

The antifertility activity of these compounds is in progress at CDRI, Lucknow and will be reported later.

The authors express their sincere thanks to the Head of Department of Chemistry for facilities.

16 June 1983; Revised 10 October 1983.

1. Rather, J. B. and Reid, E. E., *J. Am. Chem. Soc.*, 1919, 41, 75.
2. Bisagni, M., *J. Chem. Soc.*, 1955, 3688, 3693.
3. Sen, A. B. and Arora, S. L., *J. Indian. Chem. Soc.*, 1959, 36, 349.
4. Singh, H. and Kapil, R. S., *J. Org. Chem.*, 1959, 24, 2064.
5. Tiwari, S. S. and Kumar, S., *Indian. J. Appl. Chem.*, 1970, 33, 165.
6. Ischidate, M., *J. Am. Pharm. Assoc. Sci.*, 1955, 44, 132.
7. Nylon, W. L. and Busch, H., *Chem. Engg. News.*, 1958, 36, 46.
8. Buc, S. R., *J. Am. Chem. Soc.*, 1947, 69, 254.
9. King, F. E., Acheson, R. M. and Spansley, P. C., *J. Chem. Soc.*, 1949, 1401.

KINETICS AND MECHANISM OF THE BROMINATION OF AROMATIC SUBSTRATES BY N-BROMOSUCCINIMIDE IN AQUEOUS SOLUTION

T. S. RAO and S. P. DALVE

Department of Chemistry, University of Poona,
Pune 411007, India.

DESPITE the use of *N*-bromosuccinimide (NBS) as a brominating agent^{1,2} since long, the mechanism of the reaction in aqueous medium is yet not clear. It is not clear whether NBS hydrolyses to form hypobromous acid, which then attacks the substrate or whether NBS directly attacks the substrate by halogen transfer. To elucidate this problem the kinetics of the rapid bromination of acetanilide and *m*-acetotoluidide as a typical case have been studied. To confirm the deductions, the kinetics of the bromination of the substrate by hypobromous acid (HOBr) have been studied under comparable conditions. As a further probe, the effect on the specific rate of potassium bromide and hydrochloric acid added to the NBS/HOBr has also been studied.

Since the reaction is too rapid for conventional techniques, it has been studied by the use of the rotating platinum electrode (RPE)³⁻⁷. It operates on the principle that at a potential of 0.0 V vs SCE applied at the RPE, only NBS or HOBr yields diffusion current proportional to its concentration, whereas neither the substrate nor the products of the reaction yield any diffusion current. Therefore the course of the reaction can be followed by monitoring the concentration of unreacted NBS from measurement of the diffusion current at intervals of time.

Analytical grade (BDH) chemicals were used to prepare stock solutions of various reactants and the latter were maintained in a thermostat at $25 \pm 0.1^\circ\text{C}$. Equimolar solutions (4×10^{-4} M) of NBS and acetanilide containing 0.01 M potassium chloride as supporting electrolyte were rapidly mixed in a cell carrying the RPE and SCE and simultaneously a stop-watch was started. The diffusion current due to NBS at the RPE was measured with a mirror galvanometer with lamp and scale arrangement. The galvanometer deflections were earlier calibrated with NBS solutions of known concentration under identical experimental conditions. From these, the concentrations of unreacted NBS were determined at intervals of time. The experimental data fitted accurately into second order kinetic equation and a plot of $1/[\text{NBS}]$ versus time was satisfactorily linear. The slope of the curve evaluated by least square analysis was the specific rate (table 1). Repeated measurements of specific rates yielded results agreeing within $\pm 3\%$.

Table 1 Kinetics of bromination of acetanilide by *N*-bromosuccinimide in aqueous solution at 25.0°C
Calibration of galvanometer deflection = $17.6 \text{ cm}/10^{-4} \text{ M}$

Time/s	Diffusion current: galvanometer deflection/cm	Concentration of NBS unreacted [NBS]/ 10^{-4} M	$1/[\text{NBS}]$ 10^3 M^{-1}
0	35.3	2.00	5.00
20	34.2	1.94	5.16
40	33.0	1.87	5.35
60	31.9	1.81	5.53
80	31.0	1.75	5.70
100	30.2	1.71	5.85
120	29.5	1.67	5.99
140	28.6	1.62	6.18
160	27.8	1.57	6.36
180	27.2	1.54	6.50
200	26.4	1.50	6.67
220	25.8	1.46	6.84
240	25.3	1.43	6.99

