Interconversions of Hexofuranosyl Nucleosides. I. Synthesis of 9-β-L-Gulofuranosyladenine from 9-α-D-Mannofuranosyladenine[1]

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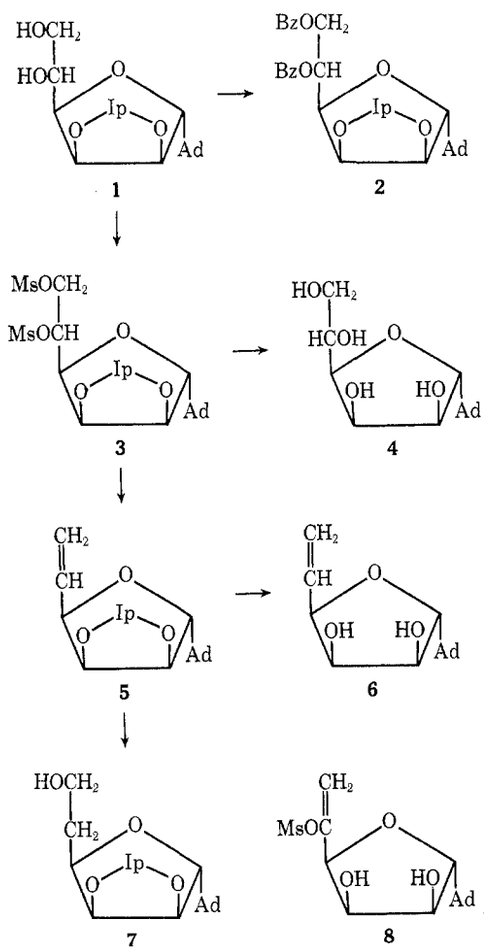
9-β-L-Gulofuranosyladenine (**4**) has been prepared from 9-α-D-mannofuranosyladenine by epimerization at C-5′. This was accomplished by formation of the 5′,6′-di-*O*-methanesulfonyl ester of 9-(2,3-*O*-isopropylidene-α-D-mannofuranosyl)adenine (**3**), followed by inversion of configuration at C-5′ in a boiling mixture of sodium benzoate in *N*,*N*-dimethylformamide. Removal of the blocking groups gave **4**. Several other derivatives prepared from **3** included the 5′,6′-dideoxy nucleoside (**5**), which was formed by elimination of the vicinal dimesyl esters, and an exocyclic enol sulfonate (**8**), which was isolated after inadvertent removal of one molecule of methanesulfonic acid. Hydroboration of **5** gave 9-(5-deoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hexofuranosyl)adenine (**7**) and acid hydrolysis of **5** gave the free nucleoside, 9-(5,6-dideoxy-α-D-*lyxo*-hex-5-enofuranosyl)adenine (**6**).

A number of hexofuranosyl nucleosides have been prepared by the author and his colleagues as biologically interesting analogs of naturally occurring nucleosides.[2,3] Such compounds have a potential use as antitumor or antimicrobial agents. Some of the rare hexose sugars required as starting materials in the synthesis of other hexofuranose-containing nucleosides are tedious to prepare in quantities which are large enough to work with. Therefore, the decision was made to prepare hexofuranosyl nucleosides from commercially available inexpensive sugars. A change in the configuration of a hydroxyl group at one or more carbon atoms could then be undertaken and would result in the desired nucleoside. This procedure offered the advantage of use of synthetic methods in nucleoside synthesis which are known to give good yields in the coupling reaction, whereas many of the rare hexose derivatives used previously have yielded low amounts of the desired products. Results such as these would not be unexpected in further experiments with rare hexoses, and the preparation of such rare hexose derivatives as are needed for these experiments would be a less than worthwhile undertaking. Hence, an investigation was begun with a study of the change in configuration at C-5′ of preformed hexofuranosyl nucleosides.

