Efficient H₂O₂ Oxidation of Alkanes and Arenes to Alkyl Peroxides and Phenols Catalyzed by the System Vanadate–Pyrazine-2-Carboxylic Acid

GEORGIY B. SHUL'PIN,[1] DONATO ATTANASIO, AND LORENZA SUBER

Istituto di Teoria e Struttura Elettronica e Comportamento Spettrochimico dei Composti di Coordinazione del CNR, P.O. Box 10, 00016 Monterotondo Stazione, Rome, Italy

H₂O₂ oxidizes cyclohexane and other alkanes in CH₃CN at 20–70°C in the presence of the catalyst Bu₄NVO₃–pyrazine-2-carboxylic acid (ratio 1 : 4) to afford, after reduction with PPh₃, the corresponding alcohol and carbonyl derivatives (the ratio decreases from 12 to 4 on raising the temperature from 20 to 70°C). The product yield reaches 46%, based on H₂O₂, and the turnover number is ca. 1000. The oxidation appears to give predominantly alkyl peroxides, which are partially decomposed in the course of the reaction. Peroxides can be formed when alkyl radicals, generated from alkanes, and radical-like species react with O₂ or abstract OOH groups from the vanadium complex. Benzene and its alkyl derivatives are oxidized to produce phenols as well as side-chain oxidation derivatives. © 1993 Academic Press, Inc.

INTRODUCTION

Although vanadium compounds have been widely used as catalysts in peroxide oxidation reactions (*1–4*), the synthesis of well-defined vanadium peroxo complexes and the study of their reactivity as an approach to the understanding of catalytic oxidation reactions have received surprisingly limited attention.

Some years ago Mimoun *et al.* (*5*) characterized a new family of V(V) oxo peroxo complexes of general formula [VO(O₂)(O–N)L₂] or [VO(O₂)(O–N)₂]⁻, where O–N represents the anion of the aromatic ligands pyridine-2-carboxylic acid or pyrazine-2-carboxylic acid. Detailed information was reported on the oxidizing properties of these compunds, which were found to be effective reagents for the stoichiometric epoxidation of alkenes and hydroxylation of aromatic hydrocarbons. However, no attempt was made subsequently to extend these results and to explore the feasibility

of catalytic-type reactions based on these compounds.

Hydrogen peroxide is one of the most attractive oxidation reagents because it is inexpensive and gives only water as a byproduct. In fact, an enormous amount of work has been carried out on the oxidation of alkanes, alkylaromatics and arenes by H₂O₂ in the presence of transition metal complexes (*1–6*). However, most of the available methods, including the well-known Fenton's reagent, do not lead to efficient, and/or synthetically useful procedures, especially for the oxidation of saturated hydrocarbons. For example, the recently described oxygenation of alkanes by a Gif-type system is carried out in pyridine (*6h*); efficient functionalization of alkanes catalyzed by manganese porphyrins occurs only in the presence of a large concentration of imidazole (*6a*), and cyclohexane oxidation catalyzed by vanadium(V) in acetic or trifluoroacetic acid requires concentrated solutions of H₂O₂ (*6c*).

On the basis of the above considerations we decided to examine the catalytic behavior of the compounds of Mimoun *et al.* (*5*).

[1] Present address: Institute of Chemical Physics, Academy of Sciences, Moscow 117977, Russia.

We now report preliminary results on the oxidation of alkanes and aromatic hydrocarbons by hydrogen peroxide under mild conditions, catalyzed by a system strictly related to the complexes defined by Mimoun et al. (5), i.e., the vanadate anion in the presence of an excess of the chelating molecule pyrazine–2-carboxylic acid.

METHODS

Materials. Bu$_4$N[VO$_3$] was prepared and purified according to a published method (7), starting from V$_2$O$_5$ and Bu$_4$NOH. The peroxo complexes [VO(O$_2$)(O–N)(H$_2$O)$_2$], with O–N= pyridine or pyrazine-2-carboxylate, were obtained following the procedure given by Mimoun et al. (5). Their purity was checked by elemental analyses. Cyclohexane (Merck, >99.5%) was purified by distillation, after shaking with conc. H$_2$SO$_4$. Other hydrocarbons (Rudi Pont, Analyticals, Aldrich) and pyrazine-2-carboxylic acid (Merck) were used as received. Hydrogen peroxide (Aldrich) was used as 30% water solution. Acetonitrile was distilled from CaH$_2$, under a stream of prepurified nitrogen, before each experiment.

