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: $\lambda_{max}^{1\ N\ HCl}$ 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 $C_{23}H_{30}N_4O_{12}S$: 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.

Acknowledgment.—The authors are indebted to Dr. R. J. Cushley for assistance in the interpretation of the nmr spectra. We thank Mr. M. J. Olsen for excellent technical assistance.

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

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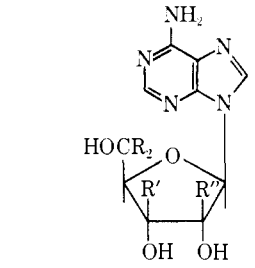
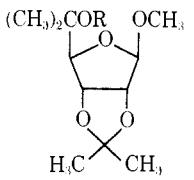
In general, there are two types of branched-chain carbohydrates—those where the branching involves one of the ring atoms and those having a branched side chain. As examples of nucleosides containing branched-chain sugars of the first type, we recently described[1] the synthesis and some biological effects 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

(1) E. Walton, S. R. Jenkins, R. F. Nutt, M. Zimmerman, and F. W. Holly, *J. Am. Chem. Soc.*, **88**, 4524 (1966).

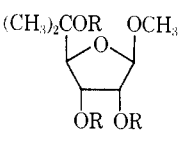
(2) E. Walton, J. O. Rodin, C. H. Stammer, F. W. Holly, and K. Folkers, *ibid.*, **80**, 5168 (1958).



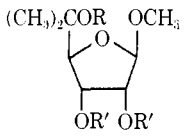
I, R = R′ = H; R″ = CH_3
II, R = R″ = H; R′ = CH_3
IV, R′ = R″ = H; R = CH_3



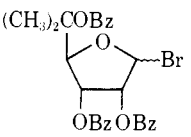
III, R = H
VIII, R = *p*-NBz



V, R = H
VI, R = Bz



IX, R = *p*-NBz; R′ = H
X, R = R′ = *p*-NBz



VII

nucleoside, 5′,5′-di-*C*-methyladenosine (IV). This was accomplished after conversion of III into a derivative suitable for reaction with chloromercuri-6-benzamidopurine.

Hydrolysis of III in methanolic hydrogen chloride removed the isopropylidene moiety and produced methyl 5,5-di-*C*-methyl-β-D-ribofuranoside (V) which was purified by chromatography on silica gel. Benzoylation of the secondary C-2 and C-3 hydroxyls of V in pyridine with benzoyl chloride occurred rapidly at room temperature, whereas benzoylation of the tertiary C-5 hydroxyl required heating. The crystalline product, methyl 2,3,5-tri-*O*-benzoyl-5,5-di-*C*-methyl-β-D-ribofuranoside (VI), was converted into the bromo sugar VII by treatment with hydrogen bromide in acetic acid. The bromo sugar VII, obtained as an impure syrup, reacted with chloromercuri-6-benzamidopurine[3] and gave 9-(2,3,5-tri-*O*-benzoyl-5,5-di-*C*-methyl-β-D-ribofuranosyl)-6-benzamidopurine which was purified by chromatography on acid-washed alumina. Removal of the benzoyl groups in methanolic sodium methoxide yielded 5′,5′-di-*C*-methyladenosine (IV). The product, even after purification by conversion to a picrate followed by regeneration of the free base, could not be obtained in crystalline form. However, the purity and identity of IV were substantiated by various physical measurements. The assignment of the β anomeric configuration to IV is based on the *trans* rule[4] and optical rotation data.

Although the impure, noncrystalline bromo sugar VII was useful in the synthesis of 5′,5′-di-*C*-methyladenosine (IV), it was felt that a more satisfactory crystalline halo sugar might be obtained if *p*-nitrobenzoyl groups were substituted for the benzoyl group blocking the C-2, -3, and -5 hydroxyls in VI. To this end, III was converted to methyl 2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-5,5-di-*C*-methyl-β-D-ribofuranoside (VIII) by treatment with *p*-nitrobenzoyl chloride in pyridine. Acid hydrolysis of the 2,3-*O*-isopropylidene moiety of VIII produced methyl 5-*O*-*p*-nitrobenzoyl-5,5-di-*C*-methyl-β-D-ribofuranoside (IX). Further reaction of this product with *p*-nitrobenzoyl chloride in pyridine gave crystalline methyl 2,3,5-tri-*O*-*p*-nitrobenzoyl-5,5-di-*C*-methyl-β-D-ribofuranoside (X). However, the low solubility of X in acetic acid complicated its conversion into a bromo sugar, and a crystalline product was not obtained.

