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Novel methods for the preparation of partially acetylated carbohydrates

Stephen Hanessian and Masahiro Kagotani
Department of Chemistry, Université de Montréal C.P. 6128, Succ. A, Montréal, Québec, H3C 3J7 (Canada)

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ABSTRACT

The selective acetylation of methyl α-D-hexopyranosides in the presence of zinc chloride shows unusual reactivity patterns compared to control experiments. Hydroperoxide ion is a mild and selective deacetylation reagent which does not attack primary acetates.

INTRODUCTION

Partially acetylated carbohydrates have been useful in a number of ways. They have been used as reference compounds in connection with the analysis of degradation products from polysaccharides[1] and other natural products[2] containing carbohydrates. Partially acetylated carbohydrates are also versatile intermediates for the preparation of other *O*-substituted derivatives, hence their utility in synthesis[3].

INTRODUCTION

Methods for the preparation of partially acetylated carbohydrates vary with the nature of the substrate[4]. Direct, preferential acetylation in a particular series may depend on such factors as the kinetic acidities of the hydroxyl groups, steric effects, the spatial disposition, and careful monitoring of reactions using stoichiometric quantities of acetylating reagents. Indirect approaches involve among others, the acetylation of partially protected carbohydrates followed by removal of the protecting groups. In this regard dialkyl stannylene acetals and triakyltin ethers have proven to be particularly useful[5]. Selective monoacetylation of a diol unit may also be achieved through the hydrolysis of orthoesters[6] and orthoamides[7]. Finally, enzymes[8] have also been used for the selective acetylation and deacetylation of carbohydrates.

RESULTS

We report here on two novel methods for the preparation of partially acetylated carbohydrate derivatives. The first relies on an initial complexation of the polyol with a

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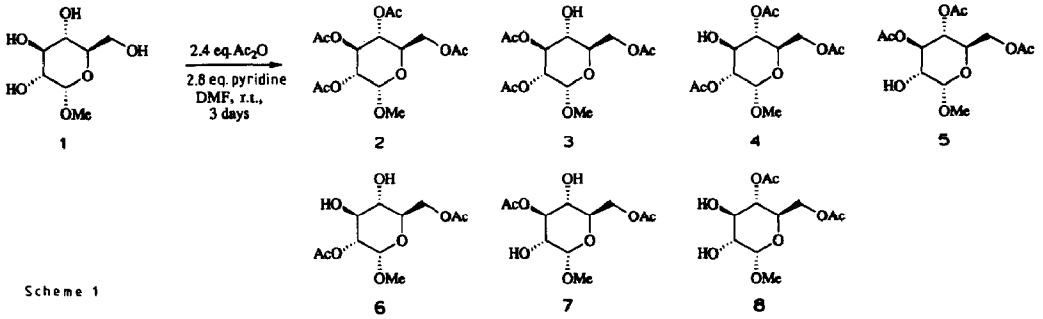
divalent metal salt, followed by acetylation of available and/or reactive hydroxyl groups. The second method is concerned with the partial deacetylation of fully acetylated carbohydrate derivatives. In both cases, partially acetylated derivatives are produced which for the most part, are not readily accessible by the presently known procedures.

Selective acetylation in the presence of zinc chloride. — It is well known that the hydroxyl groups of carbohydrates form complexes in solution with mono- and di-valent cations[9], but applications of this property in preparative carbohydrate chemistry have been sparse. For example calcium, strontium, and copper salts have been used in glycoside synthesis[10] while copper, cobalt, nickel, and zinc have been utilized in aminocyclitol chemistry[11]. Alkylation in the presence of copper salts has also been reported[12]. The known ability of zinc and other divalent ions to complex with carbohydrates in aqueous solution[13] prompted us to investigate reactions in non-aqueous aprotic media. Here we report on the acetylation of a number of carbohydrate glycosides in a mixture of *N,N*-dimethylformamide and pyridine in the presence of various divalent metal salts. The results in the case of methyl α-D-glucopyranoside are shown in Scheme 1 and Table I. In the absence of metal ions, a random pattern of acetylation was observed, with excellent overall mass balance. The two preponderant products were the triacetate **4** and the diacetate **7** (18 and 28% respectively). Although different patterns of reactivity were observed with divalent metal salts as complexing agents, zinc chloride proved to be the most selective, since it led to the 2,6-diacetate derivative **6** in 65% yield.



