was washed with tetrahydrofuran (20 ml.), and the hygroscopic product (IIIa) was dried *in vacuo* over phosphorus pentoxide at 78° for 18 hr.: yield, 170 mg.; *this solid decomposes rapidly* without melting above 200°; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 7, 320 (15.3), and at pH 13, 319 (15.7); $\bar{\nu}_{max}$ in cm.$^{-1}$ 3435 (broad, OH or NH), 2995, 2965, 2920, and 2860 (aliphatic CH), 1630, 1605, 1555, and 1540 (C=C, C=N).

Anal. Calcd. for $C_6H_3NaN_5O$: C, 38.10; H, 4.23; N, 37.05. Found: C, 37.91; H, 4.10; N, 37.17.

The Condensation of Acetylacetone with IV.—A solution of 2-allyl-5-aminotetrazole (IV, 1.0 g.) in toluene (25 ml.) containing acetylacetone (1.0 ml.) and piperidine (2 drops) was refluxed under a water separator for 21 hr. During the reflux period 20 ml. of the toluene escaped. Addition of petroleum ether (25 ml.) to the remaining liquid deposited 890 mg. of unreacted IV. The filtrate from IV was evaporated to a small volume, and the residue was distilled under high vacuum to give IIIc: yield, 100 mg.; λ_{max} in mμ at pH 7, 318, and at pH 13, 319; $\bar{\nu}_{max}$ in cm.$^{-1}$ (contact film) 3420, 3340, and 3220 (OH), 2990, 2940, and 2860 (aliphatic CH), and 1630, 1600, 1550, and 1540 (C=C, C=N).

Anal. Calcd. for $C_9H_{13}N_5O$: C, 52.20; H, 6.28; N, 33.80. Found: C, 51.84; H, 5.65; N, 33.77.

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Studies on the Azidoazomethine–Tetrazole Equilibrium. II. 4-Azidopyrimidines[1]

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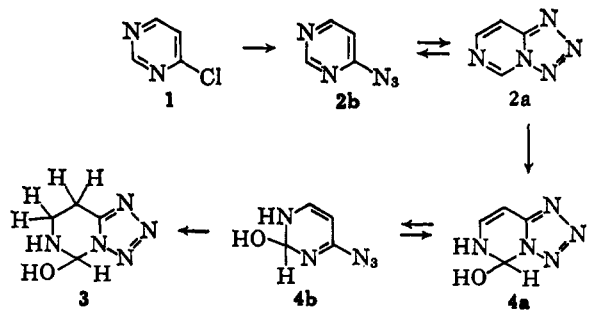
The preparation of a number of compounds for the study of the 4-azidopyrimidine–tetrazolo[1,5-*c*]pyrimidine equilibrium by means of infrared and proton magnetic resonance spectrometry is described; equilibrium constants were calculated from the ratio of the amount of the azido tautomer to that of the tetrazolo tautomer. The interaction of 4-chloropyrimidine hydrochloride (**1**) and sodium azide gave a mixture of 4-azidopyrimidine (**2b**) and tetrazolo[1,5-*c*]pyrimidine (**2a**) in which the latter is the major tautomer. This mixture readily combined with water to give a covalent hydrate, identified as 5,6-dihydro-5-hydroxytetrazolo[1,5-*c*]pyrimidine (**4a**). In the 5-amino-4-azido-6-chloropyrimidine–8-amino-7-chlorotetrazolo[1,5-*c*]pyrimidine system (**6**) the tetrazolo tautomer (**6a**) is the major form in the solid state, but only the azido form can be detected in a trifluoroacetic acid solution, a result of protonation. Also, conversion of the amino group of **6** to either an ethoxymethyleneamino or an acetamido group causes tetrazole destabilization to give mainly the azido tautomers. The presence of an acetyl or trifluoroacetyl group on the amino group of the 5-amino-4,6-diazidopyrimidine–8-amino-7-azidotetrazolo[1,5-*c*]pyrimidine system favors the (di)azido tautomers. The value of the equilibrium constant for the N-(4-amino-6-azido-5-pyrimidinyl)acetamide–8-acetamido-7-aminotetrazolo[1,5-*c*]pyrimidine system (**13**) in dimethyl sulfoxide-d_6 is larger than that of systems **11** and **12**, which suggests that the amino group of **13** is involved in hydrogen bonding.

Although the reaction of chloroazomethine heterocycles with sodium azide to give either azido derivatives or the tautomeric tetrazolo derivatives is well documented,[2] the investigation of the azidoazomethine–tetrazole equilibrium has only recently received attention.[3] In a previous paper we reported that **6** existed mainly as the 8-amino-7-chlorotetrazolo[1,5-*c*]pyrimidine (**6a**) and that **7** existed mainly as the 4-azido-6-chloro-5-ethoxymethyleneaminopyrimidine (**7b**).[3c] This observation prompted the synthesis of additional compounds of this system and a study of the effect of solvent and of certain electron-donating and electron-attracting groups on the 4-azidopyrimidine–tetrazolo-[1,5-*c*]pyrimidine equilibrium. As in a recent paper on the 2-azidopyrimidine–tetrazolo[1,5-*a*]pyrimidine equilibrium,[3f] the infrared and proton magnetic resonance spectra were used to detect and to determine the relative amounts of each tautomer in a given solvent.



