Carbonyl Oxide Chemistry. 6.[1] *N*-(Hydroperoxyalkyl)keto Nitrones and α-Oxime Ether Hydroperoxides via Disubstituted Carbonyl Oxides and Oximes[†]

M. Rosaria Iesce,* Flavio Cermola, and Antonio Guitto

Dipartimento di Chimica Organica e Biologica dell'Università di Napoli Federico II, via Mezzocannone 16, I-80134 Napoli, Italy

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Recently, we reported the synthesis of *N*-(hydroperoxyalkyl)aldo nitrones **5a′** by reacting furan *endo*-peroxide **2a′** with both aldo and keto oximes and obtained evidence that the first stage of the reaction is the rearrangement of **2a′** into carbonyl oxide **3a′**, which by oxime trapping leads to the thermally unstable α-oxime ether hydroperoxides **7a′** (Scheme 1).[1] These compounds, via the dihydro-1,2,4,5-trioxazines **6a′**, give hydroperoxy nitrones **5a′**. The latter represent the first thermally stable derivatives of the series and were successfully used for the preparation of *N*-(hydroperoxyalkyl)oxaziridines[2] as well as *N*-(hydroperoxyalkyl)-2,3-dihydroisoxazoles,[3] both previously unreported in the literature.

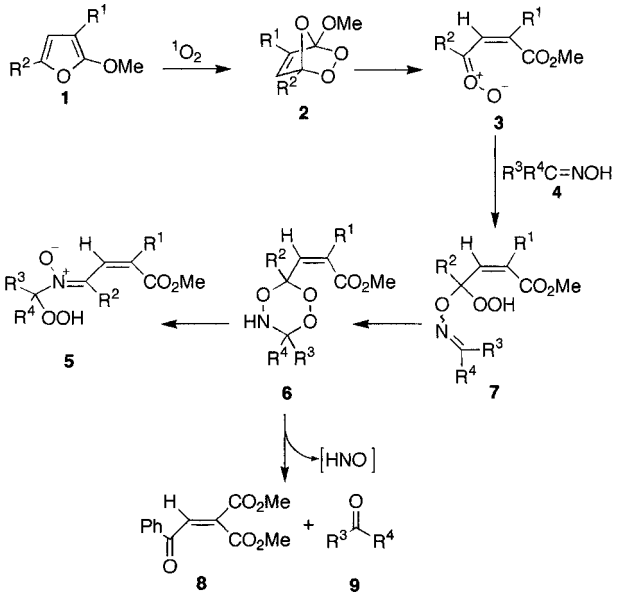
In light of these results we examined the reaction of oximes **4** toward carbonyl oxide **3a**, chosen as a representative of disubstituted derivatives, which can be generated by the dye-sensitized photooxygenation of furan **1a** via the corresponding *endo*-peroxide **2a** (Scheme 1).[4] This investigation appeared interesting since **3a** occasionally behaves differently from the monosubstituted **3a′**.[6,7] On the other hand, a behavior similar to that of **3a′** would allow the synthetic method to be extended to previously unreported *N*-(hydroperoxyalkyl)-keto nitrones which, on the basis of the results obtained from **5a′**,[2,3] could be starting materials for hydroperoxidic heterocycles.[9]

Results and Discussion

At first glance, for the series **a**, reactions with aliphatic aldo or keto oximes or aromatic oximes seemed to proceed by different paths, and only the first led to hydroperoxy nitrones **5**. A detailed investigation provided evidence that the seeming multiplicity of pathways was due to different stability of the intermediates. Indeed, when the sensitized photooxygenation of furan **1a** was carried out in CH_2Cl_2 at −20 °C in the presence of acetaldehyde oxime (**4a**), the results were similar to those reported for the series **a′** and the hydroperoxy nitrone **5a** was obtained in 58% yield.[10] Moreover, when the reaction was performed at −75 °C in $CDCl_3$−$CFCl_3$, low-temperature NMR spectroscopy evidenced the transient formation of the α-oxime ether hydroperoxide **7a**[12] and of the dihydro-1,2,4,5-trioxazine **6a** (Scheme 1).

In contrast, when the oxygenation in CH_2Cl_2 at −20 °C was performed in the presence of aliphatic keto oximes **4b**,**c**, only ketones **9b**,**c** and keto ester **8** (90% yield) were obtained in ca. 1:1 molar ratio with the loss of a HNO unit (Scheme 1).[13] Low-temperature NMR analysis of the

Scheme 1. Singlet Oxygen Oxygenation of 2-Alkoxyfurans 1 in the Presence of Aldo and Keto Oximes 4



1a; R^1=CO_2Me, R^2=Ph
1a'; R^1=R^2=H

Entry[a]	4	5	6	7	9	R^3		R^4
1	**a**	**a**	**a**	**a**	-	H		Me
2	**b**	-	**b**	**b**	**b**		-$(CH_2)_5$-	
3	**c**	-	**c**	**c**	**c**	Me		Me
4	**d**	-	-	**d**	-	H		Ph
5	**e**	-	-	**e**	-	Me		Ph
6	**f**	-	-	**f**	-	Ph		Ph

[a]Starting from **1a**.

[†]Dedicated to Professor R. Scarpati, now retired.

(1) Iesce, M. R.; Cermola, F.; Guitto, A.; Giordano, F.; Scarpati, R. *J. Org. Chem.* **1996**, *61*, 8677.

(2) Iesce, M. R.; Cermola, F.; Guitto, A. *Synthesis* **1997**, 657.

(3) Iesce, M. R.; Cermola, F.; Guitto, A. *Synthesis* **1998**, 333.

