Tetrahedron Vol. 42, No. 10, pp. 2749 to 2755, 1986
Printed in Great Britain.

0040-4020/86 $3.00 + .00
Pergamon Journals Ltd.

KINETICS AND MECHANSIM OF OXIDATION OF SOME KETONES BY N-BROMOACETAMIDE

BHARAT SINGH* and ROHIT SHRIVASTAV

Chemistry Department, University of Allahabad, Allahabad-2 (U.P.), India

(*Received in UK* 25 *October* 1985)

Abstract: The kinetics of oxidation of n-butyl methyl ketone (n-BMK) and i-butyl methyl ketone (i-BMK) by N-bromoacetamide (NBA) is studied in perchloric acid media in the presence of mercuric acetate. The main product of the oxidation is the corresponding 1,2-dicarbonyl compound. The reaction order with respect to NBA is zero while with respect to ketone and H^+ it is unity. Mercuric acetate, acetamide and sodium perchlorate have negligible effect on the reaction rate, while the dielectric effect is negative. A solvent isotope effect ($k_o(D_2O)/k_o(H_2O)$ = 1.80-2.05 and 1.70-2.06 for n-BMK and i-BMK, respectively) at 35°C is observed. On the basis of the available evidence a suitable mechanism consistent with the experimental results is proposed in which it is suggested that the mechanistic route for NBA oxidation is through the enol form of the ketone in an acidic medium.

INTRODUCTION

Although NBA has been used as an oxidising and halogenating reagent[1] in preparative organic chemistry, relatively little work appears to have been carried out on the oxidative kinetics involving NBA, and the literature about its mode of oxidation is scanty. However, its analogues, N-bromosuccinimide (NBS) and N-chlorosuccinimide (NCS), have received substantial attention.[2-5] Some workers have recently reported the kinetic study of NBA oxidation of alcohols,[6] dimethyl suphoxide[7] and a few ketones[8,9] in acidic media. The different mechanistic routes reported for these structurally related compounds prompted us to undertake this investigation. The present communication incorporates the results of the kinetic oxidation of n-BMK and i-BMK by NBA in acidic media. Mechanistic conclusions are discussed.

MATERIALS AND METHODS

NBA was prepared by the reported method,[10], and its purity was checked by iodometric titration of active bromine. The solutions of n-BMK (Fluka) and i-BMK (L.R.BDH) were prepared by dissolving weighed amounts of the samples in doubly distilled water. Perchloric acid (E. Merck) was used as a source of hydrogen ions. Acetic acid was first refluxed with chromic oxide and acetic anhydride for 3 hours and then fractionated;[11] the fraction coming over between 116-118°C was collected. E. Merck (Germany) samples of mercuric acetate and sodium perchlorate were used. Deuterium oxide (purity 99.4%) was supplied by BARC, Bombay (India). The reaction stills were blackened on the outside.

Kinetic Measurements The reaction was studied by adding the appropriate volume of the ketone to a mixture containing suitable quantities of NBA and perchloric acid maintained at a constant temperature. The kinetics were followed by estimating the remaining amount of NBA iodometrically at regular time intervals. The reactions were followed up to 75% reaction. Duplicate kinetic runs showed that the rate constants are reproducible within ± 2.8%.

RESULTS

Stoichiometry was ascertained by treating both ketones (1.00 gm, 0.01 mol) with NBA (6.95 gm, 0.05 mol) in the presence of perchloric acid (0.025-0.10 M). The residual NBA was determined iodometrically. Similar experiments with varying NBA-ketone ratios were performed. The amount of NBA consumed in each case and the corresponding 1,2-dicarbonyl compound formed (Table I) indicated the overall reaction of equation (1).

$$2\ CH_3CONHBr + CH_3COR + H_2O = 2CH_3CONH_2 + CH_3COCOR' + 2H^+ + 2Br^- \qquad (1)$$

Where R represents n-C_4H_9 and i-C_4H_9 groups in the substrate molecule whilst R' represents n-C_3H_7 and i-C_3H_7 groups in the respective diketone products. The end products 1,2-diketones were identified by adopting tlc followed by conventional spot test analysis[12] and also through the dinitrophenylhydrazine (DNP) derivative.[13]

