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Pentacoordinated manganese(III) dihydrosalen complexes as biomimetic oxidation catalysts

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Abstract

A series of seven chiral pentadentate dihydrosalen ligands, carrying an imidazole group as a fifth, axial donor was synthesized in racemic and enantiomerically pure form. All of these ligands afforded mononuclear manganese(III) complexes in good yields. In two cases, the pentacoordination of the manganese ion could be confirmed by X-ray crystallography. The complexes catalyzed the epoxidation of olefins with a variety of terminal oxidants, but most importantly, with dilute (1%) aqueous hydrogen peroxide and without any added co-ligands. With 1,2-dihydronaphthalene as substrate and 10 mol% of catalyst, enantiomeric excesses up to 66% were achieved. This value is the highest so far reported for an asymmetric epoxidation of 1,2-dihydronaphthalene, using hydrogen peroxide as oxidant and a salen-type complex as catalyst. Control experiments using a tetradentate chelate lacking the axial imidazole donor showed that the pentacoordination of the manganese ion is crucial for the peroxidase activity. Furthermore, it was shown that the enantiomeric excess of the product epoxide(s) is basically constant during the whole reaction time. Therefore, the high enantioselectivity of the oxygen transfer process must be ascribed solely to an efficient enantioface selection by the chiral catalysts, and not to secondary transformations of the product epoxide(s).

Keywords: Asymmetric epoxidation; Dihydrosalen complexes; Manganese catalysts; Peroxidase models

1. Introduction

Asymmetric catalysis is one of the most exciting fields of modern organic chemistry [1,2]. Clearly, the advantage of asymmetric catalysis over other methods of chirality transfer is its potential to multiply the chiral information present in the catalyst. As far as enantioselective epoxidations are concerned, the catalysts described by Jacobsen and co-workers [3,4] and Katsuki [5] have recently extended the synthetic scope [1] of metal-catalyzed asymmetric oxidations to unfunctionalized olefins. In this approach, oxygen transfer to the substrate is ef-

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[1] See e.g. Ref. [2] for the asymmetric Sharpless-epoxidation of allylic alcohols.

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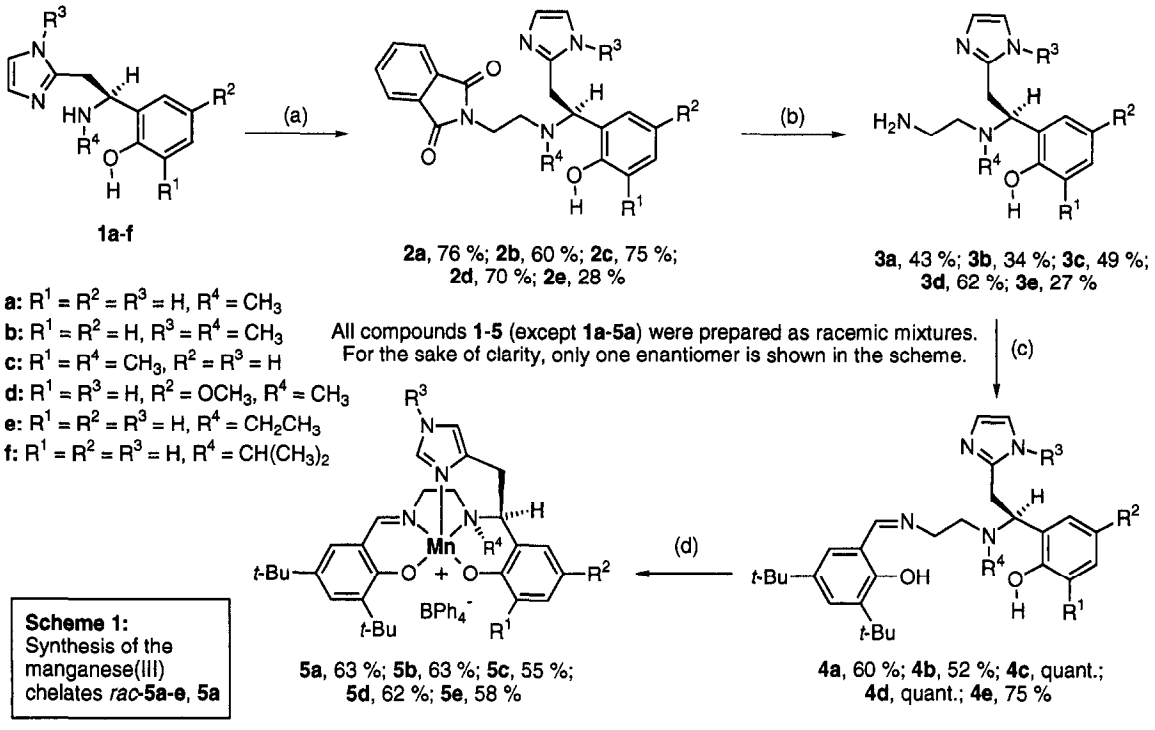


Scheme 1: Synthesis of the manganese(III) chelates *rac*-**5a-e**, **5a**

Reagents and conditions: (a) 2-(N-phthalimido)acetaldehyde, $NaBH_3CN$, methanol; (b) hydrazine hydrate, methanol; (c) 3,5-di-*tert*-butylsalicylaldehyde, methanol; (d) $MnCl_2 \cdot 4\ H_2O$, $NaBPh_4$, air, methanol.

Scheme 1. Synthesis of the pentadentate manganese(III) chelates *rac*-**5a–e**.

fected by C_2-symmetric manganese(III)-salen type complexes, using iodosylarenes or hypochlorite as the terminal oxidant [2]. As a part of our studies on biomimetic catalysts for selective oxyfunctionalizations [7,8], we addressed the question whether hydrogen peroxide could be employed as the terminal oxidant [6]. Its advantages are obvious: It is a cheap and mild reagent, with only water being formed as waste product [9]. The main challenge associated with this oxidant, however, is favoring the heterolytic O–O bond cleavage, with concomitant formation of the reactive metal–oxene species, over destructive radical pathways [10]. In many peroxidases, i.e., hydrogen peroxide utilizing enzymes, the catalytically active iron center is coordinated by the four pyrrole nitrogen atoms of its heme ligand plus an axial imidazole donor [11–13]. This proximal donor is believed to facilitate O–O heterolysis. Not surprisingly, imidazole and derivatives thereof have proven beneficial as co-ligands for manganese-complex

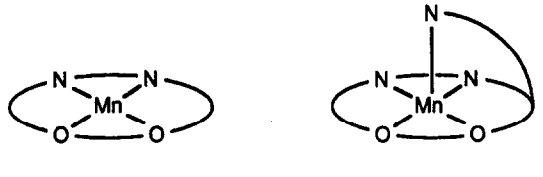


Fig. 1. Pentadentate dihydrosalen complexes of manganese as peroxidase models.

[2] The application of hydrogen peroxide in manganese-catalyzed asymmetric epoxidations has been described for salen-type catalysts in the presence of large amounts of external co-ligands in Ref. [6].

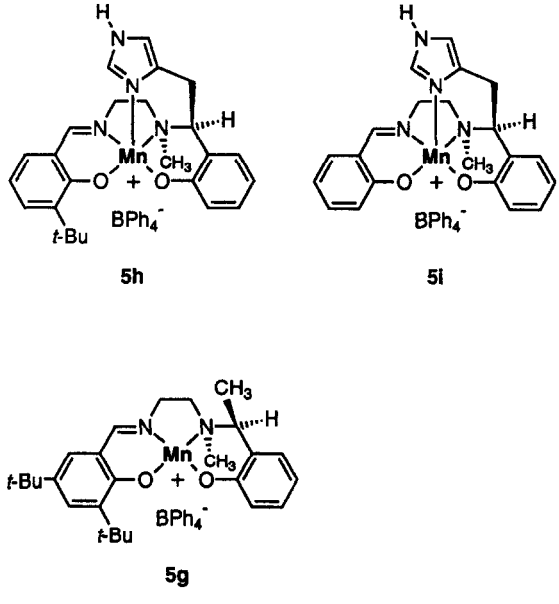
catalyzed epoxidations [14], especially with hydrogen peroxide as the source of oxygen [6,15,16]. For the efficient utilization of this oxidant in the enantioselective epoxidation of unfunctionalized olefins, it appeared desirable to combine the features of a peroxidase-like coordination sphere and a (chiral) manganese(III) salen complex (**A**, Fig. 1). In such an arrangement, a fifth, axial donor, preferably an imidazole group, should be covalently attached [3] to a salen-type complex (**B**, Fig. 1). Herein we describe the synthesis of pentadentate ligands of the dihydrosalen [7,8,17,18] type, the conversion of these ligands to manganese(III) complexes of the type **B** (Scheme 1), X-ray crystal structures of two representative chelates and the catalytic performance of these novel peroxidase models.

2. Results

2.1. Synthesis of the ligands and manganese complexes

Our three-step sequence used for the synthesis of the pentadentate dihydrosalen ligands is depicted in Scheme 1. The secondary amines **1** served as starting materials. They were prepared in racemic form by reductive amination of the corresponding ketones (see Ref. [19] for the preparation of *rac*-**1a–d**, and the experimental section for the preparation of *rac*-**1e**, **f**). Very good yields were generally obtained when methyl- or ethylamine were used. Switching to *iso*-propylamine, however, gave only 28% of the secondary amine *rac*-**1f**. As expected, only marginal yields of the amination product were found when amines of even higher steric demand, like, e.g., *tert*-butylamine, were employed. Furthermore, the *S*-configurated amine **1a** was used in enantiomerically pure form (see Ref. [19] for the separation of the enantiomers of *rac*-**1a**).

The reductive alkylation of the secondary amines *rac*-**1a–e** using 2-(*N*-phthalimino)acetaldehyde and sodium cyanoborohydride afforded the *N*-protected derivatives of ethylene diamine *rac*-**2a–e** in good yields. The analogous alkylation of the enantiomerically pure amine **1a** gave **2a** in 83% yield. Clearly, this alkylation step is again very sensitive to the steric bulk present at the amine nitrogen atom. As shown in Scheme 1, the alkylation of the *N*-ethyl amine *rac*-**1e** afforded the alkylation product *rac*-**2e** in only 28% yield. When the *N-iso*-propyl amine *rac*-**1f** was used, only trace amounts of the desired alkylation product were obtained under a variety of reaction conditions.



In the next steps, the *N*-protecting group was removed by hydrazinolysis, and subsequent condensation with 3,5-di-*tert*-butylsalicylaldehyde gave the Schiff's base ligands *rac*-**4a–e** in the yields stated in Scheme 1. The enantiomeri-

[3] For examples of tetradentate dihydrosalen complexes, see Ref. [17]; for an achiral Mn-porphyrin with a pendant imidazole group, see Ref. [18]

cally pure ligand **4a** was prepared from **2a** in just the same way. Finally, the ligands *rac*-**4a–e** and **4a** were reacted with manganese(II) chloride tetrahydrate in methanol in the presence of air and sodium tetraphenyl borate, affording the dark brown manganese(III) complexes *rac*-**5a–e** in 55–63% yield as microcrystalline powders (Scheme 1). The enantiomerically pure complex **5a** was obtained in 63% yield from the Schiff's base **4a**. Besides **5a**, the enantiomerically pure manganese(III) chelates **5h** and **5i** were also synthesized: In the case of **5h**, the corresponding Schiff's base **4h** was first isolated from the reaction of the diamine **3a** with 3-*tert*-butylsalicylaldehyde (78%). It was then subjected to the metallation conditions described above, affording the complex **5h** in 92% yield. In the case of **5i**, the diamine **3a** was condensed with salicylaldehyde and the resulting Schiff's base was reacted in situ with manganese(II) chloride as described above. The chelate **5i** was obtained in 44% yield, again as a brown, microcrystalline powder.

For comparison, the tetradentate dihydrosalen complex *rac*-**5g**, lacking the axial imidazole donor, was prepared, too. Its synthesis closely paralleled that of the pentadentate manganese chelates discussed so far: In the first step, *ortho*-hydroxyacetophenone was reductively aminated with methyl amine, affording the secondary amine (*RS*)-2-[1-(methylamino)ethyl]phenol (*rac*-**1g**, not shown) in 92% yield. The subsequent *N*-alkylation, hydrazinolysis and condensation with 3,5-di-*tert*-butylsalicylaldehyde as described above gave the products *rac*-**2g** (78%), *rac*-**3g** (48%), and *rac*-**4g** (quant.) (structures not shown). Finally, our metallation protocol (vide supra) converted the ligand *rac*-**4g** to the dark brown manganese(III) chelate *rac*-**5g** in 54% yield.

