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ISOLATION OF NITRILE OXIDES FROM THE THERMAL FRAGMENTATION OF FURAZAN N-OXIDES

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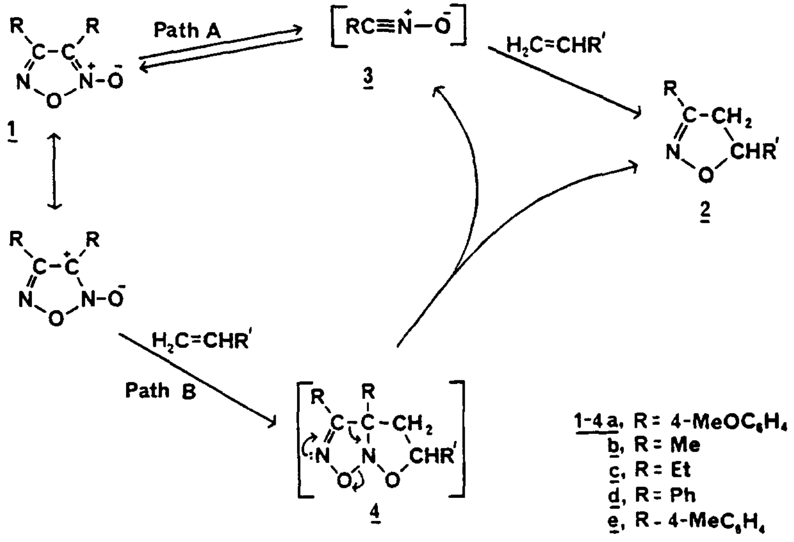
Summary: Flash vacuum pyrolysis of furoxans generates nitrile oxides, which have been reacted with alkenes to yield 2-isoxazolines, and have been examined by ^{1}H and ^{13}C nmr spectroscopy.

It has recently been established[1] that the thermolysis of 3,4-disubstituted furazan N-oxides (furoxans, 1) in the presence of alkenes at temperatures in excess of 200°C results in the formation of isoxazolines (2). The process was assumed to involve a 1,3-dipolar cycloaddition reaction between the alkene and the two nitrile oxide fragments (3) resulting from the thermal cleavage of the oxadiazole ring [Path A], thus reversing the established nitrile oxide to furoxan dimerisation.[2a] However, nitrile oxides were not detected during the course of the reaction[3] and the possibility of 2 being formed by direct interaction between the alkene and the furoxan could not therefore be ruled out; for nitrone-like cycloaddition[4] of the furoxan itself to the alkene and subsequent collapse of the intermediate adduct (4) would also lead to the observed products [Path B].



1-4a, R = 4-MeOC$_6$H$_4$
b, R = Me
c, R = Et
d, R = Ph
e, R = 4-MeC$_6$H$_4$

We have now found that, using conventional Flash Vacuum Pyrolysis (FVP) apparatus and technique,[5] it is possible to isolate and identify the nitrile oxide fragments. For example, FVP ($500^{o}C$, 10^{-3}mmHg) of dianisylfuroxan (1a) yielded anisonitrile oxide (3a), the ir and ^{1}H nmr spectra of which were indistinguishable from those of the authentic material generated by base treatment of the corresponding hydroxamic acid chloride.[2c] Further confirmation of the identity of the product was obtained by treating it with excess hex-1-ene and isolating the isoxazoline cycloadduct (2a, R' =Bu, 75%).

While the conventional methods[2d] are satisfactory for the preparation of aromatic nitrile oxides having long lifetimes, they prove cumbersome for the isolation of the short-lived aliphatic counterparts, which undergo rapid dimerisation to the corresponding furoxan.[2a] Thus acetonitrile oxide (3b) is reported[2e] to exist for less than 1 min at $18^{o}C$ and has consequently received little attention.[6] In contrast we find that FVP ($600^{o}C$, 10^{-3} mmHg) of dimethylfuroxan (1b) provides a straightforward means of generating acetonitrile oxide, thus permitting detailed examination of its properties. Recombination of the nitrile oxide fragments back to the furoxan is prevented by maintaining the FVP cold trap temperature at $<-40^{o}C$. By this technique solutions of 3b in $CDCl_3$ were prepared and its nmr spectra recorded. The ^{13}C nmr spectrum ($CDCl_3$, $-51^{o}C$) comprises the two lines marked 'n' in Fig. 1. The larger peak at 0. 8 ppm is attributed to the methyl carbon, while the broad signal centred at 35. 6 ppm, which is partially resolved into a triplet due to coupling with the ^{14}N nucleus, is assigned to the carbon of the nitrile oxide group.[7] Some contamination by 1b, either resulting from incomplete fragmentation or due to partial dimerisation of the nitrile oxide,[2a] is indicated by the presence of the four lines marked "f", this assignment being made by comparison with the spectrum obtained for the authentic material. On allowing the solution to warm to and remain at room temperature for 3 days, the lines attributed to 3b disappeared, while those due to 1b increased in intensity (Fig. 2), consistent with the expected recombination of 3b to 1b. This process may also be monitored by ^{1}H nmr. The spectrum at $-40^{o}C$ consists of three lines, the outside two at 2. 21 and 2. 40δ being due to 1b while the third line at 2. 26δ is assigned to 3. 6.[6b] On warming to 26^{o} the signal due to 1b increased at the expense of that due to 3b, the process being complete after ca 3 days.[8]

In addition to allowing spectroscopic examination of the short lived nitrile oxides, the FVP technique also broadens the scope of the synthetic route from furoxans to isoxazolines. For the range of usable alkenes is greatly extended by the removal of the necessity for them to boil at $>200^{o}C$.[9] Furthermore, the yields of the cycloadducts are increased by the reduction of the amount of tarry byproducts which were a feature of the original furoxan based route,[1] and which may be attributed to the limited thermal stability of both the alkenes and the isoxazoline products. The isoxazolines produced by the FVP technique are listed in the Table, together with the reaction conditions used.

