

An Oxidative/Reductive, Non-hydrolytic Procedure for 'Unravelling' Complex Acetals (Glycosides): a Possible Chemical Role for the *exo*-Anomeric Effect

David R. Mootoo, Vandana Date, and Bert Fraser-Reid*

Department of Chemistry, Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27706, U.S.A.

A non-hydrolytic procedure has been developed for cleavage of complex acetals/glycosides in which one of the acetal oxygen atoms undergoes oxidative, bromine-induced addition to a remote olefinic centre, with formation of a tetrahydrofuran ring, which is subsequently cleaved reductively with zinc.

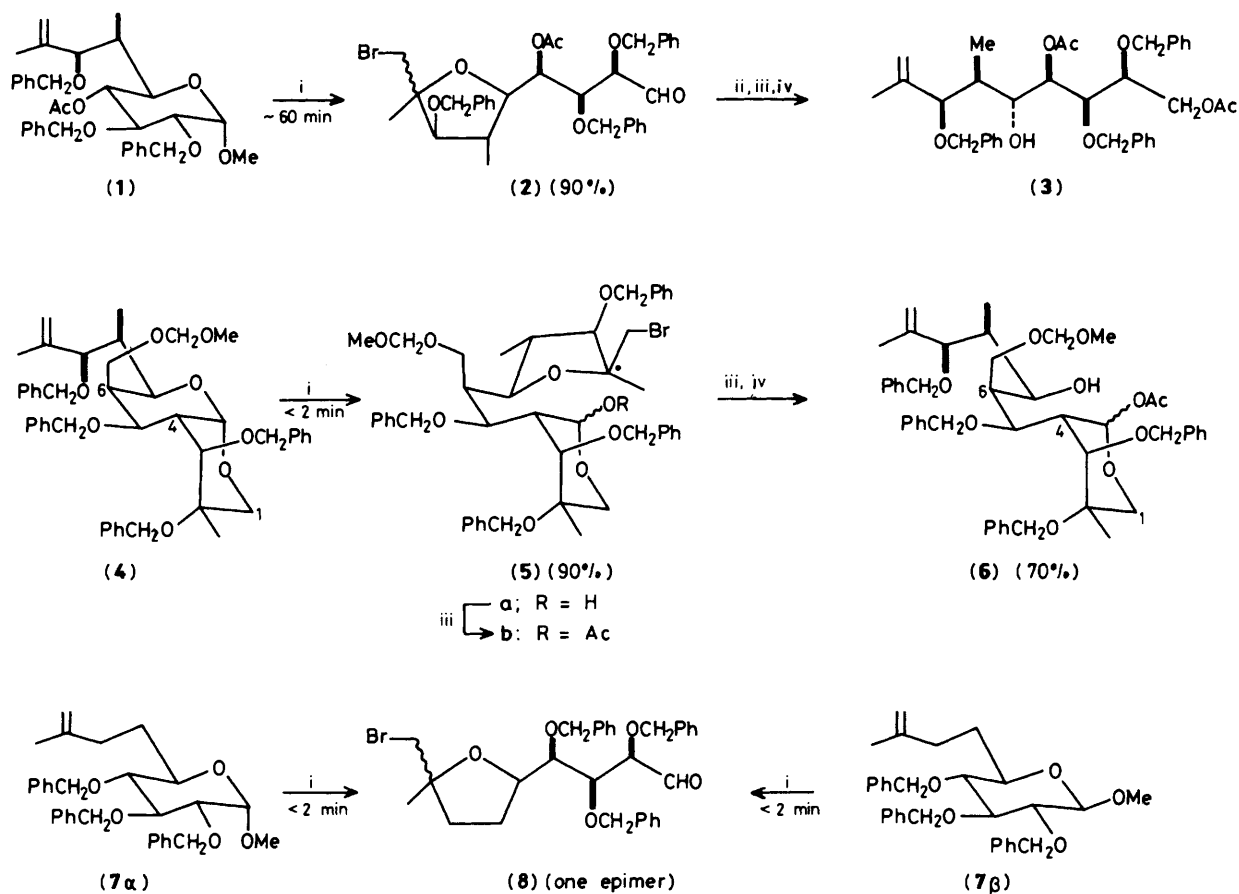
We recently described the concept of 'pyranosidic homologation' for a rational, stereocontrolled approach to systems containing multiple contiguous chiral centres, such as (**I**), in which tripyranoses, such as (**II**), were seen as advanced intermediates, the authenticity of which could be verified by simple ^1H n.m.r. analysis.¹ For the construction of this key intermediate, popular theories on stereoelectronic control² and the kinetic anomeric effect^{3,4} provided secure guidelines for predicting that the acetal oxygen atoms [*x* and *y* of (**II**)] would prefer to be axially oriented as was desired.^{1a}