2.2. X-Ray crystal structures of the manganese(III) dihydrosalen complexes rac-5a and rac-5e

Single crystals suitable for X-ray structural analyses could be obtained by slow cooling of hot, saturated solutions of the chelates *rac*-**5a**, **e** in ethanol. The results are shown in Fig. 2 and Fig. 3. As could be expected, the crystal structures of the *N*-methyl (*rac*-**5a**, Fig. 2) and of the *N*-ethyl (*rac*-**5e**, Fig. 3) complex are very similar. Most important, however, is the finding that both complexes show the desired coordination mode: The metal ion is coordinated equatorially by the oxygen (phenolate) and nitrogen

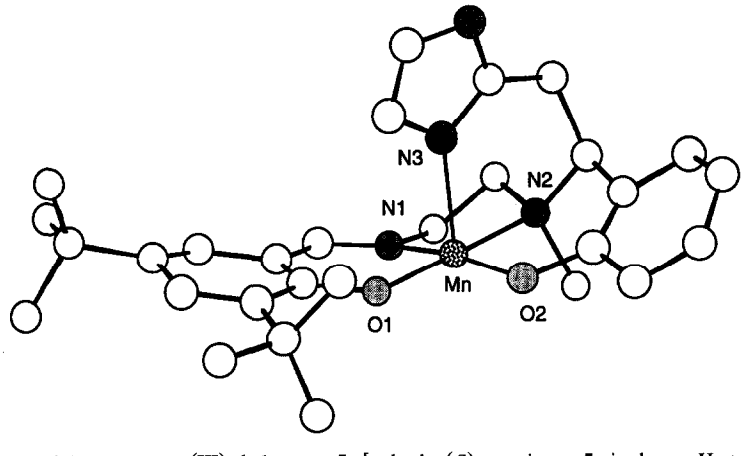


Fig. 2. X-Ray crystal structure of the manganese(III) chelate *rac*-**5a** [only the (*S*)-enantiomer **5a** is shown, H-atoms are omitted for clarity]. Selected bond lengths (Å): Mn-O1 1.82(2); Mn-O2 1.81(2); Mn-N1 1.95(2); Mn-N2 2.06(2); Mn-N3 2.20(3).

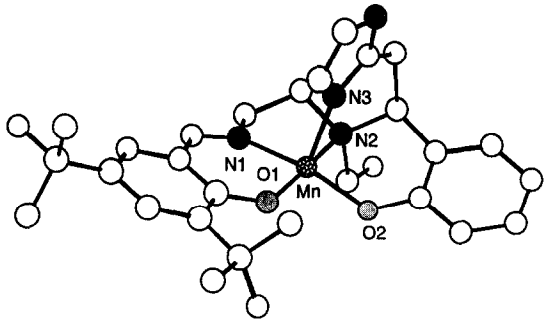


Fig. 3. X-Ray crystal structure of the manganese(III) chelate *rac*-**5e** [only the (*S*)-enantiomer **5e** is shown, H-atoms are omitted for clarity]. Selected bond lengths (Å): Mn-O1 1.853(3); Mn-O2 1.852(3); Mn-N1 1.975(3); Mn-N2 2.046(3); Mn-N3 2.160(4).

(amine and imine) donor atoms of the dihydrosalen ligand. Furthermore, the fifth imidazole donor occupies an axial position. The sixth coordination site is vacant and may thus be expected to bind and activate a hydrogen peroxide molecule, just as in heme peroxidases. As could be expected, the dihydrosalen ligand is not planar. Both the tetrahedral amine nitrogen atom and the tetrahedral carbon atom carrying the (2-imidazolyl)methyl side-chain induce significant distortion. The planes of the two benzene rings of *rac*-**5a, e** intersect at an angle of 45° and 27°, respectively. Overall, the manganese chelates **5** have two centers of chirality, namely the secondary carbon atom carrying the (2-imidazolyl)methyl side-chain, and the neighboring amine nitrogen atom. When coordinated to the manganese ion, the latter tertiary amine does not invert any more and forms a stable center of chirality. As shown in Fig. 2 and Fig. 3, the (2-imidazolyl)methyl side-chain and the alkyl substituent on the amine nitrogen atom adopt a 'transoid' orientation. It appears reasonable to assume that this type of arrangement is conserved in the other complexes (*rac*-**5b–d, g, h, i**). Since the substituent at the amine nitrogen atom is pointing 'downward', i.e., towards the face of the complex where the oxygenation of a substrate is expected to take place, significant asymmetric induction may be anticipated.

Table 1
Asymmetric epoxidation with hydrogen peroxide catalyzed by the enantiomerically pure manganese chelates **5a, h, i**

Entry	Catalyst [a]	Olefin	Oxidant	Reaction time(h)	Olefin consumed(%)	Epoxide formed [b,c](%)	ee [b](%)
1	**5a**	**6**	30% H_2O_2	12 [d]	87	60 (69)	34
2	**5a**	**6**	30% H_2O_2	1	88	68 (77)	45
3	**5a**	**6**	30% H_2O_2	1 [e]	93	73 (78)	45
4	**5a**	**6**	1% H_2O_2	1	92	77 (84)	48
5	**5a**	**6**	1% H_2O_2	1 [e]	91	65 (71)	50
6	**5a**	**6**	1% H_2O_2	1 [e]	93	72 (77)	64 [f]
7	**5h**	**6**	1% H_2O_2	1 [e]	71	47 (66)	66 [f]
8	**5i**	**6**	1% H_2O_2	1 [e]	64	52 (61)	21 [f]
9	**5a**	**7**	1% H_2O_2	2 [e]	nd	24 [g]	63 [f,g]
10	**5h**	**7**	1% H_2O_2	2 [e]	nd	nd	59 [f,g]
11	**5a**	Styrene	1% H_2O_2	2 [e]	51	51	46
12	**5h**	Styrene	1% H_2O_2	2 [e]	67	67	52

[a] The catalyst **5a** was prepared from the ligand **4a** with 81% ee.

[b] Yield and ee determined by capillary GC (heptakis(2,6-di-*O*-methyl-3-*O*-pentyl)-β-cyclodextrin column), employing 1,2-dibromobenzene as internal standard. Absolute configurations of the major enantiomers were determined by comparison with authentic samples: epoxidation of **6**: (1*R*, 2*S*)-epoxide, epoxidation of styrene: (*R*)-epoxide, epoxidation of **7**: not determined.

[c] Values in parentheses are corrected for incomplete conversion of the olefin (selectivity).

[d] In this experiment, acetonitrile was used as solvent. The oxidant was added as a solution in acetonitrile by means of a syringe pump over a period of 12 h.

[e] Epoxidation was carried out at 0°C.

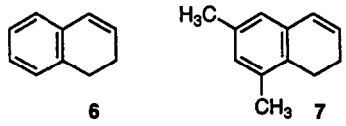
[f] Catalysts **5a, h, i** prepared from ligand **4a** of > 98% ee.

[g] Isolated yield, ee determined by HPLC on a CHIRALCEL OD-H column.

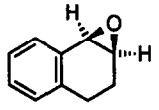
2.3. Catalytic activity of the manganese chelates 5a, h, i and rac-5a–e, g

2.3.1. Asymmetric epoxidation with hydrogen peroxide catalyzed by the enantiomerically pure manganese chelates 5a, h, i

As expected, the manganese chelates **5a**, **h**, **i** showed catalytic activity in the epoxidation of olefins with hydrogen peroxide. The results for the epoxidation of 1,2-dihydronaphthalene **6**, 6,8-dimethyl-1,2-dihydronaphthalene **7** and styrene are summarized in Table 1. As it turned out, hydrogen peroxide could either be used in homogeneous solution using acetonitrile as solvent, or in a two-phase system. In the latter case, both the olefin and the catalyst were dissolved in dichloromethane, and this solution was then layered with aqueous hydrogen peroxide, at the temperatures and concentrations stated in Table 1. Typically, 10 eq. of the oxidant were used, and 10 mol% of the catalyst (relative to the olefin). In the case of the epoxidation of 1,2-dihydronaphthalene **6**, using the enantiomerically pure complex **5a** (Table 1, entries 1–6), the best results were achieved under two phase conditions: Using 1%-hydrogen peroxide and dichloromethane at 0°C, the (1*R*, 2*S*)-epoxide **8** was obtained in high yield (72%) and enantiomeric excess (64%, Table 1, entry 6). This is the best result achieved so far in the asymmetric epoxidation of 1,2-dihydronaphthalene **6** with hydrogen peroxide. When the substrate olefin was changed to 6,8-dimethyl-1,2-dihydronaphthalene **7**, a similar ee was achieved (63%, Table 1, entry, 9), but at significantly lower yield. Finally, when styrene was subjected the epoxidation procedure, 67% of the *R*-epoxide were obtained at 46% ee (Table 1, entry 11).



6 **7**



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In the manganese(III) complex **5h**, the *tert*-butyl group in the 5-position (of complex **5a**) is omitted. When used in the epoxidation procedure, this material catalyzed the conversion of

Table 2
Asymmetric epoxidation catalyzed by the manganese chelate **5a**, using terminal oxidants other than hydrogen peroxide

Entry	Olefin	Oxidant	Reaction time(h)	Olefin consumed(%)	Epoxide formed [b,c](%)	ee [b](%)
1	**6**	$(H_2N)_2CO \cdot H_2O_2$	1	94	70 (74)	48
2	**6**	$Na_2CO_3 \cdot 1.5\, H_2O_2$	29	87	66 [d] (76)	53
3	**6**	Ph-IO [e]	1	83	68 (82)	52
4	**6**	NaOCl [f]	24	95	76 (80)	56
5	**6**	*m*CPBA [g]	1	14	11 (79)	23
6	*trans*-stilbene	Ph-IO [h]	14	nd	39 [i]	33 [i]

[a] The catalyst **5a** was prepared from the Schiff's base **4a** of 81% ee.
[b] Yield and ee determined by capillary GC (heptakis(2,6-di-*O*-methyl-3-*O*-pentyl)-β-cyclodextrin column), employing 1,2-dibromobenzene as internal standard. Absolute configurations of the major enantiomers as in Table 1, epoxidation of *trans*-stilbene: not determined.
[c] Values in parentheses are corrected for incomplete conversion of the olefin (selectivity).
[d] The yield of isolated, chromatographically purified material could be raised to 77% by driving the reaction to full conversion of the olefin.
[e] 2 eq. of iodosylbenzene (relative to olefin) was added at once.
[f] 4 eq. of sodium hypochlorite (relative to olefin) was added.
[g] Epoxidation carried out at 0°C, using 1 eq. of oxidant (relative to the olefin).
[h] 3 eq. of iodosylbenzene (relative to olefin) was added at once, 8 mol% of catalyst **5a** was used.
[i] Isolated yield, ee determined by HPLC on a CHIRALCEL OD-H column.

1,2-dihydronaphthalene **6** to the (1*R*, 2*S*)-epoxide **8** under two-phase conditions, in even higher ee (66%, Table 1, entry 7), albeit at lower chemical yield (47%). For styrene, the catalyst **5h** proved superior to **5a**: As shown in Table 1, entry 12, both the yield (67%) and the enantiomeric excess (52%) were higher compared to the catalyst **5a**. Finally, for 6,8-dimethyl-1,2-dihydronaphthalene **7** as substrate, a somewhat lower ee (59%) resulted compared to **5a** (Table 1, entries 9,10). Omission of both *tert*-butyl groups of the manganese chelate **5a** leads to the complex **5i**. In the epoxidation of 1,2-dihydronaphthalene **6**, this material proved significantly inferior to the butylated catalysts **5a** and **5h**: Only a moderate yield of the epoxide **8** was achieved (52%, Table 1, entry 8), at rather low ee (21%).

2.3.2. *Asymmetric epoxidation catalyzed by the manganese chelate **5a** using terminal oxidants other than hydrogen peroxide*

Solid adducts of hydrogen peroxide and other terminal oxidants were tested, in conjunction with the enantiomerically pure catalyst **5a**, too. The results are summarized in Table 2. As it turned out, the urea clathrate of hydrogen peroxide (Table 2, entry 1) or so-called sodium 'percarbonate' (Table 2, entry 2) could be employed as a suspension in dichloromethane, too. The enantiomeric excesses observed were generally comparable to those obtained in the two-phase system (48% and 53%, respectively). However, the chemical yields were quite reasonable. As shown in Table 2, entries 3–5, 1,2-dihydronaphthalene **6** could also be epoxidized using a suspension of iodosylbenzene, a two-phase system with sodium hypochlorite, or *meta*-chloroperbenzoic acid in homogeneous solution. In the latter case, both yield and ee's were unsatisfactory, whereas both hypochlorite and iodosylbenzene gave chemical yields almost as good as hydrogen peroxide, but at lower ee's. Interestingly, the epoxidation of trans-stilbene (Table 2, entry 6) could be achieved only with iodosylbenzene as terminal oxidant.

2.3.3. *Further variations on the catalyst structure: Epoxidation of 1,2-dihydronaphthalene **6** catalyzed by the manganese chelates rac-**5b–e** and rac-**5g***

In the manganese chelate **5a**, the 'left' benzene ring is substituted by two *tert*-butyl groups, whereas the 'right' benzene does not carry any further substituents. In the catalyst *rac*-**5c**, an additional methyl group is positioned *ortho* to the 'right' phenolic oxygen atom (Scheme 1). In *rac*-**5d**, a methoxy group occupies the *para* position relative to the 'right' phenolic oxygen atom. The manganese complex *rac*-**5b** is derived from *rac*-**5a** in that the imidazole NH is exchanged for an *N*-methyl group. Finally, the chelate *rac*-**5e** is related to the parent system *rac*-**5a** such that the methyl group at the metal-coordinating amine nitrogen atom is exchanged for an ethyl group (Scheme 1). Finally, in the complex *rac*-**5g**, the imidazole moiety is omitted.

