3.68 (d, $J_{1,2}$ = 2.4 Hz, H-1'),[31] 4–4.8 (m, CH=CH_2 and unresolved H-2', H-3'), 5.1 (m, H-4'), 7.81, 7.90 (both s, CH_3); tlc in 95:5 ethyl acetate–methanol, R_f 0.31.

Anal. Calcd for $C_{15}H_{17}N_5O_5$: C, 51.87; H, 4.93; N, 20.16. Found: C, 51.51; H, 5.01; N, 19.77.

From 14.—To a solution of 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose[26] (4.75 g) in 50 ml of dry pyridine was added 16 ml of acetic anhydride while the mixture was stirred and chilled in an ice bath. After remaining at this temperature for 1 hr, the mixture was kept at room temperature for 24 hr. The solution was evaporated to a small volume diluted with 100 ml of chloroform, and washed with water (100 ml), saturated sodium bicarbonate (two 100-ml portions), and water (100 ml), and dried. Evaporation gave an oil from which traces of pyridine were removed by coevaporation of toluene. Distillation gave 2.4 g (41%) of an unstable oil (**14**): bp 67–70° (0.15 mm); $[\alpha]^{24}D$ −12° (*c* 4, $CHCl_3$); ir (film, NaCl) 1745 (C=O), 1648 (C=C), 1414 (=CH_2), 1375 (*gem*-dimethyl), 994 cm^{-1} (-CH=CH_2) [lit.[27] bp 154–157° (0.7 mm), $[\alpha]D$ −13° (*c* 1, $CHCl_3$)].

Compound **14** (2.4 g) was converted to tri-*O*-acetate **15** in a solution of glacial acetic acid (51 ml), acetic anhydride (6.8 ml), and concentrated sulfuric acid (3.5 ml) as described above for the preparation of **2**. A yellow syrup weighing 2.52 g resulted.

The coupling reaction was performed by previously described methods. The reaction mixture consisted of 2.52 g (9.3 mmol) of **15**, 5.44 g (11.5 mmol) of 6-benzamidochloromercuripurine, 5.4 g of Celite-545, 0.7 ml of titanium tetrachloride, and 200 ml of 1,2-dichloroethane. The syrupy residue obtained was dissolved in 20 ml of warm ethanol, 22 ml of 10% ethanolic picric acid was added, and the mixture was boiled under reflux until crystals began to appear after 5 min. The picrate was allowed to crystallize at room temperature, then chilled in an ice bath to give upon filtration 1.54 g of crystals. The mother liquor deposited an additional 0.32 g (total yield 33%). Recrystallization from acetone–ethanol gave 1.2 g of tiny crystals (picrate of **12**): mp 210–214° dec; ir (KBr) 1752 (C=O), 1694 (protonated adenine ring), 1608, 1568 (purine ring), 1548, 1314 (NO_2), 1077–1042 cm^{-1} (broad CO).

Anal. Calcd for $C_{21}H_{20}N_8O_{12}$: C, 43.76; H, 3.50; N, 19.44. Found: C, 43.41; H, 3.76; N, 19.26.

(31) The low coupling constant is indicative of a *trans* relationship between C-1' and C-2' and represents additional support for the configurational assignment.

The picrate (1.06 g) was dissolved in 150 ml of 80% aqueous acetone and the yellow color was discharged with Bio-Rad AG1-X8 (CO_3^{-2}) resin. The resin was filtered off, the solvents were removed by evaporation, and the product was crystallized from ethanol in two crops to give 344 mg (54%); mp 198–201° Recrystallization produced 248 mg of colorless platelets of **12**, mp 201–203°. The mixture melting point with **12** prepared from **3** gave no depression, the ir spectra were identical, and the compounds migrated the same on tlc plates.

9-(5,6-Dideoxy-β-D-*xylo*-hex-5-enofuranosyl)adenine (13).—To a solution of 207 mg of **12** in 25 ml of methanol was added 1.5 ml of 1 *N* methanolic sodium methoxide and the mixture was boiled under reflux for 50 min.[32] The dark solution was cooled to room temperature, brought to neutrality with Dowex 50 (H^+) resin, and evaporated to dryness. The brown residue was dissolved in water, treated with activated charcoal (heat), and evaporated again. The compound failed to crystallize but could be obtained as a hard, gray foam by evaporation of acetone to give 63 mg (40%) of **13**. This substance was very hygroscopic and slowly decomposed upon storage in a desiccator at room temperature. It was homogeneous on paper chromatograms: Rad 1.25 (5% aqueous disodium hydrogen phosphate) and 1.40 (86:14 *n*-butyl alcohol–water); uv max (0.1 *N* HCl) 257 and (H_2O or 0.1 *N* NaOH) 259 mμ.

Anal. Calcd for $C_{11}H_{13}N_5O_3$: C, 50.18; H, 4.98; N, 26.60. Found: C, 50.14; H, 5.25; N, 25.26.

