Zeolite Encaged Cu(Histidine) Complexes as Mimics of Natural Cu Enzymes **

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The most abundant, active, and selective catalysts in nature are enzymes. Their operational domain is, however, relatively narrow as far as temperature and solvent are concerned. Enzyme mimicking is the building of the active center of enzymes (or an analogy of it) into a matrix which allows a larger operational temperature domain and a broader spectrum of solvents. In the case of inorganic matrices, zeolites are the obvious choice because the pore diameters and pore geometry introduce shape selectivity in the reactions. Up to now, the active center of the enzyme has been mimicked by construction of robust, rigid, and stable transition metal ion complexes in zeolite cavities and channels.[1, 2] The most prominent examples are phthalocyanine and bipyridine complexes.[3, 4] However, these complexes can only be synthesized in situ and this procedure is time-consuming. Moreover, the turnover numbers in catalytic oxidations are relatively low.

Here, we report for the first time on the immobilization of Cu(histidine) complexes in zeolites by a simple ion exchange procedure. Amino acids, like histidine, are the key building units of natural enzymes; therefore, the obtained inorganic enzyme has an active center, very close to that of its natural enzyme counterparts. In addition, the complexes are built in by a simple ion exchange procedure. Cu^{2+} was chosen as the transition metal ion, because its complexes are stable[5] and easily characterized by electron spin resonance (ESR) and diffuse reflectance spectroscopy (DRS) in the UV/VIS/NIR region.[6] Furthermore, copper proteins play a key role in both plant and animal physiology, for example hemocyanin is the oxygen-carrying protein in the hemolymph of molluscs and arthropods; ascorbate oxidase catalyzes the oxidation of L-ascorbate and galactose oxidase, which catalyzes the oxidation of galactose and many other substrates, like aliphatic and aromatic alcohols.[7–11]

Cu(histidine) complexes are typically prepared in bidistilled water with a histidine:Cu^{2+} ratio of 5:1. By using an increasing amount of preformed $[Cu(His)_2]^+$ complex at pH 7.3 in bidistilled water[12] together with a zeolite Na-Y, we have measured the amount of released Na^+, together with the amount of Cu^{2+} taken up by the zeolite material. The results are presented in Figure 1. Although there is a considerable spread of points, the data show unambiguously that ion exchange is operative. The slope of the straight line ($7Na^+/Cu^{2+}$) indicates that besides $[Cu(His)_2]^+$, His^+ is exchanged too. Chemical analysis indeed confirms that the histidine:Cu^{2+} ratio on the solid is 6:1. Thus at the low exchange levels investigated,[13] for each $[Cu(His)_2]^+$ exchanged, four His^+ cations are co-exchanged. The fact that on the average seven Na^+ ions are released and not six is indicative for charge compensation by H^+; thus some residual acidity is expected on the solids.

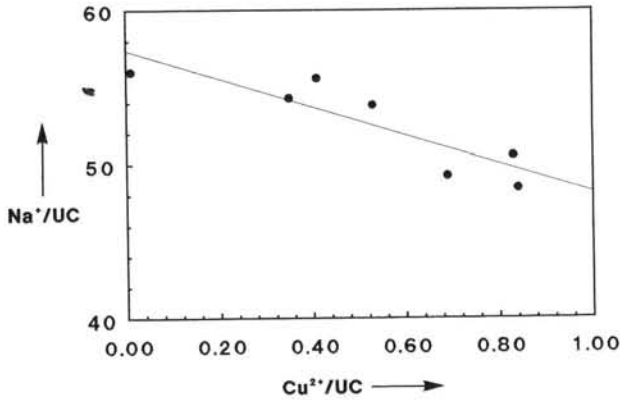

Fig. 1. The amount of released Na^+ and immobilized Cu^{2+} complex in zeolite Y for increasing concentration of Cu(histidine) complex in the ion exchange solution. UC = unit cell.

The hydrated light blue samples are characterized by an absorption band around 15600 cm^{-1} in the diffuse reflectance spectrum and a typical axially symmetric ESR spectrum with hyperfine splitting (hfs) with values for $g_\parallel$, $g_\perp$, and $A_\parallel$ of around 2.27, 2.06, and 170 G, respectively, and a seven-line superhyperfine structure (shfs) with an $A_{N\perp}$ value of 12.3 G (Fig. 2). These spectroscopic features are due to the presence of

