Reactions with 2-Mercaptopyrimidines. Synthesis of Some New Thiazolo[3,2-*a*]- and Triazolo[4,3-*a*]Pyrimidines

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Alkylation of 5-cyano-4-oxo-6-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine **I** with methyl iodide, chloroacetic acid or 3-chloro-2,4-pentanedione, afforded the *S*-alkyl derivatives **IIa-c**. 2-Carboxymethylthio and 2-(2′,4′-dioxopentan-3-ylthio) derivatives **IIb** and **IIc** could be cyclised by acetic anhydride or polyphosphoric acid to give 6-cyano-3,5-dioxo-5*H*-7-phenylthiazolo[3,2-*a*]pyrimidine **III** and 2-acetyl-6-carboxamido-5*H*-3-methyl-7-phenylthiazolo[3,2-*a*]pyrimidine-5-one **IX**, respectively. Benzoylation of 2-hydrazinopyrimidine derivative **XII**, in anhydrous dioxan, afforded the *N*-benzoyl derivative **XIII**, which could be cyclised by heating in dimethylformamide to give 5-amino-6-cyano-3,7-diphenyl-*s*-triazolo[4,3-*a*]pyrimidine (**XIV**). The 2-hydrazinopyrimidine derivatives **XII** and **XV** reacted with benzoyl isothiocyanate in dioxane to yield 4-benzoylthiosemicarbazide derivatives **XVI** and **XVII**, which were converted into the 2-*s*-trizolopyrimidine derivatives **XVIII** and **XIX**, respectively. Also, **XVI** and **XVII** reacted with 2,4-pentanedione and 3-chloro-2,4-pentanedione to yield 2-pyrazolopyrimidine derivatives **XX** and **XXI**, respectively.

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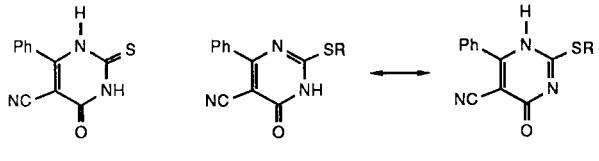
Fused pyrimidines have become of considerable interest during the last twenty years [1-12]. Many of these compouds have proved to be active anticancer [5-10], antipyretic and antiinflammatory agents [8-12]. In continuation of our interest in the chemistry of pyrimidines [13] and fused pyrimidines [14,15], we would like to report some reactions of 5-cyano-4-oxo-6-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine [16] and 4-amino-5-cyano-2-mercapto-6-phenylpyrimidine [15]. Also, we report a new synthesis for fused thiazolo[3,2-*a*]- and triazolo[4,3-*a*]pyrimidines. Thus, alkylation of 5-cyano-4-oxo-6-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine (**I**) gave the S-alkyl derivatives **IIa-d**. That alkylation took place at the sulphur atom was proved by comparison of **IIa** with an authentic sample prepared by a different method in our previous publication [14].

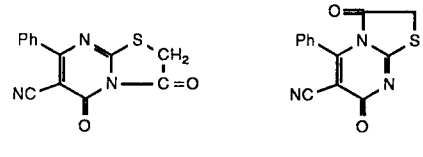


I II

a, R = CH_3
b, R = CH_2COOH
c, R = $CH(COCH_3)_2$
d, R = $CH_2COC_6H_5$

The ir spectra of compounds **II** displayed characteristic bands for NH, C≡N and amidic CO groups and the pmr spectrum (DMSO-d_6) of **IIa** showed signals at δ 2.60 (s, 3H, CH_3), 7.65 (m, 3H, aromatic protons), δ 7.95 (m, 2H, aromatic protons).

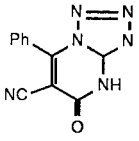
When 2-carboxymethylthio-5-cyano-6-phenyl-3,4-dihydropyrimidin-4-one (**IIb**) was heated at 100° with acetic anhydride, cyclisation took place to give product **III**, formulated as 6-cyano-3,5-dioxo-5*H*-7-phenylthiozolo[3,2-*a*]-pyrimidine (**III**) rather than the isomeric structure **III′**. Product **III** could also be obtained by heating **I** with chloroacetic acid in the presence of fused sodium acetate, acetic acid and acetic anhydride. The ir spectrum of **III** displayed signals at 2220 cm^{-1} (C≡N), 1720 and 1690 (2 CO), while its pmr spectrum (DMSO-d_6) showed signals at δ 3.55 ppm (s, 2H, CH_2), δ 7.68 ppm (m, 3H, aromatic protons) and δ 7.98 ppm (broad s, 2H, aromatic protons).



