

BINDING COOPERATIVITY IN THE SELF-ASSEMBLY OF DOUBLE STRANDED SILVER(I) TRIHELICATES

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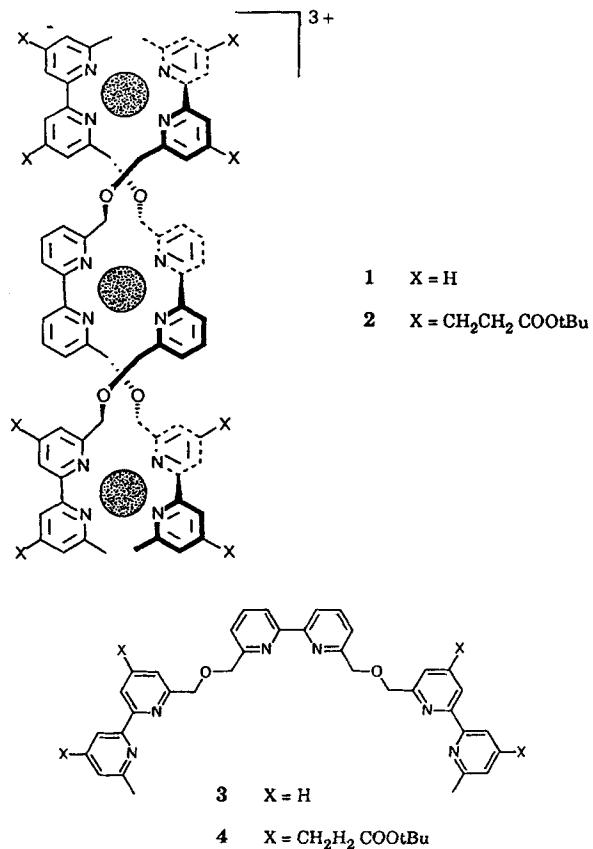
Spectroscopic and potentiometric studies of Ag(I) binding by tris-bipyridine strands indicate that the formation of trinuclear silver trihelicates is a process displaying positive cooperativity.

INTRODUCTION

Self-assembly is the process by which a supramolecular species forms spontaneously from its components.¹ Ideally, it is driven to high yield and specificity by positive thermodynamic cooperativity between the family of reactions that lead to the assembling.² It is a key step in numerous biological processes such as morphogenesis,² the formation of ribosomes,³ double-stranded DNA,⁴ viral protein coats⁵ and multiprotein complexes.⁶ Self-organizing systems, as is the case of the natural systems, should contain three levels of information input. The first is that the subunits bind one another with the correct arrangement. The second and third are that the growing supermolecule shapes itself into the desired tertiary structure and self-terminates growth when the target architecture has been achieved.

We have developed earlier a self-assembling system based on oligobipyridine ligands, where coordination of copper(I) or silver(I) ions efficiently and selectively produces complexes of double helical geometry, the helicates.⁷⁻⁹ Since these systems did not show a strong correlation between the product obtained and the stoichiometry of the reagents used, it appeared that they might display positive cooperativity.¹⁰ This led us to study the formation of the double-stranded silver trihelicates $[\text{Ag}_3(3)_2]^{3+}$, 1,⁹ and $[\text{Ag}_3(4)_2]^{3+}$, 2, from the tris-bipyridine ligands 3^{7,11} and 4¹¹ and AgCF_3SO_3 .

The complexes 1 and 2 were isolated and characterized and the binding of Ag(I) by 3 and 4 was followed by both spectrophotometric and poten-



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metric (using a silver electrode) titrations (see Experimental).

RESULTS AND DISCUSSION

Spectrophotometric titration (Figure 1) showed clean isosbestic points indicative of the formation of a single, well defined compound, in agreement also with the proton NMR data.

Positive cooperativity is a thermodynamically clearly defined process that may be revealed by several criteria

