HETEROCYCLES, Vol. 100, No. 12, 2020, pp. 2108 - 2119. © 2020 The Japan Institute of Heterocyclic Chemistry
Received, 6th September, 2020, Accepted, 3rd October, 2020, Published online, 15th October, 2020
DOI: 10.3987/COM-20-14349

SYNTHESIS OF NOVEL THIENOPYRIMIDINES AND THIENODIAZEPINES FROM ETHYL 2,4-DIAMINO-5-{[(2*E*)-2-(1-PHENYLETHYLIDENE)HYDRAZINO]CARBONYL}THIOPHENE-3-CARBOXYLATE

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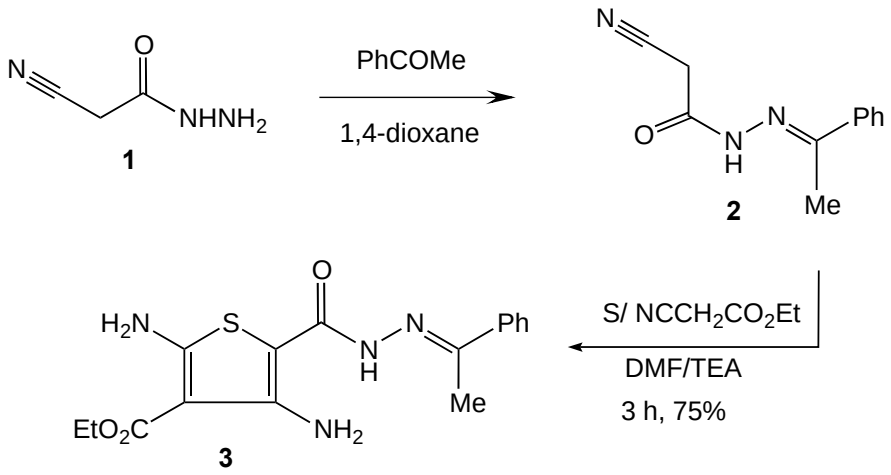
Abstract – Ethyl 2,4-diamino-5-{[(2*E*)-2-(1-phenylethylidene)hydrazino]-carbonyl}thiophene-3-carboxylate (**3**) was synthesized *via* Gewald reaction that can be readily used as precursor to potentially interesting thiophenes. Compound **3** reacted with cyanoacetamide and/or malononitrile producing thienopyrimidines **4** and **5**, respectively. Reaction of compound **3** with hydrazinecarbodithioic acid afforded pyrimidothienotriazepine **6**. Treatment of compound **3** with ethylenediamine and carbon disulfide gave (imidazolinyl)thiophene **7**. The latter compound can be used as building blocks for the synthesis of various heterocycles. Structures of the newly synthesized compounds were deduced based on their analytical and spectral data.

In 1966 Gewald reported that aliphatic ketones, aldehydes or 1,3-dicarbonyl compounds react with activated nitriles and sulfur in the presence of a base at room temperature to give 2-aminothiophenes.[1-3] Thiophenes comprise an important heterocyclic class with diverse applications ranging from the design of advanced materials[4-6] to the treatment of various diseases.[7-10] Also, thiophene derivatives are a very important class of heterocyclic compounds that are widely used as building blocks in many industrials and pharmaceuticals.[11–14] Moreover, fused thiophenes showed interesting therapeutic activity in the field of medical chemistry.[15–22] Thienopyrimidines are played a vital role in a variety of biological activities, such as antipyretics, antimicrobial, anti-inflammatory, anticancer, antiviral, anticonvulsant, antianaphylactic, antihistaminic and immunostimulant properties.[23-31] On the other hand, limited work has been carried out on the synthesis of fused thienoazepines. Also, 1,4-diazepine ring-based drugs have been found as the prototype of a distinct structure with a wide range of applications in human medicine and

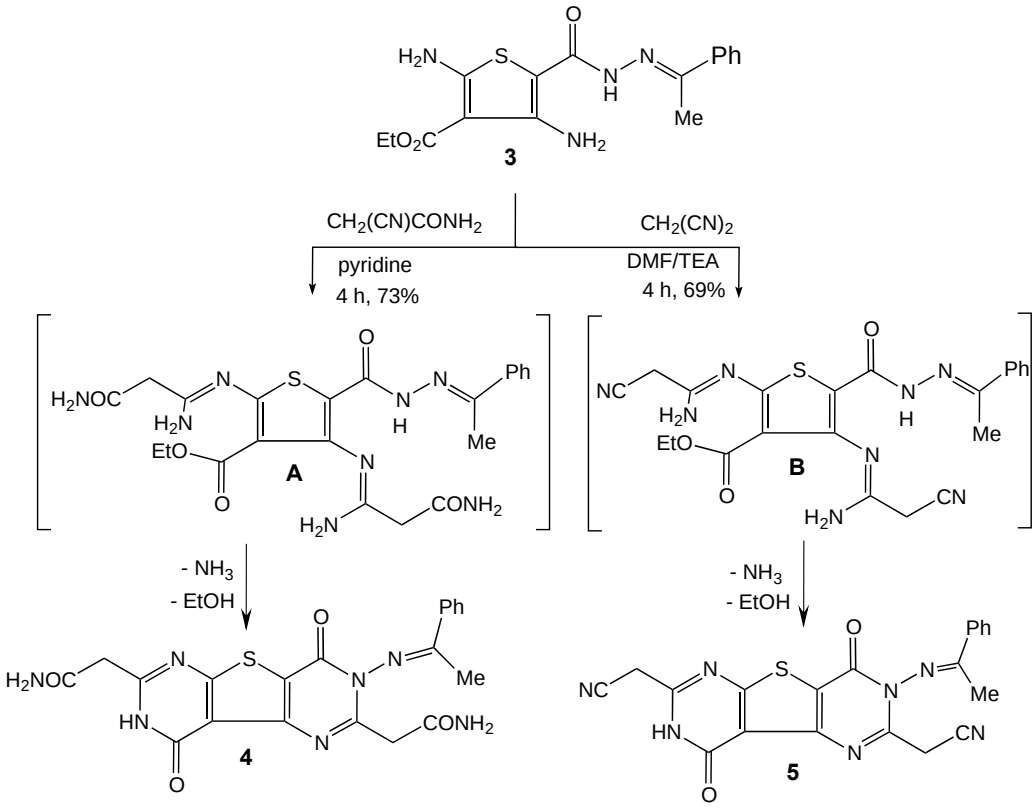
biological activities.[32] In the light of the above observations and as a continuation of our previous work on thienopyrimidines,[33-35] we describe herein the synthesis and characterization of the title compounds. We aimed to construct some new heterocyclic systems bearing thiophene moiety which would be expected that they may potentially have biological activities.

