Helicate Self-organisation: Positive Cooperativity in the Self-assembly of Double-helical Metal Complexes

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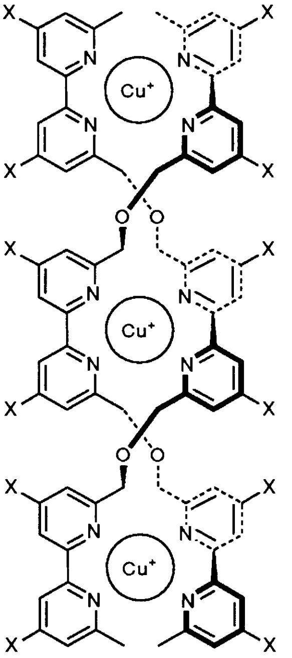
Analysis of the binding of Cu^I ions to the tris-bipyridine ligand **3** indicates that the assembly of the resulting trihelicate **1** is a self-organisation process displaying positive cooperativity.

Self-organisation is the process by which specific components spontaneously assemble in a highly selective fashion into a well-defined, discrete supramolecular architecture. It is self-assembling driven to completion by positive cooperativity, phase change and/or energy flow. It displays non-linearity since positive cooperativity results when a given step in the self-assembly sets the stage for and facilitates the following one. It requires binding interactions and implies that information must be stored in the components and read out by following a given algorithm. Three levels of information input may be distinguished: (*i*) selective binding of complementary components *via* molecular recognition; (*ii*) growth through sequential binding of the components in the correct relative orientation; (*iii*) termination of the process, requiring a built in feature, a stop signal, that specifies the end point and signifies that the process has reached completion; this may be a closure relation generating a closed structure. Such programmed supramolecular systems generate organized entities following a plan based on molecular recognition events.[1]

Thus, self-organisation may be considered to be a non-linear process involving binding, information and positive cooperativity. In addition, it requires reversibility of the connecting interactions, *i.e.* sufficiently fast kinetics, in order to allow the exploration of the energy hypersurface to the system.

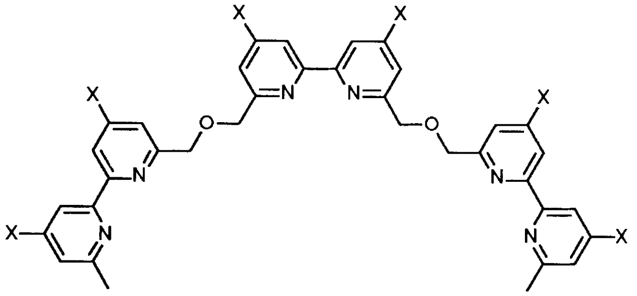
In view of the general significance of self-organisation in science as well as its importance in living organisms, it is of particular interest to design systems that undergo self-assembly with positive cooperativity, and to study in detail their physico-chemical behaviour.



1 X = CO$_2$Et
2 X = H

Such may be the case for the spontaneous formation of double-helical metal complexes, the *helicates*, from oligo-2,2′-bipyridine (oligo-bpy) ligands and suitable metal ions presenting tetrahedral coordination (*e.g.* Cu^I, Ag^I [2–4]). We present here an analysis of the physico-chemical properties of this process in the case of the cuprohelicate **1** resulting from the binding of three Cu^I ions by two strands of the tris-bpy ligand **3**.[5a] Additional studies have been conducted with the unsubstituted parent ligand **2**, as well as with the tetraester bis-bpy analogue of **1**. The present report will concentrate on the results obtained with **1**. Similar work has also been performed for silver(I) trihelicates.[6]

The formation of the cuprotrihelicates **1** and **2** was followed by spectrophotometric titration of ligands **3** and **4** with CuBF$_4$ in CH$_2$Cl$_2$/MeCN 1/1. The colourless solution of **3** becomes immediately red on addition of the solution of salt, owing to the appearance of an MLCT (metal to ligand charge transfer) absorption at λ_{max} = 500 nm (ϵ = 26 000). The titration spectra (Fig. 1) display two sharp isosbestic points between 250 and 700 nm over the complete titration. Furthermore, the excess absorbance diagrams[7] (EA) for several wavelengths (EA$_\lambda$ *versus* EA$_{360}$ plots) are linear even at very low metal : ligand ratio. Both features indicate the presence of only two absorbing species, *i.e.* the clean generation of a single species, to which the dodecaester trihelicate structure **1** may be



