Investigation of the Preparation of Pyrimidine Isocyanates (1a,b)

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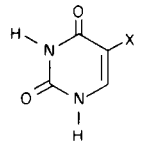
Uracil-5-yl isocyanate and 1,3-dimethyluracil-5-yl isocyanate were prepared from the corresponding new carboazides. 1,3-Dimethyluracil-5-ylmethyl isocyanate obtained from the chloro compound and silver cyanate, was polymerized with an anionic initiator to the cyclic trimer. Attempts to isolate uracil-6-yl isocyanate, 1,3-dimethyluracil-6-yl isocyanate, pyrimidinyl-4-isocyanate, and 2,6-dichloropyrimidinyl-4-isocyanate were unsuccessful. Ethyl carbamate derivatives were made from all new azides and isocyanates. Other new pyrimidine derivatives included *N,N'*-bis(pyrimidine-4-carbonyl)hydrazine, *N,N'*-bis(1,3-dimethyluracil-5-yl)urea, *N,N'*-bis(1,3-dimethyluracil-6-yl)urea and *N,N'*-bis(2,5,6-trichloro-4-pyrimidinyl)oxamide.

The possibility of using pyrimidine isocyanates as monomers for the synthesis of polyamides carrying pyrimidine rings led to this investigation. At the time the work was started, there was only one example of an isolated pyrimidine having the isocyanate group directly attached to the ring, 6-chloro-1,3-dimethyluracil-5-yl isocyanate, obtained by Taylor and Sowinski (3). In 1971, von Gizycki reported (4) the isolation of 2-isocyanato and 4-isocyanato derivatives of pyrimidines when there were two or more chlorine substituents on the ring.

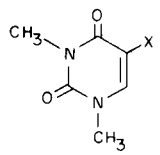
In the current work, 5-isocyanato derivatives of uracil (**2**) and of 1,3-dimethyluracil (**6**) were prepared by decomposition of the uracil-5-carboazides **1** and **5**. Spectral evidence only of the formation of the azide **1** from the corresponding hydrazide was observed by Ross, Goodman, and Baker (5). The preparation of the pure solid azide **1** has now been shown to require a large excess of nitrous acid. The azide **5** was easily obtained from 1,3-dimethyluracil-5-carbohydrazide (**4**). The azides **1** and **5** were identified by analyses and spectra and also by conversion with ethanol to the carbamates **3** and **7**; **3** was previously made from 5-aminouracil and ethyl chloroformate (6).

Heating the azide **1** in xylene or mesitylene and the azide **5** in benzene or toluene gave good yields of the isocyanates **2** and **6**, which were convertible to carbamates **3** and **7**, respectively. Attempts to prepare the isocyanate **2** by pyrolysis of carbamate **3**, which is accessible by a more convenient route than the azide **1**, were impracticable. The isocyanate **2**, on warming with water, gave 5-aminouracil in 87% yield, whereas the isocyanate **6** gave with water a 55% yield of the symmetrical urea, *N,N'*-bis(1,3-dimethyluracil-5-yl)urea (**11**).

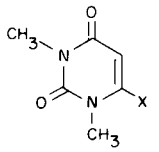
Attempts were made to isolate the 6-isocyanate from the known uracil-6-carboazide (orotyl azide). Since this azide was previously obtained as a hemihydrate (5), it was prepared and analyzed in anhydrous condition for the present work. By decomposing the azide under dry nitrogen in a nujol mull between salt plates heated at 110-125°, the disappearance of the azide absorption in



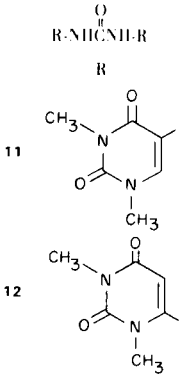
1 X CON_3
2 X NCO
3 X $NHCO_2C_2H_5$



4 X $CONHNH_2$
5 X CON_3
6 X NCO
7 X $NHCO_2C_2H_5$



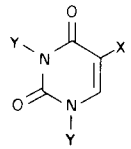
8 X $CONHNH_2$
9 X CON_3
10 X $NHCO_2C_2H_5$



