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Study on Oxazolopyrimidines. V. Preparation of 9-Substituted Hypoxanthines *via* 7-Aminooxazolo[5,4-*d*]pyrimidines

Yozo Ohtsuka

Sagami Chemical Research Center, Onuma, Sagamihara, Kanagawa

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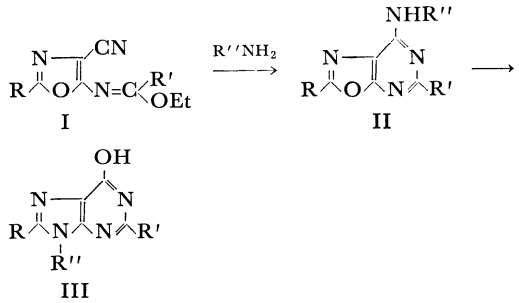
Reaction of 4-cyano-5-ethoxymethylenaminooxazoles with aliphatic amines gave 7-alkylaminooxazolo[5,4-*d*]pyrimidines. The structure of these compounds was discussed on the basis of spectroscopic properties. These oxazolopyrimidines were converted to 9-alkylhypoxanthines by treatment with aqueous alkali (Method A) or by heating in formamide (Method B). Reaction of the ethoxymethylenamino compounds with aromatic amines gave 9-arylhypoxanthines directly (Method C).

Conversion reaction of 7-aminooxazolo[5,4-*d*]pyrimidines into hypoxanthine derivatives has been reported in a previous paper.[1] The present work is concerned with the extension of this reaction to the preparation of 9-substituted hypoxanthines.

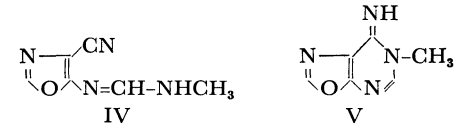
The procedure for the synthesis of fused pyrimidines by reaction of amines and heteroaromatic compounds which have a cyano and an ethoxymethylenamino group at adjacent positions has been applied to several systems.[2-5] The application of this method is convenient for preparing variously substituted fused pyrimidines which may be useful to biochemical studies.

Treatment of 4-cyano-5-ethoxymethylenaminooxazoles (I) with ammonia has been shown to afford 7-aminooxazolopyrimidines.[6] Analogous treatment of I with aliphatic amines gave the corresponding products II, most of which were led to 9-alkylhypoxanthines (III) under suitable conditions. The reaction of I with aromatic amines, however, required rather severe conditions, under which the conversion reaction of 7-arylamino intermediates (II) into 9-arylhypoxanthines (III) took place.



I II III

Synthesis and Structure of 7-Aminooxazolo[5,4-*d*]pyrimidines (II). Treatment of Ia (R=R'=H) with a cold aqueous solution of methylamine gave colorless crystals immediately. Its structure was supposed to be an amidine intermediate (IV) on the ground of its spectra (the presence of nitrile band in IR spectrum and the absence of ethoxyl group in NMR spectrum), considering the analogous reaction path with pyrazole derivatives.[2] The compound IV was easily converted into a second product, 7-methylaminooxazolpyrimidine (IIa), on standing in a basic medium. The structure of the latter compound was distinguished from that of 6-methyl-7(6*H*)iminooxazolopyrimidine (V) by the following reasons; *i*) From the study on 7-aminooxazolopyrimidines, a relatively low electron density on the pyrimidine moiety has been suggested,[6,7] and the rate of the Dimroth rearrangement has been known to be greatly enhanced with the pyrimidine derivatives having electron-withdraw-



IV V

1) Y. Ohtsuka, This Bulletin, **43**, 954 (1970).

2) E. C. Taylor and K. S. Hartke, *J. Amer. Chem. Soc.*, **81**, 2456 (1959); E. C. Taylor and P. K. Loeffler, *ibid.*, **82**, 3147 (1960).

3) R. N. Prasad and R. K. Robins, *ibid.*, **79**, 6401 (1957).

