Kinetics & Mechanism of Oxidation of Aliphatic Ketones by Sodium Metaperiodate: A Comparative Study of Uncatalysed versus OsO₄-catalysed Oxidation

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Kinetics of oxidation of acetone, ethyl methyl ketone (EMK), isobutyl methyl ketone, diisopropyl ketone and pentane-2-one in aqueous alkaline medium by sodium metaperiodate in the absence and presence of OsO₄ have been studied. The uncatalysed reaction is first order with respect to both [ketone] and [periodate] and shows marginal dependence on [OH⁻]. The oxidation rate of acetone > EMK in the uncatalysed reaction. In the presence of OsO₄ the kinetic picture changes, the dependence being first order each on [ketone], [OH⁻] and [OsO₄] and zero order in [IO₄⁻]. In the catalysed oxidation reaction rate for EMK > acetone. k_H/k_D values of 1·3 and 2·6 are observed for the uncatalysed and catalysed reactions respectively.

THE periodate oxidation of acetone to acetic acid[1] and formaldehyde has been reported to be sluggish even at 100°. Singh *et al.* have studied the kinetics of OsO₄-catalysed hexacyanoferrate(III) oxidation of acetone and ethyl methyl ketone (EMK)[2] in carbonate and bicarbonate buffer. Contrary to the literature findings that IO₄⁻ oxidizes only diketones and active methylene compounds, preliminary investigations showed that acetone and EMK are oxidized readily by periodate in alkaline medium. Hence it was thought worth while to study the kinetics of periodate oxidation of acetone, EMK, isobutyl methyl ketone, diisopropyl ketone and pentane-2-one, both in the presence and absence of OsO₄ in aqueous alkaline medium.

Materials and Methods

The ketones (BDH, AR) were distilled before use. Details of the kinetic procedure are the same as described earlier[3].

Stoichiometry and product analysis — One mole of ketone requires 3 moles of IO₄⁻ and acetic acid is the major product. In the OsO₄-catalysed hexacyanoferrate(III) oxidation of acetone and EMK[2], the major product reported is oxalic acid. This difference is understandable because once a hydroxy ketone or diketone moiety is produced, IO₄⁻ will cleave such structures with facility[4].

Results and Discussion

Uncatalysed oxidation — The facile oxidation of aliphatic ketones by IO₄⁻ at 35° contradicts the earlier report that higher temperature is necessary for these oxidations[1]. The uncatalysed reactions show first order dependence on both [ketone] and [IO₄⁻]. The reaction rate is not affected by a change in the ionic strength.

The marginal dependence of rate on [OH⁻] (Table 1) is significant and is in contrast to what has been observed in the alkaline oxidation of

ketones by hexacyanoferrate(III)[5,6]. The [OH⁻] dependence in the latter originates because of electron transfer from the enolate anion. The marginal rate difference between *p*H 10 and 14 also points in a way to direct attack on the ketone by periodate.

Structure and reactivity — The second order rate constants for the oxidations of ketones by IO₄⁻ are recorded in Table 2. The order of reactivity among the ketones studied is: acetone > EMK > pentane-2-one > isobutyl methyl ketone > diisopropyl ketone. A plot of log k_2 vs Taft substituent constants[7] (σ*) is perfectly linear with slope (ρ), ρ = 0·9.

It is interesting to recall that in the oxidation of acetone and EMK by hexacyanoferrate(III)[5,6] and Ce(IV)[8,9], the order of reactivity is EMK > acetone which is quite in the order of the enol content and its thermodynamic stability. The present reactivity order, acetone > EMK, points to a probable direct attack on the ketone by periodate and supports the view that the oxidation does not involve electron transfer from the enolate or enol as in the case of Ce(IV) oxidation[8].

Kinetic isotope effect — When the oxidation was repeated with acetone-d_6, a k_H/k_D value of 1·3 was observed and this points to the fact that cleavage of α-CH bond is not involved in the rate-determining step. The rate-limiting step may involve a nucleophilic attack of IO₄⁻ on the carbonyl group of the keto form of the substrate.

Catalysed oxidation: periodate dependence — Oxidation in the presence of OsO₄ shows zero order kinetic dependence on [IO₄⁻] as seen from constancy of k_0 values at varying [IO₄⁻] (Table 2).

The increase in k_0 values at higher [IO₄⁻] is probably due to the simultaneous oxidation of intermediate oxidation products[2].

Substrate dependence — The catalysed oxidation shows first order dependence with respect to [substrate] (Table 4).

