freshly prepared 1.0 *N* solution of hydrogen chloride in methanol (2.0 l.) and allowed to stand at ambient temperature for 6 days. The precipitate which formed was collected by filtration, washed with a small amount of methanol, and vacuum dried to give 1-(β-D-arabinofuranosyl)thymine (65.4 g, 0.242 mole, 86%): mp 246–248°, $[\alpha]^{27.0}D$ +97.9° (*c* 0.5, H_2O), $\lambda_{max}^{pH\ 1}$ 268 mμ (ε 9810), $\lambda_{min}^{pH\ 1}$ 229 mμ (ε 1750), $\lambda_{max}^{pH\ 7}$ 268 mμ (ε 9890), $\lambda_{min}^{pH\ 7}$ 234 mμ (ε 2320), $\lambda_{max}^{pH\ 13}$ 269 mμ (ε 8130), $\lambda_{min}^{pH\ 13}$ 246 mμ (ε 4130); lit.[6] mp 248–249°, $[\alpha]^{20}D$ +90° (*c* 0.5, H_2O), $\lambda_{max}^{pH\ 1}$ 268 mμ (ε 9590), $\lambda_{max}^{pH\ 7}$ 268 mμ (ε 9530), $\lambda_{max}^{pH\ 13}$ 270 mμ (ε 7870). The material was homogeneous in two paper chromatographic systems[9] with R_{Ad} 0.92 (*n*-BuOH–H_2O) and R_{Ad} 1.87 (5% Na_2HPO_4), respectively.

Anal. Calcd for $C_{10}H_{14}N_2O_6$ (258.2): C, 46.51; H, 5.47; N, 10.85; O, 37.18. Found: C, 46.82; H, 5.65; N, 10.76; O, 37.70.

The material could be recrystallized from 25% aqueous methanol with 80% recovery, mp 246–248°, $[\alpha]^{26}D$ +92° (*c* 0.5, water), with no appreciable change in spectral or microanalytical behavior.

Nucleosides and Related Substances. V. A Synthetic Procedure for Nucleosides with the Use of Phosphorus Pentoxide as Dehydrating Agent

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Fischer and Delbrück[1] first reported a procedure for the synthesis of β,β-trehalose by eliminating a water molecule from two molecules of 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose with the use of phosphorus pentoxide (P_4O_{10}). Since then, the procedure has been applied to the synthesis of some oligosaccharides without significant success. After that, Schramm, Grötsch, and Pollmann[2] reported a more simplified method for the synthesis of *N*- and *O*-glycosides, which consisted of the direct condensation of aglycons with unsubstituted monosaccharides in *N*,*N*-dimethylformamide (DMF) in the presence of ethyl polyphosphate. Both methods seem to be based on a similar principle in that a molecule of water is eliminated during the condensation. It would be interesting to examine the synthesis of nucleosides by applying the method of Fischer and Delbrück,[1] because nucleosides might be obtained in higher yields than those reported by Schramm, Grötsch, and Pollmann.[2]

In the course of our recent work on the synthesis of polysaccharides with the use of P_4O_{10} as dehydrating agent,[3] not only the polymerization of monosaccharides but also the condensation of monosaccharides with aglycons was observed to occur. The present work describes the synthesis of some nucleosides in DMF in the presence of P_4O_{10}.

