Oxidations by the reagent "O₂–H₂O₂–vanadium derivative–pyrazine-2-carboxylic acid'. Part 12.[1] Main features, kinetics and mechanism of alkane hydroperoxidation †

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Various combinations of vanadium derivatives (n-Bu₄NVO₃ is the best catalyst) with pyrazine-2-carboxylic acid (PCA) catalyse the oxidation of saturated hydrocarbons, RH, with hydrogen peroxide and air in acetonitrile solution to produce, at temperatures <40 °C, alkyl hydroperoxides, ROOH, as the main primary products. These compounds are easily reduced with triphenylphosphine to the corresponding alcohols, which can then be quantitatively determined by GLC. Certain aminoacids similar to PCA can play the role of co-catalyst; however the oxidation rates and final product yields are lower for picolinic and imidazole-4,5-dicarboxylic acids, while imidazole-4-carboxylic and pyrazole-3,5-dicarboxylic acids are almost inactive. The oxidation is induced by the attack of a hydroxyl radical on the alkane, RH, to produce alkyl radicals, R•. The latter further react rapidly with molecular atmospheric oxygen. The peroxyl radicals, ROO•, thus formed can be converted to alkyl hydroperoxides. We conclude on the basis of our kinetic investigation of the oxidation of cyclohexane that the rate-limiting step of the reaction is the monomolecular decomposition of the complex containing one coordinated PCA molecule: $V^V(PCA)(H_2O_2) \rightarrow V^{IV}(PCA) + HOO• + H^+$. The V^{IV} species thus formed reacts further with a second H₂O₂ molecule to generate the hydroxyl radical according to the equation $V^{IV}(PCA) + H_2O_2 \rightarrow V^V(PCA) + HO• + HO^-$. The concentration of the active species in the course of the catalytic process has been estimated to be as low as $[V(PCA)H_2O_2] \approx 3.3 \times 10^{-6}$ mol dm⁻³. The effective rate constant for the cyclohexane oxidation ($d[ROOH]/dt = k_{eff}[H_2O_2]_0[V]_0$) is $k_{eff} = 0.44$ dm³ mol⁻¹ s⁻¹ at 40 °C, the effective activation energy is 17 ± 2 kcal mol⁻¹. It is assumed that the accelerating role of PCA is due to its facilitating the proton transfer between the oxo and hydroxy ligands of the vanadium complex on the one hand and molecules of hydrogen peroxide and water on the other hand. For example: $(pca)(O=)V \cdots H_2O_2 \rightarrow (pca)(HO–)V–OOH$. Such a "robot's arm mechanism" has analogies in enzyme catalysis.

Introduction

Soluble vanadium derivatives are known to be efficient reagents and catalysts in oxidations of various organic compounds.[2] Vanadium plays an important role in living nature;[3] particularly some enzymes containing vanadium ions are capable of oxidizing C–H bonds in organic compounds. For example, vanadium-containing haloperoxidases[4] catalyse the halogenation of organic compounds, RH, in the presence of hydrogen peroxide and the indirect disproportionation of H₂O₂ in the presence of a halide anion.[5]

We have previously demonstrated that hydrogen peroxide oxidizes some organic substances, mainly alkanes (including very inert methane) in air, if a combination of tetrabutyl-ammonium vanadate and pyrazine-2-carboxylic acid (PCA) is used as a catalyst.[1,6,7] Almost no reaction occurs in the absence of PCA. Acetonitrile has been used as a solvent. At ambient

temperature the reaction with alkanes gives rise predominantly to the formation of alkyl hydroperoxides. Substantially lower amounts of the corresponding alcohols and ketones (alde-hydes) are formed simultaneously. It was shown that atmospheric oxygen participates in this reaction, and when it is absent no oxygenation occurs. The oxidation of cyclohexane in an atmosphere of ¹⁸O₂ provided convincing evidence that the oxidation products contain a considerable amount of labeled oxygen, and it has been concluded that hydrogen peroxide is a promoter in the oxidation of alkanes, while atmospheric oxygen plays the role of oxidant. This reagent gives a convenient method for efficient hydroperoxidation and oxygenation of alkanes under very mild conditions (for alkane oxygenation see books and reviews[2a,8]). It should be noted that recently, in analogous alkane oxidations, encapsulated vanadium complexes have been used.[9] An accelerating influence of PCA has been also observed in H₂O₂ oxidations catalysed by methyltrioxorhenium.[10] The aim of the present work is to investigate the vanadium-catalysed alkane oxygenation with H₂O₂ in more detail. We will particularly i) demonstrate that various vanadium derivatives can serve as catalysts in addition to the previously studied tetra-n-butylammonium vanadate, ii) com-

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† Electronic supplementary information (ESI) available: Appendix 1. On the possibility of radical-chain oxygenation of alkanes. Appendix 2. Comparison with other alkane-oxygenating systems. Additional references. See http://www.rsc.org/suppdata/p2/b1/b101442k/

pare the accelerating action of various chelating nitrogen-containing ligands with that of PCA, iii) check possible solvents for the reaction, iv) follow the formation of oxo and peroxo complexes of vanadium in the course of the oxidation by an NMR method, v) prove the formation of free radicals, vi) study the kinetics of the alkane oxygenation and propose the mechanism of the process.

Results and discussion

The system investigated in this work contains a vanadium derivative as a catalyst, VL_n, where L are various ligands, obligatory co-catalyst (pyrazine-2-carboxylic acid), promoter (H_2O_2) and "true" oxidant (molecular oxygen from air). An alkane, RH, was used as a substrate. The oxidation of an alkane by the system under consideration gives, according to GLC analysis, the corresponding ketone (aldehyde) and alcohol. If, prior to GLC analysis, an excess of solid triphenylphosphine is added to a sample of the reaction solution, the amount of the ketone (aldehyde) decreases, while that of the alcohol increases. This difference is due to the complete decomposition of the primary product alkyl hydroperoxide in the GLC injector to give the corresponding ketone (aldehyde) and alcohol. It should be noted that in some cases, when a GLC with quartz-lined injector and quartz capillary column was used, it is possible to detect peaks in the chromatograms due to alkyl hydroperoxides.[6f,g] Triphenylphosphine reduces the alkyl hydroperoxide easily and quantitatively to the corresponding alcohol. By comparing the concentrations of the ketone (aldehyde) and of the alcohol measured before and after the treatment of the sample with PPh_3, it is possible to estimate the *real* concentrations, not only of the carbonyl compound and of the alcohol, but also that of the alkyl hydroperoxide (for this method, see refs. 6, 7, 8c, d, 11). In order to precisely determine the rates of the reactions, however, it is more convenient to measure by GLC the concentrations only of ketones (aldehydes) and alcohols after the treatment of the sample with PPh_3. The sum of the amounts of all products determined after the reduction corresponds to the reaction rate. In this kinetic study we are not interested in the alkyl hydroperoxide/ketone (aldehyde)/alcohol ratio.

Vanadium-based catalysts

In our previous work on alkane oxidation with H_2O_2, we used tetra-*n*-butylammonium vanadate, *n*-Bu_4NVO_3, as the starting vanadium-containing component of the catalyst. This salt is readily soluble in acetonitrile and can be easily prepared starting from V_2O_5 and *n*-Bu_4NOH.[12] It was important to explore the possibility of using other vanadium derivatives as catalysts, especially those which do not contain oxo ligands. The oxidation reactions with all the vanadium-containing catalysts were carried out using PCA as a co-catalyst and cyclohexane as a substrate in acetonitrile at 50 or 40 °C. We have found that an efficient catalytic system can be prepared in the form of a complex of oxovanadate with PCA. For this purpose, vanadium(v) salt NH_4VO_3 (insoluble in acetonitrile), and PCA were stirred in hot acetonitrile before the catalytic oxidation (see Experimental section for details). The reaction course of the cyclohexane oxidation at various V : PCA ratios is shown in Fig. 1. It can be seen that the highest rate of the reaction is attained when the following concentrations of the components are used: 1.0×10^{-4} mol dm^{-3} of NH_4VO_3 and 5.0×10^{-4} mol dm^{-3} of PCA (Fig. 1d). When the ratio V : PCA = 1 : 2 the reaction rate is noticeably lower (Fig. 1a). If an efficient trap for alkyl radicals, CCl_3Br, is added to the reaction solution, cyclohexyl bromide is formed at the expense of oxygenated products (Fig. 1c).

An analogous system can be prepared using a derivative of vanadium(IV), $VOSO_4$, which is insoluble in acetonitrile. In this
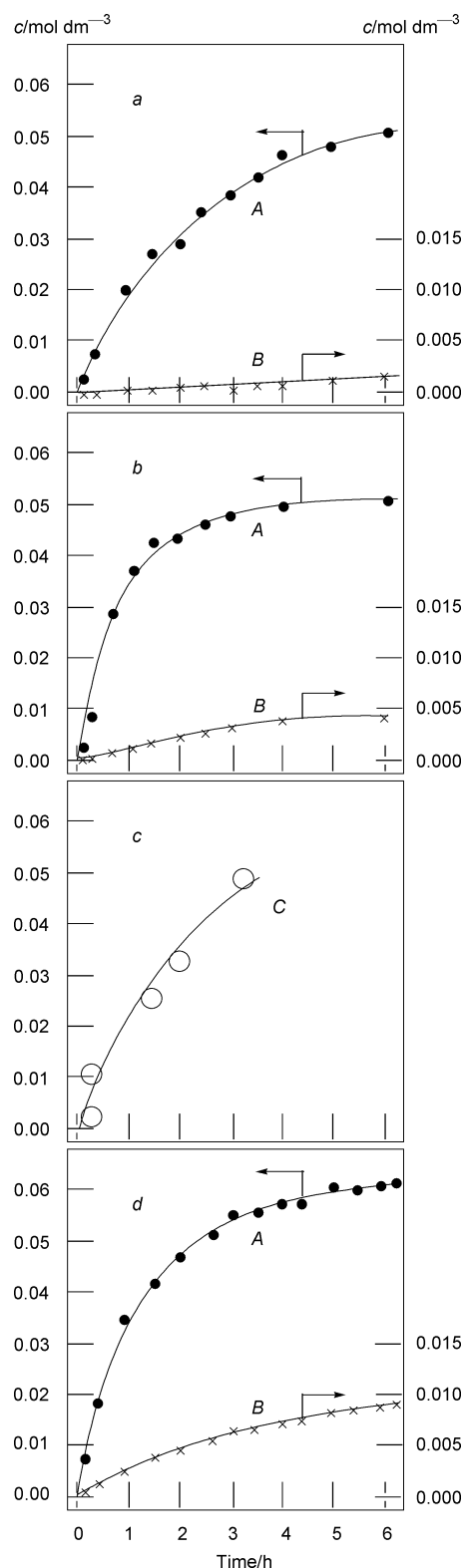

Fig. 1 Profiles of cyclohexane (initial concentration 0.4 mol dm^{-3}) oxidations by hydrogen peroxide (initial concentration 0.2 mol dm^{-3}) in acetonitrile at 50 °C catalysed by salt NH_4VO_3 (1.0×10^{-4} mol dm^{-3}) in the presence of PCA at various concentrations: 2.0×10^{-4} (a), 4.0×10^{-4} (b, c), and 5.0×10^{-4} mol dm^{-3} (d). Compound CCl_3Br (1.0 mol dm^{-3}) was added to the reaction solution in the experiment shown in graph 1(c). Concentrations, c, of cyclohexanol (curve A), cyclohexanone (curve B) and cyclohexyl bromide (curve C) were measured after the addition of an excess of solid triphenylphosphine.

case (Fig. 2) the reaction is slightly more rapid in comparison with the system based on NH_4VO_3 (compare with Fig. 1b). Fig. 3 presents results on the oxidation catalysed by derivatives of vanadium(III), VCl_3, and vanadium(IV), $VO(acac)_2$ which are
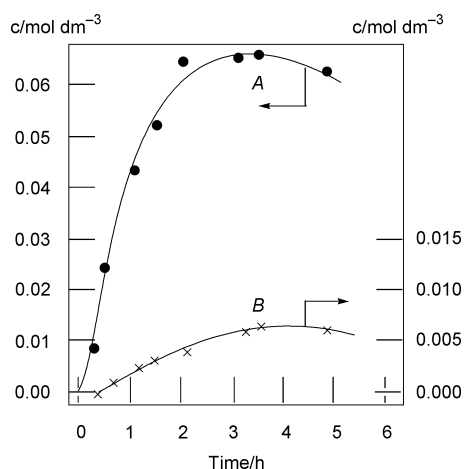
Fig. 2 Accumulation of cyclohexanol (*A*) and cyclohexanone (*B*) (measured after the addition of an excess of solid triphenylphosphine) during cyclohexane (0.4 mol dm^{-3}) oxidation by hydrogen peroxide (0.2 mol dm^{-3}) in acetonitrile at 50 °C catalysed by salt VOSO$_4$ (1.0 × 10^{-4} mol dm^{-3}) in the presence of PCA (4.0 × 10^{-4} mol dm^{-3}).
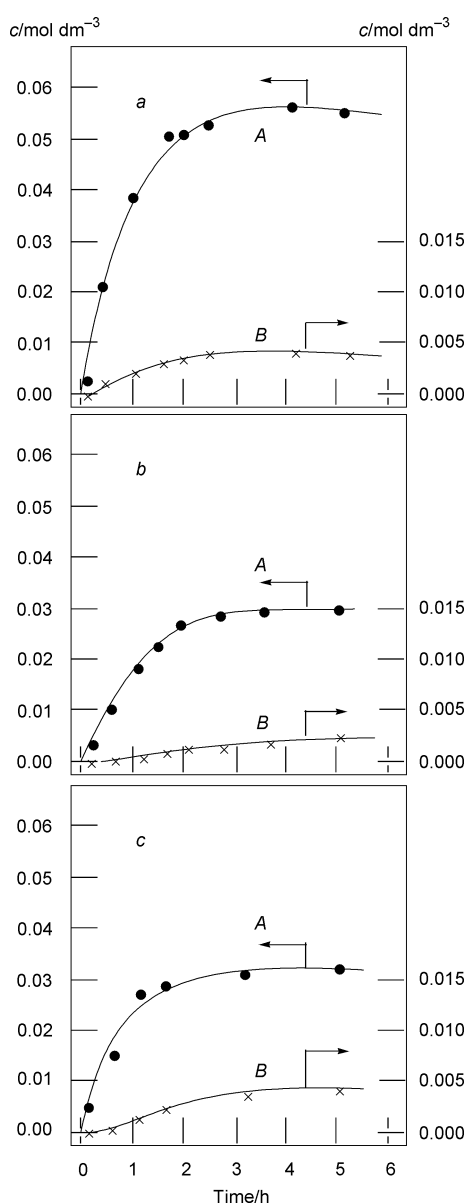
Fig. 3 Cyclohexane (0.4 mol dm^{-3}) oxidation by hydrogen peroxide (0.2 mol dm^{-3}) in acetonitrile at 50 °C in the presence of PCA (4.0 × 10^{-4} mol dm^{-3}) catalysed by certain vanadium derivatives (1.0 × 10^{-4} mol dm^{-3}): *n*-Bu$_4$NVO$_3$ (*a*), VCl$_3$ (*b*), and VO(acac)$_2$ (*c*). Concentrations of cyclohexanol (*A*) and cyclohexanone (*B*) were measured after the addition of an excess of solid triphenylphosphine.

Table 1 Oxidation of cyclohexane with H$_2$O$_2$ in acetonitrile (concentration of products, × 10^3, is given) using different samples of stock solution of *n*-Bu$_4$NVO$_3$[a]

	Stock solution of (*n*-Bu$_4$N)$^+$[VO$_3$]$^-$		
Time/min	Freshly prepared prior to experiment	Kept at −5 °C for 1 month	Kept at room temperature for 2 weeks
5	2.5	2.5	0.4
10	4.5	4.3	0.6
15	6.7	6.8	1.0

[a] Conditions: cyclohexane, 0.46 mol dm^{-3}, H$_2$O$_2$, 0.2 mol dm^{-3}, *n*-Bu$_4$NVO$_3$, 1.0 × 10^{-4} mol dm^{-3}, PCA, 4.0 × 10^{-4} mol dm^{-3}, 40 °C. Concentrations of cyclohexanol and cyclohexanone were measured after the addition of an excess of solid triphenylphosphine.

soluble in acetonitrile and turned out to be less efficient than *n*-Bu$_4$NVO$_3$. It is important to note that in all cases the presence of PCA as a co-catalyst is obligatory. Indeed, the concentration of all oxygenates after 3 h under catalysis with VO(acac)$_2$ in the absence of PCA was only 0.5 × 10^{-4} mol dm^{-3}. The vanadium-containing cluster (*p*-MeC$_6$H$_4$-iPr)$_4$Ru$_4$V$_6$O$_{19}$ (the synthesis of which has been described recently in ref. 13) catalyses the cyclohexane oxygenation in the presence of PCA (Fig. 4). Finally, a catalyst can be prepared *in situ* from V$_2$O$_5$, H$_2$O$_2$ and PCA (Fig. 5). Details of this experiment are described in the Experimental section.

It can be concluded that *n*-Bu$_4$NVO$_3$ is one of the most efficient and available vanadium-containing catalysts. This compound was used in this work in almost all experiments. The catalyst was introduced into the reaction mixture in the form of an aliquot of a stock solution of *n*-Bu$_4$NVO$_3$ in acetonitrile. Before conducting precise kinetic measurements, it was important to study the dependence of the efficiency of this stock solution on the time of its storage prior to the experiment. Table 1 summarises the initial rates of cyclohexane oxygenation. It can be seen that the activity of the catalyst is not changed if the stock solution is kept at −5 °C for a period of 1 month.

