Solvent Effects in the Two-phase Nitration of Anisole

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Depending on the nature of the organic solvent, anisole can be quantitatively nitrated by 65% nitric acid in a nitrite-catalysed two-phase system.

Recently, a two-phase system, consisting of an acidic aqueous solution of sodium nitrate and diethyl ether, has been developed for the nitration of phenols.[1–4] As under homogeneous conditions,[5–7] the reaction is catalysed by nitrites.[3,4] The method is specific for nitration of phenols. This was demonstrated by the lack of reaction with anisole,[4] and could be explained by the formation of a phenoxyl radical intermediate.[4,6–8] It was also claimed that the nature of the solvent had no effect.

In contrast with these assertions, we describe in this work an easy and effective two-phase nitration of anisole and we show that the nature of the organic solvent is of prime importance.

Table 1 Nitration of anisole with 65% HNO_3 at 25 °C[a]

Solvent	Relative permittivity[b]	Yield (%)[d] after 10 min	*Para/ortho*
n-C_5H_{12}	1.84	75.6	2.9
Iso-C_8H_{18}	1.94	75.2	2.9
cyclo-C_6H_{12}	2.02	64.2	3.1
$CFCl_2CF_2Cl$	2.41	56.8	3.0
CCl_4	2.24	35.3	3.2
$PhNO_2$	34.82	32.0	1.7
CS_2	2.64	30.1	3.6
$CHBr_3$[c]	4.39	27.7	3.6
CH_2Cl_2[c]	9.08	26.0	1.8
$PhCF_3$	9.18	24.4	2.7
$CCl_2{=}CHCl$	3.42	17.9	3.1
PhF	5.42	15.7	2.8
PhCl	5.71	14.8	3.0
C_6H_6	2.28	13.3	2.9
$CHCl_3$[c]	4.81	9.7	3.0
Et_2O	4.33	0	

[a] Anisole, 2.5×10^{-3} mol; $NaNO_2$, 0.35×10^{-3} mol; 65% HNO_3, 1 cm^3; solvent, 5 cm^3. [b] From ref. 13. [c] Washed with water then dried with molecular sieves and distilled. [d] Determined by gas chromatography using an internal standard.

Using carbon tetrachloride (5 cm^3), commercial 65% nitric acid (14.4 mmol) and sodium nitrite (0.35 mmol) at 25 °C, anisole (2.5 mmol) is totally converted (>98%) after 5 h. The products are exclusively *ortho*- and *para*-nitroanisoles with an unusual *para*-preference (*para* : *ortho* = 3.7 : 1). From the beginning of the reaction, the liquid turned violet and reddish-brown vapour was evolved. These observations are indications of the formation of radical species and nitrogen dioxide respectively.

The effect of various water-immiscible solvents on the reactivity was determined by stopping the reaction after 10 min. Results in Table 1 show a large variation in reactivity. The absence of reaction with diethyl ether is confirmed, while alkanes are the most effective solvents. The exact nature of the solvent effect is not yet clear. A single solvent parameter cannot correlate with all these results. For example, if a low relative permittivity is favourable as shown in the case of alkanes, the order of reactivities does not follow exactly the inverse order of relative permittivity values. From this point of view, the high reactivity in nitrobenzene is unexpected and the lack of reaction in diethyl ether cannot be the result of the relative permittivity only. Likewise, no relations are observed with the polarizability which was put forward by Laszlo.[9] However, the basicity, or the donicity,[10] of the solvent is an inhibiting factor, as exemplified with diethyl ether. In the case of aromatic solvents, the π-donor ability has more influence than the basicity, according to the reactivity order: $PhNO_2 > PhCF_3 > PhF > PhCl > C_6H_6$.

In all examples the *para*-selectivity is high and the lowest *para* : *ortho* ratios are obtained with the most polar solvents ($PhNO_2$; CH_2Cl_2).

All these results are consistent with the NO^+-induced electron-transfer mechanism first proposed by Giffney and Ridd.[11] The position selectivity is a reflection of the spin density of the radical cation of anisole as determined by its hyperfine coupling constants.[12] A partial participation of the classical electrophilic substitution may explain the lowest *para*-selectivity in the most polar solvents.

From a preparative point of view, alkanes show two disadvantages: firstly nitroanisoles, which are not soluble enough, crystallize in these solvents; secondly tars are formed. Thus, among the tested solvents, carbon tetrachloride is the best for such reactions.

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