4) K. Suzuki, T. Meguro, I. Kumashiro and T. Takenishi, Abstract of Papers, 21st Annual Meeting of Chemical Society of Japan, Osaka, March 1968, No. 3, p. 1775; K. Suzuki and I. Kumashiro, Brit. 1134974 (1968).

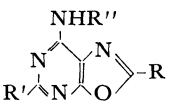
5) E. C. Taylor and E. E. Garcia, *J. Org. Chem.*, **29**, 2116 (1964); P. Rajagopalan and C. N. Talaty, *Tetrahedron*, **23**, 3541 (1967).

6) Y. Ohtsuka, This Bulletin, **43**, 187 (1970).

7) Y. Ohtsuka and K. Sugimoto, *ibid.*, **43**, 2281 (1970).

ing substituents.[8] Thus, the compound V was expected to be easily converted into IIa under such conditions as used in this experiment. Moreover, the previously isolated iminopyrimidines have been reported to be somewhat unstable on standing in moist air or on being treated in a polar solvent.[2,9] These properties are completely different from that of the product obtained here. *ii*) The UV spectrum of this compound was investigated at pH 1 and pH 10, and the difference of λ_{max} in acidic and in basic solution were compared with the values of 6-methylaminopurine ($\Delta\lambda=5$ mμ)[10] and of 1-methyl-6-(1*H*)iminopurine ($\Delta\lambda=11$ mμ).[11] While a relatively large value of $\Delta\lambda$ was expected for imino structure (V), the experimental value ($\Delta\lambda=3$ mμ) indicates that the structure of the product is IIa. Little pH-dependence has been observed also with the UV spectrum of 7-aminooxazolopyrimidine.[6] *iii*) Other spectroscopic properties of the compound seem to support the above conclusion. Its IR spectrum shows a band due to a secondary amine. In the mass spectrum, it preferentially expels 28 mass units from the molecular ion. Such a process has been observed previously with 6-methylaminopurine,[12] in which the initial fragmentation was attributed to loss of a methylamino group with concomitant transfer of one or two hydrogen atoms to the purine nucleus.

TABLE 1. 7-ALKYLAMINOOXAZOLO[5,4-*d*]PYRIMIDINE DERIVATIVES



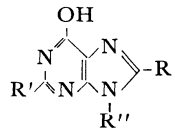
Compd	Substituent			Yield (%)	Mp (°C)
	R	R′	R″		
IIa	H	H	CH_3	80	182—184
IIb	H	CH_3	CH_3	62	170—171
IIc	H	C_2H_5	CH_3	82	140—142
IId	CH_3	H	CH_3	27	194—195
IIe	CH_3	CH_3	CH_3	67	184—185
IIf	H	H	C_2H_5	49	144—145
IIg	H	H	*n*-Pr	31	104—105
IIh	H	H	*i*-Pr	24	121—122
IIi	H	H	*n*-Bu	26	81— 82
IIj	H	H	*t*-Bu	—	—

8) D. J. Brown and J. S. Harper, *J. Chem. Soc.*, **1963**, 1276.
9) D. J. Brown, E. Hoerger and S. F. Mason, *ibid.*, **1955**, 4035.
10) G. B. Elion, E. Burgi and G. H. Hitchings, *J. Amer. Chem. Soc.*, **74**, 411 (1952).
11) N. J. Leonard and J. A. Deyrup, *ibid.*, **84**, 2148 (1962).
12) J. M. Rice and G. O. Dudek, *ibid.*, **89**, 2719 (1967).

By the reaction of I with various aliphatic amines, a number of oxazolopyrimidines were obtained. The IR, NMR and mass spectra of these products exhibit the characteristic patterns closely related with those of IIa, indicating that these products have 7-alkylamino structures (II). As shown in Table 1, both the yields and the mp's of these oxazolopyrimidines are dependent mainly upon the substituent R″. The bulkiness of R″ seems to be unfavorable to the reaction. The cyclized product was not obtained from the reaction of Ia with *t*-butylamine. The effect of other substituents, R and R′, seems to be small but the introduction of 2-substituent (R=CH_3) causes the oxazole ring to be somewhat unstable to alkali.

