Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 3219–3227

TETRAHEDRON: *ASYMMETRY*

Asymmetric sulfoxidation of a β-carbonyl sulfide series by chloroperoxidase

Reinaldo R. Vargas,* Etelvino J. H. Bechara, Liliana Marzorati and Blanka Wladislaw

Instituto de Química, Universidade de São Paulo, C.P. 26077, CEP 05599-970, São Paulo, S.P. Brazil

Received 6 July 1999; accepted 9 July 1999

Abstract

The chloroperoxidase (CPO)-catalyzed oxidation of a series of β-carbonyl sulfides to sulfoxides has been studied at room temperature in aqueous citrate buffer. For dialkyl β-carbonyl sulfides, the products with methyl and ethyl substituents are obtained in ca. 100% yield. However when the alkyl group is *n*-propyl or *i*-propyl the yield drops dramatically (25%). An aryl sulfide derivative afforded product in very low yield (4%), but when the phenyl group bears a carbonyl, and the sulfur substituents are methyl or ethyl, the oxidation occurs with high yields (91–95%). Steric control of the sulfoxidation reaction is also confirmed with cyclohexanone derivatives, where a low product yield is observed even at high enzyme concentrations. Noteworthy are the yields obtained with cyclopentanone sulfide (65%) and an unexpected quantitative yield obtained with the γ-butyrolactone sulfide.

1. Introduction

One of the most powerful stereodirecting groups in asymmetric synthesis of natural products is an enantiomerically pure sulfoxide, which has been the subject of several comprehensive reviews.[1] Optically active sulfoxides have been obtained in many different ways: optical resolution; asymmetric synthesis; kinetic resolution; and stereospecific synthesis. Chiral β-ketosulfoxides are generally available by the condensation of (−)-(*R*)-*p*-tolylmethyl sulfinyl anion and an ester,[2] although this method is restricted to aryl ketosulfoxides. The synthesis of a β-ketosulfoxide with a chiral methylsulfinyl group was recently achieved using the diacetone D-glucose (DAG) method.[3] Enantiomerically enriched β-ketosulfoxides have also been obtained through the Sharpless's modified kinetic resolution of racemic β-ketosulfoxides using furylhydroperoxides as oxidants.[4]

Studies of organic sulfide oxidation to pure sulfoxides using enzymes as catalysts have intensified in this decade. In particular, a chloroperoxidase (CPO) extracted from the marine fungus *Caldariomyces*

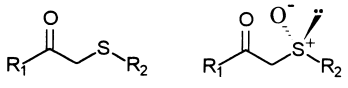
* Corresponding author. Fax: 55-11-8155579; e-mail: rrvargas@quim.iq.usp.br

0957-4166/99/$ - see front matter
PII: S0957-4166(99)00339-0

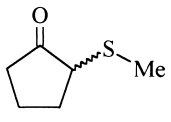
fumago has been shown to be a useful catalyst, because it is readily available, relatively stable, and does not require any cofactor. Kobayashi et al.[5] demonstrated that, with CPO as catalyst, the oxygen atom of the sulfoxide product of *p*-methoxythioanisole arises exclusively from H_2O_2. Colonna et al.[6] showed that CPO-catalyzed oxidation of prochiral sulfides, using H_2O_2 or *t*-BuOOH as the stoichiometric oxidant, is very effective in providing a variety of important aryl methyl sulfoxides with high enantiomeric excess (e.e.). This work focuses on the oxidation behavior of β-carbonyl sulfides in the presence of CPO/H_2O_2, for which a series of dialkyl and alkyl aryl derivatives and cyclic carbonyl sulfides was used.

2. Results and discussion

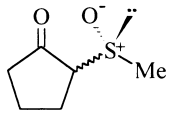
The oxidation of a series of β-carbonyl sulfides by H_2O_2 in the presence of CPO was examined in 0.05 M citrate buffer, pH 5 at 25°C.



