Photosensitized Oxidation of Furans; Part 17:[1] A Simple Method for the Synthesis of 5-Hydroperoxyfuran-2(5*H*)-ones

M. Rosaria Iesce, Flavio Cermola, M. Liliana Graziano, Rachele Scarpati*

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

Received 25 January 1994; revised 22 April 1994

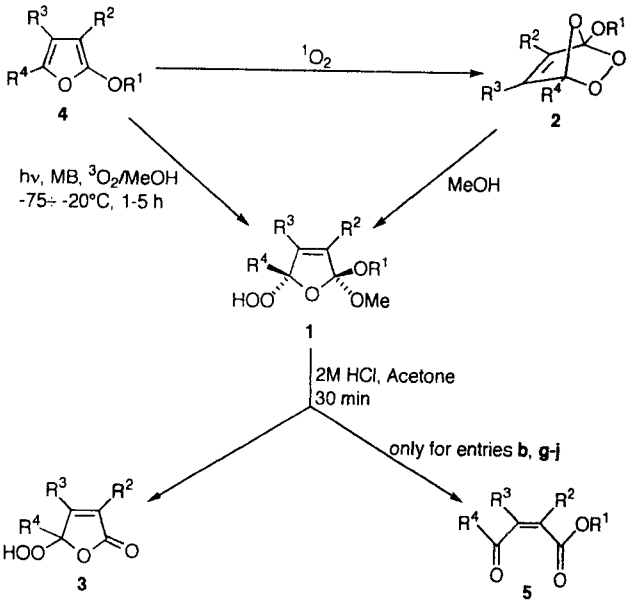
The 5-hydroperoxyfuran-2(5*H*)-ones **3** are synthesized by acid hydrolysis of the dihydrofurans **1** which are prepared in one-pot procedure by reaction of the corresponding furans **4** with singlet oxygen and methanol. The synthetic method has a wide range of applicability; however, compounds **3** unsubstituted at C-4 cannot be prepared since the corresponding dihydrofurans **1** are not formed.

The furan-2(5*H*)-one skeleton appears in diverse classes of biologically active natural and synthetic products:[2] from cytotoxic[3] to antiinflammatory[4] compounds, from antibacterial agents[5] to enzyme inhibitors.[6] The wide sphere of activity of Δ^2-butenolides has stimulated considerable research on the synthesis of these valuable compounds.[7] However, before our preliminary communication, which *inter alia* provides entries to the synthesis of 5-hydroperoxyfuran-2(5*H*)-ones,[8] a sole example of this system was reported in the chemical literature,[9] despite some peroxylactones isolated from marine organisms being cytotoxic agents.[10]

In a previous communication,[8] we reported that methyl 5-hydroperoxy-2,2-dimethoxy-4-methyl-5-phenyl-2,5-dihydrofuran-3-carboxylate (**1a**), previously obtained by methanol addition to the corresponding 1-methoxy-2,3,7-trioxabicyclo[2.2.1]hept-5-ene **2a**,[11] leads by acid hydrolysis to the lactone **3a** (Scheme). The methanol addition to the *endo*-peroxide **2a**, prepared by dye-sensitized photo-oxygenation of the furan **4a**, to form the dihydrofuran **1a** is typical of the 1-alkoxy *endo*-peroxides **2** obtained up to now,[11,12] with the sole exception of those unsubstituted at C-5 which quantitatively lead to the open chain α-methoxy hydroperoxides via carbonyl oxides.[13] However, at −70 °C the furan **4b**, in addition to **1b**, led to its regioisomer, though the latter was formed in very small amounts.[12] Therefore, in order to develop a suitable procedure for the preparation of compounds **3**, it was desirable not only to evaluate the range of applicability of the synthesis of the dihydrofurans **1** as well as of the hydrolysis of the latter into the lactones **3**, but also to select the best conditions for both the reactions.

