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Chemical Synthesis of Some Novel 6-Aminouracil-2-Thiones and Their Glycoside Analogues

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6-AMINOURACIL-2-THIONE (1) and its 5-bromo derivative 2 underwent alkylation yielding their respective S-alkyl products 4_{a-j}. The reaction of compound 1 and aldehydes in the presence of chloroacetic acid afforded the respective thiazolopyrimidinyl acetamides 7_{a-d}. The C-glycosides $8_{a,b}$ and 9_{c-e} were successfully prepared through condensing compound 1 and the appropriate sugar in the presence of chloroacetic acid. The behavior of certain S-alkyl derivative 4 towards amines and hydrazines was also studied. Structure elucidations for the new products were supported by compatible chemical and spectral measurements.

Keywords : Aminothiouracil , Glycoside , Nucleoside, NMR and IR .

6-Amino-2-thiouracil (1) and its derivatives are chemically and biologically active compounds. They are used as antithrombotic[(1)], antimicrobial[(2)], anti-inflammatory[(3)], antiviral[(4)], antidotal[(2)], anticancer agents[(2,5)] and potent inhibitors of interleukin-8-induced neutrophil chemotaxis[(6)]. Also, they are utilized in other medicinal purposes[(7)] and as stabilizers in photographic emulsions[(8)].

Thiouracil derivatives are well-established medications toward cancer diseases. In continuation to our research in drug discovery program, to find new chemical structures acting toward cancer and AIDS, we report here synthesizing new structures based on reacting 6-amino-2-thiouracil with mono- and multi-function groups as well as glucosidation of the new synthesized compounds.

As obvious from all mentioned above, 6-amino-2-thiouracil has a wide range of applications which promote us to use new synthetic routes to gain end products which could be used in many applications.

Results and Discussion

Treatment of 6-amino-2-thiouracil (or 6-aminouracil-2-thione) (1) with an equimolecular amount of bromine in acetic acid yielded 6-amino-5-bromo-2-thiouracil (2) (Scheme 1).

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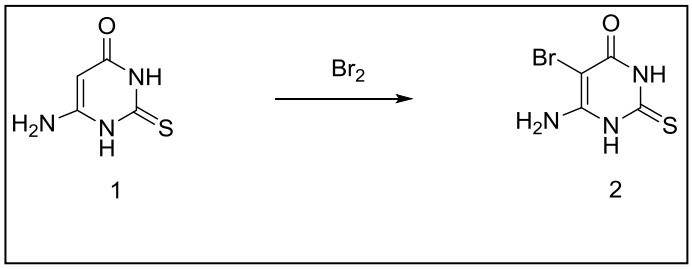
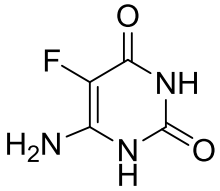


Scheme 1.

Assignment of structure **2** was based on elemental analyses and spectral data. The ^{1}H-NMR spectrum (DMSO-d_6) shows the lack of the methine proton present at δ 4.90 ppm in the spectrum of compound **1**. Besides, the elemental analysis indicates the presence of bromine atom in the molecule. (See Experimental).

Compound **2** is a very important derivative to us, since it simulates 5-fluorouracil **3** which is a well-known anticancer drug.



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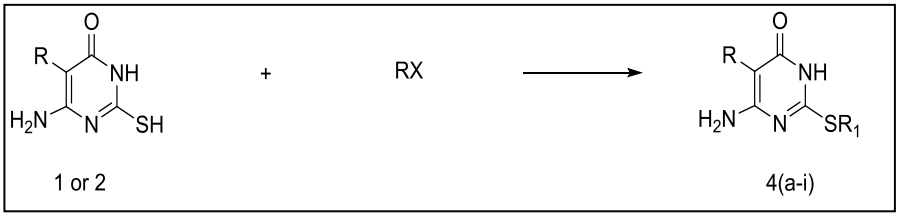
Reaction of compound **1** or **2** with the alkylating reagents in ethanolic sodium ethoxide solution produced the 2-alkylthio derivatives **4a-i** . (Scheme 2).

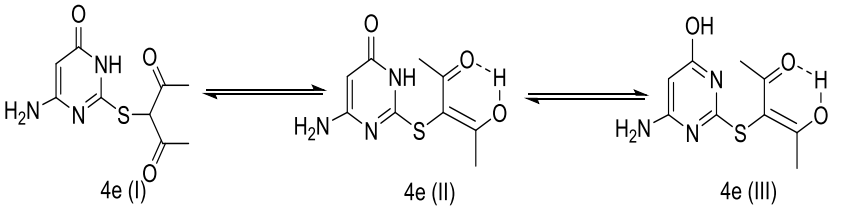


4a; R=H, R1= Me, 4b; R=H, R_1=Et, 4c; R=H, R_1=CH_2COOEt, 4d; R=H, R_1=CH_2COph, 4e; R=H, R_1=$CH(COH_3)_2$, 4f; R=Br, R_1=Me, 4g; R=Br, R_1=Et, 4h; R=Br, R_1= CH_2COph, 4i; R=Br, R_1= $CH(COH_3)_2$

Scheme 2.

Compound **4b** has been now prepared by a method different from those previously reported[1,9] to give us a better yield and purity. The ^{1}H-NMR spectrum (DMSO- d_6) of compound **4e** as an example showed signals at δ 2.15

ppm (s, 3H, Me), δ 2.55 ppm (s, 3H, Me), δ5.20 ppm (s, 1H, methine proton of the uracil ring), δ 6.50 ppm (br. s, 2H, NH_2, D_2O exchangeable), δ 7.56ppm (br. s, 1H, NH, disappeared after D_2O exchange), δ 10.19 ppm (br. s, 1H, OH, D_2O exchangeable). We noticed disappearance of the methine proton in derivative **4i** because of the existence of bromine atom at position 5.

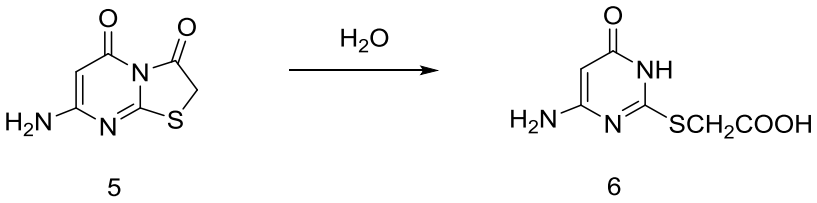


Scheme 3.

Compound **4e** exists mostly in the form **4e (II)**. This belief is inferred from the data obtained from **DEPT** (see Experimental).

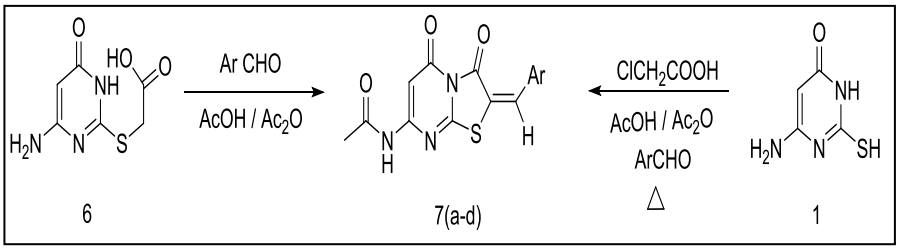
The idea of the existence of an equilibrium in the above equation is not appealing for this case since the DEPT experiment duration is long and this experiment ensures so strongly the existence of structure **4e (II).**

Compounds **4e** could exist in the enolic form **4(III),** based on the positive result with ferric chloride which develops a deep violet color. That could be understood because the form **4(III)** is stabilized by aromaticity and intramolecular hydrogen bonding (Scheme 3).



Scheme 4.

The S-carboxymethyl derivative **6** was previously prepared [8,10]but in a low yield. We report here an alternative method for preparing the same compound in high yield and purity by boiling 2,3-dihydro-5*H*-7-amino-thiazolo[3,2-*a*]pyrimdine-3,5-dione **(5)** with water. The spectral and elemental data were identical to those reported in the literature[11,12].

