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Shape selective epoxidation of alkenes by metalloporphyrin-dendrimers

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Abstract

A series of oxidatively robust manganese-porphyrin-dendrimers were synthesized in good yields for use as shape-selective oxidation catalysts. The poly(phenylester) dendrimers with the bulky *tert*-butyl terminal groups were synthesized with a convergent approach. These cascade dendrimers were linked at the *meta*-phenyl positions of the 5,10,15,20-tetrakis(3',5'-dihydroxyphenyl)porphinato manganese(III) chloride to produce a sterically hindered metal center. The regioselectivity of these catalysts was determined for epoxidation of non-conjugated dienes and 1:1 intermolecular mixture of linear and cyclic alkenes using iodosylbenzene as the oxygen donor. Metalloporphyrin dendrimers exhibit significantly higher substrate selectivity compared to unsubstituted Mn(TPP)(Cl), but only moderate selectivity relative to the extremely hindered bis-pocket porphyrin, 5,10,15,20-tetrakis(2',4',6'-triphenylphenyl)porphinato manganese(III) acetate. Molecular modeling was performed on the porphyrin dendrimers to elucidate the extent of steric crowding around the porphyrin. There is a relatively large cavity for substrate entrance in the manganese-porphyrin-dendrimers relative to extremely hindered bis-pocket porphyrin.

Keywords: Metalloporphyrin; Porphyrin; Dendrimer; Oxidation catalysis; Epoxidation

1. Introduction

Sterically hindered high-valent metalloporphyrin complexes of bis-pocket [1–3], basket handle [4], cholesterol porphyrins [5], and others [6] have been employed to mimic the substrate selectivity of cytochrome P450. The synthesis of such sterically constrained metal centers for shape-selective catalysis continues to be of great interest. In this aspect, dendritic polymers could be of considerable importance because of their

synthetic diversity which leads to varying shape, size, and surface functionality [7]. Furthermore, dendritic architecture can be controlled by simple variation in building blocks and reaction conditions. Recent studies on organic poly-ether based dendrimers appended at the peripheral positions of porphyrins showed unusual physical properties [8,9]. Interestingly, the presence of a redox active metal center at the exterior part of an organosilane (non-porphyrin) dendrimer exhibited some catalytic capabilities for carbon bond formation [10]. However, all these reported dendrimers are susceptible to oxidative degradation.

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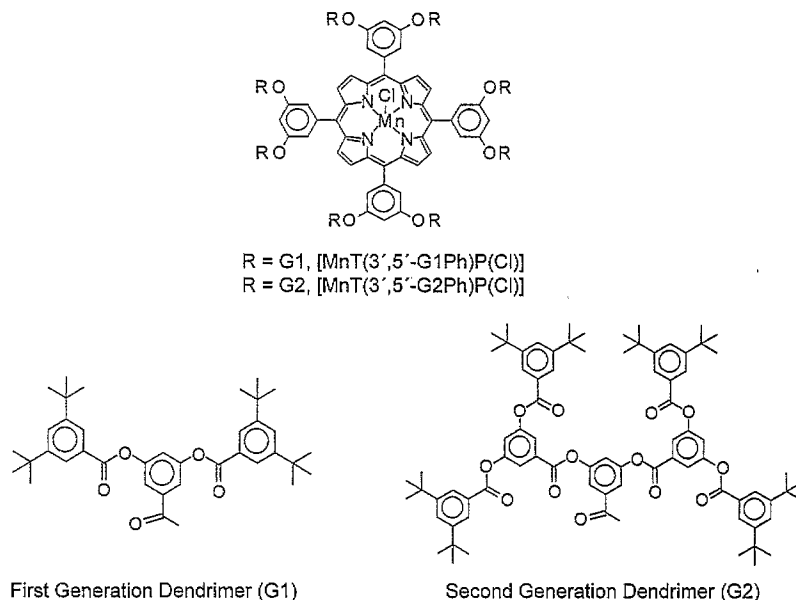


Fig. 1. Molecular structure of the dendrimers and the metalloporphyrin-dendrimers.

