

Note

Regioselective heterogeneous O-deacylation of polyacylated sugars*

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(Received November 8th, 1985; accepted for publication, January 3rd, 1986)

The advantages (selectivity, mildness, and operational simplicity) of organic reactions effected by reagents immobilised on solid supports have prompted an investigation of the deacylation of acylated sugar derivatives catalysed by solid insoluble catalysts such as magnesium oxide or alumina. Chemical reactions carried out on alumina surfaces have been reviewed², and the deacetylation of a primary steroidal acetate group during chromatography on alumina has been reported³.

We have reported on the cyanide-catalysed methanolysis of acyl groups for a variety of sugar derivatives¹ and we now report on the regioselective methanolysis of polyacylated carbohydrates catalysed by magnesium oxide or alumina.

Magnesium oxide has not been employed hitherto as a general catalyst for transesterification. Malmstrom reported⁴ the transesterification of several acetates by alcohols, catalysed by basic metal oxides, and showed that magnesium oxide was more active than alumina. We have found that magnesium oxide catalysed non-selective and quantitative methanolysis of polyacylated sugars during 0.5–6 h at room temperature (Table I). In many respects, the deacylation resembles the cyanide-catalysed reaction, but magnesium oxide is non-toxic. Moreover, a comparison with the classic Zemplén deacylation⁵ reveals that the use of sodium methoxide is not always desirable because of its strong basicity, nucleophilicity, air sensitivity, *etc.*, whereas magnesium oxide is easy to handle, stable, and readily removable by filtration.

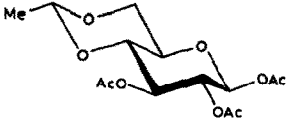
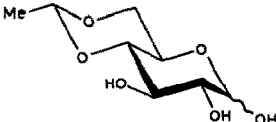
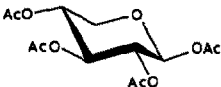
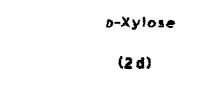
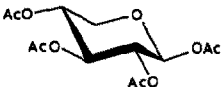
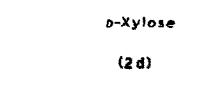
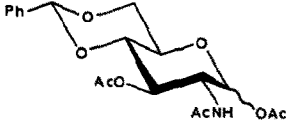
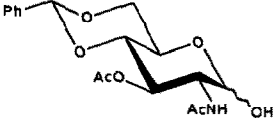
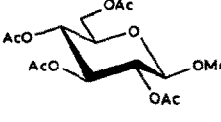
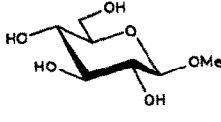
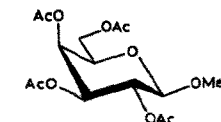
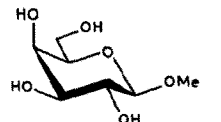
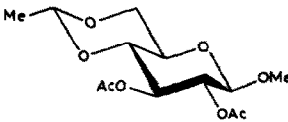
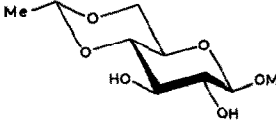
El-Shenawy and Schuerch⁶ have described the use of methanolic magnesium methoxide for the deesterification of galactopyranosides. Using a 10-mol excess of $Mg(OMe)_2$, no reaction took place during 6 h, whereas with $MgO/MeOH$ as a heterogeneous mixture, deacylation was complete within 6 h, implying a different

*Studies in Sugar Chemistry, Part III. For Part II, see ref. 1.

