Electronic Supplementary Material (ESI) for RSC Advances.

Electronic Supplementary Information

Synthesis of Schiff and Mannich bases of new s-triazole derivatives and their potential applications for removal of heavy metals from aqueous solution and antimicrobial activities

Zeinab A. Hozien,[a] Ahmed F. M. EL-Mahdy,*[a,b] Ahmad Abo Markeb,[a] Laila S. A. Ali [a] and Hassan A. H. El-Sherief *[a]

[a] Chemistry department, Faculty of Science, Assiut University, Egypt.

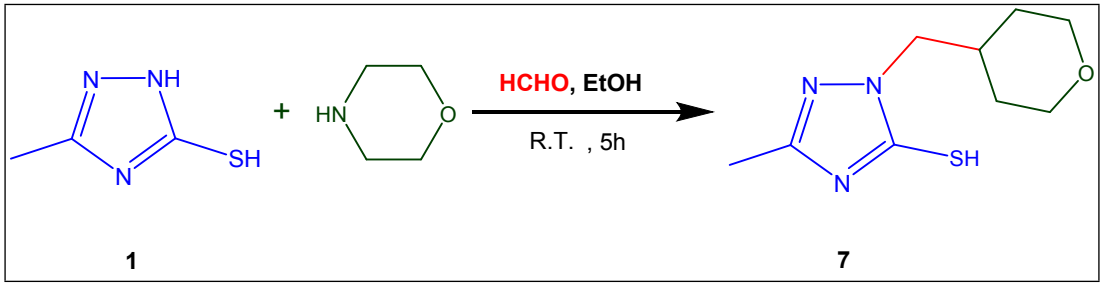
[b]*Department of Materials and Optoelectronic Science, National Sun Yat-Sen University, Kaohsiung, 80424, Taiwan.*

Email: dr_hassanahmed@yahoo.com

ahmedelmahdy@mail.nsysu.edu.tw

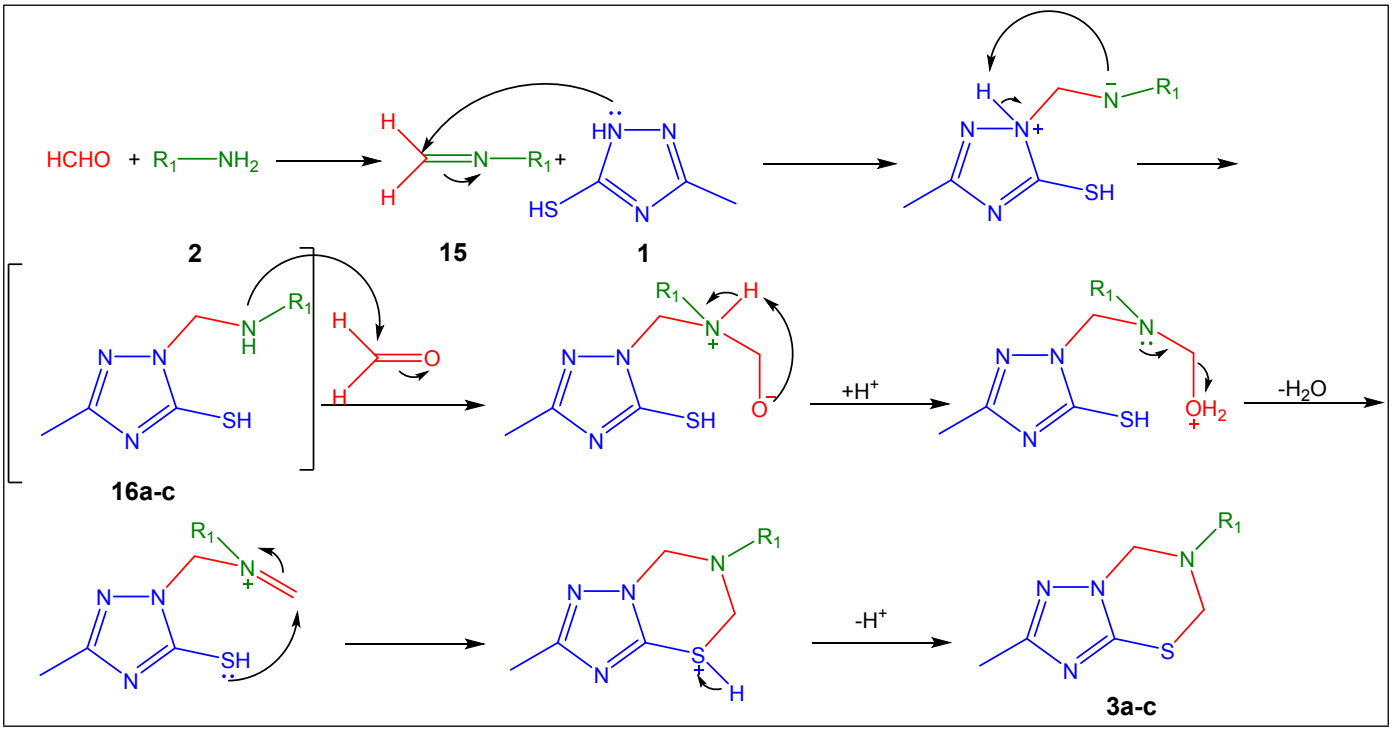
Table of contents

S1. Schematic synthesis of 3-methyl-1-(morpholinomethyl)-1H-s-triazole-5-thiol

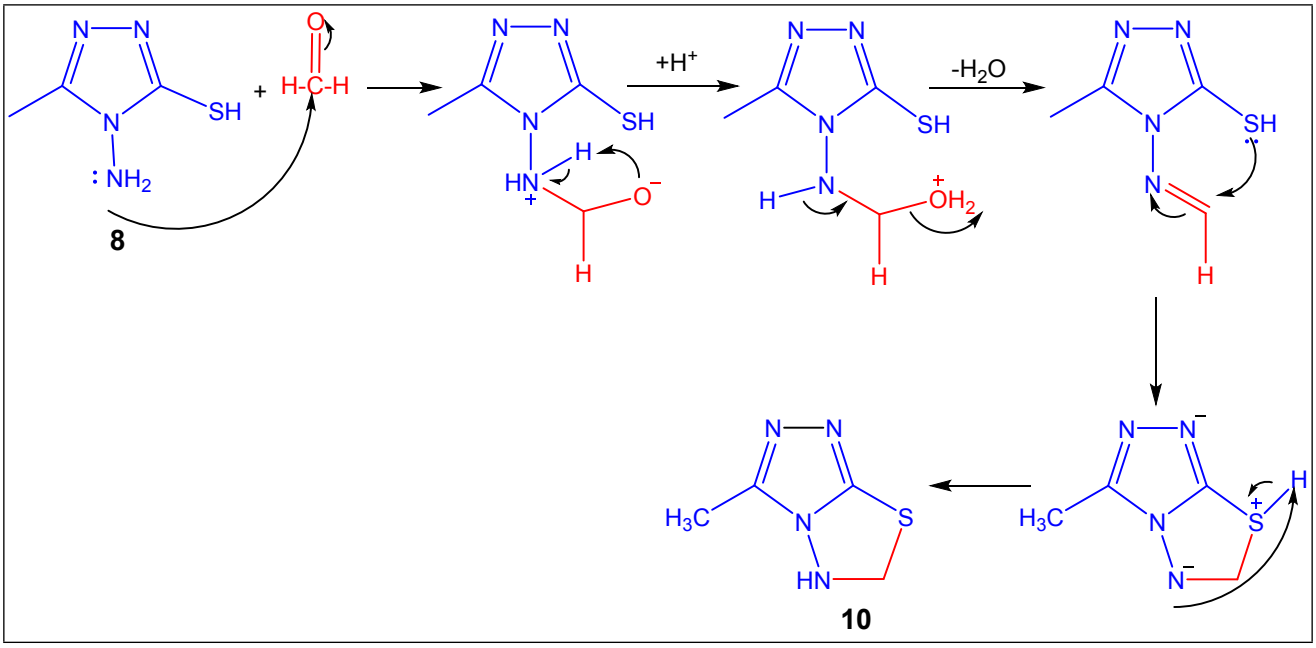


Scheme S1. Synthesis of 3-methyl-1-(morpholinomethyl)-1*H*-*s*-triazole-5-thiol.

S2. Reaction mechanisms



Scheme S2. Plausible mechanism for the formation of compounds **3a-c** and **5a-d**.



Scheme S3. Plausible mechanism for the formation of compound **10**.

S3. Experimental

S3.1. Materials

All reagents and solvents were used as received from Merck, Sigma-Aldrich, or Alfa Aesar without further purification.

S3.2. Charaterization

Melting points were determined using a Gallenkamp melting point apparatus in open capillary tubes. Infrared spectra were recorded using KBr discs on a Perkin Elmer 1430 FT-FTIR spectrometer at room temperature. ^{1}H-NMR and ^{13}C-NMR spectra were recorded at room temperature using DMSO-d_6 or $CDCl_3$ as a solvent on a Bruker Advance 400 NMR spectrometer or a Varian EM-390 90 MHz spectrometer (Spectral Unit, Chemistry department, Assiut University, Egypt). Chemical shifts were donated in ppm on d scale, relative to TMS as internal standard and coupling constants (J) are given in Hz. Mass spectra were recorded on a JEOL JMS-600 mass spectrometer using a dFTIRect inlet system. Elemental analyses were measured on a Perkin Elmer 240 C elemental analyzer.

The concentration of heavy metals and metal ions were determined using UV/VIS spectrophotometer (Perkin Elmer) and standard methods for the examination of water and wastewater. Validation of the obtained results was performed using Atomic Absorption Spectroscopy (Contra AA 700, Analytik Jena).

S3.3. Synthetic Procedures

2-methyl-6-substituted-6,7-dihydro-5*H*-s-triazolo[5,1-*b*]-1,3,5-thiadiazines (3a-c)

General procedure: A solution of 3-methyl-s-triazole-5-thiol [S1] **1** (1 gm, 8.69 mmol) in ethanol (5 mL) was added dropwise to a stired solution of formaldehyde (37% 1 mL) and primary aliphatic amines **2** (8.69 mmol) in ethanol (15 mL) and the resulting reaction mixture stired at room temperature for 5 hours. The resulting precipitate thus formed was filtered and washed with ethanol and then dried. the solid products were recrystallized from the alcohol to give the corresponding products **3a-c** in very good yield.

2-methyl-6-isobutyl-6,7-dihydro-5*H*-s-triazolo[5,1-*b*]-1,3,5-thiadiazine (3a)

Yield: (91.84%); white crystals (EtOH), mp 108-110 °C. FTFTIR: 2960-2870 (C-H aliph.), 1582 (C=N), 1427 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.94-0.96 (d, *J* = 17.6 Hz, 6H, CH(C<u>H</u>$_3$)$_2$), 1.67-1.98 (m, 1H, C<u>H</u>(CH$_3$)$_2$), 2.38 (s, 3H, CH$_3$ triazole), 2.54 (d, *J* = 7.4 Hz, 2H, C<u>H</u>$_2$-CH), 4.66 (s, 2H, N-CH$_2$-S), 5.07(s, 2H, N-

CH_2-N). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 159.20 (C5), 147.78 (C3), 68.03(N-C10-N), 58.33(N-C8-S), 56.16(C11), 26.38(C12), 20.31(2CH_3), 13.89(CH_3) triazole. m/z (EI, 70 eV) 213 [M^++1], 212.08 [M^+]. Anal. Calcd. % for $C_9H_{16}N_4S$ (212.11): C, 50.91; H, 7.60; N, 26.39; S, 15.10 Found: C, 50.88; H, 7.47; N, 26.30; S, 15.35 %.

2-methyl-6-propyl-6,7-dihydro-5*H*-s-triazolo[5,1-*b*]-1,3,5-thiadiazine (3b)

Yield: (93.56%); white crystals (EtOH), mp 110-112 °C. FTFTIR: 2959-2880 (C-H aliph.), 1618 (C=N), 1465 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 7.3 Hz, 3H, $CH_2C\underline{H}_3$), 1.60 (m, *J* = 7.4 Hz, 2H, $C\underline{H}_2CH_3$), 2.35 (s, 3H, CH_3 triazole), 2.73 (t, *J* = 14.6 Hz, 2H, $C\underline{H}_2CH_2$), 4.69 (s, 2H, N-CH_2-S), 5.05(s, 2H, N-CH_2-N). m/z (EI, 70 eV) 199 [M^++1], 198.02 [M^+]. Anal. Calcd. % for $C_8H_{14}N_4S$ (198.09): C, 48.46; H, 7.12; N, 28.26; S, 16.17 Found: C, 48.38; H, 7.20; N, 28.30; S, 16.12 %.

2-methyl-6-benzyl-6,7-dihydro-5*H*-s-triazolo[5,1-*b*]-1,3,5-thiadiazine (3c)

Yield: (91.16%); white crystals (EtOH), mp 120-122 °C. FTFTIR:3030 (C-H arom.), 2960-2850 (C-H aliph.), 1580 (C=N), 1495 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3H, CH_3 triazole), 3.93 (s, 2H, CH_2), 4.60(s, 2H, N-CH_2-S), 5.09(s, 2H, N-CH_2-N), 7.29-7.37 (m, 5H, H-arom.). m/z (EI, 70 eV) 246.09 [M^+]. Anal. Calcd. % for $C_{12}H_{14}N_4S$ (246.09): C, 58.51; H, 5.73; N, 22.74; S, 13.01 Found: C, 58.58; H, 5.48; N, 22.60; S, 13.34 %.

3-methyl-1-((substitutedamino)methyl)-1*H*-s-triazole-5-thiol (5a-d)

General procedure: A solution of 3-methyl-s-triazole-5-thiol **1** (1 gm, 8.69 mmol) in ethanol (5 mL) was added dropwise to a stired solution of formaldehyde (37% 1 mL) and primary aromatic amines **2** (8.69 mol) in ethanol (15 mL) and the resulting reaction mixture stired either at room temperature or under reflux for 5 hours. The reaction mixture was cooled and the separated precipitate was isolated by filtration, washed with ethanol and then dried. the solid products were recrystallized from the alcohol to give the corresponding products **5a-d** in excellent yield.

3-methyl-1-((phenylamino)methyl)-1*H*-s-triazole-5-thiol (5a)

Yield: (94.20%); yellow crystals (EtOH), mp 134-136 °C. FTIR: 3346 (NH), 3034 (C-H arom.), 2960 (C-H aliph.), 1574 (C=N) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.29 (s, 3H, CH_3 triazole), 5.48 (d, *J* = 7.9 Hz, 2H, CH_2-NH), 6.79 (t, J =9.3 Hz, 1H, CH_2-NH), 6.91 (d, 2H, H-arom.), 7.22 (t, 3H. H-arom), 12.60 (s, 1H, SH). m/z

(EI, 70 eV) 220 [M^+]Anal. Calcd. % for $C_{10}H_{12}N_4S$ (220.08): C, 54.52; H, 5.49; N, 25.43; S, 14.55 Found: C, 54.40; H, 5.11; N, 25.68; S, 14.81 %.

3-methyl-1-((*p*-tolylamino)methyl)-1*H*-s-triazole-5-thiol (5b)

Yield: (93.59%); orange crystals (EtOH), mp 198-200 °C. FTIR: 3340 (NH), 3098 (C-H arom.), 2914 (C-H aliph.), 1594 (C=N) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 2.40 (s, 3H, CH_3 triazole), 5.50 (d, *J* = 7.9 Hz, 2H, CH_2-NH), 6.47 (d, 2H, H-arom), 6.91 (t, 1H, NH), 7.09 (d, 2H. H-arom), 12.80 (s, 1H, SH). Anal. Calcd. % for $C_{11}H_{14}N_4S$ (234.09): C, 56.38, H; 6.02; N, 23.91; S, 13.68 Found: C, 56.15; H, 6.33; N, 23.71; S, 13.81 %.

3-methyl-1-(((*p*-chlorophenyl)amino)methyl)-1*H*-s-triazole-5-thiol (5c)

Yield: (90.45%); white crystals (EtOH), mp 180-182 °C. FTIR: 3355 (NH), 3100(C-H arom.), 2966(C-H aliph.), 1580 (C=N) cm^{-1}. ^{1}H-NMR (90 MHz, DMSO): δ = 2.39(s, 3H, CH_3 triazole), 5.52 (d, *J* = 7.9 Hz, 2H, CH_2-NH), 6.58(d, 2H, H-arom), 7.00 (t, 1H, NH), 7.03 (d, 2H, H-arom), 12.99 (s, 1H, SH). m/z (EI, 70 eV) 254.01 [Cl^{37}, M], 256.01 [Cl^{35}, M+1]. Anal. Calcd. % for $C_{10}H_{11}ClN_4S$ (254.04): C, 47.15; H, 4.35; Cl, 13.92; N, 21.99; S, 12.59 Found: C, 47.10; H, 4.30; Cl, 13.97; N, 21.95; S, 12.68 %.

3-methyl-1-(((*p*-bromophenyl)amino)methyl)-1*H*-s-triazole-5-thiol (5d)

Yield: (92.27%); pale yellow (EtOH), mp 186-188 °C. FTIR: 3369 (NH), 3080(C-H arom.), 2987(C-H aliph.), 1570 (C=N) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.18 (s, 3H, CH_3 triazole), 5.37 (d, *J* = 20.3 Hz, 2H, CH_2-NH), 6.89 (d, *J* = 8.8 Hz, 2H, H-arom), 7.13 (t, *J* = 7.3 Hz, 1H, NH), 7.26 (d, *J* = 15.4 Hz, 2H. H-arom), 13.25 (s, 1H, SH). m/z (EI, 70 eV) 298 [Br^{79}, M^+](4.72%), 300 [Br^{81} , M^+](2.21%). Anal. Calcd. % for $C_{10}H_{11}BrN_4S$ (297.99): C, 40.15; H, 3.71; Br, 26.71; N, 18.73; S, 10.72 Found: C, 40.25; H, 3.50; Br, 26.85; N, 18.66; S, 10.74 %.

3-methyl-1-(morpholinomethyl)-1*H*-s-triazole-5-thiol (7)

General procedure: A solution of 3-methyl-s-triazole-5-thiol **1** (1 gm,8.69 mmol) in ethanol (5 mL) was added dropwise to a stirred solution of formaldehyde (37% 1 mL) and morpholine (8.69 mmol) in ethanol (15 mL) and the resulting reaction mixture stirred at room temperature for 5 hours. The resulting precipitate thus formed was filtered and washed with ethanol and then dried. the solid products were recrystallized from ethanol to give the corresponding compound **7** in very good yield. Yield: (93.54%); white crystals (EtOH), mp 170-172 °C. FTIR:

3100 (SH), 2983(C-H aliph.), 1569(C=N) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3H, CH_3 triazole), 2.76 (t, *J* = 19.6 Hz, 4H, N-$(CH_2)_2$), 3.70 (t, *J* = 9.1 Hz, 4H, O-$(CH_2)_2$), 4.99 (s, 2H, CH_2), 12.50 (s, 1H, SH). m/z (EI, 70 eV) 214.03 [M^+]. Anal. Calcd. % for $C_9H_{15}N_3OS$ (213.30): C, 50.68; H, 7.09; N, 19.70; S, 15.03 Found: C, 50.77; H, 7.15; N, 19.50; S, 15.12 %.

3-methyl-5,6-dihydro-s-triazolo[3,4-b]-1,3,4-thiadiazole (10)

Procedure a: A mixture of amino triazole **8** (1 gm, 76.9 mmol) and formaldehyde (1 mL) and glacial acetic acid (25 mL) containing a catalytic amount of concentrated H_2SO_4 was stirred either at room temperature or refluxing for 3 hours. The resulting precipitate thus formed was filtered and washed with water and crystallized from dioxane to give the corresponding **10** in excellent yield.

Procedure b: A mixture of amino triazole **8** (1 gm, 76.9 mmol) and formaldehyde (1 mL) and ethanol (25 mL) was stFTIRred refluxing for 3 hours. The resulting precipitate thus formed was filtered and washed with ethanol and crystallized from dioxane to give the corresponding **10** in excellent yield.

Yield: (90.82%); white powder (dioxane); mp 264-266 °C. FTIR: 3236 (NH.), 2989 (C-H aliph), 1586 (C=N), 1445 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, DMSO): δ =2.31 (s, 3H, CH_3 triazole), 5.34 (d, 2H, CH_2), 7.38 (t, 1H, NH). m/z (EI, 70 eV) 142 [M^+] (26.60%). Anal. Calcd. % for $C_4H_6N_4S$ (142.03): C, 33.79; H, 4.25; N, 39.41; S, 22.55. Found: C, 33.70; H, 4.30; N, 39.51; S, 22.49.

4-arylidenamino-3-methyl-s-triazole-5-thiones (12a-c)

General procedure: A mixture of amino triazole [S2] **8** (1 gm, 76.9 mmol) and aromatic aldehydes (76.9 mmol) and glacial acetic acid (25 mL) containing a catalytic amount of concentrated H_2SO_4 was stirred either at room temperature or refluxing for 3 hours. The resulting precipitate thus formed was filtered and washed with water and crystallized from the appropriate solvent to give the corresponding **(12a-c)** in excellent yield.

4-Benzylideneamino-3-methyl-2,4-dihydro-3H-s-triazole-5-thione (12a)

Yield: (89.33%); white crystals (EtOH-benzene); mp 202-203 °C. FTIR: 3110 (NH), 3080 (C-H arom.), 2957(C-H aliph.), 1656 (C=N), 1487 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, DMSO): δ = 2.37 (s, 3H, CH_3 triazole), 7.58 (t, *J* = 16.3 Hz, 3H, H-arom.), 7.92(d, *J* = 8.5 Hz, 2H, H-arom.), 10 (s, 1H, -N=CH-), 13.77 (s, 1H, NH). ^{13}C-NMR (101 MHz, DMSO) δ = 163.78 (C5=S), 161.68 (C3=N), 148.86 (CH=N), 133.07 (CH-arom.), 132.64 (CH-

arom.), 129.61 (2CH-arom.), 129.02 (2CH-arom.), 11.22 (CH_3 triazole). Anal. Calcd. % for $C_{10}H_{10}N_4S$ (218.27): C, 55.03; H, 4.62; N, 25.67; S, 14.69 Found: C, 55.24; H, 4.55; N, 25.61; S, 14.60%.

4-((4-Methoxybenzylidene)amino)-3-methyl-2,4-dihydro-3H-s-triazole-5-thione (12b)

Yield: (94.24%); white crystals (ethanol-benzene); mp 200-202 °C. FTIR: 3107 (NH), 3069 (C-H arom.), 2960 (C-H aliph.), 1606 (C=N), 1453 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, DMSO): δ = 2.33 (s, 3H, CH_3 triazole), 3.86 (s, 3H, OCH_3), 7.14 (d, *J* =15.7 Hz, 2H, H-arom.), 7.84 (d, *J* =15.7 Hz, 2H, H-arom.), 9.70 (s, 1H, -N=CH-), 13.57 (s, 1H, NH). ^{13}C-NMR (101 MHz, DMSO) δ = 163.08 (C5=S), 162.59 (C3=N), 161.68 (O-CH-arom.), 147.66 (CH=N), 130.63 (2CH-arom.), 125.13 (CH-arom.), 114.38 (2CH-arom.), 55.50 (-O-CH_3), 11.06 (CH_3 triazole). Anal. Calcd. % for $C_{11}H_{12}N_4OS$ (248.30): C, 53.21; H, 4.87; N,22.56; S, 12.91. Found: C, 53.40; H, 4.70; N, 22.37; S, 12.55.

4-((4-Chlorobenzylidene)amino)-3-methyl-2,4-dihydro-3H-s-triazole-5-thione (12c)

Yield: (87.44%); white crystals (ethanol-benzene); mp 188-190 °C. FTIR: 3102 (NH), 3056 (C-H arom.), 2942 (C-Haliph.), 1586 (C=N), 1489 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, DMSO): δ = 2.37 (s, 3H, CH_3 triazole), 7.58 (d, *J* = 8.5 Hz, 2H, H-arom.), 7.92 (d, *J* = 11.1 Hz, 2H, H-arom.), 9.99(s, 1H, -N=CH-), 13.77 (s, 1H, NH). Anal. Calcd. % for $C_{10}H_9ClN_4S$ (252.72): C, 47.53; H, 3.59; Cl, 14.03; N, 22.17; S, 12.69. Found: C, 47.65; H, 3.25; Cl, 14.13; N, 22.37; S, 12.60.

4-arylidenamino-1-[(morpholino/piperidino/N-methylpiperazino)methyl]-3-methyl-s-triazole-5-thiones (13a-i):

General procedure: A mixture of 4-arylidenamino-3-methyl-s-triazole-5-thiones **12a-c** (1 gm, 4.58 mmole, 4.o3 mmole and 3.96 mmole respectively), formaldehyde (1 mL) and secondary amines was stirred at room temperature for 3 hours, then the crude product was collected by filtration and crystallized from appropriate solvent.

