Asymmetric Epoxidation of Alkenes in Fluorinated Media, Catalyzed by Second-Generation Fluorous Chiral (Salen)manganese Complexes

Marco Cavazzini,[a] Amedea Manfredi,[b] Fernando Montanari,[b] Silvio Quici,[a] and Gianluca Pozzi*[a]

Dedicated to Professor Guy Ourisson on the occasion of his 75th birthday

Keywords: Biaryls / Biphasic catalysis / Epoxidations / Fluorinated ligands / Manganese

The synthesis of sterically hindered chiral (salen)manganese complexes bearing perfluoroalkyl ponytails and their use in asymmetric epoxidation reactions are described. For better understanding of the relative influences of steric and electronic effects on the enantioselectivity of the fluorous catalysts, the epoxidation of 1,2-dihydronaphthalene and benzosuberene was first studied under homogeneous conditions. It was shown that the presence of sterically demanding *tert*-butyl groups and, to a lesser degree, the displacement of the electron-withdrawing perfluoroalkyl substituents from the ligand core provide *ee*s higher than those attainable with first generation fluorous chiral (salen)manganese complexes featuring perfluoroalkyl substituents in the key positions (3,3′ and 5,5′) in the ligand. Second generation catalysts (Mn-**6**)$C_7F_{15}COO$ and (Mn-**7**)$C_7F_{15}COO$ were successfully employed in the fluorous biphase epoxidation of alkenes with PhIO as the oxidant and pyridine *N*-oxide as an additive. Epoxide yields (68–98%) and *ee*s (50–92%) were similar to those obtained with the same oxidizing system and standard (salen)manganese complexes under homogeneous conditions. When the reaction was complete, the fluorous layer in which the catalyst was immobilized was easily recoverable by simple phase separation at room temperature and could be used up to three times before significant decline in yield and enantioselectivity was observed.

Introduction

The use of non-traditional reaction media such as supercritical fluids,[1] ionic liquids,[2] and liquid biphasic systems (both aqueous/organic and purely organic)[3,4] in synthetic organic chemistry is arousing increasing interest.[5] Investigations in this field have been stimulated by safety and environmental concerns, but also by the search for unusual selectivities and new catalyst immobilization and recovery strategies.[6]

Perfluorocarbons share chemical and physical properties (such as low dielectric constants, chemical inertness, lack of toxicity, low miscibilities with common organic solvents and water) that differ quite markedly from those of the corresponding hydrogenated compounds.[7] These fluids have been found to be very useful in organic reactions involving unstable reagents, such as transesterification of polymerizable alcohols and enamine formation.[8] A partially fluorinated solvent − benzotrifluoride (α,α,α-trifluorotoluene) − has been proposed as a substitute for CH_2Cl_2 because it has a similar dielectric constant, but lower toxicity.[9] In the last six years, a number of reagents and catalysts bearing appropriate perfluoroalkyl substituents R_F (“fluorous compounds”) have been prepared and used in “fluorous biphase chemistry”,[10] an expression used to describe the whole set of stoichiometric and catalytic reactions, phase separations and immobilization techniques that profit from use of perfluorinated media.[11] Principles and applications of fluorous biphase chemistry are described in several reviews.[12] Fluorous chemistry has great potential in asymmetric synthesis, in which solvation effects and effective recovery of precious chiral reagents or catalysts can have critical importance.[13] The asymmetric catalytic epoxidation of unfunctionalized alkenes is a good benchmark test for this notion.

Since the discovery of the catalytic activity of chiral (salen)manganese complexes,[14,15] a wide variety of *cis*-disubstituted and tri- and tetrasubstituted alkenes has been epoxidized in the presence of stoichiometric oxidants − iodosylarenes and *m*-chloroperbenzoic acid/*N*-methylmorpholine *N*-oxide (MCPBA/NMO) among them[16,17] − to give enantiomerically enriched epoxides in good yields and with moderate to excellent *ee*s. Several approaches towards the immobilization of (salen)manganese(III) complexes on organic and inorganic supports have been described, with the aim of recycling the chiral catalysts.[18] As recently discussed, this strategy still presents some drawbacks, including poor enantioselectivities due to the inaccessibility of the substrate to the catalytic sites and severe leaching of the complexes.[19] Fluorous (salen)manganese(III) complexes

[a] Centro CNR Sintesi e Stereochimica di Speciali Sistemi Organici,
Via Golgi 19, 20133 Milano, Italy
Fax: (internat.) + 39-02/2663354
E-mail: gianluca.pozzi@unimi.it
[b] Dipartimento di Chimica Organica e Industriale dell’Università,
Via Golgi 19, 20133 Milano, Italy

  1434−193X/01/1224−4639 $ 17.50+.50/0

(Mn-**1**)Cl − (Mn-**3**)Cl (Figure 1) were thus synthesized and used as catalysts in the aerobic epoxidation of alkenes under fluorous biphase conditions.[20] Despite the good chemoselectivity and efficiency generally observed, these first generation fluorous catalysts gave promising enantioselectivities only in the epoxidation of indene (*ee* = 90%). Later, a few other chiral fluorous compounds were described, and some of these were tested in the fluorous biphase version of reactions such as the asymmetric alkylation of aromatic aldehydes with diethylzinc or the asymmetric protonation of enolates.[21−23] The results obtained were somewhat encouraging, but further data are required for better understanding of the actual influence of the fluorous environment.

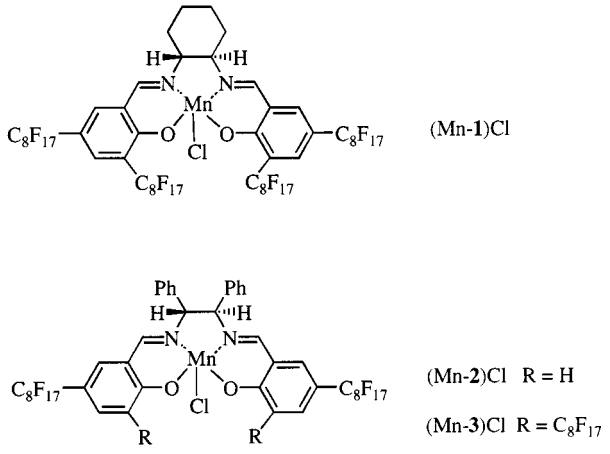


Figure 1. First generation fluorous chiral (salen)manganese(III) complexes

In a recent communication, the synthesis of new fluorous, sterically hindered, chiral (salen)manganese(III) complexes was outlined.[24] Here we describe in detail the preparation of these compounds and their use as catalysts in the asymmetric epoxidation of alkenes, under both homogeneous and fluorous biphase conditions. The improved ligand design and the careful choice of reaction conditions enabled the scope of the reaction to be widened considerably.

Results and Discussion

One of the most appealing features of chiral (salen)manganese(III) complex-catalyzed asymmetric epoxidation of alkenes is the opportunity to maximize the level of stereoinduction for a given substrate by fine-tuning of the catalyst's steric and electronic properties. In many instances, an increase in the steric bulk at the 3,3′- and 5,5′-positions in the ligand results in enhanced enantioselectivities. The presence of bulky substituents (such as *tert*-butyl groups) is thought to force the approach of the substrate to the metal site along productive directions, over the chiral diamine backbone, for instance.[25] On the other hand, electron-donating substituents usually have a positive influence on the enantioselectivity, while the presence of electron-withdrawing substituents results in decreased enantioselectivity because of the enhanced reactivity of the Mn-oxo intermediate, which is the actual oxygen-transfer agent in epoxidation reactions.[26] Although other factors such the conformational flexibility of the ligand and the choice of the stoichiometric oxidant might also play important roles, the results obtained with first generation fluorous (salen)manganese(III) complexes (Figure 1) fitted this picture. The low enantioselectivities were tentatively ascribed to a combination of low steric hindrance provided by the R_F substituents in the 3,3′- and 5,5′-positions in the ligands and inadequate electronic shielding of the metal site from the strongly electron-withdrawing effect of these substituents.[20b] On these grounds, a new set of fluorous chiral catalysts for the asymmetric epoxidation of alkenes was designed. Second generation fluorous (salen)manganese(III) complexes (Mn-**4**)Cl − (Mn-**7**)X (Figure 2) are all characterized by the presence of sterically demanding *tert*-butyl substituents in the key 3,3′-positions. R_F substituents are retained in the 5,5′-positions of (Mn-**4**)Cl and (Mn-**5**)Cl, but are replaced by perfluoroalkyl-substituted aryl moieties in the case of (Mn-**6**)X and (Mn-**7**)X. A different degree of electronic shielding of the metal site within this series of compound is thus ensured. It should be noted that the biaryl framework offers additional flexibility in the design of salen ligands. The overall number of R_F substituents can be increased to attain the desired preferential solubility in perfluorocarbons and proper spacers can be inserted between R_F substituents and the core structure of the ligand in order to achieve fine-tuning of the electron-withdrawing effect. The biaryl framework was also expected to influence the three-dimensional structure of the catalyst and to generate more steric hindrance, possibly enhancing the enantioselectivity.

The synthesis of salen ligands is readily accomplished by condensation of two equivalents of a salicylaldehyde derivative with a chiral 1,2-diamine. This method also gave good results in the case of the fluorous ligands **1**−**3**, but the synthesis of the corresponding perfluoroalkyl-substituted *o*-hydroxybenzaldehydes, especially that of 3,5-disubstituted compounds, was rather tedious. Since direct perfluoroalkylation of benzaldehydes (whether electrophilic, free-radical or through metal-mediated coupling reactions) affords only traces of the desired products,[27] we fell back on the perfluoroakylation of a protected 3,5-diiodosalicylic acid derivative followed by reduction/oxidation of the carboxylate group and deprotection of the hydroxy group.[20] Such a procedure is unsuited for the synthesis of *o*-hydroxybenzaldehydes bearing *tert*-butyl groups, due to the difficulty of access to the corresponding starting compound. The direct perfluoroalkylation of 5-bromo-3-*tert*-butylsalicylaldehyde **8** was thus undertaken, in the hope that hydrogen bonding with the hydroxy group and the steric bulk of the *tert*-butyl group would protect the carbonyl group during the reaction (Scheme 1). *ortho*-Formylation of 2-*tert*-butylphenol mediated by $SnCl_4$ was easily performed according to the classic procedure of Casiraghi.[28] Bromination of the resulting 3-*tert*-butyl-2-hydroxybenzaldehyde with Br_2 in CH_3COOH afforded **8** in 56% overall yield, which compares favourably with the overall yield of 15% obtained by following the reverse order of bromination/formylation as

