Carbonyl Oxide Chemistry. 5.[1] Nucleophilic Trapping Reaction with Aldo and Keto Oximes. Synthesis of Hydroperoxynitrones

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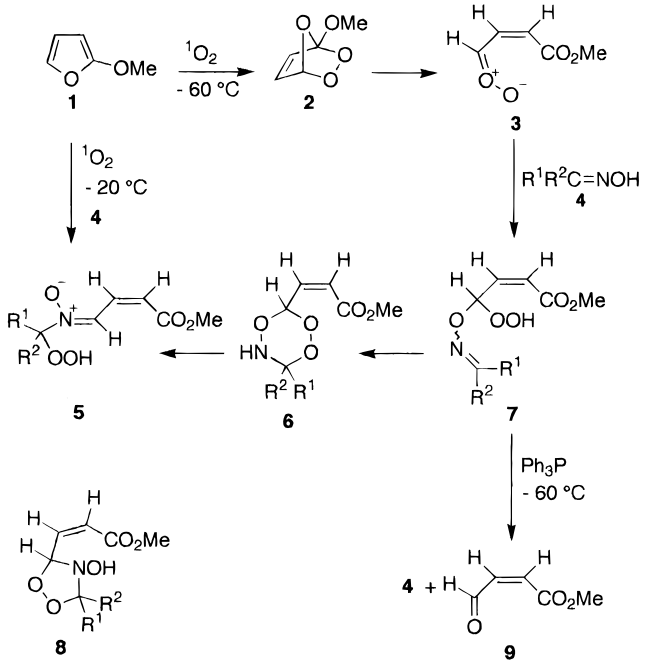
Recently, we reported that 1-methoxy-2,3,7-trioxabicyclo-[2.2.1]hept-5-ene (**2**), obtained by dye-sensitized photooxygenation at −78 °C of the furan **1**, in participating solvents leads to cyclic or acyclic adducts *via* carbonyl oxide **3**.[1] We have now investigated the behavior of *endo*-peroxide **2** with aldo and keto oximes in order to verify if, toward carbonyl oxide **3**, the nucleophilic character of the oxime oxygen[2] prevailed over the dipolarophilic character of the oxime carbon−nitrogen double bond.[4] The research was also part of a program on the preparation and use of organic peroxides.[5,7]

Unexpectedly, hydroperoxynitrones **5** were obtained that were generally isolated and characterized. These results were especially surprising in light of the fact that the only previously reported hydroperoxynitrones were obtained by singlet oxygen oxygenation of some nitrones at −78 °C. The latter were characterized by ^{1}H NMR spectra recorded at −60 °C, since upon warming to room temperature they led to complex mixtures of compounds *via* cyclic peroxides.[8]

Results and Discussion

We carried out the tetraphenylporphyrin-sensitized photooxygenation of 2-methoxyfuran (**1**) in $CDCl_3$−$CFCl_3$ at −60 °C in the presence of an excess of cyclohexanone oxime (**4a**).[9] After 90 min the ^{1}H and ^{13}C NMR spectra of the reaction mixture were recorded at −60 °C and, in addition to unreacted **4a**, showed the presence of a single compound. Upon triphenylphosphine reduction at −60 °C the latter led to the known[1] (*Z*) unsaturated aldehyde **9**. In addition to the ester signal (δ 165.2 ppm), the ^{13}C NMR spectrum of the reaction product showed a C=N resonance (δ 163.2 ppm) similar to that of the starting oxime (δ 160.5 ppm). A single signal (δ 88.4 ppm) in the typical δ range for carbons bearing two heteroatoms was also present. These data are in agreement with the structure of α-oxime ether hydroperoxide **7a**,[11] and therefore, the 1,2,4-dioxazolidine structure **8a** must be excluded[13] (Scheme 1). It follows that the carbon−nitrogen double bond of oxime **4a** is unable to give [3 + 2] cycloaddition to the carbonyl oxide **3**, and an oxygen nucleophilic trapping reaction takes place. The fact that both cyclohexanone *O*-methyl and *O*-acetyl oxime under the same conditions were recovered unchanged provides strong evidence for the suggested mechanism. At −20 °C compound **7a** is converted to the hydroperoxynitrone **5a**. To our knowledge, a rearrangement of this type has never been observed. Here it occurred through certain

Scheme 1. Singlet Oxygen Oxygenation of 2-Methoxyfuran (1) In the Presence of Aldo and Keto Oximes 4



a; R^1, R^2 = -$(CH_2)_5$-
b; R^1 = R^2 = Me
c; R^1 = Me, R^2 = Ph
d; R^1 = Me, R^2 = H
e; R^1 = Ph, R^2 = H

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(1) Iesce, M. R.; Cermola, F.; Guitto, A.; Scarpati, R.; Graziano, M. L. *J. Org. Chem*. **1995**, *60*, 5324.

