Enantioselective epoxidation of olefins with chiral metalloporphyrin catalysts

Eric Rose,* Bruno Andrioletti, Samia Zrig and Mélanie Quelquejeu-Ethève

Received 18th February 2005
First published as an Advance Article on the web 18th April 2005
DOI: 10.1039/b405679p

The intent of this *tutorial review* is to cover the recent progress accomplished in iron and manganese porphyrin-catalyzed enantioselective epoxidation of terminal olefins. The literature is covered up to the beginning of 2005. In the first part of the manuscript, we will present the results obtained with simple catalysts in the early eighties, before describing the pickets and strapped series reported more recently. We will also place a special emphasis on the biomimetic approach that oriented most of this research throughout the years. As a conclusion, we will demonstrate that easy-to-prepare porphyrin catalysts should play an important role in the future and should compete with other well-known, successful systems. Among those, the popular titanium tartrate-catalyzed Sharpless–Katsuki asymmetric epoxidation allows the conversion of allylic alcohols to chiral epoxides with high enantiomeric excesses and high conversion.[1] We will also cite the chiral metallosalen complexes independently reported by Jacobsen and Katsuki in 1990.[2] Using manganese-salens, *cis*-1,2-disubstituted, trisubstituted and some tetrasubstituted olefins are efficiently epoxidized with high enantiomeric excess. However, they suffer from two major drawbacks. They often require low temperature for the epoxidation of monosubstituted (57% ee for styrene at 5 °C; 80% at −78 °C). More importantly, they proceed with low turnover numbers, TON (TON $\approx$ 40 for styrene). More recently, a new approach involving metal-free chiral dioxiranes was also reported.[3] In some cases, they constitute an interesting alternative to the more common systems previously discussed.

Compared to the three pre-cited systems, chiral metalloporphyrins allow the enantioselective epoxidation of unfunctionalized terminal olefins with high enantiomeric excess (>97% ee for styrene) and impressive turnover numbers (>16000) when PhIO is used as oxidant. These results highlight the remarkable potential of porphyrin-based catalysts.

*rose@ccr.jussieu.fr

Eric Rose

Eric Rose was born in Nancy, France. He first worked on steroids in Nancy and then on the total synthesis of alkaloids in Paris. He entered the Scientific National Research Center (CNRS) and obtained his PhD degree in 1975 with Prof. J. Levisalles from the Université Pierre et Marie Curie, Paris. After postdoctoral training in 1976 and 1977 in porphyrin synthesis at the University of Stanford, California, USA with Prof. Jim Collman, he then moved back to Paris working on organometallic chemistry (arene–metal complexes of Cr, Mn and Fe) and on the synthesis of models of hemoproteins (myoglobin, cytochrome P450).

Bruno Andrioletti was born in Troyes-France in 1968. He studied chemistry at the University of Burgundy (Dijon-France) and received his PhD degree in 1997 under the joint supervision of Prof. R. Guilard and Dr. B. Boitrel. His PhD focused on the development of new porphyrinic systems, models of the cytochrome c oxidase active center. Then, he joined Prof. J.L. Sessler's group at the University of Texas at Austin for 2 years' postdoctoral training. There, he studied the chemistry of expanded porphyrins and carried out the development of new anions sensors. In 1999, he was appointed CNRS researcher at the Université Pierre et Marie Curie (Paris-France) in the group headed by Dr. E Rose. His current research interests concern the development of porphyrin and porphyrin-type macrocycles and their use in catalysis and molecular recognition. He is also interested in the preparation of chiral, regioregular oligothiophenes for the preparation of new materials active for NLO applications.

Bruno Andrioletti

1. Introduction

Cytochrome P-450 enzymes are heme-containing monooxygenases that catalyze the incorporation of an oxygen atom from molecular dioxygen into organic substrates with the simultaneous reduction of the other oxygen into water, eqn. (1).[4]

$$RH + O_2 + NAD(P)H + H^+ \xrightarrow[\text{P-450}]{\text{cytochrome}} ROH + H_2O + NAD(P)^+ \quad (1)$$

In 1976, the discovery that the use of exogenous oxygen source—the so-called peroxide shunt—could circumvent the O_2 binding in liver microsomes, gave an incredible impetus to the development of cytochrome P-450 models.[5]

Indeed, this reaction proceeds in the absence of NADPH and O_2. Hence, cytochrome P-450 acts as an oxene transferase in the presence of an oxidant such as iodosobenzene. The main accepted features of cytochrome P-450 cycle are represented in Fig. 1.[6]

When a substrate (RH = alkane, alkene, phenyl ring, amine, thioether) approaches the six-coordinated low-spin iron(III) metal center of the heme in the resting state, the water molecule bound to the distal face of the porphyrin is expelled, affording a high-spin five coordinate Fe^{III}, RH complex. The spin change facilitates the uptake of an electron giving an iron(II) complex that can bind O_2 giving a low spin iron(III)–superoxide complex. A second electron transfer affords a ferric-peroxy species $[Fe^{III}–O–O]^-$ or a ferrous-superoxide species $[Fe^{II}–O–O]$. This second reduction is believed to be the rate-determining step in the cycle. After a proton transfer, a ferric-hydroperoxo intermediate $[Fe^{III}–O–OH]$ is formed and the O–O bond is cleaved liberating a water molecule and an active high-valent iron-oxo intermediate. It is important to note that this pathway can be shortened if an oxidant directly oxidizes the high spin five coordinate iron(III) complex. This so-called "peroxide shunt reaction" directly generates the high-valent iron intermediate. Then, the latter transfers the oxygen atom to the substrate and regenerates the resting state of the enzyme. The authors would like to draw the attention of the reader to the fact that the exact nature of the active species responsible for the oxygen insertion step is still a matter of controversy. However, as a recent review deals with the mechanistic aspects of the active intermediates involved in cytochrome P-450 oxidations, we will not discuss this aspect.[7]

2. General requirements

Groves *et al.* first reported in 1979 a model of the peroxide shunt pathway. They used a TPP–FeCl system (TPP = 5,10,15,20-tetraphenylporphyrin) that catalyzed an oxygen transfer from iodosobenzene PhIO to alkenes and alkanes.[8] Using this strategy, they obtained cyclohexeneoxide from cyclohexene and cyclohexanol from cyclohexane in 55% and 8% yield, respectively (Scheme 1). Unfortunately, the catalyst was found to rapidly degrade.

