# Nucleophilic catalysis of nitrosation: relationship between nitrosating agent equilibrium constant and catalyst nucleophilicity

*J. Chem. Research (S),* 2002, 589–590
*J. Chem. Research (M),* 2002, 1215–1232

**Gabriel da Silva, Eric M. Kennedy* and Bogdan Z. Dlugogorski**

*Process Safety and Environment Protection Research Group, School of Engineering, The University of Newcastle, Callaghan, NSW 2308, Australia*

Equilibrium constants for the formation of nitrosating agents from various nucleophiles and nitrous acid are predicted from Edwards' nucleophilic parameter.

**Keywords:** nitrosation, nucleophilic catalysis, thermodynamic nucleophilicity

Nitrosation reactions are well-known to be catalysed by a range of nucleophilic species[1] (designated $X^-$), according to Equation (1). The equilibrium constant for this reaction, $K_{ONX}$, is given by Equation (2).

$$HNO_2 + X^- + H^+ \overset{K_{ONX}}{\rightleftharpoons} ONX + H_2O \qquad (1)$$

$$K_{ONX} = \frac{[ONX]}{[HNO_2][X^-][H^+]} \qquad (2)$$

The nitrosating agents formed from these catalysts subsequently affect the nitrosation of a substrate (designated S) according to Equation (3), where $k_N$ is the rate constant for the second-order nitrosation reaction.

$$ONX + S \xrightarrow{k_N} ONS^+ + X^- \qquad (3)$$

During nitrosation under mildly acidic conditions, formation of the nitrosating species is generally found to be at equilibrium, while the nitrosation reaction itself is rate determining. This has led to the establishment of the following rate equation to describe the overall rate of nitrosation.

$$r = K_{ONX} k_N [S][HNO_2][X^-][H^+] \qquad (4)$$

Equation (4) shows that the efficiency of a particular catalyst is partitioned between its equilibrium and rate constants. Of these two constants, $K_{ONX}$ shows the greatest variation between catalysts, thus making it the critical rate-determining factor. However, many equilibrium constants for a number of common nitrosating agents have not been well established in the literature, often because their small magnitude precludes their determination via conventional experimental techniques.

In order to predict $K_{ONX}$ values, we have developed a model, Equation (19), based on Edwards' $E_n$ parameter[4]. Here, $\alpha_n$ is a constant which lies between 0 and 1, and represents the ON–X bond order as a function of that in the two species $X^-$(bond order 0) and $X_2$ (bond order 1).

$$1n\ K_{ONX} = \left[\frac{F(1-\alpha_n)}{RT}\right] E_n + \frac{70180 - \Delta G^\circ_5 - 2.60F(1-\alpha_n)}{RT} \qquad (19)$$

Literature values of $K_{ONX}$ may be plotted against $E_n$, so as to determine the parameters of Equation (5). This has been performed in Fig. 1, and an excellent correlation is seen between the model and the data. From this plot we determine $\alpha_n$ to be 0.46 and $\Delta G°_5$ as 8906 J/mol, with the $\alpha_n$ value indicating that the ON–X bond order is intermediate between that of $X_2$ and $X^-$. Nitrosyl iodide has long been known to effect nitrosation, however no accurate value for $K_{ONX}$ was available. The value was estimated, however, to be greater than 100 $M^{-2}$. We may now use our model to predict a $K_{ONX}$ value of 1800, being considerably greater than the previous estimate.

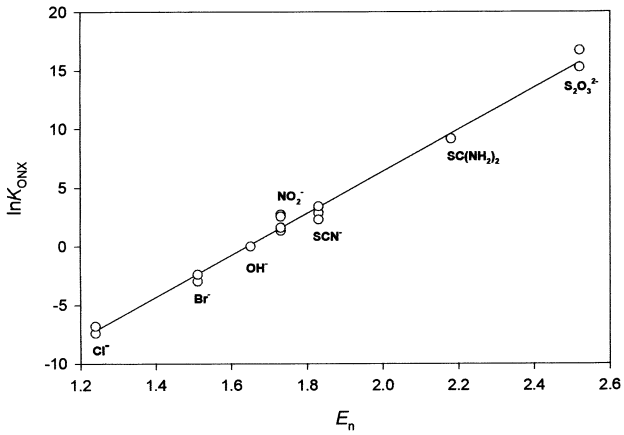


**Fig. 1** Comparison of the model with the experimental measurements.

Dix and Williams[24] studied the iodide catalysed nitrosation of various aniline derivatives, but were unable to present rate constants due to the absence of an equilibrium constant for nitrosyl iodide. These rate constants may now be determined using our predicted $K_{ONX}$ value. They are $2.6 \times 10^7$, $2.9 \times 10^6$, $2.6 \times 10^6$, $1.9 \times 10^6$ and $8.8 \times 10^4$ $M^{-1}$ $s^{-1}$ for the amines *p*-methoxyaniline, *p*-chloroaniline, aniline, *m*-methoxyaniline and *p*-carboxyaniline, respectively. These values place nitrosyl iodide below both nitrosyl acetate and nitrosyl thiocyanate in an order of kinetic reactivity.

Nitrosyl acetate is another compound for which a $K_{ONX}$ value has not been experimentally obtainable due to its low value. Again an estimate exists, based on an analysis of reaction rates with various secondary amines[20]. This estimate of $1.4 \times 10^{-8}$ $M^{-2}$ is considerably lower than our predicted value of $4.4 \times 10^{-6}$. This new $K_{ONX}$ value has been used to effect a re-analysis of existing kinetic data, as shown in Table 3 compared to values obtained using dinitrogen trioxide as nitrosating agent[26]. While the $k_N$ values obtained with dinitrogen trioxide appear to be at the encounter-controlled limit, those with nitrosyl acetate are not. This is in spite of the fact that nitrosyl acetate should be a more reactive nitrosating agent. As such, it is suggested that the original kinetic data or kinetic analysis is in error.

**Table 3** Rate constants for the nitrosation of three secondary amines by nitrosyl acetate, as compared to nitrosation via dinitrogen trioxide

| | $k_N$ ($CH_3COONO$) $M^{-1}$ $s^{-1}$ | $k_N$ ($N_2O_3$) $M^{-1}$ $s^{-1}$ |
|---|---|---|
| Morpholine | $2.8 \times 10^6$ | $2.2 \times 10^8$ |
| *N*-Methylaniline | $5.6 \times 10^5$ | $4.0 \times 10^8$ |
| Piperazine | $3.5 \times 10^4$ | $1.3 \times 10^8$ |

* To receive any correspondence.
E-mail: Eric.Kennedy@newcastle. edu.au

We would like to thank Orica Pty. Ltd. for project funding, and the Australian Research Council for the provision of a student scholarship to G.D.

Equations: 22

Figures: 2

References: 28

Tables: 3

*Received 15 October 2002; accepted 29 October 2002*
*Paper 02/1610*

### References cited in this synopsis

1 J.H. Ridd, *Quart. Revs*., 1961, **15**, 418.
4 J.O. Edwards, *J. Am. Chem. Soc*., 1954, **76**, 1540.
20 J. Casado, A. Castro, M. Mosquera, M.F.R. Prieto and J.V. Tato, *Monatsh. Chem*., 1984, **115**, 669.
21 L. Dozsa, I. Szilassy and M.T. Beck, *Inorg. Chim. Acta*, 1976, **17**, 147.
24 L.R. Dix and D.L.H. Williams, *J. Chem. Res. (S)*, 1984, 96.
26 M.R. Crampton, J.T. Thompson and D.L.H. Williams, *J. Chem. Soc. Perkin Trans. 2*, 1979, 18.