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Copper-catalyzed homolytic and heterolytic benzylic and allylic oxidation using *tert*-butyl hydroperoxide

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Allylic and benzylic alcohols were oxidized in good yields to the respective ketones by *tert*-butyl hydroperoxide (TBHP) in the presence of copper salts under phase-transfer catalysis conditions. This dehydrogenation was found to proceed *via* a heterolytic mechanism. $CuCl_2$, CuCl, and even copper powder were equally facile as catalysts, as they were all transformed *in situ* to Cu(OH)Cl which was extracted into the organic phase by the phase-transfer catalyst (PTC). Deuterium labeling experiments evidenced the scission of the benzylic C–H bond in the rate-determining step. Nonproductive TBHP decomposition was not observed in the presence of the alcohol substrates. Conversely, the oxygenation of π-activated methylene groups in the same medium was found to be a free radical process, and the major products were the appropriate *tert*-butyl peroxides. Catalyst deactivation, solvent effects, and extraction effects are discussed. By applying Minisci's postulations concerning the relative reactivity of TBHP molecules towards *tert*-butoxyl radicals in protic and nonprotic environments, the coexistence of the homolytic and the heterolytic pathways can be explained. A complete reaction mechanism is proposed, wherein the free-radical oxidation obeys Kochi's mechanism, and the heterolytic dehydrogenation is based on either a high-valent Cu^{IV}=O species or a $[Cu(OH)Cl]_2$ species.

Introduction

The mechanism of oxidation using Fenton-type reagents has been the subject of recent debate, with specific regard to the participation of free-radical intermediates in the oxidation of aliphatic and aromatic compounds with H_2O_2–M and ROOH–M reagent systems. Sawyer *et al.* have stated that free carbon radicals are not produced in Fenton oxidation systems,[1] while Walling, and MacFaul *et al.* have argued that Fenton and Fenton-type reagents (*i.e.* H_2O_2 or TBHP with Fe/Co/Cu catalysts) would have to include free-radical intermediates if they are to provide a satisfactory explanation of the observed kinetic and product studies.[2,3]

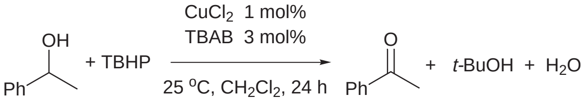
Allylic and benzylic oxidation reactions are the foundation of many important current industrial and fine-chemical processes,[4] covering a diverse field from natural product chemistry to "buckybowl" synthesis.[5] Traditionally, these reactions have been performed with stoichiometric chromium reagents, *e.g.* CrO_3,[6a] or Cr–pyridine complexes.[6b,6c] However, today's environmental restrictions render most of the stoichiometric metal oxidants obsolete. Using TBHP as an alternative oxygen source[7a] has been investigated with several transition-metal catalysts, including Cr, Ru, Rh, and Cu.[7b–g] The latter is interesting because it is both cheap and relatively benign.[8] Recent oxidations with TBHP and copper catalysts show that the immediate surroundings of the Cu atom can influence reaction enantioselectivity,[9a,9b] and maybe tell us something about the activity of copper-containing monooxygenases.[9c]

Herein we present the results of product studies and kinetic investigations of the title reactions, and explain the fundamental mechanistic differences between the oxidation of alcohols and activated methylene groups in the TBHP–Cu–PTC system.

Results

Oxidation of alcohols[10]

In the presence of catalytic amounts of $CuCl_2$ and a phase-transfer catalyst such as n-$Bu_4N^+Br^-$ (TBAB), a smooth oxidative dehydrogenation of alcohols to the appropriate aldehydes or ketones was observed with 70% aqueous TBHP. Good conversions and excellent selectivities were observed for various substrates, as shown in Table 1. Primary and unactivated alcohols could also be oxidized, but yields were lower. 1-Phenylethanol **1** was chosen as a model substrate for a mechanistic investigation of the oxidation of benzylic alcohols with TBHP [eqn. (1)].