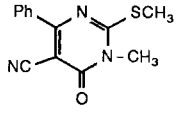
III III′

In favour of structure **III** for the reaction product is the following. It can be seen that the phenyl group in **III′**, like that in compound **IV** [14], must be twisted out of plane of the pyrimidine ring because of steric interference. This phenyl group would be expected to give compact signals in the pmr spectrum. However, the phenyl group in **III** should be co-planar with the pyrimidine ring, and in agreement there is a complex two-protons signal at low field. Since the pmr data of the reaction product shows

that the *ortho* phenyl protons are deshielded by about 0.3 ppm relative to the *meta*- and *para*-protons, similar to the nonsubstituted N-1 pyrimidine compound **V** [14], this indicates that structure **III** is the correct one for the reaction product. This is in agreement with the reported pmr data for other compounds with similar system [17,18].



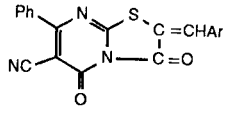
IV



V

In support of structure **III**, the reaction product was converted into the arylmethylene derivatives **VIa,b**, by direct condensation with aromatic aldehydes, and compound **VIa** was found to be identical with an authentic sample prepared by an independent route, see below.

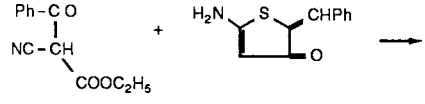
Compound **III** condensed with benzaldehyde in acetic acid in the presence of fused sodium acetate to give the benzylidene derivative **VIa**. However, the arylmethylene derivatives **VIa,b** were prepared directly from compound **I** by the action of chloroacetic acid and the aromatic aldehyde in glacial acetic acid and acetic anhydride containing anhydrous fused sodium acetate. The ir spectra of **VI** displayed absorption bands at 2220 (C≡N), 1700 and 1690 cm^{-1} (2 CO), while the pmr spectrum (DMSO-d_6) of **VIb**) showed signals at δ 3.1 (s, 6H, $2CH_3$), δ 7.68 and 8.1 ppm (m, 10H, 9 aromatic protons + ethylenic proton).



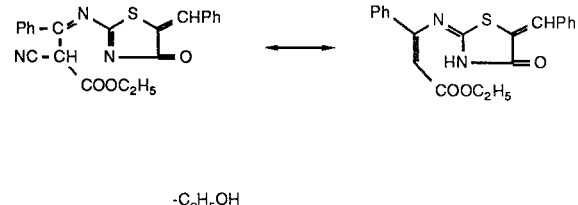
VI

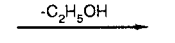
a, Ar = C_6H_5
b, Ar = $C_6H_4N(CH_3)_2$

Compound **VIa** could also be synthesised by heating ethyl benzoylcyanoacetate (**VII**) [19] with 5-benxalpseudothiohydantoin (**VIII**) [20] in acetic acid containing few drops of hydrochloric acid. The reaction of **VII** and **VIII** is assumed to proceed according to the following sequence.



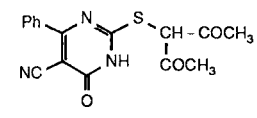
VII VIII



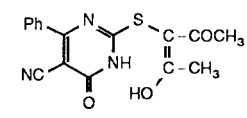


VIa

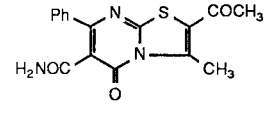
Heating 5-cyano-2-(2′,4′-dioxopentan-3′-ylthio)-6-phenyl-3,4-dihydropyrimidin-4-one (**IIc**), which most probably exists in the enolic form **II′c** with polyphosphoric acid at 100-120° resulted in partial hydrolysis of the cyano group besides cyclisation. The 2-acetyl-6-carboxamido-5*H*-3-methyl-7-phenylthiazolo[3,2-*a*]pyrimidin-5-one (**IX**) was obtained.