Preparation of 9-Substituted Hypoxanthine (III). 7-Alkylaminooxazolopyrimidines (IIa and IIb) were treated with aqueous alkali under the conditions similar to those with 7-amino compounds,[1] and the corresponding hypoxanthines (IIIa and IIIb) were obtained as shown in Table 2 (Method A). This treatment, however, has a limitation since the isolation of water-soluble products is tedious and hydrolysis with strong alkali is accompanied by the conversion reaction. In these cases, the conversion was carried out by heating II in formamide at around 200°C (Table 2, Method B). As for the reaction of I with aromatic amines, prolonged heating at higher temperatures was needed in contrast to the case of aliphatic amines, and the corresponding hypoxanthines were obtained directly (Table 2, Method C). Method C gave a better result than Method B in reaction of Ia with *n*-butylamine.

TABLE 2. TOTAL YIELDS OF HYPOXANTHINES DERIVATIVES



Compd	Substituent			Method[a]	Total yield from I (%)
	R	R′	R″		
IIIa	H	H	CH_3	A, B	69
IIIb	H	CH_3	CH_3	A	31
IIIe	CH_3	CH_3	CH_3	B	20
IIIf	H	H	C_2H_5	B	43
IIIg	H	H	*n*-Pr	B	27
IIIi	H	H	*n*-Bu	B	26
				C	48
IIIk	H	H	Ph	C	42
IIIl	H	H	*β*-Naph	C	17

a) A: Isolation of oxazolopyrimidine followed by treatment with aqueous NaOH.
B: Isolation of oxazolopyrimidine followed by heating in formamide.
C: One-step method.

The decreased yield of hypoxanthines having a bulky substituent at 9-position may be related partly with the formation of isomeric products. Thus, the treatment of IIh by Method B yielded an isomeric product, but the rearrangement accompanying this reaction will be reported in a subsequent paper.

This new route from oxazole derivatives to hypoxanthines may be applied best for the preparation of hypoxanthines having an *n*-alkyl substituent at 9-position.

Experimental

Melting points were measured on a hot-stage apparatus and uncorrected. The IR, NMR and UV spectra were determined with a Perkin-Elmer 337, a Varian HA-100 and a Carry-14 spectrometer, respectively. Mass spectra were recorded at ionization voltage of 70 eV, and samples were introduced directly into the ion source of a Hitachi RMU-6E mass spectrometer. Preparations of starting materials (I) from 5-amino-4-cyanooxazole derivatives and ortho-esters have been described in a previous paper.[6]

7-Methylaminooxazolo[5,4-*d*]pyrimidine (IIa). To an ice-cooled aqueous solution of methylamine (30%, 1 m*l*), 4-cyano-5-ethoxymethylenaminooxazole (Ia, 1.65 g) was added in one portion. A solid started to precipitate immediately from solution,[13] but on continued stirring it rapidly dissolved. After 10 min, a second solid precipitated. Filtration and washing with a small quantity of water gave a crystalline (1.20 g). For analytical purpose, recrystallization from water or ethanol gave colorless needles, mp 182—184°C. λ_{max}^{MeOH} mμ (log ε): 207 (4.20), 258 (4.20), 283 sh (3.71). $\lambda_{max}^{pH\ 1}$: 255 (4.03). $\lambda_{max}^{pH\ 10}$: 258 (3.84). ν_{max}^{KBr} cm^{-1}: 3295 (NH), 3071 (CH), 1630, 1604, 1535, 1492, 1142, 1062, 795. NMR (DMSO-d_6) δ: 3.03 (broad s, 3H, *N*-methyl protons), 8.12 (broad s, 1H, =*N*-proton), 8.33 (s, 1H, C_2-proton), 8.61 (s, 1H, C_5-proton). Mass spectrum (assignment, relative intensity, metastable peak) *m/e*: 150 (M^+, 100), 122 (M^+-28, 42, 99.0), 94 ([121]$^+$—HCN, 23, 73.0), 67 ([94]$^+$—HCN, 31, 48.7).

