Ameen Ali Abu-Hashem[a,b]*

[a]Photochemistry Department (Heterocyclic Unit), National Research Center, 12622, Dokki, Giza, Egypt
[b]Chemistry Department, Faculty of Science, Jazan University, 2097 Jazan, Saudi Arabia
*E-mail: aminaliabuhashem@yahoo.com

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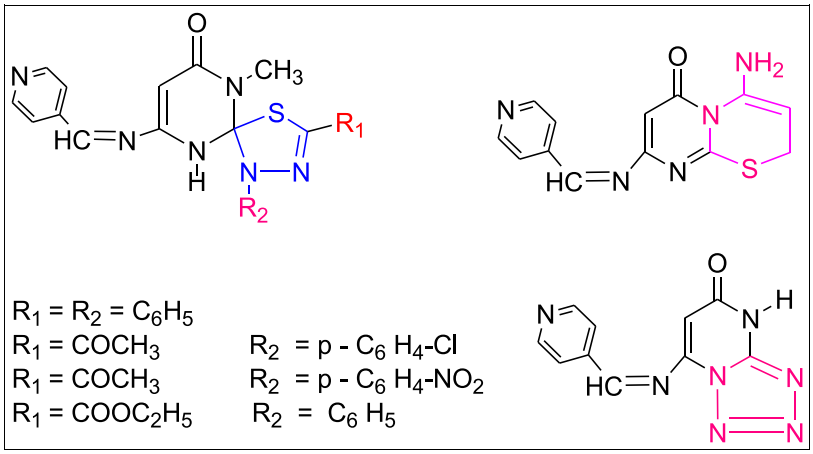

2-Mercapto-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one **1** was synthesized from Schiff base reaction of 6-amino-2-thiouracil with isonicotinaldehyde. The reaction of **1** with hydrazonyl chloride **2a–d** afforded the novel pyrimidin-4-one **3a–d**. Compounds **3a–d** reacted with methyl iodide to give **4a–d**. Subsequently, reaction of **4a–d** with triethylamine as a catalyst in dry chloroform yielded tetraaza-spiro [4.5]deca-2, 8-dien-7-one **5a–d**. In addition, reaction of **1** with acrylonitrile gave pyrimidin-propionitrile **6**. The cyclization of **6** by reacting with sodium ethoxide to give pyrimido [2, 1-b] [1,3] thiazin-6-one **7**. The refluxing of **1** with bromine in acetic acid yielded 2-bromo-pyrimidin-4-one **8**. The latter compound **8** reacted with sodium azide gave tetrazolo-pyrimidine **10**. The chemical structures of the newly synthesized compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR, and mass spectral analysis.

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INTRODUCTION

Several new organic compounds play an important role in the drug discovery. Therefore, the syntheses of polyfunctionalized heterocyclic compounds have received the attention of many researchers all over the world. Especially, pyrimidine derivatives and new hetero ring are known to exhibit promising antiviral [1], antibacterial [2], anti-aids [3], and antinociceptive activities [4], inhibitors for multidrug resistance (MDR) [5], antiplatelet and antithrombotic drugs [6] have been firmly established by clinical trials. These classes of pyrimidine based spirocyclic systems containing one carbon atom common to two rings are structurally interesting [7]. The asymmetric characteristic of the molecule due to the chiral spiro carbon is one of the important criteria of the biological activities. There are many products in the natural organic compounds called spiro compounds [8] have been discovered and proved. Therefore, spiro compounds represent an important class of naturally occurring substances characteristic by their highly pronounced biological properties [9,10].

As a result to that, most of synthetic methodologies have been developed for constructing these spiro cycles, most of which were based on cycloaddition or condensation reactions [11–19]. In this report, we have been and continue to discuss the development of new and simple synthetic methods for the efficient preparation of spiro heterocycles containing pyrimidine ring. Given the importance of the biological activity of fused pyrimidines, we have prepared heterocyclic compounds [20–26].

In this manuscript, we use new methods in the synthesis of compounds derived thia-tetraaza-spir [4.5 deca-2, 8-dien-7-one derivative. To our knowledge, this is the second report [29–32] on the synthesis of 4-amino-8-[(pyridin-4-ylmethylene)-amino]-2*H*-pyrimido [2, 1-b] [1,3] thiazin-6-one and 7-[(pyridin-4-ylmethylene)-amino]-4*H*-tetrazolo [1, 5-a]pyrimidin-5-one.

RESULTS AND DISCUSSION

This article describes our approach to the synthesis of polyfunctional heterocyclic compounds. We reported here

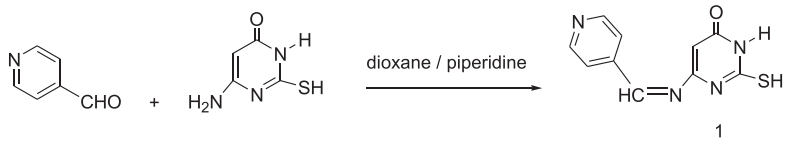
a convenient method for synthesis of tetraaza-spiro[4.5] deca-2, 8-dien-7-one and tetrazolopyrimidines derivatives. Thus, the Schiff base **1** was obtained by condensation of 6-amino thiouracil with isonicotinaldehyde in dioxane/piperidine. The structure assignments to new compounds were based on their elemental analysis and spectral (IR, ^{1}H, ^{13}C NMR, and mass) data, (Scheme 1).

Moreover, stirring under reflux 2-mercapto-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one **1** with hydrazonoyl chloride derivatives **2a–d** [27,28] in dry chloroform for 4 h under TLC control afforded 2-(*S*-p-(*S*)-phenylazo-methylsulfanyl)-6-[(pyridine-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one **3a–d**, respectively. IR, ^{1}H NMR, and ^{13}C NMR spectra of **3a–d** were given in the experimental section. Their corresponding ^{1}H NMR spectra of **3a** showed two singlet signal at δ 4.10, 5.85 ppm for phenyl protons and multiplet signal at 7.06–7.30 ppm for 10 protons phenyl group and multiplet signal at 7.82–7.92 ppm for four protons phenyl group and singlet signal at 8.07 ppm for methine proton and singlet broad signal 8.65 ppm for one proton NH group with D_2O exchangeable. The ^{13}C NMR showed at δ 65.5 ppm for one carbon atom in CH-phenyl, 112.5 ppm for one carbon atom in pyrimidin ring, 122.4–150.5 ppm for aromatic carbon atoms, 159.1, 162.5 ppm for two carbon atoms in pyrimidin ring, 163.8 ppm for one carbon atom for methine proton, and 169.6 ppm for one amid carbonyl group. Structure **4a–d** was prepared by alkylation **3a–d**.with methyl iodide and ethanolic KOH. These data are included within the assigned structures (Scheme 2).

