Study on the Reaction of Methyl *N*-Methyl-*N*-(6-substituted-5-nitropyrimidin-4-yl)glycinates with Sodium Alkoxides

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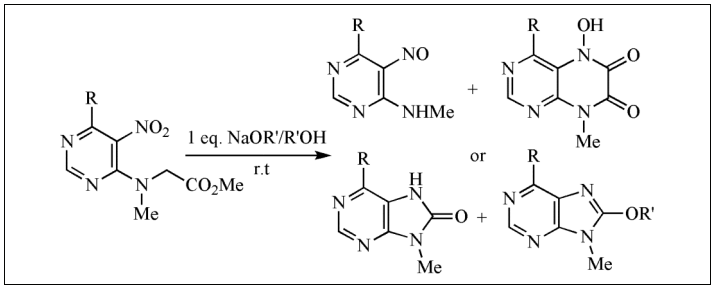

Methyl *N*-methyl-*N*-(6-substituted-5-nitropyrimidin-4-yl)glycinates (**4a-n**), obtained from 6-substituted-4-chloro-5-nitropyrimidines and sarcosine methyl ester (methyl 2-(methylamino)acetate), in the reaction with sodium alkoxides underwent transformations to give different products. *N*-methyl-*N*-(5-nitropyrimidin-4-yl)glycinates (**4a,i,j**) bearing amino and arylamino groups in the position 6 of the pyrimidine ring gave corresponding 6-substituted-4-methylamino-5-nitrosopyrimidines (**5a,i,j**). In the reaction of *N*-(6-alkylamino-5-nitropyrimidin-4-yl)-*N*-methylglycinates (**4b,f-h**) with sodium alkoxides the corresponding 6-alkylamino-4-methylamino-5-nitrosopyrimidines (**5b,f-h**) and 5-hydroxy-8-methyl-5,8-dihydropteridine-6,7-diones (**6b,f-h**) were formed. The main products of the reaction of *N*-(6-dialkylamino-5-nitropyrimidin-4-yl)-*N*-methylglycinates (**4c-e,k,l**), after work-up, were the corresponding 6-dialkylamino-9-methylpurin-8-ones (**7c-e,k,l**) and 8-alkoxy-6-dialkylamino-9-methylpurines (**9c,l**, **10c,l**). Methyl *N*-methyl-*N*-{[6-(2-methoxy-oxoethyl)thio]-5-nitropyrimidin-4-yl}glycinate (**4n**) under the same conditions gave methyl 7-methylaminothiazolo[5,4-*d*]pyrimidine-2-carboxylate (**13**). Mechanisms of the observed transformations are discussed.

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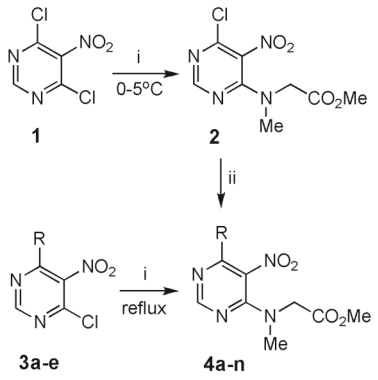
Introduction.

Nitropyrimidines due to versatility of the nitro group are often used for the synthesis of various types of heterocyclic compounds [1-4]. However transformations of 5-nitropyrimidines under basic non-reductive conditions are still studied insufficiently. Literature survey on these reactions reveals only few reports on the cyclisation reactions of 5-nitropyrimidines, bearing an active methyleneamino group in position 4 of the pyrimidine ring. For example, 5-nitro-4-phenacylaminopyrimidines in aqueous sodium hydroxide solution were shown to undergo a cyclocondensation reaction with the formation of 9*H*-purine-7-oxides [5-8]. Recently in our preliminary report [9] it has been shown that methyl *N*-methyl-*N*-(6-substituted-5-nitropyrimidin-4-yl)glycinates on treatment with sodium alkoxides undergo transformations into 6-substituted 4-methylamino-5-nitrosopyrimidines **5** or 9-methylpurin-8-ones **7**. Now we report on more detail and extensive study on these transformations.

Results and Discussion.

For the synthesis of methyl *N*-methyl-*N*-(5-nitropyrimidin-4-yl)glycinates (**4a-n**) readily available 6-substituted 4-chloro-5-nitropyrimidines (**1, 3a-e**) [10-13] were used as starting materials. Substitution of one chlorine atom in **1** with sarcosine methyl ester was achieved at 5° to give **2** in 91 % yield. 6-Substituted 4-chloro-5-nitropyrimidines (**3a-e**) reacted with sarcosine methyl ester at reflux temperature of methanol to give the corresponding

Scheme 1



	R
a	NH_2
b	MeNH
c	Me_2N
d	$(CH_2)_4N$
e	$(CH_2)_6N$
f	PrNH
g	$PhCH_2NH$
h	$PhCH_2CH_2NH$
i	PhNH
j	$3\text{-}CF_3C_6H_4NH$
k	$MeNCH_2CO_2Me$
l	MeNPh
m	PhS
n	SCH_2CO_2Me

Reagents and conditions: i - $MeNHCH_2CO_2Me \cdot HCl$, Et_3N, MeOH; ii - amine, or $NaSCH_2CO_2Me$ or PhSNa, MeOH, reflux.

N-methyl-*N*-(pyrimidin-4-yl)glycinates **4a-e**. Analogously, reaction of methyl *N*-methyl-*N*-(6-chloro-5-nitropyrimidin-4-yl)glycinate (**2**) with selected amines or sodium salts of methyl mercaptoacetate or thiophenol, prepared *in situ*, furnished compounds **4f-n** (Scheme 1).

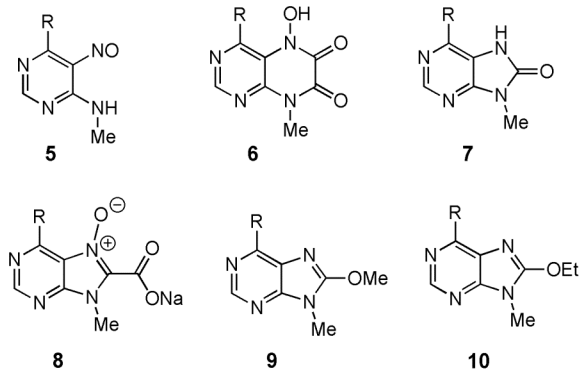


Figure 1

The reactions of the title compounds **4a-n** with sodium alkoxides in alcohols (methanol, ethanol, propanol) reveal a variety of behavior depending on the nature of substituent in position 6 of the pyrimidine ring. (Figure 1, Table 1). It should be noted that all reactions were carried out under the same reaction conditions: room temperature and an equivalent amount of the appropriate sodium alkoxide was used.

Compounds **4a,i,j** bearing primary amino or arylamino groups in position 6 of the pyrimidine ring in the reaction with alkoxides afforded the corresponding 6-substituted-4-methylamino-5-nitrosopyrimidines (**5a,i,j**) as the only products. However reaction of 6-alkylamino derivatives **4b,f-h** with sodium alkoxides gave a mixture of 5-nitrosopyrimidines **5b,f-h** and sodium salts of 8-methyl-5-hydroxypteridine-6,7-diones **6b,f-h** in yields higher for the latter compounds (Table 1). Similar behavior also showed 6-phenylthio derivative **4m**. Its reaction with sodium methoxide gave the corresponding 8-methyl-5-hydroxypteridine-6,7-dione **6m** as the main product

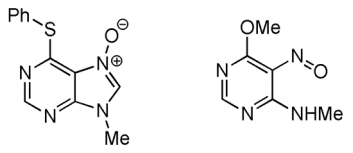
Table 1

Products from the reactions of methyl *N*-methyl-*N*-(6-substituted-5-nitropyrimidin-4-yl)glycinates (**4a-n**) with sodium alkoxides.

