

Entry 5. The directed product eluted second on Carbowax and was identified as above: δ 3.49 (lit.¹⁴ δ 3.48). The other product gave a resonance at δ 3.09 (lit.¹⁴ δ 3.02).

Entry 6. The directed product eluted first and was identified by ¹H NMR: δ 4.09 (lit.¹⁴ δ 4.02).

Entry 7. The directed product eluted second and was identified by ¹H NMR: δ 3.78 (lit.¹⁴ δ 3.75).

Entry 8. The directed isomer eluted before the other and was identified from the mp of 37–38 °C (lit.¹⁵ mp 34.5–35 °C). The other isomer melted at 47–48 °C (lit.¹⁵ mp 46–47 °C).

Entry 9. The directed product eluted before the other and was shown to be identical (GC, NMR) with the LAH reduction product of the directed product of entry 12. The counterdirected products were also identical.

Entry 10. The directed product eluted before the other and was identified from its ¹³C NMR (22.4, 29.4, 32.6, 34.5, 39.9, 68.0 ppm) by comparison with the literature²⁸ data (40.8, 30.0, 35.1, 33.3, 22.8, 68.9 ppm).

Entry 11. The directed isomer eluted second (¹³C NMR 42.1, 28.2, 33.5, 31.2, 21.5, 175.1, 50.1 ppm)²⁹ and was identified by ¹³C NMR as above. In addition, MeMgBr converted this directed isomer to the directed isomer obtained in entry 8 (GC, NMR).

(28) Kitching, W.; Olszowy, H.; Adcock, W. *Org. Magn. Reson.* 1981, 15, 230.

(29) Senda, Y.; Ishiyama, J.; Imaizumi, S. *Bull. Chem. Soc. Jpn.* 1976, 49, 1359.

Entry 12. The directed product eluted second [¹H NMR (CDCl₃) δ 2.09 (s, COMe), 0.85 (d, J = 5.7 Hz, CHMe)] and was converted with MeMgBr to the directed isomer obtained in entry 8 (GC NMR).

Entry 13 (See Text). We were not able to determine the stereochemistry in this case, but the isomer which predominates on reduction with the iridium catalyst is probably the directed product. This isomer eluted second on Carbowax.

Entry 14. The directed isomer [¹H NMR δ 3.15 (s, OMe), 0.85 (d, J = 6.6 Hz, CHMe)] eluted second and was identical with the methyl ether of the directed product formed for entry 1.

Entry 15. The directed isomer eluted first [¹H NMR (CDCl₃) δ 3.30 (s, OMe), 0.90 (d, J = 5.5 Hz, CHMe)] and was identical with the methyl ether of the directed product formed in entry 2.

From 6. We postulate that the isomer formed to the extent of 99% with the iridium catalyst is the directed isomer [¹H NMR (CDCl₃) δ 0.83 (d, J = 6.6 Hz, CHMe), 2.09 (s, COMe)].

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Metal Catalysis in Oxidation by Peroxides.¹ Molybdenum- and Tungsten-Catalyzed Oxidations of Alcohols by Diluted Hydrogen Peroxide under Phase-Transfer Conditions

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A synthetic procedure is described which allows the oxidation of primary and secondary alcohols to the corresponding carbonyl compounds with dilute hydrogen peroxide, employing Mo(VI) and W(VI) as catalysts, under phase-transfer conditions (Aliquat 336), characterized by high yields and selectivities.

Transition-metal-catalyzed oxidations with dilute hydrogen peroxide under phase-transfer conditions are increasingly attractive synthetic procedures² overcoming most of the drawbacks of homogeneous systems^{2b} and allowing the use of dilute aqueous solutions of the oxidant.

In a previous paper^{2b} we described a two-phase method of oxidation of organic sulfides and alkenes with 30% w/v hydrogen peroxide, molybdenum (VI) or tungsten (VI) catalysts, and neutral lipophilic ligands as extracting agents characterized by high yields and selectivities. By means of the ligand, *neutral* peroxo complexes MO(O₂)₂, which formed in water¹ by addition of an excess of H₂O₂ to H₂MO₄ (M = Mo, W), were extracted in the organic phase. Owing to the acidic character of MO₅, addition of acid was required to neutralize^{1,3} the anionic form.

