addition was completed, the cooling bath was removed and the reaction mixture refluxed for 2.5 h. Treatment with IM borane–THF solution (4.5 mL, 4.5 mmol) was followed by stirring of the reaction mixture at ambient temperature for 24 h, and then solvent removal at reduced pressure. The residue was purified by flash chromatography (hexane) and then by recrystallization from hexane–acetone (2:1) to afford 264 mg (18.7% yield) of the pure product: mp 158–159 °C; ^{1}H (90 MHz, $CDCl_3$) δ 1.2–3.0 (m, 10 H), 7.3 (m, 5 H), 7.5 (m, 6 H), 7.8 (m, 4 H); ^{13}C NMR in Table I; ^{31}P NMR (36.23 MHz $CDCl_3$) δ 20.31; ^{11}B NMR (28.69 MHz, $CDCl_3$) δ −39.53. Anal. Calcd for $C_{24}H_{28}BP$: C, 80.45; H, 7.87. Found: C, 80.66; H, 7.72.

(*cis*-4-*tert*-Butylcyclohexyl)diphenylphosphine–borane (6) was similarly prepared from *trans*-4-*tert*-butylcyclohexyl methanesulfonate (1.0 g, 4.2 mmol; prepared from *trans*-4-*tert*-butylcyclohexanol[43] according to the usual procedure).[42] The desired product was purified by flash chromatography (ethyl acetate/hexane (90:10)) and recrystallization from methylene chloride–hexane to furnish 260 mg (15.8% yield) of pure **6**: mp 124–125 °C; ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.83 (s, 9 H), 1.0–3.15 (m, 10 H), 7.3–8.1 (m, 10 H); ^{13}C NMR in Table I; ^{31}P NMR (36.23 MHz, $CDCl_3$) δ 20.06; ^{11}B NMR (28.69 MHz, $CDCl_3$) δ −38.87. Anal. Calcd for $C_{22}H_{32}BP$: C, 78.11; H, 9.53. Found: C, 77.78; H, 9.47.

(*trans*-4-*tert*-Butylcyclohexyl)diphenylphosphine–borane (7) was similarly prepared from *cis*-4-*tert*-butylcyclohexyl methanesulfonate (0.65 g, 2.7 mmol; prepared from *cis*-4-*tert*-butylcyclohexanol[44] according to the usual procedure).[42] The crude product was purified by flash chromatography (hexane) and recrystallization from hexane–chloroform to afford 288 mg (17.5% yield) of pure **7**: mp 143–144 °C; ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.84 (s, 9 H), 0.9–3.0 (m, 10 H), 7.5 (m, 6 H), 7.8 (m, 4 H); ^{13}C NMR in Table I; ^{31}P NMR (36.23 MHz, $CDCl_3$), δ 21.11; ^{11}B NMR (28.69 MHz, $CDCl_3$) δ −41.72. Anal. Calcd for $C_{22}H_{32}BP$: C, 78.11; H, 9.53. Found: C, 77.92; H, 9.75.

(*cis*-4,*cis*-6-Dimethyl-1,3-dithian-2-yl)- and (*trans*-4,*trans*-6-Dimethyl-1,3-dithian-2-yl)-*rel*-2-(diphenylphosphine–Borane) (11 and 12). *cis*-4,6-Dimethyl-1,3-dithiane[21] (0.8 g, 5.4 mmol) was placed in a dry round-bottom flask provided with a magnetic stirring bar and capped with a rubber septum. The flask was flushed with nitrogen prior to the addition of 50 mL of dry THF via a cannula, after which the solution was cooled to −20 °C and *n*-butyllithium (2.6 mL of a 2.3 M hexane solution, 6.0 mmol, 10% excess) was syringed into it dropwise. The resulting solution was stirred for 90 min at −20 °C, following which it was added to a THF solution (ca. 40 mL) of chlorodiphenylphoshine (1.2 g, 5.4 mmol) also at −20 °C. The reaction mixture was stirred at this temperature for 90 min and then treated with 8.0 mL of 1 M borane·THF solution. The reaction mixture was then left standing in the refrigerator for 24 h, and concentrated at reduced pressure. The desired products were purified by flash chromatography (hexane) and then recrystallized from hexane–acetone to afford 161 mg (8.6% yield) of **11** and 506 mg (27.1% yield) of **12**.

11: mp 167–169 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.26 (d, *J* = 7 Hz, 6 H), 1.35 (m, 1 H), 2.1 (dm, *J* = 11 Hz, 1 H), 2.9 (m, 2 H), 4.9 (d, *J* = 12 Hz, 1 H), 7.5 (m, 6 H), 7.95 (m, 4 H); ^{13}C NMR in Table II; ^{31}P NMR (36.23 MHz, $CDCl_3$) δ 27.59; ^{11}B NMR (28.69 MHz, $CDCl_3$) δ −38.46. Anal. Calcd for $C_{18}H_{24}BPS_2$: C, 62.43; H, 6.98. Found: C, 62.96; H, 7.02.

14: mp 193–195 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.16 (d, *J* ≈ 6 Hz, 6 H), ca. 1.2 (m, 1 H), 2.1 (dm, *J* = 11 Hz, 1 H), 3.7 (m, 2 H), 4.56 (d, *J* = 14.4, 1 H), 7.58 (m, 6 H), 7.9 (m, 4 H); ^{31}P NMR (36.23 MHz, $CDCl_3$) δ 27.79; ^{11}B NMR (28.69 MHz, $CDCl_3$) δ −38.19. Anal. Calcd for $C_{18}H_{24}BPS_2$: C, 62.43; H, 6.98. Found: C, 62.03; H, 6.82.

Reaction of Phosphine–Boranes with Triethylamine. A solution of the phosphine–borane (50–100 mg) in 1–2 mL of triethylamine was kept under nitrogen at 50 °C for 48 h. Excess triethylamine was removed in vacuo, and the residual, air-sensitive phosphine was redissolved in deuterated solvent and transferred via a cannula to the NMR tube for analysis.

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(42) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, pp 1179–1181.

(43) Obtained by Birch reduction of the corresponding ketone: Huffman, J. W.; Charles, J. T. *J. Am. Chem. Soc.* **1968**, *90*, 6486–6492.

(44) Obtained by reduction of 4-*tert*-butylcyclohexanone with hydrogen over platinum oxide[45] or with Li(*s*-Bu)$_3$BH.[46]

(45) Eliel, E. L.; Ro, R. S. *J. Am. Chem. Soc.* **1957**, *79*, 5992–5994.

(46) Krishnamurthy, S.; Brown, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 3383–3384.

Selective Oxidation of Alcohols and Aldehydes with Hydrogen Peroxide Catalyzed by Methyltrioctylammonium Tetrakis(oxodiperoxotungsto)phosphate(3−) under Two-Phase Conditions

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The use of methyltrioctylammonium tetrakis(oxodiperoxotungsto)phosphate(3−) (**1c**) in combination with hydrogen peroxide as the primary oxidant in an aqueous/organic biphase system provides a cheap, efficient, and versatile catalytic method for alcohol and aldehyde oxidation. By this method, a variety of water-insoluble primary and secondary alcohols and aldehydes were oxidized to carboxylic acids and ketones in good yields under mild conditions and after relatively short reaction times.

The oxidation of organic substrates by aqueous hydrogen peroxide is very attractive from a synthetic and industrial viewpoint since this reagent is relatively inexpensive, of low equivalent weight, environmentally clean, and easy to handle. The help of a metal catalyst is often required, and in recent years a considerable effort has been devoted to the search for new efficient metal derivatives suited to this purpose.[1]

In this context, our earlier studies on selective oxidative processes with hydrogen peroxide catalyzed by the tungstate–phosphate (arsenate) ion association[2,3] led us to discover a new family of tungsten peroxo complexes with unusual oxidizing properties, namely, quaternary ammonium (phosphonium) tetrakis(oxodiperoxotungsto)phosphates or -arsenates(3–) 1.[4] Structural characterization by X-ray diffraction analysis was made in the case of **1a**, which revealed for the $[PW_4O_{24}]^{3-}$ anion a structure consisting of four distorted $W(O_2)_2O_3$ pentagonal bipyramids, in edge-shared pairs, joined to a tetrahedral central PO_4 group.[5a] From crystallographic data the analogous complex with arsenic in place of phosphorus as the heteroatom, **1b**, turned out to be isostructural with **1a**.[5b]

$$Q^+_3\{XO_4[W(O)(O_2)_2]_4\}^{3-}$$

1

Q^+ = "onium group"; X = P, As

a: $Q^+ = [(n\text{-}C_6H_{13})_4N]^+$; X = P

b: $Q^+ = [(n\text{-}C_6H_{13})_4N]^+$; X = As

c: $Q^+ = [(n\text{-}C_8H_{17})_3NCH_3]^+$; X = P

d: $Q^+ = \{[n\text{-}C_{18}H_{37}(76\%) + n\text{-}C_{16}H_{33}(24\%)]_2N(CH_3)_2\}^+$; X = P

Notably, besides being good stoichiometric oxidants for a variety of organic substrates in nonprotic solvents, complexes 1 were found to act as highly effective and versatile oxidation catalysts as well, when used in conjunction with hydrogen peroxide as the primary oxidant in an aqueous/organic biphasic system.

