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Note

A new, efficient method for hydrolysis of the anomeric acetyl group in substituted hexopyranoses

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Protected hexopyranoses having the anomeric hydroxyl group unsubstituted are useful in the synthesis of trehaloses[1–3], trehalosamines[4–6], glycosides and oligosaccharides[7–9].

Many methods for the solvolysis of an anomeric acetyl group have been reported[9,10]. The reaction with hydrogen halide followed by silver carbonate-mediated hydrolysis of glycosyl halides[11] has been the main method for the removal of AcO-1 from aldose derivatives and we have sought a direct and simple method. AcO-1 is a good leaving-group and is amenable to nucleophilic displacement. Thus, AcO-1 in 1,2-*trans*-acetylated pyranoses can be exchanged for an alkoxyl[12,13], thioalkyl[14], or sugar moiety[13] in the presence of Lewis acids as catalysts. The susceptibility of AcO-1 in aldose derivatives to solvolysis was demonstrated in studies of the formation of acetoxonium ions on treatment with Lewis acids[14,15]. However, this reaction has not been used on a preparative scale for hexopyranose derivatives having HO-1 unsubstituted. We now report such an approach using stannic tetrachloride and water.

The reaction of 1-*O*-acetyl-α- and -β-hexopyranoses, protected in other positions with ester or ether groupings (Table I), with water and stannic tetrachloride in acetonitrile resulted in solvolysis of AcO-1 within 1 h at room temperature for compounds containing 1,2-*trans*-acetoxy groups, and at 40° for 1,2-*cis* compounds, to give the product compounds in high yields (Table I). 1,2,3,4,6-Penta-*O*-acetyl-α-D-glucopyranose underwent 75% solvolysis only, and 25% of the substrate was recovered. Such a lowered reactivity accords with observations[14] of the rate of exchange of AcO-1 in 1,2-*cis* and -*trans* acetylated pyranoses catalysed by Lewis acids, and confirms the anchimeric assistance provided[14] by the ester group at C-2.

Removal of AcO-1 from benzylated pyranose derivatives proceeded cleanly and in nearly quantitative yield, leaving the benzyl groups intact. The scope of the reaction was demonstrated further with 1,6-di-*O*-acetyl-2,3,4-tri-*O*-benzyl-α,β-D-galactopyranose (**10**), for which solvolysis of AcO-1 by alkaline reagents is excluded. Since the solvolysis of **10** as well as of 1,2-*cis* acetylated aldoses cannot

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TABLE I

YIELDS AND PHYSICAL CONSTANTS OF SUBSTITUTED HEXOPYRANOSES HAVING HO-1 UNSUBSTITUTED[a]

Starting derivative	*T.l.c. solvent system*	*Yield (%)*	*M.p. (degrees)*		$[\alpha]_D$ (c, *chloroform*) *(degrees)*		*Ref.*
			This work	*Lit.*	*This work*	*Lit.*	
1,2,3,4,6-Penta-*O*-acetyl-α-D-galactose (**1**)	*A*	88	136–138	133	133 (1.9)	144 (1.0)	16
1,2,3,4,6-Penta-*O*-acetyl-β-D-galactose (**2**)	*A*	92	139–140		139 (2.4)		
1,2,3,4,6-Penta-*O*-acetyl-α-D-glucose (**3**)	*A*	67	126–129	107	96 (1.5)	139 (0.9)	17
1,2,3,4,6-Penta-*O*-acetyl-β-D-glucose (**4**)	*A*	79	107–110		48 (1.5)		
1,2,3,4,6-Penta-*O*-acetyl-α-D-mannose (**5**)	*A*	98	95–96	93	30 (1.7)	26	18
1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucose (**6**)	*D*	80	170–171[a]	178	59 (1.7)	74 (0.5)	19
1,3,6-Tri-*O*-acetyl-4-deoxy-2-*O*-tosyl-α-D-xylose (**7**)	*A*	64	syrup[b]		58 (1.5)		
1-*O*-Acetyl-2,3,4,6-tetra-*O*-benzyl-α-D-glucose (**8**)	*B*	97	152–155	148	21 (1.6)	21 (2.5)	1
1-*O*-Acetyl-2,3,4-tri-*O*-benzyl-6-deoxy-α-L-mannose (**9**)	*B,C*	91	88–89	90	15 (1.1)	15 (1.0)	20
1,6-Di-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-galactose (**10**)	*B*	87	syrup[c]		14 (1.5)		

