Enantioselective Catalysis in Fluorinated Media – Synthesis and Properties of Chiral Perfluoroalkylated (Salen)manganese Complexes

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Chiral (salen)manganese complexes, which are selectively soluble in perfluorocarbons, were synthesized and tested as epoxidation catalysts in fluorous-organic two-phase systems. The immiscibility of the perfluorocarbons with regular organic solvents allowed a quick and effective separation of the catalyst from the products. These unprecedented perfluoroalkylated salen complexes were found to be efficient and chemoselective catalysts in the presence of several oxygen donors, but enantioselectivities were generally poor. An interesting exception to this behaviour was observed in the asymmetric epoxidation of indene that provides indene oxide with 70–92% enantiomeric excess.

Introduction

Most organic chemists still regard perfluorocarbons (fluids made up only of C and F, or C, F and O, or C, F and N) as exotic compounds for special industrial applications, devoid of any interest in preparative chemistry. Such a belief arises mainly from the chemical inertness of these fluids and on their very low solvent strength for almost all organic compounds, two features that are perceived to clash with any synthetic role.[1] Rather paradoxically, the same peculiar physico-chemical properties, together with the thermo- and pressure-controlled miscibility of perfluorocarbons with regular organic solvents, spurred several groups to investigate perfluorocarbons as a reaction media in preparative organic chemistry and homogeneous catalysis.[2] In this context, the value of the phase-separation and immobilization technique developed by Horváth and Rábai and known as FBS (Fluorous Biphase Systems) is now well recognized.[3] The principles of this approach can be summarized as follows. Perfluorocarbons (the "fluorous" phase) are almost immiscible with solvents such as acetonitrile or toluene at room temperature and under atmospheric pressure. Two-phase systems can be thus obtained, in which a catalyst soluble in the fluorous phase is segregated from reagents and products during the whole process. Since phase miscibility can sharply increase with temperature and pressure it is also possible to work under homogeneous conditions during the reaction step and to return to two-phase conditions at the end of it.

As clearly illustrated by Cornils,[2d] this technique brings about potential advantages over classical homogeneous catalysis, including the easy and effective separation and recycling of the catalyst. Nevertheless, a wide industrial use of FBS is hampered by possible environmental drawbacks related to the use of perfluorocarbons and by the cost of the ligands for FBS catalysis. Engineering aspects of FBS processes on industrial scale (e.g. elimination of leakages and complete recycle of the effluents) need to be investigated in order to meet environmental concerns.[4] We are currently tackling the other side of the question by studying the effective design and preparation of efficient catalysts selectively soluble in perfluorocarbons. As already pointed out elsewhere, this study is basic to all cost-effective applications of FBS and to the assessment of its true potential.[5]

Enantioselective transformations were recognized as an extremely interesting domain for the application of FBS at a very early stage of its development.[3a] It was suggested that, besides helping recovery and reuse of precious chiral reagents or catalysts, the unique solvation environment provided by perfluorocarbons might have unforeseen and possibly positive effects on the selectivity of the reactions[6]. Substantiation of these hypotheses calls for experimental data and therefore for the synthesis of chiral metal complexes suited for FBS. In a recent communication we reported the first example of an enantioselective reaction under FBS conditions,[5d] namely the epoxidation of indene in the presence of two different optically active perfluoroalkylated (salen)manganese(III) complexes (Jacobsen-Katsuki catalysts).[7][8] Herein, the synthesis of these catalysts is fully described together with the results obtained in the epoxidation of alkenes both under FBS and homogeneous conditions in the presence of various oxygen donors.

Results and Discussion

Asymmetric epoxidation of unfunctionalized alkenes holds a considerable interest in organic synthesis, because enantiomerically pure epoxides are versatile intermediates in the preparation of several classes of compounds.[8b] A major breakthrough in this field was the introduction in 1990 of (salen)manganese(III) complexes as chiral catalysts.[7][8] A variety of alkenes have been thus epoxidized

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enantioselectively with simple oxidants such as iodosylarenes,[7a] aqueous hypochlorite,[9] hydrogen peroxide,[10] and the couple *m*-chloroperbenzoic acid/*N*-methylmorpholine *N*-oxide.[11] The straightforward access to chiral salen ligands, based on the condensation of diamines with salicylaldehyde derivatives, provides the unique opportunity of finely tuning the steric and electronic properties of the catalyst. A wide number of chiral (salen)manganese(III) complexes have, in fact, been reported in the literature, and optimal enantioselectivities for a given substrate were achieved by choosing the proper catalyst and the best reaction conditions.[7b,8b] Although some commercially available (salen)manganese(III) complexes (e.g. Jacobsen's catalyst, Figure 1) can be successfully used for the epoxidation of several alkenes, the importance of this complementarity of substrate, catalyst, and oxidizing system should not be underestimated.

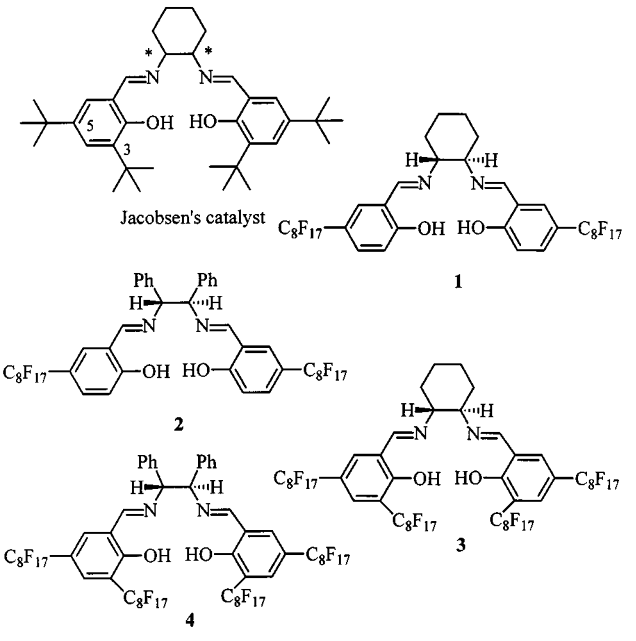
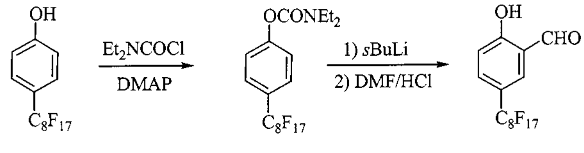


Figure 1

The abundance of literature examples for salen ligands soluble in common organic solvents is matched by the total absence of similar compounds bearing perfluoroalkyl substituents (R_F). This characteristic is paramount if selective solubility of the catalyst in perfluorocarbons is envisaged, so we planned the synthesis of a series of ligands featuring R_F tails. The overall number of R_F substituents, their location as well as the possible insertion of spacers between them and the core structure of the ligand were taken into account. At first we decided to study the properties of salen ligands in which R_F groups are connected to the salicylaldehyde moieties through carbon−carbon bonds. As a matter of fact, the comparison of the catalytic activity of various perfluoroalkylated (tetraarylporphyrin)Mn^{III} complexes showed that the presence of heteronuclear bonds such as amido bonds between the R_F substituents and the porphyrin ring can be detrimental.[5]