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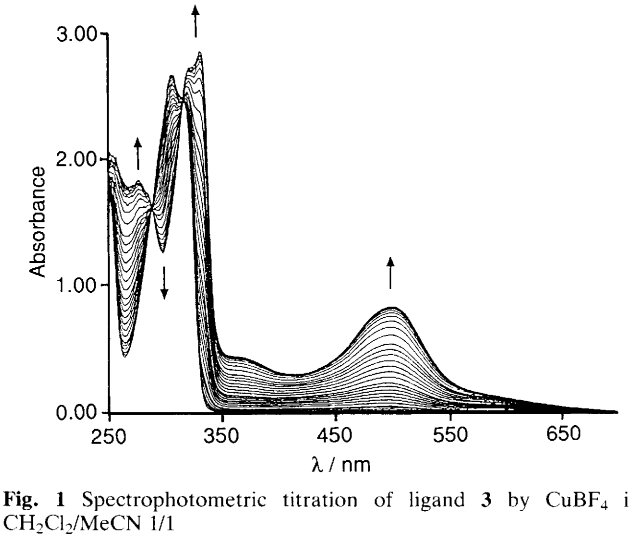

Fig. 1 Spectrophotometric titration of ligand **3** by CuBF$_4$ in CH$_2$Cl$_2$/MeCN 1/1

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† URA 422 of the CNRS.

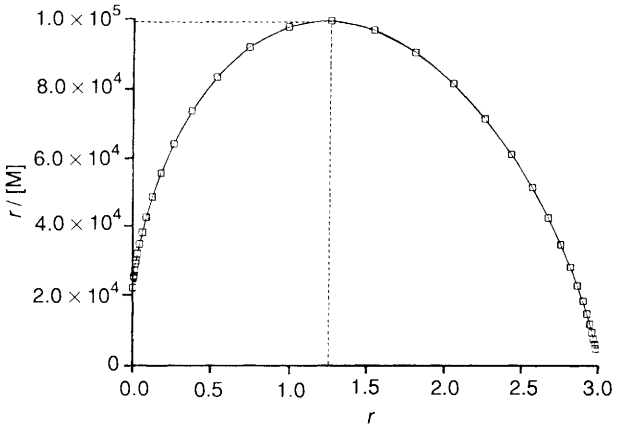

Fig. 2 Scatchard plot for the formation of the trihelicate **1**, obtained from analysis of the titration data (Fig. 1); [M]: concentration of free metal, mol dm^{-3}; r_{max} = 1.25 (see also text)

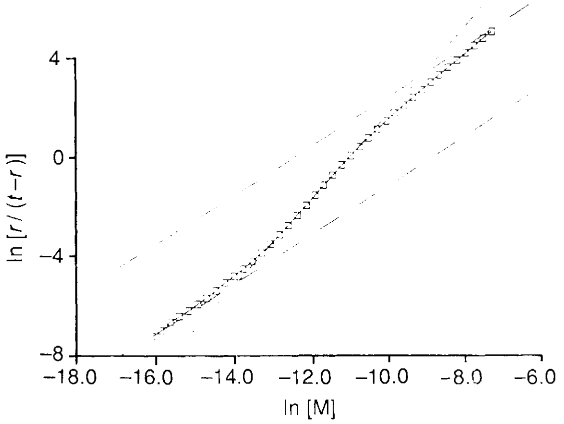

Fig. 3 Hill plot for the formation of the trihelicate **1**, obtained from analysis of the titration data (Fig. 1); maximum slope = 1.75 (see also text)

ascribed,[8] by analogy with the formation of **2** from **4**.[2] Similar results were obtained for the titration of the unsubstituted ligand **2** itself.

Analysis of the titration data should provide the thermodynamic parameters of trihelicate formation. A typical titration of **1**, which gave highly reproducible values, was exploited for 30 titration points and at 16 wavelengths using the LETAGROP-SPEFO program,[9] which performs a non-linear best fit of the spectrophotometric data. This program calculates the binding constants β_{ml} for each species M_mL_l of a proposed chemical model by iterative comparison of calculated with experimental absorbance values, searching for the global minimum of the error function. Models that do not fit the data are rejected; the one that fits best should be closest to the real situation.

