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Reactivity of furylhydroperoxides in asymmetric oxidation and kinetic resolution

Alessandra Lattanzi*,[a,*] Francesco Bonadies[b] and Arrigo Scettri*[a]

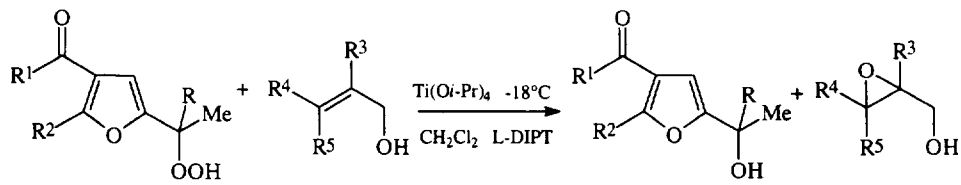
[a] Dipartimento di Chimica, Università degli Studi di Salerno, 84081 Baronissi (Salerno), Italy

[b] Centro di Studio CNR per la Chimica delle Sostanze Organiche Naturali, Dipartimento di Chimica, Università "La Sapienza", P. le A. Moro 5, 00185 Roma, Italy

Abstract: Furylhydroperoxides can be successfully employed in the enantioselective oxidation of allylic alcohols and sulfides under Sharpless-type conditions. Their kinetic resolution provides a mean both to chiral furylhydroperoxides and furylalcohols. © 1997 Elsevier Science Ltd

Over the past decade Sharpless titanium–chiral tartrate catalyst mediated oxidation of allylic alcohols with *t*-butyl hydroperoxide has received a lot of attention as a powerful tool to obtain chiral epoxyalcohols.[1] Subsequent investigations in this field led to a modification of this procedure (concerning different ratios of reagents involved) to realize the asymmetric oxidation of sulfides to chiral sulfoxides.[2] A further interesting aspect of Sharpless asymmetric epoxidation is the possibility to kinetically resolve secondary allylic alcohols, obtained at half conversion, with very high e.e. (>90%).[3] Although the complementary kinetic resolution of racemic hydroperoxides gave only low e.e. values (≤28%),[4] in principle it could open the way to optically active hydroperoxides which can be used as stereoselective oxidizing reagents.[5] Actually a better approach to the synthesis of few chiral hydroperoxides is kinetic resolution performed with enzymes such as chloroperoxidase,[6] horseradish peroxidase,[7] lipase.[8]

Our interest in the reactivity of hydroperoxides began a few years ago, when we reported an efficient route[9] to a new class of heteroaromatic hydroperoxides **1**. Their easy access and excellent stability in the presence of transition metal compounds has suggested a careful investigation on their reactivity, devoted to the elaboration of new procedures for asymmetric oxidation.[10] The results obtained with two representative furylhydroperoxides (Scheme 1) in the Sharpless asymmetric epoxidation of allylic alcohols **2** are reported in Table 1. As expected the enantioselectivity was strongly dependent on the substitution near the reactive site.[11]



1 **2** **3** **4**

Scheme 1.

With the use of tertiary furylhydroperoxide **1b** the epoxyalcohol (entry 2) was obtained with high enantiomeric excess in comparison to the modest result reached with the secondary **1a** (entry 1). We

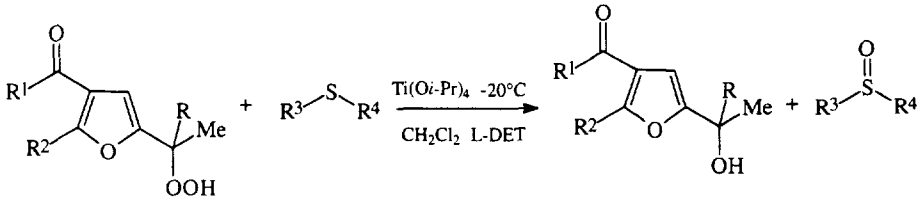
* Corresponding author. Email: lattanzi@axrma.uniroma1.it

Table 1. Asymmetric epoxidation of allylic alcohols with furylhydroperoxides **1a** and **1b**

Entry	1	2 R^3, R^4, R^5	t(h)	yield **4** (%)[a]	e.e. **4** (%)[b]
1	R=H, R^1=OEt R^2=Me **1a**	H, C_3H_7, H	18	74	52
2	R=Me, R^1=OEt R^2=Me **1b**	H, C_4H_9, H	"	65	95
3	"	H, $C_2H_4CHC(CH_3)_2$, Me	2.5	76	>95
4	"	H, Me, Me	3	50	>95

[a]Isolated yields. Molar ratios used **1** / **2** / Ti(O*i*-Pr)$_4$ / L-DIPT 1 / 1 / 1 / 1.25. [b]E.e. have been determined by ^{1}H-NMR analysis on the corresponding acetyl derivative in the presence of tri[3-(heptafluoropropylhydroxymethylene-(+)-camphorat]europium(III) as shift reagent.

noticed the same behaviour in the asymmetric oxidation of prochiral sulfides to chiral sulfoxides, adopting conditions as those reported by Modena[2b] (Scheme 2, Table 2).



