

# Kinetics and mechanism of nitrosation of toluene, *o*-xylene, and *m*-xylene in trifluoroacetic acid, or in acetic–sulfuric acid mixtures, under nitric oxide

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The title reactions give good yields with *m*-xylene, and modest yields with toluene and *o*-xylene which are successfully directly nitrosated for the first time. The advantages of purging with nitric oxide are demonstrated and discussed. The kinetics have been successfully interpreted in terms of a mechanism in which both the aromatic substrate and the nitrosoaromatics form, reversibly, complexes with nitrosonium ion. The nitrosoaromatics are unstable under the acid conditions and the method is successful only because of the protective complexation with the nitrosonium ion.

## Introduction

Electrophilic aromatic nitrosation is a reaction restricted to electron-rich aromatic compounds.<sup>1</sup> Studies are few. A major problem in preparative work, and also in mechanistic investigation, is the instability of the aromatic nitroso-compounds formed. These can decompose in a number of ways, one of which is by oxidation, notably<sup>2</sup> by NO<sub>2</sub>, to the corresponding nitroaromatic. However in the investigation of nitrosation in which the observed products are nitroaromatics it is important to consider the possibility that these were formed, not by this nitrosation oxidation route but by nitration, whether nitrous acid catalysed<sup>3</sup> or directly following aerobic oxidation of nitrous to nitric acid.<sup>4</sup> Earlier studies need to be considered with caution in this respect.<sup>5</sup> Oxidation is not the only reaction to which nitrosoaromatics are prone. Their conjugate acids<sup>6</sup> are peculiarly susceptible to nucleophilic attack as, for instance, in the formation of nitrosophenols following the reaction of aryl ethers with nitrous acid,<sup>5–7</sup> the formation of *p*-benzoquinone monoxime from 4-chloronitrosobenzene and self-condensation of nitrosobenzenes leading to *N*-aryl-*N*-4-nitrosoarylhydroxylamines.<sup>8</sup> The complex chemistry of protonated aromatic nitrosocompounds in the presence of activated aromatic compounds has been probed.<sup>9</sup>

These difficulties in the way of preparative nitrosation have been circumvented in large part by the use of the non-acidic, non-nucleophilic, anhydrous and anaerobic conditions provided by solutions of nitrosonium tetrafluoroborate in acetonitrile under nitrogen.<sup>10</sup> With this system anisole and some substituted anisoles have been quantitatively or near-quantitatively nitrosated, as have polymethyl benzenes of reactivity equal to or greater than that of *m*-xylene. However the reaction is slow (85% conversion of *m*-xylene takes 24 h) and the method is unsuccessful with *o*-xylene and with toluene.<sup>10</sup> We have described in a preliminary communication<sup>11</sup> the use of nitric oxide saturation (as a means of reducing the problems of oxidation of both the nitrous acid and the aromatic) under acidic, non-aqueous conditions without using pre-prepared nitrosonium salts, and we give here a more detailed analysis of the kinetics and products of these reactions, as they relate to methylbenzenes.

## Results and discussion

### The method of introduction of nitrous acid, and the choice of acid solvent

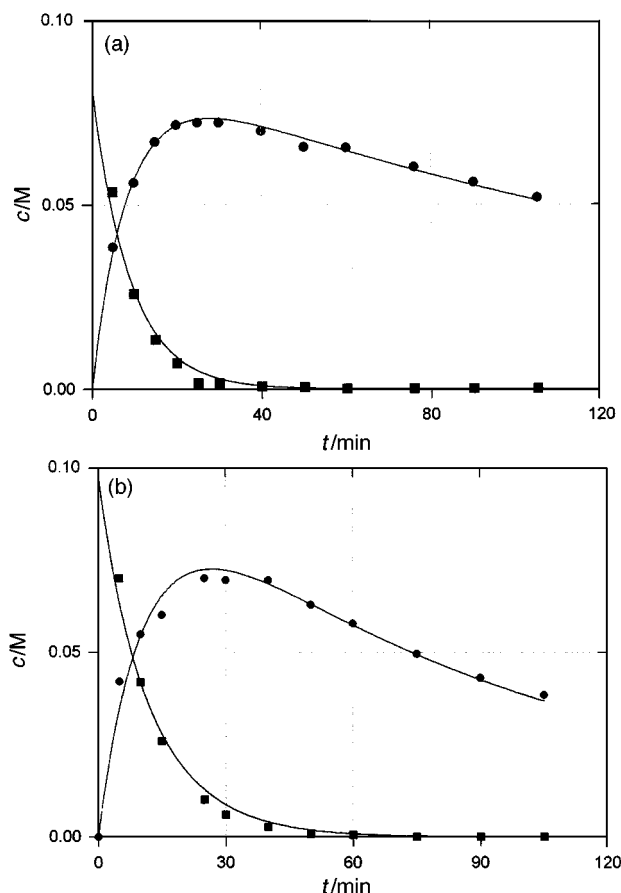
“Nitrous acid” is used here globally to include the N<sup>III</sup> species HNO<sub>2</sub>, N<sub>2</sub>O<sub>3</sub>, N<sub>2</sub>O<sub>3</sub>H<sup>+</sup>, and NO<sup>+</sup> which may be present in mobile equilibrium in acid solution.<sup>1,12</sup> The traditional way to introduce nitrous acid is by the addition of sodium nitrite to an acid solution. This presented difficulties in the present work. Two alternative methods were adopted. For acetic–sulfuric mixtures, commercially available 40% nitrosyl sulfuric acid was used in admixture with acetic and sulfuric acids. Tests showed this gave the calculated concentration of nitrous acid. In the alternative method, use was made of the purging stream of nitric oxide, the inlet tube for which was fitted with a glass bulb into which oxygen was injected by gas syringe through a septum. This reacts with excess NO to form N<sub>2</sub>O<sub>3</sub> [eqn. (1)] which



is carried into solution generating an equilibrium mixture of N<sup>III</sup> species.

