on paper electrophoresis at pH 5.7. Heating V in 6 *N* HCl at 110° for 18 hr gave 1% III and 99% IV, the identity of which was confirmed by paper chromatography and electrophoresis at pH 5.7.

Registry No.—DL-Phenylalanine, 150-30-1; L-phenylalanine, 63-91-2; Ia, 16055-11-1; N-acetyl derivative of Ia, 16055-13-3; Ib, 16055-12-2; copper chelate of Ib, 16165-21-2; N-acetyl derivative of Ib, 16055-14-4; III, 16055-15-5; hydrochloride of IV, 16055-16-6; V, 16109-66-3.

Acknowledgment.—The authors thank Miss Ann Washington for valuable assistance and Miss Audrey L. Hughes for experiments in the initial stages of this work. We are indebted to Dr. George B. Brown and staff for some of the nmr spectra and to Dr. Anna Fang for help in interpreting spectra.

Preparation of Nucleosides *via* Isopropylidene Sugar Derivatives. III. Synthesis of 9-β-D-Gulofuranosyladenine and 9-α-L-Lyxofuranosyladenine[1]

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2,3:5,6-Di-*O*-isopropylidenegulonolactone was reduced to the corresponding gulofuranose derivative with sodium borohydride. A halogenose was prepared with thionyl chloride and condensed with 6-benzamidochloromercuripurine. Removal of all blocking groups yielded 9-β-D-gulofuranosyladenine. An intermediate in the reaction sequence, 9-(2,3-*O*-isopropylidene-β-D-gulofuranosyl)adenine was treated with sodium periodate and sodium borohydride to give, after removal of the isopropylidene group, 9-α-L-lyxofuranosyladenine. Assignment of anomeric configuration to this compound was made on the basis that it was shown to be the enantiomorph of 9-α-D-lyxofuranosyladenine, the structure of which had been demonstrated previously. Knowledge of the anomeric configuration of the α-L- and α-D-pentofuranosyl nucleosides enabled assignment of anomeric configuration to the hexofuranosyl nucleosides from which they were derived, 9-β-D-gulofuranosyladenine and 9-α-D-mannofuranosyladenine, respectively.

Because of potentially interesting biological properties of the products the preparation of hexofuranosyl nucleosides has received some attention in the last few years.[2] One such nucleoside, 9-β-D-gulofuranosyladenine (**6**), was first synthesized by the reduction of tetra-*O*-benzoyl-D-gulono-γ-lactone to tetra-*O*-benzoyl-D-gulofuranose with disiamylborane[3] followed by preparation of the halogenose, which was coupled with 6-benzamidochloromercuripurine.[4] Removal of the blocking groups gave the nucleoside in small yield (6%).

In a recent communication[5] the feasibility of using 2,3:5,6-di-*O*-isopropylidene hexofuranosyl halides for the preparation of hexofuranosyl nucleosides was demonstrated. In that case, 2,3:5,6-di-*O*-isopropylidene mannofuranosyl chloride was condensed with 6-benzamidochloromercuripurine, and the blocking groups were removed to give 9-α-D-mannofuranosyladenine in good yield. Application of this pathway with other hexoses, though possible, is not readily achieved because the acid-catalyzed acetonation of hexoses gives mixtures of isopropylidene derivatives, except in the case of mannose. This would lead to a great deal of waste of some difficulty obtainable rare sugars. However, in a recent report[6] it was demonstrated that 2,3:5,6-di-*O*-isopropylidene-D-gulono-γ-lactone could be reduced to the corresponding aldose. That report led to the application of the pathway for the preparation of the title compounds.

2,3:5,6-Di-*O*-isopropylidene-D-gulono-γ-lactone (**1**) was subjected to the sodium borohydride–ethyl ether–acetic acid medium described by Hulyalkar,[6] but it was found that a longer reaction time than that reported gave better results. When a reaction time of 20–24 hr was used, a yield of about 70% of 2,3:5,6-di-*O*-isopropylidene-D-gulofuranose (**2**) was consistently obtained. The anomeric hydroxyl group was exchanged for a chloro by reaction with thionyl chloride in pyridine.[7] A new halogenose, 2,3:5,6-di-*O*-isopropylidene-D-gulofuranosyl chloride (**3**), was obtained as an analytically pure oil by vacuum distillation. This oil (**3**) was coupled with 6-benzamidochloromercuripurine in refluxing xylene.[8] The isopropylidene group blocking positions 5′ and 6′ was removed with 70% aqueous acetic acid at 50°, and the *N*-benzoyl group was removed with sodium methoxide. The product, 9-(2,3-*O*-isopropylidene-β-D-gulofuranosyl)adenine (**5**), was obtained as irregular white crystals in good yield. The structure of **5** was concluded from the elementary analysis; the presence of the isopropylidene group was confirmed by the infrared peak at 1375 cm^{-1} (*gem*-dimethyl). The position of the isopropylidene group was verified by the formation of formaldehyde after periodate cleavage.

