STRUCTURAL EFFECTS IN THE OXIDATION OF KETONES BY ACID IODATE

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The kinetics of oxidation of aliphatic, alicyclic and aryl alkyl ketones by acid iodate has been studied in aqueous methanol medium. The reaction exhibits first order dependence each on [iodate] and [ketone]. The reaction is acid catalysed and a medium of low dielectric constant is favourable for the oxidation process. The oxidation rates are slower than the enolisation rates of the ketones. The mechanism proposed involves rate limiting attack of IO_2^+ on the enol form of the ketone leading to the formation of an intermediate carbonium ion which undergoes solvolysis, ultimately leading to the formation of a methoxy derivative. The order of reactivity of these structurally different ketones is discussed in terms of stability of the enol formed from the ketone and of the stability of the carbonium ion formed due to attack of the oxidant species in the slow step.

The mechanism of oxidation of ketones using various oxidants has been the subject of study of several authors[1-10]. Two different views on the form of ketone (keto or enol form) which reacts with the oxidant have been expressed in these studies. In the oxidation of aliphatic and cyclic ketones and acetophenones by potassium permanganate[9], Radhakrishna, Murthy et al. proposed an attack of Mn(VII) on the enol form of the ketone in the rate limiting step. In the oxidation of acetophenone by Mn(III) it was proposed[7], however, that the keto form is attacked by the oxidant species in the rate limiting step. The authors studied the kinetics and substituent effect in the oxidation of acetophenones by acid iodate in aqueous methanol[11] and proposed the attack of oxidant species on the enol form of the ketone. In continuation of our earlier work[11,12] kinetic investigations have been extended to different ketones, namely alkyl (acylic and cyclic) and aryl alkyl ketones to discuss the effect of their structure on the rate of their oxidation.

EXPERIMENTAL

Acetophenone, acetone, ethyl methyl ketone, isobutyl methyl ketone, methanol and potassium iodate were of BDH, AR grade. Cyclopentanone, cyclohexanone, cycloheptanone and 1-propyl methyl ketone were E. Merck samples. Cyclooctanone was Fluka AG sample. Propiophenone and butyrophenone were supplied by Koch-Light and Aldrich, respectively. The solid samples were recrystallized and liquid samples were distilled wherever necessary before use.

The reactions were carried under the conditions of [ketone] $\gg$ [iodate] in 50% (v/v) aqueous methanol in the presence of sulfuric acid and in temperature range 30—50°C. The progress of the reaction was followed by estimating the unreacted iodate iodometrically. The compounds studied were listed in the preceding paragraph.

RESULTS AND DISCUSSION

The stoichiometric study shows that one mole of iodate oxidizes three moles of ketone. The product is identified as the corresponding methoxy derivative.

The kinetic data of the experiments conducted at different iodate and ketone concentrations (Tables I and II) establish first order dependence of rate on both iodate and ketone. The rate is enhanced due to increase in the concentration of H_2SO_4 (Table III), suggesting an acid catalyzed process. Correlation of log k_{obs} (k_{obs} is the pseudo-first order rate constant) with Hammett's acidity function[13], H_0, gives a linear plot with nearly unit slope in each case. These observations point at a rate law:

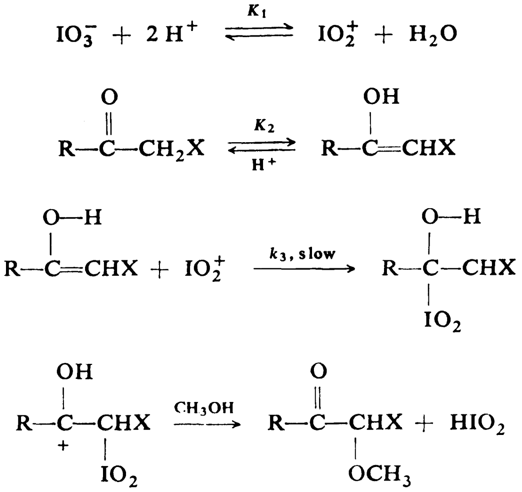
$$\frac{-d[IO_3^-]}{dt} = k_2[IO_3^-]\,[\text{ketone}]\,h_0\,,$$

where k_2 is the second order rate constant. A similar rate law has been observed in the oxidation of acetophenones[11] and 1- and 2-acetylnaphthalenes[12].

