Chemistry of Diaminomaleonitrile. 3. Reaction with Isocyanate: A Novel Pyrimidine Synthesis[1]

Yozo Ohtsuka

Sagami Chemical Research Center, Nishi-Ohnuma, Sagamihara, Kanagawa 229, Japan

Received February 28, 1978

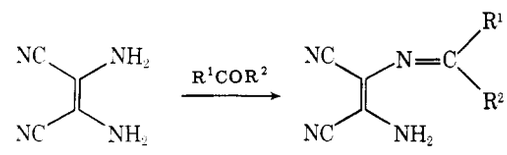
New urea derivatives of diaminomaleonitrile (DAMN, **1**) are prepared and their cyclization reactions investigated. 3-Substituted 5-alkylideneamino-6-cyanocytosines (**7**) are obtained from DAMN Schiff bases (**2**) and isocyanates by a novel trans cyclization. Similar cyclization of DAMN urea derivatives (**3**) with ketones and aldehydes was accompanied with hydration of the nitrile group to give 3-substituted 5-alkylideneaminocytosine-6-carboxamides (**9**) and 3,6-disubstituted 4-aminopyrimido[5,4-*d*]pyrimidine-2,8-diols (**10**), respectively.

Several nitrogen heterocycles, including imidazoles,[1-3] pyrazines,[4] and diazepines,[1,3] have been prepared from diaminomaleonitrile (DAMN, **1**), the tetramer of hydrogen cyanide. These syntheses have generally been based on a single reaction pattern in which **1** is used as a *cis*-1,2-diaminoethylene component. To extend synthetic versatility, a variety of the reaction pattern of **1** is desirable. One approach is exemplified by the photochemical conversion of **1** to 4-amino-5-cyanoimidazole,[5] which appears to result from the trans isomer, diaminofumaronitrile.[6] No chemical reactions of the trans isomer, however, are known mainly because it reverts to the cis isomer (**1**) under the influence of acid, base, charcoal, or light or on heating.[7] Some derivatives of **1**, such as tetramethyl[3] and bisanil compounds,[8] are known to have the trans geometry about the central carbon–carbon double bond of the skeleton of **1**. Again the chemical properties of these compounds have not yet been examined.

Here, we want to present a new reaction pattern of DAMN, in which **1** is used as a *trans*-1,2-diaminoethylene component. This is demonstrated by the successive reaction of **1** with carbonyl compounds and isocyanates to give pyrimidine derivatives.

Results and Discussion

Open-Chain Compounds. Condensation of **1** with aldehydes or ketones is known to afford Schiff bases.[1,3] These compounds are generally believed to have maleonitrile structure **2** (cis configuration) from their IR spectra, the presence of two nitrile bands near 2230 and 2200 cm^{-1}, and their chemical properties, especially the facile formation of



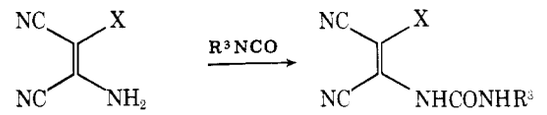
1 **2**

a, R^1 = Ph; R^2 = H
b, R^1 = 4-ClC_6H_4; R^2 = H
c, R^1 = 4-$CH_3OC_6H_4$; R^2 = H
d, R^1 = 4-$NO_2C_6H_4$; R^2 = H
e, R^1 = 2-furyl; R^2 = H
f, R^1 = R^2 = Ph

1,4-diaza heterocycles. DAMN Schiff bases **2a–f**[1,3,9] were prepared for the present study.

Synthesis of the phenylurea derivative **3e** (see Table I) from **1** and phenyl isocyanate[3] has been extended here to the preparation of alkyl derivatives. The reaction proceeded at room temperature without catalyst in acetonitrile solvent to give the corresponding monourea derivatives **3a–d** in moderate yields as shown in Table I. *N*-Benzyl DAMN's **4a–c**, prepared from **2a–c** by sodium borohydride reduction,[3] reacted similarly with isocyanates, and *N*-benzyl-*N'*-urea derivatives **5a–c** were obtained (Table I). Table I also includes an *N*-benzylidene-*N'*-urea derivative (**6a**) which was isolated by a base-catalyzed reaction of **2b** and methyl isocyanate in acetone, but the latter reaction generally afforded cyclized products (vide post).

