Photosensitized Oxidation of Furans. 20.[1] A Novel Thermal Rearrangement of Suitably Substituted Alkoxyfuran Endoperoxides via Neighboring-Group Mechanism: Synthesis and Reactivity of the First Functionalized 2-Oxetanyl Hydroperoxides

M. R. Iesce,*,† F. Cermola,† F. De Lorenzo,†
I. Orabona,‡ and M. L. Graziano†

Dipartimento di Chimica Organica e Biochimica and Dipartimento di Chimica, Università degli Studi di Napoli Federico II, Complesso Universitario Monte Sant' Angelo, via Cinthia, I-80126, Napoli, Italy

iesce@unina.it

Received February 26, 2001

Introduction

Our recent studies on the dye-sensitized photooxygenation of 2-alkoxyfurans **1** have strongly evidenced the high synthetic potential of the related endoperoxides **2**. These compounds are thermally unstable and take different rearrangement pathways strictly depending on the nature of the substituent at C5.[2] In any case, the driving-force of these conversions is the facile loosening of the C1−O2 bond due to the presence of an ortho ester function in a strained bicyclic structure.[2] The rationale of the mechanisms involved has provided the development of selective synthetic procedures for a large variety of organic compounds, from new peroxidic systems to already known compounds but whose classical approach is difficult or unsuccessful.[2,3]

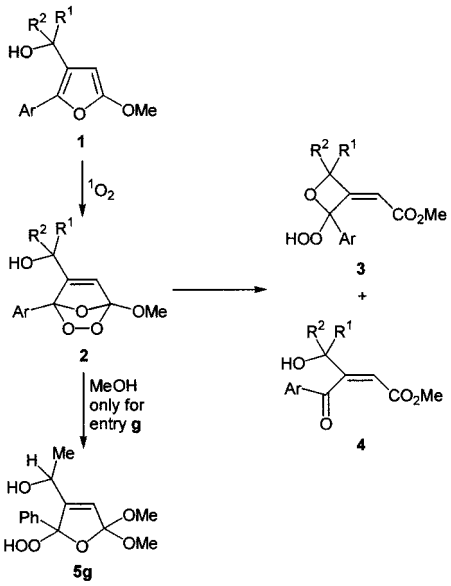
Within the research work on synthesis and use of organic peroxides,[2,3] we have now examined the reaction of singlet oxygen with the hydroxyalkyl-substituted 2-alkoxyfurans **1** purposely prepared to enlarge the synthetic applicability of the related endoperoxides **2**.

Results and Discussion

The methylene blue-sensitized oxygenation of **1a** was carried out at −20 °C in CH_2Cl_2. Unexpectedly, the reaction product was the hydroperoxy oxetane **3a**, in addition to trace amounts of the *Z*-keto ester **4a** (Scheme 1). The peroxidic nature of **3a** was tested by treatment with Et_2S, which rapidly and quantitatively led to **4a**. The latter was isolated and fully characterized (see below),[4] while compound **3a** decomposed on contact with chromatographic adsorbents.

Similar behavior was also observed starting from the 2-methoxyfurans **1b**−**f** which provided the corresponding

Scheme 1



Entry	R^1	R^2	Ar
a	Et	Et	Ph
b	Ph	Ph	Ph
c	Et	Et	4-Br-C_6H_4
d	Ph	Ph	4-Br-C_6H_4
e	Me	Et	Ph
f	Me	Ph	Ph
g	Me	H	Ph

oxetanes **3b**−**f** in very high yields. As expected due to the presence of an additional stereogenic center, **3e** and **3f** were obtained as diastereomeric mixtures in ca. 1:1 and 2:1 molar ratios, respectively.[5] For entry **g**, the only reaction product was the *Z*-keto ester **4g**,[4] and evidence for oxetane **3g** was just obtained by carrying out the oxygenation at −75 °C.[6]

The structural assignments of hydroperoxy oxetanes **3** were based on the spectral data, in particular, on the appearance in the ^{13}C NMR spectra of signals in the range of δ 80−115 for the saturated carbon atoms in the heterocyclic ring and, in addition to the ester values, of signals in the range of δ 160−165 due to the ring carbon which is part of the exocyclic double bond. In the MS spectra the molecular ions are not observed but all of them displayed fragment ions at $[M - 33]^+$ due to the loss of the OOH radical.[7] The structure of **3b**, which was solid and could be purified by recrystallization, was additionally proven by X-ray diffraction.[8]

† Dipartimento di Chimica Organica e Biochimica.
‡ Dipartimento di Chimica.