Treatment of freshly sublimed 4-chloropyrimidine hydrochloride (**1**) with sodium azide in N,N-dimethylformamide at 85° gave a 23% yield of system **2**. In contrast to the isomeric 2-azidopyrimidine–tetrazolo-[1,5-*a*]pyrimidine system,[3f,4] **2** readily combined with water to give a covalent hydrate. When water was involved in the work-up, the hydrate was the only product isolated from the reaction of the hydrochloride of **1** with sodium azide in dimethyl sulfoxide at room temperature; it was assigned the structure **4a**, which would result from the addition of water to the 5,6 C=N bond of **2a**.[5] The structure of **4a** was indicated by (1) elemental analyses, (2) a molecular weight de-

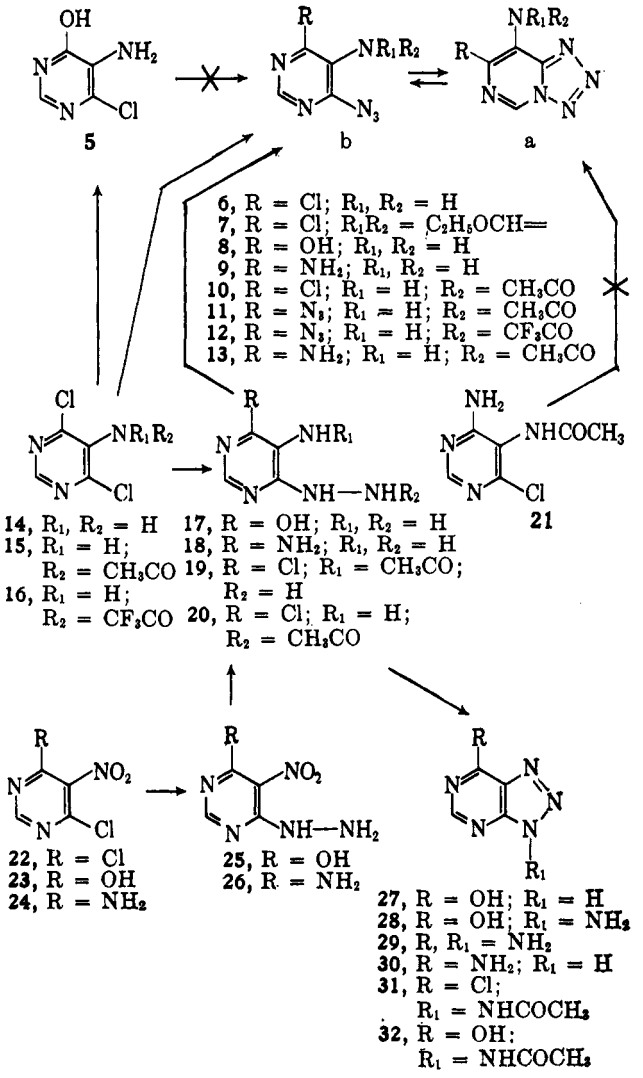
(1) *This investigation was supported by funds from the C. F. Kettering* Foundation and the Cancer Chemotherapy National Service Center, National Cancer Institutes, National Institutes of Health, Contract No. PH-43-64-51.

(2) F. R. Benson, L. W. Hartzel, and E. A. Otten, *J. Am. Chem. Soc.*, **76**, 1858 (1954), and references therein.

(3) (a) J. H. Boyer and E. J. Miller, Jr., *ibid.*, **81**, 4671 (1959); (b) J. H. Boyer and H. W. Hyde, *J. Org. Chem.*, **25**, 458 (1960); (c) C. Temple, Jr., R. L. McKee, and J. A. Montgomery, *ibid.*, **27**, 1671 (1962). (d) Y. N. Sheinker, I. Ya. Postovskii, N. P. Bednyagina, L. B. Senyavina, and L. F. Lipatova, *Dokl. Akad. Nauk. SSSR*, **141**, 1388 (1961); (e) I. Ya. Postovskii and I. N. Goncharova, *Zh. Obshch. Khim.*, **33**, 2334 (1963); (f) C. Temple, Jr., and J. A. Montgomery, *J. Org. Chem.*, **30**, 826 (1965).

(4) K. Shirakawa, Japanese Patent 777 (Feb. 6, 1957); *Chem. Abstr.*, **52**, 4699*h* (1958).

(5) In addition a solid sample of **2** in a vial was converted to **4a**—apparently by the absorption of atmospheric moisture.



termination, (3) strong absorption in the 265-mμ region of the ultraviolet spectrum, which eliminated the structure that would result from the addition of water to the 7,8 C=C bond,[6] (4) the infrared spectrum in which tetrazole ring absorption bands were present between 1100–1000 cm.$^{-1}$ [3a] and in which azido absorption bands were absent, and (5) the proton magnetic resonance spectrum in dimethyl sulfoxide-d_6, which exhibits five different proton signals. The chemical shifts (in p.p.m. on the τ-scale), multiplicity, and apparent coupling constants (c.p.s.) are summarized in Table I.[7] The appearance of the 7-proton signal as a quartet is attributed to the coupling of this proton with the 8-proton and with the proton on the adjacent 6-nitrogen. As expected, the 7-proton appeared as a doublet after the 6-NH proton was exchanged for deuterium by the addition of D_2O. The covalent hydration of **2a** is probably due to the positive character of the 5-carbon caused by the electron-attracting tetrazole ring.[3a,9] The dehydration of **4** was attempted by sublimation under high vacuum at 120° but the melting point (122–125°) of the sublimate indicated that **2** was not obtained. Catalytic hydrogenation of **4a** with a palladium-on-charcoal catalyst reduced the 7,8 C=C bond to give **3**. The structure of **3** is consistent with its elemental analyses and with the transparency of the 260-mμ region of its ultraviolet spectrum.[6] In the p.m.r. spectrum of **3** in dimethyl sulfoxide-d_6 the spin–spin coupling patterns for the hydrogens at the 6-, 7-, and 8-positions indicated that this part of the spectrum is an A_2B_2X system. The assignments of the protons for this spectrum are presented in Table I.