At constant $[H_2SO_4]$ and temperature, increase in methanol content of the medium is found to enhance the rate of oxidation (Table IV), indicating that a medium of low dielectric constant is favourable for the reaction. Therefore, the reaction can be either ion–ion type or ion–dipole type. However, the absence of salt effect on the rate of oxidation excludes the possibility of the reaction being ion–ion type. Further, the plots of log k_{obs} versus the reciprocal of dielectric constant of the medium are linear with positive slope, confirming cation–dipole type of reaction according to Amis[14].

Since the medium is highly acidic, one has to decide whether the enolisation of ketone is the rate determining step or not. If enolisation is the rate controlling step, the rate of oxidation would be independent of [iodate]. But the kinetic data (Table I) show that the rate is not independent of [iodate]. Furthermore, under identical conditions the authors found also that the iodination rates of these ketones are much faster than the oxidation rates, suggesting that the enolisation step is not the rate controlling one.

In view of the solvent effect on oxidation rate, cationic form of the oxidant is proposed as the active species which attacks the enol form in the rate limiting step. Keeping all these experimental facts in view, a plausible mechanism is proposed as shown in Scheme 1.



$$IO_3^- + 2\,H^+ \overset{K_1}{\rightleftharpoons} IO_2^+ + H_2O$$

$$R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}CH_2X \underset{H^+}{\overset{K_2}{\rightleftharpoons}} R{-}\overset{\overset{\displaystyle OH}{|}}{C}{=}CHX$$

$$R{-}\overset{\overset{\displaystyle O{-}H}{|}}{C}{=}CHX + IO_2^+ \xrightarrow{k_3,\,\text{slow}} R{-}\overset{\overset{\displaystyle O{-}H}{|}}{C}{-}\underset{\underset{\displaystyle IO_2}{|}}{C}HX$$

$$R{-}\overset{\overset{\displaystyle OH}{|}}{\underset{+}{C}}{-}\underset{\underset{\displaystyle IO_2}{|}}{C}HX \xrightarrow{CH_3OH} R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\underset{\underset{\displaystyle OCH_3}{|}}{C}HX + HIO_2$$

R = alkyl, aryl
X = H, CH_3, C_2H_5

SCHEME 1

The slow step involves the attack of oxidant species IO_2^+ on the methylene group of enol form, giving an intermediate carbonium ion which undergoes solvolysis and ultimately forms the methoxy derivative. This is similar to that proposed earlier[11,12]. However, with 1- and 2-acetyl naphthalenes[12], the product is identified as the corresponding ω-hydroxynaphthalene. This may be obtained by the attack of OH^- on the intermediate in the fast step while in the present case the attack is by OCH_3^- on the intermediate carbonium ion. Similar product is identified with acetophenones[11], too.

Thus, the reaction rate depends on two factors: (i) ease of enol formation from the ketone, which is being attacked in the slow step and (ii) the stability of the carbonium ion which is being formed in the slow step. The formation of enol is assisted by the electron releasing group adjacent to carbonyl group, while the ease of formation of carbonium ion, which is a result of C=C polarisation, is decreased.

Depending on the relative rates of these two steps, structural factors influence the overall rate of oxidation. In the case of four aliphatic ketones studied, the order of reactivity (Table V) is found to be: ethyl methyl ketone > 1-propyl methyl ketone > > acetone > isobutyl methyl ketone.

The ease of enol formation increases as we go from acetone to isobutyl methyl ketone since the size of the alkyl group adjacent to carbonyl group increases. This is also evident from an independent study (by the authors) of iodination of these ketones at 45°C in 50% (v/v) aqueous methanol in the presence of 0·5M-H_2SO_4.

The iodination rate constants are 9·98, 13·05, 11·24, and 16·24 . 10^{-2} mol l^{-1} s^{-1} with acetone, ethyl methyl ketone, 1-propyl methyl ketone and isobutyl methyl ketone, respectively. But as we go from acetone to isobutyl methyl ketone, as the size of the alkyl group adjacent to carbonyl group increases, the ease of C=C polarization decreases and hence the carbonium ion is not easily formed. With an excep-

TABLE I

Effect of [iodate] (mol l^{-1}) on k_{obs}(s^{-1}) of oxidation of ketones; [ketone] = 0·1 mol l^{-1}, [H_2SO_4] = 4·0 mol l^{-1}, 50% (v/v) aq. MeOH, 45°C

Ketone	k_{obs} . 10^4 at [iodate]			
	0·001	0·002	0·004	0·008
Acetone[a]	5·18	6·91	5·76	6·33
1-Propyl methyl ketone[a]	12·15	11·70	9·97	—
Cyclooctanone[a]	11·90	10·27	10·06	—
Propiophenone	5·24	5·22	5·31	5·29
Butyrophenone	2·28	2·30	2·37	2·29

[a] [ketone] = 0·05 mol l^{-1}, [H_2SO_4] = 2·0 mol l^{-1}, 35°C.

