Oxidation of 7,8-Diaminotheophylline with Lead Tetraacetate and Reaction of the Oxidation Product, 6-Cyanoimino-5-diazo-1,3-dimethylpyrimidine-2,4-dione with Alcohols or Amines

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Oxidation of 7,8-diaminotheophylline (**1**) with lead tetraacetate in refluxing toluene gave a mixture of 3-amino-5,7-dimethylpyrimido[4,5-*e*][1,2,4]triazine-6,8-dione (**2**) and 6-cyanoimino-5-diazo-1,3-dimethylpyrimidine-2,4-dione (**4**). The latter was transformed to **2** by the reaction with 1-propanethiol in quantitative yield. The reaction of **4** with methanol, ethanol and 1-propanol in the presence of rhodium (II) acetate gave 5-alkoxy-6-(2-alkyl-3-isoureido)-1,3-dimethylpyrimidine-2,4-diones (**7a-c**). A similar reaction of **4** with alkylamines such as *n*-propylamine, *n*-butylamine, isobutylamine and *n*-hexylamine gave a mixture of 7-alkyl-8-aminotheophyllines (**8a-d**) and (5-alkylamino-1,3-dimethyl-2,4-dioxopyrimidin-6-yl)cyanamides (**9a-d**).

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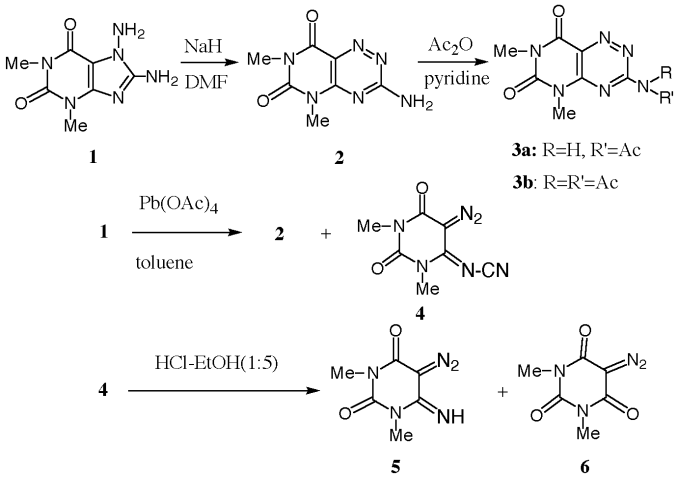
Theophylline is an important drug with diuretic, cardiac stimulant and smooth muscle relaxant activities [1]. In the course of medicinal and chemical studies of theophylline derivatives we previously synthesized 7,8-diaminotheophylline (**1**) [2] and examined its reactivity [3]. During the examination of the alkylation of **1** with alkyl halide in the presence of sodium hydride, the nitrene reaction product 3-amino-5,7-dimethylpyrimido[4,5-*e*][1,2,4]triazine-6,8-dione (**2**) was found to be formed. This paper reports on the oxidation of **1** and the reaction of the oxidation product, 6-cyanoimino-5-diazo-1,3-dimethylpyrimidine-2,4-dione (**4**) with alcohols or amines.

Our finding that tricyclic fused purines [4] were formed by the reaction of 8-aminotheophylline [5] with α,ω-dibromoalkanes induced us to examine facile synthesis of fused tricycles from **1**. However, to our surprise the reaction of **1** with alkyl halides such as 1,2-dibromoethane, ethyl bromoacetate, and ethyl bromopropionate in the presence of sodium hydride in *N*,*N*-dimethylformamide did not give the expected products, but rather provided **2** [6] in 17% yield. The structural confirmation of **2** was carried out by proton nuclear magnetic resonance and mass spectra. Moreover, acetylation of **2** with acetic anhydride in pyridine gave 3-acetylamino-5,7-dimethylpyrimido[4,5-*e*][1,2,4]-triazine-6,8-dione (**3a**) and 3-diacetylamino-5,7-dimethylpyrimido[4,5-*e*][1,2,4]triazine-6,8-dione (**3b**).

