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ARTICLE

New aqua-soluble dicopper(II) aminoalcoholate cores for mild and water-assisted catalytic oxidation of alkanes

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Tiago A. Fernandes, Carla I. M. Santos, Vânia André, Sara S. P. Dias, Marina V. Kirillova*, Alexander M. Kirillov*

Two new dicopper(II) aminoalcoholate compounds, namely a discrete 0D complex $[\{Cu(Hdea)(H_2dea)\}_2(\mu_2\text{-}H_2pma)]\cdot 3H_2O$ (**1**) and a 1D coordination polymer $[Cu_2(\mu_2\text{-}H_2tea)_2(\mu_2\text{-}nda)]_n\cdot 2nH_2O$ (**2**), were self-assembled from copper(II) nitrate, aminoalcohol {diethanolamine (H_2dea) or triethanolamine (H_3tea)} and carboxylic acid {pyromellitic (H_4pma) or 2,6-naphthalenedicarboxylic (H_2nda)} building blocks. Both products were isolated as stable and water-soluble microcrystalline solids and fully characterized by IR spectroscopy, ESI-MS(±), elemental analysis and single-crystal X-ray diffraction, revealing distinct types of dicopper(II) units. The structures of **1** and **2** are further extended by intermolecular hydrogen bonds giving rise to 3D or 2D H-bonded nets with the **pcu** or **sql** topology, respectively. Both compounds act as efficient pre-catalysts for the mild homogeneous oxidation, by aqueous H_2O_2 in $MeCN/H_2O$ medium, of different cycloalkanes to the corresponding cyclic alcohols and ketones, which are obtained in up to 34% total yields (based on alkanes). The influence of various reaction parameters such as amount and type of pre-catalyst and acid promoter, solvent composition and substrate scope were investigated, also showing that the oxidation of cycloalkanes and the activity of a catalytic system can be restarted upon addition of new portions of oxidant and substrate. Besides, an unusual promoting role of water was found when using both pre-catalysts **1** and **2**. The bond-, regio- and stereo-selectivity parameters were established using different alkane substrates, supporting a free radical oxidation mechanism. The model $\mathbf{1}/H^+/H_2O_2$ and $\mathbf{2}/H^+/H_2O_2$ solutions were investigated by ESI-MS(±), allowing to propose some possible catalytically active species.

Introduction

The search for new and highly efficient transition metal catalytic systems and single-pot protocols for the selective oxidation of alkanes under mild conditions continues to attract a high current interest in modern catalysis.[1–5] Although alkanes are naturally highly abundant, relatively cheap and thus very attractive substrates for a direct synthesis of different added value oxidation products, the intrinsic inertness of these hydrocarbons limits their wide usage as raw materials for the atom efficient and selective oxidation processes undergoing under mild temperatures and pressures.[4–8] Nevertheless, the combination of a certain metal-complex-catalyst and appropriate oxidant, along with well-adjusted reaction parameters (e.g., temperature, solvent, relative ratios of reagents and catalyst), can potentially lead to rather efficient catalytic systems and protocols for the mild oxidative functionalization of alkanes.[2,3,5,8–10]

In pursuit of our general research interest devoted to the design of different multicopper(II) complexes and coordination polymers with significance in oxidation catalysis,[10,11] the main objectives of the present study consisted in (1) the preparation of new aqua-soluble coordination compounds bearing distinct dicopper(II) cores based on aminoalcoholate and carboxylate blocks, and (2) the evaluation of their catalytic potential in the mild homogeneous oxidation of cycloalkanes to the corresponding alcohols and ketones. Diethanolamine (H_2dea) and triethanolamine (H_3tea) were selected as principal *N*,*O*-building blocks on account of their water-solubility and stability, low cost, coordination flexibility and recognized application in bio-inspired catalytic systems.[9,12] On the other hand, the obtained dicopper(II) aminoalcoholate derivatives can show some relevance to particulate methane monooxygenase (pMMO), a unique enzyme that not only possesses a multicopper active site with an *N*,*O*-environment, but is also capable of catalyzing the hydroxylation of alkanes.[13]

Bearing these points in mind, we report herein a simple aqueous-medium self-assembly synthesis, full characterization, and catalytic application of two new water-soluble dicopper(II) aminoalcoholate compounds (Scheme 1), a discrete 0D complex $[\{Cu(Hdea)(H_2dea)\}_2(\mu_2\text{-}H_2pma)]\cdot 3H_2O$ (**1**) and an

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Centro de Química Estrutural, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais, 1049-001 Lisboa, Portugal, Tel: 351 218419264;
E-mail: kirillova@tecnico.ulisboa.pt, kirillov@tecnico.ulisboa.pt

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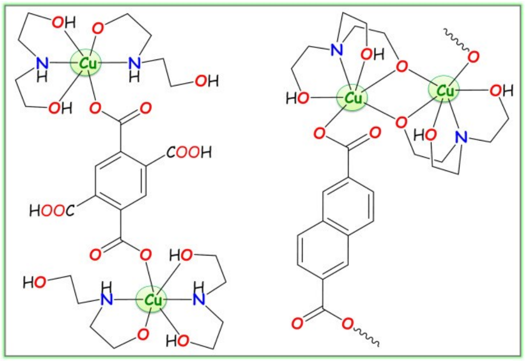
infinite 1D coordination polymer [$Cu_2(\mu_2$-$H_2tea)_2(\mu_2$-nda)]$_n$·$2nH_2O$ (**2**), derived from aminoalcohols (H_2dea or H_3tea) and aromatic carboxylic acids of different size {pyromellitic (H_4pma) or 2,6-naphthalenedicarboxylic (H_2nda) acid}. Both compounds act as efficient pre-catalysts for the mild homogeneous oxidation, by H_2O_2 in aqueous MeCN medium, of different alkanes to the corresponding alcohols and ketones. The effects of various reaction parameters were investigated and discussed in detail.



Scheme 1. Structural formulae of compounds **1** (left) and **2** (right).

Experimental

Materials and methods

All chemicals were obtained from commercial sources and used as received. The synthetic work was performed in air and at room temperature (r.t., ~25 °C). C, H, and N elemental analyses were carried out by the Microanalytical Service of the Instituto Superior Técnico. Infrared spectra (4000–400 cm^{-1}) were recorded on a JASCO FT/IR-4100 instrument in KBr pellets (abbreviations: vs – very strong, s – strong, m – medium, w – weak, br. – broad, sh. – shoulder). ESI-MS(±) spectra were run on a LCQ Fleet mass spectrometer with an ESI source (Thermo Scientific), using ~10^{-3} M solutions of **1** and **2** or their model mixtures with HNO_3 and H_2O_2 in aqueous solution. Gas chromatography (GC) analyses were run on an Agilent Technologies 7820A series gas chromatograph (He as carrier gas) equipped with the FID detector and BP20/SGE (30 m × 0.22 mm × 0.25 μm) capillary column.

