Preliminary Communication

Stereoselective ring-opening of β-D-mannopyranose 1,2-(alkyl orthoacetates)

D-Mannopyranosyl residues are common in the carbohydrate prosthetic groups of glycoproteins, structural studies on which suffer from a dearth of well-characterized oligosaccharides. With a view to synthesizing oligosaccharides containing D-mannose, particularly those having α-D-(1→2) linkages, the ring opening of β-D-mannopyranose 1,2-(alkyl orthoacetates) was investigated.

Earlier work has been directed toward the ring opening of the 1,2-(alkyl orthoacetates) of 3,4,6-tri-*O*-acetyl-β-D-mannopyranose[1] and 3,4,6-tri-*O*-acetyl-α-D-glucopyranose[2,3]. In order to avoid any embarassment in later conversions because of acetyl migration, the present studies were made with 3,4,6-tri-*O*-benzyl-β-D-mannose 1,2-(methyl orthoacetate) (**1**), m.p. 78–81°, $[\alpha]_D$ + 12.1° (*c* 1.65)*, which was prepared from the corresponding triacetate (**2**).

The acid-catalyzed ring opening of **1** (0.4M) in dichloromethane containing *p*-toluenesulfonic acid (0.04M), excluding water or any alcohol, showed complete rearrangement within 20 min at 46.5°, with almost exclusive formation of methyl α-D-glycoside derivatives. The reaction was performed in the n.m.r. sample tube, and followed by observing the decrease of orthoacetate C–Me signals at τ 8.35 and 8.56 with concomitant appearance of an *O*-acetyl peak at τ 7.91. The final, equilibrium mixture was analyzed by column chromatography on silica gel, whereby methyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannoside (**3**), $[\alpha]_D$ +27.9° (*c* 2.24), and methyl 3,4,6-tri-*O*-benzyl-α-D-mannoside (**4**), $[\alpha]_D$ + 59.7° (*c* 1.85), were isolated in 82% and 7% yield, respectively. A small proportion of the β-D anomer (**5**) of **4** was identified by t.l.c. No other products were observed. A similar reaction, with 0.012M mercuric bromide as catalyst in nitromethane[3], was slower, but otherwise gave the same results.

The presence of methanol in the reaction mixture appeared to have little or no effect upon the direction of the ring opening, but there was more extensive loss of the 2-acetoxy group. Treatment of **1** (0.4 mmole) with methanol (0.4 mmole) and

*The reactions were followed by t.l.c. on silica gel G (E. Merck, Darmstadt, Germany) with 1:1 chloroform–ethyl acetate as eluent and detection of the components by sulfuric acid. The products were purified either by recrystallization, usually from ether–petroleum ether, or by chromatography on silica gel (0.05–0.2 mm), with successive elution by dichloromethane, ethyl acetate, and methanol. The melting points (Fisher–Johns apparatus) are uncorrected. The n.m.r. spectra were obtained in chloroform or chloroform-*d*, with a tetramethylsilane external standard, by using a Varian A-60 spectrometer. All optical rotations were observed in dichloromethane.

p-toluenesulfonic acid (0.4 mmole) in dichloromethane (1 ml) for 10 min at 46.5° gave an equilibrium mixture containing 74% of **3**, 20% of **4**, and 6% of **5**. Similar treatment of 3,4,6-tri-*O*-acetyl-α-D-glucose 1,2-(alkyl orthoacetate) has previously[2] been shown to result in the complete removal of the 2-acetoxy group from the products, which were a mixture of 3,4,6-tri-*O*-acetyl-D-glucose and the corresponding alkyl α-(and β)-D-glycosides[2]. The stereoselectivity of the ring opening was not so pronounced in this D-glucose series as is described above for **1**. Almost exclusive formation of **4** was achieved by heating **1** in 2% methanolic HCl for 24 h or longer under reflux. Similarly, aqueous acetic acid hydrolyzed **1** to 3,4,6-tri-*O*-benzyl-D-mannose, m.p. 98–9°, $[\alpha]_D$ +22.7° (*c* 1.92), which was characterized by oxidation, with periodate, to the known 2,3,5-tri-*O*-benzyl-D-arabinose, m.p. 77–80°, undepressed on admixture with an authentic sample.

The acid-catalyzed rearrangements of the 1,2-(cyclohexyl orthoacetate) and 1,2-(isopropyl orthoacetate) of 3,4,6-tri-*O*-benzyl-β-D-mannose proceed with equal stereoselectivity, to give the corresponding α-D-mannoside. Studies are continuing to extend the reaction to other orthoesters.

ACKNOWLEDGMENT

This work was supported by a U. S. Public Health Service research grant (HE 06717) from the National Heart Institute.

Department of Biochemistry,
University of Iowa,
Iowa City, Iowa 52240 (U. S. A.)

NEAL E. FRANKS
REX MONTGOMERY

REFERENCES

1 A. S. PERLIN, *Can. J. Chem.*, 41 (1963) 555.
2 R. U. LEMIEUX, *Chem. Can.*, 16 (10), (1964) 14.
3 N. K. KOCHETKOV, A. J. KHORLIN, AND A. F. BOCHKOV, *Tetrahedron Letters*, (1964) 289.

(Received September 6th, 1966; in revised form, November 25th, 1966).