A serious limitation of the dihydrofuran **1** synthesis was encountered in the difficult handling of the *endo*-peroxides **2**, which can be considered stable only at −80 °C and rearrange at higher temperature by different routes.[1,8,14] This difficulty was overcome by one-pot synthesis, carrying out the methylene blue sensitized photo-oxygenation of the furans **4** in anhydrous methanol. Under the experimental conditions reported in Table 1, the ^{1}H NMR analysis of the crude reaction mixtures showed that the combination of the oxygenation of the furans **4a–j** and of the addition of methanol to the formed *endo*-peroxides **2a–j** results in the formation of only the dihydrofurans **1a–j**, although four isomeric addition products could, in principle, be formed. Therefore, under the reported conditions, methanol addition to the *endo*-peroxides **2a–j** is not only stereoselective,[15] but it is also regioselective. As regards the regioselectivity, it should be noted that the driving force which determines the reactivity of the *endo*-peroxides **2** is connected with the presence of the three oxygen atoms at C-1 in a strained cyclic structure;[1,8,13,14] so the methanol addition occurs leading to the hydroperoxides **1**.

The dihydrofurans **1a–j** are obtained in almost quantitative yields (with the sole exception of **1j** which was obtained in addition to ca. 10% of an unidentified compound stable under mild hydrolysis and showing two ester functions in its ^{13}C NMR spectrum). They can be isolated by silica gel chromatography[16] but partially decompose during the isolation processes; therefore, after removal of methanol,[17] the crude reaction mixtures of



Scheme

1-4	R^1	R^2	R^3	R^4
a	Me	CO_2Me	Me	Ph
b	Me	CO_2Me	CO_2Me	Ph
c	Me	CO_2Et	Ph	Ph
d	Et	H	Me	Ph
e	Me	CO_2Me	Me	CH_2Ph
f	Me	CO_2Me	Et	Et
g	Me	CO_2Me	CO_2Me	CH_2Ph
h	Me	H	CO_2Me	Ph
i	Me	H	CO_2Me	4-BrC_6H_4
j	Me	H	COMe	Ph

Table 1. Dihydrofurans **1** Prepared[a,b]

Product	Reaction Conditions[c]			Ref.	IR ($CHCl_3$) ν (cm^{-1})	^1H NMR ($CDCl_3$) δ, J (Hz)
	Conc ($M \times 10^2$)	T (°C)	t (h)			
1a	2	−40	1	11		
1b	10	−20	5	19		
1c	5	−20	2		3520, 3210, 1723, 1673	0.97 (t, J = 7.1, 3H, CH_3), 3.61 and 3.66 (2s, 6H, 2 × OCH_3), 4.07 (q, J = 7.1, 2H, OCH_2), 7.10–7.40 (m, 10H, 2 × C_6H_5), 9.11 (brs, 1H, OOH)
1d	2	−75	5			1.30 (t, J = 7.0, 3H, CH_3), 1.73 (d, J = 1.6, 3H, 4-CH_3), 3.47 (s, 3H, OCH_3), 3.80 (m, 2H, OCH_2), 5.84 (q, J = 1.6, 1H, CH), 7.30–7.60 (m, 5H, C_6H_5), 8.55 (brs, 1H, OOH)
1e	2	−20	2			2.21 (s, 3H, CH_3), 3.12 (s, OCH_3) and 3.11 (AB system, J_{AB} = 14.7, CH_2), (together 5H), 3.45 (s, 3H, OCH_3), 3.81 (s, 3H, CO_2CH_3), 7.26 (s, 5H, C_6H_5), 8.41 (brs, 1H, OOH)
1f	5	−40	2		3536, 3422, 1719, 1674[d]	0.99 (t, J = 7.1, 3H, CH_3), 1.19 (t, J = 7.1, 3H, CH_3), 1.66–2.16 (m, 2H, 5-CH_2), 2.40–2.70 (m, 2H, 4-CH_2), 3.38 and 3.50 (2s, 6H, 2 × OCH_3), 3.82 (s, 3H, CO_2CH_3), 8.27 (brs, 1H, OOH)
1g	5	−20	2		3523, 3067, 1732, 1681	3.31 (s, OCH_3) and 3.29 (AB system, J_{AB} = 14.6) (together 5H), 3.50 (s, 3H, OCH_3), 3.76 and 3.84 (2s, 6H, 2 × CO_2CH_3), 7.27 (s, 5H, C_6H_5), 9.94 (brs, 1H, OOH)
1h	2	−40	2	19		
1i	2	−40	3		3507, 3223, 1734, 1683	3.49 and 3.51 (2s, 6H, 2 × OCH_3), 3.74 (s, 3H, CO_2CH_3), 6.95 (s, 1H, CH), 7.40–7.60 (m, 4H, C_6H_4), 8.64 (brs, 1H, OOH)
1j	2	−40	3	19		

