265° dec,[24] $[\alpha]^{23}D$ +150° (c 0.5, H_2O). *Anal.* ($C_{10}H_{15}N_3O_5$) C, H, N.

4-Acetylamino-1-β-D-arabinofuranosyl-2(1H)-pyrimidinone (4a, R = $COCH_3$).[25]—The HCl salt of 1-β-D-arabinofuranosylcytosine (**4a**, R″ = H, 1.1 g) was dissolved in H_2O and added to a Dowex 1 (OH^-) column. After elution with ~2.5 l. of H_2O, the eluate was concentrated to dryness *in vacuo*. The fine crystalline, free nucleoside (880 mg) was dissolved in 100 ml of MeOH and refluxed with 0.9 ml of Ac_2O for 5 hr. Additional 0.9-ml portions of Ac_2O were added during the reflux period at hourly intervals. The reaction mixture was separated from a small amount of insoluble material, and the filtrate was concentrated *in vacuo* to 10 ml and treated with Et_2O. A crystalline product was obtained; 0.95 g (92%), mp ~170°. Recrystallization from hot EtOH gave pure product, mp 194–195°. Uv-absorption properties (see Table I) were generally similar to those for N^4-acetylcytidine.[11] *Anal.* ($C_{11}H_{15}N_3O_6$) C, H, N.

5,6-Dihydro-4,6-dihydroxylamino-1-β-D-ribofuranosyl-2(1H)-pyrimidinone (6).—To a solution of 1.18 g (0.0045 mole) of 4-thiouridine[8,26] in 40 ml of MeOH containing 1 ml of H_2O was added 1.5 g (0.045 mole) of anhydrous NH_2OH.[27] The mixture was left for 1 hr at room temperature. An immediate evolution of H_2S occurred. After 1 hr, the uv absorption maximum of the thione peak at 328 mμ had disappeared with a corresponding rise of a new maximum at 226 mμ. The reaction mixture was evaporated *in vacuo* to a thin syrup which was treated with a large volume of Et_2O. A flocculent precipitate thus obtained was decanted through a filter and washed with Et_2O. The solid, crystallized from hot EtOH, afforded 110 mg, mp 170–171°.[28] This compound had a single, selective, uv, absorption maximum at 223 mμ. On treatment with 1 *N* HCl, the short-wavelength maximum rapidly disappeared with the concurrent appearance of a new maximum at 280 mμ. This behavior is essentially identical with that of the "bis" hydroxylamino compound reported previously.[12] *Anal.* ($C_9H_{16}N_4O_7$) C, H; N: calcd, 19.17; found, 18.73.

After removal of the "bis" compound, the mother liquor was treated with HCl and, after subsequent neutralization, afforded a product which resembled in all respects the known N^4-hydroxycytidine.[8]

4-Hydroxylamino-1-β-D-ribofuranosyl-2(1H)-pyrimidinone (5a, R″, R‴ = OH).—To 1.06 g (0.004 mole) of 4-thiouridine[8,26] in 50 ml of MeOH was added NH_2OH[22] (0.04 mole) in MeOH (200 ml). The mixture was held at room temperature for 80 min after which time the uv absorption at 328 mμ had completely disappeared, and a new absorption maximum at 272 mμ had appeared. The MeOH was removed *in vacuo* and EtOH was added and removed *in vacuo* three times. The residue was taken up in 75 ml of cold EtOH, the insoluble material was removed, and the filtrate was taken to dryness *in vacuo*. HCl (36 ml, 1 *N*) was added, and the mixture was heated on a steam bath for 6 min.[29] The acid was removed *in vacuo*, and the residue was taken to dryness *in vacuo* six times, three times with 25 ml of C_6H_6, and three times with 25-ml portions of EtOH. The resulting residue was dissolved in 50 ml of cold EtOH, and the product was precipitated by the addition of 200 ml of Et_2O. The solution (in EtOH) and reprecipitation were repeated to obtain a pale, straw-colored powder, 661 mg (55%), mp 182–183° dec, with darkening at 181°. The HCl salt thus obtained has spectral data which are essentially identical with those previously reported.[12]

1-(2-Deoxy-β-D-ribofuranosyl)-5-fluoro-4-methylthio-2(1H)-pyrimidinone.[30]—To a solution of 1.6 g (0.006 mole) of 2′-deoxy-5-fluoro-4-thiouridine[3] in MeOH was added excess CH_2N_2 in Et_2O. The reaction mixture was allowed to stand 1 hr and taken to dryness *in vacuo*. The crystalline product was recrystallized from MeOH and afforded an essentially quantitative yield of pale yellow needles, mp 141.5–143°, shown to be a single component by tlc (*n*-BuOH–H_2O, 86:14). *Anal.* ($C_{10}H_{13}FN_2O_4S$) C, H, N.

