Photocatalytic Enantiodiscriminating Oxygenation with Cyclodextrin-linked Porphyrins and Molecular Oxygen

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2,6-Permethylated β-cyclodextrin-linked iron and manganese porphyrins catalyse the enantioselective oxygenation of a racemic mixture of (*S*)-α-pinene and (*R*)-α-pinene with molecular oxygen under irradiation with visible light.

Recently, we reported the photocatalytic oxygenation of alicyclic alkenes with μ-oxo-bis(tetraphenylporphyrinato)-iron(III)[1] or tetraarylporphyrinatomanganese(III)[2] and molecular oxygen yielding allylic oxygenation products and/or epoxides depending on the structure of the alkene and the porphyrin used. We describe here for the first time a photocatalytic enantioselective oxygenation of a racemic α-pinene mixture using chiral modified porphyrins and molecular oxygen. The work was stimulated by the fact that the bark beetle *Ips paraconfusus*, a common wood parasite, utilizes only (*S*)-α-pinene from the (*S*)-α-pinene–(*R*)-α-pinene mixture occurring in the turpentine of coniferous trees for the cytochrome P-450 mediated formation of its main pheromone component (*S*)-*cis*-verbenol.[3]

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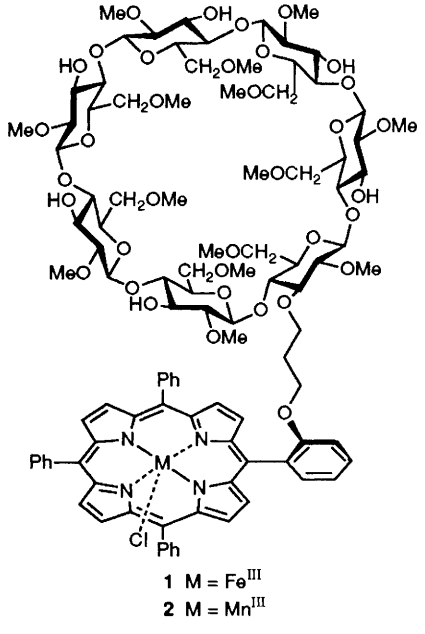
Although various chiral porphyrins have been used with different success to mimic enantioselective oxygenation reactions of cytochrome P-450 enzymes, none of the previous authors used molecular oxygen as the oxygen source or light irradiation to generate the catalytically active species.[4] Similarly, cyclodextrin-linked porphyrins or cyclodextrin–porphyrin mixtures with iodosylbenzene have already been used in oxygen transfer reactions but no enantioselectivity was observed.[5]

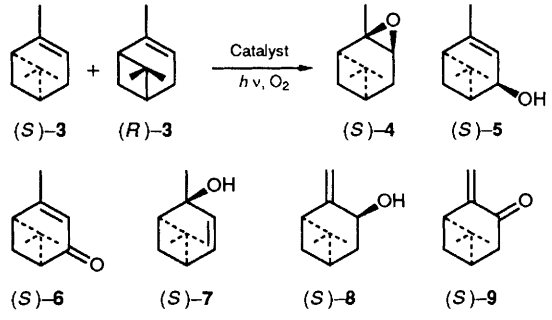
However, it is well known from chiral glass-capillary gas chromatography that heptakis-(2,6-di-*O*-methyl)-β-cyclodextrin (DMCD) is capable of separating the (*S*)-(−)- and (*R*)-(+)-α-pinene enantiomers although it was not determined which enantiomer forms a more favourable inclusion complex; moreover, no direct correlation exists between retention times and formation of inclusion complexes.[6] We decided to connect this modified cyclodextrin with a metalloporphyrin

Table 1 Photocatalytic oxygenation of a racemic α-pinene mixture [(*S*)-α-pinene : (*R*)-α-pinene = 1 : 1] with various iron and manganese porphyrins[a]

Catalyst	Solvent	Catalyst turnover[b]	Products, mol %[c] (enantiomeric excess, e.e. %)[d]					
			4	**5**	**6**	**7**	**8**	**9**
1	Benzene	144	35 (5)	18 (5)	30 (6)	14 (4)	3 (10)	—
1	MeCN	15	51 (11)	26 (18)	23 (3)	—	—	—
1	Acetone	16	29 (20)	26 (8)	17 (4)	14 (3)	8 (21)	6 (16)
1 + 2-MePy[e]	Benzene	4	41 (41)	11 (49)	10 (5)	9 (58)	11 (67)	9 (23)
2 + 2-MePy[e]	Benzene	3	36 (67)	15 (57)	12 (13)	11 (67)	15 (59)	11 (33)
FeTPPCl + DMCD + 2-MePy[f]	Benzene	3	50 (51)	17 (6)	17 (7)	—	16 (11)	—
MnTPPCl + DMCD + 2-MePy[f]	Benzene	58	26 (0)	22 (9)	38 (7)	4 (7)	5 (12)	5 (0)