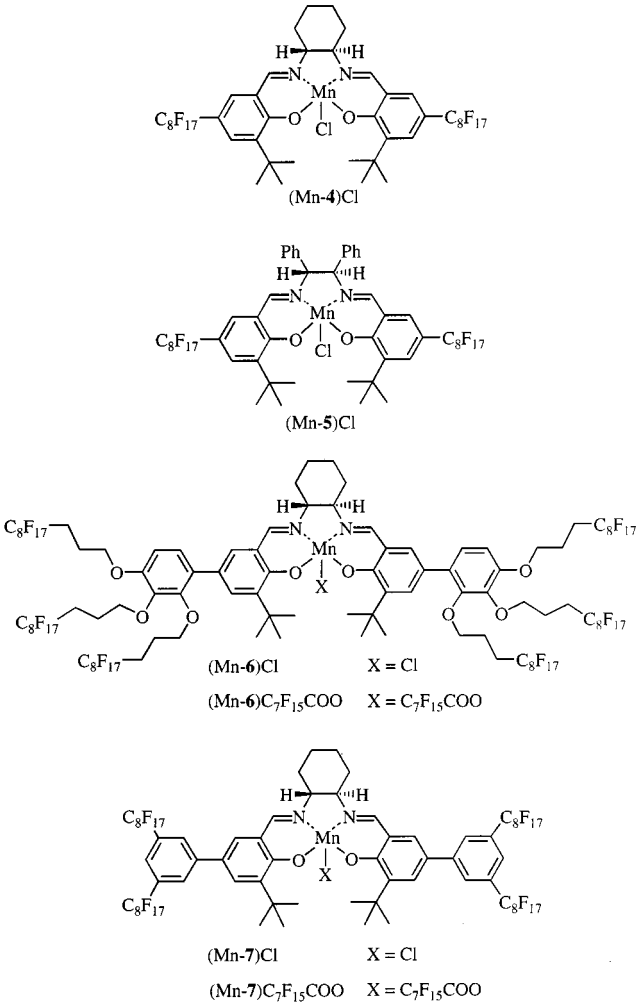
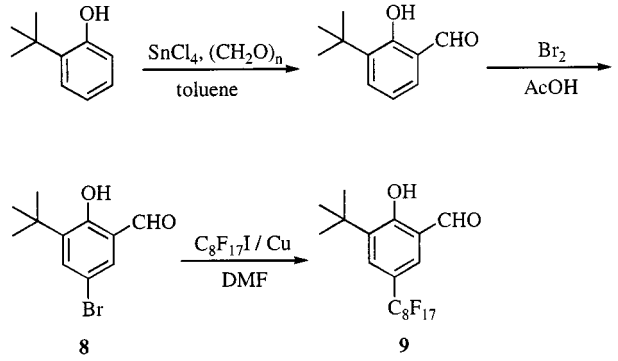


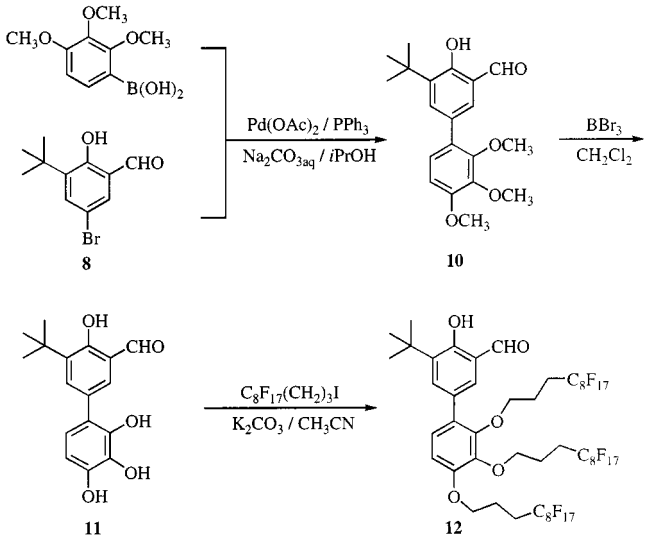
Figure 2. Second generation fluorous chiral (salen)manganese(III) complexes

proposed in the literature.[29] After some unfruitful attempts, the coupling of **8** with $C_8F_{17}I$ was achieved by portionwise addition of the perfluoroalkylating agent to a suspension of **8** and Cu powder in DMF, the temperature of which was carefully maintained at 125 °C during the whole reaction. The fluorous *o*-hydroxybenzaldehyde **9** was isolated in 75% yield.

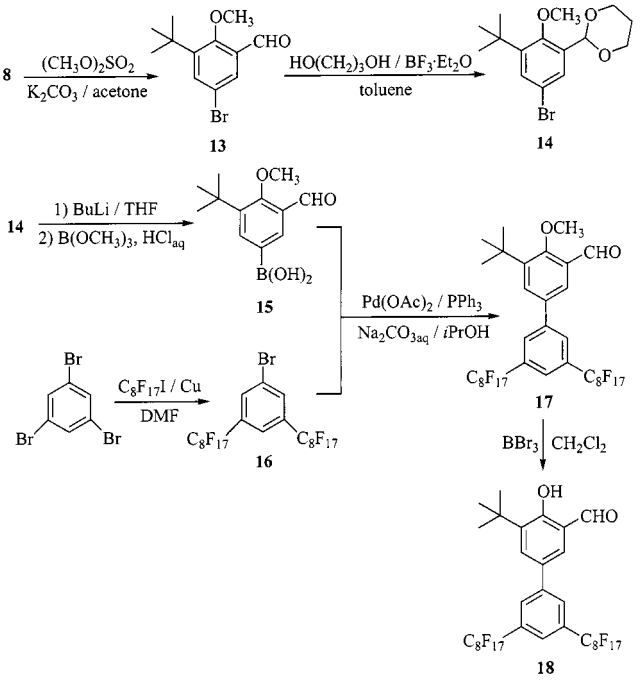


Scheme 1. Synthesis of compound **9**

Aldehyde **8** is also a convenient starting compound for the preparation of the fluorous biaryl *o*-hydroxyaldehydes **12** and **18** (Schemes 2 and 3).



Scheme 2. Synthesis of compound **12**



Scheme 3. Synthesis of compound **18**

It had previously been shown that *O*-alkylation of hydroxy groups with $R_F(CH_2)_nLG$ (LG = I, $OSO_2C_4F_9$) can profitably be used to insert long R_F chains into aromatic compounds.[30] Accordingly, biaryl aldehyde **10**, obtained from 2,3,4-trimethoxyphenyl boronic acid and aldehyde **8** by a modified Suzuki cross-coupling (yield = 86%) was *O*-deprotected (89%) and successively *O*-alkylated with $C_8F_{17}(CH_2)_3I$ to give the fluorous salicylaldehyde **12** (37%) (Scheme 2).[31,32] A minor drawback of this otherwise straightforward sequence resides in the low-yielding *O*-al-

kylation step. Although the free OH group of the salicyl moiety is less accessible to the alkylating agent than those on the other aryl ring, mild reaction conditions were necessary if complete *O*-alkylation of aldehyde **11** was to be avoided. This resulted in the formation of considerable amounts of mono- and bis-*O*-alkylated compounds, which could nevertheless be isolated and reused in following runs.

The second fluorous biaryl *o*-hydroxyaldehyde, compound **18**, was prepared according to the procedure outlined in Scheme 3. In this case, aldehyde **8** was protected by *O*-methylation (92%) followed by acid-catalyzed treatment with 1,3-propanediol (86%). Cyclic acetal **14** was lithiated and quenched with $B(OCH_3)_3$. ^1H NMR analysis of the crude product obtained after acidic hydrolysis of the reaction mixture showed the presence of boronic acid **15** and of the corresponding acetal as the main products. Although **15** could be isolated by column chromatography, the crude mixture was found to be better used as such for the palladium(0)-catalyzed cross-coupling reaction with perfluoroalkyl-substituted aryl bromide **16**. This compound was prepared by means of a copper-mediated cross-coupling reaction between 1,3,5-tribromobenzene and two equivalents of $C_8F_{17}I$. A careful choice of reaction conditions allowed the bis(perfluoroalkyl) derivative to be obtained as the main product in reasonable yields (60%) after crystallization from CH_2Cl_2 and then Et_2O. In spite of the use of crude aryl boronic acid **15**, the cross-coupling reaction afforded aldehyde **17** in good yield (63%); this was then *O*-deprotected to give the desired salicylaldehyde **18** in quantitative yield.

The fluorous salen ligands **4**−**7** were obtained in good yields (72−95%) through condensation of two equivalents of salicylaldehydes **9**, **12**, or **18** with the appropriate chiral 1,2-diamine. The corresponding manganese(III) complexes (Mn-**4**)Cl − (Mn-**7**)Cl (Figure 1) were prepared by treatment of the ligand with an excess of $Mn(OAc)_2{\cdot}4H_2O$ in refluxing ethanol under aerobic conditions, followed by anion exchange with LiCl.

As expected, complexes (Mn-**4**)Cl and (Mn-**5**)Cl, each of which possess a relatively low fluorine load (47.5 and 44.3%, respectively), were found to be soluble in benzotrifluoride and CCl_2FCF_2Cl, but only sparingly soluble in boiling *n*-perfluorooctane. Complexes (Mn-**6**)Cl and (Mn-**7**)Cl are also soluble in low-fluorinated solvents. More interestingly, these complexes, richer in fluorine (54.9. and 55.0%, respectively) and bearing multiple R_F ponytails are also soluble in *n*-perfluorooctane, but these solutions are not stable and aggregation phenomena were observed on standing. This behaviour can be explained by mutual interactions among the extended organophilic frameworks of the molecules and by the very low ion-solvating power of perfluorocarbons. An exchange of the chloride counterion of (Mn-**6**)Cl and (Mn-**7**)Cl for the fluorophilic $C_7F_{15}COO^-$ anion provided a solution to this problem. Partition coefficients between *n*-perfluorooctane and organic solvents, determined by UV/Vis spectroscopy at 25 °C (see Table 1),[33] were found to be quite similar for the resulting (Mn-**6**)$C_7F_{15}COO$ and (Mn-**7**)$C_7F_{15}COO$ complexes. When the organic solvent was CH_3CN or toluene, which are commonly used in fluorous biphase chemistry, both complexes were confined in *n*-perfluorooctane (partition coefficient > 100). It should be noted that (Mn-**6**)$C_7F_{15}COO$ and (Mn-**7**)$C_7F_{15}COO$ strongly absorb in the UV/Vis, and so even traces of these complexes should easily be detected in the organic phase. Other organic solvents, such as chlorinated ones, show a minimal ability to dissolve (Mn-**6**)$C_7F_{15}COO$ and (Mn-**7**)$C_7F_{15}COO$, but only in the case of *n*-perfluorooctane/hexane mixtures did these fluorous complexes partition significantly between the two layers. The results obtained with (Mn-**6**)$C_7F_{15}COO$ are summarized in Table 1.

