

The Stability of Partially Methylated Methyl α -L-Arabinofuranosides towards Trifluoroacetylolysis

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Trifluoroacetylolysis is a versatile method for studies on glycoconjugates. Under trifluoroacetylolysis conditions that will effect transamidation of 2-acetamido-2-deoxy functions in sugar residues into 2-deoxy-2-trifluoroacetamido groups,¹ most reducing sugars and glycosides are stable and are converted into their pertrifluoroacetylated derivatives.^{2,3} The reason for the stability of glycosides and reducing sugars is that the *O*-trifluoroacetyl groups which are rapidly introduced exert strong inductive effects which reduce the electron density of the ring and glycosidic oxygens. Using trifluoroacetylolysis, methods have been devised for the isolation of *N*- and *O*-glycosidically linked carbohydrate chains in glycoproteins,⁴⁻⁶ for specific cleavage of the glycosidic linkage between the oligosaccharide and ceramide portions in glycolipids,⁷ and for specific degradation of reducing 2-acetamido-2-deoxyhexose residues.^{2,4-6} In order to elucidate the effect of differently positioned *O*-trifluoroacetyl groups in preventing solvolysis of glycosides, detailed investigations have been carried out using partially methylated methyl α -D-glucosides and xylopyranosides as models.^{8,9} In this communication the model compound studies are extended to trifluoro-

acetylolysis of partially methylated methyl α -L-arabinofuranosides.

The partially methylated methyl α -L-arabinofuranosides were synthesized from methyl α -L-arabinofuranoside¹⁰ using conventional techniques. All compounds were obtained as chromatographically pure syrups and their purity and identity was established by GLC-MS of their peracetylated derivatives.

The partially methylated methyl α -L-arabinofuranosides were treated with trifluoroacetic acid (TFA) and trifluoroacetic anhydride (TFAA) in the proportions 1:1 and 1:50 at 100 °C for 48 h. The reaction mixtures were then de-*O*-trifluoroacetylated, reduced, acetylated and analyzed by GLC-MS. The results are summarized in Table 1.

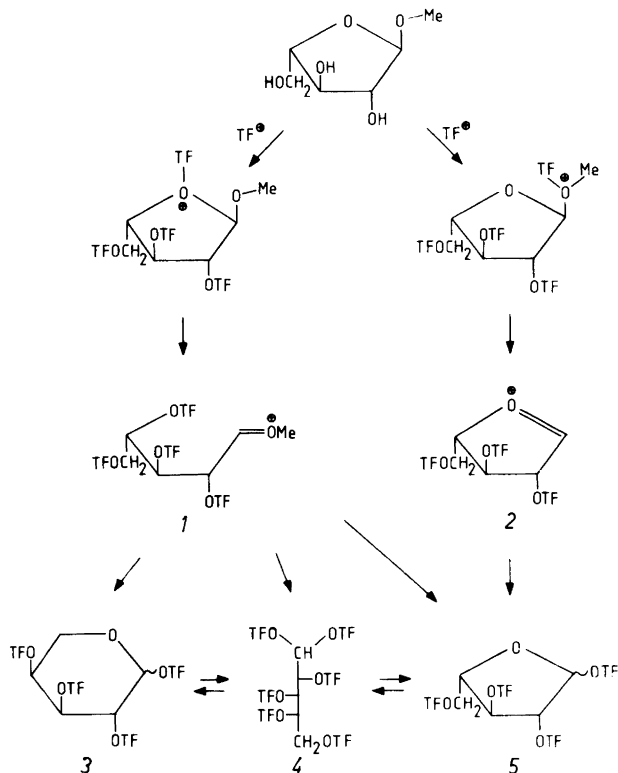
As can be seen from Table 1, methyl α -L-arabinofuranoside is stable as its pertrifluoroacetylated derivative during trifluoroacetylolysis using TFA/TFAA 1:50, whereas methyl 2,3,5-tri-*O*-methyl- α -L-arabinoside is completely solvolysed and further degraded. When the 3- or 5-position is methylated, the glycosidic bond is still essentially stable, but when the hydroxyl group in the 2-position is methylated, there is a slight decrease in stability.

Since solvolysis can be initiated by oxonium ion formation of the ring oxygen or the exocyclic glycosidic oxygen (Scheme 1), a 2-*O*-trifluoroacetyl group is the most effective in retarding this step since it is situated adjacent to C-1. *O*-Trifluoroacetyl groups in the 3- or 5-position can only effectively protect the ring oxygen from electrophilic attack. When only one *O*-trifluoroacetyl group can be introduced, the protective action decreases in the order 2->3->5-position. When trifluoroacetylolysis was carried out using TFA/TFAA in the proportions 1:1, methyl α -L-arabinofuranoside could only be recovered in about 70% yield. The rest was con-

Table 1. Trifluoroacetylolysis of partially methylated methyl α -L-arabinofuranosides using TFA/TFAA 1:1 and 1:50 at 100 °C for 48 h.

