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Metal-Mediated Enantioselective Access to Unfunctionalized Aliphatic Oxiranes: Prochiral and Chiral Recognition

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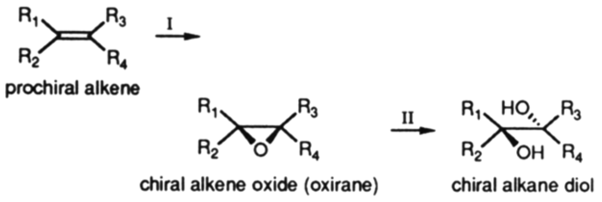
I. Introduction

Chiral unfunctionalized aliphatic oxiranes are reactive (pro-1,2-bifunctional) educts (chirons) for the synthesis of optically active natural, pharmaceutical, and synthetic products.[1] It has been remarked that *the value of epoxides as synthetic intermediates, as well as an end in themselves, emphasizes the need and desirability of obtaining these compounds in a high state of enantiomeric purity.*[2] The availability of enantiomerically pure oxiranes with established absolute configuration is also a prerequisite for chiroptical studies.[3-5] Nonracemic aliphatic oxiranes are accessible by a number of fundamental enantioselective strategies: (1) chiral carbon pool transformation,[6] (2) nonenzymatic asymmetric epoxidation,[7] (3) enzymatic asymmetric epoxidation,[8-12] (4) nonenzymatic kinetic resolution,[13-15] (5) enzymatic kinetic resolution,[16-20] (6) chromatographic resolution,[21,22] and (7) inclusion (e.g. into tri-*o*-thymotide).[23]

While the Pasteur-type resolution via diastereomeric salts is not available for unfunctionalized aliphatic oxiranes, only the chiral carbon pool approach[2] and the microbial production[12] yield simple aliphatic epoxides in good chemical and high enantiomeric yield at present.

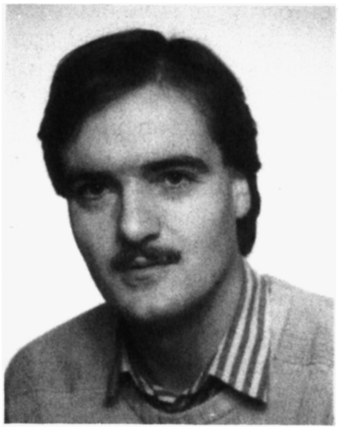
Chiral oxiranes are key intermediates in the metabolic pathway involving C–C-double bonds.



(1)

In the reaction sequences I and II, enantioselectivity can arise (i) by epoxidation of an alkene possessing enantiotopic faces (prochiral recognition, product enantioselectivity) and (ii) by kinetic resolution of the intermediary oxirane (chiral recognition, substrate enantioselectivity).[15,19]

Volker Schurig was born in 1940 in Dresden and began studies in chemistry in 1959 at the Universität Tübingen, where he received his doctorate under Ernst Bayer in 1968. He then spent two years in Israel as a postdoc at the Weizmann Institute of Science, where be began his work on the gas-chromatographic separation of enantiomers with Gil-Av. After pursuing this work at the University of Houston, he completed his "Habilitation" in Tübingen with work on complexation gas chromatography. He has been a guest professor at the Université Paris-Sud and the Weizmann Institute. His areas of interest include homogeneous catalysis with soluble polymeric metal compounds, the formation of highly ordered solid-state structures by chiral control, enzymatic epoxidations, chiral NMR shift reagents, chromatographic enantiomer separations, and the stereochemical analysis and synthesis of flavors and pheromones.



Frank Betschinger was born in Tübingen in 1962 and began studies in chemistry in 1984 at the Universität Tübingen, where he is currently working on his doctorate under Volker Schurig. He is a scholar of the Studienstiftung des Deutschen Volkes.

While enantiomerically highly enriched α-(hydroxyalkyl)oxiranes can be obtained by asymmetric Katsuki–Sharpless epoxidation of allylic alcohols with *tert*-butyl hydroperoxide/titanium(IV) dialkyl tartrate,[24,25] no such versatile procedure is yet available for the peroxometal-mediated epoxidation of *unfunctionalized* aliphatic alkenes devoid of auxiliary anchoring groups

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to favor high ee's and rates. In the absence of secondary chelation, asymmetric induction (prochiral recognition) must entirely rely on nonbonded interactions. The osmium tetraoxide-catalyzed asymmetric dihydroxylation of aliphatic alkenes to vicinal diols with ee = 87%[26] and ee = 100%,[27] followed by the elaboration of the diol functionality to cyclic sulfates as epoxide equivalents,[28] represents an important alternative to chiral oxiranes for certain synthetic purposes.

Although a breakthrough in metal-mediated enantioselective epoxidation of aliphatic alkenes is still lacking, some interesting approaches have been developed which will be reviewed here. It is noted that also microsomal cytochrome P-450-catalyzed asymmetric epoxidations of aliphatic, xenobiotic alkenes exhibit only modest, species-dependent, enantioselectivities[10] while bacterial epoxidation produces oxiranes of high ee.[8,9,12]

In the metal-mediated kinetic resolution of racemic oxiranes one enantiomer is recovered as unreacted educt while the other is transformed to the chiral (or achiral) product. If only one enantiomer reacts, 50% conversion yields a mixture of 50% pure residual educt enantiomer and of 50% product. At incomplete kinetic resolution, the chemical yield must be balanced against the enantiomeric yield. The efficient kinetic resolution of aliphatic oxiranes by polymerization[13,14] and by enzymatic transformations (catalyzed by epoxide hydrolase or glutathion *S*-transferase)[16-20] is outside the scope of this review.

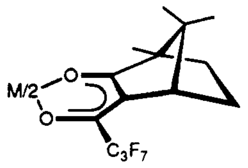
The *preparative* chromatographic separation of oxirane enantiomers on chiral nonracemic stationary phases constitutes a direct method for the access to pure aliphatic oxirane enantiomers. At present, however, only the semipreparative enantiomer separation of 2,2-dimethyl-3-phenyloxirane by complexation gas chromatography has been described.[29]

Yet, the *analytical* gas chromatographic enantiomer separation of small aliphatic oxiranes employing packed[21] or high-resolution capillary columns[22] offers a valuable tool for the reliable determination of ee of oxiranes formed by enzymatic and nonenzymatic reactions. The analysis can often be performed continuously without isolation of the volatile oxirane.[30]

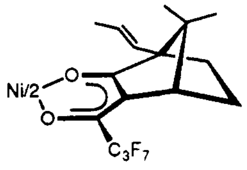
The separation of oxirane enantiomers on chiral metal chelates not only provides interesting insights in inherent thermodynamics of chiral recognition via coordination but also allows different enantioselective phenomena to be discerned. The metal-mediated chromatographic approach (featuring chiral recognition) will be discussed first.

II. Metal-Mediated Gas-Chromatographic Resolution of Racemic Aliphatic Oxiranes

In complexation gas chromatography, electronically and coordinatively unsaturated metal complexes are added to the stationary liquid in order to introduce chemical selectivity into the separation process.[15] Using nonracemic metal complexes such as manganese(II), cobalt(II), nickel(II), and zinc(II) bis[3-(heptafluorobutanoyl)-(1*R*)-camphorate] 1–4 the enantiomers of simple aliphatic oxiranes, e.g., methyloxirane—representing one of the smallest (nonisotopic) chiral molecules—can be resolved quantitatively.[22,31,32] An improved separation of oxiranes on nickel(II) bis[3-(heptafluorobutanoyl)-10-ethylidene-(1*S*)-camphorate] 5 is shown in Figure 1.[15]



1: M = Mn
2: M = Co
3: M = Ni
4: M = Zn



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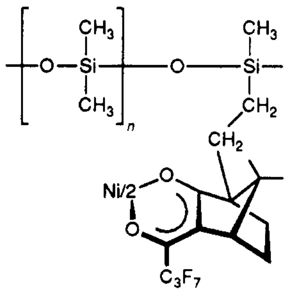
Unequivocal proof of enantiomer separation is provided by using the *racemic* metal complex as stationary phase leading to the collapse of resolution (peak *coalescence* of the first kind) or by using the *oppositely configurated* metal complex leading to the reversal of the elution order of the oxirane enantiomers (peak *inversion* of the first kind). Recently, nickel(II) bis-[3-(heptafluorobutanoyl)-(1*R*)-camphorate] has been linked via the C10-methyl group of camphor to a polysiloxane (Chirasil-Metal) 6,[33] involving platinum-catalyzed hydrosilylation[34] and affording a thermally stable stationary phase which can be thermally immobilized on the inner surface of the capillary column. This chiral stationary phase tolerates carbon dioxide in the supercritical state as mobile phase and involatile oxiranes may thus be investigated by supercritical fluid chromatography (SFC).[33] In chromatographic enantiomer separation of oxiranes, useful informations can be obtained from the following peak parameters (cf. Scheme I).



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It has been previously shown that thermodynamic data, describing chemical selectivity and enantioselectivity (cf. 1 and 2 in Scheme I), may readily be obtained from relative retention data by complexation gas chromatography.[15,32] The association equilibria between twelve mono-, di-, and trialkylsubstituted oxiranes and eleven nonracemic nickel(II) bis[α-(heptafluorobutanoyl) terpene ketonates] 7–17 in squalane ($C_{30}H_{62}$) have been measured at 60 °C.[35] The association selectivities of alkyl-substituted oxiranes and the metal chelates followed a common trend. It was interpreted in terms of opposing electronic and steric effects of the oxiranes. The relationship between the strength of mo-

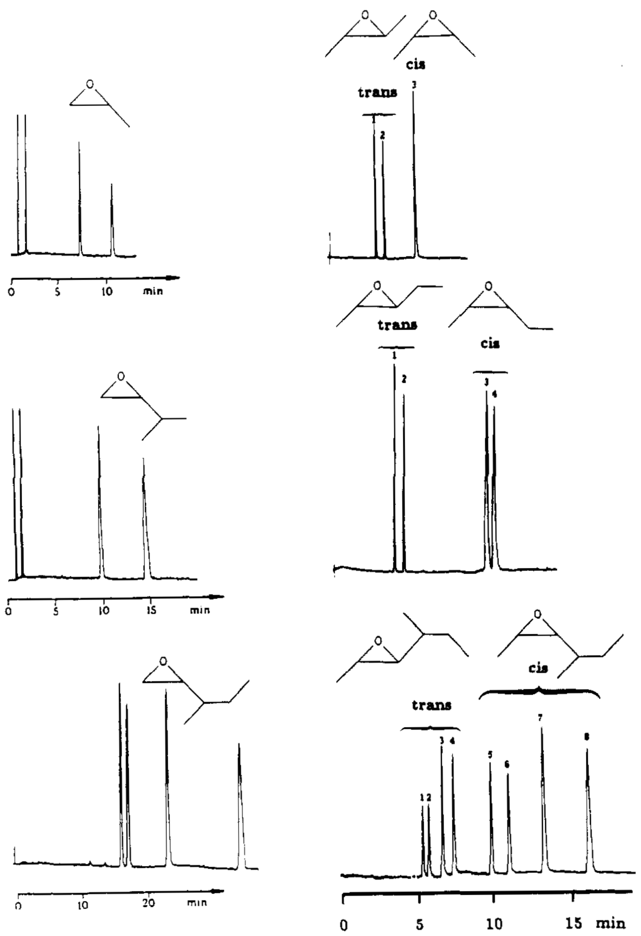


Figure 1. Enantiomer separation of aliphatic oxiranes by complexation gas chromatography on nickel(II) bis[3-(heptafluorobutanoyl)-(1*S*)-10-ethylidenecamphorate] (0.125 m in OV-101) between 70 and 90 °C. [Column: 25-m × 0.25-mm glass capillary.[15]]

Scheme I. Five Peak Parameters in Chromatographic Enantiomeric Separation[15,32]

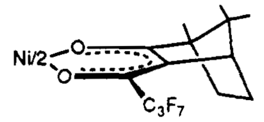
(1)	peak retention:	chemoselectivity	ΔG°
(2)	peak separation:	enantioselectivity	$\Delta_{R,S}\Delta G^\circ$
(3)	peak coalescence (3rd kind):	enantiomerization barrier	$\Delta G^\ddagger$
(4)	peak ratio:	enantiomer ratio	ee
(5)	peak assignment:	enantiomer configuration	*R*,*S*

lecular association and the magnitude of enantiomer discrimination, i.e., the chiral recognition factor, varied at random.[35] For chiral alkyl-substituted oxiranes a

$$\chi = -\Delta_{R,S}\Delta G^\circ / -\Delta G^\circ \qquad (2)$$

consistent relationship between the enantiomer configuration and the order of elution (cf. 5 in Scheme I) was observed for essentially all oxiranes[35] in accordance with a quadrant rule proposed earlier.[36] The magnitude and the sign of enantioselectivity, $\pm\Delta_{R,S}\Delta G^\circ$, between alkyl-substituted oxiranes and the nickel(II) chelates **7–17** could neither be predicted nor rationalized by simple molecular models.[36] This situation is further complicated by the temperature dependence of the enantioselective association equilibria.