Comp.	R	Base	Yields (%) [a]			
			5	**6**	**7**	Others
4a	NH_2	NaOMe	60	-	-	-
4a	NH_2	NaOEt	55			
4a	NH_2	NaOPr	49			
4b	MeNH	NaOMe	15	52	-	-
4c	Me_2N	NaOMe	-	-	25 [b]	**8c** (25%), **9c** (31%)
4c	Me_2N	NaOEt	-	-	27 [b]	**8c** (27%), **10c** (3%)
4c	Me_2N	NaOPr	-	-	80	-
4d	$(CH_2)_4N$	NaOMe	-	-	33 [b]	**8d** (33%)
4e	$(CH_2)_6N$	NaOMe	-	-	52	-
4e	$(CH_2)_6N$	NaOEt			55	
4e	$(CH_2)_6N$	NaOPr			50	
4f	PrNH	NaOMe	8	48	-	-
4g	$PhCH_2NH$	NaOMe	30	48	-	-
4g	$PhCH_2NH$	NaOEt	24	45		
4g	$PhCH_2NH$	NaOPr	20	30		
4h	$Ph(CH_2)_2NH$	NaOMe	32	54	-	-
4i	PhNH	NaOMe	65	-	-	-
4i	PhNH	NaOEt	58			
4i	PhNH	NaOPr	49			
4j	$3\text{-}CF_3\text{-}C_6H_4NH$	NaOMe	85	-	-	-
4j	$3\text{-}CF_3\text{-}C_6H_4NH$	NaOEt	79			
4j	$3\text{-}CF_3\text{-}C_6H_4NH$	NaOPr	60			
4k	$MeNCH_2CO_2Me$	NaOMe	-	-	64	-
4l	PhNMe	NaOMe	-	-	55	**9l** (31%)
4l	PhNMe	NaOEt			42	**10l** (4%)
4l	PhNMe	NaOPr			28	-
4m	PhS	NaOMe	-	44	traces	**11m** (3%), **12** (5%)
4m	PhS	NaOPr	-	30	-	-
4n	SCH_2CO_2Me	NaOMe	-	-	-	**13** (78%)
4n	SCH_2CO_2Me	NaOEt				**13** (40%)
4n	SCH_2CO_2Me	NaOPr				**13** (35%)

[a] Yields after isolation of products; [b] obtained after acidification of salts **8c,d**.

(Table 1). However, traces of purin-8-one **7m**, 6-phenylthio-9-methyl-9*H*-purine 7-oxide (**11m**) and 6-methoxy-4-methylamino-5-nitrosopyrimidine (**12**) (Table 1, Figure 2) were isolated from the reaction mixture using dry column vacuum chromatography [14]. Compound **12** is possibly formed from nitrosopyrimidine **5m** during nucleophilic substitution reaction of the phenylthio group with sodium methoxide. The reaction of **4m** with sodium propoxide gave only 5-hydroxy-8-methyl-4-phenylthio-5,8-dihydropteridine-6,7-dione (**6m**) as well as unreacted **4m**. Structure of 4-methylamino-5-nitrosopyrimidines **5** was unambiguously proved using single crystal X-ray diffraction analysis [9] and NMR spectroscopy. It should be mentioned that 6-amino-, 6-alkylamino and 6-arylamino-4-methylamino-5-nitrosopyrimidines (**5a,b,g-j**) in solutions exist as a mixture of two conformers [9] and two sets of signals are observed in their ^{1}H NMR spectra (see Experimental).



11m **12**

Figure 2

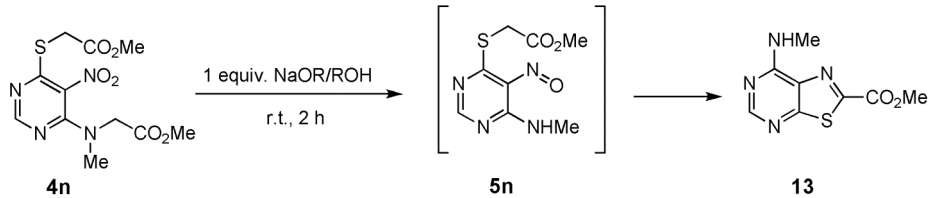
Reaction of compound **4n** bearing SCH_2CO_2Me substituent in position 6 of the pyrimidine ring reacted with sodium alkoxides to give methyl 7-methylaminothiazolo[5,4-*d*]pyrimidine-2-carboxylate (**13**) as the only reaction product (Scheme 2). The reaction outcome could be explained by the formation of nitroso derivative **5n** and subsequent intramolecular cyclisation reaction between the nitroso and SCH_2 groups to form thiazolo[5,4-*d*]-pyrimidine **13**.

could be in an equilibrium with their *aci*-forms **I** stabilised by the primary or secondary amino groups in position 6 of the pyrimidine ring (Scheme 3). This allows to form the pyrimido[4,5-*e*][2,1,4]oxadiazine intermediate **II**. When R is H or aryl, O-H_b bond becomes more polar due to stronger hydrogen bond between H_a and oxygen of the nitro group and ring opening of the oxadiazine **II** occurs preferably by an attack of a base on H_b (route i) to form intermediate **III** leading to the nitroso derivatives **5** after elimination of $OHCCO_2Me$. When R is alkyl an acidity of H_b should be lower than in previous case. Therefore ring opening of oxadiazine **II** is realised by competitive abstraction of either H_b (route i) or H_c (route ii) and formation of a mixture of nitrosopyrimidines **5** and pteridine-5,8-diones **6** is observed.

On the other hand, formation of nitrosopyrimidines **5** by a competitive mechanism *via* methyl purine-6-carboxylate 7-oxides **IV** (route iii) must be also considered. Isolation of purine 7-oxide **11m** in the reaction of **4m** with sodium methoxide and data of the analogous reactions of methyl *N*-(6-dialkylamino-5-nitropyrimidin-4-yl)-*N*-methylglycinates (**4c-e,k,l**) (see below) confirm that Dieckmann's type cyclocondensation of methyl *N*-(5-nitropyrimidin-4-yl)-*N*-methylglycinates **4** can occur in some cases. Then addition of hydroxide to **IV** causes the imidazole ring opening to give intermediate **III**. The preference for a hydroxide ion to attack C8 of purine **IV** is probably determined by the increased reactivity of C8 towards nucleophiles due to the interaction of substituent in position 6 of the purine with the oxygen of the 7-oxide group.

Neither 5-nitrosopyrimidines **5** nor 5-hydroxy-8-methyl-5,8-dihydropteridine-6,7-diones **6** formed in the reaction of methyl *N*-(6-dialkylamino-5-nitropyrimidin-4-yl)-*N*-methylglycinates (**4c-e,k,l**) with sodium alkoxides. 6-Dimethylamino derivative **4c** in the reaction with sodium

Scheme 2

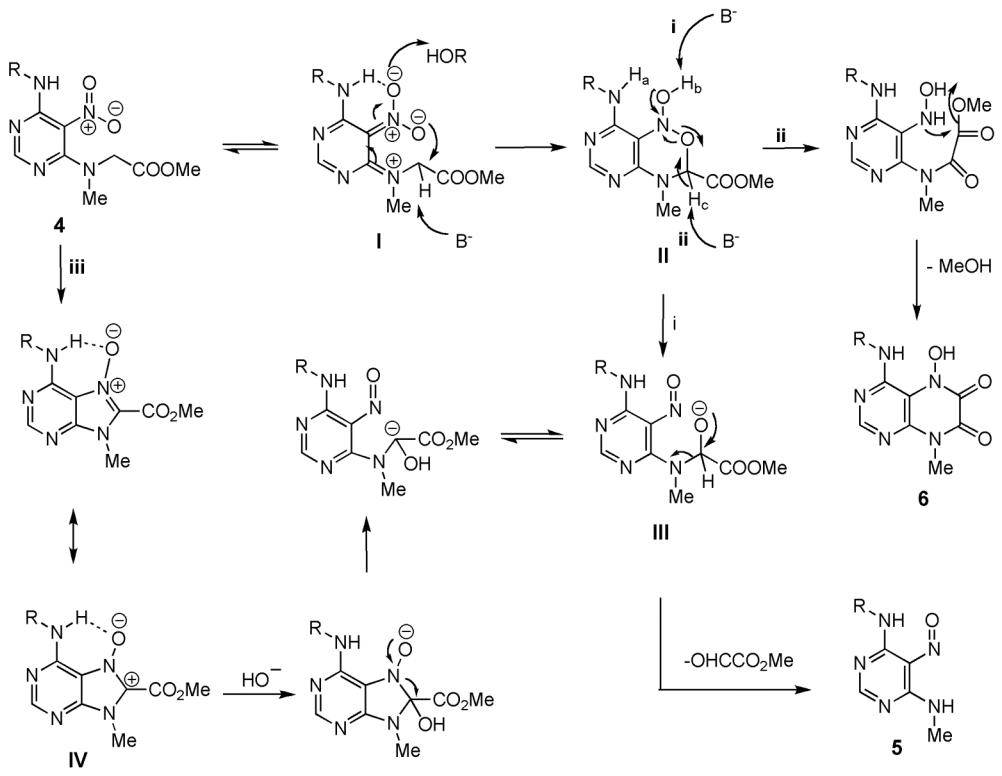


4n **5n** **13**

Results obtained for the reactions of methyl *N*-[6-amino-, 6-alkylamino-, 6-arylamino-, or 6-(substituted thio)-5-nitropyrimidin-4-yl]-*N*-methylglycinates (**4a,b,f-j,m,n**) with sodium alkoxides could be rationalised by a following mechanism. According to the data obtained in the investigation of transformations of *o*-nitrophenylglycine esters [15-17] nitro compounds in basic media