4-(benzylideneamino-3-methyl-2-(piperidinmethyl)-2,4-dihydro-3H-s-triazole-5-thione (13a)

Yield: (93.42%); white crystals (cyclohexane); mp 110-111°C. FTIR: 3075 (C-H arom.), 2910-2830 (C-H aliph.), 1525 (C=N), 1455 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.27-1.46 (m, 2H, CH_2 piper.), 1.48-1.69 (m, 4H, 2CH_2 piperidine), 2.46 (s, 3H, CH_3 triazole), 2.77 (t, , *J* = 10.6 Hz, 4H, N(CH_2)$_2$), 5.09 (s, 2H, N-CH_2-N), 7.52 (t, , *J* = 14.6 Hz, 3H, H-arom.), 7.87 (d, *J* = 4.9 Hz, 2H, H-arom.), 10.48(s, 1H, -N=CH-). ^{13}C-

NMR (101 MHz, $CDCl_3$) δ = 162.62 (C5=S), 160.81 (C3=N), 147.77 (CH=N), 134.47 (CH-arom.), 132.75 (CH-arom.), 129.01 (2CH-arom.), 128.92 (2CH-arom.), 68.81 (N-CH_2-N), 51.79 (piperidine 2N-CH_2), 25.94 (piperidine 3CH_2),11.17 (CH_3 triazole).). m/z (EI, 70 eV) 315 [M^+](8.36%), 316 [M^++1](1.72). Anal. Calcd. % for $C_{16}H_{21}N_5S$ (315.43): C, 60.92; H, 6.71; N, 22.20; S, 10.16. Found: C, 60.71; H, 6.58; N, 22.37; S, 10.34.

4-(4-methoxybenzylidene)amino-3-methyl-2-(piperidinmethyl)-2,4-dihydro-3H-s-triazole-5-thione (13b)

Yield: (91.36%); pale yellow crystals (ethanol-cyclohexane); mp 108-110 °C. FTIR: 3015(C-H arom.), 2923-2849 (C-Haliph.), 1585 (C=N), 1455 (C=C) cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 1.38-1.59 (m, 6H, 3CH_2 piperidine), 2.48 (s, 3H, CH_3 triazole), 2.80 (t, 4H, 2CH_2 piperidine), 3.40 (s, 3H, O<u>CH_3</u>), 5.10 (s, 2H, N-CH_2-N), 7.20 (d, 2H, H-arom.), 7.80 (d, 2H, H-arom.), 10.60 (s, 1H, -N=<u>CH</u>-).). m/z (EI, 70 eV) 345.30 [M^+](5.47), 346 [M^++1](3.29%). Anal. Calcd. % for $C_{17}H_{23}N_5OS$ (345.16): C, 59.10; H, 6.71; N,20.27; S, 9.28. Found: C, 59.50; H, 6.55; N, 20.37; S, 9.55.

4-(4-chlorobenzylidene)amino-3-methyl-2-(piperidinmethyl)-2,4-dihydro-3H-s-triazole-5-thione (13c)

Yield: (92.75%); pale green crystals (cyclohexane); mp 115-117 °C. FTIR: 3063 (C-H arom.), 2930-2809 (C-Haliph.), 1593 (C=N), 1453 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): = 1.30-1.48 (m, 2H, CH_2 piperidine), 1.59 (m, 4H, 2CH_2 piperidine), 2.46 (s, 3H, CH_3 triazole), 2.77 (t, *J* = 10.5 Hz, 4H, N(CH_2)$_2$), 5.08 (s, 2H, N-CH_2-N), 7.45 (d, *J* = 8.5 Hz, 2H, H-arom.), 7.80 (d, *J* = 11.1 Hz, 2H, H-arom.), 10.58 (s, 1H, -N=<u>CH</u>-). ^{13}C-NMR (101 MHz, $CDCl_3$)) δ = 163.78 (C5=S), 161.68 (C3=N), 148.86 (CH=N), 136.90 (CH-arom.), 131.60 (CH-arom.), 130.90 (2CH-arom.), 129.00 (2CH-arom.), 51.79 (piperidine N(CH_2)$_2$), 25.94 (piperidine 3CH_2),11.22(CH_3 triazole). MS (EI, 70 eV): m/z (%) = 372 [M+Na]. Anal. Calcd. % for $C_{16}H_{20}ClN_5S$ (349.88): C, 54.93; H, 5.76; Cl, 10.13; N, 20.02; S, 9.16. Found: C, 54.69; H, 5.55; Cl, 10.35, N, 20.37; S, 9.04.

4-(benzylideneamino-3-methyl-2-(morpholinomethyl)-2,4-dihydro-3H-s-triazole-5-thione (13d)

Yield: (91.72%); white crystals (cyclohexane); mp 126-128 °C. FTIR: 3087 (C-H arom.), 2950-2865(C-H aliph.), 1603 (C=N), 1415 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ =2.46 (s, 3H, CH_3 triazole), 2.85 (t, *J* =13.6 Hz, 4H, N(CH_2)$_2$), 3.71 (t, 4H, O(CH_2)$_2$), 5.09 (s, 2H, N-CH_2-N), 7.36-7.63 (t, *J* =17.9, 26.4 Hz, 3H, H-arom.), 7.87(d, *J* =8.4 Hz, 2H, H-arom.), 10.45 (s, 1H, -N=<u>CH</u>-). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 162.84 (C5=S), 161.04 (C3=N), 148.03 (CH=N), 132.66 (CH-arom.), 132.37 (CH-arom.), 128.95 (2CH-arom.), 129.72 (2CH-

arom.), 68.89 (N-CH_2-N), 66.89 (morpholine O-CH_2), 50.87 (morpholine N-CH_2),11.14 (CH_3 triazole). m/z (EI, 70 eV) 317 [M^+] (24.48%).

Anal. Calcd. % for $C_{15}H_{19}N_5OS$ (317.13): C, 56.76; H, 6.03; N, 22.06; S, 10.10. Found: C, 56.69; H, 6.10; N, 22.13; S, 10.15.

4-(4-methoxybenzylidene)amino-3-methyl-2-(morphilinomethyl)-2,4-dihydro-3*H*-s-triazole-5-thione (13e)

Yield: (92.92%); white crystals (ethanol-cyclohexane); mp 138-140 °C. FTIR: 3090 (C-H arom.), 2967-2850 (C-H aliph.), 1606 (C=N), 1422 (C=C) cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 2.40 (s, 3H, CH_3), 2.70 (t, 4H, N(CH_2)$_2$), 3.60 (t, 4H, O(CH_2)$_2$), 3.90 (s, 3H, O$\underline{CH_3}$), 5.00 (s, 2H, N-CH_2-N), 7.20 (d, 2H, H-arom.), 7.80 (d, 2H, H-arom.), 9.70(s, 1H, -N=$\underline{CH}$-). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 163.08 (C5=S), 162.59 (C3=N), 161.68 (O-CH-arom.), 147.66 (CH=N), 130.63 (2CH-arom.), 125.13 (CH-arom.), 114.38 (2CH-arom.), 68.53(N-CH_2-N), , 66.89 (morpholine O-CH_2), 55.50 (-O-CH_3), 50.87 (morpholine N-CH_2), 11.06 (CH_3).). m/z (EI, 70 eV) 347 [M^+] (23.24%). Anal. Calcd. % for $C_{16}H_{21}N_5O_2S$ (347.14): C, 55.31; H, 6.09; N,20.16; S, 9.23. Found: C, 55.40; H, 6.05; N, 20.11; S, 9.12.

4-(4-chlorobenzylidene)amino-3-methyl-2-(morpholinomethyl)-2,4-dihydro-3H-s-triazole-5-thione (13f)

Yield: (92.80%); white crystals (cyclohexane); mp 152-154 °C. FTIR: 3078 (C-H arom.), 2965 (C-H aliph.), 1610 (C=N), 1449.59 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.46 (s, 3H, CH_3), 2.82 (t, 4H, 2CH_2), 3.69 (t, *J* = 11.1 Hz, 4H, 2CH_2), 5.08 (s, 2H, CH_2), 7.46 (d, *J* = 8.5 Hz, 2H, H-arom.), 7.81 (d, J = 8.5 Hz, 2H, H-arom.), 10.55 (s, 1H, -N=CH-). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 163.78 (C5=S), 161.68 (C3=N), 148.86 (CH=N), 136.90 (CH-arom.), 131.60 (CH-arom.), 130.90 (2CH-arom.), 129.00 (2CH-arom.), 66.89 (morpholine O-CH_2), 50.87 (morpholine N-CH_2),11.22(CH_3 triazole). MS (EI, 70 eV): m/z (%) = 351.00 [M], 353.05[M+2]. Anal. Calcd. % for $C_{15}H_{18}ClN_5OS$ (351.09): C, 51.20; H, 5.16; Cl, 10.08; N, 19.90; S, 9.11

Found: C, 51.12; H, 5.09; Cl, 10.02, N, 19.57; S, 9.01.

4-(benzylideneamino-3-methyl-2-(N-methylpiperazinomethyl)-2,4-dihydro-3H-s-triazole-5-thione (13g)

Yield: (89.22%); white crystals (cyclohexane); mp 118-120 °C. FTIR: 3040 (C-H arom.), 2950-2890 (C-H aliph.), 1604 (C=N), 1414 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ =2.27 (s, 3H, N-CH_3), 2.43 (s,3H, CH_3), 2.44-2.87 (m, 8H, 4CH_2), 5.13 (s, 2H, CH_2), 7.49(t, 3H, H-arom.), 7.86 (d, *J* =8.3 Hz, 2H, H-arom.), 10.42 (s,

1H, -N=CH-). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 162.62 (C5=S), 160.81 (C3=N), 147.77 (CH=N), 134.47 (CH-arom.), 132.75 (CH-arom.), 129.01 (2CH-arom.), 128.92 (2CH-arom.), 68.81 (N-CH_2-N), 54.90 ($2CH_2$),50.23($2CH_2$), 46.01(N-CH_3),11.17 (CH_3). MS (EI, 70 eV): m/z (%) = 330 [M^+] (100%). Anal. Calcd. % for $C_{16}H_{22}N_6S$ (330.16): C, 58.16; H, 6.71; N, 25.43; S, 9.70. Found: C, 58.35; H, 6.65; N, 25.40; S, 9.60.

4-(4-methoxybenzylidene)amino-3-methyl-2-(N-methylpiperazinomethyl)-2,4-dihydro-3H-s-triazole-5-thione (13h)

Yield: (91.03%); white crystals (ethanol-cyclohexane); mp 142-144 °C. FTIR: 3058 (C-H-arom.), 2968-2840 (C-Haliph.), 1605 (C=N), 1424 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, DMSO): δ =2.28 (s, 3H,N-CH_3), 2.41 (s, 3H, CH_3), 2.44-2.88 (t, 8H, $4CH_2$), 3.88 (s, 3H, OCH_3), 5.13 (s, 2H, CH_2), 7.01(d, *J* = 13.9 Hz, 2H, H-arom.), 7.83(d, 2H, *J* = 25.2 Hz, H-arom.), 10.13 (s, 1H, -N=CH-). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 163.08 (C5=S), 162.59 (C3=N), 161.68 (O-CH-arom.), 147.66 (CH=N), 130.63 (2CH-arom.), 125.13 (CH-arom.), 114.38 (2CH-arom.), 68.53(N-CH_2-N), 55.50 (-O-CH_3), 54.90 ($2CH_2$),50.23($2CH_2$), 46.01(N-CH_3), 11.06 (CH_3).

MS (EI, 70 eV): m/z (%)= 360.08 [M^+], 361.12 [M^++1]. Anal. Calcd. % for $C_{17}H_{24}N_6OS$ (360.17): C, 56.64; H, 6.71; N, 23.31; S, 8.89. Found: C, 56.69; H, 6.25; N, 23.37; S, 8.55.

4-(4-Chlorobenzylidene)amino-3-methyl-2-(N-methylpiperazinomethyl)-2,4-dihydro-3H-s-triazole-5-thione (13i)

Yield: (90.27%); pale white crystals (cyclohexane); mp 112-114 °C. FTIR: 3060 (C-H arom.), 2950-2835 (C-H aliph.), 1601 (C=N), 1418 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, DMSO): δ = 2.27 (s, 3H, N-CH_3), 2.44 (s, 3H, CH_3), 2.45-2.89 (m, 8H, $4CH_2$), 5.13 (s, 2H, CH_2), 7.48(d, *J*= 8.5 Hz, 2H, H-arom.), 7.86 (d, *J*= 8.3 Hz, 2H, H-arom.), 10.42 (s, 1H, -N=CH-). ^{13}C-NMR (101 MHz, DMSO) δ = 163.78 (C5=S), 161.68 (C3=N), 148.86 (CH=N), 136.90 (CH-arom.), 131.60 (CH-arom.), 130.90 (2CH-arom.), 129.00 (2CH-arom.), 54.90 ($2CH_2$), 50.23 ($2CH_2$), 46.01(N-CH_3), 11.22(CH_3).). m/z (EI, 70 eV) 364.93 [M^+] (9.22%). Anal. Calcd. % for $C_{16}H_{21}ClN_6S$ (364.89): C, 52.67; H, 5.80; Cl, 9.72; N, 23.03; S, 8.79. Found: C, 52.69; H, 5.61; Cl, 9.50, N, 23.37; S, 8.83.

4(4-chlorobenzylideneamino)-3-methyl-1-((propyl/4-chlorophenylamino)methyl)-1*H*-s-triazole-3-thione 14a,b

General procedure: A mixture of 4-((4-Chlorobenzylidene)amino)-3-methyl-2,4-dihydro-3H-s-triazole-5-thione **12c** (1 gm, 3.96 mmole,), formaldehyde (1 mL) and primary amine such as propyl amine and *p*-chloro aniline

(3.96 mmole) was stirred at room temperature for 3 hours, then the crude product was collected by filtration and crystallized from appropriate solvent.

4(4-chlorobenzylideneamino)-3-methyl-1-((propylamino)methyl)-1*H*-s-triazole-3-thione (14a)

Yield: (86.61%); white crystals (cyclohexane); mp 170-172 °C. FTIR: 3235 (NH.), 3048 (C-H arom.), 2959 (C-H aliph), 1588 (C=N), 1447 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ =1.05 (t, , *J* = 18.6 Hz, 3H, $CH_2C\underline{H}_3$), 1.45 (m, 2H, $C\underline{H}_2CH_3$), 2.37 (s, 3H, CH_3 triazole), 2.38 (q, *J* = 24.5 Hz, 2H, NH -CH_2- CH_2), 5.40 (m, 1H, CH_2-NH.), 5.53 (d, 2H, $C\underline{H}_2$-NH), 7.51 (d, *J* = 41.3 Hz, 2H, H-arom.), 7.78 (d, *J* = 33.5 Hz, 2H, H-arom.), 10.52 (s, 1H, -N=CH-). m/z (EI, 70 eV) 323 [M^+] (29.76%). Anal. Calcd. % for $C_{14}H_{18}ClN_5S$ (323.10): C, 51.92; H, 5.60; Cl, 10.95; N, 21.63; S, 9.90. Found: C, 51.99; H, 5.75; Cl, 10.70, N, 21.73; S, 9.83.

4(4-chlorobenzylideneamino)-3-methyl-1-((4-chlorophenylamino)methyl)-1*H*-s-triazole-3-thione (14b)

Yield: (96.96%); white crystals (cyclohexane); mp 170-172 °C. FTIR: 3389 (NH.), 3050 (C-H arom.), 2944 (C-H aliph), 1594 (C=N), 1427 (C=C) cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ =2.41 (s, 3H, CH_3 triazole), 5.30 (t, 1H, NH), 5.52 (d, *J* = 6.8 Hz, 2H, $C\underline{H}_2$-NH), 6.86 (d, *J* = 8.8 Hz, 2H, H-arom.), 7.15(d, *J* = 8.7 Hz, 2H, H-arom.), 7.44 (d, *J* = 8.4 Hz, 2H, H-arom.), 7.78 (d, *J* = 8.5 Hz, 2H, H-arom.), 10.46 (s, 1H, -N=CH-). m/z (EI, 70 eV) 392 [Cl^{35}, M^+] (2.50%). Anal. Calcd. % for $C_{17}H_{15}Cl_2N_5S$ (392.30): C, 52.05; H, 3.85; Cl, 18.07; N, 17.85; S, 8.17. Found: C, 52.10; H, 3.80; Cl, 18.14, N, 17.78; S, 8.18.

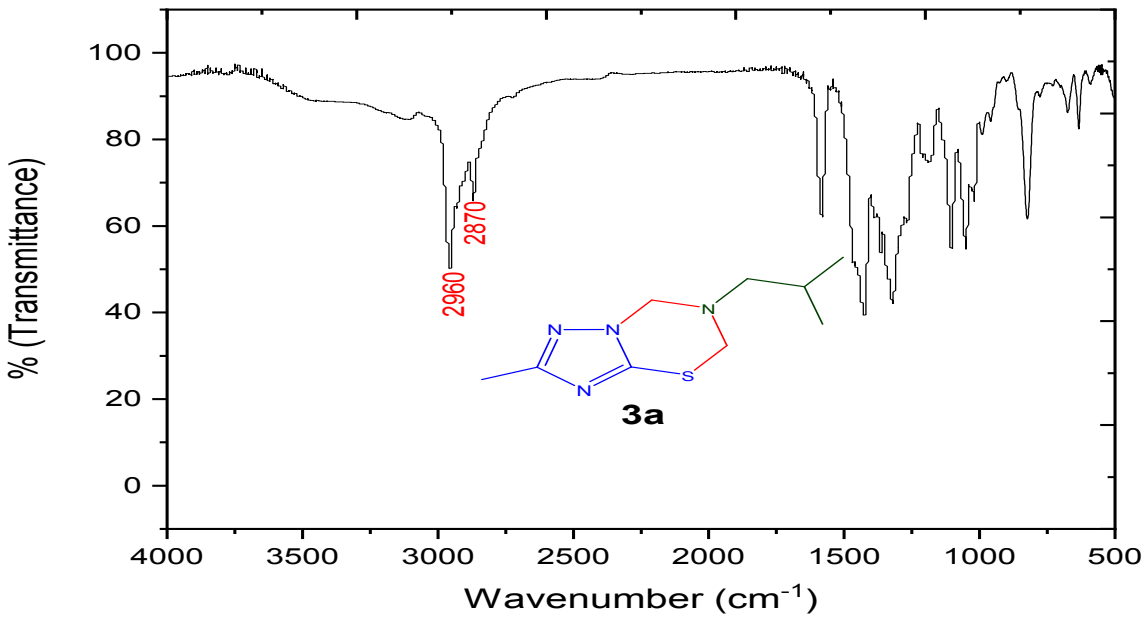
S4. Assay of antimicrobial activity

The antimicrobial activities of the synthesized compounds were evaluated using the well diffusion method [S3]. All synthesized compounds were dissolved in dimethyl sulfoxide (DMSO) to prepare a stock solution of 25 µg/mL**.** Fifteen milliliters of PDA medium for fungi and NA medium for bacteria were poured into sterile Petri dishes seeded with 1 mL of the tested microbial suspension (10^7 CFU/ml). Then, a well with a diameter of 10 mm is punched with a sterile cork borer under aseptic conditions, 100 µL of the antimicrobial agent solution is introduced into the well. Thereafter, agar plates are incubated at 28 °C and 24 h for bacteria and 5 days for fungi. One well loaded with the solvent was used as positive control. The presence of inhibition zones was measured and recorded which indicated that antimicrobial agent diffuses in the agar medium and inhibits the growth of the microbial strain tested.

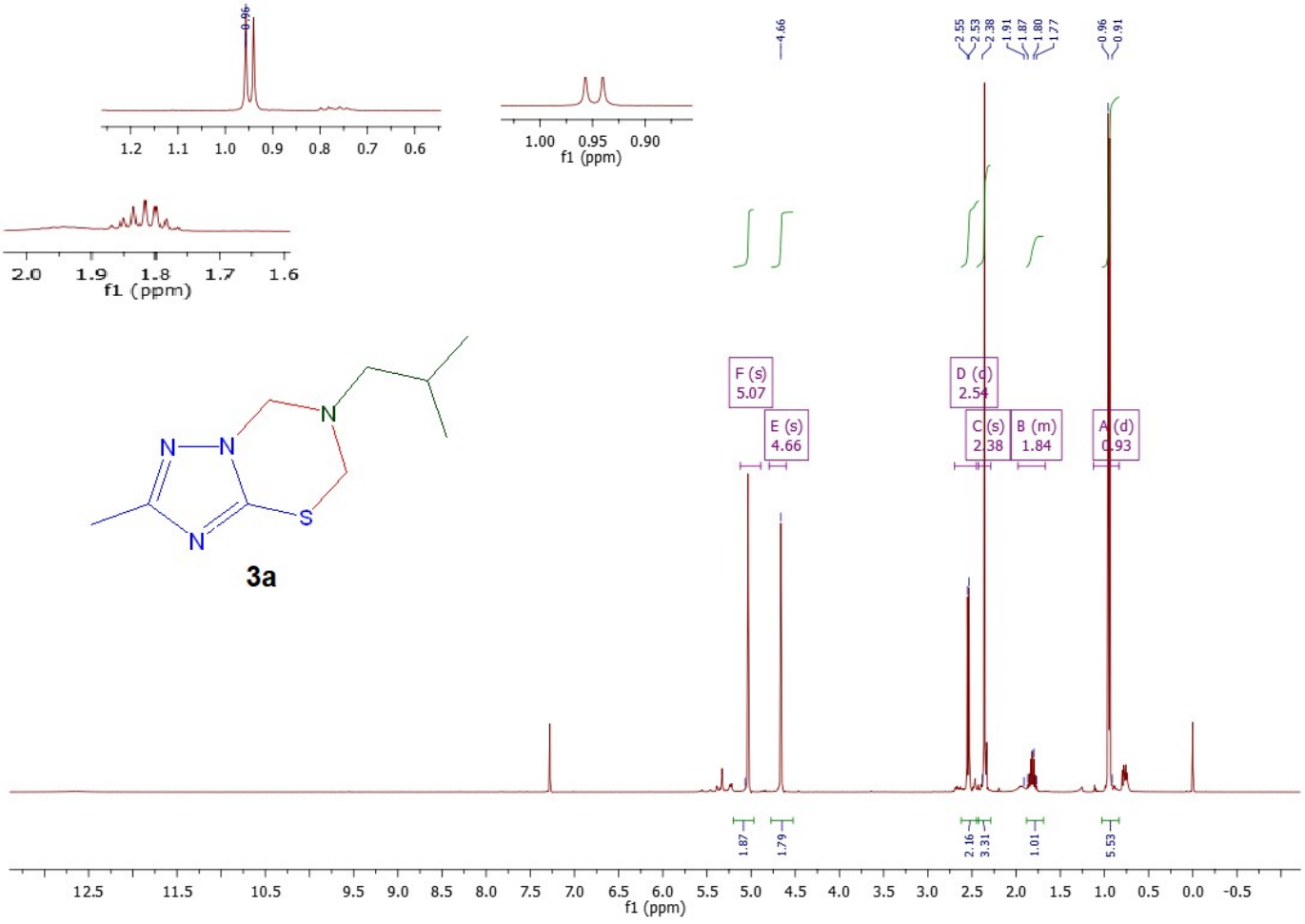
S5. Adsorption studies

Efficiency of the synthesized compounds towards the metal and heavy metal ions removal was evaluated using batch mode [S4, S5]. The adsorption behavior of the compounds under investigation towards heavy metals (Pb^{+2} and Cd^{+2}), and metal ions (Ca^{+2} and Mg^{+2}) was carried out by batch adsorption experiments. A dose of adsorbent (W) (g/L) was added into a 100 mL conical flask containing heavy metal or metal ion solution with an initial concentration (C_0). Typically, 25 mg of each synthesized compounds as adsorbent was added into the conical flask which contains 25 mL of the metal/ heavy metal ion solution (100 mg/L) as initial concentration. Depending on the experiment, pH of the solution was adjusted to 6.0 using NaOH or HCl, both at 0.1 M. The flask was shaken (180 rpm) at 25 °C using an incubating shaker (JSSI-100C, JSR, Korea) and the mixture was left for 24 h to achieve the equilibrium. Next, the adsorbent was separated from the medium by filteration using 0.45 µm Nylon membrane filter. Then, the residual concentration of Pb^{+2}, Cd^{+2}, Ca^{+2} and Mg^{+2} in the solution, C_e, was determined by Atomic Absorption Spectroscopy (ContraAA 700, Analytik Jena, Germany) after digestion in HNO_3 (10 %) overnight. UV/VIS spectrophotometer (Perkin Elmer) was used to confirm the equilbrium concentration of Pb^{+2} and Cd^{+2} in a form of complex that is extracted with chloroform after the reaction and lead and cadmium with dithizone [S6]. The removal percentage (Removal, %), were calculated as presented in Equation 2:

