Cycloaddition of Aroyl Isothiocyanate: A Novel Synthesis of Triazine, Oxazine, Pyrimidine, and Pyridine Derivatives

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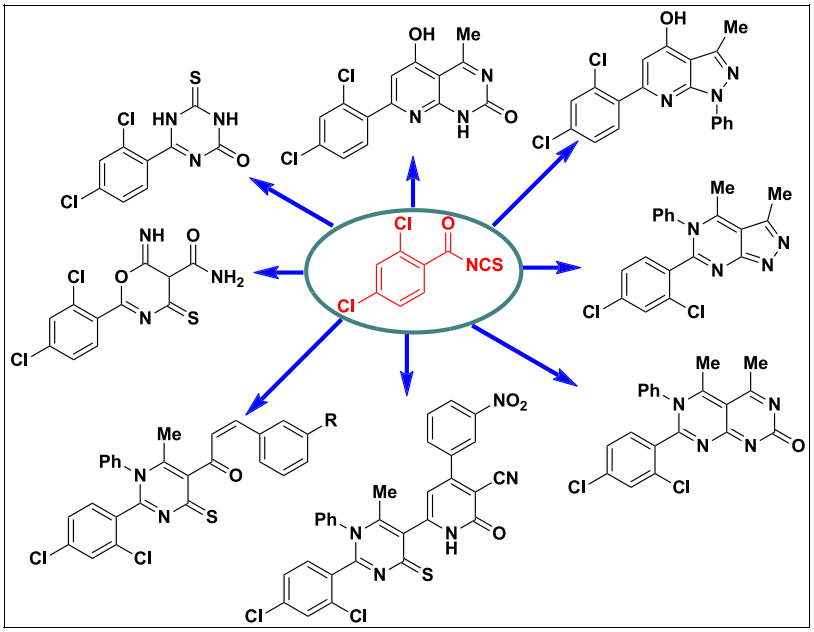


A simple and direct synthetic methodology for a novel series of azines and their annulated systems was performed. Heterocyclization of acyl isothiocyanate **2** with urea or malononitrile gave *s*-triazine **4** and 1,3-oxazine **7** derivatives, respectively. The reaction of heteroallene **1** with acetylacetone tolerated 2-thioxopyridine derivative **9**. The latter compound underwent heterocyclization with urea, hydrazine hydrate, or phenyl hydrazine to give the annulated pyridines **10**–**12**. Pyrimidinethione **14** was resulted from reaction of acylisothiocyanate with enamine **13**. Condensation of compound **14** with hydrazine hydrate, phenyl hydrazine, urea, and 3-nitrobenzaldehyde in the presence of ethyl cyanoacetate or sodium hydroxide afforded **15**–**20**, respectively.

INTRODUCTION

The synthesis of nitrogen containing heterocyclic systems attracted organic chemistry very much, due to their enormous applications as drugs and agrochemicals. For example, pyrimidine scaffolds (Fig. 1) are well-known dihydrofolate reductases inhibitor [1] and are associated with a wide area of pharmaceutical properties. Further, pyrimidines and their fused systems have been reported as antimicrobial [2], anti-inflammatory [3], antipyretic [4], anti-HIV [5], antitumor agents [6], and antihypertensive [7]. Similarly, pyridine ring is an important six-membered heterocycle core present in enormous applicable compounds, such as insecticides, herbicides, dyes, photoluminescences, electroluminescences, and metal steel anticorrosion agents [8]. The presence of triazines and oxazines in agrochemical and pharmaceutical used compounds is the main reason for their extensive study by the chemists. For instance, there are many compounds containing triazine core reported as antimalarial [9], herbicidal [10], antimicrobial [11], anticancer [12]. Furthermore, acyl isothiocyanates are used as reaction intermediates in construction of variety heterocycles systems such as poly-functional triazines, pyridazines, pyrimidines, pyridines, triazoles, thiazines, thiadiazoles, pyrazoles, isothiazoles, and pyrans [13–15]. Recently, our research area directed to design and synthesis of biologically important heterocyclic systems from readily available reagents [8,13,15]. Herein, we hope to use a simple and rapid approach to synthesize a novel series of