Additionally, they showed that the use of *cis*- and *trans*-stilbenes, PhIO and TPP–FeCl only afforded the *cis*-stilbene oxide. Later on, Lindsay-Smith *et al.* reported a similar observation[9] that shed light on the influence of the steric constraints on the approach of the olefin toward the active site.[8,10]

They also cared about the stability of the macrocycle toward oxidative degradation and introduced electron-withdrawing groups on the porphyrin ring. Chang *et al.* first described the synthesis of a porphyrin preventing the oxidation of the *meso*-carbons. Using a tetrakis-(pentafluorophenyl)porphyrinato iron(III) chloride **1** (Table 1, entry 1),[11] cyclohexene was converted to the corresponding cyclohexene oxide in 95% yield in the presence of PhIO. Similarly, Traylor *et al*. reported high turnover numbers (TON) for the epoxidation of alkenes using tetrakis-(2′,6′-dichlorophenyl)porphyrin **2a**-FeCl and tetrakis-(pentachlorophenyl)porphyrin **2b**-FeCl (Table 1, entry 2) in the presence of pentafluoroiodosobenzene.[12] As these catalysts

Samia Zrig

Samia Zrig was born in Trappes, France in 1980. She studied Chemistry at the Université René Descartes, Paris V, France and received her Master's degree from Université Pierre et Marie Curie, Paris in 2003. Then, she enrolled on a bilateral PhD program between the Université Pierre et Marie Curie, Paris VI, France and the Katholieke Universiteit, Leuven, Belgium. Her supervisors are Prof. André Persoons (Leuven) and Dr. Eric Rose (Paris). Her current work concerns the synthesis of regioregular, chiral oligothiophenes and the study of their nonlinear optic properties.

Mélanie Quelquejeu-Ethève

Mélanie Quelquejeu-Ethève was born in Lille, France in 1970. She obtained her PhD in 1997 at the Université Pierre et Marie Curie, Paris VI, France under the supervision of E. Rose, CNRS Research Director. Her PhD focused on the study of atropoisomerization of tetrakis-(o-aminophenyl)porphyrin derivatives and on the synthesis of biomimetic heme precursors. She conducted postdoctoral studies first at Stanford University in California with Prof. J.P. Collman (1997), and then at Santa Barbara University with Prof. B. Lipshutz (1998). In September 1999, she joined, as Assistant Professor, Prof. J. M. Valery's group at the Université Pierre et Marie Curie, where she works in the field of carbohydrate and nucleoside chemistry.

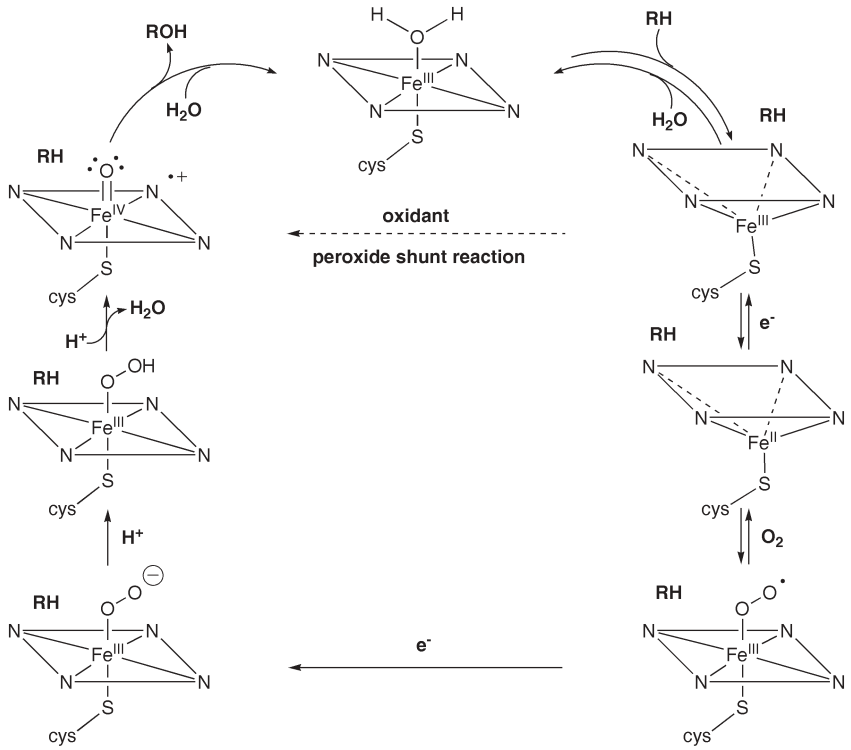
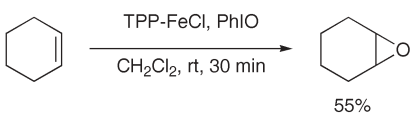


Fig. 1 Cytochrome P-450 reaction cycle.

do not undergo μ-oxo dimer formation and oxidative destruction, they were found to be unusually robust with TON reaching 10000 for the epoxidation of norbornene in 20 min! This review does not intend to give an exhaustive list of results already reported in recent reviews,[13–15] but means to shed light on key data described in the literature.

In natural hemoproteins, the protein chain present in the vicinity of the metal ion controls access to the active site. Thus, if one wants to mimic the natural enzyme, special care has to be dedicated to the design of the superstructure of the model in order to accurately control the access of the substrate to the metal center. Numerous chiral porphyrin structures appeared during the last twenty-five years but only a few were very successful in enantioselective epoxidation catalysis. Among these, we will first describe the single-faced protected porphyrins before moving on to the bis-faced porphyrins. The latter can be divided in two subgroups: the bis-faced picket porphyrins and the bis-faced ansa porphyrins.[16]

Most of the chiral porphyrins described in the literature have been prepared using the classical condensation of pyrrole with an aldehyde in the presence of a catalyst. Thus, chiral porphyrins were obtained either by condensation of pyrrole with chiral aldehydes or by attachment of chiral units to amino- or hydroxy- substituted tetraphenylporphyrins.



Scheme 1 Epoxidation of cyclohexene.

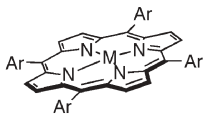
3. Single faced protected porphyrins 3 and 4

Collman *et al.* contributed most significantly to the development of this type of catalyst. In particular, they reported the synthesis of a chiral "picnic basket porphyrin" **3** (Fig. 2).[17] The rigidity of the system was insured by isophthalate amide "loops" that connected two adjacent *meso*-positions of the tetrakis-(2-aminophenyl)porphyrin. In addition, different diether linkers were used to strap the two opposite isophthalate moieties.

First attempts to epoxidize alkenes using **3**-MnCl failed to achieve shape selectivity because epoxidation reactions mostly occurred on the achiral, open face. They solved this problem using a bulky anionic ligand to block this face. Indeed, the use of the binaphthyl-strapped derivative **3** with PhIO in the presence of a large excess of 3,5-di-*tert*-butylphenoxide epoxidized styrene with 13% ee and TON reaching 600. Based on a similar strategy, the same group also described very flexible syntheses of threitol porphyrins (Fig. 3).[18] The simplest one consists in porphyrins that were prepared by reacting a ketal-protected ditosylthreitol with the tetrakis(2′-hydroxyphenyl)porphyrin. This condensation afforded two isomers differing from the relative orientation of the threitol straps up/up **4R$_4$** and up/down (not represented).