In terms of stoichiometry, four M_mL_l complexes were considered, involved in the following four equililbria (1)–(4) described by four stability constants β_{ml}. The species M_2L and M_3L were neglected.

$$M + L \rightleftharpoons ML \qquad \log\beta_{11} = 4.6 \tag{1}$$

$$ML + L \rightleftharpoons ML_2 \qquad \log\beta_{12} = 8.2 \tag{2}$$

$$ML_2 + ML \rightleftharpoons M_2L_2 \qquad \log\beta_{22} = 13.5 \tag{3}$$

$$M_2L_2 + ML \rightleftharpoons M_3L_2 \qquad \log\beta_{32} = 18.6 \tag{4}$$

(with M = Cu$^+$ and L = **1**).

The calculations were performed using first only the equilibria (2)–(4) and thereafter adding equilibrium (1).‡ They gave the values log β_{ml} (±10% estimated) listed above. These data allow the computation of the distribution diagram for the M_mL_l species and provide the basis for investigating the cooperative character of the formation of the M_3L_2 trihelicate **1**.

Positive cooperativity is a thermodynamically clearly defined feature that may be revealed by several criteria or tests.[10] A multiequilibria system presents positive cooperativity if the ratio $K_{m+1}:K_m$ is higher than the value calculated from eqn. (5); it is non-cooperative (statistical) if the ratio is the same as this value and has negative cooperativity if it is smaller.

$$\frac{K_{m+1}}{K_m} = \frac{m(t-m)}{(m+1)(t-m+1)} \tag{5}$$

(with m: number of occupied sites in species M_mL_l; t: total number of sites). The *occupancy r* (average number of occupied sites) is given by eqn. (6).

$$r = \frac{\Sigma m\beta_{ml}[M]^m[L]^{(l-1)}}{1 + \Sigma l\beta_{ml}[M]^m[L]^{(l-1)}} \tag{6}$$

With the β_{ml} values shown above, $K_4 > K_3/3$, which is sufficient for indicating positive cooperativity. There are a number of tests for cooperativity, mainly graphical ones, based on eqn. (6). Scatchard plots[11] $r/[M] = f(r)$ present respectively a concave downward curve, a straight line, and a concave upward curve for positive cooperativity, no cooperativity and negative cooperativity. The Hill coefficient n_H giving the degree of cooperativity (positive for $n_H > 1$), is calculated at the maximum of the plot [eqn. (7)].

$$n_H = \frac{t}{t - r_{max}} \tag{7}$$

The Hill plot[12] $\ln r/(t - r) = f(\ln[M])$ yields a curve presenting a region with a slope higher than unity in the case of positive cooperativity, the maximal slope giving n_H.

Finally the binding curve $r/t = f([M_0]/[L_0])$ represents the degree of saturation as a function of added substrate and a sigmoidal curve indicates positive cooperativity.

Figs. 2 and 3 show respectively the Scatchard and Hill plots for the formation of the trihelicate **1**. The marked downward curvature of the first and the slope >1 of the second clearly indicate that the process leading to the self-assembly of the trihelicate **1** from its components, ligand **3** and Cu^I ions, occurs with positive cooperativity. The Hill coefficients obtained from the two plots are n_H = 1.72 and 1.75 (maximum slope), respectively. It is also found that the binding curve is slightly sigmoidal; however this criterion is less sensitive than the others.

It is possible to estimate the enthalpy $\Delta H°$ and entropy $\Delta S°$ of formation of **1** from absorbance data measured as a function of temperature. The temperature range explored (15–25 °C) was narrow owing to solvent problems (CH_2Cl_2–MeCN, 1 : 1). The approximate values obtained, $\Delta H°$ = −168 ± 10 kJ mol^{-1} and $\Delta S°$ = −218 ± 30 J mol^{-1} K^{-1}, indicate that helicate formation $3M + 2L \rightleftharpoons M_3L_2$ displays, not unexpectedly, a large negative entropy. This may be due to the pronounced organisation of the components that takes place in the process.

The present results indicate that the helicate formation process is driven to completion by positive cooperativity. Helicate formation is thus a true self-organisation process, along the lines discussed above.

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‡ The difficulties encountered for determining log β_{11} may be ascribed to the presence of only a very small amount of ML and perhaps to other preequilibria.

We thank Professor B. Perlmutter-Hayman for very valuable discussions, Dr Anne-Marie Albrecht for use of the LETAGROP program and NATO–DAAD for a research fellowship to A. P.

Received, 18th March 1992; Com. 2/01442D

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