Table I. Effect of the Acidity of the Aqueous Phase on the Oxidation of Cyclohexanol to Cyclohexanone with H₂O₂, Catalyzed by Mo(VI) or W(VI) Complexes in the Presence of Aliquat 336, at 60 °C, under Phase-Transfer Conditions (10 mL of DCE–1 mL of H₂O)

run ^a	catalyst	pH ^b	time, min	cyclohexanone, mmol
1	Mo(VI)	4.50	60 ^c	(4.2) ^c
2	Mo(VI)	3.10	120	5.0
3	Mo(VI)	2.95	120	5.5
4	Mo(VI)	2.60	120	3.0
5	Mo(VI)	2.10	120	1.1
6	W(VI)	2.85	50	4.0
7	W(VI)	2.05	50	8.2
8	W(VI)	1.40	50	9.8
9	W(VI)	1.25	50	6.2

^a Cyclohexanol (50 mmol), H₂O₂ (10.1 mmol), Aliquat 336 (0.5 mmol), WO₄²⁻ or MoO₄²⁻ (0.25 mmol), and added acid, H₂SO₄.
^b Reference 6. ^c Complete consumption of H₂O₂.

On the other hand, the occurrence of acid–base equilibria of MO₅ implies that, at lower acidities (i.e., higher pH), it should be possible to transfer anionic peroxo compounds from an aqueous to an organic phase by using cationic phase-transfer agents. Anionic Mo(VI) and W(VI)

(1) Metal Catalysis in Oxidation by Peroxides. Part 25. Part 24: Bortolini, O.; Bragante, L.; Di Furia, F.; Modena, G. *Can. J. Chem.*, in press.

(2) (a) Venturello, C.; Alneri, E.; Ricci, M. *J. Org. Chem.* 1983, 48, 3831. (b) Bortolini, O.; Di Furia, F.; Modena, G.; Seraglia, R. *Ibid.* 1985, 50, 2688 and references therein. (c) Bortolini, O.; Di Furia, F.; Modena, G. Italian Patent Application 25720 A and 25721 A, 1981.

(3) (a) Di Furia, F.; Modena, G. *Rev. Chem. Intermed.* 1985, 6, 51. (b) Arcoria, A.; Ballistreri, F. P.; Tomaselli, G. A.; Di Furia, F.; Modena, G. *J. Mol. Catal.* 1983, 18, 177.

Table II. Effects of Various Parameters on the Oxidation of Cyclohexanol to Cyclohexanone with H₂O₂ Catalyzed by Mo(VI) or W(VI) Complexes, under Phase-Transfer Conditions

run ^a	cyclohexanol, mmol	H ₂ O ₂ , mmol	catalyst (mmol)	R ₄ N ⁺ X ⁻ , mmol	T, °C	t, min	yield, %
1	50.0	10.1	Mo(VI) (0.25)	0.5	60	150	71 ^b
2	50.0	10.1	W(VI) (0.25)	0.5	60	49	98 ^b
3	10.0	20.2	Mo(VI) (0.25)	0.5	60	2000	70 ^c
4	10.0	20.2	W(VI) (0.25)	0.5	60	210	83 ^c
5	10.0	40.4	Mo(VI) (0.5)	1.0	60	1000	89 ^c
6	10.0	20.2	W(VI) (0.5)	1.0	60	150	89 ^c
7	10.0	60.6	Mo(VI) (0.5)	1.0	75	300	84 ^c
8	10.0	30.3	W(VI) (0.5)	1.0	75	90	94 ^c
9	10.0	40.4	Mo(VI) (1.0)	2.0	75	150	88 ^c
10	10.0	40.4	W(VI) (1.0)	2.0	75	49	97 ^c

^a Added acid, H₂SO₄: pH 3.0, Mo(VI): pH 1.4, W(VI). ^b Based on H₂O₂. In all cases complete consumption of the oxidant is observed. ^c Based on cyclohexanol initially added.

