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Synthesis and Evaluation of New Non-nucleoside Compounds Based on Theinopyrimidine Nucleus with Expected Biological Activity against Microorganisms

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ABSTRACT

A series of substituted thieno[2,3-d]pyrimidines was synthesized starting from ethyl 2- amino-4,5-dimethylthiophene-3-carboxylate and ethyl 2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene- 3-carboxylate. Reaction of 2-hydrazino-5,6-dimethylthieno[2,3-d]pyrimidin-4(3H)-one, 2-hydrazino- 5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one and its 3-allyl analogue with different reagents afforded thieno [2,3-d]triazolo[4,3-a]pyrimidines and thieno[3,2-e]triazolo[4,3- a]pyrimidines, beside open chain derivatives.

Keywords: Thieno[2,3-d]triazolo[4,3-a]pyrimidines; Thieno[3,2-e]triazolo[4,3-a]pyrimidines; Thieno[3,2-e]tetrazolo[1,5-a]pyrimidines; Thiosemicarbazides; Hydrazones

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INTRODUCTION

Thienopyrimidine derivatives have received considerable attention due to their wide range of biological activities such as antimicrobial [1,2], antiviral [3], anticancer [4,5], anti-inflammatory [6,7], antihistaminic [8], antipyretics [9], antianaphylactic [10], anticonvulsant [11] and immunostimulant [12] properties. Besides, many thienopyrimidine compounds exhibited analgesic [13], neurotropic [14], molluscicidal and larvicidal [15] activities. In fact, some of them have been reported to display good activity as Phosphodiesterase [16,17], dihydrofolate reductase (DHFR) [18], VEGF kinase [19] inhibitors, in addition to prevention of cartilage destruction in articular disease [20,21]. In continuation of our previous work on searching antiviral compounds [22-26] and on the title compounds [27], we reported herein the synthesis a new series of thienopyrimidine derivatives.

EXPERIMENTAL SECTION

Melting points are uncorrected. IR spectra were recorded with PERKIN – ELMER MODEL 1720 FTIR spectrometer. ^{1}H NMR and ^{13}CNMR spectra were determined with a varian EM 390 and Bruker AC – 250 spectrometers. The chemical shifts in ppm are expressed in the δ scale using tetramethylsilane as internal standard. Coupling constants are given in Hz. Mass spectra were recorded on an AEIMS 30 spectrometer. TLC was performed on Merck silica gel 60-F 254 precoated plastic plates. Microanalyses were performed in the unit of microanalysis at the universities of Qassim and Abdul-Aziz (KSA); the results were in satisfactory agreement with the calculated values.

General Procedure for Synthesis of Ethyl-2-Amino-4,5-Disubstitutedthiophene-3-Carboxylate ($1_{a,b}$)
To a stirred mixture of corresponding ketones (50 mmol), ethylcyanoacetate (5.65 g, 50 mmol), morpholin (4.5 g, 50 mmol) and absolute ethanol (3.00 ml), sulfur (1.6 g, 50 mmol) was added gradually with continuous stirring in

water bath (60ºC) for 6 hours. The reaction mixture was cooled and poured into crushed ice (100 ml). The separated solid was filtered, washed and crystallized from ethanol.

Ethyl-2-amino-4,5-dimethylthiophene-3-carboxylate (1_a):
From butane-2-One (3.61 g, 50 mmol) as described, Yield (7.5 g, 75%) as yellow crystals, m.p.: 50-52°C; IR (KBr) ν = 1565 (C=C), 1710 (C= O), 3180, 3215 cm^{-1} (NH_2); ^{1}H NMR (DMSO-d_6) δ = 1.28 (t, J = 7.2 Hz, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 4.23 (q, J = 7.1 Hz, 2H, CH_2), 7.21 (s, 2H, NH_2).

Ethyl-2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (1_b):
From cyclohexanone (4.91 g, 50 mmol) as described, Yield (7.9g, 70%) as dark yellow crystals, m.p.: 58-60°C; IR (KBr) ν = 1568 (C=C), 1690 (C=O), 3195, 3216 cm^{-1} (NH_2); ^{1}H NMR (DMSO-d_6) δ = 1.48 (t, J = 8.1 Hz, 3H, CH_3), 1.75 (bm, 4H, $2CH_2$), 2.66 (bt, 2H, CH_2), 2.81 (bt, 2H, CH_2), 4.22 (q, J = 7.6 Hz, 2H, CH_2), 7.32 (s, 2H, NH_2).

General Procedure for Synthesis of Ethyl-2-(3-Allylthioureido)-4,5-Disubstitutedthiophene-3-Carboxylate ($2_{a,b}$)
A mixture of $\mathbf{1_{a,b}}$ (10 mmol) and methylisothiocyanate (0.73 g, 10 mmol) in absolute ethanol (10 ml), was boiled under reflux for 3 hours. The reaction mixture was cooled and poured onto cold water. The separated solid was filtered, washed with H_2O, dried and crystallized from ethanol.

Ethyl 2-(3-allylthioureido)-4,5-dimethylthiophene-3-carboxylate (2_a):
From ester 1_a (1.99 g, 10 mmol) as described to give brown crystals. Yield (2.38 g, 80%), m.p.: 80f -82°C; IR (KBr) ν = 1573 (C=C), 1655 (C= O), 3217 cm^{-1} (NH); ^{1}H-NMR (*DMSO*-d_6) δ= 1.32 (t, 3H, *J*= 7.3 Hz, CH_3), 2.18 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 4.27(m, 2H, CH_2), 4.30 (q, 2H, j = 7.1 Hz, CH_2), 5.20 (dd, 1H, J_{cis}= 10.4 Hz, 3'-Ha), 5.24(dd, 1H, J_{trans}= 17.2 Hz, 3'- Hb), 5.93 (m, 1H, 2'-H), 11.13 (s, 1H, NH), 11.97 (s, 1H, NH); $C_{13}H_{18}N_2O_2S_2$, (298.2)(Calc/ Foud) C (52.35/52.11), H (6.04/5.83), N (9.40/ 9.14).

Ethyl-2-(3-allylthioureido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (2_b):
From ester 1_b (2.25 g, 10 mmol) as described to give dark brown crystals. Yield (2.66 g, 82%), m.p.: 100-102°C; IR (KBr) ν = 1570 (C=C), 1651 (C= O), 3201 cm^{-1} (NH); ^{1}H-NMR (*DMSO*-d_6) δ= 1.31 (t, 3 H, *J* = 7.3 Hz, CH_3), 1.71 (bm, 4H, $2CH_2$), 2.56 (bt, 2H, CH_2), 2.70 (bt, 2H, CH_2), 4.25 (m, 2H, NCH_2), 4.29(q, 2H, *J*= 7.1 Hz, CH_2), 5.20(dd, 1H, J_{cis}=10.5 Hz, 3'-Ha), 5.24 (dd, 1H, J_{trans}= 17.1 Hz, 3'-Hb), 5.88(m, 1H, 2'-H), 9.57 (s, 1H, NH), 11.52 (s, 1H, NH); MS, m/z = 324; $C_{15}H_{20}N_2O_2S_2$, (324.2); (Calc/ Foud), C (55.56/ 55.21), H (6.17 / 5.80), N (8.64/ 8.33).

General Procedure for Synthesis of 2-Mercapto-5,6-Disubstitutedthieno[2,3-d]Pyrimidin- 4(3H)-one ($3_{a,b}$)
A stirred mixture of $1_{a,b}$ (10 mmol) and excess of potassium thiocyanate (1.94 g, 20 mmol) in dioxan (25 ml) and absolute ethanol (5 ml) was stirred with gradually addition of hydrochloric acid 37% (5 ml). The reaction mixture was boiled under reflux for 6 hours, cooled and poured into crushed ice. The separated solid was boiled in sodium hydroxide solution (1 M, 50 ml) for 10 minutes, then cooled and neutralized by hydrochloric acid (1M). The precipitate was filtered, washed and crystallized from ethanol.

2-Mercapto-5,6-dimethylthieno[2,3-d]pyrimidin-4(3H)-one (3_a):
A stirred mixture of 1_a (1.99 g, 10 mmol) as described to give white ppt. Yield (1.65 g, 78%), m.p.: 220-222°C. IR (KBr) ν = 1540 (C=C), 1667 cm^{-1} (C=O); ^{1}H-NMR (*DMSO*-d_6) δ: 2.15 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 12.24, 13.32 (2s, 2H, 2NH); ^{13}CNMR δ: 22.65 (2Me), 11.35, 115.80, 145.60, 153.11 (Thiophene), 157.43 (C=O), 173.14 (C=S).

2-Mercapto-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (3_b):
A stirred mixture of 1_b (2.25 g, 10 mmol) as described to give white ppt. Yield (1.88 g, 79%), m.p.: 230-232ºC. IR (KBr) ν = 1548 (C=C), 1669 cm^{-1} (C=O); ^{1}H-NMR (*DMSO*-d_6) δ: 2.41 (bm, 4H, $2CH_2$), 2.87 (bm, 2H, CH_2), 3.15 (bm, 2H, CH_2), 12.39, 13.46 (2s, 2H, 2NH).

Allyl-2-mercapto-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (4_b):
A solution of 2_b (3.24 g, 10 mmol) in (2M) Aqueous solution of sodium hydroxide (15 ml) was boiled under reflux for 1 hour. After cooling the reaction mixture was neutralized by hydrochloric acid (2M). The precipitate was filtered, dried and crystallized from ethanol as pale brown crystals. Yield (1.95 g, 70%), m.p.: 232-234ºC. IR (KBr), ν = 1539, 1628 (C=C, C=N), 1671 (C=O), 3267, 3302 cm^{-1} (NH); ^{1}H-NMR (*DMSO-d_6*) δ= 1.80 (bm, 4H, $2CH_2$), 2.77 (bm, 2H, CH_2), 2.86(bm, 2H, CH_2), 4.57 (bm, 2H, NCH_2), 5.31 (bm, 2H, $=CH_2$), 5.91 (bm, 1H, 2'-H), 14.08 (s,

1H, NH); MS, m/z = 278; $C_{13}H_{14}N_2OS_2$, (278.1), (Calc/ Foud) C (56.09 / 55.71), H (5.03 / 4.70), N (10.07 / 9.72).

General Procedure for Synthesis of 5,6-Disubstituted-2-(methylthio)thieno[2,3-d]pyrimidin- 4(3H)-one ($5_{a,b}$)
A solution of $3_{a,b}$ (10 mmol) in (150 ml) of sodium hydroxide (0.1 M) and dimethylsulphate (15 ml) was stirred for 5 minutes. Produced precipitate was dissolved by through addition of sodium hydroxide (4 N). The solution was heated at (70°C) for 10 minutes. After cooling the solution was filtered off and neutralized by hydrochloric acid (2N). The precipitate was filtered, dried and recrystallized from ethanol.

5,6-Dimethyl-2-(methylthio)thieno[2,3-d]pyrimidin-4(3H)-one (5_a):
From 3_a (2.12 g, 10 mmol) as described before to give pale brown crystals. Yield (1.65 g, 73%), m.p.: 250-252ºC; IR (KBr) ν = 1550 (C=C), 1666 cm^{-1} (C=O), 3210 cm^{-1} (NH); ^{1}H-NMR (*DMSO-d_6*) δ: 1.95 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.58 (s, 3H, SCH_3), 12.52 (bs, 1H, NH).

2-Methyl-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (5_b):
From 3_b (2.38 g, 10 mmol) as described before to give gray crystals. Yield (1.54 g, 70%), m.p.: 258-260°C; IR (KBr) ν = 1612 (C=C), 1680 cm^{-1} (C=O), 3225 cm^{-1} (NH); ^{1}H-NMR (*DMSO-d_6*) δ: 1.77 (bm, 4H, $2CH_2$), 2.60 (s, 3H, SCH_3), 2.77 (bt, 2H, CH_2), 2.92 (bt, 2H, CH_2), 12.11 (bs, 1H, NH).

2-Allyl-2-hydrazino-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (6_b):
A mixture of 4_b (2.78 g, 10 mmol) and $NH_2NH_2.H_2O$ (5 ml) in absolute ethanol (15 ml) was boiled under reflux for 3 hours. The precipitate that separated on cooling was filtered off and recrystallized from ethanol to provide yellowish white crystals. Yield (2.10 g, 76%), m.p.: 198-20°C; IR (KBr) ν = 1539, 1628 (C=C, C=N), 1670 (C=O), 3267, 3302 cm^{-1} (NH); ^{1}H- NMR (*DMSO-d_6*) δ = 1.74 (bm, 4H, $2CH_2$), 2.61 (bt, 2H, CH_2), 2.80 (bt, 2H, CH_2), 4.35 (bd, 2H, NH_2), 4.58 (m, 2H, NCH_2), 4.98 (dd, 1H, J_{cis}= 10.3 Hz, 3'-Ha), 5.11 (dd, 1H, J_{trans}= 17.2 Hz, 3'- Hb), 5.83 (m, 1H, 2'-H), 8.23 (s, 1H, NH); $C_{13}H_{16}N_4OS$, (276.1), (Calc/ Foud) C (56.50 / 56.19), H (5.80 / 5.56), N (20.28 / 19.89).

2-hydrazinyl-5,6-disubstitutedthieno[2,3-d]pyrimidin-4(3H)-one ($7_{a,b}$):
A mixture of $5_{a,b}$ (10 mmol) and $NH_2NH_2.H_2O$ (5 ml) in absolute ethanol (15 ml) was boiled under reflux for 3 hours. The precipitate that separated on cooling was filtered off and recrystallized from ethanol.

2-hydrazinyl-5,6-dimethylthieno[2,3-d]pyrimidin-4(3H)-one (7_a):
From 5_a (2.26 g, 10 mmol) as described before to provide white precipitate. Yield (1.66 g, 79%), m.p.: 200-202ºC; IR (KBr) ν = 1620 (C=C, C=N), 1710 (C=O), 3264 cm^{-1} (NH); ^{1}H-NMR (*DMSO*-d_6) δ: 1.85 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 4.80 (bs, 2H, NH_2), 8.29, 8.44 (bs, 2H, 2NH); ^{13}CNMR δ: 22.73 (2Me), 108.70, 124.16, 146.07, 155.62 (Thiophene), 156.80, (C=N), 164.72 (C=O) .

2-Hydrazino-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (7_b):
From 5_a (2.20 g, 10 mmol) as described before to provide white precipitate. Yield (1.84 g, 78%), m.p.: 189-191ºC; IR (KBr) ν = 1550, 1618 (C=C, C=N), 1669 (C=O), 3260, 3290 cm^{-1} (NH); ^{1}H-NMR (*DMSO-d_6*) δ = 1.96 (bm, 4H, $2CH_2$), 2.71 (bt, 2H, CH_2), 2.90 (bt, 2H, CH_2), 4.42 (bd, 2H, NH_2), 8.33, 8.48 (bs, 2H, 2NH).

General Procedure for Synthesis of Compounds ($8_{a,b}$)
A solution of 7_b (0.236 g, 1 mmol) and excess of appropriate isocyanate (2 mmol) in ethanol (10 ml) was boiled under reflux for 4 hours. The product that separated after cooling was filtered off and recrystallized from ethanol.

2-(4-Oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2-yl)-N phenylhydrazinecarboxamide (8_a):
From 7_b and phenylisocyanate (0.24 g, 2 mmol), Yield (0.30 g, 85%) of white crystals, m.p.: 177-179°C. IR (KBr) ν = 1550 (C=C, C=N), 1625 (NHCONH), 1672 (C=O), 3325, 3380 cm^{-1} (NH); ^{1}HNMR (*DMSO* - d_6) δ = 1.75 (bm, 4H, $2CH_2$), 2.65 (bt, 2H, CH_2), 2.70 (bt, 2H, CH_2), 6.96 (t, 1H, Ar-H), 7.25 (t, 2H, Ar-H), 7.46(d, 2H, Ar-H), 8.01 (s, 1H, NH), 9.22 (s, 1H, NH), 11.80 (s, 1H, NH), 12.02 (s, 1H, NH); $C_{17}H_{17}N_5O_2S$, (355.2), (Calc/ Foud) C (57.43 / 57.11), H (4.79 / 4.44), N (19.71 / 20.12).

N-allyl-2-(4-oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2- yl)hydrazinecarboxamide (8_b):
From 7_b and propylisocyanate (0.17 g, 2 mmol), Yield (0.26 g, 80%) of white crystals, m.p.: 207-209ºC. IR (KBr) ν

= 1546 (C=C, C=N), 1620 (NHCONH), 1671 (C=O), 3318, 3379 cm^{-1} (NH); ^{1}HNMR (*DMSO* - d_6) δ = 0.85 (m, 2H, CH_2), 1.75 (bm, 4H, $2CH_2$), 2.62 (bm, 2H, CH_2), 2.79 (bm, 2H, CH_2), 3.00 (m, 2H, CH_2), 6.48 (t, 1H, NH), 7.80 (s, 1H, NH), 8.28 (s, 1H, NH), 10.81(s, 1H, NH); $C_{14}H_{19}N_5O_2S$, (321.1),(Calc/ Foud) C (52.32 / 52.51), H (5.92 / 6.21), N (21.80 / 22.16).

General Procedure for Synthesis of Compounds (9_{a-c})
A solution of $7_{a,b}$ (1 mmol) and the appropriate ketones (1 mmol) in 30 ml ethanol containing few drops of glacial acetic acid, was boiled under reflux for 3 hours. The product that separated out on cooling was filtered off, dried and crystallized from ethanol.

2-[N'-(1-Phenyl-ethylidene)-hydrazino]-5,6,7,8-tetrahydro-3H-benzo[4,5] thieno[2,3- d]pyrimidin-4-one (9_a):
From 7_b (0.236 g, 1 mmol) and acetophenone (0.12 g, 1 mmol) as described to undergo yellow precipitate, Yield (0.27 g, 81%), m.p.: 223-225°C; IR (KBr) ν = 1608 (C=C, C=N), 1668 (C=O), 3228 cm^{-1} (NH); ^{1}HNMR (*DMSO* - d_6) δ = 1.77 (bm, 4H, $2CH_2$), 2.32(s, 3H, CH_3), 2.52(bm, 2H, CH_2), 2.82(bm, 2H, CH_2), 7.43 (m, 3H, Ar-H), 8.01 (m, 2H, Ar-H), 10.62(s, 1H, NH), 10.91(s, 1H, NH); MS, m/z = 338 [M^+]; $C_{18}H_{18}N_4OS$, (338.2), (Calc/ Foud) C (63.91/ 63.62), H (5.33 / 5.14), N(16.57 / 16.79).

2-{N'-[1-(4-Chloro-phenyl)-ethylidene]-hydrazino}-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (9_b):
From **7_b** (0.236 g, 1 mmol) and p-chloroacetophenone (0.15 g, 1 mmol) as described to provide white precipitate, Yield (0.29 g, 77%), m.p.: 214-216°C; IR (KBr) ν = 1605 (C=C, C=N), 1662 (C=O) , 3377 cm^{-1} (NH); ^{1}H-NMR (*DMSO* - d_6) δ = 1.78 (bm, 4H, $2CH_2$), 2.32 (s, 3H, CH_3), 2.66 (bm, 2H, CH_2), 2.76 (bm, 2H, CH_2), 7.46 (d, *J*= 8.6Hz, 2H, Ar-H) , 8.05 (d, *J*=8.7 Hz, 2H, Ar-H), 10.65 (s, 1H, NH), 11.06 (s, 1H, NH); ^{13}C-NMR, δ = 14.51 (CH_3)22.18, 23.29, 24.79, 25.86, ($4CH_2$), 111.27, 117.01, 127.21, 134.29 (thiophene), 114.14, 119.88, 128.98, 130.98, (Ar-C), 148.85, 150.74(2C=N), 159.13 (C=O); MS, m/z = 372; $C_{18}H_{17}ClN_4OS$, (372.6), (Calc/ Foud) C (57.97 / 58.22), H (4.56 / 4.88), N (15.03 / 14.77).

2-(2-(1-(4-chlorophenyl)ethylidene)hydrazinyl)-5,6-dimethylthieno[2,3-d]pyrimidin-4(3H)- one (9_c):
From 7_a (0.21 g, 1 mmol) and p-chloroacetophenone (0.15 g, 1 mmol) as described to give white precipitate, Yield (0.26 g, 74%), m.p.: 183-185°C; IR (KBr) ν = 1605 (C=C, C=N), 1662 (C=O) , 3217, 3375 cm^{-1} (NH); ^{1}H-NMR (*DMSO* - d_6) δ = 2.28 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 7.48 (d, 2H, Ar-H), 8.06 (d, 2H, Ar-H), 10.65 (s, 1H, NH), 11.03 (s, 1H, NH); ^{13}C-NMR, δ = 12.71, 13.31, 14.50 ($3CH_3$), 111.27, 119.06, 128.06, 136.92, (thiophene), 114.14, 117.18, 128.61, 128.74, (Ar-C), 150.75, 158.37(2C=N), 159.52 (C=O); MS, m/z = 346; $C_{16}H_{15}ClN_4OS$, (346.6), (Calc/ Foud) C (55.40 / 55.71), H (4.33 / 4.71), N (16.16 / 15.88).

General Procedure for Synthesis of Compounds ($10_{a,b}$)
A solution of 7_b (0.236 g, 1 mmol) and excess of isothiocyanate (2 mmol) in ethanol (15 ml) was boiled under reflux for 4 hours. The product that separated after cooling was filtered off and recrystallized from ethanol.

N-allyl-2-(4-oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2- yl)hydrazinecarbothioamide (10_a):
From 7_b (0.236 g, 1 mmol) allylisothiocyanate (0.20 g, 2 mmol) as described to provide white precipitate, Yield (0.27 g, 80%), m.p.: 199-201ºC; IR (KBr) ν = 1577 (C=C, C=N), 1693 (C=O) , 3120, 3336 cm^{-1} (NH); ^{1}H-NMR (*DMSO* - d_6) δ = 1.82 (bm, 4H, $2CH_2$), 2.66 (bm, 2H, CH_2), 2.86 (bm, 2H, CH_2), 3.92 (bm, 2H, N- CH_2), 5.17 (dd, 1H, J_{cis}=10.0 Hz, 3'- Ha), 5.31(dd, 1H, J_{trans}= 17.3 Hz, 3'- Hb), 6.06 (m, 1H, 2'-H), 7.27, 8.21, 9.30, 12.77 (4s, 4H, 4 NH); $C_{14}H_{17}N_5OS_2$, (335.2), (Calc/ Foud) C (50.12 / 49.87), H (5.07 / 4.81), N(20.88 / 20.61).

N-benzyl-2-(4-Oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2-yl)hydrazinecarbothioamide (10_b):
From 7_b (0.236 g, 1 mmol) benzylisothiocyanate (0.30 g, 2 mmol) as described to provide white precipitate, Yield (0.33 g, 85%), m.p.: 175-177ºC; IR (KBr) ν = 1595(C=C, C=N), 1689 (C=O), 3120, 3346 cm^{-1} (NH); ^{1}H-NMR (*DMSO* - d_6) δ= 1.85 (bm, 4H, $2CH_2$), 2.64 (bm, 2H, CH_2), 2.88 (bm, 2H, CH_2), 4.75 (bm, 2H, N-CH_2), 7.27 (m, 5H, Ar-H), 7.41(s, 1H, NH), 8.49 (s, 1H, NH), 8.75 (t, 1H, NH), 11.25 (s, 1H, NH); $C_{18}H_{15}N_5OS_2$, (385.2), (Calc/ Foud) C (56.07 / 55.81), H (4.93 / 5.28), N (18.17 / 17.79).