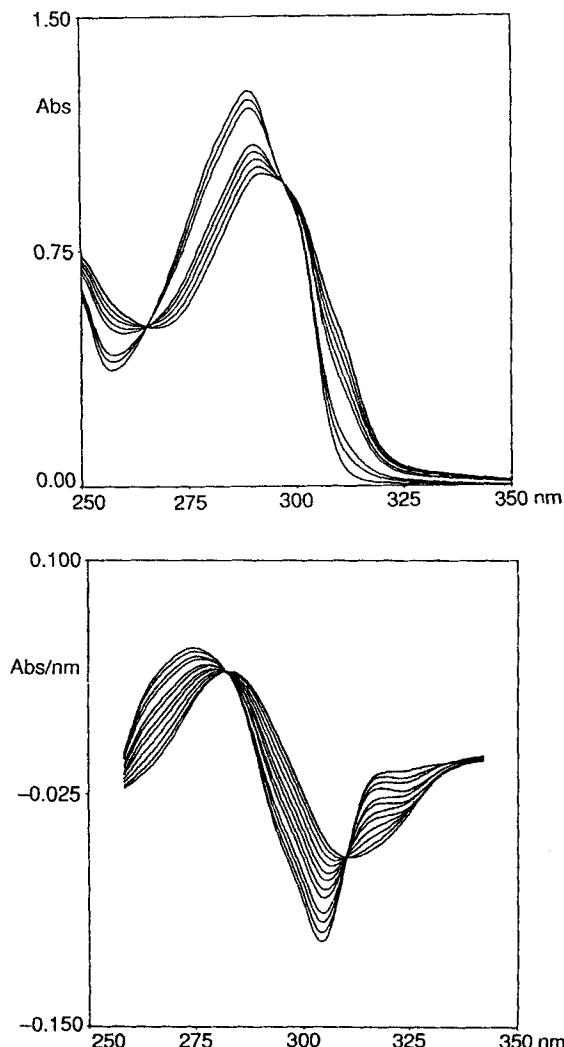


Figure 1. (Top) changes in the absorption spectrum observed in the course of titration of ligand 4 with AgCF_3SO_3 in $\text{CH}_3\text{CN}-\text{CHCl}_3$ (1:1, v/v); (bottom) first derivative of the absorption spectrum

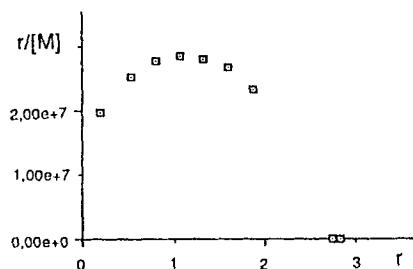
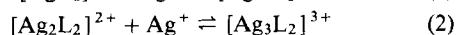
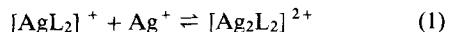


Figure 2. Scatchard plot obtained from the potentiometric titration of ligand 4 with AgCF_3SO_3 in $\text{CH}_3\text{CN}-\text{C}_6\text{H}_5\text{Cl}$ (1:1, v/v); r is the saturation of the ligand and varies from 0 to 3; $[M]$ is the concentration of free metal ion

or tests (for an excellent general presentation, see Ref. 12). Thus, both the spectrophotometric and the potentiometric experiments yielded concave downward Scatchard plots¹³ (Figure 2), indicating that the assembly of the helicates proceeded in a positively cooperative manner.¹² This could be seen as arising from a homotropic process where the stability constant K_2 for reaction (2) is greater than that for reaction (1), K_1 . In fact, for positive cooperativity to occur in reaction (2) it would be sufficient to have $K_2 > K_1/3$.



A positively cooperative heterotropic process, where ligand 'dimerization' would occur concomitantly with metal binding, could in principle also take place. Even if the most favoured pathway for assembly is not known, one may rationalize the existence of cooperativity in the self-assembly by arguments based on a homotropic path (see above). Bardsley and Wyman¹⁴ have described a general method for the determination of the sign of homotropic cooperativity in the case of ligand aggregation in addition to metal binding. All data collected for the present system demonstrate positive cooperativity by this test.

A series of Hill plots^{13,15} (Figure 3), using both the UV and silver electrode data sets, yield Hill coefficients greater than unity, confirming the result of positive cooperativity indicated by the Scatchard plots and the Bardsley and Wyman criteria. However, the two types of data sets do not give the same Hill coefficient. At 0.4 mM ligand, the silver electrode titrations yield $n_H = 1.45(5)$, whereas the UV titrations with 0.03 mM ligand give $n_H = 2.05(15)$. Since the Hill coefficient can be taken to be a quantitative measure of the amount of cooperativity present in a system, it would appear that the more dilute the system, the greater is the cooperativity in helicate formation. The lower values of n_H at high concentration could be due to the presence of small amounts of species which have lower stability

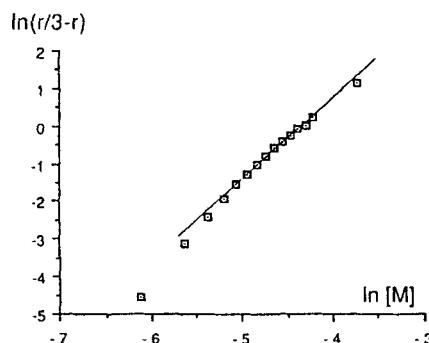


Figure 3. Hill plot obtained from the UV titration of ligand **4** with AgCF_3SO_3 in $\text{CH}_3\text{CN}-\text{CHCl}_3$ (1 : 1, v/v); for r and $[\text{M}]$, see Figure 2

constants, and are less cooperative in their formation, than the final helicate product. Such extraneous substances have been detected by proton NMR studies of the $[\text{Cu}_3(\mathbf{4})_2]^{3+}$ helicate in the presence of excess ligand;¹⁶ dilution of the sample resulted in a decrease in their signals. Since these species contain a defect of copper with respect to the helicates, this confirms that they assemble along a less cooperative path. Their absence at low concentrations is in line with the isobestic behavior of the UV titrations of the silver complexes (Figure 1).

