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Alkane oxygenation with H_2O_2 catalysed by $FeCl_3$ and 2,2′-bipyridine

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Abstract—The H_2O_2–$FeCl_3$–bipy system in acetonitrile efficiently oxidises alkanes predominantly to alkyl hydroperoxides. Turnover numbers attain 400 after 1 h at 60 °C. It has been assumed that bipy facilitates proton abstraction from a H_2O_2 molecule coordinated to the iron ion (these reactions are stages in the catalytic cycle generating hydroxyl radicals from the hydrogen peroxide). Hydroxyl radicals then attack alkane molecules finally yielding the alkyl hydroperoxide.

Iron ions surrounded with certain *N*-containing ligands can activate molecular oxygen and they play an extremely important role in nature, particularly in oxidations of alkanes and other hydrocarbons (see reviews[1–7]). Surprisingly, in vitro 'simple' iron derivatives are usually poor catalysts for hydrocarbon oxidations with hydrogen peroxide.[8,9] Iron complexes containing *N*-ligands exhibit higher catalytic activity in comparison with 'simple' salts, and amines added to the reaction solutions either accelerate oxidations or/and significantly change their selectivity.[10–28]

In the course of our systematic studies of iron-catalysed hydrocarbon oxygenations with peroxides[4,5,7,12,23,24,27,28] we decided to explore the possibility of enhancing the efficiency of the reaction by addition of certain amines (see a review on the dramatic role of additives in metal-catalysed hydrocarbon oxygenations in solutions[4]). In the present paper we report that 2,2′-bipyridine (bipy) added to iron(III)

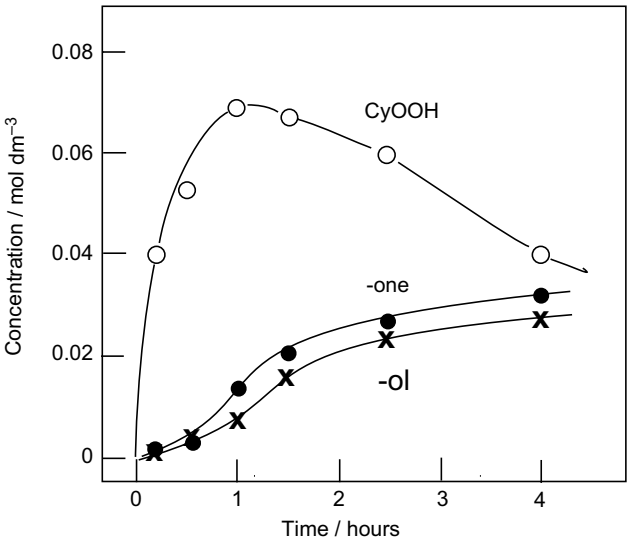

Figure 1. Cyclohexane (0.55 mol dm^{-3}) oxidation with 35% aqueous H_2O_2 (1.2 mol dm^{-3}) catalysed by $FeCl_3$ (5×10^{-4} mol dm^{-3}) and bipy (5×10^{-3} mol dm^{-3}). Accumulation of cyclohexyl hydroperoxide (ROOH), cyclohexanol (–ol) and cyclohexanone (–one) (concentrations of –ol and –one were measured twice before and after reduction of the reaction mixture with PPh_3) with time is shown. The temperature was 60 °C, and the solvent was acetonitrile.

Keywords: Alkanes; Alkyl hydroperoxides; Biomimetics; Homogeneous catalysis; Hydrogen peroxide; Hydroperoxidation; Iron complexes; Oxygenation.
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chloride used as a catalyst dramatically accelerates oxidation of alkanes with hydrogen peroxide in acetonitrile solution. The oxidations were carried out in air in thermostated (60 °C) Pyrex cylindrical vessels with vigorous stirring. The total volume of the reaction solution was 5 mL. In our experiments, aqueous solutions of hydrogen peroxide were used: either 35% ('Fluka') or 70% ('Peróxidos do Brasil'). The catalyst, $FeCl_3 \cdot 6H_2O$, and the co-catalyst, bipy, were introduced into the reaction mixture in the form of stock solutions in acetonitrile. After given time intervals, samples (about 0.2 mL) were taken. Samples of the reaction solutions were usually analysed by GC (instruments 'HP Series 6890' and 'DANI-86.10'; fused silica capillary columns) twice, before and after addition of an excess of solid triphenylphosphine. Triphenylphosphine reduces hydrogen peroxide to water and the alkyl hydroperoxide to the corresponding alcohol, and the comparison of the reaction chromatograms before and after the reduction allowed us to estimate the real concentrations of the alkyl hydroperoxide, formed from the alkane, as well as the concentrations of the alcohol and the ketone. This method was developed and used by us previously.[4,5,7,12,23,24,27–30] In the kinetic studies presented below, we measured the concentrations of the cyclohexanone and cyclohexanol only after reduction with PPh_3 because in this way we obtained more precise values of the initial reaction rates.

