piperidine-4-carboxylate hydrochloride (295 g., 0.9 mole) was added portionwise during 0.5 hr. to a vigorously stirred mixture of 120 g. (1.0 mole) of thionyl chloride, 1 ml. of pyridine and 2 liters of benzene. After the addition was completed, the mixture was stirred 0.5 hr. at room temperature, and then refluxed for 2 hr. After cooling, the crystalline product was collected and washed with ether; yield 307 g. (98%), m.p. 189–192°.

Anal. Calcd. for $C_{17}H_{24}ClNO_2 \cdot HCl$: C, 58.96; H, 7.28; Cl, 20.47. Found: C, 59.00; H, 7.01; Cl, 20.18.

Method A: Reaction between Ethyl 4-Phenylpiperidine-4-carboxylate and Arylaminoalkyl Halides. Preparation of Ethyl 1-[2-(4-Methylphenylamino)-ethyl]-4-phenylpiperidine-4-carboxylate Dihydrochloride.—A mixture of ethyl 4-phenylpiperidine-4-carboxylate hydrochloride (13.5 g., 0.05 mole), 2-(4-methylanilino)-ethyl bromide hydrobromide (14.7 g., 0.05 mole), 20 g. of anhydrous sodium carbonate and 100 ml. of butanol was refluxed for 24 hr. with vigorous stirring. The cooled solution was filtered to remove inorganic salts and concentrated *in vacuo* on the steam-bath to a light yellow oil. The oil was taken up in 100 ml. of ether and several small pieces of Dry Ice added. A small quantity of the carbamate of ethyl 4-phenylpiperidine-4-carboxylate was filtered off and the filtrate treated with a solution of hydrogen chloride in ether. A white gum precipitated which turned solid on standing. Crystallization from ethanol-ethyl acetate gave 5.4 g. (25%) of product, m.p. 212–218° dec.

Anal. Calcd. for $C_{25}H_{30}N_2O_2 \cdot 2HCl$: C, 62.86; H, 7.34; Cl, 16.14. Found: C, 62.98; H, 7.16; Cl, 16.01.

Method B: Reaction between Ethyl 1-(ω-Chloroalkyl)-4-phenylpiperidine-4-carboxylate and Aromatic Amines. Preparation of Ethyl 1-(2-Phenylaminoethyl)-4-phenylpiperidine-4-carboxylate Sulfamate.—Ethyl 1-(2-chloroethyl)-4-phenylpiperidine-4-carboxylate hydrochloride (100 g., 0.3 mole) in 500 ml. of water was added in a steady stream to a well stirred mixture of aniline (112 g., 1.2 moles), 100 g. of anhydrous sodium carbonate and 500 ml. of water heated to 90°. After the addition was completed the mixture was stirred on the steam-bath for 3 hr. After cooling, the organic layer was separated and the aqueous layer extracted three times with benzene. The extracts and the organic layer were combined and the benzene removed on the steam-bath under reduced pressure. The excess aniline was removed by distillation at 78° (18 mm.). The residual oil weighed 104 g. The crude free base (38 g., 0.117 mole) was dissolved in 100 ml. of ethanol and a solution of 11.3 g. (0.117 mole) of sulfamic acid in 60 ml. of 50% ethanol was added. On cooling and scratching, a heavy precipitate formed which was collected and washed with ether. On recrystallization from ethanol there was obtained 30 g. (60%) of product, m.p. 153.4–157.2°.

Anal. Calcd. for $C_{22}H_{28}N_2O_2 \cdot NH_2SO_3H$: C, 58.67; H, 6.92; N, 9.32. Found: C, 58.60; H, 6.85; N, 8.96.

Method C: Reaction between Ethyl 1-(ω-Chloroalkyl)-4-phenylpiperidine-4-carboxylate with Aromatic Amines in the Presence of Sodamide. Preparation of Ethyl 1-[2-(4-Meth-oxyphenylamino)-ethyl]-4-phenylpiperidine-4-carboxylate Dihydrochloride.**—To a stirred, refluxing suspension of sodamide (11.7 g., 0.3 mole) in 200 ml. of dry toluene was added 12.3 g. (0.1 mole) of *p*-anisidine. The mixture was refluxed 1.5 hr. and then cooled. Ethyl 1-(2-chloroethyl)-4-phenylpiperidine-4-carboxylate hydrochloride (33.2 g., 0.1 mole) was added all at once and the mixture stirred and refluxed for 3.5 hr. After cooling, the mixture was hydrolyzed with 500 ml. of water. The toluene layer was separated, the aqueous layer extracted with ether, the organic layers combined and concentrated *in vacuo* on the steam-bath. The residue was dissolved in isopropyl alcohol, filtered to remove some insoluble salts and the solution was saturated with HCl gas. On cooling and scratching the product precipitated out. After recrystallization from isopropyl alcohol there was obtained 9.7 g. (21%) of product melting at 181–189°.