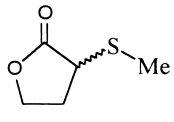
Sulfide	Sulfoxide	R_1	R_2
1	**13**	$-CH_3$	$-CH_3$
2	**14**	$-CH_3$	$-C_2H_5$
3	**15**	$-CH_3$	$-C_3H_7$
4	**16**	$-CH_3$	$-C_3H_7$ *i*
5	**17**	$-CH_3$	$-C_6H_5$
6	**18**	$-C_6H_5$	$-CH_3$
7	**19**	*p*$-CH_3C_6H_4$	$-C_2H_5$
8	**20**	$-OC_2H_5$	$-CH_3$



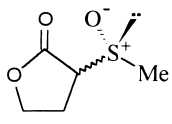
9



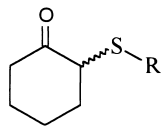
21

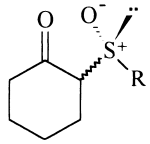


10



22





Sulfide	Sulfoxide	R
11	**23**	$-CH_3$
12	**24**	$-C_2H_5$

The crude products were purified by preparative TLC or by column chromatography, and the enantiomeric excess evaluated by optical rotation measurements and ^{1}H NMR spectroscopy. Table 1 summarizes the data obtained upon addition of H_2O_2 at 5 min intervals during 1 h (method A). Control experiments in the absence of CPO gave β-carbonyl sulfoxide yields below 2%.

Table 1 shows that the chemical yield of CPO-catalyzed oxidation of β-carbonyl sulfides can be as high as 100% when H_2O_2 is added within 1 h. No sulfone was detected in the final reaction mixture, and when the sulfoxide is formed in low yield, the remaining ketosulfide was completely recovered. Table 1 shows that only substrates **5** and **12** were not significantly oxidized in the presence of enzyme. This lack of oxidation may have been due to an effect of organic solvent. While the use of organic solvents is necessary to solubilize the organic substrates, solvents such as methanol and dimethylsulfoxide are not efficient because they are substrates for CPO,[7] and acetonitrile and acetone have been reported to lower the enantiomeric excess in sulfoxidation reactions.[8] Accordingly, when substrate **5** was studied in co-solvents such as ethanol (15% v/v), acetonitrile (8–10% v/v) and acetone (20% v/v), oxidation did not

Table 1
Chemical yields of CPO-catalyzed oxidation of β-carbonyl sulfides, according to method A

Sulfide	Sulfoxide Yield (%)	e.e. (%)	d.e. (%)
1	100	> 99	-----
2	100	>99	-----
5	3	n.d.	-----
7	31	92	-----
8	97	94	-----
10	45	> 95	63
12	10	n.d.	n.d.

n.d.- not determined, e.e.- enantiomeric excess, d.e.- diastereomeric excess

take place at all. The use of acetonitrile (30% v/v) to improve the solubility of substrate **7** decreased the product yield from 31 to 5%.

Deurzen et al.[9] showed that the procedure of oxidant addition is crucial for obtaining high product yields from CPO-catalyzed sulfoxidation reactions. It is important to keep the H_2O_2 concentration as low as possible, preferably in a rate limiting condition. This is due to the inactivation of CPO by excess H_2O_2 in the reaction mixture. Recently Deurzen et al.[10] proposed the use of a H_2O_2-controlled reaction catalyzed by CPO to improve the enzyme performance. Probably, the CPO deactivation by H_2O_2 involves internal oxidation of the porphyrin moiety, which is generally seen to occur with heme proteins such as cytochrome P450 and horseradish peroxidase (HRP).[11]

Therefore, aiming to improve the product yields, H_2O_2 addition was carried out over a long period, specifically 5 h (method B). Table 2 attests to significant yield increases relative to that obtained during 1 h of H_2O_2 addition (method A).

Using substrate **5**, sulfoxide formation occurred to a low extent when the addition time was 5 h. Similarly, Deurzen et al.[12] reported CPO-catalyzed propyl phenyl sulfide oxidation at a low yield (3%). This substrate is presumably too large to fit readily into the small active site of CPO, slowing the enzymatic oxidation of the sulfide. Methylphenyl sulfide (substrate **5**) is of similar size to propyl phenyl sulfide, and therefore the oxidation might have failed for steric factors as well. Substrate **5** was then oxidized upon continuous addition of H_2O_2 for 20 h, which raised the product yield to 15%, but with $[\alpha]_D$ +29.7 (c=0.38, methanol), indicating a low enantiomeric excess (ca. 10%).[13] This low enantiomeric specificity suggests that a chemical oxidation was competing with the enzymatic process. Because substrate **6** is liquid at the experiment temperature, a clear solution was obtained after 20 min of stirring, and sulfoxide was formed in 80% yield. When the dialkyl and alkyl aryl sulfides were *S*-methyl or *S*-ethyl substituted, the enzyme worked efficiently. The *n*-propyl and *i*-propyl substituted derivatives (substrates **3** and **4**) gave yields lower than those of the methyl and ethyl analogs, although their reactions proved to be very enantioselective (e.e.>99%).