Measurements. Qualitative and quantitative analysis of products were performed by g.l.c., eventually co-injecting authentic samples, using a Perkin–Elmer 8500 gas chromatograph equipped with a packed column (length 2 m, filling 5% Carbowax on Chromosorb W 80/100) and with an HP 3390A integrator.

Oxidations. Reactions were performed in thermostated cylindrical vessels in air under vigorous stirring. Total volume of the reaction solution was 10 ml. Addition of the aqueous 30% H$_2$O$_2$ solution was considered to be the starting point of the reaction, which was afterwards followed by g.l.c. analysis of aliquot samples. Each sample was analyzed twice, before and after addition of triphenylphosphine.

RESULTS AND DISCUSSION

We have found that the system hydrogen peroxide–vanadate anion–pyrazine-2-car-

boxylic acid oxidizes cyclohexane in acetonitrile as a solvent in the temperature range 20–70°C. No oxidation was noted in the absence of pyrazine-2-carboxylic acid (PCA), and the optimal ratio between cocatalyst and catalyst (i.e., between the organic ligand and vanadate) was found to be about 4. Several other organic chelating molecules (e.g., salicylic acid, anthranilic acid, L-alanine, 8-hydroxyquinoline, and especially pyridine-2-carboxylic acid) as well as the pure V(V) peroxo complex [VO(O$_2$) (pyrazine-2-carboxylate)(H$_2$O)$_2$] were found to be active in the oxidation of cyclohexane. However, the vanadate–PCA system proved to be definitely more efficient and was used for all the experiments described in this paper. Some evidence that this system behaves as the pure peroxo complex in the presence of excess ligand has been obtained and is reported below.

There is a linear dependence of the initial rate of cyclohexane oxidation on the catalyst concentration. However, when the concentration [VO$_3^-$ + 4PCA] is larger than 10^{-4} mol/dm^3 the rate of oxidation becomes constant. The reaction order in cyclohexane is close to zero because at [C$_6$H$_{12}$]$_0$ > 0.2 mol/dm^3 the initial rate of the oxidation does not depend on [C$_6$H$_{12}$]$_0$. Similarly, when the initial concentration of hydrogen peroxide was varied it was found that the growth of the initial rate of oxidation with increasing [H$_2$O$_2$]$_0$ stopped at [H$_2$O$_2$]$_0$ = 0.2 mol/dm^3. Comparison of the oxidation rates of c-C$_6$H$_{12}$ and c-C$_6$D$_{12}$ showed a small kinetic isotope effect (ca. 1.2 at 50°C).

Products of the cyclohexane oxidation were analyzed by g.l.c. When a sample of the reaction solution is injected into the chromatograph formation of cyclohexanol and cyclohexanone, in approximately equal amounts, can be detected. Formation of these products does not occur in the injector of the column of the chromatograph because the amount of cyclohexane oxygenation derivatives is negligible at the beginning, when the concentration of H$_2$O$_2$ is high. If the sample of the reaction solution is treated with an excess of triphenyl-
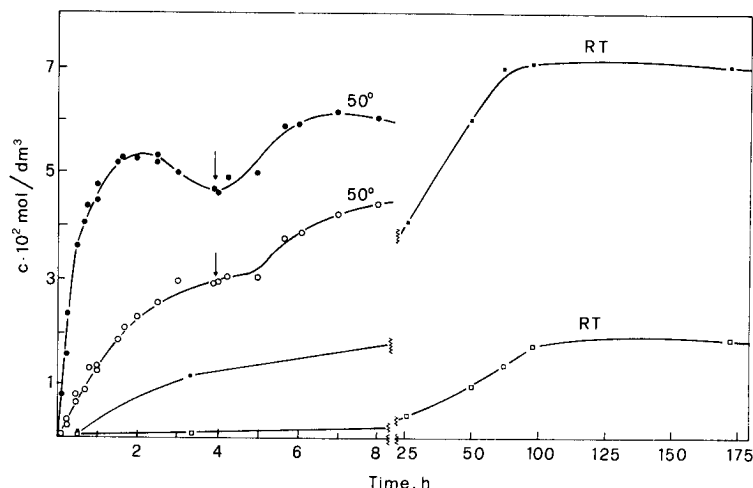
FIG. 1. Kinetics of the accumulation of cyclohexyl hydroperoxide (●, ■) and total cyclohexanol and cyclohexanone (○, □) in the oxidation of cyclohexane (0.23 mol/dm³) by H₂O₂ (0.2 mol/dm³) in CH₃CN catalyzed by Bu₄NVO₃ (0.1 mmol/dm³) and pyrazine-2-carboxylic acid (0.4 mmol/dm³) at 50°C (circles) and room temperature (squares). Arrows indicate addition of fresh H₂O₂ (0.2 mol/dm³). Data from two different experiments are used for the reaction at 50°C.

