Supported metalloporphyrin catalysts for alkene epoxidation

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This review is devoted to the recent advances in the preparation of immobilised metalloporphyrins and their use as heterogeneous catalysts for alkene epoxidation. The wide range of supports, nature of attachments, and metalloporphyrins that have been reported is detailed and a comparison is made between the activities of the resulting catalysts in the epoxidation of different alkenes. The important issue of recyclability of the metalloporphyrins is also covered.

Introduction

Oxidation reactions such as epoxidations are essential in organic synthesis. Three classes of catalyst can epoxidise a range of alkenes: titanium(IV) complexes, in the presence of an optically active tartrate ester (Sharpless catalyst) epoxidise allylic alcohols with high yield and selectivity.[1,2] Manganese complexed with salens (Jacobsen catalyst), are highly efficient asymmetric catalysts for the epoxidation of a wide range of alkenes.[3,4] Finally, metalloporphyrins are arguably the least known catalyst family for alkene epoxidation. An iron porphyrin surrounded by proteins is known to be the active site of the enzyme P450 monooxygenase, which is capable of selectively catalysing the oxidation and in particular, the epoxidation of a wide range of substrates.[5] Synthetic iron and manganese porphyrins have also been found to achieve high enantioselectivity in the epoxidation of styrene systems.[6–8]

However the synthesis of metalloporphyrins is challenging and low-yielding. Immobilisation onto a solid support can counteract this problem, enabling the easier recovery and reuse of the catalysts, which makes them cost-effective. Moreover, the support can also reduce the instability of the metalloporphyrins during the epoxidation reaction, *i.e.* self-oxidation leading to the formation of a catalytically-inactive μ-oxo porphyrin dimer in solution. The first investigations of immobilised metalloporphyrins date back to the mid-seventies.[9–13] Reports have since appeared in the eighties about porphyrins successfully attached to organic and inorganic supports *via* coordinative anchorage,[14,15] electrostatic interactions[16–19] and covalent binding,[20–24] and this has been the topic of a chapter in a book.[25] However, only a few successful studies of asymmetric epoxidation have been published. Therefore, most of the studies reported so far involve the immobilisation of non-chiral porphyrins and their use as catalysts in alkene epoxidation. Despite the numerous reports in the last ten years, no review has yet been devoted to this topic. As a result, this review summarises the research in this area during the past decade

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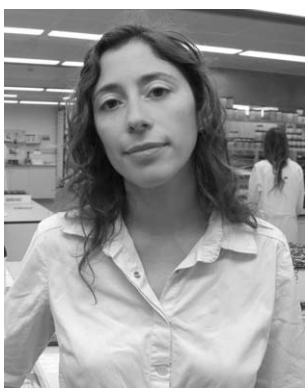
Emilie Brulé



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by comparing the activities of the supported metalloporphyrins depending on the different modes of anchorage. The investigations on their recyclability are also described.

Coordinative binding

Metalloporphyrins can be immobilised *via* coordinative binding between their metal centre and a nitrogenous axial ligand, which is covalently anchored to a support. Pyridine ligands have been anchored onto organic supports to form polyvinylpyridines (PVP) **1** (Fig. 1) and have also been immobilised on inorganic supports, such as silica gel (Si–Py) **2**. Imidazole attached to polystyrene (PS–Im) or silica gel (Si–Im) **3**, have also been utilised.

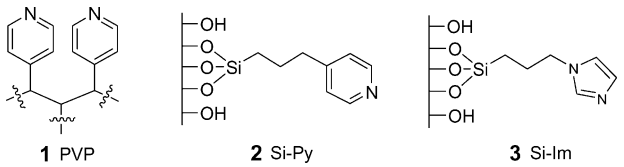

Fig. 1 Immobilised axial ligands.

Several different metalloporphyrins have been anchored to these supports. The well-known symmetric porphyrins **4–6** (Fig. 2) were chosen because of their ease of preparation and because of the presence of Cl atoms on the benzene rings. It was demonstrated that these electron-withdrawing groups decrease the electron density of the metalloporphyrin which helps reduce its self-oxidation and the formation of the inactive μ-oxo-Mn(IV) dimer. Fluorinated porphyrins have also been utilised and in particular, the unsymmetrical iron porphyrin **7**, containing a sulfonate group.[26]

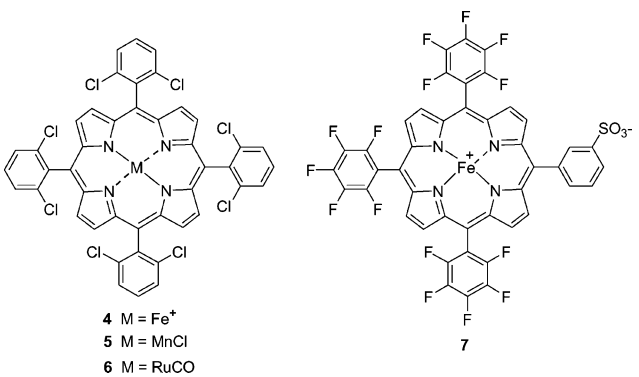

Fig. 2 Metalloporphyrins halogenated on the benzene rings.

The halogens may also be introduced on the pyrrolic β-positions of the metalloporphyrins. Novel complexes **8–10** of this kind (Fig. 3) were prepared by Meunier *et al.*[27]

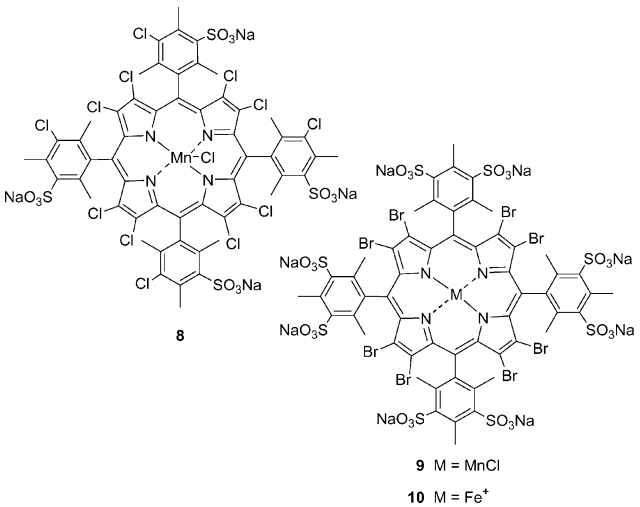

Fig. 3 Metalloporphyrins halogenated on the pyrrolic β-positions.

