mixture was evaporated to dryness under reduced pressure. The residue was extracted with ether and the ether solution was extracted with two 30-ml portions of 5% sodium hydroxide. The combined base extract was neutralized in the cold with 5% hydrochloric acid and reextracted into ether. The ether solution was washed with water and dried. Removal of the solvent under reduced pressure afforded 7.7 g of an oil. Low-boiling material was distilled to 128° (0.2 mm) and the residue (5.0 g) was crystallized from ether to obtain XV: mp 71–77°; ir 3700–2400 cm^{-1} (broad band, acid hydroxyl) and 1721 cm^{-1} (strong, ketone); analytical sample, mp 77–78°.

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.42; H, 9.05.

The thiosemicarbazone derivative had mp 185–186°.

Anal. Calcd for $C_{12}H_{21}N_3SO_2$: C, 53.11; H, 7.80; N, 15.48; S, 11.82. Found: C, 53.35; H, 7.62; N, 15.32; S, 11.63.

1,4,4-Trimethylcyclohexan-2-oneacetic Acid Enol Lactone (XVI).—1,4,4-Trimethylcyclohexan-2-oneacetic acid (XV, 200 mg) was heated for 12 hr in 5 ml of acetic anhydride containing 100 mg of anhydrous potassium acetate. The solution was cooled and water was added. The resultant acetic acid solution was extracted with ether; the combined ether extracts were washed with saturated sodium bicarbonate and water. Removal of the solvent under reduced pressure afforded 165 mg of an oil. The analytical sample was obtained by adsorption of the material on Florisil (30:1) followed by elution with benzene: ir 1802 cm^{-1} (strong, lactone carbonyl), 1701 cm^{-1} (unsaturation); mp 44.5–45°.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.11; H, 8.88.

The nmr spectrum showed the following: three methyl singlets at τ 9.01 (3 H), 8.93 (3 H), and 8.80 (3 H); singlets at τ 7.63 (2 H) and 5.03 (1 H); and two multiplets centered at τ 8.41 (2 H) and 8.31 (2 H).

Registry No.—I, 15356-74-8; II, 16778-27-1; VI, 7500-42-7; VII, 16797-54-9; X, 16797-55-0; XIV, 16778-23-7; thiosemicarbazene derivative of XIV, 16778-24-8; XV, 16778-25-9; thiosemicarbazene derivative of XV, 16797-44-7; XVI, 16778-26-0.

Pyrimidine Nucleosides. I. The Synthesis of 6-Methylcytidine, 6-Methyluridine, and Related 6-Methylpyrimidine Nucleosides[1]

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The first successful synthesis of 6-methylpyrimidine nucleosides has been realized. 6-Methylcytidine (VIII) and 6-methyl-2′-deoxycytidine (XI) have now been prepared by direct utilization of 6-methylcytosine (IV) *via* silylation and subsequent treatment with the appropriate acetohalo sugar in acetonitrile. Conversion of 6-methylcytidine into 6-methyluridine (IX) has been achieved in 65% yield. This direct glycosidation procedure applied to 6-methyluracil gave 6-methyl-3-β-D-ribofuranosyluracil (IIa) as the major product. Utilization of this general method has resulted in preparation of 5,6-dimethyluridine (XIII). A new route to the synthesis of 6-methylcytosine (IV) is reported.

Although thymidine, 5-methyl-2′-deoxycytidine,[2] 5-methylcytidine,[3,4] and 5-methyluridine[4,5] have been isolated from various sources of nucleic acid and each has been synthesized chemically[6,7] the corresponding 6-methylpyrimidine nucleosides are unknown. Various unsuccessful attempts to prepare N_1-glycosyl derivatives of 6-methyluracil have been recorded[8,9] and date back to the work of Fischer.[10] The only direct N_1-glycosidation of a 6-substituted uracil, cytosine, or thymine derivative disclosed in the literature is the preparation of orotidine reported by Curran and Angier[11] by coupling the mercury derivative of *n*-butyl orotate. In this latter instance the yield reported was very low and 3-β-D-ribofuranosylorotic acid was the main product.[11]

Newmark and Goodman[8] utilized 6-methyl-2,4-diethoxypyrimidine and 6-methyl-2-ethylthio-4-ethoxypyrimidine in an unsuccessful attempt to prepare 6-methylpyrimidine *N*-glycosides by the Hilbert–Johnson method.

Recent success in utilizing trimethylsilyloxypyrimidine derivatives[12,13] in a *modified* Hilbert–Johnson procedure[14] suggested a reinvestigation of the problem of the synthesis of 6-methylpyrimidine nucleosides. The readily available 6-methyluracil was converted into 6-methyl-2,4-bis(trimethylsilyloxy)pyrimidine (I) with hexamethyldisilazane.[12] Treatment of I with 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide in acetonitrile gave a 16% yield of crystalline 3-(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl)-6-methyluracil (II). Treatment of II with sodium methoxide gave a 66% yield of 3-β-D-ribofuranosyl-6-methyluracil (IIa) (see Scheme I).

Assignment of glycosidation at N_3 was made on the basis of the significant bathochromic shift of 25 mμ in basic solution accompanied by a substantial increase in ϵ_{max} which is characteristic of N_3-substituted uracils.[15–17]

Treatment of I with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide under similar conditions yielded after fractionation a homogeneous syrup, 3-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-6-methyluracil (III) which exhibited a coupling constant $J_{1',2'}$ of less than 1 cps for $H_{1'}$ which established the anomeric config-

(1) This work was supported by Research Grants CA-08109 and CA-08109-02 from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

(2) J. W. Littlefield and D. B. Dunn, *Nature*, **181**, 254 (1958); see also C. A. Dekker and D. T. Elmore, *J. Chem. Soc.*, 2864 (1951).

(3) J. W. Littlefield and D. B. Dunn, *Biochem. J.*, **70**, 642 (1958).

(4) R. H. Hall, *Biochemistry*, **4**, 661 (1965).

(5) D. B. Dunn, *Biochim. Biophys. Acta*, **38**, 176 (1960).

(6) J. J. Fox, D. Van Praag, I. Wempen, I. L. Doerr, L. Cheong, J. E. Knoll, M. L. Eidinoff, A. Bendich, and G. B. Brown, *J. Amer. Chem. Soc.*, **81**, 178 (1959).

(7) J. J. Fox, N. Yung, J. Davoll, and G. B. Brown, *ibid.*, **78**, 2117 (1956).

(8) P. Newmark and I. Goodman, *ibid.*, **79**, 6446 (1957).

(9) J. J. Fox and I. Wempen, *Advan. Carbohyd. Chem.*, **14**, 335 (1959).

(10) E. Fischer and B. Helferich, *Ber.*, **47**, 210 (1914).

(11) W. V. Curran and R. B. Angier, *J. Org. Chem.*, **31**, 201 (1966).

