Some Reactions of 9-(2,3-Anhydro-5-deoxy-β-D-pentofuranosyl)adenines[1]

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The reactions of 9-(2,3-anhydro-5-deoxy-β-D-lyxofuranosyl)adenine (1) and 9-(2,3-anhydro-5-deoxy-β-D-ribofuranosyl)adenine (12) with sodium benzylmercaptide and sodium azide were studied. The anhydrolyxoside (1) consistently gave a mixture of the 3-substituted arabinoside and the 2-substituted xyloside with the 3-substitution product generally predominating. The products from the anhydroriboside (12) depended on the nucleophile used. Sodium benzylmercaptide gave the 3-*S*-benzylthioxyloside (13) exclusively, whereas sodium azide gave a mixture of 3-azidoxyloside (15), 2-azidoarabinoside (18), and probably 3,3′-anhydro nucleoside (19). The differences in product in the reaction of the anhydroriboside (12) with nucleophiles can be explained on steric grounds.

A previous report from these laboratories[2] described the preparation of 9-(2,3-anhydro-5-deoxy-β-D-lyxofuranosyl)adenine (**1a**) and 9-(2,3-anhydro-5-deoxy-β-D-ribofuranosyl)adenine (**12**) and the subsequent reaction of each of these epoxides with sodium benzoate in *N*,*N*-dimethylformamide (DMF). The lyxoside (**1a**) yielded a mixture of 9-(5-deoxy-β-D-arabinofuranosyl)-adenine (**2**) and 9-(5-deoxy-β-D-xylofuranosyl)adenine (**7**) in the ratio 2:1. The anhydroriboside (**12**) gave only cyclonucleoside (**19**) as evidenced by the ultraviolet spectrum of the reaction product.

The relatively large amounts of xyloside (**7**) formed in the reaction of epoxide (**1a**) with sodium benzoate in DMF is in contrast to the almost exclusive formation of arabinoside when this same reagent was used to open 9-(2,3-anhydro-β-D-lyxofuranosyl)adenine[3] (**1b**). It was of interest from a chemical standpoint to investigate the behavior of other nucleophiles toward this same pair of 2,3-anhydro nucleosides. In addition, a number of interesting nucleosides of potential biological significance could be obtained. The results of this investigation are described below.

Treatment of 9-(2,3-anhydro-5-deoxy-β-D-lyxofuranosyl)adenine (**1a**) with sodium benzylmercaptide in methanol gave a mixture of 9-(3-*S*-benzyl-5-deoxy-3-thio-β-D-arabinofuranosyl)adenine (**3**) and 9-(2-*S*-benzyl-5-deoxy-2-thio-β-D-xylofuranosyl)adenine (**8**) in the ratio 1:1–2:1. Separation was effected by means of ion-exchange chromatography on Dowex 1 (OH).[4] Since the 2′-benzylthioxyloside (**8**) contains no free C-2′ hydroxyl, it would be expected to be eluted more easily than the 3′-benzylthio nucleoside (**3**). This proved to be the case and elution with 30% methanol in water gave the 2′-benzylthioxyloside (**8**) while the nucleoside eluted with 60% methanol in water was the 3′-benzylthioarabinoside (**3**). The nmr spectra of **3** and **8** were in agreement with the assigned structures. The 3′-benzylthioarabinoside (**3**) with a *cis* H′-1–H′-2 relationship exhibited H-1 absorption as a doublet (J = 5 cps) at τ 3.76 whereas the 2′-benzylthioxyloside (**8**) with a *trans* H′-1–H′-2 relationship showed H′-1 absorption as a doublet (J = 3 cps) at τ 4.10. Desulfurization of **3** and **8** gave crystalline 9-(3,5-dideoxy-β-D-*threo*-pentofuranosyl)adenine (**4**) and 9-(2,5-dideoxy-β-D-*threo*-pentofuranosyl)adenine (**9**), respectively. The nmr spectra of **4** and **9** confirmed the structural assignments. Thus the 3,5-dideoxy nucleoside (**4**) showed H′-1 as a doublet (J = 6 cps) at τ 3.99, while the 2,5-dideoxy nucleoside (**9**) showed H′-1 as the expected multiplet at τ 3.9.

