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THE OXIDATION OF ALDOSES AND ALDONIC ACIDS WITH PENTAVALENT VANADIUM IN M SULPHURIC ACID

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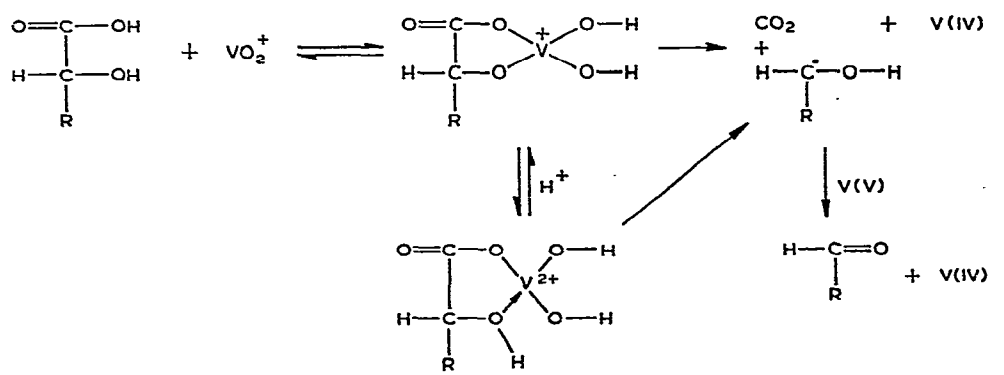
ABSTRACT

Aldoses are degraded by vanadium pentaoxide in M sulphuric acid into formic acid and the next lower aldose, and aldonic acids are degraded into carbon dioxide and the next lower aldose. Each reaction consumes two equivalents of oxidant. Glycolaldehyde is oxidized to formic acid *via* glyoxal, and glycolic acid is oxidized to carbon dioxide and formic acid *via* glyoxylic acid.

INTRODUCTION

It has been postulated[1,2] that the oxidation of aldoses with pentavalent vanadium in sulphuric acid yields aldonic acids that are then oxidized to the next lower aldonic acid with the liberation of carbon dioxide. Thus, the total oxidation of an aldohexose yields 5 mol of carbon dioxide and one mol of formic acid, with the consumption of 20 mol of oxidant.

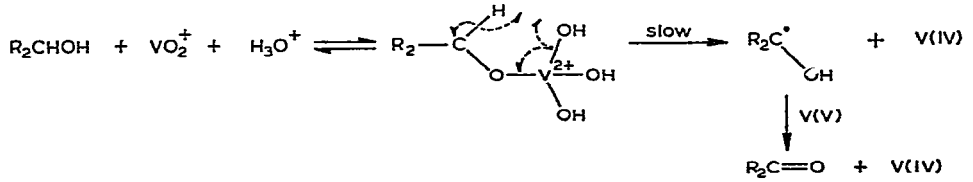
These results are not in accordance with the conclusions of Waters and Littler[3] that α-hydroxy acids are oxidized[4] to carbon dioxide and the next lower aldehyde. Vanadium(V) oxidizes α-hydroxy acids by C–C bond fission of a cyclic complex, in a manner similar to the oxidation of pinacol[4–6] and shown in the annexed scheme.



Apparently, the oxidation of short-chain α-hydroxy aldehydes with vanadium(V) has not been investigated, but aliphatic aldehydes yield formic acid and the next lower

aldehyde[7]. Therefore, α-hydroxy aldehydes would be expected to behave in a similar manner. Formic acid and arabinose have been reported[8] as the oxidation products of glucose.

In the oxidation of polyfunctional compounds, several pathways may be possible. The hydroxyl groups of primary and secondary alcohols and glycols are converted into carbonyl groups[6,9], and oxidation proceeds *via* a vanadium–alcohol complex and an acyclic mechanism. A C–H bond fission is involved in the rate-determining step, as shown in the annexed scheme.



Oxidations with pentavalent vanadium have been mainly studied kinetically, and not analytically, and have been performed under more acidic conditions[1,2] than those reported in this paper.