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TABLE I

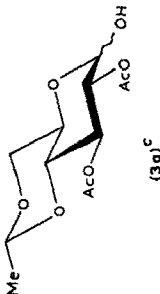
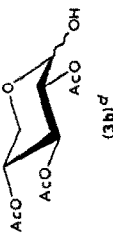
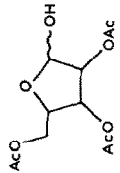
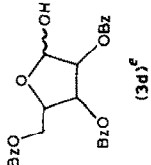
MAGNESIUM OXIDE-CATALYSED METHANOLYSES

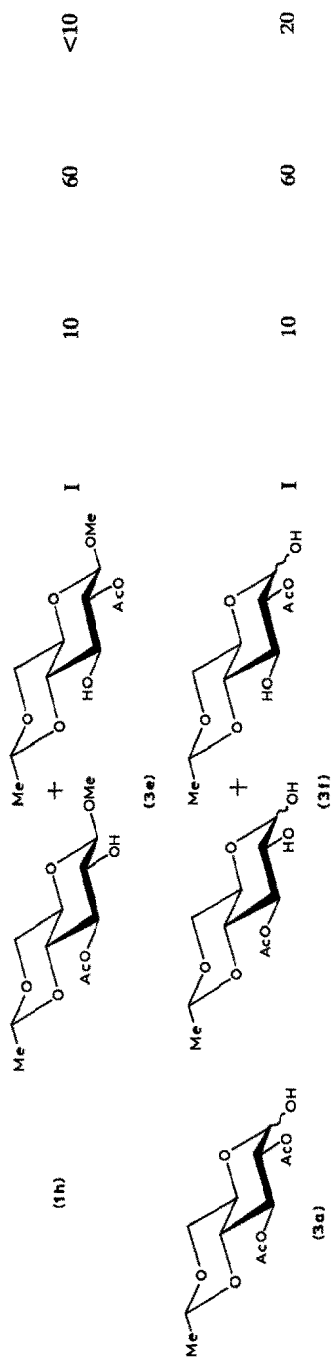
Starting material	Product	Reaction time	Isolated yield (%)
Sucrose octa-acetate 1a	Sucrose 2a	1 h	90
		30 min	93
(1b)^a	(2b)		
D-Glucose penta-acetate (1c)	D-Glucose (2c)	40 min	90
			
(1d)	(2d)	25 min	^c
			
(1e)^b	(2e)	30 min	89
			
(1f)^a	(2f)	45 min	^c
			
(1g)^a	(2g)	38 min	^c
			
(1h)^a	(2h)^a	6 h	^c
			

^aRef. 7. ^bRef. 8. ^cQuantitative conversion (t.l.c.); not isolated.

TABLE II

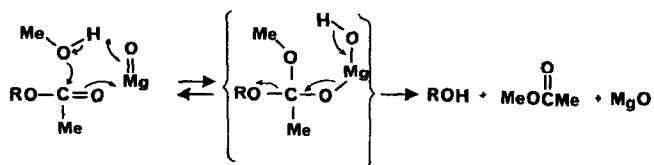
ALUMINA-CATALYSED METHANOLYSES

Starting material	Product	Catalyst ^e	Reaction time (h)	Reaction temp.	Conversion (%)
1b	 (3a) ^c	I	10	60	75 (61) ^b
1d	 (3b) ^d	II	2	55	55
(11)	 (3c) ^f	I	15	60	75
(11)	 (3d) ^f	I	14	60	85 (71) ^b



^a1, Woelm-200-N super I; II, Merck 1097/I. ^bIsolated yield. ^cRef. 7. ^dRef. 9. ^eRef. 10.

mechanism. The postulated mechanism, shown in Scheme 1, involves interaction of the MgO with the carbonyl group and hence an enhancement of its polarisation and electrophilicity toward the solvolysing methanol.



Scheme 1.

By analogy with cyanide-catalysed deacylation¹, those sugar derivatives (**1a–g**) which possess either an anomeric or a primary acetate group react considerably faster than those sugars where the anomeric position is blocked and/or which lack a primary acetate group (**1h**). The significance¹ of the participation of a neighboring group in the solvolysis of an adjacent acetyl group is highlighted in the regio-selective removal of AcO-1 in **1e**. Since the isolated AcO-3 reacts much slower than AcO-1, it is possible, by stopping the reaction after 30 min, to isolate 89% of the product **2e**. The reaction is selective for ester groups, leaving the acetamido function intact.