TABLE 1 — RATES OF UNCATALYSED OXIDATION OF KETONES BY IO$_4^-$ AT VARYING [OH$^-$]

($IO_4^- = 6 \cdot 1 \times 10^{-4}M$; $KCl = 2 \cdot 5 \times 10^{-2}M$; temp. $= 35°$)

10^2 [OH$^-$] M	10^2 $k_2 M^{-1}$ min^{-1}	10^2 [OH$^-$] M	10^2 $k_2 M^{-1}$ min^{-1}
ACETONE $3 \cdot 1 \times 10^{-2}M$		EMK $3 \cdot 4 \times 10^{-2}M$	
1·30	7·5	1·30	3·65
2·61	8·4	2·60	3·94
5·23	10·0	5·60	4·24
8·14	12·5	11·10	5·17
10·76	13·5	(pH 10)	(2·60)
(pH 10)	(4·5)	—	—

TABLE 2 — RATES OF UNCATALYSED OXIDATION OF KETONES BY PERIODATE

($IO_4^- = 8 \cdot 0 \times 10^{-4}M$; $KCl = 2 \cdot 5 \times 10^{-2}M$; $OH^- = 2 \cdot 5 \times 10^{-1}M$)

Substrate	σ^*	10^2 $k_2 M^{-2}$ min^{-1} at		
		35°	45°	60°
Acetone	+0·49	8·35	18·7	52·2
EMK	0·0	3·74	10·3	39·3
Isobutyl methyl ketone	−0·19	2·13	6·6	30·5
Diisopropyl ketone	−0·28	1·84	4·0	13·6
Pentane-2-one	−0·10	2·58	7·06	32·9

A marginal decrease in the reaction rate has been observed with increase in [ketone]. This was also observed by Singh *et al.*[2] in the hexacyano-ferrate(III) oxidation and who attributed this decrease to the dielectric effect of medium. However, we do not agree with this view. In our view a more rigorous approach would be to use equilibrium concentration of enol in the computation of k_0/[ketone] and not the stoichiometric concentrations of ketones. This probably causes a marginal decrease. In fact in chromic acid oxidation of pinacol[10] decrease in first order rate with increasing chromic acid concentration has been traced to the participation of acid chromate ion rather than dichromate ion in view of the hydration equilibria between the two.

Osmium(VIII) and [OH$^-$] dependence — The rate constants with varying [Os(VIII)] and [OH$^-$] suggest first order dependence in each.

Effect of added bases — In view of the reported observation[11] that catalytic activity of OsO$_4$ is greatly diminished by added 2,2′-bipyridyl and 1,10-phenanthroline due to the formation of inactive complexes of Os(VIII), the effect of these bases has been studied. There is a marked retardation in the rate in the presence of these complexing bases (Table 3).

Structure and reactivity — The k_0/[S] values for the various aliphatic ketones are recorded in Table 5. However, no correlation of log k_1 with σ^* was observed in the OsO$_4$-catalysed oxidation. This points to the importance of the enol form in the catalysed process.

The order of reactivity in the presence of OsO$_4$ is EMK > pentane-2-one > isobutyl methyl ketone > acetone > diisopropyl ketone, and this order parallels the Ce(IV) sulphate oxidation of aliphatic
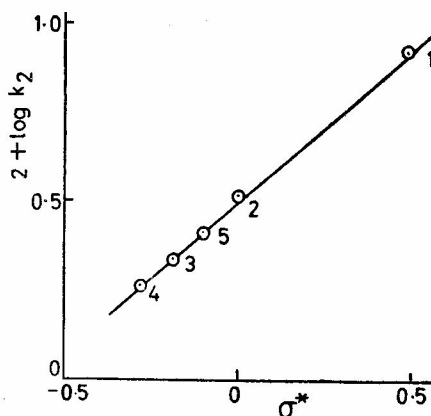

Fig. 1 — Plot of σ^* versus $2+\log k_2$; 1, acetone; 2, ethyl methyl ketone; 3, isobutyl methyl ketone; 4, diisopropyl ketone; 5, pentane-2-one

TABLE 3 — RATES OF OsO$_4$-CATALYSED OXIDATION OF KETONES BY IO$_4^-$ AT VARYING [IO$_4^-$]

($OH^- = 2 \cdot 6 \times 10^{-2}M$; $KCl = 2 \cdot 5 \times 10^{-2}M$; $OsO_4 = 3 \cdot 93 \times 10^{-6}M$; temp. $= 35°$)

10^2 [ketone] M	10^3 [IO$_4^-$] M	10^5 $k_0 M$ min^{-1}	10^4 k_0/[ketone] min^{-1}
ACETONE			
4·5	0·51	1·14	2·81
4·05	0·71	1·25	3·10
3·64	0·75	1·35	3·67
—	—	0·38*	1·28*
—	—	0·81†	2·67†
3·94	0·89	1·67	4·25
3·94	1·52	1·83	4·64
4·04	2·67	1·80	4·41
EMK			
4·23	0·50	6·27	14·8
4·23	0·71	7·13	16·9
3·56	0·75	7·53	21·1
3·87	1·54	8·57	22·1
3·90	2·67	9·71	24·9

*In the presence of 1,10-phenanthroline ($5 \cdot 25 \times 10^{-4}M$).
†In the presence of 2,2′-bypyridyl ($4 \cdot 94 \times 10^{-4}M$).

