Oxidations by the "hydrogen peroxide–manganese(IV) complex–carboxylic acid" system. Part 4.† Efficient acid-base switching between catalase and oxygenase activities of a dinuclear manganese(IV) complex in the reaction with H_2O_2 and an alkane

Georgiy B. Shul'pin,* Galina V. Nizova, Yuriy N. Kozlov and Irina G. Pechenkina

Semenov Institute of Chemical Physics, Russian Academy of Sciences, ul. Kosygina, dom 4, Moscow 119991, Russia. E-mail: Shulpin@chph.ras.ru, http://members.fortunecity.com/shulpin

Received (in Montpellier, France) 19th November 2001, Accepted 22nd April 2002
First published as an Advance Article on the web 18th July 2002

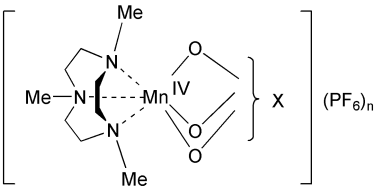
Whereas the dinuclear manganese(IV) complex $[LMn(O)_3MnL](PF_6)_2$ (**1a**, L = 1,4,7-trimethyl-1,4,7-triazacyclononane) does not react with H_2O_2 in acetonitrile solution containing cyclohexane, acetic acid added to this mixture in small amounts induces the catalytic decomposition of hydrogen peroxide to O_2 and H_2O (catalase activity) and the transformation of cyclohexane to cyclohexyl hydroperoxide (oxygenase activity). Addition to the acetic acid containing solution only 2 equivalents (relative to the Mn catalyst) of a base enhances the catalase activity and suppresses the oxygenase activity. The proposed mechanism includes the formation of dinuclear dihydroperoxy derivatives of manganese, which can be transformed under the action of acetic acid to O=Mn(V)–Mn(IV)–OOH species. The latter can abstract a hydrogen atom from an alkane. The interaction of the so-formed R$^\bullet$ radical with Mn(IV)–OOH can give the alkyl hydroperoxide, ROOH, which is the main primary product of the oxidation process.

Introduction

Manganese-containing enzymes as well as synthetic manganese-containing complexes are known to catalyse very efficiently the decomposition of hydrogen peroxide.[1] The mechanism of H_2O_2 dismutation by Mn catalase involves oxidation of a dimanganese(II) intermediate followed by reaction with a second hydrogen peroxide molecule, leading to O_2 formation (Scheme 1).[2] Added bases accelerate significantly the H_2O_2 decomposition catalysed by manganese complexes.[3] It has been demonstrated that the lack of proton donor and acceptor groups around the catalytic centre of synthetic manganese complexes may be the reason for the intense suppression of the rate compared to the natural Mn enzyme.[3a] The photosynthetic water oxidation enzyme contains a polynuclear manganese core in the oxygen-evolving center (OEC).[4]

Complexes of certain transition metals with 1,4,7-triazacyclononane (TACN) and its derivatives, for example with 1,4,7-trimethyl-1,4,7-triazacyclononane (TMTACN), have been used as models of metal-containing proteins and are known to catalyse oxidations of organic compounds.[5] Note also that a dinuclear iron complex with TACN[6] is a model for O_2-transporting hemerythrin proteins.[7]

Recently, we discovered that the manganese(IV) complex $[(TMTACN)Mn(O)_3Mn(TMTACN)](PF_6)_2$ (**1a**) catalyses the efficient oxidation of saturated hydrocarbons with hydrogen peroxide in acetonitrile at room temperature only in the presence of a small amount of acetic acid.[8] The reaction in the beginning yields predominantly alkyl hydroperoxides.[9] The oxidation of alkanes containing tertiary C–H bonds proceeds stereoselectively: the reaction with decalin isomers gives (after treatment with triphenylphosphine) alcohols hydroxylated in the tertiary positions, the *cis*/*trans* ratio being ~2 in the case of the oxidation of *cis*-decalin, and the *trans*/*cis* ratio being ~30 in the case of *trans*-decalin.[8c,d]



1a X = Mn^{IV}TMTACN, n = 2
1b X = $(CH_3)_3$, n = 1

Here, we report the study of unusual catalase and oxygenase activities of complex **1a**. Note that enzymes called catalases disarm hydrogen peroxide by converting it into oxygen and water (dismutation reaction) according to:

$$2\ H_2O_2 = 2\ H_2O + O_2$$

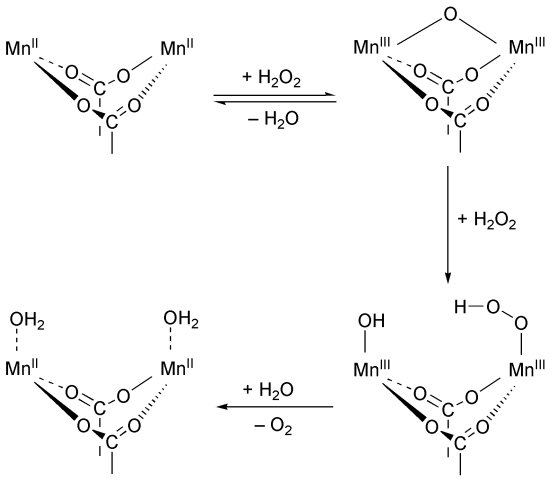
Metal complexes that decompose hydrogen peroxide mimic catalase (exhibit catalase activity). Enzymes that catalyse oxygen atom incorporation into the substrate are known as oxygenases. For example, methanemonoxygenase transforms methane into methanol in the presence of a reducing agent AH_2:

$$CH_4 + O_2 + AH_2 = CH_3OH + H_2O + A$$

Thus, metal complexes that take part in oxygen incorporation catalysis exhibit oxygenase activity.

† For parts 1–3 see ref. 8(*b*)–(*d*), respectively. A preliminary communication of previous parts has been also published.[8a]

 DOI: 10.1039/b110594a



Scheme 1 Key steps proposed for the hydrogen peroxide dismutation by Mn catalase.

