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Note

Some observations on the reaction of ammonia with methyl 2,3-anhydro-α-D-ribofuranoside*

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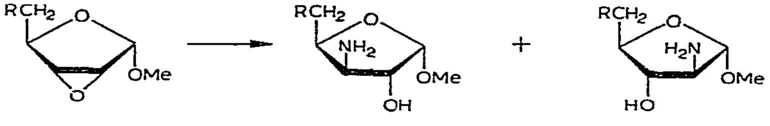
Nucleophilic attack on α-*lyxo* epoxides occurs exclusively[1–5] at C-3 because of both polar and steric effects. These two effects oppose each other in α-*ribo* epoxides and either 2- or 3-substitution occurs[6–9]. Reaction of ammonia with methyl 2,3-anhydro-α-D-ribofuranoside (**1a**) is reported to occur at C-3, giving methyl 3-amino-3-deoxy-α-D-xylofuranoside (**2a**). However, Baker *et al.*[10] reported an 88% yield of **2a**, described as a hygroscopic, waxy solid (no m.p. given) that could not be crystallized from usual solvents, $[\alpha]^{25}_{589}$ +131° (*c* 2, chloroform), whereas Schaub and Weiss[11] described **2a**, obtained in 10% yield from a mixture of **1a** and the corresponding pyranose, as a white crystalline solid, m.p. 122–123°, $[\alpha]^{25}_{D}$ +236° (*c* 0.4, chloroform), after recrystallization from alcohol–pentane. Furthermore, Schaub and Weiss established the identity of their product by its conversion into 3-amino-3-deoxy-D-xylose hydrochloride. Kuzuhara and Emoto[12], following the work of Baker *et al.*, opened the epoxide ring of methyl 2,3-anhydro-5-deoxy-α-D-ribofuranoside (**1b**) with ammonia and obtained a single product which they, by analogy, identified initially as methyl 3-amino-3,5-dideoxy-α-D-xylofuranoside (**2b**). They later reinvestigated the structure of their product by chemical degradation[13] and corrected their structure to methyl 2-amino-2,5-dideoxy-α-D-arabinofuranoside (**3b**).



1 2 3

a series : R = OH
b series : R = H

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Because of the discrepancy in the characteristics of the products obtained by Baker *et al.*[10] and by Schaub and Weiss[11], and because the results of these investigators[10,11] and those of Kuzuhara and Emoto[12] appeared to be contradictory, as pointed out but not resolved by the latter[12], we decided to reinvestigate the ammonolysis of these epoxides.

Treatment of methyl 2,3-anhydro-5-deoxy-α-D-ribofuranoside (**1b**) with ammonium hydroxide according to Kuzuhara and Emoto[12] gave a syrup, the p.m.r. spectrum of which revealed it to be about a 1:1 mixture of two sugars. These sugars were separated with difficulty by recrystallization and were identified as methyl 3-amino-3,5-dideoxy-α-D-xylofuranoside (**2b**) and methyl 2-amino-2,5-dideoxy-α-D-arabinofuranoside (**3b**) on the basis of several features of their p.m.r. spectra (see Table I). Foremost among them were the apparent *trans* relations of H-1 and H-2 of **3b** ($J_{1,2}$ 3.1 Hz) and the chemical shift of H-1 of **3b**; this proton resonates at higher field than the anomeric proton of **2b**, as would be expected. Additionally, H-2 of **3b** resonates at considerably higher field than H-2 of **2b**, presumably the result of its being attached to a carbon atom bearing an NH_2 group rather than an OH group and because of shielding from OCH_3 and OH groups on the same side of the ring. Assignments of individual peaks were verified by spin-decoupling experiments. Compound **3b** appears to be identical to the material reported by Kuzuhara and Emoto as the sole product of their reaction[12].

TABLE I

PMR DATA

Compound	*Chemical shifts, p.p.m.*	
	H-1 ($J_{1,2}$, Hz)	*H-2*
2a	4.65 (4)	3.6 (m)
2b	4.65 (4)	3.6 (m)
3a	4.5 (2)	2.9 (m)
3b	4.4 (3)	2.9 (m)

Similarly, treatment of methyl 2,3-anhydro-α-D-ribofuranoside (**1a**) with concentrated ammonium hydroxide according to Baker *et al.*[10] gave a syrup, the p.m.r. spectrum of which revealed it to be a mixture of two amino sugars (1:1.5). Again, these sugars were separated with difficulty and identified as methyl 3-amino-3-deoxy-α-D-xylofuranoside (**2a**) and methyl 2-amino-2-deoxy-α-D-arabinofuranoside (**3a**) by their p.m.r. spectra (see Table I), which were very similar to those of the corresponding deoxy compounds (see foregoing discussion) and were assigned for similar reasons. Both H-1 and H-2 of **3a** absorbed at higher field than H-1 and H-2 of **2a**, and again there appeared to be a *trans* relation between H-1 and H-2 of **3a** ($J_{1,2}$ <3 Hz). Compound **2a** appears to be identical to the material prepared by Schaub and Weiss[11].