TABLE 4 — RATES OF OsO$_4$-CATALYSED OXIDATION OF KETONES BY IO$_4^-$ AT VARYING [KETONE] AT 35°

($OsO_4 = 3 \cdot 9 \times 10^{-6}M$; $IO_4^- = 7 \cdot 5 \times 10^{-4}M$; $KCl = 2 \cdot 5 \times 10^{-2}M$; $OH^- = 2 \cdot 6 \times 10^{-2}M$)

10^2 [ketone] M	10^5 $k_0 M$ min^{-1}	10^3 k_0/[ketone] min^{-1}
ACETONE		
1·27	0·50	0·40
2·43	1·03	0·40
3·66	1·40	0·37
5·37	1·90	0·36
EMK		
1·46	3·88	2·6
2·11	5·30	2·5
3·56	7·52	2·1

ketones reported by Shorter[8] who had envisaged the importance of the enols in the oxidation. Lower reactivity for acetone has also been observed by Shorter. EMK and pentane-2-one show increased reactivity over acetone in the catalysed oxidation. It is worth recalling that in the $Fe(CN)_6^{3-}$ and Ce(IV) oxidations of acetone and EMK the trend is EMK > acetone and the higher reactivity of EMK has been traced to a dominant hyperconjugative effect which is called into play to meet the demand of a suitably placed double bond. We presume this difference in the reactivity order is due to the change in the reacting species of the substrate and this might well be the ketone and enolate anion in the absence and presence of OsO_4 respectively.

That the enolate reacts in the presence of OsO_4 also finds support from the fairly linear correlation (Fig. 2, corr. coeff. 0·92) between rates of enolization (r_e) (pertaining to enols derived from α-CH_2 or α-CH groups in the case of unsymmetrical ketones) and the rates of oxidation. Shorter[8] has observed for a series of unsymmetrical ketones a similar linear correlation. Acetone does not fit into the plot, an observation ·also recorded by Shorter[8]. The reason can be traced to absence of α-CH_2 or α-CH in acetone. In spite of this, the correlation provides a sound basis for the enolate reaction. But such a correlation was totally absent in the uncatalysed periodate oxidation of the aliphatic ketone. This leads one to believe that enolization is not important in the uncatalysed process in spite of the fact that the oxidations have been carried out in alkaline medium. A change in the substrate species can also be rationalized on the basis of kinetic isotope effect.

Kinetic isotope effect — A k_H/k_D value of 2·6 is observed in the OsO_4-catalysed oxidation of acetone-d_6 and acetone. A primary isotope effect of the order of ~5 should be expected if a cleavage of the α-CH bond is involved; the small positive k_H/k_D may be due to the fact that in acetone-d_6, enolization is appreciably retarded compared to ketonization and hence the complex formation across the enolate double bond with OsO_4, likely to be the rate-determining step, is consequently retarded.

The isotopic exchange between the solvent and acetone-d_6 is ruled out as it is well known that
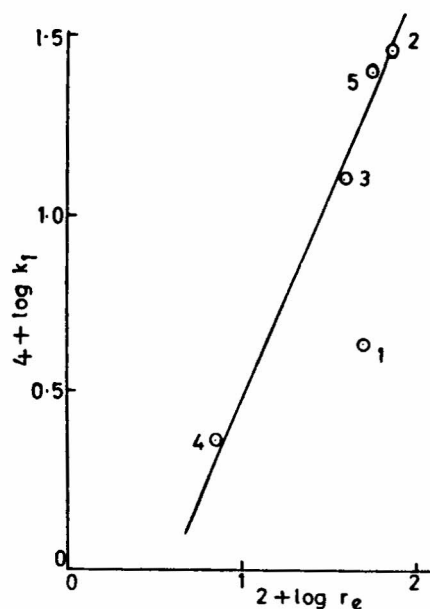

Fig. 2 — Plot of rates of enolization (r_e) versus rates of oxidation: 1, acetone; 2, ethyl methyl ketone; 3, isobutyl methyl ketone; 4, diisopropyl ketone; 5, pentane-2-one

the time taken for attainment of the exchange equilibrium is much longer than that for ketone-enol equilibrium.