Table 1. Partition coefficients *P* for Mn-**6**($C_7F_{15}COO$) between *n*-perfluorooctane and an organic solvent

Entry	Solvent[a]	*P*
1	Hexane	1.21
2	Dichloromethane	39
3	Toluene	>100
4	Acetonitrile	>100

[a] Organic solvent (1 mL) was added to a solution of the catalyst in *n*-perfluorooctane (0.01 M, 1 mL). The mixture was stirred at 20 °C for 3 h. The two phases were separated and the concentration of the catalyst in each phase was determined by measurement of the UV/Vis absorbances at 297 and 441 nm of a sample diluted as necessary in $CF_2ClCFCl_2$ and by comparison of the values obtained with a calibration curve.

First generation fluorous (salen)manganese(III) complexes had primarily been tested as catalysts for the fluorous biphase epoxidation of alkenes with molecular oxygen in the presence of a sacrificial aldehyde. Indeed, perfluorocarbons dissolve large quantities of O_2 and it was supposed that this property might favourably influence the activity of the catalytic system. Second generation fluorous complexes (Mn-**4**)Cl and (Mn-**5**)Cl were thus first examined in conjunction with this oxidizing system with the aim of verifying whether the increased steric bulk would have any beneficial effect. Benzotrifluoride, which is able to dissolve both first and second generation catalysts, was chosen as the fluorinated medium. The aerobic epoxidation of 1,2-dihydronaphthalene and benzosuberene was carried out in the dark at 20 °C under atmospheric pressure of O_2 (Table 2). A solution of the catalyst in benzotrifluoride was added to a solution of the substrate plus *N*-hexylimidazole dissolved in CH_2Cl_2. Pivalaldehyde was gradually added to the homogeneous solution, until the aldehyde/starting alkene molar ratio was equal to 3. The degrees of conversion observed in blank experiments carried out under the same conditions, but in the absence of a catalyst, were negligible.

Previous studies had shown that different reaction pathways are possible in the presence of O_2/aldehyde. In particular, the partial inversion of the relative configuration during the epoxidation of *cis*-stilbene pointed to a free radical mechanism contribution. This might be deleterious with respect to the enantioselectivity of the catalytic system, as confirmed by the results obtained with second generation catalysts (*ee*s = 10−34%). Most interestingly, it appeared that the presence of a *tert*-butyl group in the 3,3′-positions

Table 2. Homogeneous epoxidation of 1,2-dihydronaphthalene and benzosuberene with O_2/pivalaldehyde at 20 °C

Entry	Substrate[a]	Catalyst	*t* [h]	Yield[b] (%)	*ee*[c] (%)
1	1,2-Dihydronaphthalene	(Mn-**1**)Cl	2	70	10
2	1,2-Dihydronaphthalene	(Mn-**3**)Cl	2	62	5
3	1,2-Dihydronaphthalene	(Mn-**4**)Cl	22	44	25
4	1,2-Dihydronaphthalene	(Mn-**5**)Cl	22	77	10
5	Benzosuberene	(Mn-**1**)Cl	2	92	7
6	Benzosuberene	(Mn-**3**)Cl	3	91	12
7	Benzosuberene	(Mn-**4**)Cl	22	40	34
8	Benzosuberene	(Mn-**5**)Cl	22	78	10

[a] Conditions. Catalyst: 0.01 mmol; substrate: 0.2 mmol; pivalaldehyde: 0.6 mmol; *N*-hexylimidazole: 0.02 mmol; solvent: CH_2Cl_2/$PhCF_3$ (2 mL, 1:1 v/v). [b] Determined by capillary GC (HP-5 5% phenylmethylsiloxane column, internal standard method). [c] Determined by capillary GC (Cyclodex-B chiral column).

of the catalyst reduced reaction rates (entries 3 vs. 1, for example). In many cases this did not result in increased selectivities in epoxide because the incidence of by-products increased with reaction times. A considerable enhancement of the level of stereoinduction was observed in reactions catalyzed by (Mn-**4**)Cl, in comparison with those carried out with the first generation catalyst (Mn-**1**)Cl derived from the same chiral diamine (entries 3 vs. 1 and 7 vs. 5), but a similar comparison between (Mn-**5**)Cl and (Mn-**3**)Cl showed meaningless differences (entries 4 vs. 2 and 8 vs. 6).

In order to avoid all interference due to the puzzling nature of the O_2/aldehyde oxidizing system, a second set of experiments with MCPBA/NMO was undertaken. Jacobsen and co-workers had shown that the epoxidation of most substrates with this combination of oxidants proceeds smoothly at −78 °C, to afford high *ee*s.[17] Benzotrifluoride solutions of the fluorous (salen)manganese(III) complexes are not stable at such a low temperature, and so reactions were carried out at −50 °C, the lowest temperature compatible with the solubility of the catalysts, with CH_2Cl_2 used to dissolve the oxidants. The results obtained (Table 3) were all in agreement with a positive influence of the higher steric bulk of second generation fluorous catalysts, as evidenced by comparisons between (Mn-**1**)Cl and (Mn-**4**)Cl and between (Mn-**3**)Cl and (Mn-**5**)Cl. In the case of 1,2-dihydronaphthalene (entries 1 vs. 3 and 2 vs. 4), substitution of the R_F substituents in 3,3′-positions with *tert*-butyl groups produced Δ*ee*s of up to +200%, although the level of stereoinduction remained rather low. Moderate to good enantioselectivities were obtained in the epoxidation of benzosuberene catalyzed by second generation catalysts (Mn-**4**)Cl and (Mn-**5**)Cl (entries 11 and 12), with Δ*ee*s of up to +125% with respect to those obtained with (Mn-**1**)Cl and (Mn-**3**)Cl (entries 9 and 10).

As expected, further improvements in the enantioselectivities were observed in the epoxidation of 1,2-dihydronaphthalene catalyzed by (Mn-**6**)$C_7F_{15}COO$ and (Mn-**7**)$C_7F_{15}COO$. The *ee*s obtained with these complexes were almost identical (entries 5 and 7), with Δ*ee* = +300% relative to those obtained in the reaction catalyzed by the first generation catalyst (Mn-**1**)Cl, the framework of which contains the same chiral diamine unit (entry 1). It is worth noting that (Mn-**6**)$C_7F_{15}COO$ and (Mn-**7**)$C_7F_{15}COO$ afforded only a slight improvement (Δ*ee* = +36%) over (Mn-**4**)Cl, still with two R_F substituents attached at the salycilidene core of the ligand. Given that the epoxidation of 1,2-

Table 3. Homogeneous epoxidation of 1,2-dihydronaphthalene and benzosuberene with MCPBA/NMO at −50 °C

Entry	Substrate[a]	Catalyst	*t* [h]	Yield[b] (%)	*ee*[c] (%)
1	1,2-Dihydronaphthalene	(Mn-**1**)Cl	1	68	16
2	1,2-Dihydronaphthalene	(Mn-**3**)Cl	1	59	12
3	1,2-Dihydronaphthalene	(Mn-**4**)Cl	0.5	84	47
4	1,2-Dihydronaphthalene	(Mn-**5**)Cl	0.5	88	33
5	1,2-Dihydronaphthalene	(Mn-**6**)$C_7F_{15}COO$	0.5	69	62
6	1,2-Dihydronaphthalene	(Mn-**6**)Cl	0.5	65	64
7	1,2-Dihydronaphthalene	(Mn-**7**)$C_7F_{15}COO$	0.75	70	63
8	1,2-Dihydronaphthalene	(Mn-**7**)Cl	0.75	73	63
9	Benzosuberene	(Mn-**1**)Cl	1	83	36
10	Benzosuberene	(Mn-**3**)Cl	1	76	28
11	Benzosuberene	(Mn-**4**)Cl	0.5	82	81
12	Benzosuberene	(Mn-**5**)Cl	0.5	72	57
13	Benzosuberene	(Mn-**6**)$C_7F_{15}COO$	0.5	83	63
14	Benzosuberene	(Mn-**7**)$C_7F_{15}COO$	0.5	88	74

[a] Conditions. Catalyst: 0.01 mmol; substrate: 0.2 mmol; MCPBA: 0.4 mmol; NMO: 0.5 mmol; solvent: CH_2Cl_2/$PhCF_3$ (2 mL, 1:1 v/v). [b] Determined by capillary GC (HP-5 5% phenyl methyl siloxane column, internal standard method). [c] Determined by capillary GC (Cyclodex-B chiral column).

dihydronaphthalene catalyzed by (Mn-**6**)Cl and (Mn-**7**)Cl proceeded exactly as in the cases of (Mn-**6**)$C_7F_{15}COO$ and (Mn-**7**)$C_7F_{15}COO$ (entries 6 vs. 5 and 8 vs. 7), it is likely that the nature of the counterion does not influence the behaviour of the second generation catalysts to any appreciable extent.

On the other hand, the more efficient shielding of the metal site of the catalysts from the electron-withdrawing action of the R_F substituents did not have any positive effect in the case of the epoxidation of benzosuberene, in which the biaryl catalysts afforded *ee*s even lower than those obtained with (Mn-**4**)Cl (entries 13 and 14 vs. 11). It should be also pointed out that removal of two R_F substituents from the 3,3′-positions of the ligand without introduction of any sterically demanding substituents did not improve enantioselectivities.[20b] The picture emerging from all these data is coherent with the idea that steric effects play a major role in determining the level of stereoinduction obtained with fluorous (salen)manganese(III) complexes in the epoxidation of alkenes.

The otherwise useful MCPBA/NMO oxidizing system was not suitable for fluorous biphasic epoxidations in the presence of (Mn-**6**)$C_7F_{15}COO$ and (Mn-**7**)$C_7F_{15}COO$, due to the low solubility of these complexes in *n*-perfluorooctane at the low temperatures at which MCPBA/NMO works best. Test reactions in CH_2Cl_2/benzotrifluoride were thus carried out with other oxidizing agents commonly used in association with (salen)manganese(III) complexes. At 25 °C, PhIO in the presence of small amounts of pyridine *N*-oxide (PNO) gave results comparable to those obtained with MCPBA/NMO at −50 °C, [for example: epoxide yield = 81%, *ee* = 61% in the epoxidation of 1,2-dihydronaphthalene catalyzed by (Mn-**7**)$C_7F_{15}COO$]. This oxidizing system was thus used in the next fluorous biphase reactions, which were run in *n*-perfluorooctane/CH_3CN. The organic solvent was chosen in view of the favourable partition coefficients of the catalysts and the consideration that homogeneous epoxidation reactions with PhIO/PNO are conveniently carried out in CH_3CN at 0−25 °C.[34]