Synthesis and characterization of 1 and 2

[{Cu(Hdea)(H_2dea)}$_2$(μ_2-H_2pma)]·$3H_2O$ (**1**). To an aqueous solution (10 mL) of $Cu(NO_3)_2$·$2.5H_2O$ (1.00 mmol, 233 mg) were added dropwise an aqueous solution (2 mL) of diethanolamine (H_2dea; 2.0 mmol) and pyromellitic acid (127 mg, 0.50 mmol) in this order and with continuous stirring at room temperature. The obtained mixture was stirred for 2 h and then filtered off. The filtrate was left to evaporate in a beaker at ambient temperature. Blue crystals were formed in 1–2 weeks, then collected and dried in air to furnish compound **1** in ~60% yield (based on copper(II) nitrate). X-ray quality crystals of [{Cu(Hdea)(H_2dea)}$_2$(μ_2-H_2pma)]·2MeOH (**1'**) were obtained by diluting a part of filtrate with methanol, followed by a slow evaporation in air at room temperature. Compound **1** is moderately soluble in H2O ($S_{25°C}$ ~5 mg mL^{-1}). Anal. calcd (%) for **1**: $C_{26}H_{54}Cu_2N_4O_{19}$ (MW 852): C 36.66, H 6.15, N 6.58; found C 36.33, H 6.17, N 6.51. ESI-MS(±) (H_2O), MS(−): *m/z*: 797 [{Cu(Hdea)(H_2dea)}$_2$(Hpma)]$^-$, 585 [{Cu(Hdea)}$_2$(Hpma)]$^-$, 314 [Cu(Hpma)]$^-$. MS(+): *m/z*: 587 [{Cu(Hdea)}$_2$(H_3pma)]$^+$, 526 [Cu(H_2dea)$_2$(H_3pma)]$^+$. FT-IR (KBr): 3408 (s br) ν(H_2O/OH), 3187 (s) ν(NH), 2962 (w) and 2887 (w) ν(CH), 1573 (vs br) ν_{as}(COO), 1490 (m), 1426 (m), 1363 (m) and 1326 (m) νs(COO), 1139 (m), 1095 (m), 1067 (m), 1046 (m), 899 (w), 866 (w), 690 (m), 540 (m), and 459 (w) cm^{-1}.

[$Cu_2(\mu_2$-$H_2tea)_2(\mu_2$-nda)]$_n$·$2nH_2O$ (**2**). To an aqueous solution of $Cu(NO_3)_2$·$2.5H_2O$ (10 mL, 1.00 mmol, 233 mg) was added dropwise an aqueous solution (1 mL) of triethanolamine (H_3tea, 1.0 mmol) with continuous stirring at room temperature. Then, an organic linker, 2,6-naphthalenedicarboxylic acid (H_2nda; 108 mg, 0.50 mmol) and an aqueous solution of NaOH (3 mL, 3 mmol) were added to the reaction mixture. The resulting solution was stirred for 1 day and then filtered off. The filtrate was left to evaporate in a beaker at room temperature resulting in the formation of blue crystals (including those of X-ray quality) in 2–4 weeks. These were collected and dried in air to furnish the compound **2** in ~50% yield (based on copper(II) nitrate). Compound **2** is slightly soluble in H_2O ($S_{25°C}$ ~2 mg mL^{-1}). Anal. calcd for **2**: $C_{24}H_{38}Cu_2N_2O_{12}$ (MW 674): C 42.79, H 5.69, N 4.16; found: C 43.14, H 5.77, N 4.08. ESI-MS(+) (H_2O): *m/z*: 843 [$Cu_4(Htea)_4$ + H]$^+$, 633 [$Cu_3(Htea)_3$ + H]$^+$, 421 [$Cu_2(Htea)_2$ + H]$^+$. FT-IR (KBr): 3440 (s br) and 3200 (s br) ν(H_2O/OH), 2958 (w) ν_{as}(CH), 2903 (w) and 2868 (m) ν_s(CH), 1605 (w sh) and 1569 (s) ν_{as}(COO), 1496 (w), 1454 (w) and 1401 (vs) ν_s(COO), 1360 (s), 1197 (w), 1091 (s), 1054 (m), 1026 (w), 1003 (m), 906 (m), 792 (w), 766 (m), 636 (m), 573 (w), and 486 (m) cm^{-1}.

X-ray crystallography

Crystals of **1'** and **2** suitable for X-ray diffraction study were mounted with Fomblin© in a cryoloop. Data were collected on a Bruker AXS-KAPPA APEX II diffractometer with graphite-monochromated radiation (Mo Kα, λ=0.17073 Å) at 298 K. The X-ray generator was operated at 50 kV and 30 mA and the X-ray data collection was monitored by the APEX2 program.[14] All data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs.[14] SIR-97[15] and SHELXS-97[16] were used for structure solution and SHELXL-97[16] was applied for full matrix least-squares refinement on F^2. These three programs are included in the package of programs WINGX-Version 1.80.05.[17] Non-hydrogen atoms were refined anisotropically. A full-matrix least-squares refinement was used for the non-hydrogen atoms with anisotropic thermal parameters. All the hydrogen atoms were inserted in idealized positions and allowed to refine at the parent carbon or oxygen atom.

*Crystal data for **1'**:* $C_{26}H_{46}Cu_2N_4O_{16}$, M = 861.85, λ = 0.71073 Å (Mo-*K*α), T = 273(2) K, monoclinic, space group $P2_1/c$, a = 9.2907(5), b = 13.3305(6), c = 15.2281(7) Å, β = 107.358(2)°, V = 1800.11(15) Å^3, Z = 2, D_c = 1.590 g/cm^3, μ = 1.264 mm^{-1}, 60810 reflections collected, 6297 unique, $I > 2\sigma(I)$ (R_{int} = 0.0369), R_1 = 0.0524, wR_2 = 0.1587. *Crystal data for **2**:* $C_{12}H_{16}CuNO_5$, M = 335.82, λ = 0.71073 Å (Mo-$K\alpha$), T = 273(2) K, triclinic, space group P-1, a = 7.5973(6), b = 8.1060(6), c = 12.4901(12) Å, α = 89.576(3), β = 86.095(2), γ = 69.787(2)°, V = 720.03(10) Å^3, Z = 2, D_c = 1.540 g/cm^3, μ = 1.540 mm^{-1}, 24178 reflections collected, 2943 unique, $I > 2\sigma(I)$ (R_{int} = 0.0422), R_1 = 0.0316, wR_2 = 0.0786.