Thermodynamic parameters — Thermodynamic parameters for OsO_4-catalysed and the uncatalysed oxidations have been evaluated and are given in Table 6.

It is significant that differences in E, $\Delta H^{\ddagger}$, ΔS and log A values for the various ketones observed in the uncatalysed reaction have vanished in the OsO_4-catalysed reaction.

In both catalysed and uncatalysed oxidations, negative entropies of activation have been observed, the $\Delta S^{\ddagger}$ being more negative in the presence of OsO_4, which obviously means that the transition state in the presence of OsO_4 is more rigid.

Periodate species and mechanism of the uncatalysed process — The effective species of sodium periodate in alkaline medium is IO_4^- or $H_4IO_6^-$ as suggested by Maros et al.[12]. We, therefore, presume periodate monoanion (IO_4^- or $H_4IO_6^-$) as the species responsible for the oxidation.

The experimental results lead to the rate law (1).

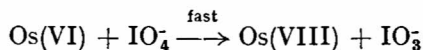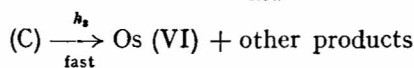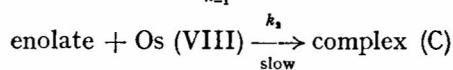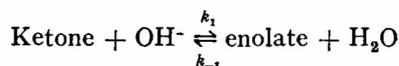$$v = k_{obs} [\text{ketone}][IO_4^-] \qquad \ldots(1)$$

The experimental observations recorded for uncatalysed oxidation suggest a nucleophilic attack by the periodate species on the carbonyl group of the ketone molecule giving rise to an S_N2 type of transition state, although it is difficult to picturize the transition state. Nucleophilic attack by IO_4^- in diketone oxidations is well known[13,14].

Rate law and mechanism of the catalysed oxidation — The hydroxide dependence in the OsO_4-catalysed oxidation points clearly to the enolate ion as the

TABLE 5 — RATES OF OsO_4-CATALYSED OXIDATION OF KETONES BY IO_4^- AT DIFFERENT TEMPERATURES

($OH^- = 2·6 \times 10^{-2}M$; $KCl = 2·5 \times 10^{-2}M$; $OsO_4 = 11·8 \times 10^{-6}M$)

Substrate	$10^3 k_1$ min^{-1} ($= k_0/[S]$)			*r_e
	25°	30°	35°	
Acetone	0·43	0·57	0·90	0·50
EMK	2·80	3·90	5·60	0·75
Isobutyl methyl ketone	1·20	1·50	2·60	0·44
Diisopropyl ketone	0·23	0·28	0·46	0·07
Pentane-2-one	2·48	3·50	5·30	0·58

*r_e = rate of enolization.

TABLE 6 — THERMODYNAMIC PARAMETERS FOR THE
OXIDATION OF KETONES BY IO_4^- AT 35°

Substrate	E kcal/ mole	$\Delta H\ddagger$ kcal/ mole	$-\Delta S\ddagger$ e.u.	$\log A$
UNCATALYSED OXIDATION				
Acetone	15·2	14·6	24·3	8·0
EMK	19·0	18·4	13·5	10·3
Isobutyl methyl ketone	19·6	19·0	13·0	10·4
Diisopropyl ketone	15·2	14·6	27·3	7·3
Pentane-2-one	21·1	20·5	7·8	11·6
CATALYSED OXIDATION				
Acetone	13·7	13·1	38·1	5·0
EMK	12·3	11·7	39·1	5·0
Isobutyl methyl ketone	13·7	13·1	36·0	5·4
Diisopropyl ketone	12·3	11·7	44·0	3·8
Pentane-2-one	13·0	12·4	37·0	5·2

important species reacting with OsO_4. The steps envisaged are:

$$\text{Ketone} + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{enolate} + H_2O$$

$$\text{enolate} + Os\,(VIII) \xrightarrow[\text{slow}]{k_2} \text{complex (C)}$$

$$(C) \xrightarrow[\text{fast}]{k_3} Os\,(VI) + \text{other products}$$

$$Os(VI) + IO_4^- \xrightarrow{\text{fast}} Os(VIII) + IO_3^-$$

Two possibilities may arise: (i) Electron transfer can occur from the enolate or (ii) OsO_4 can hydroxylate the enolate double bond. Schemes 1 and 2 depict the nature of enolate-OsO_4 interaction for the catalysed oxidation of acetone. Both the schemes lead to the same rate equation (2), if one applies the steady state condition to the enolate ion and the complex

$$-\frac{d[IO_4^-]}{dt} = \frac{Kk_2[\text{ketone}][OH^-][Os(VIII)]}{[H_2O] + k_2/k_{-1}[Os(VIII)]} \quad \dots(2)$$

where $K = k_1/k_{-1}$.

