A New and Efficient Biomimetic System for Hydrocarbon Oxidation by Dioxygen using Manganese Porphyrins, Imidazole, and Zinc

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Epoxidation of alkenes and hydroxylation of alkanes by dioxygen and Zn as a reducing agent, with good yields (up to 50%) based on Zn and rates (up to 200 turnovers of the catalyst per hour), were achieved by using manganese porphyrin catalysts in the presence of 1-methylimidazole and acetic acid.

Cytochromes P-450 catalyse the mono-oxygenation of hydrocarbons not only by O_2 and a reducing agent like NADPH [reaction (1)], but also by various single-oxygen atom donors.

$$RH + O_2 + 2e^- + 2H^+ \xrightarrow{\text{P-450}} ROH + H_2O \quad (1)$$

Very efficient biomimetic systems for alkene epoxidation and alkane hydroxylation, using iron or manganese porphyrins as catalysts and oxygen donors such as PhIO, ClO^-, amine oxides, alkyl hydroperoxides, and H_2O_2, have been reported.[1] In the case of the two latter oxidants containing an O–O bond, the use of imidazoles as cocatalysts seems to be necessary.[1f,1g,2] The problem of biomimetic hydrocarbon oxidations by O_2 itself in the presence of a reducing agent is more difficult because of secondary reactions between the highly reactive oxygenating intermediate and the reducing agent in excess.[3,4] The different systems described so far, where a metalloporphyrin catalyst was associated with various reducing agents, *i.e.*, $NaBH_4$,[5] NBu_4BH_4,[6] sodium ascorbate,[3] H_2 in the presence of Pt,[4,7] and electrons,[8] have generally led to low oxidation rates and/or poor yields based on the reducing agent. Better results for both the epoxidation rates and yields based on the reducing agent have been reported recently for a system using a dihydropyridine as reducing agent in the presence of a flavin and a water soluble Mn porphyrin catalyst.[9]

In this communication, we describe a new system where O_2 is reductively activated by a simple reducing agent, Zn, in the presence of an Mn porphyrin and imidazole,[10] which epoxidizes alkenes with yields based on the reducing agent of up to 50%, with satisfactory rates when compared to cytochrome P-450 itself, and with satisfactory alkene conversion.

In a typical experiment, Zn powder (150 equiv. with respect to Mn catalyst) and AcOH (87 equiv.) were slowly added (during 0.5 h) to a MeCN solution of cyclo-octene (385 mM) containing AcOH (87 mM), 1-methylimidazole (50 mM), and Mn(TPP)(Cl) (TPP = *meso*-tetraphenylporphyrin) (1 mM). The reaction mixture was stirred under an atmosphere of dioxygen at 20 °C. In 0.5 h, about 75 mol of cyclo-octene epoxide were formed per mol of Mn(TPP)(Cl). Under these conditions, Mn(TPP)(Cl) was unchanged at the end of the reaction and a further addition of identical amounts of Zn and AcOH to the reaction mixture within 0.5 h led to similar turnovers. Four components of the system were found necessary for the epoxidation to occur: (i) the reducing agent Zn and the proton donor AcOH [reaction (2)], which are the

$$RH + O_2 + Zn + 2AcOH \xrightarrow[\text{1-Me-Im}]{\text{Mn(TPP) (Cl)}} ROH + H_2O + Zn(AcO)_2 \quad (2)$$

equivalents of NADPH and H^+ of the enzymatic system [reaction (1)], (ii) the Mn porphyrin catalyst and the imidazole cocatalyst. As shown in Table 1, almost no epoxidation occurred within 0.5 h if one of these components was omitted. Mn(TPP)(Cl) gave better results in that system than Mn(TMP)(Cl) (TMP = *meso*-tetramesitylporphyrin) and Mn(TDCPP)(Cl) (TDCPP = *meso*-tetra-2,6-dichlorophenylporphyrin) (11 and 10 turnovers in 0.5 h respectively). This result is quite different from that observed with systems using H_2O_2[1g] or PhIO[11] as oxidant, for which Mn(TDCPP)(Cl) was the best catalyst. Among the nitrogen bases tested as cocatalysts, 1-methylimidazole was superior to imidazole and

Table 1. Epoxidation of cyclo-octene by O_2 and Zn: influence of the catalyst and of the other components of the system.

Conditions	Catalytic activity[b]	Cyclo-octene epoxide yield (%) based on Zn
Complete system[a]	75	50
Without 1-Me-Im	3	2
Without Mn(TPP)(Cl)	0	0
Without AcOH	0	0
With H_2O (5%)	13	8
Im instead of 1-Me-Im	20	13
Py instead of 1-Me-Im	28	18
Mn(TMP)(Cl) instead of Mn(TPP)(Cl)	11	7
Mn(TDCPP)(Cl) instead of Mn(TPP)(Cl)	10	6

[a] Complete system: slow addition of Zn [150 equiv. relative to Mn(TPP)(Cl)] and of AcOH (87 equiv.) during 0.5 h at 20 °C to a cyclo-octene : acetic acid : 1-methylimidazole : Mn(TPP)(Cl) mixture (385 : 87 : 50 : 1) in MeCN : CH_2Cl_2 (95 : 5); [Mn(TPP)(Cl)] = 1 mM. Dioxygen was bubbled through the reaction mixture during 5 min, then the reaction was performed under an O_2 atmosphere. 1-Me-Im = 1-methylimidazole; Im = Imidazole; Py = Pyridine. [b] Mol of epoxide per mol of catalyst formed in 0.5 h.