[a] All compounds are oils.
[b] Satisfactory microanalyses were obtained (C ± 0.25, H ± 0.18, O_{act} ± 0.4) except for **1d** and **1e** which are unchromatographable.
[c] One-pot procedure: MB sensitized photo-oxygenation in MeOH. Almost quantitative yield with the sole exception of **1j** (85–90%).
[d] Recorded in CCl_4.

the furans **4a–j** were hydrolyzed in acetone solution by addition of dilute hydrochloric acid. In this way, the lactones **3a–j** were obtained and isolated, in the yields reported in Table 2, by rapid chromatography on a short column of silica gel.

The hydrolysis of the dihydrofurans **1** into the lactones **3**, although carried out under standardized conditions, is selective for some of the dihydrofurans while for some it competes with the formation of the substituted *cis*-acylacrylates **5** (Table 2).[18] The product ratio of **3** and **5** (Table 2) shows that the formation of **5** is closely dependent on the presence of an electron-withdrawing substituent at C-4 of the dihydrofuran **1** and increases with the increasing electron-withdrawing power of the substituent.

The synthetic method for the hydroperoxylactones **3** is very convenient for its simplicity and as regards the yields. Moreover, it has a wide range of applicability, although it does not permit obtention of those unsubstituted at C-4. In this connection, for the rigorous exclusion of the formation of the dihydrofurans **1** starting from the *endo*-peroxides **2** unsubstituted at C-5, additional control experiments were performed. For example, the methyl 2-methoxy-5-phenylfuran-3-carboxylate photo-oxygenation and methanol addition was carried out under various conditions, in particular by working at very low temperature. In all cases only methyl 4-hydroperoxy-4-methoxy-2-methoxycarbonyl-4-phenylbut-2-enoate was obtained as a methanol adduct. Therefore, the lactone previously reported[9] is still the only example of a 5-hydroperoxyfuran-2(5*H*)-one unsubstituted at C-4.

Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. The IR spectra were obtained on a Perkin-Elmer 1760X-FT spectrophotometer. The NMR spectra were recorded with a Varian XL-200 or a Bruker AC-270 spectrometer using TMS as internal standard. C and H microanalyses were obtained using a Carlo Erba EA 1108-elemental analyzer. Compounds **4c,e,f,g,i** and **5i** gave C, H analysis ± 0.2%. MeOH used in the photo-oxygenation reactions was anhydrous. Silica gel (0.05–0.20 mm Merck) and light petroleum (bp 40–60°C) were used for column chromatography. 1-Phenyl-1-propyne, methyl propiolate, ethyl phenylpropiolate, methyl 2-butynoate, dimethyl acetylenedicarboxylate, 3-hexyne, methylene blue (MB), tetraphenylporphyrin (TPP), diethyl sulfide and benzophenone were used as purchased from Aldrich Chemical Co.

The furans **4b**,[19] **4d**,[20] **4h**,[19] **4j**[19] and methyl 2-methoxy-5-phenylfuran-3-carboxylate[19] were prepared according to the literature procedures.

Methyl 2-Methoxy-4-methyl-5-phenylfuran-3-carboxylate (4a):[11]
This compound was prepared by photolysis of dimethyl diazomalonate in 1-phenyl-1-propyne in the presence of benzophenone, according to a procedure previously outlined for some 5-alkylfurans.[21] A mixture of dimethyl diazomalonate[22] (0.632 g, 4.00 mmol) and benzophenone (0.728 g, 4.00 mmol) in 1-phenyl-1-propyne (0.928 g, 8.00 mmol) was irradiated with a 500 W high pressure mercury lamp (Helios Italquartz) in a Pyrex vessel for 12 h and chromatographed (silica gel, 130 g) under N_2. Elution with light petroleum/Et_2O (19:1, 9:1) gave a mixture of unreacted 1-phenyl-1-propyne and benzophenone and, successively, the furan **4a**.[11] Yield: 0.296 g (30%).

