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RING CONTRACTION DURING THE LEAD TETRAACETATE OXIDATION OF REDUCING SUGARS[1]

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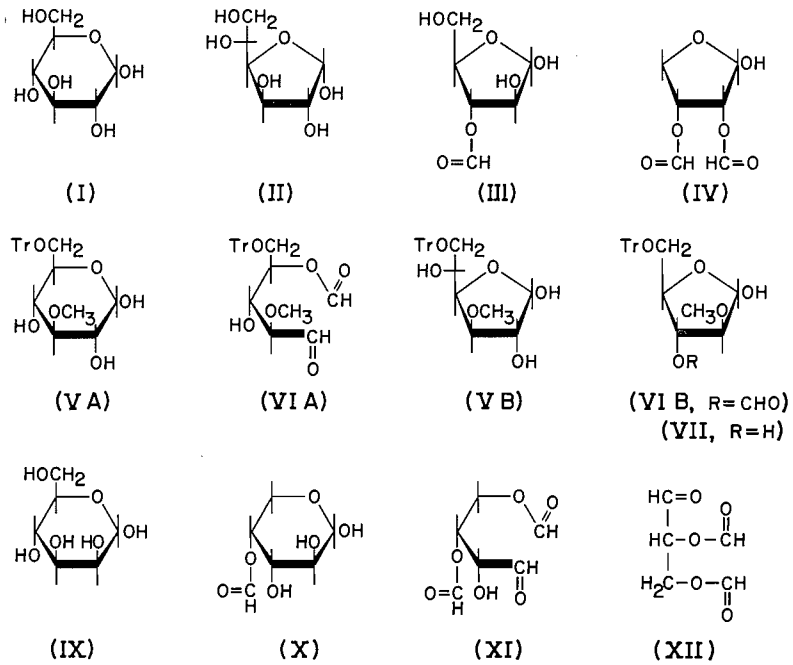
ABSTRACT

The rate of oxidation of D-glucose by lead tetraacetate in acetic acid is affected little by a large change in concentration of reactants, showing that the glycol cleavage step is not rate-controlling. Oxidation of 3-*O*-methyl-6-*O*-trityl-D-glucose yields 3-*O*-formyl-2-*O*-methyl-5-*O*-trityl-D-arabinose; the latter is not derived by production initially of a 4-*O*-formyl derivative that undergoes acyl migration. It is probable that the oxidation of D-glucose proceeds with conversion of the pyranose sugar into a furanose intermediate. By contrast, D-mannose appears to be oxidized mainly in the pyranose form, as shown by the oxidation patterns of D-mannose-1- and -2-^{14}C and 5-*O*-methyl-D-mannofuranose, and the effects of concentration change on the reaction of D-mannose and derivatives. The proximity of the ring oxygen atom to the 1,2-diol group may contribute to the unusually high reactivity of D-mannopyranose as compared with other types of monocyclic six-membered ring *vic*-diols.

Intermediate proportions of furanose and pyranose pathways characterize the lead tetraacetate oxidation of the other six aldohexoses. Similarities in the behavior of glucose and idose, gulose and mannose, and allose and talose may originate in steric similarities between these pairs of sugars.

The lead tetraacetate oxidation (1, 2) of reducing sugars in acetic acid involves primarily the cleavage of α-hydroxy hemiacetal glycol groups, and results in a stepwise shortening of the carbon chain (3, 4, 5). However, the uptake of oxidant in these reactions is lower than might be anticipated. For example, D-glucose (I) consumes only 2 moles of lead tetraacetate per mole rather than the 3 moles theoretically possible for the 1,2,3,4-tetrol grouping of the pyranose sugar (I), yielding a diformate ester of D-erythrose rather than of D-glycerose. A possible explanation for these results is to assume that a complex (6) between the tetravalent lead and the 1,2-diol group of α-D-glucofuranose (II) is an intermediate in the reaction. This complex could be formed directly from the pyranose sugar, by analogy with the formation of D-glucofuranose 1,2-acetals and borate complexes (7, 8), or from the furanose sugar if present in solution even as a minor constituent. Dissociation of the complex would give 3-*O*-formyl-D-arabinose, which, oxidized as a furanose sugar (III), would yield 2,3-di-*O*-formyl-D-erythrose (IV). Thus, involvement of a reactive structure such as II accounts for the high rate of the reaction (5, 9), as well as the consumption of only 2 moles of oxidant per mole. Consistent with these possibilities is the fact that derivatives of D-glucose that are prevented from going over to a furanose form by substituents at C-4 are oxidized much more slowly than D-glucose itself, whereas the rate is essentially unaltered by a substituent at C-3 or C-6 (10).