Many highly enantioselective salen complex catalysts are characterized by the presence of bulky substituents (e.g. *tert*-butyl groups) in the 3,3′ and 5,5′ positions of their salicylidene core (Figure 1). Their presence is assumed to force the approach of the substrate to the metal site where the oxygen transfer takes place along productive directions, for instance over the chiral diamine backbone. It should be also noted that the enantioselective epoxidation of some alkenes with catalysts bearing hydrogen atoms in the 3,3′ and 5,5′ positions was described, even though the *ee* values were less than or equal to 50%.[12] The solubility of organic compounds in perfluorocarbons is affected by their fluorine load. It was then decided to synthesize a series of salen ligands devoid of "organic" substituents and to switch to the synthesis of more complex ligands only after verification that the simplest models were suitable for catalytic FBS reactions, both in term of fluorous behaviour and enantioselectivity. Based on pure steric effects it was reasonable to suppose that the presence of R_F substituents in the 3,3′ and/or 5,5′ positions of ligands **1−4** (Figure 1) should somewhat assist the correct approach of the substrate to the catalyst. Indeed, in the solid state, R_F substituents with more than 6 C atoms assume a rigid, fully extended *anti* conformation with a quite high thermal motion.[13][14] Enantioselectivities at least of the same level of those reported in the presence of the previously cited unsubstituted salen derivatives were thus anticipated.

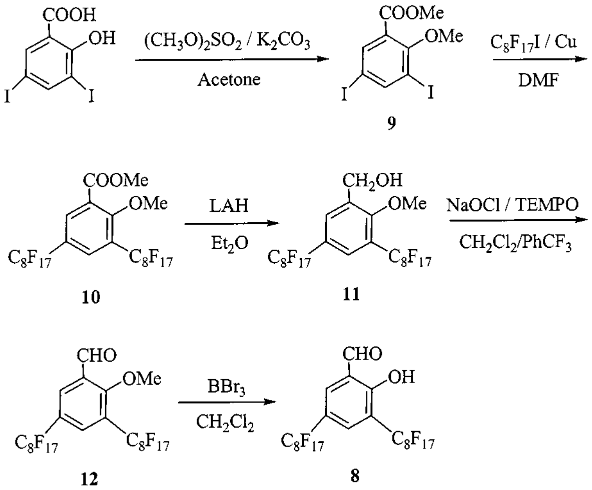
The synthesis of salen **1** and **2** (Figure 1) required a ready access to the mono(perfluoroalkylated) 2-hydroxyaldehyde **5** (Scheme 1). Of the many methods available for the synthesis of salicylaldehydes, *ortho*-formylation of phenols according to the procedures of Casiraghi and Duff proved to be the most convenient for the preparation of salen precursors.[15−17] In our hands, all attempts to obtain aldehyde **5** by formylation of 4-(*n*-heptadecafluorooctyl)phenol (**6**)[18] with paraformaldehyde or hexamethylenetetraamine in the presence of Lewis or protic acids, respectively, failed. Good results were obtained by using a simple two-step procedure involving carbamoylation of **6** and *ortho*-lithiation of carbamate **7** followed by reaction with DMF and hydrolysis (Scheme 1).[19] This alternative pathway afforded perfluoroalkylated salicylaldehyde **5** in 65% overall yield with respect to phenol **6**.



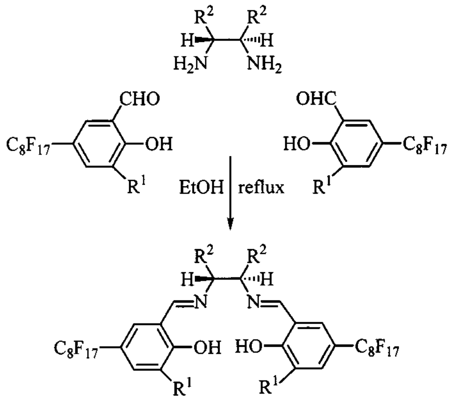
6 **7** **5**

Scheme 1. Synthesis of (perfluoroalkyl)salicylaldehyde **5**

Bis(perfluoroalkylated) salicylaldehyde **8**, the starting material for the synthesis of salen ligands **3** and **4**, was prepared according to the procedure outlined in Scheme 2. The detour from *ortho*-formylation procedures was due to the fact that, in contrast with diiodophenols, methyl esters of diiodobenzoic acids are excellent substrates for the copper-catalyzed introduction of R_F substituents on the aryl ring.[5b,5c] Moreover, 3,5-diiodosalicylic acid is readily available from commercial sources, whereas 2,4-diiodophenol is not. The free OH groups of 3,5-diiodosalicylic acid were protected by methylation with $(CH_3O)_2SO_2$ before the coupling reaction with 2 equivalents of $C_8F_{17}I$ mediated by Cu powder, carried out according to the classical and very effective procedure of McLoughlin and Thrower.[20] Indeed, the same reaction carried out on 3,5-diiodosalicylic acid gave a mixture of compounds from which the bis(perfluoroalkylated) acid could be hardly obtained. Preliminary attempts to reduce ester **10** directly to aldehyde **12** with diisobutylaluminium hydride were unsuccessful. This transformation was then carried out by reduction to benzyl alcohol **11** (70% yield) followed by oxidation to aldehyde (85% yield). The proper choice of reaction conditions was crucial for both these two simple steps. In the case of the LAH reduction of ester **10**, the temperature must be strictly controlled during the addition of the substrate to a suspension of the reducing agent in Et_2O (see Experimental Section). Under more forcing conditions the main reaction product was found to be 3,5-bis(*n*-heptadecafluorooctyl)benzyl alcohol, whereas the starting compound was recovered unchanged when the reaction mixture was kept at a temperature below 0 °C for more than 30 min. The partial oxidation of **11** to aldehyde **12** was also rather troublesome, one reason being the low solubility of the substrate in organic solvents at low temperature. The oxidation with active MnO_2 in refluxing benzene (50% yield) was found to be a useful method, but even better results were obtained by slightly modifying a mild aqueous-organic two-phase procedure previously reported by us.[21] The use of benzotrifluoride [(trifluoromethyl)benzene] as solvent greatly improved the yield of the oxidative step, which was conveniently carried out with aqueous NaOCl in the presence of catalytic amounts of KBr and 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) radical. The halogenated solvents used in the original procedure could not dissolve benzyl alcohol **11** at 5 °C. On the other hand, benzotrifluoride can replace CH_2Cl_2 in some oxidation reactions, because it has a similar dielectric constant.[22] This solvent is able to solubilize both fluorinated and hydrogenated organic compounds, and in our case it allowed the presence of the catalyst TEMPO and of the alcohol **11** in the same liquid phase. Consequently, all the advantages of the original oxidation methodology were retained, and aldehyde **12** was obtained in 85% yield by a quick and selective reaction. Demethylation of **12** with BBr_3 did not present particular problems and afforded salicylaldehyde **8** in 88% yield.



