of this period the crystalline product was triturated with ethyl acetate, and the product collected and washed with ether. Except as noted, the analytical samples formed colorless crystals from ethanol. The results of these experiments are summarized in Table II.

Cyclization of Oximes. One gram of the oxime was refluxed with 5–10 ml. of 48% hydrobromic acid, after which the hydrobromic acid was removed under reduced pressure (aspirator). About 10 ml. of ethanol was added, removed under vacuum, and the residue crystallized from ethanol. The results of these experiments are summarized in Table III.

4-Methylacridizinium Picrate. (a) *Attempted synthesis by the Oxime Method.* Quaternization of 6-methylpyridine-2-aldoxime (XIII oxime) with benzyl bromide was attempted by the usual method. The product, m.p. 208–209°, obtained by recrystallization was not the expected quaternary salt, and had the approximate composition for the hydrobromide of the original oxime.

(b) *By the Picolinic aldehyde method.*[14] Two grams of benzyl chloride and 2 g. of 6-methylpyridine-2-carboxaldehyde were refluxed for 14 hr. in 5 ml. of absolute methanol. The methanol was removed under vacuum and the residue washed with ether. The residue was dissolved in 25 ml. of conc. hydrochloric acid and refluxed for 8 hr. The residue (after removal of the hydrochloric acid *in vacuo*) was dissolved in ethanol and treated with ethanolic picric acid. The crude picrate was obtained as a dark yellow solid, m.p. 200–208° dec., yield 0.2 g. (2.5%). The analytical sample formed fine yellow needles from acetone, m.p. 230–233° dec.

Anal. Calcd. for $C_{20}H_{14}N_4O_7$: C, 56.87; H, 3.34; N, 13.27. Found[15]: C, 56.69; H, 3.89; N, 13.21.

Cyclization of 1-(3-methoxybenzyl)-2-(1-hydroximinoethyl)-pyridinium bromide (XII) *in hydrogen fluoride.* In a polyethylene bottle was placed 0.8 g. of the quaternary bromide (XII) to which 50 ml. of liquid hydrogen fluoride was added. The hydrogen fluoride was allowed to evaporate over a 2 day period. The gummy residue was dissolved in ethanol and treated with ethanolic picric acid. The picrate, crystallized from acetonitrile, was demonstrated to be *8-hydroxy-11-methylacridizinium picrate* by comparison of melting points and infrared spectra with those obtained from the sample prepared by the hydrobromic acid cyclization, yield 0.78 g. (75%).

DURHAM, N. C.

(14) This experiment was by J. H. Jones.

(15) Analysis by Micro Laboratories, Skokie, Illinois.

[CONTRIBUTION FROM THE ORGANIC CHEMICAL RESEARCH SECTION, LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID CO.]

1,2- and 3-Monoalkyl and 2-(β-D-Ribofuranosyl) Derivatives of 7-Dimethylamino-v-triazolo(d)pyrimidine and Related Compounds

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Three monoethyl derivatives have been isolated from the reaction of ethyl iodide and 7-dimethylamino-v-triazolo(d)-pyrimidine (VII). Each of these monoethyl derivatives has been assigned a definite structure by comparison of their ultraviolet absorption spectra with the spectra of 7-dimethylamino-3-ethyl-3H-v-triazolo(d)pyrimidine (V) and 7-dimethylamino-2-(2,4,6-trichlorophenyl)-2H-v-triazolo(d)pyrimidine (XVIII), which have been synthesized by unequivocal methods. By the same methods the riboside obtained from the chloromercuri derivative of VII was shown to be 7-dimethylamino-2-(β-D-ribofuranosyl)-2H-v-triazolo(d)pyrimidine (IX). Similar results were obtained with 7-dimethylamino-5-methylmercapto-v-triazolo(d)pyrimidine (VI).

Analogs of 6-dimethylamino-9(3-amino-3-deoxy-β-D-ribofuranosyl)purine[1] (I) (the aminonucleoside derived from puromycin) are of interest because of the carcinostatic[2] and trypanocidal[3] properties of I. Previous reports have been concerned primarily with analogs of I containing variations either in the carbohydrate portion of the molecule[4] or in the substituents on the purine nucleus.[5] In this paper we wish to report on the results of some work carried out during an attempt to prepare the triazolo(d)pyrimidine analog 7-dimethylamino-3(3-amino-3-deoxy-β-D-ribofuranosyl)-3H-v-triazolo(d)pyrimidine (II).

When this work was begun the only reported v-triazolo(d)pyrimidines containing substituents on the triazole portion of the molecule were some 2-phenyl derivatives.[6] Therefore, in order to have available a model compound for ultraviolet absorption spectra studies, 7-dimethylamino-3-ethyl-3H-v-triazolo(d)pyrimidine (V) was synthesized by unequivocal methods. 5-Amino-6-dimethylamino-4-ethylamino-2-methylmercaptopyrimidine (III)[7] when treated with nitrous acid gave the expected 7-dimethylamino-3-ethyl-5-methylmercapto-3H-v-triazolo(d)pyrimidine (IV), which was then desulfurized with Raney nickel catalyst to give V.

(1) B. R. Baker, J. P. Joseph, and J. H. Williams, *J. Am. Chem. Soc.*, **77**, 1 (1955).

(2) P. L. Bennett, S. L. Halliday, J. J. Oleson, and J. H. Williams, *Antibiotics Annual 1954–1955*, Medical Encyclopedia, Inc., New York, N. Y., 1954, pp. 766–769.

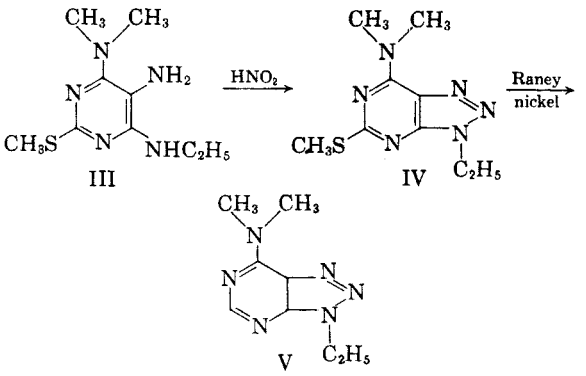
(3) R. I. Hewitt, A. R. Gamble, W. S. Wallace, and J. H. Williams, *Antibiotics and Chemotherapy*, **4**, 1222 (1954).