Scheme 1

TABLE I

Selective acetylation of methyl α-D-glucopyranoside. Products and isolated yields (%)

Run	*Additive*[a]	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*mono Ac*[c]	*Total %)*
1	NOne	7	7	(18)[b]	(8)[b]	9	28	10	12	99
2	$ZnCl_2$	4	9	21	trace	65	trace		99	
	$ZnCl_2$[d]	12	17	38	trace	32		trace	trace	
99										
3	$Hg(OAc)_2$	4	8	19	trace	54	3	1	10	99
4	$MgCl_2$[e]	4	3	5	trace	24	4	5	53	98
5	$CaCl_2$[e]	4	3	14	trace	29	9	11	26	96

[a] 1.0 eq. of metal salt was employed; [b] determined by means of n.m.r.; [c] mixture of regioisomers; [d] −15°, 4 eq. Ac_2O, 4.8 eq. pyr, 1.2 eq. salt; [e] 2.05 eq. of Ac_2O and 10 eq of pyr. were used.

TABLE II

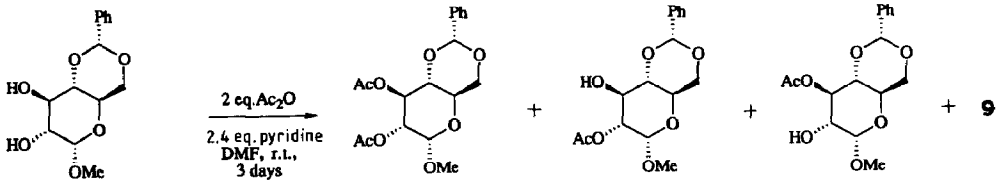
^{1}H-n.m.r. spectroscopic data for selected acetylated monosaccharides

Compound	*Chemical shift (δ CDCl$_3$, 90 MHz)*										*Coupling constants (Hz)*						
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*OMe*	*Ac*	*OH*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
									2.13								
3	4.92	4.86	5.31	3.56	3.85	4.46	4.27	3.40	2.09	3.21	2.4	8.8	8.8	9.0	4.1	2.3	12.0
									2.08								
									2.15								
4	4.93	4.80	4.04	4.94	3.92	4.09	4.29	3.40	2.12	2.64	3.5	9.0	9.0	9.0	4.7	2.6	12.0
									2.10								
									2.10								
5	4.83	4.90	5.23	4.99	3.91	4.29	4.07	3.47	2.08	3.66	3.8	8.4	8.4	8.4	4.7	2.0	10.0
									2.03								
6	4.90	4.74	3.96	3.42	3.76	4.49	4.27	3.39	2.15	3.4	3.8	10.0	9.0	10.0	4.1	2.0	11.0
									2.13								
7	4.80	3.67	5.08	3.45	3.80	4.48	4.24	3.45	2.16	2.98	3.8	9.4	9.4	10.0	4.1	2.4	13.0
									2.13	2.30							
8	4.83	3.78	3.85	4.89	3.58	4.27	4.07	3.45	2.11	2.88	3.5	10.0	10.0	10.0	4.7	2.4	14.7
									2.09	2.48							
11	4.79	4.83	3.84		3.55	4.31	4.03	3.41	2.16	2.53	3.8	9.4	9.0	9.0	4.0	2.9	8.2
12	4.80	4.31	5.33	3.53	3.02			3.47	2.12	2.26	3.8	9.0	9.0				
15	4.74	3.63	5.09		3.5	3.83	3.9	3.39	2.16	2.84	3.9	9.4	9.4		3.0	~0	~0
16	4.88	4.70	3.62	4.15			3.88	3.32	2.14	3.0	3.5	9.6			~3.0	~0	~0
									2.10								
18	4.77	4.02	5.22	5.35	~4.0	4.30	4.11	3.41	2.08	2.71	2.3	3.0	9.0	9.0	5.0	2.3	12.5
									2.03								
19	4.78	3.95	3.91	5.04	3.9	4.32	4.12	3.39	2.12	2.7	~0	3.3	9.0	9.0	5.3	2.6	11.0
									2.09								
20	4.74	4.02	3.85	3.82	5.09	4.53	4.29	3.40	2.17	2.85	1.8	4.0	9.0	7.0	4.1	2.0	12.0
									2.13	2.55							
23	4.71	4.29	3.84	5.42		4.22	3.96	3.39	2.10	2.6	1.4	3.5	10.0	10.0	5.0	3.0	10.0
24	4.72	5.24		3.8			4.3			3.42	2.20	2.5	1.6	3.5			

Mercuric acetate was somewhat less selective, and magnesium or calcium chlorides favored the formation of mixtures of monoacetates, among other products. Using an excess of acetic anhydride at a reaction temperature of $-15°$ did not appreciably change the ratios, except in the case of zinc cloride, where with four equivalents of acetic anhydride, there was formed 38% of the triacetate **4** and 32% of the diacetate **6**. The n.m.r. data of the various acetates are given in Table II. Assignments were based on direct comparison with known authentic samples and by analysis of the ^{1}H-n.m.r. spectra of partially d_3-acetylated samples, a protocol nicely worked out by Horton and Lauterbach[14].