Alumina-catalysed methanolysis is not specific with regard to the anomeric acetyl substituent. However, the reaction is sufficiently selective to allow the products **3a–d** to be isolated in fair to good yields, depending on the type of alumina (Woelm W-200-N Super I or Merck 1097 activity I), reaction time, and temperature. The latter type of alumina effected a higher reaction rate, but with lower selectivity. Prolonged reaction resulted in a larger percentage of polydeacylated products. The configuration at the anomeric centre had no significant effect on the rate of deacylation. By analogy with the cyanide- and magnesium oxide-catalysed methanolyses, compounds lacking acetoxyl groups at the anomeric centre reacted considerably slower than those having an acetyl group at position 1 (**1h, 3a** vs. **1b, 1d, 1i, and 1j**). Both primary and secondary acetates react considerably slower than anomeric ones. It appears that acyl transfer does not play a significant role in the overall deacylation process, since the rates of deacylation of **1h** and **3a** were essentially the same, in contrast to the reaction in the presence of KCN or MgO. An acyl migration in a steroidal system, from a secondary inactive position to a primary reactive position, has been described³. In contrast to the reactions described here, where the reaction proceeded during 10 h in the presence of neutral alumina, the reported migration³ involved treatment of the substrate with basic alumina for 7 days. Tables I and II list the compounds studied and the respective products obtained.

It is concluded that magnesium oxide is a mild, non-selective, deacylating agent for polyacylated sugars, whereas the reactivity of alumina may be modulated. Thus, by choosing the appropriate catalyst and conditions, deacylation at the

anomeric position may be readily effected regioselectively. For MgO, the overall rate of reaction is greatly influenced by the substituent at the anomeric position (OAc-1>OR-1).

EXPERIMENTAL

General methods. — ¹H-N.m.r. spectra were recorded on a Bruker AM-300 spectrometer for solutions in CD₃OD (internal Me₄Si). The starting sugars for which no reference is given are commercially available. MgO (Merck 5866) and alumina (Woelm W-200-N Super I) were used as such. Alumina (Merck 1097) activity II–III was dried overnight at 110° in order to afford activity I. Flash chromatography was carried out on silica gel (Merck 9385), using ethyl acetate–hexane mixtures. Reactions were monitored by t.l.c. on silica gel (Merck, 5554), using chloroform–methanol mixtures for polyhydroxy products, ethyl acetate–hexane mixtures for monohydroxy products, and detection by charring with sulfuric acid.

Deacylation procedures. — (a) *Magnesium oxide.* To a solution of a polyacetylated sugar (1 mmol) in methanol (15 mL) was added MgO (~1.0 g). The mixture was stirred at room temperature until the starting material had disappeared (t.l.c.), then filtered, and concentrated to dryness, and the residue was slurried in methanol, filtered, and dried. 2-Acetamido-3-O-acetyl-4,6-O-benzylidene-2-deoxy-D-glucose (**2e**) was obtained as a 5:1 α,β-mixture, m.p. 169–171°.

Anal. Calc. for C₁₇H₂₁NO₇ · 0.5 H₂O: C, 56.66; H, 6.15; N, 3.89. Found: C, 56.51; H, 6.02; N, 4.06.

(b) *Alumina.* To a stirred solution of a polyacetylated sugar (1 mmol) in methanol (15 mL) was added alumina (~3 g). The mixture was heated at 55–60° until no further increase in the amount of HO-1 product could be detected. The mixture was cooled to room temperature and filtered. The alumina cake was slurried in dichloromethane (~10 mL), the combined filtrates were filtered and concentrated to dryness, and the residue was subjected to flash chromatography.

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