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Fluorous biphasic oxidation of sulfides catalysed by (salen)manganese(III) complexes

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Dedicated to Professor Renato Ugo on the occasion of his 65th birthday

Abstract

Quadridentate Schiff base ligands derived from 1,2-diamines and fluorous derivatives of salicylaldehyde were prepared and the corresponding manganese(III) complexes were tested as catalysts in the selective oxidation of alkyl aryl sulfides with PhIO. Complexes bearing two fluorinated ponytails were soluble in standard organic solvents and were used under classical homogeneous conditions, whereas heavily fluorinated complexes could be used in a CH_3CN/perfluorooctane biphasic system. In both cases, sulfoxides were obtained as the main products, together with variable amounts of sulfones ($\leq$10%), depending on the nature of the substrate and the catalyst. When reactions were carried out under fluorous biphasic (FB) conditions, the selectivity for sulfoxides was improved and the catalyst could be easily recovered by simple phase separation and reused up to four times. Despite their good chemoselectivity, catalytic efficiency and recyclability, chiral fluorous (salen)manganese(III) complexes showed low enantioselectivities in preliminary experiments run under fluorous biphasic conditions.

Keywords: Biphasic catalysis; Fluorinated compounds; Manganese; Schiff bases; Sulfoxides

1. Introduction

The selective oxidation of organic sulfides to sulfoxides or sulfones has been thoroughly investigated for many years and the use of several oxidizing agents in connection with classic catalytic as well as enzymatic systems have been proposed [1,2]. A promising development in this field is represented by the introduction of fluorous biphasic (FB) catalytic systems based on the selective solubilisation of suitable perfluoroalkylated organometallic complexes in perfluorocarbons [3]. This approach is currently attracting considerable interest, in view of some potential advantages over classical homogeneous catalytic systems, in particular the easy recovery and recycling of the perfluorinated organometallic complexes by simple phase separation [4]. The few examples of FB catalytic oxidation of sulfides reported up to now indicate that this and related methodologies offer a viable access to sulfoxides and sulfones. Metal complexes of fluorinated 1,3-diketones proved to be efficient and recoverable catalysts for reactions carried out with molecular oxygen in the presence of a reducing agent such as a branched alkyl aldehyde [5]. Bégué and co-workers discovered the beneficial role played by hexafluoro-2-propanol in the stoichiometric oxidation of sulfides to sulfoxides with aqueous 30% hydrogen peroxide [6]. High yields and complete selectivity for

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sulfoxides were obtained under mild reaction conditions. The same authors also examined the use of solid $Mn(OAc)_3{\cdot}2H_2O$ as a catalyst for the oxidation of sulfides with dioxygen/2,2-dimethypropanal in perfluoro-2-butyltetrahydrofurane, but in this case no particular solvent effect was observed [7]. The positive features of the FB approach were partly hidden by the heterogeneous nature of the catalyst. We have recently reported the FB catalytic oxidation of alkyl aryl sulfides using molecular oxygen and a sacrificial aldehyde as the oxidising system, and the cobalt complexes of perfluoroalkylated tetradentate *N*-ligands (tetraarylporphyrins and phthalocyanines) as homogeneous FB catalysts [8]. Unfortunately, the effective recycling of these catalysts was prevented by their progressive bleaching in this peculiar reaction environment. Nevertheless, good chemoselectivities and catalytic efficiencies were observed, comparable to those attained with nickel complexes of fluorinated 1,3-diketones. It was found in a parallel study that fluorous (salen)manganese(III) complexes can be conveniently employed as recyclable catalysts in the FB epoxidation of alkenes [9]. Since metal complexes of salen ligands share some features with metalloporphyrins with respect to their structure and catalytic activity, it was decided to investigate the potential of fluorous (salen)manganese(III) complexes (Fig. 1) for the FB oxidation of alkyl aryl sulfides.

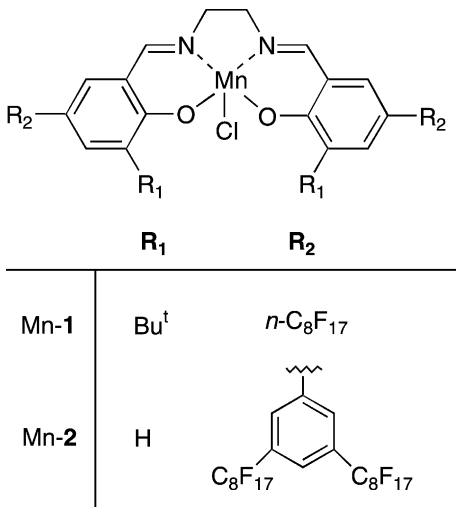


Fig. 1. Achiral (salen)manganese(III) complexes tested as catalysts in the oxidation of alkyl aryl sulfides.