[1]*Issued as N.R.C. No. 8101.*



In the oxidation route depicted above, the initial product is a 3-, rather than a 4-, formate ester. Support for this step is provided by examining the oxidation of 3-*O*-methyl-6-*O*-trityl-D-glucose to mono-*O*-formyl-2-*O*-methyl-5-*O*-trityl-D-arabinose. If the pyranose sugar (VA) were to be degraded directly, the product should be a 4-formate of the *aldehydo*-pentose (VIA), whereas a furanose intermediate (involving VB) should yield a 3-formate of the pentofuranose (VIB). Nuclear magnetic resonance (n.m.r.) spectral evidence strongly favors the latter formulation for the oxidation product. Its spectrum (Fig. 1*a*) is affected little by deacylation (Fig. 1*b*), aside from the expected shift towards

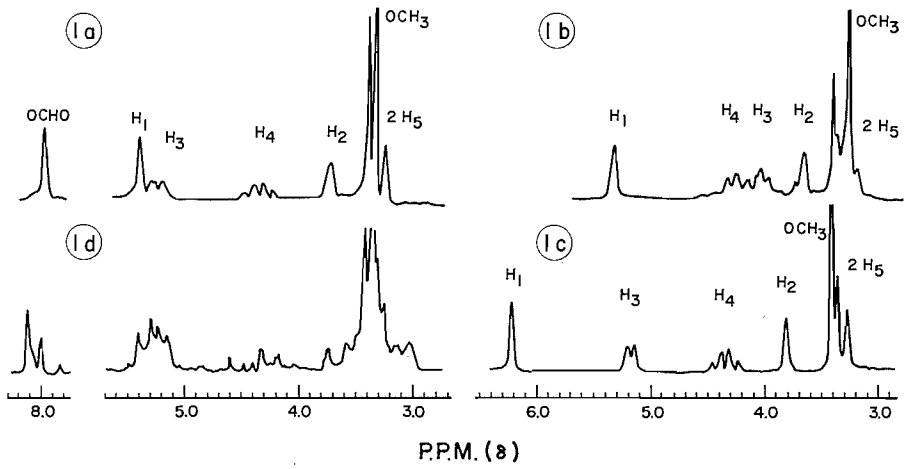


FIG. 1. The n.m.r. spectra of (*a*) 3-*O*-formyl-2-*O*-methyl-5-*O*-trityl-D-arabinose (VIB); (*b*) 2-*O*-methyl-5-*O*-trityl-D-arabinose (VII); (*c*) 1,3-di-*O*-acetyl-2-*O*-methyl-5-*O*-trityl-D-arabinose (signals for the acetyl protons are not shown); (*d*) the product (VIII) formed by oxidation with lead tetraacetate in benzene solution of 3-*O*-methyl-6-*O*-trityl-D-glucose.

higher field for the signal of the proton α to the formate group. If the oxidation product were acyclic (VIA), the gross conformational change inherent in its conversion into 2-*O*-methyl-5-*O*-trityl-D-arabinofuranose (VII) should surely be accompanied by greater differences than found between the spectra of these compounds. By contrast, the changes actually observed are those to be expected on simple deacylation of VI B to yield VII. Steric similarities between these latter two are emphasized further by acetylating VII. A n.m.r. spectrum is then obtained (Fig. 1*c*) that closely simulates the original spectrum (Fig. 1*a*), except that the H_1 signal has been shifted to lower field by the presence of the 1-acetoxy group.

Proton–proton coupling in Fig. 1*a* leads to the conclusion that H_3 of the oxidation product is located α to the formate group. The singlet at low field (5.4 p.p.m.) may be ascribed to H_1 (11)[2] and the singlet at 3.75 p.p.m. to its neighbor H_2, which appears at relatively high field because of the adjacent methoxyl group (12). Since H_2 is not coupled with H_3, the latter is undoubtedly the doublet at 5.25 p.p.m. which is split by coupling with H_4. Also, a proton situated at position-4 most readily accounts for the quartet at 4.40 p.p.m., since coupling is then permitted both with H_3 and the H_5 protons. Therefore, these data strongly support the conclusion that the product formed initially on oxidation of D-glucose is the 3-formate (III).

The oxidation of D-glucose to IV can be accounted for also by an alternative route whereby D-glucopyranose yields 4-*O*-formyl-D-arabinose, which then is converted into the 3-formate (III) by acyl migration (4).[3] This possibility could be favored even more with the trityl derivative (V), since migration of the formate from position-4 to position-3 (VIA $\rightarrow$ VIB) would permit ring closure. However, it is unlikely that such a transformation takes place, as shown by the following experiment in which V was treated with lead tetraacetate in benzene solution.