Epoxidation of styrene with **4R$_4$**-MnCl occurred in 64% yield and 39% ee with PhIO as oxidant. Ee values reaching 59% were measured for the epoxidation of *cis*-β-methylstyrene. They also prepared strapped versions of porphyrins **4R$_4$**, with a bridge spanning the center of the macrocycle.[18] The catalysts showed a favorable effect upon the addition of bulky nitrogen ligands. Indeed, epoxidation of styrene with the best candidate **4H$_2$-out/out-**MnCl afforded (*R*)-(+)-styrene oxide in 86% yield

Table 1 Structures of *meso*-aryl and -cyclopropyl catalysts



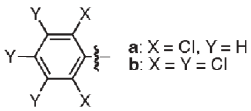
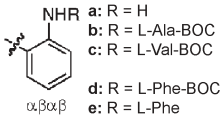
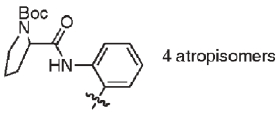
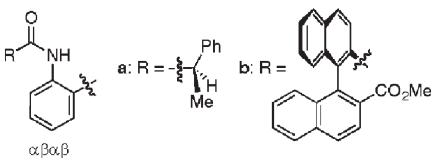
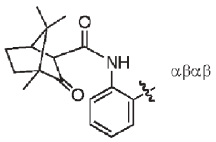
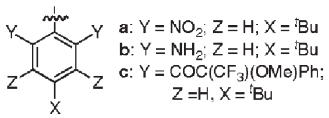
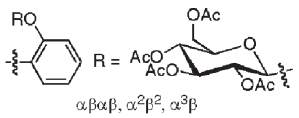
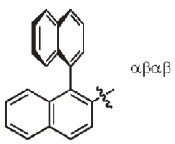
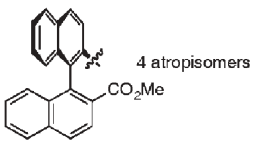
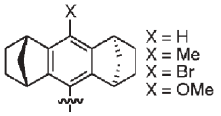
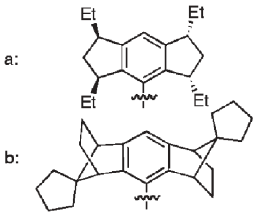
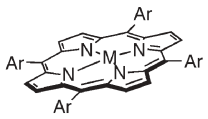
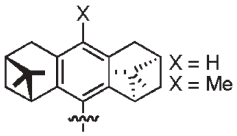
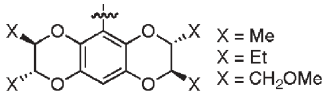
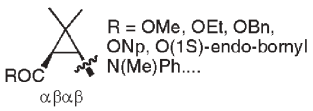
Entry	Catalyst number	M	Ar	Authors	Year
1	**1**	FeCl		Chang *et al.*	1981
2	**2**	FeCl	 **a**: X = Cl, Y = H **b**: X = Y = Cl	Traylor *et al.*	1984
3	**6**	FeCl	 **a:** R = H **b:** R = L-Ala-BOC **c:** R = L-Val-BOC **d:** R = L-Phe-BOC **e:** R = L-Phe αβαβ	Rose *et al.* Mansuy *et al.*	1985 1985
4	**7**	FeCl	 4 atropisomers	Boitrel *et al.*	2003
5	**8**	FeCl	 **a**: R = **b**: R = αβαβ	Groves *et al.*	1983
6	**9**	MnCl	 αβαβ	Paolesse *et al.*	1991
7	**10**	FeCl	 **a**: Y = NO_2; Z = H; X = ^{t}Bu **b**: Y = NH_2; Z = H; X = ^{t}Bu **c**: Y = $COC(CF_3)(OMe)Ph$; Z =H, X = ^{t}Bu	Rose *et al.*	1996
8	**12**	MnCl or FeCl	 αβαβ, $\alpha^2\beta^2$, $\alpha^3\beta$	Momenteau *et al.*	1996
9	**13**	MnCl	 αβαβ	Kodadek *et al.*	1989
10	**14**	FeCl MnCl	 4 atropisomers	Salvadori *et al.*	2000
11	**15X**	MnCl	 X = H X = Me X = Br X = OMe	Halterman *et al.*	1991 1997
12	**16**	MnCl	 **a:** **b:**	Halterman *et al.*	1997

Table 1 Structures of *meso*-aryl and -cyclopropyl catalysts



Entry	Catalyst number	M	Ar	Authors	Year
13	**17X**	MnCl		Kodadek *et al.*	1997
14	**18X**	FeBr		Higushi *et al.*	2004
15	**20**	MnCl		Marchon *et al.*	1999

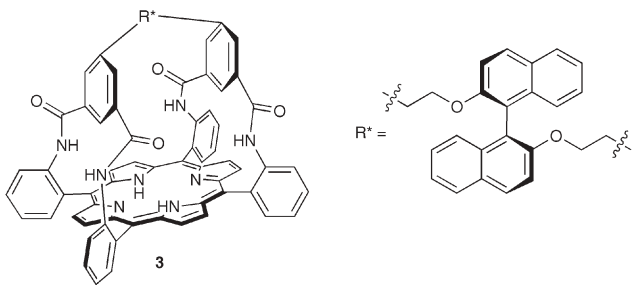


Fig. 2 The "picnic basket" porphyrin **3**.

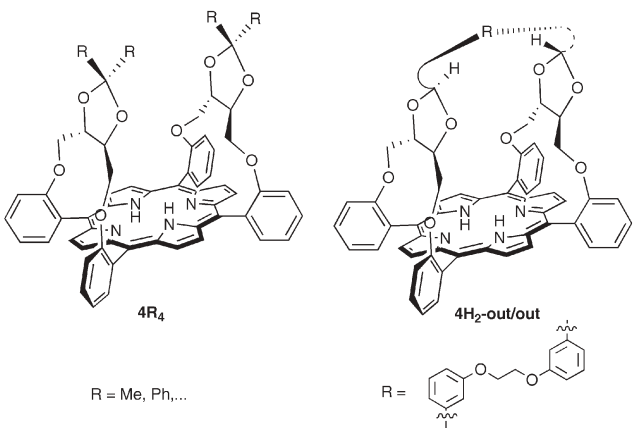


Fig. 3 The threitol porphyrins **4**.

and 69% ee in the presence of 1,5-dicyclohexylimidazole (Fig. 3). Unfortunately, the catalyst became less effective after 100 turnovers, most likely because of threitol bleaching. Using the same conditions, the epoxidation of 1,2-dihydronaphthalene led to the corresponding epoxide in 88% yield.

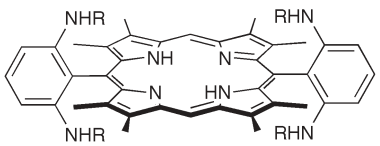
4. Double faced picket porphyrins

4.1 Amidophenyl porphyrins 5–11

In 1984, Rose *et al.* described the synthesis of tetraamino, tetraacetamido and tetrapivalamido porphyrins **5a–c** (Fig. 4).[19,20] In 1985, they reported that condensation of *tert*-butoxycarbonyl and benzyloxycarbonyl chiral amino acids with **5a** yielded picket-fence porphyrins bearing chiral protected pickets **5d–f**. After deprotection, porphyrins **5g–h** were isolated, and strapped using different diacyl chlorides affording the so-called "gyroscope" and bis-ansa porphyrins.[21] Studies concerning the latter will be discussed in section 5.5.