R-NHCNH-R
R
11
12

TABLE I

5-Substituted Derivatives of Uracil and of 1,3-Dimethyluracil



Cpd. No.	X	Y	Method	Yield % (a)	M.p., °C (b)	Ir, cm^{-1}	Formula	Analyses, % Calcd. (Found) C	H	N
1	CON_3	H	B	78	176 (c)	2170-2175 and 2130-2135 (N_3)	$C_5H_3N_5O_3$	33.16 (33.41)	1.67 (1.69)	
2	NCO	H	C	98	318 dec.	2240-2245 (NCO), 1705-1710 and 1660-1665 (CO)	$C_5H_3N_3O_3$	39.23 (39.11)	1.98 (2.35)	31.34 (d) (31.47) (d)
4	$CONHNH_2$	CH_3	A	86	202-203	3265-3270 (NH_2), 3170-3175 (NH), 1705-1710, 1670-1675, 1695-1700 (CO)	$C_7H_{10}N_4O_3$	42.42 (42.14)	4.01 (4.97)	28.27 (28.09)
5	CON_3	CH_3	B	80	105 (e)	2165-2170 (N_3), 1705-1710, 1690-1695, 1700-1705 (CO)	$C_7H_7N_5O_3$	40.19 (40.45)	3.37 (3.54)	
6	NCO	CH_3	C	95	150-151	2240-2245 (NCO), 1710-1715, 1655-1660 (CO)	$C_7H_7N_3O_3$	46.41 (46.38)	3.90 (4.02)	23.20 (22.88)
7	$NHCO_2Et$	CH_3	E	100	186-187	3225-3230 (NH), 1735-1740, 1705-1710, 1665-1670 (CO)	$C_9H_{13}N_3O_4$	47.55 (47.69)	5.76 (5.54)	18.49 (18.74)
17	CH_2Cl	CH_3	F	26	147-148	1705-1710, 1650-1655, 1640-1645 (CO)	$C_7H_9N_2O_2Cl$	44.58 (44.65)	4.81 (4.94)	18.75 (f) (18.69) (f)
18	CH_2NCO	CH_3	G	52	81-82	2255-2260 (NCO), 1680-1710 and 1660-1665 (CO)	$C_8H_9N_3O_3$	49.23 (49.35)	4.65 (4.77)	21.53 (21.34)
19	CH_2NHCO_2Et	CH_3	E	91	105-106	3320-3325 (NH), 1715-1720, 1690-1695, 1665-1670, 1750-1765 (CO)	$C_{10}H_{15}N_3O_4$	49.77 (49.83)	6.27 (6.14)	

(a) Yields before recrystallization. (b) M.p. of pure compound. (c) With explosion. (d) Analysis for O. (e) Rapid bubbling followed by solidification and melting at temperature of **6**. (f) Analysis for Cl.

the infrared and the formation of a strong NCO band at 2265-2270 cm^{-1} were observed. However, the isocyanate could not be isolated because of its very rapid reaction with atmospheric moisture; after exposure of the salt plates to air for one minute, one-fourth of the NCO absorption was gone, and after three minutes about one-half was lost, with the appearance of the absorption of 6-aminouracil. Duynstee observed (7) similar sensitivity to atmospheric moisture in attempting to isolate 2,4-diphenyl-6-isocyanato-*s*-triazine.

Cingolani and coworkers reported (8) that heating uracil-6-carboazide in toluene or xylene gave a relatively insoluble polymer. Repetition of these experiments with the anhydrous azide produced a similar intractable material.

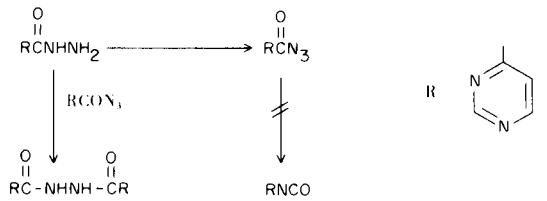
The 1,3-dimethyluracil-6-carboazide (**9**) was prepared from the hydrazide **8** by careful control of reaction conditions. If the amount of nitrous acid was greater than one equivalent, or the reaction time too long, the product was not the azide but the red-violet 6-amino-1,3-dimethyl-5-nitrosouracil. The formation of this product can be explained by assuming decomposition of the azide to the isocyanate and hydrolysis of the isocyanate to 6-amino-1,3-dimethyluracil, which is easily nitrosated to the colored compound (9).