Next, the preparation of some disubstituted derivatives of **2**, such as systems **6–13**, was attempted. Only the synthesis of systems **8** and **9** was unsuccessful. The first route aimed at the preparation of **8** involved treatment of 4,6-dichloro-5-nitropyrimidine (**22**) with hot 98% formic acid. This caused hydrolysis of one of the chloro groups of **22** to give 4-chloro-6-hydroxy-5-nitropyrimidine (**23**) in about 73% yield. The same yield of **23** was obtained when the reactants were refluxed either for 30 min. or for 1 hr., but using the shorter time a 20% yield of **22** was recovered and using the longer period an appreciable amount of 4,6-dihydroxy-5-nitropyrimidine was produced. Reaction of **23** with two or more equivalents of methanolic hydrazine at room temperature deposited the free base of 4-hydrazino-6-hydroxy-5-nitropyrimidine (**25**) in 88% yield. Reduction of the nitro group of **25** with a Raney nickel catalyst gave 5-amino-4-hydrazino-6-hydroxypyrimidine (**17**), usually contaminated with 4,5-diamino-6-hydroxypyrimidine resulting from the reductive cleavage of the hydrazino group of **17**.[10] Although nitrosation of **17** could give at least five products, the main product was expected to be system **8**, since the previous nitrosation of 5-amino-6-chloro-4-hydrazinopyrimidine gave mainly the tetrazolo[1,5-*c*]pyrimidine **6a**.[3c] The only identifiable product of this reaction, however, was the known 7-hydroxy-3H-*v*-triazolo[4,5-*d*]pyrimidine (**27**).[11] The formation of **27** from the 4,5-diamino-6-hydroxypyrimidine present as an impurity was expected, but the yield of **27** was high enough to indicate that 3-amino-7-hydroxy-3H-*v*-triazolo[4,5-*d*]pyrimidine (**28**) was initially formed and reacted further with nitrous acid to give **27** (see below).

The second route attempted for the preparation of **8** involved treatment of 5-amino-4,6-dichloropyrimidine (**14**) with hot 98% formic acid. As with **22** this resulted in the hydrolysis of one chloro group to give 5-amino-4-chloro-6-hydroxypyrimidine (**5**). However, this chloro group was more inert than expected in that **5** did not react with excess hydrazine at 100° or with sodium azide in N,N-dimethylformamide at 160°.[12]

The attempted synthesis of the diamino system **9** started with the treatment of 4-amino-6-chloro-5-nitro-

(6) L. F. Cavalieri and A. Bendich [*J. Am. Chem. Soc.*, **72**, 2587 (1950)] reported that 4,5-dihydro-2,6-dihydroxypyrimidine showed no maximum in its ultraviolet spectrum.

(7) The assignments of the CH protons are substantiated by the order in which the proton signals appear in the p.m.r. spectrum of pyrimidine itself. See ref. 8.

(8) (a) S. Grcnowitz and R. A. Hoffman, *Arkiv Kemi*, **16**, 459 (1961); (b) G. S. Reddy, R. T. Hobgood, Jr., and J. H. Goldstein, *J. Am. Chem. Soc.*, **84**, 336 (1962).

(9) A. Albert and G. B. Barlin, *J. Chem. Soc.*, 5156 (1963).

(10) G. D. Daves, Jr., R. K. Robins, and C. C. Cheng, *J. Am. Chem. Soc.* **84**, 1724 (1962).

(11) R. O. Roblin, Jr., J. O. Lampen, J. P. English, Q. P. Cole, and J. R. Vaughan, Jr., *ibid.*, **67**, 290 (1945).

(12) Previously, replacement of the chloro group in similar pyrimidines containing electron-donating groups in the 5- and 6-positions was successful in one case (ref. 13) and unsuccessful in another (ref. 14).

(13) E. C. Taylor, J. W. Barton, and W. W. Paudler, *J. Org. Chem.*, **26**, 4961 (1961).

(14) M. H. Krackov and B. E. Christensen, *ibid.*, **26**, 2677 (1963).

TABLE I

EQUILIBRIUM CONSTANTS AND PM.R. SPECTRAL ASSIGNMENTS[a]

System	Solvent[b]	% concn. (w./v.)	K_T[c]	τ-values (multiplicity) (J in c.p.s.)[d] — Tetrazolo tautomer					Azido tautomer			
3	DMSO-d_6	10	~0	8-CH_2	7-CH_2	5-H	6-NH	5-OH				
				6.87	6.50	1.98	1.98	−4.52				
4[e]	DMSO-d_6	10	~0	8-H	7-H	5-H	6-NH	5-OH[f]	5-H	6-H	2-H	
				4.17 (d)	2.55 (q)	1.52 (s)	−0.60 (d)	−5.00 (s)	...	...	...	
				J_{78} = 9.3	J_{67} = 11.7							
	CF_3COOH	10	∞	...	...	...	...	...	2.63 (q)	1.30 (q)	0.80	
									J_{25} = 1.50		J_{23} = 1.00	
									J_{56} = 6.95			
6	DMSO-d_6	20	~0	8-NH_2	5-H				5-NH_2	2-H		
				2.94	0.54				...	...		
	CF_3COOH	10	∞	...	...				g	1.51		
	Pyridine	10	h	2.00	0.55				...	...		
11	DMSO-d_6	10	0.94[i]	8-CH_3CO	5-H	8-NH			5-CH_3CO	2-H	5-NH	
				7.87	−0.10	−0.15			8.00	1.35	0.53	
	CF_3COOH	10	∞	...	...	...			7.55	1.20	g	
	Acetone-d_6	<3	3.1[i]	7.79	0.07	6.36[j]			7.95	1.43	6.36[j]	
	Pyridine	6.7	2.7[i]	7.65	k	k			7.72	k	k	
12	DMSO-d_6	10	1.6[l]	5-H	8-NH				2-H	5-NH		
				−0.20	−1.40[j]				1.23	−1.40[j]		
	CF_3COOH	10	∞	...	...				1.14	g		
	$CDCl_3$	<5	∞	...	...				1.41	2.65		
13	DMSO-d_6	10	3.3[i]	8-CH_3CO	7-NH_2	8-NH	5-H		5-CH_3CO	4-NH_2	2-H	5-NH
				7.90	4.16	0.52	0.35		8.00	6.87	1.90	1.10
	CF_3COOH	10	∞	...	...	...	...		7.57	k	1.52	k
	Acetone-d_6	<2.5	h	...	...	...	...		k	6.33	1.88	m
	Pyridine	5	h	...	...	...	...		7.78	k	1.55	−0.21