1-(2-Deoxy-β-D-ribofuranosyl)-5-fluoro-4-hydroxylamino-2(1H)-pyrimidinone (5, R′ = F; R″ = OH; R‴ = H).—A solution of 3.6 g (0.013 mole) of the S-methylated precursor in 200 ml of MeOH was treated with MeOH–NH_2OH[22] (0.13 mole), and the mixture was left at room temperature for 18 hr. The course of reaction was monitored by the disappearance of the uv absorption at 315 mμ. The solution was taken to dryness *in vacuo*. EtOH was added to the residue in three consecutive 50-ml portions, evaporating the solution to dryness each time. The residue was taken up in cold EtOH (100 ml), and the insolubles were removed by filtration. The filtrate was concentrated to *ca.* 10 ml and EtOAc was added followed by petroleum ether. The amorphous, white precipitate which resulted was purified by repeating the solution and reprecipitation step. Attempts to obtain a crystalline compound were unsuccessful. The product (1.2 g) was hygroscopic and had no definite melting point. Uv-absorption properties of the compound are in 6 *N* HCl, maxima at 219 and 290 mμ (ε 7660, 10,590), minimum at 248 mμ (ε 2040); at pH 7, maxima at 234 and 267 mμ (ε 9780, 7740), minimum at 255 mμ (ε 6920). *Anal.* ($C_9H_{12}FN_3O_5 \cdot 0.5H_2O$) C, H, N.

1-(2-Deoxy-β-D-ribofuranosyl-4-hydroxylamino-5-methyl-2(1H)-pyrimidinone (5, R′ = CH_3; R″ = NHOH; R‴ = H).—A solution of 3.4 g (0.013 mole) of 4-thiothymidine[8] and NH_2OH[22] (0.13 mole) in MeOH (200 ml) was heated at 38° for 5 hr. The completion of the reaction was determined by the absence of uv absorption in the 334-mμ region and cessation of H_2S evolution. The mixture was evaporated to dryness *in vacuo* and 50 ml of EtOH was added and evaporated *in vacuo*. The addition and evaporation were repeated three times. The resulting white residue was taken up in cold EtOH (100 ml), and the insoluble material was removed. To the filtrate was added 5 ml of a solution of HCl in EtOH (saturated at 0°) and 50 ml of Et_2O. Crystallization occurred slowly. The compound was recrystallized from EtOH–Et_2O. The yield was 3.4 g (88%), mp 160° dec. The uv-absorption properties are essentially identical with those previously reported for the free nucleoside.[8]

(24) A melting point of 257–260° for the crude, free base was reported by J. H. Hunter, U. S. Patent 3,116,282 (Dec 31, 1963).

(25) The synthesis of this compound was performed by Dr. Naotaka Yamaoka of these laboratories.

(26) This compound has been reported as a crystalline solid by N. K. Kochetkov, E. I. Budowsky, V. N. Shibaev, G. I. Yeliseeva, M. A. Grachev, and V. P. Denushkin, *Tetrahedron*, **19**, 1207 (1963).

(27) C. D. Hurd, *Inorg. Syn.*, **1**, 87 (1939).

(28) The melting point of the unrecrystallized compound is reported in ref 12 as 130–135°.

(29) No attempt was made to isolate the "bis" compound. However, the filtrate from the acid treatment did exhibit a nonultraviolet-absorbing component on a thin layer chromatogram (*n*-BuOH–H_2O 86:14) which was visualized by spraying with a FeCl₃ solution. The resulting pink spot has been reported as characteristic of the "bis" hydroxylamino derivatives.[12] The monohydroxylamino derivative exhibits a blue spot when treated with the same reagent.[12]

(30) This compound was previously reported[31] as a crude intermediate which was not characterized.

(31) T. Ueda and J. J. Fox, *J. Med. Chem.*, **6**, 697 (1963).

