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Enantioselective epoxidation of chalcones and naphthoquinones mediated by (+)-norcamphor-derived hydroperoxide

Alessandra Lattanzi,* Maria Cocilova, Patrizia Iannece and Arrigo Scettri

Dipartimento di Chimica, Università di Salerno, Via S. Allende, 84081 I Baronissi, Salerno, Italy

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Abstract—(+)-Norcamphor-derived hydroperoxide has been employed in the asymmetric epoxidation of electron poor alkenes such as *trans*-chalcones and naphthoquinones. Optimization of the reaction conditions required the employment of *n*-BuLi/THF at −20 °C to achieve ees up to 58%. The epoxide of vitamin K_3 has now been obtained with the best up to now reported value of enantioselectivity (51% ee).

1. Introduction

Asymmetric oxidations are amongst the most important transformations in organic synthesis.[1] Only recently, have investigations on enantioselective oxidations, mediated by enantiomerically pure hydroperoxides such as stereoselective reagents, attracted significant attention.[2] We have reported that tertiary renewable hydroperoxides **1** and **2** can be easily obtained from common and low cost compounds such as (*R*)- and (*S*)-camphor, respectively (Fig. 1).[3] These oxidants have been employed in the absence of any chiral ligand in the Ti(O*i*-Pr)$_4$-catalyzed epoxidation of allylic alcohols[3] and oxidation of sulfides[4] achieving moderate, or as in some examples, the best levels of asymmetric induction reported so far with the use of enantiomerically pure alkyl hydroperoxides. In order to gain a better insight into the factors, which affect the asymmetric induction in the oxidations, we synthesized a less sterically hindered hydroperoxide **3** derived from (+)-norcamphor in very high yield.[5] This oxidant provided higher reaction rates in the asymmetric sulfoxidation[5] while the stereoconvergent kinetic resolution of racemic sulfoxides helped to raise the ees of the final sulfoxides.

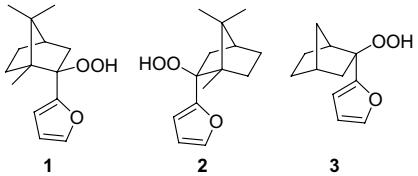

Figure 1.

Encouraged by the promising results and easy access to hydroperoxides **1**–**3**, we herein report our investigation on the asymmetric epoxidation of α,β-enones mediated by these oxidants.

2. Results and discussion

Enantiomerically pure α,β-epoxy ketones are building blocks in organic synthesis and intermediates for the production of pharmaceuticals, hence intensive research has been developed over the recent decades for their synthesis.[6] Different procedures for the enantioselective epoxidation of electron poor alkenes are available, which include: asymmetric phase-transfer catalysis,[7] epoxidation using enantiomerically pure hydroperoxides,[2e,8] polyamino acid-catalyzed epoxidation,[9] chiral ligand–metal peroxide protocol.[10] Our exploratory studies focused on the epoxidation of *trans*-chalcone **4a** (R = R^1 = Ph, Table 1). Considering the variety of reaction conditions previously reported to perform this oxidation, a screening of bases, solvents and additives is needed to be studied.

In the presence of *n*-BuLi at −20 °C in THF, hydroperoxide **1** reacted sluggishly with the epoxide isolated in

* Corresponding author. Tel.: +39 089 965370; fax: +39 089 965296; e-mail: lattanzi@unisa.it

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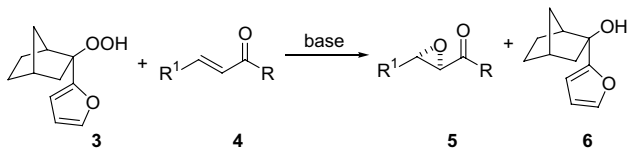
Table 1. Asymmetric epoxidation of **4a** (R = R^1 = Ph) mediated by **3** under various reaction conditions[a]