1 **5** **3** **6**

Scheme 2.

Furylhydroperoxide **1a** led to good e.e. values for aryl methyl sulfoxides (entries 1, 2, 3) and moderate ones for dialkyl sulfoxides (entries 4 and 5). A notable improvement in e.e. was detected with **1b** as oxidant expecially for dialkyl sulfoxides (entries 4 and 5) generally synthesized with lower enantiomeric excess than alkyl aryl sulfoxides.

We carried out the experiments with (+)-diethyl tartrate (L-DET) as the chiral ligand, because it worked better than (+)-diisopropyl tartrate (L-DIPT) in the asymmetric oxidation of sulfides.

So we confirmed previous reports[11,2c] showing that a tertiary hydroperoxide (furylhydroperoxide **1b**) affords the best results both in asymmetric epoxidation and oxidation, representing a valuable alternative to the most commonly used *t*-butyl hydroperoxide (TBHP) and cumyl hydroperoxide

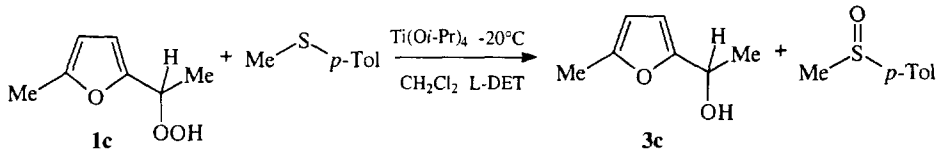
Table 2. Asymmetric oxidation of sulfides with furylhydroperoxides **1a** and **1b**

Entry	**5**	t (h)	**1a** yield **6** (%)[a]	**1a** e.e. **6** (%)[b]	t (h)	**1b** yield **6** (%)[a]	**1b** e.e. **6** (%)[b]
1	R^3=Me, R^4=C_6H_5	23	81	88 (R)	22	79	91 (R)
2	R^3=Me, R^4=*p*-Me-C_6H_4	24	83	80 (R)	28	53	90 (R)
3	R^3=Me, R^4=*p*-Cl-C_6H_4	23	78	82 (R)	-	-	-
4	R^3=Me, R^4=*n*-C_8H_{17}	21	64	57 (R)	24	77	78 (R)
5	R^3=Me, R^4=$C_6H_5CH_2$	20	84	50 (R)	24	75	74 (R)

[a]Isolated yields. Molar ratios used **1** / **5** / Ti(O*i*-Pr)$_4$ / L-DET 1 / 1 / 1 / 4. [b]E.e. have been determined on a representative sample obtained after mixing all the sulfoxide fractions coming from the chromatography[12] by ^{1}H-NMR analysis in the presence of R-(-)-3,5-dinitrobenzoyl)-α-methylbenzyl amine as shift reagent[13]. Absolute configurations established by comparison of the sign of $[\alpha]^{20}_D$ to literature data[2].

(CHP). Then we pointed out that the ester group (or more generally an electronwithdrawing group) on the furan ring was necessary to assure both chemical stability of furylhydroperoxides and high enantioselectivity in the oxidation.

