

Mercuricyclisation in Carbohydrate Chemistry: A Highly Stereoselective Route to α -D-C-Glucopyranosyl Derivatives

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Summary Mercuricyclisation of an olefin which is prepared from the carbohydrate 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose using a Wittig reaction provides the axial chloromercuri-ether as the only isolated product, thus offering the first stereospecific route to 1,5-*trans*-(e.g. α -D)-C-glucopyranosyl derivatives.

CHIRAL, substituted tetrahydropyranoid rings bearing various appendages contiguous to oxygen in either a *cis* or *trans* relationship are encountered as components of a variety of natural compounds.¹ In a carbohydrate context, these molecules may be regarded as C-glycopyranosyl derivatives.

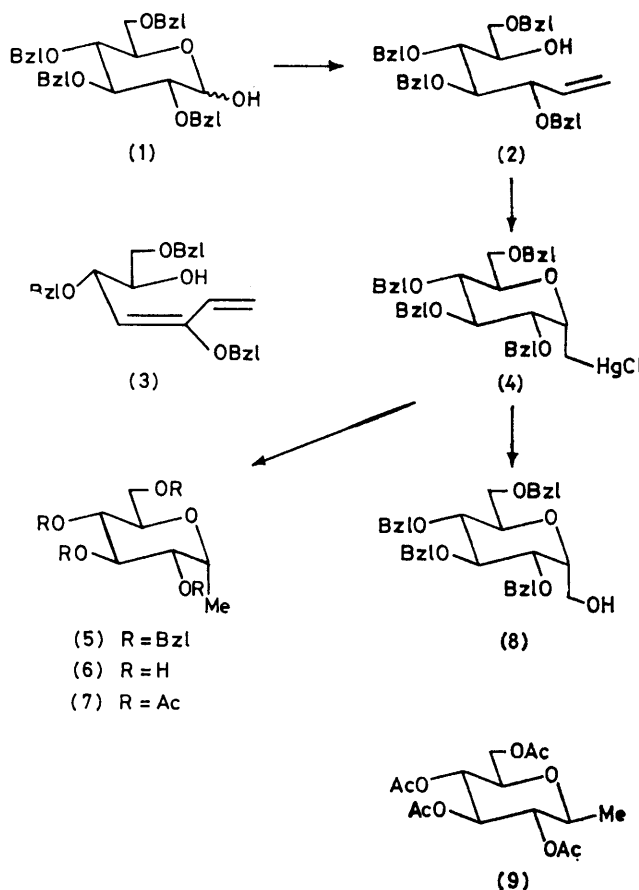
β -D-C-Glucopyranosyl derivatives, bearing C-1 and C-5 substituents in a *cis* relationship, may be prepared with a high degree of stereoselectivity from the reaction of per-*O*-acylglucosyl halide with various nucleophiles, and this approach is well documented.² However, as far as we know, no stereospecific route to 1,5-*trans*-(e.g. α -D)-C-glucopyranosyl derivatives has been reported to date, either intramolecular cyclisation of acyclic precursors^{3,4} or nucleophilic displacements at the anomeric centre resulting in a mixture of α - and β -D-C-glucopyranosyl derivatives. We report in this communication a novel highly stereoselective route to α -D-C-glucopyranosyl derivatives.

When the commercially available† 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (1) was submitted to a Wittig reaction with methylenetriphenylphosphorane ($\text{Ph}_3\text{PMeBr}^-$, Bu^nLi , toluene, 20 °C, 48 h) the unsaturated derivative (2)‡ was obtained after chromatography on silica (80%), b.p. (6×10^{-5} mmHg) 200 °C, $[\alpha]_D + 23^\circ$. Other conditions ($\text{Ph}_3\text{PMeBr}^-$, NaH, dimethyl sulphoxide) resulted in quantitative elimination to give the diene (3) (96%), $[\alpha]_D - 3^\circ$. Mercury-mediated cyclisation of the olefin (2) [i, $\text{Hg}(\text{OAc})_2$, tetrahydrofuran, 20 °C; ii, aqueous KCl] provided, after crystallisation, a single product to which we assigned structure (4) (98%), m.p. 104.5 °C (ether–light petroleum), $[\alpha]_D + 5.6^\circ$. Confirmation of this stereochemical assignment was obtained after the following transformations. Reductive demercuration of the chloromercuri-ether (4) using phase-transfer catalysis⁵ ($\text{BuEt}_3\text{N}^+\text{Cl}^-$, aqueous NaOH, NaBH_4 , CH_2Cl_2 , 10 min, 20 °C) provided the α -D-glucopyranosylmethane (5) (73%), m.p. 48 °C (hexane), $[\alpha]_D + 19.7^\circ$. Debenzylation (H_2 , Pd–C 10%, MeOH) gave (6) (100%), m.p. 184–185 °C (chloroform–methanol), $[\alpha]_D + 91^\circ$ (*c* 1, MeOH), which was easily converted (Ac_2O , pyridine) into the acetate (7) (91%), m.p. 64–65 °C (ether–hexane), $[\alpha]_D + 60.7^\circ$.

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‡ All new compounds had satisfactory microanalytical and spectral properties. Optical rotations were measured for solution in chloroform at 20 °C, unless otherwise stated.

§ C-Glucopyranosyl derivatives usually obey Hudson's rule of isorotation; see ref. 3.



Bzl = PhCH_2

The acetate (7) was easily distinguished on g.l.c. from the acetate (9), m.p. 81–82 °C, $[\alpha]_D + 1^\circ$, independently prepared by us.⁶ Using this analytical tool, we proved that less than 2% of the β -C-isomer was generated during the cyclisation process. This minute amount of β -chloromercuri-compound was readily eliminated after crystallisation, so that the reported procedure may be considered as stereospecific for preparative purposes.

¹H and ¹³C N.m.r. data and optical rotation data§ for compounds (5), (6), (7), and (9) indicated the α -D-configuration for (6), and a single-crystal X-ray diffraction study⁷ confirmed this assignment.

The remarkable selectivity of the mercuricyclisation may reasonably be explained by the strong directing effect of suitably oriented *O*-benzyl groups which are known⁸ to co-ordinate with the incoming mercurated species.

Interestingly, oxidative demercuration⁹ of the chloromercuri-ether (**4**) (O₂, NaBH₄, *NN*-dimethylformamide, 2 h) provided the alcohol (**8**) (81%), m.p. 64.5–65 °C (ethyl acetate–hexane), $[\alpha]_D +18.6^\circ$, so that the axially oriented one-carbon mercurated group is indeed well adapted for a variety of subsequent functionalizations.

In conclusion, this cyclisation provides the first stereospecific entry to 1,5-*trans*-(*e.g.* α -D)*C*-glucopyranosyl deri-

vatives. More generally, we feel that this reaction appears to be very attractive for the preparation of anomerically functionalized *C*-glycopyranosyl derivatives.

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¹ For some typical examples, see D. T. Connor, R. C. Greenough, and M. von Strandtman, *J. Org. Chem.*, 1977, **42**, 3664; E. W. Colvin, S. Malchenko, R. A. Raphael, and J. S. Roberts, *J. Chem. Soc., Perkin Trans. 1*, 1978, 658; F. J. McDonald, D. C. Campbell, D. J. Vanderah, F. J. Schmitz, D. M. Washecheck, J. E. Burks, and D. van der Helm, *J. Org. Chem.*, 1975, **40**, 665.

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