Nucleosides. XLVIII. Synthesis of 1-(5-Deoxy-β-D-arabinosyl)cytosine and Related Compounds[1]

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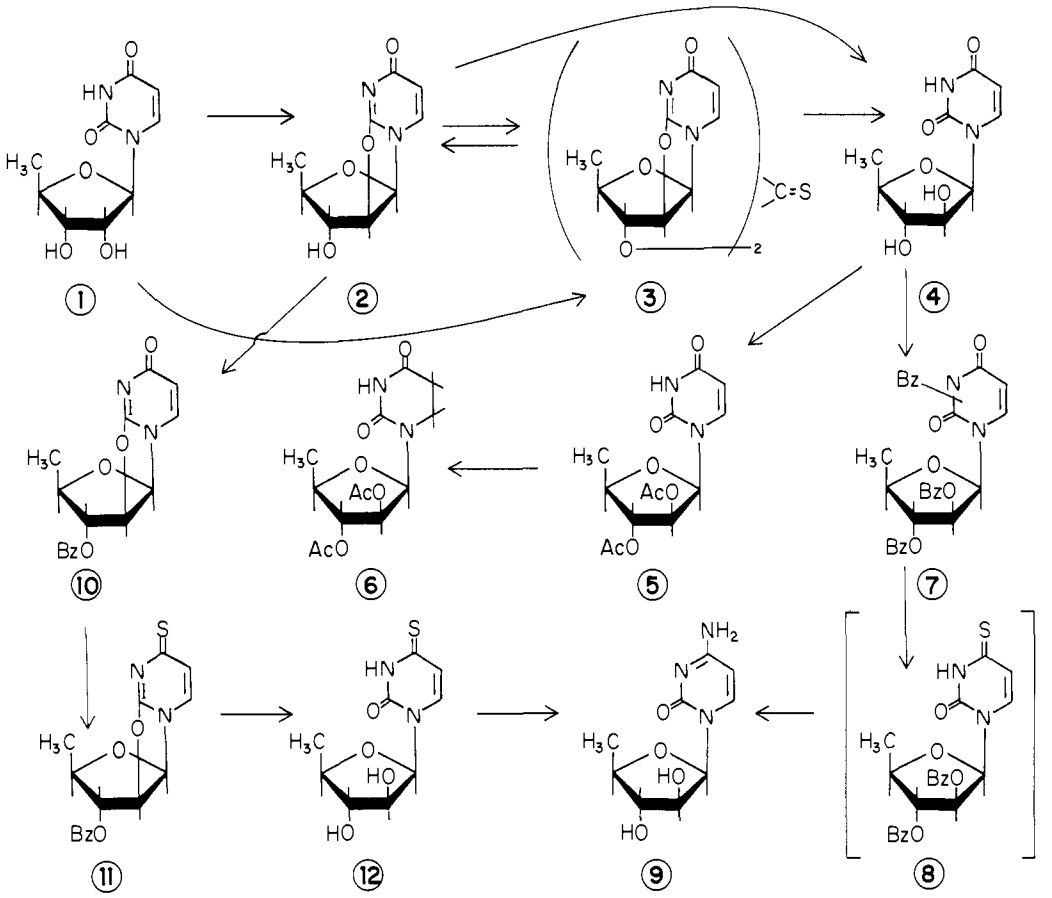
In the course of biochemical and biological studies[2,3] on analogs of 1-β-D-arabinofuranosylcytosine (*ara*-C), it became necessary to synthesize 5′-deoxy-*ara*-C (**9**, see Scheme I) as a possible substrate and/or inhibitor of deoxycytidine deaminase present in human liver or mouse kidney homogenates. This paper describes the synthesis of 5′-deoxy-*ara*-C by two routes from 5′-deoxyuridine by use of anhydro nucleoside intermediates.

(1) This investigation was supported in part by funds from the National Cancer Institute (Grant No. CA 08748).

(2) M. R. Dollinger, J. H. Burchenal, W. Kreis, and J. J. Fox, *Biochem Pharmacol.*, **16**, 689 (1967).

(3) I. Wempen, N. Miller, E. A. Falco, and J. J. Fox, *J. Med. Chem.*, in press.