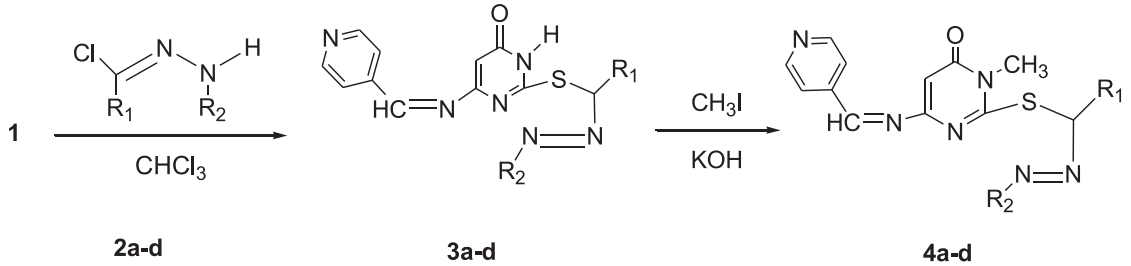
Stirring under reflux, compounds **4a–d** with few drops of triethylamine as a catalyst in dry chloroform for a long time under TLC control afforded the cyclized product 6-methyl-1,3-(sub)-9-[(pyridin-4-ylmethylene)-amino]-4-thia-1,2,6,10-tetraaza-spiro[4.5]deca-2,8-dien-7-one **5a–d**. IR, ^{1}H NMR, and ^{13}C NMR spectra of **5a–d** gave data that are in agreement with the assigned structures and experimental. The ^{1}H NMR spectrum of **5b** showed two singlet signal at δ 2.24 and 2.93 ppm for two methyl groups, singlet signal 5.75 ppm for one proton in pyrimidin ring, multiplet signals 7.32–7.41, 7.74–7.85 ppm for eight protons on phenyl groups, singlet signal 7.98 ppm for one methine proton, and an exchangeable broad signal at 8.30 ppm for one proton of the NH group. The ^{13}C NMR spectrum showed signals at δ 22.8 and 25.6 ppm for two methyl groups, signal 91.8 ppm for one spiro[4.5] carbon atom, 93.7 ppm for one carbon atom in pyrimidin ring, 121.1–150.1 ppm for aromatic carbon atoms, 152.4 ppm for carbon atom in pyrimidin ring, 162.3 ppm carbon atoms in thiadiazol ring, 163.9 ppm for one carbon atom for methine proton, 2 CO signals at 165.4, 182.2 ppm for the amid carbonyl and acetyl carbonyl groups. MS, *m/z* 440 (M^+, 81%); Scheme 3.

Treatment of **1** undergo Michael type addition to acrylonitrile [29] to give the corresponding 3-(6-oxo-4-[(pyridine-4-ylmethylene)-amino]-1,6-dihydropyrimidin-

Scheme 1. Synthesis of 2-mercapto-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one (1) from isonicotinaldehyde with 6-amino-2-thiouracil (Schiff base reaction) in high yield.

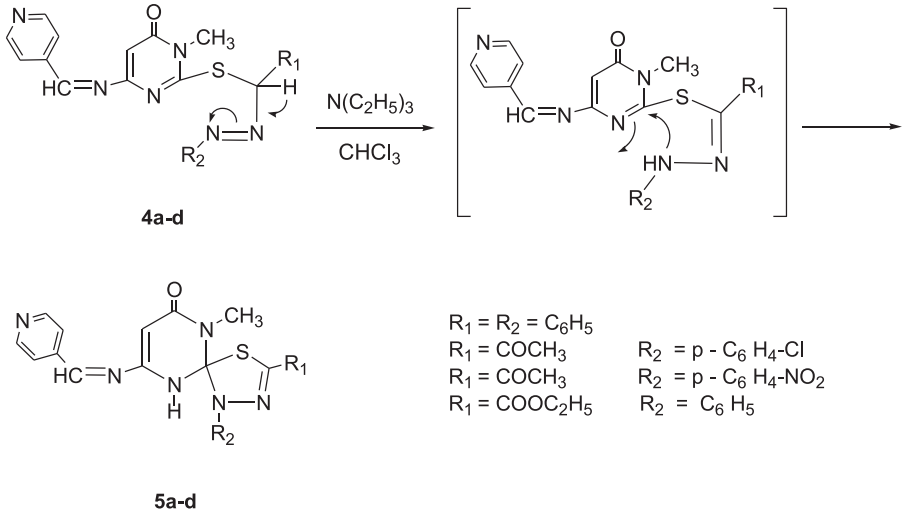


Scheme 2. Synthesis of 3-methyl-2-(azo-methyl sulfanyl)-6-[(pyridin)-amino]-pyrimidin (**4a–d**) from **3a–d** and compound **1** with hydrazonyl chloride derivatives in high yields.



$R_1 = R_2 = C_6H_5$
$R_1 = COCH_3$ $R_2 = p\text{-}C_6H_4\text{-}Cl$
$R_1 = COCH_3$ $R_2 = p\text{-}C_6H_4\text{-}NO_2$
$R_1 = COOC_2H_5$ $R_2 = C_6H_5$

Scheme 3. Synthesis of 6-methyl-1, 3-(sub.)-9-[(pyridin-4-ylmethylene)-amino]-4-thia-1, 2, 6, 10-tetraaza-spiro[4.5]deca-2, 8-dien-7-one (**5a–d**) from **4a–d** and triethylamine as a catalyst in dry chloroform in high yields.