(1) Part 19: Iesce, M. R.; Cermola, F.; Guitto, A.; Scarpati, R.; Graziano, M. L. *Synlett* **1995**, 1161.

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

(3) See for example: Iesce, M. R.; Cermola, F.; Guitto, A. *Synlett* **1999**, 417; Iesce, M. R.; Cermola, F.; Guitto, A. Giordano F. *J. Chem. Soc., Perkin Trans. 1* **1998**, 475; and references therein.

(4) Stereochemistry has been assigned on the basis of the upfield value of the CO_2Me protons (δ 3.46) in the ^1H NMR due to the anisotropy of the aromatic ring which lies at the same side.

(5) Stereochemistry not assigned.

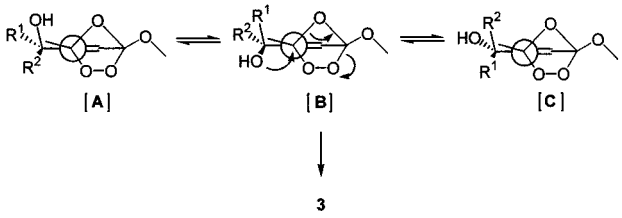
(6) Control experiments showed that **3g** does not convert into **4g** under oxygenation conditions (see Experimental Section).

(7) Other fragment ions were also observed mainly due to primary and secondary fragmentations of oxetane system: Searles, S. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: New York, 1984; Vol. 7, part 5, p 368.

(8) Crystal structure of compound **3b** is available in Supporting Information. Crystallographic data have been deposited with Cambridge Crystallographic Data Center, 12 Union Road, Cambridge, CB2 1EZ, UK.

10.1021/jo0102112 CCC: $20.00
Published on Web 06/02/2001

Scheme 2



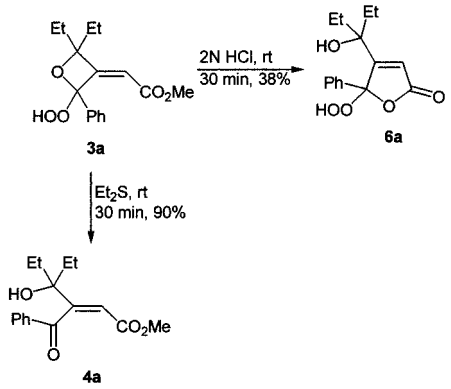
Oxetanes **3a**−**f** were similarly obtained even when the oxygenation was performed in methanol at −20 °C. Usually, this solvent adds to furan endoperoxides affording the corresponding 2,5-dihydrofurans, and the reaction represents one of the most significant trapping modes for these unstable peroxidic species.[2,9] Neverthless, no traces of dihydrofurans were present in the reaction mixtures from **1a**−**f** while the exception was still observed for **1g** which led quantitatively to the corresponding 2,5-dihydrofuran **5g**.

For entries **a**−**f**, the inability of methanol to trap the related endoperoxides **2** suggests that compounds **3** are formed by an intramolecular reaction faster than the methanol addition. Indeed, the obtaining of **3** can be explained considering that a neighboring-group mechanism is operating in the thermal conversion of the unstable corresponding endoperoxides **2**.[10] While the C1−O2 bond is loosening,[11] the hydroxy substituent, when well oriented as in [**B**], gives an intramolecular nucleophilic attack to C4, as shown in Scheme 2.[13]

The different course for **2g** can be explained by two factors: i, the lower nucleophilicity of the secondary OH (entry **g**) than that of the tertiary ones (entries **a**−**f**); ii, the conformer [**B**] which is well oriented to the nucleophilic attack is sterically unfavored when R^2 is a hydrogen. Thus, at −20 °C for **2g** the interconversion of the rotamers is slower than the thermal decomposition into **4g** in CH_2Cl_2,[14] or than the methanol trapping. The formation of **3g**, albeit in low yield, at −75 °C in CH_2Cl_2 confirms this hypothesis.