When the concentration of ketone is in excess, the plot of [NBA] against time shows that the reaction consists of two successive reactions. The initial slow reaction is followed by a faster reaction. Such an observation has been recorded in NBS oxidation also[2-4] and the faster reaction was attributed to bromine oxidation. We also observed a yellow colour (perhaps of liberated bromine) in the reaction mixture after about 20% reaction. The liberation of the yellow colour and the second faster reaction were supressed by the addition of 0.005 M mercury(II) acetate. All reactions were, therefore, investigated in the presence of 0.005 M mercury(II) acetate. Under these conditions, the zero-order plots were linear for over 75% of the reaction and the rate of the reaction in the presence of mercury(II) was nearly the same as the rate of the slow initial reaction without mercury(II).[2-4]

The zero order dependence in NBA and first order dependence both in the ketone and H^+ were established by effecting a manifold variation in the respective concentration at constant concentration of other components (Table II). Zero order in NBA was further supported through the plots of remaining [NBA] and time for varying [NBA] where a set of parallel lines were obtained (Fig. 1: for n-BMK). A proportional increase in the zero order rate constant in NBA was observed with the increase in initial concentrations of ketone (Fig. 2B: for i-BMK). The average values of the first order rate constants k_1' (k_1' = k_0/[ketone]) were found as 1.74, 2.65; 0.69, 1.02 x 1^{-3} min^{-1} at 35° and 40° for n-BMK and i-BMK oxidations, respectively.

A strong dependence on hydrogen ion concentration was observed. Zero order rate constants in NBA increased linearly (Fig. 2A : for n-BMK) with increasing hydrogen ion concentration, and $k_0/[HClO_4]$ had a fairly constant value in the oxidation of both ketones. The average values of the first order rate constants k_1'= $k_0/[HClO_4]$) were 2.22, 3.35; 3.70, 5.36 x 10^{-4} min^{-1} at 35° and 40° for n-BMK and i-BMK oxidations, respectively.

The addition of acetamide, mercuric acetate and sodium perchlorate had an insignificant effect on the reaction rate. Successive addition of acetic acid to the reaction mixture increased the rate of the reaction (Table III), indicating an ion-dipole interaction in the rate determining step. Solvent isotope effect studied in different D_2O-H_2O mixture at 35° showed an increase of the rate constant values (Table III).

DISCUSSION

Ketones are readily protonated in the presence of strong acids to form oxonium salts. Oxygen being more electronegative than the carbon, facilitates larger contribution from the second resonating structure than the first.

$$\rangle C=O + H^+ \rightleftharpoons \Big[\underset{I}{C=O^+-H} \leftrightarrow \underset{II}{C^+-O-H}\Big] \qquad (2)$$

NBA is reported to exist[6,8,9] in equilibria (3,4) or (5,6) which are indistinguishable on the present kinetic data.

$$MeCONHBr + H_2O \rightleftharpoons MeCONH_2 + HOBr \qquad (3)$$

$$HOBr + H_3O^+ \rightleftharpoons H_2OBr^+ + H_2O \qquad (4)$$

or

$$MeCONHBr + H_3O^+ \rightleftharpoons MeCON^+H_2Br + H_2O \qquad (5)$$

$$MeCON^+H_2Br + H_2O \rightleftharpoons MeCONH_2 + H_2OBr^+ \qquad (6)$$

Mukherjee et al[6] have reported that below $[H^+] = 0.2$ M the rate of oxidation of alcohols increases slowly but beyond this concentration of hydrogen ion a proportional increase in the oxidation rate with acidity is observed. They concluded that in the absence of mineral acid HOBr (3) is likely to be the oxidising species while in acidic media cationic bromine, i.e. H_2OBr^+ (4,6) is oxidising species. Contrary to their observations, the present redox reactions do not proceed in absence of mineral acid. Hence HOBr as oxidising species in our case is ruled out. Thus NBA itself, H_2OBr^+ and protonated NBA, i.e. $MeCON^+H_2Br$, seem to be possible oxidising species of NBA in acidic media.