Accordingly, Colonna et al.[14] reported high chemical (>98%) and optical yields (>98%) with the

Table 2
Chemical yields of CPO-catalyzed oxidation of β-carbonyl sulfides, according to method B

Sulfide	Sulfoxide Yield (%)	e.e. (%)	d.e. (%)
3	26	>99	-----
4	25	>99	-----
5	4	n.d.	-----
6	80	91	-----
7	55	92	-----
9	46	>95	70
10	100	>95	63
11	20	>95	70
12	22	>95	68

n.d.- not determined, e.e.- enantiomeric excess, d.e.- diastereomeric excess

cyclopentyl methyl sulfide/CPO system, but when the cycloalkane chain was extended to six carbons (cyclohexyl methyl sulfide), the chemical and optical yields decreased appreciably (85% for both).

Allenmark and Andersson,[15] when studying the CPO-catalyzed oxidation of a series of rigid aromatic sulfides had also observed a very low chemical yield for the six-membered heterocyclic compound, albeit with high e.e. (>96%). A similar five-membered substrate afforded quantitative yield (99% e.e.). Additions of co-solvents, aiming to increase the substrate solubility, had no effect on the product yield. Neither increased temperature nor prolonged reaction time altered the outcome of the reaction.

During oxidation studies of sterically well-designed sulfides with CPO, Allenmark and Andersson[16] observed that when the amount of enzyme was increased sixfold, the yield was significantly increased to 80%, with an e.e. of 96%. In contrast, in the present work, when the enzyme concentration was increased, no yield increases were obtained with *n*-propyl, *i*-propyl group and cyclohexanone derivatives (Table 3). As expected, the substrates **6**, **7** and **9**, with *S*-methyl or *S*-ethyl substituents, and the cyclopentanone derivative gave enzyme concentration-dependent product yields.

Substrate **6** gave 95% product yield using a substrate/enzyme ratio of 35 000 (Table 3). Nevertheless, in an attempt to reach large scale production (10 times, 150 mL solution), the yield of **18** was initially only 33%. By using very fast stirring, attested to by vortex formation from the solution top toward the magnetic bar, 90% yield was obtained. This reaffirms that homogeneity of the solution is crucial for proper interaction between substrate and enzyme, especially in the cases where the solubility of the substrate is low.

The data with the series of racemic cyclic carbonyl sulfides of differing size (compounds **9**, **10**, **11**, **12**) confirmed a positive influence on the product yields of a small size[17] to fit the CPO heme cleft. Indeed, substrates **11** and **12** (cyclohexanone derivatives) being bulkier than substrate **9** (cyclopentanone sulfide) gave a twofold lower yield than the smaller substrate. An effect of a carbonyl group in the β-position was observed by Allenmark and Andersson[16] when 2,3-dihydrobenzo[*b*]thiophene and

Table 3
Enzyme concentration effect on sulfoxide yield obtained by oxidation of the corresponding sulfide with the CPO/H_2O_2 system (method B)

Sulfide	[Substrate]/[Enzyme]	Sulfoxide Yield (%)
3	70,000	26
	35,000	25
	23,500	25
4	70,000	25
	35,000	25
	23,500	25
6	70,000	80
	35,000	96
7	70,000	55
	35,000	82
	23,500	94
9	70,000	46
	35,000	52
	23,500	65
11	70,000	20
	35,000	20
	23,500	19
12	70,000	22
	35,000	25
	23,500	25

benzo[*b*]thiophen-3-one were oxidized with CPO yielding 99.5% (99% e.e.) and 7% (37% e.e.) sulfoxide product, respectively. Unexpectedly the γ-butyrolactone sulfide **10** afforded the corresponding sulfoxide in quantitative yields, indicating that an oxygen atom neighbor to the carbonyl completely altered the enzyme selectivity.