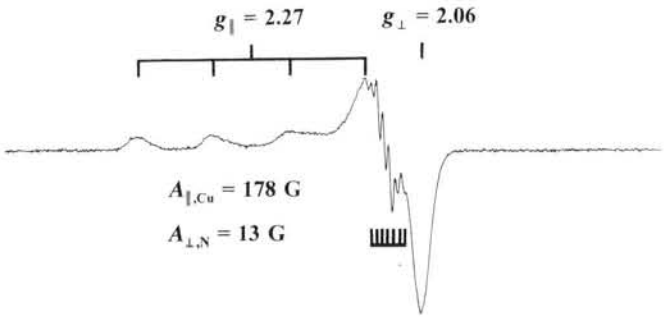

Fig. 2. ESR spectrum of a $[Cu(His)_2]^+$ complex in zeolite Y.

three nitrogen atoms ($2 \times I_N \times n_N + 1 = 7$) in the first coordination sphere of the Cu^{2+} ion. Comparable spectroscopic parameters are observed for copper proteins (e.g. galactose oxidase with an absorption at 15900 cm^{-1} and ESR parameters:[8] $g_\parallel = 2.24$; $g_\perp = 2.06$; $A_\parallel = 175$ G (hfs); $A_\perp < 0.5$ G with shfs : $A_{N\perp} = 15.1$ G) with an NNNO coordination around the Cu^{2+} ion. The intensity of the d–d absorption band in the diffuse reflectance spectrum and the amount of Cu^{2+}, as determined by quantitative ESR measurements, are given in Figure 3 for increasing Cu(histidine) loading in zeolite Y. The d–d absorption band of Cu^{2+} linearly increases with increasing Cu loading. The same holds for the intensity of the ESR signal, suggesting the presence of only one type of occluded Cu(histidine) complex. In addition, the amount of ESR-visible Cu^{2+} equals the amount determined by chemical analysis, confirming the absence of uncomplexed Cu^{2+}.

The occluded $[Cu(His)_2]^+$ can be envisaged as a complex with a Cu^{2+} center surrounded by three nitrogen atoms and one oxygen atom by ligation of two histidine molecules, one coordinating by two N ligands, the other only by one O and N atom. The fourth ligand is thus an oxygen atom of the carboxy group of histidine. A possible representation of this Cu complex is shown in Figure 4. Molecular modeling shows that the

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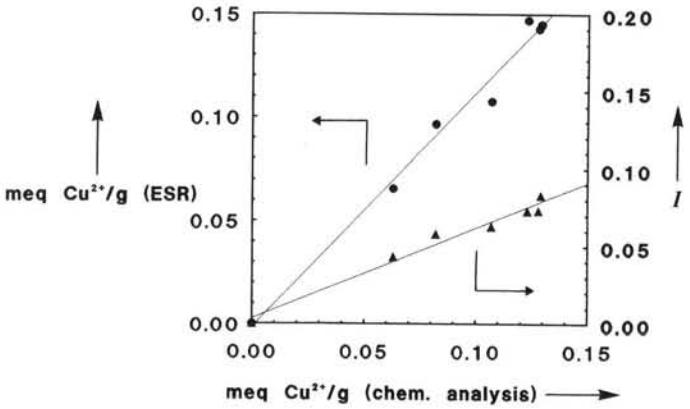

Fig. 3. Intensities of the Cu^{2+} signals in the diffuse reflectance spectrum (I) and ESR spectrum as function of the loading of the [Cu(His)] complex in zeolite Y. meq = milliequivalents.

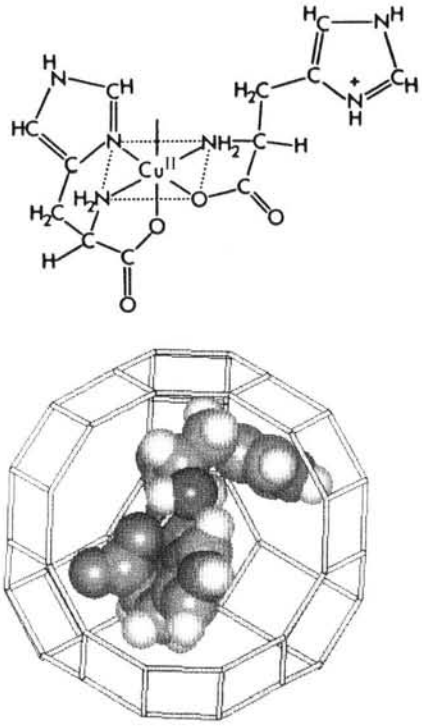

Fig. 4. Representation of $[Cu(His)_2]^+$ occluded in the supercage of zeolite Y. Top: schematic representation of the $[Cu(His)_2]^+$ complex; Bottom: space-filling molecular model, as generated by Hyperchem (light blue, carbon; black, hydrogen; green, copper; red, oxygen; dark blue, nitrogen).

