



Kinetics And Mechanistic Investigation of Oxidation of D-Mannitol By Periodate In Aqueous Alkaline Medium

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ABSTRACT

The kinetics of oxidation of D-Mannitol (D-Man) by periodate in aqueous alkaline medium at 298 K and at a constant ionic strength of 0.04 mol dm^{-3} was studied. The reaction exhibits 1:2 stoichiometry ([D-Man]:[periodate]). The reaction shows first order kinetics in [periodate] and less than unit order both in [D-Man] and [OH]. The ionic strength has positive effect and dielectric constant of the medium did not affect the rate significantly. The main products were identified by spot tests, FT-IR and LC-MS spectral studies. Based on the experimental results, the possible mechanisms were proposed. The reaction constants involved in the different steps of the mechanisms were evaluated. The activation parameters with respect to the slow step of the mechanisms were computed and also thermodynamic quantities determined. Kinetic studies suggest that the active species of periodate was found to be $[\text{H}_2\text{IO}_6^{3-}]$.

Keywords: Periodate, D-Mannitol, Oxidation, Mechanism.

INTRODUCTION

D-mannitol is used as a sweetener for people with diabetes, and in chewing gums. It is mainly used in the circuit prime of a heart lung machine during cardiopulmonary bypass. The presence of D-mannitol preserves the renal function during the time of low blood flow and pressure, while the patient is on bypass. D-mannitol is first drug of choice for the treatment of acute glaucoma in veterinary medicine.

Periodic acid is widely used as specific diol cleaving reagent. Periodate as periodic acid in acid medium is extensively used as an oxidant due to the fact that it has specific action towards α -dicarbonyl compounds which is useful in elucidating the structure. In alkaline medium it is relatively weak oxidant and is used rarely. In alkaline medium, periodate is known to exist as different species involving multiple equilibria[1] and it needs to know the active form of the oxidant in the reaction.

Some work on oxidation of D-mannitol by diperiodatoargentate(III) has been documented[2]. Literature survey reveals that there is no reports on oxidation of D-mannitol by periodate in alkaline medium. In order to investigate the redox chemistry and in view of potential pharmaceutical importance of D-Man and

to know the active species of oxidant in such media and to propose the appropriate mechanisms of the reactions on the basis of kinetic and spectral results, the title reaction is investigated in detail.

MATERIALS AND METHODS

All chemicals used were of reagent grade and double distilled water was used throughout this study. The stock solution of periodate (0.02 mol dm^{-3}) was prepared by dissolving 2.30 g of potassium metaperiodate (S.D.Fine Chem.) in 500 cm^3 water and the solution was used after keeping for 24 h. The concentration of the solution was verified[3] by titration with standard sodium thiosulfate iodometrically at neutral pH maintained by adding 5 cm^3 5% potassium dihydrogen phosphate and 5 cm^3 of 5% dipotassium hydrogen phosphate solution, using starch solution as an indicator.

A solution of D-mannitol was prepared by dissolving an appropriate amount of recrystallized sample in double distilled water. The purity of D-mannitol sample was checked by comparing its melting point (167°C) with the literature data ($165\text{-}168^\circ\text{C}$). The required concentration of D-mannitol was obtained from its stock solution.

Sodium thiosulfate (Thomas Baker Chemicals Ltd.) solution was prepared in water. It was standardized[4] against potassium iodate as follows- to the potassium iodide solution containing 1.0 mol dm^{-3} sulfuric acid in iodine flask, a known volume of standard potassium iodate solution was added. The liberated iodine was titrated against sodium thiosulfate solution using starch indicator. Potassium hydroxide and potassium nitrate were employed to maintain the required alkalinity and ionic strength respectively. Potassium dihydrogen phosphate (Thomas Baker Chemicals Ltd.) and potassium iodide (S.D. Fine Chem.) were used in iodometric determination of periodate at neutral pH.

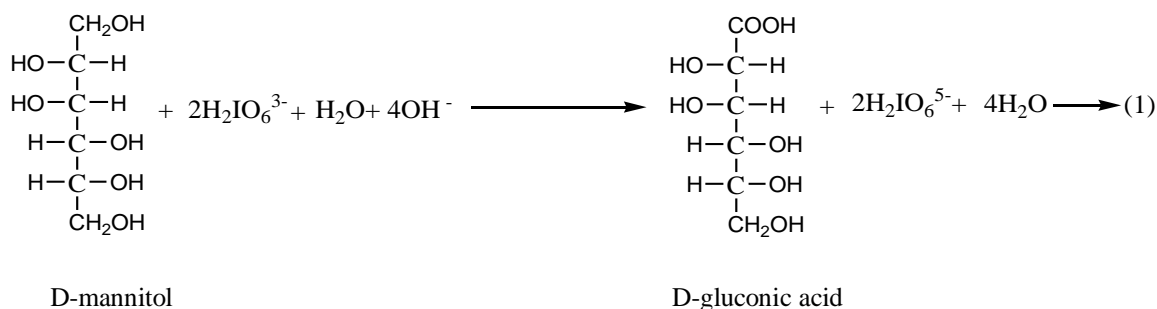
Instruments used : For product analysis, the LC/ESI/MS instrument using a Finnigan (Thermo Finnigan, San José, CA, USA) LCQ DECA ION trap instrument equipped with Xcal-ibur software and Nicolet 5700- FT-IR spectrometer (Thermo, USA) were used. For pH measurements ELICO pH meter model LI 120 (Hyderabad, India) was used.