Spectroscopic data of these open-chain ureas are presented in the supplement of Table I (see supplementary material). Two nitrile absorptions in the IR spectra of **3, 5,** and **6a** are observed in regions at 2250–2228 and 2210–2195 cm^{-1}. The spectral similarity with Schiff bases **2** and the facile formation of **3** and **5** without any acid or base catalyst suggest that the compounds in Table I also have cis configurations. The



1, X = NH_2
4, X = $NHCH_2Ar$
2b, X = $N{=}CHC_6H_4Cl$
3, X = NH_2
5, X = $NHCH_2Ar$
6a, X = $N{=}CHC_6H_4Cl$

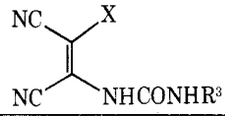
characteristic mass pattern is a molecular ion of low intensity and the fragmentation by loss of alkyl- or arylamine.

Cytosine Derivatives (Table II). By reaction of isocyanates and DAMN Schiff bases (**2a–c** and **2f**), 3-substituted 5-alkylideneamino-6-cyanocytosines (**7a–d**) were obtained. Proof of the structure rests primarily on microanalytical and spectral evidence. The IR spectra of **7** exhibit one nitrile band at 2200 cm^{-1} and two characteristic absorptions in the 1733–1740 and 1630–1660 cm^{-1} regions. The mass spectra contain a molecular ion of moderate intensity, loss of the substituent at position 3 and loss of alkyl or aryl cyanide at position 5, indicating the presence of a stable ring. The lack of alkyl- or arylamine splitting in the major fragmentation process almost excludes the possibility that the products are open-chain compounds (Table I) or 4-alkylamino- or 4-arylaminocytosines by the Dimroth rearrangement. The NMR spectra of **7** exhibit two NH protons (exchangeable), for **7d** at δ 8.93 and 8.62, and a diffused signal at δ 11–12.[10] In the spectra of **7a–c**, the azomethine proton on the side chain at position 5 is observed as two signals: for **7b** at δ 8.47 and 8.43. When **7a,b** were subjected to sodium borohydride reduction, the spectra of the products (**8a,b**) showed the signal of benzyl protons at δ 4.4 and no azomethine proton signal. The structure having an azomethine side chain was confirmed by the above result, but attempts to hydrolyze either the 5-azomethine or 6-cyano groups were unsuccessful. In most cases, **7** was recovered unchanged. Prolonged treatment of **7a** with CH_3CO_2H–H_2O_2 gave 4-amino-3,6-diphenylpyrimido[5,4-*d*]pyrimidine-2,8-diol (**10g**).

Cytosine **7b** was prepared by the reaction of **2b** and CH_3NCO with Et_3N in acetonitrile. As mentioned above, the open-chain compound **6a** was isolated when the same reaction was performed in acetone, in which **6a** is sparingly soluble. Therefore, it seems that **6a** is an intermediate of the reaction

0022-3263/78/1943-3231$01.00/0

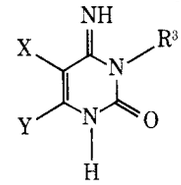
Table I. Open-Chain Urea Derivatives of Diaminomaleonitrile



Compd[a,b]	R^3	X	Yield, %	Recrystn solvent	Decompn point, °C
3a	Me	NH_2	85	CH_3CN	~167
3b	*i*-Pr	NH_2	67	CH_3CN	~184
3c	*n*-Bu	NH_2	62	$CH_3COOC_2H_5$	~162
3d	Cyclohexyl	NH_2	40	$CH_3COOC_2H_5$	~173
3e	Ph	NH_2	92	CH_3CN	~230[c]
5a	Me	$PhCH_2NH$	47	$CH_3COOC_2H_5$	151–152
5b	Me	$4\text{-}ClC_6H_4CH_2NH$	20	$CH_3COOC_2H_5$	174–175
5c	*i*-Pr	$4\text{-}CH_3OC_6H_4CH_2NH$	42	$CH_3COOC_2H_5$ + *n*-hexane	138–141
6a	Me	$4\text{-}ClC_6H_4CH{=}N$	75	CH_3CN	208–210

[a] Satisfactory analytical data (±0.4% for C, H, N, and Cl) were reported for all new compounds listed in the table (see the supplementary material). [b] For spectral data, see the supplementary material. [c] Reference 3.

