Mendeleev Commun., 1992, 2(1), 7–8

Oxidation of Alkanes by Dioxygen in the Presence of an Iron Complex immobilized on Modified Silica. Chemical Model of Methane Monooxygenase

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A model is proposed for the activation of O_2 by methane monooxygenase using a supported binuclear iron complex as a catalytic centre in the presence of Zn as a reducing agent, methylviologen as a mediator, and acetic acid as an effector.

Nonhaem protein methane monooxygenase (MMO), containing an iron active site, catalyses the oxidation of methane and its homologues.[1] An O_2 reductive activation proceeds according to a scheme typical for all monooxygenases, with one of the two oxygen atoms being incorporated into the substrate and the other going into the water molecule which is formed [eqn. (1)], where $NADH_2$ is a reduced nicotineadeninedinucleotide.

$$CH_4 + O_2 + NADH_2 \xrightarrow{MMO} MeOH + NAD + H_2O \quad (1)$$

Recently it was shown[2] that there is a binuclear μ-oxo (or μ-hydroxo) iron complex in the MMO site, similar to the binuclear iron complexes in haemerythrin and ribonucleotide reductase,[3,4] the iron in these proteins having as ligands imidazole and carboxylate moieties of protein amino acids. It has been suggested that the active species which oxidizes hydrocarbons in the MMO catalytic cycle is a binuclear iron (IV) oxocomplex, $Fe^{IV}/^{O}\backslash Fe^{IV}{=}O$.[1,5]

Recently attempts have been made to develop chemical models of MMO.[6–8] These homogeneous catalytic systems proved to be rather ineffective due to some bimolecular side-reactions which decrease the concentration of the active particle.[9] In particular, since both reduced and oxidized iron complexes are formed in the process of reductive activation of dioxygen, they readily react with each other in homogeneous solution in side-reactions, thereby reducing the activity of the system towards a substrate. Fixation of the catalytic complex on a surface may help to avoid these reactions.

This communication presents data on the activation of O_2 on the catalytic site, which is an iron complex immobilized on imidazole-modified silica in the presence of a reductant (Zn dust), electron relay [methylviologen $MV(ClO_4)_2$] and an effector (acetic acid).

Oxidation of alkanes was carried out under ambient conditions (20 °C) with constant stirring in solution in dry acetonitrile. Methane and ethane were oxidized under pressures 50 and 7 atm, respectively. Imidazole-containing silica $Si-(CH_2)_2Ph-CH_2-Im$ (SiO_2–Im) was synthesized as described in ref. 10. The number of imidazole groups on the surface was found to be 0.12 mmol g^{-1} or one molecule per 330 Å^2. The iron complex on the surface of the modified silica was synthesized as follows: a solution of 18 mg $Fe(ClO_4)_3 \cdot 9H_2O$ and 11 mg $NaOAc \cdot 3H_2O$ in 1 ml H_2O was added to 1 g of the modified silica SiO_2–Im, followed by stirring for 10 min. It was then filtered off and dried *in vacuo*. The amount of iron on the surface was found to be 0.014 mmol g^{-1}. Ratio Im:Fe = 8.

The proposal that the binuclear iron complex is formed during this synthesis is supported by the following considerations.

(*i*) The synthesis is carried out by a procedure generally used for syntheses of binuclear complexes.[3]

(*ii*) No iron is adsorbed on the surface in the absence of acetate, which presumably forms acetate bridges.

(*iii*) An EPR signal with a *g*-factor of 4.3 at $T = 77$ K was observed for the supported catalyst. The intensity of the signal corresponds to only about 10% of the total iron concetnration on the support. The absence of a signal from most of the complex is apparently due to antiferromagnetic coupling in the binuclear complex.