SCHEME I



Reaction of 5′-deoxyuridine[4] (**1**) with 1 equiv of thiocarbonyldiimidazole according to procedures previously described[5] gave directly 2,2′-anhydro-1-(5-deoxy-β-D-arabinosyl)uracil (**2**). Treatment of anhydro nucleoside **2** with alkali in dilute ethanol gave a fair yield of 1-(5-deoxy-β-D-arabinosyl)uracil (**4**). Proof of the arabinosyl configuration of **4** was obtained as follows. Acetylation of **4** gave the 2′,3′-diacetate (**5**) which, upon hydrogenation over 5% rhodium on alumina, afforded the 5,6-dihydro 2′,3′-diacetate (**6**). The nmr spectrum of **5** in DMSO-d_6 showed τ values for the 3′- and 2′-acetoxy resonances at 7.88 and 8.01, respectively. In the dihydro nucleoside (**6**), the corresponding resonances were centered at τ 7.90. Cushley, *et al.*,[6] have demonstrated with acetylated furanosylpyrimidine nucleosides bearing a *cis* relationship between the $C_{1'}$–$C_{2'}$ substituents that the $C_{2'}$ acetoxy resonance is shifted to lower field when the anisotropic effect of the 5,6 double bond is removed. They showed, further, that in the corresponding *trans*-$C_{1'}$–$C_{2'}$ nucleosides, an upfield shift for the C-2′ acetoxy signal occurs upon removal of the 5,6 double bond. The nmr signals for the acetoxy resonances of nucleosides **5** and **6** are consistent only with a *cis* relationship between the aglycon and the C-2′ substituent.

Benzoylation of **4** with an excess of benzoyl chloride in pyridine yielded the tribenzoate **7**. That an excess of this reagent will benzoylate the aglycon as well as the sugar moiety had been noted previously with thymidine and uridine.[7] Thiation of **7** according to procedures previously employed[7] gave the 4-thio nucleoside **8** which was isolated as a crude syrup and converted to 5′-deoxy-*ara*-C (**9**) with alcoholic ammonia. 5′-Deoxy-*ara*-C consumed 1 mole of metaperiodate per mole *slowly* (~40 hr) consistent with an α-*trans*-glycol system in **9**. The ultraviolet absorption spectrum and the pK_a (4.2) of **9** were similar to those for *ara*-C.

An interesting aspect of the reaction of **1** with thiocarbonyldiimidazole is noted when an excess of this reagent is used. Reaction of **1** with 1.5 moles of this reagent gave *ca.* 50% yield of **3** whose elemental analysis was consistent with a dinucleoside thionocarbonate.[8] The same dinucleoside thionocarbonate was obtained in near quantitative yield by reaction of **2** with 0.5 equiv of thiocarbonyldiimidazole. Dinucleoside **3** is converted to **2** when refluxed in 50% methanol. In 0.5 *N* NaOH **3** is rapidly converted to **4**. These data

(4) I. Wempen, I. L. Doerr, L. Kaplan, and J. J. Fox, *J. Am. Chem. Soc.*, **82**, 1624 (1960).

(5) J. J. Fox, N. Miller, and I. Wempen, *J. Med. Chem.*, **9**, 101 (1966); J. J. Fox and I. Wempen, *Tetrahedron Letters*, 643 (1965).

(6) R. J. Cushley, K. A. Watanabe, and J. J. Fox, *J. Am. Chem. Soc.*, **89**, 394 (1967).

(7) 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, *ibid.*, **81**, 178 (1959).

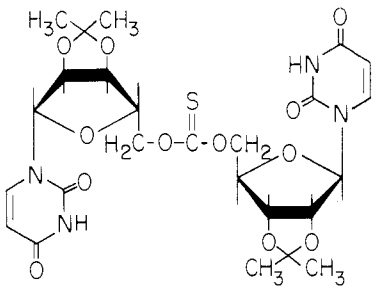
(8) It should be noted that the ultraviolet absorption spectrum of **3** is *qualitatively* similar to those for 2,3′-anhydro nucleosides.[9] However, this "similarity" is due to the contribution made by the thiono group to the spectrum. Horton and Turner[10] have observed selective uv absorption at 238 and 274 mμ for 1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-thionocarbonate.

(9) J. F. Codington, I. L. Doerr, and J. J. Fox, *J. Org. Chem.*, **30**, 476 (1965).

(10) D. Horton and W. N. Turner, *Tetrahedron Letters*, 2531 (1964).

establish **3** as bis[2,2′-anhydro-1-(5-deoxy-β-D-arabinosyl)uracil] 3′-thionocarbonate. As an extension of this observation, we treated 2′,3′-*O*-isopropylideneuridine with thiocarbonyldiimidazole and obtained a nearly quantitative yield of the 2′,3′-acetonide of diuridylyl 5′→5′-thionocarbonate (compound A).[11]

An alternate and simpler method to 5′-deoxy-*ara*-C was achieved from **2**. Benzoylation of **2** with benzoyl chloride in pyridine gave the monobenzoate **10**, mp 197°.[12-15] The conversion of the 2,2′-anhydro nucleoside **10** to **9** utilized the previously described process for thiation of anhydro nucleosides.[16] Thiation of **10** produced the 4-thione (**11**) which was converted to 5′-deoxy-*ara*-4-thiouracil (**12**). Treatment of **12** with alcoholic ammonia at 100° afforded a high yield of 5′-deoxy-*ara*-C.