Slope of $1/[\text{NBS}]$ versus time curve = specific rate (k_2)
= $8.5 \text{ M}^{-1} \text{ s}^{-1}$

The kinetics were similarly studied at various temperatures from which the energy of activation was evaluated. Further, the kinetics with hypobromous acid as the brominating agent and also with NBS/HOBr in the presence of added potassium bromide or hydrochloric acid were also similarly studied.

There are diverse opinions^{8,9} on the mechanism of the bromination by NBS. According to some, in aqueous solution NBS may hydrolyse to form HOBr and the latter may be the brominating agent.

If NBS is slowly hydrolysed, the formation of HOBr would be the rate-determining step in the overall bromination reaction and hence the specific rates of the bromination of acetanilide and *m*-acetotoluidide would be the same. But experiments show that these specific rates are $8.5 \text{ M}^{-1} \text{ s}^{-1}$ and $70 \text{ M}^{-1} \text{ s}^{-1}$ respectively, at 25°C . Hence the slow hydrolysis of NBS, as a step preceding the bromination is not correct.

In contrast, if NBS is hydrolysed rapidly, the rates of brominations by NBS and HOBr should be identical. But the specific rate of the bromination of acetanilide by NBS is $8.5 \text{ M}^{-1} \text{ s}^{-1}$ while that by HOBr is $32.5 \text{ M}^{-1} \text{ s}^{-1}$. Therefore, there is no significant hydrolysis of NBS in aqueous solution relevant to the bromination reaction implying that NBS itself is the active agent.

In probing further into this aspect, the kinetic studies on the bromination of acetanilide by NBS and by HOBr, each in the presence of equimolar potassium bromide or hydrochloric acid are highly significant. The specific rates and energies of activation for the bromination by the two reagents in the presence of added KBr/HCl are considerably different (table 2). Evidently, the reaction does not proceed *via* HOBr, and hence NBS itself is the brominating agent.

Table 2 Comparative study of the bromination of acetanilide by *N*-bromosuccinimide and hypobromous acid in aqueous solution

Bromination with/agent	Specific rate at 25.0°C $k_2/\text{M}^{-1} \text{ s}^{-1}$	Energy of activation $E_a/\text{kJ mole}^{-1}$
<i>N</i> -bromosuccinimide	8.5	13.4
Hypobromous acid	32.5	12.2
<i>N</i> -bromosuccinimide + potassium bromide	12.2	9.6
Hypobromous acid + potassium bromide	61.3	7.1
<i>N</i> -bromosuccinimide + hydrochloric acid	21.8	28.7
Hypobromous acid + hydrochloric acid	685	23.7

