

## Bringing an “Old” Biological Buffer to Coordination Chemistry: New 1D and 3D Coordination Polymers with [Cu<sub>4</sub>(Hbes)<sub>4</sub>] Cores for Mild Hydrocarboxylation of Alkanes

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New water-soluble 1D and 3D Cu<sup>II</sup>/Na coordination polymers **1–3** bearing unprecedented [Cu<sub>4</sub>(Hbes)<sub>4</sub>] cores have been easily generated by aqueous-medium self-assembly and fully characterized, thus opening up the use of the common biological buffer H<sub>3</sub>bes, (HO<sub>3</sub>SCH<sub>2</sub>CH<sub>2</sub>)N(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>2</sub>, in synthetic coordination chemistry. Apart from representing the first isolated and structurally characterized coordination compounds derived from H<sub>3</sub>bes, **1–3** show a remarkable promoting effect in the mild aqueous-medium hydrocarboxylation, by CO and H<sub>2</sub>O, of gaseous alkanes (C<sub>3</sub>H<sub>8</sub> and *n*-C<sub>4</sub>H<sub>10</sub>) to the corresponding carboxylic acids, which are obtained in up to 95% yields based on the alkane.

Since the discovery by Good et al. in 1966, *N,N*-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid (H<sub>3</sub>bes) has become a well-known low-interference buffer with a recognized use in biochemical and biomedical research.<sup>1</sup> However, in spite of its commercial availability, aqueous solubility, and interesting structure with different functional groups, the application of H<sub>3</sub>bes as a multidentate N,O ligand in synthetic coordination chemistry has remained virtually unexplored. Although the formation of some metal complexes with H<sub>3</sub>bes in solution has been documented,<sup>2</sup> searches of the literature and the Cambridge Structural Database (CSD)<sup>3</sup> show that there is no single example of a coordination compound derived from H<sub>3</sub>bes that has been isolated and

structurally characterized in the solid state. This contrasts with the rich family of compounds with the related amino-polyalcohol triethanolamine.<sup>3,4</sup>

Bearing these features in mind and following our interest in the design, by aqueous-medium self-assembly with amino-polyalcohol ligands, of catalytically active multicopper(II) compounds,<sup>4</sup> the main objectives of the present work consist of (i) opening up the use of H<sub>3</sub>bes for the synthesis of novel multicopper cores and (ii) establishing their application for the selective oxidative functionalization of alkanes as bioinspired catalysts relevant to particulate methane monooxygenase (pMMO).<sup>5</sup>

Hence, we report herein the new series of water-soluble Cu<sup>II</sup>/Na coordination polymers **1–3** having the general formulas [Cu<sub>4</sub>(Hbes)<sub>4</sub>(RC<sub>6</sub>H<sub>4</sub>COO){Na(H<sub>2</sub>O)<sub>*x*</sub>}]<sub>*n*</sub> · *y*<sub>*n*</sub>H<sub>2</sub>O [R = 4-HO- (**1**), H- (**2**), and 2-MeO- (**3**)], which represent the first structurally characterized examples of coordination compounds derived from H<sub>3</sub>bes (Scheme 1). We also show that their water-soluble [Cu<sub>4</sub>(Hbes)<sub>4</sub>] cores efficiently promote mild hydrocarboxylation, by CO and H<sub>2</sub>O, of propane and butane to the corresponding carboxylic acids.

The 1D (**1**) and 3D (**2** and **3**) polymers have been generated via a facile self-assembly route that is based on the combination, in an aqueous solution and at room temperature, of copper(II) nitrate (metal source) and H<sub>3</sub>bes (main ligand source), with the corresponding benzoic acid RC<sub>6</sub>H<sub>4</sub>COOH (auxiliary ligand source) and sodium hydroxide (pH-regulator)

