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Original Scientific Paper

Kinetics and Mechanism of Reduction of *p*-Nitroso-*N*,*N*-dimethylaniline by Sulphite Ions in Acetate—Acetic Acid Buffer Solutions

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The kinetics of the title reduction was studied spectrophotometrically in acetate-acetic acid buffer solutions at different temperatures in the range 20 ° to 40 °C. The effect of varying [H$^+$] on the reduction rate was investigated at a constant ionic strength of 0.06 mol md^{-3}. The rate-order was found to be 1.0 with respect to both reactants and —0.5 with respect to the hydrogen ion. The rate of reaction decreased with increasing hydrogen ion concentrations. The [H$^+$] dependency indicates the presence of two competitive rate-determining steps. The experimental data gave a good fit to

$$-d[\text{nitroso compound}]/dt = k_{\text{obs}}\ [\text{nitroso compound}]$$
$$= [\text{nitroso compound}]\ [\text{sulphite}] \cdot \frac{k_a K_1 + k_b K_2 K_p\ [\text{H}^+]}{1 + K_p\ [\text{H}^+]} \cdot$$

Activation parameters were determined and found to be $\Delta S^{\ddagger} =$ —176.09 JK^{-1} mol^{-1}, $\Delta H^{\ddagger} = 17.82$ kJ mol^{-1} and $\Delta G^{\ddagger} = 70.30$ kJ mol^{-1}. A mechanism consistent with the experimental results has been suggested.

INTRODUCTION

Synthetic and naturally occurring nitroso compounds are important because they contain compounds such as antibiotics and carcinogens.[1(a)] The metabolic effects of nitroso compounds are involved in some of the most important biochemical reactions occurring in living systems.[1(b),2] A number of *N*-nitroso compounds, *e. g.* *N*-nitroso-*N*-methylurethane and dimethylnitrosamine, are highly toxic, producing liver and lung damage, bleeding, convulsions, and coma.[1(c)] Others, *e. g.* some nitrosopyrazoles, exhibit fungicidal activities.[1(d)]

Kinetics of the reduction of inorganic compounds by sulphite ions has been reported earlier.[3,4] However, much less attention has been focussed on its application to organic compounds. Details of the sulphite ion reduction of the nitroso compounds are not yet known although the kinetics of reduction of these compounds by other reductants[5–12(a)] has been reported. In this work, the kinetics of reduction of the nitroso group in one of the nitroso compounds (*p*-nitroso-*N*,*N*-dimethylaniline) by SO_3^{2-} ions in HOAc—NaOAc buffer solutions was performed with the aim of elucidating the reduction mechanism. It is felt than an important result of the present work is calling attention to the possibility of conversion of the nitroso compounds, which have potential toxicological hazards and other threats to health, to hydroxylamines using sulphite ions as a reducing agent.

EXPERIMENTAL

Materials and Methods

Sodium sulphite, acetic acid and sodium acetate were of Analar (BDH) grade, and *p*-nitroso-*N*,*N*-dimethylaniline (nitroso compound *I*) was of GR (E. Merck) grade. All other reagents were chemically pure. All the solutions were prepared in doubly distilled conductivity water.

Stock solution of the nitroso compound *I* was prepared by dissolving an accurately weighed amount of the compound in an appropriate volume of water. Stock solution of sodium sulphite was prepared by dissolving the appropriate weighed recrystallized salt in water and standardized against iodine.[13] Acetic acid-sodium acetate buffer solutions with $[H^+]$ in the range $(0.13—39.81) \times 10^{-5}$ M were prepared according to Perrin.[14]

Kinetic Measurements

Kinetic experiments were carried out in a temperature controlled (± 0.1 °C) water bath. The reaction was initiated by adding to an equilibrated mixture of the nitroso compound *I* and HOAc—NaOAc buffer solution the requisite quantity of pre-equilibrated sodium sulphite solution. The course of the reaction was followed by monitoring the disappearance of compound *I* as a function of time at the CT band maximum absorption (440 nm) against the same solvent containing the same amount of sodium sulphite as in the kinetic solutions as blanks. Absorption measurements were followed on a Shimadzu UV-200 S double beam spectrophotometer, using a cell of 1 cm path length. The spectral change of the reaction is shown in Figure 1. It was verified that there was no interference of other reagents or reduction product at λ_{max} of the nitroso compound *I*. The reactions were usually followed up to not less than three half-lives. The pH measurements were carried out at 18 °C on a WG PYE model 290 pH-meter accurate to + 0.005 pH units.