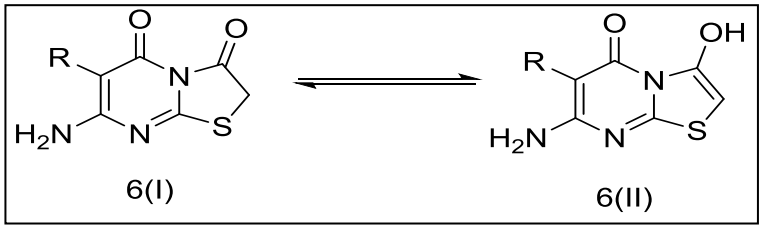


7a; Ar= C_6H_5, 7b; Ar= C_6H_4OMe-*p*, 7c; Ar= C_6H_4Cl-*p*, 7d; Ar=C_4H_3S.

Scheme 5.

Heating under reflux a mixture of **1** with chloroacetic acid, an appropriate aromatic aldehyde, anhydrous sodium acetate, glacial acetic acid, and acetic anhydride afforded N-(2-arylidene-6- alkyl-3,5- dioxo-3,5- dihydro-2*H*-thiazolo [3,2-*a*] pyrimidin-7-yl) acetamide (**7a-d)** (see Experimental).

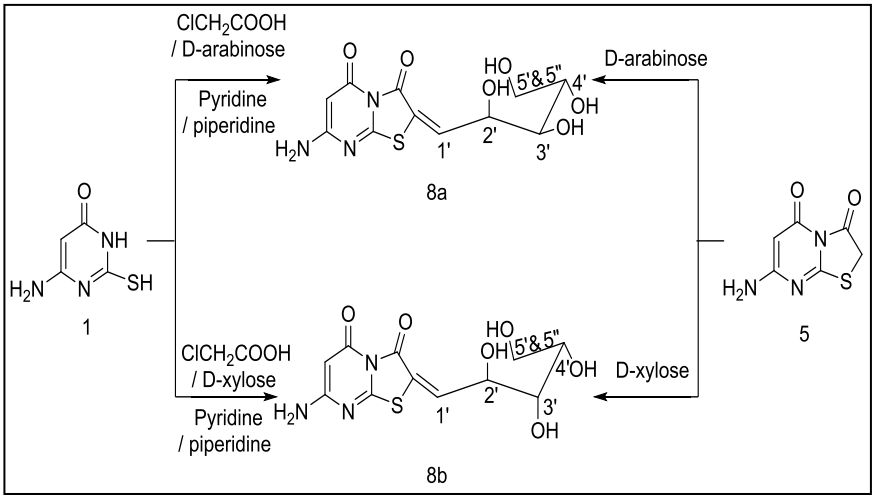
The chemical structure of compound **7d** as an example was inferred through reaction of **6** with 2-thiophene aldehyde in glacial acetic acid and acetic anhydride. The IR spectrum of compound **7d** displayed three carbonyl groups at 1710, 1696 and 1660 cm^{-1} (see Experimental). Also, its ^{1}H-NMR spectrum (DMSO-d_6) showed signal at δ 7.30 ppm (br. s, 1H, disappeared after D_2O exchange, corresponding to the NH group) and at δ 8.10 ppm (s, 1H, sp^2 methine proton).



C-Glycosides have been a field of broad interests for their antiviral activities and high selectivity against several viruses like HIV-1[13]. These facts encouraged us to synthesize a new C-glycoside from 6-amino-2-thiouracil (**1**).

Compound **6**[14] possesses two possible reaction centers to react with aldoses which are the amino group and the methylene group. We report here that the priority for such reaction is the methylene group, which was unexpected. Moreover in a previous work from our research group[15], the reaction was expected to take place on the amino group, due to the tautomerization which makes the reaction on the amino group easier.

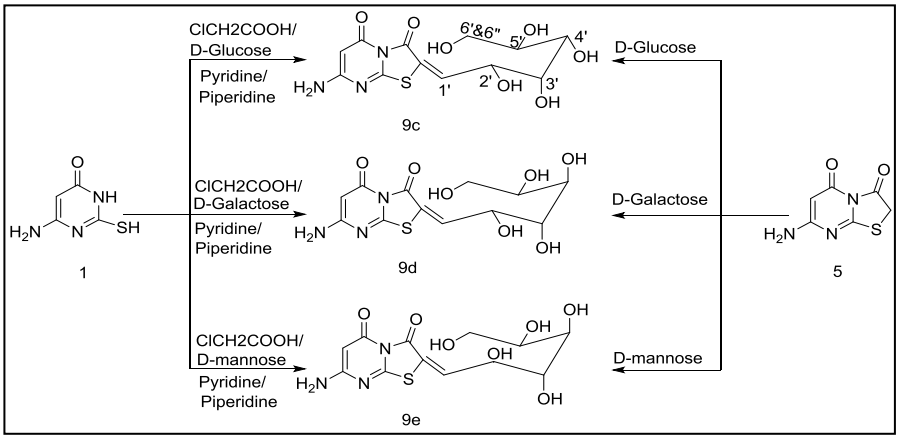
So, heating compound **5** under reflux in absolute alcohol with aldopentoses namely D-arabinose and D-xylose yielded the corresponding C-glycoside **8(a,b)**.



Scheme 6.

The same reaction could be achieved in one pot-step synthesis starting from **1** and chloroacetic acid in pyridine and a few drops of piperdine[16] (Scheme 6) .

Taking as an example the product with D-arabinose **8a**, its IR spectrum displayed absorption bands at 3500 cm^{-1} (br. corresponding to the 4 (OH) groups) , 3250 cm^{-1} for NH_2 group , 1685 cm^{-1} ,1740 cm^{-1} for the(CO) of true ketone and tert. amide. The ^{1}H-NMR spectrum (DMSO-d_6) of compound **8a** revealed signals at δ 03.70 ppm (m, 4H, OH-2`, OH-3`, OH-4`, OH-5`, D_2O exchangeable), 4.35 (m, 1H, H-3`), 04.45 (m, 1H, H-4`), 4.60 (m, 2H, H-5`, H-5``), 5.40 (dd,1H, *J*= 7.50 Hz, H-2`), 5.45 (s, 1H, uracil methine proton), 6.50 (br., s., 2H,$NH_2$, $D_2O$ exchangeable), 7.40 (d,1H,7.50 Hz, H-1`), (for the rest of data see Experimental).

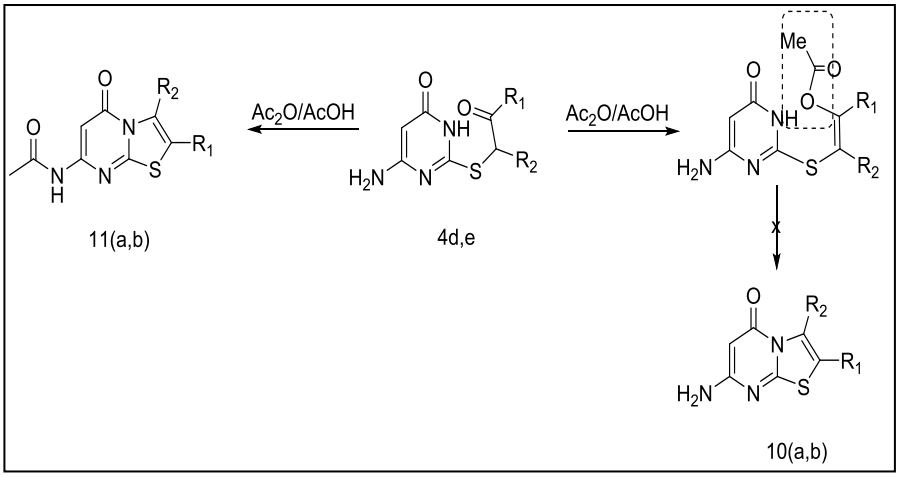


Scheme 7.