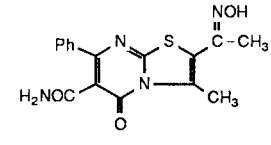
II



II′c



IX

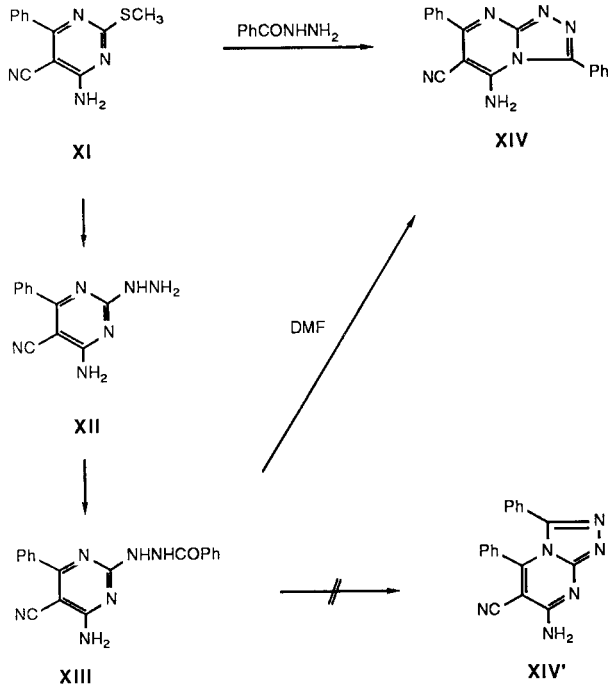


X

Structure **IX** was inferred from the following facts: (a) Compound **IX** gives no colour with ferric chloride solution while its precursor **IIc** gives a deep red colour. (b) The ir spectrum of **IX** showed no absorption in the C≡N region. (c) The pmr spectrum (DMSO-d_6) of **IX** showed signals at δ 2.65 (s, 3H, CH_3), δ 3.28 (s, 3H, CH_3), δ 7.5 (m, 3H, aromatic protons) and δ 7.81 ppm (m, 4H, 2 aromatic protons + NH_2). The oxime derivative **X** was obtained in good yield by the reaction of **IX** with hydroxylamine hydrochloride in acetic acid in the presence of sodium acetate. The ir spectrum of **X** showed an absorption band at 3300 (OH), 1690, 1670 (2 CO).

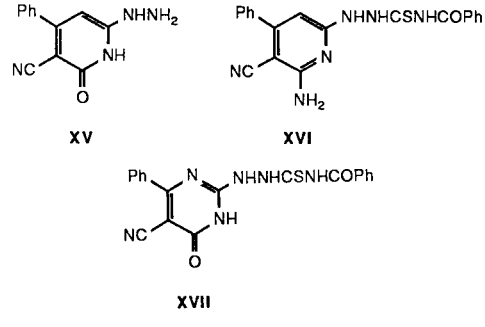
When 4-amino-5-cyano-2-hydrazino-6-phenylpyrimidine (**XII**), prepared from the 2-methylthio derivative **XI** [15], was heated with benzoyl chloride in anhydrous dioxan, the *N*-benzoyl derivative **XIII** was obtained. Compound **XIII** on refluxing with dimethylformamide underwent ring closure to give a product which could be formulated as 5-amino-6-cyano-3,7-diphenyl-*s*-triazolo[4,3-*a*]pyrimidine (**XIV**) or the isomeric structure **XIV′**. Compound **XIV** could be directly obtained by the reaction of **XI** with benzhydrazide in dimethylformamide. The pmr (DMSO-d_6) of

XIV exhibited signals at δ 7.67 (m, 6H, aromatic protons) and δ 7.93 (m, 6H, 4 aromatic protons + NH_2). Addition of deuterium oxide led to a decrease in the low field signal by two protons (NH_2). The ir spectrum of **XIV** showed absorption bands at 3380, 3360 (NH_2), 2220 (C≡N) and 1650 cm^{-1} (NH_2).



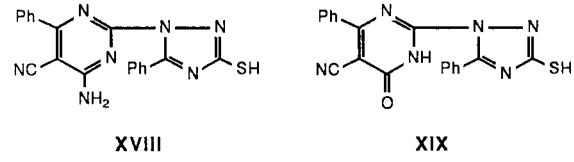
The assignment of structure **XIV** to the reaction product is based on the study of its pmr spectrum. Thus, as we reported before, since the *ortho* phenyl protons in **XIV** are deshielded by about 0.3 ppm relative to the *meta*- and *para*-protons, similar to the non-substituted N-1 pyrimidine derivative **V**, this indicates that structure **XIV** is favoured for the reaction product [14,17,18].