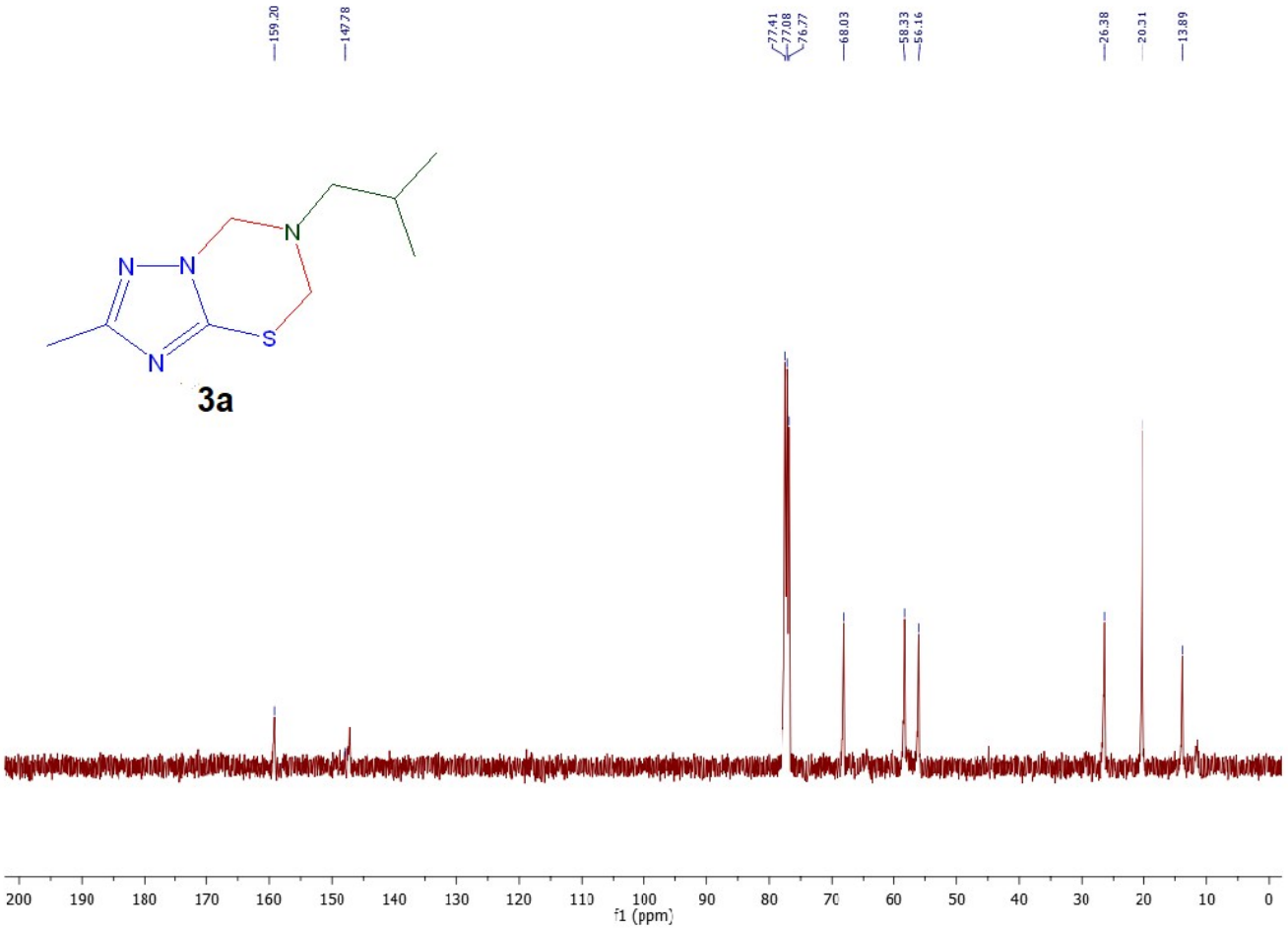
$$Removal, \% = \frac{C_o - C_e}{C_o} x\ 100 \qquad \text{Equation}$$



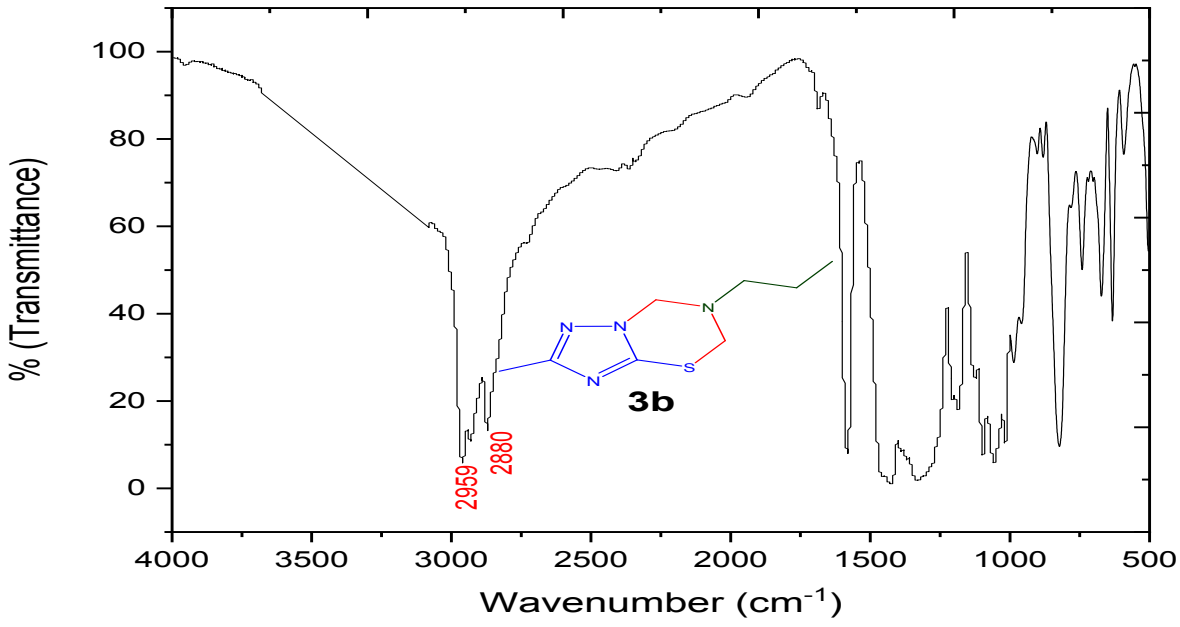
FTIR spectrum of compound **3a**



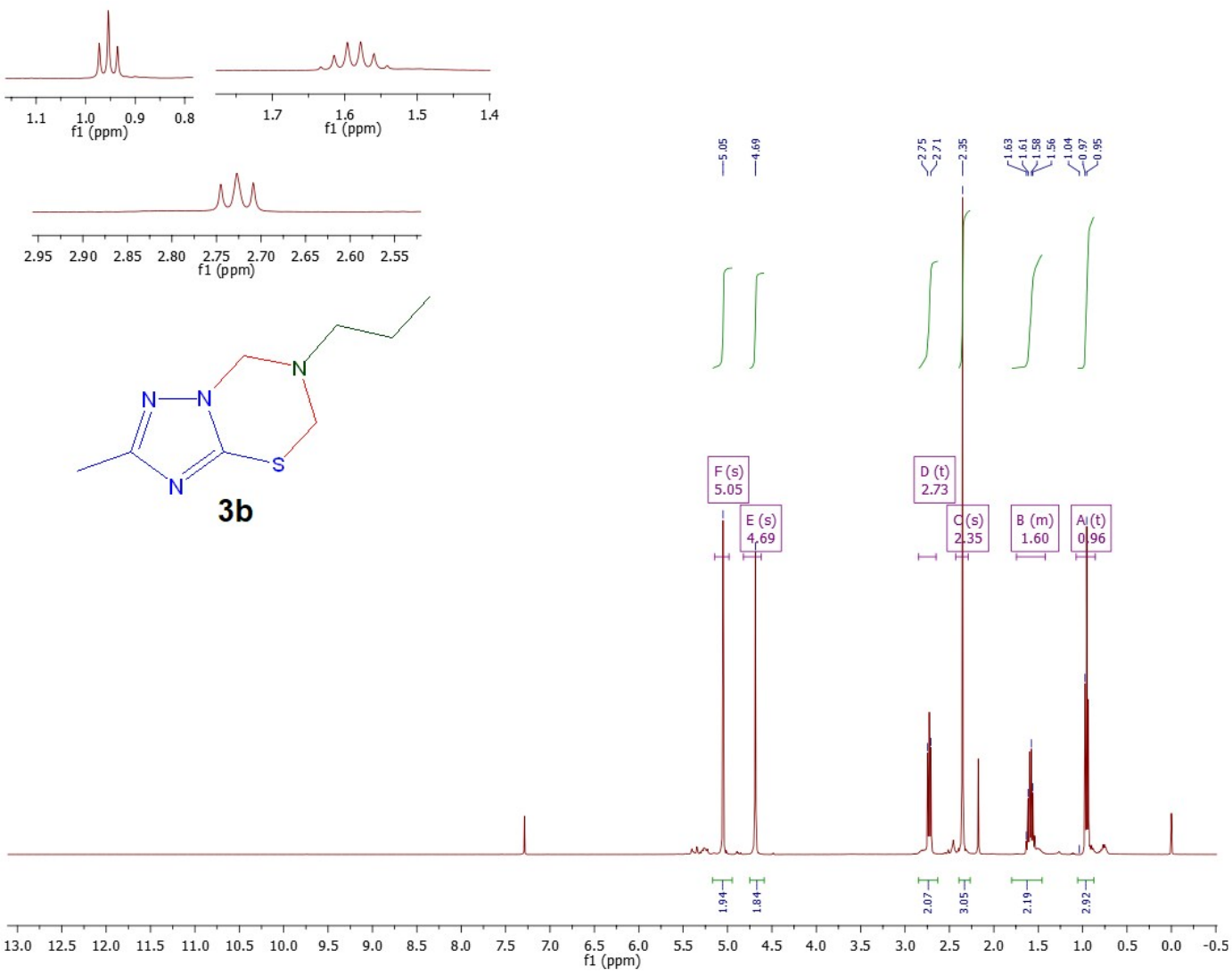
^{1}H-NMR spectrum of compound **3a** (400 MHz, $CDCl_3$).



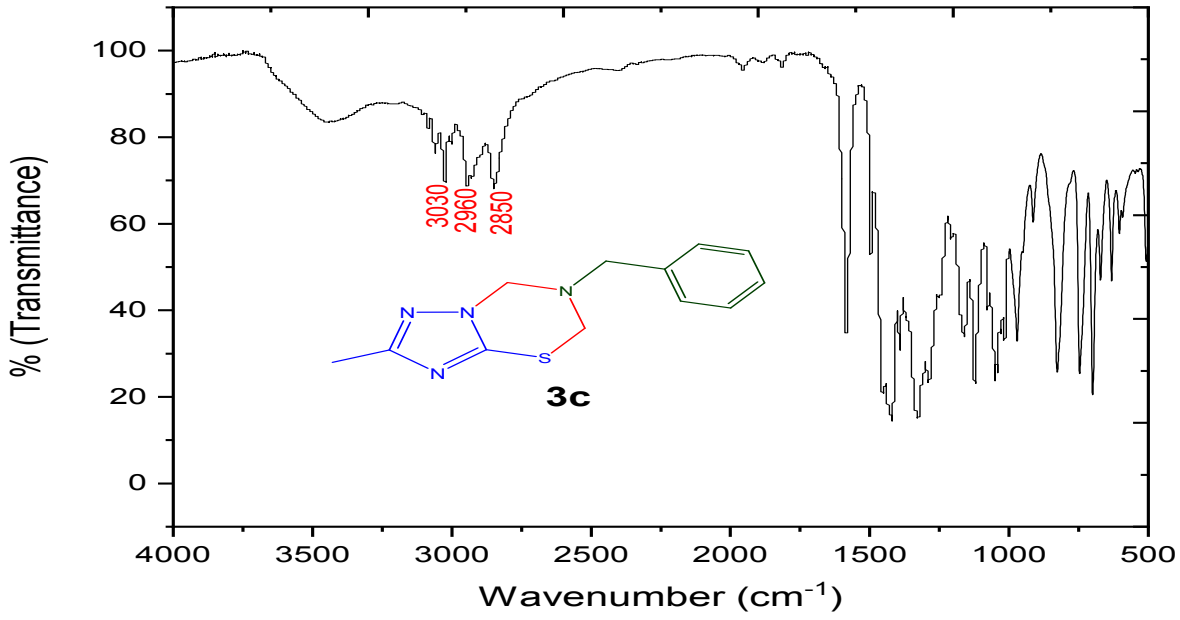
^{13}C-NMR spectrum of compound **3a** (400 MHz, $CDCl_3$).



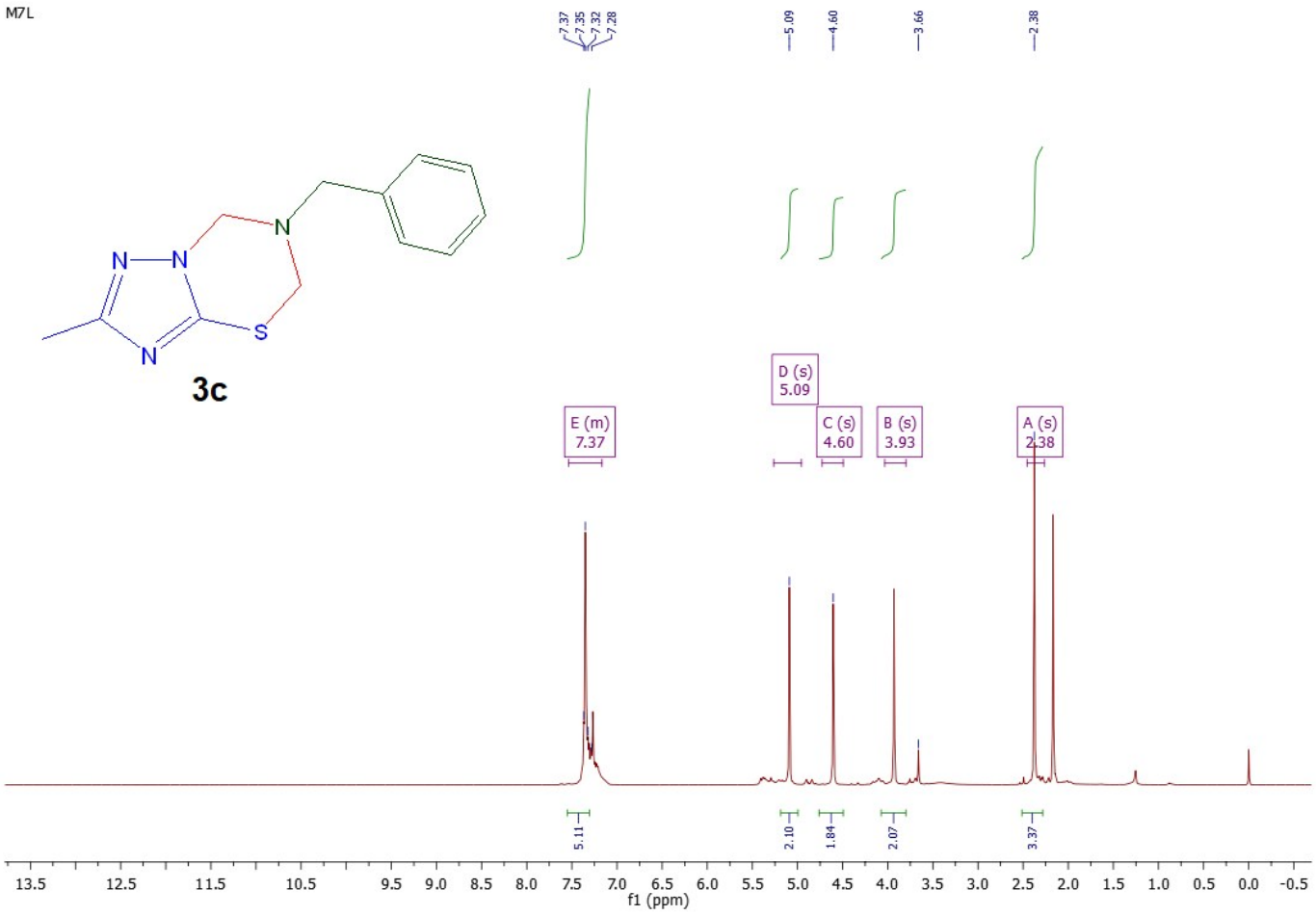
FTIR spectrum of compound **3b**



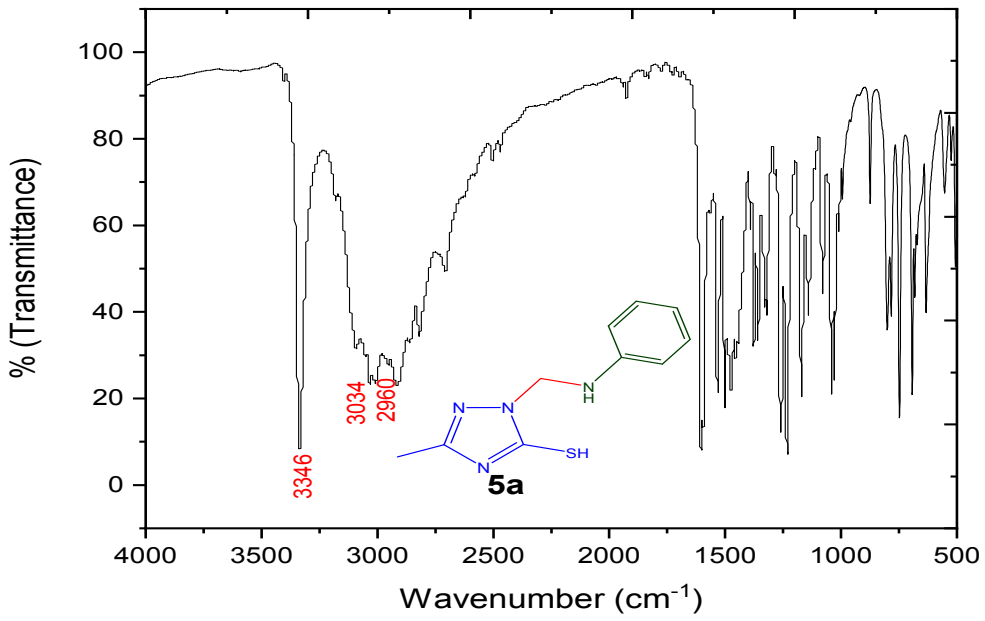
^{1}H-NMR spectrum of compound **3b** (400 MHz, $CDCl_3$).



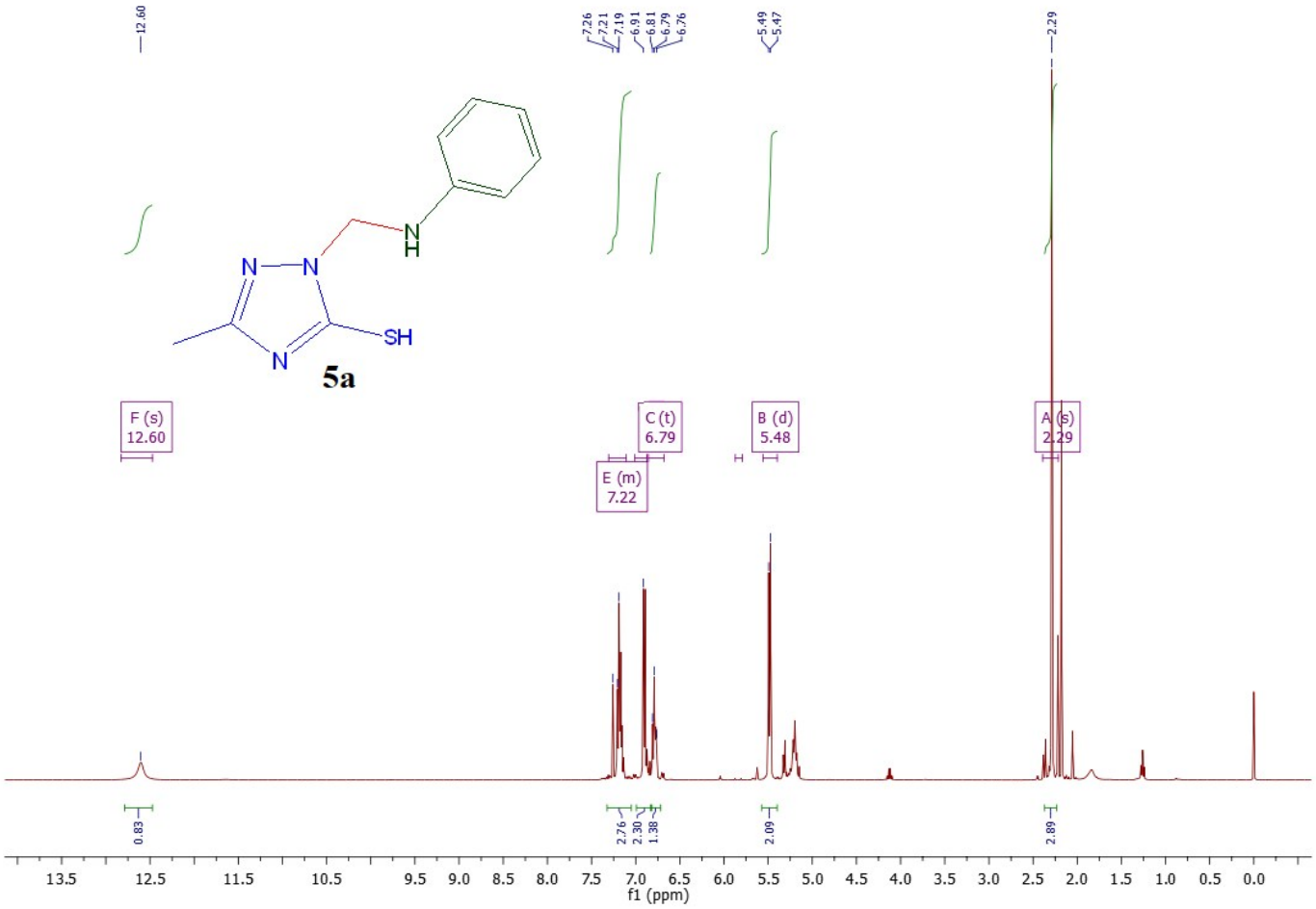
FTIR spectrum of compound **3c**



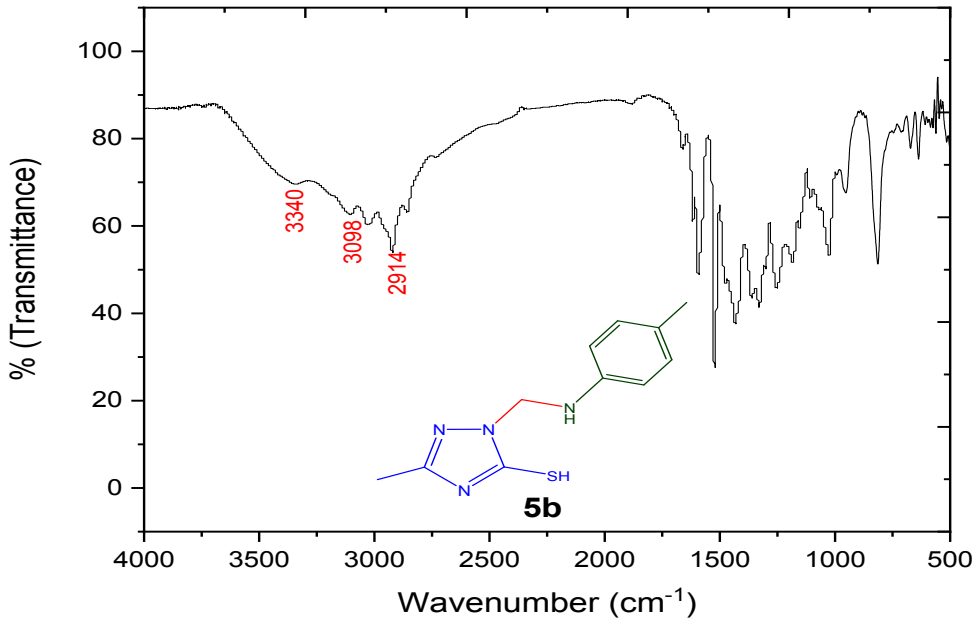
^{1}H-NMR spectrum of compound **3c** (400 MHz, $CDCl_3$).