Kinetic measurements: The kinetics was followed under pseudo first order condition where $[\text{D-mannitol}] > [\text{Periodate}]$ in reaction at $25 \pm 0.1^\circ\text{C}$, unless specified. The reaction was initiated by mixing periodate with the D-mannitol solution which contained required concentrations of KNO_3 and KOH . The reaction was followed by measuring the decrease in concentration of periodate titrimetrically using sodium thiosulfate, at regular intervals of time. In view of the modest concentration of OH^- used in the reaction medium, attention was also directed to the effect of the reaction vessel surface on the kinetics. Use of polythene/acrylic wares gave the same results, indicating that the surface did not have any significant effect on the reaction rates.

In view of the ubiquitous contamination of carbonate in the basic medium, the effect of carbonate was also studied. Added carbonate had no effect on the reaction rates. However, fresh solutions were nevertheless used for carrying out each kinetic run. Regression analysis of experimental data to obtain regression coefficient r and the standard deviation S of points from the regression line was performed with the Microsoft Office Excel 2003 program.

RESULTS AND DISCUSSION

Stoichiometry and Product analysis : Different sets of mixtures containing varying ratios of periodate to D-mannitol in presence of constant amount of OH^- (0.02 mol dm^{-3}) and KNO_3 (0.02 mol dm^{-3}) in a reaction with constant ionic strength of 0.04 mol dm^{-3} , were kept for 8 hours in a closed vessel under nitrogen atmosphere at 25°C and then analyzed. Under the condition $[\text{IO}_4^-] > [\text{D-Man}]$, the periodate in the reaction was estimated iodometrically at neutral pH. The results show 1:2 stoichiometry for title reaction as given in equation(1).



The main oxidation product, D-gluconic acid (aldonic acid), was identified by spot test[5]. To detect the aldonic acid, dinaphthol sulphuric test[6] was carried out by treating a little amount of the final reaction mixture with a few drops of β , β^1 - dinaphthol solution in concentrated sulphuric acid and was heated to 1hr in a water bath at 85°C . Characteristic green color indicates the presence of D-gluconic acid (aldonic acid). The product D- gluconic acid was also confirmed by IR and LC-MS spectra. The nature of the carboxylic acid was confirmed by the IR spectrum, which has shown a carbonyl ($>\text{C}=\text{O}$) stretch at 1705 cm^{-1} and O-H stretching of the acid at 2934 cm^{-1} (Figure 1). The product D-gluconic acid was also confirmed by LC-MS analysis data. The mass spectrum showed molecular ion peak at 195 amu, which confirms the product, D-gluconic acid (Figure 2). It was observed that D-gluconic acid did not undergo further oxidation under the present kinetic conditions.

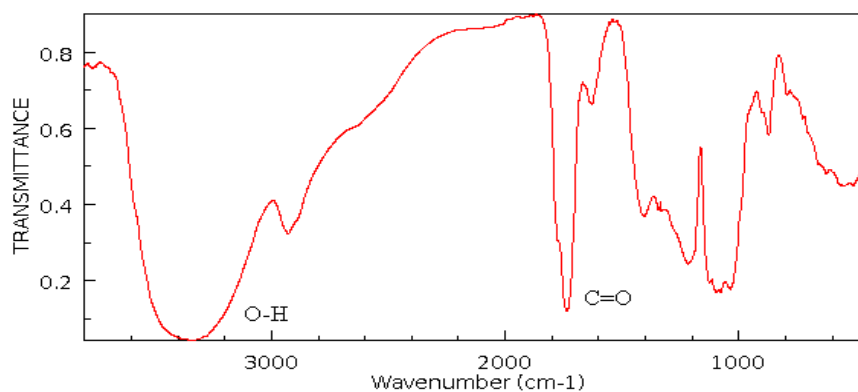


Figure 1: FTIR Spectrum of D-Gluconic acid (Aldonic acid)