Since oxidations are much more rapid in benzene than in acetic acid (6), the pyranose form (VA) might itself be attacked in benzene with sufficient vigor to offset the displacement towards a furanose pathway, as presumably occurs in acetic acid. In fact, the product of oxidation in benzene (VIII) differs notably from the 3-formate (VIB), as seen in the contrast between its n.m.r. spectrum (Fig. 1*d*) and spectrum 1*a*. The major signal due to the formate proton is at slightly lower field in Fig. 1*d*; other signals are poorly resolved, with the broad multiplet at 3.3 p.p.m. accounting for about 7 of the remaining 10 protons. Relatively weak signals at 8.0, 5.4, 4.3, and 3.7 p.p.m., respectively (Fig. 1*d*), indicate that the 3-formate (VIB) is a minor constituent (about 25%) of this oxidation product. On deacylation, VIII yielded the same product as obtained from the 3-formate, i.e., VII (identified by chromatography and by the close identity of its n.m.r. spectrum with that shown in Fig. 1*b*). It is probable that VIII consists mainly of the 4-formate (VIA). Although VIII was not prepared in acetic acid, it was found to be quite stable in this solvent, showing that, if VIA had been produced by oxidation in acetic acid, it would not have rearranged readily to VIB. Therefore, a 3-formate must be derived from the D-glucose ether (V) and, undoubtedly, also from D-glucose itself by the initial cleavage of the α-hydroxy hemiacetal group in acetic acid.

Further evidence that D-glucose is oxidized in acetic acid via a reactive intermediate such as II is provided by examining the effect of dilution on the rates of cleavage of different *vic*-diols (Table I). The rate for the acyclic 3,4-diol group of 1,2:5,6-di-*O*-isopropylidene-D-mannitol is lowered by a factor of about 100 on dilution of the reaction mixture

[2]*This is supported by the effect of acetylation on the original (Fig. 1c) (12).*
[3]*This alternative has been regarded as highly likely (13).*

TABLE I

Influence of concentration on oxidation rate

	$T_{\frac{1}{2}}$(min)*		
	10^{-4} M†	10^{-2} M†	Ratio
1,2:5,6-Di-*O*-isopropylidene-D-mannitol	60	0.6	100
Cellobiose	450	9	50
Maltose	130	3	43
3-*O*-Methyl-D-glucose	2.5 (k_{27} 1 700)‡	0.7	3.5
3,5-Di-*O*-methyl-D-glucofuranose	— (k_{27} 100 000)‡	—	—
D-Glucose	2.5	0.5	5.0
4,6-*O*-Ethylidene-D-glucose	(very slow)	65	—
D-Mannose	3.5	0.1	35
4,6-*O*-Ethylidene-D-mannose	8.5	0.2	42

*Time required for uptake of 0.5 mole of lead tetraacetate per mole.
†Concentration of diol; the lead tetraacetate was present in 20% molar excess.
‡min^{-1} $mole^{-1}$ l; measured under the more dilute conditions.

100-fold. Similarly, a large decrease in rate is shown for D-glucopyranose when a change of ring size is prohibited, as with maltose or cellobiose (the reducing end-unit of which is oxidized preferentially (10)). By contrast, the rate of scission of the 1,2-diol group of 3-*O*-methyl-D-glucose is lowered by a factor of only 3.5 upon dilution.[4] This latter oxidation is controlled, not by the glycol cleavage step, but by the availability of some reactive species formed in an equilibrium displacement. That D-glucofuranose could function as such a species is suggested by the extreme reactivity of 3,5-di-*O*-methyl-D-glucofuranose compared with pyranose derivatives, its second-order rate constant being about 60 times that of even the 3-*O*-methyl derivative. With reactivity of this order, there need only be a small proportion of D-glucofuranose in the sugar solution to ensure its preferential oxidation in the presence of the dominant pyranose form. The ensuing equilibrium displacement step should be much less sensitive to a change in concentration than is the bimolecular oxidation step.

