Stereoselective Reaction of Methyl α- and β-D-Glycopyranosides with Acetic Anhydride in the Presence of Trimethylsilyl Trifluoromethanesulphonate

Pierre Angibeaud and Jean-Pierre Utille
Centre de Recherches sur les Macromolécules Végétales, CNRS, B.P. 53X, 38041 Grenoble cedex, France

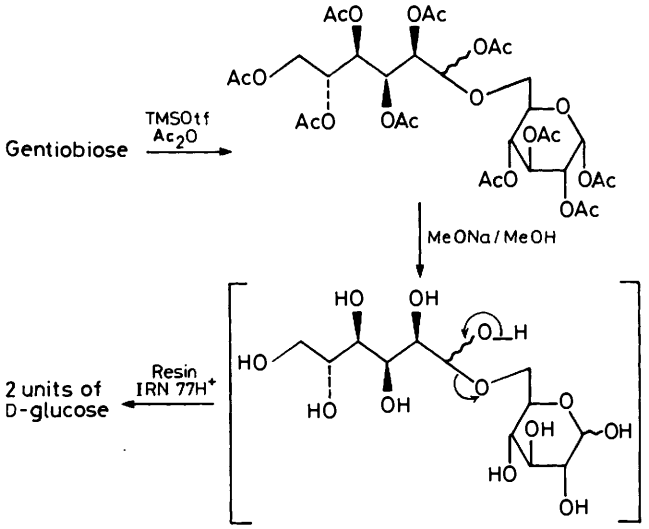
Treatment of methyl β-D-glycopyranosides with TMSOtf–Ac_2O gives acyclic products by selective cleavage of the ring carbon–oxygen bond, whereas methyl α-D-isomers undergo replacement of the anomeric methoxy by an acetoxy group with retention of configuration.

In a recent report,[1] we described the reaction at 0 °C of TMSOtf–Ac_2O with a disaccharide, namely 6-*O*-(β-D-glucopyranosyl)-D-glucopyranose (gentiobiose), to give, in good yield, two isomeric (*R,S*) deca-acetates resulting from ring opening of the non-reducing moiety and simultaneous peracetylation (Scheme).

This reaction was shown to be highly specific for the (1→6)-β-D-linkage (*e.g.* gentiotriose), whereas with (1→6) α-D-glucobiose (isomaltose) or other glucobioses no appreciable quantities of ring-opened products were detected, the expected octa-acetates with an axial anomeric acetoxy group being formed instead.

Interestingly, as observed with gentiobiose, treatment of the resulting ring-opened compounds with the Zemplén reagent (a catalytic amount of MeONa in MeOH) led to the cleavage of the initial interglycosidic (1→6) β-D-linkage(s) *via* hemiacetal species (Scheme).

In the light of these results, we have, in an extended study, examined the reaction of methyl α- and β-D-glucopyranosides (**1**) and (**2**) and three other methyl glycosides [mono-(**3**), di-(**4**) and tri-(**5**) saccharides] with TMSOtf–Ac_2O under identical conditions and made similar observations (Table). For example, treatment of methyl β-D-glucopyranoside (**1**) at 0 °C gave two products (thin layer chromatography), which were separated by



Scheme.

flash chromatography, identified by ^{1}H(300 MHz) and ^{13}C(75 MHz) NMR spectroscopy and mass spectrometry, and shown to be the acyclic enantiomers (**6a,b**)[2] 1,2,3,4,5,6-hexa-*O*-acetyl (*R,S*) 1-methoxy aldehydo-D-glucose. In contrast, similar treatment of methyl α-D-glucopyranoside[3] gave exclusive formation of 1,2,3,4,6-penta-*O*-acetyl-α-D-glucopyranose (retention of configuration).

The generality of this selective reaction was confirmed with other examples such as methyl α-D-mannopyranoside (**3**), methyl β-D-maltopyranoside (**4**), and methyl 6-*O*-(β-D-maltopyranosyl)-α-D-glucopyranoside (**5**) (see Table). With compound (**3**), 1,2,3,4,6-penta-*O*-acetyl-α-D-mannopyranose (**8**) is formed and with the disaccharide (**4**) the two nona-acetyl isomers (**9a,b**) 4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-1,2,3,5,6-penta-*O*-acetyl(*R,S*)-1-methoxyaldehydo-D-glucose; with (**5**) concomitant ring-opening and substitution of the methoxy by an α-acetoxy group occurs to give the two derivatives (**10a,b**). As seen for gentiobiose,[1] the Zemplén reaction applied to the resulting ring-opened products furnishes maltose from (**9a,b**) and maltose plus glucose from (**10a,b**); these compounds were identified, after re-acetylation by conventional methods, as their penta- and octa-acetyl derivatives (^{1}H and ^{13}C NMR and MS).