A temperature-dependent reversal of the enantioselectivity (i.e., of the sign of $\Delta_{R,S}\Delta G^\circ$) for isopropyloxirane resolved on nickel(II) bis[3-(heptafluorobutanoyl)-8-methylene-(1*R*)-camphorate] (**18**) has been discovered recently.[15] This phenomenon arises from the temperature term in the Gibbs–Helmholtz equation as the result of enthalpy/entropy compensation[37–40] (the subscripts refer to enantiomers *R* and *S*):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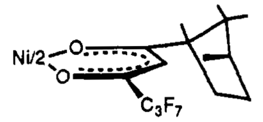
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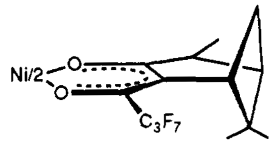
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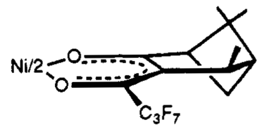
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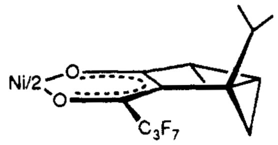
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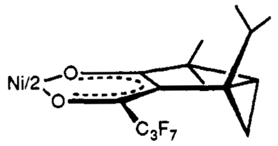
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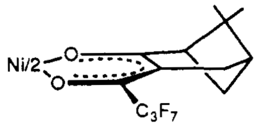
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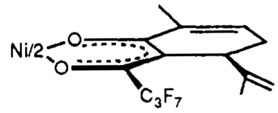
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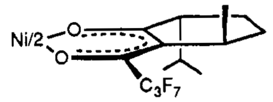
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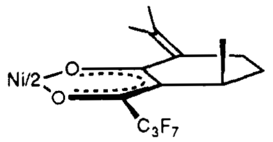
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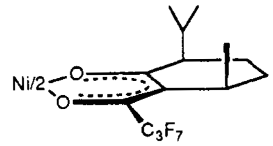
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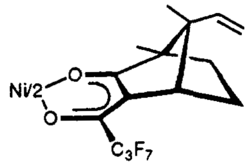
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$$RT \ln (K_R/K_S) = -\Delta_{R,S}\Delta G^\circ = -\Delta_{R,S}\Delta H^\circ + T\Delta_{R,S}\Delta S^\circ \qquad (3)$$

When $\Delta_{R,S}\Delta G^\circ = 0$ ($K_R = K_S$; no enantiomer separation), the isoenantioselective temperature T_{isoenant}, is reached. At T_{isoenant}, peak *coalescence* of the second

$$T_{\mathrm{isoenant}} = \Delta_{R,S}\Delta H^\circ / \Delta_{R,S}\Delta S^\circ \qquad (4)$$

kind occurs. Below it, the sign of enantioselectivity $\Delta_{R,S}\Delta G^\circ$ is governed by $-\Delta_{R,S}\Delta H^\circ$ and above it, by $\Delta_{R,S}\Delta S^\circ$. At the coalescence temperature T_{isoenant} (no enantiomer separation) the sign of enantioselectivity will change (peak *inversion* of the second kind). Gas chromatographic evidence for a reversal of enantioselectivity is shown in Figure 2.[15]

The coordination interaction between the enantiomers of isopropyloxirane and nickel(II) bis[3-(heptafluorobutanoyl)-8-methylene-(1*R*)-camphorate] (**18**) steadily decreases between 55 and 110 °C. While no

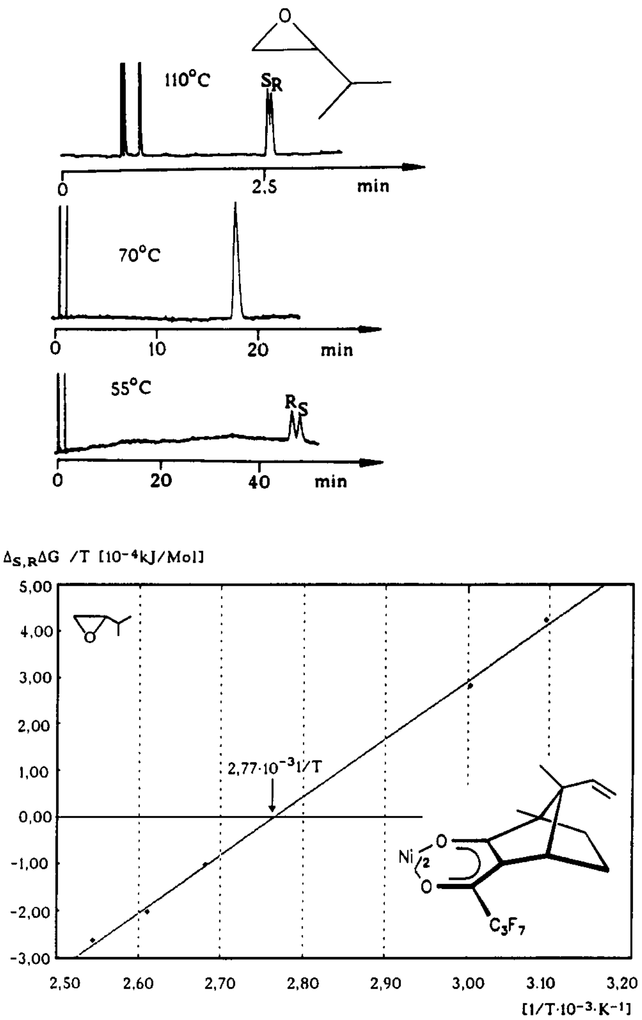
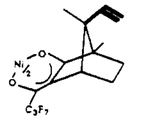
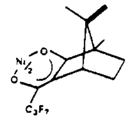
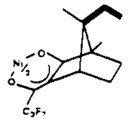


Figure 2. (Top) Temperature-dependent reversal of enantioselectivity for the enantiomers of isopropyloxirane by complexation gas chromatography on nickel(II) bis[3-(heptafluorobutanoyl)-(1*R*)-8-methylenecamphorate].[15] (Bottom) Linear van't Hoff plot and determination of the isoenantioselective temperature T_{isoenant}.

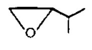
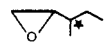
separation of the enantiomers is observed between 70 and 90 °C, the *S* enantiomer is eluted after the *R* enantiomer at 55 °C while the reverse is true at 110 °C. Above the coalescence region at T_{isoenant}, $+\Delta_{R,S}\Delta G°$ increases and so does separation. As expected from the thermodynamic origin of the phenomenon the van't Hoff plot of $R \ln (K_R/K_S)$ versus $1/T$ in 5-deg intervals between 55 and 110 °C is linear, yielding $-\Delta_{R,S}\Delta H° = 0.297$ kcal/mol and $\Delta_{R,S}\Delta S° = -0.82$ cal/mol deg, and $T_{\text{isoenant}} = 362$ K (~89 °C) (cf. Figure 2). Minor structural modifications of the metal chelate in a position opposite to the coordination site (at C8 of camphor) remarkably influences T_{isoenant} for isopropyloxirane (cf. Scheme II). Minor changes of oxirane configuration also dramatically influence T_{isoenant} (cf. Scheme III). Thus, for the diastereomeric *sec*-butyloxiranes one enantiomeric pair (unlike, u) shows a low T_{isoenant} similar to that observed for isopropyloxirane while for the other pair (like, l) T_{isoenant} is more than 500 degrees higher (cf. Scheme III).[15]

These findings are of importance for the understanding of mechanistic aspects of enantiomer recognition in chiral environments. Above T_{isoenant} preferential recognition of one enantiomer is caused by an entropy effect due to a higher degree of disorder in the resulting chemical interaction, while below T_{isoenant} enantiomer recognition is caused by the enthalpy effect of chemical bonding.[40] Thus, entropic contributions to chiral recognition represent an important parameter not to be neglected in mechanistic considerations (e.g., by molecular modeling) of enantioselectivity.

Scheme II. Enantioselective Thermodynamic Data for Isopropyloxirane and Different Nickel(II) Chelates Determined by Complexation Gas Chromatography[15]

	$-\Delta_{R,S}(\Delta H°)$ (cal/mol)	$\Delta_{R,S}(\Delta S°)$ (cal/mol K)	T_{iso} (°C)
	297	- 0,82	89
	270	- 0,80	64
	152	- 0,52	19

Scheme III. Enantioselective Thermodynamic Data for Isopropyl- and *sec*-Butyloxirane and Nickel(II) Bis[3-(heptafluorobutanoyl)-(1*R*)-camphorate] Determined by Complexation Gas Chromatography[15]

		$-\Delta_{R,S}(\Delta H°)$ (cal/mol)	$\Delta_{R,S}(\Delta S°)$ (cal/mol K)	T_{iso} (°C)
		270	- 0,80	64
	unlike	286	- 0,78	94
	like	179	- 0,20	622

Complexation gas chromatography not only represents a useful quantitative method to measure thermodynamic data of enantioselectivity but it can also be used to obtain kinetic data of enantiomerization (dynamic chromatography, cf. 3 in Scheme I).[32] Oxiranes, possessing configurationally labile chiral centers, may be prone to enantiomerization (change of configuration in a racemic mixture) or racemization (in enantiomerically enriched oxiranes) during enantiomer separation by complexation gas chromatography. In this case, characteristic chromatographic interconversion profiles are produced[32] from which inversion barriers can be derived by peak-shape analysis.[41,42] The occurrence of enantiomerization is recognized by the appearance of an overlapping zone (plateau) caused by inverted molecules between the terminal peaks originating from noninverted molecules. Two examples involving oxiranes are shown in Figure 3.

If enantiomerization is rapid only one peak will be observed (peak *coalescence* of the third kind).

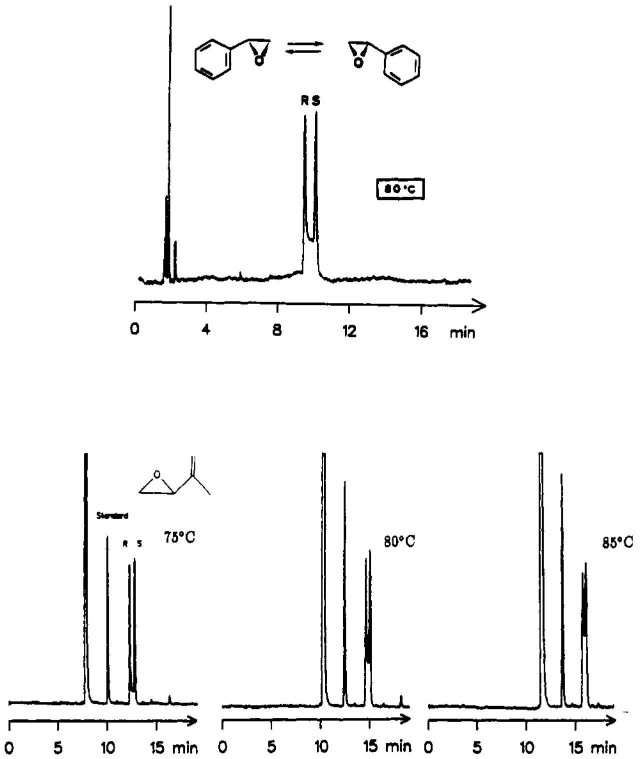
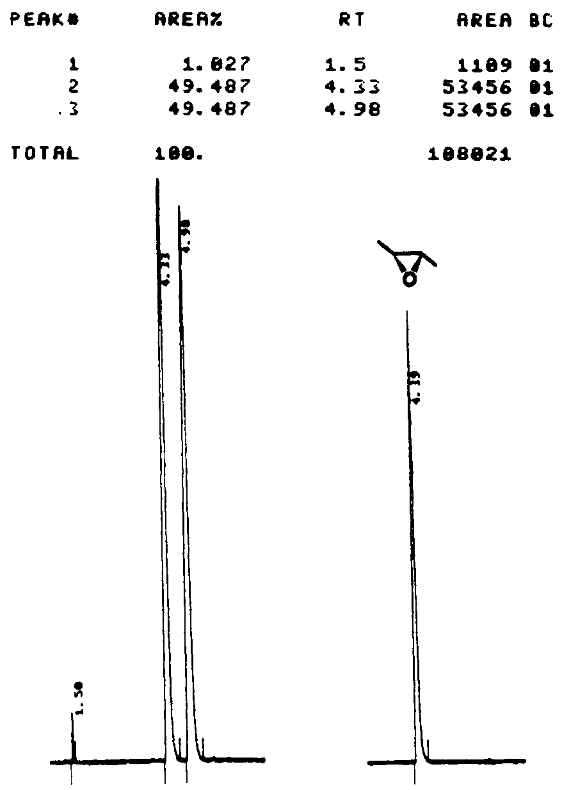


Figure 3. Interconversion profiles due to inversion of configuration in phenyloxirane and isopropenyloxirane observed by complexation gas chromatography on manganese(II) bis[3-(heptafluorobutanoyl)-(1*R*)-camphorate] (1).[15]

The observed interconversion profiles represent an important diagnostic tool for the recognition of configurational inversion. While the barrier of the enantiomerization of *trans*-2,3-dimethyloxirane via conrotary thermal ring opening has been determined to be $\Delta G^{\ddagger}$ = 54 kcal/mol using a single-pulse shock tube between 940 and 1030 K,[43] phenyloxirane[15] and isopropenyloxirane[44] undergo inversion of configuration during enantiomer separation on 1 already at low temperatures (cf. Figure 3). Since saturated alkyl-substituted oxiranes do not show this phenomenon, the metal-mediated enantiomerization is likely assisted by the presence of unsaturated substituents at the oxirane ring.

