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### **Mild homogeneous oxidation and hydrocarboxylation of cycloalkanes catalyzed by novel dicopper(II) aminoalcohol-driven cores**<sup>1</sup>

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<sup>1</sup>This article is dedicated to Prof. Georgiy B. Shul'pin on the occasion of his 70th birthday.

#### **Graphical abstract**



### Research highlights:

Two new dicopper(II) coordination compounds were synthesized and fully characterized;

These compounds catalyze the mild homogeneous oxidation of alkanes;

Effects of different reaction parameters were evaluated;

Unusual promoting role of water was detected and investigated;

The compounds also catalyze the hydrocarboxylation of alkanes to carboxylic acids.

#### ABSTRACT

*N*-benzylethanolamine (Hbea) and triisopropanolamine (H<sub>3</sub>tipa) were applied as unexplored aminoalcohol N,O-building blocks for the self-assembly generation of two novel dicopper(II) compounds,  $[Cu_2(\mu-bea)_2(Hbea)_2](NO_3)_2$  (1) and  $[Cu_2(H_3tipa)_2(\mu-pma)]\cdot 7H_2O$  (2) {H<sub>4</sub>pma = pyromellitic acid}. These were isolated as stable and aqua-soluble microcrystalline products and were fully characterized by IR spectroscopy,  $ESI-MS(\pm)$ , and single-crystal X-ray diffraction, the latter revealing distinct Cu<sub>2</sub> cores containing the five-coordinate copper(II) centers with the  $\{CuN_2O_3\}$  or  $\{CuNO_4\}$  environments. Compounds 1 and 2 were used as homogeneous catalysts for the mild oxidation of C5-C8 cycloalkanes to give the corresponding cyclic alcohols and ketones in up to 23% overall yields based on cycloalkane. The reactions proceed in aqueous acetonitrile medium at 50 °C using  $H_2O_2$  as an oxidant. The effects of different reaction conditions were studied, including the type and loading of catalyst, amount and kind of acid promoter, and water concentration. Despite the fact that different acids (HNO<sub>3</sub>, H<sub>2</sub>SO<sub>4</sub>, HCl, or CF<sub>3</sub>COOH) promote the oxidation of alkanes, the reaction is exceptionally fast in the presence of a catalytic amount of HCl, resulting in the TOF values of up to 430  $h^{-1}$ . Although water typically strongly inhibits alkane oxidations due to the reduction of H<sub>2</sub>O<sub>2</sub> concentration and lowering of the alkane solubility, in the systems comprising 1 and 2 we observed a significant growth (up to 5-fold) of an initial reaction rate in the cyclohexane oxidation on increasing the amount of H<sub>2</sub>O in the reaction mixture. The bond-, regio- and stereo-selectivity parameters were investigated in oxidation of different linear, branched, and cyclic alkane substrates. Both compounds 1 and 2 also catalyze the hydrocarboxylation of C<sub>5</sub>-C<sub>8</sub> cycloalkanes, by CO, K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>, and H<sub>2</sub>O in a water/acetonitrile medium at 60 °C, to give the corresponding cycloalkanecarboxylic acids in up to 38% yields based on cycloalkanes.

*Keywords:* C–H Functionalization; Oxidation; Hydrocarboxylation; Cycloalkanes; Homogeneous Catalysis; Copper compounds.

#### 1. Introduction

Different copper compounds constitute a vast variety of catalytic systems and are widely applied in the areas of both heterogeneous and homogeneous catalysis [1–4]. The use of Cu-containing catalysts is primarily governed by the versatile redox properties of this metal, its natural abundance and relatively low cost, low toxicity, and rich inorganic and

coordination chemistry [1–5]. Besides, copper ions are present in the active sites of diverse oxidation enzymes, such as catechol oxidase, laccase, multicopper oxidases, and particulate methane monooxygenase (pMMO), thus justifying an extensive research in the fields of copper bioinorganic chemistry and related areas of biomimetic and/or bioinspired catalysis focused on the search for efficient C–H functionalization protocols [4–6]. Among the above-mentioned enzymes, pMMO represents an especially interesting case given its multicopper active site with an N,O-environment that is capable of catalyzing the hydroxylation of such inert substrates as alkanes.<sup>7</sup>

In fact, alkanes are very abundant in nature and relatively inexpensive substrates for the synthesis of various important oxidation products [8–10]. However, a high inertness of alkanes toward the oxidative C–H functionalization under mild conditions prevents their broad use as raw materials for the direct or single-step production of alcohols, ketones, aldehydes, or carboxylic acids. [8,9,11]. Nevertheless, the design of new bioinspired metal complex catalysts, incorporating metal ions with a recognized function in oxidation catalysis as well as simple and commercially available ligands, can potentially result in the discovery of active catalytic systems, capable of oxidizing alkanes with high efficiency and under mild temperatures and pressures [4,8,11–16].

As a continuation of our recent research on the synthesis and catalytic application of novel multicopper(II) cores [17] the main aim of the current work consisted of the self-assembly generation of new dicopper(II) compounds bearing aminoalcohols as principal *N*,*O*-ligands, and the investigation of their catalytic function toward the mild homogeneous oxidation or hydrocarboxylation of cycloalkanes to give the corresponding cyclic alcohols and ketones or carboxylic acids, respectively.

Thus, the present study reports the synthesis, characterization, crystal structures, and application in oxidation catalysis of two novel dicopper(II) coordination compounds,  $[Cu_2(\mu-bea)_2(Hbea)_2](NO_3)_2$  (1) and  $[Cu_2(H_3tipa)_2(\mu-pma)]\cdot7H_2O$  (2) (Scheme 1). Apart from featuring aqueous solubility and having distinct dicopper(II) cores, the obtained complexes act as homogeneous catalysts for (i) the oxidation of different C<sub>5</sub>–C<sub>8</sub> cycloalkanes by hydrogen peroxide to give a mixture of alcohols and ketones and (ii) the hydrocarboxylation of C<sub>5</sub>–C<sub>8</sub> cycloalkanes by carbon monoxide, peroxodisulfate oxidant, and water, to give the corresponding cycloalkanecarboxylic acids with one additional carbon atom. For alkane oxidations, the effects of various reaction parameters, substrate scope, different selectivity features, and possible catalytically active species were studied in detail.



Scheme 1. Structural formulae of dicopper(II) compounds 1 (top) and 2 (bottom).

#### 2. Experimental

#### 2.1. Materials and methods

All chemicals were obtained from commercial sources and used as received. Triisopropanolamine (racemic mixture) was purchased from Across Organics. The synthetic work was performed in air and at room temperature (r.t., 25 °C). Infrared spectra (4000–400 cm<sup>-1</sup>) 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(±) analyses were run on a LCQ Fleet mass spectrometer with an ESI source (Thermo Scientific), using  $\cdot 10^{-3}$  M solutions of **1** and **2** or their model mixtures with HNO<sub>3</sub> and H<sub>2</sub>O<sub>2</sub> 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.

