

Kinetics of Oxidation of *myo*-Inositol by Potassium Periodate in Alkaline Medium†

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Kinetics of oxidation of *myo*-inositol by potassium periodate both in alkaline and acid media were studied. The reactions were found to be first order in case of periodate in both media. In the case of base catalyzed reactions, a decrease in the rate of the reaction was observed with an increase in the concentration of substrate. An inverse fractional order with respect to substrate in alkaline shows the substrate inhibition. A positive fractional order was observed for substrate in acid catalyzed reactions. The dependence on hydrogen ions and hydroxide ions was found to be inverse fractional order. Arrhenius parameters were calculated for both the reactions conducted in acid and alkali media. Plausible mechanism is postulated based on experimental results.

Key Words: Kinetics, Substrate inhibition, Inositol, Potassium periodate, Alkaline medium, Acid medium.

INTRODUCTION

myo-Inositol is a six-member carbon ring polyol that is synthesized by both eukaryotes and prokaryote¹. Inositol occurs in animal tissues in both free and combined forms. *myo*-Inositol and its various biochemical derivatives are widely distributed in mammalian tissues, higher plants, fungi and some bacteria, where they are important in many crucial cellular compounds, including those involved in signal transduction such as phosphatidylinositol phosphates and *myo*-inositol phosphates² gene expression³, auxin perception and phosphorus storage^{4,5}, membrane tethering⁶ and oligosaccharide synthesis⁷.

Oxidation of inositol was studied by different oxidants like alkaline hexacyanoferrate(III) ion in presence of Osmium (VIII)⁸, vanadium(V) in acid medium in absence⁹ and presence of copper (II)¹⁰, periodate¹¹, periodic acid¹²⁻¹⁴.

Since the periodate ion is a large and negatively charged entity that is unlikely to permeate membranes passively at lower temperatures, glycoinositol phospholipids at the cell surface were detected by sodium periodate oxidation reaction¹⁵⁻¹⁷ and hence used for topological studies. In view of the biological importance of inositol and its derivatives oxidation by periodate, it was decided to study the oxidation of inositol by periodate in aqueous alkaline medium and for the purpose of comparison, reactions were also carried out in acid medium.

EXPERIMENTAL

myo-Inositol, potassium periodate, perchloric acid, potassium hydroxide, boric acid, DMSO and all other reagents used in these experiments were of analytical reagent grade. The reaction kinetics was followed by iodometry. In the oxidation of inositol, 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 into iodate. This was also confirmed by non oxidation of inositol by iodate.

RESULTS AND DISCUSSION

Variation of [periodate]: The oxidant periodate concentration was varied in the range of 0.00025 to 0.001 M and fairly constant k_1 value indicates that order with respect to [periodate] was unity (Tables 1 and 2). This was also confirmed by linearity of the plots of $\log(a-x)$ versus time upto 85 % completion of reaction.

Reaction orders of acid /alkali and substrate: The reaction orders were determined from the slope of $\log k_1$ vs. \log [variant] plots by varying the concentrations of inositol, acid/alkali in turn while keeping all other concentrations and conditions constant.

Variation of [acid]/[alkali]: The effect of increase in concentration of acid/alkali on the reaction was studied at

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constant concentration of periodate and inositol at constant temperature of 35 °C. In both cases, the rate constants decreased with an increase in acid/alkali concentrations (Tables 1 and 2), indicating inverse fractional order dependence of rate on acid/alkali.

In the alkaline medium, the dissociative equilibria (1-3) of the IO_4^- was detected and the corresponding equilibrium constants were determined at 298.2 K by Aveston¹⁸.



The distribution of all species of periodate in aqueous alkaline solution can be calculated from equilibria (1-3). K_1 , K_2 and K_3 are the equilibrium constants in the above equations 1-3, respectively. In the $[\text{OH}^-]$ range used in this work the amount of dimer ($\text{H}_2\text{I}_2\text{O}_{10}^{4-}$) and IO_4^- species of periodate can be neglected. The main species of periodate are $\text{H}_2\text{IO}_3^{6-}$ and $\text{H}_3\text{IO}_6^{2-}$, which are consistent with the result calculated from Crouthamel's data¹⁹ and other recent results reported in the literature²⁰⁻²².