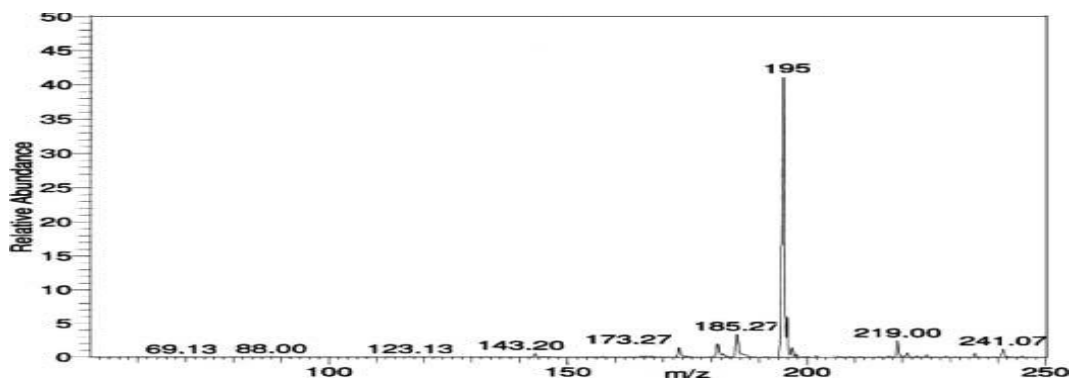


Figure 2: LC-MS of D-Gluconic acid with its molecular ionic peak at 195 m/z

Reaction orders: The reaction orders with respect to D-mannitol and alkali concentration were determined from the slopes of $\log k_{\text{obs}}$ versus \log (concentration) plots by varying the concentrations of D-mannitol, OH^- in turn while keeping all other concentrations and conditions constant.

Effect of [Periodate]: The oxidant periodate concentrations was varied in the range of 1.0×10^{-3} to 1.2×10^{-2} mol dm^{-3} at fixed [D-Man], $[\text{OH}^-]$ and ionic strength. The non variation in the pseudo-first order rate constants at various concentration of KIO_4 indicates the order in $[\text{IO}_4^-]$ as unity (Table 1) for k_{obs} . This was also confirmed from the linearity of \log (concentration) versus time up to 80% completion of the reactions.

Table 1: Effect of variation of [Periodate], [D-Man] and $[\text{OH}^-]$ concentrations on the oxidation of D-mannitol by periodate in aqueous alkaline medium at 25°C and $I = 0.04$ mol dm^{-3}

$[\text{IO}_4^-] \times 10^3$ (mol dm^{-3})	[D-Man] $\times 10^2$ (mol dm^{-3})	$[\text{OH}^-] \times 10^2$ (mol dm^{-3})	$k_{\text{obs}} \times 10^4$ (s^{-1})	
			Found	Calculated
1.0	4.0	2.0	9.71	9.90
2.0	4.0	2.0	9.60	9.90
4.0	4.0	2.0	9.94	9.90
6.0	4.0	2.0	9.71	9.90
8.0	4.0	2.0	9.94	9.90
12.0	4.0	2.0	9.94	9.90
4.0	1.0	2.0	3.67	4.10
4.0	2.0	2.0	6.36	6.66
4.0	4.0	2.0	9.98	9.90
4.0	8.0	2.0	13.9	14.8
4.0	10.0	2.0	15.1	17.2
4.0	20.0	2.0	18.3	19.8
4.0	4.0	0.5	3.67	4.20
4.0	4.0	1.0	6.84	6.80
4.0	4.0	2.0	9.98	9.90
4.0	4.0	3.0	11.7	11.2
4.0	4.0	4.0	12.9	13.8

Effect of [D-mannitol]: The substrate, [D-Man] was varied in the range of 1.0×10^{-2} to 2.0×10^{-1} mol dm^{-3} at 25°C keeping all other reactants concentrations and conditions constant. The k_{obs} values increased with the increase in concentration of D-mannitol indicating an apparent less than unit order dependence on [D-Man] under the conditions of experiment and concentration range used. This was also confirmed by the plots of k_{obs} versus $[\text{D-Man}]^{0.6}$, which was linear rather than the direct plot of k_{obs} versus [D-Man] (Figure 3; $r \geq 0.977$, $S \leq 0.015$).

Effect of $[\text{OH}^-]$: The effect of $[\text{OH}^-]$ on the rate of reaction was studied in the range of 0.005 to 0.04 mol dm^{-3} at constant concentrations of D-mannitol, IO_4^- and ionic strength of 0.04 mol dm^{-3} . The rate increased with increase in concentration of alkali. The order with respect to [alkali] was found to be less than unit order.