(12) E. Wittenburg, *Z. Chem.*, **4**, 303 (1964).

(13) T. Nishimura and I. Iwai, *Chem. Pharm. Bull.* (Tokyo), **12**, 352, 357 (1964).

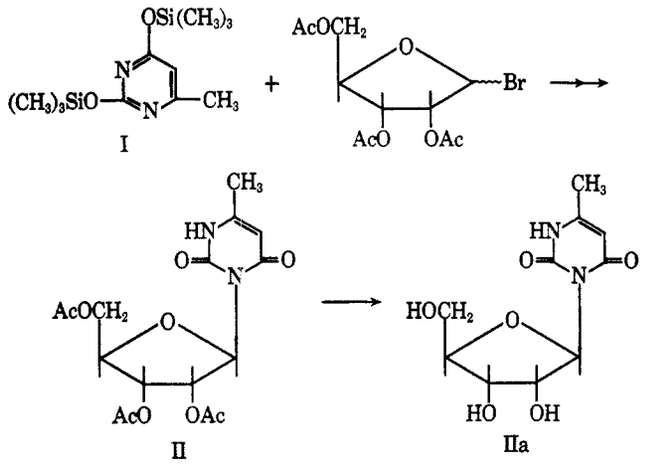
(14) M. G. Stout and R. K. Robins, *J. Org. Chem.*, **33**, 1219 (1968).

(15) D. Shugar and J. J. Fox, *Biochim Biophys. Acta*, **23**, 295 (1957).

(16) J. P. Scannell and F. W. Allen, *J. Org. Chem.*, **25**, 2143 (1960).

(17) M. Sano, *Chem. Pharm. Bull.* (Tokyo), **10**, 320 (1962).

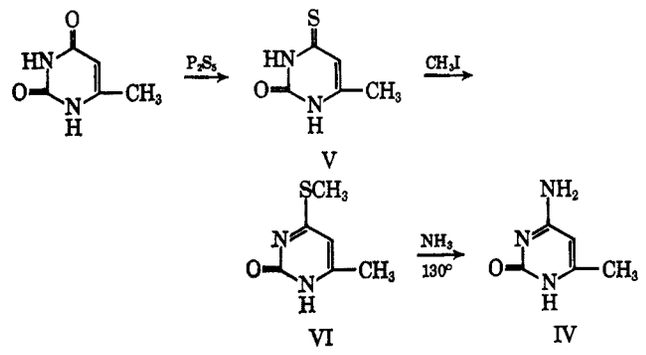
SCHEME I



uration[18] as β. Debenzoylation of III with methanolic ammonia gave a residual syrup which could not be crystallized but was acetylated to yield crystalline II in an over-all 18% yield from I. The identity of the product II obtained *via* 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide or *via* III established the β configuration for II.

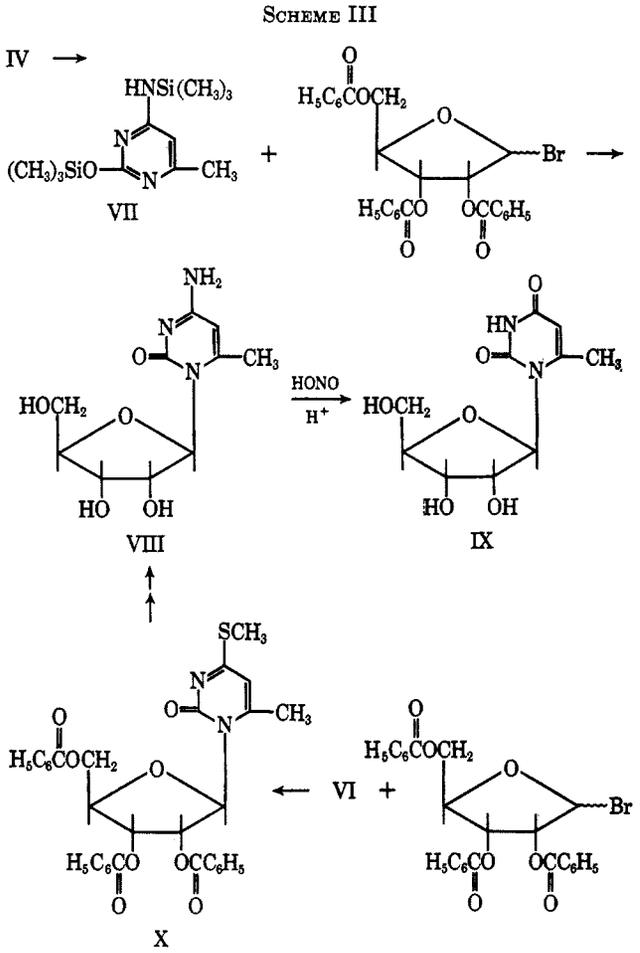
The isolation of the N_3-glycoside of 6-methyluracil is not wholly unexpected since the work of Curran and Angier[11] has shown that with a 6 substituent the mercury coupling procedure resulted in the 3-β-D-ribofuranosyl derivative as the major product. In the present study however, none of the desired 1-(β-D-ribofuranosyl)-6-methyluracil could be isolated from direct glycosidation of I. In view of these results 6-methylcytosine[19] (IV) was selected for further glycosidation studies. Since rather large quantities of 6-methylcytosine were required a new synthesis was devised in our laboratory which now makes 6-methylcytosine readily available from 6-methyluracil. 6-Methyluracil was treated with phosphorus pentasulfide in pyridine to yield 6-methyl-4-thio-2-pyrimidone (V) which was methylated with methyl iodide to provide 6-methyl-4-methylthio-2-pyrimidone (VI) in excellent yield. Replacement of the 4-methylthio group was accomplished with alcoholic ammonia at 130° to provide large white needles of 6-methylcytosine (IV) in excellent yield (Scheme II). Treatment of

SCHEME II



6-methylcytosine (IV) with hexamethyldisilazane gave an intermediate hexamethyldisilyl derivative VII which was utilized directly in the present study (Scheme III). Treatment of VII with 2,3,5-tri-*O*-benzoyl-D-

SCHEME III



ribofuranosyl bromide in acetonitrile gave a 40% yield of pure 6-methylcytidine (VIII) after chromatography and debenzoylation. Treatment of 6-methylcytidine in 2 *N* acetic acid in the presence of sodium nitrite gave 6-methyluridine (IX) in 65% yield. The 6-methylpyrimidine nucleosides VIII and IX were not hydrolyzed with 1 *N* sodium hydroxide at 100° for 2.5 hr and were resistant to 0.1 *N* hydrochloric acid at 100° for 2 hr. These conditions are known to hydrolyze *O*-glycosides.[20] The infrared spectrum of IX exhibited strong carbonyl absorption bands at 1660, 1675, and 1700, 1725 cm^{-1}, respectively. These data eliminate *O*-glycoside structures.[16]

