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Mechanism of the Oxidation of Some Substituted Acetophenones by *N*-Bromosuccinimide in Acidic Media

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The kinetics of the reaction of three substituted acetophenones with *N*-Bromosuccinimide was studied in perchloric acid media in presence of mercuric acetate. The reactions were found to be zero order with respect to *NBS* while the order with respect to ketones and [H^+] was found to be unity. The addition of succinimide mercuric acetate and sodium perchlorate has no effect on the rate of oxidation and the rate increases with the decrease in dielectric constant of the medium. Kinetic investigations have revealed that the order of reactivity is *m*-nitroacetophenone > *p*-chloroacetophenone > *p*-methylacetophenone. The *Arrhenius* equation has been found to be valid in the temperature range 35-55°. Thermodynamic parameters have been calculated. Mechanistic pathways of the reactions are discussed and a rate equation is derived. *Hammett*'s plot gives a ρ value of $+ 0.60$ for methyl-aryl-ketones.

Keywords: Hammet parameter; Kinetics; Mechanism; Thermodynamic parameters)

Mechanismus der Oxidation einiger substituierter Acetophenone mit N-Bromsuccinimid in saurem Medium

Die Kinetik der Reaktion von drei substituierten Acetophenonen mit Bromsuccinimid in Perchlorsäure in Gegenwart von Quecksilberacetat wurde untersucht. Die Reaktion war von nullter Ordnung gegenüber *NBS*, erster Ordnung gegenüber den Ketonen und [H^+]. Mögliche Mechanismen der Reaktion werden diskutiert und auch eine Geschwindigkeitsgleichung wird abgeleitet. Es wurden die thermodynamischen Parameter der Reaktion bestimmt und auch ein *Hammet*'scher ρ-Wert ($+ 0{,}6$) für die Oxidation der Methylarylketone ermittelt.

Introduction

Oxidative investigations involving acetophenone, substituted acetophenones and various oxidising agents have been a subject of several recent kinetic studies[1–5]. *N*-Bromosuccinimide is a potent

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oxidising agent and has been used in the determination of several organic compounds[6, 7].

Some investigations involving *NBS* oxidation of esters[8] and alcohols[9, 10] are reported in the literature. In continuation of our earlier work on the kinetics of oxidation of aliphatic[11] and cyclic ketones[12] and -amino acids[13, 14] using *NBS* as an oxidant, we report in this paper the oxidation of *p*-methylacetophenone (**1**), *p*-chloroacetophenone (**2**) and *m*-nitroacetophenone (**3**) with *NBS* in acidic media.

Experimental

Koch-Light (England) samples of **1** and **2**, Fluka A. G. sample of **3** and G. R. S. Merck sample of *NBS* were used. Succinimide and mercuric acetate used were of H & W (England) and E. Merck grade respectively. Sodium perchlorate freshly and its strength was checked by iodometric method. Ketones **1** and **2** were prepared in 50% A. R., B. D. H. methanol and ketone **3** was prepared in 50% A. R., B. D. H. methanol and 5% acetic acid. Triple distilled water was used throughout the course of investigations and reaction stills were blackened from outside.

All reactants except ketone were allowed to mix and the reaction was initiated by adding appropriate amount of ketone. The progress of the reaction was followed by estimating unconsumed *NBS* iodometrically using starch as indicator. Rate studies were carried out at constant temperature (± 0.1°).

Results

Several sets of experiments with varying ratios of *NBS* over ketone were carried out. The excess of *NBS* left in each set was estimated. These studies showed that one mole of ketone consumes two moles of

Table 1. *Effect of reactants concentration on the reaction rate.* $[HClO_4] = 0.16\,M$, $[Hg(OAc)_2] = 2.0 \times 10^{-3}\,M$

