ChemComm
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Remarkable axial ligand effect on regioselectivity towards terminal alkenes in epoxidation of dienes by a robust manganese porphyrin

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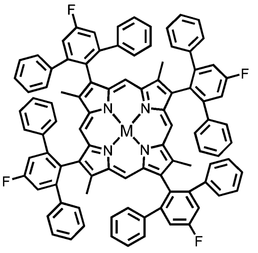
Received (in Cambridge, UK) 30th October 2002, Accepted 20th January 2003
First published as an Advance Article on the web 28th January 2003

With a highly encumbered manganese porphyrin as catalyst, significant improvements in regioselectivity towards less substituted C–C double bond in diene epoxidation were attained by simply adding organic bases as axial ligand.

Much effort has been directed to the design and synthesis of molecular superstructures on the porphyrin platform to attain regio-, enantio-, diastereo-, and shape-selectivity[1–5] for synthetically useful organic oxygenations and related appealing reactions.[6] Reports that highlight the effect of axial ligation on the selectivity of metalloporphyrins and metallosalens in the reactions have increasingly appeared.[7] It is well documented that the active site of biochemically functioning proteins such as haemoglobin and cytochrome P-450 are axially coordinated by imidazole and thiolate of amino acid residues respectively. Also, the chemical, electrochemical, and spectroscopic properties of the related transition metal complexes are profoundly influenced by the fifth coordination.[8] Because of the *trans*-relationship of the axial ligand to the transferable oxygen atom, it is presumably feasible to modulate the selectivity by screening axial bases of various electronic properties.[9] We herein describe a remarkable axial ligand effect for substantially enhancing regioselectivity in diene epoxidation by a barrel-shaped manganese porphyrin **2**. Based on computer modeling (TITAN) the porphyrin ligand **1**, 2,7,12,17-tetramethyl-3,8,13,18-tetra[2,6-bis(4-phenyl)-4-fluorophenyl]porphyrin features steric crowdedness and a hydrophobic cavity of ~0.6 nm for accommodation of organic substrates. With iodosylbenzene (PhIO) as oxidant, **2** has been shown to exhibit moderate selectivity towards a terminal C–C double bond in epoxidation.[5]



1 M = 2H
2 M = MnCl

The porphyrin **1** was prepared in high yield (50%) according to literature method.[10] Its structure was determined by X-ray crystallography† and depicted in Fig. 1 as stick models for clarity. The solid state structure of **1** indicates its conceptual resemblance to the cytochrome P-450 metalloproteins. Also, shielding of a high degree is accomplished by the four terphenyl wings that have two sets of inclination angles at 70.5(3)° and 58.2(3)° to the porphyrin plane. Complex **2** was obtained in 92% yield by refluxing hydrated manganese(II) chloride and **1** in DMF. A number of alkenes including styrene and 1-decene, were epoxidized by the catalyst **2** according to Collman's procedure[11] with high turnovers (900–2 800) within 24 h despite the steric nature of the catalyst. Epoxides were the major products in all cases as indicated by GC analysis. The high turnover values are attributed to the steric hindrance that effectuates site isolation and prevents the porphyrin π-structure from oxidative degradation.[12] UV-vis spectroscopy revealed that 77% catalyst remained intact after reaction. Epoxidation of limonene was used to benchmark various axial ligands containing *N*-donor atoms for enhancement of regioselectivity. The results are collected in Table 1. In these internal competition experiments, a 3 : 1 alkene to oxidant ratio was used in order to avoid the formation of over-oxidized products. In general, addition of pyridine-type ligands could lead to a leap of regioselectivity. The selectivity to produce 8,9-limonene oxide was 33% without axial ligand (entry 1). Interestingly, 4-phenyl- and 4-cyano- pyridines, with significance differences in electronic property, gave comparable terminal selectivity (entry 2 and 3). Good results of terminal selectivity from 64–66%, were obtained with DMAP, 4-*tert*-butylpyridine and pyridine (entry 4, 5 and 6) and these are slightly higher than that obtained with Mn(TTPPP)(OAc) reported by Suslick.[5] For imidazole (entry 7) having concentrated π-electrons (6π electrons in a five-membered aromatic ring), there was a moderate enhancement in regioselectivity but no improvement in turnover was observed. In the case of morpholine containing a sp^3 *N*-donor atom (entry 8), the improvement was comparatively less when compared to the more electron–rich counterpart (entry 9), *N*-methylmorpholine. On the whole, the results indicate an indirect evidence of 'aminophilicity' of the high valent manganese intermediate in the catalytic cycle and some dependence on electronic properties of the amines, however, there is no obvious dependence on the electron donating power of substituted pyridines. Thus, the increase in regioselectivity cannot be solely attributed to electronic effect. Plausible explanations for the general im-

