Tetrahedron Letters,Vol.26,No.6,pp 807-808,1985
Printed in Great Britain

0040-4039/85 $3.00 + .00

A NOVEL APPROACH TO THE SYNTHESIS OF 1,2-cis-GLYCOPYRANOSIDES

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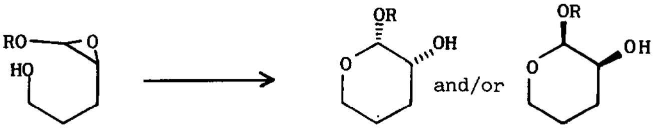
Summary: Methyl 3,4,6-tri-O-benzyl-α-D-glucopyranoside and methyl 3,4,6-tri-O-benzyl-β-D-mannopyranoside were directly obtained by m-chloroperbenzoic acid treatment of (Z)-(2R,3R,4R)-6-methoxy-1,3,4-tribenzyloxy-5-hexen-2-ol.

Stereospecific synthesis of glycosides is one of the most important problems in carbohydrate chemistry. Different glycoside-linking methods, which utilize the combination of a glycosyl activated component and a hydroxyl component have been employed.[1] However, the synthesis of 1,2-cis-glycosides from an activated sugar is still a difficult task.[1] On the other hand, the presence of the 1,2-cis-glycopyranosidic linkage in various naturally occurring oligo- and polysaccharides makes new synthetic methods welcome.

We wish here to report a novel approach according to which 1,2-cis-glycopyranosides of the type 2 and/or 3 are formed from an open chain precursor such as 1, with the aglycone moiety and the substituent at C-2 in the proper steric relationship (scheme 1), by intramolecular nucleophilic attack of the hydroxyl group at C-5 on an activated C-1.

SCHEME 1



1 2 3

2,3,5-Tri-O-benzyl-D-arabinose[2] was transformed, by reaction with diphenyl(methoxymethyl)phospine oxide, according to the procedure of Suzuki and Mukaiyama,[3] into (Z)-(2R,3R,4R)-6-methoxy-1,3,4-tribenzyloxy-5-hexen-2-ol 4[4,5](40%) and its E isomer 5[6](20%), easily separated by flash-chromatography. Treatment of 4(0.2 mmol)(scheme 2) with m-chloroperbenzoic acid(1.1 molar eq.) in $CHCl_3$ (r.t., overnight) and usual work-up afforded directly, without isolation of the intermediate epoxides 6 and 7, methyl 3,4,6-tri-O-benzyl-α-D-glucopyranoside 8[7] (35%) and methyl 3,4,6-tri-O-benzyl-β-D-mannopyranoside 9[8](20%), which were easily separated by silica gel chromatography. The structures of these compounds were confirmed by comparison with authentic samples.[9]

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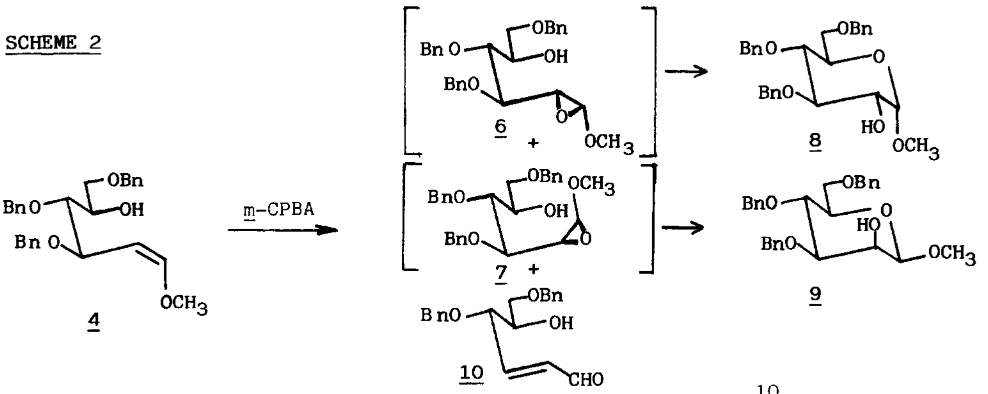
‡Fondazione "Guido Donegani" Fellow, June 1984-May 1985.

SCHEME 2



A small amount of (E)-(4S,5R)-4,6-dibenzyloxy-5-hydroxy-2-hexenal 10[10] (12%) was also obtained from the starting Z-enolether, owing to the slightly acidic reaction conditions.

These preliminary results indicate that the epoxidation of easily obtainable Z-enolethers such as 1, followed by the "in situ" spontaneous cyclization of the formed epoxides, constitutes an one-pot synthesis of 1,2-cis-glycopyranosides. The above procedure seems therefore quite attractive. Work is in progress to improve and extend these results.

References and Notes

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2. S. Tejima and H.J. Fletcher, J. Org. Chem., 28, 2999 (1963).
3. K. Suzuki and T. Mukaiyama, Chem. Lett., 683 (1982).
4. Satisfactory elemental analyses and spectroscopic data were obtained for all new compouns.
5. 4: oil, $[\alpha]_D^{20}$=-12.5°(c 1.2 in $CHCl_3$), ^1H-NMR($CDCl_3$,80MHz):δ 6.15, (d, 1H, J=5.5Hz, H-6).
6. 5: m.p. 53-54°C (from hexane), $[\alpha]_D^{20}$=-32°(c 1.0 in $CHCl_3$), ^1H-NMR($CDCl_3$,80MHz):δ 6.45, (d, 1H, $J_{5,6}$=13.5Hz, H-6); 4.83, (dd, 1H, $J_{5,6}$=13.5Hz, $J_{4,5}$=9Hz, H-5).
7. 8: m.p. 87-88°C (from hexane), $[\alpha]_D^{20}$= 98°(c 1.0 in $CHCl_3$); (lit.[11] m.p. 87-89°C, $[\alpha]_D^{20}$=100°)
8. 9: oil, $[\alpha]_D^{20}$=-13.2°(c 1.0 in $CHCl_3$); (lit.[12] $[\alpha]_D^{20}$=-10.2°).
9. 8 was obtained from the known methyl 2-O-acetyl-3,4,6-tri-O-benzyl-α-D-glucopyranoside[13] by CH_3ONa/CH_3OH hydrolysis.[14] 9 was obtained from the known methyl 3,4,6-tri-O-benzyl-β-D-arabino-hexosidulose[11] by $NaBH_4$ reduction according to Shaban and Jeanloz.[15]
10. 10: ^1H-NMR($CDCl_3$,80MHz):δ 9.59, (d, 1H, $J_{1,2}$=8Hz, H-1); 6.86, (dd, 1H, $J_{2,3}$=16Hz, $J_{3,4}$=5.5Hz, H-3); 6.30, (ddd, 1H, $J_{1,2}$=8Hz, $J_{2,3}$=16Hz, $J_{2,4}$=0.8Hz, H-2).
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(Received in UK 30 November 1984)