Rather unexpectedly, both reaction yield and enantioselectivity rose with temperature under fluorous biphase conditions (Table 4). Only traces of 1,2-dihydronaphthalene epoxide were detected at 0 °C in the presence of both catalysts, with very low *ee*s (entries 1 and 2). Yields reached their maximum level at 40 °C, whereas the *ee*s increased regularly, moving towards the upper value of 60% found under homogeneous conditions (entry 7). The reasons for this behaviour, exemplified in the case of (Mn-**4**)$C_7F_{15}COO$ (Entries 3−6), were not thoroughly investigated, but it is likely that at low temperature the reaction occurs at the interface of the two phases, where distortion of the catalyst structure could be severe.[20b] Although the biphase mixture we used did not become homogeneous even at 100 °C, the miscibility of the organic and fluorous component of the system should be enhanced, thus facilitating both mass transfer and the correct approach of the substrate to the catalytic site.[7,12a] Emergence of temperature-dependent micellar effects cannot be ruled out either. The results obtained in the fluorous biphase epoxidation of 1,2-dihydronaphthalene with PhIO/PNO at 100 °C, the boiling point of *n*-perfluorooctane and the highest operating temperature of the solvent system, are comparable to those reported for the same reaction in CH_3CN in the presence of the commercially available Jacobsen's catalyst (entry 8).[35]

Table 4. Fluorous biphase epoxidation of 1,2-dihydronaphthalene with PhIO/PNO, catalyzed by Mn-**7**($C_7F_{15}COO$), at increasing temperatures

Entry	T[a] [°C]	t [h]	Yield[b] (%)	*ee*[c] (%)
1	0	3	4.5	8
2[d]	0	3	3	6
3	20	3	46	26
4	40	3	76	32
5	70	2	74	42
6	100	1	77	50
7[e]	25	1	81	61
8[f]	room temp.	24	70	46

[a] Conditions: see Exp. Sect. [b] Determined by capillary GC (HP-5 5% phenylmethylsiloxane column, internal standard method). [c] Determined by capillary GC (Cyclodex-B chiral column). [d] Catalyst: (Mn-**6**)$C_7F_{15}COO$. [e] Homogeneous conditions. Catalyst: 0.01 mmol; substrate: 0.2 mmol; PhIO: 0.3 mmol; PNO: 0.05 mmol; solvent: CH_2Cl_2/$PhCF_3$ (2 mL, 1:1 v/v). [f] See ref.[35] Catalyst: Jacobsen's catalyst.

Reger and Janda recently described an interesting approach to recoverable, polymer-supported (salen)manganese(III) complexes.[19] They showed that the use of gel-type resins offers an improvement over earlier immobilization systems, which suffered from poor selectivity and/or recyclability of the catalysts, and suggested that their system may find utility in high-throughput organic synthesis. In summary, a catalyst supported on a specific insoluble resin with good swelling properties afforded yields ranging between 71% and 81%, with *ee*s = 51−88%, in the epoxidation of three substrates with MCPA/NMO at −78 °C. This catalyst was readily recovered by filtration of the reaction mixture and it could be used three times in the epoxidation of styrene and *cis*-β-methylstyrene without any significant drop in selectivity, but it suddenly lost activity in the fourth run. With 1,2-dihydronaphthalene, the catalyst could stand only one recycle. Epoxide yields throughout recycles were not reported.

Under the optimized fluorous biphase conditions described above, reactions catalyzed by second generation (salen)manganese complexes (Mn-**6**)$C_7F_{15}COO$ and (Mn-**7**)$C_7F_{15}COO$ afforded epoxide yields (68−98%) and *ee*s (50−92%) close to those obtained by Reger and Janda (Tables 5 and 6). As had also been found in the case of homogeneous reactions (Table 3), we did not observe major differences between the two catalysts, although (Mn-**7**)$C_7F_{15}COO$ usually gave slightly better results. Recycling of the fluorous catalysts could be performed quickly by simple phase separation at room temperature, and the catalytic activity of the fluorous layer significantly dropped in the fourth run. This set of results clearly indicates that the fluorous biphase approach is in no way inferior to the im-

mobilization of (salen)manganese complexes onto gel-type resins. Some experimental findings, however, deserve a brief comment. It is well known that a low-temperature methodology is required for the highly enantioselective epoxidation of styrene derivatives.[36] Accordingly, the attempted fluorous biphase epoxidation of *cis*-β-methylstyrene at 100 °C afforded a mixture of *cis*- and *trans*-epoxide (3.6:1 ratio) in 68% yield. In this respect, the fluorous biphase approach still requires some efforts to match the results obtained with resin-supported catalysts. On the other hand, the fluorous biphase epoxidation of suitable substrates such as triphenylethylene (Table 5, entries 17−20; Table 6, entries 21−23) and indene (Table 6, entries 13−16) did not show any significant drop in enantioselectivity and epoxide yield over three subsequent reaction cycles: the fluorous catalysts were still reasonably active even in the fourth cycle, a result not achieved with resin-supported catalysts.

Table 5. Fluorous biphase epoxidation of alkenes with PhIO/PNO, catalyzed by Mn-**6**($C_7F_{15}COO$), at 100 °C

Entry	Substrate[a]	*t* [h]	Yield[b] (%)	*ee*[c] (%)
1	1,2-Dihydronaphthalene	1	68	50
2[d]	1,2-Dihydronaphthalene	1	68	48
3[e]	1,2-Dihydronaphthalene	1	60	44
4[f]	1,2-Dihydronaphthalene	1	30	31
5	Benzosuberene	0.5	84	69
6[d]	Benzosuberene	0.5	79	69
7[e]	Benzosuberene	0.5	75	69
8[f]	Benzosuberene	0.5	51	54
9	1-Methylindene	0.5	96	70
10[d]	1-Methylindene	0.5	95	68
11[e]	1-Methylindene	0.5	92	66
12[f]	1-Methylindene	1	76	50
13	1-Methylcyclohexene	0.5	95	52
14[d]	1-Methylcyclohexene	0.5	95	50
15[e]	1-Methylcyclohexene	0.5	74	31
16[f]	1-Methylcyclohexene	1	50	20
17	Triphenylethylene	0.5	98	80[g]
18[d]	Triphenylethylene	0.5	98	81[g]
19[e]	Triphenylethylene	0.5	95	79[g]
20[f]	Triphenylethylene	1	78	66[g]

[a] Conditions: see Exp. Sect. [b] Determined by capillary GC (HP-5 5% phenyl methyl siloxane column, internal standard method). [c] Determined by capillary GC (Cyclodex-B chiral column). [d] First reuse of the fluorous layer. [e] Second reuse of the fluorous layer. [f] Third reuse of the fluorous layer. [g] Determined by ^{1}H NMR spectroscopy in the presence of the chiral shift reagent Eu(hfc)$_3$.

Finally, effective recycling of second generation fluorous catalysts through a very high number of reaction runs appears to be mainly hampered by the oxidative decomposition of the catalyst, as evidenced by the progressive disappearance of the characteristic UV/Vis absorption bands of the (salen)manganese(III) in the fluorous phase and by the absence of such bands in the organic phase. This is in agreement with previous literature reports dealing with the fate of immobilized (salen)manganese complexes during oxidation reactions,[35] and also with the behaviour of catalysts attached to gel-type resins.[19]

Table 6. Fluorous biphase epoxidation of alkenes with PhIO/PNO, catalyzed by Mn-**7**($C_7F_{15}COO$), at 100 °C

Entry	Substrate[a]	*t* [h]	Yield[b] (%)	*ee*[c] (%)
1	1,2-Dihydronaphthalene	1	77	50
2[d]	1,2-Dihydronaphthalene	1	67	45
3[e]	1,2-Dihydronaphthalene	1	63	46
4[f]	1,2-Dihydronaphthalene	1	19	40
5	Benzosuberene	0.5	92	68
6[d]	Benzosuberene	0.5	92	66
7[e]	Benzosuberene	0.5	83	64
8[f]	Benzosuberene	0.5	43	60
9	1-Methylindene	0.5	98	77
10[d]	1-Methylindene	0.5	99	77
11[e]	1-Methylindene	0.5	82	76
12[f]	1-Methylindene	1	52	57
13	Indene	0.25	98	92[g]
14[d]	Indene	0.25	95	92[g]
15[e]	Indene	0.25	93	93[g]
16[f]	Indene	0.5	76	79[g]
17	1-Methylcyclohexene	0.5	91	58
18[d]	1-Methylcyclohexene	0.5	87	53
19[e]	1-Methylcyclohexene	0.5	76	40
20[f]	1-Methylcyclohexene	1	45	25
21	Triphenylethylene	0.5	98	87[g]
21[d]	Triphenylethylene	0.5	96	85[g]
22[e]	Triphenylethylene	0.5	92	83[g]
23[f]	Triphenylethylene	1	80	71[g]

[a] Conditions: see Exp. Sect. [b] Determined by capillary GC (HP-5 5% phenyl methyl siloxane column, internal standard method). [c] Determined by capillary GC (Cyclodex-B chiral column). [d] First reuse of the fluorous layer. [e] Second reuse of the fluorous layer. [f] Third reuse of the fluorous layer. [g] Determined by ^{1}H NMR spectroscopy in the presence of the chiral shift reagent Eu(hfc)$_3$.

Conclusion

The synthesis of new chiral fluorous catalysts and their evaluation for use in fluorous chemistry is of considerable interest. We have now demonstrated that sterically encumbered chiral (salen)manganese complexes bearing a suitable number of R_F substituents can be used as catalysts in the asymmetric epoxidation of several substrates, affording results that compare favourably to those obtained with other immobilized chiral catalytic systems. Our previous hypotheses about the role of steric and electronic effects in determining the level of stereoinduction of fluorous (salen)manganese(III) complexes have been experimentally confirmed. The choice of proper reaction conditions is also very important if satisfactory results are to be achieved. In order to switch a homogeneous asymmetric catalytic reaction into its fluorous biphase version, many parameters must be adjusted, as exemplified here by the striking increase in enantioselectivity observed upon raising the temperature. Moreover, the solubility of charged fluorous complexes in perfluorocarbons can be strongly enhanced by choice of a fluorinated counterion.

We are currently investigating the use of second generation fluorous chiral salen ligands in other asymmetric reactions, such as the hydrogen-transfer reduction of ketones,[37] with the aim of widening the scope of these versatile ligands.

Experimental Section

General Remarks: Solvents were purified by standard methods and dried if necessary, except for perfluorocarbons, which were used as received. All commercially available reagents were used as received. − TLC was carried out on 60 F_{254} silica gel. Column chromatography (CC) was carried out on SI 60 silica gel, mesh size 0.040−0.063 mm (Merck, Darmstadt, Germany). − Melting points (uncorrected) were determined with a Büchi SMP-20 capillary melting point apparatus. − Optical rotations were measured using a Perkin−Elmer 241 polarimeter. − UV/Vis spectra were measured using a Lambda 6 Perkin−Elmer spectrometer. − ^{1}H NMR (300 MHz), ^{13}C NMR (75.4 MHz), and ^{19}F NMR (282 MHz) spectra were recorded on a Bruker AC 300 spectrometer with tetramethylsilane (δ = 0), $CDCl_3$ (δ = 77) and $CFCl_3$ (δ = 0) as internal standard respectively, unless otherwise indicated. − GC analyses were performed on a Hewlett−Packard 5890 instrument (column: 30 × 0.5 mm RSL-200 polymethylsiloxane or Cyclodex-B, 30 × 0.25 mm chiral column). − Elemental analysis: Redox S.n.C. (Monza, Italy) and Departmental Service of Microanalysis (University of Milano).