Effect of initially added products: The initially added products, D-gluconic acid and IO_3^- did not have any significant effect on the rate of reaction. Thus, from the observed experimental results, the experimental rate law for the reaction is given as

$$\text{Rate} = k_{\text{obs}} [\text{IO}_4^-]^{1.0} [\text{D-Man}]^{0.6} [\text{OH}^-]^{0.5}.$$

Effect of ionic strength (I) and Dielectric constant of the medium (D): The effect of ionic strength was studied by varying the potassium nitrate concentration. The ionic strength of the reaction medium was varied from 0.04 to 0.12 mol dm⁻³ at constant [IO₄⁻], [D-Man] and [OH⁻]. The k_{obs} values increased with increase in ionic strength. The relative permittivity (D) effect was studied by varying the t-butyl alcohol–water content in the reaction mixture with all other conditions being maintained constant. Attempts to measure the relative permittivities were not successful. However, they were computed from the values of pure liquids[7] the dielectric constants of the reaction medium at various composition of t- butyl alcohol (V/V)-water were calculated by using the following equation,

$$D = D_w V_w + D_B V_B$$

where V_w and V_B are volume fractions and D_w and D_B are dielectric constants of water and t-butyl alcohol. There was no reaction of the solvent with the oxidant under the experimental conditions. The rate constant, k_{obs} did not change with increase in the dielectric constant of the medium.

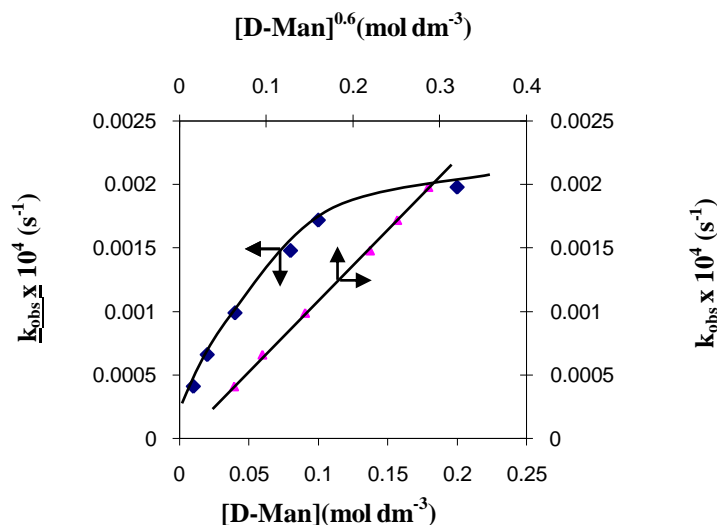


Figure 3. Plot of k_{obs} versus [D-Man]^{0.6} and k_{obs} versus [D-Man]

Effect of [OH⁻]: The effect of [OH⁻] on the rate of reaction was studied in the range of 0.005 to 0.04 mol dm⁻³ at constant concentrations of D-mannitol, IO₄⁻ and ionic strength of 0.04 mol dm⁻³. The rate increased with increase in concentration of alkali. The order with respect to [alkali] was found to be less than unit order.

Effect of initially added products: The initially added products, D-gluconic acid and IO₃⁻ did not have any significant effect on the rate of reaction. Thus, from the observed experimental results, the experimental rate law for the reaction is given as

$$\text{Rate} = k_{\text{obs}} [\text{IO}_4^-]^{1.0} [\text{D-Man}]^{0.6} [\text{OH}^-]^{0.5}$$

Effect of ionic strength (I) and Dielectric constant of the medium (D): The effect of ionic strength was studied by varying the potassium nitrate concentration. The ionic strength of the reaction medium was varied from 0.04 to 0.12 mol dm⁻³ at constant [IO₄⁻], [D-Man] and [OH⁻]. The k_{obs} values increased with increase in ionic strength. The relative permittivity (D) effect was studied by varying the t-butyl alcohol–water content in the reaction mixture with all other conditions being maintained constant. Attempts to measure the relative permittivities were not successful. However, they were computed from the values of pure liquids[7] the dielectric constants of the reaction medium at various composition of t- butyl alcohol (V/V)-water were calculated by using the following equation,

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Test for free radicals (polymerization): The intervention of free radicals in the reaction was examined as follows: The reaction mixture was mixed with acrylonitrile monomer and kept for 2 h and 1 h respectively, under nitrogen atmosphere. On dilution with methanol, a white precipitate was formed, indicating the intervention of free radicals in the reactions. The blank experiments of either periodate or D-mannitol alone with acrylonitrile did not induce any polymerization under the same conditions as those induced for the reaction mixture. Initially added acrylonitrile decreased the rate of reaction indicating free radical intervention, which is the case in earlier work[8].

Effect of temperature (T): The influence of temperature on the rate of reaction was studied for reaction at different temperatures (25, 30, 35 and 40 °C) under varying concentrations of D-mannitol and OH^- keeping other conditions constant. The rate constants were found to increase with increase in temperature. The rate constant (k) of the slow step of the reaction was obtained from the slopes and intercept of plots of $1/k_{obs}$ versus $1/[\text{D-Man}]$ and $1/k_{obs}$ versus $1/[\text{OH}^-]$ at four different temperatures and were used to calculate the activation parameters. The energy of activation corresponding to these constants was evaluated from Arrhenius plot of $\log k$ versus $1/T$ ($r \geq 0.999$, $S \leq 0.001$) and other activation parameters obtained are tabulated in table 2.