Effect of pyrazine-2-carboxylic acid and other possible co-catalysts

If a vanadium derivative is used at a concentration of 1.0 × 10^{-4} mol dm^{-3} and no PCA is added the rate of alkane oxidation is negligible. In the case when *n*-Bu$_4$NVO$_3$ is introduced into the reaction mixture in a higher concentration (1.0 × 10^{-3} mol dm^{-3}) some amount of cyclohexanol can be detected even in the absence of PCA as a co-catalyst (Fig. 6). However, the turnover number (TON, moles of products per mole of a catalyst) only slightly exceeds unity, that is to say the reaction is close to stoichiometric. The concentration of cyclohexanol after 10 min is only 0.26 × 10^{-3} mol dm^{-3}. The amount of cyclohexanone formed is negligible, which shows that in this case pure cyclohexyl hydroperoxide is formed. When a relatively small amount of PCA (4.0 × 10^{-4} mol dm^{-3}) is added to this solution, the concentration of the alcohol rises up to 1.5 × 10^{-2} mol dm^{-3}, which means an acceleration of the reaction by a factor of 55.

It is reasonable to assume that the vanadium derivative employed as a catalyst forms, under the reaction conditions, oxo and oxo-peroxo complexes (see below). We investigated the cyclohexane oxidation catalysed by isolated complexes of this type in the absence of free PCA. Fig. 7*a* shows the accumulation of oxygenates during the oxidation catalysed by a dioxo complex of vanadium(v), [V(O)$_2$(pca)$_2$]$^-$ (**1**), where pcaH = PCA. The oxidations catalysed by oxo-peroxo complexes [V(O$_2$)(O)(pca)$_2$]$^-$ (**2**) (for preparation, see ref. 7*f*) and [V(O$_2$)(O)(pca)]·2H$_2$O[14a] are illustrated by Fig. 8*a,b*. It is evident that the
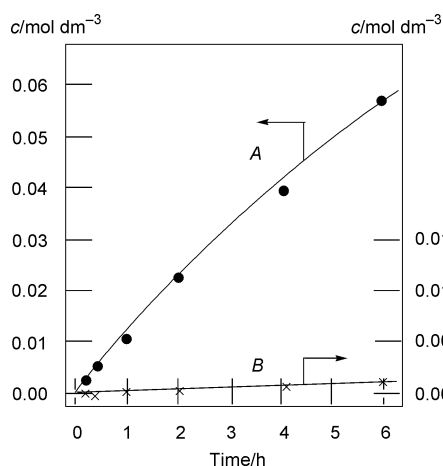
Fig. 4 Accumulation of cyclohexanol (*A*) and cyclohexanone (*B*) (measured after the addition of an excess of solid triphenylphosphine) during cyclohexane (0.4 mol dm^{-3}) oxidation by hydrogen peroxide (0.5 mol dm^{-3}) in acetonitrile at 40 °C catalysed by cluster complex (*p*-MeC$_6$H$_4$-iPr)$_4$Ru$_4$V$_6$O$_{19}$ (1.0 × 10^{-4} mol dm^{-3}) in the presence of PCA (4.0 × 10^{-4} mol dm^{-3}).
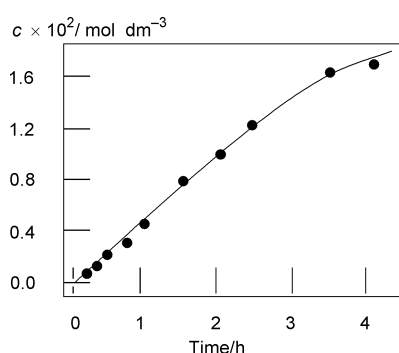
Fig. 5 Cyclohexane (0.46 mol dm^{-3}) oxidation by hydrogen peroxide (0.17 mol dm^{-3}) in acetonitrile at 40 °C catalysed by a mixture prepared previously starting from V$_2$O$_5$ (concentration of V ions 1.0 × 10^{-4} mol dm^{-3}), PCA (4.0 × 10^{-4} mol dm^{-3}) and H$_2$O$_2$ (see Experimental section). Concentration of cyclohexanol (●) was measured after the addition of an excess of solid triphenylphosphine. Concentration of cyclohexanone was less than 0.8 × 10^{-4} mol dm^{-3} in all cases.
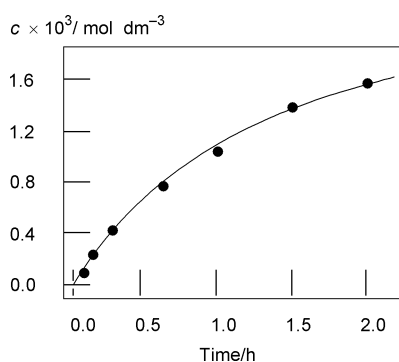
Fig. 6 Accumulation of cyclohexanol (measured after the addition of an excess of solid triphenylphosphine) during cyclohexane (0.46 mol dm^{-3}) oxidation by hydrogen peroxide (0.2 mol dm^{-3}) in acetonitrile at 40 °C in the presence of Bu$_4$NVO$_3$ (1.0 × 10^{-3} mol dm^{-3}) in the absence of PCA.

Fig. 7 Cyclohexane (0.4 mol dm^{-3}) oxidation by hydrogen peroxide (0.5 mol dm^{-3}) in acetonitrile at 40 °C catalysed by complex (*n*-Bu$_4$N)$^+$[V(O)$_2$(pca)$_2$]$^-$ (**1**) (1.0 × 10^{-4} mol dm^{-3}) in the absence of HClO$_4$ or free PCA (*a*), in the presence of HClO$_4$ (2.0 × 10^{-4} mol dm^{-3}) (*b*), and in the presence of free PCA (2.0 × 10^{-4} mol dm^{-3}) (*c*). Concentrations of cyclohexanol (*A*) and cyclohexanone (*B*) were measured after addition of an excess of solid triphenylphosphine.

complexes **1** and **2** used in a concentration of 1.0 × 10^{-4} mol dm^{-3} (in the absence of added PCA) catalyse the oxidation, however the efficiency of this catalysis is relatively low (compare Figs. 7*a* and 8*a*,*b* with Fig. 8*c*; the latter graph presents the oxidation catalysed with the combination "*n*-Bu$_4$NVO$_3$ + 4PCA" under the same conditions). It is noteworthy that the addition of free PCA to the reaction mixture gives rise to an acceleration of the oxidation and enhances the yield of

oxygenates, getting close to that obtained with "*n*-Bu$_4$NVO$_3$ + 4PCA" (compare Figs. 7*a*,*c*, 8*c*). This clearly demonstrates that the system needs free PCA in addition to the amount which is necessary for the formation of a complex between an oxo-vanadium derivative and PCA.

We have also found that perchloric acid can be used as a co-catalyst; however the accelerating effect of HClO$_4$ is much less pronounced than that for PCA (compare Fig. 9*a* and Fig. 8*c*). The dependence of the initial reaction rate on the HClO$_4$ concentration is shown in Fig. 10. When PCA is added to the mixture containing HClO$_4$, the reaction proceeds much faster (Fig. 9*c*,*d*), especially for a PCA concentration of 4.0 × 10^{-4} mol dm^{-3} (Fig. 9*d*). However, the latter experiment demonstrates that the addition of HClO$_4$ to the "standard" catalyst composition (*n*-Bu$_4$NVO$_3$ + 4PCA) does not enhance the rate of oxygenation (this rate is even slightly lower in comparison with the experiment in the absence of perchloric acid: compare Fig. 9*d* and Fig. 8*c*). Unlike perchloric acid, the weak acetic acid does not affect the oxidation at all.
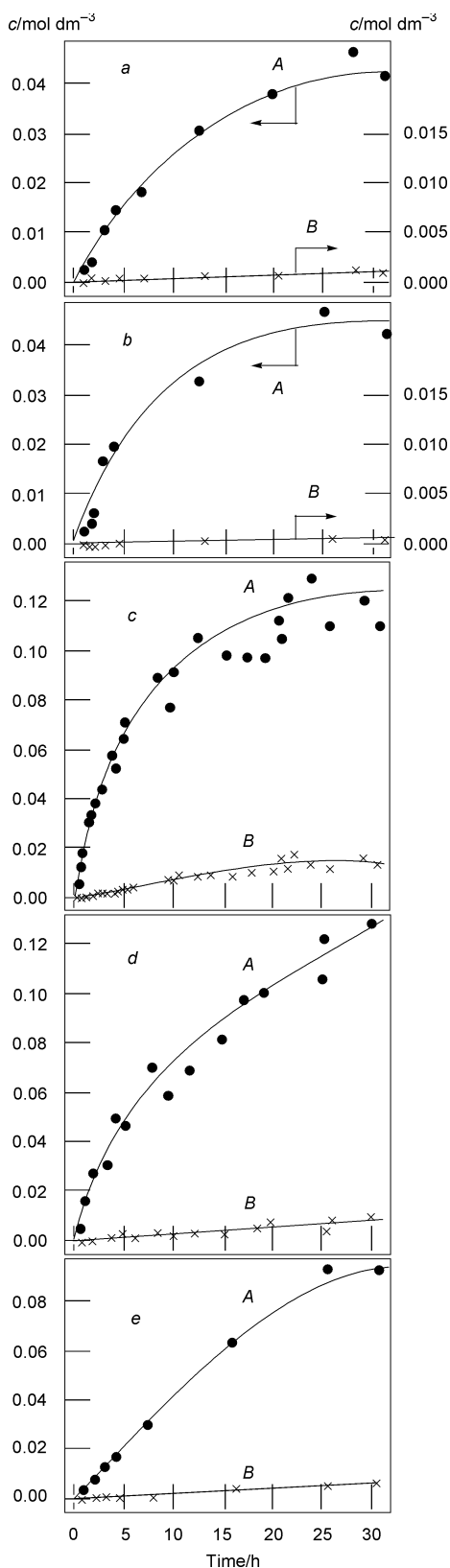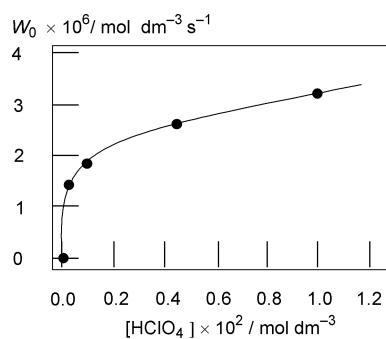
Fig. 8 Cyclohexane (0.4 mol dm^{-3}) oxidation by hydrogen peroxide (0.5 mol dm^{-3}) in acetonitrile at 40 °C catalysed by complexes NH$_4$[V(O$_2$)(O)(pca)$_2$] (**2**) (*a*) and [V(O$_2$)(O)(pca)]·2H$_2$O (*b*) (1.0 × 10^{-4} mol dm^{-3}) in the absence of free PCA and catalysed by *n*-Bu$_4$NVO$_3$ (1.0 × 10^{-4} mol dm^{-3}) in the presence of certain co-catalysts (4.0 × 10^{-4} mol dm^{-3}): PCA (*c*), pyrazine-2,3-dicarboxylic acid (*d*), and picolinic acid (*e*). Concentrations of cyclohexanol (*A*) and cyclohexanone (*B*) were measured after the addition of an excess of solid triphenyl-phosphine.

It was important to check the co-catalytic activity of other compounds whose structure is similar to that of PCA. It turned out that the chelating nitrogen-containing carboxylic
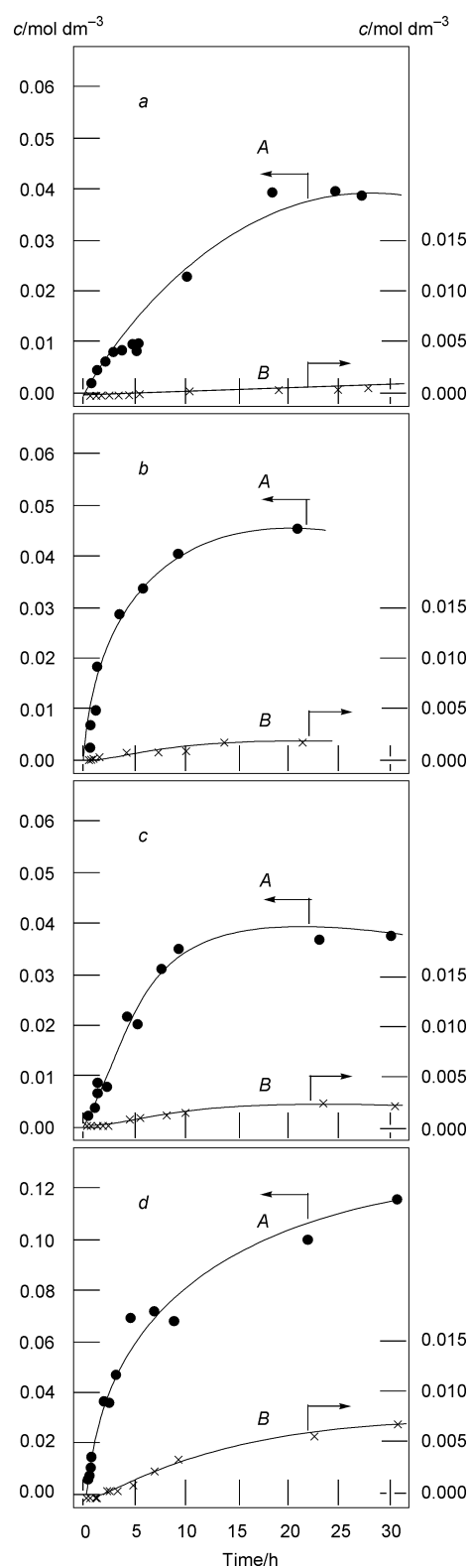
Fig. 9 Profiles of cyclohexane (0.4 mol dm^{-3}) oxidations by hydrogen peroxide (0.5 mol dm^{-3}) in acetonitrile at 40 °C catalysed by salt *n*-Bu$_4$NVO$_3$ (1.0 × 10^{-4} mol dm^{-3}) in the presence of HClO$_4$ (4.0 × 10^{-4} mol dm^{-3}) (*a*), PCA (2.0 × 10^{-4} mol dm^{-3}) (*b*), HClO$_4$ (3.0 × 10^{-4} mol dm^{-3}) + PCA (2.0 × 10^{-4} mol dm^{-3}) (*c*), and HClO$_4$ (4.0 × 10^{-4} mol dm^{-3}) + PCA (4.0 × 10^{-4} mol dm^{-3}) (*d*). Concentrations of cyclohexanol (*A*) and cyclohexanone (*B*) were measured after the addition of an excess of solid triphenylphosphine.

acids closest to PCA, pyrazine-2,3-dicarboxylic acid, PDCA, (Fig. 8*d*) and picolinic acid (Fig. 8*e*) also play the role of efficient co-catalysts, although the initial rates of the oxidation in the case of these compounds are lower in comparison with that of PCA (Fig. 8*c*). When PCA as a co-catalyst was replaced

Fig. 10 Plot of the initial rate of cyclohexane (0.46 mol dm^{-3}) oxidation by hydrogen peroxide (0.2 mol dm^{-3}) in acetonitrile at 40 °C catalyzed by salt n-Bu$_4$NVO$_3$ (1.0 × 10^{-4} mol dm^{-3}) and PCA (4.0 × 10^{-4} mol dm^{-3}) *versus* initial concentration of HClO$_4$ added.
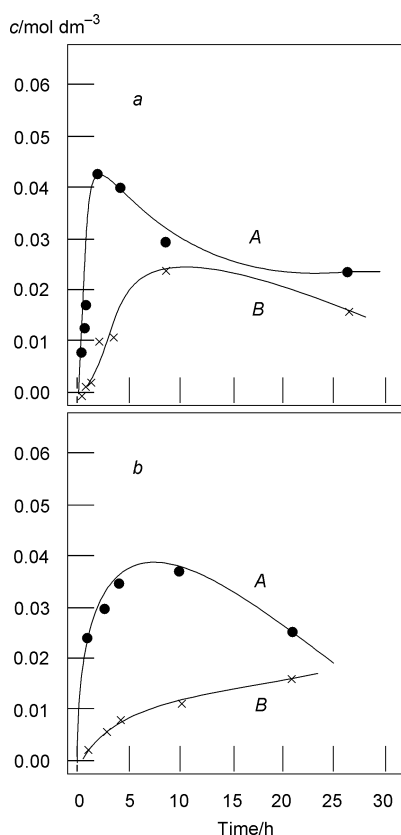
Fig. 11 Cyclohexane (0.45 mol dm^{-3}) oxidation by hydrogen peroxide (0.5 mol dm^{-3}) in a mixture acetic acid–water (99 : 1 v/v) at 40 °C catalysed by NaVO$_3$ (1.0 × 10^{-4} mol dm^{-3}) in the presence of PCA (4.0 × 10^{-4} mol dm^{-3}) (*a*) and in the absence of PCA (*b*). Concentrations of cyclohexanol (*A*) and cyclohexanone (*B*) were measured after the addition of an excess of solid triphenylphosphine. The catalyst (NaVO$_3$) was introduced as a stock solution in water.

by imidazole-4,5-dicarboxylic acid, the yield of oxygenates was found to be 2–3 times lower. It is very interesting that the similar compounds pyrazole-3,5-dicarboxylic acid, imidazole-4-carboxylic acid and 5-methyl-2-phenyl-1,2,3-triazole-4-carboxylic acid turned out to be almost inactive in the cyclohexane oxidation. One can assume that the efficient accelerating effect of PCA, and cyclic amino acids very similar to it, is associated with the ability of these compounds to form chelating six-membered cycles with vanadium ion and possibly also to form zwitterionic structures (see below for more detailed discussion).