(1) (a) For parts I and II of this series, see ref 5 and 11. (b) Supported in part by Grant T-442 from the American Cancer Society and by Grant CA-07960 from the U. S. Public Health Service.

(2) See ref 4 and 5 for references to papers dealing with this subject.

(3) P. Kohn, R. H. Samaritano, and L. M. Lerner, *J. Amer. Chem. Soc.*, **87**, 5475 (1965).

(4) P. Kohn, R. H. Samaritano, and L. M. Lerner, *J. Org. Chem.*, **31**, 1503 (1966).

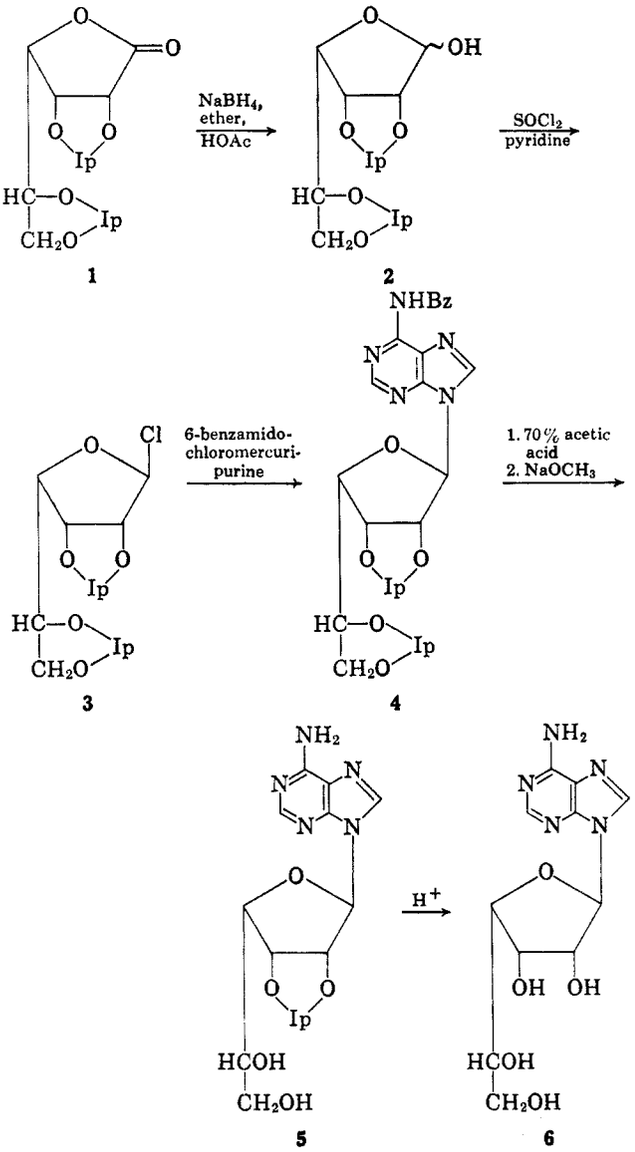
(5) L. M. Lerner and P. Kohn, *ibid.*, **31**, 339 (1966).

(6) R. K. Hulyalkar, *Can. J. Chem.*, **44**, 1594 (1966).

(7) K. Freudenberg, A. Wolf, E. Knopf, and S. H. Zaheer, *Chem. Ber.* **61**, 1743 (1928).

(8) J. Davoll and B. A. Lowy, *J. Amer. Chem. Soc.*, **73**, 1650 (1951).