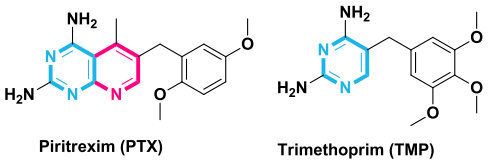


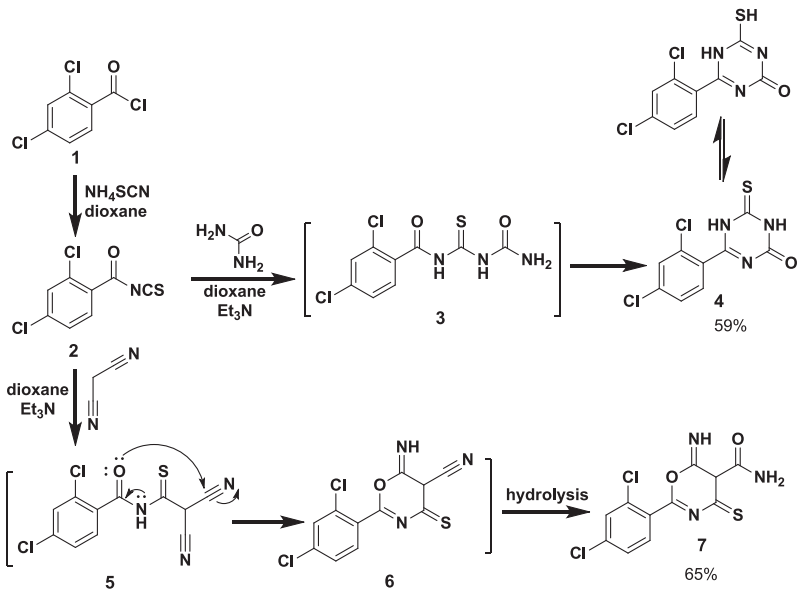
Figure 1. Pyrimidine and pyridine scaffolds as antifolate agents. [Color figure can be viewed at wileyonlinelibrary.com]

heterocyclic systems utilizing 2,4-dichlorobenzoyl isothiocaynate as a simple synthetic precursor.

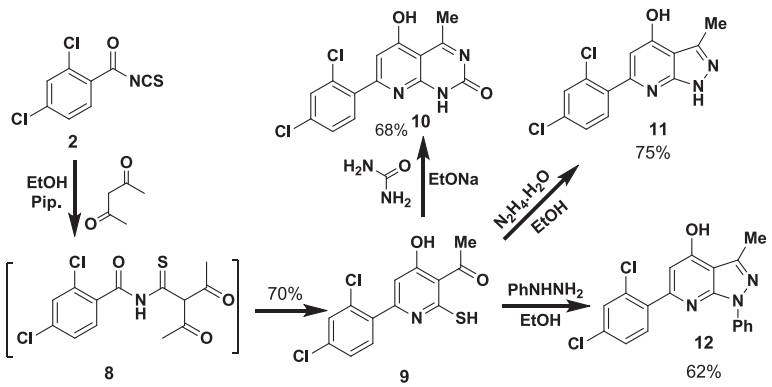
RESULTS AND DISCUSSION

Nucleophilic nitrogen of urea was added to heteroallen **2** carbon followed by cyclodehydration to furnish triazine derivative **4** (Scheme 1). The chemical structure of triazine **4** was supported by IR spectrum which leads to NH, C=O, and C=S absorption bands at 3344, 3251, 1685, and 1234 cm^{-1}, respectively. The ^{1}H-NMR revealed the presence of triazine in two tautomeric forms from the downfield signals at 9.59, 9.36, and 11.65 ppm of NH protons, in addition to aryl protons in the region 7.74–7.51 ppm as two doublets and singlets. Malononitrile and aroyl isothiocyanate derivative **2** underwent [4 + 2] cycloaddition to produce oxazine derivative **7** presumably via acyclic form **5** that underwent addition of enolic OH to cyano function followed by partial hydrolysis of cyano group (Scheme 1). The structure of target oxazine **7** was shown from IR bands that contain NH, amide C=O, C=N, and C=S at υ 3344, 3325, 3195, 1680, and 1233 cm^{-1}, respectively. Its ^{1}H-NMR displayed downfield signals at δ

Scheme 1. Intermolecular ring closure of aroyl isothiocyanate into triazine **4** and oxazine **7**.