5-Bromo-3-*tert*-butyl-2-hydroxybenzaldehyde (8): A solution of Br_2 (0.53 mL, 10.3 mmol) in CH_3COOH (2 mL) was added dropwise at room temperature over 15 min to a solution of 3-*tert*-butyl-2-hydroxybenzaldehyde (1.78 g, 9.98 mmol) in CH_3COOH (5 mL). After 1 h the reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed with H_2O (10 mL), saturated aqueous $Na_2S_2O_5$ (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL). The organic phase was dried with Na_2SO_4 and the solvents were evaporated, to afford the title compound as a yellow solid (2.45 g, 95%, m.p. 59−62 °C). The product thus obtained was pure enough for further reactions as shown by ^{1}H NMR. Crystallization from MeOH (10 mL, recovery: 60%) afforded an analytically pure sample; m.p. 63−64 °C (ref.[29] 63.3−65.5 °C). ^{1}H NMR ($CDCl_3$): δ = 1.39 [s, 9 H, C(C*H*$_3$)$_3$], 7.50 (d, *J* = 2.5 Hz, 1 H), 7.57 (d, *J* = 2.5 Hz, 1 H), 9.81 (s, 1 H, C*H*O), 11.71 (s, 1 H, O*H*). ^{13}C NMR ($CDCl_3$): δ = 29.2, 35.4, 121.9, 124.6, 133.8, 137.1, 141.5, 160.3, 195.8. $C_{11}H_{13}BrO_2$ (257.0): calcd. C 51.38, H 5.10; found C 51.27, H 5.23.

3-*tert*-Butyl-2-hydroxy-5-*n*-heptadecafluorooctylbenzaldehyde (9): Copper powder (1.91 g, 30.1 mmol) was added to a solution of *o*-hydroxybenzaldehyde **8** (1.54 g, 5.99 mmol) in dry DMF (20 mL) in a flame-dried Schlenk vessel. The suspension was purged with nitrogen and warmed whilst stirring to 120 °C. $C_8F_{17}I$ (3.20 mL, 12.1 mmol) was added under nitrogen to the stirred suspension in four 0.80 mL portions, with a pause of 40 min between each addition. After 3 h the suspension was allowed to cool to room temperature, treated with H_2O (20 mL) and Et_2O (40 mL), and filtered using a Büchner funnel. The aqueous phase was extracted with Et_2O (3 × 15 mL): The combined organic layers were washed with brine (20 mL) and dried with Na_2SO_4. Purification by CC (silica gel, petroleum ether/Et_2O 95:5) afforded the title compound as a white solid (2.72 g. 75%); m.p. 54 °C. ^{1}H NMR ($CDCl_3$): δ = 1.43 [s, 9 H, C(C*H*$_3$)$_3$], 7.66 (br. s, 1 H), 9.93 (s, 1 H, C*H*O), 12.13 (s, 1 H, O*H*). ^{19}F NMR ($CDCl_3$): δ = −81.1 (t, *J* = 10.0 Hz, 6 F), −111.2 (t, *J* = 13.0 Hz, 4 F), −121.8 (br. s, 4 F), −122.3 (br. s, 12 F), −123.0 (br. s, 4 F), −126.4 (br. s, 4 F). ^{13}C NMR ($CDCl_3$): δ = 28.9, 35.2, 104−119 (m, C_8F_{17}), 120.1, 131.0, 131.5, 139.8, 163.7, 196.5. $C_{19}H_{13}F_{17}O_2$ (596.3): calcd. C 38.20, H 2.20; found C 38.73, H 2.36.

3-*tert*-Butyl-2-hydroxy-5-(2,3,4-trimethoxyphenyl)benzaldehyde (10): *o*-Hydroxybenzaldehyde **8** (1.03 g, 4.01 mmol) and 2,3,4-trimethoxyphenyl boronic acid (0.89 g, 4.20 mmol)[31] were dissolved at room temperature under nitrogen in deaerated 1-propanol (7 mL) in a Schlenk tube. PPh_3 (9.5 mg, 36 μmol) and $Pd(OAc)_2$ (2.7 mg, 12 μmol) were then added, followed by aqueous Na_2CO_3 (1.2 M, 4.80 mL). The stirred suspension was warmed in an oil bath set at 110 °C. After 2 h the suspension was allowed to cool to room temperature and water (5 mL) was added. The mixture was stirred for 1 h and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with 5% aqueous $NaHCO_3$ (2 × 10 mL) and brine (20 mL), and dried with $MgSO_4$. The solvent was evaporated. and the crude product was purified by CC (silica gel, light petroleum ether/CH_2Cl_2/EtOAc 7:2:1) to give the title compound as a pale yellow solid (1.19 g, 86%); m.p. 74 °C. ^{1}H NMR ($CDCl_3$): δ = 1.48 [s, 9 H, C(C*H*$_3$)$_3$]. 3.74 (s, 3 H, OC*H*$_3$), 3.93 (s, 3 H, OC*H*$_3$), 3.95 (s, 3 H, OC*H*$_3$), 6.77 (d, *J* = 8.6 Hz, 1 H), 7.04 (d, *J* = 8.6 Hz, 1 H), 7.56 (d, *J* = 2.2 Hz, 1 H), 7.72 (d, *J* = 2.2 Hz, 1 H), 9.93 (s, 1 H, C*H*O), 11.8 (s, 1 H, O*H*). ^{13}C NMR ($CDCl_3$): δ = 29.7, 35.4, 56.5, 61.3, 61.4, 108.1, 120.9, 124.7, 127.8, 129.6, 132.6, 135.8, 138.3, 143.1, 151.7, 153.7, 160.6, 197.7. $C_{20}H_{24}O_5$ (344.4): calcd. C 69.75, H 7.02; found C 69.54, H 7.31.

3-*tert*-Butyl-2-hydroxy-5-(2,3,4-trihydroxyphenyl)benzaldehyde (11): BBr_3 (1 M in CH_2Cl_2, 7 mL, 7 mmol) was added at −78 °C under nitrogen to a solution of trimethoxybenzaldehyde **10** (0.69 g, 2.01 mmol) in dry CH_2Cl_2 (8 mL). After 10 min the external temperature was raised to −18 °C and the solution was stirred for 1 h. Ice (10 g) was slowly added and the resulting mixture was stirred until two liquid layers were formed. The aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with brine (15 mL), dried with $MgSO_4$ and concentrated under reduced pressure. Purification by CC (silica gel, CH_2Cl_2/MeOH 95:5) afforded the title compound as a pale yellow solid (0.54 g, 89%); m.p.>200 °C. ^{1}H NMR (CD_3OD): δ = 1.45 [s, 9 H, C(C*H*$_3$)$_3$], 4.83 (br. s, 3 H, O*H*),), 6.43 (d, *J* = 8.4 Hz, 1 H), 6.64 (d, *J* = 8.4 Hz, 1 H), 7.66 (d, *J* = 2.2 Hz, 1 H), 7.79 (d, *J* = 2.2 Hz, 1 H), 9.89 (s, 1 H, C*H*O). ^{13}C NMR (CD_3OD): δ = 29.8, 35.8, 108.5, 121.1, 121.9, 132.0, 133.5, 134.6, 136.6, 138.2, 144.7, 146.6, 153.2, 160.4, 199.6. $C_{17}H_{18}O_5$ (302.3): calcd. C 67.54, H 6.00; found C 66.98, H 6.34.

3-*tert*-Butyl-2-hydroxy-5-[2,3,4-tris(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-*n*-perfluoroundecyl)phenyl]benzaldehyde (12): A flame-dried Schlenk tube was charged with compound **11** (0.60 g, 2.00 mmol), anhydrous K_2CO_3 (1.66 g, 12.0 mmol) and dry CH_3CN (15 mL). The mixture was stirred under nitrogen for 10 min at 70 °C, after which $C_8F_{17}(CH_2)_3I$ (1.76 g, 2.99 mmol)[38] was added in three portions over 3 h. The reaction was vigorously stirred at 70 °C overnight. Evaporation of the solvent under reduced pressure afforded a residue that was taken up in Et_2O (75 mL). The inorganic salts were removed by filtration through a Celite pad that was thoroughly washed with Et_2O. The clear ether layer was washed with brine (30 mL) and dried with $MgSO_4$. Flash CC (silica gel, light petroleum ether/CH2Cl$_2$ = 75:25) afforded the title compound (1.24 g, 37%) as a white solid; m.p. 90−91 °C. ^{1}H NMR ($CDCl_3$): δ = 1.45 [s, 9 H, C(C*H*$_3$)$_3$], 1.75−1.82 (m, 2 H), 1.95−2.20 (m, 8 H), 2.26−2.41 (m, 4 H), 4.09−4.14 (m, 4 H), 6.75 (d, *J* = 8.6 Hz), 7.03 (d, *J* = 8.6 Hz, 1 H), 7.50 (d, *J* = 2.0 Hz, 1 H), 7.68 (d, *J* = 2.0 Hz, 1 H), 9.90 (s, 1 H, C*H*O), 11.82 (br. s, 1 H, O*H*). ^{19}F ($CDCl_3$): δ = −82.7 (m, 9 F), −115.0 (m, 6 F), −122.5 (br. s, 18 F), −123.3 (br. s, 6 F), −123.9 (br. s, 62 F), −126.7 (br. s, 6 F). ^{13}C NMR ($CDCl_3$): δ = 29.7, 35.4, 56.5, 61.3, 61.4, 105−120 (m, C_8F_{17}), 105.7, 120.9, 124.7, 127.8, 129.6, 132.6, 135.8, 138.3, 143.1, 151.7, 153.7, 160.6, 197.7. $C_{50}H_{33}F_{51}O_5$ (1682.7): calcd. C 35.69, H 1.98; found C 35.86, H 1.72.

5-Bromo-3-*tert*-butyl-2-methoxybenzaldehyde (13): Dimethylsulfate (1.51 g, 12.0 mmol) was added to a mixture of *o*-hydroxybenzaldehyde **8** (2.57 g, 10.0 mmol) and solid K_2CO_3 (2.76 g, 20.0 mmol) in acetone (30 mL). The mixture was stirred at room temperature overnight before being quenched with H_2O (10 mL) and concentrated under reduced pressure. The residue was extracted with CH_2Cl_2 (3 × 25 mL) and the combined organic layers were washed with brine (20 mL) and dried with Na_2SO_4. Evaporation of the solvent afforded the title compound as a pale yellow solid (2.49 g, 92%); m.p. 82 °C − ^{1}H NMR ($CDCl_3$): δ = 1.38 [s, 9 H, C(C*H*$_3$)$_3$], 3.92 (s, 3 H, OC*H*$_3$), 7.61 (d, *J* = 2.4 Hz, 1 H), 7.78 (d, *J* = 2.4 Hz, 1 H), 10.24 (s, 1 H, C*H*O). ^{13}C NMR ($CDCl_3$): δ = 30.9, 35.8, 66.7, 117.6, 130.7, 136.5, 189.3. $C_{12}H_{15}BrO_2$ (271.0): calcd. C 53.16, H 5.58; found C 53.35, H 5.63.

