A New and Versatile Method for the Preparation of Unsaturated Sugars

By MICHEL BESSODES, ELIE ABUSHANAB,* and RAYMOND P. PANZICA*
(*Department of Medicinal Chemistry, University of Rhode Island, Kingston, Rhode Island* 02881)

Summary Reaction of vicinal diols with iodoform, triphenylphosphine, and imidazole gives the corresponding olefin in high to moderate yields.

In recent years the use of sugars as chiral synthons[1] has received increasing attention. Specifically, di- and trideoxyhexoses have been employed in the synthesis of complex natural products.[2,3] The most frequently used methods for the preparation of these compounds involve catalytic hydrogenation of di- and tri-deoxyhexenopyranosides.

The synthetic methods employed in the preparation of unsaturated sugars depend upon the stereochemical relationship of the starting vicinal diols. For example, in *cis* systems, cyclic acetals,[4] cyclic thiocarbonate *O*-esters,[5] and bisdithiocarbonates[6] are decomposed to form the olefins, whereas reductive elimination of a *trans* 1,2-diol system usually proceeds by treatment of a 1,2-disulphonate ester[7] with zinc and sodium iodide or by treating a 1,2-bisdithiocarbonate with tri-n-butyltin hydride.[6] Recently, two new methods have been reported which involve either the treatment of an unprotected 1,2-diol with triphenylphosphine, imidazole, and tri-iodoimidazole[8] or the decomposition of a 1,2-diol monotosylate with a mixture of sodium iodide, zinc–copper couple, dimethylformamide, and 1,2-dimethoxyethane at 130 °C.[9]

All of these methods suffer from certain drawbacks as they involve either multistep reactions or require the preparation of tri-iodoimidazole, whose synthesis is a cumbersome process especially on a large scale. The work described here avoids these drawbacks by using readily available starting materials and reagents to produce unsaturated sugars in high to moderate yields.

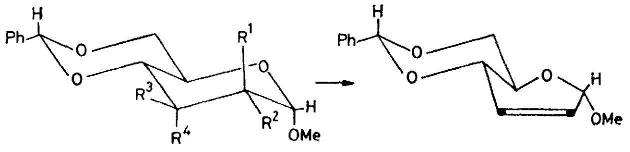
Since tri-iodoimidazole was used as an iodinating reagent,[8] it was rationalized that a similarly reactive iodinated compound might successfully replace it. Indeed, when the readily available iodoform was substituted for tri-iodoimidazole, the reaction proceeded smoothly during 1 h in refluxing toluene. In a typical experiment, to a solution of the diol (1 equiv.) in toluene was added triphenylphosphine (4 equiv.), iodoform (2 equiv.), and imidazole (2 equiv.), and the mixture was refluxed for 1 h with vigorous stirring. The cooled solution was washed with saturated sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated to dryness to yield a brown residue which was extracted with hot hexane. Evaporation of the hexane extract furnished the crude product which was crystallized from methanol–water (*ca.* 3:1).

Table. Conversion of methyl 4,6-*O*-benzylidene-α-D-hexopyranosides into the corresponding hex-2-enopyranosides

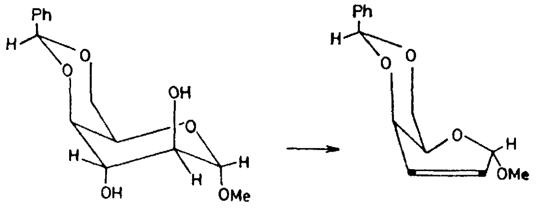
	Product	% Yield
(**1**) (*gluco*)	(**4**)[a]	80
(**2**) (*altro*)	(**4**)	65
(**3**) (*manno*)	(**4**)	45
(**5**) (*ido*)	(**6**)[b]	75

[a] M.p. 118—120 °C (lit. 119—120 °C: E. Albano, D. Horton, and T. Tsuchiya, *Carbohydr. Res.*, 1966, **2**, 349). [b] M.p. 150—151 °C (lit.,[6] 148—150 °C).

