

Copper(I)-induced activation of dioxygen for the oxidation of organic substrates under mild conditions. An evaluation of ligand effects

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Abstract

Under the appropriate reaction conditions and stoichiometries the combination of a Cu(I) complex, *t*-BuOOH and molecular oxygen generates a catalyst that is capable of oxidizing alkanes, alkenes, alcohols and triphenyl phosphine under one atmosphere oxygen pressure and at room temperature. Particularly impressive is the performance of those catalysts over substrates containing allylic methylenes in terms of both reaction efficiencies and selectivities. For instance, for ethylbenzene the system 3.5 mM/*t*-BuOOH 10 mM; O₂ 1 atm/PhCH₂Me 1 M in ac:py (1:2) as the solvent forms 57.7 mM acetophenone. Cyclohexene under similar reaction conditions yields 85.4 mM 2-cyclohexene-1-one and 3.5 mM 2-cyclohexene-1-ol. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Mononuclear Cu(I) complexes; Organic substrates; Dioxygen; Oxygen activation; Hydrogen peroxide; *t*-Butylhydroperoxide; Catalytic oxidations

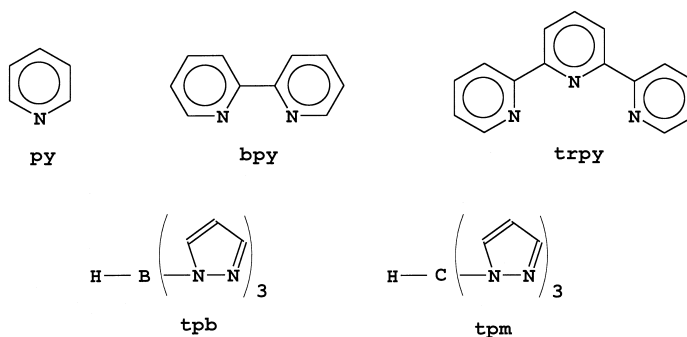
1. Introduction

Oxygen activation through transition metal complexes under mild conditions is a very active field of research due to its interest to both bioinorganic chemists and the technological world [1–11]. Elucidation of oxidation reaction mechanisms catalyzed by oxygenase non-haem type of metalloenzymes is still a major challenge in the field of oxidation chemistry. On the other hand, the abundance of hydrocarbons in nature allows them to be used as convenient industrial and chemical feedstocks. Therefore it is of primary importance to unfold the different parameters that govern system performance in order to establish successful models.

There have been previous reports on oxygen activation using non-porphyrinic ligands by several groups [12–18] aiming to model non-haem type of proteins using different metal complexes under mild conditions. Most notably Barton's group has developed systems that use Fe(II) and Fe(III) metal complexes within the so-called Gif chemistry [14–16].

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In the present report we describe the performance of Cu(I) complexes, which have been much less used, containing different ligands in order to evaluate ligand effects over system performance. The following chart shows the chosen ligands:



where py stands for (pyridine), bpy (2,2'-bipyridine), trpy (2,2':6',2''-terpyridine), tpb (tris(1-pyrazolyl)borate) and tpm (tris(1-pyrazolyl)methane). Their Cu(I) complexes $[\text{Cu}^{\text{I}}(\text{py})_4]^+$ **1**, $[\text{Cu}^{\text{I}}(\text{py})(\text{tpm})]^+$ **2**, $[\text{Cu}^{\text{I}}(\text{py})(\text{tpb})]$ **3**, $[\text{Cu}^{\text{I}}(\text{bpy})_2]^+$ **4** and $[\text{Cu}^{\text{I}}(\text{py})_2(\text{trpy})]^+$ **5** have been tested as oxygen activators for the oxidation of a variety of substrates.

2. Experimental

2.1. Equipment

The reaction products were separated and identified with a Shimadzu GC-17A gas chromatograph equipped with a Trb-5 capillary column (cross-linked methyl–silicone–gum phase, 30 m \times 0.25 mm i.d.) and by gas chromatography–mass spectrometry, Hewlett-Packard 5790A Series gas chromatograph with a mass-selective detector. UV-Vis spectroscopy was performed in a diode array HP-89532A-UV-Vis with 1 cm quartz cells.

Cyclic voltammetric experiments were performed in a PAR 263A EGandG potentiostat using a three electrode cell. Glassy carbon disk electrodes (1.5 mm diameter) from BAS were used as working electrode, platinum wire as auxiliary and SSCE as the reference electrode. All cyclic voltammograms presented were recorded at 100 mV/s scan rate under either nitrogen or argon atmosphere. The complexes were dissolved in previously degassed ac:py (1:2) as the solvent, containing the necessary amount of (*n*-Bu)₄NPF₆ to yield a 0.1 M ionic strength solution. The concentration of the complexes were approximately 5 mM.

