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# A SYNTHESIS OF DL-2, 3, 4, 5, 6-PENTA-O-BENZYLMYOINOSITOL

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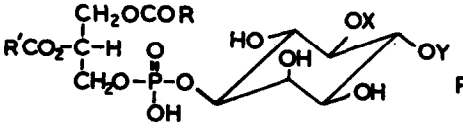
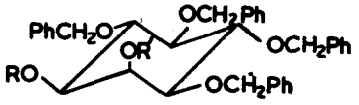
Phosphatidylinositol ["monophosphoinositide", 1, 2-di-O-acyl-L-glycerol 3-(L-myoinositol 1-phosphate), (I, X = Y = H)] is a widely distributed phospholipid and in the brain it is the precursor of the metabolically active phosphate esters "diphosphoinositide" (I, X = H, Y = $PO_3H_2$), and "triphosphoinositide" (I, X = Y = $PO_3H_2$) (1). Mono-, di-, tri-, tetra- and pentamannosides of phosphatidylinositol are present in the lipids of Mycobacterium tuberculosis and Mycobacterium phlei (2) and a substituted myoinositol phosphate also occurs in the phytoglycolipids (3). The complete structure of phosphatidylinositol has been established (1) and the inositol phosphate portion of the molecule has the configuration L-myoinositol 1-phosphate as shown in formula I (X = Y = H).




I




II

Synthetic work in this field has been limited by the lack of suitably substituted derivatives of myoinositol. DL-1, 3, 4, 5, 6-penta-O-acetyl-myoinositol has been used in a synthesis of racemic 1, 2-di-O-octadecanoylglycerol 3-(myoinositol 2-phosphate) (4) but compounds corresponding to the natural material have not been synthesised. Gero (5) has recently described a preparation of 2, 3, 4, 5, 6-penta-O-benzoyl-1-O-tosyl-(-)-inositol which might serve as an intermediate for the synthesis of phosphatidylinositol.

DL-2, 3, 4, 5, 6-penta-O-benzylmyoinositol (II, R' = $CH_2Ph$, R = H) would be a suitable intermediate for the synthesis of racemic phosphatidylinositol and Angyal and Tate (6) have described a preparation of this compound in very low yield (approx. 1%) by the partial benzylation of 3, 4, 5, 6-tetra-O-benzylmyoinositol (II, R = R' = H). Since the equatorial hydroxyl group was preferentially benzylated in this reaction the major product was 1, 3, 4, 5, 6-penta-O-benzylmyoinositol (II, R' = H, R = $CH_2Ph$).

We have shown recently (7) that the allyl ether is an effective protecting group in the preparation of benzyl ethers of carbohydrates and have now used the method in a synthesis of the title compound (II, R = H, R' = $CH_2Ph$). Compound II (R = R' = H) (2 g.) was treated with allyl bromide (1.5 mole) and powdered sodium hydroxide in refluxing benzene. The course of the reaction was followed by thin layer chromatography which showed an efficient conversion to the monoallyl derivatives (predominantly one isomer). The product was chromatographed on alumina to separate traces of starting material and the diallyl derivative. Recrystallisation of the monoallyl derivatives from light petroleum gave compound (II, R = $CH_2CH{=}CH_2$; R' = H), (1.1 g.), m.p. 63-66°(Found: C, 76.2; H, 6.6. $C_{37}H_{40}O_6$ requires C, 76.5; H, 6.9%. This compound was benzylated with benzyl chloride and sodium hydroxid and the product (II, R = $CH_2CH{=}CH_2$; R' = $CH_2Ph$) was purified by chromatography on alumina. The allyl group was removed by conversion to the prop-1-enyl group and subsequent acid hydrolysis (7) to give DL-2, 3, 4, 5, 6-penta-O-benzylmyoinositol (II, R = H, R' = $CH_2Ph$), m.p. 93-94° (from

light petroleum), 0.8 g., (35% yield from 3,4,5,6-tetra-O-benzyl-myoinositol) (Found: C, 78.2; H, 6.7. Calc. for $C_{41}H_{42}O_6$: C, 78.1; H, 6.7%) (lit.[6] m.p. 94-95°).

Angyal and Tate (6) have distinguished between the two isomers (II, R = H, R' = $CH_2Ph$, m.p. 94-5°) and (II, R = $CH_2Ph$, R' = H, m.p. 128-9°) by methylation and subsequent hydrogenation of the latter compound to give the known DL-2-O-methylmyoinositol.

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