However, 'unravelling' of condensed systems such as (**II**) [in order to obtain the linear equivalent (**I**)] was more problematic, since the 'rules' for cleavage of acetals/glycosides are not as well formulated as those for their creation. Furthermore, acid-catalysed procedures are ill-suited to these complex substrates in view of the threat of multiple side reactions. In

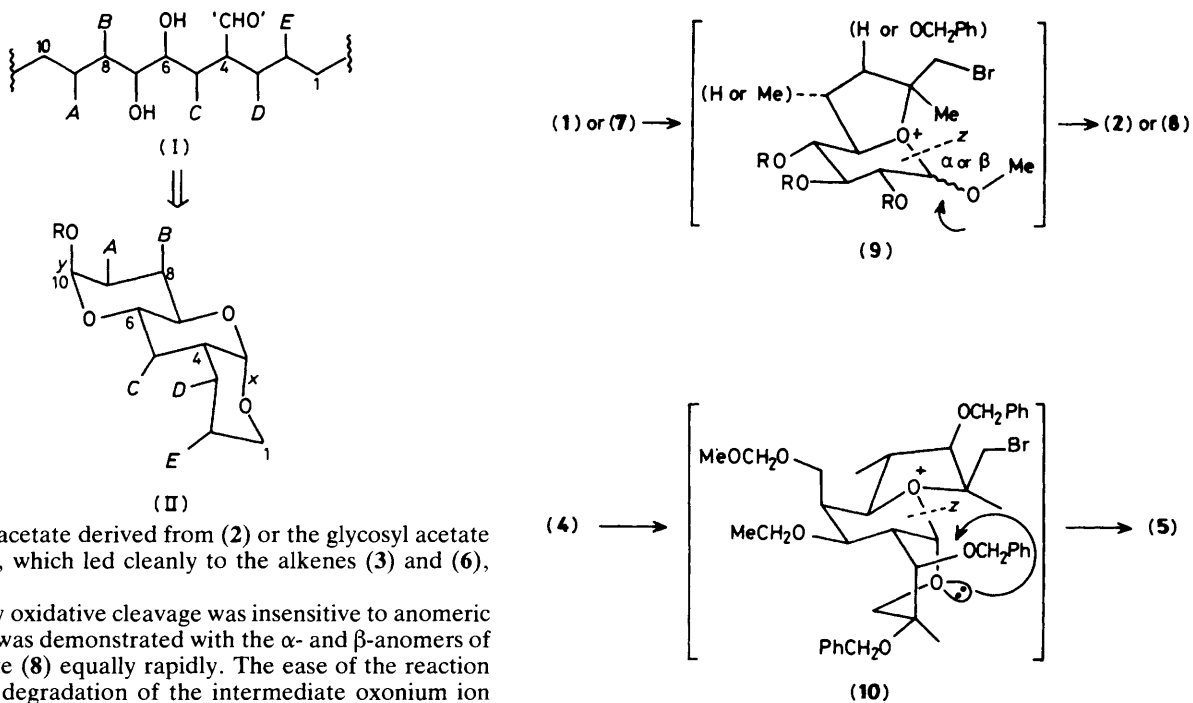
this manuscript, we describe a tandem oxidative/reductive protocol for unravelling complex acetals which *appears* to make use of concepts based on the *exo*-anomeric effect.⁵