Ethyl 2-Methoxy-4,5-diphenylfuran-3-carboxylate (4c):
This compound was prepared as for **4b**[19] by heating a mixture of 5-methoxy-4-methyl-2-phenyloxazole (0.500 g, 2.64 mmol) and ethyl phenylpropiolate (0.920 g, 5.28 mmol) at 90°C; it was isolated by silica gel chromatography under N_2 (light petroleum/Et_2O, 9:1). Yield: 0.213 g (25%), mp 100–103°C (hexane/Et_2O).

^1H NMR ($CDCl_3$): δ = 1.02 (t, J = 7.1 Hz, 3H, CH_3), 4.07 (q, J = 7.1 Hz, 2H, OCH_2), 4.23 (s, 3H, OCH_3), 7.10–7.50 (m, 10H, 2 × C_6H_5).

Table 2. Hydroperoxylactones **3** Prepared[a]

Product	Yield (%)[b]	mp (°C)	IR ($CHCl_3$) ν (cm^{-1})	^1H NMR ($CDCl_3$) δ, J (Hz)	Ratio **3/5**[c]
3a	68	oil[8]			100 : 0
3b	50	oil	3506, 3041, 1796, 1746, 1673	3.85 and 3.90 (2s, 6H, 2 × OCH_3), 7.30–7.60 (m, 5H, C_6H_5), 9.90 (brs, 1H, OOH)	86 : 14
3c	60	114–116[d]	3510, 3197, 1785, 1727, 1651	1.14 (t, J = 7.1, 3H, CH_3), 4.22 (q, J = 7.1, 2H, OCH_2), 7.10–7.50 (m, 10H, C_6H_5), 10.42 (brs, 1H, OOH)	100 : 0
3d	74	97–98[d]	3510, 3224, 1768, 1657	1.96 (d, J = 1.8, 3H, CH_3), 5.88 (q, J = 1.8, 1H, CH), 7.30–7.60 (m, 5H, C_6H_5), 10.19 (brs, 1H, OOH)	100 : 0
3e	62	127–128[d]	3509, 3200, 1790, 1723, 1670	2.41 (s, 3H, CH_3), 3.20 (AB system, J_{AB} = 14.2, 2H, CH_2), 3.78 (s, 3H, CO_2CH_3), 7.10–7.40 (m, 5H, C_6H_5), 9.19 (brs, 1H, OOH)	100 : 0
3f	70	oil	3522, 3332, 1774, 1728, 1662[e]	0.90 (t, J = 7.0, 3H, 5-$CH_2C\underline{H}_3$), 1.25 (t, J = 7.0, 3H, 4-$CH_2C\underline{H}_3$), 1.90 (m, A part of ABX_3 system, J_{AB} = 15.9, J_{AX} = 7.0) and 2.15 (m, B part of ABX_3 system, J_{AB} = 15.9, J_{BX} = 7.0) (together 2H, 5-CH_2), 2.61 (m, A part of ABX_3 system, J_{AB} = 13.7, J_{AX} = 7.0) and 2.81 (m, B part of ABX_3 system, J_{AB} = 13.7, J_{BX} = 7.0) (together 2H, 4-CH_2), 3.86 (s, 3H, CO_2CH_3), 10.60 (brs, 1H, OOH)	100 : 0
3g	50	oil	3602, 3037, 1791, 1737, 1672	3.43 (AB system, J_{AB} = 14.30, 2H, CH_2), 3.82 and 3.93 (2s, 6H, 2 × CO_2CH_3), 7.25–7.35 (m, 5H, C_6H_5), 9.50 (brs, 1H, OOH)	87 : 13
3h	60	oil	3500, 3120, 1782, 1738, 1687	3.84 (s, 3H, OCH_3), 6.81 (s, 1H, CH), 7.40–7.60 (m, 5H, C_6H_5), 9.51 (brs, 1H, OOH)	70 : 30
3i	50	88–91[d]	3508, 3192, 1785, 1738, 1650	3.85 (s, 3H, OCH_3), 6.81 (s, 1H, CH), 7.40–7.60 (m, 4H, C_6H_4), 9.48 (brs, 1H, OOH)	75 : 25
3j	16	oil	3515, 3198, 1776, 1699, 1628	2.41 (s, 3H, CH_3), 6.71 (s, 1H, CH), 7.40–7.60 (m, 5H, C_6H_5)	14 : 86

[a] Satisfactory microanalyses were obtained: C ± 0.27, H ± 0.18, O_{act} ± 0.3.
[b] Yield of isolated **3** based on the furans **4**.
[c] Product distribution determined by ^1H NMR on the crude hydrolysis mixtures of **1a–j**.
[d] Solvent recrystallization: hexane/Et_2O.
[e] Recorded in CCl_4.