(1)

1 **2**

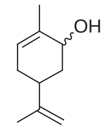
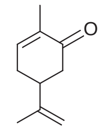
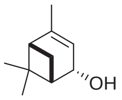
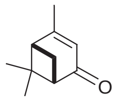
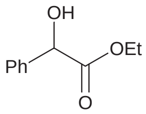
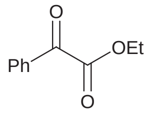
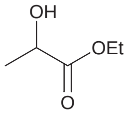
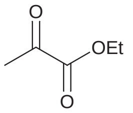
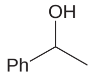
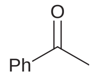
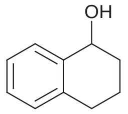
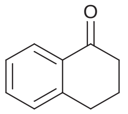
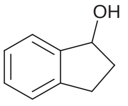
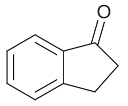
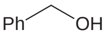
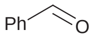
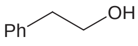
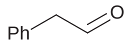
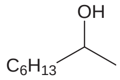
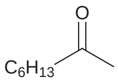
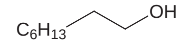
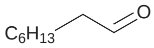
Remarkably, no unproductive decomposition of TBHP was observed in this system. Yields were nearly quantitative and no excess of TBHP was required. Consequently, the oxidant can be added in one batch without overheating risks. It should be noted, however, that when the reagents were mixed without the alcohol substrate, a free-radical chain decomposition of TBHP *was* observed.[11]

Examination of various organic solvents showed that CH_2Cl_2 and PhCN were superior to $PhNO_2$ and cyclohexanone (Fig. 1). This probably reflects different partition coefficients for the catalytic species between the organic and aqueous phases.

We have also carried out the reaction in a dry monophasic system, using t-BuOH or MeCN as solvents. The copper catalysts were soluble in these media, which was an advantage, and high conversions and selectivities were obtained (GC indicated over 95% conversion with **2** being the sole product after 45 h). The main drawback of the monophasic approach was that it made product separation difficult, while from the biphasic medium the product could be purified by simply separating the phases and washing the organic phase with water. A further disadvantage of the monophasic system was that unproductive decomposition of TBHP occurred.

The presence of both catalysts was found to be essential. No reaction was observed in the absence of copper, and very low conversions were obtained in the absence of TBAB. Bubbling O_2 or Ar through the reaction mixture (with TBHP) did not

Table 1 Copper-catalyzed oxidation of alcohols with TBHP^a

Entry	Substrate	% Conversion^b	Product	% Selectivity^b
1		35^b		100
2		80 (17)		100 (100)
3		96 (4)		100 (100)
4		60^b		100
5		75 (3)		100 (100)
6		71 (4)		100 (100)
7		67 (3)		97 (100)
8		38 (7)		100 (100)
9		6^c		66
10		20^c		100
11		6^c		100
12		53 (24)		59 (58)

[a] Reaction conditions: 25.0 mmol substrate, 25.0 mmol 70% aq. TBHP, 24 h, 1 mol% $CuCl_2$, 3 mol% TBAB, 25 °C, 10 ml CH_2Cl_2. [b] The conversion and selectivity in the absence of TBAB are indicated in brackets. [c] No conversion was detected in the absence of TBAB.

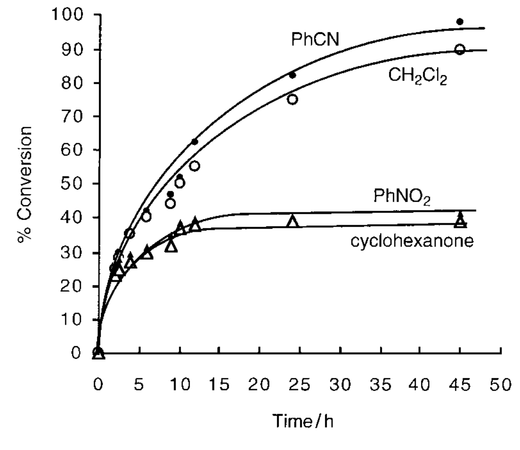


Fig. 1 Oxidation of **1** using different solvents. Reaction conditions: 26.0 mmol **1**, 26.0 mmol TBHP, 2 mol% $CuCl_2$, 3 mol% TBAB, 25 °C, 10 ml solvent.

alter the results, while substitution of the TBHP with H_2O_2 gave no products, and a nonproductive decomposition of H_2O_2 was observed.

Several phase-transfer catalysts were tested. Similar results were obtained with n-$Bu_4N^+Cl^-$, TBAB, n-$Bu_4N^+I^-$, $(C_{10}H_{21})_2$-$Me_2N^+Br^-$, $C_{16}H_{33}(Me)_3N^+Br^-$, and Aliquat 336, indicating that cation symmetry and halide anion type do not influence the catalytic activity. Ammonium salts that lack a halide counterion, *e.g.* n-$Bu_4N^+HSO_4^-$, were inactive. Nevertheless, it is not the halide ion alone that is responsible for the catalysis, as KBr and Br_2 failed to catalyze the reaction. The hydrophilic PTC $Me_4N^+Br^-$ was also inactive, as expected for biphasic systems in which the reaction takes place in the organic phase.[12]