Scheme 2. Synthetic route for annulated pyridines **10**–**12**.

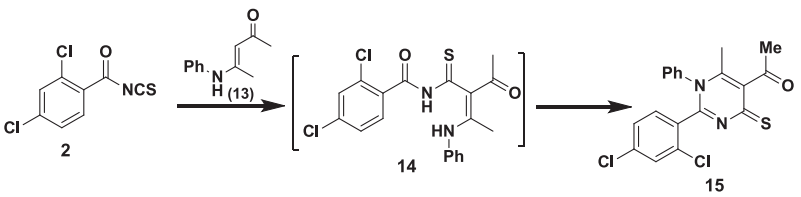


9.05 and 10.65 ppm for amino and imino protons, respectively.

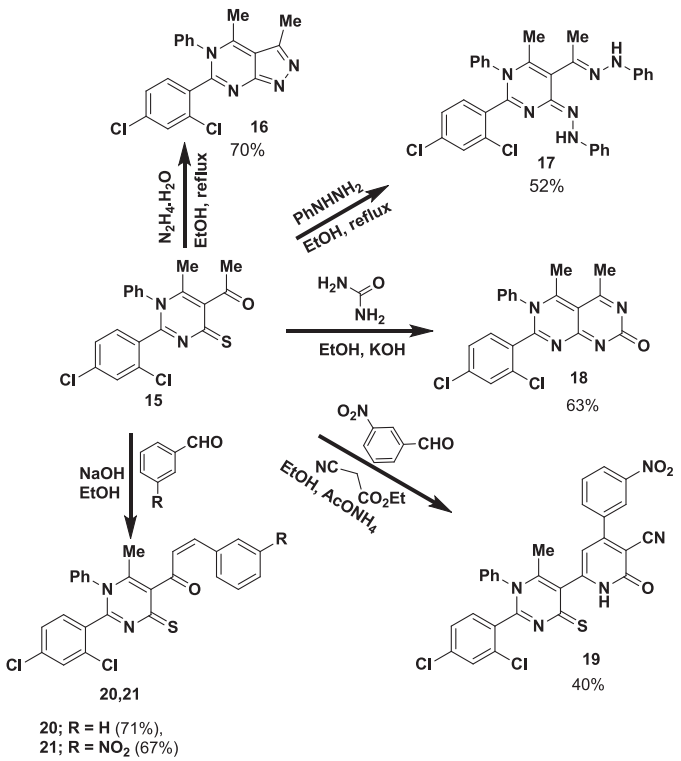
Acetylacetone and acyl isothiocyanate underwent cyclocondensation of type [3 + 3] in the presence of triethyl amine to provide pyridinethione derivative **9** (Scheme 2). The pyridine derivative **9** has absorption bands at 3375, 1697, and 1234 cm^{-1} for N-H, C═O, and C═S, respectively. Its ^{1}H-NMR contained deshielded signals at δ 7.92 and 13.69 ppm for OH and SH protons, respectively. Upon reaction of pyridine **9** with urea, the pyridopyrimidine **10** was produced as a result of nucleophilic attack of urea to carbonyl and thiocarbonyl functions (Scheme 2). 3-Acetylpyridine **9** was condensed with hydrazine hydrate to form pyrazolopyridine derivative **11**. ^{1}H-NMR data of compound **11** contain two downfield signals at δ 12.99 ppm for NH proton. The structure of compound **10** was confirmed from the IR, ^{1}H, and ^{13}C-NMR data (cf. Experimental section). Cyclocondesation of pyridine **9** with phenylhydrazine afforded 1-phenylpyrazolo[3,4-*b*]pyridine **12** in 62% yield (Scheme 2).

Enaminic carbon of enaminone derivative **13** underwent nucleophilic attack to heteroallene **2** to furnish acetyl pyrimidinethione derivative **15**. The reaction started with the formation of a non-isolable acyclic intermediate **14** that loss a molecule of H_2O (Scheme 3). Its structure was supported by IR and ^{1}H-NMR spectra, where the IR bands illustrate the presence of conjugated C═O and C═S at 1701 and 1242 cm^{-1}, respectively. The ^{1}H-NMR signals indicated the presence of two methyl groups as individual singlets at δ 1.81 and 2.50 ppm, in addition to aromatic protons as multiplet in range 7.39–7.68 ppm. Its ^{13}C-NMR signals revealed 17 signals at δ 17.83, 30.85, 126.9, 127.5, 129.0, 130.0, 130.9, 132.2, 132.4, 132.5,

Scheme 3. Synthesis of pyrimidine thione **15**.