These immobilised metalloporphyrins have been investigated mainly in the epoxidation of cyclooctene with PhIO as the oxidant. Cyclooctene is usually chosen as the substrate as cyclic alkenes are often epoxidised in high yield. In catalytic systems utilising PhIO, the alkene is added in excess, as PhIO can also be oxidised by the oxo-metalloporphyrin to form $PhIO_2$. The yields of epoxide obtained with these metalloporphyrin catalysts immobilised on various supports are therefore based on PhIO consumed during the reaction (determined by GC) and are summarised in Table 1.

In early studies,[28] the reactions were performed in methanol, which is the only solvent found to completely dissolve PhIO. A higher yield was obtained with the iron porphyrin **4** immobilised on Si–Im than on the organic supports PVP and PS–Im (entries 1 and 2), because of the better compatibility of the silica gel with methanol. Recyclability studies with this system showed that leaching of the metalloporphyrin had occurred due to competitive binding (as axial ligands for the metalloporphyrin) between methanol and the support. As a result, other solvent systems were examined, and dichloromethane and acetonitrile were found to be more suitable, even though PhIO is not completely soluble in these solvents. Using dichloromethane, the formation of the epoxide was nearly quantitative for both manganese and iron porphyrins[29] **4** and **5** (entries 3 and 4). The presence of the support affects the

Table 1 Epoxidation of cyclooctene with coordinatively bound metalloporphyrins

Entry	Porphyrin	Support	Solvent	% Yield[a,b] cyclooctene oxide	Recyclability
1	**4**	Si–Im	CH_3OH	90	Leaching
2	**4**	PS–Im or PVP	CH_3OH	80	Leaching
3	**4**	Si–Im	CH_2Cl_2	99	Good
4	**5**	Si–Im	CH_2Cl_2	100	Good
5	**4**	Si–Py	CH_2Cl_2	90	Good
6	**8**	PVP	CH_2Cl_2	100	No data
7	**9**	PVP	CH_2Cl_2	80	No data

[a] Similar catalyst loadings (*ca.* 1 mol%) were used. [b] Yield based on PhIO consumed after 24 h.

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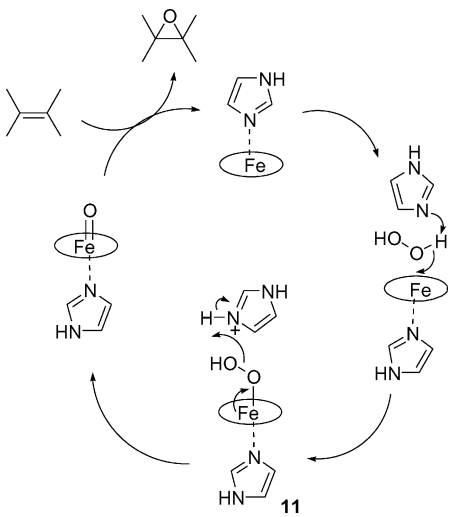
reactivity because of a slower diffusion of the reactants to the metalloporphyrins on solid support compared with the equivalent species in solution.

The iron porphyrin **4** has also been anchored to Si–Py.[30] It has been proposed that an equilibrium between bis- and mono-ligation of pyridine molecules with the iron atom occurs, thus forming pentacoordinated and hexacoordinated complexes. This may explain the stronger binding of iron porphyrins with this support than manganese porphyrins, which only form pentacoordinated complexes by mono-ligation. A 90% yield (entry 5) was achieved with the iron porphyrin **4** anchored to the pyridine-based support (Si–Py), which is slightly lower than with the imidazole-based support Si–Im (entry 3). Styrene and *para*-substituted styrenes (Me, OMe, Cl) were also tested as substrates and high yields (83–90%) were obtained. These are slightly lower than those obtained with homogeneous catalysts. Finally, the epoxidation of *trans*- and *cis*-alkenes was examined. In solution, *cis*-alkenes are more reactive, as the epoxidation usually occurs in a *syn*-stereospecific manner.[31] Indeed, it was observed that *cis*-4-methylpent-2-ene was epoxidised in 97% yield, while *trans*-4-methylpent-2-ene was not epoxidised at all.

Manganese porphyrins **8** and **9** were also bound to PVP **1**. The supported catalyst **8** containing additional halogens on the benzene rings was slightly more efficient (entry 6) than the brominated catalyst **9** (entry 7).

All these catalysts were recovered from the reaction mixture and recycled. They proved to be robust since no loss of activity was observed. This suggests that coordinative binding is strong enough to prevent leaching of the catalyst and that the use of PhIO as the oxidant does not degrade the metalloporphyrin during the catalytic reaction.

The replacement of PhIO by H_2O_2 has been the subject of some interest, since the latter oxidant is commercially available, cheap and uses environmentally friendlier aqueous systems. The catalytic reaction requires the presence of an additional ligand such as imidazole. This co-catalyst helps cleave the O–O of the iron hydroperoxo porphyrin **11** heterolytically (Scheme 1), formed by reaction between the iron porphyrin and H_2O_2,[32] a step required for the formation of the active iron oxo species. The presence of electron-withdrawing groups on the porphyrins also facilitates the heterolytic cleavage of the O–O bond.[33]



Scheme 1 Catalytic mechanism using H_2O_2 as oxidant.

Lower yields are usually achieved using H_2O_2 instead of PhIO. The best system so far involved the iron monosulfonated porphyrin **7** (Fig. 2) immobilised on Si–Im, which formed epoxycyclooctane with a good yield of 50%[26] (compared to only 12% yield with the homogeneous analogue). It was suggested by the authors that the charge of the sulfonate group, in addition to the presence of the polar environment created by the support, further facilitated the heterolytic cleavage. This explanation may be arguable since the sulfonate group is situated far from the metal centre. No recycling studies were reported.

