Asymmetric Epoxidation of Alkenes catalysed by a 'Basket-handle' Iron–Porphyrin bearing Amino Acids

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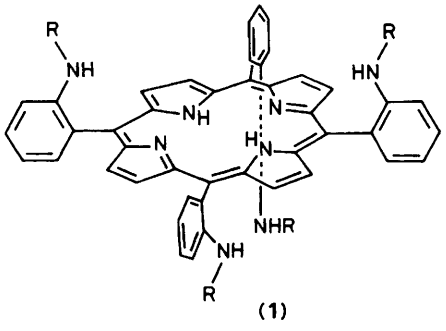
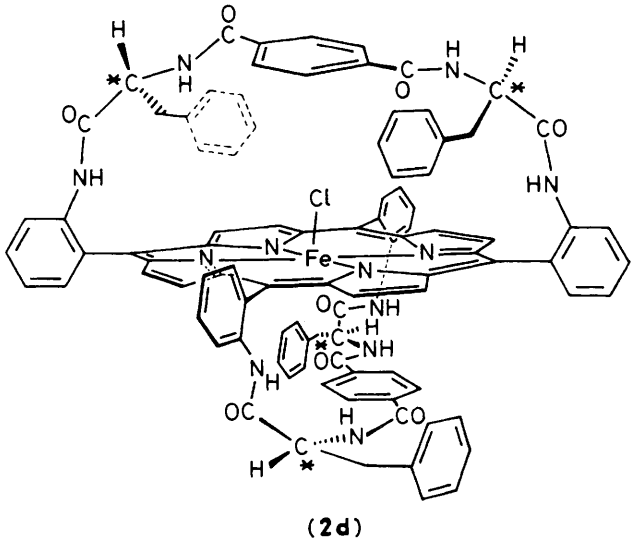
A 'basket-handle' iron–porphyrin bearing L-phenylalanine residues has been prepared and found to catalyse the epoxidation of *p*-chlorostyrene with a 50% excess of the (*R*)-epoxide, whereas 'picket' iron–porphyrins bearing the same amino acid have led to a 10—20% excess of the (*S*)-epoxide.

Mono-oxygenase-like oxygen atom transfer from iodosylbenzene to alkanes or alkenes is catalysed by simple iron–porphyrins.[1] In order to mimic the chiral recognition and asymmetric oxygenation of a substrate by cytochrome P-450 for instance, a possible method is to use iron–porphyrin catalysts bearing chiral groups in close proximity to the oxygenating centre. The first results concerning asymmetric epoxidation of alkenes by the use of an iron–porphyrin catalyst bearing chiral 'pickets' on both sides of the porphyrin plane have recently been reported.[2] We report here the first synthesis of a 'basket-handle'[3] iron–porphyrin bearing amino acids which contains a more rigid chiral environment for the iron. We also report preliminary results showing that this iron–porphyrin gives better results for asymmetric epoxidation of alkenes than the corresponding iron–porphyrins which bear 'pickets' containing the same amino acids.



(1)

a, R = H
b, R = $COCH(CH_2Ph)NHCO_2Bu^t$
c, R = $COCH(CH_2Ph)NH_2$
d, free porphyrin corresponding to (**2d**)

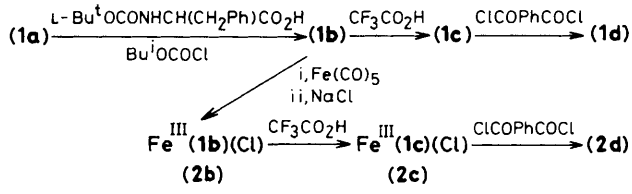


(**2d**)

Structures (**2a—c**) are the $Fe^{III}Cl$ complexes corresponding to (**1a—c**).

