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Preliminary communication

Selective removal of *O*-acetyl groups in the presence of *O*-benzoyl groups by acid-catalysed methanolysis

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As a rule, selective deacylation of sugar derivatives requires basic catalysts, often in combination with nontrivial acyl protecting-groups[1]. Acid catalysis is less widely applied; the selective removal of *O*-formyl[2] and *O*-acetyl[3] groups in the presence of *O*-benzoyl groups, using methanolic hydrogen chloride, is documented.

Attempts to deacetylate **1a** selectively by transesterification, catalysed even by such a weak base as magnesium methoxide in methanol[4], failed. We now report the selective deacetylation of some monosaccharide (**1a**–**6a**) and disaccharide (**7a** and **8a**) derivatives, using methanolic hydrogen chloride; compound **9a**, which contains a primary acetate, was used for purposes of comparison.

Typically, a solution of the compound (1 mmol) in chloroform (1–2 mL) was treated with methanolic hydrogen chloride [prepared by addition at 0° of acetyl chloride (0.2 mL) to dry methanol (5 mL)] at room temperature. The reaction was monitored by t.l.c. and, when complete, the mixture was treated with excess of aqueous potassium hydrogencarbonate, diluted with chloroform (30–40 mL), washed with water, dried, and concentrated. The product was isolated from the residue by crystallisation or by column chromatography on silica gel. The properties of the deacetylated products are listed in Table 1*. For the conversion *H-C*-OAc → *H-C*-OH, the n.m.r. signal for *H* is shifted upfield and those of carbon atoms adjacent to *C* are shifted downfield.

Complete deacetylation of the 2-*O*-acetyl derivatives **1a**, **2a**, and **7a** occurred during 12–16 h, and the corresponding alcohols **1b**, **2b**, and **7b** were obtained in yields of 74–88% after chromatography. Likewise, deacetylation of **6a** gave 87% of **6b** (isolated by crystallisation).

Deacetylation of the rhamnose cyanoethylidene derivatives **4a** and **5a** was complete in 2–3 h, but there was a side-reaction, namely, addition of methanol to the cyano group to give the corresponding imidate and its subsequent hydrolysis product. Thus, **4a**[5]

*All new compounds gave correct C, H, and N analyses, and the ^{1}H- and ^{13}C-n.m.r. spectra were in accord with the structures assigned.

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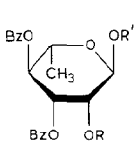
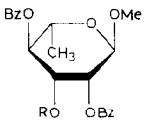


1 R′ = Me
2 R′ = Bzl



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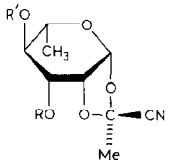
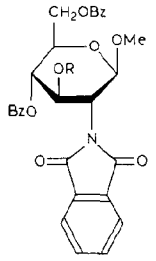


4 R′ = Ac
5 R′ = Bz



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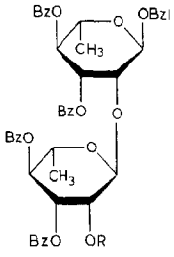

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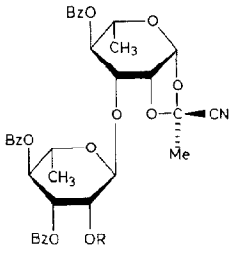

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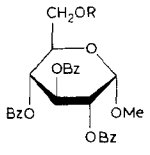

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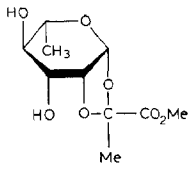

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a series, R = Ac; b series, R = H

gave the alcohol **4b** (65–70%) and the methyl ester **10** (~20%). Deacetylation of **5a** occurred within 3 h, and ~90% of the alcohol **5b** was isolated by crystallisation despite the formation (t.l.c.) of a minor proportion of an imidate.

It is the formation of imidate (the presence of which becomes apparent after 2–3 h) and the prolonged reaction time, which is necessary to remove the 2-acetate group, that determine the relatively low yield of **8b** from the disaccharide cyanoethylidene derivative **8a**. After 0.5–1 h, the reaction mixture contained four components (t.l.c.), namely, **8a**, its imidate, **8b**, and its imidate. When the reaction was stopped after 2.5–3 h, 25–30% of **8a**, 35–45% of **8b**, and the corresponding imidates (~10% of each) could be isolated easily by conventional column chromatography.

Deacetylation of **3a** required 5–6 h, and this reaction time was also sufficient to deacetylate the primary acetate **9a**. Magnesium methoxide-catalysed deacetylation of **9a** was accompanied by benzoyl migration. In contrast, no benzoyl migration was detected in any of the above reactions.