The reaction of **1a** with sodium azide in 2-methoxyethanol also gave a mixture of nucleosides which was separated by ion-exchange chromatography. Again the 2-substituted compound was eluted first so that elution with 30% methanol in water followed by 98% methanol in water gave 9-(2-azido-2,5-dideoxy-β-D-xylofuranosyl)adenine (**10**) followed by 9-(3-azido-3,5-dideoxy-β-D-arabinofuranosyl)adenine (**5**) in the ratio 1:3. Hydrogenation of the two azides gave the corresponding crystalline amino nucleosides (**6** and **11**).

The reaction of 9-(2,3-anhydro-5-deoxy-β-D-ribofuranosyl)adenine (**12**) proceeded in a different fashion. Thus, treatment of **12** with sodium benzylmercaptide in methanol gave yields of up to 90% of 9-(3-*S*-benzyl-5-deoxy-3-thio-β-D-xylofuranosyl)adenine (**13**). Ion-exchange chromatography of the mother liquors of the crystallization revealed no traces of the isomeric 9-(2-*S*-benzyl-5-deoxy-2-thio-β-D-arabinofuranosyl)-adenine (**17**). Desulfurization of **13** with sponge nickel gave the corresponding 9-(3,5-dideoxy-β-D-*erythro*-pentofuranosyl)adenine (**14**). The nmr spectrum of **14** confirmed the assigned 3,5-dideoxy structure and hence the structure of the benzylthio nucleoside (**13**).

When the anhydro nucleoside (**12**) was treated with sodium azide in 2-methoxyethanol, a mixture of azides was produced which was resolved by ion-exchange chromatography to give a 4:1 mixture of 9-(3-azido-3,5-dideoxy-β-D-xylofuranosyl)adenine (**15**) and 9-(2-azido-2,5-dideoxy-β-D-arabinofuranosyl)adenine (**18**). The ultraviolet spectrum of the crude reaction product showed significant absorption at 294 mμ at pH 1 and 7 which suggested that appreciable cyclization of the starting material to cyclonucleoside (**19**) had occurred. Efforts to characterize this material were unsuccessful. Hydrogenation of the 3-azide (**15**) over palladium on carbon gave crystalline 9-(3-amino-3,5-dideoxy-β-D-xylofuranosyl)adenine (**16**) (Scheme I).

The difference in point of opening of **1a** compared with **12** can be largely ascribed to differences in steric effects. Thus, sodium benzylmercaptide gives exclusive C-3′ opening with **12** because C-2′ is sterically unavailable to the large nucleophile. With the smaller azide ion, some C-2′ attack is noticed although the

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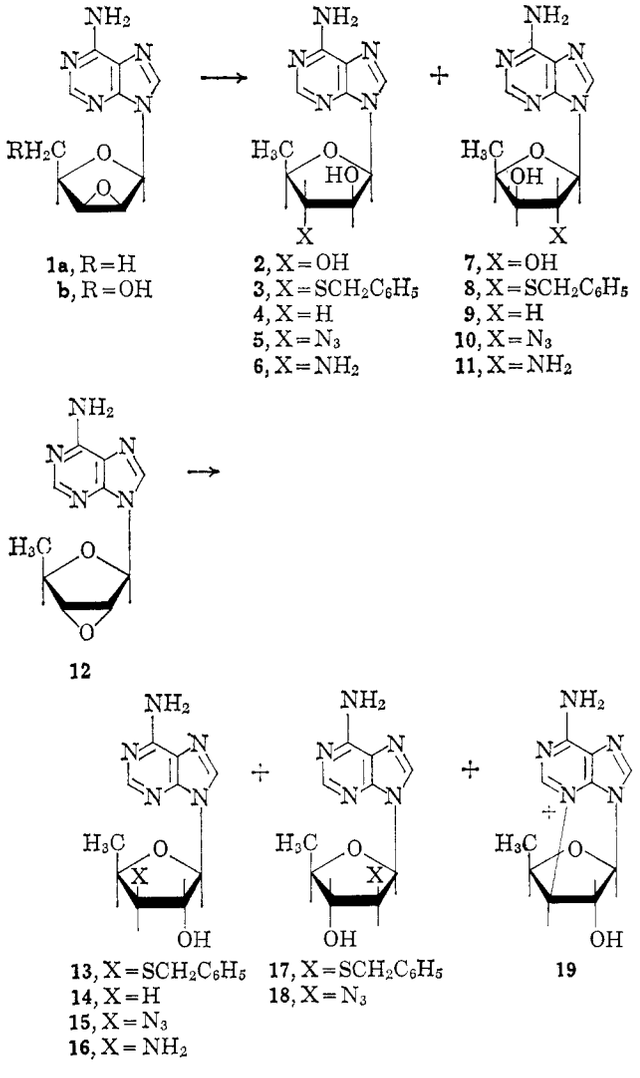
(2) E. J. Reist V. J. Bartuska, D. F. Calkins, and L. Goodman, *J. Org. Chem.*, **30**, 3401 (1965).