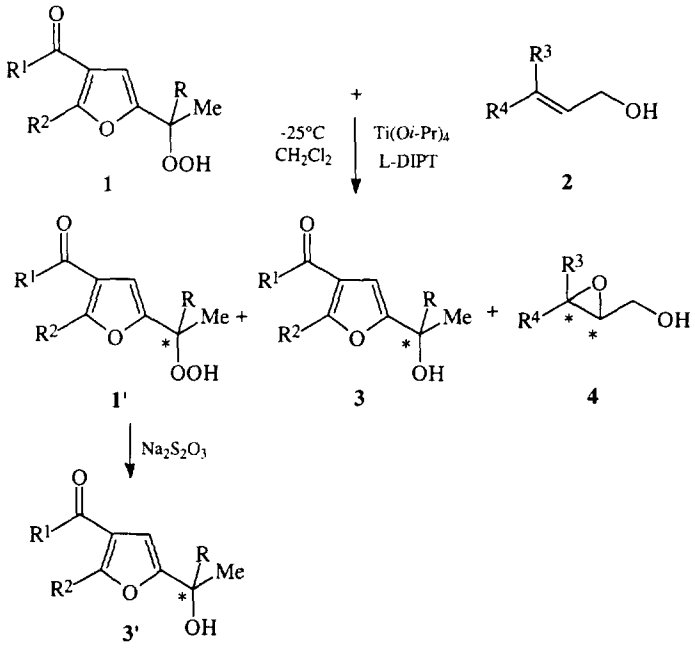
In fact, **1c**, accessible from the corresponding furylalcohol after treatment with H_2O_2,[14] showed a significant tendency to decompose in the presence of Ti(O*i*-Pr)$_4$ so that in the asymmetric oxidation (Scheme 3) of methyl *p*-tolyl sulfide, the sulfoxide was isolated in low chemical yield and with a modest enantiomeric excess if compared to that obtained with **1a** (Table 2, entry 2).



yield 37%
e.e. 66%

Scheme 3.

Since then, in our opinion, kinetic resolution of hydroperoxides by means of titanium–tartrate catalyzed oxidation has not been investigated thoroughly. So in consideration of satisfactory results achieved with furylhydroperoxides in asymmetric oxidation, we thought it interesting to analyse the possibility of their kinetic resolution in Sharpless epoxidation of allylic alcohols (Scheme 4, Table 3).



Scheme 4.

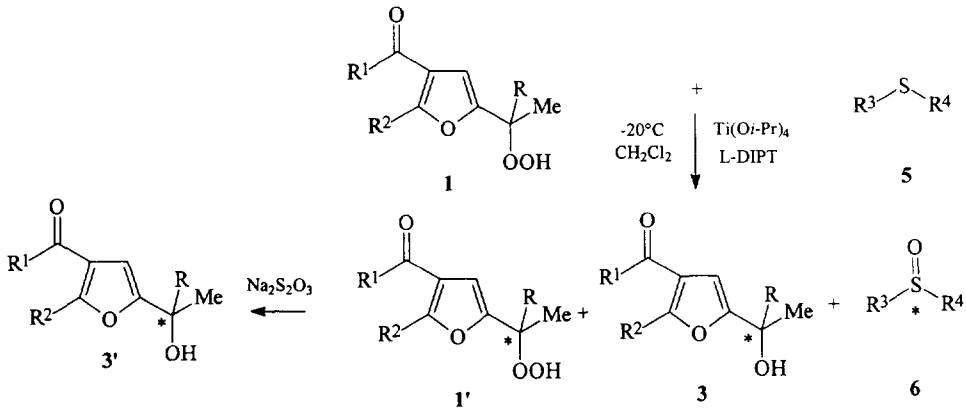
Except for entry 4, performed with catalytic amounts of Ti(O*i*-Pr)$_4$ (10% molar), we recovered unreacted secondary furylhydroperoxides **1′** and furylalcohols **3** with modest enantiomeric excess, but encouraging respect to the few data previously reported[4] on kinetic resolution of tertiary benzylic hydroperoxides. E.e.s of epoxyalcohols were those expected with the employment of less sterically demanding[2c] secondary hydroperoxides.

Table 3. Kinetic resolution of furylhydroperoxides in asymmetric epoxidation

Entry	1 R=H	2	t (h)	4 yield (%)[a] e.e. (%)[b]	1' yield (%)[a] e.e. (%)[c] (-)[d]	3 yield (%)[a] e.e. (%)[c] (+)[d]
1	**1a**	R^3=H R^4=C_3H_7	16	76 74	53 29	40 40
2	"	R^3=Me R^4=$C_2H_4CHC(CH_3)_2$	14	83 61	48 40	42 50
3[e]	"	R^3=H R^4=C_3H_7	22	85 70	47 31	43 40
4[f]	"	"	62	81 30	52 3	41 4
5	R^1=R^2=-$(CH_2)_3$- **1d**	"	16	76 62	55 36	39 33
6	R^1=OEt **1e** R^2=$(CH_2)_3CO_2Et$	"	15	61 71	62 23	32 50

[a]Isolated yields. Molar ratios used **1** / **2** / Ti(O*i*-Pr)$_4$ / L-DIPT 2 / 1 / 1 / 1.25. [b]E.e. have been determined by ^{1}H-NMR analysis on the corresponding acetyl derivative in the presence of tris[3-(heptafluoropropylhydroxymethylene-(+)-camphorat]europium(III) as shift reagent [c]E.e. have been determined by ^{1}H-NMR analysis in the presence of tris [3-(heptafluoropropylhydroxymethylene-(+)-camphorato]europium(III) as shift reagent on the corresponding alcohols **3'** and **3**.[d]Sign of specific rotation. [e]In this case L-DET was used as chiral ligand. [f]The reaction was carried out with 10% molar of Ti (O*i*-Pr)$_4$.