The reaction of each of compound **XII** and 5-cyano-2-hydrazino-6-phenyl-4-oxopyrimidine (**XV**) [15] with benzoyl isothiocyanate led to the formation of 4-amino-2-(4′-benzoylthiosemicarbazide-1′-yl)-5-cyano-6-phenylpyrimidine (**XVI**) and 2-(4′-benzoylthiosemicarbazide-1′-yl)-5-cyano-6-phenyl-3,4-dihydropyrimidin-4-one (**XVII**), respectively.



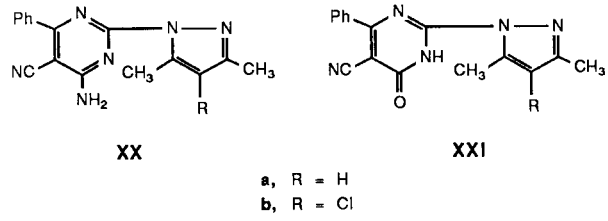
The structures of **XVI** and **XVII** were inferred from the facts that: (a) The ir spectra of **XVI** and **XVII** displayed characteristic absorption bands for NH, C≡N and CO groups. (b) Compounds **XVI** and **XVII** failed to condense with aromatic aldehydes under different conditions. (c) Acylthiosemicarbazides are known in literature [20] to undergo cyclisation on treatment with alkali, (see below).

Refluxing each of **XVI** and **XVII** in dilute aqueous sodium hydroxide afforded 4-amino-5-cyano-2-(3′-mercapto-5′-phenyl-*s*-triazole-1′-yl)-6-phenylpyrimidine (**XVIII**) and 5-cyano-2-(3′-mercapto-5′-phenyl-*s*-triazole-1′-yl)-6-phenyl-3,4-dihydropyrimidin-4-one (**XIX**), respectively.



The pmr spectrum (DMSO-d_6) of **XVIII** showed signals at δ 2.75 ppm (s, 1, SH) and δ 7.68 ppm (m, 12, Ar-H + NH_2). Addition of deuterium oxide led to the disappearance of the sulfhydryl proton and a decrease in the low field signal by two protons (NH_2). The ir spectra of **XVIII** and **XIX** displayed characteristic absorption bands for SH and C≡N groups.

The hydrazino derivatives **XII** and **XV** reacted with each of 2,4-pentanedione and 3-chloro-2,4-pentanedione in anhydrous dioxane to yield the 2-pyrazolopyrimidine derivatives **XXa,b** and **XXIa,b**, respectively.



The pmr spectrum (DMSO-d_6) of **XXb** showed signals at δ 2.28 ppm (s, 3, CH_3), δ 2.68 ppm (s, 3, CH_3), δ 7.6 ppm (m, 3, Ar-H), δ 8.0 ppm (m, 2, Ar.H) and δ 8.2 ppm (broad s, 2, NH_2). Addition of deuterium oxide led to the disappearance of the latter signal. The ir spectra of **XX** and **XXI** displayed characteristic bands for NH and C≡N groups.

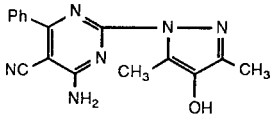
When compounds **XXb** and **XXIb** were refluxed with 5% sodium hydroxide solution, followed by acidification, they were converted into the corresponding hydroxy derivatives **XXII** and **XXIII**, respectively. The structure of which were derived from analytical data, ir spectra and the development of deep colour of their solutions with ferric chloride.

