

^{15}N -CIDNP Investigations during Nitration of Anisole with Nitric Acid and Sulfuric Acid in Acetic Acid†

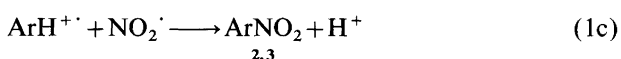
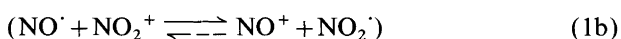
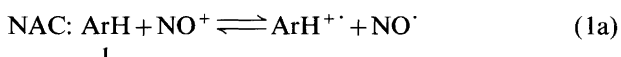
Manfred Lehnig

Fachbereich Chemie, Universität Dortmund, Otto-Hahn-Straße 6, D-44221 Dortmund, Germany

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During nitration of anisole (**1**) with ^{15}N -enriched nitric acid and sulfuric acid in acetic acid, the ^{15}N NMR signals of 2- and 4-nitroanisole (**2**, **3**) exhibit emission indicating their formation by a recombination reaction of radical cations $1^{+\cdot}$ with NO_2 . It is concluded from the magnitude of the ^{15}N -CIDNP effect that **2** is formed only via free radicals, whereas **3** may also be formed via a non-radical pathway.

The nitration of highly reactive arenes follows various reaction mechanisms depending on the reaction conditions.¹ Ridd and coworkers have shown by ^{15}N -CIDNP that the nitration of activated arenes, such as *p*-substituted phenols, polymethylbenzenes, amines and naphthalene, with nitric acid occurs, at least partially, via a nitrous acid catalysed reaction (NAC).²



1, Anisole; **2**, 2-Nitroanisole; **3**, 4-Nitroanisole

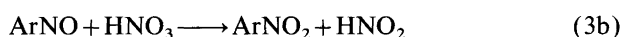
Eqn. (1b) is enclosed in parentheses, as it shows only the stoichiometry of the reaction. It does not involve free NO_2^+ but a more complex and as yet unidentified route. The key step is the one-electron transfer reaction to nitronium ion to give radical cation species.

A quantitative analysis of the ^{15}N -CIDNP effect observed during reaction of 1,2-dimethoxybenzene with nitric acid in acetic acid indicated that nitration occurs mainly or exclusively via NAC [eqns. (1)].³ The reaction did not take place in the presence of sodium azide which is a nitrous acid trap. It was concluded therefore that there is no electrophilic aromatic nitration (EAN) via nitronium ions.



A reaction through nitrosation followed by oxidation

$(\text{NOX})^4$ might be possible but in fact played a minor role, if any at all.



We could find no reference to a fourth mechanism, an electron transfer between the nitronium ion and the arene which might be an intermediate step during EAN [eqn. (2)].⁵

In the following, a ^{15}N -CIDNP study during nitration of **1** with nitric acid and sulfuric acid in acetic acid is described. This system is widely used as a nitration agent in synthetic organic chemistry.⁶ The reaction is known to give **2** and **3** as the main products,^{7–9} although large variations have been observed in the product distribution under different reaction conditions.¹⁰ This might be explained by the occurrence of EAN in some cases and of NAC or NOX in others.¹¹ Since the 2-/4- ratio should be 2.2–2.6 for EAN,^{10–12} 0.6–0.8 for NAC^{11,13} and 0.03–0.09 for NOX,^{10,11,14} the operating mechanisms can also be discussed in terms of the yields of **2** and **3**.

Experimental

^{15}N -CIDNP experiments were performed with a Bruker DPX-300 NMR spectrometer. The reactants were placed in 10 mm NMR tubes, after which the tubes were shaken, transferred to the probe head of the NMR spectrometer and locked (internal lock: D_2O) within 2 min. ^{15}N NMR spectra were then recorded using single pulses with a pulse angle of 90° . This procedure was repeated every 0.75–5 min. The intensities of the emission signals I during the reaction and the product signals I_0 after

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completion of the reaction were determined from the signal-to-noise ratios in the spectra or by integration. ^{15}N nuclear relaxation times T_1 were determined after completion of the reaction under the conditions of the experiment applying π - $\pi/2$ pulse sequences. All the compounds were commercial samples and used without further purification. The nitric acid was 9.4 mol dm^{-3} in H_2O and labelled with 60.3 atom % ^{15}N (Isotec Inc.).

