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ENANTIOMERIC FORMS OF 9-(5-DEOXY-β-*erythro*-PENT-4-ENOFURANOSYL)ADENINE AND A NEW PREPARATION OF 5-DEOXY-D-LYXOSE

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ABSTRACT

Methyl 5-deoxy-5-iodo-2,3-*O*-isopropylidene-β-D-ribofuranoside (**3**) was obtained in three steps from D-ribose. Exchange of the isopropylidene group for benzoate groups and acetolysis gave 1-*O*-acetyl-2,3-di-*O*-benzoyl-5-deoxy-5-iodo-D-ribofuranose which was coupled with 6-benzamidochloromercuripurine by the titanium tetrachloride method to afford the blocked nucleoside. Treatment with 1,5-diazabicyclo[5.4.0]undec-5-ene in *N,N*-dimethylformamide and removal of the blocking groups gave 9-(5-deoxy-β-D-*erythro*-pent-4-enofuranosyl)adenine (**9**). A similar route starting from methyl 5-deoxy-5-iodo-2,3-*O*-isopropylidene-α-D-lyxofuranoside (**14**) afforded the enantiomeric nucleoside, 9-(5-deoxy-β-L-*erythro*-pent-4-enofuranosyl)adenine (**20**). Methyl 2,3-*O*-isopropylidene-α-D-mannofuranoside was treated with sodium periodate and then with sodium borohydride to give methyl 2,3-*O*-isopropylidene-α-D-lyxofuranoside (**11**). Acid hydrolysis afforded D-lyxose. Tosylation of **11** gave methyl 2,3-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-lyxofuranoside (**12**) which was converted into **14** with sodium iodide in acetone. Reduction of **12** gave methyl 5-deoxy-2,3-*O*-isopropylidene-α-D-lyxofuranoside which was hydrolyzed to give 5-deoxy-D-lyxose.

INTRODUCTION

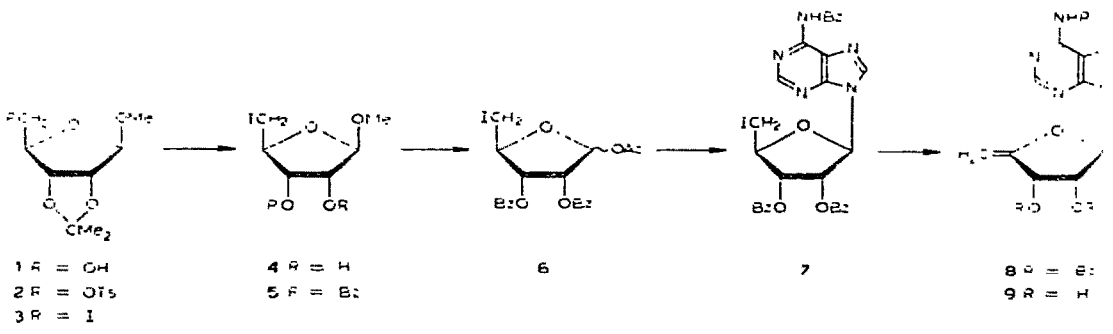
9-(5-Deoxy-β-D-*erythro*-pent-4-enofuranosyl)adenine (**9**), an analog of the antibiotic decoyinine (angustmycin A), was originally prepared from 2′,3′-*O*-ethoxymethylidene-5′-*O*-*p*-tolylsulfonylneadenosine by elimination of the sulfonate group under strong, basic conditions followed by hydrolysis of the blocking group under very mild acid conditions[1]. Another preparation of **9** has recently been published[2]. The 5′ position of 6,6-di-*N*-benzoyl-2′,3′-di-*O*-benzoyladenosine was iodinated and the unsaturated nucleoside prepared by elimination with either silver fluoride in pyridine or 1,5-diazabicyclo[4.3.0]non-5-ene in *N,N*-dimethylformamide. The use of benzoyl blocking groups enabled their removal under basic conditions, which was a distinct

advantage since the nucleoside **9** is extremely unstable under acidic conditions. Furthermore, protection of the 6-amino group clearly helped to prevent the formation of the cyclonucleoside[3], a reaction in which the 5'-methylene group forms a bond with N-3 of the purine ring. Another important innovation in the synthesis of decoyinine and some of its analogs is the use of preformed ω-terminal iodo sugar derivatives[2]. The required nucleoside is prepared only after the appropriate iodo sugar has been synthesized. Thus, blocking groups can be removed without formation of the cyclonucleoside or hydrolysis of the desired, unsaturated nucleoside. The publication of this latter procedure[2] motivated the publication of the present synthesis of **9** and its enantiomer **20**. The chemotherapeutic interest for these compounds has been ably reviewed[2].