A mathematical peak-shape analysis based on the plate model of chromatography predicts that the rate of enantiomerization is *different* for the enantiomers in the presence of the chiral metal coordination compound.[41,42] Thus, the nonracemic metal chelate enantioselectivity mediates the extent of configurational change of interconverting oxiranes. The theory requires that the weak interacting oxirane enantiomer will be inverted at a higher rate as compared to the strong interacting oxirane. Since, however, the strong interacting oxirane has a longer residence time in the column an overall change of the racemic composition (enantiomeric enrichment) is absent due to the principle of microscopic reversibility.[41,42]

The quantitative gas chromatographic enantiomer separation is the prerequisite for the precise determination of enantiomeric compositions ee (cf. 4 in Scheme I)[45] in the synthesis of chiral aliphatic oxiranes. The method is particularly successful in two borderline cases, i.e., in the detection of minute enantiomeric excesses (e.g., ee ≈ 0%) and for the determination of traces of



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PEAK#      AREA%       RT        AREA BC

  1        1.027      1.5        1109 01
  2       49.487      4.33      53456 01
 .3       49.487      4.98      53456 01

TOTAL     100.                 108021
```

Figure 4. Enantiomer separation of *trans*-2,3-dimethyloxirane by complexation gas chromatography on nickel(II) bis[3-(heptafluorobutanoyl)-(1*R*)-camphorate] (3) at 80 °C. Integration was with a Spectra-Physics SP 4100 instrument. (Left) Racemic *trans*-2,3-dimethyloxirane (peak areas: first, 53456; second, 53456). (Right) *trans*-(2*R*,3*R*)-2,3-Dimethyloxirane (only one peak is identified).[43,49]

enantiomeric impurities (e.g., ee ≈ 100%).[45] The unambiguous determination of small ee's is indicated in experiments devoted to the amplification of optical activity under abiotic conditions, as in, e.g., the kinetic resolution of methyloxirane on metal-doped *d*- or *l*-quartz[46,47] where polarimetry may give ambiguous results.[48] Enantiomeric impurities as little as 0.1% and less must be detected in the synthesis of highly enantiomerically pure oxiranes. The results in Figure 4 demonstrate that the challenge of determining extraordinary values of ee of oxiranes can be met by the experiment.[43,49]

Thus, integration of the separated elution profiles of racemic *trans*-2,3-dimethyloxirane showed an unprecedented agreement of the peak areas, i.e. (arbitrary scale): 53456 versus 53456, ee = 0.0000%. The corresponding optically active compound, *trans*-(2*R*,3*R*)-2,3-dimethyloxirane, prepared without racemization from enantiomerically pure (2*R*,3*R*)-butane-2,3-diol by the chiral carbon pool approach,[1] showed only a single peak with no trace of the antipode present within the detection limit of the instrumental setup (~0.1%).[43,49]

A serious error in the determination of enantiomeric compositions may be caused by preferential loss of one enantiomer during the gas chromatographic separation process. Nonenantioselective decomposition of the oxirane leads to a depletion of the second eluted enantiomer which spends a longer time in the column. Enantioselective decomposition mediated by the chiral metal coordination compound may lead to a depletion of the first or the second eluted enantiomer. Both phenomena have been observed with strained ox-

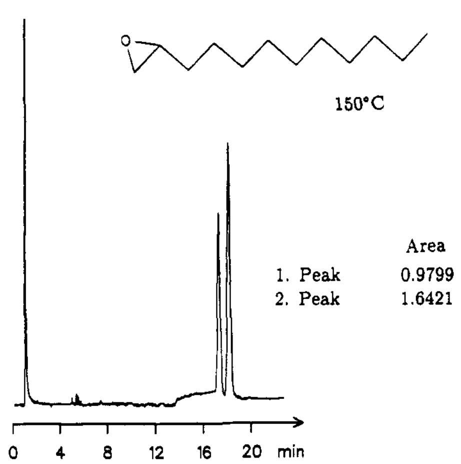


Figure 5. Deviation from the expected 1:1 ratio (*first* peak diminished) upon enantiomer separation of *racemic* *n*-decyloxirane on Chirasil-Dex 6 by complexation gas chromatography at 150 °C.[50]

iranes.[15,49] A deviation from the expected 1:1 ratio for racemic *n*-decyloxirane separated at 150 °C on Chirasil-Metal[33] is shown in Figure 5.[50]

Apart from the preferential depletion of the first eluted enantiomer a new broad elution zone, likely created by an unidentified reaction product, occurs. Reversing the chirality of the metal coordination compound will not alter the peak profiles since two enantioselective processes are involved, i.e., chromatographic resolution and kinetic resolution.

Still another metal-mediated enantioselective phenomenon involving a trans-disubstituted oxirane has been observed for the first time in chromatographic enantiomer separation.[50] It is thought to be related to different rates of coordination. As shown in Figure 6, the first eluted enantiomer shows a considerably broader peak width (recognized by the reduced peak height) as compared to the second eluted enantiomer although the peak areas are strictly identical. Since in chromatography peak broadening is related to the rate of the association process, the kinetics of coordination are obviously different for the two enantiomers. This result may imply that two different coordination sites of the (planar) metal chelate are involved in the exclusive association of each individual enantiomer.

In summary, the interaction of simple oxiranes with chiral nickel(II) bis[3-(heptafluorobutanoyl)-(1*R*)-camphorates], or derivatives thereof, may give rise to four different enantioselective processes: (1) enantioselective coordination (via distinct thermodynamics), peak ratio 1:1 (chromatographic resolution mediated by the chiral metal chelate) (cf. Figures 1 and 4); (2) enantioselective enantiomerization, terminal peak ratio 1:1 and plateau formation in between (different rate of enantiomerization mediated by the chiral metal chelate) (cf. Figure 3); (3) enantioselective reaction, peak ratio 1 $\neq$ 1 (kinetic resolution mediated by the chiral metal chelate) (cf. Figure 5); and (4) enantioselective coordination (via distinct kinetics), peak ratio 1:1, different peak width (different sites of coordination) (cf. Figure 6).

These enantioselective processes are easily detected in the chromatographic reactor. The observations will guide further investigations in static reaction devices (e.g., kinetic resolution).

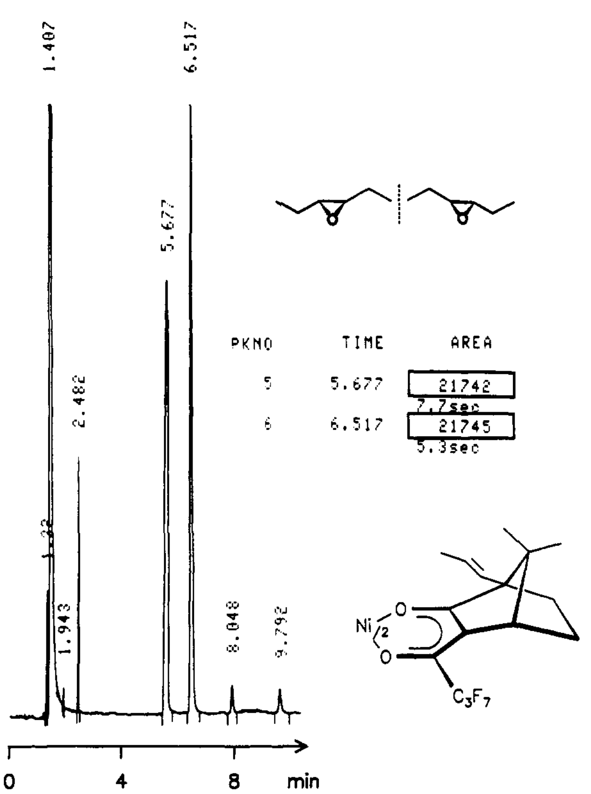


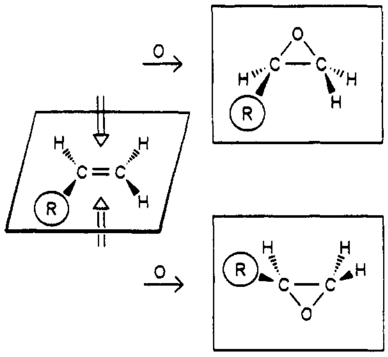
Figure 6. Deviation from the expected peak width (*first* peak broadened) upon enantiomer separation of racemic *trans*-2,3-diethyloxirane on nickel(II) bis[3-(heptafluorobutanoyl)-10-ethylidene-(1*S*)-camphorate] (5).[50]

The analytical enantiomer separation of simple oxiranes by complexation gas chromatography facilitates investigations on their metal-mediated enantioselective access. Examples are given in Figures 7, 8, and 10.

The chromatographic resolution of racemic oxiranes may also be performed by inclusion GC using cyclodextrin derivatives[51] and by HPLC.[52]

III. Access to Nonracemic Aliphatic Oxiranes via Metal-Mediated Epoxidation of Prochiral Alkenes

Asymmetric epoxidation of prochiral alkenes to nonracemic oxiranes may involve transition metal ions or not. Important metal-free asymmetric epoxidations of varying degree of enantiomer enrichment have been described inter alia by Wynberg et al.,[53-55] Juliá et al.,[56,57] Montanari et al.,[58,59] Davis et al.,[60,61] and Curci et al.[62]

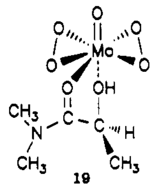


Transition metal-catalyzed epoxidations have been reviewed by Jørgensen,[63] and where appropriate, the enantioselective version of this fundamental reaction has also been mentioned. First reports on the catalytic asymmetric epoxidation of allylic alcohols appeared in 1977 from the groups of Sharpless[64] and Yamada.[65] Only moderate enantiomeric yields were observed in, e.g., the molybdenum(VI)-catalyzed asymmetric epoxidation of alkenes with *tert*-butyl hydroperoxide/Mo(O)$_2$(acac)L with L = *N*-ethylephedrine,[65] L-*N*-methylprolinol,[66] and sugar derivatives and tartrate esters.[67] However, as mentioned in the introduction, these investigations evolved into the spectacular Katsuki–Sharpless *tert*-butyl hydroperoxide/titanium(IV) dialkyl tartrate epoxidation system for allylic alcohols.[24] Extensive reviews are available on this versatile epoxidation reaction, its evolution, progress, and scope.[25,68]

Efficient asymmetric epoxidations mentioned above succeeded only with activated C–C double bonds (styrenes, conjugated ketones, quinones, allylic alcohols). The metal-mediated asymmetric epoxidation of simple unfunctionalized aliphatic alkenes still represents a particular challenge because of the lack of pendant groups favoring stereocontrol by conformational rigidity via auxiliary interactions. Higher enantiomeric bias can be attained in the asymmetric epoxidation of phenyl-substituted alkenes by chiral porphyrin metal(III) compounds (cf. section III.3) and, notably, of *Z*-disubstituted aromatic alkenes by (salen)manganese(III) complexes (cf. section III.4).

1. Stoichiometric Asymmetric Epoxidation Employing Chiral Oxodiperoxomolybdenum(VI) Reagents

Aided by the efficient enantiomer analysis of simple oxiranes by complexation gas chromatography (cf. section II) the enantioselective epoxidation of unfunctionalized aliphatic alkenes by a chiral oxodiperoxomolybdenum(VI)–hydroxy acid amide reagent was discovered by Kagan and Schurig et al. in 1979.[7] Employing the epoxidation reagent MoO(O$_2$)$_2$L of Mimoun[69] with L = (*S*)-*N*,*N*-lactic acid dimethylamide, **19**, prochiral aliphatic alkenes such as propene, (*E*)-2-butene and 2-methyl-2-butene were stoichiometrically transformed into oxiranes in nitrobenzene at 20 °C (1 bar) with chemical yields up to 70% and enantiomeric yields up to ee = 34% (cf. Table I).