Oxidation of alkanes by H_2O_2

The alkane oxidation reactions were carried out in air atmosphere in thermostated glass reactors equipped with a condenser under vigorous stirring at 50 °C and using MeCN as solvent (up to 2.5 mL total volume). In a typical experiment, pre-catalyst **1** or **2** (5 μmol) and gas chromatography (GC) internal standard ($MeNO_2$, 25 μL) were introduced into MeCN solution, followed by the addition of an acid promoter (typically 0.05 mmol, optional) used as a stock solution in MeCN. The alkane substrate (1 mmol) was then introduced, and the reaction started upon addition of hydrogen peroxide (50% in H_2O, 5 mmol) in one portion. The reactions were monitored by withdrawing small aliquots after different periods of time, which were treated with PPh_3 (following a method developed by Shul'pin[18]) for reduction of remaining H_2O_2 and alkyl hydroperoxides that are typically formed as primary products in alkane oxidations. The samples were analyzed by GC using nitromethane as an internal standard. Attribution of peaks was made by comparison with chromatograms of authentic samples. Blank tests confirmed that alkane oxidations do not proceed in the absence of copper pre-catalyst.

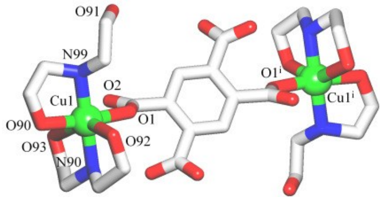
Results and discussion

Synthesis and structures of 1 and 2

The copper(II) compounds $[\{Cu(Hdea)(H_2dea)\}_2(\mu_2\text{-}H_2pma)]\cdot 3H_2O$ (**1**) and $[Cu_2(\mu_2\text{-}H_2tea)_2(\mu_2\text{-}nda)]_n\cdot 2nH_2O$ (**2**) were synthesized by a self-assembly protocol in H_2O solution at room temperature (~25 °C). Thus, the reaction of aqueous solution of $Cu(NO_3)_2\cdot 2.5H_2O$ with diethanolamine (H_2dea) as a main building block and pyromellitic acid (H_4pma) as an ancillary ligand, followed by subsequent crystallization (slow evaporation in air) resulted in the generation of a discrete dicopper(II) complex **1**. Single X-ray quality crystals of $[\{Cu(Hdea)(H_2dea)\}_2(\mu_2\text{-}H_2pma)]\cdot 2MeOH$ (**1'**) were obtained from a mother liquor of **1** (diluted by MeOH) and then used for structure determination. The treatment of copper(II) nitrate with triethanolamine (H_3tea) and 2,6-naphthalenedicarboxylic acid (H_2nda) and in the presence of NaOH as a pH-regulator, gave rise to the formation of a 1D coordination polymer **2**. Both compounds were isolated in good yields as blue and stable microcrystalline solids and characterized by IR spectroscopy, ESI-MS(±), elemental analysis, and single crystal X-ray diffraction. Both products **1** and **2** are relatively stable in aqueous medium (as confirmed by mass spectrometry data) and feature some solubility in water ($S_{25\,°C}$ ~2–5 mg mL^{-1}), thus making them suitable for the application in homogeneous aqueous medium catalytic transformations.[12c,12d,19]

The discrete 0D structure of **1'** is composed of a neutral dicopper(II) $[\{Cu(Hdea)(H_2dea)\}_2(\mu_2\text{-}H_2pma)]$ unit (Fig. 1a) and two methanol molecules of crystallization. The Cu_2 unit comprises two symmetry equivalent $\{Cu(Hdea)(H_2dea)\}^+$ moieties that are interlinked by the μ2-bridging doubly protonated pyromellitate(2–) spacer. The six-coordinate Cu1 atoms display a distorted octahedral $\{CuN_2O_4\}$ environment with the equatorial positions taken by two nitrogen (N1 and N2, mutually *trans*) and one oxygen (06) atoms of diethanolamine ligands and a carboxylate O1 atom of $\mu_2\text{-}H_2pma$ [Cu1–N1 2.019(3), Cu1–N2 2.0171(18), Cu1–O6 1.990(2), Cu1–O1 1.9615(17) Å]. The axial sites are occupied by the O5 and O7 atoms belonging to HO groups of the H_2dea moiety, with the elongated Cu–O distances of 2.376(3) and 2.744(4) Å, respectively; these are still well below the sum of the van der Waals radii of Cu and O atoms [~2.92 Å].[20] The Cu1···Cu1^i separation between the adjacent $\{Cu(Hdea)(H_2dea)\}^+$ moieties is 11.1250(7) Å. Extensive hydrogen bonding pattern between the $[\{Cu(Hdea)(H_2dea)\}_2(\mu_2\text{-}H_2pma)]$ units and involving MeOH molecules of crystallization leads to a 0D→3D extension of the structure into an intricate 3D H-bonded network. This network can be topologically classified[21] as a uninodal 6-connected underlying net with the **pcu** topology (Fig. 1b).

(a)



(b)

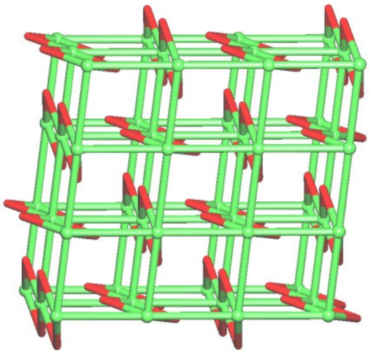


Fig. 1. Structural fragments of **1'**: (a) dicopper(II) $[\{Cu(Hdea)(H_2dea)\}_2(\mu_2\text{-}H_2pma)]$ unit with atom labelling scheme; (b) topological representation of the 3D H-bonded underlying net showing a uninodal 6-connected framework with the **pcu** topology and point symbol of ($4^{12}.6^3$). Further details: (a) H atoms are omitted for clarity, symmetry code: (i) –*x*, 1–*y*, 1–*z*, color codes: Cu (green balls), O (red), N (blue), C (gray); (b) centroids of 6-connected $[\{Cu(Hdea)(H_2dea)\}_2(\mu_2\text{-}H_2pma)]$ nodes (green balls), centroids of 2-connected MeOH linkers (red); view along the *a* axis.