(3) W. W. Lee, A. Benitez, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **82**, 2648 (1960).

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

SCHEME I



major attack is at C-3′ and there is considerable competition from N-3 to give 3,3′-anhydro nucleoside (**19**). Sodium benzoate in DMF gave 3,3′-anhydro nucleoside only.[2] The anhydrolyxoside (**1a**), on the other hand, always gives a mixture of 3-substitution and 2-substitution regardless of the nucleophile used. Furthermore, more powerful nucleophiles are less selective than the weaker nucleophiles with **1a**. This was also illustrated in the reaction of 9-(2,3-anhydro-β-D-lyxofuranosyl)adenine (**1b**) with these same three nucleophiles. Thus, sodium benzoate in DMF gave almost exclusive formation of arabinoside (attack at C-3′).[3] Sodium benzylmercaptide with **1b** gave a 5:1 ratio of products resulting from attack at C-3′ over C-2′.[5] Sodium azide with **1b** gave a mixture of 3-substituted product to 2-substituted product in the ratio 15:1.[6]

The difference in selectivity in attack of nucleophiles at the epoxide on **1a** and **1b** can be rationalized by the postulate that the greater electronegativity of the 5′-hydroxyl in **1b** compared with the 5′ hydrogen in **1a** makes C-3′ more electron deficient relative to C-2′ in **1b** than in **1a**. It is also possible that the difference in the side-chain hydroxymethyl of **1b** compared to the methyl of **1a** affects the distortion of the furanose ring so that the C-3′ position is more accessible to attack. This latter possibility seems less likely, however.[7]

(5) A. P. Martinez, W. W. Lee, and L. Goodman, *J. Org. Chem.*, **31**, 3263 (1966).

(6) W. W. Lee and A. P. Martinez, unpublished data.

Experimental Section[8]

9-(3-*S*-Benzyl-5-deoxy-3-thio-β-D-arabinofuranosyl)adenine (3) and 9-(2-*S*-Benzyl-5-deoxy-2-thio-β-D-xylofuranosyl)adenine (8).—A solution of 200 mg (0.86 mmole) of 9-(2,3-anhydro-5-deoxy-β-D-lyxofuranosyl)adenine (**1a**)[2] in 5 ml of absolute methanol was added to a stirred solution of 0.50 ml (4.3 mmoles) of α-toluenethiol and 186 mg (3.44 mmoles) of sodium methoxide in 20 ml of methanol. The reaction was stirred at reflux for 18 hr, then was cooled to room temperature and neutralized to pH 7 with Amberlite IRC 50 (H). The neutralized solution was evaporated to dryness *in vacuo* to give an oil which was triturated with 20 ml of hot benzene. The insoluble residue was discarded and the benzene filtrate was evaporated to dryness *in vacuo*. The residue was dissolved in 15 ml of 30% aqueous methanol, applied to the top of a column of Dowex 1-X 2 (OH)[4] (2.2 cm × 23 cm) and eluted with 30% aqueous methanol until there was no further ultraviolet-absorbing material coming off the column. Further elution was carried out with 60% aqueous methanol, again until no further ultraviolet absorbing material was eluted.

The two aqueous methanol fractions were evaporated to dryness *in vacuo*. The 60% aqueous methanol contained 66 mg (21.5%) of the 3-*S*-benzylthioarabinoside (**3**) as a crystalline solid, which was homogeneous on paper chromatography with R_{ad} 0.69. Recrystallization from absolute methanol gave the analytical sample of **3** with mp 179.5–180.0, $[\alpha]^{21}D$ +86° (*c* 0.7, pyridine).