The catalytic performance of these derivatives of the parent system *rac*-**5a** was explored under two-phase conditions, using 1%-hydrogen peroxide as terminal oxidant and 1,2-dihydro-

Table 3
Epoxidation of 1,2-dihydronaphthalene **6** with 1% hydrogen peroxide in a two-phase system, catalyzed by the manganese chelates *rac*-**5b–e** and *rac*-**5g**

Entry	Catalyst	Reaction time [a] (h)	Olefin consumed (%)	Epoxide formed [b,c] (%)
1	*rac*-**5b**	2	quant.	53
2	*rac*-**5c**	2.5	96	82 (86)
3	*rac*-**5d**	2.5	69	58 (84)
4	*rac*-**5e**	1	95 [d]	41 [d] (43)
5	*rac*-**5g** [e]	4	0	0

[a] All reactions were carried out at 0°C.
[b] Yields determined by capillary GC (heptakis(2,6-di-*O*-methyl-3-*O*-pentyl)-β-cyclodextrin column), employing 1,2-dibromobenzene as internal standard.
[c] Values in parentheses are corrected for incomplete conversion of the olefin.
[d] Using 0.1 M phosphate buffer (pH 7.2) and elongation of the reaction time (1.5 h) raised the yield of the epoxide to 59%, full conversion of the olefin was observed.
[e] The addition of 2-methylimidazole (up to 20 eq. relative to catalyst) did not change this result.

naphthalene **6** as substrate. The results are summarized in Table 3: The *ortho*-methylated catalyst *rac*-**5c** indeed showed a higher efficiency than the parent system *rac*-**5a**: The epoxide *rac*-**8** was formed in 82% yield (Table 3, entry 2). All other alterations of the structure resulted in a lowering of the epoxide yield. Most importantly, the tetradentate manganese complex *rac*-**5g** showed no catalytic activity at all, even in the presence of a large excess of 2-methylimidazole (up to 20 eq., relative to the complex *rac*-**5g**).

*2.3.4. Asymmetric epoxidation of 1,2-dihydronaphthalene **6** using the catalyst **5a** under two-phase conditions: Enantiomeric excess of the epoxide **8** as a function of time*

1,2-Dihydronaphthalene **6** was epoxidized under two-phase conditions with 1%-hydrogen peroxide, using the catalyst **5a**. When the concentrations of the starting material **6**, the product epoxide **8**/*ent*-**8** and the ratio of **8**/*ent*-**8** were followed by gas chromatography, the time profile shown in Fig. 4 was obtained. The most striking features are the induction period and the fact that the enantiomeric excess of the product epoxide changed only very little with time (initial value: 69%, final value: 64%).

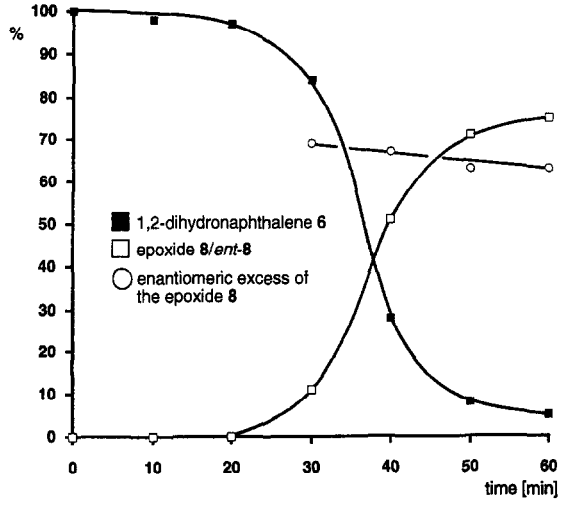

Fig. 4. Time course of the asymmetric epoxidation of 1,2-dihydronaphthalene **6** with hydrogen peroxide using the catalyst **5a**.

3. Discussion

For the sake of clarity the results presented in this paper shall briefly be summarized again: (a) The synthetic sequence depicted in Scheme 1 allows for the preparation of a wide variety of novel pentadentate dihydrosalen manganese(III) complexes. Depending on whether the starting secondary amines **1** are used in racemic or enantiomerically pure form, the chelates **5** are obtained enantiomerically pure or as racemates. In principle, many other metal ions can be complexes with the ligands **4**. (b) The pentadentate manganese(III) chelates **5** act as peroxidase models. They efficiently epoxidize olefins using dilute aqueous hydrogen peroxide as terminal oxidant. In enantiomerically pure form, the chiral catalysts **5** induce high enantiomeric excesses in the product epoxides. Oxidants other than hydrogen peroxide can be used as well. (c) The pentacoordination of the manganese(III) ion is a prerequisite for peroxidase activity: Omitting the axial imidazole donor eliminates the catalytic activity. (d) The enantiomeric excess of the product epoxide changes only very little in the course of the reaction. Therefore, a secondary stereospecific transformation of the primary epoxidation product appears not to take place.

3.1. Pentadentate manganese(III) complexes of the dihydrosalen type as peroxidase models and as new epoxidation catalysts

In view of the above results, it appears that our initial concept of using pentadentate manganese(III) chelates as peroxidase models (Fig. 1) actually afforded a new class of biomimetic oxidation catalysts. As in heme-peroxidases, it may be assumed that the axial ligand facilitates the O–O bond heterolysis of hydrogen peroxide coordinated to the 'opposite' axial site at the

manganese(III) ion [11–13]. The substrate spectrum of the catalysts **5** appears to be similar to that of the manganese(III) salen catalysts described by Jacobsen and co-workers [3,4] and Katsuki [5]: *cis*-1,2-disubstituted, conjugated olefins, like e.g. 1,2-dihydronaphthalene **6** are epoxidized best, whereas *trans*-olefins or terminal alkenes like 1-octene give at best poor yields of epoxide. In this context, it is interesting to note that our catalyst **5a** did epoxidize *trans*-stilbene (Table 2, entry 6), but *only* with iodosylbenzene as terminal oxidant, and not with any other. It has been pointed out before [20] that the mechanistic pathway for metal-catalyzed oxygen transfer from iodosylbenzene may be different from other oxygen donors: In the former case, an adduct of the catalyst with intact iodosylbenzene may be the active, oxidizing entity, as opposed to the $M{=}O$ 'oxene species' usually postulated [5].

3.2. On the mechanism of asymmetric induction

It was recently found that the high enantioselectivity of the epoxidation of 1,2-dihydronaphthalene **6** with Jacobsen's catalysts is in part due to a subsequent, stereospecific hydroxylation of the minor enantiomer of the initially formed epoxide mixture [21]. In other words, the enantiomeric excess of the product epoxide is increased by a subsequent kinetic resolution. As an experimental indicator, the ee of the product increases as the reaction proceeds [21]. In our case, the ee of the product epoxide remains basically constant (Fig. 4), and there is no indication for a secondary process. Consequently, the enantioselectivities observed must occur exclusively at the epoxidation stage. In fact, inspection of space filling models revealed that the enantioselectivity observed can consistently be explained by nonbonding interactions between the approaching substrate olefin and the non-planar catalyst: In the case of 1,2-dihydronaphthalene **6**, the approach of the (3*Re*)-face of the prochiral olefin **6** to the oxygen atom of an intermediate Mn=O species is strongly disfavored [4]. Model studies of this type also indicate that the introduction of substituents on the 'right' benzene ring of the catalyst **5a** (Fig. 2) should further direct the approach of the olefin and thus increase the face selectivity of the oxygen transfer.

3.3. Stability of the catalysts

As with other oxidation catalysts, the major weakness of our catalytic system is its limited stability. In fact, the epoxide yields stated in this article reflect the kinetic competition between oxygen transfer to a substrate and oxidative degradation of the catalyst. Experimentally, the brown solutions of the manganese(III) catalysts **5** bleach as the reaction proceeds. Once they are colorless, the catalytic activity is lost. At first glance, the imidazole NH of the catalyst may appear as an excellent target for the induction of oxidative decay. However, this seems not be the case, since the *N*-methylated derivative *rac*-**5b** does not show increased stability compared to the parent system *rac*-**5a** (Table 3, entry 1). It was already shown by Jacobsen [4] that the catalyst stability is increased when the positions *ortho* and *para* to the phenolic oxygen atoms are blocked. Most likely, substituents at these positions prevent oxidative phenol coupling reactions. Furthermore, sterically demanding substituents at these positions increase the enantioselectivity of the oxygen transfer reactions. In line with this argumentation, we found that the *ortho*-methylated complex *rac*-**5c** (Scheme 1) gives indeed higher epoxidation yields (Table 3, entry 2). As may have been expected, the electron rich methoxylated catalyst *rac*-**5d** is degraded even faster than the parent system *rac*-**5a** (Table 3, entry 3). Exchanging the *N*-methyl group of the catalyst *rac*-**5a** (Fig. 2) for an

[4] Assuming a coordination state of the manganese ion as shown in Fig. 2 and Fig. 3, with the oxene–oxygen atom bonded *trans* to the imidazole nitrogen, and a perpendicular attack [3,5,4] of this intermediate Mn=O species on the C=C double bond.

N-ethyl group in *rac*-**5e** (Fig. 3) did not significantly alter the stability of the catalyst (Table 3, entry 4). Thus, an intramolecular attack of an intermediate Mn=O oxene species on the *N*-alkyl group apparently does not constitute the major degradative pathway. Taken together, the above results indicate that a substitution of both the *ortho* and the *para* position (relative to the phenolic oxygen atom) of the 'right' benzene ring in **5a** with bulky alkyl substituents should provide higher stability towards oxidative degradation.

In summary, we have shown that pentacoordinate manganese(III) chelates of the dihydrosalen type show peroxidase activity and that they may be used as catalysts for the asymmetric epoxidation of olefins with hydrogen peroxide as terminal oxidant. Their synthetic value is presently limited by their relatively complex synthesis. We are presently aiming at (a) a significant simplification of the synthesis, and simultaneously at (b) increasing the stability of this promising new class of oxidation catalysts.

4. Experimental section

4.1. General methods

^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker AM 300 spectrometer. Chemical shifts were calibrated relative to solvent signals. Coupling patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; mc, centered multiplet; m, multiplet, br, broad; ι, pseudo. IR-Spectra were obtained on a Bruker IFS 66 instrument. Mass spectroscopy (MS) was performed on a Finnigan 3200 spectrometer (chemical ionisation: CI, methane) and Finnigan MAT 8200 spectrometer (field desorption: FD); high resolution mass spectroscopy (HRMS) on a VG Micromass ZAB-2F instrument. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Microanalyses were performed at the Institut für Organische Chemie, Universität Frankfurt/M. or at the Mikroanalytisches Labor der Chemischen Institute, Universität Heidelberg. Analytical GC: HP 5890 Series II capillary GC with flame ionisation detector and HP 3396 Series II integrator using a heptakis(2,6-di-*O*-methyl-3-*O*-pentyl)-β-cyclodextrin column. Analytical HPLC: Knauer HPLC pump 64 with Knauer UV/VIS filter-photometer, ERC differential refractometer ERC-7512 and HP 3396 Series II integrator, using a Daicel CHIRALCEL OD-H column. Column chromatography was usually carried out on silica gel 63–200 mesh, flash chromatography on silica gel 230–400 mesh. Unless otherwise stated, an adsorbent to substrate ratio of 100:1 was used.

4.2. Materials

2-(*N*-Phthalimido)acetaldehyde was obtained in two steps starting from 2-bromo-1,1-dimethoxyethane [22], 3,5-di-*tert*-butylsalicylaldehyde was prepared from 2,4-di-*tert*-butylphenol [23], 3-*tert*-butylsalicalylaldehyde from 2-*tert*-butylphenol [24]. 6,8-Dimethyl-1,2-dihydronaphthalene **7** was synthesized from commercially available 3,5-dimethyl-α-tetralone by reduction with sodium borohydride and subsequent acid-catalyzed dehydration. Details of our synthesis of 1-(2-hydroxyphenyl)-2-(1*H*-imidazol-2-yl)ethanone hydrochloride, the secondary amines *rac*-**1a–d** and of enantiomerically pure amine **1a** are described elsewhere [19].

