

The study of reaction mechanism for the transformation of nitronate into nitrile by phosphorus trichloride

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Abstract—Nitronate was generated using β -nitrostyrene and the anion of dimethyl malonate in THF at 0 °C. Subsequent treatment with PCl_3 in the presence/absence of DMAP either in THF or pyridine afforded nitroalkane, chloroxime, and nitrile. Pyridine, THF, and THF–pyridine co-solvent as solvents were investigated under different conditions. With different anions of malonates containing dipolarphiles, cyclic compounds were obtained as major products indicating nitrile oxides were generated during the reaction. Based on the results, compared to that of the one reported in literature, a plausible mechanism involving nitrile oxide intermediate was proposed.

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1. Introduction

Nitrile oxides are the most important intermediates in the synthesis of heterocyclic compounds via 1,3-dipolar cycloaddition.¹ Two widely used methods to produce nitrile oxides are (i) reaction of aldoximes with oxidizing agents or halogenating species² and (ii) reaction of primary nitroalkanes with dehydrating agents such as PhNCO and Et_3N ,³ POCl_3 ,⁴ diketene and Na ,⁵ H_2SO_4 ,⁶ Me_3SiCl and Et_3N ,⁷ Ac_2O and AcONa ,⁸ AcCl and MeONa ,⁹ p - TsOH ,¹⁰ $\text{PhSO}_2\text{-Cl}$ or ClCOOEt and Et_3N ,¹¹ SOCl_2 and Et_3N ,¹² $(\text{BOC})_2\text{O}$ and DMAP,¹³ BURGESS and DAST or $(\text{COCl})_2$.¹⁴

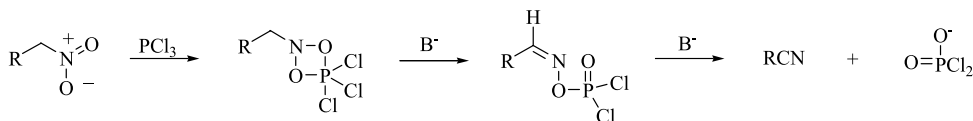
Nitrile is also a valuable synthetic intermediate for organic chemistry including pharmaceuticals, agricultural chemicals, dyes and material science and is also a key constituent in many natural products.¹⁵ Some of the useful methods for the preparation of alkylnitrile includes (i) the direct nucleophilic substitution of alkyl halides with inorganic cyanides,^{16a,b} (ii) the exchange of alcohols into cyanides either by using HCN or acetone cyanohydrins under Mitsunobu conditions^{16c} and (iii) the use of n - $\text{Bu}_3\text{P/KCN/18-crown-6}$ for the conversion of only primary alcohols to nitriles.^{16d} However, these reactions are frequently accompanied by elimination of hydrogen halides especially when bulky alkyl halides were used and gives lower yields

of the products with hindered primary and secondary alcohols. Recently, Iranpoor et al. have reported that alcohols, thiols, and trimethylsilyl ethers can be converted into their corresponding nitriles by using $\text{PPh}_3/\text{DDQ}/n\text{-Bu}_4\text{NCN}$ in acetonitrile solution at rt.^{16e} Usually, α,β -unsaturated nitriles can be obtained through a Wittig reaction of aldehyde with cyanoalkyl phosphonates. However, it always results in an unbiased form of *E*- and *Z*-isomeric nitriles.¹⁷ Preparation of nitrile by means of dehydration of amides or aldoximes with an appropriate nonmetal dehydrating agent is an alternative method, which also suffers from disadvantages, such as inconvenient preparation of the reagents, limited substrate scope or incompatibility of sensitive groups to the reaction condition.¹⁸ Several main or transition metal complexes were also used as dehydrating agents to affect this transformation.¹⁹ The conversion of primary nitro compounds into nitrile were also reported by different electrophilic phosphorus derivatives^{20a-c} such as $(\text{EtO})_2\text{PCl}$, P_2I_4 , and PCl_3 , sulfur compounds^{21a-d} such as SO_2 , $\text{Me}_3\text{SiSSiMe}_3$, and CS_2 , silyl derivatives²² such as Me_3SiI , radical chemistry,²³ or isocyanides.²⁴ Wehrli et al. used PCl_3 in pyridine to generate nitriles from primary nitro compounds in moderate yields and the following reaction mechanism (Scheme 1) has been proposed.^{20c}

Our previous studies established that β -nitrostyrenes react with different nucleophiles to generate nitroalkanes, halooximes, nitrile oxides, and polycyclic compounds under different reaction conditions.²⁵ As part of our incessant research efforts with nitroolefin chemistry, we

Keywords: Reaction mechanism; Nitrile; β -Nitrostyrene; Malonate ester; PCl_3 ; Nitrile oxide intermediate; Cyclic compounds.

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Scheme 1.

wish to report the reaction of *trans*- β -nitrostyrene **1** with different anions of malonate esters to generate nitronates and subsequent treatment with PCl_3 in the absence/presence of DMAP to afford nitroalkane **4** or **7**, chlorooxime **5**, nitrile **6**, **9** or **12**, and cyclic products **8** or **11** under different conditions and also to propose a plausible reaction mechanism.