Assignment of the D-ribose moiety to N_1 in 6-methylcytidine was made on the basis of ultraviolet absorption spectral data. The ultraviolet absorption spectra of 6-methylcytidine (VIII) closely resembles that of cytidine and at pH 11 exhibits a band at λ_{max} 271 mμ. This is vastly different from the spectrum of 3-methylcytosine which exhibits a band at λ_{max} 294 at pH 12. Similarly comparison of the ultraviolet absorption spectra of 6-methyluridine (IX) and uridine shows considerable similarity. 6-Methyluridine exhibits absorptions at $\lambda_{max}^{pH\ 1}$ 261 mμ (ε 11,200) and $\lambda_{max}^{pH\ 11}$ 262 mμ (ε 9400). The ultraviolet absorption spectra of

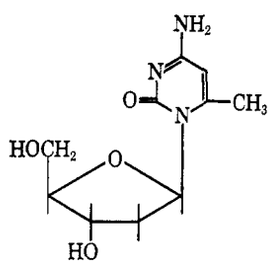
(18) K. L. Rhinehart, Jr., W. S. Chilton, M. Hickens, and W. J. von Phillips, *J. Amer. Chem. Soc.*, **84**, 3216 (1962); see also R. U. Lemieux and D. R. Lineback, *Ann. Rev. Biochem.*, **32**, 155 (1963).

(19) C. O. Johns, *Amer. Chem. J.*, **40**, 348 (1908).

(20) T. L. V. Ulbricht and G. T. Rogers, *J. Chem. Soc.*, 6125 (1965).

3-β-D-ribofuranosyluracil[16] on the other hand is characterized by a bathochromic shift in alkali from $\lambda_{max}^{pH\ 2}$ 261 mμ (ε 8000) to $\lambda_{max}^{pH\ 12}$ 292 mμ (ε 11,400) and is accompanied by a characteristic increase in the extinction coefficient. Assignment of β configuration to 1-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-6-methylcytosine was made since this derivative in deuteriochloroform exhibited a sharp singlet at δ 5.91 due to $H_{1'}$ proton.[18] This established β configuration for both 6-methylcytidine (VIII) and 6-methyluridine (IX).

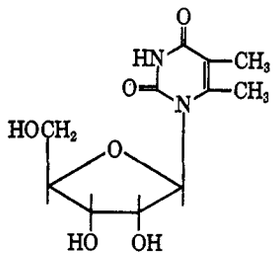
A second route to the synthesis of 6-methylcytidine (VIII) was from 6-methyl-4-methylthio-2-pyrimidone (VI) and 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide which gave a crude syrup (X) which was treated with alcoholic ammonia at 80° to give a product (8% yield) identical with 6-methylcytidine (VIII) prepared from 6-methylcytosine (IV). The successful preparation of 6-methylcytidine suggested that this procedure might be applicable to the synthesis of 6-methyl-2′-deoxycytidine (XI).



XI

Thus 3,5-di-*O*-*p*-toluyl-2-deoxy-D-ribofuranosyl chloride[21] and the hexamethyldisilyl derivative VII were mixed in dry acetonitrile in the presence of molecular sieves. Chromatography of the crude reaction syrup on alumina gave two major fractions consisting of the β and α anomers, respectively. Treatment of the first fraction with methanolic ammonia yielded a 14% yield of crystalline 6-methyl-2′-deoxycytidine, the β anomer XI. Similar treatment of the second fraction yielded 1-(2′-deoxy-α-D-ribofuranosyl)-6-methylcytosine (XII). The assignment of anomeric configuration was readily made by a comparison of the pmr spectra of XI and XII measured in deuterium oxide with an internal standard of sodium 2,2-dimethyl-2-silapentane 5-sulfonate. The anomeric proton of XII consisted of a multiplet of four peaks centered at δ 6.33 ppm (width 14.2 cps, "$J_{H_1'}$" = 6.2 and 8.0 cps). The anomeric proton of XI exhibited a pseudo triplet centered at δ 6.22 ppm (width 13.5 cps, $J_{1',2'}$ = 6.7 cps). These data clearly allow assignment of XII as the α anomer and XI as the β anomer.[22-24] It is noteworthy that in the case of the present reaction procedure the β anomer predominated whereas with 3,5-di-*O*-*p*-toluyl-2-deoxy-D-ribofuranosyl chloride in the Hilbert–Johnson synthesis of 2′-deoxyribofuranosylpyrimidines the major, and often the sole product, is the α anomer.[24]

The importance of substituent groups in the pyrimidine ring on the orientation of the entering sugar moiety is illustrated by the fact that, although 2,4-bis(trimethylsilyloxy)-6-methylpyrimidine gave almost exclusively ribosidation at position N_3 when 2,4-bis(trimethylsilyloxy)-5,6-dimethylpyrimidine was employed, under similar conditions the main product was the N_1 isomer 5,6-dimethyluridine (XIII). Thus 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide and 2,4-bis(trimethylsilyloxy)-5,6-dimethylpyrimidine gave XIII in 17% over-all yield after removal of the acetyl groups. Structural assignment for XIII follows similar lines as discussed for 6-methyluridine (IX).



XIII

Nishimura and Iwai[13] report that acetohalogenosugars did not condense with trimethylsilyloxypyrimidines in boiling benzene or xylene and preferred fusion as a method of nucleoside formation.[13,25] The present work and employment of a similar procedure in the recent synthesis of 1-β-D-ribofuranosyl-2,4-quinazolinedione[14] is convincing evidence that in many instances the general method of pyrimidine nucleoside formation here described is to be preferred and often succeeds where older procedures fail. The extension of these procedures to other sugars and additional 6-substituted pyrimidines is a subject presently under detailed investigation in our laboratory.

Experimental Section

Melting points were determined with a Thomas–Hoover capillary melting point apparatus and are uncorrected. Specific rotations were measured in a 2-dm tube with a Rudolph precision polarimeter. Proton magnetic resonance (pmr) spectra were measured with appropriate internal standards of tetramethylsilane or sodium-2,2-dimethyl-2-silapentane 5-sulfonate with a Varian A-60 nmr spectrometer. Detection of components on SilicAR 7GF (Mallinkrodt) and alumina HF 254 (Brinkmann) was by ultraviolet light. Solvent proportions were by volume. Evaporations were performed under diminished pressure at 35° with a Buchi "Rotovapor."

Trimethylsilyl derivatives of various pyrimidines were prepared using the general procedure of Wittenburg.[12] The pyrimidines were heated under reflux in an excess of hexamethyldisilizane with a catalytic quantity of ammonium sulfate under anhydrous conditions until complete solution was achieved. The time of heating varied from 1 or 2 hr to approximately 20 hr. The excess hexamethyldisilazane was removed by distillation under diminished pressure and the residue (oil or crystalline solid) was used directly without further purification.