This laboratory has been engaged in the synthesis of a number of nucleoside analogs having an exocyclic, unsaturated group[4], including compounds[5] related to either decoyinine or **9**. It was recognized early in this work that cyclonucleoside formation was a serious problem, either during the substitution at C-5' or during the elimination step. Since most of the nucleosides had to be prepared from their component sugars and bases, it seemed reasonable to devise a route in which the group to be eliminated was incorporated into the sugar prior to nucleoside synthesis. Since adenine was already blocked at N-6, no additional work had to be undertaken to selectively block this position in the nucleoside in order to prevent cyclonucleoside formation. Therefore, the substitution of a good leaving group at C-5, protection of N-6 of the purine ring, and the elimination reaction could be accomplished as part of a total synthesis starting from the component parts of the nucleoside. Based on this work, a new and simple synthesis of D-lyxose and 5-deoxy-D-lyxose from various sugar intermediates was devised.

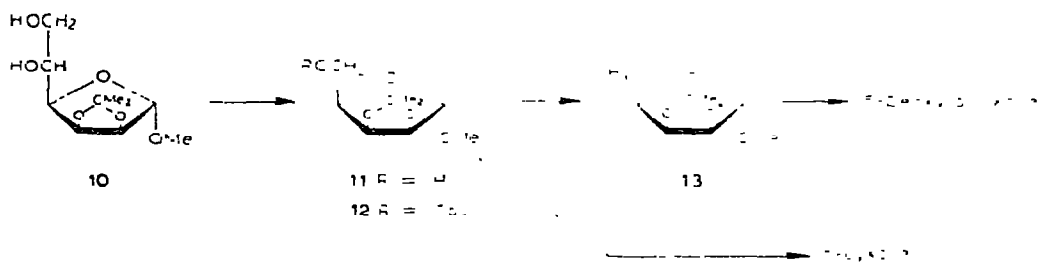
RESULTS AND DISCUSSION

In the synthesis of the nucleoside **9** from D-ribose, the procedure of Evans and Parrish[6] gave methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (**1**), which was used without purification. Treatment of **2** with sodium iodide in boiling 2-butanone gave methyl 5-deoxy-5-iodo-2,3-*O*-isopropylidene-β-D-ribofuranoside (**3**). The latter was



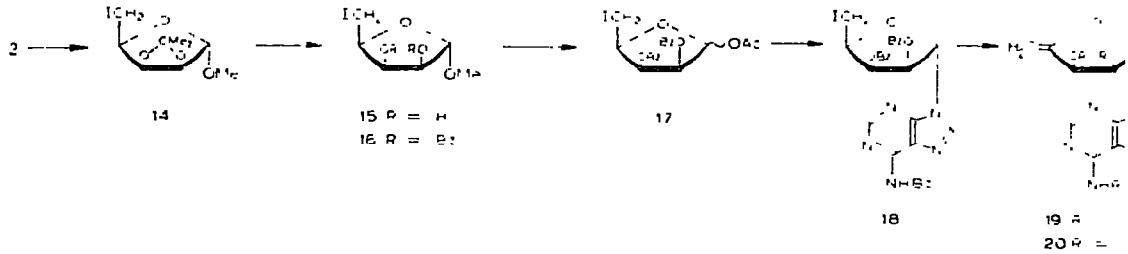
treated with 9:1 trifluoroacetic acid–water, which selectively removed the isopropylidene group to give crude **4**, which was benzoylated to form **5**. Examination of the n.m r. spectrum indicated that this crude product contained the methoxyl group in large proportion. This group was replaced with an acetoxy group by acetolysis to afford the anomeric mixture **6**. Coupling of **6** to the purine was achieved by the titanium tetrachloride method[7], and the blocked nucleoside **7** was partially purified on a column of silicic acid. Hydriodic acid was removed with 1,5-diazabicyclo[5.4.0]-undec-5-ene in *N*,*N*-dimethylformamide, to give **8** which was not purified, but immediately treated with ammonium hydroxide in methanol to remove the benzoyl groups. The nucleoside **9** crystallized after purification on an ion-exchange column[8], and showed physical properties identical with that reported in the earlier publications[1,2]. The values of the chemical shifts in the n.m.r. spectrum differed slightly, but the pattern was identical.