(2) The nucleophile trapping reaction of carbonyl oxides with methanol has been extensively used to verify the production of the dipolar species, but the behavior of these elusive entities toward nucleophiles other than alcohols has not yet been well defined.[3]

(3) Bunnelle, W. H. *Chem. Rev*. **1991**, *91*, 335.

(4) As 1,3-dipoles, carbonyl oxides participate in the cycloaddition chemistry characteristic of this class of reactive intermediates, and a number of π-bonded systems have been found to be suitable dipolarophilic partners.[3,5] Hence, the reaction with imines is quite efficient, and 1,2,4-dioxazolidines are obtained generally in high yields.[6]

(5) Reference 1 and references therein.

(6) McCullough, K. J.; Mori, M.; Tabuchi, T.; Yamakoshi, H.; Kusabayashi, M.; Nojima, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 41 and references therein.

(7) (a) Iesce, M. R.; Cermola, F.; Guitto, A.; Scarpati, R.; Graziano, M. L. *Synlett* **1995**, 1161 and references therein. (b) Iesce, M. R.; Cermola, F.; Graziano, M. L.; Cimminiello, G.; Scarpati, R. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1855. (c) Iesce, M. R.; Graziano, M. L.; Cermola, F.; Scarpati, R. *J. Chem. Soc., Chem. Commun*. **1991**, 1061.

(8) Erden, I.; Griffin, A.; Keeffe, J. R.; Brinck-Kohn, V. *Tetrahedron Lett*. **1993**, 793. Cf. also: Ching, T. Y.; Foote, C. S. *Tetrahedron Lett*. **1975**, 3771.

(9) Control experiments showed that oximes are unreactive at −20 °C with both singlet oxygen and with dimethyl 1-methoxy-4-phenyl-2,3,7-trioxabicyclo[2.2.1]hept-5-ene-5,6-dicarboxylate; the latter is an *endo*-peroxide that does not open into the corresponding carbonyl oxide and was stable at the temperature of the experimental conditions used.[7b,10]

(10) Graziano, M. L.; Iesce, M. R.; Cimminiello, G.; Scarpati, R. *J. Chem. Soc., Perkin Trans. 1* **1989**, 241.

(11) In the ^{1}H NMR spectrum the broad singlet at δ 14.11 ppm is unusually low for a OOH group that ordinarily absorbs at *ca.* δ 8−9 ppm. This observed shift can be attributed to intramolecular H-bonding to the unsaturated nitrogen.[12]

(12) Richardson, W. H. In *The Chemistry of Peroxides*; Patai, S., Ed.; J. Wiley and Sons: New York, 1983; Chapter 5, p 152.

(13) ^{13}C NMR data also exclude the structure of nitrone derived from the nitrogen trapping of **3** by the oxime since the ^{13}C nitronyl chemical shift appears in the range δ 125−150 ppm.[14]

(14) Dopp, D.; Dopp, H. In *Houben-Weyl*; Klamann, D., Hagemann, H., Eds.; Thieme: Stuttgart, 1990; Band E14b/2, p 1379.

S0022-3263(96)01375-8 CCC: $12.00

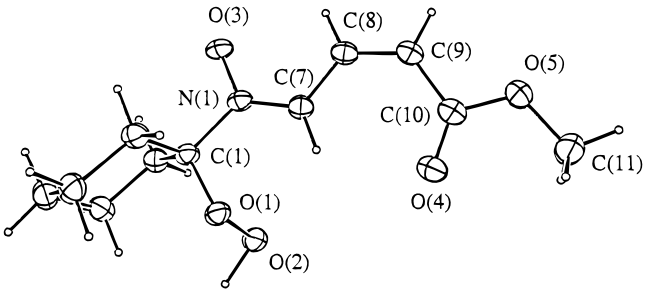


Figure 1.