A series of blank reactions were run in order to elucidate the nature and structure of the active catalytic species. We discovered that the oxidation can be carried out with equal facility using $CuCl_2$, CuCl, and even plain copper metal as the catalyst (*cf.* reaction profiles in Fig. 2). A colloidal dispersion of copper in CH_2Cl_2 had the same catalytic activity as ordinary copper

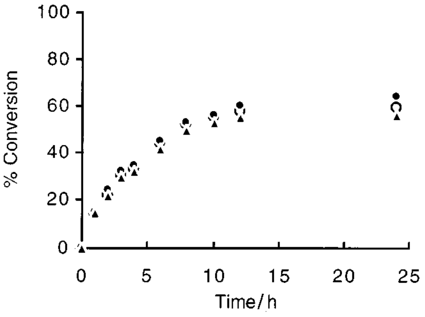


Fig. 2 Oxidation of **1** using ○, $CuCl_2$; ●, CuCl; ▲, Cu. Reaction conditions: 15.4 mmol **1**, 15.4 mmol TBHP, 2 mol% catalyst, 3 mol% TBAB, 25 °C, 18 ml CH_2Cl_2.

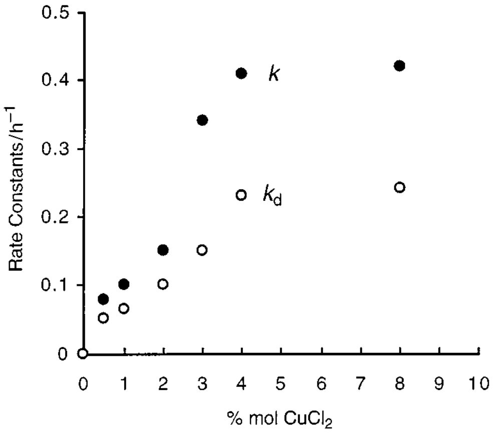


Fig. 3 Dependence of k and k_d on the initial concentration of $CuCl_2$. Reaction conditions: 15.0 mmol **1**, 15.0 mmol TBHP, 0.5–8 mol% $CuCl_2$, 2 mol% TBAB, 25 °C, 18 ml CH_2Cl_2.

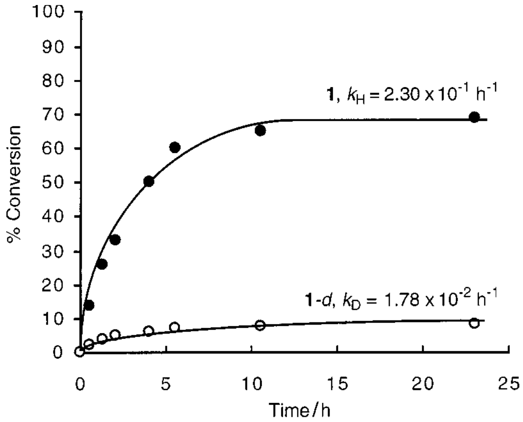


Fig. 4 Oxidation of **1** and **1**-*d*. Reaction conditions: 26.0 mmol substrate, 26.0 mmol TBHP, 0.33 mol% $CuCl_2$, 1 mol% TBAB, 25 °C, 10 ml CH_2Cl_2.

powder. Atomic absorption (AA) and UV–visible spectra of the aqueous and the organic phases showed that *$CuCl_2$ was not extracted* into CH_2Cl_2 by TBAB. Conversely, $Cu(OH)_2$ and Cu(OH)Cl were extracted efficiently into CH_2Cl_2.[13]

Note that the final conversion in Fig. 2 is lower than that in Fig. 1. This system is sensitive to concentration changes, especially of the metallic catalyst. The catalyst undergoes a deactivation process, which is much more pronounced at low concentrations. Fig. 3 shows the dependence of the reaction rate constant k, and the catalyst deactivation rate constant k_d, on the initial amount of the copper catalyst.

The kinetics of the oxidation reaction were found to fit a first-order profile with first-order deactivation of the catalyst [eqn. (2), where $[A]_t$ is the concentration of the substrate at

$$\ln\left(\ln\frac{[A]_t}{[A]_\infty}\right) = \ln\frac{k}{k_d} - k_d t \qquad (2)$$

time t, $[A]_\infty$ is the concentration of the substrate at time ∞, k is the reaction rate constant, and k_d is the catalyst deactivation rate constant; see experimental section for the derivation of eqn. (2)]. Experimental measurements (for 1 mol% $CuCl_2$) gave $k = 3.88 \times 10^{-5}\ s^{-1}$, and $k_d = 2.77 \times 10^{-5}\ s^{-1}$ ($r^2 = 0.996$). Further rate measurements indicated 1st order in the substrate and zero order for the oxidant ($r^2 = 0.983$). Altering the stirring rate (50–1000 rpm) did not affect the reaction, indicating that the rate-determining step (RDS) is chemically, rather than diffusively, controlled. This was supported by calculating the Arrhenius energy of activation, which gave $E_a = 50$ kJ mol^{-1} (12 kcal mol^{-1}, $r^2 = 0.991$ for four measurements at 1, 11, 28 and 39 °C), a typical value for a chemically controlled RDS.