The possibility of this non-hydrolytic procedure emanated from our recent observations of ready RO(5) participation of pyranoside ring oxygen in electrophilic reactions.⁶ Thus, attempts to obtain a bromohydrin by reaction of (**1**) with *N*-bromosuccinimide (NBS) in aqueous tetrahydrofuran at 0°C, led to the aldehyde(**2**). We have subsequently found that NBS in acetonitrile achieves the same transformation in *ca.* 60 min. It is noteworthy that under the latter conditions reaction of the complex array, (**4**), was complete within 2 min, giving the hemiacetal (**5a**) as the only isolable product.

The second stage in the unravelling procedure required cleavage of the bromomethyltetrahydrofuran ring of (**2**) and (**5**). This was also readily accomplished, nonhydrolytically, by



Scheme 1. Reagents: i, NBS/MeCN/NaHCO₃ (solid), 0°C; ii, NaBH₄/EtOH, 0°C; (iii), Ac₂O/EtOAc/4-dimethylaminopyridine; (iv), Zn/EtOH/NH₄Cl, reflux



treating the diacetate derived from (2) or the glycosyl acetate (5b) with zinc, which led cleanly to the alkenes (3) and (6), respectively.

That the key oxidative cleavage was insensitive to anomeric configuration was demonstrated with the α - and β -anomers of (7), which gave (8) equally rapidly. The ease of the reaction implies ready degradation of the intermediate oxonium ion

(9). Regardless of the anomeric configuration, there is an electron pair on the methoxy group which is ideally poised to assist in the breakage of bond z. This process may be regarded as a chemical consequence of the *exo*-anomeric effect.⁵

For these stereoelectronic demands to be met in the case of (4), it would be necessary for the lower ring to assume a boat-like conformation in order for the *exo*-anomeric effect to be expressed. An unrelated case in which conformation change is postulated as a prelude to 'spontaneous hydrolysis' has been described by Kirby and Martin.⁷

The differences in the rates of brominolysis of (1), (4), and (7) are intriguing and it is imperative to note that the study involving (1) and (4) was carried out competitively in the same medium. Experiments designed to provide a mechanistic rationalization are under way.

We thank the National Science Foundation (CHE 8304283) and the National Institutes of Health (GM 32569) for support of this research.

Received, 27th May 1987; Com. 721

References

- 1 (a) B. Fraser-Reid, L. Magdzinski, and B. Molino, *J. Am. Chem. Soc.*, 1984, **106**, 731; (b) B. Molino, L. Magdzinski, and B. Fraser-Reid, *Tetrahedron Lett.*, 1983, **24**, 5819; (c) L. Magdzinski, B. Cweiber, and B. Fraser-Reid, *ibid.*, 5823.
- 2 P. Deslongchamps, 'Stereoelectronic Effects in Organic Chemistry,' Pergamon, New York, 1983.
- 3 (a) R. Lemieux and N. J. Chu, Abstracts of Papers, Am. Chem. Soc., 1958, **31N**, 133rd Meeting, San Francisco, Calif., Apr. 13—18; (b) R. Lemieux in 'Molecular Rearrangements', ed. P. De Mayo, Interscience, New York, 1964, vol. 2, p. 702
- 4 A. J. Kirby, 'The Anomeric Effect and Related Stereoelectronic Effects at Oxygen,' Springer-Verlag, New York, 1983.
- 5 R. U. Lemieux, S. Kato, and D. Voisin, in 'The Anomeric Effect: Origin and Consequences,' eds. W. A. Szarek and D. Horton, Am. Chem. Soc. Symposium Series, no. 81, Washington, 1979.
- 6 D. R. Mootoo and B. Fraser-Reid, *J. Chem. Soc., Chem. Commun.*, 1986, 1570.
- 7 (a) A. J. Kirby and R. J. Martin, *J. Chem. Soc., Chem. Commun.*, 1979, 1079; (b) A. J. Kirby and R. J. Martin, *ibid.*, 1978, 803.