(4) R. E. Schaub, M. J. Weiss, and B. R. Baker, *J. Am. Chem. Soc.*, **80**, 4692 (1958); F. J. McEvoy, M. J. Weiss and B. R. Baker, *J. Am. Chem. Soc.*, **82**, 209 (1960).

(5) L. Goldman, J. W. Marsico, and R. B. Angier, *J. Am. Chem. Soc.*, **78**, 4173 (1956).

(6) F. R. Benson, L. W. Hartzel and W. L. Savell, *J. Am. Chem. Soc.*, **72**, 1816 (1950).

(7) B. R. Baker, R. E. Schaub, and J. P. Joseph, *J. Org. Chem.*, **19**, 638 (1954).



An attempt was then made to prepare a 3-ribosyl derivative of 7-dimethylamino-5-methylmercapto-v-triazolo(d)pyrimidine[8] (VI) (the more readily available ribose was used instead of 3-amino-ribose). Compound VI, treated with mercuric chloride gave a bis(triazolo(d)pyrimidyl) mercury derivative. The reaction between this derivative and 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride by a slight variation of the method of Kissman *et al.*[9] gave a crude gum from which was isolated in small yield a crystalline riboside (VIII). A comparison of the ultraviolet absorption spectra of the riboside (VIII) with the spectra of IV quickly proved that VIII was not the 3-ribosyl derivative of VI but, as substitution may have occurred on either the 1- or 2- position, no positive assignment of structure could be made.

In conjunction with the above work a simple alkylation of VI was attempted. The reaction between VI and dimethyl sulfate in an aqueous alkaline solution gave a product which was separated by fractional crystallization into two isomeric monomethyl derivatives of VI. A study of their ultraviolet absorption spectra showed that the lower melting isomer (X, m.p. 186–188°) was 7-dimethylamino-3-methyl-5-methylmercapto-3H-v-triazolo-(d)pyrimidine while the other isomer (XI, m.p. 236–238°) had spectra very similar to the spectra of the riboside VIII).

As conversion of VI to the ribosyl derivative had not given the desired isomer, a similar reaction was run using 7-dimethylamino-v-triazolo(d)pyrimidine (VII). Compound VII was prepared by the action of nitrous acid on 4,5-diamino-6-dimethylaminopyrimidine, which was in turn prepared by a Raney nickel desulfurization of 4,5-diamino-6-dimethylamino-2-methylmercaptopyrimidine.[10] The chloromercuri derivative prepared from VII was treated with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride in the usual manner to give a satisfactory yield of a single crystalline riboside (IX). Examination of the ultraviolet absorption spectra of IX demonstrated that it was not a 3-substituted derivative of VII.

Once again a simple alkylation reaction was performed. The treatment of VII with ethyl iodide in an aqueous alkaline solution gave a crude product which was separated by fractional crystallization into three isomeric monoethyl derivatives of VII. By direct comparison with an authentic sample the lowest melting isomer (V, m.p. 80–81°) was shown to be 7-dimethylamino-3-ethyl-3H-v-triazolo(d)pyrimidine (V). One of the other isomers (XIII, m.p. 117–119°) had ultraviolet absorption spectra very similar to the spectra of the riboside IX, prepared from VII, while the spectra of the third isomer (XIV, m.p. 205–206°) were very different. Thus, although a certain relationship had been established between the ribosides VIII and IX and the various alkyl derivatives, the only structures that were established were those of X (7-dimethylamino-3-methyl-5-methylmercapto-3H-v-triazolo(d)pyrimidine) and V (7-dimethylamino-3-ethyl-3H-v-triazolo(d)pyrimidine).

As this portion of the work was completed several papers appeared describing the preparation of v-triazolo(d)pyrimidines containing substituents on the triazole portion of the ring. Among these were descriptions[8,11,12] of the syntheses of a number of ribosides. In one case[8] a riboside of VI was prepared and then desulfurized with Raney nickel to give a riboside of 7-dimethylamino-v-triazolo(d)-pyrimidine (VII). No evidence of any kind was offered to prove the structure of this riboside. However, during the process of publication, the final compound was named, inadvertently but unequivocally, 7-dimethylamino-3-(β-D-ribofuranosyl)-v-triazolo(d)pyrimidine. The comparison of a sample of this product, kindly supplied by Dr. Andrews, with our compound (IX) showed them to be identical. Therefore, this product[8] could not have been a 3-ribosyl derivative.

Although several 3-alkyl derivatives of certain v-triazolo(d)pyrimidines[11,12,13] and two 1-glycosyl-5,7-dihydroxy-1H-v-triazolo(d)pyrimidines[12] have been described recently, these were not readily useful in determining the structures of our compounds. Likewise the 2-phenyl derivatives of VI and VII, which could easily be made, would be of little use as the increased conjugation due to the phenyl groups would result in ultraviolet absorption spectra entirely different from the spectra of a 2-alkyl derivative. However, our experience with the steric inhibition of resonance exhibited by 3′,5′-dichloromethotrexate[14] led us to believe that

(8) K. J. M. Andrews and W. E. Barber, *J. Chem. Soc.*, 2768 (1958).

(9) H. M. Kissman, C. Pidacks, and B. R. Baker, *J. Am. Chem. Soc.*, **77**, 18 (1955).

(10) B. R Baker, J. P. Joseph, and R. E. Schaub, *J. Org. Chem.*, **19**, 631 (1954).

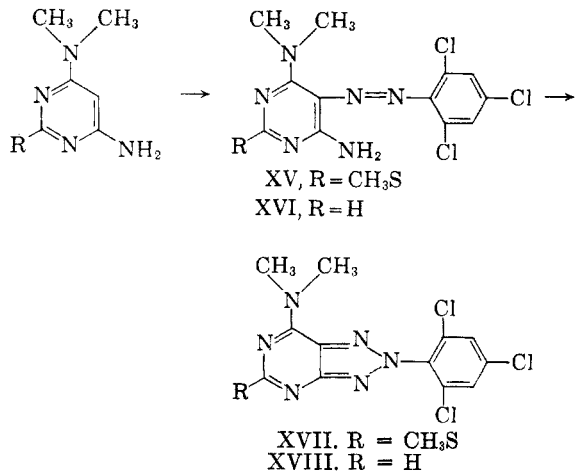
(11) J. Davoll, *J. Chem. Soc.*, 1593 (1958).

(12) J. Baddiley, J. G. Buchanan, and G. O. Osborne, *J. Chem. Soc.*, 1651 and 3606 (1958).