Oxidation of racemic substrate **11** with 30% H_2O_2 in acetic acid gave 70% d.e. sulfoxide, albeit without optical activity. A similar result was reported elsewhere when the chiral sulfide **11** was oxidized with an oxaziridine derivative: 70% d.e. product was obtained.[18] The α-sulfinyl cyclic ketones **21**, **23** and **24** or lactone **22**, containing an α-hydrogen, are known to exhibit a keto–enol tautomerism in organic solution,

and therefore substrate enolization may be responsible for the observed d.e.[19] Thus, kinetic resolution of the cyclic carbonyl sulfides must be occurring to explain the e.e., but product enolization leads to d.e. loss.

In summary, our results show that the oxidation of a series of β-carbonyl sulfides with CPO at room temperature in aqueous citrate buffer is enantioselective. For the first time, chiral dialkyl ketosulfoxides are prepared in high chemical and optical yields. The reaction proved to be dramatically sensitive to steric factors and leads predominantly to the (*R*)-sulfoxides[6] (see Experimental, products **17**, **18** and **20**). When the solubility of the substrate in aqueous buffer is low, the chemical yield is very low or no reaction occurs. In these cases, addition of co-solvents such as ethanol, acetonitrile or acetone do not enhance the yield. When H_2O_2 is added slowly, the chemical yield may be enhanced without affecting the optical yield.

3. Experimental

3.1. Instrumentation

The optical rotations were determined with a Jasco DIP 370 polarimeter at λ=589 nm. The ^{1}H NMR spectra of the products were recorded in $CDCl_3$ on a Bruker DPX 300 instrument with TMS as an internal standard. GC–MS analyses were performed on an HP 5890 Series II gas chromatograph equipped with a 25 m SE-30 column. A Gilson peristaltic pump Miniplus 3 was used to add H_2O_2 continuously.

3.2. Materials

Chloroperoxidase from *Caldariomyces fumago* was obtained from Sigma as a crude suspension and used as received. Solvents were of p.a. purity.

3.3. Preparation of sulfides

All ketosulfides were prepared by the classical substitution reaction between the α-chloro or bromo-carbonyl derivative and the corresponding sodium thiolate,[20] only compound **8** was purchased from Aldrich.

3.4. Enzymatic oxidation

Ketosulfide (0.24 mmol) and CPO (6.7×10^{-6} mmol, 145 U) were magnetically stirred for 5 min in 15 mL of aqueous citrate buffer (0.05 M), pH 5 at 25°C. Hydrogen peroxide (0.26 to 0.48 mmol) in 5 mL of buffer solution was added according to method A (1 h addition at 5 min intervals) or method B (5 h continuous addition). The reaction was then quenched with Na_2SO_3, and saturated with NaCl. Extraction with six portions (50 mL each) of CH_2Cl_2, followed by drying in anhydrous $MgSO_4$ and evaporation of the organic solvents, gave the crude product. The product was isolated and purified by preparative TLC using chloroform as eluent or by column chromatography using hexane:acetone (80:20) as eluent.

3.5. Determination of product yield and enantiomeric excess

Enantiomeric excesses were determined by ^{1}H NMR with the aid of Eu(tfc)$_3$ (10–15% molar/molar) as a chiral shift reagent in $CDCl_3$:CCl_4 (4:1).[21]

3.6. Identification of sulfoxides

The β-carbonyl sulfoxides were characterized by ^{1}H NMR and by MS.

3.6.1. 1-(Methylsulfinyl)-2-propanone **13**

^{1}H NMR ($CDCl_3$) δ 2.37 (s, 3H), 2.70 (s, 3H), 3.65–3.91 (AB system, 2H, δ_A 3.70, δ_B 3.86, J_{AB}=13.7 Hz); MS, *m/e* (rel. intensity) 120 ($M^{\cdot+}$, 21), 78 (12), 63 (48), 61 (32), 58 (20), 43 (100); $[\alpha]_D^{20}$ +54.2 (c=1.2, $CHCl_3$).