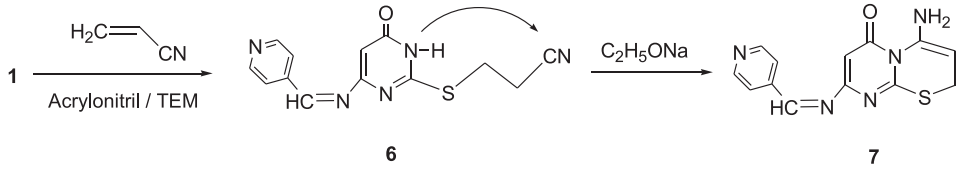
2-ylsulfanyl) propionitrile (**6**). The latter compound 4-cyanoethylmercaptopyrimidine (**6**) underwent reductive cyclization upon heating under reflux in sodium ethoxide resulting in 4-amino-8-[(pyridin-4-ylmethylene)-amino]-2*H*-pyrimido [2, 1-b] [1,3] thiazin-6-one (**7**). Its IR spectrum compound **6** displayed one group carbonitrile absorption bands at 2200 cm^{-1} (CN), beside the absence of the CN group of compound **7**. Hence, the ^1H NMR spectrum of **7** showed doublet signal at δ 3.68 ppm for two protons CH_2 group, triplet signal 3.99 ppm for one proton on thiazin ring, singlet signal 5.90 ppm for one proton on pyrimidin ring, an exchangeable broad signal at 6.72 ppm for the two protons of the amino group, doublet signal 7.94 ppm for two protons $J = 7.56$ Hz pyridine ring, doublet signal 7.98 ppm for two protons $J = 7.59$ Hz pyridine ring, and singlet signal 8.10 ppm for methine proton. The ^{13}C NMR spectrum showed at δ 20.8 ppm for one carbon atom in CH_2 group, 79.2 ppm for one carbon atom within thiazin ring, 112.3 ppm for one carbon atom in pyrimidin ring, 124.1, 138.2 ppm for three carbon atoms in pyridine ring, 145.1 ppm for one carbon atom in C–NH_2 group, 149.9 ppm for two carbon atoms in pyridine ring, 158.4, 160.8 ppm for two carbon atoms in pyrimidin ring, 163.5 ppm for one carbon atom methine proton, and 165.2 ppm for carbonyl group (Scheme 4).

The bromonation of **1** by bromine in acetic acid yielded the 2-bromo-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one (**8**).The conversion of **1** into **8** may be proceeded through the formation of pyrimidine-2-sulphonyl bromide that liberate SO_2 to give **8** [29,30]. Electron deficient nature of pyrimidine ring facilitates the synthesis of large number of pyrimidine derivatives through nucleophilic aromatic substitution of suitable leaving groups. The halogens have been especially useful in this regard [31,32]. Thus, compound **8** that reacts with sodium azide gave the corresponding tetrazolopyrimidine **10** presumably *via* the formation of azido form **9**. The structure of **10** was proved by the disappearance of azido group in IR spectrum. IR, ^1H, ^{13}C NMR, and mass spectra of **8** and **10** supported the structures (Scheme 5).

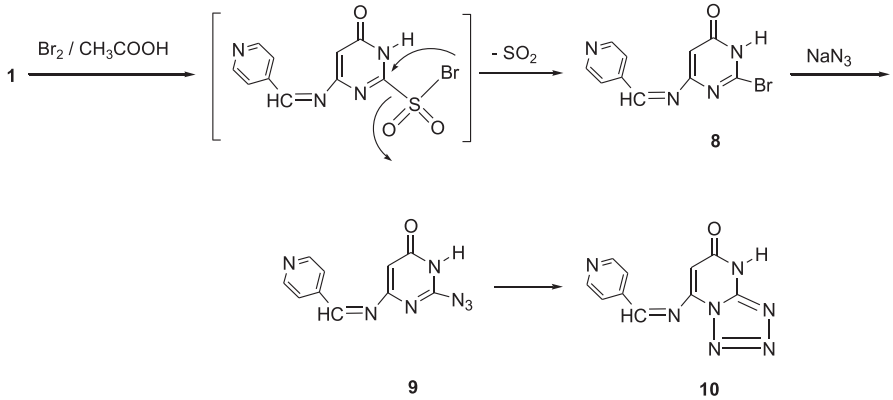
CONCLUSION

New ring compounds were prepared. In continuation, this paper describes our interest in the development of synthetic strategy to polyfunctionalized spiro organic heterocyclic compounds such as the synthesis of tetraaza-spiro[4.5]deca-2,8-dien-7-one, pyrimido[2,1-b][1,3]thiazin-6-one derivatives, and tetrazolo[1, 5-a]pyrimidin-5-one.

Scheme 4. Synthesis of 4-amino-8-[(pyridin-4-ylmethylene)-amino]-2*H*-pyrimido [2,1-b][1,3] thiazin-6-one (**7**) from compound (**1**) with acrylonitril afforded (**6**).This compound **6** refluxing in C_2H_5ONa to gave (**7**) in high yields.



Scheme 5. Synthesis of 7-[(pyridin-4-ylmethylene)-amino]-4*H*-tetrazolo[1, 5-a]pyrimidin-5-one (**10**) from compound (**1**) with bromine afforded 2-bromo-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one (**8**). The latter compound **8** refluxing in NaN_3 to gave (**10**) in high yields.



EXPERIMENTAL

All melting points are in °C and were determined on Gallenkamp electric melting point apparatus. The IR spectra were recorded potassium bromide (KBr) on a Perkin–Elmer 1430 spectrometer. The ^{1}H NMR and ^{13}C NMR spectra (δ, ppm) were recorded on JEOL-ECA 500 and JEOL JNM-LA-400 FT NMR spectrometers (Japan), and chemical shifts were expressed as δ values against TMS as an internal standard. Mass spectra were recorded on GCMS-QP 1000 EX (Shimadzu) (gas chromatography–mass spectrometer). Microanalytical data were obtained at the Microanalytical Center at Cairo University and National Research Center, Egypt.