Table III. Oxidation of Various Alcohols with H₂O₂ Catalyzed by Mo(VI) or W(VI) Complexes, under Phase-Transfer Conditions, at 75 °C

run ^a	alcohol	(mmol)	catalyst	H ₂ O ₂ , mmol	t, min	yield, % ^b
1	cyclohexanol	(10.0)	Mo(VI)	40.0	150	88
2	cyclohexanol	(10.0)	W(VI)	40.4	49	97
3	menthol	(10.0)	Mo(VI)	60.6	210	97
4	menthol	(10.0)	W(VI)	50.5	120	89
5	borneol	(10.0)	Mo(VI)	40.4	120	100
6	borneol	(10.0)	W(VI)	20.2	45	96
7	2-octanol	(10.0)	W(VI)	40.4	75	97
8	benzyl alcohol	(10.0)	W(VI)	20.2	30	85

^a Aliquat 336 (2.0 mmol): catalyst (1.0 mmol): pH 3.0, Mo(VI); pH 1.4, W(VI): added acid, H₂SO₄. ^b Based on alcohol initially added.

peroxo complexes have been employed as effective oxidants of secondary alcohols to the corresponding carbonyl compounds.⁴ Moreover, recent results indicate that molybdenum-catalyzed oxidations of alcohols with hydrogen peroxide are much faster in basic media than in neutral ones.⁵ Therefore we have developed an oxidizing procedure that permits the oxidation of primary and secondary alcohols, under phase-transfer conditions, using hydrogen peroxide, Mo(VI) or W(VI) salts as catalysts, and a lipophilic tetraalkylammonium compound as extracting agent. The results collected indicate that such a procedure may be of significant synthetic relevance, providing, particularly with secondary and benzyl alcohol, very high selectivities.

Results and Discussion

The results of a preliminary investigation on cyclohexanol, selected as model substrate, on the effect of various parameters on the oxidation of alcohols by Mo(VI)- or W(VI)-H₂O₂ systems are summarized in Tables I and II.

The experimental details are reported in the appropriate section. As previously mentioned, a strong dependence of the efficiency of the oxidant on the pH of the aqueous phase is observed.⁶ In fact the best yields of cyclohexanone, in the shortest reaction times, are obtained at pH 3.0 and 1.4 for Mo(VI) and W(VI), respectively. At higher acidities the reactions are much slower. On the other hand, at lower acidities, the selectivity of the reaction is greatly reduced because of the concomitant decomposition of hydrogen peroxide. This is likely related to the formation of less stable metal-peroxo species such as

M(O₂)₄²⁻.⁸ Under the best conditions of acidity, we have studied the dependence of cyclohexanol oxidation rates on the concentration of the various reagents and of the temperature.

The data of Table II indicate that the yields are usually very high in all cases, and, most important, complete conversion of the alcohol to the ketone may be obtained when an excess (2–6-fold) of the oxidant over the substrate is employed. As expected the reaction rates increase with increasing concentration of the catalyst. Independent experiments have shown that, under the experimental conditions adopted, quantitative extraction of the peroxo anion is achieved by using only a 2-fold excess of the quaternary ammonium salt.⁹ Contrary to the behavior of olefin epoxidation under phase-transfer conditions, where tungsten catalyst was less efficient than the corresponding molybdenum derivative,^{2b} here W(VI)-peroxo complexes are much more effective than peroxo-molybdenum ones. This has been observed also in the homogeneous oxidation of secondary alcohols with anionic Mo(VI)- and W(VI)-peroxo complexes.⁴

As far as the effect of the temperature is concerned, it may be noticed that an increase from 60 to 75 °C produces a significant acceleration of reaction rates. At the same time the yields in ketone remain unchanged and the decomposition of the oxidant is only slightly enhanced.

Under the optimized conditions, five model alcohols were oxidized. The pertinent results are collected in Table III.