A picrate prepared from **13** in methanol[30] had mp 209–211° dec on recrystallization. This material was very light sensitive.

Anal. Calcd for $C_{17}H_{16}N_8O_{10}$: C, 41.47; H, 3.28; N, 22.76. Found: C, 41.46; H, 3.30; N, 22.14.

Registry No.—**2**, 32653-56-8; **3**, 32653-57-9; **3** (picrate), 32653-58-0; **4**, 32653-59-1; **7** (picrate), 32781-70-7; **8**, 32653-60-4; **11** (picrate), 32653-67-1; **12**, 32653-61-5; **12** (picrate), 32653-62-6; **13**, 32653-63-7; **13** (picrate), 32653-64-8; **14**, 17225-57-9.

Acknowledgment.—The author would like to give acknowledgment to Mr. Philip Schiffman, who performed some of the preliminary experiments connected with this work.

(32) It is better to run this reaction overnight at room temperature to prevent degradation of the product.

Interconversions of Hexofuranosyl Nucleosides. III. Synthesis of a 4',5'-Unsaturated Hexofuranosyl Nucleoside[1]

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6-Deoxy-2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-L-mannofuranose (**1**) was converted to the α-L-chloride (**2**) by reaction with thionyl chloride in pyridine. Compound **2** was coupled with 6-benzamidopurine and 9-(6-deoxy-2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-α-L-mannofuranosyl)adenine (**4**) was isolated *via* its picrate **3**. Proof of the structure of **4** was obtained by removal of the tosyl group, which gave the known isopropylidene nucleoside **5**. When **4** was allowed to react with sodium benzoate in boiling *N*,*N*-dimethylformamide, the unsaturated nucleosides, 9-(5,6-dideoxy-2,3-*O*-isopropylidene-β-D-*erythro*-hex-4-enofuranosyl)adenine (**6**) and 9-(5,6-dideoxy-α-L-*lyxo*-hex-5-enofuranosyl)adenine (**7**), were unexpectedly isolated. The yield of **6** was 35% and could be raised to 54% by reaction of **4** with potassium *tert*-butoxide in hot *N*,*N*-dimethylformamide. The nucleosidic bond of **6** was extremely acid labile and attempts to remove the isopropylidene group resulted in immediate degradation and release of adenine. Interest in the unsaturated free nucleoside **10** is due to its structural relationship to the nucleoside antibiotic, decoyinine. Another nucleoside derivative, 9-(6-deoxy-2,3-di-*O*-acetyl-5-*O*-*p*-toluenesulfonyl-α-L-mannofuranosyl)adenine (**13**), was prepared as a potentially useful starting material toward the synthesis of **10**. Reaction of **1** under acetolysis conditions gave the triacetate **12** which was condensed with 6-benzamidochloromercuripurine by the titanium tetrachloride method. Removal of the *N*-benzoyl group gave **13**, whose chemical properties did not favor its transformation to **10**.

It was shown in the preceding two papers[2,3] that the transformation of a hexofuranosyl nucleoside into its 5' epimer was dependent to a great extent upon the configuration of the exocyclic group at C-4' relative to the configuration of the purine ring at C-1'. When they were both on the same side of the furan ring of the sugar, it became difficult to achieve a successful epimerization

(1) This work was supported, in part, by Grant No. T-442 from the American Cancer Society.

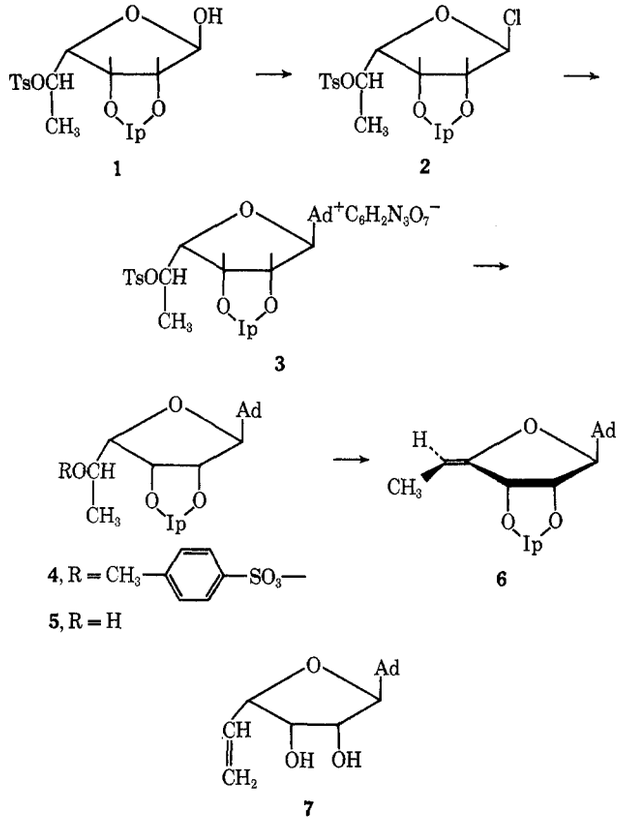
(2) L. M. Lerner, *J. Org. Chem.*, **37**, 470 (1972).