The reaction of D-mannose (IX) with lead tetraacetate contrasts sharply with that of D-glucose. Oxidation proceeds rapidly to a value of 2.8 moles per mole (4) and the product is chiefly di-*O*-formyl-D-glycerose (XII), with D-erythrose diformate (XI) being only a minor product. The oxidation is initiated primarily at the α-hydroxy hemiacetal group, as shown by the high yield of D-arabinose monoformate produced by limited oxidation (4). In addition, when D-mannose-1-^{14}C or -2-^{14}C is treated with 2.7 moles of lead tetraacetate per mole, products XI and XII account for almost all of the carbon-14, i.e.,

D-Mannose-1-^{14}C → products XI and XII,
(77 mμc/mmole CO_2) (76 mμc/mmole CO_2)

D-Mannose-2-^{14}C → products XI and XII.
(133 mμc/mmole CO_2) (126 mμc/mmole CO_2)

These results are readily explicable if the major reaction pathway proceeds in stepwise fashion, yielding at first 4-*O*-formyl-D-arabinose (X),[5] then 3,4-di-*O*-formyl-D-erythrose (XI), and finally the triose diformate (XII). Carbon-1 and carbon-2 of the original

[4]*Although not strictly comparable because of the overall greater uptake of oxidant involved, the reaction of* D-*glucose itself illustrates this same behavior. Thus, the time required for an uptake of 0.5 mole/mole is extended, on dilution, by a factor of only five.*

[5]*It was concluded earlier that 4-O-formyl-*D-*arabinose (X) cannot be the product formed initially in the oxidation of* D-*glucose. This is consistent with the oxidative behavior of* D-*mannose, for otherwise the two epimeric sugars should show the same overall reaction pattern.*

hexose are then retained in XII and carbon-3 is liberated.[6]

According to these data, a furanose pathway plays only a minor role in the oxidation of D-mannose. Nevertheless, D-mannofuranose should be highly reactive because it contains a *cis*-2,3-diol group on a five-membered ring, in addition to that potentially available at C-1 and C-2. As a model compound, 5-*O*-methyl-D-mannofuranose (14) was found to consume 1 mole of lead tetraacetate per mole very rapidly (k_{27} for this stage in dilute solution was estimated to be about 65 000) and additional oxidant much more slowly. Although acetal formation (15) and borate complexing (8) favor the 2,3- over the 1,2-diol group of D-mannofuranose, oxidation occurred chiefly at the 1,2-positions, since a pentose derivative was produced in 60% yield. Almost identical behavior was shown by 5-*O*-methyl-D-glucofuranose, in which the 2,3-diol group is *trans*. Clearly, then, the oxidation behavior of D-mannose itself cannot be reconciled with a high proportion of a furanose pathway, for the overall reaction should resemble more closely that of D-glucose.

Two other observations are consistent with a pyranose pathway predominantly for the D-mannose oxidation: the effect on reaction rates of (*a*) substitution at C-4, and (*b*) dilution. 4,6-*O*-Ethylidene-D-mannose[7] is oxidized at a rate comparable with that of the parent hexose both at low and high dilution, in marked contrast to the strong retarding effect of the same type of bicyclic system in the D-glucose series (Table I). In addition, a 100-fold dilution of the reaction mixture lowers the oxidation rate of D-mannose much more than that of D-glucose, showing that different types of pathways are operative for the two sugars.

The effect of a large change in concentration is seen in yet another way. The rapid uptake of 2.8 moles per mole by D-mannose (reported earlier) was measured at the higher concentration (ca. 10^{-2} *M*). Although this level of oxidation is reached with the more dilute reaction mixture (10^{-4} *M*), there is a marked decrease in rate after about 2 moles per mole have been taken up (Fig. 2). With the 4,6-*O*-ethylidene derivative there is also a sharp break in the curve, but this occurs at a level of 1 mole per mole. The 6-deoxy sugar (L-rhamnose) has been shown to consume rapidly about the same proportion of oxidant as does D-mannose (4). In dilute solution, its behavior is more akin to that of the *O*-ethylidene derivative. It is probable that the more rapid phases of these reactions involve cyclic forms of the sugars, and that the slower oxidations involve acyclic products (16). Thus, D-mannose and 4-*O*-formyl-D-arabinose (X) could together account for the rapid uptake of 2 moles per mole, whereas the resulting α-hydroxy aldehyde 3,4-di-*O*-formyl-D-erythrose (XI)[8] would be oxidized in the slow step. Similarly, *aldehydo* derivatives are produced by the initial degradation of 4,6-*O*-ethylidene-D-mannose to 3,5-*O*-ethylidene-4-*O*-formyl-D-arabinose (chromatographic evidence confirms a pentose product exclusively in this reaction) and of L-rhamnose to a 4-formate of 5-deoxy-L-lyxose. This could account for the rapid uptake of only 1 mole per mole by these latter sugars. By contrast, well-defined stages of this kind are not observed in the oxidation of D-glucose or of 6-substituted derivatives of it under the same conditions; however, no oxidizable acyclic products are expected in these reactions. D-Glucofuranose 5,6-carbonate, which initially should yield a 3,4,5-trisubstituted *aldehydo*-pentose,[9] is characterized by a two-