Compound A

Preliminary studies[17] showed that **9** was completely deaminated by both human liver and mouse kidney homogenates indicating, in agreement with previous studies,[2,18] that conversion to the nucleotide is not a prerequisite for enzymatic deamination. 5′-Deoxy-*ara*-C is a weak deaminase inhibitor. No activity was observed for 5′-deoxy-*ara*-C against L1210 leukemia or against Burkitt's cell cultures in agreement with the proposed mechanism for the action[19] of *ara*-C as a phosphorylated derivative.

(11) Compound A (and **3**) may be viewed as analogs of dinucleoside phosphates.

(12) Monobenzoate **10** had been reported from this laboratory[13] with mp 204–206°. The method of synthesis used involved the treatment of 2,2′-anhydro-1-(5-deoxy-3-*O*-mesyl-β-D-arabinosyl)uracil (B) with sodium benzoate in DMF at reflux temperature for 4 hr. Subsequent studies[14] have shown that such reactions produce 2′,3′-orthoester ions which can lead subsequently to both 2,2′-anhydro-3′-*O*-benzoyl and 2,3′-anhydro-2′-*O*-benzoyl derivatives. The mechanism would involve first the attack by benzoate on C-2′ of B followed by attack of the 2-carbonyl on 3′ to form the 2,3′-anhydro-2′-*O*-benzoyl derivative C. It has also since been demonstrated that 2,3′-anhydronucleosides of type C will rearrange to the 2,2′-anhydro-3′-*O*-benzoyl isomer with heat.[15] Therefore it was deemed possible that the monobenzoate previously reported[13] may have been a mixture of isomers. A reinvestigation by Dr. J. F. Codington in our laboratory showed that, indeed, the reaction of B with sodium benzoate in DMF produced two isomeric products with mp 197–198 and 231–233°, respectively. The higher melting product was converted to the lower melting isomer by heating at ~212° for 20 min. A mixture melting point of **10** with the lower melting isomer was undepressed and their ir spectra were identical. These data establish the lower melting isomer as **10** and the higher melting isomer (231–233°) as the 2,3′-anhydro-1-(5-deoxy-2-*O*-benzoyl-β-D-arabinosyl)uracil isomer.

(13) J. F. Codington, R. Fecher, and J. J. Fox, *J. Am. Chem. Soc.*, **82**, 2794 (1960).

(14) J. J. Fox and N. C. Yung, *J. Org. Chem.*, **28**, 936 (1963).

(15) N. C. Yung and J. J. Fox, *J. Am. Chem. Soc.*, **83**, 3060 (1961).

(16) N. C. Yung and J. J. Fox, *J. Org. Chem.*, **27**, 1477 (1962).

(17) M. Dolfinger, personal communication.

(18) G. W. Cuniener, *Biochem. Pharmacol.*, in press.

(19) M. Y. Chu and G. A. Fischer, *ibid.*, **11**, 423 (1962); **14**, 333 (1965).

Experimental Section[20]

2,2′-Anhydro-1-(5-deoxy-β-D-arabinosyl)uracil (2).—To 250 ml of dry toluene was added 2.74 g (0.012 mole) of 5′-deoxyuridine[4] (**1**). The suspension was stirred and brought to 80°, whereupon a solution of 2.3 g (0.013 mole) of thiocarbonyldiimidazole in dry toluene (40 ml) was added in one portion. The reaction mixture was then heated under reflux for about 1 hr whereupon the yellow color was completely discharged and a precipitate formed. The reaction mixture was cooled, the toluene was decanted, and the residue was washed with three 50-ml portions of Et_2O. The crude product crystallized from hot EtOH in colorless microneedles and was chromatographically pure (tlc, $CHCl_3$–MeOH, 4:1). The yield was 2.1 g (83%). A further crystallization from MeOH–EtOAc gave a crystalline product melting at 207–208°; $\lambda_{max}^{H_2O}$ 223 and 248 mμ (ε 7500 and 7100); λ_{min} 241 and 234 mμ (ε 5600 and 6000).

Anal. Calcd for $C_9H_{10}N_2O_4$: C, 51.43; H, 4.76; N, 13.33. Found: C, 51.44; H, 4.76; N, 13.22.

