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ScienceDirect
Mendeleev Commun., 1992, **2(2)**, 57–58

Mendeleev
Communications

Activation of Dioxygen by Catecholate Binuclear Iron Complexes for Alkane Hydroxylation. A Chemical Model for Methane Monooxygenase

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A new model is proposed for methane monooxygenase activation of O_2 on binuclear catecholate iron complexes as catalytic centres in the presence of hydrazobenzene as a reducing agent, to oxidize alkanes (including methane).

The activation of dioxygen for the hydroxylation of light alkanes by methane monooxygenase (MMO) requires a two-electron reductant.[1] The centre of the enzyme is a binuclear μ-hydroxo complex of iron.[2] Recently, attempts to develop chemical models of MMO have been undertaken, using iron complexes, reductants and O_2. In these systems a binuclear iron complex was either introduced into the reaction mixture as a catalyst[3,4] or postulated as an active intermediate formed *in situ* during O_2 activation by a mononuclear iron complex.[5,6] Hitherto, there has been no convincing evidence for a higher efficiency of binuclear iron complexes compared with mononuclear ones. Herein, we present data on the synthesis of new binuclear iron complexes and their catalytic activity in alkane oxidation.

Binuclear iron complexes may be synthesized using the $(Et_4N)_2Fe_2OCl_6$ 'synthon'.[7] The reaction of a 2:1 mixture of catechol or 3,5-di-*tert*-butylcatechol (DTBC) with $(Et_4N)_2Fe_2OCl_6$ in MeCN results in violet (**1**; λ_{max}/nm 358 and 587) or dark blue (**2**; λ_{max}/nm 360 and 623) solutions of complexes **1** and **2**, respectively. Two equivalents of catechols is sufficient for formation of the complexes, an excess of catechols does not change the spectrum. It should be noted that mixing mononuclear $FeCl_2$ or $FeCl_3$ complexes with catechols does not give compounds with spectra similar to those of the violet or dark blue complexes **1** and **2**. The presence of an absorption band near 360 nm and the ESR silence of complexes **1** and **2** provide evidence for the conservation of binuclearity.[7] From a 1:2 mixture of $(Et_4N)_2Fe_2OCl_6$ and DTBC in MeCN we were able to obtain crystals of complex **2** $(Et_4N)_2Fe_2OCl_4$ (dtbc^{2-}) (dtbc)MeCN (yield 45%).† The IR and visible spectra are consistent with a catecholate rather than a semiquinone ligand.[8] Apparently, the catecholate ligands form additional bridges in the stabilized binuclear complex.

The complexes formed are active catalysts in cyclohexane oxidation by O_2 in the presence of reductants (Table 1). During the reaction the visible bands at 583 nm and 630 nm for **1** and **2** do not change, thus confirming the stability of the binuclear complexes. The maximum efficiency and alcohol selectivity are achieved with the complex **2**–PhNHNHPh system. It is interesting that substitution of the binuclear iron complex by a mononuclear one ($FeCl_3$) leads to a more than tenfold decrease in activity.

The activation of O_2 by the system complex **2**–PhNHNHPh–O_2 for hydrocarbon oxidation was studied in more detail (Table 2). Methane was oxidized to methanol with a turnover number of less than one. Although we have previously observed cata-

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† *Characteristic data* for **2**: λ_{max}/nm 360 and 623 (ϵ_0 4650 mol^{-1} dm^3 cm^{-1}); IR (KBr) ν_{FeOFe}/cm^{-1} 860 s, ν_{CO}/cm^{-1} 1260 m; satisfactory elemental analyses were obtained.

Table 1 Hydroxylation of cyclohexane by the system iron complex–reductant–O_2[a]

Complex	Ligand	Reductant	Cyclohexanol concn./mmol dm^{-3}
$(Et_4N)_2(Fe_2OCl_6)$	Catechol	Hydroquinone	0.2
$(Et_4N)_2(Fe_2OCl_6)$	Catechol	Phenylhydrazine	1.7
$(Et_4N)_2(Fe_2OCl_6)$	Catechol	Hydrazobenzene	10.5
$(Et_4N)_2(Fe_2OCl_6)$	None	Hydrazobenzene	5.9
$(Et_4N)_2(Fe_2OCl_6)$	dtbc	Hydrazobenzene	12.5
$FeCl_3$	dtbc	Hydrazobenzene	0.8

