SYNTHESIS OF α,β-UNSATURATED, CARBONYL SUGAR DERIVATIVES BY METHYL SULFOXIDE OXIDATION AND ELIMINATION

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ABSTRACT

Oxidation of some partially *O*-acylated sugar derivatives with methyl sulfoxide in the presence of sulfur trioxide and triethylamine is described With a few exceptions, compounds possessing a free primary, secondary, or anomeric hydroxyl group are smoothly oxidized, and when an acyloxy group is suitably situated α,β elimination also occurs The last conditions have permitted the synthesis of a variety of α,β-unsaturated carbonyl compounds, namely, derivatives of 4-deoxy-6-*aldehydo*-L-*threo*-hex-4-enodialdo-1,5-pyranose, their L-*erythro* analogs, and 3-deoxyglyc-2-enono-1,5-lactone It appears that the α-*threo* and α-*erythro* isomers adopt the H_2^1 conformation, and the β-*threo* and β-*erythro* isomers adopt the H_1^2 conformation, and that the anomeric effect contributes importantly to these tendencies The overall rates and extent of the oxidation–elimination sequence are strongly dependent on the concentration of sulfur trioxide and of triethylamine, and on the order of mixing of the reagents Under the reaction conditions selected, the rates are largely insensitive to the position of the hydroxyl group and to the initial, relative disposition of the proton and acyloxy group eliminated Although the benzoyloxy (but not benzyloxy) group was readily eliminated in some instances, in others the requisite, initial oxidation step could not be effected

INTRODUCTION

Oxidation of carbinols with methyl sulfoxide[1-3] is promoted by a variety of reagents, for example, *N*,*N*′-dicyclohexylcarbodiimide[1], acid anhydrides[4,5], aminoacetylenes[6], and sulfur trioxide–triethylamine[7], and these sometimes differ importantly in their effectiveness For example, attempts to oxidize the primary hydroxyl group of 1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose with methyl sulfoxide–acetic anhydride yielded mainly the 6-*O*-(methylthio)methyl derivative of the compound[8-10], whereas the aldehyde is by far the major product when *N*,*N*′-dicyclohexylcarbodiimide[11] or sulfur trioxide–triethylamine[10] is the promoter. Use of the latter with some

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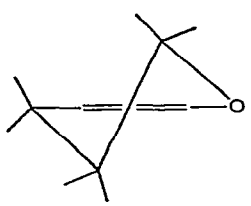
partially *O*-acetylated sugar derivatives results not only in formation of carbonyl products, but also in rapid elimination of β-acetoxyl groups[10]. The present article deals with certain characteristics of this oxidation–elimination sequence, describes a variety of α,β-unsaturated carbonyl derivatives synthesized through its use, and examines their conformational characteristics

RESULTS AND DISCUSSION

1. Oxidation of primary hydroxyl groups — A D-gluco *and* D-galacto *Isomers* Aldohexopyranose derivatives containing a free, primary hydroxyl group and a 4-*O*-acetyl group undergo oxidation–elimination Thus, methyl 2,3,4-tri-*O*-acetyl-α-D-galactopyranoside and methyl 2,3,4-tri-*O*-acetyl-α- and β-D-glucopyranoside yield the corresponding 4-deoxy-6-*aldehydo*-hex-4-enodialdopyranosides possessing either the β- or α-L-*threo* configuration (**1** or **2**, respectively)[10,12] Related compounds in these series (**3**–**8**) have now been synthesized, respectively, from 1,2,3,4-tetra-*O*-acetyl-α- and β-D-glucopyranose, 1,2,4-tri-*O*-acetyl-3-*O*-methyl-α- and β-D-glucopyranose, methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside and phenyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranoside The fourth compound furnishes an example of the successful elimination of a 4-benzoyloxy group under these conditions

Based on p m r. spectral data, the α-L-*threo* isomer (**2**) appears to exist in the H_2^1 conformation (**9**), whereas its anomer (**1**) adopts the H_1^2 conformation[12] (**10**). This



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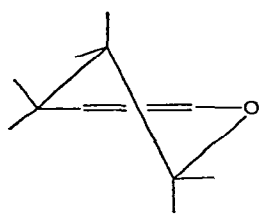

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difference could account for the fact that H-4 and H-2 of **2** exhibit long-range coupling* (about 1 Hz), whereas the corresponding protons of **1** do not The p m r spectral data for compounds **3**–**8** (see Table I) show these same characteristics Thus, signal H-4 in the spectrum of **4**, **6**, or **8** is a quartet containing a spacing of about 1 Hz attributable to long-range coupling with H-2 By contrast, signal H-4 of **3**, **5**, or **7** shows coupling only with H-3, and hence appears as a doublet** Together with other data in Table I [for example, $J_{1,2}$ of the α-L-*threo* isomers is much smaller than that of the β-L anomers (see also, refs 14 and 15)], these findings illustrate the general-

*A recent description of the conformational dependence of long-range H–H coupling is given by Barfield[13].

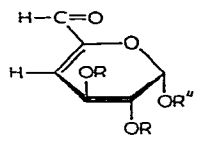
The specific assignment of signals in the spectra of **3 and **4** was greatly facilitated by reference to the spectra of **5** and **6** An upfield shift of H-3 in the latter spectra permitted a clear differentiation between that signal and H-2, and, hence, between H-1 and H-4. This choice was not possible directly for **3** and **4**, because of the greater symmetry of their spectra.

TABLE I

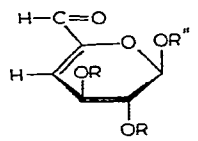
P M R. DATA FOR 4 DEOXY-6-*aldehydo*-L-*threo*-HEX-4-ENODIALDO-1,5-PYRANOSE DERIVATIVES

Compound	*Solvent*[a]	*Chemical shifts and spacings*[b]				
		H 6	*H-4*	*H-3*	*H-2*	*H-1*
1	P	9 34 s)	6 14 (d) (2 9)	5 93 (q) (2 6, 7 5)	5 42 (q) (2 9, 7 5)	5.38 (d) (2 6)
2	P	9 35 (s)	6 14 (q) (1 1, 4 0)	5 83 (m) (0 8)	5 32 (m) (1 1)	5.22 (q) (0 8, 3.8)
3	C	9 28 (s)	5 92 (d) (3 2)	5 64 (q) (3 2, 7 5)	5 29 (q) (2 5, 7 5)	6 43 (d) (2 5)
4	C	9 28 (s)	6 14 (q) (1 2, 4 8)	5.32 (o) (1.1, 2 1, 4 8)	5 19 (o) (1 2, 2 1, 3.2)	6 44 (q) (1 1, 3.2)
5	C	9 25 (s)	6 08 (d) (3 4)	4.23 (q) (3 4, 7 1)	5 21 (q) (2 6, 7.1)	6 46 (d) (2 6)
6	C	9 42 (s)	6.23 (q) (1 2, 4 8)	3 98 (m) (1 0, 4 7, 4 8)	5 35 (m) (1 2,3.2, 4 7)	6 46 (q) (1.0, 3 2)
7	A	9 28 (s)	6 06 (d) (3 0)	6 18 (q) (3 0, 8 6)	5 61 (q) (2 8, 8 6)	5 41 (d) (2 8)
8	A	9 25 (s)	6 14 (q) (1 1, 4.2)	5 41 (m)	5 14 (m)	5.87 (q) (0 9, 3.5)
11	C	9 26 (s)	6 02 (q) (1 5, 5 0)	5 26 (m)	5 06 (m)	4 42 (o) (1.5, 3 2, 12.5) 4 08 (q) (1 9, 12 5)