Anal. Calcd for $C_{17}H_{19}N_5O_2S$: C, 57.2; H, 5.36; N, 19.6; S, 8.96. Found: C, 57.3; H, 5.36; N, 19.3; S, 9.29.

The nmr spectrum showed the purine ring protons as two singlets at τ 1.75 and 1.89. The H-1′ proton occurred as a doublet (J = 5.5 cps) at τ 3.76. From the 30% aqueous methanol fraction was obtained 62 mg (20%) of the 2-*S*-benzylthioxyloside (**8**) as a crystalline solid which was homogeneous on paper chromatography with R_{ad} 1.3. Recrystallization from aqueous methanol gave the analytical sample of **8**: mp 90–93°; $[\alpha]^{21}D$ +61° (*c* 0.7, pyridine); $\lambda_{max}^{pH\ 1}$ 258 mμ (ε 13,300); $\lambda_{max}^{pH\ 7}$ 261 mμ (ε 13,700); $\lambda_{max}^{pH\ 13}$ 260 mμ (ε 34,000).

Anal. Found: C, 57.6; H, 5.50; N, 19.3; S, 8.44.

The nmr spectrum showed the purine ring protons as two singlets at τ 1.90 and 1.96. The H-1′ proton occurred as a doublet (J = 3 cps) at τ 4.10. In a subsequent reaction, 1.08 g of epoxide (**1a**) gave a 44% yield of 3-*S*-benzylthioarabinoside (**3**) and 39% yield of 2-*S*-benzylthioxyloside (**8**).

9-(3,5-Dideoxy-β-D-*threo*-pentofuranosyl)adenine (4).—A mixture of 125 mg of 9-(3-*S*-benzyl-5-deoxy-3-thio-β-D-arabinofuranosyl)adenine (**3**) and 1.2 g of Davison sponge nickel in 40 ml of DMF was stirred at 90–100° under a hydrogen atmosphere for 3 hr. The mixture was filtered and the filtrate was evaporated to dryness *in vacuo* to leave 48 mg of a yellow oil which crystallized on standing and was homogeneous on chromatography and had R_{ad} 1.4. Recrystallization from water gave the analytical sample with mp 208.5–210.5°; $[\alpha]^{21}D$ −15° (*c* 0.9, methanol); $\lambda_{max}^{pH\ 1}$ 257 mμ (ε 11,400); $\lambda_{max}^{pH\ 7,13}$ 260 mμ (ε 11,500).

Anal. Calcd for $C_{10}H_{13}N_5O_2$: C, 51.0; H, 5.58; N, 29.8. Found: C, 50.8; H, 5.71; N, 29.5.

The nmr spectrum showed the purine ring protons as two doublets at τ 1.95 and 1.97. The H-1′ proton was a doublet (J = 6 cps) at τ 3.99.

(7) An alternative suggestion has been made by the referee that this difference in selectivity of attack by nucleophiles on **1a** and **1b** may be due to a control caused by hydrogen bonding between the 5′-hydroxyl and the oxygen atom of the epoxide. This could result in a preferential weakening of the C-3′–O bond and hence would make C-3′ more vulnerable to attack.

(8) Melting points are corrected. Optical rotations were determined with a Rudolph photoelectric polarimeter. Paper chromatograms were run by the descending technique on Whatman No. 1 paper using 5% aqueous disodium phosphate. The spots were located by visual examination with an ultraviolet lamp. Adenine was used as the standard in all cases and was arbitrarily assigned a value of R_{ad} 1.00. The nmr spectra were measured in dimethyl sulfoxide-d_6 unless otherwise noted. The chemical shifts are expressed as τ values using 5% tetramethylsilane in tetrachloromethane as an external standard. The nmr spectrometer used was the Varian A-60 or HA-100.