2-(3,5-Dimethyl-pyrazol-1-yl)-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4- one (11):
A mixture of 7_b (0.236 g, 1 mmol) and pentane-2,4-dione (0,12 g, 1.2 mmol) was heated under reflux for 6 hours in absolute ethanol (30 ml). The reaction mixture was allowed to cool. The solid product that separated out was filtered

and recrystallized from ethanol as pale orange crystals. Yield (0.26 g 86%), m.p.: 204-206°C; IR (KBr) ν = 1593(C=C, C=N), 1677 (C=O) , 3211 cm^{-1} (NH); ^{1}H-NMR (*DMSO* - d_6) δ= 1.83 (bm, 4H, $2CH_2$), 2.23(s, 3H, CH_3), 2.56 (s, 3H, CH_3), 2.72 (bm, 2H, CH_2), 2.89 (bm, 2H, CH_2), 6.24(s, 1H, =CH), 11.77(s, 1H, NH); $C_{15}H_{16}N_4OS$, (300.1), (Calc/ Foud) C (59.98 / 59.69), H (5.37 / 5.73), N (18.65 /18.73).

4-Allyl-6,7,8,9-tetrahydro-4H-10-thia-2,3,4,10b-tetraaza-cyclopenta[a]fluoren-5-one (12):
A solution of 6_b (0.28 g, 1 mmol) in either formic acid or trimethylorthoformate (10 ml) was heated under reflux for 6 hours. The reaction mixture was allowed to cool and poured onto ice cold water (100 ml). The product that separated out was filtered, washed with water, dried and crystallized from ethanol as colorless crystals. Yield (0.26 g, 90%), m.p.: 215-217ºC; IR (KBr), ν = 1593 (C=C, C=N), 1666 cm^{-1} (C=O); ^{1}H-NMR, δ= 1.78 (bm, 4H, $2CH_2$), 2.75 (bm, 2H, CH_2), 2.85 (bm, 2H, CH_2), 4.72 (bm, 2H, N-CH_2), 5.15 (dd, 1H, J_{cis}=10.2 Hz, 3'-Ha) 5.24(dd, 1H, J_{trans}= 17.3 Hz, 3'- Hb), 5.93 (m, 1H, 2'-H) , 9.12 (s, 1H, CH); ^{13}C-NMR, δ= 21.28, 22.21, 24.01, 24.92 ($4CH_2$), 43.89, (NCH_2), 130.11, 131.28, 135.43, 138.25,(thiophene), 117.31, 132.36 (allyl C=C), 145.62, 147.59 (2 C=N), 155.13 (C=O); $C_{14}H_{14}N_4OS$, (286.1), (Calc/ Foud) C (58.72 / 58.51), H (4.89 / 5.11), N (19.57 / 19.23).

4-allyl-1-methyl-6,7,8,9-tetrahydro-4H-10-thia-2,3,4,10b-tetraaza-cyclopenta[a]fluoren-5- one (13):
A solution of 6_b (0.28 g, 1 mmol) in either acetic acid or triethylorthoformate (10 ml) was heated under reflux for 6 hours. The reaction mixture was allowed to cool and poured onto ice cold water (100 ml). The product that separated out was filtered, washed with water, dried and crystallized from ethanol as colorless crystals. Yield (0.27 g, 89%), m.p.: 228-230ºC; IR (KBr), ν = 1589(C=C, C=N), 1670 cm^{-1} (C=O); ^{1}H-NMR, δ = 1.76 (bm, 4H, $2CH_2$), 2.59(s, 3H, CH_3), 2.73 (bm, 2H, CH_2), 2.84 (bm, 2H, CH_2), 4.66 (bm, 2H, N-CH_2), 5.13 (dd, 1H, J_{cis}= 9.9 Hz, 3'- Ha) , 5.19 (dd, 1H, J_{trans}= 16.8 Hz, 3'- Hb) 5.90 (m, 1H, 2'-H); $C_{15}H_{16}N_4OS$, (300.1), (Calc/ Foud) C (59.99 / 60.31), H (5.33 / 5.66), N(18.66 / 19.01).

4-allyl-1-mercapto-6,7,8,9-tetrahydro-4H-10-thia-2,3,4,10b-tetraaza-cyclopenta[a]fluoren- 5-one (14):
A mixture of 6_b (2.76 g, 10 mmol) and CS_2 (0.9 g, 10 mmol) in pyridine (15 ml) was heated under reflux for 6 hours and then allowed to cool. The solid product was washed and recrystallized from ethanol to give white powder. Yield (2.89 g, 91%), m.p. : 244–246°C; IR (KBr), ν = 1620(C=C, C=N), 1678 (C=O), 3174 cm^{-1} (NH); ^{1}H-NMR, δ = 1.77 (bm, 4H, $2CH_2$), 2.76(bm, 2H, CH_2), 2.87 (bm, 2H, CH_2), 4.55 (bm, 2H, N-CH_2), 5.14 (dd, 1H, J_{cis}= 10.4 Hz, 3'-Ha) , 5.26 (dd, 1H, J_{trans}= 17.2 Hz, 3'- Hb) 5.92(m, 1H, 2'-H), 14.04 (s, 1H, NH); $C_{14}H_{14}N_4OS_2$, (318.1), (Calc/ Foud) C (52.81 / 53.12), H (4.40 / 4.63), N (17.60 / 17.92).

General Procedure for Synthesis of Compounds (15_{a-c})
A solution of 6_b (0.276 g, 1 mmol) and excess of isothiocyanate (2 mmol) in ethanol (10 ml) was boiled under reflux for 4 hours. The product was separated out cooled, filtered off and recrystallized from ethanol.

N-Allyl-2-(3-allyl-4-oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2-yl)hydrazinecarbothioamide (15_a):
From 6_b (0.276 g, 1 mmol) and allylisothiocyanate (0.2 g, 2 mmol), Yield (0.28 g, 84%), m.p. : 211–213°C; IR (KBr), ν = 1531(C=C, C=N), 1681 (C=O), 3201, 3244 cm^{-1} (NH); ^{1}H-NMR, δ= 1.74 (bm, 4H, $2CH_2$), 2.63(bm, 2H, CH_2), 2.79 (bm, 2H, CH_2), 4.01 (bm, 2H, N-CH_2), 4.62 (bm, 2H, N-CH2), 5.00 (dd, 1H, J_{cis}= 9.9 Hz, 3'- Ha) , 5.06 (dd, 1H, J_{trans}= 16.7 Hz, 3'- Hb), 5.13 (dd, 1H, Jcis= 10.1 Hz, 3''-Ha), 5.17 (dd, 1h, Jtrans= 17.1 Hz, 3''-Hb), 5.86 (m, 1h, 2'-H), 5.93(m, 1H, 2''-H), 8.04 (t, 1H, NH), 9.09 (d, 1H, NH), 9.38 (d, 1H, NH); $C_{17}H_{21}N_5OS_2$, (375.1), (Calc/ Foud) C (54.39 / 54.78), H (5.60 / 5.22), N (18.66 /18.31).

2-(3-Allyl-4-oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2-yl)Nphenylhydrazinecarbothioamide (15_b):
From 6_b (0.276 g, 1 mmol) and phenylisothiocyanate (0.34 g, 2 mmol), Yield (0.34 g, 81%), m.p. : 247–249°C; IR (KBr), ν = 1620(C=C, C=N), 1666 (C=O), 3194 cm^{-1} (NH);^{1}H-NMR, δ= 1.76 (bm, 4H, $2CH_2$), 2.75(bm, 2H, CH_2), 2.87(bm, 2H, CH_2), 4.55 (bm, 2H, N-CH_2), 5.00 (dd, 1H, J_{cis}= 10.1 Hz, 3'- Ha) , 5.26 (dd, 1H, J_{trans}= 17.2 Hz, 3'-Hb), 5.92 (m, 1H, 2'-H), 7.12-7.35(m, 5H, Ar-H), 8.11 (t, 1H, NH), 9.15 (d, 1H, NH), 9.75 (d, 1H, NH); $C_{20}H_{21}N_5OS_2$, (411.1), (Calc/ Foud) C (58.38 / 57.91), H (5.11 / 4.87), N (17.03 / 16.78).

2-(3-Allyl-4-oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2-yl)N-benylhydrazinecarbothioamide (15_c):
From 6_b (0.276 g, 1 mmol) and benzylisothiocyanate (0.30 g, 2 mmol), Yield (0.36 g, 85%), m.p. : 221–223°C; IR

(KBr), ν = 1531, 1570(sh) (C=C, C=N), 1666, 3344 cm^{-1} (NH); ^{1}H-NMR, δ= 1.76 (bm, 4H, $2CH_2$), 2.67 (bm, 2H, CH_2), 2.80 (bm, 2H, CH_2), 4.59 (bt, 2H, N-CH_2), 4.76 bt, 2H, N-CH2), 5.05 (dd, 1H, J_{cis}=10.1 Hz, 3'-Ha) 5.13(dd, 1H, J_{trans}= 17.2 Hz, 3'- Hb), 5.86 (m, 1H, 2'-H) , 7.20- 7.35 (m, 5H, Ar-H), 8.49(bt, 1H, NH), 9.18 (s, 1H, NH), 9.48 (s, 1H, NH); ^{13}C-NMR, δ= 21.87 22.65, 24.29, 25, 18 ($4CH_2$), 40.15, 40.43, ($2NCH_2$), 130.25, 131.91, 135.22, 139.66,(thiophene), 115.31, 132.37 (allyl C=C), 126.39, 126.71, 127.95, 129.9(Ar-Cl, 151.21, 159.11, 166.21 (C=N, C=O, C=S); $C_{21}H_{23}N_5OS_2$, (425.1), (Calc/ Foud) C (59.28 / 58.88), H (5.41 / 5.13), N (16.47 / 16.11).

General Procedure for Synthesis of Compounds (16_{a-d})

A solution of 6_b (0.276 g, 1 mmol) and excess of isocyanate (2.5 mmol) in ethanol (15 ml) was boiled under reflux for 4 hours. The product was separated out cooled, filtered off and recrystallized from ethanol.

N-allyl-2-(3-Allyl-4-oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2-yl)hydrazinecarboxamide (16_a):

From 6_b (0.276 g, 1 mmol) and allylisocyanate (0.21 g, 2.5 mmol), Yield (0.29 g, 80%), m.p. : 231–233°C; IR (KBr), ν = 1528 (C=C, C=N), 1674 (C=O), , 3367 cm^{-1} (NH); ^{1}H-NMR, δ= 1.76 (bm, 4H, $2CH_2$), 2.67 (bm, 2H, CH_2), 2.79 (bm, 2H, CH_2), 3.65 (bt, 2H, N-CH_2), 4.65 (bt, 2H, N-CH2), 4.98 (dd, 1H, J_{cis}=10.1Hz,H, 3'-Ha) 5.06(dd, 1H, J_{cis}= 10.2Hz, 3''- Ha), 5.13 (dd, 1H, Jtrans= 17.2 Hz, 3'- Hb), 5.20 (dd, 1H, Jtrans= 17.1 Hz, 3''-H), 5.64 (m, 1H, 2'-H), 5.96 (m, 1H, 2''-H), 6.57 (t, 1H, NH), 7.90 (s, 1H, NH), 8.83(s, 1H, NH); ^{13}C-NMR, δ= 21.87 22.63, 24.24, 25, 19 ($4CH_2$), 41.28, 41.39, ($2NCH_2$), 114.13, 114.35, 130.25, 131.94(allyl C=C), 116.08, 126.50, 136.39, 151.59 (thiophene), 157.31, 159.44, 163.79(C=N, 2 C=O); $C_{17}H_{21}N_5O_2S$, (359.1), (Calc/ Foud) C (56.81 / 56.42), H (5.85 / 5.49), N (19.49 / 19.18).

2-(3-allyl-4-oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2-yl)-N-tollylhydrazinecarboxamide (16_b):

From 6_b (0.276 g, 1 mmol) and p-tollylisocyanate (0.33 g, 2.5 mmol), Yield (0.34 g, 80%), m.p.: 237–239°C; IR (KBr), ν = 1603 (C=C, C=N), 1662 (C=O), 3317 cm^{-1} (NH); ^{1}H-NMR, δ= 1.74 (bm, 4H, $2CH_2$), 2.22(s, 3H, CH_3), 2.61 (bm, 2H, CH_2), 2.80 (bm, 2H,CH_2), 4.68 (bd, 2H, N-CH_2), 5.05 (dd, 1H, J_{cis}=10.2 Hz, 3'-H_a), 5.17(dd, 1H, J_{trans}= 17.1 Hz, 3'- H_b), 5.93 (m, 1H, 2;-H), 7.05 (d, 2H, Ar-H), 7.35 (d, 2H, Ar-H), 8.16(s, 1H, NH), 8.61 (s, 1H, NH), 8.94 (s, 1H, NH); ^{13}C-NMR, δ= 20.26 (CH_3), 21.85, 22.60, 24.22, 25.18($4CH_2$), 41.44 (NCH_2), 114.12, 130.74 (allyl C=C), 116.27, 126.59, 136.91, 151.61 (thiophene), 118.17, 128.95, 131.80, 137.07 (Ar-C), 156.01, 157.22, 163.62 (C=N, 2C=O); $C_{21}H_{23}N_5O_2S$, (409.1), (Calc/ Foud) C (61.60 / 61.26), H (5.62 / 5.41), N (17.11 / 16.83).

2-(3-allyl-4-oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2-yl)-N-phenylhydrazinecarboxamide (16_c):

From 6_b (0.276 g, 1 mmol) and phenylisocyanate (0.30 g, 2.5 mmol), Yield (0.32 g, 79%), m.p.: 262–264°C; $C_{20}H_{21}N_5O_2S$, (395.1), (Calc/ Foud) C (60.74 / 60.46), H (5.32 / 5.11), N (17.72 / 17.43).

2-(3-allyl-4-oxo-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidin-2-yl)-N-propylhydrazinecarboxamide (16_d):

From 6_b (0.276 g, 1 mmol) and propylisocyanate (0.21 g, 2.5 mmol), Yield (0.29 g, 82%), m.p.: 262–264°C; $C_{17}H_{23}N5O_2S$, (361.1), (Calc/ Foud) C (56.49 / 56.11), H (6.37 / 6.13), N (19.39 / 19.17).

General Procedure for Synthesis of Compounds (17_{a-f})

A solution of 6_b (2.76 g, 10 mmol) and the appropriate aromatic aldehyde (10 mmol) in 30 ml ethanol containing few drops of glacial acetic acid, was boiled under reflux for 3 hours. The product that separated out on cooling was filtered off, dried and crystallized from ethanol.

3-allyl-2-[N'-(3-bromo-4-chloro-benzylidene)-hydrazino]-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3d]pyrimidin-4-one (17_a):

From 6_b (2.76 g, 10 mmol) and 3-bromo-4-fluorobenzaldehyde (2.03 g, 10 mmol) as described, Yield (3.96 g, 83%), m.p.: 200–202°C; IR (KBr), ν = 1558 (C=C, C=N), 1616 (C=C, C=N), 1647 (C=O), 3263 cm^{-1} (NH); ^{1}H NMR, δ= 1.74 (bm, 4H, $2CH_2$), 2.63(bm, 2H, CH_2), 2.76 (bm, 2H, CH_2), 4.60 (bm, 2H, NCH_2), 5.12 (bm, 2H, =CH2), 5.88 (m, 1H, HC=), 7.43(m, 1H, Ar-H), 7.93 (bd, 1H, Ar-H), 8.28 (bd, 1H, Ar-H), 8.31 (s, 1H, =CH),11.62(s, 1H, NH); $C_{20}H_{18}BrFN_4OS$, (461), (Calc/ Foud) C (52.06 / 51.73), H (3.90 / 4.16), N (12.15 / 11.78).

3-allyl-2-[N'-(4-methyl-benzylidene)-hydrazino]-5,6,7,8-tetrahydro-3H-benzo [4,5]thieno[2,3-d]pyrimidin-4-one (17_b):

From 6_b (2.76 g, 10 mmol) and p-methylbenzaldehyde (1.20 g, 10 mmol) as described, Yield (3.01 g, 84%), m.p. : 197–199°C; IR (KBr), ν = 1577, 1612, (C=C, C=N), 1647, 1678 (C=O), 3228 cm^{-1} (NH); ^{1}H-NMR, δ= 1.76 (m, 4H, $2CH_2$), 2.34(s, 3H, CH_3), 2.65 (m, 2H, CH_2), 2.81 (m, 2H, CH_2), 4.59 (bd, 2H, N-CH_2), 4.82, 5.71, 5.11, 5.15 (m, 2H, =-CH_2)5.95 (m, 1H, =CH, 5.95 (m, 1H, =CH), 7.23, 7.58, 7.83 (4d, 4H, Ar-H), 8.28, 8.32, (2s, 1H,=CH), 10.43, 11.54(2s, 1H, NH); ^{13}C-NMR, δ= 21.04, 21.85 (CH_3, syn & anti), 21.12, 22.61, 23.75, 24.30, 25.02, 25.23 ($4CH_2$), 41.59, 41.83 (NCH_2), 111.09, 114.44, 130.33, 130.70 (allyl C=C), 115.66, 116.20, 124.94, 126.35, 139.19, 139.53, 146.20, 147.91(thiophene), 127.19, 127.62, 129.04, 129.40, 131.54, 132.76, 132.63, 132.81(Ar-C), 149.45, 149.98, 152.24, 157.11, 163.72 (2C=N, C=O); $C_{21}H_{22}N_4OS$, (378.1), (Calc/ Foud) C (66.65 / 67.01), H (5.82 / 6.21), N (14.81 / 15.18).

3-allyl-2-[N'-(2-nitro-benzylidene)-hydrazino]-5,6,7,8-tetrahydro-3H-benzo[4,5] thieno[2,3-d]pyrimidin-4-one (17_c):

From 6_b (2.76 g, 10 mmol) and 2-nitrobenzaldehyde (1.51 g, 10 mmol) as described, Yield (3.56 g, 87%), m.p. : 294–296°C; IR (KBr), ν = 1550, 1570, 1605 (C=C, C=N), 1658 (C=O), 1658 (C=O), 3255 cm^{-1} (NH); ^{1}H-NMR, δ= 1.76 (bm, 4H, $2CH_2$), 2.63(bm, 2H, CH_2), 2.76 (bm, 2H, CH_2), 4.62(bm, 2H, NCH_2), 4.82 (2bd, 2H, NCH2), 5.00, 5.15 (2m, 2H, =CH2), 5.92 (m, 1H, =CH), 7.60, 8.15(m, 4H, Ar-H), 8.58, 8.80 (2s, 1H, =CH), 10.94, 11.76 (2s, 1H, NH)**;** $C_{20}H_{19}N_5O_3S$, (409.1), (Calc/ Foud) C (58.67 / 58.39), H (4.64 / 4.28), N (.17.11 / 16.80)

3-allyl-2-[N'-(2,3,5,6-tetrafluoro-benzylidene)-hydrazino]-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (17_d):

From 6_b (2.76 g, 10 mmol) and 2,3,5,6-tetrafluorobenzaldehyde (1.78 g, 10 mmol) as described. Yield (3.71 g, 85%), m.p. : 215–217 °C; IR (KBr), ν = 1562, 1600 (C=C, C=N), 1678 (C=O), 3325 cm^{-1} (NH); ^{1}H-NMR, δ= 1.76 (bm, 4H, $2CH_2$), 2.64(bm, 2H, CH_2), 2.80 (bm, 2H, CH_2), 4.75 (bd, 2H, NCH_2), 5.13, 5.28 (2d, 2H, =CH2), 5.92 (m, 1H, =CH2), 7.91 (m, 1H, Ar-H), 8.42(m, 4H, Ar-H), 8.53 (2s, 1H, =CH), 11.06, 11.67 (2s, 1H, NH); ^{13}C-NMR, δ= 21.81, 22.55, 23.73, 24.33, 24.95, 25.19 (4CH2), 41.79, 42.11 (NCH2), 106.86, 115.22, 130.42, 132.30 (allyl C=C), 116.45, 144.96, 147.35 (thiophene-C), 125.92, 132.30, 134.16, 139.99(Ar-C), 151.18, 156.84, 163.12 (2C=N, C=O); $C_{20}H_{16}F_4N_4OS$, (436.1, (Calc/Foud) C (55.03 / 54.81), H (3.67 / 3.29), N (12.84 / 12.55).

3-allyl-2-[N'-(4-methoxy-benzylidene)-hydrazino]-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (17_e):

From 6_b (2.76 g, 10 mmol) and p-anisaldehyde (2.76 g, 10 mmol) as described, Yield (3.47 g, 88%), m.p.: 266–268°C; IR (KBr), ν = 1597 (C=C, C=N), 1654 (C=O), 3209 cm^{-1} (NH); ^{1}H-NMR, δ= 1.76 (bm, 4H, $2CH_2$), 2.62(bm, 2H, CH_2), 2.82(bm, 2H, CH_2), 3.84, 3.87(2s, 3H, OCH_3), 4.60, 4.83 (2d, 2H, NCH2), 5.12 (m, 1H, =CH2), 5.93 (m, 1H, =CH2), 6.98, 8.39 (m, 4H, Ar-H), 8.57, 8.70(2s, 1H, =CH), 10.54, 11.58 (2s, 1H, NH)**;** $C_{21}H_{22}N_4O_2S$, (394.1), (Calc/ Foud) C (63.94 / 64.18), H (5.58 / 5.88), N (14.21 / 13.82).

3-allyl-2-[N'-(4-chloro-benzylidene)-hydrazino]-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (17_f):

From 6_b (2.76 g, 10 mmol) and p-chlorobenzaldehyde (1.41 g, 10 mmol) as described, Yield (3.55 g, 89%), m.p. : 194–196°C; IR (KBr), ν = 1600 (C=C, C=N), 1670 (C=O), 3367 cm^{-1} (NH); ^{1}H-NMR, δ= 1.75 (bm, 4H, $2CH_2$), 2.62(bm, 2H, CH_2), 2.81(bm, 2H, CH_2), 4.37(bd, 21, NCH_2), 4.61, 4.81, 5.13 (m, 2H, =CH2), 5.92 (m, 1H, =CH), 7.48, 7.50, 7.95, 7.99 (4d, 4H, Ar-H), 8.32, 8.70(s, 1H, =CH), 11.25, 11.58 (2s, 1H, NH)**;** $C_{20}H_{19}ClN_4OS$, (398.6), (Calc/ Foud) C (60.21 / 59.85), H (4.77 / 4.51), N(14.05 / 13.88)**.**

3-allyl-1-(3-bromo-4-flurophenyl)-6,7,8,9-tetrahydro[1]benzothieno[3,2-e][1,2,4]triazolo[4,3-a]pyrimidin-5(4H)-one (19):

A solution of ferric chloride (0.4 gm) in ethanol (5 ml) was added dropwise to a boiling solution of aldehydehydrazones 17_a (0.96 g, 2 mmol) in ethanol (50 ml). Heating was continued for 30 min. and the mixture was then kept overnight at room temperature. Evaporation of the solvent under reduced pressure, washing the residue with water, drying and crystallized from ethanol to give pale brown crystals. Yield (0.64 g, 70%), m.p. : 169–171°C; IR (KBr), ν = 1585(C=C, C=N), 1674 cm^{-1} (C=O); ^{1}H-NMR, δ= 1.74 (bm, 4H, $2CH_2$), 2.64(bm, 2H, CH_2), 2.86 (bm, 2H, CH_2), 4.76 (bm, 2H, NCH_2), 5.18 (dd, 1H,Jcis= 10.2 Hz, 3'-Ha), 5.29 (dd, 1H, Jtrans= 17.3 Hz, 3'-Hb),5.96 (m, 1H, 2'-H), 7.66 (d, 1H, Ar-H), 7.83(s, 1H, Ar-H), 8.16 (d, 1H,, Ar-H); ^{13}C-NMR, δ= 21.46, 22.25, 23.91, 24.33, 24.91(4CH2), 43.89 (NCH2), 108.53, 130.67 (allyl C=C), 117.55, 123.52, 138.64, 144.48 (thiophene-

C), 131.26, 132.21, 132.27, 135.61, 148.48(Ar-C), 155.21, 159.07, 161.06(2C=N, C=O); $C_{20}H_{16}BrFN_4OS$, (459.1), (Calc/ Foud) C (52.28 / 51.91), H (3.49 / 3.11), N (12.20 / 11.87).