P_4O_{10} and SO_3 were effective as dehydrating agents for the synthesis of nucleosides, but concentrated H_2SO_4, $ZnCl_2$, P_4O_{10}–trace of HCl, and P_4O_{10}–trace of *p*-toluenesulfonic acid were ineffective. DMF was effective as solvent for the synthesis of nucleosides, but dimethyl sulfoxide (DMSO), chloroform, acetone, ethanol, formamide, dioxane, and dinitromethane were ineffective. In the reaction in DMSO in the presence of P_4O_{10}, the oxidation of hydroxyl groups in carbohydrate molecules[4] and the introduction of a $-CH_2SCH_3$ group into reactants[5] were observed to occur. The formation of nucleosides was observed with the reaction in DMF in the presence of P_4O_{10} or SO_3. The isolation of nucleosides was achieved in the yields as high as 37 and 48% in some reactions of purine bases with 2,3,4-tri-*O*-acetyl-D-xylopyranose, 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose, and 2,3,4-tri-*O*-acetyl-D-ribopyranose, respectively. In addition to the nucleosides described in the Experimental Section, some other nucleosides were observed by paper chromatographic examination to be produced in the following reactions: the reactions of theophylline with 2-acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-D-glucopyranose and 2,4-di-*O*-acetyl-D-glucurono-6,3-lactone, respectively, and the reactions of 6-benzamidopurine with tri-*O*-acetyl-D-arabinose, 2,4-di-*O*-acetyl-D-glucurono-6,3-lactone, and 2,3,5-tri-*O*-acetyl-D-ribofuranose, respectively. From these reaction mixtures, it was impossible to isolate the corresponding nucleosides because of very low yield. The method was also applied to the condensation of purine bases with unsubstituted monosaccharides of D-glucose, D-xylose, and D-fructose, but any of the corresponding nucleosides were not observed to be produced in these reactions. It was also observed not to produce any nucleosides in the reaction of 6-benzamidopurine with 2,3,4,6-tetra-*O*-benzoyl-α-D-fructofuranose.

Experimental Section

All melting points are uncorrected. All nmr spectra were recorded at 60 Mc and chemical shifts on the nmr spectra were expressed on δ scale in parts per million downfield displacement from tetramethylsilane or sodium 2,2-dimethyl-2-silapentane-5-sulfonate as internal standard. Paper chromatographic examination was carried out on Toyo Roshi No. 51 filter paper by the descending technique, using 1-butanol–water (86:14, v/v) as developing solvent.

7-β-D-Xylopyranosyltheophylline.—Theophylline (4.3 g) was dissolved at 40–50° in DMF (150 ml) containing P_4O_{10} (2.5 g). To the solution was added 2,3,4-tri-*O*-acetyl-D-xylopyranose (5.0 g) dissolved in DMF (50 ml.). The mixture was allowed to stand at 60–70° for 5 days with exclusion of moisture. After being allowed to cool at room temperature, the mixture was poured into about 300 ml of a mixture of ice–water and $CHCl_3$ (1:1, v/v), and this mixture was shaken vigorously. The chloroform layer was collected, washed three times with ice–water, dried with anhydrous Na_2SO_4, and finally concentrated under reduced pressure to a syrup. This was deacetylated in methanol saturated with ammonia according to the usual procedure. A crystalline product produced was collected by filtration and the filtrate was concentrated to a syrup. This was dissolved in a small volume of ethanol and the mixture was allowed to stand in a refrigerator overnight to produce a crystalline product. The combined crystalline products were recrystallized from hot ethanol: yield 2.1 g (37.2%); mp 255–256°; $[\alpha]^{21}D$ −23° (*c* 0.5, water); $\lambda_{max}^{H_2O}$ 274 mμ, $\lambda_{min}^{H_2O}$ 246 mμ; ν_{max}^{KBr} 3350–3450, 1700, 1670, 1630, 1600, 780, 760, and 740 cm^{-1}; nmr (in D_2O), δ 3.35 and 3.55 (CH_3N-1 and -3, 6 H), 8.28 (HC-8, 1 H), and 9.7 (HC-1′, 1 H), $J_{1',2'}$ = 9.0 cps; R_f 0.29.

(1) E. Fischer and K. Delbrück, *Ber.*, **42**, 2776 (1909). For a review, see J. Staněk, M. Černý, and J. Pacák, "The Oligosaccharides," Academic Press Inc., New York, N. Y., 1965, p 60.

(2) G. Schramm, H. Grötsch, and W. Pollmann, *Angew. Chem.*, **74**, 53 (1962).

(3) Paper presented at the Annual Meeting of the Agricultural Chemical Society of Japan, Tokyo, April 3, 1965.

(4) K. Onodera, S. Hirano, and N. Kashimura, *J. Am. Chem. Soc.*, **87**, 4651 (1965).