6-Methyl-3-(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuransoyl)uracil (II). Method 1.—To Tetra-*O*-acetyl-β-D-ribofuranose (21.2 g) in dry dichloromethane (100 ml) at −60° was added a solution of dry dichloromethane (originally 100 ml) which had been saturated at −60° with dry hydrogen bromide gas. The mixture was protected from moisture and allowed to warm to near room temperature. The solution was evaporated to near dryness and the resulting syrup was treated with azeotropically dried toluene and the excess toluene removed. To the residue was added crystalline 2,4-bis(trimethylsilyloxy)-6-methylpyrimidine (18 g) followed by 250 ml of dry "Nanograde" acetonitrile.[26] The re-

(21) M. Hoffer, *Ber.*, **93**, 2777 (1960).
(22) M. J. Robins and R. K. Robins, *J. Amer. Chem. Soc.*, **87**, 4934 (1965).
(23) T. Nishimura and B. Shimizu, *Chem. Pharm. Bull.*, **13**, 803 (1965).
(24) (a) K. J. Ryan, E. M. Acton, and L. Goodman, *J. Org. Chem.*, **31**, 1181 (1966); (b) M. Prystas, J. Farkas, and F. Šorm, *Collect. Czech. Chem. Commun.*, **30**, 3123 (1965).
(25) T. Nishimura, B. Shimizu, and I. Iwai, *Chem. Pharm. Bull.*, **11**, 1470 (1963); **12**, 1471 (1963); T. Nishimura and B. Shimizu, *ibid.*, **13**, 803 (1965).
(26) Purchased from Mallinkrodt Chemical Works, St. Louis, Mo.

action mixture was sealed and stirred until solution occurred. After 3 days at room temperature the mixture was evaporated to a syrup and excess sodium bicarbonate was added. Water (50 ml) and ethanol (50 ml) were added and the mixture was evaporated to dryness. Coevaporation with absolute ethanol removed the last traces of moisture. The residue was extracted several times with dichloromethane and the dichloromethane solution was evaporated to dryness.

The residual syrup was dissolved in benzene (70 ml) and applied to a column (5.0 × 48 cm) of alumina[27] prepacked in benzene. The material was washed onto the column with benzene (1500 ml). Elution was started with benzene–ethyl acetate (4:1, 2 l.) and then continued with ethyl acetate. One-hundred milliliter fractions were collected beginning with the benzene–ethyl acetate (4:1), and the fractionation was monitored by tlc on alumina HF 254 with ethyl acetate as developer. The fast-moving sugar degradation products were removed by elution with benzene–ethyl acetate (4:1) in the early fractions. Fractions 33–72 which contained a single nucleoside component were pooled and evaporated to dryness. Trituration with ether yielded 4.0 g (16%) of II, mp 157–159°. Recrystallization of this product from dichloromethane–ether yielded 3.70 g of pure material: mp 159–160°; $\lambda_{max}^{pH\ 1}$ 264 mμ (ε 9200), $\lambda_{min}^{pH\ 1}$ 233 (1500), $\lambda_{max}^{pH\ 11}$ 289 (10,400), $\lambda_{min}^{pH\ 11}$ 246 (1100); λ_{max}^{KBr} 1740 (OAc), 1720 (shoulder of peak at 1740), and 1650 cm^{-1} [C=O of 6-methyluracil moiety; 6-methyluracil has absorptions at 1720 and 1650 cm^{-1}]; pmr ($CDCl_3$), δ 2.08 (s, 9, OAc), 2.17 (s, 3, 6-CH_3), 4.00–4.63 (m, 3, 5′-CH_2OH overlapped by a sugar ring H), 5.48–5.84 (m, 3, 5-H and sugar ring H's), 6.45 (d, 1, 1′-H, $J_{1',2'}$ = 1.7 cps), 10.40 ppm (s, 1, 1-NH).

Anal. Calcd for $C_{16}H_{20}N_2O_9$: C, 49.99; H, 5.24; N, 7.29. Found: C, 49.77; H, 5.44; N, 7.46.

Method 2.—To tri-*O*-benzoyl-D-ribofuranosyl bromide prepared from 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (20 g) was added 2,4-bis(trimethylsilyloxy)-6-methylpyrimidine (23 g) and dry acetonitrile (480 ml). The mixture was protected from moisture and stirred until solution was achieved. After 6 days at room temperature the solution was evaporated to a syrup. Sodium bicarbonate (excess), water and ethanol were added and the mixture was evaporated to dryness as in method 1. The residue was extracted with dichloromethane and the dichloromethane solution was evaporated to a syrup. A solution of the syrup in tetrahydrofuran (50 ml) was poured with stirring into pentane (1200 ml) to give a semisolid, yield 21.3 g. This material was dissolved in a small volume of benzene and applied to a column (5.0 × 48 cm) of alumina prepacked in benzene. Benzene (1500 ml) was added and the benzene fractions were discarded. The elution was effected in a manner similar to that outlined above for the acetylated nucleoside. The ethyl acetate fractions were pooled and evaporated to a yellow syrup (8.4 g) which was dissolved in a small volume of benzene and fractionated once more on another column (3.0 × 45 cm) of alumina. The appropriate fractions (as determined by tlc were pooled and evaporated to dryness to yield 5.98 g of homogeneous material). The pmr spectrum of this syrup in deuteriochloroform displayed peaks at δ 2.08 (s, 3, 6-CH_3), 4.52–4.90 (3, 5′-CH_2OH and a sugar ring H), 5.56 (s, 1, 5-H), 6.00–6.35 (m, 2, sugar ring H's), 6.68 (s, 1,1′-H, $J_{1',2'}$ < 1 cps), 7.12–7.70, 7.82–8.20 (m, 15, benzoate H's), 10.44 ppm (s, 1, 1-NH). The small value for $J_{1'2'}$ (<1 cps) of the pmr signal for the anomeric proton established the anomeric configuration as β. To the above syrup (4.98 g) was added a solution of methanol (150 ml) saturated at 0° with ammonia and the mixture sealed in a steel bomb and heated at 80° overnight. The solution was filtered and evaporated to dryness. The residue was stirred with dichloromethane and the resulting gummy solid was removed by filtration, yield 2.80 g. This solid was dissolved in acetic anhydride (20 ml)–pyridine (20 ml) and left at room temperature overnight. The solution was poured into water and ice and the mixture was extracted with dichloromethane. The dichloromethane extract was washed consecutively with two 100-ml portions of water, 1 *N* hydrochloric acid, aqueous sodium bicarbonate solution, and then finally with water. The dried ($MgSO_4$) solution was evaporated to dryness and the residue was crystallized from ether to yield 2.30 g (18%), mp 157–158°. Recrystallization produced pure material, mp 159–160°, which did not depress the melting point of the product prepared by method 1.