General Procedure for Synthesis of Compounds ($20_{a,b}$)

A solution of semicarbazides $16_{b,c}$ (1 mmol) and sodium hydroxide (2 N, 25 ml) was boiled for 1 hour then was cooled and neutralized by addition of hydrochloric acid (2 N). The precipitate formed was collected, washed and crystallized from ethanol.

4-allyl-1-anilino-6,7,8,9-tetrahydro[1]benzothieno[3,2-e][1,2,4]triazolo[4,3-a]pyrimidin- 5(4H)-one (20_a):

From 16_c (0.41 g, 1 mmol) as described and undergo white powder, Yield (0.26 g, 69%), m.p.: 201–203°C. IR (KBr), ν = 1620(C=C, C=N), 1666 (C=O), 3194 cm^{-1} (NH); ^{1}H-NMR, δ= 1.77 (bm, 4H, $2CH_2$), 2.66(bm, 2H, CH_2), 2.80 (bm, 2H, CH_2), 4.66(bm, 2H, NCH_2), 5.15 (bm, 2H, =CH2), 5.93 (m, 1H, =CH), 7.50, 8.35(m, 5H, Ar-H), 11.6 (6s, 1H, NH); $C_{20}H_{19}N_5OS$, (377.4). (Calc/Foud) C (63.64 / 63.23), H(5.07/4.83), N (18.55 / 18.21).

4-allyl-1-(4-methylanilino)-6,7,8,9-tetrahydro[1]benzothieno[3,2-e][1,2,4]triazolo[4,3-a]pyrimidin-5(4H)-one (20_b):

From 16_b (0.42 g, 1 mmol) as described and undergo white powder, Yield (0.31 g, 68%), m.p.: 181–183°C. ^{1}H-NMR, δ= 1.68 (bm, 4H, $2CH_2$), 2.22(s, 3H, CH_3), 2.48(bm, 2H, CH_2), 2.70 (bm, 2H, CH_2), 4.53(bm, 2H, NCH_2), 5.11 (dd, J_{cis}= 9.9 Hz, 3'-Ha), 5.18 (dd, J_{trans}= 16.8 Hz, 3'-Hb), 5.87 (m, 1H, 2'-H), 7.05(d, 2H, Ar-H), 7.38 (d, 2H, Ar- H), 7.83, 8.32 (2s, 1H, NH); $C_{21}H_{21}N_5OS$ (391.4). (Calc / Foud) C (64.43 / 64.11), H (5.41 / 5.13), N (17.89 / 18.12) (Figures 1-58).