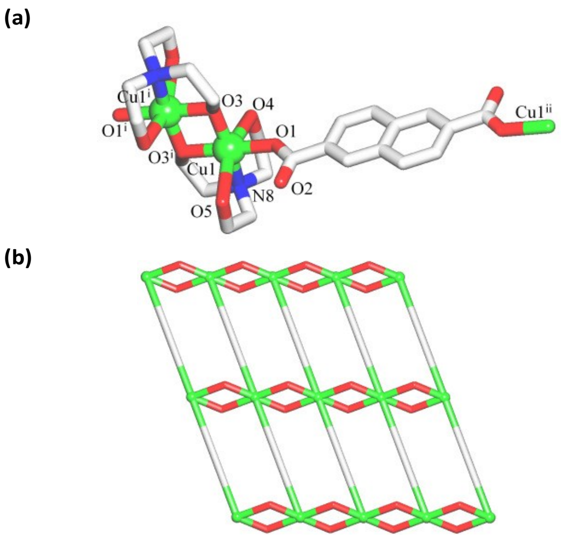
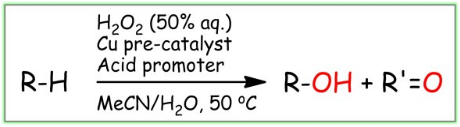


Fig. 2. Structural fragments of **2**: (a) repeating dicopper(II) [$Cu_2(\mu_2\text{-}H_2tea)_2(\mu_2\text{-}nda)$] unit with atom labelling scheme; (b) topological representation of the 2D H-bonded underlying net showing a uninodal 4-connected layer with the **sql** topology and point symbol of ($4^4.6^2$). Further details: (a) H atoms are omitted for clarity, symmetry codes: (i) –*x*, –*y*, –*z*, (ii) 1–*x*, 1–*y*, 1–*z*, color codes: Cu (green balls), O (red), N (blue), C (gray); (b) centroids of 4-connected [$Cu_2(\mu_2\text{-}H_2tea)_2]^{2+}$ nodes (green balls), centroids of 2-connected nda (gray) and H_2O (red) linkers; view along the *b* axis.

The crystal structure of **2** reveals an infinite 1D metal-organic network assembled from the dicopper(II) {$Cu_2(\mu_2\text{-}H_2tea)_2\}^{2+}$ secondary building units (SBUs) and μ_2-nda(2–) linkers (Fig. 2a). Within the dicopper(II) SBUs, the symmetry equivalent Cu1 atoms are six-coordinate and adopt a distorted octahedral {$CuNO_5$} geometry. The equatorial sites are occupied by the N8, O3, and O3^i atoms of μ_2-H_2tea moiety and the O1 atom from the μ_2-nda ligand [Cu1–N8 2.0452(15), Cu1–O3 1.9394(13), Cu1–O3^i 1.9394(13), Cu1–O1 1.9483(15) Å], whereas the axial positions are taken by the O4 and O5 atoms from the OH groups of triethanolaminate ligand [Cu1–O4 2.5526(17), Cu1–O5 2.4798(18) Å]. The {$Cu_2(\mu\text{-}O)_2$} core possesses a rather short Cu1···Cu1^i separation of 2.9075(6) Å, while the distance between the neighboring Cu1 atoms interlinked via the μ_2-nda moiety equals to 13.5229(10) Å. The bonding parameters in **2** are comparable to those found in related dicopper(II) aminoalcoholate compounds.[22] Due to the presence of water molecules of crystallization and multiple H-bonding interactions in **2**, the adjacent metal-organic 1D chains are extended (1D→2D) into H-bonded layers. From the topological viewpoint,[21] such layers can be classified as uninodal 4-connected underlying nets with the **sql** topology (Fig. 2b).

Mild homogeneous oxidation of cycloalkanes

The catalytic behavior of compounds **1** and **2** was evaluated in the mild oxidation of cycloalkanes by H_2O_2 to produce a mixture of the corresponding alcohols and ketones (Scheme 2). Cyclohexane was investigated in more detail as a model substrate, given an industrial importance of cyclohexanone and cyclohexanol as intermediates in the nylon production.[6,23] Other cycloalkanes were tested under optimized reaction conditions (Table 1).

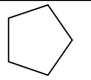
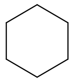
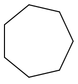
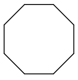


Scheme 2. Mild homogeneous catalytic oxidation of alkanes to alcohols and ketones.

Both copper(II) compounds **1** and **2** act as rather efficient pre-catalysts for the oxidation of C_5–C_8 cycloalkanes by H_2O_2, in aqueous acetonitrile medium at 50 °C in air, and in the presence (optional) of an acid promoter, resulting in the maximum total product yields up to 34%, based on cycloalkane (Table 1). It should be highlighted that such yields are considered rather high in the field of alkane functionalization, given the intrinsic inertness of these hydrocarbons and mild reaction conditions applied.[6] Although pre-catalyst **1** exhibits an appreciable activity (total product yields of ~14–18%) in the absence of an acid promoter, the yields can be duplicated (~25–34%) by adding a small quantity of trifluoroacetic acid (TFA). In contrast, compound **2** is only active in the presence of an acid promoter, leading to 14–26% yields, with a maximum value achieved in the cycloheptane oxidation.

Oxidation of cyclohexane by the **1**/TFA/H_2O_2 (Fig. 3a) system results in 34% total product yield, with cyclohexanol being formed predominantly to cyclohexanone (3:2). The maximum total yield is attained in 2 h and does not increase on prolonging the reaction time. Under the same conditions, the **2**/TFA/H_2O_2 system (Fig. 3b) results in a maximum total yield of 20% after 2 h of the reaction.

Table 1. Mild homogeneous oxidation of cycloalkanes by H_2O_2 in the presence of pre-catalysts **1** and **2**.[a]

Cycloalkane		Total Product Yield (Alcohol + Ketone), %[b]		
		1	**1**/TFA	**2**/TFA
	C_5H_{10}	13.6	25.1	13.6
	C_6H_{12}	15.8	33.5	19.6
	C_7H_{14}	16.4	32.1	25.6
	C_8H_{16}	17.5	29.5	20.8

[a] Reaction conditions: pre-catalyst **1** or **2** (5 µmol), acid promoter (optional, TFA, 0.05 mmol), cycloalkane (1 mmol), H_2O_2 (aq. 50%, 5 mmol), CH_3CN (up to 2.5 mL of the total volume), 50 °°C, 5 h. [b] Yields are based on alkanes [(moles of products per mol of cycloalkane)×100%].

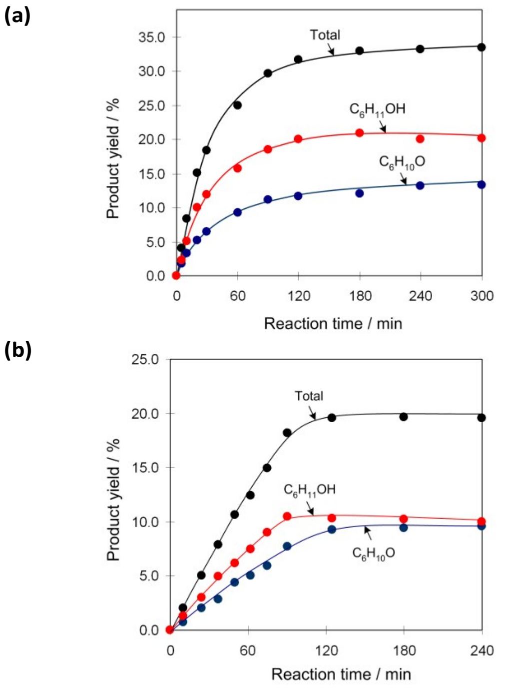


Fig. 3. Kinetic curves of product accumulation in the cyclohexane oxidation by H_2O_2 catalyzed by **1** (a) and **2** (b) in the presence of TFA promoter. Reaction conditions: pre-catalyst **1** or **2** (5 µmol), TFA (0.05 mmol), C_6H_{12} (1.0 mmol), H_2O_2 (5.0 mmol), CH_3CN (up to 2.5 mL of the total volume), 50 °C.