Scheme 4. Synthetic routes for pyrimidines **16**–**21**.



135.5, 136.6, 137.0, 144.1, 152.3, 193.5, and 201.1 ppm for 2 SP^3 and 15 SP^2 carbons, respectively.

Pyrimidinethione **15** underwent heteroannulation via its refluxing with hydrazine hydrate in ethanol for 3 h affording pyrazolo[3,4-*d*]pyrimidine **16** in good yield (70%) (Scheme 4). The IR of compound **16** confirm its formation by the absence of C═O and C═S bands. Its ^{1}H-NMR confirmed the presence of two methyl groups as two individual singlets at 2.44 and 2.50 ppm, in addition to the aryl protons that are present at the predicted field. Its ^{13}C-NMR signals are exact with the chemical structure. Acetyl pyrimidinethione **15** was condensed with of phenylhydrazine to form the hydrazone derivative **17** (Scheme 4). The IR bands of pyrimidine **17** leads to NH and C═N at υ 3390, 3244, and 1620 cm^{-1}, respectively. ^{1}H-NMR contained two NH's signals at δ 9.60 and 9.64 ppm in addition to aromatic multiplet and aliphatic protons that present at the predicted field. Pyrimidine derivative **16** was allowed to react with urea to furnish pyrimido[4,5-*d*]pyrimidine of type **18** (Scheme 4). The analytical of compound **18** are exact with its chemical structure (cf. Experimental section). One-pot condensation of acetyl derivative **15** with 3-nitrobenzaldehyde, ammonium acetate, and ethyl cyanoacetate furnish pyridin-5-yl-nicotinonitrile analogue **19** in moderate yield (40%) (Scheme 4). The spectral data confirm the formation of compound **19** by the presence of absorption bands at 3414, 2218, 1701, and 1242 cm^{-1} for NH, C≡N, C═O, and C═S groups, respectively, in its IR bands. Its ^{1}H-NMR revealed new singlet and multiplet at δ 6.98 and 7.39–7.68 ppm for pyridine and aryl protons, respectively. Its ^{13}C-NMR is exact with the chemical structure (cf. Experimental section). Finall, actyl pyrimidine **15** underwent aldol condensation with aromatic aldehydes (namely, benzaldehyde and 3-nitrobenzaldehyde to form cinnamoylpyrimidine derivative **20** and **21**(Scheme 4). Their ^{1}H-NMR indicate the presence aromatic and olefinic multiplet signals in addition to aliphatic CH_3 (cf. Experimental section).

CONCLUSION

In summary, we described the utility of 2,4-dichlorobenzoyl isothiocyanate as reactive intermediate to synthesize a series of triazines, pyrimidines, and pyridines and their annulated systems via cycloaddition and intramolecular cyclization reactions.

EXPERIMENTAL

All melting points are uncorrected and were measured using an Electro-thermal IA 9100 apparatus. IR spectra (KBr) were measured on a Nexus 670 FTIR Nicolet, Fourier Transform infrared spectrometer. The ^{1}H and ^{13}C-NMR spectroscopy were determined with a JEOL-JNM-LA 500 MHz spectrometer. The chemical shifts are expressed on the δ (ppm) scale using tetramethylsilane as the standard reference. Elemental analysis determined on a PerkinElmer 240 (microanalysis), Microanalysis Center, Cairo University, Cairo, Egypt. (E. Merck).