Given the successful development of chiral salen complexes as catalysts for the enantioselective oxidation of sulfides, [10,11] we became also interested in testing similar fluorous complexes (Fig. 2) for FB versions of this reaction. Preliminary results of these studies are reported in the present paper.

2. Experimental

2.1. General remarks

Solvents were purified by standard methods and dried if necessary, except perfluorooctane which was used as received. All commercially available reagents were used as received. Complexes Mn-**3**, Mn-**4**, Mn-**5** and Mn-**6** were prepared according to reported procedures [9]. Partition coefficients of complexes Mn-**2** and Mn-**5** between CH_3CN and *n*-perfluorooctane were measured by UV-Vis spectroscopy at 25 °C [8,9]. Both complexes were confined in *n*-perfluorooctane (partition coefficient > 50). 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). Melting points (uncorrected) were determined with a capillary melting point apparatus Büchi SMP-20. 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 ($\delta = 0$), $CDCl_3$ ($\delta = 77$) and $CFCl_3$ ($\delta = 0$) as internal standard. GC analyses were performed on a Hewlett-Packard 5890 instrument (column: HP-5 5% phenyl methyl siloxane 30 m × 320 μm × 0.25 mm). HPLC analyses were performed on an Agilent 1100 Series instrument (columns: Chiralcel OD, Chiralpak AD). Elemental analysis: Departmental Service of Microanalysis (University of Milano).

2.2. 5-[3,5-Bis(perfluorooctyl)phenyl)]-2-methoxybenzaldehyde ***8***

3-Formyl-4-methoxyphenylboronic acid [12] (1.00 g), 1,3-bis(perfluorooctyl)-5-bromobenzene [9]

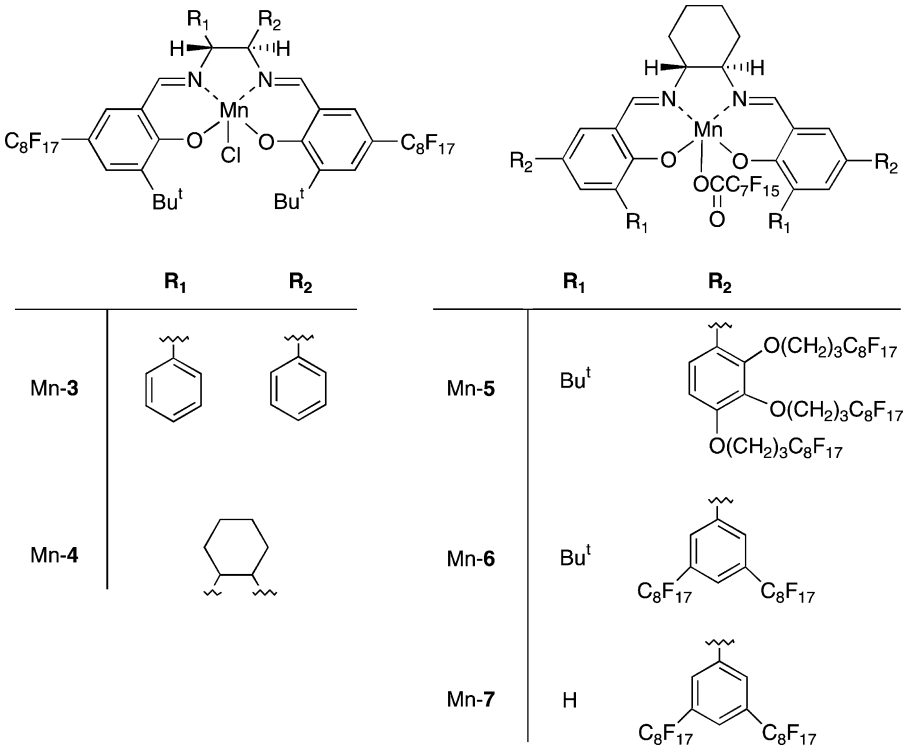


Fig. 2. Chiral (salen)manganese(III) complexes tested as catalysts in the oxidation of alkyl aryl sulfides.