phosphine for a few minutes, before g.l.c. analysis, a sharp increase of cyclohexanol concentration, at the expense of the amount of cyclohexanone, can be observed. This behavior can be interpreted as follows. Cyclohexane is oxidized to afford predominantly cyclohexyl hydroperoxide, which is well known (8) to decompose in the chromatograph with the formation of approximately equal amounts of cyclohexanol and cyclohexanone. Triphenylphosphine readily reduces the alkyl hydroperoxide to give quantitative conversion to the corresponding alcohol (8). Therefore, chromatographic analysis of the reaction solution before and after triphenylphosphine reduction allows one to estimate the amounts of peroxide as well as of cyclohexanol and cyclohexanone formed at selected time intervals.

Figure 1 shows the accumulation of cyclohexane oxidation products at 50°C and at room temperature. In both cases cyclohexyl peroxide is the main product but the amount of this derivative relative to cyclohexanol and cyclohexanone is higher if the oxidation is carried out at low temperature. Indeed at room temperature (r.t.) the maxi-

mum concentration of cyclohexanol and cyclohexanone after reduction with PPh₃ is obtained after 75 h (85.1 × 10⁻³ and 7.3 × 10⁻³ mol/dm³, respectively; ratio alcohol : ketone ca. 12), whereas at 70°C the reaction is completed within 45 min (63.1 × 10⁻³ and 15.4 × 10⁻³ mol/dm³ and the ratio mentioned above is much lower (ca. 4). The highest yield of products and selectivity (i.e., ratio alcohol : ketone after PPh₃ reduction) was achieved at r.t. after 75 h. In this case the yield of the oxygenation products based on hydrogen peroxide (and assuming that only one molecule of H₂O₂ is necessary to produce a product molecule, *vide infra*) reaches 46%, the turnover number being ca. 1000.

Linear alkanes can also be oxidized by the system under discussion. The data are summarized in Table 1 (it should be noted that the aim was only to determine the selectivity and not to obtain maximum yields of the oxidation products). Benzene is oxidized by H₂O₂ in the presence of the catalytic system to afford phenol (Fig. 2). Toluene gives rise to benzaldehyde as well as isomeric cresols, the ratio *ortho* : *meta* : *para* being 54 : 12 : 34. 1-Phenylethanol

TABLE 1

Oxidation of Alkanes by H_2O_2 in CH_3CN Catalyzed by
VO_3^-–Pyrazine-2-carboxylic Acid[a]

Alkanes	Products ($\times 10^{-3}$ mol/dm³)		Regioselectivity[c]
	Alcohols[b]	Carbonyl derivatives[b]	
n-Hexane	25.2	5.7	$C^1 : C^2 : C^3 = 1 : 8.3 : 6.8$
n-Heptane	22.9	6.0	$C^1 : C^2 : C^{(3+4)} = 1 : 8.6 : 7.0$
2-Methylhexane	23.2	4.8	$1° : 2° : 3° = 1 : 5.5 : 24$
3-Methylhexane	15.0	4.5	$1° : 2° : 3° = 1 : 13.7 : 64$

[a] Conditions: 50°C, 2 h; 0.23 mol/dm³ of alkane, 0.2 mol/dm³ of H_2O_2, 1×10^{-4} mol/dm³ of Bu_4NVO_3 and 4×10^{-4} mol/dm³ of pyrazine-2-carboxylic acid. Triphenylphosphine was added to the reaction solution before g.l.c. analysis.