(13) K. L. Dille, M. L. Sutherland, and B. E. Christiansen, *J. Org. Chem.*, **20**, 171 (1955); F. L. Rose, *J. Chem. Soc.*, 4116 (1954).

(14) R. B. Angier and W. V. Curran, *J. Am. Chem. Soc.*, **81**, 2814 (1959).

2(2,4,6-trichlorophenyl) derivatives of VI and VII would have spectra very similar to the corresponding 2-alkyl or 2-ribosyl derivatives. Therefore, 4-amino - 6 - dimethylamino - 2 - methylmercapto - 5-(2,4,6-trichlorophenylazo)pyrimidine (XV) was prepared and converted to 7-dimethylamino-5-methylmercapto-2(2,4,6-trichlorophenyl)-2H-v-triazolo-(d)pyrimidine (XVII) by conventional methods. The ultraviolet absorption spectra of XVII were very similar to the spectra of the riboside VIII and also similar to one (XI, m.p. 236–238°) of the two methyl derivatives obtained by the methylation of VI.



An attempt to desulfurize XVII with Raney nickel was unsuccessful because of a simultaneous reductive dechlorination. Therefore, 4-amino-6-dimethylamino - 2 - methylmercaptopyrimidine was desulfurized to give 4-amino-6-dimethylaminopyrimidine which was then converted *via* the azo compound (XVI) to 7-dimethylamino-2-(2,4,6-trichlorophenyl) - 2H - v - triazolo(d)pyrimidine (XVIII). The ultraviolet absorption spectra of XVIII were very similar to the spectra of the riboside IX and also similar to the spectra of one (XIII, m.p. 117–119°) of the three *N*-ethyl derivatives obtained by the action of ethyl iodide on VII.

To tie the two series together further XI (7-dimethylamino-5-methylmercapto-2-methyl-2H-v-triazolo(d)pyrimidine) was desulfurized with Raney nickel to give a compound (XII) with spectra identical to the spectra of XIII (7-dimethylamino-2-ethyl-2H-v-triazolo(d)pyrimidine).

Ultraviolet absorption spectra and structure. An examination of the spectra (Table I and Fig. 1) of the 2-(2,4,6-trichlorophenyl) (XVII) and the postulated 2-methyl (XI) and 2-ribosyl (VIII) derivatives of 7-dimethylamino-5-methylmercapto-v-triazolo(d)pyrimidine (VI) shows that, although the curves are almost superposable, there is a bathochromic shift of some 5–10 mμ for most parts of the curve as one proceeds from XI to VIII to XVII. As only two of the likely three possible *N*-monomethyl derivatives of VI had been prepared. it could be argued that the unknown third methyl derivative might have spectra very similar to XI. However, when one examines the spectra (Table I and Figs. 2 +3)of the derivatives of VII (7-dimethylamino-

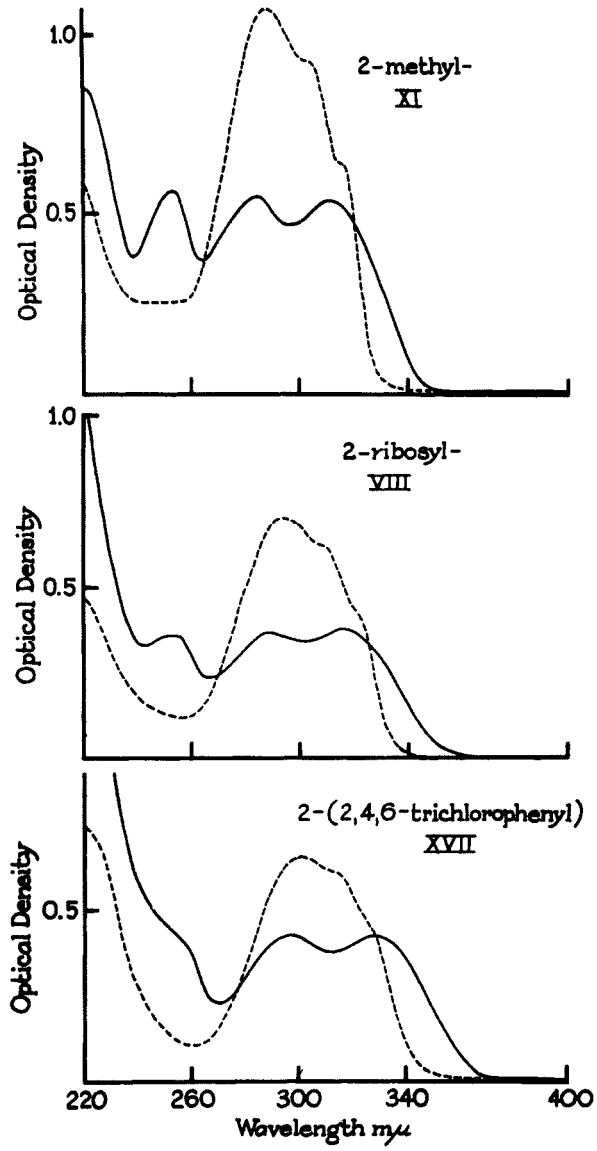


Fig. 1. Ultraviolet absorption spectra of derivatives of 7 - dimethylamino - 5 - methylmercapto - v - triazolo(d)-pyrimidine: ——, 0.1*N* sodium hydroxide or methanol (10γ/ml); – – – –, 0.1*N* hydrochloric acid (10γ/ml.)

v-triazolo(d)pyrimidine), any reasonable doubt of the structures is dispelled. The spectra of the 2-(2,4,6-trichlorophenyl) (XVIII) and the postulated 2-ethyl (XIII) and 2-ribosyl (IX) derivatives of VII again are essentially superposable when allowance is made for a small bathochromic shift from XIII to IX to XVIII. In this case all three of the likely *N*-monoethyl derivatives had been isolated and close inspection showed that only one of them (XIII) had spectra resembling the spectra of the known 2-(2,4,6-trichlorophenyl) - 7 - dimethylamino - 2H - v - triazolo(d)pyrimidine (XVIII). Although superficial examination may not quickly reveal this fact, it does become quite evident when one notes that the 2-(2,4,6-trichlorophenyl) derivative (XVIII) exhibits a bathochromic shift of its maximum when passing from the cation (0.1*N* HCl) to the neutral molecule. An examination of the other derivatives of VII then shows that the postulated 2-ethyl (XIII) and 2-ribosyl (IX) derivatives exhibit this same bathochromic shift while the