Accordingly, various synthetic applications were patented. Thus, complexes 1, especially **1c** and **1d**, were shown to catalyze the epoxidation of simple unactivated alkenes, including the terminal ones, by dilute (15%) hydrogen peroxide.[4-6] Under particular acidic conditions and with the use of very dilute (2–4%) hydrogen peroxide, they also made it possible to achieve the direct and selective synthesis of water-soluble *vic*-diols from water-insoluble olefins via epoxidation–hydrolysis.[7,8] Furthermore, under the catalytic influence of 1, it was possible to accomplish the oxidative cleavage of *vic*-diols and alkenes to carboxylic acids[9] and the ketonization of alcohols[10] by aqueous hydrogen peroxide.

Selective oxidation of hydroxyl functions plays an important role in organic synthesis, and from the environmental and economical points of view there is a growing interest in devising valuable catalytic alternatives to more conventional reagents.[11] Before[12,13] and after[14,15] our patent[10] on secondary alcohol oxidation, several reports appeared in the literature on the tungsten- and molybdenum-catalyzed oxidation of these substrates by hydrogen peroxide. These procedures, however, are of limited preparative value. Indeed, they require very long reaction times (from 1[15] to a few days[13]) and/or high catalyst/substrate ratios (1:10–1:50),[13-15] rather large excesses of oxidant,[13-15] and sometimes high hydrogen peroxide concentrations (up to 90%).[12] By contrast, the application of catalyst complexes 1 in conjunction with hydrogen peroxide avoids all these inconveniences while allowing a facile oxidation.

We were thus prompted to explore in more detail the potential of our approach to alcohol oxidation with hydrogen peroxide. On the one hand, this study allowed us to broaden the scope of the procedure for alcohol ketonization; on the other hand, it led us to find that also primary alcohols could be satisfactorily oxidized to carboxylic acids by the same catalyst–oxidant system. It should be pointed out that primary alcohols, with the exception of the benzylic ones,[14] are poorly oxidized with hydrogen peroxide by the aforementioned alternative procedures and aldehydes[14,15] or esters[13] are obtained predominantly or exclusively in all cases.[16]

As a result of our investigation, we could develop an efficient, versatile, and cheap catalytic methodology for oxidation of both primary and secondary hydroxy groups. In the present paper, we report full details of ketonization of secondary alcohols and a complete account of the newly studied oxidation of primary alcohols to carboxylic acids with aqueous hydrogen peroxide catalyzed by the very active complex **1c**. Further, the use of catalyst complex **1c** in combination with hydrogen peroxide has been extended to the oxidation of aldehydes, frequently a troublesome problem.

Results and Discussion

Oxidation of Secondary Alcohols. The ketonization of alcohols is accomplished by vigorously stirring at 90 °C a biphase mixture containing the appropriate alcohol, 40% w/v aqueous hydrogen peroxide (usually in a 50% molar excess over the substrate), the catalyst **1c**, and a solvent immiscible with the water phase, when needed, until the charged substrate has almost completely disappeared. A substrate/catalyst molar ratio of 200:1 is used. Table I lists the results of the oxidation of a variety of secondary alcohols by this procedure.

As illustrated by entries 1–10 of Table I, saturated aliphatic (open-chain and cyclic), aromatic, terpenoid as well as steroidal alcohols are oxidized to the corresponding ketones in good to excellent yields after rather short reaction times.

Some features of the present method merit attention. The reaction appears to be relatively insensitive to geo-

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(1) (a) Pralus, M.; Lecoq, J. C.; Schirmann, J. P. In *Fundamental Research in Homogeneous Catalysis*; Tsutsui, M., Ed.; Plenum: New York, 1979; Vol. 3, pp 327–343. (b) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidation of Organic Compounds*; Academic: New York, 1981. (c) Mimoun, H. In *The Chemistry of Functional Groups, Peroxides*; Patai, S., Ed.; Wiley: New York, 1982; pp 463–482.

(2) (a) Venturello, C.; Alneri, E.; Lana, G. Ger. Offen. 3027349, 1981 (It. Appl. 24478A/79); *Chem. Abstr.* **1981**, *95*, 42876. (b) Venturello, C.; Alneri, E.; Ricci, M. *J. Org. Chem.* **1983**, *48*, 3831.

(3) (a) Venturello, C.; Ricci, M. Eur. Pat. Appl. 123495, 1984 (It. Appl. 20605A/83); *Chem. Abstr.* **1985**, *102*, 78375. (b) Venturello, C.; Ricci, M. *J. Org. Chem.* **1986**, *51*, 1599.

(4) Venturello, C.; D'Aloisio, R.; Ricci, M. Eur. Pat. Appl. 109273, 1984 (It. Appl. 24154A/82); *Chem. Abstr.* **1984**, *101*, 191668.

(5) (a) Venturello, C.; D'Aloisio, R.; Bart, J. C. J.; Ricci, M. *J. Mol. Catal.* **1985**, *32*, 107. (b) Bart, J. C. J.; Venturello, C. Unpublished results.

(6) Venturello, C.; D'Aloisio, R. *J. Org. Chem.* **1988**, *53*, 1553.

(7) Venturello, C.; Gambaro, M. Eur. Pat. Appl. 146374, 1985 (It. Appl. 24203A/83); *Chem. Abstr.* **1985**, *103*, 195855.

(8) Venturello, C.; Gambaro, M. *Synthesis* **1989**, 295.

(9) Venturello, C.; Ricci, M. *Eur. Pat. Appl.* 122804, 1984 (It. Appl. 20604A/83); *Chem. Abstr.* **1985**, *102*, 95256.

(10) Venturello, C.; Gambaro, M.; Ricci, M. Eur. Pat. Appl. 232742, 1987 (It. Appl. 19098A/86); *Chem. Abstr.* **1988**, *108*, 131028.

(11) See ref 1b, pp 94, 177, 182, 350–357.

(12) Jacobson, S. E.; Muccigrosso, D. A.; Mares, F. *J. Org. Chem.* **1979**, *44*, 921.

(13) (a) Trost, B. M.; Masuyama, Y. *Tetrahedron Lett.* **1984**, *25*, 173. (b) Trost, B. M.; Masuyama, Y. *Isr. J. Chem.* **1984**, *24*, 134.

(14) Bortolini, O.; Conte, V.; Di Furia, F.; Modena, G. *J. Org. Chem.* **1986**, *51*, 2661.

(15) (a) Yamawaki, K.; Nishihara, H.; Yoshida, T.; Ura, T.; Yamada, H.; Ishii, Y.; Ogawa, M. *Synth. Comm.* **1988**, *18*, 869. (b) Ishii, Y.; Yamawaki, K.; Ura, T.; Yamada, H.; Yoshida, T.; Ogawa, M. *J. Org. Chem.* **1988**, *53*, 3587.

(16) Recently, it has been reported that the H_2O_2–$RuCl_3$ system, besides oxidizing secondary alcohols to ketones, oxidizes primary alcohols to carboxylic acids. Also this method, however, requires a large excess of H_2O_2, as a result of the simultaneous decomposition of the latter in the presence of the metal catalyst: Barak, G.; Dakka, J.; Sasson, Y. *J. Org. Chem.* **1988**, *53*, 3553.