Among the tested acid promoters, TFA provides the highest influence on the catalytic activity of **1** (Fig. 4a) in the cyclohexane oxidation, namely resulting in an increase of both the initial reaction rate (W_0) and total product yield. Interestingly, other acid promoters such as HCl and H_2SO_4 lead to a slight inhibition of the activity of **1** if compared with the acid-free system, whereas the introduction of HNO_3 results in a modest improvement of the activity. Although compound **2** does not catalyze the cyclohexane oxidation in the absence of an acid promoter (Fig. 4b), the introduction of 10 equivalents of TFA, H_2SO_4, or HNO_3 into the reaction mixture dramatically improves the activity of **2**, giving rise to 20% total yields in **2** h. On the other hand, the reaction rate of the cyclohexane oxidation practically does not depend on the type of an acid promoter applied, being similar among these three acids. However, an introduction of HCl (10 equivalents relatively to pre-catalyst) drastically accelerates the cyclohexane oxidation without affecting a maximum total yield, which is already 19% after 10 min of the reaction.

Inspired by these results, we have also studied an effect of the TFA amount on the total yield in the cyclohexane oxidation by the **1**/TFA/H_2O_2 and **2**/TFA/H_2O_2 systems (Fig. 5). The addition of TFA to the system containing **1** has almost no influence on an initial reaction rate of the C_6H_{12} oxidation, which is close to that observed in the absence of an acid promoter.

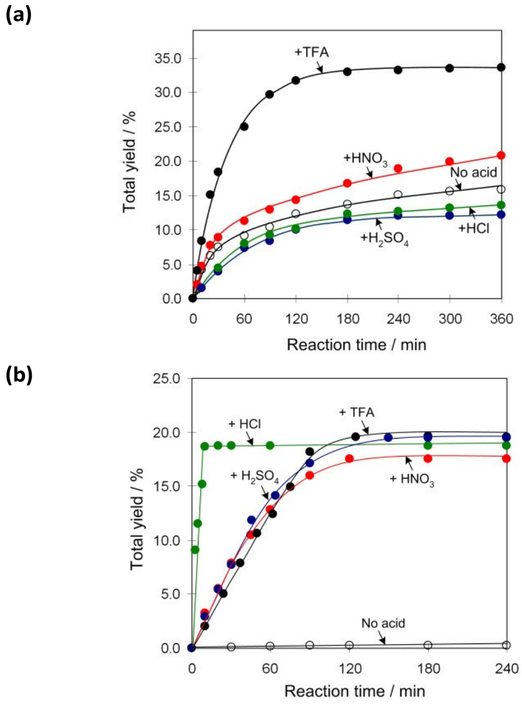


Fig. 4. Effect of different acid promoters on the total yield of products in the cyclohexane oxidation catalyzed by **1** (a) and **2** (b). Reaction conditions: pre-catalyst **1** or **2** (5 µmol), acid promoter (0.05 mmol), C_6H_{12} (1.0 mmol), H_2O_2 (5.0 mmol), CH_3CN (up to 2.5 mL of the total volume), 50 °C.

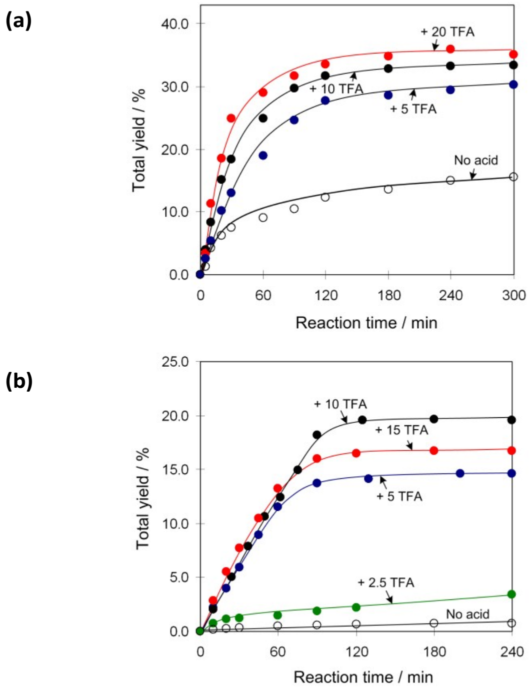


Fig. 5. Effect of TFA amount on the total yield of products in the cyclohexane oxidation catalyzed by **1** (a) and **2** (b) in the presence of H_2O_2. Reaction conditions: pre-catalyst **1** or **2** (5 µmol), TFA (0.0125–0.1 mmol), C_6H_{12} (1.0 mmol), H_2O_2 (5.0 mmol), CH_3CN (up to 2.5 mL of the total volume), 50 °C.

However, the presence of TFA noticeably improves a total yield of the products from 16% in an acid-free system to 36% when using 20 equivalents of TFA relatively to the pre-catalyst (Fig. 5a). The increase of the TFA amount from 5 to 20 equivalents leads to a slight yield growth from 30 to 36% and a small acceleration of the reaction. The role of an acid promoter[10,18] consists of activating the pre-catalysts by protonation of ligands and/or generation of oligomeric species (in case of **2**), facilitating proton transfer steps (also with an involvement of *N*,*O*-aminoalcoholate ligands[9,24,25a,b]), and improving the oxidation power of hydrogen peroxide by preventing its partial decomposition. Among the tested acid promoters, a superior promoting behavior of TFA on the catalytic activity of **1** and **2** can possibly be related to the ability of this very strong carboxylic acid to not only protonate ligands and partially replace the carboxylate moieties in the pre-catalysts, but also stabilize the newly generated copper species by acting as an ancillary trifluoroacetate ligand. Moreover, the combination of TFA with H_2O_2 may lead to a synergic effect and may substantially enhance the oxidation ability of an oxidant, as was previously observed in some other copper-containing catalytic systems.[25c,d]

The maximum product yield in the cyclohexane oxidation by the **2**/TFA/H_2O_2 system rises from 5% (6 h) to 20% (2 h) on increasing the TFA amount from 2.5 to 10 equivalents relatively to the pre-catalyst (Fig. 5b). Higher TFA excess (15 equivalents) results in a slight yield drop to 17% (2 h). The initial reaction rate is growing with the TFA amount up to 5 equivalents relatively to **2**, while further increase of the TFA loading (up to 15 equivalents) practically does not affect W_0.