(3) L. M. Lerner, *ibid.*, **37**, 473 (1972).

at C-5′, especially if the C-6′ position was occupied by a tosyloxy group. If an acyloxy group occupied the C-6′ position, there was still the possibility of a participation and the success of this synthesis became dependent to some degree on the reaction conditions used, especially as concerned the solvent and temperature. In this paper are reported attempts at inversion of configuration at C-5′ of a hexofuranosyl nucleoside having the exocyclic carbons on the opposite side of the sugar ring from the purine and a 6′-deoxy carbon. The intention was to prepare 9-(6-deoxy-β-D-gulofuranosyl)-adenine from a nucleoside derivative of 6-deoxy-L-mannose (L-rhamnose).

It was first necessary to undertake the synthesis of 9-(6-deoxy-2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-α-L-mannofuranosyl)adenine (**4**). The route chosen was similar to those which have been used several times before for the preparation of nucleosides having a nonparticipating acetal group blocking the hydroxyls at C-2 and C-3 (Scheme I).[4] The anomeric hydroxyl

SCHEME I



group of 6-deoxy-2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-L-mannofuranose[5] (**1**) was exchanged for a chloride by reaction with thionyl chloride in pyridine. The chloro sugar **2** was shown to have the α-L configuration by nmr spectroscopy which revealed a singlet for the anomeric hydrogen at τ 3.96. This is consistent with a trans configuration between H-1 and H-2. Condensation of **2** with 6-benzamidopurine under conditions developed by Yamaoka, Aso, and Matsuda[6] was successfully carried out and the crude product was converted to the picrate[7] **3**, which was in turn treated with an anion exchange resin[8] to give **4**. Both **3** and **4** probably contained small amounts of their β-L anomers; however, it has been demonstrated that only trace amounts of the 1′,2′-cis nucleosides are obtained from reactions of purines with glycosyl halides having nonparticipating blocking groups.[4] Proof of the structure of **4** was obtained by preparation of 9-(6-deoxy-2,3-*O*-isopropylidene-α-L-mannofuranosyl)adenine[4] (**5**) by removal of the tosyl group at C-5′ of **4** with sodium amalgam. These experiments represent further evidence that these coupling reactions proceed by an SN1 mechanism. The anomeric configuration of nucleoside **4** is the same as that of the glycosyl chloride **2** and the only effect directing the configuration appears to be steric in origin.[4]

In one of the early attempts to invert the configuration at C-5′ by reaction of **4** with sodium benzoate in boiling, moist *N*,*N*-dimethylformamide,[9] the crude product was treated directly with base, then acid, and subsequently chromatographed on an anion-exchange column.[10] All that was obtained from the column were very small amounts of two substances, one of which was identified as 9-(5,6-dideoxy-α-L-*lyxo*-hex-5-enofuranosyl)adenine (**7**) from its elemental analysis and by comparison of its melting point, ir spectrum, and specific rotation to those of the D enantiomer prepared previously.[2] Paper and thin layer chromatography of a similar preparation prior to column chromatography revealed that the nucleoside bond had broken, giving adenine as the major uv-absorbing spot. Since it was not expected that 9-(6-deoxy-2,3-*O*-isopropylidene-β-D-gulofuranosyl)adenine would be degraded under the acidic conditions used and it was known that the nucleosidic bond of the enantiomer of **7** was fairly stable to mild acid conditions,[2] it was felt that further investigation of the immediate product of the sodium benzoate–dimethylformamide reaction was warranted. When this was done, a crystalline substance was obtained which decolorized solutions of bromine and potassium permanganate. Elementary analysis also supported an unsaturated product. Because the isopropylidene derivative of the D enantiomer of compound **7** was a known compound[2] whose properties differed considerably from those obtained here, it appeared most likely that elimination had occurred between positions 4′ and 5′ to give 9-(5,6-dideoxy-2,3-*O*-isopropylidene-β-D-*erythro*-hex-4-enofuranosyl)adenine (**6**). This interpretation was supported by the nmr spectrum which showed a methyl resonance at τ 8.39 as a doublet which was assigned to the protons at C-6′. The chemical shift for the proton at C-5′ (τ 5.11) was identified by a decoupling experiment performed by irradiation at the resonance frequency of the C-6′ methyl group. It should perhaps be noted that the anomeric proton gave a singlet at τ 3.69 which would indicate a trans relationship between H-1′ and H-2′ and, therefore, a β-D configuration for the nucleoside, further evidence for the assigned anomeric

(4) L. M. Lerner and Y. Y. Cheng, *Carbohyd. Res.*, **14**, 297 (1970), and references cited therein.

(5) P. A. Levene and J. Compton, *J. Biol. Chem.*, **116**, 169 (1936).

2778 (1957).

(6) N. Yamaoka, K. Aso, and K. Matsuda, *J. Org. Chem.*, **30**, 149 (1965).