Table I. Oxidation of Alcohols to Carbonyl Derivatives with H_2O_2 Catalyzed by Tetrakis(oxodiperoxotungsto)phosphate 1c[a]

entry	substrate	time (min)	product(s)	% yield[b]
1	2-octanol (**2**)	90	2-octanone (**3**)	96[c,d]
2	1-phenylethanol (**4**)	10	acetophenone (**5**)	91
3	5α-cholestan-3β-ol[e] (**6**)	45	5α-cholestan-3-one (**7**)	88
4	benzhydrol (**8**)	60	benzophenone (**9**)	99
5	(−)-borneol[e] (**10**)	45	(−)-camphor (**11**)	95
6	(±)-isoborneol[e] (**12**)	45	(±)-camphor (**11**)	95
7	cyclohexanol[f] (**13**)	45	cyclohexanone (**14**)	86[c,g]
8	2,6-dimethylcyclohexanol[f,h] (**15**)	30	2,6-dimethylcyclohexanone[h] (**16**)	97[c]
9	cyclopentanol[f] (**17**)	75	cyclopentanone (**18**)	81[c,g]
10	(−)-menthol (**19**)	120	(−)-menthone[i] (**20**)	88
11	1-octen-3-ol[f,j] (**21**)	120	1,2-epoxy-3-octanol[k] (**22**)	64
			1-octen-3-one (**23**)	18[l] (20)[c]
			1,2-epoxy-3-octanone (**24**)	6
12	**21**[j,m]	270	**22**[k]	24
			23	54[l] (62)[c]
			24	4
13	**21**[f,j,n]	120	**22**[k]	19
			23	60[l] (70)[c]
			24	4
14	2-ethyl-1,3-hexanediol[h] (**25**)	60	2-ethyl-1-hydroxy-3-hexanone (**26**)	71[o]
15	benzyl alcohol[f,p] (**27**)	45	benzaldehyde (**28**)	77[c,q]
16	4-methylbenzyl alcohol[f,p] (**29**)	30	4-methylbenzaldehyde (**30**)	84[c,d,r]

[a] Unless otherwise stated, all reactions were performed without solvent at 90 °C (bath) using 25 mmol of substrate, 37.5 mmol of 40% w/v aqueous H_2O_2, and 0.125 mmol of **1c** and nearly complete conversions were obtained. [b] Unless otherwise stated, the yield (based on substrate charged) refers to the product isolated by column chromatography. Elution conditions ((entry), eluant, R_f): (3), CH_2Cl_2, 0.55; (4, 14), Et_2O/hexane (1:1), 0.74, 0.32; (2, 5, 6), Et_2O/pentane (1:4), 0.67, 0.72, 0.72; (10), id. (1:1), 0.85 (determined in Et_2O/hexane (1:2)); (11–13), id. (1:4; to eluate **23** and **24** (further purified on finer silica (230 mesh) to have an analytically pure sample)), then Et_2O (to eluate **22**), 0.80, 0.56, 0.24 (determined in Et_2O/hexane (1:2)). Product purity (checked by GLC) was ≥96% in all cases. [c] GLC value using an internal standard. [d] Conversion was 97%. [e] Tetrachloroethylene (1 mL (entries 5,6) and 10 mL (entry 3)) was added to the reaction mixture. [f] 27.5 mmol (entries 11, 13) and 30 mmol (entries 7–9, 15, 16) of H_2O_2 instead of 37.5 mmol was used. [g] Conversion was 96% in entry 7 and 92% in entry 9. The presence of Baeyer–Villiger reaction products, namely 6-hydroxyhexanoic acid (entry 7), 5-hydroxypentanoic acid (entry 9), and compounds arising from their further oxidation, was observed in the reaction mixture. [h] Mixture of isomers. [i] Prior to isolation of the product, the organic phase was stirred with a little solid Na_2SO_3 and a few drops of water until complete destruction of the peroxides present in the solution. [j] Reaction carried out at 70 °C; 1,2-dichloroethane (10 mL) as the solvent. [k] Threo/erythro (55:45 (entry 11) and 51:49 (entries 12, 13)) diastereomeric mixture. [l] Due to its high volatility, 1-octen-3-one was lost in part during workup. [m] 16% w/v H_2O_2 instead of 40% w/v (27.5 mmol) and 0.0434 mmol of **1c** instead of 0.125 mmol were used. [n] Benzyltriphenylphosphonium μ-oxobis(oxodiperoxotungstate)[21] (0.125 mmol) in place of **1c** was used as the catalyst. [o] Butyric acid (24% in mols of the substrate charged) was formed along with small amounts of 4-heptanone and propionic acid. These byproducts arise from overoxidation reactions of **26**, as ascertained in a control experiment. Under the reaction conditions, butyric acid was not formed from 4-heptanone. [p] Reaction carried out under a nitrogen atmosphere. [q] Benzoic acid (14%) was formed. [r] 4-Methylbenzoic acid (7%) was formed.

metric constraints. Indeed, the terpene alcohols borneol (**10**) and isoborneol (**12**) were both oxidized to camphor (**11**) at similar rates (entries 5, 6). By contrast, steric factors seem to play a role in these oxidations, as shown by the lower reactivity of cyclohexanol (**13**) compared to the sterically hindered 2,6-dimethylcyclohexanol (**15**) (entries 7, 8). In this respect, it was found that, in the oxidation of an equimolar mixture of **13** and **15** using an insufficient amount of hydrogen peroxide, the latter compound was oxidized about 1.4 times faster than the former.[17] It is noteworthy, however, that under the same reaction conditions the oxidation of menthol (**19**) to menthone (**20**) proceeded rather sluggishly compared to the other substrates examined (entry 10). Interestingly, cyclopentanol (**17**) was oxidized more slowly than cyclohexanol (**13**) (compare entries 7 and 9).[18a] Finally, oxidations of alcohols containing adjacent chiral centers (entries 5, 10) gave products without any detectable racemization.

The oxidation of 1-octen-3-ol (**21**) deserves some comment. As can be seen from Table I (entry 11), olefin epoxidation predominates over alcohol ketonization. Indeed, a diastereomeric mixture (55:45) of *threo*- and *erythro*-1,2-epoxy-3-octanol (**22**) was obtained as the major product (64%) together with 1-octen-3-one (**23**, 20%) and minor amounts of 1,2-epoxy-3-octanone (**24**). The trend of the reaction, however, may be reversed by simply curtailing the amount of catalyst and using more dilute hydrogen peroxide. Thus, when oxidation of **21** was performed with 16% instead of 40% w/v hydrogen peroxide and about one-third the standard amount of catalyst, the enone **23** was formed in preference to the epoxy alcohol **22** (molar ratio **23**:**22** = 2.6:1) (entry 12). The inverted chemoselectivity should be ascribed to the higher concentration of peroxotungstate moieties in the reaction medium, as a result of the more extensive hydrolysis[6] of the peroxo heteropoly anion of the catalyst complex under the particular experimental conditions adopted. In fact, unlike **1**,[19] negatively charged tungsten (molybdenum) peroxo complexes, while reactive toward alcohols,[12–14] are known to be poor oxidants of weakly nucleophilic substrates such as alkenes.[20,21] Accordingly, replacement of **1c** with benzyltriphenylphosphonium μ-oxobis(oxodiperoxo-

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(17) A similar result has been obtained in a competitive oxidation of **13** and **15** with H_2O_2 catalyzed by ammonium molybdate under basic conditions.[13b]

(18) (a) Such a behavior has been reported for **17** in an oxidation with tetrabutylammonium oxodiperoxo(picolinate *N*-oxide)molybdate(VI) as a reagent.[18b] (b) Bortolini, O.; Campestrini, F.; Di Furia, F.; Modena, G. Valle, G. *J. Org. Chem.* **1987**, *52*, 5467.

(19) The high reactivity toward nucleophilic olefins exhibited by complexes **1**,[4–6] in spite of their anionic nature, may be ascribed to an enhancement of the electrophilic character of the peroxo moieties, as a result of the presence of triply shared peroxo oxygens[5] and of the PO_4 (AsO_4) group linked to the metal in place of the basic ligand, by which metal peroxo complexes are usually stabilized.[1b,c]

(20) (a) Di Furia, F.; Modena, G. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 181. (b) Bortolini, O.; Di Furia, F.; Scrimin, P.; Modena, G. *J. Mol. Catal.* **1980**, *7*, 59. (c) Arcoria, A.; Ballistreri, F. P.; Tomaselli, G. A.; Di Furia, F.; Modena, G. *Ibid.* **1983**, *18*, 177. (d) Di Furia, F.; Fornasier, R. *Ibid.* **1983**, *19*, 81.

(21) Prandi, J.; Kagan, H. B.; Mimoun, H. *Tetrahedron Lett.* **1986**, *27*, 2617.