#### 2.2. Synthesis and characterization of 1 and 2.

 $[Cu_2(\mu-bea)_2(Hbea)_2](NO_3)_2$  (1). To a MeOH solution (10 mL) of  $Cu(NO_3)_2 \cdot 2.5H_2O$  (1.0 mmol, 233 mg) was added dropwise an aqueous 1 M solution of *N*-benzylethanolamine (Hbea; 2.0 mmol, 2 mL) with continuous stirring at room temperature. Then, an aqueous 1 M solution of NaOH (3.0 mmol, 3 mL) was introduced and the resulting mixture was stirred for 2 h and then filtered off. The filtrate was left to evaporate in a beaker at r.t. Blue X-ray quality crystals were formed in 1–2 weeks, then collected and dried in air to furnish

compound **1** in -35% yield (based on copper(II) nitrate). Compound **1** is moderately soluble in H<sub>2</sub>O (S<sub>25°C</sub> ~3 mg mL<sup>-1</sup>). FT-IR (KBr): 3230 (m) v(OH), 3183 (m) v(NH), 2940 (w), 2885 (w), and 2628 (w) v(CH), 1455 (m), 1384 (vs br) and 1361 (sh) v(NO<sub>3</sub>), 1076 (m), 1049 (m), 1015 (w), 755 (m), and 702 (m) cm<sup>-1</sup>. ESI-MS(+) (H<sub>2</sub>O), *m/z*: 853 [Cu<sub>2</sub>( $\mu$ -H<sub>0.5</sub>bea)<sub>2</sub>(Hbea)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub>]<sup>+</sup>, 640 [Cu<sub>2</sub>( $\mu$ -bea)<sub>2</sub>(Hbea)(NO<sub>3</sub>)]<sup>+</sup>, 551 [Cu<sub>2</sub>( $\mu$ -H<sub>0.5</sub>bea)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub>]<sup>+</sup>, 364 [Cu<sub>2</sub>( $\mu$ -bea)<sub>2</sub>(Hbea)<sub>2</sub>]<sup>2+</sup>. ESI-MS(-) (H<sub>2</sub>O), *m/z*: 851 [Cu<sub>2</sub>( $\mu$ -bea)<sub>2</sub>(H<sub>0.5</sub>bea)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub>]<sup>-</sup>, 745 [Cu<sub>2</sub>( $\mu$ -bea)<sub>2</sub>(H<sub>0.5</sub>bea)(H<sub>2</sub>O)]<sup>-</sup>, 593 [Cu<sub>2</sub>( $\mu$ -bea)<sub>2</sub>(bea)(OH)]<sup>-</sup>, 576 [Cu<sub>2</sub>( $\mu$ -bea)<sub>2</sub>(bea)]<sup>-</sup>.

 $[Cu_2(H_3tipa)_2(\mu-pma)]$ ·7H<sub>2</sub>O (2). To a MeOH solution (10 mL) of Cu(NO<sub>3</sub>)<sub>2</sub>·2.5H<sub>2</sub>O (1.0 mmol, 233 mg) was added dropwise triisopropanolamine (H<sub>3</sub>tipa; 1.0 mmol, 191 mg) and pyromellitic acid (1.0 mmol, 254 mg) as a solid, with continuous stirring at room temperature. Then, an aqueous 1 M solution of NaOH (3.0 mmol, 3 mL) was introduced and the resulting mixture was stirred for 2 h and then filtered off. The filtrate was left to evaporate in a beaker at r.t., 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 compound 2 in  $\sim$ 45% yield (based on copper(II) nitrate). Compound 2 is slightly soluble in H<sub>2</sub>O ( $S_{25^\circC} \sim 2 \text{ mg mL}^{-1}$ ). FT-IR (KBr): 3484 (s br), 3398, and 3277 (s br) v(OH/H<sub>2</sub>O), 2973 (w) and 2930 (w) v(CH), 1631 (w sh)  $\delta(H_2O)$ , 1596 (s) and 1560 (w sh)  $v_{as}(COO)$ , 1483 (w), 1420 (w) and 1379 (vs)  $v_s(COO)$ , 1174 (w), 1138 (s), 1034 (m), 977 (m), 867 (w) and 812 (w) cm<sup>-1</sup>. ESI-MS(+) (H<sub>2</sub>O), m/z: 781 [Cu<sub>2</sub>(H<sub>3</sub>tipa)<sub>2</sub>(µ-pma) + Na]<sup>+</sup>, 759 [Cu<sub>2</sub>(H<sub>3</sub>tipa)<sub>2</sub>(µ-Hpma)]<sup>+</sup>, 742  $[Cu_2(H_3tipa)_2(\mu-H_2pma) - OH]^+$ , 703  $[Cu_2(H_3tipa)_2(\mu-H_2pma) - C_3H_7OH]^+$ , 552  $[Cu_2(H_3tipa)(\mu-H_2pma) - OH]^+$ . ESI-MS(-) (H<sub>2</sub>O), poor fragmentation, m/z: 779  $[Cu_2(H_2tipa)_2(\mu-pma) + Na]^-$ .

#### 2.4. X-ray crystallography

Crystals of **1** and **2** suitable for X-ray diffraction study were mounted with Fomblin<sup>©</sup> in a cryoloop. Data were collected on a Bruker AXS-KAPPA APEX II diffractometer with graphite-monochromated radiation (Mo K $\alpha$ ,  $\lambda = 0.71073$  Å) at 273 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 [18]. All data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs [18]. SIR97 [19] and SHELXS-97 [20] were used for structure solution and SHELXL-97 [20] 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 [21]. 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 in the parent carbon or oxygen atom, except for the OH and NH moieties that were located from the electron density map. Water hydrogen atoms that were not accurately located from the electron density map were not included. PLATON [22] and TOPOS [23] were used for hydrogen bond interactions and topological analysis, respectively. Only one type of the dicopper(II) unit was identified in the crystal structure of 2 that represents one diastereoisomer. We believe, different diastereoisomers are present in the bulk sample of 2.

*Crystal data for 1*: C<sub>36</sub>H<sub>50</sub>Cu<sub>2</sub>N<sub>6</sub>O<sub>10</sub>, M = 853.90,  $\lambda = 0.71073$  Å (Mo-K $\alpha$ ), T = 273(2) K, monoclinic, space group  $P2_1/c$ , a = 22.536(2), b = 9.2705(9), c = 22.142(2) Å,  $\beta = 117.139(3)^{\circ}$ , V = 4116.6(7) Å<sup>3</sup>, Z = 4,  $D_c = 1.378$  g/cm<sup>3</sup>,  $\mu = 1.093$  mm<sup>-1</sup>, 99706 reflections collected, 5195 unique,  $I > 2\sigma(I)$  ( $R_{int} = 0.1571$ ),  $R_1 = 0.0639$ ,  $wR_2 = 0.1552$ . *Crystal data for* **2**: C<sub>14</sub>H<sub>22</sub>CuNO<sub>14</sub>, M = 491.88,  $\lambda = 0.71073$  Å (Mo-K $\alpha$ ), T = 273(2) K, monoclinic, space group  $P2_1/n$ , a = 12.4448(7), b = 11.0336(6), c = 17.9095(10) Å,  $\beta = 108.936(2)^{\circ}$ , V = 2326.1(2) Å<sup>3</sup>, Z = 4,  $D_c = 1.402$  g/cm<sup>3</sup>,  $\mu = 1.002$  mm<sup>-1</sup>, 31187 reflections collected, 4027 unique,  $I > 2\sigma(I)$  ( $R_{int} = 0.0398$ ),  $R_1 = 0.0444$ ,  $wR_2 = 0.1206$ . CCDC 1436749 and 1436750.