Compounds **3** are the first examples of functionalized 2-oxetanyl hydroperoxides[16] and, as exemplified by derivative **3a**, exhibit interesting chemical properties.

Scheme 3



Indeed, treatment with an equimolecular amount of Et_2S quantitatively and stereoselectively led to the *Z*-keto ester **4a**, while acid-catalyzed hydrolysis gave, in fair yield, the 5-hydroperoxyfuran-2(5*H*)-one **6a** in addition to **4a** (Scheme 3).[17] It is interesting to note that a similar behavior has been previously observed for the methanol-trapped products such as 2,5-dihydrofurans **5**.[18,19]

Conclusion

This work reports an easy one-pot method for the first functionalized 2-oxetanyl hydroperoxides **3**, starting from the furans **1**, via a novel thermal conversion of methoxyfuran endoperoxides **2**. As indicated by preliminary investigations, compounds **3** can be used as starting material both for the highly functionalized *Z*-keto esters **4**, very usable intermediates in organic synthesis,[18] and for furanones **6**, which belong to a class of compounds of both biological and applicative interest.[19]

Experimental Section

General Methods. 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. Chemical shifts are reported in ppm referenced to TMS. Elemental analyses were obtained using a Carlo Erba EA 1108-Elemental Analyzer. Low-resolution electron impact mass spectra were obtained operating at 70 eV on a GCMS-QP5050A (Shimadzu). The solvents used for the reactions were anhydrous. Methylene blue (MB) (Fluka), ethylmagnesium bromide (1 M in *tert*-butyl methyl ether, Aldrich), phenylmagnesium bromide (3 M in diethyl ether, Aldrich), sodium borohydride (Aldrich), and diethyl sulfide (Aldrich) were used without purification. Methyl 2-methoxy-5-phenylfuran-4-carboxylate,[20] methyl 2-methoxy-5-(4-bromophenyl)furan-4-carboxylate,[19] and 4-acetyl-2-methoxy-5-phenylfuran[20] used as starting compounds for **1** were prepared as previously reported. 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.

Substrates **1a**−**f** were prepared by reactions of methyl 2-methoxy-5-phenylfuran-4-carboxylate (for **1a**,**b**), methyl 2-methoxy-5-(4-bromophenyl)furan-4-carboxylate (for **1c**,**d**), and 4-acetyl-

(9) Gollnick, K.; Griesbeck, A. *Tetrahedron* **1985**, *41*, 2057.

(10) Although the neighboring-group participation is important when a five- or six-membered intermediate is formed, the likelihood of four-membered analogue is increased when there are alkyl groups α or *β* to the neighboring-group: *Advanced Organic Chemistry*; March, J., Ed.; Wiley: New York, 1992; p 311.

(11) The presence of the OMe group is determinant. Indeed, control experiments showed that in the oxygenation, in CH_2Cl_2, of the 2,5-diphenylfuran substituted in *β* as **1a** no trace of an oxetanyl hydroperoxide as **3a** was observed and, as reported for other diarylfurans,[12] only the corresponding *cis*-1,2-dibenzoyloxirane was detected [Selected ^1H NMR signals ($CDCl_3$): *δ* 1.13 and 1.26 (2 × t, J = 7.0 Hz, 6 H, 2 × CH_3), 1.60−1.90 (m, 4 H, 2 × CH_2), 4.78 (s, 1 H, $CH_{epoxidic}$), 7.40−8.20 (m, 10 H, Ar)].

(12) Graziano, M. L.; Iesce, M. R.; Chiosi, S.; Scarpati, R. *J. Chem Soc., Perkin Trans. 1* **1983**, 2071.

(13) On the basis of the proposed mechanism, the diastereoselectivity observed for entries **f**, **g** should be the same to the face-selectivity in the endoperoxide formation step. If and how this selectivity is influenced by the hydroxy group, it has not been investigeted.

(14) *cis*-1,4-Dicarbonyl compounds are generally formed in the singlet oxygen oxygenation of furans via the corresponding endoperoxides.[2,15]

(15) Bloodworth, A. J.; Eggelte, H. J. In *Singlet O_2*; Frimer, A. A., Ed.; CRC Press: Boca Raton, FL, 1985; Vol. II, p 166.