methoxide or ethoxide gave a mixture of two products – sodium salt of purine-8-carboxylic acid 7-oxide **8c** and the corresponding 8-alkoxy-6-dimethylamino-9-methylpurines (**9c** or **10c**) (Figure 1, Table 1). It is noteworthy, that in the reaction of **4c** with sodium propoxide, as well as of **4e** and **4k** with other sodium alkoxides purinones **7c**, **7e** and **7k** were formed as the only reaction products. Reaction of

Scheme 3



compound **4l** with sodium methoxide or ethoxide led to a mixture of purin-8-one **7l** and 8-alkoxypurines **9l**, **10l**, respectively. Compound **4d** with sodium methoxide gave sodium salt of purine-8-carboxylic acid 7-oxide **8d** as the sole product. In order to obtain carboxylic acids **14** sodium salts **8c,d** were acidified with hydrochloric acid. However, compounds **8c,d** underwent spontaneous decarboxylation and products formed appeared to be purin-8-ones **7c**,**d** but not expected purin-7-oxides **11c,d**. Structure of **7c**, obtained after acidification of salt **8c**, was confirmed by X-ray analysis. The crystallografic data of **7c** indicated that this compound was obtained as hydrochloride: protonation occurred at N1 atom of the purine system (Figure 3).

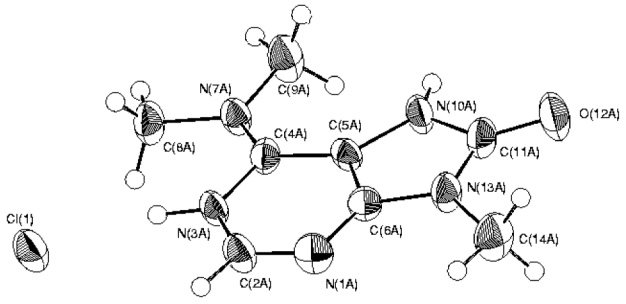
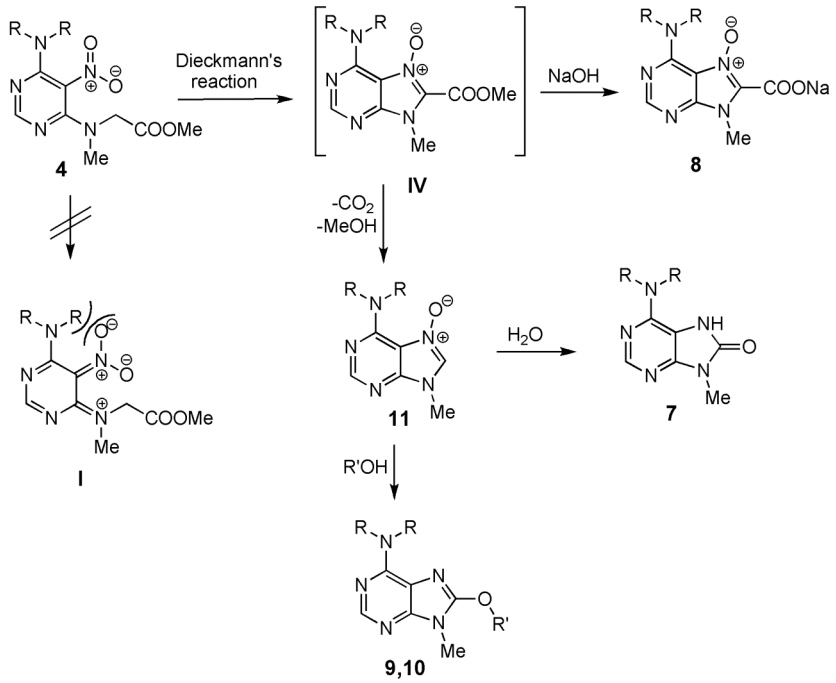


Figure 3. Ortep drawing of compound **7c**.

Nevertheless, acidification of **8d** at 0° allowed to obtain the corresponding carboxylic acid **14d**. However, due its instability, it was impossible to characterise **14d** and to record its nmr spectra. Already during dissolving **14d** in dimethylsulfoxide-d_6 spontaneous decarboxylation was observed and the ^{1}H-nmr spectrum of the sample contained signals of purine 7-oxide **11d** (d 1.99 (t, J = 4.8 Hz, 4H, $(CH_2)_2$), 3.61 (t, J = 4.8 Hz, 4H, $N(CH_2)_2$), 3.66 (s, 3H, NMe), 8.14 (s, 1H, C2-H), 8.63 (s, 1H, C8-H)) and purin-8-one **7d** (see Experimental) in a ratio 7:3. The ^{1}H-nmr spectrum recorded after sample's heating contained only the signals of compound **7d**. Purinone **7d** was also obtained by heating of crude carboxylic acid **14d** in anhydrous xylene.

Formation of purine-8-carboxylic acid 7-oxides and their conversion into purin-8-ones indicates that Dieckmann's type cyclocondensation of 6-dialkylamino derivatives occurs in the first step of rearrangement (Scheme 4). Due to steric hindrance of 6-dialkylamino groups realisation of *aci*-forms **I** of **4c-e,k,l** fails. Nitro group turns out of a plane of the pyrimidine ring and it makes Dieckmann's reaction to become more favorable. Then attack of the hydroxide ion takes place at the ester carbonyl of **IV** to form purine 7-oxides **11c-e,k,l,m**. Finally, purine 7-oxides **11** undergo rearrangement to give

Scheme 4

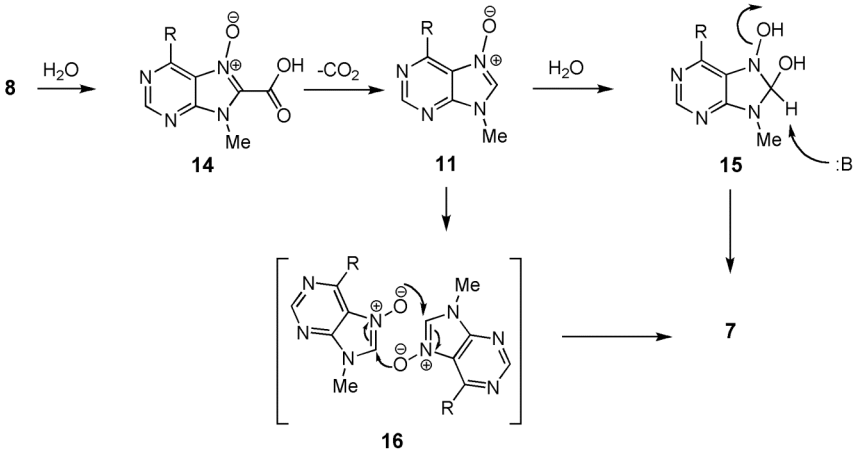


purine-8-ones **7c-e** or corresponding 8-alkoxypurines **9c,l**, **10c,l**.