In spite of extensive work on metalloporphyrin catalyzed oxidations of organic substrates [11], their use in shape-selective catalysis has been less explored [12]. Variety of simple substituted tetraphenylporphyrin complexes have been employed as shape-selective catalysts. The selectivity of the catalyst originates from control of substrate access through the steric and van der Waals contacts of the substituents at the periphery of the porphyrin. Among these catalysts, bis-pocket porphyrin, 5,10,15,20-tetrakis(2',4',6'-triphenylphenyl)porphyrin, is the most extremely hindered porphyrin, and its high-valent metal derivatives exhibited intriguing regio- and shape-selectivity [1–3].

Recently, we reported on a *new* class of metalloporphyrin-dendrimers as shape-selective catalysts [13]. In continuation of this work, here we report the synthesis of metalloporphyrin-dendrimers in which bulky cascade dendrimers have been attached at the periphery of the porphyrin for the use in shape-selective catalysis. Two generations of cascade dendrimers (G1 and G2 in Fig. 1) were employed to determine the effect of dendrimer size on the substrate selectivity. Poly(phenylester) dendrimers with bulky

tert-butyl groups as the exterior surface of the dendrimer were chosen for several reasons. The presence of *tert*-butyl groups gives substantial steric constraint around the porphyrin, enhances solubility, and provides a high level of oxidative robustness. In addition, the phenyl ester linkages are themselves very robust towards oxidative degradation, since there are no benzylic or secondary carbons present.

2. Results and discussion

The dendrimers were synthesized using standard techniques [14]. They were then appended to the *meta*-hydroxyphenyl positions of the 5,10,15,20-tetrakis(3',5'-dihydroxyphenyl)porphyrin, $H_2T(3',5'-OHPh)P$ or to its metal derivative $[Mn(T(3',5'-OHPh)P)(Cl)]$ through a DCC coupling reaction (Fig. 1). All the synthesized dendritic porphyrins were purified by HPLC and spectroscopically characterized by UV-visible absorption and low resolution matrix-assisted laser desorption time of flight (MALD-TOF) mass spectroscopic techniques, as described in the Section 4.

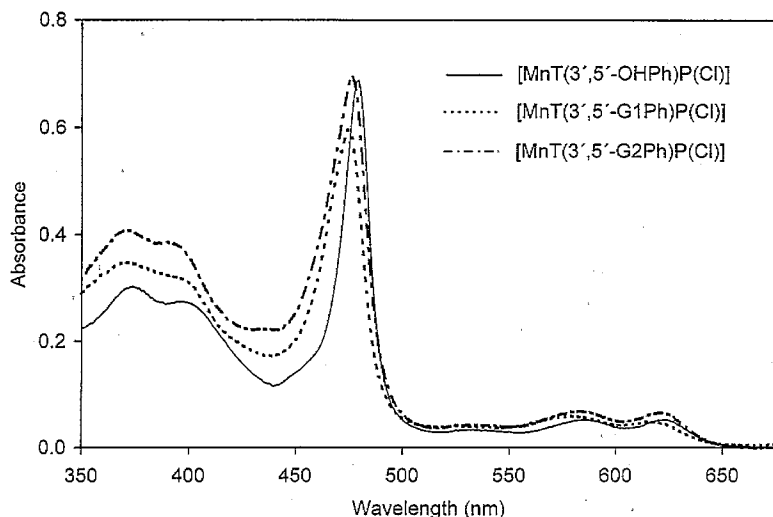


Fig. 2. Electronic absorption spectrum of manganese(III) porphyrin-dendrimers in CH_2Cl_2 .

The manganese-porphyrin-dendrimers exhibited interesting physical properties. These complexes are very soluble in non-polar solvents (even *n*-alkanes) and less soluble in polar solvents such as acetonitrile, methanol, and benzonitrile. The UV–visible absorption spectra of

the manganese first and second generation dendrimer porphyrin complexes are shown in Fig. 2. Electronic absorption spectra of these complexes are found to be similar to that of $[\text{Mn}(\text{T}(3',5'\text{-OHP})\text{P})(\text{Cl})]$, but with a small blue-shift. This is probably due to the presence