The kinetics of the present work was conducted under pseudo-first-order conditions where [sulphite] $\gg$ [nitroso compound]. Under these conditions, the rate equation can be written as follows:

$$-\frac{d\,[\text{nitroso compound}]}{dt} = k_{obs}\,[\text{nitroso compound}] \qquad (1)$$

where k_{obs} is the observed pseudo-first-order rate constant, which may be expressed by the equation:

$$k_{obs} = k_2\,[\text{sulphite}] \qquad (2)$$

and k_2 is the second-order rate constant.

RESULTS

1. *Stoichiometry and Product Analysis*

The stoichiometry of the overall reaction of sulphite ions with excess of the nitroso compound *I* was determined spectrophotometrically at 25 °C. The unreacted [nitroso compound] was estimated periodically till it attained a constant value, *i. e.* completion of reaction. A stoichiometric ratio of 1 within experimental error ($[\text{nitroso compound}]_{consumed}/[\text{sulphite}]_o$) was obtained with ten different initial concentrations of compound *I*. The reduction product was isolated from the reaction mixture containing a large excess of sulphite ions after completion of the reaction. A successive extraction with ether followed by drying over anhydrous sodium sulphate under aerobic conditions gave a solid product confirmed by elemental and IR spectral analysis as *p*-hydroxylamine-*N*,*N*-dimethylaniline (compound *II*).

From the above results, the stoichiometry of the overall reaction can be represented by Eq. (3).

$$C_8H_{10}N_2O + SO_3^{2-} + H_2O = C_8H_{12}N_2O + SO_4^{2-} \qquad (3)$$

The convertion of nitrosoarenes into hydroxylamines by other mild reducing agents has been reported earlier.[7,11,12(a)]

2. *Rate Dependence on the [Nitroso Compound]*

The rate-order with respect to compound *I* was determined by studying the reaction at different initial concentrations of the substrate with constant [sulphite]. The [nitroso compound] was varied in the range (1.13—11.30) × 10^{-5} M, whereas [sulphite] suitable for kinetic measurements was 1.0 × 10^{-3} M, the $[H^+]$ was 1.04 × 10^{-5} M at 33 °C. Under the conditions where [sulphite] $\gg$ [nitroso compound], the plots of log (absorbance) *versus* time were linear, indicating the first-order dependence of rate on [nitroso compound] (Figure 2(a)). The average value of k_{obs} was found to be (3.26 ± 0.07) × 10^{-3} sec^{-1}.

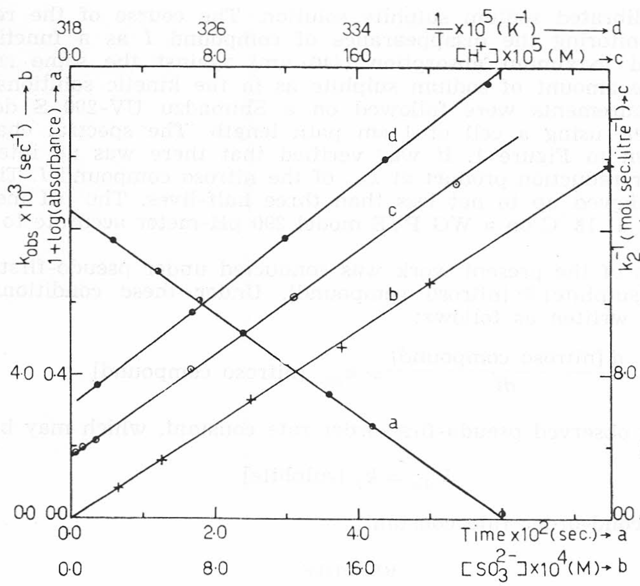


Figure 2. (a) Plot of $1 + \log(\text{absorbance})$ *versus* time ([nitroso compound] $= 4.37 \times 10^{-5}$ M, $[SO_3^{2-}] = 1.0 \times 10^{-3}$ M, $[H^+] = 1.04 \times 10^{-5}$ M; temperature = 33 °C).
(b) Plot of k_{obs} *versus* $[SO_3^{2-}]$: ([nitroso compound] $= 4.37 \times 10^{-5}$ M, $[H^+] = 1.04 \times 10^{-5}$ M; temperature = 33 °C).
(c) Plot of k_2^{-1} *versus* $[H^+]$: ([nitroso compound] $= 4.37 \times 10^{-5}$ M, $[SO_3^{2-}] = 1.0 \times 10^{-3}$ M, temperature = 33 °C).
(d) Eyring plot of $-\ln \frac{h}{kT} k_2$ *versus* $1/T$.