Reaction of 2-cyanoacetohydrazide **(1)** with acetophenone gave (*E*)-2-cyano-*N*'-(1-phenylethylidene)acetohydrazide **(2)**.[36] The key intermediate ethyl 2,4-diamino-5-{[(2*E*)-2-(1-phenylethylidene)hydrazino]carbonyl}thiophene-3-carboxylate **(3)** was prepared by treating (*E*)-2-cyano-*N*'-(1-phenylethylidene)acetohydrazide **(2)** with ethyl cyanoacetate and elemental sulfur in DMF and a catalytic amount of triethylamine (Scheme 1). The ^{1}H NMR spectrum of compound **3** displayed triplet and quartet signals at δ 1.12 and 4.12 ppm for the protons of CH_3 and CH_2 of the ester group, respectively. The ^{13}C NMR spectrum showed distinct signals at δ 159.2 and 165.8 ppm attributed to two C=O carbons. The mass spectrum revealed molecular ion peak at *m/z* 346 with a base peak at 55.



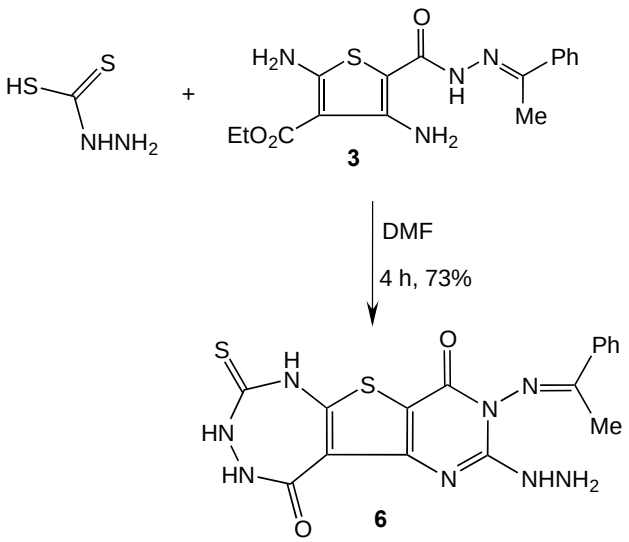
Scheme 1. Synthesis of ethyl 2,4-diaminothiophene-3-carboxylate **3**

The reactivity of compound **3** towards some active methylene reagents was studied. Thus, compound **3** reacted with two equivalents of cyanoacetamide in pyridine to give diacetamide **4**. Formation of compound **4** was supposed to achieve through the intermediate formation of **A**, followed by intramolecular cyclization *via* ammonia and ethanol elimination. In addition, diacetonitrile **5** was synthesized from the reaction of compound **3** (1 mmol) with malononitrile (2 mmol) in DMF containing a catalytic amount of triethylamine under reflux conditions. This reaction is assumed to proceed through nucleophilic attack to form intermediate **B**, which underwent intramolecular cyclization *via* ammonia and ethanol elimination (Scheme 2).[37]



