A Model for Methane Mono-oxygenase: Dioxygen Oxidation of Alkanes by Use of a μ-Oxo Binuclear Iron Complex

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Adamantane and cyclohexane are oxidised with dioxygen in CH_2Cl_2 in the presence of acetic acid, Zn powder, and a μ-oxo binuclear iron complex.

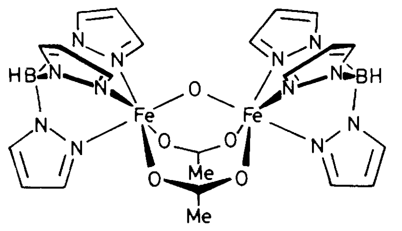
Methane mono-oxygenase is a non-heme mono-oxygenase which shows remarkable catalytic activity for dioxygen oxidation of a wide variety of alkanes, including methane under ambient conditions.[1—3] The mechanism, especially the mode of dioxygen activation, is of interest in relation to that of cytochrome P-450 which is believed to involve an oxo-iron(IV) porphyrin cation radical intermediate as an active oxygen species.[4,5] Very recently, the active site of methane mono-oxygenase has been suggested[6] to consist of a binuclear iron site, very similar to that of hemerythrin. Here we have attempted to mimic dioxygen oxidation of alkanes using a synthetic analogue of hemerythrin (**1**).

Compound (**1**) was prepared by the method described by Lippard *et al.*[7] In a typical experiment, 0.03 mmol of (**1**) were dissolved in 20 ml of CH_2Cl_2 and stirred under 1 atm. O_2 with the substrate in the presence of 0.05 ml of acetic acid (proton source) and 0.5 g Zn powder (electron donor). The results are summarized in Table 1. Adamantane (**2**) was found to be oxidised to give adamantan-1-ol (**5**) (248% yield based on the complex), adamantan-2-ol (**3**) (50%) and adamantan-2-one (**4**) (108%). The relatively low ratio of the tertiary position oxidation to the secondary position, C-3/C-2 = 2.2, implies that the present catalytic reaction is distinct from a Fenton type free-radical oxidation reaction in which typical ratios are

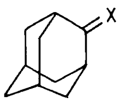
Table 1. Dioxygen oxidation of hydrocarbons.[a]

	Complex	Substrate[b]	Zn/g	Proton source (0.05 ml)	Time/h	Product yield[c] /%
1	(**1**)[d]	(**2**)	0.5	AcOH	30	(**3**) 50, (**4**) 108, (**5**) 248
2	(**1**)[e]	(**2**)	0.5	—	30	no reaction
3	(**1**)[e]	(**2**)	—	AcOH	30	no reaction
4	$Fe(acac)_3$[f]	(**2**)	0.5	AcOH	24	(**3**) trace, (**5**) trace
5	FeClTPP[e]	(**2**)	0.5	AcOH	24	no reaction
6	$[Fe(salen)]_2O$[g]	(**2**)	0.5	AcOH	30	(**5**) trace
7	(**1**)[e]	(**6**)	0.5	AcOH	30	(**7**) 99, (**8**) 84
8	(**1**)[e]	(**9**)	0.5	AcOH	30	(**10**) 54, (**11**) 73, (**12**) 20

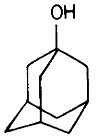
[a] Experiments were performed under 1 atm. of O_2 at room temperature in 20 ml of CH_2Cl_2. [b] 3.7 mmol were used, except in no. 1 where 3.9 mmol was used. [c] Based on the complex. [d] 0.034 mmol. [e] 0.030 mmol. [f] 0.064 mmol. [g] 0.032 mmol.