[a] Spectra were obtained on a Varian A-60 spectrometer using tetramethylsilane as internal reference. Probe temperature was about 38°. [b] DMSO-d_6 = dimethyl sulfoxide-d_6. [c] The estimated mean deviation in K_T was less than 10%. [d] s = singlet, d = doublet, q = quartet. Apparent values of J. [e] Dilution of a 10% solution of **4** in DMSO-d_6 to 6.7% with CF_3COOH gave a mixture containing about equal amounts of the tetrazolo and azido tautomers. [f] When this solution was degassed with helium for 5 min., this peak shifted to τ −2.30. [g] Exchanged with solvent. [h] Only one tautomer detected, possibly because of solvent interference. [i] Ratio of the integrated intensities of the methyl signal from **11a** to that of **11b**. [j] Exchanged with NH of other tautomer. [k] Position uncertain because of solvent interfence. [l] Ratio of the integrated intensities of the 2-H proton signal of **12a** to that of the 5-H proton signal of **12b**. [m] Not detected.

pyrimidine (**24**)[15] with methanolic hydrazine to give 4-amino-6-hydrazino-5-nitropyrimidine (**26**). Nitrosation of 4,5-diamino-6-hydrazinopyrimidine (**18**), obtained by the catalytic reduction of the nitro group of **26**, produced a mixture from which only 3,7-diamino-3H-*v*-triazolo[4,5-*d*]pyrimidine (**29**) was obtained pure. Further nitrosation of **29** provided **30**. The formation of **28** and **29** must result from the interaction of nitrous acid with the amino groups instead of hydrazino groups of **17** and **18**. This implies that the amino group of **17** and **18** is at least as basic as the hydrazino group and is more basic than the amino group of 5-amino-4-chloro-6-hydrazinopyrimidine in which preferential attack is on the hydrazino group.[3c]

The preparation of system **10** was attempted by the reaction of N-(4,6-dichloro-5-pyrimidinyl)acetamide (**15**)[16] with excess aqueous hydrazine followed by nitrosation of the resultant compound. The nitrosation reaction, however, gave 3-acetamido-7-chloro-3H-*v*-triazolo[4,5-*d*]pyrimidine (**31**) instead of **10**. The compound initially believed to be **19** was found to be identical with the known 4-(2-acetylhydrazino)-5-amino-6-chloropyrimidine (**20**),[16] which on nitrosation can give only **31**. Compound **19** must be the initial product in the reaction of **15** with hydrazine, but under the conditions of the reaction the acetyl group of **19** rearranges from the amino group to the 2-position of the hydrazino group.[17] **31** was unstable[18] and was converted to 3-acetamido-7-hydroxy-3H-*v*-triazolo[4,5-*d*]-pyrimidine (**32**).

The successful preparation of **10** in 29% yield involved the direct interaction of **15** with sodium azide in N,N-dimethylformamide. The action of excess sodium azide on **15** replaced both chloro groups to give system **11** in 59% yield. Surprisingly, **11** is stable in the solid state and in most solutions at room temperature, except aqueous sodium hydroxide. In 0.1 *N* sodium hydroxide **11** decomposed to an unidentified nonultraviolet-absorbing material, indicating that opening of the pyrimidine ring occurred in this medium.[19]

Similarly reaction of N-(4,6-dichloro-5-pyrimidinyl)-trifluoroacetamide (**16**)[16] with sodium azide gave **12**, also a stable compound. The first attempt to prepare system **13** was made by reaction of **21** with sodium azide. The presence of the acetyl group on the 5-amino group was expected to increase the reactivity of the chloro group but no reaction occurred between **21** and sodium azide in N,N-dimethylformamide at 135°. The controlled reduction of **11** with a palladium-on-charcoal catalyst, however, gave a 47% yield of **13** and only a 15% yield of N-(4,6-diamino-5-pyrimidinyl)acetamide.

Discussion

Equilibrium constants and proton magnetic resonance spectra assignments for some of the systems in this study are given in Table I. Absorption in either the

(15) W. R. Boone, W. G. M. Jones, and G. R. Ramage, *J. Chem. Soc.*, 99 (1951).

(16) C. Temple, Jr., R. L. McKee, and J. A. Montgomery, *J. Org. Chem.* **28**, 923 (1963).

(17) R. A. Abramovitch and K. Schofield [*J. Chem. Soc.*, 2331 (1955)] reported that acyl groups migrated from the hydrazino group to the amino group in *o*-hydrazinoanilines under acidic conditions.

(18) The instability of similar compounds has been noted. See Y. F. Shealy, J. D. Clayton, C. A. O'Dell, and J. A. Montgomery, *J. Org. Chem.*, **27**, 4518 (1962).

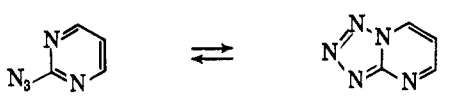
(19) The pyrimidine ring of tetrazolo[1,5-*a*]pyrimidine is opened in aqueous sodium hydroxide. See ref. 3f.

TABLE II
INFRARED ABSORPTION SPECTRA[a,b]

System	Solvent[c]	% concn. (w./v.)	Azido bands (2200–2100 cm.$^{-1}$)[d]	Tetrazolo bands (1100–1000 cm.$^{-1}$)[d]
2	KBr	..	2155 (w), 2135 (w)	1080 (s), 1040 (w), 1015 (m)
	DMF	5	2160 (w)	*e*
	CH_3OH	10	2165 (vw), 2140 (w)	*e*
3	KBr	..	*h*	1100 (w), 1080 (w), 1060 (m), 1035 (w), 1020 (w)
	CF_3COOH	5	*h*	*f*
4	KBr	..	*h*	1095 (w), 1060 (w), 1040 (w), 1018 (w)
	CF_3COOH	5	2140 (m)	*f*
6	KBr	..	*h*	1095 (w), 1070 (s), 1060 (s), 1000 (s)
	DMSO	5	*h*	*e*
	CF_3COOH	5	2160 (s)	*f*
7	*i*	..	2150 (s)	1100 (w), 1060 (w), 1010 (w)
	$CHCl_3$	10	2145 (s)	1105 (w), 1080 (w), 1000 (m)
10	KBr	..	2160 (s)	1080 (vw), 1035 (vw), 1010 (vw)
11	KBr	..	2160 (s)	1080 (vw), 1040 (vw), 1010 (w)
	DMF	5	2155 (s)	*f*
	DMSO	5	2145 (s)	*e*
	$CHCl_3$	*g*	2155 (s)	*h*
12	KBr	..	2175 (s), 2160 (s)	*h*
	$CHCl_3$	6.7	2160 (s), 2105 (m)	1090
13	KBr	..	2135 (s)	1090 (vw), 1065 (vw), 1040 (vw), 1010 (w)
	DMF	3	2140 (s)	*f*