(4) Carbonyl oxides can be generated by dye-sensitized photooxygenation of 2-alkoxyfurans provided that the latter are C-4 unsubstituted.[5]

(5) Scarpati, R.; Iesce, M. R.; Cermola, F.; Guitto A. *Synlett* **1998**, 17.

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

(7) Carbonyl oxide **3a** gives [3 + 2] cycloaddition to phenyl isocyanate leading to 1,2,4-dioxazolidin-3-one.[8] In contrast, **3a′** under the same conditions gives only resinous material.[5]

(8) Iesce, M. R.; Cermola, F.; Giordano, F.; Scarpati, R.; Graziano, M. L. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3295.

(9) For nitrone applications see, among others: (a) Breuer, E. In *The chemistry of amino, nitroso, and nitro compounds and their derivatives*, Part 1; Patai, S., Ed.; Wiley: New York, 1982; Chapter 13, p 459. (b) Sandler, S. R.; Karo, W. *Organic Functional Group Preparations*; Academic Press: New York, 1986; Vol. III, p 355.

(10) Keto ester **8**[11] was also present in 10% yield (see below).

(11) Graziano, M. L.; Iesce, M. R.; Cimminiello, G.; Scarpati, R. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1699.

(12) The stereochemistry of the carbon−nitrogen double bond was not assigned.

(13) Attempts to trap this species as nitrosyl hydride (HNO) by an ene reaction with 2,3-dimethylbut-2-ene[14] failed; however, the gas collected from the reaction apparatus reacted strongly to the Griess test[15] revealing the presence of nitrosating derivatives.

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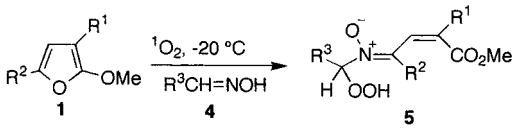
mixture obtained by reacting **1a** in the presence of cyclohexanone oxime (**4b**) at −70 °C in $CDCl_3$−$CFCl_3$ showed that trioxazine **6b**, in contrast to **6a**, did not rearrange into the corresponding nitrone but, at 0 °C, led to keto ester **8** and ketone **9b** (Scheme 1).[16] Although the mechanism of trioxazine−nitrone conversion has not yet been clarified, it is evident that the full substitution at the two ring carbons of trioxazines **6b**,**c** prevents this rearrangement completely. Thus, the breakage of O−O, C3−O, and C6−N bonds[17] occurs in a fashion similar to that observed for the decomposition, in refluxing C_6H_6, of stable *N*-substituted dihydro-1,2,4,5-trioxazines.[18,20]

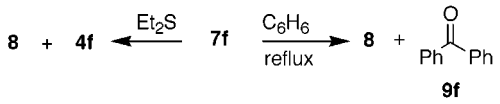
In the photooxygenation reaction of furan **1a** in the presence of aromatic oximes **4d**−**f**, α-oxime ether hydroperoxides **7d**−**f** were obtained in addition to small amounts of keto ester **8**, and they were stable even at room temperature.[22] The enhanced stability of these compounds in comparison with that of the others herein and previously reported[1] may be associated with both steric and conjugative effects which prevent the rearrangement into trioxazines **6d**−**f**. Indeed, for the series **a** the presence of at least one bulky aryl group on the oxime moiety of **7** raises the steric crowding in going from the trigonal ground state to the transition state for cyclization; in addition, conjugative energy is lost in trioxazine formation.[24] Compounds **7d**−**f** are the first examples of thermally stable oxime adducts to a carbonyl oxide; however, under chromatographic conditions they decompose, as observed for structurally related hemiperacetals.[5] The structures of **7d** and **7e**[12] were deduced by carefully analyzing the ^1H and ^{13}C NMR spectra of the corresponding crude reaction mixtures and by comparing these data with those of **7f**; the latter was obtained in the pure state by precipitation with *tert*-buthyl methyl ether followed by dissolution in Et_2O and, hence, was fully characterized. On treating **7f** with Et_2S, it converted quantitatively into keto ester **8** and oxime **4f** in 1:1 molar ratio; when dissolved in dry C_6H_6, it was stable at room temperature for several days, while at reflux it led to a mixture of cleavage products, among which the sole identifiable products were keto ester **8** and ketone **9f**.[25]

Scheme 2. One-Pot Synthesis of Hydroperoxy Nitrones 5



1	R^1	R^2	4	R^3	5	Yield %[a]
a	CO_2Me	Ph	**a**	Me	**a**	58
a	CO_2Me	Ph	**g**	Et	**b**	54
a	CO_2Me	Ph	**h**	Me_2CH	**c**	34
a	CO_2Me	Ph	**i**	$Me(CH_2)_5$	**d**	35
a	CO_2Me	Ph	**j**	Cyclohexyl	**e**	48
a	CO_2Me	Ph	**k**	Bn	**f**	65
b	CO_2Me	4-$MeOC_6H_4$	**a**	Me	**g**	50
c	CO_2Me	3-$MeOC_6H_4$	**a**	Me	**h**	55
d	CO_2Me	4-BrC_6H_4	**a**	Me	**i**	35
e	CO_2Me	4-MeC_6H_4	**a**	Me	**j**	61
f	COMe	Ph	**a**	Me	**k**	55