Anal. Calcd. for $C_{23}H_{30}N_2O_3 \cdot HCl$: C, 60.65; H, 6.63; Cl, 15.57. Found: C, 60.54; H, 7.13; Cl, 15.40.

Method D: Reaction between Ethyl 1-(ω-Chloroalkyl)-4-phenylpiperidine-4-carboxylate and Aromatic Amines in Cellosolve. Preparation of Ethyl 1-[2-(4-Chlorophenylamino)-ethyl]-4-phenylpiperidine-4-carboxylate Dihydrochloride.—A mixture of ethyl 1-(2-chloroethyl)-4-phenylpiperidine-4-carboxylate hydrochloride (16.6 g., 0.05 mole), *p*-chloroaniline (25.2 g., 0.2 mole) and 110 ml. of Cellosolve was refluxed 16 hr. The red-orange solution was concentrated *in vacuo* on the steam-bath to a red oil which solidified on cooling. Crystallization first from 25 ml. of Cellosolve, then from ethanol, gave 12.0 g. (56.6%) of product, m.p. 200–202°.

Anal. Calcd. for $C_{22}H_{26}N_2O_2 \cdot 2HCl$: Cl, 16.75; N, 6.82. Found: Cl, 16.81; N, 6.53.

Reduction of Ethyl 1-[3-(3-Nitrophenylamino)-propyl]-4-phenylpiperidine-4-carboxylate.—Ethyl 1-[3-(3-nitrophenylamino)-propyl]-4-phenylpiperidine-4-carboxylate hydrochloride (35 g., 0.079 mole) was suspended in 300 ml. of ethanol. Hydrazine hydrate (100%, 16 g., 0.316 mole) was added and the mixture heated to 50° on the steam-bath. Small portions of Raney nickel catalyst were then added over about 30 minutes, until the color change from yellow to colorless indicated reduction was complete. The solution was heated to boiling to remove any gases, filtered hot and then cooled in an ice-bath. The crystalline product was collected and dried at 50°. There was obtained 23 g. (72%) of product melting 100–108°, and requiring no further purification.

Anal. Calcd. for $C_{23}H_{31}N_3O_2 \cdot H_2O$: C, 69.14; H, 8.33; N, 10.6; H_2O, 4.50. Found: C, 69.14; H, 8.40; N, 10.82; H_2O, 4.55.

RENSSELAER, N. Y.

Chemistry of Pyrimidines. II. The Conversion of 5-Bromo- to 5-Hydroxyuracils[1,2]

BY SHIH YI WANG

Neither silver oxide nor lead oxide causes a conversion of 5-bromopyrimidines to the corresponding 5-hydroxy derivatives. Sodium bicarbonate, however, brings about such a conversion quite successfully. 5-Bromo-6-hydroxy-5,6-dihydropyrimidines can also be used for this preparation. The mechanism of this reaction is discussed and a general method of preparation is presented.

