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Chemical, Photochemical and Enzymatic Approach to Furylhydroperoxides

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Abstract: Furylhydroperoxides are accessible by three different methodologies. In the enzymatic approach, lypoxygenase is employed on non lipid-like substrates. Transition metal catalyzed epoxidation of allylic alcohols is strongly dependent on the structure of the involved hydroperoxide.

Introduction

Organic hydroperoxides represent a family of compounds accessible through a variety of methodologies.[1-4] Unfortunately, many of them lack efficiency and selectivity either because of side reactions deriving from their instability under the required reaction conditions (for ex. transition metal catalyzed auto-oxidation) or the formation of isomeric hydroperoxides (for ex. ene reaction).[5] Furthermore, the employment of hydroperoxides, as oxygen donors in oxidative processes, may be limited by this intrinsic thermal or chemical instability. Additional limitations can be caused by structural requirements,[6-8] so that well-known procedures for stereo- and enantioselective oxidations (Sharpless epoxidation, sulfoxidation, etc.) are essentially based on *t*-butyl and cumyl hydroperoxide, while the use of other hydroperoxides has been only occasionally reported.[6,9,10]

5-alkylidene-4,5-dihydrofurans of type **1** represent a class of compounds readily accessible through an efficient two-step sequence starting from 2-(2-alkenyl)-substituted 1,3-dicarbonyl compounds (80-90% overall yield).[11] Predictably, they suffer a rapid conversion into the more stable furan derivatives **3** under acid or basic conditions; nevertheless, because of the presence of an electronwithdrawing function on the five-membered heterocyclic nucleus they are relatively stable and can be isolated and purified through routine chromatographic procedures. Furthermore, they show a strong tendency to undergo a process of spontaneous oxidation: in fact, on standing in the air for 24-48 h samples of **1** in $CDCl_3$ solution are converted in 25-30% yield into hydroperoxides **2** (Scheme 1).

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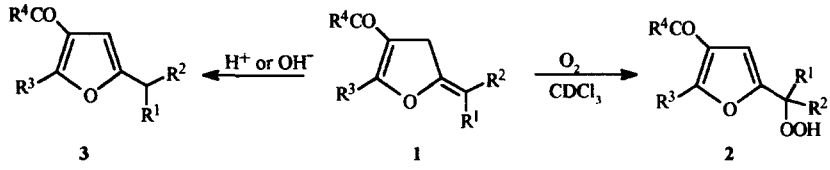
Scheme 1



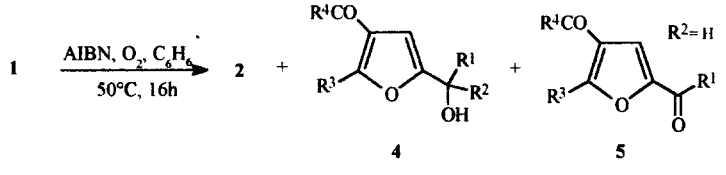
3 1 2

The possibility of elaboration of an efficient methodology for the synthesis of **2** has stimulated our interest, most of all in view of their employment in diastereoselective and enantioselective oxidative processes.[10, 12]

Auto-Oxidation of Compounds 1

The conversion **1**→**2** could be reasonably explained through a chemically or photochemically induced auto-oxidation reaction. Therefore, a variety of compounds **1** were submitted to the typical conditions of a radical chain reaction, catalytic amounts of bis-azoisobutironitrile (AIBN) in benzene solution and bubbling O_2 (Scheme 2). Oxidation proceeded with high values of conversion (> 90%) and very satisfactory selectivity (Table 1).

Scheme 2



4 5

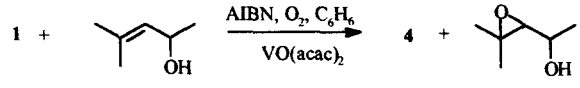
Table 1. Auto-Oxidation of compounds **1** by O_2/AIBN system

Entry	R^1	R^2	R^3	R^4	Product	Yield (%)[a)]
a	Me	H	Me	OEt	**2a**	69%
b	Me	H	*i*-Pr	OEt	**2b**	70%
c	Me	H	-$(CH_2)_2$OMe	OMe	**2c**	71%
d	Me	H	-$(CH_2)_2$COOEt	OEt	**2d**	71%
e	Me	H	-$(CH_2)_3$-		**2e**	60%
f	Me	Me	Me	OEt	**2f**	55%
g	Me	Et	Me	OEt	**2g**	63%
h	Me	H	Me	O*t*-Bu	**2h**	45%

[a)] All the yields refer to isolated chromatographically pure compounds.