[b] Sum of all isomers.

[c] Relative reactivity of hydrogen atoms at carbons 1, 2, 3, and 4 of the chain of unbranched alkanes and at primary, secondary, and tertiary carbons 1°, 2°, and 3° of branched alkanes are calculated taking into account the number of hydrogen atoms at each carbon.

(9.7×10^{-3} mol/dm³), acetophenone (2.5×10^{-3} mol/dm³), and 2-phenylethanol (0.8×10^{-3} mol/dm³) are the main products (after

FIG. 2. Kinetics of the accumulation of cyclohexanone (●) and phenol (○) in the oxidation of cyclohexanol (0.23 mol/dm³) and benzene (1.0 mol/dm³), respectively, by H_2O_2 (0.2 mol/dm³) in CH_3CN catalyzed by Bu_4NVO_3 (0.1 mmol/dm³) and pyrazine-2-carboxylic acid (0.4 mmol/dm³) at 50°C. Concentrations of the products were determined by g.l.c. after reduction with PPh_3.

PPh₃ reduction) of the ethylbenzene (0.21 mol/dm³) side-chain oxidation (40°C, 6 h); however, small amounts of styrene epoxide and benzaldehyde were also detected. Cumene (0.18 mol/dm³) is oxidized to yield 2-phenylpropanol (7.7×10^{-3} mol/dm³) and acetophenone (1.1×10^{-3} mol/dm³) in addition to nucleus hydroxylation products. Finally, cyclohexanol gives cyclohexanone (Fig. 2) with 30% yield based on hydrogen peroxide and cyclohexene is transformed predominantly into allylic hydroxylation products.

The mechanism of the reaction is not fully clear. However, one may assume the following sequence of reaction steps. A molecule of hydrogen peroxide is coordinated within the sphere of vanadium (it is interesting to note that no oxidation reaction proceeds in the presence of the tridentate dipicolinic acid) and then cleavage of the O–O bond occurs. Vanadium is known to generate hydroxyl radicals in biological systems (9). Hydroxyl radicals thus formed attack a molecule of hydrocarbon to abstract a hydrogen atom. The selectivities shown by the system under discussion are close to the values which we obtained for the uncatalyzed oxidations by H_2O_2 in
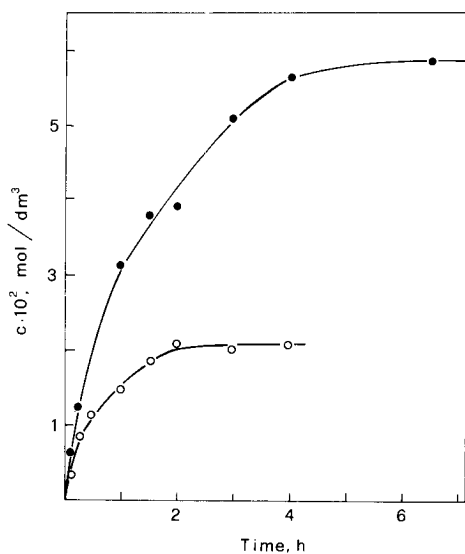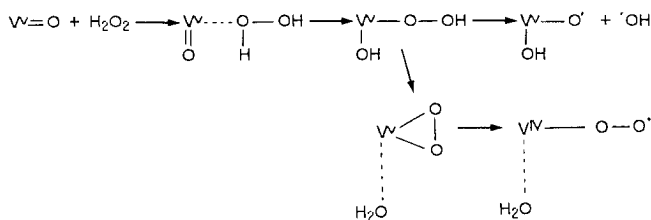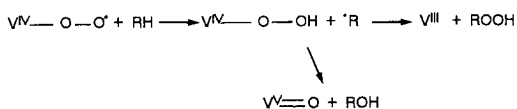
SCHEME 1