Eqn. (1) implies that one mole of oxygen gives rise to four moles of nitrous acid. Independent tests showed that this reaction was quantitative for small injected volumes of oxygen, and reproducible but less than quantitative for higher volumes, dropping to about 3 moles nitrous acid per mole of oxygen at the higher injection volumes used in this work. A calibration graph was used to deduce nitrous acid concentrations from injected volumes of oxygen.

Trifluoroacetic acid as solvent is just sufficiently acidic to make nitrosonium ion the predominant N<sup>III</sup> species present<sup>13</sup> and therefore presented itself as a suitable reaction medium. We also investigated the cheaper alternative of acetic–sulfuric mixtures. The ionisation ratio,  $I = [\text{NO}^+]/[\text{HNO}_2]$ , was measured (see Experimental section) for dilute solutions of nitrous acid in various acetic–sulfuric mixtures and found to be related to  $H_0$  (data for which is available<sup>14</sup>) by  $\log I = -1.86H_0 - 4.24$ . Thus NO<sup>+</sup> is the predominant N<sup>III</sup> species for dilute solutions of nitrous acid in acetic–sulfuric mixtures containing more than 4% by mass of sulfuric acid.



**Fig. 1** Concentrations of *m*-xylene (■) and 1,3-dimethyl-4-nitrosobenzene (●) in the nitrosation of *m*-xylene in acetic–sulfuric acid mixtures containing 36.9% by mass of sulfuric acid, under NO at 28 °C. (a)  $[\text{NO}^+] = 0.464 \text{ mol dm}^{-3}$ . (b)  $[\text{NO}^+] = 0.308 \text{ mol dm}^{-3}$ .

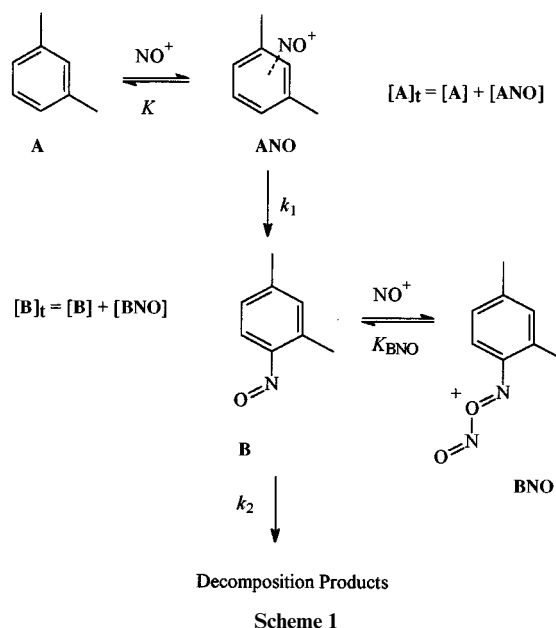
#### Nitrosation of *m*-xylene in acetic–sulfuric acid mixtures

Preliminary investigations showed that solutions containing 30–40% sulfuric acid by mass gave optimal yields in the nitrosation of *m*-xylene. A standard concentration of 36.9% by mass of sulfuric acid was adopted. In such solutions  $\text{N}^{\text{III}}$  is present almost entirely as  $\text{NO}^+$ . This was introduced using nitrosyl sulfuric acid.

The concentration/time curves, examples of which are Figs. 1(a) and (b), showed that increasing initial  $[\text{NO}^+]$  increased the maximum yield, but did not shorten the time needed to achieve it. Thus it is not, as might have been expected, the rate of formation of 1,3-dimethyl-4-nitrosobenzene that has been significantly enhanced by increasing  $[\text{NO}^+]$ , but rather that the rate of its decomposition has been diminished.

This can be understood in terms of the mechanism shown in Scheme 1.

It is known<sup>10,15</sup> that aromatics (like **A** in Scheme 1) and nitrosoaromatics (like **B**) form complexes with  $\text{NO}^+$ . The former are EDA (electron donor–acceptor) complexes (**ANO** in the scheme). Formation constants  $K$  (acetonitrile, room temperature) for *o*- and *p*-xylenes in the range 27–46  $\text{dm}^3 \text{ mol}^{-1}$  have been reported.<sup>15</sup> The complexes formed from **B** are thought to have structures like **BNO** in the scheme. Formation constants  $K_{\text{BNO}}$  for this type of complex are very much larger,<sup>10</sup> and for *m*-xylene our measured value<sup>16</sup> (trifluoroacetic acid, 25 °C) is 38000  $\text{dm}^3 \text{ mol}^{-1}$ . To avoid too many fitting parameters, this value for  $K_{\text{BNO}}$  was used in the fitting procedure. These equilibria are rapid and reversible, and in the analytical procedure **A** and **B** are released from their complexes so that the concentrations measured are  $[\text{A}]_t$  and  $[\text{B}]_t$  (see Scheme 1). The value of  $K$  was sought which led to the most constant value of  $k_1$  over the range of initial values of  $[\text{NO}^+]$ . This value of  $K$  was



**Table 1** Kinetics of nitrosation of *m*-xylene in acetic–sulfuric acid (containing 36.9% by mass of sulfuric acid) at 28 °C

| $[\text{NO}^+]/$<br>$\text{mol dm}^{-3}$ | $[m\text{-Xylene}]/$<br>$\text{mol dm}^{-3}$ | $10^4 k_1^a/$<br>$\text{s}^{-1}$ | $k_2^a/\text{s}^{-1}$ | Max yield <sup>b</sup><br>(%) | $T^c/\text{min}$ |
|------------------------------------------|----------------------------------------------|----------------------------------|-----------------------|-------------------------------|------------------|
| 0.464                                    | 0.0852                                       | 25                               | 1.07                  | 86                            | 28               |
| 0.400                                    | 0.107                                        | 22                               | 0.94                  | 82                            | 29               |
| 0.350                                    | 0.121                                        | 26                               | 0.88                  | 78                            | 25               |
| 0.308                                    | 0.099                                        | 22                               | 1.05                  | 73                            | 27               |
| 0.253                                    | 0.115                                        | 27                               | 0.78                  | 67                            | 24               |

<sup>a</sup> See Scheme 1. Values used for  $K$  and  $K_{\text{BNO}}$ : 10  $\text{dm}^3 \text{ mol}^{-1}$  and 38000  $\text{dm}^3 \text{ mol}^{-1}$  respectively. Rate constants deduced by the least squares fitting procedure of the “Scientist” software. <sup>b</sup> Maximum yield of 1,3-dimethyl-4-nitrosobenzene calculated using the kinetic and equilibrium constants given. <sup>c</sup> Calculated time of achievement of this maximum yield.

