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Note

The stability of partially methylated methyl α-D-xylopyranosides and D-xyloses towards trifluoroacetolysis

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Trifluoroacetolysis is carried out in mixtures of trifluoroacetic acid (TFA) and trifluoroacetic anhydride (TFAA) in various proportions and at different temperatures. 2-Acetamido-2-deoxy groups in sugar residues are converted into 2-deoxy-2-trifluoroacetamido groups by trifluoroacetolysis[1], using TFA/TFAA in proportions varying from 1 : 1 to 1 : 50, at 100° for 48 h. Under these conditions, most free sugars[2] and glycosides[3] are stable, due to the strong, inductive effects exerted by the *O*-trifluoroacetyl groups that are rapidly formed by the action of TFA/TFAA on hydroxyl groups in the sugar moieties. Peptide bonds are cleaved by transamidation, and thus proteins and the protein part of glycoproteins are degraded, whereas the carbohydrate portion of glycoproteins remains virtually intact, apart from some degradation at the reducing end[4]. *N*-Glycosylically linked carbohydrate-chains are cleaved from glycoproteins by transamidation[4], and *O*-glycosylically linked carbohydrate-chains (to serine or threonine) are cleaved by acid-catalysed elimination[4,5]. Trifluoroacetolysis can also be used for specific cleavage of the glycosidic linkage between the oligosaccharide and ceramide portions in glycolipids[6].

In order to study the stabilising effects of *O*-trifluoroacetyl groups in preventing solvolysis of glycosides, the trifluoroacetolysis of partially methylated methyl α-D-glucopyranosides[7] was investigated. We now report on an extension of these studies to partially methylated methyl α-D-xylopyranosides and partially methylated D-xyloses.

The model compounds were treated with TFA/TFAA in the proportions 1 : 1 and 1 : 50 for 48 h, together with a stable, internal standard (xylitol or methyl α-D-glucopyranoside).

After *O*-detrifluoroacetylation, reduction, and acetylation, the resulting mixtures were analysed by g.l.c.–m.s.[8] (Tables I and II). The data in Table I show that methyl 2,3,4-tri-*O*-methyl-α-D-xyloside was completely destroyed under both trifluoroacetolysis conditions, presumably *via* solvolysis and acid-catalysed elimination reactions occurring on the pertrifluoroacetate (*cf.* Table II). For the analogues having one free-hydroxyl group, some unchanged glycoside could be recovered after the 1 : 50 tri-

TABLE I

TRIFLUOROACETOLYSIS OF PARTIALLY METHYLATED METHYL α-D-XYLOPYRANOSIDES WITH TFA/TFAA

Location of methyl group(s)	*Recovery (mol%)*[a]					
	Starting material		*Free sugar*		*Total recovery*	
	1:1	*1:50*	*1:1*	*1:50*	*1:1*	*1:50*
0	92	99	4	—[b]	96	99
2	4	91	18	9	22	100
3	43	97	18	<1	70[c]	97
4	47	97	8	1	55	98
2,3	—	25	4	8	4	33
2,4	—	2	—	<1	—	2
3,4	—	12	—	2	—	14
2,3,4	—	—	—	—	—	—

[a]Determined after *O*-detrifluoroacetylation, reduction ($NaBD_4$), and acetylation. [b]Not detected. [c]This value includes 9% of anomerised product.