The azide **9** reacted with ethanol to give the carbamate **10**, with wet benzene to give *N,N'*-bis(1,3-dimethyluracil-6-yl)urea (**12**), and with excess water to form the known 6-amino-1,3-dimethyluracil (10). Attempts to isolate the isocyanate by decomposition of azide **9** in anhydrous benzene or toluene were unsuccessful. Spectral evidence of the presence of isocyanate was obtainable, but the very rapid reaction of the isocyanate with adventitious moisture led to the formation of mixtures of the urea **12** and 6-amino-1,3-dimethyluracil.

The fact that isocyanate derivatives of uracil or of 1,3-dimethyluracil could be isolated when the NCO was in the 5- but not in the 6-position may be explained by the fact that the 5-position of uracil is less electron-deficient than the 6-position. For example, uracil-5-carboxylic acid is a weaker acid (p*K* 4.16) than uracil-6-carboxylic acid (p*K* 2.07) (11). Even the presence of two methyl groups on uracil (compound **9**) was not sufficient to retard the very rapid hydrolysis of the 6-NCO group.

Work was also done on the possibility of isolating isocyanates of unoxygenated pyrimidines. Pyrimidine-4-carboazide was known to be convertible to ethyl 4-pyrimidinecarbamate (6), presumably through an isocyanate intermediate. Current efforts to isolate the isocyanate were unsuccessful, however. By heating pyrimidine-4-carboazide in anhydrous benzene, a dark insoluble, high-melting material was obtained. When the carboazide was heated in a nujol mull between sodium bromide plates, the infrared absorption of the azide (at 2140 and 2195 cm^{-1}) disappeared with no evidence of NCO absorption.

In the preparation of pyrimidine-4-carboazide from pyrimidine-4-carbohydrazide and nitrous acid, the observation was made that insufficient acidity or too high a temperature produced *N,N'*-bis(pyrimidine-4-carbonyl)hydrazine (**13**), instead of the azide. Conditions similar to these have been reported to favor the reaction of a freshly formed azide with unchanged hydrazide to give a secondary hydrazide (12a,b).



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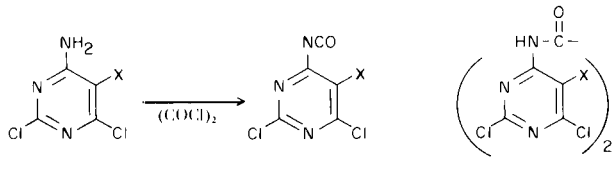
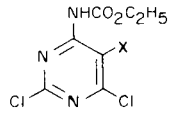
In order to decrease the electron deficiency at the 4-position of the pyrimidine ring, chlorine atoms were introduced at the 2- and 6-positions. The known 4-amino-2,6-dichloropyrimidine was treated with oxalyl chloride by the method used by von Gizycki (4) with 2,5,6-trichloro-4-aminopyrimidine:



14 X = H
X = Cl (Ref. 1)

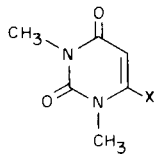


15 X = H
16 X = Cl

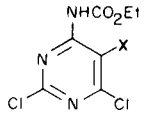
When a toluene solution of 4-amino-2,6-dichloropyrimidine and oxalyl chloride was refluxed, strong NCO absorption in the infrared was developed. This at least indicated the formation of 2,6-dichloro-4-isocyanatopyrimidine. However, attempts to isolate this isocyanate after distillation of excess reactant and solvent gave only 4-amino-2,6-dichloropyrimidine. It was concluded that the desired isocyanate was extremely sensitive to adventitious moisture. By treating the reaction mixture containing the isocyanate with ethanol at room temperature, the new carbamate **15** was obtained in 62% yield. When the ethanol reaction was carried out at reflux, a mixture of **15**