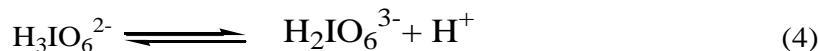
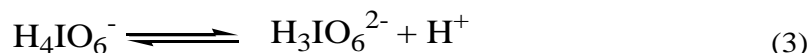
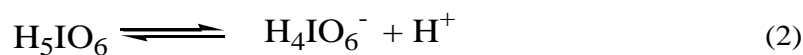
Table 2: Activation parameters and thermodynamic quantities for the oxidation of D-Man by periodate in aqueous alkaline medium with respect to the slow step of Scheme 1: (A) effect of temperature; (B) activation parameters; (C) effect of temperature to calculate K_1 and K_2 ; and (D) thermodynamic quantities using K_1 and K_2 .

(A)		
Temperature (K)	$k_1 \times 10^4 (\text{s}^{-1})$	
298	9.38	
303	12.0	
308	15.3	
313	18.8	
(B)		
Parameters	values	
E_a (kJ mol ⁻¹)	37.0 ± 1.2	
ΔH^\ddagger (kJ mol ⁻¹)	34.0 ± 1.0	
ΔS^\ddagger (J K ⁻¹ mol ⁻¹)	-180.0 ± 8	
$\Delta G^\ddagger_{(298\text{K})}$ (kJ mol ⁻¹)	88 ± 2	
log A	3.8 ± 0.3	
(C)		
Temperature (K)	$K_1 \times 10^{-1}$ (dm ³ mol ⁻¹)	$K_2 \times 10^{-1}$ (dm ³ mol ⁻¹)
298	1.24	9.09
303	1.99	5.96
308	2.71	4.20
313	3.46	3.21

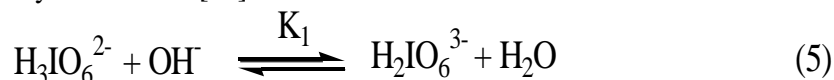
(D)

Thermodynamic quantities	Values from K ₁	Values from K ₂
ΔH (kJ mol ⁻¹)	55.2	-56.5
ΔS (J K ⁻¹ mol ⁻¹)	206	-152
ΔG_{298} (kJ mol ⁻¹)	-6.2	-10.2

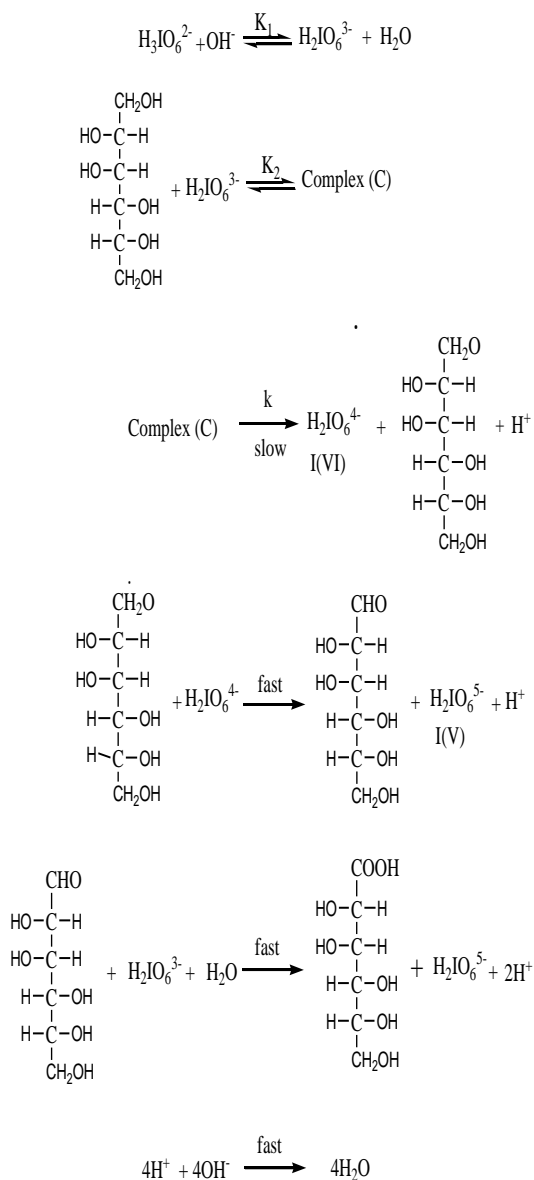
The activity of periodate as an oxidizing agent varies greatly as a function of pH and is capable of subtle control. In acidic solution known, where as in alkaline solution it is slightly less so. However in aqueous alkaline medium and in the pH ranges employed in the present study, periodate cannot exist as H₄IO₆ because in aqueous solution periodate is involved[9,10]in the following equilibria, depending on the pH of the solution.



