CHEMICAL KINETICS
AND CATALYSIS

Substrate Inhibition: Oxidation of D-Sorbitol and D-Mannitol by Potassium Periodate in Alkaline Medium[1]

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Abstract—In the oxidation of D-sorbitol and D-mannitol by potassium periodate in alkaline mediam, substrate inhibition was observed with both the substrates, i.e., a decrease in the rate of the reaction was observed with an increase in the concentration of substrate. The substrate inhibition was attributed to the formation of stable complex between the substrate and periodate. The reactions were found to be first order in case of periodate and a positive fractional order with hydroxide ions. Arrhenius parameters were calculated for the oxidation of sorbitol and mannitol by potassium periodate in alkali media.

Keywords: kinetics, substrate inhibition, D-sorbitol, D-mannitol, potassium periodate, alkaline medium.

INTRODUCTION

Studying the oxidation of sugars is very significant because in most of the living organisms, the major amount of energy is obtained from carbohydrates [1]. Polyols (viz., inositol, mannitol, sorbitol) are important osmolytes in various animals, plants and procaryote organisms [2–4]. Sorbitol and inositol are significant osmolytes in the renal medulla of mammals [5–7]. D-mannitol is abundant in nature, such as in plants, algae, yeasts, fungi, and bacteria. Mannitol is a major storage polysaccharide in fungi that also plays an important role as a metabolite in stress tolerance [8, 9] from the physiological functions fulfilled by mannitol in lower and higher eukaryotes [10]. Sorbitol finds many applications in food, pharmaceutical and cosmetic industries and as additives in many end-products. It was used as a key intermediate in the synthesis of ascorbic acid [11].

Acid catalysed oxidation of sugars and sugar alcohols with different oxidants was reported by earlier researchers [12–14]. Most of the studies carried out in perchloric acid media reported that the reaction was acid catalysed [15, 16]. The kinetics and mechanism of cerium (IV) oxidation of hexitols (D-sorbitol and D-mannitol) in aqueous sulfuric acid media have been studied in the presence and absence of surfactants [17]. The ruthenium (III) catalysed oxidation of D-mannitol by cerium (IV) was studied spectrophotometrically in aqueous sulfuric acid medium [18]. Odebunmi and marufu [19] studied oxidation of D-mannitol and D-sorbitol by $KMnO_4$ in $NaHCO_3/NaOH$

buffer and $IrCl_6^{2-}$ in sodium acetate/acetic acid buffer. Vanadium (V) oxidation of D-sorbitol was studied in the presence of externally added surfactants [20].

The literature survey shows that the oxidation of sugar alcohols has received modest thought compared to studies on the oxidation of sugars. Taking these facts into consideration, recently the present authors have carried out periodate oxidation of cyclic polyol—inositol in alkaline medium and reported substrate inhibition due to stable complex formation between inositol and periodate [21]. In continuation, this paper describes the kinetics and mechanism of periodate oxidation of sugar alcohols like D-sorbitol and D-mannitol in alkaline medium. Authors are interested to check the possibility of exhibition of substrate inhibition by these acyclic polyols.

EXPERIMENTAL

All the reagents used in these experiments were of analytical reagent grade. Requisite volumes of oxidant and substrate solutions were thermostated at 35 ± 0.1°C to attain equilibrium. After rapid mixing an equal volume of oxidant solution to the substrate solution, progress of the reaction was followed by assaying aliquots of the reaction mixture for periodate, iodometrically using starch as an indicator after suitable time intervals. In the oxidation of sorbitol and mannitol, one oxygen loss or two electrons transfer per periodate molecule was observed i.e., oxidation capacity of oxidant was observed till the conversion of periodate

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[1] The article is published in the original.

Table 1. The rate constants ($k_1 \times 10^4$, min^{-1}) of oxidation of sorbitol and mannitol by periodate in alkaline medium

Variant	c, M	D-Sorbitol	D-Mannitol
Periodate	0.00025	3.881	18.810
	0.0005	2.854	19.000
	0.001	2.897	19.370
Sorbitol	0.005	3.608	46.800
	0.025	2.854	19.000
	0.05	1.677	12.730
	0.1	1.909	
Alkali	0.05	2.246	12.350
	0.1	2.854	19.000
	0.2	3.182	24.880
	0.5	4.182	33.890
	1.0	9.355	
Temperature	35	2.854	19.000
	45	9.197	71.460
	55	43.127	240.250
Boric Acid	0	2.854	19.000
	0.01	3.012	27.03
	0.025	3.677	33.130
	0.05	4.629	49.268
No Salt	–	2.854	19.000
KNO$_3$	0.1	2.217	17.353
KCl	0.1	2.747	21.854
KI	0.1	3.192	23.374
KBr	0.1	3.250	69.999

Note: [Periodate] = 0.0005 M, [Substrate] = 0.025 M, [OH$^-$] = 0.1 M, temperature 35°C, c is concentration of variant.