The addition of mercuric acetate completely masks the possibility of any possible bromine oxidation which would have formed as a result of an interaction between NBA and HBr as follows:

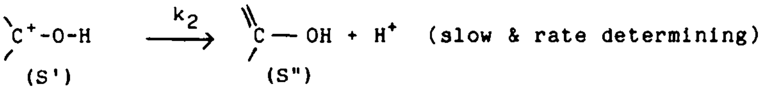
$$MeCONHBr + HBr \rightarrow MeCONH_2 + Br_2 \qquad (7)$$

Scavenging of Br_2 formed (7) by mercuric acetate as unionised $HgBr_2$ ensures pure NBA oxidation through the present investigation.

The possibility of one electron oxidation (which produces free radicals) is highly unlikely as the oxidation of ketones by NBA in an atmosphere of nitrogen failed to induce polymerisation of acrylonitirile[14].

Two-electron oxidants are reported[15] to attack the enol rather than the keto form of the substrate. Assuming therefore the enolisation step to be slowest and rate determining, the following mechanistic routes for the oxidation of ketones by NBA are proposed, in which S represents the ketone, S' its conjugate acid, S" the enol form, and A denotes acetamide.

$$\underset{(S)}{\rangle C=O} + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{(S')}{\rangle C^+-O-H} \qquad \text{(fast)} \qquad (8)$$



$$\underset{(S')}{>C^{+}\text{-}O\text{-}H} \xrightarrow{k_2} \underset{(S'')}{>C{-}OH} + H^{+} \quad \text{(slow \& rate determining)} \qquad (9)$$

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

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

Application of steady state treatment with the approximation $k_{-1} >> k_2$ yields the rate law as:

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

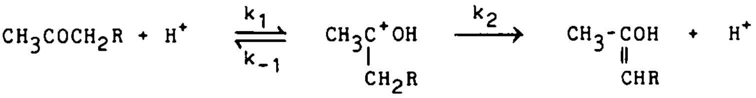
The rate law (12) was derived assuming NBA itself as the oxidising species. The same rate law can also be obtained on assuming either protonated NBA, i.e. $MeCON^+H_2Br$ or cationic bromine i.e. H_2OBr^+ (obtained from equations 10a and 10b) as oxidising species (10 and 11).

$$MeCONHBr + H_3O^+ \underset{k'_{-2}}{\overset{k'_2}{\rightleftharpoons}} MeCON^+H_2Br + H_2O \quad \text{(fast)} \qquad (10a)$$

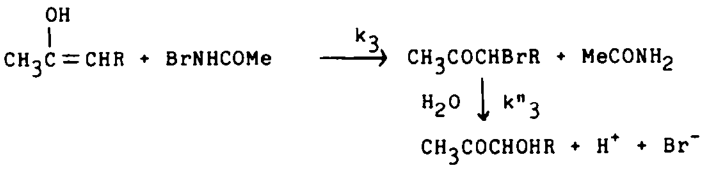
$$MeCON^+H_2Br + H_2O \underset{k'_{-3}}{\overset{k'_3}{\rightleftharpoons}} MeCONH_2 + H_2OBr^+ \quad \text{(fast)} \qquad (10b)$$

Thus it is clear from the above statement that any of the NBA species discussed above would fit the proposed mechanism. Hence the proposed mechanism is a most valid one. The negligible effect of ionic strength and a negative dielectric effect support the contention that the rate of the reaction as indicated in step (9) is controlled by the enolic form of the ketone.