The nitration products 2- and 4-nitroanisole **2**, **3** were identified by comparing the ^{15}N , ^{13}C and ^1H NMR spectra with NMR spectra of authentic material. The yields were determined from ^{15}N NMR spectra after completion of the reaction, see Fig. 1(c).

Enhancement factors V_{max} were taken from the maximum emission intensity I_{max} and I_0 .¹⁵

$$V_{\text{max}} = (I_{\text{max}} - I_0) / I_0 \quad (4)$$

Results and discussion

During the treatment of anisole **1** with nitric acid in acetic acid, 2-nitroanisole **2** and 4-nitroanisole **3** were formed as the main products at room temperature or at higher temperatures,⁷⁻⁹ however the reaction was too slow to permit the observation of CIDNP effects at room temperature. This is in contrast with the behaviour of 1,2- and 1,4-dimethoxybenzene, whose reactions with nitric acid in acetic acid are complete within a few minutes. ^{15}N -CIDNP effects were observed in the nitration products 1,2-dimethoxy-4-nitrobenzene and 1,4-dimethoxy-2-nitrobenzene under these conditions.³

After addition of 20% sulfuric acid to a solution of **1** and nitric acid in acetic acid, however, the reaction was complete within a few minutes. A ^{15}N NMR spectrum taken after the reaction is given in Fig. 1(c). Compounds **2** and **3** were the main products and formed in yields of 25% and 65%. ^{15}N NMR shifts and yields of **2** and **3** and of two additional products, **4** and **5** showing ^{15}N NMR signals at $\delta = -2.7$ and -5.4 are listed in Table 1.

While the reaction was running within the probehead of the spectrometer, the ^{15}N NMR signals of **2-5** indicated emission 5 min after the tube had been placed in the probehead. The CIDNP signals disappeared within an additional 5-12 min. Intensities I of the signals are

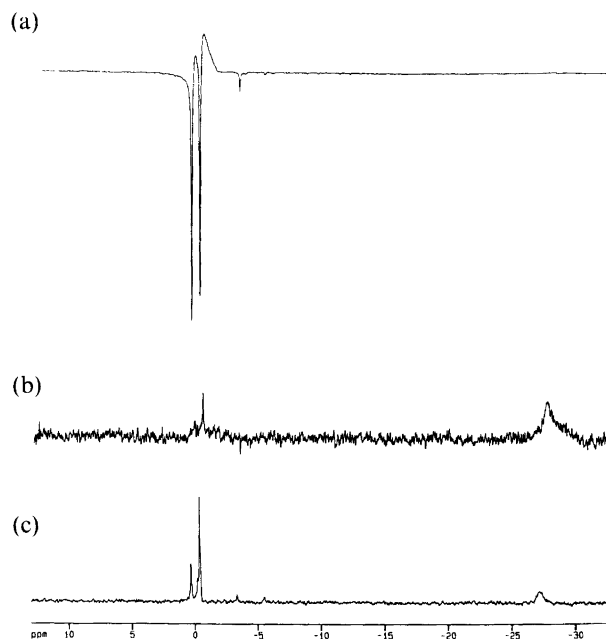


Fig. 1. ^{15}N NMR spectra taken from **1** in $\text{AcOH-H}_2\text{SO}_4$; (a) 8.75 min after addition of H^{15}NO_3 taken with a single 90° pulse; (b) ≈ 10 min later taken with a single 90° pulse; the intensity is enhanced by a factor of 20; (c) 1-2 h later taken with 32 pulses.

given in Table 2, and typical spectra are shown in Fig. 1(a),(b). The poor quality of the spectrum in Fig. 1(a) is probably due to foaming during the reaction. After the reaction compound **3** was the only product detected in a ^{15}N NMR spectrum taken with one pulse giving $I_0 = 4$, see Fig. 1(b). I_0 values of **2**, **4** and **5** were taken from ^{15}N NMR spectra recorded with 32 pulses or more, see for example Fig. 1(c). V_{max} values were determined according to eqn. (4) and are listed in Table 2.

The proportion of nitration via nitronium ion [EAN, eqn. (2)], in the presence of sodium azide as a scavenger for nitrous acid was studied. No reaction took place under these conditions indicating the absence of EAN. This is as expected from the observations of Schofield and coworkers who reported the occurrence of a nitration reaction in the presence of nitrous acid traps only at concentrations of sulfuric acid higher than 54.2%.¹⁶

Table 1. ^{15}N -CIDNP during nitration of anisole **1** (0.3 mol dm^{-3}) with nitric acid (1 mol dm^{-3}) at 298 K.