In all cases the complete conversion of the substrates is obtained when excesses ranging from 2-fold to 6-fold of hydrogen peroxide are used. With the exception of benzyl alcohol, no appreciable amounts of products arising from further oxidation of ketones were detected under the experimental conditions adopted. With benzyl alcohol, larger excesses of H₂O₂ over the substrate lead to the formation of small amounts of benzoic acid. Data not reported in

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

(5) (a) Trost, B. M.; Masuyama, Y. *Tetrahedron Lett.* 1984, 25, 173.

(b) Bortolini, O.; Conte, V.; Di Furia, F.; Modena, G., unpublished results.

(6) pH values reported in Tables I–III refer to the actual acidity of the aqueous phase in the presence of the organic one which is lower than that measured in its absence. This might indicate that small amounts of acid (H₂SO₄) are transferred in DCE solutions; cf. ref 1 and: Zahalka, H. A.; Sasson, Y. *J. Chem. Soc. Commun.* 1984, 1581.

(7) Bortolini, O.; Conte, V.; Di Furia, F.; Modena, G. *Nouv. J. Chim.* 1985, 9, 147, and references therein.

(8) Connor, J. A.; Ebsworth, E. A. V. *Adv. Inorg. Chem. Radiochem.* 1964, 6, 279.

(9) Bortolini, O.; Di Furia, F.; Modena, G., unpublished results.

Table III, referring to aliphatic primary alcohols, indicate that under the same conditions, the oxidation does proceed, though at lower rates and selectivities. Thus 1-octanol (50 mmol) is oxidized by W(VI) (0.5 mmol)-H₂O₂ (10 mmol) at 60 °C in 3 h to the corresponding octanal (4 mmol, 40% yield). However caprylic acid (1.2 mmol) is also produced, likely as a result of the lower reactivity of primary alcohols coupled with the ease of autoxidation of the aldehydes.¹⁰

The effect of the nature of the phase-transfer agent has also been examined. Therefore hexadecyltrimethylammonium sulfate [(CTA)₂SO₄] and methyltrioctylammonium chloride (Aliquat 336) [AliCl] have been compared in cyclohexanol oxidation. The oxidation in the presence of AliCl is slightly faster than that in the presence of (CTA)₂SO₄. As an example cyclohexanol (10 mmol) was oxidized by H₂O₂ (40 mmol), W(VI) (1 equiv) catalyst, at 75 °C in the presence of equal amounts (2 equiv) of AliCl or (CTA)₂SO₄. Quantitative yields (>95%) of cyclohexanone were obtained in 49 and 65 min, respectively. On this basis it appears that the use of the commercially available AliCl may be recommended.

Finally we have carried out the oxidation of cyclohexanol using two different phase-transfer systems previously described in the literature, which allow the oxidation of nucleophilic substrates, such as sulfides and alkenes, by using either a neutral ligand^{2b} or the association phosphate-tetraalkylammonium ions.^{2a} In both cases much lower yields of cyclohexanone are obtained under the best conditions preferred for olefin epoxidation.¹¹

Conclusions

The data presented here confirm the synthetic value of the two-phase oxidative procedure, which is now extended to alcohol oxidation. It should be noted that the oxidizing agent in this system is an anionic peroxy complex which is known to be a poor oxidant of nucleophilic substrates.^{3b} Therefore, from a mechanistic point of view, this may suggest a different route of oxidation for the two classes of substrates.

Work aimed to clarify the reactivity of anionic peroxy complexes is currently in progress.

(10) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic: New York, 1981; Chapter 12, p 350.

(11) According to the procedure of ref 2b, the oxidation was carried out in two-phase system consisting of DCE (25 mL), cyclohexanol (100 mmol), tridodecylphosphoric triamide (1.0 mmol), and aqueous (2 mL) H₂O₂ (20.2 mmol)-Na₂MoO₄·2H₂O (0.5 mmol), pH 2 (H₂SO₄), at 50 °C. After 5 h only 50% of hydrogen peroxide was consumed, and 0.8 mmol of cyclohexanone were produced (yield 4%). In the other system, see ref 2a, the organic phase was composed of DCE (8 mL), cyclohexanol (100 mmol), Aliquat 336 (AliCl, 1 mmol), and aqueous (29 mL) H₂O₂ (84 mmol), H₃PO₄ (5 mmol), Na₂WO₄·2H₂O (2.5 mmol), pH 1.7 (H₂SO₄), at 70 °C. After 7 h hydrogen peroxide was totally consumed, yielding 47.3 mmol (56% yield) of cyclohexanone.