The total product yield in the C_6H_{12} oxidation in the absence of an acid promoter gradually increases from 3 to 16% on raising the pre-catalyst **1** amount from 1.25 to 5 µmol (Fig. 6a). However, a higher catalyst loading (10 µmol) does not lead to a yield growth. The initial reaction rate has a linear dependence on the pre-catalyst **1** concentration (Fig. 6b), thus indicating the first-order reaction kinetics with respect to the pre-catalyst and supporting a probable involvement of one Cu-containing species in the rate-limiting step of the oxidation reaction.

The unusual promoting effect of water on the cyclohexane oxidation was observed for both the **1**/TFA/H_2O_2 and **2**/TFA/H_2O_2 systems. Interestingly, the addition of water to the reaction mixture leads to the acceleration of the cyclohexane oxidation without a significant change in the final product yields (Fig. 7). The initial reaction rate W_0 in the **1**/TFA/H_2O_2 system exhibits a linear dependence (Fig. 7b) when raising the H_2O concentration in the reaction medium from 4.0 M (corresponding the amount of H_2O present in 50% aqueous H_2O_2) to 17.2 M (after introduction of an additional amount of water to the reaction mixture). Besides, water plays a similar beneficial role in the cyclohexane oxidation by the **2**/TFA/H_2O_2 system (Fig. 7c). It should be mentioned that the formation of a minor amount of water as a result of cyclohexane oxidation has a negligible effect on the reaction mechanism, given ca. 20-40 fold higher initial content of water that comes with 50% aqueous H_2O_2.

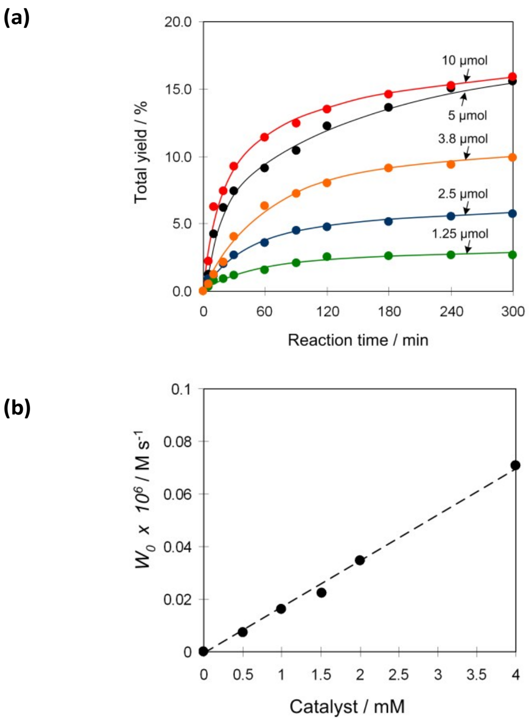


Fig. 6. Effect of pre-catalyst **1** amount on (a) the total yield of products and (b) the initial reaction rate (W_0) in the cyclohexane oxidation by H_2O_2. Reaction conditions: pre-catalyst **1** (1.25–10 µmol), C_6H_{12} (1.0 mmol), H_2O_2 (5.0 mmol), CH_3CN (up to 2.5 mL of the total volume), 50 °C.

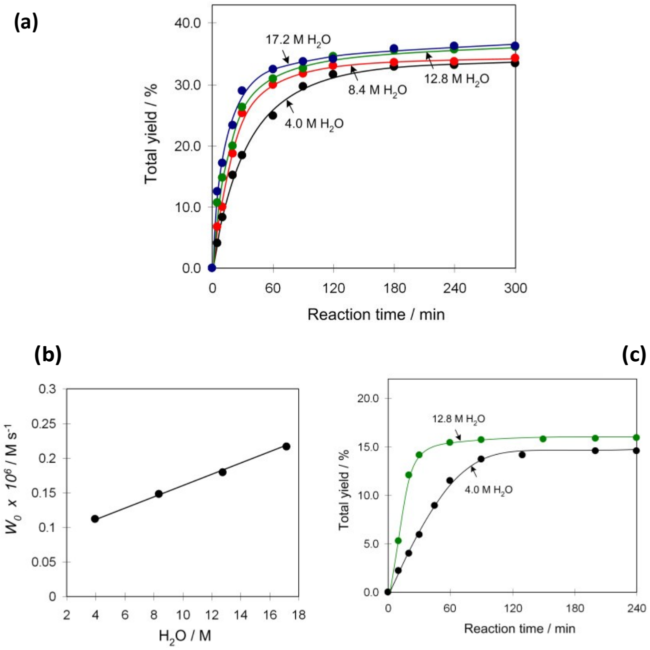


Fig. 7. Effect of H_2O amount on (a, c) the total yield of products and (b) the initial reaction rate (W_0) in the cyclohexane oxidation by **1**/TFA/H_2O_2 (a, b) or **2**/TFA/H_2O_2 (c) systems. Reaction conditions: pre-catalyst **1** or **2** (5 µmol), TFA (0.05 (a, b) or 0.025 (c) mmol), C_6H_{12} (1.0 mmol), H_2O_2 (aq. 50%, 5.0 mmol, corresponds to 4.0 M of H_2O), CH_3CN (up to 2.5 mL of the total volume), added H_2O (up to 17.2 M total), 50 °C.

The observed promoting role of water indicates a direct involvement of H_2O in the rate-limiting step of the hydroxyl radical generation in the cycloalkane oxidation. In fact, a H_2O-assisted pathway for the generation of hydroxyl radicals in vanadium(V) and rhenium(VII) catalyzed alkane oxidation was earlier suggested by DFT calculations.[26] Besides, H_2O was reported to play a crucial role as a hydroxylating reagent and solvent component in mild copper-catalyzed alkane hydrocarboxylations.[10,27] In addition, the promoting role of water opens several advantages toward a possibility of using diluted in-situ generated aqueous solutions of H_2O_2.

To understand whether the oxidation of cyclohexane stops after a certain period of time due to the deactivation of the pre-catalyst or full consumption of the oxidant, we performed a number of additional tests (Figs. 8 and 9). The oxidation of C_6H_{12} in the presence of **1**/TFA attains a plateau after 3 h of the reaction (Fig. 8, black curve), possibly owing to an almost full consumption of H_2O_2. In fact, the evolution of O_2 due to a partial catalase activity[10] of **1** was observed. An addition of a new portion of H_2O_2 into the reaction mixture after 3 h leads to the consumption of the products (Fig. 8, red curve) but not to the oxidation of residual cyclohexane. However, an addition of a new portion of C_6H_{12} at 4 h of the reaction time restores the alkane oxidation, as confirmed by the increase of the yields of cyclohexanol and cyclohexanone. In a separate experiment (Fig. 9), we performed a stepwise addition of new portions of both C_6H_{12} and H_2O_2 after 1, 2, 3, and 4 h of the reaction, resulting in a considerable growth of the products content until 2.5 h. After this time, an inverse trend is observed, since the cyclohexane oxidation slows down, most likely due to a high water content (H_2O comes with aqueous H_2O_2 and is formed as a product in H_2O_2 decomposition and, to a lesser extent, in C_6H_{12} oxidation) and a competitive oxidation of products, cyclohexanol and cyclohexanone. Given these observations and the fact that the oxidation of cyclohexane and products is still observed after a prolonged reaction time, we conclude that the **1**/TFA catalytic system can maintain its activity for a long time, while the decline in the overall system efficiency is associated with the consumption of oxidant. To a lesser extent, a similar behavior is observed for the **2**/TFA catalytic system.