2.2. Chemicals and reagents

The reagents for the investigations were of the highest purity commercially available and were used without further purification. Burdick and Jackson 'distilled in glass' grade pyridine (py, 0.007% H₂O), acetonitrile (MeCN, 0.002% H₂O) and glacial acetic acid (HOAc, ACS grade, Fischer) were used as solvents.

All the ligands used in this work are commercially available from Aldrich except tpm that was prepared according to literature procedures [19].

2.3. $Cu^I(CH_3CN)_4ClO_4$

This complex was prepared by dissolution of Cu_2O with $HClO_4$ (0.2 M) in acetonitrile [20].

2.4. $Cu(I)$ complexes

The $Cu(I)$ complexes **1–5** were prepared in situ by dissolving $[Cu^I(CH_3CN)_4]ClO_4$ in a ac:py (1:2) and adding stoichiometric amounts of the corresponding ligand under either nitrogen or argon atmosphere.

3. Methods

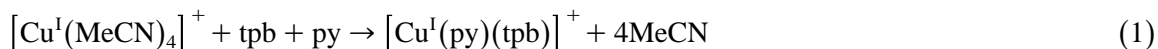
The investigation of the $HOOH$ and t -BuOOH activation by the $Cu(I)$ complexes (5 mM) used 7 ml solutions that contained 1 M substrate in the appropriate solvent mixture. Hydrogen peroxide (30% in water) or t -BuOOH (5.5 M in 2,2,4-trimethylpentane) were injected to give the desired concentration. After 24 h reaction time under constant stirring at room temperature ($24 \pm 2^\circ C$) under N_2 or O_2 (1 atm), samples of the reaction solution were injected into a capillary-column gas chromatograph for analysis. Product species were characterized by GC retention times when the product species obtained were commercially available and by GC–MS. Reference samples were used to produce standard curves for the quantitative analysis. The concentration of the products obtained in each case were determined with respect to the naphthalene concentration (15 mM) that was always added to the reaction mixtures as an internal standard.

The experiments were designed to be limited by $HOOH$ or t -BuOOH in order to evaluate reaction efficiency with respect to them and also to minimize secondary products.

4. Results

4.1. Synthesis and characterization of the $Cu(I)$ catalysts

Complexes **1–5** were prepared in situ by mixing equimolecular amounts of the desired ligand with $[Cu^I(MeCN)_4] (ClO_4)$ in 2:1 ac:py (acetonitrile:pyridine) as the solvent. For the tpb ligand the reaction can be written as follows,



The resulting mononuclear complexes were characterized by UV-Vis spectroscopy and cyclic voltammetry. Complexes **1–4** present a tetrahedral type of coordination around the $Cu(I)$ metal center [21]. A five coordination is expected for **5**, according to the literature [22] and our experimental results, due to the meridional type of coordination imposed by the trpy ligand.

Complexes **1–5** are featureless in the visible region but they highly absorb in the UV region (below 480 nm) as expected for MLCT type of bands and for $\pi - \pi^*$ aromatic ligand transitions.

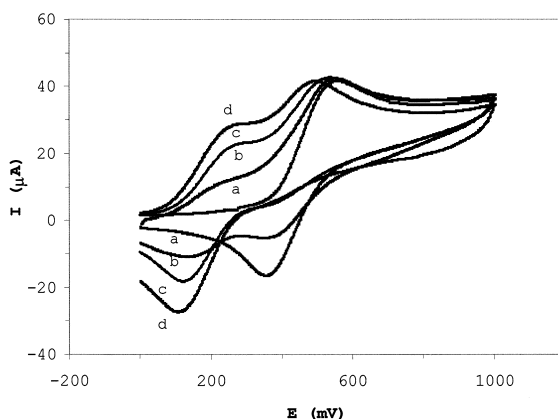


Fig. 1. Cyclic voltammograms of: (a) 0.5 mM $[\text{Cu}^{\text{I}}(\text{py})_4]^+$ complex in pure pyridine; (b) (a) + 0.25 equivalents of the trpy ligand; (c) (a) + 0.75 equivalents of trpy; (d) (a) + 1 equivalent of trpy. Working conditions are described in the Section 2.

Cyclic voltammetric experiments show that complexes **1–4**, exhibit a single chemically reversible and electrochemically pseudoreversible wave with $E_{1/2}$ values ranging from 313 to 402 mV (ΔE values range from 200 mV for **2** up to 318 mV for **4**, see Table 3) which is assigned to the Cu(II)/Cu(I) redox couple. For the $[\text{Cu}^{\text{I}}(\text{py})_2(\text{trpy})]^+$ complex a second chemically irreversible oxidation process is observed (Fig. 1) at higher potentials which is assigned to the Cu(III)/Cu(II) redox couple.