[a]αβ-Mixtures, except **6**, which was isolated as the β anomer. [b]N.m.r. data ($CDCl_3$): *inter alia*, δ 5.15–5.40 (m, 1 H, $J_{3,4}$ 10 Hz, H-3), 4.70 (pd, 1 H, $J_{2,3}$ 10 Hz, H-2), 4.03–4.22 (m, 3 H), 1.9–2.2 (m, 8 H, H-4,4' and 2 OAc). *Anal.* Calc. for $C_{17}H_{22}O_9S$: C, 50.74; H, 5.51; S, 7.97. Found: C, 51.02; H, 5.55; S, 7.82. [c]N.m.r. data ($CDCl_3$): *inter alia*, δ 7.1–7.2 (m, 15 H, 3 Ph), 4.4–5.0 (m, 7 H), 3.8–4.2 (m, 6 H). *Anal.* Calc. for $C_{29}H_{32}O_7$: C, 70.71; H, 6.55. Found: C, 70.93; H, 6.68.

proceed through a 1,2-acyloxonium ion, the reaction probably involves an S_N2 mechanism.

We believe that the above one-step procedure is markedly superior to the traditional methods.

EXPERIMENTAL

The homogeneity and structures of the solvolysis products of **1–10** were assigned on the basis of t.l.c., analytical, and spectral data, by comparison with authentic compounds. The $\alpha\beta$-ratios of the products were not determined. Therefore, some physicochemical data differ from those in the literature (see Table I).

^{1}H-N.m.r. spectra were recorded with a Jeol-4H-100 spectrometer. Optical rotations were measured with a Perkin–Elmer 141 automatic polarimeter. T.l.c. was performed on Silica Gel HF_{254} (Merck) with *A*, hexane–ethyl acetate (1:1); *B*, hexane–ethyl acetate (4:1); *C*, hexane–acetone (3:1); *D*, toluene–acetone (7:3).

Solvolysis procedures. — (*a*) To a solution of each of the 1,2-*trans*-substituted derivatives **2** and **4–6** (0.39 g, 1 mmol) in acetonitrile (5 mL) was added stannic tetrachloride (0.24 mL, 2 mmol) with stirring at 0°. After 1 h at room temperature, the mixture was treated with 2M water in acetonitrile (1 mL) and stirring was continued until t.l.c. showed that disappearance of the substrate was complete. The mixture was then poured into saturated aqueous sodium hydrogencarbonate and extracted with ether. The extract was dried and concentrated to give the 2,3,4,6-tetra-*O*-acetyl-α,β-D-hexopyranose (Table I) which was then crystallised, or purified by filtration through a short column of silica gel if necessary.

(*b*) Each of the 1,2-*cis*-substituted derivatives **1, 3**, and **7** was treated as in (*a*), except that water was added as a 2M solution in acetonitrile containing 0.2M *N,N*-dimethylformamide and the mixture was heated at 40°.

(*c*) A solution of each of the derivatives **8–10** (1 mmol) in acetonitrile (4 mL) containing water (0.072 mL) and *N,N*-dimethylformamide (0.016 mL) was treated with stannic tetrachloride (0.09 mL, 0.7 mmol) added at −20° with stirring. After 1 h, the bath temperature was raised to 15° and stirring was continued until the disappearance of the starting material was complete (t.l.c.). The product was then isolated as described in (*a*); the product from **8** crystallised directly from the reaction mixture.

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