It should be noted that, under normal conditions using stoichiometric quantities of acetic anhydride in pyridine, the diacetate **6** should be the major product, based on the known[4] kinetic acidity of the C-2 hydroxyl group in **1**. In this regard, the formation of the triacetate **4** in the control reaction (run 1, Table I) is of interest. We eliminated the possibility of acetyl migration or transterification during the workup conditions based on simulated workups of initially obtained products, and by monitoring the progress of the acetylation reaction. It is also of interest that the proportion of triacetate **4** increased (38%) in the presence of zinc chloride at lower temperature, indicating preferential masking of the 3-hydroxyl group under these conditions. Of major significance was the observation that acetylation of methyl β-D-glucopyranoside under the conditions described for the α anomer led to a random esterification much the same as in the acetylation of **1** in the absence of zinc chloride (run 1, Table I).

Application of the same acetylation protocol to methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**9**) led to a preferential acetylation of the 2-hydroxyl group, with appreciable amounts of the diacetate also being formed (Scheme 2). Interestingly, in the absence of zinc chloride, equal amounts of the two monoacetates **11** and **12** were formed.

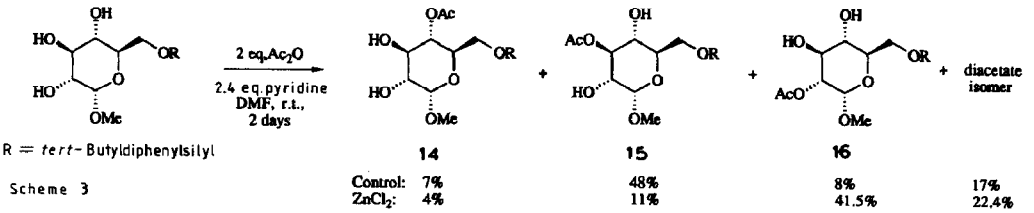


Scheme 2

Control:	6%	29%	32%	23%
$ZnCl_2$:	23%	53%	13%	10%

Acetylation of methyl 6-*O*-*tert*-butyldiphenylsilyl-α-D-glucopyranoside (**13**) in the presence of zinc chloride gave 41.5% of the 2-acetate **16** and 22.4% of a mixture of diacetates. In the absence of zinc chloride, the major monoacetate was **15**. In both instances, small quantities of the 4-acetate **14** were also formed (Scheme 3).

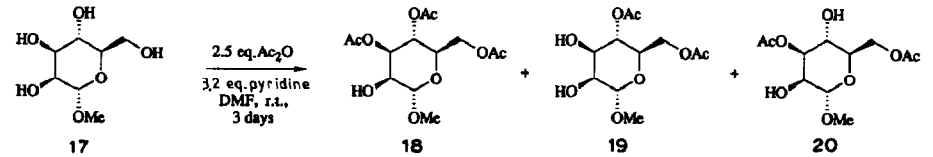
In order to study the influence of the vicinal disposition of diols, we next investigated the reaction with methyl α-D-mannopyranoside (**17**) (Scheme 4). The major



R = *tert*-Butyldiphenylsilyl

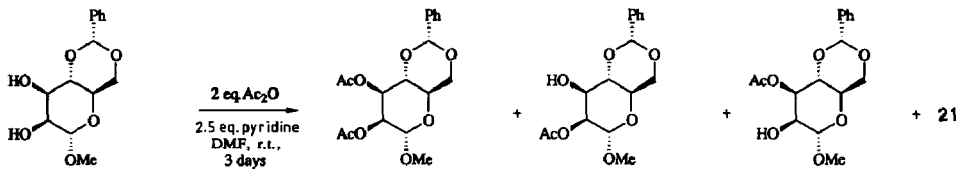
Scheme 3

	14	15	16	
Control:	7%	48%	8%	17%
$ZnCl_2$:	4%	11%	41.5%	22.4%



Scheme 4

	17	18	19	20
Control:		25.7%	48%	trace
$ZnCl_2$:		26%	trace	53.5%



Scheme 5

	21	22	23	24	
Control:		25.4%	9.4%	53.5%	11%
$ZnCl_2$:		10%	6.7%	64.6%	10%

products were found to be the 3,4,6-triacetate **18** (26%), and the 3,6-diacetate **20** (53.5%). Minor quantities of other triacetates and a trace of the 4,6-diacetate **19** were also formed. In contrast, the uncatalyzed reaction produced compounds **18** and **19** in yields of 25.7 and 48% respectively.

Finally, methyl 4,6-*O*-benzylidene-*α*-D-mannopyranoside (**21**) was subjected to acetylation under the same conditions, with and without zinc chloride (Scheme 5). In both cases, the major product was the 3-acetate **24**, but the amount of diacetate **22** was significantly higher than in the catalyzed reaction.

