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THE SYNTHESIS OF 5-DEOXY-(±)-ALLOSE DERIVATIVES AND 4-DEOXY-(±)-RIBOSE FROM *myo*-INOSITOL

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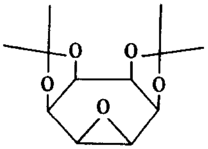
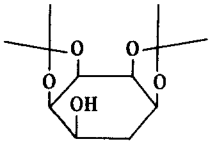
As part of a research program directed to exploring a general synthetic route to monosaccharides from cyclitols *via* the seven membered hemi-acetal lactones which we have described previously$^{1)}$, we wish now to report the synthesis of 5-deoxy-(±)-allose derivatives and 4-deoxy-(±)-ribose from *myo*-inositol.

On preparation of 1:2-anhydro-3:4,5:6-di-*O*-isopropylidene-*cis*-inositol (I) from *myo*-inositol *via* (±)-1:2,3:4-di-*O*-isopropylidene-5,6-di-*O*-*p*-toluenesulfonyl-*epi*-inositol according to the procedure reported by S.J.Angyal *et al.*$^{2)}$, a small modification was made. The ditosylate (10 g.) was refluxed with sodium methoxide (metallic sodium 1.8 g. in methanol 100 ml.) in tetrahydrofuran (100 ml.) for 5 hrs to give the 1:2-anhydro-*cis*-inositol derivative I, m.p. 142°, (2.6 g.), accompanied with a small amount of 5:6-anhydro-1:2,3:4-di-*O*-isopropylidene-*allo*-inositol, m.p. 97°, (0.22 g.) and (±)-1:2,3:4-di-*O*-isopropylidene-6-*O*-methyl-*epi*-inositol, m.p. 105°, (0.18 g.). When refluxed for a prolonged time, for example, 48 hrs, the last mentioned *O*-methyl-compound was produced as a main product$^{1)}$.

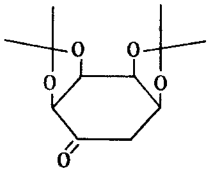
The reduction of the 1:2-anhydro-*cis*-inositol derivative I with lithium aluminum hydride gave (±)-6-deoxy-1:2,3:4-di-*O*-isopropylidene-*cis*-inositol (II), m.p. 102-104°, in 83% yield. This compound (1.61 g.) was oxidized with dicyclohexyl carbodiimide (4.83 g.) and pyridinium trifluoroacetate (630 mg.) in dimethyl sulfoxide (40 ml.), the Pfitzner-Moffat reagent$^{3)}$, for 48 hrs to give (±)-6-deoxy-2:3,4:5-di-*O*-isopropylidene-*cis*-inosose-1 (III), m.p. 143-144°, in 82% yield. When the deoxy-*cis*-inositol derivative II (300 mg.) was oxidized with active manganese dioxide$^{4)}$ (7.5 g., added portionwise) in acetonitrile (30 ml.) for 5 days, a normal oxidation product III (58 mg.) was obtained and an oxygen insertion reaction which was observed on manganese dioxide oxidation of (±)-1:2,3:4-di-*O*-isopropylidene-6-*O*-methyl-*epi*-inositol$^{1)}$ did not occur.