*4.2.1. General procedure for the preparation of the amines rac-**1e–g***

*4.2.1.1. (RS)-2-[2-(1H-Imidazol-2-yl)-1-(ethylamino)ethyl]phenol rac-**1e***. A 300 ml autoclave was charged with a solution of the 1-(2-hydroxyphenyl)-2-(1*H*-imidazol-2-yl)ethanone hydrochloride (5.00 g, 21.0 mmol) in 100 ml of dry methanol. A solution of ethylamine in methanol (18%, 23.7 ml, 105 mmol) and 10% palladium on activated charcoal (370 mg, 1.7 mol%) were added. The autoclave was pressur-

ized with hydrogen to 65 atm. The reaction mixture was stirred at room temperature for 24 h. The mixture was then filtered through Celite, which was rinsed with methanol (2 × 50 ml). The combined filtrates were concentrated, and the residue was partitioned between 300 ml of saturated aqueous sodium bicarbonate and 150 ml of dichloromethane. After extraction of the aqueous layer with dichloromethane (2 × 150 ml), the combined organic phases were dried with anhydrous potassium carbonate. Evaporation of the solvent afforded a yellow foam. After purification by column chromatography [adsorbent/substrate 40:1, dichloromethane/methanol (saturated with ammonia) 9:1] a pale brown solid (2.86 g, 60%) was obtained. mp. 70°C; TLC $R_f = 0.56$ [dichloromethane/methanol (saturated with ammonia) 85:15]; ^{1}H-NMR ($CDCl_3$): δ 1.11 (t, $J = 7.0$ Hz, 3H), 2.63 (q, $J = 7.0$ Hz, 2H), 3.00 (dd, $J = 15.1$ Hz and $J = 5.5$ Hz, 1H), 3.21 (dd, $J = 15.1$ and 8.8 Hz, 1H), 4.17 (dd, $J = 8.8$ and 5.5 Hz, 1H), 6.70–6.90 (m, 3H), 6.96 (s, 2H), 7.14 (mc, 1H); ^{13}C-NMR ($CDCl_3$): δ 14.8 (q), 34.9 (t), 41.9 (t), 62.8 (d), 116.8 (d), 119.2 (d), 121.9 (brd), 124.8 (s), 128.5 (d), 128.7 (d), 145.1 (s), 157.5 (s); IR (KBr): 3600–2200 (br), 3049, 2969, 2922, 2870, 2732, 1900, 1590, 1493, 1454, 1428, 1411, 1383, 1257, 1152, 1121, 1100, 934, 753, 733 cm^{-1}; HRMS calcd. for $C_{13}H_{17}N_3O$: 231.1372; found: 231.1364.

*4.2.1.2. (RS)-2-[2-(1H-Imidazol-2-yl)-1-(isopropylamino)ethyl]phenol rac-**1f***. Pale yellow foam (1.43 g, 28%), obtained from 1-(2-hydroxyphenyl)-2-(1*H*-imidazol-2-yl)ethanone hydrochloride (5.00 g, 21.0 mmol) and *iso*-propylamine (8.95 ml, 105 mmol). The reductive amination was run at a hydrogen pressure of 23 atm. mp. 45°C; TLC $R_f = 0.61$ [dichloromethane/methanol (saturated with ammonia) 85:15]; ^{1}H-NMR ($CDCl_3$): δ 1.02 (d, $J = 6.3$, 3H), 1.04 (d, $J = 6.3$ Hz, 3H), 2.75 (sept, $J = 6.3$ Hz, 1H), 3.02 (dd, $J = 14.7$ Hz and 5.5 Hz, 1H), 3.16 (dd, $J = 14.9$ and 8.8 Hz, 1H), 4.26 (dd, $J = 9.2$ and 5.5 Hz, 1H), 6.66–6.81 (m, 3H), 6.96 (s, 2H), 7.11 (mc, 1H); ^{13}C-NMR ($CDCl_3$): δ 21.2 (q), 23.5 (q), 35.2 (t), 46.7 (d), 60.3 (d), 116.9 (d), 119.2 (d), 121.8 (brd), 125.2 (s), 128.3 (d), 128.7 (d), 145.1 (s), 157.8 (s); IR (KBr): 3291, 3150, 3049, 2966, 2927, 2870, 1608, 1590, 1492, 1476, 1455, 1386, 1371, 1259, 1166, 1152, 1099, 1037, 932, 843, 754, 724 cm^{-1}; HRMS calcd. for $C_{14}H_{19}N_3O$: 245.1528; found: 245.1512.

*4.2.1.3. (RS)-2-[1-(methylamino)ethyl]phenol rac-**1g***. Colorless solid (5.67 g, 92%), obtained from 2-hydroxyacetophenone (5.65 g, 41.4 mmol) and a solution of methylamine in methanol (33%, 25.0 ml, 200 mmol). The reductive amination was run at a hydrogen pressure of 40 atm. Following work-up, analytically pure material was obtained without further purification. mp. 68°C (Ref. [25]: 60°C); TLC $R_f = 0.82$ [dichloromethane/methanol (saturated with ammonia) 9:1]; ^{1}H-NMR ($CDCl_3$): δ 1.44 (d, $J = 6.7$ Hz, 3H), 2.42 (s, 3H), 3.82 (q, $J = 6.7$ Hz, 1H), 6.75–6.83 (m, 2H), 6.94–6.98 (m, 1H), 7.11–7.18 (m, 1H); ^{13}C-NMR ($CDCl_3$): δ 22.3 (q), 33.9 (q), 60.9 (d), 116.6 (d), 119.0 (d), 126.4 (s), 128.2 (d), 128.3 (d), 157.2 (s); Anal. calcd. for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26; found: C, 71.54; H, 8.60; N, 9.22.

*4.2.2. General procedure for the preparation of the N-phthalimido protected ethylene diamines rac-**2a–e,g**, **2a***

*4.2.2.1. (RS)-2-[2-[[1-(2-Hydroxyphenul)-2-(1H-imidazol-2-yl)ethyl]methyl-amino]ethyl]-1H-isoindole-1,3(2H)-dione rac-**2a***. A 250 ml flask was charged with a solution of the amine *rac*-**1a** (4.28 g, 19.7 mmol) and of 2-(*N*-phthalimido)acetaldehyde (3.78 g, 19.7 mmol) in 110 ml of dry methanol. Sodium cyanoborohydride (867 mg, 13.8 mmol) was added in one portion and the resulting solution was stirred for 30 min at room temperature. Then, 1.6 ml of a solution

of hydrogen chloride in methanol (4.2 M) were added. Stirring was continued until the reaction was complete (ca. 7 h). By the addition of concentrated hydrochloric acid at 0°C, the pH of the solution was adjusted to 2. After removal of the solvent, the semi-solid residue was extracted (3 × 200 ml) with a 95:5 mixture of dichloromethane/methanol (saturated with ammonia). The extract was dried over anhydrous potassium carbonate, and the solvent was removed in vacuo. After purification by column chromatography [adsorbent/substrate 40:1; dichloromethane/methanol (saturated with ammonia) 95:5], the product was obtained as a colorless foam (5.85 g, 76%). mp. 90–110°C (dec.); TLC R_f = 0.50 [dichloromethane/methanol (saturated with ammonia) 95:5]; ^{1}H-NMR ($CDCl_3$): δ 2.45 (s, 3H), 2.69–2.75 (m, 1H), 2.82–2.86 (m, 1H), 2.98 (dd, J = 14.2 and 9.7 Hz, 1H), 3.36 (dd, J = 14.3 and 5.1 Hz, 1H), 3.68–3.87 (m, 2H), 4.00 (dd, J = 9.7 and 5.1 Hz, 1H), 6.22–6.25 (m, 1H), 6.52–6.64 (m, 2H), 6.75 (s, 2H), 6.90–6.96 (m, 1H), 7.67–7.78 (m, 4H); IR (KBr): 3148, 3057, 2941, 2854, 1711, 1467, 1454, 1436, 1396, 1358, 1253, 1085, 755, 719 cm^{-1}; Anal. calcd. for $C_{22}H_{22}N_4O_3$: C, 67.66; H, 5.68; N, 14.36; found: C, 66.79; H, 5.80; N, 13.75; HRMS (EI) calcd. for $C_{22}H_{22}N_4O_3$: 390.1687; found: 390.1681.

*4.2.2.2. (RS)-2-[2-[[1-(2-Hydroxyphenyl)-2(1-methyl1H-imidazol-2-yl)-ethyl]-methylamino]-ethyl]-1H-isoindole-1,3(2H)-dione rac-**2b**.* Colorless foam (1.92 g, 60%), obtained from the amine *rac*-**1b** (1.84 g, 7.96 mmol) and 2-(*N*-phthalimido)acetaldehyde (1.64 g, 8.65 mmol). Stirring at room temperature was continued for an additional 3 d. Purification by column chromatography (ethyl acetate/methanol 9:1). mp. 76°C; TLC R_f = 0.27 (ethyl acetate/methanol 9:1); ^{1}H-NMR ($CDCl_3$): δ 2.60 (s, 3H), 2.64–2.76 (m, 1H), 2.74 (s, 3H), 2.93 (dd, J = 13.6 and 11.0 Hz, 1H), 3.05 (mc, 1H), 3.38 (dd, J = 13.6 and 4.4 Hz, 1H), 3.67–3.77 (m, 1H), 3.86 (dd, J = 11.0 and 4.4 Hz, 1H), 3.94–4.04 (m, 1H), 6.28 (mc, 1H), 6.35 (mc, 1H), 6.48 (d, J = 1.1 Hz, 1H), 6.51 (mc, 1H), 6.86 (d, J = 1.5 Hz, 1H), 6.97 (mc, 1H), 7.72 (mc, 2H), 7.83 (mc, 2H), 10.53 (brs, 1H), signal at δ = 10.53 exchangeable with D_2O; ^{13}C-NMR ($CDCl_3$): δ 28.6 (t), 31.6 (q), 35.1 (t), 38.8 (q), 53.0 (t), 69.7 (d), 116.4 (d), 119.3 (d), 120.2 (d), 123.2 (d), 124.9 (s), 127.2 (d), 128.5 (d), 128.8 (d), 132.3 (s), 133.8 (d), 144.9 (s), 156.5 (s), 168.3 (s); IR (KBr): 3600–3200 (br), 2946, 2858, 1772, 1711, 1615, 1589, 1491, 1438, 1397, 1254, 1085, 758, 721 cm^{-1}.

*4.2.2.3. (RS)-2-[2-[[1-(2-Hydroxy-3-methyl-phenyl)-2-(1H-imidazol-2-yl)-ethyl]methylamino]ethyl]-1H-isoindole-1,3(2H)-dione rac-**2c**.* Colorless foam (2.61 g, 75%), obtained from the amine *rac*-**1c** (2.00 g, 8.65 mmol) and 2-(*N*-phthalimido)acetaldehyde (1.64 g, 8.65 mmol). Stirring at room temperature was continued for 3 d. For the extraction of the crude product, dichloromethane/methanol (saturated with ammonia) 9:1 was used. mp. 90–105°C; TLC R_f = 0.30 (dichloromethane/methanol (saturated with ammonia) 95:5); ^{1}H-NMR ($CDCl_3$): δ 1.67 (s, 3H), 2.57 (s, 3H), 2.61–2.66 (m, 1H), 2.98 (dd, J = 14.0 Hz and 10.7 Hz, 1H), 2.93–3.02 (m, 1H), 3.47 (dd, J = 14.0 and 4.4 Hz, 1H), 3.69–3.76 (m, 1H), 3.84 (dd, J = 10.7 and 4.4, 1H), 3.90–3.96 (m, 1H), 6.39–6.50 (m, 2H), 6.76 (s, 2H), 6.86–6.88 (m, 1H), 7.71–7.84 (m, 4H); ^{13}C-NMR ($CDCl_3$): δ 14.9 (q), 29.8 (t), 35.0 (t), 38.2 (q), 52.4 (t), 68.4(d), 118.9 (d), 123.2 (d), 124.0 (s), 125.2 (s), 126.2 (d), 130.1 (d), 132.2 (s), 133.8 (d), 144.9 (s), 154.2 (s), 168.3 (s); IR (KBr): 3600–3000 (br), 3055, 2918, 2853, 1772, 1712, 1614, 1595, 1557, 1466, 1436, 1397, 1084, 720 cm^{-1}.

*4.2.2.4. (RS)-2-[2-[[1-(2-Hydroxy-5-methoxy-phenyl)-2-(1H-imidazol-2-yl)-ethyl]methylamino]ethyl]-1H-isoindole-1,3(2H)-dione rac-**2d**.* Colorless foam (1.25 g, 70%), obtained from the amine *rac*-**1d** (1.05 g, 4.22 mmol) and

2-(*N*-phthalimido)acetaldehyde (798 mg, 4.22 mmol). Stirring at room temperature was continued for an additional 3d. Extraction with dichloromethane/methanol (saturated with ammonia) 9:1 was followed by column chromatography [dichloromethane/methanol (saturated with ammonia) 98:2]. mp. 85–105°C; TLC R_f = 0.15 [dichloromethane/methanol (saturated with ammonia) 98:2]; ^{1}H-NMR ($CDCl_3$): δ 2.52 (s, 3H), 2.69–2.77 (m, 1H), 2.95 (dd, J = 14.0 and 10.3 Hz, 1H), 2.91–3.00 (m, 1H), 3.43 (dd, J = 14.0 and 4.8 Hz, 1H), 3.52 (s, 3H), 3.71–3.95 (m, 3H), 6.13–6.55 (m, 3H), 6.77 (s, 2H), 7.70–7.82 (m, 4H); ^{13}C-NMR ($CDCl_3$): δ 30.0 (t), 35.2 (t), 38.6 (q), 52.4 (t), 55.7 (q), 68.1 (d), 113.7 (d), 114.7 (d), 117.1 (d), 123.2 (d), 125.6 (s), 132.2 (s), 133.8 (d), 144.8 (s), 149.6 (s), 152.7 (s), 168.3 (s); IR (KBr): 3600–2500 (br), 3057, 2943, 2832, 1772, 1711, 1615, 1556, 1495, 1464, 1436, 1396, 1359, 1217, 1085, 1041, 720 cm^{-1}.