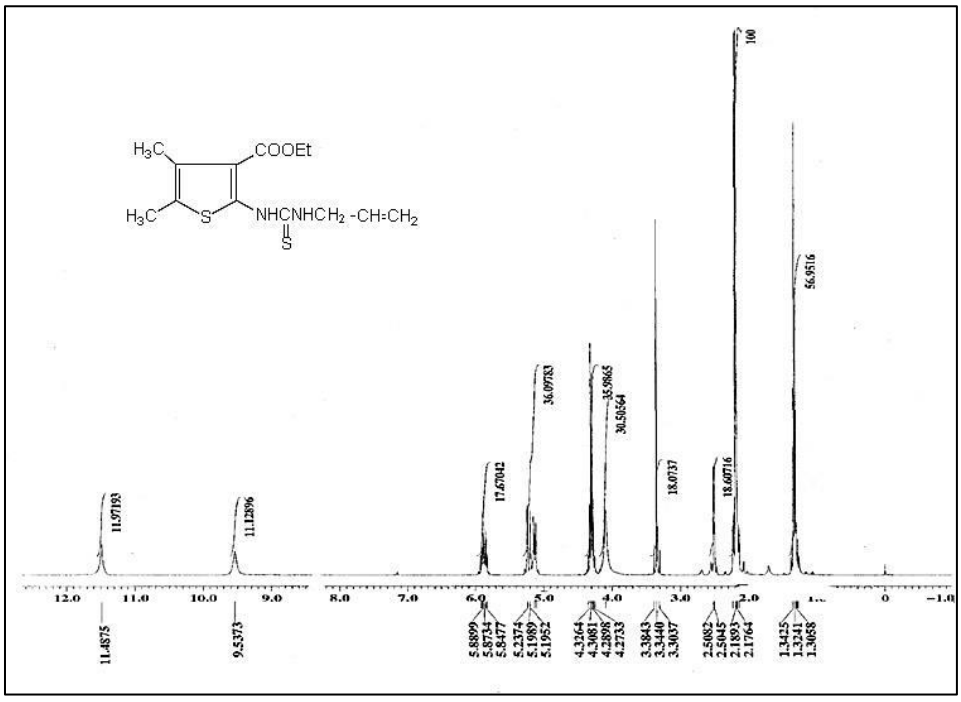


Figure 1: ^{1}H-NMR spectrum of 2_a in DMSO-d_6

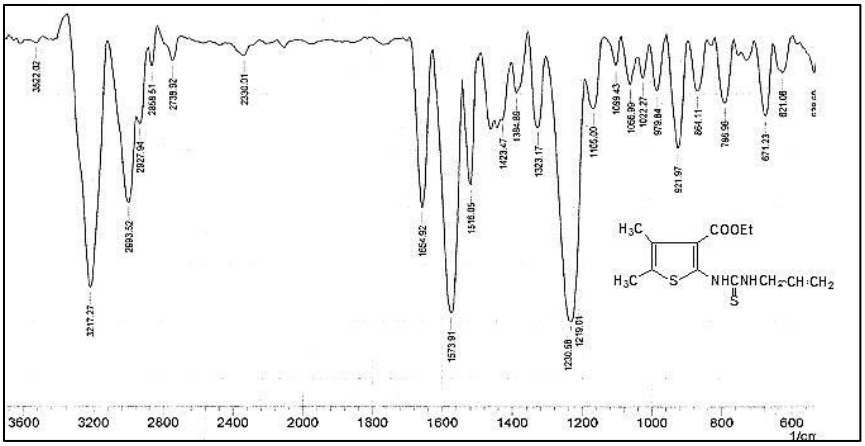


Figure 2: IR spectrum of 2_a in KBr

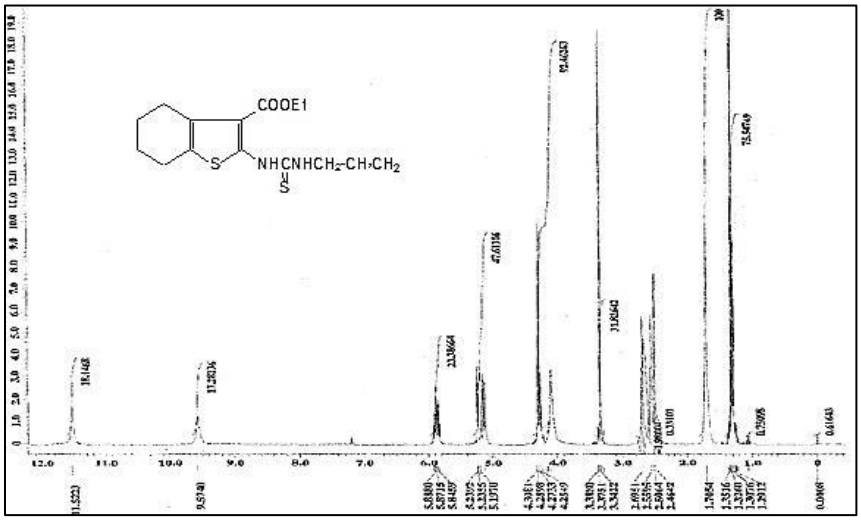


Figure 3: ^{1}H-NMR spectrum of 2_b in DMSO-d_6

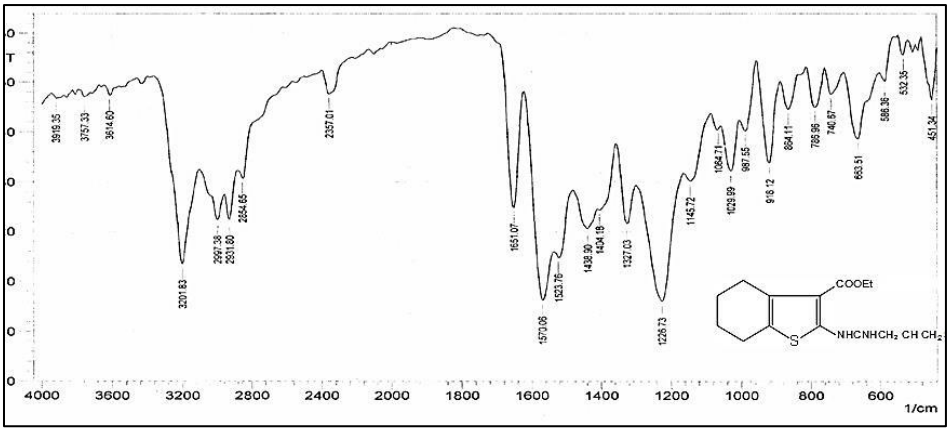


Figure 4: IR spectrum of 2_b in KBr

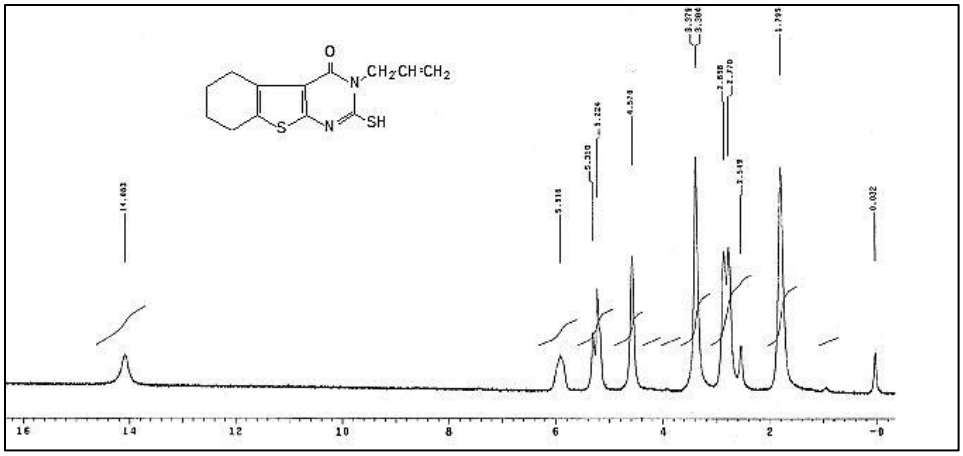


Figure 5: ^{1}H-NMR spectrum of 4_b in DMSO-d_6

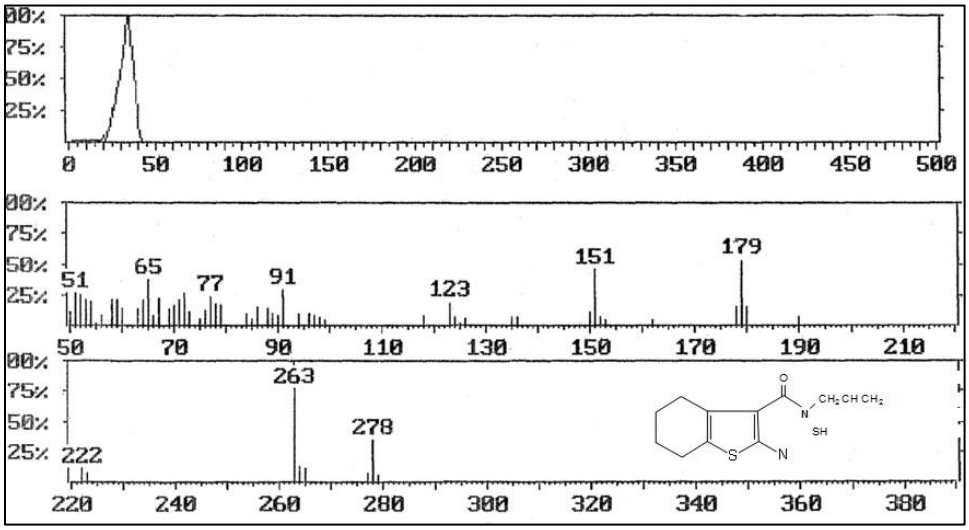


Figure 6: MS spectrum of 4_b in DMSO

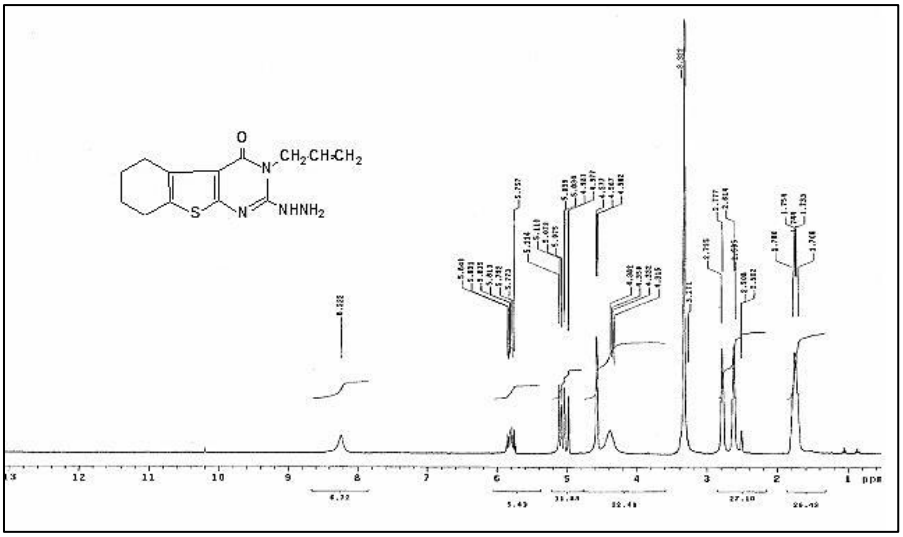


Figure 7: ^{1}H-NMR spectrum of 6_b in DMSO-d_6

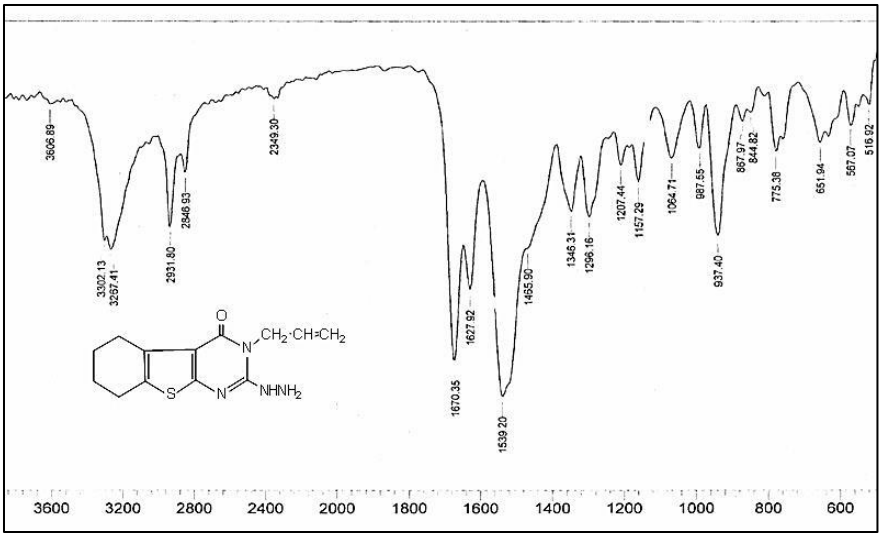


Figure 8: IR spectrum of 6_b in KBr

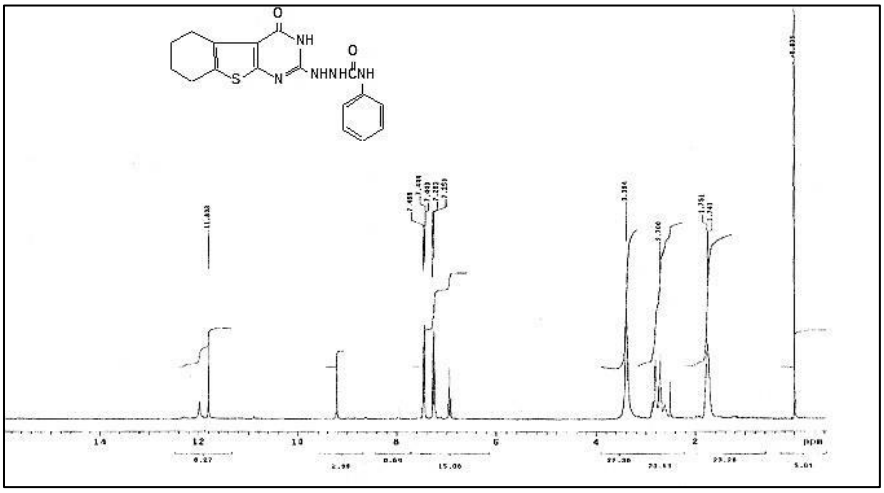


Figure 9: ^{1}H-NMR spectrum of 8_a in DMSO-d_6

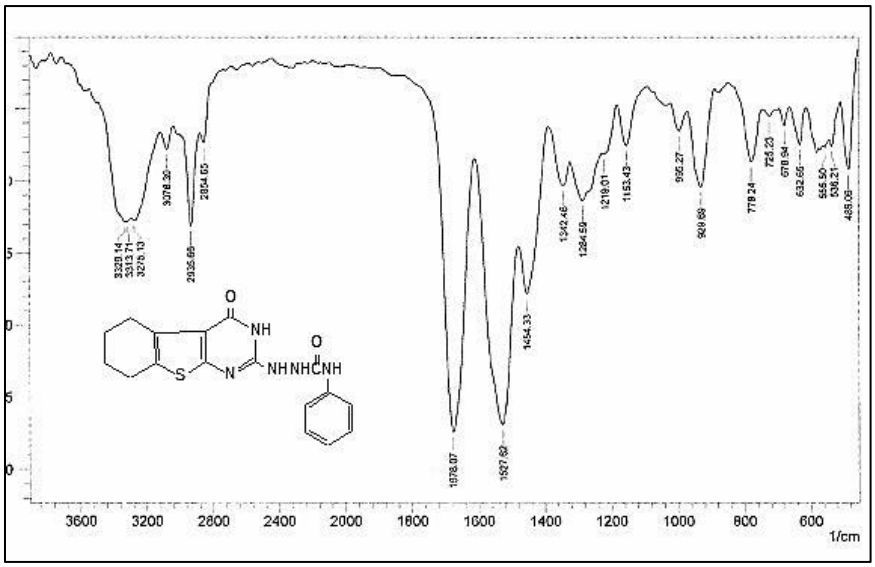


Figure 10: IR spectrum of 8_a in KBr

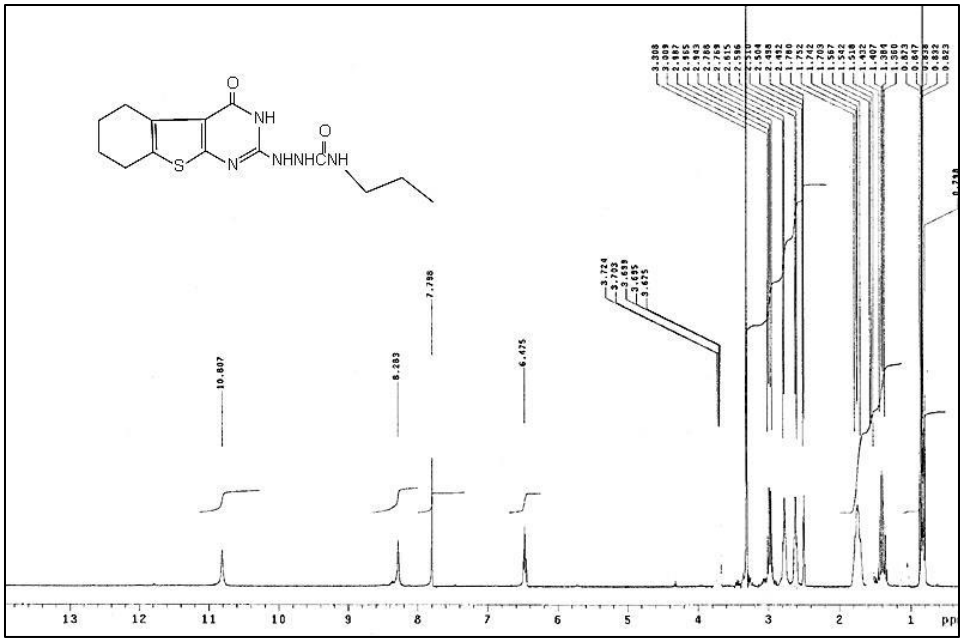


Figure 11: ^{1}H-NMR spectrum of 8_b in DMSO-d_6

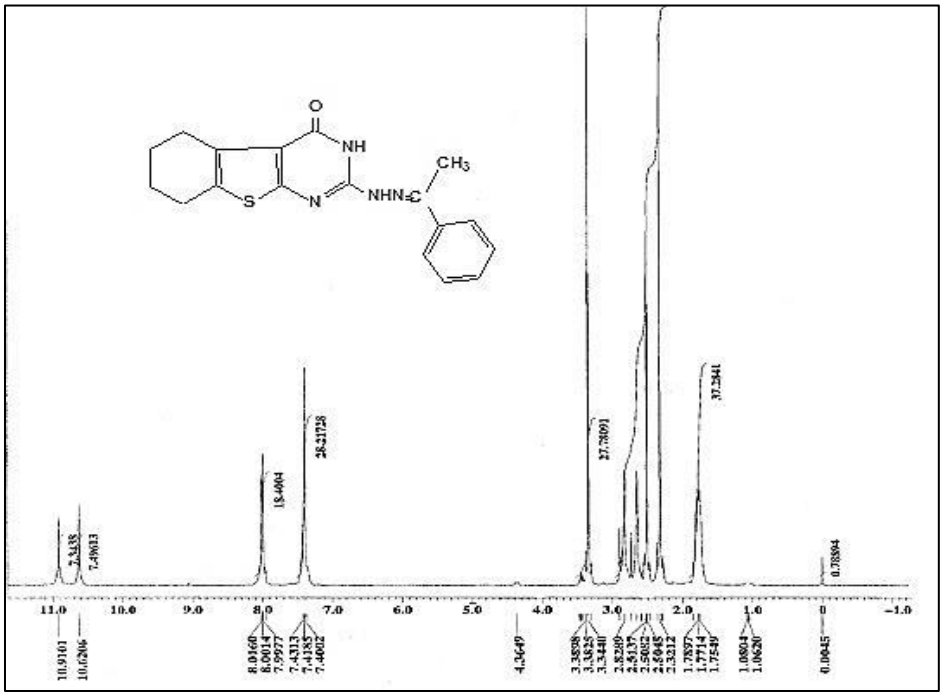


Figure 12: ^{1}H-NMR spectrum of 9_a in DMSO-d_6

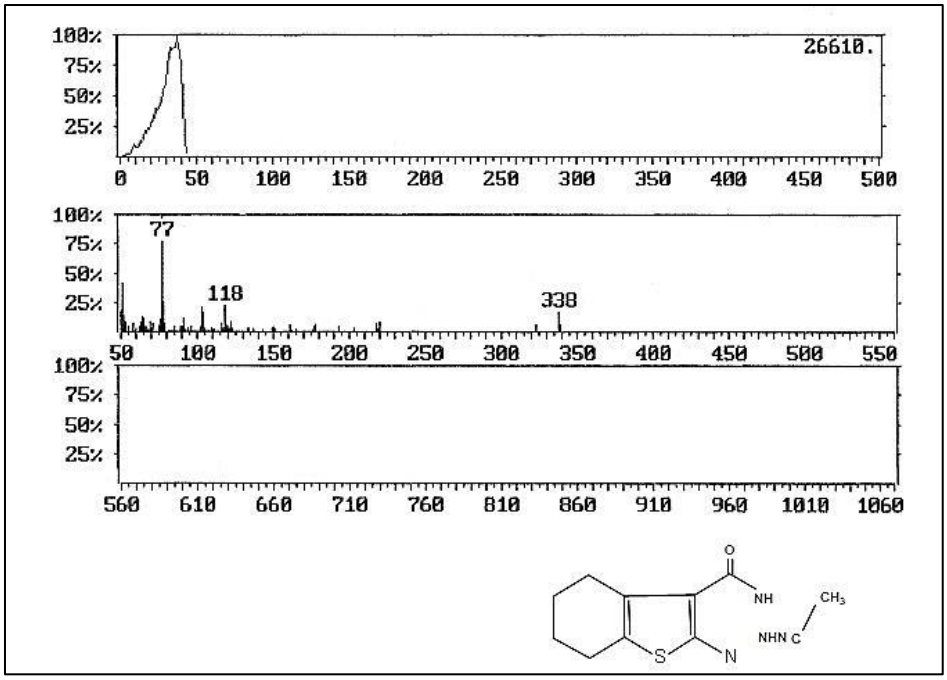


Figure 13: MS spectrum of 9_a in KBr

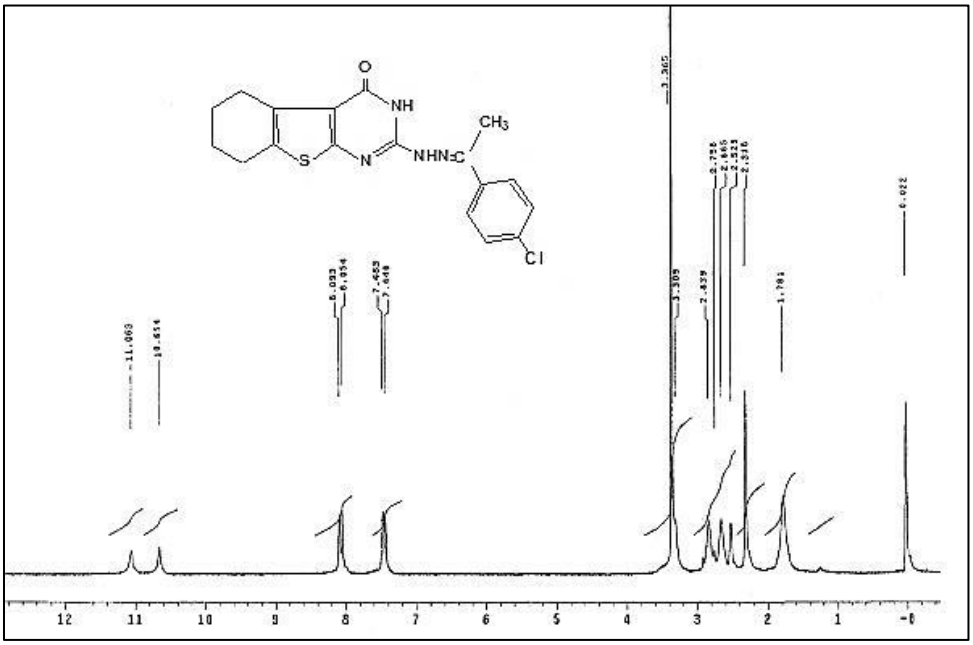


Figure 14: ^{1}H-NMR spectrum of 9_b in DMSO-d_6

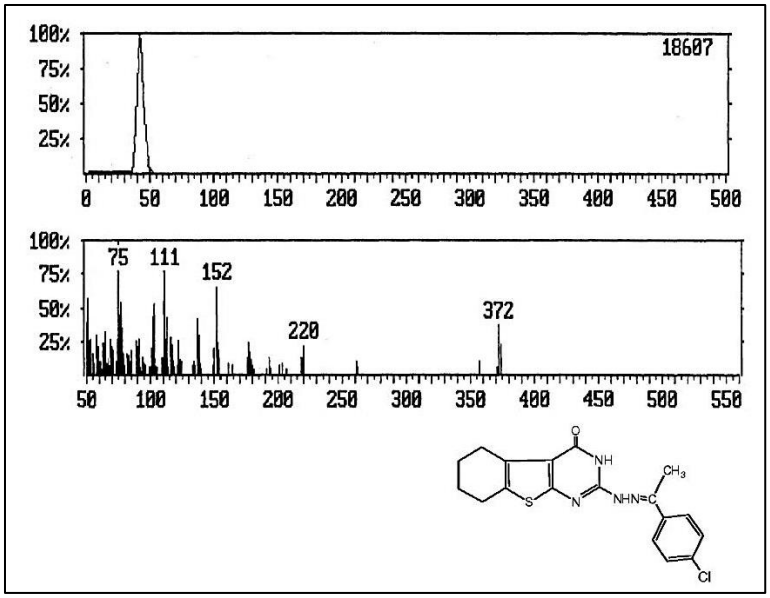


Figure 15: MS spectrum of 9_b in KBr

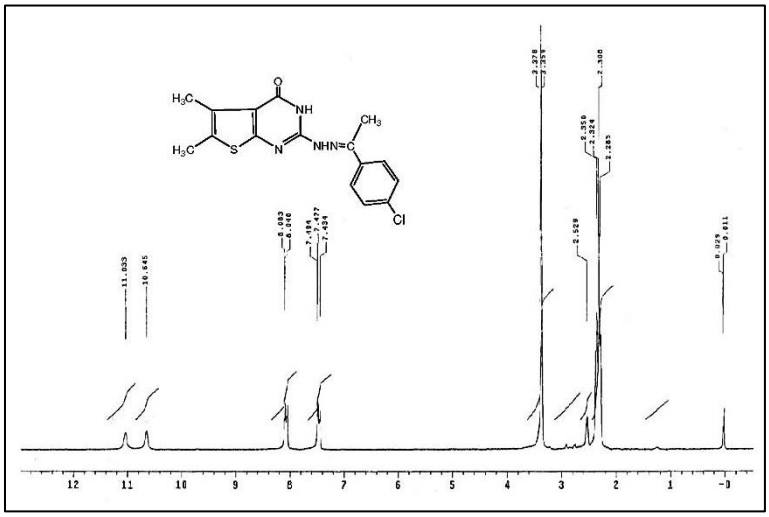


Figure 16: ^{1}H-NMR spectrum of 9_c in DMSO-d_6

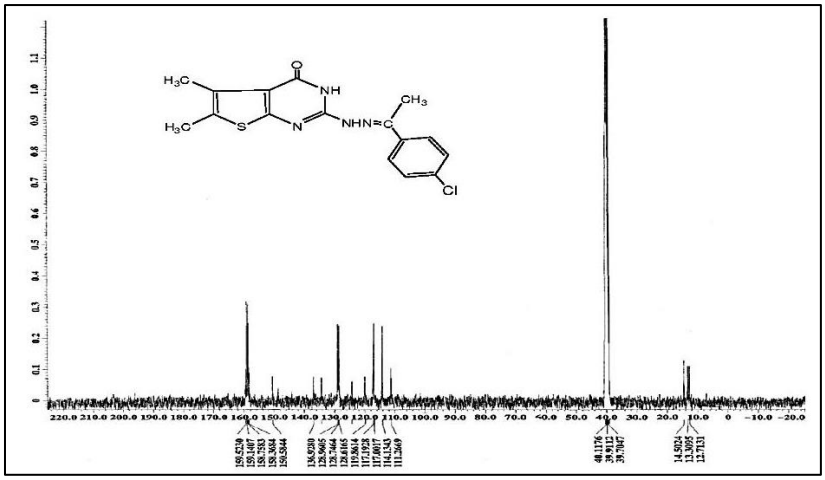


Figure 17: ^{13}C-NMR spectrum of 269c in DMSO-d_6

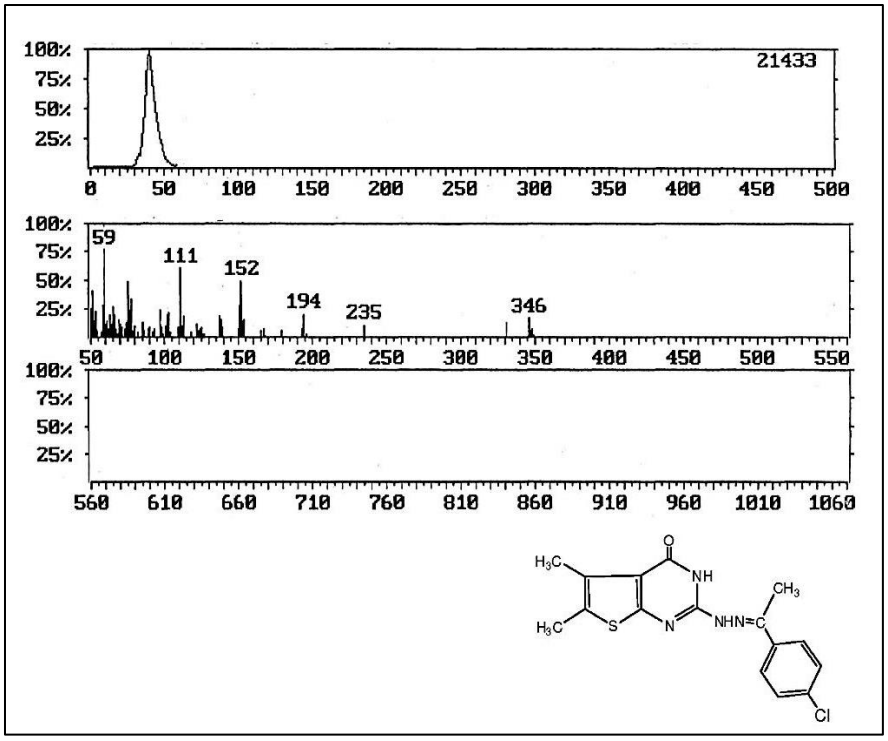


Figure 18: MS spectrum of 9_c in DMSO