DISCUSSION

In a previous study on complex formation between zinc chloride and methyl *β*-D-glucopyranoside in aqueous solution[13] it was concluded that the vicinal hydroxyl groups on C-2 and C-3 were principally involved, particularly at high concentrations (~8M) of salt. Reversible complexes of divalent metal cations with carbohydrates and cyclitols in aqueous solution require the presence of an *ax–eq–ax* sequence of three contiguous hydroxyl groups in a six-membered ring[10].

From the behavior of methyl *α*-D-hexopyranosides and their derivatives toward the acetylation conditions in the presence of zinc chloride in aprotic media as reported

here, it is clear that, if complex formation is indeed the case, it must be different than in aqueous solution. The orientation of the anomeric methoxyl group in relation to the other hydroxyl groups in the molecule appears to be critical, at least in the case of methyl *α*-D-glucopyranoside. Assuming octahedral coordination geometry around the zinc atom[15], a plausible hypothesis could involve complex formation with the axially disposed methoxyl group as a resident anchor or ligand, and one or more hydroxyl groups, possibly in a dimeric or oligomeric structure, comprising two or more sugar molecules. The available hydroxyl groups are then acetylated under the slightly basic conditions of the reaction, presumably starting with the primary hydroxyl group, but virtually excluding the 3-position in the D-*gluco* series and the 2-position in the D-*manno* series. The partially acetylated products are then protected from further acetylation, either because of insufficient reagent or the presence of a complex. Another possibility may involve a series of complexes in dynamic equilibrium, undergoing the acetylation reaction at available sites and at different rates. Of course, the involvement of DMF and pyridines as additional ligands cannot be excluded.

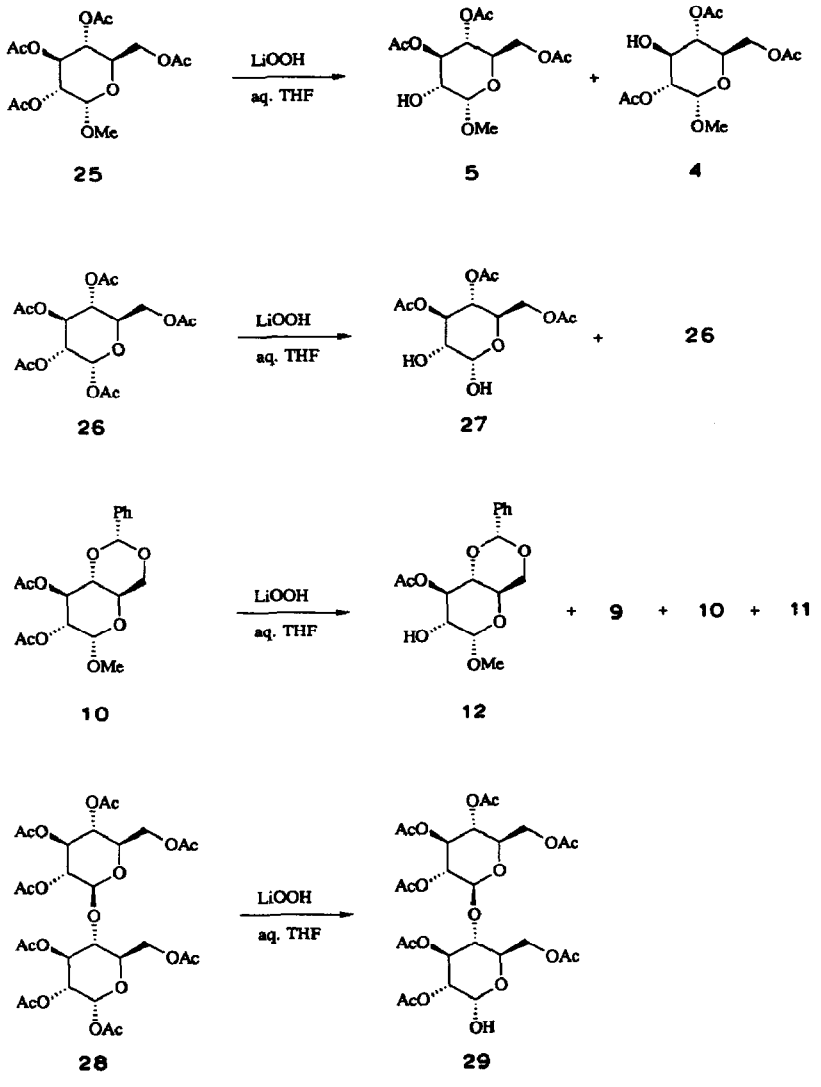
That selective acetylation is due to the existence in solution of a sterically demanding acetylating-reagent complex comprising zinc chloride can be excluded. Such a species cannot account for the larger proportion (~20%) of the 2,4,6-trisubstituted ester **4**, nor does it explain the similar reactivities between methyl *β*-D-glucopyranoside and the control using the *α* anomer but in the absence of zinc chloride.