(27) Reagent aluminum oxide for chromatographic adsorption purchased from Merck and Co., Rahway, N. J.

6-Methyl-3-(β-D-ribofuranosyl)uracil (IIa).—To II (1.50 g) in anhydrous methanol (50 ml) was added sodium (0.2 g). The resulting solution was sealed and left at room temperature overnight. To the stirred solution diluted with methanol was added portionwise Dowex 50 (H^+, X4, 200–300 mesh) until the solution was no longer basic. The resin was removed by filtration and washed well with methanol. The filtrate and washings were evaporated to smaller volume and decolorized with charcoal. The solution was evaporated to a syrup which was crystallized slowly from isopropyl alcohol. The yield of IIa was 0.80 g (66%), mp 142–145°. Recrystallization from methanol–isopropyl alcohol produced pure material: mp 144–146°; $[\alpha]^{27}D$ −27.6 (*c* 1, water); λ_{max}^{KBr} 1650, 1725 cm^{-1} (C=O of 6-methyluracil moiety); $\lambda_{max}^{pH\ 1\ and\ pH\ 4}$ 265 mμ (ε 8700), $\lambda_{min}^{pH\ 1\ and\ pH\ 4}$ 235 (1500), $\lambda_{max}^{pH\ 11}$ 289 (9800), $\lambda_{min}^{pH\ 11}$ 244 (800), $\lambda_{max}^{pH\ 14}$ 289 (11,300), $\lambda_{min}^{pH\ 14}$ 247 (500); pmr (D_2O), δ 2.17 (s, 3, 6-CH_3), 3.60–4.15 (m, 3, 5-CH_2OH centered at 3.85 overlapped by 4′-H), 4.42 (t, 1, width 13.0 cps, $J_{3',2'}$ = 6.5 cps, 3′-H), 4.58–4.93 (2′-H overlapped by solvent centered at 4.72), 5.67 (s, 1, 5-H), 6.25 ppm (d, 1, $J_{1',2'}$ = 3.0 cps, 1′-H).

Anal. Calcd for $C_{10}H_{14}N_2O_6$: C, 46.51; H, 5.47; N, 10.85. Found: C, 46.61; H, 5.67; N, 10.65.

5,6-Dimethyluridine (XIII). Method 1.—To syrupy 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide prepared from tetra-*O*-acetyl-β-D-ribofuranose (10 g) was added crystalline 2,4-bis(trimethylsilyloxy)-5,6-dimethylpyrimidine (10 g) and dry acetonitrile (250 ml) and the mixture was stirred until solution occurred. After 3 days at room temperature the solution was evaporated to a syrup. This syrup was treated as in the synthesis of II, method 1, and the fractionation was monitered by tlc on alumina HF 254 with ethyl acetate–methanol (9:1) as developer. The crude carbohydrate fraction was eluted with benzene–ethyl acetate (4:1) and the crude nucleoside was then eluted with ethyl acetate. The ethyl acetate fractions were evaporated to dryness to yield 5.0 g of crude syrup which was again applied to an alumina column (3.2 × 48 cm) and the elution was achieved with benzene–ethyl acetate (4:1); 100-ml fractions were collected. Fractions 19–23 were pooled and evaporated to dryness. The residue was dissolved in methanol (50 ml) and the solution was saturated at 0° with ammonia. After remaining at room temperature overnight the solution was filtered and the filtrate evaporated to near dryness. The residue was crystallized from isopropyl alcohol to give crystals: mp 178–180°; yield 1.44 g (17%). Recrystallization from aqueous isopropyl alcohol produced pure material: mp 179–180°; $[\alpha]^{30}D$ −30.6° (*c* 1.47, water); λ_{max}^{KBr} 1650 and 1710 cm^{-1} (C=O of 5,6-dimethyluracil moiety, 5,6-dimethyluracil has the same absorptions); $\lambda_{max}^{pH\ 1\ and\ pH\ 4}$ 268 mμ (ε 10,400), $\lambda_{min}^{pH\ 1\ and\ pH\ 4}$ 236 (1700), $\lambda_{max}^{pH\ 11}$ 269 (7800), $\lambda_{min}^{pH\ 11}$ 246 (3800) and $\lambda_{max}^{pH\ 14}$ 271 (7600), $\lambda_{min}^{pH\ 14}$ 247 (3100); pmr (D_2O, CD_3COOD), δ 1.96 (s, 3, 5-CH_3), 2.40 (s, 3, 6-CH_3), 3.73–4.22 (m, 3, 5′-CH_2OH centered at 3.90 overlapped by 4′-H), 4.51 (t, 1, width 12.5, $J_{3',2'}$ = 6.0 cps, 3′-H), 4.92 (q, 1, width 10.0, $J_{2',3'}$ = 6.0 $J_{2',1'}$ = 3.7 cps, 2′-H), 5.79 (d, 1, $J_{1',2'}$ = 3.7 cps, 1′-H), 6.3–6.7 ppm (solvent).

Anal. Calcd for $C_{11}H_{16}N_2O_6$: C, 48.51; H, 5.92; N, 10.29. Found: C, 48.70; H, 6.15; N, 10.18.

Method 2.—Similar treatment of 2,4-bis(trimethylsilyloxy)-5,6-dimethylpyrimidine (14 g) with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide (prepared from 25 g of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose) gave after alumina chromatography a homogeneous syrup residue of 2′,3′,5′-tri-*O*-benzoyl-5,6-dimethyluridine which exhibited the following pmr spectrum in $CDCl_3$: 2.00 (s, 3, 5-CH_3), 2.30 (s, 3, 6-CH_3), 4.50–4.97 (m, 3, 5′,CH_2OH and a sugar ring H), 5.85 (s, 1, $J_{1',2'}$ < 1 cps, 1′-H), 6.12–6.30 (m, 2, sugar ring H's), 7.10–7.60 (m, 9, benzoate), 7.70–8.20 (m, 6, benzoate), 9.60 ppm (s, 1, 3-NH). The singlet at δ 5.85 ppm for the anomeric proton established the β configuration.[18] To this syrup was added methanol (200 ml) saturated with ammonia at 0° and the mixture was heated at 80° overnight in a steel bomb. The brown solution was filtered and evaporated to dryness. The residue was extracted with dichloromethane and the dichloromethane discarded. The residue was dissolved in acetic anhydride (50 ml)–pyridine (50 ml) and the solution was left at room temperature overnight. The solution was poured into water and ice and extracted with dichloromethane. The extract was washed consecutively with three portions of 1 *N* hydrochloric acid, water, aqueous sodium bicarbonate, and two portions of water. The dried ($MgSO_4$) solution was evaporated to dryness and the residue was dissolved in methanol (70 ml) saturated at 0° with ammonia. After standing overnight

the reaction solution was filtered and the filtrate was evaporated to dryness. The residue was crystallized from methanol–isopropyl alcohol to yield 1.50 g (11%), mp 179–180°. This product was identical with that prepared by method 1.

