Nitration of dimethoxybenzenes, mesitylene and toluene with nitric acid and mixed acid studied by ^{15}N-CIDNP

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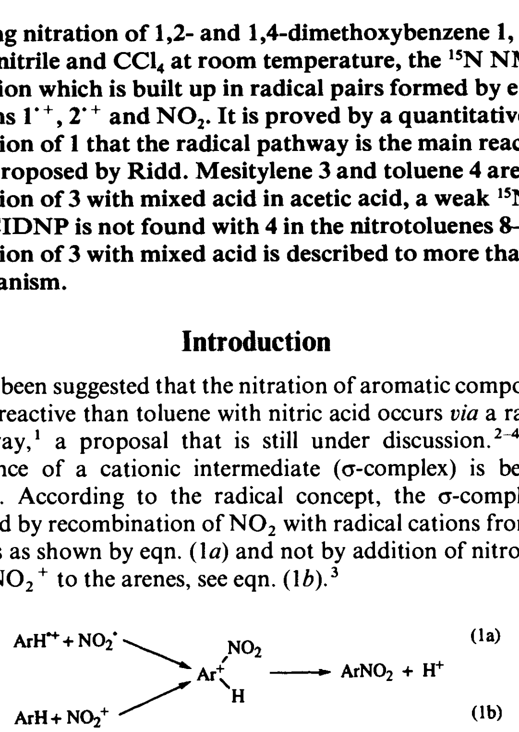
During nitration of 1,2- and 1,4-dimethoxybenzene 1, 2 with ^{15}N-labelled nitric acid in acetic acid, acetonitrile and CCl_4 at room temperature, the ^{15}N NMR signals of the nitration products 5, 6 exhibit emission which is built up in radical pairs formed by encounters of independently generated radical cations $1^{\cdot+}$, $2^{\cdot+}$ and NO_2. It is proved by a quantitative analysis of the ^{15}N-CIDNP effect during nitration of 1 that the radical pathway is the main reaction, which is a nitrous acid catalysed nitration first proposed by Ridd. Mesitylene 3 and toluene 4 are not nitrated under these conditions. During nitration of 3 with mixed acid in acetic acid, a weak ^{15}N-CIDNP effect is observed in nitromesitylene 7. ^{15}N-CIDNP is not found with 4 in the nitrotoluenes 8–10, but in the side products 12 and 13. The nitration of 3 with mixed acid is described to more than 95% and of 4 exclusively by Ingold's classical mechanism.

Introduction

It has been suggested that the nitration of aromatic compounds more reactive than toluene with nitric acid occurs *via* a radical pathway,[1] a proposal that is still under discussion.[2–4] The existence of a cationic intermediate (σ-complex) is beyond doubt. According to the radical concept, the σ-complex is formed by recombination of NO_2 with radical cations from the arenes as shown by eqn. (1*a*) and not by addition of nitronium ions NO_2^+ to the arenes, see eqn. (1*b*).[3]



1–4 (σ-complex) 5–10

1 1,2-Dimethoxybenzene
2 1,4-Dimethoxybenzene
3 Mesitylene
4 Toluene
5 1,2-Dimethoxy-4-nitrobenzene
6 1,4-Dimethoxy-2-nitrobenzene
7 Nitromesitylene
8, 9, 10 *o*-, *m*-, *p*-Nitrotoluene

A radical mechanism of the nitration reaction has been found with various nitration agents under different reaction conditions by Kochi and co-workers.[4] Using time-resolved spectroscopy during photochemical nitration of 1,2- and 1,4-dimethoxybenzene **1**,**2** with tetranitromethane in acetonitrile, they showed that the nitration products **5** and **6** are formed *via* radical pairs $[ArH^{\cdot+}, NO_2]$.[4a] Supplementary to these results, EPR spectra of $\mathbf{2}^{\cdot+}$ have been observed during irradiation of tetranitromethane with **2** in 1,1,1,3,3,3-hexafluoropropan-2-ol.[2b]

It has long been known that **5** and **6** are formed by nitration of **1** and **2** with nitric acid in acetic acid.[5] It was assumed that free radicals would be involved in these reactions as well.[4a] However, their existence as intermediates has not been proved. Radical cations and NO_2 also appear during irradiation of some less reactive arenes like mesitylene **3** and toluene **4** with *N*-nitropyridinium salts. Using $MeOPyNO_2^+$ as a nitrating agent, the isomeric ratio of *o*-, *m*- and *p*-nitrotoluene **8–10** corresponds to that found after nitration with many other reagents.[3,4b] The treatment of **4** with NO_2 in the presence of O_3 leads to the same isomeric ratio of **8–10**, a reaction that follows eqn. (1*a*), too.[6] It has been argued that the results from radical nitration, as reflected in product distributions, are indistinguishable from those obtained by following the electrophilic route.[4b,c]