#### 2.5. Alkane oxidation reactions

The alkane oxidation reactions were performed in air atmosphere in thermostated glass reactors equipped with a condenser under vigorous stirring at 50 °C and using MeCN as solvent (up to 5 mL total volume). In a typical experiment, catalyst **1** or **2** (10  $\mu$ mol) and gas chromatography (GC) internal standard (MeNO<sub>2</sub>, 50  $\mu$ L) were introduced into the MeCN solution, followed by the addition of an acid promoter (typically 0.1 mmol, optional) used as a stock solution in MeCN. An alkane or alcohol substrate (2 mmol) was then introduced, and the reaction started upon addition of hydrogen peroxide (50% in H<sub>2</sub>O, 10 mmol) in one portion. The oxidation reactions were monitored by withdrawing small aliquots after different periods of time, which were treated with PPh<sub>3</sub> (following the Shul'pin's method [24]) for the reduction of remaining H<sub>2</sub>O<sub>2</sub> 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. For comparative purposes, the oxidation of cyclohexanol to cyclohexanol was also investigated, following the above-mentioned experimental

#### 2.6. Alkane hidrocarboxylation reactions

The alkane hydrocarboxylation experiments were performed following a previously developed protocol [12]. In a typical experiment the reaction mixtures were prepared as follows: to 0.01 mmol of the compound 1 or 2 contained in a 20.0 mL stainless steel autoclave, equipped with a Teflon-coated magnetic stirring bar, were added 1.50 mmol of K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>, 2.0 mL of H<sub>2</sub>O, 4.0 mL of MeCN (total solvent volume was 6.0 mL), and 1.00 mmol of alkane. Then the autoclave was closed and flushed with CO three times to remove the air, and finally pressurized with 20 atm of CO. CAUTION: Due to the toxicity of CO, all operations should be carried out in a well-ventilated hood! The reaction mixture was typically stirred for 4 h at 60 °C using a magnetic stirrer and an oil bath, whereupon it was cooled in an ice bath, degassed, opened and transferred to a flask. Diethyl ether (9.0 mL) and 45 µL of cycloheptanone (typical GC internal standard) were added. In the case of cycloheptane hydrocarboxylation, cyclohexanone (45 µL) was used as a GC standard. The obtained mixture was vigorously stirred for 10 min, and the organic layer was analyzed by gas chromatography (internal standard method), revealing the formation of the corresponding monocarboxylic acids as major products Attribution of peaks was made by comparison with chromatograms of authentic samples.

#### 3. Results and discussion

#### 3.1. Synthesis of catalysts 1 and 2.

Treatment of copper(II) nitrate with an excess of *N*-benzylethanolamine (Hbea) and sodium hydroxide in MeOH/H<sub>2</sub>O medium at ~25°C led to the self-assembly generation of a dicopper(II) complex [Cu<sub>2</sub>( $\mu$ -bea)<sub>2</sub>(Hbea)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub> (**1**). A related synthetic procedure using a mixture of Cu(NO<sub>3</sub>)<sub>2</sub>, triisopropanolamine (H<sub>3</sub>tipa), pyromellitic acid (H<sub>4</sub>pma), and NaOH resulted in the self-assembly of a different dicopper(II) compound [Cu<sub>2</sub>(H<sub>3</sub>tipa)<sub>2</sub>( $\mu$ -pma)]·7H<sub>2</sub>O (**2**) (Scheme 1). Both products were isolated as blue air-stable microcrystalline solids and were characterized by IR spectroscopy, ESI-MS(±), and single crystal X-ray diffraction. The latter also shows the formation of H-bonded networks in the solid state which, however, disaggregate upon the dissolution of the compounds. In fact, both complexes **1** and **2** are slightly soluble in water (S<sub>25°C</sub> ~2–3 mg mL<sup>-1</sup>) and relatively stable in solution, as

attested by ESI-MS data. These characteristics open up their possible use as homogeneous catalysts (or pre-catalysts) for the mild oxidation reactions in aqueous medium [17,25].

#### 3.2. Structures of compounds 1 and 2.

The crystal structure of 1 is composed of a dicopper(II)  $[Cu_2(\mu-bea)_2(Hbea)_2]^{2+}$  cation and two nitrate anions. The Cu<sub>2</sub> cation (Figure 1a) comprises two symmetry non-equivalent copper(II) centers, a pair of terminal Hbea ligands, and two bridging deprotonated  $\mu$ -bea(1–) moieties. Both Cu1 and Cu2 atoms are five-coordinate and display well distorted {CuN<sub>2</sub>O<sub>3</sub>} square-pyramidal geometries with the  $\tau_5$  parameters of 0.33 and 0.39, respectively (parameter  $\tau_5 = 0$  for an ideal square-pyramidal geometry,  $\tau_5 = 1$  for an ideal trigonal-bipyramidal geometry) [26]. The equatorial sites around the Cu1 center are taken by the N7, N8, O3, and O60 atoms of the µ-bea/Hbea moieties [Cu1-N7 2.024(4), Cu1-N8 2.058(4), Cu1-O3 1.953(3), Cu1–O60 1.935(3) Å], while the axial position is occupied by the OH group of Hbea [Cu1–O4 2.347(5) Å]. The coordination environment and bonding distances around the Cu2 atom are similar to those of Cu1; the Cu1…Cu2 separation of 3.0010(7) Å is rather short. The bond distances and angles in 1 are in agreement with those encountered in some related dicopper(II) aminoalcohol compounds [17a,27]. Furthermore, in 1 the  $Cu_2$  cations and nitrate anions are assembled, via the repeating N-H···O and O-H···O hydrogen bonds, into a 2D Hbonded network. From the topological viewpoint [23], this network can be classified as uninodal 3-connected underlying net with the hcb topology (Fig. 1b).



**Figure 1.** Structural fragments of **1**. (a) Dicopper(II)  $[Cu_2(\mu_2-bea)_2(Hbea)_2]^{2+}$  unit with atom labelling scheme; H atoms and NO<sub>3</sub><sup>-</sup> anions are omitted for clarity; color codes: Cu (green balls), O (red), N (blue), C (gray). (b) Topological representation of a 2D H-bonded underlying net showing a decorated uninodal 3-connected layer with the **hcb** topology and point symbol of (6<sup>3</sup>); centroids of 3-connected  $[Cu_2(\mu_2-bea)_2(Hbea)_2]^{2+}$  cationic nodes (green balls), centroids of 2-connected NO<sub>3</sub><sup>-</sup> anionic linkers (gray), view along the *a* axis.



