

Self-assembly of a constitutional dynamic library of Cu(II) coordination polygons and reversible sorting by crystallization†

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A small coordination constitutional dynamic library (CDL) is self-assembled from Cu²⁺ ions and the *ortho* bis-(3-acetylacetone) benzene ligand. Two coordination polygons, a rhomboid and a triangle, establish a dynamic equilibrium. Quantitative sorting of the rhomboidal polygon is reversibly obtained by crystallization. Thermodynamic and kinetic aspects ruling the CDL system have been elucidated.

Introduction

Coordination polygons and polyhedra generated by self-assembly of metal centres and well designed polytopic ligands are attracting increasing attention as suitable units for the development of functional molecular materials. Due to their peculiar structural features, such as for instance the presence of confined nanometer sized pockets, these systems find applications as molecular vessels, as molecular reactors for space confined catalysis and for inclusion of compounds;¹ they can be regarded as mimics of the active sites of enzymes. The self-assembly of polygonal or polyhedral assemblies depends on the coordination vectors and angles between the ligand binding groups and on the coordination geometry of the metal site. During the self-assembly of these architectures the formation of mixtures of oligomers in dynamic equilibrium² is not uncommon. As excellently reviewed,³ the failure in unequivocally predicting the final assembly using the bonding directional approach is related to conformational flexibility. Such

flexibility coupled to the reversibility of coordination bonds paves the way to the formation of equilibrating architectures. Probably, the most reported case is the formation of triangular and square molecular polygons by self-assembly of linear ligands and 90° metal corners.^{2a,c,e,h-k}

When more assemblies are thermodynamically accessible and reversible interactions are working, a dynamic system is established. Such equilibrium is based on the continuous change of its constituents through dissociation and recombination of the different components. Nice examples of equilibrating systems are the so-called Constitutional Dynamic Libraries (CDL).^{4a} The Constitutional Dynamic Chemistry (CDC) concepts are general and can be applied to biological systems as well as to organic and coordination compounds.⁴ A CDL is an ensemble of molecular or supramolecular objects in dynamic equilibrium. A major goal is to achieve control of these dynamic libraries by application of physical stimuli or chemical effectors leading to adaptive systems.⁴

In this context, we are exploring coordination driven architectures based on a family of bis-(3-acetylacetone)benzene ligands.⁵ Recently, we presented a system that in solution gives a mixture of Cu(II) coordination boxes: a rhomboidal dimer (**D**) and a triangular trimer (**T**). We also demonstrated how the system can be piloted toward **T** through a chemical effector by guest induced selection or templated self-assembly.^{5c} This molecular recognition driven selection is under study for a large family of guests. Besides that, we are currently investigating the possibility to express a specific constituent through a physical stimulus such as constitutional crystallization.^{4,6} To this aim, the accurate study of the self-assembled CDL is mandatory. Here, we report on the characterization of the equilibrium between the CDL constituents and how **D** self-sorts upon crystallization. By the combined use of mass spectrometry (ESI-MS) and UV-Vis absorption spectroscopy we found that the sorting is reversible and that the CDL is promptly restored as **D** crystals are redissolved. Moreover, we demonstrated that the restoring of CDL equilibrium is characterized by pseudo-first-order kinetics.

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Results and discussion

The CDL under study is based on Cu^{2+} ions and the *ortho* bis-(3-acetylacetonate)benzene (*o*-LH₂) ligand. The presence of the rigid aromatic spacer and the coordinating vectors is designed *ad hoc* in order to orientate the two acetylacetonate groups with a 60° relative angle, Fig. 1b. By coordinating this ligand to Cu^{2+} ions, closed molecular boxes are likely to be assembled. At variance to the common strategy, the metal ions lie on the sides of the molecular polygon and not at the corners, and their coordination spheres are unsaturated so that guests can directly interact with the metal centres.^{5c,7} On