Similarly, the αβαβ-tetrakis-(2′-aminophenyl)porphyrin atropisomer **6a** was condensed with N-protected (L)-Ala, -Val, and -Phe[22] amino acids, affording amino acid picket porphyrins **6b**, **6c**, **6d** (Table 1, entry 3), the last having also been independently prepared.[23] **6d** and **6e** afforded (*S*)-*p*-chlorostyrene-oxide in 12% and 21% ee, respectively, by treating *p*-chlorostyrene with PhIO but they rapidly bleached.[23] On the other hand, the other catalysts[22] have not been tested.

The atropisomers αβαβ, $\alpha^2\beta^2$, $\alpha^3\beta$, α^4 of chiral-L-prolinoyl picket porphyrins **7** were prepared similarly in 2003. The best ee's were measured using α^4-**7**-FeCl (Table 1, entry 4). In this case, 1,2-dihydronaphthalene was epoxidized in 34% ee in the presence of 1-*tert*-butyl-5-phenyl imidazole.[24]



5a: R = H
5b: R = Ac
5c: R = CO^{t}Bu
5d: R = L-Ala-Bz
5e: R = L-Ala-Boc
5f: R = L-Phe-Bz
5g: R = L-Ala
5h: R = L-Phe

Fig. 4 *meso*-5,15-(2′,6′-Diaminophenyl)porphyrin derivatives **5**.

Oxidation of styrene using αβαβ-tetrakis-(2′-(*R*)-hydratropamidophenyl)porphyrin **8a** and αβαβ-tetrakis-(*o*-[(*S*)-2′-carboxymethyl-1,1′-binaphthyl-2-carboxamido]phenyl)porphyrin **8b** iron complexes (Table 1, entry 5) afforded (*R*)-(+) styrene oxide in 31 and 48% ee respectively, in the presence of PhIO with a TON ranging 100. The best ee (51%) was measured for the epoxidation of *p*-chlorostyrene.[10]

αβαβ-Tetrakis-(2′-camphanylamidophenyl)porphyrin **9** was prepared similarly and tested (Table 1, entry 6).[25] **9**-MnCl gave low enantiomeric excesses for the epoxidation of styrene (20%). Paolesse *et al.* concluded that the low enantiomeric excesses could be ascribed to the difficult access of the substrate to the catalytic center.

Knowing that condensation of 2,6-dinitrobenzaldehyde with pyrrole gave insoluble material, octa-nitro and amino-*tert*-butylphenyl porphyrins **10a** and **10b** (Table 1, entry 7) as well as octa-Mosher picket porphyrin **10c** were prepared.[26,27] Accordingly, mixed condensation of 2,6-dinitro-4-*tert*-butylbenzaldehyde, pentafluorobenzaldehyde and pyrrole gave a mixture of soluble di-, tetra- and hexa-nitroporphyrins that afforded di-, tetra- and hexa-Mosher picket porphyrins (Fig. 5).[28] Epoxidation of styrene using **11**-FeCl in the presence of PhIO afforded styrene oxide with very low ee values. However, an interesting trend emerged from this study. The least crowded analogue **11a** gave the "least bad" ee (6%)! Despite the very low selectivities, the authors came to the conclusion that providing more access to the catalytic active site increased the enantioselectivity and facilitated the approach of the olefin.

4.2 The glucosyl porphyrins 12

Attachment of acetylated glucose units to *ortho*-substituted TPP *via* ether linkages afforded catalysts **12** which contain interesting multistereogenic centers. Unfortunately, **12a**-MnCl or **12a**-FeCl (Table 1, entry 8) catalyzed the epoxidation of styrene derivatives with PhIO, NaOCl or $KHSO_5$ with poor enantiomeric excesses. Depending on the nature of the atropisomers (αβαβ,ααββ or αααβ), the best ee's reached only 33%.[29]

4.3 The binaphthyl porphyrins 13 and 14

Using the "chiral wall" catalyst **13**-MnCl (Table 1, entry 9), Kodadek *et al.* reported 2800 turnovers but the ee remained around 20% for the epoxidation of styrene.[30] Studying other substrates, they measured ee values reaching 40% in the case of *cis*-β-methylstyrene.

Salvadori *et al.* prepared the four atropisomers of *meso*-binaphthyl porphyrins **14** as well as the corresponding iron and manganese complexes (Table 1, entry 10).[31] The best results were obtained using $\alpha^2\beta^2$-**14**-FeCl. Indeed, epoxidation of styrene with $\alpha^2\beta^2$-**14**-FeCl afforded (*S*)-(−)-styrene in 57% ee and 47% yield. This interesting result may be ascribed to an easy access of the olefin to the metal iron for this isomer. Stabilizing π–π electronic interactions between the styrene π system and the binaphthyl ring bearing the methoxy group are suggested during the *re* face olefin approach.

4.4 The D_4-symmetric porphyrins 15–17

Good optical yields were obtained with the D_4-chiral porphyrin **15H** described by Halterman *et al.* (Table 1, entry 11).[32] Indeed, *cis*-β-methylstyrene was efficiently epoxidized (Y > 90%) in 76% ee using **15H**-MnCl and an excess of sodium hypochlorite in the presence of 4-*tert*-butylpyridine. Identically, (*S*)-(−)-styrene oxide was obtained in 52% ee in 3 h. Turnovers exceeding 6800 were measured over 24 h. They even reused the recovered complex for subsequent asymmetric epoxidation reactions and obtained identical results. In parallel, complexes **15H**-Ru were recently prepared and studied by Che *et al.*[33] As this review only focuses on iron and manganese complexes, those results will not be discussed here. On the other hand, catalysts **15Br**-MnCl, **15Me**-MnCl, and **15OMe**-MnCl showed modest electronic effects. The authors also demonstrated that (+)-**15H**-MnCl and (−)-**15Br**-MnCl or (−)-**15OMe**-MnCl gave epoxides with opposite configurations. Subsequently, Chang *et al.* demonstrated that the use of multifarious organic bases in manganese porphyrin catalyzed enantioselective *cis*-β-methylstyrene epoxidation is beneficial. For instance, when 4-(*N*,*N*-dimethylamino)pyridine and oxone ($KHSO_5$) were employed **15**H-MnCl epoxidized *cis*-β-methylstyrene in 86% ee in aqueous acetonitrile (*vs.* 43% ee with no base).[34] More recently, new sterically and electronically modified analogues **16a** and **16b** were prepared but they did not appear to be more efficient for epoxidation reactions (Table 1, entry 12).[35]

Kodadek *et al.* also prepared the D_4-symmetric porphyrins **17H** and **17Me** (Table 1, entry 13).[36] Unfortunately, the chiral source synthesis was really tedious. Epoxidation of styrene with **17H**-MnCl afforded (*R*)-(+)-styrene oxide in 70% yield and 70% ee with about 2500 turnovers when LiOCl was used