5-Methoxy-4-methyl-2-phenyloxazole:

This was prepared according to the literature procedure[23] for the corresponding 5-ethoxyoxazole. Yield: 74% of an oil after silica gel chromatography eluting with light petroleum/Et_2O (4:1).

Elemental analysis: C, H ± 0.2%.

^1H NMR ($CDCl_3$): δ = 2.12 (s, 3H, CH_3), 3.98 (s, 3H, OCH_3), 7.20–8.00 (m, 5H, C_6H_5).

Methyl 5-Benzyl-2-methoxy-4-methylfuran-3-carboxylate (4e):

This compound was prepared as for **4b**[19] by heating a mixture of 2-benzyl-5-methoxy-4-methyloxazole (1.00 g, 4.92 mmol) and methyl 2-butynoate (0.965 g, 9.80 mmol) at 90 °C; it was isolated as an oil by silica gel chromatography under N_2 (light petroleum/Et_2O, 9:1). Yield: 0.128 g (10%).

^1H NMR ($CDCl_3$): δ = 2.16 (s, 3H, CH_3), 3.80 and 4.01 (2 s, 6H, 2 × OCH_3), 3.86 (s, 2H, CH_2), 7.27 (s, 5H, C_6H_5).

2-Benzyl-5-methoxy-4-methyloxazole:

This was prepared according to the literature procedure[23] for the corresponding 5-ethoxyoxazole. Yield 50% of an oil after chromatography (silica gel; light petroleum/Et_2O, 4:1).

Elemental analysis: C, H ± 0.3%.

^1H NMR ($CDCl_3$): δ = 2.02 (s, 3H, CH_3), 3.87 (s, 3H, OCH_3), 3.95 (s, 2H, CH_2), 7.27 (s, 5H, C_6H_5).

Methyl 4,5-Diethyl-2-methoxyfuran-3-carboxylate (4f):

This compound was prepared as reported above for **4a** starting from dimethyl diazomalonate (0.632 g, 4.00 mmol) and 3-hexyne (0.657 g, 8.00 mmol). Yield: 0.085 g (10%) of an oil by chromatography carried out under N_2 (silica gel; light petroleum/Et_2O, 9:1).

^1H NMR ($CDCl_3$): δ = 1.08 (t, J = 7.3 Hz, CH_3) and 1.15 (t, J = 7.3 Hz, CH_3) (together 6H), 2.49 (q, J = 7.3 Hz, 4H, $2CH_2$), 3.77 and 4.03 (2 s, 6H, 2 × OCH_3).

Dimethyl 5-Benzyl-2-methoxyfuran-3,4-dicarboxylate (4g):

This compound was prepared as for **4b**[19] by heating a mixture of 2-benzyl-5-methoxy-4-methyloxazole (0.507 g, 2.50 mmol) and dimethyl acetylenedicarboxylate (0.710 g, 5.00 mmol) at 90 °C; it was isolated by silica gel chromatography (light petroleum/Et_2O, 9:1). Yield: 0.380 g (50%), mp 50–53 °C (hexane/Et_2O).

^1H NMR ($CDCl_3$): δ = 3.79, 3.85 and 4.01 (3 s, 9H, 3 × OCH_3), 4.08 (s, 2H, CH_2), 7.25–7.35 (m, 5H, C_6H_5).

Methyl 5-(4-Bromophenyl)-2-methoxy-4-methylfuran-3-carboxylate (4i):

This compound was prepared as for **4b**[19] by heating a mixture of 2-(4-bromophenyl)-5-methoxy-4-methyloxazole (0.500 g, 1.86 mmol) and methyl propiolate (0.314 g, 3.73 mmol) at 90 °C; it was isolated by silica gel chromatography (light petroleum/Et_2O, 19:1). Yield: 0.145 g (25%), mp 77–79 °C (hexane/Et_2O).