XR diffraction spectroscopy of the powder residue containing the catalyst at the end of the reaction indicated the presence of $Cu_2Cl(OH)_3$ (*d*-values: 5.46, 2.76, 2.27) and $CuCl_2$ (*d*-values: 5.44, 4.02, 2.64), but no Cu^I species were detected. The binuclear species $Cu_2Cl(OH)_3$ has been proposed previously as the deactivated catalyst in copper-catalyzed oxidations.[14]

In order to gain additional insight into the reaction mechanism, the deuterated substrate Ph-CDOH-CH_3 **1**-*d* was prepared and oxidized. Fig. 4 shows the reaction profiles for **1** and **1**-*d*, respectively. An uncommonly large kinetic isotopic effect (KIE) was observed, $k_H/k_D = 12.9$. This asserts that the RDS involves breaking the benzylic C–H bond.

We have found that the RDS in the oxidation of **1** and analogous compounds in this system is heterolytic, *i.e.* involves the transfer of two electrons rather than free radicals. This was supported by several observations: *(1)* Addition of a radical scavenger (1,6-di-*tert*-butyl-4-methylphenol, BHT) to the reaction mixture had no effect on the reaction rate.[15] *(2)* No hydroperoxide or peroxide intermediates were detected by iodometric titration. *(3)* UV–Visible and XR diffraction spectra indicated the presence of Cu(II) species, but not Cu(I), making a one-electron transfer harder to envisage. *(4)* Single products were obtained in high selectivities, which is uncommon in free-radical processes. *(5)* No changes were observed when oxygen was bubbled through the reaction mixture, indicating that the presence of alkyl radicals is unlikely.

Significantly, no benzylic oxidation was observed at the 4- and 3-positions of 1-tetralol (tetrahydro-1-naphthol) and indan-1-ol, respectively. This finding suggests a mechanistic difference between the oxidation of alcohols and that of π-activated methylenes in this system.

Oxygenation of π-activated methylenes[16]

The oxidation of 1,2,3,4-tetrahydronaphthalene (tetralin, **3**) proceeded to 50% substrate conversion when a 1 : 1 molar ratio of TBHP : Substrate was employed [eqn. (3)]. The major

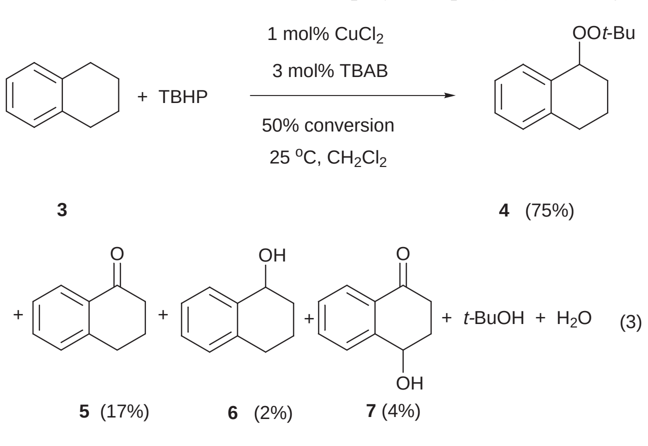


Table 2 Oxidation of π-activated methylenes with TBHP[a]

Entry	Substrate	Time/h	Conversion (%)	Product (% selectivity)
1	Tetralin	4	50	1-*t*-Bu-peroxytetralin (75), 1-tetralone (17), 4-hydroxytetralone (8), 1-tetralol (2)
2	Tetralin[b]	4	8	1-*t*-Bu-peroxytetralin (50), 1-tetralol (50)
3	Indane	6	50	1-*t*-Bu-peroxyindane (70), indan-1-one (25), indan-1-ol (4), 1-indene (1)
4	Indane[b]	24	18	1-*t*-Bu-peroxyindane (28), indan-1-one (55), indan-1-ol (17)
5	Diphenylmethane	4	32	1-*t*-Bu-peroxydiphenylmethane (16), benzophenone (78), diphenylcarbinol (6)
6	Diphenylmethane[b]	48	10	1-*t*-Bu-peroxydiphenylmethane (40), benzophenone (55), diphenylcarbinol (5)
7	Fluorene	4	50	1-*t*-Bu-peroxyfluorene (tr), fluorenone (86), fluorenol (14)
8	Fluorene[b]	4	6	1-*t*-Bu-peroxyfluorene (14), fluorenone (86)
9	(*R*)-Limonene	14	17	*t*-Bu-peroxylimonene[c] (17), carvone (20), limonene oxide (26)
10	α-Pinene	14	18	*t*-Bu-peroxypinene[c] (15), verbenone (22), pinene oxide (29)
11	Cumene[d]	4	12	*t*-Bu-peroxycumene (17), 1-phenylpropan-2-ol (83)
12	Ethylbenzene[d]	9	36	1-Phenyl-1-*t*-Bu-peroxyethane (10), acetophenone (72), 1-phenylethanol (18)