Eqs. (4) and (5) can be obtained²³ from (2) and (3):

$$[\text{H}_2\text{IO}_6^{3-}] = \frac{\beta_3[\text{OH}^-]^2}{1 + \beta_2[\text{OH}^-] + \beta_3[\text{OH}^-]^2} [\text{IO}_4^-]_{\text{ex}} = f([\text{OH}^-])[\text{IO}_4^-]_{\text{ex}} \quad (4)$$

$$[\text{H}_3\text{IO}_6^{2-}] = \frac{\beta_2[\text{OH}^-]}{1 + \beta_2[\text{OH}^-] + \beta_3[\text{OH}^-]^2} [\text{IO}_4^-]_{\text{ex}} = \phi([\text{OH}^-])[\text{IO}_4^-]_{\text{ex}} \quad (5)$$

Here $[\text{IO}_4^-]_{\text{ex}}$ represents the concentration of the original overall periodate ion and is approximately equal to the sum of $[\text{H}_2\text{IO}_6^{3-}]$ and $[\text{H}_3\text{IO}_6^{2-}]$. At lower concentration of alkali (0.05 M), the concentrations of $\text{H}_3\text{IO}_6^{2-}$ and $\text{H}_2\text{IO}_6^{3-}$ are 0.0003076 M and 0.00018 M respectively, whereas at higher concentrations of alkali (0.833 M), the corresponding concentrations are 0.0000465 M and 0.000453387 M respectively. Hence, $\text{H}_3\text{IO}_6^{2-}$ is the predominant species at lower concentration of alkali whereas $\text{H}_2\text{IO}_6^{3-}$ is the predominant species at higher concentration of alkali. Based on such distribution, we can conclude that inositol complexes with either $\text{H}_3\text{IO}_6^{2-}$ or the less protonated ionic species $\text{H}_2\text{IO}_6^{3-}$. If two or more hydroxyl groups in a polyol are in a sterically favourable arrangement they may displace two or more molecules, respectively, of water from the solvation sphere of periodate ion. In alkaline solution hydroxyl groups can, after losing a proton, form much stronger complexes.

Barker²⁴ described the existence of triesters of periodate ion with inositol and suggested that the iodine atom is attached to an ax-eq-ax sequence of oxygen atoms. The NMR spectrum confirmed the suggested structure (Fig. 1). Out of the three hydroxyls, one is axial hydroxyl second is equatorial and third is axial hydroxyl and these three OH's have complexed with the periodate species $\text{H}_3\text{IO}_6^{2-}$ in alkaline medium.

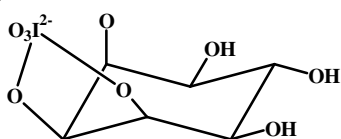


Fig. 1. Periodate ion and inositol complex

Lower rate of reaction in alkali medium: The rate of reaction between periodate and inositol in alkaline medium is lower compared to acid medium, which 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. Perlin and Von Rudolff²⁵ reported that the cleavage of complex between diols and periodate is slower in weakly alkaline compared to that in acid medium. In addition, the rate of glycol scission by periodate may be retarded as the pH is raised^{26,27}.

Variation of [inositol]: The effect of inositol concentration on the rate of reaction was studied at constant concentration of acid/alkali and periodate at 35 °C. The k_1 values increased with an increase in concentration of inositol in the case of acid medium and the apparent order with respect to [inositol] was found to be positive fractional (Table-2). In the case of alkali medium, substrate inhibition was observed *i.e.*, the rate of the reaction decreased with an increase in the inositol and an inverse fractional order was found w.r.t. inositol (Table-1). Similar effects have been observed with hexacyanoferrate(III) of carbohydrates²⁸ and ceric sulphate oxidation of alcohols²⁹. Substrate inhibition *i.e.*, a decrease in rate of reaction with an increase in substrate concentration can be contributed to the formation of periodate-inositol 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.