In tests carried out by Dr. C. O. Gitterman of these laboratories, IV caused a 50% inhibition of the growth of KB cells in culture at a concentration of 100 μg/ml, whereas the same effect was produced by I and II at concentrations of 10 and 3 μg/ml, respectively. Studies[5] on the metabolism of 5′,5′-di-*C*-methyladenosine by Ehrlich ascites cells have shown that it is not phosphorylated. Under the same conditions 3′-*C*-methyladenosine (II) is converted to the 5′-mono- and triphosphate. It is entirely likely that the inability of the enzymes of Ehrlich ascites cells to phosphorylate IV results from the tertiary nature of the C-5′ hydroxyl and/or the local, adverse steric effects of the *gem*-dimethyl groups. The conformational difference of the pentose moiety of IV (see ref 6) as compared with that of adenosine is hardly an important factor when one considers that IV is conformationally related to II[7] which is phosphorylated by Ehrlich ascites cells.[5]

Experimental Section[8]

Methyl 2,3,5-Tri-*O*-benzoyl-5,5-di-*C*-methyl-β-D-ribofuranoside (VI).—A solution of 5 g (21.5 mmoles) of III[2] in 100 ml of MeOH was treated with 12.5 ml of a solution made by diluting 1.5 ml of concentrated HCl to 15 ml with MeOH. The reaction was followed by tlc on silica gel in EtOAc–$CHCl_3$ (4:1) (R_f 0.9, III; 0.3, V). After 3.5 hr, 3 g of $NaHCO_3$ was added. After being stirred, the mixture was filtered and the solids were washed with 150 ml of warm EtOAc in four portions. Concentration of the filtrate gave 5.5 g of residual oil. Chromatography of the oil on 100 g of silica gel in EtOAc–$CHCl_3$ (4:1) gave 1.8 g of unhydrolyzed III and 1.7 g (42%) of noncrystalline V: τ^{Me_4Si} 5.11 (d, C-1 H, $J_{1,2}$ = 1.3 cps), 5.72 (q, C-3 H), 5.97 (q, C-2 H, $J_{2,3}$ =

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(4) B. R. Baker, Ciba Foundation Symposium, Chemistry and Biology of Purines, Little, Brown and Co., Boston, Mass., 1957, p 120.

(5) H. T. Shigeura and S. D. Sampson, *Nature*, **215**, 419 (1967).

(6) A comparison of the coupling constants shown in the nmr spectrum of IV with those calculated by C. D. Jardetzky, *J. Am. Chem. Soc.*, **84**, 62 (1962), for some maximally puckered five-membered ring conformations indicates that the pentose moiety of IV exists in an approximate C-2′ *endo* conformation. This is qualitatively similar to that of the ribose moiety of adenosine; however, the magnitude of the *J* values shown by IV indicates a more highly puckered arrangement of its sugar-ring atoms than that of the ribose-ring atoms of adenosine. On the other hand, the nmr spectra of the methyl glycosides V, VI, VIII–X show that they approximate a C-3′ *endo* conformation in solution.

(7) Based on nmr data to be published.

(8) Nmr spectra were determined by Dr. B. Arison using a Varian Associates Model A-60 spectrometer. Microanalyses were by Mr. R. N. Boos and his associates, the ultraviolet spectral measurements by Mr. E. A. MacMullin and his associates. The ORD curve was determined by Dr. J. J. Wittick. All melting points (micro hot stage) are corrected. Except where noted, the tlc zones were made visible by spraying the plates (silica gel G, aluminum oxide G) with a solution of 100 mg of 1,3-dihydroxynaphthalene in 50 ml of ethanol containing 2.5 ml of H_3PO_4. On warming on the steam cone, a blue color is produced by those derivatives of 5,5-di-*C*-methyl-D-ribofuranose having the C-5 hydroxyl acylated. Those derivatives having a free C-5 hydroxyl give a green color which turns to blue on standing. Fritted-glass Büchner funnels of medium porosity were used for column chromatographic separations. The packing (aluminum oxide, acid-washed, Merck; silica gel, J. T. Baker) had a height:diameter ratio of about 1:1. Unless noted otherwise, all concentrations were carried out in a rotary evaporator at reduced pressure.