Table II. Substituted Cytosines



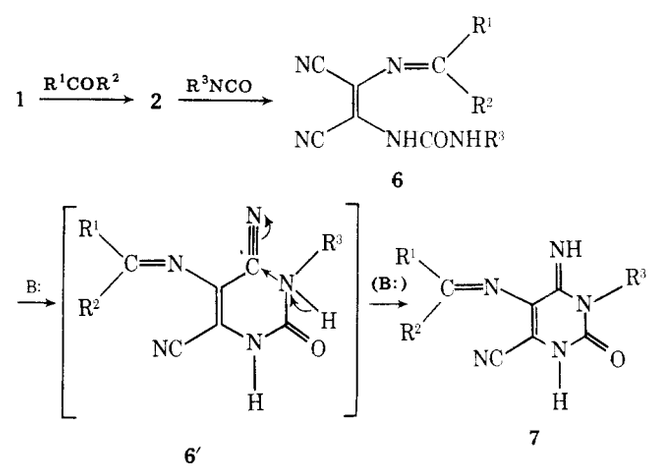
Compd[a,b]	Y	X	R^3	Reaction time, h (temp, °C)	Yield, %	Recrystn solvent	Mp, °C
7a	CN	$PhCH{=}N$	Ph	0.1 (70)	97	CH_3CN	233–235 dec
7b	CN	$4\text{-}ClC_6H_4CH{=}N$	Me	0.2 (70)	64	CH_3NO_2	235–238 dec
7c	CN	$4\text{-}CH_3OC_6H_4CH{=}N$	*i*-Pr	18 (RT)[c]	90	CH_3CN	213–215 dec
7d	CN	$Ph_2C{=}N$	*n*-Bu	2 (RT)	18	C_2H_5OH (aq)	196–197 dec
8a	CN	$PhCH_2NH$	Ph	0.25 (5)	85	CH_3CN	159–160 dec
8b	CN	$4\text{-}ClC_6H_4CH_2NH$	Me	0.25 (5)	82	CH_3CN	172–173 dec
9a	$CONH_2$	$Me_2C{=}N$	Ph	1 (RT)	59	CH_3CN	>300
9b	$CONH_2$	$4\text{-}NO_2C_6H_4C(Me){=}N$	Me	3 (RT)	58	CH_3CN	>300

[a] Satisfactory analytical data (±0.4% for C, H, N, and Cl) were reported for all new compounds listed in the table (see supplementary material). [b] For spectral data, see the supplementary material. [c] RT = room temperature.

to give **7b**, and it was separated as a precipitate at an early stage of the reaction by the latter experiment. In fact, treatment of **6a** with aqueous sodium hydroxide followed by neutralization gave **7b**. Compound **7b** was also obtained by oxidation of **5b** with manganese dioxide in dimethylformamide. The oxidation conditions have been developed by Begland[8] for the preparation of benzylidene derivatives of **1** from the corresponding benzyl derivatives. Hence, the oxidation of **5b** gave presumably **6a**, which would afford **7b** in situ by the same mechanism.

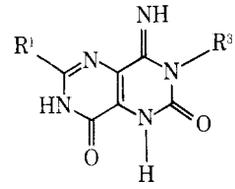
The reaction to give **7** seems to demand the presence of a base catalyst since **6a** is recovered unchanged from the hot acetonitrile solution. Previous preparations of DAMN derivatives have generally been carried out under neutral or acidic conditions, and the trans-type (fumaronitrile-type) reaction of **1** has not been observed (except in a case[8] that will be discussed below). We postulated that the cytosine **7** synthesis proceeded through a base-catalyzed isomerization of **6** to **6′**, as illustrated in Scheme I.

Scheme I



Oxidation of **1** is known to result in a trans compound, diiminosuccinonitrile.[11] The patent on a bisanil dye,[8] Ar-CH=NC(CN)=C(CN)N=CHAr′, states that the trans compound is prepared from **1** and an aldehyde with concentrated sulfuric acid, whereas the cis isomer is obtained under milder conditions, and that the cis isomer can be converted into the trans isomer by heating it in benzene containing a small amount of iodine. Hydrogen abstraction from **1** is presumably the initiation step of the photochemical cis–trans isomerization of **1**.[6] These previous examples seem to indicate the importance of oxidation [probably at the amino or imino group adjacent to the C=C bond] for the isomerization. Accordingly, it is probable to consider that the isomerization of **6** into **6′** in Scheme I is initiated by such a hydrogen abstraction with triethylamine, but further evidence was not obtained in the present investigation. We are seeking clearer evidence