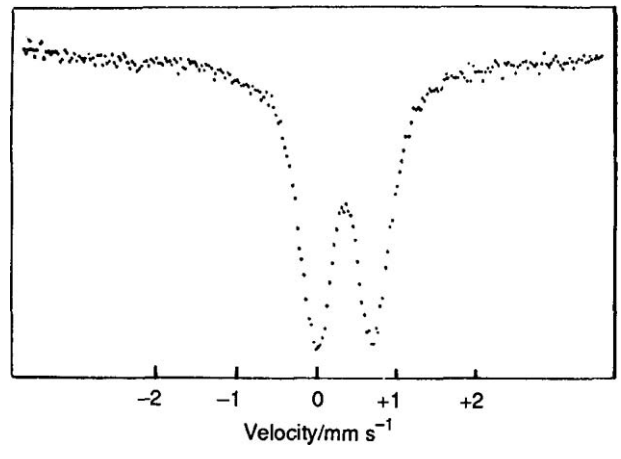

Fig. 1 Mössbauer spectra of SiO_2–Fe–Im at 300 K; the line width (Γ) is 0.46 mm s^{-1}

(*iv*) Mössbauer spectroscopy of the supported ^{57}Fe catalyst shows a narrow doublet with high-spin octahedral ferric complexes ($\delta = 0.36$ mm s^{-1}, $\Delta E_Q = 0.69$ mm s^{-1} at 300 K) (Fig. 1). A very similar spectrum was obtained for MMO ($\delta = 0.44$ mm s^{-1}, $\Delta E_Q = 0.63$ mm s^{-1} at 200 K).[11] The values of the quadrupole splitting parameter ΔE_Q for model and enzyme are unusual for binuclear μ-oxo ferric complexes ($\Delta E_Q = 1.5$–2.5 mm s^{-1}) but are, however, close to the value of ΔE_Q obtained for μ-hydroxo ferric complexes.[12]

(*v*) The visible spectrum of SiO_2–Im–Fe shows a shoulder near 360 nm, characteristic of binuclear iron complexes.[12] Thus, on the basis of the above data a structure for the SiO_2–Im–Fe complex may be proposed as shown in Fig. 2. For even distribution of imidazole on the surface, the closest distance between two imidazole groups should be *ca.* 18 Å. In fact, an uneven distribution may be suggested and the molar ratio of [Im]/[Fe] = 8 may be in agreement only with that portion of the Im pairs which are available for binuclear complex formation.

Cyclohexane oxidation using the complete catalytic system revealed that the supported catalyst SiO_2–Im–Fe is 3–5 times more active than known mono- and bi-nuclear catalysts in homogeneous solution.[9] For an iron complex supported on silica without attached imidazole groups the activity of the catalyst is at least half that of SiO_2–Im–Fe.

The oxidation of methane, ethane, hexane, cyclohexane and

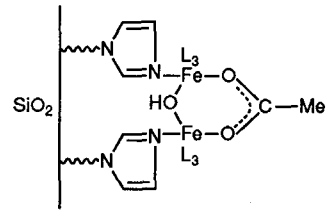

Fig. 2

Table 1 Oxidation of alkanes catalysed by SiO_2–Im–Fe[a]

Substrate	Products[b]	Concentration /mmol dm^{-3}
Methane	Methanol	0.20
	Formaldehyde	0.17
	Methanol[c]	0.30
	Formaldehyde[c]	1.10
Ethane	Ethanol[d]	1.9
Hexane	Hexan-1-ol[e]	0.6
	Hexan-2-ol	2.0
	Hexan-3-ol	2.1
Cyclohexane	Cyclohexanol	4.0
	Cyclohexanone	2.0
DMSO	Dimethylsulfone[d,f]	10.0
DMSO	Dimethylsulfone[d,g]	2.0

[a] *Reaction conditions*: 1 mmol substrate, 0.001 mmol SiO_2–Im–Fe, 0.08 mmol AcOH, 0.0025 mmol $MV(ClO_4)_2$, 0.4 mmol of Zn dust, 1 ml of acetonitrile, temp. 20 °C, time 30 min. [b] Concentrations of products were determined by GLS analysis using authentic smaples as references on a Carbowax 6000 3 m × 3 cm steel column. Formaldehyde was determined by calorimetric analysis. [c] *Reaction conditions*: 0.0004 mmol SiO_2–Im–Fe, 0.4 mmol AcOH, time 4 h, other conditions as in footnote *a*. [d] Other products were not identified. [e] The hexanols were analysed after reduction of aldehyde and ketones. [f] [DMSO] = 20 mmol dm^{-3}, conversion of DMSO 80%. [g] In the absence of catalyst. [DMSO] = 20 mmol dm^{-3} conversion of DMSO 60%.