Finally, consideration could be given to the enhancement of kinetic acidities of some of the hydroxyl groups in the complexed glycosides, either at the site of complexation or vicinal to it. This would imply acetylation of hydroxyl groups that are actually coordinated to the zinc atom or those affected by it but not complexed.

As previously mentioned, acetyl migration during the reactions or the workup process can be excluded. Thus, the products isolated from the acetylation as described are, in major part, a reflection of the reactivities of the substrates under the given reaction conditions.

Selective deacetylation with lithium hydroperoxide. — Acid- or base-catalyzed hydrolysis of esters proceeds by attack of the nucleophile on the carbonyl carbon atom, and a number of methods are available for the selective hydrolysis of carbohydrate acetates[16]. The hydroperoxide ion is well known for its high nucleophilicity and much weaker basicity as compared to hydroxide ion, and this is attributed to the *α*-effect[17]. This property has been capitalized upon by Corey and co-workers[18] in the hydrolysis of lactones, by ourselves in the hydrolysis of acetates[19], and by Evans and coworkers[20] in the hydrolysis of tertiary amides.

Scheme 6 illustrates examples of selective deacetylation of a number of fully acetylated carbohydrate derivatives with M lithium hydroperoxide in aqueous oxolane. It can be seen that methyl 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranoside (**25**) gave a 50% isolated yield of the corresponding 3,4,6-tri-*O*-acetyl derivative **5**. Based on the amount of recovered starting material (44.2%), the yield of **5** was 91%. N.m.r. analysis indicated methyl 2,4,6-tri-*O*-acetyl-*α*-D-glucopyranoside as a minor contaminant. The structure and substitution pattern of **5** was further confirmed by its conversion into the corre-



Scheme 6

sponding 2-*O*-trideuterioacetyl derivative and detailed n.m.r. analysis of the product based on assignments published by Horton and Lauterbach[14].

Similar treatment of α-D-glucose pentaacetate (**26**) gave 3,4,6-tri-*O*-acetyl-D-glucopyranoside (**27**) in 40% yield, with 59% of **26** being recovered by column chromatography. Methyl glycoside formation gave a product identical to **5**, thus establishing the original substitution pattern. Selective *O*-deacetylation took place in the case of methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**10**) to give the 3-O-acetyl derivative **12** in 44% yield. Starting material (27%) and deacetylated product (23%) were also recovered, in addition to traces of **11**. Finally, treatment of α-D-

cellobiose octaacetate (**28**) under the same deacetylating conditions as for **25** gave a 58% yield of α-cellobiose 2,2',3,3',4,6,6'-heptaacetate (**29**).

While the foregoing results do not constitute an exhaustive or complete study, they indicate a preferential hydrolysis pattern in peracetylated derivatives of D-glucopyranose under very mild conditions. Previous experience in this laboratory has shown that lithium hydroperoxide is an excellent nucleophile for effecting the hydrolysis of mono and diacetyl derivatives of polyols[19]. In this regard, we had also reported[21] that potassium cyanide in methanol is also a mild reagent for *O*-deacetylation[16,22] in the presence of other functionality.

The deacetylations with hydroperoxide ion are of interest in view of the reported relative unreactivity of this ion toward ethyl acetate[23] and, its insensitivity to steric effects[20]. Except for **28**, it appears that nucleophilic attack of the hydroperoxide ion is directed at the 2-acetoxy group in compounds **10, 25** and **26**. Since no deacetylation of primary acetate was observed, it appears that the preferential attack on the 2-acetoxy group is due to electronic or stereoelectronic factors. Control experiments showed that no acetyl migration took place under the conditions of the reaction. A recent report[16] on the methanolysis of acetylated sugars in the presence of tin oxides also shows interesting selectivity.

The observation that lithium hydroperoxide does not attack primary acetate groups prompted us to study the partial *O*-deacetylation of cellulose triacetate with the objective of producing 2- and/or 3-*O*-deacetylated derivatives. Treatment of cellulose triacetate with varying quantities of M lithium hydroperoxide in a mixture of oxolane and dichloromethane gave mixtures of partially acetylated celluloses which were analyzed by a well-documented ^{13}C-n.m.r. method[24]. At the highest ratio of hydroperoxide ion, the total d.s. was found to be 0.58, with the individual d.s. at O-6, O-3, and O-2 being 0.35, 0.15, and 0.08 respectively. Thus, as in the case of the monosaccharide acetates, the tendency for O-6 *O*-deacetylation was low compared to other sites, particularly O-2.

EXPERIMENTAL

General methods. — Optical rotations were determined in a 1-dm cell with a Perkin–Elmer model 141 photoelectric polarimeter. I.r. spectra were recorded with a Perkin-Elmer model 781 spectrophotometer. ^{1}H-N.m.r. spectra were recorded in $CDCl_3$ on a Bruker 90 MHz spectrometer and ^{13}C-n.m.r. spectra were recorded on a JEOL 6X-270 spectrometer using conditions previously reported[24]. Melting points are uncorrected. Flash chromatography was done according to Still and co-workers[25].