**Figure 2.** Structural fragments of **2**. (a) Dicopper(II)  $[Cu_2(H_3tipa)_2(\mu_2-pma)]$  unit with atom labelling scheme (representation of one diastereoisomer identified in the crystal structure); H atoms are omitted for clarity; symmetry code: (i) -x, 2-y, -z; color codes: Cu (green balls), O (red), N (blue), C (gray). (b) Fragment of a 2D H-bonded  $\{(H_2O)_{25}\}_n$  network (gray colored) composed of repeating  $(H_2O)_8$  and  $(H_2O)_{20}$  rings; this network was topologically classified as a uninodal 3-connected layer with the **fes** topology and point symbol of  $(4.8^2)$ ; for simplicity, H-bonding interactions between  $[Cu_2(H_3tipa)_2(\mu_2-pma)]$  units (their centroids are shown as green balls) and  $\{(H_2O)_{25}\}_n$  layer are omitted for clarity; rotated view along the *ab* plane.

In contrast to 1, the structure of 2 is neutral and reveals a different type of dicopper(II) block [Cu<sub>2</sub>(H<sub>3</sub>tipa)<sub>2</sub>(µ-pma)] (Fig. 2a); there are also seven water molecules of crystallization per formula unit. The Cu<sub>2</sub> block is built from two symmetry equivalent  $\{Cu(H_3tipa)\}^{2+}$ moieties which are interconnected by the  $\mu_2$ -bridging and fully deprotonated pyromellitate(4– ) linker. The five-coordinate Cu1 center adopts a significantly distorted {CuNO<sub>4</sub>} squarepyramidal environment ( $\tau_5 = 0.41$ ) wherein the equatorial sites are filled by the N2, O9, and O10 atoms from a neutral fully protonated  $H_3$  tipa ligand and the carboxylate O66 atom from a µ-pma(4-) moiety [Cu1-N2 2.010(3), Cu1-O9 1.951(2), Cu1-O10 1.967(2), Cu1-O66 1.909(2) Å]. The axial position is taken by the remaining O1 atom of H<sub>3</sub>tipa [Cu1–O1 2.298(2) Å]. The µ-pma(4-) moiety separates the adjacent copper(II) centers with the Cu1...Cu1<sup>i</sup> distance of 11.055(2) Å. An interesting feature of the crystal structure of 2 concerns the presence of numerous H<sub>2</sub>O molecules of crystallization, which are assembled into intricate 2D { $(H_2O)_{25}$ }<sub>n</sub> layers (Fig. 2b) [28]. These layers are composed of the repeating (H<sub>2</sub>O)<sub>8</sub> and (H<sub>2</sub>O)<sub>20</sub> cyclic motifs and can be topologically classified as uninodal 3-connected nets with the **fes** topology [23]. Furthermore, these  $\{(H_2O)_{25}\}_n$  layers are extensively Hbonded to  $[Cu_2(H_3tipa)_2(\mu-pma)]$  units, generating a very complex 3D supramolecular network.

#### 3.3. Catalytic activity of 1 and 2 in the oxidation of cycloalkanes

Following our general interest in the mild oxidative functionalization of alkanes catalyzed by bioinspired copper compounds [12,17], we tested the dicopper(II) derivatives **1** and **2** as homogeneous catalysts for the oxidation of cycloalkanes to the corresponding alcohols and ketones. The reactions proceed under mild conditions (50 °C, atmospheric pressure) in aqueous MeCN medium and using  $H_2O_2$  (50% in  $H_2O$ ) as an oxidant. The oxidation of cyclohexane to a mixture of cyclohexanol and cyclohexanone (Scheme 2) was studied in detail as a model reaction with industrial significance (e.g., one of the steps in nylon production) [29].



Scheme 2. Oxidation of cyclohexane to cyclohexanol and cyclohexanone.

The cyclohexane oxidation catalyzed by **1** in the presence of a catalytic amount of trifluoroacetic acid (TFA) as a promoter (Fig. 3a) proceeds with a maximum total product yield of ~20% (hereinafter, all the yields are based on an alkane substrate), which is achieved at 90 min reaction time. A slight yield decline due to an overoxidation is observed on prolonging the reaction time. In the beginning of the reaction, cyclohexanol is formed predominantly to cyclohexanone; however, after 2 h of the reaction the ketone yield approaches that of the alcohol. Compound **2** is less active under the same reaction conditions, resulting in ~16% total yield (Fig. 3b).



**Figure 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.



**Figure 4.** Effect of the type of acid promoter on the total yield of the products in the cyclohexane oxidation with  $H_2O_2$  catalyzed by **1** (a) or **2** (b). Reaction conditions: catalyst **1** or **2** (0.01 mmol), acid promoter (0.1 mmol),  $C_6H_{12}$  (2.0 mmol),  $H_2O_2$  (10.0 mmol),  $CH_3CN$  (up to 5.0 mL total volume), 50 °C.

Both catalysts **1** and **2** require the presence of a small amount of an acid promoter (Fig. 4). Such a promoter activates the catalysts via partial protonation of ligands, facilitates proton transfer steps, and enhances the oxidation properties of  $H_2O_2$  [12,13,17]. We studied the influence of different types of acid promoters and found a similar behavior of **1** and **2** (Fig. 4). The kinetic curves of products accumulation show a resembling trend when using TFA, HNO<sub>3</sub>, or  $H_2SO_4$  as promoters (acid-to-catalyst molar ratio of 10:1). In contrast, the

presence of HCl dramatically increases the reaction rate of the  $C_6H_{12}$  oxidation for both catalysts **1** and **2**, resulting in a very fast reaction with the total yields of 16–18% (TOFs = 380–430 h<sup>-1</sup>) that are achieved within several minutes.



**Figure 5.** Effect of  $H_2SO_4$  (a, b) or TFA (c) amount on the total yield of the products in the cyclohexane oxidation with  $H_2O_2$  catalyzed by **1** (a) or **2** (b, c). Reaction conditions: catalyst **1** or **2** (0.01 mmol), acid promoter ( $H_2SO_4$  or TFA, 0.01–0.15 mmol),  $C_6H_{12}$  (2.0 mmol),  $H_2O_2$  (10.0 mmol), CH<sub>3</sub>CN (up to 5.0 mL total volume), 50 °C.

To get further insight into the promoting role of acids, we investigated the influence of the amount of  $H_2SO_4$  and TFA (Fig. 5). In the cyclohexane oxidation by the  $1/H_2SO_4$ system (Fig. 5a), both the product yield and the initial reaction rate ( $W_0$ ) grow on increasing the amount of  $H_2SO_4$  up to 5 equivalents relatively to catalyst. Further increase of the  $H_2SO_4$ loading (up to 15 equivalents) has no effect on the  $W_0$  and final product yield. In the  $2/H_2SO_4$ 

system (Fig. 5b), only one equivalent of acid is required to promote the catalytic activity of the complex, leading to ~10% total yield. By increasing an amount of  $H_2SO_4$  up to 2.5 equivalents relatively to 2, the maximum total yield rises to 13%, without affecting the initial reaction rate. A bigger  $H_2SO_4$  loading (15 equivalents) does not have influence on the reaction parameters. A similar behavior was observed in the 2/TFA system (Fig. 5c).