3.6.2. 1-(Ethylsulfinyl)-2-propanone **14**

^{1}H NMR ($CDCl_3$) δ 1.36 (t, 3H, J=7.4 Hz), 2.36 (s, 3H), 2.78–2.91 (m, 2H), 3.63–3.85 (AB system, 2H, δ_A 3.68, δ_B 3.80, J_{AB}=13.6 Hz); MS, *m/e* (rel. intensity) 134 ($M^{\cdot+}$, 8), 106 (17), 77 (26), 63 (33), 46 (46), 43 (100); $[\alpha]_D^{20}$ +32.0 (c=1.0, $CHCl_3$).

3.6.3. 1-(Propylsulfinyl)-2-propanone **15**

^{1}H NMR ($CDCl_3$) δ 1.10 (t, 3H, J=7.5 Hz), 1.83 (sextet, 2H, J=7.5 Hz), 2.37 (s, 3H), 2.70–2.85 (m, 2H), 3.65–3.84 (AB system, 2H, δ_A 3.68, δ_B 3.82, J_{AB}=13.8 Hz); MS, *m/e* (rel. intensity) 148 ($M^{\cdot+}$, 1), 106 (38), 61 (22), 46 (52), 43 (100), 41 (32); $[\alpha]_D^{20}$ +14.7 (c=1.5, $CHCl_3$).

3.6.4. 1-(2-Propylsulfinyl)-2-propanone **16**

^{1}H NMR ($CDCl_3$) δ 1.30 (d, 3H, J=6.6 Hz), 1.34 (d, 3H, J=6.6 Hz), 2.39 (s, 3H), 2.94 (septet, 1H, J=6.6 Hz), 3.59–3.74 (AB system, 2H, δ_A 3.62, δ_B 3.70, J_{AB}=13.2 Hz); MS, *m/e* (rel. intensity) 148 ($M^{\cdot+}$, 0.7), 106 (34), 61 (15), 46 (47), 43 (100), 41 (36); $[\alpha]_D^{20}$ −5.0 (c=0.6, $CHCl_3$).

3.6.5. (R)-1-(Phenylsulfinyl)-2-propanone **17**

^{1}H NMR ($CDCl_3$) δ 2.24 (s, 3H), 3.76–3.93 (AB system, 2H, δ_A 3.81, δ_B 3.88, J_{AB}=13.6 Hz), 7.53–7.57 (m, 3H), 7.65–7.68 (m, 2H); MS, *m/e* (rel. intensity) 182 ($M^{\cdot+}$, 27), 125 (100), 97 (25), 77 (20); $[\alpha]_D^{20}$ +29.7 (c=0.38, MeOH), 11.7 e.e. (lit.[13] $[\alpha]_D$ +254 for pure enantiomer *R*).

3.6.6. (R)-2-(Methylsulfinyl)-1-phenylethanone **18**[3,22]

^{1}H NMR ($CDCl_3$) δ 2.77 (s, 3H), 4.29–4.52 (AB system, 2H, δ_A 4.32, δ_B 4.50, J_{AB}=14.4 Hz), 7.50–8.00 (m, 5H); MS, *m/e* (rel. intensity) 182 ($M^{\cdot+}$, 6), 120 (70) 105 (100), 91 (38), 77 (45), 51 (15); $[\alpha]_D^{20}$ +50.5 (c=1.05, $CHCl_3$); $[\alpha]_D^{20}$ −57.0 (c=1.2, EtOH) (lit.[3] $[\alpha]_D^{22}$ +63, c=1.4, EtOH, for pure enantiomer *S*); mp 84–85°C.

3.6.7. 2-(Ethylsulfinyl)-1-(4-methylphenyl)-ethanone **19**

^{1}H NMR ($CDCl_3$) δ 1.40 (t, 3H, J=7.8 Hz), 2.43 (s, 3H), 2.67–3.07 (m, 2H), 4.15–4.39 (AB system, 2H, δ_A 4.20, δ_B 4.34, J_{AB}=14.6 Hz), 7.20 (d, 2H, J=8.1 Hz), 7.70 (d, 2H, J=8.1 Hz); MS, *m/e* (rel. intensity) 210 ($M^{\cdot+}$, 0.3), 134 (83), 119 (100), 105 (16), 91 (25); $[\alpha]_D^{20}$ +29.0 (c=3.0, $CHCl_3$); mp=95–96°C (lit.[23] 94–97°C).