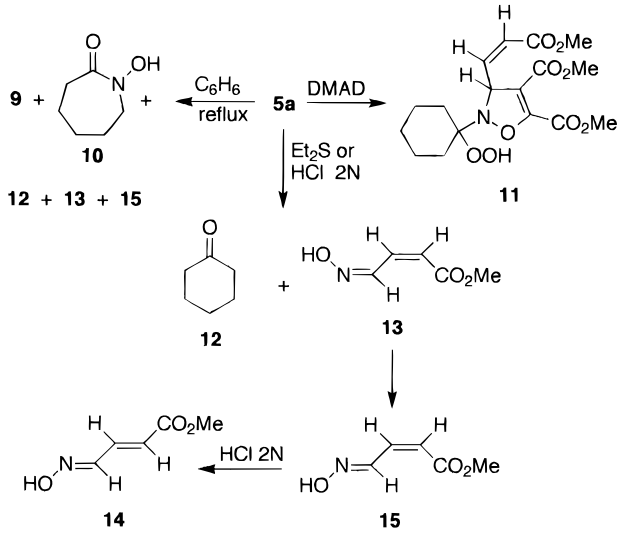
short-lived intermediates evidenced by recording the ^1H and ^{13}C NMR spectra of the reaction mixture at regular time intervals at −40 °C. At this temperature, it was found that the signals of **7a** decreased, while new signals appeared that collapsed into those of the nitrone **5a**. In particular, in addition to two singlets at δ 3.78 ppm and δ 3.79 ppm, two sets of ^1H signals due to two CHCH=CH systems were present in the range δ 6.0−6.5 ppm as well as four carbon signals at δ 92.1, 98.5, 102.6, and 104.6 ppm in the ^{13}C NMR spectrum. These data would suggest that the intermediates are two conformational isomers of dihydro-1,2,4,5-trioxazine **6a**. No further intermediate was observed in the rearrangement of **6a** to **5a**.[15]

When the sensitized photooxygenation of **1** in the presence of **4a** was carried out in CH_2Cl_2 at −20 °C, in addition to unreacted **4a**, only the nitrone **5a** was observed. Silica gel chromatography led to the isolation of **5a**, whose structure was assigned on the basis of elemental analyses and spectral data and was confirmed by X-ray crystallography (Figure 1).[16]

In addition to cyclohexanone (**12**), treatment of the hydroperoxynitrone **5a** with Et_2S led to (*Z*)-*syn*-oxime **13** (85%), which slowly converted into (*Z*)-*anti*-isomer **15** (Scheme 2). Under acid conditions the latter isomerized to (*E*)-*anti*-oxime **14**, which was directly obtained by acid hydrolysis of the hydroperoxynitrone **5a**. The functionalized nitrone **5a** reacted with dimethyl acetylenedicarboxylate (DMAD) at room temperature and, by 1,3-dipolar cycloaddition, led to the hydroperoxy-2,3-dihydroisoxazole **11** in 90% yield. In refluxing C_6H_6 compound **5a** gave a mixture of products [**9** (32%), **10** (33%), **12** (6%), and **13** + **15** (22%)] that were structurally similar to those previously obtained from thermally unstable hydroperoxynitrones.[8]

Similar results were obtained when the photooxygenation of **1** was carried out in the presence of oximes **4b**−**e** (Scheme 1).[17] However, it should be noted that (1) in contrast to nitrones **5a**,**b**,**d**,**e**, compound **5c** was stable only below −15 °C and at room temperature decomposed to the oxime **13**, acetophenone and ketone-related unidentified peroxides;[18] (2) for series **e**, the ^1H NMR spectrum of the photooxygenation reaction at −60 °C

Scheme 2. Chemical Properties of Hydroperoxynitrone 5a



showed a complex mixture that, upon warming to room temperature, led to hydroperoxynitrone **5e** and large amounts of unidentified compounds.

In conclusion, the reported results show that the carbon−nitrogen double bond of oximes is unable to give [3 + 2] cycloaddition to carbonyl oxide **3** and an oxygen nucleophilic trapping reaction takes place. The reaction, which is the first ever reported addition of an oxime to a carbonyl oxide,[3] provides a useful one-pot synthesis of hydroperoxynitrones **5**. The latter, owing to the presence of both nitrone and hydroperoxy functions, may exhibit interesting biological properties and serve as useful materials in various industrial processes.[19,20] Finally, the high yield together with the mild reaction conditions make the conversion of hydroperoxynitrone **5a** into hydroperoxy-2,3-dihydroisoxazole **11** a convenient entry to the synthesis of this compound class. Isoxazoline **11** shows an unusual stability for this ring system[21] and represents the first example of derivatives bearing a hydroperoxy substituted carbon on nitrogen.

Experimental Section

General. Melting points are uncorrected. IR spectra were recorded with chloroform as solvent. ^1H and ^{13}C NMR spectra were run in $CDCl_3$ at 400 and 100.6 MHz, unless otherwise stated. Chemical shifts are reported in ppm referenced to the TMS. DEPT techniques were employed to determine the multiplicity in the ^{13}C spectra. The solvents used for the reactions were anhydrous. 2-Methoxyfuran (Aldrich), tetraphenylporphyrin (TPP) (Fluka), cyclohexanone oxime (Fluka),

(15) The hypothesis that the rearrangement occurs through the intermediacy of an undetected oxaziridine is to be ruled out since methyl (*Z*)-3-[2-(1-hydroperoxycyclohexyl)oxaziridin-3-yl]propenoate, casually obtained by prolonged irradiation of the photooxygenation mixture (see Experimental Section), was a stable compound and under no conditions gave the nitrone **5a**.

(16) The authors have deposited X-ray data for this structure with the Cambridge Crystallographic Data Center. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Center, 12 Union Road, Cambridge, CB2 1EZ, UK.