Suitable solvents

Acetonitrile is the solvent of choice for the reaction under discussion. The oxidation in acetone proceeds less efficiently.[6e] It is known that these solvents are not completely inert towards

Table 2 Selectivity parameters for competitive oxygenations of cycloalkanes[a]

Reagent	c-C$_5$/c-C$_6$	c-C$_8$/c-C$_6$	c-C$_{12}$/c-C$_6$
O$_2$–H$_2$O$_2$–NH$_4$VO$_3$–PCA [b]	0.73	1.6	1.0
O$_2$–H$_2$O$_2$–hv[c]	0.96	1.6	0.9

[a] Normalized (*i.e.*, taking into account the number of hydrogen atoms in each hydrocarbon) reactivities of hydrogen atoms in cycloalkanes, C$_N$, relative to that in cyclohexane (c-C$_6$ = 1.0); the reactions were in acetonitrile. [b] For c-C$_8$/c-C$_6$ and c-C$_{12}$/c-C$_6$ at 50 °C, for c-C$_5$/c-C$_6$ at 30 °C; 1 h. [c] UV Irradiation at 25 °C; 20 min.

hydrogen peroxide, especially in the presence of a metal-complex catalyst.[14b,c] For example, acetonitrile, in the presence of a base in large amounts (pH of 10) as well as trichloro-acetonitrile,[14d,e] gives peroxycarboximidic acids. Acetone forms tetrameric acetone peroxide.[14f] However, we can neglect the chemical reaction between hydrogen peroxide and the nitrile group under our conditions (*i.e.*, in the absence of a base). We have also obtained preliminary results on the possibility of carrying out this oxidation in a protic solvent. The oxidation of cyclohexane under "standard" conditions in acetic acid is shown in Fig. 11. It can be concluded that in this solvent the vanadium-catalysed oxidation proceeds less efficiently in comparison with acetonitrile, and the addition of PCA does not accelerate the reaction. Since cyclohexane is insoluble in water we checked this solvent using benzene (in a very low concentration) as a substrate. The oxidation is not efficient under these conditions. Indeed, the yield of phenol after 5 h attains 14% based on benzene and TON = 14 based on [V]$_0$.

Selectivity of alkane oxygenation

In order to gain insight into the nature of the oxidizing species and evaluate the mechanism of the process we determined various selectivity parameters for the reaction under discussion with alkanes as well as for oxygenations by some other systems. These data are summarized in Tables 2–5.

Competitive reactions for pairs of cycloalkanes allowed us to determine the reactivities[17] of the hydrogen atoms in cyclopentane, cyclooctane and cyclododecane relative to those in cyclohexane (Table 2). The corresponding parameters for the oxygenation with H$_2$O$_2$ in acetonitrile under UV irradiation are also given in Table 2, since the mechanism of the action of this system is known: hydroxyl radicals are reactive intermediates in the reaction.[18] It is clear that a close similarity exists between the parameters for the two systems, "O$_2$–H$_2$O$_2$–NH$_4$VO$_3$–PCA" and "O$_2$–H$_2$O$_2$–hv". Both these oxidizing systems exhibit low selectivities in oxygenations of linear and branched alkanes (Table 3). Fenton's reagent, "O$_2$–H$_2$O$_2$–FeSO$_4$", and the system "O$_2$–H$_2$O$_2$–Fe(ClO$_4$)$_3$" similarly oxidize with low selectivities. Fenton's reagent is believed to produce hydroxyl radicals[19] (see, however, refs. 20). Experiments on the oxidation of disubstituted cyclohexanes demonstrated that vanadium-catalysed reaction occurs without retention of configuration, *i.e.*, the *trans*/*cis* ratio is approximately the same for oxidation of both *cis*- and *trans*-isomers of the substituted cyclohexane and this value is usually more than unity (Table 5). A similar situation was found for the reaction with the "O$_2$–H$_2$O$_2$–FeSO$_4$" and "O$_2$–H$_2$O$_2$–FeSO$_4$" systems. Various selectivity parameters for the oxidations with participation of PDCA and perchloric acid as co-catalysts are similar to those obtained for PCA.

It is important to note that the systems known to oxidize without the production of hydroxyl radicals exhibited different values of the selectivity parameters. For example, the oxidations of alkanes with H$_2$O$_2$ in CF$_3$COOH and with C$_6$H$_5$COOOH in benzene exhibit much higher selectivities compared to the oxidation with the "O$_2$–H$_2$O$_2$–n-Bu$_4$NVO$_3$–PCA" system (Tables 3 and 5). The oxo-peroxo complex

Table 3 Oxidation of normal and branched alkanes[a]

Reagent	n-Pentane	n-Hexane	n-Heptane	Methylbutane	2-Methylpentane	3-Methylpentane	2-Methylhexane	3-Methylhexane	2,2,4-Trimethylpentane
O$_2$–H$_2$O$_2$–n-Bu$_4$NVO$_3$–PCA[b]	1:8:7	1:9:7	1:6:6:5	1:6.5:37	1:6:25	1:6:22	1:5:5:24	1:14:64	1:3:5
O$_2$–H$_2$O$_2$–n-Bu$_4$NVO$_3$–PDCA[c]	1:5.5:6		1:6:6:6	1:7:30	1:7:32	1:6:38		1:4.5:26	
O$_2$–H$_2$O$_2$–n-Bu$_4$NVO$_3$–HClO$_4$[c]	1:5.5:12		1:7:6:7					1:4:30	
[V(O)(O$_2$)(pic)(H$_2$O)$_2$][d]		1:40:20							
O$_2$–H$_2$O$_2$–hv[e]		1:10:7	1:5:5:4.5				1:6:20	1:7:9	1:2:6
O$_2$–H$_2$O$_2$–Fe(ClO$_4$)$_3$[e]		1:9:9						1:4:12	
O$_2$–H$_2$O$_2$–FeSO$_4$[e]									1:3:6
H$_2$O$_2$ in CF$_3$COOH		1:364:363[f]							1:52:0

[a] Parameters are relative reactivities of hydrogen atoms at carbons 1, 2, 3 and 4, C(1):C(2):C(3):C(4), of the chain of unbranched alkanes and at primary, secondary and tertiary carbons, 1°:2°:3°, of branched alkanes and are normalized, i.e., calculated taking into account the number of hydrogen atoms at each carbon. The reactions were in acetonitrile. Samples were reduced with triphenylphosphine before GLC analysis. PDCA, pyrazine-2,3-dicarboxylic acid. [b] At 50 °C. [c] At 40 °C. [d] Stoichiometric oxidation at room temperature by the complex with picolinate anion (pic); the synthesis of this complex has been described in Ref. 14a. [e] At room temperature. [f] Data from Ref. 15a.

Table 4 Oxidation of cyclohexane-d_{12}, adamantane and ethylbenzene/cyclohexane[a]

Reagent	KIE,[b] k_H/k_D	2°:3°[c]	Ethylbenzene/cyclohexane[d]
O$_2$–H$_2$O$_2$–n-Bu$_4$NVO$_3$–PCA[e]	1.2	0.75	0.5
O$_2$–H$_2$O$_2$–hv[f]	2.2	0.7	0.8
O$_2$–H$_2$O$_2$–Fe(ClO$_4$)$_3$[f]	1.9	0.25	
[V(O)(O$_2$)(pic)(H$_2$O)$_2$][g]	2.8[h]		1.6
C$_6$H$_5$COOOH in benzene[i]		0.09	

[a] Samples were reduced with triphenylphosphine before GLC analysis. The reactions were in acetonitrile. [b] Kinetic isotope effect, determined by comparison of oxidations of cyclohexane and cyclohexane-d_{12}. [c] Relative normalized reactivities of hydrogen atoms at secondary and tertiary carbons of adamantane. [d] The normalized reactivities of methylene hydrogen atoms in ethylbenzene relative to those in cyclohexane. [e] At 50 °C. [f] At room temperature. [g] Stoichiometric oxidation at room temperature by the complex with picolinate anion (pic); the synthesis of this complex has been described in ref. 14a. [h] Data from ref. 14a. [i] Peroxybenzoic acid in benzene at 100 °C; data from ref. 15b.

[V(O)(O$_2$)(pic)(H$_2$O)$_2$], which contains only one molecule of chelating ligand (picolinate, pic), oxidizes alkanes stoichiometrically with high selectivity (Table 3), and the reaction of this complex with disubstituted cyclohexanes occurs with partial retention of configuration (cis-disubstituted cyclohexanes give rise to the predominant formation of cis-tert-alcohol, see Table 5). The reaction of alkanes with H$_2$O$_2$ catalysed by the combination "[L$_2$Mn$_2$O$_3$](PF$_6$)$_2$ (L = 1,4,7-trimethyl-1,4,7-triazacyclononane)–MeCOOH",[16] which is believed to proceed without formation of free hydroxyl radicals demonstrated selectivities different from those found for the "O$_2$–H$_2$O$_2$–n-Bu$_4$NVO$_3$–PCA" system. Unlike the complex [V(O)(O$_2$)(pic)(H$_2$O)$_2$], the vanadium oxo-peroxo derivative **2**, which contains two anions of pyrazine-2-carboxylic acid as ligands, exhibits stereoselectivity neither in stoichiometric nor in catalytic reactions. This shows that the oxidations in the presence of complex [V(O)(O$_2$)(pic)(H$_2$O)$_2$] and of compound **2** proceed via different mechanisms.

Production of hydroxyl radicals from hydrogen peroxide

Since the selectivity parameters obtained for oxidation by the "O$_2$–H$_2$O$_2$–n-Bu$_4$NVO$_3$–PCA" system indicate that hydroxyl radicals could be reactive intermediates in this reaction, we undertook an additional study to prove the formation of hydroxyl radicals. It should be noted that hydroxyl radicals are believed to play a very important role in various chemical and biochemical processes.[19a,d,g,21] Hydroxyl radicals can be generated from hydrogen peroxide under the action of various transition metal ions such as iron(II),[19] iron(III),[22a] and copper(I),[22b,c] copper(II),[22d] chromium(IV),[22e] (see also ref. 22f), uranium(IV),[22g] cobalt(II).[22h] Some chemical and biochemical systems involving vanadium are also known to generate hydroxyl radicals.[22g,23]

The spin trap method is widely used for the fixation of radicals that arise in various chemical and biochemical reactions.[21c,d,f,22d–h,24] In order to prove the formation of hydroxyl radicals and their participation in hydrocarbon oxidations by the "O$_2$–H$_2$O$_2$–n-Bu$_4$NVO$_3$–PCA" system we used N-(benzylidene)-tert-butylamine N-oxide (nitrone **3**). The interaction of nitrone **3** with a hydroxyl radical gives rise to the formation of the radical adduct **4** [eqn. (1)].

We have found that a signal having a triplet structure with $g = 2.0057 \pm 0.0002$, $a_N = 13.75$ mT and $a_H^\beta = 2.25$ mT appears in the EPR spectrum (Fig. 12) of a solution containing n-Bu$_4$NVO$_3$ (1.0×10^{-4} mol dm^{-3}), PCA (4.0×10^{-4} mol dm^{-3}), cyclohexane (0.46 mol dm^{-3}) and the nitrone **3** (0.05 mol dm^{-3}) in acetonitrile after the addition of a 30% aqueous solution of hydrogen peroxide (resulting concentration was 0.1 mol dm^{-3}). These parameters of the EPR spectrum agree satisfactorily with

Table 5 Oxidation of disubstituted cyclohexanes (*trans/cis* ratio) in acetonitrile [a]

	Oxidation of					
Reagent	*cis*-Decalin	*trans*-Decalin	*cis*-1,2-DMCH	*trans*-1,2-DMCH	*cis*-1,4-DMCH	*trans*-1,4-DMCH
O$_2$–H$_2$O$_2$–*n*-Bu$_4$NVO$_3$–PCA [b]	2.1	2.4	0.75	0.8	1.45	1.6
O$_2$–H$_2$O$_2$–*n*-Bu$_4$NVO$_3$ in MeCOOH [b]	0.9	5.0	0.85	0.7	1.5	1.2
O$_2$–H$_2$O$_2$–*n*-Bu$_4$NVO$_3$–PCA in MeCOOH [b]	1.0	3.8				
O$_2$–H$_2$O$_2$–*n*-Bu$_4$NVO$_3$–PDCA [c]	5.3	5.4				
O$_2$–H$_2$O$_2$–*n*-Bu$_4$NVO$_3$–HClO$_4$ [c]	5.9	1.4				
O$_2$–H$_2$O$_2$–*hv* [c]	1.3	2.7	0.9	1.0	1.5	1.4
O$_2$–H$_2$O$_2$–FeSO$_4$ [c]	3.4	8.8	1.3	1.2	1.5	1.5
O$_2$–H$_2$O$_2$–FeSO$_4$–PCA [c]	1.15	8.8	1.0	0.9	1.65	1.5
[V(O)(O$_2$)(pic)(H$_2$O)$_2$] [d]	0.24	6.0	0.26	*ca.* 8	1.0	3.4
NH$_4$[V(O$_2$)(O)(pca)$_2$] (compound **2**, stoichiometrically) [c]	3.0		0.9	0.6	1.6	1.5
O$_2$–H$_2$O$_2$–compound **2** [c]	2.5	4.5	0.8	0.8	1.3	1.3
H$_2$O$_2$ in CF$_3$COOH [e]			RC	RC		
C$_6$H$_5$COOOH in benzene [f]	0.03	32				
H$_2$O$_2$–[L$_2$Mn$_2$O$_3$]–MeCOOH [g]	0.12	33	0.34	4.09	0.50	2.15

[a] The *trans/cis* ratio of isomers of *tert*-alcohols formed in the oxidation of disubstituted cyclohexanes was measured after treatment of the reaction sample with triphenylphosphine. DMCH, dimethylcyclohexane; PDCA, pyrazine-2,3-dicarboxylic acid. [b] At 40 °C. [c] At room temperature. [d] Stoichiometric oxidation at room temperature by the complex with picolinate anion (pic); the synthesis of this complex has been described in Ref. 14a. [e] At room temperature. Data from Ref. 15c. RC = retention of configuration. [f] Peroxybenzoic acid in benzene at 100 °C; data from Ref. 15b. [g] For the catalysis with complex [L$_2$Mn$_2$O$_3$](PF$_6$)$_2$ (L = 1,4,7-trimethyl-1,4,7-triazacyclononane) in the presence of carboxylic acid see Refs. 16.

$$
\text{3} \xrightarrow{\text{HO}^\bullet} \text{4} \tag{1}
$$
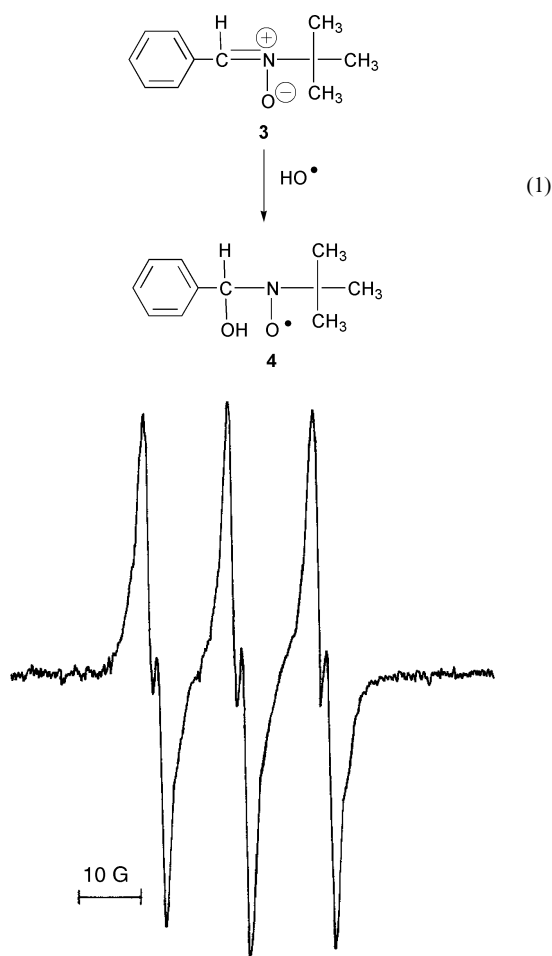
**Fig. 12** EPR Spectrum of a solution containing nitrone **3** (see the text).

the corresponding values for the adduct of nitrone **3** with hydroxyl radicals generated in the photolysis of hydrogen peroxide in acetonitrile ($g = 2.0054 \pm 0.0002$, $a_N = 15.5$ mT and $a_H^\beta = 2.35$ mT), and with the parameters for adduct **4** prepared by the photolysis of H$_2$O$_2$ in an aqueous solution [24a] ($g = 2.0057$, $a_N = 15.3$ mT and $a_H^\beta = 2.75$ mT).

We obtained additional evidence for hydroxyl radical formation in the system under discussion using the method of com-

petitive oxidation of benzene and various aliphatic alcohols.[25] According to this method, the [PhOH]$_0$/[PhOH] ratio is proportional to k_A[ROH] for the reaction between hydroxyl radicals and a mixture benzene–aliphatic alcohol, ROH. Here [PhOH]$_0$ and [PhOH] are phenol concentrations at a certain moment chosen at the beginning of the reaction in the absence and presence of the alcohol, ROH, respectively. The parameter k_A is the rate constant for the interaction of the hydroxyl radical and ROH *via* hydrogen atom abstraction from the α-position of ROH. Finally, [ROH] is the concentration of the alcohol added. The existence of a linear correlation between the [PhOH]$_0$/[PhOH] ratio and the constants k_A of several different alcohols supports the participation of hydroxyl radicals in the key stage of this reaction. We have found such a correlation [6c] in the competitive oxidation of benzene with methanol, ethanol and *n*-propanol by the "O$_2$–H$_2$O$_2$–*n*-Bu$_4$NVO$_3$–PCA" system and using some parameters from ref. 25b.