Taking into account that formation of 9-methylpurin-8-ones **7** proceeds in protic and anhydrous conditions rearrangement of purine 7-oxides **11** into purin-8-ones **7** possibly occurs by competitive mechanisms of an abnormal addition-elimination process of water (AE_a) (intermediate **15**) or bimolecular intermediate **16**, similar to that proposed for conversion of benzimidazole *N*-oxides [18].

In summary, the present investigation provides novel results on chemistry of 5-nitropyrimidines. It was found that alkoxide-induced transformations of the title compounds give products, whose formation is sometimes difficult to predict. Nevertheless, the data obtained allow to conclude that main products of the reaction of *N*-methyl-*N*-(6-substituted-5-nitropyrimidin-4-yl)glycinates (**4a,i,j**) bearing amino or arylamino groups in the position 6 are 6-substituted-4-methylamino-5-nitrosopyrimidines **5a,i,j**. Reaction of *N*-(6-alkylamino-5-nitropyrimidin-4-

Scheme 5



yl)-*N*-methylglycinates (**4b,f-h**) leads to a mixture of the corresponding 6-alkylamino-4-methylamino-5-nitroso-pyrimidines (**5b,f-h**) and 4-alkylamino-5-hydroxy-8-methyl-5,8-dihydropteridine-6,7-diones (**6b,f-h**). The main products of interaction of *N*-(6-dialkylamino-5-nitropyrimidin-4-yl)-*N*-methylglycinates (**4c-e,k,l**) with sodium alkoxides in the appropriate alcohols, after work-up, were found to be the corresponding 6-dialkylamino-9-methylpurin-8-ones (**7c-e,k,l**) and 8-alkoxy-6-dialkyl-amino-9-methylpurines (**9c,l, 10c,l**).

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were run in Nujol mulls or in KBr discs on a Perkin-Elmer FT spectrophotometer Spectrum BX II. ^{1}H nmr spectra were recorded with a Varian Unity spectrometer (300 MHz) using tetramethylsilane as internal standard. Mass spectra were performed using direct insertion probe on a Kratos MS-30 spectrometer (70 eV). Elemental analyses (C, N, H) results were found to be in good agreement (±0.4%) with the calculated values. All reactions and purity of the synthesised compounds were monitored by TLC using Silica gel 60 F_{254} aluminium plates (Merck). Visualization was accomplished by UV light.

Methyl *N*-(6-chloro-5-nitropyrimidin-4-yl)-*N*-methylglycinate (**2**).

To a cooled to 5 °C suspension of compound **1** [10] (5 g, 26 mmol) and sarcosine methyl ester hydrochloride [19] (3.6 g, 26 mmol) in chloroform (15 ml) a solution of triethylamine (5.2 g, 52 mmol) in chloroform (10 ml) was added dropwise. The reaction mixture was stirred at 5° for 30 min. Then the solution was washed with water, organic layer dried with Na_2SO_4 and evaporated under reduced pressure to dryness. The residue was recrystallised to give 6.2 g (91%) of compound **2**, mp 45-46° (from hexane); ir (nujol): 1762 (CO) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.07 (s, 3H, NMe), 3.78 (s, 3H, OMe), 4.38 (s, 2H, NCH_2), 8.37 (s, 1H, C2-H).

Anal. Calcd. for $C_8H_9ClN_4O_4$: C, 36.87; H, 3.48; N, 21.50. Found: C, 36.98; H, 3.46; N, 21.39.

General Procedure for the Synthesis of Methyl *N*-(6-Substituted-5-nitropyrimidin-4-yl)-*N*-methylglycinates (**4a-e**).

A solution of compounds **3a-e** (10 mmol), sarcosine methyl ester hydrochloride (1.4 g, 10 mmol), triethylamine (2.02 g, 20 mmol) in methanol (20 ml) was refluxed for 30 min. The solvent was evaporated under reduced pressure to dryness, the residue was washed with water and recrystallised to give compounds **4a-e**.

Methyl *N*-(6-Amino-5-nitropyrimidin-4-yl)-*N*-methylglycinate (**4a**).

This compound was obtained as a yellow solid, mp 143-145° (from methanol); yield 66%; ir (nujol): 3462, 3431 (NH_2), 1754 (CO) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.97 (s, 3H, NMe), 3.78 (s, 3H, OMe), 4.34 (s, 2H, NCH_2), 7.00 (br.s, 2H, NH_2), 7.97 (s, 1H, C2-H).

Anal. Calcd. for $C_8H_{11}N_5O_4$: C, 39.84; H, 4.60; N, 29.04. Found: C, 40.00; H, 4.65; N, 29.11.

Methyl *N*-Methyl-*N*-(6-methylamino-5-nitropyrimidin-4-yl)-glycinate (**4b**).

This compound was obtained as a yellow solid, mp 82-82.5° (from methanol); yield 51%; ir (KBr): 3351 (NH), 1746 (CO) cm^{-1}; ^{1}H nmr (acetone-d_6): δ 2.91 (s, 3H, NMe), 3.13 (d, J = 4.8 Hz, 3H, NHMe), 3.74 (s, 3H, OMe), 4.45 (s, 2H, NCH_2), 8.05 (s, 1H, C2-H), 8.31 (br.s, 1H, NH).

Anal. Calcd. for $C_9H_{13}N_5O_4$: C, 42.35; H, 5.13; N, 27.44. Found: C, 42.18; H, 4.99; N, 27.35.

Methyl *N*-Methyl-*N*-(6-dimethylamino-5-nitropyrimidin-4-yl)-glycinate (**4c**).

This compound was obtained as a yellow solid, mp 63-64° (from 2-propanol); yield 98%; ir (KBr): 1748 (CO) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.23 (s, 3H, NMe), 3.24 (s, 6H, NMe_2), 3.80 (s, 3H, OMe), 4.37 (s, 2H, NCH_2), 7.91 (s, 1H, C2-H).

Anal. Calcd. for $C_{10}H_{15}N_5O_4$: C, 44.61; H, 5.62; N, 26.01. Found: C, 44.69; H, 5.86; N, 26.20.

Methyl *N*-Methyl-*N*-(6-pyrrolidino-5-nitropyrimidin-4-yl)-glycinate (**4d**).

This compound was obtained as a yellow solid, mp 86-87° (from 2-propanol); yield 65%; ir (KBr): 1748 (CO) cm^{-1}; ^{1}H nmr (acetone-d_6): δ 1.98-2.03 (m, 4H, $(CH_2)_2$), 3.16 (s, 3H, NMe), 3.54-3.59 (m, 4H, $N(CH_2)_2$), 3.73 (s, 3H, OMe), 4.40 (s, 2H, NCH_2), 7.94 (s, 1H, C2-H).

Anal. Calcd. for $C_{12}H_{17}N_5O_4$: C, 48.81; H, 5.80; N, 23.72. Found: C, 48.98; H, 5.76; N, 23.85.

Methyl *N*-[6-(Azepan-1-yl)-5-nitropyrimidin-4-yl]-*N*-methyl-glycinate (**4e**).

This compound was obtained as a yellow solid, mp 97-98° (from 2-propanol); yield 57%; ir (KBr): 1749 (CO) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.39-1.89 (m, 8H, $(CH_2)_4$), 3.27 (s, 3H, NMe), 3.49-3.67 (m, 4H, $N(CH_2)_2$), 3.80 (s, 3H, OMe), 4.36 (s, 2H, NCH_2), 7.91 (s, 1H, C2-H).

Anal. Calcd. for $C_{14}H_{21}N_5O_4$: C, 52.00; H, 6.55; N, 21.66. Found: C, 51.95; H, 6.70; N, 21.82.

General Procedure for the Synthesis of Methyl *N*-Methyl-*N*-(6-substituted-5-nitropyrimidin-4-yl)glycinates **(4f-n)**.

To a solution of compound **2** (2 g, 7.66 mmol) in methanol (20 ml) a solution of the corresponding amine (15.32 mmol) or sodium salt of methyl mercaptoacetate, prepared from sodium (0.176 g, 7.66 mmol), anhydrous methanol (3 ml) and methyl mercaptoacetate (0.81 g, 7.66 mmol), or sodium salt of thiophenol, prepared from sodium (0.176 g, 7.66 mmol), anhydrous methanol (3 ml) and thiophenol (0.84 g, 7.66 mmol), was added. The reaction mixture was refluxed for 15 min. After cooling to room temperature the precipitate was collected by filtration, washed with water and recrystallised to give compounds **4f-n**.