[a] Cyclohexane (1 mol), reductant (0.1 mol) and iron complex (4 mmol), together with 8 mmol of catechol were combined in 1 ml of MeCN followed by admission of air into the reaction cell with 10 ml head space. Reactions were carried out at room temperature for 2 h.

lytic methane oxidation in the presence of a binuclear iron complex,[4] the quantity of methanol formed in this system is higher and is similar to that in the $Fe(ClO_4)$–H_2O_2 system.[9] The regioselectivity in hexane oxidation (C1:C2:C3 = 1:5:8) differs from that obtained using $OH^{\bullet}$ and is similar to that using Fe=O particles.[9] Evidence for the absence of $OH^{\bullet}$ radicals in this system is given by (*i*) the relatively high values of the kinetic isotope effects ($k_H/k_D = 2.2$), (*ii*) the high values of the parameter 6/5 = 5 (6/5 is a measure of the relative reactivity to oxidation of cyclohexane and cyclopentane per C—H bond; this parameter characterizes the electrophilicity of the particle) and (*iii*) the slow oxidation of benzene, compared with cyclohexane. The distribution of *tert*-alcohols in the oxidation of *cis*-1,2-dimethylcyclohexane indicates the formation of free alkyl radicals. It appears that the low regioselectivity at the tertiary position (1°:2°:3° = 1:10:11) is caused by cleavage of the C—C bond near the tertiary carbon, as in the oxidation of 2,3-dimethylbutane and of isoalkanes by Fe=O particles.[9] A comparison of hexane and adamantane regioselectivities for binuclear (Table 2) and mononuclear complexes (C1:C2:C3 = 1:4:6 and 3°:2° = 2.5 for $FeCl_3$) shows that the system containing a binuclear complex is more selective.

Hitherto, various hypotheses have been expressed about an active particle [$Fe^{III}OOH$,[10,11] $HO_2^{\bullet}$,[12] $Fe^{IV}(OH)_2$, $Fe^{III}OOFe^{III}$[6]] oxidizing hydrocarbons in the iron complex–PhNHNHPh system. An analysis of the dependence of activity and selectivity on the structure of the catalyst prompts the conclusion that an Fe^{IV}—O—Fe^{IV}=O species is the active intermediate in the complex **2**–PhNHNHPh–O_2 system. The ability of this system to hydroxylate alkanes, including methane, mimics the function of MMO. Although the activity of the model system (turnover number/min) is less than that of the enzyme and the regioslectivity of n-alkane oxidation is different ω- and ω-1 hydroxylation for MMO), the binuclear iron complex–PhNHNHPh–O_2 system is a promising base for the development of new models of MMO.

Received: Moscow, 4th September 1991
Cambridge, 5th November 1991; Com. 1/04776K

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Table 2 Activation of O_2 by complex **2**–PhNHNHPh for hydrocarbon oxidation[a]

Substrate (concn./mmol dm^{-3})	Products (concn./mmol dm^{-3})		Relative reactivities per C—H bond (6/5 ratio)
CH_4	MeOH	(0.7)	
C_2H_6	EtOH	(4.7)	
n-C_6H_{14}	n-$C_6H_{13}OH$	(0.7)	
	$Bu^nCHOHMe$	(2.0)[c]	
	$Pr^nCHOHEt$	(3.6)[c]	
$Me_2CHCHMe_2$	MeCOMe	(6.5)	
	Me_2CHOH	(5.2)	
c-C_6H_{12}(0.5)–c-C_5H_{10} (0.5)	c-$C_6H_{11}OH$	(18.0)	5.0
	c-C_5H_9OH	(3.0)	
c-C_6D_{12}(0.5)–c-C_5H_{10}(0.5)	c-$C_6D_{11}OH$	(12.0)	2.2
	c-C_5H_9OH	(4.4)[d]	
cis-1,2-dimethyl-cyclohexane	*cis-tert*-alcohol	(0.47)[e]	
	trans-tert-alcohol	(0.47)	
	sec-alcohols	(3.4)	
	prim-alcohols	(0.25)	
AdH[b]	Ad-1-ol	(2.3)	
	Ad-2-ol	(2.1)[f]	3°:2° = 3.3 ± 0.2
PhH	PhOH	(1.5)	

[a] For conditions see footnote [a], Table 1; reaction time: 6 h. [b] AdH = adamantane, $C_{10}H_{16}$. [c] C1:C2:C3 = 1:5:8. [d] $k_H/k_D = 2.2 \pm 0.1$. [e] 1°:2°:3° = 1:10:11. [f] 3°:2° = 3.3 ± 0.2.