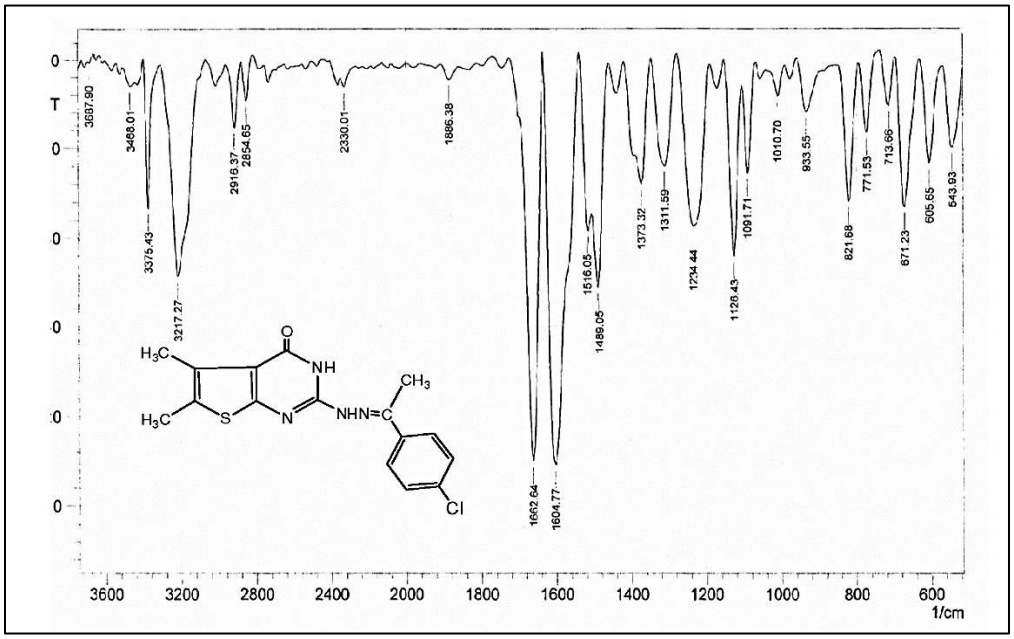


Figure 19: IR spectrum of 9_c in KBr

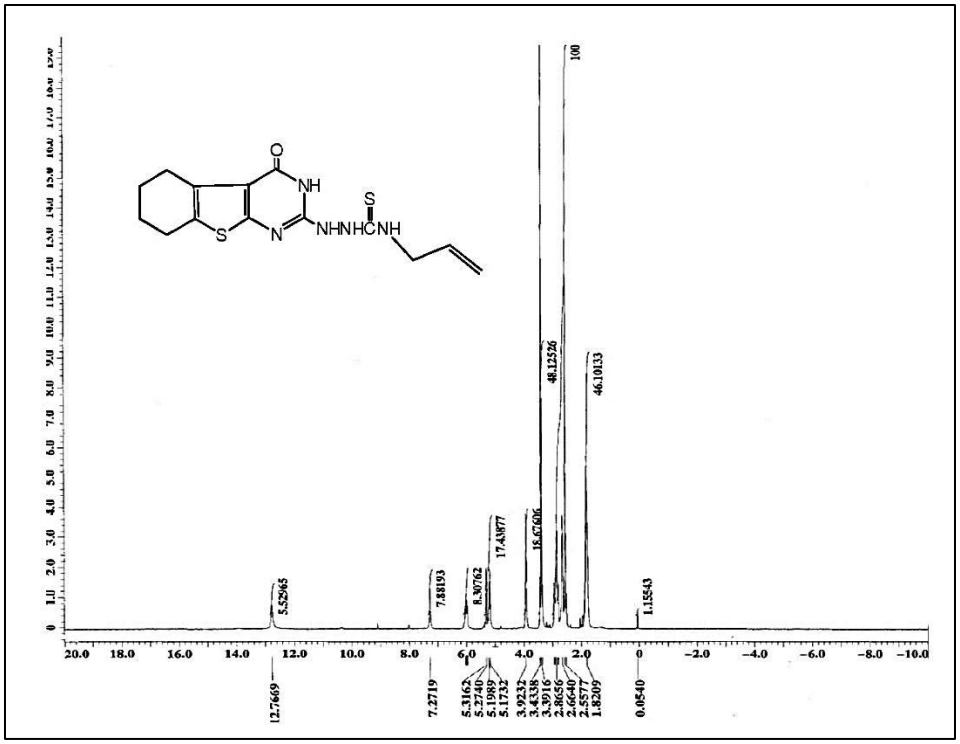


Figure 20: ^{1}H-NMR spectrum of 10_a in DMSO-d_6

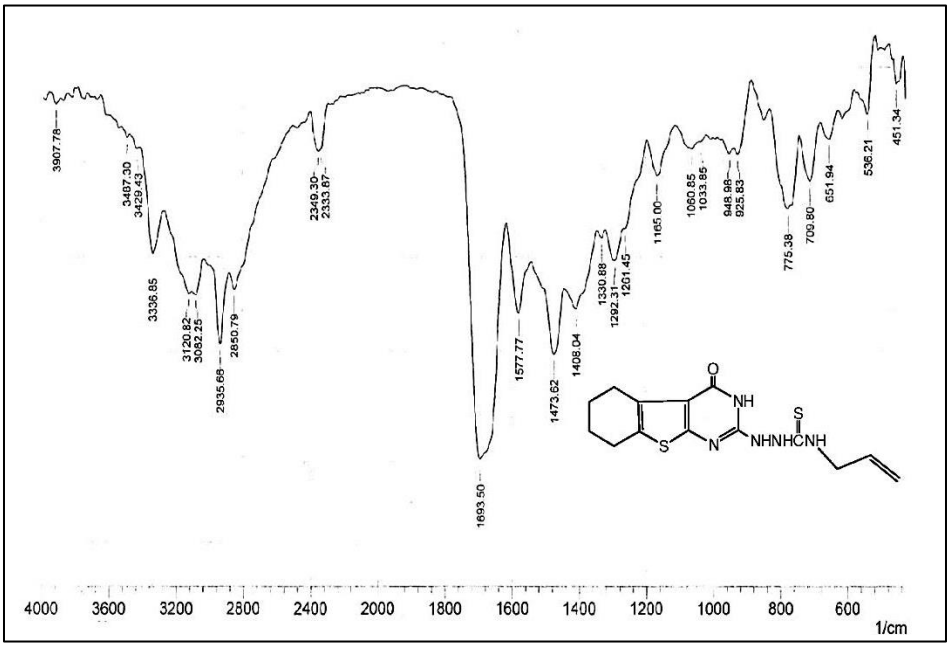


Figure 21: IR spectrum of 10_a in KBr

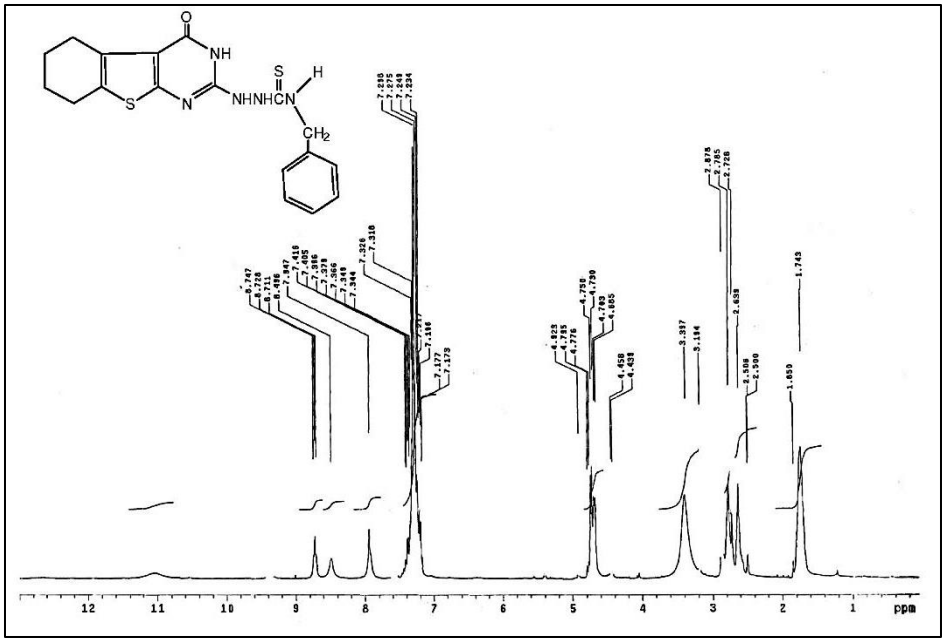


Figure 22: ^{1}H-NMR spectrum of 10_b in DMSO-d_6

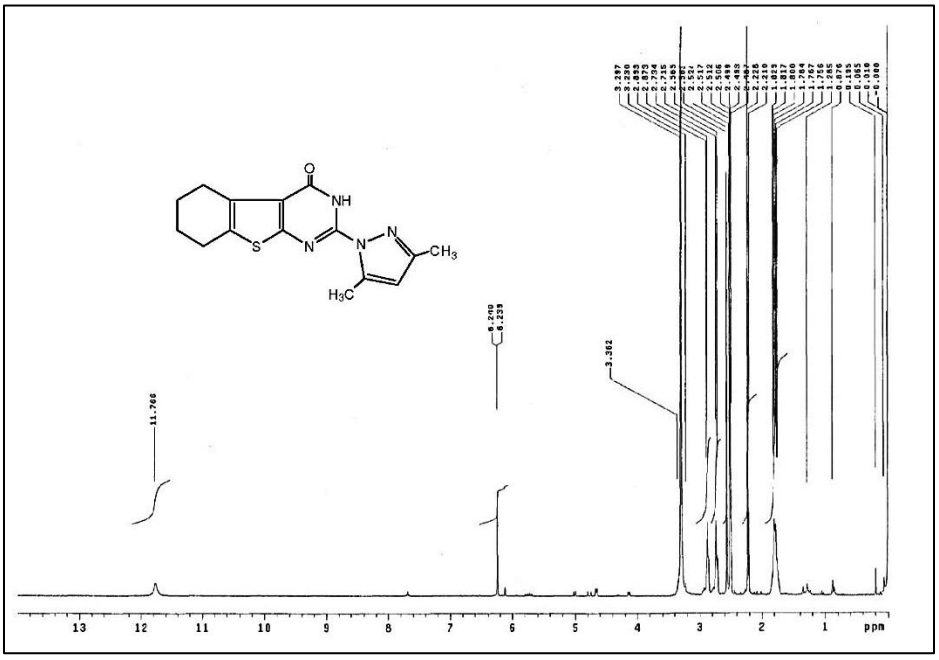


Figure 23: ^{1}H-NMR spectrum of 11 in DMSO-d_6

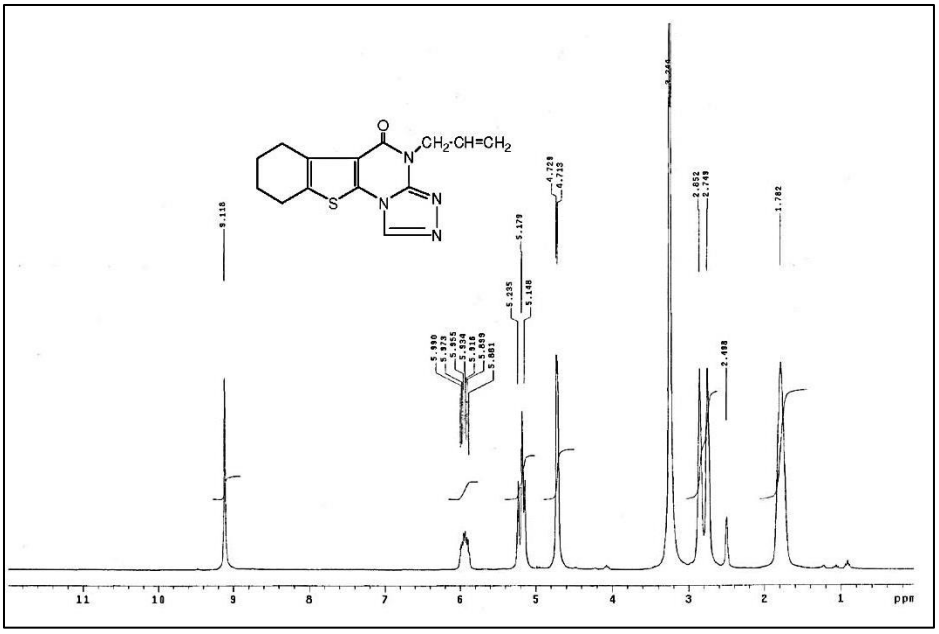


Figure 24: ^{1}H-NMR spectrum of 12 in DMSO-d$_6$

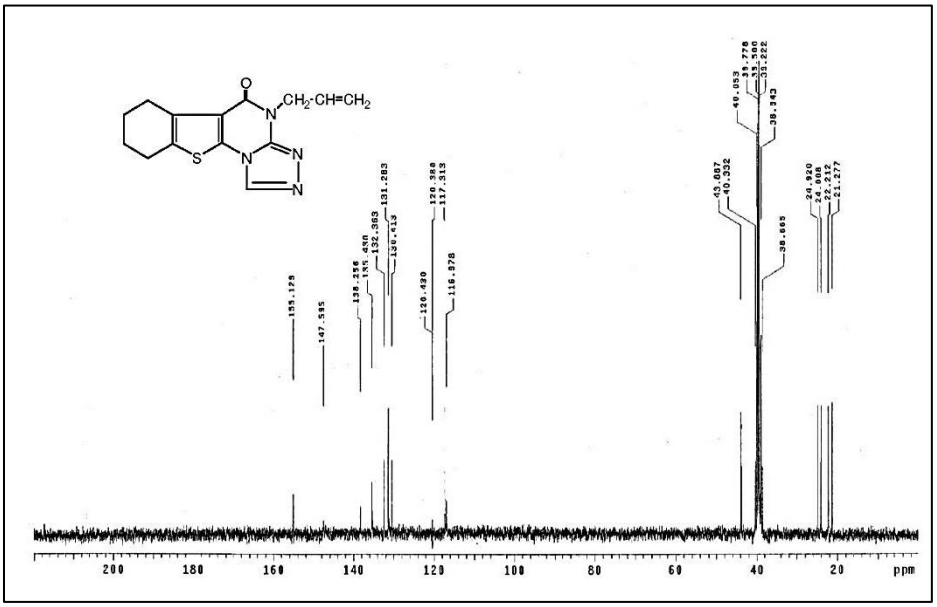


Figure 25: ^{13}C-NMR spectrum of 12 in DMSO-d$_6$

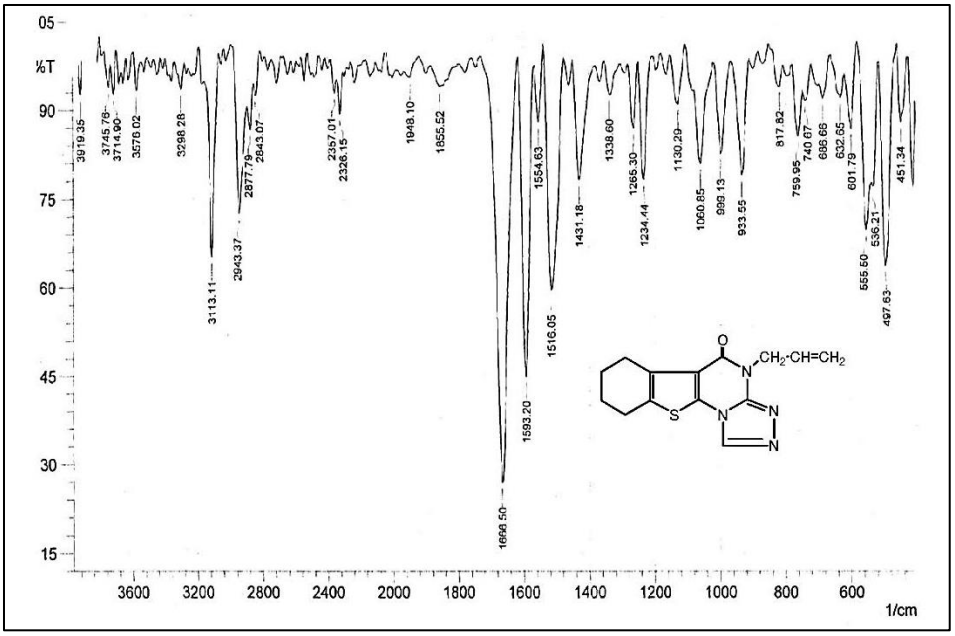


Figure 26: IR spectrum of 12 in KBr

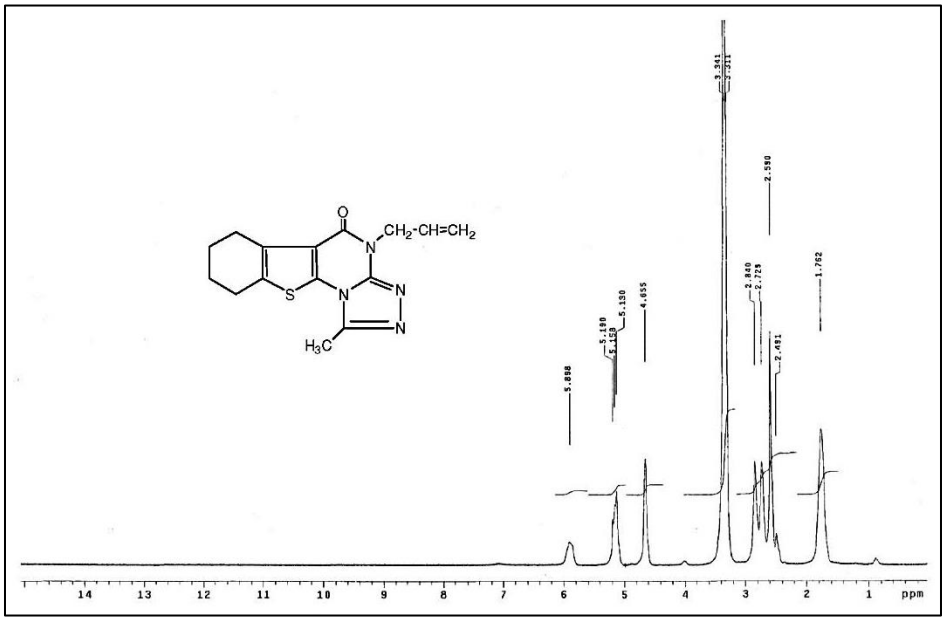


Figure 27: ^{1}H-NMR spectrum of 13 in DMSO-d_6

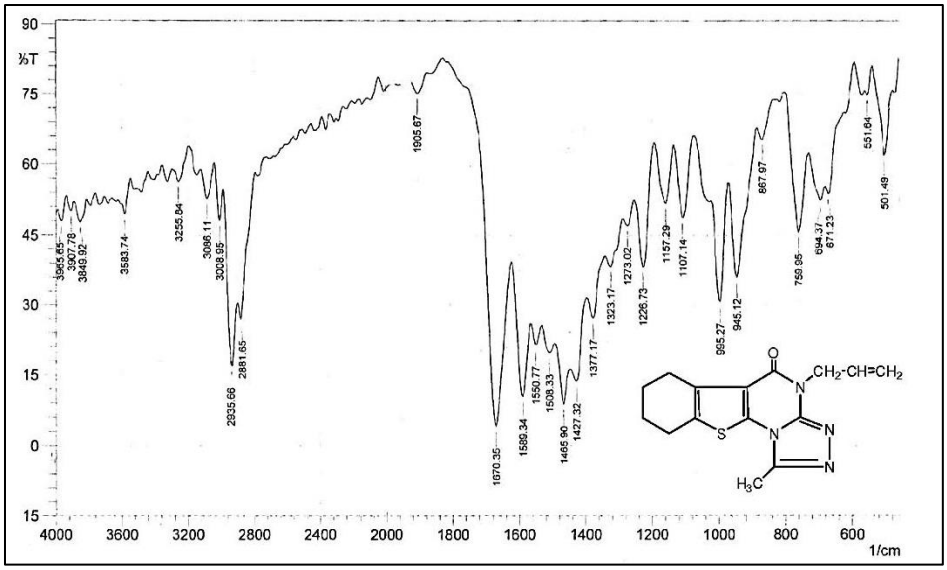


Figure 28: IR spectrum of 13 in KBr

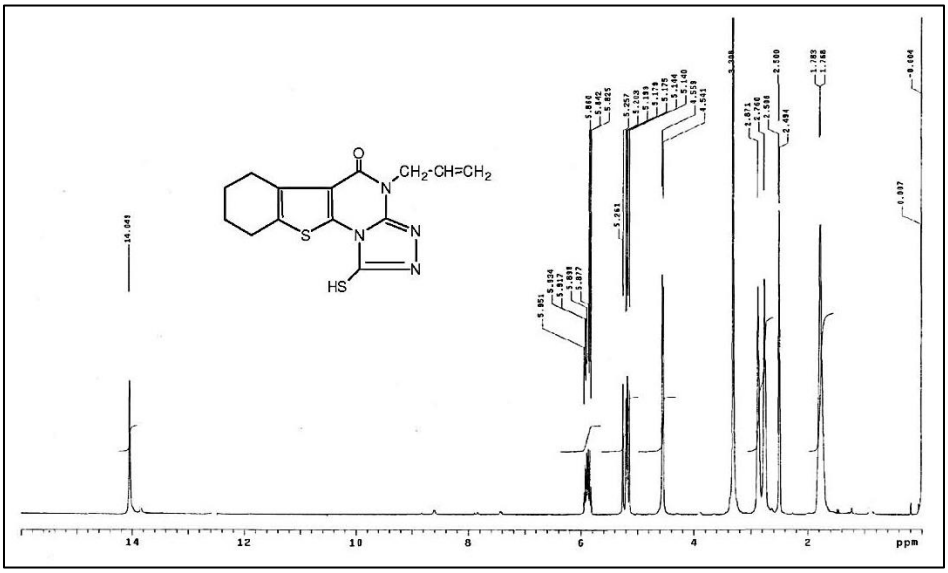


Figure 29: ^{1}H-NMR spectrum of 14 in DMSO-d_6

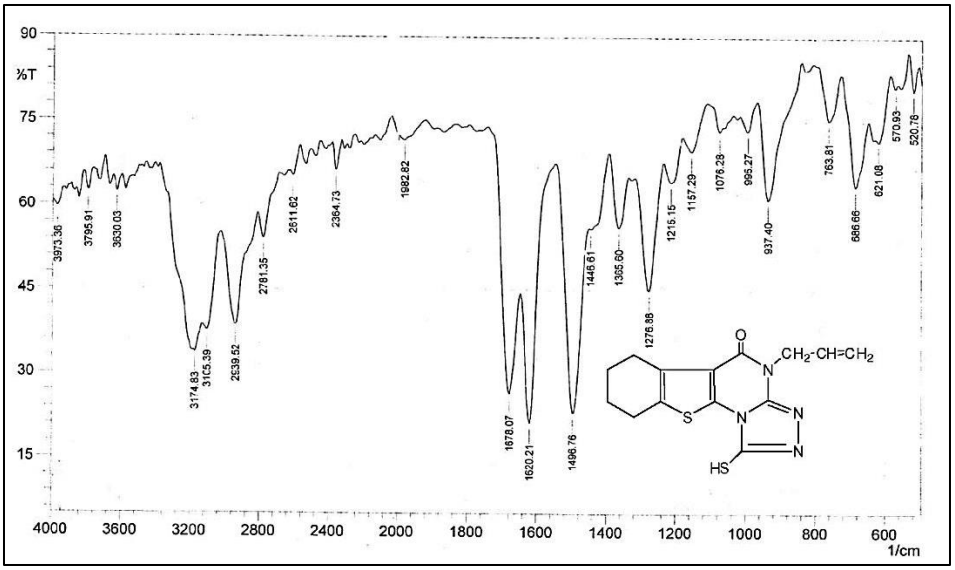


Figure 30: IR spectrum of 14 in KBr

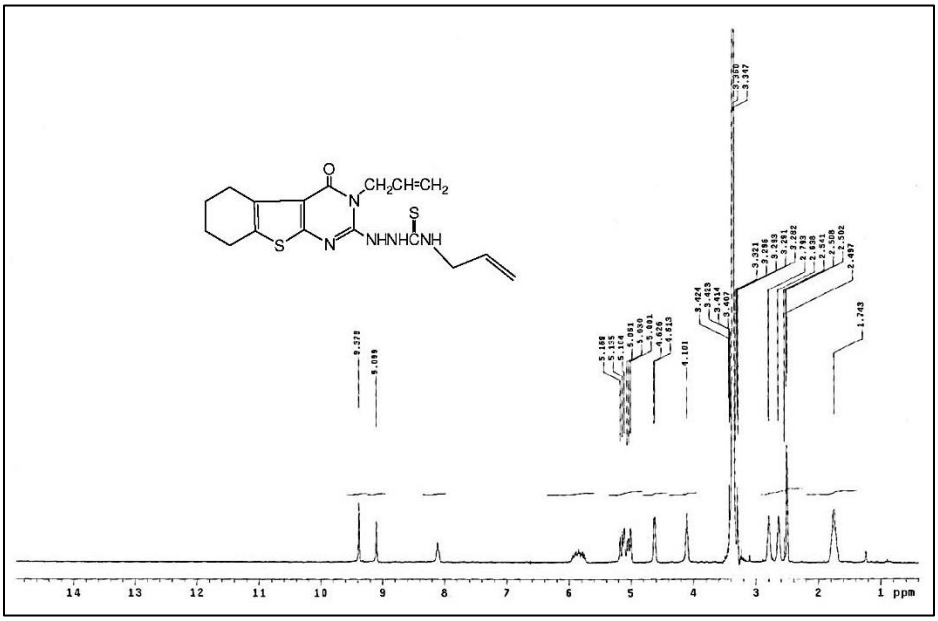


Figure 31: ^{1}H-NMR spectrum of 15$_a$ in DMSO-d$_6$

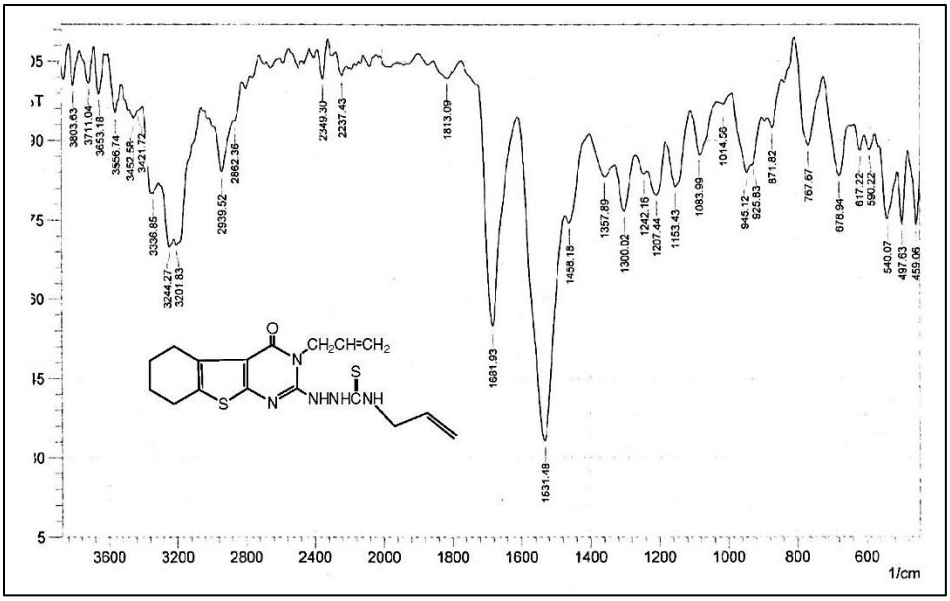


Figure 32: IR spectrum of 15_a in KBr

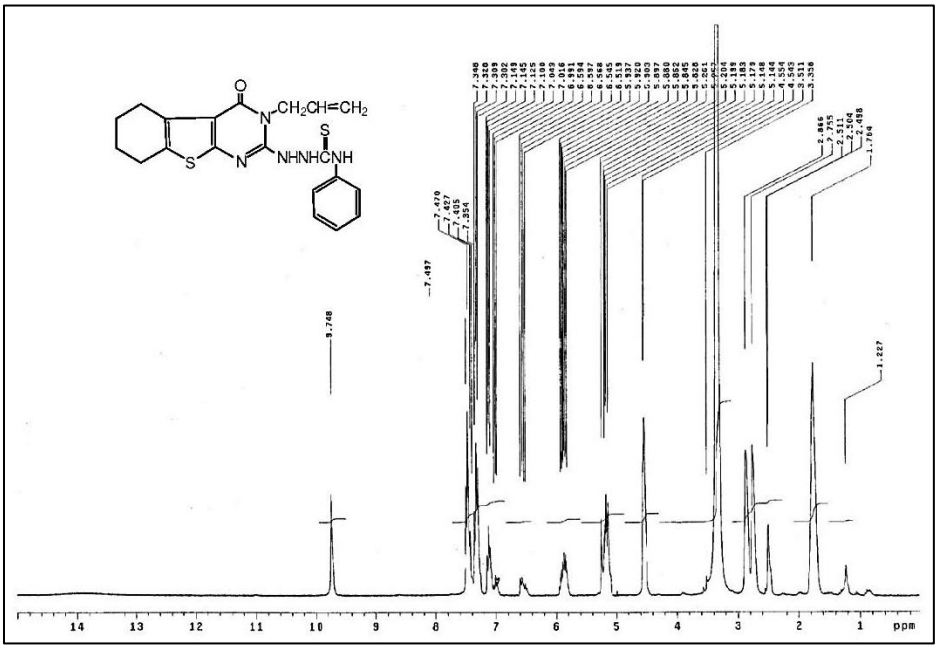


Figure 33: ^{1}H-NMR spectrum of 15_b in DMSO-d_6

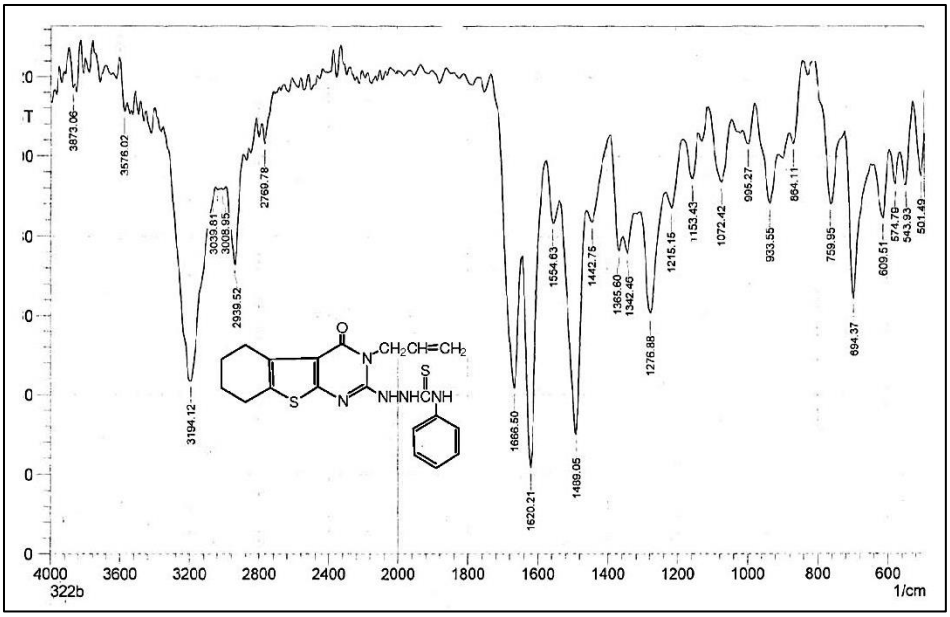


Figure 34: IR spectrum of 15_b in KBr

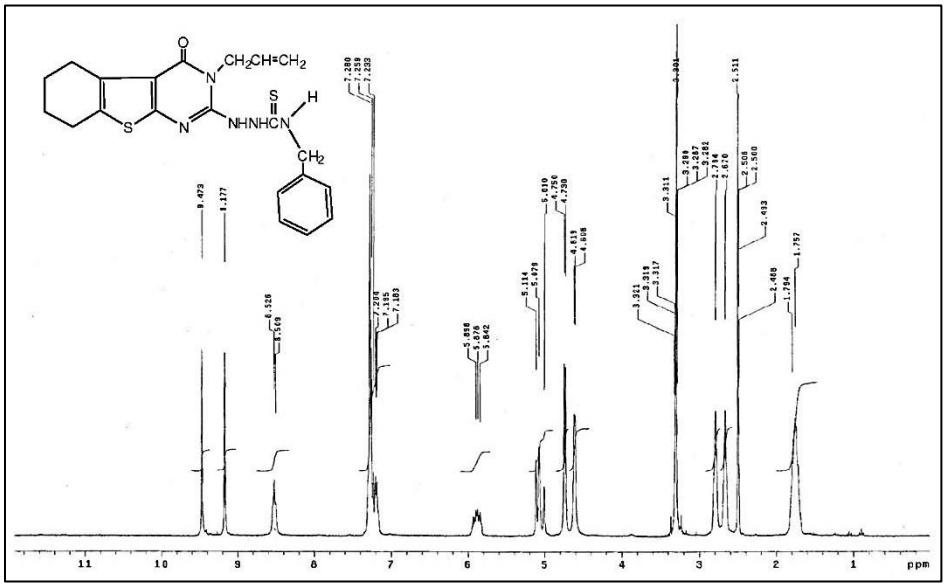


Figure 35: ^{1}H-NMR spectrum of 15_c in DMSO-d_6

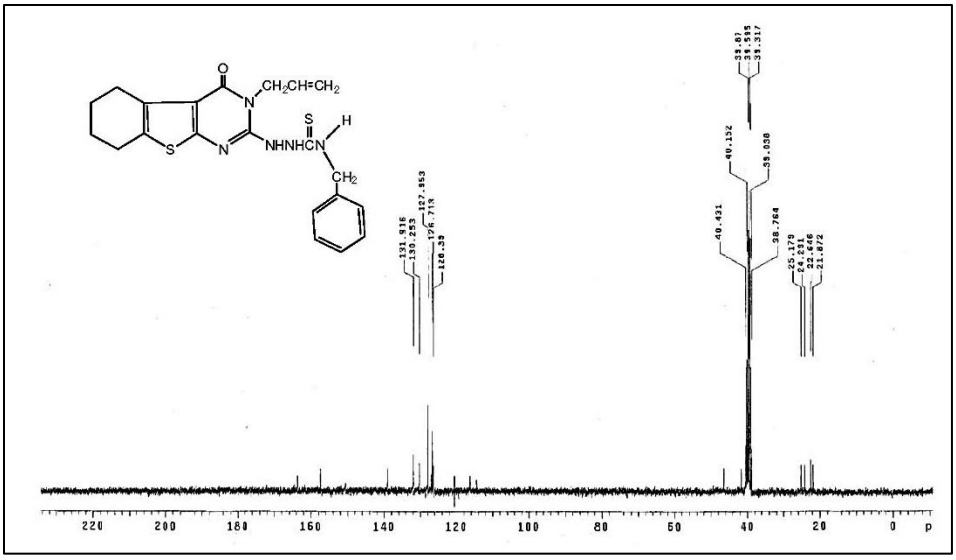


Figure 36: ^{13}C-NMR spectrum of 15c in DMSO-d$_6$