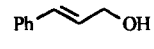
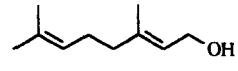
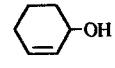
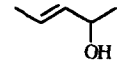
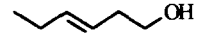
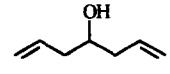
In fact, as supported by ^{1}H-NMR analysis performed directly on crude reaction mixtures, hydroperoxides **2** represented the most abundant products, since the formation of **4** and **5**, deriving from the typical processes of decomposition of **2**, took place to a reduced extent [(**4**+**5**) overall yield <15%]. Only in entry **h** was an unsatisfactory selectivity observed because of the instability of the corresponding hydroperoxide **2h** under these reaction conditions. In order to confirm the potential synthetic value of **2** we decided to carry out a series of experiments involving transition metal catalyzed epoxidation of unsaturated alcohols **6** and, in particular, to verify the compatibility of the auto-oxidation reaction with the presence of unsaturated alcohols, as oxygen acceptors, and $VO(acac)_2$, as catalyst.

Scheme 3



6 **7**

Table 2. Sharpless-type Epoxidation of Unsaturated Alcohols **6**

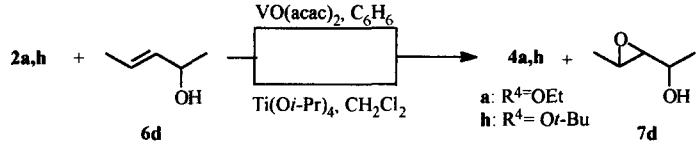
Entry	Substrate		Reac. Time (h)	Temp. (°C)	Yield (%)[a]
a		**6a**	18	60	85
b		**6b**	18	60	81[b]
c		**6c**	18	60	70 (98/2)[c]
d		**6d**	18	60	43 (39/61)[d]
e		**6f**	48	45	50
f		**6g**	48	45	35 (1/1)[e]

[a] All the yields refer to isolated chromatographically pure compounds, whose structures were confirmed by comparison with authentic samples prepared according to a known procedure.[21] [b] Citrale (18%) was isolated as additional oxidation product. [c] Value in parentheses refers to sin/anti diastereoisomeric ratio determined by GLC on acetate. [d] Value in parentheses refers to erythro/threo diastereoisomeric ratio, determined by ^{1}H-NMR analysis performed on crude reaction mixture.[13]
[e] Value in parentheses refers to sin/anti diastereoisomeric ratio determined by ^{1}H-NMR analysis.[14]

When auto-oxidation was repeated under the conditions reported in Scheme 3 for the representative compound **1a**, the formation of hydroperoxide **2a** took place with the usual efficiency: however, its accumulation was prevented by the concomitant fast consumption in a Sharpless-type reaction. In fact, epoxidation was found to proceed in a regio- and diastereoselective way (respectively entry **b** and entries **c**, **d**) (Table 2).

Satisfactory results have been obtained with homoallylic alcohols, although milder conditions had to be used to avoid extensive decompositions of the resulting β,γ-epoxyalcohols. It is noteworthy that, in the case of bis-homoallylic alcohol involved in entry **f**, only the formation of a monoepoxidation product could be observed. Alcohol **6d**, that does not possess 1,2- and 1,3- allylic strain, undergoes poorly selective epoxidation under a great variety of experimental conditions (solvent, catalyst, oxidant).[14] Therefore, in our opinion, it could be considered a good test to examine the influence of the structure of the hydroperoxide on the diastereoselectivity in Sharpless epoxidation.

Scheme 4



In Table 3 the results obtained with TBHP/$VO(acac)_2$ and TBHP/$Ti(O\textit{i}\text{-}Pr)_4$ systems are compared with those obtained with two representative furylhydroperoxides, **2a** and **2h**, characterized by a structural variation very far from the reaction site.