Table 2. Oxidation of alkenes and alkanes by the system: O_2–Zn–Mn(TPP)Cl–1-Me-Im–AcOH.[a]

Substrate	Products	Turnovers per 0.5 h	Total yield (%) based on Zn
Cyclo-octene	Cyclo-octene epoxide	75	50
2-Methylhept-2-ene	2-Methylhept-2-ene epoxide	51	34
Cyclohexene	Cyclohexene epoxide	57	49
	Cyclohexen-3-one	8	
Non-1-ene	Non-1-ene epoxide	11	7
Cyclo-octane	Cyclo-octanol	6	15
	Cyclo-octanone	8	
Adamantane[b]	Adamantan-1-ol	13	12
	Adamantan-2-ol	2	
	Adamantan-2-one	1	

[a] Standard conditions: Mn(TPP)(Cl) 1 mM, substrate 385 mM, AcOH 87 mM, 1-Me-Im 50 mM; solvent MeCN : CH_2Cl_2 (95 : 5); Zn (150 equiv.) and AcOH (87 equiv.) were continuously added during 0.5 h. [b] Same molar ratio but with the solvent mixture MeCN : CH_2Cl_2 (33 : 66) and [Mn(TPP)(Cl)] = 0.66 mM.

pyridine (respective turnovers in 0.5 h: 75, 20, and 28) (Table 1). Among the solvents tested, MeCN was the most convenient, and the presence of H_2O (5% in volume) decreased the catalytic activity (13 turnovers instead of 75 in the absence of H_2O).

Initial rates measured for reactions performed with all the reactants present at the beginning (Mn : 1-methylimidazole : AcOH : Zn : cyclo-octene = 1 : 100 : 150 : 150 : 3850) were as high as 3.3 mol of epoxide per mol of catalyst per min (200 turnovers per h). The use of an additional excess (3-fold) of either AcOH or 1-methylimidazole led to marked decreases of this rate.

This Mn(TPP)(Cl)–O_2–Zn–AcOH–1-methylimidazole system led to a selective epoxidation of various alkenes (Table 2). Cyclo-octene, 2-methylhept-2-ene, and non-1-ene led almost exclusively to the corresponding epoxide with respective turnovers in 0.5 h of 75, 51, and 11. This shows a greater reactivity of electron-rich alkenes in that system. Cyclohexene led to minor amounts of allylic oxidation products in addition to cyclohexene epoxide (57 turnovers). This system is also able to hydroxylate alkanes (Table 2). Cyclo-octane was oxidized to equivalent amounts of cyclo-octanol and cyclo-octanone with a 15% total yield based on Zn. Adamantan-1-ol was the major product of adamantane oxidation (13 turnovers per 0.5 h), as in previous biomimetic systems using Fe or Mn porphyrins and single oxygen atom donors.[1]

When compared to the previously reported Mn porphyrin-dependent biomimetic systems using O_2 and a reducing agent, the above described O_2–Zn–Mn system exhibits two interesting properties: (i) catalytic activities of about 150 mol of epoxides derived from electron-rich alkenes and 30 mol of alcohols and ketones derived from cycloalkanes, formed per mole of catalyst per hour, which are much higher than those reported for previously described Mn porphyrin-dependent systems[3—8a] using ascorbate, H_2, BH_4^-, or electrolysis (turnovers found per h: about 0.3,[3] 3,[4,5] and 2[8a] respectively for alkenes and 0.6[3] and 0.3[4] for cycloalkanes), similar to those found for the Mn porphyrin–dihydropyridine–flavin system[9] (about 150 turnovers per h for cyclohexene), and not far from those usually found for cytochrome P-450 (around 10 turnovers per min for alkenes[12] and alkanes[13]); (ii) yields based on the starting reducing agent of about 50 and 15% for cycloalkenes and cycloalkanes, which are high when compared to those found for previously reported systems[3—8a] which never exceeded a few percent (except for the systems using a dihydropyridine[9] or electrochemistry[8a] for which yields of 33 and 56% were reported for alkene epoxidation).

In fact, the efficacy of the Mn–O_2–Zn–1-methylimidazole system was illustrated by its ability to convert totally 2 mmol of cyclo-octene into its epoxide (90% yield) within 1 h at 20 °C when a molar ratio of 1 : 50 : 300 : 350 : 96 of reactants (Mn : 1-methylimidazole : Zn : AcOH : alkene) was used.

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