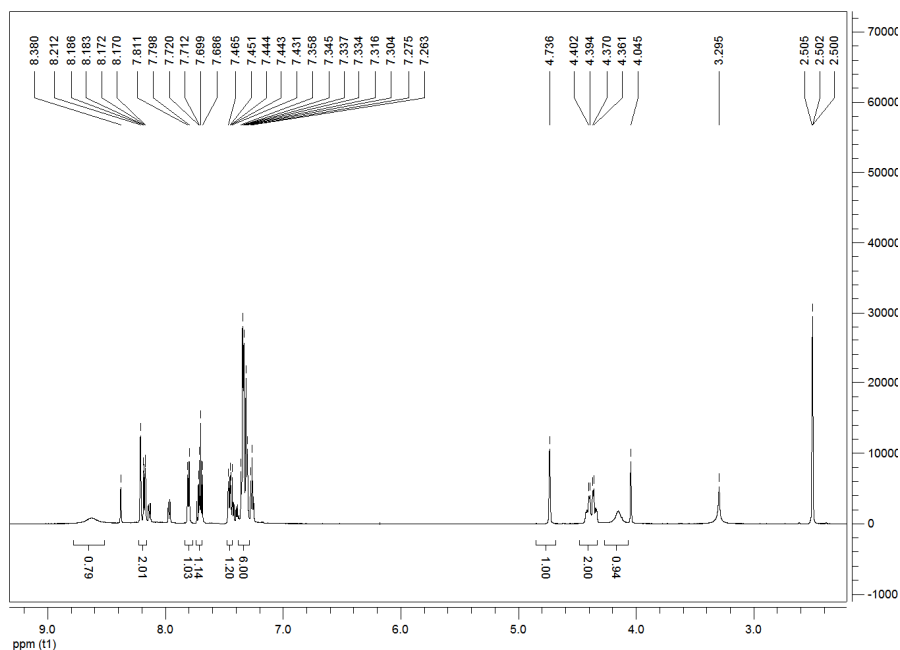
^1H NMR of **5g** (600 MHz, $\text{DMSO}-d_6$)



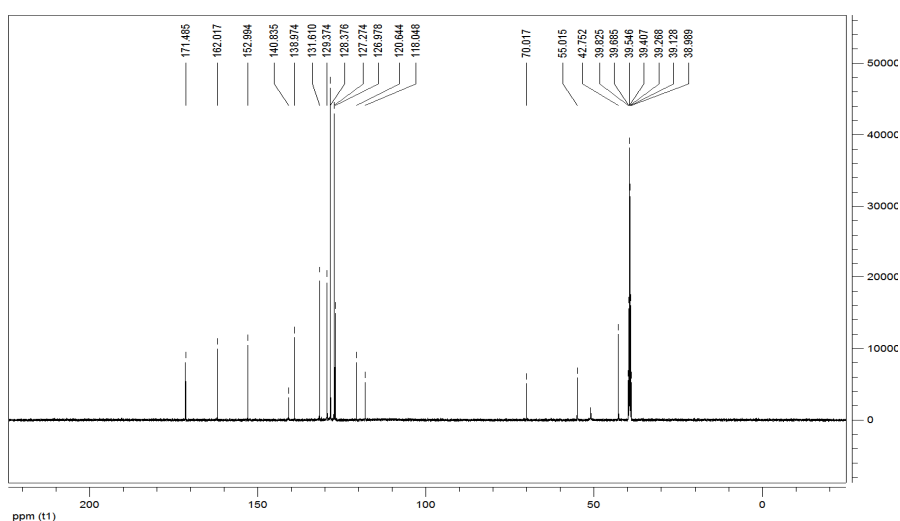
^{13}C NMR of **5g** (150 MHz, $\text{DMSO}-d_6$)

5h: white solid, 41.3%, m.p. 222~224 $^{\circ}\text{C}$; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 10.77~10.01 (brs, 1H, NH), 8.85~8.46 (brs, 1H, NH), 8.21~8.17 (m, 2H, ArH), 7.80 (d, $J = 7.8\text{Hz}$, 1H, ArH), 7.72~7.70 (m, 1H, ArH), 7.46~7.43 (m, 1H, ArH), 7.36~7.27 (m, 6H, ArH, NH_2), 4.74(s, 1H, CH), 4.40~4.36 (m, 2H, CH_2), 4.23~ 4.09 (brs, 1H, CH); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 171.4, 162.8, 153.1, 148.1, 148.0, 143.7, 139.0, 137.4, 135.2, 134.1, 134.0, 130.3, 130.2, 128.8, 128.6, 128.5, 128.3, 127.3, 127.0, 122.8, 122.5, 122.3, 121.8, 120.9, 118.0, 69.4, 55.0, 42.7, 42.3; IR(KBr) ν : 3432, 3354, 3259, 3174, 2976, 2373, 2340, 2175, 1701, 1628, 1577, 1533, 1497, 1422, 1352,

1254, 1185, 1093, 982, 873, 767; MS (m/z): 422.60 ([M-1]⁺, 100%); Anal Calcd for C₂₀H₁₇N₅O₄S: C 56.73, H 4.05, N 16.54; Found: C 56.48, H 4.51, N 16.32.



¹H NMR of **5h** (600 MHz, DMSO-*d*₆)

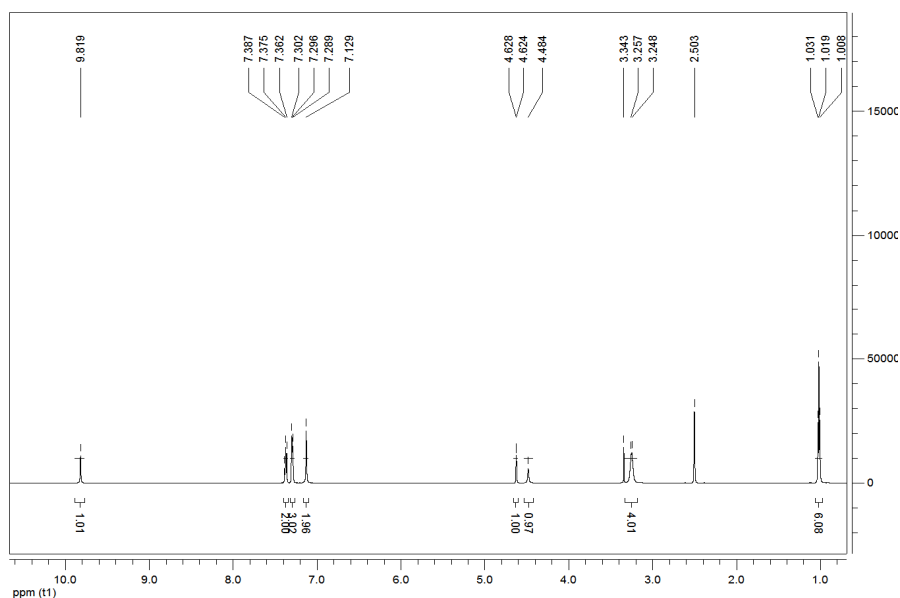


¹³C NMR of **5h** (150 MHz, DMSO-*d*₆)

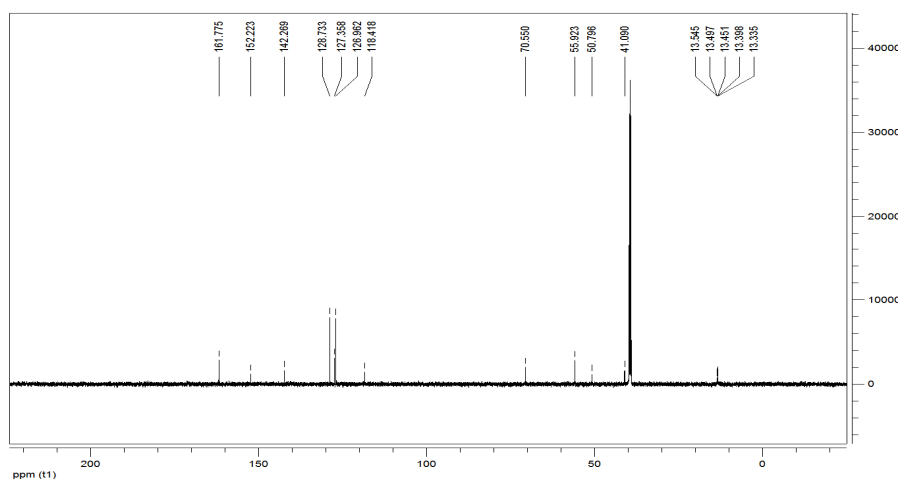
2. Typical preparation procedure of dihydrothiophene and spirocyclohexano-1,3-thiazole by one-pot four-component reaction of 1,3-thiazolidinedione, *p*-methylbenzaldehyde, malononitrile and diethylamine: A mixture of *p*-methylbenzaldehyde (8.0 mmol, 0.960g), malononitrile (8.0 mmol, 0.528 g) and diethylamine (4.0 mmol, 0.292g) in acetonitrile (5mL) was stirred at room temperature for two minutes. Then 1,3-thiazolidinedione (4.0mmol) was added and the reaction was stirred at room temperature for additional 48 hours. The resulting precipitate was collected by filtration and washed with acetonitrile. The crude product was refluxed in 50mL of

acetonitrile for two hours. After filtration the clean solution was cooled to give dihydrothiophene **6b**. The undissolved solid was filtrated out to give the product **7b**. The same reaction procedure was carried out by using other aromatic aldehydes and other amine to substitute diethylamine to give products **6a-6h** or **7a-7j**.