Scheme 2. Synthesis of (perfluoroalkyl)salicylaldehyde **8**



1	$R^1 = H$	$R^2 = -(CH_2)_4-$	Yield = 67%
2	$R^1 = H$	$R^2 = Ph$	Yield = 54%
3	$R^1 = -C_8F_{17}$	$R^2 = -(CH_2)_4-$	Yield = 75%
4	$R^1 = -C_8F_{17}$	$R^2 = Ph$	Yield = 82%

Scheme 3. Synthesis of salen ligands **1−4**

To our surprise, the C_2-symmetric salen ligands **1−4** were obtained in good yields (54−82%) through condensation of 2 equivalents of perfluoroalkylated salicylaldehydes **5** or **8** with the proper chiral 1,2-diamine (Scheme 3). Although this kind of reaction is well-established for many salicylaldehydes, we were afraid that perfluoroalkylated compounds **5** and **8** could exhibit a different behaviour. Indeed, it was previously reported that the acid-catalyzed condensation of perfluoroalkylated benzaldehydes with pyrrole barely affords tetraarylporphyrins, probably because of solubility problems.[5b,5c]

The manganese(III) complexes of salen ligands **1−4** (Mn-**1**−Mn-**4**) were prepared by refluxing an ethanolic solution of the ligand with an excess of $Mn(OAc)_2{\cdot}4H_2O$ under aerobic conditions. Complexes Mn-**1** and Mn-**2** precipitated as brown amorphous solids from the ethanolic solution, whereas Mn-**2** and Mn-**4** formed brown oily layers on the bottom of the flask. The four complexes exhibit remarkably different behaviours towards common organic solvents and perfluorocarbons. The following commercially available fluids were tested: FC-72 (3 M, mainly perfluorohexanes, b.p. 56 °C), FC-75 (3 M, mainly perfluoro *n*-butyltetrahydrofuran, b.p. 102 °C), Galden D-100 (Ausimont, mainly *n*-perfluorooctane, b.p. 100 °C). Complex Mn-**1** (fluorine load F = 52%) was found to be completely insoluble in organic solvents, in perfluorocarbons and in benzotrifluoride, both at room temperature and at reflux, therefore its catalytic properties were not further investigated. The complex Mn-**2**, bearing two R_F like Mn-**1** but with a slightly lower fluorine load (F = 48%) was soluble in cold ethers, CCl_2FCF_2Cl, and benzotrifluoride, sparingly soluble in refluxing CH_2Cl_2, but completely insoluble in perfluorocarbons. Only complexes Mn-**3** and Mn-**4** (F = 62% and 59%) bearing four R_F substituents were soluble in these fluids, as well as in benzotrifluoride and CCl_2FCF_2Cl. Their solubility in other halogenated solvents was so low that they could not be detected by UV/Vis spectroscopy despite their characteristic absorption. We took advantage of the preferential solubility of Mn-**3** and Mn-**4** in perfluorocarbons for their isolation from the reaction mixture (see Experimental Section) and for the catalytic epoxidation of alkenes under FBS conditions. Salens **1−4** belong to an expanding series of perfluoroalkylated tetradentate ligands,[5][23] the members of which are suitable for the preparation of FBS catalysis only if the fluorine load is higher than 60%. The present results also confirm that in this series the preference for perfluorocarbons or organic solvents is finely tuned by slight differences in the fluorine load. Considerable efforts are often required for the synthesis of tailored perfluoroalkylated ligands; hence it would be important to find out reliable parameters for the effective design of compounds selectively soluble in perfluorocarbons. The empiric rule "$F \geqslant 60\%$" is a useful starting point in the case of tetradentate ligands, and it can also be conveniently applied for other classes of compounds.[24] However, one should always bear in mind that fluorine load alone is not sufficient to foresee the solubility behaviour of a molecule, and other features such as the number and length of the R_F substituents must be taken into account.[2f,25]

With chiral manganese complexes **3** and **4** on hand, we were able to study the feasibility of enantioselective catalytic reactions under FBS conditions. Among the manifold oxidizing systems used in connection with (salen)manganese(III) complexes, our choice fell on molecular oxygen in the presence of a sacrificial aldehyde. This combination was originally applied in salen-mediated enantioselective epoxidation by Mukaiyama and co-workers and it was particularly appealing for our purposes.[26] Indeed, perfluorocarbons dissolve large quantities of molecular oxygen, and this property has been exploited in the aerobic epoxidation of alkenes under FBS conditions in the presence of aliphatic aldehydes.[5c,27] Complexes Mn-**3** and Mn-**4** were thus first tested adapting Mukaiyama conditions to a typical FBS procedure (see Experimental Section). Reactions were carried out in the dark at 20°C under atmospheric pressure of O_2 in two-phase systems in which Mn-**3** and Mn-**4** were immobilized in the fluorous phase and the substrate plus *N*-hexylimidazole dissolved in CH_2Cl_2. Pivalaldehyde was gradually added to the mixture until the molar ratio aldehyde/starting alkene was equal to 3. The conversions observed in blank experiments carried out under the same conditions, but in the absence of Mn-**3** and Mn-**4**, were negligible. Results reported in Tables 1 and 2 show that both complexes were active catalysts, affording epoxides isolated in yields up to 85%. As already verified in the case of the cobalt complex of a perfluoroalkylated tetraarylporphyrin, the presence of two distinct phases did not preclude the oxidation of the substrate dissolved in the organic solvent.[5c] With most substrates, the brown perfluorocarbon layer recovered by simple decantation could be used for a second run without appreciable decrease of activity and enantioselectivity. Examples are given for indene and 1,2-dihydronaphthalene (Entries 2 and 4, Tables 1 and 2).

Among the alkenes examined, only indene gave the corresponding epoxide with high enantioselectivity. This result was rather puzzling especially because very low *ee* values were obtained with similar alkenes (2-methylindene, benzosuberene and the above-cited 1,2-dihydronaphthalene) for which epoxidation catalyzed by (salen)manganese(III) complexes usually proceeds with high enantioselectivity.[7][8]

The peculiar nature of the oxidizing system justified some conjectures. There is a considerable disagreement on the role played by metal catalysts in the epoxidation of alkenes with O_2/aliphatic aldehydes. According to Valentine and Nam this role is negligible and free $RCO_3^{\cdot}$ radicals spontaneously formed are the main oxidizing agents.[28] Indeed, under particular reaction conditions (e.g. high aldehyde/alkene ratio, direct exposition to sunlight) the epoxidation of certain alkenes proceeds in the absence of metal catalysts.[29][30] On the other hand, several literature reports show that metal catalysts have a profound effect on the epoxide yields and on the selectivity of the reaction. For instance, many substrates are not epoxidized by the O_2/aldehyde system in the absence of a metal catalyst, even in fluorinated media.[31] At the same time, it should be noted that fluorinated media can influence the selectivity of reactions catalyzed by a heterogeneous manganese catalyst.[31] The high enantioselectivity levels reported by Mukaiyama and co-workers point to the participation of the metal complexes in the oxygen transfer.[26]

The most plausible picture for metal-catalyzed epoxidations in the presence of O_2/aldehyde is the coexistence of different reaction pathways,[32] as also suggested by the present results. Besides the absence of reaction product in blank experiments and the high level of enantioselectivity for the epoxidation of indene, we observed a partial inversion of relative configuration in the epoxidation of *cis*-stilbene (Table 1, Entry 12). Free-radical side-reactions could be then responsible for the low enantioselectivities usually obtained. In order to validate this hypothesis, other oxygen donors, more commonly used in combination with chiral (salen)manganese complexes, were tested. Examples are reported in Table 3 for catalyst Mn-**4** and 1,2-dihydronaphthalene.