Experimental

All reactions were carried out in MeCN at 25 °C in thermostated Pyrex cylindrical vessels with vigorous stirring. The total volume of the reaction solution was 5 mL. In a typical experiment, initially, a portion of 35% aqueous solution of hydrogen peroxide was added to the solution of the catalyst and cyclohexane in acetonitrile.

The volume of dioxygen evolved was measured using a thermostated burette. The reaction system was connected to a manometric burette with water that was saturated with oxygen prior to use. After certain time intervals, the pressure was equilibrated using a separation funnel by adjusting the water level to the same heights.

In order to determine concentrations of all cyclohexane oxidation products the samples of reaction solutions were analysed twice (before and after their treatment with PPh_3) by GC (LKhM-80-6, 2 m columns with 5% carbowax 1500 on 0.25–0.315 mm Inerton AW-HMDS; argon carrier gas), measuring concentrations of cyclohexanol and cyclohexanone. This method (an excess of solid triphenilphosphine is added to the samples 10–15 min before the GC analysis) described by us earlier[8–10] allows the detection of alkyl hydroperoxides and also to measure the real concentrations of all three products (alkyl hydroperoxide, alcohol and aldehyde or ketone) present in the reaction solution, because alkyl hydroperoxides are usually decomposed in the gas chromatograph to produce mainly the corresponding alcohol and ketone.

Synthesis of the complexes **1** has been described in the literature.[5c,11]

Results

We have found that, in the absence of a carboxylic acid, compound **1a** in acetonitrile solution at 25 °C does not catalyse alkane hydroperoxidation (oxygenase activity), and catalyses very slow the decomposition of hydrogen peroxide to molecular oxygen (catalase activity). However, addition of a small amount (only 0.02–0.05 mol dm^{-3}) of acetic acid leads to a noticeably more rapid evolution of molecular oxygen (see Fig. 1, curve 1b and Fig. 2).

At $[CH_3CO_2H] < 0.1$ mol dm^{-3}, added cyclohexane has practically no effect on the initial rate of O_2 evolution (compare curves 1 and 2 in Fig. 2) and this rate is higher than that for the cyclohexane oxidation (curve 3 in Fig. 2). However, in the presence of cyclohexane, the rate $W(O_2)$ passes through a maximum while W(CyH) rises monotonously; $W(O_2) = W$(CyH) at $[CH_3CO_2H] \approx 0.4$ mol dm^{-3}. Perchloric acid

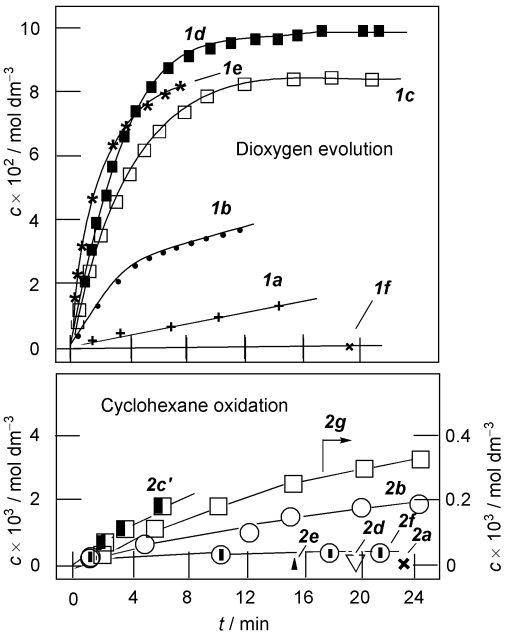


Fig. 1 Decomposition of H_2O_2 (0.25 mol dm^{-3}) in the presence of cyclohexane (0.46 mol dm^{-3}) and cyclohexane oxidation catalysed by complex **1a** (5×10^{-5} mol dm^{-3}). Kinetic curves are presented for the O_2 evolution (1) and for the sum of cyclohexanol and cyclohexanone (after PPh_3 reduction) accumulation (2) in the absence of any additive (curves a) and in the presence of acetic acid ($[CH_3CO_2H] = 0.05$ mol dm^{-3}) (curves b), in the presence simultaneously of acetic acid ($[CH_3CO_2H] = 0.05$ mol dm^{-3}) and of n-Bu_4NOH at various concentrations: 10×10^{-5} (curves c) {at $[H_2O_2]_0 = 0.75$ mol dm^{-3} (curve c′)}, 20×10^{-5} mol dm^{-3} (curves d), or of TMTACN (10×10^{-5} mol dm^{-3}) (curves e), as well as in the presence of $HClO_4$ (10×10^{-5} mol dm^{-3}) (curves f) and simultaneously CH_3CO_2H (0.05 mol dm^{-3}) and $HClO_4$ (5×10^{-5} mol dm^{-3}) (curve g).

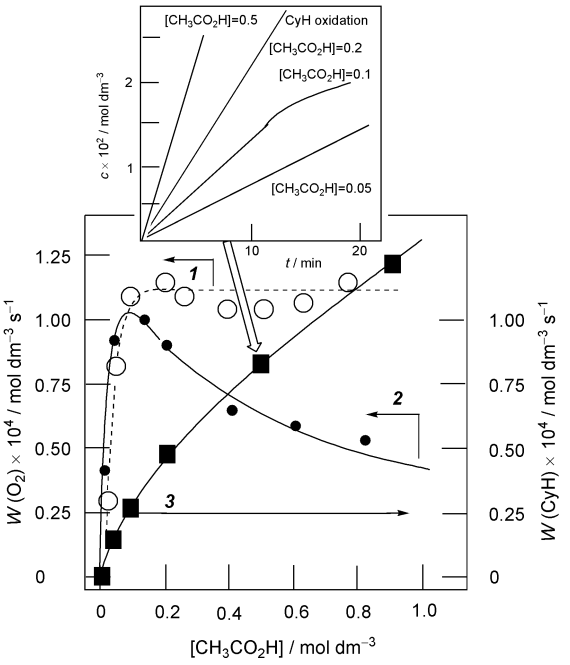


Fig. 2 Decomposition of H_2O_2 (0.25 mol dm^{-3}) catalysed by complex **1a** (5×10^{-5} mol dm^{-3}). The dependence of the O_2 evolution rate on $[CH_3CO_2H]$ in the absence (curve 1) and in the presence (curve 2) of cyclohexane (0.46 mol dm^{-3}), as well as the analogous dependence for the initial rate of cyclohexanol and cyclohexanone (after PPh_3 reduction) accumulation (curve 3) are shown. Curves of oxygenate accumulation with time in the cyclohexane oxidation at various acetic acid concentrations are shown in the inset at the top of the figure. Initial rates of these reactions are plotted as curve 3 in the main graph.