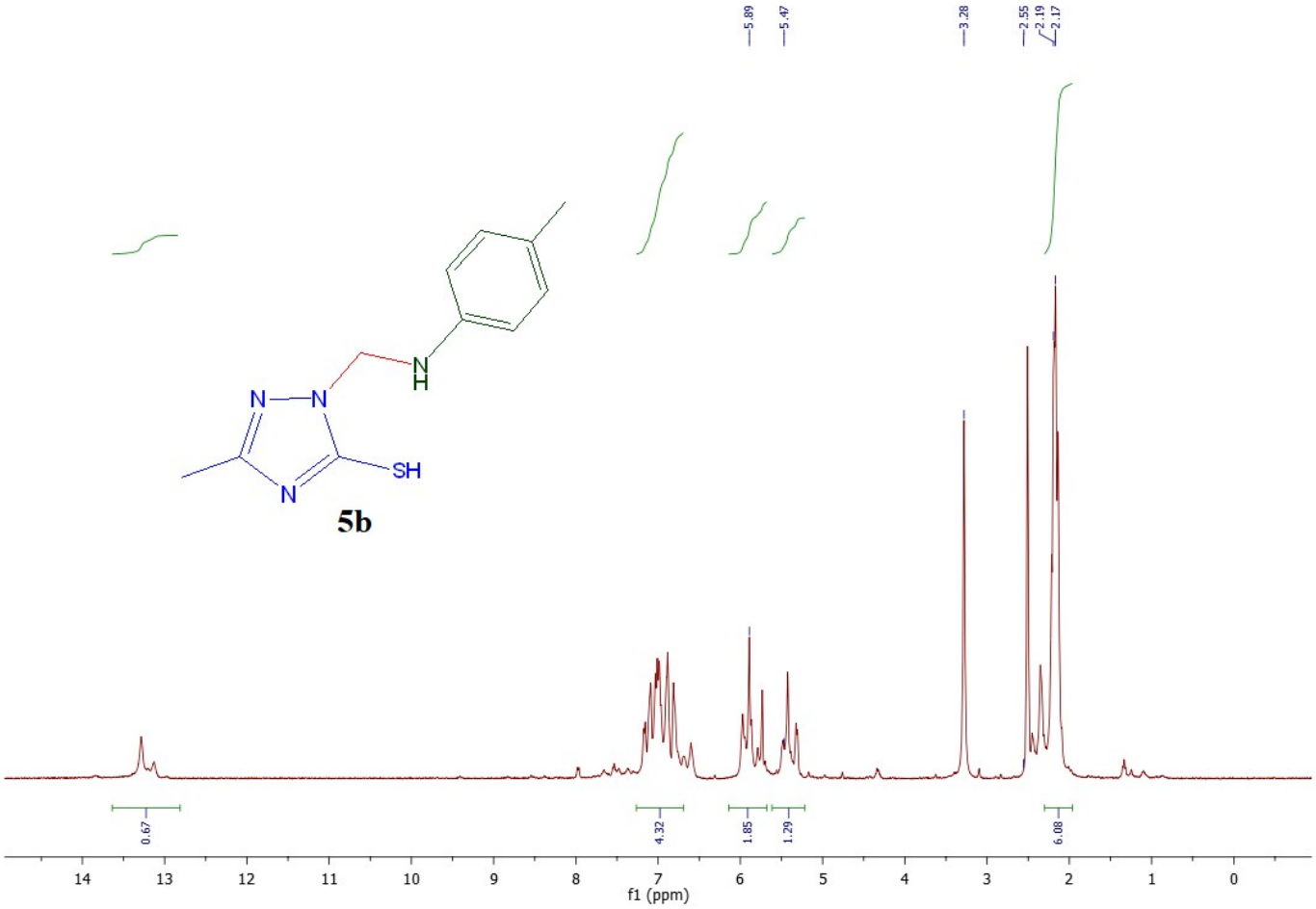
FTIR spectrum of compound **5a**



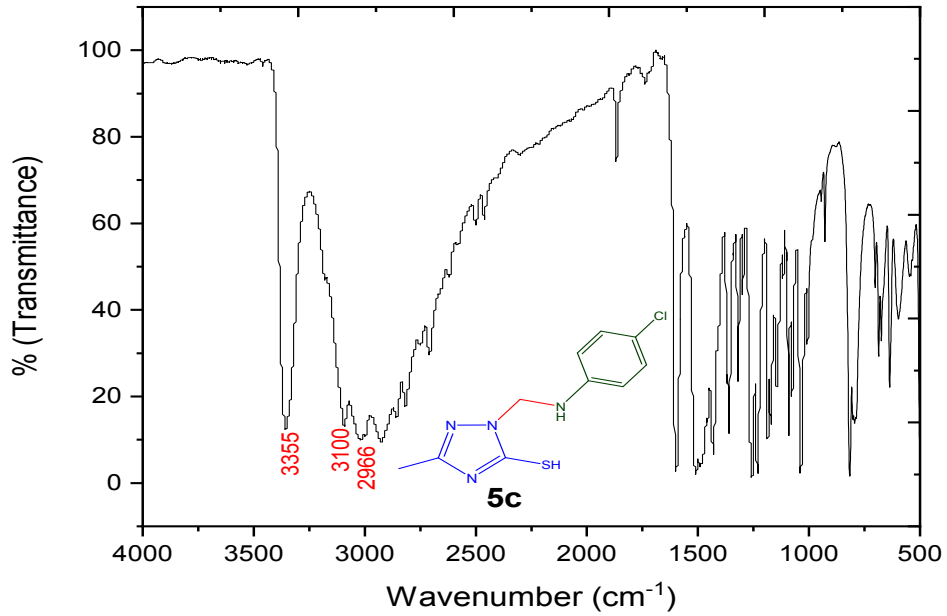
^{1}H-NMR spectrum of compound **5a** (400 MHz, $CDCl_3$).



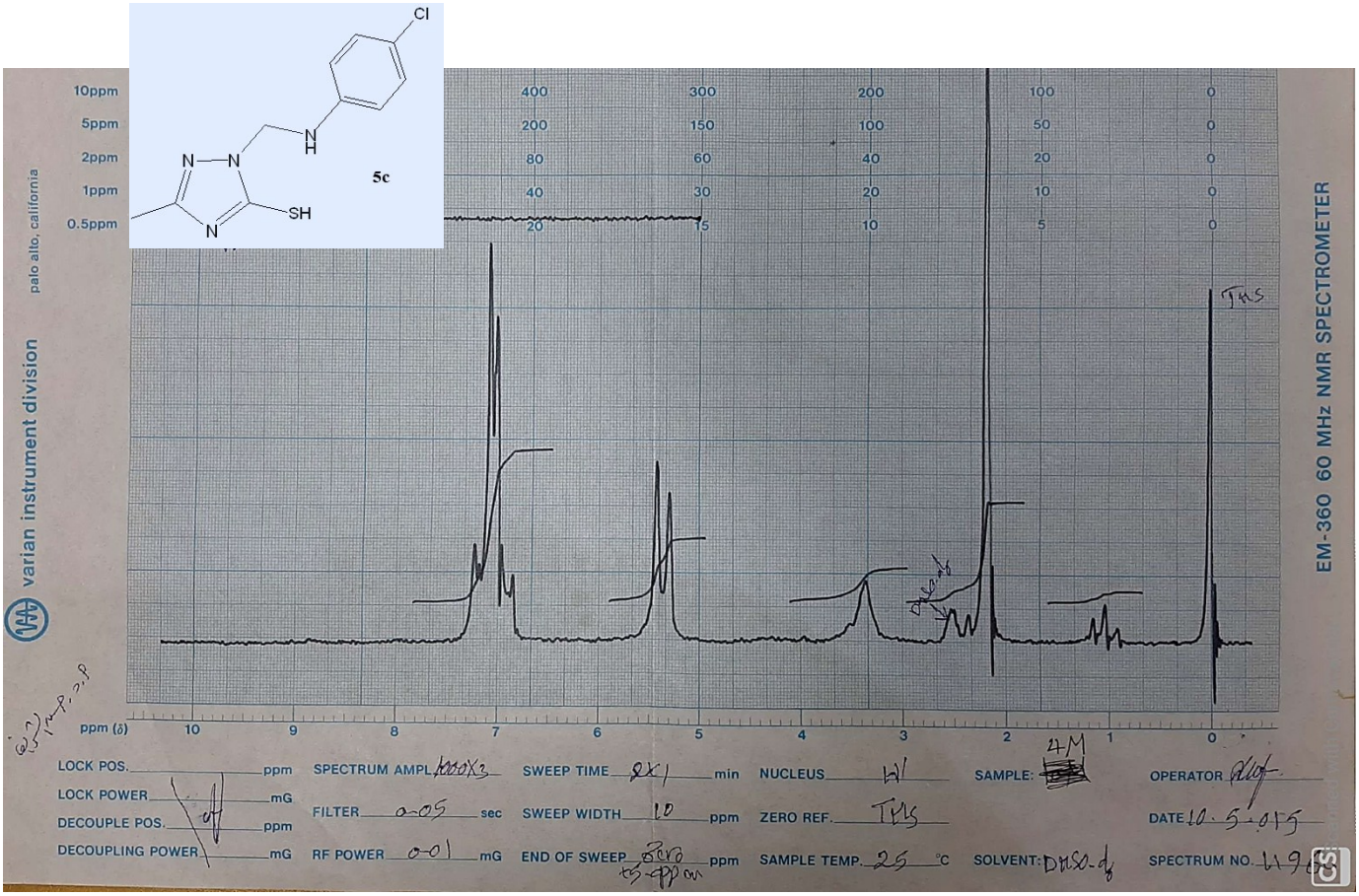
FTIR spectrum of compound **5b**



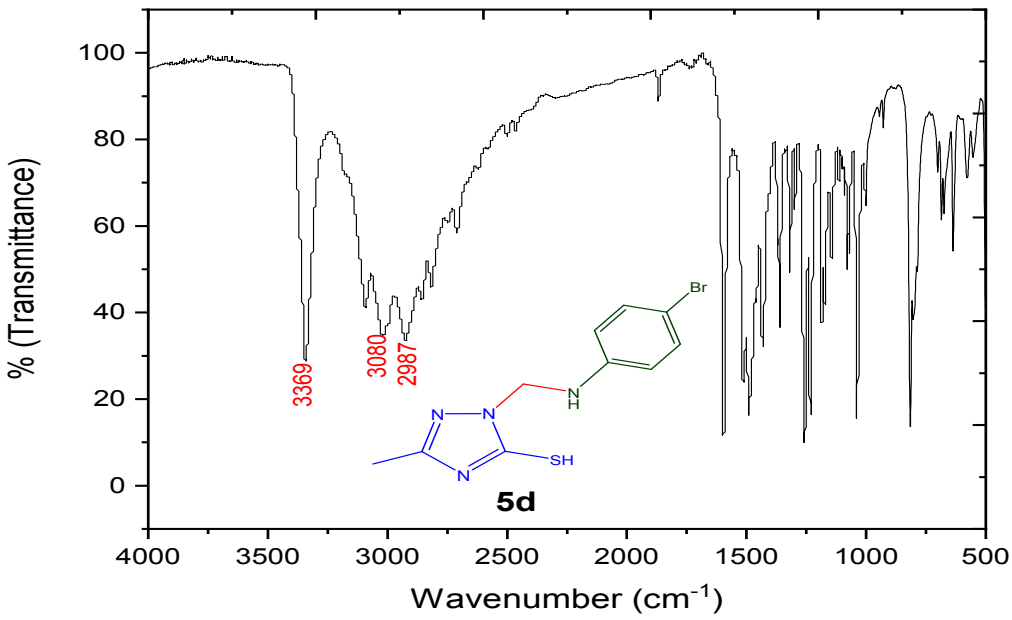
^{1}H-NMR spectrum of compound **5b** (400 MHz, DMSO-d_6).



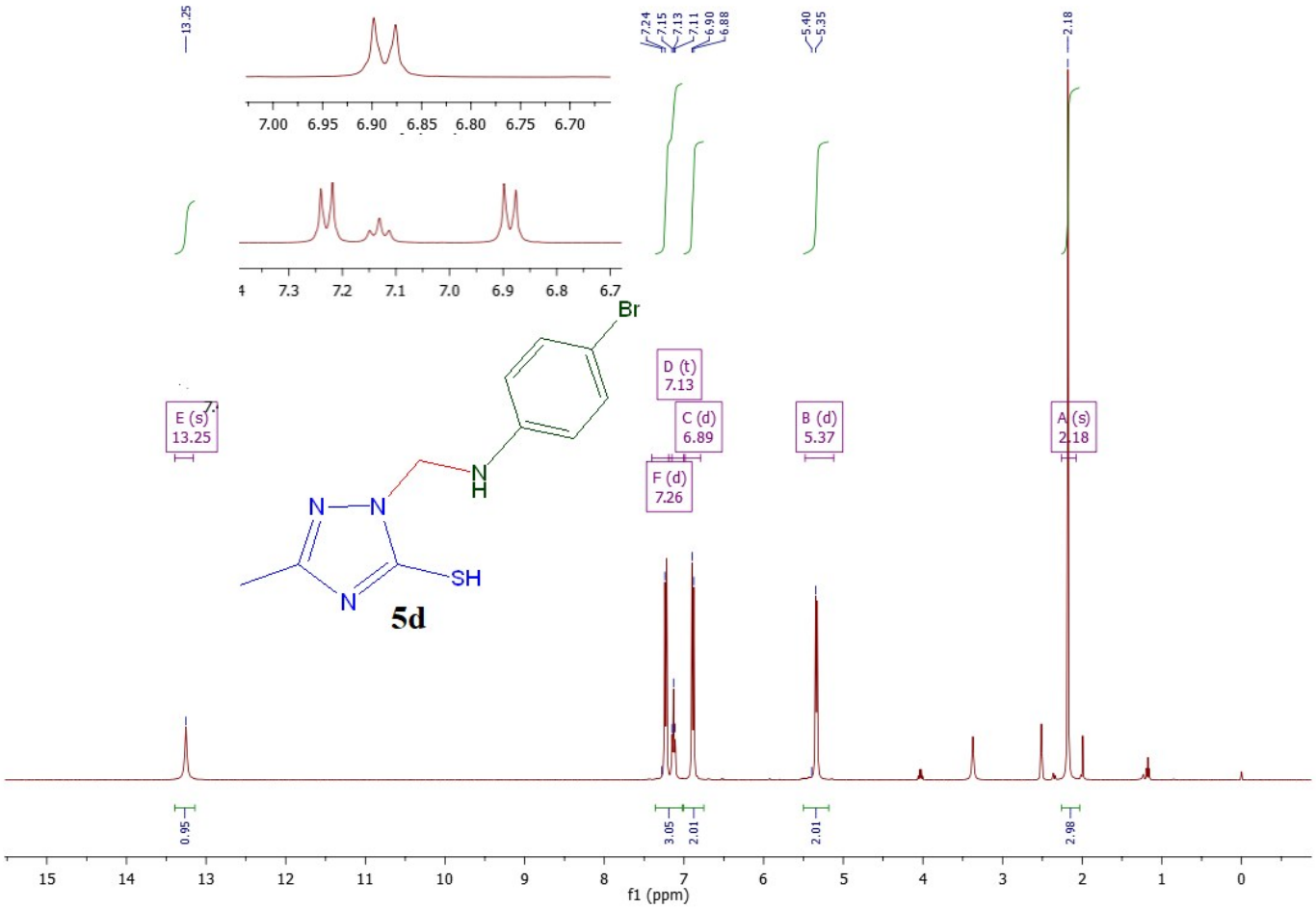
FTIR spectrum of compound **5c**



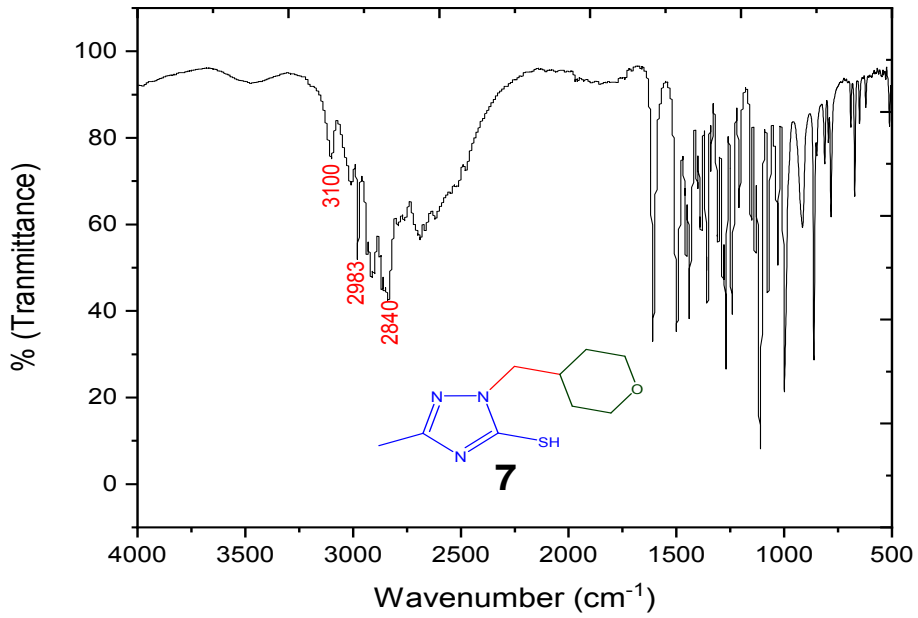
^{1}H-NMR spectrum of compound **5c** (60 MHz, DMSO-d_6).



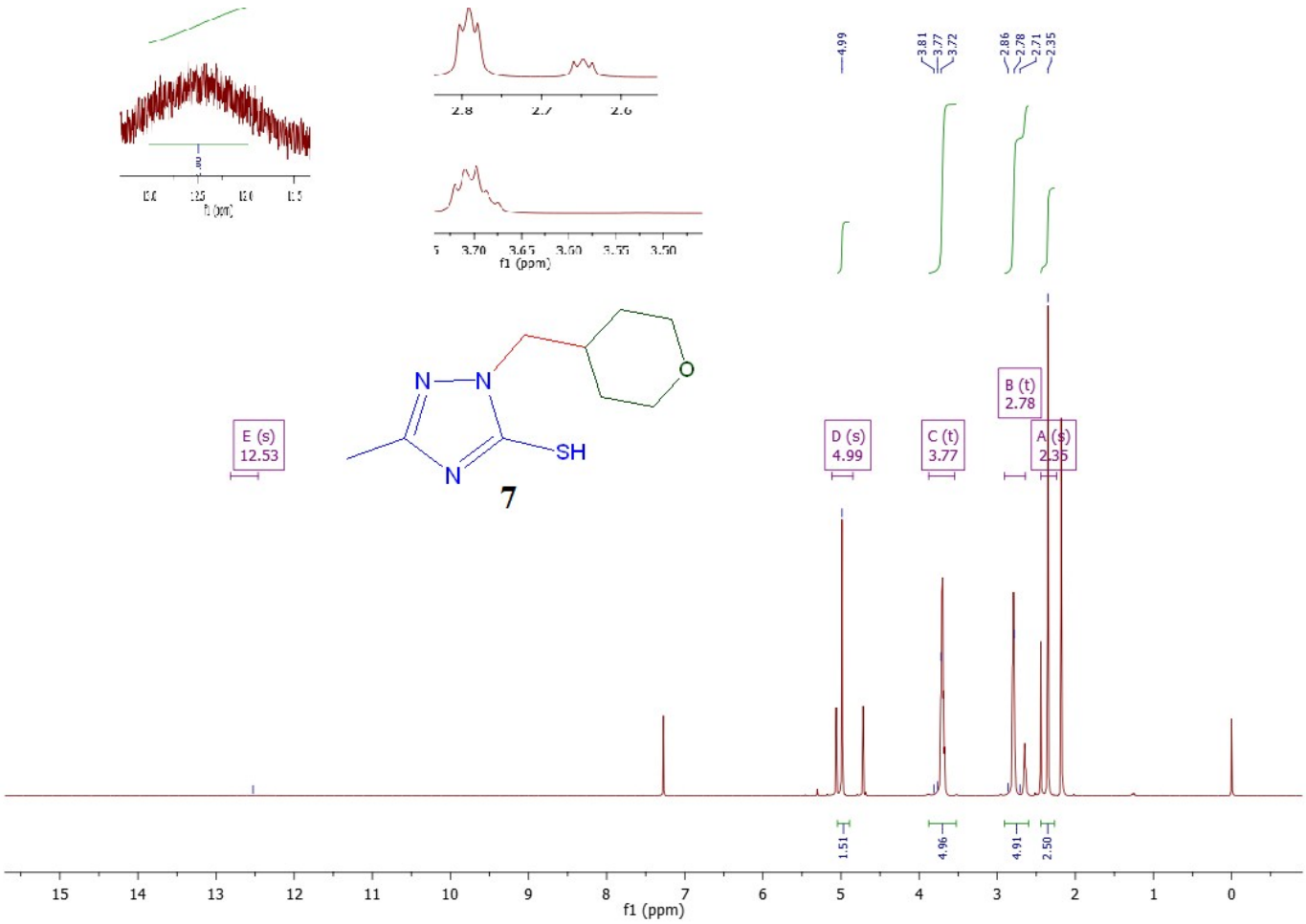
FTIR spectrum of compound **5d**



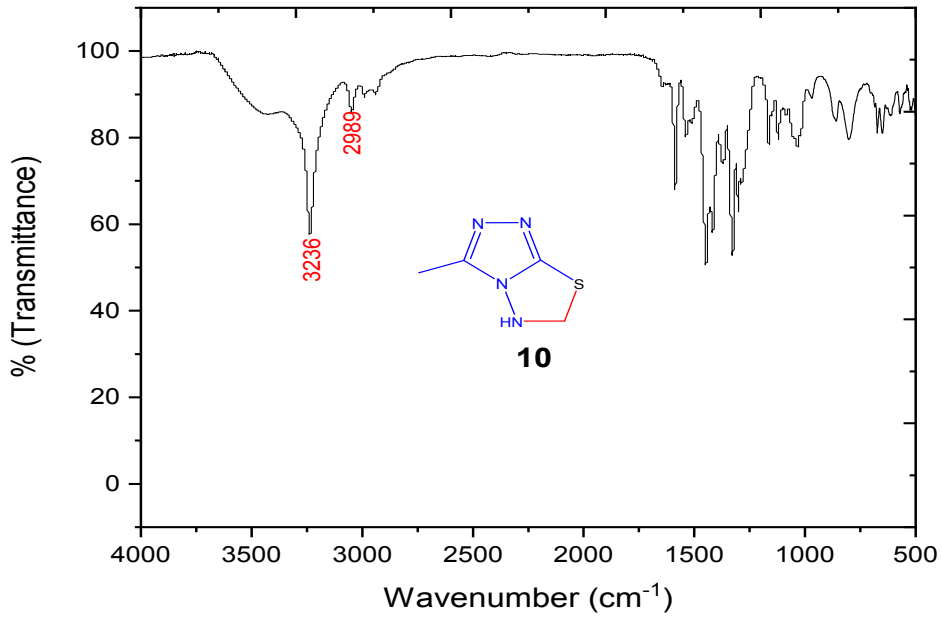
^{1}H-NMR spectrum of compound **5d** (400 MHz, DMSO-d_6).