Introduction

Although, in 1912, Levene and LaForge[3] reported the preparation of 5-hydroxy-uridine by the bromine and lead oxide method, subsequent workers have found it difficult to use their method.[4] In
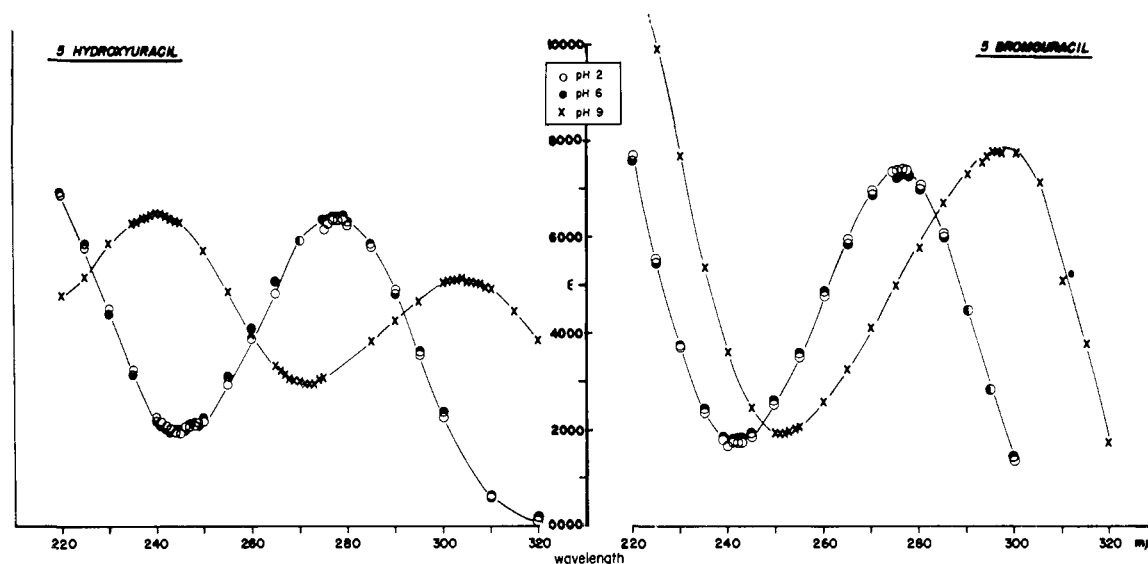
(1) This work was accomplished under the terms of Contract AT(30-1)-911 of the Atomic Energy Commission with the Physiology Department, Tufts University School of Medicine.

(2) The author wishes to thank L. A. Johnson and R. Weintraub for their able assistance.

(3) P. A. Levene and F. B. LaForge, *Ber.*, **45**, 608 (1912).

(4) M. Roberts and D. W. Visser, THIS JOURNAL, **74**, 668 (1952).

our laboratory, 5-hydroxy-1,3-dimethyluracil has been prepared in a similar manner[5] but, again, the results were variable.

Levene and LaForge had indicated that 5-bromopyrimidines are intermediates in the reaction sequence. Johnson and co-workers,[6] in the meantime, proposed that the 5-bromo atom in pyrimidines bearing amino or hydroxy groups in position 4 and 6 is extremely stable toward acid or alkali, thereby making syntheses involving such a conversion unattractive. Indeed, Bendich and Clements[7] treated 5-bromopyrimidines with hot alkali, sodium alkoxides, etc., without liberating any bromide, which further established the 5-bromo atom as unusually resistant to such treatment.

This difficulty has led to the development of various indirect methods[8-11] for the synthesis of 5-hydroxypyrimidines which do not involve bromopyrimidines as intermediates. Recently Davoll and Laney[12] achieved another synthetic approach. They, however, indicated the desirability of a direct conversion utilizing the readily available 5-halogenopyrimidines. Our experimental findings have led to a direct, general method for the preparation of 5-hydroxypyrimidines.

Results and Discussion

For the 5-bromo atom in pyrimidines to be stable, as suggested by most workers, the pyrimidine nucleus would have to be aromatic. Yet it has been suggested that in aqueous solution 2- or 4-hydroxypyrimidine exists predominantly in the lactam (ketonic) form,[13] in which the 5-bromo atom

should be fairly reactive because it is the α-bromo atom in an α,β-unsaturated ketone; and thus it should be possible to hydrolyze the 5-bromo derivatives to the hydroxy derivatives by means of relatively weak bases. In order to support this assumption experimentally, therefore, 5-bromo-1,3-dimethyluracil (IIIb) was allowed to react with different relatively weak alkalies.

When silver oxide was heated under reflux with IIIb in aqueous solution only the starting material could be isolated, the recovery being about 50%. The rest of the starting material was possibly lost as an insoluble silver salt, or oxidized in the process, since a silver mirror was formed during the reaction.