Reactions carried out in the presence of aqueous oxidants such NaOCl and diluted H_2O_2 gave the worst results. The use of the first oxidant made the system triphasic (H_2O/CH_2Cl_2/perfluorocarbon) and reactions were particularly slow (Entry 1, Table 3). Moreover, inorganic salts precipitated at all stages of the reaction, and the catalyst was not recovered. Bleaching of the catalysts occurred quickly in the presence of 30% H_2O_2; the oxidant was previously dissolved in CH_3CN, and reaction was thus carried out un-

Table 1. Epoxidation of alkenes with O_2/pivalaldehyde under fluorous two-phase conditions catalyzed by the chiral salen complex Mn-**3**[a]

Entry	Substrate	t [h]	Conversion (%)[b]	Yield (%)[c]	*ee* (%)[d]
1	Indene	2	100	83	92
2	Indene[e]	2	100	73	89
3	1,2-Dihydronaphthalene	6	85	70	10
4	1,2-Dihydronaphthalene[e]	6	83	70	9
5	2-Methylindene	2	91	86	n.d.[f]
6	Benzosuberene	2	100	92	7
7	Styrene	5	100	86	n.d.
8	1-Phenylcyclohexene	2	100	78	n.d.
9	3-Nitrostyrene	12	70	36	n.d.
10	*trans*-β-Methylstyrene	5	100	75	n.d.
11	*trans*-Stilbene	12	80	78	n.d.
12	*cis*-Stilbene	12	88	85[g]	−

[a] Reaction conditions: see Experimental Section. − [b] Determined by capillary GC integration against an internal standard. − [c] Isolated epoxide. − [d] Determined by capillary GC on a Cyclodex-B chiral column. − [e] Recycled catalyst. − [f] n.d. = not detected (< 5%). − [g] *cis*/*trans*-epoxide = 3:1.

Table 2. Epoxidation of alkenes with O_2/pivalaldehyde under fluorous two-phase conditions catalyzed by the chiral salen complex Mn-**4**[a]

Entry	Substrate	t [h]	Conversion (%)[b]	Yield (%)[c]	ee (%)[d]
1	Indene	3	100	77	90
2	Indene[e]	2	100	75	92
3	1,2-Dihydronaphthalene	8	95	70	13
4	1,2-Dihydronaphthalene[e]	8	84	61	10
5	2-Methylindene	3	100	68	n.d.[f]
6	Benzosuberene	3	100	91	12
7	Styrene	5	100	81	n.d.

[a] Reaction conditions: see Experimental Section. − [b] Determined by capillary GC integration against an internal standard. − [c] Isolated epoxide. − [d] Determined by capillary GC on a Cyclodex-B chiral column. − [e] Recycled catalyst. − [f] n.d. = not detected (< 5%).

Table 3. Epoxidation of 1,2-dihydronaphthalene with various oxygen donors under fluorous two-phase conditions catalyzed by Mn-**4**[a]

Entry	Oxidant	Solvent	t [h]	T [°C]	Conversion (%)[b]	Yield (%)[b]	*ee* (%)[c]
1	Aqueous NaOCl	CH_2Cl_2	14	0	54	36	9
2	30% H_2O_2[d]	MeCN	0.5	20	−	−	−
3	PhIO	MeCN	24	20	85	65	6
4	Bu_4NHSO_5	CH_2Cl_2	10	20	95	89	8
5	MCPBA/NMO[e]	CH_2Cl_2	4	−78	10	9	5
6	MCPBA/NMO	CH_2Cl_2	6	−50	70	56	7
7	MCPBA/NMO	CH_2Cl_2	6	−20	98	86	5
8	MCPBA/NMO[f]	CH_2Cl_2	4	−50	90	85	71

[a] Conditions: [catalyst] = 0.005 mol dm^{-3} in D-100; [substrate] = 0.1 mol dm^{-3} in CH_2Cl_2; volume of D-100 = 1 ml; volume of CH_2Cl_2 = 1 ml; oxidant: 0.2 mmol. Stirring rate = 1300 rpm. − [b] Determined by capillary GC integration against an internal standard (dichlorobenzene). − [c] Determined by capillary GC on a Cyclodex-B chiral column. − [d] The catalyst bleached in 30 min. − [e] NMO = *N*-methylmorpholine *N*-oxide (0.5 mmol). Addition of the oxidant was carried out according to the procedure described in ref.[11b] − [f] Substrate = indene.

der true FBS conditions (Entry 2). Although other oxidants such as PhIO and Bu_4NHSO_5 (Entries 3 and 4) gave better results with respect to conversion and selectivity, the enantioselectivity was low. Jacobsen and co-workers have shown that olefins susceptible to side reactions, for instance styrene, can be epoxidized enantioselectively at −78 °C in the presence of chiral (salen)manganese complexes and the couple *m*-chloroperbenzoic acid/*N*-methylmorpholine *N*-oxide (MCPBA/NMO) as the oxidant.[11] Reactions were very slow at this low temperature employed under FBS conditions, probably because of hindered mass transfer between the two liquid phases (Entry 5). Although still lower than in the case of homogeneous systems, reaction rates became reasonable already at −50 °C (Entry 6). Blank experiments proved that at this temperature the couple MCPBA/NMO also does not epoxidize the substrates. Nevertheless, low *ee* values were observed again in the presence of the fluorinated (salen)manganese catalysts, except in the epoxidation of indene (Entry 8). We concluded that the nature of the oxidant is not the cause of the low enantioselectivities observed.

Molecular modeling based on the known crystal structures of chiral (salen)manganese complexes and of perfluoroalkylated compounds suggests a bent conformation for the salicylidene moiety of complex Mn-**3**. Room would be thus left for the free approach of the substrate to the metal site. At the perfluorocarbon-organic solvent interface, where the oxygen transfer likely takes place, the structure of the catalyst could be even more distorted from the near-planar geometry commonly adopted by (salen)manganese complexes. In order to minimize the interaction with the organic solvent, the perfluorinated tails would be directed toward the bulk of the fluorous phase while the salicylidene core of the catalyst would point toward the organic phase. Such behaviour was observed for diblock lipophilic/fluorophilic molecules that play the role of "molecular dowels" between perfluorocarbons and fatty acid chains of egg yolk phospholipids.[33]

The comparison of the catalytic activities of Mn-**4** under homogeneous (Table 4) and FBS conditions (Table 2) ruled out this last hypothesis. Although reactions carried out in CH_2Cl_2/benzotrifluoride (homogeneous conditions) were generally faster than those in CH_2Cl_2/D-100 (FBS), the *ee* values were very similar. Another interesting point is that catalyst Mn-**4** was bleached under homogeneous conditions, and it was not possible to recover it from the solution. This is another sound proof of the favourable effects of the segregation of the catalysts in the fluorous phase. The use of benzotrifluoride as a solvent also allowed the direct comparison of the catalytic activities of Mn-**2** and Mn-**4**. As shown in Table 4, the presence of four R_F susbtituents in Mn-**4** did not bring about major advantages for the enantioselectivity.