[a] Spectra were determined with a Perkin-Elmer, Model 221, spectrophotometer. An Irtran-2, fixed-thickness cell was used for the dimethyl sulfoxide and trifluoroacetic acid solutions. [b] vw = very weak, w = weak, m = medium, and s = strong. [c] KBr = potassium bromide disk, DMF = N,N-dimethylformamide, and DMSO = dimethyl sulfoxide. [d] Some bands in the given region may not be due to the designated group absorption. [e] Solvent interference. [f] This region not determined. [g] Saturated solution. [h] No band(s) present. [i] Contact film.

azido region (2200–2100 cm.$^{-1}$) or the tetrazole region (1100–1000 cm.$^{-1}$) of the infrared spectrum of a number of systems provided evidence for the tautomer assignment; this data is presented in Table II.[3a] The infrared spectrum of **2** in the solid state and in methanol and N,N-dimethylformamide solutions showed that both **2b** and **2a** were present, but the weak azido band(s) indicated that **2a** was the major tautomer of the mixture. Previously we studied[3f] the spectra of the 2-azidopyrimidine–tetrazolo[1,5-*a*]pyrimidine system (**33**) and could detect only **33a** in the solid state and in dimethyl sulfoxide solution, implying that **33a** is more stable relative to **33b** than **2a** is relative to **2b**.[20] Apparently, however, the covalent hydration of **2a** to yield **4a** resulted in tetrazolo stabilization as the infrared spectrum of **4** in the solid state exhibited no azido bands. In trifluoroacetic acid protonation of the 6-nitrogen of **4a** resulted in electron withdrawal from the tetrazole ring, which favored the formation of the azido form in which the azido group is electron donating.[3f,21] Reduction of the 7,8 C=C bond of **4a** to give **3**, however, prevented the transmission of the effect of protonation, and the infrared spectrum of **3** in trifluoroacetic acid was transparent in the azido absorption region.



33b **33a**

In the potential 7,8-disubstituted tetrazolo[1,5-*c*]-pyrimidines the effect of solvents[22] as well as the electronic property of groups on tetrazole destabilization was evident.[3a-c] For system **6** only the tetrazolo tautomer **6a** was found in the solid state and in dimethyl sulfoxide solution. As in most of the other systems, only the azido form of **6** was detected in trifluoroacetic acid. Here protonation of either the 6-nitrogen or the 8-amino group of **6a** would probably result in the formation of the azido form. The effect of diminishing the electron-donating ability of the 8-amino group of **6a** was demonstrated by the preparation of systems **7** and **10** in which **7b** and **10b** were the major tautomers.

In systems **11** and **12** one of the two potential azido groups exists as such under all conditions. Except for **11** in dimethyl sulfoxide (K_T = 0.94), the diazido tautomers **11b** and **12b** appeared to be favored over the tetrazolo tautomers **11a** and **12a** in all solvents (see Table I). As expected the trifluoroacetyl group in **12** had a greater effect on tetrazole destabilization than the acetyl group in **11**. The values of the equilibrium constant for **11** indicated that tetrazole destabilization occurred more readily in acetone-d_6 or pyridine than in dimethyl sulfoxide-d_6. A similar result was found in the 2-azidopyrimidine–tetrazolo[1,5-*a*]pyrimidine series.[3f]

Unexpectedly the amount of the azido tautomer in a dimethyl sulfoxide-d_6 solution of **13** was greater than that for **11** or even **12**. A reasonable explanation for this is that the electron-donating property of the amino group in **13** is reduced by hydrogen bonding.

Experimental

The melting points reported were determined on a Kofler Heizbank apparatus and are corrected. The ultraviolet spectra were determined in aqueous solution with a Cary Model 14 spectrophotometer. The infrared spectra were determined in pressed

(20) Postovskii and Goncharova[3e] have found the same relative stabilities in the case of tetrazole–azidoazomethines derived from 2-chloro- and 4-hydrazinoquinazoline.

(21) The melting point (128–130°) of the solid obtained by evaporation of this solution was lower than that of **4**, but the infrared spectrum of this solid in a potassium bromide disk was transparent in the azido absorption region.

(22) Similar solvent effects on the tetrazole–azidoazomethine equilibrium in the compound derived from 2-chloro- or 2-hydrazinobenzothiazole has been reported.[3d]

potassium bromide disks or, when indicated, in solution, with a Perkin-Elmer Model 221 spectrophotometer.

Preparation of 2.—Sublimed 4-chloropyrimidine hydrochloride (1, 1.51 g.) was added with stirring to a suspension of sodium azide (1.3 g.) in N,N-dimethylformamide (15 ml.) and the whole was heated at 85° for 1 hr. The solid was removed by filtration, the filtrate was evaporated to a small volume *in vacuo*, and the resulting oil was extracted with ether (75 ml.). The extract was concentrated to 20 ml., filtered through Celite, and evaporated to dryness: yield, 250 mg. (21%); m.p. 77–79°; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 266 (19.6); at pH 7, 253 (broad) (20.0); and at pH 13, 261 (18.9). The molecular weight of **2** was determined by the isothermal distillation method.[23]

Anal. Calcd. for $C_4H_3N_5$: C, 39.70; H, 2.48; N, 57.80; mol. wt., 121. Found: C, 39.79; H, 2.64; N, 57.69; mol. wt., 120.

