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Mono-oxygenase-like Dioxygen Activation leading to Alkane Hydroxylation and Olefin Epoxidation by an Mn^{III}(porphyrin)–Ascorbate Biphasic System

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A biphasic H_2O–C_6H_6 system, which has Mn^{III}(tetraphenylporphyrin)(Cl) and a phase transfer agent as catalysts and ascorbate as a reducing agent, activates dioxygen leading to selective epoxidation of olefins and hydroxylation of alkanes under mild conditions.

Cytochrome P450-dependent mono-oxygenases catalyse the reductive activation of dioxygen by NADPH and the insertion of one oxygen atom into organic compounds.[1] Under anaerobic conditions, they catalyse the reduction of substrates such as nitroarenes, amine epoxides, arene epoxides, and halogenated compounds.[2] We recently described a biphasic heme model system able similarly to reduce all these substrates under anaerobic conditions.[3] This system uses ascorbate as a reducing agent in water, an iron-porphyrin to catalyse electron transfer towards the substrate in C_6H_6, and a catalytic amount of a phase transfer agent.[3] Under aerobic conditions, this system is unable to activate dioxygen and to oxidise substrates such as alkanes or olefins. However, we found very recently that, simply by replacing the Fe-porphyrin by an Mn-porphyrin, it becomes capable of oxidising many substrates. Other systems using dioxygen, Mn-porphyrins as catalysts, and either a borohydride[4,5] or H_2 (in the presence of Pt)[6] as reducing agents, have recently been described to oxidise terminal olefins to methyl ketones (borohydride)[5] and epoxidise olefins and hydroxylate adamantane (H_2–Pt).[6]

This communication reports preliminary results showing that our biphasic Mn(porphyrin)–ascorbate–O_2 system performs selective epoxidation of olefins, hydroxylation of alkanes, and oxidation of alcohols under especially simple and mild conditions.

In a typical experiment, Mn(TPP)(Cl) (TPP = dianion of tetraphenylporphyrin) (5 μmol) was dissolved in a C_6H_6–substrate (1 ml/1 ml) mixture and sodium ascorbate (0.5 mmol) was dissolved in a 1 M tris–HCl buffer pH 8.5 [tris = tris(hydroxymethyl)methylamine]. Trioctylmethylammonium chloride (TOMA) (10 μmol) was added to the biphasic medium. Dioxygen was bubbled through for 15 min and the system was then stirred at 20 °C under 1 atm of dioxygen. The organic phase was analysed by g.l.c. and mass spectrometry.

With cyclohexene as substrate, epoxycyclohexane is the only product of the reaction when all components of the system are present. In the absence of dioxygen or manganese-porphyrin, no oxidation takes place. However, in the absence of either sodium ascorbate or phase transfer agent, cyclohexenone, cyclohexenol, and epoxycyclohexane are formed in a ratio of 79:20:1 which is characteristic of cyclohexene

Table 1. Oxidation of various substrates by the system Mn(TPP)(Cl)–ascorbate–O_2.

Substrate	Products (yields, %)[a]
Styrene	Styrene oxide (600) 2-Phenylethanal (80)
Cyclohexene	1,2-Epoxycyclohexane (230)
Hex-1-ene	1,2-Epoxyhexane (30)
2,3-Dimethylbut-2-ene	2,3-Dimethyl-2,3-epoxybutane (340)
Cyclohexane	Cyclohexanol (40) Cyclohexanone (300)
Heptane	Heptan-4-one (30) Heptan-3-one (130) Heptan-2-one (70)
Toluene	Benzaldehyde (400)
Cyclohexanol	Cyclohexanone (1500)
Heptan-4-ol	Heptan-4-one (1300)
Benzyl alcohol	Benzaldehyde (8700)

[a] Yields, based on Mn(TPP)(Cl), measured after 10 h at 20 °C (conditions indicated in the text). In one experiment, with styrene as substrate, we used identical conditions except for styrene concentration which was reduced in order to have a 100:1 styrene:Mn(TPP)(Cl) molar ratio; after 10 h of reaction at 20 °C the yields of styrene oxide and 2-phenylethanal were 220 and 25% based on Mn(TPP)(Cl) or 2.2 and 0.25% based on the substrate (yield of styrene oxide, based on consumed styrene >75%).

autoxidation.[4,7] These results suggest that sodium ascorbate acts not only as a reducing agent, as expected, but also as an efficient inhibitor of the autoxidation process.

As shown in Table 1, the complete system is also able to epoxidise several other olefins and to oxidise alkanes and alcohols. With all these substrates, no oxidation occurs in the absence of any component of the system [O_2, sodium ascorbate, Mn(TPP)(Cl), TOMA]. Moreover, product formation is linear with time for days and no destruction of the manganese-porphyrin could be detected after 2 days reaction, indicating that the Mn-porphyrin acts as a real catalyst. Under these conditions (pressure of dioxygen = 1 atm, pH 8.5) the reactions stop after *ca.* 2 h, because sodium ascorbate is rapidly consumed not only in substrate oxidation but also in secondary reactions such as its direct reaction with O_2. After addition of more sodium ascorbate, the reactions start again at the same rate. When lower pH (7.4) or lower dioxygen pressure (in aerated solvents) is used, the reducing agent is consumed more slowly but the rates of substrate oxidation are lower.

Differently substituted olefins are selectively oxidised to the corresponding epoxides, except for styrene, the oxidation of which also gives minor amounts of 2-phenylethanal. It is noteworthy that, contrary to the Mn(TPP)(Cl)–O_2–borohydride system which oxidises terminal olefins to methyl ketones,[5] this system leads only to epoxides.

The Mn(TPP)(Cl)–ascorbate–O_2 system is able to oxidise alkanes leading mainly to ketones or aldehydes; minor amounts of cyclohexanol are also formed upon cyclohexane oxidation. It appears to be at least as efficient as the previously described Mn(TPP)(Cl)–O_2–H_2(Pt) system for alkane oxidation since the former oxidises cyclohexane to 420% cyclohexanone and 56% cyclohexanol in 14 h, whereas the latter hydroxylates adamantane to 330% adamantan-1-ol and adamantan-2-ol at the same time. Finally, the Mn(TPP)(Cl)–O_2–ascorbate system is very efficient for the oxidation of alcohols to ketones or aldehydes.

Very few metalloporphyrin-dependent systems able to perform oxygenation of alkanes or olefins upon dioxygen activation have been reported so far. Our system is able to perform such reactions under mild and very simple conditions (room temp., pH 8.5).

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