SCHEME I

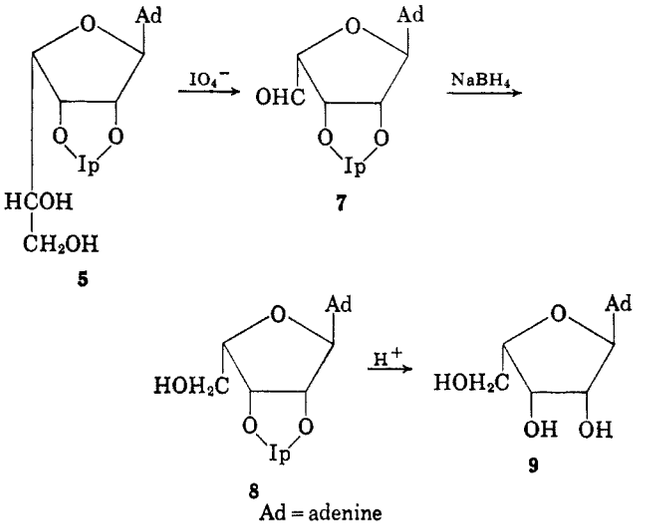


The isopropylidene group was removed from **5** using 0.1 *N* aqueous sulfuric acid at room temperature. This reagent was used by Todd and coworkers[9] to remove the isopropylidene group from nucleotides, but best results in our case was obtained by using a reaction time of 5 days rather than 2 days as used by Todd. The yield of **6** was about 50%, with virtually no cleavage of the glycosidic bond, a distinct advantage over the use of a variety of concentrations of acetic acid, which does cause cleavage of the nucleoside and which results in yields of products ranging from 35–50% depending on the concentration of the acid and the time and temperature of the reaction. With sulfuric acid the principal substance in the mother liquor is unreacted monoisopropylidene derivative (**5**), which can be subjected to acid hydrolysis again.

The final product (**6**) was identical in every respect with the material reported earlier.[4] The complete pathway is shown in Scheme I.

Previously, the anomeric configuration of **6** was assumed to be β, concluded from application of the *trans* rule[10] and by comparison of the molecular rotation of **6** with those of glycofuranosides and glycosylamines of known anomeric configuration. The availability of 9-(2,3-*O*-isopropylidene-D-gulofuranosyl)-adenine (**5**) made it possible to prove the anomeric configuration unequivocally. The same reaction sequence used previously[11] in the case of 9-(2,3-*O*-isopropylidene-α-D-mannofuranosyl)adenine was applied for this purpose and is shown in Scheme II.

SCHEME II



Oxidation of **5** with sodium periodate followed by reduction with sodium borohydride yielded compound **8** (see Scheme II). This compound had a melting point identical with that of 9-(2,3-*O*-isopropylidene-α-D-lyxofuranosyl)adenine (**10**)[11] and had a specific rotation of equal value but opposite in sign.[12] Compound **8**, therefore, is shown to be the enantiomorph of **10** and must be 9-(2,3-*O*-isopropylidene-α-L-lyxofuranosyl)adenine. Furthermore, when the isopropylidene group was removed from **8**, compound **9** was obtained. This substance had a melting point identical with that of α-D-lyxofuranosyladenine (**11**)[11] and had a specific rotation of equal value but opposite in sign. These data are summarized in Table I.

TABLE I

PHYSICAL CONSTANTS OF D- AND L-LYXOFURANOSYLADENINE NUCLEOSIDES AND THEIR MONOISOPROPYLIDENE DERIVATIVES

	9-α-Lyxofuranosyladenine		9-(2,3-*O*-Isopropylidene-α-lyxofuranosyl)adenine	
	D[a]	L	D[a]	L
Mp, °C	248–250	246–249	182–183	182–184
[α]D, deg.	+93.8	−96.6	−28	+29.1
R_{Ad}[b]	1.31	1.33	0.84	0.85

[a] Cited in ref 11. [b] Mobility compared with that of adenine using 5% aqueous disodium hydrogen phosphate as developing agent on silica gel thin layer chromatogram plates.

(9) J. Baddiley and A. R. Todd, *J. Chem. Soc.*, 648 (1947); N. Anand and A. R. Todd, *ibid.*, 1867 (1951).

(10) 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.

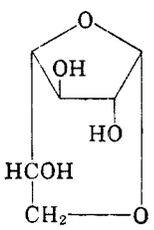
(11) P. Kohn, L. M. Lerner, and B. D. Kohn, *J. Org. Chem.*, **32**, 4076 (1967).