Selective acetylation of methyl α-D-glucopyranoside (**1**). — Methyl α-D-glucopyranoside (**1**) (450 mg, 2.32 mmol) and anhydrous $ZnCl_2$ (317 mg, 2.33 mmol) were dissolved in 10 mL of *N,N*-dimethylformamide (DMF) with gentle warming. The mixture was cooled to −15°, and then treated with Ac_2O (0.525 mL, 5.55 mmol) and pyridine (0.525 mL, 6.50 mmol) with stirring. The mixture was gently stirred for 3 days

at room temperature. The solvent was evaporated under diminished pressure to give a yellowish residue was purified by flash column chromatography (1:2 hexanes–EtOAc). The major product, methyl 2,6-di-*O*-acetyl-*α*-D-glucopyranoside (**6**, 427 mg, 65%) was obtained as a colorless syrup, $[\alpha]_D^{22}$ +102.9° (*c* 2.05, $CHCl_3$). The following compounds were also isolated, methyl 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranoside (**2**, 34 mg, 4%); methyl 2,3,6-tri-*O*-acetyl-*α*-D-glucopyranoside (**3**, 67 mg, 9%), syrup, $[\alpha]_d^{22}$ +104° (*c* 2.3, $CHCl_3$), and methyl 2,4,6-tri-*O*-acetyl-*α*-D-glucopyranoside (**4**, 156 mg, 21%); $[\alpha]_D^{22}$ +119° (*c* 2.17, $CHCl_3$). These products were found to be identical to authentic materials ($[\alpha]_D$, ^1H n.m.r.)[14].

Acetylation of the *β* anomer of **1** under the conditions just described led to a mixture of acetates similar to a control experiment using **1** but in the absence of zinc chloride. The control experiment was performed as just described, but omitting the addition of zinc chloride, and the products were isolated by chromatography (see Table I).

*Selective acetylation of methyl 4,6-*O*-benzylidene α-*D*-glucopyranoside* (**9**). — The title compound (282 mg, 1 mmol) was dissolved in 5 mL of DMF and the solution was treated with $ZnCl_2$ (150 mg, 1.1 mmol), Ac_2O (0.2 mL, 2.03 mmol), and pyridine (0.2 mL, 2.47 mmol). After stirring for 3 d, the solution was diluted with EtOAc (50 mL) and 2M HCl (20 mL). The organic layer was processed conventionally and then evaporated to give a pale-yellow syrup which was purified by column chromatography (1:2 hexanes–EtOAc). Methyl 2-*O*-acetyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (**11**, 172 mg, 53%) was thus obtained, m.p. 131–132°, $[\alpha]_D^{22}$ +109.6° (*c* 1.0, $CHCl_3$); lit.[26] m.p. 133–134°, $[\alpha]_D^{22}$ +112° (*c* 0.9, $CHCl_3$); methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (**10**, 84 mg, 23%), methyl 3-*O*-acetyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (**12**, 42 mg, 13%), and **9** (36 mg, 10%) were also isolated.

When the foregoing reaction was repeated in the absence of $ZnCl_2$, compounds **11** and **12** were obtained in 30 and 32.6% yields, respectively, and 23% of starting material was recovered.

*Selective acetylation of methyl 6-*O*-tert-butyldiphenylsilyl-α-*D*-glucopyranoside* (**13**). — The title compound (500 mg, 1.16 mmol) in 5 mL of DMF was acetylated as described for **9**. After 2 d at room temperature, the mixture was processed as for **9**, and the crude product was chromatographed. Methyl 2-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-*α*-D-glucopyranoside (**16**, 228 mg, 41.5%) was obtained as a syrup, $[\alpha]_D^{22}$ +79.2° (*c* 1.2, $CHCl_3$). The 3-*O*-acetyl derivative **15** (syrup, 59 mg, 10.8%), $[\alpha]_D^{22}$ +79.7° (*c* 1.29, $CHCl_3$), the 4-*O*-acetyl derivative **14** (syrup, 23 mg, 4.2%), and a mixture of diacetates (63.2 mg, 10.9%) were also isolated, in addition to **13** (13%).

Anal. Calc. for **16**: C, 63.27; H, 7.22. Found: C, 63.21; H, 7.08.

In the absence of $ZnCl_2$, the ratio of product **15:16:14** was 48, 8, and 7% respectively, with recovery of starting material **13** (9%).