Alkane transformations with participation of free radicals

Hydroxyl radicals are well known to be very reactive species, and it is reasonable to assume that radicals produced from hydrogen peroxide under the action of the "V–PCA" combination will attack the hydrocarbon molecules.[26] Hydroxyl radicals easily abstract hydrogen atoms from alkanes according to eqn. (2):

$$
\text{HO}^\bullet + \text{RH} \rightarrow \text{H}_2\text{O} + \text{R}^\bullet \tag{2}
$$
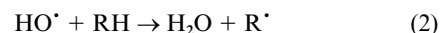
The rate constants for the reaction (2) lie in the interval between 3×10^8 dm^3 mol^{-1} s^{-1} for the relatively inert cyclohexane and *ca.* 10^9 dm^3 mol^{-1} s^{-1} for hydrogen abstraction from the methyl group of methanol at ambient temperature. The rate constant for the abstraction of methyl hydrogen atoms from acetonitrile by hydroxyl radicals is much lower, 3.5×10^6 dm^3 mol^{-1} s^{-1}. More detailed discussion of the rates of reaction (2) will be given in the next sections. Alkyl radicals R$^\bullet$ react rapidly with the molecular oxygen present in the solution [27] (see also refs. 2a, p. 21; 8a, p. 99; 8c, pp. 373, 382, 384, 406, 414, 417) according to eqn. (3) to produce the corresponding alkylperoxyl

$$
\text{R}^\bullet + \text{O}_2 \rightarrow \text{ROO}^\bullet \tag{3}
$$
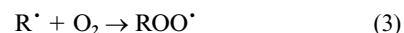
radicals, ROO$^\bullet$. The rate constants [27d,e] for reaction (3) for carbon-centred radicals range from 4×10^6 up to 5×10^9 dm^3

mol^{-1} s^{-1}. For example, values of k_3 (dm^3 mol^{-1} s^{-1})[27d] at ambient temperature have been reported as follows: benzyl, 2.5×10^7; cyclohexyl, $(3.4 \pm 0.6) \times 10^9$; hydroxymethyl, 4.8×10^9; trichloromethyl, 3.3×10^9. Although it is generally accepted that at ambient temperature recombination (3) is the sole pathway, in principle, disproportionation of two radicals ($R^{\bullet}$ and O_2) can occur to yield an alkene and the hydroperoxyl radical:[27k]

$$R^{\bullet} + O_2 \rightarrow R(-H) + HOO^{\bullet} \qquad (4)$$
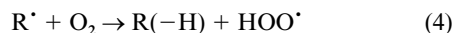
In addition, in the case of long hydrocarbon chains, iso-merisation and cyclisation reactions of peroxyalkyl radicals are possible.[28a] For example, self-abstraction in aliphatic long-chain hydroperoxyl radicals (intramolecular H-atom abstraction) can proceed, as shown in reaction (5):[28b]

$$CH_3CH_2CH_2OO^{\bullet} \rightarrow CH_3C^{\bullet}HCH_2OOH \qquad (5)$$

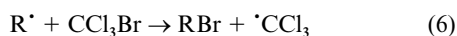It is interesting that reactions of such a type occur much more rapidly in the case of analogous organosilicon peroxy radicals.[28c] In the presence of a donor of bromine atom, CCl_3Br, there is a competition between recombination of $R^{\bullet}$ with O_2 and bromine atom abstraction, reaction (6), which readily takes place in our system (see Fig. 1c).

$$R^{\bullet} + CCl_3Br \rightarrow RBr + {}^{\bullet}CCl_3 \qquad (6)$$

It is important to remember here that alkane oxidation by the "O_2–H_2O_2–n-Bu_4NVO_3–PCA" reagent at low ($<50\,°C$) temperature gives rise to the clean formation of the alkyl hydroperoxide as the sole product, at least in the initial period of the reaction. Consequently, we have to assume that at low temperatures the alkylperoxyl radical is smoothly converted into the corresponding alkyl hydroperoxide [eqn. (7)]:
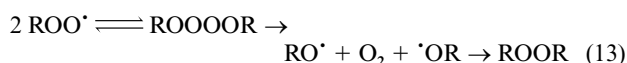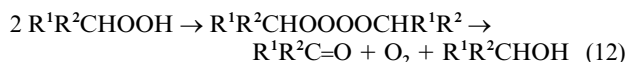
$$ROO^{\bullet} + e^- + H^+ \rightarrow ROOH \qquad (7)$$
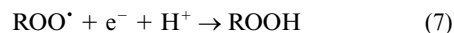
To be transformed into the relatively stable alkyl hydro-peroxide, the radical $ROO^{\bullet}$ should add a hydrogen atom or consecutively add an electron and a proton. Hydrogen peroxide could play the role of hydrogen atom donor, reaction (8), and the alkyl hydroperoxide can be also produced via recombination reactions of peroxyl radical, eqn. (9).

$$ROO^{\bullet} + H_2O_2 \rightarrow ROOH + HOO^{\bullet} \qquad (8)$$

$$ROO^{\bullet} + HOO^{\bullet} \rightarrow ROOH + O_2 \qquad (9)$$

The radical $ROO^{\bullet}$ could alternatively be reduced with V^{IV}-containing species produced in the catalytic cycle [see: reactions (10) and (11)]:

$$ROO^{\bullet} + V^{IV} \rightarrow ROO^- + V^V \qquad (10)$$
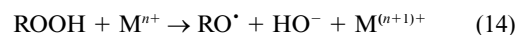
$$ROO^- + H^+ \rightarrow ROOH \qquad (11)$$
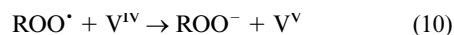
At low temperatures the reactions between peroxyl radicals affording intermediate or final stable products, i.e., so-called Russell termination[29b] (12) and Vaughan termination[29c] (13)
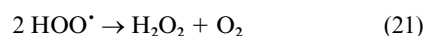
$$2\,R^1R^2CHOOH \rightarrow R^1R^2CHOOOOCHR^1R^2 \rightarrow$$
$$R^1R^2C{=}O + O_2 + R^1R^2CHOH \qquad (12)$$

$$2\,ROO^{\bullet} \rightleftharpoons ROOOOR \rightarrow$$
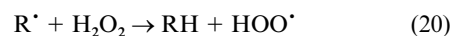$$RO^{\bullet} + O_2 + {}^{\bullet}OR \rightarrow ROOR \qquad (13)$$
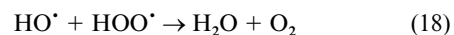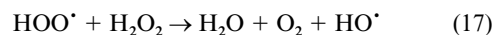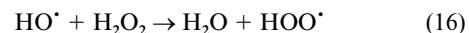
are not probable in our case, because they do not correspond with the products found in our oxidation (see also refs. 29d, e). Generation of ketone (aldehyde) and alcohol at higher ($>50\,°C$)

temperatures, with simultaneous formation of the alkyl hydro-peroxide, is in accordance with reaction (12). However, it is more reasonable to propose that the stable ketone (aldehyde) and alcohol are produced in the alkyl hydroperoxide decom-position under the action of a metal complex present in the solution via reactions (14) and (15) (see, e.g., ref. 8c, pp. 375, 376 and ref. 29f).

$$ROOH + M^{n+} \rightarrow RO^{\bullet} + HO^- + M^{(n+1)+} \qquad (14)$$

$$ROOH + M^{(n+1)+} \rightarrow ROO^{\bullet} + H^+ + M^{n+} \qquad (15)$$

Other reactions of radical species possible in the solution, especially at high temperatures, are depicted as eqns. (16)–(22).[1a,8,29g] Some of these reactions are very fast, for example,

$$HO^{\bullet} + H_2O_2 \rightarrow H_2O + HOO^{\bullet} \qquad (16)$$

$$HOO^{\bullet} + H_2O_2 \rightarrow H_2O + O_2 + HO^{\bullet} \qquad (17)$$

$$HO^{\bullet} + HOO^{\bullet} \rightarrow H_2O + O_2 \qquad (18)$$

$$ROO^{\bullet} + R^{\bullet} \rightarrow ROOR \qquad (19)$$

$$R^{\bullet} + H_2O_2 \rightarrow RH + HOO^{\bullet} \qquad (20)$$

$$2\,HOO^{\bullet} \rightarrow H_2O_2 + O_2 \qquad (21)$$

$$RO^{\bullet} + ROOH \rightarrow ROH + ROO^{\bullet} \qquad (22)$$

the rate constants for processes (16)[26f] and (18)[26a] are 2.7×10^7 and 9×10^9 dm^3 mol^{-1} s^{-1}, respectively, and $k_{22} = 2.5 \times 10^8$ dm^3 mol^{-1} s^{-1} for $R = t$-Bu at $22\,°C$ (ref. 29g). Reaction (17) proceeds very slowly, if at all.

However, since the current concentrations of free radicals should be low, in our further consideration we will ignore many of these processes, restricting the analysis to the initial period of the oxidation reaction which occurs at low temperature. The possibility of a radical chain mechanism is discussed in the Electronic Supplementary Information (Appendix 1).

Cleavage of C–C bonds in normal alkanes

In order to obtain additional evidence for the formation of alkyl hydroperoxyl radicals in the oxidation with the reagent under discussion, we decided to investigate more carefully the composition of the products of the reaction with long-chain normal saturated hydrocarbons. Destruction of the hydro-carbon chain is known for alkane oxygenation processes which involve the formation of alkoxyl radicals[30] (see also ref. 8a, pp. 12, 347). Usually this destruction occurs at high ($>100\,°C$) temperatures. We studied the oxidation of propane and n-hexane with the "O_2–H_2O_2–n-Bu_4NVO_3–PCA" reagent at room temperature. The data obtained are summarized in Table 6. It turned out that the content of the oxygenate mixture depends on the concentrations of the catalyst and hydrogen peroxide. Thus when the vanadium-containing catalyst is used at a con-centration of 1.0×10^{-4} mol dm^{-3} and $[H_2O_2]_0 = 0.16$ mol dm^{-3}, system A, only the products derived from the C–H bond split-ting (i.e., propan-1-ol and propan-2-ol) are formed even after 24 h. When the initial concentrations of H_2O_2 and the catalyst are higher (systems B and C) some products of C–C bond splitting (i.e., ethanol and methanol) can be detected in the reaction mixture. The [C–C]/[C–H] ratio attains 7.6% for system B. Similar results were obtained for the oxidation of propane with hydrogen peroxide catalysed by $Fe(ClO_4)_3$, systems E and F. It is interesting that, unlike propane, n-hexane is oxidized with the "O_2–H_2O_2–n-Bu_4NVO_3–PCA" reagent at room tem-perature without C–C bond breakage. In contrast, the "O_2–H_2O_2–$Fe(ClO_4)_3$" system oxidizes this alkane with extensive

Table 6 Oxidation of *n*-alkanes by certain H_2O_2-containing systems under various conditions (products, concentration in mmol dm^{-3})

| Products	Systems					
	nBu$_4$NVO$_3$–PCA[a] (A)	nBu$_4$NVO$_3$–PCA[b] (B)	nBu$_4$NVO$_3$–PCA[c] (C)	nBu$_4$NVO$_3$–PCA[d] (D)	Fe(ClO$_4$)$_3$[e] (E)	Fe(ClO$_4$)$_3$[f] (F)
Oxidation of propane						
Propan-2-ol	3.6	33	101		45[g]	63
Propan-1-ol	1.6	8	54		26[g]	22
Ethanol	0	2.1	1.8		2.1[g]	4.6
Methanol	0	1.0	3.3		2.0[g]	3.2
Ratio [C–C]/[C–H] (%)[h]	0	7.6	3.3		5.8	9.2
Oxidation of *n*-hexane						
Hexan-2-ol		11		15	19	16
Hexan-3-ol		8		12	21	18
Hexan-1-ol		2.0		3.2	3.8	3.6
Pentan-1-ol		<0.05		<0.05	0.1	0.3
Butan-1-ol		traces		traces	1.0	1.0
Propan-1-ol		<0.5		<0.5	0.8	1.0
Ethanol		<0.5		<0.5	3.5	5.5
Methanol		<0.5		<0.5	0.2	3.0
Ratio [C–C]/[C–H] (%)[h]		0		0	3.8	32

Conditions: solvent, MeCN; room temperature; in all cases, concentration of the products was determined after reduction of the sample with NaBH$_4$; [propane]$_0$, 1.4 mol dm^{-3}; [hexane]$_0$, 0.3 mol dm^{-3} in the oxidations catalysed by Fe(ClO$_4$)$_3$ and 0.5 mol dm^{-3} in the oxidation catalysed by nBu$_4$NVO$_3$. [a] [nBu$_4$NVO$_3$], 0.1 mmol dm^{-3}; [PCA], 0.4 mmol dm^{-3}; [H$_2$O$_2$]$_0$, 160 mmol dm^{-3}; 24 h. [b] [nBu$_4$NVO$_3$], 0.5 mmol dm^{-3}; [PCA], 2.0 mmol dm^{-3}; [H$_2$O$_2$]$_0$, 400 mmol dm^{-3}; 2 h. [c] [nBu$_4$NVO$_3$], 0.5 mmol dm^{-3}; [PCA], 2.0 mmol dm^{-3}; [H$_2$O$_2$]$_0$, 600 mmol dm^{-3}; 4 h. [d] [nBu$_4$NVO$_3$], 0.5 mmol dm^{-3}; [PCA], 2.0 mmol dm^{-3}; [H$_2$O$_2$]$_0$, 400 mmol dm^{-3}; 24 h. [e] [Fe(ClO$_4$)$_3$], 0.4 mmol dm^{-3}; [H$_2$O$_2$]$_0$, 550 mmol dm^{-3}; 60 min. [f] [Fe(ClO$_4$)$_3$], 4.0 mmol dm^{-3}; [H$_2$O$_2$]$_0$, 360 mmol dm^{-3}; 10 min. [g] Reaction time, 10 min. [h] Parameter [C–C]/[C–H] is the ratio of the total concentration of products obtained *via* C–C bond cleavage to total concentration of products derived from C–H bond splitting.

formation of lower alcohols (pentanol, butanol, propanol, ethanol and methanol), and at higher concentration of iron-containing catalyst, system F, the [C–C]/[C–H] ratio is larger.

The autoxidation of styrene, initiated by free radicals, gives benzaldehyde as a main product (ref. 8a, p. 356). It is known that (*E*)-stilbene reacts with hydroxyl radicals in the presence of oxygen in aqueous acetonitrile to afford a high yield of benzaldehyde.[30e] Recently we have found[6k] that the oxidation of styrene and stilbene with the "O$_2$–H$_2$O$_2$–*n*-Bu$_4$NVO$_3$–PCA" reagent at room temperature also proceeds with C–C bond splitting and gives benzaldehyde and benzoic acid. These data and the data given in Table 6 are in accordance with our assumption that the vanadium-based reagent generates hydroxyl radicals which are capable of converting the alkane into the alkyl hydroperoxyl radical.

Intermediate vanadium oxo and peroxo complexes

In order to obtain additional insight into the mechanism of alkane oxygenation with the "O$_2$–H$_2$O$_2$–*n*-Bu$_4$NVO$_3$–PCA" reagent, we investigated by NMR spectroscopy the transformations of various vanadium complexes under conditions close to those used in the oxidation reaction. It turned out that the ^{51}V NMR spectrum of the starting compound *n*-Bu$_4$NVO$_3$ consists of three signals at −539, −571, and −514 ppm. It is important to note that the relative intensities of these signals depended on the CD$_3$CN batch used to prepare the sample: for wet acetonitrile the two outer signals predominated, whereas for freshly dried acetonitrile the spectrum showed the central line only. Both the ^{1}H and the ^{51}V NMR spectra showed that treatment of *n*-Bu$_4$NVO$_3$ with PCA in acetonitrile-*d*$_3$ resulted in the formation of a new product. The reaction is complete at about 2 equiv. of PCA. Higher concentrations of PCA do not lead to further chemical transformations. The product formed from the initial vanadate species was the same whatever solvent batch was used. The final product has a single vanadium signal at δ −532 and three proton signals of equal intensity in the aromatic region from coordinated pca ligands: δ 9.22 (d, J = 1.5, 2 H), 8.77 (d, J = 2.7, 2 H), and 8.45 (dd, J = 2.7, 1.5, 2 H) (see the Figs. 13a, 14a). The aliphatic signals due to
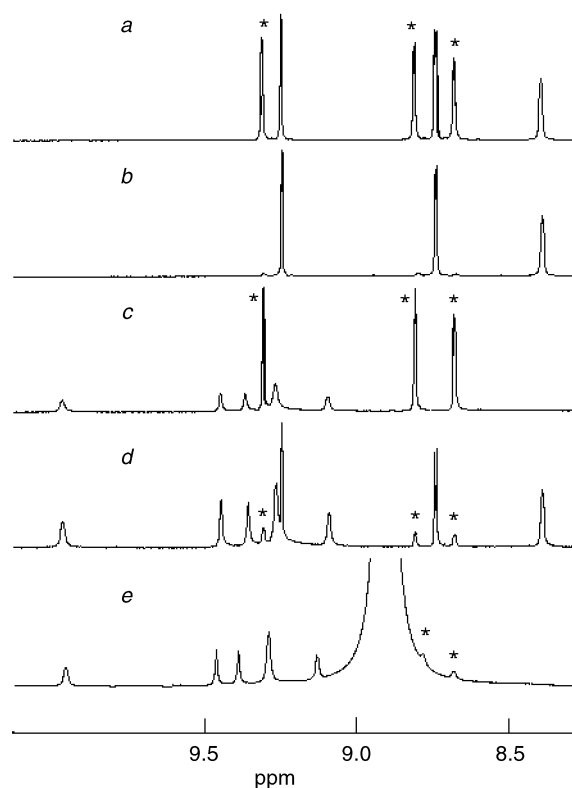
Fig. 13 500 MHz ^{1}H NMR spectra of (*a*) *n*-Bu$_4$NVO$_3$ + PCA (4 equiv.); (*b*) (*n*-Bu$_4$N)$^+$[V(O)$_2$(pca)$_2$]$^-$ (**1**); (*c*) *n*-Bu$_4$NVO$_3$ + PCA (4 equiv.) + H$_2$O$_2$ (1 equiv.); (*d*) **1** + H$_2$O$_2$ (1 equiv.); (*e*) **1** + H$_2$O$_2$ (50 equiv.). Peaks indicated by asterisks are due to free PCA. Concentration of the vanadium species was 5.0 × 10^{-3} mol dm^{-3}.

