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Note

A convenient, acyloxonium ion-mediated conversion of adenosine-2′, 3′-*ribo*-epoxide into the *lyxo*-epoxide*

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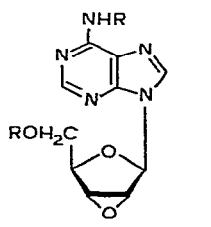
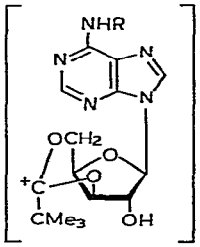
The 2′,3′-anhydro function has been widely utilised synthetically in nucleoside chemistry[2]. Whereas the 2′,3′-*ribo*-epoxide (**1**) of adenosine is relatively easily prepared[3,4], further synthetic and purification procedures[3,5] are necessary to obtain the isomeric *lyxo*-epoxide **8**. The disadvantage[6] of our published procedure[3] for the transformation **1**→**8** is that, on treating **2** with sodium benzoate, base-catalysed opening of the oxirane ring is accompanied by partial cleavage of BzO-3′, leading to **9**. Mesylation of the crude product (during which HO-3′ of **9** is selectively mesylated[6]), followed by base treatment, then gives a considerable proportion of **1** as



1 R = H
2 R = Me_3C–CO



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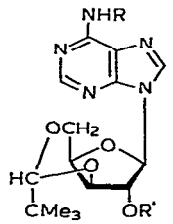
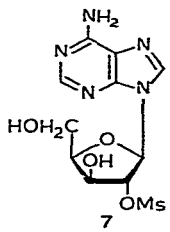


4 R = Me_3C–CO, R′ = H
5 R = R′ = H
6 R = H, R′ = Ms



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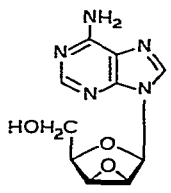

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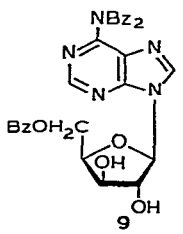

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*Nucleoside Transformation: Part VI. For Part V, see Ref. 1.

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side-product, which could be isolated only by column chromatography. When the ring opening of **2** was effected with 1 : 1 benzoic acid/sodium benzoate, the proportion of **1** in the product was lowered to 15%, but chromatography was still necessary. An earlier procedure[5] avoids these difficulties by preparation of 9-(3,5-*O*-isopropylidene-β-D-xylofuranosyl)adenine, but suffers from the disadvantage that prior preparation of 9-β-D-xylofuranosyladenine is required.

We now report a more convenient synthesis of **8** (42% yield) from **2**.

The *N*-6,*O*-5′-dipivaloyl-*ribo*-epoxide **2** was stirred briefly at room temperature with boron trifluoride etherate in acetonitrile, to give, presumably[8], the acyl-oxonium ion **3**. Addition of potassium borohydride then gave the neopentylidene derivative **4** which was indicated by p.m.r. spectroscopy to be a single diastereoisomer. The value (<1 Hz) of $J_{1',2'}$ indicated that the furanose ring was fixed in a 3′-*endo* conformation[9]. The 1,3-dioxane ring in **4** probably adopts the chair conformation having the *tert*-butyl group and the C-3′–C-2′ bond in equatorial positions. An X-ray analysis of 5-acetyl-1-(3,5-*O*-isopropylidene-β-D-xylofuranosyl)uracil revealed a 3′-*endo*,4′-*exo*-xylofuranose ring bridged by a 1,3-dioxane ring in the chair conformation[10].

Treatment of **3** with sodium borohydride partially cleaved the *N*-6-pivaloyl group from **4**, and the reaction was completed with sodium methoxide, yielding **5**. For the reaction sequence **2**→**4**, the greater the time interval between the addition of boron trifluoride etherate and sodium borohydride the smaller is the yield of **4**.

When the foregoing reaction was carried out with the *lyxo*-epoxide, neighbouring-group participation did not occur, since HO-5′ is not *trans* to the epoxide ring, and there was only a small yield of a product assumed to be 9-(3-acetamido-3-deoxy-β-D-arabinofuranosyl)adenine by analogy with the results of Fox *et al.*[11].

