

# Nitrosation of *m*-xylene, anisole, 4-nitrophenyl phenyl ether and toluene in trifluoroacetic acid or in acetic-sulfuric acid mixtures under nitric oxide

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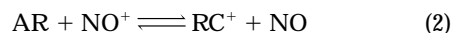
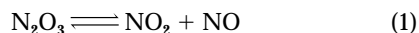
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**Nitrosation in trifluoroacetic acid or in acetic-sulfuric acid mixtures is regioselective and accompanying non-selective nitrous acid catalysed nitration can be avoided by purging with nitric oxide.**

Studies of electrophilic aromatic nitrosation in which the products have been clearly characterised are remarkably few.<sup>1</sup> Aromatic substrates strongly activated to electrophilic substitution appear to be necessary and products are often unstable under the conditions used.

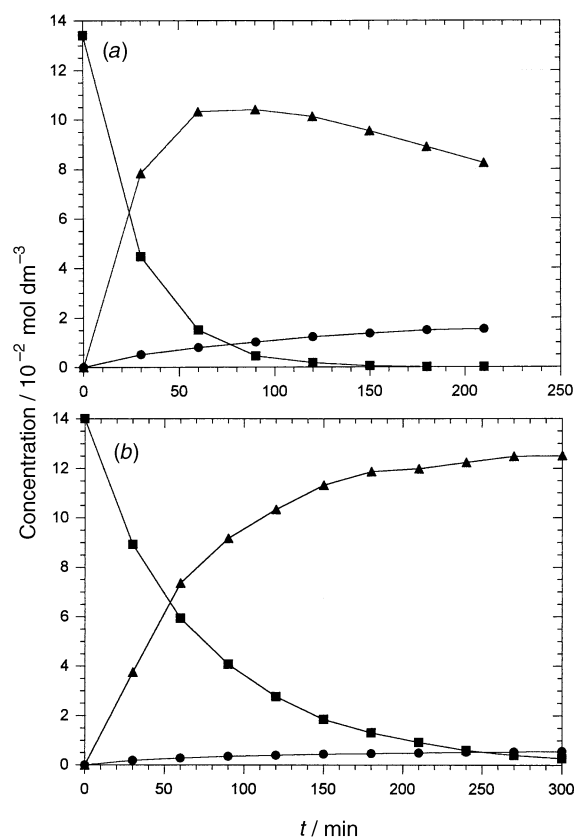
Nitrosoaryl ethers, formed by the nitrosation of aryl ethers in aqueous acid, are rapidly converted to nitrosophenols.<sup>2,3</sup> With alkylbenzenes, nitration rather than nitrosation is often the observed reaction; *m*-xylene in 65% sulfuric acid or 91% trifluoroacetic acid gives a mixture of nitro-*m*-xylenes in a reaction in which nitroso-*m*-xylenes were detected as intermediates.<sup>4</sup> The most successful method reported for aromatic nitrosation has used nitrosonium tetrafluoroborate in acetonitrile,<sup>5</sup> but the reagent is expensive and the reaction is slow, *m*-xylene for instance giving 4-nitroso-*m*-xylene in 85% yield after 24 h.

Nitrosation is much more regioselective than nitration, both with ethers and with alkyl benzenes,<sup>5</sup> and in view of the ease of oxidation of the nitroso product to the corresponding nitro compound, offers an attractive method for regioselective nitration, *i.e.* nitrosation followed by oxidation. For this purpose accompanying nitrous acid catalysed nitration, a totally different and less selective reaction in which a mixture of nitroisomers are formed by the combination of the aromatic radical cation with nitrogen dioxide<sup>6</sup> must be minimised. The use of an inert atmosphere<sup>5,7</sup> is helpful in preventing NO<sub>2</sub> production by the aerial oxidation of nitrous acid.<sup>8</sup> However nitrogen dioxide can still be formed reversibly by dinitrogen trioxide homolysis and the aromatic radical cation (RC<sup>+</sup>) can be formed, also reversibly, by electron transfer from aromatic to nitrosonium ion. We report the novel use of nitric oxide as a purging gas to prevent oxidative decomposition of nitrous acid and to reduce through equilibria (1) and (2) the concentrations of both



partners of the non-regioselective product-forming step of nitrous acid catalysed nitration.