Despite a recent debate over the mechanism of oxygen transfer from the intermediate (oxo)Mn species to the double bond, it is now accepted that both the activity and enantioselectivity of (salen)manganese complexes are tuned by a complex interplay of steric and electronic factors.[34] In this context, the lack of enantioselectivity of Mn-**3** and Mn-**4** is consistent with a strong electron-withdrawing effect exerted by the four R_F substituents on the (oxo)Mn intermediate.[35] It should be pointed out that a residual electron-withdrawing effect of the perfluoroalkyl substituents on the metal center in the complex *trans*-$[IrCl(CO)\{P[CH_2CH_2(CF_2)_5CF_3]_3\}_2]$ has been recently reported.[13] However, R_F differs from other electron-withdrawing substituents, such as Cl and Br, because the introduction of four halides also lowers the catalytic activity and the stability of (salen)manganese complexes.[36]

Conclusions

Several techniques of heterogenization of Jacobsen-Katsuki catalysts have been proposed in the literature, but in just one case the reported activities, chemoselectivities and *ee* values were as high as those obtained with one of the best homogeneous chiral (salen)manganese complexes.[37] The FBS approach here described offers distinct advantages over other immobilization methods: Stability of the catalyst toward bleaching is increased and its activity remains high. The easy separation of the products from the catalyst, which can be readily reused, is another considerable benefit. Despite the good chemoselectivity and efficiency observed, only the epoxidation of indene proceeded with high levels of enantioselectivity. The nature of the oxidizing system and the use of perfluorocarbons does not have a significative impact on this trend. Solvation effects due to perfluorocarbons or phenomena at the interface between the organic and the fluorous phase do not interfere at a great extent with the outcome of the reaction. The intrinsic stereoelectronic features of the catalysts remain the main source of enantioselectivity (or lack of it) in the epoxidation of alkenes.[38] The results reported here are a good starting point for the rational design of other chiral catalysts for FBS epoxidation of alkenes. We are currently synthesizing a second generation of chiral salen ligands in which either the salicylidene core is shielded more efficiently from the R_F substituents or "organophilic" bulky substituents replace some of the R_F substituents. These features are expected to improve enantiofacial discrimination, while still maintaining the peculiar solubility of the catalysts in fluorocarbons.

Experimental Section

General Remarks: Solvents were purified by standard methods and dried if necessary, except perfluorocarbons that were used as re-

Table 4. Epoxidation of alkenes under homogeneous conditions[a]

Entry	Substrate	Catalyst	*t* [h]	Conversion (%)[b]	Yield (%)[b]	*ee* [%][c]
1	Indene[d]	Mn-**2**	2	100	77	81
2	Indene[d]	Mn-**4**	1	100	79	90
3	1,2-Dihydronaphthalene[d]	Mn-**2**	2	75	35	14
4	1,2-Dihydronaphthalene[d]	Mn-**4**	1	93	62	5
5	Styrene[d]	Mn-**2**	2	88	70	n.d.[e]
6	Styrene[d]	Mn-**4**	2	90	70	8
7	Indene[f]	Mn-**2**	2	80	61	62
8	Indene[f]	Mn-**4**	2	74	58	76
9	1,2-Dihydronaphthalene[f]	Mn-**2**	2	68	67	13
10	Styrene[f]	Mn-**2**	2	81	44	7

[a] Conditions: [catalyst] = 0.005 mmol; [substrate] = 0.1 mmol; solvent = $CH_2Cl_2/PhCF_3$ (2 mL, 1/1 v/v). Stirring rate = 1300 rpm. The use of CH_2Cl_2 was required in order to solubilize NMO. − [b] Determined by capillary GC integration against an internal standard. − [c] Determined by capillary GC on a Cyclodex-B chiral column. − [d] Oxidant = O_2/pivalaldehyde (0.3 mmol); $T = 20°C$. − [e] n.d. = not detected (< 5%). − [f] Oxidant = MCPBA/NMO (see Table 3); $T = -50°C$.

ceived. 2-Methylindene and benzosuberene were synthesized according to literature procedures.[39] All commercially available reagents were used as received. TLC was carried out on silica gel 60 F_{254}. Column chromatography (CC) was carried out on silica gel SI 60, mesh size 0.040−0.063 mm (Merck, Darmstadt, Germany) or neutral alumina 90 Activity I, mesh size 0.063−0.200 mm (Merck, Darmstadt, Germany). − Melting points (uncorrected) were determined with a capillary melting point apparatus Büchi SMP-20. − Optical rotations were measured with a Perkin−Elmer 241 polarimeter. UV/Vis spectra were measured with 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 with a Varian XL 300 spectrometer with tetramethylsilane ($\delta = 0$), $CDCl_3$ ($\delta = 77$) and $CFCl_3$ ($\delta = 0$), respectively, as internal standards. − GC analyses were performed with a Hewlett-Packard 5890 instrument (column: 30 × 0.5 mm RSL-200 polymethylsiloxane or Cyclodex-B, 30 × 0.25 mm chiral column). − Elemental analyses: Redox S.n.C. (Cologno Monzese, Italy) and Departmental Service of Microanalysis (University of Milano).

Carbamate 7: To a solution of 4-(*n*-heptadecafluorooctyl)phenol (**6**)[18] (512 mg, 1 mmol) and 4-(dimethylamino)pyridine (DMAP, 244 mg, 2 mmol) in dry toluene (20 mL) was added diethylcarbamyl chloride (253 µl, 2 mmol). After overnight reflux, the mixture was cooled to room temperature, diluted with Et_2O (10 mL), and poured into ice (20 g). The aqueous phase was extracted with Et_2O (3 × 10 mL), and the combined organic layers were washed with brine (10 mL) and dried with Na_2SO_4. The residue was purified by CC (light petroleum ether/Et_2O, 1:1) to afford the title compound **7** as a pale yellow solid (575 mg, 94%). − M.p. 38 °C. − ^{1}H NMR ($CDCl_3$): $\delta = 1.21$ (m, 6H, CH_2CH_3), 3.40 (m, 4H, CH_2CH_3), 7.26 (d, $J = 8.7$ Hz, 2H, 2-H), 7.57 (d, $J = 8.7$ Hz, 2H, 3-H). − ^{13}C NMR ($CDCl_3$): $\delta = 13.3$, 14.2, 42.0, 42.2, 105−120 (m, C_8F_{17}), 121.9, 128.1 (t, $J = 6$ Hz), 153.3, 154.4. − ^{19}F NMR ($CDCl_3$) $\delta = -81.3$ (t, $J = 10$ Hz, 3 F), −111.8 (t, $J = 12$ Hz, 2 F), −121.8 (m, 4 F), −122.3 (m, 4 F), −123.1 (br. s, 2 F), −126.6 (br. s, 2 F). − $C_{19}H_{14}F_{17}NO_2$ (611.3): calcd. C 37.33, H 2.31, N 2.29; found C 37.56, H 2.45, N 2.18.

