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Synthesis of poly(ethylene glycol)-supported manganese porphyrins: efficient, recoverable and recyclable catalysts for epoxidation of alkenes

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Two new poly(ethylene glycol) supported manganese porphyrins have been prepared and their catalytic activity and recyclability were investigated for the epoxidation of alkenes using H_2O_2 and PhIO as stoichiometric oxidants.

The development of catalysts anchored to solid supports has been one of the areas of most intense research activity over the past years. The possibility of recovering and recycling catalysts which are often expensive has positive effects from the economical and environmental points of view. A further benefit is the ease of product isolation and purification.[1] Among the different polymeric matrixes employed, poly(ethylene glycol)s (PEGs) have recently emerged as very convenient supports for the synthesis of a variety of small organic molecules, ligands and catalysts.[2] This inexpensive, readily functionalized class of polymers provides a distinct advantage over other supports, being soluble in most organic solvents but insoluble in a few common ones, like Et_2O. Thus a reaction catalysed by a PEG-supported catalyst can be run under homogeneous (and likely best performing) conditions while the catalyst itself can be easily recovered as if it was bound to an insoluble polymer.[3] We have recently reported the synthesis of achiral phase transfer catalysts,[4] chiral organic catalysts[5] and chiral ligands[6] anchored to PEGs modified with a linker and spacer with a suitable functional group. In many cases the obtained systems showed catalytic activity and stereocontrol ability similar to (and sometimes even higher than) those displayed by the corresponding non-supported species. As a part of this project, we have also investigated the immobilisation of metalloporphyrins. Indeed, such compounds are known to be versatile catalysts for several organic reactions, but their synthesis is often tedious and low-yielding and their recovery from reaction mixtures is low. Immobilisation of porphyrins and metalloporphyrins onto insoluble organic and inorganic polymers has been investigated for many years, but the advantages of these heterogeneous systems are often counterbalanced by the limited accessibility of active sites to organic substrates, especially in the case of oxidation reactions.[7]

A few metalloporphyrins linked to PEGs have been synthesized, mainly to tune their solubility properties for biomedical applications,[8] but recently the first example of the use of similar complexes in catalysis has been reported.[9] This prompted us to disclose our preliminary results in the field. Herein we describe the synthesis of two PEG-supported manganese porphyrins **1** and **2** (Scheme 1) and the study of their catalytic activity in the epoxidation of alkenes.

Results and discussion

On the basis of our experience in the PEG-supported synthesis of small organic molecules,[10] mesylate **3** was selected as the polymeric starting material to which *meso*-tetraarylporphyrins bearing free -OH substituents could be conveniently linked. Mesylates **3a**, **3b**, **3c** were prepared in three steps and 95% overall yield starting from commercially available monomethyl ether of PEGs (MeOPEGs, *MW* 750, 2000 and 5000, respectively) as previously described.[10] Our first approach involved the attachment of four poly(ethylene glycol) chains to a single molecule of the commercially available, symmetrically substituted 5,10,15,20-tetrakis(4-hydroxyphenyl)porphyrin **4** (Scheme 1).

The reaction of 1 mol. equiv. of **4** with 4 mol. equiv. of the mesylates **3a**,**b** in DMF in the presence of 12 mol. equiv. of Cs_2CO_3 afforded the desired supported porphyrin derivatives **5a**,**b**, respectively. It is worth mentioning that **5a** with $MeOPEGs_{750}$ substituents did not precipitate as a solid upon addition of Et_2O to the reaction mixture, but it was recovered as a very thick oil (93% yield).[11] However by employing the mesylate **3b** of $MeOPEG_{2000}$ the expected PEG-supported porphyrin **5b** was obtained as a solid that precipitated out by pouring the reaction mixture in Et_2O (87% yield).[12] The PEG-supported porphyrin **5b** was then reacted with $Mn(OAc)_2 \cdot 4H_2O$ in DMF at 160 °C for 18 hours; after elimination of the solvent by distillation under vacuum, the crude mixture was dissolved in CH_2Cl_2 and shaken with saturated aqueous NaCl. Cold Et_2O was added to the organic layer to induce the precipitation of the manganese porphyrin complex **1** bound to four $MeOPEGs_{700}$ chains as a green solid in 70% yield after filtration and two washings with Et_2O. TLC analysis clearly indicated the presence of a single species with no trace of starting porphyrin. Formation of the manganese complex **1** was confirmed by UV–Vis spectroscopy, which showed a shift of the characteristic 421 nm peak of **5b** (Soret band, free-porphyrin) to 480 nm, corresponding to that of a complexed porphyrin. In order to increase the catalyst loading, the attachment of the unsymmetrically substituted 5-(4-hydroxy-2,6-dichlorophenyl)-10,15,20-tris(2,6-dichlorophenyl)porphyrin **6** to a single $MeOPEG_{5000}$ residue was envisaged (Scheme 1).