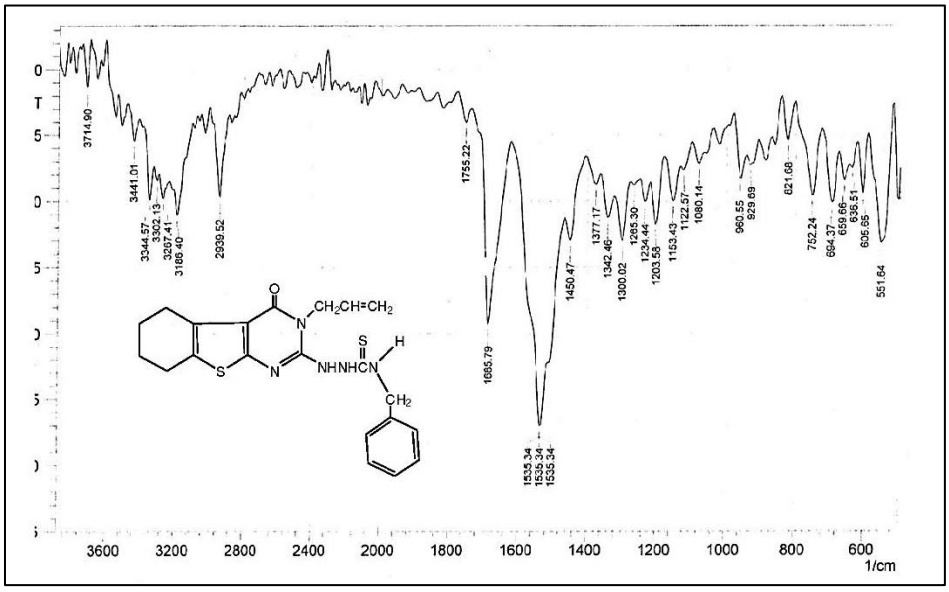


Figure 37: IR spectrum of 15$_c$ in KBr

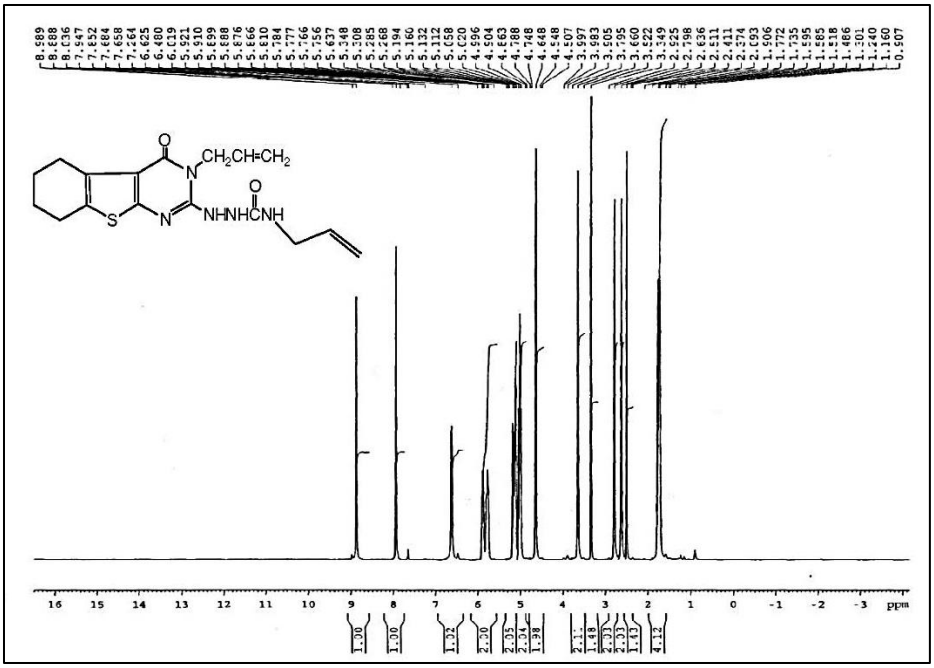


Figure 38: ^{1}H-NMR spectrum of 16$_a$ in DMSO-d$_6$

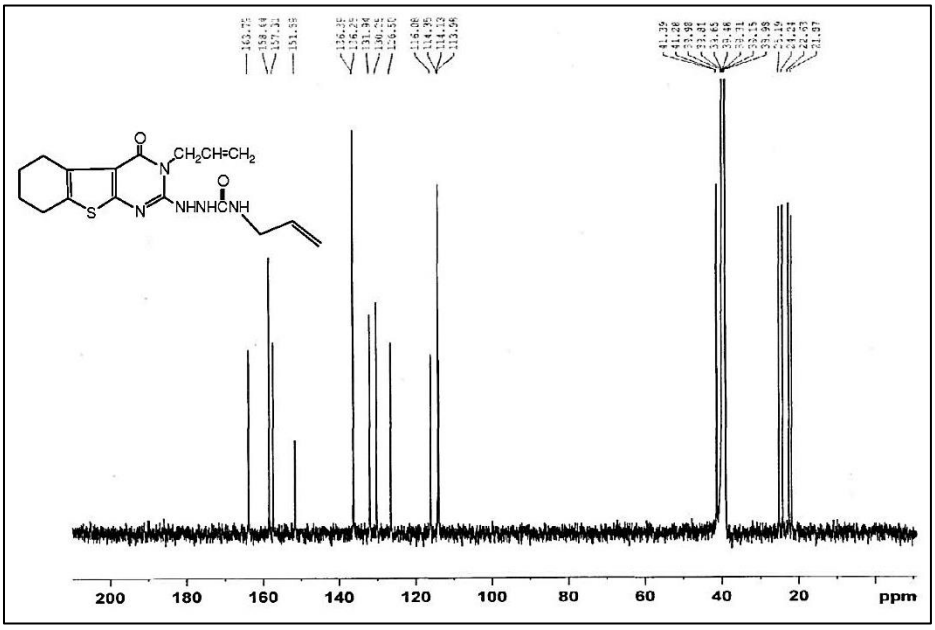


Figure 39: ^{13}C-NMR spectrum of 16$_a$ in DMSO-d$_6$

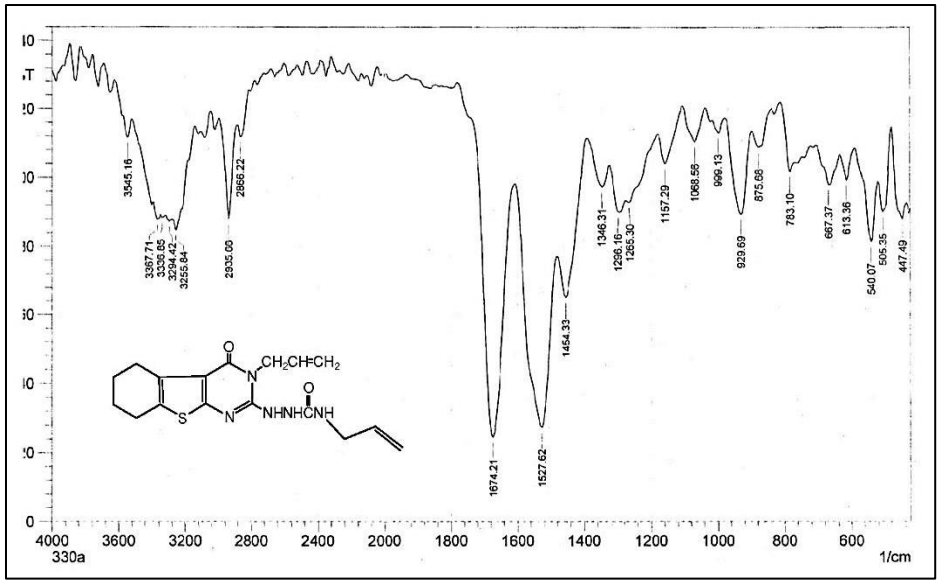


Figure 40: IR spectrum of 16_a in KBr

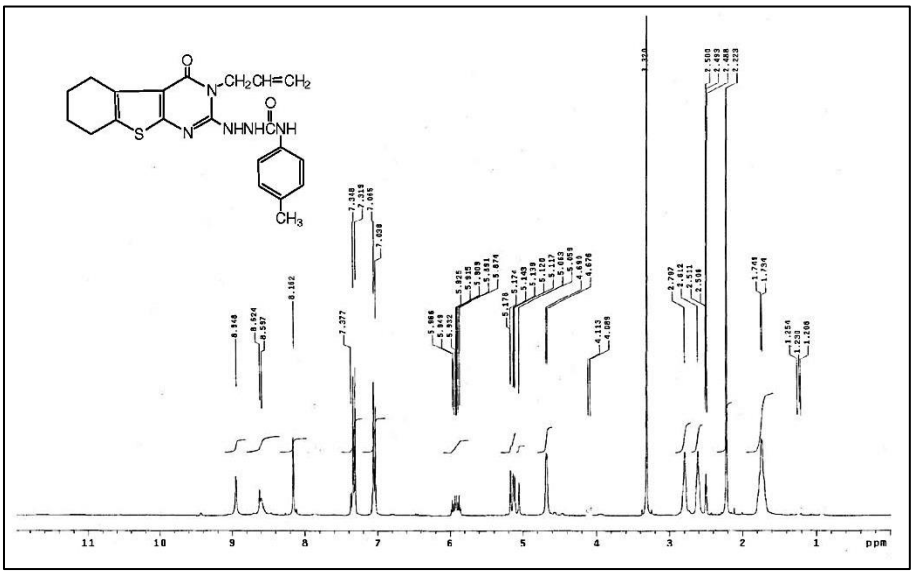


Figure 41: ^{1}H-NMR spectrum of 16_b in DMSO-d_6

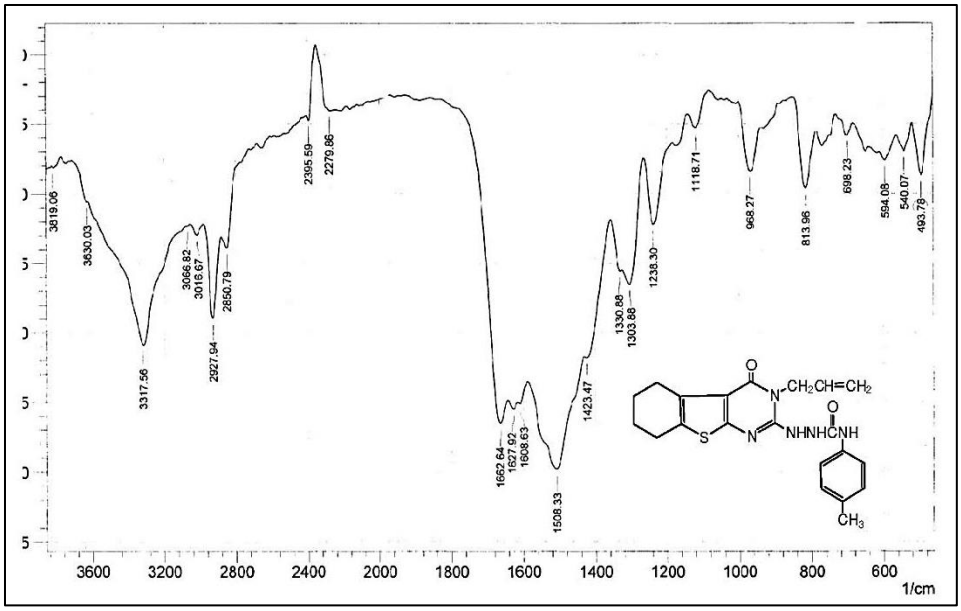


Figure 42: IR spectrum of 16_b in KBr

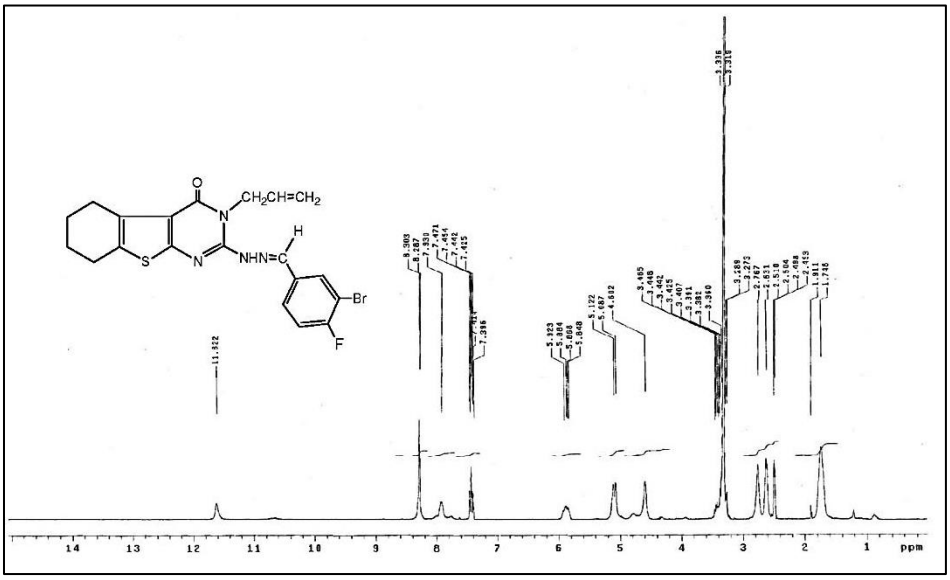


Figure 43: ^{1}H-NMR spectrum of 17_a in DMSO-d_6

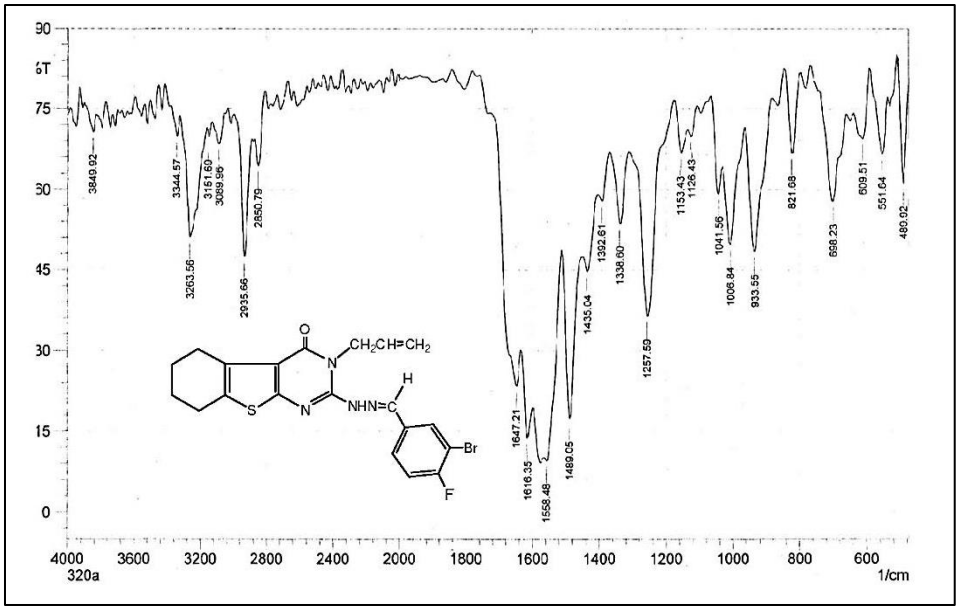


Figure 44: IR spectrum of 17_a in KBr

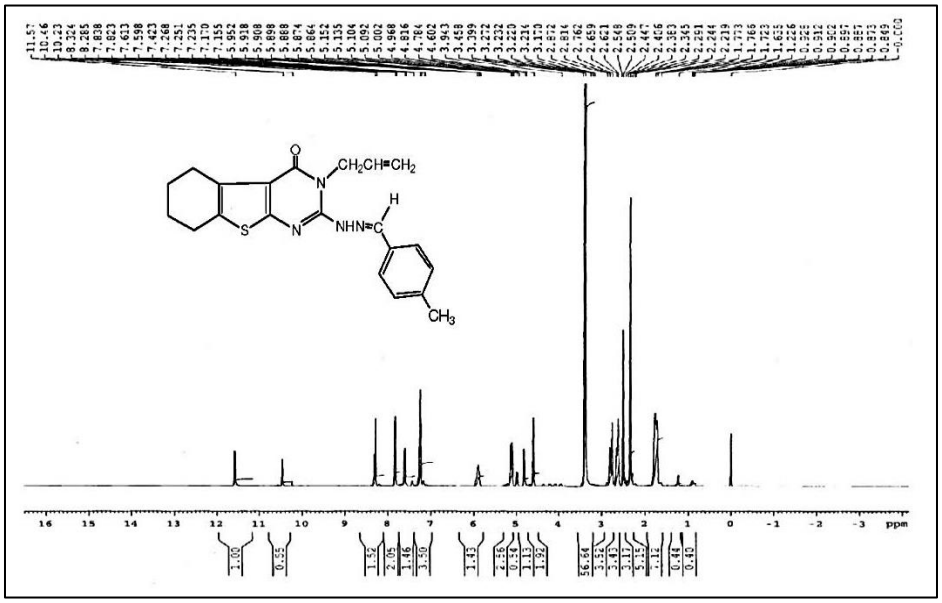


Figure 45: ^{1}H-NMR spectrum of 17_b in DMSO-d_6

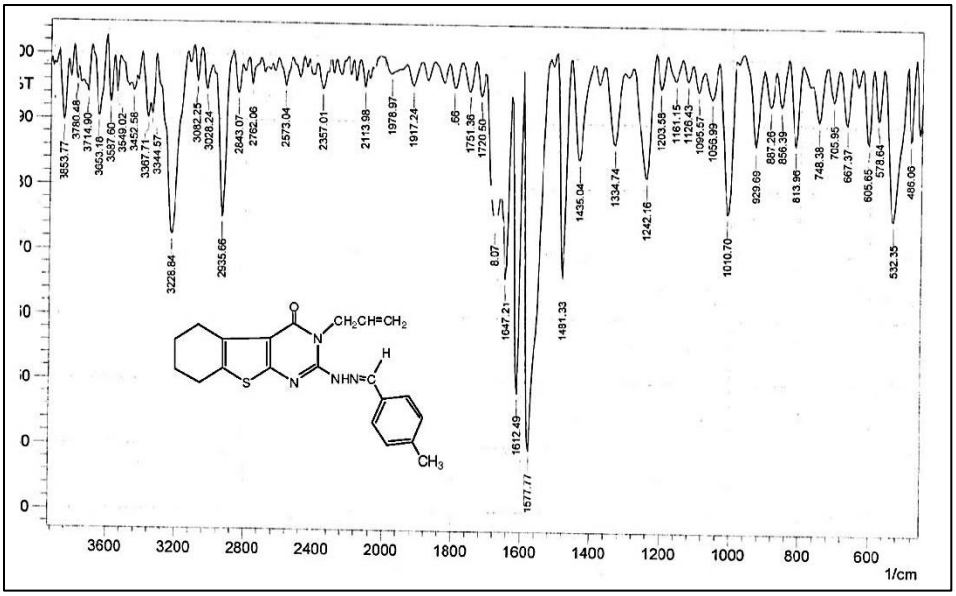


Figure 46: IR spectrum of 17_b in KBr

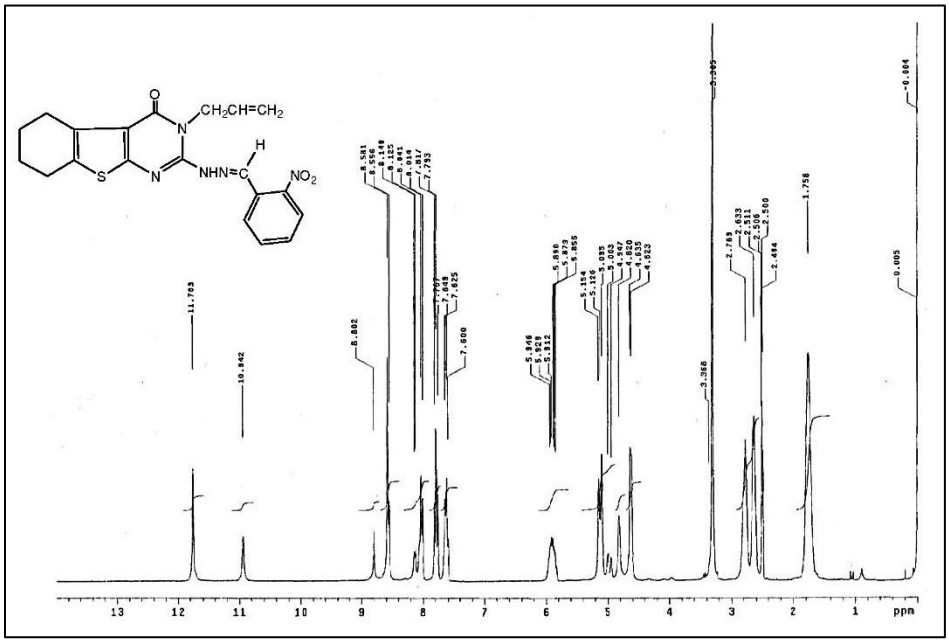


Figure 47: ^{1}H-NMR spectrum of 17_c in DMSO-d_6

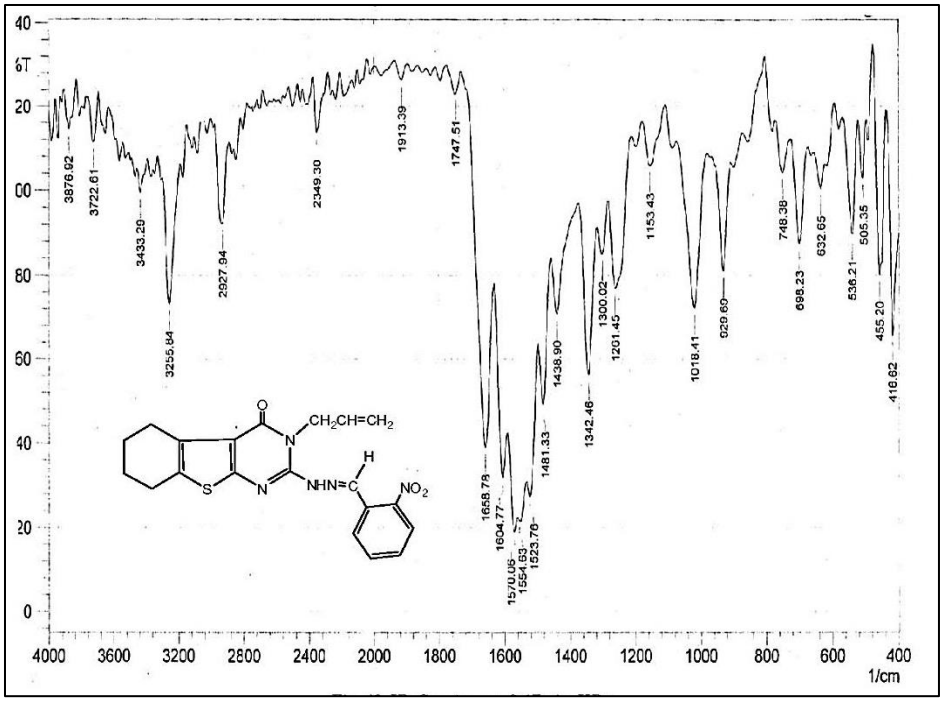


Figure 48: IR spectrum of 17_c in KBr

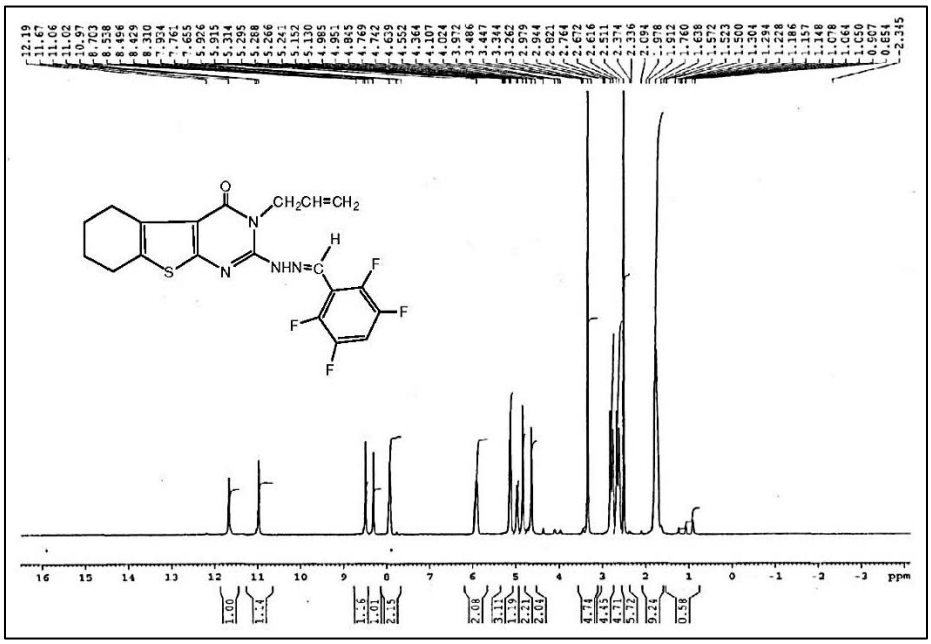


Figure 49: ^{1}H-NMR spectrum of 17_d in DMSO-d_6

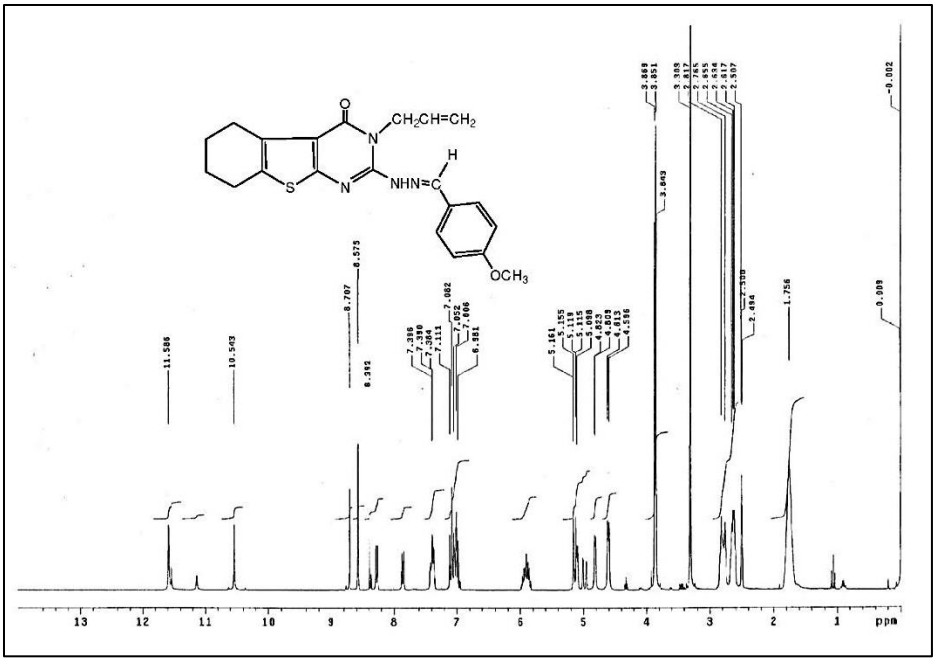


Figure 50: ^{1}H-NMR spectrum of 17$_e$ in DMSO-d$_6$

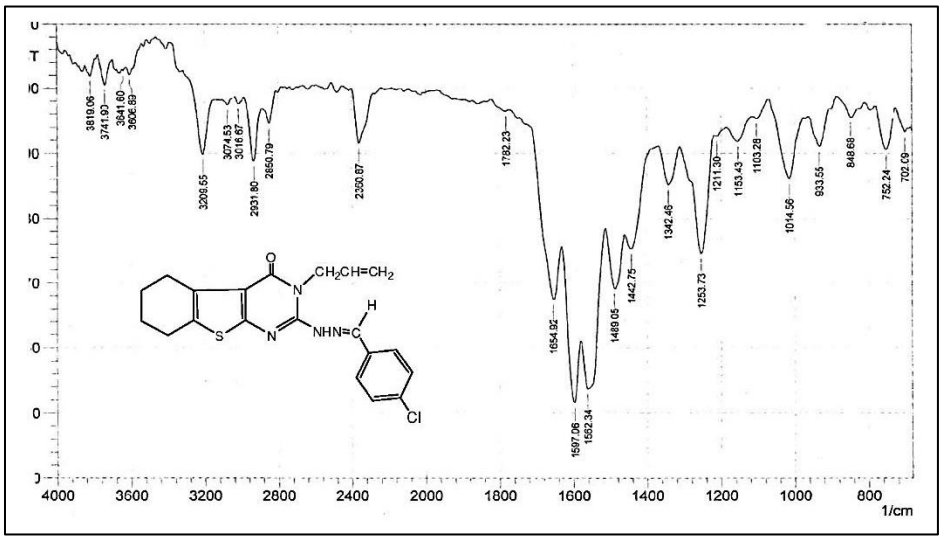


Figure 51: IR spectrum of 17$_e$ in KBr

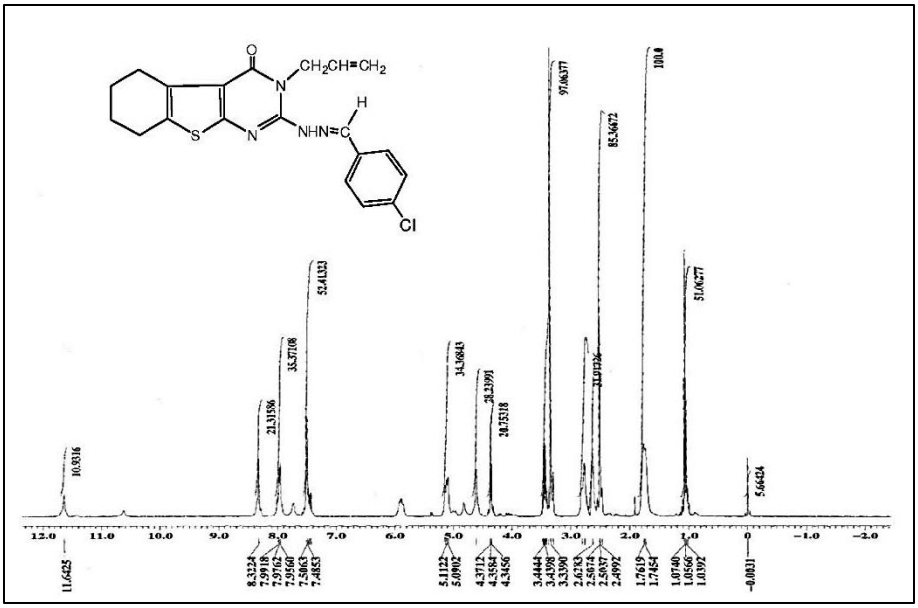


Figure 52: ^{1}H-NMR spectrum of 17$_f$ in DMSO-d$_6$

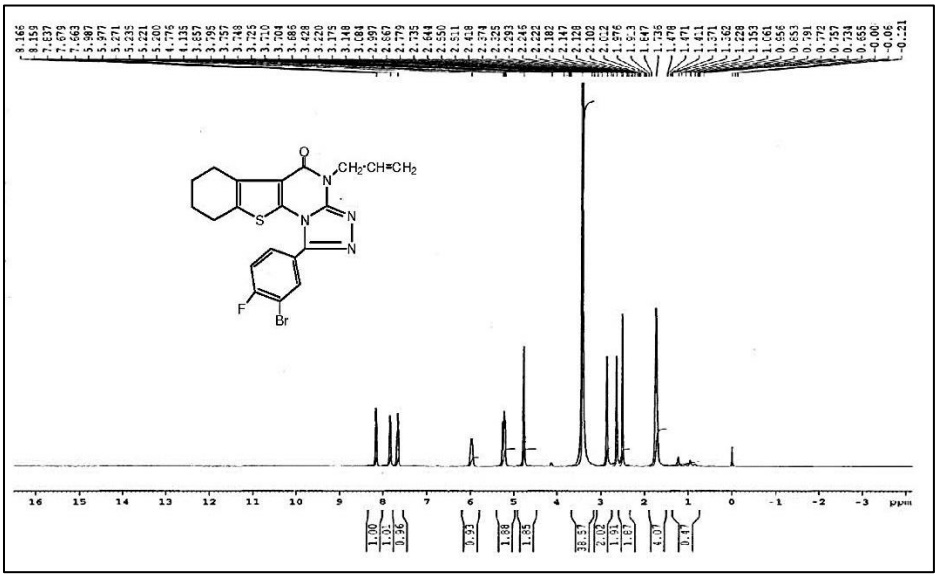


Figure 53: ^{1}H-NMR spectrum of 19 in DMSO-d$_6$

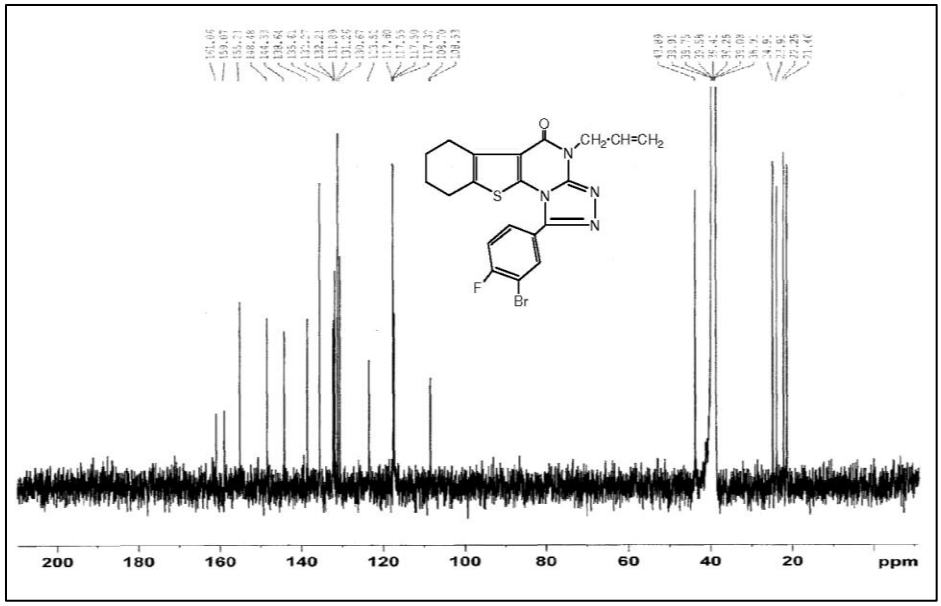