Scheme 1



1 → 2 (NaH, DMF); 2 → 3a, 3b (Ac2O, pyridine)

1 + Pb(OAc)4 → 2 + 4 (toluene)

4 + HCl-EtOH(1:5) → 5 + 6

Because **2** seemed to be formed *via* nitrene [7] which was generated during the reaction of **1** with sodium hydride and/or air in *N*,*N*-dimethylformamide, we examined the nitrene reaction of **1** with lead tetraacetate [8] as the oxidizing agent (Table 1). The yield of **2** is increased as the reaction temperature is increased, and the best yield was obtained by refluxing toluene with 1.5 molar equivalent of lead tetraacetate to give **2** (65%) along with **4** in 27% yield. By contrast, the reaction at room temperature gave better yield of **4**. When two molar equivalents of lead tetraacetate were used in benzene at room temperature, the yield of **4** was remarkably increased to 92% and that of **2** was decreased to 4%. In this way either **2** or **4**

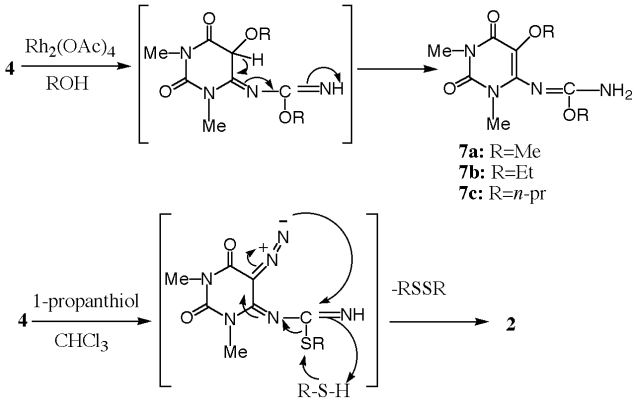
Table 1
Yields of **2** and **4** by the Oxidation of **1** with Lead Tetraacetate.[a]

Solvent	$Pb(OAc)_4$(eq)[b]	Temperature	**2**(%)	**4**(%)	**1**(%)
benzene	1	rt	6	46	48
benzene	1	40°C	12	41	46
benzene	1	reflux	36	30	24
benzene	1.5	rt	10	69	20
benzene	1.5	40°C	24	64	11
benzene	1.5	reflux	48	45	0
toluene	1.5	reflux	65	27	0
benzene	2.0	rt	4	92	0
benzene	2.0	40°C	12	85	0

[a] All reactions were carried out with **1** (0.5 mmol) in 20 ml of benzene or toluene for 20 hours.
[b] Molar equivalent to compound **1**.

can be synthesized at our option. The infrared spectra of **4** indicated the presence of a cyano group. For the confirmation of the unique structure of **4**, hydrolysis with concentrated hydrochloric acid in ethanol (1:5) was carried out by refluxing for 6 hours to give 6-imino-5-diazo-1,3-dimethylpyrimidine-2,4-dione (**5**) in 60% yield and 5-diazo-1,3-dimethylbarbituric acid (**6**) [9] in 33% yield. The reaction of **4** with refluxing concentrated hydrochloric acid gave **5** as the sole product in 95% yield. These experiments proved the presence of the cyanoimino group in **4**.

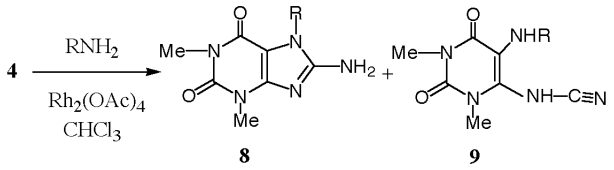
Scheme 2



Similar ring expansion of *N*-aminoimidazoles to triazines by the nitrene reaction has been reported [10]. However, the formation of the cyanoiminouracil type compounds like that of **4** is unknown. To further examine the unique structure of **4** the rhodium carbenoid OH insertion reaction [11] was employed. The reaction of the diazo compound **4** in alcohol in the presence of rhodium (II) acetate gave 5-alkoxy-6-(2-alkyl-3-isoureido)-1,3-dimethylpyrimidine-2,4-diones (**7a-c**). Among the reactions of **4** with methanol, ethanol and propanol, the reaction with propanol gave the better yield (55%) of the insertion product **7c**. However, the carbenoid reaction with butanol or 2-bromoethanol did not proceed at all. Since the carbenoid reaction with propanol gave the better yield of **7c**, the reaction of **4** with 1-propanethiol was tried. But, to our surprise this reaction gave **2** in 97% yield, and no carbenoid reaction was observed. Thus the formation of **2** from **4** appears to arise from the addition of propanethiol to a cyanoimino group.