Next, IIIb was treated with lead oxide in aqueous solution and an almost quantitative recovery of unchanged starting material was obtained. This result, together with that found with silver oxide, strongly suggests that 5-bromouridine[3,4] could not be the intermediate which reacts with lead oxide to form the 5-hydroxy derivatives V. Rather, it would appear far more likely that 5-bromo-6-hydroxy-5,6-dihydro derivatives II are the intermediates which react with lead oxide to form the 5,6-dihydroxy-5,6-dihydro derivatives IV and that these in turn dehydrate to form 5-hydroxy derivatives V. When Ia or Ib was converted to II and then treated with lead oxide, Va or Vb was obtained, but only as a mixture with IIIa and IIIb, respectively. In the case of Ib, a pure product (Vb) could be obtained after repeated recrystallization.[14] These results, therefore, suggest that II is the intermediate in the preparation of 5-hydroxypyrimidines. Incidentally, in our laboratory, 5-hydroxyuridine was obtained in over 60% of the theoretical yield by using this approach.

Finally, sodium bicarbonate was used and successfully converted the 5-bromo derivatives III to the corresponding 5-hydroxy derivatives V. Thus we now have available a simple and direct method for the preparation of V.

(5) S. Y. Wang, M. Apicella and B. R. Stone, This Journal, 78, 4180 (1956).

(6) T. B. Johnson and C. O. Johns, Am. Chem. J., 34, 175 (1905); T. B. Johnson and D. A. Hahn, Chem. Revs., 13, 193 (1933).

(7) A. Bendich and G. C. Clements, Biochim. et Biophys. Acta, 12, 470 (1953).

(8) R. Behrand and O. Roosen, Ann., 251, 235 (1889).

(9) T. B. Johnson and E. V. McCollum, J. Biol. Chem., 1, 437 (1906); T. B. Johnson and F. W. Heyl, Am. Chem. J., 38, 237 (1907); T. B. Johnson and D. B. Jones, ibid., 40, 538 (1908).

(10) J. Tafel and P. A. Houseman, Ber., 40, 3743 (1907).

(11) R. Hull, J. Chem. Soc., 2033 (1956).

(12) J. Davoll and D. H. Laney, ibid., 2124 (1956).

(13) J. R. Marshall and J. Walker, ibid., 1004 (1951); D. J.

Brown and L. N. Short, ibid., 331 (1953); and D. J. Brown, E. Hoerger and S. F. Mason, ibid., 211 (1955).

(14) S. Y. Wang, This Journal, 80, 6196 (1958).
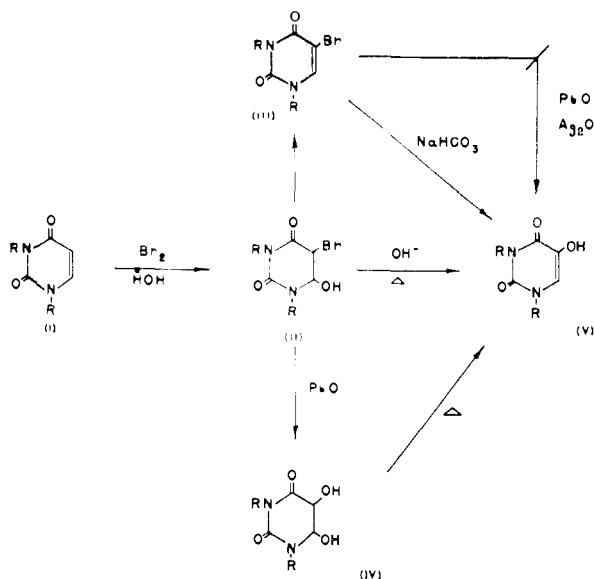
As shown in the figure there is but little difference in the ultraviolet spectra of IIIa and Va at pH 2 or 6. At pH 9, however, a marked difference occurs between IIIa and Va, and this variance was used for the differentiation of these compounds. At higher pH (>9), the optical densities of the spectrum of Va fell with time. The instability of 5-hydroxyuracil in strong bases is probably the reason for the failure to isolate compounds of this type when strong bases were used for their preparations. Indeed, the spectrum of Va was decreased by 50% within 4.5 hr. of reflux with sodium carbonate.

In conclusion, it seems probable that there are two routes for the conversion of 5-bromopyrimidines (II) or (III), to their corresponding 5-hydroxypyrimidines (V). First, if lead oxide or weaker base is used, the chemical pathway involves 5-bromo-6-hydroxy-5,6-dihydro derivatives (II)[15] as intermediates rather than 5-bromo derivatives III as previously suggested.[3] The second route, when sodium bicarbonate or stronger base is used, involves either II or III as the intermediate.