Porphyrins (**1b**) and (**1c**) bearing two 'pickets' on each side of the porphyrin ring were prepared by treatment of porphyrin (**1a**)[4] with an excess of t-butoxycarbonyl-L-phenylalanine using the mixed carbonic anhydride method[5] and removal of the N-protecting group in CF_3CO_2H–CH_2Cl_2 (1 : 1) at 20 °C (Scheme 1). The free-base (**1d**) of complex (**2d**) was obtained by reaction of (**1c**) with terephthaloyl chloride in anhydrous tetrahydrofuran (THF) under high dilution conditions [5×10^{-5} M (**1c**), 30% yield]. The elemental analysis (C,H,N), mass, and ^1H n.m.r. spectra of this 'basket-handle' porphyrin (**1d**) as well as of the 'picket' porphyrins (**1b**) and (**1c**) were in complete agreement with the indicated structures. Details of their preparation and spectral characteristics, as well as studies of their conformation in solution and optical purity will be decribed elsewhere. However, the following data are noteworthy in relation to the expected conformational rigidity of (**1d**) and the proximity of its handles to the porphyrin plane: (i) the ^1H n.m.r. signals corresponding to the amino acid protons are very much sharper in (**1d**) than in (**1b**), indicating a severe restriction of the conformational freedom; (ii) the chemical shifts of the terephthalic and N–H pyrrolic protons are respectively 3.5 and −4.0 instead of 8.1 and −2.7 in terephthalic acid and (**1b**), indicating a good proximity of the terephthalic and porphyrin rings.

The iron complex (**2b**) was prepared by treatment of (**1b**) with $Fe(CO)_5$ and I_2,[6] followed by aqueous NaCl. Complexes (**2c**) and (**2d**) were prepared from (**2b**) as indicated in Scheme 1. The elemental analysis and mass spectrum of (**2d**) as well as the ^1H n.m.r. spectrum of its Fe^{II} complex are in complete



Scheme 1

Table 1. Epoxidation of *p*-chlorostyrene by iodosylbenzene catalysed by complexes (**2b**), (**2c**), and (**2d**).[a]

Catalyst	% Yield of isolated epoxide[b]	% Enantiomeric excess (major isomer)
(**2b**)	50	12 (*S*)
(**2c**)	45	21 (*S*)
(**2d**)	35	50 (*R*)

[a] Conditions: catalyst in *p*-chlorostyrene, CH_2Cl_2, C_6H_6 (1 : 1 : 1). Slow addition of PhIO at −5 °C under argon over 2 h (*p*-chlorostyrene, PhIO, catalyst 1500 : 5 : 1). [b] Based on initial PhIO.

agreement with the proposed structure. The three complexes (**2b**), (**2c**), and (**2d**) were found to be active as catalysts for *p*-chlorostyrene epoxidation by iodosylbenzene (35—50% yield, Table 1). The epoxides were isolated under argon and their enantiomeric excess determined by ^{1}H n.m.r. with the use of a chiral shift reagent, tris-[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III).[2] As expected, the best enantiomeric excess was obtained with (**2d**) which involved the most rigid conformation of the amino acids in close proximity to the iron centre. However, the most striking result is the formation of an excess of (*S*)-epoxide with (**2b**) and (**2c**) and of an excess of (*R*)-epoxide with (**2d**). The latter result could be explained by taking into account the preferred rigid geometry of the amino acids in (**2d**) which favours the approach of the alkene[1b] presenting its *re* face to the FeO reactive species. The origin of the predominant formation of the other epoxide enantiomer with (**2b**) and (**2c**), indicating a preferred reaction of the FeO species with the *si* face, remains to be determined. This requires a conformational analysis of (**2b**) and (**2c**) in solution.

These first data on the control of chiral recognition of a substrate by amino-acids held in close proximity to the iron in ferriporphyrins suggest that studies on catalysts similar to (**2d**) should lead to the design of efficient catalysts for chiral oxidation as well as to the understanding of the role of amino acids in hemoprotein-catalysed oxidations.

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