It is noteworthy that this transformation simultaneously opens up a route to four enantiomerically enriched compounds. Besides, chiral functionalized 2-furylalcohols are accessible as useful building blocks for the synthesis of natural products.[15] With the aim of improving these results, we tried sulfides as partners for kinetic resolution of compounds **1** (Scheme 5, Table 4).



Scheme 5.

Undoubtedly the e.e. of furylhydroperoxides improved and methyl *p*-tolyl sulfoxide was recovered with high enantiomeric excess (entries 3, 4, 5). Again, (entry 6) under catalytic conditions, in the course of oxidation achiral reaction paths are involved. Also with a dialkyl sulfide (entry 7), furylhydroperoxide **1d** was efficiently resolved, while the use of symmetric sulfides (entries 8 and 9) resulted in poor kinetic resolution of the oxidant, probably ascribed to their lack of prochirality.

Table 4. Kinetic resolution of furylhydroperoxides in asymmetric oxidation of sulfides

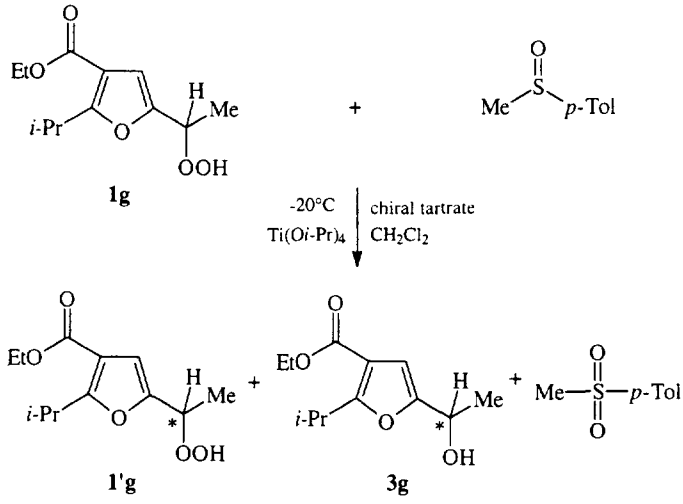
Entry	1	5	t(h)	6 yield (%)[a] e.e. (%)[b]	1' yield (%)[a] e.e. (%)[c] (-)[d]	3 yield (%)[a] e.e. (%)[c] (+)[d]
1	**1a**	R^4=*p*-Me-C_6H_4 R^3=Me	14	51 81	20 68	72 23
2	R=H, R^1=OMe, R^2=$(CH_2)_2$OMe **1f**	"	"	74 77	24 63 $[\alpha]_D^{20}$=−6.8[g]	68 28 $[\alpha]_D^{20}$=+3.1[h]
3	R=H, R^1=OEt R^2=*i*-Pr **1g**	"	"	75 95	25 81 $[\alpha]_D^{20}$=−10.4[i]	68 30 $[\alpha]_D^{20}$=+3.5[i]
4	R^1=R^2=-$(CH_2)_3$- R=H **1d**	"	"	48 >95	22 78	74 23
5[e]	**1g**	"	13	58 92	20 62	73 31
6[f]	"	"	69	84 racemic	44 4	55 4
7	"	R^4=$C_6H_5CH_2$ R^3=Me	14	55 70	15 81	76 19
8	**1a**	R^3=R^4=C_6H_5	22	-	60 8	34 16
9	"	R^3=R^4=$C_6H_5CH_2$	18	-	18 31	60 17
10	R=Et, R^1=OEt R^2=Me **1h**	R^4=*p*-Me-C_6H_4 R^3=Me	7	63 55	57 4	34 5

[a]Isolated yields. Molar ratios used **1** / **2** / Ti(O*i*-Pr)$_4$ / L-DIPT 2 / 1 / 1 / 4. In almost all the experiments sulfone was isolated in about 20% yield as overoxidation product. [b]See note b in Table 2. [c]See note c in Table 3; reported $[\alpha]_D^{20}$ values refer to corresponding alcohols **3'** and **3**. [d]Sign of specific rotation. [e]In this case L-DET was used as chiral ligand. [f]The reaction was carried out with 10% molar of Ti (O*i*-Pr)$_4$. [g] (c=0.6, acetone). [h](c=2.1, acetone). [i](c=1.2, CH_3CN).

