



A new facile way to generate Nitrile Oxides from Dichloronitroethylenes

Eva Nutz, Viktor A. Zapol'skii, Dieter E. Kaufmann*

Institute of Organic Chemistry, Clausthal University of Technology, 38678 Clausthal-Zellerfeld

Abstract

The reaction of perchloronitrobutadiene **1** with electron deficient alkenes like 4-nitroaniline does not lead to the expected C-4 diamino substitution product but under reaction of the nitro group and loss of the dichloromethylene moiety it leads to vinylidene arylhydrazines instead.¹

The proposed mechanism of this unusual reaction contains formation of an oxazinone ring which upon cycloreversion forms a chlorinated nitrile oxide.

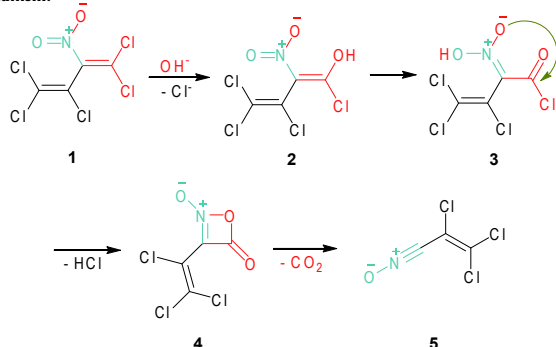
This reaction can be performed in the presence of inorganic bases such as NaOH, so that the formed nitrile oxide can be trapped easily with alkenes building the expected dihydroisoxazoles in reasonable yields. It is feasible to vary the used dichloronitroethylenes, therefore this reaction can be applied to even more complex structures, too.

Key words: nitro compounds, halides, nitrile oxides, dihydroisoxazoles, 1,3 dipolar cycloaddition.

Introduction

Nitrile oxides are valuable precursors in organic synthesis. They are prepared e.g. from primary nitroalkanes by dehydration with phenylisocyanate und triethylamine, better known as Mukaiyama-Hoshino method². An alternative method is the preparation from aldoximes via chlorination and elimination³, or via oxidation with aqueous sodium hypochlorite.⁴ The presented method is the first to use secondary nitroalkenes instead, and as only an inorganic base is necessary, the byproducts are very simple because only carbon dioxide, sodium chloride and water are formed. They are all easy to trap or to remove, so that a very clean reaction is provided.

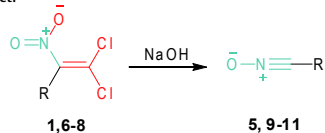
Mechanism:



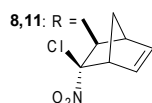
Discussion

The reaction of 2-nitroperchlorobuta-1,3-diene (**1**) with sodium hydroxide leads in the first step to the nucleophilic substitution of one chlorine atom. The next step is a rearrangement in which the hydrogen shifts to an oxygen atom in the nitro group, so that both, a nitronic acid and an acid chloride are formed simultaneously. The nitronate attacks in the next step the acid chloride to form an oxazinone-N-oxide **4** under loss of HCl. Afterwards heterocycle **4** undergoes cycloreversion to form nitrile oxide **5** and carbon dioxide.

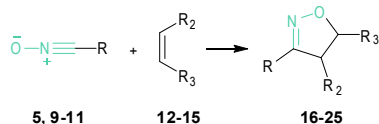
Obviously different dichloroethylenes were used (see scheme), even an additional nitro group in the sidechain is tolerated and leads to the butoxycarbonyl derivative **24**. Only the bicyclic starting material **8** did not react. Sterical hindrance might be the reason that we could not obtain any product.



1,5: R = CCICCl
6,9: R = Cl
7,10: R = CHCC(NO₂)



Trapping of the nitrile oxides with alkenes leads to dihydroisoxazoles which were almost all unknown at this time. As expected, the 5-substituted isomer is formed in the case of unsymmetrical substituted alkenes.⁵ Only by reacting the chlorinated nitrile oxide **9** with styrene (**13**) a mixture of 2 isomers were obtained. But by changing the workup procedure to a non-aqueous one it was even in that case possible to obtain only dihydroisoxazole **21** as single isomer.



Starting material	Alkene	Product	Yield
			63 %*
			52 %*
			43 %*
			29 %*
			32 %*
			22 %* 16 %**
			10 %* 22 %**
			25 %*
			28 %*
			0 %*

* aqueous workup
 ** non aqueous workup

Conclusion

Our method leads to an efficient way of generating nitrile oxides from inexpensive starting materials. As even an additional nitro group in the sidechain is tolerated, it is a good way to build up those precursors with complex structures as a sidechain. As expected, the formation proceeds with high regioselectivity in all cases. The use of norbornene as alkene probably leads to the formation of the *exo*-compound like **16** and **20**.⁶ This was examined by 2 dimensional NMR-studies on **16**.

References:

- [1] V. A. Zapol'skii, E. Nutz, J. C. Namyslo, A. E. W. Adam, D. E. Kaufmann, *Synthesis* **2006**, 17, 2927.
- [2] T. Mukaiyama, T. Hoshino, *J. Am. Chem. Soc.* **1960**, *82*, 5339.
- [3] R. Huisgen, W. Mack, *Tetrahedron Lett.*, **1982**, *17*, 583.
- [4] G. A. Lee, *Synthesis* **1982**, 508.
- [5] R. P. Litvinovskaya, V. A. Khripach, *Russian Chemical Reviews* **2001**, *5*, 405.