Nitrile Oxides; XVI.
The Dehydrodimers of Arenaldoximes as an *in situ* Source of Nitrile Oxides[1]

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Nitrile oxides are valuable intermediates for synthesis, especially of heterocyclic compounds[3]. As they are unstable under normal conditions (except for strongly sterically hindered members of the species) they have to be generated *in situ*, i.e., in the presence of a reaction partner. All known modes, however, of generating nitrile oxides from stable precursors involve somewhere in the process the presence of strong bases or acids which may interfere with the planned reaction[4,5]. Therefore, an interest exists in a method which would generate a nitrile oxide under neutral conditions.

In the long known dehydrodimers of aldoximes (**1**), we found the required neutral source for nitrile oxides. These compounds are formed from the aldoximes by oxidation with a variety of oxidizing agents, such as alkali metal hypohalites, potassium hexacyanoferrate(III), lead(IV) acetate, or oxides of nitrogen[6,8]. Our experiences in the preparation of a number of compounds **1** by some of these methods are listed in Table 1. No attempts were made to optimize the yields, but nitrogen dioxide in ethereal solution was preferred as oxidizing agent because of the purity of products **1** obtained and the simplicity of isolation.

The structure of these dehydrodimers is still in question; while the earlier proposals **1a** and **1b** have been abandoned, a decision between the aldazine-N,N′-bis-oxide- (**1c**) and the nitrone oximate- (**1d**) structure has not been reached so far. Structure **1c** may be derived from the neat conversion to the aldazine (**2**) with trivalent phosphorus compounds, a reagent specific for the deoxygenation of N-oxides[7]. However, the ease with which these compounds are oxidized to the corresponding furazan-2-oxides (**3**), as well as the I.R. spectra, are better explained by structure **1d**[8]. For these reasons, the non-committal designation of the title of this communication was preferred.

The dehydrodimers decompose thermally under mild conditions, e.g., in refluxing chloroform or benzene, forming

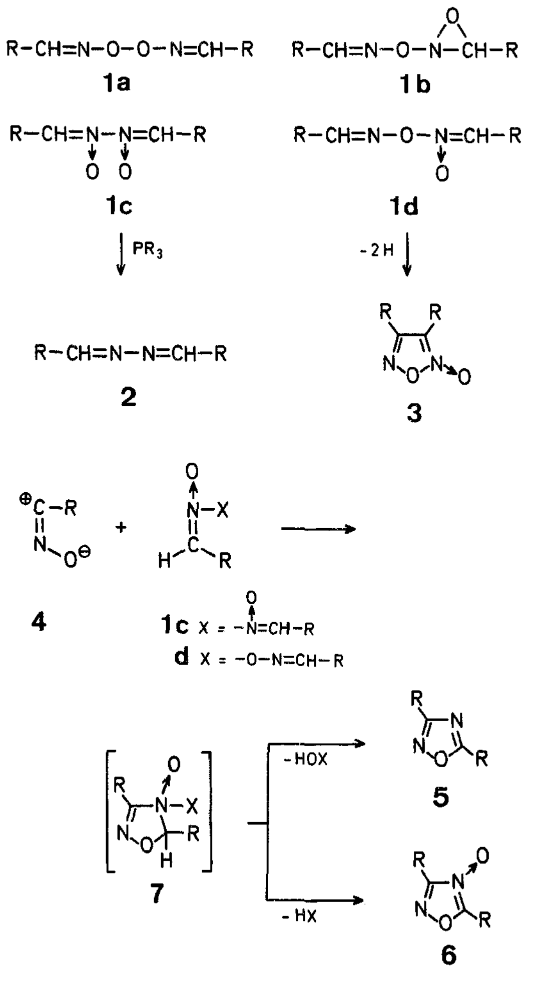
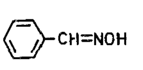
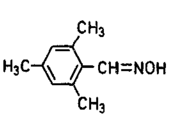
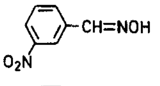
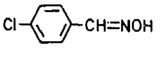
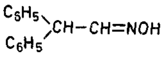


Table 1. Preparation of Dehydrodimers (1) of Aldoximes

R		Oxidizing Agent	Solvent	Reaction Conditions	Yield (%)	m.p. (dec.)	References
	(α)	J_2 and Na_2CO_3	benzene and H_2O	180 min, 25°	12[a]	97–100°	6c
	(α)	NO_2	ether	60 min, 0°	20	73–74°	
	(β)	NaOBr[b]	H_2O	60 min, 5°	63	111–112°	6a
	(β)	NO_2	ether	60 min, 0°	40	113–114°	
		NO_2	ether	60 min, 0°	15[c]	103–104°	
		NO_2	CH_2Cl_2	30 min, 0°	55	131–132°	6d
		NO_2	CH_2Cl_2	30 min, 0°	68	191–192°	6f
 $(C_6H_5)_2CH-CH=NOH$		NO_2	ether	60 min, 0°	30[d]	117–118°	
$(C_6H_5)_3C-CH=NOH$		NO_2	ether	60 min, 0°	0[d]	–	

[a] Consists of a mixture of dehydrodimers of α- and β-benzaldoxime, since iodine catalyzes the isomerization of the starting material.

