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The Mechanism of the Nitration of Donor-Activated Benzenes with Nitric and Nitrous Acid as Studied by ^{15}N CIDNP

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Abstract: ^{15}N CIDNP effects observed during nitration of phenolic compounds with nitric and nitrous acid are comparable showing that nitrous acid is not only a catalyst during nitration with nitric acid but also a reactive intermediate. The ^{15}N CIDNP effects are generated in radical pairs formed during encounters of $NO_2^{\cdot}$ and arene radical cations or aroxyl radicals. The mechanism given is valid for arenes more reactive than toluene.

Keywords: *Nitration, Electron transfer, Nitrogen oxides, Radicals and radical reactions*

The nitration of activated arenes with nitric acid has been thoroughly studied during the past [1]. Nevertheless, the mechanism is not clear in all details.

$$\underset{\mathbf{1-4}}{ArH} + HNO_3 \rightarrow \underset{\mathbf{5-8}}{ArNO_2} + H_2O \qquad (1)$$

1: Phenol
2: *p*-Fluorophenol
3: Anisole
4: 1,2-Dimethoxybenzene
5a,b: *o*-, *p*-Nitrophenol
6: 2-Nitro-4-fluorophenol
7a,b: *o*-, *p*-Nitroanisole
8: 1,2-Dimethoxy-4-nitrobenzene
9: 4-Fluoro-4-nitrocyclohexadien-1-one

Martinsen and Ingold and coworkers found that the nitration of **1** and **3** is catalyzed by nitrous acid which is formed during the reaction [2,3]. Ridd and coworkers proved the radical character of the product formation using ^{15}N CIDNP for arenes more reactive than toluene [4,5].

$$ArH^{+\cdot} + NO_2^{\cdot} \rightarrow ArNO_2 + H^+ \qquad (2)$$

The detailed effect of nitrous acid has not been specified. In the meantime, nitration reactions of *p*-substituted phenols with $NO_2^{\cdot}$ in water and with HNO_2 in trifluoroacetic acid have been studied [6,7]. It will be shown in the following that the mechanism given for the nitration reactions with $NO_2^{\cdot}$ and HNO_2 is generally valid for the nitration of donor-activated benzenes with nitric acid. For proving this, nitration reactions of **2** and **4** with $NaNO_3$, HNO_3 and $NaNO_2$ are compared. **2** and **4** have been chosen, as they give only **6** and **8** as stable nitration products, whereas **1** und **3** lead not only to nitration products **5a,b** and **7a,b,** but also to a lot of side products.

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^{15}N NMR spectra taken during and after the reaction of **2** with ^{15}N enriched $NaNO_3$ in acetic acid are given in Figure 1. During the reaction, the ^{15}N NMR signals at δ = 1.6, 7.9 and 6.4 ppm appear in emission for 847 min. They are assigned to **6** and the unstable intermediate **9** [8]. The ^{15}N NMR signals at δ = 3.2 and 204.2 ppm are due to $^{15}NO_3^-$ and $^{15}NO_2^-$. They are not polarised. $^{15}NO_3^-$ disappears according to the progress of the reaction; $^{15}NO_2^-$ is formed as an intermediate. The time dependency of the NMR signals of **6** and $^{15}NO_3^-$ is given in Table 1. An enhancement factor E = -1202 has been determined from the data, which quantitatively describes the CIDNP effect [9,10], see Table 2. During the reaction of **2** with $Na^{15}NO_2$, similar ^{15}N NMR spectra are observed, and the duration of the emission in the ^{15}N NMR signal of **6** is comparable (804 min).

The reaction of **4** with $H^{15}NO_3$ in acetic acid has been described [10]. The ^{15}N NMR signal of **8** appears in emission for 39 min with E = -962. Using $Na^{15}NO_2$, no reaction takes place. After adding 8 % H_2SO_4 to the reaction mixture, the emission of **8** is observable for 33 min, E = -770.