(12) It should be noted that 9-(2,3-*O*-isopropylidene-α-D-lyxofuranosyl)-adenine[11] has a more negative specific rotation than does the corresponding β isomer[13] and therefore does not follow Hudson's rules of isorotation. It can be assumed, therefore, that the α-L enantiomer reported here likewise fails to follow the isorotation rules.

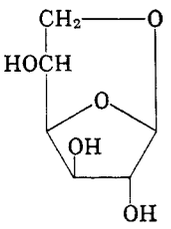
(13) E. J. Reist, D. F. Calkins, and L. Goodman, *ibid.*, **32**, 169 (1967).

That **11** was the α-D form had been demonstrated[11] by preparation of 2-*O*-[1-(9-adenyl)-2-(hydroxy)ethyl]-glycerol and comparison of its specific rotation with that of its enantiomorph prepared from adenosine, a nucleoside of known β configuration. Compound **9**, therefore, is shown to be the enantiomorph of **11**, and **9** must be α-L-lyxofuranosyladenine. The present findings also confirm the assignment of anomeric configuration to 9-β-D-gulofuranosyladenine (**6**),[4] since, if **6** had an α configuration, the lyxofuranosyladenine obtained would have been the β-L form and would have been the enantiomorph of the β-D compound prepared by Reist, *et al.*,[13] rather than of the α-D compound previously prepared in these laboratories.[11]

The synthesis of 9-α-D-mannofuranosyladenine has been shown to proceed *via* an SN1 reaction mechanism.[5,11,14] The anomeric configuration of the halogenose (α) was retained and an α-nucleoside product was produced. The data and results of the work reported here suggest an analogous situation. The large negative rotation of the halogenose (**3**) suggests a β configuration, and the nucleoside product (**6**) also has a β configuration. It is apparent that the configuration of the chloride in the halogenoses is *trans* to the hydroxyl on C-2 as a result of the bulky isopropylidene groups at C-2,3 and C-5,6 which cause steric hindrance on the *cis* side of the furanose ring. The proximity of the hydroxyl group at C-6 to the hydroxyl group at C-1 has been demonstrated by the formation of 1,6-anhydro-α-D-galactofuranose (**12**), prepared by the pyrolysis of α-D-galactose,[15] and by the formation of 1,6-anhydro-β-D-glucofuranose (**13**), prepared by the pyrolysis of



12



13

starch.[16] Compound **12** approaches the case of D-gulose, except for the configuration of the hydroxyl group at C-3, and approaches the case of D-mannose, except for the configuration at C-2. It is therefore to be expected that 2,3:5,6-diisopropylidene-D-gulofuranosyl chloride (**3**) would be more stable in the β configuration, owing to crowding on the α side. In the case of 2,3:5,6-diisopropylidene-D-mannosyl chloride, the opposite would be expected to be true, and the halide would be expected to be more stable in the α configuration. During condensation of the halogenose with the nucleophilic nitrogenous base, a carbonium ion is formed at C-1 with the departure of the chloride. The nucleophile enter son the less hindered side, resulting in retention of configuration.

The synthetic approach to the preparation of nucleosides described here should be applicable to other hexono-γ-lactones. In the case of allono- and talono-γ-lactones, which possess vicinal, *cis* hydroxyl groups at C-2,3 it is to be expected that glycosyl halides and nucleosides with structural relationships analogous to gulose and mannose, respectively, would be obtained. Investigations of these compounds are currently in progress. Furthermore, because of the successful reduction of acylated hexono-γ-lactones to acylated hexofuranoses with disiamylborane in high yield,[3] the application of this reagent to the reduction of diisopropylidene hexonolactones is being investigated as a possible means of improving the yield of furanose over that obtained with sodium borohydride.[6]

Experimental Section[17]