3 **4** **5** **6**

Entry	Base	Solvent	*T* (°C)	*t* (h)	Yield **5a** (%)[b]	Ee **5a** (%)[c]	Abs conf[d]
1[e]	*n*-BuLi	THF	−20	22	30	0	—
2	*n*-BuLi	THF	−20	3	66	43	α*R*,β*S*
3	*n*-BuLi	DME	−20	5	78	30	α*R*,β*S*
4	*n*-BuLi	Toluene	−20	4	60	0	—
5	DBU	Toluene	rt	72	—	—	—
6	DBU	THF	rt	47	38	43	α*R*,β*S*
7	LiOH	THF	−20	28	54	46	α*R*,β*S*
8	KOH	CH_3CN	−20	4	80	4	α*R*,β*S*
9	KOH	THF	−20	1.5	93	14	α*R*,β*S*
10[f]	KOH	Toluene	0	48	35	0	—
11	NaOH	THF	−20	2	100	37	α*R*,β*S*
12[g]	*n*-BuLi	THF	−20	3	86	49	α*R*,β*S*
13[g]	*n*-BuLi	THF	−78	6	20	49	α*R*,β*S*
14[h]	KOH	THF	−20	1	87	10	α*R*,β*S*

[a] Molar ratios: **3**/**4**/base 1.1/1.0/1.2.
[b] Isolated yield after flash chromatography.
[c] Determined by HPLC analysis using chiral column Chiralcel OD.
[d] Determined by comparison with specific rotation in the literature.
[e] Hydroperoxide **1** was employed.
[f] TBAB was used as PTC catalyst.
[g] 1 equiv of [12]crown-4 with respect to the base was added.
[h] 1 equiv of [18]crown-6 with respect to the base was added.

low yield and in its racemic form (entry 1). Under the same conditions, oxidant **3** reacted much faster and, more importantly that (α*R*,β*S*)-epoxide was obtained in 43% ee (entry 2). As a result further investigations were conducted employing hydroperoxide **3**. Dimethoxyethane, when used as an alternative solvent, proved to be equally effective, although the product was synthesized with lower enantioselectivity (entry 3). In nonpolar toluene, the epoxidation was completely unselective (entry 4). Epoxidation using DBU in toluene at room temperature did not proceed (entry 5). DBU in THF, even after prolonged reaction time, only furnished the epoxide in modest yield but with 43% ee (entry 6).

A LiOH/THF combination at −20 °C afforded the product in moderate yield and slightly improved ee 46% (entry 7). The epoxidation performed using KOH in CH_3CN led to an almost racemic epoxide in good yield (entry 8). A similar result was obtained with a KOH/THF combination, although a better ee was achieved (entry 9). When the reaction was carried out under phase-transfer catalysis, using aqueous KOH/TBAB in toluene at 0 °C, the racemic epoxide was isolated in low yield (entry 10). The employment of NaOH in THF at −20 °C quantitatively afforded the epoxide with 39% ee. Further experiments were performed, in order to examine if metal coordination of the enone and hydroperoxide anion by Li^+ or K^+ ions was effective in controlling the asymmetric induction. The reaction reported in entry 2 was carried out in the presence of [12]crown-4 as a Li^+ chelating agent (entry 12). The reaction was accelerated and the epoxide isolated in high yield and with 49% ee. Under these conditions, but at −78 °C, the reactivity was as expected lowered, although the enantioselectivity did not improve (entry 13). The enantiomeric excess was almost unaffected even in the presence of [18]crown-6 as a K^+ chelating agent, with respect to the epoxidation performed in its absence (compare last entry with entry 9).

A set of experiments was then carried out on *trans*-substituted chalcones under optimized conditions (*n*-BuLi/**3**/THF at −20 °C) (Table 2). *para* Substituents on the β-phenyl group strongly enhanced the reaction rate in the order: *p*-NO_2 > *p*-Cl > *p*-OMe (entries 2–4). In the case of the *p*-OMe substituent (entry 4), the reaction proceeded slowly at room temperature and in the presence of [12]crown-4, although a level of enantioselectivity was maintained.[11] This trend is in agreement with the classically accepted mechanism for this epoxidation, which consists of a conjugate addition of the peroxide anion to the enone, followed by an intramolecular nucleophilic attack of the enolate to the O–O bond and ring closure. The conjugate addition is considered as the rate and stereoselective-detemining step.[12,8] Enones having electron-withdrawing substituents on the phenyl ring increased the electrophilic character of the β-carbon, then the reactivity of the enone (entries 2–3); the opposite result can be expected with electron-donating substituents (entry 4). Substitution on the phenyl ring of the carbonyl function, while not affecting the reaction rate with respect to chalcone **4a**, slightly influenced the enantioselectivity, which was improved with the electron-donating substituent (entry 6). With the β-naphthyl group in the carbonyl function a result similar to that obtained for compound **4a** was observed (entry 7).