*Selective acetylation of methyl α-*D*-mannopyranoside* (**17**). — Methyl *α*-D-mannopyranoside (384 mg, 2.0 mmol) was dissolved in 10 mL of DMF and the mixture was treated with Ac_2O (0.55 mL, 5.83 mmol), pyridine (0.55 mL, 6.9 mmol), and $ZnCl_2$/300 mg, 2.2 mmol) After stirring for 3d the mixture was processed as described for **1** to give

methyl 3,6-di-*O*-acetyl-*α*-D-mannopyranoside (**20**, 298 mg, 53.5%), m.p. 133–134°, $[\alpha]_D^{22}$ +62.7° (*c* $CHCl_3$), and the 3,4,6-tri-*O*-acetyl derivative **18** (syrup, 26%), $[\alpha]_D^{22}$ +67.3 (*c* 1.26, $CHCl_3$). Minor quantities of other triacetates were also formed but not isolated. The aqueous layers contained small quantities of **17**, which were not recovered.

Anal. Calc. for **20**: C, 47.48; H, 6.52. Found: C, 47.37; H, 6.41.

In the absence of $ZnCl_2$, methyl 4,6-di-*O*-acetyl-*α*-D-mannopyranoside (**19**, 48.1%); $[\alpha]_D^{22}$ +51.3° (*c* 2.20, $CHCl_3$), and **18** (25.7%) were the major products, the remainder being starting material that remained in the aqueous layer.

*Selective acetylation of methyl 4,6-*O*-benzylidene-α-D-mannopyranoside* (**21**). — The title compound (290 mg, 1 mmol) was acetylated as for **9**. After 3 d and the usual workup, the following products were obtained from a chromatographic separation; methyl 3-*O*-acetyl-4,6-*O*-benzylidene-*α*-D-mannopyranoside (**24**, 215.3 mg, 64.6%); m.p. 57.5–58°, $[\alpha]_d^{22}$ +48.6° (*c* 1, $CHCl_3$); the 2-*O*-acetyl derivative **23** (22.3 mg, 6.7%), syrup; $[\alpha]_D^{22}$ +24.6° (*c* 0.5, $CHCl_3$); lit.[27] $[\alpha]_D$ 26° ($CHCl_3$); and the 2,3-di-*O*-acetyl derivative **22**.

In the absence of $ZnCl_2$, the reaction gave **22**, **23** and **24** in 25.4, 9.4, and 53.5% yields respectively.

Reaction of methyl α-D-glucopyranoside tetraacetate with lithium hydroperoxide. — A solution consisting of M LiOH (1.2 mL) and 30% H_2O_2 (3 mL) in 15 ml of THF was added dropwise to a solution of methyl *α*-D-glucopyranoside tetraacetate (**25**, 360 mg) in 10 mL of THF at 0°. The mixture was stirred for 1 h at 0°, and then for 30 min at room temperature. Saturated aq. $Na_2S_2O_3$ (3 mL) was added at 0°, most of the THF was removed by evaporation, and the remaining solution was extracted with EtOAc (50 mL). Conventional processing of the organic layer and evaporation of the solvent gave a colorless oil which was purified by flash chromatography (2:1 hexanes–EtOAc). Methyl 3,4,6-tri-*O*-acetyl-*α*-D-glucopyranoside[28] (**5**), and methyl 2,4,6-tri-*O*-acetyl-*α*-D-glucopyranoside (**4**) were isolated as a 10:1 mixture (163 mg, 51%). Recovered starting material accounted for the balance (160 mg, 45%).

A solution containing 282 mg of **5** and **4** in 1 mL of DMF was treated with *tert*-butylchlorodimethylsilane (200 mg), and imidazole (100 mg) in 2 ML of DMF and the solution was heated for 3 h at 80°. After standard workup and purification by flash column chromatography, methyl 3,4,6-tri-*O*-acetyl-2-*O*-*tert*-butyldimethylsilyl-*α*-D-glucopyranoside was obtained as a syrup (302 mg, 79%); $[\alpha]_D^{22}$ + 103.5° (*c* 1.63, $CHCl_3$); ^{1}H-n.m.r. ($CDCl_3$): *δ* 5.35 (t, 1 H, *J* 9.5 Hz, H-3 or H-4), 4.97 (t, 1 H, *J* 9.5 Hz, H-4 or H-3), 4.68 (d, 1 H, *J* 3.5 Hz, H-1), 4.30 (dd, 1 H, *J* 13 and 5 Hz, H-6), 4.16–3.9 (m, 2 H, H-6 and H-5), 3.78 (dd, *J* 9.5 and 3.5 Hz, 1 H, H-2), 3.43 (s, 3 H, OMe), 2.10 (s, 3 H, OAc), 2.01 (s, 6 H, OAc), 0.87 (s, 9 H, Bu^t), 0.08 (s, 3 H, SiMe), and 0.05 (s, 3 H, SiMe).

Anal. Calc. for $C_{19}H_{34}O_9Si$: C, 52.52; H, 7.89. Found: C, 52.27; H, 7.80.