Whereas the possibilities of a radical or a non-radical nitration of **4** are still under discussion,[4c,6,7] ^{15}N-CIDNP has been observed during the nitration of **3** with ^{15}N-labelled nitric acid in trifluoroacetic acid by Ridd and co-workers.[8] The nuclear polarisation is observed in nitromesitylene **7** and proves the formation of the nitration product *via* eqn. (1*a*). It is built up in radical pairs $[\mathbf{3}^{\cdot+}, NO_2]$ resulting from diffusion of free radicals $\mathbf{3}^{\cdot+}$ and NO_2, which are formed independently in a nitrous acid catalysed process, see eqns. (2*a*,*b*).[8]

$$ArH + NO^+ \rightleftharpoons ArH^{\cdot+} + NO^{\cdot} \qquad (2a)$$

$$(NO^{\cdot} + NO_2^+ \rightleftharpoons NO^+ + NO_2^{\cdot}) \qquad (2b)$$

The reaction is accelerated by addition of sodium nitrite and retarded by using sodium azide as a nitrous acid trap. Under the latter conditions, nitration still takes place without the appearance of ^{15}N-CIDNP indicating the formation of NO_2^+ and the occurrence of the non-radical reaction (1*b*) as well.[8] The formation rate of NO_2^+ is therefore smaller than the product formation rate without sodium azide. As a consequence, eqn. (2*b*) is considered to show only the stoichiometry of this stage and is enclosed in parentheses.[8]

In the following, thermal ^{15}N-CIDNP experiments are described during reaction of **1** and **2** in acetic acid, acetonitrile and CCl_4 with ^{15}N-enriched nitric acid. For proving the radical character of the nitration reaction, enhancement factors are determined during nitration of **1** in acetic acid and acetonitrile and compared with calculations based on Pedersen's quantitative formulation of the radical pair theory.[9] The model has been applied with success to the interpretation of ^{1}H- and ^{119}Sn-CIDNP effects observed during the reaction of independently generated carbon- and tin-centred radicals.[10,11] For verifying the results, a recent refinement of the theory developed by Fischer and co-workers[12] is used, too. The conclusions are completed by scavenger experiments. Further, the nitration of **3** and **4** with ^{15}N-labelled nitric acid in acetic acid–sulfuric acid mixtures is studied. ^{15}N-CIDNP enhancement factors are measured for determining the share of radical nitration and compared with calculations.

Experimental

NMR measurements and product identification

For performing the ^{15}N-CIDNP experiments, the reactants were put in 10 mm NMR tubes. In standard experiments, a 1.25

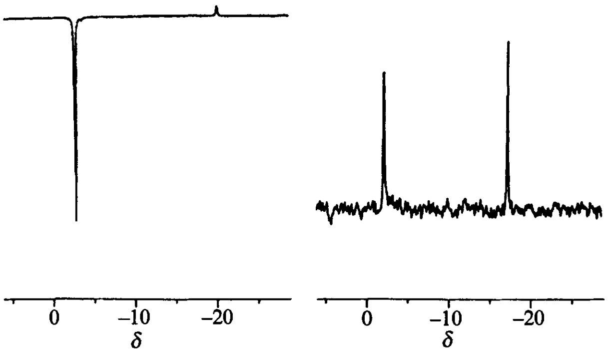


Fig. 1 ^{15}N NMR spectra taken from **1** in AcOH using a single 90° pulse. Left hand side: 6 min after addition of $H^{15}NO_3$. Right hand side: 2 h later, enhanced by a factor of 10. Further details see Table 1.

M solution of nitric acid and 0.5 M of the substrate were used. Lower concentrations of nitric acid were used in CCl_4 and lower concentrations of the substrates in acetic acid–sulfuric acid mixtures. The tubes were shaken, transferred into the probe head of a BRUKER DPX-300 NMR spectrometer and locked (internal lock: D_2O) within 2 min. ^{15}N NMR spectra were then recorded using one pulse with a pulse angle of 90°. This procedure was repeated every 1–2 min during fast reactions (duration of the emission less than ½ h) or every 5–30 min during slow reactions until the reactions were completed. The intensities of the emission signals I, the product signals after completion of the reaction I_0 and the $H^{15}NO_3$ signal during reaction $I(H^{15}NO_3)$ have been taken from the signal-to-noise ratios in the spectra or by integration. ^{15}N nuclear relaxation times T_1 have been 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 M in H_2O and labelled with 60.3 atom% ^{15}N (Isotec Inc.).