It has previously been reported that the coupling of 2,3,5,6-tetra-*O*-benzoyl-L-gulofuranosyl chloride with 6-benzamidochloromercuripurine gave a 10% yield of 9-β-L-gulofuranosyladenine.[2] This was accomplished by synthesis of the required glycosyl halide in a rather extensive series of reactions starting with D-glucuronic acid.[4,5] Furthermore, it has been demonstrated that the use of isopropylidene blocking groups in place of ester groups in nucleoside coupling reactions has resulted in increased yields[6] but the large number of steps in the reaction sequence still discouraged the use of this pathway. 9-(2,3-*O*-Isopropylidene-α-D-mannofuranosyl)adenine (**1**) is a nucleoside intermediate which can be obtained in good yield in a few, relatively simple steps.[3] What will be described below is the inversion of configuration at C-5′ of **1** as a simple method for the preparation of **4** (Scheme I).

SCHEME I[a]



[a] Ad = adeninyl; Ms = CH_3SO_3; Ip = $(CH_3)_2C$; Bz = benzoyl.

Some years ago Baker and his colleagues demonstrated that benzoate ion became a powerful nucleophile in solutions of moist *N*,*N*-dimethylformamide.[7] This reaction has since had wide application in carbohydrate chemistry.[8] To use this procedure in the preparation of **4** from **1** it was necessary to prepare the 5′,6′-di-*O*-

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p-toluenesulfonyl ester of **1**. However, the usual conditions of synthesis of tosyl esters[9] failed to give complete tosylation of **1**. When forcing reaction conditions were used which involved an excess of *p*-toluenesulfonyl chloride and heat, as many as six products were detectable on thin layer chromatograms, all of which could be approximated to be in nearly equal amounts. The lack of ease of reactivity of the hydroxyl groups of **1** may be, in part, a steric property, as ascertained by a study of molecular models and from experiments on the benzoylation of **1**. Although complete benzoylation of **1** could be achieved, a great excess of benzoyl chloride and a temperature of 100° was necessary, and the yield was still relatively low. Tosylation of **1** was abandoned in favor of methanesulfonylation, which proceeded satisfactorily under mild conditions to give **3**. When **3** was treated with an excess of sodium benzoate in moist *N*,*N*-dimethylformamide at 100°, or for 6 hr at reflux, 9-α-D-mannofuranosyladenine and **4** were isolated in a ratio of about 10:1 after removal of the blocking groups and chromatography on a Dowex 1 (OH) resin.[10] When the reaction mixture was heated at reflux for 24 hr and the blocking groups were removed, the major product was **4** in a 12% yield. Reaction mixtures became nearly black within minutes after the application of heat, a sign which is probably indicative of extensive decomposition when one considers the small yield of **4** and the inability to recover any 9-α-D-mannofuranosyladenine. Also, it is necessary to consider the often difficult problem of the removal of the isopropylidene group under conditions which will frequently hydrolyze the acid labile C–N nucleoside bond.[11] Nevertheless, the yield seems respectable enough when these results are compared to the 16% yield obtained for a similar inversion of 3-deoxy-1,2-*O*-isopropylidene-5,6-di-*O*-methanesulfonyl-α-D-galactofuranose to 3-deoxy-5,6-di-*O*-benzoyl-1,2-*O*-isopropylidene-β-L-mannofuranose.[12] Buss, *et al.*,[13] have shown that the tosyloxy group at C-6 of 3-*O*-acetyl-1,2-*O*-isopropylidene-5,6-di-*O*-*p*-toluenesulfonyl-α-D-glucofuranose is displaced much more easily and at a lower temperature than the one at C-5, and raising the temperature to the boiling point of *N*,*N*-dimethylformamide transforms this compound into 3-*O*-acetyl-5,6-di-*O*-benzoyl-1,2-*O*-isopropylidene-β-L-idofuranose in 50% yield. The better yield in this case may be due to the ability of the tosyloxy group to act as a better leaving group than the mesyloxy.[8,9] Goodman[14] has suggested that the reaction of sodium benzoate in *N*,*N*-dimethylformamide proceeds under SN2 displacement conditions at the exocyclic carbons of hexofuranose derivatives even under situations where a neighboring group participation would be expected. No clear reason for this was offered, but the recovery of 9-α-D-mannofuranosyladenine as the principal product in some of the reactions run in the present work may indicate that only the mesyloxy group at C-6 was displaced, and that the expected participation of the benzoyloxy group at that stage never occurred. Davidson and coworkers[15] have recently been studying the effects of solvent on the ability of potassium acetate to effect a displacement at C-5 of sugar derivatives possessing a benzoyloxy group at C-6 and they have concluded that both direct displacement and neighboring group participation take place in *N*,*N*-dimethylformamide.