9-(2,5-Dideoxy-β-D-*threo*-pentofuranosyl)adenine (9).—A mixture of 410 mg of 9-(2-*S*-benzyl-5-deoxy-2-thio-β-D-xylofuranosyl)-adenine (**8**) and 5 g of Davison sponge nickel in 150 ml of DMF was heated at 80% for 2 hr in the manner described for the preparation of **4**. The crystalline residue, 335 mg, after evaporation of solvent, was dissolved in water and extracted continuously with chloroform. The chloroform extract was evaporated to dryness *in vacuo* to give 172 mg (64%) of crystals which were triturated with 3 ml of chloroform to give 100 mg of needles which were homogeneous on paper chromatography with R_{ad} 1.3 and mp 212–213°; $[\alpha]^{22}D$ −63° (*c* 0.6, methanol); $\lambda_{max}^{pH\ 1}$ 262 mμ (ε 12,700); $\lambda_{max}^{pH\ 7,13}$ 260 mμ (ε 14,300).

Anal. Calcd for $C_{10}H_{13}N_5O_2$: C, 51.0; H, 5.58; N, 29.8. Found: C, 51.1; H, 5.67; N, 29.6.

The nmr spectrum showed the purine ring protons as two singlets at τ 1.75 and 1.93. The H-1′ proton occurred as a multiplet at *ca.* τ 3.85. Its complex pattern indicated that it was coupled to more than one hydrogen; hence the compound was indeed the 2′-deoxy nucleoside.

9-(3-Azido-3,5-dideoxy-β-D-arabinofuranosyl)adenine (5) and 9-(2-Azido-2,5-dideoxy-β-D-xylofuranosyl)adenine (10).—A mixture of 2.0 g (8.5 mmoles) of 9-(2,3-anhydro-5-deoxy-β-D-lyxofuranosyl)adenine (**1**), 2.2 g (34 mmoles) of sodium azide, and 1.0 g (16 mmoles) of ammonium chloride in 10 ml of 2-methoxyethanol which contained 6 ml of water was stirred at 85° for 4 days. The brown reaction mixture was evaporated to dryness *in vacuo* and the residue was partitioned between 40 ml each of chloroform and water. The aqueous phase was extracted with four 20-ml portions of chloroform; then the combined chloroform layers were evaporated to dryness *in vacuo*. This residue was dissolved in 10 ml of methanol, then applied to a column of Dowex 1 (OH) (2.8 cm × 35 cm, 150 g). The column was eluted first with 30% aqueous methanol, then with 60% aqueous methanol in the manner described for the separation of the *S*-benzyl nucleosides (**3** and **8**). Evaporation of the 30% methanol fraction gave 288 mg (11%) of 9-(2-azido-2,5-dideoxy-β-D-xylofuranosyl)adenine (**10**) as a crystalline solid. Evaporation of the 60% methanol fraction gave 977 mg (41%) of 9-(3-azido-3,5-dideoxy-β-D-arabinofuranosyl)adenine (**5**) as a crystalline solid. The analytical sample of 9-(3-azido-3,5-dideoxy-β-D-arabinofuranosyl)adenine (**5**) was obtained from ethyl acetate as fine white needles: mp 149–150°; $[\alpha]^{23.5}D$ −10° (*c* 1.0, methanol).

Anal. Calcd for $C_{10}H_{12}N_8O_2$: C, 43.4; H, 4.34, N, 40.6. Found: C, 43.2; H, 4.53; N, 40.0.

The nmr spectrum showed the purine ring protons as two singlets at τ 1.82 and 1.88. The H-1′ proton appeared as a doublet (J = 6 cps) at τ 3.85. The paper chromatograms showed a single spot at R_{ad} 1.17. The analytical sample of 9-(2-azido-2,5-dideoxy-β-D-xylofuranosyl)adenine (**10**) obtained from ethyl acetate had mp 78–80°; $[\alpha]^{22.5}D$ −50° (*c* 1.0, methanol).

Anal. Found: C, 43.1; H, 4.56; N, 37.9.

Although repeated nitrogen analyses failed to give the theoretical value, the product was homogeneous on paper chromatography with R_{ad} 1.20. The nmr spectrum was satisfactory for a pure compound and showed the purine ring protons as two singlets at τ 1.87 and 1.97. The H-1′ proton appeared as a doublet (J = 3 cps) at τ 4.22. Finally, it could be hydrogenated in high yield to give the 2-amine (**11**).