Applying the same reaction conditions on aldohexoses namely D-glucose, D-galactose, and D-manose either by using compound **1** or **5,** afforded the corresponding C-glycosides **9c-e** respectively (Scheme **7**).

The ^{1}H-NMR spectrum (DMSO-d_6) of compound **9c** as an example, showed signals at δ 3.55ppm (m,5H, 5OH, D_2O exchangeable, OH-2`, OH-3`, OH-4`, OH-5`, and OH-6`), δ 3.75 ppm (m, 1H, H-5`), δ 4.30 ppm (m, 2H, H-6`, H-6``), δ 4.50 ppm (m, 1H, H-4`), δ 4.60 ppm (m, 1H, H-3`), δ 5.00 ppm (s, 1H, uracil, methine proton), δ 5.50 ppm (m, 1H, H-2`) , δ 6.50 ppm (br. s, 2H, $NH_2$ group, $D_2O$ exchangeable), δ 7.40 ppm (d, 1H, *J*=7.5 Hz, H-1`).

A simple and conventional method is reported here for cyclization of both compounds **4d** and **4e** *via* acetylation mechanism.



10a;R_1= COMe, R_2= CH_3 , 11a; R_1= COMe, R_2= CH_3, 10b;R_1=H, R_2=Ph , 11b; R_1=H, R_2=Ph.

Scheme 8.

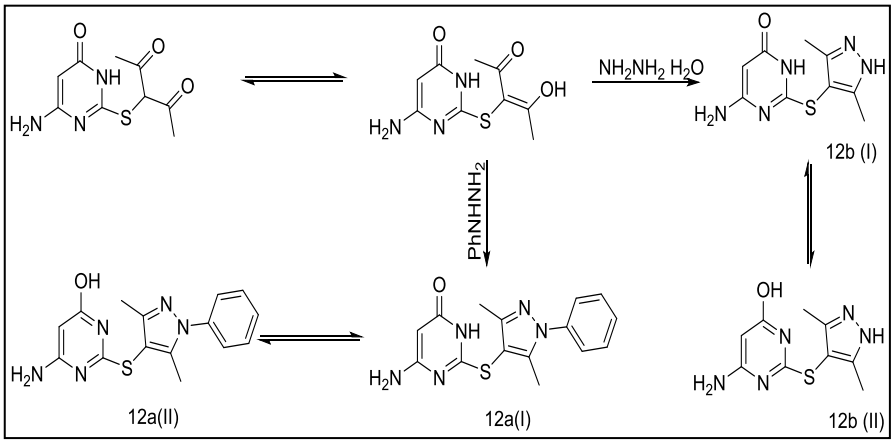
The amino group in the expected cyclized products **10a,b** was acetylated to give the final products **11a, b**.

Structure **11b** as an example was confirmed by different spectral data. The IR spectrum of **11b** showed absorption band for the NH group at 3150 cm^{-1}. ^{1}H-NMR spectrum (DMSO-d_6) of **11b**, showed signals at δ 2.10 ppm (s, 3H, methyl of acetyl group), δ 6.50 ppm (s, 1H, uracil methine proton), δ 7.40-7.60 ppm (m, 5H, aromatic protons), δ 8.10 ppm (s, 1H, sp^2 thiazole proton), δ 10.50 ppm (br. s., 1H, NH disappeared after D_2O exchange).

Since acetylation of the free amino group is undesirable from the biological activity view point, another technique was performed to prevent the amino group from acetylation.

Thus, compound **4d (**or **4e)** was heated at 120 - 140 ^{o}C with polyphosphoric acid as dehydrating agent, to furnish the corresponding thiazolo[3,2-*a*]pyrimidine derivatives **10a,b** with retaining the amino group**.**

The IR spectrum of compounds **10a,b** showed absorption around 3300 cm^{-1} (NH_2). The ^{1}H-NMR spectrum (DMSO-d_6) of compound **10b**, as an example showed signals at δ 5.08 ppm (s, 1H, uracil methine proton) , δ 6.50 ppm (br. s, 2H, amino group, disappeared by D_2O exchange), δ 7.37 ppm (s, 1H, sp^2 thiazole proton), and δ 7.40 ppm (m, 5H, aromatic protons).

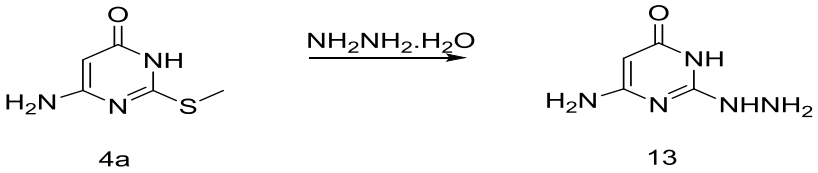


Scheme 9.

The S-alkyl product obtained from reacting compound **1** with 3-chloropentan-2,4-dione **4e** was subjected to further investigations. So, heating compound **4e** with phenyl hydrazine or hydrazine hydrate yielded compounds **12a,b** (Scheme **8**).

Compound **12a(I)** can exist in the tautomeric form **12a (II)**, which is stabilized by the aromaticity of uracil. The structure of the condensed product **12a** was based on the correct values of spectral data. The IR spectrum showed ,beside the signals of the amino group and (C=O) group of 6-amino-2-thiouracil (**1**), signals in the (OH) and (NH) regions at 3500 cm^{-1} and 3150 cm^{-1} ,which prove the existence of the amide structure **12a(I)**. The ^{1}H-NMR spectrum (DMSO-d_6) of compound **12a** showed signals at δ 02.20 ppm (s, 3H, methyl group attached to pyrazole ring) , δ 2.30 ppm (s, 3H, other methyl group attached to pyrazole ring), δ 5.00 ppm (s, 1H, methine proton of the uracil ring), δ 6.49 ppm (br., s., 2H, amino group, disappeared by deuterium oxide exchange), δ 7.50 ppm (m, 3H, aromatic protons), and δ 7.55 ppm (d, 2H, *J*= 6.8 Hz, aromatic protons).

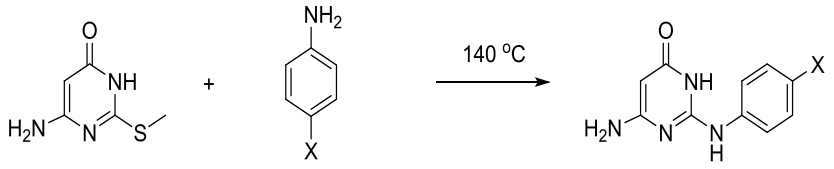
Heating compound **4a** with hydrazine hydrate in ethanol under reflux produced compound **13** in a good yield (see Experimental).



4a 13

Scheme 10.

On other hand, reacting **4a** with aromatic amines by fusion at 140 ^{o}C produced the 2-arylamino derivatives **14a,b**.



4a 14(a,b)

4a; X=H, 4b;X=Cl

Scheme 11.

The IR spectrum of **14b** proved the existence of a tautomeric structure as it showed absorption bands for NH_2, NH, OH groups in the expected places (see Experimental). The ^{1}H-NMR spectrum (DMSO-d_6) of compound **14a**, as an example showed signals at δ 5.06 ppm (s, 1H, uracil methine proton) , 7.01 (br. s.,4H, disappeared by deuterium oxide exchange, NH_2 and 2 NH groups), δ 7.50 ppm (m, 5H, aromatic protons), δ 7.55 ppm (br., s, 1H, disappeared by deuterium oxide exchange, for the enol form of the tautomer **14a)** (for the rest of data see Experimental).

Experemnetal

All reactions were carried out with the exclusion of moisture. All solvents were dried by standard methods. The melting points are uncorrected.

Thin layer chromatography (TLC) was performed by using Merck Alufolien Kieselgel 60 F_{254} aluminum sheets, and visualization under UV-absorption at 254 nm.

