Molecular mechanism of alkane oxidation involving binuclear iron complexes

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The use of substrate probes for establishing the nature of intermediates and the mechanism of alkane oxidation by peroxides upon catalysis by binuclear iron complexes {[Fe₂OL₂ (H₂O)₂](ClO₄)₄, where L = bpy, 4,4′-Me₂bpy or 5-NO₂phen (bpy = bipyridine, phen = phenanthroline)}, the analysis of the dependence of test parameters on the nature of a substituent in a ligand and the effect of dioxygen all make it possible to diagnose a two-electron mechanism for the transfer of the oxygen atom from peroxide to the C–H bond of an alkane *via* metal complexes.

Binuclear oxo-bridge iron(III) complexes catalyse the selective oxidation of alkanes by peroxides at 20 °C, presumably *via* a $2e^-$ mechanism involving the transfer of the O atom from the oxidant to the C–H bond[1–3] [reactions (1) and (2), M is a metal complex†]

$$R^1OOH + M \longrightarrow M \cdot O, \quad R^1 = Bu^t, H \qquad (1)$$

$$R^2H + M \cdot O \longrightarrow R^2OH + M \qquad (2)$$
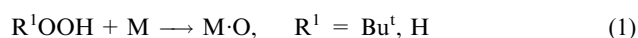
unlike the usual radical mechanism involving H atom abstraction from the alkane[4] [reactions (3)–(5)]

$$R^1OOH + M \longrightarrow R^1O \cdot \qquad (3)$$

$$R^1O \cdot + R^2H \longrightarrow R^2 \cdot + R^1OH \qquad (4)$$

$$R^2 \cdot + O_2 \longrightarrow R^2O_2 \cdot , \; etc. \qquad (5)$$

Since methane monooxygenase (MMO) has a binuclear iron centre and selectively transforms methane to methanol,[5,6] biomimetic alkane oxidation mediated by iron complexes is of considerable interest and its mechanism is worthy of investigation.[6]

The existence of a molecular mechanism has been proved for the oxidation of alkanes mediated by iron porphyrin complexes.[7] For non-heme oxidation with mononuclear iron complexes in so-called Gif systems, the molecular mechanism involving the ferryl intermediate $Fe^{IV}=O$ is assumed; however, there are arguments in favour of a radical mechanism in these systems.[9] A radical mechanism has also been suggested to explain alkane oxidation involving binuclear iron complexes.[10,11]

We have shown[12] that in the oxidation of alkanes by peroxides catalysed by the binuclear iron complexes [Fe₂OL₂(H₂O)₂](ClO₄)₄, where L = bpy or phen with a substituent X = H, Me, CH₂Cl, NO₂, the nature of X affects both the rate of catalysed decomposition of peroxide and the catalytic activity in oxidation, and we have assumed the possibility of simultaneous radical and molecular mechanisms. The results obtained in the present work give evidence for the contribution of a molecular mechanism. The oxidation by H₂O₂ in MeCN of the hydrocarbons [methane, cyclopentane, cyclohexane, [²H₁₂]cyclohexane, cyclohexene, limonene, adamantane, and *trans*-1,4-dimethylcyclohexane (DMCH)] chosen as mechanistic probes has been carried out in air at 20 °C. Table 1 presents the catalytic activity (*A*) of the complexes studied in the oxidation of methane and cyclohexane expressed as the number of catalyst turnovers during the complete decomposition of peroxide, the relative reactivity of cyclopentane and cyclohexane [*r*(5/6)], the kinetic isotope

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† The designation M·O reflects the fact that an active intermediate contains the O atom transferred to the C–H bond, but does not indicate its actual structure.

Table 1 The use of substrate probes for determining the nature of intermediates and the mechanism of alkane oxidation by binuclear iron complexes with substituents X in the ligands.

Test parameters[a]	X = Me	X = H	X = NO₂
	Methane oxidation		
$A(CH_4)$	0.6±0.1	1.4±0.2	2.1±0.2
	Cyclopentane and cyclohexane oxidation		
$A(C_6H_{12})$	14.2±1.0	11.0±1.0	4.5±0.5
$KIE(C_6H_{12})$	3.1±0.2	2.4±0.3	2.0±0.1
$r(5/6)$	0.30±0.02	0.32±0.04	0.35±0.02
	Adamantane oxidation		
2°/3°	0.160±0.002	0.220±0.005	0.290±0.005
	Limonene oxidation		
I°/II°	2.0±0.1	2.3±0.1	3.0±0.1
	trans-1,2-DMCH oxidation		
RC(%)	48±5		72±5

[a] The parameter *A* was measured at [H₂O₂] = 100 mM, the rest of the parameters at [H₂O₂] = 20 mM. Later we found that these values depend on peroxide concentration, probably due to the increasing O₂ concentration in solution and the greater contribution of chain-radical oxidation with increasing peroxide concentration. This conclusion is confirmed by the independence of the test parameters on peroxide concentration in experiments with dioxygen elimination.

effect (KIE) found by the competitive method with respect to cyclopentane $k_H/k_D = r(5/6)_D/r(5/6)_H$, the selectivity of the attack at the secondary and tertiary bonds of adamantane per bond (2°/3°), the relative selectivity of the attack to 1, 2- and 8, 9- bonds in limonene (I°/II°) and the retention of configuration (RC) in the oxidation of the *tert*-C–H bond in *trans*-DMCH, found as the ratio of alcohols (*trans–cis*)/(*trans + cis*), upon catalysis by [Fe₂OL₂(H₂O)₂](ClO₄)₄, where L is bpy (X = H), 4,4′-Me₂bpy (X = Me), and 5-NO₂phen (X = NO₂).

