

## The dichotomy between nitration of substituted 1,4-dimethoxybenzenes and formation of corresponding 1,4-benzoquinones by using nitric and sulfuric acid<sup>†</sup>

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Various alkyl-substituted *p*-dimethoxybenzenes (ArH) react readily with nitric acid and sulfuric to form nitro-products (ArNO<sub>2</sub>). When the nitric acid is used in excess, the nitro-product react via either nitration to dinitro-compound (Ar(NO<sub>2</sub>)<sub>2</sub>) or *via* oxidative demethylation to nitro-*p*-quinone (Q). As such, the competition between the nitration, polynitration and oxidative dealkylation is effectively modulated by the added nitric acid and the alkyl-substituted *p*-dimethoxybenzenes.

Aromatic nitration is conventionally carried out with nitric acid, either alone or in combination with either Lewis or Brønsted acid<sup>1</sup>. It has long been known that most of the aromatic compounds are nitrated with a mixture of nitric acid and sulfuric acid according to ionic mechanism.<sup>2</sup> For compounds as (polymethoxy)benzenes, more reactive than toluene, it has been shown that nitric acid was a sufficient nitration reagent to nitrate them.<sup>1</sup> Only in this case, it has been suggested that the nitration of the (polymethoxy)benzenes with nitric acid occurs via a radical pathway (Scheme 1).<sup>3,4</sup>

In the meantime, other nitration reagents have been studied for nitration of activated-arenes.<sup>5</sup> It has been proved that the mechanism given for the nitration reactions with NO<sub>2</sub> and HNO<sub>3</sub> (Scheme 1) is generally valid for the nitration of donor-activated benzenes with nitric acid.<sup>6</sup> Nevertheless, the mechanism is not clear in all details and it is still under discussion.<sup>1,4-8</sup>

In connection to our interest in deoxygenation of dissolved oxygen in water, we investigated the nitration of dimethoxybenzene derivatives with a mixture of nitric and sulfuric acid. For the first time, nitration and oxidative demethylation of (polymethyl)-1,4-dimethoxybenzenes were observed in the studied conditions. On the other hand, because the tetramethyl-*p*-dimethoxybenzene is oxidatively demethylated by nitrogen dioxide to form duroquinone,<sup>9,10</sup> we thought that it could be interesting to examine the dichotomy between aromatic nitration and quinone formation by using (polymethyl)-1,4-dimethoxybenzenes **1** (Scheme 2) with an excess of nitric acid (molar ratios : HNO<sub>3</sub>/H<sub>2</sub>SO<sub>4</sub> = 1.5/1.1).

### Results and discussion

Our starting point was to consider that the nitration of 1,4-dimethoxybenzene derivatives with nitric acid followed the radical reaction scheme to form quinone-type compounds by oxidative demethylation if reactions occurred in weakly acidic medium. We then investigated the nitration of (mono or polymethyl)-1,4-dimethoxybenzenes with a mixture of nitric and sulfuric acid in acetic acid (Scheme 2). Several experiments were performed at various temperatures and times, in order to find the best conditions to synthesize nitro-compounds **2** without any side products. The results are summarized in Table 1.

Results show that the nitration of aromatic compounds **1** is more important than the oxidative demethylation (Table 1, entries 2, 4, 6, 10 and 12). On the other hand, the dichotomy is less pronounced in the studied conditions (polar solvent) than Kocki's system<sup>10</sup> (entry 8). By using H<sub>2</sub>SO<sub>4</sub>, the first corresponding step is the formation of NO<sub>2</sub><sup>+</sup> to give a cation intermediate (σ-complex) and then, the electrophilic substitution of the donor-arenes to form the compounds **2** (Scheme 3, path A).<sup>9</sup> However, we cannot exclude by the presence of traces of nitrous acid in nitric acid, the formation of NO<sub>2</sub> and so the reaction between NO<sub>2</sub> and so the reaction between NO<sub>2</sub> and so the reaction between NO<sub>2</sub> with the radical cation **1**<sup>+</sup> to give the σ-complex (Scheme 3, path B).<sup>4,8</sup>

In a second step, the chemical behaviour of nitro-(mono or polymethyl)-1,4-dimethoxybenzenes **2** towards nitric acid in excess is different. Thus, the reaction of 2-nitro-1,4-dimethoxybenzene (Table 1, entry 2) with HNO<sub>3</sub>/H<sub>2</sub>SO<sub>4</sub> produce the 2,5-dinitro-1,4-dimethoxybenzene. On the other hand, tetramethyl-1,4-dimethoxybenzene (Table 1, entries 13 and 14) react with HNO<sub>3</sub>/H<sub>2</sub>SO<sub>4</sub> to produce *p*-benzoquinones *via* oxidative demethylation.<sup>10</sup> Other products are obtained by nitration and oxidative demethylation of certain *p*-dimethoxybenzene derivatives (Table 1, entries 2, 8 and 12). According to previous work,<sup>4,6,8</sup> the reaction of compounds **2** with an excess

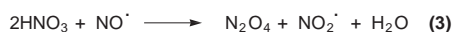
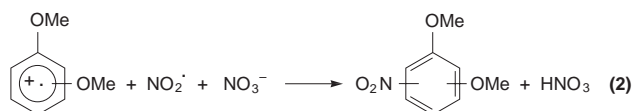
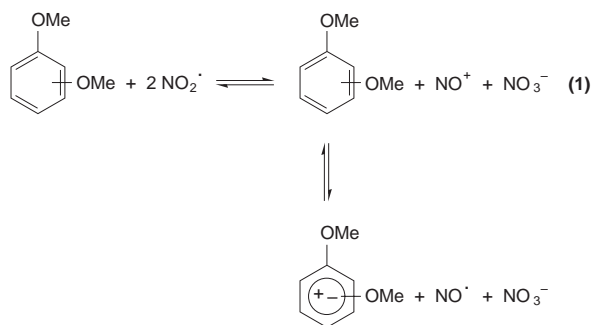
**Table 1** The dichotomy between nitration, polynitration and oxidative demethylation with HNO<sub>3</sub>/H<sub>2</sub>SO<sub>4</sub> in CH<sub>3</sub>CO<sub>2</sub>H