tetrabutylammonium cation were observed at δ 3.11 (m, 8 H), 1.62 (m, 8 H), 1.37 (sextet, J = 7.4, 8 H), 0.98 (t, J = 7.3, 12 H). It should be noted that in all systems containing NBu$_4^+$ cation we observed one set of aliphatic signals with chemical shifts equal to population-weighted means of all charged species
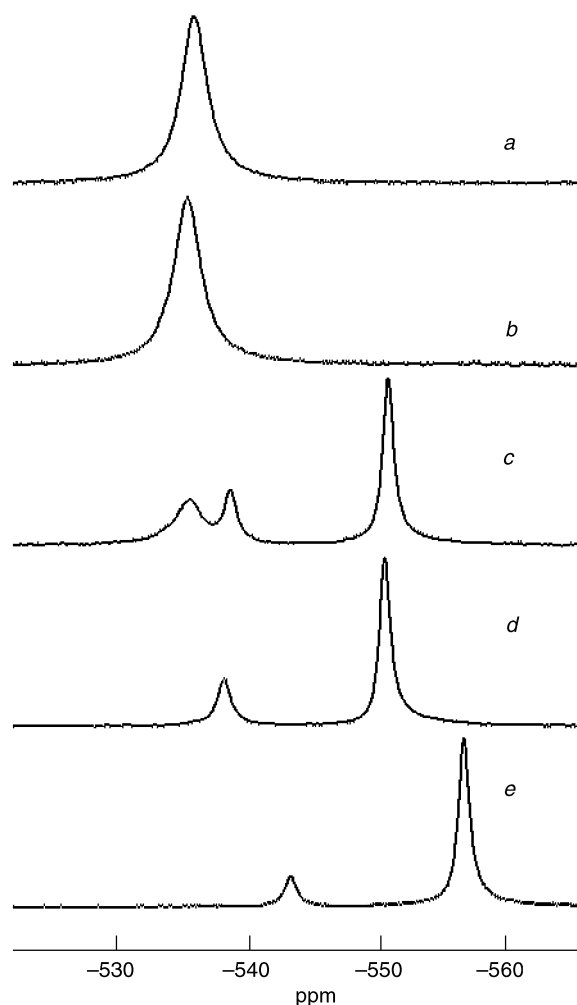
Fig. 14 131.5 MHz ^{51}V NMR spectra of (*a*) *n*-Bu$_4$NVO$_3$ + PCA (4 equiv.); (*b*) (*n*-Bu$_4$N)$^+$[V(O)$_2$(pca)$_2$]$^-$ (**1**); (*c*) **1** + H$_2$O$_2$ (1 equiv.); (*d*) *n*-Bu$_4$NVO$_3$ + PCA (4 equiv.) + H$_2$O$_2$ (1 equiv.); (*e*) *n*-Bu$_4$NVO$_3$ + PCA (4 equiv.) + H$_2$O$_2$ (100 equiv.). Concentration of the vanadium species was 5.0×10^{-3} mol dm^{-3}.

present in solution. The positions of these signals did not provide any relevant information, therefore we shall omit the aliphatic proton signals from our further discussion.

As can be seen from Figs. 13*b* and 14*b*, similar ^{1}H and ^{51}V spectra with identical chemical shifts were obtained for acetonitrile-*d$_3$* solutions of complex (*n*-Bu$_4$N)$^+$[V(O)$_2$(pca)$_2$]$^-$ (anion **1**),[7f] and we can conclude that **1** is the only vanadium complex existing in acetonitrile solutions of salt *n*-Bu$_4$NVO$_3$ and PCA when [PCA]$_0$/[*n*-Bu$_4$NVO$_3$] > 2. Addition of hydrogen peroxide (30% aqueous) to a solution of **1** or a mixture of (*n*-Bu$_4$N)$^+$[VO$_3$]$^-$ + 4PCA produced a reddish solution. The NMR spectra showed that 1–2 equiv. of H$_2$O$_2$ were enough for complete disappearance of **1**. The three aromatic proton signals mentioned above were replaced by five aromatic signals at δ 9.86 (1 H), 9.40 (1 H), 9.32 (1 H), 9.24 (2 H) and 9.08 (1 H) (see Fig. 14*c–e*). The signals are broadened, and information about coupling constants is not readily available from the spectra. It was shown earlier[7f] that H$_2$O$_2$ can easily react with compound **1** to yield the oxo-peroxo complex containing anion [V(O$_2$)(O)(pca)$_2$]$^-$ (**2**), and it is reasonable to assume that the above signals belong to **2**. The two pca ligands in **2** are not equivalent, and one might expect to observe six different aromatic signals for this compound. Obviously, two of these signals have very close chemical shifts in acetonitrile and are not resolved even at 500 MHz.

In the presence of a slight excess of hydrogen peroxide the signal observed at δ −532 in the ^{51}V NMR spectra of **1** or of a mixture of *n*-Bu$_4$NVO$_3$ + PCA was replaced by two new signals

at δ −535 and −550 with the ratio 0.3 : 1 (Fig. 14*c*, *d*). Upon increasing the concentration of H$_2$O$_2$ these signals showed small (a few ppm) upfield shifts and their ratio changed to 0.14 : 1 at 0.5 mol dm^{-3} of H$_2$O$_2$ (Fig. 14*e*). Our earlier study[7f] revealed the existence of two isomers for the peroxo complex **2**, with the two coordinated nitrogen atoms from the two *N,O*-coordinated pca ligands (**2b** and **2c**) being *cis* and *trans*. We assume that the two vanadium signals belong to these isomers. The smooth changes in the ^{51}V chemical shifts and in the isomeric ratio of **2b** and **2c** observed upon increasing the concentration of H$_2$O$_2$ can be explained by gradual changes in solvent composition. The lack of two separate sets of signals for **2b** and **2c** in the proton NMR could result from some form of dynamic exchange which leads to time-averaged pca signals with signs of exchange broadening. It is noteworthy that **2b** and **2c** are the only vanadium species existing in the studied systems in the presence of hydrogen peroxide. The ^{51}V NMR spectra show that complexes **2b** and **2c** are stable under catalytic conditions. Even at very low vanadium concentrations (about 10^{-4} mol dm^{-3}) and at high hydrogen peroxide concentrations (up to 0.5 mol dm^{-3}), which correspond to real catalytic conditions, there are no signs of dissociation of **2** or further reaction of **2** with H$_2$O$_2$ resulting in the formation of diperoxo complexes.

We have also studied the spectra of the reaction mixture models containing perchloric acid instead of PCA. A sample for ^{51}V NMR was prepared in the following way. First, an appropriate amount of 30% H$_2$O$_2$ was added to a solution of *n*-Bu$_4$NVO$_3$ in acetonitrile-*d$_3$*. Then a diluted acetonitrile solution of HClO$_4$ (0.12 mol dm^{-3}) was added to this mixture to obtain the final NMR sample with concentrations 10^{-3} mol dm^{-3} of *n*-Bu$_4$NVO$_3$ + 4×10^{-3} mol dm^{-3} of HClO$_4$ + 0.1 mol dm^{-3} H$_2$O$_2$. The resulting spectrum consisted of at least two overlapping broad signals with almost identical chemical shifts at about −600 ppm. These signals probably represent different peroxo species formed in acetonitrile solution. Recently, a wide range of peroxovanadate complexes formed in water–acetonitrile mixtures has been characterized by ^{51}V NMR.[31a] The ^{51}V signals for all peroxovanadate species moved downfield as the water concentration decreased, with particularly dramatic changes being observed at lower water concentrations. The minimum content of water in those studies was 2%. In the systems we have examined, the content of water (introduced with H$_2$O$_2$) was less than 1%, and it is not surprising that the two signals we observed were located at somewhat lower field than most of the signals of the peroxovanadate species studied in ref. 31a. We believe that our peaks belong to similar species to those observed in ref. 31a when acid was added to the [VO(O$_2$)$_2$]$^-$ solution of low water concentration. Among those species were [VO(O$_2$)$_2$]$^-$, [V$_2$O$_2$(O$_2$)$_3$] and some unidentified complexes. We showed that the system "VO(acac)$_2$ + 4PCA + H$_2$O$_2$ (excess)" exhibits a moderate catalytic activity, which is somewhat lower than for "*n*-Bu$_4$NVO$_3$ + 4PCA + H$_2$O$_2$ (excess)". It is of considerable interest to determine whether the presence of acetylacetonato ligands and the different oxidation state of the metal ion in the starting vanadium complex result in different types of catalytically active species and hence in different types of catalytic mechanisms in these two systems. Compound VO(acac)$_2$ is a paramagnetic V^{IV} complex, and no ^{51}V NMR signals can be observed in acetonitrile solution at 4×10^{-3} mol dm^{-3} of VO(acac)$_2$. The proton NMR spectrum of VO(acac)$_2$ does not reveal any signals in the diamagnetic region. In the presence of 4 equiv. of PCA the ^{51}V NMR spectrum of VO(acac)$_2$ remains "blank". However, the proton NMR spectrum shows that PCA molecules replace acetylacetonato ligands in the coordination sphere of vanadium. Indeed, two sets of diamagnetic signals appear in the ^{1}H NMR spectrum of a mixture of VO(acac)$_2$ and PCA (4 equiv.); these signals can be assigned to the keto and enol forms of free uncoordinated acetylacetone molecules. Their integral intensities correspond to a ketone/enol ratio of about 2 : 3. The

spectra demonstrate that the acac ligands in VO(acac)$_2$ are readily replaced in the presence of PCA by the stronger pca ligands, with vanadium retaining its paramagnetic oxidation state IV. In addition to the free acacH signals, the diamagnetic region of the proton spectrum of the mixture contains three broadened aromatic signals of equal integral intensities with chemical shifts corresponding to free PCA (9.28, 8.84 and 8.72 ppm) which can be assigned to uncoordinated molecules of PCA. Each vanadium ion coordinates two pca ligands, and half of the PCA molecules in a mixture VO(acac)$_2$ + 4PCA remain uncoordinated. These molecules, however, can form outer-sphere adducts with paramagnetic vanadium species, and this may be the reason for the excessive broadening of their signals.

Addition of H$_2$O$_2$ to the mixture VO(acac)$_2$ + 4PCA produced a reddish solution containing diamagnetic vanadium species with a detectable NMR spectrum. In the presence of a 10-fold excess of H$_2$O$_2$ the ^{51}V NMR spectrum consists of three signals at -522, -542, and -545 ppm with the ratio of integral intensities about $1:2:0.5$. At higher concentrations of H$_2$O$_2$, the relative intensity of the most downfield component grows, and at a 40-fold excess of H$_2$O$_2$ the ratio of integrals is close to $1:0.5:0.2$. The aromatic region of the proton spectrum reveals at least nine new broad partially overlapped signals with chemical shifts from 9.2 to 9.9 ppm, which clearly belong to coordinated pca ligands. The ^{51}V and ^{1}H NMR signals observed in systems "n-Bu$_4$NVO$_3$ + PCA (4 equiv.) + H$_2$O$_2$ (excess)" and "VO(acac)$_2$ + PCA (4 equiv.) + H$_2$O$_2$ (excess)" have different chemical shifts, and at this moment we do not know the exact nature of the species formed from VO(acac)$_2$ in the presence of PCA and H$_2$O$_2$. It is clear that a more detailed study is required in order to identify all of the vanadium complexes formed in this system. The conclusion that may be drawn from the above experiments is that these species are diamagnetic complexes of vanadium(v) in which acetylacetonato ligands are replaced by pca ligands.

We have found that pyridine-2,6-dicarboxylic acid (PyDCA), which coordinates as a tridentate ligand (vanadium complexes have been described[31b,c]), is absolutely inactive as a co-catalyst for cyclohexane oxidation in acetonitrile. To explain this fact, we prepared a vanadium-containing complex of PyDCA by mixing n-Bu$_4$NVO$_3$ and PyDCA in a 1 : 1 ratio at elevated temperature and isolated the resulting product. The vanadium spectrum of this complex, which possibly is an oxo derivative, in CD$_3$CN consists of a single sharp signal at -519 ppm, and its proton spectrum in the aromatic region consists of two signals: δ 8.46 (1 H, t, $J = 7.7$) and 8.15 (2 H, d, $J = 7.7$). Addition of 1 equivalent of H$_2$O$_2$ does not generate any changes in the spectrum. Upon increasing the concentration of H$_2$O$_2$ to 50 equivalents, the aromatic signals shift slightly downfield (δ 8.48 and 8.18 ppm, correspondingly), and along with the old signals we can clearly see small signals of a new product at 8.39 ppm (1 H, t, $J = 7.8$) and 8.15 (2 H, d, $J = 7.8$). Its vanadium signal is observed at -554 ppm. Immediately after the addition of hydrogen peroxide the concentration of the new complex (possibly an oxo-peroxo derivative) is low and does not exceed 5% of the concentration of the starting species. However, in 2 hours the spectrum of the same solution corresponds already to a 2 : 3 mixture of the old and the new species, and the spectrum obtained after 16 hours shows the complete conversion of the starting species into the new complex. Obviously, an additional study is necessary for better understanding of this process. Nevertheless, the above results already demonstrate that PyDCA forms much stronger vanadium complexes than PCA, thus hindering the coordination of hydrogen peroxide. Therefore, for systems with PyDCA the formation of peroxo complexes becomes much more difficult and proceeds much more slowly. In addition, when a rigid tridentate PyDCA ligand is coordinated to vanadium, a transformation of peroxo ligands becomes impossible because this requires a certain

Table 7 Oxidation of cyclohexane in the presence of naphthols[a]

Additive	10^4[Additive]/ mol dm^{-3}	10^2[Products]/mol dm^{-3}	
		Cyclohexanone	Cyclohexanol
None	—	0.19	5.2
α-Naphthol	1.0	0.22	6.5
	5.0	<0.01	0.43
β-Naphthol	1.0	0.13	4.7
	5.0	<0.01	0.49

[a] Conditions: Bu$_4$NVO$_3$, 1.0×10^{-4} mol dm^{-3}; PCA, 4.0×10^{-4} mol dm^{-3}; cyclohexane, 0.46 mol dm^{-3}; hydrogen peroxide, 0.5 mol dm^{-3}; in acetonitrile at 40 °C; 4 h. Concentrations of cyclohexanol and cyclohexanone were measured after the addition of an excess of solid triphenylphosphine.

flexibility of the coordination sphere. As a result, no catalysis is observed.

Effect of phenols on the oxidation of cyclohexane

It was useful for the understanding of the radical mechanism to study the influence of certain "radical traps"[8a,32] on the oxidation process. It turned out that addition of 2,6-di-*tert*-butyl-4-methylphenol (BHT, 0.01 mol dm^{-3}) to the reaction mixture (cyclohexane, 0.23 mol dm^{-3}; hydrogen peroxide, 0.2 mol dm^{-3}; n-Bu$_4$NVO$_3$, 1.0×10^{-4} mol dm^{-3}; PCA, 4.0×10^{-4} mol dm^{-3}; 50 °C, 1 h, acetonitrile) even slightly accelerates the oxidation: the total yield of oxygenates was 0.076 mol dm^{-3}, while in the absence of the additive the yield was 0.064 mol dm^{-3}. Hydroxyl radicals are known to react with BHT,[8a] giving a variety of products. The known rate constants for the reaction of BHT with other oxygen-centred radicals are as follows: 2.0×10^7 dm^3 mol^{-1} s^{-1} for Me$_3$CO$^\bullet$ at 295 K in acetonitrile[32a] and 2.5×10^4 dm^3 mol^{-1} s^{-1} for PhCH$_2$OO$^\bullet$.[32f] If we accept the rate constant 3×10^8 dm^3 mol^{-1} s^{-1} for the reaction between cyclohexane and hydroxyl radicals and ~10^8 dm^3 mol^{-1} s^{-1} for the interaction between hydroxyl radicals and BHT, and take into account the concentrations of cyclohexane and BHT in our solution (0.23 and 0.01 mol dm^{-3}, respectively) we will see that hydrogen atom abstraction from cyclohexane is one or two orders of magnitude more rapid than that from BHT.[32b] Thus it is not surprising that BHT in relatively low concentrations does not retard the oxidation of cyclohexane. Moreover, since the BHT concentration is much lower than that of cyclohexane, all of the added BHT is consumed in the beginning of the process, after which only the oxidation of cyclohexane can continue. Also no retardation of cyclohexane oxidation was detected when very low concentrations of other known "radical traps", α- and β-naphthols,[32a] were added (1.0×10^{-4} mol dm^{-3} of the naphthol per 1.0×10^{-4} mol dm^{-3} of n-Bu$_4$NVO$_3$) as shown in Table 7. This is not surprising if we take into account the above-mentioned calculations, assuming the rate constants for the oxidation of cyclohexane and the naphthol to be comparable. However, an unexpectedly sharp drop in the oxidation rate was noticed when the naphthol was added in higher concentrations (5 equivalents of the naphthol per 1 equivalent of vanadate anion).