Table II. Oxidation of Primary Alcohols to Carboxylic Acids with H_2O_2 Catalyzed by Tetrakis(oxodiperoxotungsto)phosphate 1c[a]

entry	substrate	time (h)	product(s)	% yield[b,c]
1	benzyl alcohol (**27**)	3	benzoic acid (**31**)	85[d]
2	4-methylbenzyl alcohol[e,f] (**29**)	4	4-methylbenzoic acid[g] (**32**)	59[h,i]
3	4-chlorobenzyl alcohol[f] (**33**)	3	4-chlorobenzoic acid (**34**)	85[h]
4	4-nitrobenzyl alcohol[f] (**35**)	3	4-nitrobenzoic acid (**36**)	90
5	3-methoxybenzyl alcohol[e] (**37**)	4	3-methoxybenzoic acid[g] (**38**)	55[h,i]
6	4-methoxybenzyl alcohol[e,j] (**39**)	4	4-methoxybenzoic acid[k] (**40**)	<2[h,i,l,m]
7	2-nitrobenzyl alcohol (**41**)	9	2-nitrobenzoic acid (**42**)	91[d]
8	2-chlorobenzyl alcohol[e,f] (**43**)	5	2-chlorobenzoic acid[g] (**44**)	60[h,i]
9	1-hexanol (**45**)	6	hexanoic acid (**46**)	83
10	1-heptanol (**47**)	6	heptanoic acid (**48**)	83
11	1-octanol (**49**)	6	octanoic acid (**50**)	85
12	1-decanol (**51**)	6	decanoic acid (**52**)	83[d]
13	3-methyl-1-pentanol (**53**)	6	3-methylpentanoic acid (**54**)	80
14	4-methyl-1-pentanol (**55**)	6	4-methylpentanoic acid (**56**)	80
15	2-methyl-1-pentanol (**57**)	6	2-methylpentanoic acid (**58**)	70[n]
16	2-cyclohexylethanol (**59**)	6	cyclohexylacetic acid (**60**)	83
17	cyclohexylcarbinol[e] (**61**)	6	cyclohexanecarboxylic acid (**62**)	70[o]
18	2-phenylethanol (**63**)	6	phenylacetic acid[g] (**64**)	51[p]
			benzoic acid (**31**)	17[q]
19	2,2-dimethyl-1-propanol (**65**)	6	2,2-dimethylpropionic acid (**66**)	40[l,r]
20	2-phenyl-1-propanol (**67**)	6	2-phenylpropionic acid[g] (**68**)	23[p,s]
21	3-phenyl-1-propanol (**69**)	6	3-phenylpropionic acid (**70**)	76[d,l,t]

[a] Unless otherwise stated, all reactions were performed without solvent at 90 °C (bath) using 25 mmol of substrate, 75 mmol of 40% w/v aqueous H_2O_2, and 0.125 mmol of **1c** and conversions higher than 96% were obtained. [b] The yield (based on substrate charged) refers to the isolated product. Purity (determined by GLC after methylation with CH_2N_2) was ≥96% in all cases except for **64**, which was obtained admixed with **31** in the molar ratio of 3:1. [c] With aliphatic alcohols, 6–9% of ester (see text) was obtained, while smaller amounts (<3%) were obtained with aromatic alcohols. Less than 3% of aldehyde was found at the end of the reaction if not otherwise indicated. [d] Product slightly contaminated by heavy materials. [e] 100 mmol (entry 17) and 125 mmol (entries 2, 5, 6, 8) of H_2O_2 instead of 75 mmol was used. [f] Tetrachloroethylene (2 mL) was added to the reaction mixture. [g] The crude product was freed from heavy materials by passage, after dissolution in Et_2O (30 mL (entries 5, 8, 18, 20) and 70 mL (entry 2)), through a short column (2.5-cm diameter) of silica gel (30 g), eluting then with more Et_2O (130 mL (entry 20), 160 mL (entries 5, 8, 18), and 300 mL (entry 2)). [h] 13% (entry 2), 7% (entries 3, 5), 28% (entry 6), and 19% (entry 8) of the intermediate aldehyde was found at the end of the reaction. [i] The corresponding phenol (in negligeable amounts (entries 2, 5), 6% (entry 6), and 3% (entry 8)) was detected. Large amounts of CO_2 were formed (see text). [j] Reaction carried out at 70 °C; 1,2-dichloroethane (5 mL) as the solvent. [k] Chromatographic separation of the crude product on a silica gel column (Et_2O/pentane (4:1), then Et_2O) was required to obtain a sufficiently pure product. [l] Conversion was 93%. [m] Highly colored, heavy materials were formed. [n] 2-Pentyl formate (<2%) (mass spectrum *m/e* M^+ absent, 101, 88, 73, 71 70, 55, 45 (100), 43) and 2-pentanol/2-pentanone (11–12%) were formed. [o] Cyclohexyl formate (<1%) (mass spectrum *m/e* M^+ absent, 99, 82, 67 (100), 57, 54, 41) and cyclohexanol/cyclohexanone (3%)[24] were formed. [p] Conversion was 88%. [q] Benzyl alcohol and benzaldehyde were also found in small amounts. [r] 2-Methyl-2-propanol was formed in 20% yield (determined by GLC on both aqueous and organic phase (external standard)). Small amounts of *tert*-butyl hydroperoxide were also formed. The latter originates from reaction of 2-methyl-2-propanol with H_2O_2 under the acidic conditions generated by the catalyst,[6] as ascertained in a control experiment. [s] 1-Phenylethyl formate (4%) (mass spectrum *m/e* 150 (M^+), 122, 121, 105, 104 (100)) and acetophenone (38%) were formed. [t] 2-Phenylethanol and acetophenone were formed in small amounts.

tungstate(VI)),[21] $(Ph_3PCH_2Ph)^+{}_2$ $[(O_2)_2W(O)O(O)W(O_2)_2]^{2-}$, as the catalyst in the oxidation of **21** (entry 13) led to the predominant formation of **23** [molar ratio **23**:**22** = 3.7:1).[22]

Although primary hydroxy groups can conveniently be oxidized by the present method (see next section), the difference in reactivity existing between them and the secondary ones allows chemoselective oxidation of the latter in diols possessing both hydroxy functions. This is illustrated by the oxidation of 2-ethyl-1,3-hexanediol (**25**) to 2-ethyl-1-hydroxy-3-hexanone (**26**) (entry 14). It should be noted, however, that α-hydroxy ketones cannot satisfactorily be obtained from the corresponding primary–secondary *vic*-diols by this procedure. Indeed, the former are oxidatively cleaved to carboxylic acids readily under the reaction conditions, as previously shown by us.[3b]

Oxidation of Primary Alcohols. Under the same conditions as employed for the ketonization of secondary alcohols, primary alcohols also undergo oxidation, though at lower rates and selectivities. In this case, however, the reaction mainly leads to carboxylic acids, which are obtained along with small amounts of esters ($RCOOCH_2R$, presumably deriving from oxidation of hemiacetal intermediates, $RCH(OH)OCH_2R$).[23] In general, the oxidation could not be stopped at the aldehyde stage satisfactorily. Exceptions, among the substrates examined, were benzyl and 4-methylbenzyl alcohols (**27** and **29**) whose aldehydes **28** and **30**, could be obtained in good yields together with only modest amounts of the respective acids (Table I, entries 15, 16). The preferential formation of acids must be attributed to the lower reactivity of primary alcohols coupled with the ease of oxidation of the intermediate aldehydes under the reaction conditions (see Oxidation of Aldehydes). The results of the oxidation of primary alcohols to carboxylic acids with **1c**/H_2O_2 are summarized in Table II.

As shown, a number of saturated aliphatic and alkyl aromatic alcohols are converted (at 90 °C) into the respective acids in fair to good yields (60–90%) in 3–6 h using a 1.5-fold excess of hydrogen peroxide over the stoichiometric amount in most cases.

Inspection of the data reported in Table II reveals that, in general, benzylic alcohols (entries 1–8) are oxidized to the corresponding acids faster than the aliphatic ones. The

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(22) For examples referring to the predominance of alcohol ketonization over double-bond epoxidation in the oxidation of allylic alcohols by anionic molybdenum peroxo species, see refs 13b and 18b.