TABLE II

Derivatives of Pyrimidines



Cpd. No.	X	Method	Yield % (a)	M.p., °C (b)	Ir, cm^{-1}	Formula	Analyses, % Calcd. (Found) C	H	N
8	$CONHNH_2$	A	72	212-213	3265-3270 (NH_2), 1680-1700, 1660-1665 (CO)	$C_7H_{10}N_4O_3$	42.42 (42.53)	5.09 (5.13)	28.27 (28.25)
9	CON_3	B	61	58-59	2170-2175 and 2190-2195 (N_3), 1700-1705, 1660-1665, 1685-1690 (CO)	$C_7H_7N_5O_3$	40.19 (39.89)	3.37 (3.30)	
10	$NHCO_2Et$	E	80	166-168	3125-3130 (NH), 1745-1750, 1705-1710, 1665-1670 (CO)	$C_9H_{13}N_3O_4$	47.55 (47.46)	5.76 (5.61)	



15	H	D	46	113-114 (c) at 0.04 mm.		$C_7H_7N_3O_2Cl_2$		30.04 (d) (29.87) (d)	17.79 (17.85)
16	Cl	D	39	85-86	1760-1765 (CO)	$C_7H_6N_3O_2Cl_3$	31.08 (31.47)	2.24 (2.44)	15.53 15.46

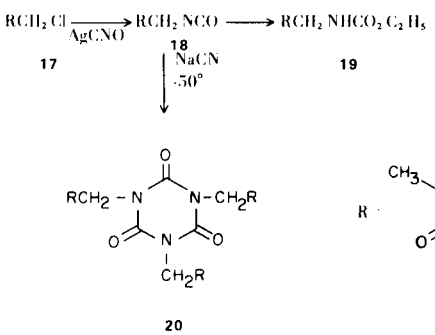
(a) Yield of unrecrystallized material. (b) Of pure substance. (c) B.p. (d) Analysis for Cl.

(20% yield) and of ethyl uracil-6-carbamate (46% yield) was obtained. The latter compound, probably formed by hydrolysis of the labile chlorine atoms (13), was previously obtained from uracil-6-carboazide by Cingolani and coworkers (14).

The 2,5,6-trichloro-4-isocyanatopyrimidine was prepared as described by von Gizycki (4). It was an unstable substance, but convertible without isolation to the ethyl carbamate derivative **16**. From the filtrate was obtained the bisoxamide **14**. Bisoxamides were mentioned as by-products by von Gizycki (4), but were not characterized.

A few tests were made on the possibility of controlled homopolymerization of the pyrimidine isocyanates. Uracil-5-yl isocyanate (**2**) had unpromising solubilities, but 1,3-dimethyluracil-5-yl isocyanate (**6**) seemed more suitable. However, a solution of **6** in dimethylformamide at -10° showed no reaction with sodium cyanide as initiator; lower temperatures could not be used because of too little solubility. Attempted polymerization of **6** with *n*-butyl lithium in toluene at 0° also gave no reaction. In both cases the ethyl carbamate **7** was obtained on quenching the reaction mixture with ethanol. This lack of reactivity of **6** could be attributed to steric inhibition of polymerization due to the carbonyl group *alpha* to the isocyanate group. Steric effects in isocyanate polymerizations were observed by Shashoua and coworkers (15); phenyl isocyanate was polymerizable but *o*-methoxyphenyl isocyanate was not.

Since pyrimidines having the isocyanate group directly on the ring were unsuitable as monomers for polymerization, a homolog of **6** with the NCO on a side-chain was prepared.



5-Chloromethyl-1,3-dimethyluracil (**17**) was prepared by the method used to chloromethylate uracil (16). Compound **17** reacted with silver cyanate to give the tractable isocyanate **18**, which formed with ethanol the carbamate **19**.

When a solution of isocyanate **18** in dimethylformamide at -50° was treated with sodium cyanaide, the trimer **20** was rapidly formed. The ir spectrum of this isocyanurate showed the *s*-triazine-trione carbonyl absorption at 1705-1710 cm^{-1} (17), together with characteristic absorptions for the 1,3-dimethyluracil structure. With the NCO in the side-chain, compound **18** does not have steric inhibition of polymerization, unlike isocyanate **6**. However, compound **18** apparently forms the trimer rather than a potentially more interesting linear homopolymer.