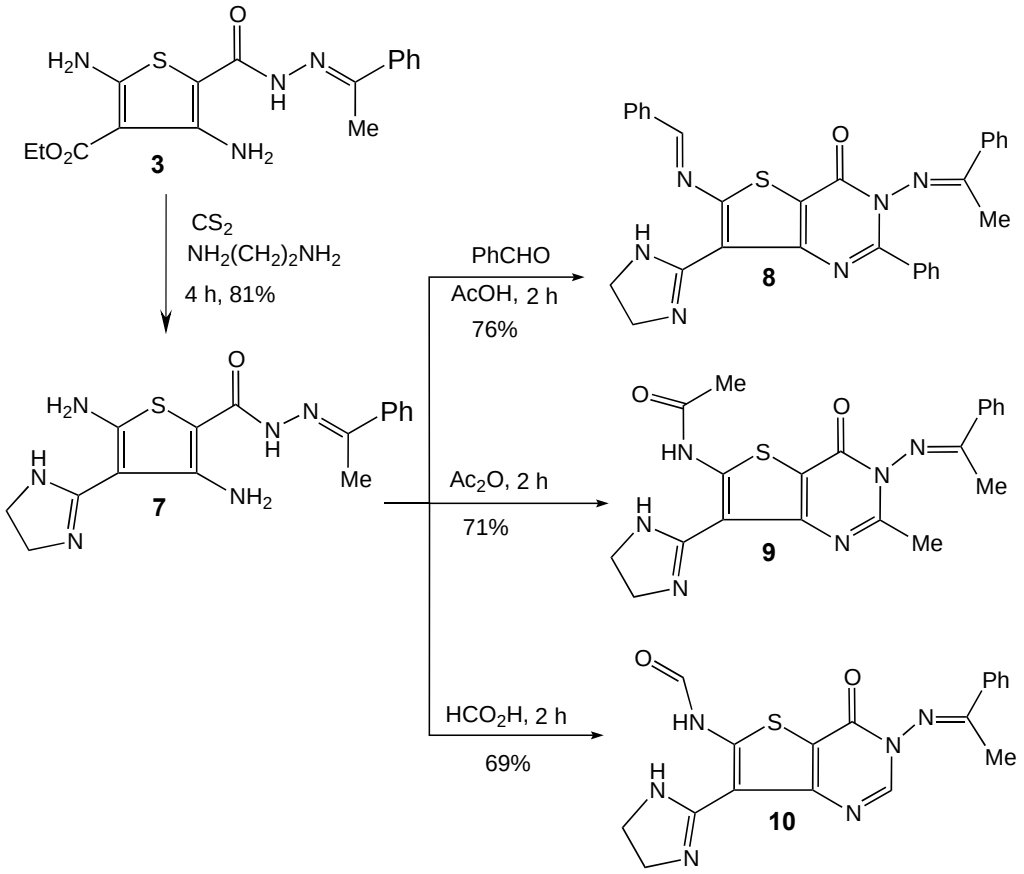
Scheme 2. Formation of pyrimidothienopyrimidines **4** and **5**

Also, cyclization of compound **3** was achieved by treatment with two equivalents of hydrazinecarbodithioic acid in DMF to give pyrimidothienotriazepine **6** (Scheme 3). The ^{1}H NMR spectrum revealed the absence of the triplet and quartet signals for the protons of CH_3 and CH_2 of the ester group. The mass spectrum of compound **6** represents a good guide to its structure and revealed the molecular ion peak at *m/z* 414 which corresponds to the suggested molecular formula $C_{16}H_{14}N_8O_2S_2$.



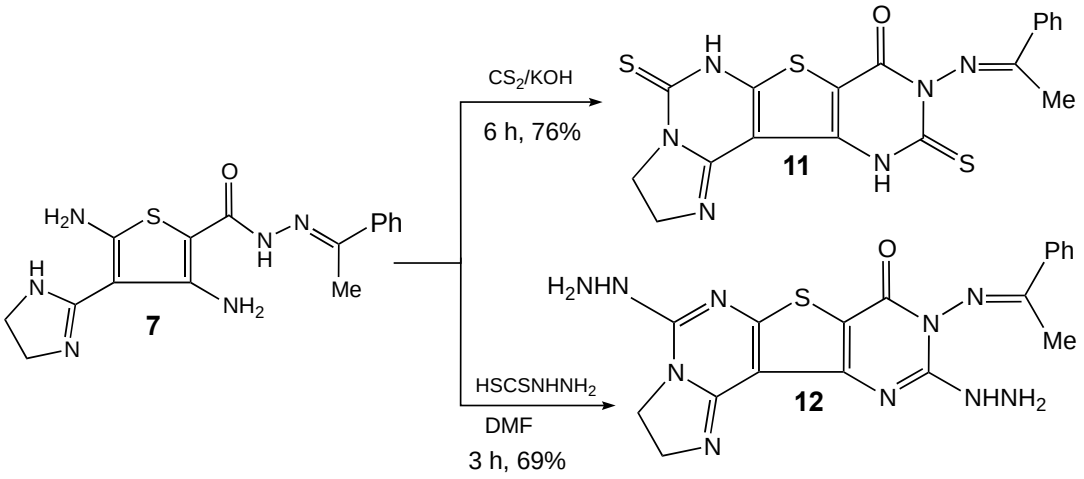
Scheme 3. Synthesis of pyrimidothienotriazepine **6**

Cyclocondensation of compound **3** with ethylenediamine in the presence of carbon disulfide[38] afforded (imidazolinyl)thiophene **7**. Further, compound **7** was reacted with two moles of benzaldehyde, acetic anhydride and/or formic acid furnished thienopyrimidines **8**-**10**, respectively, (Scheme 4). The mass spectrum of compound **10** was showed the molecular ion peak at *m/z* 379 (M-1) corresponding to the molecular formula $C_{18}H_{16}N_6O_2S$, which agrees with formula weight (380.42) and boosts the identity of the structure.