Table I

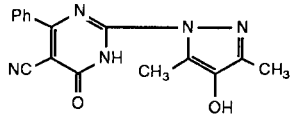
2-Pyrazolopyrimidine Derivatives

Compound	Mp °C	Yield %	Solvent	Formula	Analysis % Calcd./Found C	H	N	IR cm^{-1}
XXa	261	75	Acetic acid	$C_{16}H_{14}N_6$	66.18 65.9	4.86 5.0	28.97 28.8	3400, 3250 (NH), 3160 (CH), 2220 (C≡N).
XXb [a]	290	80	Dimethylformamide	$C_{16}H_{13}ClN_6$	59.17 59.3	4.03 4.0	25.88 25.8	3300 (NH), 3100 (CH), 2220 (C≡N)
XXIa	237	70	Dioxan	$C_{16}H_{13}N_5O$	65.97 65.9	4.50 4.5	24.04 24.1	3350 (NH), 3100 (CH), 2220 (C≡N), 1705 (CO).
XXIb [b]	300	72	Dimethylformamide	$C_{16}H_{12}ClN_5O$	59.00 59.2	3.71 3.8	21.50 21.7	3400 (NH), 3050 (CH), 2220 (C≡N), 1690 (CO).

[a] Cl, Calcd: 10.92. Found: 10.7. [b] Cl, Calcd: 10.89. Found: 10.8.



XXII



XXIII

EXPERIMENTAL

Melting points were taken on a kofler apparatus and are uncorrected. Infrared (ir) spectra were determined as potassiumbromide pellets with a Perkin-Elmer Infracord 137 instrument. The pmr spectra were determined with a Perkin-Elmer R12A instrument.

5-Cyano-2-methylthio-6-phenyl-3,4-dihydropyrimidin-4-one (**IIa**).

Compound **I** (2.29 g, 0.01 mole) was dissolved in 50 ml of ethanol to which 0.78 ml (1.2 moles) of methyl iodide was added, and the solution was refluxed for 2 hours, concentrated and allowed to cool. The precipitate was filtered off, dried and recrystallised from ethanol to give **IIa** in 60% yield, mp 275°. No depression was observed when mixed with an authentic sample [14]; pmr (deuteriodimethylsulfoxide): 2.60 (s, 3H, CH_3), 7.65 (m, 3H, aromatic protons), δ 7.95 (m, 2H, aromatic protons).

2-Carboxymethylthio-5-cyano-6-phenyl-3,4-dihydropyrimidin-4-one (**IIb**).

Chloroacetic acid (1.04 g, 0.011 mole) was dissolved in 5 ml of water and just neutralized with 1*N* potassium carbonate solution. The above solution was added to 2.67 g (0.01 mole) of the potassium salt of **I** dissolved in 30 ml of water. The reaction mixture was refluxed for 2 hours, left to cool and then acidified with acetic acid. The solid that separated was collected, dried and crystallised from ethanol to give 2.3 g (80%), mp 218°; ir: 3020 (OH and NH), 2220 (C≡N), 1700 (cyclic CO), 1660 (COOH); pmr (deuteriodimethylsulfoxide): δ 4.05 (s, 2, CH_2), 7.75 (m, 3, aromatic protons), 8.1 (m, 2, aromatic protons), 10.1 (s, 1, COOH).

Anal. Calcd. for $C_{13}H_9N_3O_3S$: C, 54.35; H, 3.16; N, 14.63; S, 11.16. Found: C, 54.6; H, 3.3; N, 14.5; S, 11.0.

5-Cyano-2-(2',4'-dioxopentan-3'-ylthio)-6-phenyl-3,4-dihydropyrimidin-4-one (**IIc**).

A stirred mixture containing 2.29 g (0.01 mole) of **I**, 20 ml of ethanol and 0.56 g (0.01 mole) of potassium hydroxide in few ml of water was heated at 70-80° for 10 minutes. After cooling the resulting solution to 30°, 1.35 g (0.01 mole) of pure 3-chloro-2,4-pentanedione was added in one portion. After standing at room temperature for 18 hours, the reaction mixture was added to 100 g of ice-water. The precipitate that formed was collected by filteration washed with water until free from chloride and crystallised from dilute dimethyl formamide to give 2.45 g (75%), mp 226°; ir: 3400, 3000 (broad, OH and NH), 2220 (C≡N), 1700, 1685 (2 CO); pmr (deuteriodimethylsulfoxide): δ 2.36 (s, 3, CH_3), 2.85 (s, 3, CH_3), 4.9 (broad s, 1, enolic OH), 7.8 (m, 5, aromatic protons).

Anal. Calcd. for $C_{16}H_{13}N_3O_3S$: C, 58.71; H, 4.00; N, 12.84; S, 9.79. Found: C, 59.0; H, 4.2; N, 12.8; S, 9.6.