$[Cu(His)_2]^+$ complex is occluded in the zeolite supercage without distortion.

Drying of the samples results in the removal of water and only a slight shift in the absorption in the diffuse reflectance spectrum (15700 cm^{-1}) and ESR parameters ($g_\parallel$, $g_\perp$, and $A_\parallel$ values are 2.26, 2.07, and 175 G,respectively). Furthermore, the occluded $[Cu(His)_2]^+$ complexes are thermally stable up to 100 °C. Admission of ammonia onto the sample dried at room temperature results in the formation of a $Cu(His)_2(NH_3)_x$ complex with an absorption at 16000 cm^{-1} and $g_\parallel$, $g_\perp$, and $A_\parallel$ values of 2.26, 2.07, and 160 G, respectively. The absence of the superhyperfine splitting in the ESR spectrum is due to a distortion of the complex. Removal of the ammonia in vacuo at 50 °C leads to the initial Cu^{2+} state and this process is totally reversible. Thus, by simple evacuation a free coordination site is produced.

The presence of such a coordination site gives catalytic potential to these materials. The oxidation of alcohols and alkenes with *tert*-butyl hydroperoxide, an environmentally friendly and cheap oxidant,[14] in the presence of $[Cu(His)_2]^+$-Y has been studied at 60 °C in batch-type reactors. The catalytic performances of $[Cu(His)_2]^+$-Y with 0.75 Cu/UC are summarized in Table 1. 1-Pentanol is oxidized to pentanoic acid with a selectivity of 100%, while the oxidation of benzyl alcohol gives both benzaldehyde and benzoic acid in a ratio of about 2:1. Similar oxidation reactions are catalyzed by galactose oxidase which has a broad substrate specificity.[15] Excellent catalytic results were, however, obtained for the epoxidation of cyclohexene. At a turnover of 3230, the major reaction product is 1,2-cyclohexanediol. This product is formed from the hydrolysis of cyclohexenoxide, on some acid sites of zeolite Y. A minor allylic oxidation is also observed, indicative of only traces of free copper. After reaction, no free Cu ions were detected in the reaction mixture and combined DRS and ESR measurements show also that the $[Cu(His)_2]^+$ complexes were maintained inside the cages of zeolite Y. This strong encapsulation can be explained by the positive charge of the complex. Furthermore, after repeated regeneration (three times), no changes in catalytic and spectroscopic properties were observed. Thus, a new stable and selective oxidation catalyst has been designed.

Table 1. Catalytic performances of $[Cu(His)_2]$ complexes encaged in zeolite Y at 60 °C [a].

Substrate [a]	Time [h]	Conversion [%]	TON [b]	Selectivity [mol%]
1-pentanol	24	12	1425	pentanoic acid [100]
benzylalcohol	24	56	2421	benzoic acid [33], benzaldehyde [66]
cyclohexene	24	28	3230	cyclohexenoxide [9], 1,2-cyclohexanediol [89], cyclohex-2-en-1-ol [0.3] and cyclohex-2-en-1-one [1.7]

[a] 100 mmol substrate, 150 mmol *tert*-butyl hydroperoxide; no Cu leaching during reaction, as determined by AAS; no catalytic activity was observed for zeolite Y and histidine exchanged zeolite Y, while Cu/zeolite Y only decomposes the peroxide. [b] TON = turnover number.

In conclusion, we have discovered that $[Cu(His)_2]^+$ complexes can be immobilized in the cages of zeolite Y by a simple ion exchange method, which results in the formation of a typical coordination geometry frequently encountered in biological Cu proteins. The presence of a free coordination site opens the way for oxidation catalysis at relatively low temperatures in the presence of peroxides, especially olefin epoxidations and alcohol oxidations. To our knowledge, this system is the first example of immobilized transition metal ion (amino acids) complexes in zeolites. Further studies on the mechanism of the oxidations and the extension to other transition metal ions, amino acids, and inorganic oxides are in progress and should increase our understanding of these occluded complexes.