Table III. Pyrimido[5,4-*d*]pyrimidines



Compd[a,b]	R^1	R^3	Method[c]	Reaction time, h	Yield, %	Recrystn solvent	Mp, °C
10a	Me	Me	A	24	37	EtOH	294–295
			B	18	44		
10b	Me	*n*-Bu	A	24	12	CH_3CN	260–261
10c	Ph	*n*-Bu	A	6	56	CH_3CN	296–298
10d	2-Furyl	Cyclohexyl	A	2	53	CH_3CN	>300
10e	H	Ph	A	6	30	CH_3CN	>300
10f	Me	Ph	A	4	82	CH_3CN	>300
10g	Ph	Ph	A	1	69	CH_3CN	>300
			B	6	15		
10h	4-$NO_2C_6H_4$	Ph	A	0.3	72	CH_3CN	>300

[a] Satisfactory analytical data (±0.4% for C, H, N, and Cl) were reported for all new compounds listed in the table (see supplementary material). [b] For spectral data, see the supplementary material. [c] Method A, from **3** and R^1CHO; method B, from **3** and R^1CO-CH_2CO_2Et.

to understand the reaction.

The cyclization, **6′** to **7** in Scheme I, seems to be a fast reaction, and attempts to isolate **6′** failed. A similar cyclization by the addition of an urea moiety to the intramolecular cyano group has been reported in the preparation of 3-alkyl-5-cyanocytosine from 3-alkylureidomethylenemalononitrile.[12]

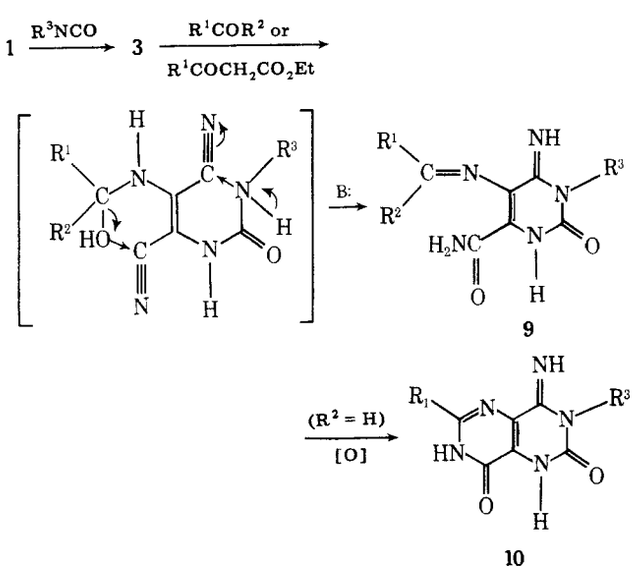
It was expected from Scheme I that cytosine **7** would also be obtained by the reversed reaction sequence: reaction of **1** and R^3NCO to give **3** followed by condensation with R^1COR^2. However, the reactions of **3** with ketones did not afford **7**, but instead the corresponding 6-carboxamides (**8a,b**) as shown in Table II. This reaction will be discussed in the next section.

Pyrimido[5,4-*d*]pyrimidines (Table III). The reaction of urea derivatives **3a–d** and aldehydes in the presence of triethylamine gave 3,6-disubstituted 4-aminopyrimido[5,4-*d*]pyrimidine-2,8-diols (**10a–h**) as colorless high-melting crystals. The structure of **10a–h** is consistent with their IR and mass spectra, which are characteristic with strong peaks attributed to the loss of $R^1C(=NH)NHCHO$ from the molecular ion (the spectroscopic data are presented in the supplement of Table III in the supplementary material). Their NMR spectra indicate the presence of three NH protons (exchangeable), one on the external nitrogen, for **10c** at δ 11.3, and two on the ring, for **10c** at δ 8.0 and 7.8. The structure **10** is confirmed by both the above-mentioned results that the hydration of **7a** gives **10g** and that the reaction of **3** and ketone gives **9**. The compound corresponding to **9a,b** is probably the precursor of **10** when R^2 is H.