(7) J. R. Parikh, M. E. Wolff, and A. Burger, *J. Amer. Chem. Soc.*, **79**, 2778 (1957).

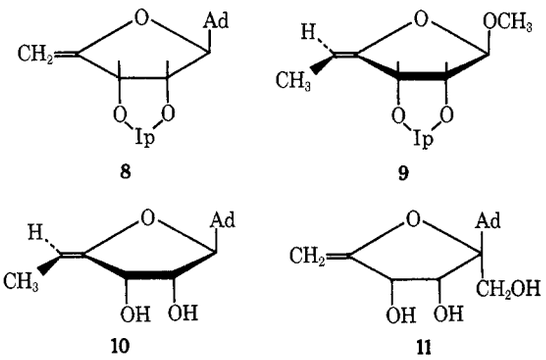
(8) M. L. Wolfrom, A. B. Foster, P. McWain, W. von Bebenburg, and A. Thompson, *J. Org. Chem.*, **26**, 3095 (1961).

(9) E. J. Reist, L. Goodman, and B. R. Baker, *J. Amer. Chem. Soc.*, **80**, 5775 (1958).

(10) C. A. Dekker, *ibid.*, **87**, 4027 (1965).

configurations used in this and previous work.[4] It is also of interest to note that when the reaction of bromine with **6** was reinvestigated, it was found that the ultraviolet peak shifted from 261 to 275 mμ. This may mean that an N-3,4′ cyclonucleoside had formed, such as isolated by McCarthy, *et al.*,[11] for a similar reaction of 9-(5-deoxy-2,3-*O*-isopropylidene-β-D-*erythro*-pent-4-enofuranosyl)adenine (**8**) (Chart I).

CHART I



Although it has been shown that anions become more basic in aprotic dipolar solvents such as *N*,*N*-dimethylformamide,[12] the 35% yield in this elimination reaction was surprising. This is especially so when one considers that Baker and coworkers[9] converted methyl 6-deoxy-2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-β-D-allofuranoside into methyl 6-deoxy-5-*O*-benzoyl-2,3-*O*-isopropylidene-α-L-talofuranoside in yields of 77–79% under similar conditions. Solutions of **4** in boiling *N*,*N*-dimethylformamide did not undergo reaction to **6**, as has been reported to happen in some cases where olefins have been prepared from sulfonate esters of secondary alcohols.[13] The yield of **6** obtained here compared favorably with the yield (40%) of olefinic sugar **9** which was obtained by reacting methyl 6-deoxy-2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-β-D-allofuranoside with potassium *tert*-butoxide in boiling *tert*-butyl alcohol.[14] Treatment of **4** with a solution of potassium *tert*-butoxide in pyridine and *tert*-butyl alcohol at room temperature did not give a reaction and **4** was recovered unchanged. Under the same conditions, 5′-*O*-*p*-toluenesulfonyl-2′,3′-*O*-isopropylideneadenosine gave a 35% yield of **8** after 5 min.[11] Treatment of **4** with sodium methoxide in *N*,*N*-dimethylformamide at either room temperature or at 100° yielded a number of substances, among them a very small amount of **6** and what appeared to be **5** from tlc data. However, when **4** was heated at reflux with potassium *tert*-butoxide in a mixture of *tert*-butyl alcohol and *N*,*N*-dimethylformamide for 22 hr, the yield of **6** was 54% or better if the mother liquors were chromatographed on silicic acid columns. The isolation of unsaturated products from reactions of tosyl derivatives of alditols with sodium benzoate in boiling dimethylformamide have been reported previously[15] and papers describing the elimination of *p*-toluenesulfonic acid under similar conditions to form enol tosylates have been referred to in a previous article.[2]

When the methyl glycoside of **1** was allowed to react under basic conditions the product obtained was the same one which was obtained from methyl 6-deoxy-2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-β-D-allofuranoside, namely **9**.[14] Since hydroboration of **9** gave the 6-deoxy-D-gulose derivative and not the 6-deoxy-L-mannose derivative, the conclusion was made that the elimination has occurred by an E2 mechanism and that the configuration of the methyl group in relation to the ring oxygen was trans. Hydroboration[14,16] of **6** resulted in darkened reaction mixtures and as many as six unidentified components as shown by tlc. Attempts to carry out a successful hydroboration were dropped and the structure of **6** as shown in Scheme I is assumed in analogy to **9**.

