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KINETICS AND MECHANISM OF THE OXIDATION OF SOME ALIPHATIC KETONES BY N-BROMOACETAMIDE IN ACIDIC MEDIA

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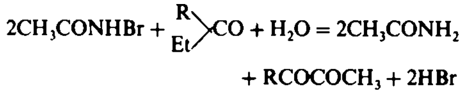
Abstract—Kinetics of the oxidation of methyl ethyl ketone (MEK) and diethyl ketone (DEK) by N-bromoacetamide (NBA) have been studied in perchloric acid media in the presence of mercuric acetate. A zero order dependence to NBA and a first-order dependence to both ketones and H^+ have been observed. Acetamide, mercuric acetate and sodium perchlorate additions have negligible effect while addition of acetic acid has a positive effect on the reaction rate. A solvent isotope effect ($K_0D_2O/k_0H_2O = 2.1$–2.4 and 2.2–2.5 for MEK and DEK, respectively) has been observed at 40°. Kinetic investigations have revealed that the order of reactivity is MEK > DEK. The rates were determined at four different temperatures and the activation parameters were evaluated. The main product of the oxidation is the corresponding 1,2-diketone. A suitable mechanism consistent with the above observations has been proposed.

Although NBA has found applications in preparative organic chemistry as an oxidising and halogenating reagent,[1] but very little attention has been paid on its mode of oxidation. Recently, kinetic investigations involving NBA oxidation of primary alcohols[2] and dimethyl sulphoxide[3] are reported. However, its analogues, N-bromosuccinimide (NBS) and N-chlorosuccinimide (NCS) have received substantial attention on the mechanism of their reaction with several substances in recent years.[4–10] The different mechanistic pathways[6] reported for these structurally related compounds prompted us to undertake this investigation. In the present communication kinetics of the oxidation of MEK and DEK by NBA has been studied in acidic media with a view to shed some light on the oxidation mechanism involving this oxidant.

Materials and methods. All the reagents used were of highest purity available. E. Merck (Germany) sample of methyl ethyl ketone, Fluka sample of diethyl ketone and Merck-Schuchardt sample of N-bromoacetamide were used. Acetamide and mercuric acetate were of E. Merck grade. Sodium perchlorate (E. Merck) was used for varying the ionic strength of the medium and perchloric acid (E. Merck) was used as a source of H ions. NBA solution was always prepared fresh and its strength was checked by iodometric method. Deuterium oxide (purity 99.0%) was supplied by BARC, Bombay (India). Triple distilled water was used throughout the course of investigations and reaction stills were blackened from outside to avoid any photochemical reactions.

All reactants except ketone were allowed to mix and the reaction was initiated by adding subsequently appropriate amount of ketone. Aliquots were withdrawn at suitable time intervals by means of a pipet and the amount of unreacted NBA was estimated by iodometric titrations. All the rate studies were carried out at constant temperature (±0.1°). The reactions were followed upto 70% reaction. Duplicate kinetic runs showed that the rate constants were reproducible within ±3%.

Stoichiometry and product analysis. Various sets of experiments with varying NBA ketone ratios were carried out and the excess of NBA left in each case was estimated. The results showed that one mole of ketone consumed two moles of NBA and accordingly the following stoichiometric equation could be formulated, where R represents Me and Et groups in MEK and DEK molecules, respectively.



$$2CH_3CONHBr + \overset{R}{\underset{Et}{}}\!\!>\!CO + H_2O = 2CH_3CONH_2 + RCOCOCH_3 + 2HBr \quad (1)$$

The end products corresponding diketones were identified by adopting TLC followed by conventional spot test analysis[11] and also through dinitrophenyl hydrazine (DNP) derivative.[12]

RESULTS AND DISCUSSION

Zero order dependence in NBA and first-order dependence both in ketone and H ion were established by effecting a manifold variation in the respective concentration at the fixed concentration of other components (Table 1). Zero order in NBA was further supported through the plots of remaining [NBA] and "t" for varying concentration of oxidant (NBA) where a set of parallel lines was obtained. A proportional increase in the zero-order rate constant in NBA was observed with the increase in initial concentrations of MEK (Fig. 1). The average values of the first order rate constants calculated as $k_1 = k_0/[\text{ketone}]$ were found as 3.78, 5.40; 3.19, 4.66 $\times 10^{-6}$ sec^{-1} at 35° and 40° for MEK and DEK, respectively. A strong dependence on H ion concentration was observed and the average values of first order rate constants in H ion calculated as $k_1' = k_0/[HClO_4]$ were found as 7.58, 11.21; 6.32, 9.72 $\times 10^{-6}$ sec^{-1} at 35° and 40° for MEK and DEK, respectively.