Encapsulation

Encapsulation of a catalyst consists of its physical entrapment in a polymer or inorganic material such as a zeolite. Very recently, Naik *et al.*[34] have micro-encapsulated the tetraphenylporphyrin manganese chloride (TPPMnCl) and the porphyrin manganese chloride **5** (Fig. 2) in a polystyrene-based polymer. The metalloporphyrins were anchored through electronic interactions between the π electrons of the benzene ring of the polymer and the vacant orbitals of the metalloporphyrin. These two immobilised catalysts were investigated in the epoxidation of styrene and *α*-methylstyrene using $NaIO_4$, $KHSO_5$ and NaOCl as oxidants. The highest yields of epoxides were obtained in the presence of $NaIO_4$: styrene oxide was formed in 94–95% yield and *α*-methylstyrene was epoxidised in 92–94% yield with both catalysts and with high TOF. Encapsulated catalyst **5** was found to be more active than the immobilised TPPMnCl using $KHSO_5$ and NaOCl, although yields of epoxides were not higher than 86% for both alkenes. The lower yields obtained with $KHSO_5$ and NaOCl were due to degradation of the catalyst during the reaction. Recycling studies were also carried out with both catalysts and the three oxidants and it was shown that both catalysts could be recycled twice without any significant decrease in the conversion of styrene in the presence of $NaIO_4$.

Hydrogen peroxide has also been used as the oxidant for the epoxidation of the deactivated double bond of an allylic alcohol (3-penten-2-ol) catalysed by the manganese porphyrin **5** (Fig. 2) encapsulated in polydimethylsiloxane (a dense hydrophobic elastomer),[35] but low yields were obtained.

The less commonly used ruthenium porphyrins **6** (Fig. 2) have also been immobilised by encapsulation into the zeolite MCM-41.[36] Ruthenium porphyrins catalyse epoxidation reactions in the presence of dichloropyridine *N*-oxide as oxidant. Epoxycyclooctane was obtained with 91% yield and the immobilised catalyst was also highly active for a wide range of alkenes such as styrene (98% conv.), *cis*-stilbene (76% conv.) and norbornene (81% conv.). It was also shown that the supported ruthenium porphyrin could be recycled three times in the epoxidation of styrene with no significant loss of activity. In conclusion, immobilised ruthenium porphyrins appear to be promising catalysts for use in synthesis.

Electrostatic interactions

Electrostatic interactions between an ionic metalloporphyrin and a counterionic group situated on the support have been shown to be stronger than the coordinative ones.[30] Anionic metalloporphyrins

containing sulfonate groups have been developed and anchored onto silica gel containing ammonium groups ($SiNR_3^+$) **12** (Fig. 4). Anionic silica gel ($SiSO_3^-$) **13** has also been prepared and bound to cationic metalloporphyrins containing pyridinium functions.

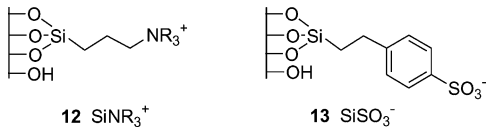


Fig. 4 Ionic silica gels.

The ionic functions situated on the metalloporphyrins may be introduced onto the four aromatic rings to form symmetric metalloporphyrins. Two symmetrical halogenated manganese porphyrins **14** and **15** (Fig. 5) containing sulfonated and pyridinium functions respectively, have been synthesised and anchored onto **12** $SiNR_3^+$ and **13** $SiSO_3^-$.[37]

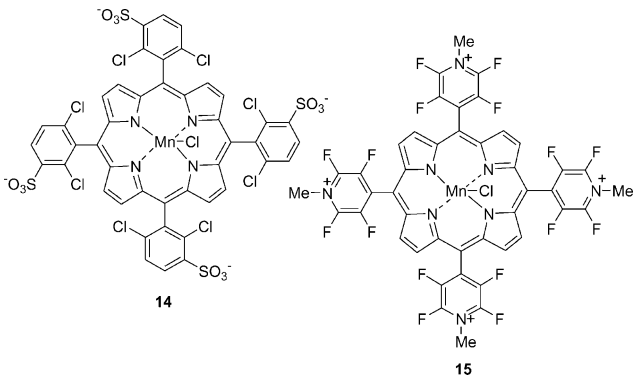


Fig. 5 Symmetrical ionic manganese porphyrins.

Despite their facile preparation, the presence of the four ionic groups is not ideal, as this may result in multiple site anchorages, which lead to cross-linking and reduced mobility of the ligand, thus lowering the yield of epoxide obtained.[38,39] Consequently, mono cationic metalloporphyrins **16–18** (Fig. 6) have also been prepared, albeit in low yields (1–9%), and attached onto **13** $SiSO_3^-$.[40]

These immobilised catalysts were also examined in the epoxidation of cyclooctene with PhIO as oxidant. The yields of epoxide obtained are presented in Table 2.

Compared with coordinatively bound manganese porphyrins (Table 1), the reaction times are considerably shorter. Both immobilised symmetric cationic and anionic manganese porphyrins

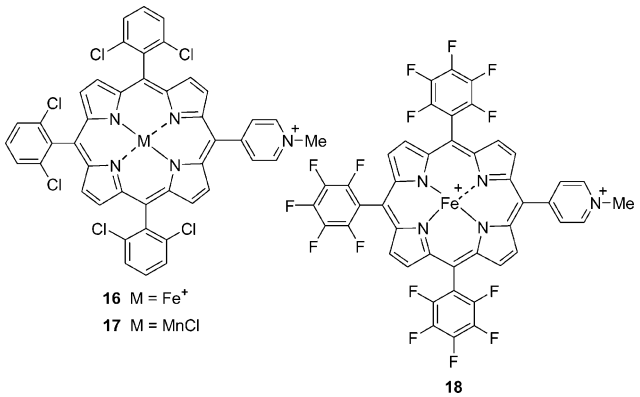


Fig. 6 Halogenated mono-cationic metalloporphyrins.