RESULTS AND DISCUSSION

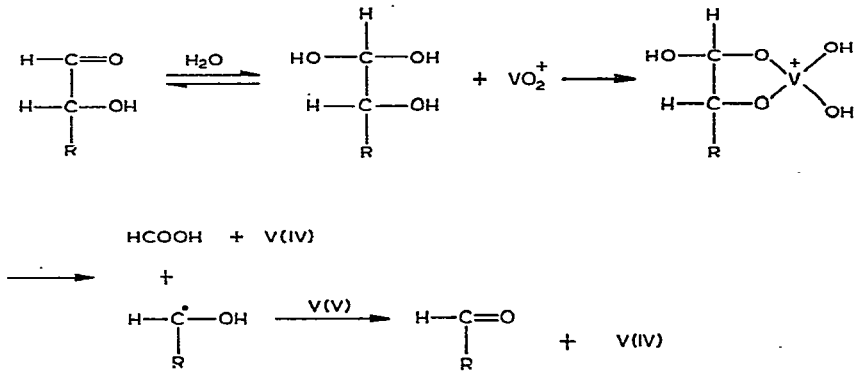
Table I shows the initial rate of formation of tetravalent vanadium (*i.e.*, rate of consumption of oxidant) on oxidizing compounds with varied functionality

TABLE I

RELATIVE REACTIVITY OF COMPOUNDS: INITIAL RATE OF DEVELOPMENT OF TETRAVALENT VANADIUM

Compound	*Relative rate of development of tetravalent vanadium*	*Temperature (degrees)*
D-Glucose	1.0	60
D-Gluconic acid	120	40
L-Arabinose	12	60
L-Arabinonic acid	220	40
D-Erythrose	1000	20
DL-Glyceraldehyde	130	40
D-Glyceric acid	120	40
Glycolaldehyde	50	40
Glycolic acid	55	40
Glyoxal	3500	10
Glyoxylic acid	2800	10
Formaldehyde	0.05	60
Formic acid	0.00	60
1-Propanol	0.1	60
Propanal	5.4	60
D-Glucitol	1.4	60
Dihydroxyacetone	2500	10

related to that of D-glucose. The reaction rates of the α-hydroxy acids and simple α-hydroxy aldehydes are much greater than those of aliphatic aldehydes or primary and secondary alcohols. Aliphatic acids are very resistant to attack by the oxidant[3]. Therefore, it is probable that the primary oxidation occurs at α-hydroxy acid or α-hydroxy aldehyde groups. The rates of formation of tetravalent vanadium on oxidizing each type of compound are of the same magnitude and the reaction mechanisms are probably similar. By analogy with α-hydroxy acids, the oxidation of the α-hydroxy aldehydes or their hydrates may be written as in the annexed scheme.



A C–C bond fission yields radicals that are rapidly oxidized further to formic acid and the next lower aldehyde, with the consumption of two equivalents of the oxidant.

The data in Table II show that, in the total degradation of aldoses, the yield (mol) of formic acid was almost the same as the number of carbon atoms (n) in the aldose. The consumption of oxidant was almost $2n$ and <0.1 mol of formaldehyde was formed. The next lower aldose was found as an intermediate product. Likewise, aldonic acids gave 1 mol of carbon dioxide, <0.1 mol of formaldehyde, almost $(n - 1)$ mol of formic acid, and $\sim 2n$ mol of vanadium(IV). The next lower aldose was also found as an intermediate product. No lower aldonic acids were detected.

The products of the total and partial oxidation of aldonic acids and aldoses were those predicted by the theory of Waters and Littler[3]. However, glycolic acid and glycolaldehyde behave differently, in that a much smaller amount of formaldehyde was obtained than expected. Formaldehyde is oxidized too slowly to explain this result, and ~90% of glycolic acid reacts[10] *via* C–H bond fission, giving glyoxylic acid as the primary product which is then rapidly oxidized to formic acid and carbon dioxide. Only ~10% of the glycolic acid is oxidized in the same way as other α-hydroxy acids, *via* a C–C fission in the first step, giving formaldehyde and formic acid.