the basis of the directional bonding approach, the formation of a $[\text{Cu}(\text{o-L})]_3$ (T) triangle would be forecast using the *o*-LH₂ ligand. Unexpectedly, single crystals of a $[\text{Cu}(\text{o-L})]_2$ rhomboidal dimer (D) have been isolated in quantitative yield.^{5a,b,8} Variation of the crystallization parameters does not affect the final result. However, after the metal-ligand self-assembly, ESI-MS patterns show the presence of the two oligomers in solution: $[\text{D} + \text{Na}^+]$ at m/z 693 and $[\text{T} + \text{Na}^+]$ at m/z 1030 (Fig. 2a). The peaks at m/z 758 and 817 derive from the fragmentation of the trimeric species. In particular, in the former T loses a ligand, while in the latter a ligand molecule partially decomposes to give an acetate group. This fragmentation also leads to a partial reduction of the metal ions: the peaks at m/z 758 and 817 are ascribed to fragments containing one Cu(II) and two Cu(I) ions, and *vice versa*, respectively. We have already described similar reduction processes during ESI-MS analysis of bis-(3-acetylacetonate)benzene derivatives.^{5b} The simulated isotopic pattern of the species highlighted in Fig. 2a confirms their identity (Fig. S1–S3, ESI†). Solutions prepared by dissolving D single crystals evidenced a time dependent evolution, Fig. 2b. Just after dissolution, ESI-MS shows the presence of the rhomboidal dimer alone. At increasing times, the intensity of the D peak decreases while T increases until equilibrium is reached.

Based on these results it can be inferred that the system is constitutionally dynamic since its components undergo continuous change through dissociation and recombination into the triangular and rhomboidal polygons. Moreover, it is evident that D can be selectively sorted from the equilibrating system by crystallization, and that through its dissolution the CDL is promptly restored (Fig. 1a).

A quantitative study on the kinetics of CDL restoring has been carried out by using UV-Vis spectroscopy, by considering that the solution turns from gold-brown, immediately after dissolution of $[\text{Cu}(\text{o-L})]_2$ crystals, to dark green, at the

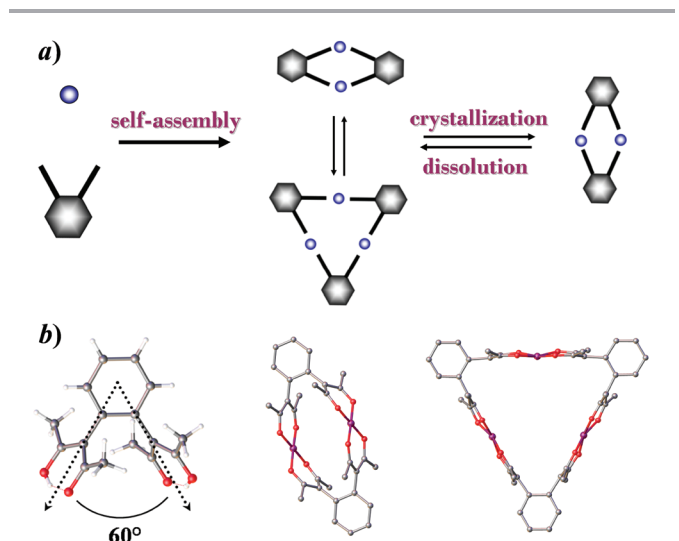


Fig. 1 (a) Scheme of the self-assembled CDL: the equilibrium between D and T constituents, the D selective crystallization and the restored $3\text{D} = 2\text{T}$ equilibrium after D single crystals dissolution. (b) The *o*-LH₂ structure; dotted arrows: coordination vectors of the two acetylacetonate groups; D X-ray structure and T energy minimized model.