The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Jeol ECA-500 run at 500 MHz for ^{1}H-NMR and 125 MHz for ^{13}C-NMR, (central Labs at National Research Center) with TMS ($SiMe_4$) as an internal standard in δ units at 295 K, unless otherwise specified. The chemical shifts were expressed in δ-scale (ppm), the coupling constants J are reported in Hz. The IR spectra were recorded as potassium bromide discs on Jasco FTIR spectrophotometer. Mass spectra were recorded at 70 ev on a GCMS-QP 1000 EX Shimadzu Japan (Gas

chromatography-Mass spectrometer). Elemental analysis data were performed by the National Research Centre.

6-Amino-5-Bromo-2-Thiouracil (2)

A solution of bromine (01.60 gm , 10 mmole) in 20 ml of glacial acetic acid was added drop- wise, with shaking, to a suspension of **1** (01.43 gm, 10 mmole) in 40 ml of glacial acetic acid. After the addition was completed and the color of bromine was completely discharged, the reaction mixture was allowed to gentle heating on a water bath for 3 hr with occasional shaking every 5 min, to ensure the ejection of hydrogen bromide gas out of the reaction mixture, then cooled and poured onto ice-water containing a solution of sodium acetate. The colorless precipitate was filtered off, washed thoroughly with water then ethanol , dried and crystallized from dioxane to furnish **2** in good yield (75%).mp 278 ^{o}C (charring); IR spectrum (KBr, υ, cm^{-1}): 3244 for NH_2 group, 3142 for NH group, 1682 for CO group; ^{1}H-NMR (500 MHz, DMSO-d_6) δppm = 3.20 (s, 1H, SH disappeared after deuterium oxide exchange), 7.61(br., s, 2H, NH_2, by after deuterium oxide exchange) 12.78 br., s, 1H, OH, disappeared by deuterium oxide exchange; Anal.calcd.for $C_4H_4BrN_3OS$ (222.06) : C, 21.63; H, 1.82; Br, 35.98; N, 18.92; S, 14.44%. Anal. Found; C, 21.36; H, 2.08; Br, 35.78; N, 19.12; S, 14.24%. MS(m/z) : 221 (41%)(M^+), 223 (45%).

Genral procedures for preparation of 6-amino-2-alkylthio-5-substituted-3,4-dihydro-pyrimldln-4-ones (4a-i). (A)

A sodium ethoxide solution (10 mmole) and compound **1** (01.43gm, 10 mmole) or 2 (2.22 gm, 10 mmole) were refluxed for 15 min. The reaction mixture was allowed to cool down to room temperature then treated with an equimolecular amount of the proper alkyl halide or α–halo ketone. The mixture was heated under reflux for 1 hr. The precipitate was separated by pouring the reaction mixture onto 10ml of ice-water. The solid that formed was filtrated and washed with 10 ml ice-water then dried and crystallized from the proper solvent to give 4c-i in good yield.

(B)

A solution of bromine (01.60 gm , 10 mmole) in 20 ml of glacial acetic acid was added dropwise , with shaking, to a suspension of 4a or 4b in 25 ml of glacial acetic. After the addition was completed and the color of bromine was completely discharged, the reaction mixture was allowed to gentle heating on a water bath for 3 hr with occasional shaking every 5 min, to ensure the complete ejection of hydrogen bromide gas, then cooled and poured onto ice-water containing a solution of sodium acetate. The solid that formed was collected with filtration and crystallized from the appropriate solvent to give 4c-i.

2-Ethyl[6-AMINO-2-THIO-3,4-dihydropyrimldln-4-ONE] Acetate (4c)

Using ethyl bromoacetate. The product was crystallized from isopropanol to furnish 4c with 70% yield. mp 161^{o}C; IR spectrum (KBr, υ, cm^{-1}): 3450 cm^{-1} (broad) for OH, 3258 cm^{-1} (broad) for NH_2 , 3150 cm^{-1} (broad) for NH, 2920 cm^{-1}

for CH, 1750 cm^{-1} for CO (ester), 1680 cm^{-1} for CO (amide); ^{1}H-NMR (500 MHz, DMSO-d_6) δppm = 1.20 (t,3H, *J*=7.1 Hz, Methyl of the ester group), 3.99 (s, 2H, CH_2), 4.10 (q, 2H, *J*=7.1Hz, CH_2 of ester group), 5.01 (s, 1H, methine proton of pyrimidine), 6.46(br., s, 2H, NH_2, D_2O exchangeable), 11.55(br.,s,1H, OH, D_2O exchangeable); Anal.calcd.for $C_8H_{11}N_3O_3S$ (229.3); C, 41.91; H, 04.84; N, 18.33; S,13.99 %. Anal. Found; C, 41.80; H, 05.07; N, 18.05; S,13.78 %. MS(m/z): 229 (20 %) (M^+).

6-Amino-2-(2-OXO-2-phenylethylthio)-3,4-DIHYDRO-PYRIMLDLN-4-ONE (4d)

Using phenacyl bromide. The product was crystallized from ethanol; to produce 4d with 85% yield, mp 169°C; IR spectrum (KBr, υ, cm^{-1}): 3450 cm^{-1} (broad) for OH group, 3268 cm^{-1} (broad) for NH_2 group, 3145 cm^{-1} (broad) for NH group, 2925 cm^{-1} for CH group, 1720 cm^{-1} for CO (ester), 1688 cm^{-1} for CO (amide); ^{1}H-NMR (500 MHz, DMSO-d_6) δppm = 03.29 (d, 1H, *J*=11.75 Hz, methine proton of the methylene group(non-diasterotropic proton), 03.66((d, 1H, *J*=11.75 Hz, methine proton of the methylene group(non-diasterotropic proton), 05.09 (s, 1H, CH, methine proton of uracil), 7.23 (m, 3H, aromatic protons), 7.56 (d, 2H, *J*=7Hz, aromatic protons), 9.14(br., s, 2H, NH_2 group, disappeared after deuterium oxide exchange). Anal.calcd.for $C_{12}H_{11}N_3O_2S$ (261.3); C, 55.16; H, 4.24; N, 16.08; S, 12.27%. Anal. Found; C, 54.16; H, 4.04; N, 16.28; S, 11.90%. MS(m/z): 261 (45.0%) (M^+).

3-(4-amino-6-oxo-1,6-dihydropyrimidin-2-yl-thio) pentane-2,4-dione (4e)

Using 3-chloropentan-2,4-dione. The product was crystallized from ethanol to produce **4e** with 81% yield. Mp. 120°C; IR spectrum (KBr, υ, cm^{-1}): 3450 cm^{-1} (broad) for OH group, 3268 cm^{-1} (broad) for NH_2 group, 3145 cm^{-1} (broad) for NH group, 2925 cm^{-1} for CH group, 1720 cm^{-1} for CO (ester), 1688 cm^{-1} for CO (amide); ^{1}H-NMR (500 MHz, DMSO-d_6) δppm = 2.15 (s, 3H, CH_3, methyl group), 2.55 (s, 3H, CH_3, methyl group), 5.20 (s, 1H, CH, methine proton of uracil), 6.50 (br., s, 2H, NH_2 group, D_2O exchangeable), 7.56(br., s, 1H, NH group, D_2O exchangeable), 10.19 (br., s, 1H, OH group, D_2O exchangeable). DEPT-NMR (125 MHz, DMSO-d_6) δppm = 30° :27.1, 30.2 (135° both up, 90°: non, 45° both displayed, 2 methyl groups); 30° : 80.1 (135° :up, 90°: displayed, 45° displayed, Pyrimidine methine sp2 carbon); 30° : 98.1 (135° non, 90°: non, 45° non, Quaternary carbon sp2 ethylenic S-carbon atom); 30° : 163 (135° non, 90°: non, 45° non, sp2 Pyrimidine NH2-carbon); 30° :165, 167 (135° non, 90°: non, 45° non, 2 CO groups not involved in hydrogen bond); 30° : 202.2 (135° non, 90°: non, 45° non, CO group involved in hydrogen bond) Anal.calcd.for $C_9H_{11}N_3O_3S$ (241.3); C,44.80; H, 4.60; N,17.42; S,13.29% Anal. Found; C,44.91; H, 4.59; N,17.46; S,13.26%. MS (m/z): 241 (15.0%) (M^+).