2-(5-Bromo-3-*tert*-butyl-2-methoxyphenyl)-1,3-dioxane (14): BF_3·Et_2O (0.30 mL, 2.39 mmol) was added to a solution of *o*-methoxybenzaldehyde **13** (2.71 g, 10.0 mmol) and 1,3-propanediol (3.80 g, 50.0 mmol) in toluene (5 mL). The yellow solution was heated to reflux for 4 h, after which it was cooled to room temperature and Et_2O (30 mL) was added. The solution was washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL), and dried with $MgSO_4$. The solvent was evaporated and the residue was purified by CC (silica gel, CH_2Cl_2/light petroleum ether 1:1) to afford the title compound as a pale yellow oil that slowly solidified on standing (2.84 g, 86%); m.p. 72.1−73.5 °C. ^{1}H NMR ($CDCl_3$): δ = 1.35 [s, 9 H, C(C*H*$_3$)$_3$], 2.23−2.41 (m, 2 H), 3.81 (s, 3 H, OC*H*$_3$), 3.99−4.01 (m, 2 H), 4.21−4.27 (m, 2 H), 5.74 [s, 1 H, C*H*(O$_2$C$_3$H$_6$)], 7.38 (d, *J* = 2.6 Hz, 1 H), 7.64 (d, *J* = 2.6 Hz, 1 H). ^{13}C NMR ($CDCl_3$): δ = 26.1, 31.2, 35.7, 64.1, 68.1, 97.8, 117.5, 129.6, 131.4, 135.0, 145.4, 156.8. $C_{15}H_{21}BrO_3$ (329.2): calcd. C 54.72, H 6.43; found C 54.57, H 6.61.

3-*tert*-Butyl-5-formyl-4-methoxybenzeneboronic Acid (15): A solution of protected aldehyde **14** (2.63 g, 7.99 mmol) in THF (15 mL) was cooled to −78 °C under nitrogen. *n*BuLi (1.6 M in hexanes, 5.50 mL, 8.80 mmol) was added dropwise over 5 min. The solution was stirred at −78 °C for 45 min before being quenched with a solution of $B(OCH_3)_3$ (2.91 mL, 26.2 mmol) in THF (5 mL). The resulting cloudy suspension was stirred at −78 °C for 2 h and then allowed to warm slowly to 0 °C. After 4 h, H_2O (10 mL) and Et_2O (50 mL) were added. The organic layer was washed three times with 10% HCl (20 mL) and once with brine (10 mL), and dried with Na_2SO_4. The solvent was evaporated and the crude title compound was obtained as a viscous orange oil (1.75 g) that was used as such for further reactions. A sample was purified by CC (silica gel, CH_2Cl_2/CH_3OH 98:2) for analytical purposes. This step resulted in an appreciable loss of product (yield = 12%) and the crude product was better used as such for the following palladium(0)-catalyzed cross-coupling reaction. ^{1}H NMR ($CDCl_3$): δ = 1.41 [s, 9 H, C(C*H*$_3$)$_3$], 3.92 (s, 3 H, OC*H*$_3$), 7.96 (d, *J* = 1.7 Hz, 1 H), 8.10 (d, *J* = 1.7 Hz, 1 H), 10.28 (s, 1 H, C*H*O). ^{13}C NMR ($CDCl_3$): δ = 31.2, 35.5, 62.4, 129.4, 135.8, 138.9, 142.9, 165.3, 191.2 (C *ipso* to boron not observed). $C_{12}H_{17}BO_4$ (236.1): calcd. C 61.05, H 7.26; found C 61.37, H 7.14.

1-Bromo-3,5-bis(*n*-heptadecafluorooctyl)benzene (16): Copper powder (2.41 g, 38.0 mmol) was added to a solution of 1,3,5-tribromobenzene (2.99 g, 9.50 mmol) in dry DMF (15 mL) in a flame-dried Schlenk vessel. The suspension was purged with nitrogen and warmed to 120 °C whilst stirring. $C_8F_{17}I$ (5.03 mL, 19.0 mmol) was added dropwise under nitrogen to the stirred suspension. After 18 h the suspension was allowed to cool to room temperature, treated with H_2O (20 mL) and filtered using a Büchner funnel. The aqueous phase was extracted with Et_2O (20 mL). The solid was washed with cold Et_2O (3 × 50 mL) and then extracted with boiling Et_2O in a Soxhlet apparatus. The combined ethereal extracts were washed with brine (30 mL) and dried with $MgSO_4$. Removal of the solvent under reduced pressure afforded a white solid residue (8.20 g), which was treated with boiling CH_2Cl_2 (70 mL). All undissolved material was discarded and the warm, clear solution was evaporated to dryness to afford a residue (7.31 g) that was crystallized twice from Et_2O (60 mL). The title compound was obtained as a white solid (5.66 g, 60%); m.p. 72 °C. ^{1}H NMR ($CFCl_2CF_2Cl$, ext. ref. $CDCl_3$): δ = 7.73 (br. s, 1 H), 7.95 (br. s, 2 H). $C_{22}H_3BrF_{34}$ (993.1): calcd. C 26.61, H 0.30, F 65.04; found C 26.52, H 0.34, F 64.71.

5-[3,5-Bis(*n*-heptadecafluorooctyl)phenyl]-3-*tert*-butyl-2-methoxybenzaldehyde (17): A suspension of crude boronic acid **15** (1.60 g), aryl bromide **16** (1.23 g, 1.24 mmol), $Pd(OAc)_2$ (13.8 mg, 61.0 μmol), PPh_3 (48.0 mg, 110 μmol), and Na_2CO_3 (0.19 g, 1.80 mmol) in deaerated 1-propanol (6 mL) was heated to 120 °C in a Schlenk tube under nitrogen. Water (0.6 mL) was added and the mixture was vigorously stirred for 4 h. Cold water (15 mL) was then added. After 1 h, the suspension was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with 5% aqueous HCl (2 × 10 mL) and brine (20 mL), and dried with $MgSO_4$. The solvent was evaporated to afford a yellow residue (1.82 g) from which the title compound was isolated by CC (silica gel, light petroleum ether/Et_2O 95:5) as a white solid (0.86 g, 63%); m.p. 79−80 °C. ^{1}H NMR ($CDCl_3$): δ = 1.48 [s, 9 H, C(C*H*$_3$)$_3$], 4.01 (s, 3 H, OC*H*$_3$), 7.73 (d, *J* = 2.5 Hz, 1 H), 7.78 (br. s, 1 H), 7.92 (d, *J* = 2.5 Hz, 1 H), 7.94 (br. s, 2 H), 10.41 (s, 1 H, C*H*O). ^{19}F NMR ($CDCl_3$): δ = −81.2 (t, *J* = 10.0 Hz, 6 F), −111.4 (t, *J* = 14.0 Hz, 4 F), −121.6 (br. s, 4 F), −122.3 (br. s, 12 F), −123.2 (br. s, 4 F), −126.6 (br. s, 4 F). ^{13}C NMR ($CDCl_3$): δ = 31.0, 35.8, 66.8, 105−120 (m, C_8F_{17}), 124.7 (t, *J* = 7.0 Hz), 126.9, 129.3 (t, *J* = 7.0 Hz), 130.7, 131.5 (t, *J* = 25.0 Hz), 132.3, 134.1, 142.6, 145.6, 164.5, 190.2. $C_{34}H_{18}F_{34}O_2$ (1104.5): calcd. C 36.97, H 1.64; found C 36.92, H 1.74.

5-[3,5-Bis(*n*-heptadecafluorooctyl)phenyl]-3-*tert*-butyl-2-hydroxybenzaldehyde (18): A solution of *o*-methoxybenzaldehyde **17** (0.50 g, 0.45 mmol) in dry CH_2Cl_2 (5 mL) was cooled under nitrogen to 0 °C. After addition of BBr_3 (1 M in CH_2Cl_2, 2 mL, 2 mmol), the solution was stirred at 0 °C for 1 h and then at room temperature for 2 h. The solution was poured into chilled water (5 mL). Et_2O (10 mL) was added and the organic phase was washed with H_2O (5 mL), 5% aqueous $NaHCO_3$ (5 mL), and brine (5 mL), and dried with $MgSO_4$. Evaporation of the solvent afforded the title compound as a white solid (0.49 g, 98%); m.p. 94−96 °C. ^{1}H NMR ($CDCl_3$): δ = 1.48 [s, 9 H, C(C*H*$_3$)$_3$], 7.61 (d, *J* = 2.3 Hz, 1 H), 7.70 (d, *J* = 2.3 Hz, 1 H), 7.77 (br. s, 1 H), 7.92 (br. s, 2 H), 9.99 (s, 1 H, C*H*O), 11.94 (s, 1 H, O*H*). ^{19}F NMR ($CDCl_3$): δ = −81.2 (t, *J* = 10.0 Hz, 6 F), −111.3 (t, *J* = 14.0 Hz, 4 F), −121.5 (br. s, 4 F), −122.2 (br. s, 12 F), −123.2 (br. s, 4 F), −126.5 (br. s, 4 F). ^{13}C NMR ($CDCl_3$): δ = 29.1, 35.2, 105−120 (m, C_8F_{17}), 120.9, 123.9 (t, *J* = 7.0 Hz), 128.6 (t, *J* = 7.0 Hz), 129.4, 130.4, 130.8 (t, *J* = 25.0 Hz), 132.8, 139.9, 142.3, 161.8, 196.9. $C_{33}H_{16}F_{34}O_2$ (1090.4): calcd. C 36.35, H 1.48; found C 36.24, H 1.70.

Salen 4: *o*-Hydroxyaldehyde **9** (1.79 g, 3.00 mmol) was dissolved under nitrogen in hot EtOH (40 mL). (*R*,*R*)-1,2-Diaminocyclohexane (0.17 g, 1.50 mmol) was added to the stirred solution. The solution was refluxed for 3 h before being cooled to room temperature and concentrated under reduced temperature. Purification by flash CC (silica gel, light petroleum ether/Et_2O 98:2) afforded the title compound (1.60 g, 84%) as a yellow foam. − $[\alpha]_D^{20}$ = −165.6 (*c* = 0.5, Et_2O). ^{1}H NMR ($CDCl_3$): δ = 1.38 [s, 18 H, C(C*H*$_3$)$_3$],

1.90−2.01 (m, 8 H, *c*C_4H_8CHN), 3.31−3.43 (m, 2 H, *c*C_4H_8C*H*N), 7.17 (d, *J* = 2.3 Hz, 2 H), 7.38 (d, *J* = 2.3 Hz, 2 H), 8.28 (s, 2 H, ArC*H*=N), 14.4 (s, 2 H, O*H*). ^{19}F NMR ($CDCl_3$): δ = −81.3 (t, *J* = 10.0 Hz, 6 F), −111.5 (t, *J* = 12.0 Hz, 4 F), −121.6 (br. s, 8 F), −122.3 (br. s, 8 F), −123.1 (br. s, 4 F), −126.6 (br. s, 4 F). ^{13}C NMR ($CDCl_3$): δ = 24.5, 29.3, 33.1, 35.3, 72.5, 105−120 (m, C_8F_{17}), 118.0, 127.8, 129.0, 138.8, 163.8, 165.4. $C_{44}H_{36}F_{34}N_2O_2$ (1270.7): calcd. C 41.59, H 2.86, N 2.06; found C 41.42, H 2.91, N 1.95.

