Comparative solvolytic stabilities of copper(II) nanoballs and dinuclear Cu(II) paddle wheel units

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ABSTRACT

The self-assembly of copper(II) ions and 5-(2-(2-hydroxyethoxy)ethoxy)benzene-1,3-dicarboxylic acid (**2**) leads to hollow nanoballs in which 12 dinuclear copper(II) paddle wheel units are interconnected via 24 ligands, as determined by single crystal X-ray structure analysis. The nanoball dissociates in aqueous solutions, and in the presence of an excess of ligand it transforms into a three-dimensional network, but is stable in organic solvents. The thermodynamic stability of the nanoball against dissociation in aqueous solution is studied and compared to simple copper(II) paddle wheel complexes. The results reveal enhanced thermodynamic stability of the nanoball as compared to discrete copper(II) paddle wheel complexes due to chelate effects and positive cooperativity.

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1. Introduction

A broad range of existing and future applications for nanometer-sized hollow molecules is currently under discussion in literature: they can serve for instance as nanoreactors, which are a simple mimic of enzymes for a diverse range of thermal and photochemical reactions [1]. Further present applications for (drug) delivery, storage, and separation technology [2] involve molecular recognition, host–guest chemistry and chiral recognition, while long-term goals are focused on the design of new materials with desirable properties and the manufacturing of nanoscale devices and molecular machinery [3,4].

Tracking these aims, metal-organic polyhedra (MOPs, also named nanoballs, nanocontainers or nanocages) [4–7], have come to the foreground in the last few years, in addition to the well-established organic molecular containers [8]. MOPs are built through the interconnection of metal ions or clusters with simple, polyfunctional organic ligands (so-called linkers, mostly containing nitrogen or carboxylate groups as complex builders). One way to obtain nanoballs in high yield is to interconnect copper(II) paddle wheel complexes at a 120° angle with the bifunctional ligand ben-

zene-1,3-dicarboxylate (bdc) or its derivatives [4–7]. By changing the substituent R in the 5-position of bdc, nanoballs which are highly soluble in polar solvents (e.g. alcohols or N,N-dimethylformamide (DMF) for R = OH [5a], DMF or dimethyl sulfoxide (DMSO) for R = OC_2H_5OH [6]), or in nonpolar solvents (e.g. toluene, dichloromethane or THF for R = $OC_{12}H_{25}$ [5d]) are obtained.

Especially for the applications mentioned above, knowledge about *kinetic* and *thermodynamic* stability of these molecular containers is crucial. Studies on the *disassembly kinetics* of smaller supramolecular architectures (such as helices [9] and organic self-assemblies) [10] have been intensively performed, but to date only a few studies focus on the *kinetic stability* of larger, nanometer-sized metal-organic polyhedra [6,7]. To the best of our knowledge, no studies concerning the *thermodynamic stability* of metal-organic polyhedra or similar compounds have been carried out in detail yet.

We have already shown earlier that nanoballs based on interconnected copper(II) paddle wheels are *kinetically* far more stable in solvents like DMF or DMSO than the (kinetically labile) dinuclear copper(II) paddle wheel complexes such as copper acetate or benzoate, which is presumably due to their more rigid structure (as shown for R = OC_2H_5OH in 5-position of bdc by spectrophotometry) [6].

Since the *kinetic stability* compared to simple paddle wheel units is increased due to the structural features of the nanoball,

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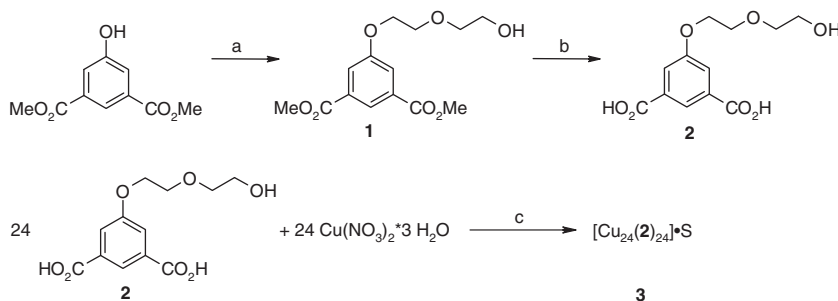
Scheme 1. Synthetic route for linker **2** and nanoball **3**. a: KI, K$_2$CO$_3$, CH$_3$CN, reflux, 24 h; b: (1) KOH, EtOH/H$_2$O (1:1), reflux, 6 h (2) HCl; c: 2 equivalents 2,6-dimethylpyridine, methanol, room temperature, 1 min. S: solvent molecules.

the question about the influence on the *thermodynamic stability* arises. Dinuclear copper(II) carboxylates (to which we refer as a reference standard) are remarkably dissociated in aqueous solution [11], whereas the dissociation is strongly decreased for less polar solvents [12]. For hydroxylated nanoballs (R = OH in 5-position of bdc) in methanol solution, spectroscopic studies even showed no detectable dissociation at all [13], qualitatively showing the increased thermodynamic stability above the underlying dinuclear copper(II) carboxylates. Since the thermodynamic stability of these nanoballs seems to be most interesting for aqueous solutions, we thus prepared a new nanoball based on a bis(ethylene glycol)-functionalized linker which is soluble in H$_2$O:DMF (1:1) to quantify the thermodynamic stability, as existing functionalised nanoballs [5,6] in our hands showed poor solubility in aqueous solvents.