TABLE-1
OXIDATION OF MYO-INOSITOL BY POTASSIUM
PERIODATE IN AN ALKALI MEDIUM

Variant	Concentration of variant (M)	$k_1 \times 10^4 (\text{sec}^{-1})$
Periodate	0.00025	2.110
	0.00050	2.117
	0.00100	1.873
OH ⁻	0.050	2.780
	0.100	2.117
	0.200	1.345
	0.500	1.070
	0.833	0.763
	Inositol	0.0005
0.0010		12.113
0.0025		7.529
0.0125		2.662
0.0250		2.117
0.0500		1.340
0.1000		0.648
Temperature		35 °C
	45 °C	4.372
	55 °C	19.133
Boric acid	0	2.117
	0.010	2.136
	0.025	2.536
	0.050	3.234

Conditions: [Inositol] = 0.025 M; [OH⁻] = 0.1 M; [Pot. periodate] = 0.0005 M; Temperature = 35 °C

Effect of addition of solvent-dimethyl sulphoxide: Dimethyl sulphoxide is a dipolar aprotic solvent and it has a dielectric constant less than that of water. To find out the effect

of dielectric constant (D) on the rate of oxidation in acid medium, the reactions have been carried out at various proportions of DMSO in the medium. The D values were calculated from the equation $D = D_w V_w + D_D V_D$, where D_w and D_D are dielectric constants of pure water and DMSO respectively and V_w and V_D are the volume fractions of components of water and DMSO respectively in the total mixture. With an increase in the percentage of DMSO, the rate of the reaction decreased (Table-2). In other words, the decrease in dielectric constant of the reaction medium had retarded the rate of reaction. It appears that these reactions are between negative ion and a dipole. Hence, in acid medium, the reaction is between ion $[IO_4^-]$ and molecule [inositol].

TABLE-2
OXIDATION OF MYO-INOSITOL BY POTASSIUM PERIODATE IN AN ACID MEDIUM

Variant	Concentration of variant (M)	$k_1 \times 10^4 (\text{sec}^{-1})$
Periodate	0.00025	5.883
	0.0005	6.102
	0.001	6.081
$HClO_4$	0.0125	7.097
	0.025	9.000
	0.05	9.229
	0.1	6.102
	0.2	3.669
	0.5	2.720
	1.0	2.661
	2.0	1.788
Inositol	0.0125	4.641
	0.025	6.105
	0.05	8.104
	Temperature	
Temperature	30 °C	2.912
	35 °C	5.343
	40 °C	5.883
	45 °C	7.770
Solvent composition (DMSO:Water)	0:100	6.102
	5:95	5.574
	10:90	4.122
	20:80	1.195
Boric acid	0	6.102
	0.01	6.231
	0.025	6.132
	0.05	5.973

Conditions: [Inositol] = 0.025 M; $[HClO_4]$ = 0.1 M; [Pot. periodate] = 0.0005 M; Temperature = 35 °C

Effect of temperature: The rate constants (k_1) increased with an increase temperature in both the media. The plot of $\ln(k)$ vs. $1/T$ yields a straight line and the values of activation parameters viz. enthalpy of activation (ΔH^\ddagger), entropy of activation ($-\Delta S^\ddagger$) and Gibb's free energy (ΔG^\ddagger) evaluated from the slope of the plot by using the Eyring equation^{30,31} and tabulated (Tables 3 and 4).

Effect of boric acid: Addition of boric acid didn't influence the rate of reaction in acid medium because acid medium suppress the dissociation of boric acid and hence repress complex formation between inositol and borate. However, an increase in rate was observed in alkali medium due to favouring conditions for complex formation between inositol and highly dissociating potassium borate (Fig. 2), which competes with the stable complex formation between inositol and periodate.

Such observations were reported earlier by other authors in sodium borate solution. The three axial oxygen atoms of hydroxyl groups are on the same side of the *cis*-inositol molecule in either of its two chair conformations, which facilitates the formation of tridentate borate ester anions (I) in sodium borate solution. The creation of tridentate borate ester anions is reminiscent by their strong mobility towards the anode in electrophoresis³² and changes in NMR spectrum^{33,34}.