6-Methylcytidine (VIII) from 6-Methyl-4-methylthio-2-pyrimidone (VI). Method 1.—To 2-trimethylsilyloxy-6-methyl-4-methylthiopyrimidine (prepared from 5 g of VI) was added 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide (prepared from 15 g of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose) in dry acetonitrile (70 ml). After 3 days at room temperature the solution was evaporated to a syrup and treated with sodium bicarbonate, water, and ethanol as in the preparation of II.

The crude syrup was dissolved in a small volume of benzene and applied to a column (5.0 × 35 cm) of alumina prepacked in benzene and the material was washed on with benzene (2 l.). Elution was achieved with benzene–ethyl acetate (19:1) and the fractionation was monitered by tlc with alumina HF 254 with chloroform, as developer. The first three fractions were of 200-ml volume and thereafter of 100-ml volume. Fractions 9–24 were pooled and evaporated to dryness to yield 2.34 g of a yellow syrup. To this syrup was added methanol (100 ml) saturated at 0° with ammonia. The solution was sealed in a steel bomb and heated at 80° overnight. The solution was filtered and evaporated to dryness. Water was added and the mixture was extracted twice with chloroform. The aqueous phase was evaporated to a crystalline solid. This material was dissolved in hot aqueous ethanol, treated with charcoal, and filtered. The filtrate was evaporated and the residue was crystallized three times from water–ethanol–isopropyl alcohol to yield white crystals: 0.66 g (8%); mp 230–232° dec (yellow crystals from *ca.* 208°); $[\alpha]^{30}D$ −41.5° (*c* 1.55, water); $\lambda_{max}^{pH\ 1}$ 278 mμ (ε 14,700), $\lambda_{min}^{pH\ 1}$ 241 (1500), $\lambda_{max}^{pH\ 4}$ 271 (9500), $\lambda_{min}^{pH\ 4}$ 251 (6400), $\lambda_{max}^{pH\ 11}$ 271 (9300), $\lambda_{min}^{pH\ 11}$ 253 (6400), $\lambda_{max}^{pH\ 14}$ 273 (9900), $\lambda_{min}^{pH\ 14}$ 252 (5800); pmr (D_2O), δ 2.37 (s, 3, 6-CH_3), 3.73–4.20 (m, 3, 5′-CH_2OH at 3.88 overlapped by 4′-H), 4.44 (t, 1, width 12.5 $J_{3',2'}$ = 6.0 cps, 3′-H), 4.67 (solvent), 4.85 (q, 1, width 10.5, $J_{2',3'}$ = 6.0, $J_{2',1'}$ = 3.5 cps, 2′-H), 5.73 (d, 1, $J_{1',2'}$ = 3.5 cps, 1′-H), 5.88 ppm (s, 1, 5-H).

Anal. Calcd for $C_{10}H_{15}N_3O_5$: C, 46.68; H, 5.88; N, 16.33. Found: C, 46.78; H, 5.94; N, 16.30.

6-Methylcytidine (VIII) from 6-Methylcytosine (IV). Method 2.—To the crystalline trimethylsilyl derivative prepared from 10 g of 6-methylcytosine, was added 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide (from 25 g of the 1-*O*-acetyl derivative) and dry acetonitrile (150 ml). The mixture was sealed and stirred until solution occurred. After 3 days at room temperature the solution was evaporated to a syrup and treated with sodium bicarbonate, water, and ethanol and the mixture was evaporated to dryness. The last traces of moisture were removed by successive evaporations with absolute ethanol. The residue was extracted with dichloromethane and the extract was evaporated to dryness. This residue was again extracted with dichloromethane and the extract evaporated to yield 31.0 g of a syrup.

The bulk of the above syrup (22.43 g) was dissolved in a small volume of benzene and applied to a column (5.0 × 46 cm) of alumina prepacked in benzene. The material was washed on with benzene (1 l.). Elution was carried out with benzene–ethyl acetate (4:1), ethyl acetate, ethyl acetate–methanol (19:1), ethyl acetate–methanol (10:1), and finally with ethyl acetate–methanol (4:1). The fractionation was monitored by tlc on alumina HF 254 with ethyl acetate–methanol (4:1) as solvent and on SilicAR 7GF with ethyl acetate methanol (9:1) as solvent. Two-hundred milliliter fractions were collected up to fraction 32 and 100-ml fractions were collected thereafter. At fraction 10 the solvent was changed to ethyl acetate and at fraction 25 the solvent was changed to ethyl acetate–methanol (19:1). Fractions 32–71 which contained the main nucleoside component were pooled and evaporated to dryness to yield 10.28 g. The material remaining on the column (a mixture of two components) was finally eluted with ethyl acetate–methanol (9:1, 2 l.) and ethyl acetate–methanol (4:1, 3 l.) to yield 6.82 g of crude mixture which proved to be approximately 50% 6-methylcytidine. The contaminating component was not further identified.

The pmr spectrum of the major component in $CDCl_3$ exhibited peaks at δ 2.34 (s, 3, 6-CH_3), 4.50–4.95 (m, 3, 5′-CH_2OH at 4.79 overlapped by a sugar ring H), 5.91 (s, 1, $J_{1',2'}$ < 1 cps, 1′-H), 6.12 (s, 1, 5-H), 6.23–6.63 (m, 2, sugar ring H's), 7.17–7.68, 7.86–8.30 (m, 17, benzoate overlapping 4-NH_2). The signal assigned to the anomeric proton at δ 5.91 ppm had $J_{1',2'}$ < 1 cps and therefore[18] the anomeric assignment made was that of β. The residue, 10.28 g, representing the major component was dissolved in methanol (200 ml) saturated at 0° with ammonia and left at room temperature for 3 days. The solution was filtered and the filtrate was evaporated to a small volume. Crystallization occurred while the solution was being evaporated. Isopropyl alcohol was added and the volume was reduced further. The yield of white crystalline material was 3.70 g (40% from 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose), mp 232–236°. The infrared spectrum was identical with that of VIII prepared by method 1. Attachment of the sugar moiety to N_3 was excluded since the ultraviolet spectrum of 3-substituted cytosines exhibit a bathochromic shift in alkali.[28]