Fig. 1 shows the cyclic voltammograms obtained when a sequential addition of trpy ligand (0.25, 0.75 and 1.0 equivalents) is added to the $[\text{Cu}^{\text{I}}(\text{py})_4]^+$ complex using neat pyridine as the solvent. The experiment unambiguously demonstrate that complex **5** is progressively formed at the expenses of **1** and that after 1 equivalent addition of trpy, only complex **5** is observed with complete elimination of complex **1**. The $[\text{Cu}^{\text{I}}(\text{py})_2(\text{trpy})]^+$ complex now remains perfectly stable under the present system conditions. Further support for the stability of complex **2–5** in our system conditions comes from the strong formation constants displayed by this type of bidentate and tridentate ligands with Cu(I) [23]. (For similar type of complexes Lei and Anson [24] have reported that the chemical and electrochemical results obtained isolating first the metal complexes as salts and then dissolving them into the solution were identical to those of the in situ generation).

The formal $E_{1/2}$ redox potentials for the Cu(II)/Cu(I) couple decreases as the π -acceptor character of the ligand increases. This is in agreement with a strong dependence of the Cu(II)/Cu(I) couple with σ type of electron density, a fact that had been previously observed in other transition metal complexes [25]. The $[\text{Cu}^{\text{I}}(\text{py})_2(\text{trpy})]^+$ complex ends up with the lowest $E_{1/2}$ as a result of the latter and also due to the presence of one more N-donor bonded to the copper metal center. This in turn favors the accessibility of the Cu(III) higher oxidation state which is only observed for the trpy complex **5**. The five coordination in this complex is also supported by the fact that the trpy complex by far has the lowest ΔE . This in turn suggests that the Cu(II)/Cu(I) electrochemical quasireversibility of complexes **1–4** might be caused by the formation of a pentacoordinate Cu(II) species.

4.2. The oxidation of ethylbenzene by $[\text{Cu}^{\text{I}}(\text{py})(\text{tpb})]$, **3**

Complex **3** and PhCH_2Me were used as probe catalyst precursor and probe substrate respectively in order to optimize system conditions. Table 1 summarizes the results obtained when the optimization was carried out in terms of solvent, oxidant and [oxidant]/[catalyst] (Ox/Cat) ratio.

Table 1
The oxidation of ethylbenzene by the [Cu^I(py)(tpb)]⁺ (**3**) complex^a

Ent. no.	Solvent, ac:py	Oxidant	Products, mM (±0.5%) ^b	React. eff. ^c , % (no. of metal cycles)
1	1:4	10 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 15.3; PhCH(OH)Me, < 1.0	306 (3.1)
2	1:2	10 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 57.7; PhCH(OH)Me, < 1.0	1154 (11.5)
3	1:1	10 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 42.3; PhCH(OH)Me, < 1.0	846 (8.5)
4	2:1	10 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 33.4; PhCH(OH)Me, < 1.0	668 (6.7)
5	4:1	10 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 41.3; PhCH(OH)Me, < 1.0	826 (8.3)
6	4:1	O ₂	PhC(O)Me, 0.0; PhCH(OH)Me, 0.0	0 (0.0)
7	4:1	200 mM HOOH in N ₂	PhC(O)Me, 12.7; PhCH(OH)Me, 0.0	12.7 (2.5)
8	4:1	200 mM HOOH in O ₂	PhC(O)Me, 14.2; PhCH(OH)Me, 0.0	14.2 (2.8)
9	4:1	200 mM <i>t</i> -BuOOH in N ₂	PhC(O)Me, 14.1; PhCH(OH)Me, < 1.0; PhCH(OOtBu)Me, 19.3	23.7 (6.7)
10	4:1	200 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 83.9; PhCH(OH)Me, < 1.0	83.9 (16.8)
11	1:2	200 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 168.2; PhCH(OH)Me, 1.6; PhCH(OOtBu)Me, 1.7	169.9 (34.3)
12	1:2	100 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 141.9; PhCH(OH)Me, 1.4; PhCH(OOtBu)Me, 1.4	286.6 (28.9)
13	1:2	50 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 105.7; PhCH(OH)Me, 1.0	424.8 (21.3)
14	1:2	25 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 79.5; PhCH(OH)Me, < 1.0	636 (15.9)
15	1:2	10 mM <i>t</i> -BuOOH in O ₂	PhC(O)Me, 57.7; PhCH(OH)Me, < 1.0	1154 (11.5)
16	1:2	10 mM <i>t</i> -BuOOH in air	PhC(O)Me, 35.9; PhCH(OH)Me, < 1.0	718 (7.2)
17	1:2	10 mM <i>t</i> -BuOOH in N ₂	PhC(O)Me, 3.1; PhCH(OH)Me, < 1.0; PhCH(OOtBu)Me, 2.7	89 (1.2)

^aReaction conditions are described in Section 2. Typically, the required amount of **3** and the substrate (1 M) were dissolved in 7 ml of the desired solvent under N₂. Then the selected oxidant was added and the reaction allowed to react for a period of 24 h under constant magnetic stirring.