**Figure 6.** The effect of catalyst amount on (a) the total product yield and (b) the maximum initial reaction rate ( $W_0$ ) in the cyclohexane oxidation with H<sub>2</sub>O<sub>2</sub> catalyzed by **1**/TFA. Reaction conditions: catalyst **1** (0.0025–0.01 mmol), TFA promoter (0.1 mmol), C<sub>6</sub>H<sub>12</sub> (2.0 mmol), H<sub>2</sub>O<sub>2</sub> (10.0 mmol), CH<sub>3</sub>CN (up to 5.0 mL total volume), 50 °C.

The effects of the catalyst amount on the total yield and the reaction rate of the cyclohexane oxidation in the 1/TFA (Fig. 6) and 2/TFA (Fig. 7) systems are rather similar, although the reaction is slightly faster in the case of 1/TFA. A gradual growth of the total product yield on rising the catalyst amount from 0.0025 to 0.01 mmol was observed. The initial reaction rates have a linear dependence on the concentration of 1 and 2 (Figs. 6b and 7b), thus indicating the first-order reaction kinetics with respect to catalyst and supporting a probable involvement of one Cu-containing species in the rate-limiting step of the oxidation reaction.

An unusual accelerating effect of water on the initial reaction rate was observed for both catalysts **1** and **2** (Fig. 8). The increase in water concentration from 4.1 M (corresponding to the amount of  $H_2O$  present in 50% aqueous  $H_2O_2$ ) to 12.9 M (via an introduction of additional  $H_2O$  into the reaction mixture) leads to a linear increase of the initial reaction rate in both catalytic systems. In the  $1/H_2SO_4$  system (Fig. 8a), such a

behavior is also accompanied by a slight improvement of the maximum product yield; however, upon a prolonged reaction time, an yield drop was observed. This process is more evident at a high water concentration (12.9 M), thus suggesting that an additional amount of water in the system may promote the overoxidation reactions. In fact, a detailed GC-MS analysis of reaction mixtures containing a higher water content revealed the presence of different isomeric dicyclohexanols, dicyclohexanones, hidrohycyclohexanones, and even adipic acid. A similar trend was observed when studying the effect of water in the **2**/TFA (Fig. 8b) and **1**/TFA (Fig. 8c) systems. For both the **1**/H<sub>2</sub>SO<sub>4</sub> and **2**/TFA systems, a linear dependence of  $W_0$  on water concentration was detected (Fig. 8d), revealing a 5- or 4-fold growth of the  $W_0$  on increasing the H<sub>2</sub>O concentration from 4.1 to 12.9 M, respectively.



**Figure 7.** The effect of catalyst amount on (a) the total product yield and (b) the maximum initial reaction rate ( $W_0$ ) in the cyclohexane oxidation with H<sub>2</sub>O<sub>2</sub> catalyzed by 2/TFA. Reaction conditions: catalyst 2 (0.0025–0.01 mmol), TFA promoter (0.1 mmol), C<sub>6</sub>H<sub>12</sub> (2.0 mmol), H<sub>2</sub>O<sub>2</sub> (10.0 mmol), CH<sub>3</sub>CN (up to 5.0 mL total volume), 50 °C.

To get further insight, we performed additional experiments using the incubation of the 1/TFA catalytic system (Fig. 8c). The addition of a high amount of water (up to 12.9 M total) into the reaction mixture leads to the acceleration of the  $C_6H_{12}$  oxidation but results in a lower total yield (15% vs. 20%). The incubation of the reaction mixture containing 1/TFA,  $H_2O_2$ , and  $H_2O$  for 1 h at 50 °C with a posterior addition of  $C_6H_{12}$  does not lead to cyclohexane oxidation due to the consumption of peroxide (catalase activity). The addition of a new portion of  $H_2O_2$  to this reaction mixture restores the  $C_6H_{12}$  oxidation. The incubation of the reaction mixture containing 1/TFA and water for 1 h with a posterior addition of both  $H_2O_2$  and  $C_6H_{12}$  results in a less efficient cyclohexane oxidation, which proceeds with the

same reaction rate as the reaction without incubation. This can be due to the shift of an equilibrium toward the formation of different catalytically active species in the presence of a high amount of water.



**Figure 8.** The effect of H<sub>2</sub>O amount on (a, b, and c) the total product yield and (d) the maximum initial reaction rate ( $W_0$ ) of the cyclohexane oxidation with H<sub>2</sub>O<sub>2</sub> catalyzed by (a)  $1/H_2SO_4$ , (b) 2/TFA, (c) 1/TFA, and (d)  $1/H_2SO_4$  and 2/TFA systems. Reaction conditions: catalyst 1 or 2 (0.01 mmol), acid promoter (0.1 mmol), C<sub>6</sub>H<sub>12</sub> (2.0 mmol), H<sub>2</sub>O<sub>2</sub> (10.0 mmol), added H<sub>2</sub>O (up to 0.8 mL), CH<sub>3</sub>CN (up to 5.0 mL total volume), 50 °C.

All the above-discussed effects of H<sub>2</sub>O indicate a direct involvement of water in the rate-limiting step (generation of hydroxyl radicals) of the cycloalkane oxidation. In fact, the H<sub>2</sub>O-assisted pathways for the generation of hydroxyl radicals in V- or Re-catalyzed alkane

oxidations were earlier suggested by DFT calculations [30]. Furthermore,  $H_2O$  showed a remarkable promoting behavior in some related Cu-containing catalytic systems [17a,b] as well as acted as unusual hydroxylating reagent and solvent component in mild coppercatalyzed alkane hydrocarboxylations [12,31]. However, such a promoting role of water is still uncommon but may open a possibility of applying diluted in situ generated aqueous solutions of  $H_2O_2$  as a green oxidant in alkane oxidation processes.

The effect of the oxidant amount on the cyclohexane oxidation catalyzed by the  $1/H_2SO_4$  system was also investigated. As expected, the  $H_2O_2$  concentration affects both the initial reaction rate and total product yield (Fig. 9a). With a high  $H_2O_2$  amount (10 mmol), the oxidation of  $C_6H_{12}$  is faster and more efficient, resulting in 17% total yield (vs. 10% with a low oxidant loading, 2.5 mmol).



**Figure 9.** (a) The effect of  $H_2O_2$  amount on the total product yield in the cyclohexane oxidation catalyzed by  $1/H_2SO_4$ . (b) The cyclohexane oxidation with  $H_2O_2$  catalyzed by the 2/TFA system using fresh and recovered catalyst. Reaction conditions: catalyst 1 (a) or 2 (b) (0.01 mmol),  $H_2SO_4$  (a) or TFA (b) promoter (0.1 mmol),  $C_6H_{12}$  (2.0 mmol),  $H_2O_2$  (2.5 (a) or 10.0 (a, b) mmol),  $CH_3CN$  (up to 5.0 mL total volume), 50 °C.