In the case of a radical mechanism the active oxidant is RO· (or HO·) and the parameters in Table 1 should not depend on the nature of the metal complex and racemization should be observed in the oxidation of *trans*-DMCH. For Bu^tO· $k_H/k_D = 3.5$, $r(5/6) = 0.73$, $2°/3° = 0.11–0.07$ and similar values are expected for other RO· radicals,[8,13] but for HO·, $k_H/k_D = 1.0–1.7$, $2°/3° = 0.4$ and $r(5/6) = 1$.[14] Since RO₂· is involved in the radical mechanism, the double bond can be epoxidized; however, in this case the parameter I°/II° should be independent of the nature of metal complexes. Conversely, many parameters should be expected to depend on the nature of a metal complex in the molecular mechanism.

The sensitivity of the parameters presented in Table 1 to a change in the catalyst nature and their values unambiguously indicate that the M·O intermediate takes a part in alkane oxidation catalysed by these binuclear complexes. The increase in catalytic activity in CH₄ oxidation with increasing M·O electronegativity (X = Me < H < NO₂) is in accord with the electrophilic attack on the C–H bond and is similar to that observed for metal porphyrin[15] complexes. The reverse dependence for cyclohexane has been interpreted earlier[12] by a decrease in the contribution of chain-radical oxidation in

Table 2 The influence of O_2 on the parameter $2°/3°$ in adamantane oxidation by binuclear iron complexes with substituents X in ligands.

Conditions	X = Me	X = H	X = NO$_2$
Air	0.16	0.22	0.29
Oxygen	0.13	–	0.25
in vacuo	0.20	0.30	0.62

Table 3 The influence of O_2 on product yield and the parameter $I°/II°$ in limonene epoxidation.

Conditions	X = Me	X = H	X = NO$_2$
Air			
I°/II°	2.0±0.1	2.3±0.1	3.0±0.1
Yield (mM)	1.3	1.1	0.8
in vacuo			
I°/II°	1.7±0.1	1.9±0.1	2.7±0.1
Yield (mM)	0.7	0.6	0.6

this series. A decrease in the isotope effect is also in accordance with an increase in the activity of an intermediate in this series. The parameter $r(5/6)$ is substantially lower than values characteristic of a radical mechanism, which indicates the contribution of a metal complex intermediate.[13] As expected,[16,17] an increase in the electrophilicity of M·O results in an increase in the parameter $2°/3°$ for adamantane and the $I°/II°$ ratio for limonene. A partial retention of the configuration is observed for hydroxylation of the *tert*-C–H bond in *trans*-1,4-DMCH. The changes in A, KIE and $2°/3°$ might be explained by the change in the nature of attacking radicals (RO·, HO·), but this is more difficult in the case of $I°/II°$, because there are no other radicals, except RO$_2$·, which could epoxidize the double bond, and the low values of $r(5/6)$ and the partial retention of configuration can be reconciled only by the implication of M·O in the oxidation.

The contribution of radical reactions can be checked by comparing experiments under O_2 and *in vacuo* (or under inert gas purge‡) in the cases when a substrate and products are nonvolatile. When adamantane is oxidized under an O_2 atmosphere, a decrease in the $2°/3°$ parameter is observed, but it increases under vacuum compared to that for experiments conducted in air (Table 2). It is easy to notice that the $2°/3°$ value of 0.13 for X = Me in O_2 is close to that for RO· radicals, and that the $2°/3°$ value of 0.62 for X = NO$_2$ is considerably greater than this value. We assume that the $2°/3°$ values obtained in vacuum are caracteristic of M·O particles. The correlation between $(2°/3°)_{vac}$ and the Hammett parameters σ_p of substituent X in ligands favours this assumption (Figure 1).

We have also observed the effect of dioxygen on the yield of products and the $I°/II°$ parameter on the epoxidation of limonene (Table 3), which indicates that epoxides can be formed by the attack of both the RO$_2$· radical and the M·O intermediate. In fact, as follows from Figure 1, values of $(I°/II°)_{vac}$ for various complexes are also correlated by Hammett parameters (σ_p) of the substituents X in the ligands.

An active intermediate M·O can have one of the following structures: ferryl (1), peroxocomplex (2) or bis-μ-oxocomplex (3), and structures (1) and (2) also assume the possibility of a mononuclear complex. The mononuclear intermediate has recently been identified[18] in the system for alkane oxidation by alkylhydroperoxides catalysed by binuclear iron complexes, although there is no proof of its involvement in alkane oxidation. The small values of KIE, found by us $2°/3°$ and $I°/II°$, and the fact of retention of configuration in oxidation of the *tert*-C–H bond in *trans*-DMCH agree better with structures (2) and (3) for the active intermediate than with structure (1). However, the available date are not enough for definite conclusions.

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‡ We observed the same effect at inert gas purge, but in the case of the experiments *in vacuo* we obtained more reproducible values.
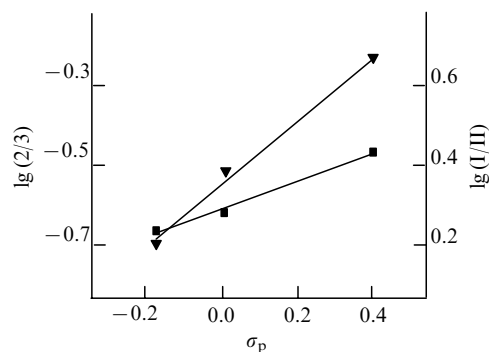

Figure 1 Correlation of the parameters $2°/3°$ for adamantane and $I°/II°$ for limonene with Hammett constants (σ_p) for substituents in the ligands of the iron complexes.

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