TABLE II

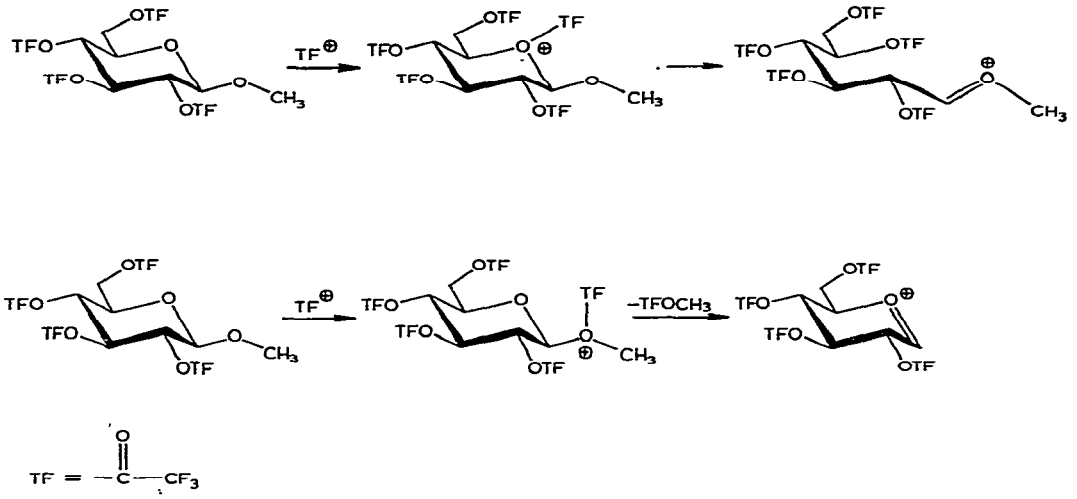
TRIFLUOROACETOLYSIS OF PARTIALLY METHYLATED D-XYLOSES WITH TFA/TFAA

Location of methyl group(s)	*Recovery (mol%)*[a]	
	Starting material	
	1:1	*1:50*
0	97	100
2	71	98
3	62	94
4	6	65
2,3	12	60
2,4	—[b]	<1
3,4	—	3
2,3,4	—	—

[a]Determined after *O*-detrifluoroacetylation, reduction ($NaBD_4$), and acetylation. [b]Not detected.

fluoroacetolysis. The stabilising effects were somewhat larger for a 4-*O*-trifluoroacetyl group than for a 2-*O*-trifluoroacetyl group; a 3-*O*-trifluoroacetyl group had a small, protective effect.

The first step in the trifluoroacetolysis reaction on the glycosidic bond should involve ionisation of the ring oxygen or the exocyclic aglycon-oxygen (Scheme 1). It is therefore not surprising that a 4-*O*- or a 2-*O*-trifluoroacetyl group is more effective than a 3-*O*-trifluoroacetyl group in lowering the rate of solvolysis. Methyl α-D-xylopyranosides having two free hydroxyl groups were essentially stable in 1:50 TFA/TFAA, but considerable solvolysis occurred in the 1:1 reagent (Table I). Little or



Scheme 1. Possible mechanisms for the solvolysis of a glycosidic bond by trifluoroacetolysis.

no anomerisation was observed, except for methyl 3-*O*-methyl-α-D-xylopyranoside in 1:1 TFA/TFAA.

The partially methylated D-xyloses were rapidly converted into their pertrifluoroacetylated derivatives. Pertrifluoroacetylated 2,3,4-tri-*O*-methyl-D-xylose was completely degraded in both 1:50 and 1:1 TFA/TFAA. This degradation is probably initiated by acid-catalysed elimination reactions, and a 4-*O*-trifluoroacetyl group is more effective in preventing this degradation than 2-*O*- or 3-*O*-trifluoroacetyl groups (Table II).

EXPERIMENTAL

Concentrations were performed at reduced pressure with bath temperatures not exceeding 40°. G.l.c.–m.s. was performed on a Varian MAT 311A combined gas chromatograph–mass spectrometer. Separations were performed at 170° on glass-capillary columns (50 m × 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 by using the above column fitted in a Perkin–Elmer 3920 gas chromatograph equipped with a flame-ionisation detector.

Partially methylated methyl α-D-xylopyranosides. — These were obtained by standard, synthetic procedures. The identity and purity of the compounds were established by g.l.c.–m.s. of the corresponding acetates[8].

Partially methylated D-xyloses[9]. — These were obtained from the corresponding methyl glycoside by hydrolysis with 0.25M sulphuric acid at 100° for 18 h. The identity and purity of the compounds were established by g.l.c.–m.s. of the corresponding alditol acetates.

Trifluoroacetolysis experiments. — Each partially methylated methyl α-D-xylopyranoside or partially methylated D-xylose (9 mg) and xylitol or methyl α-D-glucopyranoside (6 mg; as stable, internal standard) were dissolved in methanol (3 ml), and 1 ml of the mixture was analysed by g.l.c.–m.s. after acetylation (xylosides) and reduction–acetylation (xyloses), to obtain response factors for the quantitative determinations. Other portions (1 ml) were evaporated to dryness, and solutions of the residues in TFA/TFAA (1 : 1 or 1 : 50; 4 ml) were then heated in a sealed glass-tube at 100° for 48 h (caution: corrosive mixture under pressure).

Each mixture was then cooled to room temperature and evaporated to dryness. The residue was dissolved in methanol (2 ml) and the solution was evaporated to dryness. The residue was then dissolved in ethanol–water (2:1, 2 ml) and reduced with sodium borodeuteride (10 mg). Each reduced product was acetylated, and analysed by g.l.c.–m.s. The identity of each component was established by its mass spectrum and retention time in g.l.c., as compared with an authentic sample.

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