CH₃CN under UV irradiation. In the case of linear hexane the relative, normalized selectivities of nonequivalent carbons along the chain are $C^1 : C^2 : C^3 = 1 : 10 : 7$. When branched alkanes, such as 2- or 3-methylhexane are used, the selectivities, referred to primary, secondary, and tertiary carbon atoms, $1° : 2° : 3°$, are found to be $1 : 6 : 20$ and $1 : 4 : 12$, respectively. These data may be compared with the results obtained for the catalyzed reactions, which are reported in Table 1. The reactivities of methylene hydrogens in ethylbenzene relative to that of cyclohexane, for the vanadium catalyzed or light-stimulated oxidations, are also similar (0.5 and 0.8, respectively).

Hydroxyl radicals may be generated in the decomposition of a peroxo complex as shown in Scheme 1. An alternative possibility is the formation of a V–O–O· species which can also abstract the hydrogen atom from the alkane. Such a mechanism was proposed by Mimoun et al. (5) for the oxidation of alkanes by vanadium peroxo complexes. We determined the selectivities for the stoichiometric oxidation by Mimoun's peroxo complex [VO(O₂)(O–N)(H₂O)₂] (O–N = pyridine-2-carboxylate). The experimental results give $C^1 : C^2 : C^3 = 1 : 40 : 20$ for n-hexane, $1° : 2° : 3° = 1 : 7 : 9$ for 3-methylhexane, and 1.6 for the relative reactivity of CH₂ in ethylbenzene and cyclohexane. The oxidation by the complex appears to be more selective than the catalytic reaction. It is noteworthy that we detected the formation of alkyl peroxides in large concentrations in the stoichiometric oxidation of alkanes by Mimoun's peroxo complex. Thus it is reasonable to assume that three

types of radical-like species, including hydroxyl radicals, may arise in the reaction, as shown in Scheme 1. The contribution of each species in the stoichiometric and catalytic processes may be different, this being reflected by the different selectivities of the oxidations. A radical-like species abstracts the hydrogen atom from the alkane, RH. The alkyl radical R· thus formed reacts very rapidly with a molecule of oxygen to form ROO· which then is transformed into alkyl hydroperoxide (with the participation of an hydrogen atom donor or via reduction by V(IV) and addition of a proton).

In another route to alkylhydroperoxide, R· may abstract an OOH group from the vanadium derivative (Scheme 2). Such abstraction of an OH group leads to the formation of alcohol as proposed in Ref. (5a). The failure to oxidize cyclohexane using 70% aqueous tert-butyl hydroperoxide instead of H₂O₂ supports the hydroxyl radical participation in the reaction under discussion. Hydroxyl radicals appear to be the species which oxidize arenes in the reaction with H₂O₂. In this case molecular oxygen does not participate in the process and the yield of phenol is low compared with the yield of cyclohexane oxidation products. It should be noted that the formation of alkyl hydroperoxides was found in the oxidation by Gif-type systems (10).

SCHEME 2

The oxidation by H_2O_2 catalyzed by vanadate and pyrazine-2-carboxylic acid does not appear to be a chain process because 2,6-bis(tert-butyl)-4-methylphenol (concentration 0.01 mol/dm³), the inhibitor of free radical chain reactions, does not decrease the rate of cyclohexane oxidation. The presence of 2-propanol (0.1 mol/dm³) also does not influence dramatically the rate of cyclohexane oxidation. On the other hand in the presence of CCl_4 (1.23 mol/dm³) or CBr_4 (0.04 mol/dm³), which easily react with alkyl radicals, the rate of cyclohexane oxygenation is ca. 10 times lower.

The fact that pyrazine-2-carboxylic acid is by far the most active cocatalyst among a series of several bidentate chelating organic molecules has been already pointed out. In addition we note the complete inactivity of tridentate ligands such as dipicolinic acid or 2,2'-bipyridine. In this context the recent observation (11) that alkane oxidation by hydrogen peroxide catalyzed by iron complexes (a Gif-type system) is significantly accelerated in the presence of picolinic acid and other related acids is particularly interesting.