3. *Rate Dependence on [Sulphite]*

The rate-order with respect to sulphite ion was deduced from the measurement of the reaction rates at several [sulphite] and constant [nitroso compound]. The [sulphite] was varied in the range $(2.5-30.0) \times 10^{-4}$ M, whereas [nitroso compound] $= 4.37 \times 10^{-5}$ M, $[H^+] = 1.04 \times 10^{-5}$ M at 33 °C. The plot of k_{obs} *versus* [sulphite] was found to be linear passing through the origin (Figure 2(b)). This indicates that the reaction is also first-order with respect to $[SO_3^{2-}]$ ion, Table I.

TABLE I

Effect of varying [sulphite] on the reduction rates.
[Nitroso compound] = 4.37×10^{-5} M, $[H^+] = 1.04 \times 10^{-5}$ M, temperature = 33 °C

10^4 [sulphite] (M)	$k_{obs} \times 10^3$ (s^{-1})	$10\ k_{obs}$/[sulphite] ($l\ mol^{-1}\ s^{-1}$)
2.5	0.82	32.80
5.0	1.62	32.40
10.0	3.26	32.60
15.0	4.80	32.00
20.0	6.51	32.55
30.0	9.77	32.57

4. *Rate Dependence on [Hydrogen Ion]*

To clarify the influence of $[H^+]$ on the reduction rates and to elucidate the reduction mechanism, the reaction of 4.3×10^{-5} M compound *I* with 1.0×10^{-3} M Na_2SO_3 at 18 °C was investigated in a series of HOAc—NaOAc buffer solutions[14] of different pH values and constant ionic strength of 0.06 mol dm^{-3}. The dependence of k_{obs} on $[H^+]$ is presented in Table II. The increase in hydrogen ion concentration decreases the reaction rate. The power dependence of $[H^+]$ on k_2 was determined from the empirical relation:

TABLE II

Effect of varying [H⁺] on the rate of reduction.
[Nitroso compound] = 4.37×10^{-5} M, $[SO_3^{2-}] = 1.0 \times 10^{-3}$ M, temperature = 18 °C

$10^5\ [H^+]$ M	0.31	0.71	1.39	6.65	12.39	21.53
$10^4\ k_{obs}$ s^{-1}	27.32	25.25	23.15	12.08	8.09	5.37

$$\ln k_2 = \ln [H^+]^n \tag{4}$$

The value of n was found to be —0.5. A plot of k_2^{-1} *versus* $[H^+]$ gives a good straight line with an intercept on k_2^{-1} axis, Figure 2(c).

5. *Rate Dependence on Temperature*

The reaction was studied at 20, 25, 30, 35 and 40 °C, [nitroso compound] = 4.37×10^{-5} M, $[SO_3^{2-}] = 1.0 \times 10^{-3}$ M and $[H^+] = 1.2 \times 10^{-5}$ M. The second-order rate constants (k_2) were calculated from the rate expressions. The plot of $-\ln (h/kT)\, k_2$ against $1/T$ of Eyring equation[15] was a good straight line (Figure 2(d)). The values of the enthalpy and entropy of activations were determined from the slope and the intercept of the straight line obtained, respectively. These values are summarized in Table III.

TABLE III

Activation parameters of the reaction

Parameter	Value
$k_2 \times 10^2$ ($l\ mol^{-1}\ s^{-1}$) (298 °K)	289.63
E_a* (kJ mol^{-1})	18.61
$\log_{10} A$* (kJ mol^{-1})	13.90
$\Delta H^{\ddagger}$** (kJ mol^{-1}) (298 °K)	17.82
$\Delta G^{\ddagger}$** (kJ mol^{-1}) (298 °K)	70.30
$\Delta S^{\ddagger}$** ($JK^{-1}\ mol^{-1}$) (298 °K)	—176.09

* Calculated using Arrhenius equation.
** Calculated using Eyring equation.