(17) The stereochemistry of the carbon−nitrogen double bond of **7c**,**d**, derived from the asymmetric oximes **4c**,**d**, was not assigned.

(18) This mixture was also obtained when the reaction was carried out in CH_2Cl_2 at −20 °C. The low stability of **5c** can be related to that observed for nitrones similarly substituted on the hydroperoxidic carbon.[8]

(19) For nitrone applications see among others: Kato, K.; Nakano, M.; Richaado, G. K. Jpn. Patent 06239737, 1994; *Chem. Abstr.* **1995**, *122*, 1096k. Krimer, M. Z.;, Styngin, E. P.; Rekhten, M. A.; Grushetskaya, G. N.; Uzhavka, Z. N.; Panasenko, A. A.; Molchanov, O. Yu.; Abelentsev, V. I. *Zh. Org. Chim.* **1993**, *29*, 1859. Sandler, S. R.; Karo, W. *Organic Functional Group Preparations*; Academic Press: New York, 1986; Vol. III, p 355.

(20) For hydroperoxide applications see among others: Oda, K.; Takei, K. Jpn. Patent 0710709, 1995; *Chem. Abstr.* **1995**, *122*, 207776r. Inoi, T. Jpn. Patent 0211501, 1990; *Chem. Abstr.* **1990**, *113*, 120874m. *Organic Peroxides*; Ando, W., Ed.; Wiley: Chichester, 1992. Sheldon, R. A. In *The Chemistry of Peroxides*; Patai, S., Ed.; Wiley: Chichester, 1983; p 161. Kropf, H.; Torkler, F. In *Houben-Weyl*; Kropf, H., Ed.; Thieme: Stuttgart, 1990; Band E14b/2; p 39.

(21) Freeman, J. P. *Chem. Rev.* **1983**, *83*, 241.

acetone oxime (Fluka), acetaldehyde oxime (mixture of *syn* and *anti*) (Fluka), benzaldehyde oxime (Fluka) and dimethyl acetylenedicarboxylate (DMAD) (Aldrich) were used without purification. Acetophenone oxime[22] was prepared according to the literature procedure. Silica gel (0.063−0.2 mm Macherey-Nagel) and light petroleum (bp 40−60 °C) were used for column chromatography. CAUTION: since organic peroxides are potentially hazardous compounds, they must be handled with care. No particular difficulties were experienced in handling any of the new peroxides reported in this work.

General Procedure for the TPP-Sensitized Photooxygenation of 2-Methoxyfuran (1) in the Presence of Oximes 4 in $CFCl_3/CDCl_3$. Each solution (5×10^{-2} M) of the furan **1** (0.5 mmol) and the oxime **4** (2.5 mmol) in $CFCl_3/CDCl_3$ (1:2 v/v), after the addition of the sensitizer (1.8×10^{-4} mmol), was irradiated at −60 °C with a halogen-superphot lamp (Osram, 650 W). During irradiation, dry oxygen was bubbled through the solution, which was kept at this temperature. When the reaction was complete (90 min), the ^{1}H and ^{13}C NMR spectra recorded at −60 °C showed the presence of **7**, in addition to the unreacted oxime **4**, except for entry **e**. Compounds **7a**−**d** converted slowly at −40 °C and rapidly at −20 °C into intermediates **6a**−**d** (^{1}H NMR), which in turn rearranged into the corresponding hydroperoxynitrones **5a**−**d**. For entry **e**, the ^{1}H NMR of the irradiation reaction at −60 °C showed a complex mixture which evolved continuously upon heating, leading to the hydroperoxynitrone **5e** and large amounts of unidentified products at rt. Nitrones **5a**,**b**,**d**,**e** were stable at rt, while **5c** decomposed to a mixture of oxime **13**, acetophenone, and ketone-related unidentified peroxidic compounds.[23] Selected spectral data of compounds **7a**−**d**, **6a**−**d**, and **5c** were deduced by a careful analysis of the ^{13}C and/or ^{1}H NMR spectra of the related reaction mixtures, recorded at −60, −40, and −20 °C, respectively, after the signals of the other products were subtracted. It was not possible to run satisfactory ^{13}C NMR spectra for **6b** and **6d** owing to their low concentration in the reaction mixtures.

Cyclohexanone oxime *O*-[(*Z*)-1-hydroperoxy-3-(methoxycarbonyl)-2-propenyl] ether (7a): ^{1}H NMR ($CFCl_3/CDCl_3$) δ 3.77 (s, 3 H), 6.19 (d, J = 11.7 Hz, 1 H), 6.51 (dd, J = 11.7, 7.0 Hz, 1 H), 7.54 (d, J = 7.0 Hz, 1 H) and 14.11 (br s, 1 H); ^{13}C NMR ($CFCl_3/CDCl_3$) δ 52.2 (q), 88.4 (d), 124.9 (d), 137.0 (d), 163.2 (s), 165.2 (s).