A similar pathway was used for the preparation of **20** starting from a D-lyxose derivative. Methyl 2,3-*O*-isopropylidene-α-D-mannofuranoside (**10**), prepared from D-mannose[6], was treated with sodium metaperiodate. Reduction of the aldehyde group with sodium borohydride gave methyl 2,3-*O*-isopropylidene-α-D-lyxofuranoside (**11**). D-Lyxose, was conveniently obtained by acid hydrolysis of the protective groups. Brimacombe *et al.*[9] have followed a similar route from D-mannose; the present method, however, obviates the prior synthesis of 2,3:5,6-di-*O*-isopropylidene-D-mannose, and the subsequent benzylation and selective acid hydrolysis. In the present case, **10** was prepared in a two-step procedure that does not require processing or isolation of the fully protected intermediate.



Tosylation of **11** afforded methyl 2,3-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-lyxofuranoside (**12**). The sulfonate group was reductively cleaved with sodium borohydride in dimethyl sulfoxide[10] to give methyl 5-deoxy-2,3-*O*-isopropylidene-α-D-lyxofuranoside (**13**), which was hydrolyzed into 5-deoxy-D-lyxose. The preceding steps represent a convenient preparation of this rare sugar. Previously, 5-deoxy-D-lyxose had been prepared by the Wohl degradation of 2,3,4,5-tetra-*O*-acetyl-D-fucononitrile[11].

Very little conversion of **12** into methyl 5-deoxy-5-iodo-2,3-*O*-isopropylidene-α-D-lyxofuranoside (**14**) occurred upon treatment with sodium iodide in boiling 2-butanone. At 115° in a sealed vessel for several days, however, **12** in acetone solution



was converted into **14**. The L forms of the methyl lyxosides **11–14** have been prepared from D-galactono-1,4-lactone[12].

From this point on, the pathway to **20** was identical with the preparation of **9**. The only significant difference was in the hydrolysis during the preparation of **15**, so that a portion of the compound lost the methoxyl group, as shown by the n.m.r. spectrum of the benzoate derivative **16** which showed a much weaker methyl peak than expected. Thus, in addition to **16**, the crude syrup also contained the 1-benzoate. This was not considered to be a serious problem, however, because the 1-benzoate was expected to react under the coupling conditions to provide the nucleoside, although not necessarily with as high a yield. The protected nucleoside **18** was obtained after chromatography, and the final two reactions, elimination of hydroiodic acid and removal of protective groups, afforded **20**. As expected, the physical properties of **20** were identical to those of **9**, except for the sign of the optical rotation.

EXPERIMENTAL

General methods. — I.r. spectra were recorded on a Perkin-Elmer Model 21 spectrophotometer, and u.v. spectra on a Beckman DK-2 spectrophotometer. Optical rotations were recorded on a Rudolph polarimeter and n.m.r. spectra with a Varian T-60A spectrometer, tetramethylsilane being the internal reference. The n.m.r. spectra of nucleosides **9** and **20** were recorded on solutions in dimethyl sulfoxide-d_6 and those of the sugar derivatives in solutions in $CDCl_3$. Melting points were determined on a Kofler hot-stage and correspond to corrected values. Moist, organic solutions were dried with $MgSO_4$. Evaporations were performed *in vacuo* with a rotary evaporator unless otherwise stated. The chloroform used contained 0.75% ethanol. Elementary analyses were performed by the Spang Microanalytical Laboratory, Ann Arbor, Michigan.

Methyl 2,3-O-isopropylidene-5-O-p-tolylsulfonyl-β-D-ribofuranoside (**2**). — A mixture containing D-ribose (50 g), acetone (190 ml), methanol (190 ml), and conc. HCl (5 ml) was heated under reflux for 2 h. The orange solution was poured into water (500 ml), the organic solvents were evaporated, and the aqueous solution was extracted with chloroform, first with 100 ml, then three times with 50-ml portions. Drying of the extract and evaporation afforded 55.3 g of **1** as an oil. It was dissolved

in dry pyridine (100 ml), the solution chilled in an ice-bath, and *p*-toluenesulfonyl chloride (65 g) added. The mixture was stirred for 15 h at room temperature, chilled in an ice-bath, and water (5 ml) was slowly added. After 0.5 h, chloroform (200 ml) was added and the solution was washed with 0.05M H_2SO_4 (300 ml), 0.2M NaOH (3 × 300 ml), and water (300 ml). After drying and evaporation of the solvent, **2** was obtained as a syrup which began to crystallize immediately; **2** was recrystallized from ethanol to yield 64.1 g (54% from D-ribose) in several crops, m.p. 85–86°; lit.[13]: m.p. 83–84°.

