

## Rate-limiting NO<sup>+</sup> Formation in Nitrosation Reactions in Acetonitrile

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Acid-catalysed nitrosation of methanol, thioglycolic acid, and water in acetonitrile using alkyl nitrites or nitrous acid (except in the case of water), is kinetically zero order in the substrate, consistent with rate-limiting NO<sup>+</sup> formation.

It has recently been suggested<sup>1</sup> that the use of alkyl nitrites (particularly *t*-butyl nitrite) in chloroform or acetonitrile, is a good synthetic procedure for the nitrosation of amines, alcohols, and thiols. Although much is known about the mechanism of nitrosation in aqueous media,<sup>2</sup> this is not the case for reactions in other solvents. We have examined the kinetics of nitrosation of alcohols [equation (1)], thioglycolic acid (R'SH) [equation (2)], and water, using alkyl nitrites in acetonitrile, and also the nitrosation of alcohols and the thiol using nitrous acid in the same solvent.

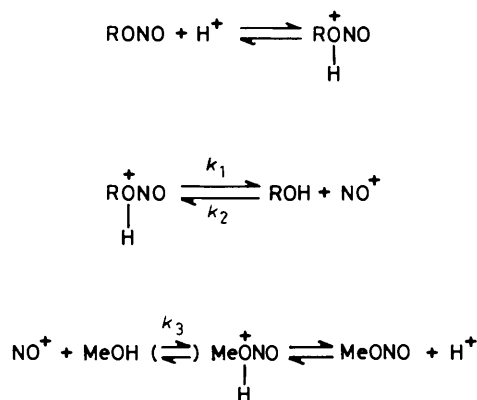


Reaction occurs very readily in the absence of any acid catalyst, but the measured rate constants are not very reproducible and tend to increase with the age of the reactant solutions. With acid catalysts, there is still an 'ageing effect,' but reproducible rate constants (to  $\pm$  ca. 7%) were obtained after fresh acid solutions had stood for ca. 1 h. The explanation of this curious effect is deferred to a later fuller publication. With [RONO]<sub>0</sub> or [HNO<sub>2</sub>]<sub>0</sub>  $\ll$  [Substrate]<sub>0</sub> reactions were followed by stopped-flow spectrophotometry, at ca. 410 nm for the alcohols and at 330 nm for R'SH. Good first-order behaviour was found for R = Bu<sup>t</sup>, Pr<sup>i</sup>, isopentyl, and H. With alcohols, the reactions are reversible and equilibrium constants were obtained spectrophotometrically for reactions with methanol: 12.8  $\pm$  1.9 (for Bu<sup>t</sup>ONO), 4.5  $\pm$  1.0 (for Pr<sup>i</sup>ONO), and 2.5  $\pm$  0.7 (for isopentyl-ONO). Under the kinetic conditions however, reaction is essentially quantitative from left to right. There is no evidence of reversibility with the thiol reactant.

The interesting feature however, is that for all three alkyl nitrites, and also for nitrous acid, the measured first-order rate constant is independent of the concentration (0.01–0.1 M) and nature of the substrate (MeOH, Pr<sup>i</sup>OH, Bu<sup>t</sup>OH, R'SH, and H<sub>2</sub>O). Some of the results for Bu<sup>t</sup>ONO and HNO<sub>2</sub> reactions are shown in Table 1. Similar results were found for Pr<sup>i</sup>ONO and isopentyl-ONO, giving the relative reactivity sequence HNO<sub>2</sub>: Bu<sup>t</sup>ONO: Pr<sup>i</sup>ONO: isopentyl-ONO 8.5:4.6:1.9:1.0. All reactions are acid catalysed with a rate

dependence very close to first-order in [H<sub>2</sub>SO<sub>4</sub>], up to 0.015 M. The relative reactivity sequence derived from the rate constant-[acid] profile was very similar to the one above.