The species H₄IO₆⁻ exists near pH 7.0. Hence under the alkaline conditions employed in the present system, the main species expected to be trihydrogenparaperiodate(H₃IO₆²⁻). At higher concentration periodate can also undergo dimerization. The observed fractional order in alkali concentration may be understood in terms of H₂IO₆³⁻ as the main species in alkaline medium with the following equilibrium, which is also supported by earlier work[11].



Mechanism of reaction: The reaction between D-mannitol and periodate in alkaline medium presents a 1:2 stoichiometry of reductant to oxidant. Since the reaction was first order dependence in [IO₄⁻] and an apparent order of less than unit order in [D-Man] and [OH⁻]. No effect of added products was observed. Based on the experimental results, a mechanism is proposed for which all the observed orders in each constituent such as [IO₄⁻], [D-Man] and [OH⁻] may be well accommodated (Scheme 1). The less than unit order in [D-Man] presumably results from formation of a complex (C) between periodate species and D-mannitol prior to the formation of the products. This complex (C) decomposes in a slow step to give a free radical of D-mannitol and intermediate I(VI) species. Further this free radical species reacts with I(VI) species in a fast step to form a gluconaldehyde intermediate and I(V) species. This gluconaldehyde reacts with one more mole of periodate species in a further fast step to form products such as gluconic acid and periodate. Such type of free radical is observed in literature in the oxidation of D-mannitol[2]. Free radical experiments also revealed such a possibility. All these reactions can be accommodated in Scheme 1



Scheme 1.Detailed Scheme for oxidation of D-Mannitol by alkaline periodate.

The Michaelis- Menten plot provides the complex formation between periodate and D-mannitol, which explains less than unit order dependence on [D-Man]. Scheme 1 leads to the rate law (Eq.6)

$$\begin{aligned}
 \text{Rate} &= \frac{k K_1 K_2 [\text{Man}]_T [\text{H}_3\text{IO}_6^{2-}]_T [\text{OH}^-]_T}{1 + K_1[\text{OH}^-] + K_1 K_2 [\text{Man}][\text{OH}^-]} \\
 k_{\text{obs}} &= \frac{\text{Rate}}{[\text{H}_3\text{IO}_6^{2-}]} = \frac{k K_1 K_2 [\text{Man}]_T [\text{OH}^-]_T}{1 + K_1[\text{OH}^-] + K_1 K_2 [\text{Man}][\text{OH}^-]} \quad \rightarrow (6)
 \end{aligned}$$

Which explains all the observed kinetic orders of different species.

The rate law (6) can be arranged in the following form, which is suitable for verification.

$$\frac{1}{k_{\text{obs}}} = \frac{1}{k K_1 K_2 [\text{Man}] [\text{OH}^-]} + \frac{1}{k K_2 [\text{Man}]} + \frac{1}{k} \longrightarrow (7)$$

According to equation (7), other conditions being constant, plot of $1/k_{\text{obs}}$ versus $1/[\text{D-Man}]$ (Figure 4) ($r \geq 0.995$, $S \leq 0.003$), $1/k_{\text{obs}}$ versus $1/[\text{OH}^-]$ (Figure 5) ($r \geq 0.997$, $S \leq 0.002$) should be linear with an intercept supporting the D-mannitol complex, which is verified in Fig 4. From the intercepts and slopes of such plots lead to the values of K_1 , K_2 and k were calculated as $12.4 \text{ dm}^3 \text{ mol}^{-1}$, $90.9 \text{ dm}^3 \text{ mol}^{-1}$ and $2.32 \times 10^{-3} \text{ s}^{-1}$ respectively. These reaction constants are in good agreement with the earlier work[12].

A high negative value of ΔS^\ddagger ($-180 \text{ J K}^{-1} \text{ mol}^{-1}$) suggests that intermediate complex (C) is more ordered than the reactants[13]. These constants were used to calculate the rate constants and compared with the experimental values and found to be reasonable agreement with each other given in Table 1 which fortities Scheme 1.

