Enantiomeric Epoxidation of 4-Chlorostyrene with H_2O_2 catalysed by Robust Chloro Manganese(III) *meso*-5,10,15,20-Tetrakis[2-chloro-6-(2,3,4,6-tetraacetyl-*O*-β-glucosyl)-phenyl] Porphyrins

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Three new chiral porphyrins bearing chloro and glucosyl groups are obtained by Lindsey's method; their chloro manganese(III) complexes are robust catalysts for the asymmetric epoxidation of 4-chlorostyrene with diluted hydrogen peroxide.

In the last fifteen years, many enantioselective epoxidations of unfunctionalized alkenes catalysed by metal complexes of porphyrins[1] or salens[2] have been developed. In these approaches, oxygen transfer to the substrate can be effected by high-valent metal oxo species formed by oxidizing Fe^{III} or Mn^{III} prophyrins with molecular oxygen, iodosoarenes, sodium hypochlorite, alkyl hydroperoxides and hydrogen peroxide, amine *N*-oxides, potassium persulfate and organic peroxy acids as oxygen atom sources.[3] Such reactions dealt with the shunt mechanism occurring in catalytic cycle of cytochrome P-450 enzymes.

Among these, diluted hydrogen peroxide is attractive because it is a cheap and mild reagent with only water being formed in the waste product. However, the catalytic reactions with hydrogen peroxide have been limited because it is often too reactive in transition metal catalysed oxidations giving a fast oxidative destruction of the catalyst.[4] Thus, few papers described the asymmetric oxidation using H_2O_2 as the source of oxygen.[5]

In our effort to develop new chiral porphyrins in goal to obtain catalysts for an enantioselective epoxidation of alkenes, we have recently synthesized porphyrins bearing acetylated sugar substituted at the *ortho* position of the *meso* phenyl groups.[6] The manganese and iron complexes of these glycosylated compounds are both oxidatively robust and able to epoxidize stereoselectivity 4-chlorostyrene in presence of iodosylbenzene.[7] Unfortunately, the use of H_2O_2 gives a partially destruction of these catalysts.†

Here, we report the synthesis of chloro Mn^{III} *meso*-5,10,-15,20-tetrakis[2-chloro-6-(2,3,4,6-tetraacetyl-*O*-β-glucosyl)-phenyl] porphyrins and the preliminary results of oxidative properties towards 4-chlorostyrene as substrate. In these molecules, the glucosyl substituents linked at the one *ortho* position of the *meso* phenyl groups give the chiral environment of catalytic site whereas the presence of strong electron-withdrawing chloro atoms at the other *ortho* position induces stability of catalysts.[8]

The required *meso*-5,10,15,20-tetrakis[2-chloro-6-(2,3,4,6-tetraacetyl-*O*-β-glucosyl)-phenyl] porphyrins **1a**, **2a**, **3a** were prepared following the method described by Lindsey *et al.*[9] from the reaction of **6** and pyrrole in 9% yield. The condensation of compound **5** previously obtained by NaOH hydrolysis from 2-fluoro-6-chloro benzaldehyde **4**[10] with α-bromoacetylglucose in a heterogeneous phase following the Halazy's[11] method afforded the corresponding *ortho* glycosylated benzaldehyde **6** in 55% yield (Scheme 1). TLC on silica gel showed that the mixture contained only three atropisomers: **1a** (αβαβ), **2a** (ααββ), **3a** (αααβ) obtained in 1, 3, 5% yield, respectively. These compounds were characterized by ^1H NMR spectroscopy.† Thermal atropoisomerisation of these compounds to obtain the αααα atropisomer was unsuccessful even when they were refluxed in xylene. This contrasted to that observed for the *ortho* glucosylated compounds without chloro groups.[12]