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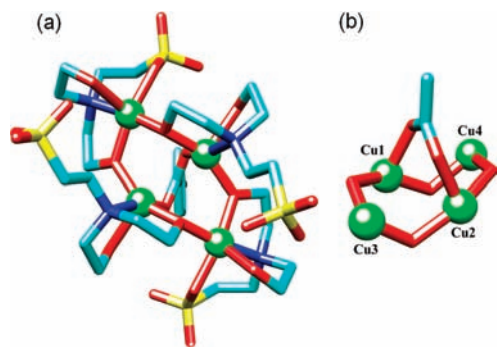
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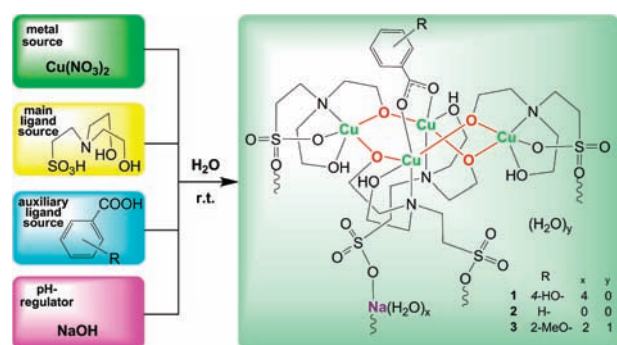
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**Figure 1.** Crystal structure of **1** (partial view) representing the  $[\text{Cu}_4(\text{Hbes})_4(4\text{-HO-C}_6\text{H}_4\text{COO})]^-$  unit (a) and its  $[\text{Cu}_4(\mu\text{-O})_4(\mu\text{-COO})]$  core (b).  $\mu\text{-Na}(\text{H}_2\text{O})_4$  moieties and H atoms are omitted for clarity. Color codes: Cu, green; O, red; N, blue; C, cyan; S, yellow. Selected bonding parameters (Å): Cu–OHbes 1.918(2)–1.931(2), Cu–OCOO 2.012(2), Cu1...Cu2 3.0563(5), Cu1...Cu3 3.3510(7), Cu3...Cu4 5.9013(9).

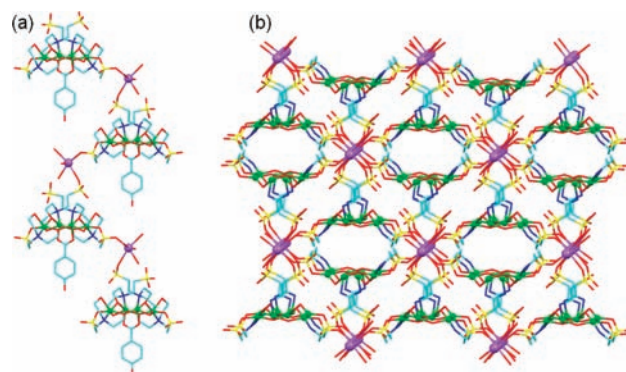
### Scheme 1. Aqueous-Medium Self-Assembly Synthesis of 1–3



(Scheme 1). The crucial role in defining the dimensionality of the obtained networks is eventually played by the type of auxiliary benzenecarboxylate ligand. The obtained products have been isolated as air-stable crystalline solids and characterized by IR spectroscopy, electrospray ionization mass spectrometry (ESI-MS), elemental analyses, and X-ray crystallography.<sup>6</sup>

The X-ray crystal structures of all of the compounds bear structurally similar tetracopper(II)  $[\text{Cu}_4(\text{Hbes})_4(\text{carboxylate})]^-$  blocks (as a typical example, see Figure 1) that are further assembled, via the charge-balancing sodium moieties and the sulfonate groups of Hbes, into the different 1D or 3D coordination networks (Figure 2). In all compounds, the tetracopper(II) cores are composed of four  $\mu\text{-O}$  bridging Hbes ligands (acting in different  $\text{N}_2\text{O}_2$ - and  $\text{N}_2\text{O}_3$ -coordination modes) and one  $\mu\text{-COO}$  carboxylate ligand, which provides an additional interlinkage of the “central” Cu

(6) Crystal data for **1**:  $\text{C}_{31}\text{H}_{64}\text{Cu}_4\text{N}_4\text{NaO}_{27}\text{S}_4$ , MW = 1331.26, monoclinic, space group  $P2_1/c$ ,  $a = 17.502(3)$  Å,  $b = 21.080(3)$  Å,  $c = 13.7686(9)$  Å,  $\beta = 106.664(7)^\circ$ ,  $V = 4866.5(11)$  Å<sup>3</sup>,  $T = 120(2)$  K,  $Z = 4$ ,  $D_{\text{calcd}} = 1.817$  Mg m<sup>-3</sup>,  $\mu = 1.999$  mm<sup>-1</sup>,  $F(000) = 2744$ ,  $\theta = 1.93\text{--}27.5^\circ$ , GOF = 1.061, 85 491 reflns measured, 11 162 unique ( $R_{\text{int}} = 0.0565$ ),  $R1 = 0.0351$ ,  $wR2 = 0.0628$ . Crystal data for **2**:  $\text{C}_{31}\text{H}_{57}\text{Cu}_4\text{N}_4\text{NaO}_{25}\text{S}_4$ , MW = 1243.20, monoclinic, space group  $C2/c$ ,  $a = 18.0367(13)$  Å,  $b = 21.0944(15)$  Å,  $c = 14.0941(10)$  Å,  $\beta = 116.122(3)^\circ$ ,  $V = 4814.7(6)$  Å<sup>3</sup>,  $T = 292(2)$  K,  $Z = 4$ ,  $D_{\text{calcd}} = 1.715$  Mg m<sup>-3</sup>,  $\mu = 2.006$  mm<sup>-1</sup>,  $F(000) = 2552$ ,  $\theta = 1.93\text{--}27.10^\circ$ , GOF = 0.913, 18 403 reflns measured, 5291 unique ( $R_{\text{int}} = 0.0780$ ),  $R1 = 0.0518$ ,  $wR2 = 0.1250$ . Crystal data for **3**:  $\text{C}_{32}\text{H}_{50}\text{Cu}_4\text{N}_4\text{NaO}_{26}\text{S}_4$ , MW = 1321.22, monoclinic, space group  $C2/c$ ,  $a = 18.6049(12)$  Å,  $b = 21.0872(11)$  Å,  $c = 14.0954(9)$  Å,  $\beta = 118.396(2)^\circ$ ,  $V = 4864.6(5)$  Å<sup>3</sup>,  $T = 150(2)$  K,  $Z = 4$ ,  $D_{\text{calc}} = 1.804$  Mg m<sup>-3</sup>,  $\mu = 1.997$  mm<sup>-1</sup>,  $F(000) = 2712$ ,  $\theta = 2.49\text{--}26.41^\circ$ , GOF = 1.041, 19 293 reflns measured, 5001 unique ( $R_{\text{int}} = 0.0415$ ),  $R1 = 0.0624$ ,  $wR2 = 0.1549$ .