TABLE I

Substituent	Ultraviolet Absorption Spectra[a] λ_{max}, mμ (ϵ) 0.1*N* HCl	Methanol or 0.1*N* NaOH[b]
7-Dimethylamino-5-methylmercapto-v-triazolo(d)pyrimidine (VI)		
VI	250 (8,800)	248 (18,900)[b]
	286 (22,900)	296 (15,100)
2-Methyl (XI)	288 (24,000)	254 (13,000)
	302Sh (20,800)	284 (12,100)
	315Sh (14,400)	311 (12,400)
2-(β-D-Ribofuranosyl)[17] (VIII)	294 (23,600)	254 (12,100)
	309Sh (20,800)	290 (12,300)
	321Sh (14,400)	318 (12,700)
2-(2,4,6-Trichlorophenyl) (XVII)	300 (26,600)	254Sh (13,600)
	312Sh (25,000)	297 (13,300)
		328 (13,300)
3-Methyl (X)	253 (13,400)	255 (17,300)
	284 (19,700)	300 (13,700)
3-Ethyl (IV)	252 (14,500)	255 (19,700)
	283 (18,400)	300 (15,200)
2-Phenyl	303 (21,200)	250 (27,200)
	336 (26,600)	304 (15,400)
		347 (19,400)
7-Dimethylamino-v-triazolo(d)pyrimidine (VII)		
VII	286 (12,400)	292 (18,200)[b]
2-Methyl (XII)	303 (16,200)	309 (15,100)
2-Ethyl (XIII)	303 (16,500)	308 (15,300)
2-(β-D-Ribofuranosyl)[17] (IX)	310 (17,000)	314 (14,800)
2-(2,4,6-Trichlorophenyl) (XVIII)	314 (16,000)	323 (14,200)
1-Ethyl (XIV)	308 (17,800)	299 (14,800)
3-Ethyl (V)	275 (14,400)	296 (15,000)

[a] Sh = shoulder. [b] Except for VI and VII the spectra in methanol and 0.1*N* NaOH are essentially identical for any one compound. The spectra for VI and VII were run in 0.1*N* NaOH.

postulated 1-ethyl derivative[15] (XIV) shows a hypsochromic shift of its maximum in passing from the cation (0.1*N* HCl) to the neutral molecule.

Although ultraviolet absorption spectra comparisons alone may not be considered a rigorous proof of structure the authors feel that the evidence for the correctness of the assigned structures is very strong.

During the course of this work XVII was treated with refluxing 6*N* hydrochloric acid for seven hours and gave an easily separable mixture of 5,7-dihydroxy-2(2,4,6-trichlorophenyl)-2H-v-triazolo(d)-pyrimidine and 7-dimethylamino-5-hydroxy-2-(2,4,6-trichlorophenyl)-2H-v-triazolo(d)pyrimidine.

EXPERIMENTAL[16]

4-Amino-6-dimethylaminopyrimidine. 4-Amino-6-dimethylamino-2-methylmercaptopyrimidine[10] (2.0 g., 11 mmoles), 75 ml. of 2-methoxyethanol and excess Raney nickel were mixed and heated on the steam bath for 2 hr. with stirring. Fresh Raney nickel was added and the mixture was heated another hour. The mixture was filtered and the catalyst was extracted with warm 2-methoxyethanol. The filtrates were combined and evaporated to 10 ml. *in vacuo*, diluted with water, and the product collected; yield: 0.3 g. of recovered starting material; melting point and mixed melting point with the starting material, 164–166°.

The filtrate was evaporated to dryness and the residue dissolved in a minimum amount of hot ethanol and cooled;

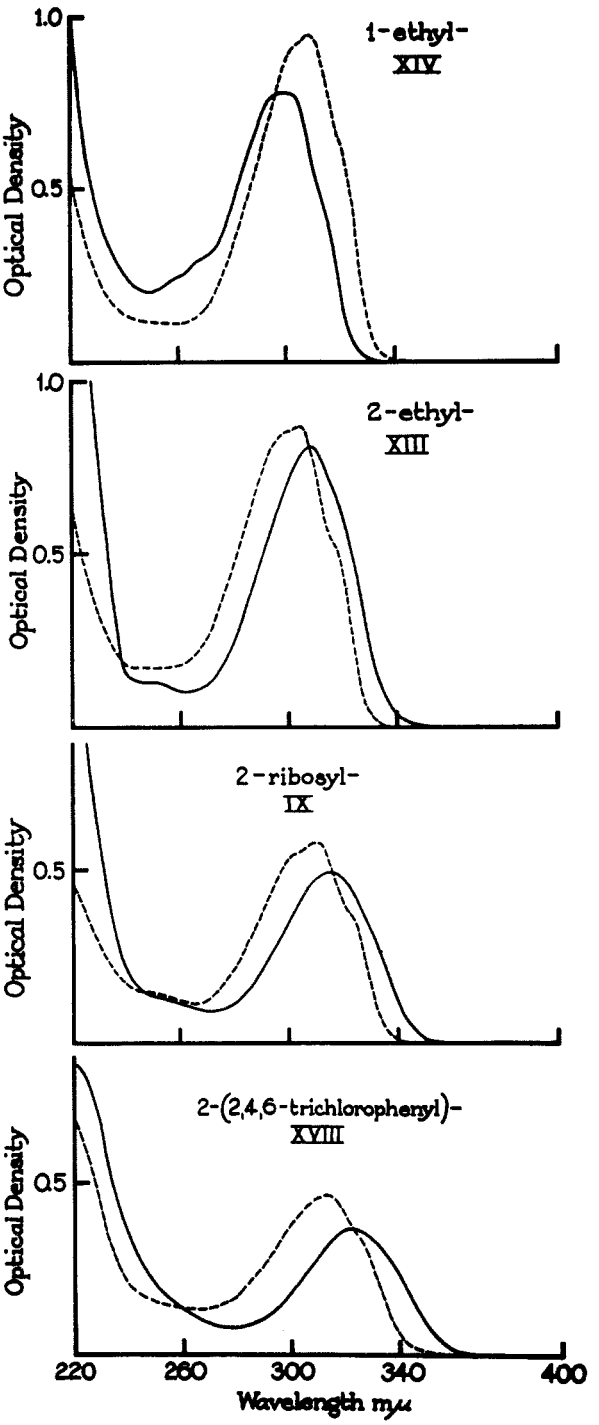
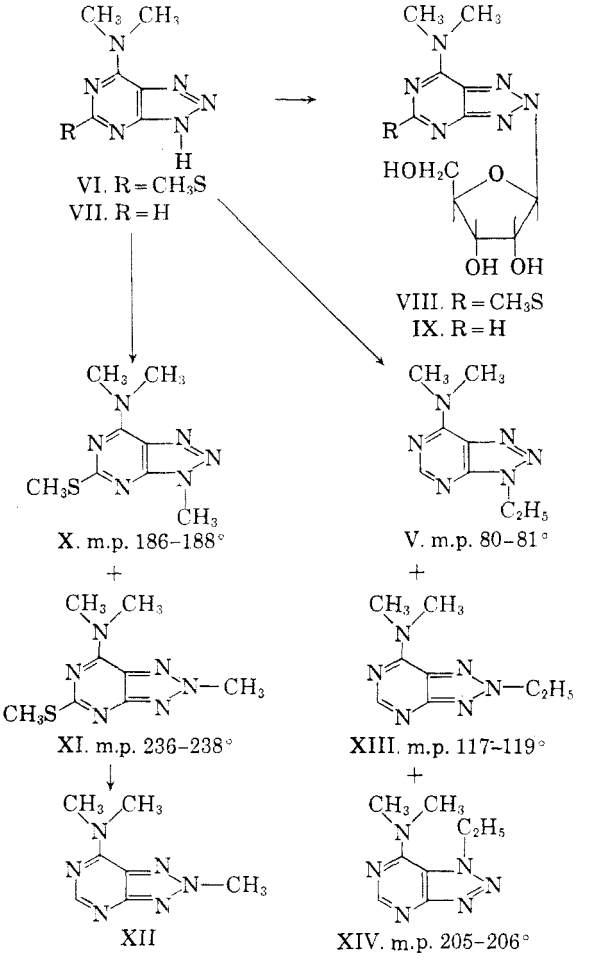