A notable feature of the catalyst 2 consists in the possibility of its reuse. After a standard cyclohexane oxidation reaction by the 2/TFA system (Fig. 9b), we recovered a solid residue of the catalyst by filtration. It was washed by CH<sub>3</sub>CN, dried in air, and analyzed by the IR spectroscopy, revealing a spectrum that is very similar to that of the parent compound 2. This experiment confirms the stability of 2 in the course of catalytic tests. In fact, the cyclohexane oxidation using a recovered catalyst 2 reveals a similar product accumulation curve (Fig. 9b), although with a slightly decreased total yield of 13%. Such a yield decrease

may be associated with the use of a decreased catalyst amount (due to a partial loss of the catalyst during a recycling experiment).

To evaluate the substrate scope of the present catalytic systems, we tested the oxidation of other cycloalkanes under selected reaction conditions, using the 1/TFA and 2/TFA systems (Table 1). Among the tested cycloalkanes, the highest activity (23% total yield) was observed for the cycloheptane oxidation, followed by cyclooctane (22–18%) and cyclohexane (19–15%) substrates. Cyclopentane oxidation is less efficient, leading to 9–6% total product yields. For the oxidation of the C<sub>6</sub>–C<sub>8</sub> cycloalkanes, the obtained product yields are comparable to those attained in some other copper based catalytic systems [12,17]. Despite not being very high, the total yields of cyclohexanol and cyclohexanone achieved in the present work are superior than those in an industrial DuPont process for the oxidation of cyclohexane, which uses cobalt naphthenate as a homogeneous catalyst and proceeds under harsher reaction conditions [10,29].

Furthermore, in spite of being more reactive substrate, cyclohexanol is not readily oxidized into cyclohexanone by the present 1/TFA and 2/TFA systems (only 5–6% yields of cyclohexanone were obtained), thus suggesting that possible overoxidation reactions of the formed alcohol products in the course of the alkane oxidations do not proceed to a significant extent, if avoiding prolonged reaction times. These data also confirm a rather high overall selectivity (typically above 90% in the first hours of the reaction) toward the main products, cyclohexanol and cyclohexanone, in the cyclohexane oxidation catalyzed by 1 and 2. It should also be mentioned that both the 1/TFA and 2/TFA catalytic systems show a significantly lower activity when using *tert*-butyl hydroperoxide (*t*-BuOOH) as oxidant instead of hydrogen peroxide. In fact, the total yields of products in the oxidation of cyclohexane by *t*-BuOOH do not exceed ~3%.

Cycloalkane	Total product yield (alcohol + ketone), % <sup>b</sup>		
<u> </u>	1	2	
C <sub>5</sub>	9	6	
C <sub>6</sub>	19	15	
<b>C</b> <sub>7</sub>	23	23	

**Table 1.** Mild oxidation of  $C_5$ – $C_8$  cycloalkanes with  $H_2O_2$  catalyzed by 1 and 2.<sup>a</sup>



<sup>a</sup>Reaction conditions: catalyst **1** or **2** (0.01 mmol), acid promoter (TFA, 0.1 mmol), cycloalkane (2 mmol),  $H_2O_2$  (10 mmol),  $CH_3CN$  (up to 5 mL total volume), 50 °C, 3 h. <sup>b</sup>Yields are based on alkanes [(moles of products per mol of cycloalkane)×100%]. <sup>c</sup>Under similar reaction conditions, the oxidation of cyclohexanol with  $H_2O_2$  leads to ~6 or 5% yield of cyclohexanone when using **1** or **2**, respectively. <sup>d</sup>Under similar reaction conditions, the oxidation of  $C_6H_{12}$  by *t*-BuOOH (70% in  $H_2O$ , 5 mmol) results in only 3 or 1% total yields of products (cyclohexanol + cyclohexanone) when using **1** or **2**, respectively.

#### 3.4. Investigation of model solutions by ESI-MS.

To get additional information on possible species present in solution, we investigated the parent compounds 1 and 2 and the corresponding  $1/H^+/H_2O_2$  and  $2/H^+/H_2O_2$  model catalytic mixtures by the ESI-MS( $\pm$ ) method. The MS(+) spectrum of  $[Cu_2(\mu-bea)_2(Hbea)_2](NO_3)_2$  (1) reveals a characteristic peak of a doubly charged cation  $[Cu_2(\mu-bea)_2]^{2+}$  (*m*/*z* 364) and a molecular ion  $[Cu_2(\mu-H_{0.5}bea)_2(Hbea)_2(NO_3)_2]^+$  (m/z 853), followed by further fragmentation with the loss of benzylethanolamine moieties, as confirmed by the detection of the  $[Cu_2(\mu-bea)_2(Hbea)(NO_3)]^+$  (m/z)640) and  $[Cu_2(\mu-H_{0.5}bea)_2(NO_3)_2]^+$  (m/z 551) peaks. The MS<sup>2</sup> fragmentation of the molecular ion,  $[Cu_2(\mu-H_{0.5}bea)_2(Hbea)_2(NO_3)_2]^+$  (m/z 853), produced the following fragments:  $[Cu_2(\mu-H_{0.5}bea)_2(Hbea)_$  $bea)_2(H_{0.5}bea)_2(H_2O)_2]^+$  (*m*/*z* 765),  $[Cu_2(\mu-bea)_2(bea)]^+$  (*m*/*z* 576),  $[Cu_2(\mu-H_{0.5}bea)_2(NO_3)_2]^+$  (*m*/*z* 551), and  $[Cu_2(\mu-bea)_2]^+$  (m/z 426). In the MS(-) mode, we were able to detect the molecular ion,  $[Cu_2(\mu-bea)_2]^+$ bea)<sub>2</sub>(H<sub>0.5</sub>bea)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub><sup>-</sup> (m/z 851), and the derived adducts [Cu<sub>2</sub>( $\mu$ -bea)<sub>2</sub>(H<sub>0.5</sub>bea)(H<sub>2</sub>O)]<sup>-</sup> (m/z 745),  $[Cu_2(\mu-bea)_2(bea)(OH)]^-$  (*m/z* 593), and  $[Cu_2(\mu-bea)_2(bea)]^-$  (*m/z* 576). Additional less characteristic fragments corresponding to various nitrate adducts were also observed in both positive and negative ESI modes. In acidic medium and after the introduction of hydrogen peroxide, we can still identify in the ESI-MS(+) spectrum the molecular ion,  $[Cu_2(\mu-H_{0.5}bea)_2(Hbea)_2(NO_3)_2]^+$  (*m*/z 853), and typical derived dicopper fragments with expected isotopic distribution patterns, suggesting that such Cu<sub>2</sub>aminoalcohol cores can correspond to catalytically active species in the  $1/H^+/H_2O_2$  system.