Experimental[16]

Treatment of 5-Bromo-1,3-dimethyluracil (IIIb) with Silver Oxide.—One millimole (219 mg.) of IIIb was heated under reflux with 1.5 mmoles of silver oxide in 10 cc. of water for 5 hr. The solution was stirred during the reaction and a silver mirror was formed. The reaction mixture was then filtered and the product was isolated. This product (120 mg.) was found to be identical with the starting material by m.m.p. and infrared spectrum.

Treatment of 5-Bromo-1,3-dimethyluracil (IIIb) with Lead Oxide.—One millimole of IIIb was treated with lead oxide in a manner similar to that of the above procedure. The filtrate was evaporated to dryness and the organic material was taken up with chloroform. This product (204 mg.) was also found to be identical with the starting material.

(15) S. Y. Wang, Nature, 180, 91 (1957); J. Org. Chem., 24, 11 (1959).

(16) All melting points are uncorrected and were taken with a Fisher–Johns melting point apparatus. Elementary analyses were carried out by Dr. S. M. Nagy and his associates, Microchemical Laboratory, M.I.T. Ultraviolet spectra were determined with a Beckman spectrophotometer, model DU. Infrared spectra were determined with an Infracord spectrophotometer, Perkin–Elmer, in potassium bromide disks.

Conversion of 5-Bromouracil (IIIa) to 5-Hydroxyuracil (Va) with NaHCO₃.—In a typical reaction, 573 mg. (3 mmoles) of IIIa was heated under reflux in 30 cc. of water with 378 mg. (4.5 mmoles) NaHCO₃ for 20 hours under nitrogen. The solution turned to light yellow and upon cooling a small amount of crystals appeared. It was acidified to pH 1–2 and subsequently was allowed to stand in a refrigerator overnight. More than 200 mg. of crude product was obtained which was "digested" twice in 5-cc. portions of methanol at room temperature to get rid of the trace of IIIa present and over 50% of the theoretical yield was obtained. For analysis, this material was recrystallized from water. The infrared and ultraviolet spectra were identical with authentic material.

Anal. Calcd. for $C_4H_4N_2O_3$: C, 37.50; H, 3.15; N, 21.87. Found: C, 37.79; H, 3.25; N, 21.91.

Compound Va, lacking both a reasonable melting point and an appreciable solubility in ordinary solvents, presents a slight problem in its purification. Since these technical difficulties are characteristic of most uracils, a brief account of the purification of Va seems desirable. We have used both infrared and ultraviolet spectra for comparison and identification purposes. Both the increase of the absorbance at ν_{OH}^{KBr} 3398 cm.$^{-1}$ in the infrared spectrum and the decrease of the end absorption in the ultraviolet spectrum at pH 9 indicated that IIIa was gradually being removed as a contaminant of Va. However, contamination of a small amount of IIIa in Va does not significantly change the spectra of pure Va. But this contamination leads to incorrect elementary analyses. However, we found that it was ultimately possible to remove the last traces of IIIa from Va by "digestion" with a small amount of absolute methanol (solubility of IIIa about 5 mg./cc., of Va less than 1 mg./cc.). The product, then, was recrystallized from water and gave correct elementary analyses.

Conversion of 5-Bromo-1,3-dimethyluracil (IIIb) to 5-Hydroxy-1,3-dimethyluracil (Vb) with NaHCO₃.—In a typical reaction, 657 mg. (3 mmoles) of IIIb was heated under reflux in 30 cc. of water with 378 mg. (4.5 mmoles) of NaHCO₃ for 5–6 hours. After cooling, the solution was acidified with 12 drops of 6 N HCl and was then extracted six times with 15-cc. portions of chloroform. The chloroform extract was evaporated to dryness. The residue was taken up in ethanol for crystallization. Over 65% of the theoretical yield was obtained and gave m.p. 198–199°. Both infrared and ultraviolet spectra were identical with authentic Vb, and m.m.p. was 198–199° without depression.