EXPERIMENTAL

Melting points are corrected. Infrared spectra (in potassium bromide) were obtained on Perkin-Elmer 137 or 337 spectrophotometers. Nmr spectra were done on a Varian A-60A spectrometer for the uracil derivatives, and on a Jeol Co. 4-H 100 spectrometer for the unoxygenated pyrimidines, all with TMS as internal standard; the solvent was dimethylsulfoxide-d_6 unless specified. Analyses were performed by Micro-Analysis, Wilmington, Delaware, by Galbraith Laboratories, Knoxville, Tennessee, and by M-H-W Laboratories, Garden City, Michigan.

In Tables I and II are shown certain properties of new compounds and their analyses. Further details are in the lettered sections.

A. Preparation of Carbohydrazides, **4** and **8**.

A mixture of 21.2 g. (0.10 mole) of 1,3-dimethyl-5-carbethoxyuracil (18), 10.0 g. (0.20 mole) of 85% hydrazine hydrate, and 500 ml. of 1-butanol was refluxed for 24 hours. Cooling gave 17.1 g. of **4**, m.p. 201-202°, purified by recrystallization from ethanol: nmr δ 3.23 (s, 3, 3-NCH_3), 3.48 (s, 3, 1-NCH_3), 4.5 (br, 2, NH_2), 8.65 (s, 1, C*H*), 9.7 (br, 1, N*H*).

Compound **8** was made from 1,3-dimethyluracil-6-carboxylic acid (19) by esterifying 13.7 g. (0.75 mole) of this acid with 500 ml. of 1-butanol and 10 ml. of concentrated sulfuric acid. After azeotropic distillation for 48 hours, the mixture was concentrated to 100 ml., poured into 100 ml. of water, made basic (*p*H 8-9) with sodium carbonate, and extracted with ether. The yellow oil obtained by drying and evaporating the ether extracts was dissolved in 300 ml. of 1-butanol and added slowly to 150 ml. of 1-butanol containing 0.20 mole of 85% hydrazine hydrate. After refluxing for 3 hours, 10.7 g. of **8**, m.p. 206-209°, was obtained and purified as for **4**; nmr δ 3.18 (s, 3, 3-NCH_3), 3.27 (s, 3, 1-NCH_3), 4.7 (br, 1, N*H*), 5.72 (s, 1, C*H*); mol. wt. 198 (mass spectrum, 70 eV).

B. Preparation of Carboazides **1**, **5**, and **9**.

To a solution at 0° of 2.35 g. (0.0125 mole) of uracil-5-carbohydrazide (5) in 171 ml. of 0.74 *N* hydrochloric acid was added dropwise over 20 minutes, a solution of 8.7 g. (0.125 mole) of sodium nitrite in 50 ml. of water. After stirring at 0° for 20 minutes, the precipitated azide **1** was filtered, washed successively with cold water, acetone, and ether, and dried at 1 mm. at ambient temperature. Azide **1** showed nmr δ 8.22 (s, 1, C*H*), 11.4 (br, 1, 1-N*H*), 11.7 (br, 1, 3-N*H*).

Azide **5** was prepared by adding dropwise over 15 minutes to a stirred solution of **4** (0.01 mole) and sodium nitrite (0.02 mole) in 40 ml. of water, 3.3 ml. of 6*N* hydrochloric acid. Compound **5** showed nmr δ 3.18 (s, 3, 3-NCH_3), 3.45 (s, 3, 1-NCH_3), 8.63 (s, 1, C*H*).

Azide **9** was prepared by adding to a solution of **8** (0.01 mole) and sodium nitrite (0.01 mole) in 30 ml. of water at -5 to 0° 3.7 ml. of 3*N* hydrochloric acid over 5 minutes. After 5 minutes more at 0°, the azide was isolated; nmr δ 3.10 (s, 3, 3-NCH_3), 3.28 (s, 3, 1-NCH_3), 6.22 (s, 1, C*H*). If the same reaction mixture was allowed to stand at temperatures up to room temperature, a red-violet precipitate of 1,3-dimethyl-5-nitroso-6-aminouracil, dec., 255-257° was slowly formed. Because the decomposition temperature in the literature was 233° (9), the composition of the nitroso compound was confirmed by analysis.

Anal. Calcd. for $C_6H_8N_4O_3$: C, 39.12; H, 4.38. Found: C, 39.37; H, 4.51.

Uracil-6-carboazide (5) was obtained in pure, anhydrous condition by drying to constant weight over phosphorus pentoxide at 70°.