Porphyrin **6** was prepared in 14% yield following the procedure previously described for the synthesis of its isomer 5-(3-hydroxy-2,6-dichlorophenyl)-10,15,20-tris(2,6-dichlorophenyl)-porphyrin.[13] Reaction of mesylate **3c** with **6** in DMF gave the PEG-supported porphyrin **7** which was isolated after precipitation with Et_2O in 90% yield. Treatment of **7** with $Mn(OAc)_2 \cdot 4H_2O$ and anion exchange with saturated aqueous NaCl afforded the PEG-supported manganese porphyrin **2** in 78% yield. The UV–Vis spectra of **2** showed the diagnostic peak at 478 nm and the total absence of the Soret band of the free-porphyrin **7** at 417 nm. The inverse reaction sequence (complexation of porphyrin **6** followed by immobilisation of the manganese complex onto PEG) was also feasible and it afforded **2** in comparable overall yield (73% *vs.* 71%). The

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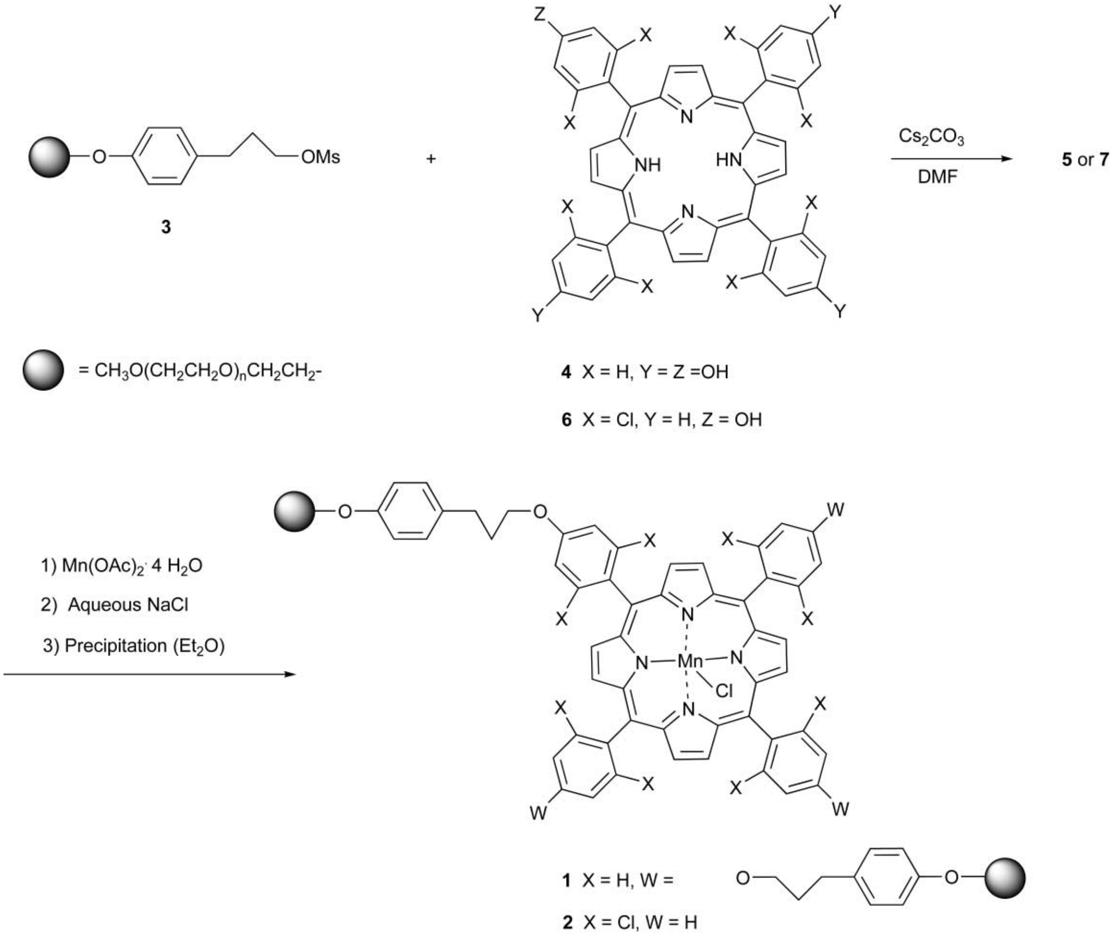
Table 1 Epoxidation of alkenes catalysed by PEG-supported manganese porphyrin **2**^{a}