The reaction to afford **10** proceeds smoothly at room temperature in an alcohol solvent, and the products are separated gradually as precipitates. An aqueous solution of aldehyde can be used as the reactant: formaline for **10a** and a 90% solution of acetaldehyde for **10b** and **10f**. Using ethyl acylacetate (method B) instead of aldehyde (method A) gave the same product **10**. The use of ethyl acylacetate had been developed for the preparation of imidazoles in a previous study[1] to introduce an RC≤ component by elimination of ethyl acetate. In the present study, however, imidazole formation giving rise to purine derivatives by cyclization with the 4-imino group is not observed, but further investigation under modified conditions is being undertaken.

Yamada and his co-workers[13] reported the formation of 4,8-diaminopyrimido[5,4-*d*]pyrimidine from hydrogen cyanide and formamidine in anhydrous liquid ammonia, and they explained the result by reaction of 2 mol of formamidine and diaminofumaronitrile, a postulated intermediate. Since the formation of **1** in their system was proved, the present study indicates another possibility of the mechanism, this being that the pyrimidopyrimidine resulted from an *N,N′*-bis(aminomethylene) derivative of **1** by a trans cyclization.

Scheme II



By the successive reaction **1** → **2** → **7** (Scheme I), one of the nitrile groups of **1** is left unchanged. Hydration of the C-6 nitrile group of **7** did not occur under the mild conditions used in the present synthesis. On the other hand, no nitrile compound was isolated by the reaction of reversed sequence, (**1** → **3**) → **9** or **10**, although the same type of trans cyclization occurred under closely similar reaction conditions. The nitrile group seems to be hydrated along with the carbonyl condensation. Thus, a mechanism involving intramolecular transfer of a water molecule is proposed as illustrated in Scheme II.

Oxidative cyclization of **9** into **10** occurs presumably by atmospheric oxygen. Oxidation during the workup of a *cis*-2,3-dihydropyrazine derivative into the corresponding pyrazine has been reported.[14]

Experimental Section

NMR spectra were determined using Me_2SO-d_6 solutions in a Varian HA-100 spectrometer, infrared (IR) spectra by KBr discs on a Hitachi EPR-G3 Infracord spectrometer, and mass spectra on a Hitachi RMU-6E mass spectrometer. All melting points were measured on a Yanagimoto MP-21 micro hot-stage apparatus and were corrected.

Diaminomaleonitrile (DAMN, **1**) was purchased from the Nippon Soda Co., Ltd. (grade A; 98% purity). DAMN Schiff bases (**2a**,[9a] **2b**,[3] **2c**, **2d**,[9b] **2e**,[9c] and **2f**[1]) were prepared from **1** and aldehydes or benzophenone. *N*-Benzyl derivatives of **1** were prepared by the sodium borohydride reduction[3] of **2a–c**: ***N*-(4-chlorobenzyl)diaminomaleonitrile (4b)**, mp 130–131 °C dec (recrystallized from benzene), was prepared in a solvent mixture of methanol (50 mL), tetrahydrofuran (75 mL), and dimethyl sulfoxide (40 mL) from **2b** (9.2 g) and sodium borohydride (14.0 g) in 94% yield; ***N*-(4-methoxybenzyl)-diaminomaleonitrile (4c)**, mp 137–138 °C dec (recrystallized from benzene), was similarly prepared from **2c** in 96% yield.

General Procedure for DAMN Urea Derivatives 3a–e and 5a–c (Table I). A mixture of isocyanate (0.09 mol), **1** or **4a–c** (0.03 mol), and acetonitrile (50 mL) was stirred at room temperature for 24 h. The reaction mixture was then chilled and filtered to yield a solid product, which was washed with cold acetonitrile. When the reaction was carried out in other solvents than acetonitrile, such as tetrahydrofuran, major parts of the reactants were recovered unchanged.

***N'*-Methylurea Derivative of *N*-(4-Chlorobenzylidene)diaminomaleonitrile (6a).** Three drops of triethylamine were added to a mixture of 3.0 g of **2b**, 4.8 g of methyl isocyanate, and 50 mL of acetone. The reaction mixture was warmed gently at about 40–50 °C until precipitates separated (within few minutes) and then stirred at room temperature. After 15 min the solid product was collected by filtration and washed with acetone to give 2.8 g of a yellow-white powder. Recrystallization gave colorless needles (see Table I). Its NMR spectrum showed an azomethine proton at δ 7.50.