DISCUSSION

The first-order dependence on both sulphite ions and the nitroso compound molecules leads to the following simple rate equation

$$-\frac{d\,[\textit{nitroso compound}]}{dt} = -\frac{d\,[\text{sulphite}]}{dt} = \frac{d\,[\text{product}]}{dt} \tag{5}$$

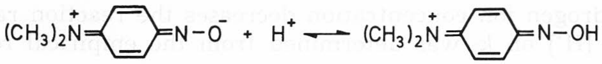
$$= k_2\,[\text{nitroso compound}]\,[\text{sulphite}]$$

Owing to the concerted interaction of the electron-releasing dimethylamino group and the electron-withdrawing nitroso group, the structure of the nitroso compound *I* is found to be noticeably shifted to the side of the quinonoid[16] form (*III*), and it may be described as a resonance hybrid:

(6)

(I) (III)

This is detected by the enhanced dipole moment (6.90 D),[12(b)] the bathochromic shift of light absorption and the inability to form a dimer.[17] In acid medium, the following equilibrium is stabilized:



(7)

(III) (IV)

The retardation of the reduction rate on increasing $[H^+]$ may be interpreted by the formation of the inactive ion (*IV*) (*cf.* Mechanism). The large negative values of the entropy of activation obtained (—176.09 JK^{-1} mol^{-1}) can be explained in part by a necessity to overcome the formation of this inactive protonated form.

Mechanism

The power dependence of the second order rate constant on $[H^+]$ at moderate pH's used and the linearity plot shown in Figure 2(c) with an intercept on k_2^{-1} axis indicates that the reaction between the nitroso compound *I* and SO_3^{2-} in the presence of hydrogen ions proceeds through two reaction paths.

Equation (7) shows that compound *I* molecules are protonated in acid medium and the protonation constant (K_p) is given by the equilibrium:

$$A + H^+ \overset{K_p}{\rightleftharpoons} AH^+ \tag{7'}$$

The presence of A and AH^+ species is in accordance with the observed data.

Introducing the protonation constant (K_p) defined by Eq. (7') and the total concentration of compound *I*,

$$[A]_{total} = [A] + [AH^+] \tag{8}$$

we can express the concentrations of [A] and $[AH^+]$ species by the equations:

$$[A] = \frac{[A]_{total}}{1 + K_p\,[H^+]} \tag{9}$$

$$[AH^+] = \frac{K_p\,[A]_{total}\,[H^+]}{1 + K_p\,[H^+]} \tag{10}$$

The simple interpretation of the effect of varying $[H^+]$ suggests the presence of competitive reactions[18] (11) and (12):

$$A + SO_3^{2-} \underset{\text{fast}}{\overset{K_1}{\rightleftharpoons}} [*] \underset{\text{slow}}{\overset{k_a}{\longrightarrow}} \text{product} \qquad (11)$$

$$AH^+ + SO_3^{2-} \underset{\text{fast}}{\overset{K_2}{\rightleftharpoons}} [*] \underset{\text{slow}}{\overset{k_b}{\longrightarrow}} \text{product} \qquad (12)$$

Both Eqs. (11) and (12) involve the rate-determining step where two equilibrium forms [*] involving both reagents, possibly $O_3S^+ \ldots O \ldots N\ Ar$, are produced initially and subsequently undergo further dissociation to give rise to the products. Thus, the change of the rate constant with change in $[H^+]$ may be expressed by Eq. (13):

$$Rate = \frac{k_aK_1 + k_bK_2K_p\,[H^+]}{1 + K_p\,[H^+]}\,[A]_{total}\,[SO_3^{2-}] \qquad (13)$$

Comparing Eqs. (13) and (5), one can conclude that

$$k_2 = \frac{k_aK_1 + k_bK_2K_p\,[H^+]}{1 + K_p\,[H^+]} \qquad (14)$$

Assuming that SO_3^{2-} and A are the reactive species under the experimental conditions, the value of k_bK_2 is nearly zero. Consequently, Eq. (14) can be recast in the form:

$$\frac{1}{k_2} = \frac{K_p\,[H^+]}{k_aK_1} + \frac{k_aK_1}{1} \qquad (15)$$

$$\frac{1}{k_2} = \frac{K_p\,[H^+]}{k'} + \frac{1}{k'} \qquad (16)$$

where $k' = k_a K_1$. According to Eq. (16) the plot of k_2^{-1} *versus* $[H^+]$ will be linear with an intercept and slope corresponding to $(k')^{-1}$ and $(K_p\,k'^{-1})$, respectively, as experimentally obtained. The values of K_p and k' were evaluated at 18 °C and found to be 2.0×10^4 M^{-1} and 2.9 litre mol^{-1} min^{-1}, respectively.