Prior to the publication of papers by Davidson and colleagues[15,16] and by Chalk, *et al.*,[17] which demonstrated that reactions of acetate ion in boiling acetic anhydride proceeded by neighboring group participation reactions, **3** was treated with Dowex 1 (acetate) resin in acetic anhydride under the expectation that a simple displacement would occur.[18] Removal of the blocking groups gave, instead of **4**, what appeared to be an unsaturated enol mesylate (**8**). The structure shown is only tentatively assigned on the basis of elemental analysis, stability of the compound under conditions where allylic mesylates (4′,5′-olefinic bond) would be expected to be highly reactive, a characteristic infrared band at 885 cm^{-1} for a *gem*-vinyl group, and the expectation that the mesyl group at C-6′ would be more labile than the one at C-5′. Similarly, enol tosylates and mesylates in the rings of sugars[19a] and cyclitols[19b] have been isolated after reactions with sodium benzoate in *N*,*N*-dimethylformamide, and in one case a straight-chain enol tosylate of an alditol was prepared.[19c]

Dimesylate **3** was next subjected to reaction conditions which are known to give unsaturated products in compounds containing acyclic vicinal sulfonyloxy groups.[20] When **3** was treated with sodium iodide in acetone at 100° for only 1.5 hr,[20a] very little happened and what was recovered was primarily the starting material. It was found necessary to increase the reaction time to at least an overnight reaction, whereupon a substantial yield of 9-(5,6-dideoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hex-5-enofuranosyl)adenine (**5**) was obtained. That **5** had a double bond between carbons 5′ and 6′ and not between carbons 4′ and 5′ was supported by an nmr spectrum which showed no C-6′ methyl peak near τ 8.4. Acid hydrolysis of the isopropylidene of **5** gave compound **6**. Application of hydroboration reactions[21] to **5** were not very successful under the various conditions employed,[22] but one of the reactions yielded a very small quantity of what is believed to be 9-(5-deoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hexofuranosyl)adenine (**7**). The position of the deoxy carbon was based upon the known course of this addition reaction, which yields anti-Markovnikoff products.[21,22]

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Experimental Section[23]

9-(5,6-Di-*O*-benzoyl-2,3-*O*-isopropylidene-α-D-mannofuranosyl)adenine (2).—To a suspension of 9-(2,3-*O*-isopropylidene-α-D-mannofuranosyl)adenine (1)[3] (0.75 g, 2.2 mmol) in 14 ml of dry pyridine was added 1.8 ml of benzoyl chloride. The mixture was stirred at room temperature for 15 min, and then kept on a steam bath for 4.5 hr, protected from moisture. After allowing the mixture to cool to room temperature, it was poured into a mixture of ice and saturated sodium bicarbonate and stirred for 1 hr. The insoluble gum was extracted into chloroform and the chloroform solution was washed with saturated sodium bicarbonate and water, dried, and evaporated. The gum was dissolved in 15 ml of warm absolute ethanol, treated with 10 ml of 10% ethanolic picric acid,[24] and heated at reflux for 20 min, whereupon crystallization began. The flask was kept at room temperature for 2 hr, and the yellow crystals were filtered off and thoroughly washed with ethanol, giving 0.55 g (32%) of the picrate of **2**, mp 225–227° dec. Recrystallization of a portion of this from methanol gave fine needles: mp 229–230° dec; ir (KBr) 1722 (benzoate C=O), 1548 (NO_2), 1360 (*gem*-dimethyl), 1316 (NO_2), and 712 cm^{-1} (monosubstituted phenyl).