The identification of the nitration products **5** and **6** has been performed by comparing the ^{13}C NMR spectra with ^{13}C NMR data of authentic material. The formation of any other reaction product during nitration of **1** and **2** with nitric acid could not be proved, in accordance with the literature.[4a,5] **7** has been identified using ^{13}C NMR and ^{15}N NMR spectroscopy.[8] ^{15}N NMR shifts of **8**, **9** and **10** have been assigned by adding authentic material to the reaction mixture.

Determination of enhancement factors V_{max} and E

The magnitude of CIDNP effects is described by enhancement factors in different ways. Enhancement factors V_{max} are taken from the maximum emission intensity I_{max} and I_0.[13]

$$V_{max} = (I_{max} - I_0)/I_0 \qquad (3)$$

V_{max} values are dependent on the reaction time t and on T_1 and are useful only for qualitative descriptions of CIDNP. To avoid this, an enhancement factor E has been introduced,[14] which is the ratio between the intensity of the NMR signal immediately after formation of the polarised product at $t \ll T_1$ and the NMR signal of the product after stopping the reaction. If the reaction follows first-order kinetics with a rate constant k and if $1/k \gg T_1$, k and E are taken from the emission intensity at the beginning of the reaction ($t = 0$) and the time τ at which emission is no longer observed.[15]

$$I(t = 0) = I_0\, EkT_1 \qquad (4a)$$

$$\tau = 1/k \ln(-EkT_1 + 1) \qquad (4b)$$

Eqns. (4*a*,*b*) were applied for the 50 min after starting the nitration of **1** in acetonitrile. Within the first 50 min and during the nitration of **1** in acetic acid and of **3** in mixed acid, E has been determined from eqn. (5).

$$E = \Sigma I_i \Delta t(i,i + 1)/I_0 T_1 \qquad (5)$$

I_i is the intensity of the i^{th} measurement, $\Delta t(i,i + 1)$ the time interval between the i^{th} and the $(i + n)^{th}$ pulse. The summation is carried out as long as the emission continues. Eqn. (5) is an extension of the relation $E = It/I_0T_1$ which has been used for 0^{th} order reactions.[10] It is valid if $\Delta t \gg T_1$ and $I \gg I_0$ and is used as an approximation.

Results

Nitration of 1 and 2 with nitric acid in acetic acid

After adding $H^{15}NO_3$ to a solution of **1** in acetic acid and putting the NMR tube into the probe head of the ^{15}N NMR spectrometer, the signal of the nitration product **5** at $\delta = -2.3$ ppm shows emission, see Fig. 1. The ^{15}N-CIDNP effect reaches its maximum 4 min after taking the first spectrum indicating an induction period of the reaction of *ca.* 6 min. 33 min later, the emission signal disappears. After 2 h, the reaction is complete, and **5** shows a ^{15}N NMR signal with an intensity corresponding to the yield of the product. The reaction conditions and the assignment of the signals are given in Table 1, relative intensities I/I_0 in Table 2. $V_{max} = -62$ has been taken from I_{max}/I_0 following eqn. (3). To determine the enhancement factor E, the first 2 min of the reaction before taking the spectra have been neglected. $E = -962$ has been determined from eqn. (5) with $T_1 = 35$ s, see Table 3. The nitration of **1** does not take place in the presence of sodium azide.

During nitration of **2**, the ^{15}N NMR signal of the nitration product **6** at $\delta = -1.1$ ppm exhibits emission. The I/I_0 values given in Table 2 indicate a high reaction rate; the emission disappears 7 min after taking the first spectrum. An induction period and an emission maximum are not observed. $V_{max} = -71$ is derived from the spectrum taken at $t = 0$. E has not been determined. A second emission signal appears at $\delta = -5.0$ ppm. Its intensity is about 5% of the emission intensity of **6**. A ^{15}N NMR signal is not observed at $\delta = -5.0$ ppm after the reaction. The emission signal is therefore assigned to an intermediate the structure of which has not been investigated. The nitration of **2** is stopped by adding sodium azide, too.

Nitration of 1 and 2 with nitric acid in acetonitrile and CCl_4

Using acetonitrile as solvent for the nitration of **1**, the ^{15}N NMR signal of the nitration product **5** also appears in emission. The reaction rate is smaller than in acetic acid. $I_{max} = -2.25$ is observed after 50 min giving $V_{max} = -3.25$. The emission disappears after about 500 min. For determining E, it is necessary to take into account the increase of the product concentration during the reaction. E is divided into two parts, $E = E_r + E_d$. E_r is determined from the rise and E_d from the decline of the CIDNP effect. During the first 50 min, about 5% of the product is formed. If the product formation is neglected, the application of eqn. (5) gives $E_r = -33$. The intensity of the $H^{15}NO_3$ signal, $I(H^{15}NO_3)$ decreases by 40% during the reaction. It is treated as a measure of product formation and taken into account by determining $I/I(H^{15}NO_3)$; values are given in Table 4. It is assumed that the reaction is first order from $t = 50$ min. By applying eqns. (4*a*,*b*), $E_d = -572$ is determined with $T_1 = 90$ s, $I(t = 0)/I_0 = -2.25$ and $\tau = 450$ s, see Table 3.