Methyl 5-deoxy-5-iodo-2,3-O-isopropylidene-β-D-ribofuranoside (**3**). — To a solution of **2** in 2-butanone (560 ml) was added NaI (54 g), and the mixture was stirred and heated under reflux for 24 h. After the mixture had cooled to room temperature, the precipitate of sodium *p*-toluenesulfonate was filtered off (38 g, 91% yield). The filtrate was evaporated and the residual oil was dissolved in dichloromethane (200 ml), washed with water (2 × 200 ml), and dried and the solvent evaporated. Distillation afforded 52.8 g (94% yield), b.p. 75° (0.05 Torr), $[\alpha]_D^{24}$ −69.7° (*c* 2.55, chloroform); lit.[14]: b.p. 75–80° (0.1 Torr), $[\alpha]_D^{24}$ −68.6 (*c* 2, chloroform).

9-(5-Deoxy-β-D-erythro-pent-4-enofuranosyl)adenine (**9**). — Compound **3** (3.14 g, 10 mmol) was dissolved in freshly prepared 9:1 (v/v) trifluoroacetic acid–water (35 ml) and kept for 0.5 h at room temperature. The solvents were evaporated and the residue was dried by several additions and evaporations of 15-ml portions of 1:1 (v/v) methanol–benzene, and then of benzene alone. A solution of the syrup (**4**) in dry pyridine (22 ml) was chilled in an ice-bath, and treated with benzoyl chloride (4.5 ml). After 1 h, the mixture was kept for 22 h at room temperature, poured into a mixture of ice and saturated $NaHCO_3$ solution (200 ml), and stirred for 1 h. The mixture was extracted several times with dichloromethane (50 ml and 2 × 25 ml). The combined extracts were washed with a saturated $NaHCO_3$ solution (100 ml), water (100 ml), and dried. Evaporation and coevaporation with toluene (3 × 20 ml) gave an orange syrup containing **5** and some benzoic anhydride (n.m.r.: δ 3.41, Me). The syrup was dissolved in a mixture of glacial acetic acid (39 ml) and acetic anhydride (4.5 ml), chilled in an ice-bath, and conc H_2SO_4 (2.3 ml) added, dropwise. After 19 h at room temperature, the mixture was poured on ice (300 g) and stirred until the ice melted. Chloroform (50 ml) was added with stirring and upon separation of the layers, the aqueous layer was extracted again with chloroform (2 × 25 ml), the extracts were combined and washed with water (2 × 200 ml), saturated $NaHCO_3$ solution, and again with water. Each of these washings required the addition of NaCl to break down an emulsion. Evaporation and several coevaporations with benzene afforded 4.8 g of syrup (**6**) (n.m.r.: disappearance of s for OMe, appearance of δ 2.03, $COCH_3$).

A mixture containing the sugar derivative **6** (4.7 g), 6-benzamidochloromercuripurine (5.1 g), Celite-545 (5.1 g), $TiCl_4$ (1.3 ml), and 1,2-dichloroethane (430 ml) was heated at reflux for 24 h and processed in the usual fashion[4,7]. The crude product was chromatographed on a column (24 × 3.4 cm) of silicic acid (130 g, Mallinckrodt, 100 mesh) packed in benzene, and elution with 5:1 benzene–ethyl acetate removed unreacted sugar derivatives. Elution with 3:1 benzene–ethyl acetate

afforded 2.39 g of a foam which was shown to be the desired nucleoside **7** by u.v. spectrum (λ_{max}^{MeOH} 278 nm) and by a positive Beilstein test for halogen. The foam was dissolved in dry *N*,*N*-dimethylformamide (25 ml) and 1,5-dizabicyclo[5.4.0]undec-5-ene (1.10 g) in *N*,*N*-dimethylformamide (5 ml) was added. The solution was kept for 25 h at room temperature, evaporated (33°, *in vacuo*), and the residue was dissolved in methanol (40 ml) and conc. NH_4OH (40 ml) slowly added. After 25 h at room temperature, the solvents were evaporated (38°) and the yellow syrup dissolved in a small amount of water and placed on a column (26 × 2 cm) of Bio-Rad AGI-X2 (200–400 mesh, OH^-). The column was eluted with water, fractions (13 ml) were collected, and tubes 15–29 and 45–155, the two major u.v.-absorbing peaks, were pooled.