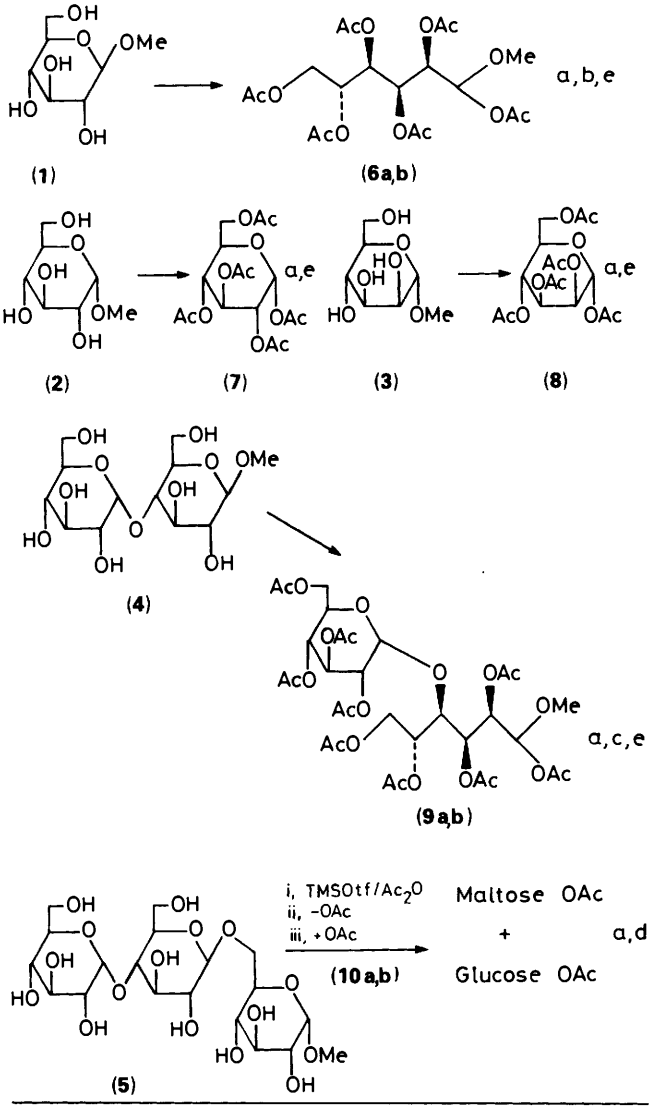
It is noteworthy that when the reaction is carried out with triflic anhydride in place of TMSOtf, identical results are obtained independent of whether the sugars were peracetylated or not; this shows the potentiality of this promotor.

This phenomenon of ring opening, indicative of a cleavage of the endocyclic carbon–oxygen bond, specifically observed both with methyl β-D-glycosides and compounds possessing (1→6) linkages in the β-D-configuration must be compared to that reported by Y. Guindon *et al.*[4] who studied the action of dimethylboron bromide (Me_2BBr) in the presence of a nucleophile towards methyl α- or β-D-glycopyranosides giving similar ring-opened products.

In our case, greater specificity is observed between methyl α-and β-D-isomers under milder experimental conditions (0 °C), and two different paths are strictly followed according to the configuration of the C-1 methoxy group; furthermore, when the substituent at the anomeric centre is a sugar linked by its C-6 primary hydroxy [see gentiobiose or (**5**)] the same stereospecificity is maintained.

The present selective reactivity can be explained by stereoelectronic considerations which will be discussed elsewhere. In addition to its theoretical interest, this reaction is also an easy way to prepare optically active acyclic molecules[5] of synthetic importance and whatever the anomer involved, a deacetylation under Zemplén conditions leads overall to the loss of the anomeric methoxy group under mild conditions.

Table. Reaction of methyl α- and β-D-glycopyranosides with acetic anhydride in the presence of TMSOtf.



[a] Identical results are obtained with starting peracetylated products. [b] NMR and MS data for these stereoisomers will be described elsewhere. [c] As expected, the product is a mixture of diastereoisomers as shown from the ^{13}C NMR spectrum. [d] The intermediary opened forms (**10a,b**) have not been isolated; only the two final peracetylated saccharides were identified. [e] Zemplén reaction gives anomerically deprotected sugar. No significant amount of by-product is observed and the final compounds are obtained in high yields (80–90%).

Experimental

The saccharide (acetylated or not, 1 mmol) was magnetically stirred in acetic anhydride (10–15 ml) at 0 °C (ice bath); trimethylsilyl trifluoromethanesulphonate (50% solution in dry dichloromethane; 1 mmol) was slowly added. When the reaction was over (1.5–2 h, TLC) the mixture was poured into $NaHCO_3$–ice-water and extracted with chloroform and the

extract dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

Pure diastereoisomers from compounds (**6a,b**) and (**9a,b**) were separated by flash chromatography (diethyl ether–hexane, 1.5:1 v/v). The products were characterized by ^1H and ^{13}C NMR and by FAB mass spectrometry. Free saccharides were obtained in good yields by deacetylation under Zemplén conditions followed by treatment with IRN 77 H^+ resin.

Acknowledgements

The authors thank Dr. H. Driguez (C.E.R.M.A.V) for useful discussions.

References

1 P. Angibeaud, C. Bosso, and J. P. Utille, *Carbohydr. Res.*, in press.
2 These acyclic forms were obtained in different experimental conditions by other authors; M. L. Wolfrom, M. Konigsberg, and F. B. Moody, *J. Am. Chem. Soc.*, 1940, **62**, 2343.
3 N. C. Barua, R. P. Sharma, and J. N. Baruah, *Tetrahedron Lett.*, 1983, **24**, 1189. Note: It has been argued that such a mixture of reagents would generate acylonium ions $MeC^{+}{=}O$ and it seems to be the case in our experimental conditions with the exocyclic C–O bonds giving acetate with retention of configuration.
4 Y. Guindon and P. C. Anderson, *Tetrahedron Lett.*, 1987, **28**, 2385.
5 S. Hanessian, 'Total synthesis of natural products: the chiron approach,' Pergamon Press, Oxford, 1983.

Paper 0/00512F
Received 6*th December* 1989
Accepted 2*nd February* 1990