TABLE II

Effect on [ketone] (mol l^{-1}) on k_{obs}(s^{-1}) of the oxidation; [IO_3^-] = 0·002 mol l^{-1}, [H_2SO_4] = = 4·0 mol l^{-1}, 50% (v/v) aq. MeOH, 45°C

Ketone	k_{obs} . 10^4 at [ketone]				
	0·025	0·050	0·075	0·100	0·200
Acetone	1·98	3·33	—	6·91	14·58
Ethyl methyl ketone	—	6·78	8·73	13·27	—
1-Propyl methyl ketone	2·69	5·57	—	11·70	22·46
Isobutyl methyl ketone	0·86	—	—	3·26	—
Cyclooctanone[a]	5·10	10·27	—	23·21	—
Propiophenone	1·34	2·45	—	5·22	10·83
Butyrophenone	0·58	1·20	—	2·30	4·82

[a] [H_2SO_4] = 2·0 mol l, 35°C.

tion of isobutyl methyl ketone, the oxidation rates are in the same order as the iodination rates, indicating that the enol formation is the dominant factor when compared to the carbonium ion formation. The low oxidation rate of isobutyl

TABLE III

Effect of $[H_2SO_4]$ (mol l^{-1}) on $k_{obs}(s^{-1})$ of the oxidation; [ketone] = 0·1 mol l^{-1}, $[IO_3^-]$ = = 0·002 mol l^{-1}, 50% (v/v) aq. MeOH, 45°C

Ketone	$k_{obs} . 10^4$ at $[H_2SO_4]$				
	2·0	2·5	3·0	3·5	4·0
Acetone	0·51	0·92	2·35	3·58	7·00
Ethyl methyl ketone	3·22	4·61	10·17	16·69	23·27
Cyclopentanone[a]	—	—	6·43	9·84	14·08
Cyclohexanone[a]	2·69	3·07	5·18	7·48	9·88
Cyclooctanone[a]	10·27	18·61	32·30	—	—
Propiophenone[b]	0·49	0·73	1·05	2·44	5·22

[a] [ketone] = 0·05 mol l^{-1}, 35°C; [b] [ketone] = 0·05 mol l^{-1}.

TABLE IV

Effect of solvent composition on $k_{obs}(s^{-1})$ of the oxidation; [ketone] = 0·1 mol l^{-1}, $[IO_3^-]$ = = 0·002 mol l^{-1}, $[H_2SO_4]$ = 3·0 mol l^{-1}, 45°C

Ketone	$k_{obs} . 10^4$ at % (v/v) aq. MeOH			
	40	50	60	70
Acetone	1·80	2·35	3·53	6·14
Ethyl methyl ketone	6·91	10·17	12·28	18·04
1-Propyl methyl ketone	2·90	5·37	7·23	8·92
Cyclopentanone[a]	3·75	4·42	5·09	6·14
Cyclohexanone[a]	6·14	7·68	9·21	11·32
Cyclooctanone[a]	9·50	10·27	14·67	19·76
Propiophenone	1·78	2·16	2·68	3·26

[a] [ketone] = 0·05 mol l^{-1}, $[H_2SO_4]$ = 2·0 mol l^{-1}, 35°C.

methyl ketone (in spite of its high iodination rate) suggests the role of steric factor. In the molecular model constructed, the distance between the methyl group and hydroxyl group is less than the sum of Van der Waals radii, which results in repulsive interactions.

Correlation of log k_{obs} with the substituent constant σ^* shows a considerable scatter. This poor correlation may be attributed to the fact that the ease of enol formation increases while the stability of the carbonium ion decreases from acetone to isobutyl methyl ketone, the magnitude of the structural effects being different.

Among the four cyclic ketones studied, the order of reactivity is observed to be C-8 > C-6 > C-5 > C-7. Similar trend in the reactivity has been observed by Venkatasubramanian et al. in the chlorination of ketones by 1-chlorobenzotriazole[15], in which enolisation of the ketone is the rate limiting step. According to Gero[16] and Alinger et al.[17] alicyclic ketones with even number of carbon atoms have higher enolic content than their adjacent analogues with odd number of carbon atoms. Hence, in the oxidation of cyclic ketones the formation of enol from the ketone is playing a major role compared to the stability of the corresponding carbonium ion.