[a]Of isolated products



The above investigation showed that only the reaction of **1a** in the presence of acetaldehyde oxime (**4a**) afforded nitrone **5a**. Thus, to extend the one-pot synthesis of **5**, the photooxygenation reaction of furan **1a** was carried out in the presence of various aliphatic aldo oximes such as **4g**−**k**. In this way, nitrones **5b**−**f** were formed and isolated in good yields by silica gel chromatography (Scheme 2). Similar success was obtained by extending the photooxygenation, in the presence of acetaldehyde oxime (**4a**), to different C-4 unsubstituted 5-aryl-2-alkoxyfurans such as **1b**−**f**, which resulted in the formation of nitrones **5g**−**k** (Scheme 2). All nitrones obtained were fully characterized by analytical and spectroscopic data. As expected for keto nitrones,[9a] their IR spectra exhibit two characteristic bands resulting from N−O and C=N bond stretching vibrations which appear between 1233−1260 and 1590−1605 cm^{-1}, respectively; in the ^{13}C NMR spectra the nitronyl carbon singlet appears in the region of δ 144−148 ppm.[26]

From their ^1H and ^{13}C NMR spectral data, the isolated nitrones **5** appeared to consist only of a single diastereomer in each case, and there was no evidence for the presence of the other isomer in the residual product mixtures. NOE experiments carried out on **5h** allowed *E*-configuration to be assigned. Straightforward comparison of spectral data for the other nitrones obtained with those for **5h**, and in particular of the chemical shifts of the unsaturated CH proton (δ 8.17−8.05 ppm) with

(14) Ensley, H. E.; Mahadevan, S. *Tetrahedron Lett.* **1989**, *30*, 3255.
(15) Green, L. C.; Wagner, D. A.; Glogowski, J.; Skipper, P. L.; Wishnok, J. S.; Tannenbaum, S. R. *Anal. Biochem.* **1982**, *126*, 131.
(16) Careful analysis showed that the formation of ketone **9b** took place via a labile intermediate to which it was not possible to assign any structure owing to its low concentration in the reaction mixture.
(17) Control experiments performed using $^{18}O_2$ in the photooxygenation of **1a** in the presence of **4b** revealed the incorporation of ^{18}O both in **9b** and in the benzoyl group of **8** (see Experimental Section).
(18) These products, which were stable at room temperature, decomposed by refluxing in C_6H_6 into the related carbonyl and oxime compounds.[19] It is significant that derivatives bearing two groups on each carbon of the trioxazine ring could not be obtained even when using the reported route.[19.]
(19) Mori, M.; Sugiyama, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. *J. Org. Chem.* **1992**, *57*, 2285.
(20) The hypothesis that cleavage compounds **8** and **9b** could derive from an undetected thermally unstable nitrone should be rejected since no hydroperoxy nitrone previously reported showed a similar decomposition route.[1,21]
(21) Erden, I.; Griffin, A.; Keeffe, J. R.; Brinck-Kohn, V. *Tetrahedron Lett.* **1993**, *34*, 793 and references therein.
(22) It is evident that trioxazines **6d**−**f** are not responsible for the obtaining of keto ester **8**. Formation of the latter can be explained taking into account that it is a usual product in the photooxygenation of **1a** in nonparticipating solvents; thus, for entries 4−6, **8** should derive directly from *endo*-peroxide **2a** via carbonyl oxide **3a**.[23] Conversely, in entry 1, the formation of **8** takes place via trioxazine **6a** decomposition (^1H NMR, see Experimental Section).
(23) Iesce, M. R.; Cermola, F.; Graziano, M. L.; Scarpati, R. *J. Chem. Soc., Perkin Trans. 1* **1994**, 147.
(24) The loss of conjugative energy in trioxazine formation should contribute to a lesser extent; indeed, for series **a**′ the peroxides **7** thermally rearranged into the corresponding trioxazines even when aromatic oximes were used.[1]
(25) Compounds **8** and **9f** are structurally related to those obtained by the thermal decomposition of trioxazine **6b**; therefore, it is likely that upon heating α-oxime ether hydroperoxide **7f** leads partly to trioxazine **6f** which immediately decomposes owing to the high temperature.
(26) Clack, D. W.; Khan, N.; Wilson, D. A. *J. Chem. Soc., Perkin Trans. 2* **1981**, 860.

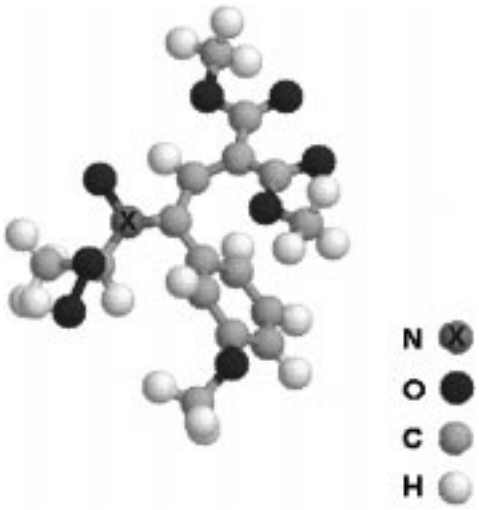


Figure 1. Optimized structure of **5h** by MM+ calculation.

that of **5h** (δ 8.11 ppm), gave *E*-configurations to all of them. Stereochemical assignment was also supported by MM+ calculations which indicated that *E*-nitrone **5h** was more stable than *Z*-isomer.[27] Figure 1 reports the calculated minimized conformation of **5h**. As shown in this figure, one methoxycarbonyl group lies just in front of the aromatic ring, and this accounts for the unusually upfield ^{1}H NMR signal (δ 3.17 ppm) due to ring anisotropy. Similarly, in all other nitrones prepared the signal of the shielded methoxycarbonyl group falls in the δ range 3.15−3.27 ppm.