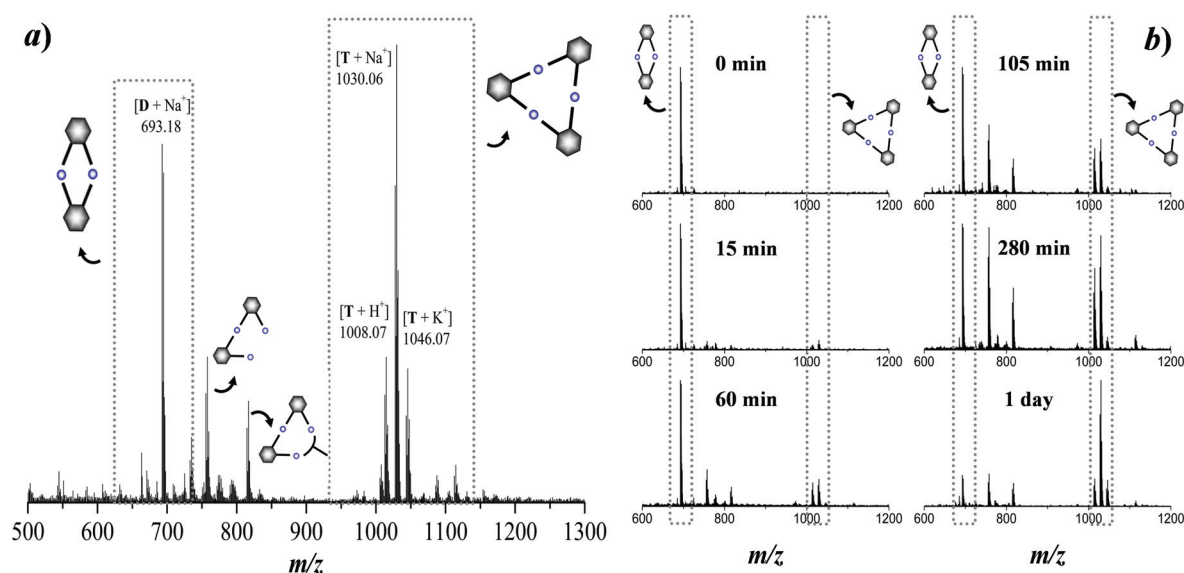


Fig. 2 (a) ESI-MS positive mode of a $[\text{Cu}(\text{o-L})]_n$ solution ($n = 2, 3$); (b) ESI-MS positive mode, time evolution of the CDL equilibrium restoring.

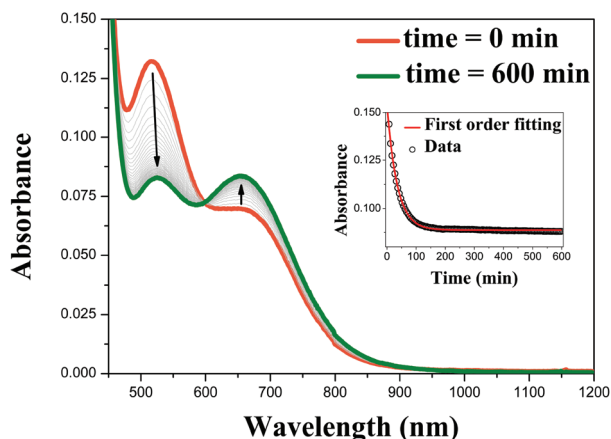


Fig. 3 Evolution of absorption spectra during CDL equilibrium restoring starting from **D** single crystals (1.0 mM, CHCl_3 solution). Inset: absorbance decrement at 512 nm and first order fitting.

equilibrium (Fig. 3). The absorbance profile changes significantly over time; the band at 512 nm decreases in intensity and presents a red-shift to 525 nm, while the band at 655 nm increases in intensity. The spectrum shows also a strong charge transfer band below 500 nm and a clear isosbestic point at 602 nm.

From these spectra it can be deduced that both polygonal species contribute to the two absorption bands in the visible region. However, during conversion of $[\text{Cu}(\text{o-L})]_2$ crystals into the **D**–**T** system at equilibrium, the band centred at 525 nm shows its major variation. This suggests a predominant contribution of **D** to the 525 nm band and of **T** to the one centred at 655 nm. The absorbance decrement at 512 nm is fitted with high precision by a first-order kinetics. By varying the concentration, the k value changes according to a pseudo-first order. The concentration dependence of the pseudo-first order kinetic constant has not yet been clarified and is still under study. However, for concentrations in the 1–10 mM range, k values are on the order of *ca.* 10^{-3} s^{-1} .