2-Mercapto-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one (1). ***General procedure.*** A suspension of compound 6-aminothiouracil and isonicotinaldehyde (1.07 g, 10 mmol) in dioxane (40 mL) containing piperidine (0.5 mL) as a catalyst was stirred and heated under reflux for 6 h. The reaction mixture was cooled, the formed precipitate filtered off, dried, and recrystallized from DMF to afford **1**. Yellow crystal, yield, 85%, mp 305–307°C (dec.). IR (KBr) ν_{max}, cm^{-1}: 3230 (br, NH), 3025 (br, CH, aryl), 2995 (br, CH, aliph.) 1690 (CO), 1610 (CN), 1350 (CS). ^{1}H NMR (DMSO-d_6) δ 5.80 (s, 1H, C_5-H), 7.85–7.95 (m, 4H, Ar–H), 8.05 (s, 1H, CH methine), 8.35 (s, 1H, SH), 8.55 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 113.1 ($1C_5$, CH), 123.9, 138.6, 150.2 (5C pyridin), 159.4, 160.2 ($2C_2$, $_6$ pyrimidin), 164.1 (1C, CH methine),169.3 (CO amid). MS (70 ev, %) *m/z* 234 ($M^+ + 2$, 8.2%), 233($M^+ + 1$, 40.3%), 232 (M^+, 100%). *Anal.* Calcd for $C_{10}H_8N_4OS$ (232.26): C, 51.71; H, 3.47; N, 24.12; S, 13.81. Found: C, 51.78; H, 3.40; N, 24.19; S, 13.88.

2-(S-p-(S)-phenylazo-methylsulfanyl)-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one (3a–d). A suspension of compound **1** (2.32 g, 10 mmol) and the appropriate hydrazonoyl chlorides **2a–d** (10 mmol) in (35 mL) dry chloroform were stirred under reflux for 4 h under TLC control. The deposited so-precipitate was filtered off, washed with 40 mL chloroform, dried, and crystallized from appropriate solvent to produce (**3a–d**) in high yields.

2-(Phenyl-phenylazo-methylsulfanyl)-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one (3a). The compound was obtained from **1** (2.32 g,10 mmol) and N-phenylbenzene-carbo-hydrazonoyl chloride **2a** (2.310 g, 10 mmol) as pale brown crystals, crystallized from dioxane in 70% yield, mp 252–254°C (melted); IR (KBr) ν_{max}, cm^{-1}: 3220 (br, NH), 3023 (br, CH, aryl), 2992 (br, CH, aliph.) 1688 (CO), 1615 (CN). ^{1}H NMR (DMSO-d_6) δ 4.10 (s, 1H, CH-phenyl), 5.85 (s, 1H, C_5-H), 7.06–7.30 (m, 10H, Ar–H) 7.82–7.92 (m, 4H, Ar–H), 8.07 (s, 1H, CH, methine), 8.65 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 65.5(1C,CH-phenyl), 112.5 ($1C_5$, CH pyrimidin), 122.4, 123.5, 125.4, 126.5, 127.4, 128.8, 129.2, 138.7, 141.3, 149.9, 150.5 (Ar–C), 159.1, 162.5 (2C, $C_{2,6}$ pyrimidin)163.8 (1C, CH methine),169.6 (CO amid). MS (70 ev, %) *m/z* 428 ($M^+ + 2$, 6.8%), 427($M^+ + 1$, 20.6%), 426 (M^+, 80%). *Anal*. Calcd for $C_{23}H_{18}N_6OS$ (426.49): C, 64.77; H, 4.25; N, 19.70; S, 7.52. Found: C, 64.70; H, 4.29; N, 19.78; S, 7.48.

2-[1-(4-Chloro-phenylazo)-2-oxo-propylsulfanyl]-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one (3b). The compound was obtained from **1** (2.32 g,10 mmol) and 1-p-chlorophenyl-azo-1-chloroacetone **2b** (1.96 g, 10 mmol) as pale brown crystals, crystallized from DMF in 60% yield, mp 195–197°C (melted); IR (KBr) ν_{max}, cm^{-1}: 3223 (br, NH), 3027 (br, CH, aryl), 2996 (br, CH, aliph.) 1682, 1725 (2CO), 1619 (CN).^{1}H NMR (DMSO-d_6) δ 2.1(s, 3H, CH_3), 4.01 (s, 1H, CH acetyl), 5.92 (s, 1H, C_5-H), 7.21–7.30 (m, 4H, Ar–H) 7.82–7.92 (m, 4H, Ar–H), 8.02 (s, 1H, CH methine), 8.74 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 22.2 (1C, CH_3), 75.8 (1C, CH-acetyl), 111.9 ($1C_5$, CH pyrimidin),123.5, 124.3, 129.6, 138.6, 148.8, 150.1 (Ar–C), 159.8, 162.7 (2C, $C_{2,6}$ pyrimidin) 163.9 (1C, CH methine), 169.8, 190.2 (2C, CO amid, CO acetyl). MS (70 ev, %) *m/z* 428 ($M^+ + 2$, 11.2%), 427 ($M^+ + 1$, 27.8%), 426 (M^+, 70%). *Anal.* Calcd for $C_{19}H_{15}ClN_6O_2S$ (426.88): C, 53.46; H, 3.54; Cl, 8.31; N, 19.69; S, 7.51. Found: C, 53.40; H, 3.59; Cl, 8.28; N, 19.60; S, 7.59.

2-[1-(4-Nitro-phenylazo)-2-oxo-propylsulfanyl]-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one (3c). The compound was obtained from **1** (2.32 g,10 mmol) and 1-p-nitrophenyl-azo-1-chloroacetone **2c** (2.41 g, 10 mmol) as pale yellow crystals, crystallized from dioxane in 61% yield, mp 210–212°C (melted); IR (KBr) ν_{max}, cm^{-1}:3229 (br, NH), 3028 (br, CH, aryl), 2988 (br, CH, aliph.) 1685, 1730 (2CO), 1615 (CN). ^{1}H NMR (DMSO-d_6) δ 2.08 (s, 3H, CH_3),4.03 (s, 1H, CH_{acetyl}), 5.97 (s, 1H, C_5-H), 7.35–7.43 (m, 4H, Ar–H) 7.80–7.90 (m, 4H, Ar–H), 8.01 (s, 1H, CH, methine), 8.70 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 22.4 (1C, CH_3), 73.2 (1C, CH-acetyl), 112.5 ($1C_5$, CH pyrimidin),123.3, 124.2, 124.6, 138.5, 145.2, 150.2, 155.9 (Ar–C), 158.8, 162.9 (2C, $C_{2,6}$ pyrimidin) 163.6 (1C, CH methine),169.5, 178.6 (2C, CO

amid, CO acetyl). MS (70 ev, %) *m/z* 439 ($M^+ + 2$, 11.2%), 438 ($M^+ + 1$, 27.8%), 437 (M^+, 70%). *Anal*. Calcd for $C_{19}H_{15}N_7O_4S$ (437.43): C, 52.17; H, 3.46; N, 22.41; S, 7.33. Found: C, 52.10; H, 3.40; N, 22.49; S, 7.38.