Location of methyl group(s)	Starting material		Recovery/mol % ^a				Total recovery	
	1:1	1:50	Anomerized product		Free sugar		1:1	1:50
O	68	101	20	<1	14	<1	102	101
2	<1	92	— ^b	6	87	5	87	103
3	20	98	8	<1	64	1	92	99
5	27	97	9	2	59	1	95	100
2,3	—	8	—	3	2	84	2	95
2,5	<1	41	—	<1	6	59	6	100
3,5	5	70	3	6	12	25	20	101
2,3,5	—	—	—	—	—	5	0	5

^a Determined after de-*O*-trifluoroacetylation, reduction (NaBD₄) and acetylation. ^b — = not detectable.



Scheme 1.

verted into the β -anomer or the solvolysed product(s). If the 2-position was blocked, the solvolysis was complete, whereas 20–30% of the glycoside was recovered when the 3- or 5-position was blocked. For glycosides with only one free hydroxyl the 2-hydroxyl compound was the only one that was not completely solvolysed.

The intermediate *1* may rearrange to give the anomerized product (Table 1) and by reacting further it could form the solvolysis products *3*, *4* or *5*, although none of these products were detected by the analytical method used which involved reduction (NaBD_4) and acetylation. The possible intermediate *2* could only react further to yield the solvolysis product *5* which then could produce *3* and *4*. The intermediates *1* and *2* and the pertrifluoroacetylated solvolysis products (*3*, *4* and *5*) may be degraded further *via* acid catalyzed eliminations. The results obtained in this investigation demonstrate that furanosidic bonds may be stable towards trifluoroacetylation using TFA/TFAA 1:50 providing that at least two hydroxyl groups are unsubstituted.

Experimental. Concentrations were performed at reduced pressure with bath temperatures not ex-

ceeding 40 °C. GLC-MS was carried out on a combined gas chromatograph-mass spectrometer (Varian MAT 311A). Separations were performed at 170 °C on glass capillary columns (50 m \times 0.25 mm) wall-coated with SE-30 (LKB-Products, Sweden). Mass spectral data were processed with an on-line computer system (Spectrosystem 100, Varian MAT). Quantitative analyses were performed using the above column fitted in a Perkin-Elmer 3920 gas chromatograph equipped with a flame ionisation detector.

Partially methylated methyl α -L-arabinofuranosides^{10,11} were obtained by standard synthetic procedures. The identity and purity of the compounds were established by GLC-MS of the corresponding acetates using principles previously outlined.¹² The identity was further corroborated by GLC-MS¹³ of the alditol acetates after hydrolysis, reduction, and acetylation.

Trifluoroacetylation experiments. The partially methylated methyl α -L-arabinofuranosides (12 mg) and xylitol or methyl α -D-glucopyranoside (6 mg) (as stable internal standard)³ were dissolved in methanol (3 ml) and 1 ml of the mixture was

analyzed by GLC-MS after acetylation to obtain response factors for the quantitative determinations. Other portions (1 ml) were dried and dissolved in TFA/TFAA (1:1 or 1:50, v/v) (4 ml) and were then heated in a sealed glass tube at 100 °C for 48 h (Caution! Corrosive mixture under pressure).

The mixtures were then cooled to room temperature and evaporated to dryness. The residues were dissolved in methanol (2 ml) and the solutions were evaporated to dryness. These residues were then dissolved in ethanol:water (2:1, v/v) (2 ml) and reduced with sodium borodeuteride (10 mg). The reduced products were acetylated and analyzed by GLC-MS. The identity of each component was established by its mass spectrum and retention time on GLC as compared with an authentic sample.

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1. Nilsson, B. and Svensson, S. *Carbohydr. Res.* 62 (1978) 377.
2. Nilsson, B. and Svensson, S. *Carbohydr. Res.* 65 (1978) 169.
3. Nilsson, B. and Svensson, S. *Carbohydr. Res.* 69 (1979) 292.
4. Nilsson, B. and Svensson, S. *Carbohydr. Res.* 72 (1979) 183.
5. Nilsson, B., Nordén, N. E. and Svensson, S. *J. Biol. Chem.* 254 (1979) 4545.
6. Lindberg, B., Nilsson, B., Norberg, T. and Svensson, S. *Acta Chem. Scand. B* 33 (1979) 230.
7. Lundsten, J., Svensson, S. and Svennerholm, L. *FEBS Lett. In press.*
8. Franzén, L.-E. and Svensson, S. *Carbohydr. Res.* 73 (1979) 309.
9. Franzén, L.-E. and Svensson, S. *Carbohydr. Res. In press.*
10. Augestad, I. and Berner, E. *Acta Chem. Scand.* 8 (1954) 251.
11. Maher, G. G. *Adv. Carbohydr. Chem.* 10 (1955) 262.
12. Kochetkov, N. K. and Chizhov, O. S. *Adv. Carbohydr. Chem.* 21 (1966) 39.
13. Björndal, H., Hellerqvist, C. G., Lindberg, B. and Svensson, S. *Angew. Chem. Int. Ed. Engl.* 9 (1970) 610.

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