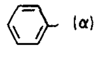
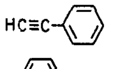
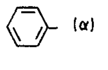
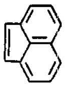
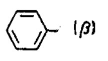
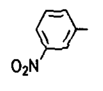
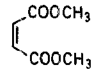
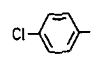
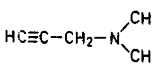
[b] Only 0.5 mol of sodium hypobromide per mol of oxime, otherwise 1 is oxidized to the nitrile oxide.

[c] $C_{20}H_{24}N_2O_2$ calc. C 74.04 H 7.46 N 8.64
(324.4) found 73.98 7.54 8.55

[d] $C_{28}H_{24}N_2O_2$ calc. C 79.97 H 5.75 N 6.67
(420.5) found 80.14 5.80 6.52

[e] Instead of 1, a mixture of starting material and triphenylacetonitrile oxide was obtained from which 56% of the latter was isolated by recrystallization from ethanol.

Table 2. Cycloaddition Products From **1** and Dipolarophiles

1 R =	Starting Materials Dipolarophiles	Cyclooadducts	Yield (%)	References
		3,5-Diphenyl-1,2-oxazole	52	9
		3-Phenyl-3a,9a-dihydroacenaphtho[1,2-*d*]-1,2-oxazole	28	10
		3-Phenyl-4,7-methanooctahydrobenzo[*d*]-1,2-oxazole	13	11
		4,5-*trans*-Dimethoxycarbonyl-3-(3-nitrophenyl)-4,5-dihydro-1,2-oxazole	64	12
	 $HC{\equiv}C{-}CH_2{-}N(CH_3)_2$	3-(4-Chlorophenyl)-5-dimethylaminomethyl-1,2-oxazole	48	13

one equivalent of nitrile oxide (**4**). If this nitrile oxide is trapped *in situ* by a suitable dipolarophile, the expected 1,3-cycloaddition products are obtained and the second half of **1** is found as the aldoxime. A number of such reactions are listed in Table 2; the yields could very likely have been improved by consideration of the suggestions below.

Cycloaddition of Dehydrodimers (1) of Aldoximes and Dipolarophiles; General Procedure:

The reactions were carried out by refluxing equimolar amounts (mostly, 0.01 mol) of the components in chloroform (50 ml) for 3 hr. After evaporation of solvent, the residue was recrystallized from ethanol and the product identified by I. R. spectrum, m.p., and comparison with an authentic specimen.

If the dehydrodimers are decomposed thermally without the presence of a suitable reaction partner, usually a large number of products are formed. Aside from the trivial products, such as the corresponding aldehyde, oxime, nitrile, and carboxylic acid, the more interesting products are the 1,2,4-oxadiazole **5** and the 1,2,4-oxadiazole-4-oxide **6**. Nitrile oxides are known to dimerize to compounds of the type **6** and to react with oximes to give **5** (through the intermediate **7**, X = H, with subsequent loss of water), but both reactions occur only in the presence of strong Lewis acids[14]. Thus, a different mechanism could be operative in this case[6e]: the nitrile oxide **4**, formed by thermal decomposition of **1**, adds to yet undecomposed **1** to give an intermediate **7** which in turn eliminates the oxime to form **6**, or the nitromethane-equivalent to give **5**[15]. In cases where either **4** or **1** are not prone to reaction with each other for electronic or steric reasons, the nitrile oxide will finally undergo the normal dimerization to the furazan-2-oxide **3**[6d]. It is obvious that these reactions leading to **3**, **5**, or **6** will compete with the desired cycloaddition, and may become prevalent if the generated nitrile oxide and the dipolarophile have little affinity towards each other.

The merit of the method described is the possibility to carry out cycloaddition of nitrile oxides with sensitive dipolarophiles. Because of the sensitivity of the dipolarophiles it will in all cases be advantageous to use a considerable excess of **1** to ensure complete conversion of the dipolarophile.

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[1] Part XV of the series: C. Grundmann, P. Kochs, J. R. Boal, *Liebigs Ann. Chem.* **761**, 162 (1972).

[2] Part of this work is taken from the Ph. D. Thesis of G. F. K., Carnegie-Mellon University, 1973.

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(b) G. Ponzio, G. Busti, *Gazz. Chim. Ital.* **36** II, 338 (1906).
(c) P. Robin, *Ann. Chim. (Paris)* [9] **16**, 77 (1921).
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[15] Phenylnitromethane and benzaldoxime have indeed been observed among the products of the thermal decomposition of **1** ($R = C_6H_5$); R. Ciusa, E. Parisi, *Gazz. Chim. Ital.* **55**, 416 (1925).