6a: white solid, 34.5%, m.p. 174~177 °C; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ : 9.82 (s, 1H, NH), 7.39~7.36 (m, 2H, ArH), 7.30~7.29 (m, 2H, ArH), 7.31 (s, 2H, NH_2), 4.62 (d, $J = 2.4\text{Hz}$, 1H, CH), 4.48 (s, 1H, CH), 3.30~3.20 (m, 4H, CH_2), 1.02 (t, $J = 7.2\text{Hz}$, 6H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ : 161.7, 152.2, 142.2, 128.7, 127.3, 126.9, 118.4, 70.5, 55.9, 50.7, 41.0, 13.5, 13.4, 13.4, 13.3, 13.3; IR(KBr) ν : 3416, 3328, 3231, 1976, 2933, 2175, 1670, 1635, 1574, 1482, 1359, 1337, 1304, 1261, 1204, 1152, 1081, 891, 852, 780, 747; MS (m/z): 343.40 ($[\text{M}-1]^+$, 100%); Anal Calcd for $\text{C}_{17}\text{H}_{20}\text{N}_4\text{O}_2\text{S}$: C 59.28, H 5.85, N 16.27; Found: C 59.24, H 6.23, N 16.02.

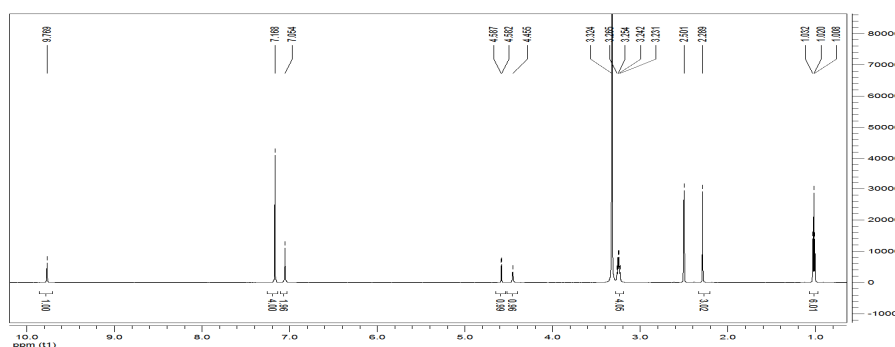


^1H NMR of **6a** (600 MHz, $\text{DMSO-}d_6$)

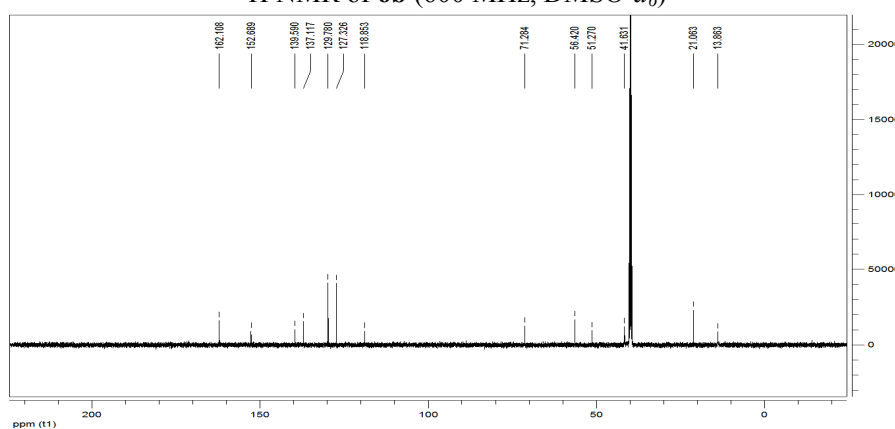


¹³C NMR of **6a** (150 MHz, DMSO-*d*₆)

6b: light yellow solid, 11.3%, m.p. 176~178 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.77 (s, 1H, NH), 7.17 (s, 4H, ArH), 7.05 (s, 2H, NH₂), 4.58 (d, *J* = 3.0 Hz, 1H, CH), 4.45 (s, 1H, CH), 3.27–3.23 (m, 4H, CH₂), 2.29 (s, 3H, CH₃), 1.02 (t, *J* = 7.2 Hz, 6H, CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 162.1, 152.6, 139.5, 137.1, 129.7, 127.3, 118.8, 71.2, 56.4, 51.2, 41.6, 21.0, 13.8; IR (KBr) ν: 3408, 3325, 3228, 2977, 2932, 2180, 1672, 1579, 1481, 1353, 1259, 1201, 1152, 1093, 896, 815; MS (m/z): 358.62 ([M-1]⁺, 100%); Anal Calcd for C₁₈H₂₂N₄O₂S: C 60.31, H 6.19, N 15.63; Found: C 60.48, H 6.57, N 15.84.

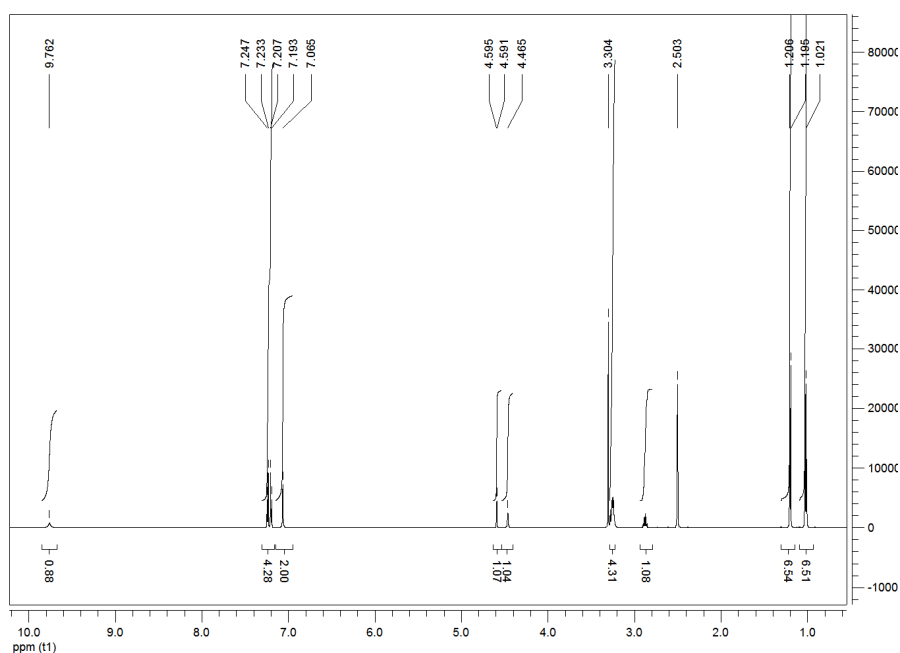


¹H NMR of **6b** (600 MHz, DMSO-*d*₆)

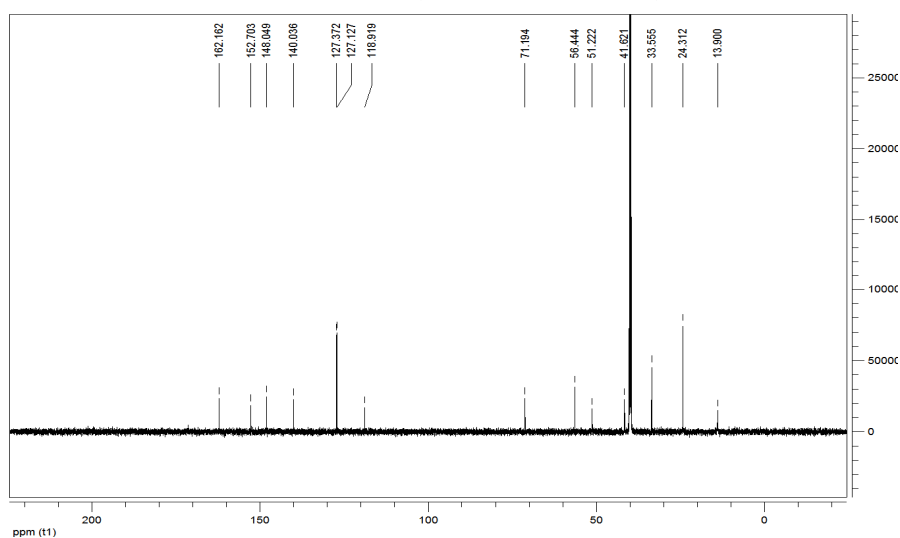


¹³C NMR of **6b** (150 MHz, DMSO-*d*₆)

6c: white solid, 10.4%, m.p. 180~182 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.85–9.67 (brs, 1H, NH), 7.24 (d, *J* = 8.4 Hz, 2H, ArH), 7.20 (d, *J* = 8.4 Hz, 2H, ArH), 7.06 (s, 2H, NH₂), 4.59 (d, *J* = 2.4 Hz, 1H, CH), 4.46 (s, 1H, CH), 3.28–3.23 (m, 4H, CH₂), 2.91–2.85 (m, 1H, CH), 1.20 (d, 6H, CH₃), 1.02 (t, *J* = 6.6 Hz, 6H, CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 162.1, 152.7, 148.0, 140.0, 127.3, 127.1, 118.9, 71.1, 56.4, 51.2, 41.6, 33.5, 24.3, 13.9; IR (KBr) ν: 3407, 3330, 3230, 2969, 2178, 1676, 1636, 1577, 1481, 1352, 1308, 1257, 1200, 1152, 1093, 1019, 897, 824, 747; MS (m/z): 385.55 ([M-1]⁺, 100%); Anal Calcd for C₂₀H₂₆N₄O₂S: C 62.15, H 6.78, N 14.50; Found: C 61.88, H 6.9, N 14.27.