The thermodynamic quantities for the different equilibrium steps in Scheme 1 can be evaluated as follows. The $[\text{D-Man}]$ and $[\text{OH}^-]$ concentrations as in Table 1 were varied at different temperatures. From the slopes and intercepts, the values of K_1 and K_2 were calculated at different temperatures and these values are given in table 2. The van't Hoff's plots were made for the variation of K_1 and K_2 with temperature [i.e. $\log K_1$ versus $1/T$ ($r \geq 0.981$, $S \leq 0.013$)] and [$\log K_2$ versus $1/T$ ($r \geq 0.993$, $S \leq 0.005$)] and the values of the enthalpy of reaction ΔH , entropy of reaction ΔS and free energy of reaction ΔG were calculated for first and second equilibrium steps. These values are given in Table 2. A comparison of the ΔH value of first step ($55.2 \text{ k J mol}^{-1}$) with ΔH^\ddagger value from Scheme 1 ($34.4 \text{ k J mol}^{-1}$) obtained for the slow step of the reaction shows that these values mainly refer to the rate limiting step, supporting the fact that the reaction before the rate determining step is fairly slow and involves high activation energy[14,15]. In the same manner, K_2 values were calculated at different temperatures and the corresponding values of thermodynamic quantities are given in Table 2.

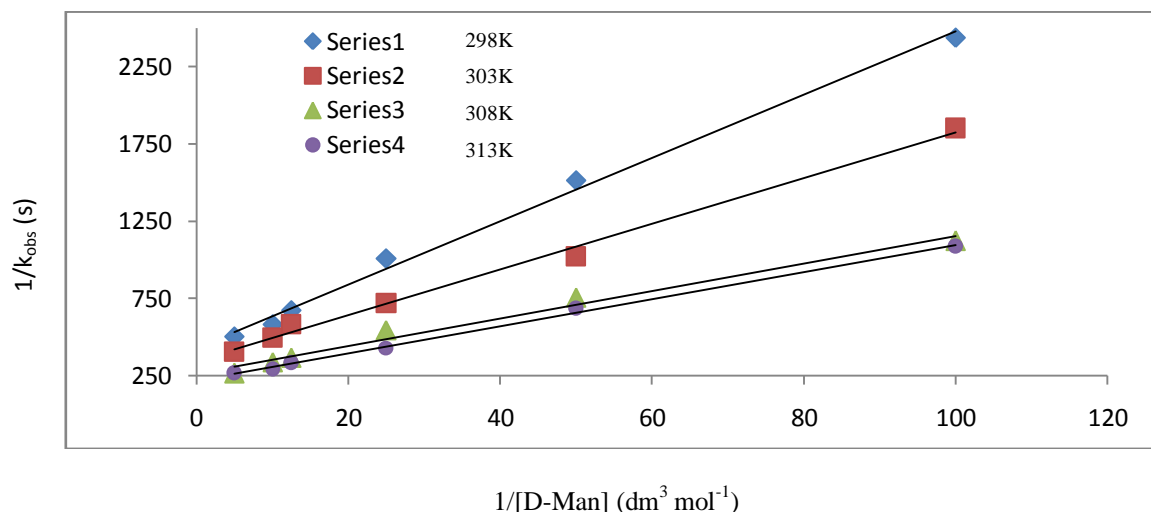


Figure 4: Verification of rate law (Eq. 7) for the oxidation of D- mannitol by periodate. Plots of $1/k_{\text{obs}}$ versus $1/[\text{OH}^-]$ at four different temperatures (Conditions as given in Table 1).

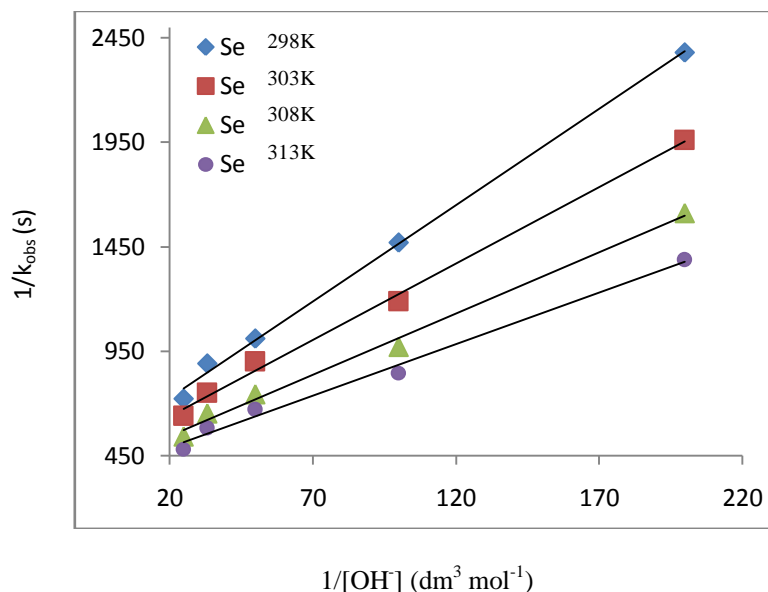


Figure 5: plot of $1/k_{\text{obs}}$ vs $1/[\text{OH}^-]$

APPLICATIONS

The rate of reactions and the various conditions under which they occur are crucial for determining certain aspects of environmental protection. In view of potential pharmaceutical importance of D-Man and periodate, understanding the active species of $[\text{IO}_4^-]$ and the mechanism is of importance.