6-Methyluridine (IX).—To 6-methylcytidine (VIII) (3.0 g) in 2 *N* acetic acid (600 ml) was added sodium nitrite (12 g). The resulting solution was sealed and left at room temperature for 2 days. The volume of the solution was reduced by evaporation at 35° and the solution was neutralized to pH 7 with dilute sodium hydroxide solution. Acid-washed AU-4 charcoal[29] (45 g) was added and the mixture was stirred for 2 hr. The mixture was filtered on a Celite pad and the charcoal was washed well with water. The charcoal pad was stirred with ethanol (500 ml), which had been saturated with ammonia at 0°, and filtered. This process was repeated three times. The combined filtrates were evaporated to dryness. The residue was dissolved in water (75 ml) and applied to a column (39 × 2.0 cm) of Dowex 50 (H^+, X4, 200–400 mesh). The nucleoside was washed off with water (1,500 ml). The acid (pH 1) eluate was evaporated at 35° to small volume and the solution treated with ethanol and evaporated to dryness. This process was repeated several times until a syrup was obtained. This syrup was crystallized from ethanol–ethyl acetate to yield 1.94 g (65%), mp 174–176°. Recrystallization from methanol–ethyl acetate produced pure material: mp 177–178°; $[\alpha]^{30}D$ −28.6° (*c* 1.52, water); λ_{max}^{KBr} 1660, 1675 cm^{-1} and 1700, 1725 cm^{-1} (carbonyl absorptions of the 6-methyluracil moiety). These strong carbonyl bands at 1660, 1675 cm^{-1} and 1700, 1725 cm^{-1} attest to existence of two carbonyl groups in the nucleoside. The compound also exhibited uv bands at $\lambda_{max}^{pH\ 1\ and\ pH\ 4}$ 261 mμ (ε 11,200), $\lambda_{min}^{pH\ 1\ and\ pH\ 4}$ 232 (1900), $\lambda_{max}^{pH\ 11}$ 262 (9400), $\lambda_{min}^{pH\ 11}$ 239 (4300), $\lambda_{max}^{pH\ 14}$ 264 (7900), $\lambda_{min}^{pH\ 14}$ 244 (4200); pmr (D_2O) signals were at δ 2.42 (s, 3, 6-CH_3), 3.77–4.22 (m, 3, 5′-CH_2OH at 3.91 overlapped by 4′-H), 4.45 (t, 1, width 12.5, $J_{3',2'}$ = 6.2 cps, 3′-H), 4.69 (solvent), 4.76–5.00 (q, 1, width 10.0, $J_{2',3'}$ = 6.2, $J_{2',1'}$ = 3.7 cps, 2′-H), 5.76 (d, 1, $J_{1',2'}$ = 3.7 cps, 1′-H), 5.83 ppm (s, 1, 5-H).

Anal. Calcd for $C_{10}H_{14}N_2O_6$: C, 46.51; H, 5.47; N, 10.85. Found: C, 46.34; H, 5.54; N, 10.72.

6-Methyl-4-thio-2-pyrimidone (V).—To a warm stirred solution of 6-methyluracil (12.6 g) dissolved in reagent grade pyridine (400 ml) was added phosphorus pentasulfide (6.6 g). The stirred solution was heated under reflux overnight. The solution was evaporated to dryness. The residue was boiled with ethanol and the mixture was filtered. The solid was dissolved in warm dilute aqueous ammonia and glacial acetic acid was added to precipitate the crude compound. This precipitate was dissolved in warm dilute ammonia and the solution was treated with charcoal and filtered. The hot filtrate was acidified with glacial acetic acid to give 8.25 g of yellow crystals, mp 337° (darkening at 325°). The reprecipitation process was twice repeated to give pure yellow crystals of V: mp 339–341°; $\lambda_{max}^{pH\ 1}$ 327 mμ (ε 23,400), $\lambda_{max}^{pH\ 11}$ 330 (22,200).

Anal. Calcd for $C_5H_6N_2OS$: C, 42.24; H, 4.25; N, 19.71; S, 22.55. Found: C, 42.33; H, 4.12; N, 19.86; S, 23.04.

Wheeler and McFarland[30] recorded mp >250° for this compound, prepared by another procedure.

Preparation of 6-Methyl-4-methylthio-2-pyrimidone (VI).—To 22.72 g of 6-methyl-4-thio-2-pyrimidone (V) in cold 1 *N* sodium hydroxide (500 ml, cooled in ice) was added methyl iodide (22.72 g) and the mixture was stirred vigorously for several hours during which time the reaction was gradually allowed to come to room temperature. The mixture was acidified with glacial acetic acid and the volume was reduced to one-fourth. The crude methylated product crystallized on cooling. The product was removed by filtration and the mother liquor evaporated to give another crop. The total yield was 20.8 g, mp 150–157°. The product was recrystallized from water to yield 17.7 g (71%),

(28) P. Brookes and P. D. Lawley, *J. Chem. Soc.*, 1348 (1962).

(29) Purchased from Barneby-Cheney, Columbus 19, Ohio.

(30) H. L. Wheeler and D. F. McFarland, *Amer. Chem. J.*, **42**, 431 (1909).

mp 163–167°. Two recrystallizations from ethyl acetate afforded pure material: mp 178–180°; $\lambda_{max}^{pH\ 1}$ 265 mμ (ε 3600), 321 (22,000), $\lambda_{max}^{pH\ 11}$ 298 (11,200).

Anal. Calcd for $C_6H_8N_2OS$: C, 46.13; H, 5.19; N, 17.94; S, 20.52. Found: C, 46.16; H, 5.30; N, 17.94; S, 20.59.

Wheeler and McFarland[30] recorded mp 174–175° for this compound prepared by another procedure.

Preparation of 6-Methylcytosine (IV).—6-Methyl-4-methylthio-2-pyrimidone (VI, 7.35 g) was dissolved in methanol, and the solution was filtered into a glass bomb liner. The solution was evaporated to dryness on a steam bath. Methanol (200 ml) saturated at 0° with ammonia was added and the vessel sealed in a bomb. The mixture was heated at 130° overnight. The resulting cooled solution contained large white needles: yield 5.66 g (96%); mp 361–363° dec; $\lambda_{max}^{pH\ 1}$ 276 mμ (ε 13,000), $\lambda_{min}^{pH\ 1}$ 238 (880), $\lambda_{max}^{pH\ 11}$ 267 (8000), $\lambda_{min}^{pH\ 11}$ 246 (3800), $\lambda_{max}^{pH\ 14}$ 280 (8900), $\lambda_{min}^{pH\ 14}$ 249 (1400).

Anal. Calcd for $C_5H_7N_3O$: C, 48.01; H, 5.64; N, 33.59. Found: C, 47.91; H, 5.76; N, 33.54.

Johns[19] reported mp >300° for this compound, prepared by another procedure.