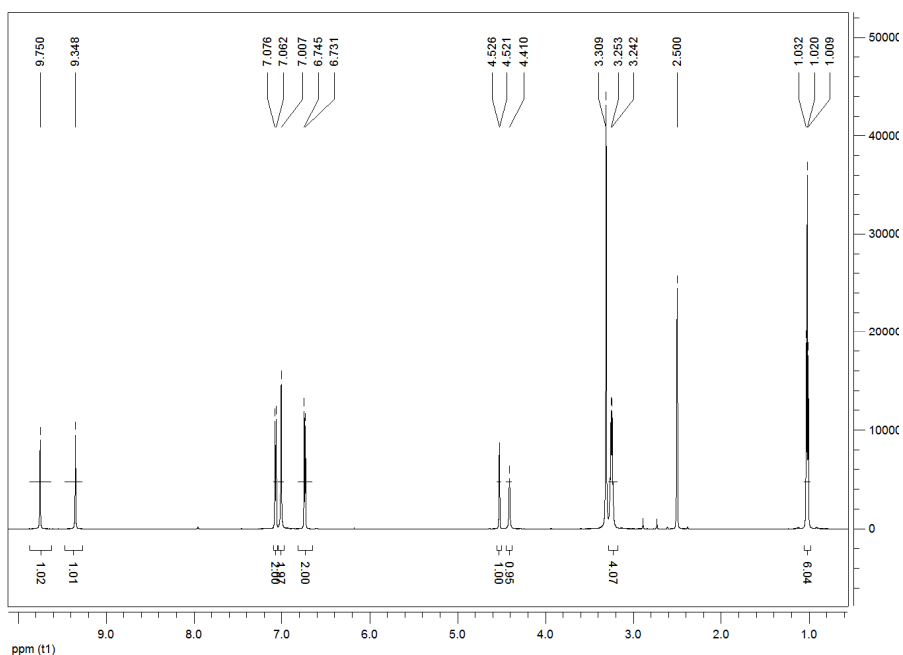


¹H NMR of **6c** (600 MHz, DMSO-*d*₆)

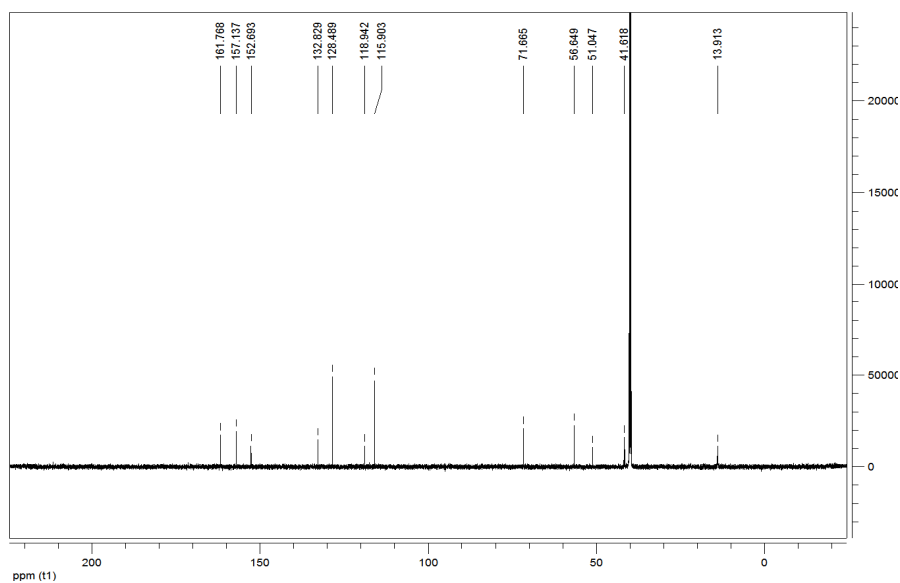


¹³C NMR of **6c** (150 MHz, DMSO-*d*₆)

6d: white solid, 35.4%, m.p. 184~186 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.75 (s, 1H, NH), 7.35 (s, 1H, OH), 7.07((d, *J* = 8.4Hz, 2H, ArH), 7.01(s, 1H, ArH), 6.74(d, *J* = 8.4Hz, 2H, NH₂), 4.52(d, *J* = 3.0Hz, 1H, OH), 4.41 (s, 1H, CH), 3.28~3.20 (m, 4H, CH₂), 1.02 (t, *J* = 7.2Hz, 6H, CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 161.1, 157.1, 152.6, 132.8, 128.4, 118.9, 115.9, 71.6, 56.6, 51.0, 41.0, 13.9; IR(KBr) ν: 3405, 3320, 3202, 3001, 2192, 1679, 1652, 1587, 1512, 1486, 1358, 1300, 1263, 1211, 1177, 1087, 1016, 889, 827, 802, 751; MS (*m/z*): 359.45 ([*M*-1]⁺, 100%); Anal Calcd for C₁₇H₂₀N₄O₃S: C 56.65, H 5.59, N 15.54; Found: C 56.37, H 5.84, N 15.35.



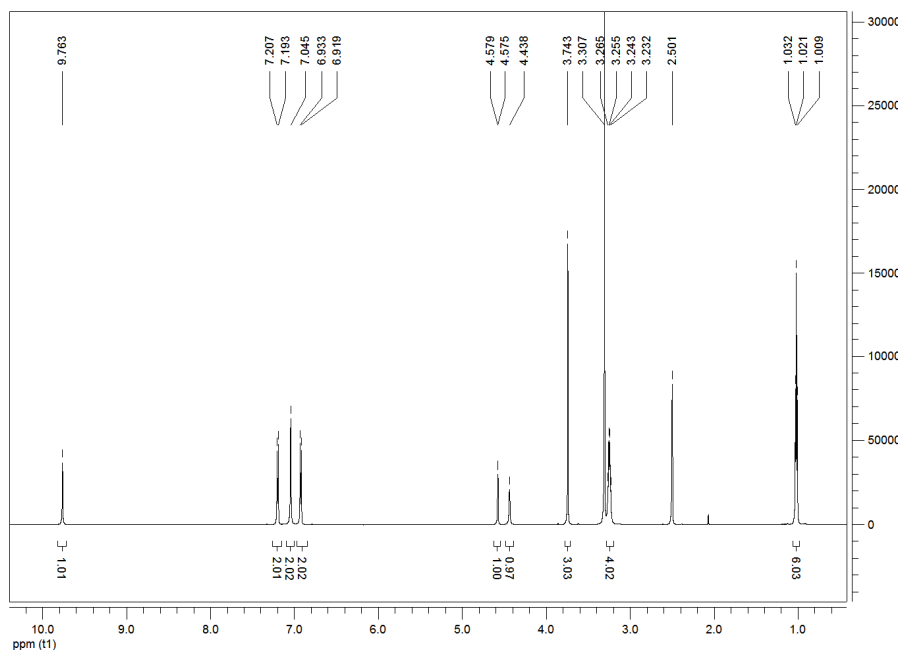
^1H NMR of **6d** (600 MHz, $\text{DMSO-}d_6$)



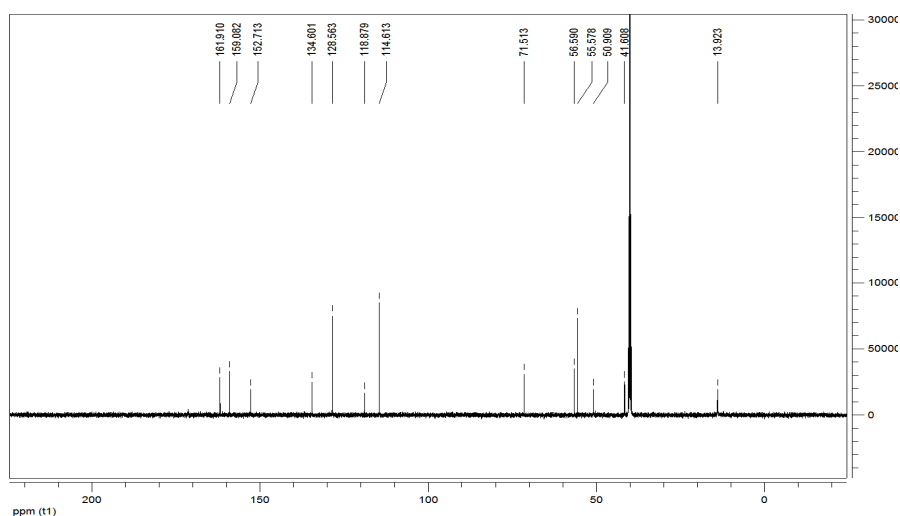
^{13}C NMR of **6d** (150 MHz, $\text{DMSO-}d_6$)

6e: grey solid, 49.3%, m.p. 159~160 °C; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ : 9.76 (s, 1H, NH), 9.20 (d, $J = 8.4\text{Hz}$, 2H, ArH), 7.04 (s, 2H, NH_2), 6.92 (d, $J = 8.4\text{Hz}$, 2H, ArH), 4.57 (d, $J = 2.4\text{Hz}$, 1H, CH), 4.44 (s, 1H, CH), 3.74 (s, 3H, OCH_3), 3.27~3.23 (m, 4H, CH_2), 1.02 (t, $J = 6.6\text{Hz}$, 6H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ : 161.9, 159.0, 152.7, 134.6, 128.5, 118.8, 114.6, 71.5, 56.5, 55.5, 50.9, 41.6, 13.9; IR(KBr) ν : 3402, 3306, 3221, 2992, 2935, 2837, 2176, 1681, 1626, 1582, 1510, 1481, 1344, 1299, 1250, 1203, 1177, 1151, 1090, 1033, 901, 828, 803, 749; MS (m/z):

374.54 ($[M-1]^+$, 100%); Anal Calcd for $C_{18}H_{22}N_4O_3S$: C 57.73, H 5.92, N 14.96; Found: C 57.62, H 6.36, N 14.65.