Preparation of 5-Hydroxyuracil (Va) via 5-Bromo-6-hydroxy-5,6-dihydrouracil (IIa) with NaHCO₃.—In a typical reaction, 336 mg. (3 mmoles) of Ia was dissolved in 100 cc. of hot water and was cooled to less than 5°. Bromine (0.18 ml., 3.3 mmoles) was added and was stirred into solution with a magnetic stirrer. When all the bromine was reacted, 756 mg. (9 mmoles) of NaHCO₃ was added in small portions. Then the solution was refluxed for 10 hours under nitrogen. After cooling, a small amount of red precipitate (formed due to the presence of dibromo compound) was removed by filtration. The filtrate was acidified to less than pH 2, and was then lyophilized. The yellowish-white powder so obtained was washed on a funnel with 2 cc. of cold water to remove inorganic material. The organic residue, 245 mg., so obtained gave an infrared curve for Va. It was "digested" twice with 5 cc. of abs. methanol and 177 mg. of the product was obtained.

Preparation of 5-Hydroxy-1,3-dimethyluracil (Vb) via 5-Bromo-6-hydroxy-1,3-dimethyl-5,6-dihydrouracil (IIb) with NaHCO₃.—In a typical reaction, 560 mg. (4 mmoles) of Ib was dissolved in 15 cc. of water and was cooled to about 5°. Bromine (0.21 ml., 4 mmoles) was added to the solution with swirling. As soon as all the bromine droplets disappeared, 12 mmoles of sodium bicarbonate was added in small portions. When the sodium bicarbonate was all reacted, the solution was refluxed for 2 hours. After cooling, it was acidified and the product was isolated in the usual manner. About 350 mg. of the product was obtained with m.p. 198–199°.

Effect of Sodium Carbonate on 5-Hydroxyuracil (Va).—Compound Va, 1 mmole, was dissolved by boiling in 10 cc. of water and then 4.5 mmoles of sodium carbonate was added. At time intervals, a 0.1-ml. sample of the refluxing solution was withdrawn and was diluted with pH 9 buffer to 100 ml. The ultraviolet spectrum of each sample was determined. The readings at 305 mμ decreased with increasing

time as:

Time, hr.	0	2.5	4.5	7	9
$\epsilon_{305} \times 10^{-3}$	5.15	4.18	3.48	2.46	1.88

The experiment was done under nitrogen. The solution turned gradually from yellow to dark brown in color.

BOSTON 11, MASS.

[CONTRIBUTION OF THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

Purines. VIII. The Aminolysis of Certain Chlorosubstituted Purines[1]

BY S. R. BRESHEARS, S. S. WANG, S. G. BECHTOLT AND B. E. CHRISTENSEN

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2,6-Dichloropurine and 2,6,8-trichloropurine were treated with a number of nitrogenous bases. The reactions were found to be stepwise with the 6-position being preferentially aminated. In the case of very active aminating agents the stepwise reaction was accomplished by using aqueous solutions of the amine. For complete aminolysis of the less reactive amines it was necessary to employ pressure equipment. The proof of structure of the partially aminated purines was established by the dehalogenation of the substituted chloropurine and comparison of the product with known compounds. The dehalogenation of 2,6,8-trichloropurine resulted in partial reduction of the nucleus, while 2,6-dichloropurine yielded the 2-chloropurine.

Largely through the efforts of Davoll,[2a] Bendich,[2b] Elion,[3] and their respective co-workers, 6-chloropurine, 2,6-dichloropurine and 2,6,8-trichloropurine have been made available as intermediates for the synthesis of purine derivatives.

The discovery of the effect of kinetin on cell division has stimulated activity in the search for methods for the synthesis of other 6-substituted purines, many of which have been prepared from 6-chloropurine.[4] Little attention, however, has been directed to the use of 2,6-[5] and 2,6,8-halogen substituted purines for such purposes.

TABLE I

COMPARISON OF DEHALOGENATED PURINES WITH KNOWN 6-SUBSTITUTED PURINES

	M.p., °C.	Mixed m.p., °C.	pH	λ_{max}	$E \times 10^4$
2-Chloropurine[12]	231–234		1	270.5	0.807
2-Chloropurine[c]	231–234		1	271	.800
6-Dimethylamino-purine·HCl[d]	251–253		1	277	1.56
6-Dimethylamino-purine·HCl[b]	249–250		1	277	1.47
6-Furfurylaminopurine[d]	265–266		1	274	1.69
6-Furfurylaminopurine[a]	264–266	264–266			
6-Furfurylaminopurine[b]	269–270		1	274	1.59
6-Morpholinopurine[d]	300–302		6	282	1.89
6-Morpholinopurine[a]	301–303	301–303			
6-Morpholinopurine[b]	299–301		[e]	282	1.77
6-Piperidinopurine[d]	274–275		1	281	1.70
6-Piperidinopurine[a]	273–275	272–274			
6-Piperidinopurine[b]	272–275	272–275			