9-(3-Amino-3,5-dideoxy-β-D-arabinofuranosyl)adenine (6).—A mixture of 282 mg of 9-(3-azido-3-deoxy-β-D-arabinofuranosyl)-adenine (**5**) and 125 mg of 5% palladium on carbon in 80 ml of 95% ethanol was stirred under an atmosphere of hydrogen for 1.5 hr. The mixture was filtered through a Celite pad and the filtrate was evaporated to dryness *in vacuo* to give 250 mg of the amine (**6**) as a white solid. Recrystallization from 9 ml of ethyl acetate–ethanol (10:1) gave 199 mg (78%) of product as white needles: mp 102.5–105.5°; $[\alpha]^{24}D$ −34° (*c* 0.5, methanol).

Anal. Calcd for $C_{10}H_{14}N_6O_2 \cdot 0.75\ H_2O$: C, 45.6; H, 5.93; N, 31.8. Found: C, 45.6; H, 6.07; N, 31.7.

The nmr spectrum showed the purine ring protons as two singlets at τ 1.94 and 1.99. The H-1′ proton was a doublet (J = 6 cps) at τ 3.87.

9-(2-Amino-2,5-dideoxy-β-D-xylofuranosyl)adenine (11).—A mixture of 480 mg of 9-(2-azido-2,5-dideoxy-β-D-xylofuranosyl)-adenine (**10**) and 100 mg of 5% palladium on carbon in 70 ml of 95% ethanol was hydrogenated for 2 hr at atmospheric pressure. The mixture was filtered through a Celite pad to give a white solid which was dissolved in water and applied to a Dowex 1 (OH) column. The column was eluted with 200 ml of water. The water was evaporated to dryness to give a white solid. Trituration with refluxing ethyl acetate which contained 1 ml of ethanol gave 390 mg (90%) of white crystalline product: mp 208–210°; $\alpha^{22}D$ −79° (*c* 1.0, methanol).

Anal. Calcd for $C_{10}H_{14}N_6O_2$: C, 48.0; H, 5.64; N, 33.6. Found: C, 48.1; H, 5.80; N, 33.3.

The nmr spectrum showed the purine ring protons as two singlets at τ 1.81 and 1.92. The H-1′ proton occurred as a doublet (J = 3 cps) at τ 4.40.

9-(3-S-Benzyl-5-deoxy-3-thio-β-D-xylofuranosyl)adenine (13).—To a solution of 196 mg (3.5 mmoles) of sodium methoxide and 0.49 ml (4.2 mmoles) of α-toluenethiol in 10 ml of methanol was added 163 mg (0.7 mmole) of 9-(2,3-anhydro-5-deoxy-β-D-ribofuranosyl)adenine (**12**). The mixture was heated at reflux under nitrogen for 22 hr, then was concentrated to 5 ml *in vacuo* and cooled in an ice bath. On filtration there was obtained 233 mg (94%) of product **13** as a white powder, mp 233–234°. The analytical sample from a previous reaction was recrystallized from 95% ethanol and had mp 237–238°; $[\alpha]^{22}D$ −175° (*c* 0.7, pyridine).

Anal. Calcd for $C_{17}H_{19}N_5O_2S$: C, 57.1; H, 5.36; N, 19.6; S, 8.97. Found: C, 57.2; H, 5.12, N, 19.6; S, 8.90.

The product was homogeneous on paper chromatography with R_{ad} 0.90. The nmr spectrum showed the purine ring protons as two singlets at τ 1.87 and 1.98. The H-1′ proton occurred as a doublet (J = 5 cps) at τ 4.37.

9-(3,5-Dideoxy-β-D-*erythro*-pentofuranosyl)adenine (14).—A mixture of 400 mg of 9-(3-*S*-benzyl-5-deoxy-3-thio-β-D-xylofuranosyl)adenine (**13**) and 3.9 g of Davison sponge nickel in 40 ml of DMF under a hydrogen atmosphere was heated at 80–90° for 2 hr in the manner described for the preparation of **4**. The crystalline residue, 250 mg, after evaporation of solvent was recrystallized from 9 ml of water to give 136 mg (52%) of product as white needles: mp 200–201°; $[\alpha]^{21}D$ −54° (*c* 1.0, methanol).

Anal. Calcd for $C_{10}H_{13}N_5O_2 \cdot H_2O$: C, 47.5; H, 5.97; N, 27.7. Found: C, 47.4; H, 5.88; N, 27.9.