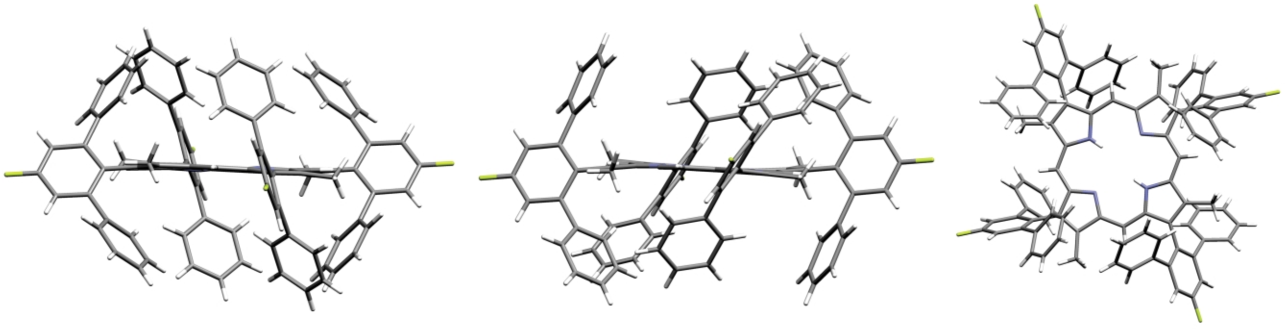


Fig. 1 Top and side views of molecule structure of $C_{96}H_{66}F_4N_4$ **1** based on X-ray crystallographic study.

DOI: 10.1039/b210645k

Table 1 The effect of various organic bases in regioselective epoxidation of limonene by catalyst **2** using Clorox as oxidant[a]

Entry	Axial ligand	Turnover number	% of the less substituted epoxide[b]
1	Chloride	259	33
2	4-Cyanopyridine	521	57
3	4-Phenylpyridine	501	57
4	DMAP[c]	560	65
5	4-*tert*-Butylpyridine	532	66
6	Pyridine	593	64
7	Imidazole	216	54
8	Morpholine	461	42
9	Methylmorpholine	371	61

[a] Reaction condition: all reactions were carried out in CH_2Cl_2 at room temperature, with a catalyst:axial ligand:oxidant:alkenes molar ratio of 1:30:800:2000 and stirred for 24 h; [b] Determined by GC-MS with HP-5 capillary column. [c] DMAP = 4-*N*,*N*-dimethylaminopyridine.