We next examined the carbenoid reaction with alkylamines. The reaction of **4** with alkylamines, such as *n*-propylamine, *n*-butylamine, isobutylamine, and *n*-hexylamine in the presence of rhodium (II) acetate gave 7-alkyl-8-aminotheophyllines (**8a-d**) and (5-alkyl-1,3-dimethyl-2,4-dioxopyrimidin-6-yl)cyanamides (**9a-d**). These reactions even proceeded in the absence of rhodium (II) acetate, though the yields of **8a-d** and **9a-d** were poor. 7-Propyl-8-aminotheophylline (**8a**) and 7-butyl-8-aminotheophylline (**8b**) were identical with those obtained previously by us [12] during the reaction of 8-aminotheophylline with propyl bromide or butyl bromide.

Scheme 3



8a: R=*n*-propyl
8b: R=*n*-butyl
8c: R=isobutyl
8d: R=*n*-hexyl

9a: R=*n*-propyl
9b: R=*n*-butyl
9c: R=isobutyl
9d: R=*n*-hexyl

Consequently we could synthesize **2** or **4** by the nitrene reaction of 7,8-diaminotheophylline at our option. Since **4** is easily transformed to **2** in excellent yield, our method makes a facile synthesis of **2** from **1**. The carbenoid reaction of **4** with alcohols or amines gave new pyrimidinones (**7a-c**, **9a-d**).

EXPERIMENTAL

All melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. The infrared spectra were measured with a JASCO IR-810 spectraphotometer. Mass spectra were measured with a JEOL JMS-DX 300 mass spectrometer. Proton nuclear magnetic resonance spectra were recorded with a JEOL JNM-LA-400 and JNM-EX-270 spectrometer using tetramethylsilane as internal standard. Abbreviations are as follows: s, singlet; d, doublet; q, quartet; br, broad; m, multiplet.

3-Amino-5,7-dimethylpyrimido[4,5-*e*][1,2,4]triazine-6,8-dione (**2**).

To a solution of 7,8-diaminotheophylline (**1**) (2.1 g, 10 mmol) in *N*,*N*-dimethyl formamide (130 ml) was added sodium hydride (60% dispersion in mineral oil 840 mg) at 100° and the reaction mixture was stirred for 8 hours. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure, diluted with water (10 ml) and neutralized with 5% aqueous hydrochloric acid. The mixture was extracted with ethyl acetate (5x30 ml). The organic layer was washed with water (30 ml), dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was chromatographed on silica gel with a mixture of chloroform:methanol (10:1) as eluent to give compound **2** (0.36 g, 17%), fine crystals, mp>300° (from methanol); ^{1}H nmr (deuteriochloroform): δ 3.27 (3H, s, Me), 3.38 (3H, s, Me), 8.30 (2H, br, NH_2); ir (potassium bromide): ν max 3350 and 3330 cm^{-1} (NH_2), 1690 cm^{-1} (C=O); ms: m/z 208 (M^+).

Anal. Calcd. for $C_7H_8N_6O_2$: C, 40.37; H, 3.88; N, 40.38. Found: C, 40.29; H, 4.08; N, 40.15.

3-Acetylamino-5,7-dimethylpyrimido[4,5-*e*][1,2,4]triazine-6,8-dione (**3a**) and 3-Diacetylamino-5,7-dimethylpyrimido[4,5-*e*]-[1,2,4]triazine-6,8-dione (**3b**).

To a solution of compound **2** (208 mg, 1 mmol) in pyridine (3 ml) was added acetic anhydride (3 ml) at 100° and stirred for

12 hours. The reaction mixture was concentrated under reduced pressure and the residue was chromatographed on silica gel with a mixture of chloroform:methanol (15:1) to give compound **3a** (138 mg 55%) and **3b** (26 mg, 9%).

Compound **3a**: mp 244-246° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 2.28 (3H, s, C-Me), 3.31 (3H, s, N-Me), 3.45 (3H, s, N-Me), 8.31 (1H, br, NH); ir (potassium bromide): ν max 3210 cm^{-1} (NH), 1740 and 1680 cm^{-1} (C=O); ms: m/z 250 (M^+).