During nitration of **2** in acetonitrile, CIDNP effects are observed, which are similar to those in acetic acid, see Tables 1 and 2. The emission intensity of the unknown intermediate is about 30% of that assigned to **6**. This indicates the occurrence of a second reaction leading to CIDNP. E has therefore not been determined.

With CCl_4 as a solvent, only a few qualitative experiments

Table 1 ^{15}N-CIDNP during nitration of **1**–**4** with nitric acid[a] and mixed acid

Compound	Solvent[b]	^{15}N-Signals[c]	V_{max}[d]	τ_E[e]
1, 0.5 M	$AcOH/H_2O + D_2O = 9/1$	−2.3 (**5**) E −20 ($H^{15}NO_3$)	−62	37[f]
1, 0.5 M	$ACN/H_2O + D_2O = 9/1$	+3.3 (**5**) E −5 ($H^{15}NO_3$)	−3.25	500
2, 0.5 M	$AcOH/H_2O + D_2O = 9/1$	−1.1 (**6**) E −5.0 (?) E[g] −10 ($H^{15}NO_3$)	−71	7[f]
2, 0.5 M	$ACN/H_2O + D_2O = 9/1$	+4.8 (**6**) E +0.5 (?) E[g] −5 ($H^{15}NO_3$)	−8	50
3, 0.5 M	$AcOH/H_2O + D_2O = 9/1$			N.r.
3, 0.05 M[h]	$AcOH/H_2O + D_2O/H_2SO_4 = 6/1/2$	+10.2 (**7**) E −30 ($H^{15}NO_3$)	−3.8	6
4, 0.5 M	$AcOH/H_2O + D_2O = 9/1$			N.r.
4, 0.2 M	$AcOH/H_2O + D_2O/H_2SO_4 = 6/1/3$	+15.1 (**12**) E +4.6 (**8**) +0.6 (**13**) E[i] +0.3 (**10**) −32 ($H^{15}NO_3$)	−31[j]	8

[a] $[HNO_3] = 1.25$ M, $T = 298$ K. The ^{15}N NMR signal of $H^{15}NO_3$ may change its position during reaction. [b] v/v mixture. [c] δ in ppm against $Ph^{15}NO_2$, high field values negative, assignment in brackets. E = emission. [d] V_{max} determined from eqn. (3). [e] τ_E: Duration of the emission in min, N.r.: no reaction within 2 h. [f] No reaction within 2 h in the presence of sodium azide ($[NaN_3] = 0.1$ M). [g] The signal could not be assigned. Intensity: *ca.* 5% of **6** in acetic acid, *ca.* 30% in acetonitrile. [h] A ^{15}N-CIDNP effect in **7** has first been observed in trifluoroacetic acid with $V_{max} = -220$ ($[\mathbf{3}] = 0.84$ M, $[H^{15}NO_3] = 2.10$ M, $[NaNO_2] = 0.084$ M.[8] [i] The ^{15}N NMR signal due to **9** also appears at $\delta = 0.6$ ppm. [j] Calculated with an estimated yield of 3%.

Table 2 Relative ^{15}N NMR signal intensities I/I_0[a] of the nitration products **5**, **6**, **7** and **13** during reaction of **1**, **2** with nitric acid and of **3**, **4** with mixed acid in acetic acid[b]

	t/min[c]		I/I_0[a]		t/min[c]		I/I_0[a]
1	0	**5**	−14	**2**	0	**6**	−70
	1		−26		1		−41
	2		−51		2		−27
	4		−61		3		−7.1
	6		−60		5		−1.1
	7		−45		7		0
	9		−29	**3**	0	**7**	−1.8
	10		−18		1		−2.8
	12		−13		2		−2.7
	14		−7.5		4		−1.8
	15		−5.4		6		0
	17		−4.9	**4**	0	**13**[d]	0
	20		−3.7		1		−8
	22		−2.1		3		−30
	25		−1.1		5		−20
	32		−0.3		7		−8
	37		0		8		0

[a] I: Signal intensity during reaction; I_0: signal intensity after reaction. [b] Reaction conditions see Table 1. [c] $t = 0$:2 min after mixing the reactants and 1 min after putting the tube into the probe head of the spectrometer. [d] Calculated with an estimated yield of 3%, see text.