Our results with ammonia are in keeping with those of other recent investigators[6–9] of the reactions of **1a** with other nucleophiles, such as the fluoride ion[9] and the benzylthioxide ion[7]. In our hands, reaction of **1a** with sodium azide gave, in very poor yield, two sugars, presumably resulting from attack at C-2 and C-3.

EXPERIMENTAL

General. — Melting points were determined with a Mel-Temp apparatus and are not corrected. The p.m.r. spectra were determined in $(CD_3)_2SO$ (Me_4Si) with a Varian XL-100-15 spectrometer; chemical shifts quoted for multiplets were measured from the approximate centers. Chromatographic analyses were carried out on Analtech silica gel G plates. The spots were detected by charring after spraying the plates with aqueous ammonium sulfate and by ninhydrin spray. Compounds **2a** and **3a** were separated into two discrete spots by 1:1 methanol–water and compounds **2b** and **3b** by 3:1 chloroform–methanol.

*Methyl 3-amino-3-deoxy-α-*D*-xylofuranoside* (**2a**) *and methyl 2-amino-2-deoxy-α-*D*-arabinofuranoside* (**3a**). — A solution of 2.0 g (13.7 mmoles) of methyl 2,3-anhydro-α-D-ribofuranoside (**1a**) in 15 ml of concentrated ammonium hydroxide was heated for 16 h at 100° in a bomb. The mixture was diluted with water, filtered through Celite, and the filtrate evaporated to dryness. The resultant syrup was azeotropically dried by distillation of benzene from it. The p.m.r. spectrum of this residue showed it to be a 1:1.5 mixture of **2a** and **3a**. These isomeric sugars were separated with difficulty and low recovery by recrystallization from ethyl acetate. Compound **2a** crystallized from the solution and, after one additional recrystallization, gave 239 mg (11%) of white crystals, m.p. 117–119°, $[\alpha]_D^{25}$ +194.0 ±0.6° (*c* 0.835, chloroform), lit.[11] m.p. 116–118°, $[\alpha]_D^{25}$ +236° (*c* 0.4, chloroform).

Anal. Calc. for $C_6H_{13}NO_4$: C, 44.16; H, 8.03; N, 8.58. Found: C, 44.47; H, 7.80; N, 8.47.

From the filtrate was obtained by further recrystallization from ethyl acetate 100 mg (4.5%) of **3a**, m.p. 75–77°, $[\alpha]_D^{25}$ +100.8 ±0.9° (*c* 0.75, chloroform).

Anal. Calc. for $C_6H_{13}NO_4$: C, 44.16; H, 8.03; N, 8.58. Found: C, 44.07; H, 7.67; N, 8.38.

In a second run, 1.7 g of **2a** and 3.8 g of **3a** (containing about 20% of **2a**) were obtained from 11.7 g of the epoxide **1a**.

*Methyl 3-amino-3,5-dideoxy-α-*D*-xylofuranoside* (**2b**) *and methyl 2-amino-2,5-dideoxy-α-*D*-arabinofuranoside* (**3b**). — A solution of methyl 2,3-anhydro-5-deoxy-α-D-ribofuranoside (10.4 g) in concentrated ammonium hydroxide (200 ml) was heated for 12 h at 100°. The solution was evaporated to dryness, and the residue was azeotropically dried by distillation of benzene and ethyl acetate from it. The p.m.r. spectrum of the dried residue (60% yield) indicated that it was a mixture of **2b** and **3b**, with the latter preponderating slightly. Recrystallization from ethyl acetate gave 3.3 g (28%) of pure **3b**, m.p. 118–121°, $[\alpha]_D^{26}$ +114.3 ±1.4° (*c* 0.485, water), lit. m.p. 122–123°, $[\alpha]_D^{25}$ +126° (*c* 1.34, water). Concentration of the filtrate gave 5.9 g (50%) of a mixture containing mainly **2b**. Repeated recrystallization gave a small amount of pure **2b**, m.p. 86–87°, $[\alpha]_D^{26}$ +179.5 ±0.2° (*c* 0.58, water).

Anal. Calc. for $C_6H_{13}NO_3$: C, 48.96; H, 8.90; N, 9.52. Found: C, 48.86; H, 8.51; N, 9.23.

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