We assume that the naphthol enters the coordination sphere of the vanadium complex and thus prevents coordination of a hydrogen peroxide molecule to the vanadium ion. Indeed, we have found that phenol itself interacts with the vanadium peroxo species formed in acetonitrile solution, leading to rather slow changes in the UV-visible spectrum of this solution (Fig. 15, curves *a*, *b*, *c* and *d*). These changes might be associated with pca substitution by phenol in the vanadium coordination sphere and its subsequent oxidation. It is noteworthy that BHT, when added to the solution, causes only negligible changes (compare Fig. 15, curves *a* and *e*). Such a small effect could be explained if we take into account the very strong spatial shielding of the hydroxy group in BHT by its two bulky
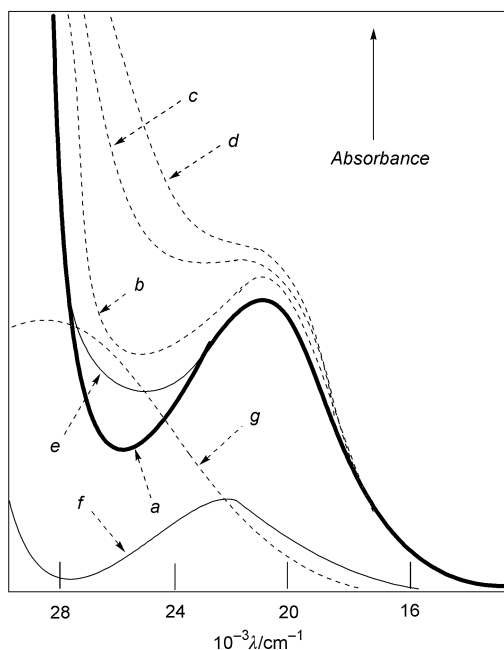
Fig. 15 UV-visible spectra of a solution of n-Bu$_4$NVO$_3$ (2.0×10^{-3} mol dm^{-3}), PCA (8.0×10^{-3} mol dm^{-3}) and H$_2$O$_2$ (2.5×10^{-2} mol dm^{-3}) in the absence of any additive (a), in the presence of phenol (1.0×10^{-2} mol dm^{-3}) after 20 (b), 60 (c) and 120 (d) min at room temperature, as well as the same solution in the presence of BHT (1.0×10^{-2} mol dm^{-3}) after 120 min (e). For comparison, spectra of quinone solution (1.0×10^{-2} mol dm^{-3}) (f) and the solution containing n-Bu$_4$NVO$_3$ (0.4×10^{-3} mol dm^{-3}) and H$_2$O$_2$ (0.625×10^{-3} mol dm^{-3}) (g) are also shown.
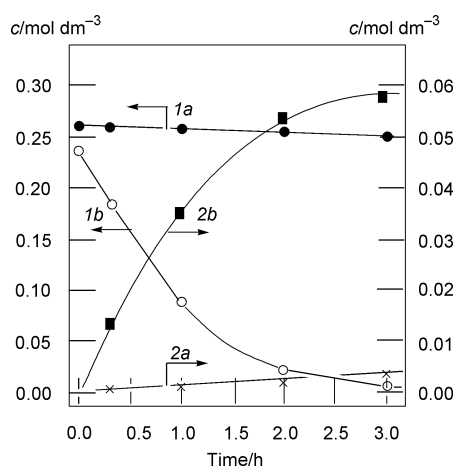

Fig. 16 Profiles of cyclohexane (0.46 mol dm^{-3}) oxidations by hydrogen peroxide (0.24 mol dm^{-3}) in acetonitrile at 20 (a) and 50 °C (b) catalysed by salt n-Bu$_4$NVO$_3$ (1.0×10^{-4} mol dm^{-3}) and PCA (4.0×10^{-4} mol dm^{-3}). Consumption of H$_2$O$_2$ (curves 1) and accumulation of the sum of the products (measured after addition of an excess of solid triphenylphosphine) (curves 2) are shown.

tert-butyl groups. Due to this spatial hindrance BHT is unable to coordinate to a vanadium centre *via* its hydroxy group and thus to inhibit the oxidation. Simple phenols, which have no steric hindrance around the hydroxy group, can possibly be oxidized on the vanadium-containing reaction centre, but these substrates have to be coordinated to vanadium prior to oxidation. Such a coordination suggests a different reaction mechanism from that proposed for alkane oxidation.

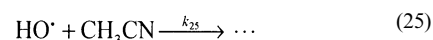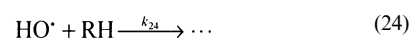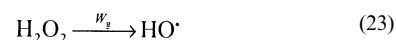**Kinetics of the oxygenation (hydroxyl radical generation)**

Discussing the kinetics and mechanism of cyclohexane, CyH, oxidation by the "O$_2$–H$_2$O$_2$–n-Bu$_4$NVO$_3$–PCA" reagent, we first of all must note that at temperatures <60 °C, the classical radical-chain mechanism (see Electronic Supplementary
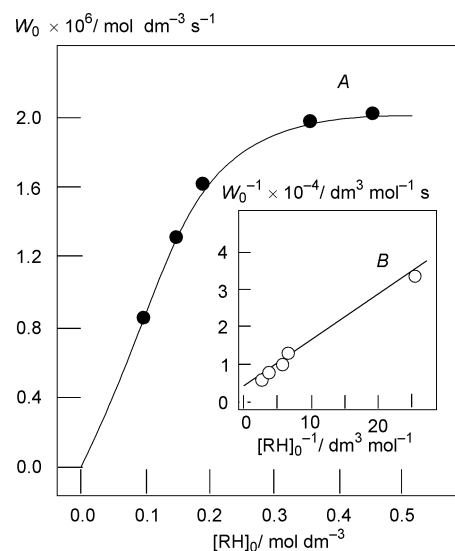
Fig. 17 Plot of the initial cyclohexane oxidation rate, W_0, *versus* cyclohexane initial concentration (curve A) and its anamorphosis (curve B) which was obtained using eqn. (26). Reaction conditions: [n-Bu$_4$NVO$_3$]$_0$ = 1.0×10^{-4} mol dm^{-3}; [PCA]$_0$ = 4.0×10^{-4} mol dm^{-3}; [H$_2$O$_2$]$_0$ = 0.20 mol dm^{-3}, 40 °C, acetonitrile.

Information, Appendix 1) is impossible. The rate found experimentally for the cyclohexane oxidation by the reagent under consideration is 3×10^{-6} mol dm^{-3} s^{-1}. Due to the low reactivity of the cyclohexyl peroxyl radicals, the value for the oxidizability parameter will be consequently rather low,[33a] 6.6×10^{-5} mol$^{-1/2}$ dm$^{3/2}$ s$^{-1/2}$ at 60 °C. For such a value of the oxidizability parameter, the experimentally measured rate of the oxidation will be attained if the initiation rate equals 2×10^{-3} mol dm^{-3} s^{-1} at [CyH]$_0$ = 1 mol dm^{-3}. Thus the chain length for such a process is much less than unity, *i.e.*, the process is not a chain one. At low temperature and high hydrocarbon concentration, when the oxidation rate does not depend on [CyH]$_0$, the yield of alkyl hydroperoxide approximately corresponds[6f] to one half of the amount of H$_2$O$_2$ consumed (Fig. 16), which also supports the non-chain mode of the oxidation. In our experiments at low temperatures, the yield of oxygenates never exceeded 1 mole per 2 moles of hydrogen peroxide. At relatively high temperature (*e.g.*, 50 °C) some non-productive H$_2$O$_2$ decomposition to O$_2$ and H$_2$O occurs (the so-called catalase activity of the vanadium catalyst) (Fig. 16).

Fig. 17 (curve A) demonstrates the dependence of the cyclohexane oxidation rate on the cyclohexane initial concentration. Such a behavior corresponds to the competition between cyclohexane, RH, and acetonitrile for the same oxidative species, *i.e.*, hydroxyl radical [eqns. (23)–(26)]:

$$H_2O_2 \xrightarrow{W_g} HO^\bullet \qquad (23)$$

$$HO^\bullet + RH \xrightarrow{k_{24}} \cdots \qquad (24)$$

$$HO^\bullet + CH_3CN \xrightarrow{k_{25}} \cdots \qquad (25)$$

$$-\frac{d[RH]}{dt} = \frac{W_g}{1 + \dfrac{k_{25}[CH_3CN]}{k_{24}[RH]}} \qquad (26)$$

Treatment of the data presented in Fig. 17, curve A using eqn. (26) allows us to determine value $W_g = 2.5 \times 10^{-6}$ mol dm^{-3} s^{-1} and the rate constant ratio $k_{25}/k_{24} = 8.3 \times 10^{-3}$. Value W_g coincides with the maximum cyclohexane oxidation rate at its high concentration. The k_{25}/k_{24} ratio is close to the ratio of rate constants for the reactions between acetonitrile and cyclohexane with hydroxyl radical. These parameters, taken from the literature,[33b,c] are as follows: $k_{25} = 3.5 \times 10^6$ dm^3 mol^{-1}

s^{-1}, $k_{24}^{cyclohexane} = 3.0 \times 10^8$ dm^3 mol^{-1} s^{-1} and $k_{25}/k_{24} = 1.2 \times 10^{-2}$. It is of interest to calculate the relative reactivities of methane and acetonitrile in their reactions with hydroxyl radicals. Since k_{24} for CH$_4$ is $k_{24}^{methane} = 1.1 \times 10^8$ dm^3 mol^{-1} s^{-1} (taken from ref. 33d) and accepting [CH$_4$] ≈ 1.0 mol dm^{-3} (at reasonably high pressures) we obtain $k_{24}^{methane}$[CH$_4$] $\approx 1.1 \times 10^8$ s^{-1} and k_{25}[MeCN] $\approx 0.5 \times 10^8$ s^{-1}. This means that the rate of hydroxyl attack on methane will be approximately two times higher than that on acetonitrile and, consequently, in the acetonitrile solution methane will be oxidized, although oxygenates from acetonitrile can also be expected in the mixture of products.[6h,j]

It has been shown in previous sections and ref. 7f that vanadate anions in acetonitrile solution are capable of forming complexes with one and two PCA molecules. In the presence of hydrogen peroxide, peroxo derivatives of vanadium(v) are generated, as well as peroxo complexes of vanadium and PCA. Based upon these data we can propose the following formal sequence [eqns. (27)–(32)] of complexing stages in the system under consideration:

$$V + PCA \xrightleftharpoons{K_{27}} V(PCA) \qquad (27)$$

$$V(PCA) + PCA \xrightleftharpoons{K_{28}} V(PCA)_2 \qquad (28)$$

$$V(PCA) + H_2O_2 \xrightleftharpoons{K_{29}} V(PCA)H_2O_2 \qquad (29)$$

$$V(PCA)H_2O_2 \xrightleftharpoons{K_{30}} V(H_2O_2) + PCA \qquad (30)$$

$$V(PCA)_2 + H_2O_2 \xrightleftharpoons{K_{31}} V(PCA)_2H_2O_2 \qquad (31)$$

$$V(PCA)_2H_2O_2 \xrightleftharpoons{K_{32}} V(PCA)H_2O_2 + PCA \qquad (32)$$
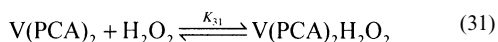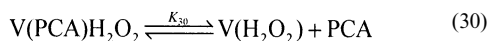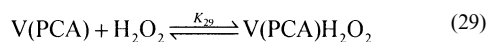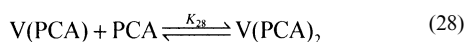
It has been demonstrated in previous sections that, at [PCA]$_0$ > [V]$_0$ (these parameters are initial concentrations of PCA and a vanadium derivative, respectively), vanadium ions not bound to PCA are practically absent in the solution. Taking this into account we can neglect the concentration of V, compared with the concentration of PCA–V, complexes present in the equation of balance. The first two equations simplify the situation since the real stoichiometry of these stages should be written as eqns. (27a) and (28a):

$$n\text{-Bu}_4\text{N}^+\text{VO}_3^- + \text{pcaH} \xrightleftharpoons{}$$
$$\text{VO}_2(\text{pca}) + n\text{-Bu}_4\text{NOH} \quad (27a)$$

$$\text{VO}_2(\text{pca}) + \text{pcaH} + n\text{Bu}_4\text{NOH} \xrightleftharpoons{}$$
$$n\text{-Bu}_4\text{N}^+[\text{VO}_2(\text{pca})_2]^- + \text{H}_2\text{O} \quad (28a)$$
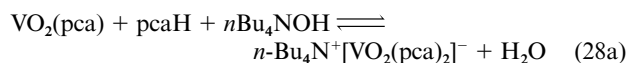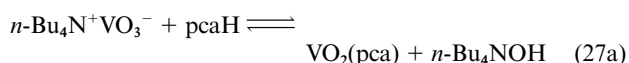
In accordance with eqn. (27a) the interaction of vanadate anion tetrabutylammonium salt with PCA gives rise to the formation of n-Bu$_4$NOH, which will be further involved in reaction (28a) when the second PCA molecule enters the vanadium coordination sphere. We have demonstrated in special experiments that the tetrabutylammonium cation (added in small amounts in the form of the PCA salt) does not affect the hydrocarbon oxidation rate. Water present in substantial concentrations slightly retards the alkane oxidation (see below). However the amount of water liberated in reaction (28a) should not exceed 10^{-4} mol dm^{-3} (at the standard concentration of vanadium derivative which we used in almost all the experiments). Taking into account all these arguments, in our kinetic calculations we can replace eqns. (27a) and (28a) by the more simple eqns. (27) and (28), respectively, in which we consider PCA as a indivisible ligand. This ligand can be conventionally added or replaced as a whole in various reactions.
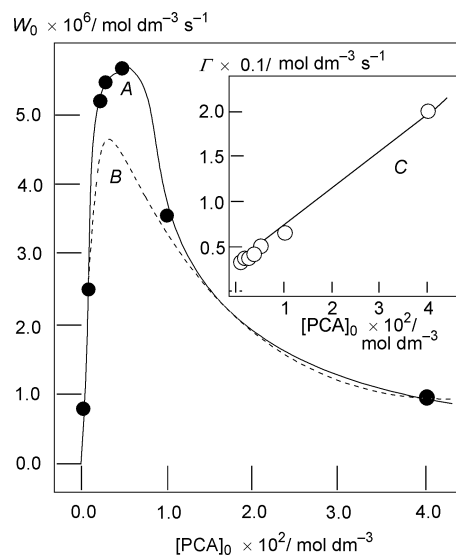
Fig. 18 Dependence of the oxidation rate on the initial concentration of PCA: A—plot of the experimentally obtained dependence; B—curve for the dependence A obtained by calculation in accordance with eqn. (37); C—linear anamorphosis of curve A in coordinate $\Gamma - [\text{PCA}]_0$, where Γ is governed by eqn. (42). Reaction conditions are as described in the caption to Fig. 17.

Fig. 18 shows the experimental dependence of the cyclohexane oxidation rate on the initial PCA concentration. An increase of the rate upon addition of the co-catalyst at low concentration unambiguously shows that hydroxyl radical generation is associated with the formation of complexes between vanadium and PCA. The bell-shaped curve A observed in Fig. 18 can be interpreted in terms of a mechanism corresponding to eqns. (27)–(32) if a vanadium complex containing one PCA molecule takes part in the rate-determining stage of the oxidation. Vanadium complexes containing none or two PCA molecules are much less efficient as catalysts. The dependence of the reaction rate on the initial H$_2$O$_2$ concentration also exhibits a maximum (Fig. 19, curve A). In special experiments we showed that water added to the reaction solution retards the oxidation process. The lowering of the oxidation rate at high hydrogen peroxide concentration is due to the increase in concentration of water introduced into the reaction mixture simultaneously with hydrogen peroxide (usually we employed 30 or 35% aqueous solution of H$_2$O$_2$). Taking this influence into consideration we can see that at constant H$_2$O concentration the reaction rate approaches an ultimate value (curve B in Fig. 19). This means that a monoperoxo vanadium complex is a catalytically active species.

Given the fact that the cyclohexane oxidation is a non-chain process and considering the data presented in Figs. 18 and 19, we conceive that the rate-determining step of the oxidation process is the monomolecular transformation of complex V(PCA)H$_2$O$_2$. Therefore, the generation of hydroxyl radicals can be described by the sequence shown as eqns. (33)–(35):

$$\text{V}^\text{V}(\text{PCA})\text{H}_2\text{O}_2 \xrightarrow{k_{33}} \text{V}^\text{IV}(\text{PCA}) + \text{H}^+ + \text{HOO}^\bullet \quad (33)$$

$$\text{V}^\text{IV}(\text{PCA}) + \text{H}_2\text{O}_2 \rightarrow \text{V}^\text{V}(\text{PCA}) + \text{HO}^\bullet + \text{HO}^- \quad (34)$$

$$\text{V}^\text{V}(\text{PCA})\text{H}_2\text{O}_2 + \text{HOO}^\bullet \rightarrow$$
$$\text{V}^\text{V}(\text{PCA}) + \text{HO}^\bullet + \text{H}_2\text{O} + \text{O}_2 \quad (35)$$

Reaction (33) is a rate-limiting step. Because at high cyclohexane concentrations all the hydroxyl radicals generated in the system will interact with this hydrocarbon, the reaction rate can be expressed by eqn. (36):

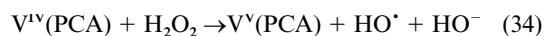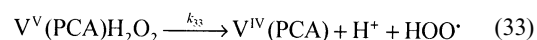$$W = -\frac{d[\text{RH}]}{dt} = \frac{d[\text{ROOH}]}{dt} = 2k_{33}[\text{V}(\text{PCA})\text{H}_2\text{O}_2] \quad (36)$$

$$\frac{d[ROOH]}{dt} = \frac{2k_{33}K_{29}[H_2O_2]_0[PCA]_0[V]_0}{K_{28}(1 + K_{31}[H_2O_2]_0)[PCA]_0^2 + (1 + K_{29}[H_2O_2]_0)[PCA]_0 + K_{29}K_{30}[H_2O_2]_0} \tag{37}$$
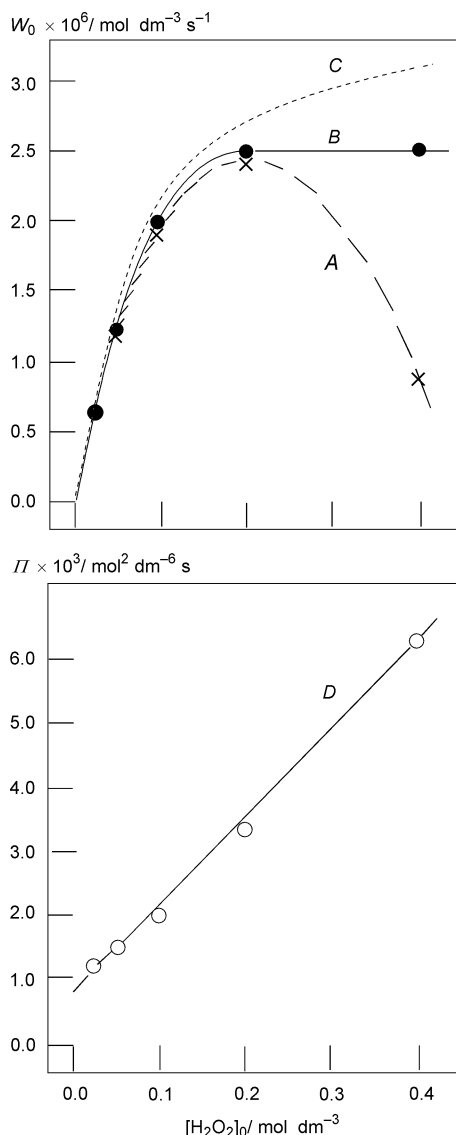
Fig. 19 Dependence of the oxidation rate on the initial concentration of hydrogen peroxide: *A*—plot of the experimentally obtained dependence of the initial rate W_0 on the initial H_2O_2 concentration; *B*—curve for the same dependence taking into account the retarding influence of water; *C*—curve obtained from curve *B* using eqn. (37); *D*—linear anamorphosis of curve *B* in coordinate Π—$[H_2O_2]_0$, where Π is governed by eqn. (39). Reaction conditions are as described in the caption to Fig. 17.