Table 3 Experimental enhancement factors E of ^{15}N-CIDNP effects in **5** and **7** and calculated ones E_{calc} using Pedersen's[a] and Fischer's[b] treatment of the radical pair theory

Compound	EPR and NMR parameters[c]	Enhancement factors
5 in AcOH ($\eta = 1.056$ cP)	$g(\mathbf{1}^{\cdot+}) = 2.003\,74$[34] T_1 (**5**) = 35 s	$E = -962$ $E_{calc} = -1296$[a] $E_{calc} = -970$[b]
5 in ACN ($\eta = 0.369$ cP)	$g(\mathbf{1}^{\cdot+}) = 2.003\,74$[34] T_1 (**5**) = 90 s	$E = -605$ $E_{calc} = -1088$[a] $E_{calc} = -861$[b]
7 in $AcOH/H_2SO_4$ ($\eta = 2$ cP[d])	$g(\mathbf{3}^{\cdot+}) = 2.002\,3$ T_1 (**7**) = 25 s	$E = -33$ $E_{calc} = -1196$[a]
7 in CF_3CO_2H ($\eta = 0.808$ cP)	$g(\mathbf{3}^{\cdot+}) = 2.002\,3$ T_1 (**7**) = 70 s	$E = -189$[e] $E = -960$[f] $E_{calc} = -1295$[a]

[a] Determined with $\lambda = 0.46, p = 0.32, d = 4$ Å $= 2r$. [b] Determined with $\lambda = 0.46$, $\lambda_D = 2$ Å, $r(NO_2) = 1$ Å, $r(\mathbf{1}^{\cdot+}) = 3$ Å, $J_0 = 10^{14}$ rad s^{-1}, $r_{ex} = 5$ Å. [c] EPR data of NO_2: $a_N(^{15}NO_2) = 76.4$ G; $g(NO_2) = 2.0000$; $1/T_2 = 2 \times 10^9$ s^{-1}.[33] [d] Estimated from viscosity data of acetic acid and H_2SO_4. [e] Determined with eqn. (5) from data given in ref. 8 (Table 3), $[\mathbf{3}] = 0.84$ M, $[H^{15}NO_3] = 2.10$ M, $[AcONa] = 0.084$ M. [f] Determined with eqn. (5) from data given in ref. 8 (Table 3), $NaNO_2$ in the place of AcONa.

have been performed. After adding nitric acid to the solution, a binary phase system is formed, and nitric acid is not observed by ^{15}N NMR in the organic phase. Nevertheless, strong emission signals for **5** and **6** are observed which disappear within 15 min. After shaking the probe, the emission signals reappear.

Nitration of 3 and 4 with mixed acid in acetic acid

Mesitylene **3** and toluene **4** are not nitrated in acetic acid under the conditions given in Table 1 indicating that the radical reaction leading to CIDNP is of minor or no importance. Mixed acid has therefore been used which is known to be a more powerful nitrating agent than pure nitric acid.[3]

During nitration of **3** with nitric acid in mixtures of acetic acid and sulfuric acid, the ^{15}N signal of **7** shows emission for 7 min. Relative ^{15}N NMR intensities I/I_0 are listed in Table 2. The application of eqns. (3) and (5) gives $V_{max} = -3.8$ and $E = -33$ with $T_1 = 25$ s. The results are listed in Table 3.

^{15}N-CIDNP during nitration of **3** with nitric acid has first been observed in trifluoroacetic acid by Ridd and co-workers. $V_{max} = -220$ has been found in the presence of sodium nitrite.[8] $E = -960$ is calculated from the data given in ref. 8 with eqn. (5). It follows by comparison of the enhancement factors that the radical mechanism is of minor importance during the nitration of **3** with mixed acid (< 5%). The absolute contribution of the radical reaction in trifluoroacetic acid is discussed below.

The main products of the nitration of **4** with mixed acid in acetic acid are the nitrotoluenes **8** and **10**,[3,16] the ^{15}N NMR signals of which $\delta = 4.6$ and 0.3 ppm do not show CIDNP, see Fig. 2. Additionally, two emission lines at $\delta = 0.6$ ppm and

Table 4 Relative ^{15}N NMR signal intensities I/I ($H^{15}NO_3$)^a during reaction of **1** (0.5 M) with ^{15}N enriched nitric acid (1.25 M) in acetonitrile at 298 K

t/min^b	$I/I(H^{15}NO_3)^a$	t/min^b	$I/I(H^{15}NO_3)^a$
0	−20	219	−48
6	−36	281	−34
11	−46	329	−22
21	−72	391	−14
32	−80	445	−8
50	−90	500	0
83	−88	561	10
99	−76	685	20
130	−68	754	24
158	−64	1430	67

^{a} × 10^{-2}. I signal intensity of **5** during reaction. I ($H^{15}NO_3$) signal intensity of $H^{15}NO_3$ during reaction. ^{b} t = 0: 2 min after mixing the reactants and 1 min after putting the tube into the probe head of the spectrometer.