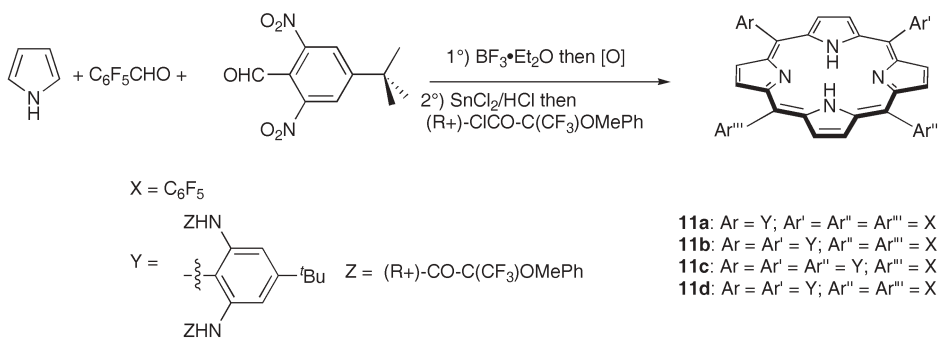


Fig. 5 The "Mosher-picket series" **11**.

as oxidant in the presence of 1,5-dicyclohexylimidazole in a phase transfer system. In parallel, epoxidation of α-methylstyrene gave (1*R*)-α-methylstyrene oxide in 91% yield and 65% ee, with TON reaching 19000.

In 2004, Higushi *et al.* described the efficient preparation of novel D_4-symmetric chiral porphyrins **18X** that utilized commercially available C_2-symmetric diols as the chiral source (Table 1, entry 14).[37] The catalytic activity remained quite moderate with for instance 47% ee and 68% yield for the epoxidation of styrene using **18CH$_2$OMe**-FeBr. Interestingly, contrary to the general tendency of most porphyrin catalysts, they observed higher enantioselectivity for the epoxidation of *trans*-β-methylstyrene.

4.5 The 2,6-dialkoxyphenylporphyrins 19

In 2003, Lindsay-Smith and Reginato reported that mixed condensation of pentafluorobenzaldehyde with (*R*,*R*)-2,6-di-(1-phenylbutoxy)benzaldehyde afforded four porphyrins **19a–d** (Fig. 6).[38] The sterically crowded **19a**-FeCl bearing four dialkoxyphenyl units was a poor epoxidation catalyst (16% ee). The introduction of a *meso*-pentafluorophenyl group increased the reactivity, stability and selectivity of the catalysts. Thus, catalyst **19c**-FeCl converted styrene to (*S*)-(−)-styrene oxide in 99% yield and 23% ee in the presence of PhIO.

4.6 The chiroporphyrins 20

A series of αβαβ-tetraalkylporphyrins **20** named "chiroporphyrins" derived from a chiral cyclopropylaldehyde (biocartol) were described by Marchon *et al.* (Table 1, entry 15). Thus, unlike most of the porphyrin-based catalysts, the chiral residues are borne directly on the *meso* carbon atoms. Interestingly, it was reported that **20**-MnCl gave good ee's (60–86%) for the epoxidation of 1,2-dihydronaphthalene.[39]

5. Double-faced bis-handle or ansa-porphyrins

5.1 The bridled chiroporphyrins 21

Marchon *et al*. also prepared a series of bridled manganese chiroporphyrins **21**-MnCl in which the distortions of the porphyrin ring are controlled by the length of the bridles (n = 8–12, 14, 16, Fig. 7).[40] Interestingly, it appeared that ruffling the porphyrin ring led to higher enantioselectivities. Thus, when n = 8, epoxidation of dihydronaphtalene occurred with 44% ee but reached 64% for the more twisted n = 16 bridled porphyrin.

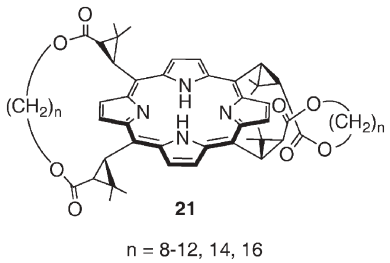


Fig. 7 The bridled chiroporphyrins **21**.

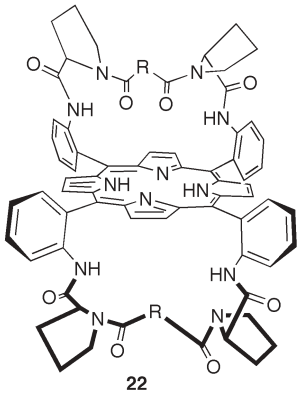


Fig. 8 The prolinoyl porphyrins **22**.

5.2 The prolinoyl porphyrins 22

Other bis-strapped chiral porphyrins **22** derived from L-prolinoyl residues were reported by Boitrel *et al.* Whereas the αβαβ geometry did not induce any good enantioselectivity, the $\alpha^2\beta^2$ atropisomer (Fig. 8) gave ee never exceeding 31% for the epoxidation of 4-chlorostyrene.[41] Furthermore, autooxidation of the handle was observed.

5.3 The "vaulted" porphyrins 23

In 1990, Groves and Viski synthesized porphyrin **23** from αβαβ-tetrakis-(2′-aminophenyl)porphyrin and (*R*)-(+)-2,2′-dimethoxy-1,1′-bis-6-naphthoylchloride in 79% yield (Fig. 9). The iron complex afforded a moderate enantioselectivity (ee = 30% for the styrene) and limited activity (TON = 300).[42]

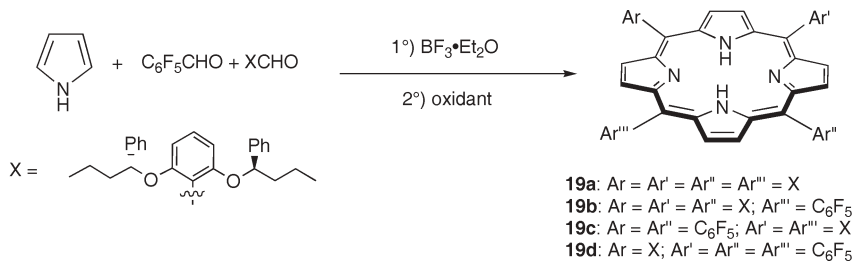


Fig. 6 The 2,6-dialkoxyphenylporphyrins **19**.

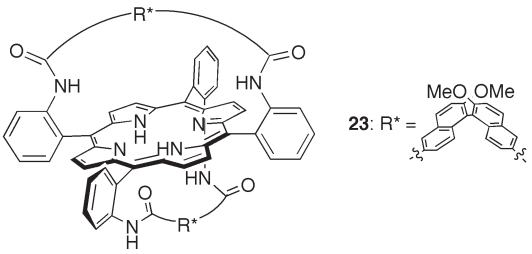


Fig. 9 The "vaulted" porphyrin **23**.