$10^3[NBS]$ M	10^2 [Ketone] M	$k_0 \cdot 10^7$ mol l^{-1} s^{-1} **1** 40°	45°	**2** 40°	45°	**3** 40°	45°
0.8	1.0	3.83	5.87	6.83	9.50	12.50	17.33
1.0	1.0	4.00	6.23	7.00	9.73	12.83	17.84
1.2	1.0	4.10	6.00	7.17	9.83	13.00	18.00
1.4	1.0	4.33	6.33	7.00	10.00	13.00	18.00
1.6	1.0	4.50	6.50	7.33	9.67	13.16	18.17
1.0	0.6	2.50	3.50	4.33	5.67	7.82	10.83
1.0	1.4	5.67	8.37	10.00	13.67	18.00	24.66
1.0	1.8	7.66	11.53	12.33	17.00	22.67	32.00
1.0	2.2	9.33	14.00	15.17	21.66	27.66	39.00

NBS according to the stoichiometric equation (1); *R* represents p-CH_3—C_6H_4-, p-Cl—C_6H_4- and m-NO_2—C_6H_4- for **1**, **2** and **3** respectively. The obtained phenyl glyoxals were tested by a conventional method[15].

$$(CH_2CO)_2NBr + RCOCH_3 + H_2O = 2\,(CH_2CO)_2NH + RCOCHO + 2\,HBr \quad (1)$$

The oxidation of ketones by *NBS* was studied over a wide range of concentrations of the reactants at constant hydrogen ion concentration (Table 1). The rate of the reaction was found to be independent of initial *NBS* concentration. A proportional increase in the zero order rate constant in *NBS* was observed with the increase in initial concentrations of ketone (Fig. 1 for p-methylacetophenone). The average values of the first order rate constants calculated as $k_1' = k_0/[\text{ketone}]$ were found as 4.15, 6.16; 7.02, 9.65; 12.78, 17.80 × $10^{-5}\,s^{-1}$ at 40°, 45° for **1**, **2** and **3** respectively.

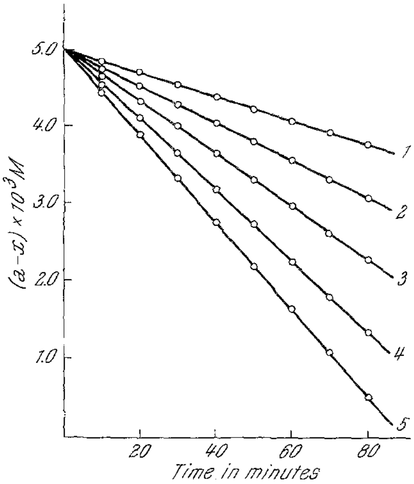


Fig. 1. Zero order rate plots at 40°. $[NBS] = 1.0 \times 10^{-3} M$, $[HClO_4] = 0.16 M$, $[Hg(OAc)_2] = 2.0 \times 10^{-3} M$, $[p\text{-}Me\text{-}PhCOMe] = 0.6$, 1.0, 1.4, 1.8 and $2.2 \times 10^{-2} M$ in 1, 2, 3, 4 and 5 respectively

A strong dependence of the rate to the hydrogen ion concentration was observed (Fig. 2 for p-methylacetophenone). An increase in hydrogen ion concentration increased the zero order rate constant in *NBS* almost linearly (Table 2) and the average values of first order rate constants calculated as $k_1' = k_0/[HClO_4]$ were found as 2.59, 3.85; 4.40, 6.03; 8.0, 10.93 × $10^{-6}\,s^{-1}$ at 40°, 45° for **1**, **2** and **3** respectively.

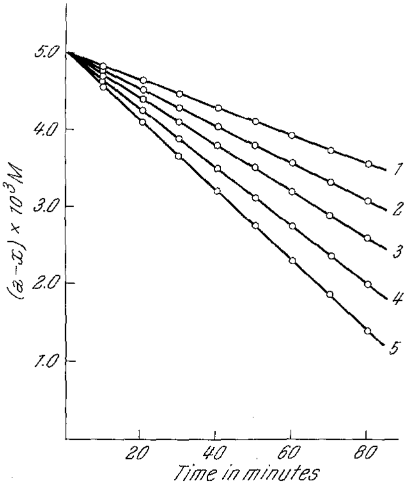


Fig. 2. Zero order rate plots at 40°. $[NBS] = 1.0 \times 10^{-3} M$; $[p\text{-}MePhCOMe] = 1.0 \times 10^{-2} M$; $[Hg(OAc)_2] = 2.0 \times 10^{-3} M$; $[HClO_4] = 1.2, 1.6, 2.0, 2.4$ and $2.8 \times 10^{-1} M$ in 1, 2, 3, 4 and 5 respectively