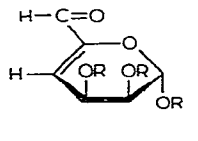
[a]P, pyridine-d_5, C, chloroform-*d*, A, acetic acid-d_4 [b]Chemical shifts (no parentheses) are in p p m (δ), spacings (Hz) are the numbers in parentheses, d, doublet, m, multiplet, o, octet, q, quartet, s, singlet



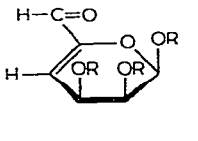
1 R=R=Ac R″=Me
3 R=R′=R″=Ac
5 R=Me, R′=R=Ac
7 R=R=Bz, R″=Me



2 R=R=Ac, R″=Me
4 R=R=R″=Ac
6 R=Me, R=R″=Ac
8 R=R=Ac, R″=Ph
11 R=R′=Ac, OR″=H



12 R=Ac R=Me
15 R=R=Ac



16 R=R=Ac

ity already cited, namely, that, among glycals of this class, the conformation is dependent upon the configuration at the anomeric center Because these same spectral differences are found among the related 4,5-unsaturated 4-deoxy hexuronic acids[12], they provide a basis for assigning anomeric configuration in unsaturated oligosaccharides formed from glycuronans (polyuronides) by enzymic β-elimination[12]

Assumption of the H_2^1 or H_1^2 conformation involves, in each instance, a pseudo-axial orientation for the anomeric substituent, an indication that the anomeric effect is operative in these glycals* Such an orientation should be favored additionally in such compounds, as compared with their saturated analogs, by the absence of an unfavorable interaction with H-5 However, the disposition of the 2- and 3-acetoxyl groups appears also to be an important factor, this is suggested by the characteristics of the product (**11**) obtained from 2,3,4-tri-*O*-acetyl-1,5-anhydro-D-glucitol, a glycal of this series in which the 1-*O*-substituent has been replaced by a hydrogen atom Thus, the p m r spectrum of **11** (see Table I) shows long-range coupling between H-2 and H-4 (as well as between H-1 and H-3), constituting evidence that this compound is in the H_2^1 conformation Probable stabilizing factors in this instance are the *quasi*-axial orientation of the allylic 2-acetoxyl group (the "allylic effect", which amounts to about[17] 0 8 kcal mol^{-1}) and the elimination of a 2,3-*gauche* interaction that would be present in the H_1^2 conformation Presumably, then, in the β-L-*threo* isomers, these factors are minor in comparison to a relatively stronger tendency for the anomeric *O*-substituent to be oriented axially The latter, therefore, amounts to a value of at least 1 7 kcal mol^{-1} in these half-chair, six-membered-ring compounds

B D-manno *Isomers* Related oxidations have been conducted in the D-*manno* series with derivatives having an unprotected, primary hydroxyl group and a 4-*O*-acetyl group, this work furnished 4,5-unsaturated 6-*aldehydo* products having the 2,3-L-*erythro* configuration, and, also, information about the effect of configurational inversion at C-2 on the conformation of these kinds of glycals

On treatment with the Parikh–Doering modification of the methyl sulfoxide oxidant[7], methyl 2,3,4-tri-*O*-acetyl-α-D-mannopyranoside yields crystalline methyl 2,3-di-*O*-acetyl-4-deoxy-6-*aldehydo*-β-L-*erythro*-hex-4-enodialdo-1,5-pyranoside (**12**) This product was characterized by analysis, by chemical tests, by the fact that it

*A strong orientation effect is observed in glycals in which the anomeric carbon is allylic to the double bond[16]

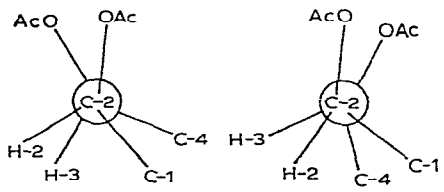
TABLE II

P.M.R. DATA FOR 4-DEOXY-6 *aldehydo*-L-*erythro*-HEX-4-ENODIALDO-1,5-PYRANOSE DERIVATIVES

Compound	*Solvent*[a]	*Chemical shifts and spacings*[b]				
		H-6	*H-4*	*H-3*	*H-2*	*H-1*
12	A	9.27 (s)	6.00 (q) (1.6, 2.0)	5.82 (q) (3.0, 8.6)	5.40 (m) (1.6, 2.9, 4.5)	5.19 (d) (2.9)
15	C	9.31 (s)	5.85 (m)	5.85 (m)	5.36 (m) (1.8, 3.9)	6.49 (d) (3.9)
16	C	9.27 (s)	5.94 (q) (0.6, 4.5)	5.80 (m) (1.1, 5.0)	5.41 (o) (0.6, 2.5, 5.0)	6.52 (q) (1.1, 2.1)

[a]A, acetic acid-d_4, C, chloroform-*d*. [b]Chemical shifts (no parentheses) are in p.p.m. (δ), spacings (Hz) are the numbers in parentheses, d, doublet, m, multiplet, o, octet, q, quartet, s, singlet

affords erythritol tetraacetate after ozonolysis, and by its spectral characteristics In the p m r spectrum of this compound (see Table II), the vinylic proton (H-4) signal is a quartet containing a spacing of 1 6 Hz that arises from long-range coupling with H-2 Also, the 1-, 2-, and 3-proton signals show relatively small splitting, suggesting that these protons are attached *quasi*-equatorially and, hence, that the anomeric methoxyl group is *quasi*-axially attached Accordingly, compound **12** may be assigned the H_1^2 conformation A molecular model suggests that this conformation can accommodate two extreme arrangements about the C-2,3 bond, as in **13** and **14** Of these, the latter appears more likely to permit the particularly strong (1 6 Hz) long-range H-2,H-4 coupling observed.



13 14

Analogous results were obtained with 1,2,3,4-tetra-*O*-acetyl-α-D-mannopyranose, the corresponding, crystalline glycal (**15**) being isolated in 72% yield The p m r spectral characteristics of this product (see Table II), including strong (2 0 Hz) H-2,H-4 coupling, again indicate that the β-L-*erythro* configuration is associated with the H_1^2 conformation and the arrangement about the C-2,3 bond depicted in **14**

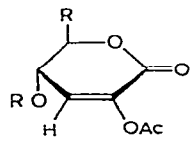
When oxidized in the same way as for its anomer, 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose yielded 1,2,3-tri-*O*-acetyl-4-deoxy-6-*aldehydo*-α-L-*erythro*-hex-4-enodialdo-1,5-pyranose (**16**) The structure of this product was determined chemically and spectroscopically, as described for the compounds already discussed Particularly noteworthy in the p m r spectrum of **16** (see Table II) is the evidence of long-range coupling *both* between H-1 and H-3 (1 1 Hz) and between H-2 and H-4 (0 6 Hz) Inspection of Dreiding models indicates that these couplings are possible in the H_2^1 conformation, but not in the alternative half-chair conformation, and it also appears probable that the relative disposition of the 2,3-substituents is as in compound **14**

Hence, there is overall a close parallelism between *erythro* and *threo* diastereoisomers, in that α-L anomers favor the H_2^1 conformation, whereas β-L anomers assume the H_1^2 conformation In all instances, a marked tendency is observed for the anomeric C—OR bond to assume a *pseudo*-axial orientation