Figure 54: ^{13}C-NMR spectrum of 19 in DMSO-d$_6$

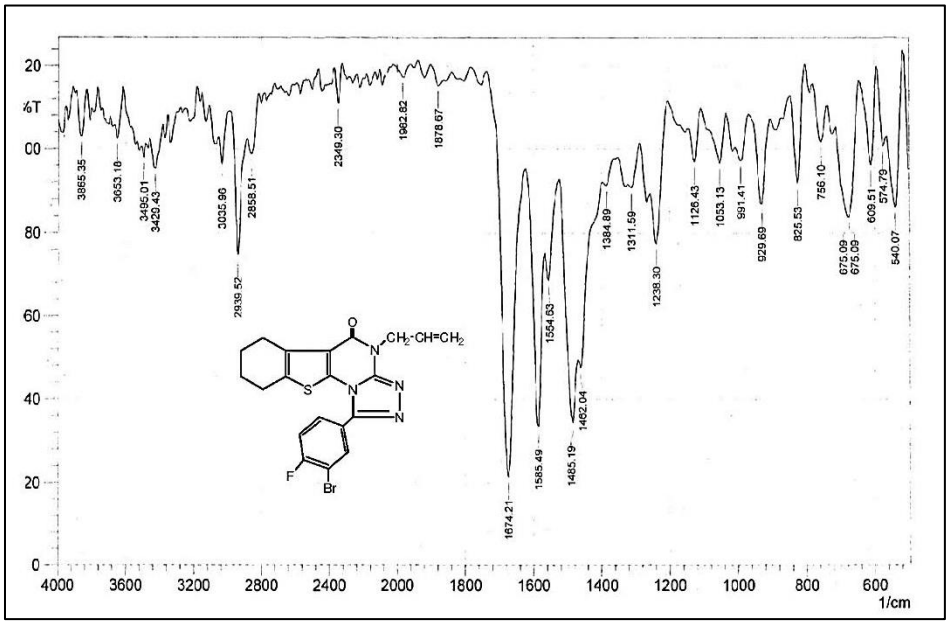


Figure 55: IR spectrum of 19 in KBr

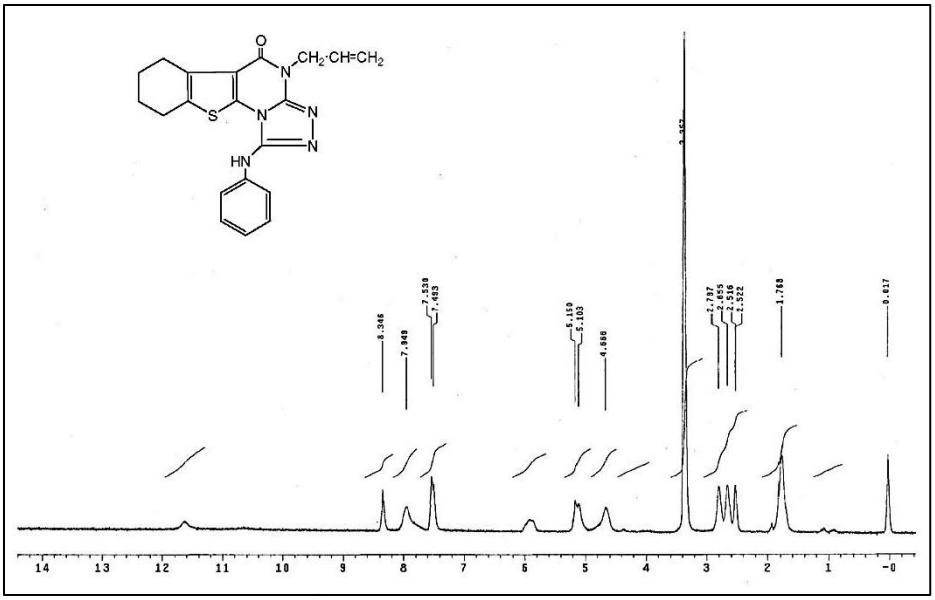


Figure 56: ^{1}H-NMR spectrum of 20$_a$ in DMSO-d$_6$

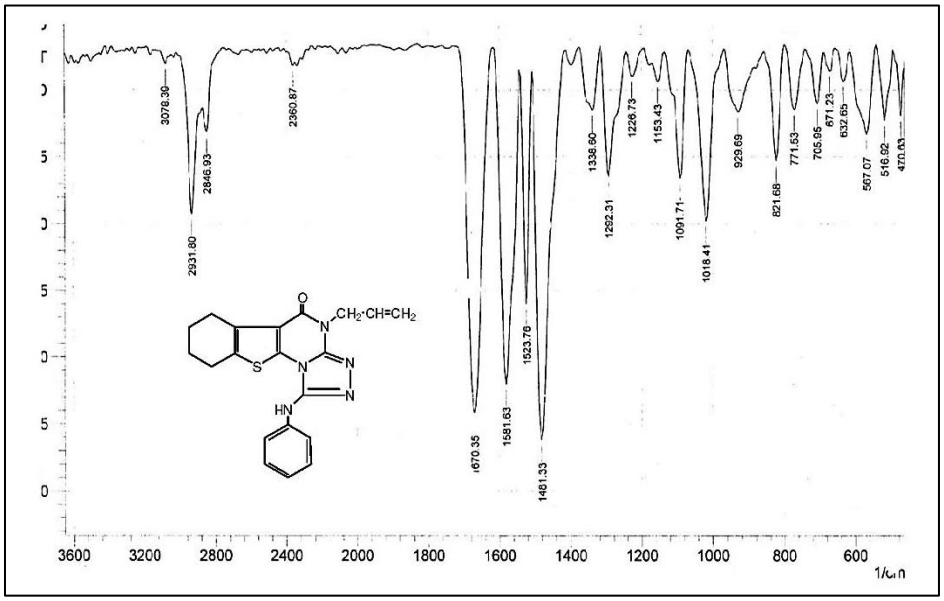


Figure 57: IR spectrum of 20$_a$ in KBr

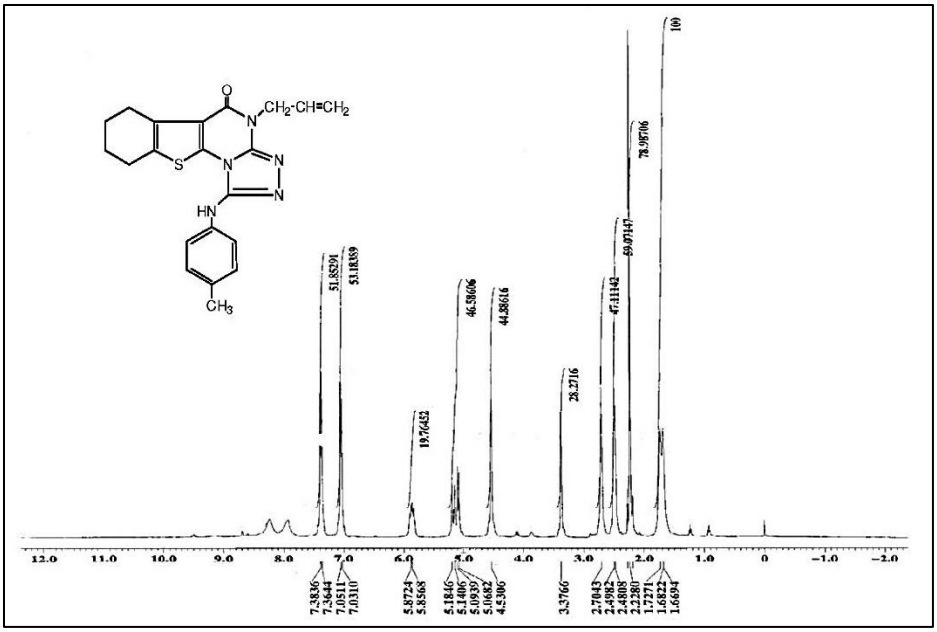


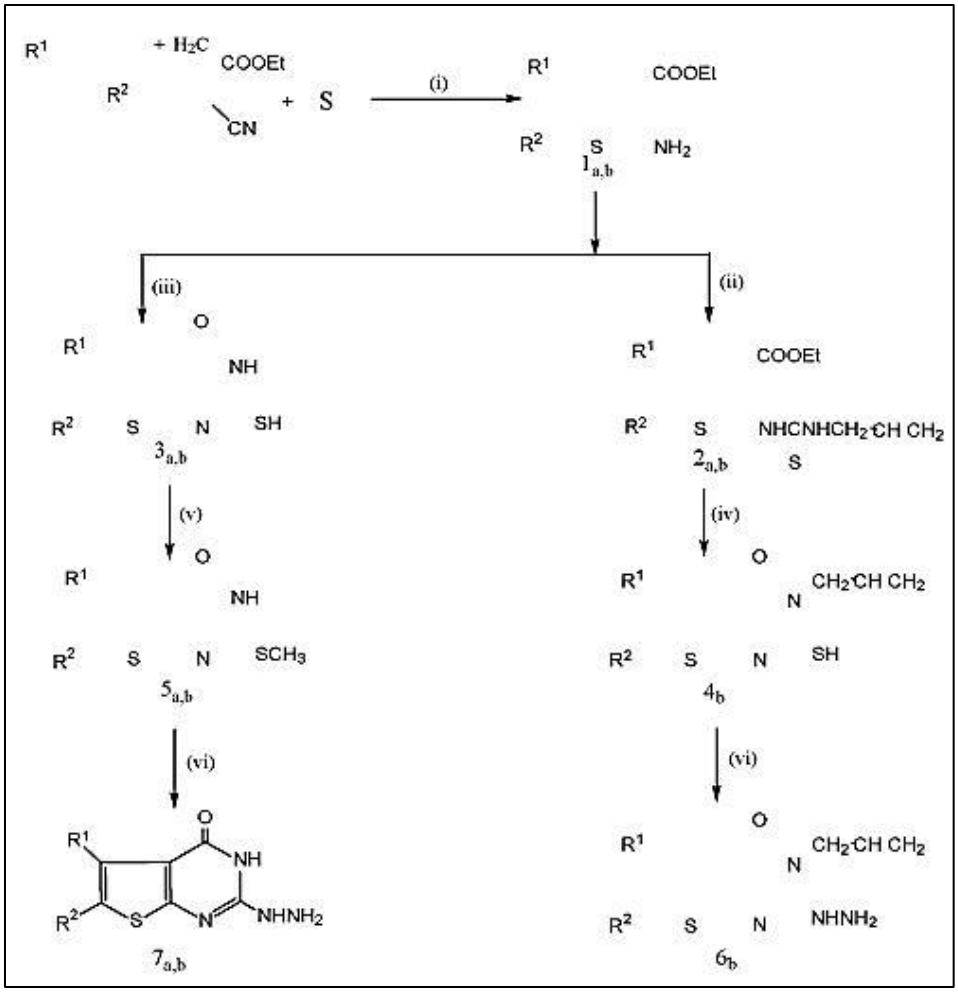
Figure 58: ^{1}H-NMR spectrum of 20_b in DMSO-d_6

RESULTS AND DISCUSSION

The starting enamino ester, Ethyl- 2-amino-4,5-dimethylthiophene-3-carboxylate 1_a and Ethyl- 2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate 1_b are prepared according to *Karel Gewald* procedure [28]. Their reactions with thiourea or potassium thiocyanate in dioxane gave the corresponding thienopyrimidines $3_{a,b}$. Subsequent methylation with dimethylsulphate and aqueous NaOH afforded corresponding 2-methylthio derivatives $5_{a,b}$ which upon nucleophilic displacement of the S*Me* group with hydrazine hydrate furnished the respective hydrazino derivatives $7_{a,b}$. On the other hand, addition of allylisothiocyanate to 2- aminothiophene derivatives $1_{a,b}$ gave the corresponding thiourea derivatives $2_{a,b}$ which are followed by alkaline cyclization with 2N sodium hydroxide to thienopyrimidine 4_b. Subjection of 4_b to hydrazine hydrate resulted in the formation of the 3-allyl-2-hydrazinothienopyrimidin derivative 6_b (Scheme 1). It is necessary to emphasize that the compounds, 1, 3, 5 and 7 were previously synthesized according to literatures [29] and were used for other purposes.