^1H NMR ($CDCl_3$): δ = 3.82 and 3.91 (2 s, 6H, 2 × OCH_3), 5.60 (s, 1H, CH), 7.40–7.90 (m, 4H, C_6H_4).

2-(4-Bromophenyl)-5-methoxy-4-methyloxazole:

This was prepared according to the procedure reported above for the corresponding 2-phenyloxazole; it was isolated by silica gel chromatography (light petroleum/Et_2O, 9:1). Yield: 70%, mp 58–60 °C (hexane/Et_2O).

Elemental analysis: C, H ± 0.2%.

^1H NMR ($CDCl_3$): δ = 2.12 (s, 3H, CH_3), 3.99 (s, 3H, OCH_3), 7.40–7.80 (m, 4H, C_6H_4).

5-Hydroperoxyfuran-2(5*H*)-ones (3); General Procedure:

A solution of each of the furans **4** (0.5 mmol) in dry MeOH at the concentration reported in Table 1 was irradiated with a halogen superphot lamp (Osram 650 W) in the presence of MB (4×10^{-3} mmol). During the irradiation, dry oxygen was bubbled through the solution which was cooled at the temperature reported in Table 1. Progress of each reaction was checked by periodically monitoring (^1H NMR) of the disappearance of furan **4**. When each reaction was complete (Table 1), MeOH was removed on a rotary evaporator at r.t. Inspection of the ^1H NMR spectrum of each residue showed the presence of only each dihydrofuran **1** except for entry **j** (10% of an unidentified compound). Each residue, dis-

solved in acetone (15 mL) and treated with 2 M HCl (0.15 mL), was kept at r.t. After 30 min, the acetone was removed on a rotary evaporator and each residue was treated with H_2O (2 mL) and extracted with $CHCl_3$ (3 × 5 mL). The combined organic layers of each preparation were dried ($MgSO_4$), the solvent was removed on a rotary evaporator and each residue analyzed by ^1H NMR spectroscopy. For entries **a,c,d,e**, and **f** the ^1H NMR spectrum of each residue showed the presence of only the hydroperoxylactones **3a,c,d,e,f**, respectively, which were isolated with the yields reported in Table 2, by filtration through a short column of silica gel (5 g) using light petroleum/Et_2O (7:3) as eluent. For entries **b**, **g–j** the ^1H NMR spectrum of each residue showed the presence of the hydroperoxylactones **3** and of the *cis*-acylacrylates **5** with the product distribution reported in Table 2 (for entry **j** the unidentified compound was still present). For entries **b,h** and **i**, each residue was chromatographed on a short column (silica gel, 5 g; light petroleum/Et_2O, 4:1 and 7:3) giving the acrylates **5** and the lactones **3**, successively. For entry **g** silica gel chromatography of the residue (benzene/Et_2O, 97:3 and 17:3) gave the acrylate **5g**, in addition to its byproducts, and the lactone **3g**, successively. For entry **j** silica gel chromatography of the residue [benzene, benzene/Et_2O (19:1) and benzene/Et_2O (9:1)] gave the acrylate **5j**, the lactone **3j** and the unidentified product, successively. Physical, analytical[24] and spectral data of the lactones **3** are reported in Table 2 together with the yields of isolated compounds. The acrylates **5b**,[12] **5h**,[12] **5j**[12] were identified by comparison (^1H NMR) with authentic samples and **5g** with a sample to this end prepared (see below); the acrylate **5i** was identified on the basis of the analytical and spectral data.

Methyl 4-(4-Bromophenyl)-3-methoxycarbonyl-4-oxo-2-butenoate **(5i)**:

Mp 71–73 °C (hexane/Et_2O)

IR ($CHCl_3$): ν = 1728, 1682, 1639 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.64 and 3.78 (2 s, 6H, 2 × OCH_3), 7.09 (s, 1H, CH), 7.60–7.80 (m, 4H, C_6H_4).