(16) Only the parent 2-oxetanyl hydroperoxide has been reported whose data are not easily consultable: Rakhimova, T. F.; Litinskii, A. O.; Nikishin, G. I.; Glukhovtsev, V. G. *Khim. Khim. Teknol.* **1986**, *29*, 38; *Chem. Abstr.* **1986**, *105*,133097v.

(17) The presence, in **3a**, of keto ester **4a** as the impurity has no influence since the latter is a reaction product in both the cases.

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

(19) Iesce, M. R.; Cermola, F.; Graziano, M. L.; Scarpati, R. *Synthesis* **1994**, 944.

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

2-methoxy-5-phenylfuran (for **1e**, **f**) with EtMgBr or PhMgBr according to standard protocols.[21,22] A representative example is here reported for **1a**: to the stirred commercial solution of EtMgBr (3 equiv, 3 mL) was added methyl 2-methoxy-5-phenylfuran-4-carboxylate (1 mmol) in dry Et_2O (3 mL) dropwise. After stirring for 5 h at room temperature, the mixture was poured into water (3 mL) and slightly acidified with 2 N HCl, the ether layer separated, and the aqueous layer extracted with Et_2O (3 × 3 mL). The combined organic solutions were dried over $MgSO_4$. Then the solvent was evaporated and the mixture chromatographed on a short column of silica gel with light petroleum/Et_2O (8:2) to give **4-(1-ethyl-1-hydroxypropyl)-2-methoxy-5-phenylfuran (1a):** yield 90%; oil; IR ($CHCl_3$) 3600, 3460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 7.1 Hz, 6 H), 1.59 (brs, 1 H), 1.77 (q, J = 7.1 Hz, 4 H), 3.84 (s, 3 H), 5.10 (s, 1 H), 7.20−7.70 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 8.1, 34.4, 57.6, 75.1, 81.5, 127.2, 127.4, 127.7, 128.8, 132.0, 139.5, 160.2. Anal. Calcd for $C_{16}H_{20}O_3$ (260.32): C, 73.82; H, 7.74. Found: C, 73.7; H, 7.8.

4-(Hydroxydiphenylmethyl)-2-methoxy-5-phenylfuran (1b): yield 88%; oil; IR ($CHCl_3$) 3589 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.05 (brs, 1 H), 3.78 (s, 3 H), 4.74 (s, 1 H); 7.20−7.50 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 57.7, 78.5, 84.8, 127.0, 127.3 (overlapping doublets), 128.0 (overlapping doublets), 128.9, 131.1, 139.9, 146.7, 159,5. Anal. Calcd for $C_{24}H_{20}O_3$ (356.40): C, 80.88; H, 5.66. Found: C, 80.7; H, 5.6.

5-(4-Bromophenyl)-4-(1-ethyl-1-hydroxypropyl)-2-methoxyfuran (1c): yield 92%; oil; IR ($CHCl_3$) 3598 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, J = 7.1 Hz, 6 H), 1.65 (brs, 1 H), 1.75 (q, J = 7.1 Hz, 4 H), 3.86 (s, 3 H), 5.08 (s, 1 H), 7.40−7.65 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 8.0, 34.1, 57.5, 75.3, 81.8, 121.1, 128.2, 130.2, 130.8, 131.8, 138.6, 160.4. Anal. Calcd for $C_{16}H_{19}O_3Br$ (339.23): C, 56.65; H, 5.65. Found: C, 56.7; H, 5.6.

5-(4-Bromophenyl)-4-(hydroxydiphenylmethyl)-2-methoxyfuran (1d): yield 65%; mp 156−158 °C; IR ($CHCl_3$) 3597 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.89 (brs, 1 H); 3.79 (s, 3 H); 4.73 (s, 1 H), 7.20−7.50 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 57.7, 78.4, 85.0, 120.8, 127.2, 127.4, 127.8, 128.0, 128.6, 129.6, 129.9, 130.9, 146.3, 159.6. Anal. Calcd for $C_{24}H_{19}O_3Br$ (435.31): C, 66.21; H, 4.40. Found: C, 66.1; H, 4.4.