The reaction solutions (trifluoroacetic acid or acetic-sulfuric acid mixtures) were flushed first with nitrogen and then with nitric oxide. Initially N<sup>III</sup> was introduced as solid sodium nitrite, but subsequently and more conveniently by injection of oxygen gas into a bulb in the inlet tube for nitric oxide. Tests of diluted samples showed that this procedure gave a reaction solution containing 3–4 moles of N<sup>III</sup> per mole of oxygen injected. The N<sup>III</sup> is present as an equilibrium mixture<sup>1,9</sup> of 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> in as yet unknown proportions, though we have evidence<sup>10</sup> that in 100% trifluoroacetic acid under our conditions NO<sup>+</sup> predominates. The aromatic, mixed with a GC reference compound, was added by injection



**Fig. 1** Concentrations of *m*-xylene (■), 4-nitroso-*m*-xylene (▲) and 4-nitro-*m*-xylene (●) as they vary with time in (a) 91% aqueous trifluoroacetic acid and (b) 100% trifluoroacetic acid containing 0.37 mol dm<sup>-3</sup> trifluoroacetic anhydride. Solutions were flushed with NO throughout and contained 0.48 mol dm<sup>-3</sup> N<sup>III</sup>, added by injection of oxygen into the inlet NO gas stream prior to addition of *m*-xylene.

through a septum. Purging with nitric oxide or nitrogen was continued during the experiment and samples of reaction solution were removed at intervals for analysis by gas chromatography. Fig. 1 shows representative time profiles. Results are summarised in Table 1.

Reaction of *m*-xylene with N<sup>III</sup> in 91% trifluoroacetic acid is reported<sup>4</sup> to give 4- and 2-nitro-*m*-xylenes in 5:1 proportion. Our results show that regioselectivity is greatly improved by purging with N<sub>2</sub> and still more by using NO. Substitution at the 2-position is eliminated. The yield of the product, in these circumstances 4-nitroso-*m*-xylene, goes through a maximum [Fig. 1(a)], its further reaction giving in part 4-nitro-*m*-xylene and in part unidentified products. A range of acetic-sulfuric mixtures were also investigated as solvents. The results were similar; those for the optimum mixtures are reported (Table 1).

Using 100% trifluoroacetic acid with sufficient added trifluoroacetic anhydride to react with the water formed in the production of NO<sup>+</sup>, leads to near quantitative production of 4-nitroso-*m*-xylene. The reaction is somewhat slower, but there

**Table 1** Yields expressed as percentages of starting aromatic (initial concentration 0.09–0.14 mol dm<sup>-3</sup>) for reaction with N<sup>III</sup> (initial concentration 0.30–0.48 mol dm<sup>-3</sup>)