(3.50 g, 3.5 mmol), palladium acetate (0.0094 g, 0.042 mmol), triphenylphosphine (0.018 g, 0.084 mmol) and sodium carbonate (1.04 g, 12.6 mmol) were stirred in degassed propan-1-ol (15 ml). The mixture was heated under stirring to 120 °C and water (1 ml) was added. The reaction was stirred at 120 °C overnight and then cooled, quenched with water and extracted three times with ether. The ether extract was washed with 10% HCl, brine and then dried over magnesium sulphate. The ether was removed to leave the crude product which was purified by CC (silica gel, petroleum ether/ethyl acetate 7/3) to give pure **8** as a white solid (0.76 g, 20%). M.p. 76–77 °C. ^{1}H NMR ($CDCl_3$) $\delta = 4.01$ (s, 3H), 7.15 (d, $J = 8.7$ Hz, 1H), 7.75 (br s, 1H), 7.80 (dd, $J = 8.7$ Hz, $J = 2.5$ Hz, 1H), 7.96 (br s, 2H), 8.08 (d, $J = 2.5$ Hz, 1H), 10.53 (s, 1H). ^{13}C NMR ($CDCl_3$) $\delta = 56.43$, 110.6, 124.4, 125.6, 127.4, 128.9, 131.1, 134.8, 141.9, 162.7, 189.6. ^{19}F NMR ($CDCl_3$) $\delta = -81.3$ (t, $J = 10$ Hz, 6F), −111.4 (t, $J = 14$ Hz, 4F), −121.6 (br s, 4F), −122.3 (m, 12F), −123.2 (br s, 4F), −126.6 (br s, 4F). Calculated C 34.37, H 0.96; found C 34.61, H 0.85.

*2.3. 5-[3,5-Bis(perfluorooctyl)phenyl)]-2-hydroxybenzaldehyde **9***

A sample of **8** (1.28 g, 1.22 mmol) was dissolved in dry dichloromethane (20 ml) and cooled in an ice bath to 0 °C under nitrogen. Boron tribromide (1 M in CH_2Cl_2, 3.66 ml, 3.66 mmol) was added dropwise and the reaction was stirred at 0 °C for 30 min and at room temperature for 2 h. The reaction was quenched with water and extracted three times with ether. The organic phase was washed with saturated sodium bicarbonate solution, brine and dried over magnesium sulphate. The solvent was removed under vacuum to leave the product as a white solid (1.15 g, 90%). M.p. 100–101 °C. ^{1}H NMR ($CDCl_3$) $\delta = 7.17$ (d, $J = 8.6$ Hz, 1H), 7.79 (m, 3H), 7.96

(br s, 2H), 10.04 (s, 1H), 11.15 (s, 1H). ^{13}C ($CDCl_3$) NMR δ = 119.4, 121.3, 124.5, 128.8, 130.4, 131.1, 132.6, 135.9, 141.7, 162.6, 196.7. ^{19}F NMR ($CDCl_3$) $\delta = -81.2$ (t, $J = 10$ Hz, 6F), -111.4 (t, $J = 14$ Hz, 4F), -121.5 (br s, 4F), -122.2 (br s, 12F), -123.1 (br s, 4F), -126.6 (br s, 4F). Calculated C 34.27, H 0.89; found C 34.87, H 1.10.

2.4. Salen ligand **1**

3-*tert*-Butyl-2-hydroxy-5-*n*-perfluorooctylbenzaldehyde [9] (1.51 g, 2.54 mmol) was stirred and refluxed under nitrogen until it dissolved in trifluorotoluene/ethanol (20 ml, 1/1 (v/v)). To this solution was added ethylenediamine (80 μl, 1.27 mmol,) and the solution was stirred and refluxed for 2 h. The solvents were evaporated off and the residue was dissolved in diethyl ether and was washed with water, brine and dried over magnesium sulphate. The solvent was removed under vacuum and the crude product which was purified by CC (silica gel, petroleum ether/ethyl ether 9/1) to give pure **1** as a pale yellow solid (1.29 g, 72%). M.p. 107–108 °C. ^{1}H NMR ($CDCl_3$) $\delta = 1.40$ (s, 18H), 3.98 (s, 4H), 7.31 (d, $J = 2.1$ Hz, 2H), 7.45 (d, $J = 2.1$ Hz, 2H), 8.42 (s, 2H), 14.4 (s, 2H). ^{13}C ($CDCl_3$) NMR δ = 29.4, 35.4, 59.4, 118.4, 128.0, 129.1, 139.1, 163.8, 167.1. ^{19}F NMR ($CDCl_3$) $\delta = -81.2$ (t, $J = 10$ Hz, 6F), -110.2 (t, $J = 14$ Hz, 4F), -121.7 (br s, 4F), -122.1 (br s, 12F), -123.1 (br s, 4F), -126.5 (br s, 4F). UV-Vis (1.8×10^{-5} M, CH_2Cl_2) λ_{max} ($\log \varepsilon$) = 231 nm (5.04), 257 nm (4.56), 317 nm (4.21). Calculated C 36.80, H 2.16, N 2.15; found C 37.10, H 2.20, N 2.11.