14 and **15** displayed the same activity with high yields of 91–92% (entries 1 and 2). The epoxidation catalysed by the unsymmetrical mono-cationic iron porphyrin **18** bound to $SiSO_3^-$ *via* a single site, was quantitative (entry 4). This may be due to the reduced steric hindrance imposed by the support. The reuse of these immobilised symmetric and unsymmetric metalloporphyrins was investigated and it was shown that no leaching of the porphyrin from the support occurred. Furthermore, the heterogeneous metalloporphyrins could be reused several times without any significant loss of activity (entries 3 and 6).

To reinforce the strength of the bonding between a metalloporphyrin and its support, the use of a novel type of silica gel **19** (Fig. 7a), which allows the combination of coordinative (with imidazole) and electrostatic (with SO_3^-) interactions, was examined.[41]

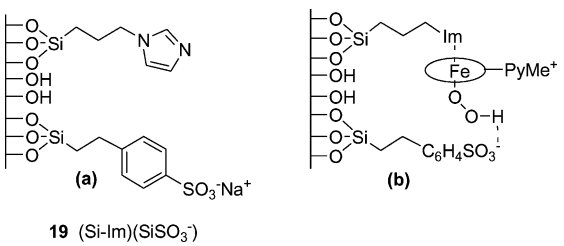


Fig. 7 (a) Multi-functional support; (b) effect of the support with H_2O_2 as oxidant.

Using support **19**, epoxycyclooctane was formed quantitatively in the presence of the unsymmetrical cationic manganese porphyrin **17** (entry 7). The symmetric cationic supported manganese

Table 2 Epoxidation of cyclooctene using metalloporphyrins bound electrostatically

Entry	Metalloporphyrin	Mol% cat.	Support	Solvent	Time (h)	% Yield[a]
1	**14**	0.7	$SiNMe_3^+$	CH_3CN	2	91
2	**15**	0.7	$SiSO_3^-$	CH_2Cl_2	2	92
3	**15**[b]	0.7	$SiSO_3^-$	CH_2Cl_2	2	91
4	**18**	1	$SiSO_3^-$	DCE	3	100
5	**16**	1	$SiSO_3^-$	DCE	3	75
6	**16**[c]	1	$SiSO_3^-$	DCE	3	75
7	**17**	0.9	**19**	DCE	24	100
8	**15**	0.9	**19**	DCE	24	94

[a] Yield based on PhIO consumed. [b] 8th cycle. [c] 2nd cycle.

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porphyrin **15** gave a yield of 94% (entry 8), which is slightly higher compared to that obtained in the presence of $SiSO_3^-$ alone (entry 2). Nevertheless, much slower reaction rates were observed.

Hydrogen peroxide has also been examined as the oxidant with the manganese porphyrins **15** and **17** immobilised on (Si–Im)($SiSO_3^-$) **19**, but low yields were obtained. Nevertheless, 52% yield of epoxycyclooctane was reached using the monocationic iron porphyrin[26] **16** bound to support **19** compared to 11% and 26% yield obtained with porphyrin **16** anchored to Si–Im and $SiSO_3^-$ respectively. It was suggested that the binding between the porphyrin and the support was mostly coordinative, since the porphyrin only contains one pyridinium function, and that the sulfonate group from the support helped in the heterolytic cleavage of the O–O bond of the hydroperoxo species **11** (Fig. 7b) in a similar manner as shown in Scheme 1. As a result, this support presents advantages compared to the simpler supports Si–Im and $SiSO_3^-$.

Few studies have been carried out on the epoxidation of alkenes other than cyclooctene. Cyclohexene was epoxidised in the presence of PhIO using a symmetrical tetrapyridyl manganese porphyrin encapsulated in zeolite MCM-41.[42] The manganese porphyrin was anchored to the support *via* Mn–O coordinative binding, as well as *via* electrostatic interactions between the pyridyl groups of the porphyrin and the anionic species of the zeolite. Epoxycyclohexane was formed in 91% yield (*vs* 46% with the homogeneous analogue). The complex was also recycled several times without any major degradation of activity after five cycles.

In contrast, no epoxycyclohexane was formed using the porphyrin immobilised on a different zeolite, Al–MCM-41.[43] It was suggested that the smaller pore size of the Al–MCM-41 prevents the formation of the transition state. For that reason, the reactivity of encapsulated catalysts may depend on the zeolite utilised.

Tangestaninejad *et al.*[44–49] investigated the epoxidation of a variety of alkenes using sodium periodate as the oxidant. This was catalysed by a symmetrical tetrasulfonated porphyrin **20** immobilised on ionic exchange resins such as IRA-900 or 400 (macroporous and microporous resins, respectively, with quaternary ammonium functionality) and polyvinylpyridine (PVP) (Fig. 8).

The results are presented in Table 3. For the epoxidation of cyclooctene, the three catalysts gave similar yields between 95–96% (entry 1). Good yields between 70–93% were also obtained with cyclohexene (entry 2) with PVP–**20** displaying the highest yield of 93%. Styrene was epoxidised in high yields between 94–95% with both ion exchange resins (entry 3). However the presence of PVP decreased the yield to 75%. IRA-900–**20** exhibited the highest yield (94%) for the epoxidation of *α*-methylstyrene, compared to 89% and 85% with IRA-400 and IRA-900 respectively (entry 4). In contrast, aliphatic linear alkenes, such as 1-octene, displayed lower yields between 40–55% (entry 5). In all cases, the recyclability of the catalysts was claimed to be excellent, although no details of the relevant data were provided.

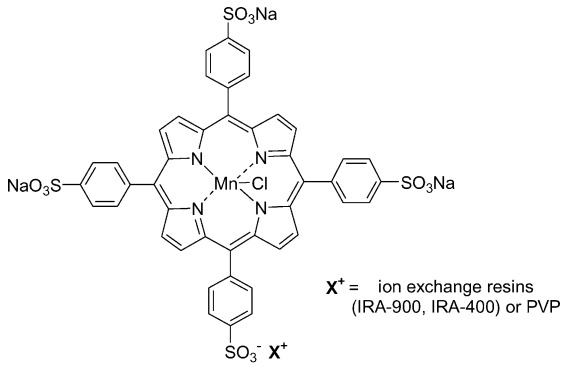

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Fig. 8 Manganese porphyrin bound to cationic exchange resins or polymers.