provement by axial ligation is the presence of structural modulation that the binding of the organic bases in the highly crowded environment would restrict the rotational freedom of the terphenyl rings against the porphyrin plane leading to a comparatively more rigid pocket on the other side for efficient molecular regionalization results. Also, the increase in regioselectivity may be due to a subtle alteration of the pocket shape caused by conformational changes such as ruffling of the porphyrin plane upon coordination. One of the complications could be the involvement of *N*-oxides as axial ligand because the amines are prone to oxidation although it is regarded as a minor problem in alkene epoxidation.[13] Another important consideration is the involvement of different reactive species generated depending on axial ligands.[14] By spectrophotometric titration, the binding constant K_{eq} for DMAP to coordinate to **2** was determined to be 7.48×10^3 dm^3 mol^{-1} (298.0 K) that is comparable to that for the reaction between Zn(TPP) and pyridine. Thus, no extra difficulty is encountered for the axial coordination in the steric environment. DMAP was used in the following experiments. The same scenario repeated for 1-methyl-1,2,4,5-cyclohexadiene, 1,2,5,6-undecadiene and 7,7-dimethyl-1,2,5,6-octadiene. Fig. 2 provides a pictorial comparison for the dienes among MCPBA, **2**–Clorox and **2**–Clorox–DMAP. For 1-methyl-1,2,4,5-cyclohexadiene, a three-fold increase in regioselectivity towards the less substituted one (from 11% to 33%) was observed. In oxidation to the two linear non-conjugated dienes, above 90% less substituted epoxides were produced. This selectivity is complementary to that of most conventional epoxidizing reagents such as peracids and $Mo(CO)_6$–TBHP. In fact, the regioselectivity is intrinsically difficult to achieve as the reactivity of 1,2-disubstituted alkenes is at about 21 times faster than that of mono-substituted alkenes in epoxidation.[15] To our knowledge, this is an unprecedented example that the utilization of axial ligand can lead to a dramatic increase in regioselectivity for metalloporphyrin catalyzed alkene epoxidation although the mechanistic aspects have not been amply understood.

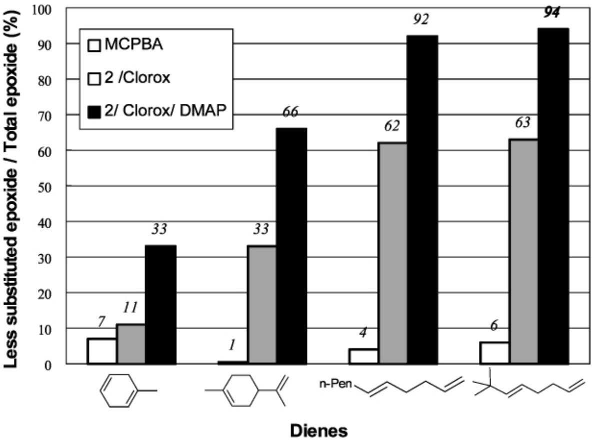


Fig. 2 Percentage of less substituted epoxides formed by epoxidation of dienes using MCPBA, **2**–Clorox and **2**– Clorox–DMAP.

We acknowledge support from Research Grant Council of Hong Kong (HKUST 6182/99P & AoE/P-10/01).

Notes and references

† Crystallographic data for (**1**): $C_{96}H_{66}F_4N_4{\cdot}2CH_2Cl_2$, M = 1350.52, crystal dimension = 0.40 mm × 0.20 mm × 0.20 mm, monoclinic, space group $P2_1/n$, a = 11.0987(10), b = 24.357(2), c = 14.4675(12) Å, α = 90, β = 98.770(2), γ = 90°, U = 3865.3(6) Å^3, T = 100 K, Z = 2, D_c = 1.307 Mg m^{-3}, Mo-Kα (λ = 0.71073 Å), absorption coefficient = 0.216 mm^{-1}, F(000) = 1580, max and min. transmission 0.9581 and 0.9187, reflections collected = 21372, independent reflections = 7867 [R(int) = 0.0397], total parameters = 518, R1 = 0.0650 and wR2 = 0.1487 for $I > 2\sigma(I)$, GOF = 1.018, the final difference map give maxima and minima 0.693 and −0.577 e Å^{-3} respectively. CCDC 196833. See http://www.rsc.org/suppdata/cc/b2/b210645k/ for crystallographic data in CIF or other electronic format.

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