^bProduct solutions were analyzed by GC and GC–MS.

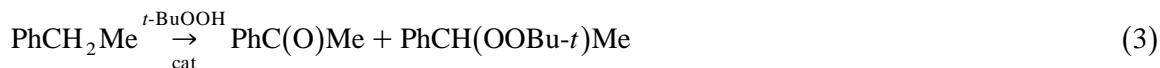
^cReaction efficiencies are reported with regard to HOOH or *t*-BuOOH. It is assumed that the formation of one molecule of PhC(O)Me requires 2 molecules of the oxidant whereas the formation of PhCH(OH)Me and PhCH(OOtBu)Me requires only one.

The solvents tested included methanol, acetic acid, acetonitrile, pyridine and mixtures of them. The best results were obtained when using different combinations of acetonitrile and pyridine (see entries 1–5, Table 1).

Complex **3** is not capable of activating dioxygen. However is capable of activating HOOH for the oxidation of ethylbenzene with low to moderate yields. The presence of an oxygen atmosphere does not significantly change product profiles or yields (see entries 7–8, Table 1).



Using *t*-BuOOH as the oxidant in the same conditions under a nitrogen atmosphere, generates similar amounts of acetophenone plus the *t*-butyl coupling product,



An spectacular increase in product yield and selectivity takes place when the former reaction is performed under an oxygen atmosphere (entries 9–10); 83.9 mM acetophenone is now formed as the only significant product with traces of the corresponding alcohol.

System performance was also studied as a function of the Ox/Cat ratio (see entries 11–15, Table 1). An exponential increase of the reaction efficiency is observed as the Ox/Cat ratio decreases from 40 down to 2 (Fig. 2).

It is important to point out the protocols used when running the systems. The best performance is obtained when *t*-BuOOH and O₂ are added simultaneously to the solution containing the complex and

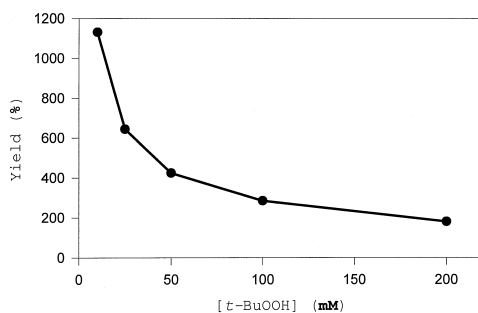


Fig. 2. System optimization. $[\text{Cu}^{\text{I}}(\text{py})(\text{tpb})]$ 5 mM/ t -BuOOH a mM; O_2 1 atm/PhEt 1 M/ac:py 1:2.

the substrate under inert atmosphere. Sequential addition of O_2 followed by the addition of hydroperoxide after one minute, causes a drop in reaction efficiencies of about 20% which is evidence against a one electron reduction of oxygen to superoxide, being the major pathway. A similar effect is observed when the sequential addition is carried out by adding first the hydroperoxide and a minute later oxygen.

Replacement of the oxygen atmosphere by air produces a drop of reaction efficiencies of 36% as shown on entries 15–16 of Table 1 leaving the selectivity unchanged.

4.3. The oxidation of organic and inorganic substrates by $[\text{Cu}^{\text{I}}(\text{py})(\text{tpb})]$, **3**

Table 2 summarizes the product distribution and reaction efficiencies for different substrates including alkanes, alkenes, alcohols and triphenylphosphine that result from the catalytic activation of dioxygen using **3**, as the catalyst precursor under optimized conditions. It is interesting to underline the high selectivity and efficiencies obtained under this specific system conditions. Particularly impressive is the performance of the system, **3** 5 mM/ t -BuOOH 10 mM; O_2 1 atm/PhCH₂Me 1 M in ac:py (1:2) as the solvent forming 57.7 mM acetophenone as basically the only product,



This represents nearly 11 oxygen cycles with regard to the metal complex. When the $[\text{t-BuOOH}]$ is increased up to 100 mM, then 141.9 mM PhC(O)Me is formed, again with high selectivity, which

Table 2

Substrate oxidation by the system: $[\text{Cu}^{\text{I}}(\text{py})(\text{tpb})]$ 5 mM/ t -BuOOH a mM; O_2 1 atm/subs. 1 M/ac:py 1:2