The duration of the reactions of **2** and **4** with $NaNO_3$ and HNO_3 and with $NaNO_2$ is comparable, and the magnitudes of the ^{15}N CIDNP effects are similar indicating identic mechanisms for the nitration with nitrous and nitric acid.

$$H^+ + NO_2^- \rightleftharpoons HNO_2 \tag{3}$$

$$HNO_2 + NO_3^- + H^+ \rightleftharpoons 2\ NO_2^{\cdot} + H_2O \tag{4}$$

$$2\ HNO_2 \rightleftharpoons NO^{\cdot} + NO_2^{\cdot} + H_2O \tag{5}$$

$$NO_2^{\cdot} + ArH \rightarrow NO_2^- + ArH^{+\cdot} \tag{6}$$

$$ArH + HNO_2 \rightarrow ArH^{+\cdot} + NO^{\cdot} + OH^- \tag{7}$$

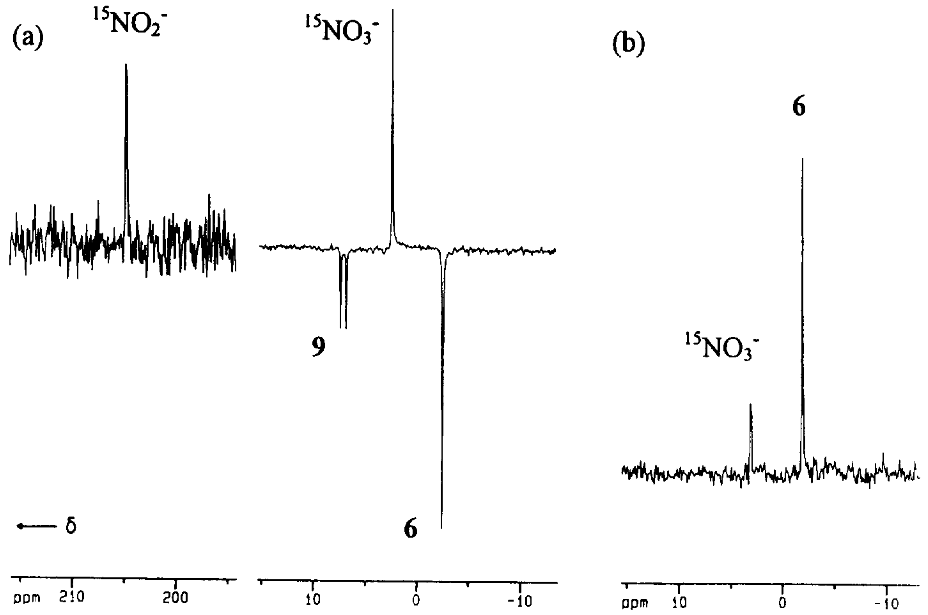

Figure 1. ^{15}N NMR spectra, taken (a) with 176 pulses 313-847 min., (b) with 10 pulses 2880-2930 min. after starting the reaction of **2** with $Na^{15}NO_3$ in acetic acid/ D_2O. δ values against nitrobenzene-^{15}N.

Table 1. ^{15}N NMR signal intensities $I^{[a]}$ of **6**, **8** and $^{15}NO_3^-$ at 300 K during the reaction of (a) **2** (0.2 M) with $NaNO_3$ (0.1 M), (b) **2** (0.2 M) with $NaNO_2$ (0.3 M), (c) **4** (0.2 M) with $NaNO_2$ (0.1 M) with H_2SO_4 (8%) in acetic acid with 10% D_2O as lock, $NaNO_3$ 64% atom % ^{15}N, $NaNO_2$ 99.3% atom % ^{15}N.