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In all cases, the configuration of the dominant oxirane enantiomer formed was *R*. The ee of the oxiranes was continuously monitored during the whole reaction period and it remained invariant throughout the course of the reaction (cf. Figure 7). Thus, it was demonstrated that olefin epoxidation was asymmetrically induced (prochiral recognition) and that enantiomeric enrichment was not due a kinetic resolution taking place in a subsequent oxidation reaction (chiral recognition) (cf. Figure 7).[15] Consequently, the system exhibited product enantioselectivity and no substrate enantioselectivity (cf. section IV, however).

Table I. Asymmetric Epoxidation of Prochiral Olefins by Oxodiperoxomolybdenum(VI)–(*S*)-Lactic Acid Dimethylamide in Nitrobenzene at 20 °C (1 bar)

olefin	oxirane	ee (%)	abs config
propene	methyloxirane	28.8	*R*
1-butene	ethyloxirane	31.1	*R*
3-methyl-1-butene	isopropyloxirane	15.5	*R*
(*E*)-2-butene	*trans*-2,3-dimethyloxirane	34.8	2*R*,3*R*
2-methyl-2-butene	trimethyloxirane	5.1	*R*
		30.2 (−5 °C)	*R*

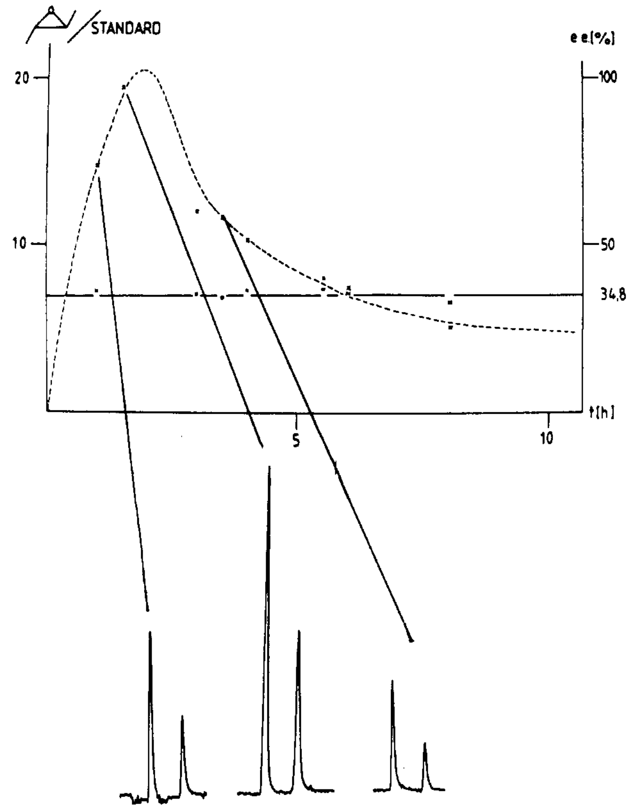


Figure 7. Stoichiometric enantioselective epoxidation of (*E*)-2-butene with oxodiperoxomolybdenum(VI)–(*S*)-lactic acid dimethylamide (**19**) in nitromethane at 22 °C: chemical versus enantiomeric yield.

A subsequent oxidation of the oxiranes by **19** was suppressed by an excess of olefin[7] or by adding aprotic polar additives such as amides.[70] For example, addition of 1 equiv dimethylformamide or (*S*)-lactic acid *N*,*N*-pentanedi-1,5-ylamide (PLA) to the reaction mixture did not affect the enantiomeric yield in the asymmetric epoxidation of (*E*)-2-butene while the chemical yield remained high.[71]

The rate of epoxidation increased by about 2 orders of magnitude along the series:[7] ethene (48 h) < 1-butene < (*E*)-2-butene < 2-methyl-2-butene (15 min), which coincided with the strength of π-complexation of these olefins by MoO(O$_2$)$_2$(HMPT).[72] In subsequent studies, a number of different chiral ligands L in MoO(O$_2$)$_2$L have been screened.[70,71,73] Of them, only (*S*)-*N*,*N*-lactic acid dimethylamide (DMLA) and (*S*)-lactic acid *N*,*N*-pentanedi-1,5-ylamide (PLA) induced the highest ee in the epoxidation of (*E*)-2-butene. In the reaction of

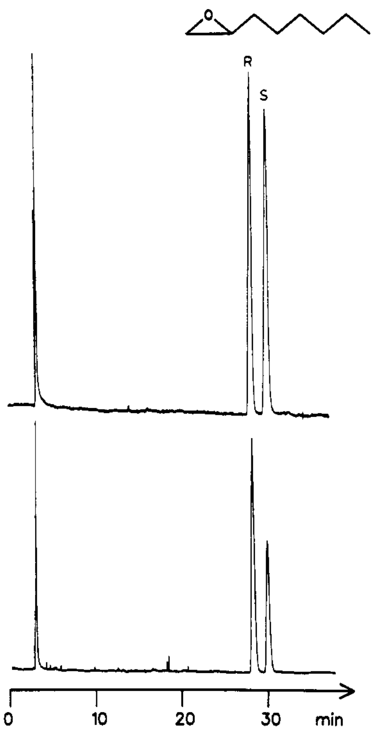
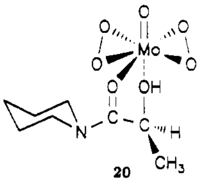


Figure 8. Determination of the enantiomeric yield of (*R*)-*n*-hexyloxirane formed by preparative asymmetric epoxidation of 1-octene with oxodiperoxomolybdenum(VI)–(*S*)-lactic acid *N*,*N*-pentanedi-1,2-ylamide (**20**) [ee = 27% (22 °C)] by complexation gas chromatography on manganese(II) bis[3-(heptafluorobutanoyl)-(1*R*)-camphorate] (**1**) (0.125 m in OV 101) at 70 °C. [Column: 40-m × 0.25-mm glass capillary. Carrier: 1 bar N_2.] (Top) Racemic sample. (Bottom) Enantiomerically enriched product.[71]

PLA with MoO_3 and H_2O_2 not only the expected yellow complex $MoO(O_2)_2$·PLA (**20**) was found but another



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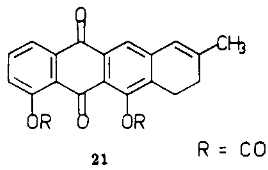
yellow-orange compound with a Mo/O ratio of 1:7, with better solution properties in organic solvents, had been isolated.[71] This complex of unidentified structure "Mo·PLA" produced ee = 55% for *trans*-2,3-dimethyloxirane at −20 °C.[71] Attempts to recycle the $MoO(O_2)_2$·L reagents by reoxidation with H_2O_2 for use in consecutive asymmetric epoxidations failed.[73]

The stoichiometric asymmetric epoxidation of simple aliphatic alkenes with chiral oxodiperoxomolybdenum(VI) complexes was also performed in a (gram scale) preparative way. Thus, epoxidation of 1-octene with oxodiperoxomolybdenum(VI)–(*S*)-lactic acid *N*,*N*-pentanedi-1,5-ylamide, $MoO(O_2)_2$·PLA (**20**), in dichloromethane for 13 h at 22 °C led to a 53% isolated yield of (*R*)-*n*-hexyloxirane with ee = 27% (cf. Figure 8).

With **20** also the preparative stoichiometric epoxidation of the prochiral tetracyclic anthracyclinone precursor **21** containing a methyl-substituted endocyclic double bond at −20 °C with ee = 53% was reported.[74] The *α*-epoxide **22** was formed as a major enantiomer and the absolute configuration was later proven by conversion to the daunosamin glycoside **23**.[75]



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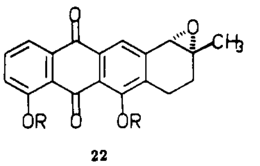
R = COC(CH3)3



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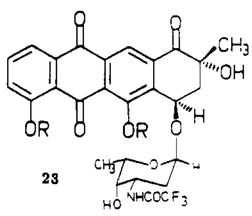

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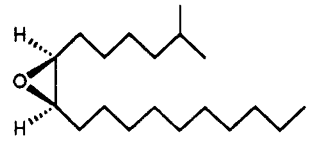
By employing the reagent in high dilution (in dichloromethane) and by cooling the reaction mixture to −70 °C the enantiomeric yield could be raised to ee = 73%.[76] However, the enantioselectivity was substrate dependent and exchanging the pivaloyl group (R) in **21** for methyl or hydrogen gave lower ee values (31–59%) and the exchange of the methyl group for an ethyl group in **21** also decreased the ee. Interestingly, a steady increase of the enantiomeric yield of the epoxide **22** was observed,[76] and this was attributed to different modes of enantiofacial discrimination in the oxygen transfer of the first and the second peroxo group of **20**. A similar interpretation has recently been advanced in enantioselective osmylation.[26]

Oxodiperoxomolybdenum(VI) complexes with L = dimethyl 2-piperidinosuccinate and dimethyl (−)-2-morpholinosuccinate have also been used for the attempted enantioselective epoxidation of (*Z*)-2-methyl-*n*-octadec-7-ene to the insect pheromone (−)-disparlure (**24**).[77]



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Some oxodiperoxomolybdenum(VI) reagents bearing chiral monodentate ligands, i.e., L = (−)-menthylphosphoric acid triamide, *N*,*N*-dimethyl-(−)-menthylamine *N*-oxide, (+)-(*α*-phenylethyl)phosphoric acid triamide and *N*,*N*-dimethyl-(+)-*α*-phenylethylamine *N*-oxide have shown only low asymmetric induction in the epoxidation of (*E*)-2-octene (chemical yield of epoxide: 8–70%, ee = 0.7–8.5%) at 25 °C in 1,2-dichloroethane.[78]

The crystal structure determination of chiral oxodiperoxomolybdenum(VI)–*N*,*N*-dimethyllactamide (**19**) revealed a distorted pentagonal-bipyramidal coordination sphere of molybdenum with two peroxo groups and the carbonyl oxygen of L in equatorial positions and the oxo ligand and the hydroxyl function of L in axial positions (cf. Figure 9).[79]

The mechanism of the stoichiometric epoxidation of alkenes by oxodiperoxomolybdenum(VI) complexes is still in doubt.[63,80] According to the Mimoun mechanism[81] an equatorial ligand is replaced by the olefin. Upon coordination, the alkene loses its nucleophilic character and, being electrophilic, becomes susceptible to nucleophilic attack by the peroxo group. Intramolecular 1,3-dipolar cycloaddition of the peroxo group to the coordinated electrophilic alkenes yields a five-membered dioxametallacycle which eventually collapses

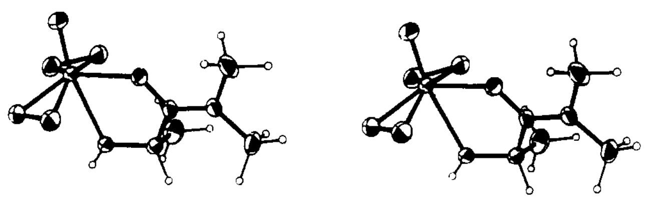
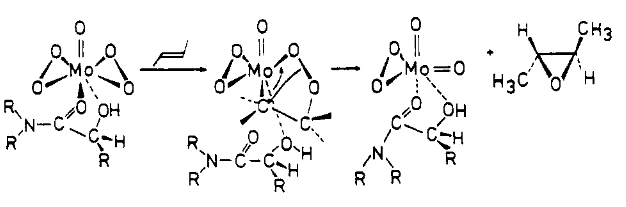


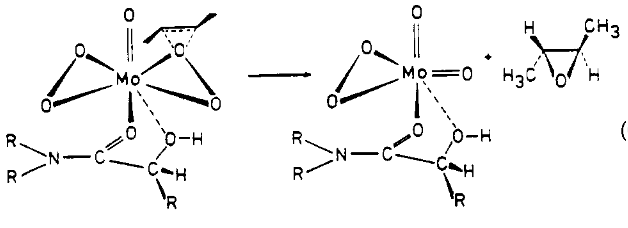
Figure 9. ORTEP plot of oxodiperoxomolybdenum(VI)-(*S*)-lactic acid dimethylamide (**19**).[79]

to a dioxoperoxomolybdenum(VI) species and the oxirane by a 1,3-dipolar cycloreversion.



(5)

The alkene–metal bonding can only be σ, since Mo(VI) is devoid of π-electrons for back-donation. An increase of the Lewis donor property of the alkene by alkyl substitution at the C–C double bond has increased the rate of epoxidation.[7,72] According to the Mimoun mechanism, the carbonyl function of the bidentate ligand must dissociate from the equatorial position. This is in contradiction to structural data, which show a very strong equatorial (2.07 Å) but a weak axial (2.36 Å) bond of the DMLA ligand in the oxodiperoxomolybdenum(VI) reagent **19**.[79] On the other side, the position of the hydroxyl group in different chiral hydroxy acid amides L exerts a strong influence on enantioselection,[73] and also monodentate chiral ligands L in $MoO(O_2)_2 \cdot L$ have been found to induce an (modest) asymmetric epoxidation although the mechanism of the oxygen transfer from the oxodiperoxomolybdenum(VI) complex to the olefin could not be established.[78] According to the Modena mechanism[82] the olefin is not coordinated to the oxodiperoxomolybdenum(VI) reagent at all, but is directly oxidized by electrophilic attack of the peroxo group, similar to the epoxidation of alkenes with peroxo acids.[83]



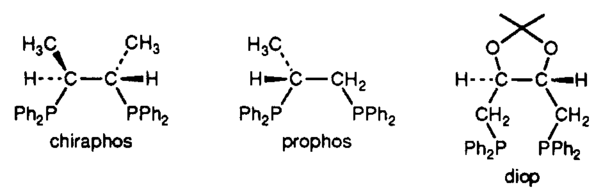
(6)

A third mechanism, advanced by Sheldon, involves molybdenum-diol complexes, in which the diol is thought to originate from the epoxide formed.[84]

Very high ee's up to 95% for the oxiranes were found when enantiomerically pure 1,2-alkanediols were added to the epoxidation reagent oxodiperoxomolybdenum(VI)-(*S*)-lactic acid *N*,*N*-pentanedi-1,5-ylamide, $MoO(O_2)_2 \cdot PLA$.[71,73] Further investigations led to the discovery of an efficient kinetic resolution of oxiranes catalyzed by oxodiperoxomolybdenum(VI)–hydroxy acid amide/diol reagents as discussed in section IV.