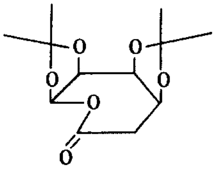
I



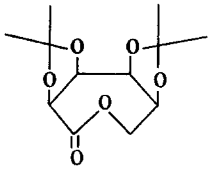
II



III



IVa



IVb

The *cis*-inosose derivative III was subjected to the Baeyer-Villiger reaction with perbenzoic acid in moist chloroform to give the hemi-acetal lactone IVa, m.p. 171-173°, in 84% yield. Its IR spectrum[*] showed a strong band at 1725 cm^{-1} and its nmr spectrum indicated the presence of two isopropylidene groups (τ 8.61, 8.55, 8.47, 8.33) as well as six ring protons, which were not so well resolved that these physical data gave us no reliable ground for choice between the hemi-acetal lactone structure IVa and the lactone structure IVb. The latter structure is, however, excluded by the following experimental evidences: The treatment of the hemi-acetal lactone IVa with lithium aluminum hydride gave 2-deoxy-3:4-*O*-isopropylidene-(±)-allitol (V), m.p. 73-76°, in quantitative yield as a result of reduction and concomitant elimination of an isopropylidene group. The 2-deoxy-allitol derivative V was subjected to the oxidative cleavage with periodate to give 4-deoxy-2:3-*O*-isopropylidene-(±)-ribose (VI), m.p. 48.5-49.5°, which was, in turn, hydrolyzed with 50% acetic acid to afford 4-deoxy-(±)-ribose as a colorless syrup. The reduction of the 4-deoxy-ribose derivative VI with sodium borohydride and the subsequent elimination of the isopropylidene group with 50% acetic acid produced an oily substance, which was, without further purification, treated with benzoyl chloride in pyridine to give 2-deoxy-(±)-ribitol tetrabenzoate, m.p. 145°. This racemic

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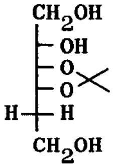
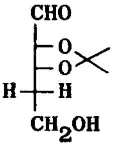
[*] Unless otherwise mentioned, IR spectra were measured in nujol mull, nmr spectra in deuterio-chloroform solution with a Varian A-60 (with tetramethylsilane as internal standard). We are indebted to Dr. Tetsuro Shingu for the nmr spectra.

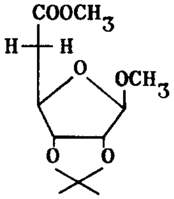
tetrabenzoate showed an identical infrared spectrum (in chloroform) with that of the D-isomer, m.p. 130-131°, $(\alpha)_D^{26} = -15.3°$ (in chloroform), (lit.[5] m.p. 128-130°, $(\alpha)_D = -17°$ (in chloroform)), prepared from 2-deoxy-D-ribose.



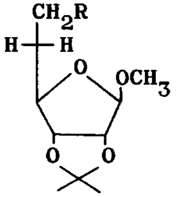
V



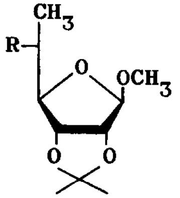
VI



VII



VIIIa:R=OH
VIIIb:R=H



IXa:R=H
IXb:R=OTs

The hemi-acetal lactone IVa (1.8 g.) was heated in methanol (90 ml.) in the presence of a catalytic amount of sulfuric acid for 2 hrs and the resultant oily product was chromatographed over alumina with chloroform to afford a colorless oil (710 mg.), which was assigned to be methyl (methyl 5-deoxy-2:3-*O*-isopropylidene-β-(±)-allofuranosid)uronate (VII) on the basis of the following evidences: The nmr spectrum of the compound VII indicated the presence of an isopropylidene group (τ 8.68, 8.52), an *O*-methyl (τ 6.68), a methyl ester (τ 6.28), C-1 proton (τ 5.07, singlet), C-5 protons (τ 7.37, doublet $J_{4,5}$= 7.5 c.p.s.), and three ring protons (in a range of τ 5.27 to 5.52). A definite evidence for the structure was given by the reduction of VII with lithium aluminum hydride, which afforded a colorless syrup of methyl 5-deoxy-2:3-*O*-isopropylidene-β-(±)-allofuranoside (VIIIa), (its 3,5-dinitrobenzoate, m.p. 84-86°), giving identical nmr data with those of its β-D-isomer reported by K.J.Ryan *et al.*[6] Another evidence was also given by the fact that methyl 5,6-dideoxy-2:3-*O*-isopropylidene-β-(±)-allofuranoside (VIIIb), which was derived from VIIIa through mesylation with methanesulfonyl chloride and subsequent reduction with lithium aluminum hydride, showed identical infrared (in chloroform) and nmr spectra with those of its β-D-isomer IXa, $(\alpha)_D^{24}$ = -70.4° (in methanol). This β-D-isomer was prepared from methyl 6-deoxy-2:3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-β-D-allofuranoside (IXb)$^{7)}$ by treatment with sodium iodide in acetone in a sealed tube and the subsequent hydrogenolysis of the resultant 5-iodo-compound with Raney nickel.

The structurr of the uronate VII indicates that an isopropylidene group of the starting hemi-acetal lactone IVa migrates from the original position during the acid treatment of IVa. The reaction mechanism for this migration is left to be confirmed.

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