2.5. Salen ligand **2**

This compound was prepared analogously to salen **1**, starting from aldehyde **9** and ethylenediamine. However, column chromatography was not required, since salen **2** precipitated out from the reaction mixture as an off white solid which was collected, washed with cold ethanol and dried under vacuum (yield = 74%). M.p. 156–157 °C. ^{1}H NMR ($CDCl_3$, CCl_2FCF_2Cl) $\delta = 4.06$ (s, 4H), 7.10 (d, $J = 12.9$ Hz, 2H), 7.47 (d, $J = 3.3$ Hz, 2H), 7.56 (dd, $J = 12.9$ Hz, $J = 3.3$ Hz, 2H), 7.76 (br s, 2H), 7.92 (br s, 4H), 8.49 (s, 2H). UV-Vis (1×10^{-5} M, CCl_2FCF_2Cl) λ_{max} ($\log \varepsilon$) = 255 nm (4.79), 277 nm (4.55), 331 nm (3.90). Calculated C 33.44, H 0.96, N 1.34; found C 33.64, H 0.87, N 1.41.

2.6. Salen ligand **7**

5-[3,5-Bis(perfluorooctyl)phenyl)]-2-hydroxybenzaldehyde **9** (0.60 g, 0.58 mmol) was stirred and refluxed under nitrogen until it dissolved in trifluorotoluene/ethanol (20 ml, 1/1 (v/v)). To this solution was added (*R*,*R*)-1,2-diaminocyclohexane (0.033 g, 0.29 mmol) and the solution was stirred and refluxed for 2 h. The solvents were evaporated off and the residue was dissolved in diethyl ether and was washed with water, brine and dried over magnesium sulphate. The solvent was removed under vacuum to leave the Salen as an off white solid (0.53 g, 82%). M.p. 79–82 °C. $[\alpha]_D^{20} = -26.0$ (c = 0.1, CCl_2FCF_2Cl). ^{1}H NMR ($CDCl_3$) δ = 1.42–2.02 (m, 8H), 3.35 (m, 2H), 7.02 (d, $J = 12.8$ Hz, 2H), 7.31 (d, $J = 3.3$ Hz, 2H), 7.45 (dd, $J = 12.8$ Hz, $J = 3.3$ Hz, 2H), 7.67 (br s, 2H), 7.78 (br s, 4H), 8.47 (s, 2H). ^{13}C ($CDCl_3$) NMR δ = 24.1, 29.7, 32.8, 72.8, 115.2, 119.0, 123.4, 128.2, 128.7, 130.1, 130.5, 131.0, 142.1, 161.8, 164.7. ^{19}F NMR ($CDCl_3$) $\delta = -81.2$ (t, $J = 10$ Hz, 12F), -111.4 (t, $J = 14$ Hz, 8F), -121.5 (br s, 8F), -122.2 (br s, 24F), -123.2 (br s, 8F), -126.6 (br s, 8F). UV-Vis (1×10^{-5} M, CCl_2FCF_2Cl) λ_{max} ($\log \varepsilon$) = 249 nm (4.81), 275 nm (4.58), 329 nm (3.92). Calculated C 36.42, H 1.34, N 1.33; found C 36.42, H 1.65, N 1.05.

2.7. (Salen)manganese(III) complex Mn-**1**

Salen ligand **1** (1.29 g, 1.06 mmol) was dissolved in refluxing trifluorotoluene/ethanol (20 ml, 1/1 (v/v)) under nitrogen. Manganese(II) acetate tetrahydrate (0.58 g, 2.38 mmol) was added and the reaction was refluxed under nitrogen for 5 h. The reaction was opened to the air and lithium chloride (0.01 g, 2.38 mmol) was added. The reaction was refluxed for another 2 h. The solvents were evaporated off and the residue was recrystallised from EtOH to give a green brown solid (1.11 g, 80%). UV-Vis (6.4×10^{-6} M, Et_2O) λ_{max} ($\log \varepsilon$) = 236 nm (4.70), 402 nm (3.72). Calculated C 33.04, H 0.83, N 1.28; found C 33.54, H 1.25, N 1.59.

2.8. (Salen)manganese(III) complex Mn-**2**

This complex was prepared from the corresponding salen ligand according to the procedure described for Mn-**1**. Recrystallisation of the crude product from trifluorotoluene gave a green brown solid (0.55 g, 60%). UV-Vis (1×10^{-5} M, CCl_2FCF_2Cl) λ_{max} ($\log \varepsilon$) = 294 nm (4.76), 424 nm (4.61), 331 nm (3.90). Calculated C 33.04, H 0.83, N 1.28; found C 33.54, H 1.25, N 1.59.