Thus, in order to obtain a kinetic expression for the oxidation rate, it is sufficient to establish the dependence of [V(PCA)-H₂O₂] on the initial concentrations of the reagents. In the steady-state approximation the value [V^V(PCA)H$_2$O$_2$] can be easily obtained if we accept $[PCA]_0/[V]_0 > 4$, *i.e.*, $[PCA]_0 - [V]_0 \approx [PCA]_0$, $[V]_0/[PCA]_0 << 1$ and $[V^V] >> [V^{IV}]$. Using this expression for the steady-state concentration of species V^V(PCA)H$_2$O$_2$ we will come to the kinetic equation for the initial reaction rate given by eqn. (37).

To check the applicability of the proposed kinetic expression to the experimental data we studied the dependence d[ROOH]/dt on $[V]_0$ under the condition $[V]_0/[PCA]_0 \leq 1/4$ and quantitatively analysed the data presented in Figs. 18 and 19. Firstly, in accordance with kinetic eqn. (37) the reaction rate is proportional to the vanadium concentration (Fig. 20). The experimental dependences depicted in Figs. 18 and 19 are tolerably

described by eqn. (37) at $[PCA]/[n\text{-}Bu_4NVO_3] \geq 4$ if we use corresponding values of the equilibrium and rate constants (see below). Secondly, the dependence of the reciprocal reaction rate on the reciprocal hydrogen peroxide concentration [eqn. (38)] should give a straight line:

$$\frac{1}{\frac{d[ROOH]}{dt}} = \frac{1}{2k_{33}K_{29}[PCA]_0[V]_0} \times \left\{ K_{28}K_{31}[PCA]^2 + \right.$$
$$\left. K_{29}[PCA] + K_{29}K_{30} + (K_{28}[PCA]^2 + [PCA])\frac{1}{[H_2O_2]} \right\} \tag{38}$$

More simply, in accordance with eqn. (37) the dependence of function Π [eqn. (39)] on $[H_2O_2]_0$ should be linear. Indeed,

$$\Pi = \frac{[H_2O_2]_0[V]_0[PCA]_0}{W} \tag{39}$$

the straight line *D* in Fig. 19 demonstrates the very close correspondence of the model, *i.e.*, eqn. (37), with experimental data. Thirdly, the dependence of the reaction rate on the PCA concentration is also in accordance with the experimental data. Really, in accordance with eqn. (37) the maximum value for the reaction rate at the fixed H₂O₂ concentration is attained at the PCA concentration magnitude governed by expression (40).

$$[PCA]_{max} = \sqrt{\frac{K_{29}K_{30}[H_2O_2]_0}{K_{28}(1 + K_{31}[H_2O_2]_0)}} \tag{40}$$

Using eqn. (40) and the kinetic expression for the reaction rate (37) we can obtain eqn. (41). It follows from this expression that the left-hand side value of eqn. (41), which can be easily

$$\frac{[V]_0[H_2O_2]_0}{[PCA]_0 - [PCA]_{max}}\left\{\frac{[PCA]_0}{W} - \frac{[PCA]_{max}}{W_{max}}\right\} = \frac{1}{2k_{33}K_{29}} \times \tag{41}$$
$$\{(1 + K_{29}[H_2O_2]_0) + K_{28}(1 + K_{31}[H_2O_2]_0)([PCA]_0 + [PCA]_{max})\}$$

calculated using the experimental data, should be a linear function of the PCA concentration at a fixed H₂O₂ concentration. Such a dependence of parameter Γ [eqn. (42)] on the PCA

$$\Gamma = \frac{[V]_0[H_2O_2]_0}{[PCA]_0 - [PCA]_{max}}\left\{\frac{[PCA]_0}{W} - \frac{[PCA]_{max}}{W_{max}}\right\} \tag{42}$$

concentration has been observed in reality and shown in the form of line *C* in Fig. 18.

We can state that the reaction rate dependences on $[V]_0$, $[H_2O_2]_0$ and $[PCA]_0$ are adequately characterized, if one accepts the following values (at 40 °C) for the equilibrium constants: $K_{28} \leq 10$ dm³ mol⁻¹; $K_{29} = 0.55$ dm³ mol⁻¹; $K_{30} = 8 \times 10^{-3}$ dm³ mol⁻¹; $K_{31}K_{28} = 0.9 \times 10^3$ dm⁶ mol⁻², and for the rate constant $k_{33} = 0.4$ s⁻¹. For our typical experimental conditions ($[H_2O_2]_0 = 0.1$ mol dm⁻³, $[V]_0 = 1.0 \times 10^{-4}$ and $[PCA]_0 = 1.0 \times 10^{-3}$ mol dm⁻³) we can calculate the following concentrations of transient species (mol dm⁻³): $[V(PCA)_2] \leq 6 \times 10^{-7}$, $[V(PCA)] \approx 6 \times 10^{-5}$, $[V(PCA)H_2O_2] \approx 3.3 \times 10^{-6}$, $[VH_2O_2] \approx 2.8 \times 10^{-5}$, $[V(PCA)_2H_2O_2] \approx 5.6 \times 10^{-6}$. The results of the calculations are illustrated in the forms of curve *B* in Fig. 18 and curve *C* in Fig. 19. Thus, it can be concluded that the proposed kinetic scheme for this process adequately describes the whole
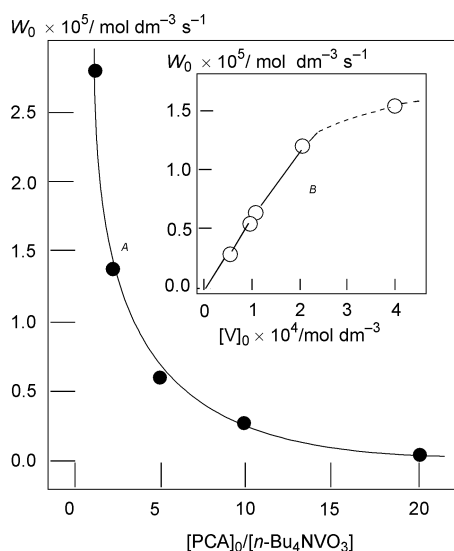
Fig. 20 Plots of the initial cyclohexane oxidation rate, W_0, *versus* the [PCA]/[n-Bu$_4$NVO$_3$] ratio at constant [PCA] = $(1.0 \times 10^{-3}$ mol dm^{-3}) (curve *A*) and *versus* the concentration of the catalyst composition [V]$_0$ (1 equiv. of n-Bu$_4$NVO$_3$ + 4 equiv. of PCA) (curve *B*). Initial concentration of H$_2$O$_2$ was 0.2 mol dm^{-3}. Other conditions are as described in the caption to Fig. 17.

set of the experimental data and properly expresses the main features of the considered oxidation reaction. It is necessary to emphasize that the conclusion about the direct proportionality between the reaction rate (*i.e.*, hydroxyl radical generation rate) and concentration of the complex containing only one PCA molecule is by no means in contradiction with our experimental data. Indeed, on the one hand, at [PCA]$_0$ > [V]$_0$ practically all the vanadium ions exist as complexes with PCA. According to our NMR data, mixing vanadate, PCA and H$_2$O$_2$ in a ~1 : 4:1 ratio gives rise to the formation of the complex containing two pca ligands per one vanadium. On the other hand, the maximum reaction rate has been observed at [PCA]$_0$/[V]$_0$ > 4 rather than at [PCA]$_0$/[V]$_0$ = 1. This excess of the PCA concentration over the vanadium concentration, necessary to reach the maximum reaction rate, is due to the competition between H$_2$O$_2$ and PCA for the sites in the vanadium coordination sphere. The equilibrium constant K_{31} is reasonably high ($\approx 10^4$ dm^3 mol^{-1}) and it is also evident that the concentration of the catalytically active species V^V(PCA)H$_2$O$_2$ [eqns. (29) and (32)] should be low ($\approx 3 \times 10^{-6}$ mol dm^{-3} as stated above).

When the concentrations of hydrogen peroxide and PCA are not high, *i.e.*, [H$_2$O$_2$]$_0$ ≤ 0.1 mol dm^{-3} and [PCA]$_0$ ≤ 2 × 10^{-3} mol dm^{-3} and 10 ≥ [PCA]$_0$/[V]$_0$ ≥ 4, kinetic eqn. (37) can be simplified to eqn. (43). Taking into consideration the constants given above, we can transform eqn. (43) into expression (44),

$$\frac{d[ROOH]}{dt} = \frac{2k_{33}K_{29}[H_2O_2]_0[PCA]_0[V]_0}{[PCA]_0 + K_{29}K_{30}[H_2O_2]_0} \quad (43)$$

$$\frac{d[ROOH]}{dt} = \frac{0.44[H_2O_2]_0[PCA]_0[V]_0}{[PCA]_0 + 0.44 \times 10^{-3}[H_2O_2]_0} \quad (44)$$

which can be easily used for the evaluation of the expected cyclohexane oxidation rates. If the hydrogen peroxide concentration is low, [PCA]$_0$ > $K_{29}K_{30}$[H$_2$O$_2$]$_0$, and the equation for the reaction rate will be even simpler [eqn. (45)]. These conditions

$$\frac{d[ROOH]}{dt} = 2k_{33}K_{29}[H_2O_2]_0[V]_0 \quad (45)$$

have been used to study the temperature dependence of the cyclohexane oxidation rate. The following parameters were obtained: i) effective activation energy, which equals the sum

of true activation energy for the monomolecular decomposition of complex V(PCA)H$_2$O$_2$ and enthalpy for equilibrium (29), $E_{eff} = 17 \pm 2$ kcal mol^{-1}; ii) effective value for preexponent factor $A_{eff} = 7.2 \times 10^{11}$ dm^3 mol^{-1} s^{-1}, which corresponds to iii) effective rate constant $k_{eff} = 2k_{33}K_{29} = 0.44$ dm^3 mol^{-1} s^{-1} at 40 °C.

Catalytic cycle for hydroxyl radical generation

In accordance with our experiments we assume that in the initial period of the reaction any vanadium derivative under the action of hydrogen peroxide (and possibly also dioxygen and other components of the reaction mixture) is rapidly transformed into a reactive form of the catalyst. Because the most efficient reaction is the oxidation catalysed by vanadate anion, such transformations of ligands at the vanadium centre for the case VCl$_3$ can be conventionally presented as eqn. (46):

$$V^{III}\text{–}Cl \xrightarrow{H_2O} V^{III}\text{–}OH \xrightarrow{H_2O_2} V^V\text{=}O \quad (46)$$
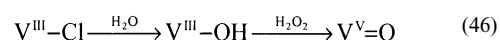
It has been shown above that the interaction between the vanadate anion and a PCA ($\equiv$pcaH) molecule results in the formation of the neutral dioxo complex (**5**) (Scheme 1) of vanadium(v) having one pca ligand. This complex is in equilibrium with the anionic dioxo complex (**1**) containing two pca ligands [eqn. (28)]. However, our kinetic analysis established that complex **5** is the precursor of the catalytically active species responsible for generating hydroxyl radicals. Generation and subsequent transformations of complex **5** were expressed formally by eqns. (27), (29) and (33). In more detail these reactions are depicted by eqns. (27a) and (28a). Complex **5** can coordinate a H$_2$O$_2$ molecule as shown previously in the formal eqn. (29). More detailed presentation of this reaction is depicted by Step 1 in Scheme 1. The following transformation is the reduction of vanadium(v) to vanadium(IV) by a hydrogen peroxide molecule. This reaction, which is a rate-determining stage, corresponds to a hydrogen atom abstraction by the ligand of a V^V complex, which gives hydroperoxyl radical, HOO$^•$, and oxo-hydroxy V^{IV} derivative **8**. It is reasonable to assume that the reduction occurs in two steps: proton transfer from coordinated H$_2$O$_2$ to one of the two oxo ligands with simultaneous formation of a new covalent V–O bond (Step 2) and the subsequent homolysis of this V–OOH bond (Step 3). The oxidation of hydrogen peroxide by metal complexes is not surprising. For example, according to the Haber–Weiss mechanism for the "Fe^{III}–Fe^{II}–H$_2$O$_2$–H$_2$O" system (see also Electronic Supplementary Information, Appendix 2), the initiation stage of hydrogen peroxide decomposition [reaction (47)] proceeds[8b,19a] with the

$$H_2O_2 + Fe^{III} \rightarrow HOO^• + H^+ + Fe^{II} \quad (47)$$
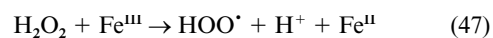
effective rate constant $k_{47} = 2 \times 10^{-4}$ dm^3 mol^{-1} s^{-1} at 25 °C and [H$^+$] = 1.0×10^{-2} mol dm^{-3}.

The second hydrogen peroxide molecule adds to a vacant site of complex **8**, forming in Step 4 the V^{IV} complex **9**. The other proton transfer (Step 5) results in the formation of a dihydroxy-hydroperoxy V^{IV} derivative which can exist in two forms, **10a** and **10b**. Both forms are known for various metals. We assume that complex **10a** decomposes *via* the homolysis of the O–O bond in the hydroperoxy ligand (Step 6), generating a free hydroxyl radical. This reaction seems to be favorable because it leads to an oxygen-centred radical V^{IV}–O$^•$ (**11a**) which is a mesomeric form of the stable oxo-vanadium(v) complex (**11b**). The formation of a stable species can be "a driving force" for the liberation of hydroxyl radicals. The mesomeric forms **11a** can be considered as the excited state of species **11b**, existing in the ground state. Oxo complexes of the type **11b** can be transformed into their excited states of the type **11a** by light

irradiation. Excited oxo complexes are stronger oxidizing re-agents and easily abstract hydrogen atoms from alkanes;[8b–d,34a–d] this has been utilised in photocatalytic aerobic alkane oxygenations.[8b–d,34e–k] Vanadium oxo-peroxo complexes are also more active in alkane oxidation if irradiated with light.[34l] In all these cases light irradiation stimulates the electron transfer from a ligand to a high-valent metal ion. A transformation analogous to $10a \rightarrow 11a$ (Step 6) with the O–O cleavage, for the case of the V^V derivative 7 looks less probable, because such a decomposition of 7 could lead to an unfavorable V^V–O˙. This is why complex 7 decomposes with V–O bond rupture (Step 3). Finally, in order to transform complex 11b to the starting species 5 active in catalysis, we need to transfer a proton from one oxo ligand of 11b to another one and then to eliminate a water molecule (Steps 7 and 8).

In this discussion we have not considered the role PCA in the proposed transformations. However, it should be emphasized that in the absence of PCA no catalytic oxidation takes place. Moreover, PCA is the most efficient co-catalyst and some PCA analogues turned out to be very poor co-catalysts. We therefore propose that the pca ligand plays the role of "a robot-manipulator's arm", facilitating the proton transfer within the vanadium complex. Scheme 2A illustrates this mechanism using the transformation $6 \rightarrow 7$ (Step 2 in Scheme 1). The nitrogen atom of the pca ligand can be de-coordinated from vanadium and abstract a proton from the coordinated H_2O_2 molecule to form an ammonium base which, after rotation of "the robot's arm", approaches another =O ligand of the complex and pro-tonates it to produce an –OH ligand. After re-coordination of the nitrogen to vanadium, complex 7 is formed. Analogously, a pca ligand can facilitate the transformation $9 \rightarrow 10a$ (Step 5 in Scheme 1). Another possible role of this ligand is proton transfer between two hydroxy ligands of the vanadium com-plex, resulting in water molecule extrusion from complex 11b and formation of the catalytically active starting species 5 (Scheme 2B). Obviously, a close spatial correspondence should be realized, i.e., all distances and angles between atoms must accommodate these atoms properly to provide for the possi-bility of the $H^+ \rightarrow$:N<, $H^+ \rightarrow \ddot{O}$= and $H^+ \rightarrow H\ddot{O}$– transfers. For example, imidazole-4-carboxylic acid and pyrazole-3,5-dicarboxylic acid as ligands do not fulfil this condition and are

very poor co-catalysts.[7f] Tridentate pyridine-2,6-dicarboxylic acid strongly binds to the vanadium ion and cannot rotate, which leads to the inactivity of this compound as a co-catalyst. We can assume that the pca-assisted proton transfer between an H_2O_2 molecule and the nitrogen atom of the pca ligand (Scheme 2C) as well as between the protonated nitrogen and the oxo ligand (Scheme 2D) proceeds via four-membered transition states 13 and 14, respectively.