4-(1-Hydroxy-1-methy1propyl)-2-methoxy-5-phenylfuran (1e): yield 60%; oil; IR ($CHCl_3$) 3597 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 7.1 Hz, 3 H), 1.49 (s, 3 H), 1.60 (brs, 1 H), 1.81 (q, J = 7.1 Hz, 2 H), 3.87 (s, 3 H), 5.16 (s, 1 H), 7.30−7.70 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 8.4, 29.0, 35.6, 57.4, 72.2, 81.4, 127.1, 127.7, 128.7, 129.1, 131.9, 138.9, 160.0. Anal. Calcd for $C_{15}H_{18}O_3$ (246.29): C, 73.14; H, 7.37. Found: C, 73.2; H, 7.3.

4-(1-Hydroxy-1-phenylethyl)-2-methoxy-5-phenylfuran (1f): yield 90%; oil; IR ($CHCl_3$) 3596 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.83 (s, 3 H), 2.40 (brs, 1 H), 3.90 (s, 3 H), 5.35 (s, 1 H), 7.10−7.70 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 32.5, 57.7, 73.3, 82.7, 125.4, 127.0, 127.1, 127.4, 128.0, 128.2, 129.4, 131.3, 139.3, 147.8, 160.0. Anal. Calcd for $C_{19}H_{18}O_3$ (294.33): C, 77.53; H, 6.16. Found: C, 77.6; H, 6.1.

Furan **1g** was prepared as follows: to the solution of 4-acetyl-2-methoxy-5-phenylfuran (1 mmol) in MeOH (3 mL), cooled to 0 °C, was added $NaBH_4$ (1 mmol) in portions. After warming up to room temperature, the reaction mixture was stirred for 12 h. Then the solution was concentrated and water (2.5 mL) was added. The resulting mixture was extracted with CH_2Cl_2 (3 × 5 mL), the combined organic phases were dried, and, after evaporation of the solvent, the residue was chromatographed on silica gel (light petroleum/Et_2O 3:2) to give **4-(1-hydroxyethyl)-2-methoxy-5-phenylfuran (1g):** yield 85%; oil;[21] IR ($CHCl_3$) 3600, 3320 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.53 (d, J = 6.5 Hz, 3 H), 1.92 (brs, 1 H), 3.89 (s, 3 H), 5.11 (q, J = 6.5 Hz, 1 H), 5.39 (s, 1 H), 7.20−7.60 (m, 5 H, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 23.5, 57.6, 62.6, 79.7, 125.6, 126.7, 128.5, 130.6, 139.2, 160.9. Anal. Calcd for $C_{13}H_{14}O_3$ (218.24): C, 71.54; H, 6.47. Found: C, 71.4; H, 6.5.

MB−Sensitized Photooxygenation of 2-Methoxyfurans 1a−f in CH_2Cl_2 at −20 °C. Each solution (5 × 10^{-2} M) of the furans **1a−f** (0.5 mmol), after the addition of the sensitizer (4 × 10^{-3} mmol), was irradiated at −20 °C with a halogen lamp (General Electric, 650 W). During irradiation, dry oxygen was bubbled through the solution, which was kept at this temperature. When each reaction was complete (3 h), the solvent was removed under reduced pressure at room temperature and the residue analyzed by ^1H NMR. After removal of the solvent, for entries **a**,**c−f** each residue was taken up in dry Et_2O, the suspension filtered to remove Methylene Blue, and the filtrate evaporated to give the hydroperoxy oxetanes **3a−f**. All the attempts to purify **3** chromatographically failed since they decompose on contact with the adsorbents. Derivative **3b** was obtained pure by two subsequent recrystallizations with CH_2Cl_2/*n*-hexane.

Methyl 2-(4,4-diethyl-2-hydroperoxy-2-phenyl-3-oxetanylidene)acetate (3a): 88% yield (with a purity of 90%); oil; IR ($CHCl_3$) 3510, 3316, 1724 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 and 1.00 (2 x t, J = 7.3 Hz, 6 H), 1.58−2.20 (m, 4 H), 3.78 (s, 3 H), 5.89 (s, 1 H), 7.35−7.80 (m, 5 H), 9.68 (brs, 1 H); ^{13}C NMR ($CDCl_3$) δ 7.4, 7.9, 28.0, 28.2, 52.1, 88.6, 112.1, 113.3, 127.1, 128.2, 129.6, 136.8, 162.7, 165.5; MS (EI) *m*/*z* 259 (M^+ − 33), 227, 215, 105, 77, 57.