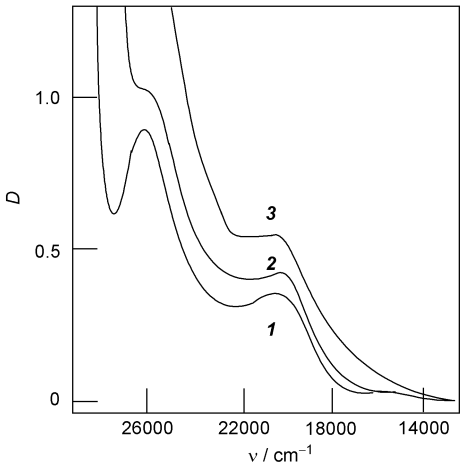


Fig. 3 Electronic spectra of compound **1a** (1×10^{-3} mol dm^{-3}) in CH_3CN in the absence of additives (curve 1), and in the presence of $HClO_4$: 1×10^{-4} mol dm^{-3} (curve 2) and 7×10^{-4} mol dm^{-3} (curve 3) (D = optical density).

accelerates neither catalase nor oxygenase reactions if acetic acid is absent (Fig. 1, curves 1f and 2f, respectively). Even in the presence of acetic acid, addition of a low concentration of $HClO_4$ (5×10^{-5} mol dm^{-3}; 1 equiv. relative the catalyst) gives rise to a much lower oxygenase activity of the system (compare curves 2g and 2b in Fig. 1). The activity loss under the action of the very strong perchloric acid could be explained by the transformation of complex **1a**, for example, into a mononuclear species that is not capable of catalysing both the peroxide dismutation and the alkane oxygenation. Fig. 3 shows changes in the visible spectrum caused by addition of low concentrations of perchloric acid. Addition of acetic acid does not change the spectrum of the **1a** solution, however, if both acetic acid and H_2O_2 are added some changes can be noticed.

It is noteworthy that in the presence of both acetic acid (0.05 mol dm^{-3}) and HO^- anion, used in the form of n-Bu_4NOH (20×10^{-5} mol dm^{-3}, see Fig. 1, curve 1d) the $W(O_2)$ value is much higher than that for reactions in the presence of acetic acid only.

The second very interesting feature is that when only 2 equiv. of HO^-, relative to the catalyst, are added to the reaction solution containing acetic acid and $[H_2O_2]_0 < 0.3$ mol dm^{-3} the oxygenase activity of **1a** is suppressed very significantly. The yield of oxygenates from the reaction with cyclohexane after 20 min is 85 times lower when only 4 equiv. of n-Bu_4NOH are added to the solution containing CH_3CO_2H (compare curves 2b and 2d in Fig. 1). Thus, it can be concluded that the system requires the presence of either a carboxylic acid or a base (free amine TMTACN has been found to affect the reaction analogously, see Fig. 1, curve 1e) to exhibit catalase activity whereas only acetic acid in relatively high concentration induces oxygenase activity. The highest catalase activity has been found when an acetate buffer at very low concentration was used. It should be noted that at relatively high concentrations of hydrogen peroxide ($[H_2O_2]_0 = 0.75$ mol dm^{-3}) the addition of small amounts of Bu_4NOH affects the oxygenase activity less dramatically (compare curves 2b and 2c′ in Fig. 1).

The rate dependences of both cyclohexane oxygenation and O_2 evolution catalysed by **1a** in the presence of CH_3CO_2H are first-order for the initial $(Mn)_2$ complex [Fig. 4(A,B)] in relatively low concentrations and for cyclohexane [Fig. 4(C)]. It is, however, noteworthy that for both catalase and oxygenase routes a second-order dependence has been found for hydrogen peroxide [Fig. 5(A)]. When lower concentrations of the catalyst were used in the presence of n-Bu_4NOH (only

