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Preliminary communication

Synthesis of a sugar occurring in an antibiotic: ezoaminuroic acid, the first example of a naturally occurring 3-amino-3-deoxyhexuronic acid

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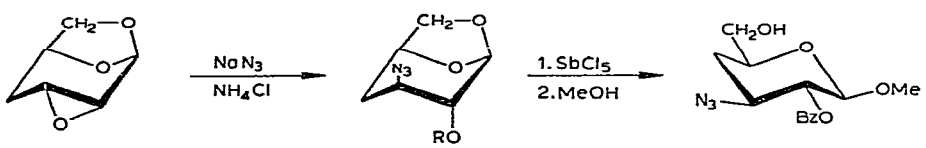
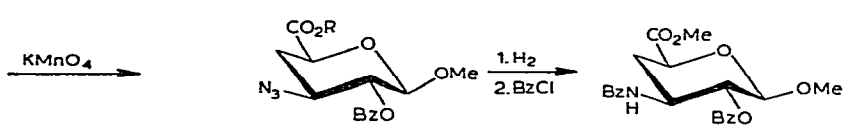
The isolation and determination of structure of ezomycin, an antibiotic exhibiting specific antifungal activity, was recently reported by Sakata *et al.*[1]. In the course of their structural investigation, a derivative (**7**) of ezoaminuroic acid, the first naturally occurring 3-amino-3-deoxyhexuronic acid, was obtained by chemical degradation of ezomycin.

As part of a project on achieving carbohydrate transformations by employing molecules having a rigid conformation, we now report the first, stereospecific synthesis of the ezoaminuroic acid derivative **7** in seven steps starting from the Černý epoxide[2] **1**.

Treatment of epoxide **1** with sodium azide in aqueous ethanol in the presence of a catalytic amount of ammonium chloride gave azide **2**, $[\alpha]_D^{25}$ −12.2° (*c* 0.63, methanol), by stereospecific, epoxide opening due to the rigid conformation of the molecule[3]. Benzoylation gave the monobenzoate **3** (in 88% yield from **1**); m.p. 52–55°, $[\alpha]_D^{25}$ +100°



1 **2** R = H, **3** R = Bz **4**



5 R = H, **6** R = Me **7**

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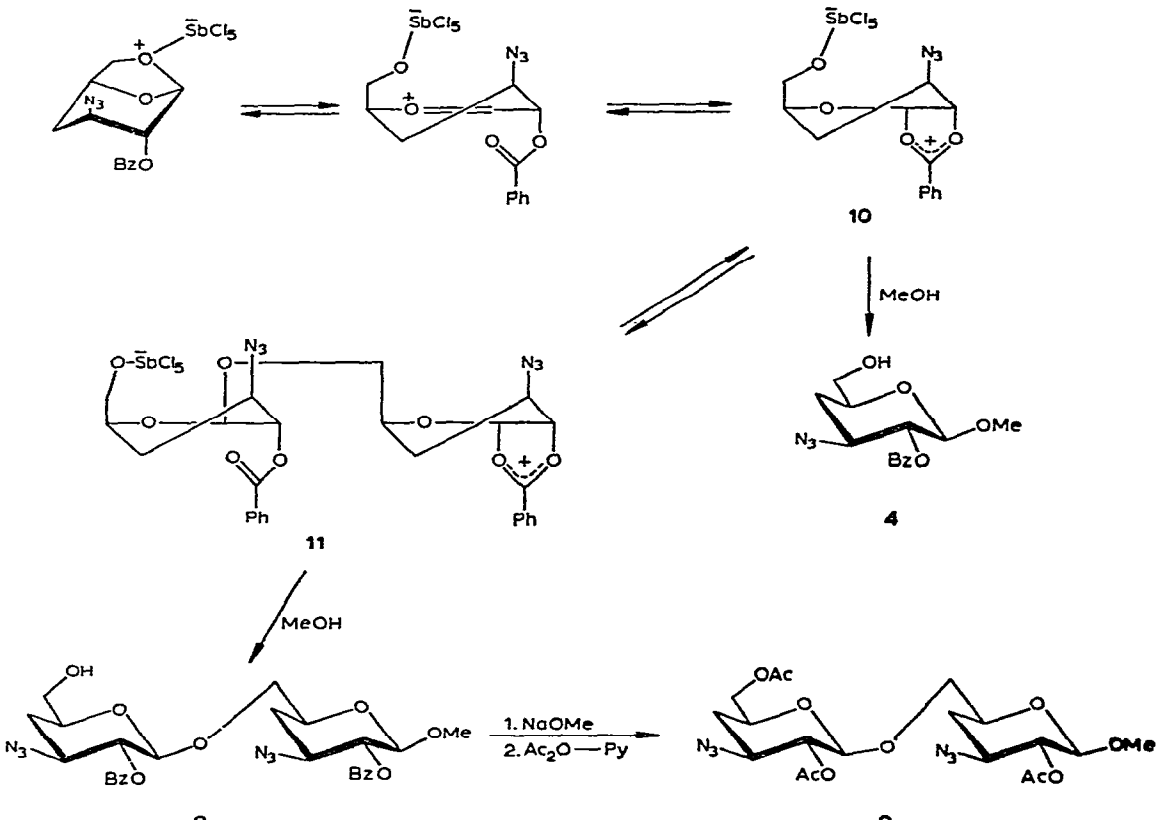
(*c* 1.1, chloroform); ν_{max}^{Nujol} 2070 cm^{-1} (N_3); ^1H n.m.r. ($CDCl_3$): δ 4.90 (1 H, s, H-1), 5.56 (1 H, s, H-2).