Compared to results in entry 5, L-DIPT (entry 3) afforded better values of enantiomeric excess for the resolution of **1g** than L-DET as chiral ligand. In the last entry, surprisingly, oxidation carried out with a tertiary furylhydroperoxide **1h** led to methyl *p*-tolyl sulfoxide with low e.e. and it proceeded without kinetic resolution.

Clearly structural modifications of compounds **1** (pattern of substitution in the furan ring and nearby the reaction site) are crucial for the success of asymmetric oxidation and kinetic resolution. Since sulfoxides may be good ligands for the titanium chiral complex,[16] we thought to investigate if they could act as potential resolving agents, considering that sulfone was detected as overoxidation product (note a, Table 4). Hydroperoxide **1g** and methyl *p*-tolyl sulfoxide were chosen as model compounds in this investigation (Scheme 6).

We performed different runs adopting the usual conditions, whose results are collected in Table 5,



Scheme 6.

Table 5. Kinetic resolution of **1g** with methyl *p*-tolyl sulfoxide

Entry	sulfoxide	chiral ligand	t (h)	**1'** yield (%)[a] e.e. (%)[b] (-)[c]	**3** yield (%)[a] e.e. (%)[b] (+)[c]	E[d]
1	R	L-DIPT	21	60 31	35 30	3.6
2	S	"	22	45 45	46 36	3.3
3	(###)	"	21	43 49	49 48	3.5
4	"	L-DET	16	49 52	46 44	4.9
5	"	D-DET	22	46 54 (+)	49 47 (-)	4.5

[a]Isolated yield. Molar ratios used 1 / **sulfoxide** / Ti(O*i*-Pr)$_4$ / chiral ligand 2 / 1 / 1 / 4. [b]See note c in Table 3. [c]Sign of specific rotation. [d]Evaluation of stereoselectivity factor $E=k_R/k_S$[17].

employing starting pure and racemic sulfoxide. In all the experiments we found furylhydroperoxide **1'g** and furylalcohol **3g** enantiomerically enriched.

The absolute configuration of sulfoxide (entries 1 and 2) had no influence in the stereochemical course of kinetic resolution as the sign of optical rotation of **1'g** was the same in both the examples.

The use of L-DET (entry 4) instead of L-DIPT (entry 3) had a moderate effect in the process. At last (entry 5) only absolute configuration of chiral tartrate determined the stereochemical outcome of the resolution, since the sign of optical rotation of **1'g** was reversed with D-DET.

From these trials coming back to Table 4, we can hypothesize that a first kinetic resolution of furylhydroperoxides is operating during the oxidation of sulfides to chiral sulfoxides and the enantiomeric enrichment continues in the oxidation of sulfoxides to sulfones as described above. We checked this hypothesis carring out an experiment with molar ratios **1g**/methyl *p*-tolyl sulfide/Ti(O*i*-Pr)$_4$/L-DIPT 2/1/1/4 at −20°C for 2 hours. After this time no sulfone was recovered from the reaction

mixture and we isolated (−)-**1′g** with 25% e.e. and 52% yield, while (+)-**3g** with 15% e.e. and 43% yield (E=2.1).

Thus, it turns out that good values of enantiomeric excess of furylhydroperoxides **1′** in Table 4 derive as a sum of both enantioconvergent kinetic resolutions of compounds **1** in the oxidation of sulfides to sulfoxides and sulfoxides to sulfones.

In conclusion herein we described that furylhydroperoxides **1** are suitable reagents for asymmetric epoxidation and oxidation under Sharpless type-conditions and how structural modifications influence the course of these processes. Besides, we reported their reactivity under kinetic resolution conditions, showing that the availability of chiral furylhydroperoxides and furylalcohols is attainable employing allylic alcohols and more interestingly sulfides and sulfoxides as resolving agents. In fact, in this last case we can exploit the two enantioconvergent kinetic resolutions to improve e.e. of compounds **1′**.