4-(2,4-Dichlorophenyl)-6-thioxo-5,6-dihydro-1,3,5-triazin-2(1*H*)-one (4). A mixture of 2,4-dichlorobenzoyl isothiocyanate (0.02 mol) with urea (0.022 mol) and catalytic triethyl amine in dioxane was heated at refluxing temperature for 4 h and cooled, and the obtained solid was crystallized from ethanol, mp 188–190°C, yield 59%. IR (υ, cm^{-1}): 3344, 3251 (2NH), 1685 (C═O), 1234 cm^{-1} (C═S). ^{1}H-NMR (DMSO-d_6/D_2O, ppm): δ 7.51 (d, 1H, ^3J = 8.32 Hz, H_{aryl}), 7.59 (d, 1H, ^3J = 8.32 Hz, H_{aryl}), 7.74 (s, 1H, H_{aryl}), 9.59 and 9.63, 11.65 (3 s, 3H, 3NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6, ppm): δ 127.7, 129.5, 130.9, 131.6, 133.9, 136.1, 142.2, 166.8, 181.9 (SP^2-C). *Anal*. Calcd for $C_9H_5Cl_2N_3OS$ (274.13): C, 39.43; H, 1.84; N, 15.33. Found: C, 39.34; H, 1.89; N, 15.42.

2-(2,4-Dichlorophenyl)-6-imino-4-thioxo-5,6-dihydro-4*H*-1,3-oxazine-5-carboxamide (7). A mixture of 2,4-dichlorobenzoyl isothiocyanate (0.02 mol) with malononitrile (0.02 mol) and catalytic triethyl amine in dioxane was heated at refluxing temperature for 4 h and cooled, and the obtained solid was crystallized from ethanol, mp 210–212°C, yield 65%. IR (υ, cm^{-1}): 3344, 3325, 3195 (NH, NH_2), 1680 (C═O), 1608 (C═N), and 1233 cm^{-1} (C═S). ^{1}H-NMR (DMSO-d_6, ppm): δ 2.99 (s, 1H, $H_{oxazine\ ring}$), 7.51 (d, 1H, ^3J = 8.28 Hz, H_{aryl}), 7.59 (d, 1H, ^3J = 8.28 Hz, H_{aryl}), 7.74 (s, 1H, H_{aryl}), 9.05 (s, 2H, NH_2), 10.65 (s, H, NH). ^{13}C-NMR (DMSO-d_6, ppm): δ 48.00 (SP^3-C), 127.7, 129.5, 131.0, 131.6, 133.9, 136.1, 142.3, 158.6, 166.8, 181.9 (SP^2-C). *Anal*. Calcd for $C_{11}H_7Cl_2N_3O_2S$ (316.16): C, 41.79; H, 2.23; N, 13.29. Found: C, 41.88; H, 2.17; N, 13.36.

1-(6-(2,4-Dichlorophenyl)-4-hydroxy-2-mercaptopyridin-3-yl)ethanone (9). A mixture of 2,4-dichlorobenzoyl isothiocyanate (0.02 mol) with acetyl acetone (0.02 mol) and catalytic piperidine in dioxane was heated at refluxing temperature for 4 h and cooled, and the obtained pyridine derivative was crystallized from acetic acid, mp 310–312°C, yield 70%. IR (υ, cm^{-1}): 3375, (OH, NH), 1697 (C═O), and 1234 cm^{-1} (C═S). ^{1}H-NMR (DMSO-d_6, ppm): δ 1.90 (s, 3H, H_{acetyl}), 7.51 (d, 1H, $^{1,3}J$ = 8.28 Hz, H_{aryl}), 7.59 (d, 1H, $^{1,3}J$ = 8.28 Hz, H_{aryl}), 7.67 (s, 1H, $H_{pyridine}$), 7.74 (s, 1H, H_{aryl}), 7.92 (s, 1H, OH), 13.47 (s, 1H, SH). ^{13}C-NMR (DMSO-d_6, ppm): δ 28.50 (SP^3-C), 127.6, 127.7, 127.9, 129.5, 129.7, 130.5, 132.8, 133.5, 134.7, 136.3, 137.0, 172.3 (SP^2-C). *Anal*. Calcd for $C_{13}H_9Cl_2NO_2S$ (314.19): C, 49.70; H, 2.89; N, 4.46 Found: C, 49.58; H, 2.85; N, 4.53.