Table 2. Asymmetric epoxidation of *trans*-chalcones mediated by **3**/*n*-BuLi in THF at −20 °C[a]

Entry	R	R^1	*t* (h)	Yield **5** (%)[b]	Ee **5** (%)[c]	Abs conf[d]
1[e]	Ph	Ph	3	66	43	α*R*,β*S*
2	Ph	*p*-$NO_2C_6H_4$	1	98	45	α*R*,β*S*
3	Ph	*p*-ClC_6H_4	1	80	44	α*R*,β*S*
4	Ph	*p*-$MeOC_6H_4$	3	30	42	α*R*,β*S*
5	*p*-BrC_6H_4	Ph	3	65	38	α*R*,β*S*
6	*m*-MeC_6H_4	Ph	4.5	67	50	α*R*,β*S*
7	β-Naphthyl	Ph	4	60	40	α*R*,β*S*

[a] Molar ratios: **3**/**4**/base 1.1/1.0/1.2.
[b] Isolated yield after flash chromatography.
[c] Determined by HPLC analysis using chiral columns.
[d] Determined by comparison with specific rotation in the literature.
[e] The reaction was carried out at room temperature in the presence of 1 equiv of [12]crown-4 with respect to the base.

Experimental data in Tables 1 and 2 showed a reduced reactivity and no enantioselectivity in apolar toluene, which led us to the conclusion that tight ion pairing of the metal ion and the hydroperoxide anion was detrimental to the reaction in all respects (Table 1, entries 4–5). Moreover, the enantioselectivity is not affected by the presence of metal ions, indicating the lack of templating structures (made up of alkaline ions, hydroperoxide anion and enone) in modulating the stereodifferentiation through steric interactions of the three partners (Table 1, entries 2, 12, 9 and 14).

This result is in contrast to what has been previously observed when using secondary enantiopure alkyl hydroperoxides in the KOH/CH_3CN and DBU/toluene mediated epoxidation of α,β-enones. In this case the templating agent, either the potassium ion (K^+), or the ammonium ion ($DBUH^+$), via chelation of the hydroperoxide anion and the enone, was found to affect the sense and level of the asymmetric induction.[8] In our case, the 'naked' sterically demanding hydroperoxide anion is more reactive and the enantiocontrol would be regulated by non-bonded steric interactions of the approaching anion with the substituents on β-carbon of chalcone.[13]

A reasonable mechanistic proposal for the enantiofacial discrimination in the epoxidation of chalcones is depicted in Figure 2. When the hydroperoxide anion, with the large furyl group (Fu) pointing outward in the less crowded direction, is approaching the *Si*-face in the **TS-A** structure, a pronounced steric interaction is supposed to develop between the C_3–hydrogens in the norcamphor skeleton and the R group of the enone. When the anion approaches the *Re*-face in **TS-B**, a smaller steric interaction, between the R group and C_1–hydrogen in the norcamphor skeleton is envisaged. **TS-B** should be favoured in view of the minimized steric interactions leading to (α*R*,β*S*)-epoxide, which was the observed major enantiomer in Tables 1 and 2.

Amongst the classes of valuable enantiopure epoxides, natural products containing the epoxycyclohexenone core show antimicrobial and anticancer activity or play an important role in metabolic processes as the epoxide of vitamin K_3.[14] The asymmetric epoxidation of cyclic enones as α-substituted naphthoquinones is a more difficult task to succeed and both the magnitude and the sense of enantioselectivity were found to be strongly dependent on the nature of the α-side chain R.[6a] As a consequence, there is an opportunity to observe significant improvements in levels of asymmetric induction. The most important asymmetric methodologies of epoxidation have been reported by Colonna et al. using bovine serum albumine (BSA) and TBHP,[15] by Arai et al. using phase-transfer catalysts[16] and by Taylor et al. using sugar-derived hydroperoxides.[17]

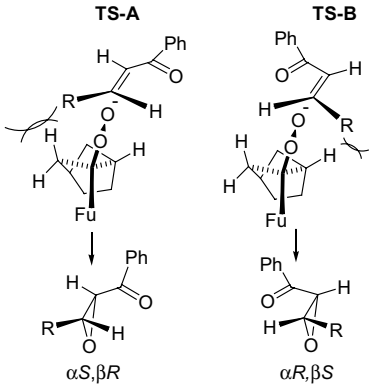
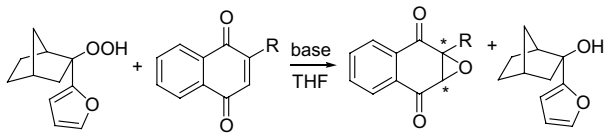


Figure 2.