Fig. 2. Ultraviolet absorption spectra of derivatives of 7-dimethylamino-v-triazolo(d)pyrimidine: ——, 0.1*N* sodium hydroxide or methanol (10γ/ml); – – – –, 0.1*N* hydrochloric acid (10γ/ml.)

(15) It would have been desirable to have had an authentic sample of 7-dimethylamino-1-ethyl-1H-v-triazolo(d)-pyrimidine (XIV) available for direct comparison. However, several attempts to convert 4-amino-6-dimethylamino-6-ethylaminopyrimidine to XIV by the use of nitrous acid failed to give the desired product.

(16) The melting points were corrected for the exposed stem of the thermometer.



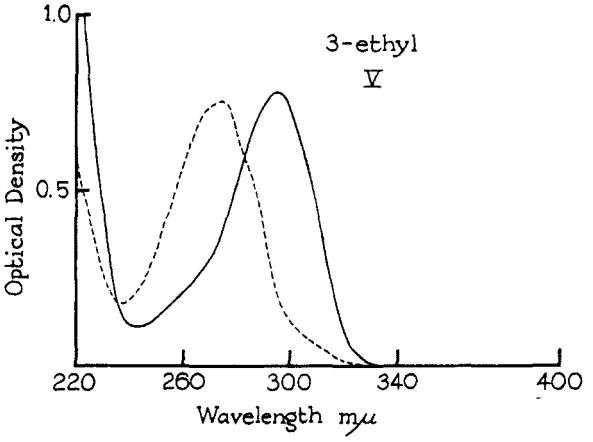


Fig. 3. Ultraviolet absorption spectra of 7-dimethylamino - 3 - ethyl - 3H - v - triazolo(d)pyrimidine (V): ——, 0.1*N* sodium hydroxide 10γ/ml.); – – – –, 0.1*N* hydrochloric acid (10γ/ml)

yield: 0.5 g. (39% based on recovered starting material); m.p. 206–208°. This was recrystallized from 5 ml. of ethanol; yield: 0.3 g., m.p. 207–209°.

Anal. Calcd. for $C_6H_{10}N_4$ (138): C, 52.2; H, 7.2; N, 40.6. Found: C, 52.1; H, 7.3; N, 40.8.

4,5-Diamino-6-dimethylaminopyrimidine. 4,5-Diamino-6-dimethylamino-2-methylmercaptopyrimidine[10] (20 g., 0.1 mole) was dissolved in 400 ml. of 2-methoxyethanol and slurried with 200 g. of Raney nickel catalyst. The mixture was heated on the steam bath with stirring for 1 hr. The catalyst was removed by filtration and the filtrate was evaporated to dryness *in vacuo*. The residue was recrystallized from 350 ml. of benzene; yield varied from 6 to 10 g. (39—65%); m.p. 157–159°. This material was satisfactory for subsequent reactions. For analyses a small sample was sublimed; m.p. 158–160°.

Anal. Calcd. for $C_6H_{11}N_5$ (153): C, 47.0; H, 7.2; N, 45.7. Found: C, 47.5; H, 7.5; N, 45.5.

7-Dimethylamino-v-triazolo(d)pyrimidine (VII). 4,5-Diamino-6-dimethylaminopyrimidine (4.3 g., 28 mmoles) was was dissolved in a solution of 30 ml. of water and 5 ml. of acetic acid. After the addition of a solution of 2.0 g. (29 mmoles) of sodium nitrite in 5 ml. of water a solid appeared. The mixture was cooled and the product collected; yield: 4.4 g. (95%), m.p. 279–281°.

Anal. Calcd. for $C_6H_8N_6$ (164): C, 43.9; H, 4.9; N, 51.2. Found: C, 44.2; H, 5.2; N, 51.6.

7-Dimethylamino-3-ethyl-5-methylmercapto-3H-v-triazolo(d)pyrimidine (IV). A solution of 2.0 g. (8.3 mmoles) of 6-dimethylamino-4-ethylamino-2-methylmercapto-5-nitrosopyrimidine[7] in 40 ml. of warm acetone was added to a solution of 4.0 g. of sodium hydrosulfite in 20 ml. of water. This was shaken and warmed until the blue color disappeared. The mixture was diluted with 80 ml. of water and extracted with three 50-ml. portions of chloroform. The chloroform solution was dried with magnesium sulfate and filtered and the filtrate was evaporated to dryness. The residue (crude triamine III) was dissolved in a solution of 100 ml. of warm water and 10 ml. of acetic acid and mixed with a solution of 600 mg. of sodium nitrite in 10 ml. of water. A precipitate formed immediately. After 5 min. on the steam bath the mixture was cooled; yield: 1.4 g. (70%). This product was recrystallized from a solution of 25 ml. of acetic acid and 50 ml. of water; yield: 0.6 g. (30%), m.p. 114–115°.