Salen 5: *o*-Hydroxyaldehyde **9** (1.79 g, 3.00 mmol) and (*R*,*R*)-1,2-diphenylethylenediamine (0.32 g, 1.50 mmol) were condensed according to the procedure described for the synthesis of salen **4**. Purification by flash CC (silica gel, light petroleum ether/Et_2O 98:2) afforded the title compound (1.79 g, 87%) as a pale yellow foam. − $[\alpha]_D^{20}$ = −46.8 (*c* = 0.5, Et_2O). ^{1}H NMR ($CDCl_3$): δ = 1.40 [s, 18 H, C(C*H*$_3$)$_3$], 4.75 (s, 2 H, PhC*H*N), 7.21 (d, *J* = 2.3 Hz, 2 H), 7.15−7.30 (m, 10 H), 7.41 (d, *J* = 2.3 Hz, 2 H), 8.35 (s, 2 H, ArC*H*=N), 14.3 (s, 2 H, O*H*). ^{19}F NMR ($CDCl_3$): δ = −81.3 (t, *J* = 10.0 Hz, 6 F), −111.3 (t, *J* = 14.0 Hz, 4 F), −121.8 (br. s, 8 F), −122.3 (br. s, 8 F), −123.1 (br. s, 4 F), −126.6 (br. s, 4 F). ^{13}C NMR (CDCl3): δ = 28.9, 35.0, 79.8, 105−120 (m, C_8F_{17}), 118.0, 118.2 (t, *J* = 25.0 Hz), 127.8 (t, *J* = 6.5 Hz), 127.9, 128.0, 128.6, 128.8 (t, *J* = 6.5 Hz), 138.5, 163.2, 166.3 − $C_{52}H_{38}F_{34}N_2O_2$ (1368.8): calcd. C 45.63, H 2.80, N 1.92; found C 45.84, H 2.86, N 2.07.

Salen 6: Biaryl aldehyde **12** (1.35 g, 0.80 mmol) was dissolved under Ar in boiling EtOH (20 mL). (*R*,*R*)-1,2-Diaminocyclohexane (46.0 mg, 0.40 mmol) was added to the stirred solution, and the yellow solution was refluxed for 5 h. Evaporation of the solvent afforded a yellow oil that was washed with cold EtOH (5 mL). The residue was redissolved in Et_2O (40 mL) and washed with water (10 mL) and brine (10 mL). The organic phase was dried with Na_2SO_4 and the crude product was further purified by flash chromatography (silica gel, light petroleum ether/Et_2O 95:5) to give the title compound as a yellow foam (0.91 g, 72%). − $[\alpha]_D^{20}$ = −13.7 (*c* = 0.5, Et_2O) − ^{1}H NMR ($CDCl_3$): δ = 1.40 [s, 18 H, C(C*H*$_3$)$_3$], 1.45−2.08 (m, 8 H, *c*C_4H_8CHN), 1.67−1.72 (m, 4 H), 1.94−2.17 (m, 12 H), 2.24−2.39 (m, 8 H), 3.32−3.43 (m, 2 H, *c*C_4H_8C*H*N), 3.59−3.67 (m, 4 H), 4.04−4.11 (m, 8 H), 6.67 (d, *J* = 8.6 Hz, 2 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 7.10 (d, *J* = 1.9 Hz, 2 H), 7.45 (d, *J* = 1.9 Hz, 2 H), 8.32 (s, 2 H, ArC*H*=N), 14.21 (br. s, 2 H, O*H*). ^{19}F NMR ($CDCl_3$): δ = −81.3 (t, *J* = 10.0 Hz, 18 F), −111.5 (t, *J* = 14.0 Hz, 12 F), −121.6 (br. s, 12 F), −122.3 (br. s, 36 F), −123.2 (br. s, 12 F), −126.6 (br. s, 12 F). ^{13}C NMR ($CDCl_3$): δ = 21.0, 21.5, 21.7, 24.6, 28.2, 29.7, 30.7, 33.4, 35.2, 67.8, 72.2, 72.6, 72.7, 105−120 (m, C_8F_{17}), 109.4, 119.2, 125.3, 127.8, 129.6, 130.3, 130.8, 137.4, 142.0, 150.6, 152.0, 160.0, 165.8. $C_{106}H_{76}F_{102}N_2O_8$ (3443.6): calcd. C 36.97, H 2.22, N 0.81; found C 36.90, H 2.25, N 0.77.

Salen 7: Condensation of biaryl aldehyde **18** (1.09 g, 1.00 mmol) and (*R*,*R*)-1,2-diaminocyclohexane (57.0 mg, 0.50 mmol) in boiling EtOH (20 mL) and benzotrifluoride (5 mL) and subsequent workup were carried out according to the procedure described for the synthesis of salen **3**. Evaporation of the solvent under reduced pressure gave the title compound as a yellow foam (1.08 g, 95%). − $[\alpha]_D^{20}$ = −14.6 (*c* = 0.5, Et_2O) − ^{1}H NMR ($CDCl_3$): δ = 1.39 [s, 18 H, C(C*H*$_3$)$_3$], 1.45−2.08 (m, 8 H, *c*C_4H_8CHN), 3.38−3.48 (m, 2 H, *c*C_4H_8C*H*N), 7.15 (d, *J* = 2.2 Hz, 2 H), 7.39 (d, *J* = 2.2 Hz, 2 H), 7.67 (br. s, 2 H), 7.76 (br. s, 4 H), 8.38 (s, 2 H, ArC*H*=N), 14.21 (br. s, 2 H, O*H*). ^{19}F NMR ($CDCl_3$): δ = −81.3 (t, *J* = 10.0 Hz, 12 F), −111.5 (t, *J* = 14.0 Hz, 8 F), −121.7 (br. s, 8 F), −122.3 (br. s, 24 F), −123.2 (br. s, 8 F), −126.6 (br. s, 8 F). ^{13}C NMR ($CDCl_3$): δ = 24.7, 29.3, 33.2, 35.3, 72.9, 105−120 (m, C_8F_{17}), 119.2, 123.5, 128.3, 128.7, 128.8, 130.8 (t, *J* = 25.0 Hz), 139.2, 143.5, 161.7, 165.8. $C_{72}H_{42}F_{68}N_2O_2$ (2259.0) calcd. C 38.28, H 1.87, N 1.24; found C 38.36, H 1.90, N 1.18.

Complex (Mn-4)Cl: Solid $Mn(OAc)_2{\cdot}4H_2O$ (0.46 g, 1.90 mmol) was added under nitrogen in three portions to a solution of ligand **4** (1.27 g, 1.00 mmol) in boiling EtOH (40 mL). The brown mixture was stirred at reflux for 2 h. LiCl (0.12 g, 2.80 mmol) was added and reflux was continued for 1 h, after which the mixture was allowed to cool to room temperature. The solvent was removed under reduced pressure and the residue was dissolved in CH_2Cl_2 (70 mL). The solution was washed with water (15 mL) and brine (15 mL), and dried with Na_2SO_4. Evaporation of the solvent under reduced pressure afforded the title compound as a brown solid (1.29 g, 95%). − $[\alpha]_D^{20}$ = −188.6 (*c* = 0.01, CH_3OH). UV/Vis ($1{\cdot}10^{-5}$ M, CH_3OH): λ_{max} (lg ε) = 235 nm (4.74). $C_{44}H_{34}ClF_{34}MnN_2O_2$ (1359.1): calcd. C 38.88, H 2.52, N 2.06; found C 39.15, H 2.41, N 1.99.

Complex (Mn-5)Cl: Complexation of ligand **5** (1.37 g, 1.00 mmol) and subsequent workup were carried out as described for (Mn-**4**)Cl. The title compound (0.76 g, 52%) was obtained as a brown solid. − $[\alpha]_D^{20}$ = −88.1 (*c* = 0.01, CH_3OH). UV/Vis ($1{\cdot}10^{-5}$ M, CH_3OH): λ_{max} (lg ε) = 237 nm (4.73). $C_{52}H_{36}ClF_{34}MnN_2O_2$ (1457.2): calcd. C 42.86, H 2.49, N 1.92; found C 43.11, H 2.60, N 1.68.

Complex (Mn-6)Cl: Solid $Mn(OAc)_2{\cdot}4H_2O$ (245 mg, 1.00 mmol) was added under nitrogen in three portions to a solution of ligand **6** (860 mg, 0.25 mmol) in boiling EtOH (20 mL) and benzotrifluoride (5 mL). The brown mixture was stirred at reflux for 4 h. LiCl (85.0 mg, 2.00 mmol) was added and reflux was continued for 1 h, after which the mixture was allowed to cool to room temperature. The solvent was removed under reduced pressure and the residue was extracted with $CFCl_2CF_2Cl$ in a Soxhlet apparatus for 6 h. The solution obtained was evaporated and the brown solid residue was further purified by flash CC (silica gel, light petroleum ether/Et_2O 4:1) to afford the title compound (565 mg, 64%). − $[\alpha]_D^{20}$ = −290 (*c* = 0.01, $CFCl_2CF_2Cl$). UV/Vis ($2{\cdot}10^{-5}$ M, $CFCl_2CF_2Cl$): λ_{max} (lg ε) = 284 nm (4.71), 451 nm (3.63). $C_{106}H_{74}ClF_{102}MnN_2O_8$ (3532.0): calcd. C 36.05, H 2.11, N 0.79; found C 36.05, H 2.11, N 0.79.

Complex (Mn-6)C_7F_{15}COO: Complex (Mn-**6**)Cl (353 mg, 0.10 mmol) was dissolved in Et_2O (5 mL) and *n*-perfluorooctane (10 mL) at room temperature. A large excess of solid $C_7F_{15}COONH_4$ (1.29 g, 2.99 mmol) was added and the mixture was vigorously stirred for 24 h under nitrogen. Water (5 mL) was added and the organic layer was evaporated under reduced pressure. The residue was taken up in *n*-perfluorooctane (10 mL), washed with water (3 × 5 mL) and dried with Na_2SO_4. Evaporation of the solvent afforded the title compound as a dark brown solid (381 mg, 97%). − $[\alpha]_D^{20}$ = −218 (*c* = 0.01, $CFCl_2CF_2Cl$). UV/Vis ($3{\cdot}10^{-5}$ M, $CFCl_2CF_2Cl$): λ_{max} (lg ε) = 272 nm (4.80), 442 nm (3.74). $C_{114}H_{74}ClF_{117}MnN_2O_{10}$ (3909.6): calcd. C 35.02, H 1.91, N 0.72; found C 35.36, H 1.99, N 0.70.