Acetone oxime *O*-[(*Z*)-1-hydroperoxy-3-(methoxycarbonyl)-2-propenyl] ether (7b): ^{1}H NMR ($CFCl_3/CDCl_3$) δ 2.39 and 2.57 (2 × s, 6 H), 3.79 (s, 3 H), 6.21 (d, J = 11.5 Hz, 1 H), 6.47 (dd, J = 11.5, 7.9 Hz, 1 H), 7.48 (d, J = 7.9 Hz, 1 H), 14.04 (br s, 1 H); ^{13}C NMR ($CFCl_3/CDCl_3$) δ 20.9 (q), 21.4 (q), 52.3 (q), 88.7 (d), 125.4 (d), 136.3 (d), 157.6 (s), 165.2 (s).

Acetophenone oxime *O*-[(*Z*)-1-hydroperoxy-3-(methoxycarbonyl)-2-propenyl] ether (7c):[17] ^{1}H NMR ($CFCl_3/CDCl_3$) δ 2.70 (s, 3 H), 3.53 (s, 3 H), 6.17 (d, J = 11.3 Hz, 1 H), 6.68 (dd, J = 11.3, 8.1 Hz, 1 H), 7.33 (d, J = 8.1 Hz, partially overlapping to phenyl hydrogens), 13.74 (br s, 1 H); ^{13}C NMR ($CFCl_3/CDCl_3$) δ 21.9 (q), 52.0 (q), 91.2 (d), 157.7 (s), 164.3 (s).

Acetaldehyde oxime *O*-[(*Z*)-1-hydroperoxy-3-(methoxycarbonyl)-2-propenyl] ether (7d):[17] ^{1}H NMR ($CFCl_3/CDCl_3$) δ 2.21 (d, J = 6.2 Hz, 3 H), 3.78 (s, 3 H), 6.20 (d, J = 11.5 Hz, 1 H), 6.42 (dd, J = 11.5, 7.9 Hz, 1 H), 6.84 (d, J = 7.9 Hz) and 7.53 (q, J = 6.2 Hz) partially overlapping to the two quartet signals of the unreacted *syn*- and *anti*-oximes **4d**, 13.5 (br s, 1 H); ^{13}C NMR ($CFCl_3/CDCl_3$) δ 13.0 (q), 52.2 (q), 97.0 (d), 125.7 (d), 136.5 (d), 144.3 (d), 165.3 (s).

Methyl (*Z*)-3-(1,2,4-triox-5-azaspiro[5.5]undec-3-yl)propenoate (6a) (two isomers): ^{1}H NMR ($CFCl_3/CDCl_3$) δ 3.78 and 3.79 (2 × s), 6.00−6.60 (m), 8.28 and 8.45 (2 × br s); ^{13}C NMR δ 92.1 (s), 98.5 (s), 102.6 (d), 104.6 (d).

Methyl (*Z*)-3-(dihydro-6,6-dimethyl-1,2,4,5-trioxazin-3-yl)propenoate (6b) (two isomers): ^{1}H NMR ($CFCl_3/CDCl_3$) δ 1.43 (s), 1.60 (two overlapping s) and 1.65 (s) (together 12 H), 3.81 and 3.82 (2 × s, 6 H), 6.10−6.70 (m), 8.41 and 8.75 (2 × br s).

Methyl (*Z*)-3-(dihydro-6-methyl-6-phenyl-1,2,4,5-trioxazin-3-yl)propenoate (6c) (one isomer): ^{1}H NMR ($CFCl_3/CDCl_3$) δ 1.80 (s, 3 H), 3.63 (s, 3 H), 6.00 (d, J = 6.3 Hz, 1 H), 6.10 (d, J = 11.9 Hz), 6.42 (dd, J = 11.9, 6.3 Hz, 1 H), 8.49 (br s, 1 H); ^{13}C NMR ($CFCl_3/CDCl_3$) δ 21.2 (q), 53.4 (q), 92.5 (s), 105.2 (d), 165.7 (s).

Methyl (*Z*)-3-(dihydro-6-methyl-1,2,4,5-trioxazin-3-yl)-propenoate (6d) (two isomers): ^{1}H NMR ($CFCl_3/CDCl_3$) δ 1.39 and 1.54 (2 × d, J = 5.3 Hz, 6 H), 4.78 and 4.95 (2 × q, J = 5.3 Hz, 2 H), 8.24 and 8.31 (2 × br s).