2,3:5,6-Di-*O*-isopropylidene-D-gulono-γ-lactone (1).—D-Gulono-γ-lactone (30 g) was suspended in 1500 ml of stirring acetone which contained 0.2% sulfuric acid. The contents of the flask were protected from moisture and stirred for 18 hr at room temperature. Concentrated aqueous ammonia (sp gr 0.88, 7.6 ml) was used to neutralize the acid, and the ammonium sulfate which precipitated was removed by filtration. The acetone was removed by evaporation, and the residue was triturated with chloroform. The mixture was filtered to separate 2,3-*O*-isopropylidene-D-gulono-γ-lactone, and the chloroform solution was concentrated to yield still more of this by-product. A total of 9 g of 2,3-*O*-isopropylidene-D-gulono-γ-lactone was recovered in this manner. The chloroform filtrate was washed once with water and dried. The solution was concentrated to a small volume, and petroleum ether (bp 30–60°) was added to near turbidity. A yield of 20.9 g of product (**2**) was obtained in three crops, mp 150–151° (oil bath, uncorrected), $[\alpha]^{25}D$ −67.8° (*c* 4.16, $CHCl_3$), lit.[18] mp 153–153.5°. The ir spectrum revealed no hydroxyl group and had a strong γ-lactone peak at 1790 cm^{-1}. The *gem*-dimethyl group was easily recognized at 1375 cm^{-1}.

2,3:5,6-Di-*O*-isopropylidene-D-gulofuranose (2).[6]—Twenty grams of **1** was dissolved in 3 l. of anhydrous ethyl ether. While the solution was vigorously stirred, 20 g of sodium borohydride was added, and a mixture of 60 ml of acetic acid in 500 ml of ethyl ether was added dropwise. The reaction mixture was stirred for 22 hr at room temperature. Acetone (200 ml) was added and after 1 hr, 450 ml of 2 *N* aqueous sodium hydroxide solution was added very slowly (*caution!*). The ether layer was removed, washed once with saturated aqueous sodium chloride solution, and dried. The bulk of the ether was removed by distillation, and the remaining 400 ml was evaporated in a rotary evaporator. A clear, slightly yellow syrup was obtained. The product was crystallized from ethyl ether–petroleum ether (1:1) in an open flask overnight. Large, long, rectangular, plate-like crystals were obtained in two crops, 14.4 g (71.5%), mp 114–115°, $[\alpha]^{25}D$ −2.6° (*c* 4.12, $CHCl_3$), lit.[6] mp 114–115°. This material gave a postive Benedict's test after removal of the isopropylidene groups with dilute sulfuric acid. The ir spectrum showed a prominent hydroxyl peak at 3360 cm^{-1}, and the lactone peak at 1790 cm^{-1} had disappeared.

2,3:5,6-Di-*O*-isopropylidene-D-gulofuranosyl Chloride (3).—The method of preparation used was that used previously for the corresponding mannose derivative.[5,7] The product was a viscous orange oil which was distilled *in vacuo*, bp 127° (2.6 mm). From 8 g of **2**, a clear, straw-colored, viscous oil weighing 4.4 g (51%) was obtained: $[\alpha]^{25}D$ −40.2° (*c* 9.61, $CHCl_3$). This substance gave an instantaneous positive alcoholic silver nitrate test.

(14) J. B. Lee and T. J. Nolan, *Tetrahedron*, **23**, 2789 (1967).

(15) B. H. Alexander, R. S. Dimler, and C. L. Mehltretter, *J. Amer. Chem. Soc.*, **73**, 4658 (1951).

(16) R. J. Dimler, H. A. Davis, and G. E. Hilbert, *ibid.*, **68**, 1377 (1946).

(17) Elementary analyses were performed by the Spang Microanalytical Laboratory, Ann Arbor, Mich. Melting points were obtained on either a Kofler hot stage or a Fisher-Johns block and are corrected values. Optical rotations were determined on a Rudolph polarimeter, ir spectra on a Perkin-Elmer Model 21 spectrophotometer, and uv spectra on a Beckman DK-2 spectrophotometer. Evaporations were performed *in vacuo* on a rotary evaporator with a bath temperature of 40–45°. All moist solutions were dried over anhydrous magnesium sulfate. Chloroform used in these experiments was freed of ethanol by percolating through a column of activated alumina. Acetone was distilled from potassium permanganate and dried over calcium sulfate prior to use. Tlc refers to thin layer chromatography on silica gel HF plates (E. Merck, A. G. Darmstadt) using Desaga equipment. Spots were visualized with an uv lamp. The plates were sprayed with a solution of chromic acid and heated carefully in an open flame to detect non-uv-absorbing material.

(18) K. Iwadare, *Bull. Chem. Soc. Jap.*, **18**, 226 (1943).

An nmr spectrum of **3** revealed a singlet for the anomeric hydrogen at τ 3.85. This is consistent with a *trans* configuration[14] between H_1 and H_2, and it can be concluded that the chloro substituent was oriented in the β configuration.