Anal. Calcd. for $C_9H_{14}N_6S$ (238): C, 45.4; H, 5.9; N, 35.3; S, 13.4. Found: C, 45.7; H, 6.2; N, 35.3; S, 13.9.

7-Dimethylamino-3-ethyl-3H-v-triazolo(d)pyrimidine (V). A solution of 0.5 g. (2.1 mmoles) of IV in 40 ml. of warm 2-methoxyethanol was treated with several spoonfuls of Raney nickel catalyst and heated on the steam bath for 1 hr. The mixture was filtered and the filtrate was evaporated to dryness. The residue was recrystallized once from 7 ml. of water (yield 120 mg.) and a second time from 7 ml. of heptane; yield: 80 mg. (20%), m.p. 80–81°.

Anal. Calcd. for $C_8H_{12}N_6$ (192): C, 50.0; H, 6.3; N, 43.7. Found: C, 50.2; H, 6.1; N, 43.3.

Methylation of 7-dimethylamino-5-methylmercapto-v-triazolo(d)pyrimidine. A solution containing 4.1 g. (19.5 mmoles) of 7-dimethylamino-5-methylmercapto-v-triazolo(d)pyrimidine (VI),[8] 0.8 g. (20 mmoles) of sodium hydroxide, 80 ml. of water, 30 ml. of methanol, and 1.6 ml. (3.65 g., 25.6 mmoles) of methyl iodide was heated to reflux on a steam bath for 1 hr. The mixture was cooled and the product collected; yield 2.8 g. The solid was dissolved in a minimum amount (about 250 ml.) of hot acetone and allowed to cool slowly to room temperature. The solid was collected and recrystallized from 135 ml. of hot acetone; yield 0.45 g. (10%); m.p. 236–238°. As described in the discussion, this was shown to be 7-dimethylamino-5-methylmercapto-2-methyl-2H-v-triazolo(d)pyrimidine (XI).

Anal. Calcd. for $C_8H_{12}N_6S$ (224): C, 42.9; H, 5.4; N, 37.5; S, 14.3. Found: C, 43.1; H, 5.4; N, 37.0; S, 14.2.

The acetone filtrate remaining after removing the higher melting material was evaporated to about 65% of its original volume and cooled to 0°; yield 1.2 g. This was redissolved in 70 ml. of hot acetone, cooled just to room temperature, and filtered. The filtrate was cooled to 0° and the product collected; yield 0.85 g. (19%); m.p. 186–188°. This had ultraviolet absorption spectra essentially identical with those of IV and was therefore 7-dimethylamino-5-methylmercapto-3-methyl-3H-v-triazolo(d)pyrimidine (X).

Anal. Calcd. for $C_8H_{12}N_6S$ (224): C, 42.9; H, 5.4; N, 37.5; S, 14.3. Found: C, 43.1; H, 5.4; N, 37.4; S, 14.6.

7-Dimethylamino-2-methyl-2H-v-triazolo(d)pyrimidine (XII). 7-Dimethylamiro-5-methylmercapto-2-methyl-2H-v-triazolo(d)pyrimidine (XI) (500 mg.; 2.22 mmoles) in 75 ml. of 2-methoxyethanol was desulfurized with Raney nickel in the usual manner. After removal of the catalyst the solution was evaporated to dryness. The residue was extracted with 12 ml. of boiling acetone which upon cooling gave 140 mg. (35% yield) of a crystalline product; m.p. 193–195°. Recrystallization from acetone did not change the melting point.

Anal. Calcd. for $C_7H_{10}N_6$ (178): C, 47.2; H, 5.6; N, 47.2. Found: C, 47.6; H, 5.9; N, 46.8.

Ethylation of 7-dimethylamino-v-triazolo(d)pyrimidine. A solution containing 2.0 g. (12.2 mmoles) of 7-dimethylamino-v-triazolo(d)pyrimidine (VII), 15 ml. of methanol, 6.5 ml. of 2*N* sodium hydroxide, and 1.06 ml. (2.05 g., 13 mmoles) of ethyl iodide was heated at reflux for 135 min. The clear yellow solution was evaporated to a gum *in vacuo*. The gum was dissolved in 15 ml. of a 10% sodium hydroxide solution and extracted with 40 ml. of chloroform followed by three 25-ml. portions of chloroform. The chloroform solution was dried over sodium sulfate and evaporated to a gum. The addition of heptane gave a solid which was collected; yield 414 mg. (fraction I). Upon standing the filtrate gave more solid; yield 545 mg. (fraction II); m.p. 65–105°. The filtrate from fraction II was evaporated to a gum and heptane added again to give 250 mg. of solid which was added to fraction II.

Fraction I (414 mg.) was recrystallized from 35 ml. of benzene; yield: 230 mg., m.p. 205–206°. As described in the discussion this was shown to be 7-dimethylamino-1-ethyl-1H-v-triazolo(d)pyrimidine (XIV).

Anal. Calcd. for $C_8H_{12}N_6$ (192): C, 50.0; H, 6.3; N, 43.7. Found: C, 50.2; H, 6.6; N, 43.7.

When fraction II was recrystallized from heptane and cooled in an ice bath, the product (fraction III) had essentially the same melting point as fraction II. However, the filtrate from fraction III was evaporated to dryness and the residue was recrystallized from heptane to give a product with m.p. 80–81°. This was shown by mixed melting point and ultraviolet absorption spectra to be identical with authentic 7-dimethylamino-3-ethyl-3H-v-triazolo(d)pyrimidine (V).

When fraction III was dissolved in hot heptane and cooled slowly to room temperature the product melted at 116–119°. Another recrystallization from heptane gave a product melting at 117–119°. This was shown to be 7-dimethylamino-2-ethyl-2H-v-triazolo(d)pyrimidine (XIII).

Anal. Calcd. for $C_8H_{12}N_6$: C, 50.0; H, 6.3; N, 43.8. Found: C, 50.5; H, 6.6; N, 43.7.

Bis(7-dimethylamino-5-methylmercapto-v-triazolo(d)pyrimidine) mercury. A solution of 0.33 g. (1.6 mmoles) of 7-dimethylamino - 5-methylmercapto - v - triazolo(d)pyrimidine (VI)[8] in 40 ml. of warm 50% ethanol was treated with 0.8 ml. of 2*N* sodium hydroxide followed by 0.22 g. (0.85 mmole) of mercuric chloride dissolved in 3A ethanol. The salt precipitated immediately. The mixture was cooled and the product collected; yield: 0.45 g. (93%).