Methyl 2-(2-hydroperoxy-2,4,4-triphenyl-3-oxetanylidene)acetate (3b): 90% (with a purity of 90%) [57% isolated yield by recrystallization]; mp 167−168 °C (dec); IR ($CHCl_3$) 3500, 3318, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.78 (s, 3 H), 6.20 (s, 1 H), 7.20−7.65 (m, 15 H), 9.46 (brs, 1 H); ^{13}C NMR δ 52.1, 88.3, 113.2, 116.6, 126.1, 126.5, 127.3, 127.8, 127.9, 128.2, 128.6, 129.4, 135.5, 141.3, 142.5, 160.4, 165.2. Anal. Calcd for $C_{24}H_{20}O_5$ (388.40): C, 74.21; H, 5.19. Found: C, 74.4; H, 5.3; MS (EI) *m*/*z* 355 (M^+ − 33), 323, 295, 250, 206, 105, 77.

Methyl 2-[2-(4-bromophenyl)-4,4-diethyl-2-hydroperoxy-3-oxetanylidene]acetate (3c): 92% yield (with a purity of >90%); IR ($CHCl_3$) 3509, 3309, 1729 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 and 0.98 (2 × t, J = 7.7 Hz, 6 H); 1.53−2.28 (m, 4 H); 3.77 (s, 3 H), 5.90 (s, 1 H), 7.40−7.65 (m, 4 H), 9.99 (brs, 1 H); ^{13}C NMR ($CDCl_3$) δ 7.3, 7.4, 27.8, 28.2, 52.0, 89.1, 112.1, 113.6, 123.8, 129.0, 131.2, 135.7, 162.1, 164.9; MS (EI) *m*/*z* 337/339 (M^+/M^++2 − 33), 305/307, 183/185, 155/157, 57.

Methyl 2-[2-(4-bromophenyl)-2-hydroperoxy-4,4-diphenyl-3-oxetanylidene]acetate (3d): 93% yield (with a purity of >90%); IR ($CHCl_3$) 3516, 3271, 1728 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.77 (s, 3 H), 6.18 (s, 1 H), 7.20−7.70 (m, 14 H), 9.40 (brs, 1 H); ^{13}C NMR ($CDCl_3$) δ 52.2, 88.6, 112.6, 116.8, 124.0, 126.0, 126.4, 128.0, 128.2, 128.3 (two overlapping d), 129.2, 131.0, 134.6, 141.1, 142.3, 160.0, 165.0; MS (EI) *m*/*z* 433/435 (M^+/M^++2 − 33), 401/403, 373/375, 183/185, 155/157, 105, 77.

Methyl 2-(4-ethyl-2-hydroperoxy-4-methyl-2-phenyl-3-oxetanylidene)acetate (3e) (mixture of diastereomers in ca. 1:1): 90% yield (with a purity of 90%); ^1H NMR ($CDCl_3$) δ 0.92 and 1.04 (2 × t, J = 7.3 Hz, 6 H), 1.44 (s, 3 H), 1.55−2.20 (m) and 1.60 (s) (together 7 H), 3.75 and 3.76 (2 × s, 6 H), 5.85 (s, 2 H), 7.25−7.80 (m, 10 H), 10.05 (brs, 1 H), 10.24 (brs, 1 H); ^{13}C NMR ($CDCl_3$) δ 7.6, 8.0, 22.6, 23.0, 32.0, 32.2, 51.8 (two overlapping q), 86.1, 86.5, 112.0, 112.4, 113.0, 113.5, 127.2 (two overlapping d), 128.1(two overlapping d), 128.5, 129.4, 136.3, 136.6, 162.9, 163.4, 165.1 (two overlapping s); MS (EI) *m*/*z* 245 (M^+ − 33), 213, 201, 105, 77, 43.