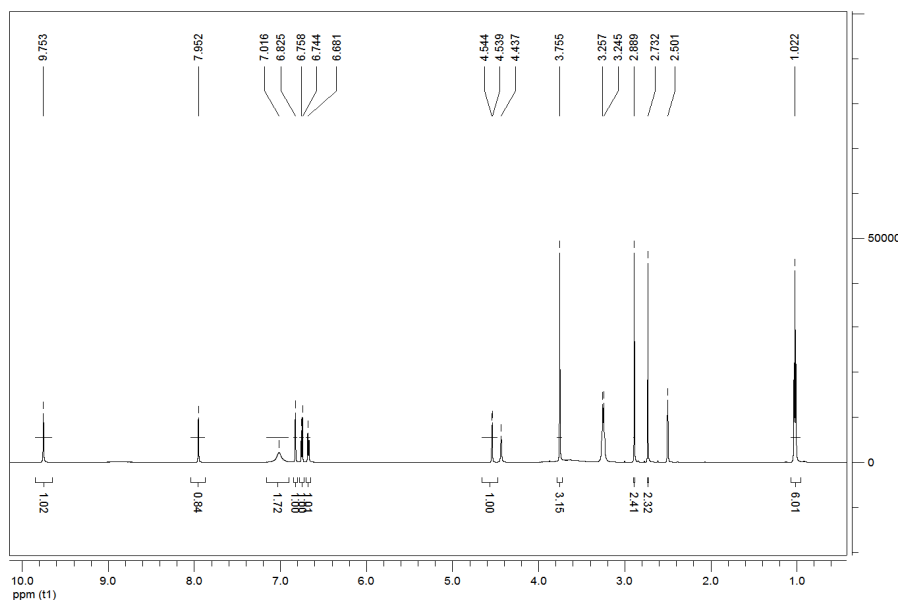
^1H NMR of **6e** (600 MHz, $\text{DMSO}-d_6$)



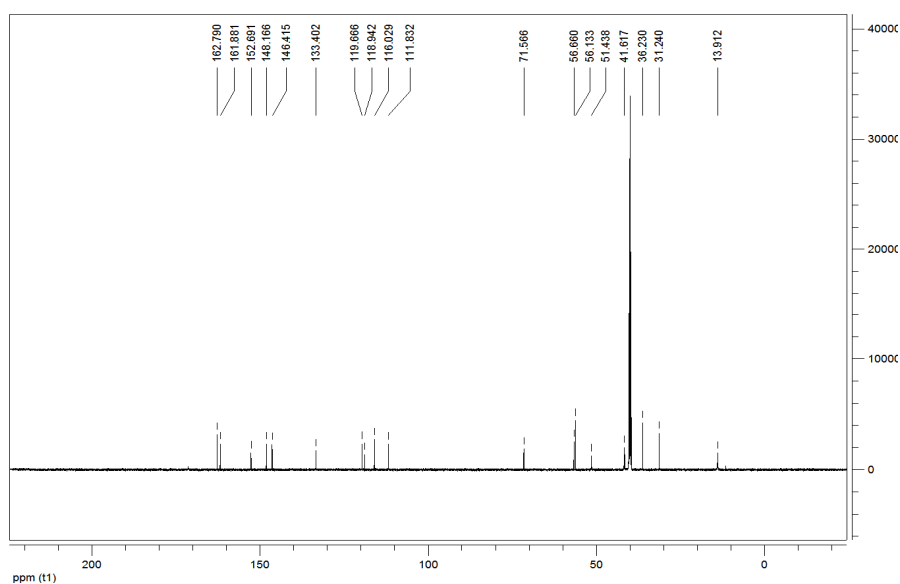
^{13}C NMR of **6e** (150 MHz, $\text{DMSO}-d_6$)

6f: white solid, 41.3%, m.p. 180~182 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 9.75 (s, 1H, NH), 7.95 (s, 1H, OH), 7.12~6.93 (brs, 2H, NH_2), 6.83 (s, 1H, ArH), 6.75 (d, $J = 8.4\text{ Hz}$, 1H, ArH), 6.67 (d, $J = 8.4\text{ Hz}$, 1H, ArH), 4.54 (d, $J = 3.0\text{ Hz}$, 1H, CH), 4.44 (s, 1H, CH), 3.76 (s, 3H, OCH_3), 2.89 (s, 2H, CH_2), 2.73 (s, 2H, CH_2), 1.02 (t, $J = 7.2\text{ Hz}$, 6H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 162.7, 161.8, 152.6, 148.1, 146.4, 133.4, 119.6, 118.9, 116.0, 111.8, 71.5, 56.6, 56.1, 51.4, 41.6, 36.2, 31.2, 13.9; IR (KBr) ν : 3357, 3201, 2986, 2936, 2183, 1663, 1580, 1513, 1387, 1340, 1263,

1197, 1152, 1124, 1099, 1032, 902, 874, 850, 814, 749; MS (m/z): 391.34 ($[M-1]^+$, 100%); Anal Calcd for $C_{18}H_{22}N_4O_4S$: C 55.37, H 5.68, N 14.35; Found: C 55.42, H 5.83, N 14.37.



^1H NMR of **6f** (600 MHz, $\text{DMSO}-d_6$)

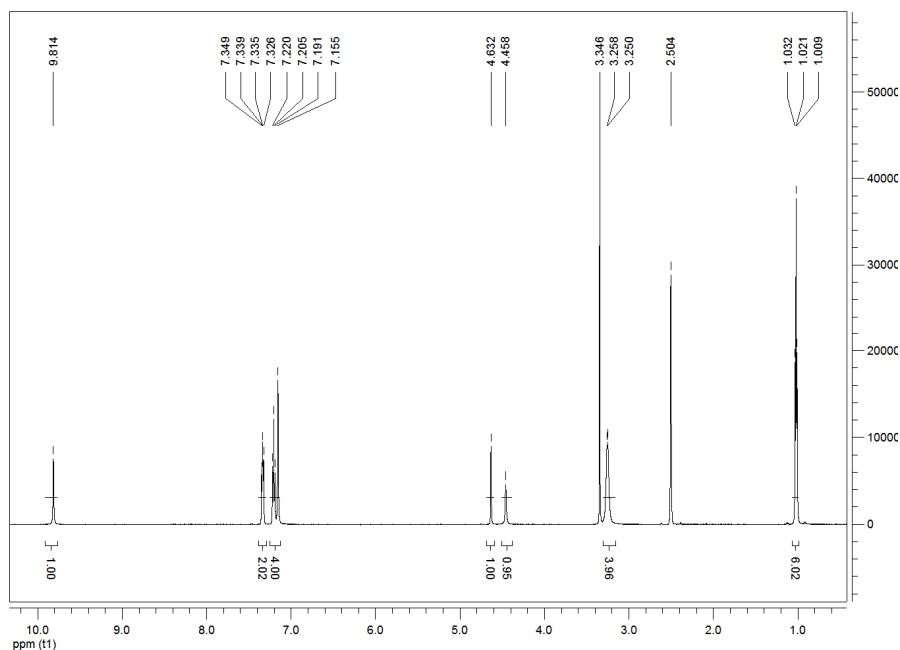


^{13}C NMR of **6f** (150 MHz, $\text{DMSO}-d_6$)

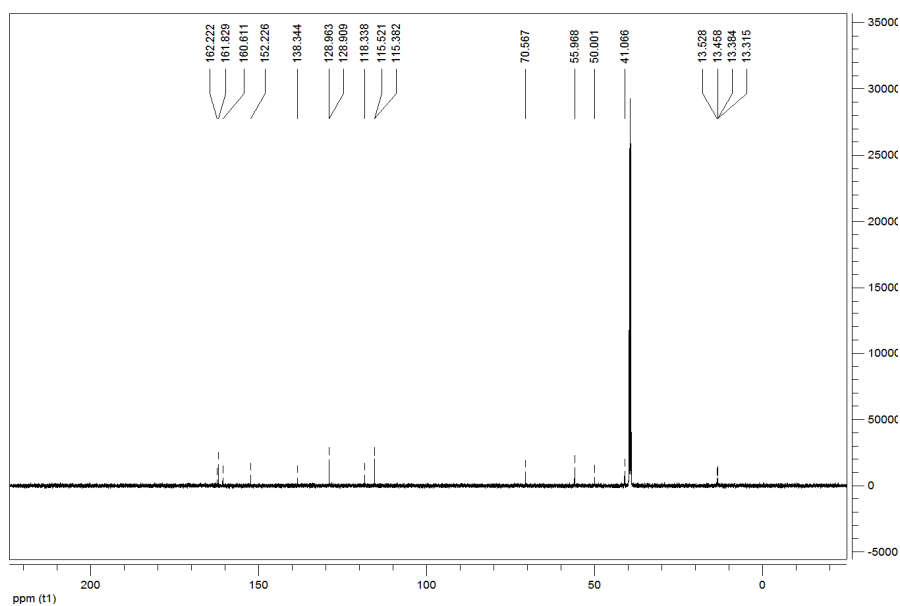
6g: white solid, 26.9%, m.p. 176~178 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 9.81 (s, 1H, NH), 7.33~7.35 (m, 2H, ArH), 7.21 (t, $J = 9.0\text{ Hz}$, 2H, ArH), 7.16 (s, 2H, NH_2), 4.63 (s, 1H, CH), 4.46 (s, 1H, CH), 7.21 (d, $J = 4.8\text{ Hz}$, 4H, CH_2), 1.02 (t, $J = 6.6\text{ Hz}$, 6H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ : 162.2, 161.8, 160.6, 152.2, 138.4, 128.9, 128.9, 118.3, 115.5, 115.3, 70.5, 55.9, 50.0, 41.0, 13.5, 13.4, 13.3, 13.3; IR(KBr) ν : 3445, 3317, 3227, 2971, 2932, 2183, 1691, 1581, 1483,

1380, 1356, 1259, 1212, 1151, 1095, 1020, 907, 836, 789, 748; MS (m/z): 361.40 ([M-1]⁺, 100%);

Anal Calcd for C₁₇H₁₉FN₄O₂S: C 56.34, H 5.28, N 15.46; Found: C 56.75, H 5.60, N 15.29.