(*Z*)-1-Hydroperoxy-1-phenyl-*N*-[(*Z*)-3-(methoxycarbonyl)-2-propenylidene]ethylamine *N*-oxide (5c): ^{1}H NMR ($CFCl_3/CDCl_3$) δ 2.22 (s, 3 H), 3.77 (s, 3 H), 6.21 (d, J = 11.3 Hz, 1 H), 9.19 (d, J = 10.1 Hz, 1 H) and 12.91 (br s, 1 H); ^{13}C NMR ($CFCl_3/CDCl_3$) δ 23.5 (q), 52.1 (q), 106.2 (s), 166.3 (s).

Triphenylphosphine Reduction of the Ethers 7a−d. To 0.5 mL of the solution of **7a**−**d** in $CFCl_3/CDCl_3$ at −60 °C was added a solution of triphenylphosphine (10 mg, 0.037 mmol) in $CDCl_3$ (0.2 mL) precooled at this temperature. After 4 h the ^{1}H NMR, recorded at −60 °C, showed, in addition to the oximes **4a**−**d**, only the presence of the (*Z*)-unsaturated aldehyde **9**.[1]

General Procedure for the TPP-Sensitized Photooxygenation of 2-Methoxyfuran (1) in the Presence of Oximes 4 in CH_2Cl_2. Each 2×10^{-2} M solution of the furan (1 mmol) in CH_2Cl_2 and the oxime (5 mmol), after the addition of the sensitizer (3.6×10^{-4} mmol), was photooxygenated at −20 °C. When each reaction was complete (90 min) the solvent was removed under reduced pressure at rt and the residue analyzed by ^{1}H NMR. In addition to the unreacted oximes **4**, the spectra for entries **a**,**b**,**d** showed the presence of only **5a**,**b**,**d**, and for entry **e**, a mixture of **5e** and unidentified compounds. Chromatography on a short column of silica gel, eluting with light petroleum/ether (8:2, 1:1), gave successively the oxime **4** and the hydroperoxynitrones **5a**,**b**,**d**,**e**. For series **c** no nitrone **5c** was detected spectroscopically and silica gel chromatography, using light petroleum/ether (8:2) as eluent, gave the oxime **4c** as well as complex mixtures of **13** and **15** along with acetophenone and ketone-related peroxidic unidentified products.

(*Z*)-1-Hydroperoxy-*N*-[(*Z*)-3-(methoxycarbonyl)-2-propenylidene]cyclohexylamine *N*-oxide (5a): 65% yield; mp 76−78 °C (from diethyl ether/hexane); IR 3530, 3161, 1713, 1606, 1074 cm^{-1}; ^{1}H NMR δ 1.50−2.30 (m, 10 H), 3.77 (s, 3 H), 6.05 (dd, J = 11.7, 1.4 Hz, 1 H), 7.35 (dd, J = 11.7, 10.5 Hz, 1 H), 8.97 (dd, J = 10.5, 1.4 Hz, 1 H) and 10.58 (br s, 1 H); ^{13}C NMR δ 22.2 (t), 24.6 (t), 31.6 (t), 51.7 (q), 105.6 (s), 123.4 (d), 131.0 (d), 131.6 (d), 166.3 (s). Anal. Calcd for $C_{11}H_{17}NO_5$: C, 54.31; H, 7.04; N, 5.76. Found: C, 54.1; H, 6.8; N, 5.6.

(*Z*)-2-Hydroperoxy-*N*-[(*Z*)-3-(methoxycarbonyl)-2-propenylidene]-2-propylamine *N*-oxide (5b): 80% yield; mp 77−78 °C (from *tert*-butyl methyl ether/hexane); IR 3526, 3160, 1713, 1606, 1078 cm^{-1}; ^{1}H NMR δ 1.77 (s, 6 H), 3.78 (s, 3 H), 6.06 (dd, J = 11.7, 1.0 Hz, 1 H), 7.35 (dd, J = 11.7, 10.2 Hz, 1 H), 8.89 (dd, J = 10.2, 1.0 Hz, 1 H), 9.82 (br s, 1 H); ^{13}C NMR δ 22.4 (q), 51.1 (q), 103.7 (s), 123.0 (d), 130.5 (d), 131.1 (d), 165.7 (s). Anal. Calcd for $C_8H_{13}NO_5$: C, 47.29; H, 6.45; N, 6.89. Found: C, 47.1; H, 6.3; N, 6.6.

(*Z*)-1-Hydroperoxy-*N*-[(*Z*)-3-(methoxycarbonyl)-2-propenylidene]ethylamine *N*-oxide (5d): 80% yield; oil; IR 3522, 3120, 1715, 1609, 1081 cm^{-1}; ^{1}H NMR δ 1.60 (d, J = 5.9 Hz, 3 H), 3.78 (s, 3 H), 5.46 (q, J = 5.9 Hz, 1 H), 6.14 (dd, J = 11.7, 1.0 Hz, 1 H), 7.37 (dd, J = 11.7, 10.3 Hz, 1 H), 8.77 (dd, J = 10.3, 1.0 Hz, 1 H), 11.59 (br s, 1 H); ^{13}C NMR δ 16.8 (q), 51.8 (q), 101.2 (d), 124.3 (d), 130.5 (d), 132.4 (d), 166.1 (s). Anal. Calcd for $C_7H_{11}NO_5$: C, 44.44; H, 5.86; N, 7.41. Found: C, 44.2; H, 5.6; N, 7.3.