We can also propose that PCA facilitates the proton transfer participating in the process either in the zwitterionic form (structure 15 in Scheme 3) or as an amino acid with an inter-molecular hydrogen bond (structure 16 in Scheme 3). In both cases the close geometrical conformity between the parameters of the vanadium complex and PCA molecule is very important. It is not clear, however, whether in catalytic reactions PCA molecules exist in solution as monomers or as H-bonded self-associates. In order to detect the potential intermolecular self-association we studied the concentration dependence of the chemical shifts of the PCA aromatic protons in acetonitrile solutions. One could expect that, in the case of intermolecular hydrogen bonding, dilution will lead to the destruction of the H-bonded self-associates, accompanied by changes in the NMR chemical shifts of interacting molecules. It turned out that the chemical shifts remained constant upon 200-fold dilution of PCA from 1.2×10^{-2} to 6×10^{-5} mol dm^{-3}: δ 9.28 (d, $J = 1.4$, 1 H), 8.83 (d, $J = 2.4$, 1 H) and 8.72 (dd, $J = 2.4$, 1.4, 1 H). The fact that the chemical shifts of PCA are not con-centration dependent can be explained by considering that self-association for PCA is negligible. At the same time, PCA molecules have both donor and acceptor groups capable of strong hydrogen bonding. The most plausible interpretation is that the hydroxy hydrogen of the PCA carboxylate group is involved in intramolecular H-bonding with the adjacent nitrogen atom (structure 16) and therefore is not available for intermolecular complexation.

It is known that in some biological systems vanadium(v) derivatives play the role of catalysts for hydroxyl radical generation, which causes these compounds to be toxic. The following processes [reactions (48)–(52)] occurring in the presence of the biological reducing agent, NADPH, have been proposed[23h,35a,b] for these systems:
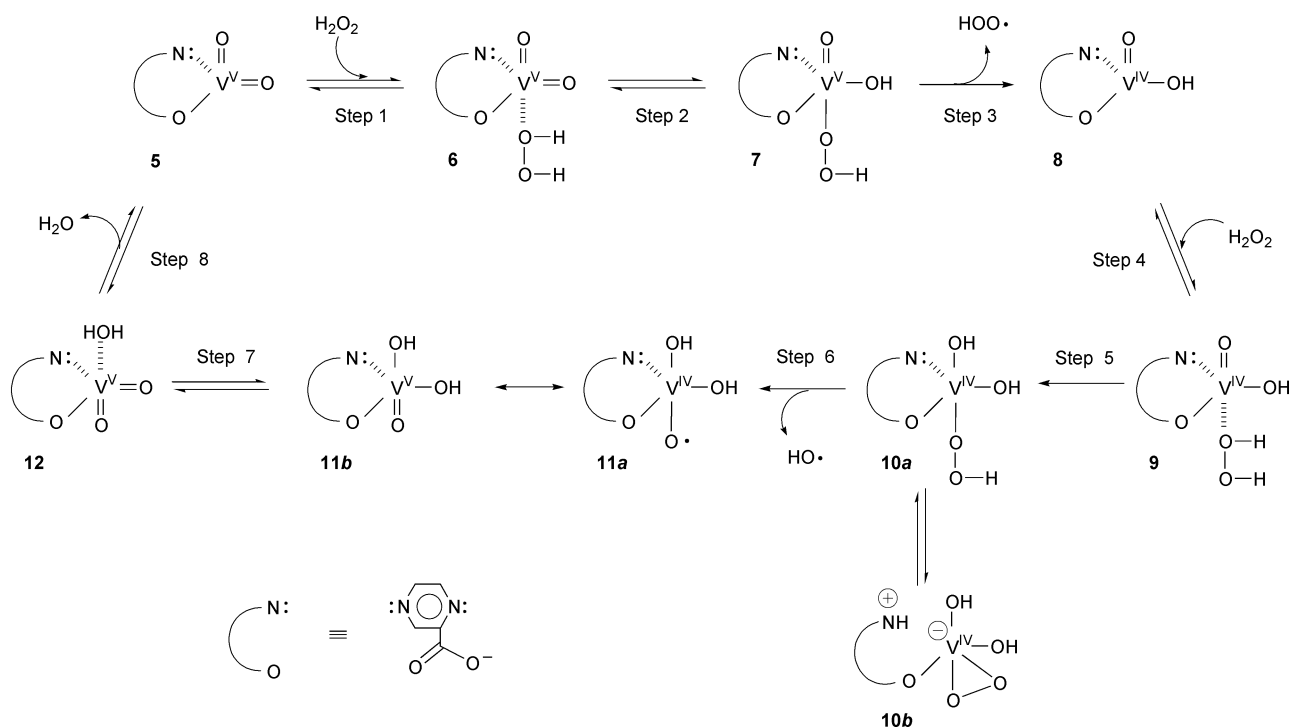
Scheme 1 Proposed catalytic cycle for hydroxyl radical generation.

A:

6

7

B:

12

5

C:

13

D:

14
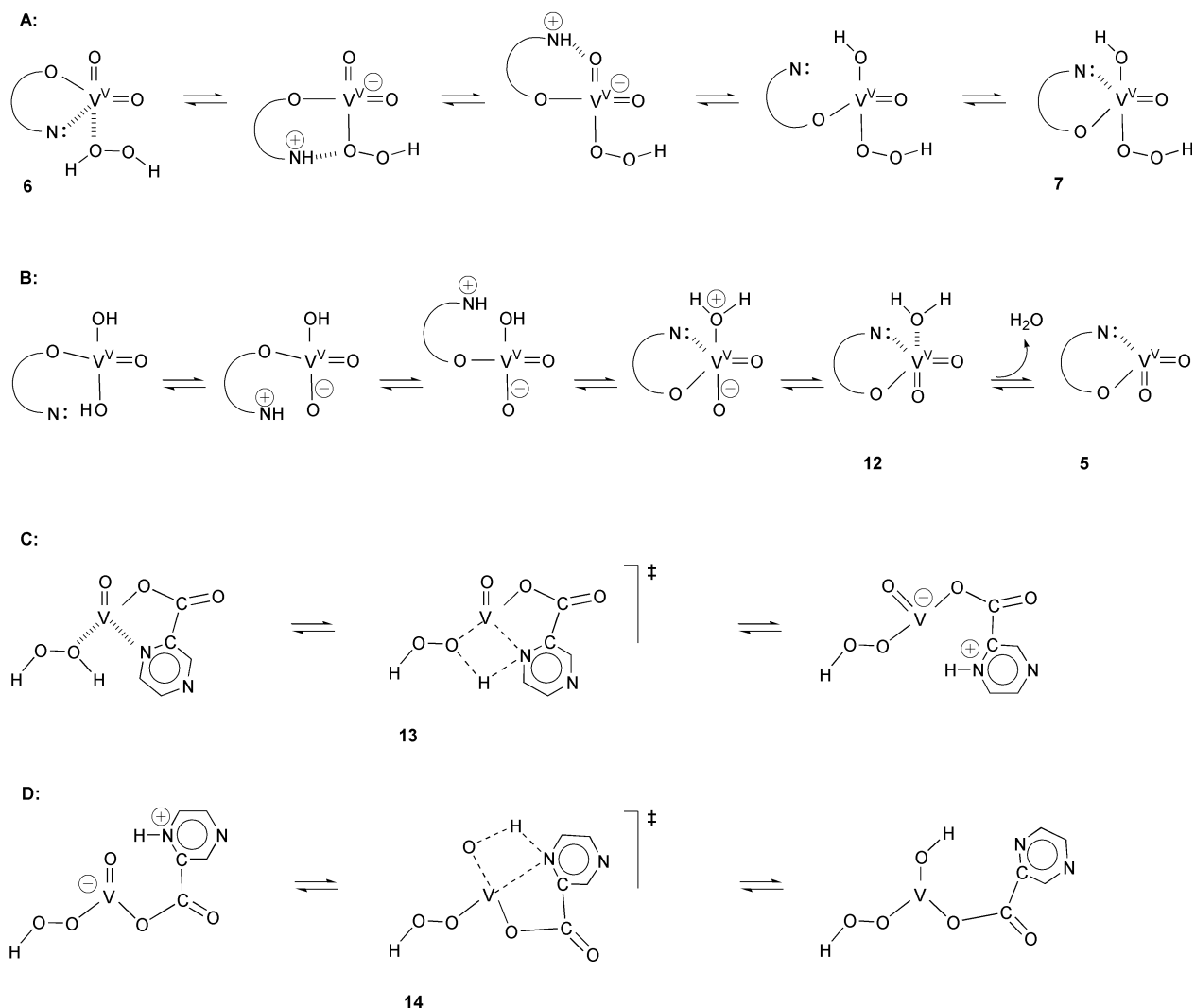
Scheme 2 Possible role of PCA in proton transfer ("robot's arm mechanism") between coordinated H_2O_2 molecule and OH ligand (**A**) and between two OH ligands (**B**).

$$V^V + O_2^{-\bullet} \rightarrow V^{IV}\text{–}OO^{\bullet} \qquad (48)$$

$$V^{IV}\text{–}OO^{\bullet} + NADPH \rightarrow V^{IV}\text{–}OOH + NADP^{\bullet} \qquad (49)$$

$$V^{IV}\text{–}OOH + H^+ \rightarrow V^V + H_2O_2 \qquad (50)$$

$$NADP^{\bullet} + O_2 \rightarrow NADP^+ + O_2^{-\bullet} \qquad (51)$$

$$V^{IV} + H_2O_2 \rightarrow V^V + HO^{\bullet} + HO^- \qquad (52)$$
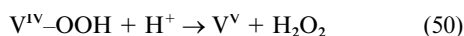
The mechanism of step $(52)^{23e}$ has not been discussed in detail.[23h,35a,b] However, it is clear that there is some similarity between the reactions (48)–(52) occurring in living cells and the steps of the catalytic cycle depicted in Scheme 2. We can assume that the accelerating role of PCA in the generation of hydroxyl radicals which we have found for the "O_2–H_2O_2–n-Bu$_4$NVO$_3$–PCA" reagent is played in living organisms by amino acids of peptides or free amino acids of various cell components. Thus we can conclude that processes that occur under the action of the reagent mimic some biological reactions and this reagent can be considered as a biomimetic system. Proton transfer processes are of great importance for biochemical systems (see, *e.g.*, refs. 35*c*–*h*).

Creating the total catalytic cycle for the system under discussion, we should take into consideration not only the process of hydroxyl radical production but also the interaction of these radicals with the alkane molecules and all subsequent reactions. These reactions were discussed above; see eqns. (2)–

15

16
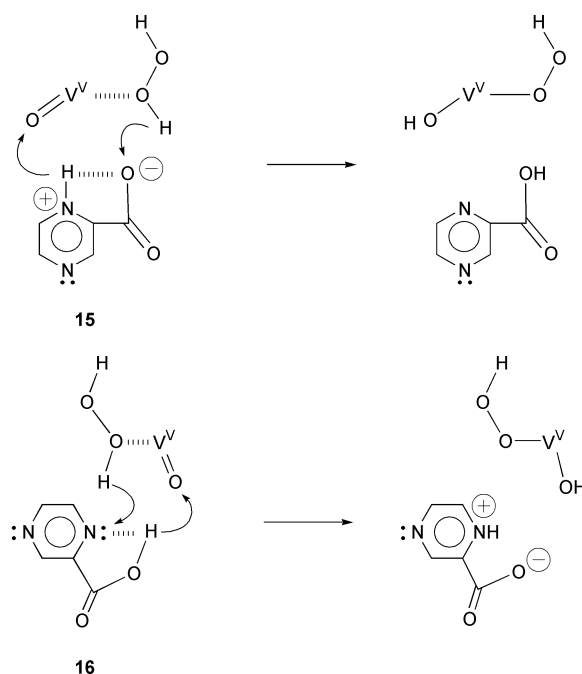
Scheme 3 Facilitation of proton transfer by PCA molecules *via* six-membered transition states.

(4), (7)–(22). The closed catalytic cycle is depicted in Scheme 4. All starting compounds coming in to the cycle are shown
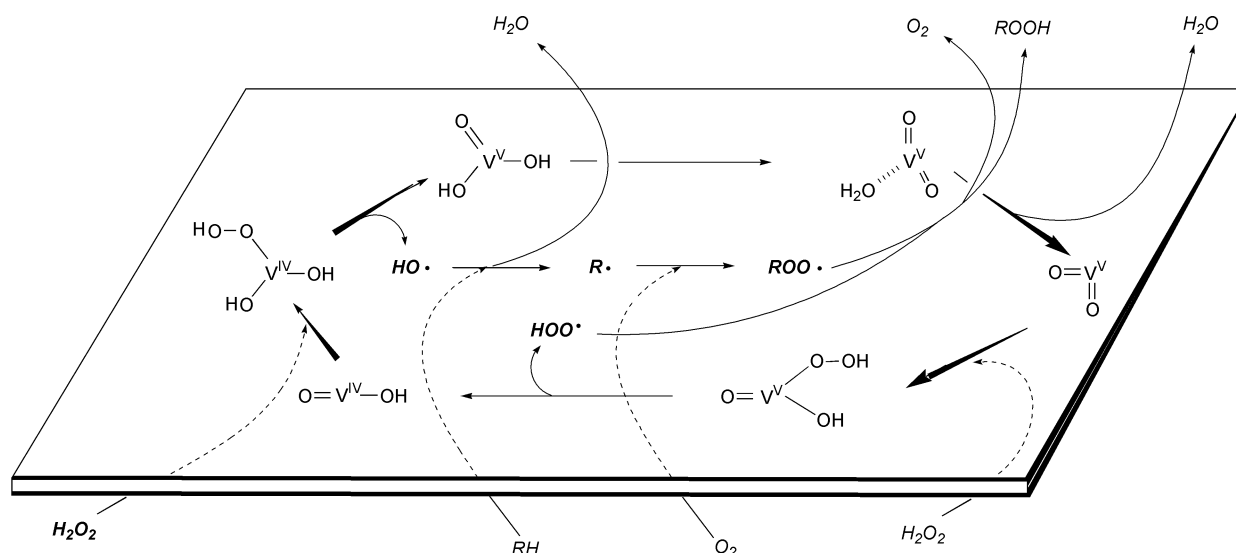
Scheme 4 Simplified catalytic cycle for alkane hydroperoxidation.

beneath the cycle and all outgoing, relatively stable products are shown above. We realize, of course, that this is only a very simplified formal scheme combining the various processes that proceed in reality.

Conclusions

The reagent described in the present paper consists of any derivative of vanadium(v), (IV) or even (III) and should contain PCA as an obligatory co-catalyst. Such a combination very efficiently produces hydroxyl radicals from H_2O_2 at relatively low temperatures (<50 °C) if acetonitrile is used as the solvent. These radicals can be used to initiate the aerobic oxidation of saturated hydrocarbons. At higher temperatures extensive decomposition of hydrogen peroxide occurs under the action of V–PCA to give molecular oxygen and water. PCA turns out to be a unique co-catalyst and only pyrazine-2,4-dicarboxylic acid and picolinic acid can be compared with PCA. The role of PCA in the process is thought to facilitate the proton transfer between an H_2O_2 molecule coordinated to vanadium and oxo ligands. Similar mechanisms operate in enzymatic catalysis.

Experimental

The compound n-Bu$_4$NVO$_3$, easily soluble in acetonitrile, was prepared[12] by adding V$_2$O$_5$ (4.0 g) to 200 mL of aqueous n-Bu$_4$NOH solution (0.4 mol dm^{-3}), stirring the solution for 18 h, filtering off the small amount of insoluble material, and then evaporating the solution to complete dryness under vacuum at 60 °C. This and other compounds soluble in acetonitrile, such as VCl$_3$ and VO(acac)$_2$, were used as stock solutions in acetonitrile. Aliquots of these vanadium-containing stock solutions and stock solutions of PCA or other co-catalysts were introduced into the reaction mixture and the reaction started by the addition of hydrogen peroxide. In the cases of the vanadium derivatives insoluble in acetonitrile, the stock solution containing both catalyst and co-catalyst was prepared prior to the oxidation reaction. Thus, stirring a suspension of NH$_4$VO$_3$ (2.9 mg) or VOSO$_4$·5H$_2$O (6.1 mg) and PCA (12.5 mg) in 100 mL of hot acetonitrile over a few hours gave a stock solution, which was used (2 mL) to prepare the reaction mixture (5 mL) containing vanadium (1.0 × 10^{-4} mol dm^{-3}) and PCA (4.0 × 10^{-4} mol dm^{-3}). The oxidations of higher hydrocarbons were carried out in air in thermostatted Pyrex cylindrical vessels with vigorous stirring. The total volume of the reaction solution was 5 or 10 mL.

The samples of the reaction solutions were analysed by GC (instruments LKhM 80/6; column 2 m; 5% Carbowax on Inerton AW-HMDS and DANI-86.10; fused silica capillary column 25 m × 0.32 mm × 0.25 μm, CP-WAX52CB; integrator SP-4400) 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, from which it is possible to determine the *real* concentrations of the alkyl hydroperoxide, alcohol, and ketone (aldehyde). This addition of PPh$_3$ allows us also to avoid the simultaneous injection into the GC of a substrate and hydrogen peroxide.

^{1}H and ^{51}V NMR spectra were recorded on a JEOL Eclipse+500 NMR spectrometer at room temperature, with neat VOCl$_3$ as external standard for ^{51}V NMR ($\delta = 0$). The instrument was operated at 131.46 MHz for recording ^{51}V NMR spectra. Normally, a total of 4096 points were collected over a spectral width of 52 630 Hz. The pulse width was 45°. Vanadium spectra of 5×10^{-3} mol dm^{-3} species could be obtained with good signal-to-noise ratio by accumulating 2000–4000 transients, at about 11 per second. Spectra of diluted solutions with 10^{-4} mol dm^{-3} concentration of vanadium species required the accumulation of 100 000–500 000 transients. The processing of the vanadium spectra included exponential multiplication with the line broadening 15–50 Hz to improve signal-to-noise ratio. All NMR spectra were obtained in acetonitrile-d_3. Unless it is stated otherwise, the concentration of vanadium species in the NMR samples was kept between 3×10^{-3} and 9×10^{-3} mol dm^{-3}.

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1 For parts 1–11 see refs. 6(*a*)–(*k*), respectively. Preliminary communications of previous parts and related papers have also been published (ref. 7).

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