Table 2. *Effect of hydrogen ion concentration on the reaction rate*
$[NBS] = 1.0 \times 10^{-3} M$, $[\text{Ketone}] = 1.0 \times 10^{-2} M$, $[Hg(OAc)_2] = 2.0 \times 10^{-3}$

$[HClO_4]$ M	$k_0 \cdot 10^7$ mol l^{-1} s^{-1}					
	1		**2**		**3**	
	40°	45°	40°	45°	40°	45°
0.12	3.03	4.67	5.50	7.33	9.83	13.33
0.16	4.00	6.23	7.00	9.73	12.83	17.84
0.20	5.00	7.50	8.83	12.17	16.83	22.32
0.24	6.33	9.50	10.33	14.67	18.82	24.50
0.28	7.50	11.00	12.00	16.66	21.70	30.83

Table 3. *Second order rate constants for oxidation of ketones with NBS at 40°*
$[NBS] = 1.0 \times 10^{-3} M$, $[\text{Ketone}] = 1.0 \times 10^{-2} M$, $[HClO_4] = 0.16 M$,
$[Hg(OAc)_2] = 2.0 \times 10^{-3} M$

Substrate	$k_2 \cdot 10^4$ mol^{-1} l s^{-1}
p-methylacetophenone	2.50
p-chloroacetophenone	4.38
m-nitroacetophenone	8.02

The overall second order rate constants k_2 calculated as $k_2 = k_o/[HClO_4]$ [ketone] are compiled in Table 3.

The reactivity order *m*-nitroacetophenone > *p*-chloroacetophenone > *p*-methylacetophenone indicates that electron withdrawing groups in benzene ring facilitate the oxidation and electron releasing groups retard the process. The electron withdrawing groups increase the relative stability of the enol form and hence the higher reactivity.

Sodium perchlorate, mercuric acetate and succinimide variations had negligible effect on the rate of the reaction while methanol addition had a positive effect (Table 4).

Table 4. *Effect of methanol on the reaction rate at 40°*
$[NBS] = 1.0 \times 10^{-3} M$, $[\text{Ketone}] = 1.0 \times 10^{-2} M$,
$[HClO_4] = 0.16 M$, $[Hg(OAc)_2] = 2.0 \times 10^{-3} M$

[Methanol] %	$k_o \cdot 10^7$ mol l^{1} s^{-1} 1	2	3
0	4.00	7.00	12.83
10	4.50	7.52	13.37
20	4.93	7.98	14.07
30	5.33	8.49	14.69
40	5.80	9.05	15.34

The rate study measurements carried out at five different temperatures (35-55°) gave values for the energy of activation ($\Delta E^{\ddagger}$), frequency factor (A), entropy of activation ($\Delta S^{\ddagger}$) and heat of activation ($\Delta H^{\ddagger}$) as 17.3, 15.3, 11.9 kcal mol^{-1}; 2.5×10^8, 1.7×10^7, 1.0×10^5 l mol^{-1} s^{-1}; -21.2, -26.7, -36.8 e.u.; 16.6, 14.6, 11.3 kcal mol^{-1} for **1, 2** and **3** respectively.

Further the values of $T\Delta S^{\ddagger}$ (kcal mol^{-1}) were plotted against the corresponding $\Delta H^{\ddagger}$ values in order to test the validity of the compensation effect which is usually observed in processes within a homologous series. It is found that the points corresponding to various substitutents lie on a linear plot of approximately unit slope.

Discussion

NBS is known to exist in three different forms viz. *NBS* itself, Br$^+$ or $\overset{+}{N}BS$H in acidic media.