(*Z*)-1-Hydroperoxy-*N*-[(*Z*)-3-(methoxycarbonyl)-2-propenylidene]benzylamine *N*-oxide (5e): 20% yield; oil; IR 3520, 3113, 1715, 1604, 1078 cm^{-1}; ^{1}H NMR δ 3.77 (s, 3 H), 6.08 (dd, J = 11.8, 1.1 Hz, 1 H), 6.28 (s, 1 H), 7.35 (dd, J = 11.8, 10.3 Hz) and 7.30−7.55 (m) together 6 H, 8.91 (dd, J = 10.3, 1.1 Hz, 1 H), 11.47 (br s, 1 H); ^{13}C NMR δ 51.8 (q), 104.3 (d), 124.4 (d), 127.1 (d), 128.7 (d), 130.4 (d), 130.5 (d), 131.4 (s), 132.6 (d), 166.1 (s). Anal. Calcd for $C_{12}H_{13}NO_5$: C, 57.37; H, 5.22; N, 5.58. Found: C, 57.2; H, 5.1; N, 5.4.

***syn*-Methyl (*Z*)-4-(Hydroxyimino)-2-butenoate (13).** A solution of **5a** (243 mg, 1 mmol) in CCl_4 (20 mL) was treated with Et_2S (135 mg, 1.5 mmol). When the reduction was complete (30 min) the ^{1}H NMR showed the presence of the (*Z*)-*syn*-oxime

(22) Campbell, K. N.; Campbell, B.; Chaput, E. P. *J. Org. Chem.* **1943**, *8*, 99.

(23) When a sample of this mixture was treated with Et_2S, acetophenone was formed in addition to Et_2SO, and after completion of the reduction, the oxime **13** and the ketone were present in *ca.* 1:1 molar ratio (^{1}H NMR).

13 in addition to Et_2S and Et_2SO. Removal of the solvent and of the unreacted Et_2S gave a residue that was rapidly chromatographed on a short column of silica gel using light petroleum/ether (8:2) as eluent to give 108 mg (84%) of **13**: mp 40−42 °C (from hexane); IR 3579, 3316, 1719, 1631, 1601 cm^{-1}; ^1H NMR δ 3.79 (s, 3 H), 6.05 (dd, J = 11.7, 1.0 Hz, 1 H), 7.30 (dd, J = 11.7, 9.8 Hz, 1 H), 8.38 (dd, J = 9.8, 1.0 Hz, 1 H), 9.30 (br s, 1 H); ^{13}C NMR δ 51.8 (q), 124.4 (d), 128.4 (d), 143.8 (d), 165.7 (s). Anal. Calcd for $C_5H_7NO_3$: C, 46.51; H, 5.47; N, 10.85. Found: C, 46.4; H, 5.3; N, 10.7.

Compound **13** slowly converted into (*Z*)-*anti*-isomer **15**: mp 74−75 °C (from diethyl ether/hexane); IR 3572, 3346, 1719, 1629, 1603 cm^{-1}; ^1H NMR δ 3.77 (s, 3 H), 6.03 (d, J = 11.5 Hz, 1 H), 6.64 (dd, J = 11.5, 9.7 Hz, 1 H), 7.60 (br s, 1 H), 8.91 (d, J = 9.7 Hz, 1 H); ^{13}C NMR δ 51.7 (q), 123.2 (d), 136.8 (d), 148.9 (d), 165.8 (s). Anal. Calcd for $C_5H_7NO_3$: C, 46.51; H, 5.47; N, 10.85. Found: C, 46.4; H, 5.3; N, 10.8.

***anti*-Methyl (*E*)-4-(Hydroxyimino)-2-butenoate (14).** A solution of **5a** (243 mg, 1 mmol) in acetone (25 mL) was treated with 2 M HCl (0.05 mL) and kept at rt. After 1 h, the acetone was removed in vacuo, and the residue was treated with H_2O and extracted three times with $CHCl_3$. The organic layers were dried over $MgSO_4$ and evaporated to a residue that was chromatographed on silica gel with light petroleum/ether (17:3) to give 103 mg (80%) of **14**: mp 90−93 °C (from *tert*-butyl methyl ether/hexane); IR 3569, 3346, 1718, 1647, 1600 cm^{-1}; ^1H NMR δ 3.80 (s, 3 H), 6.18 (d, J = 16.1 Hz, 1 H), 7.34 (dd, J = 16.1, 10.2 Hz, 1 H), 7.89 (d, J = 10.2 Hz, 1 H), 9.39 (br s, 1 H); ^{13}C NMR δ 52.1 (q), 126.8 (d), 137.6 (d), 149.4 (d), 166.5 (s). Anal. Calcd for $C_5H_7NO_3$: C, 46.51; H, 5.47; N, 10.85. Found: C, 46.4; H, 5.4; N, 10.6. Control experiments showed that, under the conditions used for **5a**, both (*Z*)-*syn*-oxime **13** and (*Z*)-*anti*-oxime **15** isomerized to (*E*)-*anti*-oxime **14**.