REFERENCES

1. H. Feuer, *The chemistry of the nitroso groups.* Interscience Publishers a division of John Wiley & Sons., New York, London, Sydney, Toronto. Part 2. 1970. a) p. 212; b) p. 201; c) p. 243; d) p. 238.
2. P. N. Magee and J. M. Barnes, *Advan. Cancer Res.* **10** (1967) 164.
3. C. R. Dennis, S. S. Basson, and J. G. Leipoldt, *Polyhedron* **2** (1983) 1357.
4. A. V. Kalyakina, E. A. Buketov, A. A. Kozhakova, and A. N. Polukarov, *Tr. Khim.-Met. Inst., Akad. Nauk kaz. SSR* **16** (1970) 22.
5. J. S. Wessels, *Biochim. Biophys. Acta* **109** (1965) 357.
6. R. N. Cochran, F. H. Horne, J. L. Dye, J. Ceraso, and C. H. Suelter, *J. Phys. Chem.* **84** (1980) 2567.
7. A. R. Becker and L. A. Sternson, *Bioorg. Chem.* **9** (1980) 305.
8. J. I. G. Cadogan and A. Cooper, *J. Chem. Soc. B* **7** (1969) 883.
9. T. Sato, K. Hamamura, and S. Kanbara, *Nenryo Kyokaishi* **60** (1981) 106.

10. H. Awano and W. Tagaki, *Chem. Lett.* 5 (1985) 669.
11. H. Awano, T. Hirabayashi, and W. Tagaki, *Tetrahedron Lett.* 25 (1984) 2005.
12. F. R. S. D. Barton and F. R. S. D. Ollis, *Comprehensive Organic Chemistry.* I. O. Sutherland. Vol. 2. *Nitrogen compounds, Carboxylic Acids, Phosphorus Compounds.* Pergamon Press Ltd. Oxford, New York, Toronto, Sydney, Paris, Frankfurt, 1979. a) p. 317; b) p. 315.
13. A. I. Vogel, *Text-book of Quantitative Inorganic Analysis,* 3rd Edn., Longmans, London, 1961, p. 370.
14. D. D. Perrin and B. Dempsey, *Buffers for pH and Metal Ion Control,* Science Paperbacks, Chapman and Hall, London, 1979, p. 153.
15. S. Glasstone, K. J. Laidler, and H. Eyring, *The Theory of Rate Processes.* Mc Graw-Hill Book Company, New York, 1941, p. 417.
16. C. Romming and H. J. Talberg, *Acta Chem. Scand.* (1973) 2246.
17. S. Patai, *Supplement. F. The Chemistry of Amino, Nitroso and Nitro Compounds and their Derivatives,* Part 1. John Wiley & sons. An Interscience Publication. 1982. p. 44.
18. R. M. Hassan and M. M. Girgis, *Indian J. Chem.* **26 A** (1987) 936.

SAŽETAK

Kinetika i mehanizam redukcije *p*-nitrozo-*N,N*-dimetilanilina sa sulfitnim ionom u sistemu octena kiselina—acetat ion

Maher M. Girgis

Primjenom spektroskopije studirana je kinetika redukcije *p*-nitrozo-*N,N*-dimetilanilina sa sulfitnim ionom u octenoj kiselini u prisustvu acetatnog iona. Posebna je pažnja posvećena utjecaju temperature i koncentracije H^+ iona na brzinu reakcije. Na temelju rezultata o ovisnosti brzine reakcije o koncentraciji H^+ iona zaključeno je da reakcija uključuje dva kompetitivna stupnja koja određuju brzinu reakcije. Izračunati su i aktivacijski parametri i ukratko diskutiran mehanizam reakcije.