Rhamnosides **1a** {m.p. 94–96° (from ether–hexane), $[\alpha]_D^{20}$ +46.5° (*c* 2, chloroform)} and **2a** {syrup, $[\alpha]_D^{20}$ +24.5° (*c* 2.4, chloroform)} were obtained by the reaction of 2-*O*-acetyl-3,4-di-*O*-benzoyl-L-rhamnopyranosyl bromide[6] (**11**) with methanol and benzyl alcohol under Helferich conditions. The rhamnoside **1a** was also prepared by benzoylation of 1,2-*O*-(1-methoxyethylidene)-β-L-rhamnopyranose followed by mercuric bromide-catalysed isomerisation[7] and by selective benzoylation of methyl 4-*O*-benzoyl-α-L-rhamnopyranoside (**12**) followed by acetylation. Selective acetylation of **12** followed by

TABLE I

PROPERTIES OF DEACETYLATED COMPOUNDS[a]

Compound	*Yield (%)*	*M.p. (deg.) (solvent)*	$[\alpha]_D^{20}$ *(deg.)* (c *1–2, $CHCl_3$*)	*Characteristic n.m.r. chemical shifts ($CDCl_3$, δ)* a *series* → b *series*
1b	84	155–160	+26	C-1 98.7 → 100.8; C-3 70.2 → 72.8
2b	74	syrup	+13	H-2 5.46 → 4.43
3b	85	amorphous	+63	H-3 5.68 → 4.30
4b	65	113–114 (ether–hexane)	−25	H-3 5.27 → 3.49
5b	91	155–157 (ethyl acetate–hexane)	−13	H-3 5.50 → 4.11
6b	87	221–222 (ethanol)	+18	H-3 6.05 → 4.70
7b	88	amorphous	+64	H-2 5.72 → 4.44
8b	35–45	207–209 (ethyl acetate–hexane)	+107	C-1′ 100.3 → 102.8; C-3′ 70.2 → 72.2
9b	94	amorphous	+49	H-6 4.21 → 3.76; H-6′ 4.32 → 3.87
10	19	170–172 (ethyl acetate–methanol–hexane)	−12	H-4 → 4.90; H-3 → 3.86

[a] Methyl 3,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**1b**); benzyl 3,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**2b**); methyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**3b**); 4-*O*-acetyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-β-L-rhamnopyranose (**4b**); 4-*O*-benzoyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-β-L-rhamnopyranose (**5b**); methyl 4,6-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**6b**); benzyl 3,4-di-*O*-benzoyl-2-*O*-(3,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**7b**); 4-*O*-benzoyl-3-*O*-(3,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-1,2-*O*-[1-(*exo*-cyano)ethylidene]-β- L-rhamnopyranose (**8b**); methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (**9b**); 1,2-*O*-(1-methoxycarbonylethylidene)-β-L-rhamnopyranose (**10**).

benzoylation gave **3a**, $[\alpha]_D^{20}$ +72° (*c* 1.4, chloroform). Conventional tritylation of methyl α-D-glucopyranoside followed by benzoylation, detritylation, and acetylation gave **9a**, $[\alpha]_D^{20}$ +51° (*c* 2.2, chloroform). The cyanoethylidene derivative **5a** {m.p. 115–117° (from methanol), $[\alpha]_D^{20}$ +47.5° (*c* 1.8, chloroform)} was obtained as follows. Acetolysis of **12** gave 1,2,3-tri-*O*-acetyl-4-*O*-benzoyl-α-L-rhamnopyranose, the glycosyl bromide of which reacted with sodium cyanide in acetonitrile[5] to give **5a** (major product) and its *endo*-cyano isomer. The disaccharide cyanoethylidene derivative **8a** was obtained as described previously[6] and also by Helferich glycosylation of **5b** using the bromide **11**. Reaction of **11** with the alcohol **2b** yielded the disaccharide derivative **7a**, $[\alpha]_D^{20}$ +50° (*c* 1.8, chloroform). The 2-amino-2-deoxy-D-glucose derivative **6a** {m.p. 169.5–170.5° (from ethanol), $[\alpha]_D^{20}$ +42.5° (*c* 3.7, chloroform)} was obtained from methyl 2-deoxy-2-phthalimido-β-D-glucopyranoside by sequential benzylidenation, acetylation, debenzylidenation (pyridinium perchlorate in nitromethane–methanol[8]), and benzoylation. Details of the syntheses of these compounds will be given elsewhere.

The selective *O*-deacetylation procedure reported above should be of general value in synthetic carbohydrate chemistry*.

REFERENCES

1 A. H. Haines, *Adv. Carbohydr. Chem. Biochem.*, 39 (1981) 13–70.
2 J. Thiem, M. Gerken, and K. Bock, *Justus Liebigs Ann. Chem.*, (1983) 462–470.
3 (a) E. J. Corey, D. A. Clark, G. Goto, A. Marfat, C. Mioskowski, B. Samuelsson, and S. Hammarström, *J. Am. Chem. Soc.*, 102 (1980) 1436–1439; (b) E. Petráková and J. Schraml, *Collect. Czech. Chem. Commun.*, 48 (1983) 877–888.
4 S. Josephson and D. Bundle, *J. Chem. Soc., Perkin Trans. 1*, (1980) 297–301.
5 V. I. Betaneli, M. V. Ovchinnikov, L. V. Backinowsky, and N. K. Kochetkov, *Carbohydr. Res.*, 94 (1981) C1–C4.
6 V. I. Betaneli, L. V. Backinowsky, N. É. Byramova, M. V. Ovchinnikov, M. M. Litvak, and N. K. Kochetkov, *Carbohydr. Res.*, 113 (1983) C1–C5.
7 A. F. Bochkov, V. I. Betaneli, and N. K. Kochetkov, *Bioorg. Khim.*, 3 (1977) 39–44.
8 N. K. Kochetkov, B. A. Dmitriev, N. É. Byramova, and A. V. Nikolaev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (1978) 652–656.

*Analogous, high-yielding deacetylations of methyl di-*O*-acetyl-*O*-benzoyl-β-D-xylopyranosides have been recently described[3b].