4.8 cps), 6.15 (d, C-4 H, $J_{3,4}$ = 7.0 cps) ppm; τ^{CDCl_3} 5.20 (s, C-1 H), 6.22 (d, C-4 H, $J_{3,4}$ = 6.5 cps) ppm.

A solution of 1.7 g (9.0 mmoles) of V in 50 ml of dry pyridine was stirred at ~5° and treated with 7.5 g (54 mmoles) of benzoyl chloride. The course of the reaction was followed by tlc on silica in $CHCl_3$–EtOAc (4:1). Monobenzoylation (R_f 0.2) occurred rapidly (<1 min) while conversion to the 2,3-di-*O*-benzoyl derivative (R_f 0.6) required about 15 min. The completely benzoylated product (R_f 0.9) was obtained after heating at 95° for 20 hr. About 2 ml of H_2O was added, the mixture was stirred for 15 min, poured into ice–H_2O and $CHCl_3$ and acidified with cold 10% HCl. The H_2O layer was extracted with two portions of $CHCl_3$. The $CHCl_3$ extracts were washed with 10% $KHCO_3$ and dried. Concentration gave 5.55 g of oil which was chromatographed on 80 g of silica gel in $CHCl_3$–EtOAc (19:1). About 3.9 g of purified product was obtained which, when recrystallized from benzene–petroleum ether, gave 3.3 g (73%) of VI: mp 131–133°; $[\alpha]_D$ +86° (*c* 1.41, $CHCl_3$); τ^{CDCl_3} 4.84 (s, C-1 H, $J_{1,2}$ = 0 cps), 4.27 (d, C-2 H), 3.96 (q, C-3 H, $J_{2,3}$ = 5.0 cps), 5.30 (d, C-4 H, $J_{3,4}$ = 7.0 cps) ppm.

Anal. Calcd for $C_{29}H_{28}O_8$: C, 69.04; H, 5.59. Found: C, 69.33; H, 5.42.

2,3,5-Tri-*O*-benzoyl-5,5-di-*C*-methyl-D-ribofuranosyl Bromide (VII).—A solution of 3 g (6.0 mmoles) of VI in 15 ml of HOAc was cooled to 5° and treated with 0.5 ml of AcBr and 15 ml of a 32% (w/w) solution of HBr in AcOH. The mixture was kept at 25° for 18 min. The mixture was concentrated, and three portions of dry toluene were distilled from the residue to remove last traces of HBr and AcOH. The residual VII[9] was used in the next step without further purification.

9-(2,3,5-Tri-*O*-benzoyl-5,5-di-*C*-methyl-β-D-ribofuranosyl)-6-benzamidopurine.—A suspension of 2.82 g (5.95 mmoles) of chloromercuri-6-benzamidopurine in 200 ml of xylene was dried by distilling about 100 ml of xylene; the mixture was cooled to 30°. Bromide VII (from 3.0 g (6 mmoles) of VI) in 30 ml of dry xylene was added, and the stirred mixture was refluxed for 80 min. The hot mixture was filtered, and the precipitate (1.5 g) was washed with 20 ml of xylene. The filtrate was diluted with 400 ml of petroleum ether (bp 30–60°) and cooled. The solid (2.7 g) which separated was removed, dissolved in 300 ml of $CHCl_3$, and washed with two 20-ml portions of 30% aqueous KI. The $CHCl_3$ solution was concentrated, and the residue (2.1 g) was chromatographed on 70 g of acid-washed alumina in $CHCl_3$–C_6H_6 (4:1). Fractions showing a single zone (R_f 0.5) on alumina in $CHCl_3$–C_6H_6 (9:1) were pooled and concentrated affording 1.42 g (34%) of 9-(2,3,5-tri-*O*-benzoyl-5,5-di-*C*-methyl-β-D-ribofuranosyl)-6-benzamidopurine as a glass: λ_{max}^{EtOH} [mμ ($\epsilon \times 10^{-3}$)] 280 (22.0), 230 (49.5); $[\alpha]_D$ −94° (*c* 1.42, $CHCl_3$). For analysis a sample was dried for 8 hr at 78° and reduced pressure.

Anal. Calcd for $C_{40}H_{33}N_5O_8$: C, 67.50; H, 4.67; N, 9.84. Found: C, 67.32; H, 4.44; N, 9.67.