Experimental

General

^{1}H-NMR and ^{13}C-NMR spectra were recorded with Varian Gemini-200 and Varian XL-300 spectrometers. 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. Signs of optical rotation were measured with a JASCO Dip-370 digital polarimeter at λ=589 nm at temperature of 20°C at c=1–2 in acetone as solvent on the corresponding alcohols **3′** and **3**. 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. Melting points of compounds **1** were not determined because of their termal instability. The enantiomeric excesses of sulfoxides were determined by ^{1}H-NMR in the presence of (R)-(−)-(3,5-dinitrobenzoyl)-α-phenylethylamine, while the e.e. of furylalcohols **3** and **3′**, in the presence of tris-[3-(heptafluoropropylhydroxymethylene-(+)-camphorato]europium(III) Eu(hfc)$_3$ as shift reagent. Molecular sieves 4Å used for asymmetric epoxidation (also in kinetic resolution experiments) were activated under *vacuo* for 24 h at 300°C. Dicloromethane was stored over activated 4 Å molecular sieves (2 days at 160°C). Other chemicals (Aldrich or Fluka) were used as commercial products without further purification. With the exception of **1c** all the hydroperoxides have been prepared according to the procedures reported in Ref.[9]

*Enantioselective epoxidation by furylhydroperoxides **1a** and **1b**. General procedure*

To a solution of CH_2Cl_2 (6 mL), at room temperature and under argon atmosphere, are added molecular sieves 4 Å (30% wt based on allylic alcohol), Ti(O*i*-Pr)$_4$ (1 mmol), L-DIPT (1.25 mmol), allylic alcohol (1 mmol). The stirred mixture is cooled to −20°C for 20 minutes. Then **1a**, or **1b**, dissolved in 6 mL of CH_2Cl_2 is added. After complete conversion of hydroperoxide (detected by TLC), 4 mL of water are added to the solution at −20°C and a vigorous stirring is mantained at room temperature for 1 h. The white gel is filtered over celite and thoroughly washed with CH_2Cl_2. The organic phase is dried over Na_2SO_4 and then evaporated. Flash chromatography of the residue (*n*-hexane/diethyl ether) affords epoxyalcohols. The e.e. are determined on the corresponding acetylated epoxylacohols by ^{1}H-NMR analysis in the presence of tris[3-(heptafluoropropylhydroxymethylene-(+)-camphorat]europium(III) Eu(hfc)$_3$ as shift reagent. The absolute configurations of epoxyalcohols are identic to those obtained with Sharpless procedure employing TBHP as oxidant.

*Enantioselective oxidation of sulfides by furylhydroperoxides **1a–c**. General procedure*

To a solution of CH_2Cl_2 (7 ml) at room temperature and under argon atmosphere, Ti(O*i*-Pr)$_4$ (1 mmol), L-DET (4 mmol), and sulfide (1 mmol) are added and the stirred mixture is cooled at −20°C for 20 minutes. Then **1a**, or **1b**, dissolved in 7 mL of CH_2Cl_2 is added. After complete conversion

of hydroperoxide (detected by TLC), the reaction is quenched with 4 mL of water at −20°C and a vigorous stirring is mantained at room temperature for 1 h. The white gel is filtered over celite and thoroughly washed with CH_2Cl_2. The organic phase is dried over Na_2SO_4 and then evaporated. Flash chromatography of the crude product (AcOEt) affords sulfoxides.

5-(1-Hydroperoxyethyl)-3-ethoxycarbonyl-2-methylfuran ***1a***

White needles; ^{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-Hydroperoxy-1-methylethyl)-3-ethoxycarbonyl-2-methylfuran ***1b***

White needles; ^{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%.

Oxidation of (5-methyl-2-furyl) methylcarbinol ***3c*** *to* ***1c*** *with* H_2O_2

A suspension of **3c** (2 mmol), at room temperature, is treated with H_2O_2 (4 mL, 35% v/v) and 10 μL of acetic acid and is stirred until disappearance of the substrate; the progress of reaction was monitored by TLC. Then water is added and the mixture is extracted with diethyl ether. The organic extracts are dried over Na_2SO_4 and solvent is evaporated at room temperature. The residue is purified on silica gel by flash chromatography using *n*-hexane/ethyl ether, obtaining **1c** in 41% yield.

(5-Methyl-2-furyl)methyl carbinol ***3c***

Colourless oil; ^{1}H-NMR ($CDCl_3$):1.47 (d, 3H, *J*=6,6 Hz), 2.29 (s, 3H), 2.32 (bs, 1H), 4.76 (q, 1H, *J*=6.6 Hz), 5.85 (dd, 1H, J_1=3.3., J_2=1.0 Hz), 6.04 (d, 1H, *J*=3.3 Hz); ^{13}C-NMR ($CDCl_3$): 13.2, 20.8, 63.3, 105.9, 151.6, 156.0. Anal. Calcd. for $C_7H_{10}O_2$: C, 66.63; H, 7.99%. Found: C, 66.55; H, 7.90%.