2.9. (Salen)manganese(III) complex Mn-**7**

Salen ligand **7** (0.39 g, 0.17 mmol) was dissolved in refluxing trifluorotoluene/ethanol (20 ml, 1/1 (v/v)) under nitrogen. Manganese(II) acetate tetrahydrate (0.17 g, 0.68 mmol) was added and the reaction was refluxed under nitrogen for 2 h. A second portion of manganese acetate tetrahydrate (0.17 g, 0.68 mmol) was added and the reaction was refluxed for another 2 h. The reaction was opened to the air and lithium chloride (0.056 g, 1.32 mmol) was added. The reaction was refluxed for another 2 h. The solvents were evaporated off and the residue was dissolved in trifluorotoluene, washed with water, brine and dried over magnesium sulphate. Unreacted starting material was removed by adsorbing the crude complex onto a small amount of silica, placing it in a fritted funnel and eluting with diethyl ether to remove the unreacted salen and then with *n*-perfluorooctane to elute the (salen)manganese(III) chloride complex that was obtained as a green brown solid (0.16 g, 41%). $[\alpha]_D^{20} = -375$ ($c = 0.016$, CCl_2FCF_2Cl). UV-Vis (1.3×10^{-5} M, CCl_2FCF_2Cl) λ_{max} ($\log \varepsilon$) = 294 nm (4.84), 423 nm (3.79). Calculated C34.96, H 1.31, N 1.25; found C 35.4, H 1.57, N 1.22.

To the (salen)manganese(III) chloride complex (0.15 g, 0.07 mmol) dissolved in trifluorotoluene/diethyl ether (20 ml, 1/1 (v/v)), $C_7F_{15}COONH_4$ (0.21 g, 0.5 mmol) was added and the reaction was stirred at room temperature for 48 h. The solvents were evaporated off and the residue dissolved in *n*-perfluorooctane washed with water and dried over magnesium sulphate. The solvent was removed under vacuum to leave a green brown solid (0.13 g, 68%). $[\alpha]_D^{20} = -150$ ($c = 0.027$, CCl_2FCF_2Cl). UV-Vis (1×10^{-5} M, CCl_2FCF_2Cl) λ_{max} ($\log \varepsilon$) = 286 nm (4.77), 351 nm (4.08), 413 nm (3.49). Calculated C 33.40, H 1.10, N 1.05; found C 32.87, H 1.19, N 1.07.

2.10. Oxidation of sulfides under homogeneous conditions: general procedure

In a 10 ml Schlenk tube placed in a thermoregulated bath at 25 °C, 0.2 ml of a 0.5 M solution of alkyl aryl sulfide in CH_3CN containing anisole (0.25 M, internal standard for GC) was added under nitrogen to 1 ml of a 0.001 M solution of the catalyst (Mn-**1**, Mn-**3** or Mn-**4**) in CH_3CN/CH_2Cl_2 1/1 (v/v). PhIO (22 mg, 0.1 mmol) was quickly added under a nitrogen stream. The homogeneous mixture was magnetically stirred at 1300 ± 50 rpm and the progressive disappearance of the substrate was followed by TLC. An amount of 0.3 ml of solution was then diluted with 0.3 ml of CH_2Cl_2, washed with 0.5 ml of saturated aqueous $NaHCO_3$ and dried over Na_2SO_4. Products yields were then determined by GC analysis of this solution. For reactions catalyzed by chiral salen complexes, ee of the sulfoxide was evaluated by HPLC analysis (hexane/*i*-PrOH 9/1 (v/v), 1 ml/min).

2.11. Oxidation of sulfides under fluorous biphasic conditions: general procedure

In a 10 ml Schlenk tube placed in a thermoregulated bath at 25 °C, 1 ml of a 0.1 M solution of alkyl aryl sulfide in CH_3CN containing anisole (0.05 M, internal standard for GC) was added under nitrogen to 1 ml of a 0.001 M solution of the catalyst (Mn-**2**, Mn-**5**, Mn-**6** or Mn-**4**) in *n*-perfluorooctane. PhIO (22 mg, 0.1 mmol) was quickly added under a nitrogen stream. The two-phase mixture was magnetically stirred at 1300 ± 50 rpm and the progressive disappearence of the substrate was followed by TLC of the organic upper layer. When the substrate was consumed, the brownish fluorous layer was separated, washed with CH_3CN (2 × 1 ml) and reused in further runs (see text). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (1 ml), brine (1 ml) and dried (Na_2SO_4). Products yields were determined by GC analysis of the organic solution. For reactions catalyzed by chiral salen complexes, ee of the sulfoxide was evaluated by HPLC analysis (hexane/*i*-PrOH 9/1 (v/v), 1 ml/min).