Anal. Calcd for $C_{34}H_{30}N_8O_{14}$: C, 52.72; H, 3.88; N, 14.48. Found: C, 53.48; H, 3.98; N, 14.75.

The picrate was dissolved in 80% aqueous acetone and treated with Bio-Rad AG 1-X8 (CO_3^{-2}) resin to remove the picrate ion.[25] The resin was removed by filtration and the solvents were evaporated off. Crystallization of **2** was not achieved, but a hard foam was obtained by evaporation of absolute ethanol and dried at 64° under high vacuum. The product appeared homogeneous on tlc plates,[26] R_f 0.74 in 1:1 ethyl acetate–methanol: ir (film, NaCl) 1720 (benzoate C=O), 1370 (*gem*-dimethyl), and 710 cm^{-1} (monosubstituted phenyl).

Anal. Calcd for $C_{28}H_{27}N_5O_7$: C, 61.64; H, 4.99; N, 12.84. Found: C, 61.55; H, 5.10; N, 12.30.

9-(2,3-*O*-Isopropylidene-5,6-di-*O*-methanesulfonyl-α-D-mannofuranosyl)adenine (3).—A solution of 3.03 g (9 mmol) of **1** in 150 ml of dry pyridine was chilled in an ice bath and 4.3 ml of methanesulfonyl chloride was added dropwise. The mixture was stirred for 1 hr, kept at room temperature for 48 hr, and poured into an ice-saturated sodium bicarbonate mixture. The product was extracted with chloroform, washed with saturated sodium bicarbonate and water, and dried. Evaporation left a hard gum: 2.9 g (64.5%); ir (film, NaCl) 1360, 1333 sh (*gem*-dimethyl and sulfonate) and 1174 cm^{-1} (sulfonate). Tlc revealed that there were two trace components contaminating the main substance, which had R_f 0.53 in 1:1 ethyl acetate–methanol. Preparations such as this were found to be sufficiently pure for the reactions described below.

9-β-L-Gulofuranosyladenine (4).—To a solution of **3** (2.9 g, 5.8 mmol) in 290 ml of *N*,*N*-dimethylformamide was added 12.8 g of sodium benzoate and the mixture was stirred and heated at reflux for 24 hr.[7,13] During the first few minutes at reflux the reaction mixture became nearly black. It was cooled to room temperature, 150 ml of water was added, and the solution was extracted several times with chloroform (total volume, 400 ml). The organic layer was washed with saturated sodium bicarbonate (two 200-ml portions) and water (200 ml), dried, and evaporated to yield a thick, dark brown syrup weighing 2.6 g. Tlc in 1:1 methylene chloride–ethyl acetate revealed a major spot at R_f 0.17 and trace components at R_f 0.24 and 0.03. A similar pattern occurred on tlc in 9:1 ethyl acetate–methanol, R_f 0.37 for the major component and R_f 0.57 and 0.28 for the minor components.

The syrup was treated with 70 ml of 0.25 *N* methanolic sodium methoxide at room temperature for 19 hr and brought to neutrality with Dowex 50 (H) resin. The solvent was evaporated off and the residue was dissolved in 214 ml of hot 25% aqueous acetic acid and kept on a steam bath for 3.5 hr. Evaporation to dryness was followed by several coevaporations with absolute ethanol and then the brown residue was dissolved in hot water and decolorized with Darco G-60. The water was evaporated off and the residue was dissolved in 10 ml of 60% aqueous methanol and placed on top of a column (30 × 2 cm) of Bio-Rad AG 1-X2 (OH, 200–400 mesh)[10] which had been packed in the same solvent. Fractions were collected which were 10 ml in volume and tubes 175–250, the only tubes containing substantial uv absorption, were collected and the contents pooled. The solvents were removed by evaporation and **4** was crystallized from ethanol–water to give 211 mg (12%): mp 231–233°; $[\alpha]^{26}D$ +56.3° (*c* 1.13, 1 *N* HCl). Admixture with an authentic sample[2] of **4** gave no depression of melting point. The ir spectra and mobilities on paper chromatograms in two solvent systems were identical.