Since the employment of enantiomerically pure hydroperoxides has been demonstrated a useful tool for the epoxidation of naphthoquinones, some runs were carried out on vitamin K_3 as model compound employing hydroperoxide **3** (Table 3).

Under the best reaction conditions, previously found for chalcones, (2*S*,3*R*)-epoxide was obtained in high yield and with 51% ee, which represents the best, up to now reported value of enantioselectivity for this biologically important compound (entry 1). Either at lower (−78 °C) or higher (0 °C) temperatures, a decreased asymmetric induction was observed (entries 2–3). With the addition of [12]crown-4 at −20 °C (entry 4), the reaction was more rapid, but this time, the enantioselectivity was strongly reduced. The NaOH promoted epoxidation furnished the product in quantitative yield and moderate ee (entry 5). Under bifunctional catalysis,[18] using DBU/LiCl at 0 °C, a satisfactory yield of the product was

Table 3. Asymmetric epoxidation of naphthoquinones mediated by **3**[a]



3 **7** **8** **6**

Entry	R	Base	T (°C)	t (h)	Yield **8** (%)[b]	Ee **8** (%)[c]	Abs conf[d]
1	Me	*n*-BuLi	−20	5	80	51	2*S*,3*R*
2	Me	*n*-BuLi	−78	48	76	41	2*S*,3*R*
3	Me	*n*-BuLi	0	3	70	13	2*S*,3*R*
4[e]	Me	*n*-BuLi	−20	3	94	26	2*S*,3*R*
5	Me	NaOH	−20	1.5	100	29	2*S*,3*R*
6[f]	Me	DBU	0	7	60	21	2*S*,3*R*
7	*i*-Pr	*n*-BuLi	−20	24	32	58	2*R*,3*S*
8	*n*-Pr	*n*-BuLi	−20	7	51	20	2*R*,3*S*
9	Ph	*n*-BuLi	−20	3	78	17	2*R*,3*S*

[a] Molar ratios: **3**/**7**/base 1.1/1.0/1.2.
[b] Isolated yield after flash chromatography.
[c] Determined by HPLC analysis using chiral columns.
[d] Determined by comparison with specific rotation in the literature.
[e] 1 equiv of [12]crown-4 with respect to the base was added.
[f] 1 equiv LiCl with respect to the base was added.

obtained in an acceptable reaction time, but without improving the enantiomeric excess (entry 6). More sterically demanding groups on the naphthoquinones had a strong effect on reaction rate, level and sense of asymmetric induction, which was inverted (entries 7–9).

Data in Table 3 are more difficult to rationalize and it seems likely that a different enantiocontrol would be in act. In fact, in this case, the lack of templating structures cannot be ruled out in controlling the asymmetric induction. On the other hand, they confirm the synthetic problem of achieving generally high enantioselectivities in the epoxidation of naphthoquinones, although improvements can be accomplished on particular substrates by different methods.

3. Conclusions

In conclusion, we have shown that (+)-norcamphor-derived hydroperoxide **3** can be used in the enantioselective epoxidation of *trans*-chalcones achieving epoxides in good yields and moderate enantioselectivity. We have disclosed a different stereocontrol in the epoxidation of chalcones with the bulky tertiary hydroperoxide **3**. In fact, no templating structures made of alkaline cations, hydroperoxide anion and chalcone direct the asymmetric induction, as previously reported when employing secondary enantiopure alkyl hydroperoxides.[8] Nonbonded steric interactions of the approaching hydroperoxide anion with the β-substituents on chalcones would account for the observed enantioselectivity.

In the epoxidation of α-substituted naphthoquinones, the epoxide of vitamin K_3 has been obtained with the best ee reported to date. Finally, excellent recovery (95%) of enantiopure alcohol **6** at the end of epoxidations allowed a straightforward and convenient regeneration of **3** making this enantiomerically pure hydroperoxide of competitive synthetic utility.[19] It is interesting to note at this point how the steric modifications of the bicyclic framework of hydroperoxides **1**–**3** provided marked effects on reactivity and level of asymmetric induction. Hence by investigations on structurally modified enantiopure hydroperoxides of this type, it seems likely that their performance as stereoselective reagents could be susceptible to further improvements.