NaOCl, H_2O_2 and *t*-BuOOH have also been used as oxidants for the epoxidation of styrene with anionic manganese porphyrins immobilised on cationic polymer latexes in aqueous media.[50] Although these supported metalloporphyrins displayed higher reactivities than the homogeneous analogues, only moderate yields were obtained.[51,52]

Covalent anchorage

Inorganic supports

Unsymmetrical metalloporphyrins have been covalently anchored onto inorganic supports such as aminopropyl silica (APS). The aromatic substitution of the *p*-fluorine of monopentaflurophenylporpyhrins[20,53] **21–23** (synthesised in a 4% yield) with APS were used to prepare the various immobilised halogenated metalloporphyrins[54,55] **24–26** (Scheme 2).

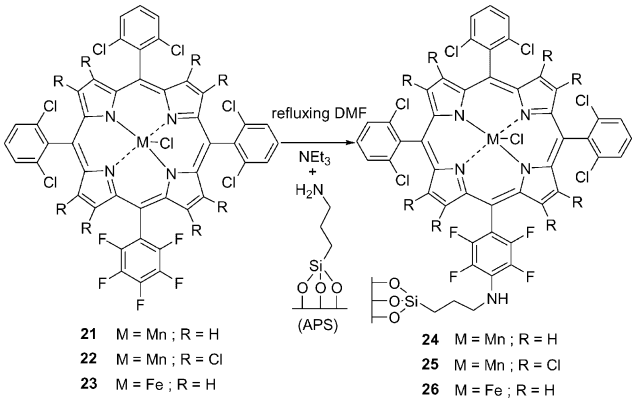
Amide or sulfonamide linkages were also used by other groups. The acid function situated on the benzene ring of an unsymmetrical iron porphyrin was activated through conversion to an acid chloride, which was then reacted with APS to form the supported iron porphyrin[56] **27** (Fig. 9).

A manganese porphyrin functionalised with amino groups was reacted with silica gel containing an acid chloride to form the catalyst **28** (Fig. 9). Similarly, the catalyst **29** was obtained from the reaction between an amine group supported on a type of clay called montmorillonite $\mathbf{K_{10}}$ and a sulfonate functionality on the porphyrin. Symmetrical manganese porphyrins have also been

Table 3 Epoxidation of alkenes catalysed by immobilised anionic porphyrin **20**

Entry	Alkene	% Yield[a] for IRA-900–**20**	% Yield[a] for IRA-400–**20**	% Yield[a%] for PVP–**20**
1	Cyclooctene	95	96	95
2	Cyclohexene	70	82	93
3	Styrene	94	95	75
4	*α*-Methylstyrene	94	89	85
5	1-Octene	55	—	40

[a] Yield based on starting material after 4 h and similar catalyst loadings of 1.4 mol% were used



Scheme 2 Aromatic substitution of *p*-fluorine with aminopropyl silica (APS).

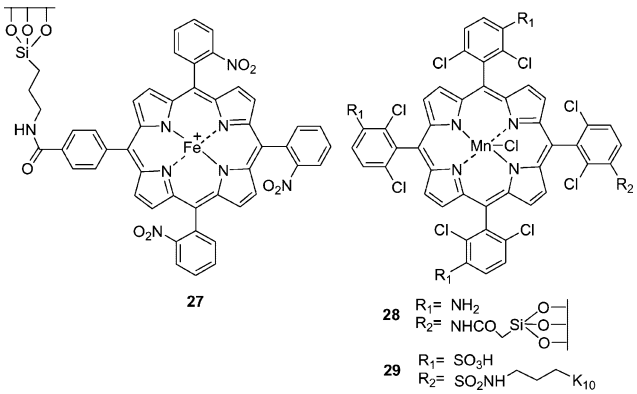


Fig. 9 Covalent binding *via* amide or sulfonamide bond.

used with montmorillonite $\mathbf{K_{10}}$,[57] although in this case the control of single-site binding with the support is not possible.

These immobilised metalloporphyrins were examined in the epoxidation of cyclooctene and cyclohexene using PhIO. The various yields obtained are summarised in Table 4.

The immobilised manganese porphyrin **24** displayed a similar activity (entries 1 and 2) to its homogeneous counterpart for the epoxidation of both alkenes, whereas lower yields were obtained using the supported catalyst **25**, which contains electron-withdrawing groups on the pyrrolic *β*-positions (entries 3 and 4). It was suggested that the chlorines imposed too much steric hindrance. The iron porphyrin **26** was less efficient than the manganese analogue in the epoxidation of cyclooctene (entry 5), whereas cyclohexene was epoxidised in higher yield (entry 6). No explanation was offered for the difference in reactivity of different metals. The iron porphyrin **27**, bound to APS *via* an amide linkage, also exhibited high activity for the epoxidation of cyclooctene (95% yield, entry 7). The presence of the nitro group may increase the stability of the metalloporphyrin toward self-oxidation. Using a higher amount of catalyst, epoxycyclooctane was formed in high yield (entry 9) using the manganese porphyrin anchored to montmorillonite **29** compared to the metalloporphyrin **28** attached to silica gel (entry 8). This may be due to the presence of free reactive amines on the benzene rings of **28**, which inhibit the reactivity of the metalloporphyrin towards the epoxidation reaction. In general, all of these catalysts are very efficient but most of them are not recyclable. No leaching was observed during the reaction but degradation of the metalloporphyrin may be responsible for the decrease in activity.

Hydrogen peroxide was examined as the oxidant for the epoxidation reaction catalysed by **28** and **29**. 70% yield was obtained for the epoxidation of cyclooctene using **28**, which is high compared to other studies,[58] including that of the homogeneous analogue. Other alkenes such as cyclohexene or *cis*-stilbene were also epoxidised in high yields. Moreover, no loss of activity was observed after several cycles using the recovered catalyst, which makes the use of H_2O_2 promising. In contrast, a low yield of epoxycyclooctane was obtained with **29** and may have been caused by the reaction between H_2O_2 and the metal ions present on the montmorillonite.