In conclusion, the reported results show that toward oximes the disubstituted carbonyl oxide **3a** behaves like the monosubstituted **3a′** and an oxygen nucleophilic trapping reaction takes place leading to α-oxime ether hydroperoxide **7**. The fomation of final nitrones **5** depends on the nature of the substituents at the oxime moiety and only occurs when aliphatic aldo oximes are used. In the case of aliphatic keto oximes, the formation of trioxazines **6b,c** is not followed by the rearrangement into nitrones, but bond breakage occurs most probably due to steric hindrance. Both steric and conjugative effects could be responsible for the nonformation of trioxazines **6d**−**f** from the unusually stable α-oxime ether hydroperoxides **7d**−**f** obtained when using aryl oximes.

From a preparative standpoint, the reaction represents a highly stereoselective one-pot synthesis to previously unreported (*E*)-*N*-(hydroperoxyalkyl)keto nitrones **5** and can be accomplished using a variety of both aliphatic aldo oximes and C-4 unsubstituted 2-alkoxyfurans.

Experimental Section

General. Melting points are uncorrected. IR spectra were recorded with chloroform as solvent. ^{1}H 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 TMS. MS were run on a TRIO 2000 (Micromass). Furans **1a**,**1g**,[11] **1b**,**1d**,[23] **1c**,[28] and **1e**,[8] heptaldehyde oxime[29] (**4i**), acetophenone oxime[30] and benzophenone oxime[31] were prepared according to the literature procedure. Oximes **4g,h**,**j**,**k** were prepared as reported for heptaldehyde oxime (**4i**).[29] The Griess reagent was freshly prepared.[16] Oxygen-$^{18}O_2$ (^{18}O, 50%) was obtained from Cambridge Isotope Laboratories, Andover, MA. Other chemicals (Aldrich or Fluka) were used without further purification. The solvents used for the reactions were anhydrous. Silica gel (0.063−0.2 mm Macherey-Nagel) and light petroleum ether (bp 40−60 °C) were used for column chromatography. TLC was performed on silica gel layers (Whatman PK6F). 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 Methyl 2-Methoxy-5-phenylfuran-3-carboxylate (1a) in the Presence of Oximes 4a−f in CH_2Cl_2. Each 2×10^{-2} M solution of the furan (1 mmol) in CH_2Cl_2 and the oxime **4** (5 mmol, 1.2 mmol for **4f** owing to its scarce solubility in the reaction conditions), after the addition of the sensitizer (3.6×10^{-4} mmol), was irradiated at −20 °C with a halogen-superphot lamp (Osram, 650W). During the irradiation, dry oxygen was bubbled through the solution, which was kept at this temperature. When each reaction was complete (90 min), the solvent was removed under reduced pressure at room temperature and the residue was analyzed by ^{1}H NMR.

For entry 1 (Scheme 1), the spectrum showed the presence of nitrone **5a** in addition to the unreacted oxime **4a** and little amount of keto ester **8**. After evaporation of the solvent and volatile oxime **4a**, the residue was chromatographed on a short column of silica gel, eluting with light petroleum/ether (8:2, 1:1), to give keto ester **8**[11] (10%) and pure hydroperoxy nitrone **5a**, successively.

(*E*)-1-Hydroperoxy-*N*-[3,3-(dimethoxycarbonyl)-1-phenyl-2-propenylidene]ethylamine *N*-oxide (5a): 58% yield; mp 75−77 °C (from *tert*-butyl methyl ether/hexane); IR 3520, 3190, 1733, 1612, 1256 cm^{-1}; ^{1}H NMR δ 1.45 (d, J = 6.2 Hz, 3 H), 3.17 (s, 3 H), 3.78 (s, 3 H), 5.76 (q, J = 6.2 Hz, 1 H), 7.30−7.55 (m, 5 H), 8.17 (s, 1 H), 11.72 (brs, 1 H); ^{13}C NMR δ 16.3, 52.1, 52.8, 95.1, 128.8, 129.7, 130.3, 130.4, 132.2, 132.3, 145.6, 164.1, 164.3. Anal. Calcd for $C_{15}H_{17}NO_7$: C, 55.72; H, 5.30; N, 4.33. Found: C, 55.4; H, 5.1; N, 4.2.

No nitrone was detected spectroscopically in the reaction of **1a** with cyclohexanone oxime (**4b**) and, in addition to the unreacted oxime **4b**, only keto ester **8** and ketone **9b** were present (entry 2, Scheme 1).[32] Silica gel chromatography of the reaction mixture obtained by carrying out the oxygenation in the presence of 1 equiv of oxime **4b**, using light petroleum/ether (8:2) as eluent, gave the ester **8** in 90% yield.[33] When the oxygenation was performed at −20 °C in $CDCl_3$ using both 5 and 1 equiv of oxime **4b**, the ^{1}H NMR spectrum of each reaction mixture showed the presence of keto ester **8** and ketone **9b** in ca. 1:1 molar ratio. Similar results were obtained when the oxygenation reaction was performed in the presence of both 5 and 1 equiv of acetone oxime (**4c**).

For entries 4−6 (Scheme 1), the ^{1}H NMR spectra of the reaction mixtures showed the presence of oxime ethers **7d**−**f** in addition to keto ester **8** and some amount of unidentified products. All attempts to obtain pure **7d**−**f** by chromatography failed since they partly polymerize and partly hydrolyze on contact with adsorbents. Quantification of **7d** (40%), **7e** (33%), and **7f** (53%) was based on the relative areas of the signals at δ 3.78 (OMe), 2.41 (Me), and 3.45 (OMe), respectively, and the methoxy signals of all products present in the corresponding crude mixtures. Compound **7f** was obtained pure by precipitation with *tert*-buthyl methyl ether from the crude mixture followed by dissolution in Et_2O. Attempts to perform this

(27) MM+-minimized conformations were obtained with routines built into Hyperchem and developed from MM2.