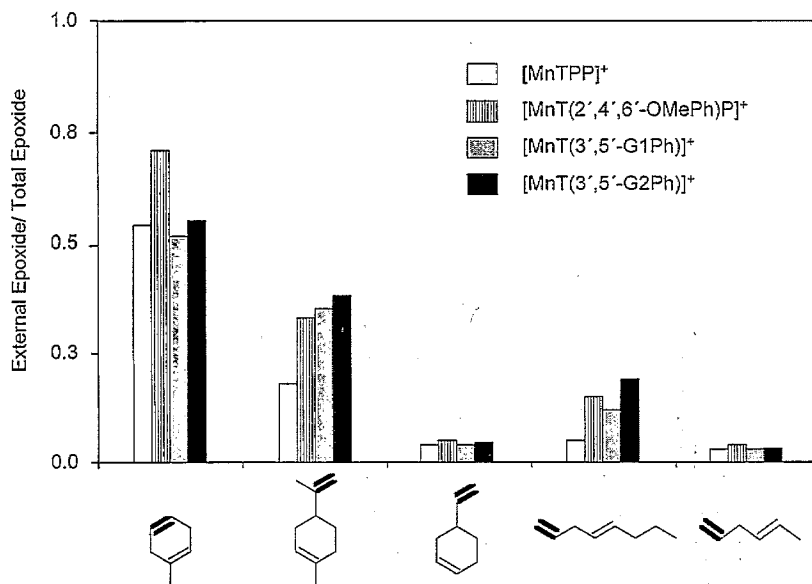


Fig. 3. Epoxidation results for the intramolecular selectivity of non-conjugated dienes for the various metalloporphyrin catalysts. Data for the $[\text{Mn}(\text{T}(2',4',6'\text{-OMePh})\text{P})(\text{OAc})]$ is taken from Ref. [3]. The more accessible double bonds are shown in heavy lines.

of hydrophobic dendrimers at the periphery of the porphyrin, which will lower the local polarity felt by the porphyrin π -system. Similar behavior was observed in the case of zinc-porphyrin-dendrimers [8,9].

Epoxidation reactions using the manganese porphyrin-dendrimers were carried out with iodosylbenzene as the oxygen donor. To determine the regioselectivity of these catalysts, two types of tests were performed. In the first case, a series of non-conjugated dienes with varying shapes and sizes were used to test the catalysts *intramolecular* selectivity. The dienes employed in the present study bear both less sterically-hindered (external) and more sterically-hindered (internal) double bonds. In the second class of tests, several mixed solutions containing equimolar concentrations of two alkenes were employed for *intermolecular* selectivity studies: the solutions contained *cis*-cyclooctene as the standard with a second alkene (1-pentene, 1-hexene, 1-octene, *cis*-2-octene, or cyclohexene) or they contained *cis*-2-octene as the standard with either *trans*- β -methylstyrene or 2-methyl-2-pentene. Control epoxidation reactions were

carried out with $\text{Mn}(\text{TPP})(\text{Cl})$ and are similar to those of previously reported results [3,4].

Epoxidation results for several linear and cyclic dienes are shown in Fig. 3 for manganese porphyrin-dendrimers along with the moderately hindered $[\text{Mn}(\text{T}(2',4',6'\text{-OMePh})\text{P})(\text{OAc})]$ catalyst [3]. A comparison of catalysis results between the porphyrin-dendrimers with other simple substituted porphyrins is to demonstrate the extent of steric crowding arising from the peripheral dendrimers. From Fig. 3, the dendrimer metalloporphyrins are more selective than $\text{Mn}(\text{TPP})(\text{Cl})$ and are similar to the moderately hindered $\text{Mn}(\text{T}(2',4',6'\text{-OMePh})\text{P})(\text{OAc})$. Fig. 4 shows the epoxidation data for intermolecular mixture of alkenes. Dendrimer catalysts show two to three times higher selectivity than the parent $\text{Mn}(\text{TPP})(\text{Cl})$. Marginal increase in selectivity was observed for the longer linear alkenes 1-octene or 1-hexene compared to 1-pentene. For the mixtures of alkenes, 2-methyl-2-pentene / *cis*-2-octene, *trans*- β -methylstyrene / *cis*-2-octene and cyclohexene / *cis*-cyclooctene dendrimer metalloporphyrins exhibit higher selectivity relative