For the alkyl nitrite reactions, the rate constants are substantially reduced by the addition of the alcohol from which the alkyl nitrite is derived (*i.e.* Bu<sup>t</sup>OH for Bu<sup>t</sup>ONO, *etc.*), and similarly, for the nitrous acid reaction the rate constants are reduced by the addition of small amounts of water. Further, at high [added ROH] the reaction has a rate dependence upon the substrate *e.g.* for methanol in its nitrosation by Bu<sup>t</sup>ONO with high [added Bu<sup>t</sup>OH]. All of these observations can be accommodated by the mechanism outlined in Scheme 1 (for methanol nitrosation) for reactions with RONO generally and also with HNO<sub>2</sub>. In the absence of any added ROH, the results are readily explained by the inequality  $k_2[\text{ROH}] \ll k_3[\text{MeOH}]$ . This is not unreasonable given the large concentration differences. Under these conditions, the rate limiting step ( $k_1$ ) is the formation of NO<sup>+</sup> from the protonated form of the alkyl nitrite (or of nitrous acid). However, when ROH is added,  $k_2[\text{ROH}]$  becomes more comparable with  $k_3[\text{MeOH}]$  and we get an overall rate reduction and the reaction of NO<sup>+</sup> with MeOH becomes at least partly rate-limiting.



Scheme 1. R = H, Bu<sup>t</sup>, Pr<sup>i</sup>, or isopentyl.

Table 1. First-order rate constants<sup>a</sup> for the reactions of Bu<sup>t</sup>ONO and HNO<sub>2</sub> with various substrates.

Substrate	Bu <sup>t</sup> ONO [Substrate]/M	$k_0/s^{-1}$	Substrate	HNO <sub>2</sub> [Substrate]/M	$k_0/s^{-1}$
MeOH	0.023	32	MeOH	0.025	27
MeOH	0.046	36	MeOH	0.050	25
MeOH	0.070	32	MeOH	0.077	28
MeOH	0.093	32	Pr <sup>i</sup> OH	0.0149	25
MeOH	0.117	33	Pr <sup>i</sup> OH	0.0446	26
R'SH	0.009	36	Bu <sup>t</sup> OH	0.0161	24
R'SH	0.014	35	R'SH	0.0265	22
			R'SH	0.0443	24

<sup>a</sup>  $k_0/s^{-1}$  at 25°C. Individual  $k_0$  values were reproducible to ca.  $\pm 2 s^{-1}$ .

This is, as far as we are aware, the first time that nitrosation by  $\text{HNO}_2$  or  $\text{RONO}$  has shown a fully zero-order dependence upon [substrate], thus kinetically identifying the nitrosonium ion  $\text{NO}^+$  as the electrophile, in this case in acetonitrile solvent. The situation is analogous to that which is well known<sup>3</sup> in the nitration of reactive aromatic systems, where a zero-order substrate dependence is consistent with rate-limiting  $\text{NO}_2^+$  formation. Previously, for some nitrous acid nitrosations in water, the observation of curved [substrate] vs. rate constant plots (for reaction with hydrogen peroxide),<sup>4</sup> and the existence of a small zero-order (in substrate) term in the rate equation (for reaction with thiosulphate ion),<sup>5</sup> have been interpreted in terms of  $\text{NO}^+$  reactions where  $\text{NO}^+$  formation is thought to be rate-limiting. However, in neither of these cases is the reaction fully zero-order with respect to the substrate concentration and both have an alternative explanation, based on a medium effect<sup>6</sup> (in the hydrogen peroxide case, where very high  $\text{H}_2\text{O}_2$  concentrations are used) and the existence of a minor pathway via  $\text{N}_2\text{O}_3$ , where  $\text{N}_2\text{O}_3$  formation is rate limiting<sup>7</sup> (in the thiosulphate case).

The results presented here show that both alkyl nitrites and nitrous acid in acetonitrile, react by an acid-catalysed pathway

to yield a nitrosating species in a rate-limiting stage. The most likely inference is that this species is the (solvated) nitrosonium ion  $\text{NO}^+$ , but other possibilities, such as a species where  $\text{NO}^+$  is covalently bonded to one solvent molecule, cannot be ruled out.

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