Table 3. Diastereoselective Epoxidation of Allylic Alcohol **6d**

Entry	Hydro peroxide	Catalyst	Solvent	Temp. (°C)	Reac. Time (h)	E/T[a)]
a	**2a**	$VO(acac)_2$	C_6H_6	r.t.	16	39/61
b	TBHP	$VO(acac)_2$	C_6H_6	r.t.	16	71/29[14]
c	**2a**	$Ti(O\textit{i}\text{-}Pr)_4$	CH_2Cl_2	-17	16	21/79
d	TBHP	$Ti(O\textit{i}\text{-}Pr)_4$	CH_2Cl_2	-17	16	34/66[14]
e	**2h**	$Ti(O\textit{i}\text{-}Pr)_4$	CH_2Cl_2	-17	4	87/13

[a)] All the reactions have been prolonged until >90% conversion. Erythro/Threo diastereoisomeric ratios have been determined by ^{1}H-NMR analysis performed on crude reaction mixtures.[13]

In the presence of $VO(acac)_2$ the epoxidation of **6d** by **2a** took place with a reverse but again poor diastereoselectivity. More interestingly, when **2a** and **2h** were used as oxidants, the $Ti(Oi\text{-}Pr)_4$-catalyzed epoxidation proceeded with higher diastereoselectivity (with respect to Ti^{+4}/TBHP system) and opposite erythro/threo ratios were observed in entries **c** and **e**. This result clearly shows that the stereochemical outcome of Sharpless epoxidation does not depend only on the type of allylic alcohol and/or metal catalyst, but a strong influence can be exerted by the particular hydroperoxide employed.

Photochemical Auto-Oxidation of 1

The spontaneous conversion **1**→**2** could be reasonably explained through a photochemical process where compounds **1** play the role both of substrates and photosensitizers. The possibility of formation of **2** by ene reaction of singlet oxygen $^1O_2$ on **1** was rapidly excluded. In fact, photo-oxidation of **1a** with a 300W lamp in $CHCl_3$ solution at -78°C in the presence of tetraphenylporphine, led to a complex reaction mixture. Rather surprisingly, by irradiation with a 60W desk lamp under O_2 atmosphere in the presence of catalytic amounts of rose bengal (RB), as photo-sensitizer, neat **1** were converted into hydroperoxides **2** in an efficient way (Table 4).

Scheme 5

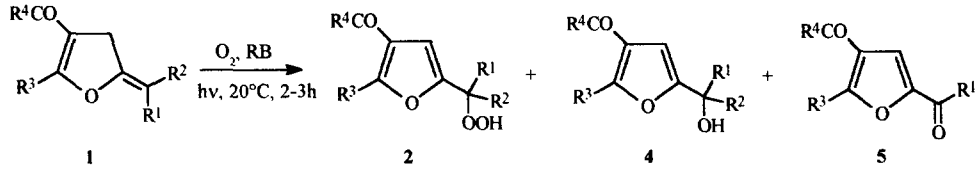


Table 4. Photochemical Auto-Oxidation of Compounds **1**

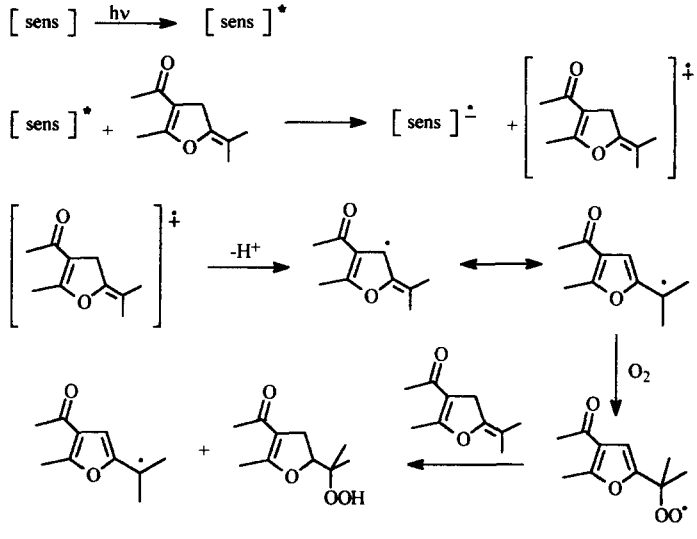
Entry	Compound 1	R^1	R^2	R^3	R^4	Yield (%)[a]
a	**1a**	Me	H	Me	OEt	66
b	**1h**	Me	H	Me	O*t*-Bu	80
c	**1i**	H	H	Me	OEt	85
d	**1j**	H	H	Me	Me	48[b]

[a] All the yields refer to isolated chromatographically pure compounds. [b] Hydroperoxide **2j** suffered a noticeable process of decomposition in the course of purification procedure.