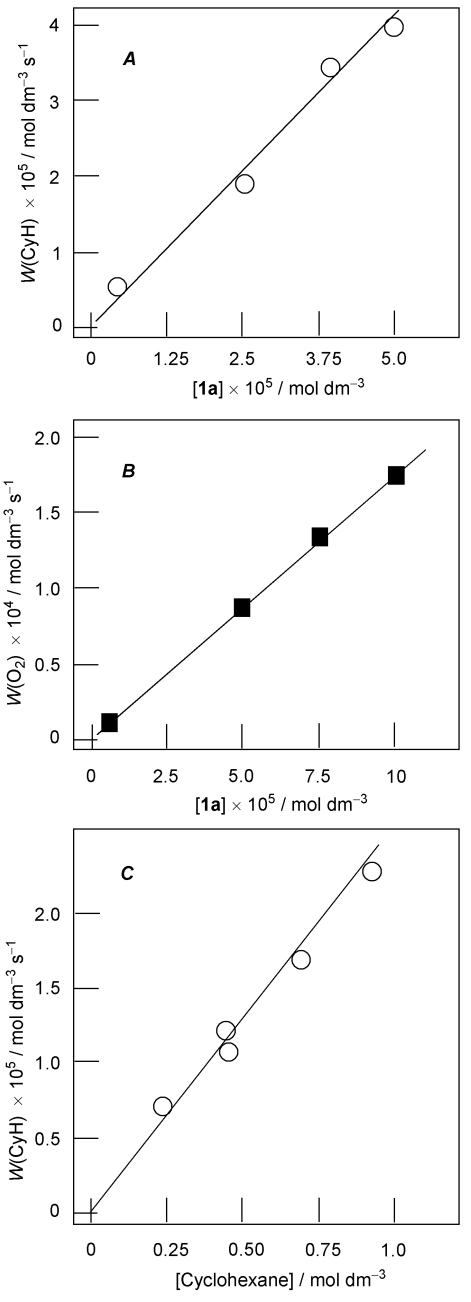


Fig. 4 Plots of the cyclohexane oxygenation rate (graph A) and the O_2 evolution rate (graph B) *versus* initial concentration of catalyst **1a** and *versus* initial concentration of cyclohexane (graph C). Conditions: cyclohexane (0.46 mol dm^{-3} for graphs A and B), **1a** (5×10^{-5} mol dm^{-3} for graph C), H_2O_2 (0.25 mol dm^{-3}), CH_3CO_2H (0.05 mol dm^{-3}).

4×10^{-5} mol dm^{-3}) a sigmoidal shape of the dependence for the O_2 evolution rate *versus* H_2O_2 concentration was found [Fig. 5(B)]. It should be noted that the sigmoidal shape of the dependence of the initial cyclohexane oxygenation rate on $[H_2O_2]_0$ was not found under the conditions used. This could be due to the relatively low accuracy of the ROOH analysis. Effective activation energies have been measured to be 8 and 14 kcal mol^{-1} for oxygenation and O_2 evolution, respectively (Fig. 6). Comparison of the initial oxygenation rates of cyclohexane and cyclohexane-d_{12} allowed us to estimate the kinetic isotope effect at 1.3. This value is only slightly higher than that for alkane oxidation with participation of non-selective hydroxyl radicals ($k_H/k_D = 1.1$) so such a small difference requires additional investigation and explanation. It is noteworthy that, according to our[12a] preliminary results, k_H/k_D

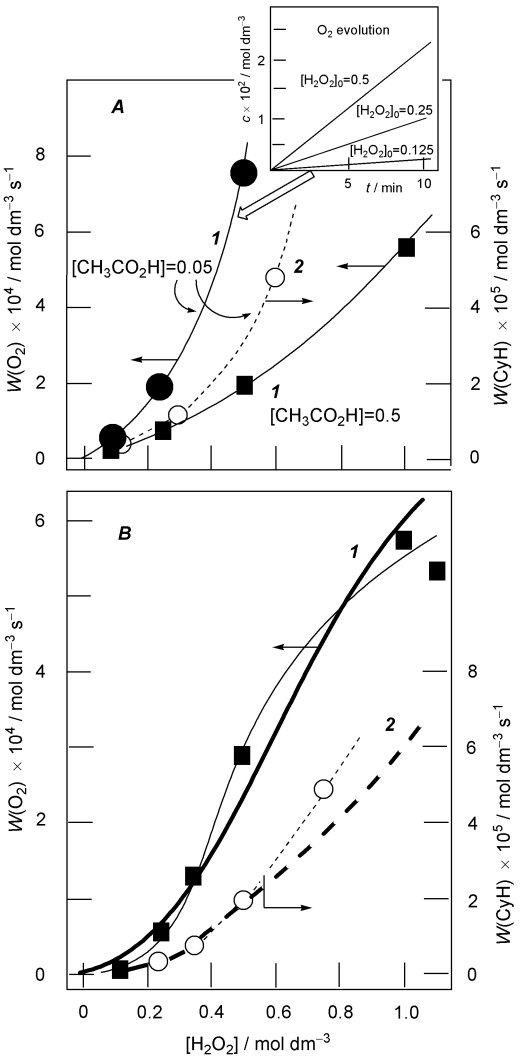


Fig. 5 Dependence of the O_2 evolution rate (curves 1) and the cyclohexane oxygenation rate (curves 2) on initial concentration of hydrogen peroxide. Graph A: CH_3CO_2H (0.05 or 0.5 mol dm^{-3}), **1a** (5×10^{-5} mol dm^{-3}). Graph B: CH_3CO_2H (0.05 mol dm^{-3}), **1a** (1×10^{-5} mol dm^{-3}), *n*-Bu_4NOH (4×10^{-5} mol dm^{-3}) and (for curve 2) cyclohexane (0.46 mol dm^{-3}). On graph B bold curves for the O_2 evolution (curve 1) and for the cyclohexane oxygenation (curve 2) were simulated using eqns. (1)–(7) and the conditions in eqns. (8)–(11). Curves of dioxygen evolution with time in the hydrogen peroxide decomposition at various hydrogen peroxide concentrations are shown in the inset at the top of the figure. Initial rates of these reactions are plotted as curve 1 in graph A.