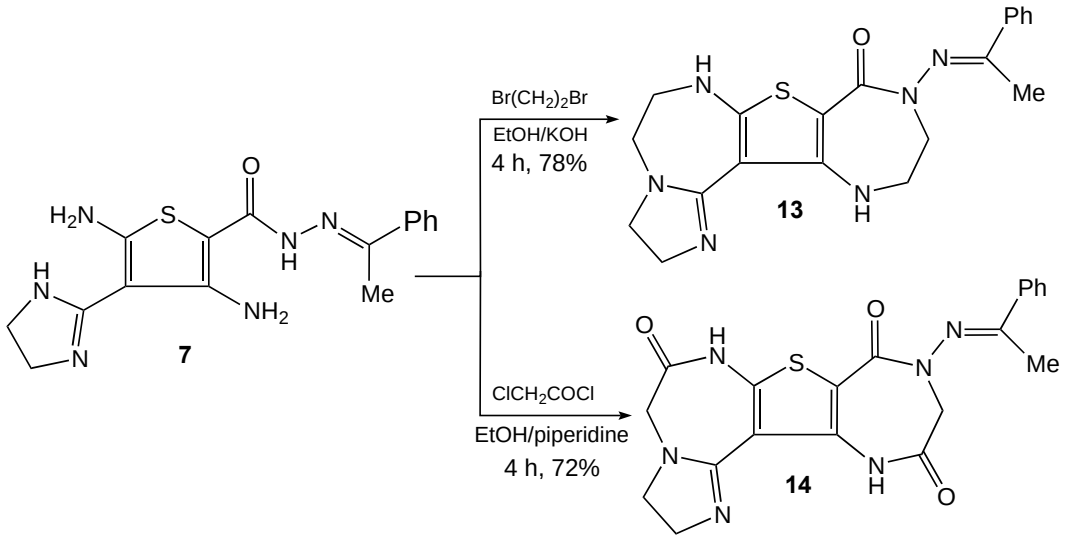
Scheme 4. Formation of (imidazolinyl)thiophene **7** and thienopyrimidines **8**-**10**

Cyclization of compound **7** with two equivalents of carbon disulfide in KOH and/or hydrazinecarbodithioic acid in DMF gave pyrimidothienopyrimidines **11** and **12**, respectively (Scheme 5). The mass spectra of compounds **11** and **12** showed their molecular ion peaks at *m/z* 426 and 422, respectively, which confirm the postulated structures. The ^{13}C NMR spectrum of compound **11** displayed signals at δ 176.5 and 183.2 ppm attributed to two C=S carbons.



Scheme 5. Reaction of compound **7** with carbon disulfide and hydrazinecarbodithioic acid

Finally, treatment of (imidazolinyl)thiophene **7** with 1,2-dibromoethane and/or chloroacetyl chloride in a basic medium led to the formation of diazepinothienodiazepines **13** and **14**, respectively (Scheme 6). The IR spectra of compounds **13** and **14** showed the absence of the NH_2 band. The mass spectra of compounds **13** and **14** revealed their molecular ion peaks at *m/z* 394 and 422 that is fully consistent with the suggested formula weights.



Scheme 6. Formation of diazepines **13** and **14**

In conclusion, synthesis of the key ethyl 2,4-diamino-5-{[(2*E*)-2-(1-phenylethylidene)hydrazino]-carbonyl}thiophene-3-carboxylate (**3**) was accomplished *via* Gewald reaction. We demonstrated that *o*-aminothiophene ester **3** can be used as available building blocks for the synthesis of novel fused heterocyclic thiophenes.

EXPERIMENTAL

General. Melting points were determined on a digital Stuart SMP3 apparatus. Infrared spectra were measured on FTIR Nicolet IS10 spectrophotometer (cm^{-1}), using KBr disks. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured on Mercury-300BB, using DMSO-d_6 as a solvent and TMS (δ) as the internal standard. Mass spectra were obtained using GC-2010 Shimadzu Gas chromatography instrument mass spectrometer (70 eV). Elemental microanalyses were performed on a Perkin–Elmer CHN-2400 analyzer.

Ethyl 2,4-diamino-5-{[(2*E*)-2-(1-phenylethylidene)hydrazine]carbonyl}thiophene-3-carboxylate (3). A mixture of compound **2** (0.2 g, 1 mmol), sulfur (0.032 g, 1 mmol) and ethyl cyanoacetate (0.11 mL, 1 mmol) in DMF (5 mL) containing five drops of TEA was heated under reflux for 3 h. The reaction mixture was cooled and poured onto crushed ice. The solid obtained was filtered off and recrystallized from dioxane to give compound **3** as pale brown crystals (0.26 g, 75%): mp 149-150 ºC; IR (ν cm^{-1}) 3454-3111 ($2NH_2$, NH), 3040 ($CH_{arom.}$), 2959 ($CH_{aliph.}$), 1692, 1680 ($C=O_{ester}$ and $C=O_{amide}$), 1621 (C=N), 1570 (C=C); ^1H NMR (300 MHz, DMSO-d_6) δ 1.12 (t, 3H, $CH_2\boldsymbol{CH_3}$, J = 7.2 Hz), 2.28 (s, 3H, CH_3), 3.82 (brs, 2H, NH_2 exchangable with D_2O), 4.12 (q, 2H, $\boldsymbol{CH_2}CH_3$, J = 7.2 Hz), 4.21 (brs, 2H, NH_2 exchangable with D_2O), 7.57-7.73 (m, 5H, Ar-H), 9.29 (s, 1H, NH exchangable with D_2O); ^{13}C NMR (75 MHz) δ 13.8 ($CH_2\mathbf{CH_3}$), 14.2 (CH_3), 60.9 ($\mathbf{CH_2}CH_3$), 126.3, 127.1, 128.6, 129.1, 131.7, 135.3, 137.9, 143.4, 149.1 (C=N), 159.2 ($C=O_{amidic}$), 165.8 ($C=O_{ester}$); MS *m/z* (%): $[M]^{\cdot+}$ 346 (1.6), 200 (24.4), 149 (7.0), 119 (12.7), 109 (15.6), 92 (28.0), 77 (55.3), 55 (100); Anal. Calcd for $C_{16}H_{18}N_4O_3S$ (%): C, 55.48; H, 5.24; N, 16.17; S, 9.26%. Found: C, 55.42; H, 5.27; N, 16.21; S, 9.22%.