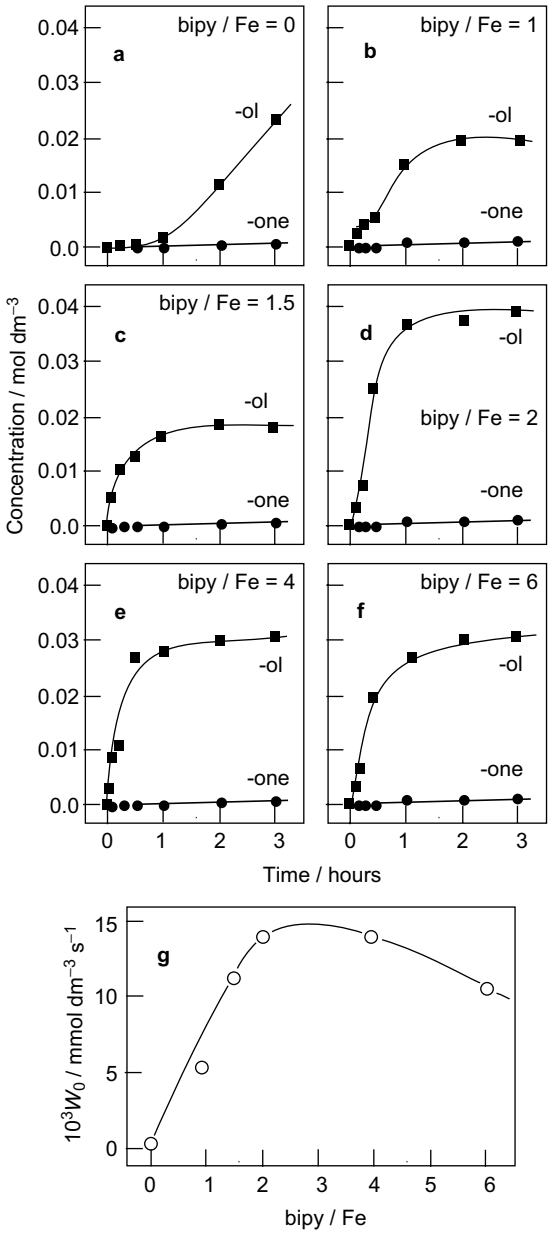


Figure 2. Cyclohexane (0.5 mol dm^{-3}) oxidation with 70% aqueous H_2O_2 (0.5 mol dm^{-3}) catalysed by $FeCl_3$ (1×10^{-4} mol dm^{-3}) at various concentrations of added bipy. Accumulation of cyclohexanol (–ol) and cyclohexanone (–one) (concentrations were measured after reduction of the reaction mixture with PPh_3) (graphs a–f) and dependence of initial rate of formation of oxygenates W_0 on the bipy/Fe ratio (graph g) are shown. The temperature was 60 °C, the solvent was acetonitrile.