9-(5,6-Dideoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hex-5-enofuranosyl)adenine (5).—Dimesylate **3** was prepared from 3 g of **1** and was dissolved in 50 ml of acetone. Sodium iodide (10.5 g) was added and the solution was placed in a stainless steel bomb and kept at 100° for 16 hr.[20] The bomb was cooled to room temperature and the contents were diluted with chloroform. The organic solution was washed with water, three times with a mixture of sodium thiosulfate and aqueous sodium bicarbonate, once more with water, and dried. The solvent was evaporated, leaving a light brown syrup which solidified after an hour. Crystallization from methanol over several days gave pink-colored crystals. These were dissolved in chloroform, silicic acid[27] was added, and the solvent was removed by evaporation. The silicic acid was placed on top of a column (26 × 3.5 cm) of silicic acid[27] which had been packed in benzene and the column was washed with 600 ml of ethyl acetate. The product was eluted with 1:1 ethyl acetate–methanol. The first 400 ml was discarded and the next 300 ml contained **5**. Evaporation of the solvents and crystallization of **5** as hemispherical colonies from ethyl acetate–petroleum ether (bp 60–110°) gave 1.3 g (48%) in several crops; mp 180.5–181° with a change in form to needles above 165°; $[\alpha]^{24}D$ −76° (*c* 1.2, $CHCl_3$); ir (KBr) 3080 ($CH=CH_2$), 1730, 1671, 1598, 1565 (C=C and purine ring), 1372 (*gem*-dimethyl), 995 cm^{-1} ($CH=CH_2$); nmr ($CDCl_3$) τ 3.96 (s, 1, H-1′), 4–5.3 (m, $CH=CH_2$ and unresolved H-2′, H-3′, H-4′), 8.42 and 8.58 (both s, 6, *gem*-dimethyl); tlc in 95:5 ethyl acetate–methanol, R_f 0.30.

Anal. Calcd for $C_{14}H_{17}N_5O_3$: C, 55.47; H, 5.65; N, 23.09. Found: C, 55.39; H, 5.61; N, 23.02.

9-(5,6-Dideoxy-α-D-*lyxo*-hex-5-enofuranosyl)adenine (6).—A solution of 317 mg of **5** in 18 ml of 0.1 *N* sulfuric acid was kept at room temperature for 5 days.[6] It was neutralized with barium carbonate, heated at 90° for 1 hr, filtered by suction through a pad of Celite, and evaporated to a small volume. Two days later the crystals were filtered off. This turned out to be a mixture of spherical colonies (**6**) and tiny needles (**5**). The large spheres were easily separated with a tweezers to give 168 mg (61%), mp 237–240° dec. Two recrystallizations from water gave 116 mg: mp 245–246.5° dec; $[\alpha]^{26}D$ +53° (*c* 0.92, 1 *N* HCl); uv max (H_2O) 259 mμ (ε 15,100); Rad[28] 1.49 in 5% aqueous disodium hydrogen phosphate; Rad 1.09 in 86:14 *n*-butyl alcohol–water; tlc in 95:5 ethyl acetate–methanol, R_f 0.10.

Anal. Calcd for $C_{11}H_{13}N_5O_3$: C, 50.18; H, 4.98; N, 26.60. Found: C, 50.47; H, 4.80; N, 26.87.

Recrystallization of the tiny needles obtained above and comparison against a sample of **5** (mixture melting point, ir, tlc) verified its identity.

9-(5-Deoxy-2,3-*O*-isopropylidene-α-D-*lyxo*-hexofuranosyl)adenine (7).—Compound **5** (415 mg) was dissolved in 35 ml of tetrahydrofuran, 268 mg of sodium borohydride was added, and the mixture was stirred in a nitrogen atmosphere.[22b] A solution