2. Catalytic Asymmetric Epoxidation Employing Chiral (Diphosphine)platinum(II) Complexes

The asymmetric epoxidation of propene and 1-octene with hydrogen peroxide catalyzed by chiral (diphosphine)platinum(II) complexes of composition $P_2{}^*Pt(CF_3)X$ ($P_2{}^*$ = chiraphos, prophos, diop; X = OH and CH_2Cl_2/BF_4) **25a–c** have been investigated and ee up to 41% was claimed via polarimetric evidence.[85,86] The rate of epoxidation was chiraphos > prophos ≫ diop. The following sets of equilibria have been formulated (ol = olefin).



$[(chiraphos)Pt(CF_3)(CH_2Cl_2)](BF_4)$ **25a**

$[(prophos)Pt(CF_3)(CH_2Cl_2)](BF_4)$ **25b**

$[(diop)Pt(CF_3)(CH_2Cl_2)](BF_4)$ **25c**

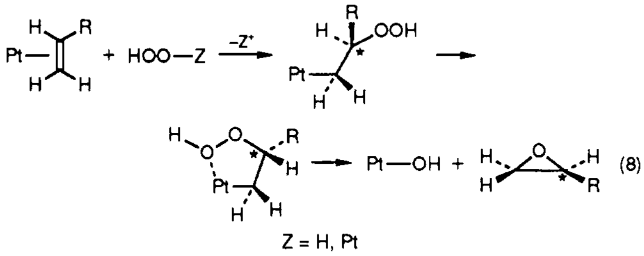
$$Pt\text{-}OH \rightleftharpoons Pt^+ + {}^-OH$$

$$^-OH + H_2O_2 \rightleftharpoons {}^-OOH + H_2O$$

$$Pt^+ + {}^-OOH \rightleftharpoons Pt\text{-}OOH$$

$$Pt^+ + ol \rightleftharpoons Pt(ol)^+ \tag{7}$$

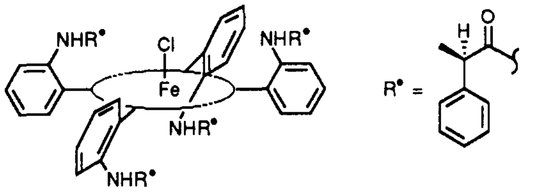
Epoxide formation is proposed to arise from external nucleophilic attack of hydroperoxide on the π-coordinated alkene to produce a platinum alkyl hydroperoxide existing in an open chain structure (giving a ketone) and a dioxametallacycle (giving the oxirane). The catalysts are air stable and can be recovered unchanged.[85,86] The use of H_2O_2 is useful from a practical point of view. There is a consistent relationship in regard to the preferred configuration of the oxirane formed in each catalytic system. In comparison to the asymmetric epoxidation of 1-alkylcyclohexenes by *tert*-butyl hydroperoxide with a $Mo(O)_2(acac)_2$ catalyst in the presence of diisopropyl (+)-tartrate producing ee's up to 10%,[67] the higher ee's for simple oxiranes observed with (diphosphine)platinum catalysts are thought to arise from the stereochemical rigidity of, e.g., the chiraphos system favoring efficient discrimination in the enantiofacial π-complexation of the prochiral alkene to the metal.[86]



At the first sight, the incomplete enantioselectivity observed in metal diphosphine-catalyzed oxidation of alkenes contrasts that of asymmetric hydrogenations. Yet, the highly enantioselective asymmetric hydrogenation and asymmetric Sharpless epoxidation pertains only to functionalized alkenes containing an auxiliary anchoring group favoring high ee's and rates via chelation.

3. Catalytic Asymmetric Epoxidation Employing Chiral (Porphyrinato)metal(III) Compounds

Although microsomal epoxidation of simple aliphatic alkenes is only moderately enantioselective and is strongly dependent on mammalian species and enzyme induction,[10] high enzymatic enantioselectivities are observed with styrene[87] and with aromatic hydrocarbons.[88] Following the report of Groves et al.[89] and Chang et al.[90] that iron(III) porphyrin catalysts are model compounds for cytochrome P-450 for the epoxidation of alkenes, the asymmetric epoxidation of unfunctionalized aromatic alkenes with iodosylarenes, catalyzed by iron and manganese complexes of chiral (nonracemic) porphyrins, were investigated by a number of groups. Thus, Groves et al. prepared the chiral "picket" porphyrin **26** starting from 5α,10β,15α,20α-tetrakis(*o*-aminophenyl)porphyrin of Collman et al.[91] by amide formation with (*R*)-2-phenylpropanoyl chloride.[92] In the $\alpha\beta\alpha\beta$ atropisomer the faces of the iron porphyrin complex are topologically identical (homotopic). The catalytic asymmetric epoxidation of styrene and 1-octene with iodosylbenzene in the presence of **26** gave ee = 31% and ee = 9%, respectively.[92] In order to increase the steric hindrance in the amide portion of the iron porphyrin, the catalyst **27** was prepared which contains axially chiral binaphthylcarboxyamido residues and the enantiomeric yield was raised to ee = 48% (phenyloxirane) and to ee = 20% (*n*-hexyloxirane).[92]



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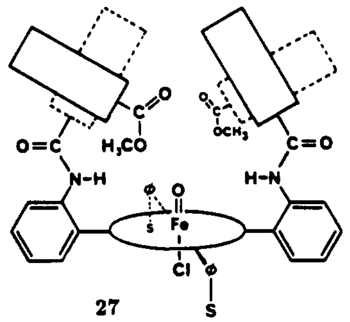

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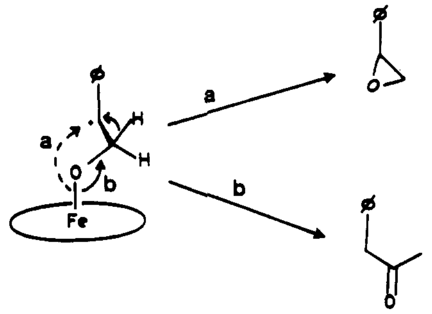
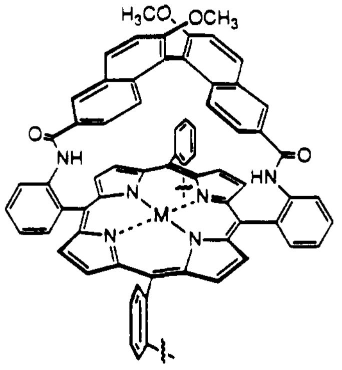
A reactive iron–oxo intermediate was proposed in the iron porphyrin-catalyzed oxygen transfer to the alkene and not only the oxirane but aldehyde was also formed as expected from the proposed mechanism of the epoxidation.[92,93] The $\alpha\beta\alpha\beta$ "basket-handle" porphyrin **28** containing two rigid axially chiral binaphthyl bridges was used by Groves et al. as iron(III) chloride or manganese(III) chloride porphyrin catalyst (1 equiv) with iodosylbenzene (100 equiv) as oxidant for the asymmetric epoxidation of olefins (1000 equiv) yielding ee = 30% for phenyloxirane and ee = 32% for *trans*-2-ethyl-3-methyloxirane.[94] The ee of *cis*-2-methyl-3-phenyloxirane was as high as 72%.[94]



(9)

The asymmetric epoxidation of alkenes catalyzed by a "basket-handle" and two "picket" iron porphyrins containing L-phenylalanine residues **29–31** was investigated by Mansuy et al.[95,96] The two $\alpha\beta\alpha\beta$ "picket" iron porphyrins catalyzed the epoxidation of *p*-chlorostyrene with iodosylbenzene with ee = 12 and 21% for the (*S*)-oxirane, respectively, while the "basket-handle" iron porphyrin containing the same amino acid produced ee = 50% for the (*R*)-oxirane.[95]

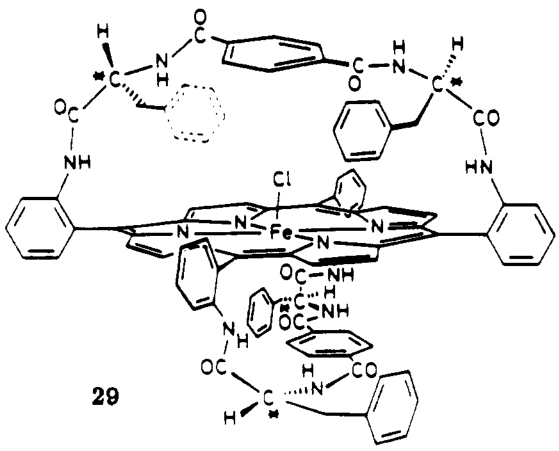


28 M = Mn, Fe

The iron(III)–chloro complexes of the "twin coronet" porphyrins **32** catalyzed the asymmetric epoxidation of styrene and derivatives with iodosobenzene as oxidant.[97,98] The best enantiomeric yields were obtained in the oxidation of electron-deficient olefins and the highest ee = 89% was recorded in the case of 2-nitrostyrene. This is the highest value reported so far in the epoxidation with chiral porphyrin catalysts.

Unfortunately, these previous porphyrin catalysts suffer from stability problems due to the presence of electron-donating substituents on the phenyl groups, which sensitize the porphyrin toward oxidative degradation. The highest turnover number of 500 with slight decomposition of the catalyst was achieved in the case of complex **28**. On the contrary, the manganese(III) complex of the "chiral wall" 5α,10β,15α,20β-tetrakis[(*R*)-1,1′-binaphthyl-2-yl]porphyrin **33** proved to be robust under oxidative conditions.

The complex catalyzes the asymmetric epoxidation of styrene or (*Z*)-1-phenylpropene with ee = 20 and 40%, respectively, with hypochlorite as oxidant in a two-phase system.[99] Regeneration of the catalyst after 250 turnover numbers did not change the ee and after 2800 catalytic cycles the catalyst showed still 86% of the UV absorption band at 479 nm.[99]



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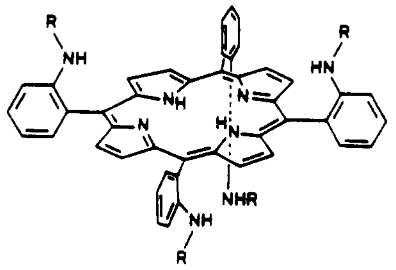
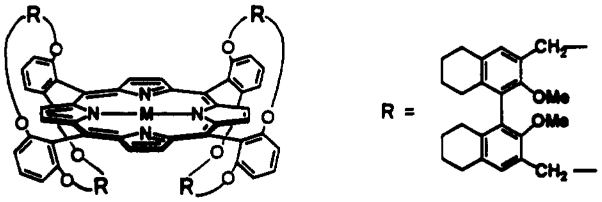
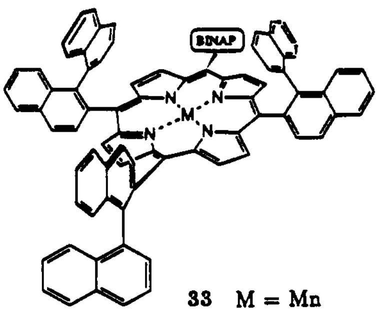


30 R = $COCH(CH_2Ph)NHCO_2Bu$

31 R = $COCH(CH_2Ph)NH_2$



32 M=FeCl



33 M = Mn

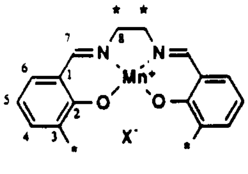
Solvent effects on the epoxidation of styrene with sodium hypochlorite were determined using a bovine serum albumin-modified manganese(III) tetraphenylporphyrin system, which showed rather low enantioselectivity.[100]

The results on metal porphyrin-catalyzed asymmetric epoxidation of unfunctionalized alkenes demonstrate that efficient prochiral recognition can be affected via nonbonded interactions. The catalysts represent interesting synthetic model compounds for the asymmetric oxygen transfer to prochiral alkenes by cytochrome P-450.[101]

4. Catalytic Asymmetric Epoxidation Employing Chiral (Salen)manganese(III) Complexes

Although in the following systems mainly phenyl-substituted alkenes are involved in the metal-mediated asymmetric epoxidation, these enantioselective systems are nevertheless mentioned as they might in principle prove useful also for aliphatic alkenes.

Following the report of Kochi et al. that the cationic (salen)manganese(III) complex 34 was an efficient catalyst for the epoxidation of alkenes[102] the asymmetric epoxidation of unfunctionalized aromatic alkenes with iodosylbenzene, iodosylmesitylene, or sodium hypochlorite, catalyzed by chiral (nonracemic) C_2-symmetric manganese(III) Schiff's base derivatives of 34, i.e., 35–42, has been investigated by Katsuki et al.[103-106] and Jacobsen et al.[107-111]



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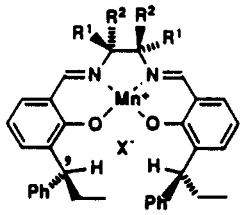
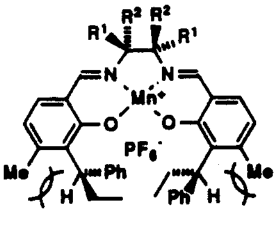
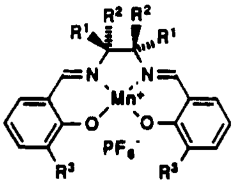


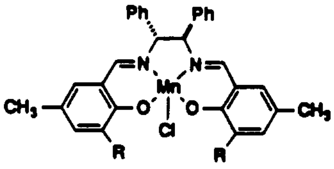
35: R^1=Ph, R^2=H, X=AcO
36: R^1=H, R^2=Ph, X=AcO



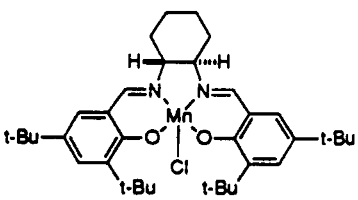


37: R^1=Ph, R^2=H
38: R^1=H, R^2=Ph

39: R^1=Ph, R^2=H, R^3=H
40: R^1=H, R^2=Ph, R^3=t-Bu



41: R=t-Bu

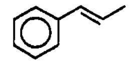
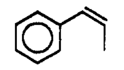


42

The salen-based catalysts offer an important advantage over known chiral porphyrin systems because the asymmetric centers are located closer to the metal center than those in porphyrin complexes, resulting in better stereochemical control in the epoxidation step.