2 Oxidation at the anomeric center — Onodera *et al*[18] have reported that the oxidation of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose with methyl sulfoxide–phosphorus pentaoxide gives a 20% yield of methyl 2,3,4,6-tetra-*O*-acetyl-D-gluconate With acetic anhydride as the promoter, Kuzuhara and Fletcher[19] obtained conversion of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose into the corresponding lactone, whereas other oxidants (chromic anhydride[20], oxygen–platinum[20], or *N*-bromocarbamide[21])

have been found unsatisfactory for oxidation of these and related derivatives at the anomeric center

As reported earlier[10], when 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose is treated with methyl sulfoxide–triethylamine–sulfur trioxide, oxidation and elimination both occur readily and afford, in 81% yield, 2,4,6-tri-*O*-acetyl-3-deoxy-D-*erythro*-hex-2-enono-1,5-lactone (**17**)* Characterization of this product by chemical and spectroscopic means is now described in fuller detail Under the same reaction conditions, 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranose also yields **17**, providing additional support for the structure proposed for this product In the aldopentose series, 2,3,4-tri-*O*-acetyl-α-D-xylopyranose was found to undergo rapid oxidation–elimination to afford the corresponding 1,5-lactone (**18**)



17 R = CH_2OAc, R′ = Ac
18 R = H, R′ = Ac
21 R = CH_2OAc, R′ = 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl

The p m r spectrum of **17** (see Table III) suggested that this compound exists largely in the H_0^5 conformation (**19**), the observed value of 5 2 Hz for $J_{4,5}$ is more consistent with a *quasi*-diequatorial than a *quasi*-diaxial orientation for these two protons Similarly, a *quasi*-equatorial orientation for H-4 is supported by the observed value of 4 6 Hz for $J_{3\,4}$, which corresponds[24] to a dihedral angle of about 45° between vicinal allylic and vinylic C–H bonds Although both the 5-(acetoxymethyl) and 4-acetoxyl groups are *quasi*-axial in the H_0^5 conformation, there are no substituents

TABLE III

P M R DATA FOR 3-DEOXYGLYC-2-ENONO-1,5-LACTONE DERIVATIVES

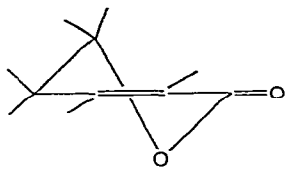
Compound	*Chemical shifts and spacings*[a]					
	H-3	*H-4*	*H-5*	*2H-6*	*Enol acetate*	*Ester acetate*
17[b]	6 43 (d) (4 6)	5 60 (q) (4 6, 5 2)	4 71 (m)	4 30 (o)	2 23 (s)	2 10 (s), 2 15 (s)
18[c]	6 62 (q) (1 0, 5 9)	5 45 (m) (2 3, 3 1, 5 9)	4 56 (5,5′) (m) (1 0, 2 3, 3 1, 13 0)	—	2 28 (s)	2 10 (s)
21[b]	6 59 (d) (2 0)	4 65 (4,5) (m)		4 26 (m)	2 29 (s)	2 02-2 14 (3 s)

[a]Chemical shifts (no parentheses) are in p p m (δ), spacings (Hz) are in parentheses, d, doublet, m, multiplet, o, octet, q quartet, s, singlet [b]Chloroform-*d* as solvent [c]Acetic acid-d_4 as solvent

*See refs 22 and 23 for analogous reactions

oriented unfavorably in opposition to the former group, and the latter, being an allylic ester function, probably favors the axial disposition, as in related glycal derivatives[17]

The p m r spectrum of the 5-carbon, unsaturated lactone **18** provides even clearer evidence that this product exists in the H_0^5 conformation Thus, the spin–spin couplings of 2 3 and 3 1 Hz (see Table III) exhibited by the C-4 and 5 protons indicate that H-4 is *gauche* with respect to both H-5 and H-5′, and hence is *quasi*-equatorial It is noteworthy that H-3 and H-5 of **18** are long-range coupled (1 0 Hz, see Table III), whereas this is not true of **17** Possibly, this difference means that the H_5^0 conformation (**20**) contributes importantly to a fuller representation of **17**, but that only the H_0^5 conformation need be considered in depicting **18**



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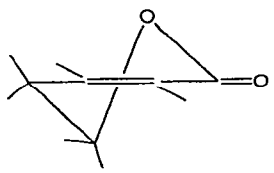

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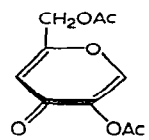

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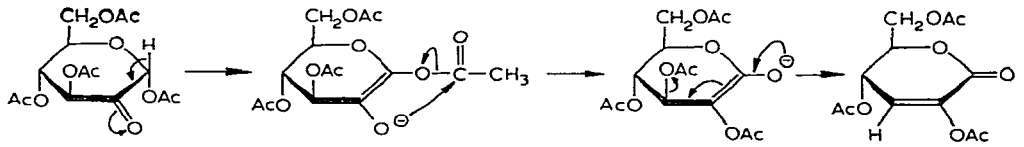
Treatment of 2,3,4,6,2′,3′,6′-hepta-*O*-acetylcellobiose with the methyl sulfoxide oxidant afforded the crystalline, unsaturated lactone **21** Among evidence supporting the latter formulation is the fact that ozonolysis of the compound, followed by borohydride reduction, gave 2-*O*-β-D-glucopyranosyl-D-erythritol[25] Although the p m r spectrum of **21** was only partially resolved (see Table III), signal H-3 of the lactone residue (at 6 59 p p m) is a doublet of 2 0-Hz spacing, that is, it is much smaller than $J_{3,4}$ for **17** and **18** This narrow spacing is not inconsistent with the possibility that the glycal residue of **21** favors the H_5^0 conformation Perhaps this contrasting behavior, relative to **17** and **18**, is associated with the presence in **21** of a 4-ether substituent, which thereby removes possible stabilization of the H_0^5 conformation by an allylic-ester effect

Treatment of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose with methyl sulfoxide–sulfur trioxide–triethylamine afforded the saturated 1,5-lactone, just as found by previous workers[19] who used methyl sulfoxide–acetic anhydride as the oxidant That is, the 3-benzyloxy group is not eliminated under these conditions More surprising, however, was the finding that 2,3,4,6-tetra-*O*-benzoyl-D-glucopyranose, and also the D-*manno* tetrabenzoate, are *totally unreactive, even towards initial oxidation**

3 Oxidation at a secondary position — Oxidation of 1,3,4,6-tetra-*O*-acetyl α-D-glucopyranose with methyl sulfoxide in the presence of either sulfur trioxide–triethylamine[10] or acetic anhydride[26 27] is accompanied by the elimination of *two* molecules of acetic acid The product is di-*O*-acetylkojic acid[26 27] (**22**), and a mechanism that reasonably accounts for its formation has been presented by Chittenden[27]

*The free hydroxyl group adjacent to an *O*-benzoyl substituent in a derivative of *epi*-inositol is reported[45] to be resistant to a variety of oxidants, including the reagent used here

In the present study, **22** was also synthesized from 1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose and -mannopyranose and, in addition, all of the reactions were accompanied by formation of a minor product With the D-*gluco* and D-*manno* isomers, this product was identified as the unsaturated lactone **17** The latter could conceivable arise from the intermediate ketone (**23**) *via* enolization, migration, and elimination, as illustrated. However, its main origin undoubtedly lies in migration of the 1-*O*-acetyl group to the 2-position *prior* to oxidation, under the conditions normally employed in these reactions Thus, when a solution of 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose in methyl sulfoxide–triethylamine was kept for 8 h (*i e* , much longer than usual) before addition of the sulfur trioxide, the lactone was the major, and **22**, the minor, product Conversely, when all three components of the oxidant were pre-mixed and the carbohydrate then added (see later), kojic acid diacetate was formed almost exclusively.