(5-Methyl-2-furyl)-1-hydroperoxyethane ***1c***

Colourless oil; ^{1}H-NMR ($CDCl_3$):1.50 (d, 3H, *J*=6,7 Hz), 2.25 (s, 3H), 4.97 (q, 1H, *J*=6.7 Hz), 5.90 (dd, 1H, J_1=3.0, J_2=1.0 Hz), 6.22 (d, 1H, *J*=3.0 Hz), 8.20 (ss, 1H); ^{13}C-NMR ($CDCl_3$): 13.2, 16.0, 76.4, 106.2, 109.7, 151.5, 152.6. Anal. Calcd. for $C_7H_{10}O_3$: C, 59.13; H, 7.09%. Found: C, 59.20; 7.01%.

Kinetic resolution of furylhydroperoxides. General procedure

The procedure is the same described for the asymmetric epoxidation of allylic alcohols. The molar ratios of reagents are **1/2**/Ti(O*i*-Pr)$_4$/L-DIPT 2/1/1/1.25 and the solvent (0.08 M in **1**) employed is doubled. The crude product is purified on silica gel using mixtures of *n*-hexane/ethyl ether. Furylalcohols **3** are generally eluted with the chiral ligand; so **3** and L-DIPT are treated with NaOH 3N (20 mL) at 0°C for 1 h.

The organic phase is then washed with brine, dried over Na_2SO_4 and evaporated affording pure **3**. Furylhydroperoxides **1′** (0.3 mmol) are reduced with $Na_2S_2O_3$ in excess in 9 mL of water plus 1 mL of ethanol at room temperature for 2 h. Then the mixture is extracted with diethyl ether, the organic phase is dried over $MgSO_4$ and then evaporated affording pure **3′**.

In the case of kinetic resolution with sulfides **5** (Table 4) and methyl *p*-tolyl sulfoxide (Table 5) molecular sieves are not added to the solution and the molar ratios of reagents are those indicated in Tables 4 and 5 (0.08 M in **1**).

3-(1-Hydroperoxyethyl)-6-oxo-2-oxa-bicyclo[4.3.0]-1,3-nonadiene ***1d***

White needles; ^{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-Hydroperoxyethyl)-3-ethoxycarbonyl-2-(3-ethoxycarbonylpropyl)furan ***1e***

White needles; ^{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*=7.0 Hz), 3.94 (q, 2H, *J*=7.0 Hz), 4.26 (q, 2H, *J*=7.0 Hz), 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%.

5-(1-Hydroperoxyethyl)-3-methoxycarbonyl-5-(2-methoxyethyl)furan ***1f***

White needles; ^{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-isopropylfuran ***1g***

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*=7.0 Hz), 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-Hydroperoxy-1-methylpropyl)-3-ethoxycarbonyl-2-methylfuran ***1h***

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-Hydroxyethyl)-3-ethoxycarbonyl-2-methylfuran ***3a***

Colourless oil; ^{1}H-NMR ($CDCl_3$): 1.15 (t, 3H, *J*=7.0 Hz), 1.60–1.40 (bs, 1H), 1.35 (d, 3H, *J*=7.0 Hz), 2.50 (s, 3H), 4.11 (q, 2H, *J*=7 Hz), 4.65 (q, 1H, *J*=7 Hz), 6.32 (s, 1H). ^{13}C-NMR ($CDCl_3$): 13.4, 13.9, 20.8, 59.9, 62.9, 105.9, 113.8, 155.7, 158.7, 164.3. Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.58; H, 7.12%. Found: C, 60.48; H, 7.07%.

5-(1-Hydroxyethyl-1-methylethyl)-3-ethoxycarbonyl-2-methylfuran ***3b***

Colourless oil; ^{1}H-NMR ($CDCl_3$): 1.15 (t, 3H, *J*=7.0 Hz), 1.54 (s, 6H), 2.50 (s, 3H), 4.24 (q, 2H, *J*=7.0 Hz), 6.40 (s, 1H). ^{13}C-NMR ($CDCl_3$): 13.4, 14.0, 20.8, 59.8, 63.1, 106.0, 114.0, 154.9, 160.9, 165.0. Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.23; H, 7.60%. Found: C, 62.29; H, 7.53%.