Anal. Calcd. for $C_{14}H_{18}N_{12}S_2Hg$ (619): C, 27.2; H, 2.9; N, 27.2. Found: C, 27.3; H, 3.3; N, 27.1.

7-Dimethylamino-5-methylmercapto-2-(β-D-ribofuranosyl)-2H-v-triazolo(d)pyrimidine (VIII).[17] 1-Acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribose[9] (2.5 g., 5 mmoles) was dissolved in 10 ml. of acetyl chloride and the solution was poured into 50 ml. of anhydrous ether saturated with dry hydrogen chloride at ice-bath temperature. The solution remained at 3° for 3 days. It was then evaporated to a gum *in vacuo* on a steam bath and evaporated three times with 45-ml. portions of benzene. Meanwhile, 1.3 g. (2.1 mmoles) of bis(7-dimethylamino-5-methylmercapto-v-triazolo(d)pyrimidine) mercury was suspended in 100 ml. of dry xylene and 20 ml. distilled with stirring to dry the solid. The sugar derivative was dissolved in 20 ml. of dry xylene and added to the mercury derivative suspension. Another 25 ml. of xylene was distilled and the mixture was refluxed and stirred for 2.5 hr. The hot mixture was filtered and the filtrate was evaporated to dryness. The residue was dissolved in 100 ml. of chloroform, filtered from traces of solid material, and washed with 15 ml. of 30% aqueous potassium iodide solution followed by 20 ml. of water. The chloroform solution was dried over sodium sulfate, filtered, and the filtrate concentrated to a yellow glass *in vacuo*. This was dissolved in 30 ml. of methanol containing 1.0 ml. of 1.0*N* methanolic sodium methoxide, refluxed for 45 min., and evaporated to a gum. Trituration with ether gave a white crystalline product which was recrystallized from water to give 250 mg. of crude product. This was recrystallized from 10 ml. of methanol; yield 87 mg. (5.5%); m.p. 171–172°.

Anal. Calcd. for $C_{12}H_{18}O_4N_6S \cdot CH_3OH$ (374): C, 41.7; H, 5.9; N, 22.5; S, 8.6; CH_3O, 8.3. Found: C, 42.1; H, 6.1; N, 22.6; S, 8.7; CH_3O, 7.6.

7-Dimethylamino-2-(β-D-ribofuranosyl)-2H-v-triazolo(d)-pyrimidine (IX).[17] 1-Acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribose[9] (2.5 g., 5 mmoles) was converted to the corresponding ribosyl chloride just as described for compound VIII above. The reaction between this sugar derivative and 2.0 g. (5 mmoles) of chloromercuri-7-dimethylamino-v-triazolo(d)pyrimidine[18] was also carried out just as described for compound VIII. After washing with potassium iodide solution and drying, the solution was evaporated *in vacuo* to a gum. The gum was dissolved in 35 ml. of methanol containing 2 ml. of 1.0*N* methanolic sodium methoxide and refluxed for 45 min. The solution was neutralized with acetic acid and evaporated to a solid. Methanol (50 ml.) was added and heated to boiling, the solution was filtered, and the filtrate allowed to cool to room temperature; yield: 517 mg., m.p. 220–221°. Recrystallization from 50 ml. of methanol gave 435 mg. (29%) of product with same melting point.

Anal. Calcd. for $C_{11}H_{16}O_4N_6$ (296): C, 44.6; H, 5.4; N, 28.4. Found: C, 44.6; H, 5.5; N, 28.5.

4-Amino-6-dimethylamino-2-methylmercapto-5-(2,4,6-trichlorophenylazo) pyrimidine (XV). 2,4,6-Trichloroaniline (10.0 g., 51.0 mmoles) was suspended in a solution of 100 ml. of concd. hydrochloric acid and 50 ml. of water and warmed to convert to the hydrochloride. This was cooled in an ice bath with stirring and treated with a solution of 3.7 g. of sodium nitrite in 30 ml. of water. The solid dissolved. The excess nitrous acid was destroyed with urea and the solution was then poured into 1300 ml. of water and ice containing 115 g. of sodium bicarbonate.

A solution of 8.0 g. (37.0 mmoles) of 4-amino-6-dimethylamino-2-methylmercaptopyrimidine hydrochloride[10] in 350 ml. of warm water was added, with stirring, to the diazonium solution. An orange precipitate appeared during the addition. The product was collected and recrystallized from 600 ml. of 2-methoxyethanol; yield 11.4 g. (79%); orange-red crystals; m.p. 247–249°.

Anal. Calcd. for $C_{13}H_{13}N_6SCl_3$ (391.6); C, 39.9; H, 3.4; N, 21.4. Found: C, 40.1; H, 3.4; N, 21.6.

4-Amino-6-dimethylamino-5-(2,4,6-trichlorophenylazo)-pyrimidine (XVI). A solution of 0.41 g. (3 mmoles) of 4-amino-6-dimethylaminopyrimidine in 15 ml. of water was added to the diazonium chloride solution prepared from 0.8 g. (4 mmoles) of 2,4,6-trichloroaniline in the manner described above. The initial gelatinous product was converted to a solid by heating a short time on the steam bath. After cooling the product was collected; yield: 1.1 g. (88%),

(17) The *beta* configuration is assumed on the basis of analogy and theoretical grounds for which see B. R. Baker in *The Chemistry and Biology of Purines*, Ciba Foundation Symposium, Little, Brown and Co., Boston, Mass., 1957, p. 120; B. R. Baker *et al.*, *J. Org. Chem.*, 19, 1786 (1954).

(18) The chloromercuri derivative of VII was prepared just as described for the mercury derivative of VI except that one mole of mercuric chloride was used.

m.p. 225–227°. Recrystallization from 60 ml. of 2-methoxyethanol gave 0.9 g. (72%) of product; orange needles; m.p. 230–232°.

Anal. Calcd. for $C_{12}H_{11}N_6Cl_3$ (345.6): C, 41.8; H, 3.2; N, 24.4. Found: C, 41.5; H, 3.7; N, 24.8.

7-Dimethylamino-5-methylmercapto-2-(2,4,6-trichlorophenyl)-2H-v-triazolo(d)pyrimidine (XVII). A mixture of 0.8 g. (2 mmoles) of 4-amino-6-dimethylamino-2-methylmercapto 5-(2,4,6-trichlorophenylazo)pyrimidine (XV), 2.5 g. of copper sulfate pentahydrate, 7.0 ml. of water, and 14.0 ml. of pyridine was heated at reflux for 4 hr. The solution was then diluted with 50 ml. of water and cooled overnight; yield 0.75 g. (94%); m.p. 214–216°. This was recrystallized from 7 ml. of 2-methoxyethanol; yield: 0.58 g. (72%), m.p. 216–217°.