5.4 The "twin-coronet" porphyrins 24 and 25

Naruta *et al.* described the synthesis and the catalytic activity of the "twin coronet" porphyrins **24** and **25** based on an octahydroxyphenylporphyrin scaffold and 3,3′-bis-methylenebinaphthalene (Fig. 10). Thus, the chiral auxiliaries (binaphthyl and bitetralin) are connected to the two faces of the porphyrin *via* ether bonds. **24**-FeCl afforded very high ee for the epoxidation of 2-nitrostyrene (80%) using PhIO as oxidant. Using the same conditions, styrene was converted to styrene oxide with a low 22% ee. In parallel, **25**-FeCl was used and afforded 56% ee for the epoxidation of styrene and very good 89% and 96% ee values for 2-nitro- and 3,5-dinitrostyrene, respectively.[43] Thus the best results were obtained with electron deficient substrates. To explain this result, the mechanism of chiral induction was discussed.

5.5 The "gyroscope" and "basket handle" porphyrins 26–28

The gyroscope porphyrin **26b** and the basket handle porphyrin **27c** with one terephthalic and one pyridinic handle were synthesized to mimic the nitrogen chelation of the proximal nitrogen of imidazole ring in Mb and Hb natural hemoproteins.[16,21] Similarly, the porphyrins **26a, 26c**, **27a, 27b, 27e** and **28** with identical handles were prepared (Fig. 11). The L-phenylalanine catalyst **28**-FeCl was tested for the epoxidation of *p*-chlorostyrene. Using PhIO as oxidant, (*R*)-(+)-*p*-chlorostyrene oxide was isolated in 35% yield and 50% ee.[23] The poor robustness of the catalyst might be ascribed to the proximity of the handle to the metal. Indeed, in the L-Ala series, Boitrel and Rose demonstrated that the handle lies only 3.5Å above the mean plane of the porphyrin.[44]

5.6 The 3,3′-bis-binaphthyl porphyrins 29–31

The $\alpha^2\beta^2$-tetrakis-(2′-aminophenyl)porphyrin atropisomer was used to prepare the catalyst **29** (Fig. 12).[16] Using **29**-FeCl, (*S*)-(−)-styrene oxide and (*S*)-(−)-pentafluorostyrene oxide were obtained in 83% and 88% ee and 95 and 75% yield, respectively.[45] At that time, those results jointly obtained in Stanford and in Paris exceeded the highest values reported by any catalytic systems, including the remarkable Mn(salen) derivatives.[46] Recently, the versatility of our catalyst **29**-FeCl was also tested for other different types of catalyses.[47,48]

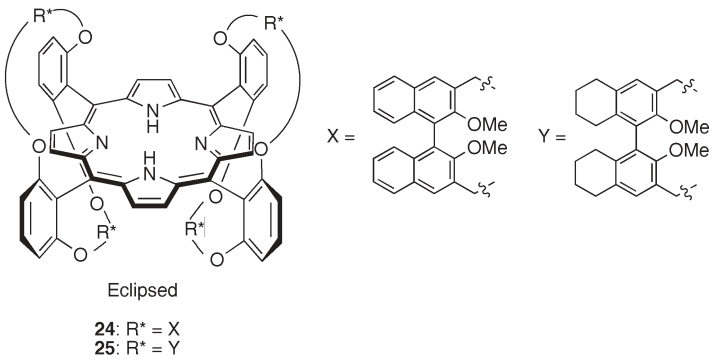
Condensation of the binaphthyl diacyl chloride with the 5,10-pentafluorophenyl-15,20-(2,6-diamino-4-*tert*-butylphenyl)porphyrin[16,26] afforded **31**, a robust and soluble C_2-symmetrical binaphthyl catalyst (Fig. 12). If **31**-FeCl appeared to be less effective than **29**-FeCl for the epoxidation of styrene and pentafluorostyrene (ee = 59% and 85%, respectively) it showed a better enantioselection for the epoxidation of 2-nitrostyrene (70% ee *vs.* 55%). On the other hand, epoxidation of 3-nitrostyrene occurred in the same range (72% ee *vs.* 73%).

We also prepared the so-called "homologated" catalyst **30**-FeCl, hoping that **30**-FeCl would provide more access to the metal center than **29**-FeCl and also would prevent any C–O bond cleavage. This strategy appeared extremely successful as **30**-FeCl epoxidized styrene and afforded (*R*)-(+)-styrene oxide in 96% yield and 97% ee at −10 °C and 90% ee at rt![49] Furthermore, the catalyst appeared really stable as the ee values remained close to 80% after 16000 TON at rt. The authors also demonstrated that catalyst **29**-FeCl and **30**-FeCl gave epoxides with opposite configurations. Therefore, **29**-FeCl and **30**-FeCl constitute an efficient pair of catalysts for the epoxidation of both (*R*) and (*S*) styrene oxides.

6. Conclusion

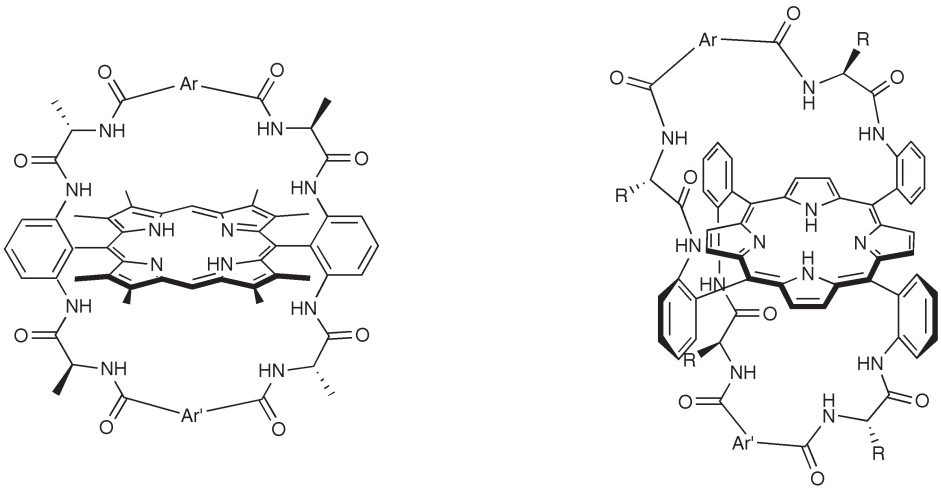
The main results concerning iron or manganese porphyrin-based enantioselective epoxidation of styrene are gathered in Table 2. Analyses of these data point out that the binaphthyl residues linked to the porphyrin ring appear to constitute efficient moieties for inducing good enantioselectivity and turnover frequency in chiral porphyrin-based catalysis.

From the numerous examples reported in this review, it appears that chiral porphyrins can play a key role as effective catalytic systems for olefin epoxidation. In difficult cases like



24: R* = X
25: R* = Y

Fig. 10 The "twin coronet" porphyrins **24** and **25**.