Found: C, 47.66; H, 4.09; N, 37.45%. Calcd for $C_6H_6N_4O$: C, 48.00; H, 4.03; N, 37.32%.

9-Methylhypoxanthine (IIIa). Method A. A mixture of IIa (1 g) and a 4N aqueous NaOH (5 m*l*) was stirred at room temperature for 30 min and then warmed gradually to dissolve the solid into the solution. After cooling, the solution was neutralized with HCl and resulting precipitate (0.8 g) was collected by filtration.

Method B. The compound IIa (1 g) was heated in formamide (5 m*l*) to a vicinity of 200°C for 40 min and then evaporated to nearly dryness under reduced pressure. Recrystallization from water gave 0.8 g of colorless crystals.

These products were identified as 9-methylhypoxanthine.[14]

13) A crude material was rapidly isolated from the reaction mixture. Its IR spectrum showed a nitrile band and its NMR spectrum showed no ethoxyl group. Furhter purification of the material gave IIa.

5-Methyl-7-methylaminooxazolo[5,4-*d*]pyrimidine (IIb). This compound was prepared from 4-cyano-5-ethoxyethylenaminooxazole (Ib) and methylamine by the procedure described above with 69% yield. Recrystallization from ethanol gave colorless needles, mp 170—171°C. ν_{max}^{KBr} cm^{-1}: 3249 (NH), 3118 (CH), 1677, 1600, 1555, 1519, 1160, 1040, 771. NMR (DMSO-d_6) δ: 3.54 (broad s, 3H, *N*-methyl protons), 7.21 (s, 1H, =N-proton), 8.35 (s, 1H, C_2-proton), 2.50 (s, 3H, C_5-methyl protons). Mass spectrum, *m/e*: 164 (M^+, 100), 149 (M^+-15, 16, 135.4), 136 (M^+-28, 16, 112.8), 96 ([136]$^+-C_2H_2N$, 19, -), 69 ([96]$^+$ -HCN, 47, 49.6).

Found: C, 51.08; H, 4.62; N, 34.61%. Calcd for $C_7H_8N_4O$: C, 51.21; H, 4.91; N, 34.13%.

2,9-Dimethylhypoxanthine (IIIb). This compound was prepared from IIb by Method A with 74% yield. Recrystallization from water gave colorless crystals, mp>320°C. The IR spectrum of the compound exhibited a broad band in the 2800—2600 cm^{-1} region which is characteristic of all the hypoxanthines studied here and a band due to a secondary amine was absent. Mass spectrum, *m/e*: 164 (M^+, 100), 123 (M^+-CH_3CN, 98, 92.3), 95 ([123]$^+-28$, 97, 73.4), 68 ([95]$^+$—HCN, 116, 48.7), 53 ([68]$^+-CH_3$, 50, 41.3), 41 ([68]$^+$—HCN, 84, 25.8).

Found: C, 51.36; H, 4.94; N, 34.29%. Calcd for $C_7H_8N_4O$: C, 51.21; H, 4.91; N, 34.13%.

5-Ethyl-7-methylaminooxazolo[5,4-*d*]pyrimidine (IIc). This compound was prepared from 4-cyano-5-ethoxypropylenaminooxazole (Ic) and methylamine with 82% yield. Recrystallization from ethanol gave colorless needles, mp 140—142°C. ν_{max}^{KBr} cm^{-1}: 3218 (NH), 3085 (CH), 1663, 1600, 1540, 1509, 1147, 1049, 810, 797. NMR (DMSO-d_6) δ: 3.56 (s, 3H, *N*-methyl protons), 8.40 (s, 1H, C_2-proton), 1.22 and 2.84 (5H, ethyl protons). Mass spectrum, *m/e*: 178 (M^+, 100), 177 (M^+–H, 47, 176.0), 163 (M^+-CH_3, 46, 149.3), 150 (M^+-28, 22, 126.4), 149 ([150]$^+$—H, 15, 148.0), 123 ([150]$^+$—HCN, 8, 100.9), 96 ([124]$^+$—28, 11, 74.3), 69 ([96]$^+$—HCN, 33, 49.6), 42 ([69]$^+$—HCN, 53, 25.6).