The first peak yielded 303 mg of benzamide as prisms (from water), m.p. 131.5–132°, which was further characterized by comparison of its i.r. and n.m.r. spectra with authentic benzamide.

The second peak afforded 683 mg of crystalline material which was recrystallized from acetone to give 432 mg of **9**, m.p. 184–187°. When the determination of the m.p. was repeated on a preheated block as described previously[1], the sample melted at 192–193°, $[\alpha]_D^{24}$ −47° (*c* 1.02, *p*-dioxane); u.v.: λ_{max}^{MeOH} 258 nm (ε 14,700); n.m.r.: δ 8.25, 8.08 (both s, 1 H each, H-2, H-8), 7.23 (broad s, 2 H, NH_2), 6.12 (d, 1 H, $J_{1',2'}$ 4 Hz, H-1'), 5.53 (m, 2 H, 2'- and 3'-OH), 4.77 (m, 2 H, H-2', H-3'), 4.28, and 4.20 (both broad s, 1 H each, CH_2=); lit.[1]: m.p. 195–196°, $[\alpha]_D^{26}$ −46.4° (*c* 1, *p*-dioxane), λ_{max}^{MeOH} 258 nm (ε 14,700).

Methyl 2,3-O-isopropylidene-α-D-lyxofuranoside (**11**). — Methyl 2,3-*O*-isopropylidene-α-D-mannofuranoside (**10**) was prepared from D-mannose as previously described[6,13]. The syrup (44.6 g) was dissolved in water (1 l) and treated with $NaIO_4$ (44 g). After 1.25 h, the water was evaporated (38°), the residue was triturated with acetone (200 ml), and the solids were removed by filtration and washed well with acetone (100 ml). Evaporation (35°) of the solvent left a syrupy residue which was dissolved in methanol (900 ml). The solution was chilled in an ice-bath, and treated with $NaBH_4$ (9.0 g) in water (100 ml). The reaction was allowed to proceed for 2 h at room temperature, the pH was adjusted to 7 with acetic acid, and the solvents were removed by evaporation. The residue was dissolved in chloroform (200 ml), washed with water (250 ml), dried, and the chloroform evaporated. The oil was purified by vacuum distillation to afford 30.9 g (79%) of **11**, b.p. 66–69° (0.02 Torr), $[\alpha]_D^{24}$ +74.7° (*c* 3.20, chloroform), n_D^{20} 1.4518; i.r.: ν_{max}^{film} 3430 cm^{-1} (broad peak, OH); n.m.r.: δ 4.80 (s, 1 H, H-1), 4.72–4.40 (m, 2 H, H-2, H-3), 4.02–3.72 (m, 3 H, H-4, H-5a, H-5b), 3.23 (s, 3 H, OCH_3), 2.98 (s, 1 H, 5-OH), 1.38, and 1.23 (both s, 6 H, *gem*-diMe); lit.[12]: methyl 2,3-*O*-isopropylidene-α-L-lyxofuranoside (not distilled), $[\alpha]_D$ −51° (*c* 2, chloroform), n_D^{23} 1.4506.

Anal. Calc. for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 52.94; H, 7.95.

Methyl 2,3-O-isopropylidene-5-O-p-tolylsulfonyl-α-D-lyxofuranoside (**12**). — A solution of methyl 2,3-*O*-isopropylidene-α-D-lyxofuranoside (**11**, 29 g) in dry pyridine (60 ml) was chilled in an ice-bath, and *p*-toluenesulfonyl chloride (34.1 g)

added. The mixture was stirred for 15 min in the cold, then at room temperature for 15 h, and chilled again. Water (3 ml) was added slowly, and stirring continued for another 0.5 h. The mixture was poured into ice–water (600 ml), whereupon an oil settled out which rapidly crystallized. The crystals were collected by filtration, washed extensively with water, and dried (50.29 g, 98.8%); they were statisfactory for further work.