5-Cyano-2-phenacylthio-6-phenyl-3,4-dihydropyrimidin-4-one (**IId**).

A mixture of 2.29 g (0.01 mole) of **I**, 1.38 g (0.01 mole) of potassium carbonate, 2.19 g (0.011 mole) of phenacyl bromide and ethanol (30 ml) was heated under reflux for 2 hours and concentrated. The reaction mixture after cooling was poured into 100 ml of water. The crude **IId** that separated was collected and crystallised from dioxan to give 2.43 g (70%), mp 225-226°; ir: 2900 (broad NH with hydrogen bond), 2220 (C≡N), 1700 and 1685 (2 CO); pmr (deuteriodimethylsulfoxide): δ 4.9 (s, 2, CH_2), 7.2-8.3 (m, 10, aromatic protons).

Anal. Calcd. for $C_{19}H_{13}N_3O_2S$: C, 65.69; H, 3.77; N, 12.10; S, 9.23. Found: C, 65.9; H, 3.7; N, 12.0; S, 9.2.

6-Cyano-3,5-dioxo-5*H*-7-phenylthiazolo[3,2-*a*]pyrimidine (**III**).

A) One g of **IIb** was heated with 5 ml of acetic anhydride for 3 hours. The reaction mixture was allowed to cool and the solid which separated was filtered off, dried and crystallised from dimethylformamide-ethanol to give 1.6 g (60%) of **III**, mp 304°; ir: 2220 (C≡), 1720 and 1690 (2 CO); pmr (deuteriodimethylsulfoxide): δ 3.55 (s, 2, CH_2), δ 7.68 (m, 3, aromatic protons), 7.98 (broad s, 2, aromatic protons).

Anal. Calcd. for $C_{13}H_7N_3O_2S$: C, 57.99; H, 2.62; N, 15.60; S, 11.91. Found: C, 58.1; H, 2.6; N, 15.6; S, 12.0.

B) A mixture of 2.29 g (0.01 mole) of **I**, 0.95 g (0.01 mole) of chloroacetic acid, 0.9 g (0.011 mole) of anhydrous fused sodium acetate, 20 ml of acetic acid and 10 ml of acetic anhydride was heated on a boiling water bath for 2 hours. The reaction mixture was left to cool and poured into water. The solid that separated was filtered off, dried and crystallised to give 1.4 g (52%) of **III**, mp and mixed mp 304°.

2-Arylmethylene-6-cyano-7-phenyl-5*H*-thiazolo[3,2-*a*]pyrimidine-3,5(2*H*)-diones (**VI**).

A) A mixture of 2.69 g (0.01 mole) of **III**, 1.06 g (0.01 mole) of benzaldehyde and 3 g of anhydrous sodium acetate was refluxed in 30 ml of glacial acetic acid for 4 hours. The reaction mixture was then poured on cold water, the separated solid was filtered off, washed with water and crystallised from dilute dimethylformamide to give 2.5 g (71%) of **VI**, mp 298°; ir: 2220 (C≡N), 1700, 1690 (2 CO).

Anal. Calcd. for $C_{20}H_{11}N_3O_2S$: C, 67.22; H, 3.10; N, 11.76; S, 8.97. Found: C, 67.4; H, 3.1; N, 11.7; S, 9.1.

B) A mixture of 2.29 g (0.01 mole) of **I**, 1.03 g (0.011 mole) of chloroacetic acid, 2 g of fused sodium acetate and 0.01 mole of the aromatic aldehyde was refluxed in 20 ml of glacial acetic acid and 10 ml of acetic anhydride for 4 hours. The reaction mixture was then worked up as in method A to give **VI**.

Compound **VIa** was obtained in 75% and found to be identical with **VIa** prepared in method A, mp and mixed mp 298°.

Compound **VIb** was crystallised from dilute dimethylformamide and obtained in 80% yield, mp 290°; ir: 2220 (C≡N), 1770, 1685 (2 CO); pmr (deuteriodimethylsulfoxide): δ 3.1 (s, 6H, 2 CH_3), δ 7.68 and δ 8.1 (m, 10H, 9 aromatic protons + ethylenic proton).