The material was homogeneous on paper chromatography with R_{ad} 1.3. The nmr spectrum showed the purine ring protons as a singlet at τ 1.82. The H-1′ proton occurred as a doublet (J = 2 cps) at τ 4.17.

9-(3-Azido-3,5-dideoxy-β-D-xylofuranosyl)adenine (15) and 9-(2-Azido-2,5-dideoxy-β-D-arabinofuranosyl)adenine (18).—A mixture of 2.0 g of 9-(2,3-anhydro-5-deoxy-β-D-ribofuranosyl)-adenine (**12**), 2.2 g of sodium azide, and 1.0 g of ammonium chloride in 90 ml of 2-methoxyethanol which contained 5 ml of water was stirred at 90° for 3 days. The reaction mixture was worked up and chromatographed on Dowex 1 (OH) in the manner described for the preparation of **5** and **10** to give a 15% yield of the 3-azide (**15**) (eluted with 98% methanol) and a 4% yield of the 2-azide (**18**) (eluted with 60% aqueous methanol). Recrystallization of the 3-azide (**15**) from 95% ethanol gave the analytical sample: mp 175–176°; $[\alpha]^{24}D$ −76° (*c* 1.0, methanol).

Anal. Calcd for $C_{10}H_{12}N_8O_2$: C, 43.4; H, 4.34; N, 40.6. Found: C, 43.4; H, 4.55; N, 40.3.

The product was homogeneous on paper chromatography and had R_{ad} 1.3. The nmr spectrum showed the purine ring protons as two singlets at τ 1.74 and 1.80. The H-1′ proton occurred as a doublet (J = 4 cps) at τ 4.17. The 2-azide (**18**) could not be crystallized; so it was characterized as its picrate. Recrystallization of the picrate from 50% ethanol gave material, mp 202–203°.

Anal. Calcd for $C_{10}H_{12}N_8O_2 \cdot C_6H_3N_3O_7 \cdot {}^1/_3C_2H_5OH$: C, 38.5; H, 3.29; N, 29.6. Found: C, 38.6; H, 3.29; N, 29.6.

Treatment of the picrate with Dowex 2 (CO_3) regenerated the 2-azide (**18**) as a colorless glass, $[\alpha]^{21}D$ + 24° (*c* 0.9, methanol). This material was homogeneous on paper chromatography and had R_{ad} 1.3. The nmr spectrum showed the purine ring protons as two singlets at τ 1.57 and 1.73. The H-1′ proton appeared as a doublet (J = 6 cps) at τ 4.02.

9-(3-Amino-3,5-dideoxy-β-D-xylofuranosyl)adenine (16).—A mixture of 190 mg of 9-(3-azido-3,5-dideoxy-β-D-xylofuranosyl)-adenine (**15**) and 150 mg of 5% palladium on carbon in 45 ml of 95% ethanol was hydrogenated at room temperature and atmospheric pressure for 1.25 hr as described for the preparation of **6** and **11**. Recrystallization of the crude product gave 96 mg (56%) of white crystals: mp 180–181°; $[\alpha]^{22}D$ −74° (*c* 1.0, methanol).

Anal. Calcd for $C_{10}H_{14}N_6O_2$: C, 48.0; H, 5.64; N, 33.6. Found: C, 48.0; H, 5.60; N, 33.5.

The product was homogeneous on paper chromatography and had R_{ad} 1.5. The nmr spectrum showed the purine ring protons as two singlets at τ 1.55 and 1.85. The H-1′ proton occurred as a doublet (J = 3 cps) at τ 4.26.

Registry No.—**3,** 13116-37-5; **4,** 13116-38-6; **5,** 13116-39-7; **6,** 13116-40-0; **8,** 13116-41-1; **9,** 13116-42-2; **10,** 13137-25-2; **11,** 13137-26-3; **13,** 13137-28-5; **14,** 13137-27-4; **15,** 13143-63-0; **16,** 13116-43-3; **18,** 13116-44-4; **18** picrate, 13116-45-5.