26a: Ar=Ar'=*p*-C_6H_4

26b: Ar=*p*-C_6H_4; Ar'=*m*-C_5H_3N

26c: Ar=Ar'=*m*-C_5H_3N

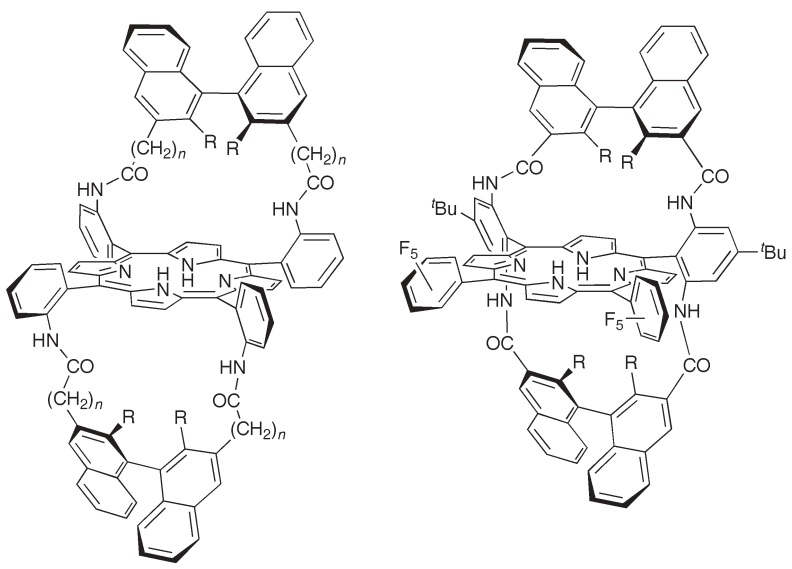
27a: n = 0; **27b**: n = 1 — R = Me; Ar=Ar'=$(CH_2)_n$-*p*-C_6H_4-$(CH_2)_n$

27c: n = 0; **27d**: n = 1 — R = Me; Ar=$(CH_2)_n$-*p*-C_6H_4-$(CH_2)_n$; Ar'=*m*-C_5H_3N

27e: R = Me; Ar=Ar'=*m*-C_5H_3N

28: R = Phe; Ar=Ar'=*p*-C_6H_4

Fig. 11 The "gyroscope" and "basket handle" porphyrins **26–28**.



R = OMe

29: n = 0
30: n = 1

R = OMe

31

Fig. 12 The bis-binaphthyl porphyrins **29–31**.

Table 2 Enantiomeric excesses obtained for the epoxidation of styrene using the different metalloporphyrins listed in this review

Catalyst	Config.	Yield [%]	ee [%][a]
11c-FeCl	nd	nd	1
11b-FeCl	nd	nd	3
16b-MnCl	(*S*)-(−)	nd	5
11a-FeCl	nd	nd	6
19d-FeCl	(*S*)-(−)	95	7
19c-MnCl	(*S*)-(−)	87	7
19b-FeCl	(*S*)-(−)	80	8
αβα$\tilde{\beta}$**14**-MnCl	(*S*)-(−)	37	8
(+)**15H**-FeCl	(*S*)-(−)	70	8
3-MnOAr	(*R*)-(+)	nd	13 (600)
19a-FeCl	(*R*)-(+)	49	16
13-MnCl	nd	nd	20 (2800)
9-MnCl	nd	51	20
(*S*)-**24**-FeCl	(*R*)-(+)	nd	20 (49)
$\tilde{\alpha}^4$ **14**-FeCl	(*S*)-(−)	44	21
(*R*)-**24**-FeCl	(*S*)-(−)	nd	22 (50)
19c-FeCl	(*S*)-(−)	99	23
23-FeCl	(*R*)-(+)	23	30 (300)
8a-FeCl	(*R*)-(+)	65	31
23-MnCl	(*R*)-(+)	21	36
4R$_4$-MnCl	(*R*)-(+)	64	39
$\alpha^3\tilde{\beta}$**14**-FeCl	(*S*)-(−)	40	39
(−)**15Br**-MnCl	(*R*)-(+)	nd	40
(−)**15OMe**-MnCl	(*R*)-(+)	nd	40
18CH$_2$OMe-FeBr	(*S*)-(−)	68	47 (68)
8b-FeCl	(*R*)-(+)	67	48
αβα$\tilde{\beta}$**14**-FeCl	(*S*)-(−)	35	48
(+)**15H**-MnCl	(*S*)-(−)	90	52 (6800)
$\alpha^2\beta^2$-**14**-FeCl	(*S*)-(−)	47	57
(*R*)-**25**-FeCl	(*S*)-(−)	nd	58 (485)
31-FeCl	nd	nd	59
15H-RuO$_2$	(*R*)-(+)	61	65
4H$_2$out/out-MnCl	(*R*)-(+)	86	69 (100)
17H-MnCl	(*R*)-(+)	70	70 (2500)
29-FeCl	(*S*)-(−)	95	83 (10000)
30-FeCl	(*R*)-(+)	96	97 (16000)

[a] TON in parenthesis.

the epoxidation of terminal olefins, they give better ee values than those obtained with other catalytic systems such as the much studied Mn(salen) derivatives. In addition, compared to the classical catalysts, they generally afford higher turnover numbers and frequencies. However, several new challenges still remain. First, it is necessary to obtain equally good results using hydrogen peroxide, *tert*-butylhydroperoxide, or sodium hypochlorite as is obtained with the commonly used PhIO. Secondly, it is important to develop the synthesis of the catalysts using inexpensive and easy-to-prepare ligands. Thirdly, it appears more and more crucial to use computer modeling in order to have an exact idea of the nature of the active site and how the geometry of the porphyrin ring influences the enantioselective differentiation of the prochiral faces. And fourthly, an ultimate achievement would involve the use of molecular dioxygen itself. Inspiration from Nature should continue to guide chemists toward this goal.

Acknowledgements

We thank all the graduate students and postdocs who have at some point been involved in this project. Their names appear in the publications from recent years. The CNRS and the NATO (Grant No. 960485) are also gratefully acknowledged for financial support. ER thanks J. P. Collman for helpful discussions and a fruitful Stanford–Paris collaboration over the years.

Eric Rose,* Bruno Andrioletti, Samia Zrig and Mélanie Quelquejeu-Ethève
UMR CNRS 7611 de Chimie Organique, Laboratoire de Synthèse Organique et Organométallique, Tour 44, 1er Et., BP 181, 4 Place Jussieu, 75252 Paris Cedex 05 E-mail: rose@ccr.jussieu.fr