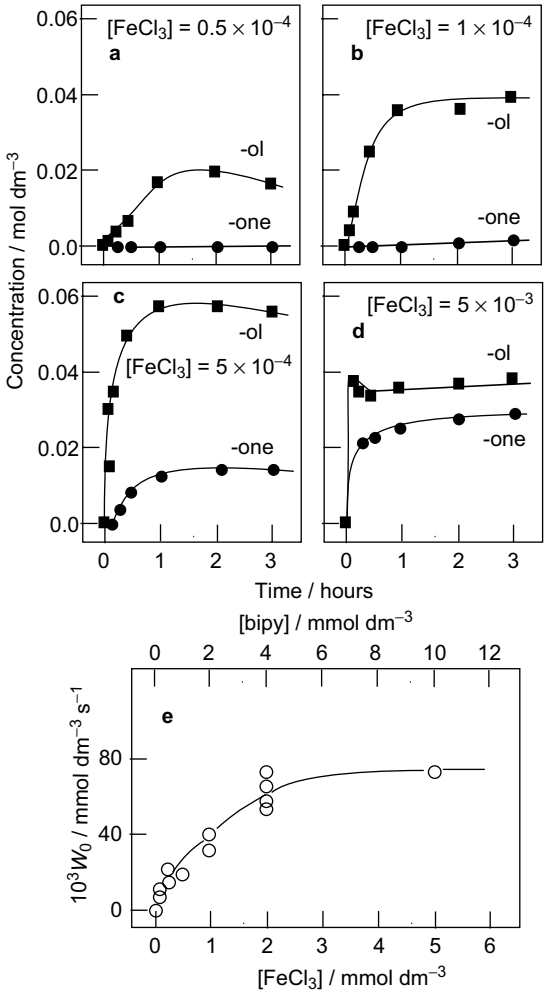


Figure 3. Cyclohexane (0.5 mol dm^{-3}) oxidation with 70% aqueous H_2O_2 (0.5 mol dm^{-3}) catalysed by the '$FeCl_3$–bipy' system at various concentrations of both $FeCl_3$ and bipy at constant ratio bipy/$FeCl_3$ = 2. Accumulation of cyclohexanol (–ol) and cyclohexanone (–one) (concentrations were measured after reduction of the reaction mixture with PPh_3) (graphs a–d) and dependence of initial rate of formation of all oxygenates W_0 on the concentration of $FeCl_3$ and bipy (graph e) are shown. The temperature was 60 °C, the solvent was acetonitrile.

Oxidation of cyclohexane by the H_2O_2–$FeCl_3$–bipy system gave rise to formation of cyclohexyl hydroperoxide predominantly which was transformed in the course of the reaction into cyclohexanol and cyclohexanone (Fig. 1). Turnover numbers (total moles of products produced per one mole of a catalyst; TONs) attained 205 after 2.5 h at $[FeCl_3] = 5 \times 10^{-4}$ mol dm^{-3}.

When the concentration of $FeCl_3$ was lower (1×10^{-4} mol dm^{-3}) we measured TON = 410 after 1 h (Fig. 2, graph d). At this catalyst concentration, the maximum initial rate of the cyclohexane oxygenation was found for the ratio bipy/Fe = 2–4 (Fig. 2, graph g). It should be noted that the initial oxidation rate was ca. 35 times higher in the reaction co-catalysed by bipy in comparison with the reaction in the absence of bipy (compare graphs a, d and e in Fig. 2).

Figure 3 demonstrates reaction profiles for cyclohexane oxidations at various catalyst concentrations (with fixed ratio bipy/Fe = 2). Maximum initial rate was attained at $[FeCl_3] = 2 \times 10^{-3}$ mol dm^{-3} and [bipy] = 4×10^{-3} mol dm^{-3} (graph e). It is interesting that at high concentrations of the catalytic system, the cyclohexyl hydroperoxide formed in the alkane oxygenation process decomposed extensively to produce substantial amounts of the corresponding ketone (compare graph a with graph c and especially with graph d). Thus, it

Table 1. Selectivities of alkane oxidations by various systems in MeCN[a]

Entry	System	Hydrocarbon oxidised (the selectivity parameter)				
		n-Hexane	3-MH	2,4,4-TMP	MCH	*cis*-1,2-DMCH
		1:2:3	1°:2°:3°	1°:2°:3°	1°:2°:3°	*trans*/*cis*
1	H_2O_2–$FeCl_3$–bipy	1:5.1:6.7	1:2.0:8.8	1:3.7:10.5	1:4.7:14.7	0.85
2	H_2O_2–$FeCl_3$			1:7:57		1.0[b]
3	H_2O_2–$Fe(ClO_4)_3$	1:9:9	1:4:30	1:5: 45	1:4:30	
4	H_2O_2–hν	1:10:7	1:4:12	1:2:6		0.9
5	H_2O_2–VO_3^-–PCA[c]	1:8:7	1:5.7:22	1:4:9	1:6:22	0.75
6	H_2O_2–$[LMn^{IV}(O)_3Mn^{IV}L]^{2+}$[d]	1:42:37:34[e]	1:22:200	1:5:55	1:26:200	0.34