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Pyrrolidine Sugars. Synthesis of 9-(4-Acetamido-4-deoxy-β-D-xylofuranosyl)adenine and Other Derivatives of 4-Amino-4-deoxy-D-xylose[1]

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Derivatives of 4-amino-4-deoxy-D-xylose have been prepared starting from methyl β-L-arabinopyranoside (**1**). Selective benzoylation of the equatorial hydroxyls of **1** gave methyl 2,3-di-*O*-benzoyl-β-L-arabinopyranoside (**2**). Tolylsulfonation of **2** followed by nucleophilic displacement of the tosylate by azide ion, then debenzoylation, and hydrogenation gave methyl 4-amino-4-deoxy-α-D-xylopyranoside (**8**). Acetylation of **8** followed by acetolysis gave 4-acetamido-1,2,3,5-tetra-*O*-acetyl-4-deoxy-D-xylofuranose (**14**) together with a trace amount of pyranose (**16**). Conversion of **14** to 9-(4-acetamido-4-deoxy-β-D-xylofuranosyl)adenine (**17**) was accomplished in the usual fashion. The nmr spectrum of **17** in D_2O exhibited the phenomenon of hindered internal rotation.

In recent years, there has been great interest in the preparation of derivatives of monosaccharides in which the ring oxygen has been substituted by some other heteroatom such as nitrogen or sulfur. Our interest in the preparation of fraudulent nucleosides as compounds of potential biological significance directed us to the synthesis of monosaccharides in which the sulfur or nitrogen atom was on C-4 in order that the resulting ring closed sugar would have the desired furanose configuration. The preparation of D-ribose analogs, the derivatives of 4-thio-D-ribose,[2] and 4-acetamido-D-ribose[3] has been reported previously. Subsequently, it was desired to prepare similar nucleoside derivatives with the configuration of D-xylose, since some biological activity has been reported for 9-(β-D-xylofuranosyl)adenine.[4]

Numerous reports have been published which describe the preparation of substituted 4-aminoxylose sugars, *e.g.*, 4-acetamido-4,5-dideoxy-D-xylose,[5] 4,5-diacetamido-4,5-dideoxy-L-xylose,[5,6] 4-acetamido-4-deoxy-L-xylose,[7] and sulfonylated 4-azido-4-deoxy-D-xylose.[8] None of the approaches described seemed applicable to our purposes, however; so an alternative route was investigated which proved successful for the preparation of derivatives of the desired 4-acetamido-4-deoxy-D-xylose. The results are described in this paper. A subsequent paper will describe the preparation of 4-thio-D-xylose.

The selective benzoylation of methyl α-D-galactopyranoside at the primary and secondary equatorial hydroxyls[9,10] proved to be an entré to derivatives of 4-amino-4-deoxy-D-glucose.[9] Since the configuration about the ring of the functional groups of D-glucose is the same as that of D-xylose, a similar approach seemed logical for the 4-amino-4-deoxy-D-xylose series. With this idea in mind, methyl β-L-arabinopyranoside[11] (**1**) was treated under controlled conditions with benzoyl chloride in pyridine to give a fair yield of a crystalline dibenzoate which was tentatively assigned the structure of the desired methyl 2,3-di-*O*-benzoyl-β-L-arabinopyranoside (**2**). This dibenzoate **2** could be treated with *p*-toluenesulfonyl chloride in pyridine or methanesulfonyl chloride in pyridine to give crystalline methyl 2,3-di-*O*-benzoyl-4-*O*-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (**3**) or methyl 2,3-di-*O*-benzoyl-4-*O*-methylsulfonyl-β-L-arabinopyranoside (**4**), respectively. That the sulfonate of **3** and **4** was indeed at C-4 was demonstrated when **4** was debenzoylated with excess methanolic sodium methoxide to give a high yield of methyl 4-*O*-methylsulfonyl-β-L-arabinopyranoside (**5**). If the methylsulfonate had been located on either C-2 or C-3, it would have been adjacent to a *trans* hydroxyl function and epoxide formation should have occurred. Only with a 4-sulfonate was epoxide formation not possible.

Methyl 2,3-di-*O*-benzoyl-4-*O*-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (**3**) was treated with sodium azide in *N*,*N*-dimethylformamide (DMF) to give crystalline methyl 4-azido-2,3-di-*O*-benzoyl-4-deoxy-α-D-xylopyranoside (**6**). Debenzoylation of **6** with methanolic sodium methoxide gave a good yield of crystalline methyl

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