Found: C, 53.64; H, 5.30; N, 31.75%. Calcd for $C_8H_{10}N_4O$: C, 53.92; H, 5.66; N, 31.45%.

2-Methyl-7-methylaminooxazolo[5,4-*d*]pyrimidine (IId). This compound was prepared from 4-cyano-5-ethoxymethylenamino-2-methyloxazole (Id) and methylamine with 62% yield. Recrystallization from water gave colorless needles, mp 194—195°C. ν_{max}^{KBr} cm^{-1}: 3240 (NH), 3048 (CH), 1665, 1630, 1585, 1502, 1134, 911, 791. NMR (DMSO-d_6) δ: 2.99 (d, 3H, *N*-methyl protons), 7.90 (broad s, 1H, =N-proton), 8.22 (s, 1*H*, C_5-proton), 2.58 (s, 3*H*, C-methyl protons). Mass spectrum, *m/e*: 164 (M^+, 100), 136 (M^+-28, 77, 112.8), 108 ([135]$^+$—HCN, 27, 86.4).

Found: C, 51.18; H, 5.01; N, 33.66%. Calcd for $C_7H_8N_4O$: C, 51.21; H, 4.91; N, 34.12%.

2,5-Dimethyl-7-methylaminooxazolo[5,4-*d*]pyrimidine (IIe). An aqueous solution of methylamine (30%, 3.8 m*l*) was cooled with ice-salt mixture. To this, cooled and powdered 4-cyano-5-ethoxyethylenamino-2-methyloxazole (Ie, 5.4 g) was added in one

14) R. K. Robins and H. H. Lin, *J. Amer. Chem. Soc.*, **79**, 490 (1957).

portion. The mixture was stirred at room temperature for 30 min. The resulting semi-solid was dissolved in chloroform and the aqueous layer was separated. The colorform solution was poured into a large volume of ether. On cooling the mixture, white crystalline material separated gradually and filtration gave an amorphous solid (3.5 g). The solid was dissolved in water (10 ml) and the solution was heated under reflux for 1.5 hr. Filtration after cooling gave light-yellow needles (2.2 g), mp 181—182°C. For analytical purpose, recrystallization from water-ethanol gave colorless needles, mp 184—185°C. ν_{max}^{KBr} cm^{-1}: 3245 (NH), 3045 (CH), 1630, 1580, 1520, 1505, 1141, 1036, 791. NMR (DMSO-d_6) δ: 2.97(d, 3H, *N*-methyl protons), 7.70 (broad s, 1H, =N-proton), 2.53 s, 3H, C_2-methyl protons), 2.42 (s, 3H, C_5-methyl protons). Mass spectrum, *m/e*: 178 (M^+, 100), 150 (M^+-28, 48, 126.4), 137 (M^+-CH_3CN, 21, 105.4), 109 ([137]$^+-28$, 29, 86.7), 108 ([150]$^+-CH_3CNH$, 49, 77.8).

Found: C, 53.85; H, 5.79; N, 31.24%. Calcd for $C_8H_{10}N_4O$: C, 53.92; H, 5.66; N, 31.45%.

2,8,9-Trimethylhypoxanthine (IIIe). This compound was prepared from IIe by Method B with 74% yield. Recrystallization from acetonitrile gave colorless crystals, mp>330°C. The IR spectrum of the compound exhibited a broad band at around 2900 cm^{-1} and a band due to a secondary amine was absent. NMR (D_2O) δ: 2.01 (s, 6H, *C*-methyl protons), 3.88 (s, 3H, *N*-methyl protons). Mass spectrum, *m/e*: 178 (M^+, 100), 164 (M^+-CH_2, 14, —), 137 (M^+-CH_3CN, 28, 105.4), 95 ([137]$^+-CH_3CNH$, 18, 65.9).

Found: C, 53.88; H, 5.76; N, 31.54%. Calcd for $C_8H_{10}N_4O$: C, 53.92; H, 5.66; N, 31.45%.

