Anomeric Nucleosides of the Furanose Forms of 2-Amino-2-deoxy-D-glucose and 2-Amino-2-deoxy-D-ribose

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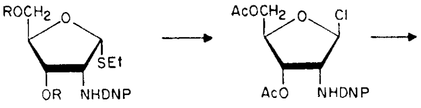
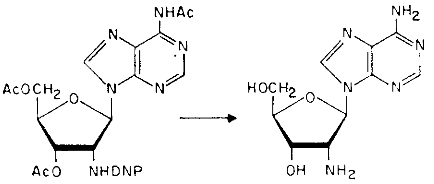
THE synthesis of nucleosides of 2-amino-2-deoxy-sugars has presented many difficulties. The introduction of the 2,4-dinitrophenyl group as a protective group for the amino-function in amino-sugars[1,2] allowed the syntheses of the anomeric forms of 9-(2-amino-2-deoxy-D-glucopyranosyl)-adenine.[3] We have now used this route for the successful synthesis of a crystalline furanosyl nucleoside of 2-amino-2-deoxy-D-ribose, a rare sugar first synthesized in this laboratory.[4] A 6-dimethylaminopurine nucleoside of the furanose form of this sugar has been reported by Baker and co-workers[5] as' 'a non-crystalline substance of somewhat doubtful purity". The starting point for their synthesis was methyl 3-amino-3-deoxy-4,6-*O*-benzylidene-α-D-altropyranoside.

We have recently prepared ethyl 2-deoxy-2-(2,4-dinitroanilino)-1-thio-α-D-ribofuranoside[6] (I) from 2-amino-2-deoxy-D-xylose, in turn prepared[7] from 2-amino-2-deoxy-D-glucose. Crystalline (I) was acetylated to the syrupy acetate (II).* Treatment of (II) with chlorine[8] in dichloromethane produced the glycosyl chloride (III) which was treated immediately with 6-acetamidochloromercuripurine in refluxing toluene. Thin-layer chromatography on silica gel indicated a complex mixture of products. A major component (IV) was isolated as a pure syrup in an overall yield from (I) of 15%. (IV) was converted, in 81% yield, into a non-crystalline solid picrate; m.p. 178—180°, $[\alpha]^{23}_{D}$ $-163 \pm 2°$ (*c*, 1·22; acetone). Treatment of the picrate with Dowex I(OH$^-$) resin in aqueous acetone resulted in 9-(2-amino-2-deoxy-β-D-ribofuranosyl)adenine (V) in 48% yield, m.p. 190—191°, $[\alpha]^{24}_{D}$ $-67 \pm 2°$ (*c*, 1·01; methanol), λ_{max} (H_2O) 262 mμ (ε 14,700). Attempts to isolate the possible α-D-anomer are in progress.†

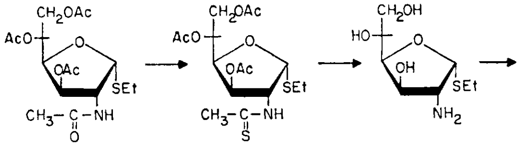
Ethyl 2-acetamido-3,5,6-tri-*O*-acetyl-2-deoxy-1-thio-α-D-glucofuranoside (VI)[6,9] was converted, in 69% yield, into ethyl 3,5,6-tri-*O*-acetyl-2-deoxy-1-thio-2-thioacetamido-α-D-glucofuranoside {(VII, m.p. 111—112°, $[\alpha]^{21}_{D}$ $+ 125 \pm 1°$ (*c*, 3·72; chloroform)} by treatment with phosphorus pentasulphide in pyridine. Complete deacylation of this 1-thioglycoside was achieved using methanolic ammonia at 100°.[10] The syrupy product (VIII) was treated with 1-fluoro-2,4-dinitrobenzene to



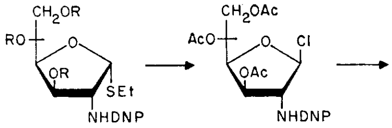
(I), R = H
(II), R = Ac
(III)