(23) The oxidation of alcohols to esters is known for various oxidants: (a) Stevens, R. V.; Chapman, K. T.; Weller, H. N. *J. Org. Chem.* **1980**, *45*, 2030. (b) Nwaukwa, S. O.; Keehn, P. *Tetrahedron Lett.* **1982**, *23*, 35. (c) Masuyama, Y.; Takahashi, M.; Kurusu, Y. *Ibid.* **1984**, *25*, 4417. (d) Abramovici, S.; Neumann, R.; Sasson, Y. *J. Mol. Catal.* **1985**, *29*, 299. The possibility that esters be formed, in part, by esterification of the acids under the acidic reaction conditions generated by the catalyst[6] cannot be excluded, however.

data also show that the presence of electron-withdrawing groups in the aromatic ring has little influence on the course of the reaction, while electron-releasing groups exert a negative effect. Thus, whereas under the standard reaction conditions linear aliphatic alcohols C_6–C_8 and C_{10} gave 83–85% yields of the corresponding alkanoic acids in 6 h (entries 9–12), under the same conditions benzyl alcohol and 4-chloro- and 4-nitrobenzyl alcohols gave comparable yields of the respective benzoic acids in only 3 h (entries 1, 3, 4). By contrast, acid yields of only 59 and 55% were obtained (in 4 h) by oxidation of 4-methyl- and 3-methoxybenzyl alcohols, respectively (entries 2, 5). In both cases, a greater excess of H_2O_2 (2.5 times instead of 1.5 times the stoichiometric amount) had to be used, and carbon dioxide was formed in large amounts (40–60% in mols of the substrate charged). Carbon dioxide evolution was even more pronounced (70% in mols of the substrate charged) in the oxidation (at 70 °C) of 4-methoxybenzyl alcohol, which only gave negligible amounts (<2%) of 4-methoxybenzoic acid (entry 6). 4-Methoxybenzaldehyde (28%) and 4-methoxyphenol (6%) were found in the reaction mixture along with unreacted alcohol (7%) and highly colored, heavy materials.

Steric effects also seem to affect the oxidation of benzylic alcohols. Thus, 2-nitrobenzyl alcohol (**41**) was oxidized much more slowly than 4-nitrobenzyl alcohol (**35**), and it required 9 h to give 91% yield of 2-nitrobenzoic acid (**42**). Likewise, 2-chlorobenzyl alcohol (**43**) exhibited a lower reactivity than 4-chlorobenzyl alcohol (**33**), affording 2-chlorobenzoic acid (**44**) in 60% yield after 5 h. With respect to **41**, however, the oxidation of **43** required a large excess of H_2O_2 (2.5 times the stoichiometric amount) and was less selective. Carbon dioxide (40% in mols of the substrate charged) was produced. 2-Chlorophenol (3%) was found in the reaction mixture together with the intermediate 2-chlorobenzaldehyde (19%).

As with benzylic alcohols, also the oxidation of aliphatic alcohols shows a large substrate effect. As illustrated by entries 9–21 of Table II, straight- or not-β-branched-chain primary aliphatic alcohols give the best conversions to the respective acids, while the oxidation selectivity is lowered, more or less remarkably, by the presence of benzyl, cyclohexyl, α-branched or α-aryl-substituted alkyl groups linked to the hydroxymethyl group. Thus, 3- and 4-methyl-1-pentanol (**53** and **55**) could be converted into the respective methylpentanoic acids **54** and **56** in 80% yields, but only a 70% yield of 2-methylpentanoic acid (**58**) was obtained, under the same conditions, by oxidation of the isomeric 2-methyl-1-pentanol (**57**). In this case, 2-pentanol and 2-pentanone were formed (11–12%) as byproducts. Similarly, while oxidation of 2-cyclohexylethanol (**59**) gave cyclohexylacetic acid (**60**) in 83% yield, oxidation of cyclohexylcarbinol (**61**) was less satisfactory, affording cyclohexanecarboxylic acid (**62**; 70% yield) along with cyclohexanol and cyclohexanone.[24] In this context, oxidations of 2-phenylethanol (**63**), 2,2-dimethyl-1-propanol (**65**), and 2-phenyl-1-propanol (**67**) are particularly indicative. The expected acids, phenylacetic acid (**64**), 2,2-dimethylpropionic acid (**66**), and 2-phenylpropionic acid (**68**), respectively, were obtained in 51, 40, and 23% yields only. Substantial quantities of, respectively, benzoic acid (17%), 2-methyl-2-propanol (20%), and acetophenone (38%) were concurrently formed. At variance with **63** and **67**, 3-phenyl-1-propanol (**69**) bearing the phenyl group remote from the hydroxy function was oxidized to 3-phenylpropionic acid (**70**) in good yield.

It should be noted that, in all the cases mentioned above where a less or scarcely satisfactory oxidation occurred, carbon dioxide evolution was observed. Its amount (in mols), with time,[25] approached that of the byproduct(s) formed.

The lower oxidation selectivities found with certain benzylic and aliphatic alcohols as reported above are likely to be due to the intervention of the same oxidative mechanism.

The byproducts of one less carbon formed in the oxidation of cyclohexyl- and benzylcarbinols **61** and **63** and of β-branched aliphatic alcohols **57**, **65**, and **67** must arise from a Baeyer–Villiger-type rearrangement occurring at the stage of aldehyde oxidation (with carbon as the migrating group instead of hydrogen) that leads to the next lower alcohol and formic acid through the intermediate formate.[26,27] Further oxidation of the alcohol gives rise to the related ketone or aldehyde/carboxylic acid, according to the substrate. Likewise, by oxidation of formic acid carbon dioxide is produced. The presence of the formate could be detected in the reaction mixtures resulting from the oxidation of **57**, **61**, and **67**. Moreover, when in a separate experiment a formate (e.g., *tert*-butyl formate) was subjected, in the presence of hydrogen peroxide, to the hydrolytic action of the acidic medium generated by the catalyst[6] under the reaction conditions, carbon dioxide evolution was observed.

A Baeyer–Villiger rearrangement in the oxidation of the intermediate benzaldehydes, leading to the corresponding phenols via aryl formates,[27,28] should likewise account for the moderate to poor yields of acids obtained with benzylic alcohols **29**, **37**, **39**, and **43**. The expected phenols, however, could only be detected in negligible (with **29** and **37**) or small quantities (see also earlier in this section). Overoxidation of the formed phenols must occur under the reaction conditions and is likely to lead to heavy materials (found in some cases) that may then undergo further extensive oxidative degradation. In fact, control experiments carried out on 4-methyl-, 3- and 4-methoxy-, and 2-chlorophenol showed that these phenols are largely demolished under these conditions, with the concomitant, substantial production of carbon dioxide. It should be noted that, in the absence of the metal catalyst, no evolution of carbon dioxide was observed and the phenol could be recovered essentially unchanged.

As will be shown in next section, the oxidation of the related aldehydes paralleled the above results.

Oxidation of Aldehydes. Since carboxylic acids are obtained easily from primary alcohols by the **1c**/H_2O_2 oxidizing system, we wondered whether the catalyst complex might play a role also in the oxidation of the intermediate aldehydes. Hydrogen peroxide itself is indeed known to oxidize aldehydes to acids in a variety of media.[27,28]

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[24] Only 3% of cyclohexanol/cyclohexanone was found at the end of the reaction. It is likely that most of the cyclohexanone formed is lost under the reaction conditions, due to its known tendency to form peroxides and Baeyer–Villiger oxidation products with hydrogen peroxide[27,37] (see also footnote *g* of Table I). This seems to be supported by the fact that in the oxidation of cyclohexanecarboxaldehyde (Table III, entry 8), where only a slight excess of H_2O_2 was used and the reaction time was much shorter, a larger amount of cyclohexanone and related byproducts was found.

[25] Due to the lower oxidation rate of formic acid relative to the other organic components of the reaction mixture, a longer time and/or use of a larger excess of H_2O_2 with respect to the standard reaction conditions were required to convert most of the formic acid formed to carbon dioxide.

[26] Spath, E.; Pailer, M.; Schmid, M. *Chem. Ber.* **1941**, *74*, 1552.

[27] Hassal, C. H. *Organic Reactions*; Wiley: New York, 1957; Vol. 9, pp 73–106 and references cited therein.

[28] Matsumoto, M.; Kobayashi, H.; Hotta, Y. *J. Org. Chem.* **1984**, *49*, 4740.