Salicylaldehyde 5: In a flame-dried flask, a solution of carbamate **7** (611 mg, 1 mmol) and tetramethylethylenediamine (190 µl, 1.2 mmol) in dry THF (20 mL) was cooled under Ar to −78 °C. *s*BuLi (1.17 M in hexane, 1.2 mL, 1.4 mmol) was added dropwise over 15 min. After 1 h, the solution was treated with DMF (0.30 mL) and then set aside at room temperature overnight. The reaction mixture was hydrolyzed with 10% HCl and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried with Na_2SO_4. The residue was purified by CC (light petroleum ether/Et_2O, 3:2) to afford the title compound **5** as a white solid (391 mg, 72%). − M.p. 61−62 °C. − ^{1}H NMR ($CDCl_3$): $\delta = 7.08$ (d, $J = 8.6$ Hz, 1H, 3-H), 7.63 (dd, $J = 8.6$ Hz, $J = 2.3$ Hz, 1H, 4-H), 7.72 (d, $J = 2.3$ Hz, 1H, 6-H), 9.95 (s, 1H, CHO), 11.31 (s, 1H, OH). − ^{13}C NMR ($CDCl_3$): $\delta = 105-120$ (m, C_8F_{17}), 118.6, 120.1, 132.6 (t, $J = 6$ Hz), 134.7 (t, $J = 6$ Hz), 164.1, 195.9. − ^{19}F NMR ($CDCl_3$): $\delta = -81.1$ (t, $J = 9.5$ Hz, 3 F), −111.2 (t, $J = 12.5$ Hz, 2 F), −121.8 (m, 4 F), −122.3 (m, 4 F), −123.0 (br. s, 2 F), −126.4 (br. s, 2 F). − $C_{15}H_5F_{17}O_2$ (540.2): calcd. C 33.35, H 0.93; found: C 33.51, H 0.87.

Salen 1: Aldehyde **5** (540 mg, 1 mmol) was dissolved in hot EtOH (20 mL) under Ar. To the stirred solution was added (*R*,*R*)-1,2-diaminocyclohexane (57 mg, 0.5 mmol). The mixture was heated at reflux for 7 h and then cooled slowly to 0 °C. The title compound **1** precipitated as a yellow solid that was recovered by filtration and washed with EtOH (388 mg, 67%). − M.p. 115−117 °C. − UV/Vis (10^{-4} M, Et_2O): $\lambda = 311$ nm, 253. − $[\alpha]_D^{20} = -84.2$ ($c = 0.5$, Et_2O). − ^{1}H NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 1.43-2.13$ [m, 8 H, c-$C_4H_8(CHN)_2$], 3.25−3.42 [m, 2 H, c-$C_4H_8(CHN)_2$], 6.98 (d, $J = 8.6$ Hz, 2 H, 3-H), 7.35 (d, $J = 2.2$ Hz, 2H, 6-H), 7.42 (dd, $J = 8.7$ Hz, $J = 2.2$ Hz, 2H, 4-H), 8.30 (s, 2 H, ArCH=N), 11.57 (s, 2 H, OH). − ^{13}C NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 23.1$, 32.3, 71.2, 105−120 (m, C_8F_{17}), 118.7, 119.3, 129.7, 134.1, 163.2, 164.9. − $C_{36}H_{20}F_{34}N_2O_2$ (1158.5): calcd. C 37.32, H 1.74, F 55.76, N 2.42; found C 37.38, H 1.65, F 54.98, N 2.52.

Salen 2: Aldehyde **5** (540 mg, 1 mmol) was dissolved in hot EtOH (20 mL) under Ar. To the stirred solution was added (*R*,*R*)-1,2-diphenylethylendiamine (106 mg, 0.5 mmol). The mixture was heated at reflux for 4 h and then cooled slowly to 0 °C. The title compound **2** precipitated as a yellow solid that was recovered by filtration and washed with cold EtOH. (340 mg, 54%). − M.p. 139−141 °C. − UV/Vis (10^{-4} M, Et_2O): $\lambda = 316$ nm, 259. − $[\alpha]_D^{20} = -0.2$ ($c = 0.5$, Et_2O). − ^{1}H NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 4.78$ (s, 2 H, PhCHN), 7.07 (d, $J = 8.7$ Hz, 2 H, 3-H), 7.09−7.28 (m, 10 H, Ph), 7.36 (d, $J = 2.3$ Hz, 2 H, 6-H), 7.46 (dd, $J = 8.7$ Hz, $J = 2.3$ Hz, 2 H, 4-H), 8.31 (s, 2 H, ArCH=N), 13.74 (s, 2 H, OH). − ^{13}C NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 80.5$, 105−120 (m, C_8F_{17}), 118.3, 118.5, 128.1, 128.5, 128.8, 129.4, 131.4, 131.7, 139.3, 165.2, 166.6. − $C_{44}H_{22}F_{34}N_2O_2$ (1256.6): calcd. C 42.06, H 1.76, F 51.40, N 2.23; found C 42.15, H 1.77, F 50.81, N 2.12.

Mn^{III} Complex of Salen 2: Hot EtOH (20 mL) was added to salen **2** (251 mg, 0.2 mmol) in a two-neck flask equipped with a reflux condenser and a funnel for the addition of solids. The mixture was heated to reflux as $Mn(OAc)_2 \cdot 4H_2O$ (98 mg, 0.4 mmol) was added in 10-mg portions. At the end of the addition, the brown mixture was kept under stirring at reflux for 6 h. LiCl (34 mg, 0.8 mmol) was added, and reflux was continued for 1 h before the mixture was allowed to cool to room temperature. The solvent was removed under vacuum, and the residue, placed in a Soxhlet thimble, was extracted with refluxing CH_2Cl_2 for 24 h. The brown organic solution was concentrated to afford the title compound as a brown solid (189 mg, 70%). − UV/Vis (10^{-4} M, $CFCl_2CF_2Cl$): $\lambda = 391$ nm, 307. − $[\alpha]_D^{20} = +30$ ($c = 0.01$, $CFCl_2CF_2Cl$). − $C_{44}H_{20}ClF_{34}MnN_2O_2$ (1345.0): calcd. C 39.29, H 1.50, N 2.08; found C 39.16, H 1.62, N 1.95.

