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

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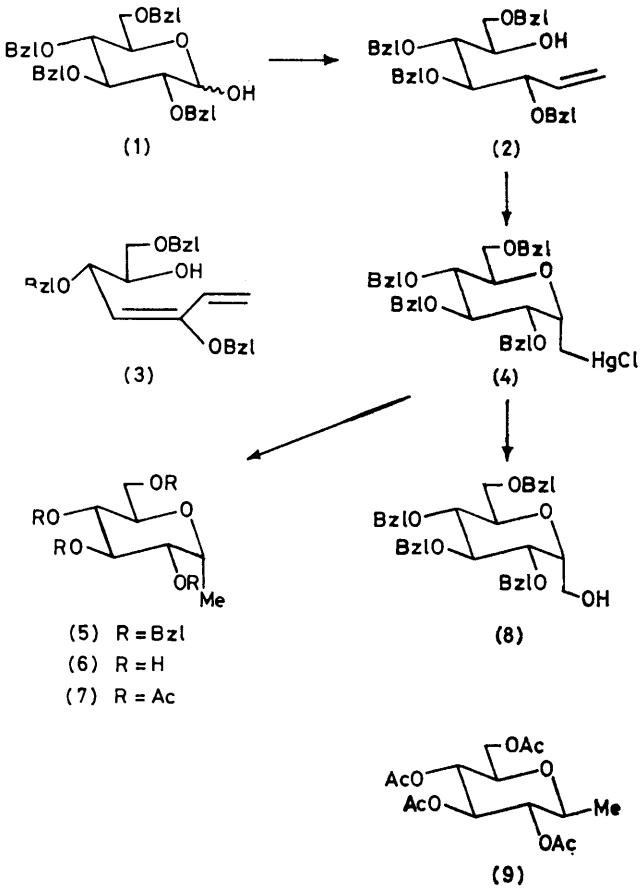
Summary Mercuricyclisation of an olefin which is prepared from the carbohydrate 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose using a Wittig reaction provides the axial chloromercuri-ether as the only isolated product, thus offering the first stereospecific route to 1,5-*trans*-(*e.g.* α-D)*C*-glucopyranosyl 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 ($Ph_3\overset{+}{P}MeBr^-$, 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°. Other conditions ($Ph_3\overset{+}{P}MeBr^-$, NaH, dimethyl sulphoxide) resulted in quantitative elimination to give the diene (**3**) (96%), $[\alpha]_D$ −3°. Mercury-mediated cyclisation of the olefin (**2**) [i, $Hg(OAc)_2$, 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°. Confirmation of this stereochemical assignment was obtained after the following transformations. Reductive demercuration of the chloromercuri-ether (**4**) using phase-transfer catalysis[5] ($BuEt_3N^+Cl^-$, 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°. Debenzylation (H_2, Pd–C 10%, MeOH) gave (**6**) (100%), m.p. 184—185 °C (chloroform–methanol), $[\alpha]_D$ + 91° (*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°.



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°, 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 ^{13}C 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 study[7] confirmed this assignment.

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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.

The remarkable selectivity of the mercuricyclisation may reasonably be explained by the strong directing effect of suitably oriented *O*-benzyl groups which are known[8] to co-ordinate with the incoming mercurated species.

Interestingly, oxidative demercuration[9] of the chloromercuri-ether (**4**) (O_2, $NaBH_4$, *NN*-dimethylformamide, 2 h) provided the alcohol (**8**) (81%), m.p. 64·5—65 °C (ethyl acetate–hexane), $[\alpha]_D$ +18·6°, 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 derivatives. 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.
[2] S. Hanessian and A. C. Pernet, *Adv. Carbohydr. Chem. Biochem.*, 1976, **33**, 111.
[3] B. Fraser-Reid, R. D. Dawe, and D. B. Tulshian, *Can. J. Chem.*, 1979, **57**, 1746. An *unsaturated* α-*C*-hex-2-enopyranosyl derivative has however been obtained in 85% yield by these authors from the Claisen rearrangement of a glycal.
[4] A. P. Kozikowski, R. J. Schmiesing, and K. L. Sorgi, *J. Am. Chem. Soc.*, 1980, **102**, 6577.
[5] M. C. Benhamou, G. Etemad-Moghadam, V. Speziale, and A. Lattes, *Synthesis*, 1979, 891.
[6] J.-R. Pougny, M. A. M. Nassr, and P. Sinaÿ, *Carbohydr. Res.*, to be published.
[7] A. Neuman, *Acta Crystallogr.*, to be published.
[8] H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 1959, 227.
[9] C. L. Hill and G. M. Whitesides, *J. Am. Chem. Soc.*, 1974, **96**, 870.