*4.2.2.5. (RS)-2-[2-[Ethyl[1-(2-hydroxyphenyl)-2-(1H-imidazol-2-yl)ethyl]-amino]ethyl]-1H-isoindole-1,3(2H)-dione rac-**2e***. Colorless foam (980 mg, 28%), obtained from the amine *rac*-**1e** (2.00 g, 8.65 mmol) and 2-(*N*-phthalimido)acetaldehyde (2.02 g, 10.7 mmol) and sodium cyanoborohydride (480 mg, 7.64 mmol). Stirring at room temperature was continued for an additional 4 d. Purification by column chromatography (ethyl acetate/methanol 9:1). mp. 105°C; TLC R_f = 0.69 [dichloromethane/methanol (saturated with ammonia) 9:1]; ^{1}H-NMR ($CDCl_3$): δ 1.15 (t, J = 7.2 Hz, 3H), 2.77–3.04 (m, 4H), 3.10 (dd, J = 14.0 and 10.7 Hz, 1H), 3.46 (dd, J = 14.3 and 4.0 Hz, 1H), 3.83 (mc, 2H), 4.24 (mc, 1H), 6.37 (dd, J = 8.4 and 1.1 Hz, 1H), 6.59–6.71 (m, 2H), 6.81 (s, 2H), 7.01 (mc, 1H), 7.71–7.75 (m, 2H), 7.81–7.85 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ 10.7 (q), 29.3 (t), 35.6 (t), 44.0 (t), 47.5 (t), 64.3 (d), 116.5 (d), 119.6 (d), 123.3 (d), 125.0 (s), 128.6 (d), 128.9 (d), 132.1 (s), 134.0 (d), 144.8 (s), 156.1 (s), 168.4 (s); IR (KBr): 3600–2300 (br), 3058, 2973, 2934, 2852, 1772, 1712, 1612, 1588, 1555, 1466, 1454, 1434, 1397, 1252, 1087, 754, 719 cm^{-1}.

*4.2.2.6. (S)-2-[2-[[1-(2-Hydroxyphenyl)-2-(1H-imidazol-2-yl)ethyl]methyl-amino]ethyl]-1H-isoindole-1,3(2H)-dione **2a***. Colorless foam (1.50 g, 83%), obtained from the enantiomerically pure amine **1a** (835 mg, 3.84 mmol) and 2-(*N*-phthalimido)acetaldehyde (725 mg, 3.84 mmol) as described for *rac*-**2a**. mp. 90–110°C; TLC R_f = 0.50 [dichloromethane/methanol (saturated with ammonia) 95:5]; ^{1}H-NMR ($CDCl_3$): δ 2.53 (s, 3H), 2.72–2.80 (m, 1H), 2.91–2.99 (m, 1H), 2.99 (dd, J = 14.2 and 10.1 Hz, 1H), 3.44 (dd, J = 14.2 and 4.6 Hz, 1H), 3.71–3.78 (m, 1H), 3.92 (dd, J = 10.2 and 4.7 Hz, 1H), 3.80–3.94 (m, 1H), 6.32–6.34 (m, 1H), 6.56–6.60 (m, 2H), 6.77 (s, 2H), 6.97–7.02 (m, 1H), 7.71–7.83 (m, 4H); IR (KBr): identical with *rac*-**2a**; HRMS (EI) calcd. for $C_{22}H_{22}N_4O_3$: 390.1687; found: 390.1714. The enantiomeric purity of **2a** (ee > 96%) was determined by an ^{1}H-NMR shift experiment using 4.0 equivalents of *R*(+)-1,1'-bi-(2-naphthol) in $CDCl_3$.

*4.2.2.7. (RS)-2-[2-[[1-(2-Hydroxyphenyl)ethyl]-methylamino]ethyl]-1H-isoindole-1,3(2H)-dione rac-**2g***. Colorless solid (3.34 g, 78%), obtained from the amine *rac*-**1g** (2.00 g, 13.2 mmol), 2-(*N*-phthalimido)acetaldehyde (2.50 g, 13.2 mmol) and sodium cyanoborohydride (584 mg, 9.27 mmol). Stirring at room temperature was continued for an additional 2 d. Extraction with a 9:1 mixture of dichloromethane/methanol (saturated with ammonia) was followed by column chromatography (hexane/ethyl acetate 2:1). mp: 90–92°C; TLC R_f = 0.38 (hexane/ethyl acetate 2:1); ^{1}H-NMR ($CDCl_3$): δ 1.37 (d, J = 6.6 Hz, 3H), 2.49 (s, 3H), 2.77 (t, J = 5.9 Hz, 2H), 3.82 (m, 3H), 6.24–7.04 (m, 4H), 7.71–7.89 (m, 4H), 10.6 (s, 1H), signal at δ = 10.6 exchangeable with D_2O; ^{13}C-NMR ($CDCl_3$): δ 12.7 (q), 35.3 (t), 37.7 (q), 50.9 (t), 62.8 (d), 116.3 (d), 119.2 (d), 123.2 (d), 123.4 (s), 126.9 (d), 128.6 (d), 132.3 (s), 133.8 (d),

157.0 (s), 168.3 (s); IR (KBr): 3650–2500 (br), 3058, 3032, 2944, 2849, 1771, 1710, 1611, 1586, 1494, 1466, 1437, 1393, 1290, 1256, 1086, 1039, 759, 717 cm^{-1}; MS (CI) calcd. for $C_{19}H_{20}N_2O_3$: 324; found: 325 $(M+H)^+$.

*4.2.3. General procedure for the preparation of the unprotected ethylene diamines rac-**3a–e, g, 3a***

*4.2.3.1. (RS)-2-[1-[(2-Aminoethyl)methylamino]-2-(1H-imidazol-2-yl)ethyl]-phenol rac-**3a***. A 100 ml flask was charged with a solution of the phthalimide *rac*-**2a** (5.22 g, 13.4 mmol) in 50 ml of dry ethanol. 99%-Hydrazine hydrate (670 mg, 13.4 mmol) was added, and the resulting mixture was stirred for 18 h at room temperature. A colorless solid precipitated. The mixture was poured into 200 ml of 2 M hydrochloric acid, and stirring at room temperature was continued for an additional hour. After removal of the solvent in vacuo, the residue was extracted (2 × 100 ml) with a mixture of dichloromethane/methanol (saturated with ammonia) 9:1. The extract was dried over anhydrous potassium carbonate, and the solvent was removed in vacuo. Column chromatography [adsorbent/substrate 40:1; dichloromethane/methanol/methanol (saturated with ammonia) 35:60:5] afforded a colorless foam. The crude material was dissolved in chloroform. Slow evaporation of the solvent afforded a colorless solid (1.49 g, 43%). mp. 137°C (dec.); TLC $R_f = 0.14$ [dichloromethane/ methanol (saturated with ammonia) 9:1]; ^{1}H-NMR (CD_3OD): δ 2.31 (s, 3H), 2.57–2.63 (m, 2H), 2.76–2.81 (m, 2H), 3.10 (dd, $J = 14.5$ and 9.0 Hz, 1H), 3.40 (dd, $J = 14.5$ Hz and 6.4 Hz, 1H), 4.35 (dd, $J = 8.8$ and 6.2 Hz, 1H), 6.61–6.66 (m, 1H), 6.72–6.75 (m, 1H), 6.83 (s, 2H), 6.86–6.88 (m, 1H), 7.02–7.07 (m, 1H); ^{13}C-NMR ($CDCl_3$): δ 29.8 (t), 38.1 (q), 39.6 (t), 56.8 (t), 65.4 (d), 117.2 (d), 120.0 (d), 122.2 (d), 126.2 (s), 129.5 (d), 129.5 (d), 147.3 (s), 157.9 (s); IR (KBr): 3600–2100 (br), 3353, 3281, 3137, 3113, 3038, 2968, 2942, 2873, 2838, 2821, 2100–1750 (br), 1599, 1451, 1398, 1274, 1250, 982, 721 cm^{-1}; Anal. calcd. for $C_{14}H_{20}N_4O \cdot 0.5\ H_2O$: C, 62.43; H, 7.86; N, 20.80; found: C, 62.36; H, 7.89; N, 20.81; HRMS (EI) calcd. for $C_{14}H_{20}N_4O$: 260.1633; found: 260.1621.

*4.2.3.2. (RS)-2-[1-[(2-Aminoethyl)methylamino]-2-(1-methyl-1H-imidazol-2-yl)ethyl]phenol rac-**3b***. Colorless solid (320 mg, 34%), obtained from the phthalimide *rac*-**2b** (1.41 g, 3.47 mmol) and 99%-hydrazine hydrate (194 mg, 3.88 mmol). Stirring at room temperature was continued for an additional 2d. mp. 52°C; TLC $R_f = 0.25$ [dichloromethane/methanol (saturated with ammonia) 9:1]. ^{1}H-NMR ($CDCl_3$): δ 2.44 (s, 3H), 2.48–2.62 (m, 2H), 2.71–2.85 (m, 2H), 2.83 (s, 3H), 2.91 (dd, $J = 13.6$ and 10.3 Hz, 1H), 3.27 (dd, $J = 13.6$ and 4.4 Hz, 1H), 3.85 (dd, $J = 10.3$ and 4.4 Hz, 1H), 6.32 (mc, 1H), 6.43–6.50 (m, 2H), 6.67 (mc, 1H), 6.80 (brs, 1H), 6.99 (mc, 1H); ^{13}C-NMR ($CDCl_3$): δ 28.7 (t), 31.7 (q), 38.8 (q), 39.1 (t), 57.4 (t), 69.4 (d), 116.5 (d), 119.1 (d), 120.3 (d), 125.1 (s), 127.2 (d), 128.5 (d), 128.8 (d), 145.0 (s), 157.1 (s); IR (KBr): 3600–2200 (br), 3042, 2943, 2852, 1589, 1491, 1455, 1411, 1397, 1361, 1282, 1257, 1037, 756 cm^{-1}.

*4.2.3.3. (RS)-2-[1-[(2-Aminoethyl)methylamino]-2-(1H-imidazol-2-yl)ethyl]-6-methyl-phenol **rac-3c***. Colorless foam (345 mg, 49%), obtained from a solution of the phthalimide *rac*-**3c** (962 mg, 2.38 mmol) in 20 ml of dry methanol. 99%-Hydrazine hydrate (357 mg, 7.14 mmol) was added in three portions over a period of 30 h. The resulting solution was stirred at room temperature for 3 d, followed by work-up as described above and purification by column chromatography [dichloromethane/methanol (saturated with ammonia) 9:1]. mp. 55–60°C; TLC $R_f = 0.31$ [dichloromethane/methanol (saturated with ammonia) 9:1]. ^{1}H-NMR ($CDCl_3$): δ 2.18 (s, 3H), 2.32 (s, 3H), 2.60–2.68 (m, 2H), 2.84–2.88 (m, 2H), 3.10 (dd, $J = 14.3$ Hz and $J = 9.7$ Hz, 1H), 3.38 (dd, $J = 14.3$ and

4.4 Hz, 1H), 4.01 (dd, $J = 9.7$ and 4.4 Hz, 1H), 6.53–6.74 (m, 2H), 6.83 (s, 2H), 6.97–7.00 (m, 1H); ^{13}C-NMR ($CDCl_3$): δ 15.9 (q), 29.5 (t), 38.2 (q), 39.2 (t), 56.8 (t), 67.5 (d), 118.7 (d), 121.6 (brd), 124.4 (s), 125.3 (s), 126.0 (d), 130.0 (d), 145.1 (s), 154.9 (s); IR (KBr): 3600–2250 (br), 3050, 2917, 2855, 1594, 1563, 1464, 1342, 1294, 1258, 1230, 1220, 1101, 1086, 1048, 1020, 747 cm^{-1}; MS (CI) calcd. for $C_{15}H_{22}N_4O$: 274; found: 275 $(M + H)^+$.