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The 4-hydroxyl group of methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside was found in the current study to be completely resistant to oxidation, although the compound undergoes oxidation and elimination with methyl sulfoxide–acetic anhydride[26], and is oxidized by ruthenium tetraoxide[28] This behavior parallels that of the 2,3,4,6-tetrabenzoates discussed, and illustrates that the Parikh–Doering modification, like the Pfitzner–Moffatt reagent, is relatively sensitive towards the structure of the intended substrate

4 Some characteristics of the oxidation–elimination reaction — The reaction conditions used in this study were essentially those described by Parikh and Doering[7], although, in searching for optimal yields, several variants have been tested As stressed by these workers, the order of addition of the reagents is important, in their procedure, the substrate is dissolved in methyl sulfoxide, triethylamine is added (but is only sparingly miscible), and then a solution of the sulfur trioxide complex in methyl sulfoxide is introduced, whereupon the reaction mixture becomes homogeneous This procedure is associated with the evolution of much heat, and intense darkening of the solution When the order of addition of the last two reagents was reversed, no oxidation occurred, although this was found not to be due to competitive sulfation of the hydroxyl group However, it was possible to effect reaction by premixing the three components of the oxidant and then introducing the substrate, as already noted for the preparation of **22**, under these conditions, the sharp rise in temperature and the darkening of the reaction mixture were largely obviated Also, the procedure was equally efficient in promoting reaction, because the rates of conversion of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside into **1** under the two sets of conditions were essentially equal

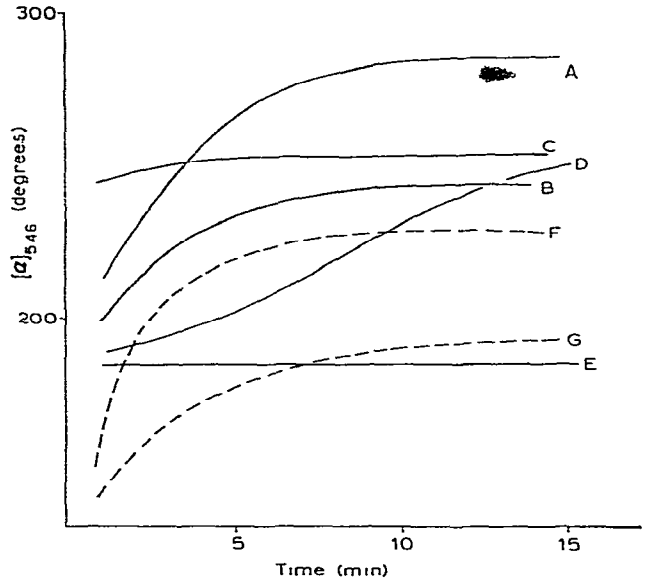

Fig. 1 Optical rotatory measurement (at 546 nm) of rates of oxidation–elimination [Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (1 mmole) plus (A) 15 mmoles of triethylamine (TEA) and 6 mmoles of sulfur trioxide–pyridine complex (SPC), (B) 15 mmoles of TEA and 3 mmoles of SPC, (C) an additional 3 mmoles of SPC introduced at 15 min into B, (D) 10 mmoles of TEA and 6 mmoles of SPC, (E) 5 mmoles of TEA and 6 mmoles of SPC Methyl 2,3,4-tri-*O*-acetyl-α-D-mannopyranoside (using reactant proportions as in A) in anhydrous methyl sulfoxide (F), with trace of water added (G)]

In the present study, it was found necessary to use a 6 1 ratio of sulfur trioxide–pyridine complex to substrate, in order to achieve complete reaction; this is a much higher ratio than that employed by Parikh and Doering[7] With a ratio of only 3 1 and the reaction terminated after the same interval of time, oxidation was incomplete, and it could not then be forced to completion by doubling the proportion of the complex at this stage of the reaction (see Fig 1) These results indicate that the initial rate of oxidation is strongly dependent upon the concentration of sulfur trioxide*, and that the maximal yield of the carbonyl product is obtainable only if the total quantity of sulfur trioxide is added at the outset The pyridine moiety appears to play no unique role, as it was replaced satisfactorily by extra triethylamine However, unless an *excess* of the base was present, no oxidation occurred. In fact, as Parikh and Doering[7] have shown, a very high proportion of triethylamine** is required, in our experiments, we preferred to use a minimum of 15 moles of the base per mole of the alcohol, to ensure rapid completion of the reaction (see Fig 1) The exclusion of moisture from the reaction mixture was also highly beneficial (see Fig 1) In some

*By contrast, when methyl sulfoxide oxidation is promoted with acetic anhydride, there is an induction period, and the kinetics appear to be zero-order[19]

**Triethylamine was replaced satisfactorily by its trimethyl, propyl or -butyl analog, although not by sodium ethoxide

instances, about half of the normal volume of methyl sulfoxide was replaced by diluent benzene or *N,N*-dimethylformamide, without noticeable effect on the reaction

In addition to the effects of the reaction conditions on the progress of these reactions, the possible influence of the stereochemistry of the substrate was examined It was, however, found that, aside from those few instances already noted in which oxidation of partially *O*-benzoylated derivatives failed to occur, the effects of structural variations on the rate were minor Thus, there was relatively little difference in the reaction rates of primary and secondary alcohols Also, approximately equal rates were found for each of the following diastereoisomeric pairs methyl 2,3,4-tri-*O*-acetyl α-D-glucopyranoside and -galactopyranoside, 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose and -mannopyranose, and 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose and -mannopyranose That is, no differences in rate were observable occasioned by different orientation of the hydroxyl group, or by different orientation of the leaving groups, whether *trans-e,e*, *trans-a,a*, or *cis-a,e*, initially It is, nevertheless, possible that there are distinct stereochemical differences, but that these were obscured under the reaction conditions used, the latter having been specifically selected to ensure efficient oxidation–elimination

EXPERIMENTAL

General — Evaporations were conducted under diminished pressure at a bath temperature below 60° Infrared spectra were recorded, for KBr discs or for solutions in carbon disulfide, with a Unicam SP200 infrared spectrophotometer Mass spectra were measured with an A E I MS902 instrument operating at 70 eV P m r spectra were recorded with a Varian HA-100 n m r spectrometer (internal standard, tetramethylsilane), the apparent coupling-constants (in Hz) reported are the directly observed line-spacings Microanalyses were performed by Dr C Daessle, Montreal

Thin-layer chromatography (t l c) was performed with Kieselgel G (Merck) as the adsorbent, and the following solvent systems *A*, ethyl acetate, *B*, 4 1 benzene–methanol, *C*, 9 1 benzene–methanol, and *D*, 1 1 benzene–ether Compounds were detected with iodine vapor, 10% sulfuric acid, or (2,4-dinitrophenyl)hydrazine in phosphoric acid–ethanol, where applicable, they were detected by viewing the plates under u v light

Measurement of rates of oxidation–elimination — The compound was dissolved in dry methyl sulfoxide, triethylamine was added, and the solution was made up to a specific volume with methyl sulfoxide Pyridine–SO_3 complex in a specific volume of dry methyl sulfoxide was then added, and optical rotatory measurements were made on the reaction mixture at chosen intervals By using 1 mmole of substrate to 15–20 mmoles of triethylamine and 6 mmoles of pyridine-SO_3 complex, most of the reactions examined in this study proceeded to completion in 10–20 min (see Fig 1)