2,2'-(4,9-Dioxo-3-{[(1*E*)-1-phenylethylidene]amino}-3,4,8,9-tetrahydropyrimido[4',5':4,5]thieno-[2,3-*d*]pyrimidine-2,7-diyl)diacetamide (4). A mixture of compound **3** (0.346 g, 1 mmol) and cyanoactamide (0.168 g, 2 mmol) in pyridine (5 mL) was heated under reflux for 4 h. The reaction mixture was cooled and poured onto crushed ice and neutralized with conc. HCl. The solid obtained was filtered off and recrystallized from EtOH to give compound **4** as brown crystals (0.33 g, 73%): mp >300 ºC; IR (ν cm^{-1}) 3350-3169 ($2NH_2$, NH), 3020 ($CH_{arom.}$), 2924 ($CH_{aliph.}$), 1672 ($2C=O_{amidic}$), 1645 ($2C=O_{pyrimidinone}$), 1602 (C=N), 1580 (C=C); ^1H NMR (300 MHz, DMSO-d_6) δ 2.26 (s, 3H, CH_3), 4.77 (s, 4H, $2CH_2$), 5.12 (brs, 4H, $2NH_2$ exchangable with D_2O), 7.39-7.59 (m, 5H, Ar-H), 8.20 (s, 1H, NH exchangable with D_2O); ^{13}C NMR (75 MHz) δ 14.1 (CH_3), 44.3, 48.3 ($2CH_2$), 125, 126.9, 127.8, 128.7, 130.3, 131.1, 132.4, 136.2, 139.2, 141.9, 148.4, 158.3 (2C=O), 165.7 (2C=O); MS *m/z* (%): $[M]^{\cdot+}$ 451 (0.5), [M+1] 452 (0.1), 390 (3.9), 307 (100), 288 (43.9), 273 (37.4), 202 (22.4), 91 (32.2), 77 (70.6); Anal. Calcd for $C_{20}H_{17}N_7O_4S$ (%): C, 53.21; H, 3.80; N, 21.72; S, 7.10%. Found: C, 53.27; H, 3.72; N, 21.66; S, 7.18%.

2,2'-(4,9-Dioxo-3-{[(1*E*)-1-phenylethylidene]amino}-3,4,8,9-tetrahydropyrimido[4',5':4,5]thieno-

[2,3-*d*]pyrimidine-2,7-diyl)diacetonitrile (5). A mixture of compound **3** (0.346 g, 1 mmol), and malononitrile (0.132 g, 2 mmol) in DMF (5 mL) containing five drops of TEA was heated under reflux for 4 h. The reaction mixture was cooled and poured onto crushed ice. The solid obtained was filtered off and recrystallized from dioxane to give compound **5** as brown crystals (0.286 g, 69%): mp >300 ºC; IR (ν cm^{-1}) 3330 (NH), 3041 ($CH_{arom.}$), 2929 ($CH_{aliph.}$), 2204 (2C≡N), 1662 (2C=O), 1604 (C=N), 1591 (C=C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.27 (s, 3H, CH_3), 4.85 (s, 4H, $2CH_2$), 7.47-7.70 (m, 5H, Ar-H), 7.83 (s, 1H, NH exchangable with D_2O); ^{13}C NMR (75 MHz) δ 13.8 (CH_3), 43.3, 45.8 ($2CH_2$), 116.6 (2C≡N), 125.8, 127.1, 129.3, 129.9, 130.1, 132, 137.9, 142.6, 146.6, 150.4, 154.5, 163.9, 165.8 (2C=O); MS *m/z* (%): $[M]^{\cdot+}$ 415 (0.3), [M+1] 416 (0.2), 366 (100), 321 (21.7), 304 (23.4), 221 (12.9), 129 (4.8), 91 (7.6), 77 (36.9); Anal. Calcd for $C_{20}H_{13}N_7O_2S$ (%): C, 57.82; H, 3.15; N, 23.60; S, 7.72%. Found: C, 57.80; H, 3.17; N, 23.64; S, 7.65%.

7-Hydrazino-8-{[(1*E*)-1-phenylethylidene]amino}-2-thioxo-3,4-dihydro-1*H*-pyrimido[4′,5′:4,5]-thieno[2,3-*e*][1,2,4]triazepine-5,9(2*H*,8*H*)-dione (6). A mixture of compound **3** (0.346 g, 1 mmol) and hydrazinecarbodithioic acid (0.216 g, 2 mmol) in DMF (5 mL) was heated under reflux for 4 h. The reaction mixture was cooled and poured onto crushed ice. The solid obtained was filtered off and recrystallized from EtOH to give compound **6** as brown crystals (0.302 g, 73%): mp 112-113 ºC; IR (ν cm^{-1}) 3340-3140 (NH_2, 4 NH), 3052 ($CH_{arom.}$), 2924 ($CH_{aliph.}$), 1648 (2C=O), 1614 (C=N), 1583 (C=C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.19 (s, 3H, CH_3), 4.44 (brs, 2H, NH_2 exchangable with D_2O), 7.00, 7.10, 7.15 (s, 3H, 3NH exchangable with D_2O), 7.18-7.39 (m, 5H, Ar-H), 8.07 (s, 1H, NH exchangable with D_2O); ^{13}C NMR (75 MHz) δ 13.3 (CH_3), 124.9, 127.1, 128.7, 130.1, 134.1, 137.1, 143.2, 145.1, 149.2, 153.2, 156.1, 159.7 (2C=O), 173.8 (C=S); MS *m/z* (%): $[M]^{\cdot+}$ 414 (0.2), [M+1] 415 (0.1), 295 (1.5), 250 (12.4), 149 (5.8), 134 (18.9), 91 (9.1), 77 (11.9), 73 (100); Anal. Calcd for $C_{16}H_{14}N_8O_2S_2$ (%): C, 46.37; H, 3.40; N, 27.04; S, 15.47%. Found: C, 46.32; H, 3.42; N, 27.11; S, 15.41%.