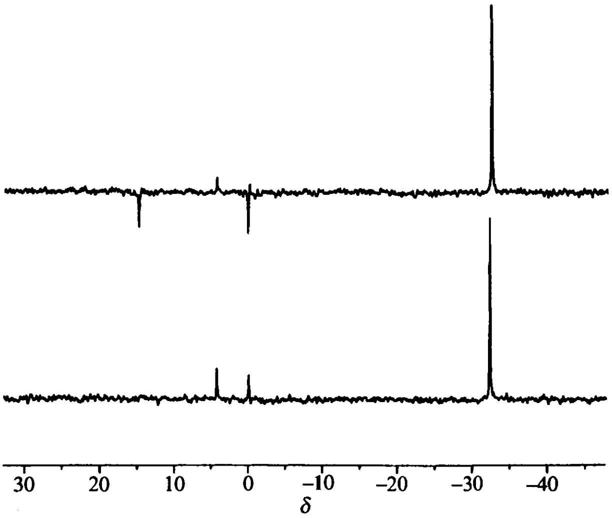
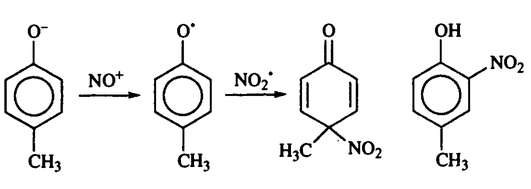


Fig. 2 ^{15}N NMR spectra taken from **4** in AcOH–H_2SO_4 using a single 90° pulse. Upper part: 6 min after addition of $^{15}NO_3$. Lower part: 1 h later. Further details see Table 1.

δ = 15.1 ppm are observed. According to the ^{15}N NMR shift value, the emission signal at δ = 0.6 ppm might be assigned to *m*-nitrotoluene **9** or to 4-methyl-2-nitrophenol **13** which both are side products of the nitration of **4** with yields of about 3%.[16–18] As **13** has also been observed in emission during nitration of 4-methylphenol **11**[19] and **11** is assumed to be the precursor of **13** during nitration of **4**,[18] we suggest that the emission signal at δ = 0.6 ppm might be due to **13**, which is formed in eqn. (6).[19]



(6)

11 **12** **13**

The I/I_0 values listed in Table 2 have been determined with the assumption of a 3% yield.[18] The emission signal at δ = 15.1 ppm might be caused by 4-methyl-4-nitrocyclohexa-2,5-dienone **12**, which exhibits emission during nitration of **11** with ^{15}N-labelled acetyl nitrate in acetic anhydride.[19]

Discussion

Reaction mechanism

The ^{15}N-CIDNP effects in **5**–**7** are explained by the reactions (1*a*) and (2) by analogy with those observed in **7** during nitration of **3** in trifluoroacetic acid.[8] They are built up in radical pairs formed by encounters of independently generated radical cations $1^{•+}$–$3^{•+}$ and NO_2.

It is well known that a σ-complex is formed by reaction of $1^{•+}$ and $2^{•+}$ with NO_2. Its formation has also been assumed during irradiation of **1**–**4** with tetranitromethane,[4] anionic nitration of **2** in the presence of $NaNO_2$,[20] reaction of **1**,**2** with NO_2[21] and during reaction of **4** with NO_2 in the presence of O_3.[6] Reaction (2*a*) is started by traces of nitrous acid, which are present in nitric acid or formed by an autocatalytic process.[22,23] As the nitration of **1** and **2** in acetic acid is completely suppressed by the addition of sodium azide, the non-radical reaction (1*b*) does not play a role. This is in accordance with the known formation rate of NO_2^+ in acetic acid, which is too small to cause nitration under the conditions described in Table 1.[24]

The addition rate of NO_2^+ to arenes more reactive than toluene is controlled by diffusion and expected to be nearly the same for **1**–**4**.[25] Scheme 2 describes a chain reaction delivering NO_2, $1^{•+}$ and $2^{•+}$ with high yields. NO^+ works as the chain carrier. Free nitronium ions NO_2^+ are not involved for kinetic reasons. A more complex route is probable for the formation of NO^+ and NO_2. The chain reaction does not occur with **3** and **4** under the applied reaction conditions, as **3** and **4** are not nitrated in acetic acid.

