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

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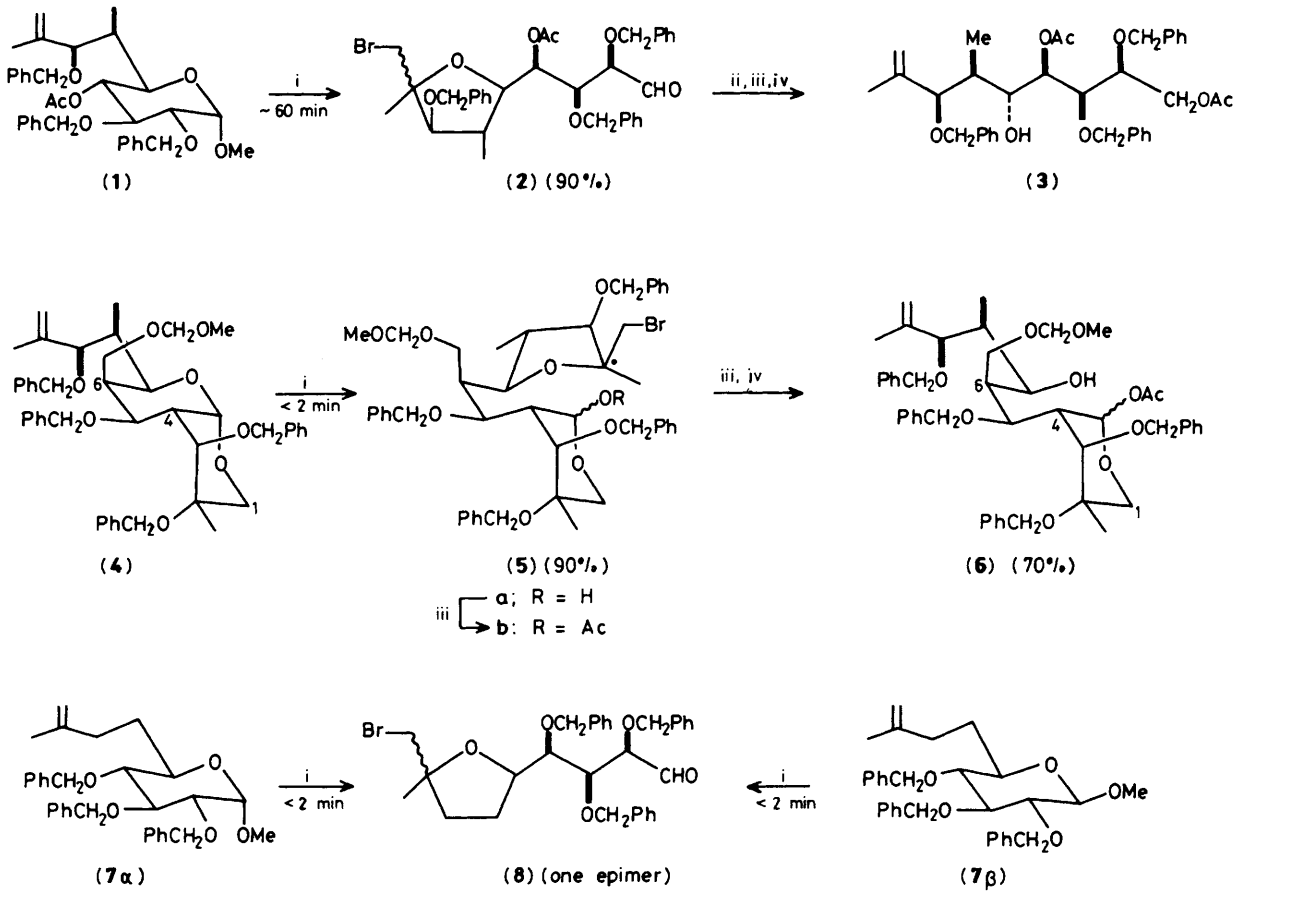
A non-hydrolytic procedure has been developed for cleavage of complex acetals/glycosides in which one of the acetal oxygen atoms undergoes oxidative, bromine-induced addition to a remote olefinic centre, with formation of a tetrahydrofuran ring, which is subsequently cleaved reductively with zinc.

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 $^1$H n.m.r. analysis.[1] For the construction of this key intermediate, popular theories on stereoelectronic control[2] 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]

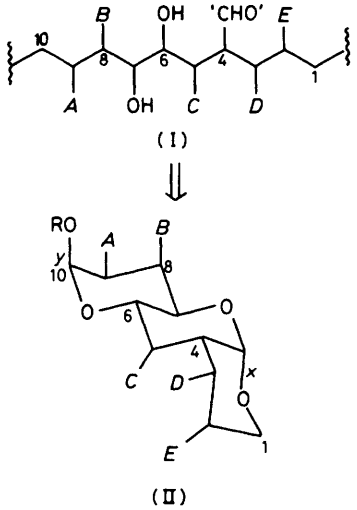
However, 'unravelling' of condensed systems such as (**II**) [in order to obtain the linear equivalent (**I**)] was more problematic, since the 'rules' for cleavage of acetals/glycosides are not as well formulated as those for their creation. Furthermore, acid-catalysed procedures are ill-suited to these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

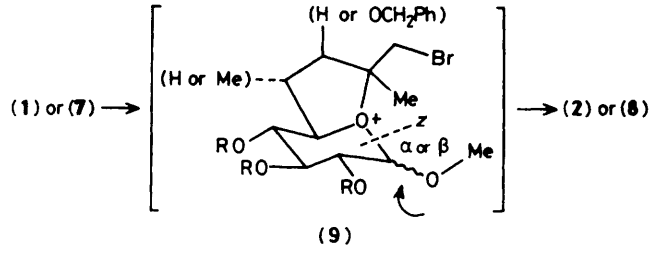
The possibility of this non-hydrolytic procedure emanated from our recent observations of ready RO(5) participation of pyranoside ring oxygen in electrophilic reactions.[6] Thus, attempts to obtain a bromohydrin by reaction of (**1**) with *N*-bromosuccinimide (NBS) in aqueous tetrahydrofuran at 0 °C, 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.

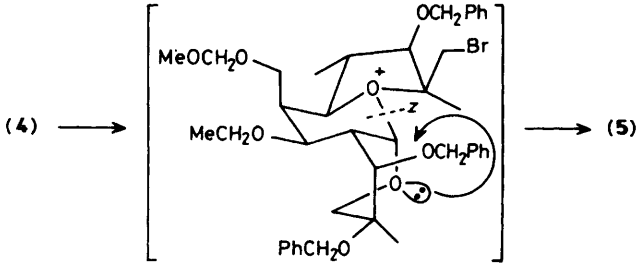
The second stage in the unravelling procedure required cleavage of the bromomethyltetrahydrofuran ring of (**2**) and (**5**). This was also readily accomplished, nonhydrolytically, by




**Scheme 1.** *Reagents:* i, NBS/MeCN/$NaHCO_3$ (solid), 0 °C; ii, $NaBH_4$/EtOH, 0 °C; (iii), $Ac_2O$/EtOAc/4-dimethylaminopyridine; (iv), Zn/EtOH/$NH_4Cl$, 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.

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