7-(2,4-Dichlorophenyl)-5-hydroxy-4-methylpyrido[2,3-*d*] pyrimidin-2(1*H*)-one (10). To a susbended 3-acetyl pyridine **9** (0.02 mol) in ethoxide solution (prepared from 0.23 g sodium metal in 20 mL of absolute ethanol), urea (0.011 mol) was added, the reaction mixture was refluxed for 6 h, ethanol was evaporated, and the residue was suspended in 50 mL of water and neutralize with HCl to give compound **10** that recrystallized from acetic acid, mp 201–203°C, yield 68%. IR (υ, cm^{-1}): 3444 (O-H), 3325 (N-H), 1693 (C═O), ^{1}H-NMR (DMSO-d_6/D_2O, ppm): δ 2.58 (s, 3H, H_{methyl}), 7.43 (d, 1H, $^{1,3}J$ = 8.40 Hz, H_{aryl}), 7.58 (d, 1H, ^3J = 8.40 Hz, H_{aryl}), 7.74 (s, 1H, H_{aryl}), 8.12 (s, 1H, OH, D_2O exchangeable), 12.57 (s, 1H, NH, D_2O exchangeable), ^{13}C-NMR (DMSO-d_6, ppm): δ 32.12 (SP^3-C), 125.6, 126.0, 126.5, 127.0, 127.9, 130.5, 130.6, 132.8, 133.5, 137.0, 142.0, 148.8, 166.2 (SP^2-C). *Anal*. Calcd for $C_{14}H_9Cl_2N_3O_2$ (322.15): C, 52.20; H, 2.82; N, 13.04. Found: C, 52.29; H, 2.85; N, 12.98.

6-(2,4-Dichlorophenyl)-3-methyl-1*H*-pyrazolo[3,4-*b*] pyridin-4-ol (11). Hydraine hydrate (0.015 mol) was added to a solution of compound **9** in ethanol, the resulted mixture was refluxed for 4 h, and after cooling, the resulted solid was filtered off and crystallized from acetic acid, mp 282–284°C, yield 75%. IR (υ, cm^{-1}): 3450 (OH), 3152 (NH). ^{1}H-NMR (DMSO-d_6/D_2O, ppm): δ 2.58 (s, 3H, H_{methyl}), 7.54–7.91 (m, 3H, H_{aryl}), 8.16 (s, 1H, OH, D_2O exchangeable), 12.89 (s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6, ppm): δ 30.28 (SP^3-C), 126.8, 127.5, 127.9, 128.1, 129.8, 130.4, 131.1, 131.9, 132.1, 132.7, 132.8, 133.0 (SP^2-C). *Anal*. Calcd for $C_{13}H_9Cl_2N_3O$ (294.14): C, 53.08; H, 3.08; N, 14.29. Found: C, 52.98; H, 3.05; N, 14.34.

6-(2,4-Dichlorophenyl)-3-methyl-1-phenyl-1*H*-pyrazolo [3,4-*b*]pyridin-4-ol (12). Phenyl hydrazine (0.015 mol) was added to a solution of compound **9** in ethanol, and the resulted mixture was refluxed for 4 h, and after cooling, the resulted solid was filtered off and crystallized from acetic acid, mp 268–270°C, yield 62%. IR (υ, cm^{-1}): 3344 (OH). ^{1}H-NMR (DMSO-d_6/D_2O, ppm): δ 2.57 (s, 3H, H_{methyl}), 7.27–7.74 (m, 3H, H_{aryl}), 8.59 (s, 1H, OH, D_2O exchangeable). *Anal*. Calcd for $C_{19}H_{13}Cl_2N_3O$ (370.23): C, 61.64; H, 3.54; N, 11.35. Found: C, 61.75; H, 3.50; N, 11.43.

1-(2-(2,4-Dichlorophenyl)-6-methyl-1-phenyl-4-thioxo-1,4-dihydropyrimidin-5-yl)ethanone (15). A mixture of 2,4-dichlorobenzoyl isothiocyanate (0.02 mol) with 4-(phenylamino)pent-3-en-2-one (**13**) (0.02 mol) and few drops of piperidine in dioxane was refluxed for 6 h and cooled, and the obtained solid was crystallized from acetic acid, mp >300°C, yield 73%. IR (υ, cm^{-1}): 1701 (C═O), 1242 (C═S). ^{1}H-NMR (DMSO-d_6, ppm): δ 1.81 (s, 3H, H_{acetyl}), 2.58 (s, 3H, $H_{methyl\ ring}$), 7.39–7.68 (m, 8H, H_{aryl}). ^{13}C-NMR (DMSO-d_6, ppm): δ 17.83, 30.85 (SP^3-C), 126.9, 127.5, 129.0, 130.0, 130.9, 132.2, 132.4, 132.5, 135.5, 136.5, 137.0, 144.1, 152.3, 193.5, 201.1 (SP^2-C). *Anal*. Calcd for $C_{19}H_{14}Cl_2N_2OS$ (389.30): C, 58.62; H, 3.62; N, 7.20. Found: C, 58.71; H, 3.58; N, 7.16.