[a] Reaction conditions: 25.0 mmol substrate, 25.0 mmol 70% aq. TBHP, 1 mol% $CuCl_2$, 3 mol% TBAB, 25 °C, 10 ml CH_2Cl_2. [b] No TBAB. [c] The exact structure could not be determined. [d] No conversion was detected in the absence of TBAB.

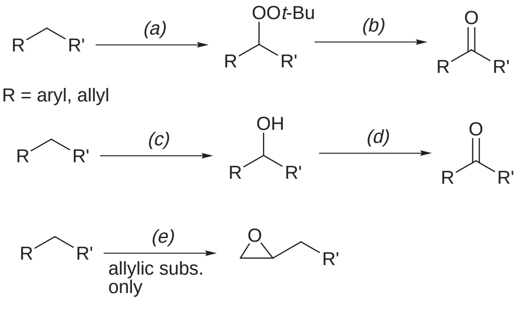
product was 1-*tert*-butylperoxytetralin **4** (75%), together with 1-tetralone **5** (17%), 1-tetralol **6** (2%), naphthalene (2%), and 4-hydroxy-1-tetralone **7** (4%). Using a 2 : 1 ratio of TBHP to tetralin, as the stoichiometry of the reaction demands, led to a higher conversion but with poorer selectivity for **4**.

Separate oxidation experiments performed on an isolated sample of the peroxide **4** showed that it could be an intermediate in the formation of **5** and **7** (**6** was not detected). This indicates that there are two possible pathways for the formation of the ketone **5**, *i.e.* **4**→**5** and **6**→**5**. The latter is not sufficiently fast for the reaction to proceed by the pathway **4**→**6**→**5**, as some **6** would have to accumulate. The decomposition of **4** to **5** and **7** was found to be temperature-sensitive. In the absence of TBHP at 25 °C, **4** was stable in the presence of Cu–TBAB, but decomposed when fresh TBHP was added. Conversely, at 60 °C, the presence of Cu–TBAB was sufficient to transform **4** to **5** and **7**. A commercial sample of **5** was oxidized (with an excess of 4 equiv. of TBHP) to **7**, but the conversion was only 9% after 3 d.

Similar results were obtained with several other benzylic and allylic olefins. The results are summarized in Table 2. Again, the presence of both catalysts was required. It is significant that some tertiary peroxide was obtained in all cases, because this could only result from the participation of the *tert*-butylperoxy radical. As expected, we found that BHT addition inhibits the oxidation of **3**.

Discussion

The TBHP–Cu–TBAB system involves a complex set of interrelated reactions (Scheme 1): *(a)* benzylic/allylic *tert*-butyl peroxide formation; *(b)* peroxide decomposition affording the ketone as the main product; *(c)* formation of the allylic/benzylic alcohol; *(d)* oxidative dehydrogenation of the alcohol to the ketone; *(e)* double-bond epoxidation (allylic substrates only).



Scheme 1 Oxidation of allylic and benzylic olefins.

Our data pertaining to the oxidation of allylic and benzylic olefins can be explained by adaption of the mechanism proposed earlier by Kochi [eqn. (4)–(8)], who used a series of redox reactions to explain the formation of the *tert*-butyl peroxides.[17]

$$Cu^{II} + TBHP \longrightarrow Cu^{I} + t\text{-BuOO}^{\bullet} + H^{+} \qquad (4)$$

$$Cu^{I} + TBHP \longrightarrow Cu^{II}OH + t\text{-BuO}^{\bullet} \qquad (5)$$

$$Cu^{II}OH + TBHP \longrightarrow Cu^{II}\text{-OO-}t\text{-Bu} + H_2O \qquad (6)$$

$$t\text{-BuO}^{\bullet} + RH \longrightarrow t\text{-BuOH} + R^{\bullet} \qquad (7)$$

$$Cu^{II}\text{-OO-}t\text{-Bu} + R^{\bullet} \longrightarrow R\text{-OO-}t\text{-Bu} + Cu^{I} \qquad (8)$$