It has been found to be impossible to remove the isopropylidene group of **6** under all of the acidic conditions tried. Adenine was liberated immediately. It was now understood why only compound **7** was obtained in the earlier experiment. During the reaction which formed **6**, a small amount of the isopropylidene derivative of **7** was also formed by elimination between C-5′ and C-6′. Acid hydrolysis degraded **6** completely, but did not hydrolyze the C–N bond of **7**, which was freed of adenine on the ion-exchange column.[10] Similar results occurred in attempts to remove the isopropylidene group of **8**.[11]

Removal of the isopropylidene group of **6** would give the free nucleoside **10**, which would be an interesting analog of the unsaturated nucleoside antibiotic, decoyinine (**11**). Preparations of other nucleoside analogs of this antibiotic have been reported.[11,17] Further attempts to obtain **10** were now made and several approaches were considered. The first one was to replace the isopropylidene group of **6** with a group which was much more acid labile, such as a methoxymethylidene group.[18] To do this it was necessary to be able to selectively hydrolyze the isopropylidene group and as of this writing this task has not been accomplished satisfactorily. Next, the synthesis of 9-(6-deoxy-2,3-di-*O*-acetyl-5-*O*-*p*-toluenesulfonyl-α-L-mannofuranosyl)-adenine (**13**) was undertaken (Scheme II). The plan here was to remove the base-labile groups in one step with a strong base and get a concomitant elimination at C-4′ to form **10** or, if that was unsuccessful, to remove the acetyl groups with catalytic amounts of sodium methoxide or other base and then form the methoxymethylidene derivative. Compound **1** was subjected to acetolysis and a compound assumed to be the tri-*O*-acetate **12** was obtained. This was condensed with 6-benzamidochloromercuripurine, using titanium tetrachloride to generate the glycosyl chloride *in situ*,[19] and **13** was prepared *via* the picrate.[7,8] The anomeric con-

(11) J. R. McCarthy, R. K. Robins, and M. J. Robins, *J. Amer. Chem. Soc.*, **90**, 4993 (1968).

(12) A. J. Parker, *Quart. Rev., Chem. Soc.*, 163 (1962).

(13) H. R. Nace, *J. Amer. Chem. Soc.*, **81**, 5428 (1959); D. V. Banthorpe, "Elimination Reactions," Elsevier, New York, N. Y., 1963, pp 33 ff.

(14) H. Arzoumanian, E. M. Acton, and L. Goodman, *J. Amer. Chem. Soc.*, **86**, 74 (1964).

(15) M. A. Bukhari, A. B. Foster, and J. M. Webber, *J. Chem. Soc.*, 2514 (1964); M. A. Bukhari, A. B. Foster, J. M. Webber, and J. Lehmann, *Carbohyd. Res.*, **1**, 485 (1966).

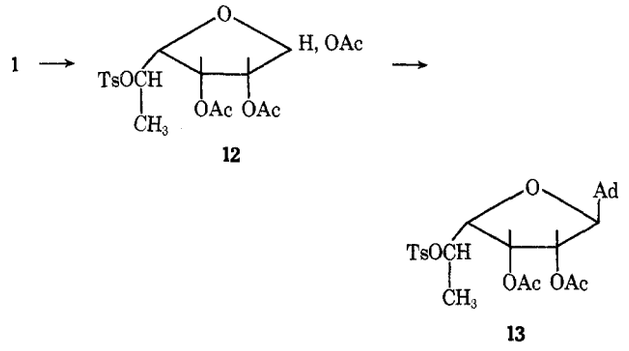
(16) M. L. Wolfrom, K. Matsuda, F. Komitsky, Jr., and T. E. Whiteley, *J. Org. Chem.*, **28**, 3551 (1963).

(17) J. P. H. Verheyden and J. G. Moffatt, *J. Amer. Chem. Soc.*, **88**, 5684 (1966).

(18) B. E. Griffin, M. Jarman, C. B. Reese, and J. E. Sulston, *Tetrahedron*, **23**, 2301 (1967).

(19) B. R. Baker, R. E. Schaub, J. P. Joseph, and J. H. Williams, *J. Amer. Chem. Soc.*, **77**, 12 (1955); J. Prokop and D. H. Murray, *J. Pharm. Sci.*, **54**, 359 (1965).

SCHEME II



figuration of **13** was assigned as α by reference to the trans rule,[20] which predicts that the α anomer will predominate because of the directive effect of the acyloxy group at C-2. Treatment of **13** with potassium *tert*-butoxide in *N*,*N*-dimethylformamide or methanolic sodium methoxide caused the mixtures to darken and resulted in complex mixtures of products as shown by tlc. This characteristic was noted by McCarthy, *et al.*,[11] during similar reactions with 5′-tosyl derivatives of adenosine and seems to be a general feature of these types of compounds which either have base-labile blocking groups at C-2′ and C-3′ or no blocking groups whatsoever.

A number of unsuccessful attempts were made to deacylate **13** using conditions which have been used successfully to deacylate sugars without detosylating them.[21] Catalytic quantities of sodium methoxide in methanol had no effect on **13** even under boiling conditions. Methanolic ammonia gave a 50% recovery of crystalline **13** and five other components which chromatographed on tlc plates similarly to some of the products derived from the complex mixtures mentioned above. Sodium hydroxide in aqueous acetone gave results which were even less hopeful.

Further work is continuing in this laboratory leading to the preparation of **10**, an interesting but elusive compound.