The $3\text{D} \rightleftharpoons 2\text{T}$ equilibrium is governed by a very subtle balance between enthalpic and entropic factors. As a general and simple rule, entropy favors the formation of the smaller oligomer (**D**) while the less strained assembly (**T**) is driven by enthalpy gain. By varying the concentration *via* dilution, it is possible to influence the speciation of the constituents according to the mass action law. The equilibrium constant can be determined once the relative distribution of **D** and **T** has been evaluated. For non-paramagnetic metal species this is usually done by NMR, but due to the presence of Cu^{2+} ions useful NMR data were not obtained. On the other hand, the system can be characterized by UV-Vis absorption spectroscopy. As mentioned before, none of the bands can be unambiguously assigned to the dimer or to the trimer. Moreover, we observed that the variation of absorbance of the CDL system presents an almost linear trend as a function of concentration (Fig. S11 and S12, ESI†): *i.e.* the ratio between the concentrations of equilibrating species is almost constant with dilution. This

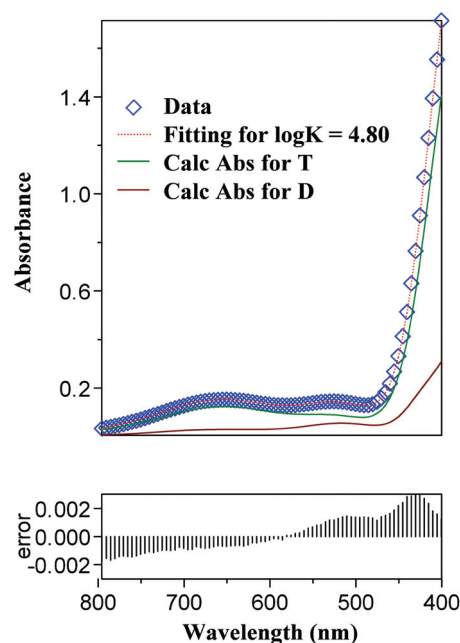


Fig. 4 Absorbance data (square) and calculated spectrum (red dotted line) for a 2.04 mM CHCl_3 solution. Green line is the **T** calculated spectrum and the wine line is the **D** one.

suggests a high value for the $3\text{D} \rightleftharpoons 2\text{T}$ equilibrium constant (K_{DT}). Due to these considerations, K_{DT} determination is challenging. Absorption spectra have been collected at different concentrations and a multivariate data analysis has been performed. The obtained value for the $\log K_{\text{DT}}$ constant is 4.8 ± 0.4 (298.15 K). Standard deviation is high, as expected based on the considerations illustrated above.

Fig. 4 reports a comparison between experimental and calculated data for the spectrum obtained using a 2.04 mM solution (concentration is calculated on a virtual monomer $[\text{Cu}(\text{o-L})]$, **M**). The calculated spectrum fits very well with the experimental data. The high K_{DT} value indicates that **T** is the predominant species in the $[\text{Cu}(\text{o-L})]_n$ ($n = 2, 3$) solution. For instance, the ratio between the trimer and the dimer is close to 3:1 for the 2.04 mM solution. Fig. 5 shows the speciation plot for the $3\text{D} \rightleftharpoons 2\text{T}$ system (range 1–100 mM).

On the basis of these reports, we hypothesized the possibility to crystallize the **T** trimer from highly concentrated solutions (up to 100 mM). In spite of our expectations, **D** crystals have been quantitatively isolated over the whole concentration range (Fig. 5). The preferential crystallization of **D** can be correlated either to a lower solubility of the rhomboidal polygon or, most likely, to kinetic reasons. Indeed, once the dimer molecules start to nucleate, the early crystallites act as seeds for the subsequent growth and quantitative crystallization of the rhomboid. As a consequence, **D** is subtracted from the equilibrium which is accordingly restored by continuous conversion of **T** into **D**. Hence, crystallization drives the quantitative CDL sorting to **D**.