(5) K. Onodera, S. Hirano, N. Kashimura, and T. Yajima, *Tetrahedron Letters*, 4327 (1965).

Anal. Calcd for $C_{12}H_{16}N_4O_8 \cdot 2H_2O$: C, 41.38; H, 5.79; N, 16.09. Found: C, 41.88; H, 5.47; N, 16.27.

The water of crystallization was lost on drying at 100° on P_4O_{10} under reduced pressure for 3 hr.

A mixture melting point with an authentic sample[6] of 7-β-D-xylopyranosyltheophylline showed no depression, and the infrared spectrum was identical with that of the authentic sample.

7-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyl)theophylline.—2,3,4,6-Tetra-*O*-acetyl-D-glucopyranose (10 g), theophylline (5.7 g), and P_4O_{10} (10 g) were dissolved in 300 ml of DMF as described above. The mixture was allowed to stand at 60–70° under vigorous stirring for 20 hr. The reaction product was repeatedly extracted with chloroform and the combined extracts were concentrated to a syrup. This was crystallized from hot ethanol and recrystallized from the same solvent: yield 7.0 g (48%); mp 145–146°; $[\alpha]^{20}D$ −14.5° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 1760, 1710, 1680, 1620, 1550, 785, 765, and 755 cm^{-1}, no OH absorption; nmr (in $CDCl_3$), δ 2.00 [$CH_3C(=O)OR$, 12 H], 3.41 and 3.58 (CH_3N-1 and -3, 6 H), and 6.20 (HC-1′, 1 H), $J_{1',2'}$ = 9.0 cps; R_f 0.82.

Anal. Calcd for $C_{21}H_{26}N_4O_{11}$: C, 49.41; H, 5.13; N, 10.98. Found: C, 49.20; H, 5.38; N, 10.95

A mixture melting point with an authentic sample[6] of 7-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)theophylline showed no depression, and the infrared spectrum was identical with that of the authentic sample.

Deacetylation of the product was carried out in methanol saturated with ammonia to produce 7-β-D-glucopyranosyltheophylline: mp 261°; $[\alpha]^{13}D$ −2.9°[7] (*c* 1.0, water); $\lambda_{max}^{H_2O}$ 273 mμ, $\lambda_{min}^{H_2O}$ 244 mμ.

9-β-D-Glucopyranosyladenine.—2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranose (3.6 g), 6-benzamidopurine (2.4 g), and P_4O_{10} (2.0 g) were dissolved in 35 ml of DMF. After the mixture was allowed to stand 75 hr at 50–60° under stirring, DMF was evaporated from the reaction mixture under reduced pressure below 60°. The residue was dissolved in 500 ml of methanol saturated with ammonia and a precipitate produced was immediately removed by filtration. The filtrate was allowed to stand at room temperature overnight, and then concentrated to a syrup. This was dissolved in water and subjected to column chromatography with the use of an IR-120 (H^+ form) column (4.5 × 30 cm). The column was thoroughly washed with water and eluted with 2 *N* NH_4OH. The fractions which showed positive ultraviolet absorption were collected and concentrated to a syrup. 9-β-D-Glucopyranosyladenine was isolated by crystallization from a mixture of water, ethanol, and ether, and recrystallization was carried out from the same solvent: yield 0.3 g (9.8%); mp 198–200°; $[\alpha]^{21}D$ −9° (*c* 1.0, water); $\lambda_{max}^{H_2O}$ 259 mμ, $\lambda_{min}^{H_2O}$ 225 mμ; ν_{max}^{KBr} 3200–3470, 1640, 800, and 730 cm^{-1}.

Anal. Calcd for $C_{11}H_{15}N_5O_5 \cdot 0.5H_2O$: C, 43.13; H, 5.27; N, 22.86. Found: C, 43.11; H, 5.27; N, 23.33.

The water of crystallization was lost on drying at 100° on P_4O_{10} under reduced pressure for 3 hr.

A mixture melting point with an authentic sample[8] of 9-β-D-glucopyranosyladenine showed no depression, and the infrared spectrum was identical with that of the authentic sample.