3-(1-Hydroxyethyl)-6-oxo-2-oxa-bicyclo[4.3.0]-1,3-nonadiene ***3d***

Colourless oil; ^{1}H-NMR ($CDCl_3$): 1.51 (d, 3H, *J*=6.6 Hz), 2.13 (qp, 2H, *J*=6.1 Hz), 2.44 (t, 2H, *J*=5.8 Hz), 2.83 (t, 2H, *J*=6.3 Hz), 4.32 (q, 1H, *J*=6.6 Hz), 6.45 (s, 1H). ^{13}C-NMR ($CDCl_3$): 20.9, 22.2, 23.0, 37.2, 62.9, 101.5, 121.5, 158.3, 167.1, 195.1. Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.64; H, 6.72%. Found: C, 66.54; H, 6.71%.

5-(1-Hydroxyethyl)-3-ethoxycarbonyl-2-(3-ethoxycarbonylpropyl)furan ***3e***

Colourless oil; ^{1}H-NMR ($CDCl_3$): 1.22 (t, 3H, *J*=7.0 Hz), 1.31 (t, 3H, *J*=7.0 Hz), 1.50 (d, 3H, *J*=7.0 Hz), 2.06–1.91 (m, 2H), 2.10 (bs, 1H), 2.31 (t, 2H, *J*=7.0 Hz), 3.00 (t, 2H, *J*=7.0 Hz), 4.08 (q, 2H, *J*=7.0 Hz), 4.24 (q, 2H, *J*=7.0 Hz), 4.79 (q, 1H, *J*=7.0 Hz), 6.45 (s, 1H). ^{13}C-NMR ($CDCl_3$): 13.8, 13.9, 20.8, 22.9, 26.6, 33.3, 59.9, 60.2, 62.9, 105.9, 114.2, 156.2, 161.1, 163.9, 173.3. Anal. Calcd. for $C_{15}H_{22}O_6$: C, 60.37; H, 7.44%. Found: C, 60.28; H, 7.51%.

5-(1-Hydroxyethyl)-3-methoxycarbonyl-2-(2-methoxyethyl)furan ***3f***

Colourless oil; ^{1}H-NMR ($CDCl_3$): 1.50 (d, 3H, *J*=7.0 Hz), 2.00 (bs, 1H), 3.24 (t, 2H, *J*=7.0 Hz), 3.33 (s, 3H), 3.67 (t, 2H, *J*=7.0 Hz), 3.80 (s, 3H), 4.75 (q, 1H, *J*=7.0 Hz), 6.50 (s, 1H). ^{13}C-NMR ($CDCl_3$): 13.9, 27.9, 51.2, 52.2, 62.9, 69.9, 105.9, 114.4, 156.5, 159.2, 164.4. Anal. Calcd. for $C_{11}H_{16}O_5$: C, 57.87; H, 7.07%. Found: C, 57.94; H, 7.14%.

5-(1-Hydroxyethyl)-3-ethoxycarbonyl-2-isopropylfuran ***3g***

Colourless oil; ^{1}H-NMR ($CDCl_3$): 1.24 (t, 6H, *J*=7.0 Hz), 1.31 (t, 3H, *J*=7.0 Hz), 1.50 (d, 3H, *J*=7.0 Hz), 1.90 (bs, 1H), 3.71 (hept, 1H, *J*=7.0 Hz), 4.25 (q, 2H, *J*=7.0 Hz), 4.80 (q, 1H, *J*=7.0 Hz), 6.45 (s, 1H). ^{13}C-NMR ($CDCl_3$): 14.0, 20.4, 20.8, 27.0, 59.9, 63.2, 106.0, 112.0, 155.4, 164.2, 166.8. Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.68; H, 8.02%. Found: C, 63.60; H, 8.10%.

5-(1-Hydroxy-1-methylpropyl)-3-ethoxycarbonyl-2-methylfuran ***3h***

Colourless oil; ^{1}H-NMR ($CDCl_3$): 0.82 (t, 3H, *J*=7.0 Hz), 1.30 (t, 3H, *J*=7.0 Hz), 1.82 (q, 2H, *J*=7.0 Hz), 1.90 (bs, 1H), 2.51 (s, 3H), 6.24 (q, 2H, *J*=7.0 Hz), 6.41 (s, 1H). ^{13}C-NMR ($CDCl_3$): 8.2, 13.5, 14.1, 25.4, 33.9, 60.0, 71.5, 105.6, 113.9, 157.4, 158.5, 164.4. Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%. Found: C, 63.63; H, 8.08%.

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