6-Methyl-2′-deoxycytidine (XI).—3,5,-Di-*O*-*p*-toluyl-2-deoxy-D-ribofuranosyl chloride (35 g prepared[21] from 50 g of methyl 2-deoxy-3,5-di-*O*-*p*-toluylribofuranoside) was added to the crystalline trimethylsilyl derivative prepared from 15 g of 6-methylcytosine. Molecular sieves[31] (type 4A, 1/16-in. pellets, 20 g) and dry acetonitrile (450 ml) was added and the sealed mixture stirred at 20° for 4 days. The mixture was diluted with dichloromethane and filtered through Celite. The filtrate was evaporated to dryness. To the residue was added sodium bicarbonate, water, and ethanol and the mixture was finally evaporated to dryness. Evaporation with absolute ethanol removed the last traces of water. The residue was extracted with chloroform and with ethyl acetate. The combined extracts were evaporated to a syrup which was dissolved in benzene and applied to a column (5.1 × 43 cm) of alumina packed in benzene. The material was washed on with benzene (500 ml). Elution was accomplished with benzene–ethyl acetate (4:1), ethyl acetate, ethyl acetate–methanol (49:2), and ethyl acetate–methanol (10:1). Two-hundred milliliter fractions were collected until fraction 43 and from then on 50-ml fractions were collected. Benzene–ethyl acetate (4:1) was the eluting solvent until fraction 5. Ethyl acetate was the eluting solvent from fraction 5 to fraction 35. Ethyl acetate–methanol (49:2) was used from fraction 35 to fraction 40. Ethyl acetate–methanol (10:1) was used from 40 onwards. Fractions 43–63 (fraction A), which contained a single nucleosidic component, were pooled and evaporated to dryness to yield 8.47 g. Fractions 64–92 (fraction B), which contained a mixture, were pooled and evaporated to dryness to yield 8.16 g of isomers which were discarded. Fractions 93–154 (fraction C), which were enriched with a slower moving component, were pooled and evaporated to dryness to yield 4.57 g. The total yield of nucleosidic material was 21.2 g.

Fraction A was dissolved in methanol (300 ml) previously saturated at 0° with ammonia and the vessel was sealed. After 3 days at room temperature the solution was filtered and the filtrate was evaporated to dryness. The residue was partitioned between chloroform and water. The aqueous phase was extracted with three 100-ml portions of chloroform, and the aqueous solution was then evaporated to dryness. Evaporation with absolute ethanol removed the last traces of water. The residual syrup was crystallized from ethanol–isopropyl alcohol to yield 3.04 g of 6-methyl-2′-deoxycytidine (14%), mp 159–162°. This slightly yellow product was dissolved in methanol, decolorized with charcoal, and evaporated to a syrup. The syrup was crystallized from methanol–isopropyl alcohol to yield 2.70 g: mp 164–166° (this process was repeated to raise the melting point to 173–176°); $[\alpha]^{34}D$ +32.2° (*c* 1, water); $\lambda_{max}^{pH\ 1}$ 278 mμ (ε 14,900), $\lambda_{min}^{pH\ 1}$ 241 (960), $\lambda_{max}^{pH\ 4\ and\ pH\ 11}$ 271 (9500), $\lambda_{min}^{pH\ 4\ and\ pH\ 11}$ 252 (6000), $\lambda_{max}^{pH\ 14}$ 273 (9800), $\lambda_{min}^{pH\ 14}$ 252 (5600); pmr (D_2O), δ 2.40 (s, 3, 6-CH_3), 2.50–2.85 (m, 2, 2′-H's), 3.80 (s, 2, 5′-CH_2OH) 4.21–4.58 (m, 2, 3′-H overlapped by 4′-H), 4.80 (solvent), 5.87 (s, 1, 5-H), 6.20 ppm (t, 1, width 13.5, $J_{1'2'}$ = 6.7 cps).

Anal. Calcd for $C_{10}H_{15}N_3O_4$: C, 49.77; H, 6.27; N, 17.42. Found: C, 49.52; H, 6.49; N, 17.32.

1-(2′-Deoxy-α-D-ribofuranosyl)-6-methylcytosine.—Fraction C from the synthesis of XI was further purified by preparative thin layer chromatography on SilicAR 7GF. The material was applied to the short edge of ten plates (400 × 200 × 2 mm) of SilicAR 7 GF and the plates were developed several times in ethyl acetate–methanol (9:1). The major bands were extracted with methanol and the extract evaporated to dryness. Extraction of the residue with dichloromethane and evaporation of the solvent yielded 3.49 g of purified material.

This material was applied to eight plates (400 × 200 × 2 mm) of alumina HF 254 and the plates were developed several times with ethyl acetate–methanol (4:1). Two bands were observed, a faster band (β anomer) and a broad slower moving band (α anomer). The broad slower band was carefully excised and the absorbent was extracted with methanol. The solvent was evaporated and the residue was extracted with dichloromethane. Evaporation of this extract gave a syrup which was treated with methanol (150 ml) previously saturated with ammonia at 0° for 3 days at room temperature. The solution was filtered and evaporated to dryness. The residue was crystallized from methanol–isopropyl alcohol to yield 0.50 g (melting point, yellows from 197° and gradually decomposes). This material was dissolved in aqueous methanol and decolorized with charcoal. The solution was evaporated to a syrup and recrystallized from ethanol–isopropyl alcohol to yield pure material: mp 197–199° sinters, gradually decomposes, yellows at 192°; $[\alpha]D$ +13.7 (*c* 1, water); $\lambda_{max}^{pH\ 1}$ 278 mμ (ε 14,900), $\lambda_{min}^{pH\ 1}$ 241 (970), $\lambda_{max}^{pH\ 4\ and\ pH\ 11}$ 271 (9700), $\lambda_{min}^{pH\ 4\ and\ pH\ 11}$ 252 (6400), $\lambda_{max}^{pH\ 14}$ 273 (9900), $\lambda_{min}^{pH\ 14}$ 252 (6200); pmr (D_2O), δ 1.95–2.50 (m, 4, 6-CH_3 (s), at 2.40 overlapped by 2′-H), 2.70–3.25 (m, 1, 2′-H), 3.75–4.22 (m, 3, 5′-CH_2OH at 3.92 overlapped by 4′-H), 4.45–5.00 (m, 3′-H overlapped by solvent at 4.77), 5.89 (s, 1, 5-H), 6.22 ppm (q, 1, width 14.2 cps, "J_H" = 6.2, 8.0 cps, 1′-H).

Anal. Calcd for $C_{10}H_{15}N_3O_4$: C, 49.77; H, 6.27; N, 17.42. Found: C, 49.98; H, 6.39; N, 17.49.

The faster component (β anomer) was isolated and deblocked as described to yield 0.24 g, mp 173–176°.

Registry No.—II, 16710-07-9; IIa, 16710-08-0; IV, 6220-50-4; V, 638-13-1; VI, 16710-11-5; VIII, 16710-12-6; IX, 16710-13-7; XI, 16710-14-8; XII, 16710-15-9; XIII, 16710-16-0.

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(31) Purchased from Fisher Scientific Co., Fair Lawn, N. J.