10  $\text{dm}^3 \text{ mol}^{-1}$ , a little smaller than those reported for *o*- and *p*-xylenes under somewhat different conditions. It led to the fitted values of  $k_1$  (the first-order rate constant for the conversion of the EDA complex between *m*-xylene and nitrosonium ion into 1,3-dimethyl-4-nitrosobenzene) and  $k_2$  (the first-order rate constant for the decomposition of uncomplexed 1,3-dimethyl-4-nitrosobenzene) in Table 1. (The value of  $K$  is not accurately determined by this technique; any value between 5 and 20  $\text{dm}^3 \text{ mol}^{-1}$  gives acceptable constancy of  $k_1$ . The values of  $k_1$  are not sensitive to the chosen value of  $K$  within this range. Similarly the relative values of  $k_2$  are not sensitive to the value of  $K_{\text{BNO}}$  provided that it is of the order of magnitude stated.)

The values of  $k_1$  and  $k_2$  show some scatter but no trend with changing  $[\text{NO}^+]$ . This is good evidence that the mechanism of Scheme 1 is broadly correct. The quality of the fit is illustrated by the curves in Fig. 1, which were generated using the “Scientist” numerical integration computer package, the least squares fitting procedure of which gave rise to the curves shown and the rate constants in Table 1.

Increasing  $[\text{NO}^+]$  only marginally enhances the rate of nitrosation because the equilibrium between *m*-xylene and its EDA complex is well over towards the complex even at the lowest concentration used. Increasing  $[\text{NO}^+]$  is however protective because it reduces still further the very small concentration of uncomplexed 1,3-dimethyl-4-nitrosobenzene, the species undergoing the decomposition reaction. This is the reason for the reduced rate of decomposition at the larger initial  $[\text{NO}^+]$  [compare Figs. 1(a) and (b)].

The practical advantage of using as high  $[\text{NO}^+]$  as is practi-

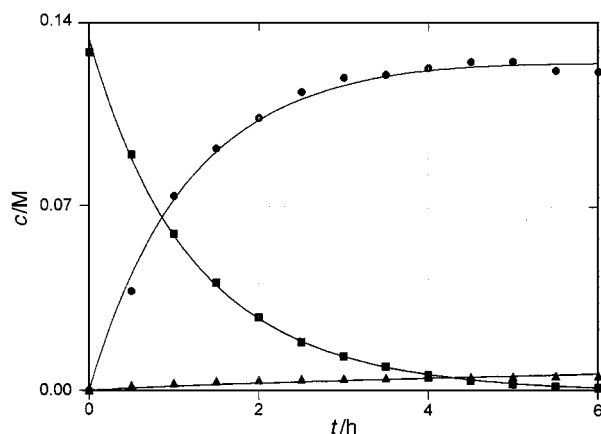


Fig. 2 Concentrations of *m*-xylene (■), 1,3-dimethyl-4-nitrosobenzene (●) and 1,3-dimethyl-4-nitrobenzene (▲) in the nitrosation of *m*-xylene in anhydrous trifluoroacetic acid under NO at 28 °C.  $[\text{NO}^+] = 0.450 \text{ mol dm}^{-3}$ .

ably possible thus lies in the enhanced maximum yield, rather than in the reduced time for its attainment.

The rate constant  $k_2$  for the decomposition of 1,3-dimethyl-4-nitrosobenzene (Table 1, mean value  $0.94 \text{ s}^{-1}$ ) indicates that in the absence of nitrosonium ion the material would be very unstable and have a half-life of less than a second. In accord with this, a sample of 1,3-dimethyl-4-nitrosobenzene in the same solvent examined by NMR was found to have decomposed completely within 2 minutes of preparation.

Products of decomposition of 1,3-dimethyl-4-nitrosobenzene have not been identified. The  $^1\text{H}$  NMR spectrum showed considerable complexity in both the aromatic and the methyl region showing that many products of varying stability are formed.

#### Nitrosation of *m*-xylene in anhydrous trifluoroacetic acid and in 91% aqueous trifluoroacetic acid

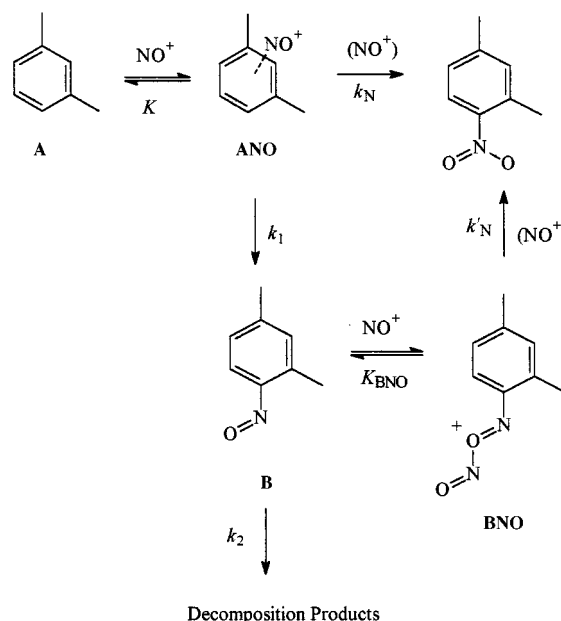
For these experiments nitrous acid was introduced by oxygen injection into the input stream of nitric oxide as described above. With anhydrous trifluoroacetic acid, sufficient trifluoroacetic anhydride was added to react with the water generated by reactions (1) and (2). (Later tests revealed however that



this precaution was unnecessary; results were very similar if trifluoroacetic anhydride was not added.)