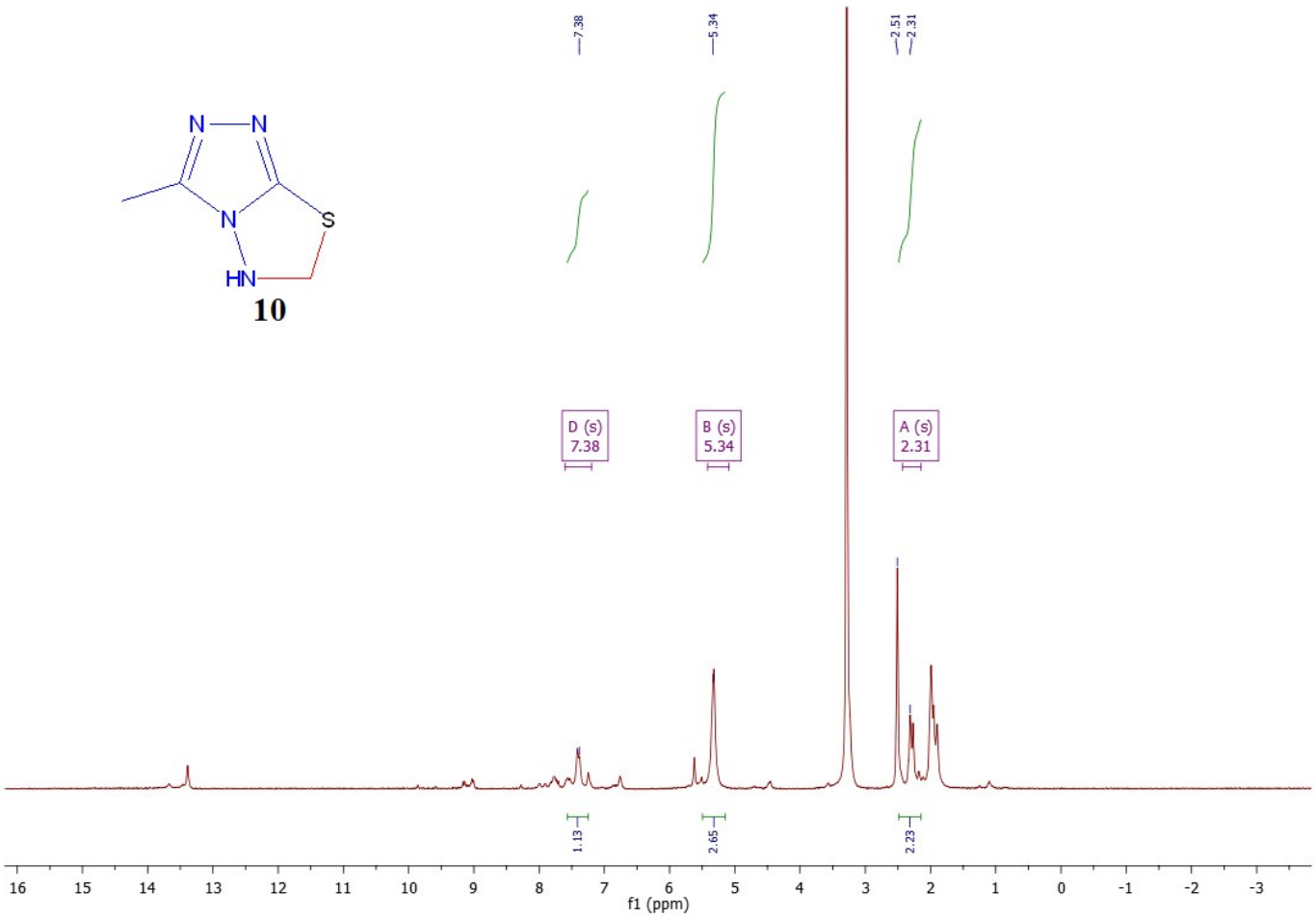
FTIR spectrum of compound **7**



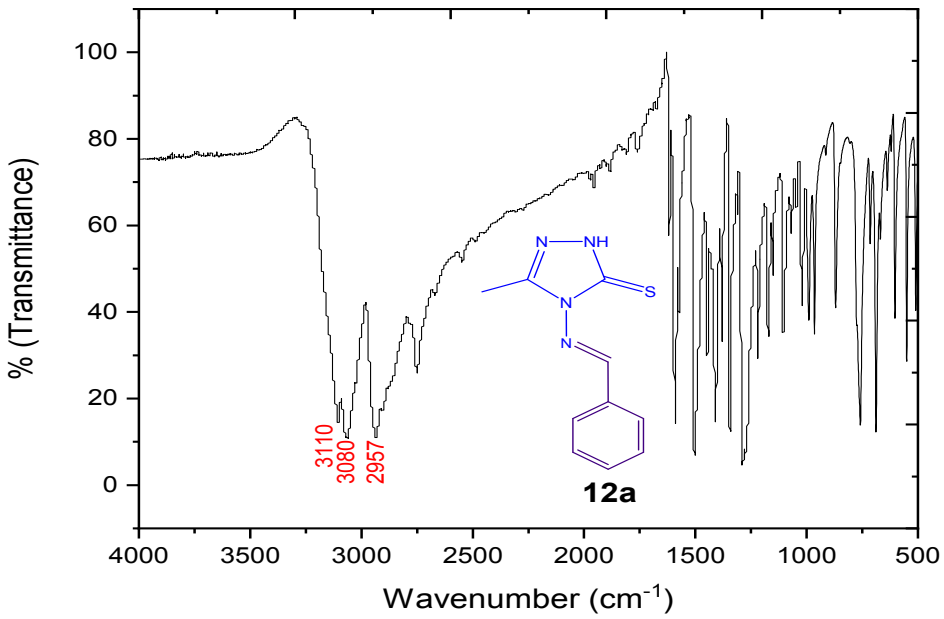
^{1}H-NMR spectrum of compound **7** (400 MHz, $CDCl_3$).



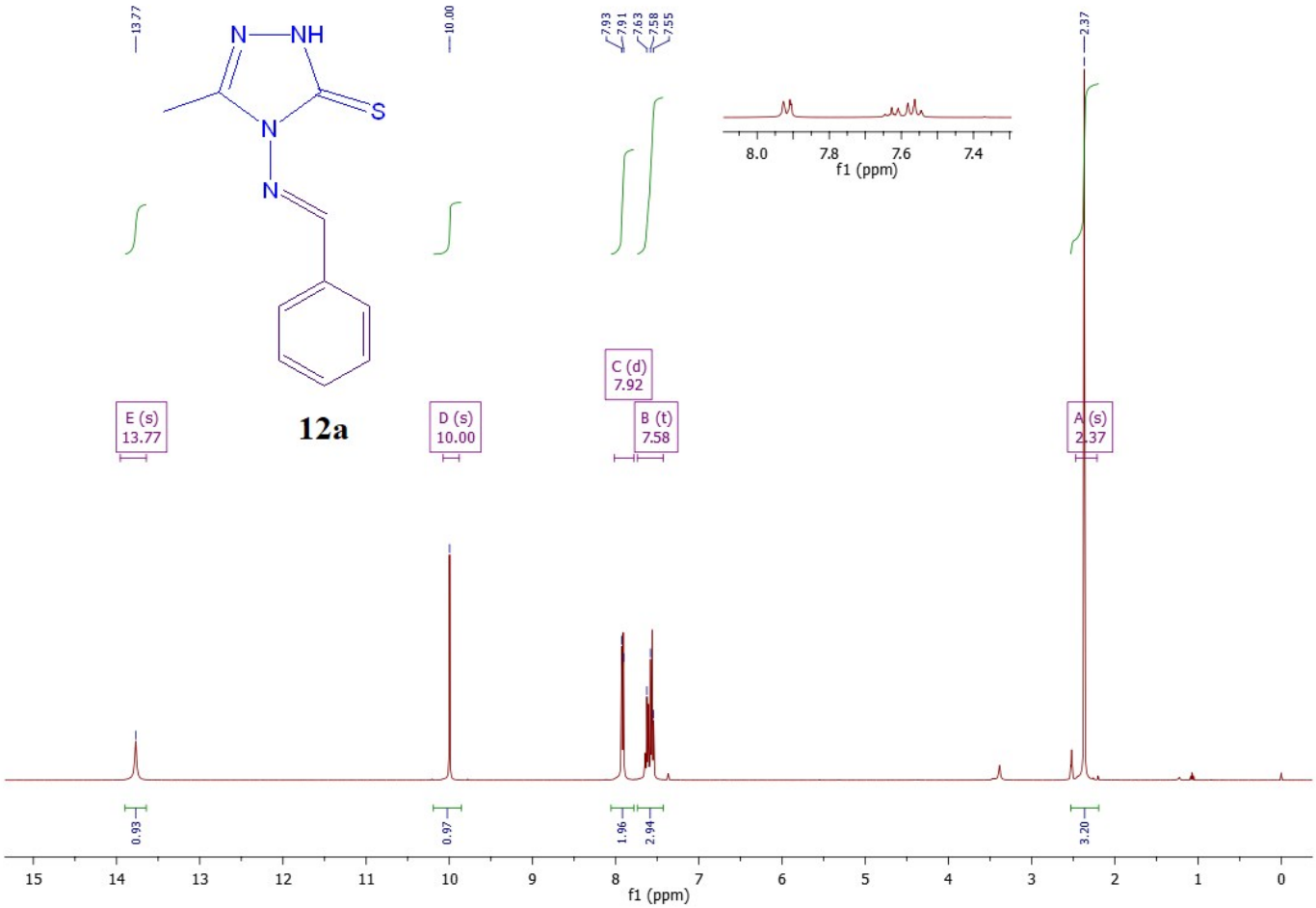
FTIR spectrum of compound **10**



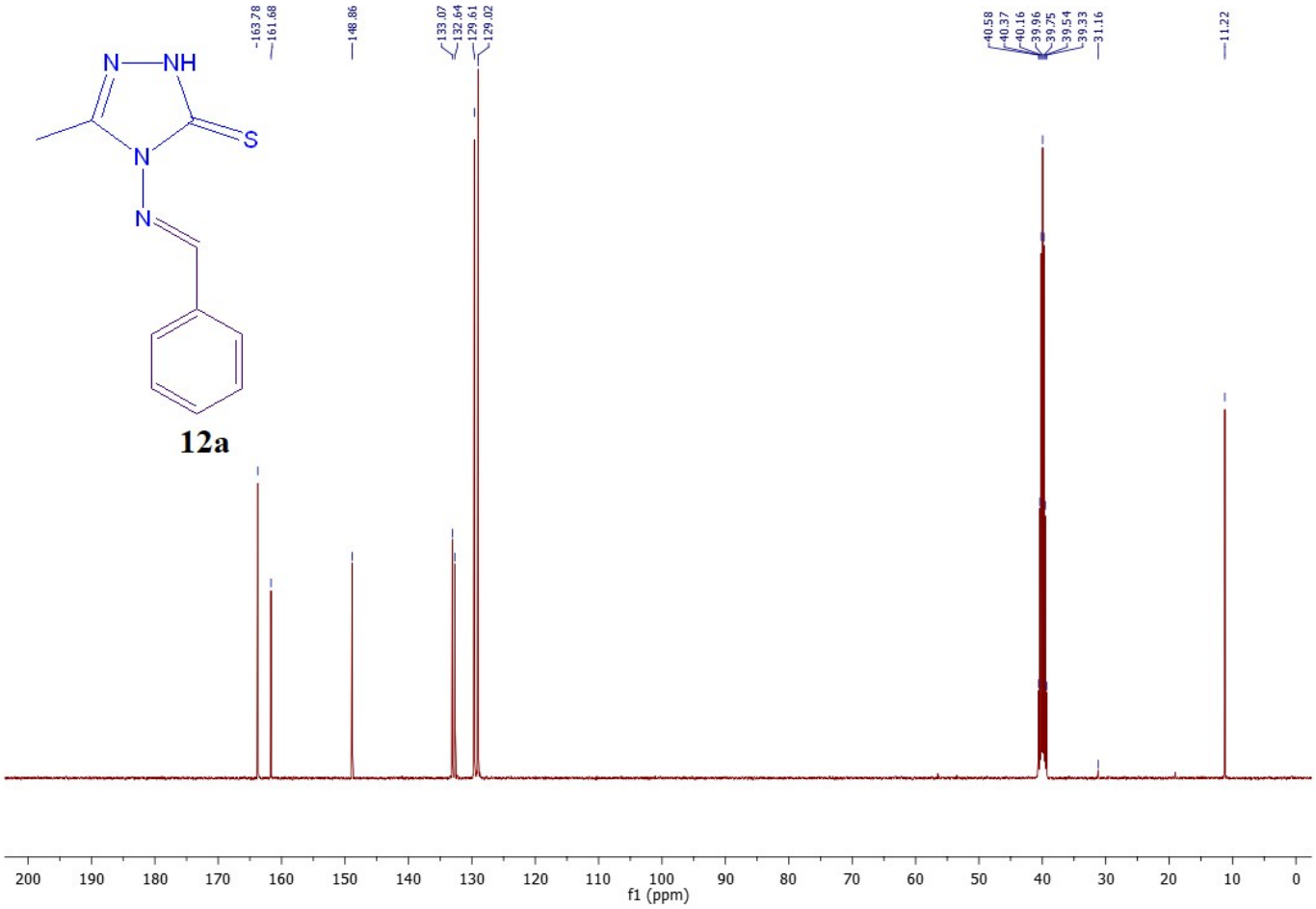
^{1}H-NMR spectrum of compound **10** (400 MHz, DMSO-d_6).



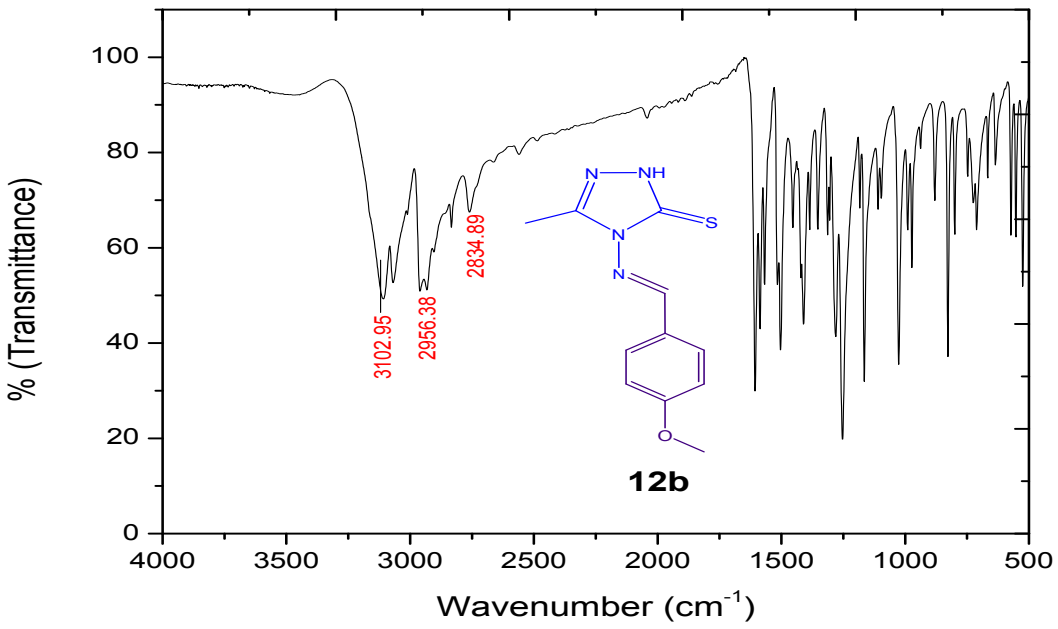
FTIR spectrum of compound **12a**



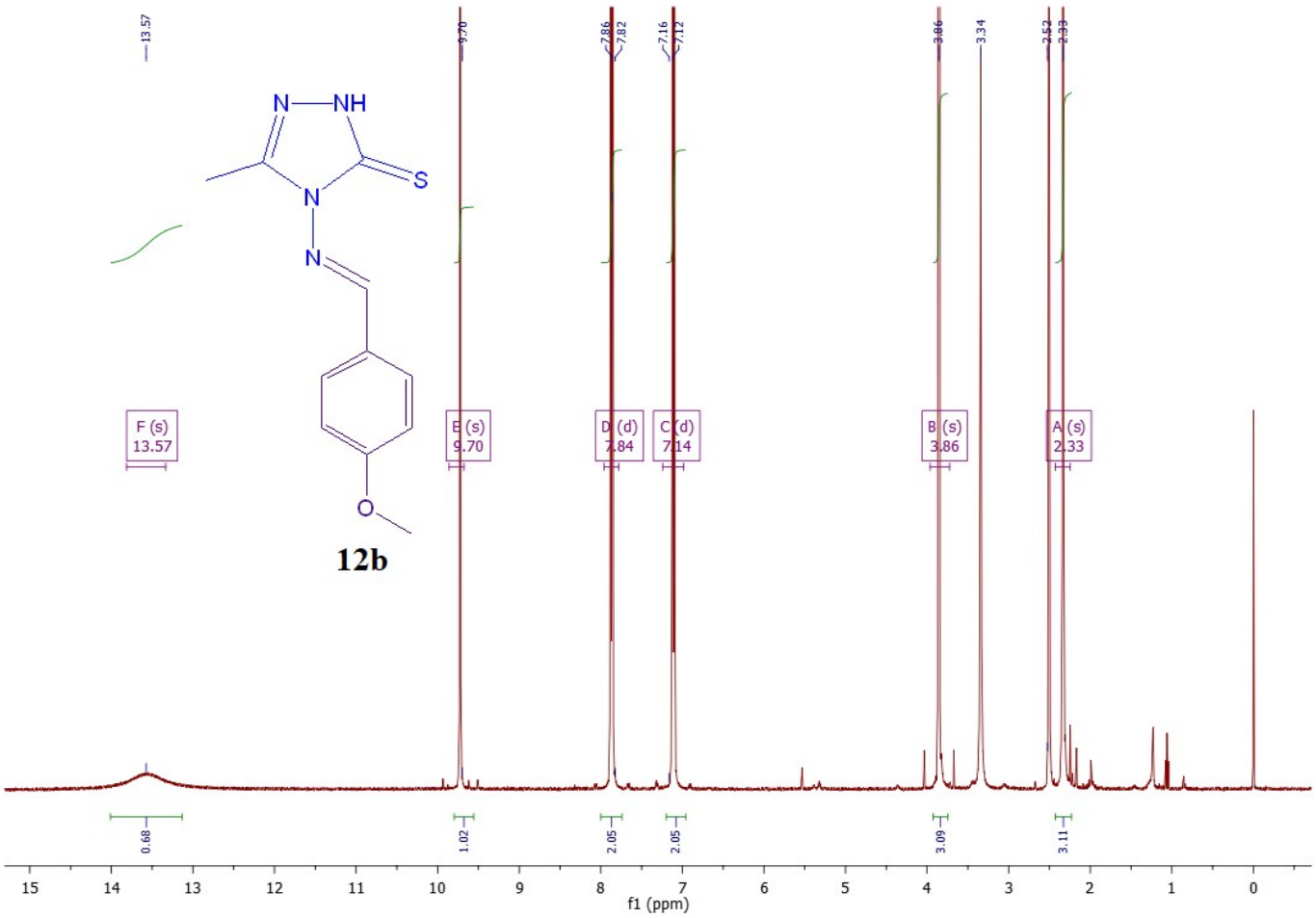
^{1}H-NMR spectrum of compound **12a** (400 MHz, DMSO-d_6).



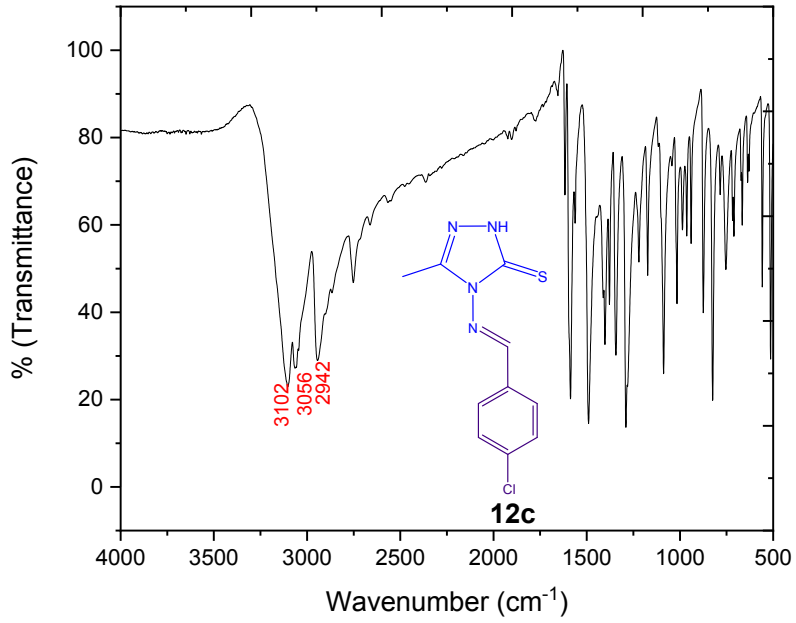
^{13}C-NMR spectrum of compound **12a** (400 MHz, DMSO-d_6).



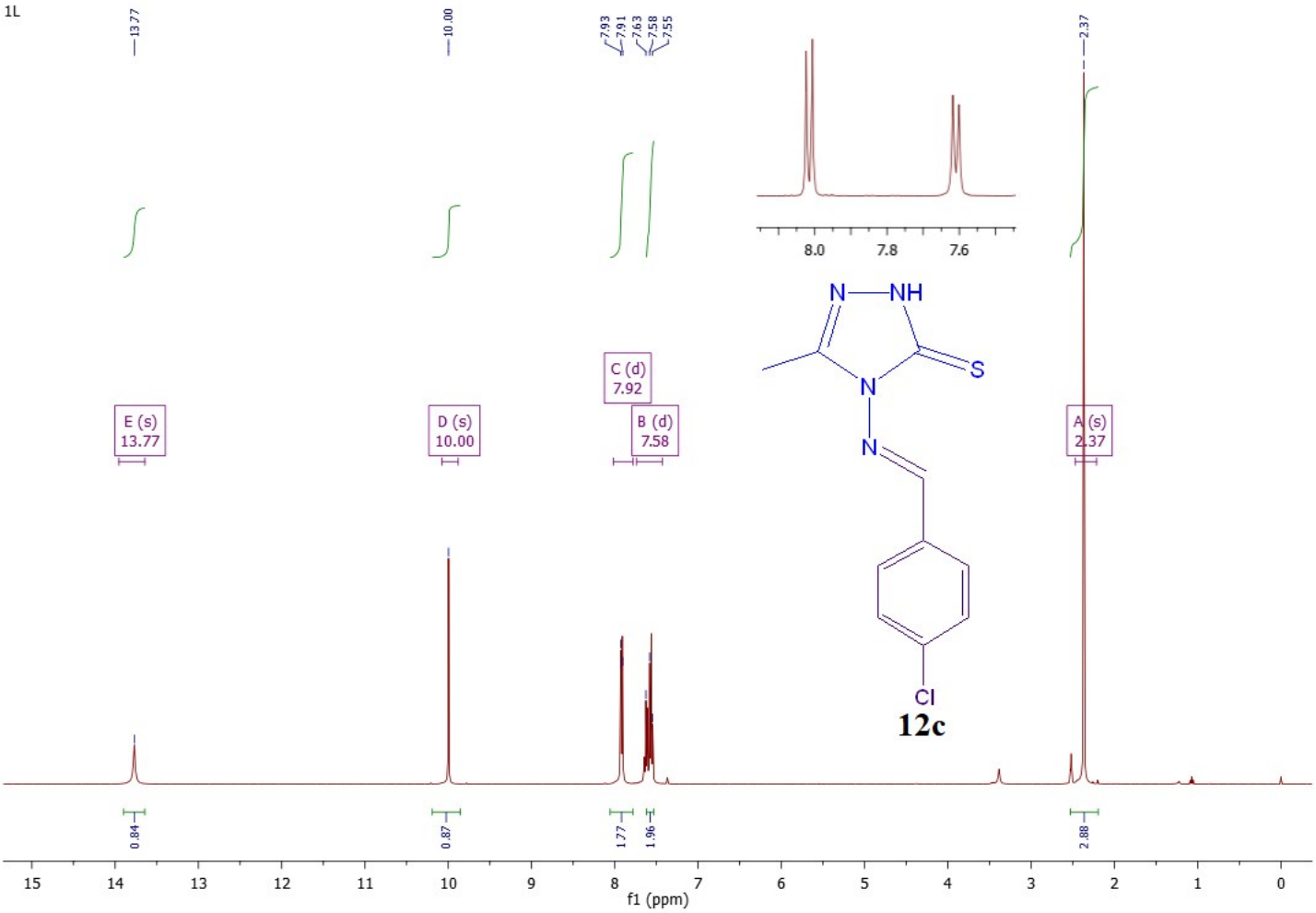
FTIR spectrum of compound **12b**



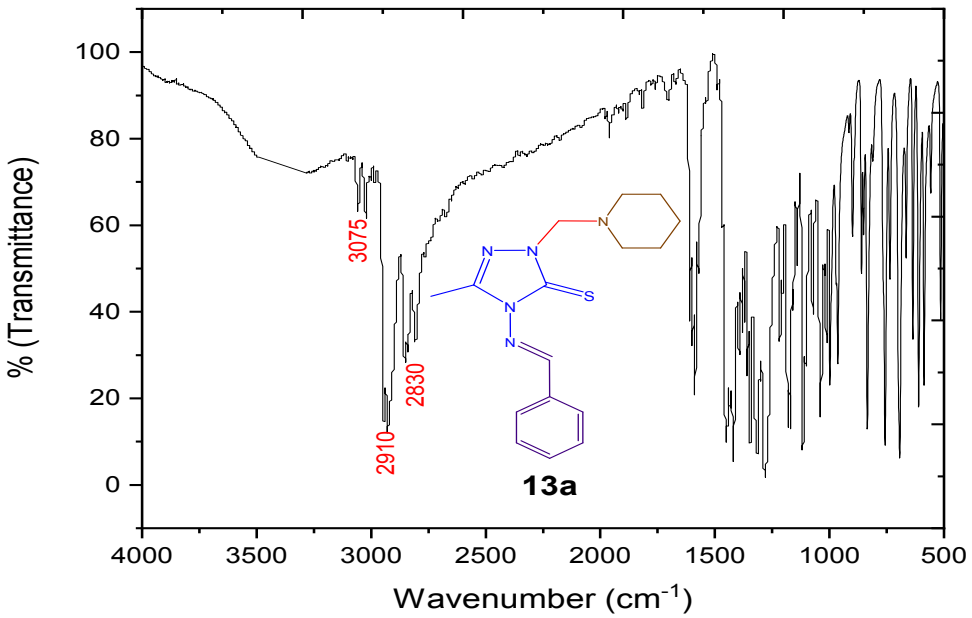
^{1}H-NMR spectrum of compound **12b** (400 MHz, DMSO-d_6).