Glycolaldehyde is probably oxidized to glyoxal in a manner similar to that of glycolic acid. Glyoxal is rapidly oxidized to give 2 mol of formic acid per mol. Only a small part of the glycolaldehyde is oxidized in a manner analogous to that of aldoses, giving formaldehyde and formic acid. Glycolaldehyde is an intermediate product

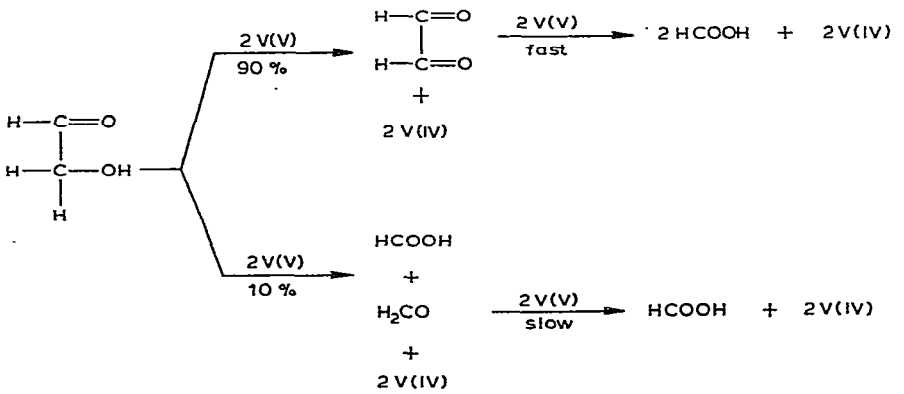
TABLE II

PRODUCTS OF PARTIAL AND TOTAL OXIDATION OF SUBSTRATES

Compound	*Intermediate products detected on partial oxidation*	*Products (mol/mol of substrate) of total oxidation*							
		Formaldehyde		*Formic acid*		*Carbon dioxide*		*Tetravalent V*	
		Theory[a]	*Found*	*Theory*[a]	*Found*	*Theory*[a]	*Found*	*Theory*[a]	*Found*
D-Glucose	D-Arabinose	1	0.09	5	5.4	0	0	10	11.2
D-Gluconic acid	D-Arabinose	1	0.09	4	4.8	1	1.0	10	12.0
L-Arabinose	L-Erythrose, L-Glyceraldehyde	1	0.09	4	4.7	0	0	8	9.4
L-Arabinonic acid	L-Erythrose, L-Glyceraldehyde	1	0.08	3	3.4	1	1.0	8	9.8
D-Erythrose	D-Glyceraldehyde	1	0.06	3	+	0	0	6	—
DL-Glyceraldehyde	Glycolaldehyde	1	0.08	2	2.7	0	0	4	5.6
D-Glyceric acid	Glycolaldehyde	1	0.07	1	+	1	+	4	—
Glycolaldehyde	Glyoxal[b]	1	0.07	1	2.0	0	0	2	4.0
Glycolic acid	Glyoxylic acid[b]	1	0.06	0	1.0	1	1.0	2	4.0
Glyoxal		0	0.00	2	2.0	0	0.0	2	2.0
Glyoxylic acid		0	0.00	1	1.0	1	1.0	2	2.0

[a]By analogy with Waters and Littler.[3] [b]Detection not conclusive. Key: —, not determined quantitatively; +, product detected.

in the oxidation of the aldoses and aldonic acids, which explains the low yield of formaldehyde on total oxidation of the other compounds (see annexed scheme).



On oxidation of aliphatic aldehydes, the reaction stops at acetaldehyde[7], indicating that the oxidation of compounds with a chain length of only two carbon atoms is probably dissimilar to that of compounds with a chain length of three or more.

The crystalline forms of glycolaldehyde and DL-glyceraldehyde are dimeric[11,12], and they slowly dissociate in neutral aqueous solution[12,13]. However, no difference

in reactivity could be observed on oxidizing a freshly prepared or aged solution of each compound, which is consistent with immediate dissociation under the experimental conditions employed. There was no significant difference in the g.l.c. pattern on silylating fresh solutions of DL-glyceraldehyde or glycolaldehyde in M sulphuric acid at 40° compared with those of the aged solutions. The chromatogram of aged DL-glyceraldehyde exhibited several peaks having retention times in the region corresponding to those of D-glucose or the silylated crystalline form of DL-glyceraldehyde. Also, two peaks with retention times shorter than those of D-erythrose were observed, probably due to the hydrated and non-hydrated monomer forms. The area of the dimer peaks indicated that ~50% of the compound exists in the monomer form. Glycolaldehyde showed a similar chromatogram.