Methyl 2-(2-hydroperoxy-4-methyl-2,4-diphenyl-3-oxetanylidene)acetate (3f) (mixture of diastereomers in ca. 2:1): 93% yield (with a purity >90%); ^1H NMR ($CDCl_3$) δ 1.84* (s, 3 H), 1.98 (s, 3 H), 3.73* (s, 3 H), 3.75 (s, 3 H), 6.08* (s, 1 H), 6.22 (s, 1 H), 7.15−7.85 (m, 20 H), 9.69* (brs, 1 H), 10.61 (brs, 1 H); ^{13}C NMR ($CDCl_3$) δ 27.9*, 28.3, 51.9 (two overlapping q), 85.5*, 86.2, 112.9*, 114.6*, 115.1, 115.3, 124.4 (two overlapping d), 126.9, 127.1, 127.6, 127.8, 128.2 (two overlapping d), 128.3, 128.6, 129.3, 129.6, 135.3, 136.4*, 142.0, 142.8*, 161.7, 162.4*, 164.7, 164.9* (* refers to the minor isomer). MS (EI) *m*/*z* 293 (M^+ − 33), 261, 233, 105, 77, 43.

Similar results were obtained when the oxygenation of **1a−f** was carried as above using MeOH as solvent.

MB-Sensitized Photooxygenation of 2-Methoxyfuran 1g. A solution of the furan **1g** (0.5 mmol) in CH_2Cl_2, after the addition of the sensitizer (4 × 10^{-3} mmol), was photooxygenated at −20 °C as above. When the reaction was complete (3 h), the solvent was removed under reduced pressure at room temperature and the residue analyzed by ^1H NMR showed the presence

(21) As previously reported for other 2-alkoxyfurans,[22] compounds **1** are sensitive to air oxidation, particularly on silica gel, so that they must be stored under N_2.

(22) Wulff, W. D.; Gilbertson, S. R.; Springer, J. P. *J. Am. Chem. Soc.* **1986**, *108*, 520.

of the only keto ester **4g** which was purified by silica gel chromatography with $CHCl_3$ as eluent.

Methyl (*Z*)-3-benzoyl-4-hydroxypent-2-enoate (4g): 87% yield; oil; IR ($CHCl_3$) 3531, 3106, 1729, 1669 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (d, $J = 6.5$ Hz, 3 H), 3.17 (brs, 1 H), 3.46 (s, 3H), 4.62 (dq, $J = 6.5$,1.5 Hz, 1 H), 6.29 (d, $J = 1.5$ Hz, 1 H), 7.40−7.90 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 22.1, 51.6, 68.5, 117.4, 128.6, 128.9, 133.6, 135.6, 161.2, 165.5, 197.4. Anal. Calcd for $C_{13}H_{14}O_4$ (234.24): C, 66.65; H, 6.02. Found: C, 66.7; H, 6.1.

When the oxygenation was carried out at −75 °C, after completion of the reaction (3 h), NMR analysis of the reaction mixture performed either at this temperature or at room temperature showed the presence of **3g** (one isomer) and keto ester **4g** in ca. 1:8 molar ratio; this ratio did not change also when the reaction mixture was kept for further 3 h under the oxygenation conditions. Selected NMR data for **3g** were deduced by a careful analysis of the reaction mixture after the signals of the keto ester **4g** were subtracted. No spectroscopic evidence for isomer of **3g** was obtained likely due to its low concentration.

Methyl 2-(2-hydroperoxy-4-methyl-2-phenyl-3-oxetanylidene)acetate (3g): Selected ^1H NMR signals ($CDCl_3$) δ 1.66 (d, $J = 6.3$ Hz, 3 H), 3.80 (s, 3 H), 5.67 (dq, $J = 6.3$, 1.8 Hz, 1 H), 5.90 (d, $J = 1.8$ Hz, 1 H), 11.04 (brs, 1 H); selected ^{13}C NMR signals ($CDCl_3$) δ 23.1, 51.7, 80.2, 110.7, 115.2, 159.0, 164.0.

When the reaction was carried out at −20 °C using methanol as solvent, after completion of the reaction (3 h), NMR analysis showed the presence of only dihydrofuran **5g** as a diastereomeric mixture in ca. 3:1 molar ratio. All attempts to isolate the diastereomers chromatographically failed since both decompose on contact with chromatographic adsorbents.