Table 2. Concentrations of periodate species at different concentrations of alkali

[OH$^-$] M	[H$_3$IO$_6^{2-}$] M	[H$_2$IO$_6^{3-}$] M
0.05	0.000307612	0.000180027
0.1	0.000228251	0.000267163
1.0	0.0000393489	0.000460572

into iodate. This was also confirmed by non oxidation of sorbitol and mannitol by iodate.
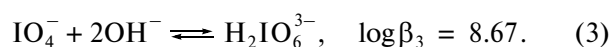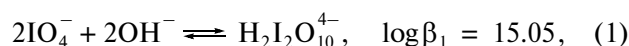
RESULTS AND DISCUSSION

The kinetic studies were carried out under pseudo-first-order conditions with the concentration of the substrate in large excess compared to that of the oxidant. The pseudo-first-order with respect to [periodate] was almost constant in the concentration range 0.00025–0.001 M (Table 1). The reaction orders of substrate(s)/alkali were determined from the slope of $\log k_1$ vs. log [variant] plots while maintaining all other concentrations and conditions constant.

The rate constants increased with an increase in alkali concentration and a fractional slope for $\log k_1$ versus log[alkali] indicates a positive fractional order dependence of rate on alkali. In the earlier studies by Okoro and Odebunmi, an increase in the rate of oxidation of sorbitol and mannitol by KMnO$_4$ was observed with an increase in the pH (range 9.60 to 11.00) of the reaction medium and was attributed to base catalyzation [22].

The three dissociative equilibria of the periodate ion in alkaline medium and the corresponding equilibrium constants at 298.2 K were given by Aveston [23]

$$2IO_4^- + 2OH^- \rightleftharpoons H_2I_2O_{10}^{4-}, \quad \log\beta_1 = 15.05, \quad (1)$$

$$IO_4^- + OH^- + H_2O \rightleftharpoons H_3IO_6^{2-}, \quad \log\beta_2 = 6.21, \quad (2)$$

$$IO_4^- + 2OH^- \rightleftharpoons H_2IO_6^{3-}, \quad \log\beta_3 = 8.67. \quad (3)$$

The composition of different species of periodate in aqueous alkaline solution can be obtained from the equilibrium constants K_1, K_2 and K_3. Within the used alkali concentrations, the amounts of both the species of periodate (dimmer—H$_2$I$_2$O$_{10}^{4-}$ and IO$_4^-$) can be neglected. From the give below calculations, it is clear that the key species of periodate are H$_2$IO$_6^{3-}$ and H$_2$IO$_6^{2-}$, which is corroborating with the earlier reports of Crouthamel's data [24] and other recent results reported in the literature [25, 26].

$$[H_2IO_6^{3-}] = \frac{\beta_3[OH^-]^2}{1 + \beta_2[OH^-] + \beta_3[OH^-]^2}[IO_4^-]_{ex}$$

$$= f([OH^-])[IO_4^-]_{cx},$$

$$[H_3IO_6^{2-}] = \frac{\beta_2[OH^-]}{1 + \beta_2[OH^-] + \beta_3[OH^-]^2}[IO_4^-]_{ex}$$

$$= \phi([OH^-])[IO_4^-]_{cx}.$$

The original overall periodate ion concentration is represented by $[IO_4^-]_{ex}$, which is approximately equal to the sum of the concentrations of two main species of periodate (H$_2$IO$_6^{3-}$ and H$_2$IO$_6^{2-}$). At different alkali concentrations, [H$_2$IO$_6^{3-}$] and [H$_3$IO$_6^{2-}$] are calculated (Table 2). The predominant species are H$_3$IO$_6^{2-}$ and H$_2$IO$_6^{3-}$ at lower (0.05 M) and higher (1.0 M) concentrations of alkali respectively. At 0.1 M alkali (where most of the reactions are carried out) both ionic species exist equally and hence the sugar alcohols complex with either H$_3$IO$_6^{2-}$ or H$_2$IO$_6^{3-}$.