Experimental Procedure

The Cu(histidine)/Y samples were prepared starting from Na-Y from Ventron (Si:Al ratio of 2.49 and cation exchange capacity of 4.32 meq g^{-1}) after the zeolite had been put in its Na^+ form by two successive exchanges with 1 M NaCl solutions, followed by washing until free from Cl^- ions, and drying in air at room temperature overnight. The zeolites obtained were then ion exchanged with a solution of Cu(histidine) in bidistilled water at a fixed pH. After ion exchange, the samples were separated from the solution by centrifugation, washed, and dried at 60 °C overnight in air. The amounts of Na^+ and Cu^{2+} were determined by atomic absorption

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spectroscopy (AAS) after dissolution of known quantities of the zeolites materials in HF/H_2SO_4. AAS measurements were performed with an Instrumentation Laboratory Inc. apparatus with a nitrous oxide/acetylene flame. Scanning electron micrographs (SEM) were obtained by using a Jeol Superprobe 733 instrument, while diffuse reflectance spectroscopy (DRS) was performed on a Varian Cary 5 UV/VIS/NIR spectrophotometer at room temperature. The diffuse reflectance spectra were recorded against a halon white reflectance standard in the range 2200–200 nm. The computer processing of the spectra consisted of the following steps: 1) subtraction of the baseline, 2) conversion to wavenumber, and 3) calculation of the Kubelka-Munk (KM) function. For ESR spectroscopy, a Bruker ESP300E spectrometer at X-band (ca. 9.5 GHz) was used. Quantitative ESR results were obtained by comparison with Cu(acetylacetonate)/KCl reference samples (spin density : 10^{16}–10^{20} $Cu^{2+}\,g^{-1}$). The molecular models were generated by the commercial software package Hyperchem™ of Autodesk.

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Self-Assembly of 1,3,5-Benzenetricarboxylic Acids (Trimesic Acids) and Several Analogues in the Solid State**

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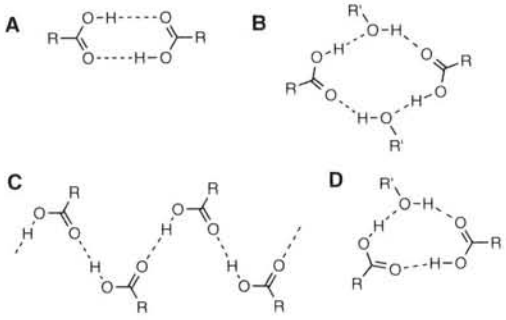
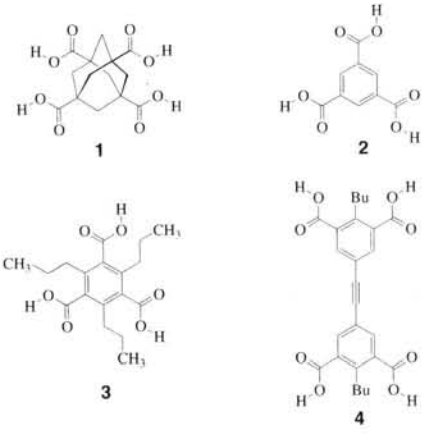
The design of organic compounds that crystallize in a predictable way remains a contemporary challenge to chemists.[1] Particular attention has recently focused on the rational design of clathrates that may be useful in separations or catalysis.[2] Hydrogen bonding can be useful in this regard[3] because it is a moderately directional intermolecular interaction that may control short-range packing. Ideally, each functional group or set of groups would form a single hydrogen bonding motif. Unfortunately, however, the complex interplay of crystal packing forces makes this less likely to occur. For example, carboxylic acids are well-known to form centrosymmetric dimers (Scheme 1, **A**), but



Scheme 1. Four hydrogen bonding motifs for carboxylic acids. **A**: symmetrical dimer, **B**: doubly bridged dimer, **C**: catemer, **D**: singly bridged dimer.

other motifs exist.[4] These alternate motifs are nonetheless rare and the reported high frequency of dimer formation suggests that carboxylic acids are attractive candidates for controlling short-range crystal packing.[1a]

Longer range packing might be controlled through compounds containing two or more such functional groups in a defined spatial arrangement. Two paradimatic examples of this approach to engineering hydrogen bonded networks are adamantanetetracarboxylic acid (**1**) and 1,3,5-benzenetricarboxylic acid (trimesic acid, **2**), which form diamondoid[5] and



hexagonal[6] networks, respectively. However, channels or cavities are not present as a result of extensive interpenentration. In the case of **2**, the "chicken-wire" networks of trimesic acid molecules are pleated and the 14 Å holes are filled by a mutual triple catenation. Herein we describe the results from three different approaches to break the interpenetration of the trimesic acid lattice to give cavity clathrates. The results bear on the issue of whether the hydrogen bonding of carboxylic acids, and by extension, related functional groups can be used to reliably control the structure of crystals.

The first approach to break interpenetration involved crystallization of trimesic acid in the presence of a guest that might pack efficiently within the 14 Å channels. Partial success using this approach was reported by Herbstein et al. in 1987.[7] How-

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