3. Results and discussion

3.1. Synthesis of the catalysts

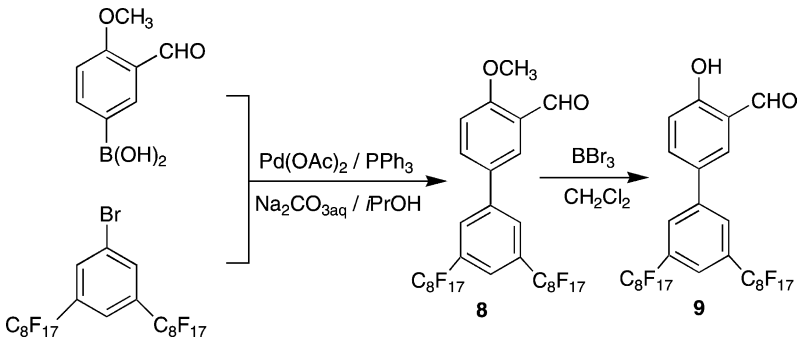
A major advantage of salen ligands over porphyrins and phthalocyanines is their synthetic accessibility. Indeed, salen ligands can be conveniently synthesized by condensation of two equivalents of a salicylaldehyde derivative with the proper 1,2-diamine. As first demonstrated by Ugo and co-workers, this procedure also provides a straightforward access to chiral quadridentate Schiff base ligands [13]. Following this earlier work, an impressive number of achiral and chiral salen ligands has been reported in the literature and the utility of their metal complexes in homogeneous catalysis is now well-recognized. In particular, chiral (salen)manganese(III) complexes are the catalysts of choice for the enantioselective epoxidation of unfunctionalized alkenes with primary oxidants such as aqueous hypochlorite, iodosylarenes and hydrogen peroxide [14,15]. We have recently shown that both "light-fluorous" and "heavy-fluorous" salen ligands are accessible through the general synthetic approach which has been now extended to the synthesis of the new complexes Mn-**1**, Mn-**2** and Mn-**7**.

Aldehyde **9**, the key-intermediate in the synthesis of ligands **2** and **7**, was prepared according to a multistep procedure (Scheme 1) involving the Pd(0)-catalysed cross-coupling reaction of 3-formyl-4-methoxyphenylboronic acid [12] with 1,3-bis(perfluorooctyl)-5-bromobenzene [9].

The fluorous salen ligands **1**, **2** were obtained in good yields (72 and 74%) by reacting 1,2-ethylenediamine with two equivalents of 3-*tert*-butyl-2-hydroxy-5-*n*-perfluorooctylbenzaldehyde [9] and **9**, respectively. Under analogous conditions, aldehyde **9** reacted with (*R*,*R*)-1,2-diaminocyclohexane to yield salen **7** in 82% yield. Reaction of the ligands with an excess of $Mn(OAc)_2{\cdot}4H_2O$ in refluxing trifluorotoulene/ethanol (1/1 (v/v)) under aerobic conditions, followed by anion exchange with LiCl, afforded the corresponding manganese(III) complexes in the form of chlorides. As expected, complex Mn-**1** (Fig. 1) having a relatively low fluorine load (48.6%) was found to be soluble in benzotrifluoride and CCl_2FCF_2Cl, but only sparingly soluble in boiling *n*-perfluorooctane. This "light-fluorous" compound was thus tested as a catalyst for the oxidation of sulfides under classical homogeneous conditions (see further). Complex Mn-**2**, richer in fluorine (57.8%) and bearing four perfluoroalkylated ponytails, was found to be soluble in *n*-perfluorooctane and it could be used as such as a catalyst in FB reactions. On the other hand, the exchange of the chloride counterion for the fluorophilic $C_7F_{15}COO^-$ anion (Scheme 1) enhanced the fluorous affinity of Mn-**7**, as already shown in the case of the related complexes Mn-**5** and Mn-**6** [9], and the carboxylate form of the complex was therefore used in the subsequent catalytic assays.

3.2. Catalytic oxidation of alkyl aryl sulfides

Fluorous (salen)manganese(III) complexes are able to catalyse the epoxidation of alkenes in the presence of molecular oxygen and a sacrificial aldehyde [16]. However, their stability in this reaction environment



Scheme 1. Synthesis of aldehyde 9.

is quite low, thus limiting the effectiveness of their recycling, which is one of the major goals of the FB approach. The use of milder primary oxidants can decrease the incidence of the catalyst decomposition: in this respect, iodosylbenzene (PhIO) was found to be the oxidant of choice for the epoxidation of alkenes. Moreover, the formation of high-valent oxometal species from (salen)metal complexes and PhIO and the mechanism of the oxygen transfer from these species to alkyl aryl sulfides have been investigated in detail [17–20]. For these reasons, it was decided to evaluate the catalytic behaviour of Mn-**1**–Mn-**7** in the oxidation of alkyl aryl sulfides using PhIO as the primary oxidant.

In a first series of experiments, the achiral (salen) manganese(III) complexes Mn-**1** and Mn-**2** were tested (Table 1). Reactions catalysed by the light-fluorous complex Mn-**1** were carried out under homogeneous conditions, in CH_3CN/CH_2Cl_2 1/1 (v/v) as a solvent, whereas standard FB conditions could be applied in the case of the fluorocarbon soluble complex Mn-**2**, which was dissolved in *n*-perfluorooctane and then mixed with a solution of the substrate and PhIO in CH_3CN to give a liquid–liquid biphasic mixture.