References

1 K. B. Sharpless, *Angew. Chem. Int. Ed.*, 2002, **41**, 2024–2032.
2 (*a*) W. Zhang, J. L. Loebach, S. R. Wilson and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1990, **112**, 2801–2803; (*b*) R. Irie, K. Noda, Y. Ito, N. Matsumoto and T. Katsuki, *Tetrahedron Lett.*, 1990, **31**, 7345–7348.
3 D. Yang, *Acc. Chem. Res.*, 2004, **37**, 497–505.
4 M. Sono, M. P. Roach, E. D. Coulter and J. H. Dawson, *Chem. Rev.*, 1996, **96**, 2841–2888.
5 F. Lichtenberger, W. Nastainczyk and V. Ullrich, *Biochem. Biophys. Res. Commun.*, 1976, **70**, 939–946.
6 S. Jin, T. M. Makris, T. H. Bryson, S. G. Sligar and J. H. Dawson, *J. Am. Chem. Soc.*, 2003, **125**, 3406–3407.
7 B. Meunier, S. P. de Visser and S. Shaik, *Chem. Soc. Rev.*, 2004, **104**, 3947–3980.
8 J. T. Groves, T. E. Nemo and R. S. Myers, *J. Am. Chem. Soc.*, 1979, **101**, 1032–1033.
9 J. R. Lindsay-Smith and P. R. Sleath, *J. Chem. Soc., Perkin Trans. 2*, 1982, 1009–1015.
10 J. T. Groves and R. S. Myers, *J. Am. Chem. Soc.*, 1983, **105**, 5791–5796.
11 C. K. Chang and F. Ebina, *J. Chem. Soc., Chem. Commun.*, 1981, 778–779.
12 P. S. Traylor, D. Dolphin and T. G. Traylor, *J. Chem. Soc., Chem. Commun.*, 1984, 279–280.
13 J. T. Groves, K. Shalyaev and J. Lee, in *The Porphyrin Handbook*, K. M. Kadish, K. M. Smith and R. Guilard, Eds., 2000, Volume **4**, Ch 27, 2000, 17–39.
14 K. S. Suslick, in *The Porphyrin Handbook*, K. M. Kadish, K. M. Smith and R. Guilard, Eds., 2000, Volume **4**, Ch 28, 41–63.
15 J. C. Marchon and R. Ramasseul, in *The Porphyrin Handbook*, K. M. Kadish, K. M. Smith and R. Guilard, Eds., 2003, Volume **11**, Ch 64, 75–132.
16 E. Rose, M. Quelquejeu, R. P. Pandian, A. Lecas-Nawrocka, A. Vilar, G. Ricart, J. P. Collman, Z. Wang and A. Straumanis, *Polyhedron*, 2000, **19**, 581–586.
17 J. P. Collman, X. Zhang, V. J. Lee, E. S. Uffelman and J. I. Brauman, *Science*, 1993, **261**, 1404–1411.
18 J. P. Collman, V. J. Lee, C. J. Kellen-Yuen, X. Zhang, J. A. Ibers and J. I. Brauman, *J. Am. Chem. Soc.*, 1995, **117**, 692–703.
19 A. Lecas, J. Levisalles, Z. Renko and E. Rose, *Tetrahedron Lett.*, 1984, **25**, 1563–1566.
20 A. Lecas-Nawrocka, J. Levisalles, C. Mariacher, Z. Renko and E. Rose, *Can. J. Chem.*, 1984, **62**, 2054–2058.
21 A. Lecas, Z. Renko and E. Rose, *Tetrahedron Lett.*, 1985, **26**, 1019–1022.
22 B. Boitrel, A. Lecas, Z. Renko and E. Rose, *J. Chem. Soc., Chem. Commun.*, 1985, 1820–1821.
23 D. Mansuy, P. Battioni, J.-P. Renaud and P. Guerin, *J. Chem. Soc., Chem. Commun.*, 1985, 155–156.
24 B. Boitrel and V. Baveux-Chambenoît, *New J. Chem.*, 2003, 942–947.
25 S. Licoccia, M. Paci, P. Tagliatesta, R. Paolesse, S. Antonaroli and T. Boschi, *Magn. Res. Chem.*, 1991, **29**, 1084–1091.
26 E. Rose, A. Kossanyi, M. Quelquejeu, M. Soleilhavoup, F. Duwavran, N. Bernard and A. Lecas, *J. Am. Chem. Soc.*, 1996, **118**, 1567–1568.
27 E. Rose, M. Quelquejeu-Ethève and B. Andrioletti, *J. Porphyrins Phthalocyanines*, 2003, **7**, 375–381.

28 E. Rose, M. Soleilhavoup, L. Christ-Tommasino, G. Moreau, J. P. Collman, M. Quelquejeu and A. Straumanis, *J. Org. Chem.*, 1998, **63**, 2042–2044.
29 S. Vilain-Deshayes, P. Maillard and M. Momenteau, *J. Mol. Cat. A: Chem.*, 1996, **113**, 201–208.
30 S. O'Malley and T. Kodadek, *J. Am. Chem. Soc.*, 1989, **111**, 9116–9117.
31 G. Reginato, L. Di Bari, P. Salvadori and R. Guilard, *Eur. J. Org. Chem.*, 2000, 1165–1171.
32 R. L. Halterman and S.-T. Jan, *J. Org. Chem.*, 1991, **56**, 5253–5254.
33 R. Zhang, W.-Y. Yu, H.-Z Sun, W.-S. Liu and C.-M. Che, *Chem. Eur. J.*, 2002, **8**, 2495–2507.
34 T.-S. Lai, K.-H Ng, H.-Y. Liu, C. K. Chang and L.-L. Yeung, *Synlett*, 2002, **9**, 1475–1478.
35 R. L. Halterman, S.-T Jan, A. H. Abdulwali and D. J. Standlee, *Tetrahedron*, 1997, **53**, 11277–11296.
36 J. F. Barry, L. Campbell, D. W. Smith and T. Kodadek, *Tetrahedron*, 1997, **53**, 7753–7776.
37 H. Nakagawa, Y. Sei, K. Yamaguchi, T. Nagano and T. Higushi, *J. Mol. Cat. A: Chem.*, 2004, **219**, 221–226.
38 J. R. Lindsay-Smith and G. Reginato, *Org. Biomol. Chem.*, 2003, **1**, 2543–2549.
39 C. Pérollier, J. Pécault, R. Ramasseul and J.-C. Marchon, *Inorg. Chem.*, 1999, **38**, 3758–3759.
40 S. Gazeau, J. Pécaut, R. Haddad, J. A. Shelnutt and J.-C. Marchon, *Eur. J. Inorg. Chem.*, 2002, 2956–2960.
41 B. Boitrel, V. Baveux-Chambenoît and P. Richard, *Helv. Chim. Acta*, 2004, **87**, 2447–2464.
42 J. T. Groves and P. Viski, *J. Org. Chem.*, 1990, **55**, 3628–3634.
43 Y. Naruta, in *Metalloporphyrins in Catalytic Oxidations*, R. A. Sheldon, Ed., M. Dekker, New York, 1994, 241–256.
44 P. Richard, E. Rose and B. Boitrel, *Inorg. Chem.*, 1998, **37**, 6532–6534.
45 J. P. Collman, Z. Wang, A. Straumanis, M. Quelquejeu and E. Rose, *J. Am. Chem. Soc.*, 1999, **121**, 460–461.
46 E. N. Jacobsen, in *Catalytic Asymmetric Synthesis*, I. Ojima, Ed., VCH, Weinheim, 1999, p. 59.
47 W. Adams, S. Prikhodovski, K. J. Roschmann and C. R. Saha-Möller, *Tetrahedron Asymmetry*, 2001, **12**, 2677–2681.
48 G. Du, B. Andrioletti, E. Rose and K. Woo, *Organometallics*, 2002, **21**, 4490–4495.
49 E. Rose, Q.-Z. Ren and B. Andrioletti, *Chem. Eur. J.*, 2004, **10**, 224–230.