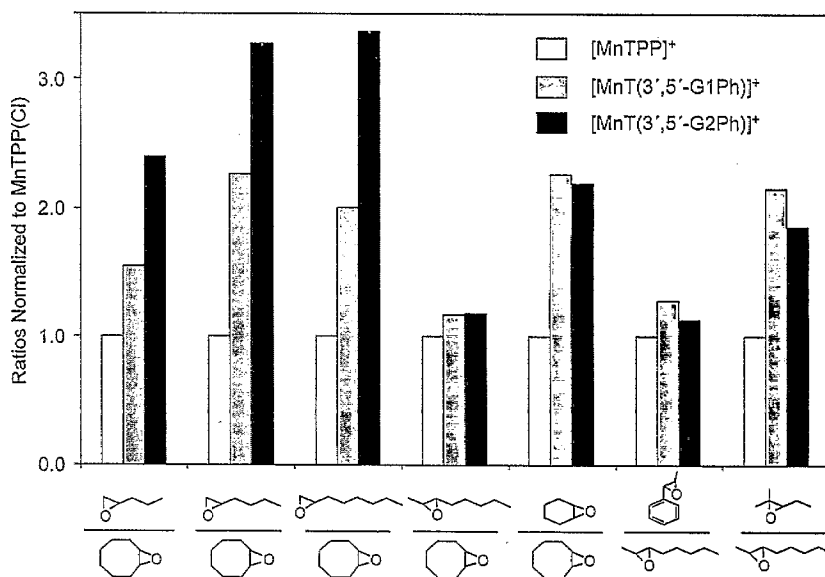


Fig. 4. Epoxidation results for the intermolecular mixture of alkenes. The ratios of the epoxides are normalized with respect to corresponding $[\text{Mn}(\text{TPP})(\text{Cl})]$ values.

to less hindered Mn(TPP)(Cl) (Fig. 4). A decrease in selectivity was observed for 1-octene/*cis*-cyclooctene to *cis*-2-octene/*cis*-cyclooctene. This is reflected in the ease of accessibility of 1-octene relative to 2-octene for the sterically hindered catalyst. The turnover numbers (T.O.N., i.e., mol product/mol metalloporphyrin/s) obtained for the manganese porphyrin dendrimers ($2\text{--}4\text{ s}^{-1}$) were not significantly different compared to unsubstituted Mn(TPP)(Cl) ($3\text{--}4\text{ s}^{-1}$). These dendrimer-porphyrin catalysts show considerable stability; less than 10% degradation was observed after 1000 turnovers (based on oxidant) as evidenced from electronic absorption spectroscopy.

Computer generated molecular modeling studies were carried out to examine the extent of steric hindrance offered by the dendrimers on both faces of the porphyrin. Comparisons were made to other sterically hindered porphyrins. Fig. 5 and Fig. 6 show the van der Waals molecular models for the complex $\text{H}_2(\text{T}(3',5'\text{-G1Ph})\text{P})$ and $\text{H}_2(\text{T}(3',5'\text{-G2Ph})\text{P})$, respectively. Surprisingly, for the porphyrin dendrimers, top access is found to be completely restricted on both faces of the porphyrin, whereas the bis-pocket porphyrin shows a top access pocket of 4 Å (see Ref. [2]). From the side view (along the porphyrin plane, as in Fig. 5 and Fig. 6), significant cavities of 10 Å and 7 Å for the G1 and G2 dendrimers, respectively, can be seen, whereas no side accessibility is possible for the bis-pocket porphyrin [2].

Docking studies for dienes and other alkenes with the porphyrin dendrimers indicated that the dienes can enter the cavity with less steric constraints compare to the extremely hindered bis-pocket porphyrin. The higher selectivity towards 1-alkenes in intermolecular mixture of alkenes is expected since the bulky cyclooctene has substantial steric constraints. The presence of bulky phenyl rings at the *ortho*-phenyl positions in the bis-pocket porphyrin are close to the metal center and provide a smaller pocket. Although the dendrimer substituents are extremely large, their attachment at the *meta*-phenyl posi-