*Methyl 2,3-di-*O*-acetyl-4-deoxy-6-*aldehydo-*β*-L-threo-*hex-4-enodialdo-1,5-pyranoside* (**1**) — Methyl 2,3,4-tri-*O*-acetyl-α-D-galactopyranoside (see later) was oxidized by the procedure used for the D-*gluco* isomer[12] The triacetate (0 32 g) was dissolved in methyl sulfoxide (3 5 ml), and triethylamine (1 5 ml) was added To this

well-stirred mixture, pyridine–SO_3 complex (0 95 g, 6 molar equiv) in methyl sulfoxide (10 ml) was added After 20 min, cold chloroform (100 ml) was introduced, and the solution was washed successively with tartaric acid solution (100 ml), sodium hydrogen carbonate (100 ml), and ice-water (2 × 100 ml), dried, decolorized with charcoal, and concentrated, affording a colorless oil (0 22 g, 83%), $[\alpha]_D$ +308° (*c* 2 0, chloroform) Its u.v. and p m r spectral characteristics (see Table I) were indistinguishable from those of **1** obtained from the corresponding D-glucoside[12], and it gave the same (2,4-dinitrophenyl)hydrazone, m p 177–179°

Ozonolysis of **1** — Compound **1** (250 mg) was dissolved in dry carbon tetrachloride, and the solution was cooled to 5° and treated with a stream of ozone Sodium borohydride (120 mg) in cold aqueous ethanol (5 ml) was added, the mixture shaken overnight, and the aqueous layer was made neutral with Amberlite IR-120 (H^+) ion-exchange resin, and concentrated Co-evaporation with methanol under diminished pressure removed the remaining boric acid An oil was obtained, $[\alpha]_D$ −35° (*c* 2, water), which, on a paper chromatogram (solvent *A*), migrated as a single spot having the mobility of threitol The oil was dissolved in pyridine (3 ml) and acetic anhydride (2 ml), and, after 5 h, analysis of the product by g l c showed the presence of a compound having the retention time of 1,2,3,4-tetra-*O*-acetyl-D-threitol

*Methyl 6-*O*-trityl-2,3,4-tri-*O*-acetyl-α-D-galactopyranoside* — Water of crystallization was removed *in vacuo* from methyl α-D-galactopyranoside monohydrate at 110° Dry methyl α-D-galactopyranoside (10 g), chlorotriphenylmethane (20 44 g), and anhydrous pyridine (75 ml) were heated together for 3 h on a steam bath, the solution was cooled, and acetic anhydride (30 ml) was added After 24 h, the solution was poured into ice–water, and the precipitate was filtered off, washed with ice–water, and air-dried. Two recrystallizations from 95% ethanol gave the pure title compound (16 4 g, 52%), m p 167–169°, $[\alpha]_D$ +49 3° (*c* 2, chloroform)

Anal Calc for $C_{32}H_{34}O_9$ C, 68 3, H, 6 0 Found C, 68 1, H, 5 8

*Methyl 2,3,4-tri-*O*-acetyl-α-D-galactopyranoside* — Removal of the trityl group from the preceding ether (5 98 g, 0.01 mole) was achieved with cold, 32% hydrobromic acid in glacial acetic acid (3 ml) After 45 sec, the bromotriphenylmethane was filtered off, the filtrate was poured into ice–water (400 ml), and the resulting suspension was extracted with chloroform (3 × 100 ml) The extracts were combined, successively washed with cold sodium hydrogen carbonate and ice–water (twice), dried (sodium sulfate), and evaporated under diminished pressure A syrup (2 16 g) was obtained that had $[\alpha]_D$ +93 5° (*c* 4, chloroform) and consisted essentially of one component, R_F 0 32 (solvent *B*) Further purification of the product by column chromatography on silica gel did not lead to crystallization, but tritylation gave back the crystalline trityl ether from which it had been prepared, indicating that acetyl migration had not occurred

*Methyl 2,3,4-tri-*O*-acetyl-β-D-galactopyranoside* — Methyl 2,3,4-tri-O-acetyl-6-*O*-trityl-β-D-galactopyranoside[30] (5 86 g) was detritylated in the way described for the α anomer A syrupy product (1 98 g) was obtained that had $[\alpha]_D$ −9 8° (*c* 3 1, chloroform); its identity was verified by re-*O*-tritylation

*Methyl 2,3-di-*O*-acetyl-4-deoxy-6-*aldehydo-α-L-threo-*hex-4-enodialdo-1,5-pyranoside* (**2**) — Methyl 2,3,4-tri-*O*-acetyl-β-D-galactopyranoside (0 32 g) was oxidized as already described, and processing of the reaction mixture yielded a chromatographically pure syrup (0 19 g, 73%) having $[\alpha]_D$ +31 9° (*c* 3 3, chloroform) Its u v and p m r. spectral characteristics (see Table I) were indistinguishable from those of **2** obtained by the oxidation of methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranoside[12] The (2,4-dinitrophenyl)hydrazone prepared from the syrup had m p 167–168°, undepressed on admixture with that from **2** prepared by the other method

*1,2,3-Tri-*O*-acetyl-4-deoxy-6-*aldehydo-α-L-threo-*hex-4enodialdo-1,5-pyranose* (**4**) — 1,2,3,4-Tetra-*O*-acetyl-β-D-glucopyranose[31] was dissolved in methyl sulfoxide (5 ml), and triethylamine (2 7 ml) was added Pyridine–SO_3 complex (1 43 g, 9 mmoles) in methyl sulfoxide (15 ml) was then added, and the mixture was shaken After 15 min, cold chloroform was introduced, and the mixture was subjected to the four-stage extraction previously described for the preparation of **1** A syrupy product (352 mg, 85 5%) was obtained that had $[\alpha]_{546}$ +10 5° (*c* 2 4, chloroform), R_F 0 73 (solvent *A*) The product was chromatographed on a column of silica gel with ethyl acetate at a flow rate of 60 ml per h, 10-ml fractions being collected Fractions 22–26 were found by t l c to contain a u v -active compound (303 mg, 65%), it had $[\alpha]_{546}$ +16 6° (*c* 4, chloroform), λ_{max}^{MeOH} 245 nm (ε 2750), it decolorized acidified potassium permanganate solution, and a solution of bromine in carbon tetrachloride, ν_{max}^{KBr} 1753 (C=O acetyl), 1715 (C=O), and 1662 cm^{-1} (conj C=C) Its p m r spectrum is described in Table I

Anal Calc for $C_{12}H_{14}O_8$ C, 50 4, H, 4 9 Found C, 49 9, H, 5 3

Semicarbazone of **4** — To a solution of **4** (57 mg) in ethanol was added dropwise a solution of sodium acetate (44 mg) and semicarbazide hydrochloride (50 mg) in water (2 ml), and the solution was warmed gently for 30 min Concentration resulted in the formation of crystals These were filtered off, and recrystallized from ethanol, m p 205–207°

Anal Calc for $C_{13}H_{17}N_3O_8$ C, 45 5, H, 5 0, N, 12 2 Found C, 45 7, H, 5 3, N, 12 3