Anal. Calcd. for $C_9H_{10}N_6O_3$: C, 43.20; H, 4.03; N, 33.59. Found: C, 43.16; H, 4.03; N, 33.60.

Compound **3b**: mp 158-160°C (from ethanol); ^{1}H nmr (deuteriochloroform): δ 2.39 (6H, s, C-Me x 2), 3.59 (3H, s, N-Me), 3.66 (3H, s, N-Me); ir (potassium bromide): ν max 1740 and 1680 cm^{-1} (C=O); ms: m/z 292 (M^+).

Reaction of 7,8-Diaminotheophylline with Lead Tetraacetate (Synthesis of **2** and **4**).

Method a: To a solution of 7,8-diaminotheophylline (105 mg, 0.5 mmol) in refluxing toluene (20 ml) was added lead tetraacetate (332 mg 0.75 mmol) and the solution was stirred for 20 hours. The reaction mixture was concentrated under reduced pressure. The residue was chromatographed on silica gel with a mixture of chloroform:methanol (50:1) as eluent to give compound **2** (64 mg, 65%) and compound **4** (26 mg, 27%).

Compound **4**: mp 197-199°C (from ethanol); ^{1}H nmr (deuteriochloroform): δ 3.35 (3H, s, N-Me), 3.43 (3H, s, N-Me); ir (potassium bromide): ν max 2190 cm^{-1} (CN), 2145 cm^{-1} (C=N=N), 1720 and 1670 cm^{-1} (C=O); ms:m/z 206 (M^+).

Anal. Calcd. for $C_7H_6N_6O_2$: C, 40.78; H, 2.93; N, 40.77. Found: C, 40.75; H, 3.05; N, 40.78.

Method b : To a solution of 7,8-diaminotheophylline (105 mg, 0.5 mmol) in refluxing benzene (20 ml) was added lead tetraacetate (443 mg, 1 mmol) and the solution was stirred for 20 hours. The reaction mixture was concentrated under reduced pressure. The residue was chromatographed on silica gel with a mixture of chloroform:methanol (50:1) as eluent to give compound **2** (4 mg, 4%) and compound **4** (95 mg, 92 %).

Hydrolysis of Compound **4**: Synthesis of 6-Imino-5-diazo-1,3-dimethylpyrimidine-2,4-dione (**5**) and 5-Diazo-1,3-dimethylpyrimidine-2,4,6-trione (**6**).

Method a: To a solution of compound **4** (206 mg, 1 mmol) in ethanol (30 ml) was added concentrated hydrochloric acid (6 ml) and the mixture was refluxed for 6 hours. The reaction mixture was concentrated under reduced pressure and the residue was chromatographed on silica gel with a mixture of chloroform:methanol (15:1) as eluent to give **5** (109 mg, 65%) and **6** (64 mg, 35%).

Compound **5**; colorless crystalline powder, mp 259-261 °C (from methanol); ^{1}H nmr (deuteriochloroform): δ 3.21 (3H, s, N-Me), 3.44 (3H, s, N-Me), 8.26 (1H, br, NH); ir (potassium bromide): ν max 3450 cm^{-1} (NH), 1720 cm^{-1}(C=O); ms: m/z 181 (M^+).

Anal. Calcd. for $C_6H_7N_5O_2$: C, 39.78; H, 3.89; N, 38.66. Found: C, 40.16; H, 4.22; N, 38.30.

Compound **6**; colorless prisms, mp 162-163 °C (from methanol); ^{1}H nmr (deuteriochloroform): δ 3.35 (s, 6H, N-Me x 2); ir (potassium bromide): ν max 2150 cm^{-1} (C=N=N), 1710 and 1660 cm^{-1} (C=O); ms: m/z 182 (M^+).

Method b: A solution of compound **4** (618 mg, 3 mmol) in concentrated hydrochloric acid (36 ml) was refluxed for 3 hours. The reaction mixture was evaporated to dryness and the residue was chromatographed on silica gel with a mixture of chloroform:methanol (15:1) as eluent to give compound **5** (514 mg, 95%).

General Procedure for the Reaction of Compound **4** with Alcohols: Synthesis of 5-Alkoxy-6-(2-alkyl-3-isoureido)-1,3-dimethylpyrimidine-2,4-diones (**7a-c**).