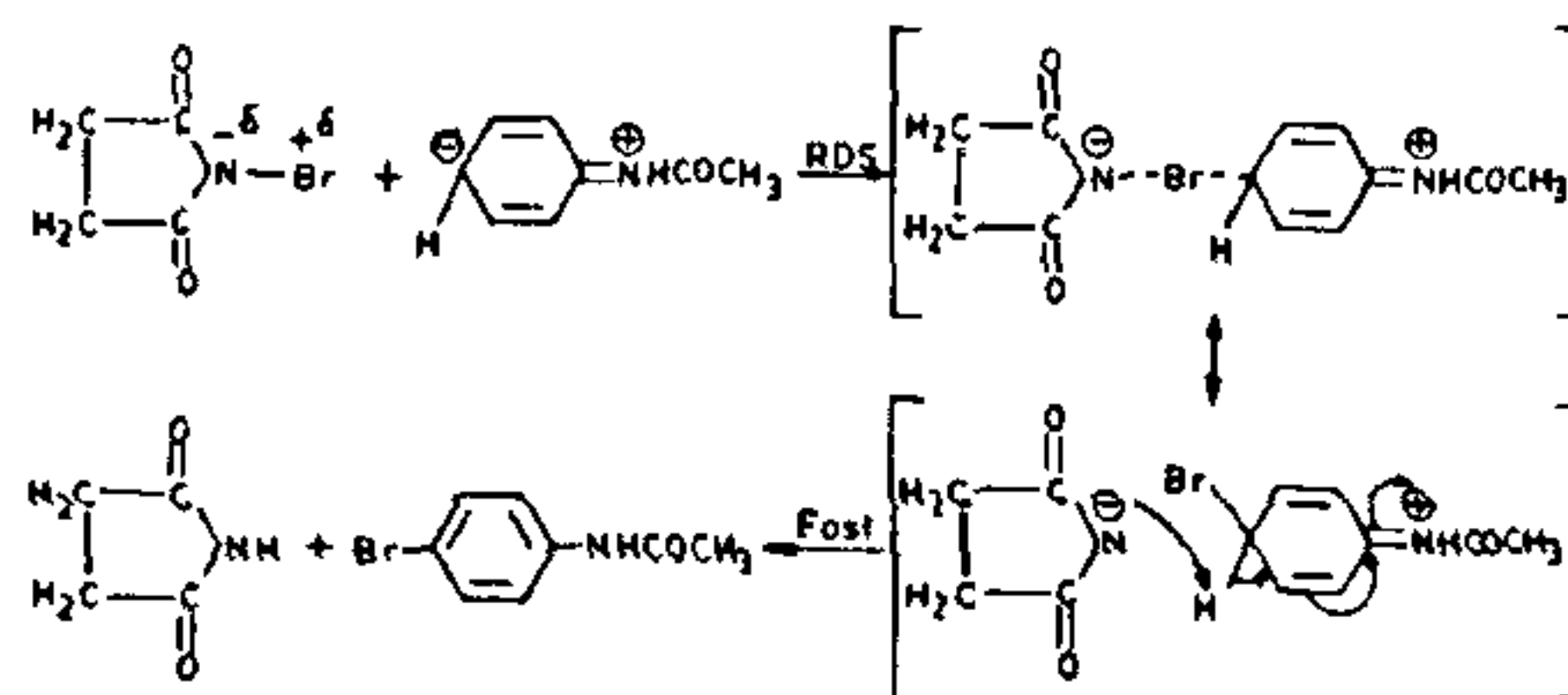


Figure 1. Mechanism of the reaction.

Keeping the above observations in view, the most likely mechanism can be proposed as figure 1.

Because of greater electronegativity of N atom than that of Br atom in *N*-bromosuccinimide, N and Br atoms carry incipient negative and positive charges respectively. The para position¹⁰ in acetanilide has high electron density, due to which it is highly reactive. Therefore, it is probable that NBS can complex with acetanilide in a rate determining step to give an intermediate¹¹ which decomposes by halogen transfer and finally the succinimide anion abstracts the proton in fast step to give the product¹².

27 August 1983

- Djerassi, C., *Chem. Rev.*, 1948, **43**, 271.
- Pearson, R. E. and Martin, J. C., *J. Am. Chem. Soc.*, 1963, **85**, 354.
- Kolthoff, I. M. and Laitinen, H. A., *J. Phys. Chem.* 1941, **45**, 1079.
- Kolthoff, I. M., *J. Assoc. Offic. Agr. Chem.* 1959, **39**, 47.
- Kolthoff, I. M. and Lingane, J. J., *Polarography*, 2nd edn., Interscience, New York, Vol. I, 1952, p. 421.
- Rao, T. S. and Mali, S. I., *Z. Naturforsch.*, 1976, **31(a)**, 1735.
- Rao, T. S., Mali, S. I. and Dangat, V. T., *Tetrahedron*, 1978, **34**, 205.
- Gopalkrishnan, G., Pai, B. R. and Venkatasubramanian, N., *Indian J. Chem.*, 1980, **19(B)**, 293.
- Radhakrishnanmurti, P. S and Sahu, S. N., *Indian J. Chem.*, 1977, **15(A)**, 785.
- Hine, J., *Physical organic chemistry*, 2nd edn. McGraw-Hill, New York, 1962, p. 370.
- Hober Field, Paul and Denis Paul, *J. Am. Chem. Soc.*, 1965, **87**, 5502.
- Kleinschmidt, E. G., Braeuniger and Harald, *Pharmazie*, 1969, **24**, 87 (Ger).