Diiodoester 9: To a mixture of 3,5-diiodosalicylic acid (390 mg, 1 mmol) and K_2CO_3 (700 mg, 5 mmol) in acetone (10 mL) was added dimethyl sulfate (0.2 mL, 2.1 mmol). The mixture was heated to reflux for 6 h. H_2O (2 mL) was added, and the mixture was stirred for 1 h; then the solvent was evaporated under vacuum, and the residue was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried with $MgSO_4$. Evaporation of the solvent afforded the title compound **7** as a white solid (401 mg, 96%). − M.p. 205 °C. − ^{1}H NMR ($CDCl_3$): $\delta = 3.86$ (s, 3 H, OCH_3), 3.91 (s, 3 H, $COOCH_3$), 8.05 (d, $J = 2.2$ Hz, 1 H, 4-H), 8.23 (d, $J = 2.2$ Hz, 1 H, 6-H). − ^{13}C NMR ($CDCl_3$): $\delta = 52.7$, 62.3, 87.7, 95.4, 126.9, 140.3, 150.6, 159.2, 164.0. − $C_9H_8I_2O_3$ (417.9): calcd. C 25.86, H 1.93; found C 25.79, H 1.91.

Perfluoroalkyl Ester 10: A few crystals of iodine were added under stirring to a suspension of copper bronze (3.18 g, 50 mmol) in acetone (20 mL). After 30 min, the liquid phase was separated and the copper washed first with HCl/acetone (2:3, v/v), then acetone. The solid was filtered and dried in vacuo for 2 h. The activated copper (636 mg, 10 mmol) was added to a solution of methyl benzoate **9** (418 mg, 1 mmol) in dry DMF (8 mL) in a Schlenk vessel. The suspension was warmed under stirring to 120 °C and purged with

N_2. $C_8F_{17}I$ (0.8 mL, 3 mmol) was added dropwise to the stirred suspension over 10 min. After 5 h, the suspension was cooled to room temperature. Water (20 mL) and Et_2O (50 mL) were added, and the suspension stirred for 30 min. The solid was removed by filtration using a Büchner funnel and washed with Et_2O (3 × 15 mL). The aqueous phase was extracted with Et_2O (20 mL). The combined ether layers were washed with brine (30 mL) and dried with $MgSO_4$. The solvent was evaporated and the residue purified by column chromatography (light petroleum ether/Et_2O, 7:3) to afford the title compound as a white solid (682 mg, 68%). − M.p. 47−48°C. − ^1H NMR ($CDCl_3$): $\delta = 3.95$ (s, 3 H, OCH_3), 4.05 (s, 3 H, $COOCH_3$), 7.88 (d, $J = 2.3$ Hz, 1 H, 4-H), 8.22 (d, $J = 2.3$ Hz, 1 H, 6-H). − ^{13}C NMR ($CDCl_3$): $\delta = 53.0$, 64.3, 105−120 (m, C_8F_{17}), 124.0 (t, $J = 22$ Hz), 124.5 (t, $J = 23$ Hz), 126.3, 131.3, 134.7, 162.6, 164.5. − ^{19}F NMR ($CDCl_3$) $\delta = -81.2$ (m, 6 F), −109.7 to −111.4 (m, 4 F), −121.5 to −122.2 (m, 16 F), −123.1 (br. s, 4 F), −126.5 (br. s, 4 F). − $C_{25}H_8F_{34}O_3$ (1002.3): calcd. C 29.26, H 0.80, F 64.45; found C 29.35, H 0.67, F 63.80.

Benzyl Alcohol 11: Under N_2, a solution of perfluoroalkyl ester **7** (1 g, 1 mmol) in Et_2O (10 mL) was addded over 10 min to a suspension of $LiAlH_4$ (38 mg, 1 mmol) in Et_2O (10 mL), cooled to 0°C. The mixture was stirred for 30 min, and then AcOEt (3 mL) was added. When the temperature reached 20°C, 10% H_2SO_4 (3 mL) was cautiously added, followed by Et_2O (10 mL). The upper organic phase was removed, washed with brine (10 mL), and dried with $MgSO_4$. The solvent was evaporated and the residue purified by column chromatography (light petroleum ether/Et_2O, 7:3) to afford **11** as a white solid (685 mg, 70%). − M.p. 62°C. − ^1H NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 2.01$ (t, $J = 5.7$ Hz, 1 H, CH_2OH), 3.90 (s, 3 H), 4.87 (d, $J = 5.7$ Hz, 2 H, CH_2OH), 7.67 (d, $J = 1.8$ Hz, 1 H, 4-H), 7.99 (d, $J = 1.8$ Hz, 1 H, 6-H). − ^{13}C NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 59.4$, 63.7, 105−120 (m, C_8F_{17}), 123.1 (t, $J = 25$ Hz), 125.2 (t, J = 25 Hz), 127.3, 131.6, 137.4, 159.8. − $C_{24}H_8F_{34}O_2$ (974.3): calcd. C 29.59, H 0.83; found C 29.67, H 0.92.

Methoxybenzaldehyde 12: A solution of benzylic alcohol **11** (487 mg, 0.5 mmol) in benzotrifluoride (2 mL) was transferred to a two-neck flask, containing KBr (6 mg, 0.05 mmol) dissolved in H_2O (0.15 mL). To the two-phase mixture, cooled to 5°C, was added a solution of 2,2,6,6-tetramethylpiperidinyloxy radical (TEMPO) in benzotrifluoride (1 mL, 10^{-2} M). Aqueous NaOCl (2 mL, 0.36 M), saturated with $NaHCO_3$, was then added dropwise under vigorous stirring, while the temperature of the reaction mixture was maintained between 0 and 5°C. After further 15 min, the two liquid layers were separated. The aqueous layer was extracted with Et_2O (10 mL). The combined organic layers were washed with brine (5 mL) and dried with $MgSO_4$. The solvent was evaporated, and the residue purified by column chromatography (light petroleum ether/Et_2O, 7:3) to afford the title compound **12** as a white solid (413 mg, 80%). − M.p. 52°C. − ^1H NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 4.07$ (s, 3 H, OCH_3), 7.96 (d, $J = 2.2$ Hz, 1 H, 4-H), 8.31 (d, $J = 2.2$ Hz, 1 H, 6-H), 10.38 (s, 1 H). − ^{13}C NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 67.4$, 105−120 (m, C_8F_{17}), 124.9 (t, $J = 24$ Hz), 125.8 (t, $J = 26$ Hz), 131.2, 132.7, 133.0, 164.9, 186.7. − $C_{24}H_6F_{34}O_2$ (972.2): calcd. C 29.65, H 0.62; found C 29.71, H 0.75.

Salicylaldehyde 8: Aldehyde **12** (972 mg, 1 mmol) was dissolved in a mixture of benzotrifluoride (2 mL) and CH_2Cl_2 (2 mL). To this solution, cooled to −78°C under N_2, a solution of BBr_3 in CH_2Cl_2 (2 mL, 1 M) was added, and the reaction mixture was allowed to warm to room temperature over 4 h. The mixture was poured into ice (5 g) and allowed to warm to room temperature. Solid $NaHCO_3$ was slowly added under stirring until the pH value of the aqueous layer was neutral. The mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (5 mL) and dried with $MgSO_4$. The solvent was evaporated, and the residue purified by column chromatography (light petroleum ether/Et_2O, 7:3) to afford the title compound **8** as a white solid (795 mg, 83%). − M.p. 80°C. − ^1H NMR ($CDCl_3$): $\delta = 7.93$ (d, $J = 2.1$ Hz, 1 H, 4-H), 8.02 (d, $J = 2.1$ Hz, 1 H, 6-H), 10.02 (s, 1 H, CHO), 12.23 (s, 1 H, OH). − ^{13}C NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 105-120$ (m, C_8F_{17}), 121.6, 134.5, 136.5, 163.1, 195.9. − $C_{23}H_4F_{34}O_2$ (958.2): calcd. C 28.83, H 0.42; found C 28.63, H 0.45.