6-amino-5-bromo-2-meylthio-3,4-dihydropyrimldln-4-one (4f)

Using iodomethane. The product was crystallized from ethanol to produce 4f with 83% yield. mp 120°C; IR spectrum (KBr, υ, cm^{-1}): 3620 cm^{-1} (sharp) for OH group, 3502 cm^{-1} (broad) for OH intramolecular hydrogen bond, 3290 cm^{-1} (broad) for NH_2 group, 3100 cm^{-1} (broad) for NH group, 2950 cm^{-1} for CH group, 1666 cm^{-1}, 1680 cm^{-1} for 2 (CO) groups; ^{1}H-NMR (500 MHz, DMSO-d_6)

δppm = 02.42 (s, 3H, methyl group), 6.47 (br., s, 2H, NH_2, D_2O exchangeable), 11.55(br., s, 1H, OH group, D_2O exchangeable). Anal. calcd. for $C_5H_6BrN_3OS$ (236.1); C,25.44; H, 2.56; Br, 33.84; N,17.80; S,13.58% Anal. Found; C,25.44; H, 2.56; Br, 33.84; N,17.80; S,13.58%. MS (m/z): 235(51 %) (M^+), 237(53 %).

6-amino-5-rromo-2-ethylthio-3,4-dihydropyrimldln-4-one (4g)

Using ethyl bromide. The product was crystallized from isopropanol to produce 4g with 89% yield. mp 230°C; IR spectrum (KBr, υ, cm^{-1}): 3250 cm^{-1} (broad) for NH_2 group, 3150 cm^{-1} (broad) for NH group, 2960 cm^{-1} for CH group, 1698 cm^{-1} for CO (amide). ^{1}H-NMR (500 MHz, DMSO-d_6) δppm = 1.42 (t, 3H, *J*= 7.3Hz, methyl of the ethyl group), 3.7 (q, 2H, *J*= 7.3Hz, methylene of the ethyl group), 6.46 (br., s, 2H, NH_2 group, D_2O exchangeable), 11.5 (br., s, OH group (enolic form) of the uracil ring, D_2O exchangeable). Anal.calcd.for $C_6H_8BrN_3OS$ (250.12); C, 28.81; H, 3.22; Br, 31.95; N, 16.80; S, 12.82%. Anal. Found; C, 28.71; H, 3.1; Br, 31.75; N, 16.90; S, 12.62%. MS(m/z): 249 (61%) (M^+), 251 (58%).

6-amino-5-bromo-2-(2-oxo-2-phenylethylthio)-3,4-dihydropyrimldln-4-one (4h)

Using phenacyl bromide. The product was crystallized from dioxane to furnish 4hr with 80% yield. mp 300°C; IR spectrum (KBr, υ, cm^{-1}): 3450 cm^{-1} (broad) for OH, 3260 cm^{-1} (broad) for NH_2 , 3150 cm^{-1} (broad) for NH, 2950 cm^{-1} for CH. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm = 3.30(d, 1H, *J*= 11.75Hz, methine proton of the methylene group (non diasterotropic protons), 3.61(d, 1H, *J*= 11.75Hz, methine proton of the methylene group (non diasterotropic protons) , 7.01 (br., s, 2H, NH_2, D_2O exchangeable), 7.23(m,3H, aromatic protons), 7.56(d,2H, *J*=7.1 Hz, aromatic protons), 9.14 (br.s, 2H, 2OH,disappeared after deuterium oxide exchange); Anal. calcd. for $C_{12}H_{10}BrN_3O_2S$ (340. 20); C, 42.37; H, 2.96; Br, 23.49; N, 12.35; S, 9.43%. Anal. Found; C, 42.17; H, 2.90; Br, 23.29; N, 12.15; S, 9.73%. MS (m/z): 339 (59%), 341 (55%) (M^+)

3-(4-amino-5-bromo-6-oxo-1,6-dihydropyrimidin-2-ylthio) pentane-2,4-dione (4i)

Using 3-chloropentan-2,4-dione. The product was crystallized from DMF to give 4i in a 90% yield. mp 180°C; IR spectrum (KBr, υ, cm^{-1}): 3720 cm^{-1} (sharp) for OH group, 3602 cm^{-1} (broad) for OH intramolecular hydrogen bond, 3350 cm^{-1} (broad) for NH_2 group, 3160 cm^{-1} (broad) for NH group,3000 cm^{-1} for CH group,1666 cm^{-1} , 1680 cm^{-1} for 2 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm = 2.15(s, 3H,CH_3, methyl group), 2.55(s, 3H, CH_3, methyl group) ,7.50 (br., s, 2H, NH_2, D_2O exchangeable), 7.65 (br., s, 1H, NH, D_2O exchangeable), 10.19 (br.s,2H, 2OH, D_2O exchangeable); Anal. calcd. for $C_9H_{10}BrN_3O_3S$ (320); C, 33.76; H, 3.15; Br, 24.96; N, 13.12; S, 10.02%. Anal. Found; C, 33.96; H, 3.45; Br, 24.70; N, 13.00; S, 10.32%. MS(m/z): 319 (58%) (M^+), 321(61%).

6-amino-2-carboxymethylthio-3,4-dlhydropyrimldin-4-one (6)

One gram of 5 in 30 ml of water was heated under reflux for 3 hr, concentrated and left to cool whereby colorless crystals separated.

Recrystallization from water gave 90% yield; which gave positive acidity test. All data matched those reported in literature [11].

General procedures for preparation of N-(2-(4-arylidene)-3,5-dioxo-3,5-dihydro-2h-thiazolo[3,2-a]pyrimidine-7-yl)acetamide (A).

A mixture of 1 (01.43 gm, 10 mmole) or 2 (02.22 gm, 10 mmole), (01.04 gm, 10 mmole) of chloroacetic acid, 10 mmole of the appropriate aldehyde and 2 gm of anhydrous sodium acetate was refluxed in 20 ml of glacial acetic acid and 10 ml of acetic anhydride for 3 hr. The reaction mixture was poured onto ice-water. The deposited precipitate, thus formed, was filtered off, washed thoroughly with water, dried and recrystallized from the appropriate solvent, to produce the pure derivatives 7(a-d).

(B)

Compound 5 (2.01 gm, 10 mmole) was refluxed for 3 hr. in 20 ml of glacial acetic acid, 10 ml of acetic anhydride, 2 gm of fused sodium acetate and 10 mmole of the appropriate aldehyde to furnish compounds 7(a-d).

n-(2-benzylidene-3,5-dioxo-3,5-dihydro-2h-thiazolo[3,2-a]pyrimidine-7-yl) acetamide (7a)

Using benzaldehyde. The product was crystallized from DMF; to give 7a in an 85% yield. mp 276^{o}C; IR spectrum (KBr, υ, cm^{-1}): 3500 cm^{-1} (sharp) for OH enolic amide form, 3150 cm^{-1} for NH group,1690 cm^{-1}, 1740 cm^{-1} for 2 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 2.00 (s, 3H,CH_3, methyl of acetyl group), 7.51(m, 3H, aromatic protons), 7.77 (d, 2H, *J*= 9.01Hz, aromatic protons), 8.1(s, 1H, methine proton of the benzylidene group), 9.10(br., s, 1H, NH, D_2O exchangeable). Anal. calcd. for $C_{15}H_{11}N_3O_3S$ (313.33) C, 57.50; H, 3.54; N, 13.41; S, 10.23%. Anal. Found; C, 57.80; H, 3.34; N, 13.11; S, 10.532%. MS(m/z): 313(100.0%) (M^+).