(23) Elementary analyses were performed by the Spang Microanalytical Laboratory, Ann Arbor, Mich., or by the Baron Consulting Co., Orange, Conn. Melting points were determined on a Kofler hot stage and correspond to corrected values. Infrared spectra were recorded on a Perkin-Elmer Model 21 spectrophotometer and ultraviolet spectra on a Beckman DK-2 spectrophotometer. Molar extinction coefficients were checked on a Beckman DU equipped with a Gilford digital readout attachment. Optical rotations were obtained on a Rudolph polarimeter and nmr spectra were recorded on a Perkin-Elmer 20A by Dr. Harry Agahigian of the Baron Consulting Co. Evaporations were performed *in vacuo* in a rotary evaporator at a bath temperature of 40–45°. All moist organic solutions were dried over anhydrous magnesium sulfate. Spots on tlc plates or on paper chromatograms were visualized with a Mineralight lamp which produced ultraviolet radiation at 254 mμ.

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(26) Tlc was performed on silica gel HF plates (E. Merck A.G., Darmstadt) of 0.25 mm thickness which were prepared with Desaga equipment.

(27) Mallinckrodt 100 mesh; dried at 150° for 16 hr prior to use.

(28) Paper chromatograms were run by a descending technique on Whatman No. 1 paper. The expression Rad refers to the ratio of the distance the nucleoside migrated to the distance which adenine migrated.

of boron trifluoride ethyl etherate [1.32 g, freshly distilled at 44° (9 mm)] in 10 ml of tetrahydrofuran was added dropwise over a period of 15 min. After 2 hr, water was carefully added to destroy excess reagent and the solution was treated with 30% hydrogen peroxide while maintaining the pH at 9 with 3 *N* sodium hydroxide. This was stirred for 1.5 hr, the solvents were evaporated, and the residue was extracted with chloroform which was washed with water and dried. Evaporation left a syrup which crystallized slowly over the next 4 months. The syrup–crystal mixture was triturated with methanol to give 22 mg (5%) of crystals which were recrystallized from methanol. Tiny, colorless prisms weighing 6 mg were obtained: mp 220–220.5°; ir (KBr) 3320 (NH, OH), 1680, 1600, 1572 ($NH_2C{=}N$, purine ring), 1384–1364 (multiplet, *gem*-dimethyl), 1092, 1064 (COC, CO).

Anal. Calcd for $C_{14}H_{19}N_5O_4$: C, 52.33; H, 5.96; N, 21.80. Found: C, 52.04; H, 5.73; N, 21.90.

Enol Mesylate (8).—A mixture of 5.1 g of **3**, Dowex 1-X10 (acetate, 200–400 mesh) resin, and 200 ml of acetic anhydride was heated at reflux for 8 hr. The resin was removed by filtration and the filtrate was evaporated to a brown foam which was coevaporated five times with a mixture of ethanol and toluene. The foam (5.4 g) was dissolved in methanol and treated with 13 ml of 1 *N* methanolic sodium methoxide at reflux for 1 hr. After neutralization with Dowex 50 (H) resin and a Darco G-60 treatment, the methanol was removed by evaporation, leaving a tan foam which was dissolved in 0.1 *N* sulfuric acid and kept at room temperature for 6 days. The neutralization step was carried out as described above for **6**. The aqueous solution was washed with chloroform and evaporated, and the residue was dissolved in a minimum amount of 30% aqueous methanol. This was applied to the top of a column of Bio-Rad AG 1-X2 (OH, 200–400 mesh)[10] (30 × 2.3 cm), the column was eluted with the same solvent, and 12 ml fractions were collected. Fractions 136–225 represented the only major uv-absorbing component. The contents of these tubes were pooled and evaporated to dryness and crystallization was achieved from ethanol–water (644 mg, 16%). Two recrystallizations yielded 380 mg of feathery platelets: mp 160°; $[\alpha]^{27}D$ +143° (*c* 0.71, 1 *N* HCl); ir (KBr) 1702, 1643, 1618, 1575 ($CH{=}CH_2$ and purine ring), 1360, 1175 (sulfonate), and 885 cm^{-1} (*gem*-vinyl); Rad 1.58 in 5% aqueous disodium hydrogen phosphate and 0.57 in 86:14 *n*-butyl alcohol–water.