Methyl 2,3-Dimethoxycarbonyl-4-oxo-5-phenyl-2-pentenoate (5g):
The acrylate **5g** was prepared by diethyl sulfide reduction of the *endo*-peroxide **2g**. A solution of the furan **4g** (0.076 g, 0.25 mmol) in $CDCl_3$ (5 mL) was irradiated as reported above at −60 °C in the presence of TPP (9×10^{-5} mmol). After completion of the reaction (90 min, ^1H NMR), a sample was transferred from the reaction apparatus into the spectrometer, the probe temperature being −60 °C. Inspection of the ^1H NMR spectrum showed the presence of only the *endo*-peroxide **2g**. To the remainder of the solution maintained at −60 °C, Et_2S (0.5 mmol), precooled to this temperature, was added and the resulting mixture was slowly warmed to −15 °C and maintained at this temperature. After 1 h, the ^1H NMR spectrum recorded at r.t. showed the signals of the acrylate **5g** in addition to those of Et_2S and diethyl sulfoxide. The solution was washed with water (3 × 3 mL) in order to remove diethyl sulfoxide. The organic layer was dried ($MgSO_4$) and the solvent and unchanged Et_2S were removed under reduced pressure to give the crude acrylate **5g** (0.076 g) with a purity of 95% (^1H NMR). Yield: 90%. All attempts to purify **5g** by chromatographic methods failed since it decomposes on contact with the adsorbents.

IR ($CHCl_3$): ν = 1733 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.72, 3.82 and 3.86 (3 s, 9H, 3 × OCH_3), 4.01 (s, 2H, CH_2), 7.26 (s, 5H, C_6H_5).

^{13}C NMR ($CDCl_3$): δ = 48.7 (t, CH_2), 53.0, 53.1 and 53.3 (3 q, 3 × OCH_3), 127.2, 128.3 and 129.9 (3 d, CH of C_6H_5), 132.1, 133.7 and 143.2 (3 s, C-1 of C_6H_5 and olefinic carbons), 162.2, 162.3 and 163.3 (3 s, 3 × CO_2), 196.7 (s, CO).

Dimethyl 4-Benzyl-1-methoxy-2,3,7-trioxabicyclo[2.2.1]hept-5-ene-5,6-dicarboxylate **(2g)**:

^1H NMR ($CDCl_3$): δ = 3.62 (AB system, J = 14.6 Hz, CH_2) and 3.74 (s, OCH_3) (together 5H), 3.83 and 3.85 (2 s, 6H, 2 × OCH_3), 7.29 (s, 5H, C_6H_5).

2,5-Dihydrofurans (1); General Procedure:
The previously unreported dihydrofurans **1c,f,g,i** were isolated by silica gel chromatography of the photo-oxygenation mixture of the related furans **4c,f,g,i** on a short column (5 g), after removal of MeOH. Elution with light petroleum/Et_2O (4:1) gave the dihydrofurans **1c** (70), **1f** (90), **1g** (80), and **1i** (95%) as oils. Physical and spectral data of analytical[24] samples are reported in Table 1. All the attempts to purify the dihydrofurans **1d** and **1e** by chromatographic methods failed since they undergo hydrolysis and polymerization on contact with the adsorbent. In Table 1 are reported the ^1H NMR data obtained by the spectra of the crude reaction mixtures.

We gratefully acknowledge the Progetto Finalizzato Chimica Fine 2 (CNR, Rome) and the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST). We would also like to thank Mr. V. Piscopo (Centro di Metodologie Chimico Fisiche, Università di Napoli Federico II) for the NMR spectra.