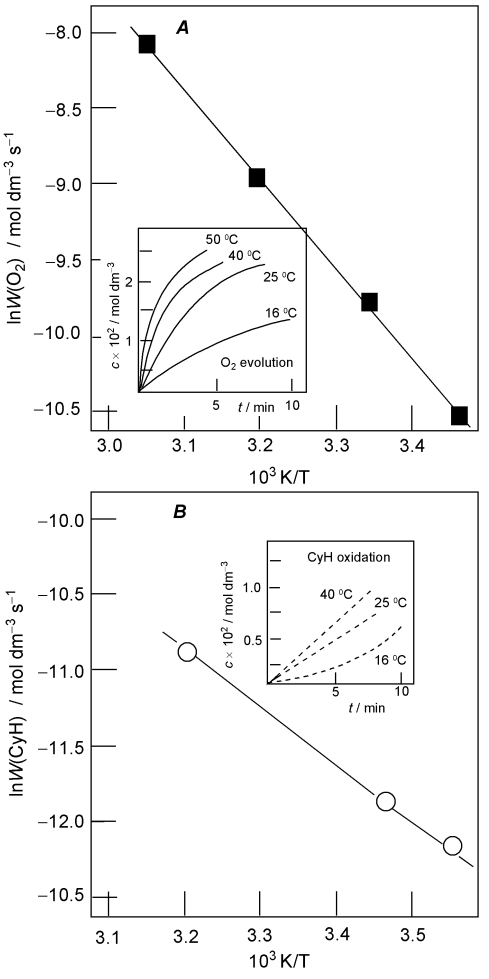


Fig. 6 Dependence of the O_2 evolution rate $W(O_2)$ (graph A) and the cyclohexane oxygenation rate W(CyH) (graph B) on temperature. Conditions: cyclohexane (0.46 mol dm^{-3}), **1a** (5×10^{-5} mol dm^{-3}), H_2O_2 (0.25 mol dm^{-3}), CH_3CO_2H (0.05 mol dm^{-3}). Curves of dioxygen evolution and oxygenate accumulation with time at various temperatures are shown in the insets. Initial rates of these reactions are plotted in the main graphs.

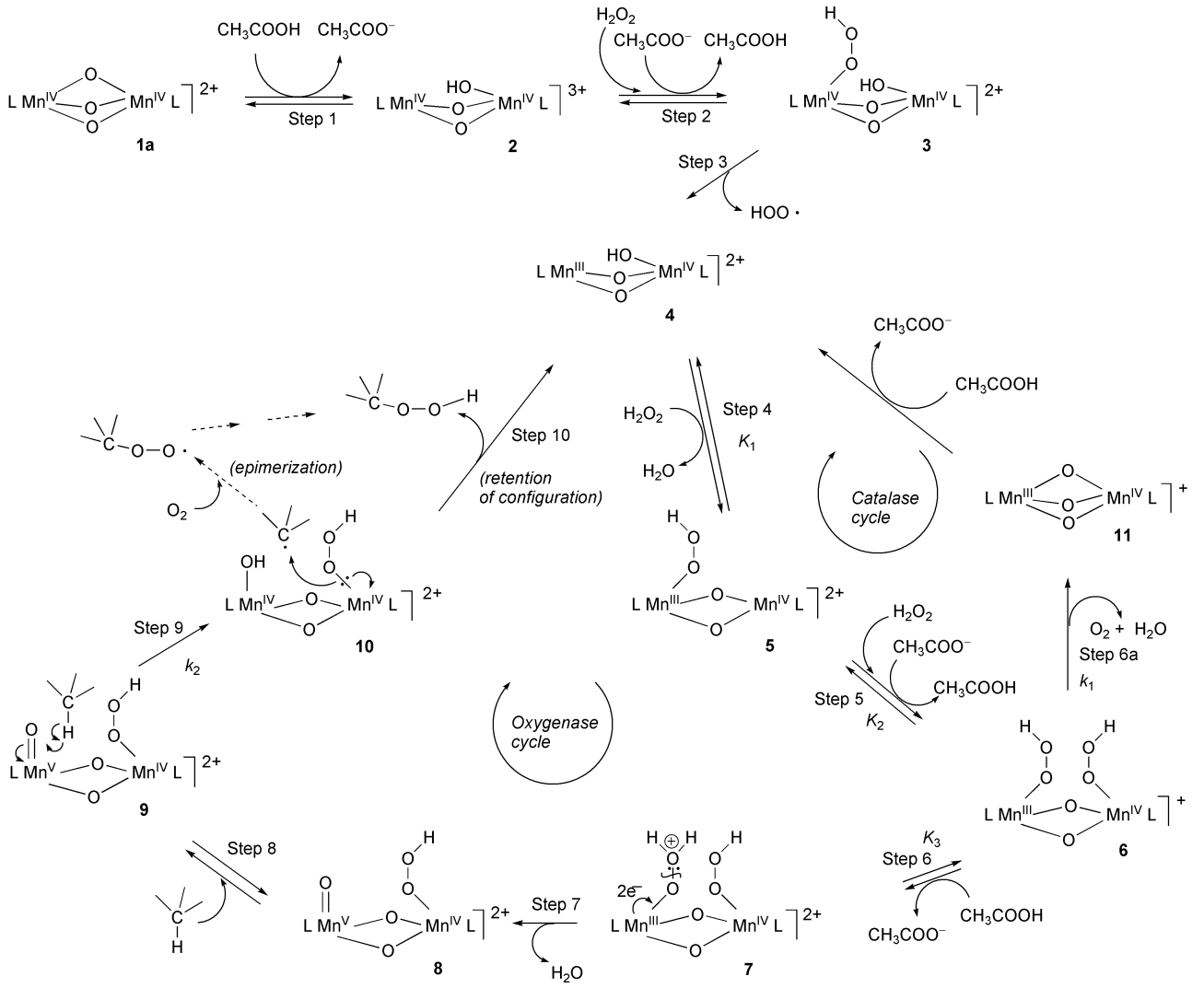
attained a value of 2.8 in the cyclohexane oxidation catalysed with the Mn(IV) complex of a polymeric ligand described in ref. 5*v*.

The data presented in Fig. 4(C) are primordial for understanding the process mechanism: the linear dependence of the ROOH formation rate on the initial cyclohexane concentration up to almost 1 mol dm^{-3} testifies that the oxidizing species in the system under consideration is not hydroxyl radical. Indeed, it is known[12*b*,*c*] that in the case of systems generating hydroxyl radicals, the ROOH formation rate becomes practically independent of the hydrocarbon concentration at [cyclohexane]$_0 > 0.3$ mol dm^{-3}, and this is in accordance with a competition between cyclohexane and acetonitrile for the reaction with the hydroxyl radical.

We have also found that mononuclear complex **1b** exhibits only very low oxygenase activity (the yield of cyclohexane oxygenates was 3×10^{-4} mol dm^{-3} after 15 min, which is 45 times less than that in the reaction catalysed by **1a**). Also negligible catalase activity (O_2 concentration was only 0.6×10^{-2} mol dm^{-3} after 11 min) has been found for this catalyst in the presence of CH_3CO_2H (0.05 mol dm^{-3}). This argues that a binuclear structure of the manganese complex is necessary for oxygenase activity.