N-(2-(4-methoxybenzylidene)-3,5-dioxo-3,5- dihydro-2h- thiazolo[3,2-a] pyrimidine-7-yl) acetamide (7b)

Using 4-methoxy-benzaldehyde. The product was crystallized from DMF to give 7b in an 85% yield. mp 280^{o}C; IR spectrum (KBr, υ, cm^{-1}): 3500 cm^{-1} (broad) for OH group, 3200 cm^{-1} (broad) for NH, 2900 cm^{-1} (broad) for NH, 2900 cm^{-1} CH group, 1660 cm^{-1}, 1698 cm^{-1} 1730 cm^{-1} for 3 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 1.91 (s, 3H,CH_3, methyl of acetyl group), 3.88(s, 3H,CH_3, methyl of methoxy group), 6.60 (s, 1H, methine proton of the uracil), 6.88(d, 2H, *J*= 10Hz, A,B system of the benzene ring) ,7.20 (br., s, 1H,NH group, D_2O exchangeable), 7.88(d, 2H, *J*= 10Hz, A,B system of the benzene ring), 8.1(s, 1H, methine proton of the benzylic proton). Anal. calcd. for $C_{16}H_{13}N_3O_4S$ (343.36); C, 55.97; H, 3.82; N, 12.24; S, 9.34%. Anal. Found; C, 55.77; H, 4.02; N, 12.04; S, 9.64%. MS(m/z): 343 (45%) (M^+).

N-(2-(4-chlorobenzylidene)-3,5-dioxo-3,5-dihydro-2h-thiazolo[3,2-a]pyrimidine-7-yl)acetamide(7c)

Using 4-chlorobenzaldehyde. The product was crystallized from DMF to give 7c in an 85% yield. mp 298°C; IR spectrum (KBr, υ, cm^{-1}): 3500 cm^{-1} (broad) for OH, 3200 cm^{-1} (broad) for NH, 2900 cm^{-1} (broad) for NH, 2900 cm^{-1} CH group, 1660 cm^{-1} , 1696 cm^{-1} 1710 cm^{-1} for 3 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 2.10 (s, 3H,CH_3, methyl of acetyl group), 7.10 (s, 1H, methine proton of the uracil ring), 6.88(d, 2H, *J*= 12Hz, A,B system of the benzene ring), 7.20 (br., s, 1H,NH group, D_2O exchangeable), 07.88 (d, 2H, *J*= 12Hz, A,B system of the benzene ring), 8.1(s, 1H, the benzylic proton). Anal. calcd. for $C_{15}H_{10}ClN_3O_3S$ (347.78); C, 51.80; H, 2.90; Cl, 10.19; N, 12.08; S, 9.22%. Anal. Found; C, 52.11; H, 2.60; Cl, 10.25; N, 12.40; S, 9.00%. MS(m/z): 347 (39%) (M^+), 349 (42%).

N-(3,5-dioxo-2- (thiophen-2- ylmethylene)-3,5- dihydro-2h-thiazolo[3,2-a] pyrimidine-7-yl)acetamide (7d)

Using 2-thiophene aldehyde. The product was crystallized from DMF to produce 7d in a 65% yield. mp 260°C; IR spectrum (KBr, υ, cm^{-1}): 3500 cm^{-1} (broad) for OH, 3200 cm^{-1} (broad) for NH, 2900 cm^{-1} CH group, 1660 cm^{-1} , 1698 cm^{-1} 1710 cm^{-1} for 3 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 2.00 (s, 3H,CH_3, methyl of acetyl group), 6.80(s, 1H, methine proton of the uracil ring), 7.30 (br., s, 1H,NH group, D_2O exchangeable), 7.67 (t, 1H, *J*= 6.65Hz, thiophene proton, H-3`), 7.60 (d, 1H, *J*= 7.75Hz, thiophene proton, H-4`), 7.67 (d, 1H, *J*= 7.75Hz, thiophene proton, H-2`), 8.1(s, 1H, the benzylic proton). Anal. calcd. for $C_{13}H_9N_3O_3S_2$ (319.36) C, 48.89; H, 2.84; N, 13.16; S, 20.08 %%. Anal. Found C, 48.77; H, 3.02; N, 13.35; S, 20.38 %%. MS (m/z): 319 (59%) (M^+).

General procedure for the preparation of 7-amino-2-aldosyl-2,3-dihyro-5h-thiazolo [3,2-a] pyrimidine-3,5-diones (8a,b) and (9c-e).

An equimolar amount of 1 (01.43gm, 10 mmole), chloroacetic acid (10 m mole, 00.93gm) and the appropriate aldoses (10 mmole) were heated under reflux in 30 ml of pyridine and a catalytic amount of piperidine for 8 hr. The mixture was controlled using TLC technique. The mixture was poured onto ice-water and the formed solid was filtered off, and recrystallized from absolute ethanol.

7-amino-2-arabinosyl-2,3-dihyro-5h-thiazolo[3,2-a]pyrimidine-3,5-dione (8a)

Obtained from D-arabinose. The product was produced in a 90% yield. mp 270°C; IR spectrum (KBr, υ, cm^{-1}), 3500 cm^{-1} (broad) for OH group, 3250 cm^{-1} (broad) for NH_2, 2900 cm^{-1} for CH group, 1740 cm^{-1} and 1685 cm^{-1} for 2 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 3.70(m, 4H, 4 OH, D_2O exchangeable), 4.35 (m, 1H, CH, H-3`), 4.45(m, 1H, CH, H-4`), 4.60(m,2H, CH_2, H-5`,H-5"), 5.40 (dd, 1H, *J*=7.5Hz, H-2`), 5.45 (s,1H, methine proton of uracil ring), 6.50 (br. s, 2H, NH_2 group, D_2O exchangeable), 7.40 (d, 1H, *J*= 7.5Hz, H-1'). Anal.calcd.for $C_{11}H_{13}N_3O_6S$ (315.05); Anal. Found; C, 41.90; H, 4.16; N, 13.33; S, 10.17% C, 41.70; H, 4.46; N, 13.03; S, 10.25%.

7-amino-2-xylosyl-2,3-dihyro-5h-thiazolo[3,2-a] pyrimidine-3,5-dione (8b)

Using D-xylose. The product was obtained in a 90% yield. mp 300 ^{o}C (charred) ; IR spectrum (KBr, υ, cm^{-1}): 3500 cm^{-1} (broad) for OH group, 3250 cm^{-1} (broad) for NH_2, 2900 cm^{-1} for CH group, 1740 cm^{-1} and 1685 cm^{-1} for 2 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 03.40(m, 4H, 4 OH, D_2O exchangeable), 04.25 (q, 1H, *J*=6Hz, CH, H-4`), 4.45(m, 2H, CH, $CH_2$ ,H-5`,H-5"`), 04.60(d, 1H,CH, *J*=5Hz, H-3`), 05.80 (dd, 1H, *J*=7.5Hz, H-2`), 5.95 (s, 1H, methine proton of uracil ring), 06.50(br. s, 2H, NH_2 group, D_2O exchangeable), 7.40 (d, 1H, *J*= 7.5Hz, H-1'). Anal. calcd. for $C_{11}H_{13}N_3O_6S$ (315.05); Anal. Found; C, 41.90; H, 4.16; N, 13.33; S, 10.17% C, 41.70; H, 4.46; N, 13.03; S, 10.25%.

7-amino-2-glucosyl-2,3-dihyro-5h-thiazolo[3,2-a]pyrimidine-3,5-dione (9c)

Using D-glucose. The product was obtained in a 90% yield. mp 301^{o}C (charred); IR spectrum (KBr, υ, cm^{-1}): 3550 cm^{-1} (broad) for OH group,3280 cm^{-1} (broad) for NH_2, 2850 cm^{-1} for CH group, 1730 cm^{-1} and 1680 cm^{-1} for 2 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 03.55(m, 5H, 5 OH, D_2O exchangeable), 3.75 (m, 1H, CH, H-5'), 04.30 (m, 2H, CH_2 ,H-6`,H-6"), 4.50(m, 1H, CH, H-4`), 04.60(m, 1H,CH, H-3` ), 5.00 ( s, 1H, methine proton of uracil ring), 05.50 (m, 1H, CH, H-2`), 06.50(br. s, 2H, NH_2 group, D_2O exchangeable), 7.40 (d, 1H, *J*= 7.5Hz,methine H-1'). Anal. calcd. for $C_{12}H_{15}N_3O_7S$ (345.33); C, 41.74; H, 4.38; N, 12.17; S, 9.29 %. Anal. Found; C, 41.56; H, 4.50; N, 12.37; S, 9.00 %.