(6-Oxo-4-[(pyridin-4-ylmethylene)-amino]-1,6-dihydro-pyrimidin-2-ylsulfanyl)-phenyl-azo-acetic acid ethyl ester (3d). The compound was obtained from **1** (2.32 g,10 mmol) and 1-phenyl azo-1-chloroethylacetate **2d** (2.26 g, 10 mmol) as pale brown crystals crystallized from n-hexane in 58% yield, mp 235–237°C (melted); IR (KBr) ν_{max}, cm^{-1}: 3230 (br, NH), 3035 (br, CH, aryl), 2975 (br, CH, aliph.) 1687, 1745 (2CO), 1610 (CN). ^{1}H NMR (DMSO-d_6) δ 1.35 (t, 3H, CH_3), 4.08 (s, 1H, CH ester), 4.21 (q, 2H, CH_2), 5.98 (s, 1H, C_5-H), 7.37–7.48 (m, 5H, Ar–H) 7.75–7.85 (m, 4H, Ar–H), 8.05 (s, 1H, CH, methine), 8 .76 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 21.8 (1C,CH_3), 58.5 (1C, CH_2), 70.1 (1C, CH ester), 112.4 (1C_5, CH pyrimidin), 122.6, 124.5, 125.7, 129.3, 138.7, 150.1, 151.2 (Ar–C), 158.6, 162.8 (2C, $C_{2,6}$ pyrimidin) 163.8 (1C, CH methine), 169.1, 172.2 (2C, CO amid, CO ester). MS (70 ev, %) *m/z* 424 ($M^+ + 2$, 15.1%), 423 ($M^+ + 1$, 21.2%), 422 (M^+, 76%). *Anal*. Calcd for $C_{20}H_{18}N_6O_3S$ (422.46): C, 56.86; H, 4.29; N, 19.89; S, 7.59. Found: C, 56.79; H, 4.32; N, 19.95; S, 7.62.

3-Methyl-2-(Sub-p-(sub)-phenylazo-methylsulfanyl)-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one (4a–d). To a warmed ethanolic potassium hydroxide solution (prepared by dissolving 0.56 g, 10 mmol of potassium hydroxide in 50 mL ethanol) was added compound 3a–d (10 mmol), and heating was continued for 30 min. The mixture was allowed to cool to room temperature, and methyl iodide (10 mmol) was added. The mixture was stirred under reflux for 6 h and then allowed to cool to room temperature and finally poured into cold water (100 mL). The solid product precipitated was filtered off and washed with 100 mL water. The compound was obtained as crystals (4a–d) in high yields.

3-Methyl-2-(phenyl-phenylazo-methylsulfanyl)-6-[(pyridin-4-ylmethylene)-amino]-3*H*-pyrimidin-4-one (4a). The compound was obtained from **3a** (4.26 g, 10 mmol) and methyl iodide (20 mmol) as brown crystals, crystallized from methanol in 80% yield, mp 275–277°C (melted); IR (KBr) ν_{max}, cm^{-1}: 3024 (br, CH, aryl), 2990 (br, CH, aliph.) 1686 (CO), 1614 (CN). ^{1}H NMR (DMSO-d_6) δ 2.75 (s, 3H, CH_3), 4.11 (s, 1H, CH-phenyl), 5.86 (s, 1H, C_5-H), 7.07–7.31 (m, 10H, Ar–H) 7.83–7.93 (m, 4H, Ar–H), 8.06 (s, 1H, CH methine); ^{13}C NMR (DMSO-d_6) δ 24.6 (1C, CH_3), 62.1 (1C, CH-phenyl), 112.4 (1C_5, CH pyrimidin), 122.5, 123.6, 125.3, 126.7, 127.2, 128.5, 129.1, 138.5, 141.1, 149.8, 150.4 (Ar–C), 159.3, 162.2 (2C, $C_{2,6}$ pyrimidin) 163.1 (1C, CH methine), 169.2 (CO, amid). MS (70 ev, %) *m/z* 442 ($M^+ + 2$, 9.5%), 441($M^+ + 1$, 18.3%), 440 (M^+, 84%). *Anal*. Calcd for $C_{24}H_{20}N_6OS$ (440.52): C, 65.44; H, 4.58; N, 19.08; S, 7.28. Found: C, 65.49; H, 4.50; N, 19.12; S, 7.32.

2-[1-(4-Chloro-phenylazo)-2-oxo-propylsulfanyl]-3-methyl-6-[(pyridin-4-ylmethylene)-amino]-3H-pyrimidin-4-one (4b). The compound was obtained from **3b** (4.26 g,10 mmol) and methyl iodide (20 mmol) as pale yellow crystals, crystallized from dioxane in 73% yield, mp 220–222°C (melted); IR (KBr) ν_{max}, cm^{-1}: 3025 (br, CH, aryl), 2991 (br, CH, aliph.) 1680, 1723 (2CO), 1614 (CN). ^{1}H NMR (DMSO-d_6) δ 2.1(s, 3H, CH_3), 2.73(s, 3H, CH_3), 4.02 (s, 1H, CH acetyl), 5.93 (s, 1H, C_5-H), 7.22–7.31 (m, 4H, Ar–H) 7.83–7.93 (m, 4H, Ar–H), 8.04 (s, 1H, CH methine); ^{13}C NMR (DMSO-d_6) δ 22.2 (1C, CH_3), 25.4 (1C, CH_3), 75.1 (1C, CH acetyl),111.7 (1C_5, CH pyrimidin), 123.4, 124.2, 129.5, 138.4, 148.7, 150.2 (Ar–C), 159.4, 162.2 (2C, $C_{2,6}$ pyrimidin) 163.8 (1C, CH methine), 169.5, 190.1 (2C, CO amid, CO acetyl). MS (70 ev, %) *m/z* 442 ($M^+ + 2$, 17.4%), 441 ($M^+ + 1$, 21.6%), 440 (M^+, 79%). *Anal*. Calcd for $C_{20}H_{17}ClN_6O_2S$ (440.91): C, 54.48; H, 3.89; Cl, 8.04; N, 19.06; S, 7.27. Found: C, 54.40; H, 3.80; Cl, 8.10; N, 19.12; S, 7.32.