9-β-D-Ribopyranosyladenine.—2,3,4-Tri-*O*-acetyl-D-ribopyranose (1.2 g), 6-benzamidopurine (1.2 g), and P_4O_{10} (1 g) were dissolved in DMF (15 ml) as described above. The mixture was allowed to stand at 70–75° for 50 hr. The reaction product, which was obtained by extraction with $CHCl_3$ as described in the preparation of 7-β-D-xylopyranosyltheophylline, was purified with the use of a Dowex-50 (H^+ form) column as described in the preparation of 9-β-D-glucopyranosyladenine. Crystallization and recrystallization were carried out from hot water: yield 0.1 g (6.0%); mp 242–243°; $[\alpha]^{21}D$ −37° (*c* 1.0, water) [lit. mp 237,[9] 254°[10,11]; $[\alpha]D$ −38,[9,11] −37°[10] (water)]; $\lambda_{max}^{H_2O}$ 258 mμ, $\lambda_{min}^{H_2O}$ 227 mμ; $R_{adenine}$ 0.54; ν_{max}^{KBr} 3200–3300 and 1640 cm^{-1}.

Anal. Calcd for $C_{10}H_{13}N_5O_4 \cdot H_2O$: C, 42.10; H, 5.30; N, 24.55. Found: C, 42.03; H, 5.34; N, 23.64.

The water of crystallization was lost on drying at 100° on P_4O_{10} under reduced pressure for 3 hr.

(6) K. Onodera, S. Hirano, and H. Fukumi, *Agr. Biol. Chem.* (Tokyo)' **28**, 173 (1964).

(7) The specific rotation is in good agreement with those reported: $[\alpha]D$ −2.33° (water) [E. Fischer and B. Helferich, *Ber.*, **47**, 210 (1914)] and $[\alpha]^{19}D$ −3.56° (*c* 1.49, water) [T. Hashizume and H. Iwamura, *Tetrahedron Letters*, 3095 (1965)], but this is different from those reported in our previous papers: $[\alpha]^{19}D$ +39.09° (*c* 0.92, water) [K. Onodera and H. Fukumi, *Agr. Biol. Chem.* (Tokyo), **27**, 864 (1963)] and $[\alpha]^{14}D$ +38° (*c* 0.9, water).[6] The positive value of the specific rotation obtained previously might be taken with the anomeric mixture of 7-D-glucopyranosyltheophylline. This is under investigation by preparing the α-D anomer.

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Hydroxylation of Ethyl 2,3-Didehydro-2,3-dideoxy-α-D-glucopyranoside

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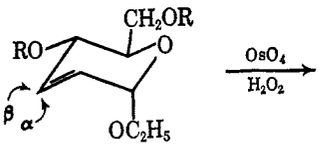
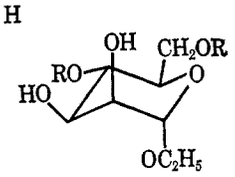
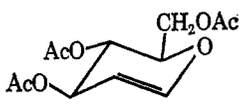
Two recent papers[2,3] have reported different syntheses of D-allose and its derivatives. While successful in their two approaches, these references still served to illustrate that difficulties remain in synthesizing that hexose. This paper reports a brief study of the stereochemical course of the osmium tetroxide catalyzed hydroxylation of unsaturated sugar derivatives[4] Ia and b, readily obtained from triacetyl glucal. Thus, it will be noted that attack of the *cis* hydroxylating



Ia, R = Ac
b, R = H





III

IIa, R = Ac
b, R = H

agent on the α face of I would yield the *allo* configuration while attack on the β face would yield the *manno* configuration. One might anticipate predominant reagent attack on the β face because of the increased steric requirements to α attack imparted by the α-ethoxy group at C-1 of I. Triacetyl glucal (III) has been shown to undergo stereoselective hydroxylation with osmium tetroxide, however, *via* α attack to yield the *gluco* configuration in great predominance.[5a] Galactal also suffers α hydroxylation affording D-galactose exclusively.[5b] No 2,3-dehydro sugars appear

(1) Summer visitor, 1965, from Laboratoire de Chimie Organique Sorbonne, Paris V[e], France.

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