For analytical purposes, a sample (1.0 g) was recrystallized by solution in warm ethanol (10 ml) followed by dilution with an equal volume of water (10 ml) to give long needles (0.666 g), m.p. 81–81.5°, $[\alpha]_D^{24}$ +43.7° (*c* 3.22, methanol); i.r.: ν_{max}^{KBr} 1379, 1354, 1335 (sh, *gem*-dimethyl, sulfonate), and 1170 cm^{-1} (sulfonate); n.m.r.: δ 7.70 (d, 2, *J* 9 Hz, Ts H *o* to sulfonate), 7.21 (d, 2 H, *J* 9 Hz, tosyl H *o* to Me), 4.52 (m, 2 H, H-2, H-3), 4.17 (m, 3 H, H-4, H-5a, H-5b), 3.22 (s, 3 H, OMe), 2.40 (s, 3 H, Me of Ts), 1.30, and 1.22 (both s, 6 H, *gem*-diMe); lit.[12]: methyl 2,3-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-L-lyxofuranoside m.p. 76–77°, $[\alpha]_D$ −41.7° (*c* 3.2, methanol).

Anal. Calc. for $C_{16}H_{22}O_7S$: C, 53.61; H, 6.19. Found: C, 53.64; H, 6.16.

β-D-Lyxose. — Methyl 2,3-*O*-isopropylidene-α-D-lyxofuranoside (700 mg) was hydrolyzed with 0.5M sulfuric acid (12 ml) on a steam bath for 2 h. The solution was neutralized with $BaCO_3$ and cooled to room temperature. The mixture was filtered through a pad of Celite and the filtrate was passed through a column (13 × 1.4 cm) of Amberlite MB-3 mixed-bed, ion-exchange resin. The water was evaporated and the syrup was dried by several coevaporations with absolute ethanol. D-Lyxose (288 mg) slowly crystallized from ethanol (after seeding) over a period of 6 days. Further processing of the mother liquor afforded two additional crops of crystals (total yield 373 mg, 72.5%), m.p. 118–122°, $[\alpha]_D^{24}$ −13.9° (*c* 2.64, water, equil); lit.[16] m.p. 117–118°, $[\alpha]_D$ −14°; in admixture with a sample of β-D-lyxose (m.p. 119–124°, Pfanstiehl Laboratories, Inc.) no depression of m.p. was observed and the i.r. spectra of the two samples were also identical.

Methyl 5-deoxy-2,3-O-isopropylidene-α-D-lyxofuranoside (**13**). — To a solution of **12** (10.9 g) in dimethyl sulfoxide (80 ml) was added $NaBH_4$ (4.6 g). The mixture was stirred for 24 h at 85°, cooled to room temperature, and poured into a solution of 1% aq. acetic acid (300 ml). The mixture was extracted with chloroform (4 × 50 ml), the chloroform solution washed with water (5 × 250 ml), dried, and evaporated. The oil was distilled (4.145 g, 72%), b.p. 29–30° (0.05 Torr), $[\alpha]_D^{24}$ +99.8° (*c* 3.88, methanol); n_D^{20} 1.4292; n.m.r.: δ 4.73 (s, 1 H, H-1), 4.45 (d, 2 H, H-2, H-3), 3.98 (q, 1 H, H-4), 3.22 (s, 3 H, OMe), 1.40, 1.25 (both s, 6 H, *gem*-diMe), and 1.26 (d, 3, terminal Me); lit.[12]: methyl 5-deoxy-2,3-*O*-isopropylidene-α-L-lyxofuranoside[12], $[\alpha]_D$ −92.7° (*c* 4.7, methanol) and n_D^{22} 1.4280.

Anal. Calc. for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.37; H, 8.54.

5-Deoxy-D-lyxose. — Compound **13** (566 mg) was hydrolyzed in 0.5M H_2SO_4 (10 ml) and processed, as just described for the preparation of D-lyxose, to give a colorless gum (363 mg, 90%, after drying under high vacuum), $[\alpha]_D^{23}$ +31.7° (*c* 1.23, water, equil.); lit.[27]: $[\alpha]_D$ +32.4°.

A phenylosazone was obtained by treating the sugar (30 mg) with phenylhydrazine hydrochloride (60 mg) and sodium acetate (90 mg) in water (2 ml) for 0.5 h in a boiling-water bath. The product was recrystallized twice from methanol–water, m.p. 180–181.5°; lit.[18]: 5-deoxy-D-xylose phenylosazone, m.p. 179–180°.