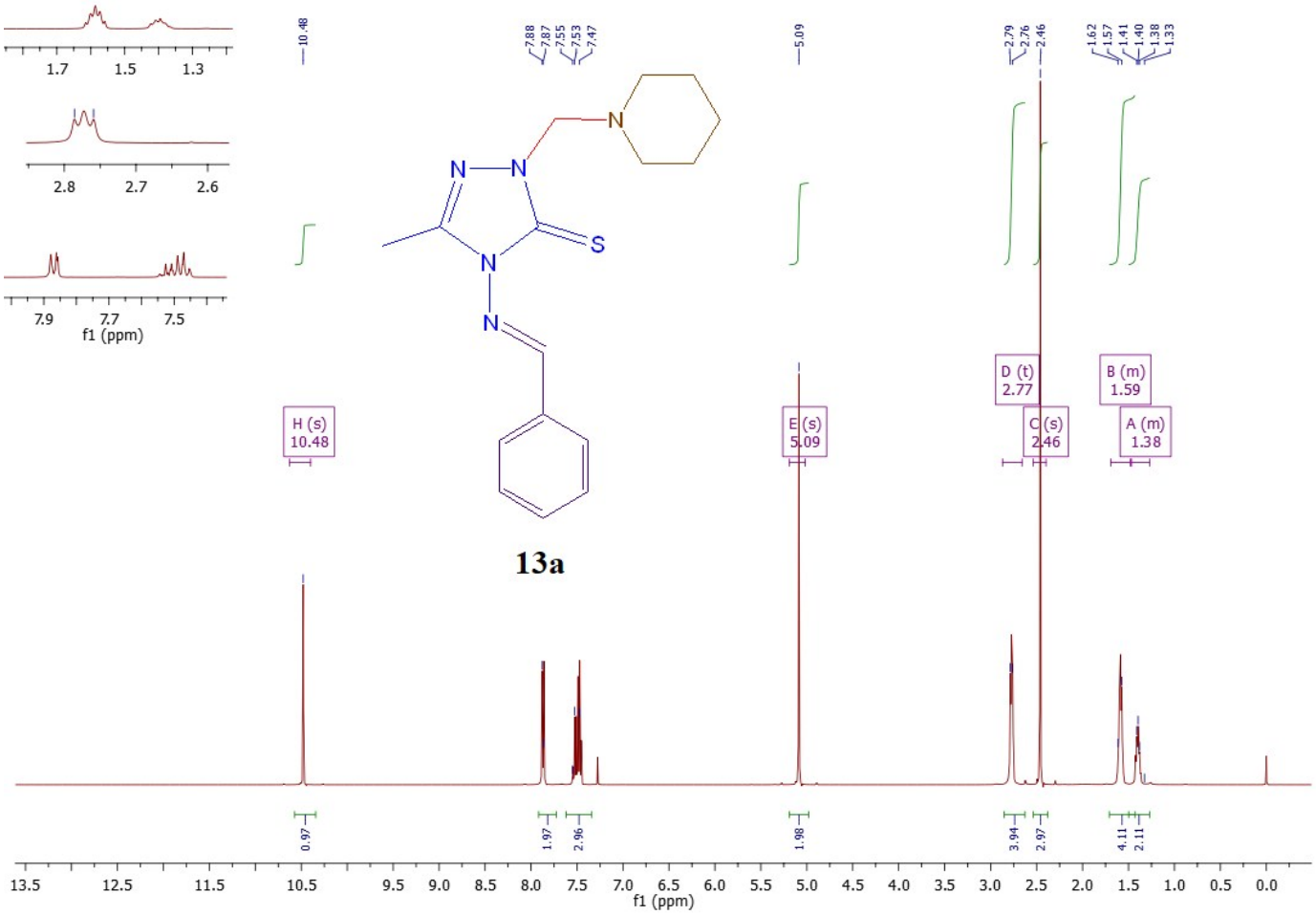


FTIR spectrum of compound **12c**

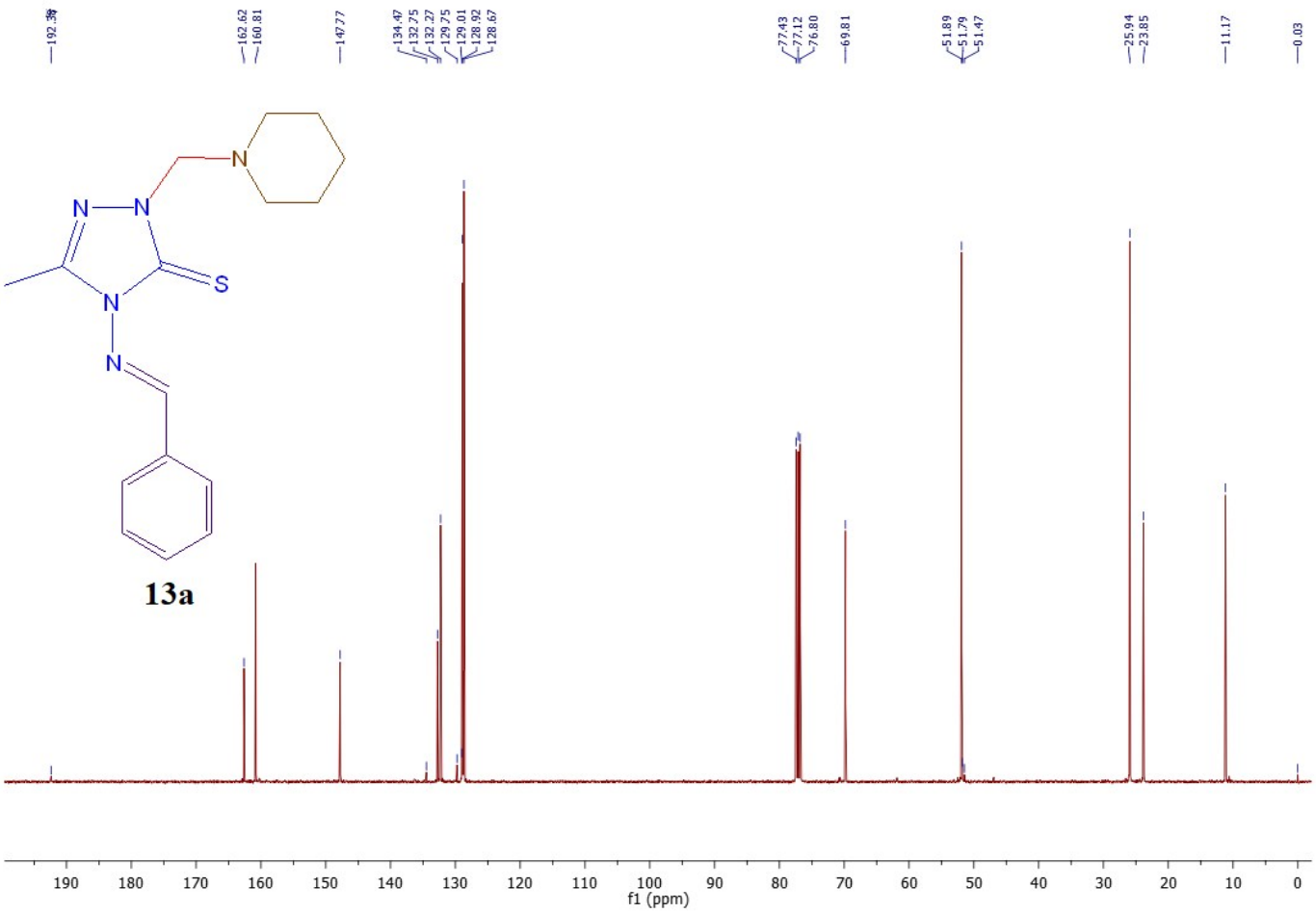


^{1}H-NMR spectrum of compound **12c** (400 MHz, DMSO-d_6).

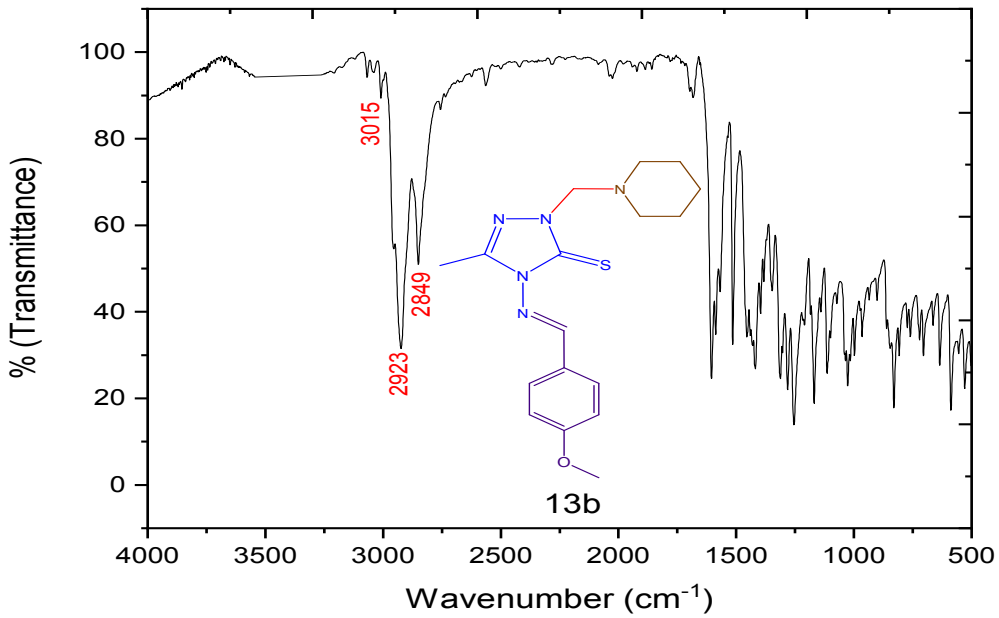




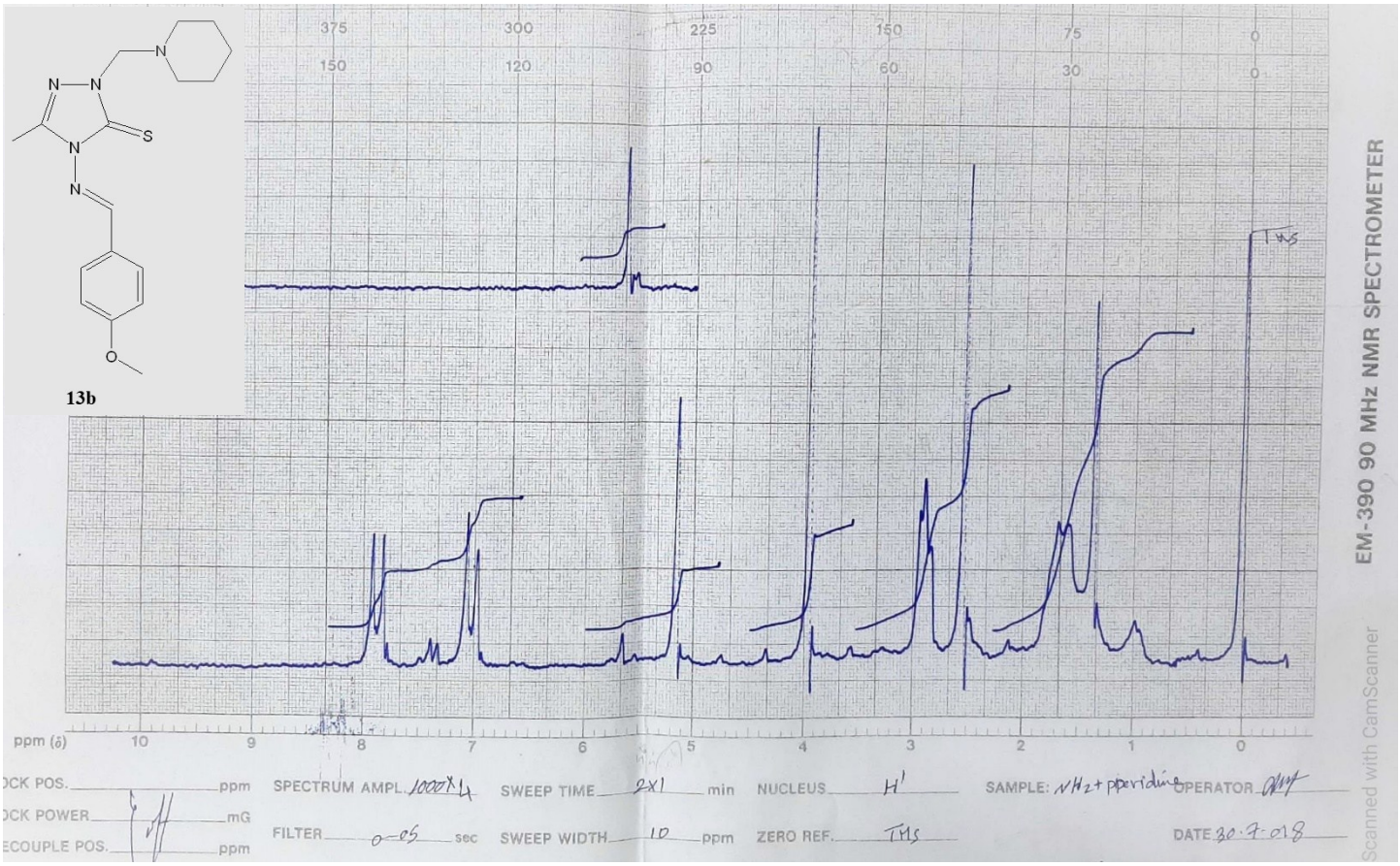
^{1}H-NMR spectrum of compound **13a** (400 MHz, $CDCl_3$).



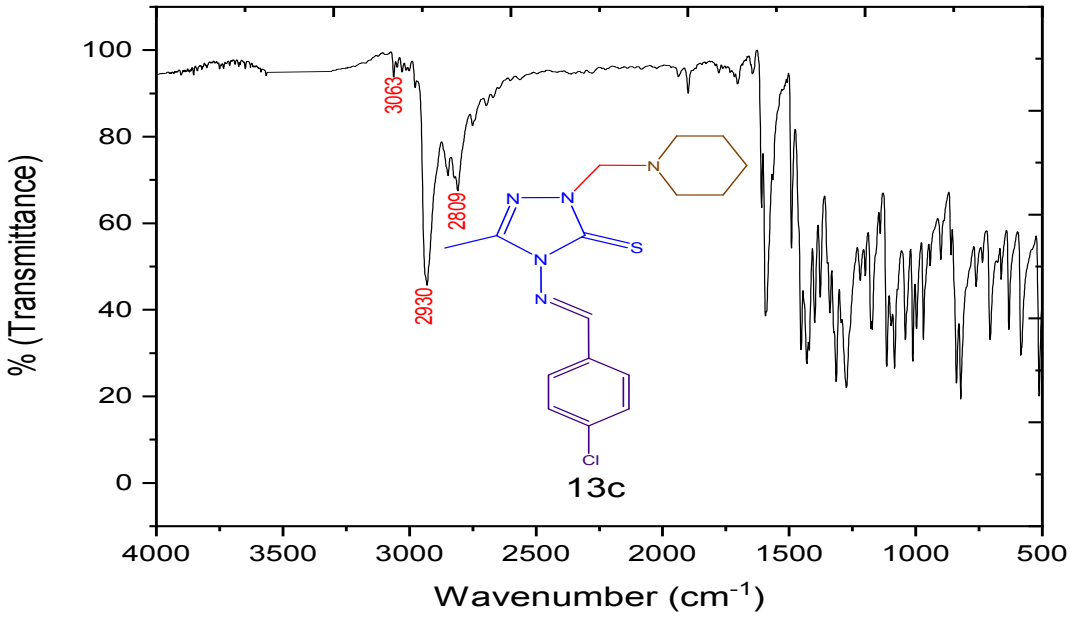
^{13}C-NMR spectrum of compound **13a** (400 MHz, $CDCl_3$).



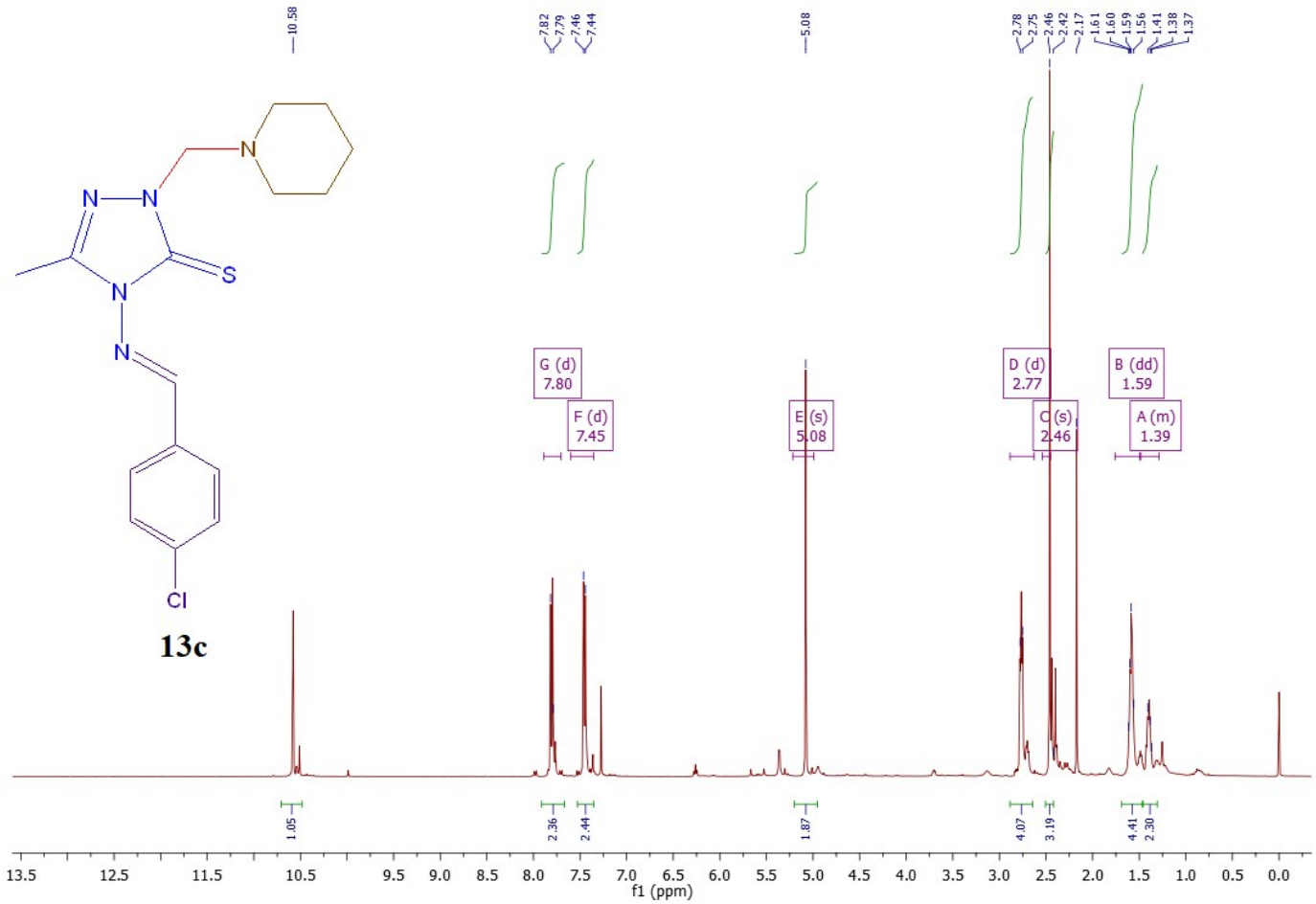
FTIR spectrum of compound **13b**



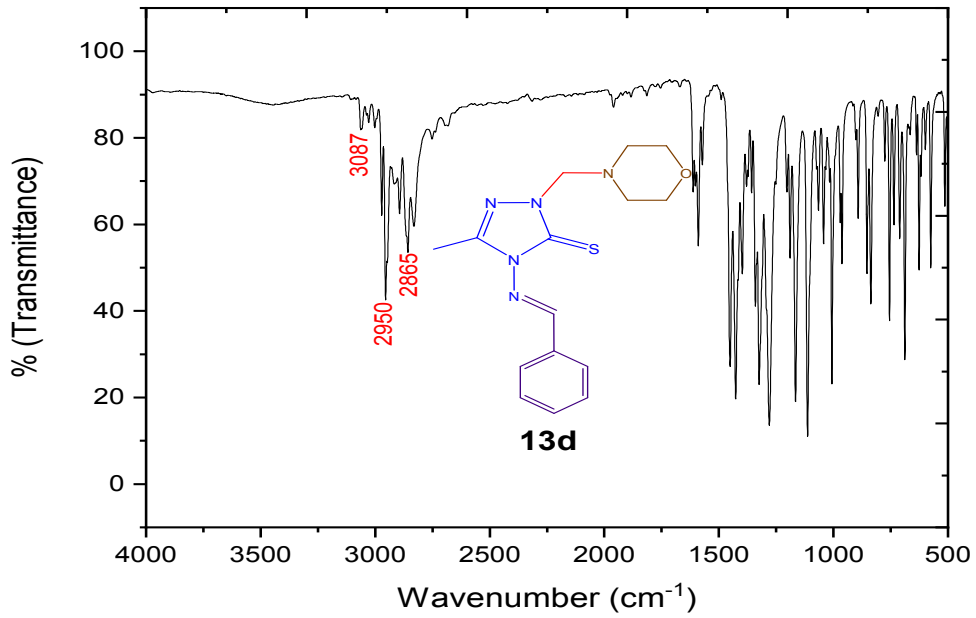
^{1}H-NMR spectrum of compound **13b** (90 MHz, $CDCl_3$).