The mechanism of the oxidative dehydrogenation of alcohols to the appropriate aldehydes or ketones is somewhat more elusive. Experimental data point to a heterolytic process, and the large kinetic isotope effect indicates cleavage of the benzylic C–H bond in the rate-determining step. Fortunately, the mechanistic picture can be elucidated by taking into account the extraction of the copper species between the aqueous and organic phases *and* Minisci's reasoning concerning the hydrogen abstraction from TBHP by the *tert*-butoxyl radical [eqn. (9)] in the presence and in the absence of alcohols. Minisci has postulated[18] that the high rate constant measured[19] for eqn. (9)

$$t\text{-BuO}^{\bullet} + TBHP \longrightarrow t\text{-BuOH} + t\text{-BuOO}^{\bullet} \qquad (9)$$

($k = 2.5 \times 10^{8}$ M^{-1} s^{-1} at 22 °C) is dramatically lowered in a medium that allows hydrogen bonding with the TBHP, in accordance with the fact that free-radical TBHP decomposition was not observed in the presence of alcohol substrates. Hydrogen-bonding between the quaternary ammonium salt and the TBHP can also occur,[20] but its effect would be limited due to the small amount (1–3 mol%) of ammonium salt present. Additional experiments showed that the rate of tetralin oxidation diminished by a factor of 3.5 in the presence of an equimolar amount of tetralol.

We therefore suggest that when 70% aqueous TBHP is added to a mixture of substrate and catalytic amounts of $CuCl_2$ and TBAB in CH_2Cl_2, eqn. (10) and (11) take place *in the aqueous phase*.

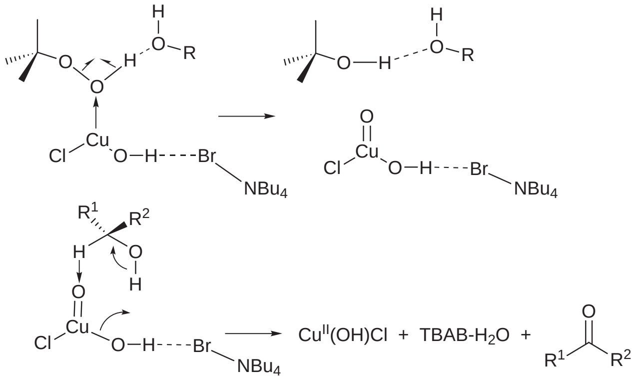
$$Cu^{II}Cl_2 + TBHP \longrightarrow Cu^{I}Cl + t\text{-BuOO}^{\bullet} + HCl \qquad (10)$$

$$Cu^{I}Cl + TBHP \longrightarrow Cu^{II}(OH)Cl + t\text{-BuO}^{\bullet} \qquad (11)$$

With substrates that cannot form a hydrogen bond with the TBHP molecule (*e.g.* tetralin), the formation of the *tert*-butoxyl radical would lead to instantaneous abstraction of the peroxidic hydrogen from another TBHP molecule, generating the *tert*-butylperoxy radical and eventually producing the peroxide **4**.

Conversely, in the case of alcohol oxidation, *e.g.* 1-tetralol, hydrogen bonding between the peroxidic hydrogen of the

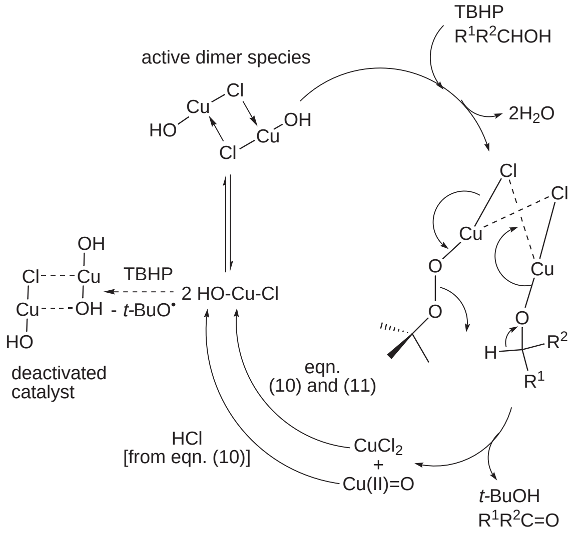
TBHP and the alcohol would inhibit the abstraction of that hydrogen by the *tert*-butoxyl radical. $Cu^{II}(OH)Cl$ which was generated in eqn. (11) would be extracted into the organic phase by TBAB [note that ammonium cations paired with a soft anion, *e.g.* HSO_4^-, cannot form hydrogen bonds with $Cu^{II}(OH)Cl$, and evidently do not catalyze the reaction], becoming a precursor for an active catalytic species: one possibility would be interaction of $Cu^{II}(OH)Cl$ with the hydrogen-bonded pair TBHP–ROH to form an active Cu^{IV}=O catalytic species[21] (Scheme 2, top). Ketone formation and regeneration of the $Cu^{II}(OH)Cl$ species would then be possible by abstraction of the geminal hydrogen from the alcohol as a hydride *via* a seven-membered pericyclic reaction (Scheme 2, bottom).