Methyl *N*-Methyl-*N*-(6-propylamino-5-nitropyrimidin-4-yl)-glycinate (**4f**).

This compound was obtained as a yellow solid, mp 85-86° (from hexane); yield 95%; ir (KBr): 3398 (NH), 1752 (CO) cm^{-1}; ^{1}H nmr (acetone-d_6): δ 0.99 (t, J = 7.5 Hz, 3H, Me), 1.66-1.75 (m, J = 7.5 Hz, 2H, CH_2), 2.98 (s, 3H, NMe), 3.61 (q, J = 7.5 Hz, 2H, $NHCH_2$), 3.74 (s, 3H, OMe), 4.45 (s, 2H, NCH_2), 8.03 (s, 1H, C2-H), 8.31 (br.s, 1H, NH).

Anal. Calcd. for $C_{11}H_{17}N_5O_4$: C, 46.64; H, 6.05; N, 24.72. Found: C, 46.58; H, 5.99; N, 24.65.

Methyl *N*-(6-Benzylamino-5-nitropyrimidin-4-yl)-*N*-methylglycinate (**4g**).

This compound was obtained as a yellow solid, mp 102-102.5° (from 2-propanol); yield 67%; ir (Nujol): 3332 (NH), 1744 (CO) cm^{-1}; ^1H nmr (acetone-d_6): δ 2.98 (s, 3H, NMe), 3.73 (s, 3H, OMe), 4.44 (s, 2H, NCH_2), 4.88 (d, J = 6 Hz, 2H, $NHCH_2$), 7.28 – 7.44 (m, 5H, ArH), 8.03 (s, 1H, C2-H), 8.71 (br.s, 1H, NH).

Anal. Calcd. for $C_{15}H_{17}N_5O_4$: C, 54.38; H, 5.17; N, 21.14. Found: C, 54.58; H, 5.23; N, 21.07.

Methyl *N*-Methyl-*N*-{6-[(2-phenylethyl)amino]-5-nitropyrimidin-4-yl}glycinate (**4h**).

This compound was obtained as a yellow solid, mp 100-101° (from ethanol); yield 94%; ir (KBr): 3379 (NH), 1749 (CO) cm^{-1}; ^1H nmr (dichloromethane-d_2): δ 2.96 (s, 3H, NMe), 2.99 (t, J = 7.2 Hz, 2H, CH_2), 3.79 (s, 3H, OMe), 3.88 (q, J = 7.2 Hz, 2H, $NHCH_2$), 4.36 (s, 2H, NCH_2), 7.29 – 7.46 (m, 5H, ArH), 8.08 (s, 1H, C2-H), 8.23 (br.s, 1H, NH).

Anal. Calcd. for $C_{16}H_{19}N_5O_4$: C, 55.64; H, 5.55; N, 20.28. Found: C, 55.77; H, 5.43; N, 20.04.

Methyl *N*-(6-Anilino-5-nitropyrimidin-4-yl)-*N*-methylglycinate (**4i**).

This compound was obtained as a yellow solid, mp 118-120° (from 2-propanol); yield 82%; ir (nujol): 3334 (NH), 1751 (CO) cm^{-1}; ^1H nmr (acetone-d_6): δ 3.03 (s, 3H, NMe), 3.76 (s, 3H, OMe), 4.52 (s, 2H, NCH_2), 7.22 – 7.77 (m, 5H, ArH), 8.11 (s, 1H, C2-H), 10.61 (br.s, 1H, NH).

Anal. Calcd. for $C_{14}H_{15}N_5O_4$: C, 52.99; H, 4.76; N, 22.07. Found: C, 53.08; H, 4.65; N, 22.03.

Methyl *N*-Methyl-*N*-(5-nitro-6-{[3-(trifluoromethyl)phenyl]-amino} pyrimidin-4-yl)glycinate (**4j**).

This compound was obtained as a yellow solid, mp 115-116° (from 2-propanol); yield 77%; ir (nujol): 3299 (NH), 1743 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.01 (s, 3H, NMe), 3.80 (s, 3H, OMe), 4.41 (s, 2H, NCH_2), 7.42 – 8.03 (m, 4H, ArH), 8.15 (s, 1H, C2-H), 10.02 (br.s, 1H, NH).

Anal. Calcd. for $C_{15}H_{14}F_3N_5O_4$: C, 46.76; H, 3.66; N, 18.18. Found: C, 46.65; H, 3.62; N, 18.20.

4,6-Bis[*N*-methyl-*N*-(2-methoxy-2-oxoethyl)amino]-5-nitropyrimidine (**4k**).

This compound was obtained as a yellow solid, mp 90-92° (from 2-propanol); yield 62%; ir (nujol): 1750 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.20 (s, 6H, 2NMe), 3.79 (s, 6H, 2OMe), 4.34 (s, 4H, $2NCH_2$), 7.91 (s, 1H, C2-H).

Anal. Calcd. for $C_{12}H_{17}N_5O_6$: C, 44.04; H, 5.24; N, 21.40. Found: C, 44.56; H, 5.34; N, 21.74.

Methyl *N*-Methyl-*N*-{6-[methyl(phenyl)amino]-5-nitropyrimidin-4-yl}glycinate (**4l**).

This compound was obtained as a yellow solid, mp 104-105° (from 2-propanol); yield 87%; ir (KBr): 1752 (CO) cm^{-1}; ^1H nmr (acetone-d_6): δ 2.95 (s, 3H, NMe), 3.03 (s, 3H, NMe), 3.73 (s, 3H, OMe), 4.38 (s, 2H, NCH_2), 7.22 – 7.40 (m, 5H, ArH), 8.18 (s, 1H, C2-H).

Anal. Calcd. for $C_{15}H_{17}N_5O_4$: C, 54.38; H, 5.17; N, 21.14. Found: C, 54.44; H, 4.99; N, 21.09.

Methyl *N*-Methyl-*N*-(5-nitro-6-phenylthiopyrimidin-4-yl)-glycinate (**4m**).

This compound was obtained as a yellow solid, mp 105-107° (from 2-propanol); yield 66%; ir (KBr): 1746 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.03 (s, 3H, NMe), 3.80 (s, 3H, OMe), 4.40 (s, 2H, NCH_2), 7.46 – 7.90 (m, 5H, ArH), 8.19 (s, 1H, C2-H),

Anal. Calcd. for $C_{14}H_{14}N_4O_4S$: C, 50.29; H, 4.22; N, 16.76. Found: C, 50.17; H, 4.35; N, 16.63.

Methyl *N*-{6-[(2-Methoxy-2-oxoethyl)thio]-5-nitropyrimidin-4-yl}-*N*-methylglycinate (**4n**).

This compound was obtained as a yellow solid, mp 129-130° (from methanol); yield 71%; ir (KBr): 1754, 1735 (CO) cm^{-1}; ^1H nmr (acetone-d_6): δ 3.03 (s, 3H, NMe), 3.71 (s, 3H, OMe), 3.74 (s, 3H, OMe), 4.06 (s, 2H, SCH_2), 4.54 (s, 2H, NCH_2), 8.35 (s, 1H, C2-H).

Anal. Calcd. for $C_{11}H_{14}N_4O_6S$: C, 40.00; H, 4.27; N, 16.96. Found: C, 40.32; H, 4.39; N, 16.75.

General Procedure for the Synthesis of Compounds **5-13**.

To a suspension of the corresponding compound **4a-n** (5 mmol) in an alcohol (methanol, ethanol, propanol) (5 ml) a solution of the sodium alkoxide, prepared from sodium (0.115 g, 5 mmol) and appropriate alcohol (3 ml), was added dropwise under stirring. The reaction mixture was stirred at room temperature for 2 h.

Isolation Procedure for Compounds **5a,i,j, 7c,e,k, 13**.

After the reaction had completed the precipitate that formed was collected by filtration, washed with small amount of alcohol and recrystallised to give compounds **5a,i,j, 7c,e,k, 13**. Mp's, spectral and analytical data of compounds **5a,i** and **7e** are given in ref. [9].

N^4-Methyl-5-nitroso-N^6-[3-(trifluoromethyl)phenyl]pyrimidine-4,6-diamine (**5j**).