This result seems to be contrary to the observation of CIDNP during the nitration reaction of **3** in trifluoroacetic acid with nitric acid and with mixed acid in acetic acid. Obviously, the rate constant for the formation of $3^{•+}$ *via* reaction (2*a*) is much smaller than for the formation of $1^{•+}$ and $2^{•+}$. Because of the higher acidities of trifluoroacetic acid and mixed acid compared with acetic acid, the formation rate of NO_2^+ is much higher in these acids giving NO^+, NO_2 and $3^{•+}$ with a yield which is sufficient for the observation of CIDNP. This is supported by the result, that the nitration of **3** in trifluoracetic acid is only partially suppressed by addition of sodium azide,[8] which shows the ocurrence of nitration of **3** *via* the classical route (1*b*). It is therefore concluded that the nitration of **3** with mixed acid follows both mechanisms (1*a*) and (1*b*). This is supported by a discussion of the CIDNP enhancement factors.

The lack of CIDNP effects in **8** and **10** excludes free radicals as intermediates during nitration of **4** with mixed acid. However, the presence of NO_2 is shown by the observation of ^{15}N-CIDNP in side products. Radical cations $4^{•+}$ are not formed from **4** by oxidation with NO^+ because of the high oxidation potential of **4** (2.61 V)[26] which is higher than the oxidation potentials of **1** (1.40), **2** (1.35) and **3** (2.35 V).[8,21,27]

The nitrous acid catalysed mechanism should be of general importance for the nitration of highly activated arenes if the nitration reaction is faster than with moderately activated arenes. A nitrous acid catalysed radical reaction has been assumed by Schofield and co-workers during the nitration of 1,2,3-trimethoxy-5-nitrobenzene with mixtures of nitrous and nitric acid in sulfuric acid.[28]

A nitrous acid catalysed reaction has been formulated during nitration of **2** with nitric acid in CCl_4 and explained by *C*-nitrosation followed by oxidation of the *C*-nitroso compound with nitric acid reforming the nitrous acid consumed in the initial stage.[29] The occurrence of radical nitration is proved by the observation of ^{15}N-CIDNP in this system now.

Generally, the occurrence of a nitrosation reaction or any non-radical nitration cannot be excluded by the observation of CIDNP. Quantitative CIDNP investigations allow the determination of whether the radical reaction is the main reaction or only a side reaction. This will be discussed below by comparing experimental and calculated ^{15}N-CIDNP intensities of **5** and **7**.

Enhancement factors of ^{15}N-CIDNP in 5 and 7

There are not many quantitative CIDNP results obtained by conventional NMR spectroscopy, because reactions showing

CIDNP are too fast for quantitative studies in most cases. Complex reaction mechanisms as well as an unknown relaxation behaviour of the radical electrons and the nuclei involved make them difficult. The properties of the nitration of **1** with nitric acid in acetic acid and acetonitrile allow the determination of the enhancement factors. Because of the long relaxation times of the ^{15}N nuclei (*ca.* 1 min), the reaction times can be chosen to be long enough (*ca.* 1 h) to allow NMR measurements by conventional pulse methods. The only reaction leading to CIDNP is the encounter of independently generated free radicals $\mathbf{1}^{\cdot+}$ and NO_2 (F pairs).

A theoretical enhancement factor E_{calc} is determined by taking into account time-dependent S–T_0 mixing in radical pairs caused by g values and hyperfine coupling constants a[30] which are known from EPR investigations.[31] Transversal relaxation times T_2 of the radical electrons are obtained from the linewidths of the EPR signals. The diffusional behaviour is described by diffusion constants $D = kT/6\pi\eta r$; η is the viscosity of the solvent, r the radius of the radical which might be estimated from models. There are several treatments leading to satisfactory values of E_{calc}.[9,12,32] We will apply Pedersen's model,[9] which has successfully been used for calculating CIDNP built up in F pairs.[10,11] More recently, time-resolved CIDNP investigations have been performed by Fischer and co-workers[12] and discussed in terms of a refined model. The results are listed in Table 3.

Pedersen's parameters are λ, the probability of reaction per radical encounter, p, the probability of at least one encounter, and d, the distance of closest approach during an encounter. $\lambda = 0.46, p = 0.32$ and $d = 4$ Å $= 2r$ are taken for calculating ^1H-CIDNP effects in recombination products of the free-diffusing carbon-centred radicals $^{\cdot}CH_3$, $^{\cdot}CHCl_2$, $^{\cdot}CH_2COMe$ and $^{\cdot}CHClCO_2H$.[10,11b] They were also suitable for describing ^{119}Sn-CIDNP in Me_6Sn_2 formed by recombination of trimethyltin radicals,[11b] and will therefore be applied here without any modification. Using $T_2(NO_2) = 5.10^{-10}$ s,[33] $a(NO_2) = 76.4$ G,[33] $g(\mathbf{1}^{\cdot+}) = 2.003\,74$,[34] η $(MeCO_2H) = 1.056$ cP and $(MeCN) = 0.369$ cP, $E_{calc} = -1296$ in acetic acid and $E_{calc} = -1088$ in acetonitrile are obtained, which agree with the experimental data ($E = -962; -605$) within a factor of 2.