Methyl 5-deoxy-5-iodo-2,3-O-isopropylidene-α-D-lyxofuranoside (**14**). — A mixture of **12** (6.1 g) and NaI (3.6 g) in acetone (40 ml) was heated at 115° in a Parr bomb. After 66 h, the bomb was cooled to room temperature and the precipitated sodium *p*-toluenesulfonate was removed by filtration and washed with acetone. The solvent was evaporated, the residue was dissolved in chloroform (50 ml), and washed with a 10% $Na_2S_2O_3$ solution (50 ml), water (50 ml), and dried. The chloroform was evaporated and the oil distilled to give 4.74 g (70%) of **14**. In a repetition of this procedure in which three separate batches were processed starting with 12.2 g of **12**, the products were combined and distilled to afford a total yield of 30.24 g (94%), b.p. 56–63° (0.02 Torr), $[\alpha]_D^{24}$ +72.6° (*c* 2.88, methanol); n_D^{20} 1.4992; n.m.r.: δ 4.83 (s, 1 H, H-1), 4.60 (m, 2 H, H-3, H-4), 4.12 (sextet, 1 H, H-4), 3.27 (s, 3 H, OMe), 3.23 (d, 2 H, H-5a, H-5b), 1.40, and 1.28 (both s, 6 H, *gem*-diMe); lit.[12]: methyl 5-deoxy-5-iodo-2,3-*O*-isopropylidene-α-L-lyxofuranoside, $[\alpha]_D$ −70.4° (*c* 2, methanol), n_D^{22} 1.4975.

Anal. Calc. for $C_9H_{15}IO_4$: C, 34.41; H, 4.81. Found: C, 34.33; H, 4.71.

9-(5-Deoxy-β-L-erythro-pent-4-enofuranosyl)adenine (**20**). — Treatment of **14** (6.28 g, 0.02 mol) with 9:1 trifluoroacetic acid–water for 0.5 h and processing as described for **3** gave a product (containing **15**) which was dissolved in pyridine (45 ml) and treated with benzoyl chloride (9 ml) for 19 h at room temperature. After the usual processing (see preparation of **5**), a syrup was obtained which appeared to be contaminated with benzoic anhydride. It also did not exhibit a very strong OMe peak in the n.m.r., indicating that some hydrolysis of the glycoside bond had occurred under the acid conditions. The syrup was acetolyzed in a mixture of acetic anhydride (6 ml), acetic acid (50 ml), and H_2SO_4 (2.7 ml) for 16 h. After processing (see preparation of **6**), 6.98 g of a syrup was obtained, which had a peak for $COCH_3$ at δ 2.07 (n.m.r.).

The blocked nucleoside **18** was prepared by reaction of this syrup (6.98 g) with 6-benzamidochloromercuripurine (8.05 g) in 1,2-dichloroethane (630 ml) containing $TiCl_4$ (1.9 ml), and Celite-545 (8 g) for 21 h under reflux. After the usual processing[4,7], a crude product was obtained that was purified on a silicic acid column, as described for **7**, to give a foam (4.58 g), u.v.: λ_{max}^{MeOH} 277 nm, and positive Beilstein test.

The blocked nucleoside **18** was treated with 1,5-diazabicyclo[5.4.0]undec-5-ene (1.72 g) in *N,N*-dimethylformamide, as described for the *ribo* compound, and the benzoyl groups were removed with 1:1 methanol–conc. NH_4OH (80 ml). After evaporation, the residue in water solution was chromatographed on a column (55 × 2 cm) of Bio-Rad AG1-X2 (200–400 mesh, OH^-) ion-exchange resin. Fractions (15 ml) were collected and the major u.v. absorbing peaks in tubes 6–41 and 63–156 were pooled. The first peak was identified as benzamide and the second peak crystallized from water to afford 690 mg. Recrystallization from acetone gave 524 mg of **20**

in three crops, m.p. 182–184°; on a preheated stage (185°), m.p. 189–192°; $[\alpha]_D^{27}$ +49° (*c* 1.04, *p*-dioxane); i.r. and n.m.r. spectra identical to those of the enantiomer **9**.

Anal. Calc. for $C_{10}H_{11}N_5O_3$: C, 48.19; H, 4.49; N, 28.10. Found: C, 48.20; H, 4.44; N, 28.13.

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