Aromatic	Solvent <sup>a</sup>	Gas <sup>b</sup>	T/°C	t/min <sup>c</sup>	Yield (%)					
					AR <sup>d</sup>	4-NS <sup>d</sup>	2-NS <sup>d</sup>	4-N <sup>d</sup>	2-N <sup>d</sup>	U <sup>d</sup>
<i>m</i> -Xylene	TFA-W	N <sub>2</sub>	28	80 (max)	12	39	Trace	42	1	6
	TFA-w	NO	28	90 (max)	3	78	0	8	0	11
	37%A	NO	32	20 (max)	7	76	0	2	0	15
	TFA	NO	28	210 (end)	5	82	0	8	0	5
	TFA-A	NO	28	300 (end)	1	96	0	3	0	0
Anisole	TFA-A <sup>e</sup>	N <sub>2</sub>	r.t.	5 (max)	0	62	1	13	7	17
	TFA-A <sup>e</sup>	NO	r.t.	5 (max)	0	88	Trace	3	1	7
	16%A <sup>f</sup>	N <sub>2</sub>	r.t.	8 (max)	0	100	0	0	0	0
	16%A	NO	r.t.	2 (max)	7	93	0	0	0	0
4-NPPE <sup>g</sup>	TFA-A <sup>c</sup>	N <sub>2</sub>	r.t.	240 (end)	26	40	0	8	4	22 <sup>h</sup>
	TFA-A <sup>e</sup>	NO	r.t.	240 (end)	23	55	0	2	0	20 <sup>i</sup>
Toluene	TFA-A	NO	28	780 (end)	<i>j</i>	16	4	0	0	<i>j</i>

<sup>a</sup> TFA = 100% trifluoroacetic acid, TFA-A = 100% trifluoroacetic acid with added trifluoroacetic anhydride (0.3–0.4 M), TFA-W = 91% aqueous trifluoroacetic acid (w/w), x%A = acetic acid solvent containing the stated percentage by weight of sulfuric acid. <sup>b</sup> Gas used for purging, sufficient to maintain saturation at 1 atm. <sup>c</sup> Time at which the yield of the 4-nitroso product was a maximum (max) or if this yield increased throughout, time at the end of the monitoring period (end). <sup>d</sup> Percentage yields, based on starting aromatic; aromatic (AR), 4-nitrosoaromatic (4-NS), 2-nitrosoaromatic, (2-NS), 4-nitroaromatic (4-N), 2-nitroaromatic (2-N) and other products, unidentified except where stated, (U). <sup>e</sup> N<sup>III</sup> added as sodium nitrite, 0.30 mol dm<sup>-3</sup>. <sup>f</sup> N<sup>III</sup> added as sodium nitrite, 0.58 mol dm<sup>-3</sup>. <sup>g</sup> 4-Nitrophenyl phenyl ether. Analysis by HPLC. Reported yields are for substitution in the initially unsubstituted ring. <sup>h</sup> 2,4-Dinitrophenol, 18% (9% based on 2 mol per mol of aromatic.) <sup>i</sup> 2,4-Dinitrophenol (trace) present. <sup>j</sup> Toluene not determined by GC, but NMR revealed ca. 40% of initial toluene remained after 25 h.

was no detectable decomposition during the 5 h monitoring period [Fig. 1(b)]. This beneficial effect of reducing the nucleophile concentration suggests that decomposition takes place by nucleophilic attack at the ring carbon *para* to the protonated nitroso group giving an oxime.<sup>4</sup>

Anisole reacts much more quickly, as it does with nitrosonium tetrafluoroborate.<sup>4</sup> In an optimum acetic-sulfuric mixture the early yield based on consumed aromatic is quantitative within experimental error with N<sub>2</sub> or NO as the purging gas (Table 1). 4-Nitrophenyl phenyl ether is much less reactive towards electrophilic substitution. In separate experiments it was found that nitration in trifluoroacetic acid under conditions used previously<sup>11</sup> gives rise to 2,4'- and 4,4'-dinitrodiphenyl ethers (yield ratio 0.55 whether or not urea was present as a nitrous trap). It was of interest to see whether regioselective nitrosation of this much less strongly activated compound could be achieved. The table shows that this is the case and that the use of NO as a purging gas almost eliminates substitution at the 2'-position.

Toluene can also be nitrosated, albeit slowly and in modest yield (Table 1). This contrasts with the NO<sup>+</sup>BF<sub>4</sub><sup>-</sup>-CH<sub>3</sub>CN system, where no nitrosation was reported.<sup>5</sup>

The preparative utility of the method has thus been demonstrated and its scope is under active investigation. A kinetic analysis will be presented in a later publication.

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