7-Ethylaminooxazolo[5,4-*d*]pyrimidne (IIf). The compound Ia (1.65 g) was added into an ice-cooled aqueous solution of ethylamine (35%, 2 ml) and stirred for 10 min. Filtration gave a solid (1.24 g), which was quickly dried *in vacuo* for 30 min and then heated under reflux in ethanol (15 ml) for 4 hr. After cooling, the mixture was filtered and the filtrate was concentrated under reduced pressure. Crystals (0.75 g) were obtained from the residue on cooling. Recrystallization from water gave colorless needles, mp 144—145°C. ν_{max}^{KBr} cm^{-1}: 3230 (NH), 3090 (CH), 1630, 1591, 1560, 1516, 1135, 1060, 796. NMR (DMSO-d_6) δ: 8.22 (broad s, 1H, =N-proton), 8.34 (s, 1H, C_2-proton), 8.63 (s, 1H, C_5-proton), 1.22 and 3.62 (5H, *N*-ethyl protons). Mass spectrum, *m/e*: 164 (M^+, 64), 149 (M^+-CH_3, 100, 135.4), 136 (M^+-28. 58, 112.8), 122 ([149]^+-HCN, 16, 99.9), 109 ([136]^+-HCN, 19, 87.4), 94 ([121]^+-HCN, 12, 73.0), 81 ([109]^+-CO, 10, 60.2), 67 ([94]^+-HCN, 28, 47.7).

Found: 51.37; H, 5.19; N, 33.87%. Calcd for $C_7H_8N_4O$: C, 51.21; H, 4.91; N, 34.13%.

9-Ethylhypoxanthine (IIIf). The above compound (IIf) was treated by Method B and the reaction product (a brown oil) was crystallized from acetone (83%). Recrystallization from water gave colorless crystals, mp 264—266°C. This product was identified as 9-ethylhypoxanthine.[15]

7-*n*-Propylaminooxazolo[5,4-*d*]pyrimidine (IIg). This compound was prepared by the method analogous to that of IIf from Ia and *n*-propylamine in water with 31% yield. Recrystallization from water gave colorless needles, mp 104—105°C. ν_{max}^{KBr} cm^{-1}: 3230 (NH), 3060 (CH), 1629, 1589, 1561, 1518, 1142, 1052, 1044, 794. NMR (DMSO-d_6) δ: 8.23 (broad s, 1H, =N-proton), 8.33 (s, 1H, C_2-proton), 8.63 (s, 1H, C_5-proton), 1.43, 1.65 and 3.53 (7H, *N*-*n*-propyl protons).

Found: C, 53.93; H, 5.85; N, 31.20%. Calcd for $C_8H_{10}N_4O$: C, 53.92; H, 5.66; N, 31.45%.

9-*n*-Propylhypoxanthine (IIIg). Avove compound (IIg) was treated by Method B and the product was recrystallized from *i*-PrOH. Yield 87%. This compound was identified as 9-*n*-propylhypoxanthine.[16]

7-*i*-Propylaminooxazolo[5,4-*d*]pyrimidine (IIh). This compound was prepared in a similar way to the preparation of IIf from Ia and *i*-propylamine with 24% yield. Recrystallization from water gave colorless crystals, mp 121—122°C. ν_{max}^{KBr} cm^{-1}: 3230 (NH). 3075 (CH), 1636, 1590, 1562, 1520, 1113, 1071, 794, NMR (DMSO-d_6) δ: 8.03 (d, 1H, =N-proton), 8.30 (s, 1H, C_2-proton), 8.61 (s, 1H, C_5-proton), 4.5 and 1.26 (7H, *i*-propyl protons).

Found: C, 53.95; H, 5.73; N, 31.42%. Calcd for $C_8H_{10}N_4O$: C, 53.92; H, 5.66; N, 31.45%.