Ent. no.	Substrate	a mM t -BuOOH	Products, mM	Reac. eff. %, (mc)
1	PhCH ₂ Me	10	PhC(O)Me, 57.7; PhCH(OH)Me, <1.0	1154 (11.5)
2		100	PhC(O)Me, 141.9; PhCH(OH)Me, 1.4; PhCH(OOtBu)Me, 1.4	286.6 (28.9)
3	c -C ₆ H ₁₂	10	c -C ₆ H ₁₀ (O), 8.5; c -C ₆ H ₁₁ OH, 1.3	183 (2.0)
4		100	c -C ₆ H ₁₀ (O), 23.0; c -C ₆ H ₁₁ OH, 2.6; c -C ₆ H ₁₁ OOtBu, 0.8	49.4 (5.3)
5	Adamantane	100	ada-1-o1, 18.1; ada-2-o1, 0.3; ada-2-ona, 6.5	31.4 (5.0)
6	c -C ₆ H ₁₀	10	c -C ₆ H ₈ (O), 85.4; c -C ₆ H ₉ OH, 3.5	1743 (17.8)
7		100	c -C ₆ H ₈ (O), 234; c -C ₆ H ₉ OH, 24.0; c -C ₆ H ₉ OOtBu, 0.4	492.4 (51.7)
8	PhCH(OH)Me	10	PhC(O)Me, 24.5	245 (4.9)
9	PhCH ₂ OH	10	PhC(O)H, 23.9	239 (4.8)
10		100	PhC(O)H, 87.9	87.9 (17.6)
11	^a PPh ₃	50	(O)PPh ₃ , 100	200 (20.0)

^aPPh₃ concentration is 0.1 M.

Table 3

Dioxygen oxidation of ethylbenzene through Cu(I) complexes and their electrochemical properties^a

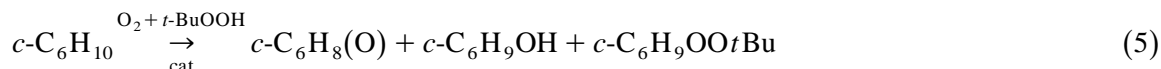
Complex	[PhC(O)Me], mM (±0.5%)	$v_i^b \times 10^6$ (M/s)	$E_{1/2}$ (V) ^c vs. SSCE (ΔE in mV)
[Cu ^I (py) ₄] ⁺ , 1	29.0	13.9	0.390 (208)
[Cu ^I (py)(tpm)] ⁺ , 2	31.9	12.8	0.370 (200)
[Cu ^I (py)(tpb)], 3	57.7	3.9	0.402 (216)
[Cu ^I (bpy) ₂] ⁺ , 4	32.7	9.5	0.313 (318)
[Cu ^I (py) ₂ (trpy)] ⁺ , 5	50.8	7.2	0.142 (156)

^aThe reactions were carried out under the following system conditions, complex X 5 mM/*t*-BuOOH 10 mM; O₂ 1 atm/PhCH₂Me 1 M in ac:py (1:2).

^b v_i : Initial rates of acetophenone formation were obtained from product profile graphs.

^c $E_{1/2}$ redox potentials were calculated from cyclic voltammetry experiments in ac:py (1:2) as the solvent. $\Delta E = E_{p,a} - E_{p,c}$.

represents more than 28 metal cycles. The best reaction efficiencies are obtained when using cyclohexene as the substrate although the selectivity is slightly lower compared to ethylbenzene. The **3** 5 mM/*t*-BuOOH 10 mM; O₂ 1 atm/*c*-C₆H₁₀ 1 M in ac:py (1:2) system yields 85.4 mM 2-cyclohexene-1-one and 3.5 mM 2-cyclohexene-1-ol representing a reaction efficiency of 1743%, with regard to *t*-BuOOH, and 17.8 metal cycles. Increasing the [*t*-BuOOH] ten times reduces the reaction efficiency by 3.5 but increases the number of metal cycles by nearly 3 times. The increase of the [*t*-BuOOH] also produces a significant decrease on the selectivity; the ketone/alcohol ratio for the 5/10 (Cat/Ox) is 24.4 whereas for the 5/100 is only 9.75. Besides, for the high Ox/Cat ratio, the *t*-butyl coupling product (*c*-C₆H₉OOtBu) is also detected



The system also oxidizes saturated alkanes like *c*-hexane and adamantane forming the corresponding ketones and alcohols. In this case, the reaction efficiencies and selectivities are substantially lower (see entries 3–5, Table 2) manifesting the difficulty of the present systems to oxidize non-activated saturated alkanes.