3,5-Diamino-4-(4,5-dihydro-1*H*-imidazol-2-yl)-*N*-[(1*E*)-1-phenylethylidene]thiophene-2-carbohydrazide (7). A mixture of compound **3** (0.346 g, 1 mmol) and ethylenediamine (2 mL) in carbon disulfide (1 mL) was heated under reflux for 4 h. The reaction mixture was cooled and poured onto crushed ice. The solid obtained was filtered off and recrystallized from dioxane to give compound **7** as pale brown crystals (0.277 g, 81%): mp 204-205 ºC; IR (ν cm^{-1}) 3350-3249 ($2NH_2$, 2NH), 3051 ($CH_{arom.}$), 2934 ($CH_{aliph.}$), 1660 (C=O), 1611 (C=N), 1557 (C=C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.37 (s, 3H, CH_3), 3.43-3.55 (m, 4H, $2CH_2$), 3.90 (brs, 4H, $2NH_2$ exchangable with D_2O), 7.18-7.52 (m, 5H, Ar-H), 7.81, 8.07 (s, 2H, 2NH exchangable with D_2O); ^{13}C NMR (75 MHz) δ 14.5 (CH_3), 44.1, 49.1 (CH_2CH_2), 125.7, 128, 129.9, 132.2, 136, 138, 142, 144.7, 147, 154.2, 164.9 (C=O); MS *m/z* (%): $[M]^{\cdot+}$ 342 (0.1), [M+1] 343 (0.1), 236 (10.3), 221 (31.2), 149 (3.6), 118 (9.6), 102 (100), 77 (38.8), 55 (11.4); Anal. Calcd for $C_{16}H_{18}N_6OS$ (%): C, 56.12; H, 5.30; N, 24.54; S, 9.36%. Found: C, 56.22; H, 5.23; N, 24.49; S,

9.11%.

7-(4,5-Dihydro-1*H*-imidazol-2-yl)-2-phenyl-3-{[(1*E*)-1-phenylethylidene]amino}-6-[(phenylmethylene)amino]thieno[3,2-*d*]pyrimidin-4(3*H*)-one (8). A mixture of compound **7** (0.342 g, 1 mmol) and benzaldehyde (0.2 mL, 2 mmol) in glacial acetic acid (5 mL) was heated under reflux for 2 h. The reaction mixture was cooled. The solid obtained was filtered off and recrystallized from dioxane to give compound **8** as white crystals (0.392 g, 76%): mp 261-262 ºC; IR (ν cm^{-1}) 3249 (NH), 3047 ($CH_{arom.}$), 2930 ($CH_{aliph.}$), 1678 (C=O), 1610 (C=N), 1518 (C=C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.31 (s, 3H, CH_3), 3.76-3.87 (m, 4H, $2CH_2$), 7.61-7.91 (m, 15H, Ar-H), 8.10 (s, 1H, NH exchangable with D_2O), 10.06 (s, 1H, CH=N); ^{13}C NMR (75 MHz) δ 14 (CH_3), 45.1, 48.7 (CH_2CH_2), 126, 127.1, 128.2, 130, 132.3, 134, 136, 137.9, 141.9, 144.2, 146.3, 147.7, 151.1, 153.7, 157.3, 159.5, 163.8 (C=O); MS *m/z* (%): $[M]^{\cdot+}$ 516 (0.2), [M+1] 517 (0.2), 406 (0.2), 221 (1.2), 200 (2.4), 171 (1.2), 118 (8.8), 102 (100), 91 (16), 77 (20.8), 55 (17.1); Anal. Calcd for $C_{30}H_{24}N_6OS$ (%): C, 69.75; H, 4.68; N, 16.27; S, 6.21%. Found: C, 69.71; H, 4.62; N, 16.31; S, 6.35%.