dimethylsulfoxide using the complete catalytic systems has been studied (Table 1). Methane was oxidized to methanol and formaldehyde, with yields of about 0.4 (±0.1) mol per mol catalyst after 30 min. The same reaction at concentration [SiO_2–Im–Fe] = 0.4 mmol dm^{-3} in the presence of AcOH (0.4 mol) over 4 h gives 0.8 (±0.2) mmol MeOH and 1.1 (±0.3) mmol CH_2O. Under the same conditions a control reaction (without the catalyst) yields 0.2 (±0.1) mmol MeOH and 0.5 (±0.2) mmol of CH_2O. Consequently, under the conditions of the experiment the pure yield of methane oxidation products per mol catalyst corresponds to *ca.* three cycles. Under the conditions presented in Table 1 ethanol was formed catalytically during ethane oxidation. In the oxidation of hexane the regioselectivity is C-1 : C-2 : C-3 = 1 : 5 : 5. A similar selectivity is observed in reactions with hydroxyl radical.[13] Therefore it is possible that OH· is an active species in the studied system. Previously, we have shown that the oxidation of dimethylsulfoxide (DMSO) to dimethylsulfone occurs with high selectivity (80–90%) in the $Fe(ClO_4)_2$–H_2O_2 system, in which Fe—O_2H and Fe=O[8] species are probably generated. In the complete catalytic system DMSO was oxidized to the sulfone with a selectivity of 62%, while that in the control experiment without catalyst was 16%. This fact may testify that after the Fe—O_2H and Fe=O species are formed they are intercepted by DMSO, but in the presence of more inert alkanes OH· formation takes place on reaction with acetic acid [eqn. (2)]. It should be noted that OH radicals (in addition to Fe=O species) are also considered to be possible active species in MMO.[5]

$$Fe{=}O + HOAc \longrightarrow FeOAc + {}^{\cdot}OH \qquad (2)$$

The dependence of the efficiency of the system on the nature of the added acid has been studied. For cyclohexane oxidation the activities of the added proton source can be placed in the following sequence: [concentration of added material 80 mmol dm^{-3}; yield of cyclohexane oxidation (in mmol h^{-1}) in parentheses]: acetic acid (10) > trifluoroacetic acid (3.1) > nicotinic acid (2.5) > benzoic acid (2.4) > picolinic acid (2.2) > pyruvic acid (1.1) > chloric acid (1) > water (0.3). Evidently, there is no definite dependence of the efficiency on the pK_a of the added acid. Acetic acid shows the highest activity. Acetic acid is used for μ-carboxo bridge formation in the synthesis of iron binuclear complexes.[3] Possibly, the efficiency of acetic acid is more pronounced not only because it is a better proton source, but also because it stabilizes the binuclear iron centres on the SiO_2 surface.

In conclusion, a catalytic system for alkane oxidation, $Zn/MV(ClO_4)_2/AcOH/SiO_2$–Im–$Fe/O_2$ has been developed, and the possibility of catalytic methane oxidation by O_2 under mild conditions, imitating the function of MMO, has been shown. However, the efficiency is still rather low and ·OH radicals may be the active species reacting with the alkanes.

Received: Moscow, 29th April 1991
Cambridge, 19th September 1991; Com. 1/02444B

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New Rearrangement in the *o*-Methoxycarbonyl-ω-diazoacetophenone Series

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Correlation analysis has been used to study a new ring–chain rearrangement in the *o*-methoxycarbonyl-ω-diazoacetophenone series.

For some years we have been investigating the intramolecular reactions of *o*-methoxycarbonyl-ω-diazoacetylquinolines[1] and *o*-methoxycarbonyl-ω-diazoacetylquinolines.[2] We have found that on reaction with sodium methoxide these compounds undergo a previously unknown ring–chain rearrangement, leading to the formation of an equilibrium mixture of isomeric *o*-methoxycarbonyldiazoacetylazines corresponding to the 2-diazo-1,3-dicarbonyl compounds. In this communication, using the series of unsymmetrical *o*-methoxycarbonyl-ω-diazoacetophenones **1a–f**, we have examined both the possibility of a similar ring–chain rearrangement occurring in these compounds and the influence of electronic factors on the ratio of products obtained.