Complex (Mn-7)Cl: Complexation of ligand **7** (903 mg, 0.40 mmol) with solid $Mn(OAc)_2{\cdot}4H_2O$ (392 mg, 1.60 mmol) in boiling EtOH (35 mL) and benzotrifluoride (5 mL) and subsequent workup were carried out as described for the synthesis of (Mn-**6**)Cl. Flash CC (silica gel, light petroleum ether/Et_2O 9:1) afforded the title compound (870 mg, 93%) as a dark brown solid. − $[\alpha]_D^{20}$ = −500 (*c* = 0.01, $CFCl_2CF_2Cl$). UV/Vis ($2{\cdot}10^{-5}$ M, $CFCl_2CF_2Cl$): λ_{max} (lg ε) =

299 nm (4.67), 514 nm (3.12). $C_{72}H_{40}ClF_{68}MnN_2O_2$ (2347.4): calcd. C 36.84, H 1.72, N 1.19; found C 36.05, H 2.11, N 0.79.

Complex (Mn-7)$C_7F_{15}COO$: Anion exchange carried out according to the procedure described for the synthesis of (Mn-**6**)$C_7F_{15}COO$ gave the title compound (270 mg, 99%) as a dark brown solid. $-[\alpha]_D^{20} = -324$ (c = 0.025, $CFCl_2CF_2Cl$). UV/Vis ($1.85\cdot10^{-5}$ M, $CFCl_2CF_2Cl$): λ_{max} (lg ε) = 297 nm (4.71), 441 nm (3.53). $C_{80}H_{40}ClF_{83}MnN_2O_4$ (2725.0): calcd. C 35.26, H 1.48, N 1.03; found C 35.01, H 1.52, N 1.20.

General Procedure for the Asymmetric Epoxidation of Alkenes under Fluorous Biphasic Conditions: In a 10-mL Schlenk tube in a thermoregulated bath at 100 °C, a solution of alkene in CH_3CN (0.20 M, 1.00 mL) containing *o*-dichlorobenzene (0.10 M, internal standard for GC) and a solution of pyridine *N*-oxide (PNO) in CH_3CN (0.25 M, 0.20 mL) were added under nitrogen to a solution of the catalyst in *n*-perfluorooctane (0.01 M 1.00 mL). PhIO (67.0 mg, 0.30 mmol) was quickly added under a nitrogen stream. The two-phase mixture was magnetically stirred at 1300±50 rpm and cooled to room temperature at the end of the reaction. The brown fluorous layer was separated, washed with CH_3CN (2 × 0.5 mL) and reused in further runs (see text). The combined organic layers were washed with saturated aqueous Na_2SO_3 (1 mL) and brine (1 mL), and dried ($MgSO_4$). The epoxide yield and enantiomeric excess were determined by gas chromatographic analysis of the organic solution. In the case of indene and triphenylethylene, the *ee*s of the epoxides were determined by ^1H NMR in the presence of the chiral shift reagent Eu(hfc)$_3$.

Acknowledgments

The COST Action D12 "Fluorous medium: a tool for environmentally compatible oxidation processes" is gratefully acknowledged.

[1] *Chemical Synthesis in Supercritical Fluids* (Eds.: P. G. Jessop, W. Leitner), Wiley-VCH, New York, **1999**.
[2] P. Wasserscheidt, W. Keim, *Angew. Chem. Int. Ed.* **2000**, *39*, 3772−3789, and references therein.
[3] B. Cornils, *J. Mol. Catal. A: Chem.* **1999**, *143*, 1−10, and references therein.
[4] R G. da Rosa, L. Martinelli, L. H. M. da Silva, W. Loh, *Chem. Commun.* **2000**, 33−34, and references therein.
[5] *Modern Solvents in Organic Synthesis*, in: *Topics in Current Chemistry, Vol. 206* (Ed.: P. Knochel), Springer-Verlag, Berlin, **1999**.
[6] R. S. Oakes, A. A. Clifford, K. D. Bartle, M. T. Pett, C. M. Rayner, *Chem. Commun.* **1999**, 247−248. [6b] C. de Bellefon, E. Pollet, P. Grenouillet, *J. Mol. Catal. A: Chem.* **1999**, *145*, 121−126.
[7] P. Lo Nostro, *Adv. Coll. Int. Sci.* **1995**, *56*, 245−287.
[8] D.-W. Zhu, *Synthesis* **1993**, 953−954, and references therein.
[9] A. Ogawa, D. P. Curran, *J. Org. Chem.* **1997**, *62*, 450−451.
[10] I. T. Horváth, J. Rábai, *Science* **1994**, *266*, 72−75.
[11] I.T. Horváth, *Acc. Chem. Res.* **1998**, *31*, 641−650.
[12] [12a] L. P. Barthel-Rosa, J. A. Gladysz, *Coord. Chem. Rev.* **1999**, *192*, 587−605. [12b] R. H. Fish, *Chem. Eur. J.* **1999**, *5*, 1677−1680. [12c] E. De Wolf, G. van Koten, B.-J. Deelman, *Chem. Soc. Rev.* **1999**, *28*, 37−41. [12d] E. G. Hope, A. M. Stuart, *J. Fluorine Chem.* **1999**, *100*, 75−83. [12e] M. Cavazzini, F. Montanari, G. Pozzi, S. Quici, *J. Fluorine Chem.* **1999**, *94*, 183−193.
[13] J. A. Gladysz, *Science* **1994**, *266*, 55−56.
[14] E. N. Jacobsen, in: *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), VCH, Weinheim, **1993**, pp. 159−202, and references therein.
[15] Y. N. Ito, T. Katsuki, *Bull. Chem. Soc. Jpn.* **1999**, *72*, 603−619, and references therein.
[16] W. Zhang, E. N. Jacobsen, *J. Org. Chem.* **1991**, *56*, 2296−2298.
[17] M. Palucki, G. J. McCormick, E. N. Jacobsen, *Tetrahedron Lett.* **1995**, *36*, 5457−5460.
[18] L. Canali, D. C. Sherrington, *Chem. Soc. Rev.* **1999**, *28*, 85−93, and references therein.
[19] T. S. Reger, K. D. Janda, *J. Am. Chem. Soc.* **2000**, *122*, 6929−6934.
[20] [20a] G. Pozzi, F. Cinato, F. Montanari, S. Quici, *Chem. Commun.* **1998**, 877−878. [20b] G. Pozzi, M. Cavazzini, F. Cinato, F. Montanari, S. Quici, *Eur. J. Org. Chem.* **1999**, 1947−1955.
[21] Synthesis and characterization of a chiral fluorous phosphane and its iridium and rhodium complexes: A. Klose, J. A. Gladysz, *Tetrahedron: Asymmetry* **1999**, *10*, 2665−2674.
[22] Enantioselective reactions in supercritical CO_2, catalyzed by iridium and rhodium complexes of chiral fluorous ligands: [22a] S. Kainz, A. Brinkmann, W. Leitner, A. Pfaltz, *J. Am. Chem. Soc.* **1999**, *121*, 6421−6429. [22b] G. Franciò, W. Leitner, *Chem. Commun.* **1999**, 1663−1664.
[23] Enantioselective reactions in fluorinated media: [23a] S. Takeuchi, Y. Nakamura, Y. Ohgo, D. P. Curran, *Tetrahedron Lett.* **1998**, *39*, 8691−8694. [23b] H. Kleijn, E. Rijnberg, J. T. B. H. Jastrzebski, G. van Koten, *Org. Lett.* **1999**, *1*, 853−855. [23c] S. Takeuchi, Y. Nakamura, Y. Ohgo, D. P. Curran, *Tetrahedron Lett.* **2000**, *41*, 57−60. [23d] S. Takeuchi, Y. Nakamura, Y. Ohgo, D. P. Curran, *Tetrahedron* **2000**, *56*, 351−356. [23e] Y. Tian, K. S. Chan, *Tetrahedron Lett.* **2000**, *41*, 8813−8816. [23f] Y. Nakamura, S. Takeuchi, K. Okumura, Y. Ohgo, *Tetrahedron* **2001**, *57*, 5565−5571.
[24] M. Cavazzini, A. Manfredi, F. Montanari, S. Quici, G. Pozzi, *Chem. Commun.* **2000**, 2171−2172.
[25] P. J. Pospisil, D. H. Carsten, E. N. Jacobsen, *Chem. Eur. J.* **1996**, *2*, 974−980, and references therein.
[26] D. Feichtinger, D. A. Plattner, *Chem. Eur. J.* **2001**, *7*, 591−599.
[27] G. Pozzi, I. Colombani, M. Miglioli, F. Montanari, S. Quici, *Tetrahedron* **1997**, *52*, 11879−11888.
[28] G. Casiraghi, G. Casnati, G. Puglia, G. Sartori, G. Terenghi, *J. Chem. Soc., Perkin Trans. 1* **1980**, 1862−1865.
[29] J. F. Larrow, E. N. Jacobsen, Y. Gao, Y. Hong, X. Nie, C. M. Zepp, *J. Org. Chem.* **1994**, *59*, 1939−1942.
[30] D. Sinou, G. Pozzi, E. N. Hope, A. M. Stuart, *Tetrahedron Lett.* **1999**, *40*, 849−852.
[31] M. G. Banwell, J. M. Cameron, M. P. Collins, G. T. Crisp, R. W. Gable, E. Hamel, J. N. Lambert, M. F. Mackay, M. E. Reum, J. S. Scoble, *Aust. J. Chem.* **1991**, *44*, 705−728.
[32] B. E. Huff, T. M. Koenig, D. Mitchell, M. A. Staszak, *Org. Synth.* **1998**, *75*, 53−60.
[33] S. Colonna, N. Gaggero, F. Montanari, G. Pozzi, S. Quici, *Eur. J. Org. Chem.* **2001**, 181−186.
[34] H. Sasaki, R. Irie, T. Katsuki, *Synlett* **1993**, 300−302.
[35] J. M. Fraile, J. I. Garcia, J. Massam, J. A. Mayoral, *J. Mol. Catal. A: Chem.* **1998**, *136*, 47−57.
[36] M. Palucki, P. J. Pospisil, W. Zhang, E. N. Jacobsen, *J. Am. Chem. Soc.* **1994**, *116*, 9333−9334.
[37] D. Maillard, C. Nguefack, G. Pozzi, S. Quici, B. Valadé, D. Sinou, *Tetrahedron: Asymmetry* **2000**, *11*, 2881−2884.
[38] J.-M. Vincent, A. Rabion, V. K. Yachandra, R. H. Fish, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2346−2349.

Received June 18, 2001
[O01283]