The higher rate value in deuterium oxide (D_2O) indicates a pre-equilibrium fast proton transfer with specific acid-catalysed reaction. In the present investigation a solvent isotope effect corresponding to $k_0(D_2O)/k_0(H_2O) =$ 1.80-2.05 and 1.70-2.06 for n-BMK and i-BMK oxidations respectively, at 35°C in 40-80% D_2O, supports the proposed mechanism. Thus the observed solvent isotope effect is in close agreement with the reported values[16,17] which establishes that the oxidation proceeds through the enol form of the ketones and NBA itself is involved in this particular redox system. On the basis of the above argument it is established that the oxidation of ketones involves the enolisation as the slow and rate-controlling step, followed by a rapid attack of an NBA molecule on the enol of the ketone to give an intermediate which interacts immediately with another molecule of NBA yielding the products of the reaction in a fast step. The actual reaction steps involved in the reaction are shown below, where R represents $n\text{-}C_3H_7$ and $i\text{-}C_3H_7$ groups in the substrates.



$$CH_3COCH_2R + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{CH_2R}{CH_3C^+OH} \xrightarrow{k_2} \underset{CHR}{CH_3\text{-}COH} + H^+$$



$$CH_3C(OH){=}CHR + BrNHCOMe \xrightarrow{k_3} CH_3COCHBrR + MeCONH_2 \xrightarrow[H_2O]{k''_3} CH_3COCHOHR + H^+ + Br^-$$

$$CH_3COCHOHR + BrNHCOMe \xrightarrow{k_4} CH_3COC^+OHR + HBr + MeCONH^-$$

$$MeCONH^- + HBr \xrightarrow{k_5} MeCONH_2 + Br^-$$

$$CH_3COC^+OHR \xrightarrow{k_6} CH_3COCOR + H^+$$

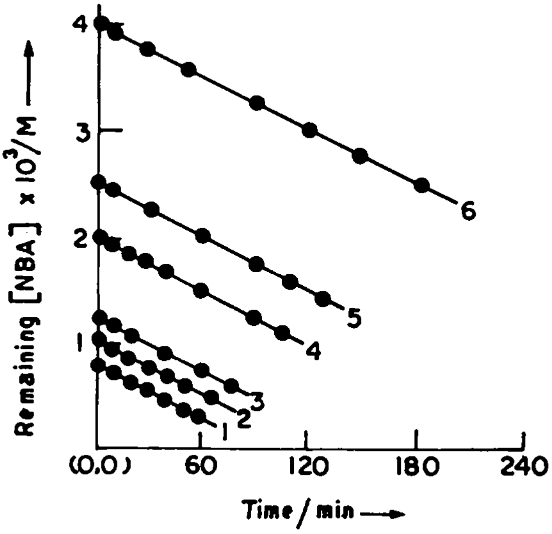


Figure 1 Zero order rate plots at 35°

[n-BMK] = 1.00 x 10^{-2} M, [$HClO_4$] = 20.00 x 10^{-2} M, [$Hg(OAc)_2$] = 5.00 x 10^{-3} M, [NBA] = 0.78 (1), 1.00 (2), 1.26 (3), 2.00 (4), 2.51 (5) and 4.00 x 10^{-3} M (6), respectively.

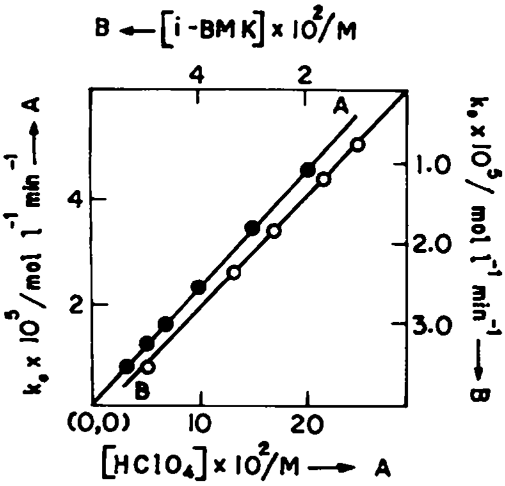


Figure 2 A: Plot of k_o vs [$HClO_4$] at 35° for n-BMK.