7-*n*-Butylaminooxazolo[5,4-*d*]pyrimidine (IIi). This compound was prepared in a similar way to the preparation of IIf from Ia and *n*-butylamine with 26% yield. Recrystallization from water-ethanol gave colorless crystals, mp 81—82°C. ν_{max}^{KBr} cm^{-1}: 3250 (NH), 3060 (CH), 1660, 1630, 1596, 1521, 1144, 1050, 798. NMR (DMSO-d_6) δ: 7.68 (s, 1H, =N-proton), 8.30 (s, 1H, C_2-proton), 8.59 (s, 1H, C_5-proton), 0.9, 1.5 and 3.5 (9H, *N*-*n*-butyl protons).

Found: C, 56.23; H, 6.50; N, 29.10%. Calcd for $C_9H_{12}N_4O$: C, 56.22; H, 6.29; N, 29.15%.

9-*n*-Butylhypoxanthine (IIIi). By Method B. Above compound IIi was treated by Method B and the product was recrystallized from water. The yield was nearly quantitative.

By Method C. To a solution of *n*-butylamine (1.5 g) in dry pyridine (25 ml), Ia (1.65 g) was added portionwise. The mixture was stirred for 15 min at room temperature and then heated under reflux for 2 hr. After concentration of the solution nearly to dryness under reduced pressure, the residual sirup was kept overnight in a refrigerator. The resulting precipitate was filtered off and washed with benzene. The product (0.8 g) was recrystallized from water and identified as 9-*n*-butylhypoxanthine.[17]

9-Phenylhypoxanthine (IIIk). Aniline (2.0 g) and Ia (3.3 g) were chilled with ice-water separately and mixed in one portion. On stirring at room temperature, the mixture changed into an amorphous solid. This was digested with 50 ml of water and the mixture was heated gradually to 70—80°C in the course of 2 hr. Light brown needles separated from the brown oil. Filtration after cooling and washing of the needles with acetone gave a product (2.0 g), which on recrystallization from 50% ethanol gave colorless needles identified

15) J. A. Montogomery and C. Temple, Jr., *J. Amer. Chem. Soc.*, **79**, 5238 (1957).

16) C. Temple, Jr., C. L. Kussner and J. A. Montogomery, *J. Med. Pharm. Chem.*, **5**, 866 (1962).

17) J. A. Montogomery and C. Temple, Jr., *J. Amer. Chem. Soc.*, **80**, 409 (1958).

as 9-phenylhypoxanthine.[18]

9-β-Naphthylhypoxanthine (IIIl). Cooled and pulverized Ia (1.65 g) was mixed with β-naphthylamine (1.43 g). On stirring at room temperature, the mixture melted and crystals separated again. After 30 min, this was digested with water (50 ml) and the mixture was heated under reflux for 1 hr. The resulting solid was collected and washed with a small quantity of acetone. Reprecipitation from DMF-ether followed by recrystallization from 50% ethanol gave colorless crystals (0.45 g), mp 320°C. Its IR spectrum showed a broad band at around 2850 cm^{-1} and an intense band at 1700 cm^{-1}. NMR (NaOD-D_2O) δ: 8.58 (s, 1H, C_2-proton), 8.17 (s, 1H, C_8-proton). 8.3 (m, 7H, β-naphthyl protons). Mass spectrum, *m/e*: 262 (M^+, 100), 261 (M^+-H, 21, 260.0), 234 ($[261]^+-HCN$, 6, 209.8), 207 ($[234]^+-HCN$, 5, 183.1), 180 ($[207]^+$-HCN, 4, 156.5).

Found: C, 68.16; H, 3.86; N, 21.09%. Calcd for $C_{15}H_{10}N_4O$: C, 68.69; H, 3.84; N, 21.37%.

This compound was shown to be identical with the product prepared by the method of Robins *et al.*[18] from 5-amino-4,6-dichloropyrimidine and β-naphthylamine.

The author wishes to thank Dr. Shizuo Nakamura for his encouragement throughout this work, and Mr. Kikuo Sugimoto and Mr. Shigeru Kiuchi for their technical assistance.

18) S. M. Greenberg, L. O. Ross and R. K. Robins, *J. Org. Chem.*, **24**, 1314 (1959).