Dimethyl 2-(1-Hydroperoxycyclohexyl)-3-[(*Z*)-2-(methoxycarbonyl)vinyl]-2,3-dihydroisoxazole-4,5-dicarboxylate (11). A solution of **5a** (243 mg, 1 mmol) in dry Et_2O (50 mL) was treated with DMAD (710 mg, 5 mmol), and the resulting mixture was stirred at rt. The ^1H NMR spectrum, recorded after 1 h, showed the presence of the hydroperoxy-2,3-dihydroisoxazole **11** in addition to the unreacted DMAD. After removal of the solvent, the residue was chromatographed on a short column of silica gel using light petroleum/ether (9:1, 3:2) as eluent to give successively the unreacted DMAD and the hydroperoxy-2,3-dihydroisoxazole **11** in 90% yield: mp 59−61 °C dec (from *tert*-butyl methyl ether/hexane); IR 3532, 3420, 1753, 1719, 1658, 1603 cm^{-1}; ^1H NMR δ 1.30−2.20 (m, 10 H), 3.69, 3.77 and 3.90 (3 × s, 9 H), 5.84 (d, J = 11.7 Hz, 1 H), 6.15 (dd, J = 11.7, 9.3 Hz, 1 H), 6.87 (d, J = 9.3 Hz, 1 H), 7.90 (br s, 1 H); ^{13}C NMR δ 21.8 (t), 21.9 (t), 25.3 (t), 29.7 (t), 30.0 (t), 51.5 (q), 51.8 (q), 53.3 (q), 59.4 (d), 98.7 (s), 108.5 (s), 119.9 (d), 143.8 (d), 152.7 (s), 159.0 (s), 162.1 (s), 166.1 (s). Anal. Calcd for $C_{17}H_{23}NO_9$: C, 52.98; H, 6.02; N, 3.64. Found: C, 52.7; H, 5.9; N, 3.5.

Thermolysis of Hydroperoxynitrone 5a. A solution of **5a** (243 mg, 1 mmol) in dry C_6H_6 (10 mL) was kept on reflux. After 30 min the ^1H NMR spectrum showed a mixture composed of the aldehyde **9**,[1] the hydroxamic acid **10**,[24] the ketone **12**, the (*Z*)-*syn*-oxime **13**, and the (*Z*)-*anti*-oxime **15**. After removal of the solvent, the residue was chromatographed on silica gel with light petroleum/ether (9:1, 8:2, 1:1, 1:19) to give successively **12** (6%), **9** (32%), a mixture of **13** and **15** (together 22%), and **10** (33%).

Methyl (*Z*)-3-[2-(1-Hydroperoxycyclohexyl)oxaziridin-3-yl]propenoate. A solution of the photooxygenation mixture of **1** (98 mg, 1 mmol) with the oxime **4a** (565 mg, 5 mmol) and TPP in CH_2Cl_2 at −20 °C was allowed to irradiate for a long time (6 h). The ^1H NMR spectrum of a sample showed the presence of a small amount of the hydroperoxyoxaziridine in addition to the hydroperoxynitrone **5a** and unreacted oxime **4a**. Removal of the solvent gave a residue that was chromatographed on silica gel with light petroleum/ether (9:1, 8:2, 1:1) to give successively the oxime **4a**, the oxaziridine [(20 mg, 8%), mp 45−47 °C (from C_6H_6/hexane); IR 3543, 3434, 1723, 1661 cm^{-1}; ^1H NMR δ 1.30−2.30 (m, 10 H), 3.80 (s, 3 H), 5.87 (m, 2 H) and 6.21 (m, 1 H), 9.08 (br s, 1 H); ^{13}C NMR δ 21.5 (t), 21.9 (t), 25.1 (t), 30.1 (t), 31.1 (t), 51.9 (q), 68.9 (d), 95.9 (s), 127.5 (d), 142.8 (d), 165.7 (s). Anal. Calcd for $C_{11}H_{17}NO_5$: C, 54.31; H, 7.04; N, 5.76. Found: C, 54.2; H, 6.9; N, 5.6.], and the nitrone **5a** (110 mg, 45%).

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