*Reaction of methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside* (**10**) *with lithium hydroperoxide.* — The title compound (433 mg) in 15 mL of THF was treated with a solution consisting of M LiOH (1.4 mL) and 30% H_2O_2 (3.5 mL) in THF (20 mL) at 0° as in the previous example. After workup and column chromatography, methyl 3-*O*-acetyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (**12**, 220 mg, 44.4%), m.p.

173–174°, $[\alpha]_D^{22}$ + 112° (*c* 0.9, $CHCl_3$) and the 2-acetate **11** (13 mg, 2.7%) were obtained; also recovered were 120 mg (27.7%) of **10** and 77 mg (23%) of **9**; lit.[26] for **12**, m.p. 173.5–174.5°, $[\alpha]_D$ +110° (*c* 0.85 $CHCl_3$).

Reaction of α-D-glucose pentaacetate (**26**) *with lithium hydroperoxide.* — The title compound (600 mg, 1.53 mmol) in 10 mL of THF was subjected to partial deacetylation as just described using 2 mL of M LiOH and 30% H_2O_2 (5 mL) in 30 mL of THF. After workup and chromatography, 3,4,6-tri-*O*-acetyl-α-D-glucopyranose (**27**) was isolated as a syrup, (217 mg, 40.5%), $[\alpha]_D^{20}$ +89.7° (*c* 2.75, $CHCl_3$); ^{1}H-n.m.r. ($CDCl_3$): δ 5.32 (d, 1 H, *J* 4 Hz, H-1); 5.30 (t, 1 H, *J* 10 Hz, H-3), 5.18–4.90 (m, 2 H), 4.77 (m, 1 H, H-5), 2.09–4.03 (m, 3 H), 3.69 (dd, 1 H, *J* 4 and 10 Hz, H-2), 2.09 (s, 6 H), and 2.04 (s, 3 H). Starting material was also recovered (59%).

Anal. Calc. for $C_{12}H_{18}O_9$: C, 52.52; H, 7.89. Found: 52.33; H, 7.78.

A sample of **27** (412 mg, 1.35 mmol) was treated with CH_2N_2 in the presence of a catalytic quantity of $BF_3{\cdot}OEt_2$ in CH_2Cl_2 (20 mL). Neutralization (AcOH and then $NaHCO_3$), followed by usual workup and chromatography gave methyl 3,4,6-tri-*O*-acetyl-2-*O*-methyl-α-D-glucopyranoside (288 mg, 64%), m.p. 120–121°, $[\alpha]_D^{20}$ +157° (*c* 1.04, $CHCl_3$); lit.[29] m.p. 119–120°, $[\alpha]_D^{22}$ +148° ($CHCl_3$).

Reaction of α-cellobiose octaacetate with lithium hydroperoxide. — Cellobiose octaacetate (**28**, 600 mg, 0.88 mmol) in a mixture of THF (15 mL) and CH_2Cl_2 (15 mL) was treated with a solution consisting of M LiOH (1 mL) and 30% H_2O_2 (2.5 mL) in 5 mL of THF. After stirring for 1 h at 0° and for 15 min at room temperature, the mixture was processed as described for **26** to give 325 mg (58%) of 2,2′,3,3′,4,6,6′-hepta-*O*-acetyl-α-cellobiose (**29**), m.p. 208–209°, $[\alpha]_D^{22}$ +32.8° (*c* 2.38, pyridine); lit.[30] m.p.. 209°, $[\alpha]_D$ +33.4° (pyridine).

Partial deacetylation of cellulose triacetate. — *A.* Cellulose triacetate (Aldrich, 1 g) was dissolved in CH_2Cl_2 (30 mL) and the solution was mixed with a solution of M LiOH (3.5 mL) and 30% H_2O_2 (3.5 ML) in 30 mL of THF at room temperature. After stirring for 1 h, water (100 mL) was added and the mixture was vigorously stirred. Processing the organic phase and evaporation gave a colorless solid which was filtered and washed with water, then with EtOH. After being dried for 3 h at 120°, 0.82 g of a product (A) was obtained having a total d.s. of 1.90 (d.s., O-6, 0.83; O-3, 0.55; O-2, 0.52), based on ^{13}C-n.m.r. analysis[24].

B. The same experiment was repeated with 8.4 mL of LiOH, and 8.4 mL of H_2O_2 in 60 mL of THF. The product (B, 0.75 g) had a d.s. of 1.53 (d.s., O-6, 0.72; O-3, 0.36; O-2, 0.45).

C. The same experiment was repeated with 10.5 mL of LiOH and 10.5 mL of H_2O_2 in 60 mL of THF. The product (C, 0.6 g) had a d.s. of 0.58, (d.s., O-6, 0.35; O-3, 0.15; O-2, 0.08).

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