Table III. Oxidation of Aldehydes to Carboxylic Acids with H_2O_2 Catalyzed by Tetrakis(oxodiperoxotungsto)phosphate 1c[a]

entry	substrate	time (h)	product(s)	% yield[b]
1	benzaldehyde (**28**)	2	benzoic acid (**31**)	84[c]
2	4-methylbenzaldehyde[d] (**30**)	1.5	4-methylbenzoic acid[e] (**32**)	57[f]
3	pentanal (**71**)	2	pentanoic acid (**72**)	82
4	heptanal (**73**)	1	heptanoic acid (**48**)	85
5	octanal (**74**)	1	octanoic acid (**50**)	87
6	3-phenylbutanal (**75**)	1	3-phenylbutanoic acid[g] (**76**)	77[h]
7	2-methylpentanal (**77**)	0.5	2-methylpentanoic acid (**58**)	70[i]
8	cyclohexanecarboxaldehyde (**78**)	0.5	cyclohexanecarboxylic acid (**62**)	74[j]
9	phenylacetaldehyde[k] (**79**)	2	phenylacetic acid[e] (**64**)	56
			benzoic acid (**31**)	19[l]
10	2-phenylpropionaldehyde[k] (**80**)	1	2-phenylpropionic acid[e] (**68**)	22[m]
11	4-chlorobenzaldehyde[n] (**81**)	2	4-chlorobenzoic acid (**34**)	86
12	2-nitrobenzaldehyde (**82**)	4	2-nitrobenzoic acid (**42**)	94[c]
13	4-nitrobenzaldehyde[n,o] (**83**)	2	4-nitrobenzoic acid (**36**)	89
14	3-methoxybenzaldehyde[d] (**84**)	2	3-methoxybenzoic acid[e] (**38**)	69[f]
15	2-methylbenzaldehyde[d] (**85**)	1.5	2-methylbenzoic acid[p] (**86**)	23[f]
16	4-methoxybenzaldehyde[d,q] (**87**)	2	4-methoxybenzoic acid[p] (**40**)	6[f,r]
17	2,4-dimethoxybenzaldehyde[d,q] (**88**)	2	2,4-dimethoxybenzoic acid (**89**)	0[f]
18	2-chlorobenzaldehyde[d] (**90**)	3	2-chlorobenzoic acid[e] (**44**)	59[f]

[a] Unless otherwise stated, all reactions were performed without solvent at 90 °C (bath) under a nitrogen atmosphere using 25 mmol of aldehyde, 30 or 45 mmol of 40% w/v aqueous H_2O_2 (for aliphatic and aromatic aldehydes, respectively), and 0.125 mmol of **1c**; conversions ranged between 87 and 97% with aromatic aldehydes and were higher than 97% with aliphatic aldehydes. [b] See footnote *b* of Table II. [c] Product slightly contaminated by heavy materials. [d] 75 mmol (entry 14) and 100 mmol (entries 2, 15–18) of H_2O_2 instead of 45 mmol was used. [e] The crude product was purified as indicated in footnote *g* of Table II. [f] The corresponding phenol (in negligible amounts (entries 2,14), 9–10% (entries 15, 17), 13% (entry 16), and 4% (entry 18) was detected. Tars (entries 15–17) and conspicuous amounts of CO_2 were formed (see text). In entries 16 and 17, the parent aryl formate (6 and 29%, respectively) was also found. Mass spectra: 4-methoxyphenyl formate, *m/e* 152 (M^+), 124, 109 (100), 81; 2,4-dimethoxyphenyl formate, *m/e* 182 (M^+), 154, 139 (100), 111. [g] The crude product was purified as indicated for **38** in footnote *g* of Table II. The purified product slowly crystallized by scratching. [h] 2-Phenylpropyl formate (mass spectrum *m/e* 164 (M^+), 118, 105 (100), 91), 2-phenyl-1-propanol, 2-phenyl-2-propanol, acetophenone, and isopropylbenzene were formed in small amounts. [i] 2-Pentyl formate (7%) and 2-pentanol/2-pentanone (7%) were formed. [j] Cyclohexyl formate (6%) and cyclohexanol/cyclohexanone (5–6%) were formed. [k] 45 mmol of H_2O_2 instead of 30 mmol was used. [l] Benzyl formate (<1%) (mass spectrum *m/e* 136 (M^+), 108, 107, 91 (100), 90), benzyl alcohol (3%), and benzaldehyde (5–6%) were formed. 1,2-Diphenylethane was also found in the reaction mixture (mass spectrum *m/e* 182 (M^+), 91 (100), 65). [m] 1-Phenylethyl formate (12%) and acetophenone (33%) were formed. 2,3-Diphenylbutane (1:1 diastereomeric mixture, 5%) was also found in the reaction mixture (mass spectrum *m/e* 210 (M^+), 178, 105 (100), 104). [n] Tetrachloroethylene (2 mL (entry 11) and 5 mL (entry 13)) was added to the reaction mixture. [o] The addition of 2.5 mL of water to the standard reaction mixture was found to be necessary to obtain the best results. [p] The crude product was chromatographed on SiO_2 using Et_2O/hexane (1:1; entry 15) and Et_2O/pentane (9:1) then Et_2O (entry 16) as the eluant. [q] 1,2-Dichloroethane (5 mL) as the solvent. Reaction carried out at 70 °C in entry 16 and at 60 °C in entry 17. [r] Conversion was 61%.

To this end, aldehydes were reacted with hydrogen peroxide both in the presence and in the absence[29] of catalyst **1c** under the standard conditions for alcohol oxidation. Precautions were taken to conduct the reaction under a nitrogen atmosphere in order to ensure that no autoxidation took place.

Interestingly, it was found that, under the experimental conditions adopted, the presence of the metal catalyst considerably enhances the oxidation rate of aldehydes by hydrogen peroxide, so that high conversions in relatively short times are obtained. For instance, in the oxidation of octanal in the presence of **1c**, the yield of octanoic acid jumped to 87% in the same period (1 h) that gave only a 34% yield when hydrogen peroxide was used without catalyst under the same conditions.

On the other hand, attempts were made to accelerate the oxidation of aldehydes by hydrogen peroxide alone under heterogeneous conditions, using lipophilic quaternary ammonium phase-transfer catalysts (e.g., Aliquat 336), which are known to extract hydrogen peroxide from aqueous to organic media readily.[30] No appreciable results were obtained, however.

It thus follows that the use of catalyst **1c** in conjunction with hydrogen peroxide under two-phase conditions offers a simple and efficient way to oxidize a wide range of water-insoluble aldehydes to carboxylic acids. The pertinent results are collected in Table III.

Saturated aliphatic aldehydes (entries 3–10) are in most cases satisfactorily converted into the corresponding acids (70–87% yields) within 0.5–2 h (at 90 °C) with the use of only a slight excess of H_2O_2 (1.2 molar equiv). As might be expected based on the data reported in the previous section, the best results are attained with linear or not-α-branched aldehydes (entries 3–6). With substrates possessing alkyl and/or aryl substituents in the α-position to the formyl moiety or a cyclohexyl (benzyl) group directly linked to it (entries 7–10), alkyl migration competes with hydrogen migration, thereby causing a more or less appreciable decrease in the yield of the desired carboxylic acids. It is worth noting that the presence of the phenyl group β to the aldehyde function also exerts some negative influence on the oxidation selectivity, as shown in the case of 3-phenylbutanal (entry 6).

Interestingly, the oxidation of aromatic aldehydes (entries 1, 2, 11–18) needs larger excesses of H_2O_2 and also longer reaction times (usually 2 h)[31a] than the oxidation of the aliphatic ones, while the corresponding benzylic alcohols are in general oxidized to aldehydes more easily than the aliphatic alcohols. Good yields of the acids (84–94%, at 91–97% conversions; 1.8 molar equiv of H_2O_2 used) are obtained from benzaldehyde and aldehydes bearing an electron-attracting group in the ring (entries 1, 11–13). With benzaldehydes possessing electron-releasing substituents (entries 2, 14–18), however, the situ-

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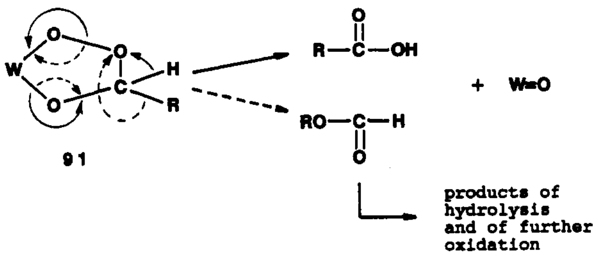
[29] In order to obtain an acidity comparable with that generated by the catalyst itself under the two-phase conditions,[6] the water phase was acidified to pH 2 by sulfuric acid.