The catalysts of Katsuki et al. 35–38 contain four pairwise homochiral (*SS* and *RR*) stereogenic centers in various diastereomeric combinations (i.e., *SS*/*SS*, *RR*/*RR*, *SS*/*RR* and *RR*/*SS*). In 37 and 38 a fixed conformation along C(3)–C(9) is created by vicinal

Table II. Asymmetric Epoxidation of (*E*)- and (*Z*)-1-Phenylpropene by 35–41

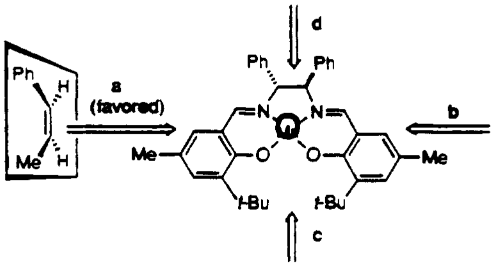
olefin	catalyst	ee (%)	abs config	yield (%)
	**35**	3	1*S*,2*S*	59
	36	32	1*R*,2*R*	61
	37	7	1*R*,2*R*	32
	38	17	1*R*,2*R*	25
	39	20	1*S*,2*S*	93
	**36**	44	1*R*,2*S*	26
	37	68	1*S*,2*R*	12
	40	84	1*R*,2*S*	88
	41	82	1*R*,2*S*	87

methyl substitution of the aromatic ring. In the catalysts of Jacobsen et al. **39–42** the homochiral stereogenic centers at C(9) and C(9′) are replaced by (achiral) hydrogens **39** or by bulky *tert*-butyl groups **40–42**, respectively. Typical results for the epoxidation of (*E*)- and (*Z*)-1-phenylpropene are summarized in Table II.[106]

From the inspection of Table II it follows that the highest asymmetric bias is achieved for the *Z*-olefin. For this substrate the stereogenic centers at C(9) and C(9′) in **35–38** have only little influence on enantioselectivity and they mainly serve as steric bulk as the *tert*-butyl groups in **40–42** at the same position. The comparison of the results for the *E*-olefin shows that the diastereomeric relationship of the stereogenic centers in **35** and **37** is unfavorable while that in **36** and **38** is favorable in determining a high enantiofacial discrimination of the *E*-olefin (prochiral recognition). In the epoxidation of (*Z*)-1-phenylpropene with **36** both *cis*- and *trans*-2-methyl-3-phenyloxirane with nearly identical ee (~45%) and consistent configuration at C(2) were formed, indicating the intervention of a free-radical intermediate as proposed by Kochi et al.[102] at the phenyl-substituted carbon atom C(3).[106]

The addition of donor ligands such as 2-methylimidazole and pyridine *N*-oxide alters the enantioselectivity and the chemical yield of the asymmetric epoxidation.[104] Another advantage of added donor ligands is that the decomposition of the epoxides formed is suppressed.[106]

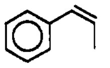
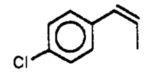
The sign and magnitude of asymmetric induction (prochiral recognition) displayed by **40** with *Z*-olefins has been rationalized by side-on perpendicular approach of the alkene to an oxomanganese(V) intermediate.[107,108] Two structural features of **40** are crucial to its selectivity. The bulky *tert*-butyl groups prevent the alkene approach from (c) away from the chiral diimine bridge while the C_2 symmetry of the chiral diimine bridge discriminates approach a (favorable) from approach b (unfavorable). Approach d is believed to be disfavored for steric reasons.[109]



(10)

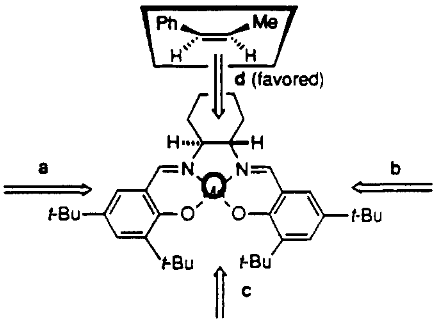
This model predicts that *Z*-disubstituted olefins or bulky terminal olefins should give the highest ee's with **40**, which is proved by the experiment.

Table III. Asymmetric Epoxidation of *Z*-Disubstituted Olefins by 42

olefin	ee (%)	yield (%)
	92	84
	92	67

To simplify the synthesis of the chiral (salen)manganese(III) complexes, methyl groups were introduced in C(5) and C(5′) position, yielding the readily accessible catalyst **41**. The selectivity and stability of **41** depends on the presence of bulky groups at C(3) and C(3′). The complex derived from 5-methylsalicylaldehyde (R = H, cf. formula **41**) catalyzes the epoxidation of (*Z*)-1-phenylpropene with only ee = 0–3% and approximately 5 catalyst turnovers, while the reaction with **41** resulted in ee = 82% and 35 catalyst turnovers.[108]

Very high enantioselectivities with *Z*-disubstituted alkenes are achieved with complex **42** (cf. Table III) where the chiral 1,2-diamino-1,2-diphenylethane in **40** was replaced by chiral *trans*-1,2-diaminocyclohexane, favoring approach d. A second set of *tert*-butyl groups was introduced at C(5) and C(5′) disfavoring approaches a and b of the olefin, resulting in a reversal of enantioselectivity as compared to the reaction with **40**.



(11)

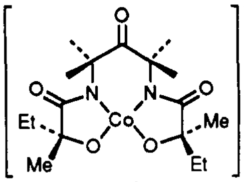
Consistent with the side-on approach model, *E*-olefins tend to be poor substrates for **42**, being epoxidized slowly and with very low selectivity.[109] The high enantioselectivity of **42** in catalytic asymmetric epoxidations with *Z*-disubstituted olefins was used for the preparative synthesis of epoxychroman chiral building blocks employing commercially available household bleach as oxygen source.[110]

In a study on electronic tuning of asymmetric catalysis, Jacobsen et al. introduced typical Hammett donor and acceptor substituents at C(5) and C(5′) in **40** and **42**. The highest enantioselectivity was obtained with the OMe substituent.[111] The effects observed were interpreted according to a Hammond postulate argument, where increase in selectivity is attributed to more product-like transition state structure in the olefin oxidation step.[111]

5. Catalytic Asymmetric Epoxidation Employing Chiral Cobalt(III) Complexes

Seven chiral square-planar cobalt(III) complexes **43–49** were prepared and used for the asymmetric epoxidation of styrenes with iodosylbenzene as oxidant.[112]

Enantioselectivity turned out to be low, however, with ee = 17% for 2-phenyl-(2′-chloro)oxirane being the highest figure reported.



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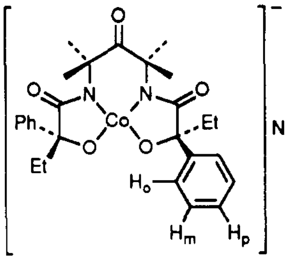

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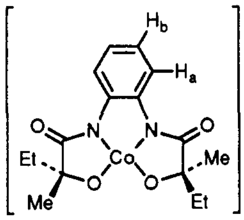

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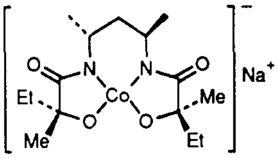

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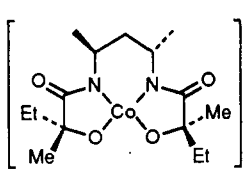

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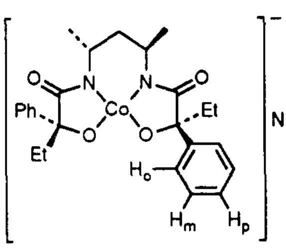

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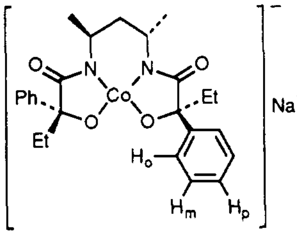

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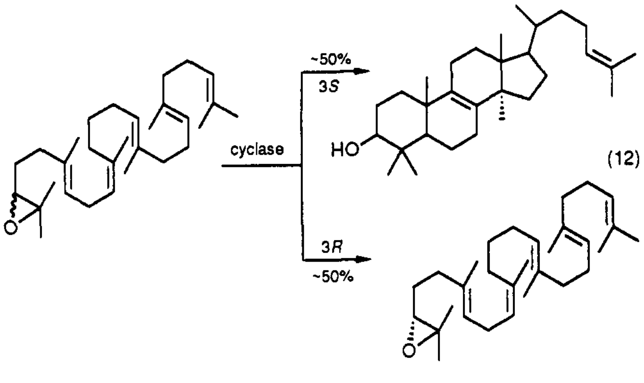
IV. Metal-Mediated Kinetic Resolution of Racemic Aliphatic Oxiranes

Metal-mediated kinetic resolution of chiral aliphatic oxiranes (chiral recognition) represents an interesting alternative to asymmetric epoxidation (prochiral recognition) because racemic oxiranes are easily accessible and often produced at a large industrial scale (e.g., methyloxirane) rendering the loss of 50% of the antipode acceptable. In a kinetic resolution experiment the enantiomeric yield must be balanced against the chemical yield. In the ideal case, a 50% turnover produces ee = 100% for the unreacted educt enantiomer. A nearly complete kinetic resolution has been observed for racemic 2,3-oxidosqualene via cyclization to lanosterol by cyclase.[113]

A highly competent survey on kinetic resolution has been advanced by Kagan and Fiaud.[114] In the formalism describing kinetic resolution the stereoselectivity factor $s = k_R/k_S$, i.e., the ratio of the reaction rates of the educt enantiomers, plays a key role. At a range of $s \geq 7$, kinetic resolutions become preparatively useful.

Both highly efficient enzymatic kinetic resolutions[16-20] and nonenzymatic kinetic resolution via polymerization[13,14] have been described involving simple aliphatic oxiranes. It is remarkable that for a hetero analogue, i.e., racemic methylthiirane the *s* factor was close to 20 when employing the atropisomeric chiral initiator [(*S*)-2,2′-dihydro-1,1′-binaphthyl]diethylzinc.[115,116]



(12)

The metal-mediated kinetic resolution of simple unfunctionalized oxiranes, excluding polymerization, will be reviewed in this section.

The kinetic resolution of racemic aliphatic oxiranes mediated by oxodiperoxomolybdenum(VI)–hydroxy acid amide/chiral diol reagents, yielding ee up to 99% for *trans*-2,3-dimethyloxirane,[117] has been found accidentally. In efforts to quench decomposition of oxiranes formed in the molybdenum(VI)-mediated epoxidation of alkenes (cf. section III.1) the addition of a nonracemic diol led to an unprecedended increase of the ee of the oxirane.[73] It was then found that oxodiperoxomolybdenum(VI)–hydroxy acid amide/chiral diol reagents are effective in the kinetic resolution of racemic aliphatic oxiranes.[73,118] The ee of the oxiranes was conveniently determined by complexation gas chromatography (cf. section II). This method readily permitted the determination of chemical yield, enantiomeric yield, and absolute configurations of the volatile oxiranes by simple head-space analysis throughout the reaction. This is demonstrated in Figure 10 for the kinetic resolution of *trans*-2,3-dimethyloxirane with $MoO(O_2)_2$·(*S*)-PLA/(2*S*,3*S*)-butane-2,3-diol at a *molar* ratio of 5:1:2 in 1,2-dichloroethane.[117] Figure 11 shows the relationship between the enantiomeric yield and the chemical yield of this kinetic resolution. The dependence of the enantiomeric and the chemical yield on the molar ratio in the kinetic resolution of ethyloxirane with $MoO(O_2)_2$·(*S*)-PLA/(2*R*,3*R*)-butane-2,3-diol has been determined.[118] Thus, low reagent concentrations (7:1:2) increase the chemical yield and decrease the enantiomeric yield, while for high reagent concentrations (4:1:2) the opposite is true.