As $[Os(VIII)]$ used is in catalytic amount, $[H_2O] \gg (k_1/k_{-1})[Os(VIII)]$ and hence the second term in the denominator can be neglected. This leads to the rate law (3)

$$-\frac{d[IO_4^-]}{dt} = \frac{Kk_2}{[H_2O]} [\text{ketone}][OH^-][Os(VIII)]$$

$$= k_{o(obs)} [\text{ketone}][OH^-][Os(VIII)] \quad \dots(3)$$

Two possibilities are open for the OsO_4 to participate in the oxidation. (i) Osmate enolate ester complex: The enolate-Os(VIII) complex (C_1) decomposes to Os(VI) and products in the presence of OH^- rapidly. Evidence for the Os(VI) has been established[3]. (ii) Addition complex: Addition of OsO_4 to the double bond of the enolate with concomitant electron transfer so that osmium is in 6 + oxidation state in the addition complex (C_2). In both the cases the complex formation is rate-determining. Wiberg[15] in the acetone oxidation by alkaline MnO_4^- has considered both the possibilities.
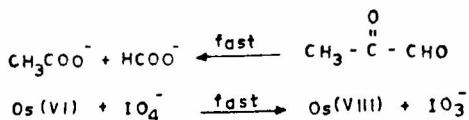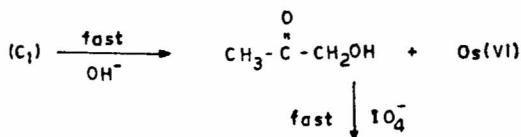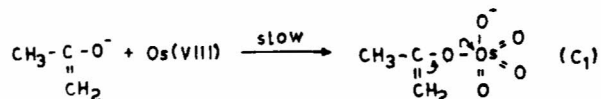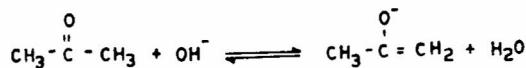
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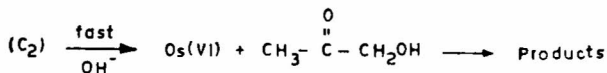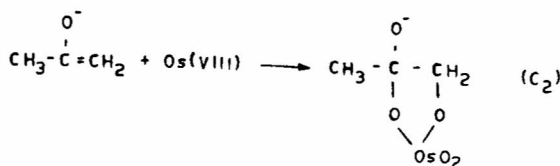
SCHEME - 2

If MnO_4^- is to hydroxylate the double bond of the enolate, the rate constant $k_2(M^{-1}$ min$^{-1})$ must be of comparable magnitude to the rate of addition of MnO_4^- to olefinic bonds. The rates for MnO_4^- addition to olefinic functions lie in the range 400–$600 M^{-1}$ min^{-1} whereas simple electron transfer from the enolate to MnO_4^- would be faster which in fact is seen in the values of MnO_4^- oxidations of the order of $10^7 M^{-1}$ min^{-1}.

Singh et al.[2] have postulated Scheme 1 for the OsO_4-catalysed $Fe(CN)_6^{3-}$ oxidation. $k_0/[\text{ketone}][OsO_4]$ values in the present study lie in the range 100–$500 M^{-1}$ min^{-1} and hence it is more tempting to accept the addition model as a more realistic approach to the nature of OsO_4 participations. It may be pertinent here to compare the relative rates of oxidation of the compounds with olefinic functions under identical conditions, viz. acetone

(7·67), EMK (37·0), maleate (6·0), fumarate (210·0) and cinnamate (400·0) $\times 10^{-4}$ min^{-1}.

Rate acceleration is pronounced in systems with available double bonds[16].

The large negative entropies of activation in the OsO-catalysed oxidations point to the cyclic nature of the transition state and an addition mechanism is more likely. The high negative entropy values for the catalysed process must be a consequence of the enolate-OsO$_4$ complex. The enol double bond opens up to give two single bonds which attach directly to the osmium atom of OsO$_4$ and the restriction of the osmium-oxygen vibrations will account for the entropy decrease. The addition of the single carbon bonds to two oxygens of the OsO$_4$ is unlikely in view of the specific acceleration provided by OsO$_4$ whereas other oxides fail to do so. The log A values are in agreement with the processes with negative entropies of activation.

Acknowledgement

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