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A convenient approach to renewable hydroperoxides

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Abstract—2-(1-Hydroperoxyalkyl)-furans and 6-hydroperoxy-2*H*-pyran-3(6*H*)-ones are alternatively accessible by acid-catalyzed oxidation of 2-furyl alcohols with hydrogen peroxide under appropriate conditions. Representative compounds of both classes of hydroperoxides have been used, as easily renewable oxygen donors, in asymmetric sulfoxidation reactions. © 2001 Published by Elsevier Science Ltd.

Cheap, safe, environmentally acceptable, energy- and resource-saving processes represent some of the main features of advanced chemical methodologies; besides, the availability of highly efficient and selective procedures is particularly important from the preparative point of view, since it may often allow the direct use of either crude intermediates or reagents, avoiding tedious and expensive purification processes.

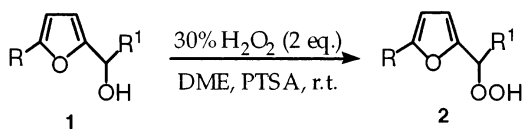
In connection with our previous research concerning the employment of new oxygen donors in highly enantioselective epoxidation[1] and sulfoxidation[2,3] reactions, achieving an efficient approach to easily renewable hydroperoxides, to be used in stereoselective oxidative processes, seemed to be an important preparative target.

One of the typical procedures for the synthesis of hydroperoxides, involving treatment of alcohols with hydrogen peroxide in an acidic medium,[4,5] suffers from some disadvantages: the reaction, usually performed on tertiary or benzylic alcohols, often requires low values of conversion in order to reduce significant decomposition of the hydroperoxides, promoted by temperature and/or acidic catalyst. Moreover, because of the relative stability of the final products, isolation and purification may represent further difficult aspects of this approach.

We wish to report a very simple and cheap procedure for the conversion of 2-furylcarbinols of type **1** into the corresponding furylhydroperoxides **2**: the reaction takes places at room temperature by treatment of **1** with 30% hydrogen peroxide (2 equiv.) in 1,2 dimethoxyethane (DME) solution in the presence of catalytic amounts (0.12 equiv.) of *p*-toluenesulfonic acid (PTSA) (Scheme 1).

Compounds **2** have shown satisfactory stability under both the reaction conditions and in the course of isolation and purification procedures so that they can be obtained in good yields as pure products by silica gel column chromatography (Table 1).

It is noteworthy that no decomposition of **2** could be observed after 1 month at –4°C.



1 **2**

Scheme 1.

Table 1. Conversion of furylalcohols **1** into furylhydroperoxides **2**

Product	R		Reaction time (h)	Yield (%)
2a	H	*n*-Hexyl	14	65
2b	Me	*n*-Hexyl	7	75
2c	Me	*n*-Pentyl	8	71
2d	Me	*n*-Octyl	7	65

All the yields refer to isolated chromatographically pure compounds whose structures were confirmed by spectroscopic data (IR, ^{1}H NMR and ^{13}C NMR).

Keywords: sulfoxides; asymmetric reaction; oxidation.
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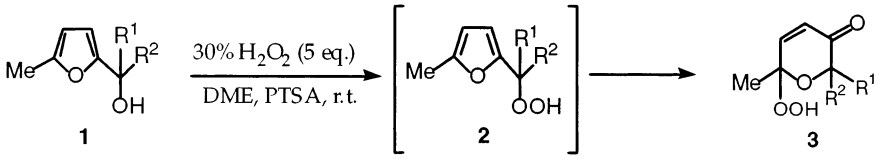


Scheme 2.

More interestingly, in the presence of greater amounts of 30% hydrogen peroxide (5 equiv.) and PTSA (0.40 equiv.), intermediates of type **2** have been shown to suffer further oxidation to give 6-hydroperoxy-2*H*-pyran-3(6*H*)-one derivatives **3** in very high yields (usually >85%), as supported by ^{1}H NMR analysis (400 MHz) on crude **3** (Scheme 2).