3-Methyl-2-[1-(4-nitro-phenylazo)-2-oxo-propylsulfanyl]-6-[(pyridin-4-ylmethylene)-amino]-3H-pyrimidin-4one (4c). The compound was obtained from **3c** (4.37 g,10 mmol) and methyl iodide (20 mmol) as yellow crystals, crystallized from dimethyl formamide in 63% yield, mp 240–242°C (melted); IR (KBr) ν_{max}, cm^{-1}: 3032 (br, CH, aryl), 2979 (br, CH, aliph.) 1682, 1736 (2CO), 1612 (CN). ^{1}H NMR (DMSO-d_6) δ 2.07 (s, 3H, CH_3) 2.76 (s, 3H, CH_3), 4.08 (s, 1H, CH acetyl), 5.98 (s, 1H, C_5-H), 7.37–7.45 (m, 4H, Ar–H) 7.82–7.92 (m, 4H, Ar–H), 8.02 (s, 1H, CH methine); ^{13}C NMR (DMSO-d_6) δ 22.2 (1C, CH_3), 25.8 (1C, CH_3), 73.1 (1C, CH acetyl), 112.2 (1C_5, CH pyrimidin), 123.2, 124.3, 124.7, 138.3, 145.3, 150.1, 155.1 (Ar–C), 158.6, 162.5 (2C, $C_{2,6}$ pyrimidin) 163.2 (1C, CH methine), 169.2, 178.4 (2C, CO amid, CO acetyl). MS (70 ev, %) *m/z* 453 ($M^+ + 2$, 15.9%), 452 ($M^+ + 1$, 20.1%), 451 (M^+, 65%). *Anal*., Calcd for $C_{20}H_{17}N_7O_4S$ (451.46): C, 53.21; H, 3.80; N, 21.72; S, 7.10. Found: C, 53.28; H, 3.87; N, 21.76; S, 7.19.

(1-Methyl-6-oxo-4-[(pyridin-4-ylmethylene)-amino]-1,6-dihydro-pyrimidin-2-ylsulfanyl) phenylazo-acetic acid ethyl ester (4d). The compound was obtained from **3d** (4.22 g,10 mmol) and methyl iodide (20 mmol) as yellow crystals, crystallized from dioxane in 68% yield, mp 265–267°C (melted); IR (KBr) ν_{max}, 3032 (br, CH, aryl), 2973 (br, CH, aliph.) 1682, 1743 (2CO), 1609 (CN). ^{1}H NMR (DMSO-d_6) δ 1.34 (t, 3H, CH_3), 2.78 (s, 3H, CH_3), 4.09 (s, 1H, CH ester), 4.23 (q, 2H, CH_2), 5.99 (s, 1H, C_5-H), 7.38–7.49(m, 5H, Ar–H) 7.76–7.86 (m, 4H, Ar–H), 8.07 (s, 1H, CH, methine); ^{13}C NMR (DMSO-d_6) δ 21.8, 25.9 (2C, 2CH_3), 58.6 (1C, CH_2), 70.2(1C, CH-ester), 112.7 (1C_5, CH pyrimidin), 122.8, 124.7, 125.9, 129.5, 138.8, 150.4, 151.4 (Ar–C), 158.7, 162.9 (2C, $C_{2,6}$ pyrimidin) 163.4 (1C, CH methine), 169.3, 172.5 (2C, CO amid, CO ester). MS (70 ev, %) *m/z* 438 ($M^+ + 2$, 19.3%), 437 ($M^+ + 1$, 27.5%), 436 (M^+, 79%). *Anal*. Calcd for $C_{21}H_{20}N_6O_3S$ (436.49): C, 57.79; H, 4.62; N, 19.25; S, 7.35. Found: C, 57.70; H, 4.58; N, 19.17; S, 7.30.

6-Methyl-1, 3-(sub.)-9-[(pyridin-4-ylmethylene)-amino]-4-thia-1, 2, 6, 10-tetraaza-spiro[4.5]deca-2, 8-dien-7-one (5a–d). A mixture from compound 4a-d (10 mmol) was stirred under reflux in dry chloroform (40 mL) and 4 drops of triethylamine as a catalyst for a long time under TLC control for 7 h. The solvent was evaporated under reduced pressure. The solid produced was washed four times with 50 mL methanol and crystallized form an appropriate solvent to produce 5a-d in high yields.

6-Methyl-1, 3-diphenyl-9-[(pyridin-4-ylmethylene)-amino]-4-thia-1, 2, 6, 10-tetraaza-spiro[4.5]deca-2, 8-dien-7-one (5a). The compound was obtained from **4a** (4.40 g, 10 mmol) and tri-ethyl amine (1 mL as a catalyst); as white crystals, crystallized from benzene in 71% yield, mp 340–342°C (melted); IR (KBr) ν_{max}, cm^{-1}: 3240 (br, NH), 3045 (br, CH, aryl), 2970 (br, CH, aliph.) 1673 (CO), 1627 (CN), 1570 (CC).^{1}H NMR (DMSO-d_6) δ 2.95 (s,3H,CH_3),5.72 (s, 1H, CH, pyrimidin), 7.05 –7.30 (m, 10H, Ar–H) 7.75–7.88 (m, 4H, Ar–H), 7.96 (s, 1H, CH methine), 8.35 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 22.1 (1C,CH_3), 92.01(1C,spiro[4.5] carbon atom), 93.6 (1C, CH pyrimidin), 122.4, 124.3, 128.5, 128.8, 129.4,130.1, 131.5, 138.3,143.5,149.7 (Ar-C), 154.1, 162.2 (2C, C, pyrimidin, C, thiadiazol), 163.1 (1C, CH methine),165.5 (CO). MS (70 ev, %) *m/z* 442 ($M^+ + 2$, 15.3%), 441($M^+ + 1$, 14.2%), 440 (M^+,

87%). *Anal*. Calcd for $C_{24}H_{20}N_6OS$ (440.52): C, 65.44; H, 4.58; N, 19.08; S, 7.28. Found: C, 65.50; H, 4.55; N, 19.15; S, 7.34.