Whether the thermodynamic stability is increased, or even decreased, depends on the cooperativity of the system. Cooperativity [14] arises from the interplay of two or more interactions, so that the system as a whole behaves differently from expectations based on the properties of the individual interactions acting in isolation. Coupling of interactions can lead to positive or negative cooperativity, depending on whether one interaction favours or disfavours another. Positive cooperativity implies a low concentration of intermediates. Positive cooperativity leads to a low peak concentration of intermediates and a sharp transition from unbound to bound. In other words, as the system approaches the limit of strong positive cooperativity, only the extreme states are significantly populated. Cooperativity exhibited in the folding of proteins and supramolecular self-assemblies is driven by the difference in strength between the intermolecular and intramolecular interactions, and is a consequence of the molecular architecture. This phenomenon gives rise to the chelate effect [15], and is thus also called chelate cooperativity.

Already small organic assemblies [16], inorganic cylindrical architectures [17] or double helicates [9a–c] show increased thermodynamic stabilities due to positive cooperative effects, and an even more pronounced influence on the nanoball built from 48 subunits might be expected.

Furthermore, the formation of insoluble coordination polymers is always given as a possible concurrence to the dissociation of a supramolecular self-assembly into its constituents: by linking copper(II) paddle wheel complexes with functionalised benzene-1,3-dicarboxylate (bdc), two- or three-dimensional networks [18,19] might be obtained instead of nanoballs. Which of these competing products occurs depends on the formation of kinetic products, the concentrations of the educts, the ligand-to-metal ratio, pH, solvent effects, template molecules which direct the course of the assembly, and temperature [1,20–22]. Among these, the concentrations and the ligand-to-metal ratio are the most crucial for the self-assembly of cyclic or spherical self-assemblies.

2. Results and discussion

The linker 5-(2-(2-hydroxyethoxy)ethoxy)benzene-1,3-dicarboxylic acid **2** was synthesized from dimethyl-5-hydroxybenzene-1,3-dicarboxylate and 2-(2-chloroethoxy)ethanol to give the intermediate **1**, which was subsequently saponified and afterwards protonated to yield **2** in an overall yield of 77% (Scheme 1).

From an equimolar solution of **2** and Cu(NO$_3$)$_2$·3H$_2$O in methanol, the nanoball [Cu$_{24}$(C$_{12}$H$_{12}$O$_7$)$_{24}$]·24MeOH **3** immediately precipitates upon adding two equivalents of 2,6-dimethylpyridine.[1] Recrystallisation from dimethylsulfoxide (DMSO) and butanol afforded **3b** as green crystals suitable for single crystal X-ray diffraction studies.

To evaluate the dissociation stability of **3**, it is necessary to facilitate the dissociation of the complexes by adding an acid, since the dissociation of the nanoball is kinetically hindered. For this purpose, it might seem reasonable to add the diprotonated ligand **2** to a solution of the nanoball **3**. Consequently, a closed spherical structure starts to compete with open polymeric structures if the ratio in solution after dissociation mismatches the stochiometry of the spherical structure: compared to open polymeric structures, an increased number of bonds between the constituents is possible in a cyclic or spherical arrangement, and will be favoured from the enthalpic point of view (since the donor and acceptor sites at each end of the polymer will always remain uncoordinated). However, when the ligand-to-metal ratio in solution mismatches the stochiometry of the cyclic or spherical supramolecular assembly, the enthalpic advantage diminishes due to the present excess of donor or acceptor sites [1,20–22]. Accordingly, when the nanoball **3** is dissolved in H$_2$O:DMF (1:1) together with three equivalents of the ligand **2** per copper atom, the nanoball slowly transforms throughout several weeks into single crystals of the three-dimensional network [Cu(C$_{12}$H$_{12}$O$_7$)]·0.5 H$_2$O·0.5 DMF **4**. This course from least stable to more stable (as well as less dense to more dense) polymorph of Cu(C$_{12}$H$_{12}$O$_7$) follows the classical Ostwald–Volmer rule [23]. Only slow dissociation and no transformation is observed after the addition of acetic acid, emphasising the strong influence of the ligand-to-metal ratio for the stability of the nanoball over open polymeric structures. Therefore, the dissociation constant of **3** can be determined after the addition of acetic acid (see below).

Noteworthly, no transformation of **3** into a three-dimensional network is observed for solutions in anhydrous DMF or DMSO. These solutions have remained unchanged for up till now more than 12 months – even when up to 500 equivalents of the diacid ligand **2** per copper atom are present in these solutions. These results show, in analogy to the strongly increased stability against

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[1] The exact number and kind of coordinated solvent molecules is difficult to determine for this class of substances [4a] and was chosen according to elemental and thermogravimetric analyses.