The reaction was found to be applicable to sugars containing *cis*- and *trans*-1,2-diols. Inspection of the Table reveals that sugar analogues having a *trans*-1,2-diol arrangement give better yields of the desired unsaturated compounds than their *cis* counterparts as illustrated with the glucose and mannose derivatives (**1**) and (**3**).

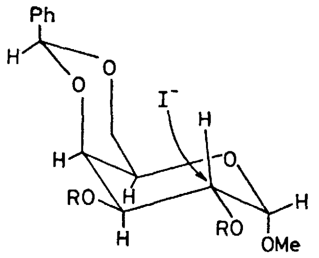


(1) $R^1 = R^4 = H$; $R^2 = R^3 = OH$
(2) $R^1 = R^4 = OH$; $R^2 = R^3 = H$
(3) $R^1 = R^3 = OH$; $R^2 = R^4 = H$ (4)



(5) (6)

A proposed mechanism involves iodide displacement of the oxyphosphonium groups resulting in the formation of a vicinal di-iodo derivative. Highest yields are observed when the iodo-substituent can assume a 1,2-diaxial configuration. Indeed, triphenylphosphine with tri-iodoimidazole or iodoform was found to convert sugars into iodosugars with inversion of configuration.[10,11] Reductive elimination of the di-iodo intermediate with imidazole then furnishes the unsaturated product. The postulated role imidazole plays in this reaction is supported by the fact that when it is eliminated from the reaction mixture, no unsaturated product is observed, while its replacement with zinc restores the formation of the olefin, but in poor yield.



$R = \overset{+}{P}Ph_3$

(7)

Methyl 4,6-*O*-benzylidene-α-D-galactopyranoside (**7**, R = H), a diequatorial 1,2-diol, failed to undergo this reaction. This led us to conclude that the formation of a 1,2-diaxial di-iodo derivative is not feasible in this case, possibly owing to a 1,3-diaxial interaction between the approaching iodide ion and the benzylidene oxygens. The fact that the 1,2-diaxial diols (**2**) and (**5**) undergo this elimination suggests that the pyranose form is in equilibrium with a skew form which allows the formation of the required di-iodide intermediate. The recent work of Angyal on methyl 4,6-*O*-benzylidene-α-D-idopyranoside supports this conclusion.[12]

This new method of reductive elimination is considered to be complementary to the already existing methods.

We thank Professor Leon Goodman for helpful discussions. This research was supported by a grant from the National Cancer Institute, National Institutes of Health, U.S. Public Health Service.

(*Received*, 17*th September* 1980; *Com.* 1024.)

---

[1] S. Hanessian, *Acc. Chem. Res.*, 1979, **12**, 159.
[2] A. H. Haines, *Carbohydr. Res.*, 1972, **21**, 99.
[3] S. Hanessian and R. Frenette, *Tetrahedron Lett.*, 1979, 3391.
[4] S. Hanessian, A. Bargiotti, and M. La Rue, *Tetrahedron Lett.*, 1978, 737.
[5] E. J. Corey and R. A. E. Winter, *J. Org. Chem.*, 1976, **41**, 896.
[6] A. G. M. Barrett, D. H. R. Barton, R. Bielski, and S. W. McCombie, *J. Chem. Soc., Chem. Commun.*, 1977, 866.
[7] R. S. Tipson and A. Cohen, *Carbohydr. Res.*, 1965, **1**, 338.
[8] P. J. Garegg and B. Samuelsson, *Synthesis*, 1979, 813.
[9] B. K. Radatus and I. S. Clarke, *Synthesis*, 1980, 47.
[10] P. J. Garegg and B. Samuelsson, *J. Chem. Soc., Chem. Commun.*, 1979, 978.
[11] M. Bessodes, D. C. J. Wu, E. Abushanab, and R. P. Panzica, unpublished results.
[12] S. J. Angyal and Y. Kondo, *Carbohydr. Res.*, 1980, **81**, 35.