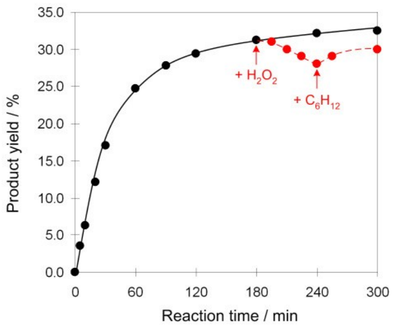


Fig. 8. Kinetic curves of products accumulation (total yield of cyclohexanol and cyclohexanone) in the cyclohexane oxidation by H_2O_2 catalyzed by **1** in the presence of TFA promoter. Black line corresponds to standard reaction. Red line corresponds to the addition of new portions of H_2O_2 (5.0 mmol, at 180 min reaction time) and C_6H_{12} (1.0 mmol, at 240 min reaction time). Reaction conditions are those of Figure 3a.

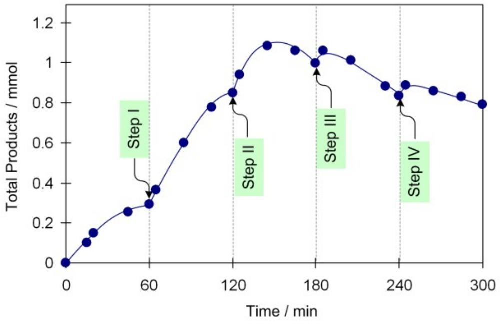


Fig. 9. Kinetic curve of products accumulation (total yield of cyclohexanol and cyclohexanone) in the stepwise oxidation of cyclohexane by H_2O_2 catalyzed by **1** in the presence of TFA promoter. On each step, a new portion of C_6H_{12} (1.0 mmol) and H_2O_2 (5.0 mmol) was added. Reaction conditions: pre-catalyst **1** (10 µmol), TFA (0.1 mmol), C_6H_{12} (1.0 mmol), H_2O_2 (5.0 mmol), CH_3CN (up to 5.0 mL of the total volume), 50 °C.

ESI-MS studies of catalytic mixtures

To get further insight into the nature of catalytically active species, we studied by ESI-MS(±) both the parent copper(II) compounds and the respective **1**/H^+/H_2O_2 and **2**/H^+/H_2O_2 model mixtures, using the conditions typical to those of catalytic tests. Thus, in the ESI-MS(–) plot of $[\{Cu(Hdea)(H_2dea)\}_2(\mu_2\text{-}H_2pma)]\cdot 3H_2O$ (**1**), we were able to identify a characteristic peak corresponding to the molecular ion, $[\{Cu(Hdea)(H_2dea)\}_2(Hpma)]^-$ (*m/z* 797), followed by its subsequent fragmentation with the loss of diethanolamine moieties, as attested by the detection of the $[\{Cu(Hdea)\}_2(Hpma)]^-$ (*m/z* 585) and $[Cu(Hpma)]^-$ (*m/z* 314) ions. In the MS(+) mode, the fragmentation was very poor, although some derived peaks can also be detected, namely $[\{Cu(Hdea)\}_2(H_3pma)]^+$ (*m/z* 587) and $[Cu(H_2dea)_2(H_3pma)]^+$ (*m/z* 526). Notably, in acidic medium and after introduction of hydrogen peroxide, we still observe in the MS(–) mode an intense peak of the parent $[\{Cu(Hdea)(H_2dea)\}_2(Hpma)]^-$ (*m/z* 797) molecular ion with an expected isotopic distribution pattern, suggesting that this ion can correspond to a catalytically active species in the **1**/H^+/H_2O_2 system. In addition, new highly intense fragments were also detected, which are the dicopper(I) pyromellitate $[Cu_2(Hpma) + (H_4pma)]^-$ (*m/z* = 631) and $[Cu_2(Hpma)]^-$ (m/z 377) moieties, revealing a facile ESI-induced loss of aminoalcoholate ligands due to their additional protonation in acidic medium.

In contrast to **1**, the compound $[Cu_2(\mu_2\text{-}H_2tea)_2(\mu_2\text{-}nda)]_n\cdot 2nH_2O$ (**2**) has a 1D polymeric structure that is relatively stable in solution, on account of poor fragmentation observed in both positive and negative modes. However, upon addition of an acid promoter and H_2O_2, the ESI-MS(–) fragmentation pattern improves (most likely due to a partial disaggregation of the polymeric network), leading to the detection of a very characteristic tetracopper(I) $[Cu_4(H_3tea)_3(H_2tea)(nda)_2]^-$ (*m/z* =

1277) fragment as the heaviest and intense ion with the expected isotopic distribution. This fragment represents a ~$Cu_2(H_2tea)_2$–nda–$Cu_2(H_2tea)_2$–nda~ part of the polymeric chain of **2**. We believe that such a type of oligomeric ion can constitute a catalytically active species in alkane oxidation by the **2**/H^+/H_2O_2 system, given also the analysis of subsequent fragmentation patterns and the identification of derived tetracopper species in the MS(+) mode. Hence, both compounds **1** and **2** act as aqua-soluble pre-catalysts and, upon treatment with an acid promoter and oxidant, partially dissociate generating homogeneous di- or tetracopper catalytically active species, respectively.