Solvent ^a	^{15}N -signals ^b	Yield ^c	V_{max} ^d	τ_E ^e
$\text{AcOH-H}_2\text{O} + \text{D}_2\text{O}$ 4:1				n.r. ^f
$\text{AcOH-H}_2\text{O} + \text{D}_2\text{O-H}_2\text{SO}_4$ 3:1:1	0.3 (2) E	25	-1300 ^g	6
	-0.4 (3) E	65	-500 ^g	5
	-2.7 (4) ^h E	5	-130	12
	-5.4 (5) ^h E	5	-140	5
	-26 (H^{15}NO_3)			
+ NaN_3 (0.1 mol dm^{-3})				n.r. ^f

^a v/v mixture. ^b δ in ppm against $\text{Ph}^{15}\text{NO}_2$, high-field values negative, assignment in parentheses. E = emission. ^c In%, determined from ^{15}N NMR spectra after reaction. ^d V_{max} determined according to eqn. (4). ^e τ_E : duration of the emission in min. ^f n.r. = no reaction within 2 h. ^g $E_{\text{calc}} = -1309$ has been calculated using Pedersen's treatment.¹⁹ ^h The signal has not been assigned.

Table 2. Relative ^{15}N NMR signal intensities I^a during reaction and I_0^b after reaction of **1** (0.3 mol dm^{-3}) with nitric acid (1 mol dm^{-3}) in $\text{AcOH-H}_2\text{O} + \text{D}_2\text{O-H}_2\text{SO}_4$ ($v/v = 3:1:1$) at 298 K.

t/min	$I(2)$	$I(3)$	$I(4)$	$I(5)$
0–3 ^c	0	0	0	0
4	–10	–10	0	0
5	≈ -2000	≈ -2000	–25	–40
5.75	–400	–400	–30	–5
6.50	–40	–35	–25	–3
7.25	–20	–15	–20	–3
9	–2	1	–10	0
30	≈ 1	≈ 4	<1	<1
60–360 ^b	I_0 1.5	I_0 4	I_0 0.3	I_0 0.3

^a I determined from the signal-to-noise ratio. ^b I_0 determined from ^{15}N NMR spectra taken after reaction with 150 pulses and scaled to a spectrum recorded after 30 min with a single pulse. ^c $t=0$: taken 2 min after mixing the reactants and 1 min after placement of the tube into the probehead.

V_{max} values of –1300 and –500 obtained for **2**, **3** were much higher than those of determined (–130 and –140) for **4**, **5**. It is concluded that the polarisations in **2**, **3** are built up in radical pairs generated by free radical encounters of NO_2 and $1^{+\cdot}$ which are formed by NAC [eqns. (1)]. The polarisations observed in **4**, **5**, whose structures have not been elucidated, might be due to a side-reaction. For instance, attack by the *O*-end of NO_2 would give a species that could lose NO in a secondary reaction and after dealkylation end up as *o*- or *p*-quinone, as has been described for phenols.^{17,18} The emission signals of **2**, **3**, **5** declined within 5–6 min corresponding to a decay time similar to the nuclear relaxation time T_1 of **3** (20 s). It follows that the reaction that forms **2**, **3**, **5** occurred within less than 1 min, after an induction time of about 5 min. In contrast with this, the emission of **4** appeared later and continued for 12 min, see Fig. 1(b) and the Tables 1 and 2, indicating that **4** might be the product of a secondary reaction.

In the following, V_{max} values of **2**, **3** are compared with enhancement factors per molecule E_{calc} calculated according to the radical pair theory of CIDNP. $E_{\text{calc}} = -1309$ was obtained by applying Pedersen's treatment¹⁹ of the radical pair theory with $g(1^{+\cdot}) = 2.00351$,²⁰ $\eta = 1.4 \text{ cP}$ and the parameters used for the calculation of the enhancement factors of 1,2-dimethoxy-4-nitrobenzene in acetic acid.³