Discussion

On the basis of the obtained data we propose the mechanism shown in Scheme 2. In the first step of the process acetic acid protonates one of the oxygen bridges between two manganese(IV) centres, resulting in the formation of a vacant site at one Mn(IV). Although acetic acid is a weak protonating agent we believe that such a process is possible in acetonitrile solution (in aqueous or methanol solutions oxo bridges can be protonated by strong acids;[3*e*,13*a*] see also a very recent paper on Mn–OH complexes[13*b*]). "Formation of a weak Mn–O(hydroxo) bond instead of a strong Mn–O(oxo) bond at the active site of OxMnCAT will greatly reduce the relative stability of the oxidized site and thus ensure the necessary driving force for the peroxide oxidation reaction".[13*c*] The formed complex then adds one hydrogen peroxide molecule, acetate anion being the proton acceptor. The hydroperoxo derivative **3** eliminates hydroperoxyl radical to afford the catalytically active Mn(III)Mn(IV) species, **4**. For oxidations of hydrogen peroxide by transition metal complexes see, for example, ref. 13*d*,*e*. Binuclear Mn(III)Mn(IV) derivatives with various ligands



Scheme 2 Mechanism proposed for hydrogen peroxide decomposition and alkane hydroperoxidation catalysed by a $(Mn)_2$ complex in the presence of acetic acid.

are well known and in some cases were obtained by the reduction of Mn(IV)Mn(IV) species.[3g,13a,f,g] Steps 4 and 5 lead to the formation of the dihydroperoxo complex of Mn(III)Mn(IV), **6**. Acetate anion and acetic acid (both in low concentrations) catalyse the formation and decomposition of complex **6**, yielding H_2O and O_2 and the derivative **11**. If acetic acid is present in higher concentration, the protonation of the –OOH ligand in **6** can occur and the dinuclear Mn^{V}=O derivative **8** is formed (such a mononuclear Mn^{V}=O species has been proposed and even detected in the literature[14]). The high-valent oxomanganese species abstracts a hydrogen atom from the alkane RH (step 9) to produce an alkyl radical, $R^{\bullet}$, and the

Table 1 Activities of some Mn-containing systems in H_2O_2 dismutation

Entry	System[a] (Mn-containing catalyst)	k_{cat}/s^{-1}	Reference
1	*Thermus thermophilus*	2.6×10^5	2*a*, 15*a*
2	*Lactobacillus plantarum*	2.0×10^5	2*a*, 15*b*
3	*Thermoleophilum album*	2.6×10^4	2*a*, 15*c*
4	Liver arginase	30	2*a*, 15*d*
5	$[Mn_4O_6(bpea)_4]^{3+}$–TMTACN	405	3*f*
6	$[Mn^{IV}(salpn)O]_2$	250	15*e*, 16
7	$[(TMTACN)Mn(O)_3Mn(TMTACN)]^{2+}$–*n*-$Bu_4NOH$	> 140	This work
8	$[Mn^{III}(2\text{-}OHsalpn)]_2$	22	16*a*
9	$[Mn^{III/IV}(TMTACN)(O)_2(OAc)(bpy)]^{2+}$	13	16*a*, 17*a*
10	$[Mn^{III}(saltnO)]_2$	13	3*d*, 17*b*
11	$[Mn^{III/IV}(TMTACN)(O)_2(\mu\text{-}OAc)(OAc)_2]$	5	16*a*, 17*a*
12	[Mn(salen)Cl]	0.24	3*d*
13	[Mn(TPP)Cl]	0.013	3*d*, 17*c*

[a] Abbreviations: bpea = *N*,*N*-bis(2-pyridylmethyl)ethylamine; salpn = 1,3-bis(salicylidenamino)propane; 2-OHsalpn = 1,3-bis(salicylideneamino)-2-propanol; H_2saltn = *N*,*N*′-propane-1,3-diylbis(salicylideneamine); H_2salen = *N*,*N*′-ethylenebis(salicylideneamine); TPP = tetraphenyltetraphenylporphyrinate.

Table 2 Comparison of various systems for the oxidation of organic compounds with hydrogen peroxide that are based on Mn–TACN derivatives as catalysts