*4.2.3.4. (RS)-2-[1-[(2-Aminoethyl)methylamino]-2-(1H-imidazol-2-yl)ethyl]-4-methoxy-phenol rac-**3d**.* Colorless foam (494 mg, 62%), obtained from a solution of the phthalimide *rac*-**3d** (1.15 g, 2.74 mmol) in 15 ml of dry methanol. 99%-Hydrazine hydrate (411 mg, 8.22 mmol) was added in three portions over a period of 30 h. The resulting solution was stirred at room temperature for 3 d, followed by work-up as described above and purification by column chromatography [dichloromethane/methanol (saturated with ammonia) 95:5]. mp. 131–135°C (dec.); TLC $R_f = 0.21$ (dichloromethane/methanol (saturated with ammonia) 9:1); ^{1}H-NMR (CD_3OD): δ 2.35 (s, 3H), 2.59–2.65 (m, 2H), 2.76–2.81 (m, 2H), 3.06 (dd, $J = 14.4$ and 9.2 Hz, 1H), 3.40 (dd, $J = 14.4$ and 6.1 Hz, 1H), 3.60 (s, 3H), 4.26 (dd, $J = 9.1$ and 6.1 Hz, 1H), 6.41–6.42 (m, 1H), 6.62–6.66 (m, 2H), 6.85 (s, 2H); ^{13}C-NMR (CD_3OD): δ 30.0 (t), 38.3 (q), 39.6 (t), 56.2 (q), 57.1 (t), 66.1 (d), 115.1 (d), 115.2 (d), 117.7 (d), 122.3 (br d), 126.9 (s), 147.2 (s), 151.4 (s), 154.0 (s); IR (KBr): 3600–2250 (br), 3350, 3283, 3134, 3108, 3041, 2990, 2874, 2843, 2834, 1589, 1498, 1449, 1432, 1273, 1217, 1109, 984, 752 cm^{-1}; MS(CI) calcd. for $C_{15}H_{22}N_4O_2$: 290; found: 291 $(M + H)^+$.

*4.2.3.5. (RS)-2-[1-[(2-Aminoethyl)ethylamino]-2-(1H-imidazol-2-yl)ethyl]phenol rac-**3e**.* Colorless solid (55 mg, 27%), obtained from the phthalimide *rac*-**2e** (305 mg, 755 μmol) and 99%-hydrazine hydrate (58.7 mg, 1.16 mmol). Stirring at room temperature was continued for 3 d, followed by work-up as described above and purification by column chromatography [dichloromethane/methanol (saturated with ammonia) 9:1]. The crude product was obtained as an oil and was crystallized from chloroform. mp. 75°C; TLC $R_f = 0.10$ [dichloromethane/methanol (saturated with ammonia) 9:1]; ^{1}H-NMR (CD_3OD): δ 1.06 (t, $J = 7.1$ Hz, 3H), 2.55–2.86 (m, 6H), 3.10 (dd, $J = 14.3$ and 9.2 Hz, 1H), 3.38 (dd, $J = 14.5$ and 6.1 Hz, 1H), 4.55 (dd, $J = 9.2$ and 6.1 Hz, 1H), 6.65 (mc, 1H), 6.73 (mc, 1H), 6.85 (s, 2H), 6.87–6.93 (m, 1H), 7.06 (mc, 1H); IR (KBr): 3600–2200 (br), 3054, 2969, 2929, 2871, 2000–1700 (br), 1591, 1452, 1405, 1386, 1298, 1275, 1253, 1168, 1097, 754 cm^{-1}.

*4.2.3.6. (S)-2-[1-[(2-Aminoethyl)methylamino]-2-(1H-imidazol-2-yl)ethyl]phenol **3a**.* Colorless solid (140 mg, 42%), obtained from the phthalimide **2a** (210 mg, 538 μmol) and 99%-hydrazine hydrate (53.8 mg, 1.08 μmol) as described for *rac*-**3a**. Stirring was continued at room temperature for 24 h. TLC $R_f = 0.14$ [dichloromethane/methanol (saturated with ammonia) 9:1]; ^{1}H-NMR, IR (KBr): identical with *rac*-**3a**; HRMS (EI) calcd. for $C_{14}H_{20}N_4O$: 260.1633; found: 260.1628. The enantiomeric purity was determined by derivatization to the Schiff's base **4a**.

*4.2.3.7. (RS)-2-[1-[(2-Aminoethyl)methylamino]ethyl]phenol rac-**3g**.* Colorless oil (698 mg, 48%), obtained from the phthalimide *rac*-**2g** (2.44 mg, 7.52 mmol) and 99%-hydrazine hydrate (1.13 g, 22.6 mmol). Purification was done by column chromatography [dichloromethane/methanol (saturated with ammonia) 9:1]. TLC $R_f = 0.32$ [dichloromethane/methanol (saturated with ammonia) 9:1]; ^{1}H-NMR ($CDCl_3$): δ 1.39 (d, $J = 6.8$ Hz, 3H), 2.27 (s, 3H), 2.52–2.59 (m, 2H), 2.83–2.88 (m, 2H), 3.90 (q, $J = 6.8$ Hz, 1H), 6.77–6.78 (m, 4H); ^{13}C-NMR ($CDCl_3$): δ 12.5 (q), 36.8 (q), 39.6 (t), 56.6 (t), 62.4 (d), 116.4 (d), 119.0 (d), 127.0 (d), 127.1 (s), 128.6

(d), 157.8 (s); IR (KBr): 3600–2200 (br), 3041, 2947, 2890, 1607, 1588, 1490, 1453, 1289, 1256, 944, 843, 755 cm^{-1}.

*4.2.4. General procedure for the preparation of the ligands rac-**4a–e, g, 4a, h***

*4.2.4.1. (RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxyphenyl)-2-(1H-imidazol-2-yl)methyl]amino]ethyl]imino]methyl]phenol rac-**4a***. A 25 ml flask was charged with a solution of 3,5-di-*tert*-butylsalicylaldehyde (900 mg, 3.84 mmol) in 10 ml of dry methanol, and the diamine *rac*-**3a** (1.00 g, 3.84 mmol) was added. The yellow solution was stirred at room temperature for 15 min. Removal of the solvent in vacuo and recrystallization from dry ethanol gave a yellow, microcrystalline solid (1.09 g, 60%). mp. 163°C; TLC R_f = 0.66 (ether/methanol 9:1); ^{1}H-NMR ($CDCl_3$): δ 1.30 (s, 9H), 1.43 (s, 9H); 2.48 (s, 3H), 2.87–3.00 (m, 2H), 3.06 (dd, J = 14.0 and 9.9 Hz, 1H), 3.46 (dd, J = 14.0 and 4.8 Hz, 1H); 3.73 (ut, J = 6.6 Hz, 2H); 4.03 (dd, J = 9.6 and 4.8 Hz, 1H), 6.62–6.63 (m, 2H), 6.75–6.85 (m, 2H), 7.05–7.40 (m, 4H), 8.32 (s, 1H); ^{13}C-NMR ($CDCl_3$): δ 29.4 (q), 30.7 (t), 31.5 (q), 34.1 (s), 35.0 (s), 39.3 (q), 54.9 (t), 56.9 (t), 67.9 (d), 116.8 (d), 117.8 (s), 119.3 (d), 126.0 (d), 127.1 (d), 127.2 (s), 128.7 (d), 129.0 (d), 136.7 (s), 140.2 (s), 144.9 (s), 156.6 (s), 157.9 (s), 167.4 (d); IR (KBr): 3151, 3060, 2960, 2908, 2866, 2709, 1632, 1593, 1453, 1361, 1275, 1252, 753, cm^{-1}; Anal. calcd. for $C_{29}H_{40}N_4O_2$: C, 73.07; H, 8.46; N, 11.75; found: C, 73.12; H, 8.38; N, 11.71.

*4.2.4.2. (RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxyphenyl)-2-(1-methyl-1H-imidazol-2-yl)methyl]amino]ethyl]imino]methyl]-phenol rac-**4b***. Yellow crystals (300 mg, 52%), obtained from the diamine *rac*-**3b** (320 mg, 1.17 mmol) and 3,5-di-*tert*-butylsalicylaldehyde (273 mg, 1.17 mmol). Stirring was continued at room temperature for an additional hour. Upon work-up as described above, an oily residue was obtained. The crude material was crystallized from a mixture of ether/methanol 99:1. mp. 134°C; TLC R_f = 0.80 [dichloromethane/methanol (saturated with ammonia) 9:1]; ^{1}H-NMR ($CDCl_3$): δ 1.30 (s, 9H), 1.43 (s, 9H), 2.56 (s, 3H), 2.80 (s, 3H), 2.90–3.09 (m, 3H), 3.43 (dd, J = 13.8 Hz and J = 4.1 Hz, 1H), 3.78 (mc, 2H), 4.01 (dd, J = 10.6 Hz and J = 4.0 Hz, 1H), 6.39 (mc, 1H), 6.54 (d, J = 1.1 Hz, 1H), 6.56 (mc, 1H), 6.77 (mc, 1H), 6.93 (d, J = 1.1 Hz, 1H), 7.06–7.13 (m, 2H), 7.37 (d, J = 2.6 Hz, 1H), 8.37 (s, 1H); ^{13}C-NMR ($CDCl_3$): δ 29.0 (t), 29.4 (q), 31.5 (q), 31.6 (q), 34.1 (s), 35.0 (s), 39.9 (q), 55.1 (t), 56.8 (t), 69.4 (d), 116.7 (d), 117.8 (s), 119.2 (d), 120.3 (d), 124.8 (s), 126.0 (d), 127.1 (d), 127.2 (d), 128.5 (d), 128.9 (d), 136.7 (s), 140.2 (s), 145.0 (s), 157.1 (s), 157.9 (s), 167.3 (d); IR (KBr): 3044, 2958, 2866, 2799, 2783, 1632, 1590, 1469, 1454, 1391, 1361, 1274, 1252, 1203, 1174, 1038, 881, 829, 772, 754 cm^{-1}; Anal. calcd. for $C_{30}H_{42}N_4O_2$: C, 73.43; H, 8.63; N, 11.42; found: C, 73.30; H, 8.75; N, 11.30.

*4.2.4.3. (RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxy-3-methyl-phenyl)-2-(1H-imidazol-2-yl)methyl]amino]ethyl]imino]methyl]-phenol rac-**4c***. Yellow crystals (84 mg, quant.), obtained from the diamine *rac*-**3c** (45 mg, 164 μmol) and 3,5-di-*tert*-butylsalicylaldehyde (38.4 mg, 164 μmol). mp. 157°C; TLC R_f = 0.57 (ether/methanol 9:1); ^{1}H-NMR ($CDCl_3$): δ 1.30 (s, 9H), 1.43 (s, 9H), 2.16 (s, 3H), 2.49 (s, 3H), 2.86–2.99 (m, 2H), 3.07 (dd, J = 14.0 and 10.7 Hz, 1H), 3.48 (dd, J = 14.0 and 4.4 Hz, 1H), 3.74 (t, J = 6.6 Hz, 2H), 3.95 (dd, J = 10.3 and 4.4 Hz, 1H), 6.43–6.56 (m, 2H), 6.80 (s, 2H), 6.98–7.00 (m, 1H), 7.07 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 2.4 Hz, 1H), 8.35 (s, 1H); ^{13}C-NMR ($CDCl_3$): δ 15.7 (q), 29.5 (q), 30.4 (t), 31.3 (q), 39.2 (q), 54.7 (t), 56.8 (t), 68.3 (d), 117.8 (s), 118.7 (d), 124.2 (s), 125.6 (s), 126.1 (d), 126.3 (d), 127.1 (d), 130.2 (d), 136.7 (s), 140.2 (s), 144.9 (s), 154.8 (s), 157.9 (s), 167.4 (d); IR (KBr): 3500–2250 (br), 3049, 2958, 2911, 2867, 1631, 1595, 1466, 1440, 1392, 1362, 1271, 1253, 1147, 1085, 1024, 830, 745 cm^{-1}; Anal. calcd. for $C_{30}H_{42}N_4O_2 \cdot 1.5\ H_2O$:

C, 69.90; H, 8.76; N, 10.82; found: C, 69.66; H, 8.32; N, 10.38.

*4.2.4.4. (RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxy-5-methoxy-phenyl)-2-(1H-imidazol-2-yl)methyl]amino]ethyl]imino]methyl]phenol rac-**4d***. Yellow crystals (412 mg, quant.), obtained from the diamine *rac*-**3d** (237 mg, 818 μmol) and 3,5-di-*tert*-butylsalicylaldehyde (191 mg, 818 μmol). Stirring at room temperature was continued for 30 min. Analytically pure material was obtained by recrystallization from chloroform. mp. 163°C; TLC R_f = 0.61 (ether/methanol 9:1); ^{1}H-NMR ($CDCl_3$): δ 1.30 (s, 9H), 1.43 (s, 9H), 2.48 (s, 3H), 2.82–3.00 (m, 2H), 3.03, (dd, J = 13.8 and 9.7 Hz, 1H), 3.46 (dd, J = 13.8 and 4.6 Hz, 1H), 3.55 (s, 3H), 3.73 (m, 2H), 3.96 (dd, J = 9.7 and 4.6 Hz, 1H), 6.17–6.18 (m, 1H), 6.64–6.73 (m, 2H), 6.80 (s, 2H), 7.07 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 2.4 Hz, 1H), 8.35 (s, 1H); ^{13}C-NMR ($CDCl_3$): δ 29.4 (q), 30.8 (t), 31.5 (q), 34.1 (s), 35.0 (s), 39.4 (q), 54.9 (t), 55.7 (q), 56.9 (t), 68.2 (d), 113.8 (d), 114.9 (d), 117.4 (d), 117.8 (s), 125.3 (s), 126.1 (d), 127.2 (d), 136.7 (s), 140.2 (s), 144.9 (s), 150.1 (s), 152.7 (s), 157.9 (s), 167.4 (d); IR (KBr): 3600–2500 (br), 3050, 2957, 2908, 2868, 1631, 1596, 1496, 1467, 1440, 1390, 1361, 1272, 1250, 1215, 1174, 743 cm^{-1}; Anal. calcd. for $C_{30}H_{42}N_4O_3 \cdot 0.5\ H_2O$: C, 69.87; H, 8.40; N, 10.86; found: C, 70.03; H, 8.48; N, 10.70.