Experimental Section[22]

6-Deoxy-2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-α-L-mannofuranosyl Chloride (2).—6-Deoxy-2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-L-mannofuranose[6] (8.2 g, 24 mmol) was dissolved in 14 ml of dichloromethane[23] and added dropwise to a stirring ice-cold mixture containing 4.6 ml of thionyl chloride in 11.5 ml of dry pyridine and 14 ml of dichloromethane. The reaction was allowed to proceed for 6 hr at 0° and then poured onto 100 g of ice. When the ice had melted, 50 ml of dichloromethane was added and the organic layer was separated. Two more extractions of the aqueous layer with 35-ml portions of dichloromethane were carried out, and the extracts were all combined and washed twice with 75-ml portions of ice-cold 1 *N* sodium hydroxide solution and twice with 100-ml portions of ice-cold water, and dried. The solution was evaporated to a syrup from which toluene was coevaporated two times to remove traces of pyridine. An orange syrup was obtained which gave an instantaneous positive alcoholic silver nitrate test: ir (film NaCl) 1174 cm^{-1} (sulfonate); nmr ($CDCl_3$) τ 2.25 (d, phenyl protons ortho to sulfonate), 2.75 (d, phenyl protons ortho to CH_3), 3.96 (s, H-1), 4.99 (m, unresolved H-2, H-3, H-4), 5.68 (m, H-5), 7.56 (s, CH_3 of tosyl group), 8.55 (d, C-6 CH_3), 8.75, 8.84 (both s, *gem*-dimethyl). This compound was used directly in reactions without further purification because it was rather unstable.

9-(6-Deoxy-2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-α-L-mannofuranosyl)adenine (4).—From a mixture of 5.5 g of 6-benzamidopurine, 6.9 g of mercuric cyanide, and 350 ml of nitromethane was distilled 50 ml of the latter to remove any traces of moisture. The mixture was cooled to below the boiling point and 12 g of anhydrous calcium sulfate was added, followed by the entire sample of **2** in 50 ml of dry nitromethane.[6] The mixture was heated at reflux for 4 hr and filtered while still warm, and the filter cake was washed with two 25-ml portions of warm nitromethane. The solvent was evaporated, and the residue was extracted with 300 ml of dichloromethane, filtered, washed three times with 150-ml portions of 30% potassium iodide and twice with 150-ml portions of water, and dried. Evaporation gave 8.4 g of a thick, orange syrup which was dissolved in 35 ml of absolute ethanol and treated with 50 ml of 10% ethanolic picric acid at reflux for 10 min, at which time crystals began to appear.[7] Crystallization was allowed to continue at room temperature to yield 4.31 g (26% from **1**) of yellow crystals in two crops: mp 190–196° dec. A 300-mg sample was recrystallized from methanol: mp 194–196°; $[\alpha]^{26}D$ −24° (*c* 1.13, acetone); ir (KBr) 1690 (protonated adenine ring), 1604 (phenyl and purine ring), 1544 (NO_2), 1375 sh, 1358 (*gem*-dimethyl and sulfonate), 1316 (NO_2), 1173 (sulfonate), and 1076 cm^{-1} (COC, CO).

Anal. Calcd for $C_{27}H_{28}N_8O_{13}S$: C, 46.02; H, 4.01; N, 15.90. Found: C, 45.65; H, 4.01; N, 15.79.

In other preparations of **3**, yields ranging up to 46% from **1** were obtained by this procedure.

A solution of 4.0 g of **3** in 175 ml of 80% aqueous acetone was stirred with Bio-Rad AG1-X8 (CO_3^{-2}) resin until the yellow color due to picrate ion was removed.[8] Some orange color due to a contaminant was removed by treatment with Darco G-60, affording a clear, colorless solution. Evaporation gave a hard white foam which was dried by evaporation of absolute ethanol. The foam weighed 1.4 g (52%): $[\alpha]^{26}D$ −15° (*c* 1.5, *N*,*N*-dimethylformamide); ir (film, NaCl) 3360 (NH) 1640, 1595 (phenyl and purine ring), 1378 sh, 1360 (*gem*-dimethyl and sulfonate), 1175 (sulfonate), 1074 cm^{-1} (broad CO). Tlc showed that the foam was not homogeneous, but was contaminated by trace amounts of two slower moving components: R_f of **4** in 1:1 ethyl acetate–methanol, 0.59.

Anal. Calcd for $C_{21}H_{25}N_5O_6S$: C, 53.04; H, 5.30; N, 14.73; S, 6.74. Found: C, 52.54; H, 5.52; N, 14.17; S, 6.07.

When addition of the ion-exchange resin and of the charcoal was more cautiously controlled, yields such as 71 and 97% were obtained, indicating that the product was being absorbed by these materials.