This compound was obtained as green needles, mp 151-152° (from methanol); yield 85% (using sodium methoxide in methanol); 72% (using sodium ethoxide in ethanol); 60% (using sodium propoxide in propanol); ir (KBr): 3344, 3249 (NH) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.12, 3.30 (2d, J = 5,1 Hz, 3H, NHMe), 7.45-7.97 (m, 4H, ArH), 8.12, 11.38 (2q, J = 5.1Hz, 1H, NHMe), 8.31, 8.38 (2s, 1H, C2-H), 9.95, 13.38 (br.s., 1H, NH); ms: m/z 297 (M^+).

Anal. Calcd. for $C_{12}H_{10}F_3N_5O$: C, 48.49; H, 3.39; N, 23.56. Found: C, 48.67; H, 3.21; N, 23.59.

9-Methyl-6-dimethylamino-7,9-dihydro-8*H*-purin-8-one (**7c**).

This compound was obtained as a colorless solid, mp 232-234° (from 2-propanol); yield 80% (using sodium propoxide in propanol); ir (KBr): 3175 (NH), 1710 (CO) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 3.16 (s, 6H, $N(Me)_2$), 3.30 (s, 3H, NMe), 7.98 (s, 1H, C2-H), 10.73 (br.s., 1H, NH); ^{13}C nmr (dimethylsulfoxide-d_6): δ 25.1, 37.9, 103.9, 147.1, 148.4, 149.6, 152.8.

Anal. Calcd. for $C_8H_{11}N_5O$: C, 49.73; H, 5.74; N, 36.25. Found: C, 50.01; H, 5.68; N, 36.19.

Crystal Data of Compound **7c**.

$C_8H_{12}ClN_5O$, M = 229.671, monoclinic, space group $P2_1/c$, a = 17.0490(3), b = 8.8346(7), c = 20.2167(7) Å, β = 94.657(2)°; V = 3035.0(3) Å^3, Z = 12, D_c = 1.508 g·cm^{-3}, μ = 0.359 mm^{-1}, F(000) = 1440. Total number of reflection measured 20174, unique 6643; 3967 observed reflections with $I > 2\sigma(I)$ were used for refinement. Final R_1 = 0.0968, wR_2 = 0.2262.

X-ray diffraction data were collected on a Nonius Kappa CCD diffractometer at the temperature 293 K using graphite-monochromated MoK$_\alpha$ radiation (λ = 0.71073 Å). Structure **7c** was solved by direct methods with SIR97 program [20] and refined by full-matrix least squares techniques with anisotropic non-hydrogen atoms. Hydrogen atoms were refined in the riding model. The refinement calculations were carried out with the help of SHELX97 program [21]. ORTEP [22] view of the molecule is shown in Figure 2. Full crystallographic data for structure **7c** have been deposited at the Cambridge Crystallographic Data Center (CCDC number 283166).

Methyl *N*-Methyl-*N*-(9-methyl-8-oxo-8,9-dihydro-7*H*-purin-6-yl)-glycinate (**7k**).

This compound was obtained as a colorless solid, mp 191-192° (from 2-propanol); yield 64% (using sodium methoxide in methanol); ir (KBr): 3161 (NH), 1730 (CO) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.43 (s, 6H, 2NMe), 3.76 (s, 3H, OMe), 4.41 (s, 2H, NCH$_2$), 8.22 (s, 1H, C2-H), 10.49 (br.s., 1H, NH); ms: m/z 251 (M$^+$).

Anal. Calcd. for $C_{10}H_{13}N_5O_3$: C, 47.81; H, 5.22; N, 27.87. Found: C, 48.00; H, 5.28; N, 27.78.

Methyl 7-Methylaminothiazolo[5,4-*d*]pyrimidine-2-carboxylate (**13**).

This compound was obtained as a colorless needles, mp 231-232° (from dimethylformamide); yield 78% (using sodium methoxide in methanol); 40% (using sodium ethoxide in ethanol); 35% (using sodium propoxide in propanol); ir (KBr): 3410 (NH), 1723 (CO) cm^{-1}; ^{1}H nmr (dimethylsulfoxide-d_6): δ 2.97 (d, J = 4.5 Hz, 3H, NHMe), 3.96 (s, 3H, OMe), 8.46 (s, 1H, C2-H), 8.67 (q, J = 4.5 Hz, 1H, NH); ^{13}C nmr (deuterio-chloroform): δ 27.7, 54.0, 132.3, 153.5, 157.1, 160.5, 163.5, 174.7; ms: m/z 224 (M$^+$).

Anal. Calcd. for $C_8H_8N_4O_2S$: C, 42.85; H, 3.60; N, 24.99; S 14.3. Found: C, 42.88; H, 3.65; N, 25.02; S 14.00

Isolation Procedure for Compounds **5b,f-h, 6b,f-h**.

After the reaction had completed the precipitate formed was collected by filtratoin, dissolved in water and acidified with concentrated hydrochloric acid to give compounds **6b,f-h**. The alcoholic mother liquor was concentrated under reduced pressure to dryness, the solid obtained was recrystallised to give compounds **5b,f-h**. Mp, spectral and analytical data of compound **5b** are given in ref. [9].

N^4-Methyl-*N*^{6}-propyl-5-nitrosopyrimidine-4,6-diamine (**5f**).

This compound was obtained as a green solid, mp 54-55° (from hexane); yield 8% (using sodium methoxide in methanol); ir (KBr): 3349 (NH) cm^{-1}; ^{1}H nmr (acetone-d_6): δ 0.97, 1.03 (2t, J = 8Hz, 3H, Me), 1.67, 1.79 (2m, J = 8 Hz, 2H, CH$_2$), 3.05, 3.23 (2d, J = 5 Hz, 3H, NHMe), 3.54, 3.72 (2q, J = 8 Hz, 2H, NHCH$_2$), 8.14 (s, 1H, C2-H), 8.89 (br.s., 1H, NH), 11.39, 11.59 (2 br.s., 1H, NH).

Anal. Calcd. for $C_8H_{13}N_5O$: C, 49.22; H, 6.71; N, 35.87. Found: C, 49.17; H, 6.55; N, 36.00.

N^4-Benzyl-*N*^{6}-methyl-5-nitrosopyrimidine-4,6-diamine (**5g**).

This compound was obtained as a green solid, mp 130-132° (from octane); yield 30% (using sodium methoxide in methanol); 24% (using sodium ethoxide in ethanol); 20% (using sodium propoxide in propanol); ir (KBr): 3287, 3333 (NH) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.07, 3.25 (2d, J = 5.4 Hz, 3H, NHMe), 4.76, 4.90 (2d, J = 6 Hz, 2H, NHCH$_2$), 7.31-7.40 (m, 5H, ArH), 8.04, 8.26 (2br.s., 1H, NH), 8.25 (s, 1H, C2-H), 11.46, 11.75 (2 br.s., 1H, NH); ^{13}C nmr (deuteriochloroform): δ 26.0, 27.6, 43.2, 44.6, 127.3, 127.4, 128.4, 139.2, 136.1, 136.6, 145.7, 146.8, 162.8, 163.4, 164.8, 164.9.

Anal. Calcd. for $C_{12}H_{13}N_5O$: C, 59.25; H, 5.39; N, 28.79. Found: C, 59.45; H, 5.41; N, 28.56.

N^4-Methyl-*N*^{6}-(2-phenylethyl)-5-nitrosopyrimidine-4,6-diamine (**5h**).

This compound was obtained as a green solid, mp 129-130° (from hexane); yield 32% (using sodium methoxide in methanol); ir (KBr): 3278, 3271 (NH) cm^{-1}; ^{1}H nmr (dichloromethane-d_2): δ 2.95, 2.96 (2t, J = 6 Hz, PhCH_2), 3.06, 3.24 (2d, J = 5.4 Hz, 3H, NHMe), 3.83, 3.99 (2d, J = 6 Hz, 2H, NHCH_2), 7.27-7.40 (m, 5H, ArH), 8.15, 8.20 (2br.s., 1H, NH), 8.20, 8.21 (2s, 1H, C2-H), 11.45, 11.53 (2 br.s., 1H, NH); ^{13}C nmr (dichloromethane-d_2): δ 26.5, 28.0, 35.5, 35.8, 41.4, 42.5, 126.8, 126.9, 128.8, 128.9, 129.01, 138.8, 138.9, 140.0, 146.6, 147.5, 163.6, 164.1, 165.2, 165.93.