The reaction gave 1,3-dimethyl-4-nitrosobenzene in nearly quantitative yield. Some 1,3-dimethyl-4-nitrobenzene was also formed (Fig. 2) as it was in the other two runs to be described in this section. Attempts to fit the results including the observed profile for 1,3-dimethyl-4-nitrobenzene, were successful when the latter was assumed to arise in part from ANO and in part from BNO. These extensions to Scheme 1 are shown in Scheme 2. Rate constants are in Table 2. Compared with the acetic-sulfuric system (Table 1) both formation and decomposition of 1,3-dimethyl-4-nitrosobenzene are slower, but the latter effect is more significant and accounts for the superior maximum yield.

Reactions in 91% aqueous trifluoroacetic acid both under nitric oxide and under nitrogen, [Fig. 3(a) and (b)] were studied in order to make direct comparison with reported results for reaction in this solvent system under aerobic conditions<sup>17</sup> where 1,3-dimethyl-4-nitro- and 1,3-dimethyl-2-nitrobenzene are formed in 5 : 1 ratio *via* their corresponding nitroso-compounds. Reaction under nitric oxide gives no 2-substitution. The major product is 1,3-dimethyl-4-nitrosobenzene, but a small amount of 1,3-dimethyl-4-nitrobenzene is also formed. Their combined yields account quantitatively for the *m*-xylene consumed. Reaction under nitrogen gives traces of 2-substitution [1,3-dimethyl-



Scheme 2

2-nitrosobenzene (<1%), and 1,3-dimethyl-2-nitrobenzene (1.5% after 3 h), less 1,3-dimethyl-4-nitrosobenzene and more 1,3-dimethyl-4-nitrobenzene [Fig. 3(b)].

Thus when nitrogen rather than air is the saturating gas, 2-substitution is much reduced, and when nitric oxide is used, 2-substitution is eliminated. Nitric oxide also drastically reduces formation of the 4-nitro compound.

These results can be explained as follows: The major factor is the effect of the saturating gas on the concentration of  $\text{NO}_2$ . When nitrogen is used, preventing the oxidation which occurs under aerobic conditions [eqns. (3) and (4)],  $[\text{NO}_2]$  is diminished. When nitric oxide is the saturating gas, the high  $[\text{NO}]$  shifts equilibrium (3) to the left, causing a further decrease in  $[\text{NO}_2]$ .



Nitroso compounds react with  $\text{NO}_2$  to form nitro compounds,<sup>2</sup> so the efficacy of  $\text{N}_2$ , and the greater efficacy of  $\text{NO}$ , in reducing nitroso-to-nitro conversion is explained. The effect on positional selectivity is less clear. One route<sup>3</sup> to both 2- and 4-nitro compounds would be through nitrous acid catalysed nitration, that is reaction of *m*-xylene radical cation with  $\text{NO}_2$ , with the former generated by reversible homolysis of either the EDA or the Wheland intermediate (Scheme 3). A high concentration of  $\text{NO}$  would inhibit this pathway by reducing the concentrations of both *m*-xylene radical cation and  $\text{NO}_2$ , the radicals which combine in relatively unselective radical formation of nitro compounds. However in such a reaction nitroso compounds are not intermediates and this does not explain the reported formation of the 2-nitrosocompound as a precursor of the 2-nitrocompound under aerobic conditions.<sup>17</sup>

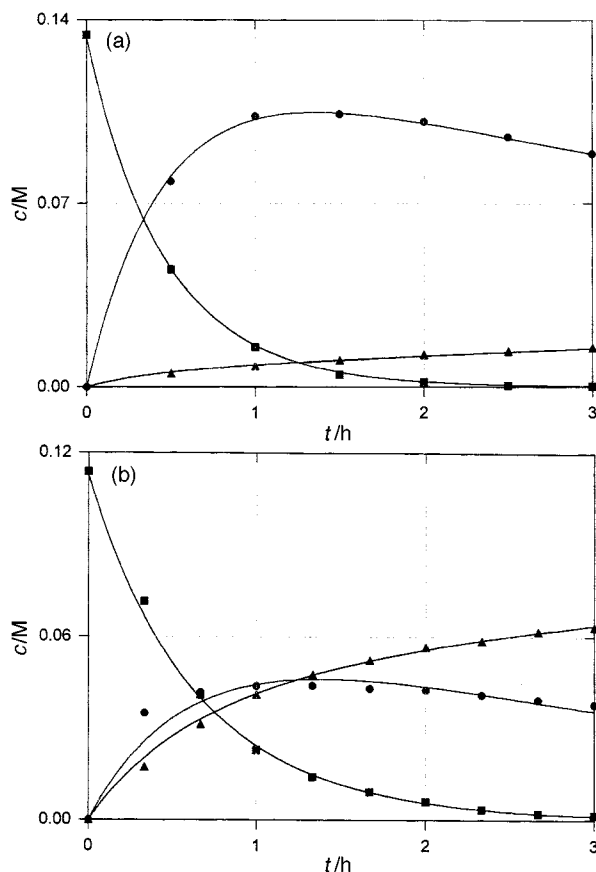
#### Nitrosation of toluene and *o*-xylene

Direct nitrosations were successfully achieved for the first time, in modest yield, using anhydrous trifluoroacetic acid (38 °C) flushed with nitric oxide as the reaction medium (Figs. 4 and 5). (Similar attempts to nitrosate toluene with acetic-sulfuric mixtures, and with 91% aqueous trifluoroacetic acid, as reaction media were by contrast disappointing, with maximum yields of 2% and 3% respectively.)