9-(6-Deoxy-2,3-*O*-isopropylidene-α-L-mannofuranosyl)adenine (5).—To a solution of 1 g of **4** in 50 ml of 80% aqueous methanol was added 25 g of 2.5% sodium amalgam in small portions, while stirring vigorously. After 24 hr, the solution was decanted, the mercury was washed a few times with methanol, and the washings were decanted. The washings were combined with the original solution, and carbon dioxide gas was bubbled through the solution for several hours. Following filtration, the solvents were removed by evaporation and the residue was partitioned between 30 ml each of water and chloroform. The aqueous layer was extracted two more times with 30-ml portions of chloroform, and the chloroform extracts were combined and dried. Evaporation and crystallization from ethyl acetate afforded 240 mg of **5**, mp 218–224°. Recrystallization from 30% aqueous methanol raised the melting point to 224–229°. There was no depression of melting point upon admixture of an authentic sample[4] of **5**, and the ir spectra and mobility on tlc plates were also identical.

9-(5,6-Dideoxy-2,3-*O*-isopropylidene-β-D-*erythro*-hex-4-enofuranosyl)adenine (6). Method A.—A mixture consisting of 7.2 g (15.1 mmol) of **4**, 10.9 g of sodium benzoate, and 640 ml of *N*,*N*-dimethylformamide was boiled under reflux for 24 hr and then evaporated to a dark brown residue.[9] This was partitioned between 250 ml each of chloroform and water and the chloroform layer was washed with 300 ml of saturated sodium bicarbonate and again with 300 ml of water. The solution was dried and the chloroform was removed by evaporation. A white solid formed when the residue was triturated with 30% aqueous methanol and most of the dark colored material was washed away with the fil-

(20) B. R. Baker, in Ciba Foundation Symposium, "Chemistry and Biology of Purines," G. E. W. Wolstenholme and C. M. O'Connor, Ed., Little, Brown and Co., Boston, Mass., 1957, p 120.

(21) R. S. Tipson, *Advan. Carbohyd. Chem.*, **8**, 107 (1953).

(22) General methods and instrumentation are described in the first paper of this series.[2] Tlc was carried out on silica gel HF (E. Merck A. G., Darmstadt) using plates of 0.25 mm thickness. Rad (adenine) = 1.00.

(23) Dried over molecular sieve 3A.

trate. The solid weighed 1.57 g (35%), mp 193–195°. Two recrystallizations from methanol gave the analytical sample: mp 209–210.5°, with fine needles forming during heating; $[\alpha]^{24}D$ +87° (*c* 1.4, $CHCl_3$); uv max (CH_3OH) 261 mμ; nmr (DMSO-d_6) τ 1.82, 1.88 (both s, 1 proton each, H-2, H-8), 3.69 (s, 1, H-1′), 4.28 (s, 1, H-3′), 4.70 (s, 1, H-2′), 5.11 (m, 1, H-5′), 8.39 (d, 3, C-6′ CH_3), 8.56, 8.65 (both s, 6, *gem*-dimethyl); tlc in 9:1 ethyl acetate–methanol, R_f 0.41; paper chromatography on Whatman No. 1 paper, Rad 2.58. This compound rapidly decolorized solutions of bromine in carbon tetrachloride and potassium permanganate in aqueous ethanol.

Anal. Calcd for $C_{14}H_{17}N_5O_3$: C, 55.47; H, 5.65; N, 23.09. Found: C, 55.29; H, 5.58; N, 23.06.

Additional **6** can sometimes be obtained from the brown filtrates by chromatography on silicic acid[24] with 9:1 ethyl acetate–methanol. This chromatographic system worked well for the isolation of **6** in those cases where it would not crystallize easily from aqueous methanol.

Method B.—To a solution of 9 g (18.9 mmol) of **4** in 225 ml of *N*,*N*-dimethylformamide under a nitrogen atmosphere was added dropwise 225 ml of 1 *N* potassium *tert*-butoxide in *tert*-butyl alcohol and the mixture was heated at reflux for 22 hr. The dark brown residue obtained after evaporation of the solvents was partitioned between 150 ml each of chloroform and water. The water layer was extracted several more times with chloroform, and the extracts were combined, dried, and evaporated to dryness. Crystallization from methanol afforded 3.15 g (54%) of **6**. One recrystallization gave analytically pure material, mp 208.5–209.5°. This material was identical in every way to the crystals obtained from method A.

Anal. Found: C, 55.56; H, 5.76; N, 23.12.

9-(5,6-Dideoxy-α-L-*lyxo*-hex-5-enofuranosyl)adenine (7).—Compound **4** (4.5 g) was treated as described in method A for the preparation of **6**. The crude product was treated directly with 90% formic acid for 19 hr. The residue obtained after evaporation of the acid was dissolved in 30% aqueous methanol and chromatographed on a column of Bio-Rad AG1-X2 (OH, 200–400 mesh) using the same solvent system. Two uv-absorbing peaks were obtained, one of which was identified as **7** after crystallization from aqueous ethanol: yield 34 mg; mp 246–247° dec; $[\alpha]^{27}D$ −52.1° (*c* 0.305, 1 *N* HCl). The ir spectrum of **7** was identical with that of the D enantiomer prepared earlier.