Alcohols can also be oxidized by the system with moderate to high reaction efficiencies (see entries 8–10, Table 2). The oxidation of *sec*-phenethyl alcohol gives acetophenone whereas benzylalcohol forms benzaldehyde. The amount of acetophenone generated by *sec*-phenethyl alcohol is nearly five

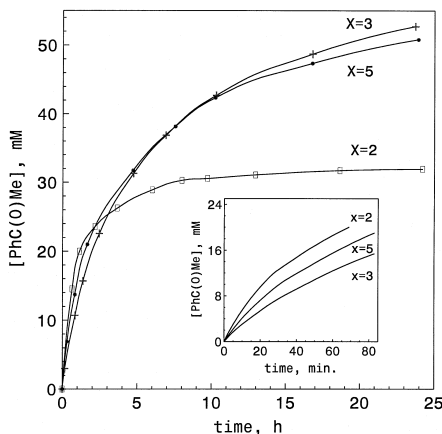


Fig. 3. Time course of acetophenone formation for the systems: Complex X 5 mM/*t*-BuOOH 10 mM; O₂ 1 atm/PhCH₂Me 1 M in py:ac (2:1) at 24°C with X = 2, 3 and 5. The inset shows the first 60–80 min reaction time.

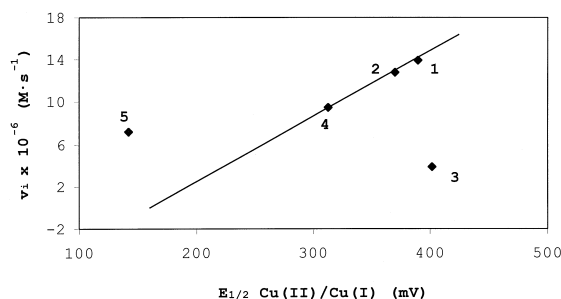


Fig. 4. $E_{1/2}$ Cu(II)/Cu(I) redox potentials vs. v_i for the Cu(I) complexes 1–5.

times lower than the generated from ethylbenzene under the same system conditions (entries 1,8; Table 2). This result clearly indicates that in our systems, alcohols are not intermediates for the formation of acetophenone.

Finally PPh_3 is quantitatively oxidized to its oxide (entry 11, Table 2). In this experiment the $[\text{PPh}_3]$ is only 0.1 M; higher substrate concentrations produce lower yields due to the coordination of the phosphine into the copper metal center which deactivates the catalyst.

4.4. The ligand effects on the oxidation of ethylbenzene

The oxidation of ethylbenzene was performed with Cu(I) complexes containing different type of ligands. Table 3 shows the concentration of acetophenone obtained when using complexes 1–5 as catalysts, all under the same reaction conditions. Together with the acetophenone yield produced, Table 3 also contains electrochemical information regarding the Cu(I) complexes and the calculated initial PhC(O)Me formation rates. Those rates have been calculated from $[\text{PhC(O)Me}]$ vs. time graphs like the ones depicted in Fig. 3.

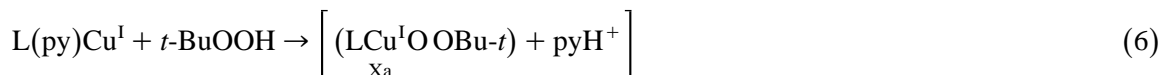
The results displayed in Table 3 clearly show a strong dependence of the catalyst performance with regard to the ligand attached to the metal center. It can be observed that, except for 3, there is an inverse correlation of v_i vs. overall yield of acetophenone formation. This can be understood upon examination of the product profile as a function of time graphs (Fig. 3). It turns out that the systems with higher v_i also deactivate sooner and finally end up giving lower yields.

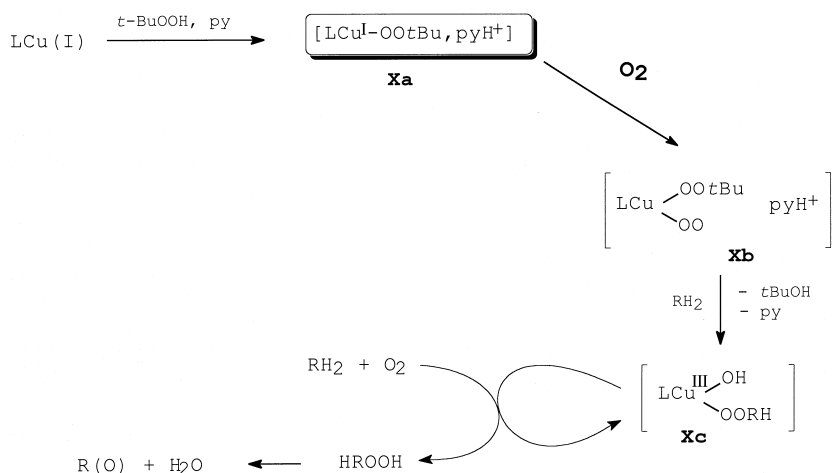
Table 3 also exhibits a direct correlation of v_i vs. $E_{1/2}$ as plotted in Fig. 4 (except for 3), indicating that species with easily accessible higher oxidation states have lower v_i . This suggests the presence of an intermediate reactive species bearing a high oxidation state. Complex 3 being an exception, which can be attributed to anionic nature of the *tpb* ligand with regard to the rest of the ligand series which are neutral. Complex 5 has a much higher v_i than expected as a consequence of the influence that the meridional *trpy* ligand exerts into the stability of the intermediate reactive species.