[30] Dehmlow, E. V.; Slopianka, M. *Chem. Ber.* **1979**, *112*, 2768.

[31] (a) A slower oxidation of aromatic aldehydes compared to the aliphatic ones has been reported also for the $PhSeO_2H/H_2O_2$ oxidizing system.[31b] (b) Choi, J.-K.; Chang, Y.-K.; Hong, S. Y. *Tetrahedron Lett.* **1988**, *29*, 1967.

Scheme I



ation, as expected, is quite different. The oxidation requires 3–4 molar equiv of H_2O_2 in all cases and is accompanied by a more or less substantial production of carbon dioxide. Nevertheless, it still proceeds fairly well (57–69% of acids, at 92–93% conversion) if the substituent is only mildly activating (e.g., CH_3) and not ortho to the aldehyde (entry 2) or if it is in the meta position (entry 14), but alternative/secondary reactions predominate in the other cases (entries 15–17), leading to the corresponding phenol and to its subsequent, oxidative degradation, as discussed in the previous section.

A borderline behavior close to that of aldehydes with meta-oriented (or also para-oriented, if weakly activating) electron-releasing groups (see entries 2, 14) is exhibited by 2-chlorobenzaldehyde (**90**). Also in this case, formation of the phenol and of carbon dioxide accompanied the oxidation to the acid, which was obtained in only 59% yield at 87% conversion after 3 h (entry 18). An analogous result revealing the occurrence of aryl migration to a significant extent has been reported for the oxidation of **90** by peroxomonosulfate.[32] Likewise, the lower reactivity exhibited by 2-chlorobenzaldehyde (**90**), as well as by 2-nitrobenzaldehyde (**82**), with respect to the para isomer (compare entries 11, 18 and 12, 13) has been observed also with other oxidizing systems.[31b,32]

Despite the aforementioned limitations, the present method for aldehyde to acid conversion is competitive with existing methods[33] and may represent in many cases a valuable alternative to the use of alkaline hydrogen peroxide[27,34] and of hydrogen peroxide activated by selenium compounds.[31b,35]

From the mechanistic point of view, the fact that the aldehyde oxidation with the **1c**/H_2O_2 oxidizing system follows the Baeyer–Villiger pattern, as it does using hydrogen peroxide alone[26–28] or peracids[32,36] as oxidants, suggests that metal peroxo complexes like **1** react with aldehydes similarly to peroxide-containing reagents. The oxidation of aldehydes with **1** can be envisaged to proceed through the formation of a tungsten ozonide **91** by insertion of the carbonyl group of the aldehyde into the tungsten–oxygen bond of the peroxo moiety. Rearrangement of **91** would lead to the observed products (Scheme I). A metal ozonide has been proposed as an intermediate in the Baeyer–Villiger lactonization of cyclic ketones with hydrogen peroxide catalyzed by molybdenum peroxo complexes.[37] Experiments aimed at providing evidence for the postulated intermediate **91** are in progress.

Experimental Section

IR spectra were run on a Perkin-Elmer Model 983 spectrophotometer. ^1H NMR (300-MHz) spectra were recorded on a Bruker AM-300 spectrometer, using $CDCl_3$ as solvent with $CHCl_3$ at 7.25 ppm as reference. ^{13}C NMR spectra were recorded on the Bruker instrument operating at 75.4 MHz, with $CDCl_3$ as solvent and $(CH_3)_4Si$ as an internal standard. Mass spectra were obtained on a Varian MAT 112S, a Finnigan Incos 50 (EI), or a Finnigan MAT 8400 (EI and CI) instrument. GLC analyses were performed on a HRGC 5300 Carlo Erba flame ionization instrument, using a 25 m × 0.32 mm i.d. OV-1 (0.1–0.15-μm film, Carlo Erba Strumentazione) or a 30 m × 0.32 mm i.d. SPB-1 (1.0-μm film, Supelco) bonded-phase, fused silica capillary column with column temperature programming. A 2 m × 2 mm i.d. glass column packed with Porapak Q (190 °C) was used for 2-methyl-2-propanol determination. TLC analyses were performed on Merck precoated silica gel 60F-254 plates, and spots were detected by observation under a 254-nm source, by exposure to iodine fumes, or by spraying with a potassium permanganate or Bromophenol Blue solution, according to the product. Products were identified by combustion analysis and spectral data (when isolated) or by the GLC/MS analysis (after methylation by diazomethane in the case of carboxylic acids) in comparison with authentic samples and the literature values. Carbon dioxide evolved from the reaction mixture was absorbed in a $Ba(OH)_2$ solution and determined gravimetrically as $BaCO_3$. Optical rotations were measured with a Perkin-Elmer Model 141 polarimeter. Melting and boiling points are uncorrected.

Materials. Catalyst complex methyltrioctylammonium tetrakis(oxodiperoxotungsto)phosphate (**1c**) was prepared according to the reported procedure.[6] All alcohols and aldehydes used in this work were commercial products (Fluka or Aldrich) and were purified by distillation or recrystallization before use, as appropriate. Hydrogen peroxide (40% w/v, Fluka) was used as such or after appropriate dilution.

Oxidation of Alcohols to Carbonyl Derivatives. General Procedure. A two-necked round-bottomed flask equipped with a Teflon-coated magnetic bar stirrer, a thermometer, and a reflux condenser was charged with methyltrioctylammonium tetrakis(oxodiperoxotungsto)phosphate (**1c**; 0.125 mmol),[38] the appropriate alcohol (25 mmol), 40% w/v H_2O_2 (25 mmol plus a 10–50% molar excess), and a solvent immiscible with the aqueous phase (1–10 mL) when needed (see Table I). The flask was immersed in a water bath preheated to 90 °C, and the resultant biphase mixture was vigorously stirred at this temperature for the prescribed time (see Table I). At the end, the stirred mixture was cooled, CH_2Cl_2 (10 mL) was added, and then the organic layer was separated from the aqueous layer, which was extracted with CH_2Cl_2 (3 × 5 mL). In entries 2–6 and 10–14 (Table I), to the combined organic layers was added 10–15 g of silica gel (Merck Kieselgel 60, 70–230 mesh). The resulting slurry was further dried[39] by rotary evaporation to yield a powder, which was poured onto the top of a chromatographic column (3-cm diameter) filled with silica gel (120 g). Et_2O/*n*-pentane (-hexane) or CH_2Cl_2 was then passed through the column, collecting the fraction(s) of appropriate R_f (for details, see Table I). Removal of the solvent on a rotavapor afforded the desired product(s). In the other cases (entries 1, 7–9, 15, 16; Table I), the combined organic layers were analyzed by GLC.

Notice. In the initial stage, the reaction is, in general, quite exothermic and control of the temperature by a cold water bath may be necessary. Operating at a larger scale (>0.1 mol), an adequate thermal control is achieved by gradual addition of

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[32] Renganathan, R.; Maruthamuthu, P. *J. Chem. Soc., Perkin Trans. 2* **1986**, 285.

[33] (a) Augustine, R. L. *Oxidation*; Dekker: New York, 1969; Vol. 1, pp 81–86. (b) *Houben-Weyl Methoden der Organischen Chemie, Bd E 3, Aldehyde*; Farbe, J., Ed.; Georg Thieme Verlag: Stuttgart, 1983; pp 634–635. (c) March, J. *Advanced Organic Chemistry*, 3rd. ed.; Wiley: New York, 1985; pp 629–631.

[34] *Peroxygen Compounds in Organic Synthesis*, Interox publication A 0.1.2.

[35] Ishii, Y.; Murai, S.; Sonoda, N. *Technol. Rep. Osaka Univ.* **1976**, *26*, 623.

[36] Royer, J.; Beugelmans-Verrier, M. *C. R. Acad. Sc. Paris, Ser. C* **1971**, *272*(22), 1818.

[37] Jacobsen, S. E.; Tang, R.; Mares, F. *J. Chem. Soc., Chem. Commun.* **1978**, 888.

[38] For the sake of convenience, due to its syrupy nature the catalyst was preferably added as a dichloromethane solution of known titre, then removing the solvent.

[39] Precautions are always to be taken during workup to prevent concentration of peroxidic species: the reaction product should be analyzed for peroxides, and any present destroyed reductively (see Table I, footnote *i*).

hydrogen peroxide to the stirred, warm substrate–catalyst mixture.

