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THE SYNTHESIS OF (1S, 2R, 4R, 5S, 6R)-1,2,4,5,6-PENTA-O-BENZOYLMYOINOSITOL.

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Phosphoinositides are widely distributed in both the animal and plant kingdoms (1). The structure of the simplest monophosphoinositides (I) and also of the most complex phosphatidylmyoinositol mannosides (2) of Mycobacteria have been established. In view of biogenetic relationship to the naturally occuring phosphoinositides (3), the availability of the monophosphoinositide (I) would be of considerable chemical and biological interest.

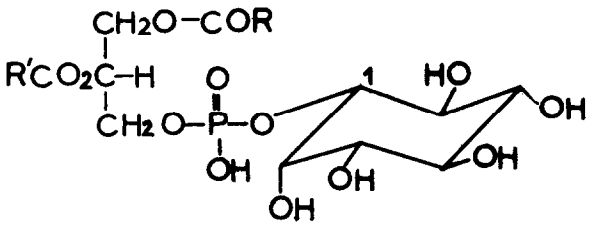
In order to synthesize monophosphoinositides (I) and other derivatives of myoinositol, optically active partially substituted myoinositols are required as intermediates. Such derivatives have not yet been synthesized. Partially substituted racemic derivatives of myoinositols have been reported (4,5,6).

In this communication we report the preparation of the (1S, 2R, 4R, 5S, 6R)-1,2,4,5,6-pento-O-benzoyl-myoinositol (III) and its tetrahydropyranyl ether (IV).

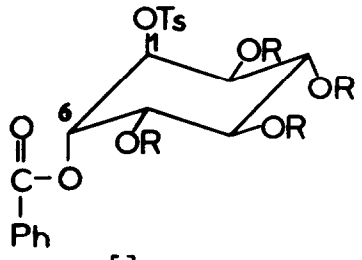
Recently (7) the smooth conversion of quebrachitol to 2,3,4,5,6-penta-O-benzoyl-1-O-tosyl-(-)-inositol (II) has been described. This system having an antiperiplanar arrangement of the functional groups seems quite ideal for an intramolecular displacement. It appears, however, that the conversion of the O-tosyl-ester (II) into the C(1)-C(2)-C(3)-cis-cis-cis-configuration (III) presents serious difficulties from a stereoselective point of view. The conversion of a trans-2-O-acyl-O-p-toluenesulphonate to the corresponding cis-diol on either the sugar pyranose ring or cyclitol derivatives by the classical Winstein procedure has not been successful (8).

The introduction of the sodium benzoate-dimethylformamide reagent by Baker et al. (9) for displacing O-sulphonyl esters has found wide application in the carbohydrate and nucleoside chemistry. However, recently reported cases (10,11,12) of 1,4- and 1,5-migration of the methoxy group, olefin formation and ring contraction following such displacement reactions suggested that it might not be applicable for our problem.

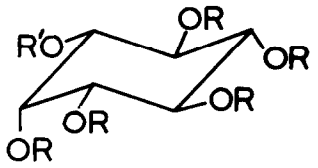
Treatment of (III) with sodium fluoride in dimethylformamide at 140° for 72 hours caused the complete loss of the tosyl group as indicated by N.M.R. and infrared spectroscopy.



[I]



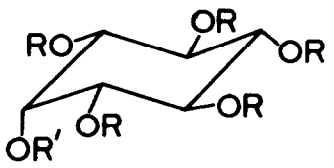
[II] R=COPh



[III] R=COPh; R′=H

[IV] R=COPh; R′=THP

[V] R=H; R′=THP



[VI] R=COPh; R′=H

[VII] R=COPh; R′=THP

[VIII] R=H; R′=THP

Thin layer chromatography showed the presence of two major components. It was expected that the two products would be (1S, 2R, 4R, 5S, 6R)-1,2,4,5,6- and 1,3,4,5,6-penta-O-benzoylmyoinositols (III, VI). Paper chromatography after debenzoylation showed only the presence of myoinositol.

The crude reaction mixture after solvolysis was pyranylated with dihydropyran in the presence of an acidic catalyst. Crystals were isolated in 70% yield, but proved to be a mixture of two components (in the ratio 1 to 1) which could be separated on preparative thin layer plate. On the basis of mechanistic considerations we assign the structures 1,2,4,5,6-penta-O-benzoyl-3-O-(2-tetrahydropyranyl) myoinositol (IV), m.p. 173-175°, $[\alpha]_D^{25°}$ - 19.2° (c, 2 ; $CHCl_3$) and 1,3,4,5,6-penta-O-benzoyl-2-O-(2-tetrahydropyranyl) myoinositol (VII), m.p. 226-230°, respectively. Recently, the tetrahydropyranyl esters of myoinositol were synthesized (13). Consequently, the unequivocal structural assignment of the two pyranlylated products (IV, VII) can be made.

Debenzoylation of (IV) and (VII) with methanolic sodium methoxide gave (V) and (VIII), which were shown by comparison to be identical with the authentic DL-1-O-tetrahydropyranyl (V) and 2-O-tetrahydropyranylmyoinositol (VIII) (13), respectively.

The tetrahydropyranyl groups of (IV) and (VII) were removed by treatment with acid, furnishing (1S, 2R, 4R, 5S, 6R)-1,2,4,5,6-penta-O-benzoylmyoinositol (III), m.p. 123-125°, $[\alpha]_D$ - 59.5° (c, 1.8 ; $CHCl_3$), and 1,3,4,5,6-penta-O-benzoylmyoinositol (VI), m.p. 227-232°, respectively.

The formation of the cis-hydroxyesters (III) and (VI) from the trans-O-benzoyl-p-toluenesulphonate (II) is in accordance with the recent results of King and Allbutt (14) on the stereoselective hydrolysis of acyloxonium ions and ortho esters fused to trans-decalin system.

Recently Reist and his colleagues reported (15) the preparation of methyl β-L-lyxopyranosides, using sodium fluoride in DMF. The low yield of 30% contrasts with our yield of 70% and illustrates the importance of the diaxial orientation of the trans-O-acyl-p-toluene-sulphonates in such displacement reactions.

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