The manganese complexes **1b**, **2b**, **3b**§ were prepared by treatment of free base porphyrins with $MnCl_2$ in presence of excess of 4-nitrophenol at reflux in DMF under argon.[13] These metalloporphyrins were used to catalyse the epoxidation of 4-chlorostyrene with iodosylbenzene and hydrogen peroxide

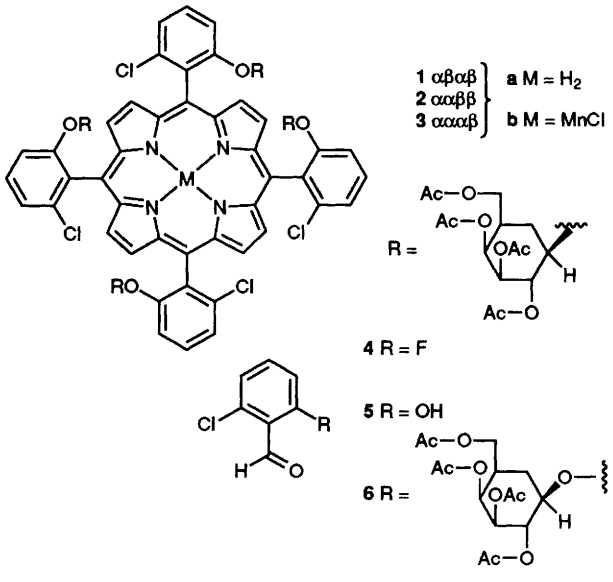

Table 1 Asymmetric epoxidation of 4-chlorostyrene by Mn(TDCPP)Cl, Mn(2-Cl-6-GlucOAc$_4$)$_4$Cl αβαβ **1b**, ααββ **2b**, αααβ **3b**

	4-Chlorostyrene + PhIO[a]			4-Chlorostyrene + H_2O_2[b]		
	Total yield	EE[c]	Turnover[d]	Total yield	EE	Turnover
Mn(TDCPP)Cl	25	0	39	66*	0	132
1b	25	20	49	24.5	23	64
2b	26	19	49	31	22	62
3b	45	16	57	29**	22	58

[a] Reaction was run for 1 h in the dark with 416 μmol of alkene, 150 μmol of PhIO, 0.4–0.6 μmol of catalyst, 200 μmol of 4-picoline in 1 ml of CH_2Cl_2 under argon at 25 °C. Yields were based upon PhIO consumed and determined by calibrated GC integrations. [b] Reaction was performed for 4 h (or for 2 h 30* and or for 5 h 30**) after an addition of H_2O_2 (30% in H_2O, 400 equiv. relative to catalyst) over 15 min at 25 °C to a mixture of 100 μmol of 4-chlorostyrene, 200 μmol of 4 *tert*-butylpyridine, 20 μmol of benzoic acid and 0.38–0.5 μmol of catalyst in 1 ml of CH_2Cl_2. Yields were based on the initial quantity of 4-chlorostyrene. [c] Determined in the presence of Eu(hfc)$_3$. [d] Turnover number = mol of 4-chlorostyrene converted per mol of catalyst.

in CH_2Cl_2. The epoxidized products were analysed by GC and isolated by silica gel column chromatography with pentane–ether (85:15, v/v) as eluent. Enantiomeric excess was determined by ^1H NMR using paramagnetic chiral shift reagent.[14] Results of epoxidation reactions are presented in Table 1 and compared with those obtained with the chloro Mn^{III} *meso*-5,10,15,20-tetrakis(2,6-dichlorophenyl)porphyrin [Mn(TDCPP)Cl][15] known to have a remarkable stability towards oxidation degradation.[4]

Reactions using PhIO gave 4-chlorostyrene epoxide with a similar yield to those obtained with the no-chlorinated glucosylated porphyrins.[7] Furthermore, complexes **1b**, **2b**, **3b** proved to be good catalysts for the epoxidation of 4-chlorostyrene by H_2O_2 in the presence of 4-*tert*-butylpyridine as axial ligand.[16] They led to give the epoxidation derivative in 24–31% yield. The catalytic efficiency of these systems was relatively low in comparison with that observed with Mn(TDCPP)Cl (66%) used under identical conditions. Note that a mixture of the three atropoisomers gave a similar enantiomeric excess (16 and 22% with PhIO and H_2O_2) and a yield of epoxidation lightly weaker than individual isomers (22 and 23% with PhIO and H_2O_2).