The overall second-order rate constants k_2 calculated as $k_2 = k_0/[HClO_4][\text{ketone}]$ were found to be 1.89, 2.70; 1.59, 2.33 $\times 10^{-4}$ mole^{-1} l sec^{-1} at 35° and 40° for MEK and DEK, respectively.

The reactivity order MEK > DEK is explained on the basis of the steric factors[13] operative in the

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* For correspondence.

Table 1. Effect of concentration of reactants and [H^+] on the rate [$Hg(OAc)_2$] = 2.00 × 10^{-3} M

10^3[NBBA]	10^2[ketone]	10^2[$HClO_4$]	$k_0 \times 10^7$ mol l^{-1} sec^{-1}			
M	M	M	MEK		DEK	
			35°	40°	35°	40°
0.5	4.0	2.0	1.55	1.98	1.27	1.88
0.8	4.0	2.0	1.54	2.10	1.28	1.83
1.0	4.0	2.0	1.55	2.20	1.27	1.93
1.6	4.0	2.0	1.56	2.16	1.28	1.90
2.0	4.0	2.0	1.54	2.30	1.27	1.93
2.5	4.0	2.0	1.55	2.33	1.28	1.98
1.0	1.0	2.0	0.38	0.53	0.32	0.43
1.0	2.0	2.0	0.76	1.15	0.66	0.97
1.0	5.0	2.0	1.88	2.53	1.58	2.30
1.0	8.0	2.0	3.06	3.93	2.54	3.78
1.0	10.0	2.0	3.82	5.20	3.16	4.55
1.0	4.0	1.0	0.76	1.16	0.63	0.97
1.0	4.0	3.0	2.20	3.40	1.86	3.00
1.0	4.0	4.0	3.10	4.63	2.54	3.90
1.0	4.0	5.0	3.70	5.48	3.16	5.17
1.0	4.0	8.0	6.08	8.72	5.14	7.15

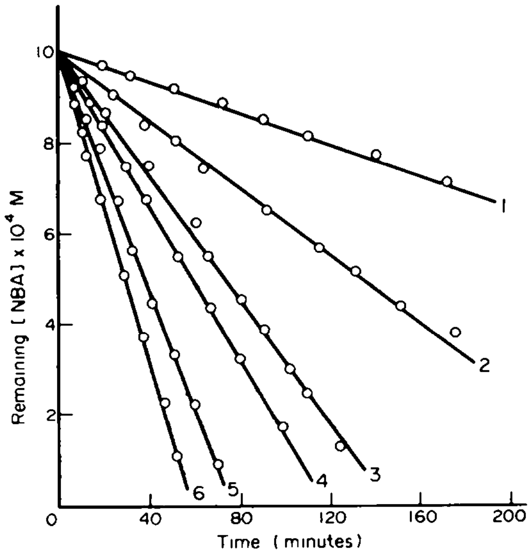


Fig. 1. Zero order rate plots at 40° [NBA] = 1.0 × 10^{-3} M, [$HClO_4$] = 2.00 × 10^{-2} M, [$Hg(OAc)_2$] = 2.00 × 10^{-3} M, [MEK] = 1.00, 2.00, 4.00, 5.00, 8.00 and 10.00 × 10^{-2} M, in 1, 2, 3, 4, 5 and 6 respectively.

neighbourhood of the ketonic group. The larger the alkyl group in a particular substrate the slower is the rate of its oxidation. Sodium perchlorate, mercuric acetate and acetamide variations had negligible effect on the rate of oxidation while acetic acid addition had a positive effect (Table 2), i.e. negative dielectric effect. Solvent isotope effect studied in different D_2O–H_2O mixtures at 40° showed an increase in the rate constant values (Table 3). The rate study measurements carried out at four different temperatures ((Table 2) led to compute the energy of activation ($\Delta E^{\neq}$), frequency factor (A) and entropy of activation ($\Delta S^{\neq}$) as 14.08, 15.92 kcal mol^{-1}, 1.91 × 10^6, 3.09 × 10^6 l mol^{-1} sec^{-1} and −31.89 e.u., −26.35 e.u. for MEK and DEK, respectively.

In acidic media[2] NBA is known to exist in equilibria (2, 3) or (4, 5) and these two alternatives of equilibria are not kinetically distinguishable.

$$MeCONHBr + H_2O \rightleftharpoons MeCONH_2 + HOBr \quad (2)$$

$$HOBR + H_3O^+ \rightleftharpoons H_2OBr^+ + H_2O \quad (3)$$

or

$$MeCONHBr + H_3O^+ \rightleftharpoons (MeCONH_2Br)^+ + H_2O \quad (4)$$

Table 2. Effect of temperature and [acetic acid] variations on the reaction rate. [NBA] = 1.00 × 10^{-3}M, [ketone] = 4.00 × 10^{-2}M, [$HClO_4$] = 2.00 × 10^{-2}M, [$Hg(OAc_2)$] = 2.00 × 10^{-3}M