Anal. Calcd. for $C_5H_3N_5O_3$: C, 33.16; H, 1.67; O, 26.50. Found: C, 33.19; H, 1.89; O, 26.47.

When the anhydrous uracil-6-carboazide was refluxed in methanol to prepare the known methyl carbamate (14), a 50% yield of methyl uracil-6-carboxylate (20) was obtained along with a 45% yield of the methyl carbamate. Other examples of nucleophilic attack on this azide have been reported (14).

Pyrimidine-4-carboazide (6) was prepared by standard methods (6,21), provided the reaction temperature was 0-5° and the product immediately extracted with chloroform. Precursors of the azide were pyrimidine-4-carboxylic acid (22), its ethyl ester and hydrazide (23).

C. Decomposition of Azides. Isocyanates **2** and **6**.

A suspension of 1.72 g. (9.5 mmoles) of uracil-5-carboazide (**1**) in 250 ml. of dry xylene was slowly heated to reflux during stirring and under a stream of dry nitrogen. After refluxing for 4 hours and cooling, the product was filtered and washed with anhydrous ether to give 1.44 g. of crude **2**. Analytical purity was obtained only by sublimation of 0.2-0.3 mm., first rapidly at 180-240°, then slowly at 185-190°. The solubility of **2** was too limited for an nmr determination.

Attempts to prepare isocyanate **2** by heating carbamate **3** showed that at a pressure of 5 mm., **3** sublimed unchanged at 180-183°, while at 180-225° (5 mm.) or at 225° (760 mm.) the sublimate consisted of difficultly separable mixtures of **3** and **2**. A carbamate of a non-oxygenated pyrimidine, ethyl 2-pyrimidinyl carbamate, also sublimed quantitatively without decomposition at 110-125° (5 mm.).

Isocyanate **6** was prepared by refluxing a solution of 1.24 g. (5.9 mmoles) of azide **5** in 125 ml. of anhydrous benzene for 2 hours under dry nitrogen. After concentrating the solution to 25 ml., the product was precipitated as long needles by adding 100 ml. of heptane. Filtration under anhydrous conditions and recrystallization from dry benzene-heptane (1:5) gave pure **6**; nmr (deuteriochloroform) δ 3.43 (s, 6, 1, 3-NCH_3), 7.10 (s, 1, C*H*). Traces of moisture led to contamination by the less soluble urea **11**.

Many attempts to prepare uracil-6-yl isocyanate by heating a suspension of anhydrous uracil-6-carboazide in anhydrous xylene or mesitylene gave difficultly soluble yellow powders which were unmelted below 350°, showed no azide nor NCO absorption in the infrared, and gave multiplet C_5-H absorptions in the nmr.

Neither column chromatography nor Soxhlet extraction yielded a homogeneous substance, and the solubility was too small for a molecular weight determination.

Heating pyrimidine-4-carboazide in anhydrous benzene until gas evolution ceased gave an insoluble, reddish-brown solid, melting above 360°.

D. Reaction of Aminopyrimidines with Oxalyl Chloride. Compounds **15** and **16**.

A 0.02 mole sample of 4-amino-2,6-dichloropyrimidine (24), obtained from 2,4,6-trichloropyrimidine (25), was treated with excess oxalyl chloride in toluene according to the procedure of von Gizycki (4). After 7 hours of refluxing, the reaction mixture showed a strong isocyanate absorption at 2245-2250 cm^{-1}. However, distillation of excess oxalyl chloride at 30 mm. and evaporation of the remaining solvent at ambient temperature gave a 90% recovery of 4-amino-2,6-dichloropyrimidine.

When another such reaction mixture, after removal of oxalyl chloride, was treated with 20 ml. of ethanol and refluxed for 16 hours, a precipitate of 0.8 g. (20%) of 6-ethoxycarbamoyluracil, m.p. 338-339°, was obtained, identical in nmr and analyses with the compound of Cingolani and coworkers (14).