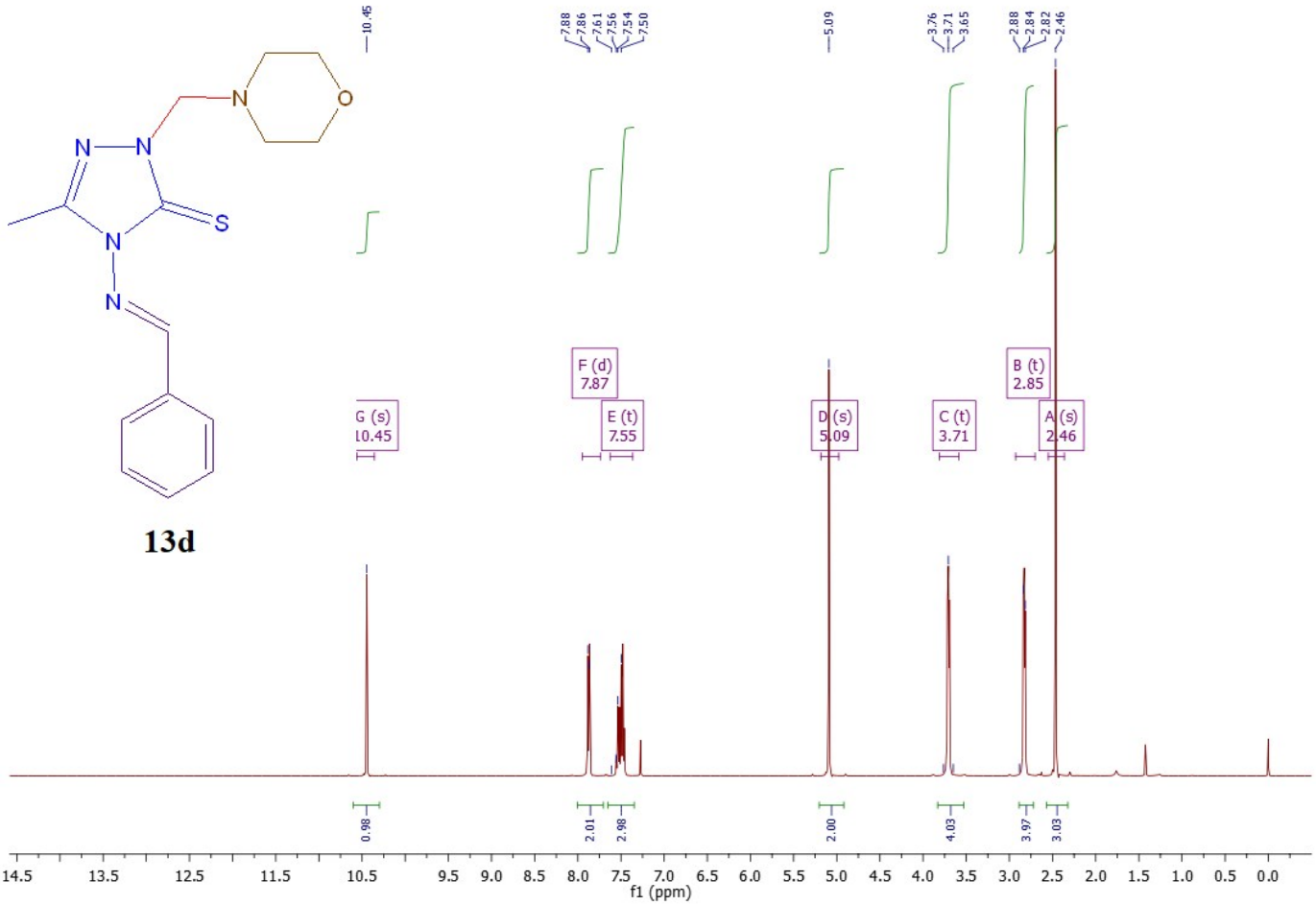
FTIR spectrum of compound **13c**



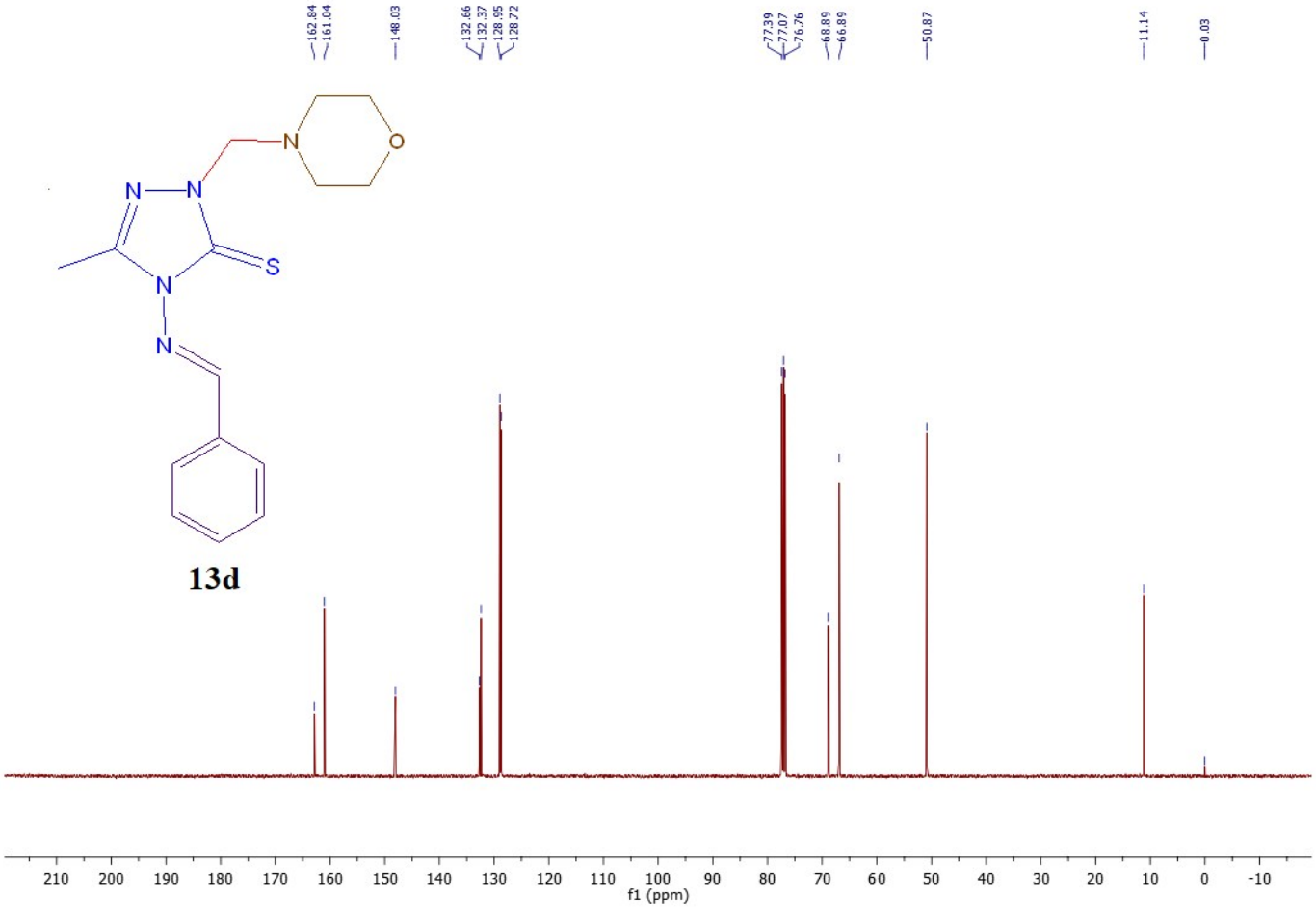
^{1}H-NMR spectrum of compound **13c** (400 MHz, $CDCl_3$).



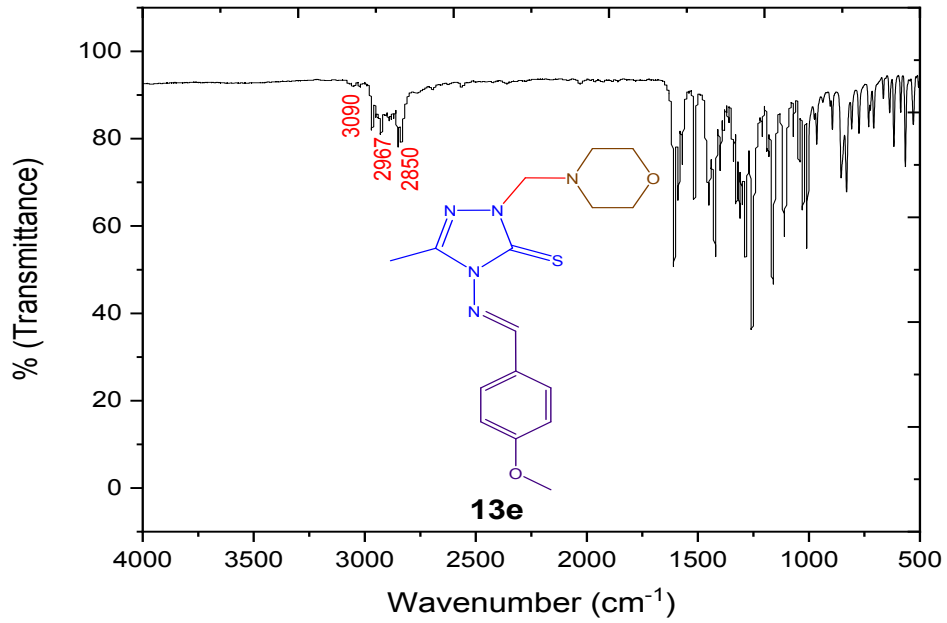
FTIR spectrum of compound **13d**



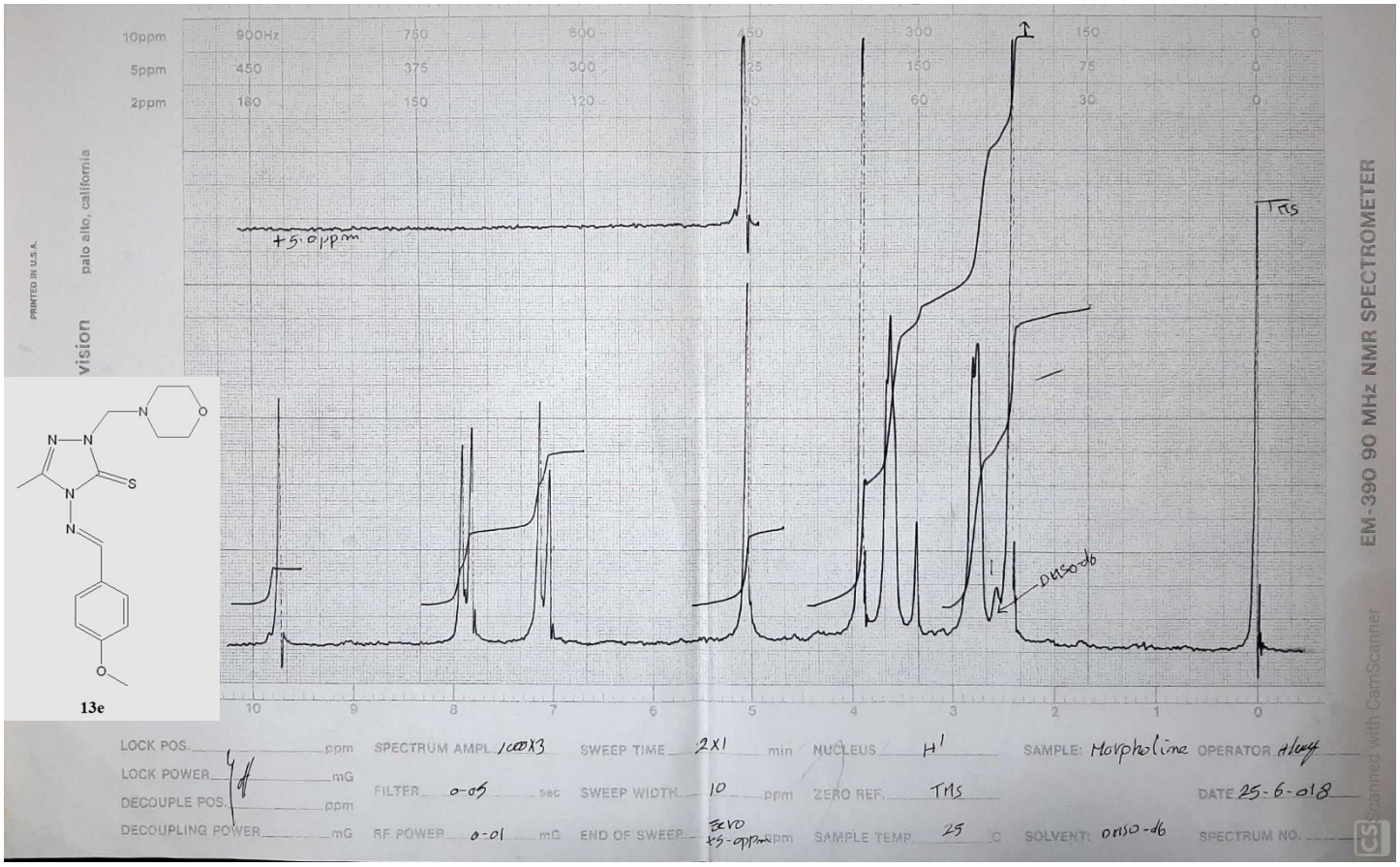
^{1}H-NMR spectrum of compound **13d** (400 MHz, $CDCl_3$).



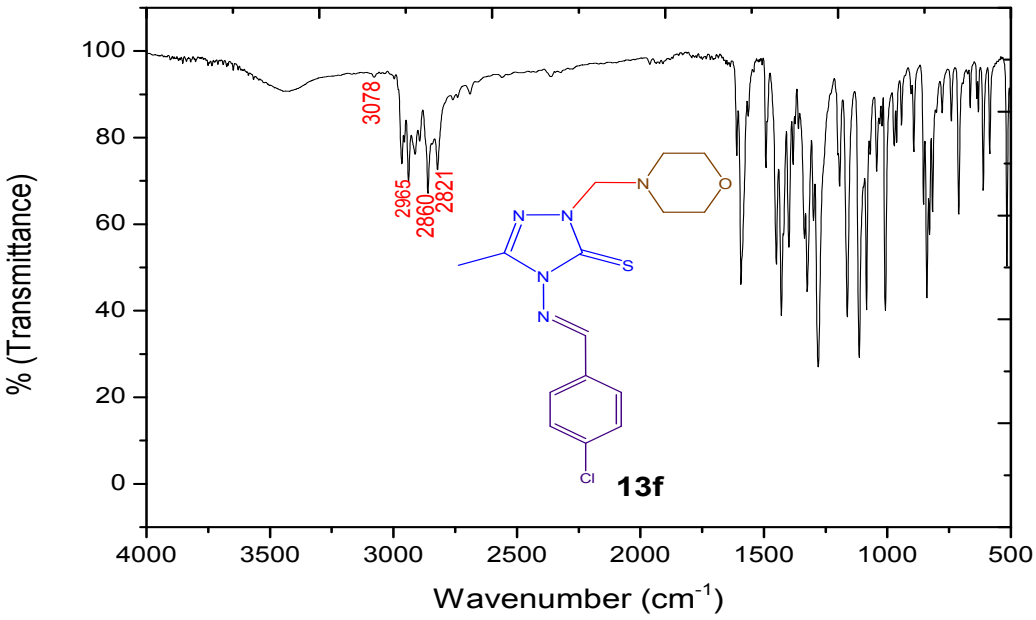
^{13}C-NMR spectrum of compound **13d** (400 MHz, $CDCl_3$).



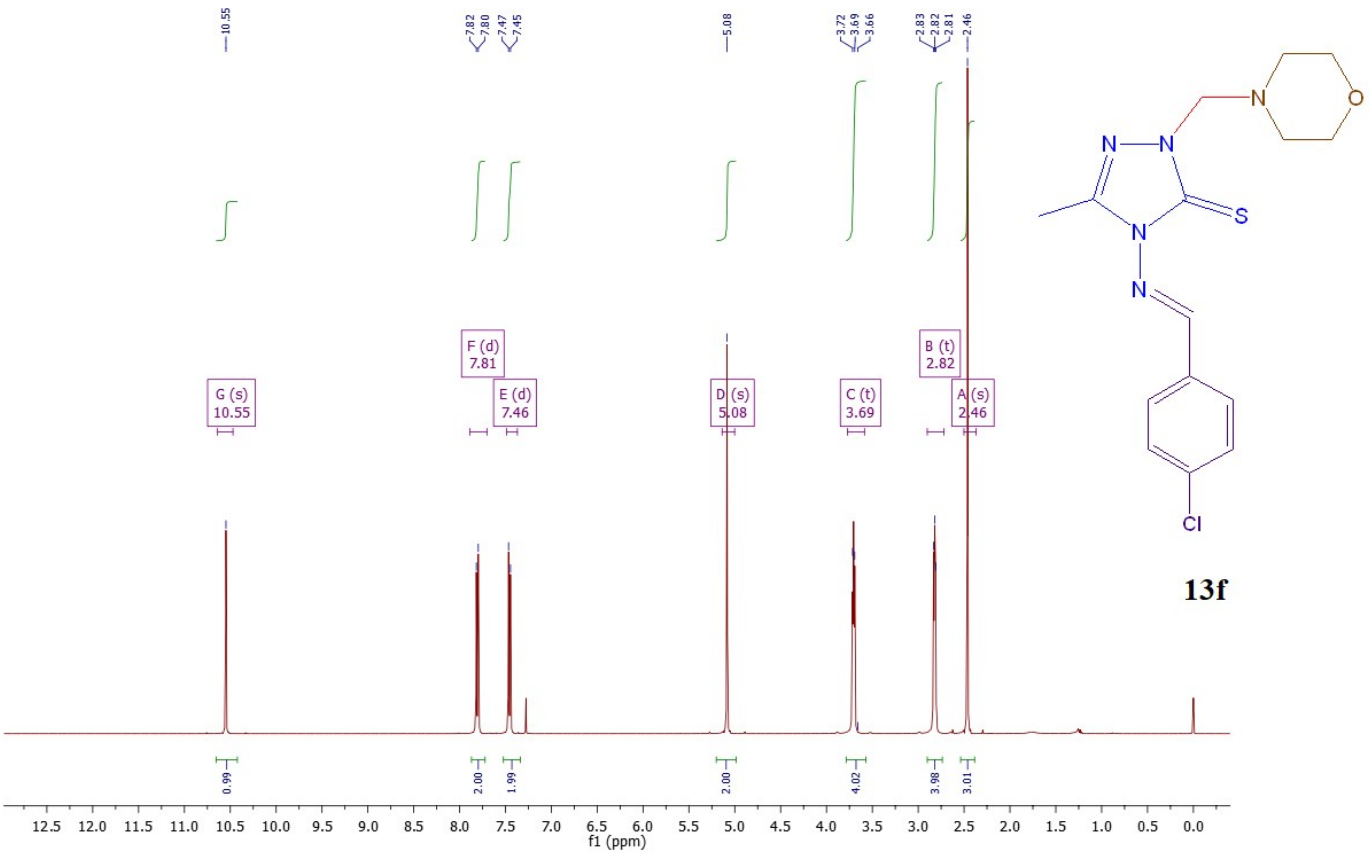
FTIR spectrum of compound **13e**



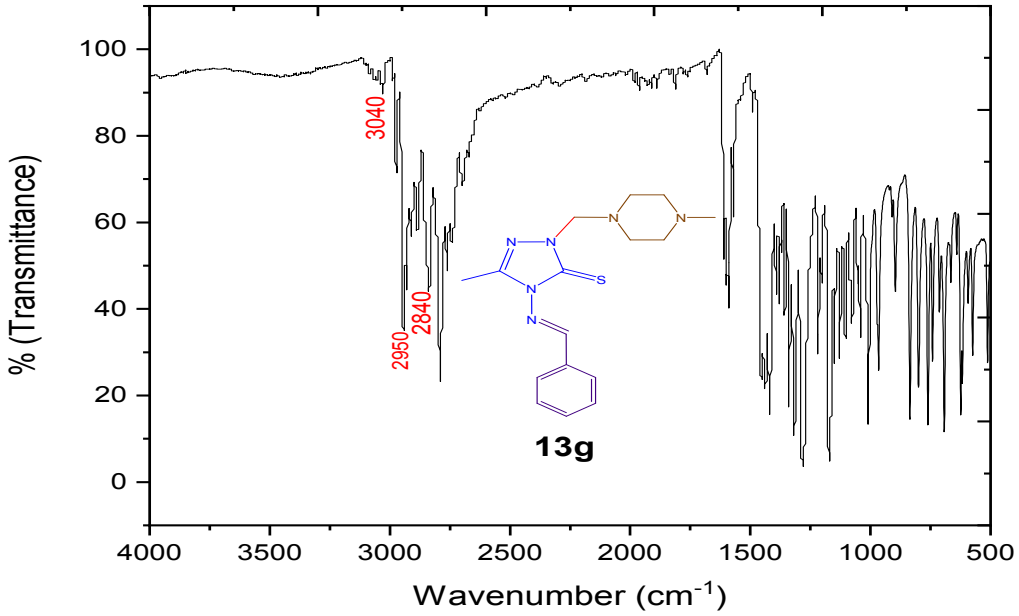
^{1}H-NMR spectrum of compound **13e** (90 MHz, DMSO-d_6).



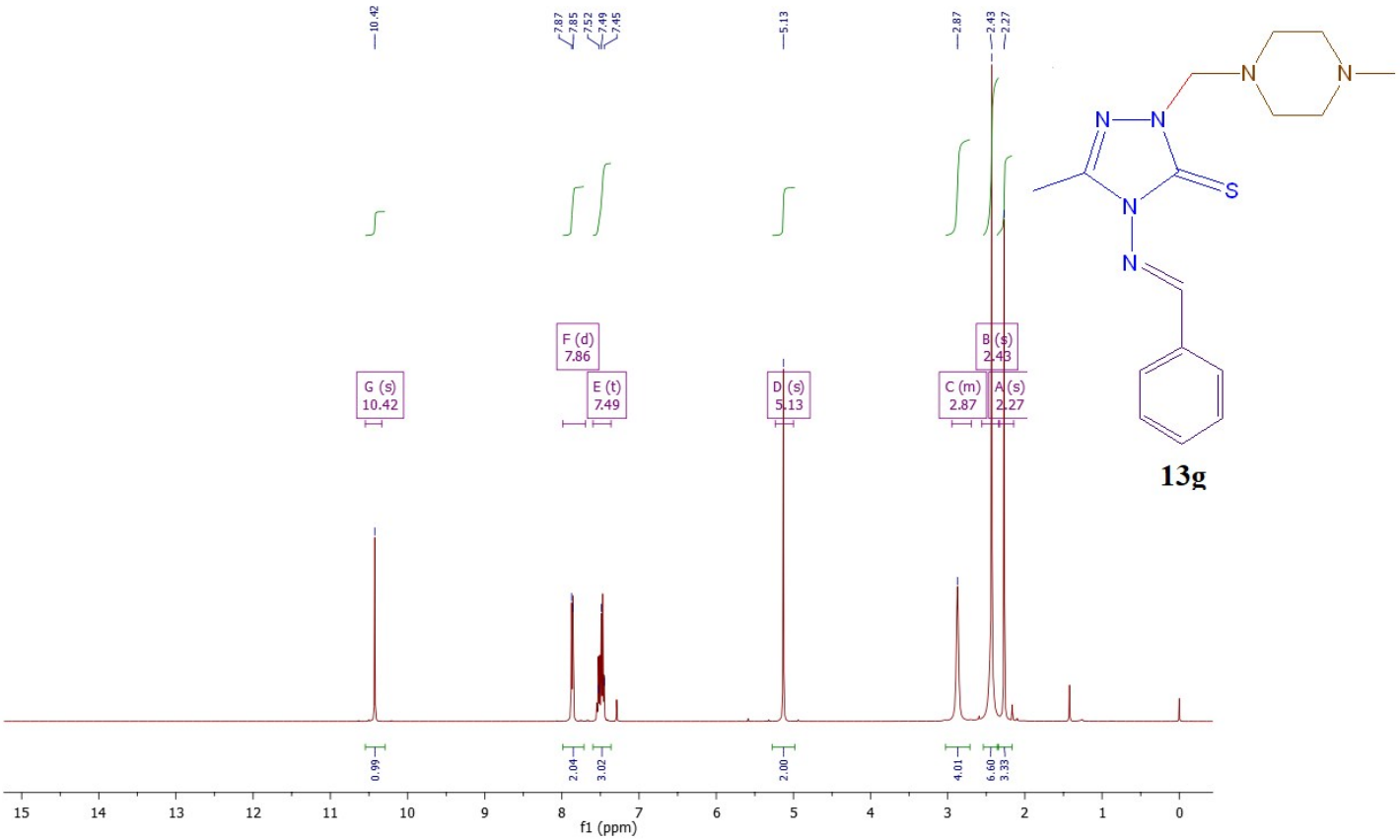
FTIR spectrum of compound **13f**



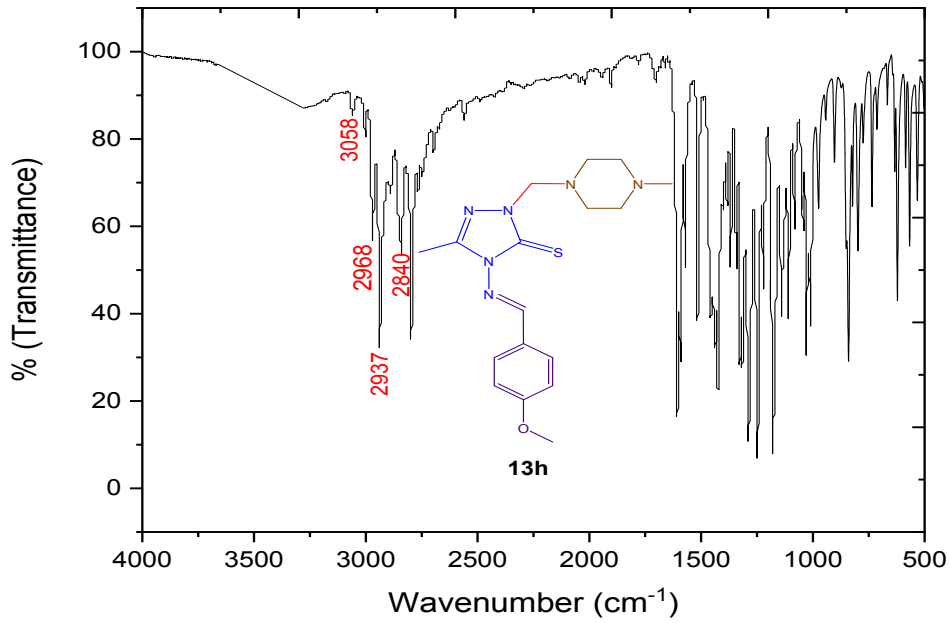
^{1}H-NMR spectrum of compound **13f** (400 MHz, $CDCl_3$).