Temperature °C	[Acetic Acid] v/v (%)	$k_0 \times 10^7$ mol l^{-1} sec^{-1}	
		MEK	DEK
35	0	1.55	1.27
40	0	2.20	1.93
45	0	3.20	2.90
50	0	4.72	4.57
40	10	2.83	2.60
40	20	3.32	3.00
40	40	4.07	3.97
40	70	5.80	5.55

Table 3. Solvent Isotope effect on the reaction rate at 40° [NBA] = 1.00×10^{-3}M, [ketone] = 4.00×10^{-2} M [$HClO_4$] = 2.00×10^{-2}M, [$Hg(OAc)_2$] = 2.00×10^{-3}M

$D_2O - H_2O$ %	$k_0 \times 10^7$ mol l^{-1} sec^{-1} MEK	DEK
0–100	2.26	1.93
30–70	4.75	4.25
50–50	5.02	4.49
70–30	5.44	4.83

$$(MeCOHN_2Br)^+ + H_2O \rightleftharpoons MeCOHN_2 + H_2OBr^+. \quad (5)$$

Thus NBA itself or H_2OBr^+ formed in equilibibria (3) or (5) are the possible oxidising species.

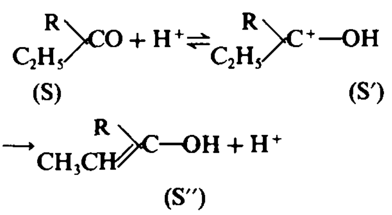
Mukherjee and Banerji[2] observed that the reaction rate increases slowly at lower acidity but above [H^+] = 0.2 M the linear increase in the rate of reaction with acidity is observed. They concluded that in the absence of added mineral acid HOBr (2) is likely to be oxidising species while protonated HOBr, i.e. cationic bromine species (3) is oxidising species in acidic media. Our observations do not allow HOBr at all to be oxidising species as in absence of added mineral acid the oxidation does not proceed. Now if H_2OBr^+ of either equilibria (3) or (5) is assumed to be real oxidising species of NBA the rate expression would require negative effect of acetamide contrary to our observed zero acetamide effect. Thus possibility of H_2OBr^+ as the real oxidising species is ruled out.

It may be pointed out that all kinetic studies have been made in presence of $Hg(OAc)_2$ in order to avoid any possible bromine oxidation which may be produced as:

$$MeCOHNBr + HBr \rightarrow MeCONH_2 + Br_2. \quad (6)$$

Mercuric acetate acts as scavenger[14] for any Br^- formed in the reaction and exists as [$HgBr_4^{2-}$] or unionised $HgBr_2$ and ensures that oxidation takes place purely through NBA.

Ketones are known to enolise in acidic media as follows:



(7)

where, S represents the ketone, S′ the conjugate acid and S″ its enolic form.

It has been established through kinetic investigations that the reaction follows zero order in NBA and taking into consideration Littler and Water's[15] contention that in such cases enolisation step will be slow and rate determining, following mechanistic scheme is formulated in which NBA itself acts as an oxidising species.

$$S + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} S' \text{ --- fast} \quad (8)$$

$$S' \xrightarrow{k_2} S'' + H^+ \quad (9)$$

slow and rate determining step

$$S'' + NBA \xrightarrow{k_3} X \quad \text{— fast} \quad (10)$$

(Intermediate species)

$$X + NBA \xrightarrow{k_4} \text{Products} \quad \text{--- fast.} \quad (11)$$

Application of steady state treatment to S′, S″ and X gives the rate law as:

$$-\frac{d}{dt}[NBA] = \frac{2k_1k_2}{k_{-1} + k_2}[S][H^+]. \quad (12)$$

The above mechanism is supported by the following experimental observations:

(1) The rate law derived above, is in accordance with the experimental observations.

(2) The experimental stoichiometry is in good agreement with the mechanism proposed.

(3) A negative dielectric effect is supported by the above machanism.

(4) The magnitude of the solvent isotope effect also supports the proposed mechanism. The higher rate value in D_2O indicates a pre-equilibrium fast proton transfer with specific acid catalysed reaction. A solvent isotope effect (kD_2O/kH_2O) of about 2.0 to 2.5 for any proton catalysed reaction has been reported in the literature[16] and a value of $kD_2O/kH_2O = 2.1$ has been found for the rate of acid catalysed enolisation of acetone.[17] In the present investigation a solvent isotope effect corresponding to $kD_2O/kH_2O = 2.1 - 2.4$ and $2.2 - 2.5$ for MEK and DEK, respectively, has been obtained in 30%–70% D_2O. Thus the observed solvent isotope effect is in the close agreement with the reported values and further establishes that the oxidation proceeds through the enol and not through the ketoform.

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