It was not possible to determine experimentally the forms in which DL-glyceraldehyde or glycolaldehyde were oxidized, as the equilibrium between the different forms was established very rapidly. However, when the reactive functions are masked, *e.g.*, in ethers[4], hemiacetals, or glycosides[14], the reactivity is much lower. Also, cyclic compounds react much slower than corresponding open-chain compounds, *e.g.*, *cis*- and *trans*-1,2-dimethylcyclohexane-1,2-diols react slowly compared with pinacol[6]. In the oxidation of *myo*-inositol, the reaction stops at inosose[15]. This contrasts with dihydroxyacetone, which is very reactive (Table I). The formation of a nearly planar, five-membered chelate ring is greatly hindered if this ring is fused to a six-membered ring[6], indicating that it is mainly the monomeric form of DL-glyceraldehyde or glycolaldehyde that is being oxidized. The high reactivity of D-erythrose indicates that it exists mainly in the acyclic monomeric form in M sulphuric acid.

Reactivity increases with chain length for the compounds glycolaldehyde, DL-glyceraldehyde, and D-erythrose. The consumption of oxidant by glycolaldehyde due to C–C bond scission is only ~10% of the total. Thus, the relative reactivities should be 5 for glycolaldehyde, 130 for DL-glyceraldehyde, and 1000 for D-erythrose.

Equilibrated solutions of D-glucose in distilled water at 20° have[16] a carbonyl concentration of 0.002%. The ratio of the acyclic form to the pyranoid form of D-glucose is 1:50,000. The ratio of the reaction rates of D-glucose and DL-glyceraldehyde is 1:130 in M sulphuric acid at 40°, with ~50% of the DL-glyceraldehyde in the acyclic form. The reason for this large difference may be that (*a*) forms other than *aldehydo*-D-glucose are oxidized, (*b*) there is a much higher aldehyde content under the experimental conditions employed, and (*c*) *aldehydo*-D-glucose has a much higher reaction rate than that of monomeric DL-glyceraldehyde.

The rates of formation of blue vanadium(IV) in the oxidation of D-glucose and D-glucitol are approximately the same, but, since carbon dioxide was not formed, ketones are excluded as intermediates. Also, a C–C bond fission of a cyclic complex, as for pinacol, is improbable[6], as no such scission has been reported for primary or secondary glycols[6,17]. The transition state would require a five-membered chelate ring fused to a six-membered ring, which is greatly hindered[6].

The possibility of oxidation at C-6 giving a 1,6-dialdehyde cannot be excluded; the steady-state concentration of such a compound would be small.

TABLE III

THE RELATIVE AMOUNT OF ALDEHYDO FORM COMPARED WITH THE RELATIVE OXIDATION RATE OF SUGARS

Sugar	*Relative amount of aldehyde*		*Relative rate of development of V(IV)*[c]
	Circular dichroism[a]	*Polarography*[b]	
D-Glucose	1.0	1.0	1.0
D-Galactose	8	3.4	1.8
D-Mannose	2.5	2.7	1.2
L-Arabinose	15	11.7	12
D-Xylose	7	7.1	7.2
D-Ribose	21	354	7.2

[a]Sugar concentration, 0.2 to 1M; pH 5.2 to 7.0; 20°. Value obtained by dividing the circular dichroic ($\Delta\varepsilon$) value of Table I in Ref. 16 with the $\Delta\varepsilon$ value for D-glucose. [b]Sugar concentration, 0.25M; pH 7; 25° (Ref. 25). [c]Sugar concentration, 0.10M; 0.1M vanadium pentaoxide in M sulphuric acid at 60°.

The data in Table III show, with the exception of ribose, a correlation between the percentage of aldehydo form[16] and the initial rate of formation of tetravalent vanadium, which indicates that each sugar is oxidized in the aldehydo form (see also Ref. 8). This conclusion is supported by the finding that there was no correlation between the equilibrium ratios of the anomeric forms[19,20] and the rates of oxidation. The aldehydo form has also been invoked for oxidations with sodium peroxide[18], which convert aldoses into the next lower aldose and formic acid.

EXPERIMENTAL

Solutions were concentrated under reduced pressure at <40°. T.l.c. of sugars was performed on silica gel G–Kieselguhr (2:1) with (*A*) toluene–acetic acid–methanol (2:2:1), and detection with 0.1M vanadium pentaoxide in M sulphuric acid[14] or with diphenylamine–aniline–phosphoric acid[21]. T.l.c. of 2,4-dinitrophenylhydrazones was performed on silica gel G with (*B*) chloroform–methanol (10:1), and detection (after drying) by treatment with diethylamine vapour.

