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Electrophilic reaction of nitric oxide with Wittig reagents

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Abstract—Reaction of nitric oxide (NO) with *p*-substituted benzyl triphenylphosphonium chlorides or bromides (Wittig reagents) in CH_2Cl_2 under argon undergoes electrophilic attack of NO on the carbon center of phosphonium ylides, producing benzonitriles.
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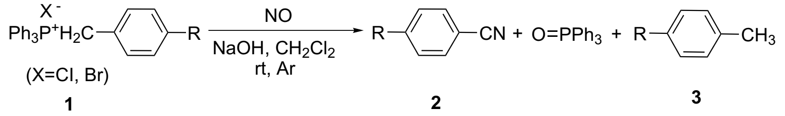
Increasing interest in NO in biological systems[1] promoted us to perform a research project designed to investigate the chemical behaviors of NO. In general, the chemistry of NO has been learned in two categories: free radical and oxidant. As a radical species, it reacts rapidly with other radicals.[2] NO can be oxidized to the nitrosonium or reduced to the nitroxyl anion.[3] Recently, we reported that reaction of epoxides with NO obtained the corresponding ring-opened products.[4] The aromatization of Hantzsch dihydropyridines and the deamination of aromatic primary amines by the reaction of substrates with NO exhibit the oxidative reactivity of NO, particularly in the presence of a catalytic amount of oxygen.[5,6] Although the electrophilic reactions of NO are very rare, they have been observed for a long time. Reaction of amides with NO[7] seems to undergo an electrophilic reaction. The rapid reaction of NO with $O_2^{-\bullet}$ yields peroxynitrite[8] and the diffusion-controlled reaction of NO with radical anions[2c] imply the electrophilic property of NO, although it is considered to possess some negative charge character on its nitrogen.[9] In fact, the synthetic investigation of the clear electrophilic reaction of NO started from Joseph's work.[10] Traube[11] found that NO reacted with enolate anions to produce compounds with N_2O_2 bound to nitrogen. We let the strong nucleophilic *p*-substituted benzyl triphenylphosphonium ylides (Wittig reagents) react with NO and benzonitriles were obtained. We believe that the reactions most probably proceed on an electrophilic reaction of NO with the carbon center of ylides.

In a representative experiment, a 15 mL CH_2Cl_2 solution of (*p*-nitrobenzyl)triphenylphosphonium bromide (**1b**) (1 mmol) was thoroughly deaerated by bubbling argon through for about 30 min. A 3 mL via the same way deaerated of aqueous solution of sodium hydroxide (25%) was then slowly added under Ar and stirring. NO was immediately passed through the mixed solution for ca. 5 h at room temperature. The total amount of NO passing through the solution was estimated to be roughly 100 mmol at the local atmosphere pressure using the ideal gas law. Preparation, purification, and transportation of NO were carried out under an argon atmosphere. The mixture was then extracted with three 10 mL portions of ether. The ethereal extract was washed with 3 × 10 mL of water. Afterwards, the organic phase was dried with magnesium sulfate over night. Product identification indicates the formation of *p*-nitrobenzonitrile (**2b**), *p*-nitrotoluene[12] (**3b**) and triphenylphosphine oxide ($Ph_3P{=}O$) (Scheme 1). IR



Scheme 1.

Keywords: Electrophilic reaction; Nitric oxide; Wittig reagents.

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identification of the residual compounds in the aqueous phase presented the generation of sodium nitrite (KBr, *v* NO_2^- 1269 cm^{-1}) in the reaction. The experimental results are summarized in Table 1. The solvent effect on product yields was investigated using **1b** as a substrate. The yields listed in Table 2 suggest that (1) aprotic solvents such as CCl_4, CH_2Cl_2 are greatly favorable for the formation of benzonitriles; (2) solubility of Wittig reagents is another key factor of influencing the yield of **2**.

On the basis of our experimental results, we believe that the reaction of NO with Wittig reagents most likely undergoes an electrophilic reaction of NO with the carbon center of phosphonium ylides, which are formed by deprotonation of phosphonium salts in the presence of a strong base, giving a betaine-like zwitterionic **4** shown in Scheme 2. An oxaphosphetane-like four-membered ring (**5** in Scheme 2) in a species and lastly the opening of the four-member ring occurs,[13] generating two fragments, one with a phosphorus–oxygen double bond, that is, $Ph_3P{=}O$ and the other with a carbon–nitrogen double bond, that is, phenylimino radical (**6** in Scheme 2). In the past several decades, Ingold and co-workers[14] had done embedded work focus on such imino radicals. As a result, nitriles were obtained as a major product during these courses.[15] The byproduct, toluene (**3**), is directly formed from the Wittig reagent under alkaline conditions.[12] In conclusion, we describe a novel reaction of NO with Wittig reagents to give nitriles and it was considered to attribute to the electrophility of NO.

Table 1. Formation of benzonitriles and toluenes from the reaction of NO with Wittig reagents in CH_2Cl_2 under an Ar atmosphere

Entry	Wittig reagent	R	Yield of **2**[a] (%)	Yield of **3**[a] (%)
1	**1a**	H	80	15
2	**1b**	NO_2	95	5
3	**1c**	Cl	55	40
4	**1d**	CN	78	20
5	**1e**	OC_2H_5	65	32
6	**1f**	CH_3	72	25

[a] Products were characterized by GC-MS.

Table 2. Solvent effect on the reaction of NO with **1b**

Solvent	Yield of **2** (%)	Yield of **3** (%)
CCl_4	98	Trace
CH_2Cl_2	95	5
$CHCl_3$	40	60
DCE[a]	60	38
CH_3CN	35	65
Benzene	45	55
THF[b]	30	70
DMSO[c]	Trace	Trace

[a] 1,2-Dichloroethane.
[b] Tetrahydrofuran.
[c] Dimethylsulfoxide.

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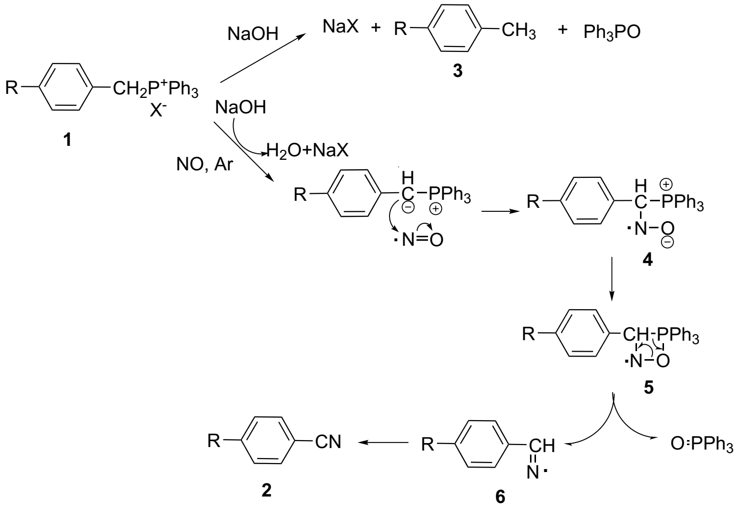

Scheme 2.

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