Organic supports

Metalloporphyrins have also been covalently anchored to organic supports.[59–62] Recently Benaglia and co-workers[63] anchored a manganese porphyrin to a PEG chain to obtain the catalyst **30** (Fig. 10). The advantage of this support is its solubility in

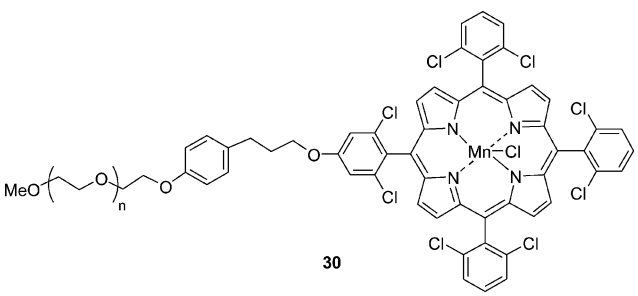


Fig. 10 Manganese porphyrin anchored to a soluble PEG chain.

Table 4 Alkene epoxidation catalysed by metalloporphyrins covalently bound to silica

Entry	Alkene	Catalyst	Mol% cat.	% Yield[a] epoxide	Reuse
1	Cyclooctene	**24**	0.8	95	No leaching detected, but activity decreased upon reuse
2	Cyclohexene	**24**	0.8	80	
3	Cyclooctene	**25**	0.8	67	
4	Cyclohexene	**25**	0.8	49	
5	Cyclooctene	**26**	0.8	88	
6	Cyclohexene	**26**	0.8	88	
7	Cyclooctene	**27**	1	95	No data
8	Cyclooctene	**28**	5	88	Good
9	Cyclooctene	**29**	5	98	Good

[a] Determined by GC and based on PhIO consumed after 8 h

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most organic solvents. As a result, the catalytic reaction occurs in homogeneous conditions, but the catalyst can be easily recovered upon addition of ether, in which it is insoluble.

Polystyrenes containing different spacer chains have also been used to covalently attach manganese porphyrins. For instance, Tangestaninejad *et al.*[64,65] have prepared the catalysts **31** and **32** (Fig. 11). Supported ruthenium porphyrins **33** and **34** have also been synthesised by reaction with Merrifield resin[66] and soluble PEG chains.[67]

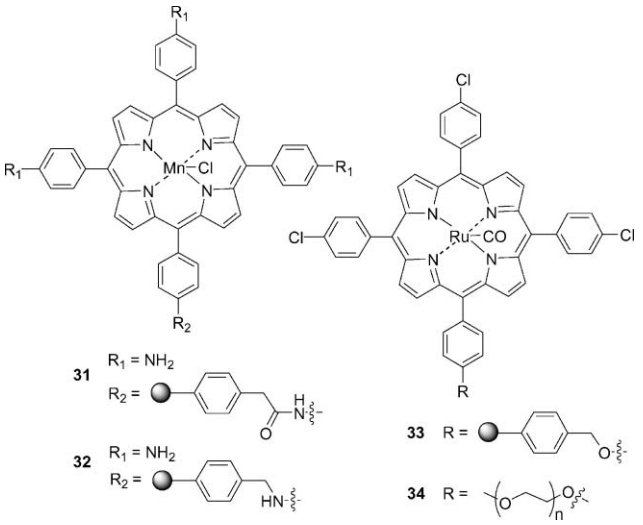


Fig. 11 Metalloporphyrins covalently bound to organic polymers.

The immobilised catalysts were investigated for the epoxidation of a variety of alkenes, using PhIO as an oxidant with the catalyst **30**, $NaIO_4$ with **31** and **32**, and dichloropyridine *N*-oxide with **33** and **34**. The data obtained are summarised in Table 5.

All the catalysts displayed high activity for most of the electron-rich alkenes (entries 1–7, Table 5). It can be pointed out that reaction times were shorter in the presence of catalyst **30** due to the presence of the soluble PEG chain, which allows homogeneous conditions for the reaction. More unreactive alkenes such as α,β-unsaturated ketones (entry 8) or protected α-amino alkenes (entry 10) were also epoxidised in high yields using the immobilised ruthenium porphyrins **33** and **34**. Glycal, which is an enol ether, is an election-rich alkene which explains its moderate yield (entry 9). With regards to the issue of recyclability, the manganese porphyrin **30** anchored to the PEG chain was reused four times without significant loss of activity. The polystyrene-supported manganese porphyrin **31** and **32** were said to be reusable (although no data were reported). In contrast, the ruthenium porphyrins were shown to be robust upon reuse and did not undergo any decrease in activity.

Our group prepared the catalyst **35**[68] by anchoring hydroxytetraphenylporphyrin to Argogel chloride (PS–PEG copolymer) followed by metallation with manganese dichloride (II) (Fig. 12). Catalyst **35** catalysed in high yields the epoxidation of a wide range of alkenes using sodium periodate as oxidant, but it was observed that some metalloporphyrin leached from the support during the epoxidation reaction due to cleavage of the PEG chain. It was shown that the same porphyrin anchored to Merrifield resin was more robust and the resulting catalyst

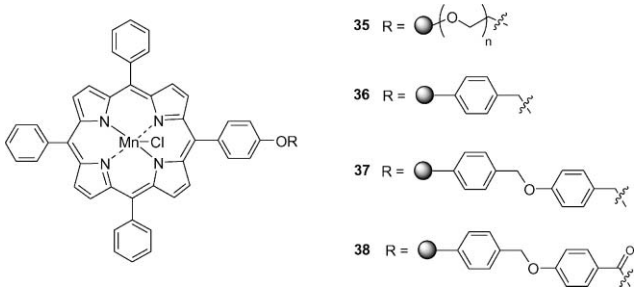
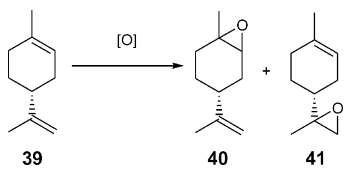


Fig. 12 Polymer-supported manganese porphyrin containing different spacer chains.