In fact, as supported by ^{1}H-NMR data, an efficient conversion (> 85%) was usually observed and the formation of decomposition products **4** and **5** was limited to < 10% overall yield. It should be noted that

photo-oxidations in solution proceeded in a very disappointing way: for example, after irradiation of 0.1 M solutions of **1i** in acetone, methanol or acetonitrile under the standard conditions, the starting material was recovered respectively in 81, 94, and 76%; very complex reaction mixtures were obtained after more prolonged reaction times. The inhibition of solvent-free photo-oxygenation by 2,6-di-*t*-butyl-phenol seems to be in agreement with the mechanistic pathway reported in Scheme 6.

Scheme 6



It has to be noted that an analogous mechanism, involving the formation of a radical cation , followed by a radical chain process, was proposed for the photosensitized oxygenation of alkylbenzenes with 9,10-dicyanoanthracene.[15] Because of the very mild conditions this alternative procedure allows a more satisfactory approach to less stable hydroperoxides **2** (for ex., **2h** and **2j**).

Enzymatic Hydroperoxidation of Compounds 1

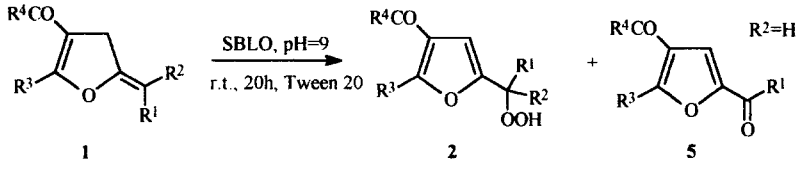
Lipoxygenase (EC 1.13.11.12) is a non-heme iron containing enzyme, ubiquitously distributed in plants and animals, characterized by multiple activities as dioxygenase, hydroperoxidase and leucotriene synthetase.[16] The main feature of lipoxygenase is represented by its high substrate specificity: in fact, the major substrates are long chain polyunsaturated fatty acids presenting a Z,Z-1,4-pentadiene system and a carboxylic function situated at a suitable distance from this system. High substrate specificity has hitherto limited the employment of lipoxygenase as catalyst in organic synthesis, so that few known applications concern lipid-like compounds.[17,18] Recent reports[19] have shown that lipid hydroperoxides and reactive radicals

produced in the course of oxidation of polyunsaturated fatty acids are capable of performing reactions of epoxidation, N-oxidation, sulfoxidation on non-conventional substrates, but the preparative aspects of these co-oxidations have not yet been the object of a deeper investigation.

However, although 5-alkylidene-4,5-dihydrofurans **1** do not possess any of the structural features required for the enzymatic reaction by lipoxygenase, we equally decided to perform a series of experiments devoted to verify the possibility of an enzymatic hydroperoxidation leading to products **2**.

When the representative compounds **1b,d** were submitted to the action of soybean lipoxygenase (SBLO) under O_2 atmosphere in buffer solution (pH=9), in the absence of any co-oxidant, the formation of the expected hydroperoxide **2b,d** was found to occur although in rather low yield (entries **g** and **h**, Table 5).