[6]*If the total reaction proceeds in this way, the product should actually be slightly more radioactive than the original hexose, since one unlabelled carbon atom would be lost as formic acid in the formation of XII.*

[7]*This derivative was kindly provided by Dr. D. M. Ball.*

[8]*At this stage, in fact, degradation has produced mainly tetrose formate, and very little triose formate has appeared. This was shown by chromatographic examination of the product formed on treating* D-*mannose with only 2 molar equivalents of lead tetraacetate under these dilute conditions.*

[9]*By oxidation of the hexose carbonate with 1 molar equivalent of lead tetraacetate,* D-*arabinose carbonate is obtained in high yield (17).*

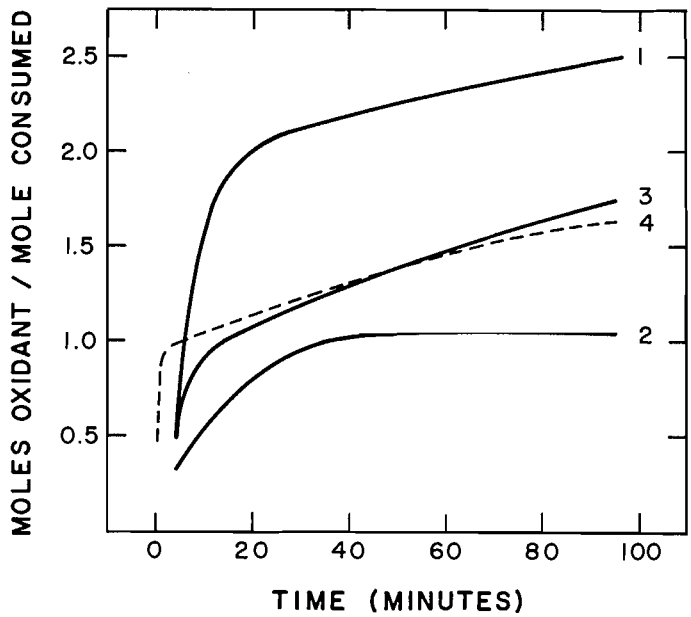


FIG. 2. Rates of lead tetraacetate consumption at high dilution (ca. 10^{-4} *M*) of (1) D-mannose; (2) 4,6-*O*-ethylidene-D-mannose; (3) 6-deoxy-L-mannose; (4) D-glucofuranose 5,6-carbonate (closely similar curves are given by D-erythrose and D-threose).

stage reaction. It is noteworthy that this latter curve is closely paralleled by those for D-erythrose and D-threose, each of which should afford an α-hydroxy aldehyde, viz. 3-*O*-formyl-D-glycerose.

The overall consistency of these different types of data leads to the conclusion that the oxidation of D-glucose in acetic acid involves preferential attack on D-glucofuranose or formation of a furanose intermediate, whereas, in the oxidation of D-mannose a pyranose form is involved chiefly. Apparently, the relative inertness of D-glucopyranose permits an equilibrium displacement in favor of the furanose pathway. However, even glucopyranose can be relatively reactive as compared with other kinds of monocyclic six-membered ring compounds; for example, the reducing unit of maltose or cellobiose is oxidized far more rapidly than is the nonreducing end-unit (10). D-Mannopyranose is a remarkably reactive monocyclic six-membered ring diol. This property of reducing sugars would not be predicted on steric grounds by comparing molecular models of pyranose forms with those of glycopyranosides and related cyclic polyhydric alcohols. In a free sugar, however, the unshared electron pair of the ring oxygen atom could aid materially in attracting the strongly electrophilic tetravalent lead atom towards the 1,2-diol group, increasing the effective concentration of oxidant about this region of the molecule. The models suggest that an orienting influence of this kind should be particularly noticeable with β-D-mannopyranose, the 1- and 2-oxygen atoms of which lie relatively close to the ring oxygen atom, but less so with α-D-glucopyranose (in accord with the higher reactivity of D-mannose).

Oxidation of Other Aldohexoses

The six other aldohexoses rapidly consume lead tetraacetate in proportions ranging between the values for D-glucose and D-mannose (4, 5) (Table II). Their oxidations have not been examined as extensively as those of the latter two sugars. A high yield of pentose