The ESI-MS(+) plot of  $[Cu_2(H_3tipa)_2(\mu-pma)]\cdot 7H_2O$  (2) shows the characteristic peak corresponding to the molecular ion  $[Cu_2(H_3tipa)_2(\mu-Hpma)]^+$  (*m*/*z* 759) and its adduct  $[Cu_2(H_3tipa)_2(\mu-pma) + Na]^+$  (*m*/*z* 781), pursued by further fragmentation with the ESI-induced cleavage or loss of triisopropanolamine moieties. This is confirmed by the detection of the ions:  $[Cu_2(H_3tipa)_2(\mu-H_2pma) - OH]^+$  (*m*/*z* 742),  $[Cu_2(H_3tipa)_2(\mu-H_2pma) - C_3H_7OH]^+$  (*m*/*z* 703), and  $[Cu_2(H_3tipa)(\mu-H_2pma) - OH]^+$  (*m*/*z* 552). Despite poor fragmentation in the MS(–) mode, an adduct of the molecular ion  $[Cu_2(H_2tipa)_2(\mu-pma) + Na]^-$  (*m*/*z* 779) was detected. In the MS(+) mode, some of the above dicopper(II) fragments become more intense in acidic medium and after the introduction of H<sub>2</sub>O<sub>2</sub>, suggesting a partial decoordination of triisopropanol moieties and further fragmentation of dicopper cores in the course of catalytic reactions. However, these processes appear to be reversible given the

#### 3.5. Investigation of different selectivity parameters in alkane oxidation.

Aiming at evaluating the type of the reaction mechanism and nature of the involved oxidizing species, we carried out the oxidation of different linear and cyclic alkanes in the presence of both 1/TFA and 2/TFA systems and measured various selectivity parameters (Table 2). Interestingly, the oxidation of a linear alkane, *n*-hexane, proceeds with some specific preference to the third C(3) secondary carbon atom, as attested by the regioselectivity C(1):C(2):C(3) parameters of 1:8:15 or 1:10:18 for the 1/TFA or 2/TFA systems, respectively. In the case of *n*-heptane, an increased reactivity of the forth C(4) carbon atom was also observed, with the respective C(1):C(2):C(3):C(4) parameters of 1:12:16:26 (1/TFA) or 1:10:12:15 (2/TFA). Besides, the oxidation of *n*-octane proceeds with some preference to the C(3) and C(4) atoms (Table 2). Within all the tested  $C_6-C_8$  linear alkanes, the secondary atoms are oxidized with an increased preference over the primary C atoms. The oxidation reactions of methylcyclohexane and adamantane result in moderate bond selectivities, with the 1°:2°:3° parameters of 1:5:27 (1/TFA) and 1:8:31 (2/TFA) in the case of methylcyclohexane. If both cis- or trans-1,2-dimethylcyclohexanes are used as substrates, the oxidation reactions are non-stereoselective, as evidenced by the trans/cis ratios of 0.6-0.9 between the generated isomeric tertiary alcohols with the mutual trans and cis orientation of the methyl groups. The cis isomers are predominant products in the oxidation of trans-1,2dimethylcyclohexane, suggesting a partial inversion of the configuration.

Table 2. Selectivity parameters in the oxidation of various alkane substrates.<sup>a</sup>

	catalyst		
Selectivity parameter	1	2	
Regioselectivity			
$C(1):C(2):C(3)^{b} (n-C_{6}H_{14})$	1:8:15	1:10:18	
$C(1):C(2):C(3):C(4)^{b}$ ( <i>n</i> -C <sub>7</sub> H <sub>16</sub> )	1:12:16:26	1:10:12:15	
$C(1):C(2):C(3):C(4)^{b}$ ( <i>n</i> -C <sub>8</sub> H <sub>18</sub> )	1:15:18:18	1:12:16:16	
Bond selectivity			
$1^{\circ}:2^{\circ}:3^{\circ}$ (methylcyclohexane) <sup>c</sup>	1:5:27	1:8:31	
2°:3° (adamantane) <sup>d</sup>	1:1.6	1:1.6	
Stereoselectivity			
trans/cis (cis-dimethylcyclohexane) <sup>e</sup>	0.6	0.7	
trans/cis (trans-dimethylcyclohexane) <sup>e</sup>	0.9	0.8	

<sup>a</sup>Reaction conditions: catalyst **1** or **2** (0.005 mmol), TFA (0.05 mmol), alkane (1.0 mmol), H<sub>2</sub>O<sub>2</sub> (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. <sup>b</sup>Parameters C(1):C(2):C(3):(C(4)) are the relative reactivities of hydrogen atoms at carbons 1, 2, 3, (and 4) of the *n*-hexane, *n*-heptane or *n*-octane chain. <sup>c</sup>Parameters 1°:2°:3° are the relative normalized reactivities of the hydrogen atoms at primary, secondary and tertiary carbon atoms of methylcyclohexane. <sup>d</sup>Parameters 3°/2° are the relative normalized reactivities of the hydrogen atoms at tertiary and secondary carbon atoms of adamantane, determined as the ratio of the formed tertiary and secondary alcohol isomers. <sup>e</sup>Parameter *trans/cis* is determined as the ratio of the formed tertiary and secondary alcohol and *cis* orientation of the methyl groups.

The above-discussed selectivity parameters in the alkane oxidations with  $H_2O_2$  catalyzed by the **1**/TFA and **2**/TFA systems (Table 2) as well as prior literature data<sup>12,13,17,32</sup> indicate an involvement of a powerful and rather indiscriminate oxidizing species such as HO<sup>•</sup> radicals. A somewhat increased regioselectivity in the oxidation of linear alkanes can be associated with some bulkiness of the dicopper catalysts. On the basis of the obtained selectivity data, observed kinetic features, and literature background for related Cucontaining catalytic systems [12,13,17] a number of simplified mechanistic steps can be mentioned. (1) Hydrogen peroxide reacts with a Cu<sub>2</sub> catalyst generating hydroxyl radicals; (2) they abstract hydrogen atoms from alkane to give alkyl radicals R<sup>•</sup>; (3) these radicals react further with O<sub>2</sub> (e.g., from air or via partial H<sub>2</sub>O<sub>2</sub> decomposition) to furnish ROO<sup>•</sup> radicals; (4) the latter are transformed to alkyl hydroperoxides (ROOH) as primary intermediate products; and finally (5) ROOH rapidly decomposes (eventually via a Cu-catalyzed processes and additionally after the treatment by PPh<sub>3</sub>) to result in alcohols and ketones as oxidation products [12,17].

#### 3.6. Catalytic activity of 1 and 2 in the hydrocarboxylation of cycloalkanes

In addition to the oxidation of cycloalkanes by  $H_2O_2$ , we also investigated the catalytic performance of the compounds **1** and **2** in the mild hydrocarboxylation of cycloalkanes to give carboxylic acids with one more carbon atom (Scheme 3). This method consists of the reaction of  $C_n$  alkane with CO (carbonyl source), potassium peroxodisulfate (oxidant), and  $H_2O$  (hydroxyl source) to form directly a  $C_{n+1}$  carboxylic acid,  $C_n$ –COOH. Cyclic ketones and alcohols are also formed as minor products as a result of the competing alkane oxidation reaction. The hydrocarboxylation reactions were carried out under optimized conditions [12,31], namely at 60 °C in water-acetonitrile medium (v/v 1:2) and using p(CO) of 20 atm. The obtained results are summarized in Table 3.



Scheme 3. Hydrocarboxylation of  $C_n$  cycloalkanes into  $C_{n+1}$  cycloalkanecarboxylic acids.