36 could be reused three times with only a small decrease of activity for the epoxidation of styrene (from 86 to 75%).[68] Two other supported catalysts[69] **37** and **38** were also prepared using Wang and carboxy Wang resins respectively. Moderate to excellent yields were obtained in the epoxidation of a range of alkenes. More interestingly, three dienes (limonene, cyclooctadiene and 7-methyl-1,6-octadiene) were also used as substrates in order to study the chemoselectivity induced by these catalysts.[69] Only a few studies on chemoselectivity, mainly carried out by Tangestaninejad *et al.*,[44, 46, 47, 49, 64, 65] have been reported so far.

Using our catalysts **37** and **38**, (*R*)-limonene **39** (Scheme 3) was epoxidised selectively to epoxide **40** (no diastereoisomeric excess was observed) in a good ratio of 2.7 : 1 compared to the epoxide **41**. The same trend was observed in previous studies. The chemoselectivity was even higher in the case of cyclooctadiene, as the monoepoxide was formed exclusively in 70–80% yield with the three catalysts **36–38**. In the case of the linear aliphatic diene 7-methyl-1,6-octadiene, the tri-substituted epoxide was obtained exclusively in 90–100% yield. The recyclability was also investigated and the catalysts **36–38** were reused up to four times in the epoxidation of limonene. It was shown that no significant decrease in activity occurred with catalyst **38** and that a similar ratio of epoxide **40/41** was obtained after the 4th cycle.[69]



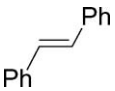
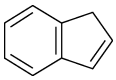
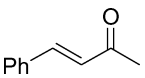
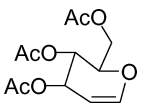
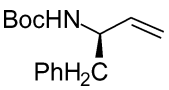
Scheme 3 Epoxidation of (*R*)-limonene.

Heterogeneous chiral metalloporphyrins

To date, only a few studies on asymmetric epoxidation catalysed by supported metalloporphyrins have been published. Different approaches were considered. Sasaki *et al.*[70,71] have focused their research on the mimic of the P450 enzyme with its hydrophobic pocket formed by the protein. A peptide–manganese porphyrin conjugate has been prepared and has been bound to the inorganic support Si–Im to form the asymmetric catalyst **42** (Fig. 13).

It was suggested that the α-helical peptide, attached to the porphyrin *via* the side chain of two cysteine residues, would create a chiral hydrophobic pocket. The feasibility of the sequence of amino acids was confirmed by molecular modelling. The potential selectivity displayed by the chiral catalyst **42** was examined in

Table 5 Epoxidation of alkenes catalysed by polymer-supported metalloporphyrins

Entry	Alkene	%Yield[a] with **30**	%Yield[b] with **32**	%Yield[c,d] with **33**	%Yield[c,e] with **34**
1		100	91	98	98
2		82	68	66	37
3		80	85	96	98
4		—	70	—	—
5		—	55	90	87
6		100	75	62	87
7		—	—	98	95
8		—	—	89	—
9		—	—	56	60
10		—	—	88	
Recyclability		Good	No detailed data reported	Excellent	Excellent

[a] Catalyst loading of 0.2 mol% was used, yield determined by GC after 2 h and based on an internal standard. [b] Catalyst loading of 4 mol% was used and yield determined by GC after 8 h and based on the alkene. [c] Yield determined by GC after 24 h and based on an internal standard. [d] Catalyst loading of 0.1 mol% was used. [e] Catalyst loading of 0.06 mol% was used.

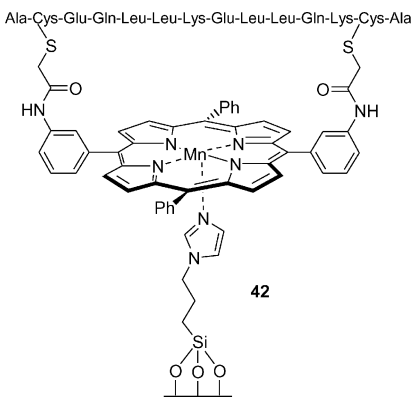


Fig. 13 Supported peptide–metalloporphyrin conjugate.

the epoxidation of a variety of alkenes such as styrene, *cis*- and *trans*-stilbene using PhIO. Despite the fact that the corresponding epoxides were formed in a wide range of yields (15–84%), no enantioselectivity was detected for any of the epoxidation reactions.

The origins of these results have been the subject of a detailed study.[72] It was suggested that several different parameters could explain the absence of enantioselectivity. Firstly, some degradation of the supported porphyrin was observed during the reaction, which could have led to some loss of stereoselectivity, though it was thought that this could not be the only reason. Secondly, by comparing successful homogeneous asymmetric metalloporphyrins, it was believed that the binding pocket of **42** was too symmetrical and that a precise amino acid sequence of the peptide chain might be crucial for substrate recognition.

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Inspired by Sasaki's work, our group prepared a large library of peptide–metalloporphyrin conjugates bound to polystyrene polymer, based on the scaffold shown on Fig. 14.[73] Various sequences of peptides were synthesised, and attached *via* an amide bond to an acid-functionalised porphyrin, in which the *ortho* position of one of the benzene rings had been used to introduce the desired spacer chain.

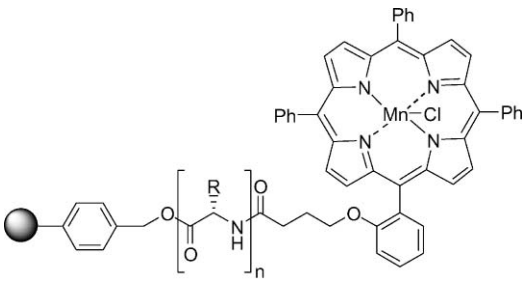

Fig. 14 Scaffold of peptide–metalloporphyrin conjugates on solid support.

The resulting catalysts were tested in the epoxidation of styrene using sodium periodate as an oxidant. Unfortunately, the catalysts of the library did not exhibit any enantioselectivity during the reaction of epoxidation. Nevertheless, some of these catalysts which contained amino acids with an N- or S-donor such as **44** and **45** (Fig. 15) (containing histidine and cysteine respectively) were found to exhibit excellent chemoselectivity in the epoxidation of dienes such as limonene. A ratio of 5 : 1 of limonene oxide **40**/**41** was obtained with catalyst **44** and 3.7 : 1 with catalyst **45**. Moreover, recylability studies showed that the same chemoselectivity was observed in a 2nd cycle with both catalysts. It was thought that the presence of the imidazole of histidine could stabilise the manganese porphyrin by acting as axial ligands during the epoxidation reaction.