Evaporation of the ethanol filtrate from the 6-ethoxycarbamoyluracil gave a 46% yield of 2,6-dichloro-4-ethoxycarbamoylpyrimidine, **15**, a colorless liquid, b.p. 113-114° (0.04 mm.); nmr (deuteriochloroform) δ 1.33 (t, 3, J = 6 Hz, -C*H*$_3$), 4.31 (q, 2, J = 6 Hz, -C*H*$_2$), 8.07 (s, 1, -N*H*), 7.99 (s, 1, -5C*H*).

By treating 0.02 mole of 4-amino-2,5,6-trichloropyrimidine (26) with oxalyl chloride in toluene as described (4), an unstable isocyanate was formed; its NCO absorption disappeared on standing overnight in a vacuum desiccator over phosphorus pentoxide.

Another such reaction mixture was treated with 20 ml. of ethanol after removal of oxalyl chloride, and the solution allowed to stand for 15 hours. Removal of solvents and distillation of the residual syrup at 175° (0.5 mm.) gave a solid distillate which was separated by extraction with hot ethanol into the more soluble 4-ethoxycarbamoyl-2,5,6-trichloropyrimidine, **16** (39%) and the less soluble *N,N'*-bis(2,5,6-trichloro-4-pyrimidinyl)oxamide, **14** (11%). Carbamate **16** was recrystallized from ethanol; nmr δ 1.35 (t, 3, J = 6 Hz, -C*H*$_3$), 4.33 (q, 2, J = 6 Hz, -C*H*$_2$), 7.75 (s, 1, -N*H*).

E. Carbamates **7**, **10**, and **19**.

1,3-Dimethyl-5-ethoxycarbamoyluracil (**7**), prepared from either **5** or **6**, was recrystallized from ethanol; nmr δ 1.22 (t, 3, J = 7 Hz, C*H*$_3$), 3.22 (s, 3, 3-NC*H*$_3$), 3.33 (s, 3, 1-NC*H*$_3$), 4.10 (q, 2, J = 7 Hz, C*H*$_2$), 9.90 (s, 1, C*H*).

1,3-Dimethyl-6-ethoxycarbamoyluracil (**10**), prepared from **9**, was recrystallized from benzene; nmr δ 1.28 (t, 3, J = 7 Hz, C*H*$_3$), 3.18 (s, 3, 3-NC*H*$_3$), 3.37 (s, 3, 1-NC*H*$_3$), 4.22 (q, 2, J = 7 Hz, C*H*$_2$), 5.90 (s, 1, C*H*), 9.7 (br, 1, N*H*).

1,3-Dimethyl-5-ethoxycarbamoylmethyluracil (**19**), prepared from the isocyanate, was recrystallized from benzene-heptane (1:3); nmr (deuteriochloroform) δ 1.22 (t, 3, C*H*$_3$), 3.33 (s, 3, 3-NC*H*$_3$), 3.38 (s, 3, 1-NC*H*$_3$), 3.92-4.27 (m, 4, C*H*$_2$O and C*H*$_2$N), 5.6 (br, 1, N*H*), 7.33 (s, 1, C*H*).

F. 5-Chloromethyl-1,3-dimethyluracil (**17**).

The procedure, using 0.05 mole of 1,3-dimethyluracil, was the same as for uracil (16) with the omission of hydrogen chloride gas and the continuation of the stirring for 12 hours. The product was recrystallized from benzene-hexane (1:4); nmr (deuteriochloroform) δ 3.50 (s, 3, 3-NC*H*$_3$), 3.58 (s, 3, 1-NC*H*$_3$), 4.58 (s, 2, C*H*$_2$), 7.57 (s, 1, C*H*).

G. 1,3-Dimethyluracil-5-yl isocyanate (**18**).

A suspension of 0.90 g. (6 mmoles) of dry, freshly prepared silver cyanate and 0.95 g. (5 mmoles) of **17** in 100 ml. of anhydrous benzene was refluxed for 5 hours during stirring. After cooling, filtration of the salts, concentration of the filtrate to 25 ml. and pouring it into 75 ml. of dry hexane, a precipitate of 0.51 g. of isocyanate, m.p. 73-82°, was obtained. Recrystallization from dry hexane gave the pure isocyanate; nmr (deuteriochloroform) δ 3.33 (s, 3, 3-NC*H*$_3$), 3.43 (s, 3, 1-NC*H*$_3$), 4.23 (s, 2, C*H*$_2$), 7.30 (s, 1, C*H*).