Table 3. Arrhenius parameters at 308K

Substrate	$\Delta E^{\neq}$, kJ/mol	$\Delta H^{\neq}$, kJ/mol	$-\Delta S^{\neq}$, J K^{-1} mol^{-1}	$\log P_{Z}$	$\Delta G^{\neq}$, kJ/mol
D-Sorbitol	113.8336	111.2728	13.31927	13.9511	115.3752324
D-Mannitol	106.5674	104.0066	6.150066	13.57661	105.900888

Two or more molecules of water are displaced from the trimester sphere of periodate ion when three or more hydroxyl groups in a polyol are in a sterically favourable arrangement. Hydroxyl groups lose a proton in alkaline medium and form much stronger complexes. Barker [27] described the existence of trimesters of periodate ion with inositol and suggested that the iodine atom is attached to an ax−eq−ax sequence of oxygen atoms which was confirmed by N. M. R. spectrum. Out of the three hydroxyls which have complex one is axial hydroxyl second equatorial third axial hydroxyl these three OH's have complexed with the periodate species $H_3IO_6^{2-}$ in alkaline medium.

Relative Oxidation of Sorbitol and Mannitol by Periodate

The kinetic data (Table 1) clearly indicates that in alkaline medium, rates of oxidation of mannitol are very much higher as compared to those of sorbitol. This report is quite remarkable because the reports demonstrate that sorbitol is the most reactive while mannitol is the least reactive in their oxidation by alkaline $KMnO_4$ [22] and by vanadium pentoxide (V_2O_5) in acidic medium [28].

Current observations can be explained based on the geometry of 5, 6 hydroxyls in these compounds. No stable complex formation takes place between periodate and mannitol due to the trans geometry of 5, 6 hydroxyls in mannitol. Whereas, in the case of sorbitol, due to the cis geometry of 5, 6 hydroxyls a stable complex forms which is responsible for the lower oxidation rate in sorbitol. In sorbitol oxidation, the breakdown of the complex leads to c−c fission and gives two aldehydes (a) formaldehyde and (b) arabinose. In the case of mannitol, there is no stable complex formation because of the trans geometry of 5, 6 hydroxyls. Hence oxidation rates are quite higher for mannitol as compared to sorbitol.

We envisage differential mechanism for mannitol which may be an acyclic pathway leading to the corresponding aldehyde as the primary major product. The inhibition observed with increasing concentration of mannitol can be traced to competing cyclic mechanism operating to a lesser extent, because of unstable complex formation with mannitol along with acyclic mechanism which is the cause the higher rate observed with mannitol. Oxidation of sorbitol yields by cyclic mechanism as primary products D-arabinose and formaldehyde, whereas oxidation of mannitol yields

D-mannose as a primary product. The products formation was confirmed by spot tests [29].

Substrate Inhibition

A decrease in k_1 values with an increase in concentration of sorbitol/mannitol was observed and an inverse fractional with respect to substrate was found (Table 1). Much attention was not paid by the earlier workers who observed similar effects with hexacyanoferrate (III) oxidation of carbohydrates [30] and ceric sulphate oxidation of alcohols [31]. Olusanya and Odebunmi studied copper (II) inhibition in the oxidation of maltose and xylose by hexacyanoferrate (III) in alkaline medium and reported that the order of reaction in sugar decreased from one to zero at higher sugar concentration, but actually, their data shows that a 12% decrease in rate of reaction at higher concentration of maltose can be observed [32].

Substrate inhibition, i.e., a decrease in rate of reaction with an increase in substrate concentration can be contributed to the formation of periodate-sugar alcohol complex which resists oxidation. The inert complexes must contain a higher proportion of substrate molecules because of 1:1 complexes, which take part in the oxidation. Similar substrate inhibition was reported by us in the oxidation of myoinositol by periodate in alkaline medium [21].

Effect of Temperature

The rate constants (k_1) increased with an increase in temperature with both substrates. The plot of $\ln k$ vs. $1/T$ yielded a straight line and the values of activation parameters viz. enthalpy of activation ($\Delta H^{\neq}$), entropy of activation ($-\Delta S^{\neq}$) and Gibb's free energy ($\Delta G^{\neq}$) were evaluated from the slope of the plot by using the Eyring equation [33, 34] and tabulated (Table 3). The high +ve value of free energy of activation ($\Delta G^{\neq}$) indicates highly solvated transition state, while −ve value of entropy of activation ($-\Delta S^{\neq}$) suggest the formation of an activated complex with reduction in the degree of freedom of molecules.

Effect of Boric Acid

Increase in rate was observed with an addition of boric acid due to favouring conditions for complex formation between substrates and highly dissociating potassium borate, which competes with the stable complex formation between sorbitol/mannitol and

periodate. Such observations were reported earlier by other authors in sodium borate solution with other hexose like inositol. One of the first reports on the formation of boronic esters from diols and polyols, described the preparation of several esters of phenylboronic acid by reaction of the latter, in warm water, with sugars like mannitol and sorbitol, and 1,2-diols like catechol and pinacol [35]. Similar formation of tridentate borate ester anions (I) in sodium borate solution by cyclic polyols was reminiscent by their strong mobility towards the anode in electrophoresis [36] and changes in NMR spectrum [37, 38].