Entry	Oxidant^b	Substrate	Cat. (mol. %)	t/h	Conv.^{c} (%)	Yield^c (%)
1	PhIO	Cyclooctene	0.2	0.8	100	100
2^d	PhIO	Cyclooctene	0.5	18	63	61
3	PhIO	Cyclooctene	0.01	28	100	96
4	PhIO	Cyclooctene	2	0.3	97	97
5^e	PhIO	Cyclooctene	2	0.3	91	90
6^f	PhIO	Cyclooctene	2	0.3	65	63
7	H_2O_2	Cyclooctene	0.1	4	70	67
8^g	H_2O_2	Cyclooctene	0.1	1	72	70
9	PhIO	Dodec-1-ene	1.5	5	40	38
10	H_2O_2	Dodec-1-ene	0.1	5	24	21
11^g	H_2O_2	Dodec-1-ene	0.1	5	26	25
12	PhIO	Cyclohexene	0.2	18	82	82
13	PhIO	Styrene	0.2	1.5	85	80
14	PhIO	Indene	0.2	0.3	100	100

^{a} Reactions were carried our as described in ref. 12 and 13. ^{b} Axial ligand = *N*-methylimidazole, catalyst–ligand = 1 : 1 molar ratio (PhIO); *N*-hexylimidazole–PhCOOH, catalyst–ligand–acid = 1 : 3 : 4 (30% H_2O_2). ^{c} Determined by GC analysis (column HP-5 5% phenyl methyl siloxane, 30 m × 0.32 mm) in the presence of diphenyl ether as internal standard. ^{d} Catalyst = **1**. ^{e} Catalyst recovered from entry 4: 4th consecutive run. ^{f} Catalyst recovered from entry 4: 7th consecutive run. ^{g} Catalyst = 5,10,15,20-tetrakis(2,6-dichlorophenyl)porphyrinMn(III) chloride complex.



Scheme 1 Synthesis of PEG-supported manganese porphyrins **1** and **2**.

loading for the manganese porphyrin **2** is 0.165 mmol g^{-1} and favourably compares to the loading of **1** (0.110 mmol g^{-1}).

The new compounds were tested as catalysts in the epoxidation of alkenes with PhIO or 30% H_2O_2 as terminal oxidants, in the presence of *N*-alkylimidazoles as axial ligands (Table 1). In a typical experiment, a 10 ml Schlenk tube placed in a thermoregulated bath at 25 °C, was charged under nitrogen with: 1 ml of a 0.1 M solution of alkene in CH_3CN containing diphenyl ether (0.05 M, internal standard for GC); 1 ml of a 0.0001 M solution of the catalyst in CH_3CN; 0.010 ml of a 0.01 M solution of *N*-methylimidazole in CH_3CN; after 5 minutes stirring PhIO (44 mg, 0.2 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 GC. The presence of bulky, electron-withdrawing substituents in the 2,6-positions of the *meso* aryl rings of the PEG-supported manganese porphyrins enhances their catalytic activity and stability, analogously to what was found in the case of their polymer-free counterparts.[7] Thus, complex **2** was found to be superior to **1** in the epoxidation of cyclooctene with PhIO (entries 1 and 2), affording complete substrate conversion in 30 min when a ratio substrate–catalyst = 200 was used. Up to 10 000 turnovers were attained in 28 h in a reaction carried out in the presence of 0.01% molar equivalents of catalyst with respect to cyclooctene (entry 3). Recycling of **2** by precipitation with Et_2O and filtration was also demonstrated (entries 4–6, selected data). After being reused four times, **2** showed only a marginal decrease in the catalytic efficiency, while a drop of activity was observed in the seventh run, parallel by the almost complete disappearance of the 478 nm absorption in the UV–Vis spectrum. Complex **2** was also found to be active in the oxidation promoted by 30% H_2O_2 in the presence of *N*-hexylimidazole and benzoic acid as co-catalysts (entry 7).[14] Only robust metalloporphyrins can withstand this particular oxidising environment and can catalyse the oxygen transfer to the substrate (see entry 8 in Table 1).[15]

The applicability of **2** in the epoxidation of other alkenes has been also examined (entries 9–14). Good results have been obtained, except for dodec-1-ene, which is a terminal alkene chosen as a model of poorly reactive substrates. Nevertheless, the overall turnover numbers and the turnover frequency observed in the epoxidation of dodec-1-ene with 30% H_2O_2 (240) are close to those attained in the presence of other oxidatively robust manganese porphyrins (see entry 10–11 in Table 1).[15] Thus, the presence of the electron-donating MeOPEG substituent does not seem to negatively affect the catalytic activity of the complex.

In conclusion, we have demonstrated that soluble, PEG-supported manganese porphyrins can be easily prepared and conveniently used as recoverable and recyclable catalysts in the epoxidation of alkenes with readily available oxidants. We are currently investigating the use of similar compounds in other catalytic reactions.

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11 MeOPEGs of *MW* > 2000 are solid, and they are known to be insoluble in Et_2O, hexanes or isopropanol; tethering four $MeOPEG_{750}$ chains to **4** should provide in principle a porphyrin embedded in a poly(ethylene glycol) matrix of *MW* > 3000, able to precipitate as a solid under the proper conditions. Apparently, the core macrocycle plays a decisive role in preventing a cooperative effect of the PEG chains.

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