5-Hydroxy-5,6,7,8-tetrahydrotetrazolo[1,5-*c*]pyrimidine (3).—A solution of **4** (250 mg.) in ethanol containing 5% palladium on charcoal (200 mg.) was hydrogenated at room temperature and atmospheric pressure. In 58 hr. 91% of the calculated amount of hydrogen was absorbed. The residue was removed by filtration, the filtrate was evaporated to dryness, and the solid was extracted with hot ethyl acetate (75 ml.). Evaporation of the extract to dryness gave 150 mg. of white solid, m.p. 144–145° dec.

Anal. Calcd. for $C_4H_7N_5O$: C, 34.04; H, 4.96; N, 49.60. Found: C, 34.27; H, 5.42; N, 49.36.

Preparation of 4.—Sublimed 4-chloropyrimidine hydrochloride (1, 1.76 g.) was added to a suspension of sodium azide (1.5 g.) in dimethyl sulfoxide (4 ml.), and the whole was stirred at room temperature for 2 hr. The mixture was diluted with benzene (15 ml.), the solid was removed by filtration, and the filtrate was evaporated to a small volume *in vacuo*. Extraction of a solution of this residue in water (50 ml.) with six 100-ml. portions of ether gave 1.25 g. (77%) of solid, m.p. 144–147°. Recrystallization of this solid from benzene yielded 925 mg.: m.p. 150–152°; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 265 (20.5); at pH 7, 262 (19.4); and at pH 13, 261 (19.3). The molecular weight of **4** was determined by the isothermal distillation method.[23]

Anal. Calcd. for $C_4H_5N_5O$: C, 34.50; H, 3.60; N, 50.30; mol. wt., 139. Found: C, 34.77; H, 3.45; N, 50.09; mol. wt., 146.

5-Amino-4-chloro-6-hydroxypyrimidine Hydrochloride (5).—A solution of 5-amino-4,6-dichloropyrimidine (**14**, 5.0 g.) in 98–100% formic acid (100 ml.) was refluxed for 1.5 hr., evaporated to dryness, and the residue was boiled in petroleum ether (b.p. 85–105°) to dissolve unchanged **14**. The solid was collected and dried *in vacuo* over phosphorus pentoxide: yield, 4.0 g.; m.p. 221–222°.

The above solid (3.3 g.) was dissolved by warming for 10 min. in 1 *N* hydrochloric acid (150 ml.), the residue was removed by filtration, and the filtrate was evaporated to dryness *in vacuo*. The hydrochloride was dried *in vacuo* over phosphorus pentoxide: yield, 3.3 g.; m.p. 240–242° with decomposition and sublimation; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 265 (sh) (7.44) and 288 (8.52); at pH 7, 265 (sh) (7.50) and 288 (8.52); and at pH 13, 258 (6.96) and 279 (7.76); $\bar{\nu}_{max}$ in cm.$^{-1}$ 3390, 3290, 3225, 3180, 3125, and 3100 (NH), 3040 (aromatic CH), 2900–2200 (acidic H), 1705 (C=O), 1640 (NH), and 1615, 1570 (sh), and 1560 (C=C, C=N).

Anal. Calcd. for $C_4H_4ClN_3O \cdot HCl$: C, 26.35; H, 2.75; Cl, 39.00; N, 23.10. Found: C, 26.64; H, 2.84; Cl, 38.58; N, 23.08.

From the petroleum ether filtrate 500 mg. of **14** was recovered.

Preparation of 10.—A solution of N-(4,6-dichloro-5-pyrimidinyl)acetamide (**15**,[16] 1.00 g.) in dimethylformamide (10 ml.) containing sodium azide (330 mg.) was stirred at room temperature for 4 hr., the residue was removed by filtration, and the filtrate was diluted with water (50 ml.). The aqueous solution was extracted with four 100-ml. portions of ether; the combined extracts were dried with magnesium sulfate and evaporated to dryness under reduced pressure. The solid was washed with two 25-ml. portions of ether and dried *in vacuo* over phosphorus pentoxide: yield, 300 mg. (29%); m.p. 176–177° dec.; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 244 (7.57), 272 (8.3), and 279 (sh) (8.1); and at pH 7, 244 (7.57), 273 (8.1), and 280 (sh) (8.0).

Anal. Calcd. for $C_6H_5ClN_6O$: C, 33.85; H, 2.35; Cl, 16.70; N, 39.52. Found: C, 33.86; H, 2.44; Cl, 15.62; N, 39.89.

Recrystallization of this solid from benzene–methanol lowered the melting point as well as the chlorine content indicating instability.

Preparation of 11.—Solid sodium azide (750 mg.) was added to a solution of N-(4,6-dichloro-5-pyrimidinyl)acetamide (**15**,[16] 1.00 g.) in N,N-dimethylformamide (5 ml.), and the mixture was stirred at room temperature for 45 hr. The residue was removed by filtration, the filtrate was evaporated to dryness *in vacuo* at 55°, and the residue was washed with water (50 ml.) to give 630 mg. (59%) of solid, m.p. 196–197° dec. Precipitation of this solid from a tetrahydrofuran solution with petroleum ether (85–105°) did not raise the melting point; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 232 (21.3) and 288 (15.2); and at pH 7, 231 (20.8) and 287 (15.1).

Anal. Calcd. for $C_6H_5N_9O$: C, 32.85; H, 2.28; N, 57.50. Found: C, 33.23; H, 2.05; N, 57.44.

Preparation of 12.—Sodium azide (1.2 g.) was added to a cooled solution of N-(4,6-dichloro-5-pyrimidinyl)trifluoroacetamide (**16**,[16] 2.0 g.) in N,N-dimethylformamide (10 ml.). The mixture was stirred at room temperature for 18 hr., evaporated to a small volume *in vacuo*, and the residue was washed with water (20 ml.). The solid was collected by filtration and dried *in vacuo* over phosphorus pentoxide: yield, 1.0 g. (48%); m.p. 140–141° with sublimation. Recrystallization of this solid from petroleum ether (b.p. 85–105°) did not raise the melting point; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 233 (26.8) and 287 (16.1); and at pH 7, 222 (13.0) and 296 (15.3).