Anal. Calcd for $C_{11}H_{13}N_5O_3$: C, 50.18; H, 4.98; N, 26.60. Found: C, 49.88; H, 5.04; N, 26.24.

9-(6-Deoxy-2,3-di-*O*-acetyl-5-*O*-*p*-toluenesulfonyl-α-L-mannofuranosyl)adenine (13).—A reaction mixture containing 13 g (38 mmol) of **1**, 22.4 ml of acetic anhydride, 224 ml of glacial acetic acid, and 12.5 ml of concentrated sulfuric acid was made up by a previously described procedure[3] and kept at room temperature for 48 hr. The mixture was poured on 500 g of ice, stirred until the ice melted, and extracted with chloroform (three 100-ml portions). The chloroform solution was washed with saturated aqueous sodium bicarbonate and sodium chloride (300 ml), and again with sodium chloride solution (250 ml). The organic layer was dried and evaporated, and traces of acetic acid were removed by evaporation of toluene, leaving 10 g (59%) of an oil (**12**).

The preparation of the nucleoside was carried out by previously described procedures. The oil was added to a reaction mixture consisting of 13.5 g of 6-benzamidochloromercuripurine, 13.5 g of Celite-545, 3.1 ml of titanium tetrachloride, and 1050 ml of 1,2-dichloroethane.[19] A hard syrup (11.1 g) was obtained which was dissolved in 100 ml of ethanol and treated at reflux with 56 ml of 10% ethanolic picric acid for 30 min.[7] Crystallization of the picrate of **13** ensued in the boiling solution at this point and was continued for several hours at room temperature, then in the refrigerator overnight. Recrystallization from acetone–ethanol gave 7.45 g (44%) of yellow crystals, mp 157–160°.

A solution containing 7.05 g of the picrate in 500 ml of 80% aqueous acetone was stirred for 3 hr with Bio-Rad AG1-X8 (CO_3^{-2}) resin.[8] The clear, colorless solution was filtered to remove the resin and evaporated, whereupon crystallization occurred. Recrystallization from acetone afforded 2.22 g of **13**: mp 179–181° to a viscous liquid which decomposed at about 200°; $[\alpha]^{26}D$ +36° (*c* 1.7, $CHCl_3$); ir (KBr) 3380 (NH), 1745 (C=O of acetate), 1678, 1608, 1572 (purine ring), 1170 (sulfonate) 1094, 1075 cm^{-1} (CO).

Anal. Calcd for $C_{22}H_{25}N_5O_8S$: C, 50.86; H, 4.85; N, 13.48. Found: C, 51.19; H, 4.82; N, 13.49.

Registry No.—**2**, 32658-92-7; **3**, 32658-93-8; **4**, 32658-94-9; **5**, 29847-42-5; **6**, 32658-96-1; **7**, 32658-97-2; **13**, 32658-98-3.

(24) Mallinckrodt, 100 mesh.

Ring Expansion of Hydroxyoxetanes to Dihydrofurans

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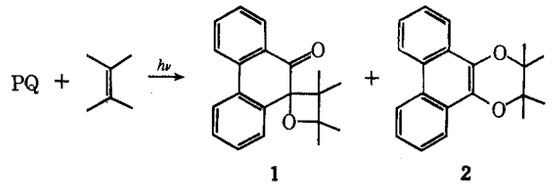
Reduction of the ketooxetanes **1** to the secondary alcohols **3** followed by treatment with acid led to rearrangement to the diols **4**, which, on dehydration, yielded the dihydrophenanthrofurans **5**. This reaction sequence and lanthanide-induced shift data were applied in elucidating the stereochemistry of **1**. The dehydration **4** → **5** proceeds either with retention or with inversion of the configuration depending on the nature of substituents.

α-Ketooxetanes can be prepared by the photoaddition of *o*-quinones or α diketones to olefins.[2] Most of these reactions have been carried out with phenanthrenequinone (PQ) which, in competing 1,2- and 1,4-cycloadditions, yields the ketooxetanes **1** and the dihydrophenanthrodioxins **2**, respectively.[3]



1 **2**

Oxetanes in general are known to undergo a number of acid catalyzed reactions, which may be used for different syntheses (for a review *cf.* ref 4). Rearrangement of oxetanes is, however, quite an unusual reaction.[4]

We have found that reduction of derivatives of **1** with $NaBH_4$ to the hydroxyoxetanes **3** and subsequent acid treatment led to rearrangement to the 1,4-diols **4**, which were readily dehydrated to the dihydrophenanthrofurans **5**.

In this way, the compounds **5a–g** could be prepared from the corresponding oxetanes (**1a–g**). The struc-

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(2) S. Farid, D. Hess, and C. H. Krauch, *Chem. Ber.*, **100**, 3266 (1967).

(3) S. Farid and D. Hess, *ibid.*, **102**, 3747 (1969).

(4) S. Searles, Jr., in "The Chemistry of Heterocyclic Compounds," Vol. 19, Part 2, A. Weissberger, Ed., Interscience, New York, N. Y., 1964, Chapter 9.