Bis[2,2′-anhydro-1-(5-deoxy-β-D-arabinosyl)uracil] 3′-Thionocarbonate (3). (a) From 5′-Deoxyuridine.—To a stirred suspension of 2.28 g (0.010 mole) of **1** in 250 ml of dry toluene, previously heated to 80°, was added all at once a solution of thiocarbonyldiimidazole (2.79 g, 0.016 mole) in about 50 ml of warm toluene. The reaction mixture which was heated at reflux temperature lost color slowly over a period of 1 hr. The mixture was cooled, the toluene was decanted from the pale tan precipitate, and the solid was washed twice with Et_2O. The residue was warmed with 50 ml of EtOH and the insoluble precipitate was collected and washed with several portions of cold EtOH. Thin layer chromatography showed only one component with MeOH–$CHCl_3$ (4:1). The yield of **3** was 1.2 g (52%). The filtrate contained several components including a small proportion of **2**. Recrystallization of the crude precipitate from a large volume of 98% EtOH gave a compound which decomposed at 243–245°; $\lambda_{max}^{H_2O}$ 225 mμ (ε 25,400); λ_{min} 208 mμ (ε 14,100), shoulder 237–255 mμ, inflection at 248 mμ.

Anal. Calcd for $C_{19}H_{18}N_4O_8S$: C, 49.35; H, 3.90; N, 12.12; S, 6.93. Found: C, 49.56; H, 4.11; N, 11.94; S, 6.83.

(b) From 2.—To 240 mg (0.001 mole) of **1** in 50 ml of dry toluene stirred at 80° was added 94 mg (0.0005 mole) of thiocarbonyldiimidazole. The mixture was heated at reflux temperature until the yellow color was discharged (8 hr). The reaction mixture was worked up as in a and the resulting compound (230-mg crude yield) was found to be identical with the compound described above (mixture melting point showed no depression).

Alkaline Hydrolysis of 3 to 4.—Several milligrams of **3** was placed in 0.5 *N* NaOH for a few minutes, neutralized with AcOH, and examined spectrophotometrically. The uv peak of starting material at 225 mμ had disappeared and a new peak was noted at 262 mμ. The migration of this hydrolysis product was compared with the hydrolysis product of **2** (*i.e.*, **4**) and **1** (paper electrophoresis, borate buffer, pH 7.0, 3.5 hr, 600 v). The alkaline hydrolysis products of both **2** and **3** have the same mobility. They migrate toward the cathode (**1** cm), while 5′-deoxyuridine migrates (3.5 cm) toward the anode in this buffer.

Hydrolysis of 3 to 2.—To 30 ml of 50% MeOH was added 150 mg of **3** and the solution was heated to reflux for 24 hr. When the evolution of a sulfur-containing gas, detected with lead acetate paper, ceased, the ultraviolet spectrum of the mixture was measured and found to be identical with that obtained from **2**. Thin layer chromatography also showed the product to be the same as **2**.

2,2′-Anhydro-1-(3-*O*-benzoyl-5-deoxy-β-D-arabinosyl)uracil (10).—Compound **2** (4.3 g, 0.021 mole) in 50 ml dry pyridine and 3.54 g (0.025 mole) of benzoyl chloride were allowed to stand for 72 hr at room temperature. Pyridine was removed under vacuum to half volume and the resulting syrup was poured over ice (100 g) while stirring. The crude precipitate was filtered and washed with H_2O. The product (5.2 g, 78%) was recrystallized from EtOAc and melted at 197°.[12]

2,2′-Anhydro-1-(3-*O*-benzoyl-5-deoxy-β-D-arabinosyl)-4-thiouracil (11).—To a clear, refluxing solution of 65 ml of dry pyridine

(20) Pmr spectra were taken on a Varian A-60 spectrometer using DMSO-d_6 as solvent and TMS as internal reference. Values are given in τ. Microanalyses were performed by the Spang Microanalytical Laboratories, Knoxville, Tenn. Melting points were determined on a Thomas–Hoover capillary melting point apparatus.

containing 5 g (0.022 mole) of P_2S_5 was added 3 g (0.0095 mole) of **10**. The solution was heated at reflux temperature for 0.5 hr, the pyridine was removed under vacuum, and the residue was treated with about 250 ml of H_2O. The yellow precipitate crystallized from EtOH in yellow needles (2.55 g, 81%): mp 233° dec; $\lambda_{max}^{H_2O}$ 233, 327 mμ; λ_{min} 212, 258 mμ.

Anal. Calcd for $C_{16}H_{14}N_2O_4S$: C, 58.18; H, 4.24; N, 8.48; S, 9.70. Found: C, 58.02; H, 4.56; N, 8.41; S, 9.66.