***N*-{7-(4,5-Dihydro-1*H*-imidazol-2-yl)-2-methyl-4-oxo-3-{[(1*E*)-phenylethylidene]amino}-3,4-dihydrothieno[3,2-*d*]pyrimidin-6-yl}acetamide (9).** A mixture of compound **7** (0.342 g, 1 mmol) and acetic anhydride (5 mL) was heated under reflux for 2 h. The reaction mixture was cooled and poured onto crushed ice. The solid obtained was filtered off and recrystallized from EtOH to give compound **9** as brown crystals (0.29 g, 71%): mp 101-102 ºC; IR (ν cm^{-1}) 3462 (2NH), 3026 ($CH_{arom.}$), 2942 ($CH_{aliph.}$), 1690 (2C=O), 1613 (C=N), 1570 (C=C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.91 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 2.73 (s, 3H, CH_3), 3.12-3.45 (m, 4H, $2CH_2$), 7.68-7.93 (m, 5H, Ar-H), 8.39 (s, 1 H, NH exchangable with D_2O), 8.73 (s, 1H, NH exchangable with D_2O); ^{13}C NMR (75 MHz) δ 13.9, 18.2, 22.2 ($3CH_3$), 45.8, 46.6 (CH_2CH_2), 125, 129.1, 132.8, 136.5, 139.6, 142.5, 145.2, 149.9, 152.6, 157.4, 158.6, 163.1, 167.1 (2C=O); MS *m/z* (%): [M-2] 406 (0.4), 362 (4.2), 320 (2.4), 261 (36.9), 219 (100), 191 (7.3), 115 (21.6), 102 (29.7), 77 (31.5), 55 (12.2); Anal. Calcd for $C_{20}H_{20}N_6O_2S$ (%): C, 58.81; H, 4.94; N, 20.57; S, 7.85%. Found: C, 58.83; H, 4.88; N, 20.59; S, 7.81%.

***N*-{7-(4,5-Dihydro-1*H*-imidazol-2-yl)-4-oxo-3-{[(1*E*)-phenylethylidene]amino}-3,4-dihydrothieno-[3,2-*d*]pyrimidin-6-yl}formamide (10).** A mixture of compound **7** (0.342 g, 1 mmol) and formic acid (5 mL) was heated under reflux for 3 h. The reaction mixture was cooled and poured onto crushed ice. The solid obtained was filtered off and recrystallized from EtOH to give compound **10** as white crystals (0.262 g, 69%): mp 169-170 ºC; IR (ν cm^{-1}) 3188 (2NH), 3059 ($CH_{arom.}$), 2906 ($CH_{aliph.}$), 1682, 1666 (2C=O), 1607 (C=N), 1549 (C=C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.87 (s, 3H, CH_3), 3.48-3.54 (m, 4H, $2CH_2$), 7.45-7.92 (m, 6H, Ar-H), 8.43 (s, 1H, NH exchangable with D_2O), 9.21 (s, 1H, CHO), 10.03 (s, 1H, NH exchangable with D_2O); ^{13}C NMR (75 MHz) δ 14.1 (CH_3), 46.1, 48 (CH_2CH_2), 124.8, 126.3, 129.6, 132.1, 133.9, 135.9, 138.1, 142, 145.7, 147.4, 151.4, 158.8, 165.2 (2C=O); MS *m/z* (%): [M-1] 379 (0.3),

295 (1.4), 277 (1.1), 221 (1.8), 167 (4.2), 130 (19.8), 102 (21.7), 77 (14.9), 67 (25.6), 57 (100); Anal. Calcd for $C_{18}H_{16}N_6O_2S$ (%): C, 56.83; H, 4.24; N, 22.09; S, 8.43%. Found: C, 56.87; H, 4.28; N, 22.12; S, 8.40%.

3-{[(1*E*)-1-Phenylethylidene]amino}-2,7-dithioxo-2,3,6,7,9,10-hexahydroimidazo[1,2-*c*]pyrimido-[4',5':4,5]thieno[2,3-*d*]pyrimidin-4(1*H*)-one (11). A mixture of compound **7** (0.342 g, 1 mmol) and carbon disulfide (2 mL) in aqueous solution of KOH (5%, 5 mL) was heated under reflux for 6 h. The reaction mixture was cooled and poured onto crushed ice and neutralized with conc. HCl. The solid obtained was filtered off and recrystallized from EtOH to give compound **11** as yellow crystals (0.324 g, 76%): mp 269-270 ºC; IR (ν cm^{-1}) 3249 (NH), 3062 ($CH_{arom.}$), 2947 ($CH_{aliph.}$), 1668 (C=O), 1601 (C=N), 1514 (C=C), 1204 (C=S); ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.23 (s, 3H, CH_3), 2.91-3.13 (m, 4H, $2CH_2$), 7.39-7.54 (m, 5H, Ar-H), 7.88 (s, 1H, NH exchangable with D_2O), 7.91 (s, 1H, NH exchangable with D_2O). ^{13}C NMR (75 MHz) δ 14.7 (CH_3), 44.7, 46.9 (CH_2CH_2), 124.8, 126.7, 131.1, 134.1, 138, 143, 145.9, 149.2, 153.6, 157.7, 166.4 (C=O), 176.5, 183.2 (2C=S); MS *m/z* (%): $[M]^{\cdot+}$ 426 (0.1), 327 (0.1), 236 (14.4), 221 (38.8), 159 (5.8), 132 (2.5), 118 (8.1), 102 (100), 77 (28.6), 59 (3.5); Anal. Calcd for $C_{18}H_{14}N_6OS_3$ (%): C, 50.69; H, 3.31; N, 19.70; S, 22.55%. Found: C, 50.74; H, 3.28; N, 19.75; S, 22.51%.