Scheme 7



1 **2** **5**

Table 5. SBLO Catalyzed Oxidation of Compounds **1**

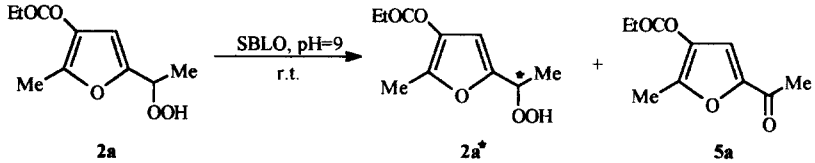
Entry	R^1	R^2	R^3	R^4	React. Time (h)	Product	Yield (%)[a]	e.e. (%)[b]
a	Me	H	Me	OEt	20	**2a**	40(10)	8
b	Me	H	*i*-Pr	OEt	20	**2b**	35(6)	5
c	Me	H	$-(CH_2)_2OMe$	OMe	42	**2c**	24(14)	6
d	Me	H	$-(CH_2)_3COOEt$	OEt	20	**2d**	80(8)	5
e	Me	Me	$-(CH_2)_3COOEt$	OEt	20	**2k**	85	-
f	Me	Et	$-(CH_2)_3COOEt$	OEt	20	**2l**	80	0
g	Me	H	$-(CH_2)_3COOEt$	OEt	20	**2d**	28(9)[c]	13
h	Me	H	*i*-Pr	OEt	23	**2b**	15(5)[c]	5
i	Me	H	$-(CH_2)_3COOEt$	OEt	20	**2d**	3[d]	0

[a] All the yields refer to isolated, chromatographically pure compounds; values in parentheses refer to isolated **5**.
[b] E.e of products **2** have been determined by ^{1}H-NMR analysis in the presence of $Eu(hfc)_3$ as chiral reagent shift performed on the corresponding 2-furylcarbinols **4**, obtained by in situ reduction of **2** with an excess of 0.1 N $Na_2S_2O_3$ solution. [c] Without Tween 20. [d] Without SBLO

It is noteworthy that furylketones **5b,d** were isolated as additional oxidation products and **2d** was found to be enantiomerically enriched although to a very poor extent.

A significant improvement in the formation of hydroperoxides **2** was observed by addition of Tween 20,[20] a non-ionic surfactant previously employed as a solubilizing agent for polyunsaturated fatty acids, (entries **a-f**); in particular, very satisfactory results were obtained when a side chain containing a terminal polar group was situated on the furan nucleus. Unfortunately, in the presence of this additive, enantiomeric excesses of **2** were scarcely detectable. The isolation of **2l** as a completely racemic mixture suggested the possibility that enantioselectivity was not involved in hydroperoxidation reaction, while enantiomeric enrichment could originate by enantioselective dehydration of furylhydroperoxides **2** to furylketones **5** by lipoxygenase. In order to confirm this hypothesis racemic **2a** was submitted to treatment with SBLO under the conditions reported in Scheme 8.

Scheme 8



2a **2a*** **5a**

In the absence of Tween 20, **5** was obtained in 56% yield while the recovered **2a** (42% yield) had 44% e.e..

Although the mechanistic aspects have not been investigated, in every case, the enzyme proved to play a determining role in the hydroperoxidation reaction: in fact, a control experiment performed in the absence of SBLO afforded **2d** only in 3% yield (entry **i**, Table 5). These results represent, to our knowledge the first example of direct synthetic application of SBLO on non-conventional substrates.

In conclusion, the easy access to furylhydroperoxides in achiral, racemic and chiral forms should disclose new possibilities of investigation on asymmetric oxidation and, in particular, on the stereochemical outcome deriving from the use of chiral oxidants.

Acknowledgements

We wish to thank MURST and CNR (Roma) for financial support.

Experimental

General information: ^{1}H-NMR and ^{13}C-NMR spectra were recorded with Varian Gemini-200 spectrometer. Splitting patterns are designated as s (singlet), d (doublet), t(triplet), q (quartet), qp (quintet), hept (heptuplet), m (multiplet), dd (double doublet), ss (sharp singlet), bs (broad singlet). Chemical shifts are reported in (δ) ppm relative to internal $CHCl_3$ δ (7.27) for ^{1}H-NMR and $CDCl_3$ δ (77.0) for ^{13}C-NMR. Silica gel (230-400 mesh Merck) was used for flash chromatography. Analytical thin layer chromatography (TLC) were carried out on Merck Kieselgel F_{254} plates. Spots on TLC were visualized under UV light, iodine and by spraying with H_2SO_4 (10% in ethanolic solution) followed by heating.

Starting materials **1** have been prepared according a literature procedure[11] and their structures were confirmed by ^{1}H-NMR and ^{13}C-NMR data. Other chemicals (Aldrich or Fluka) were used as commercial products without further purification.