¹H NMR of **6g** (600 MHz, DMSO-*d*₆)

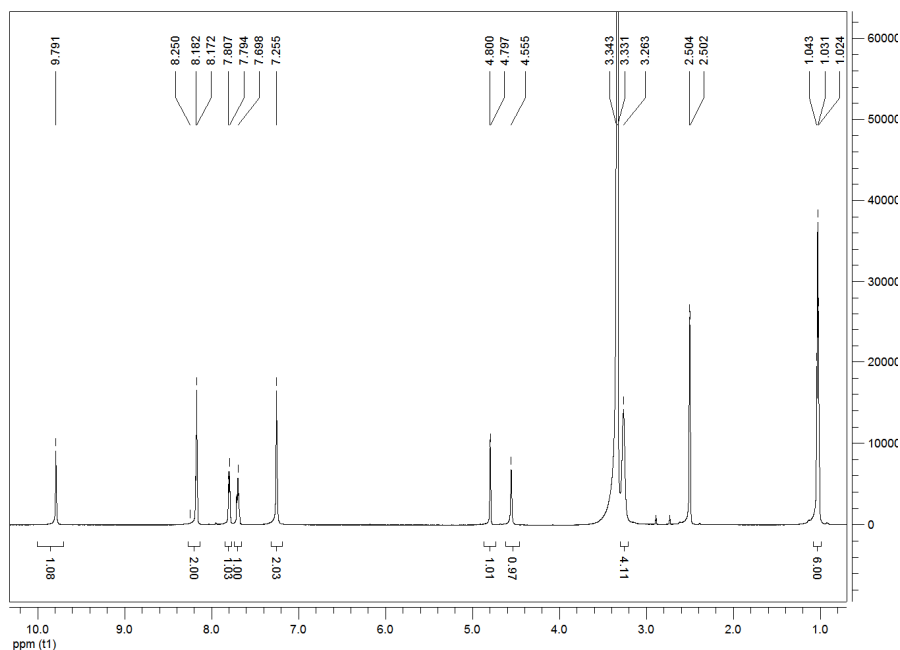


¹³C NMR of **6g** (150 MHz, DMSO-*d*₆)

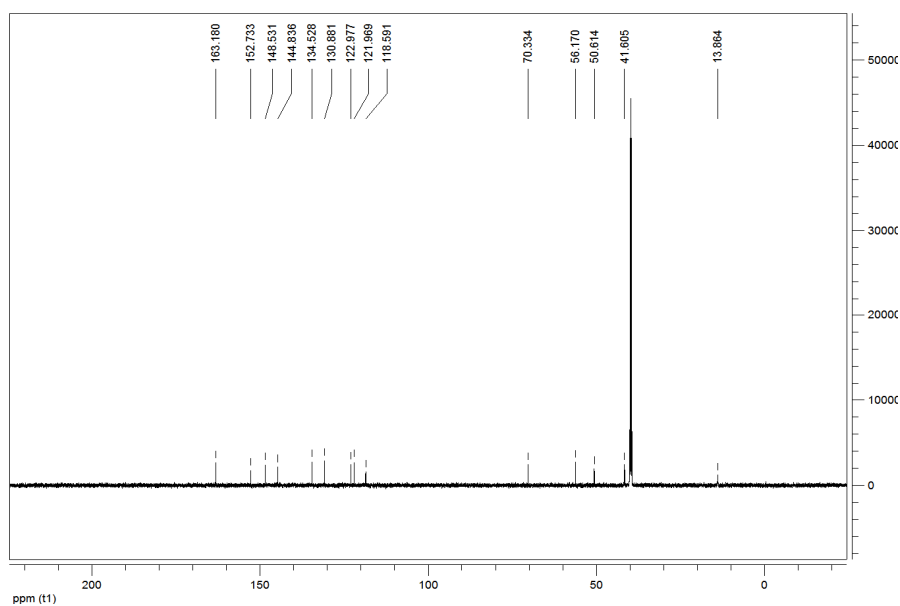
6h: yellow solid, 45.4%, m.p. 206~208 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 9.79 (s, 1H, NH), 8.18~8.14 (m, 2H, ArH), 7.83~7.77 (m, 1H, ArH), 7.73~7.66 (m, 1H, ArH), 7.26 (s, 2H, NH₂), 4.81~4.77 (m, 1H, CH), 4.56 (s, 1H, CH), 3.30~3.21 (m, 4H, CH₂), 1.05~1.00 (m, 6H, CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 163.1, 152.7, 148.5, 144.8, 134.5, 130.8, 122.9, 121.9, 118.5, 70.3, 56.1, 50.6, 41.6, 13.8; IR(KBr) ν: 3421(m), 3318, 3233, 3201, 3088, 2983, 2934, 2178, 1691, 1669,

1574, 1528, 1481, 1351, 1262, 1200, 1152, 1087, 933, 869, 814; MS (m/z): 388.42 ([M-1]⁺, 100%);

Anal Calcd for C₁₇H₁₉N₅O₄S: C 52.43, H 4.92, N 17.98; Found: C 52.27, H 5.31, N 17.66.



¹H NMR of **6h** (600 MHz, DMSO-*d*₆)

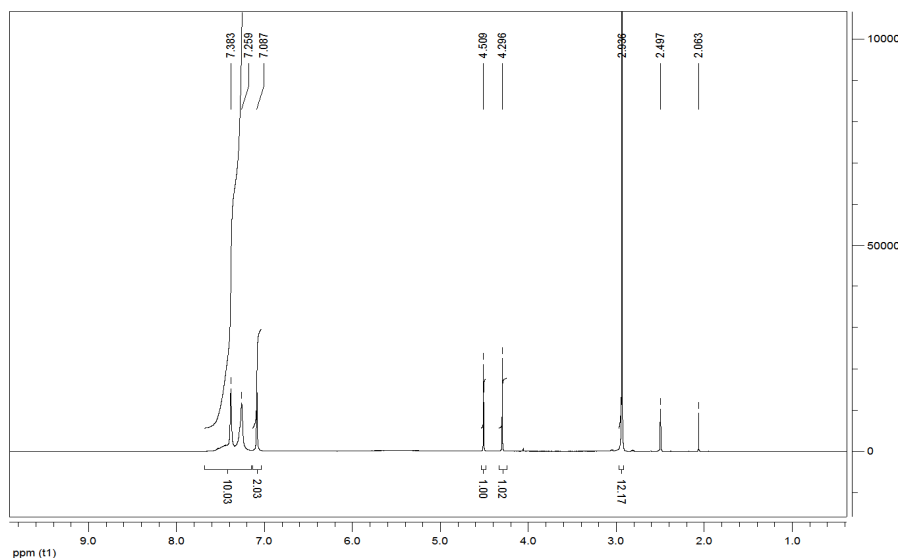


¹³C NMR of **6h** (150 MHz, DMSO-*d*₆)

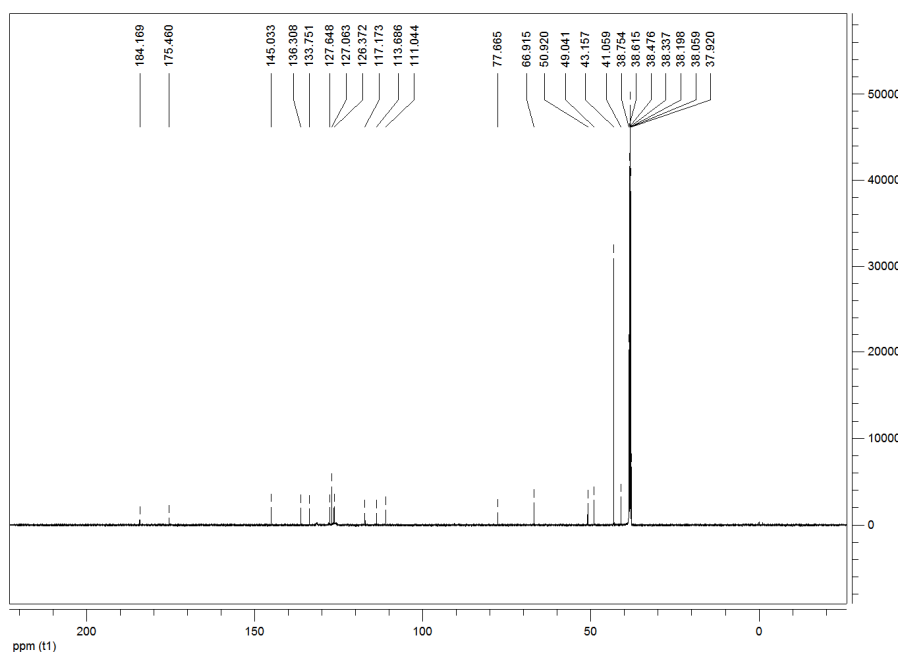
7a: (From the reaction of DBU as base) white solid, 30%, m.p. 233~235 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 7.64~7.17 (m, 10H, ArH), 7.09 (s, 2H, NH₂), 4.51 (s, 1H, CH), 4.30 (s, 1H, CH), 2.97(s, 12H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 184.2, 175.5, 145.0, 136.3, 133.8, 127.6, 127.1, 126.4, 117.2, 113.7, 111.0, 77.7, 66.9, 50.9, 49.0, 43.2, 41.1, 38.6; IR(KBr) ν: 3445, 3307, 3159, 2967, 2793, 2194, 1692, 1646, 1584, 1493, 1458, 1354, 1266, 1234, 1052, 998, 936, 832; MS

(m/z): 424.33 ([M-1]⁺, 100%); Anal Calcd for C₂₃H₁₅N₅O₂S.C₆H₁₂N₂: C 64.93, H 3.55, N 16.46;

Found: C 64.79, H 3.84, N 16.22.