For the molybdenum-mediated kinetic resolution of phenyloxirane a number of reaction products have been identified by GC/MS analysis.[15,119] The main reaction is the oxidative cleavage of the oxirane to carbonyl compounds.

It can be seen from Figure 11 that the oxidation of the oxirane is not totally stoichiometric but requires the presence of free dioxygen.[70,118,119] Thus, an experiment performed in a nitrogen atmosphere resulted only in a stoichiometric decomposition of the oxirane.[117] Activation of dioxygen in the presence of diols by the oxodiperoxomolybdenum(IV)–pyridine-2-carboxylate *N*-oxide anion has recently described also by Di Furia and Modena et al.[120]

Enantioselectivity in the kinetic resolution of oxiranes with oxodiperoxomolybdenum(VI)–hydroxy acid amide/

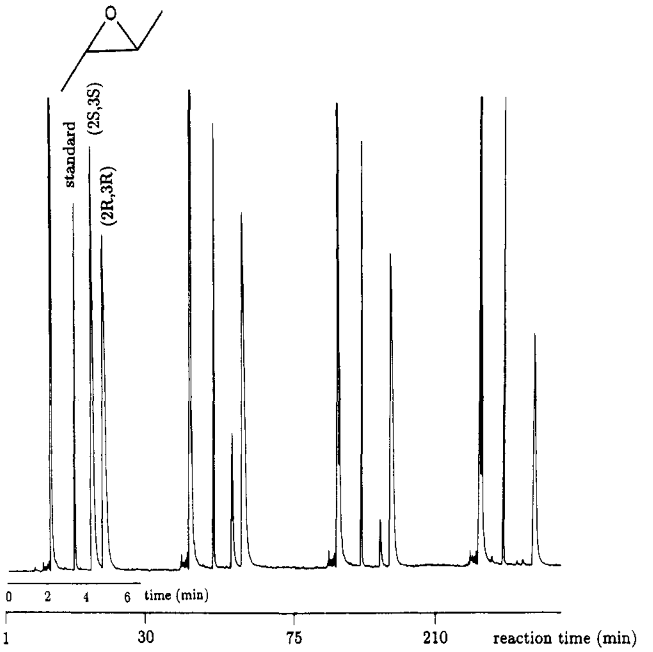


Figure 10. Determination of the enantiomeric and chemical yield of *trans*-2,3-dimethyloxirane, recovered after kinetic resolution with $MoO(O_2)_2$·(*S*)-PLA/(2*S*,3*S*)-butane-2,3-diol, by complexation gas chromatography on nickel(II) bis[3-(heptafluorobutanoyl)-(1*R*)-camphorate] (3) (0.125 m in SE 30) at 70 °C. [Column: 25-m × 0.25-mm fused silica capillary. Carrier: 1 bar N_2.[50]]

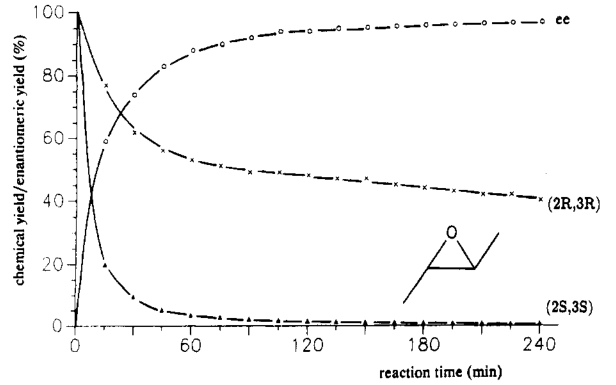


Figure 11. Enantiomeric yield versus chemical yield in the kinetic resolution of *trans*-2,3-dimethyloxirane by $MoO(O_2)_2$·(*S*)-PLA/(2*S*,3*S*)-butane-2,3-diol at a stoichiometric ratio of 5:1:2 in 1,2-dichloroethane at 23 °C.[50]

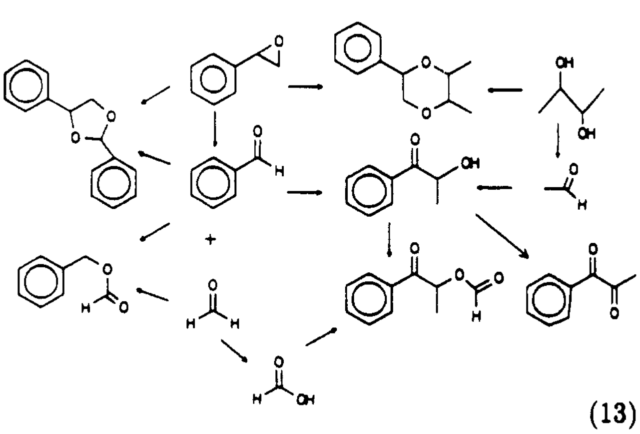


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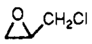
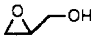
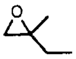
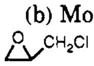
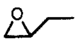
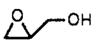
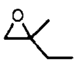
Table IV. Enantiomeric Yield, Absolute Configuration, and Yield of Oxirane Recovered after Kinetic Resolution with Oxodiperoxomolybdenum(VI)-Lactic Acid Amide/(3*S*)-2-Methylbutane-2,3-diol Reagents

oxirane	reaction time (min)	ee (%)	yield (%)
(a) $MoO(O_2)_2$·(*S*)-DMLA/(3*S*)-2-Methylbutane-2,3-diol			
	180	53 (*S*)	42
	120	91 (*R*)	26
	120	78 (*R*)	27
	60	86 (*R*)	13
	120	84 (*R*)	60
	240	99.6 (*R*,*R*)	46
	120	54 (*R*)	63
(b) $MoO(O_2)_2$·(*S*)-PLA/(3*S*)-2-Methylbutane-2,3-diol			
	240	45 (*S*)	42
	180	66 (*R*)	44
	180	63 (*R*)	37
	60	90 (*R*)	14
	180	55 (*R*)	74
	240	80 (*R*,*R*)	68
	120	37 (*R*)	60

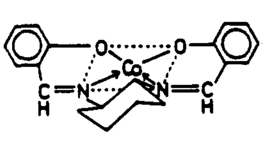
chiral diol reagents is clearly controlled by the chirality of the diol.[118] Inverting the chirality of the diol led to a reversal of enantioselectivity for the unreacted oxirane, and with racemic diol or in the absence of diol the oxiranes were not resolved.[118]

Table IV summarizes the results for the kinetic resolution of a series of simple oxiranes performed with $MoO(O_2)_2$·(*S*)-DMLA/(3*S*)-2-methylbutane-2,3-diol and $MoO(O_2)_2$·(*S*)-PLA/(3*S*)-2-methylbutane-2,3-diol in 1,2-dichloroethane at 23 °C.[121]

Temperature-dependent studies showed an optimum of the enantiomeric yield at 30 °C.[118,119] A preparative kinetic resolution was performed with *trans*-2,3-dimethyloxirane by $MoO(O_2)_2$·(*S*)-PLA/(3*S*)-2-methylbutane-2,3-diol. Workup of this reaction gave a 60% isolated yield of (2*R*,3*R*)-dimethyloxirane with ee = 83%.[121]

The metal-mediated kinetic resolution of small aliphatic oxiranes such as methyl- and ethyloxirane has been investigated by Tsuruta et al.[122,123] Low enantiomeric yields (based on polarimetric evidence) of recovered methyl- and ethyloxirane were achieved in the rearrangement of the epoxides to acetone and ethyl methyl ketone, respectively, mediated by a chiral (salen)cobalt(I) complex obtained by reduction of the Co(II) complex **50** with $LiAlH_4$ or butyllithium.[122,123]

The access to chiral oxiranes in kinetic resolution may not only be based on the epoxide employed as the educt, but may arise from the epoxide formed enantioselectively as the product. Thus, Tsuruta et al. used the (salen)cobalt(II) complex **50** as catalyst in the kinetic resolution of halohydrins to give chiral oxiranes as reaction products. Cyclization of propylene chloro- or



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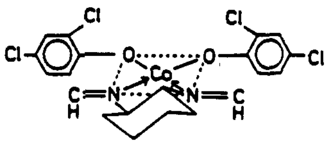

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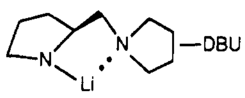
bromohydrins in presence of chiral **50** and K_2CO_3 yielded methyloxirane with ee = 27% at 40% conversion.[124,125] Modification of the complex and extension of the reaction to other oxiranes resulted in lower enantioselectivities.[125,126] Higher enantioselectivities were observed by enantiotopos discrimination of achiral 1,3-dichloro-2-propanol with **51**, yielding epichlorohydrin with ee up to 60% in a reaction based on prochiral recognition.[126]

A chiral lithium amide prepared from (*S*)-2-(pyrrolidin-1-ylmethyl)pyrrolidine, **52**, was applied in the kinetic resolution of oxiranes by Asami et al.[127] This reaction showed a high ee for cis-disubstituted oxiranes such as *cis*-2-methyl-3-*n*-hexyloxirane and *cis*-2-methyl-3-phenyloxirane (ee = >95%) but gave only moderate chemical yields (31%). In efforts to mimic enzymatic kinetic resolution of 2,3-oxidosqualene,[113] Yamamoto et al. reported on a kinetic resolution of 2-methylhept-2-ene-6-one oxide by a chiral organoaluminum reagent derived from (*R*)-binaphthol.[128] The nearly completely resolved keto epoxide was employed in the synthesis of juvenile hormone.[129] The kinetic resolution of 1-phenyl-1,2-epoxycyclohexane (ee = 52%) was also investigated.[128]



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Note Added in Proof

Very recently, interesting contributions relevant to section III.3 appeared in the literature.

Catalytic asymmetric epoxidation of unfunctionalized alkenes using the first D_4-symmetric metallotetraphenylporphyrin. Halterman, R. L.; Jan, S.-T. *J. Org. Chem.* **1991**, *56*, 5253.

Synthesis of chiral bitetralin-strapped twin coronet porphyrins. Catalytic and asymmetric epoxidation of styrene derivatives. Naruta, Y.; Ishihara, N.; Tani, F.; Maruyama, K. *Chem. Lett.* **1991**, 1933.

Asymmetric epoxidation of olefins catalyzed by manganese complexes of chiral "strapped" porphyrins with diastereotopic faces. A novel strategy for stereochemical modeling of the active site of cytochrome P-450. Konishi, K.; Oda, K.; Nishida, K.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1992**, *114*, 1313.

Photocatalytic enantiodiscriminating oxygenation with cyclodextrin-linked porphyrins and molecular oxygen. Weber, L.; Imiolczyk, I.; Haufe, G.; Rehorek, D.; Hennig, I. *J. Chem. Soc., Chem. Commun.* **1992**, 301.

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References

(1) Schurig, V.; Koppenhoefer, B.; Bürkle, W. *J. Org. Chem.* **1980**, *45*, 538.
(2) Scott, J. W. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 4, pp 1–226.
(3) Barron, L. D.; Vrbancich, J. *Mol. Phys.* **1983**, *11*, 1.
(4) Gedanken, A.; Schurig, V. *J. Phys. Chem.* **1987**, *91*, 1324.
(5) Rodger, A. *J. Am. Chem. Soc.* **1988**, *110*, 5941.
(6) Koppenhoefer, B.; Schurig, V. *Organic Syntheses* **1988**, *66*, 160.
(7) Kagan, H. B.; Mimoun, H.; Mark, C.; Schurig, V. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 485.
(8) May, S. W. *Enzyme Microb. Technol.* **1979**, *1*, 15.
(9) Ohta, H.; Tetsukawa, H. *J. Chem. Soc., Chem. Commun.* **1978**, 849.
(10) Wistuba, D.; Nowotny, H.-P.; Träger, O.; Schurig, V. *Chirality* **1989**, *1*, 127.
(11) Habets-Crützen, A. Q. H.; Carlier, S. J. N.; de Bont, J. A. M.; Wistuba, D.; Schurig, V.; Hartmans, S.; Tramper, J. *Enzyme Microb. Technol.* **1985**, *7*, 17.
(12) Weijers, C. A. G. M.; de Bont, J. A. M. *Microbiol. Sci.* **1988**, *5*, 156.
(13) Tsuruta, T. *J. Polym. Sci.* **1972**, *D*, 180.
(14) Spassky, N.; Leborgne, A.; Sepulchre, M. *Pure Appl. Chem.* **1981**, *53*, 1735.
(15) Schurig, V.; Wistuba, D.; Laderer, H.; Betschinger, F. *Organic Synthesis via Organometallics*; Dötz, K. H., Hoffmann, R. W., Eds.; Vieweg: Braunschweig, 1991; pp 241–265.
(16) Weijers, C. A. G. M.; de Haan, A.; De Bont, J. A. M. *Appl. Microbiol. Biotechnol.* **1988**, *27*, 337.
(17) Belluci, G.; Chiappe, C.; Couti, L.; Marioni, F.; Pierini, G. *J. Org. Chem.* **1985**, *54*, 5978.
(18) Berti, G. *Enzymes as Catalysts in Organic Synthesis*; Schneider, M. P., Ed.; Reidel: Dordrecht, 1986; p 349.
(19) Wistuba, D.; Schurig, V. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1032.
(20) Wistuba, D.; Träger, O.; Schurig, V. *Chirality* **1992**, *4*, 185.
(21) Golding, B. T.; Sellars, P. J.; Wong, A. K. *J. Chem. Soc., Chem. Commun.* 1977, 570.
(22) Schurig, V.; Bürkle, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 132.
(23) Arad-Yellin, R.; Green, B. S.; Knossow, M. *J. Am. Chem. Soc.* **1980**, *102*, 1157.
(24) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
(25) Finn, M. G.; Sharpless, K. B. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, pp 247–308.
(26) Wai, J. S. M.; Markó, I.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 1123.
(27) Oishi, T.; Hirama, M. *J. Org. Chem.* **1989**, *54*, 5834.
(28) Gao, Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *120*, 7538.