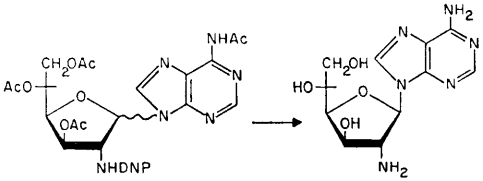
(IV)
(V)



(VI)
(VII)
(VIII)



(IX), R = H
(X), R = Ac
(XI)



(XII)
(XIII)
(XIV), α-D-anomer

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* Unless otherwise noted, all compounds were crystalline, gave satisfactory elemental analyses, and were homogeneous by thin-layer chromatography.

† *Note added in proof:* This has now been done by Dekker's method (ref. 11); m.p. 149—151°, $[\alpha]^{23}_{D}$ $+ 90 \pm 2°$ (*c*, 0·65; MeOH).

give, in 63% yield from (VII), crystalline ethyl 2-(2,4-dinitroanilino)-2-deoxy-1-thio-α-D-glucofuranoside (IX); m.p. 136—137° $[\alpha]^{21}_D$ −43 ± 2° (*c*, 1·75-methanol). Acetylation to give (X) followed by treatment with chlorine in dichloromethane produced the syrupy glycosyl halide (XI) which was immediately treated with 6-acetamidochloromercuripurine in hot toluene. The crude syrupy nucleosidic material was isolated by thin-layer chromatography on silica gel and was converted, in 48% yield from (IX), into a crystalline picrate, m.p. 187—192° decomp. Complete removal of the blocking groups from the picrate was effected by treatment with Dowex I (OH^-) resin in aqueous acetone to give, in 49% yield, an anomeric mixture; m.p. 214—222°, $[\alpha]^{25}_D$ −41° (*c*, 1·12; water), λ_{max} (H_2O) 262 mμ (ε 14,400). The anomers were separated by elution from a column of with Dowex I (OH^-) aqueous methanol according to Dekker's method[11] to give, in 63% yield, 9-(2-amino-2-deoxy-β-D-glucofuranosyl)adenine (XIII); m.p. 225—226° decomp., $[\alpha]^{22}_D$ −57 ± 2° (*c*, 1·23; water), λ_{max} (H_2O) 262 mμ (ε 14,400), and, in 31% yield, 9-(2-amino-2-deoxy-α-D-glucofuranosyl)adenine (XIV); m.p. 223—224° decomp., $[\alpha]^{22}_D$ −3 ± 1° (*c*, 1·00; water), λ_{max} (H_2O) 262 mμ (ε 14,500).

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[1] P. F. Lloyd and M. Stacey, *Tetrahedron*, 1960, **9**, 116.
[2] P. F. Lloyd and G. Roberts, *J. Chem. Soc.*, 1963, 2962.
[3] M. L. Wolfrom, H. G. Garg, and D. Horton, *Chem. and Ind.*, 1964, 930; *J. Org. Chem.*, 1965, **30**, 1556.
[4] M. L. Wolfrom, F. Shafizadeh, R. K. Armstrong, and T. M. Shen Han, *J. Amer. Chem. Soc.*, 1959, **81**, 3716.
[5] F. J. McEvoy, B. R. Baker, and M. J. Weiss, *J. Amer. Chem. Soc.*, 1960, **82**, 209.
[6] M. L. Wolfrom and M. W. Winkley, *J. Org. Chem.*, 1966, **31**, 1169.
[7] M. L. Wolfrom and K. Anno, *J. Amer. Chem. Soc.*, 1953, **75**, 1038.
[8] M. L. Wolfrom and W. Groebke, *J. Org. Chem.*, 1963, **28**, 2986.
[9] M. L. Wolfrom, S. M. Olin, and W. J. Polglase, *J. Amer. Chem. Soc.*, 1950, **72**, 1724.
[10] K. A. Watanabe, J. Beranek, A. Friedman, and J. J. Fox, *J. Org. Chem.*, 1965, **30**, 2735.
[11] C. A. Dekker, *J. Amer. Chem. Soc.*, 1965, **87**, 4027.