Conventional mesylation of **5** gave **6** in almost quantitative yield. Treatment of **6** with M HCl for 2 h at 65° gave **7** and, surprisingly, no adenine. Glycosylic cleavage occurred only above 65°, and adenine was then detectable by chromatography. Treatment of **7** with a basic ion-exchange resin gave the *lyxo*-epoxide **8**.

EXPERIMENTAL

T.l.c. was performed on Kieselgel F 1500 LS 254 (Schleicher und Schüll) with chloroform–methanol (10:1). ^{1}H-N.m.r. spectra were recorded on a JEOL JNM MH-100 instrument (external lock) for solutions in Me_2SO-d_6 (internal Me_4Si). U.v. spectra were recorded on a Cary 15 spectrophotometer, and optical rotations were measured with a Perkin–Elmer Model 241 MC polarimeter (10-cm path-length). Melting points are uncorrected.

9-(3,5-O-Neopentylidene-β-D-xylofuranosyl)adenine (**5**). — To a solution of **2**[2] (0.4 g, 0.92 mmol) in acetonitrile (10 ml) was added BF_3OEt_2 (2 ml, 15 mmol). The mixture was stirred for 2 min at room temperature and then cooled in an ice bath, KBH_4 (560 mg, 10.4 mmol) was added, and stirring was continued for 80 min. The mixture was poured into saturated, aqueous $NaHCO_3$ (40 ml) and extracted with ethyl acetate (3 × 20 ml), and the combined extracts were dried (Na_2SO_4) and

concentrated. To a solution of the residue in MeOH (10 ml) was added 5% methanolic NaOMe (6 ml), and, after being stirred for 16 h at room temperature, the yellow solution was neutralised with acetic acid and concentrated to dryness. A solution of the residue in water (30 ml) was extracted with ethyl acetate (3 × 20 ml). The combined extracts were dried (Na_2SO_4) and concentrated, and methanol was distilled several times from the residue (182 mg, 59%) which was crystallised from methanol to yield **5**, m.p. 268–270°, $[\alpha]_D^{25}$ −75° (*c* 0.38, *N*,*N*-dimethylformamide), λ_{max}^{MeOH} 258 nm (log ε 4.16). N.m.r. data: δ 0.85 (s, 9 H, CMe_3), 4.0–4.42 (m, 6 H, H-2′,3′, 4′,5′,5′, CMe_3-C*H*), 5.98 (s, 1 H, H-1′), 6.14 (d, 1 H, $J_{HO,2'}$ 4 Hz, HO-2′), 7.25 (bs, 2 H, NH_2-6), 8.16 (s, 1 H, H-2), and 8.23 (s, 1 H, H-8).

Anal. Calc. for $C_{15}H_{21}N_5O_4$: C, 53.72; H, 6.31; N, 20.89. Found: C, 53.70; H, 6.43; N, 20.97.

Conventional treatment of **5** with mesyl chloride–pyridine gave the 2′-mesylate **6**, m.p. 225–228° (from ethanol), $[\alpha]_D^{25}$ −54° (*c* 0.42, *N*,*N*-dimethylformamide), λ_{max}^{MeOH} 258 nm (log ε 4.18).

Anal. Calc. for $C_{16}H_{23}N_5O_6S$: C, 46.48; H, 5.60; N, 16.93. Found: C, 46.52; H, 5.60; N, 16.72.

9-(2,3-Anhydro-β-D-lyxofuranosyl)adenine (**8**). — A solution of **6** (0.9 g) in M HCl (25 ml) was kept for 4 h at 65° and then cooled at room temperature, neutralised by portionwise addition of Dowex-1 X2 (HO^-) resin, filtered, and concentrated. The residue was triturated with MeOH, to yield **8** (380 mg, 70%) which was recrystallised from 95% EtOH–pentane; m.p. 205–210° (dec.); mass spectrum: molecular peak at *m/e* 249; lit.[3] m.p. 208–210° (dec.). The n.m.r. data for the crude product are identical with the published data[3].

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