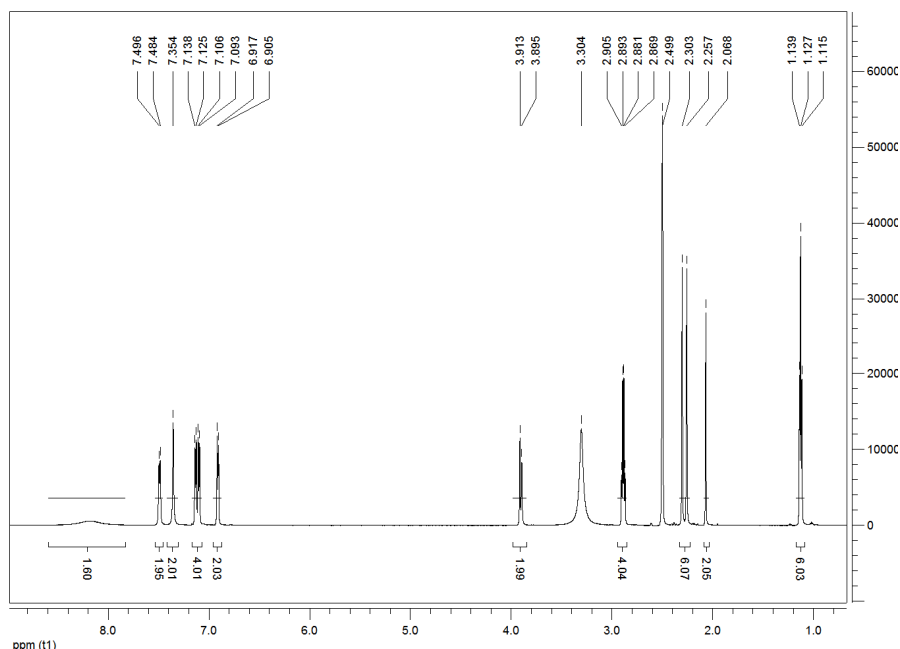
¹H NMR of **7a** (600 MHz, DMSO-*d*₆)



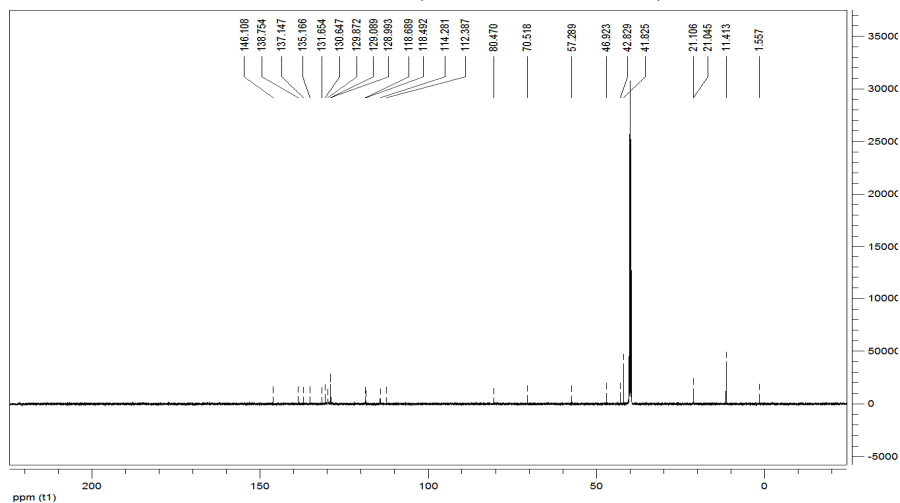
¹³C NMR of **7a** (600 MHz, DMSO-*d*₆)

7b: (From the reaction of diethylamine as base), white solid, 29.6%, m.p. 180~182 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 8.41~7.93 (brs, 1H, NH), 7.49 (d, *J* = 7.2Hz, 2H, ArH), 7.35 (s, 2H, NH₂), 7.13 (d, *J* = 7.8Hz, 2H, ArH), 7.10 (d, *J* = 7.8Hz, 2H, ArH), 3.91 (s, 1H, CH), 3.89 (s, 1H, CH), 2.89 (brs, 4H, 2CH₂), 2.50 (s, 6H, CH₃), 1.13 (t, *J* = 7.2Hz, 6H, 2CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 146.1, 138.7, 137.1, 135.1, 131.6, 130.6, 129.8, 129.0, 128.9, 118.6, 118.4, 114.2,

112.3, 80.4, 70.5, 57.2, 46.9, 42.8, 41.8, 21.1, 21.0, 11.4, 1.5; IR(KBr) ν : 3413, 3342, 3228, 2987, 2791, 2496, 2255, 2208, 1706, 1625, 1515, 1454, 1366, 1317, 1206, 1120, 1047, 881, 825, 783; MS (m/z): 452.56 ($[M-1]^+$, 100%); Anal Calcd for $C_{25}H_{19}N_5O_2S \cdot C_4H_{11}N$: C 66.14, H 5.74, N 15.96; Found: C 65.83, H 6.02, N 15.47.



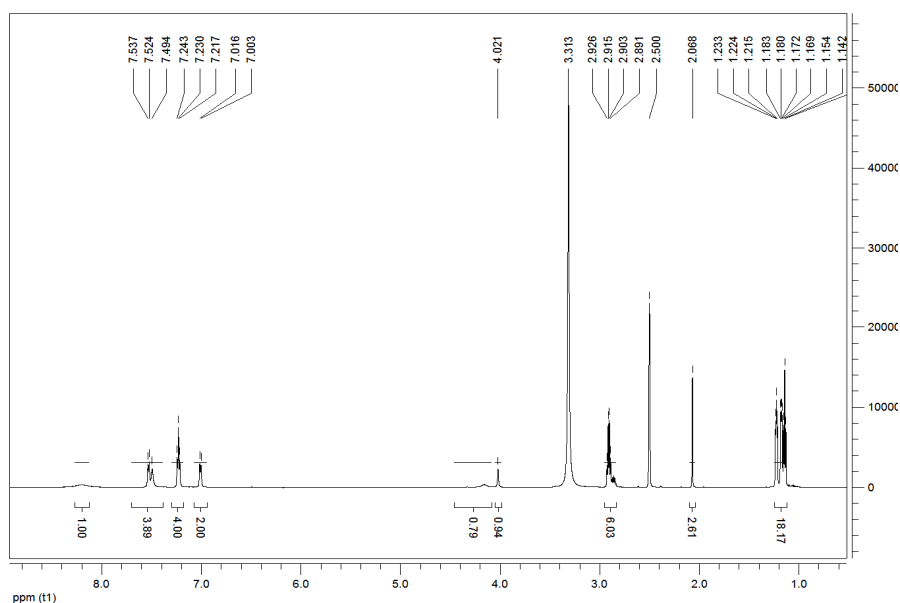
1H NMR of **7b** (600 MHz, $DMSO-d_6$)



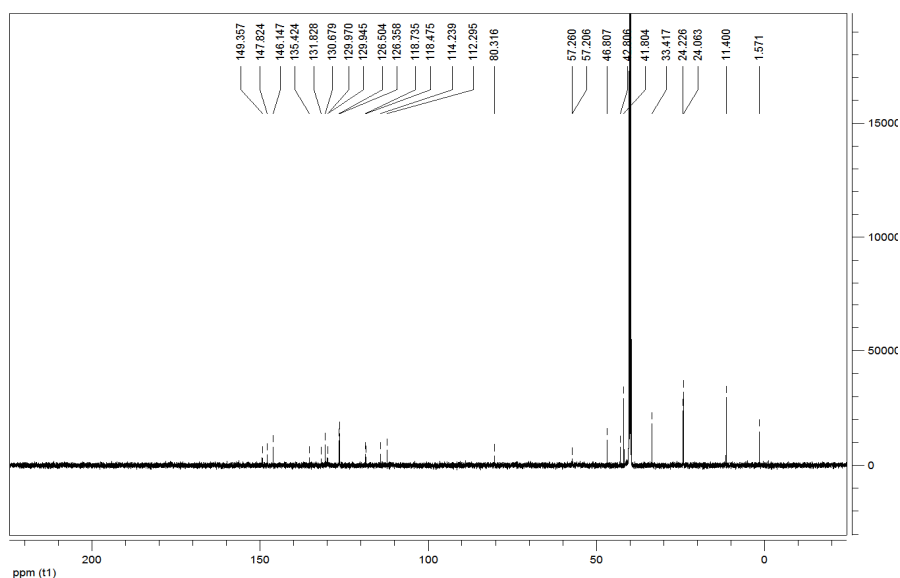
^{13}C NMR of **7b** (150 MHz, $DMSO-d_6$)

7c: (From the reaction of diethyl amine as base), light yellow solid, 25.3%, m.p. 178~180 °C; 1H NMR (600 MHz, $DMSO-d_6$) δ : 8.35~8.06 (brs, 1H, NH), 7.53 (d, $J = 7.8$ Hz, 2H, ArH), 7.49 (s, 2H, NH₂), 7.23 (d, $J = 7.8$ Hz, 4H, ArH), 7.01 (d, $J = 7.8$ Hz, 2H, ArH), 4.25~4.09 (brs, 1H, CH), 4.02 (s, 1H, CH), 2.93~2.89 (m, 6H, CH, CH₂), 1.18~1.13 (m, 18H, CH₃); ^{13}C NMR (150 MHz, $DMSO-d_6$) δ : 149.4, 147.8, 146.1, 135.4, 131.8, 130.7, 130.0, 129.9, 126.5, 126.4, 118.7, 118.5,

114.2, 112.3, 80.3, 57.3, 57.2, 46.8, 42.8, 41.8, 33.4, 24.2, 24.0, 11.4, 1.5; IR(KBr) ν : 3404, 3337, 3218, 2963, 2870, 2501, 2262, 2201, 1700, 1656, 1622, 1584, 1512, 1461, 1424, 1364, 1321, 1191, 1094, 1058, 1020, 948, 887, 833, 795; MS (m/z): 509.72 ($[M-1]^+$, 100%); Anal Calcd for $C_{29}H_{27}N_5O_2S \cdot C_4H_{11}N$: C 68.35, H 5.34, N 13.74; Found: C 68.97, H 5.64, N 13.96.