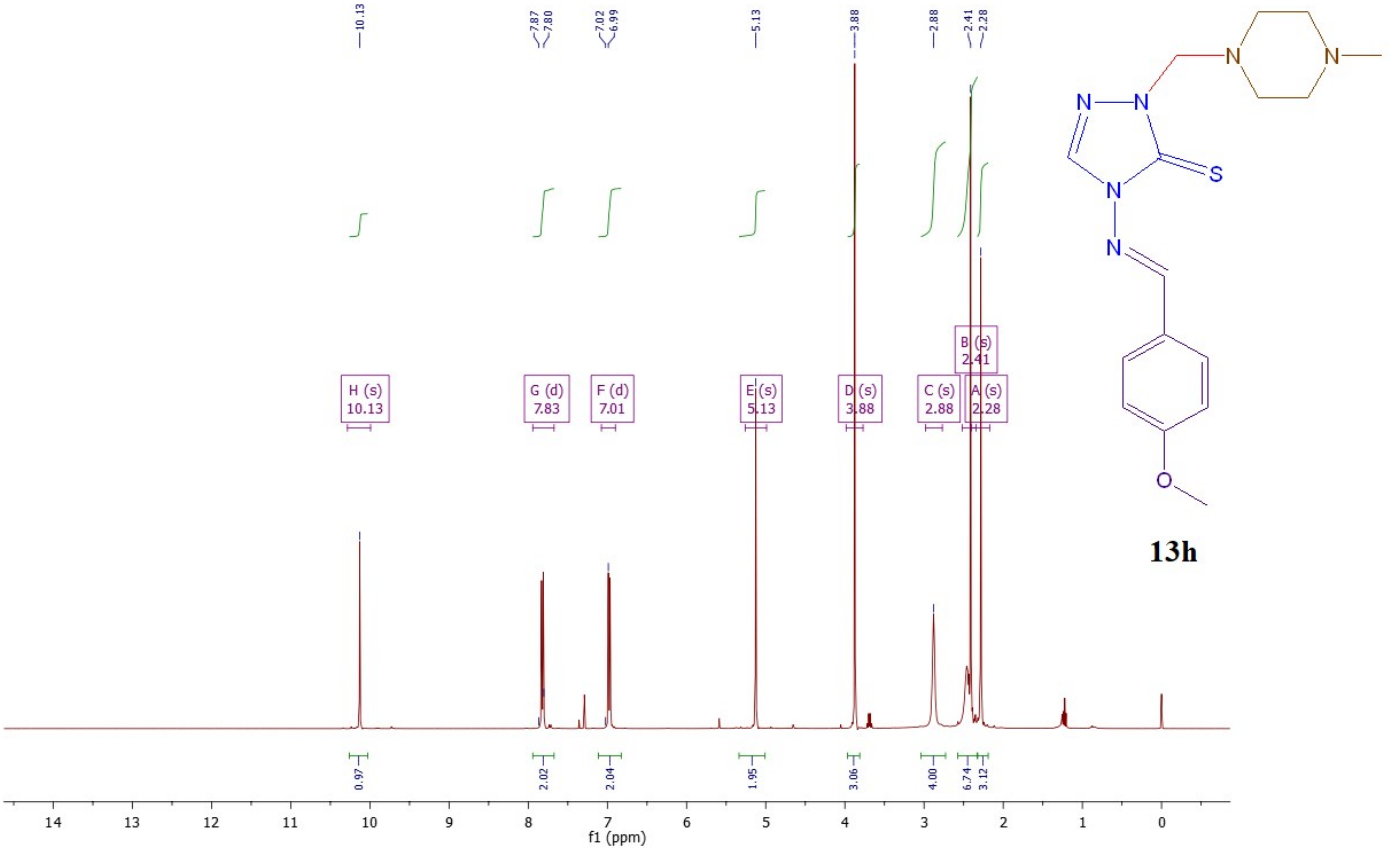
FTIR spectrum of compound **13g**



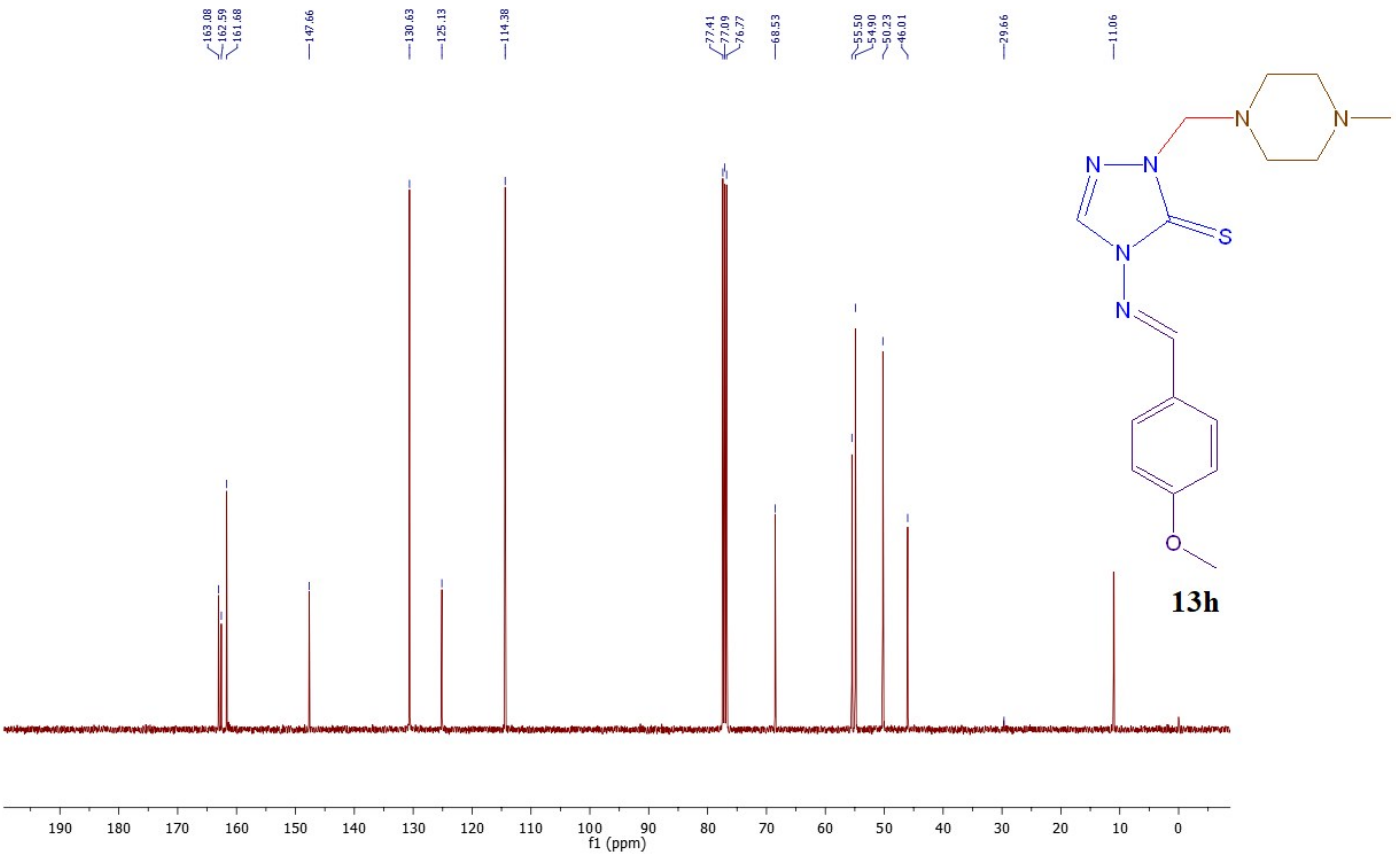
^{1}H-NMR spectrum of compound **13g** (400 MHz, $CDCl_3$).



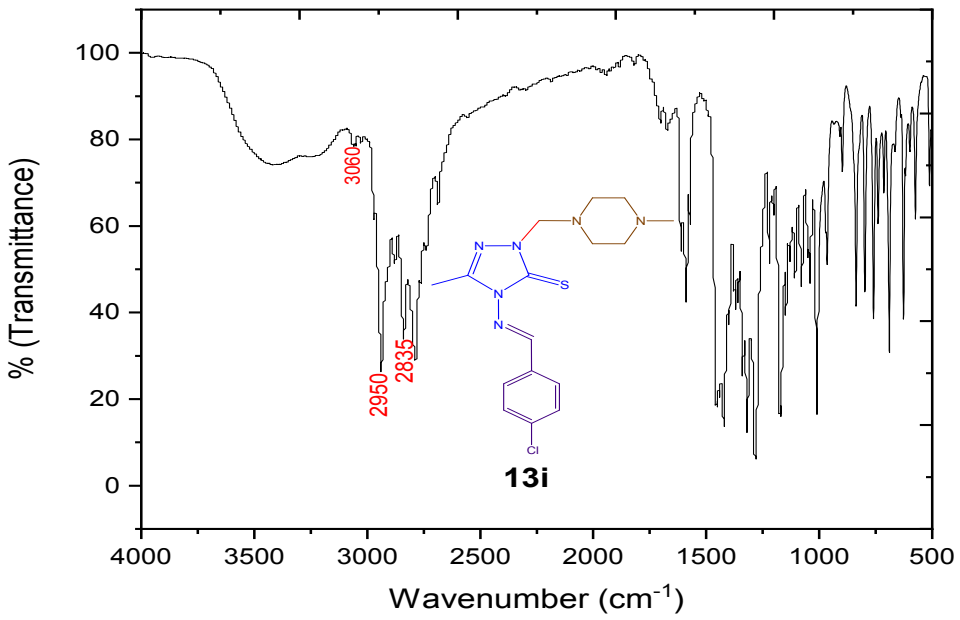
FTIR spectrum of compound **13h**

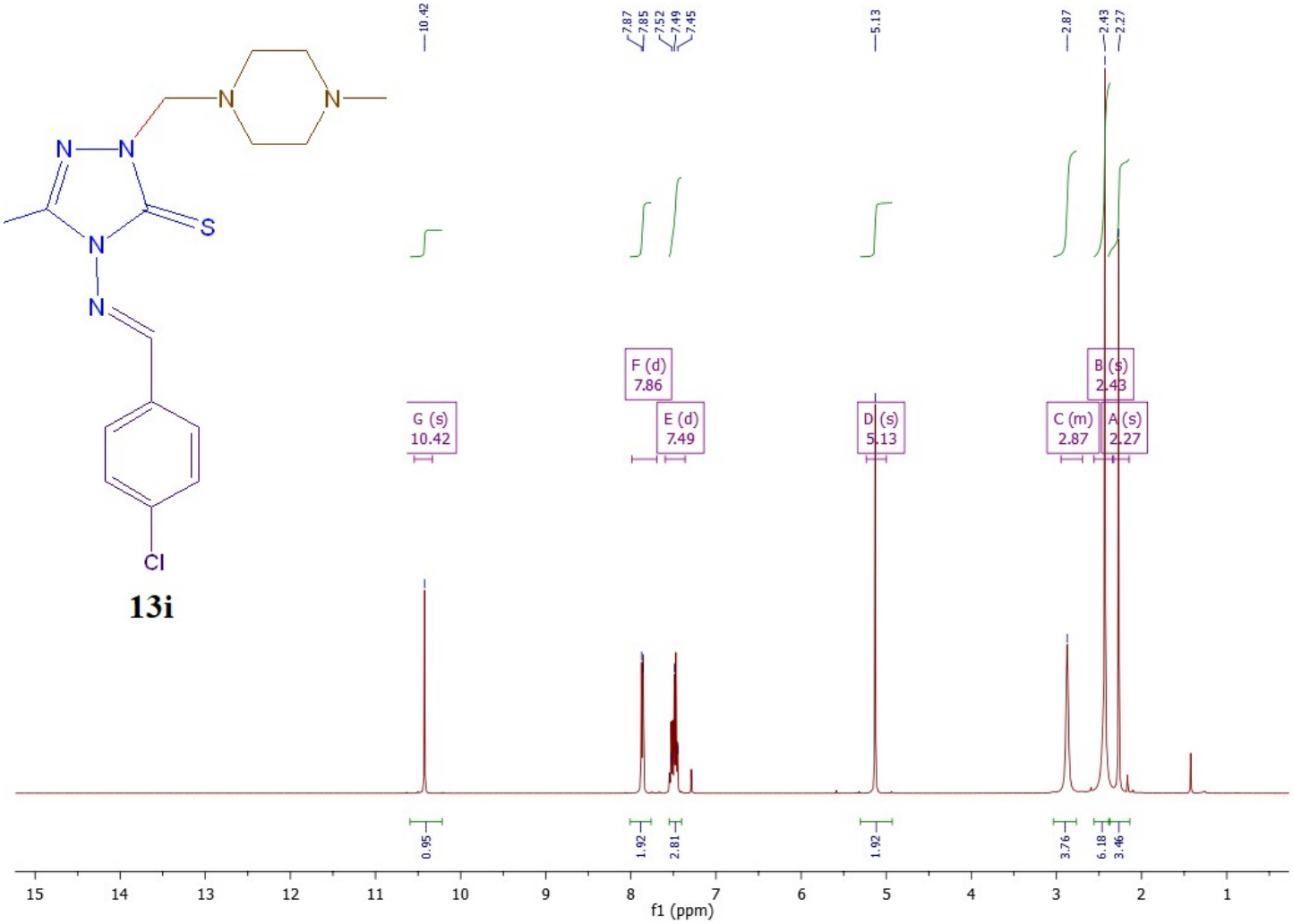


^{1}H-NMR spectrum of compound **13h** (400 MHz, $CDCl_3$).

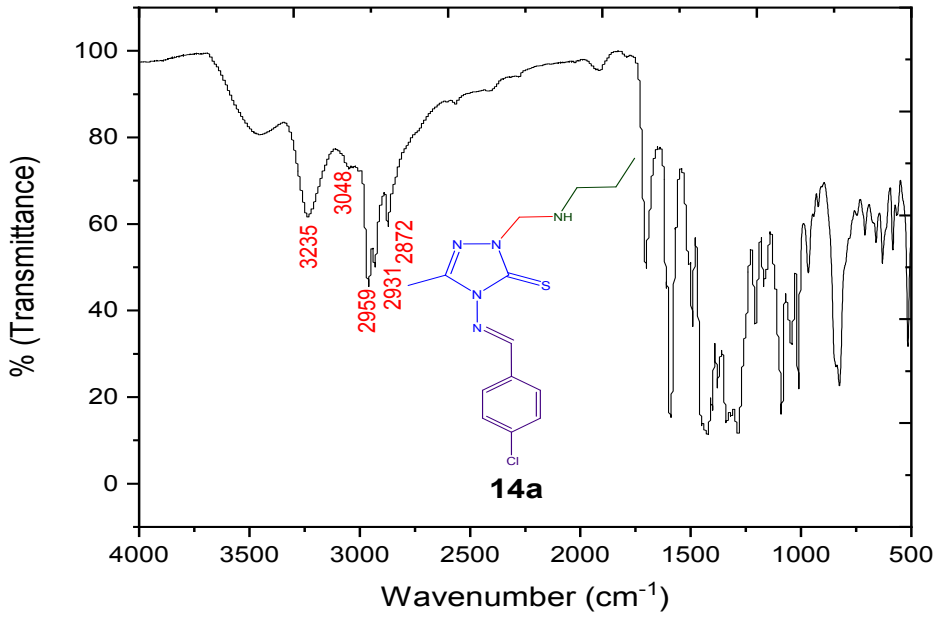


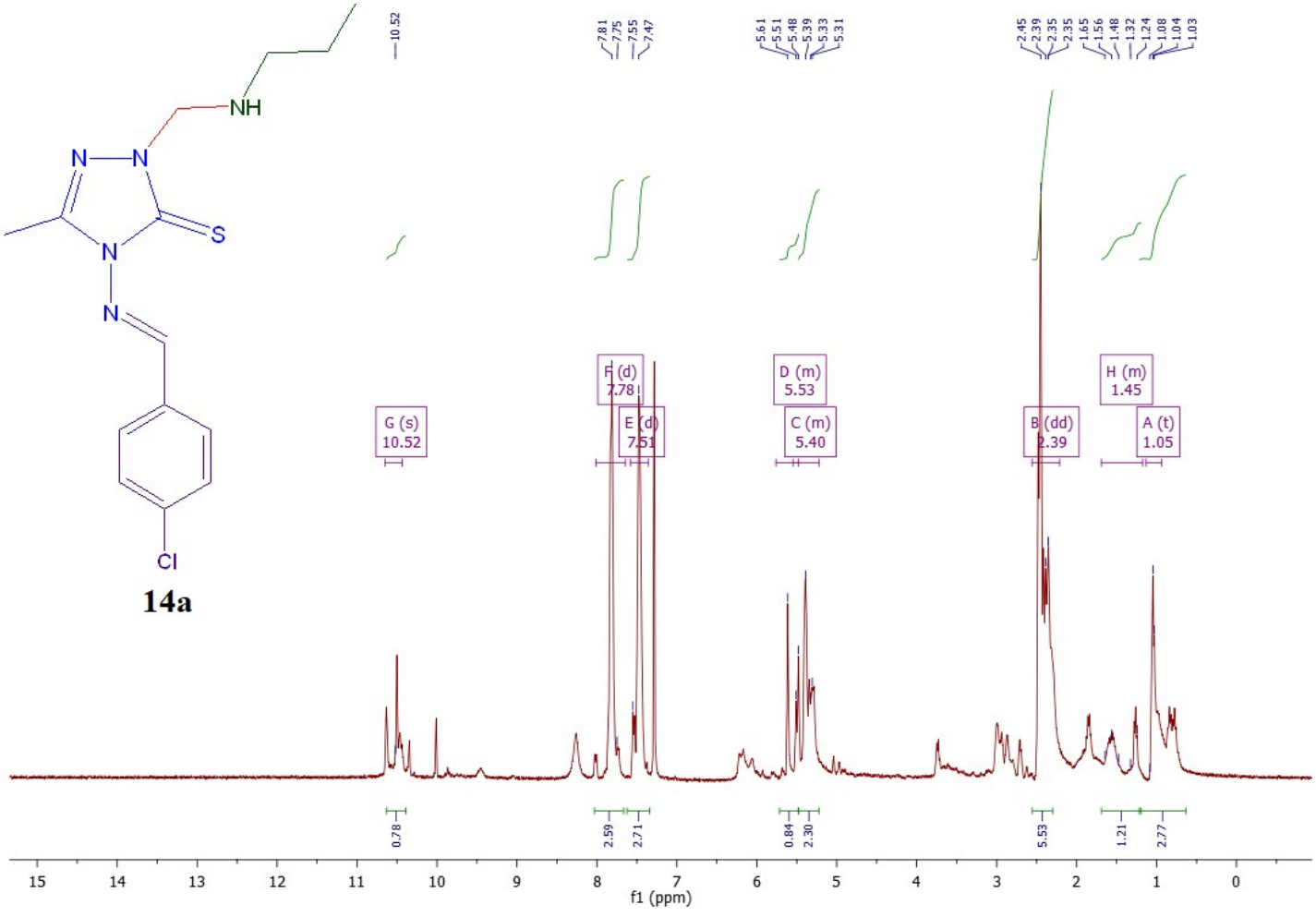
^{13}C-NMR spectrum of compound **13h** (400 MHz, $CDCl_3$).



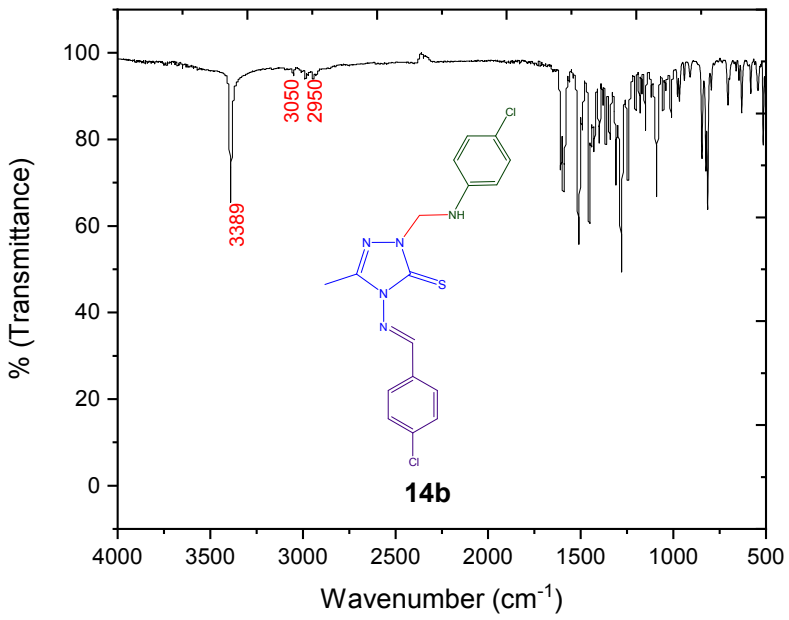


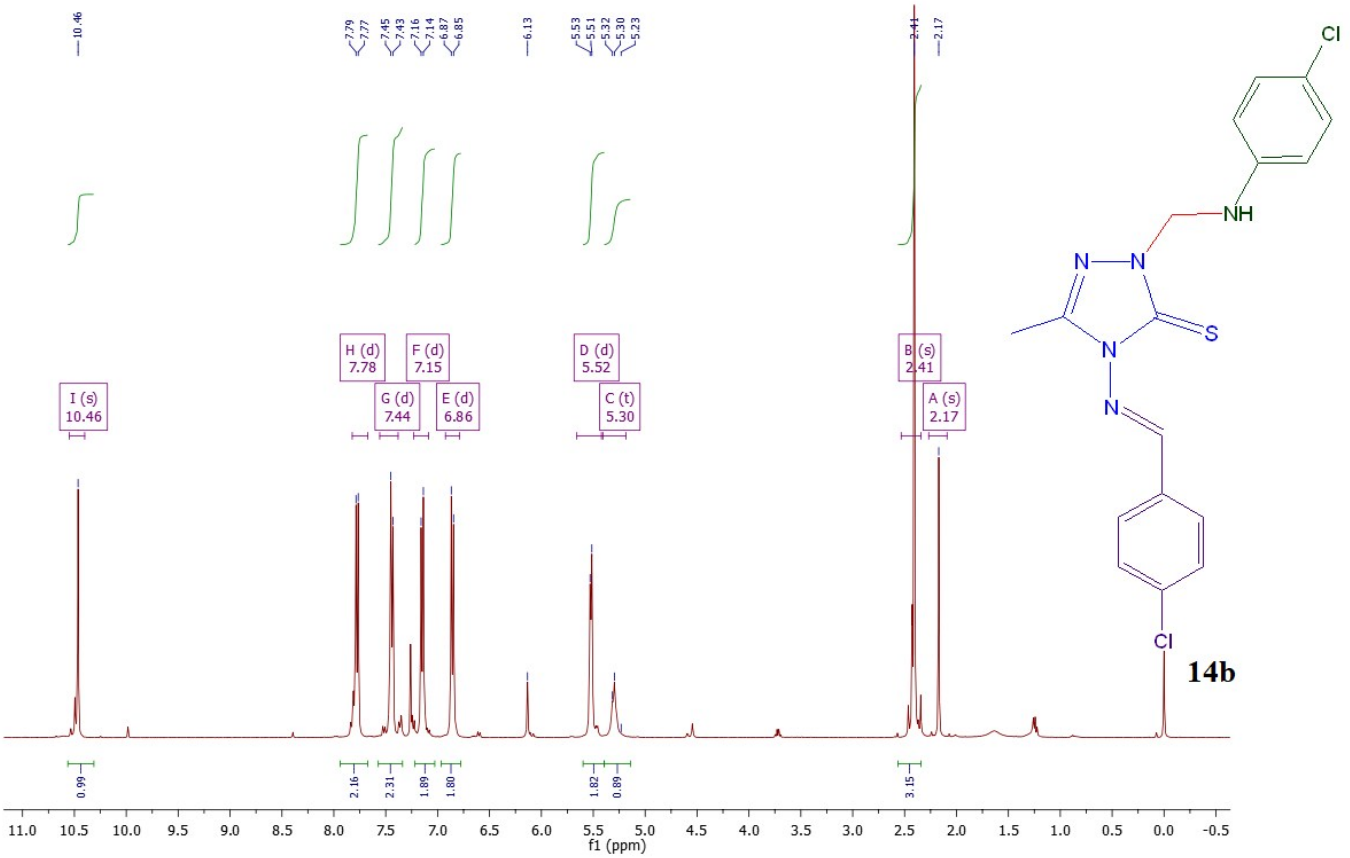
^{1}H-NMR spectrum of compound **13i** (400 MHz, $CDCl_3$).





^{1}H-NMR spectrum of compound **14a** (400 MHz, $CDCl_3$).





^{1}H-NMR spectrum of compound **14b** (400 MHz, $CDCl_3$).

S6. references

S1. R. M.Shaker and A.A. Aly, Recent trends in the chemistry of 4-amino-1,2,4-triazole-3-thiones. Phosphorus, Sulfur, and Silicon and the Related Elements, 2006, 181(11), 2577-2613.

S2. P. D. R. Kumari, J. Nayak and A.N. Shetty, 3-Methyl-4-amino-5-mercapto-1,2,4-triazole as corrosion inhibitor for 6061/Al-15(Vol-%) Sic (p) composite on 0.5M sodium hydroxide solution. Journal of Materials and Environmental Science, 2011, 2, 387-402.

S3. S. Magaldi, S. Mata-Essayag, C. H. D. Capriles, C. Perez, M. T. Colella, C. Olaizola and Y. Ontiveros, Well diffusion for antifungal susceptibility testing. International Journal of Infectious Diseases, 2004, 8(1), 39-45.

S4. A. A. Markeb, A. Alonso, A. Sánchez and X Font. Adsorption process of fluoride from drinking water with magnetic core-shell Ce-Ti@Fe3O4 and Ce-Ti oxide nanoparticles. Science of The Total EnvFTIRonment, 2017, 598, 949-958.

S5. A. A. Markeb, L. A. Ordosgoitia, A. Alonso, A. Sanchez and X. Font, Novel magnetic core–shell Ce–Ti@Fe3O4 nanoparticles as an adsorbent for water contaminants removal. RSC Adv., 2016, 6(62), 56913-56917.

S6. APHA, Standard Methods for the Examinations of Water and Wastewater, 23rd ed., American Public Health Association, Washington, DC, (2017), 248–257.