1-(5-Deoxy-β-D-arabinosyl)-4-thiouracil (12).—To 2 g of **11** (0.006 mole) in 300 ml of 50% MeOH was added 30 ml of 1 *N* NaOH and the mixture was stirred at 60° for 5 min. The reaction mixture was cooled and passed through an Amberlite IR-120 (H^+) column. The eluate was extracted with $CHCl_3$, and the $CHCl_3$ was discarded. The aqueous layer was concentrated under vacuum to about 15 ml, whereupon there separated 1.16 g (78%) of a pale yellow solid. A portion crystallized from EtOAc yielded pale yellow needles which melted at 202–202.5°. Thin layer chromatography, BuOH–H_2O (86:14) indicated only one component; $\lambda_{max}^{H_2O}$ 243, 332 mμ; λ_{min} 276 mμ.

Anal. Calcd for $C_9H_{12}N_2O_4S$: C, 44.26; H, 4.92; N, 11.48. Found: C, 44.34; H, 4.95; N, 11.45.

1-(5-Deoxy-β-D-arabinosyl)uracil (4).—Compound **2** (1.5 g, 0.007 mole) was added to a stirred solution of 100 ml of 50% EtOH and 11 ml of 1 *N* NaOH. The solution was stirred for 2 hr at room temperature, neutralized with 1 *N* HCl, and evaporated under vacuum. The residue was taken up in three 100-ml portions of hot Me_2CO, the Me_2CO was concentrated to dryness, and the residue was dissolved in hot EtOH–EtOAc. After treatment with charcoal and filtration there precipitated microcrystals (600 mg, 37%), mp 155–158°, $\lambda_{max}^{H_2O}$ 262 mμ, $\lambda_{min}^{H_2O}$ 231 mμ (only one component by tlc, MeOH–$CHCl_3$ 4:1).

Anal. Calcd for $C_9H_{12}N_2O_5$: C, 47.37; H, 5.26; N, 12.30. Found: C, 47.26; H, 5.16; N, 12.22.

1-(5-Deoxy-2,3-di-*O*-acetyl-β-D-arabinosyl)uracil (5).—To 250 mg of **4** was added 1 ml of dry pyridine and 3 ml of Ac_2O. The mixture was allowed to stand at room temperature for 72 hr and the flask contents was evaporated under vacuum. MeOH was added twice and removed under vacuum each time. A recrystallization of the residue from H_2O afforded 140 mg of flat, shiny plates (mp 208–209°). A single component was noted by means of thin layer chromatography.

Anal. Calcd for $C_{13}H_{15}N_2O_7$: C, 50.16; H, 4.82; N, 9.00. Found: C, 49.97; H, 5.15; N, 8.88.

1-(5-Deoxy-2,3-di-*O*-acetyl-β-D-arabinosyl)-5,6-dihydrouracil (6).—The acetyl compound **5** (130 mg) was dissolved in 50 ml of EtOH, and about 50 mg of 5% rhodium-on-alumina catalyst and one drop of HCl were added. The hydrogenation was carried out at atmospheric pressure for 12 hr. The catalyst was removed, the filtrate was concentrated to 5 ml under vacuum, and the resulting precipitate was recrystallized from hot EtOH. The compound formed white needles, mp 182–183° (43 mg). The compound was homogenous by thin layer chromatography (BuOH–H_2O, 86:14) (visualized by means of MnO_4^- spray).

Anal. Calcd for $C_{13}H_{17}N_2O_7$: C, 49.84; H, 5.43; N, 8.95. Found: C, 49.55; H, 5.67; N, 8.81.

5′-Deoxytribenzoyl-1-β-D-arabinosyluracil (7).—To 4.3 g (0.02 mole) of **4** in 150 ml of dry pyridine was added benzoyl chloride (11.2 g, 0.08 mole), and the mixture was allowed to stand for 24 hr at 70°. Half of the pyridine was removed under vacuum and the residual syrup was poured over a slurry of ice–H_2O. The granular precipitate was removed and washed with Et_2O. The crude compound thus obtained (6 g, 55%) gave a single spot (tlc) (MeOH–$CHCl_3$ 4:1). A portion recrystallized from EtOH melted at 223–224°.

Anal. Calcd for $C_{30}H_{24}N_2O_8$: C, 66.66; H, 4.44; N, 5.19. Found: C, 66.58; H, 4.45; N, 5.15.

