

SELECTIVE NITRATION OF PHENOLS CATALYZED BY LANTHANUM (III) NITRATE

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Phenols are easily mononitrated at room temperature by NaNO_3 in a two-phase system (water - ether) in the presence of HCl and a catalytic amount of $\text{La}(\text{NO}_3)_3$. The experimental conditions leave completely unaltered many other aromatic systems.

Phenols are very reactive towards various nitrating agents but isolated yields are often low. Several methods of nitration have been proposed¹.

We report here a new method for the nitration of phenols which affords very high yields under mild experimental conditions, and which leaves unaltered many other aromatic systems.

For several years, we have investigated the use of lanthanide derivatives either as reagents or as catalysts^{8,9}. In 1975, we described the air oxidation of benzoin to benzil catalyzed by ytterbium trinitrate⁹ in an acidic medium. We have now found that it is possible to carry out efficient nitrations of phenolic derivatives in the presence of catalytic amounts of some lanthanide nitrates. We selected a procedure where the nitrating agent is 1 equivalent of NaNO_3 and an excess of HCl. The reaction medium is a mixture of water and ether (1:3) so as to have 1 M nitrate ion in the water phase. We determined that the system is completely ineffective in the nitration of phenol or many types of aromatic compounds in the absence of lanthanum, but the phenol nitration starts immediately after the addition of 0.01 molar equivalent of $\text{La}(\text{NO}_3)_3$. Yields obtained after the completion of the reaction are very high¹⁰; representative results and procedure are presented in Table 1. Phenol itself gives 2:1 ortho/para nitration, while phenols substituted in the para position (para-cresol, 2,4-dimethylphenol) give nearly exclusive ortho nitration, with some meta nitration. We investigated the influence of the reaction medium acidity on the yield and regioselectivity in the nitration of phenol. The reaction does not proceed in the absence of HCl, but reasonable reactivity is observed in a weakly acidic medium (0.5 eq. of HCl). This reaction might be useful for the nitration of acid-sensitive compounds. Another feature of the reaction is the ortho/para ratio of the products as a function of the acidity. Increasing the acid content of the aqueous phase from 0.5 eq. to 13 eq. of HCl allows the reaction to go from predominantly para to ortho nitration products. Unfortunately, in both cases the major isomer does not exceed 63-67%. $\text{La}(\text{NO}_3)_3$ certainly operates as a homogeneous catalyst and is efficient in very small amount (1% mole of phenol).

Without the catalyst nitration is negligible even after 24 hours. As soon as $\text{La}(\text{NO}_3)_3$ is added to the reaction medium a strong coloration develops and the reaction starts. Other lanthanum salts, for example LaCl_3 , are as efficient as the nitrate. We tested a large variety of rare-earth nitrates $\text{Ln}(\text{NO}_3)_3$ ($\text{Ln} = \text{Nd}, \text{Eu}, \text{Sm}, \text{Tb}, \text{Yb}$ and Tm) and found that they are almost equivalent to $\text{La}(\text{NO}_3)_3$. Our reagent requires mild conditions and routinely gives 80-90% yield of product during the nitration of many types of phenols.

Another important feature of our catalyst is the selective nitration of phenols in the presence of several types of aromatic compounds. For example with an equimolar mixture of phenol, naphthalene and para-xylene our standard procedure (1 eq. NaNO_3 , 0.01 eq. $\text{La}(\text{NO}_3)_3$, 5 ml HCl) affords only the nitration of phenol. Yield and selectivity are quite similar to those described in Table 1, while naphthalene and para-xylene remain completely unreacted. The same mixture of aromatic compounds was also treated by a limited amount of HNO_3 in concentrated sulfuric acid under the conditions of Ref. 11 but the nitration was not selective with respect to phenol. The selective nitration of phenols can be very useful in organic synthesis. For example, 1 was nitrated only on the phenolic ring (Table 1). Nitration of a 1:1 mixture of 1 and 4,4'-dimethoxy 1,1'-diphenyl 2 under the standard conditions gave products derived from 1. Investigations of the mechanism of the lanthanide catalyzed nitration as well as on the use of these reagents in the nitration of more complex molecules are currently in progress.