With PhIO and H_2O_2, the low ee in favour of the (*R*)-epoxide compound suggest that the flexibility of glucosylated substituents is too important to induce a specific stereoselective approach of the substrate.

With the *ortho* glucosylated unchlorinated porphyrins,[6] rapid autooxidation of the catalyst occurred† whereas a high stability of compounds **1b**, **2b**, **3b** is likely a result of the presence of chloro atoms. On progressive addition of a large excess of H_2O_2 to the reaction mixture at 25 °C results only a very low destruction of the catalysts (*ca.* 5%) at the end of the epoxidation. Thus, when a sample of used catalyst was isolated, purified and committed to another oxidation of 4-chlorostyrene, the same ee was obtained. This indicates that the catalyst has not been altered during the oxidation.

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Footnotes

† After a progressive addition of H_2O_2 (30% m/m in H_2O, 500 equiv. relative to catalyst), 50% of catalysts is destroyed in 30 min.

‡ ^1H NMR ($CDCl_3$) δ **1a**: 8.78 (s, 4H, pyr), 8.56 (s, 4H, pyr), 7.64 (m, 12H, phenyl), 4.7 (t, 4H, H ose, *J* 9 Hz), 4.66 (d, 4H, H ose, *J* 8 Hz), 4.33 (t, 4H, H ose, *J* 9 Hz), 4.20 (m, 12H, H ose), 3.55 (m, 4H, H ose), 2.14(s), 1.84(s), 1.20(s), −1.24 (s, 48H, acetyl), −2.74 (s, 2H, NH).

2a: 8.75 (d, 2H, pyr), 8.66 (d, 2H, pyr), 8.66 (s, 2H, pyr), 8.56 (s, 2H, pyr), 7.80–7.51 (m, 12H, phenyl), 4.91 (d, 4H, H ose *J* 8 Hz), 4.82–4.60 (m, 6H, H ose), 4.48 (m, 2H, H ose), 4.30–4.07 (m, 12H, H ose), 3.94 (dd), 3.76(m), 3.42(m) (6H, H ose), 2.16(s), 2.04(s), 1.87(s), 1.77(s), 1.32(s), 0.76(s), −0.95(s), −1.83(s) (48H, acetyl), −2.63 (s, 2H, NH).

3a: 8.75–8.50 (m, 8H, pyr), 7.61(m), 7.55(m) (12H, phenyl), 5.32(d), 5.25(d), 4.97(d), 4.92(d) (4H, H_1 ose, *J* 8 Hz), 4.88–4.45(m), 4.35–4.05(m), 3.95–3.60(m), 3.11(m) (24H, H ose), 2.17(s), 2.15(s), 2.11(s), 1.98(s), 1.90(s), 1.89(s), 1.86(s), 1.75(s) (24H, acetyl), 1.46 (s, 6H, acetyl), 1.30(s), 0.88(s), −0.24(s), −0.37 (broad), −0.66(s), −1.49 (broad) (18H, acetyl), −2.67 (s, 2H, NH).

§ UV–VIS spectra of metallic complexes in $CHCl_3$: λ_{max}/nm, (ε mmol dm^{-3}): **1b**: 376.5 (34.8); 399.5 (33.1); 469.5 (60); 566 (8.1). **2b**: 377 (47.7); 400.5 (44.5); 470.5 (85.3); 566 (11.2). **3b**: 377 (51); 400 (50.4); 469 (102.6); 564.5 (15.4).

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