Refined r values are used in Fischer's treatment[12] which should lead to a better correspondence. $D = 1.91 \times 10^{-5}$ cm^2 s^{-1} is given for the radical cation of naphthalene in acetonitrile.[35] As the molecules of naphthalene and of **1** are similar in magnitude, we adopt this value for $\mathbf{1}^{\cdot+}$ and calculate r $(\mathbf{1}^{\cdot+})$ *ca.* 3 Å. $r(NO_2) = 1$ Å is estimated from the bond length and the bond angle of NO_2[36] giving $D(NO_2) = 5.73 \times 10^{-5}$ cm^{-1} s^{-1}. We adopt $\lambda = 0.46$, a jump length of diffusion $\lambda_D = 2$ Å, an exchange integral $J_0 = 10^{14}$ rad s^{-1} and an exchange radius $r_{ex} = 5$ Å. $E_{calc} = -970$ in acetic acid and $E_{calc} = -861$ in acetonitrile are obtained, which agree well with the experimental values $E = -962$ in acetic acid and $E = -605$ in acetonitrile.

For determining E_{calc} values for **7** during nitration of **3**, $g(\mathbf{3}^{\cdot+}) = 2.0023$ is assumed which is the g value of the hexamethylbenzene radical cation.[37] $\eta = 2$ cP is used for mixed acid in acetic acid and $\eta = 0.808$ cP for trifluoroacetic acid leading to $E_{calc} = -1196$ and $E_{calc} = -1295$. The comparison with $E = -33$ for the nitration with mixed acid confirms the small participation of radicals of less than 5% discussed above. The experimental value $E = -960$ for the nitration in trifluoroacetic acid in the presence of $NaNO_2$ agrees nicely with $E_{calc} = -1296$ indicating the radical character of this reaction. An experimental value $E = -189$ is derived with eqn. (5) from the data given for trifluoroacetic acid without $NaNO_2$.[8] It is concluded that the radical nitration of **3** in trifluoroacetic acid is of less importance than the non-radical reaction (*ca.* 20%).

Conclusions

The nitration of the activated arenes **1–4** with nitric acid has been studied by ^{15}N-CIDNP under conditions customary in synthetic work. The long relaxation times of the ^{15}N nuclei in the nitration products allow a quantitative analysis of the effects. The nitration of **1**,**2** with nitric acid in acetic acid, acetonitrile and CCl_4 and of **3**,**4** with mixed acid in acetic acid follows different mechanisms. The highly activated anisoles **1** and **2** are nitrated *via* a radical chain reaction catalysed by nitrous acid as has been found with moderately electron-rich aromatics like *p*-substituted phenols, polymethylbenzenes, amines and naphthalene.[8] The rate-determining step is an electron transfer from the arene to NO^+. There is no indication for an electron transfer between **1–4** and $NO_2{}^+$, which should lead to enhanced absorption in the ^{15}N-NMR spectra of the nitration products.

Compounds **3** and **4** are nitrated by nitric acid only in the presence of sulfuric acid. A quantitative analysis of the weak emission in the nitration product **7** shows the occurrence of the nitrous acid catalysed radical reaction as a side reaction. More than 95% of **7** are formed *via* Ingold's classical route. The nitrotoluenes **8–10** do not show CIDNP indicating the absence of a radical nitration, as toluene is not oxidized by NO^+. The presence of NO^+ is indicated by the observation of ^{15}N-CIDNP in the side products **12** and **13**.

The results are in accord with Perrin's proposal[1] of the incursion of free radical processes in the nitration of only those arenes that are more reactive than toluene,[1] but not with his suggestion that the radicals are generated by electron transfer between the arene and $NO_2{}^+$. Our work confirms the importance of NO^+ ion as the oxidizing agent. Although the occurrence of a radical process with toluene, under different conditions as observed by Kochi,[4b] cannot be excluded, it would be nice to confirm these results by CIDNP investigations.

Acknowledgements

The financial support by the Fonds der Chemischen Industrie, Frankfurt, is gratefully acknowledged. The author thanks Professor Dr H. Fischer, Zürich, for making a program available which allows simulations of CIDNP enhancement factors, and Dipl. Chem. K. Schürmann for helping with the calculations.

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Paper 6/01417H
Received 28*th February* 1996
Accepted 18*th April* 1996