General procedure for auto-oxidation of 1: A solution of **1** (2 mmol) and AIBN (0.2 mmol) in benzene (70 ml) was stirred overnight at 50°C under bubbling O_2. The reaction was monitored by TLC. Then the solvent was removed under a reduced pressure and crude **2** were purified by silica gel column chromatography by elution with light petroleum/diethyl ether mixtures.

General procedure for photo-oxidation of 1: **1** and rose bengal (0.01 mmol) were dissolved in acetone (5 ml) and, then, the solvent was removed under a reduced pressure. The resulting mixture was irradiated, under an O_2 atmosphere, with an Ilesa 60 Watt lamp at 20°C. The reaction was monitored by TLC. At last the crude **2** were purified as above reported.

General procedure for enzymatic hydroperoxidation of 1: starting materials **1** (0.5 mmol) and SBLO (Fluka) (1/1 w/w ratio) were dissolved in a borate buffer solution (pH=9) (50 ml) containing Tween 20 (0.25 ml). The mixture was stirred under O_2 atmosphere in the dark (to avoid photo-oxidation) and the reaction was monitored by TLC. Finally the solid residue was separated by filtration and the aqueous phase was extracted with AcOEt (3x 25 ml). After the neutral extracts were dried over anhydrous Na_2SO_4, the solvent was evaporated and crude **2** were purified as reported above.

General procedure for one-pot epoxidation of allylic alcohols with 1: A solution of **1a** (1.2 mmol), AIBN (0.12 mmol), $VO(acac)_2$ (0.03 mmol) and unsaturated alcohol (1 mmol) in benzene (50 ml) was stirred under a slow stream of O_2 under the conditions reported in Table 2. The reaction was prolonged until >80% conversion of unsaturated alcohols. Then the solvent was removed under a reduced pressure and the crude products were purified through flash chromatography by n-hexane/AcOEt mixtures. $VO(acac)_2$ and $Ti(O\textit{i}\text{-}Pr)_4$ catalyzed epoxidations were performed respectively according to ref. 21. and 22.

5-(1-hydroperoxyethyl)-3-ethoxycarbonyl-2-methylfuran (2a): White needles; Crystd from n-hexane/CH_2Cl_2 (6:1) mp 62-63°; ^{1}H-NMR ($CDCl_3$):1.32 (t, 3H, *J*=7.0 Hz), 1.52 (d, 3H, *J*=6.8 Hz), 2.56 (s, 3H), 4.26 (q, 2H, *J*=7.0 Hz), 4.99 (q, 1H, *J*=6.8 Hz), 6.62 (s, 1H), 8.20 (ss, 1H); ^{13}C-NMR ($CDCl_3$): 13.5, 13.9, 15.9, 60.2, 75.8, 109.6, 114.0, 151.6, 159.6, 164.4. Anal. Calcd.for $C_{10}H_{14}O_5$: C, 56.05; H, 6.59%. Found: C, 56.10; H, 6.64%.

5-(1-hydroperoxyethyl)-3-ethoxycarbonyl-2-isopropylfuran (2b): White needles; ^{1}H-NMR ($CDCl_3$): 1.24 (d, 6H, *J*=7.0 Hz), 1.32 (t, 3H, *J*=7.0 Hz), 1.52 (d, 3H, *J*=7.0Hz), 3.73 (hept, 1H, *J*=7.0 Hz), 4.26 (q, 2H, *J*=7.0 Hz), 5.00 (q, 1H, *J*=7.0 Hz), 6.62 (s, 1H), 7.83 (ss, 1H). ^{13}C-NMR ($CDCl_3$): 13.9, 15.9, 20.3, 27.1, 60.0, 75.9, 109.4, 112.1, 151.2, 164.2, 167.4. Anal. Calcd. for $C_{12}H_{18}O_5$: C, 59.48; H, 7.49%. Found: C, 59.40; H, 7.41%.