4. Experimental

4.1. Materials and general methods

All reactions requiring anhydrous conditions were conducted in flame-dried apparatus under an argon atmosphere. Tetrahydrofuran (THF) was distilled from lithium aluminium hydride under argon. CH_2Cl_2 and toluene were distilled from calcium hydride under argon. Petrol refers to the fraction of petroleum ether boiling in the range of 40–60 °C. Standard techniques were used in handling air sensitive reagents. All commercially available reagents were purchased from Aldrich and Fluka. Reactions were monitored by thin layer chromatography (TLC) on Merck silica gel plates (0.25 mm) and visualized by UV light or by 10% H_2SO_4/ethanol spray test. Flash chromatography was performed on Merck silica gel (60, particle size: 0.040–0.063 mm). Spectroscopic characterizations of hydroperoxide **3** and alcohol **6** have been previously reported.[5] Enantiomeric excesses of epoxides **5**/**8** were determined by HPLC analysis on chiral columns Chiralcel OD and Chiralpak AD and their absolute configurations determined by comparison with specific rotations in the literature.[8,16b,20]

4.2. General procedure for asymmetric epoxidation of *trans*-chalcones and naphthoquinones

To a solution of hydroperoxide **3** (100 mg, 0.515 mmol) in dry THF (3 mL) under an argon atmosphere at −20 °C, *n*-BuLi (224 μL, 0.561 mmol, 2.5 M solution) was added. After 15 min, enone **4** or **7** (0.468 mmol) dissolved in dry THF (2 mL) was cannulated into the flask. At the end of the reaction, as verified by TLC, a solution of Na_2SO_3 (0.5 mL, 1 M solution) was added and the mixture was stirred for 10 min at room temperature. The organic phase was diluted with diethyl ether (30 mL) and then washed with water. After drying with Na_2SO_4, the solvent was removed under reduced pressure and the crude product was purified by flash chromatography (petrol/diethyl ether 99/1) to give epoxide **5** or **8** and alcohol **6**. Physical and spectroscopic data of epoxides **5** and **8** matched those reported.[8,16b,20]