To a solution of compound **4** (0.49 mmol) in alcohol (30 ml) was added rhodium(II) acetate (4.4 mg, 0.0098 mmol) at room temperature and stirred at 65° for 15 hours. The reaction mixture was concentrated under reduced pressure and the residue was chromatographed on silica gel with a mixture of chloroform:-methanol (20:1) as eluent.

5-Methoxy-6-(2-methyl-3-isoureido)-1,3-dimethylpyrimidine-2,4-dione (**7a**).

Compound **7a** was obtained in 19% yield as colorless prisms, mp 209-211° (from methanol); ^{1}H nmr (deuteriochloroform): δ 3.37 (3H, s, N-Me), 3.38 (3H, s, N-Me), 3.66 (3H, s, O-Me), 3.87 (3H, s, O-Me), 4.87 (2H, br, NH_2); ir (potassium bromide): ν max 3380 and 3320 cm^{-1} (NH_2), 1695 cm^{-1} (C=O); ms: m/z 242 (M^+).

Anal. Calcd. for $C_9H_{14}N_4O_4$: C, 44.63; H, 5.83; N, 23.13. Found: C, 44.34; H, 5.64; N, 23.18.

5-Ethoxy-6-(2-ethyl-3-isoureido)-1,3-dimethylpyrimidine-2,4-dione (**7b**).

Compound **7b** was obtained in 37% yield as colorless prisms, mp 140-141° (from chloroform); ^{1}H nmr (deuteriochloroform): δ 1.24 (3H, t, J = 7.1 Hz, CH_2CH_3), 1.35 (3H, t, J = 7.1 Hz, CH_2CH_3), 3.35 (3H, s, N-Me), 3.37 (3H, s, N-Me), 3.88 (2H, q, J = 7.1 Hz, CH_2CH_3), 4.30 (2H, q, J = 7.1 Hz, CH_2CH_3), 4.99 (2H, br, NH_2); ir (potassium bromide): ν max 3395 and 3315 cm^{-1} (NH_2), 1690 cm^{-1} (C=O); ms: m/z 270 (M^+).

Anal. Calcd. for $C_{11}H_{18}N_4O_4$: C, 48.88; H, 6.71; N, 20.73. Found: C, 48.73; H, 6.69; N, 20.78.

5-Propoxy-6-(2-propyl-3-isoureido)-1,3-dimethylpyrimidine-2,4-dione (**7c**).

Compound **7c** was obtained in 55% yield as colorless prisms, mp 110-111°(from chloroform); ^{1}H nmr (deuteriochloroform): δ 0.92 (3H, t, J = 7.3 Hz, $CH_2CH_2CH_3$), 1.00 (3H, t, J = 7.3 Hz, $CH_2CH_2CH_3$), 1.59-1.68 (2H, m, $CH_2CH_2CH_3$), 1.69 (2H, m, $CH_2CH_2CH_3$), 3.33 (3H, s, N-Me), 3.36 (3H, s, N-Me), 3.75 (2H, t, J = 6.6 Hz, $CH_2CH_2CH_3$), 4.19 (2H, t, J = 6.6 Hz, $CH_2CH_2CH_3$), 5.10 (2H, br, NH_2); ir (potassium bromide): ν max 3400 and 3350 cm^{-1} (NH_2), 1700 cm^{-1} (C=O); ms: m/z 298 (M^+).

Anal. Calcd. for $C_{13}H_{22}N_4O_4$: C, 52.34; H, 7.43; N, 18.78. Found: C, 52.58; H, 7.40; N, 18.78.

Reaction of Compound **4** with 1-Propanethiol.

To a solution of compound **4** (51.5 mg, 0.25 mmol) in chloroform (5 ml) was added 1-propanethiol (380 mg, 5 mmol) at room temperature and the mixture was refluxed for 2 hours. The reaction mixture was evaporated under reduced pressure, and the residue was chromatographed on silica gel with chloroform:methanol (15:1) as eluent to give compound **2** (46 mg, 92%).

General Procedure for the Reaction of **4** with Alkylamines: Synthesis of 7-Alkyl-8-aminotheophyllines (**8a-d**) and (5-Alkylamino-1,3-dimethyl-2,4-dioxopyrimidin-6-yl)carbodiimides (**9a-d**).