G.l.c. of trimethylsilylated sugars[22] was performed at 100° for 5 min, and then a temperature programme of 4°/min, on a glass column (6 ft × 1.5 mm) containing 3% of XE-60 on Chromosorb G AW-KMCS (80–100 mesh) and a nitrogen flow-rate of 20 ml/min.

Determination of reaction rates. — To 0.1M vanadium pentaoxide in M sulphuric acid (5 ml, prepared as described in Ref. 14), at the temperatures shown in Table II, the substrate (0.5 mmol) was added. Aliquots (250 µl) were added to water (2.5 ml), and the amount of tetravalent vanadium formed was measured at 700 nm.

Investigation of intermediate products. — Barium carbonate (6 g) was added to the oxidation mixture (5 ml) described above until the colour changed from blue to beige. Barium hydroxide (15 ml, 0.1M) was then added until precipitation was complete. The mixture was centrifuged, and the supernatant solution was neutralised with Amberlite IR-120(H^+) resin (3 g) and then concentrated to 0.2 ml. A portion

was subjected to t.l.c. (solvent *A*) and the remainder was concentrated to dryness. The syrupy residue was dissolved or suspended in ethanol (5 ml) and boiled under reflux with 2,4-dinitrophenylhydrazine (20 mg) for 6 h. The mixture was concentrated to ~0.5 ml and subjected to t.l.c. (solvent *B*).

For g.l.c., aliquots (250 μl) of oxidation mixture were mixed with 0.1M barium hydroxide (5 ml) and centrifuged, and the supernatant solution was neutralized with Amberlite IR-120(H^+) resin (1 g) and then concentrated to dryness before silylating.

Investigation of composition of compounds in solution. — Aliquots (10 μl) of fresh solutions of D-glucose, DL-glyceraldehyde, and glycolaldehyde in M sulphuric acid, in the oxidant, and solutions aged in distilled water, were added to a mixture of pyridine (2 ml), chlorotrimethylsilane (0.1 ml), and hexamethyldisilazane (0.2 ml). The mixture was centrifuged and then concentrated to dryness, and the residue was dissolved in 0.1 ml of light petroleum (b.p. 60–80°) before g.l.c.

Total oxidation of substrates. — To 0.1M vanadium pentaoxide in M sulphuric acid (5 ml) was added M substrate (10 μl) (Table II), and the mixture was heated at 60° for 6 h for D-glucose and L-arabinose, and 3 h for the other compounds.

Determination of formaldehyde. — To the oxidation mixture (250 μl) was added 0.1M barium hydroxide (5 ml). After centrifugation, the supernatant solution was neutralized with Amberlite IR-120(H^+) resin. The chromophore was generated by heating 1 ml of formaldehyde solution with 2.5 ml of Hantzsch reagent [pentane-2,4-dione (2 ml), acetic acid (3 ml), and ammonium acetate (150 g) diluted to 1 litre] for 10 min at 60°, and measured[23] at 412 nm. The molar absorptivity (ε) of the chromophore was taken[23] as 8000.

Determination of total volatile acids. — The oxidation mixture (10 ml) was concentrated to dryness *in vacuo* and the distillate (2 ml) was titrated (to phenolphthalein) with 0.01M sodium hydroxide. Formic acid was assumed to be the only volatile acid present.

After removal of formaldehyde with phenylhydrazine and subsequent distillation, formic acid was identified by a modification of the spot-test method[24]. Formic acid was reduced to formaldehyde by stirring the distillate with magnesium turnings and Dowex 50W(H^+) resin (200–400 mesh), and determined using the Hantzsch reagent[23].

The oxidation mixture was neutralized, and concentrated to dryness, and the residue was stirred in methanol with dry, methanol-washed Dowex 50W(H^+) resin (200–400 mesh). Methyl formate was detected by g.l.c. on an XE-60 column at <35°.

Determination of carbon dioxide. — Carbon dioxide-free nitrogen was passed through the reaction vessel containing oxidant (10 ml) and 0.1 mmol of substrate, and into 0.1M barium hydroxide (5 ml). The barium hydroxide solution was centrifuged and then back-titrated with 0.05M hydrochloric acid (to Methyl Orange).

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