7-amino-2-galactosyl-2,3-dihyro-5h-thiazolo[3,2-a]pyrimidine-3,5-dione (9d)

Using D-galactose. The product was obtained in a 90% yield. mp 311^{o}C (charred); IR spectrum (KBr, υ, cm^{-1}): 3550 cm^{-1} (broad) for OH group, 3280 cm^{-1} (broad) for NH_2, 2850 cm^{-1} for CH group, 1730 cm^{-1} and 1680 cm^{-1} for 2 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 03.75(m, 5H, 5 OH, D_2O exchangeable), 4.20 (m, 2H, CH_2 ,H-6`,H-6"), 4.50 (m, 3H, 3CH, H-3' , H-4' , H-5' ), 5.00 ( s, 1H, methine proton of uracil ring), 5.20 (d, 1H, *J*=7.5Hz, CH, H-2`), 06.40(br. s, 2H, NH_2 group, D_2O exchangeable), 7.40 (d, 1H, *J*= 7.5Hz, methine H-1'). Anal. calcd. for $C_{12}H_{15}N_3O_7S$ (345.33); C, 41.74; H, 4.38; N, 12.17; S, 9.29 %. Anal. Found; C, 41.56; H, 4.50; N, 12.37; S, 9.00 %.

7-amino-2-mannosyl-2,3-dihyro-5h-thiazolo[3,2-a]pyrimidine-3,5-dione (9e)

Using D-mannose. The product was obtained in a 90% yield. mp 305^{o}C (charred); IR spectrum (KBr, υ, cm^{-1}): 3550 cm^{-1} (broad) for OH group,3280 cm^{-1} (broad) for NH_2, 2850 cm^{-1} for CH group, 1730 cm^{-1} and 1680 cm^{-1} for 2 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 03.60 (m, 5H, 5 OH, D_2O exchangeable), 4.25 (m, 1H, CH ,H-3`), 4.35 (m, 2H, $CH_2$ ,H-6`,H-6"), 4.50 (m, 2H, 2CH, H-3' , H-4'), 5.00 (s, 1H, methine proton of uracil ring), 5.20 (dd, 1H, *J*=7.5Hz, CH, H-2`), 6.55(br. s, 2H, NH_2 group, D_2O exchangeable), 6.65 (d, 1H, *J*= 7.5Hz, methine H-1'). Anal. calcd. for $C_{12}H_{15}N_3OS$ (345.33); C, 41.74; H, 4.38; N, 12.17; S, 9.29 %. Anal. Found; C, 41.56; H, 4.50; N, 12.37; S, 9.00 %.

General procedure for the preparation of 2-alkyl-7-amino-3-substituted-5h-thiazolo[3,2-a]pyrimidin -5-one (10a-b). (A)

A mixture of 2 gm of 4d (or 4e) in 10 gm of polyphosphoric acid (prepared by dissolving 5 gm of phosphorus pentoxide in 5 ml of ortho-phosphoric acid) was heated at 140 °C on an oil bath for 1 hr. The solution was allowed to cool, poured with stirring onto ice-water and basified with ammonium hydroxide solution. The solid that formed was collected, washed with water and crystallized from the appropriate solvent to give 10(a,b) and also 11(a,b).

(B).

Compound 4d or 4e was dissolved in 20 ml of sulfuric acid (40%) and wormed, then left to cool at room temperature for 24 hr. The solution was poured onto ice-water and basified with ammonium hydroxide solution. The solid that formed, was separated with filtration, washed and recrystallized from the appropriate solvent.

2-Acetyl-7-amino-3-methyl-5h-thiazolo[3,2-a]pyrimidin-5-one(10a)

Using compound 4d. The product was crystallized from dioxane in a 60% yield. mp 305^{o}C; IR spectrum (KBr, υ, cm^{-1}): 3250 cm^{-1} (broad) for NH_2 group, 2900 cm^{-1} for CH, 1720 cm^{-1} and 1680 cm^{-1} for 2 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 2.08(s, 3H, CH_3, methyl of acetyl group), 03.04 (s, 3H,CH_3 methyl group), 6.00 (s, 1H, methine proton of the pyrimidine ring), 7.20 (br., s, 2H, NH_2, D_2O exchangeable). Anal. calcd. for $C_9H_9N_3O_2S$ (223.25); C, 48.42; H, 4.06; N, 18.82; S, 14.36%. Anal. Found; C, 48.12; H, 4.36; N, 18.72; S, 14.45%. MS (m/z): 223 (48%) (M^+).

7-Amino-3-Phenyl-5h-Thiazolo[3,2-a]Pyrimidin -5-ONE (10b)

Using compound 4e. The product was crystallized from DMF in a 70% yield, mp 320^{o}C; IR spectrum (KBr, υ, cm^{-1}): 3250 cm^{-1} (broad) for NH_2 group, 2930 cm^{-1} for CH, 1695 cm^{-1} for (CO) group. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 5.08(s, 1H, methine proton of the pyrimidine ring), 6.50 (br., s, 2H, NH_2, D_2O exchangeable), 7.37 (s, 1H, CH, thiazole proton), 7.40(m., 5H, aromatic protons). Anal.calcd.for $C_{12}H_9N_3OS$ (243.28): C, 59.24; H, 3.73; N, 17.27; S, 13.18%. Anal. Found; C, 59.04; H, 3.53; N, 17.57; S, 12.88%. MS (m/z): 243 (41%) (M^+).

N-(2-alkyl-7- amino-3- substituted-5h- thiazolo [3,2-a] pyrimidine-7-yl) acetamide (11a,b)

Compound 4d or 4e (10 mmole) was dissolved in a mixture of 10 ml pyridine and 10 ml acetic anhydride. The reaction mixture was heated under reflux for 5hr, then poured onto ice-hydrochloric acid/water mixture. The deposited precipitate, thus formed, was filtered off, washed thoroughly with water then ethanol, dried and recrystallized from DMF, to furnish derivatives 11 (a,b).

N-(2-acetyl-3-methyl-5-oxo-5h-thiazolo[3,2-a] pyrimidine-7-yl) acet- amide (11a)

Using compound 4d. The product was produced in a (70%) yield. mp 330 ^{o}C; IR spectrum (KBr, υ, cm^{-1}): 3150 cm^{-1} for NH group, 2930 cm^{-1} for CH, 1720 cm^{-1}, 1700 cm^{-1} and 1665 cm^{-1} for 3 (CO) groups ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 1.99 (s, 3H, CH_3, methyl of acetyl group), 2.20 (s, 3H, CH_3, methyl of acetyl group), 3.00 (s, 3H,CH_3 methyl group attached to the thiazole ring), 6.90 (s, 1H, methane proton of the pyrimidine ring), 10.82 (br., s, 1H, NH, D_2O exchangeable). Anal. calcd. for $C_{11}H_{11}N_3O_3S$ (265.28); C, 49.80; H, 4.18; N, 15.84; S, 12.09%. Anal. Found; C, 49.64; H, 3.93; N, 15.59; S, 12.29%. MS (m/z): 265 (43.0%) (M^+).