*1,2,3-Tri-*O*-acetyl-4-deoxy-6-*aldehydo-β-L-threo-*hex-4-enodialdo-1,5-pyranose* (**3**) — 1,2,3,4-Tetra-*O*-acetyl-α-D-glucopyranose[32] (696 mg, 2 mmoles) was oxidized as described for its β anomer, affording an oil (483 mg, 87%) Chromatography on a column (20 × 2 cm) of silica gel with ethyl acetate as the eluant gave **3** as a slightly colored oil, $[\alpha]_D$ +111° (*c* 2 4, chloroform), λ_{max}^{MeOH} 246 nm (ε 4205), it decolorized a solution of bromine in carbon tetrachloride, ν_{max}^{KBr} 1750 (C=O, acetyl), 1715 (HC=O), and 1668 cm^{-1} (C=C, conj) The p m r spectrum is described in Table I

Anal Calc for $C_{12}H_{14}O_8$ C, 50 4, H, 4 9 Found C, 50 9, H, 4 7

Semicarbazone of **3** — Compound **3** (75 mg) was treated with semicarbazide hydrochloride as described for its α anomer The resulting crystals were recrystallized from 70% ethanol, m p 190–192°

Anal Calc for $C_{13}H_{17}N_3O_8$ C, 45 5, H, 5 0, N, 12 2 Found C, 45 8, H, 4 7, N, 12 0

1,2,4-Tri-O-acetyl-3-O-methyl-6-O-trityl-α-D-glucopyranose — 1,2,4-Tri-*O*-acetyl-3-*O*-methyl-6-*O*-trityl-β-D-glucopyranose was prepared essentially by the method described earlier[33] On prolonged standing, the mother liquor of the β-acetate yielded plate-like crystals (3 86 g), $[\alpha]_D$ +79 5°. Recrystallization from ethanol yielded pure title compound (3 29 g, 19 5%), m p 145°, $[\alpha]_D$ +92 2° (*c* 2, chloroform)

Anal Calc for $C_{32}H_{34}O_9$ C, 68 3, H, 6 0; Found C, 68 3; H, 5 7

1,2,4-Tri-O-acetyl-3-O-methyl-β-D-glucopyranose — A solution of 1,2,4-tri-*O*-acetyl-3-*O*-methyl-6-*O*-trityl-β-D-glucopyranose (5 69 g, 0 01 mole) in glacial acetic acid (20 ml) was cooled to 5°, and 32% hydrobromic acid in glacial acetic acid (3 5 ml) was added After 45 sec, the precipitated bromotriphenylmethane was filtered off, and washed with acetic acid (10 ml) The filtrate was immediately poured into ice–water and chloroform The chloroform extract was washed twice with ice–water, dried (sodium sulfate), and evaporated under diminished pressure to a syrup Crystallization and recrystallization from ether–hexane gave long, needle-shaped crystals (1 87 g, 60 5%), m p 121–122°, $[\alpha]_D$ +13 2° (*c* 3, chloroform)

Anal Calc for $C_{13}H_{20}O_9$· C, 48 8, H, 6 3 Found C, 49 2; H, 6 1

*1,2-Di-O-acetyl-4-deoxy-3-O-methyl-6-*aldehydo-α-L-threo-*hex-4-enodialdo-1,5-pyranose* (**6**) — 1,2,4-Tri-*O*-acetyl-3-*O*-methyl-β-D-glucopyranose (0 320 g, 1 mmole) was dissolved in methyl sulfoxide (3 5 ml), and triethylamine (1 5 ml) was added, followed by pyridine–SO_3 complex (0 98 g, 6 mmoles) dissolved in methyl sulfoxide (10 ml) After 15 min, the mixture was poured into cold chloroform, and processed, to give a syrup (0 193 g, 74 5%), $[\alpha]_D$ −69 8° (*c* 1, chloroform), λ_{max}^{MeOH} 246 nm (ε 3,760), ν_{max}^{KBr} 1750 (C=O, acetyl), 1708 (H–C=O), and 1645 cm^{-1} (C=C, conj) The compound decolorized a solution of bromine in carbon tetrachloride The p m r spectrum is described in Table I

The (2,4-dinitrophenyl)hydrazone of **6**, prepared in the usual way, was recrystallized from acetonitrile; m p 127–129°

Anal. Calc. for $C_{17}H_{18}N_4O_{10}$· C, 46.8; H, 4.1, N. 12 8. Found. C, 46 7, H, 4 4; N, 13 2

1,2,4-Tri-O-acetyl-3-O-methyl-α-D-glucopyranose — 1,2,4-Tri-*O*-acetyl-3-*O*-methyl-6-*O*-trityl-α-D-glucopyranose[33] (2 99 g; 5 3 mmoles) was dissolved in acetic acid and cooled to 5°, 32% hydrobromic acid in acetic acid (1 5 ml) was added, and the mixture was shaken for 45 sec The resulting bromotriphenylmethane was filtered off, the filtrate was immediately poured into ice–water (250 ml), the suspension was filtered, the filtrate was extracted with chloroform (3 × 50 ml), and the extracts were combined, successively washed with cold water, cold sodium hydrogen carbonate, and cold water (2 × 100 ml), dried, and evaporated to a syrup (0 948 g), $[\alpha]_D$ +124 5° (*c* 1, chloroform) This syrup was chromatographically pure (R_F 0 42 in Solvent *A*, 0 31 in Solvent *B*)

*1,2-Di-O-acetyl-4-deoxy-3-O-methyl-6-*aldehydo-β-L-threo-*hex-4-enodialdo-1,5-pyranose* (**5**) — 1,2,4-Tri-*O*-acetyl-3-*O*-methyl-α-D-glucopyranose (320 mg) was oxidized in the way described for its anomer, to yield **5** as an oil (194 mg, 67 5%); $[\alpha]_D$ +242° (*c* 3 3, chloroform); λ_{max}^{MeOH} 247 nm (ε 2,150), ν_{max}^{KBr} 1755 (C=O, acetyl),

1715 (H–C=O), and 1660 cm^{-1} (C=C, conj) The p m r spectrum is described in Table I

A crystalline (2,4-dinitrophenyl)hydrazone was prepared, m p 140–143°

2,3,4-Tri-O-acetyl-1,5-anhydro-6-O-trityl-D-glucitol —1,5-Anhydro-D-glucitol[34] (8 9 g, 0 05 mole) and chlorotriphenylmethane (1 48 g, 0 05 mole) were slowly added to anhydrous pyridine (150 ml) and, after 24 h, acetic anhydride (80 ml) was introduced slowly into the cooled mixture, which was then kept for 18 h at room temperature Water was added to turbidity, the mixture was poured into ice-water (1 1 liters), and the granular precipitate formed was filtered off, washed, and air-dried Two recrystallizations from ethanol gave pure product (17 52 g, 65 9%), m p 92–93°, $[\alpha]_D$ +82° (*c* 3 4, pyridine)

Anal Calc for $C_{31}H_{32}O_8$. C, 69 9, H, 5 9 Found C, 70 4, H, 6 2

2,3,4-Tri-O-acetyl-1,5-anhydro-D-glucitol — Removal of the trityl group from the foregoing anhydride (11 9 g, 0 02 mole) was effected with cold acetic acid–32% hydrobromic acid (5 ml) for 60 sec at 5° The oil obtained after treatment with ice–water and extraction into chloroform was crystallized from anhydrous ether–hexane with the aid of vigorous scratching, yield, 5 9 g Recrystallization from ether–hexane gave pure product (5 32 g, 80 5%), m p. 111–113°, $[\alpha]_D$ +49 9° (*c* 3, chloroform)