Selectivity features in alkane oxidations and proposed mechanism

In order to evaluate both the type of the reaction mechanism and reactive species involved, we tested the oxidation of linear and substituted cyclic alkanes by the **1**/TFA/H_2O_2 and **2**/TFA/H_2O_2 systems and determined the corresponding bond-, regio- and stereo-selectivity parameters (Table 2). Oxidation of *n*-heptane in the presence of both pre-catalysts proceeds without a specific preference to any secondary carbon atom of the hydrocarbon chain, resulting in the regioselectivity C(1):C(2):C(3):C(4) parameters of 1:5:4:4 and 1:7:7:7. The oxidation of methylcyclohexane and adamantane results in a moderate bond selectivity, suggesting that the tertiary C atom is oxidized with some preference over the secondary C atoms; the bond selectivity 1°:2°:3° parameters are 1:5:15 and 1:6:23 in the methylcyclohexane oxidation in the presence of **1** and **2**, respectively (Table 2). The oxidations of both *cis*- or *trans*-1,2-dimethylcyclohexanes proceed rather non-stereoselectively, as confirmed by the *trans*/*cis* ratios of 0.5–0.8 between the generated isomeric tertiary alcohols with the mutual *trans* and *cis* orientation of the methyl groups. A partial inversion of the configuration was also detected, with the *cis* isomers being predominant products in both *cis*- and *trans*-1,2-dimethylcyclohexane oxidations. The observed bond-, regio- and stereo-selectivity parameters in both the **1**/TFA/H_2O_2 and **2**/TFA/H_2O_2 systems (Table 2) are indicative of an involvement of a powerful and rather indiscriminate oxidizing species.[9,18,25a,b] Moreover, these selectivity parameters are close to those reported earlier for other Cu-containing catalytic systems operating with $HO^•$ radicals.[10,11,28] Therefore, based on the selectivity parameters in the oxidation of linear and substituted cyclic alkanes as well as on some kinetic data obtained in the oxidation of cyclohexane, we can propose an involvement of hydroxyl radicals as principal oxidizing species. These are generated from H_2O_2 via an interaction with a Cu pre-catalyst. Then, the hydroxyl radicals abstract H atoms from an alkane substrate forming the alkyl radicals $R^•$, which further react with O_2 (e.g., from air or via partial H_2O_2 decomposition) resulting in the $ROO^•$ radicals. These are then transformed to alkyl hydroperoxides ROOH as primary intermediate products. However, alkyl hydroperoxides rapidly decompose (eventually via Cu-catalyzed processes and additionally after the treatment by PPh_3) to furnish the corresponding alcohols and ketones as final oxidation products.[10,11]

Table 2. Selectivity parameters in the oxidation of linear and substituted cyclic alkanes.[a]

Selectivity parameter	System **1**/TFA/H_2O_2	 **2**/TFA/H_2O_2
Regio-selectivity		
C(1):C(2):C(3):C(4) (*n*-C_7H_{16})[b]	1:5:4:4	1:7:7:7
Bond selectivity		
1°:2°:3° (methylcyclohexane)[c]	1:5:15	1:6:23
3°/2° (adamantane)[d]	4.7	3.4
Stereo-selectivity		
trans/*cis* (*cis*-dimethylcyclohexane)[e]	0.8	0.5
trans/*cis* (*trans*-dimethylcyclohexane)[e]	0.6	0.8

[a] Reaction conditions: pre-catalyst **1** or **2** (5 µmol), TFA (0.05 mmol), alkane (1.0 mmol), H_2O_2 (5.0 mmol), MeCN up to 2.5 mL total volume, 3 h, 50 °C. All parameters were calculated based on the ratios of isomeric alcohols. The calculated parameters were normalized, i.e., recalculated taking into account the number of H atoms at each carbon atom. [b] Parameters C(1):C(2):C(3):C(4) are the relative reactivities of H atoms at carbon atoms 1, 2, 3, and 4 of the *n*-heptane chain. [c] Parameters 1°:2°:3° are the relative normalized reactivities of the H atoms at primary, secondary and tertiary carbon atoms of methylcyclohexane. [d] Parameters 3°/2° are the relative normalized reactivities of the H atoms at tertiary and secondary carbon atoms of adamantane, determined as the ratio of the formed tertiary and secondary alcohol isomers. [e] Parameter *trans*/*cis* is determined as the ratio of the formed tertiary alcohol isomers with mutual trans and *cis* orientation of the methyl groups.

Conclusions

In the current work, we have self-assembled, isolated, and fully characterized two novel aqua-soluble coordination compounds that are composed of distinct dicopper(II) blocks, namely [{Cu(Hdea)(H_2dea)}$_2$(μ_2-H_2pma)] and [Cu_2(μ_2-H_2tea)$_2$(μ_2-nda)] in **1** and **2**, respectively. These products not only widen the coordination chemistry of versatile aminoalcohols (diethanolamine and triethanolamine), but also represent noteworthy examples of such compounds that can be applied as highly active pre-catalysts toward the homogeneous oxidation of alkanes under mild conditions.

In fact, the present study has shown that **1** and **2** can act as efficient pre-catalysts for the oxidation, by aqueous hydrogen peroxide in H_2O/MeCN medium, of the C_5–C_8 cycloalkanes to give the corresponding cyclic alcohols and ketones. Cyclohexane has been selected as a model substrate on account of the industrial importance of its oxidation products in the nylon production.[6] Hence, the effects of various reaction parameters have been investigated in the cyclohexane oxidation by the **1**/H^+/H_2O_2 and **2**/H^+/H_2O_2 systems, including the type of acid promoter, relative amounts of reagents, influence of water and substrate scope. The maximum overall yields of up to 34% (relative to alkane substrate) have been attained in the oxidation of cyclohexane, which are rather high in the field of alkane oxidation under mild temperature and atmospheric pressure.[1–6]

To further highlight the novelty of the present work with respect to prior state-of-the-art studies, the following main points should be accounted for:

(a) Two new copper(II) coordination compounds have been prepared and structurally characterized;

(b) They extend the scope of self-assembly synthetic methods and broaden the application of aqua-soluble, low cost, and versatile aminoalcohol building blocks (H_3tea and H_2dea) for the generation of the bio-inspired catalytic systems.

(c) Apart from showing some interesting structural and topological features, compounds **1** and **2** also exhibit rather high activity in the mild homogeneous oxidation of cycloalkanes;

(d) A rare promoting behavior of water has been detected and studied in both the **1**/H^+/H_2O_2 and **2**/H^+/H_2O_2 systems, despite the fact that H_2O typically shows a strongly inhibiting effect in the mild oxidation of alkanes;

(e) Such a promoting role of H_2O can potentially find practical implications, allowing the use of diluted in-situ generated aqueous solutions of H_2O_2 as a green oxidant.[29]

We believe that further studies should focus on the widening of both synthetic and catalytic directions, namely by preparing and evaluating novel metal-complex-catalysts and broadening the substrate scope of alkane oxidations. The content of water in the reaction medium should be monitored and accounted for in future developments, aiming at the establishment of efficient reaction protocols capable of utilizing aqueous H_2O_2 in low concentrations.

Acknowledgements

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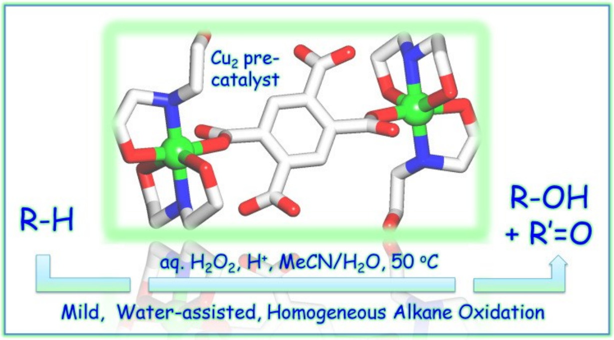
TOC graphic and text



Two new dicopper(II) pre-catalysts were synthesized, fully characterized, and applied for the mild homogeneous oxidation of alkanes.