5. Discussion

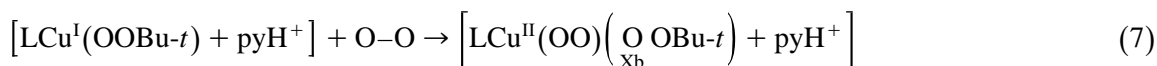
5.1. The proposed reaction mechanism

Mononuclear Cu(I) complexes 1–5 are inactive with regard to oxygen activation. However, reaction of complexes 1–5 with *t*-BuOOH produces an intermediate Xa (X = 1, 2, 3, 4 or 5),

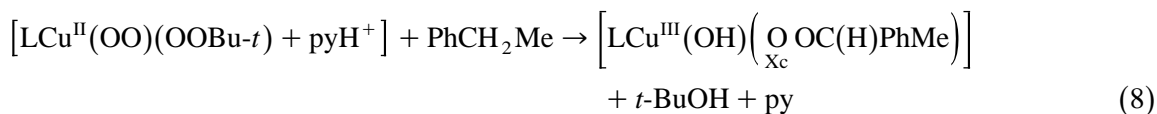




that reacts very fast with oxygen to form species Xb,



Species Xb represents an oxygenated Fenton type of reagent that reacts with organic substrates. Xb is now capable of abstracting a H atom, for instance from ethylbenzene forming a radical ($\text{R}\cdot$; $\text{PhC}\cdot(\text{H})\text{Me}$) that is trapped by the bound dioxygen to give species Xc.



Xc is also capable of abstracting a H-atom from ethylbenzene producing the corresponding hydroperoxide, ROOH, that decomposes to acetophenone and water yielding again Xc ready for the next cycle (see Scheme 1).

5.2. First step: the formation of Xa

From the early work of Halperin and Taube [26], there is mounting evidence that the *major* chemistry of hydroperoxides with transition metal complexes in organic solvents is nucleophilic substitution or addition rather than generation of free hydroxyl or alkoxy radicals [27–33] as shown in Eq. (6).

Further evidence is obtained here, where no radically derived coupling products like R–py, R–R or ROOR are detected at all in either N_2 or O_2 atmospheres and in different Ox/Cat ratios. For instance, in the present system conditions, under nitrogen atmosphere adamantane gave only the corresponding alcohol and ketone species whereas with free $t\text{-BuO}\cdot$ radicals it yields mainly pyridyladamantyl coupling products (65.6% of the overall products) [34].

Electrochemical data also provides compelling evidence that the following reaction does not significantly proceed under our system conditions,



since ligands which form Cu(I) complexes with the lower formal $E_{1/2}$ Cu(II)/Cu(I) redox potentials would be expected to have the higher initial rate constants and we observe just the opposite [35] (see Table 3). This suggests that the reactive intermediates that interact with the substrates have oxidation states higher than Cu(I).

A significant increase on reaction efficiencies is observed when the ionic strength of the medium is progressively increased up to $\mu = 0.4$ M (n -Bu)₄NPF₆, for Cu catalysts containing neutral ligands (**1**, **2**, **4** and **5**). This result is also consistent with the cationic nature of their proposed reactive intermediates Xa, Xb and Xc.

5.3. The formation of Xb and Xc

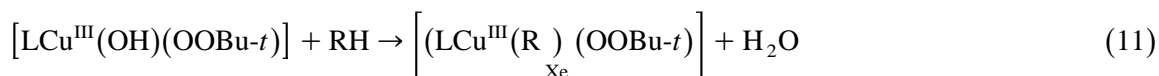
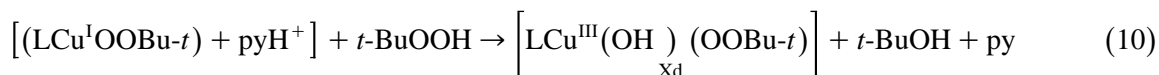
In the presence of an oxygen atmosphere Xa reacts rapidly with oxygen forming Xb, formally a Cu(II) complex containing a superoxide ligand. Related oxygenation reactions with mononuclear pyridyl Cu(I) complexes at 298 K have rate constants close to 10^8 M/s [36]. Once Xb is formed it can react with the substrate to form Xc. Those species have been proposed as reactive intermediates instead of the formation of free t -BuO· radicals based on the absence of typical free radical coupling products mentioned in Section 5.2.