*4.2.4.5. (RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxyphenyl)-2-(1H-imidazol-2-yl)ethyl]amino]ethyl]imino]methyl]phenol rac-**4e***. Yellow crystals (36 mg, 75%), obtained from the diamine *rac*-**3e** (27.0 mg, 98.0 μmol) and 3,5-di-*tert*-butylsalicylaldehyde (23.0 mg, 98.0 μmmol). Stirring at room temperature was continued for an additional 15 min. The crude material was dissolved in ethanol and precipitated by the addition of ether. Analytically pure material was obtained by an additional recrystallization from methanol/ether. mp.162°C; TLC R_f = 0.76 [dichloromethane/methanol (saturated with ammonia) 9:1]; ^{1}H-NMR ([D_6]DMSO): δ 1.15 (t, J = 7.2 Hz, 3H), 1.30 (s, 9H), 1.43 (s, 9H), 2.75–3.15 (m, 5H), 3.48 (dd, J = 14.2 and 4.2 Hz, 1H), 3.75 (mc, 2H), 4.23 (dd, J = 10.5 Hz and 4.2 Hz, 1H), 6.62–6.69 (m, 2H), 6.74 (brs, 1H), 6.92 (brs, 1H), 6.99–7.12 (m, 2H), 7.22 (d, J = 2.2 Hz, 1H), 7.30 (d, J = 2.2 Hz, 1H), 8.45 (s, 1H); 11.72 (brs, 1H), signal at δ = 11.72 ppm exchangeable with D_2O; ^{13}C-NMR ([D_6]DMSO): δ 10.7 (q), 29.4 (q), 30.7 (t), 31.5 (q), 34.2 (s), 35.0 (s), 44.6 (t), 50.0 (t), 57.5 (t), 65.4 (d), 116.8 (d), 117.8 (s), 119.3 (d), 125.1 (s), 126.1 (d), 127.2 (d), 128.7 (d), 129.0 (d), 136.7 (s), 140.2 (s), 144.8 (s), 156.9 (s), 157.9 (s), 167.4 (d); IR (KBr): 3600–2400 (br), 3061, 2959, 2909, 2867, 1632, 1594, 1541, 1453, 1393, 1363, 1275, 1252, 1098, 753 cm^{-1}; Anal. calcd. for $C_{30}H_{42}N_4O_2$: C, 73.43; H, 8.63; N, 11.42; found: C, 73.24; H, 8.61; N, 11.30.

*4.2.4.6. (S)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxyphenyl)-2-(1H-imidazol-2-yl)methyl]amino]ethyl]imino]methyl]phenol **4a***. Yellow crystals (149 mg, 58%), obtained from the diamine **3a** (140 mg, 538 μmol) and 3,5-di-*tert*-butylsalicylaldehyde (126 mg, 538 μmol) as described for *rac*-**4a**. The crude material was crystallized from ether/methanol 9:1. mp. 159°C; TLC R_f = 0.56 (ether/methanol 9:1); ^{1}H-NMR, IR (KBr): identical with *rac*-**4a**; $[\alpha]_D^{20}$ = +85.8° (c = 0.43, methanol); Anal. calcd. for $C_{29}H_{40}N_4O_2$: C,73.07; H, 8.46; N, 11.75; found: C, 73.00; H, 8.51; N, 11.52; The enantiomeric purity (ee > 95%) was determined by an ^{1}H-NMR shift experiment using 5.0 equivalents of R(+)-1,1′-bi-(2-naphthol) in $CDCl_3$.

*4.2.4.7. (RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[[1-(2-hydroxyphenyl)ethyl]-methylamino]ethyl]imino]methyl]phenol rac-**4g***. Yellow solid (870 mg, quant.), obtained from the diamine *rac*-**3g** (482 mg, 2.06 mmol) and 3,5-di-*tert*-butylsalicylaldehyde (400 mg, 2.06 mmol). Stirring at room temperature was continued for an additional hour. mp. 57–68°C; TLC R_f = 0.76 (ether/methanol 9:1); ^{1}H-NMR ($CDCl_3$): δ

1.30 (s, 9H), 1.42 (d, $J = 6.6$ Hz, 3H), 1.43 (s, 9H), 2.40 (s, 3H), 2.87 (t, $J = 6.6$ Hz, 2H), 3.74 (ιt, $J = 6.6$ Hz, 2H), 3.94 (q, $J = 6.6$ Hz, 1H), 6.78–6.82 (m, 2H), 7.00–7.03 (m, 1H), 7.08 (d, $J = 2.4$ Hz, 1H), 7.13–7.19 (m, 1H), 7.37 (d, 2.4 Hz, 1H), 8.37 (s, 1H); ^{13}C-NMR ($CDCl_3$): δ 13.3 (q), 29.4 (q), 31.5 (q), 34.1 (s), 35.0 (s), 38.2 (q), 53.9 (t), 57.8 (t), 62.9 (d), 116.6 (d), 117.8 (s), 119.1 (d), 126.0 (d), 126.9 (s), 127.1 (d), 128.7 (d), 136.7 (s), 140.1 (s), 157.6 (s), 157.9 (s), 167.3 (d); IR (KBr): 3600–2250 (br), 3042, 2958, 2908, 2868, 1631, 1588, 1467, 1442, 1287, 1273, 1253, 1173, 753 cm^{-1}.

4.2.4.8. (S)-2-(1,1-dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxyphenyl)-2-(1H-imidazol-2-yl)methyl]amino]ethyl]imino]methyl]phenol ***4h***. Yellow crystals (102 mg, 78%), obtained from the diamine **3a** (81.0 mg, 311 μmol) and 3-*tert*-butylsalicylaldehyde (55.4 mg, 311 μmol) as described above. The crude material was crystallized from ether/methanol 9:1. mp. 167°C; TLC $R_f = 0.55$ (ether/methanol 9:1); ^{1}H-NMR ($CDCl_3$): δ 1.42 (s, 9H), 2.52 (s, 3H), 2.93–3.05 (m, 2H), 3.06 (dd, $J = 13.6$ and 10.3 Hz, 1H), 3.50 (dd, $J = 14.0$ Hz and 4.8 Hz, 1H), 3.76 (ιt, $J = 6.8$ Hz, 2H), 3.97 (dd, $J =$ 10.3 and 4.4 Hz, 1H), 6.58–7.33 (m, 9H), 8.35 (s, 1H); IR (KBr): 3149, 3107, 3056, 2957, 2912, 2858, 2711, 1632, 1599, 1451, 1358, 1272, 753 cm^{-1}.

*4.2.5. General procedure for the preparation of the manganese(III) complexes rac-***5a–e, g, 5a, h, i**

*4.2.5.1. [(RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxyphenyl)-2-(1H-imidazol-2-yl)methyl]amino]ethyl]imino]methyl]-phenolato(2-)-N,N″,N^3,O,O″]manganese(1 +)tetraphenylborate rac-***5a***. A 10 ml flask was charged with a suspension of the ligand *rac*-**4a** (500 mg, 1.05 mmol) in 2 ml of dry methanol. A solution of manganese(II) chloride tetrahydrate (208 mg, 1.05 mmol) in 2 ml of dry methanol was added, and a homogenous brown solution was obtained. A solution of sodium tetraphenylborate (719 mg, 2.10 mmol) in 6 ml of dry methanol was added and the mixture was stirred at room temperature for an additional hour. A brown solid precipitated, and the mixture was kept at −20°C for 48 h. The brown microcrystalline solid was filtered off (561 mg, 63%). Analytically pure material was obtained by recrystallization from dry ethanol. mp. 180–182°C; TLC $R_f = 0.49$ (dichloromethane/ethanol 9:1); IR (KBr): 3054, 2960, 2906, 2868, 1611, 1480, 1269, 1252, 737, 708 cm^{-1}; Anal. calcd. for $C_{53}H_{58}MnBN_4O_2$: C, 74.96; H, 6.89; N, 6.60; found: C, 74.87; H, 6.87; N, 6.73; MS (FD) calcd. for $C_{29}H_{38}MnN_4O_2$: 529; found: 529.

*4.2.5.2. (RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[[1-(2-hydroxyphenyl)-2-(1-methyl-1H-imidazol-2-yl)ethyl]methylamino]ethyl]imino]methyl]phenolato(2-)-N,N″,N^3,O,O″]manganese(1 +)-tetraphenylborate rac-***5b***.* Brown crystals (110 mg, 63%), obtained from the ligand *rac*-**4b** (100 mg, 204 μmol), manganese(II) chloride tetrahydrate (40.4 mg, 204 μmol) and sodium tetraphenylborate (139 mg, 407 μmol). The crude material was recrystallized from methanol. Analytically pure material was obtained by an additional recrystallization from ethanol. mp. 235°C; IR (KBr): 3600–3200 (br), 3122, 3055, 2958, 2906, 2869, 1609, 1580, 1536, 1479, 1391, 1361, 1267, 1251, 1176, 1031, 953, 877, 846, 737, 706, 612, 558 cm^{-1}; Anal. calcd. for $C_{54}H_{60}BMnN_4O_2$: C, 75.17; H, 7.01; N, 6.49; found: C, 75.33; H, 7.25; N, 6.60; MS (FD) calcd. for $C_{30}H_{40}MnN_4O_2$: 543; found: 543.

*4.2.5.3. [(RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[[1-(2-hydroxy-3-methyl-phenyl)-2-(1H-imidazol-2-yl)ethyl]methylamino]ethyl]imino]methyl]-6-methyl-phenolato(2-)-N,N″,N^3,O,O″]manganese(1 +)tetraphenylborate rac-***5c***.* Brown crystals (100 mg, 55%), obtained from the ligand *rac*-**4c** (100 mg, 208 μmol), manganese(II) chloride tetrahydrate (40.3 mg, 208 μmol) and sodium tetraphenylborate (139 mg, 408 μmol). Analytically pure material was obtained by re-

crystallization from methanol. mp. 180°C; IR (KBr): 3600–3200 (br), 3054, 2960, 2908, 2869, 1609, 1558, 1536, 1475, 1460, 1307, 1252, 1176, 870, 846, 749, 736, 708 cm^{-1}; Anal. calcd. for $C_{54}H_{60}BMnN_4O_2 \cdot 0.5\ H_2O$: C, 74.39; H, 7.05; N, 6.43; found: C, 74.45; H, 7.18; N, 6.41.

*4.2.5.4. [(RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[[1-(2-hydroxy-5-methoxy-phenyl)-2-(1H-imidazol-2-yl)ethyl]methylamino]ethyl]imino]methyl]-4-methoxy-phenolato(2-)-N,N'',N^3,O,O'']-manganese(1 +)tetraphenylborate rac-**5d**.* Brown crystals (102 mg, 62%), obtained from the ligand *rac*-**4d** (94.0 mg, 186 μmol), manganese(II) chloride tetrahydrate (36.7 mg, 186 μmol) and sodium tetraphenylborate (127 mg, 371 μmol). Analytically pure material was obtained by recrystallization from dry methanol. mp. 180–182°C; IR (KBr): 3600–3200 (br), 3054, 2959, 2907, 2870, 1611, 1537, 1486, 1391, 1362, 1253, 749, 708 cm^{-1}; Anal. calcd. for $C_{54}H_{60}BMnN_4O_3 \cdot H_2O$: C, 72.32; H, 6.97; N, 6.25; found: C, 72.25; H, 7.05; N, 6.64.

*4.2.5.5. [(RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxyphenyl)-2-(1H-imidazol-2-yl)ethyl]amino]ethyl]imino]methyl] phenolato-(2-)-N,N'',N^3,O,O'']manganese(1 +)tetraphenylborate rac-**5e**.* Brown crystals (89.0 mg, 58%), obtained from the ligand *rac*-**4e** (88.0 mg, 179 μmol), manganese(II) chloride tetrahydrate (35.5 mg, 179 μmol) and sodium tetraphenylborate (123 mg, 358 μmol). Stirring at room temperature was continued for an additional 2 h. Analytically pure material was obtained by recrystallization from ethanol. mp. 165°C; IR (KBr): 3600–3200 (br), 3055, 2961, 2907, 2870, 1612, 1581, 1562, 1537, 1480, 1444, 1391, 1362, 1303, 1269, 1251, 1176, 1093, 873, 845, 752, 737, 611, 556 cm^{-1}; Anal. calcd. for $C_{54}H_{60}BMnN_4O_2$: C, 75.17; H, 7.01; N, 6.49; found: C, 74.98; H, 7.18; N, 6.67; MS (FD) calcd. for $C_{30}H_{40}MnN_4O_2$: 543; found: 543.