1-(5-Deoxy-β-D-arabinosyl)cytosine (9). (a) From 12.—Compound **12** (1.1 g, 0.0045 mole) was placed in a sealed tube with 200 ml of EtOH saturated with NH_3 at 0°. The vessel was heated for 17 hr at 100° and cooled, and the tube contents was concentrated under vacuum. The resulting residue was taken up in hot EtOH, decolorized with carbon, and filtered. A further recrystallization from H_2O yielded 920 mg (90%) of material in white needles which melted at 166–168° dec. Paper electrophoresis (pH 7.0 borate buffer, 6 hr, 600 v) indicates one spot which migrates toward the cathode. Infrared, nmr, and tlc indicated that the material is identical with the material described in preparation b below; spectral data: $\lambda_{max}^{0.1\,N\,HCl}$ 280 mμ (ε 12,800), λ_{min} 241 mμ (ε 1700); $\lambda_{max}^{pH\,7}$ 272 mμ (ε 8900), λ_{min} at 248 mμ (ε 5700)), inflection at 229 mμ.

Anal. Calcd for $C_9H_{13}N_3O_4 \cdot H_2O$: C, 44.08; H, 6.12; N, 17.14. Found: C, 44.27; H, 6.20; N, 17.42.

Spectrophotometrically calculated pK_a = 4.20 (±0.05). Rotation shows $[\alpha]^{23}D$ +114°, and metaperiodate consumption is complete over 40 hr consistent with an α-*trans*-glycol system.

(b) From 7.—To a stirred mixture of 5.0 g (0.0093 mole) of **7** in pyridine (150 ml) was added 9.2 g (0.041 mole) of P_2S_5 and 0.2 ml of H_2O. The mixture was heated at reflux temperature for 3 hr and the pyridine was reduced to half volume under vacuum. The residual syrup was poured into ice H_2O, stirred for 1 hr, and extracted into $CHCl_3$. The $CHCl_3$ was washed with H_2O and dried (Na_2SO_4). All attempts to crystallize the syrup obtained on the evaporation of the dried $CHCl_3$ solution failed. The crude syrup (**8**) was therefore used for the preparation of **9**. The crude syrup (3.5 g) was heated in a sealed tube at 100° for 12 hr with 150 ml of EtOH saturated at 0° with NH_3. The tube contents was brought to dryness under vacuum, taken up in H_2O, and shaken with $CHCl_3$. The aqueous layer was concentrated to 10 ml and on cooling there was obtained 240 mg of white crystals. Further concentration of the aqueous layer yielded an additional 200 mg of crystals. These two fractions are identical in all respects with the compound obtained by method a (*vide supra*) ir, nmr, tlc. However the former precipitate melts at 189–192° while the recrystallized sample of the latter melts at 166–168°.

Di(2,3-*O*-isopropylideneuridylyl) 5′→5′-Thionocarbonate (A).—To 980 mg of 2′,3′-*O*-isopropylideneuridine (0.003 mole) in 50 ml of dry toluene heated to 80° was added a solution of thiocarbonyldiimidazole (640 mg, 0.003 mole) in 20 ml of toluene. The reaction was stirred at reflux temperature for 4 hr. The yellow color faded and the reaction mixture was then cooled. The toluene was decanted and the insoluble residue was washed twice with Et_2O. The residue was then recrystallized twice from EtOH to give white needles which decomposed slowly up to 140°, $\lambda_{max}^{H_2O}$ 260 mμ (ε 12,900), λ_{min} 237 mμ (ε 11,400).

Anal. Calcd for $C_{33}H_{30}N_4O_{12}S$: C, 49.18; H, 4.92; N, 9.18; S, 5.24. Found: C, 48.68; H, 4.91; N, 9.71; S, 5.67.

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Branched-Chain Sugar Nucleosides. II. 5′,5′-Di-*C*-methyladenosine

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In general, there are two types of branched-chain carbohydrates—those where the branching involves one of the ring atoms and those having a branched side chain. As examples of nucleosides containing branched-chain sugars of the first type, we recently described[1] the synthesis and some biological effects of both 2′-*C*-methyladenosine (I) and 3′-*C*-methyladensoine (II). Earlier, as a consequence of work on the naturally occurring branched-chain sugar noviose, we synthesized[2] methyl 2,3-*O*-isopropylidene-5,5-di-*C*-methyl-β-D-ribofuranoside (III), a sugar which is examplary of branching of the second type. In view of the interesting biological properties of 2′- and 3′-*C*-methyladensosine, it seemed worthwhile to convert III into the related

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