Similar intermediates have been recently proposed by Sawyer [3] and Sawyer et al. [12] for related Cu(I) complexes and by Kim et al. [37] for Fe(III) complexes based on electrochemical and electrospray ionization mass spectral experiments, respectively.

Xc has the thermodynamic power to abstract a hydrogen atom from ethylbenzene ($\Delta H_{\text{DBE}} = 85$ kcal/mol) and cyclohexene ($\Delta H_{\text{DBE}} = 87$ kcal/mol) to generate the corresponding hydroperoxide ROOH, that finally yields ketone and water, but it can not perform a similar reaction with saturated hydrocarbons like for instance cyclohexane ($\Delta H_{\text{DBE}} = 95.5$ kcal/mol) [38].

5.4. Other pathways: the formation of ROOBu-*t* and ROH

Under nitrogen atmosphere (entries 9, 17; Table 1) or under a high ratio Ox/Cat (entry 7; Table 2) significant amounts of the t -butyl coupling product (t -BuOOCH(Me) (Ph), t -BuOOC₆H_{9-c}) are being formed. This can be rationalized by assuming the existence of a parallel pathway that competes with the dioxygen pathway shown in Scheme 1, and that is favored in the absence of the latter.



Finally Xe collapses forming ROOBu- t and the initial Cu(I) complex.

The existence of this anaerobic parallel pathway is further corroborated by a competitive substrate experiment whose results are described in Table 4.

A measure of the influence of C–H bond energies on reaction probabilities is the ratio of the ketone product per methylenic carbon (CH₂) for ethylbenzene ($\Delta H_{\text{DBE}} = 85$ kcal/mol) and cyclohexane ($\Delta H_{\text{DBE}} = 95.5$ kcal/mol),

$$\{R\} = \left[k_{\text{PhCH}_2\text{Me}} / (k_{\text{c-C}_6\text{H}_{12}} / 6) \right] \quad (12)$$

From Table 4, it can be observed that $\{R\}$ values for the formation of ROOR' remain relatively unaffected by the presence or absence of an oxygen atmosphere but dramatically change for the

Table 4

Cyclohexane vs. ethylbenzene competitive substrate oxidations. System conditions: $[\text{Cu}^{\text{I}}(\text{py})(\text{tpb})]$ 5 mM / *t*-BuOOH 100 mM / *c*-C₆H₁₂ 0.5 mM; PhCH₂Me 0.5 mM / ac:py 1:2 under oxygen and nitrogen atmospheres

	O ₂			N ₂		
	alc	ket	ROOBu- <i>t</i>	alc	ket	ROOBu- <i>t</i>
<i>c</i> -C ₆ H ₁₂	1.4	12.9	0.4	–	3.0	8.4
PhCH ₂ Me	0.6	84.9	0.9	–	8.7	18.3
{ <i>R</i> } ^a	2.6 ^b	39.5 ^b	13.5	–	17.4	13.1

^a{*R*} = $[k_{\text{PhCH}_2\text{Me}} / (k_{c\text{-C}_6\text{H}_{12}} / 6)]$, relative reactivity per (CH₂) for PhCH₂Me vs. *c*-C₆H₁₂.

^bSimilar {*R*} values are obtained for the 10/5 (Ox/Cat) ratio case.

formation of ketone. Thus the formation of ROOR' takes place through the same reaction pathway which is independent of the [O₂]. In sharp contrast, for the formation of ketone, {*R*} values increase from 17.4 till 39.5 upon changing from N₂ to O₂ atmosphere, respectively, which clearly indicates the presence of different reaction pathways.

Finally, small amounts of alcohol can be obtained by slow deactivation of the cycling species Xc, forming both ketone and alcohol.

In summary, the combination of a Cu(I) complex **1–5**, and *t*-BuOOH in the appropriate conditions activates molecular oxygen for the oxidation of a variety of organic and inorganic substrates including alkanes, alkenes, alcohols and triphenylphosphine. Those reactions take place under very mild conditions: at room temperature and under 1 atm pressure of oxygen or air. The system performance is highly dependent on the ligands attached to the metal center and can be rationalized in terms of electronic and geometric effects induced by the nature of the ligand. Cyclohexene and ethylbenzene are exceptional substrates in terms of both absolute reaction efficiencies and absolute concentrations obtained of 2-cyclohexene-1-one and acetophenone, respectively.

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