Effect of Salts

Salt effect was studied on the oxidation of sorbitol and mannitol by periodate. Ions like chloride, iodide and nitrate didn't show an appreciable effect on the rate of reaction, where as bromide increased the rate. Earlier, a positive catalytic effect of bromide ion was reported in the oxidation of dextrose [39] and fructose [40] by Ce (IV) in aqueous sulphuric acid medium.
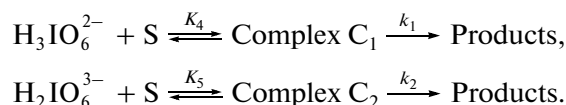
Product Analysis

Sugar oxidation occurs under different conditions of pH, temperature and ionic strength giving product that depend on the reactions used [14]. The kinetics and mechanism of oxidation of monosacharides and disaccharides have been studied in both acidic and alkaline media, employing different transition metal ions, inorganic acids, complex ions and hydrogen peroxide as oxidants. The results showed that the mechanism may depend on the nature of the substrates, in some cases it involves the formation of intermediate complex, free radical or transition states [12]. In the present case, the spectral analysis of hydrazone deriv-

ative of the product indicates the products to be an aldehydes as indicated above. Agarwal et al. [1] also reported the aldehydes in the oxidation of mannitol by Ce(IV) in acid medium.

Faster Reactions in Acid Medium

The rates of reaction between periodate and sorbitol/mannitol were instantaneous in acid medium and hence were unable to follow kinetics as per the method described above in the experimental section. However, these reactions were slow in alkaline medium. This observation was in parallel with our earlier studies of oxidation of inositol by periodate [21]. The lower rates of oxidation of sorbitol/mannitol in alkaline medium can be attributed to the slow scission of substrate as well as slow cleavage of the complex between oxidant and substrate. Such reports also are available in the literature in the case of reaction between alcohols and periodate. According to Bunton and colleagues [42, 43] the monocyclic type formed as a transient intermediate in glycol scission reactions is a dianion at pH 9. They regard dianion as highly stable because it cannot likewise suffer dehydration thus accounting for the relatively slow rate of periodate oxidations at high pH. Perlin and Von Rudolff [44] reported that the cleavage of complex between diols and periodate is slower in weakly alkaline compared to that in acid medium.

Rate Law in Alkali Medium

$$H_3IO_6^{2-} + S \underset{K_4}{\overset{}{\rightleftharpoons}} \text{Complex } C_1 \overset{k_1}{\longrightarrow} \text{Products},$$

$$H_2IO_6^{3-} + S \underset{K_5}{\overset{}{\rightleftharpoons}} \text{Complex } C_2 \overset{k_2}{\longrightarrow} \text{Products}.$$

Since, the $[IO_4^-]$ and $[H_2I_2O_{10}^{4-}]$ are negligible, the total concentration of periodate can be written as

$$[IO_4^-]_T = [H_3IO_6^{2-}] + [H_2IO_6^{3-}] + [\text{Complex } C_1] + [\text{Complex } C_2]$$

$$= K_2[IO_4^-][OH^-] + K_3[IO_4^-][OH^-]^2$$

$$+ k_1K_2K_4[S][IO_4^-][OH^-] + k_2K_3K_5[S][IO_4^-][OH^-]^2,$$

$$[IO_4^-] = \frac{[IO_4^-]_T}{[OH^-]\{K_2 + K_3[OH^-] + k_1K_2K_4[S] + k_2K_3K_5[S][OH^-]\}},$$

$$\text{Rate} = k_1[\text{Complex } C_1] + k_2[\text{Complex } C_2]$$

$$= k_1K_4[H_3IO_6^{2-}][S] + k_2K_5[H_2IO_6^{3-}][S]$$

$$= k_1K_2K_4[IO_4^-][OH^-][S] + k_2K_3K_5[IO_4^-][OH^-]^2[S]$$

$$= [IO_4^-][OH][S]\{k_1K_2K_4 + k_2K_3K_5[OH^-]\}$$

$$= \frac{[IO_4^-]_T[S]\{k_1K_2K_4 + k_2K_3K_5[OH^-]\}}{K_2 + K_3[OH^-] + k_1K_2K_4[S] + k_2K_3K_5[S][OH^-]}.$$

CONCLUSION

Substrate inhibition was observed in the oxidation of D-sorbitol/D-mannitol in alkaline medium due to stable complex formation between the substrate and periodate.

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SPELL: 1. catalysed, 2. hexitols, 3. marufu