*3.6.8. (*R*)-Ethyl methylsulfinyl acetate **20***

^{1}H NMR ($CDCl_3$) δ 1.32 (t, 3H, J=7.4 Hz), 2.76 (s, 3H), 3.64–3.81 (AB system, 2H, δ_A 3.68, δ_B 3.76, J=13.5 Hz), 4.26 (q, 2H, J=7.4 Hz); MS, *m/e* (rel. intensity) 150 ($M^{\cdot+}$, 12), 105 (39), 88 (100), 77 (24), 64 (44), 63 (66), 61 (37), 60 (35); $[\alpha]_D^{20}$ +29.5 (c=2.0, $CHCl_3$), $[\alpha]_D^{20}$ −56.0 (c=1.5, acetone) (lit.[24] $[\alpha]_D$ −31.3 (acetone), enantiomer *R*).

*3.6.9. 2-Methylsulfinyl cyclopentanone **21***

^{1}H NMR ($CDCl_3$) δ 1.98–2.69 (m, 6H, 3×CH_2), 2.73[a] (s, 3H), 2.81[b] (s, 3H), 3.06[b] (dd, 1H, J=6.6 Hz, J=8.4 Hz), 3.34[a] (t, 1H, J=7.5 Hz), a/b=70%; MS, *m/e* (rel. intensity) 146 ($M^{\cdot+}$, 29), 91 (25), 87 (27), 83 (23), 74 (58), 55 (100); $[\alpha]_D^{20}$ −100.0 (c=0.9, $CHCl_3$).

*3.6.10. Methylsulfinyl-γ-butyrolactone **22***

^{1}H NMR ($CDCl_3$) δ 2.40–2.90 (m, 2H), 2.82[a] (s, 3H), 2.87[b] (s, 3H), 3.47[b] (dd, 1H, J=4.9 Hz, J=9.0 Hz), 3.71[a] (dd, 1H, J=6.5 Hz, J=9.4 Hz), 4.4–4.5 (m, 2H), a/b=63%; MS, *m/e* (rel. intensity) 148 ($M^{\cdot+}$, 7), 86 (100) 85 (82), 64 (43), 63 (15), 57 (21), 55 (69), 41 (77); $[\alpha]_D^{20}$ −22.9 (c=1.4, $CHCl_3$).

*3.6.11. 2-Methylsulfinyl cyclohexanone **23***

^{1}H NMR ($CDCl_3$) δ 1.73–2.25 (m, 6H, 3×CH_2), 2.42–2.55 (m, 2H), 2.58[b] (s, 3H), 2.70[a] (s, 3H), 3.38[b] (t, 1H, J=6.0 Hz), 3.45[a] (dd, 1H, J=5.7 Hz, J=9.3 Hz), a/b=70%; MS, *m/e* (rel. intensity) 160 ($M^{\cdot+}$, 20), 98 (12), 97 (100), 69 (54), 55 (40), 41 (55); $[\alpha]_D^{20}$ +5.5 (c=1.1, $CHCl_3$) (lit.[18] $[\alpha]_D$ −4.1 (c=1.3, ethanol), d.e.=70%).

*3.6.12. 2-Ethylsulfinyl cyclohexanone **24***

^{1}H NMR ($CDCl_3$) δ 1.34[b] (t, 3H, J=7.5 Hz), 1.38[a] (t, 3H, J=7.5 Hz), 2.78–2.98 (m, 10H, 5×CH_2), 3.32[b] (t, 1H, J=5.2 Hz), 3.48[a] (dd, 1H, J=5.4 Hz, J=8.4 Hz), a/b=68%; MS, *m/e* (rel. intensity) 174 ($M^{\cdot+}$, 17), 98 (72), 97 (100) 69 (66), 55 (947), 41 (60); $[\alpha]_D^{20}$ −2.2 (c=1.4, $CHCl_3$).