N-(2-acetyl-5-oxo-3-phenyl-5h-thiazolo[3,2-a] pyrimidine-7-yl)acet- amide (11b)

Using compound 4e. The product was obtained in a 70% yield. mp 330^{o}C; IR spectrum (KBr, υ, cm^{-1}): 3150 cm^{-1} for NH group, 2930 cm^{-1} for CH, 1700 cm^{-1} and 1665 cm^{-1} for (2 CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 2.10 (s, 3H, CH_3, methyl of acetyl group), 2.20 (s, 3H, CH_3, methyl of acetyl group), 6.50 (s, 1H, methane proton of the pyrimidine ring), 10.50 (br., s, 1H, NH, D_2O exchangeable). Anal. calcd. for $C_{14}H_{11}N_3O_2S$ (285.28); C, 58.93; H, 3.89; N, 14.73; S, 11.24%. Anal. Found; C, 59.09; H, 3.70; N, 14.43; S, 11.54%. MS (m/z): 285 (32.0%) (M^+).

General procedure for the preparation of 6-Amino-2-(3,5-Dimethyl-1-Aryl-1h-Pyrazol-4-Yl)Thio)Pyrimidine-4(3h) - One(12a,b)

A mixture of compound 4e (02.41gm, 10 mmole) and phenyl hydrazine (01.08gm, 10 mmole) or hydrazine hydrate 99% (00.50gm, 10 mmole) was heated under reflux in dry dioxane for 3 hr. The reaction mixture was poured onto acidified water. The separated solid was filtrated off, washed and recrystallized from dioxane to furnish 12(a,b).

6-amino-2-((3,5-dimethyl-1-phenyl-1h-pyrazol-4-yl)thio)pyrimidine-4(3h)-one (12a)

Using phenyl hydrazine. The product was obtained in an 87% yield. mp 220^{o}C; IR spectrum (KBr, υ, cm^{-1}): 3500 cm^{-1} for OH group, 3400 cm^{-1} (Broad) for NH_2 group, 3150 cm^{-1} for NH, 2920 cm^{-1} CH, 1700 cm^{-1} for (CO) group. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 2.20(s, 3H, methyl group), 2.30 (s, 3H, methyl group), 5.00 (s, 1H, CH, methine proton of the pyrimidine ring), 6.49(br., s, 2H, NH_2, D_2O exchangeable), 7.50 (m, 3H, aromatic protons), 7.55 (d., 2H, *J*=6.8Hz, aromatic protons), 11.55 (br., s, 1H, OH group, D_2O exchangeable). Anal. calcd. for $C_{15}H_{15}N_5OS$ (313.38); C, 57.49; H, 4.82; N, 22.35; S, 10.23%. Anal. Found; C, 57.19; H, 4.92; N, 22.05; S, 10.53%. MS (m/z): 313 (49%) (M^+).

6-amino-2-((3,5-dimethyl-1h-pyrazol-4-yl)thio)pyrimidine-4(3h)-one (12b)

Using hydrazine hydrate. The product was obtained in a 80% yield. mp 200^{o}C; IR spectrum (KBr, υ, cm^{-1}): 3500 cm^{-1} for OH group,3300 cm^{-1} (broad) for NH_2 group, 3150 cm^{-1} for NH, 2920 cm^{-1} CH, 1720 cm^{-1} for (CO) group. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 2.30(s, 6H, two methyl groups), 5.00 (s, 1H, CH, methine proton of the pyrimidine ring), 6.49(br., s, 2H, NH_2, D_2O

exchangeable), 11.50 (br., s, 1H, OH group, D2O exchangeable). Anal. calcd. for $C_9H_{11}N_5OS$ (237.28); C, 45.56; H, 4.67; N, 29.51; S, 13.51%. Anal. Found; C, 45.77; H, 4.92; N, 29.25; S, 13.53%. MS(m/z): 237 (42%) (M^+).

6-amino-3,4-dihydro-2-hydrazinopyrlmidin-4-one(13)

A solution of (01.57gm, 10 mmole) of 4a in 50 ml of ethanol was treated with an excess (1 ml, 02.00 mmole) of hydrazine hydrate 99%. The solution was heated under reflux till evolution of methane-thiol ceased. The hydrazino derivative which precipitated during reflux was collected and recrystallized from ethanol/water (1:1) to produce 13 in a 75% yield; m.p. 245 °C, not depressed when admixed with an authentic sample. All spectral and elemental data were identical to those reported in literature [17].

General procedure for the preparation of 2-arylamino-6-amino -3,4-dihydro-pyrlmldln-4-one(14a-b)

A mixture of 4a (1.57 gm, 10 mmole) and either aniline (0.93 gm, 10 mmole) or p-chloroaniline (01.28 gm, 10 mmole) was heated at 140 ^oC till evolution of methane-thiol ceased. The residue was triturated with ethanol and the solid, so obtained, was filtered off, washed with ethanol, dried and recrystallized from the appropraite solvent to give 14 (a,b).

6-amino -3,4-dihydro-2-phenylamino-pyrlmldln-4-one (14a)

Using aniline. The product was crystallized from ethanol to produce 14a in a 60% yield. .mp 285^oC; IR spectrum (KBr, υ, cm^{-1}): 3300 cm^{-1} for NH_2 group , 3100 cm^{-1} (broad) for NH group, 1675 cm^{-1} for 2 (CO) groups.; ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 5.06 (s, 1H, CH, methine proton of pyrimidine ring), 7.01 (br., s, 4H, NH_2, 2NH, D_2O exchangeable), 7.50 (m, 5H, aromatic protons), 10.55 (br., s, 1H, OH group, D_2O exchangeable). Anal. calcd. for $C_{10}H_{10}N_4O$ (202.21); C, 59.40; H, 4.98; N, 27.71%. Anal. Found; C, 59.10; H, 5.18; N, 27.52%. MS(m/z) : 202 (53%) (M^+).

6-amino-3,4-dihydro-2-(4-chlorophenylamino)-pyrlmldln-4-one (14b)

Using p-chloroaniline. The product was crystallized from DMF to give 14b in a 60% yield. mp 310^oC; IR spectrum (KBr, υ, cm^{-1}): 3300 cm^{-1} for NH_2 group, 3100 cm^{-1} -2870cm^{-1} (Broad) for CH and NH with intramolecular hydrogen bond, 1675 cm^{-1} for 2 (CO) groups. ^{1}H-NMR (500 MHz, DMSO-d_6) δppm: 5.00 (s, 1H, CH, methine proton of pyrimidine ring), 7.00 (br., s, 4H, NH_2, 2NH, D_2O exchangeable), 7.20-7.40 (dd, 2H, *J*= 8.5Hz, 2H, AB system aromatic protons), 7.50-7.60(dd, 2H, *J*= 8.5Hz, 2H, AB system aromatic protons), 10.50(br., s, 1H, OH group, D_2O exchangeable). Anal. calcd. for $C_{10}H_9ClN_4O$ (236.66); C, 50.75; H, 3.83; Cl, 14.98; N, 23.67%. Anal. Found; C, 50.55; H, 3.60; Cl, 15.09; N, 23.37%. MS(m/z): 236 (25%) (M^+), 238 (22 %).

Conclusion

As evidenced from all the above arguments, 6-amino-2-thiouracil (1) has a wide range of applications which encourage us to use it for developing new synthetic routes with the possibility to obtain end products which could be used in many applications.

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تشييد كيميائى لمشتقات 6-امينو-2-ثيويوراسيل وجليكوسيدتها

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تم الكلة 6-امينو-2-ثيويوراسيل بالكواشف الهاوجينية المختلفة لانتاج مشتقات على ذرة الكبريت كما تم تفاعلة مع البروم لانتاج مشتق البروم منة فى الوضع 5. ايضا تم حلوقة المشتقات المختلفة لتفاعل الالدهيدات المختلفة. تم ادماج بعض نتائج الحلوقة مع السكاكر المختلفة لانتاج الجلكوسيدات. كما تم مفاعلته مع مشتقات الهيدرازين لانتاج مشتقات الثيازولوبريمدين والبيرازول. كما تم ايضا انتاج مشتق الهيدرازين عند مفاعلة احدى مشتقان الالكة مع الهيدرازين هيدرات.

تم التاكد من التراكيب الناتجة بواسطة التحاليل الدقيقة والتحاليل الطيفية المختلفة.