The structure proposal of the prepared compounds was derived from the analytical data (^{1}H NMR, ^{13}C NMR, IR) and satisfactory elemental analyses. For example the most characteristic bands of IR spectrum in KBr appeared in the range $\bar{\upsilon}$ = 1651-1680 cm^{-1} for C=O groups and $\bar{\upsilon}$ = 3201-3303 cm^{-1} corresponding to NH groups. The ^{1}H-NMR spectrum of Ethyl 2-(3-allylthioureido)-4,5-disubstituted thiophene-3-carboxylate ($2_{a,b}$) are in accordance with their structures, The ethyl group for (- $COOCH_2CH_3$) showed two bands, the first appeared as triplet at δ = 1.32 ppm with coupling constant *J* = 7.3 Hz and integration equal to 3 protons for (-CH_3), the second displayed as quartet at higher chemical shift δ = 4.30 ppm with coupling constant *J*=7.2 Hz and integration equal to 2 protons for (- CO-CH_2-) group, as they deshielded with oxygen atoms, the other two remaining methyl groups of compound 2_a displayed as two singlet peaks at δ = 2.18, 2.19 ppm. Compound 2_b showed three broad bands at δ = 1.71, 2.56, 2.72 ppm for 4H, 2H, and 2H respectively, while its allyl group in N-3 position displayed as follow: δ = 4.25 (m, 2H, NCH_2), 4.29 (q, 2H, *j*= 7.1 Hz, CH_2), 5.20 (dd, 1H, J_{cis}=10.5 Hz, 3'-H_a), 5.24 (dd, 1H, J_{trans} = 17.1 Hz, 3'-H_b), 5.88(m, 1H, 2'-H), in addition of two singlet peaks at δ = 9.57, 11.52 ppm for 2 NH groups. The mass spectra exhibited ion molecular peak [M^+] at m/z = 324 corresponding to molecular formula [$C_{15}H_{20}N_2O_2S_2$] of compound 2_b.

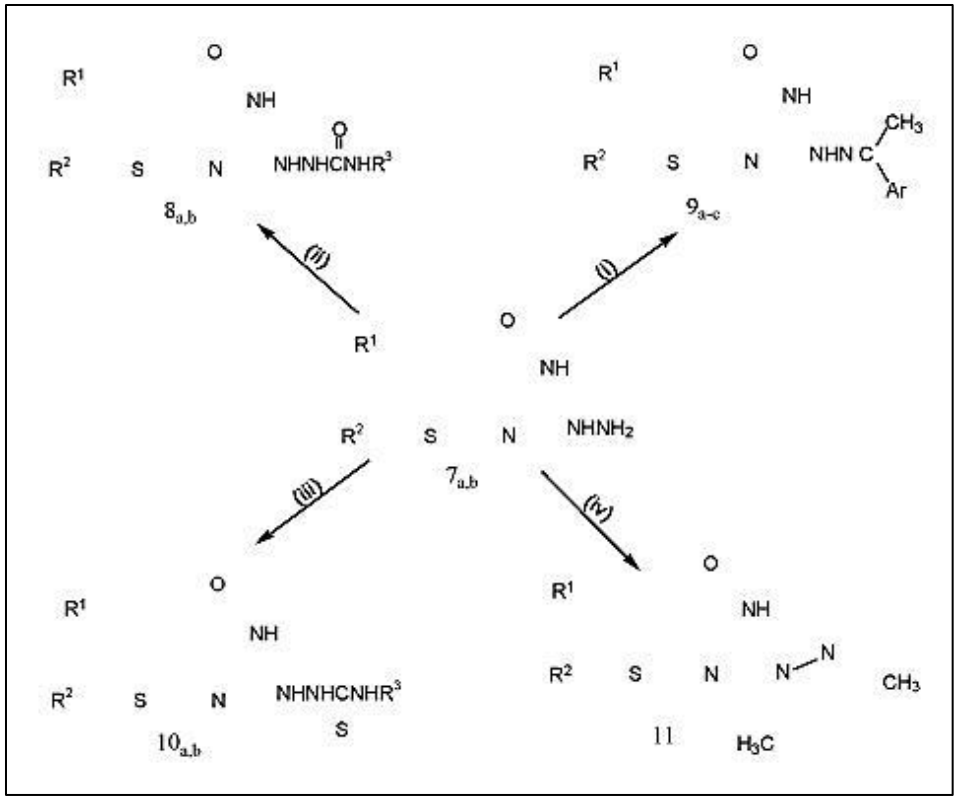
The ^{1}H-NMR spectrum of 3-Allyl-2-mercapto-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3- d]pyrimidin-4-one 4_b showed three multiplet bands at δ = 1.80, 2.77, 2.86 ppm for 4H, 2H, and 2H respectively while its allyl group in N-3 position appeared at δ = 4.57 (bd, 2H, NCH_2), 5.31 (bm, 2H, 3'-H_a, 3'-H_b), 5.91 (bm, 1H, 2'-H_b), beside one band at δ = 14.08 ppm for NH group and its molecular ion peak[M^+] at m/z = 278 corresponding to formula [$C_{15}H_{20}N_2O_2S_2$].



Reagents and conditions: i)Morpholin, EtOH, 60°C; ii)CH_2=CH-CH_2NCS, EtOH, Δ; iii)KSCN, dioxan, EtOH, HCl, Δ; iv)NaOH(aq.), Δ, HCl; **v)** NaOH(aq.),$(CH_3)_2SO$; **vi)** $NH_2NH_2.H_2O$, EtOH, Δ.

Scheme 1: 3-allyl-2-hydrazinothienopyrimidin derivative

The resulted data of ^{1}H-NMR spectrum of starting materials 3-Allyl-2-hydrazino-5,6,7,8-tetrahydro- 3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (6_b) showed three multiplet bands at δ = 1.74, 2.61, 2.80 ppm for 4H, 2H, and 2H respectively in addition of allyl group bands at δ = 4.58 (m, 2H, NCH_2), 4.98 (dd, 1H,J_{cis}=10.3 Hz, 3'-H_a), 5.11 (dd, 1H, J_{trans} = 17.2 Hz, 3'-H_b), 5.83 (m, 1H, 2'-H) beside bands of hydrazino group at δ = 4.35, 8.23 ppm corresponding to (2H) and (1H). Starting materials 2-hydrazinyl-5,6-disubstitutedthieno[2,3-d]pyrimidin-4(3H)-one ($7_{a,b}$) condensed with various one–carbon donors, for instance, they reacted with isocyanates and isothiocyanates to provide the corresponding semi and thiosemicarbazides $8_{a,b}$ and $10_{a,b}$ respectively. Condensation of $7_{a,b}$ with acetophenone derivatives in the presence of few drops of acetic acid furnished the corresponding hydrazones 9_{a-c}. Starting compound 7_b condensed with 2,4-pentadione resulted in the formation of the corresponding pyrazole derivative 11 in good yield (Scheme 2). The constitution of the prepared compounds was secured by their NMR, IR, and MS spectra, for instance, ^{1}H-NMR spectrum of 8_a showed three bands at δ = 1.75, 2.65, 2.70 ppm for 4H, 2H, and 2H respectively besides five protons of phenyl group appeared in three bands δ = 6.96, 9.22, 11.80, 12.02 ppm corresponding to four NH group. Acetophenone hydrazone compounds 9_{a-c} showed absorbance in IR spectra at ν = 1662-1668 cm^{-1} for stretching C=O group and absorbance peak at ν = 3228-33.77 cm^{-1} for NH group.^{1}H-NMR spectrum of 9_a displayed three bands at δ = 1.77, 2.52, 2.82 ppm for 4H, 2H, and 2H respectively besides one singlet band at δ = 2.32 ppm for methyl group, in addition to five protons of phenyl group appeared in the range δ = 7.43-8.0 ppm while the protons of NH group resonate at δ = 10.62, 10.91 ppm, the structure is finally mass spectra showed molecular ion peak[M^+] at m/z = 338 closed with formula [$C_{18}H_{18}N_4OS$].



Comp.	R1 R2	R3	Ar
8a	$(CH_2)_4$	C_6H_5	-----
8b	$(CH_2)_4$	$CH_2CH_2CH_3$	-----
9a	$(CH_2)_4$	-----	C_6H_5
9b	$(CH_2)_4$	-----	4–Cl–C_6H_4
9c	CH_3 CH_3	-----	4–Cl–C_6H_4
10a	$(CH_2)_4$	$CH_2CH{=}CH_2$	-----
10b	$(CH_2)_4$	CH_2–C_6H_5	-----
11	$(CH_2)_4$	-----	-----

Reagents and conditions: i) $ArCOCH_3$, EtOH, Δ; ii) R^3NCO, EtOH, Δ; iii) R^3NCS, EtOH, Δ; iv) $(CH_3CO)_2$ CH_2, Δ.

Scheme 2: Pyrazole derivative

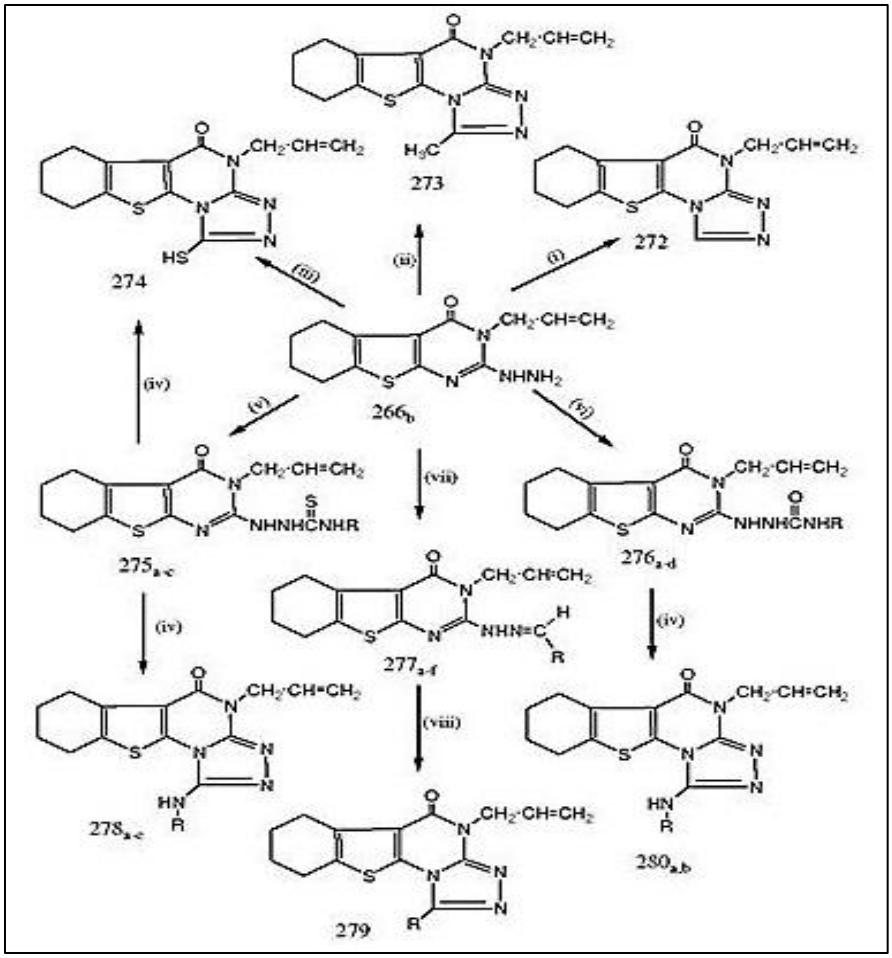
Similarly ^{1}H-NMR spectrum of 9_b exhibited three bands at δ = 1.78, 2.66, 2.76 ppm for 4H, 2H, and 2H respectively besides one singlet band at δ = 2.32 ppm for methyl group, in addition to four protons of phenyl group showed two doublet bands in model AA' XX' at δ = 7.46 ppm for (H- 2', H-6') with coupling constant *J* = 8.6 Hz, the other two aryl protons (H-3', H-5') appeared at δ = 8.05 ppm, *J* = 8.6 Hz, the remaining two protons for NH group showed two singlet bands at δ = 10.65, 11.01 ppm, the structure also confirmed by The ^{13}C-NMR spectrum measured in DMSO-d_6 showed all 18 carbons of compound 9_b, one absorption band at δ = 14.5 for CH_3 group, and three bands at δ = 22.1, 23.3, 24.8, 25.9 corresponding to ($4CH_2$) groups in addition of four bands for thiophene ring at δ = 111.27, 117.01, 127.21, 134.29, while the aryl carbons appeared at δ = 114.14, 119.88, 128.98, 130.98 ppm. In addition of three absorption bands at δ = 148.85, 150.74, 159.13 corresponding to (2C=N) and (C=O) respectively. Finally mass spectra showed molecular ion peak [M^+] at m/z = 372 closed with formula [$C_{18}H_{17}ClN_4OS$].

^{1}H-NMR spectrum of 9_c displayed three bands at δ = 2.28, 2.30, 2.35 ppm for 3 methyl groups, beside absorption doublet bands at δ = 7.48, 8.06 with coupling constant *J* = 8.6 Hz corresponding to 4 protons of aryl group, in addition of two bands at δ = 10.65, 11.03 ppm for 2NH group. The structure also confirmed with ^{13}C-NMR spectrum which showed all 16 carbons of compound 9_c, it gave three absorption bands at δ = 12.71, 13.31, 14.50 ppm for $3CH_3$ groups, while the absorption bands of thiophene carbons appeared at δ = 111.27, 119.06, 128.06, 136.92 ppm in addition of four absorption bands of aryl carbons appeared at δ = 114.14, 117.18, 128.61, 128.74 ppm. Furthermore three bands at δ = 150.75, 158.37, 159.52 corresponding to (2C=N) and (C=O) respectively, also

mass spectra showed molecular ion peak [M^+] at m/z = 346 identical with formula [$C_{16}H_{15}ClN_4OS$]. For thiosemicarbazide compounds $10_{a,b}$ showed IR absorption $\bar{\upsilon}$ = 1693 cm^{-1} for C=O groups and absorption peaks around $\bar{\upsilon}$ = 3120, 3336 cm^{-1} for NH groups. The resulted data of ^{1}H-NMR spectrum of 10_a showed three multiplet bands at δ = 1.82, 2.66, 2.86 ppm for 4H, 2H, and 2H respectively in addition of one band at δ = 4.92 for NCH_2 group while protons of allyl appeared as follow: δ = 5.17 (dd, 1H, J_{cis}=10.0 Hz, 3'- Ha), 5.31(dd, 1H, J_{trans}= 17.3 Hz, 3'- Hb), 6.06 (m, 1H, 2'-H), the protons of 4NH groups resonate at δ = 7.27, 8.21, 9.30, 12.77 ppm.
The resulted data of ^{1}H-NMR spectrum of 10_b showed three multiplet bands at δ = 1.85, 2.64, 2.88 ppm for 4H, 2H, and 2H respectively in addition of one broad band at δ = 4.75 for NCH_2 group while protons of aryl group appeared multiplet around δ = 7.27 ppm. In addition of four bands for NH appeared at δ = 7.41, 8.49, 8.79 and 11.25 ppm.
For compound 11 showed its ^{1}H-NMR spectrum showed three multiplet bands at δ = 1.83, 2.72, 2.89 ppm for 4H, 2H, and 2H respectively in addition of two singlet bands at δ = 2.32 and 2.56 ppm for 2 CH_3 groups in addition of two protons of pyrazole ring absorbed at δ = 6.24 ppm in addition of other absoprption band at δ = 11.77 ppm for one proton of NH group. See experimental part.

Synthesis of Triazolo-thienopyrimidine Derivatives

Starting material 3-Allyl-2-hydrazino-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (6_b) condensed with various one–carbon donors such as acetic acid, formic acid, triethylorthoformate, isothiocyanates, isocyanates, carbondisulphide and aldehydes to give poly condensed triazolo-thienopyrimidine derivatives. For instance, treatment of the hydrazino compound 6_b with formic acid or triethylorthoformate gave exclusively the product angular triazolo-thienopyrimidine (272), since N-3 is blocked by allyl group, while it reacted with glacial acetic acid or triethylorthoacetate to provide methyl substituted triazolo- thienopyrimidine derivative (273), while 6_b refluxed with alcoholic solution of carbon disulphide in the presence of pyridine resulted in the formation of mercaptotriazolo- thienopyrimidine (274). Addition of isocyanates and isothiocyanates to starting material (6_b) provide the corresponding semi and thiosemi-carbazides 276_{a-d} and 275_{a-c} respectively. An expected cyclization of semi-carbazide derivatives take place upon treatment of compounds 276_{a-d} with a solution of NaOH (2N) to provide amino-triazolothienopyrimidines $270_{a,b}$, while treatment of thiosemi-carbazode with NaOH (2N) didn't provide an expected cyclization, all derivatives gave mercaptotriazolo-thienopyrimidine (274). Condensation of 266_b with aromatic aldehydes furnished the corresponding hydrazones (277_{a-f}). Dehydrogenative cyclization of 277_a by ethanolic $FeCl_3$ solution afforded the triazolothienopyrimidines 279 (Scheme 3).
The constitution of the prepared compounds was secured by their NMR, IR, and MS spectra, for instance, compound 272 showed absorbance in IR spectra at υ = 1666 cm^{-1} for stretching C=O group while no any appearance of any stretched absorbance peak for NH group. Its ^{1}H-NMR spectrum showed three bands at δ = 1.78, 2.75, 2.85 ppm for 4H, 2H, and 2H respectively for aliphatic ring, protons of allyl group appeared as follow: δ = 4.72 (bm, 2H, NCH_2), 5.15 (dd, 1H, J_{cis}=10.2 Hz, 3'-H_a), 5.24 (dd, 1H, J_{trans}= 17.3 Hz, 3'-H_b), 5.93(m, 1H, 2'-H), finally the proton of triazole ring resonate at δ = 9.12 ppm. the structure of compound 272 also confirmed by ^{13}C-NMR spectrum measured in DMSO-d_6 showed 4 absorption bands at δ = 21.28, 22.21, 24.01, 24.928 ppm for carbons of aliphatic ring while allyl group absorption appeared at δ = 43.89 (NCH_2), 117.31, 132.36 (C=C) in addition of 4 absorption bands at δ = 130.11, 131.28, 135.43, 138.25 ppm corresponding to carbons of thiophene ring, furthermore 3 bands at δ =145.62, 147.59, 155.13 ppm for 2C=N and C=O groups respectively. The structure proposal of compound 273 was derived from the analytical data (^{1}H-NMR, IR) and satisfactory elemental analyses (see experimental part). The compound mercaptotriazole 274 showed absorbance in IR spectra at υ = 1678 cm^{-1} for C=O group also ^{1}H-NMR spectrum showed singlet absorption band at δ = 14.04 ppm for NH group. In other hand, thiosemi-carbazide derivatives 275_{a-c} exhibit absorption bands for IR spectra in the range υ = 1666-1681 cm^{-1} for carbonyl C=O.
The structures also confirmed by ^{1}H-NMR and ^{13}C-NMR spectra for instance compound 275_c showed three multiplet broad bands at δ = 1.76, 2.67, 280 ppm corresponding to four CH_2 groups of aliphatic ring (4H, 2H, and 2H respectively), while allyl group appeared as follow: δ = 4.76 (bt, 2H, NCH_2), 5.05 (dd, 1H, J_{cis}=10.1 Hz, 3'-H_a), 5.13 (dd, 1H, J_{trans}= 17.2 Hz, 3'-H_b), 5.86 (m, 1H, 2'-H), while the protons of benzoyl group appeared at δ = 4.59 (bt, 2H, NCH_2), 7.20–7.35 (m, 5H, ph-H), in addition of three absorption bands for NH groups two of them showed singlet absorption at δ = 9.47, 9.17 ppm while the remaining one appeared triplet at δ = 8.52 ppm.
^{13}C-NMR spectrum measured in DMSO-d_6 showed 4 absorption signals at δ = 21.87, 22.65, 24.29, 25.18 ppm for aliphatic carbons ring and two absorption lines for NCH_2 at δ = 40.15, 40.43 ppm in addition of four absorption bands at δ = 130.25, 131.91, 135.20, 139.60 ppm corresponding to thiophene ring carbons and two absorption lines at δ = 115.31, 132.37 ppm for sp^2 allyl carbon atoms while phenyl carbons appeared at δ = 126.39, 126.71, 127.95, 129.90 ppm followed by three signals at 151.21, 159.11 and 166.21 corresponding to C=N, C=O and C=S respectively.



Comp.	R
275a	$CH_2CH=CH_2$
275b	C_6H_5
275c	$CH_2–C_6H_5$
276a	$CH_2CH=CH_2$
276b	4-CH_3-C6H_4
276c	C_6H_5
276d	$CH_2CH_2CH_3$
277a	3-Br-4-F-C_6H_3
277b	4-CH_3-C6H_4
277c	2-NO_2–C_6H_4
277d	2,3,5,6-(F)4–C_6H
277e	2-OCH_3–C_6H_4
277f	4-Cl–C_6H_4
279	3-Br-4-F-C_6H_3
280a	C_6H_5
280b	4-CH_3-C_6H_4

Reagents and conditions: i) HCOOH, or $HC(OEt)_3$, Δ; ii) CH_3COOH, or $CH_3C(OEt)_3$, Δ; iii) CS_2, pyridine, Δ; iv) 2N NaOH, Δ, HCl; v) RNCS, EtOH,Δ; vi) RNCO, EtOH, Δ; vii) RCHO, EtOH, Δ; viii) $FeCl_3$, EtOH, Δ

Scheme 3: Condensation of 266b with aromatic aldehydes

While the semi-carbazide compounds 276_{a-d} showed IR absorption bands around ν = 1674 cm^{-1} for carbonyl C=O and ν = 3367 cm^{-1} for NH group, the structures also confirmed by ^{1}H-NMR and ^{13}C-NMR spectra for instance compound 276_a showed three multiplet absorption bands of four CH_2 groups at δ = 1.76, 2.67, 2.79 ppm, while two allyl groups appeared as follow: first group at δ = 3.65, 4.98, 5.06, 5.86 (5H), and second group at δ = 4.65, 5.20, 5.60, 5.95 (5H) in addition of three absorption bands for NH groups at δ = 6.56, 7.90, 8.83 ppm.

^{13}C-NMR spectrum measured in DMSO-d_6 showed four absorption lines for four sp^3 carbon atoms at δ = 21.87,

22.63, 24.24, 25.19 ppm in addition of four bands for allyl sp^2 carbon atoms at δ = 114.13, 114.35, 130.25, 131.54 ppm furthermore other four bands corresponding to four sp^2 thiophene carbon atoms at δ = 116.08, 126.50, 136.39, 151.59 ppm, while C=N and 2C=O showed absorption bands at δ = 157.31, 159.44, 163.79 respectively. The structure proposal of the prepared aldehydehydrazones 277_{a-f} were derived from the analytical data (^{1}H NMR, ^{13}C NMR, IR) and satisfactory elemental analyses, for instance IR spectra showed absorption at ν = 1647-1678 cm^{-1} for carbonyl C=O and around ν = 3317 cm^{-1} for NH group. The ^{1}H-NMR spectra of the hydrazones 277_{a-f} indicated their existence as a mixture of the two conformations Syn- and Anti-isomers as indicated by the presence of two doublets for HC=N proton. The analytical data of compound 279 proved that dehydrogenative cyclization of 277_a by ethanolic solution of $FeCl_3$ took place, its ^{1}H-NMR showed three absorption bands of four CH_2 groups of aliphatic rings at δ = 1.76, 2.64, 2.86 ppm, in addition of three absorption lines of allyl group appeared at δ = 4.76, 5.18, 5.29, 5.96 (5H), while the three protons of aryl group appeared at δ = 7.66, 7.83, and 8.16 ppm with the disappearance of protons of NH and imine N=CH-Ar groups, ^{13}C-NMR and elemental analysis also confirmed the structure of compound 279.

CONCLUSION

^{1}H-NMR spectra showed the presence of only one NH group in compound 280_a indicate to dehydrogenation cyclization of compound 276_c while ^{1}H-NMR of compound 280_b showed there's an endo & exo equilibrium of NH group and thiazole ring.

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