3-Acetyl-1-(4-chloro-phenyl)-6-methyl-9-[(pyridin-4-ylmethylene)-amino]-4-thia-1, 2, 6, 10-tetraaza-spiro[4.5]deca-2, 8-dien-7-one (5b). The compound was obtained from **4b** (4.40 g,10 mmol) and triethylamine (1 ml as a catalyst) as yellow crystals, crystallized from DMF in 69% yield, mp 260–262°C (melted); IR (KBr) ν_{max}, cm^{-1}: 3245 (br, NH), 3048 (br, CH, aryl), 2975 (br, CH, aliph.)1675, 1730 (2CO),1625 (CN),1575 (CC).^{1}H NMR (DMSO-d_6) δ 2.24 (s, 3H, CH_3), 2.93 (s, 3H, CH_3), 5.75 (s, 1H, CH pyrimidin),7.32–7.41 (m, 4H, Ar–H) 7.74–7.85 (m, 4H, Ar–H), 7.98 (s, 1H, CH methine), 8.30 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 22.8, 25.6 (2C, $2CH_3$), 91.8 (1C,spiro[4.5] carbon atom), 93.7 (1C,CH pyrimidin), 121.1, 122.5, 124.3, 129.8, 138.2, 141.7, 150.1 (Ar-C), 152.4, 162.3 (2C,C pyrimidin, C thiadiazol),163.9 (1C, CH methine), 165.4, 182.2 (2C, CO amid, CO acetyl). MS (70 ev, %) *m/z* 442 (M^+ + 2, 13.7%), 441 (M^+ + 1, 26.9%), 440 (M^+, 81%). *Anal*., Calcd for $C_{20}H_{17}Cl\,N_6O_2S$ (440.91): C, 54.48; H, 3.89; Cl, 8.04; N, 19.06; S, 7.27. Found: C, 54.38; H, 3.82; Cl, 8.12; N, 19.10; S, 7.35.

3-Acetyl-6-methyl-1-(4-nitro-phenyl)-9-[(pyridin-4-ylmethylene)-amino]-4-thia-1, 2, 6, 10-tetraaza-spiro[4.5]deca-2, 8-dien-7-one (5c). The compound was obtained from **4c** (4.51 g,10 mmol) and triethylamine (1 mL as a catalyst) as pale yellow crystals, crystallized from methanol in 66% yield, mp 271–273°C (melted); IR (KBr) ν_{max}, cm^{-1}: 3241 (br, NH),3046 (br, CH, aryl), 2970 (br, CH, aliph.) 1677, 1738 (2CO),1622 (CN), 1572 (CC).^{1}H NMR (DMSO-d_6) δ 2.25 (s, 3H, CH_3) 2.91 (s, 3H, CH_3), 5.72 (s, 1H, CH pyrimidin), 7.15–7.35 (m, 4H, Ar–H) 7.65–7.76 (m, 4H, Ar–H),7.90 (s, 1H, CH methine), 8.25 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 22.1, 25.3 (2C, $2CH_3$), 91.9 (1C, spiro[4.5]carbon atom), 93.8 (1C, CH pyrimidin), 120.2, 123.5, 124.6, 136.8, 138.5, 149.4, 150.3 (Ar– C), 153.6, 162.7 (2C; C , pyrimidin, C, thiadiazol),163.6 (1C, CH methine), 165.4, 185.3 (2C, CO amid, CO acetyl). MS (70 ev, %) *m/z* 453 (M^+ + 2, 25.1%), 452 (M^+ + 1, 22.2%), 451 (M^+, 70%). *Anal*., Calcd for $C_{20}\,H_{17}\,N_7\,O_4\,S$ (451.46): C, 53.21; H, 3.80; N, 21.72; S, 7.10. Found: C, 53.17; H, 3.85; N, 21.70; S, 7.09.

10-Methyl-9-oxo-1-phenyl-7-[(pyridin-4-ylmethylene)-amino]-4-thia-1, 2, 6, 10-tetraaza-spiro[4.5]deca-2, 7-diene-3-carboxylic acid ethyl ester (5d). The compound was obtained from **4d** (4.36 g,10 mmol) and triethylamine (1 mL as a catalyst) as brown crystals, crystallized from ethanol in 62% yield, mp 331–333°C (melted); IR (KBr) ν_{max}, 3240 (br, NH), 3040 (br, CH, aryl), 2968 (br, CH, aliph.) 1670, 1740 (2CO), 1625 (CN), 1577 (CC). ^{1}H NMR (DMSO-d_6) δ 1.35 (t,3H,CH_3), 2.94 (s,3H, CH_3), 4.25 (q, 2H,CH_2), 5.78 (s, 1H, CH pyrimidin),7.17 –7.28 (m, 5H, Ar-H) 7.79 –7.89(m, 4H, Ar-H), 8.02 (s, 1H, CH methine), 8.21 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 22.7, 25.8 (2C, $2CH_3$), 59.1 (1C,CH_2), 91.5 (1C,spiro[4.5] carbon atom), 93.7 (1C,CH pyrimidin), 120.08, 122.4,124.2,129.4, 137.9,143.4, 149.7 (Ar-C), 155.1, 162.5 (2C; C, thiadiazol, C, pyrimidin), 163.4 (1C,CH methine),165.3,179.2 (2C, CO amid, CO ester). MS (70 ev, %) *m/z* 438 (M^+ + 2, 12.1%), 437 (M^+ + 1, 17.6%), 436 (M^+, 71%). *Anal*. Calcd for $C_{21}H_{20}N_6O_3S$ (436.49): C, 57.79; H, 4.62; N, 19.25; S, 7.35. Found: C, 57.72; H, 4.55; N, 19.19; S, 7.28.