N,N'-Bis(1,3-dimethyluracil-5-yl)urea (**11**).

A suspension of 0.45 g. of the isocyanate **6** in 25 ml. of water was stirred at room temperature for 20 minutes, 50 ml. of water was added, and the solution brought to boiling. Dimethylformamide was added to just dissolve the product and the mixture was filtered hot and cooled. The precipitate of pure **11** (0.23 g., 55%) melted at 335° with decomposition; ir 3255-3260 (NH), 1705-1710 and 1655-1660 (ring C=O), 1665-1670 cm^{-1} (urea C=O).

Anal. Calcd. for $C_{13}H_{16}N_6O_5$: C, 46.42; H, 4.80; N, 24.99. Found: C, 46.38; H, 4.71; N, 24.81.

N,N'-Bis(1,3-dimethyluracil-6-yl)urea (**12**).

A solution of 1.27 g. of the azide **9** in 100 ml. of water-saturated benzene was refluxed for 1 hour. The resulting insoluble solid consisted of 0.79 g. (78%) of **12**, which decomposed at 315-316° after recrystallization from water-dimethylformamide (1:2); ir 3205-3210 (NH), 1705-1710 and 1665-1670 (ring C=O), 1690-1695 cm^{-1} (urea C=O).

Anal. Calcd. for $C_{13}H_{16}N_6O_5$: C, 46.42; H, 4.80. Found: C, 46.33; H, 4.99.

N,N'-Bis(pyrimidine-4-carbonyl)hydrazine (**13**).

To a solution of 1.0 g. of pyrimidine-4-carbohydrazide (23) in 11 ml. of glacial acetic acid at 10° was added dropwise a solution of 1.32 g. of sodium nitrite in 3.30 ml. of water, keeping the temperature at 10-15°. On addition of 20 ml. of water, 0.78 g. of **13** precipitated, which was recrystallized from 95% ethanol to give 0.43 g. (48%) of pure **13**, m.p. 220-221°; ir 1660-1710 (C=O), 3340-3370 (NH); nmr δ 8.11 (d, 1, J = 5 Hz, -5C*H*), 9.14 (d, 1, J = 5 Hz, -6C*H*), 9.41 (s, 1, -2C*H*), 11.12 (s, 1, -N*H*).

Anal. Calcd. for $C_{10}H_8N_6O_2$: C, 49.18; H, 3.30; N, 34.41. Found: C, 49.08; H, 3.20; N, 34.06.

N,N'-Bis(2,5,6-trichloro-4-pyrimidinyl)oxamide (**14**).

This by-product, isolated with **16**, melted at 251-252° after thorough washing with hot ethanol; ir 1730-1735 (C=O); nmr (deuteriochloroform) δ 11.05 (b, 1, -N*H*).

Anal. Calcd. for $C_{10}H_2N_6O_2Cl_6$: C, 26.64; H, 0.45; Cl, 47.19. Found: C, 26.69; H, 0.70; Cl, 47.60.

1,3,5-Tris(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-5-pyrimidinylmethylene)-2,4,6-trioxo-*s*-trihydrotriazine (**20**).

To a solution of 0.98 g. (5 mmoles) of 1,3-dimethyluracil-5-ylmethyl isocyanate in 10 ml. of dry dimethylformamide at -50° under nitrogen was added 0.2 ml. of a 0.72% solution of sodium cyanide in dimethylformamide. After 15 minutes of stirring, the solution was poured into 250 ml. of methanol to precipitate the product (0.50 g., 51%). Solution in dimethylformamide and reprecipitation with methanol gave the isocyanate trimer, unmelted by 325°, as a methanol complex: ir 1705-1710 (C=O) and 1630-1655 (uracil C=O); nmr (deuteriochloroform) δ 3.32 (s, 9, 3-NC*H*$_3$), 3.43 (s, 12, 1-NC*H*$_3$ and C*H*$_3$O), 4.85 (s, 7 C*H*$_2$ and O*H*),

7.47 (s, 3, CH).

Anal. Calcd. for $C_{24}H_{27}N_9O_9 \cdot CH_3OH$: C, 48.62; H, 5.02; N, 20.41. Found: C, 48.49; H, 4.78; N, 20.60.

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