Scheme 2 Suggestions for the formation of an active Cu^{IV} species (top) and the oxidation of the alcohol substrate (bottom).

However, we have not been able to prove the existence of the Cu^{IV}=O species.

Another possible pathway† involves the dimerization of $Cu^{II}(OH)Cl$ and subsequent coordination of the TBHP and ROH molecules. As depicted in Scheme 3, this mechanism could also account for the catalyst deactivation, through formation of the inactive dimer species. Further study of these mechanistic possibilities is in progress.



Scheme 3 Suggestions for alcohol oxidation *via* a dimeric catalytic species.

The oxidation of alcohols would not be affected by the presence of free-radical scavengers such as BHT, because the generation of the extractable catalytic species would occur in the aqueous phase. The *in situ* transformation of Cu^0 to soluble compounds by TBHP has been envisaged.[7g]

Conclusions

In the Fenton-type TBHP–Cu system under PTC conditions, the oxygenation of π-activated methylenes is indeed a classic free-radical Kochi[17a] process. Conversely, the oxidation of alcohols *in the same medium* follows a heterolytic mechanism. Alcohol substrates interact by hydrogen bonding with the TBHP oxidant, and this lessens the free-radical peroxidic hydrogen abstraction by the *tert*-butoxyl radical. In this case, the active catalyst may be a high-valent Cu^{IV}=O species, generated by oxidation of Cu(OH)Cl by TBHP.

Experimental

^1H NMR spectra were measured in $CDCl_3$ on a Bruker AMX 300 instrument at 300.13 MHz. δ_H values are reported in ppm downfield from TMS. GC and GCMS analysis were performed using an HP-5790 gas chromatograph with a 5% diphenyl 95% dimethyl capillary column (25 m/0.31 mm). HPLC analysis was performed on a Hewlett-Packard series 1050 instrument, using an RP18 column with 80 : 20 MeCN : H_2O as eluent (1 ml min^{-1}, UV detector, 250 nm). Atomic absorption measurements were performed on a GBC 903 single beam spectrophotometer. Powder XR diffraction spectra were measured with a Philips PW1830 diffractometer. Unless stated otherwise, reagents were purchased from Aldrich, Fluka, and Merck, and were used as received. 70% TBHP (remainder water) was purchased from Sigma. **1**-*d* was synthesized and identified by its spectral properties. Products were either isolated and identified by comparison of their ^1H NMR spectra to commercial samples, or identified by MS data and comparison of their GC retention times with commercial samples.

Preparation of a colloidal dispersion of copper in CH_2Cl_2

An aqueous solution of 0.056 g (1.5 mmol) $NaBH_4$ was added to a flask containing 40 mg (0.3 mmol) $CuCl_2$, 108 mg (0.3 mmol) $C_{16}H_{33}(Me)_3N^+Br^-$, and 10 ml CH_2Cl_2. The mixture was stirred for 2 h at 25 °C. An intense red colour indicated the presence of colloidal Cu^0 in the organic phase. The phases were separated when the green color disappeared from the aqueous phase, indicating that all of the $CuCl_2$ was reduced.

Preparation of 1-phenyl-1-deuteroethanol 1-*d*

A suspension of 0.8 g (21 mmol) $LiAlD_4$ in 25 ml of dry ether was added dropwise to a gently boiling solution of 0.49 g (41 mmol) **2** in 6.5 ml dry ether. The mixture was kept at a gentle boil for 30 min, after which the $LiAlD_4$ remnants were neutralized with EtOAc, and the solution was brought to pH = 7 with aqueous HCl. Separation of the organic phase, drying over Na_2SO_4, filtration, and evaporation of the solvent *in vacuo* afforded 4.5 g (89 mol% based on **2**) of pure **1**-*d*. δ_H: 7.22 (5H, m), 2.01 (1H, s), 1.38 (1H, s,). [*cf.* with **1**: 7.22 (5H, m), 4.78 (1H, d,), 1.79 (1H, s), 1.38 (3H, d)]; *m*/*z*: 123 (*cf.* with **1**, 122). Isotopic purity was >99.9% according to ^1H NMR.