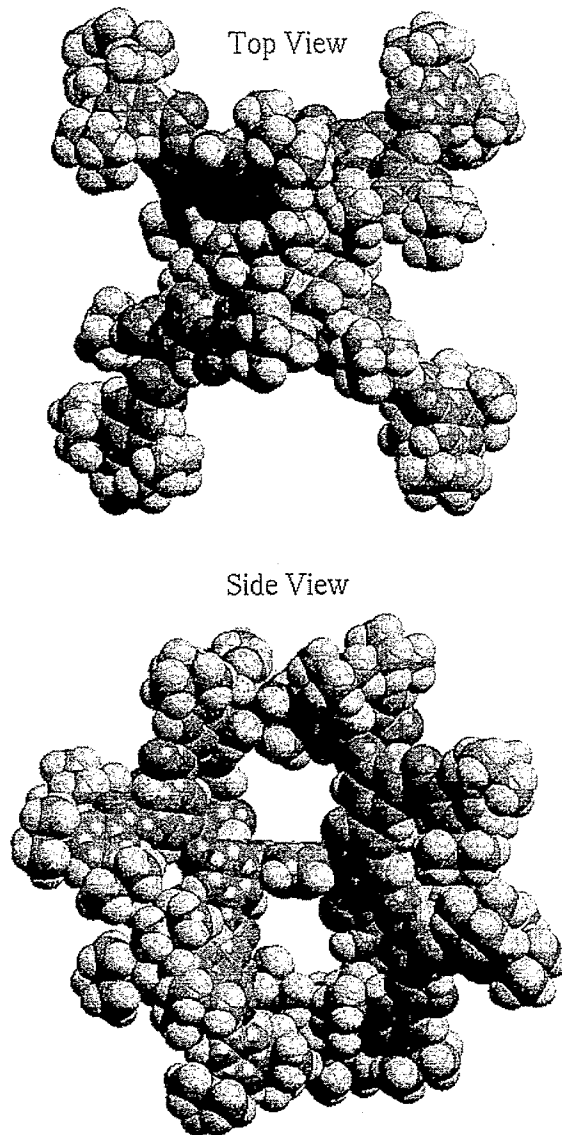


Fig. 5. Molecular models of $\text{H}_2\text{T}(3',5'\text{-G1Ph})\text{P}$ showing full van der Waals radii. The top view shows the face of the porphyrin is fully blocked by the dendrimers. The side view shows a pocket of 10 Å diameter.

tions fails to give a small cavity due to their orientation and possible fluxional behavior. From Fig. 5 and Fig. 6, it can be seen that the alkene substrate can approach the reactive manganese-oxo porphyrin intermediate from the side ways rather than from the face of the dendritic