**Table 2** Kinetics of nitrosation<sup>a</sup> of *m*-xylene<sup>b</sup> in trifluoroacetic acid and in aqueous trifluoroacetic acid at 28 °C

| TFA (%) <sup>c</sup> | Gas <sup>d</sup>            | $10^4 k_1$ s <sup>-1</sup> | $10^4 k_N$ /dm <sup>3</sup> mol <sup>-1</sup> s <sup>-1</sup> | $10^4 k'_N$ /dm <sup>3</sup> mol <sup>-1</sup> s <sup>-1</sup> | $k_2$ s <sup>-1</sup> | Max yield <sup>f</sup> (%) | $t^g$ /min      |
|----------------------|-----------------------------|----------------------------|---------------------------------------------------------------|----------------------------------------------------------------|-----------------------|----------------------------|-----------------|
| 100                  | NO                          | 3.0                        | 0.16                                                          | 1.1                                                            | 0                     | 95                         | 300             |
| 91                   | NO                          | 6.5                        | 1.3                                                           | 0.37                                                           | 0.064                 | 78                         | 84              |
| 91                   | N <sub>2</sub> <sup>h</sup> | 2.9                        | 6.2                                                           | 1.6                                                            | 0.082                 | 40                         | 72              |
| 91                   | Air <sup>i</sup>            |                            |                                                               |                                                                |                       | 50 <sup>i</sup>            | 80 <sup>i</sup> |

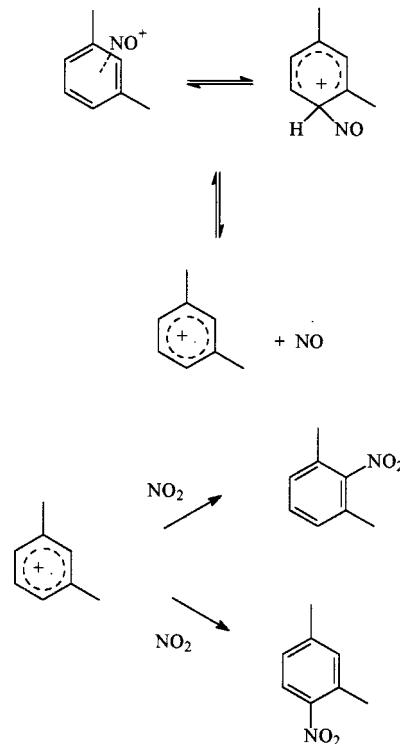
<sup>a</sup>  $[N^{III}]_0 = 0.450 \text{ mol dm}^{-3}$ . <sup>b</sup>  $[m\text{-Xylene}]_0 = 0.10\text{--}0.14 \text{ mol dm}^{-3}$ . <sup>c</sup> % by mass of trifluoroacetic acid. <sup>d</sup> Saturating gas. <sup>e</sup> See Scheme 2. Values used for  $K$  and  $K_{BNO}$  for 100% trifluoroacetic acid, where ionisation of nitrous acid to nitrosonium ion is essentially complete,<sup>13</sup> as in Table 1. Values reduced by a factor of four in 91% trifluoroacetic acid because the fraction of  $N^{III}$  present as nitrosonium ion in this medium is 0.25.<sup>13</sup> Rate constants deduced by the least squares fitting procedure of the "Scientist" software. <sup>f</sup> Maximum yield of 1,3-dimethyl-4-nitrosobenzene calculated using the kinetic and equilibrium constants given. <sup>g</sup> Calculated time of achievement of the maximum yield of 1,3-dimethyl-4-nitrosobenzene. <sup>h</sup> Traces of 1,3-dimethyl-2-nitrosobenzene (<1%) and 1,3-dimethyl-2-nitrobenzene (1.5% after 3 h) were observed amongst the products. <sup>i</sup> Results from ref. 8. Yield and time estimated from the published graph. 1,3-Dimethyl-2-nitrosobenzene and 1,3-dimethyl-2-nitrobenzene were also observed in substantial amounts (concentrations one-fifth of those of the corresponding 4-substituted compounds).



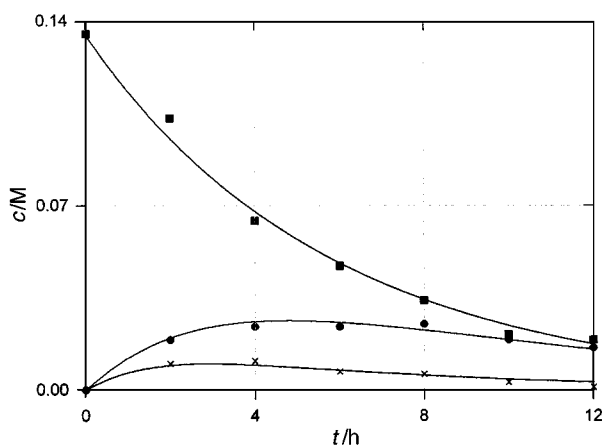
**Fig. 3** Concentrations of *m*-xylene (■), 1,3-dimethyl-4-nitrosobenzene (●) and 1,3-dimethyl-4-nitrobenzene (▲) in the nitrosation of *m*-xylene in 91% aqueous trifluoroacetic acid at 28 °C.  $[NO^+] = 0.450 \text{ mol dm}^{-3}$ . (a) Under NO. (b) Under N<sub>2</sub>.

With toluene, *o*- and *p*-nitrosotoluenes were the major initial products, but small amounts of *o*- and *p*-nitrotoluenes were also detected in steadily increasing amount throughout the 12 hour monitoring period, at the end of which their combined yield was 4.5%. *o*-Xylene (Fig. 5) gave rise to 1,2-dimethyl-4-nitrosobenzene, a small amount of 1,2-dimethyl-3-nitrosobenzene, and trace amounts only of nitrocompounds. Products of decomposition of the nitrosotoluenes and xylenes have not been identified. The <sup>1</sup>H NMR spectrum showed considerable complexity in both the aromatic and the methyl region showing that many products of varying stability are formed.