5-(1-hydroperoxyethyl)-3-methoxycarbonyl-5-(2-methoxyethyl)furan (2c): White needles; Crystd from n-hexane/CH_2Cl_2 (6:1) mp 45° (dec); ^{1}H-NMR ($CDCl_3$): 1.51 (d, 3H, *J*=7.0 Hz), 3.25 (t, 2H, *J*=7.0 Hz), 3.33 (s, 3H), 3.68 (t, 2H, *J*=7.0 Hz), 3.80 (s, 3H), 4.99 (q, 1H, *J*=7.0 Hz), 6.62 (s, 1H), 8.30 (ss, 1H). ^{13}C-NMR ($CDCl_3$): 15.9, 27.9, 51.2, 58.2, 69.9, 75.6, 109.4, 114.5, 152.4, 159.7, 164.3. Anal. Calcd. for $C_{11}H_{17}O_5$: C, 54.09; H, 6.60%. Found: C, 54.16; H, 6.69%.

5-(1-hydroperoxyethyl)-3-ethoxycarbonyl-2-(3-ethoxycarbonylpropyl)furan (2d): White needles; Crystd from n-hexane/CH_2Cl_2 (6 :1) mp 47-48°; ^{1}H-NMR ($CDCl_3$): 1.15 (t, 3H, *J*=7.0 Hz), 1.30 (t, 3H, *J*=7.0 Hz), 1.50 (d, 3H, *J*=7.0 Hz), 2.14-2.00 (m, 2H), 2.34 (t, 2H, *J*=7.0 Hz), 3.06 (t, 2H, *J*=7.0Hz), 3.94 (q, 2H, *J*=7.0 Hz), 4.26 (q, 2H, *J*=7.0Hz), 4.97 (q, 1H, *J*=7.0 Hz), 6.57 (s, 1H), 9.00 (ss, 1H). ^{13}C-NMR ($CDCl_3$): 13.8, 14.0, 15.9, 22.9, 26.7, 33.2, 60.1, 60.4, 75.8, 109.5, 114.7, 152.3, 161.6, 163.9, 173.7. Anal. Calcd. for $C_{15}H_{22}O_7$: C, 57.32; H, 7.05%. Found: C, 57.22; H 7.00%.

3-(1-hydroperoxyethyl)-6-oxo-2-oxa-bicyclo[4.3.0]-1,3-nonadiene (2e): White needles; Crystd from n-hexane/CH_2Cl_2 (6 :1) mp 75° (dec); ^{1}H-NMR ($CDCl_3$): 1.52 (d, 3H, *J*=6.8 Hz), 2.15 (qp, 2H, *J*=6.2), 2.47 (t, 2H, *J*=6.0 Hz), 2.86 (t, 2H, *J*=6.2 Hz), 5.02 (q, 1H, *J*=6.8 Hz), 6.63 (s, 1H), 8.30 (ss, 1H);^{13}C-NMR ($CDCl_3$): 16.0, 22.1, 23.0, 37.1, 75.7, 104.9, 121.4, 154.4, 167.8, 195.6. Anal. Calcd. for$C_{10}H_{12}O_4$: C, 61.20; H, 6.17%. Found: 61.29; H, 6.25%.

5-(1-hydroperoxy-1-methylethyl)-3-ethoxycarbonyl-2-methylfuran (2f): White needles; Crystd from n-hexane/CH_2Cl_2 (6 :1) mp 56° (dec); ^{1}H-NMR ($CDCl_3$):1.30 (t, 3H, *J*=7.0 Hz), 1.54 (s, 6H), 2.52 (s, 3H), 4.25

(q, 2H, *J*=7.0 Hz), 6.54 (s, 1H), 8.00 (ss, 1H); ^{13}C-NMR ($CDCl_3$): 13.6, 14.1, 24.0, 60.5, 81.5, 108.5, 116.7, 153.2, 158.9, 164.0. Anal. Calcd. for$C_{11}H_{16}O_5$: C, 57.87; H, 7.07%. Found: C, 57.95; H, 7.10%.

5-(1-hydroperoxy-1-methylpropyl)-3-ethoxycarbonyl-2-methylfuran (2g): White needles; ^{1}H-NMR ($CDCl_3$): 0.82 (t, 3H, *J*=7.5 Hz), 1.29 (t, 3H, *J*=7.0 Hz), 1.48 (s, 3H), 1.85 (q, 2H, *J*=7.5 Hz), 2.50 (s, 3H), 4.22 (q, 2H, *J*=7.0 Hz), 6.53 (s, 1H), 7.92 (ss, 1H).^{13}C-NMR ($CDCl_3$): 7.01, 13.5, 14.0, 24.8, 28.7, 60.0, 82.6, 109.0, 113.9, 153.6, 158.9, 164.3. Anal. Calcd. for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49%. Found: C, 59.38; H, 7.43%.