Experimental Section

Materials. Cyclohexanol, 1-octanol, 2-octanol, and benzyl alcohol, all commercially available products, were purified by distillation. Reagent grade Na₂WO₄·2H₂O and Na₂MoO₄·2H₂O were used as catalysts. 1,2-Dichloroethane was purified by standard procedures from highly pure commercial samples. Hexadecyltrimethyl ammonium sulfate [(CTA)₂SO₄] was obtained from the commercially available hexadecyltrimethylammonium bromide, [CTABr] according to the following procedure: 2.96 g (8.1 mmol) of CTABr were dissolved in 60 mL of methanol, and 7.06 g (22 mmol) of Ag₂SO₄ were added, maintaining the suspension under vigorous stirring for 30 min. The reaction mixture was kept in a sonicator for additional 2 h and the residue filtered off. Methanol was partially evaporated and ethyl ether was added until precipitation of the product was obtained. The above procedure was repeated using the solid separated from the organic solution. Finally the product was washed twice with ether and dried overnight, affording 1.69 g of (CTA)₂SO₄ (63% yield). All other chemicals were used as received.

Procedures. In a typical run 1 mL of H₂O₂ 70% w/v (20.0 mmol) was added to a dichloroethane solution (10 mL) containing the alcohol (10 mmol) and methyltrioctylammonium chloride [AliCl] (2.0 mmol) in a glass reactor, maintained at 75 °C and equipped with a condenser. Then, 0.5 mL of an aqueous solution containing Na₂WO₄·2H₂O (1.0 mmol) and the required amount of H₂SO₄ to adjust the pH were added under vigorous stirring. At regular intervals the stirring was suspended, and a small quantity (0.1 mL) of the organic phase was analyzed by GLC methods. In the experiments run by using an excess of alcohol over hydrogen peroxide, the yields were determined when complete consumption of the oxidant (iodometric titer) was observed. In the experiments carried out in the presence of an excess of the oxidant (see Tables I-III), yields are calculated when complete conversion of the alcohols is observed. In this case the yields are based on the alcohol initially added. The products were determined by quantitative GLC analysis (internal standard) using a 10% Carbowax 20 M or a 3% FFAP on Chromosorb WAW-DMCS column, with a Varian 3700 instrument, equipped with a Varian CDS 401 integrator.

In all cases the identity of the products was confirmed by comparison with authentic samples.

Alternatively, isolation of the products may be carried out as in the following representative example: benzyl alcohol (20.76 mmol) dissolved in DCE (20 mL) together with AliCl (4.0 mmol) was maintained at 75 °C in the presence of the aqueous phase (3 mL) containing Na₂WO₄·2H₂O (2.0 mmol) and H₂O₂ (40.0 mmol), pH 1.0, under stirring. After 30 min (see Table III) the stirring was suspended, the two phases were separated, and the organic one, after drying, was evaporated under vacuum. From the residual oil, benzaldehyde was separated by column chromatography (silica gel; CHCl₃; crude product 19.2 mmol, 92% yield). Under these conditions, AliCl was not eluted. The aldehyde has been further purified by distillation [bp 58-59 °C (5 mmHg); 17.4 mmol, 84% yield].

Registry No. H₂O₂, 7722-84-1; Na₂WO₄, 13472-45-2; Na₂MoO₄, 7631-95-0; cyclohexanol, 108-93-0; menthol, 1490-04-6; borneol, 507-70-0; 2-octanol, 123-96-6; benzyl alcohol, 100-51-6; cyclohexanone, 108-94-1; menthone, 10458-14-7; 2-bornanone, 76-22-2; 2-octanone, 111-13-7; benzaldehyde, 100-52-7.