2,7-Bis(hydrazino)-3-{(1*E*)-1-phenylethylidene)amino}-9,10-dihydroimidazo[1,2-*c*]pyrimido-[4',5':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (12). A mixture of compound **7** (0.342 g, 1 mmol) and hydrazinecarbodithioic acid (0.216 g, 2 mmol) in DMF (5 mL) was heated under reflux for 3 h. The reaction mixture was cooled and poured onto crushed ice. The solid obtained was filtered off and recrystallized from EtOH to give compound **12** as brown crystals (0.291 g, 69%): mp 119-120 ºC; IR (ν cm^{-1}) 3421-3216 (NH_2, NH), 3039 ($CH_{arom.}$), 2924 ($CH_{aliph.}$), 1679 (C=O), 1604 (C=N), 1568 (C=C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.32 (s, 3H, CH_3), 2.91-3.13 (m, 4H, $2CH_2$), 4.13 (brs, 4H, $2NH_2$ exchangable with D_2O), 7.24-7.51 (m, 5H, Ar-H), 8.23 (s, 1H, NH exchangable with D_2O), 8.31 (s, 1H, NH exchangable with D_2O); ^{13}C NMR (75 MHz) δ 14.7 (CH_3), 43.9, 47.9 (CH_2CH_2), 125.4, 129.7, 130.9, 134.4, 136, 139.6, 141.8, 145.7, 147.2, 151.4, 155.5, 158.3, 164.6 (C=O); MS *m/z* (%): $[M]^{\cdot+}$ 422 (0.1), [M+1] 423 (0.1), 376 (0.1), 306 (0.2), 258 (17.9), 221 (9.9), 192 (23.1), 159 (31.2), 128 (26.3), 118 (2.8), 102 (15.5), 77 (17.1), 64 (100); Anal. Calcd for $C_{18}H_{18}N_{10}OS$ (%): C, 51.17; H, 4.29; N, 33.15; S, 7.59%. Found: C, 51.20; H, 4.25; N, 33.19; S, 7.62%.

4-{[(1*E*)-1-Phenylethylidene]amino}-(11*H*,12*H*)-imidazo[1,2-*d*]-1,2,3,4,8,9-hexahydro[1,4]diazepino-[5',6':4,5]thieno[2,3-*e*][1,4]diazepin-5(7*H*)-one (13). A mixture of compound **7** (0.342 g, 1 mmol) and 1,2-dibromoethane (0.17 mL, 2 mmol) in ethanolic solution of KOH (5%, 10 mL) was heated under reflux for 4 h. The reaction mixture was cooled. The solid obtained was filtered off and recrystallized from EtOH to give compound **13** as yellow crystals (0.307 g, 78%): mp 283-284 ºC; IR (ν cm^{-1}) 3249

(2NH), 3062 ($CH_{arom.}$), 2963 ($CH_{aliph.}$), 1672 (C=O), 1596 (C=N), 1520 (C=C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.25 (s, 3H, CH_3), 3.76-3.85 (m, 12H, $6CH_2$), 7.38-7.54 (m, 5H, Ar-H), 7.85 (s, 2H, 2NH exchangable with D_2O); ^{13}C NMR (75 MHz) δ 14.4 (CH_3), 43.3, 45.7, 48, 49.4 ($3CH_2CH_2$), 124, 128, 130.2, 133.8, 134.6, 136.3, 140.6, 147.7, 149.9, 158.1, 164.2 (C=O); MS *m/z* (%): $[M]^{\cdot+}$ 394 (0.1), [M+1] 395 (0.1), 302 (0.1), 236 (27.1), 221 (80.7), 180 (9.7), 143 (3.6), 118 (22.7), 102 (100), 77 (77.3), 57 (7.5); Anal. Calcd for $C_{20}H_{22}N_6OS$ (%): C, 60.89; H, 5.62; N, 21.30; S, 8.13%. Found: C, 60.92; H, 5.58; N, 21.35; S, 8.09%.

4-{[(1*E*)-1-Phenylethylidene]amino}-3,4,7,9,11,12-hexahydroimidazo[1,2-*d*][1,4]diazepino[5',6':4,5]-thieno[2,3-*e*][1,4]diazepine-2,5,8(1*H*)-trione (14). A mixture of compound **7** (0.342 g, 1 mmol) and chloroacetyl chloride (0.16 mL, 2 mmol) in EtOH (10 mL) containing five drops of piperidine was heated under reflux for 4 h. The reaction mixture was cooled. The solid obtained was filtered off and recrystallized from EtOH to give compound **14** as yellow crystals (0.304 g, 72%): mp 219-220 ºC; IR (ν cm^{-1}) 3411 (2NH), 3051 ($CH_{arom.}$), 2967 ($CH_{aliph.}$), 1671 (C=O), 1613 (C=N), 1552 (C=C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.23 (s, 3H, CH_3), 3.76-3.81 (m, 4H, $2CH_2$), 4.18 (s, 4H, $2CH_2$), 7.32-7.59 (m, 5H, Ar-H), 8.33 (s, 1H, NH exchangable with D_2O), 8.43 (s, 1H, NH exchangable with D_2O); ^{13}C NMR (75 MHz) δ 14.8 (CH_3), 44.8, 46.4 (CH_2CH_2), 49.7 ($2CH_2$), 125.7, 129.5, 131.8, 134.4, 137.9, 141, 144, 147, 149.6, 158, 161.6, 164.5, 168.5 (3C=O); MS *m/z* (%): $[M]^{\cdot+}$ 422 (0.3), [M+1] 423 (0.5), 382 (1.7), 315 (3.4), 274 (85.9), 257 (55.9), 230 (100), 197 (3.3), 157 (10.6), 129 (15.6), 102 (20.6), 77 (27.7), 64 (4.8); Anal. Calcd for $C_{20}H_{18}N_6O_3S$ (%): C, 56.86; H, 4.29; N, 19.89; S, 7.59%. Found: C, 56.88; H, 4.25; N, 19.92; S, 7.53%.

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