

Crystalline Pseudo- α -D-glucopyranose

Regine Blattner and Robert J. Ferrier*

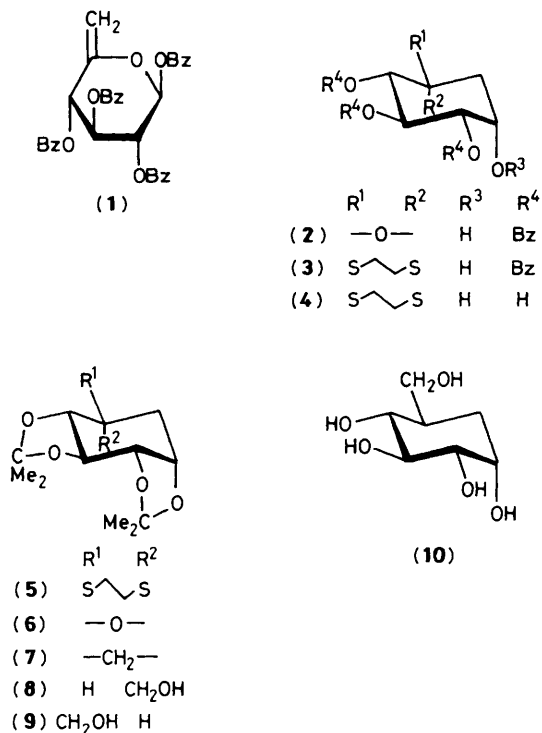
Department of Chemistry, Victoria University of Wellington, Private Bag, Wellington, New Zealand

Crystalline pseudo- α -D-glucopyranose, a compound of potential biochemical interest, has been obtained for the first time from a 6-deoxyhex-5-enopyranose derivative as starting material.

Since 'pseudo-sugar' was coined to describe monosaccharide analogues having a methylene group instead of the ring oxygen atom,¹ considerable attention has been given to these compounds, notably by S. Ogawa and his colleagues.² While recent work has reported pseudo-pentofuranoses and derived 'nucleosides',³ pseudo-ketoses,⁴ and pseudo-2-amino-2-deoxysugars,⁵ the main attention to date has been given to the pseudo-aldohexopyranoses. Initial synthetic studies were based on cyclohexene derivatives obtained as products of the Diels-Alder reaction, and they afforded racemic compounds, but recent work has concentrated on providing enantiomerically pure materials following the finding of pseudo-nucleosides,³ pseudo- α -D-galactopyranose,⁶ and related com-

pounds, for example validamine, valienamine, and validatol,⁷ in natural products, and the recognition of the potential value of carbocyclic compounds of this category in studies of specific enzymic inhibition.⁷

Our interest in the enantiomerically pure deoxyinosose derivatives, readily obtainable from 6-deoxyhex-5-enopyranosyl compounds,⁸ has led us to a synthesis of pseudo- α -D-glucopyranose which has particular potential for biochemical studies; the racemate⁹ has already been shown to inhibit glucokinase activity and glucose-stimulated insulin release.² The D-enantiomer was first reported in 1984 as a syrup with $[\alpha]_D +30^\circ$ (MeOH),¹⁰ but very recent reports record $+67^\circ$ (MeOH; synthesis from a resolved cyclohexane derivative²)



and +70° (water; synthesis by ring closure of a D-glucose-based phosphonate).¹¹ The present studies have produced a crystalline product with m.p. 151–152 °C and $[\alpha]_D^{25} +68.4^\circ$ (MeOH) and offer a relatively simple and unambiguous route.

The starting deoxyinosose (2), prepared from 1,2,3,4-tetra-O-benzoyl-6-deoxy- β -D-xylo-hex-5-enopyranose (1)¹² by treatment with mercury(II) acetate in aqueous acetone,⁸ was converted into the di-O-isopropylidene analogue (6) by way of the dithiolane triester (3), the tetraol (4), and its diacetal (5) in 78% yield. Removal of the thioacetal group was effected almost quantitatively by use of N-bromosuccinimide in aqueous acetonitrile in the presence of cadmium carbonate, and the ketone (6), on reaction with dibromomethane–zinc in dry tetrahydrofuran which had previously been treated by slow addition of titanium tetrachloride,¹³ gave the alkene (7) in 95% yield. Hydroboration afforded crystalline di-O-isopropylidene-pseudo- β -L-idopyranose (8) in 81% yield

together with small amounts (4% isolated) of the α -D-glucose isomer (9), but this desired thermodynamically preferred minor product was obtainable from the major (36% isolated crystalline) by oxidation with pyridinium dichromate in refluxing dichloromethane–dimethylformamide to give the corresponding aldehyde which was isomerised by treatment in dry methanol with solid potassium carbonate (polarimetric monitoring) and the product was reduced with sodium borohydride. Hydrolysis of the diacetal (9) was effected using hydrogen chloride in methanol and gave pseudo- α -D-glucopyranose in 96% yield (10).

¹H N.m.r. coupling analysis at 200 MHz (carbohydrate atom numbering, the ring methylene group taken as C-7) confirmed the structure of the compound: $J_{1,2}$ 3.1, $J_{1,7a}$ 2.3, $J_{1,7e}$ 4.1 (± 0.5), $J_{2,3}$ 9.8, $J_{3,4}$ 8.9, $J_{4,5}$ 10.4, $J_{5,6'}$ 5.2, $J_{5,6}$ 3.4, $J_{5,7a}$ 13.8, $J_{5,7e}$ 4.1, $J_{6,6'}$ 11.3, $J_{7a,7e}$ 15.2 Hz.

Professor H. Paulsen is thanked for providing reference 11 before its publication. We thank the Wellington Medical Research Foundation for financial support.

Received, 2nd January 1987; Com. 002

References

- G. E. McCasland, S. Furuta, and L. J. Durham, *J. Org. Chem.*, 1966, **31**, 1516.
- S. Ogawa, K. Nakamura, and T. Takagaki, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 2956 and earlier papers in this series.
- R. C. Cookson, P. J. Dudfield, and D. I. C. Scopes, *J. Chem. Soc., Perkin Trans. 1*, 1986, 393, 399.
- T. Suami, S. Ogawa, Y. Uematsu, and A. Suga, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 1261.
- D. H. R. Barton, S. D. Géro, S. Augy, and B. Quiclet-Sire, *J. Chem. Soc., Chem. Commun.*, 1986, 1399.
- S. Ogawa, Y. Iwasawa, F. Nose, T. Suami, S. Ohba, M. Ito, and Y. Saito, *J. Chem. Soc., Perkin Trans. 1*, 1985, 903.
- S. Ogawa, Y. Shibata, T. Nose, and T. Suami, *Bull. Chem. Soc. Jpn.*, 1985, **58**, 3387.
- R. J. Ferrier, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1455.
- S. Ogawa, T. Toyokuni, T. Kondoh, Y. Hattori, S. Iwasaki, M. Suetsugu, and T. Suami, *Bull. Chem. Soc. Jpn.*, 1981, **54**, 2739.
- T. Suami, K.-i. Tadano, Y. Kameda, and Y. Iimura, *Chem. Lett.*, 1984, 1919.
- W. von Deyn, Dissertation, University of Hamburg, 1986. The material has now been published: H. Paulsen and W. von Deyn, *Leibigs Ann. Chem.*, 1987, 125.
- R. Blattner, R. J. Ferrier, and P. C. Tyler, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1535; R. Blattner, R. J. Ferrier, and S. R. Haines, *ibid.*, 1985, 2413.
- L. Lombardo, *Tetrahedron Lett.*, 1982, **23**, 4293.