Analysis of the kinetics is difficult for several reasons. Firstly, the mechanism needs to be enlarged to allow for two alternative sites of reaction, as in Scheme 4. Secondly, equilibrium constants  $K_{BNO}$  (for complexation of the nitroso compounds with nitrosonium ion) are known only for 1,3-dimethyl-4-nitrosobenzene and 4-nitrosotoluene (38000 and 58000 dm<sup>3</sup> mol<sup>-1</sup>

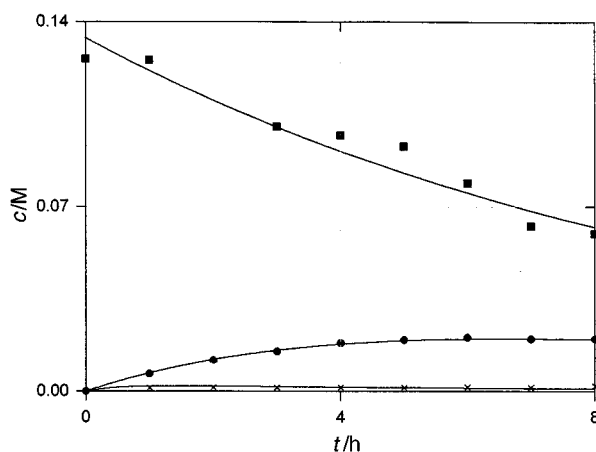


**Scheme 3**



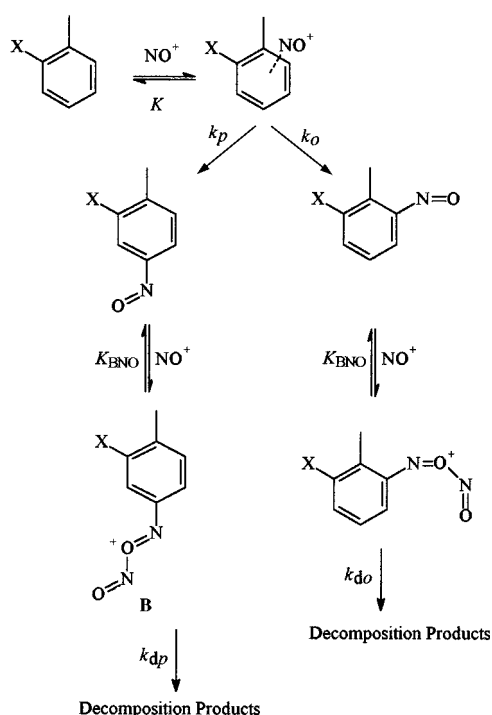
**Fig. 4** Concentrations of toluene (■), *p*-nitrosotoluene (●) and *o*-nitrosotoluene (×) in the nitrosation of toluene in anhydrous trifluoroacetic acid under NO at 38 °C.  $[NO^+] = 0.450 \text{ mol dm}^{-3}$ . Nitrotoluenes, not shown, were also formed and represented 4.5% of the consumed toluene after 12 h.

respectively<sup>16</sup>) and thirdly, nitroaromatics are also formed in small or trace amount. In order to reduce the number of fitting parameters we have ignored the nitroproducts, used the same



**Fig. 5** Concentrations of *o*-xylene (■), 1,2-dimethyl-4-nitrosobenzene (●) and 1,2-dimethyl-3-nitrosobenzene (×) in the nitrosation of *o*-xylene in anhydrous trifluoroacetic acid under NO at 28 °C.  $[\text{NO}^+] = 0.450 \text{ mol dm}^{-3}$ .

values of  $K$  and  $K_{\text{BNO}}$  (10 and  $38000 \text{ dm}^3 \text{ mol}^{-1}$  respectively) in all cases (fortunately the rate constants are rather insensitive to these values), and obtained rate constants using the mechanism of Scheme 4 and the numerical integration method used previ-



**Scheme 4** For toluene ( $X = \text{H}$ ) and *o*-xylene ( $X = \text{Me}$ ).

ously. The results are in Table 3, which includes for comparison results for nitrosation of *m*-xylene at the same temperature and analysed according to Scheme 1.

Nitrosations of toluene and *o*-xylene give a mixture of nitrosocompounds. This lack of regioselectivity is not surprising if comparison is made with nitration;<sup>18</sup> however it contrasts strongly with the nitrosations of anisole<sup>10,11</sup> and *m*-xylene (see above) which, quite unlike nitration, occur exclusively at the 4-position. The difference between nitration and nitrosation in these latter cases has been attributed<sup>10</sup> to the fact that in nitrosation, Wheland intermediate deprotonation is rate-limiting [as shown by kinetic hydrogen isotope effects (k.h.i.e.s) of 3–4<sup>5,7,10,19</sup>] whereas in nitration the formation of the Wheland intermediate is rate-limiting. This led us to check for a kinetic hydrogen isotope effect in the nitrosation of toluene.

**Table 3** Kinetics of nitrosation<sup>a</sup> of toluene, [4-<sup>2</sup>H]toluene, and *o*-xylene (according to Scheme 3), and *m*-xylene (Scheme 1), in 100% trifluoroacetic acid at 38 °C

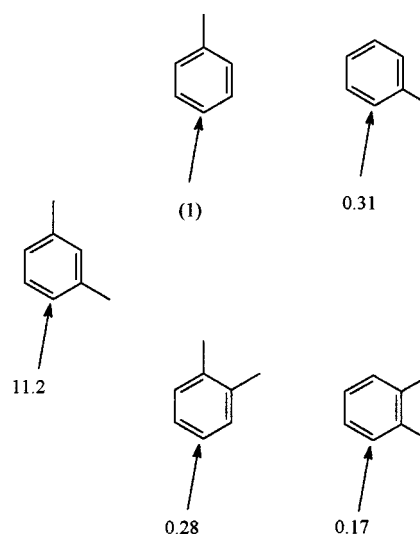
|                            | $10^4 k_p/\text{s}^{-1}$ | $10^4 k_o/\text{s}^{-1}$ | $k_{dp}/\text{s}^{-1}$ | $k_{do}/\text{s}^{-1}$ |
|----------------------------|--------------------------|--------------------------|------------------------|------------------------|
| Toluene                    | 0.408                    | 0.254                    | 0.645                  | 1.52                   |
| [4- <sup>2</sup> H]Toluene | 0.200                    | 0.254                    | 0.645                  | 1.52                   |
| <i>o</i> -Xylene           | 0.224                    | 0.140                    | 0.601                  | 6.81                   |
| <i>m</i> -Xylene           | 9.16 <sup>b</sup>        |                          | 0.507 <sup>c</sup>     |                        |

<sup>a</sup>  $[\text{NO}^+]_0 = 0.40 \text{ mol dm}^{-3}$  (toluene, [4-<sup>2</sup>H]toluene, and *o*-xylene) or  $0.45 \text{ mol dm}^{-3}$  (*m*-xylene). Values used for  $K$  and  $K_{\text{BNO}}$  in all cases: 10 and  $38000 \text{ dm}^3 \text{ mol}^{-1}$ . Rate constants deduced by the least squares fitting procedure of the "Scientist" software. <sup>b</sup> Value of  $10^4 k_1/\text{s}^{-1}$  (Scheme 1). <sup>c</sup> Value of  $k_2/\text{s}^{-1}$  (Scheme 1).