TABLE II

Lead tetraacetate uptake and configurational relations among the aldohexoses

	Furanose forms, ring configuration (19)	Pyranose forms						Lead tetraacetate uptake (moles/mole) (4, 5)
		Orientation of groups on:						
		C-1	C-2	C-3	C-4	C-5	Conformation	
α-D-Glucose	α-D-xylo-	*a*	*e*	*e*	*e*	*e*	*C 1*	2.0
β-D-Idose	α-L-xylo-	*a*	*e*	*e*	*e*	*a*	*1 C*	2.1
α-D-Galactose	α-D-arabino-	*a*	*e*	*e*	*a*	*e*	*C 1*	2.1
β-D-Altrose	α-L-arabino-	*a*	*e*	*e*	*a*	*a*	*1 C*	2.5
α-D-Allose	α-D-ribo-	*a*	*e*	*a*	*e*	*e*	*C 1*	2.3
β-D-Talose	α-L-ribo-	*a*	*e*	*a*	*e*	*a*	*1 C*	2.3
α-D-Gulose	α-D-lyxo-	*e*	*a*	*e*	*e*	*a*	*1 C*	2.7
β-D-Mannose	α-L-lyxo-	*e*	*a*	*e*	*e*	*e*	*C 1*	2.8

formate obtained by partial oxidation of D-galactose, D-allose, or D-altrose (4, 5) shows that these sugars are degraded preferentially in stepwise fashion from the reducing end. Di-*O*-formyl-D-threose is the major product obtained from D-galactose, consistent with a lead tetraacetate uptake of slightly over 2 moles per mole, whereas D-altrose, which consumes 2.5 moles per mole, affords about equimolar amounts of triose and tetrose formates.

The amounts of lead tetraacetate consumed in the oxidation of these aldohexoses may be interpreted in terms of the proportions of furanose and pyranose forms that have reacted. For example, D-idose consumes 2.1 moles of lead tetraacetate per mole, only slightly more than does D-glucose, so that its oxidation pathway probably involves chiefly a furanose form. It is noteworthy that the relative orientation of the 1-, 2-, and 3-hydroxyl groups and of C-5 in β-D-idofuranose is the same as in α-D-glucofuranose. This marked steric resemblance was emphasized by Isbell (19) in noting that these forms may be assigned the α-L-*xylo* and α-D-*xylo* configurations, respectively. Since there is little effective competition from a pyranose route in the oxidation of idose, the relative unreactivity of α-D-idopyranose is analogous to that of α-D-glucopyranose.[10] There are some notable steric similarities between these two forms. For example, in the two chair conformations (20) considered, the orientation of all substituents other than that of the C-6 carbinol groups is the same. On balance, free-energy changes accompanying the formation of the activated complexes could be lower by approximately the same amount for each furanose pathway than for each pyranose pathway, thus favoring the same oxidation pattern for the two aldohexoses.

This type of comparison, based on similar oxidation patterns and configurational resemblance, permits pairing of D-gulose with D-mannose. D-Allose and D-talose constitute a third pair for which there is good agreement, but the analogy does not hold as closely for the pair D-galactose and D-altrose.

The pyranose conformation listed for each sugar in Table II is chosen to emphasize similarities, and does not necessarily represent the most stable ground state of the individual compounds (20–24). Probably, this factor is not significant in some of the oxidations, since energy barriers separating conformers (23, 24) are small relative to, for example,

[10]*It is assumed that 1,2-cis-anomers of pyranose or furanose sugars are more likely to be attacked in these oxidations than are 1,2-trans-anomers.*

heats of reaction of lead tetraacetate oxidations (25, 26, 27). However, in an instance where both furanose and pyranose pathways are prominent (most notably, the oxidation of D-altrose), it could substantially affect the outcome, since this is dependent on the *difference* between overall free-energy changes for the competing pathways.

EXPERIMENTAL

Lead tetraacetate uptake was measured iodometrically (1, 2) with reaction mixtures in which the concentration of reactants was about 10^{-2} *M*, and spectrophotometrically (28) with reaction mixtures in which the concentration of reactants was about 10^{-4} *M*.

Proton magnetic resonance (n.m.r.) spectra were measured with a Varian A-60 high-resolution spectrometer, using chloroform or deuterochloroform as solvent and tetramethylsilane as internal standard. When the compound to be examined contained a free hydroxyl group, a preliminary deuterium exchange was carried out by shaking the chloroform solution twice with deuterium oxide.

Specific activity measurements were made by combustion analysis according to the procedure of Buchanan and Nakao (29).

Solutions were concentrated *in vacuo* at 40–45 °C.