TABLE V

Value of k_{obs} at 30°C (s^{-1}) and activation parameters for iodate–ketone system; [ketone] = = 0·1 mol l^{-1}, [IO_3^-] = 0·002 mol l^{-1}, [H_2SO_4] 4·0 mol l^{-1}, 50% (v/v) aq. MeOH

Ketone	$k_{obs} \cdot 10^4$	E_a kJ mol^{-1}	$\Delta H^{\neq}$ kJ mol^{-1}	$-\Delta S^{\neq}$ J K^{-1} . mol^{-1}	$\Delta G^{\neq}$ kJ mol^{-1}
Acetone	1·45	62·24	59·72	122	96·54
Ethyl methyl ketone	6·95	34·48	31·96	200	92·62
1-Propyl methyl ketone	4·59	51·23	48·71	148	93·66
Isobutyl methyl ketone	1·25	52·67	50·15	154	96·93
Cyclopentanone	24·83	54·11	51·59	143	94·97
Cyclohexanone	56·20	55·54	53·02	127	92·09
Cycloheptanone	17·52	52·19	49·67	153	97·74
Cyclooctanone	74·61	52·19	49·67	140	92·07
Acetophenone[a]	2·19	81·49	78·97	54	96·52
Propiophenone	1·33	71·83	69·31	91	96·77
Butyrophenone	0·71	55·55	53·03	150	98·37

[a] From ref.[11].

In the case of three aryl alkyl ketones studied, the oxidation rates were found to be in the order acetophenone > propiophenone > butyrophenone (Table V). Increase in the size of the alkyl group attached to the carbonyl group of the aryl alkyl ketone decreases the rate of oxidation. In propiophenone, the methyl group enhances the electron density compared to acetophenone at the carbon atom adjacent to the carbonyl group due to inductive effect, which results in the decreased enolic content of the propiophenone compared to acetophenone. Similarly, also the +I effect of the methyl group in propiophenone opposes the π-electron movement and decreases the extent of C=C polarisation compared to acetophenone. Consequently, the attack of electrophile is less facile and there is a decrease in the observed rate. In butyrophenone the ease of enolisation and the attack by the oxidant are further decreased, since with C_2H_5 group the +I effect becomes more pronounced, resulting in a further decrease in the oxidation rate. In an independent study of iodination of these ketones in 50% (v/v) aqueous methanol at 45°C in the presence of 0·02M-H_2SO_4, we observed that the zero order enolisation rate constants are 4·53, 1·02 and 0·88 . 10^{-2} mol l^{-1} s^{-1} with acetophenone, propiophenone and butyrophenone, respectively. These values confirm that the ease of enolisation decreases when the carbon chain length adjacent to the carbonyl group increases. Similar trend has been observed by Venkatasubramanian et al.[15] with acetophenone and propiophenone in the chlorination using 1-chlorobenzotriazole. Therefore, it can be concluded that in these ketones both factors, i.e. enol formation and stability of the carbonium ion are responsible for the observed order of reactivity.

Thus, by comparing the kinetics of oxidation of acetophenones[11], acetyl naphthalenes[12] and other ketones, namely aliphatic, alicyclic and aryl alkyl ones, we can conclude that these ketones ofllow a similar rate law and include the attack by the oxidant on the enolic form of the ketone. However, while with aliphatic ketones the order of reactivity is mainly controlled by the enolic content of the ketone, with acetylnaphthalenes[12] the order of reactivity can be explained in terms of the stability of the carbonium ion. By contrast, in the case of acetophenone, propiophenone and butyrophenone both factors should be taken into consideration in explaining the observed reactivity order.

The reactions have been studied at different temperatures and the activation parameters computed are presented in Table V. The free energy of activation, $\Delta G^{\neq}$ (95 ± 3) kJ mol^{-1}, is nearly the same, indicating a similar mechanism for all the ketones studied. The Exner's plot of log k_{obs} (at 35°C) vs log k_{obs} (at 50°C) and the isokinetic plot of $\Delta H^{\neq}$ vs $\Delta S^{\neq}$ are linear with $r = 0{\cdot}98$ and 0·97, respectively, and support thus the above conclusions.

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