(28) Iesce, M. R.; Cermola, F.; Piazza, A.; Scarpati, R.; Graziano, M. L. *Synthesis* **1995**, 439.

(29) Bousquet, E. N. In *Organic Synthesis*; Blatt, A. H., Ed.; J. Wiley and Sons: New York, 1957; Collect. Vol. II, p 313.

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

(31) Lachman, A. In *Organic Synthesis*; Blatt, A. H., Ed.; J. Wiley and Sons: New York, 1957; Collect. Vol. II, p 70.

(32) The **8**:**9b** molar ratio was barely reproducible owing to a certain degree of volatility in ketone **9b**.

(33) Quantification, by chromatography, of the reaction mixture using 5 equiv of oxime **4b** became complicated in that mixtures of oxime, ketone **9b**, keto ester **8**, and an oxime adduct of **8** were obtained. Control experiments showed that this adduct, which was not investigated, was formed slowly (rapidly by chromatography) after adding oxime **4b** to a solution of keto ester **8** in CH_2Cl_2 (^{1}H NMR).

procedure for **7d** and **7e** failed even using 1 equiv of oximes **4d** or **4e**; therefore, their selected spectral data were deduced by a careful analysis of the ^{1}H and ^{13}C NMR spectra of the related crude mixtures, after the signals of the other products were subtracted, and by comparison with data of **7f**.

Benzaldehyde oxime *O*-[1-hydroperoxy-3,3-(dimethoxycarbonyl)-1-phenyl-2-propenyl] ether (7d):[12] ^{1}H NMR δ 3.78 (s 3 H), 3.83 (s, 3 H), 7.23 (s, 1 H), 8.28 (s, 1 H), 9.49 (brs, 1 H); ^{13}C NMR δ 52.4, 52.7, 107.8, 142.5, 152.5, 163.6, 166.4.

Acetophenone oxime *O*-[1-hydroperoxy-3,3-(dimethoxycarbonyl)-1-phenyl-2-propenyl] ether (7e):[12] ^{1}H NMR δ 2.41 (s, 3 H), 3.77 and 3.78 (2s, 6 H), 7.24 (s, 1 H); ^{13}C NMR δ 13.5, 52.3, 52.6, 107.7, 142.9, 158.6, 163.6, 165.8.

Benzophenone oxime *O*-[1-hydroperoxy-3,3-(dimethoxycarbonyl)-1-phenyl-2-propenyl] ether (7f): 40% yield; white foam; IR 3512, 3286, 1735, 1658 cm^{-1}; ^{1}H NMR δ 3.45, (s, 3 H), 3.77 (s, 3 H), 7.20−7.60 (m, 16 H), 9.83 (brs, 1 H); ^{13}C NMR δ 52.1, 52.7, 108.2, 126.8, 128.1, 128.3, 128.7, 129.3, 129.5, 129.7, 130.1, 132.4, 135.7, 136.1, 142.9, 160.6, 163.6, 165.7. Anal. Calcd for $C_{26}H_{23}NO_7$: C, 67.67; H, 5.02; N, 3.04. Found: C, 67.4; H, 5.1; N, 3.1.

General Procedure for the TPP-Sensitized Photooxygenation of Furan 1a in the Presence of Oximes 4a,b in $CFCl_3$−$CDCl_3$. Each solution (5×10^{-2} M) of the furan **1a** (0.5 mmol) and the oximes **4a,b** (2.5 mmol) in $CFCl_3$−$CDCl_3$ (1:1 v/v), after the addition of the sensitizer (TPP 1.8×10^{-4} mmol), was photooxygenated at −75 °C as reported above. When the reaction was complete (90 min), for entry **a**, the ^{1}H NMR spectrum recorded at −70 °C showed, in addition to unreacted oxime **4a**, the presence of **7a** which rapidly converted to trioxazine **6a** as a mixture of two conformational isomers. The latter upon warming to −10 °C led to nitrone **5a**, keto ester **8** and a mixture of acetaldehyde and aldehyde-related unidentified compounds in ca. 5:1:1 molar ratio. For entry 2, the ^{1}H NMR spectrum recorded at −70 °C showed, in addition to unreacted oxime **4b**, the presence of *endo*-peroxide **2a** which was identified by comparison with an authentic sample.[34] Upon warming to −50 °C, a complex mixture was formed which evolved continuously leading to only trioxazine **6b** as a mixture of two conformational isomers. The latter coalesced at −10 °C and, at 0 °C, led to keto ester **8** and an unidentified compound which in turn converted into ketone **9b**.[16] After 90 min compounds **8** and **9b** were present in ca. 1:1 molar ratio. Selected spectral data of oxime ether **7a** and trioxazines **6a,b** were deduced by a careful analysis of the ^{13}C and ^{1}H NMR spectra of the related reaction mixtures, recorded at −70 and −50 °C, respectively, after the signals of the other products were subtracted. It was not possible to run satisfactory ^{13}C NMR spectrum for **7a** owing to its fast rearrangement into trioxazine **6a** even at −70 °C.

Acetaldehyde oxime *O*-[1-hydroperoxy-3,3-(dimethoxycarbonyl)-1-phenyl-2-propenyl] ether (7a):[12] ^{1}H NMR ($CFCl_3$−$CDCl_3$) δ 2.28 (d, J = 5.7 Hz, 3 H), 3.46 (s, 3 H), 3.83 (s, 3 H), 13.10 (brs, 1 H).