[NBA] = 1.00 x 10^{-3} M, [n-BMK] = 2.50 x 10^{-2} M and [$Hg(OAc)_2$] = 5.00 x 10^{-3} M.

B: Plot of k_o vs [i-BMK] at 35°

[NBA] = 0.74 x 10^{-3}, [$HClO_4$] = 8.00 x 10^{-2} M and [$Hg(OAc)_2$] = 5.00 x 10^{-3} M.

TABLE I Stoichiometry of the Oxidation of n-BMK and i-BMK by N-bromoacetamide

[H^+] 10^2/M	Moles of NBA consumed per mole of Ketone		% Yield of DNP of 1,2-dicarbonyl compound[a]	
2.5	2.02*	2.15**	85*	90**
5.0	1.95*	2.06**	88*	87**
10.0	2.08*	1.98*	84*	86**

[a] Based on NBA consumption * n-BMK and ** 2'-BMK

TABLE II Effect of [reactant]s on reaction rate at 35°C and [Hg(OAc)$_2$] = 5.00 x 10^{-3} M

[NBA] x 10^3/M	0.78	1.00	1.26	2.00	2.51	4.00
k_0^a x 10^5/mol l^{-1} min^{-1}	1.69	1.76	1.70	1.74	1.68	1.61
a — — — —	[n-BMK] = 1.00 x 10^{-2}M,		[HClO$_4$] = 20.00 x 10^{-2}M			
[NBA] x 10^3/M	0.79	1.19	1.39	1.98	2.97	4.00
k_0^b x 10^5/mol l^{-1} min^{-1}	1.57	1.58	1.56	1.60	1.60	1.51
b — — — —	[i-BMK] = 1.00 x 10^{-2}M,		[HClO$_4$] = 20.00 x 10^{-2}M			
[n-BMK] x 10^2/M	1.00	1.30	1.70	2.50	3.30	5.00
k_0^c x 10^5/mol l^{-1} min^{-1}	1.76	2.22	3.02	4.41	5.49	8.88
k_1' x 10^3/min^{-1}	1.76	1.71	1.78	1.76	1.67	1.78
c — — — —	[NBA] = 1.00 x 10^{-3}M,		[HClO$_4$] = 20.00 x 10^{-2}M			
[i-MBK] x 10^2/M	1.00	1.26	1.66	2.60	3.40	5.00
k_0^d x 10^5/mol l^{-1} min^{-1}	0.71	0.90	1.12	1.80	2.30	3.40
k_1' x 10^4/min^{-1}	7.10	7.12	6.70	6.91	6.79	6.90
d — — — —	[NBA] = 0.74 x 10^{-3}M,		[HClO$_4$] = 8.00 x 10^{-2}M			
[HClO$_4$] x 10^2/M	3.20	5.00	6.70	10.00	15.20	20.00
k_0^e x 10^5/mol l^{-1} min^{-1}	0.72	1.13	1.47	2.21	3.30	4.41
k_1'x 10^4/min^{-1}	2.25	2.26	2.19	2.21	2.17	2.21
e — — — —	[NBA] = 1.00 X 10^{-3}M,		[n-BMK] = 2.5 X 10^{-2}M			
[HClO$_4$] x 0^2/M	2.0	2.50	3.30	6.70	10.00	
k_0^f x 10^5/mol l^{-1} min^{-1}	0.70	0.95	1.19	2.47	3.70	
k_1' x 10^4/min^{-1}	3.70	3.80	3.61	3.68	3.70	
f — — — —	[NBA] = 1.14 x 10^{-3}M,		[i-BMK] = 3.40 x 10^{-2}M			

TABLE III Effect of acetamide D$_2$O, acetic acid, mercuric acetate and sodium perchlorate on reaction rate at 35°C and [Hg(OAc)$_2$] = 5.00 x 10^{-3}M (unless otherwise stated).