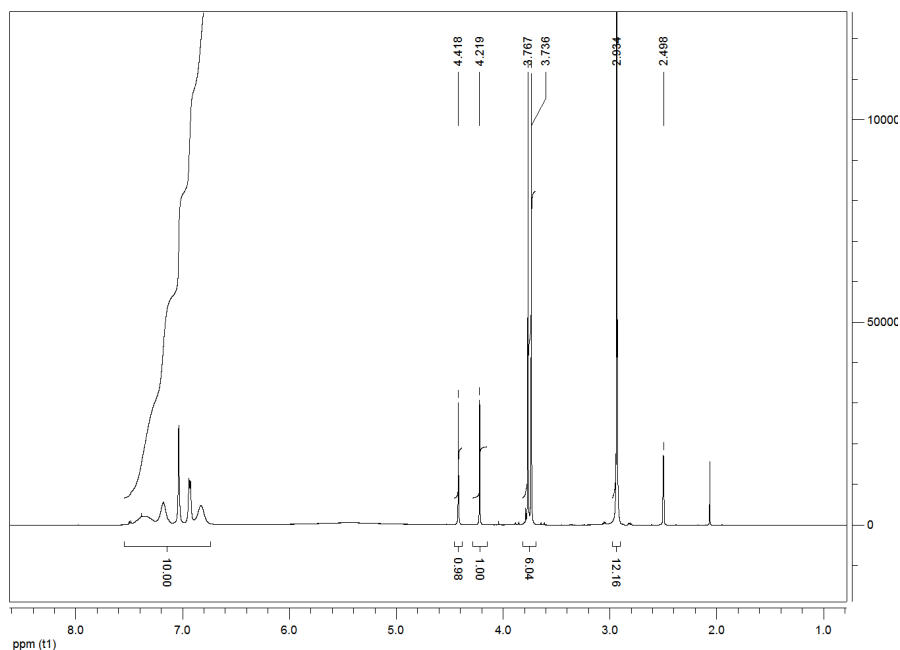
1H NMR of **7c** (600 MHz, $DMSO-d_6$)



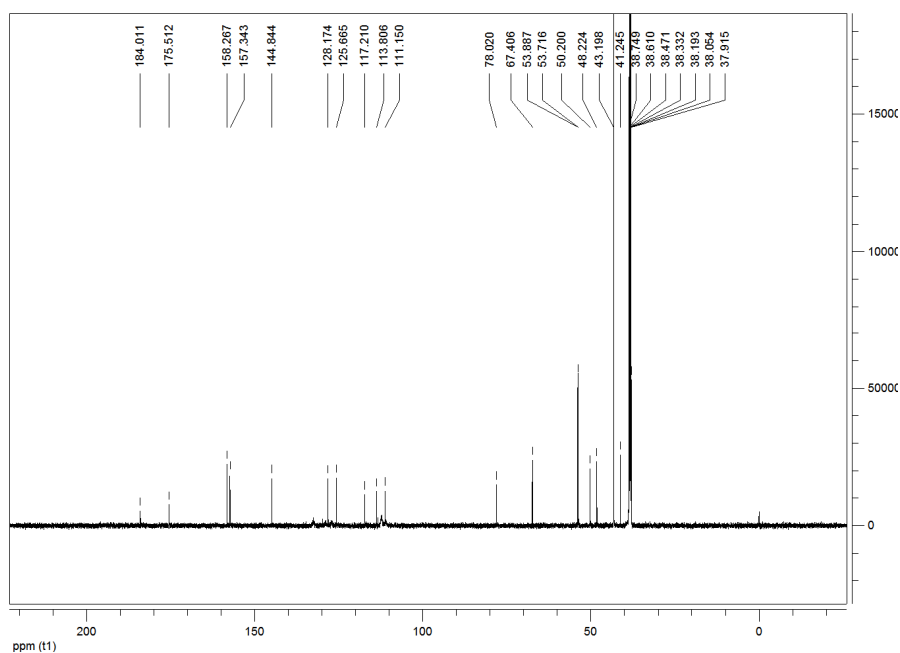
^{13}C NMR of **7c** (150 MHz, $DMSO-d_6$)

7c: (From the reaction of DBU as base), white solid, 42.0%, m.p. 247~248 °C; 1H NMR (600 MHz, $DMSO-d_6$) δ : 7.52~6.68 (m, 10H, ArH, NH₂), 4.42 (s, 1H, CH), 4.22 (s, 1H, CH), 3.77 (s, 3H, OCH₃), 3.74 (s, 3H, OCH₃), 2.93 (s, 12H, CH₂); ^{13}C NMR (150 MHz, $DMSO-d_6$) δ : 184.0, 175.5, 158.3, 157.3, 144.8, 128.2, 125.7, 117.2, 113.8, 111.2, 78.0, 67.4, 53.9, 53.7, 50.2, 48.2, 43.2, 41.3 IR(KBr) ν : 3446, 3304, 3150, 2962, 2837, 2193, 1701, 1596, 1513, 1463, 1353, 1257,

1181, 1029, 840, 809; MS (m/z): 484.33 ([M-1]⁺, 100%); Anal Calcd for C₂₅H₁₉N₅O₄S.C₆H₁₂N₂: C 62.30, H 5.23, N 16.40; Found: C 62.45, H 5.61, N 16.11.



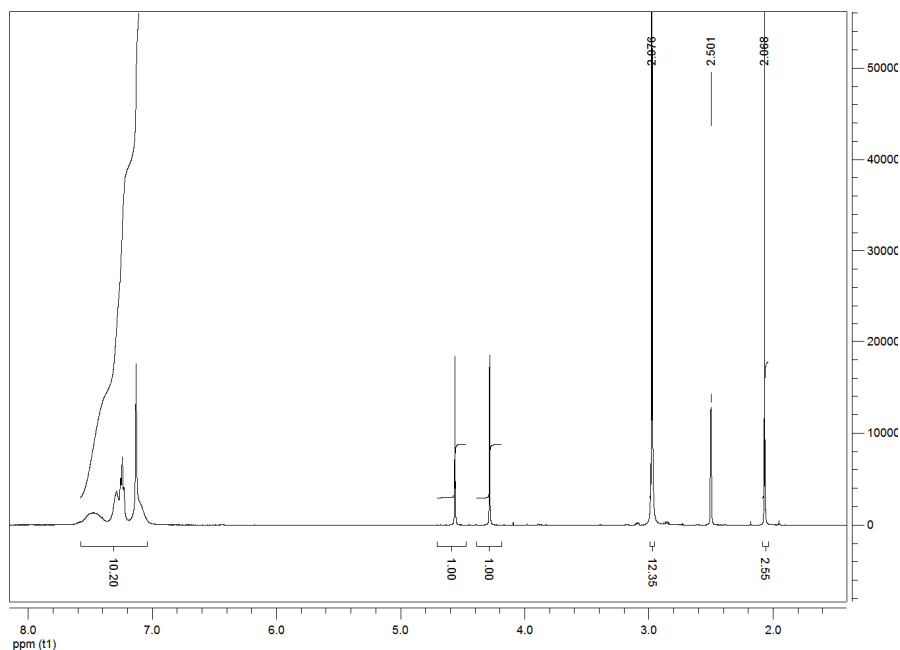
¹H NMR of **7e** (600 MHz, DMSO-*d*₆)



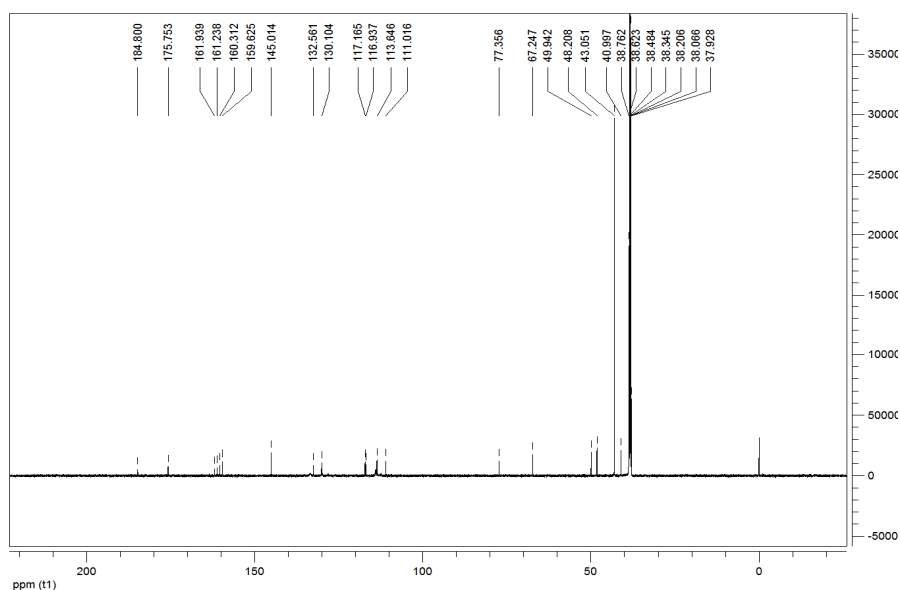
¹³C NMR of **7e** (600 MHz, DMSO-*d*₆)

7g: (From the reaction of DBU as base) white solid, 28.4%, m.p. □250 □; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 7.72□6.77 (m, 11H, ArH, NH₂, NH), 4.56 (s, 1H, CH), 4.28 (s, 1H, CH), 2.93 (s, 12H, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 184.8, 175.8, 161.9, 161.2, 160.3, 159.6, 145.0, 132.6, 130.1, 117.2, 116.9, 113.6, 111.0, 77.4, 67.2, 49.9, 48.2, 43.1, 41.0; IR(KBr) ν:3419, 3326, 3206, 2962, 2894, 2192, 1698, 1598, 1510, 1467, 1362, 1302, 1268, 1229, 1168, 1108, 1053, 989, 841,

816; MS(*m/z*): 460.35([*M*-1]⁺) 100%; Anal Calcd for C₂₃H₁₃F₂N₅O₂S.C₆H₁₂N₂: C 60.72, H 4.39, N 17.09; Found: C 60.44, H 4.07, N 16.73.