3-(6-Oxo-4-[(pyridin-4-ylmethylene)-amino]-1, 6-dihydro-pyrimidin-2-ylsulfanyl)-propionitrile (6). A mixture of **1** (2.32 g, 10 mmol) and acrylonitrile (.53 g, 10 mmol) and TEM (3 drops) in ethanol (10 mL) was heated under reflux for 2 h. After cooling, the precipitate was collected and crystallized from methanol to give white crystals in 74% yield, mp 172–174 °C (melted); IR (KBr) ν_{max}, 3230 (br, NH), 3025 (br, CH, aryl), 2960 (br, CH, aliph.), 2200 (CN), 1665 (CO), 1620 (CN), 1572 (CC). ^{1}H NMR (DMSO-d_6) δ 3.09(t, 2H, CH_2), 3.25(t, 2H, CH_2), 5.88 (s, 1H, pyrimidine), 7.92 (d, 2H, J = 7.55 Hz, pyridine), 7.96 (d, 2H, J = 7.58 Hz, pyridine), 8.08 (s, 1H, CH, methine proton), 8.35 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 20.2, 22.4 (2C, CH_2), 112.4 (1C_5, pyrimidine), 118.1(1C,CN), 124.2, 138.4, 150.1 (5C, pyridine), 158.6, 160.5 (2C, $C_{2,6}$ pyrimidin), 163.8 (1C, methine proton), 169.1 (CO, amid). MS (70 ev, %) *m/z* 287 (M^+ + 2, 11.3%), 286 (M^+ + 1, 25.4%), 285 (M^+, 100%). *Anal*. Calcd for $C_{13}H_{11}N_5OS$ (285.32): C, 54.72; H, 3.89; N, 24.55; S, 11.24. Found: C, 54.78; H, 3.42; N, 24.50; S, 11.29.

4-Amino-8-[(pyridin-4-ylmethylene)-amino]-2H-pyrimido [2, 1-b] [1,3] thiazin-6-one (7). A solution of **6** (2.85 g, 10 mmol) in sodium ethoxide (0.23 g of sodium metal in 40 cm^3 ethanol) was stirred under reflux for 7 h. After cooling the reaction mixture was neutralized with cooled 10% HCl and the solid formed was collected by filtration, washed with water, dried, and recrystallized from ethanol in 74% yield, mp 246–248°C (melted); IR (KBr) ν_{max}, 3420 (br, NH_2),3021(br, CH, aryl), 2970 (br, CH, aliph.), 1666 (CO),1628 (CN), 1578 (CC). ^{1}H NMR (DMSO-d_6) δ 3.68(d,2H,CH_2), 3.99 (t,1H, thiazin ring), 5.90 (s, 1H, pyrimidin), 6.72 (s, 1H, NH_2, D_2O exchangeable), 7.94 (d, 2H, J = 7.56 Hz, pyridine),7.98 (d, 2H, J = 7.59 Hz, pyridine), 8.10 (s, 1H, methine proton); ^{13}C NMR (DMSO-d_6) δ 20.8 (1C, CH_2),79.2 (1C, CH, thiazin ring), 112.3 (1C, pyrimidin), 124.1, 138.2, (3C, pyridine), 145.1 (1C, C-NH_2), 149.9 (2C, pyridine), 158.4, 160.8 (2C, pyrimidin), 163.5 (1C, methine proton),165.2 (CO). MS (70 ev, %) *m/z* 287 (M^+ + 2, 14.5%), 286 (M^+ + 1, 20.3%), 285 (M^+, 90%). *Anal*. Calc. for $C_{13}H_{11}N_5OS$ (285.32): C, 54.72; H, 3.89; N, 24.55; S, 11.24. Found: C, 54.69; H, 3.45; N, 24.60; S, 11.27.

2-Bromo-6-[(pyridin-4-ylmethylene)-amino]-3H-pyrimidin-4-one (8). Bromine gas was bubbled through a suspension of 1 (2.32 g, 10 mmol) in acetic acid (50 mL, 25%) for about 4 hours. The result white precipitate was collected by filtration, washed with water and dried to give **8** and recrystallized from methanol in 70% yield, mp >350°C (melted); IR (KBr) ν_{max}, 3218 (br, NH), 3030 (br, CH, aryl), 2960 (br, CH, aliph.), 1660 (CO), 1625 (CN), 1570 (CC). ^{1}H NMR (DMSO-d_6) δ 5.85 (s, 1H, pyrimidin),7.92 (d, 2H, J = 7.55 Hz, pyridine),7.95 (d, 2H, J = 7.57 Hz, pyridine), 8.07 (s,1H, methine proton), 8.30 (s, 1H, NH, D_2O exchangeable);^{13}C NMR (DMSO-d_6) δ 112.4 (1C,pyrimidin), 124.2,138.4,149.8 (5C, pyridine), 158.6,162.1 (2C, pyrimidin), 163.9 (1C, methine proton), 167.3 (CO). MS (70 ev, %) *m/z* 281 (M^+ + 2, 24.1%), 280 (M^+ + 1, 11.2%), 279 (M^+, 80%). *Anal*. Calcd for $C_{10}H_7Br\,N_4O$ 279.09): C, 43.03; H, 2.53; Br, 28.63; N, 20.07. Found: C, 43.10; H, 2.58; Br, 28.72; N, 20.11.

7-[(Pyridin-4-ylmethylene)-amino]-4H-tetrazolo[1,5-a] pyrimidin-5-one (10). A mixture of **8** (2.79 g, 10 mmol) and sodium azide (.65 g, 10 mmol) in ethanol (40 mL) were refluxed for 5 hours. The solid that separated after cooling and pouring onto water was collected by filtration and crystallized from dioxane to give pale yellow crystals of **10**, in 62% yield, mp 280–282°C (melted); IR (KBr) ν_{max}, 3232 (br, NH), 3035 (br, CH, aryl), 2970 (br, CH, aliph.), 1655 (CO), 1620 (CN), 1580 (CC). ^{1}H NMR (DMSO-d_6) δ 5.90 (s, 1H, pyrimidin),7.98 (d, 2H, J = 7.60 Hz, pyridine) ,7.99 (d, 2H, J = 7.62 Hz, pyridine), 8.12 (s,1H, methine proton), 8.38 (s, 1H, NH, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ 100.1 (1C, pyrimidin), 124.3, 138.2, 149.7 (5C, pyridine), 151.1, 159.5 (2C, pyrimidin), 163.6 (1C,

methine proton),165.1 (CO). MS (70 ev, %) *m/z* 243 ($M^+ + 2$, 20.2%), 242 ($M^+ + 1$, 16.5%), 241 (M^+, 68%). *Anal*. Calcd for $C_{10}H_7N_7O$ (241.21): C, 49.79; H, 2.93; N, 40.65. Found: C, 49.70; H, 2.98; N, 40.57.

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