In conclusion, the homogeneous system described in this paper and based on hydrogen peroxide as an oxidant and vanadate ion and pyrazine-2-carboxylic acid as a catalyst efficiently transforms alkanes into alkyl peroxides (which may be selectively reduced to afford the corresponding alcohols) and arenes into phenols. Other organic and inorganic compounds can also be oxidized by this system, and investigation in this field is in progress.

REFERENCES

1. Sheldon, R. A., and Kochi, J. K., "Metal-Catalyzed Oxidations of Organic Compounds." Academic Press, New York, 1981.

2. Shul'pin, G. B., "Organic Reactions Catalyzed by Metal Complexes." Nauka, Moscow, 1988.

3. Freeman, F., in "Organic Syntheses by Oxidation with Metal Compounds" (W. J. Mijs and C. R. H. I. de Jonge, Eds.). Plenum Press, New York, 1986.

4. Strukul, G. (Ed.), "Metal Catalysis in Hydrogen Peroxide Oxidations." Reidel, Dordrecht, The Netherlands, 1991.

5. (a) Mimoun, H., Saussine, L., Daire, E., Postel, M., Fischer, J., and Weiss, R., J. Am. Chem. Soc. 105, 3101 (1983); (b) J. Eur. Pat. 97551 (C.A. 100, 174641h (1984)).

6. (a) Battioni, P., Renaud, J. P., Bartoli, J. F., Mansuy, D., J. Chem. Soc. Chem. Commun., 341 (1986); (b) Taqui Khan, M. M., and Shukla, R. S., J. Mol. Catal. 51, 171 (1989); (c) Moiseev, I. I., Gekhman, A. E., and Shiskin, D. I., New J. Chem. 13, 683 (1989); (d) Attanasio, D., Orrù, D., and Suber, L., J. Mol. Catal. 57, L1 (1989); (e) Druzhinina, A. N., Nizova, G. V., and Shul'pin, G. B., Izvest. Akad. Nauk SSSR Ser. Khim., 210 (1990); (f) Muzart, J., and N'Ait Ajjou, J. Mol. Catal. 66, 155 (1991); (g) Muzart, J., N'Ait Ajjou, A., Nizova, G. V., and, Shul'pin, G. B., Izvest. Akad. Nauk SSSR Ser. Khim., 1454 (1991); (h) Barton, D. H. R., Eaton, P. E., and Liu, W. G., Tetrahedron Lett. 32, 6263 (1991); (i) Barton, D. H. R., Doller, D., and Geletii, Yu. V., Mendeleev Commun., 115 (1991); (j) Bonchio, M., Conte, V., Di Furia, F., and Modena, G., J. Org. Chem. 54, 4368 (1989).

7. Day, V. W., Klemperer, W. G., and Yagasaki, A., Chem. Lett., 1267 (1990).

8. Galimova, I. G., Maslennikov, S. I., and Nikolaev, A. I., Izvest. Akad. Nauk SSSR Ser. Khim., 2464 (1980).

9. (a) Butler, A., and Carranco, C. J., Coord. Chem. Rev. 109, 61 (1991). (b) Shi, X., and Dalal, N. S., Arch. Biochem. Biophys. 289, 355, (1991) and references therein.

10. (a) Barton, D. H. R., Csuhai, E., Doller, D., and Balavoine, G., J. Chem. Soc. Chem. Commun., 1787 (1990); (b) Knoght, C., and Perkins, M. J., J. Chem. Soc. Chem. Commun., 925 (1991).

11. (a) Sheu, C., Richert, S. A., Cofrè, P., Ross, B. Jr., Sobrowiak, A., Sawyer, D. T., and Kanofsky, J. R., J. Am. Chem. Soc. 112, 1936 (1990); (b) About-Jaudet, E., Barton, D. H. R., Csuhai, E., and Ozbalik, N., Tetrahedron Lett. 31, 1657 (1990).