Anal. Calcd. for $C_{22}H_{16}N_4O_2S$: C, 65.98; H, 4.03; N, 13.99; S, 8.01. Found: C, 66.1; H, 4.2; N, 14.0; S, 8.1.

C) To a solution of **VII** (2.17 g, 0.01 mole) in acetic acid (150 ml) containing few drops of hydrochloric acid was added 2.04 g (0.01 mole) of **VIII** and the reaction mixture was heated under reflux for 12 hours. The reaction mixture was allowed to cool and the precipitate which separated was filtered off, washed with ethanol and crystallised from dimethylformamide to give 2.14 g (60%) of **VIa**, mp and mixed mp 298°.

2-Acetyl-6-carboxamido-5*H*-3-methyl-7-phenylthiazolo[3,2-*a*]pyrimidin-5-one (**IX**).

A suspension of 2 g (0.006 mole) of **IIc** and 10 g of polyphosphoric acid (prepared by dissolving 5 g of phosphorus pentoxide in 5 ml of *ortho*-phosphoric acid) was heated at 100° for an hour and then at 120° for an hour. The solution was left to cool, poured into ice-water and stirred. The solid that separated was collected and crystallised from ethanol to give 1.9 g (60%) of **IX**, mp 246°; ir: 3400, 3280 (NH), 1715, 1680, 1660 (3 CO); pmr: δ 2.65 (s, 3H, CH_3), δ 3.28 (s, 3H, CH_3), δ 7.5 (m, 3H, aromatic protons) and δ 7.81 (m, 4H, 2 aromatic protons + NH_2).

Anal. Calcd. for $C_{16}H_{13}N_3O_3S$: C, 58.71; H, 4.00; N, 12.84; S, 9.79. Found: C, 58.5; H, 4.0; N, 12.8; S, 10.0.

Formation of the Oxime **X**.

A solution of 1.64 g (0.005 mole) of **IX**, 0.35 g (0.005 mole) of hydroxylamine hydrochloride and about 1 g of sodium acetate in 25 ml of glacial acetic acid was refluxed for 30 minutes. After cooling the precipitate was collected by filteration, washed with water and dried. The product was obtained in 75% yield. After crystallization from acetic acid, it melted at 255°; ir: 3300 (OH), 1690 and 1670 (2 CO).

Anal. Calcd. for $C_{16}H_{14}N_4O_3S$: C, 56.13; H, 4.12; N, 16.37; S, 9.36. Found: C, 56.2; H, 4.3; N, 16.3; S, 9.2.

4-Amino-2-(2'-benzoylhydrazino)-5-cyano-6-phenylpyrimidine (**XIII**).

A solution of 1.13 g (0.005 mole) of **XII** and 0.7 g (0.005 mole) of benzoyl chloride in 25 ml of anhydrous dioxane was refluxed for 2 hours. The reaction mixture was left to cool and poured into water. The solid that separated was collected, washed with water, dried and crystallised from ethanol to give **XIII**, with one mole of ethanol of crystallisation, in 80% yield, mp 232°; ir: 3500 (OH), 3365, 3280 (NH), 2220 (C≡N), 1680 (CO), 1650 (NH_2).

Anal. Calcd. for $C_{20}H_{20}N_6O_2$: C, 63.82; H, 5.36; N, 22.33. Found: C, 63.8; H, 5.4; N, 22.2.

5-Amino-6-cyano-3,7-diphenyl-*s*-triazolo[4,3-*a*]pyrimidine (**XIV**).

A) A solution of 1.88 g (0.005 mole) of **XIII** was heated under reflux in 30 ml of dimethylformamide. The reaction mixture was left to cool and poured into water. The solid that separated was collected, dried and crystallised from ethanol to give 1 g (65%) of **XIV**, mp 194-195°; ir: 3380, 3360 (NH_2), 2220 (C≡), 1650 (NH_2); pmr: δ 7.67 (m, 6H, aromatic protons), δ 7.93 (m, 6H, 4 aromatic protons + NH_2).

Anal. Calcd. for $C_{18}N_{12}N_6$: C, 69.04; H, 4.12; N, 26.84. Found: C, 69.0; H, 4.2; N, 26.7.

B) A mixture of 2.42 g (0.01 mole) of **XI**, 1.36 g (0.01 mole) of benzhydrazide was refluxed in 50 ml of dimethylformamide for 3 hours and then worked up as in method A to give 1.87 g (60%) of **XIV**, mp 194°, not depressed when mixed with that obtained in method A.