To a solution of alkylamine (49 mmol) in chloroform (135 ml), rhodium (II) acetate (22 mg, 0.49 mmol) was added. A solution of **4** in chloroform (15 ml) was added dropwise over 10 minutes to the above mixture. The reaction mixture was concentrated under reduced pressure and the residue was chromatographed on silica gel with chloroform:methanol (20:1) as eluent.

7-Propyl-8-aminotheophylline (**8a**).

This compound was obtained in 57% yield as colorless prisms, mp 233-234° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 0.98 (3H, t, J = 7.3 Hz, -$CH_2CH_2CH_3$), 1.77-1.90 (2H, m, -$CH_2CH_2CH_3$), 3.50 (3H, s, N-Me), 3.38 (3H, s, N-Me), 4.04 (2H, t, J = 7.3 Hz, -$CH_2CH_2CH_3$), 4.59 (2H, br, NH_2); ir (potassium bromide): ν max 3390 and 3340 cm^{-1} (NH_2), 1700 cm^{-1} (C=O); ms: m/z 237 (M^+). This compound was identical with that obtained by the reaction of 8-aminotheophylline with propyl bromide [12].

7-Butyl-8-aminotheophylline (**8b**).

This compound was obtained in 53% yield as colorless prisms, mp 202-203° (from chloroform); ^{1}H nmr (deuteriochloroform): δ 0.95 (3H, t, J = 7.3 Hz, -$CH_2CH_2CH_2CH_3$), 1.34-1.45 (2H, m, -$CH_2CH_2CH_2CH_3$), 1.68-1.79 (2H, m, -$CH_2CH_2CH_2CH_3$), 3.36 (3H, s, N-Me), 3.48 (3H, s, N-Me), 4.08 (2H, t, J = 7.3 Hz, -$CH_2CH_2CH_2CH_3$), 5.63 (2H, br, NH_2); ir (potassium bromide): ν max 3350 and 3420 cm^{-1} (NH_2), 1690 cm^{-1} (C=O); ms: m/z 251 (M^+). This compound was identical with that obtained by the reaction of 8-aminotheophylline with butyl bromide [12].

7-(2-Methylpropyl)-8-aminotheophylline (**8c**).

This compound was obtained in 38% yield as colorless prisms, mp 172-174° (from ethanol), ^{1}H nmr (deuteriochloroform): δ 0.98 (6H, d, J = 6.6 Hz, $(Me)_2CHCH_2$-), 2.17-2.27 (1H, m, $(Me)_2CHCH_2$-), 3.38 (3H, s, N-Me), 3.50 (3H, s, N-Me), 3.85 (2H, d, J = 7.6 Hz, $(Me)_2CHCH_2$-), 4.66 (2H, br, NH_2); ir (potassium bromide): ν max 3460 and 3420 cm^{-1} (NH_2), 1700 cm^{-1} (C=O); ms: m/z 251 (M^+).

Anal. Calcd. for $C_{11}H_{17}N_5O_2$: C, 52.58; H, 6.82; N, 27.87. Found: C, 52.36; H, 6.75; N, 27.64.

7-Hexyl-8-aminotheophylline (**8d**).

This compound was obtained in 43% yield as colorless prisms, mp 176-177° (from methanol); ^{1}H nmr (deuteriochloroform): δ 0.87 (3H, t, J = 7.1 Hz, $CH_2(CH_2)_4CH_3$), 1.26-1.34 (6H, m, $CH_2CH_2(CH_2)_3CH_3$), 1.74-1.82 (2H, m, $CH_2CH_2(CH_2)_3CH_3$), 3.38 (3H, s, N-Me), 3.49 (3H, s, N-Me), 4.07 (2H, t, J = 7.3 Hz, $CH_2(CH_2)_4CH_3$), 4.97 (2H, br, NH_2); ir (potassium bromide): ν max 3400 and 3350 cm^{-1} (NH_2), 1700 cm^{-1} (C=O); ms: m/z 279 (M^+).

Anal. Calcd. for $C_{13}H_{21}N_5O_2$: C, 55.88; H, 7.58; N, 25.08. Found: C, 55.81; H, 7.58; N, 25.34.

(1,3-Dimethyl-2,4-dioxo-5-propylaminopyrimidin-6-yl)-cyanamide (**9a**).