Methyl 2-(methoxycarbonyl)-3-(dihydro-6-methyl-3-phenyl-1,2,4,5-trioxazin-3-yl)propenoate (6a) (two isomers): ^{1}H NMR ($CFCl_3$−$CDCl_3$) δ 1.37 and 1.40 (2d, J = 5.9 Hz, 6 H), 3.70, 3.77, 3.78 and 3.86 (4s, 12 H), 4.71 (q, J = 5.9 Hz, 1 H), 4.88 (q, J = 5.9 Hz, 1 H), 6.99 and 7.16 (2s, 2 H), 7.26 (brs, 1 H), 7.27−7.56 (m, 10 H), 7.88 (brs, 1 H); ^{13}C NMR ($CFCl_3$−$CDCl_3$) δ 10.8, 13.9, 53.0, 53.2, 93.4, 100.0, 102.1, 105.4, 137.3, 140.1, 163.5, 163.7, 166.6, 168.3.

Methyl 2-(methoxycarbonyl)-3-(3-phenyl-1,2,4-trioxo-5-azaspiro[5.5]undec-3-yl)propenoate (6b) (two isomers): ^{1}H NMR ($CFCl_3$−$CDCl_3$) δ 3.69, 3.73, 3.77 (two overlapping s) (together 12 H), 6.96 and 7.15 (2s, 2 H), 7.20−7.57 (m, 10 H), 9.57 (brs, 2 H); ^{13}C NMR ($CFCl_3$−$CDCl_3$) δ 52.8, 53.0, 101.2, 102.4, 103.8, 106.5, 143.2, 145.9, 161.2, 163.9, 166.9.

Procedure for Griess Test. A 2×10^{-2} M solution of **1a** (0.5 mmol) and cyclohexanone oxime (**4b**) (0.5 mmol) in CH_2Cl_2 at −20 °C was photooxygenated as above, and the gas which came out from the reaction apparatus was passed through two traps containing 0.017 M NaOH (20 mL). A Griess reagent (2 mL) was added after 90 min to a sample (25 μL) from each trap, and an intense purple color appeared in the first one. No color appeared when the photooxygenation was carried out in the absence of either oxime **4b** or furan **1a**.

When the above procedure was carried out using acetone oxime (**4c**), the same results were obtained.

Decomposition of Trioxazine 6b in the Presence of 2,3-Dimethylbut-2-ene. A 2×10^{-2} M solution of **1a** (0.25 mmol) and **4b** (0.25 mmol) in $CDCl_3$ was photooxygenated at −20 °C as above. After 90 min, the ^{1}H NMR, recorded at this temperature, showed the presence of only trioxazine **6b**. The solution was carefully degassed with dry N_2, and 2,3-dimethylbut-2-ene (1.25 mmol), precooled at −20 °C, was then added. The resulting mixture was allowed to stand at room temperature. After 30 min the ^{1}H NMR showed that only keto ester **8** and ketone **9b** were formed in ca. 1:1 molar ratio. No evidence was obtained to indicate the presence of any alkene−HNO adduct.[14]

Procedure for $^{18}O_2$ Oxygenation of Furan 1a in the Presence of Cyclohexanone Oxime (4b). A 2×10^{-2} M solution of **1a** (0.25 mmol) and **4b** (0.25 mmol) in CH_2Cl_2, after the addition of TPP (1.8×10^{-4} mmol), was saturated with $^{18}O_2$ and irradiated at −20 °C. When the reaction was complete (240 min, TLC), the solution was concentrated under N_2 and chromatographed on silica gel using CH_2Cl_2 as eluent. The two fractions containing the ketone **9b** and keto ester **8**, respectively (TLC), were directly analyzed by MS. The spectra of both compounds showed that the parent and fragmentation peaks were accompanied by isotopic peaks at +2 Da more intense than those found for the unlabeled reference compounds.

Et_2S Reduction of Oxime Ether Hydroperoxide 7f. A solution of **7f** (116 mg, 0.25 mmol) in CCl_4 (5 mL) was treated with Et_2S (34 mg, 0.37 mmol). When the reduction was complete (30 min), the ^{1}H NMR showed the presence of keto ester **8** and oxime **4f** in 1:1 molar ratio in addition to Et_2S and Et_2SO. Removal of the solvent and of the unreacted Et_2S gave a residue that was chromatographed on silica gel using light petroleum/ether (9:1, 8:2) as eluent and gave oxime **4f** (48 mg, 98%) and keto ester **8** (60 mg, 97%), successively.

Thermolysis of Oxime Ether Hydroperoxide 7f. Compound **7f** (0.1 mmol, 46 mg) was refluxed in dry benzene (5 mL). After 1 h the ^{1}H NMR spectrum showed **7f** almost unchanged. Heating for a further 15 h resulted in the complete disappearance of the original compound, and keto ester **8** and benzophenone (**9f**) were present in ca. 1:1 molar ratio in addition to a certain amount of unidentified products.

One-Pot Synthesis of *N*-(Hydroperoxyalkyl)ketonitrones 5. Each solution of the furan (0.5 mmol) and oxime (2.5 mmol) in CH_2Cl_2 (25 mL) was photooxygenated at −20 °C as above. After completion of reaction (90 min, ^{1}H NMR), the solvent was removed under reduced pressure and the residue was chromatographed on a short column of silica gel. Elution with light petroleum/ether (8:2, 1:1) gave mixtures of unreacted oxime and keto ester **8** and pure hydroperoxy nitrones **5**, successively.