General procedure for oxidation of allylic and benzylic alcohols and olefins

Example: tetralin **3**. 3.46 g (26.2 mmol) of **3**, 35 mg (0.26 mmol. 1 mol%) of $CuCl_2$, 246 mg (0.78 mmol, 3 mol%) of TBAB and 10 ml CH_2Cl_2 were stirred at 25 °C. 3.4 g of TBHP (70% aq.; 26.2 mmol) and 0.2 g of *m*-$C_6H_4Cl_2$ (internal standard) were added and the mixture was stirred for 4 h. Reaction progress was monitored by GC/HPLC. Products were either identified by GCMS or purified from the organic phase by flash chromatography on silica (Merck, 0.040–0.063 mm) and identified by their ^1H NMR spectra, *e.g.* **4** was isolated in 75% yield and >99.5% purity using a gradient of petroleum ether : EtOAc from 100 : 0 to 90 : 10 with a drip rate of 90 drops min^{-1}. δ_H: 1.27 (9H, s), 1.7–1.82 (2H), 1.93 (1H, m), 2.33 (1H, m), 2.58–2.9

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† We thank a referee for this suggestion.

(2H), 5.46 (1H, t), 7.1–7.6 (4H). Good agreement was found with lit. values.[22]

Experimental procedure for kinetic studies

Example: 1.88 g (15.4 mmol) of **1**, 26 mg (0.15 mmol, 1 mol%) of $CuCl_2$, 90 mg (0.28 mmol, 1.9 mol%) of TBAB, 0.5 g of *m*-$C_6H_4Cl_2$ (internal standard) and 18 ml CH_2Cl_2 were mechanically stirred (300 rpm) at 25 °C for 24 h. Reaction progress was monitored by GC. The following parameters were studied: substrate concentration (5 expts., with [**1**] from 0.19 to 3.08 M); $CuCl_2$ amount (7 expts., with 0, 0.5, 1, 2, 3, 4 and 8 mol% of $CuCl_2$); TBAB amount (8 expts., with 0, 1, 2, 3, 4, 5, 6 and 8 mol% of TBAB); stirring rate (7 expts., at 0, 180, 270, 480, 584, 680 and 820 rpm); and temperature (4 expts. at 1, 11, 28 and 39 °C). The best fit ($r^2 = 0.993$ for 8 data points) was obtained with eqn. (2) (*vide infra*).

The derivation of eqn. (2)

Assuming that the oxidation of **1** and the catalyst deactivation are both first-order reactions, the following rate laws apply: eqn. (12) and (13), where [A] is the concentration of the substrate at time t, a is the activity of the catalyst, k_r is the reaction rate constant with no deactivation and k_d is the catalyst deactivation rate constant.

$$-r_A = \frac{-d[A]}{dt} = k_r[A]a \tag{12}$$

$$\frac{-da}{dt} = k_d a \tag{13}$$

Likewise, the change in the concentration of the substrate with time is given by eqn. (14) and (15), where N_A is the number of moles of A, V is the reaction volume, W is the weight of the catalyst, and k is the reaction rate constant with the deactivation taken into account.

$$\frac{-d[A]}{dt} = \frac{-1}{V}\frac{dN_A}{dt} \tag{14}$$

$$\frac{-d[A]}{dt} = \frac{W}{V}\left(\frac{-1}{W}\frac{dN_A}{dt}\right) = k[A]a \tag{15}$$

Integration of eqn. (13) gives eqn. (16), where a_0 is the activity of the catalyst at time $t = 0$ (it is assumed that $a_0 = 1$). Substituting eqn. (16) into eqn. (15) gives, after integration, eqn. (17) for the reaction at time t, and eqn. (18) for the reaction at time $t = \infty$. Simple mathematical operations lead from eqn. (17) and (18) to eqn. (2).

$$a = a_0 \exp(-k_d t) \tag{16}$$

$$\ln\frac{[A]_0}{[A]} = \frac{k}{k_d}[1 - \exp(-k_d t)] \tag{17}$$

$$\ln\frac{[A]_0}{[A]_\infty} = \frac{k}{k_d} \tag{18}$$

CAUTION! Although relatively safe to work with, TBHP, like almost all substances containing peroxidic bonds, should be handled cautiously. Concentrations above 95% purity should be avoided. Containers should be kept at 5–10 °C, to avoid layer separation. Strong acids should not be added to high-strength TBHP solutions. Extreme care should be taken when adding metal catalysts (we have had a minor explosion when adding $RuCl_3$ to a 70% TBHP soln). Small-scale reactions are preferable.

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