This compound was obtained in 24% yield as colorless prisms, mp 299-301°(from chloroform): ^{1}H nmr (deuteriochloroform): δ 0.98 (3H, t, J = 7.3Hz, -$CH_2CH_2CH_3$), 1.59-1.68 (2H, m, -$CH_2CH_2CH_3$), 3.32 (3H, t, J = 7.1 Hz, -$CH_2CH_2CH_3$), 3.37 (3H, s, N-Me), 3.52 (3H, s, N-Me), 5.71 (1H, br, NH), 10.88 (1H, br, NH); ir (potassium bromide) ν max 3325 cm^{-1} (NH), 3150 cm^{-1} (NH), 1700 cm^{-1} (C=O); ms: m/z 237 (M^+).

Anal. Calcd. for $C_{10}H_{15}N_5O_2$: C, 50.61; H, 6.38; N, 29.53. Found: C, 50.57; H, 6.32; N, 29.31.

(5-Butylamino-1,3-dimethyl-2,4-dioxopyrimidin-6-yl)-cyanamide (**9b**).

This compound was obtained in 25% yield as colorless prisms, mp 227-229° (from chloroform): δ 0.95 (3H, t, J = 7.1 Hz, -$CH_2CH_2CH_2CH_3$), 1.34-1.45 (2H, m, -$CH_2CH_2CH_2CH_3$), 1.51-1.62 (2H, m, -$CH_2CH_2CH_2CH_3$), 3.36 (2H, t, J = 7.3 Hz, -$CH_2CH_2CH_2CH_3$), 3.37 (3H, s, N-Me), 3.51 (3H, s, N-Me), 5.56 (1H, br, NH), 7.59 (1H, br, NH); ir (potassium bromide): ν max 3500 cm^{-1} (NH), 3300 cm^{-1} (NH), 1695 cm^{-1} (C=O); ms: m/z 251 (M^+).

Anal. Calcd. for $C_{11}H_{17}N_5O_2$: C, 52.58; H, 6.82; N, 27.87. Found: C, 52.33; H, 6.91; N, 27.84.

(1,3-Dimethyl-5-(2-methylpropylamino)-2,4-dioxopyrimidin-6-yl)cyanamide (**9c**).

This compound was obtained in 26% yield as colorless prisms, mp 254-256° (from ethanol): δ 1.00 (6H, d, J = 6.9 Hz, -$CH_2CH(CH_3)_2$), 1.84-1.96 (1H, m, -$CH_2CH(CH_3)_2$), 3.27 (2H, d, J = 6.6 Hz, -$CH_2CH(CH_3)_2$), 3.42 (3H, s, N-Me), 3.55 (3H, s, N-Me), 5.12 (1H, br, NH), 11.36 (1H, br, NH); ir (potassium bromide): ν max 3280 cm^{-1} (NH), 3170 cm^{-1} (NH), 1695 cm^{-1} (C=O); ms: m/z 251 (M^+).

Anal. Calcd. for $C_{11}H_{17}N_5O_2$: C, 52.58; H, 6.82; N, 27.87. Found: C, 52.29; H, 6.59; N, 27.61.

(5-Hexylamino-1,3-dimethyl-2,4-dioxopyrimidin-6-yl)-cyanamide (**9d**).

This compound was obtained in 33% yield as colorless prisms, mp 223-225° (from ethanol): δ 0.89 (3H, t, J = 7.1 Hz, -$CH_2(CH_2)_4CH_3$), 1.25-1.49 (6H, m, -$CH_2CH_2(CH_2)_3CH_3$), 1.60-1.72 (2H, m, -$CH_2CH_2(CH_2)_3CH_3$), 3.41 (3H, s, N-Me), 3.46 (2H, t, J = 7.1 Hz, -$CH_2(CH_2)_4CH_3$), 3.55 (3H, s, N-Me), 4.99 (1H, br, NH), 11.56 (1H, br, NH); ir (potassium bromide): ν max 3270 cm^{-1} (NH), 3130 cm^{-1} (NH), 1695 cm^{-1} (C=O); ms: m/z 279 (M^+).

Anal. Calcd. for $C_{13}H_{21}N_5O_2$: C, 55.88; H, 7.58; N, 25.08. Found: C, 55.65; H, 7.42; N, 25.00.

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