5′,5′-Di-*C*-methyladenosine (IV).—MeONa, prepared from 100 mg (4 g-atoms) of Na and 20 ml of dry MeOH, and 1.48 g (2.08 mmoles) of 9-(2,3,5-tri-*O*-benzoyl-5,5-di-*C*-methyl-β-D-ribofuranosyl)-6-benzamidopurine was refluxed for 45 min. No further change in the ultraviolet absorption spectrum of the reaction mixture was observed after 15 min. The mixture was concentrated to dryness, and 50 ml of H_2O was added to the residue. The solution was neutralized (pH 6.8) with HOAc and extracted with three portions of $CHCl_3$. The H_2O layer was filtered and concentrated to dryness. The residue was partially dissolved in 30 ml of hot EtOH, and the insoluble material was removed by filtration. The EtOH filtrate was concentrated to 10 ml, and 150 ml of Et_2O was added. The solid which separated was removed, and the filtrate was concentrated to a residual glass (520 mg). It was dissolved in 3.5 ml of H_2O and 1.7 ml was treated with a hot solution of 260 mg of 85% picric acid in 5 ml of H_2O. After cooling, the picrate of IV (350 mg, mp 188–193° dec) was obtained.

Anal. Calcd for $C_{18}H_{20}N_8O_{11}$: C, 41.22; H, 3.84; N, 21.37. Found: C, 41.67; H, 3.94; N, 20.85.

The sample of IV obtained from the picrate (3 g of Dowex 2-X8, CO_3^{2-}, 15 ml of H_2O, 60–70°) had physical properties identical with those of the analytical sample described below but could not be obtained crystalline.

The remaining H_2O solution from above (1.8 ml) was concentrated to dryness. A MeOH solution was filtered and reconcentrated; 180 mg (59%) of IV was obtained as a glass: $\lambda_{max}^{H_2O}$ [mμ ($\epsilon \times 10^{-3}$)] pH 1, 207 (19.3), 257 (14.0); pH 7, 207 (20.6), 206 (14.4); pH 13, 260 (13.8); R_f 0.62 (tlc on cellulose in water); τ^{CDCl_3} 4.09 (d, C-1′ H, $J_{1',2'}$ = 7.0 cps), 5.27 (q C-2′ H), 5.55 (q, C-3′ H, $J_{2',3'}$ = 5.5 cps), 6.02 (d, C-4′ H, $J_{3',4'}$ = 1.5 cps) ppm;[6] $[\alpha]_D$ −93° (*c* 0.24, H_2O); $[\phi]_{300}$ −1290°, $[\phi]_{280}$ −2650° (trough), $[\phi]_{267}$ 0°, $[\phi]_{254}$ +1520° (peak) (*c* 0.041, MeOH).[10] For analysis, a small sample was reprecipitated from EtOH by the addition of Et_2O and dried at 78° for 2.5 hr at reduced pressure.

Anal. Calcd for $C_{12}H_{17}N_5O_4$: C, 48.80; H, 5.80; N, 23.72. Found: C, 49.13; H, 5.60; N, 23.55.

Methyl 2,3-*O*-isopropylidene-5-*O*-*p*-nitrobenzoyl-5,5-di-*C*-methyl-β-D-ribofuranoside (VIII).—A solution of 4.65 g (0.02 mole) of III in 50 ml of dry (BaO) pyridine was cooled, stirred, and treated with 5.56 g (0.03 mole) of *p*-nitrobenzoyl chloride. The mixture was kept at 25° for 24 hr. Tlc on silica gel in $CHCl_3$–EtOAc (99:1) showed the reaction to be complete, R_f 0.74 (blue, VIII), 0.36 (green, III). The reaction mixture was worked up as in the synthesis of VI, and the crude product was chromatographed on 100 g of silica gel in $CHCl_3$–EtOAc (99:1). Fractions containing only VIII were combined and concentrated. The residue (7 g) was recrystallized from 8 ml of C_6H_6 by adding 25 ml of petroleum ether, and 4.0 g (53%) of VIII was obtained; mp 134–136°; $[\alpha]_D$ −55° (*c* 1.02, $CHCl_3$); τ^{CDCl_3} 4.87 (s, C-1 H), 5.83 (d, C-2 H, $J_{2,3}$ = 3.0 cps), 506 (q, C-3 H), 5.32 (d, C-4 H, $J_{3,4}$ = 6.5 cps) ppm.