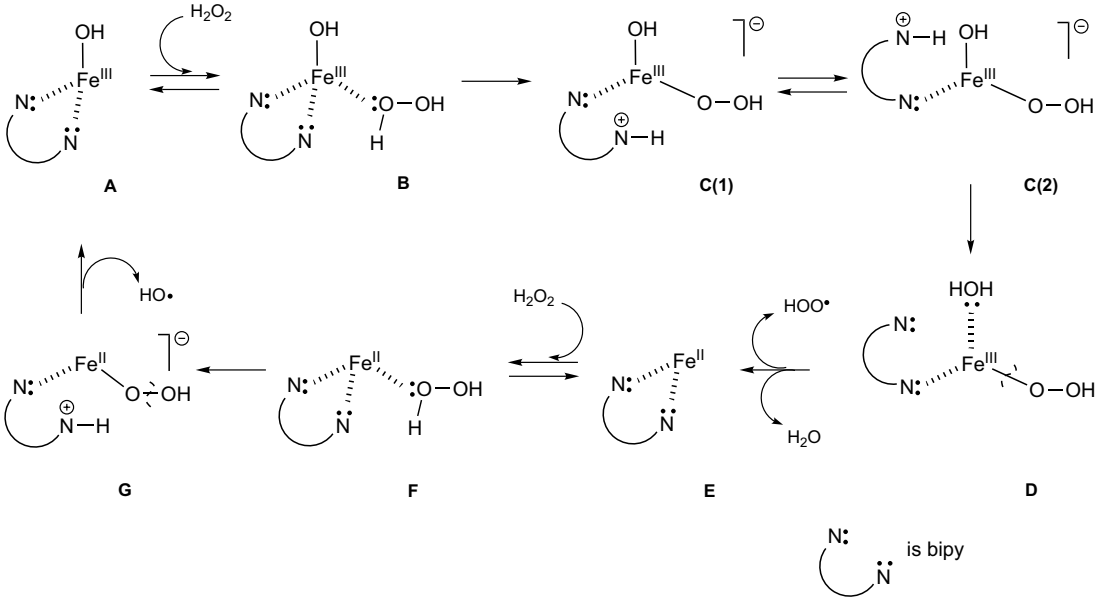
[a] The concentrations of alcohols formed in the reaction were measured after reduction with PPh_3. Substrates: 3-methylhexane, 3-MH; 2,4,4-trimethylpentane, 2,4,4-TMP (isooctane); methylcyclohexane, MCH; *cis*-1,2-dimethylcyclohexane, *cis*-1,2-DMCH. Parameter 1:2:3 is normalised (i.e., calculated taking into account the number of hydrogen atoms at each position) relative reactivities of hydrogen atoms in positions 1, 2 and 3 of the hydrocarbon chain, respectively. Parameter 1°:2°:3° is the normalised relative reactivities of hydrogen atoms at primary, secondary and tertiary carbons, respectively. Parameter *trans*/*cis* = [*trans*-ol]/[*cis*-ol] is the ratio of concentrations of tertiary alcohols *trans*-ol and *cis*-ol formed in the oxidation of *cis*-1,2-dimethylcyclohexane.

[b] *cis*-Decalin was used instead of *cis*-1,2-DMCH.

[c] PCA, pyrazine-2-carboxylic acid. For this system, see Refs. 1,2,4,5,23,29,31,32.

[d] Complex $[LMn^{IV}(O)_3Mn^{IV}L]^{2+}$, where L = 1,4,7-trimethyl-1,4,7-triazacyclononane. The oxidation at 20 °C proceeds only in the presence of CH_3COOH in low concentration. For this system, see Refs. 2,4,5,33–38.

[e] *n*-Heptane was used instead of *n*-hexane.



Scheme 1. Catalytic cycle proposed for hydroxyl radical generation from hydrogen peroxide catalysed by an iron(III) complex and assisted with bipyridine.

can be concluded that the $FeCl_3$–bipy combination in acetonitrile is a catalyst for transformation of alkyl hydroperoxides into the corresponding ketones.

Selectivity parameters for the oxidation of certain hydrocarbons by H_2O_2–$FeCl_3$–bipy are given in Table 1, which also summarises the corresponding data for other alkane-oxygenating systems, particularly for the H_2O_2–VO_3^-–PCA reagent which is known to generate hydroxyl radicals,[1,2,4,5,23,29,31,32] and for H_2O_2–$LMn^{IV}(O)_3Mn^{IV}L$–CH_3COOH (where L = 1,4,7-trimethyl-1,4,7-triazacyclononane) system[2,4,5,33–38] which is believed to oxidise alkanes via attack of Mn(V)=O species on a C–H bond. It can be seen that oxidations of all the test hydrocarbons proceeded with low selectivity parameters which are close to the parameters determined for the hydroxyl-generating systems: H_2O_2–hν and H_2O_2–VO_3^-–PCA. The oxidation of a disubstituted cyclohexane was not a stereoselective reaction.

All these data clearly testify that the mechanism of alkane oxidation by the H_2O_2–$FeCl_3$–bipy system in acetonitrile includes the formation of free hydroxyl radicals. Scheme 1 shows a catalytic cycle which we propose for hydroxyl radical generation by the system under consideration. One can assume that the role of bipy is proton transfer (via protonation–deprotonation steps of the *N*-atom) of a coordinated H_2O_2 molecule (structure **B**) to an –OH ligand resulting in the formation of a hydroperoxyl derivative **E**. Bipyridine could also assist the transformation of **F** to **G**. Species **G** generates a hydroxyl radical with the simultaneous conversion into the starting species **A**.

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