Anal. Calcd. for $C_6H_2F_3N_9O$: C, 26.35; H, 0.73; N, 46.16. Found: C, 26.62; H, 1.23; N, 46.05.

Preparation of 13.—A solution of **11** (1.0 g.) in ethanol (25 ml.) containing 5% palladium on charcoal (400 mg.) was hydrogenated at room temperature and atmospheric pressure. Although the eudiometer reading was unchanged after 4 hr., a solid had deposited from the reaction solution. The mixture was diluted with ethanol (50 ml.) and heated to boiling; the residue was removed by filtration. The filtrate was evaporated to dryness, the residue was dissolved in hot tetrahydrofuran (100 ml.), and the resulting solution was diluted with petroleum ether (b.p. 85–105°, 50 ml.) and refrigerated. The crude N-(4,6-diamino-5-pyrimidinyl)acetamide (120 mg.) that deposited was removed by filtration, and the filtrate was diluted with additional petroleum ether (50 ml.). **13** precipitated and was collected by filtration and dried *in vacuo* over phosphorus pentoxide: yield, 410 mg. This sample decomposed without melting around 210°; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 237 (16.5) and 292 (11.3); and at pH 7, 216 (18.8), 233 (15.4), 272 (6.93), and 282 (sh) (6.57).

Anal. Calcd. for $C_6H_7N_7O$: C, 37.28; H, 3.63; N, 50.75. Found: C, 37.28; H, 3.69; N, 50.75.

5-Amino-4-hydrazino-6-hydroxypyrimidine (17).—A suspension of 4-hydrazino-6-hydroxy-5-nitropyrimidine (**25**, 1.00 g.) in water (150 ml.) was hydrogenated at room temperature and atmospheric pressure in the presence of 5% palladium-on-charcoal catalyst (500 mg.). In 1.5 hr. the mixture absorbed 89% of the theoretical amount of hydrogen. The residue was removed by filtration and washed with water (25 ml.); the filtrate was evaporated to dryness *in vacuo*. The slightly gummy residue was triturated with methanol (10 ml.). The solid was collected by filtration and dried *in vacuo* over phosphorus pentoxide: yield, 460 mg. (56%); m.p. 245–248° dec. (taken fast from 200°); λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 264 (5.5); and at pH 7, 273 (5.98); $\bar{\nu}_{max}$ in cm.$^{-1}$ 3435, 3270, and 3200 (NH), 2800–2300 (acidic H), 1640 (C=O), 1615 (NH), and 1570 (C=C, C=N).

Anal. Calcd. for $C_4H_7N_5O$: C, 34.05; H, 4.96; N, 49.60. Found: C, 33.80; H, 5.16; N, 49.88.

In larger runs **17** was usually contaminated with 4,5-diamino-6-hydroxypyrimidine.

4,5-Diamino-6-hydrazinopyrimidine Dihydrochloride (18).—A suspension of 4-amino-6-hydrazino-5-nitropyrimidine (**26**, 10.5 g.) in water (350 ml.) containing Raney nickel (13 g., washed with water) was hydrogenated at room temperature and atmospheric pressure. After 18 hr. 98.5% of the calculated amount of hydrogen was absorbed. The mixture was filtered through Celite, the residue was washed with water (50 ml.), and the filtrate was evaporated to dryness *in vacuo*. The black residue (7.5 g.) was heated to boiling in 3 *N* hydrochloric acid (400 ml.), the mixture was filtered, and the filtrate was concentrated to one-fifth of its volume under reduced pressure. The solid

(23) J. E. Morton, A. D. Campbell, and T. S. Ma, *Analyst*, **78**, 722 (1953).

that precipitated was collected by filtration and dried *in vacuo* over phosphorus pentoxide: yield, 6.0 g. (45.5%). This sample decomposes rapidly above 200°; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 7, 280 (7.9); $\bar{\nu}_{max}$ in cm.$^{-1}$ 3370 and 3195 (NH), 3000–2200 (acidic H), 1670 (NH), 1610, 1580, 1560, 1548, and 1510 (C=C, C=N, NH).

Anal. Calcd. for $C_4H_5N_6 \cdot 2HCl$: C, 22.52; H, 4.69; Cl, 33.30; N, 39.43. Found: C, 22.37; H, 4.75; Cl, 33.20; N, 39.64.

4-(2-Acetylhydrazino)-5-amino-6-chloropyrimidine (20).[16]—Anhydrous hydrazine (1.0 ml.) was added with stirring to a suspension of N-(4,6-dichloro-5-pyrimidinyl)acetamide (**15**, 1.0 g.) in water, and the whole was stirred at room temperature for 60 hr. The solid was collected by filtration and recrystallized from ethyl acetate: yield, 460 mg.; m.p. 176° dec. The ultraviolet and infrared spectra of this solid were practically identical with the spectra of an authentic sample of **20**.

N-(4-Amino-6-chloro-5-pyrimidinyl)acetamide (21).—A suspension of 6-chloro-4,5-diaminopyrimidine (1.0 g.) in acetic anhydride (10 ml.) was heated to 90°, and the resulting solution was maintained at this temperature for 15 min. The solution was cooled and the solid was collected by filtration, washed with ether (50 ml.), and dried *in vacuo* over phosphorus pentoxide: yield, 0.90 g. (70%); m.p. 232–233° with sublimation; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 238 (8.54) and 277 (4.67); at pH 7, 237 (9.9) and 278 (4.17); and at pH 13, 256 (6.72) and 284 (6.68); $\bar{\nu}_{max}$ in cm.$^{-1}$ 3395, 3310, 3240, and 3180 (NH), 1680 (C=O), 1640 (NH), and 1580, 1555, and 1515 (C=C, C=N).

Anal. Calcd. for $C_6H_7ClN_4O$: C, 38.60; H, 3.75; Cl, 19.02; N, 30.00. Found: C, 38.73; H, 3.84; Cl, 18.82; N, 30.07.