Acknowledgements

We thank Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) for financial support and for a postdoctoral fellowship to one of us (R.R.V.). E.J.H.B. is also grateful for grants obtained from the Programa de Apoio a Núcleos de Excelência (PRONEX). We are grateful to Dr. Brian Bandy for a critical reading of this manuscript.

References

1. (a) Walker, A. J. *Tetrahedron: Asymmetry* **1992**, *3*, 961. (b) Carreno, M. C. *Chem. Rev*. **1995**, *95*, 1717. (c) Solladié, G.; Carreno, M. C. In *Organosulfur Chemistry. Synthetic Aspects*; Page, P. C. B., Ed.; Academic Press: New York, 1995, Chapter 1, pp. 1–47.
2. Kunieda, N.; Nokami, J.; Kinoshita, M. *Chem. Lett*. **1974**, 369.
3. Ouazzani, H. El.; Khiar, N.; Fernandez, I.; Alcudia, F. *J. Org. Chem*. **1997**, *62*, 287.
4. Lattanzi, A.; Bonadies, F.; Schiavo, A.; Scettri, A. *Tetrahedron: Asymmetry* **1998**, *9*, 2619.
5. Kobayashi, S.; Nakano, M.; Kimura, T.; Schaap, A. P. *Biochemistry* **1987**, *26*, 5019.
6. Colonna, S.; Gaggero, N.; Casella, L.; Carrea, G.; Pasta, P. *Tetrahedron: Asymmetry* **1992**, *3*, 95.
7. (a) Geigert, J.; Dewitt, S. K.; Neidleman, S. L.; Lee, G.; Daleitos, D. J.; Moreland, M. *Biochem. Biophys. Res. Commun*. **1983**, *116*, 82. (b) Geigert, J.; Daleitos, D. J.; Neidleman, S. L.; Lee, T. D.; Wadsworth, J. *Biochem. Biophys. Res. Commun*. **1983**, *114*, 1104.

8. Colonna, S.; Gaggero, N.; Manfredi, A.; Casella, L.; Gullotti, M.; Carrea, G.; Pasta, P. *Biochemistry* **1990**, *29*, 10465.
9. van Deurzen, M. P. J.; Groen, B. W.; van Rantwijk, F.; Sheldon, R. A. *Biocatalysis* **1994**, *10*, 247.
10. van Deurzen, M. P. J.; Seelbach, K.; van Rantwijk, F.; Kragl, U.; Sheldon, R. A. *Biocatalysis and Biotransformation* **1997**, *15*, 1.
11. Bagger, S.; Williams, R. J. P. *Acta Chem. Scand*. **1971**, *25*, 976.
12. Van Deurzen, M. P. J.; Remkes, I. J.; van Rantwijk, F.; Sheldon, R. A. *J. Mol. Catal. A: Chemical* **1997**, *117*, 329.
13. Iriuchijima, S.; Kojima, N. *Agric. Biol. Chem*. **1978**, *42*, 451.
14. Colonna, S.; Gaggero, N.; Carrea, G.; Pasta, P. *Chem. Commun*. **1997**, 439.
15. Allenmark, S. G.; Andersson, M. A. *Tetrahedron: Asymmetry* **1996**, *7*, 1089.
16. Allenmark, S. G.; Andersson, M. A. *Chirality* **1998**, *10*, 146.
17. Sundaramoorthy, M.; Terner, J.; Poulos, T. L. *Structure* **1995**, *3*, 1367.
18. Glahsl, G.; Herrmann, R. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1753.
19. Bravo, P.; Piovosi, E.; Resnati, G. *Synthesis* **1986**, 579.
20. Bradsher, C. K.; Brown, F. C.; Granthan, R. J. *J. Am. Chem. Soc*. **1954**, *76*, 114.
21. Kunieda, N.; Suzuki, A.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1143.
22. Ibarra, C. A.; Rodriguez, R. C.; Monreal, M. C. F.; Navarro, F. J. G.; Tesorero, J. M. *J. Org. Chem*. **1989**, *54*, 5620.
23. Olivato, P.; Bonfada, E.; Rittner R. *Magn. Reson. Chem*. **1992**, *30*, 81.
24. Dunach, E.; Kagan, H. B. *Nouv. J. Chim*. **1985**, *9*, 1.