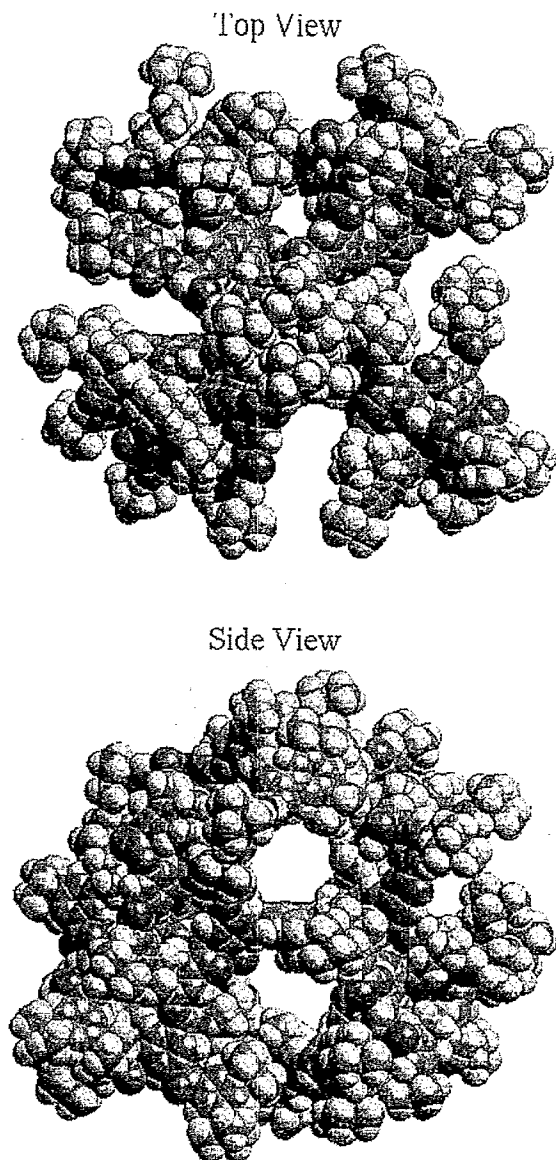


Fig. 6. Molecular models of $H_2T(3',5'-G_2Ph)P$ showing full van der Waals radii. The top view shows the face of the porphyrin is fully blocked by the dendrimers. The side view shows a pocket of 7 Å diameter.

porphyrin, consistent with the mechanism of proposed substrate approach [15]. Relatively lower selectivity observed for the porphyrin-dendrimers compared to bis-pocket porphyrin is

consistent with the presence of larger pockets in the dendritic porphyrins.

3. Conclusions

A new class of sterically hindered dendrimer-metalloporphyrins was synthesized for use as shape-selective catalysts. The series of oxidatively robust poly(phenylesters) dendrimers were prepared through a convergent synthesis. Monodendrons were appended to the *meta*-positions of the 5,10,15,20-tetrakis(3',5'-dihydroxyphenyl)porphinato-manganese(III) chloride to obtain a sterically protected metal center. These complexes have been examined as regioselective oxidation catalysts. Epoxidation of dienes and alkene mixtures of alkene and cyclooctene catalyzed by dendrimer-metalloporphyrins has been carried out using iodosylbenzene as the oxygen donor. These conjugates exhibit significantly greater regioselectivity than the corresponding parent complex, manganese(III) tetraphenylporphyrin. To examine the extent of steric crowding around the porphyrin from the dendrimers, molecular modeling studies were performed on free-base porphyrin dendrimers. Although the top access is extremely limited in the dendrimer-metalloporphyrins, a significant side opening limits the extent of regioselectivity that can be achieved with *meta*-substitution of a tetraphenylporphyrin.

4. Experimental section

4.1. Materials

Porphyrins ($H_2(3',5'-OHP)P$) [8] and its manganese derivative, $Mn(T(3',5'-OHP)P)(Cl)$ [16] were synthesized using reported procedures. Alkenes purchased from Aldrich were of high purity and used without further purification. 3,5-di-*tert*-butyl benzoic acid and 3,5-dihydroxy benzoic acid were obtained from Aldrich and were used as received. All the

solvents employed were of high purity and were distilled before use. Tetrahydrofuran obtained from Fisher Scientific was distilled from sodium/benzophenone under nitrogen before use. Dichloromethane was distilled from CaH₂ under N₂. Dicyclohexylcarbodiimide (DCC) obtained from Aldrich was used as received. 4-(dimethylamino)pyridinium 4-toluenesulphonate (DPTS) was synthesized using reported procedure [17]¹.

4.2. Instrumentation

The epoxidation products were analyzed with a Varian GL 3700 series capillary gas chromatograph and a Hewlett-Packard GCMS. UV-visible absorption spectral measurements were performed on a Hitachi UV-3300 spectrophotometer. Computer modeling studies were performed on a Silicon Graphics Iris extreme² work station using Quanta and Charmm software packages.

4.3. Synthesis of cascade dendrimers

Polyester dendrimers, first generation (G1) and second generation (G2) were prepared using literature procedures [14]. These dendrimers were not significantly different from those previously reported, except for the presence of *tert*-butyl groups at the periphery of the dendrimer. Briefly, the synthesis of G1 involves an initial protection of the carboxylate of 3,5-dihydroxybenzoic acid by condensation with 2,2,2-trichloroethanol, esterification with di-*t*-butylbenzoic acid using DCC/DPTS catalysis, followed by deprotection; synthesis of G2 simply repeats the cycle.