(29) Schurig, V.; Schleimer, M.; Wistuba, D. *Instrumentalized Analytical Chemistry and Computer Technology, InCom '90*; Günther, W., Matthes, J. P., Perkampus, H.-H., Eds.; GIT-Verlag: Darmstadt, 1990; pp 366–371.
(30) Schurig, V. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 1, pp 59–86.
(31) Schurig, V.; Weber, R. *J. Chromatogr.* **1981**, *217*, 51.
(32) Schurig, V.; Bürkle, W. *J. Am. Chem. Soc.* **1982**, *104*, 7573.
(33) Schurig, V.; Schmalzing, D.; Schleimer, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 987.
(34) Matlin, S. A.; Lough, W. S.; Chan, L.; Abram, D. M. H.; Zhou, Z. *J. Chem. Soc., Chem. Commun.* **1984**, 1038.
(35) Schurig, V.; Bürkle, W.; Hintzer, K.; Weber, R. *J. Chromatogr.* **1989**, *475*, 23.
(36) Schurig, V.; Koppenhöfer, B.; Bürkle, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 937.
(37) Koppenhoefer, B.; Bayer, E. *Chromatographia* **1984**, *19*, 123.
(38) Schurig, V.; Link, R. *Chiral Separations*; Stevenson, D., Wilson, I. D., Eds.; Proceedings of the International Meeting on Chromatography, University of Surrey, Guildford, 3-4 Sept 1987; Plenum Press: New York, 1988; p 91.
(39) Watabe, K.; Charles, R.; Gil-Av, E. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 192.
(40) Schurig, V.; Ossig, J.; Link, R. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 194.
(41) Bürkle, W.; Karfunkel, H.; Schurig, V. *J. Chromatogr.* **1984**, *288*, 1.
(42) Jung, M.; Schurig, V. *J. Am. Chem. Soc.* **1992**, *114*, 529.
(43) Ebbrecht, T. Diploma Thesis, University of Bochum, FRG, 1987.
(44) Weigand, K. Diploma Thesis, University of Tübingen, FRG, 1990.
(45) Schurig, V. *Kontakte (Darmstadt)* **1986**, *1*, 3.
(46) Terentèv, A. P.; Klabunovskii, E. I.; Patrikeev, V. V. *Doklady Akad. Nauk S.S.S.R.* **1950**, *74*, 947; *Chem. Abstr.* **1951**, *45*, 3798.
(47) Terentèv, A. P.; Klabunovskii, E. I. *Sbornik Statei Obshchei Khim.* **1953**, *2*, 1598; *Chem. Abstr.* **1955**, *49*, 5262h.
(48) Schurig, V. *Asymmetric Synthesis*, Houben-Weyl, Part 1, in print.

(49) Schurig, V. *J. Chromatographia* **1988**, *441*, 135.
(50) Betschinger, F.; Schurig, V. Unpublished results.
(51) Schurig, V.; Nowotny, H.-P. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 939.
(52) *Chiral Separations by HPLC*; Krstulovic, A. M., Ed.; Wiley: New York, 1989.
(53) Helder, R.; Hummelen, J. C.; Laane, R. W. P. M.; Wiering, J. S.; Wynberg, H. *Tetrahedron Lett.* **1976**, 1831.
(54) Pluim, H.; Wynberg, H. *J. Org. Chem.* **1980**, *45*, 2498.
(55) Wynberg, H. *Top. Stereochem.* **1986**, *16*, 87.
(56) Juliá, S.; Masana, J.; Vega, J. C. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 929.
(57) Baures, P. W.; Eggleston, D. S.: Flisak, J. R.; Gombatz, K.; Lantos, I.; Mendelson, W.; Remich, J. J. *Tetrahedron Lett.* **1990**, *31*, 6501.
(58) Montanari, F.; Moretti, I.; Torre, G. *J. Chem. Soc., Chem. Commun.* **1969**, 135.
(59) Montanari, F.; Moretti, I.; Torre, G. *Gazz. Chim. Ital.* **1974**, *104*, 7.
(60) Davis, F. A.; Harakal, M. E.; Awad, S. B. *J. Am. Chem. Soc.* **1983**, *105*, 3123.
(61) Davis, F. A.; Chattopadhyay, S. *Tetrahedron Lett.* **1986**, *27*, 5079.
(62) Curci, R.; Fiorentino, M.; Serio, M. R. *J. Chem. Soc., Chem. Commun.* **1984**, *155*.
(63) Jørgensen, K. A. *Chem. Rev.* **1989**, *89*, 431.
(64) Michaelson, R. C.; Palermo, R. E.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 1990.
(65) Yamada, S.; Mashiko, T.; Terashima, S. *J. Am. Chem. Soc.* **1977**, *99*, 1988.
(66) Coleman-Kammula, S.; Duim-Koolstra, E. T. *J. Organomet. Chem.* **1983**, *246*, 53.
(67) Tani, K.; Hanafusa, M.; Otsuka, S. *Tetrahedron Lett.* **1979**, 3017.
(68) Rossiter, B. E. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, pp 194–246.
(69) Mimoun, H.; Seree de Roch, I.; Sajus, L. *Bull. Soc. Chim. Fr.* **1969**, 1481; *Tetrahedron* **1970**, *26*, 37.
(70) Pitchen, P. Ph.D. Thesis, University of Paris-Sud, Centre d'Orsay, France, 1983.
(71) Schurig, V.; Hintzer, K.; Leyrer, U.; Mark, C.; Pitchen, P.; Kagan, H. B. *J. Organomet. Chem.* **1989**, *370*, 81.
(72) Arakawa, Y.; Moro-oka, A.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2958.
(73) Hintzer, K. Ph.D. Thesis, University of Tübingen, FRG, 1983.
(74) Broser, E.; Krohn, K.; Hintzer, K.; Schurig, V. *Tetrahedron Lett.* **1984**, *25*, 2463.
(75) Krohn, K.; Broser, K. *J. Org. Chem.* **1984**, *49*, 3766.
(76) Broser, E. Ph.D. Thesis, University of Braunschweig, FRG, 1986.
(77) Dzhemilev, U. M.; Fakhretainov, R. N.; Telin, A. G.; Tolstikov, G. A.; Rafikov, S. R. *Dokl. Akad. Nauk SSSR* **1983**, *271*, 361.
(78) Bortoloni, O.; Di Furia, F.; Modena, G.; Schionato, A. *J. Mol. Catal.* **1986**, *35*, 47.
(79) Winter, W.; Mark, C.; Schurig, V. *Inorg. Chem.* **1980**, *19*, 2045.
(80) Mark, C. Ph.D. Thesis, University of Tübingen, FRG, 1980.
(81) Mimoun, H. *Angew. Chem.* **1982**, *94*, 1853.
(82) Di Furia, F.; Modena, G. *Pure Appl. Chem.* **1982**, *54*, 1853.
(83) Sharpless, K. B.; Townsend, J. M.; Williams, D. R. *J. Am. Chem. Soc.* **1972**, *94*, 295.
(84) Sheldon, R. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 367.
(85) Strukul, G.; Michelin, R. A. *J. Chem. Soc., Chem. Commun.* **1984**, 1538; *J. Am. Chem. Soc.* **1985**, *107*, 7563.
(86) Sinigalia, R.; Michelin, R. A.; Pinna, F.; Strukul, G. *Organometallics* **1987**, *6*, 728.
(87) Watabe, T.; Ozawa, N.; Hiratsuka, A. *Biochem. Pharmacol.* **1983**, *32*, 777.
(88) Yang, S. K. *Biochem. Pharmacol.* **1988**, *37*, 61.
(89) Groves, J. T.; Nemo, T. E.; Myers, R. S. *J. Am. Chem. Soc.* **1979**, *101*, 1032.
(90) Chang, C. K.; Kuo, M.-J. *J. Am. Chem. Soc.* **1979**, *101*, 3413.
(91) Collman, J. P.; Gagne, R. R.; Reed, C. A.; Halbert, T. R.; Lang, G.; Robinson, W. T. *J. Am. Chem. Soc.* **1975**, *97*, 1427.
(92) Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5791.
(93) Myers, R. S. Ph.D. Thesis, University of Michigan, Ann Arbor, 1981.
(94) Groves, J. T.; Viski, P. *J. Org. Chem.* **1990**, *55*, 3628.
(95) Mansuy, D.; Battioni, P.; Renaud, J. P.; Guerin, P. *J. Chem. Soc., Chem. Commun.* **1985**, 155.
(96) Renaud, J. P.; Battioni, P.; Mansuy, D. *Nouv. J. Chim.* **1987**, *11*, 279.
(97) Naruta, Y.; Tani, F.; Maruyama, K. *Chem. Lett.* **1989**, 1269.
(98) Naruta, Y.; Tani, F.; Ishihara, N.; Maruyama, K. *J. Am. Chem. Soc.* **1991**, *113*, 6865.
(99) O'Malley, S.; Kodadek, T. *J. Am. Chem. Soc.* **1989**, *111*, 9116.
(100) Yoshinaga, K.; Itoh, N.; Kito, T. *Polym. J.* **1991**, *23*, 65.
(101) McMurry, T. J.; Groves, J. T. *Cytochrome P-450: Structure, Mechanism and Biochemistry*; Ortiz de Montellano, P. R., Ed.; Plenum: New York, 1986; p 1.
(102) Srinivasan, K.; Perier, S.; Kochi, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 2309.
(103) Irie, R.; Noda, K.; Ito, Y.; Matsumoto, N.; Katsuki, T. *Tetrahedron Lett.* **1990**, *31*, 7345.
(104) Irie, R.; Ito, Y.; Katsuki, T. *Synlett* **1991**, 265.
(105) Irie, R.; Noda, K.; Katsuki, T. *Tetrahedron Lett.* **1991**, *32*, 1055.
(106) Irie, R.; Noda, K.; Ito, Y.; Matsumoto, N.; Katsuki, T. *Tetrahedron: Asymmetry* **1991**, *2*, 481.
(107) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801.
(108) Zhang, W.; Jacobsen, E. N. *J. Org. Chem.* **1991**, *56*, 2296.
(109) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L. *J. Am. Chem. Soc.* **1991**, *113*, 7063.
(110) Jacobsen, E. N.; Zhang, W.; Güler, M. L. *J. Am. Chem. Soc.* **1991**, *113*, 6703.
(111) Lee, N. H.; Muci, A. R.; Jacobsen, E. N. *Tetrahedron Lett.* **1991**, *32*, 5055.
(112) Ozaki, S.; Mimura, H.; Yasuhara, N.; Masui, M.; Yamagata, Y.; Tomita, K.; Collins, T. *J. Chem. Soc., Perkin Trans. 2* **1990**, 353.
(113) Barton, D. H. R.; Jarman, T. R.; Watson, K. C.; Widdowson, D. A.; Boar, R. B.; Damps, K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1134.
(114) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249.
(115) Sépulchre, M.; Hintzer, K.; Schurig, V.; Spassky, N. *C. R. Acad. Sc. Paris, Ser. C* **1980**, *291*, 267.
(116) Sépulchre, M.; Spassky, N.; Mark, C.; Schurig, V. *Makromol. Chem., Rapid Commun.* **1981**, *2*, 261.
(117) Betschinger, F.; Hintzer, K.; Leyrer, U.; Schurig, V. *Dioxygen Activation and Homogenous Catalytic Oxidation*; Simandi, L. I., Ed.; Elsevier: Amsterdam, 1991; p 513.
(118) Leyrer, U. Ph.D. Thesis, University of Tübingen, FRG, 1985.
(119) Betschinger, F. *Diploma Thesis*, University of Tübingen, FRG, 1989.
(120) Campestrini, S.; Di Furia, F.; Modena, G.; Novello, F. *Dioxygen activation and Homogenous Catalytic Oxidation*; Simandi, L. I., Ed.; Elsevier: Amsterdam, 1991; p 375.
(121) Betschinger, F.; Schurig, V. Results to be published.
(122) Aoi, H.; Ishimori, M.; Yoshikawa, S.; Tsuruta, T. *J. Organomet. Chem.* **1975**, *85*, 241.
(123) Aoi, H.; Ishimori, M.; Tsuruta, T. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1897.
(124) Takeichi, T.; Ishimori, M.; Tsuruta, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2614.
(125) Takeichi, T.; Takakura, T.; Ishimori, M.; Tsuruta, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 603.
(126) Takeichi, T.; Arihara, M.; Ishimori, M.; Tsuruta, T. *Tetrahedron* **1980**, *36*, 3391.
(127) Asami, M.; Kanemaki, N. *Tetrahedron Lett.* **1989**, *30*, 2125.
(128) Naruse, Y.; Esaki, T.; Yamamoto, H. *Tetrahedron* **1988**, *44*, 4747.
(129) Naruse, Y.; Esaki, T.; Yamamoto, H. *Tetrahedron Lett.* **1988**, *29*, 1417.