Anal. Calcd for $C_{12}H_{19}ClO_5$: C, 51.70; H, 6.09; Cl, 12.72. Found: C, 51.78; H, 6.19; Cl, 12.84.

9-(2,3-*O*-Isopropylidene-β-D-gulofuranosyl)adenine (5).—6-Benzamidochloromercuripurine (7.15 g, 15.1 mmol) was coupled with 4.2 g (15.1 mmol) of the halogenose (**3**) in 400 ml of dry xylene.[8] After work-up[5] a foam weighing 8.4 g was obtained. This was subjected to acid hydrolysis in 150 ml of 70% aqueous acetic acid at 50° for 2.5 hr. The acetic acid was removed by evaporation, and absolnte ethanol was added and removed three times. Toluene was added and evaporated to remove a trace of acetic acid. The residue was dissolved in 135 ml of warm 0.15 *N* methanolic sodium methoxide solution, and the solution was refluxed for 1.5 hr. The solution was neutalized with glacial acetic acid,[19] and the solvent was evaporated. The syrup was dissolved in warm water, and the aqueous solution was decanted from an insoluble oil (methyl benzoate).[20] The water was evaporated using a few drops of nonyl alcohol to hold down foaming. The product (**5**) crystallized as clusters of hemispheres from a concentrated solution in methanol after it stood in an open flask overnight. Two crops of a tan-colored substance[21] were obtained, 3.33 g (71%). Two recrystallizations in the same manner gave the analytical sample as irregular white crystals, mp 154–160°. The crystallinity of this compond was verified under a polarizing microscope, $[\alpha]^{25}D$ −29.0° (*c* 1.37, H_2O). Uv and ir data were $\lambda_{max}^{H_2O}$ 259 mμ (ε 12,900); λ_{max}^{KBr} 3700–3150 (broad NH, OH), 1660–1612, 1590 (NH and purine ring), 1375 (*gem*-dimethyl), 1110–1048 cm^{-1} (plateau C–O–C, C–O–H).

A formaldehyde determination with dimedone reagent,[22] after treatment of **5** with excess periodate, yielded 0.80 mol of HCHO/mol of nucleoside.

Anal. Calcd for $C_{14}H_{19}N_5O_5$: C, 49.85; H, 5.68; N, 20.76. Found: C, 49.61; H, 5.70; N, 20.64.

(19) More recently it has been found to be a better practice to remove sodium ion with an acid resin (IRC 50). Crystallization of **5** from concentrated methanol is made difficult by cocrystallization of small amounts of sodium acetate when acetic acid is used in the neutralization step.

(20) When attempts were made to partition the residue between water and chloroform as previously described for the case of the mannosyl nucleoside,[5] an emulsion formed which was impossible to break.

(21) This contained a small amount of sodium acetate which was apparent from an uv spectrum and an ash test. See ref 19.

(22) J. R. Dyer, *Methods Biochem. Analy.*, **3**, 111 (1956).

9-β-D-Gulofuranosyladenine (6).—To 100 ml of 0.1 *N* sulfuric acid solution was added 400 mg of **5**, and the mixture was swirled until dissolution occurred.[9] The flask was stored at room temperature for 5 days after which 1 equiv of barium hydroxide was added, and the mixture was stirred for 1 hr. Barium sulfate was removed by filtration through a pad of Celite on a sintered-glass funnel using light suction. The filtrate was evaporated to dryness and the product (**6**) was crystallized from ethanol–water in two crops to yield 180 mg (51%) of **6**. Recrystallization from water gave light feathery crystals, mp 227.5–228.5°. Admixture with an authentic sample[4] of 9-β-D-gulofuranosyladenine gave no depression of the melting point. The mobilities of **6** and the authentic sample were identical on both tlc and paper chromatography using 1-butanol–water (86:14) and 5% aqueous disodium hydrogen phosphate as solvents. The ir spectra were identical: $\lambda_{max}^{H_2O}$ 259 mμ (ε 14,300), lit.[4] $\lambda_{max}^{H_2O}$ 259 mμ (ε 14,400).

When acetic acid solutions at 100° were used to remove the isopropylidene group the yields of **6** varied from 36% with 12% aqueous acetic acid to 50% for 20–25% aqueous acetic acid.