[a] Obtained by dehalogenation of the 2-chloro-6-substituted purine. [b] Obtained by dehalogenation of the 2,8-dichloro-6-substituted purine. [c] Obtained by dehalogenation of the 2,6-dichloropurine. [d] Sample prepared by aminolysis of 6-chloropurine and product used for comparison purposes. [e] Distilled water.

Inasmuch as there is evidence that the activity of the chloro substituents at the 2,6- and 8-posi-

(1) Published with the approval of the Monographs Publications Committee, Oregon State College as Research Paper No. 353, School of Science, Department of Chemistry.

(2) (a) J. Davoll and B. A. Lowy, THIS JOURNAL, **73**, 2936 (1951); (b) A. Bendich, et al., ibid., **76**, 6073 (1954).

(3) G. B. Elion and G. H. Hitchings, ibid., **78**, 3509 (1956).

(4) J. Daly and B. E. Christensen, J. Org. Chem., **21**, 117 (1956); M. L. Sutherland and B. E. Christensen, THIS JOURNAL, **79**, 2251 (1957).

(5) (a) J. A. Montgomery and L. Holum, ibid., **79**, 2185 (1957); (b) **80**, 404 (1958).

tions[6] in the purine molecule are markedly different thus permitting stepwise reactions, these intermediates offer interesting possibilities for the preferential aminolysis leading to the synthesis of possible purine antagonists. In order, therefore,

TABLE II

Purine	pH	λ_{max}	$E \times 10^4$	λ_{min}	$E \times 10^3$
2-Chloro-6-furfurylamino-	95% EtOH	270	1.92	236	4.44
2-Chloro-6-morpholino-	95% EtOH	278	2.12	238	2.64
2-Chloro-6-piperidino-	95% EtOH	280	2.19	238	2.52
2,8-Dichloro-6-morpholino-	95% EtOH	282	2.10	244	3.27
2,6-Difurfurylamino-	95% EtOH	230	3.50	267	6.57
		287	1.18		
2,8-Difurfurylamino-6-morpholino-	95% EtOH	233	2.88	282	7.16
2,8-Dihydrazino-6-morpholino-	1	295	1.72	265	7.31
2,6-Dimorpholino-	1	244	1.86		
		266	2.21		
2,8-Di-n-hexylamino-6-morpholino	95% EtOH	235	2.49	283	5.58
2,6-Dipiperidino-	1	245	1.75		
		268	2.30		
2,8-Dipiperidino-6-morpholino-	1	226	2.35	288	6.94
2-Furfurylamino-6-morpholino-	1	287	1.73	247	10.71
2-Furfurylamino-6-piperidino-	1	288	1.94	245	5.58
2-Hydrazino-6-furfurylamino-	1	282	1.36	255	6.83
2-Hydrazino-6-morpholino-	1	231	1.34		
		289	1.47		
2-Hydrazino-6-piperidino-	1	231	1.46		
		290	1.72		
2-Morpholino-6-furfurylamino-	1	240	2.26		
		290	1.29		
2-Morpholino-6-piperidino-	1	245	1.63		
		268	2.14		
2-Piperidino-6-furfurylamino-	1	241	2.40		
		292	1.20		
2-Piperidino-6-morpholino-	1	244	1.91		
		266	2.26		

to further study the aminolysis reactions of the chloropurines, to establish the structures of the partially aminated chloropurines and to investigate possible dehalogenation reactions of the chloropurines the work described herein was undertaken.

Using 2,6-dichloropurine four types of reactions were performed which included (1) preferential amination, (2) chemical reduction of 2-chloro-6-substituted purine, (3) total amination and (4) stepwise amination of 2-chloro-6-substituted purine.

(6) (a) E. Fischer, Ber., **33**, 1371 (1900); (b) **30**, 2220 (1897); (c) R. K. Robins and B. E. Christensen, THIS JOURNAL, **74**, 3624 (1952).