Blank experiments carried out both under homogeneous and FB conditions, confirmed that substrate conversions were negligible (<5%) in the absence of the (salen)manganese(III) complexes. Both fluorous complexes effectively catalyse the oxidation of *p*-substituted methyl phenyl sulfides at a substrate/catalyst molar ratio S/C = 100, with good sulfoxide selectivities (≥90%). It is also evident that the use of Mn-**2** under FB conditions yields better results in terms of catalytic activity and selectivity than the use of Mn-**1** (entries **4**, **7**, **10** versus **1**–**3**): after 5 h the FB oxidation of methyl phenyl sulfide and of the electron-poor methyl *p*-nitrophenyl sulfide catalysed by Mn-**2** were complete, while under homogeneous conditions, in the presence of Mn-**1**, conversions of the same substrates reached 70 and 64%, respectively. Although methyl *p*-bromophenyl sulfide was not oxidised completely after 5 h, the FB system afforded 88% conversion against 59% obtained under homogeneous conditions.

Recycling of the fluorous phase containing Mn-**2**, which was recovered by simple decanting from the organic solution containing the products, was also demonstrated (entries **5**, **6**, **8**, **9**, **11**, **12**). Indeed, catalytic activities and selectivities were unaffected after three consecutive recyclings.

These encouraging results stimulated our interest in the potential of fluorous chiral (salen)manganese(III) complexes for enantioselective catalytic sulfide oxidation, a challenging process for which the available catalysts are relatively limited [21]. Among the fluorous

Table 1
Oxidation of aryl methyl sulfides to sulfoxides with PhIO catalysed by fluorous achiral (salen)manganese(III) complexes[a]

Entry	Catalyst	Substrate	*t* (h)	Conversion[b] (%)	Selectivity[b,c] (%)
1	Mn-**1**	$PhSCH_3$	5	70	91
2	Mn-**1**	*p*-$BrPhSCH_3$	5	59	91
3	Mn-**1**	*p*-NO_2PhSCH_3	5	64	88
4	Mn-**2**	$PhSCH_3$	5	95	95
5[d]	1st recovery	$PhSCH_3$	5	100	91
6[d]	3rd recovery	$PhSCH_3$	5	100	92
7	Mn-**2**	*p*-$BrPhSCH_3$	5	87	96
8[d]	1st recovery	*p*-$BrPhSCH_3$	5	88	95
9[d]	3rd recovery	*p*-$BrPhSCH_3$	5	86	95
10	Mn-**2**	*p*-NO_2PhSCH_3	5	100	92
11[d]	1st recovery	*p*-NO_2PhSCH_3	5	100	90
12[d]	3rd recovery	*p*-NO_2PhSCH_3	5	100	90

[a] Reaction conditions: *T*, 25 °C; molar ratio substrate/oxidant/catalyst, 1/1/0.01; entries **1**–**3**, homogeneous conditions (CH_3CN/CH_2Cl_2 1/1); entries **4**–**12**, FB conditions (CH_3CN/*n*-perfluorooctane 1/1). See also Section 2.

[b] Determined by capillary GC (HP-5 5% phenyl methyl siloxane column, internal standard method).

[c] Only sulfones were detected as by-products.

[d] Recycling of the fluorous layer recovered from previous runs.

Table 2
Oxidation of aryl methyl sulfides to sulfoxides catalysed by fluorous chiral (salen)manganese(III) complexes[a]

Entry	Catalyst	Substrate	t (h)	Conversion[b] (%)	Selectivity[b,c] (%)	ee (%)[d]
1	Mn-**3**	*p*-NO_2PhSCH_3	2	61	71	<5
2	Mn-**4**	*p*-NO_2PhSCH_3	2	57	66	<5
3	Mn-**4**[e]	*p*-NO_2PhSCH_3	5	32	81	<5
4	Mn-**4**[f]	*p*-NO_2PhSCH_3	5	63	97	11
5	Mn-**5**	$PhSCH_3$	8	93	>99	<5
6	4th recovery	$PhSCH_3$	8	80	95	<5
7	Mn-**6**	$PhSCH_3$	8	100	>99	<5
8	4th recovery	$PhSCH_3$	8	94	93	<5
9	Mn-**7**	$PhSCH_3$	8	92	>99	<5
10	4th recovery	$PhSCH_3$	8	80	96	<5
11	Mn-**5**	*p*-$BrPhSCH_3$	8	84	96	9
12	Mn-**6**	*p*-$BrPhSCH_3$	8	80	>99	14
13	Mn-**7**	*p*-$BrPhSCH_3$	8	84	>99	10
14	Mn-**5**	*p*-NO_2PhSCH_3	8	89	95	17
15	Mn-**6**	*p*-NO_2PhSCH_3	8	78	88	12
16	Mn-**7**	*p*-NO_2PhSCH_3	8	84	98	<5