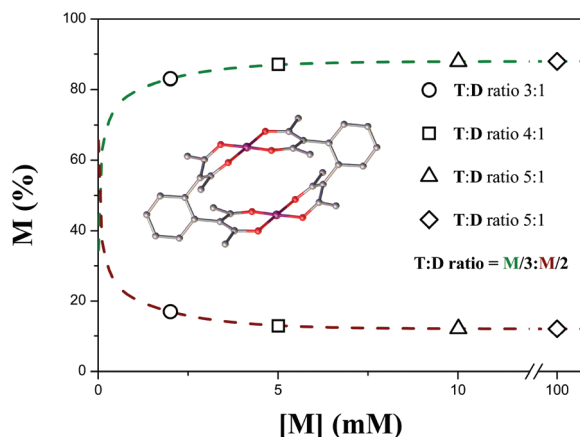


Fig. 5 Speciation of the CDL constituents: green dotted line is **T** and wine is **D**. Different concentrations (symbols) always lead to quantitative **D** crystallization. The **T** : **D** ratio in solution is highlighted on the speciation plot.

Conclusions

A coordination CDL is self-assembled from Cu^{2+} ions and the **o-LH₂** ditopic ligand. Two copper based coordination polygons – a rhomboidal dimer **D** and a triangular trimer **T** – are in dynamic equilibrium. The equilibrium constant has been determined by UV-Vis absorption spectroscopy and multivariate data analysis. In solution the predominant species is the molecular triangle **T**, although by constitutional crystallization the system evolves to **D**. This process is reversible and the dynamic system is promptly restored in solution as evidenced by ESI-MS studies and UV-Vis absorption spectroscopy.

Experimental

Synthesis: **o-LH₂** ligand and CDL self-assembly

Reagents were purchased from Aldrich and used as received. The CDL has been self-assembled^{5c} and the ligand 1,2-bis-(3-acetylaceton)benzene (**o-LH₂**)^{5b,9} has been prepared as reported in the literature.

[Cu(**o-L**)]₃ (**T**) energy minimized model

An energy minimized model for the triangular trimer has been calculated using the universal force field (UFF) implemented in the ArgusLab software.

Crystallization experiments

Single crystals of the rhomboidal dimer **D** have been obtained from chloroform and co-solvents using different conditions as reported in Table 1. The compound identity has been confirmed by X-ray single crystal unit cell determination and comparison with published data.⁸

Electrospray ionization mass spectrometry (ESI-MS)

The ESI-mass spectra were obtained using an LCQ DECA ion trap instrument (ThermoFisher Scientific, San José, CA, USA),

Table 1 Crystallization parameters

[Cu(o-L)] (mM) concentration ^a	Co-solvent		
2	Toluene	Acetone	Benzene
5	Toluene	Acetone	Benzene
10	Toluene	Acetone	Benzene
100	Toluene	Acetone	Benzene

^aThe concentration has been calculated on the basis of a virtual monomer [Cu(**o-L**)] = **M**.

operating in positive ion mode. The entrance capillary temperature was 280 °C and the capillary voltage was 4 kV. The compounds under study were firstly dissolved in chloroform and then diluted in acetonitrile to obtain a 10^{-6} M concentration. The acetonitrile solution was introduced into an ESI ion source by direct infusion at a flow rate of $10 \mu\text{L min}^{-1}$. The He pressure inside the trap was kept constant. The pressure directly read by an ion gauge, in the absence of the N_2 stream, was 2.8×10^{-5} torr. MS/MS experiments were performed by resonant excitation of the ion of interest through a supplementary r.f. voltage in the range 30–35% of its maximum value (5 V peak-to-peak). The isolation width was set at 1 mass unit.