No	Catalytic system	Oxidation reaction	Reference
1	**1a** and Mn complexes with related ligands	Bleaching of stains, epoxidation of 4-vinylbenzoic acid and styrene in water at pH 8–10 (40 °C)[a]	5*a*
2	**1b**	Oxidation in water at pH 9 (25 °C) of 4-vinylbenzoic acid to the corresponding epoxide and of styrylacetic acid to a mixture of the epoxide, diol and a ring-closed lactone[b]	5*c*
3	TMTACN–$MnSO_4 \cdot H_2O$	Epoxidation of styrene and cyclohexene in acetone (0 °C)[c]	5*d*
4	A manganese faujasite containing TMTACN	Epoxidation of styrene and cyclohexene in acetone (0 °C)[c]	5*d*
5	TMTACN–Mn^{2+}	Epoxidation of olefins in acetone (0 °C)[d]	5*e*
6	TACN derivative–$MnSO_4 \cdot H_2O$	Epoxidation of olefins in acetone or methanol (0 °C)[e]	5*f*
7	Chiral TACN derivative–$Mn(OAc)_2 \cdot 4H_2O$	Enantioselective epoxidation of olefins in methanol (0 °C)[f]	5*g*
8	TACN covalently anchored on silica–$MnSO_4 \cdot H_2O$	Epoxidation of styrene and cyclohexene in acetone or methanol (0 °C)[g]	5*h*
9	**1a**	Oxidation of benzyl alcohols to benzaldehydes in acetone at room temperature[h]	5*i*
10	Zeolite-exchanged Mn^{2+}–TMTACN	Oxidation of olefins and alkanes with H_2O_2 and *t*-BuOOH	5*j*
11	R_fTACN–$[R_f(CH_2)_2CO_2]_2Mn$	Allylic oxidations by *t*-BuOOH–O_2 (fluorous biphasic catalysis)	5*k*
12	**1a**	Oxidation of phenols in water at pH 10.5	5*l,m*
13	**1a**	Oxidation of sulfides to sulfones by periodic acid in pyridine	5*n*
14	TMTACN–$MnSO_4 \cdot H_2O$–oxalic acid–Na oxalate	Epoxidation of olefins in aqueous acetonitrile (5 °C)[i]	5*o*
15	TACN derivative anchored on solid–$MnSO_4 \cdot H_2O$	*cis*-Dihydroxylation and epoxidation of olefins in acetonitrile (0 °C)	5*p*
16	$[LMn^{IV}(O)_3Mn^{IV}L](PF_6)_2$ (L–TACN derivative)	Two-phase epoxidation of styrene and dodecene[j]	5*q*
17	$[L^1Mn^{IV}{}_2(O)_3](ClO_4)_2$	Oxidation of lignin models (epoxidation of double bonds and oxidation of hydroxyl groups) in acetone–water (30–60 °C)[k]	5*r*
18	$[L^*Mn^{III}(O)(AcO)_2Mn^{III}L^*](PF_6)_2$	Enantioselective epoxidation of olefins in acetone (−25 °C)[l]	5*s*
19	TMTACN–$Mn(OAc)_2 \cdot 4H_2O$–sodium ascorbate	Epoxidation of olefins and oxidation of alcohols to ketones and carboxylic acid in acetonitrile–water solution (0 °C)	5*t*
20	$[TPTNMn_2(O)(OAc)_2](ClO_4)_2$	Epoxidation of olefins in acetone (0 °C)[m]	5*u*
21	Polymer-bound TACN derivative–$Mn(OAc)_2 \cdot 4H_2O$–oxalic acid–sodium oxalate	Epoxidation of olefins and oxidation of alcohols in acetone–methanol–water (0 °C)	5*v*
22	**1a**–carboxylic acid	Hydroperoxidation of alkanes with partial retention of configuration in acetonitrile or nitromethane (−22 to +25 °C)[n]	8*a–d*
23	**1a**–carboxylic acid	Epoxidation of olefins, oxidation of alcohols to ketones and sulfides to sulfoxides at room temperature in acetonitrile[n]	8*d*
24	**1a**–carboxylic acid	Oxidation of alkanes by *t*-BuOOH at room temperature in acetonitrile[o]	8*d,e*

[a] The H_2O_2–substrate–catalyst ratio was 10 000:100:1; reaction time 2 h; conversion 98–99%. [b] The H_2O_2–substrate–catalyst ratio was 10 000:100:1; reaction time 1–3 h; conversion 69–98%. [c] The H_2O_2–substrate ratio was 1:1; hydrogen peroxide was gradually added; reaction time *ca.* 12 h; in methanol at 25 °C almost no epoxidation. [d] Hydrogen peroxide (2 mmol, 30%) was added gradually to the solution of olefin (1 mmol), TMTACN (1.5 μmol) and Mn^{2+} (1.0 μmol); turnover numbers (TON) were up to 1000; in methanol, isopropanol or acetonitrile, only small amounts of the epoxide were obtained; the oxidation of cyclohexane in acetone gave very low yield of cyclohexanol (TON = 9). [e] Epoxide yields were up to 98%; yields in acetonitrile or THF were much lower. [f] The epoxidation of *cis*-β-methylstyrene gave mainly (1*R*,2*R*)- *trans*-epoxide with 55% *ee*. [g] TON were up to 50 per hour. [h] TONs were up to 380. [i] Aqueous H_2O_2 was injected over 300 s into the reaction mixture contained 1 μmol of $MnSO_4 \cdot H_2O$, 1.5 μmol of TMTACN, 1.5 μmol of oxalic acid, 1.5 μmol of sodium oxalate and 0.67 mmol of an olefin; reaction time 0.3–2 h; yields 55–99%; the epoxidation occurs if the oxalate buffer is replaced with oxalic acid or sodium oxalate; no epoxide was found if acetic acid was added. [j] Reaction in dichloroethane–water–methanol; reaction time 16 h. [k] L′ is 1,2-bis-(4,7-dimethyl-1,4,7-triazacyclonon-1-yl)ethane; 1-(3,4-dimethoxyphenyl)ethanol, 1-(3,4-dimethoxyphenyl)-1-propene (mixture of *E* and *Z* isomers) and *E*-1,2-diphenylethene were used as model compounds; [l] L* is enantiopure TACN derivative; the epoxidation of styrene gave after 2 h the corresponding epoxide with 24% *ee* at 28% conversion of the styrene. [m] TPTN is *N*,*N*,*N*′,*N*′-tetrakis(2-pyridylmethyl)propane-1,3-diamine; the H_2O_2–substrate ratio was 8:1. [n] TONs attain 3300; reaction time 1–2 h; no reaction occurs in the absence of carboxylic (usually acetic) acid. [o] In the absence of acetic acid the reaction proceeds but less efficiently; olefins are not epoxidised under these conditions even in the presence of acetic acid.

Mn(IV)-hydroxy-Mn(IV)-hydroperoxy derivative, **10**. Finally, recombination of the alkyl radical R$^\bullet$ and hydroperoxy ligand HOO$^\bullet$ occurs in the solvent cage to give the reaction product, alkyl hydroperoxide, ROOH. The alkyl radicals can partially leave the solvent cages and react with molecular oxygen. The recombination step within the solvent cage with partial leaving of the alkyl radicals into the solution explains the partial retention of configuration in the alkane hydroperoxidation.