6-(2,4-Dichlorophenyl)-3,4-dimethyl-5-phenyl-5*H*-pyrazolo [3,4-*d*]pyrimidine (16). A mixture of pyrimidine thione **3** (0.02 mol) with hydrazine hydrate (0.02 mol) in ethanol (20 mL) was heated at refluxing temperature for 3 h. The resulted precipitate was filtered off and crystallized ethanol, mp 292–294°C; yield 70%. IR (υ, cm^{-1}): 1620 (C═N). ^{1}H-NMR (DMSO-d_6, ppm): δ 2.44 (s, 3H, H_{methyl}), 2.50 (s, 3H, H_{methyl}), 7.27–7.90 (m, 8H, H_{aryl}). ^{13}C-NMR (DMSO-d_6, ppm): δ 29.06, 30.85 (SP^3-C), 126.9, 127.4, 129.0, 130.1, 130.9, 132.2, 132.4, 132.5, 135.6, 136.6, 137.0, 144.0, 152.3, 158.0, 160.1 (SP^2-C). *Anal*. Calcd for $C_{19}H_{14}Cl_2N_4$ (369.25): C, 61.80; H, 3.82; N, 15.17. Found: C, 61.89; H, 3.79; N, 15.22.

2-(2,4-Dichlorophenyl)-6-methyl-1-phenyl-4-(2-phenylhydrazono)-5-(1-(2-phenylhydrazono)ethyl)-1,4-dihydropyrimidine (17). A mixture of pyrimidine thione **3** (0.02 mol) with phenyl hydrazine (0.02 mol) in ethanol (20 mL) was heated at refluxing temperature for 4 h. The resulted precipitate was filtered off and crystallized ethanol, mp 168–170°C, yield 52%. IR (υ, cm^{-1}): 3390, 3244 (2NH), 1620 (C═N). ^{1}H-NMR (DMSO-d_6/D_2O, ppm): δ 1.29 (s, 3H, H_{methyl}), 2.50 (s, 3H, H_{methyl}), 7.27–7.90 (m, 18H, H_{aryl}), 9.60, 9.64 (s, 2H, 2NH, D_2O exchangeable). *Anal*. Calcd for $C_{31}H_{26}Cl_2N_6$ (553.48): C, 67.27; H, 4.73; N, 15.18 Found: C, 67.35; H, 4.70; N, 15.23.

7-(2,4-Dichlorophenyl)-4,5-dimethyl-6-phenylpyrimido [4,5-*d*]pyrimidin-2(6*H*)-one (18). A mixture of pyrimidine thione **3** (0.02 mol), urea (0.022 mol), and potassium hydroxide (0.02 mol) in ethanol (20 mL) was heated at refluxing temperature for 5 h. The resulted precipitate was filtered off and crystallized ethanol, mp 180–182°C, yield 63%. IR (υ, cm^{-1}): 1701 (C═O), 1604 (C═N). ^{1}H-NMR (DMSO-d_6/D_2O, ppm): δ 1.81 (s, 3H, H_{methyl}), 2.58 (s, 3H, H_{methyl}), 7.39–7.68 (m, 8H, H_{aryl}). ^{13}C-NMR (DMSO-d_6, ppm): δ 17.81, 30.83, (SP^3-C), 126.9, 127.5, 129.01, 129.06, 130.0, 130.9, 132.2, 132.4, 135.5, 136.5, 136.9, 144.1, 148.0, 152.4, 158.0, 169.2 (SP^2-C). *Anal*. Calcd for $C_{20}H_{14}Cl_2N_4O$ (397.26): C, 60.47; H, 3.55; N, 14.10. Found: C, 60.56; H, 3.52; N, 14.14.