CONCLUSIONS

The study of oxidation of D-mannitol by periodate was studied and oxidation products were identified. Among the various species of periodate in alkaline medium, $[\text{H}_2\text{IO}_6^{3-}]$ is considered as active species for the title reaction. Thermodynamic quantities of individual steps in the mechanism were evaluated. Activation parameters with respect to slow step were computed. The overall sequence is consistent with the observed product, mechanistic and kinetic study.

ACKNOWLEDGEMENT

One of the authors (PAM) thanks Department of Science and Technology, New Delhi for the award of INSPIRE fellowship.

Appendix

$$\text{Rate} = -\frac{d[\text{H}_2\text{IO}_6^{3-}]}{dt} = k[\text{C}] \quad [\text{A.1}]$$

$$K_2 = \frac{[\text{C}]}{[\text{Man}] [\text{H}_2\text{IO}_6^{3-}]}$$

$$[\text{C}] = K_2 [\text{Man}] [\text{H}_2\text{IO}_6^{3-}] \quad [\text{A.2}]$$

$$K_1 = \frac{[\text{H}_2\text{IO}_6^{3-}]}{[\text{H}_3\text{IO}_6^{2-}] [\text{OH}^-]}$$

$$[\text{H}_2\text{IO}_6^{3-}] = K_1 [\text{H}_3\text{IO}_6^{2-}] [\text{OH}^-]$$

$$[\text{C}] = K_1 K_2 [\text{Man}] [\text{H}_3\text{IO}_6^{2-}] [\text{OH}^-]$$

$$\text{Rate} = k K_1 K_2 [\text{Man}] [\text{H}_3\text{IO}_6^{2-}] [\text{OH}^-] \quad [\text{A.3}]$$

The total concentration of $[\text{D-Man}]_T$ is given by,

$$[\text{Man}]_T = [\text{Man}]_f + \text{C}$$

where T and f refer to total and free concentrations.

$$[\text{Man}]_T = [\text{Man}]_f + K_1 K_2 [\text{Man}]_f [\text{H}_3\text{IO}_6^{2-}] [\text{OH}^-]$$

$$= [\text{Man}]_f (1 + K_1 K_2 [\text{H}_3\text{IO}_6^{2-}] [\text{OH}^-])$$

$$[\text{Man}]_f = \frac{[\text{Man}]_T}{1 + K_1 K_2 [\text{H}_3\text{IO}_6^{2-}] [\text{OH}^-]}$$

In view of low concentration of $[\text{H}_3\text{IO}_6^{2-}]$ used, the second term in denominator is neglected.

$$[\text{Man}]_f = [\text{Man}]_T \quad [\text{A.4}]$$

Similarly, the concentration OH^- is

$$[\text{OH}^-]_f = [\text{OH}^-]_T \quad [\text{A.5}]$$

Similarly,

$$[\text{H}_3\text{IO}_6^{2-}]_T = [\text{H}_3\text{IO}_6^{2-}]_f + [\text{H}_2\text{IO}_6^{3-}]_f + \text{C}$$

$$= [\text{H}_3\text{IO}_6^{2-}]_f + K_1 [\text{H}_3\text{IO}_6^{2-}]_f [\text{OH}^-] + K_1 K_2 [\text{Man}] [\text{OH}^-] [\text{H}_3\text{IO}_6^{2-}]_f$$

$$= [\text{H}_3\text{IO}_6^{2-}]_f (1 + K_1 [\text{OH}^-] + K_1 K_2 [\text{Man}] [\text{OH}^-])$$

$$[\text{H}_3\text{IO}_6^{2-}]_f = \frac{[\text{H}_3\text{IO}_6^{2-}]_T}{(1 + K_1 [\text{OH}^-] + K_1 K_2 [\text{Man}] [\text{OH}^-])} \quad [\text{A.6}]$$

Substituting equations (A.4), (A.5) and (A.6) in equation (A.3) we get,

$$\text{Rate} = \frac{k K_1 K_2 [\text{Man}]_T [\text{H}_3\text{IO}_6^{2-}]_T [\text{OH}^-]_T}{1 + K_1 [\text{OH}^-] + K_1 K_2 [\text{Man}] [\text{OH}^-]}$$

$$k_{\text{obs}} = \frac{\text{Rate}}{[\text{H}_3\text{IO}_6^{2-}]} = \frac{k K_1 K_2 [\text{Man}]_T [\text{OH}^-]_T}{1 + K_1 [\text{OH}^-] + K_1 K_2 [\text{Man}] [\text{OH}^-]} \quad [\text{A.7}]$$

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