The ratio of rate constants  $k_1$  for conversion of the EDA complexes of toluene and [4-<sup>2</sup>H] toluene into *p*-nitrosotoluene is  $2.0 \pm 0.1$  (Table 3). This, though smaller than previously measured k.h.i.e.s for nitrosation, shows that proton loss from the Wheland intermediate must be at least partially rate-limiting.

### Relative reactivities of ring-positions in toluene and *o*- and *m*-xylene

From the results in Table 3, reactivities of ring positions were calculated relative to that of the *p*-position in toluene and statistically corrected to take into account equivalent ring positions, and are in Scheme 5. These reactivities relate to the conversion



**Scheme 5**

of the pre-formed EDA complex into the transition state and not (as is more usually the case in other electrophilic aromatic substitutions) to the conversion of the bare aromatic into the transition state. It is clear that *o*- and *p*-methyl are activating, but it is noteworthy that *m*-methyl is deactivating (vertical comparisons in the scheme). This is why the *o*-xylene- $\text{NO}^+$  EDA complex reacts more slowly than the toluene- $\text{NO}^+$  EDA complex (Figs. 4 and 5).

### Conclusions

Electrophilic aromatic nitrosation of aromatics of reactivity comparable to or greater than that of toluene can be achieved using acid solutions, despite the instability of protonated aromatic nitroso compounds, because of the protective effect of strong complexation between aromatic nitroso compounds and nitrosonium ion. The prospects for extending the method to less reactive aromatics are not good. Decomposition rate constants (Tables 1–3) do not diminish with decreasing

aromatic reactivity. Thus maximum yields will be even smaller than with toluene.

Nitrosation differs significantly from nitration in that in the former, Wheland intermediate deprotonation is rate-limiting, and in the latter, Wheland intermediate formation is rate limiting. Prior to this work this appeared to explain the marked difference in regioselectivity in the two reactions.<sup>10</sup> Our results for toluene seem to cast doubt on this explanation. However the relatively small *k*.h.i.e (2.0) observed with toluene may be an indication that this is an aromatic for which Wheland intermediate deprotonation is only partially rate limiting, and that as one moves to less reactive aromatics, formation of the Wheland intermediate will become rate limiting, as in nitration, and abnormal regioselectivities will disappear. It is not at present possible to test this hypothesis because a method of nitrosating less reactive aromatics has yet to be devised.

## Experimental

### Materials

Trifluoroacetic acid (99%) was distilled from 10% (v/v) sulfuric acid, under nitrogen. Dichloromethane (Fischer) was distilled from calcium hydride. Oxygen was dried by passing through a column of diphosphorus pentoxide prior to use. Nitrosyl sulfuric acid (40 wt% NOHSO<sub>4</sub> in sulfuric acid) (Aldrich) was used as supplied.

### 1,3-Dimethyl-4-nitrosobenzene

50 cm<sup>3</sup> of a mixture of aristar grade glacial acetic acid (100.00 g), 40 wt% nitrosyl sulfuric acid (21.58 g) and sulfuric acid (39.46 g) were placed in a thermostatted vessel at 25 °C and nitrogen was allowed to flow for 5 minutes; following this the gas flow was changed to nitric oxide. After a further 5 minutes *m*-xylene (0.99 g, 9.32 mmol) was added by injection. The solution turned opaque dark red/brown.

Ten minutes after the addition of substrate the purging gas was switched to nitrogen. After a further 2 minutes the solution was quenched in saturated sodium hydrogen carbonate solution (1000 cm<sup>3</sup>), the crude product was extracted using dichloromethane (3 × 200 ml), the organic layers were collected, dried (MgSO<sub>4</sub>), filtered and the solvent removed on a rotary evaporator. The crude product was a brown oil with a crude yield of 0.43 g, 43%. This was purified by column chromatography [60 g flash silica, 20% hexane in dichloromethane (v/v) as eluent], the fraction at an *R*<sub>F</sub> of 0.70 was collected, the purified yield was 0.24 g, 19%. Mp (46.0–47.0 °C, lit.<sup>20</sup> 44 °C) *v*<sub>max</sub>/cm<sup>-1</sup> (CH<sub>2</sub>Cl<sub>2</sub>) 1494 (N–O), 2983, 3054 (C–H (CH<sub>3</sub>)); δ<sub>H</sub> (300 MHz, CDCl<sub>3</sub>), 7.37 (1H, s, C(2)H), 6.30 (1H, d, *J* = 7.9 Hz, C(6)H), 6.95 (1H, d, *J* = 7.9 Hz, C(5)H), 3.28 (3H, s, C(3)–CH<sub>3</sub>), 2.38 (3H, s, C(1)–CH<sub>3</sub>).

### 4-Nitrosotoluene, 1,2-dimethyl-4-nitrosobenzene, and 1,2-dimethyl-3-nitrosobenzene

These were prepared by the method described.<sup>21</sup>

**4-Nitrosotoluene.** δ<sub>H</sub> lit.<sup>22</sup> (300 MHz, CDCl<sub>3</sub>), 2.45 (3H, s, CH<sub>3</sub>), 7.40 (2H, d, *J* = 7.9 Hz, C(2)H, C(6)H), 7.80 (2H, d, *J* = 7.9 Hz, C(3)H, C(5)H).