Anal. Calcd. for $C_{13}H_{11}N_6SCl_3$ (389.6): C, 40.1; H, 2.8; N, 21.6; S, 8.2; Cl, 27.4. Found: C, 39.9; H, 3.1; N, 21.8; S, 8.4; Cl, 27.3.

7-Dimethylamino-2-(2,4,6-trichlorophenyl)-2H-v-triazolo(d)pyrimidine (XVIII). A mixture of 0.85 g. (2.5 mmoles) of 4-amino-6-dimethylamino-5-(2,4,6-trichlorophenylazo)-pyrimidine (XVI), 2.5 g. of copper sulfate pentahydrate, 7 ml. of water, and 14 ml. of pyridine were heated to reflux for 5 hr. The mixture was diluted with several volumes of water and cooled; yield 0.7 g. (83%); m.p. 262–267°. Recrystallization from 15 ml. of 2-methoxyethanol gave 0.55 g. (65% yield) of product; m.p. 266–268°.

Anal. Calcd. for $C_{12}H_9N_6Cl_3$ (343.6): C, 41.9; H, 2.7; N, 24.5; Cl, 31.0. Found: C, 41.9; H, 2.8; N, 24.8; Cl, 30.6.

Acid hydrolysis of 7-dimethylamino-5-methylmercapto-2-(2,4,6-trichlorophenyl)-2H-v-triazolo(d)pyrimidine (XVII). A solution of 300 mg. (0.77 mmole) of XVII in 15 ml. of 6*N* hydrochloric acid was heated to reflux for 8 hr. during which time a crystalline solid separated. The solid was collected (yield 60 mg. (23%)), dissolved in 3 ml. of hot 2-methoxyethanol and 2 ml. of hot water added. Cooling gave 35 mg. of 5,7-dihydroxy-2-(2,4,6-trichlorophenyl)-2H-v-triazolo(d)pyrimidine; m.p. >300°. Ultraviolet absorption spectra in 0.1*N* sodium hydroxide, λ_{max} 317 mμ (ε 7,700); methanol, λ_{max} 280 mμ (ε 10,700); 0.1*N* hydrochloric acid, λ_{max} 281 mμ (ε 11,700).

Anal. Calcd. for $C_{10}H_4N_5O_2Cl_3$ (332.6): C, 36.1; H, 1.2; N, 21.0; Cl, 32.0. Found: C, 36.2; H, 1.5; N, 20.8; Cl, 32.0.

The 6*N* hydrochloric acid filtrate from the reaction was diluted to 70 ml. with water and brought to *p*H 4 with sodium acetate. A crystalline product separated; yield: 160 mg. (57%). This was recrystallized from 5 ml. of 2-methoxyethanol to give 80 mg. of 7-dimethylamino-5-hydroxy-2-(2,4,6-trichlorophenyl)-2H-v-triazolo(d)pyrimidine; m.p. >300°. Ultraviolet absorption spectra in 0.1*N* sodium hydroxide, λ_{max} 280 mμ (ε 6,800), 334 mμ (ε 9,500); methanol, λ_{max} 287 mμ (ε 16,500), 0.1*N* hydrochloric acid, λ_{max} 299 mμ (ε 12,900).

Anal. Calcd. for $C_{12}H_9N_6OCl_3$ (359.6): C, 40.1; H, 2.5; N, 23.4; Cl, 29.6. Found: C, 39.9; H, 2.8, N, 23.3; Cl, 29.7.

4-Amino-6-dimethylamino-2-methylmercapto-5-phenylazopyrimidine. Aniline (4.7 g., 50 mmoles) was diazotized as described by Bensen *et al.*[6] and the diazonium solution was coupled with 9.2 g. (50 mmoles) of 4-amino-6 dimethylamino-2-methylmercaptopyrimidine dissolved in a solution of 300 ml. of water, 115 ml. of acetic acid, and 52 g. of sodium acetate; yield: 8.1 g. This was recrystallized from 100 ml. of 2-methoxyethanol; yield: 7.2 g. (50%) of an orange product, m.p. 197–198°.

A sample (0.45 g.) was recrystallized from 80 ml. of ethanol; yield: 0.25 g., m.p. 198–199°.

Anal. Calcd. for $C_{13}H_{16}N_6S$ (288): C, 54.2; H, 5.7; N, 29.2; S, 11.1. Found: C, 53.8; H, 5.6; N, 29.0; S, 11.0.

7-Dimethylamino-5-methylmercapto-2-phenyl-2H-v-triazolo(d)pyrimidine. A solution of 6.5 g. (22.6 mmoles) of 4-amino-6-dimethylamino-2-methylmercapto-5-phenylazopyrimidine, 16.7 g. of copper sulfate pentahydrate, 64 ml. of pyridine, and 34 ml. of water was heated at reflux for 2.5 hr. and cooled; yield of product 6.3 g. (98%); m.p. 193–194°; mixed melting point with starting material 165–180°.

A sample (0.5 g.) was recrystallized from 80 ml. of ethanol; yield of light yellow crystalline product 0.4 g.; m.p. 194–195°.

Anal. Calcd. for $C_{13}H_{14}N_6S$ (286): C, 54.6; H, 4.9; N, 29.4. Found: C, 54.4; H, 5.9; N, 29.7.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ARIZONA STATE UNIVERSITY]

Potential Purine Antagonists. XXIII. Synthesis of Some 7-Substituted Amino-v-triazolo(d)pyrimidines[1]

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The preparation of certain 7-alkylamino-v-triazolo(d)pyrimidines from 7-methylthio-v-triazolo(d)pyrimidine (XIV) has been accomplished. Some 7-alkylthio-5-amino-v-triazolo(d)pyrimidines have been synthesized by ring closure of the corresponding 6-alkylthio-2,4,5-triaminopyrimidines with nitrous acid. 5-Amino-7-methoxy-v-triazolo(d)pyrimidine has been prepared.

The antitumor activity of 5-amino-7-hydroxy-v-triazolo(d)pyrimidine[2] (8-azaguanine) and 6-amino-4-hydroxypyrazolo(3,4-d)pyrimidine[3] strongly suggested the possibility that antitumor activity similar to that exhibited by the 4-substituted-

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