4.4. Synthesis of manganese(III)-porphyrin-dendrimers

[Mn(T(3',5'-G1Ph)P)(Cl)] was synthesized by the direct DCC coupling reaction of the den-

dimer, G1-acid with the free base porphyrin, H₂T(3',5'-OHP)P, followed by manganese insertion reaction, while MnT(3',5'-G2Ph)P(Cl) was prepared by the direct DCC coupling reaction of G2-acid with the manganese porphyrin, [Mn(T(3',5'-OHP)P)(Cl)]. DCC coupling reaction was performed in two steps: first in THF, followed by CH₂Cl₂. This was essential due to the low solubility of Mn(T(3',5'-OHP)P)(Cl) in CH₂Cl₂.

4.5. Synthesis of [Mn(T(3',5'-G1Ph)P)(Cl)]

Step 1: DCC (0.062 g, 0.3 mM) in 1 mL THF was added to a THF solution containing H₂T(3',5'-OHP)P (0.002 g, 0.0025 mM), dendrimer (G1) (0.015 g, 0.025 mM), and DPTS (0.024, 0.08 mM). The reaction mixture was stirred at room temperature for 15 h under argon. At the end of this period, the reaction mixture was filtered and the solvent was removed under reduced pressure. Step 2: The residue obtained from step 1 was redissolved in CH₂Cl₂ (2–3 mL) and catalytic amounts of DPTS and excess DCC were added, and the reaction was allowed for a further period of 72 h. The reaction mixture was filtered and the filtrate was evaporated to dryness under reduced pressure to obtain a violet oily product. The desired porphyrin-dendrimer product was extracted by using pentane as the solvent. Yield of the product was found to be 0.010 g (55%).

Metallation reaction: To a solution of H₂T(3',5'-G1Ph)P (0.02 g, 0.004 mM) in THF/CH₃CN (1:1, v/v) mixture, anhydrous MnCl₂ (0.010 g, 0.08 mM), 2,6-lutidine (0.25 mL) were added and the solution was refluxed under argon for 12 h. At the end of this period, the solvent was removed under reduced pressure and the residue was extracted with *n*-pentane to obtain the desired [Mn(T(3',5'-G1Ph)P)(Cl)] complex. Yield of the product was found to be 0.016 g (80%).

HPLC analysis of the manganese-porphyrin-dendrimers was performed to demonstrate pu-

¹ The rate of DCC coupling reactions depends on the solvent employed, see Ref. [18].

urity on a normal phase silica gel column using 30% THF in CH_2Cl_2 as the eluent. The low resolution matrix assisted laser desorption ionization time of flight mass spectral technique (MALD-TOF) was very useful in characterization of the manganese porphyrin-dendrimers. MALD-TOF of the manganese porphyrin dendrimer complexes were performed using [2-(4-hydroxyphenylazo)benzoic acid] (HABA) matrix. The MOD-TOF spectrum of the free-base porphyrin dendrimer, $\text{H}_2(\text{T}(3',5'\text{-G1Ph})\text{P})$ exhibits a peak at $[\text{M}]^+$ (m/z) 5291.1 (calcd. 5292.8) while $[\text{Mn}(\text{T}(3',5'\text{-G1Ph})\text{P})(\text{Cl})]$ shows molecular ion peak at $[\text{M} - \text{Cl}]^+$ (m/z) 5344 (calcd. $\text{M} - \text{Cl} = 5346.2$), and $[\text{Mn}(\text{T}(3',5'\text{-G2Ph})\text{P})(\text{Cl})]$ exhibit molecular ion peak $[\text{M} - \text{Cl}]^+$ at 10,980 (calcd. 10,985). In the latter, two minor peaks were observed at (m/z) 9724 and 8462, possibly due to successive loss of one and two dendrimer (G2) units from the parent molecular ion (calcd. 9694 and 8437, respectively).

4.6. Epoxidation reactions

Epoxidations were performed under argon using iodosylbenzene as the oxygen donor. In a typical experiment, iodosylbenzene (10 μmol) and 0.5 M alkene in 1 mL of CH_2Cl_2 containing manganese porphyrin catalyst (1 mM). The solution was vigorously stirred under argon for 30 min. At the end of this period, an internal standard decane or octane was added and the products were analyzed by GC and GCMS. The obtained yields of epoxides were greater than 80% based on the amount of iodosylbenzene employed. Standard epoxides were purchased from Aldrich or synthesized by using *m*-chloroperbenzoic acid as the oxidant and were analyzed by GC and GCMS.

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