We have carried out the kinetic analysis of the scheme described above taking $[CH_3CO_2H]$ = const. Let us consider the following simplified kinetic scheme [eqn. (1)–(5)], where $(Mn)_2$ is a dinuclear catalytically active species.

$$(Mn)_2 + H_2O_2 \rightleftharpoons (Mn)_2 \cdot H_2O_2 \quad K_1(\text{step 4}) \tag{1}$$

$$(Mn)_2 \cdot H_2O_2 + H_2O_2 \rightleftharpoons (Mn)_2 \cdot (H_2O_2)_2 \quad K_2(\text{step 5}) \tag{2}$$

$$(Mn)_2 \cdot (H_2O_2)_2 + H^+ \rightleftharpoons (Mn)_2 \cdot (H_2O_2)_2 \cdot H^+ \quad K_3(\text{step 6}) \tag{3}$$

$$(Mn)_2 \cdot (H_2O_2)_2 \rightarrow (Mn)_2 + O_2 + 2H_2O \quad k_1(\text{step 6a}) \tag{4}$$

$$(Mn)_2 \cdot (H_2O_2)_2 \cdot H^+ + CyH \rightarrow \text{oxygenates} \quad k_2(\text{steps 7–9}) \tag{5}$$

Assuming that steps 6a and (7 + 8) (see Scheme 2) are rate-limiting steps and that the concentrations of complexes **5, 6** and **7** are at quasi-equlibrium, we obtain eqns. (6) and (7) for the rates of the catalase and oxygenase reactions, respectively:

$$\frac{d[O_2]}{dt} = \frac{k_1 K_1 K_2 [H_2O_2]^2 [(Mn)_2]_0}{1 + K_1[H_2O_2] + K_1 K_2 [H_2O_2]^2 (1 + K_3[H^+])} \tag{6}$$

$$\frac{d[RO_2H]}{dt} = \frac{k_2K_1K_2K_3[H_2O_2]^2[H^+][(Mn)_2]_0[RH]}{1 + K_1[H_2O_2] + K_1K_2[H_2O_2]^2(1 + K_3[H^+])} \quad (7)$$

These kinetic equations adequately describe the experimentally determined dependencies of both reaction rates on the initial concentrations of the catalyst [Fig. 4(A,B)] and of the cyclohexane [Fig. 4(C)] at a constant concentration of acetic acid.

Using eqns. (6) and (7) and accepting the following values for the combinations of constants that are included in these rate equations:

$$(k_1K_1K_2)^{-1} = 0.01 \text{ mol}^2 \text{ dm}^{-6} \text{ s} \quad (8)$$

$$K_1[H_2O_2] \ll 1 \quad (9)$$

$$k_1{}^{-1}(1 + K_3[H^+]) = 7 \times 10^{-3} \text{ s} \quad (10)$$

$$k_2K_1K_2K_3[H^+] = 13 \text{ mol}^{-3} \text{ dm}^9 \text{ s}^{-1} \quad (11)$$

we calculated theoretical curves for the dependencies of the rates of O_2 evolution and cyclohexane oxidation on the initial hydrogen peroxide concentration (Fig. 5, curves 1 and 2, respectively). It can be seen that although the simulated curves correctly correspond to the main features of both processes, there is not a very close coincidence of the experimental points and the theoretical curves. From this we can assume that the proposed scheme contains some simplifications and that in reality the mechanism is more complex and can involve additional steps. Nevertheless, this mechanism is consistent with all features found for the system. It follows from eqn. (10) that the constant for the monomolecular decomposition of the dimeric diperoxo manganese complex to evolve O_2 should not be less than 140 s^{-1}. The comparison of this parameter measured for the system discussed in this paper with that for other systems known from the literature (Table 1) shows that complex $[(TMTACN)Mn(O)_3Mn(TMTACN)]^{2+}$ in the presence of a small amount of *n*-Bu_4NOH in acetonitrile solution exhibits very high, for synthetic catalase models, catalytic activity in hydrogen peroxide dismutation.

We realise that although the mechanism presented in Scheme 2 adequately describes the main kinetic features of both catalase and oxygenase reactions, in reality both processes can proceed *via* more complex mechanism including a few parallel routes. For example, one can assume a similar catalytic cycle that involves participation the Mn(III)/Mn(II) couple instead of (in addition to) the proposed catalytically active Mn(IV)/Mn(III) couple (compare Scheme 1). Obviously, additional studies are required to get a full understanding of the mechanism actually operating in this very complex biomimetic system.

The system described here (that is, H_2O_2–**1a**–CH_3CO_2H in acetonitrile) exhibits unique properties in the oxidation of organic compounds. Similar systems based on manganese complexes with TACN derivatives described in the literature have absolutely different features in various oxidations and it is clear that they operate *via* different mechanisms. For example, complex **1a** catalyses olefin epoxidation in acetone solution in the absence of carboxylic acid. A manganese TMTACN derivative can be prepared *in situ* starting from a simple manganese salt and TMTACN. This derivative catalyses olefin epoxidation or benzyl alcohol oxidation without acetic acid. We have found that in acetonitrile solution no epoxidation proceeds if acetic acid is not present in the reaction mixture. Alkanes can be very efficiently oxidised (to alkyl hydroperoxides, ketones and alcohols) in acetonitrile solution only in the presence of carboxylic acid. No oxidation occurs under these conditions if the TMTACN complex is prepared *in situ*. Examples that show the differences between our system and other similar but "acid-free" systems are summarised in Table 2. It should be noted that almost nothing has been reported on the catalase activities of "acid-free" TACN–Mn systems.

Conclusions

We have demonstrated that only in the presence of small amounts of acetic acid can a dinuclear manganese complex catalyse both hydrogen peroxide decomposition and cyclohexane oxygenation by H_2O_2. The reaction pathway can be effectively controlled by addition of acids or bases in very small concentrations. The system described here mimics certain enzymes that can be "switched on" or "switched off" in living cells by the action of base or acid "switchers" such as amino acids.

Acknowledgements

We thank the Russian Basic Research Foundation (Project No. 98–03–32015a) for support. The authors are grateful to Prof. John R. Lindsay Smith for valuable discussions.

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