**Figure 2.** Fragments of crystal-packing diagrams of **1** (a) and **2** (b) (views along the  $c$  axis) showing the interlinkage of  $\text{Cu}_4$  cluster nodes into a zigzag 1D chain (a) and a 3D metal–organic framework (b). Color codes: Cu, green; Na, purple; O, red; N, blue; C, cyan; S, yellow. H atoms (in **1** and **2**),  $\text{C}_6\text{H}_5\text{COO}$ , and some  $\text{CH}_2\text{CH}_2(\text{O})$  groups of Hbes (in **2**) are omitted for clarity.

atoms. The geometries around the pentacoordinated Cu atoms can be described as square pyramids fused via common vertices into the  $[\text{Cu}_4(\mu\text{-O})_4(\mu\text{-COO})]$  cores, wherein the Cu centers are located almost in one plane, with the shortest and longest Cu...Cu separations in **1** of 3.0563(5) and 5.9013(9) Å, respectively. Such a relative planarity of the Cu atoms in **1–3** is very unusual for tetracopper(II) compounds, as confirmed by a search in the CSD.<sup>3</sup>

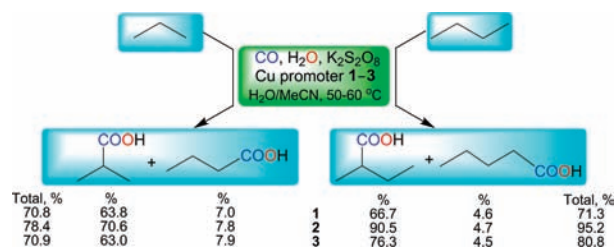
In spite of bearing similar tetracopper cores (cluster nodes), the main architectural distinctive features of **1–3** arise from the different coordination modes of the sulfonate groups in the Hbes moieties. In **1**, only two of four sulfonate groups connect to the aqua–sodium linkers, thus giving rise to 1D zigzag metal–organic chains (Figure 2a). In contrast, all four sulfonate groups within the Cu cluster node in **2** coordinate to the neighboring Na atoms, generating an infinite 3D metal–organic framework (Figure 2b). A similar 3D architecture is also observed in the structure of **3** (Figure S9 in the Supporting Information).

All of the compounds **1–3** represent rare examples<sup>4b,7</sup> of water-soluble copper-containing coordination polymers, with solubilities ( $S_{25\text{ }^\circ\text{C}}$  in  $\text{H}_2\text{O}$ ) ranging from 15 (**1** and **3**) to 130 (**2**) mg mL<sup>-1</sup>. In aqueous solution, they eventually dissociate into ionic species upon decoordination of the carboxylate ligands, in accordance with detection of the  $[\text{Cu}_4(\text{Hbes})_4\text{Na}]^+$  and  $[\text{Cu}_4(\text{Hbes})_3(\text{bes})]^-$  fragments at  $m/z$  1122 and 1098, respectively, in the ESI-MS( $\pm$ ) spectra of **1–3**. An important feature of the highly soluble compound **2** consists of its ability to recrystallize from a  $\text{H}_2\text{O}$  solution in the original form, as confirmed by IR spectroscopy and elemental analysis.

The water solubility of **1–3** and the significance of their labile tetracopper cores in terms of the active site of pMMO (a multi-copper cluster with a N,O environment)<sup>5</sup> suggest the potential application of these compounds for oxidative functionalization, in an aqueous medium, of inert gaseous alkanes. Although numerous examples of bioinspired copper complexes have been reported,<sup>8</sup> the aqueous-medium transformations of gaseous alkanes with water-soluble catalysts remain rather scant.