**1,2-Dimethyl-4-nitrosobenzene.** δ<sub>H</sub> lit.<sup>22</sup> (300 MHz, CDCl<sub>3</sub>), 2.37 (3H, s, C(1)–CH<sub>3</sub>), 2.40 (3H, s, C(2)–CH<sub>3</sub>), 7.38 (1H, d, *J* = 7.9 Hz, C(6)H), 7.61 (1H, s, C(3)H), 7.74 (1H, d, *J* = 8.0 Hz, C(5)H); *m/z* M<sup>+</sup> 135.068414, expected 135.166.

**1,2-Dimethyl-3-nitrosobenzene.** δ<sub>H</sub> (300 MHz, CDCl<sub>3</sub>), 2.55 (3H, s, C(1)–CH<sub>3</sub>), 3.37 (3H, s, C(2)–CH<sub>3</sub>), 6.05 (1H, d, *J* = 7.9 Hz, C(4)H), 7.07 (1H, tr, C(5)H), 7.54 (1H, d, *J* = 7.9 Hz, C(6)H); *m/z* M<sup>+</sup> 135.068414, expected 135.166.

### [4-<sup>2</sup>H]-Toluene

This was prepared from *p*-tolylmagnesium bromide as described.<sup>23</sup>

### Nitrosation of *m*-xylene with several concentrations of N<sup>III</sup> (Table 1 and Fig. 1)

A solution of acetic acid, sulfuric acid and 40 wt% nitrosyl sulfuric acid, of appropriate composition (50 cm<sup>3</sup>) was stirred, with nitrogen bubbling through, at 28 ± 1 °C for 30 minutes. The gas flow was changed to nitric oxide for a further 30 minutes. A mixture of 1,2,3-trichlorobenzene (GC reference standard) and *m*-xylene was added by injection. The solution quickly turned to a deep red colour which darkened over time. Nitric oxide flow was maintained. Aliquots (≈1 cm<sup>3</sup>) taken at intervals by syringe were quenched in a mixture of 30 cm<sup>3</sup> of saturated sodium hydrogen carbonate solution and 5 cm<sup>3</sup> of dichloromethane. The dichloromethane layers were extracted, washed, extracted and analysed by gas chromatography.

### Nitrosation of *m*-xylene, toluene, [4-<sup>2</sup>H]toluene, and *o*-xylene in trifluoroacetic acid (Tables 2 and 3 and Figs. 2–5)

Trifluoroacetic anhydride (4.08 g, 0.0194 mol) was added to 50 cm<sup>3</sup> of pure trifluoroacetic acid and stirred, with nitrogen bubbling through, at 28 ± 1 °C or 38 ± 1 °C for 120 minutes. The gas flow was changed to nitric oxide for 15 minutes then 180 cm<sup>3</sup> of dry oxygen gas was injected into a bulb in the gas inlet tube over 5–10 minutes. The solution turned a deep apple green. A mixture of 1,2,3-trichlorobenzene (GC reference standard) and *m*-xylene was added by injection. The solution quickly turned dark red/brown. Nitric oxide flow was maintained. Aliquots (≈1 cm<sup>3</sup>) were taken at intervals. For *m*-xylene, analysis was as above. For toluene, [4-<sup>2</sup>H]toluene and *o*-xylene, the 5 cm<sup>3</sup> of dichloromethane was replaced by 3 cm<sup>3</sup> of C<sup>2</sup>HCl<sub>3</sub> and analysis was by both GC and <sup>1</sup>H NMR.

For *m*-xylene, a reaction in which the trifluoroacetic anhydride was not added gave similar results. The same technique was used with 91% aqueous trifluoroacetic acid.

### Determination of the concentration of nitrous acid in solutions prepared by oxygen injection into the inlet nitric oxide stream, and from nitrosyl sulfuric acid

Trifluoroacetic acid solutions (50 cm<sup>3</sup>) were flushed with nitrogen, then with nitric oxide, as above. Volumes of oxygen gas (60–180 cm<sup>3</sup>) were injected into the inlet nitric oxide stream. The solution turned apple-green. Samples (2 cm<sup>3</sup>) were diluted to 100 cm<sup>3</sup> with water and the absorbance, after blank correction, was measured at 370 nm (a wavelength of maximum absorbance of nitrous acid in dilute aqueous acid solution). A calibration graph was constructed linking total N<sup>III</sup> concentrations in the trifluoroacetic acid to volumes of oxygen injected. This showed that an injection of 60 cm<sup>3</sup> oxygen gave an N<sup>III</sup> concentration of 0.20 mol dm<sup>-3</sup>, and an injection of 180 cm<sup>3</sup> oxygen gave an N<sup>III</sup> concentration of 0.45 mol dm<sup>-3</sup>. Points between gave a smooth curve. Samples of 40 wt% NOHSO<sub>4</sub> in sulfuric acid (Aldrich), diluted with nitrogen-flushed water and analysed similarly, showed that the nitrous acid content was as stated by the suppliers.

### Measurement of the nitrosonium ion/nitrous acid equilibrium ratio in acetic–sulfuric mixtures

Mixtures of acetic and sulfuric acid were purged with nitrogen, and then a solution of 40% nitrosyl sulfuric acid was added. Because of a slow drift of absorbances with time, absorbances in the range 280–330 nm were recorded at 1 minute intervals and the zero-time values obtained by back-extrapolation. The data for 0–12% sulfuric acid in the acetic–sulfuric mixtures were very similar to those for 84–98% aqueous trifluoroacetic acid<sup>13</sup>

and were analysed similarly by characteristic vector analysis.<sup>13</sup> The first scalar multiple accounted for 99.6% of the variance. (Absorbances of solutions containing more than 12% sulfuric acid fell with increasing sulfuric acid content in much the same way as in the 98–100% trifluoroacetic acid mixtures.<sup>13</sup> The reason for this is unclear.) Values of  $[\text{NO}^+]/[\text{HNO}_2]$  for the range 2–10% sulfuric acid in acetic acid were deduced as previously,<sup>13</sup> and, in the absence of  $H_f$  data for the media in question, were correlated with  $H_o$ <sup>14</sup> to give the relation in the main text above.

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