(−)-Menthone (20): bp 66 °C (5 mm) [lit.[40] bp 66–67 °C (4 mm)]; $[\alpha]^{20}_{D}$ −27.92° (neat) [lit.[41] $[\alpha]^{20}_{D}$ −28.5° (neat)].

1,2-Epoxy-3-octanol (22) (threo/erythro 55:45 diastereomeric mixture): bp 78–79 °C (4 mm); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.0 (q), 22.6 (t), 25.1 (t), 31.9 (t), 33.7 (t), 34.2 (t), 43.8 (t), 45.1 (t), 54.8 (d), 55.8 (d), 69.0 (d), 72.0 (d); MS *m/e* (relative intensity) (CI, iso-C_4H_{10}) 145 (MH^+, 100), 127 (20), 109 (10) (EI) 101 (3), 83 (38), 70 (36), 55 (100), 43 (63), 41 (58). IR and ^{1}H NMR are consistent with published spectral data of the separate isomers.[42]

1-Octen-3-one (23):[43] bp 84–85 °C (30 mm) [lit.[44] bp 58–61 °C (11 mm)]; IR (neat) 3096, 3022, 1701, 1683, 1615, 987, 962 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 3 H), 1.15–1.42 (m, 4 H), 1.61 (br quintet, J = 7.4 Hz, 2 H), 2.56 (t, J = 7.4 Hz, 2 H), 5.80 (X of ABX, J_{AX} = 10.3 Hz, J_{BX} = 1.5 Hz, 1 H), 6.12–6.42 (AB of ABX, J_{AB} = 17.7 Hz, J_{AX} = 10.3 Hz, J_{BX} = 1.5 Hz, 2 H).

1,2-Epoxy-3-octanone (24): IR (neat) 3064, 1714, 1245, 1234, 934, 871, 845 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, J = 6.9 Hz, 3 H), 1.15–1.40 (m, 4 H), 1.45–1.67 (m, C_5H_2, XX′ of ABXX′, 2 H), 2.34 (m, center of AB of ABXX′, C_4H_2, 2 H), 2.91 (center of AB of ABX, C_1H_2, J_{AB} = 5.8 Hz, J_{AX} = 4.7 Hz, J_{BX} = 2.5 Hz, 2 H), 3.41 (X of ABX, C_2H_1, J_{AX} = 4.7 Hz, J_{BX} = 2.5 Hz, 1 H); MS *m/e* (relative intensity) 142 (M^+, 3), 99 (100), 86 (32), 71 (36), 55 (12), 43 (53).

2-Ethyl-1-hydroxy-3-hexanone (26):[23a] bp 66 °C (1 mm) [lit.[45] bp 75 °C (1.5 mm)]; ^{1}H NMR ($CDCl_3$) δ 0.92 and 0.93 (t, J = 7.4 Hz, 3 H each), 1.40–1.80 (m, 4 H), 2.15 (v br s, 1 H), 2.48 (t, J = 7.3 Hz, 2 H), 2.63 (m, X of ABX, 1 H), 3.75 (center of AB of ABX, J_{AB} = 11.1 Hz, J_{AX} = 7.3 Hz, J_{BX} = 4.1 Hz, 2 H).

Oxidation of Primary Alcohols and Aldehydes to Carboxylic Acids. General Procedure. A two-necked round-bottomed flask equipped with a Teflon-coated magnetic bar stirrer, a thermometer, and a reflux condenser was charged with methyltrioctylammonium tetrakis(oxodiperoxotungsto)phosphate (1c; 0.125 mmol),[38] the appropriate alcohol (aldehyde) (25 mmol), 40% w/v H_2O_2 (50 mmol (25 mmol when the substrate was the aldehyde) plus a 20–200% molar excess), and a solvent immiscible with the aqueous phase (2–5 mL) when needed (see Tables II and III). The flask was immersed in a water bath preheated to 90 °C, and the resultant biphase mixture (kept under a nitrogen atmosphere when the substrate was the aldehyde) was vigorously stirred at this temperature for the prescribed time (see Tables II and III). At the end, the stirred mixture was cooled, CH_2Cl_2 (Et_2O in entries 5–8 (Table II) and 12, 14–18 (Table III); 10–20 mL) was added, and then the organic layer was separated, and the aqueous layer (salted out with NaCl in entry 19 (Table II) and entry 3 (Table III)) was extracted with CH_2Cl_2 (Et_2O in entries 5–8, 12 (Table II) and 12, 14–18 (Table III); 3 × 10 mL). The combined organic layers were extracted with 10% Na_2CO_3 (4 × 5 mL, 6 × 5 mL in entry 12 (Table II)). The basic extracts (washed with Et_2O (10 mL)) were acidified with concentrated HCl with stirring, salted out with NaCl in entries 19 (Table II) and 3 (Table III), and then back-extracted with Et_2O (*n*-pentane in entries 9–17, 19 (Table II) and 3–5, 7, 8 (Table III); 5 × 10 mL, 4 × 30 mL in entries 5, 7, 8 (Table II) and 12, 14, 18 (Table III)). The combined organic extracts were dried over Na_2SO_4, filtered, and evaporated[39] to give the desired product. In entries 2–4 (Table II) and 2, 11, 13 (Table III) workup was somewhat different because of solubility problems. CH_2Cl_2 (25 mL) and 10% Na_2CO_3 (25 mL) were added with stirring to the reaction mixture. After dissolution of the product, the layers were separated. The organic layer was extracted with 10% Na_2CO_3 (3 × 5 mL), and the extracts were added to the basic aqueous layer. By acidification of the latter with concentrated hydrochloric acid (or preferably by addition of the alkaline solution to the mineral acid, in entries 4 (Table II) and 13 (Table III)) a solid precipitated that was extracted with Et_2O (4 × 30 mL) and treated as above (entry 2 (Tables II and III)) or filtered, washed thoroughly with water, and dried (entries 3, 4 (Table II) and 11, 13 (Table III)).

Notice. With aliphatic alcohols the reaction does not present particular exothermicity problems in the initial stage, whereas with benzylic alcohols, aliphatic aldehydes, and aromatic aldehydes bearing electron-releasing substituents thermal control in general is needed, analogously to secondary alcohols (see corresponding notice).

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Registry No. **2**, 123-96-6; **4**, 98-85-1; **6**, 80-97-7; **8**, 91-01-0; **10**, 464-45-9; **12**, 24393-70-2; **13**, 108-93-0; **15**, 5337-72-4; **17**, 96-41-3; **19**, 2216-51-5; **21**, 3391-86-4; **22** (isomer 1), 135637-52-4; **22** (isomer 2), 135637-53-5; **23**, 4312-99-6; **24**, 114701-53-0; **25** (isomer 1), 4780-68-1; **26**, 27970-80-5; **27**, 100-51-6; **28**, 100-52-7; **29**, 589-18-4; **30**, 104-87-0; **33**, 873-76-7; **35**, 619-73-8; **37**, 6971-51-3; **39**, 105-13-5; **41**, 612-25-9; **43**, 17849-38-6; **45**, 111-27-3; **47**, 111-70-6; **49**, 111-87-5; **51**, 112-30-1; **53**, 589-35-5; **55**, 626-89-1; **57**, 105-30-6; **59**, 4442-79-9; **61**, 100-49-2; **63**, 60-12-8; **65**, 75-84-3; **67**, 1123-85-9; **69**, 122-97-4; **71**, 110-62-3; **73**, 111-71-7; **74**, 124-13-0; **75**, 16251-77-7; **77**, 123-15-9; **78**, 2043-61-0; **79**, 122-78-1; **80**, 93-53-8; **81**, 104-88-1; **82**, 552-89-6; **83**, 555-16-8; **84**, 591-31-1; **85**, 529-20-4; **87**, 123-11-5; **88**, 613-45-6; **90**, 89-98-5.

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(40) Brown, H. C.; Garg, C. P. *J. Am. Chem. Soc.* **1961**, *83*, 2952.

(41) Naves, Y. R. *Helv. Chim. Acta* **1948**, *31*, 932.

(42) Mori, K.; Otsuka, T. *Tetrahedron* **1985**, *41*, 553 and 3253.

(43) Tursch, B., Chome, C., Braekman, J. C., Daloze, D. *Bull. Soc. Chim. Belg.* **1973**, *82*, 699.

(44) Archer, S.; Dickinson, W. B.; Unser, M. Y. *J. Org. Chem.* **1957**, *22*, 92.

(45) Wear, R. L. *J. Am. Chem. Soc.* **1959**, *73*, 2390.