Cleavage of the 1,6-anhydro ring and subsequent formation of the methyl β-D-glycosidic bond was successfully achieved in one step by employing a Lewis acid as the reagent. Thus, reaction of benzoate **3** with the equivalent amount of antimony pentachloride in dichloromethane during 5 h at −10° and subsequent treatment of the reaction mixture with a large excess of methanol afforded the glycoside **4** stereospecifically, in 55% yield; m.p. 131–133°, $[\alpha]_D^{25}$ +21.5° (*c* 0.33, methanol); ^1H n.m.r. ($CDCl_3$) revealed the β stereochemistry of the methyl glycoside by showing H-1 at δ 4.50 (d, *J* 8.0 Hz) and OMe at δ 3.50 (s). A second product, **8**, isolated in 7% yield from the reaction mixture was further transformed into triacetate **9**, m.p. 116–117°, $[\alpha]_D^{25}$ −44° (*c* 0.43, chloroform); ν_{max}^{Nujol} 2100 cm^{-1} (N_3), through two successive steps, namely, saponification and acetylation. The structure of compound **9** was assigned according to the ^1H n.m.r. data, which showed two anomeric protons at δ 4.27 (d, *J* 8 Hz), 4.46 (d, *J* 8 Hz), one β-glycosidic methyl group at δ 3.48 (s), and three acetyl methyl groups at δ 2.11, 2.10, and 2.09 as singlets. The formation of **4** and **8** could be reasonably explained by the reaction path *via* the benzoxonium ions **10** and **11** shown in Scheme 1.



Scheme 1

Potassium permanganate oxidation of compound **4** in 1:1 acetic acid–acetone at room temperature gave the azido acid **5**, which was directly transformed by treatment with diazomethane into methyl ester **6**, m.p. 97–100°, $[\alpha]_D^{25}$ +34.3° (*c* 0.55, chloroform); ν_{max}^{Nujol} 2100 cm^{-1} (N_3), in 30% yield from **4**. ^1H n.m.r. spectroscopy showed the anomeric proton at δ 4.52 (1 H, d, *J* 8 Hz), the glycosidic methyl group at δ 3.50 (3 H, s), and the ester methyl group at δ 3.82 (3 H, s).

Hydrogenation of compound **6** in the presence of 10% Pd–C in methanol containing ammonium chloride, and subsequent benzoylation, gave methyl [methyl 3-(benzamido)-2-*O*-benzoyl-3,4-dideoxy-β-D-glucosid]uronate (**7**); m.p. 241–242°, $[\alpha]_D^{25}$ +60.7° (*c* 0.44, methanol), $[\theta]_{237}^{20}$ +61,300, $[\theta]_{222}^{20}$ –20,700 (methanol); lit[1]. m.p. 237.5–238°, $[\alpha]_D$ +58° (methanol); $[\theta]_{237.5}^{20}$ +64,000, $[\theta]_{222}^{20}$ –23,600 (methanol). The ^1H n.m.r. spectra ($CDCl_3$) of synthetic and natural **7** were in complete agreement, and proved the identity of the two samples. This stereospecific transformation of D-glucose into the ezoaminuroic derivative **7** through the Černý epoxide **1** confirmed the absolute stereochemistry of the natural product.

ACKNOWLEDGMENT

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