(1) For Part 16 see: Iesce, M.R.; Cermola, F.; Graziano, M.L.; Cimminiello, G.; Scarpati, R. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1855.
(2) Larock, R.C.; Riefling, B.; Fellows, C.A. *J. Org. Chem.* **1978**, *43*, 131, and references therein.
(3) For example see: Wahlberg, I.; Eklund, A.M. *Fortschr. Chem. Org. Naturst.* **1992**, *59*, 141.
Gu, Z.; Fang, X.; Rieser, M.J.; Hui, Y.; Miesbauer, L.R.; Smith, D.L.; Wood, K.V.; McLaughlin, J.L. *Tetrahedron* **1993**, *49*, 747.
(4) Fenical, W.J. *Natural Products* **1987**, *50*, 1001.
Lee, G.C.M. U.S. Patent 5013850, 1991; *Chem. Abstr.* **1991**, *115*, 135904m.
(5) Yoshioka, K. Eur. Patent Appl. 266182, 1988; *Chem. Abstr.* **1988**, *109*, 110243h.
Tanabe, A. Jpn. Kokai 63211276, 1988; *Chem. Abstr.* **1989**, *110*, 94978q.
(6) Ator, M.A.; Ortiz DeMontellano, P.R. In *The Enzymes*, 3rd ed., Vol. XIX; Sigman, D.S., Boyer, P.D., Eds.; Academic: New York, 1990; p 213.
(7) Boyd, G.V. In *The Chemistry of Acid Derivatives*, Supplement B; Vol. 1, Part 1, p 491 and Vol. 2, Part 1, p 547; Patai, S., Ed.; Wiley: New York, 1979 and 1992.
(8) Iesce, M.R.; Graziano, M.L.; Cermola, F.; Scarpati, R. *J. Chem. Soc., Chem. Commun.* **1991**, 1061.
(9) 5-Hydroperoxy-5-methylfuran-2(5*H*)-one was formed, in addition to diverse polymeric compounds, by autoxidation of 5-methylfuran-2(3*H*)-one and of 5-methylfuran-2(5*H*)-one: Rieche, A.; Schulz, M.; Seyfarth, H.E.; Gottschalk, G. *Fette, Seifen, Anstrichmittel* **1962**, *64*, 198; *Chem. Abstr.* **1962**, *57*, 4779e.
(10) Davidson, B.S. *Tetrahedron Lett.* **1991**, *32*, 7167.
(11) Graziano, M.L.; Iesce, M.R.; Cermola, F.; Cimminiello, G.; Scarpati, R. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1479.
(12) Graziano, M.L.; Iesce, M.R.; Cimminiello, G.; Scarpati, R. *J. Chem. Soc., Perkin Trans. 1* **1989**, *241*, and references therein.
(13) Iesce, M.R.; Graziano, M.L.; Cermola, F.; Cimminiello, G.; Scarpati, R. *Gazz. Chim. It.* **1990**, *120*, 629.
(14) Graziano, M.L.; Iesce, M.R.; Cermola, F.; Giordano, F.; Scarpati, R. *J. Chem. Soc., Chem. Commun.* **1989**, 1608.
(15) The X-ray structure analysis of the methanol adduct to the *endo*-peroxide of 2,5-dimethylfuran revealed a *cis* arrangement of OMe and OOH (Peters, K.; Peters, E.M.; v. Schnering, H.G.; Griesbeck, A.; Gollnick, K. *Z. Kristallogr.* **1984**, *168*, 153). Thus, **1** should also represent the *cis* isomers (cf. Gollnick, K.; Griesbeck, A. *Tetrahedron* **1985**, *41*, 2057).

(16) All the attempts to purify the dihydrofurans **1d** and **1e** by chromatographic methods failed since they undergo hydrolysis and polymerization on contact with the adsorbent.
(17) Attempts to carry out the hydrolysis on the methanol solutions of the dihydrofurans **1** were unsuccessful; the yields of the lactones **3** were very low since side-reactions became predominant.
(18) Control experiments showed that the same results were obtained carrying out the hydrolysis on the isolated compounds **1**.
(19) Graziano, M.L.; Iesce, M.R.; Cimminiello, G.; Scarpati, R. *J. Chem. Soc.. Perkin Trans. 1* **1988**. 1699.
(20) Pincock, J.A.; Moutsokapas, A.A. *Can. J. Chem.* **1977**, *55*, 979.
(21) Hendrick, M.E. *J. Am. Chem. Soc.* **1971**, *93*, 6337.
(22) Peace, B.W.; Carman, F.C.; Wulfman, D.S. *Synthesis* **1971**, 658.
(23) *The Chemistry of the Penicillin*; Clarke, H.T.; Johnson, J.R.; Robinson, R., Eds.; Princeton Univ.: Princeton, N.J. 1949.
(24) Active oxygen (O_{act}) analysis was performed according to a literature procedure: Pasto, J.D.; Johnson, C.R. In *Organic Structure Determination*; Prentice Hall: London, 1969, p 409.