Anal. Calcd for $C_{12}H_{15}N_5O_6S$: C, 40.33; H, 4.23; N, 19.60; S, 8.97. Found: C, 40.31; H, 4.21; N, 19.56; S, 8.99.

Registry No.—**1**, 32659-04-4; **2**, 32659-05-5; **2** (picrate), 32829-93-9; **3**, 32659-06-6; **4**, 10279-88-6; **5**, 32659-07-7; **6**, 32829-95-1; **7**, 32659-08-8; **8**, 32829-96-2.

Interconversions of Hexofuranosyl Nucleosides. II. Preparation of 9-α-L-Idofuranosyladenine and 5′,6′-Unsaturated Derivatives[1]

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9-(2,3-Di-*O*-acetyl-5,6-di-*O*-*p*-toluenesulfonyl-β-D-glucofuranosyl)adenine (**3**) was prepared from 1,2-*O*-isopropylidene-5,6-di-*O*-*p*-toluenesulfonyl-α-D-glucofuranose (**1**) in a four-step synthesis. Inversion of configuration at C-5′ was not possible without extensive degradation and cyclonucleoside (**4**) formation. 9-(2,3-Di-*O*-acetyl-6-*O*-benzoyl-5-*p*-toluenesulfonyl-β-D-glucofuranosyl)adenine successfully underwent inversion to the L-idose nucleoside (**8**) but in too small of a yield to be of preparative value. Therefore, 9-α-L-idofuranosyladenine (**8**) was synthesized starting from 3,6-di-*O*-acetyl-5-*O*-benzoyl-1,2-*O*-isopropylidene-β-L-idofuranose (**9**) and proceeded by condensation of the acetate **10**, prepared by acetolysis of **9**, with 6-benzamidochloromercuripurine and titanium tetrachloride. An 5′,6′-olefinic blocked nucleoside **12** was prepared from **3** in hot sodium iodide-acetone or by a pathway starting from the known unsaturated sugar derivative, 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose. This derivative was converted in two steps to an acetate **15** which was coupled to adenine by the titanium tetrachloride method. Removal of the blocking groups of **12** gave 9-(5,6-dideoxy-β-D-*xylo*-hex-5-enofuranosyl)adenine, a noncrystalline, unstable compound.

The aims of the present investigation were set forth in the previous paper of this series.[2] 9-α-L-Idofuranosyladenine (**8**) appeared to be an interesting compound to prepare because of its structural relationship to 9-β-D-xylofuranosyladenine, a compound of biological interest because of its ability to inhibit growth of some forms of animal tumors.[3] It was of interest to see if epimerization of C-5′ of a preformed D-glucofuranosyl nucleoside derivative could be effected, thereby giving the nucleoside with the L-ido configuration. To do this it was necessary to prepare a derivative of 9-β-D-glucofuranosyladenine which had a group at C-5′ that could easily be displaced by an SN2 reaction or assisted by neighboring group participation. 9-(2,3-Di-*O*-acetyl-5,6-di-*O*-*p*-toluenesulfonyl-β-D-glucofuranosyl)adenine (**3**) seemed like such a compound.

The preparation of **3** started from 1,2-*O*-isopropylidene-5,6-di-*O*-*p*-toluenesulfonyl-α-D-glucofuranose[4] (**1**) and the route used is illustrated in Scheme I. Acetolysis of **1** converted it to tri-*O*-acetate **2**, which was immediately coupled, without further purification, with 6-benzamidochloromercuripurine using the titanium tetrachloride method of nucleoside synthesis.[5] The product of this condensation was treated with picric acid,[6] and a crystalline picrate of **3** was obtained in excellent yield. Removal of the picrate ion with an ion exchange resin[7] gave **3**.

Buss, *et al.*,[8] were able to convert 3-*O*-acetyl-1,2-*O*-isopropylidene-5,6-di-*O*-toluenesulfonyl-α-D-glucofuranose to 3-*O*-acetyl-5,6-di-*O*-benzoyl-1,2-*O*-isopropylidene-β-L-idofuranose in a yield of 50% using the hot sodium benzoate–dimethylformamide system first de-

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