Anal. Calcd. for $C_{13}H_{15}N_5O$: C, 60.69; H, 5.88; N, 27.22. Found: C, 60.53; H, 5.83; N, 27.53.

5-Hydroxy-8-methyl-4-methylamino-5,8-dihydropteridine-6,7-dione (**6b**).

This compound was obtained as a colorless solid, mp 218-219° (dec) (from 2-propanol); yield 52% (using sodium methoxide in methanol); ir (KBr): 3484 (OH), 3247 (NH), 1689 (CO) cm^{-1}; ^{1}H nmr (dimethylsulfoxide-d_6): δ 2.96 (s, 3H, NHMe), 3.50 (s, 3H, NMe), 7.82 (br.s., 1H, NH), 8.24 (s, 1H, C2-H); ^{13}C nmr (dimethylsulfoxide-d_6): δ 28.4, 28.8, 106.0, 140.5, 150.2, 150.9, 151.7, 156.0.

Anal. Calcd. for $C_8H_9N_5O_3$: C, 43.05; H, 4.06; N, 31.38. Found: C, 43.21; H, 4.02; N, 31.49.

5-Hydroxy-8-methyl-4-propylamino-5,8-dihydropteridine-6,7-dione (**6f**).

This compound was obtained as a colorless solid, mp 110-112° (dec) (from 2-propanol); yield 48% (using sodium methoxide in methanol); ir (KBr): 3386 (OH), 3155 (NH), 1683 (CO) cm^{-1}; ^{1}H nmr (dimethylsulfoxide-d_6): δ 0.94 (t, J = 7 Hz, 3H, Me), 1.60 (m, J = 7 Hz, 2H, CH$_2$), 3.43 (q, J = 7 Hz, 2H, NHCH_2), 3.49 (s, 3H, NMe), 7.82 (t, J = 7 Hz, 1H, NH), 8.21 (s, 1H, C2-H); ^{13}C nmr (dimethylsulfoxide-d_6): δ 11.3, 21.9, 28.7, 42.4, 105.6, 140.7, 150.2, 150.6, 151.8, 155.9.

Anal. Calcd. for $C_{10}H_{13}N_5O_3$: C, 47.81; H, 5.22; N, 27.87. Found: C, 47.60; H, 5.62; N, 27.56.

4-Benzylamino-5-hydroxy-8-methyl-5,8-dihydropteridine-6,7-dione (**6g**).

This compound was obtained as a colorless solid, mp 181-182° (dec) (2-propanol); yield 48% (using sodium methoxide in

methanol); 45% (using sodium ethoxide in ethanol); 30% (using sodium propoxide in propanol); ir (KBr): 3379 (OH), 3204 (NH), 1687 (CO) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 3.44 (s, 3H, NMe), 4.63 (d, J = 5.7 Hz, 2H, NHCH_2), 7.17 – 7.33 (m, 5H, ArH), 7.95 (t, J = 5.7 Hz, 1H, NH), 8.04 (s, 1H, C2-H); ^{13}C nmr (dimethylsulfoxide-d_6): δ 30.3, 47.4, 106.4, 127.0, 128.8, 129.7, 131.5, 141.9, 144.2, 144.6, 145.5, 156.7.

Anal. Calcd. for $C_{14}H_{13}N_5O_3$: C, 56.18; H, 4.38; N, 23.40. Found: C, 56.55; H, 4.22; N, 23.46.

5-Hydroxy-8-methyl-4-[(2-phenylethyl)amino]-5,8-dihydropteridine-6,7-dione (**6h**).

This compound was obtained as a colorless solid, mp 142-143° (dec) (from 2-propanol); yield 54% (using sodium methoxide in methanol); ir (KBr): 3382 (OH), 3227 (NH), 1691 (CO) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 2.86 (t, J = 7.2 Hz, CH_2), 3.50 (s, 3H, NMe), 3.61 (q, J = 7.2 Hz, 2H, NHCH_2), 7.15 – 7.28 (m, 5H, ArH), 8.00 (t, J = 7.2 Hz, 1H, NH), 8.08 (s, 1H, C2-H); ^{13}C nmr (dimethylsulfoxide-d_6): δ 28.0, 35.1, 41.8, 108.3, 126.0, 128.3, 128.6, 139.5, 141.6, 151.4, 151.5, 153.7, 156.0.

Anal. Calcd. for $C_{15}H_{15}N_5O_3$: C, 57.50; H, 4.83; N, 22.35. Found: C, 57.55; H, 5.00; N, 22.44.

Isolation Procedure for Compounds **7c, 8c, 9c, 10c.**

After the reaction had completed the precipitate formed was collected by filtration, recrystallised to give sodium salt **8c**, which was dissolved in water. The resulting aqueous solution was cooled to 0° and acidified with concentrated hydrochloric acid to pH 3-4 to give compound **7c**. The alcoholic mother liquor was concentrated under reduced pressure to dryness, the solid was purified using dry column vacuum chromatography [14] (Merck silica gel 60 μm, eluent - toluene: ethylacetate 8:1) to give compounds **9c** or **10c**.

Mp, spectral and analytical data of compound **7c** are identical to those of **7c** isolated from the reaction of **4c** with sodium propoxide.

6-Dimethylamino-9-methyl-9*H*-purine-8-carboxylic Acid 7-Oxide, Sodium Salt (**8c**).

This compound was obtained as a colorless solid, mp > 300° (from methanol); yield 25% (using sodium methoxide in methanol), 27 % (using sodium ethoxide in ethanol) ir (KBr): 1692 (CO) cm^{-1}; ^1H nmr (D_2O): δ 3.20 (s, 6H, NMe_2), 3.61 (s, 3H, NMe), 7.87 (s, 1H, C2-H); ^{13}C nmr (D_2O): d 30.5, 41.1, 110.3, 136.4, 144.3, 153.0, 153.3, 159.5.

8-Methoxy-*N*,*N*,9-trimethyl-9*H*-purin-6-amine (**9c**).

This compound was obtained as a yellowish solid, mp 100-100.5° (R_f = 0.51, 50% ethyl acetate in benzene (v/v)); yield 31% (using sodium methoxide in methanol); ^1H nmr (acetone-d_6): δ 3.44 (s, 6H, NMe_2), 3.51 (s, 3H, NMe), 4.15 (s, 3H, OMe), 8.13 (s, 1H, C2-H); ^{13}C nmr (acetone-d_6): δ 28.1, 39.1, 58.0, 117.5, 152.1, 152.6, 154.6, 155.7.

Anal. Calcd. for $C_9H_{13}N_5O$: C, 52.16; H, 6.32; N, 33.79. Found: C, 52.07; H, 6.15; N, 33.95.

8-Ethoxy-*N*,*N*,9-trimethyl-9*H*-purin-6-amine (**10c**).

This compound was obtained as a yellowish solid, mp 99-100° (R_f = 0.70, 50% ethyl acetate in benzene (v/v)); yield 3% (using sodium ethoxide in ethanol); ^1H nmr (dimethylsulfoxide-d_6): δ 1.42 (t, J = 7.2 Hz, 3H, Me), 3.38 (s, 6H, NMe_2), 3.39 (s, 3H, NMe), 4.51 (q, J = 7.2 Hz, 2H, OCH_2), 8.12 (s, 1H, C2-H).

Anal. Calcd. for $C_{10}H_{15}N_5O$: C, 54.28; H, 6.83; N, 31.65. Found: C, 54.09; H, 6.55; N, 31.75.

Isolation Procedure for Compounds **7d, 8d, 14d**.

After the reaction had completed the precipitate formed was collected by filtration, recrystallised to give sodium salt **8d**, which was dissolved in water. The resulting aqueous solution was cooled to 0° and acidified with concentrated hydrochloric acid to pH 3-4 to give compound **14d**. Acidification of aqueous solution at room temperature gave compound **7d**, which was collected by filtration and recrystallised.

9-Methyl-6-pyrrolidino-7,9-dihydro-8*H*-purin-8-one (**7d**).