Anal Calc for $C_{12}H_{18}O_8$ C, 49 3, H, 6 2 Found C, 49 0, H, 6 2

*2,3-Di-O-acetyl-1,5-anhydro-4-deoxy-6-*aldehydo-L-threo-*hex-4-enitol* (**11**) — Oxidation of 2,3,4-tri-*O*-acetyl-1,5-anhydro-D-glucitol (0 61 g), as described for the preparation of compound **1**, gave a chromatographically pure oil (0 384 g, 79%), λ_{max}^{MeOH} 245 nm (ε 4,050), $[\alpha]_D$ +170° (*c* 2 4, chloroform), ν_{max}^{KBr} 1750 (C=O, acetyl), 1713 (HC=O), and 1663 cm^{-1} (C=C, conj)

The crystalline (2,4-dinitrophenyl)hydrazone was prepared, and thrice recrystallized from ethanol, m p 185–186°

Anal Calc for $C_{16}H_{16}N_4O_9$ C, 47 0, H, 3 9, N, 13 7, mol wt , 408 Found C, 47 2; H, 3 7, N, 13 4, M^+ 408

*Phenyl 2,3-di-O-acetyl-4-deoxy-6-*aldehydo-α-L-threo-*hex-4-enodialdo-1,5-pyranoside* (**8**) — Oxidation of phenyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranoside[35] (0 764 g, 2 mmoles) to give the title compound was conducted in the usual way with methyl sulfoxide (25 ml), triethylamine (3 ml), and pyridine–SO_3 complex (1 97 g, 12 mmoles) Chromatography of the resulting oil on a column (2 × 30 cm) of silica gel with ethyl acetate as the eluant gave a glass (0 487 g, 76%), $[\alpha]_D$ −107° (*c* 2, chloroform); λ_{max}^{MeOH} 248 nm (ε 3,450); ν_{max}^{KBr} 1725 (C=O, acetyl), 1716 (HC=O), and 1668 cm^{-1} (C=C, conj) The p m r spectrum is described in Table I

Anal Calc for $C_{16}H_{16}O_7$ C, 60 0, H, 5 0, Found C, 60 5, H, 5 1

*Methyl 2,3-di-O-benzoyl-4-deoxy-6-*aldehydo-β-L-threo-*hex-4-enodialdo-1,5-pyranoside* (**1**) — Oxidation of methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside[36] (0 54 g) yielded an oil (268 mg, 70 5%), $[\alpha]_D$ +253° (*c* 3, chloroform); λ_{max}^{MeOH} 250 nm (ε 4,850); ν_{max}^{KBr} 1740 (C=O, benzoyl), 1715 (C=O, aldehydic). 1650 (C=C, conj), 1600, and 1580 cm^{-1} (C=C, aromatic) The p m r spectrum is described in Table I.

Anal Calc for $C_{21}H_{18}O_7$ C, 65 7, H, 4 7 Found C, 66 1, H, 4 1

The (2,4-dinitrophenyl)hydrazone of **7** was prepared, it crystallized, with difficulty, from ethyl acetate–ethanol, m p 206–208°

*1,2,3-Tri-O-acetyl-4-deoxy-6-*aldehydo-α-L-erythro*-hex-4-enodialdo-1,5-pyranose* (**16**) — To 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose[37] (0 696 g, 2 mmoles) dissolved in methyl sulfoxide (10 ml), was added triethylamine (3 ml) Pyridine–SO_3 complex (1 98 g, 12 mmoles) in methyl sulfoxide (15 ml) was then added, and the mixture was shaken After 15 min, chloroform (100 ml) was added, and the resultant solution was processed, yielding an oil Crystallization from ether–hexane gave pure **16** (0 424 g, 74%), m p 92–93°, $[\alpha]_D$ +49° (*c* 2, chloroform), λ_{max}^{MeOH} 247 nm (ε 2,980) The product decolorized acidic potassium permanganate solution and bromine solution, and gave positive Schiff and Tollens tests, ν_{max}^{KBr} 1752 (C=O, acetyl), 1708 (C=O, aldehydic), and 1652 cm^{-1} (C=C, conj) The p m r spectrum is described in Table II

Anal Calc for $C_{12}H_{14}O_8$ C, 50 0, H, 4 9; mol wt , 286 Found· C, 50 2; H, 5 0, M^+, 286

Ozonolysis of compound **16** — Compound **16** (250 mg) was subjected to ozonolysis as already described The acetylated product, crystallized from ethanol, was tetra-*O*-acetylerythritol, m p and mixed m p , 88–89°

*1,2,3-Tri-O-acetyl-4-deoxy-6-*aldehydo-β-L-erythro*-hex-4-enodialdo-1,5-pyranose* (**15**) — 1,2,3,4-Tetra-*O*-acetyl-α-D-mannopyranose (prepared from the 6-trityl ether[33]) (700 mg) was oxidized as described for its anomer Crystallization from ethyl acetate–hexane yielded compound **15** (415 mg, 72%), m p 116–117°, $[\alpha]_D$ +284° (*c* 1, chloroform), λ_{max}^{MeOH} 248 nm (ε 3,670), Schiff and Tollens tests positive; ν_{max}^{KBr} 1750 (C=O, acetyl), 1700 (C=O, acetyl), 1700 (C=O, aldehydic), and 1650 cm^{-1} (C=C, conj) The p m r spectrum is described in Table II

Anal Calc for $C_{12}H_{14}O_8$ C, 50 0, H, 4 9 Found C, 49 8, H, 5 1

*Methyl 2,3-di-O-acetyl-4-deoxy-6-*aldehydo-β-L-erythro*-hex-4-enodialdo-1,5-pyranoside* (**12**) — Oxidation of methyl 2,3,4-tri-*O*-acetyl-α-D-mannopyranoside[38] (640 mg, 2 mmoles) gave crystalline **12** Recrystallization from ether–hexane yielded pure material (0 362 g, 70%), m p 57–59°, $[\alpha]_D$ +244° (*c* 2, chloroform), λ_{max}^{MeOH} 249 nm (ε 4,050) It gave positive Schiff and Tollens tests, decolorized bromine solution, and reacted with (2,4-dinitrophenyl)hydrazine, ν_{max}^{KBr} 1706 (C=O, aldehydic) and 1650 cm^{-1} (C=C, conj) The p m r spectrum is described in Table II

Anal Calc for $C_{11}H_{14}O_7$ C, 51 2, H, 5 4 Found· C, 51 3; H, 5 4.

*2,4,6-Tri-O-acetyl-3-deoxy-*D-erythro*-hex-2-enono-1,5-lactone* (**17**) — 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranose[39] (3 48 g, 10 mmoles) was dissolved in methyl sulfoxide (20 ml), and triethylamine (15 ml) and pyridine–SO_3 complex (9 87 g, 60 mmoles) in methyl sulfoxide (30 ml) were added sequentially After 30 min, chloroform (150 ml) was added, and the mixture was processed in the usual way The syrup obtained was subjected to short-path, vacuum distillation, to yield a chromatographically pure syrup that decolorized bromine solution; $[\alpha]_D$ +108° (*c* 3, chloroform); λ_{max}^{EtOH} 219 nm (ε 8,100); ν_{max}^{KBr} 1755 (C=O, acetyl) and 1670 cm^{-1} (C=C, conj) The p m r spectrum is described in Table III

Anal Calc for $C_{12}H_{14}O_8$· C, 50 3, H, 4 9, Found C, 50 2, H, 4 7

Ozonolysis of compound **17** — Compound **17** (500 mg) in carbon tetrachloride at 0° was subjected to ozonolysis as already described The syrup obtained was treated with pyridine–acetic anhydride for 24 h, and the solution was processed to yield tetra-*O*-acetylerythritol, m p 87–89°, mixed m p 87–88°