Both compounds **1** and **2** act as rather efficient catalysts toward the hydrocarboxylation of  $C_5-C_8$  cycloalkanes (cyclopentane, cyclohexane, cycloheptane, and cyclooctane) into the corresponding  $C_6-C_9$  cycloalkanecarboxylic acids with yields up to 38% based on the cyloalkane (Table 3). The catalytic activity of compound **1** is comparable or slightly higher than that of **2**. The hydrocarboxylation of cycloalkanes results in the formation of one monocarboxylic acid product due to the presence of a single type of carbon atom in their molecules. No dicarboxylic acid formation was detected in these tests. The highest activity for both **1** and **2** catalysts is observed for the hydrocarboxylation of cyclohexane, leading to a 38% yield of cyclohexanecarboxylic acid ( $C_6H_{11}COOH$ ), followed by cycloheptane (24–26% of  $C_7H_{13}COOH$ ) and cyclopentane (21–27% of  $C_5H_9COOH$ ). The yield of carboxylic acid drops to 13% and 10% when using cyclooctane as a substrate in the presence of **1** or **2**, respectively.

**Table 3.** Single-pot hydrocarboxylation of  $C_n$  (n = 5-8) cycloalkanes into the corresponding  $C_{n+1}$  cycloalkanecarboxylic acids catalyzed by **1** and **2**.<sup>*a*</sup>

Entry	Cycloalkane	Catalyst	Product Yield, % <sup>b</sup>			
		Cycloarkane Catalyst	Catalyst	Acid	Ketone	Alcohol
1		1	26.7	0.5	0.1	27.3
2	05	2	20.9	0.3	0.1	21.3
3	C	1	38.4	1.5	0.3	40.2
4		2	38.2	2.1	0.4	40.7
5		1	24.2	9.5	2.7	36.4
6	C <sub>7</sub>	2	26.1	8.3	2.2	36.6
7		1	13.4	11.8	4.8	30.0
8		2	10.1	10.4	3.6	24.1

<sup>*a*</sup>Cyclic ketones and alcohols are also formed as by-products. Reaction conditions (unless stated otherwise): cycloalkane (1.00 mmol), Cu catalyst (0.01 mmol), p(CO) = 20 atm,  $K_2S_2O_8$  (1.50 mmol),  $H_2O$  (2.0 mL)/MeCN (4.0 mL), 60 °C, 4 h in an autoclave (20.0 mL capacity). <sup>*b*</sup> Moles of product/100 moles of alkane. <sup>*c*</sup> Yield of all products.

The corresponding cyclic ketones and alcohols are also formed as minor products as a result of partial oxidation of cycloalkanes. However, the total yield of oxygenates (ketone is formed predominantly to alcohol) increases with the hydrocarbon size, namely from 0.5-2.5% for C<sub>5</sub>H<sub>10</sub> and C<sub>6</sub>H<sub>12</sub> to 10.5-12.6% for C<sub>7</sub>H<sub>14</sub> and C<sub>8</sub>H<sub>16</sub>.

Based on prior literature background [12,31] and the obtained experimental data, we believe that the Cu-catalyzed hydrocarboxylation reactions proceed via the following main steps. (1) The formation of the cycloalkyl radicals R<sup>•</sup> from a cycloalkane [generated via H abstraction by sulfate radical SO<sub>4</sub> - derived from homolysis of K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>]. (2) The carbonylation of R<sup>•</sup> by CO to give the cycloacyl radicals RCO<sup>•</sup>. (3) The oxidation of RCO<sup>•</sup> by copper(II) species to the cycloacyl cations RCO<sup>+</sup> [via the Cu(II)/Cu(I) redox couple] and (3') the regeneration of the Cu(II) form upon oxidation of Cu(I) by K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>. (4) The hydrolysis of RCO<sup>+</sup> to yield the corresponding cycloalkanecarboxylic acid [12].

#### 4. Concluding remarks

The present study has reported the synthesis, full characterization, and application in homogeneous oxidation catalysis of two new water-soluble coordination compounds,  $[Cu_2(\mu-bea)_2(Hbea)_2](NO_3)_2$  (1) and  $[Cu_2(H_3tipa)_2(\mu-pma)]\cdot 7H_2O$  (2). Their structures show distinct types of dicopper(II) cores driven by *N*-benzylethanolamine or triisopropanolamine and pyromellitate ligands, respectively. In spite of commercial availability and potential

coordination versatility of these aminoalcohol ligands, the obtained compounds also represent the first examples of discrete copper complexes derived from Hbea and H<sub>3</sub>tipa [17a,33]. Other novelty features of the present compounds concern their catalytic versatility, since both 1 and 2 are capable of catalyzing two distinct reactions of the oxidative functionalization of alkanes (i.e., oxidation and hydrocarboxylation).

Thus, both dicopper(II) compounds catalyze the mild homogeneous oxidation by  $H_2O_2$  of different cycloalkanes (cyclopentane, cyclohexane, cycloheptane, and cyclooctane) to form the corresponding cyclic alcohols and ketones in up to 23% overall yields based on substrate. Despite not being high, these yields can be considered as rather good especially in view of the high inertness of saturated hydrocarbons and very mild reaction conditions that were applied [34,35]. Besides, a notable feature of compound **2** consists in the possibility of its recovery and reuse in further catalytic tests. Cyclohexane has been studied as a model hydrocarbon [10,29] and the influence of various reaction parameters has been investigated, including the kind and amount of an acid promoter, catalyst loading, and solvent composition (water content).

Although water is known to inhibit alkane oxidation due to the reduction of oxidant concentration and decrease of substrate solubility, we have detected a considerable increase of an initial reaction rate in the cyclohexane oxidation by both  $1/H^+/H_2O_2$  and  $2/H^+/H_2O_2$  systems on rising the H<sub>2</sub>O content in the reaction mixture. The present work thus represents a continuation of our efforts on widening a very limited family of copper based catalytic systems [17a,b] that are active in the oxidative functionalization of alkanes and wherein water can play an unusual promoting role. By extending a series of Cu-aminoalcohol catalysts it should be possible to verify whether the type of aminoalcohol ligand and/or the nuclearity of a copper core can correlate with the promoting role of water. We believe that by identifying and studying more examples of such copper compounds, it would be possible to develop more efficient water-assisted catalytic systems and better understand the promoting role of water.

Furthermore, the compounds **1** and **2** act as efficient catalysts for the hydrocarboxylation of  $C_5$ – $C_8$  cycloalkanes in the presence of CO,  $K_2S_2O_8$ , and  $H_2O$ , resulting in the formation of the corresponding cycloalkanecarboxylic acids as principal products. Cyclic alcohols and ketones are also formed in minor amounts as products of the competing oxidation reaction. Highest yields of carboxylic acids were obtained when using cyclohexane (38% of  $C_6H_{11}COOH$ ), followed by cycloheptane (24–26% of  $C_7H_{13}COOH$ ) and cyclopentane (21–27% of  $C_5H_9COOH$ ).

By having a N,O-environment around copper centers and being active in mild alkane oxidations, the compounds **1** and **2** can also be considered as bioinspired homogeneous catalysts with some relevance to the function of particulate methane monooxygenase [7]. The design of novel multicopper cores driven by simple and low-cost aminoalcohol ligands as well as the application of such compounds toward the oxidation of different alkanes under mild conditions is currently in progress.

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