[a] Reaction conditions: molar ratio substrate/oxidant/catalyst, 1/1/0.01; T, 25 °C. Entries **1**–**4**, homogeneous conditions; solvent, CH_3CN/CH_2Cl_2 1/1. Entries **5**–**16**, FB system, CH_3CN/*n*-perfluorooctane 1/1. See also Experimental.
[b] Determined by capillary GC (HP-5 5% phenyl methyl siloxane column, internal standard method).
[c] Only sulfones were detected as by-products.
[d] Determined by HPLC ($PhSCH_3$: Chiralcel OD column; *p*-$BrPhSCH_3$ and *p*-NO_2PhSCH_3: Chiralpak AD column).
[e] In the presence of 1 M equivalent of pyridine-*N*-oxide (axial ligand) with respect to the catalyst.
[f] $T = 0$ °C.

chiral (salen)manganese(III) complexes available, the light-fluorous complexes Mn-**3** and Mn-**4** are those closer to the popular Jacobsen's catalysts [14]. They were tested under homogeneous conditions (Table 2) with disappointing results (ee's = 11%). The addition of pyridine *N*-oxide as an axial ligand for manganese did not improve the observed ee's, while decreasing temperature below 25 °C had only a minor positive effect on the enantioselectivity. The presence of electron withdrawing substituents on the 5,5′ positions of the salen ligands was reported to markedly decrease the ee's attainable in the oxidation of sulfides with Jacobsen's catalysts, possibly by enhancing the reactivity of the high valent oxomanganese intermediates [10]. The C_8F_{17} substituents on the 5,5′ positions of Mn-**3** and Mn-**4** could exert an analogous effect, in contrast with what was found in the epoxidation of alkenes where their influence is minor [9].

Another series of reactions was thus carried out using the fluorous (salen)manganese(III) complexes Mn-**5**–Mn-**7** which are selectively soluble in perfluorocarbons and are characterized by the presence of perfluoroalkyl-substituted aryl moieties on the 5,5′ positions. This feature ensures the electronic shielding of the metal site from the electron withdrawing effect of the C_8F_{17} substituents, and offers the opportunity to insert electron donor spacers between the fluorous substituents and the core structure of the ligand in order to further insulate the metal centre, as in Mn-**5**. Complexes Mn-**5**–Mn-**7** showed good catalytic activities, high selectivities and recyclabilities in the FB oxidation of methyl aryl sulfides. The drop of activity observed in the fifth consecutive run (fourth recycling. entries **6**, **8**, **10**) was due to the partial bleaching of the catalysts and not to their leaching as such into the organic phase, as shown by the absence of the characteristic UV-Vis absorptions in the latter. Nevertheless, the enantioselectivities observed in the FB oxidation of the model substrates were still poor, also in the case of Mn-**5** (entries **5**, **11**, **14**). Also the presence or the absence of sterically demanding *tert*-butyl substituents on the key-positions 3,3′ of the ligand do not have significative effects on the enantioselectivities (entries **7**, **12**, **15** versus **9**, **13**, **16**).

These experimental findings do not support the view of a direct influence of the electron withdrawing effect

of the C_8F_{17} substituents on the level of entioselectivity attainable with the chiral fluorous (salen)manganese(III) catalysts here investigated. Another possible explanation resides in the mechanism ruling the oxidation of sulfides catalysed by (salen)manganese (III) complexes. Single electron tranfer from organic sulfide to the oxomanganese complex leading to the formation of sulfur-centered radical cations has been proposed as the rate determining step in the oxygen transfer reaction from oxo(salen)manganese(V) to sulfides. The oxidation reaction thus displays a considerable radical character that could justify losses in selectivity [17]. In this respect, it has been recently suggested that chiral (salen)iron complexes could be more conveniently used for the enantioselective oxidation of sulfides, since in this case the reaction mechanism involves a direct oxygen atom transfer from a high valent oxo(salen)iron species to the sulfide [20].

4. Conclusions

The first results obtained indicate that fluorous (salen)manganese(III) complexes are efficient catalysts in the oxidation of sulfides with PhIO. The use of complexes selectively soluble in perfluorocarbons in reactions run under fluorous biphasic conditions brought about increased selectivities for sulfoxide in comparison to those obtained under homogeneous conditions in the presence of "light-fluorous" catalysts. Moreover, the fluorous layer containing the catalyst could be easily recovered and recycled as such in a new reaction. This confirms the benefits of the fluorous biphasic approach to the oxidation of sulfides. Chiral fluorous (salen)manganese(III) complexes also showed good chemoselectivities and efficiencies. These recyclable chiral complexes could in principle catalyse the asymmetric oxidation of sulfides to sulfoxides, but the enantioselectivities obtained so far were poor, even under fluorous biphasic conditions. The influence of radical pathways in (salen)manganese-catalysed oxidation of sulfides reasonably explains this experimental finding. We are currently investigating the use of other metal complexes of the same fluorous ligands in order to overcome this limitation.

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