6-(2-(2,4-Dichlorophenyl)-6-methyl-1-phenyl-4-thioxo-1,4-dihydropyrimidin-5-yl)-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (19). A mixture of pyrimidine thione **3** (0.02 mol), 4-nitrobenzaldehyde (0.02 mol), ethyl cyanoacetate (0.02 mol), and $AcONH_4$ (0.16 mol) in acetic acid (20 mL) was refluxed for 10 h, and the resulted solid was filtered off and crystallized form acetic acid, mp 180–182°C, yield 40%. IR (υ, cm^{-1}): 3414 (NH), 2218 (C≡N), 1701 (C═O), 1242 (C═S). ^{1}H-NMR (DMSO-d_6/D_2O, ppm): δ 2.58 (s, 3H, H_{methyl}), 6.98 (s, 1H, $H_{pyridine}$), 7.39–7.68 (m, 12H, H_{aryl}), 12.32 (s, 1H, NH). ^{13}C-NMR (DMSO-d_6, ppm): δ 30.83, (SP^3-C),

114.5, 125.5, 126.0, 126.6, 126.9, 127.5, 127.8, 128.2, 128.9, 129.0, 130.0, 130.9, 132.2, 132.4, 132.5, 135.5, 136.5, 137.0, 144.1, 148.2, 152.4, 154.0, 157.1, 158.1, 160.3, 169.8 (SP^2-C). *Anal*. Calcd for $C_{29}H_{17}Cl_2N_5O_3S$ (586.45): C, 59.39; H, 2.92; N, 11.94. Found: C, 59.28; H, 2.88; N, 11.89.

1-(2-(2,4-Dichlorophenyl)-6-methyl-1-phenyl-4-thioxo-1,4-dihydropyrimidin-5-yl)-3-phenylprop-2-en-1-one (20). A mixture of pyrimidine thione **3** (0.02 mol), benzaldehyde (0.02 mol), and sodium hydroxide (0.02 mol) was stirred at room temperature for overnight, and the formed solid was filtered off and crystallized from acetic acid, mp 215–217°C, yield 71%. IR (υ, cm^{-1}): 1701 (C═O), 1604 (C═N), 1242 (C═S). ^{1}H-NMR (DMSO-d_6, ppm): δ 2.58 (s, 3H, H_{methyl}), 6.80–7.68 (m, 15H, H_{aryl} and H_{olefin}). ^{13}C-NMR (DMSO-d_6, ppm): δ 30.83, (SP^3-C), 90.8, 112.5, 125.5, 126.0, 126.6, 126.9, 127.5, 129.0, 130.0, 130.9, 132.2, 132.4, 132.5, 135.5, 136.5, 136.9, 144.1, 154.2, 158.0, 169.0, 182.4 (SP^2-C). *Anal*. Calcd for $C_{26}H_{18}Cl_2N_2OS$ (477.40): C, 65.41; H, 3.80; N, 5.87. Found: C, 65.33; H, 3.77; N, 5.91.

1-(2-(2,4-Dichlorophenyl)-6-methyl-1-phenyl-4-thioxo-1,4-dihydropyrimidin-5-yl)-3-(3-nitrophenyl) prop-2-en-1-one (21). A mixture of pyrimidine thione **3** (0.02 mol), 4-nitrobenzaldehyde (0.02 mol), and sodium hydroxide (0.02 mol) was stirred at room temperature for overnight, and the formed solid was seperated and crystallized from acetic acid, mp 215–217°C, yield 67%. IR (υ, cm^{-1}): 1701 (C═O), 1604 (C═N), 1242 (C═S). ^{1}H-NMR (DMSO-d_6, ppm): δ 2.50 (s, 3H, H_{methyl}), 6.89–7.96 (m, 14H, H_{aryl} and H_{olefin}). ^{13}C-NMR (DMSO-d_6, ppm): δ 30.85, (SP^3-C), 101.0, 116.5, 125.5, 126.0, 126.6, 126.9, 127.5, 129.0, 129.06, 130.0, 130.9, 132.2, 132.4, 132.5, 135.5, 136.5, 136.8, 137.0, 152.3, 154.2, 158.0, 169.0, 182.5 (SP^2-C). *Anal*. Calcd for $C_{26}H_{17}Cl_2N_3O_3S$ (522.40): C, 59.78; H, 3.28; N, 8.04. Found: C, 59.88; H, 3.32; N, 8.09.

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SUPPORTING INFORMATION

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