(a)

$t^{[b]}$	3	6	12[c]	100	106	282	286	313[d]	847[e]	2880[f]	14400[g]
I(**6**)	-8	-13	-16	-20	-16	-13	-1	-2.6	0	3.8	5.9
$I(^{15}NO_3^-)$	2	3	4.2	5	4	5	3	2.8	2	0.9	0

(b)

$t^{[b]}$	3	6	9	12	18	79	132	180	283[h]	806[i]	14400[j]
I(**6**)	-125	-140	-100	-83	-77	-40	-25	-14	-2.2	0	15
$I(^{15}NO_3^-)$	5	6	8	8	9	6	4	3	4	3	0

(c)

$t^{[b]}$	2	4	7	10	14	18	21	25	29	33	120
I(**8**)	-600	-550	-200	-80	-40	-18	-9	-5	-2	0	9

[a] I: Relative NMR intensities determined from the signal-to-noise ratios after single 90^0 pulses. [b] t: Time after mixing the reactants (min). - [c] Average values from 28 pulses. - [d] Average values from 176 pulses. - [e] 23% nitration product. - [f] Average values from 10 pulses. - [g] After adding a single drop of H_2SO_4; average values from 9 pulses, 42% nitration product. - [h] Average values from 175 pulses. - [i] 41% nitration product. - [j] 88% nitration product.

According to eq 4, NO_3^- is in equilibrium with HNO_2 und $NO_2^\cdot$ [11]. On the other hand, HNO_2 decomposes to $NO_2^\cdot$ und $NO^\cdot$, eq 5 [12], and oxidizes the arenes following eq 8. Phenolic compounds might also be oxidized by $NO_2^\cdot$ (eq 6) [7,13]. However, the oxidation potential of $NO_2^\cdot$ (E_{ox} = 0.9 - 1.0 V) [14] is not high enough to oxidize **4** (E_{ox} = 1.4 V) [15]. **6**$^{+\cdot}$ should be deprotonated in weakly acid medium [16]. The product yields are higher than expected from eqs 3 - 7, because $NO^\cdot$ is partially oxidized by O_2 giving $NO_2^\cdot$ which takes part in the nitration.

By using the radical pair theory, enhancement factors have been calculated giving E_{calc} =-1222 for **6** and E_{calc} = -1296 for **8**. They are comparable with the measured E values indicating that the radical reaction is the main reaction under the applied reaction conditions. Non-radical reactions like a nitrosation followed by oxidation or an electrophilic substitution with NO_2^+ are of no importance. It is concluded that nitrations of donor-activated arenes with nitric acid follow the radical reaction scheme if the reactions occur in weakly acid media.

Table 2. Experimental enhancement factors E in **6** and **8** and calculated ones E_{calc}.

Reaction system	^{15}N NMR parameters	t_{max} [a]	t_E [b]	E, E_{calc}
2 with $Na^{15}NO_3$ in	T_1 = 1.6 min	100	847	E (**6**) = - 1202[c]
acetic acid	I_o = 3.2			E_{calc} (**6**) = - 1222[d]
2 with $Na^{15}NO_2$ in	T_1 = 1.6 min	8	806	E (**6**) = - 1090[c]
acetic acid	I_o = 7			E_{calc} (**6**) = - 1222[d]
4 with $H^{15}NO_3$ in	T_1 = 35 s	6	39	E (**8**) = - 962
acetic acid [10]				E_{calc} (**8**) = - 1296
4 with $Na^{15}NO_2$ in	T_1 = 35 s	2	33	E (**8**) = - 770[c]
acetic acid/H_2SO_4	I_o = 9			E_{calc} (**8**) = - 1296 [10]

[a] t_{max}: Time of maximal emission after mixing the reactants (min) - [b] t_E: Duration of the emission (min) - [c] Determined following $E = \Sigma I_i \Delta t(i,i+1)/I_0 T_1$ with I_i: signal intensities during the i^{th} measurement, $\Delta t(i,i+1)$: time intervals between the i^{th} and the $(i+1)^{th}$ measurement, I_o: yield at t_E (see Table 1), T_1: nuclear relaxation time determined after the reaction. The summation occurs during t_E. - [d] Determined following Pedersen's treatment of the radical pair theory [17] and parameters taken from [10], $g(F\text{-}C_6H_4\text{-}O^{\cdot})$ = 2.00503 [16].

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