Preparation of **17** *from 2,3,4,6-tetra*-O-*acetyl*-D-*mannose* — 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranose[40] (3 48 g) was oxidized as described for 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose, to yield **17** as a chromatographically pure oil (2 22 g, 77%), $[\alpha]_D$ +107 5°, λ_{max}^{EtOH} 218 nm (ε 7,900) The spectral characteristics of this compound were indistinguishable from those of **17** obtained by oxidation of the D-*gluco* isomer

2,4-Di-O-*acetyl-3-deoxy*-D-glycero-*hex-2-enono-1,5 lactone* (**18**) — Oxidation of 2,3,4-tri-*O*-acetyl-α-D-xylopyranose[41] (0 546 g, 2 mmoles) yielded an oil {0 231 g, 55%, $[\alpha]_D$ +130 2° (*c* 2, chloroform)} which was distilled *in vacuo* to give chromatographically pure **18**, $[\alpha]_D$ +139 9°, the compound decolorized bromine solution, $\lambda_{max}^{H_2O}$ 218 nm (ε 6,150), ν_{max}^{KBr} 1750 (C=O, acetyl), 1710 (C=O, conj), and 1650 cm^{-1} (C=C, conj) The p m r spectrum is described in Table III

Anal Calc for $C_9H_{10}O_6$ C, 50 5, H, 4 7 Found C, 50 0, H, 4 9

2,6-Di-O-*acetyl-3-deoxy-4*-O-(*2,3,4,6-tetra*-O-*acetyl-β*-D-*glucopyranosyl*)-D-erythro-*hex-2-enono-1,5-lactone* (**21**) — 2′,3′,6′,2,3,4,6-Hepta-*O*-acetyl cellobiose[42] (1 91 g) dissolved in methyl sulfoxide (10 ml) was added to triethylamine (4 5 ml), followed by a solution of pyridine–SO_3 complex (3 1 g, 0 02 mole) in methyl sulfoxide (10 ml) After 30 min, the mixture was processed in the usual way, to give an oil of R_F 0 79 and 0 57 (solvents *A* and *B*) that subsequently crystallized Recrystallization from ether–hexane gave pure **21**, m p 128–129°, $[\alpha]_D$ +27 9° (*c* 3, chloroform), λ_{max}^{MeOH} 214 nm (ε 7350) The i r spectrum showed a weak band at 1663 cm^{-1} The p m r spectrum is described in Table III

Anal Calc for $C_{29}H_{30}O_{16}$ C, 50 2, H, 5 2. Found C, 50 5; H, 4 9

Ozonolysis of compound **21** — Compound **21** (300 mg) was dissolved in dry carbon tetrachloride, and the solution was cooled to 0° Ozonolysis, reduction, and processing in the usual way afforded crystals of 2-*O*-β-D-glucopyranosyl-D-erythritol, m p 184–185°, mixed m p 185°

2,3,4,6-Tetra-O-*benzyl*-D-*glucono-1,5-lactone* — To a solution of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose[43] (0 54 g, 1 mmole) in methyl sulfoxide was added triethylamine (1 5 ml), followed by a solution of pyridine–SO_3 complex (0 987 g) in methyl sulfoxide (10 ml) After 20 min, the mixture was processed in the usual way, to give an oil (0 47 g, 87%), $[\alpha]_D$ +79° (*c* 3 3, chloroform), lit [12] $[\alpha]_D$ +79 9° The i r spectrum in carbon disulfide showed an absorption band at 1754 cm^{-1} (C=O, δ-lactone)

2,3,4,6-Tetra-O-*benzyl*-N,N-*dimethyl*-D-*gluconamide* — To a solution of the preceding lactone (3 g) in cold, anhydrous ether was added cold dimethylamine (4 ml) The solution was kept for 3 min at room temperature, and evaporated, and the product was crystallized from cyclohexane, yield, 2 7 g (84%), m p 100–102°

mixed m p 100–103°, $[\alpha]_D$ +34 9° (*c* 3 3, chloroform), lit [19] m p 101–103°, $[\alpha]_D$ +35 1°

*Oxidation of 1,3,4,6-Tetra-*O*-acetyl-α-*D*-glucopyranose to di-*O*-acetylkojic acid* (**22**) — 1,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranose[44] (3 48 g, 0 01 mole) was dissolved in methyl sulfoxide (20 ml), triethylamine (15 ml) was added, and pyridine–SO_3 complex (9 54 g, 0 06 mole) predissolved in methyl sulfoxide was introduced with stirring The temperature rose to 37°, and the solution turned yellow T l c of the mixture after 20 min (solvent *C*) showed two components (R_F 0 50 and 0 74) that were revealed by u v light and with iodine (only the minor, faster-moving compound was detected by spraying with sulfuric acid), no starting-material was present The mixture was diluted with chloroform and processed in the usual way, affording a crystalline product that was recrystallized from ether–hexane Two further recrystallizations from isopropyl ether gave pure **22** (1 4 g, 61%), m p 100–101°, undepressed on admixture with di-*O*-acetylkojic acid; $[\alpha]_D$ 0°; λ_{max}^{MeOH} 252 nm (ε 10,600); ν_{max}^{KBr} 1781 (C=O, enol Ac), 1760 (C=O, acetate), and 1678 cm^{-1} (doublet C=O, C=C) The p m r spectrum (in $CDCl_3$) contained the following signals 7 05 (1-proton singlet), 6 05 (1-proton singlet), 4 90 (1-proton singlet), 2 30 (3-proton singlet, enol Ac), and 2 15 (3-proton singlet, OAc)

Anal Calc for $C_{10}H_{10}O_6$ C, 53 1, H, 4 5, mol wt, 226 Found C, 53 5, H, 4 4, M^+ 226

The mother liquor was evaporated to a syrup (0 347 g) that did not crystallize This material had spectral characteristics indistinguishable from those of **17** prepared by the oxidation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose

*Oxidation of 1,3,4,6-tetra-*O*-acetyl-α-*D*-galactopyranose* — Treatment of the tetraacetate (3 48 g) in the way described for the D-*gluco* isomer gave di-*O*-acetylkojic acid (**22**) (1 276 g, 56%), m p 100–102°, mixed m p 100–102° The i r, u v, and p m r spectra were indistinguishable from those of the authentic compound A minor, unidentified product was obtained from the mother liquor

*Oxidation of 1,3,4,6-tetra-*O*-acetyl-β-*D*-mannopyranose.* — The tetraacetate (3 48 g) was oxidized in the way described for the D-*gluco* and D-*galacto* isomers to give di-*O*-acetylkojic acid (1 58 g, 69%); m p 100–102°, mixed m p 100–102° The i r, u v, and p m r spectra were indistinguishable from those of an authentic sample.

A minor product (0 376 g), obtained as an oil from the mother liquor, was identified as **17** by its spectral characteristics

*Effect of prolonged treatment of 1,3,4,6-tetra-*O*-acetyl-α-*D*-glucopyranose with triethylamine* — 1,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranose (3 48 g, 0 01 mole) was dissolved in methyl sulfoxide (20 ml), triethylamine (10 ml, 0 10 mole) was added, and the mixture was shaken vigorously for 8 h Pyridine–SO_3 complex (9 54 g, 0 06 mole) predissolved in methyl sulfoxide was then added After 20 min, t l c (solvent *C*) of the mixture showed the presence of only one component, moving faster than the starting material, the mixture was processed, to yield a chromatographically pure oil indistinguishable from unsaturated lactone **17**.

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