Entry	Compounds <b>1</b>	Reaction conditions <sup>a</sup>	<b>2</b> (%) <sup>b</sup>	<b>3</b> (%) <sup>b</sup>	<b>4</b> (%) <sup>b</sup>	<b>5</b> (%) <sup>b</sup>
1	R = H	A	90 <sup>c</sup>	0	0	0
2	R = H	B	65	35	0	1
3	R = Me	A	70 <sup>c</sup>	0	0	0
4	R = Me	B	45 <sup>c</sup>	0	0	22 <sup>c</sup>
5	R = 2,3-Me	A	85 <sup>c</sup>	0	0	0
6	R = 2,3-Me	B	83	5	0	0
7	R = 2,5-Me	A	68 <sup>c</sup>	0	0	0
8 <sup>d</sup>	R = 2,5-Me	B	62	0	0	7
9	R = 2,6-Me	A	78 <sup>c</sup>	0	0	0
10	R = 2,6-Me	B	71	3	0	0
11	R = 2,3,5-Me	A	70 <sup>c</sup>	0	0	0
12	R = 2,3,5-Me	B	63	0	0	12
13	R = 2,3,5,6-Me	A	0	0	2	0
14 <sup>e</sup>	R = 2,3,5,6-Me	B	0	0	19 <sup>c</sup>	0

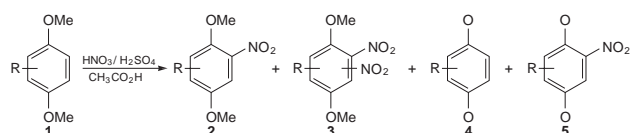
<sup>a</sup>Reaction conditions Δ: in the presence of 1.1 equiv. of HNO<sub>3</sub> 65%, 1.1 equiv. of H<sub>2</sub>SO<sub>4</sub> 5°C, 15 min; B: in the presence of 1.5 equiv. of HNO<sub>3</sub> 65%, 1.1 equiv. of H<sub>2</sub>SO<sub>4</sub>, 5°C, 15 min, then 25°C, 24h. <sup>b</sup>Yields were determined by <sup>1</sup>H NMR and HPLC. <sup>c</sup>Isolated yields, <sup>d</sup>89% of the compound **4** was obtained by Kochi<sup>10</sup>, <sup>e</sup>52% of the starting material was observed in the reaction mixture.

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<sup>†</sup> This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.



Scheme 1



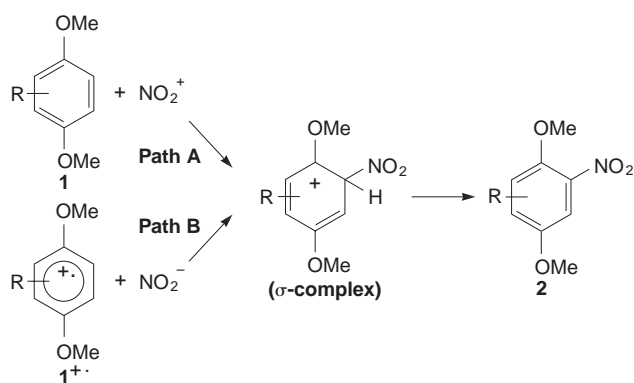
Scheme 2

of  $\text{HNO}_3$  to form nitro-benzoquinones derivatives proceeds probably via a radical pathway but we cannot confirm if the radical **2**. is generated by electron transfer between the arenes **2** and  $\text{NO}_2^{+\cdot}$  or by electron transfer from the arenes **2** to  $\text{NO}^{+\cdot}$ .

## Experimental

Melting points were determined with a Metler FP1 and are uncorrected.  $^1\text{H}$  and  $^{13}\text{C}$  spectra were recorded on a Bruker AC300 spectrometer operating at, respectively, 300.133 and 75.47 MHz in  $\text{CDCl}_3$ , using trimethylsilane as internal reference. IR spectra were recorded on a Bruker IFS 48 spectrometer. Elemental analyses were performed by the 'Service Central de Microanalyses' of CNRS, in Vernaison, France.

**General nitration procedure:** To a stirred solution of 2,5-dimethoxytoluene (26.3 mmol) in acetic acid (50 ml) at  $5^\circ\text{C}$ , was added a mixture of nitric (39.5 mmol) and sulfuric acid (28.9 mmol), and stirring was continued for 15 min and then for 24 h at  $25^\circ\text{C}$ . The crude product was collected and washed with petroleum ether.



Scheme 3

**Selected physical data:** 2-methyl-5-nitro-1,4-benzoquinone: mp  $150^\circ\text{C}$ ;  $\nu_{\text{max}}/\text{cm}^{-1}$  (KBr) 2982, 1650, 1577, 1543, 1494, 1465, 1355;  $\delta_{\text{H}}$  6.80 (s, 1H), 6.65 (s, 1H), 2.10 (s, 3H);  $\delta_{\text{C}}$  186.9, 184.7, 146.2, 139.5, 135.9, 133.6, 15.6 (Found: C, 50.25; H, 3.06; O, 38.14.  $\text{C}_7\text{H}_5\text{NO}_4$  requires C, 50.31; H, 3.02; N, 8.38; O, 38.29%).

All other compounds were characterized by comparison of their physical data with those described in the literature.<sup>2,10</sup>

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