(*E*)-1-Hydroperoxy-*N*-[3,3-(dimethoxycarbonyl)-1-phenyl-2-propenylidene]propylamine *N*-oxide (5b): 54% yield; mp 75−76 °C (from diethyl ether−hexane); IR 3518, 3085, 1737, 1603, 1236 cm^{-1}; ^{1}H NMR δ 0.86 (t, J = 7.3 Hz, 3 H), 1.86 (m, J = 7.3, 6.2 Hz, 2 H), 3.19 (s, 3 H), 3.79 (s, 3 H), 5.61 (t, J = 6.2 Hz, 1 H), 7.30−7.60 (m, 5 H), 8.15 (s, 1 H), 10.89 (brs, 1 H); ^{13}C NMR δ 8.8, 23.8, 52.0, 52.8, 99.7, 128.7, 129.6, 130.3, 130.8, 132.3, 146.7, 164.1, 164.2. The signal of a carbon is hidden in the aromatic resonances. Anal. Calcd for $C_{16}H_{19}NO_7$: C, 56.97; H, 5.68; N, 4.15. Found: C, 56.6; H, 5.8; N, 3.9.

(*E*)-1-Hydroperoxy-2-methyl-*N*-[3,3-(dimethoxycarbonyl)-1-phenyl-2-propenylidene]propylamine *N*-oxide (5c): 34% yield; mp 60−62 °C (from diethyl ether−hexane); IR 3511, 3154, 1733, 1604, 1245 cm^{-1}; ^{1}H NMR δ 0.85 and 0.93 (2d, J = 6.9 Hz, 6 H), 2.28 (m, J = 8.8, 6.9 Hz, 1 H), 3.17 (s, 3 H), 3.76 (s, 3 H), 5.37 (d, J = 8.8 Hz, 1 H), 7.35−7.50 (m, 5 H), 8.16 (s, 1 H), 11.57 (brs, 1 H); ^{13}C NMR δ 18.0, 18.2, 29.7, 52.0, 52.7, 103.2, 128.6, 129.8, 130.2, 131.2, 132.3, 132.6, 147.3, 164.1, 164.2. Anal. Calcd for $C_{17}H_{21}NO_7$: C, 58.11; H, 6.02; N, 3.99. Found: C, 58.3; H, 5.8; N, 4.0.

(*E*)-1-Hydroperoxy-*N*-[3,3-(dimethoxycarbonyl)-1-phenyl-2-propenylidene]heptylamine *N*-oxide (5d): 35% yield; oil; IR 3504, 3145, 1734, 1601, 1260 cm^{-1}; ^{1}H NMR δ 0.40−2.00 (m, 13 H), 3.17 (s, 3 H), 3.79 (s, 3 H), 5.65 (t, J = 6.4 Hz, 1 H),

(34) Iesce, M. R.; Graziano, M. L.; Cermola, F.; Cimminiello, G.; Scarpati, R. *Gazz. Chim. Ital.* **1990**, *120*, 629.

7.25−7.55 (m, 5 H), 8.15 (s, 1 H), 11.07 (brs, 1 H); ^{13}C NMR δ 13.9, 22.3, 24.2, 28.5, 30.4, 31.3, 52.0, 52.8, 98.7, 128.7, 129.6, 130.3, 130.8, 132.3, 132.4, 146.5, 164.1, 164.3. Anal. Calcd for $C_{20}H_{27}NO_7$: C, 61.05; H, 6.92; N, 3.56. Found: C, 61.2; H, 6.8; N, 3.3.

(*E*)-1-Cyclohexyl-1-hydroperoxy-*N*-[3,3-(dimethoxycarbonyl)-1-phenyl-2-propenylidene]methylamine *N*-oxide (5e): 48% yield; white foam; IR 3504, 3157, 1734, 1604, 1255 cm^{-1}; ^{1}H NMR δ 0.60−2.10 (m, 11 H), 3.15 (s, 3 H), 3.76 (s, 3 H), 5.41 (d, J = 9.0 Hz, 1 H), 7.30−7.55 (m, 5 H), 8.15 (s, 1 H), 11.54 (brs, 1 H); ^{13}C NMR δ 25.2, 25.5, 25.7, 28.1, 28.4, 38.6, 52.0, 52.7, 102.4, 128.6, 129.7, 130.2, 131.2, 132.3, 132.7, 147.5, 164.1, 164.2. Anal. Calcd for $C_{20}H_{25}NO_7$: C, 61.37; H, 6.44; N, 3.58. Found: C, 61.0; H, 6.5; N, 3.6.

(*E*)-1-Hydroperoxy-2-phenyl-*N*-[3,3-(dimethoxycarbonyl)-1-phenyl-2-propenylidene]ethylamine *N*-oxide (5f): 65% yield; white foam; IR 3505, 3145, 1733, 1603, 1251 cm^{-1}; ^{1}H NMR δ 2.94 (dd, J = 13.4, 4.1 Hz, 1 H), 3.05 (s, 3 H), 3.26 (dd, J = 13.4, 9.0 Hz, 1 H), 3.75 (s, 3 H), 5.78 (dd, J = 9.0, 4.1 Hz, 1 H), 6.63 (brs, 1 H), 7.00−7.40 (m, 10 H), 8.09 (s, 1 H); ^{13}C NMR δ 36.1, 52.0, 52.8, 99.3, 127.7, 128.2, 128.8, 128.9, 129.6, 130.0, 130.7, 132.2, 132.5, 133.3, 147.8, 164.0, 164.1. Anal. Calcd for $C_{21}H_{21}NO_7$: C, 63.15; H, 5.30; N, 3.51. Found: C, 62.9; H, 5.1; N, 3.3.