*4.2.5.6. [(S)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxyphenyl)-2-(1H-imidazol-2-yl)methyl]amino]ethyl]imino]methyl]-phenolato(2-)-N,N'',N^3,O,O'']manganese(1 +)tetraphenylborate **5a**.* Brown crystals (79.0 mg, 63%), obtained from the ligand **4a** (70.0 mg, 147 μmol), manganese(II) chloride tetrahydrate (29.2 mg, 147 μmol) and sodium tetraphenylborate (101 mg, 294 μmol). Analytically pure material was obtained by recrystallization from dry ethanol, mp. 181–183°C; TLC $R_f = 0.49$ (dichloromethane/ethanol 9:1); IR (KBr): identical with *rac*-**5a**; Anal. calcd. for $C_{53}H_{58}BMnN_4O_2 \cdot C_2H_5OH$: C, 73.82; H, 7.21; N, 6.26; found: C, 73.92; H, 7.30; N, 6.26; MS (FD) calcd. for $C_{29}H_{38}MnN_4O_2$: 529; found: 529.

*4.2.5.7. (RS)-2,4-Bis(1,1-dimethylethyl)-6-[[[2-[[1-(2-hydroxyphenyl)ethyl]-methylamino]ethyl]imino]methyl]phenolato(2-)-N,N',O,O']-manganese(1 +)tetraphenylborate rac-**5g**.* Dark brown crystals (103 mg, 54%), obtained from the ligand *rac*-**4g** (100 mg, 244 μmol), manganese(II) chloride tetrahydrate (48.2 mg, 244 μmol) and sodium tetraphenylborate (167 mg, 488 μmol). mp. 112°C; IR (KBr): 3600–3200 (br), 3055, 2960, 2906, 2868, 1607, 1557, 1536, 1478, 1447, 1295, 1250, 842, 737, 708 cm^{-1}; MS (FD) calcd. for $C_{26}H_{36}MnN_2O_2$: 463; found: 463.

*4.2.5.8. [(S)-2-(1,1-Dimethylethyl)-6-[[[2-[ethyl[1-(2-hydroxyphenyl)-2-(1H-imidazol-2-yl)methyl]amino]ethyl]imino]methyl]-phenolato(2-)-N,N'',N^3,O,O'']manganese(1 +)tetraphenylborate **5h**.* Brown crystals (87.0 mg, 92%), obtained from the ligand **4h** (50.0 mg, 119 μmol), manganese(II) chloride tetrahydrate (23.6 mg, 119 μmol) and sodium tetraphenylborate (81.4 mg, 238 μmol). Analytically pure material was obtained by recrystallization from dry *iso*-propanol, mp. 175–177°C; TLC $R_f =$ 0.23 (dichloromethane/ethanol 9:1); IR (KBr): 3600–3200 (br), 3055, 2999, 2959, 2869, 1611,

1480, 1268, 737, 708 cm^{-1}; Anal. calcd. for $C_{49}H_{50}BMnN_4O_2 \cdot H_2O$: C, 72.59; H, 6.46; N, 6.91; found: C, 72.61; H, 6.48; N, 7.09; MS (FD) calcd. for $C_{25}H_{30}MnN_4O_2$: 473; found: 473.

*4.2.5.9. [(S)-6-[[[2-[Ethyl[1-(2-hydroxyphenyl)-2-(1H-imidazol-2-yl)methyl]-amino]ethyl]imino]methyl]-phenolato(2-)-N,N'',N^3,O,O'']manganese-(1 +)tetraphenylborate **5i**.* A 5 ml flask was charged with a solution of the diamine **3a** (100 mg, 384 μmol) and salicylaldehyde (46.9 mg, 384 μmol) in 1 ml of methanol. Manganese(II) chloride tetrahydrate (76.0 mg, 384 μmol) were added. A brown microcrystalline solid (126 mg, 44%) was obtained from precipitation with sodium tetraphenylborate (263 mg, 768 μmol). Analytically pure material was obtained by recrystallization from ethanol. mp. 170–172°C; IR (KBr): 3329, 3055, 3035, 2999, 2932, 1616, 1480, 1269, 1252, 737, 708 cm^{-1}; Anal. calcd. for $C_{45}H_{42}BMnN_4O_2$: C, 73.38; H, 5.75; N, 7.61; found: C, 73.28; H, 5.91; N, 7.70; MS (FD) calcd. for $C_{21}H_{22}MnN_4O_2$: 417; found: 417.

4.3. X-Ray-structural analysis of the manganese complexes rac-5a and rac-5e

Crystals were grown by slowly cooling the hot saturated solution of *rac*-**5a** or *rac*-**5e** in ethanol. In the case of *rac*-**5a**, brown transparent platelets were obtained, and dark brown needles from *rac*-**5e**. Data were collected on an IPDS-diffractometer employing Mo Kα radiation at 203(2) K for *rac*-**5a** and 293(2) K for *rac*-**5e**.

Further details of the crystal structure investigations are available on request from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, Germany, on quoting the depository number, the names of the authors, and the journal citation.

	rac-**5a**	*rac*-**5e**
Crystal dimensions (mm)	0.6, 0.4, 0.01	0.4, 0.2, 0.03
Color and habit	brown, transparent platelet	brown, transparent needle
Crystal system	monoclinic	monoclinic
Space group	$P2_1/n$	$P2_1/n$
Unit cell dimensions (Å)	$a = 9.420(9)$	$a = 10.082(2)$
	$b = 31.07(2)$	$b = 34.742(5)$
	$c = 16.76(3)$	$c = 15.463(5)$
	$\beta = 105.51(9)$	$\beta = 104.720(10)$
V (Å^3)	4727(9)	5238(2)
Z	4	4
ρ_{calcd} (g/cm^3)	1.193	1.151
2Θ-range (°)	5.2–37.44	3.6–48.3
No. of reflectionscollected	7473	29891
No. of independentreflections	2657	7415
No. of observedreflections	1126	4948
Refinement and structuresolution	direct methods (SHELXS-86 and SHELXL-93)	
R (%) ($I > 2\sigma$ (I))	14.2	6.5
$\omega R2$ (%) ($I > 2\sigma$ (I))	34.8	17.0
Data to parameter ratio	12.96:1	12.84:1
Largest diff. peak (e Å^{-3})	0.25	0.369
CSD-depository No.	404 623	404 622

4.4. Catalytic epoxidation of olefins

4.4.1. General procedure for epoxidations using 1%-hydrogen peroxide under two phase conditions, catalyzed by the manganese chelates rac-5a–e,g and 5a,h,i

A 10 ml flask was charged at room temperature with a solution of the olefin (40.0 μmol), 1,2-dibromobenzene [9.40 mg, 40.0 μmol (as internal standard)] and the manganese catalyst (4.00 μmol, 10 mol%) in 1.5 ml of dichloromethane. Water (1.5 ml) was added and the resulting mixture was stirred vigorously. 30%-Hydrogen peroxide (45.0 mg, 400 μmol, 10 eq.) was then injected by means of a syringe. The course of the reaction was monitored by GC or HPLC. For each olefin, the identity and the yield of the oxidation product was verified by isolation. In the case of 1,2-epoxy-1,2,3,4-tetrahydronaphthalene *rac*-**8**, the isolation was done as follows: The organic phase was filtered through Celite. After evaporation of the solvent, the residue was extracted with *n*-pentane. The extract was flash-chromatographed on silica gel, eluting with *n*-pentane/ethyl ether 40:1.

4.4.2. General procedure for epoxidations catalyzed by the manganese chelate 5a, using oxidants other than 1%-hydrogen peroxide

A 10 ml flask was charged at room temperature with a solution of the olefin (40.0 μmol), 1,2-dibromobenzene [9.40 mg, 40.0 μmol (as internal standard)] and the manganese chelate **5a** (3.45 mg, 4.00 μmol, 10 mol%) in 1.5 ml of dichloromethane. With vigorous stirring, the oxidant (400 μmol, 10 eq.) was added at room temperature. The course of reaction was monitored by GC or HPLC. For each olefin, the identity and the yield of the oxidation product was verified by isolation.

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References

[1] H. Brunner and W. Zettlmeier, Handbook of Enantioselective Catalysis, Vols. I and II (VCH, Weinheim, 1993);
[2] I. Ojima, ed., Catalytic Asymmetric Synthesis (VCH, Weinheim, 1993); R. Noyori, Asymmetric Catalysis in Synthesis (Wiley, New York, 1994).
[3] E.N. Jacobsen, W. Zhang. A.R. Muci, J.R. Ecker and L. Deng, J. Am. Chem. Soc. 113 (1991) 7063; B.D. Brandes and E.N. Jacobsen, J. Org. Chem. 59 (1994) 4378.
[4] E. Jacobsen, In: ed. I. Ojima, Catalytic Asymmetric Synthesis (VCH, Weinheim, 1993) pp. 159–202.
[5] T. Katsuki, Coord. Chem. Rev. 140 (1995) 189; T. Katsuki, Tetrahedron 52 (1995) 515.
[6] P. Pietikäinen, Tetrahedron Lett. 35 (1994) 941; R. Irie, N. Hosoya and T. Katsuki, Synletter (1994) 255.
[7] A. Berkessel, J.W. Bats and C. Schwarz, Angew. Chem. 102 (1990) 81; Angew. Chem. Int. Ed. Engl. 29 (1990) 106.
[8] A. Berkessel, M. Bolte and T. Schwenkreis, J. Chem. Soc., Chem. Commun. (1995) 535.
[9] K. Dear, Topics Curr. Chem. 164 (1993) 115.
[10] B. Meunier, Chem. Rev. (1992) 1411.
[11] L.J. Marnett, P. Weller and J.R. Battista, In: ed. P.R. Ortiz de Montellano, Cytochrome P-450 (Plenum, New York, 1986) pp. 29–76.
[12] P.R. Ortiz de Montellano, Acc. Chem. Res. 20 (1987) 289.
[13] J. Zeng and R.E. Fenna, J. Mol. Biol. 226 (1992) 185.
[14] R. Irie, Y. Ito and T. Katsuki, Synletter (1991) 265.
[15] D. Mansuy and P. Battioni, In: ed. J. Reedijk, Bioinorganic Catalysis (Marcel Dekker, New York, 1993) pp. 395–424; P. Battioni, J.P. Renaud, J.F. Bartoli, M. Reina-Artiles, M. Fort and D. Mansuy, J. Am. Chem. Soc. 110 (1988) 8462.
[16] (S. Quici, S. Banfi and G. Pozzi, Gazz. Chim. Ital. 123 (1993) 597; P.L. Anelli, S. Banfi, F. Montanari and S. Quici, J. Chem. Soc., Chem. Commun. (1989) 779–780.
[17] A. Boettcher, H. Elias, B. Eisenmann, E. Hilms, A. Huber, R. Kniep, C. Roehr, M. Zehnder, M. Neuburger and J. Springborg, Z. Natutforsch. B 49 (1994) 1089; A. Boettcher, H. Elias, E.-G. Jaeger, H. Langfelderova, M. Mazur, L. Mueller, H. Paulus, P. Pelikan, M. Rudolph and M. Valko, Inorg. Chem. 32 (1993) 4131.
[18] S. Banfi, F. Legramandi, F. Montanari, G. Pozzi and S. Quici, J. Chem. Soc., Chem. Commun. (1991) 1285–1287
[19] A. Berkessel, M. Bolte, M. Frauenkron, T. Nowak, T. Schwenkreis, L. Seidel and A. Steinmetz, Chem. Ber. 129 (1996) 59.
[20] H. Volz and W. Müller, Liebigs Ann. Chem. (1992) 1097; H. Volz and T. Barth, Liebigs Ann. Chem. (1989) 171; J.A. Smegal, B.C. Schardt and C.L. Hill, J. Am. Chem. Soc. 105 (1983) 3510; J.A. Smegal and C.L. Hill, J. Am. Chem. Soc. 105 (1983) 3515; 2920.
[21] J.F. Larrow and E.N. Jacobsen, J. Am. Chem. Soc. 116 (1994) 12129.

[22] Beilsteins's Handbuch der Organischen Chemie, Vol. 21, E IV (Springer, Berlin, 1979) p. 5127; D.W. MacCorquodale and T.B. Johnson, Recl. Trav. Chim. Pays-Bas 51 (1932) 486.
[23] L. Deng and E.N. Jacobsen, J. Org. Chem. 57 (1992) 4320.
[24] C. Casiraghi, G. Casnati, G. Puglia, G. Sartori and G. Tarenghi, J. Chem. Soc., Perkin 1 (1980) 1862; G. Casiraghi, G. Casnati, M. Cornia, A. Pochini, G. Puglia and G. Sartori, J. Chem. Soc., Perkin 1 (1978) 318.
[25] L. Cazaux and P. Tisnes, J. Heterocycl. Chem. 13 (1976) 665.