10^3 x [Acetamide] M	D$_2$O-H$_2$O V/V (%)	CH$_3$COOH-H$_2$O V/V (%)	k_0 x 10^5/mol l^{-1} min^{-1}	
			n-BMK*	i-BMK**
0	0-100	0-100	1.47	0.70
0	40- 60	0-100	2.68	1.25
0	60- 40	0-100	2.88	1.34
0	80- 20	0-100	3.01	1.44
0	0-100	40- 60	2.47	1.15
0	0-100	50- 50	2.70	1.28
0	0-100	60- 40	2.98	1.43
0	0-100	0-100	1.49a	0.68a
0	0-100	0-100	1.50b	0.75b
0	0-100	0-100	1.44c	0.72c
0	0-100	0-100	1.47d	0.74d
0	0-100	0-100	1.45e	0.70e
0	0-100	0-100	1.44f	0.72f
0.62	0-100	0-100	1.46	0.69
1.48	0-100	0-100	1.49	0.71
2.52	0-100	0-100	1.51	0.74

*[NBA] = 1.00 x 10^{-3}M, [HClO$_4$] = 6.70 x 10^{-2}M and [n-BMK] = 2.50 x 10^{-2}M.

**[NBA] = 1.14 x 10^{-3}M, [HClO$_4$] = 2.00 x 10^{-2}M and [i-BMK] = 3.40 x 10^{-2}M.

[Hg (OAc)$_2$] = 1.60(a), 2.78(b) and 4.12 x 10^{-3}M (c), respectively.

[NaClO$_4$] = 4.00 (d), 6.00 (e) and 8.00 x 10^{-2}M (f), respectively.

REFERENCES

1. R. Filler, Chem. Rev., 63, 21 (1963).
2. N. Venkatasubramanian and V. Thiagarajan, Tetrahedron Lett., 3349 (1967); Can. J. Chem., 47, 694 (1969); Indian J. Chem., 8, 809 (1970).
3. Kameshwar Singh, J.N. Tiwari and S.P. Mushran, Int. J. Chem. Kin., 10, 995 (1978).
4. Bharat Singh, Lalji Pandey, J. Sharma and S.M. Pandey, Tetrahedron, 38, 169 (1982).
5. N.S. Srinivasan and N. Venkatasubramanian, Tetrahedron, 30, 419 (1974).
6. Jogeshwar Mukherjee and Kalyan K. Banerji, J. Org. Chem., 46, 2323 (1981); B. Shah, A.L. Jain and K.K. Banerji, Indian J. Chem., 22, 720 (1983).
7. P.S. Radhakrishnamurti and N.C. Sahu, Indian J. Chem., 20A, 269 (1981).
8. Bharat Singh, B.B.L. Saxena and A.K. Samant, Tetrahedron, 40, 3321 (1984).
9. Bharat Singh and Rohit Shrivastav, Curr. Sci., 54(9), 415 (1985); Oxidn. Comm., accepted, in press (1986).
10. E.P. Olevito and C. Gerold, "Organic Syntheses", Collect. Vol. IV, H. Gilman, Ed., John Wiley, New York, p.104 (1963).
11. K.J. Orton and A. Bradfield, J. Chem. Soc., 960 (1924); ibid., 983 (1927).
12. F. Feigl, "Spot Tests in Organic Analysis", Elsevier, New York, p.325 (1966).
13. I. Vogel, "Elementary Practical Organic Chemistry", Part III, Longmans Green, London, p.73 (1953).
14. A.Y. Drummond and W.A. Waters, J. Chem. Soc., 2836 (1953); J.S. Littler and W.A. Waters, ibid., 1299 (1959).
15. J.S. Littler and W.A. Waters, J. Chem. Soc., 827 (1962).
16. C.K. Rule and V.K. Lamer, J. Am. Chem. Soc., 60, 726 (1938).
17. O. Reitz, Z. Phys. Chem., A179, 119 (1937).