Acknowledgements

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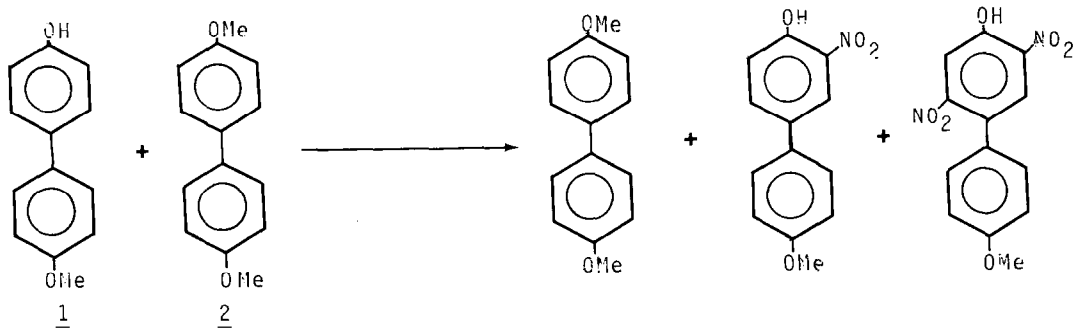
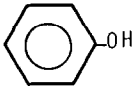
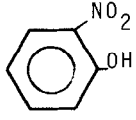
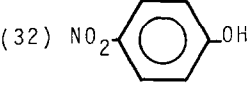
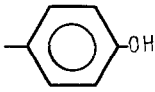
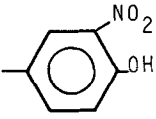
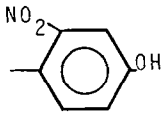
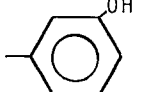
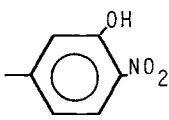
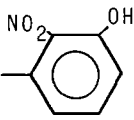
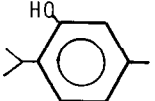
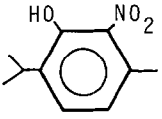
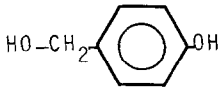
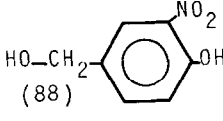
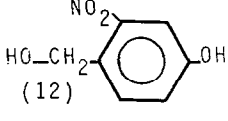
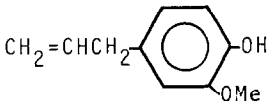
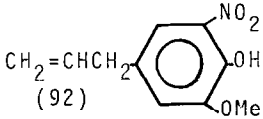
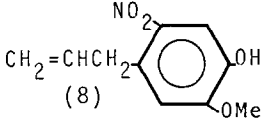
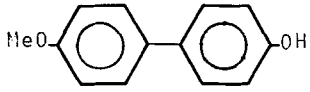
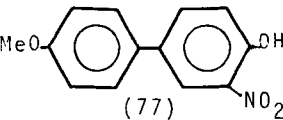
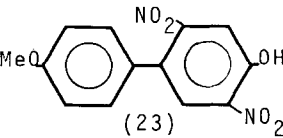


TABLE 1

Phenol nitration catalyzed by $\text{La}(\text{NO}_3)_3$

Phenol (a)	Yields (b)	Product distribution (%) (c)
	81 (8)	(68)  (32) 
	86 (14) ^(d)	(30)  (10) 
	86 (14) ^(d)	(87)  (13) 
	80 (16)	 (100)
	80 (16)	(88)  (12) 
	77 (20)	(92)  (8) 
	84 (14)	(77)  (23) 

(a) Reaction conditions :

425 mg NaNO_2 (5mmol) and 22 mg $\text{La}(\text{NO}_3)_3 \cdot 6 \text{H}_2\text{O}$ (0.05 mmol) were dissolved in 4 ml water and 4 ml concentrated HCl ($d = 1.19$). To this solution were added 5 mmol of phenolic compound dissolved in 15 ml diethylether. After 10 minutes a yellow coloration appeared turning to red when the reaction was over. The reaction mixture was stirred for 3 to 8 h, at room temperature and then extracted with chloroform. The organic phase was washed and dried (MgSO_4). The products were separated by silica preparative thin-layer chromatography (eluent: cyclohexane - ethyl acetate) and identified by comparison with the spectra of authentic sample by IR, NMR and mass spectroscopy.

(b) Yields of isolated nitrophenols (and of recovered starting material).

(c) Calculated from isolated yields of products unless stated.

(d) Yields measured on crude reaction mixture by glc (OV1 4% 2m 100°C) using an internal standard.

REFERENCES AND NOTES

- (1) Addition of phenol to a $\text{HNO}_3\text{-H}_2\text{SO}_4$ (or $\text{NaNO}_3\text{-H}_2\text{SO}_4$) mixture leads to mononitrophenols (61% yield, o/p : 1.44⁽²⁾). Phenol nitration was obtained by using either graphite nitrate³, tetranitromethane in water⁴ or sodium nitrate in trifluoroacetic acid⁵. Recently, an efficient procedure has been described for the paranitration of phenol by sodium nitrate and nitrite in sulfuric acid which uses lower oxides of nitrogen as catalyst⁶. For a recent review on aromatic nitration see ref.7.
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