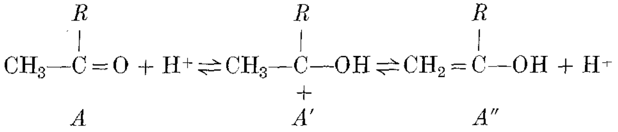
NBS reacts with HBr with the formation of Br_2 as follows:

$$NBS + HBr \rightarrow \text{Succinimide} + Br_2 \qquad (2)$$

Mercuric acetate acts as a scavenger for any bromide ion[16] (Br$^-$)

formed in the reaction and exists as $HgBr_4^{2-}$ or unionized $HgBr_2$ and thus ensuring that oxidation takes place purely through *NBS*.

Ketones enolise in acidic media [Eq. (3)], A representing the ketone, A' the conjugate acid and A'' its enolic form.



$$\underset{A}{CH_3-\overset{\overset{R}{|}}{C}=O} + H^+ \rightleftharpoons \underset{A'}{CH_3-\underset{+}{\overset{\overset{R}{|}}{C}}-OH} \rightleftharpoons \underset{A''}{CH_2=\overset{\overset{R}{|}}{C}-OH} + H^+ \qquad (3)$$

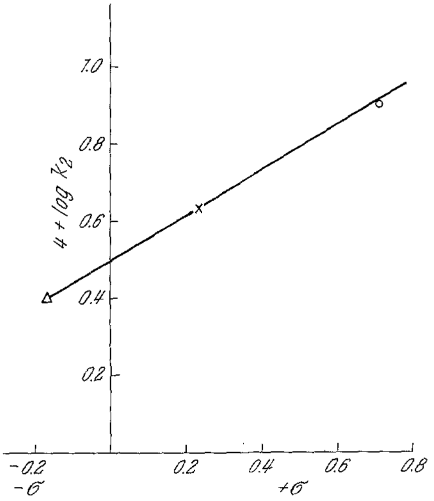


Fig. 3. Plot of log k_2 versus *Hammett* substituent constants at 40°. ○ m = nitroacetophenone; × p-chloroacetophenone; Δ p-methylacetophenone

It has been established through kinetic investigation that the order in *NBS* is zero and taking into consideration *Littler* and *Waters*[17] contention that in such cases the enolisation step will be slow and rate determining, three schemes involving Br^+, *NBS* and $\overset{+}{N}BSH$ were formulated. It was concluded that the scheme involving *NBS* as oxidising species satisfied the observed kinetic data and the other two schemes involving bromonium ion and protonated *NBS* as oxidising species were ruled out as they were found to be very unlikely. The mechanistic model for *NBS* oxidation may be represented as follows.

$$A + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} A' \text{ (fast)} \qquad (4)$$

$$A' \xrightarrow{k_2} A'' + H^+ \text{ (slow; rate determining)} \qquad (5)$$

$$A'' + NBS \xrightarrow{k_3} X \text{ (fast; intermediate species)} \qquad (6)$$

$$X + NBS \xrightarrow{k_4} \text{Products (fast)} \qquad (7)$$

Applying steady state treatment to the intermediates A', A'' and X we get the rate law:

$$-\frac{\mathrm{d}}{\mathrm{d}t}[NBS] = \frac{2k_1 k_2}{k_{-1} + k_2}[A][H^+] \qquad (8)$$

The rate law equation (8) fully satisfies the kinetic results.

NBS oxidation of ketones in acidic media thus involves the enolisation of conjugate acid of ketone A' as the slow and rate determining step followed by rapid attack of *NBS* molecule on A'' forming an intermediate which is subsequently destroyed by another molecule of *NBS* in a fast step yielding products.

Employing the appropriate values of the *Hammett* substituent constants[18], viz. —0.17, +0.73, +0.71 for p-CH_3, p-Cl and m-NO_2 groups respectively, an attempt was made to correlate the structure and reactivity for the substituted acetophenones investigated. A plot of log k_2 versus σ is linear (Fig. 3) with a positive slope giving a ρ value of +0.60 in the *Hammett* equation and establishing that electron withdrawing groups accelerate the reaction whereas the rate is appreciably retarded by electron donating groups like the methyl group.

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