Method A. This compound was obtained as a colorless solid, mp > 250° (from 2-propanol); yield 33%; ir (KBr): 3159 (NH), 1700 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.71 (t, J = 4.8 Hz, 4H, $(CH_2)_2$), 3.46 (s, 3H, NMe), 3.80 (t, J = 4.8 Hz, 4H, $N(CH_2)_2$), 8.27 (s, 1H, C2-H), 10.70 (br.s., 1H, NH); ^{13}C nmr (dimethylsulfoxide-d_6): δ 24.7, 25.4, 46.9, 103.4, 145.3, 147.9, 150.5, 153.1.

Anal. Calcd. for $C_{10}H_{13}N_5O$: C, 54.78; H, 5.98; N, 31.94. Found: C, 54.61; H, 5.78; N, 31.89.

Method B. A solution of compound **14d** (0.1g, 0.38 mmol) in anhydrous xylene (3 ml) was refluxed for 20 min. After cooling to room temperature the precipitate was collected by filtration and recrystallised to give 0.075 g (90%) of compound **7d**, whose properties are identical to those of the product obtained in method A.

9-Methyl-6-pyrrolidino-9*H*-purine-8-carboxylic Acid 7-Oxide, Sodium Salt (**8d**).

This compound was obtained as a colorless solid, mp > 300° (from methanol); yield 33% (using sodium methoxide in methanol); ir (KBr): 1690 (CO) cm^{-1}; ^1H nmr (dimethylsulfoxide-d_6): δ 1.90 (m, 4H, $(CH_2)_2$), 3.35 (m, 4H, $N(CH_2)_2$), 3.50 (s, 3H, NMe), 8.25 (s, 1H, C2-H).

9-Methyl-6-pyrrolidino-9*H*-purine-8-carboxylic Acid 7-Oxide (**14d**).

This compound was obtained as a colorless solid, mp 100-101° (dec); yield 30% (using sodium methoxide in methanol); ir (KBr): 3394 (OH), 3255 (NH), 1675 (CO) cm^{-1}; due to its unstability it was impossible to obtain reliable nmr spectra and elemental analysis data.

Isolation Procedure for Compounds **7l, 9l, 10l**.

After the reaction had completed the solution was concentrated under reduced pressure. The residue was purified by dry column vacuum chromatography [14] (Merck silica gel 40 μm, elution with 0-100% ethyl acetate in benzene (v/v) with 10% increment in ethyl acetate concentration for each fraction collected) to give compounds **9l** or **10l** and **7l** (order of elution).

Mp, spectral and elemental analysis data of compound **7l** are given in ref. [9].

8-Methoxy-*N*,9-dimethyl-*N*-phenyl-9*H*-purin-6-amine (**9l**).

This compound was obtained as a yellow solid, mp 49-50° (R_f = 0.42, 50% ethyl acetate in benzene (v/v)); yield 31% (using sodium methoxide in methanol); ^1H nmr (acetone-d_6): δ 3.52 (s,

3H, NMe), 3.83 (s, 3H, NMe), 4.00 (s, 3H, OMe), 7.25 – 7.41 (m, 5H, ArH), 8.16 (s, 1H, C2-H); ^{13}C nmr (acetone-d_6): δ 26.6, 39.2, 56.4, 116.9, 125.6, 126.8, 128.7, 146.5, 150.2, 151.9, 152.2, 154.8.

Anal. Calcd. for $C_{14}H_{15}N_5O$: C, 62.44; H, 5.61; N, 26.01. Found: C, 62.27; H, 5.46; N, 25.98.

8-Ethoxy-*N*,9-dimethyl-*N*-phenyl-9*H*-purin-6-amine (**10l**).

This compound was obtained as a yellow solid, mp 40-42° (R_f = 0.48, 50% ethyl acetate in benzene (v/v)); yield 4% (using sodium ethoxide in ethanol); ^{1}H nmr (acetone-d_6): δ 1.24 (t, J = 6 Hz, 3H, Me), 2.85 (s, 3H, NMe), 3.46 (s, 3H, NMe), 4.20 (q, J = 6 Hz, 2H, OCH_2), 7.12 – 7.44 (m, 5H, ArH), 8.13 (s, 1H, C2-H).

Anal. Calcd. for $C_{15}H_{17}N_5O$: C, 63.59; H, 6.05; N, 24.72. Found: C, 63.48; H, 6.42; N, 24.70.

Isolation Procedure for Compounds **6m, 7m, 11m, 12**.

After the reaction had completed the precipitate that formed was collected by filtration, dissolved in water and acidified with concentrated hydrochloric acid to give compound **6m**. The mother liquor was concentrated under reduced pressure to dryness, the residue was purified using dry column vacuum chromatography [14] (Merck silica gel 40 μm, elution with 0-100% ethyl acetate in benzene (v/v) with 2% increment in ethyl acetate concentration for each fraction collected) to give compounds **11m**, **12 and 7m** (order of elution).

5-Hydroxy-8-methyl-4-phenylthio-5,8-dihydropteridine-6,7-dione (**6m**).

This compound was obtained as a colorless solid, mp 220-222° (dec) (from 2-propanol); yield 44% (using sodium methoxide in methanol), 30% (using sodium propoxide in propanol); ir (KBr): 3065 (OH), 1702 (CO) cm^{-1}; ^{1}H nmr (dimethylsulfoxide-d_6): δ 3.51 (s, 3H, NMe), 7.49 (s, 5H, ArH), 8.38 (s, 1H, C2-H); ^{13}C nmr (dimethylsulfoxide-d_6): δ 28.8, 118.7, 129.2, 129.3, 129.4, 135.8, 142.4, 150.4, 150.7, 153.6, 155.7.

Anal. Calcd. for $C_{13}H_{10}N_4O_3S$: C, 51.65; H, 3.33; N, 18.53. Found: C, 51.62; H, 3.30; N, 18.42.

9-Methyl-6-phenylthio-7,9-dihydro-8*H*-purin-8-one (**7m**).

This compound was obtained as a colorless solid, mp > 250° (R_f = 0.38, 50% ethyl acetate in benzene (v/v)); yield < 1%; ir (KBr): 1715 (CO) cm^{-1}; ^{1}H nmr (acetone-d_6): δ 3.39 (s, 3H, NMe), 7.45 – 7.56 (m, 5H, ArH), 8.38 (s, 1H, C2-H), 10.37 (br.s., 1H, NH).

Anal. Calcd. for $C_{12}H_{10}N_4OS$: C, 55.80; H, 3.90; N, 21.69. Found: C, 55.60; H, 3.78; N, 21.79.

9-Methyl-6-phenylthio-9*H*-purine 7-Oxide (**11m**).

This compound was obtained as a yellow needles, mp 200-201° ((R_f = 0.95, 50% ethyl acetate in benzene (v/v)); yield 3% (using sodium methoxide in methanol); ^{1}H nmr (dimethylsulfoxide-d_6): δ 3.56 (s, 3H, NMe), 7.52 – 7.61 (m, 5H, ArH), 8.34 (s, 1H, C2-H), 8.70 (s, 1H, C8-H), ^{13}C nmr (dimethylsulfoxide-d_6): δ 27.2, 121.9, 126.7, 129.4, 129.8, 135.8, 150.8, 156.4, 156.6, 169.2

Anal. Calcd. for $C_{12}H_{10}N_4OS$: C, 55.80; H, 3.90; N, 21.69. Found: C, 55.55; H, 3.81; N, 21.47.

6-Methoxy-*N*-methyl-5-nitrosopyrimidin-4-amine (**12**).

This compound was obtained as a blue solid, mp 151-152° (R_f = 0.87, 50% ethyl acetate in benzene (v/v)); yield 5% (using sodium methoxide in methanol); ir (KBr) 3299 (NH) cm^{-1}; ^{1}H nmr (acetone-d_6): δ 3.10 (d, J = 5 Hz, 3H, NHMe), 4.28 (s, 3H, OMe), 8.44 (s, 1H, C2-H), 11.00 (q, J = 5 Hz, 1H, NH).

Anal. Calcd. for $C_6H_8N_4O_2$: C, 42.86; H, 4.80; N, 33.32. Found: C, 43.01; H, 4.85; N, 33.55.

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