[a] The photocatalytic oxygenation reactions were performed in a 50 ml thermostatted (25 °C) stirred photoreactor, equipped with a 55 W tungsten immersion lamp, with a stream of dry air (2 l h^{-1}) passing through the solution during the reaction period of 8 h. The catalysts (10 μmol) and a mixture of 5 mmol of (*S*)-α-pinene and 5 mmol of (*R*)-α-pinene were dissolved in 50 ml of dry solvent. [b] Moles of product formed per mole of catalyst. Product analysis was performed by quantitative capillary gas chromatography on a Hewlett-Packard 5890 IIA instrument, using n-decane as internal standard. [d] A 25 m fused silica CP-cyclodextrin-B-236-M-19 glass capillary column (Chrompack) was used for determination of the enantiomeric excess using authentic samples of the corresponding homochiral compounds **4–9**. In all cases the (*S*)-enantiomers were formed in excess. [e] 5 Equiv. of 2-methylpyridine were added per mole of catalytst. [f] 5 Equivalents of heptakis-(2,6-di-*O*-methyl)-β-cyclodextrin and 2-methylpyridine were added per mole of catalyst.





using a propyl spacer group,‡ thus modelling the chiral protein environment of cytochrome P-450 enzymes. The porphyrin-linked cyclodextrin iron **1** and manganese **2** complexes were used in the photocatalytic reaction with an artificial racemic mixture of (*S*)-α-pinene and (*R*)-α-pinene **3** and molecular oxygen.

On irradiating the reaction mixture with visible light (λ > 350 nm) in the presence of air, we obtained typical oxygenation products as already described with achiral iron manganese prophyrins: α-pinene oxide **4**, *trans*-verbenol **5**, verbenone **6**, *trans*-pin-3-en-2-ol **7**, *trans*-pinocarveol **8** and pinocarvone **9**.[8]

Different product compositions and enantiomeric ratios were observed, depending on the solvent and the catalyst used. However, in all cases the (*S*)-enantiomers of **4–9** were obtained in excess. The photocatalytic reaction of **1** in acetone or acetonitrile as solvent gave higher enantiomeric discrimination between both pinene enantiomers than in benzene, probably because of the higher polarity of the solvents forcing the apolar pinene into the hydrophobic cyclodextrin cavity (Table 1). The highest e.e. values were observed for both **1** and **2** upon addition of a base, 2-methylpyridine (2-MePy), to the reaction mixture. This might be due to axial complexation with the metal centre at the unprotected side of the porphyrins, thus preventing oxygenation reactions at the 'achiral site' of the porphyrins. As a consequence of complexation the turnover numbers decreased, as similarly observed for tetraphenylporphyrins.[2]

To compare the results for the supramolecular catalysts **1** or **2** with the chemoselectivity of the unlinked components, reactions with the tetraphenylporphyrins and the 2,6-permethylated cyclodextrin were carried out, resulting in products with much lower e.e. ratios. Similarly, the thermal oxygenation of the racemic pinene mixture with iodosylbenzene and **1** yielded more selectively α-pinene oxide (92%) **4** and *trans*-verbenol (8%) **5** but only low e.e. values of 5% for both compounds.

The observed enantiomeric discrimination between the two pinene enantiomers in the case of α-pinene oxide **4** as well as for **5**, **7** and **8** in the oxygenation reactions with the **1** or **2**–O_2–*hν*–2-MePy system with up to 67% e.e. points towards a common oxygenation mechanism centred at the chiral

‡ Compounds **1** and **2** were prepared from 5-(2-hydroxyphenyl)-10,15,20-tetraphenylporphyrin by reaction with excess of 1,3-dibromopropane in K_2CO_3–acetone, metallation with anhydrous $FeBr_2$ or $MnCl_2$ and treatment with heptakis-(2,6-di-*O*-methyl)-β-cyclodextrin (prepared by a procedure described by Stoddart *et al.*[7]) with NaH–dimethylformamide (DMF) at elevated temperature to form the μ-oxo dimers from which **1** and **2** were liberated with hydrochloric acid. The structures of **1** and **2** were confirmed by FAB mass spectroscopy and spectral data. Both compounds gave satisfactory combustion analysis.

porphyrin site. On the other hand, the lower e.e. values for the ketones **6** and **9** seem to correspond partially to an autoxidation mechanism for these compounds.

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