5-(1-hydroperoxyethyl)-3-t-butyloxycarbonyl-2-methylfuran (2h): White needles; Crystd from n-hexane/CH_2Cl_2 (6 :1) mp 50° (dec); ^{1}H-NMR ($CDCl_3$): 1.50 (d, 3H, *J*=7.0 Hz), 1.51 (s, 9H), 2.52 (s, 3H), 4.98 (q, 1H, *J*=7.0 Hz), 6.57 (s, 1H), 8.00 (ss, 1H). Anal. Calcd. for $C_{12}H_{18}O_5$: C, 59.48; H, 7.49%. Found: C, 59.36; H, 7.40%.

5-(hydroperoxymethyl)-3-ethoxycarbonyl-2-methylfuran (2i): Very dense oil; ^{1}H-NMR ($CDCl_3$): 1.30 (t, 3H, J=7.0 Hz), 2.50 (s, 3H), 4.20 (q, 2H, J=7.0 Hz), 4.81 (s, 2H), 6.65 (s, 1H), 8.20-8.50 (bs, 1H). Anal. Calcd. for $C_9H_{12}O_5$: C, 54.00; H, 6.04%. Found: C, 53.04; H, 6.10%.

5-(hydroperoxymethyl)-3-acetil-2-methylfuran (2j): Very dense oil; ^{1}H-NMR ($CDCl_3$): 2.40 (s, 3H), 2.55 (s, 3H), 4.85 (s, 2H), 6.65 (s, 1H), 8.50-8.90 (bs, 1H). Anal. Calcd. for $C_8H_{10}O_4$: C, 56.47; H, 5.92%. Found: C, 56.54; H, 5.85%.

5-(1-hydroperoxy-1-methylethyl)-3-ethoxycarbonyl-2-(3-ethoxycarbonylpropyl)furan (2k): Very dense oil; ^{1}H-NMR ($CDCl_3$): 1.14 (t, 3H, *J=7.0*), 1.31 (t, 3H, *J=7.0*), 1.54 (s, 6H), 1.95-2.15 (m, 2H), 2.32 (t, 2H, *J=7.0 Hz*), 3.04 (t, 2H, *J=7.0 Hz*), 3.91 (q, 2H, *J=7.0 Hz*), 4.25 (q, 2H, *J=7.0 Hz*), 6.50 (s, 1H), 8.80 (s, 1H); ^{13}C-NMR ($CDCl_3$): 13.8, 14.1, 22.8, 23.0, 26.7, 33.1, 60.1, 60.5, 79.2, 108.4, 114.8, 154.9, 161.0, 163.9, 173.9. Anal. Calcd. for $C_{16}H_{24}O_7$: C, 58.53; H, 7.37%. Found: C, 58.46; H, 7.40%.

5-(1-hydroperoxy-1-methylpropyl)-3-ethoxycarbonyl-2-(3-ethoxycarbonylpropyl)furan (2l): Very dense oil; ^{1}H-NMR ($CDCl_3$): 0.83 (t, 3H, *J=7.0 Hz*), 1.14 (t, 3H, *J=7.0 Hz*), 1.31 (t, 3H, *J=7.0 Hz*), 1.48 (s, 3H), 1.84 (q, 2H, *J=7.0 Hz*), 1.95-2.10 (m, 2H), 2.30 (t, 2H, *J=7.0 Hz*), 2.90-3.20 (m, 2H), 3.92 (q, 2H, *J=7.0 Hz*), 4.24 (q, 2H, *J=7.0 Hz*), 6.49 (s, 1H), 8.74 (s, 1H); ^{13}C-NMR ($CDCl_3$): 13.7, 14.1, 19.2, 22.8, 26.7, 28.6, 33.1, 60.0, 60.5, 82.5, 109.1, 114.7, 154.5, 161.0, 164.0, 173.8. Anal. Calcd. for $C_{17}H_{26}O_7$: C, 59.64; H, 7.65%. Found: C, 59.56; H, 7.60%.

References and Notes

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