Hydrolysis of Periodate Oxidized-reduced Glycosides

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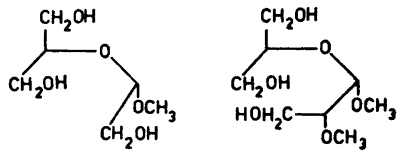
The Smith degradation of polysaccharides,[1] which is a sequence of reactions comprising oxidation, borohydride reduction and hydrolysis of the resulting polyalcohol under mild conditions, has become an important tool in polysaccharide chemistry.

The conditions of the hydrolysis are critical, and Smith and VanCleve [2] studied the rate of hydrolysis of the mixed acetal I, prepared from methyl-α-D-glucopyranoside. No other model substances seem to have been studied. Dutton and Gibney [3] have, however, recently showed how the hydrolysis of the polyalcohol could be monitored by GLC of the products.

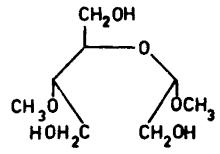
We now report hydrolysis studies on I, II, and III, the two latter prepared from methyl 2- and 4-*O*-methyl-α-D-glucopyranoside, respectively.

These glycosides, which are known substances, were prepared by conventional methods. After oxidation with periodate in aqueous methanol, they were reduced with borohydride and the products purified by distillation or preparative TLC. The products which were amorphous, were chromatographically pure (TLC).



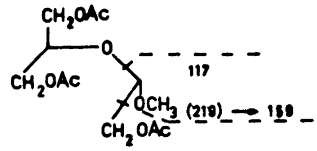
I

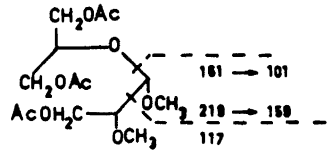
II

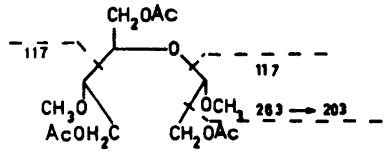


III

The acetate derivatives were also pure (GLC) and their NMR and mass spectra were in agreement with the postulated structures. The origin of some primary fragments on MS are indicated in the formulae below.







The hydrolyses of I, II, and III, each at three different temperatures, were followed polarimetrically. Inactive products should be formed from I, but II and III should give optically active products, in accordance with the experimental finding. Because of the rather low change in optical rotation during the hydrolysis, the rate constants and activation energies (Table 1) may be subject to rather large errors. Whilst I and III are hydrolysed at about the same rate, II reacts about ten times slower. This is attributed to the presence in II of electron attracting groups in both the α- and β-positions to the acetal carbon atom. The corresponding values for methyl α-D-glucopyranoside at 40°, extrapolated from published values,[4] are also given in Table 1. The differences in rate of hydrolysis for the acyclic acetals and the glucoside are considerable and it should be possible to hydrolyse the former completely without affecting the latter. The activation energy is higher for the glucoside, and the difference in rate is consequently enhanced at low temperatures. Smith and his coworkers [1] also used comparatively strong

Table 1. Rate constants and activation energies for the acid hydrolysis of the mixed acetals I, II, and III.

Compound	Temperature	$k \times 10^4$ sec^{-1}	E kcal/mol
	20	0.89	
I	30	3.62	23.5
	40	11.30	
	40	0.94	
II	50	2.40	19.6
	60	5.89	
	20	1.04	
III	30	3.49	23.3
	40	12.90	
Methyl α-D-glucopyranoside	40	0.00005	35.1

acid and low temperature for the hydrolysis of polyalcohols.

It is, however, often observed that the yields in a Smith degradation are not as high as expected from the other structural information available. Further much stronger hydrolytic conditions have to be applied than those recommended [1] and indicated in the present study. A possible reason for this discrepancy is that acetal migration, with formation of more stable cyclic acetals, competes with the hydrolysis. The formation of a cyclic acetal during a Smith degradation has been reported.[1] This complication could easily be avoided if the hydroxyl groups in the polyalcohol were protected, *e.g.* by methylation, before the hydrolysis step.

Experimental. Concentrations were performed under reduced pressure at a bath temperature below 40°. Precoated plates with Silica Gel F 254 (Merck) were used for TLC and silicic acid (230 mesh, Merck) for column chromatography. NMR spectra were recorded with a Varian A60 A instrument and chemical shifts are given as τ-values. MS were recorded with a Perkin-Elmer 270 instrument and optical rotations with a Perkin-Elmer 141 polarimeter. GLC was performed with a Perkin-Elmer model 900 instrument using a column packed with ECNSS-M 3 % on Gas-Chrom Q.