In a separate experiment the entire synthetic route was repeated from **2** without isolation of any intermediate compounds. The crude chloride (**3**) was used without distillation. The *N*-benzoyl group was removed with methanolic sodium methoxide and both isopropylidene groups were removed simultaneously by hydrolysis for 3 hr at 100° in 25% aqueous acetic acid. The yield of **6** from **2** was 11%.

9-(2,3-*O*-Isopropylidene-α-L-lyxofuranosyl)adenine (8).—The preparation of **8** was carried out exactly as described for the preparation of the corresponding D compound from 9-(2,3-*O*-isopropylidene-α-D-mannofuranosyl)adenine.[11] From 127 mg of **5**, there was obtained 30 mg of pure **8**, which began to shrink at 163–165°, mp 182–184°, $[\alpha]^{22}D$ +29.1° (*c* 0.5, pyridine).

Anal. Calcd for $C_{13}H_{17}N_5O_4$: C, 50.81; H, 5.58; N, 22.79. Found: C, 50.88; H, 5.48; N, 22.71.

9-α-L-Lyxofuranosyladenine (9).—The preparation of **9** from **8** was carried out in a manner exactly as described for the preparation of the corresponding D compound from 9-(2,3-*O*-isopropylidene-D-mannofuranosyl)adenine.[11] By this procedure, pure 9-α-L-lyxofuranosyladenine (**9**) was obtained: mp 246–249°, $[\alpha]^{23}D$ −96.6° (*c* 0.2, H_2O). Uv and ir data were $\lambda_{max}^{H_2O}$ 259 mμ (ε 13,350); λ_{max}^{KBr} 2.9–2.95 (OH, NH), 6.1, 6.25, 6.8 (NH and purine ring) 8.9, 9.4–9.6 μ (C–O–C, C–O–H).

Registry No.—**3**, 16136-64-4; **5**, 16136-60-0; **6**, 10279-87-5; **8**, 16136-62-2; **9**, 16136-63-3.

Intramolecular Displacement by Neighboring *O*-Thionobenzoate. Synthesis of 3′-Thioadenosine[1]

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Internal displacement of a tosylate by adjacent *trans*-*O*-thionobenzoate as a new neighboring group has been used to convert the 3,5-di-*O*-tosylate 2-*O*-thionobenzoate **3** of methyl α-D-xylofuranoside into 3-thio-D-ribofuranoside derivatives. Attachment of sulfur and configurational inversion at C-3 occurred upon treatment of **3** with sodium benzoate–dimethyl formamide (DMF), which also converted the 5-*O*-tosylate into 5-*O*-benzoate. The initial product was a dimer **8** of novel structure, elucidated by spectral studies; a crystalline analog of **8** was obtained in the analogous 5-deoxy series. Acid treatment of **8** afforded solely the monomeric thiol **6**, which was protected by benzoylation. Acetolysis afforded crystalline 1-*O*-acetyl-2,3,5-tri-*O*,*S*,*O*-benzoyl-3-thio-β-D-ribofuranoside (**5**). Condensation of **5** (*via* the chloro sugar obtained with titanium tetrachloride) with chloromercuri-6-benzamidopurine afforded the tetrabenzoate of 3′-thio-D-adenosine. Debenzoylation afforded 3′-thioadenosine (**11**), which was precipitated as a mercury salt and then liberated. The β configuration of **11** and location of the sulfur at C-3 were proved by nickel desulfurization to form 3′-deoxyadenosine.

The rationale for introducing a thiol function at C-3 of the D-ribose moiety of adenosine has been discussed in a recent communication[2] describing the synthesis of 3′-thioadenosine (**11**), and in earlier papers[3,4] from these laboratories describing some other studies toward this nucleoside. Structure–activity studies with the 3′-amino-3′-deoxy-D-ribo nucleoside

(1) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, U. S. Public Health Service, Contract No. PH-43-64-500. The opinions expressed are those of the authors and are not necessarily those of the Cancer Chemotherapy National Service Center.

(2) E. M. Acton, K. J. Ryan, and L. Goodman, *J. Amer. Chem. Soc.*, **89**, 467 (1967).

(3) B. R. Baker, K. Hewson, L. Goodman, and A. Benitez, *ibid.*, **80**, 6577 (1958).

(4) L. Goodman, A. Benitez, C. D. Anderson, and B. R. Baker, *ibid.*, **80**, 6582 (1958).