The time evolution of the CDL restoring has been studied as follows. A 10^{-3} M solution has been prepared in chloroform from **D** single crystals. At the detected time (0, 15, 60, 105, 280 minutes and 1 day) an aliquot of the solution has been diluted in acetonitrile to obtain a 10^{-6} M solution and the ESI-MS spectrum has been recorded.

Kinetics of the CDL restoring

D single crystals have been dissolved in chloroform and spectra have been recorded every 2 minutes. The decrement at 512 nm has been fitted according to the following equation for a first-order kinetics $A = A_{\text{inf}} + (A_0 - A_{\text{inf}})\text{e}^{-kt}$; where A is the absorbance, A_0 the absorbance at time zero, A_{inf} the absorbance at infinite time, k the kinetic constant and t the time.

All spectra collected present a very good first-order fitting ($R^2 \geq 0.99$) and the constant value is dependent on concentration.

Equilibrium constant determination

Absorption spectra of [Cu(**o-L**)]_{*n*} ($n = 2, 3$) chloroform solutions at different total concentrations (Table S3†) have been recorded at different temperatures (293.15–323.15 K, every 5 K). Data have been collected using quartz suprasil cuvettes, filled with 3 mL of the solution. Spectra are shown in Fig. S4–S10.† Data have been computed using Hyperquad software¹⁰ according to the model described here. For the sake of clarity, in the model [Cu(**o-L**)]₂ and [Cu(**o-L**)]₃ are denoted as **D** and **T**, respectively. Moreover, the minimization program required, for a correct mass balance (see eqn (2) and (5) below), the introduction of a virtual monomer [Cu(**o-L**)] denoted as **M**. Since the optical length is constant (1 cm), molar absorbance will be written as ϵ (L mol^{-1}).

The CDL absorbance (A_{λ}^i) at a given wavelength λ for the i -th concentration is:

$$A_{\lambda}^i = \varepsilon_{D,\lambda}[\mathbf{D}] + \varepsilon_{T,\lambda}[\mathbf{T}] \quad (1)$$

where $\varepsilon_{D,\lambda}$ and $\varepsilon_{T,\lambda}$ are the molar extinction coefficients of the dimer and the trimer at the same wavelength. The total concentration (calculated on the basis of a virtual monomer \mathbf{M}) is given by eqn (2).

$$C_{\text{Tot},\mathbf{M}} = 2[\mathbf{D}] + 3[\mathbf{T}] \quad (2)$$

Dimer and trimer species are related to \mathbf{M} by the following equilibria, where β_D and β_T are the dimer and trimer formation constants, respectively.



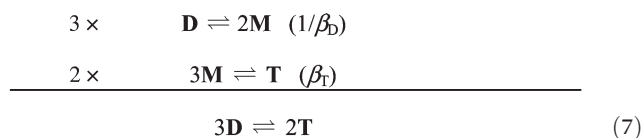
Considering eqn (3) and (4), the total concentration can be re-written as:

$$C_{\text{Tot},\mathbf{M}} = 2\beta_D[\mathbf{M}]^2 + 3\beta_T[\mathbf{M}]^3 \quad (5)$$

The Hyperquad program, by minimizing the difference between experimental and calculated absorbance values (eqn (6)), can calculate β_D , β_T , $[\mathbf{D}]$, $[\mathbf{T}]$, $\varepsilon_{D,\lambda}$ and $\varepsilon_{T,\lambda}$.

$$\Sigma(A_{\lambda}^i - A_{\text{calc}})^2 \quad (6)$$

The constant of the dimer–trimer equilibrium (eqn (7)) can be eventually calculated as follows (eqn (8)).



$$K_{\text{DT}} = \beta_T^2/\beta_D^3 \text{ or } \log K_{\text{DT}} = 2 \log \beta_T - 3 \log \beta_D \quad (8)$$

In order to improve the fit, $\varepsilon_{D,\lambda}$ values, obtained from the kinetic experiments at $t = 0$, have been input to Hyperquad as fixed parameters.

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