Methyl 2-O-methyl-α-D-glucopyranoside. Methyl iodide (3.8 g) was added over 2 h to a stirred mixture of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (7.6 g) and silver oxide (6.4 g) in dimethylformamide (60 ml), kept below 4° by external cooling. The mixture was allowed to reach room temperature and stirring was continued overnight. The mixture was filtered, concentrated and fractionated on a silicic acid column (6 × 50 cm), using toluene-ethyl acetate (1:1) as irrigant. The eluate was monitored polarimetrically and by TLC. The third component eluted (1.8 g) was pure methyl 4,6-*O*-benzylidene 2-*O*-methyl-α-D-glucopyranoside, which after crystallization showed m.p. 169–170° and $[\alpha]_D^{24}$ +97° (*c* 0.8, chloroform), in good agreement with published values.[5] This substance was hydrogenated (H_2/Pd) and the product crystallized from ethyl acetate, giving the title compound (0.7 g), m.p. 147–148°, $[\alpha]_D^{24}$ +158° (*c* 1.0, water), in good agreement with published values.[6]

Methyl 4-O-methyl-α-D-glucopyranoside was prepared essentially as described by Whistler and coworkers [7] and showed m.p. 95–96°, $[\alpha]_D^{24}$ +172° (*c* 0.8, water).

Preparation of the mixed acetals I, II, and III. Sodium metaperiodate (22 g) in water (150 ml) was added to a solution of methyl α-D-glucopyranoside (10 g) in methanol (700 ml). The mixture was kept in the dark at room temperature for 15 h, filtered and concentrated. The resulting syrup and sodium borohydride (15 g) in water (200 ml) was kept for 12 h at room temperature, excess borohydride was decomposed with acetic acid and the solution concentrated. Boric acid was removed by codistillations with methanol and the product extracted with ethanol, concentrated and distilled at 200–210°/0.2 mm. The resulting syrup (3.0 g), $[\alpha]_{578}^{24}$ −13° (*c* 2.45, water), consisted of chromatographically pure I (TLC, chloroform-ethanol, 7:3). The acetate, which gave a single peak on GLC, showed the following peaks on NMR: 5.19 (t, 1H) proton at C-1 of the original glucoside, 5.70–5.95 (m, 7H) protons at C-2, C-4, C-5 and C-6, 6.55 (s, 3H) OCH_3, 7.92 (s, 9H) $OOCCH_3$. It gave the following ions on MS (relative intensities in brackets): 43(100), 45(4), 99(2), 103(2), 117(19), 145(1), 159(12).

The mixed acetals II and III were prepared analogously, except that half of the molar amount of periodate was used and the products were not distilled, but purified by TLC (chloroform-ethanol 7:3). They were both obtained as chromatographically pure syrups and their acetates gave single peaks on GLC.

II, $[\alpha]_{578}^{24}$ +13° (*c* 2.8, water). NMR of the acetate: 5.40 (d, 1H) proton at C-1, 5.65–5.90 (m, 8H) protons at C-2, C-3, C-4, C-5 and C-6, 6.52 (s, 3H) and 6.53 (s, 3H) two OCH_3, 7.92 (s, 9H) $OOCCH_3$. MS of acetate: 43(100), 99(9),

101(23), 103(5), 117(5), 129(1), 145(3), 159(60), 161(5) and 219(3).

III, $[\alpha]_{578}^{24}$ −11.5° (*c* 2.2, water). NMR of acetate: 5.13 (t, 1H) proton at C-1, 5.55–5.98 (m, 8H) protons at C-2, C-3, C-4, C-5 and C-6, 6.53 (s, 3H) and 6.55 (s, 3H) two OCH_3, 7.81 (s, 9.11) $OOCCH_3$. MS of acetate: 43(100), 69(7), 71(5), 87(4), 101(6), 117(55), 129(1), 143(5), 161(1), 203(8) and 263(1).

Acid hydrolysis of I, II and III. The mixed acetal (approximately 0.2 M) in 0.125 M sulphuric acid (2 ml) was transferred to a jacketed polarimeter tube (10 cm), maintained at the required temperature, and the optical rotation was determined at intervals. The observed changes in rotation were approximately: I, −0.105°→0°. II, +0.155°→0.075°. III, −0.315°→0.040°. Duplicate experiments gave results in good agreement with those given in Table 1.

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Studies on Orchidaceae Alkaloids

XXXVI.* Alkaloids from Some *Vanda* and *Vandopsis* Species

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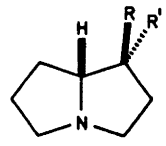
Esters of 1-hydroxymethylpyrrolizidine have previously been isolated from orchid extracts. Laburnine acetate (I) has been isolated from *Vanda cristata* Lindl.[1] and more complex esters from *Phalaenopsis*[2] and *Liparidinæ*[3–6] species. We now report similar studies on some other *Vanda* and closely related *Vandopsis* species.

From *Vandopsis lissochiloides* Pfitz. the alcohols laburnine (III) and lindelofidine (IV) were isolated, together with the corresponding acetates I and II,[1] in the *exo/endo* ratios 1/3. From *Vandopsis gigantea* Pfitz. the same alcohols and acetates were isolated in the *exo/endo* ratios 10/1. Laburnine acetate (I) has been isolated



I: $R = CH_2OAc$, $R' = H$

II: $R = H$, $R' = CH_2OAc$

III: $R = CH_2OH$, $R' = H$

IV: $R = H$, $R' = CH_2OH$

from *Vanda hindsii* Lindl., and I and III from *Vanda helvola* Bl. An extract of *Vanda luzonica* Loher contained either I or its enantiomer (GLC-MS). A small amount of hygrine was detected (GLC-MS) in an extract of *Vandopsis parishii* Schltr.

In some of the above investigations a modified reineckate procedure was used to purify and quantify small amounts of

* For number XXXV in this series, see Ref. 6.