The value of E_{calc} (–1309) is identical with $V_{\text{th}}(2)$ (–1300) but bigger than $V_{\text{th}}(3)$ (–500). It is concluded that **2** is formed exclusively via NAC [eqn. (1)] whereas the formation of **3** occurs to an extent of 60% via a non-radical pathway. The 2-/4-ratio of V_{th} reflects the participation of the non-radical reaction. This agrees with the results of Radner and coworkers if the non-radical formation of **3** occurs by NOX [eqns. (3)].¹¹

During nitration of **1** with nitric acid in acetic acid at 65 °C, compounds **2**, **3** were formed with a ratio of 0.8.⁷ It is concluded that the nitration of **1** occurs via NAC

mainly or exclusively under these conditions. The nitration mechanism of **1** in acetic acid is identical with that of 1,2-dimethoxybenzene.³ In mixed acid with 20% sulfuric acid, the nitration mechanism of **1** does not correspond to the nitration mechanism of mesitylene and toluene which are nitrated mainly or exclusively via EAN [eqn. (2)] under these conditions.³ The different behaviour is reflected in the oxidation potential of **1** (1.76 V)²¹ which is somewhat higher than that of 1,2-dimethoxybenzene (1.45 V)²¹ but much lower than those of mesitylene (2.35 V)²² and toluene (2.61 V).²³

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References

- Ebersson, L., Hartshorn, M. P. and Radner, F. *Acta Chem. Scand.* 48 (1994) 937; *Adv. Carboeat. Chem.* 2 (1995) 207.
- Giffney, J. C. and Ridd, J. H. *J. Chem. Soc., Perkin Trans. 2* (1979) 618; Ridd, J. H. *Chem. Soc. Rev.* 20 (1991) 149.
- Lehnig, M. *J. Chem. Soc., Perkin Trans. 2* (1996) 1943.
- Williams, D. L. H., *Nitrosation*, Cambridge University Press, Cambridge 1988.
- Kenner, J. *Nature (London)* 156 (1945) 369; Perrin, C. L. *J. Am. Chem. Soc.* 99 (1977) 5516.
- Olah, G. A., Malhotra, R. and Narang, S. C. *Nitration*, VCH, Weinheim 1989.
- Griffiths, P. H., Walkey, W. A. and Watson, H. B. *J. Chem. Soc.* (1934) 631.
- Bunton, C. A., Minkoff, G. I. and Reed, R. J. *J. Chem. Soc.* (1947) 1416.
- Bunton, C. A., Hughes, E. D., Ingold, C. K., Jacobs, D. I. H., Jones, M. H., Minkoff, G. J. and Reed, R. I. *J. Chem. Soc.* (1950) 2628.
- Schofield, K., *Aromatic Nitration*, Cambridge University Press, Cambridge 1980, p. 243.
- Radner, F., Wall, A. and Loncar, M. *Acta Chem. Scand.* 44 (1990) 152.
- Hoggett, J. G., Moodie, R. B. and Schofield, K. *J. Chem. Soc., Chem. Commun.* (1969) 605.
- Underwood, G. R., Silverman, R. S. and Vandervalde, A. *J. Chem. Soc., Perkin Trans. 2* (1973) 1177.
- Dix, L. R. and Moodie, R. B. *J. Chem. Soc., Perkin Trans. 2* (1986) 1097.
- Bargon, J. and Fischer, H. *Z. Naturforsch., Teil A.* 22 (1967) 1556.
- Barnett, J. W., Moodie, R. B., Schofield, K., Weston, J. B., Coombes, R. G., Golding, J. G. and Tobin, G. D. *J. Chem. Soc., Perkin Trans. 2* (1977) 248.
- Amin, M. R., Dekker, L., Hibbert, D. B., Ridd, J. H. and Sandall, J. P. B. *J. Chem. Soc., Chem. Commun.* (1986) 658.
- Thompson, M. J. and Zeegers, P. J. *Tetrahedron* 45 (1989) 191.
- Pedersen, J. B. *J. Chem. Phys.* 67 (1977) 4097.
- O'Neill, P., Steenken, S. and Schulte-Frohlinde, D. *J. Phys. Chem.* 79 (1975) 2773.
- Zweig, A., Hodgson, W. G. and Jura, W. H. *J. Am. Chem. Soc.* 86 (1964) 4124.
- Schlesener, C. J., Amatore, C. and Kochi, J. K. *J. Am. Chem. Soc.* 106 (1984) 3567.
- Ebersson, L., Jönsson, L. and Wistrand, L.-G. *Acta Chem. Scand., Ser. B* 32 (1978) 520.

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