TABLE-3
ARRHENIUS PARAMETERS FOR INOSITOL OXIDATION IN ALKALI MEDIUM AT 313 K

ΔE^\ddagger (KJ/mol)	ΔH^\ddagger (KJ/mol)	$-\Delta S^\ddagger$ (JK ⁻¹ / mol)	$\log_{10} P_z$	ΔG^\ddagger (KJ/mol)
92.485	89.924	23.558	12.011	97.186

TABLE-4
ARRHENIUS PARAMETERS FOR INOSITOL OXIDATION IN ACID MEDIUM AT 313 K

ΔE^\ddagger (KJ/mol)	ΔH^\ddagger (KJ/mol)	$-\Delta S^\ddagger$ (JK ⁻¹ / mol)	$\log_{10} P_z$	ΔG^\ddagger (KJ/mol)
52.419	49.816	148.798	5.476	96.390

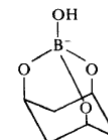


Fig. 2. Borate ion and inositol complex

Product analysis: The product was $CHO(CH.OH)_4CHO$, which was identified by its characteristic spot test³⁵ and it was quantified by gravimetric analysis, *via* their transformation into 2,4-dinitrophenylhydrazone derivative. The product as in the case of oxidation of inositol with nitric acid³⁶ is ruled out because no formation of products like tetrahydroxy quinone and dihydroxy quinone was observed with the help of UV spectra. Moreover, the minimum periodate should be two moles in the first case and four moles in second case, where as in our work it is only one oxygen that is used. So the product can be only $CHO(CH.OH)_4CHO$ under kinetic conditions³⁷.

Rate law in alkali medium:

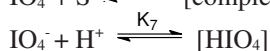


Since, the $[IO_4^-]$ and $[H_2I_2O_{10}^{4-}]$ are negligible, the total concentration of periodate can be written as:

$$\begin{aligned} [IO_4^-]_T &= [H_3IO_6^{2-}] + [H_2IO_6^{3-}] + [\text{complex } C_1] + [\text{complex } C_2] \\ &= K_2 [IO_4^-] [OH^-] + K_3 [IO_4^-] [OH^-]^2 \\ &\quad + k_1 K_2 K_4 [S] [IO_4^-] [OH^-] + k_2 K_3 K_5 [S] [IO_4^-] [OH^-]^2 \end{aligned}$$

$$[IO_4^-] = \frac{[IO_4^-]_T}{[OH^-] \{K_2 + K_3 [OH^-] + k_1 K_2 K_4 [S] + k_2 K_3 K_5 [S] [OH^-]\}}$$

$$\begin{aligned} \text{Rate} &= k_1 [\text{complex } C_1] + k_2 [\text{complex } C_2] \\ &= k_1 K_4 [H_3IO_6^{2-}] [S] + k_2 K_5 [H_2IO_6^{3-}] [S] \\ &= k_1 K_2 K_4 [IO_4^-] [OH^-] [S] + k_2 K_3 K_5 [IO_4^-] [OH^-]^2 [S] \\ &= [IO_4^-] [OH^-] [S] \{k_1 K_2 K_4 + k_2 K_3 K_5 [OH^-]\} \\ &= \frac{[IO_4^-]_T [S] \{k_1 K_2 K_4 + k_2 K_3 K_5 [OH^-]\}}{K_2 + K_3 [OH^-] + k_1 K_2 K_4 [S] + k_2 K_3 K_5 [S] [OH^-]} \end{aligned}$$

Rate law in acid medium:

$$\text{Rate} = k_3 [\text{complex C}_3] + k_4 [\text{complex C}_4]$$

$$= \frac{[\text{IO}_4^-]_T [\text{S}] \{k_3 K_6 + k_4 K_7 K_8 [\text{H}^+]\}}{1 + K_6 [\text{S}] + K_7 [\text{H}^+] (1 + K_8 [\text{S}])}$$

Conclusion

Substrate inhibition is observed in the oxidation of inositol in alkaline medium due to stable complex formation between inositol and periodate.

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