Salen 3: Salicylaldehyde **8** (1.92 g, 2 mmol) and (*R*,*R*)-1,2-diaminocyclohexane (114 mg, 1 mmol) were condensed according to the procedure described for the synthesis of salen **2**. The title compound **3** was recovered as a pale yellow solid that was recrystallyzed from EtOH (1.49 g, 75%). − M.p. 109°C. − UV/Vis (10^{-4} M, Et_2O): $\lambda = 400$ nm, 311, 253. − $[\alpha]_D^{20} = -105.2$ ($c = 0.5$, Et_2O). − ^1H NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 1.68-2.16$ [m, 8 H, c-$C_4H_8(CHN)_2$], 3.37−3.48 [m, 2 H, c-$C_4H_8(CHN)_2$], 7.47 (d, $J = 2.1$ Hz, 2 H), 7.65 (d, $J = 2.1$ Hz, 2 H), 8.29 (s, 2 H, ArCH=N), 13.45 (br. s, 2 H, OH). − ^{13}C NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 23.9$, 32.3, 71.5, 105−120 (m, C_8F_{17}), 118.6, 131.1, 134.2, 164.4, 164.6. − $C_{52}H_{18}F_{68}N_2O_2$ (1994.6): calcd. C 31.31, H 0.91, F 64.77, N 1.40; found C 31.02, H 0.99, F 64.15, N 1.29.

Salen 4: Salicylaldehyde **8** (958 mg, 1 mmol) and (*R*,*R*)-1,2-diphenylethylendiamine (106 mg, 0.5 mmol) were condensed according to the procedure described for the synthesis of salen **2**. The title compound **4** was recovered as a pale yellow solid that was recrystallyzed from EtOH (858 mg, 82%). − M.p. 49°C. − UV/Vis (10^{-4} M, Et_2O): $\lambda = 399$ nm, 314, 251. − $[\alpha]_D^{20} = -8.8$ ($c = 0.5$, Et_2O). − ^1H NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 4.82$ (s, 2 H, PhCHN), 7.05−7.27 (m, 10 H, Ph), 7.52 (d, $J = 2.1$ Hz, 2 H), 7.65 (d, $J = 2.1$ Hz, 2 H), 8.44 (s, 2 H, ArCH=N); 13.24 (br. s, 2 H, OH). − ^{13}C NMR ($CDCl_3$ + $CFCl_2CF_2Cl$): $\delta = 79.3$, 105−120 (m, C_8F_{17}), 117.4, 118.6, 119.1, 127.8, 128.5, 128.9, 131.0, 134.2, 137.1, 163.4, 165.3. − $C_{60}H_{20}F_{68}N_2O_2$ (2092.7): calcd. C 34.44, H 0.96, F 61.73, N 1.34; found C 34.58, H 0.90, F 61.36, N 1.38.

Mn^{III} Complex of Salen 3: Hot EtOH (20 mL) was added to salen **3** (399 mg, 0.2 mmol) in a two-neck flask, equipped with a reflux condenser and a funnel for the addition of solids. The mixture was heated to reflux as $Mn(OAc)_2 \cdot 4H_2O$ (98 mg, 0.4 mmol) was added in 10-mg portions. At the end of the addition, the brown mixture was kept under stirring at reflux for 1 h. LiCl (34 mg, 0.8 mmol) was added, and reflux was continued for 1 h before the mixture was cooled to 0°C. A brown, viscous oil separated on the bottom of the flask. The mixture was extracted with *n*-perfluorooctane (3 × 10 mL), and the combined perfluorocarbon layers were washed with H_2O (10 mL) and EtOH (10 mL). The fluorous phase was dried with $MgSO_4$ and concentrated to dryness to afford the title compound as a brown solid (408 mg, 98%). − UV/Vis (8×10^{-5} M, $CFCl_2CF_2Cl$): $\lambda = 465$ nm, 385, 335. − $[\alpha]_D^{20} = -780$ ($c = 0.01$, $CFCl_2CF_2Cl$). − $C_{52}H_{16}ClF_{68}MnN_2O_2$ (2082.8): calcd. C 29.99, H 0.77, N 1.35; found C 29.58, H 0.87, N 1.31.

Mn^{III} Complex of Salen 4: The title compound was obtained as a brown solid according to the procedure described for the Mn^{III} complex of salen **3** (423 mg, 97%). − UV/Vis (8×10^{-5} M, $CFCl_2CF_2Cl$): $\lambda = 480$ nm, 385, 330. − $[\alpha]_D^{20} = +90$ ($c = 0.01$, $CFCl_2CF_2Cl$). − $C_{60}H_{18}ClF_{68}MnN_2O_2$ (2180.9): calcd. C 33.05, H 0.83, N 1.28; found C 32.92, H, 0.91, N 1.16.

General Procedure for the Aerobic Epoxidation of Alkenes under Two-Phase Conditions: Reactions were carried out in the dark in a

20-mL Schlenk vessel connected to a gas burette, charged with 250 mL of O_2. The Schlenk vessel was placed in a thermoregulated bath maintained at 20 ± 0.2°C. After equilibration, it was charged with (i) 3 mL of a CH_2Cl_2 solution of the substrate (0.33 M) containing *N*-hexylimidazole (0.033 M) and the internal standard for gas chromatography (tetradecane or *o*-dichlorobenzene, 0.05 M) and (ii) 3 mL of a D-100 solution of the catalyst (0.005 M). The two-phase mixture was magnetically stirred at 1300 ± 50 rpm in order to ensure the best contact between the organic and the fluorous phase. Pivalaldehyde (0.1 mL, 3 mmol) was added to the mixture over 20 min. Samples of the organic phase (5 μl, upper layer) were taken at 1-h intevals and analyzed by GC. When the alkene was completely oxidized, or when its concentration did not change any more, 1 mL of CH_2Cl_2 was added to the mixture, and stirring was stopped after 5 min. The brown fluorous layer was separated, washed with CH_2Cl_2 (2 × 1 mL) and was ready for the use in further runs. The combined organic solutions were washed with 5% aqueous $NaHCO_3$ (2 × 1 mL) and brine (1 × 1 mL), and dried ($MgSO_4$). After evaporation of the solvent, the crude epoxide was purified by column chromatography on neutral alumina. The enantiomeric excess was determined by capillary GC (see general remarks) or by ^{1}H-NMR spectroscopy in the presence of the chiral shift reagent Eu(hfc)$_3$ (*trans*-β-methylstyrene epoxide and *trans*-stilbene epoxide).

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