Anal. Calcd for $C_{18}H_{23}NO_8$: C, 56.68; H, 6.08; N, 3.67. Found: C, 56.86; H, 5.80; N, 3.77.

Methyl 5-*O*-*p*-Nitrobenzoyl-5,5-di-*C*-methyl-β-D-ribofuranoside (IX).—A solution of 3 g (7.8 mmoles) of VIII in 75 ml of MeOH, treated with 7.5 ml of a solution made from 1 ml of concentrated HCl diluted to 10 ml with MeOH, was stirred at 25° for 4 hr. Tlc on silica in $CHCl_3$–EtOAc (6:4) showed that the reaction was almost complete, R_f 0.3 (product), 1.0 (starting material). The solution was concentrated and the residue, in $CHCl_3$, was chromatographed on 30 g of silica. Elution with $CHCl_3$–EtOAc (5:1) removed a small amount of starting material and the product (2.2 g) was eluted with $CHCl_3$–EtOAc (6:4). Recrystallization from CH_2Cl_2–petroleum ether (1:1) gave 2.0 g (75%) of IX: mp 131–133°; $[\alpha]_D$ −73° (*c* 1.6, $CHCl_3$); τ^{CDCl_3} 5.09 (s, C-1 H), 5.87 (d, C-2 H, $J_{2,3}$ = 4.5 cps), 5.42 (q, C-3 H), 5.90 (d, C-4 H, $J_{3,4}$ = 7.5 cps) ppm.

Anal. Calcd for $C_{15}H_{19}NO_8$: C, 52.78; H, 5.61; N, 4.10. Found: C, 53.11; H, 5.54; N, 3.97.

Methyl 2,3,5-Tri-*O*-*p*-nitrobenzoyl-5,5-di-*C*-methyl-β-D-ribofuranoside (X).—A cold solution of 1.2 g (3.5 mmoles) of IX in 30 ml of dry pyridine was treated with 1.95 g (10.5 mmoles) of *p*-nitrobenzoyl chloride. Tlc on silica gel in $CHCl_3$–EtOAc (9:1) showed that the reaction was complete in 1.5 hr at 25°. The reaction mixture was worked up as in the synthesis of VI, and the crude product, when recrystallized from 10 ml of $CHCl_3$ and 10 ml of petroleum ether, gave 2.0 g (89%) of X: mp 189–191°; $[\alpha]_D$ +122° (*c* 0.82, $CHCl_3$); τ^{CDCl_3} 4.77 (s, C-1 H), 4.23 (d, C-2 H, $J_{2,3}$ = 4.5 cps), 3.92 (q, C-3 H), 5.27 (d, C-4 H, $J_{3,4}$ = 7.5 cps) ppm.

Anal. Calcd for $C_{29}H_{25}N_3O_{14}$: C, 54.46; H, 3.94; N, 6.57. Found: C, 54.77; H, 3.90; N, 6.43.

(9) Tlc of VII on silica gel in C_6H_6–$CHCl_3$ (1:1) shows (I_2 vapor) a zone (R_f 0.3) for the bromo sugar and a rather large by-product zone (R_f 0.8) as well as a zone for starting material, VI, at R_f 0.9. The by-product is most likely 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-5,5-di-*C*-methyl-D-ribofuranose. Examination of the nmr spectrum shows resonances at τ^{CDCl_3} 6.55 (s, OCH_3 protons of starting material) and 7.9 ppm (s, 1-*O*-acetyl protons). The size of these peaks indicates that the bromo sugar contains about 15% of each impurity.

(10) W. A. Klee and S. H. Mudd, *Biochemistry*, **6**, 988 (1967), have recently shown that a number of adenosine derivatives substituted with a sulfur atom at the 5′ position give ORD curves showing positive Cotton effects. To explain these results, they suggested that the bulk of the sulfur atom forces the nucleoside to assume an *anti* conformation of base to sugar. As a corollary, these workers propose, contrary to the generally accepted view, that purine nucleosides which show negative Cotton effects exist in the *syn* conformation. Examination of space-filling molecular models indicate that the *gem*-dimethyl groups of IV have spacial requirements as great as if not greater than the 5′-thio moiety. The normal, negative Cotton effect shown by IV seems to require that a factor other than the bulk of the sulfur atom be invoked to explain the positive Cotton effect of the 5′-thioadenosines.