General Procedure for 3-Substituted 5-Alkylideneamino-6-cyanocytosines (7a–c; Table II). Compounds **7a**, **7c**, and **7d** were obtained by the same procedure described for **6a** at the temperature indicated in Table II from the corresponding isocyanate (R^3NCO) and **2a**, **2c**, and **2f**, respectively. Compound **7b** was obtained by the method using acetonitrile instead of acetone. A compound identical with **7b**, confirmed by its melting point and IR spectrum, was obtained by the following two methods. (1) A mixture of 0.29 g of **5b**, 0.3 g of activated manganese dioxide, and 5 mL of dimethylformamide was kept at about 70 °C for 4 h with occasionally shaking. Then the solid was removed by filtration and washed with a small quantity of dimethylformamide. The filtrate and washing were gathered and diluted by water to give 0.1 g of the product. (2) **6a** was dissolved in a 10% aqueous solution of NaOH and then neutralized with acetic acid to give **7b** as a white precipitate.

Reduction of 7 with $NaBH_4$. To an ice-cooled mixture of 1.0 g of **7a** and 25 mL of tetrahydrofuran was added 1.0 g of sodium borohydride portionwise. On stirring, **7** gradually dissolved into the solution which turned yellow to red-brown. Then the reaction mixture was poured into 300 mL of ice water. Filtration and washing with water gave 0.85 g of **8a** as a yellow powder (see Table II). By the same treatment **7b** gave **8b**.

Hydrolysis of 7. A mixture of 0.3 g of **7a**, 2 mL of hydrogen peroxide, and 10 mL of acetic acid was stirred at room temperature for 4 days. After neutralization with ammonium hydroxide, 0.1 g of a solid product was obtained in which a small amount of **7a** was included, as investigated by its IR spectrum. Recrystallization from a large volume of acetonitrile gave a compound identical in all respects with **10g** (see later). By the following treatments **7a** was recovered unchanged: (1) stirring with aqueous ammonia (28%) at room temperature for 2 h; (2) stirring with $NaOCH_3$ in methanol at room temperature for 16 h; (3) on heating at 60–80 °C with a catalytic amount of *p*-toluenesulfonic acid in dimethylformamide for 2 h.

5-Isopropylideneamino-3-phenylcytosine-6-carboxamide (9a) was prepared similarly by stirring a mixture of 1.0 g of **3e**, 1 mL of triethylamine, and 30 mL of acetone. Filtration and washing with acetone gave the product **9a** as a white powder: NMR δ 1.34 (s, 6, CH_3), 7.47 (m, 5), 7.5 (broad, 2, NH). Other spectral data are shown in the supplement of Table II (see supplementary material).

The treatment of 0.83 g of **3a**, 0.9 g of *p*-nitroacetophenone, and 20 mL of methanol gave **9b** as a yellow powder (Table II).

General Procedure for 3,6-Disubstituted 4-Aminopyrimido[5,4-*d*]pyrimidine-2,8-diol (10; Table III). Method A. Triethylamine was added to a mixture of **3** (0.01 mol), aldehyde (0.02 mol), and 80–100 mL of methanol or ethanol, and the reaction mixture was stirred for the length of time indicated in Table III. Filtration gave the first crop, and an additional crop was obtained from the filtrate after allowing it to stand for several hours. The ratio of triethylamine was varied from a catalytic amount (a few drops) to an equimolecular quantity (0.01 mol), but no substantial effect on the yield was observed. The addition of the base was carried out under cooling when aqueous solutions of aldehydes were used since a rapid decomposition was observed on heating **3** with water.

Method B. The above procedure was repeated using ethyl acylacetate (ethyl acetoacetate for **10a** and ethyl benzoacetate for **10g**) instead of aldehyde (acetaldehyde for **10a** and benzaldehyde for **10g**). The reaction proceeded in a similar manner, and identical products were obtained.