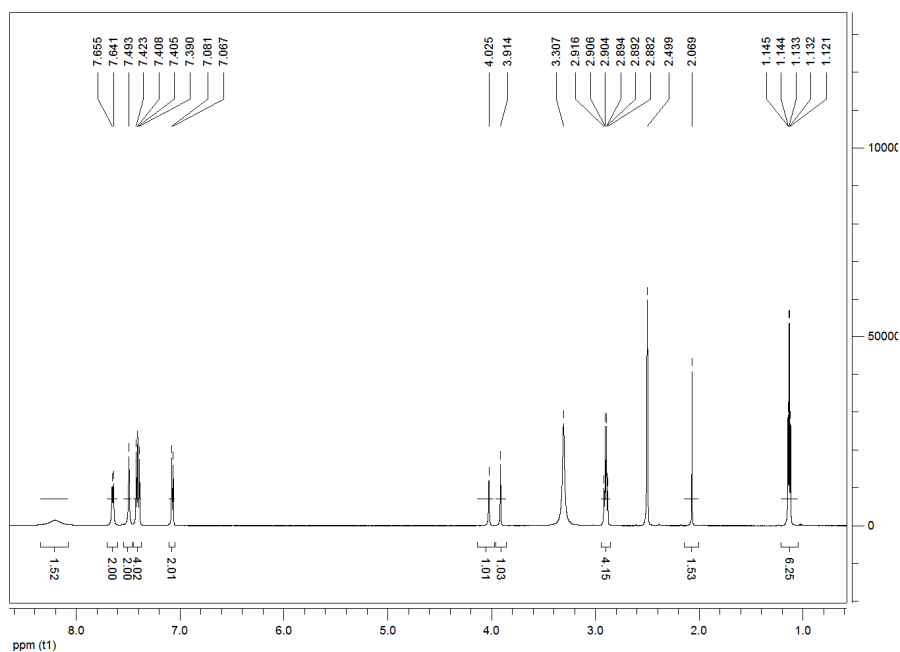
¹H NMR of **7g** (600 MHz, DMSO-*d*₆)



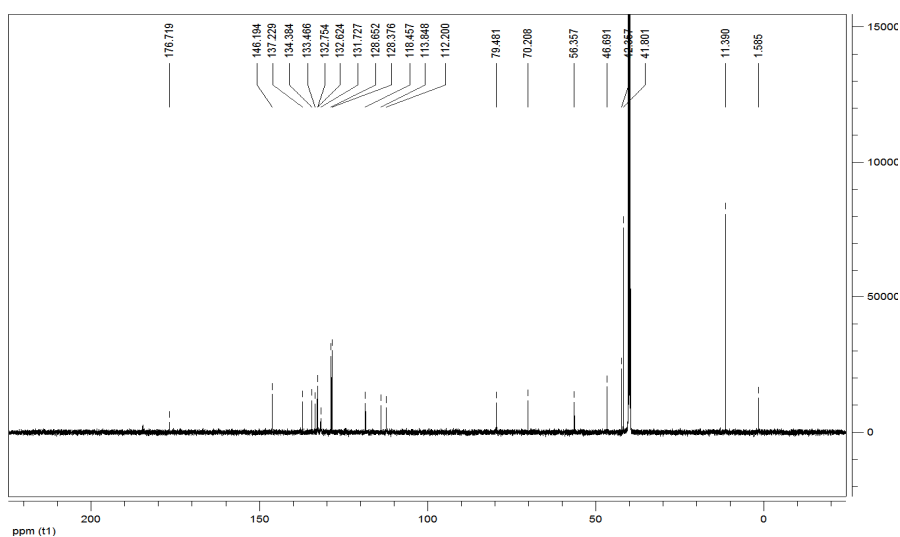
¹³C NMR of **7g** (600 MHz, DMSO-*d*₆)

7i: (From the reaction of diethyl amine as base), grey solid, 14.5%, m.p. 194~196 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 8.36~8.06 (brs, 1H, NH), 7.65 (d, *J* = 8.4 Hz, 2H, ArH), 7.49 (s, 2H, NH₂), 7.42~7.39 (m, 4H, ArH), 7.07 (d, *J* = 8.4 Hz, 2H, ArH), 4.02 (s, 1H, CH), 3.91 (s, 1H, CH), 2.90 (brs, 4H, 2CH₂), 1.13 (brs, 6H, 2CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 176.7, 146.1, 137.2, 134.3, 133.4, 132.7, 132.6, 131.7, 128.6, 128.3, 118.4, 113.8, 112.2, 79.4, 70.2, 56.3, 46.6, 42.3, 41.8, 11.3; IR(KBr) ν: 3411, 3336, 3217, 2988, 2821, 2496, 2255, 2212, 1913, 1705, 1625, 1492,

1414, 1369, 1314, 1203, 1093, 1015, 880, 831, 788; MS (m/z): 492.53 ([M-1]⁺, 100%); 494.27 ([M-1]⁺, 72%); Anal Calcd for C₂₃H₁₃Cl₂N₅O₂S.C₄H₁₁N: C 57.14, H 4.26, N 14.81; Found: C 56.78, H 3.85, N 14.36.



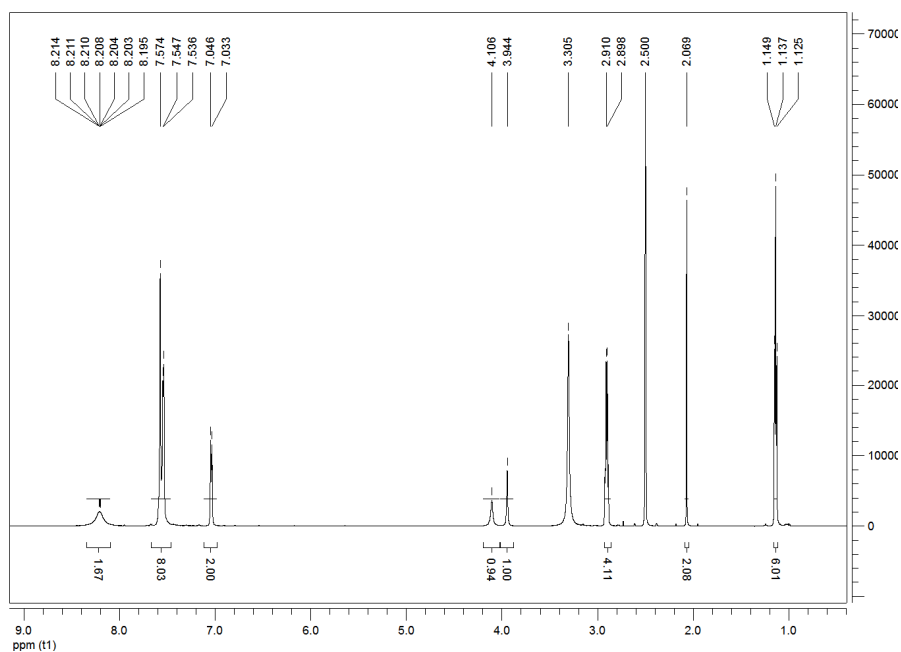
¹H NMR of **7i** (600 MHz, DMSO-*d*₆)



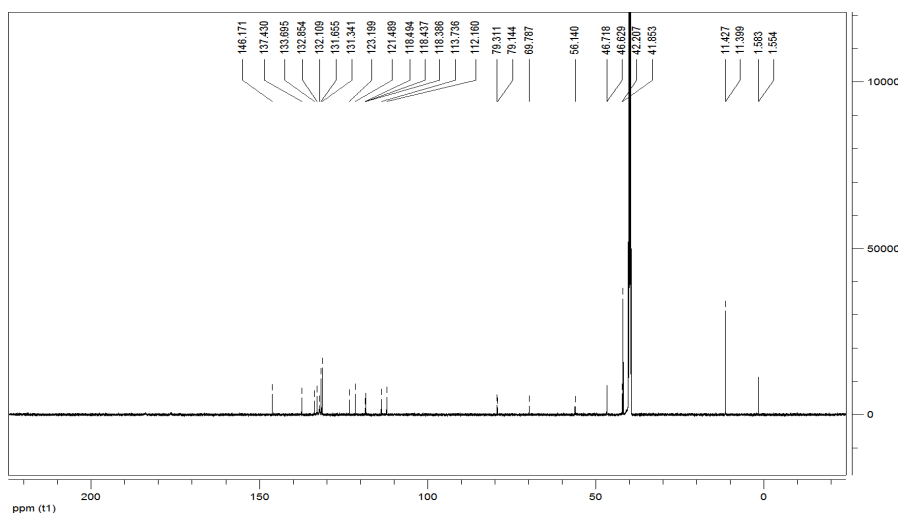
¹³C NMR of **7i** (150 MHz, DMSO-*d*₆)

7j: (From the reaction of diethylamine as base), grey solid, 31.2%, m.p. 197~199 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 8.34~8.09 (brs, 1H, NH), 7.57~7.54 (m, 8H, NH₂, ArH), 7.04 (d, *J* = 7.8Hz, 4H, ArH), 4.11 (s, 1H, CH), 3.94 (s, 1H, CH), 2.90 (q, *J* = 7.2Hz, 4H, 2CH₂), 1.14 (t, *J* = 7.2Hz, 6H, 2CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ: 146.1, 137.4, 133.6, 132.8, 132.1, 131.6, 131.3, 123.1, 121.4, 118.4, 118.4, 118.3, 113.7, 112.1, 79.3, 79.1, 69.7, 56.1, 46.7, 46.6, 42.2, 41.8, 11.4, 11.3, 1.5, 1.5; IR(KBr) ν: 3423, 3341, 3230, 3023, 2859, 2496, 2255, 2209, 1707, 1624, 1582,

1489, 1455, 1410, 1367, 1323, 1197, 1112, 1075, 1011, 880, 828, 788; MS (m/z): 582.43 ($[M-1]^+$, 100%); Anal Calcd for $C_{23}H_{13}Br_2N_5O_2S \cdot C_4H_{11}N$: C 49.40, H 3.69, N 12.80; Found: C 48.85, H 3.34, N 12.55.



1H NMR of **7j** (600 MHz, $DMSO-d_6$)



^{13}C NMR of **7j** (150 MHz, $DMSO-d_6$)