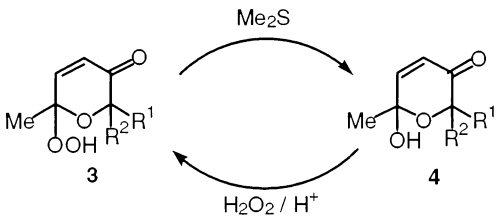
The structures of hydroperoxides **3** were confirmed by comparison of the spectroscopic data of compounds **4**, quantitatively obtained by in situ reduction with dimethylsulfide, with those of authentic samples prepared according to a literature procedure[6] (Scheme 3).

It is noteworthy that this one-pot, cheap and safe sequence allows an efficient approach to products of type **4**, which are well-known both as bio-active compounds[7] and key-intermediates in the synthesis of more complex molecules.[8–11]

In every case compounds **3** can again be obtained in very high yield (>90%) by submitting **4** to the usual treatment with hydrogen peroxide. Compounds **2a** and **3e** have been chosen as representative hydroperoxides for asymmetric sulfoxidation according to Modena's procedure[12] and very promising results have been obtained by using **2a** (Scheme 4, Table 3) both in terms of efficiency and enantioselectivity.

In all the reported experiments chiral sulfoxides were isolated as *R* predominant enantiomers pointing out the same sense of selectivity as Modena's[12] and Kagan's[13] procedures.

It is noteworthy that in all the experiments the corresponding reduction products **1a** or **4e** could be recovered and recycled as indicated in Scheme 3.



Scheme 3.

In conclusion, two different families of easily renewable hydroperoxides are accessible by a very simple and benign procedure and their potential synthetic value is confirmed by preliminary use in asymmetric sulfoxidation reactions.

Typical experimental procedure for the synthesis of hydroperoxides **2** (or **3**):
Compound **1** (or **4**) (2.0 mmol) is dissolved in 21 ml of DME (or 11 ml) and treated with 2 equiv. of 30% hydrogen peroxide (or 5 equiv.) in the presence of 0.12 equiv. of PTSA (or 0.40 equiv.) at room temperature as indicated in Table 1 (or Table 2). The reaction is

Table 2. Conversion of furyl alcohols **1** into hydroperoxides **3**

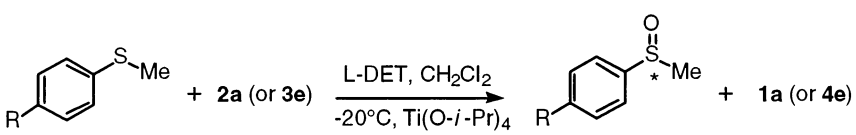
Product	R^1	R^2	Reaction time (h)	Yield (%)
3b	H	*n*-Hexyl	18	75 (90/10)
3c	H	Cyclohexyl	23	77 (93/7)
3d	H	*i*-Propyl	16	84 (92/8)
3e	Me	Me	7	77
3f	Et	*n*-Hexyl	5	65 (50/50)

All the yields refer to isolated chromatographically pure compounds whose structures were confirmed by spectroscopic data (IR, ^{1}H NMR and ^{13}C NMR). Values in parentheses refer to diastereoisomeric ratios calculated by careful integration of the signals relative to olefinic protons in the ^{1}H NMR spectra (400 MHz) performed on crude **3**.

Table 3. Asymmetric sulfoxidation with hydroperoxides **2a** and **3e**

Entry	Hydroperoxide	R	Yield (%)[a]	e.e. (%)[b]
a	**2a**	Me	61	98
b	**2a**	Cl	82	93
c	**3e**	Me	77	68
d	**3e**	Cl	80	64

[a] All the yields refer to isolated chromatographically pure compounds (*R* configuration) whose structures were confirmed by spectroscopic data (IR, ^{1}H NMR and ^{13}C NMR).
[b] E.e. values were determined by HPLC analysis using Chiralcel OB column at $\lambda = 254$ nm.



Scheme 4.

monitored by TLC and, after the disappearance of **1**, the mixture is diluted with Et_2O (70 ml). The organic phase is washed with brine and dried over magnesium sulfate. After the removal of the solvent the resulting crude product **2** (or **4**) is purified by silica gel column chromatography by elution with light petroleum/diethyl ether mixtures.

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