Registry No.—**1**, 1187-42-4; **2a**, 56029-18-6; **2b**, 51802-11-0; **2c**, 59574-37-7; **2f**, 55752-09-5; **3a**, 66483-01-0; **3b**, 66483-00-9; **3c**, 66482-99-3; **3d**, 66482-98-2; **3e**, 51802-29-0; **4a**, 51802-03-0; **4b**, 66551-64-2; **4c**, 66482-86-8; **5a**, 66483-02-1; **5b**, 66482-97-1; **5c**, 66482-96-0; **6a**, 66483-10-1; **7a**, 66483-09-8; **7b**, 66483-08-7; **7c**, 66483-07-6; **7d**, 66483-06-5; **8a**, 66483-05-4; **8b**, 66483-04-3; **9a**, 66483-03-2; **9b**, 66482-95-9; **10a**, 66482-94-8; **10b**, 66482-93-7; **10c**, 66482-92-6; **10d**, 66482-91-5; **10e**, 66482-90-4; **10f**, 66482-89-1; **10g**, 66482-88-0; **10h**, 66482-87-9; PhNCO, 103-71-9; *i*-Pr-NCO, 1795-48-8; BuNCO, 111-36-4; MeCHO, 75-07-0; PhCHO, 100-52-7; 2-furancarboxaldehyde, 98-01-1; HCHO, 50-00-0; 4-$NO_2C_6H_4$-CHO, 555-16-8; $MeCOCH_2CO_2Et$, 141-97-9; $PhCOCH_2CO_2Et$, 94-02-0.

Supplementary Material Available: Spectral and analytical data (5 pages). Ordering information is given on any current masthead page.

References and Notes

(1) Part 2: Y. Ohtsuka, *J. Org. Chem.*, **41**, 629 (1976).
(2) (a) Y. Ohtsuka, *J. Org. Chem.*, **41**, 713 (1976); (b) W. A. Sheppard and O. W. Webster, *J. Am. Chem. Soc.*, **95**, 2695 (1973).
(3) R. W. Begland, D. R. Hartter, F. N. Jones, D. J. Sam. W. A. Sheppard, O. W. Webster, and F. J. Weigert, *J. Org. Chem.*, **39**, 2341 (1974).
(4) F. D. Popp, *J. Heterocycl. Chem.*, **11**, 79 (1974).
(5) J. P. Ferris and F. R. Antonucci, *J. Am. Chem. Soc.*, **96**, 2010 (1974).
(6) T. H. Koch and R. M. Rodehorst, *J. Am. Chem. Soc.*, **96**, 6707 (1974).
(7) E. Ciganek, W. J. Linn, and O. W. Webster in "The Chemistry of the Cyano Group", Z. Rappoport, Ed., Interscience, New York, N.Y., 1970, p 508.
(8) R. W. Begland, U.S. Patents 3 912 724 and 3 914 276 (1975).
(9) (a) P. S. Robertson and J. Vaughan, *J. Am. Chem. Soc.*, **80**, 2691 (1958); (b) L. E. Hinkel, G. O. Richards, and O. Thomas, *J. Chem. Soc.*, 1432 (1937); (c) K. Onoda, *Nippon Nogei Kagaku Kaishi*, **36**, 255 (1962).
(10) These data did not give clear enough information to distinguish structure **7** from the tautomeric 4-amino structure. The ^{13}C NMR spectrum [in Me_2SO-d_6 with $Cr(AcAc)_3$] of **7b** showed two equivalent carbons at 112.9 ppm (downfield from Me_4Si) and one at 119.1 ppm for C-4, C-5, and C-6, assigned by the aid of a partial decoupling experiment and comparison with the spectrum of **2b**. The C-4 carbon of cytosine (predominant amino form) was observed at a much lower field at 171.0 ppm: M. P. Schweizer, E. B. Banta, J. T. Witkowski, and R. K. Robins, *J. Am. Chem. Soc.*, **95**, 3770 (1973). This difference suggests that structure **7** is preferable, and the reactivity of **7**, especially the lack of reactivity of the 4 substituent, seems to support this conclusion
(11) O. W. Webster, D. R. Hartter, R. W. Begland, W. A. Sheppard, and A. Cairncross, *J. Org. Chem.*, **37**, 4133 (1972).
(12) B. B. Kehm and C. W. Whitehead, "Organic Syntheses", Collect. Vol. 4, Wiley, New York, N.Y., 1967, p 515.
(13) Y. Yamada, I. Izumi, I. Kumashiro, and T. Takenishi, *Bull. Chem. Soc. Jpn.*, **42**, 1454 (1969).
(14) A. Padwa, M. Dharan, J. Smolanoff, and S. I. Wetmore, Jr., *J. Am. Chem. Soc.*, **95**, 1954 (1973).