Acknowledgements

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References

1. (a) Ojima, I. *Catalytic Asymmetric Synthesis*, 2nd ed.; VCH Publisher: New York, 2000; (b) Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*; Springer: Berlin, 1999.
2. (a) Hamann, H.-J.; Höft, E.; Mostowicz, D.; Mishnev, A.; Urbańczyk-Lipkowska, Z.; Chmielewski, M. *Tetrahedron* **1997**, *53*, 185; (b) Mostowicz, D.; Jurczak, M.; Hamann, H.-J.; Höft, E.; Chmielewski, M. *Eur. J. Org. Chem.* **1998**, 2617; (c) Adam, W.; Korb, M. N. *Tetrahedron: Asymmetry* **1997**, *8*, 1131; (d) Adam, W.; Korb, M. N.; Roschmann, K. J.; Saha-Möller, C. R. *J. Org. Chem.* **1998**, *63*, 3423; (e) Aoki, M.; Seebach, D. *Helv. Chim. Acta* **2001**, *84*, 187; (f) Adam, W.; Alsters, P. L.; Neumann, R.; Saha-Möller, C. R.; Seebach, D.; Zhang, R. *Org. Lett.* **2003**, *5*, 725; (g) Adam, W.; Alsters, P. L.; Neumann, R.; Saha-Möller, C. R.; Seebach, D.; Beck, A. K.; Zhang, R. *J. Org. Chem.* **2003**, *68*, 8222.
3. (a) Lattanzi, A.; Iannece, P.; Vicinanza, A.; Scettri, A. *Chem. Commun.* **2003**, 1440; (b) Lattanzi, A.; Scettri, A. *Curr. Org. Chem.* **2004**, *8*, 607.
4. Lattanzi, A.; Iannece, P.; Scettri, A. *Tetrahedron: Asymmetry* **2004**, *15*, 413.
5. Lattanzi, A.; Iannece, P.; Scettri, A. *Tetrahedron: Asymmetry* **2004**, *15*, 1779.
6. (a) Porter, M. J.; Skidmore, J. *Chem. Commun.* **2000**, 1215; (b) Nemoto, T.; Ohshima, T.; Shibasaki, M. *Tetrahedron* **2003**, *59*, 6889.
7. (a) Arai, S.; Ishida, T.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 8229; (b) Lygo, B.; Wainwright, P. G. *Tetrahedron* **1999**, *55*, 6289; (c) McDonald, G.; Alcaraz, L.; Lewis, N. J.; Taylor, R. J. K. *Tetrahedron Lett.* **1998**, *39*, 5433; (d) Corey, E. J.; Zhang, F.-Y. *Org. Lett.* **1999**, *1*, 1287.
8. (a) Adam, W.; Bheema Rao, P.; Degen, H.-G.; Saha-Möller, C. R. *J. Am. Chem. Soc.* **2000**, *122*, 5654; (b) Adam, W.; Bheema Rao, P.; Degen, H.-G.; Saha-Möller, C. R. *Eur. J. Org. Chem.* **2002**, 630.
9. (a) Julià, S.; Masana, J.; Vega, J. C. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 929; (b) Julià, S.; Guixer, J.; Masana, J.; Rocas, J.; Colonna, S.; Annunziata, R.; Molinari, H. J. *Chem. Soc., Perkin Trans. 1* **1982**, 1317; (c) Kroutil, W.; Lasterra-Sanchez, M. E.; Maddrell, S. J.; Mayon, P.; Morgan, P.; Roberts, S. M.; Thornton, S. R.; Todd, C. J.; Tüter, M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2837; (d) Pu, L. *Tetrahedron: Asymmetry* **1998**, *9*, 1457.
10. (a) Enders, D.; Zhu, J.; Raabe, G. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1725; (b) Elston, C. L.; Jackson, R. F. W.; MacDonald, S. J. F.; Murray, P. J. *Angew. Chem., Int. Ed.* **1997**, *36*, 410; (c) Bougauchi, M.; Watanaba, S.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1997**, *119*, 2329; (d) Nemoto, T.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2001**, *123*, 9474.
11. After 3 h at room temperature, hydroperoxide **3** was consumed showing a substantial decomposition of the oxidant.
12. (a) Bunton, C. A.; Minkoff, G. J. *J. Chem. Soc., Chem. Commun.* **1979**, 665; (b) House, H. O.; Ro, R. S. *J. Am. Chem. Soc.* **1958**, *80*, 2428; (c) Wynberg, H.; Pluim, H. *J. Org. Chem.* **1980**, *45*, 2498.
13. Another confirmation that no templating control is in act during the epoxidation by different bases is the fact that in our case, (α*R*,β*S*)-epoxides **5** (Tables 1 and 2) were always preferentially obtained, regardless of the presence of different templating agents (alkaline metal ions or ammonium ion).
14. (a) Matschiner, J. T.; Bell, R. G.; Amelotti, J. M.; Knauer, T. E. *Biochim. Biophys. Acta* **1970**, *201*, 309; (b) Willingham, A. K.; Matschiner, J. T. *Biochem. J.* **1974**, *140*, 435; (c) Preusch, P. C.; Suttie, J. W. *J. Org. Chem.* **1983**, *48*, 2291.
15. (a) Colonna, S.; Manfredi, A. *Tetrahedron Lett.* **1986**, *27*, 387; (b) Colonna, S.; Gaggero, N.; Manfredi, A.; Spadoni, M.; Casella, L.; Carrea, G.; Pasta, P. *Tetrahedron* **1988**, *44*, 5169.
16. (a) Arai, S.; Oku, M.; Miura, M.; Shioiri, T. *Synlett* **1998**, 1201; (b) Arai, S.; Tsuge, H.; Oku, M.; Miura, M.; Shioiri, T. *Tetrahedron* **2002**, *58*, 1623.
17. Dwyer, C. L.; Gill, C. D.; Ichihara, O.; Taylor, R. J. K. *Synlett* **2000**, 704.
18. Loupy, A.; Tchoubar, B. *Salt Effect in Organic and Organometallic Chemistry*; VCH: Weinheim, 1992.
19. Reaction of alcohol **6** with Amberlyst-15/50% H_2O_2 in THF at room temperature affords hydroperoxide **3** after 6 h in 85% isolated yield.[5] Overall yield for the three-step route to **3** is 83%.
20. Kumaraswamy, G.; Sastry, M. N. V.; Nivedita, J.; Ravi Kumar, K.; Vairamani, M. *Tetrahedron: Asymmetry* **2003**, *14*, 3797.