2. Results and discussion

trans- β -Nitrostyrene **1a** reacts with the anion of dimethyl malonate to afford nitronate **3a**, and subsequent treatment with 3 equiv of PCl_3 for 1.5 h at rt afforded nitroalkane **4a** (28%), chlorooxime **5a** (26%), and nitrile **6a** (23%) (Scheme 2).

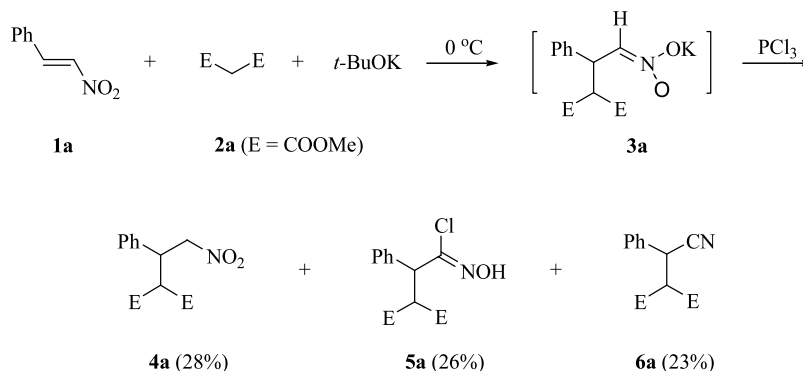
The compounds **4a**, **5a** and **6a** were characterized thoroughly using ^1H , ^{13}C NMR spectrums and the data is in consistent with the reported literature data.²¹ Although parts of the ^1H NMR pattern of **5a** are similar to **6a**, these two products can be distinguished by the following characteristics. For example, the coupling constant of the vicinal proton of chlorooxime **5a** is 12.0 Hz and that of nitrile **6a** is only 9.6 Hz. In addition to this, the D_2O exchangeable proton of $\text{ClC}=\text{NOH}$ was observed in product **5a**. Besides this, different IR absorptions were also observed for compound **5a** [3410 cm^{-1} (OH, broad) and 1639 cm^{-1} ($\text{C}=\text{N}$ stretch, weak)] and **6a** [2248 cm^{-1} (CN stretch, weak)]. In the ^{13}C NMR spectrums of these compounds absorption at δ 141.24 ppm corresponds to $\text{ClC}=\text{NOH}$ in **5a** and at δ 118.40 ppm to CN in **6a** and are also useful to distinguish between the two products.

Similar reactions were also conducted in different solvents with varying amounts of DMAP under different reaction conditions and all the experimental results were shown in Table 1. The result of entry 1 indicates that nitronate **3a** can be converted into **4a**, **5a** and **6a** by reacting with PCl_3 in THF solution. The increase in the amount of PCl_3 from 5 to 10 equiv did not improve the yields of **4a**, **5a** and **6a**.

Literature studies revealed that DMAP is one of the most effective reagents to convert the nitronate into the final products.²¹ A careful observation has led to identify two different reaction conditions during the addition of DMAP. Addition of 0.5 equiv of DMAP initially to the nitronate solution, followed by PCl_3 resulted in the formation of products **4a** (32%) with increased yield and **5a** (23%) and **6a** (25%) with decreased yield. In another variation, addition of PCl_3 followed by DMAP resulted in the increased yield of nitrile **6a** (38%) with reduced yields of **4a** (13%) and **5a** (15%). The decrease in the yields of **4a** and **5a** and the increase in the yield of **6a** clearly support the assumption that, DMAP plays an important role during reaction. Based on the above observation, increasing the amount of DMAP to 5 equiv afforded the nitrile product **6a** in 49% yield. Similarly, with further increase in the amount of DMAP to 10 equiv the yield of **6a** increased to 62%. These results clearly signify that the increase in the amount of DMAP increases the formation of nitrile product **6a** efficiently.

The effect of solvents and temperature were also investigated by employing different reaction conditions at different reaction times and proved that all the parameters play important roles and may have different effects to the same reaction. After observing the results of entries 1–7 in THF solution, pyridine was used as solvent for similar reactions by modifying the literature procedures and conditions. Only 13% of **4a** and 29% of **6a** were obtained and no product **5a** was observed when the reaction was carried out in pyridine at $95\text{ }^\circ\text{C}$ for 2 h (entry 8). However, only 34% of **6a** was isolated when the same solution was stirred at rt for 9 h (entry 9). These results indicate that **4a** can be converted into **6a** slowly in pyridine solution and also consist with literature report.^{21c}

Although the use of pyridine as solvent afforded the product **6a** only, the longer reaction times and formation of insoluble materials made the workup very difficult. In addition to this, lower yield of products, tedious workup procedures and longer reaction times limited the use of pyridine as a choice of solvent. In order to attain better yields of the nitrile, a



Scheme 2.

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