5-Hydroperoxy-3-(1-hydroxyethyl)-2,2-dimethoxy-5-phenyl-2,5-dihydrofuran (5g) (mixture of diastereomers in ca. 3:1 molar ratio): 90% (with a purity of >90%); ^1H NMR ($CDCl_3$) δ 1.18* (d, $J = 6.8$ Hz, 3 H), 1.40 (d, $J = 6.8$ Hz, 3 H), 3.47, 3.48 and 3.49 (3 x s, 12 H), 4.11 (two overlapping q, $J = 6.8$ Hz, 2 H), 6.05* and 6.08 (2 x s, 2 H), 7.30−7.60 (m, 10 H), 9.31 (brs, 1 H), 9.86* (brs, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.4*, 21.8, 49.5 (two overlapping q), 51.2 (two overlapping q), 61.6*, 63.3, 114.1, 114.8*, 122.0*, 122.1*, 122.6, 123.7, 126.1, 128.1, 128.4*, 128.7*, 136.4*, 136.7, 150.2*, 151.4, (* refers to the minor isomer).

Reduction of 3a. A solution (0.05 M) of **3a** (0.5 mmol) in CH_2Cl_2 (10 mL) was treated with Et_2S (54 mg, 0.6 mmol). After 30 min the solvent was removed together with the excess of Et_2S. The residue, analyzed by ^1H NMR, showed the presence of the only keto ester **4a** which was obtained in 90% yield by chromatography on silica gel (light petroleum/ether 1:1).

Methyl (*Z*)-3-benzoyl-4-ethyl-4-hydroxyhex-2-enoate (4a): mp 91−92 °C; IR ($CHCl_3$) 3602, 1719, 1669, 1638 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, $J = 7.2$ Hz, 6 H), 1.68 (m, 4 H), 2.13 (brs, 1 H), 3.46 (s, 3 H), 6.17 (s, 1 H), 7.35−7.90 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 7.5, 31.6, 51.5, 77.8, 118.8, 128.4 (two overlapping d), 133.0, 136.7, 161.4, 165.3, 197.2. Anal. Calcd for $C_{16}H_{20}O_4$ (276.32): C, 69.54; H, 7.30. Found: C, 69.7; H, 7.4.

Acid Hydrolysis of 3a. A solution (0.02 M) of **3a** (0.5 mmol) in acetone (25 mL) was treated with HCl (2 N, 0.2 mL) and kept at room temperature. After 30 min acetone was removed, water was added, and the mixture was extracted with $CHCl_3$ (3 × 5 mL), dried ($MgSO_4$), and evaporated. The residue, analyzed by ^1H NMR, showed the presence of keto ester **4a** and the hydroperoxyfuranone **6a** in 3:2 molar ratio, respectively. Chromatography on silica gel, eluting with $CHCl_3$−EtOAc (100:0, 9:1), gave successively the keto ester **4a** (45%) and furanone **6a** (38%).

4-(1-Ethyl-1-hydroxypropyl)-5-hydroperoxy-5-phenylfuran-2(5*H*)-one (6a): oil; IR ($CHCl_3$) 3592, 3508, 3283, 1772 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.54 (t, $J = 7.1$ Hz, 3 H), 0.81 (t, $J = 7.1$ Hz, 3 H), 0.95−1.80 (m, 4 H), 2.65 (brs, 1 H), 5.95 (s, 1 H), 7.20−7.60 (m, 5 H), 10.90 (brs, 1 H); ^{13}C NMR ($CDCl_3$) δ 6.9, 7.6, 31.2, 31.8, 76.8, 113.4, 119.1, 126.4, 128.4, 129.8, 132.9, 170.7, 172.0. Anal. Calcd for $C_{15}H_{18}O_5$ (278.29): C, 64.73; H, 6.52. Found: C, 64.9; H, 6.6.

Acknowledgment. Financial Support from Murst (PRIN 1999-2001) is gratefully acknowledged. NMR spectra were run and crystallographic work was undertaken at the Centro di Metodologie Chimico-Fisiche, Università di Napoli Federico II. MS spectra were run at the Laboratorio INCA (Interuniversity Consortium Chemistry for the Environment) of Naples.

Supporting Information Available: Crystal structure and tables of X-ray crystallographic data for compound **3b**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0102112