*3-O-Methyl-6-O-trityl-*D*-glucose (V)*

3-*O*-Methyl-D-glucose (2.0 g) in pyridine (20 ml) was treated with chlorotriphenylmethane (3.4 g) at 3 °C for 18 h. Ice water was added, the syrupy deposit was extracted into chloroform, and the chloroform layer was washed well with water, dried, and concentrated. After being dried thoroughly in a high vacuum, the syrupy product was applied in chloroform solution (25 ml) to a column of dry silicic acid (4 cm × 40 cm). The column was developed with chloroform, fractions of the eluate being examined by thin-layer chromatography (solvent—benzene:methanol (9:1); spray—30% sulphuric acid; all products containing the trityl group gave a bright yellow color, whereas that also containing the sugar residue charred when the chromatogram was heated). Chromatographically pure material isolated was extracted into benzene, and the extract was concentrated, yielding a white solid (3.3 g); $[\alpha]_D$ 35° (*c*, 2, benzene).

Calcd. for $C_{26}H_{28}O_6$: C, 71.54; H, 6.47. Found: C, 71.81; H, 6.34.

*1,2,4-Tri-O-acetyl-3-O-methyl-6-O-trityl-β-*D*-glucose*

In a second preparation of V, on twice the scale above, additional pyridine (20 ml) and acetic anhydride (20 ml) were added to the reaction mixture at 48 h, and the solution was stored at 3 °C for a further 48 h. Ice water was added; the syrupy deposit was extracted into benzene; and the benzene extract was washed successively with cold sodium bicarbonate solution, cold tartaric acid solution, and water; then dried, and concentrated. The residue afforded crystalline material (2.8 g) from ethanol; m.p. 173–175 °C, $[\alpha]_D$ 18° (*c*, 2, chloroform.

Calcd. for $C_{32}H_{34}O_9$: C, 68.31; H, 6.09. Found: C, 68.57; H, 6.20.

*Lead Tetraacetate Oxidation of 3-O-Methyl-6-O-trityl-*D*-glucose (V)*

(*A*) To a solution of V in acetic acid (165 mg, 5 ml) was added an acetic acid solution of lead tetraacetate (7 ml; 160 mg (0.95 molar equivalents)). After 10 min reaction time, when a negative test was given for tetravalent lead, the solution was concentrated and the residue was extracted with benzene. The extract was washed three times with ice water, dried, and concentrated to a syrup (120 mg); $[\alpha]_D$ 20.6° (*c*, 3.3, methanol). The syrupy product (VI) absorbed strongly in the infrared region at 1725 and 1175 cm^{-1}, characteristic of a formate ester group; the n.m.r. spectrum is reproduced in Fig. 1*a*.

The oxidation product was taken up in methanol and treated with a slight excess of sodium methoxide; the calculated $[\alpha]_D$ of the deacylated product (VII) was 17.9°. Absorption bands in the infrared region due to a formate group were no longer detectable; otherwise, the spectra of VI and VII were virtually indistinguishable. The n.m.r. spectrum of VII is reproduced in Fig. 1*b*.

(*B*) A solution of V in dry benzene (100 mg; 5 ml) was treated with lead tetraacetate (92 mg) in dry benzene containing 2% of acetic acid (4 ml). A precipitate formed immediately, and a negative test for tetravalent lead was obtained within 30 s. The filtrate from the suspension was concentrated to yield a syrup (VIII) (80 mg), $[\alpha]_D$ − 4.0° (*c*, 3.7, chloroform), which was shown by infrared spectroscopy to contain a formate ester group; the n.m.r. spectrum is reproduced in Fig. 1*d*. After deacylation with sodium methoxide, the product gave an n.m.r. spectrum essentially the same as that shown in Fig. 1*b*. In another experiment, product VIII was stored for several hours as a solution in acetic acid. After removal of the solvent, the n.m.r. spectrum was indistinguishable from that shown in Fig. 1*d*.

*1,3-Di-O-acetyl-2-O-methyl-5-O-trityl-*D*-arabinose*

The deacylated oxidation product (VII) was taken up in a mixed solvent of pyridine and acetic anhydride (3 vol.:2 vol.), the solution was stored at 3 °C for 48 h and then poured into ice water. The syrupy deposit was extracted into benzene, the extract was washed with cold sodium bicarbonate solution, cold tartaric

acid solution, and ice water, and dried. Removal of the benzene afforded a colorless syrup, $[\alpha]_D$ 46° (*c*, 2.2, acetone).

Calcd. for $C_{29}H_{30}O_7$: C, 71.00; H, 6.16. Found: C, 71.19; H, 6.21.

*3,4-O-Isopropylidene-2-O-methyl-*D*-arabinose (30)*

2-*O*-Methyl-5-*O*-trityl-D-arabinose (VII) (120 mg; about one-half of this sample was derived from VIB and one-half from VIII) was taken up in acetone (5 ml), one drop of concentrated hydrochloric acid was added, and the solution was stored at 3 °C for 72 h. Excess lead carbonate was added, followed by water (10 ml); the neutral suspension was filtered, the filtrate was concentrated, and the residue was extracted with acetone. The acetone-soluble product (52 mg) solidified; m.p. 116–119 °C; $[\alpha]_D$ −107° (*c*, 2.5, methanol; no mutarotation observed).