Reaction of **XII** and **XV** with Benzoyl Isothiocyanate.

General Procedure.

Benzoyl isothiocyanate (1.63 g, 0.01 mole) was heated under reflux with 0.01 mole of each of **XII** and **XV** in 30 ml of anhydrous dioxane. The reaction mixture was allowed to cool and then poured into water. The solid that separated was collected, washed thoroughly with water and dried to give **XVI** and **XVII**, respectively.

Compound **XVI** was crystallised from dilute dioxane in 70% yield, mp 209°; ir: 3325 (NH), 2220 (C≡N), 1670 (CO), 1650 (NH_2).

Anal. Calcd. for $C_{19}H_{15}N_7OS$: C, 58.60; H, 3.88; N, 25.18; S, 8.23. Found: C, 58.4; H, 4.0; N, 25.3; S, 8.2.

Compound **XVII** was crystallised from dilute dimethylformamide in 60% yield, mp 212°; ir: 3320 (NH), 2220 (C≡N), 1700, 1675 (2 CO).

Anal. Calcd. for $C_{19}H_{14}N_6O_2S$: C, 58.45; H, 3.61; N, 21.52; S, 8.21. Found: C, 58.5; H, 3.8; N, 21.5; S, 8.4.

Cyclisation of **XVI** and **XVII**. Formation of **XVIII** and **XIX**.

About 2 g of each of **XVI** or **XVII** was dissolved in 50 ml of 5% sodium hydroxide solution and then gently warmed. The solution was filtered and acidified with dilute hydrochloric acid. The solid separated was collected, washed with water and dried to give **XVIII** and **XIX**, respectively.

Compound **XVIII** was crystallised from dimethylformamide in 85% yield, mp > 300°; ir: 3325 (NH), 2600 (SH), 2225 (C≡), 1640 (NH_2); pmr: δ8 2.75 (s, 1H, SH), δ 7.68, (m, 12, 10 aromatic protons + NH_2).

Anal. Calcd. for $C_{19}H_{13}N_7S$: C, 61.44; H, 3.53; N, 26.40; S, 8.63. Found: C, 61.3; H, 3.7; N, 26.5; S, 8.6.

Compound **XIX** was crystallised from dimethylformamide in 80% yield, mp > 300°; ir: 3200 (NH), 2650 (SH), 2220 (C≡N), 1710 (CO).

Anal. Calcd. for $C_{19}H_{12}N_6OS$: C, 61.29; H, 3.25; N, 22.57; S, 8.61. Found: C, 61.1; H, 3.4; N, 22.5; S, 8.5.

Preparation of **XX** and **XXI**.

General Method.

Equimolecular amounts (0.01 mole) of each of **XII** or **XV** and 2,4-pentanedione or 3-chloro-2,4-pentanedione in 50 ml of absolute ethanol were heated under reflux for 6 hours and allowed to cool. The precipitate formed was filtered off, dried and recrystallised from the proper solvent to give **XXa,b** and **XXIa,b**, respectively. See Table I.

Table I

Hydrolysis of **XXb** and **XXIb**.

A mixture of 1 g of each of **XXb** or **XXIb**, 20 ml of ethanol and 20 ml of 5% sodium hydroxide solution was heated under reflux for 2 hours. The reaction mixture was left to cool and the precipitate was rejected by filteration. The filtrate was acidified with acetic acid to precipitate **XXII** and **XXIII**, respectively.

Compound **XXII** was crystallised from dimethylformamide in 65% yield, mp > 300°; ir: 3320 (OH), 3200 (NH), 3050 (CH), 2220 (C≡).

Anal. Calcd. for $C_{16}H_4N_6O$: C, 62.74; H, 4.61; N, 27.44. Found: C, 62.9; H, 4.8; N, 27.5.

Compound **XXIII** was crystallised from dioxane in 60% yield, mp 298°; ir: broad centered at 3000 (OH, NH), 2220 (C≡N), 1690 (CO).

Anal. Calcd. for $C_{16}H_{13}N_5O_2$: C, 62.54; H, 4.26; N, 22.79. Found: C, 62.5; H, 4.1; N, 22.6.

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