Another strategy for the preparation of heterogeneous chiral metalloporphyrins was reported by Che and co-workers[74] and consisted of supporting the chiral D_4-symmetric ruthenium porphyrin[75] **46** (Fig. 16) that epoxidises a wide range of alkenes with high enantioselectivity in homogeneous systems. In order to keep the D_4-symmetry of the chiral porphyrin, it was coordinatively anchored *via* an amine functionality contained on two different zeolites: MCM-41 and MCM-48, constituted of one- and three-dimensional networks, respectively. The chiral supported porphyrins **47** and **48** were first compared in the asymmetric epoxidation of styrene with dichloropyridine N-oxide after 24 h.

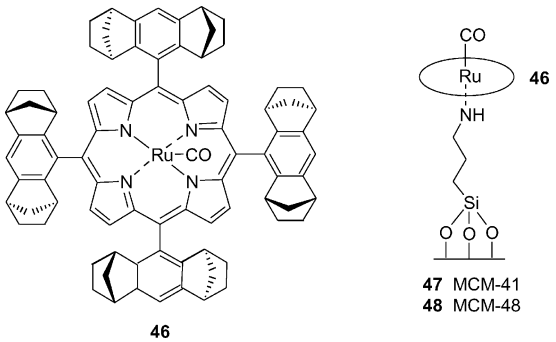

Fig. 16 Ruthenium porphyrin bound to zeolite.

Styrene oxide was formed with both catalysts with high enantioselectivity and high conversions (79–84%). Indeed, **47** displayed a similar selectivity (72% ee) to that obtained using the homogeneous counterpart,[76] and a higher ee of 75% was reached with **48**. The better results obtained with MCM-48 may be explained by the larger surface area of the support provided by the 3D network, leading to higher accessibility for the

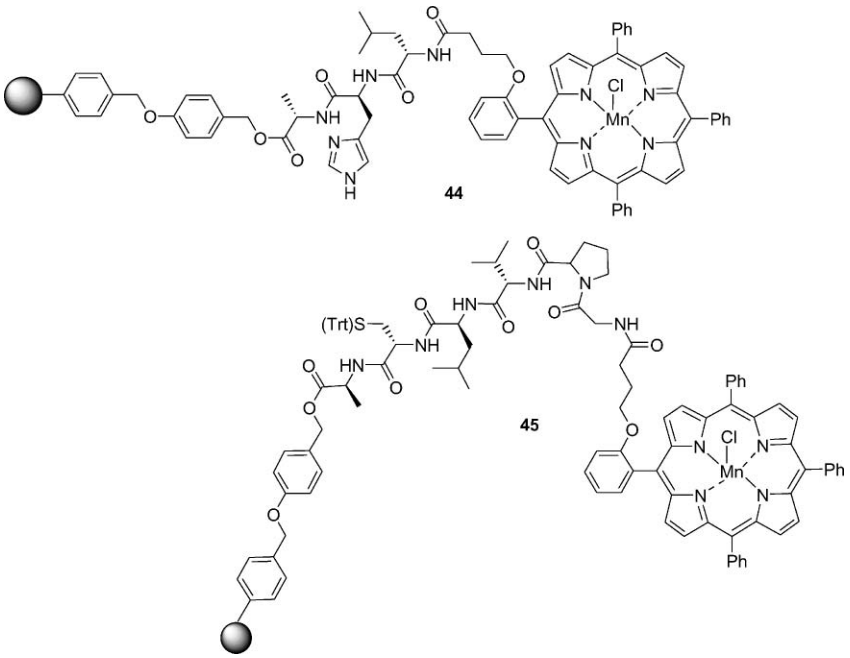

Fig. 15 Peptide–metalloporphyrin conjugates containing N- or S-donor ligands.

substrates to the active site of the porphyrin. Other alkenes, such as dihydronaphthalene or *cis*-α-methylstyrene were also epoxidised with 74–76% ee. The reuse of these successful catalysts was examined, and despite an unchanged reactivity, the selectivity decreased to 66% ee with **48** after the second cycle. Nevertheless, these preliminary results are very promising.

Conclusion

Supported metalloporphyrins successfully catalyse the epoxidation of a range of alkenes. A wide diversity of reactions has been presented, as well as a variety of methods for the immobilisation of the metalloporphyrins and variations in the nature of the support and in the oxidant used in the catalytic reaction. Covalent anchorage requires more work synthetically than the coordinative or electrostatic bindings. A phenyl ring of the metalloporphyrin needs to be functionalised in order to react with a support. However, the resulting binding is stronger and should lead to robust catalysts. Indeed several catalysts display high activity for a wide range of alkenes. Metalloporphyrins immobilised using coordinative and electrostatic bindings are also successful catalysts, although only "easy substrates" such as cyclooctene were often studied. Encapsulation is an emerging area, which seems to be promising, giving the high activity for the immobilised metalloporphyrin as well as the easy preparation of the catalyst. Furthermore, recyclability of these encapsulated metalloporphyrins was reported to be good. Indeed the reuse of supported metalloporphyrins remains challenging. Leaching of the catalyst into solution can be observed due to cleavage of the spacer chain between the porphyrin and the support. Degradation of the support and of the metalloporphyrin may also be responsible for catalyst deactivation. Nevertheless, some catalysts are already recyclable several times without loss of activity. In particular, ruthenium porphyrins have shown excellent results in terms of recyclability, although few studies have been dedicated to them.

Finally, supported chiral metalloporphyrins for asymmetric epoxidation remain the most important investigation carried out. Covalent binding seems to be a challenging route but the successful work reported by Che *et al.*[75] on the immobilisation of known chiral metalloporphyrins in zeolites showed that using coordinative or electrostatic anchoring is promising for the preparation of successful chiral supported metalloporphyrins.

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