(*E*)-1-Hydroperoxy-*N*-[3,3-(dimethoxycarbonyl)-1-(4-methoxyphenyl)-2-propenylidene]ethylamine *N*-oxide (5g): 50% yield; white foam; IR 3505, 3040, 1731, 1603, 1233 cm^{-1}; ^{1}H NMR δ 1.46 (d, J = 5.7 Hz, 3 H), 3.24 (s, 3 H), 3.79 (s, 3 H), 3.86 (s, 3 H), 5.78 (q, J = 5.7 Hz, 1 H), 6.98 (d, J = 8.8 Hz, 2 H), 7.26 (d, J = 8.8 Hz, 2 H), 8.13 (s, 1 H), 11.50 (brs, 1 H); ^{13}C NMR δ 16.3, 52.1, 52.8, 55.4, 84.4, 114.3, 121.7, 131.9, 132.2, 132.8, 145.6, 161.1, 164.1, 164.4. Anal. Calcd for $C_{16}H_{19}NO_8$: C, 54.39; H, 5.42; N, 3.96. Found: C, 54.5; H, 5.6; N, 3.7.

(*E*)-1-Hydroperoxy-*N*-[3,3-(dimethoxycarbonyl)-1-(3-methoxyphenyl)-2-propenylidene]ethylamine *N*-oxide (5h): 55% yield; mp 65−67 °C (from diethyl ether−hexane); IR 3504, 3157, 1729, 1600, 1580, 1236 cm^{-1}; ^{1}H NMR δ 1.46 (d, J = 5.9 Hz, 3 H), 3.24 (s, 3 H), 3.78 (s, 3 H), 3.85 (s, 3 H), 5.82 (q, J = 5.9 Hz, 1 H), 6.90−7.40 (m, 4 H), 8.11 (s, 1 H), 11.42 (brs, 1 H); ^{13}C NMR δ 16.4, 52.1, 52.8, 55.5, 95.2, 115.7, 116.5, 122.5, 129.9, 130.9, 132.0, 145.2, 159.8, 164.1, 164.3. The signal of a carbon is hidden in the aromatic absorption. Anal. Calcd for $C_{16}H_{19}NO_8$: C, 54.39; H, 5.42; N, 3.96. Found: C, 54.4; H, 5.6; N, 3.8.

(*E*)-1-Hydroperoxy-*N*-[1-(4-bromophenyl)-3,3-(dimethoxycarbonyl)-2-propenylidene]ethylamine *N*-oxide (5i): 35% yield; mp 69−71 °C (from diethyl ether−hexane); IR 3511, 3174, 1733, 1605, 1590, 1245 cm^{-1}; ^{1}H NMR δ 1.45 (d, J = 6.1 Hz, 3 H), 3.25 (s, 3 H), 3.78 (s, 3 H), 5.74 (q, J = 6.1 Hz, 1 H), 7.25 (d, J = 8.0 Hz, 2 H), 7.63 (d, J = 8.0 Hz, 2 H), 8.08 (s, 1 H), 11.49 (brs, 1 H); ^{13}C NMR δ 16.2, 52.1, 52.9, 95.2, 125.1, 128.8, 131.6, 132.0, 132.2, 132.3, 144.5, 163.9, 164.2. Anal. Calcd for $C_{15}H_{16}BrNO_7$: C, 44.79; H, 4.01; N, 3.48. Found: C, 44.9; H, 3.8; N, 3.3.

(*E*)-1-Hydroperoxy-*N*-[3,3-(dimethoxycarbonyl)-1-(4-methylphenyl)-2-propenylidene]ethylamine *N*-oxide (5j): 61% yield; mp 69−70 °C (from diethyl ether−hexane); IR 3510, 3154, 1729, 1605, 1245 cm^{-1}; ^{1}H NMR δ 1.45 (d, J = 6.1 Hz, 3 H), 2.42 (s, 3 H), 3.19 (s, 3 H), 3.78 (s, 3 H), 5.77 (q, J = 6.1 Hz, 1 H), 7.10−7.35 (m, 4 H), 8.14 (s, 1 H), 11.57 (brs, 1 H); ^{13}C NMR δ 16.3, 21.3, 52.0, 52.8, 94.9, 126.7, 129.5, 130.3, 132.1, 132.5, 140.7, 144.5, 163.6, 163.9. Anal. Calcd for $C_{16}H_{19}NO_7$: C, 56.97; H, 5.68; N, 4.15. Found: C, 56.7; H, 5.7; N, 4.0.

(*E*)-1-Hydroperoxy-*N*-[(*Z*)-3-(methoxycarbonyl)-4-oxo-1-phenyl-2-pentenylidene]ethylamine *N*-oxide (5k): 55% yield; mp 73−74 °C (from diethyl ether−hexane); IR 3501, 3172, 1734, 1697, 1673, 1600, 1239 cm^{-1}; ^{1}H NMR δ 1.46 (d, J = 5.9 Hz, 3 H), 2.42 (s, 3 H), 3.19 (s, 3 H), 5.73 (q, J = 5.9 Hz, 1 H), 7.30−7.70 (m, 5 H), 8.05 (s, 1 H), 9.80 (brs, 1 H); ^{13}C NMR δ 16.2, 26.6, 51.9, 95.1, 128.9, 129.5, 130.4, 130.8, 132.1, 146.4, 165.3, 195.1. The signal of a *C*H is hidden in the aromatic absorption. Anal. Calcd for $C_{15}H_{17}NO_6$: C, 58.63; H, 5.58; N, 4.56. Found: C, 58.7; H, 5.6; N, 4.3.

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