D-*Mannose-2-*^{14}*C*

D-Mannose-2-^{14}C was prepared from D-mannono-1,4-lactone-2-^{14}C (kindly furnished by A. C. Neish) by reduction with sodium borohydride in the presence of Amberlite-IR-120 (H^+), according to the procedure of Frush and Isbell (31).

Lead Tetraacetate Oxidation of D-*Mannose or* D-*Mannose-*^{14}*C*

In a typical experiment, D-mannose (250 mg) in water (0.3 ml) was taken up in acetic acid (15 ml). A solution of lead tetraacetate (1.7 g; 2.7 molar equivalents) in acetic acid (50 ml) was added to the sugar solution over a period of 15 min, and this was followed 10 min later by a solution of oxalic acid (0.3 g) in acetic acid (5 ml). The precipitate of lead oxalate was filtered off through Celite, the filtrate was concentrated, and the residue was extracted with ethyl acetate. On being concentrated, the extract yielded a syrup which was purified by distillation (bath temp. 140 °C at 0.05 mm).

Samples of the syrup, after reduction with excess sodium borohydride, gave a mixture consisting mainly of erythritol and glyceritol (paper chromatographic evidence). These products were estimated, after elution from the chromatograms, by treatment with periodate, followed by analysis of the formaldehyde produced on oxidation (32). The ratio of erythritol to glyceritol was 6.8 to 3.2.

In experiments with D-mannose-^{14}C, the distilled oxidation product was used for the specific activity measurements.

*5-O-Methyl-*D*-glucose and 5-O-Methyl-*D*-mannose (2,5-dichlorophenyl) Hydrazones*

The 5-*O*-methyl sugars were prepared as chromatographically pure syrups by procedures described elsewhere (14, 33). By treatment with a methanolic solution of (2,5-dichlorophenyl) hydrazine (34), each sugar yielded a solid product that was recrystallized from ethyl acetate – benzene.

The substituted hydrazone of 5-*O*-methyl-D-glucose had m.p. 140–142 °C.

Calcd. for $C_{13}H_{18}Cl_3N_2O_5$: C, 44.20; H, 5.10. Found: C, 44.00; H, 5.31.

An attempt to prepare the dichlorophenylosazone by use of excess reagent and a longer reflux period, as with D-erythrose (35), was unsuccessful, only the substituted hydrazone being obtained in this experiment.

The substituted hydrazone of 5-*O*-methyl-D-mannose, m.p. 129–130 °C, contained benzene as solvent of crystallization (its presence being detected by gas–liquid chromatographic analysis of a concentrated solution of the hydrazone in methyl sulphoxide).

Calcd. for $C_{13}H_{18}Cl_2N_2O_5 \cdot O \cdot 5C_6H_6$: C, 48.99; H, 5.40; Cl, 18.08. Found: C, 49.00; H, 5.75; Cl, 18.47.

*Lead Tetraacetate Oxidation of 5-O-Methyl-*D*-glucose and -mannose*

The sugar derivative (10 mg) in acetic acid (1 ml) was treated with lead tetraacetate (22 mg) in acetic acid (1 ml) for 10 min; a negative test for tetravalent lead was given within this period. Water (5 ml) was added to the reaction mixture followed by excess of Amberlite-IR-120 (H^+), and the solution was warmed on the steam bath for 0.5 h, concentrated, and examined chromatographically. Three products were detected, the major component being indistinguishable from 4-*O* methyl-D-arabinose (unpublished preparation). Based on the intensity of color developed by the latter with the orcinol ferric chloride reagent for pentose (36), the yield of 4-*O*-methyl-D-arabinose produced in the oxidation of each 5-*O*-methyl hexose was estimated to be 57% (D-gluco isomer) and 60% (D-manno isomer).

When the sugar was treated at high dilution with 2 molar equivalents of lead tetraacetate, the uptake of oxidant (moles/mole) was as follows:

Time (min)	2	5	10	15	25
5-*O*-Methyl-D-glucose	0.83	1.00	1.18	1.27	1.36
5-*O*-Methyl-D-mannose	0.95	1.10	1.20	1.30	1.40

Measurement of lead tetraacetate uptake by 5-*O*-methyl-D-mannose at the outset of the reaction gave the following data, calculated as second-order rate constants (min^{-1} $mole^{-1}$ l) at 27 °C: 67 900 (0.20 min); 70 900 (0.25 min); 64 100 (0.30 min); 54 100 (0.40 min).

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