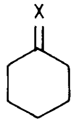
(**1**)



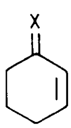
(**2**), X = H_2
(**3**), X = H,OH
(**4**), X = O



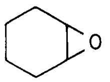
(**5**)



(**6**), X = H_2
(**7**), X = H,OH
(**8**), X = O



(**9**), X = H_2
(**10**), X = H, OH
(**11**), X = O



(**12**)

>20. Each component is essential for the oxidation reactions, but when more acetic acid (0.5 ml) was added, no oxidation was noted, owing to the formation from (**1**) of $Fe(HBPz_3)_2{}^+$ (Pz = Pyrazolyl),† which is catalytically inactive. The mononuclear iron complexes $Fe(acac)_3$ (acac = acetylacetonate) and FeClTPP (TPP = tetraphenylporphyrin) showed no catalytic activity under the same reaction conditions. Another μ-oxo binuclear complex $[Fe(salen)]_2O$ [salen = *N,N*′-ethylenebis(salicylideneaminato)] which is known to be readily converted into a mononuclear species with acetic acid was also ineffective. Not only adamantane but also cyclohexane (**6**) and cyclohexene (**9**) are oxidised catalytically to give cyclohexanol (**10**) and cyclohex-2-en-1-ol as the main product, respectively.

The time dependence of the product yields of adamantane oxidation is shown in Figure 1. No induction period was observed. Each yield increases rapidly in the initial stage, but shows a tendency to be gradually saturated.

Dioxygen oxidation of alkanes has been known to proceed in pyridine (Py) in the presence of acetic acid, Zn powder, and a μ^3-oxo trinuclear iron complex $[Fe_3O(OAc)_6Py_3]$, *i.e.* the so called Gif system.[8—10] However, the involvement of such trinuclear species in the present system is highly unlikely because μ^3-oxo trinuclear iron complexes are known to be generated only in the presence of a solvent such as pyridine which acts as a ligand of the trinuclear complex; CH_2Cl_2 has no such ligating capability.‡ Accordingly, the electronic spectra of the reaction mixture before and after the reaction did not show any absorption bands attributable to a μ^3-oxo trinuclear iron complex. Thus, we suggest that the active species is dinuclear and the reaction mechanism may be related to that of methane mono-oxygenase.

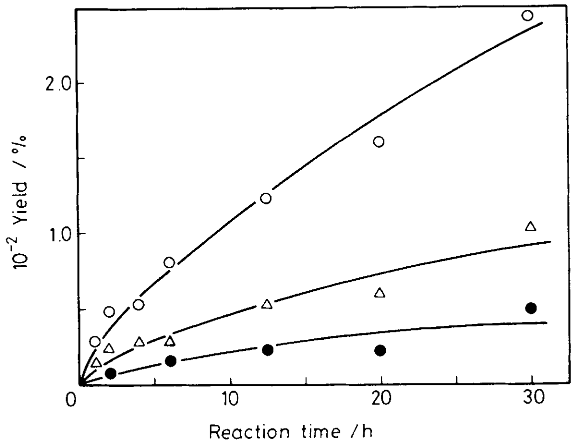


Figure 1. Time course of adamantane (3.9 mmol) oxidation with (**1**) (0.03 mmol) in 20 ml of CH_2Cl_2, with 0.05 ml of acetic acid at 25 °C. ○ = adamantan-1-ol, Δ = adamantanone, ● = adamantan-2-ol.

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† The formation of this mononuclear species was confirmed by electronic spectroscopy. The propensity of (**1**) to decompose to the mononuclear complex in highly acidic solutions was originally described by Lippard *et al.*[7]

‡ When the solvent was replaced with pyridine instead of CH_2Cl_2, this feature of the reaction was completely different. In this case, addition of a larger amount of acetic acid was necessary for the oxidation of adamantane to proceed. The reaction of 3.7 mmol of adamantane in 20 ml of pyridine in the presence of 0.5 ml of acetic acid, 0.5 g of Zn powder, and 0.03 mmol of (**1**) for 10 h, gave a 656% yield of (**3**) and 189% of (**5**). However, not only (**1**), but also $Fe(acac)_3$, FeClTPP, $FeCl_3$, $[Fe(Salen)]_2O$, and $Fe_3O(OAc)_6Py_3$ were all effective catalysts and showed almost the same activity and selectivity as (**1**), implying that the same active species, as in the Gif system, is generated under these reaction conditions.