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**Scheme 2.** Copper-Promoted Hydrocarboxylation of Propane and *n*-Butane to Carboxylic Acids<sup>a</sup>

<sup>a</sup>The molar percent yields are based on alkane.

Following our recently developed method for the mild transformation of  $C_n$  alkanes to  $C_{n+1}$  carboxylic acids in an aqueous medium,<sup>9</sup> we have tested the promoting behavior of **1–3** in such hydrocarboxylation reactions using propane and *n*-butane as substrates (Scheme 2).<sup>10</sup> These transformations were undertaken by reacting, at low temperature (50–60 °C) in a neutral  $H_2O/MeCN$  medium, an alkane with  $CO$ ,  $H_2O$ , and potassium peroxodisulfate.

Compounds **1–3** were found to exhibit a remarkable promoting behavior. Thus, the branched *i*-butyric and 2-methylbutyric acids were respectively obtained as the main products (63–91% yield) during carboxylation of  $C_3H_8$  and *n*- $C_4H_{10}$ , whereas the corresponding linear butyric and valeric acids were generated in minor amounts (5–8% yield). The structural resemblance of the  $[Cu_4(Hbes)_4]$  cores in **1–3** explains their somehow similar activity. However, the highest total yields of carboxylic acids (78 and 95% in reactions with  $C_3H_8$  and *n*- $C_4H_{10}$ , respectively) were obtained in the presence of **2** (Scheme 2). These yields are superior to those of 23 and 38% previously reported for the metal-free hydrocarboxylations or promoted by the tetracopper(II) triethanolamine complex, respectively.<sup>9a</sup>

On the basis of the previous background<sup>9</sup> on the hydrocarboxylation of alkanes  $RH$ , a free-radical mechanistic cycle can be proposed (Scheme S1 in the Supporting Information). Its main steps involve the (i) generation of alkyl radicals  $R^\bullet$  (H abstraction by sulfate radicals derived from  $K_2S_2O_8$ ), (ii) carbonylation of  $R^\bullet$  by  $CO$  to acyl radicals  $RCO^\bullet$ , (iii) oxidation of  $RCO^\bullet$  by copper(II) species (via the  $Cu^{II}/Cu^I$  redox couple) to acyl cations  $RCO^+$ , and (iv) hydrolysis of  $RCO^+$  to furnish carboxylic acid products.<sup>9</sup> The latter step was previously confirmed by us on the basis of experiments with  $^{18}O$ -labeled  $H_2O$  and theoretical calculations.<sup>9a</sup>

Apart from high product yields, important features of the present copper-promoted hydrocarboxylations include the

exceptionally *mild* and *acid-solvent-free* reaction conditions and operation in an *aqueous medium* with a rare hydroxylating role of water and with high selectivities to carboxylic acids. These represent some of the mildest methods so far reported for the efficient oxidative functionalization of gaseous alkanes. In this regard, one should mention that, because of the high inertness of gaseous alkanes, most of the state-of-the-art systems for their relatively mild transformations<sup>11</sup> require the use of strongly acidic reaction media (concentrated trifluoroacetic or sulfuric acid or a superacid).<sup>12</sup>

In summary, this study has opened up the use, for the first time, of the common biological buffer  $H_3bes$  in synthetic coordination chemistry, resulting in the self-assembly generation and isolation of the unprecedented  $Cu/Na$  coordination polymers **1–3**, which represent the first structurally characterized coordination compounds derived from  $H_3bes$ . They feature a rare type of water-soluble tetracopper(II) core, capable of efficiently promoting mild and selective hydrocarboxylations of propane and *n*-butane to the corresponding carboxylic acids. Besides, this work provides a contribution to the sweeping area of crystal engineering,<sup>13</sup> namely, toward the development of aqueous-medium processes and the synthesis of rare water-soluble coordination polymers. Further research toward the exploration of  $H_3bes$  in the design of metal–organic materials and the search for their diverse applications is currently underway in our group.

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**Supporting Information Available:** Synthetic procedures, full experimental details, additional structural representations (Figures S1–S9) and bonding parameters (Tables S1–S6) for **1–3**, the proposed mechanism for hydrocarboxylation (Scheme S1), and crystallographic files in CIF format. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(10) Reaction conditions:  $p(\text{alkane}) = 1.0 \text{ atm}$ ,  $p(\text{CO}) = 10 \text{ atm}$  (1 atm = 0.266 mmol),  $K_2S_2O_8$  (1.0 mmol),  $H_2O$  (2 mL)/ $MeCN$  (4 mL), copper promoters **1–3** (4.0  $\mu\text{mol}$ ), 50 °C (for *n*- $C_4H_{10}$ ) or 60 °C (for  $C_3H_8$ ), 6 h in an autoclave (13.0 mL), followed by workup and gas chromatographic analyses.