4-Chloro-6-hydroxy-5-nitropyrimidine (23).—A suspension of 4,6-dichloro-5-nitropyrimidine (**22**, 5.00 g.) in 98–100% formic acid (25 ml.) was heated with stirring over a 10-min. period to reflux and the resulting solution was refluxed for 50 min. A small amount of solid deposited from the solution toward the end of the reflux period. The mixture was cooled, evaporated to dryness *in vacuo*, and the residue was treated with methanol (75 ml.). The resulting mixture was chilled, the insoluble 4,6-dihydroxy-5-nitropyrimidine (770 mg., 19%) was removed by filtration, and the methanol filtrate was evaporated to dryness *in vacuo*. The residue was triturated with ether (15 ml.) and the cream-colored solid was collected by filtration and dried *in vacuo* over phosphorus pentoxide: yield, 3.28 g. (73%); m.p. 200–205° with predecomposition when taken slow; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 285 (3.2); $\bar{\nu}_{max}$ in cm.$^{-1}$ 1690 (C=O), 1590 (C=C, C=N), 1540, and 1360 (NO_2).

Anal. Calcd. for $C_4H_2ClN_3O_3$: C, 27.35; H, 1.14; Cl, 20.20; N, 23.95. Found: C, 27.11; H, 1.37; Cl, 20.72; N, 24.08.

4-Hydrazino-6-hydroxy-5-nitropyrimidine (25).—To a solution of 4-chloro-6-hydroxy-5-nitropyrimidine (**23**, 2.00 g.) in methanol (100 ml.) was added with stirring a solution of 95+% anhydrous hydrazine (0.75 ml.) in methanol (50 ml.). After 4 hr. the solid was collected by filtration and dried *in vacuo* over phosphorus pentoxide: yield, 1.71 g. (88%); m.p. >250° dec.; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 228 (14.3), 280 (sh) (3.8), and 327 (6.3); at pH 7, 229 (12.5), 295 (sh) (3.2), and 352 (6.45); $\bar{\nu}_{max}$ in cm.$^{-1}$ 3250 and 3125 (NH), 1680 (C=O), 1605, 1555, and 1500 (C=C, C=N, and NO_2).

Anal. Calcd. for $C_4H_5N_5O_3$: C, 28.05; H, 2.92; N, 40.90. Found: C, 27.81; H, 2.85; N, 40.86.

4-Amino-6-hydrazino-5-nitropyrimidine (26).—To a solution of 4-amino-6-chloro-5-nitropyrimidine (**24**, 1.0 g.) in methanol (50 ml.) was added with stirring 95+% hydrazine (0.4 ml.). After 15 min. the yellow solid that deposited was collected by filtration, washed with water (10 ml.) and then ether (5 ml.), and dried *in vacuo* over phosphorus pentoxide: yield, 890 mg. (91%); m.p. >264°; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 237 (19.0) and 335 (6.7); at pH 7, 338 (8.4); $\bar{\nu}_{max}$ in cm.$^{-1}$ 3380 3320, and 3240 (NH), 1640 (NH), 1560 (NO_2), and 1500 (C=C, C=N).

Anal. Calcd. for $C_4H_6N_6O_2$: C, 28.24; H, 3.55; N, 49.40. Found: C, 28.34; H, 3.70; N, 49.43.

3,7-Diamino-3H-*v*-triazolo[4,5-*d*]pyrimidine (29).—Solid sodium nitrite (330 mg.) was added with stirring to an ice-bath cooled solution of 4,5-diamino-6-hydrazinopyrimidine dihydrochloride (**18**, 1.0 g.) in water. After 15 min. the ice bath was removed, and the mixture was stirred at room temperature for 1 hr. The solid was removed by filtration, and the filtrate was neutralized to pH 6 with solid sodium hydrogen carbonate. The solid that deposited was collected by filtration and dried *in vacuo* over phosphorus pentoxide at 78°: yield, 180 mg. (25%); m.p. >264°; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 1, 262 (10.7); at pH 7, 278 (10.4); at pH 13, 278 (10.1); $\bar{\nu}_{max}$ in cm.$^{-1}$ 3390, 3300, and 3240 (NH), 1710, 1575, and 1510 (C=C, C=N, N=N), and 1620 (NH_2).

Anal. Calcd. for $C_4H_5N_7$: C, 31.80; H, 3.31; N, 64.85. Found: C, 31.87; H, 3.42; N, 64.59.

3-Acetamido-7-chloro- and 3-Acetamido-7-hydroxy-3H-*v*-triazolo[4,5-*d*]pyrimidine (31 and 32).—A suspension of 4-(2-acetylhydrazino)-5-amino-6-chloropyrimidine (**20**,[16] 400 mg.) in water (5 ml.) containing 1 *N* hydrochloric acid (2.0 ml.) was cooled in an ice bath and solid sodium nitrite (200 mg.) was added with stirring. After 10 min., 110 mg. of **31** was collected by filtration and dried *in vacuo* over phosphorus pentoxide: m.p. 199–200° dec.; λ_{max} in mμ ($\epsilon \times 10^{-3}$) at pH 7, 262 (6.80); $\bar{\nu}_{max}$ in cm.$^{-1}$ 3140 and 3050 (NH), 1730 and 1720 (C=O), 1595, 1580, and 1530 (C=C, C=N).

Anal. Calcd. for $C_6H_5ClN_6O$: C, 33.85; H, 2.35; N, 39.52. Found: C, 33.51; H, 2.65; N, 39.38.

From the aqueous filtrate an additional 125 mg. of **31**, m.p. 187–188° dec., was obtained by ether extraction. The total yield was 235 mg. (56%). After standing for 1 month, recrystallization of the combined crops from tetrahydrofuran–petroleum ether gave **32**: m.p. >264°; identified by comparison of its ultraviolet spectrum with that of **27**; $\bar{\nu}_{max}$ in cm.$^{-1}$ 3260–2800 (NH), 1730 and 1710 (C=O), and 1600 and 1570 (C=C, C=N).

Anal. Calcd. for $C_6H_6N_6O_2$: C, 37.10; H, 3.09; N, 43.25. Found: C, 37.19; H, 3.61; N, 43.06.

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