While these FVP results do not necessarily preclude direct reaction between the alkene and the furoxan in solution, they demonstrate both a novel means of isolating and studying even the most reactive nitrile oxides, and a more generally applicable route fro furoxans to isoxazolines.

Figure 1

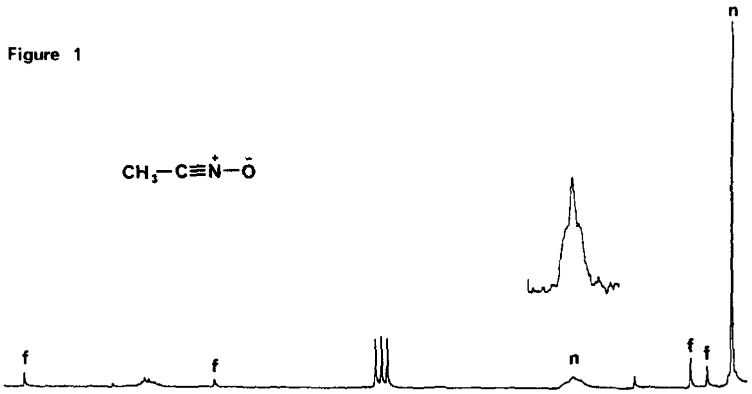


Figure 2

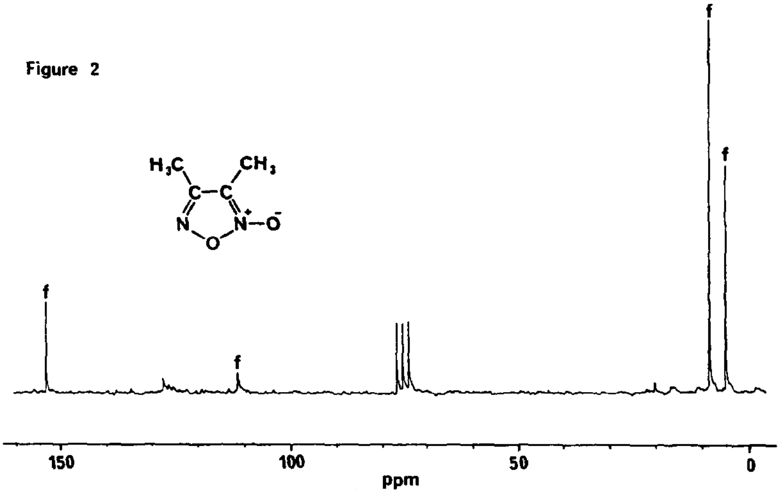


Figure 1. ^{13}C nmr spectrum (CDCl$_3$, -51°C) of solution resulting from FVP of dimethylfuroxan (1b), showing signal due to acetonitrile oxide (3b, lines marked "n") with contamination by 1b (lines marked "f").

Figure 2. ^{13}C nmr spectrum of reaction mixture after 3 days at room temperature, indicating increased concentration of 1b and absence of 3b.

TABLE

Isoxazolines(2) produced by reaction of alkenes (CH_2=CHR') with nitrile oxides (RCNO, 3) produced via FVP fragmentation of furoxans (1).

R	R'	FVP[(a)] oven temp (°C)	% Yield
4-$MeOC_6H_4$	Bu	500	75
Me	Bu	600	79
Et	Bu	650	95
Ph	Bu	550	97
4-MeC_6H_4	$C_{12}H_{25}$	500	86

(a) Pressure ca 10^{-3}mmHg.

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References and Footnotes

1. J. A. Chapman, J. Crosby, C. A. Cummings, R. A. C. Rennie, and R. M. Paton, J. C. S. Chem. Comm., 240 (1976) and references therein.
2. C. Grundmann and P. Grünanger, 'The Nitrile Oxides,' Springer-Verlag, West Berlin and Heidelberg, (1971); (a) pp. 75-81; (b) pp.62-67 and 96-111; (c) p. 55; (d) Chapter 3; (e) p. 16.
3. At temperatures in excess of 200°C the rearrangement of nitrile oxides to isocyanates and their cycloaddition reactions with alkenes are rapid; see Ref. 2b.
4. Nitrone-like character of furoxans has been invoked to explain the reactions of dibenzoylfuroxan with phenylacetylene, styrene and stilbene: M. Altaf-ur-Rahman, A.J. Boulton and D. Middleton, Tetrahedron Lett., 3469 (1972).
5. See for example: G. Seybold, Angew. Chem. Int.Edn., 16, 365 (1977).
6. (a) G. Zinner and H. Gunther, Angew. Chem. Int. Edn., 3, 383 (1964).
   (b) A. Brandi, F. De Sarlo and A. Guana, J. C. S. Perkin I, 1827 (1976).
7. M. Christl, J. P. Warren, B. L. Hawkins and J. D. Roberts, J. Am. Chem. Soc., 95, 4392 (1973).
8. The rates of disappearance of 3b and formation of 1b showed the expected second order kinetics; W. R. Mitchell and R. M. Paton, unpublished observations.
9. In the original furoxan to isoxazoline route[1] all the furoxans required >200°C for fragmentation to occur and the reactions were performed at atmospheric pressure.

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