The formation constant for $[\text{Ag}_3(\mathbf{4})_2]^{3+}$ is the same, to within experimental error, for the silver electrode and the UV titrations, $\log K = 22(1)$. This result shows little thermodynamic chelate effect, indicating that the cooperativity, although important for speciation, is not very large. Cooperativity could be more pronounced with the less hindered (but less soluble) ligand **3** than with **4**. On the other hand, the ligand-exchange kinetics observable by variable-temperature proton NMR yield a free energy of activation $\Delta G \geq 16 \text{ kcal mol}^{-1}$ for $[\text{Ag}_3(\mathbf{4})_2]^{3+}$. The literature value for $\text{Ag}(\text{phen})_2^+$ is $13.8 \text{ kcal mol}^{-1}$,¹⁷ demonstrating in our case a kinetic chelate effect of at least 2 kcal mol^{-1} ($1 \text{ kcal} = 4.184 \text{ kJ}$). Hence the special double helical structure in which two ligand strands are wrapped around three metal ions has provided significant kinetic stability to the five particles composing the helicate cation.

We have seen that the source of cooperativity need not be energetically large, and can be viewed in homotropic terms. It could arise at least in part from the π stacking seen in the crystal structure of $[\text{Ag}_3(\mathbf{3})_2](\text{CF}_3\text{CO}_3)_3$.⁹ After complexation of a metal by two ligands, the stability constants for the binding of the second and third metals is raised by the π stacking of the pyridine bases, which may induce a more favourable conformation for progressive metal coordination.

The present results demonstrate that the formation of

the double-stranded silver(I) helicates **1** and **2** displays positive cooperativity and provide a physico-chemical basis for the remarkable ability of these species to assemble spontaneously from their components with high efficiency and selectivity.

Studies of the corresponding Cu(I) helicates and of longer helicates involving more metal centres should shed further light on the origin of these self-organization processes.

EXPERIMENTAL

General. All commercially available chemicals employed were of reagent grade and used without further purification. The ^1H NMR spectra were measured on a Bruker AC 200 or Bruker AM 400 spectrometer. The microanalyses were performed at the Service Central de Microanalyse du CNRS, Institut de Chimie, Strasbourg.

The tris-bipyridine ligands **3** and **4** were synthesized as described elsewhere.¹¹

Synthesis of the helicate complex $[\text{Ag}_3(\mathbf{3})_2](\text{CF}_3\text{SO}_3)_3$, **1**. To a sonicated slurry of 50.1 mg (0.0863 mmol, 2 equiv.) of ligand **3**¹¹ in 4 ml of CH_3CN was added, dropwise, in the dark, a solution of 43.6 mg (0.170 mmol, 3.9 equiv.) silver(I) trifluoromethanesulphonate in 2 ml of CH_3CN . After dissolution of the ligand, the solution was stirred for 30 min. The reaction mixture was filtered over glass wool–Celite and concentrated. Addition of diethyl ether produced a precipitate which was collected by centrifugation and washed twice with diethyl ether. The product was dried *in vacuo* at room temperature, giving 75.7 mg (90%) of **1** as a cream-coloured powder. Analysis: calculated for $\text{C}_{75}\text{H}_{64}\text{N}_{12}\text{O}_{13}\text{Ag}_3\text{F}_9\text{S}_3 \cdot 4\text{H}_2\text{O}$, C 44.94, H 3.63, N 8.39; found, C 44.74, H 3.39, N 9.40%. ^1H NMR (CD_3CN): δ 8.05–7.40 (m, bpy), 6.95 (d, bpy), 6.81 (d, bpy), 3.90–4.15 (m, H, CH_2OCH_2), 2.35 (s, H, CH_3). FAB-MS (ortho-nitrobenzyl alcohol (NBA)): m/z 1783 [$[\text{Ag}_3(\mathbf{3})_2](\text{CF}_3\text{SO}_3)_2]^+$.

Synthesis of the helicate complex $[\text{Ag}_3(\mathbf{4})_2](\text{CF}_3\text{SO}_3)_3$, **2**. To a sonicated slurry of 25.2 mg (0.0230 mmol, 2 equiv.) of ligand **4**¹¹ in 5 ml of CH_3CN was added, dropwise, in the dark, a solution of 10.0 mg (0.0389 mmol, 3.4 equiv.) of silver(I) trifluoromethanesulphonate in 3 ml of CH_3CN . After dissolution of the ligand the solution was stirred for 1 h. It was filtered over a plug of silica gel (Merck 60, 70–230 mesh) and the solvent stripped off. The product was taken up in CH_3CN , filtered again over silica gel and the solvent evaporated. Drying *in vacuo* at room temperature yielded 29 mg (81%) of **2** as a colourless glass. Analysis: calculated for $\text{C}_{131}\text{H}_{160}\text{N}_{12}\text{O}_{29}\text{F}_9\text{S}_3\text{Ag}_3 \cdot 8\text{H}_2\text{O}$, C 50.72, H 5.47, N

5.42; found, C 50.50, H 5.24, N 5.30%. ^1H NMR (CD_3CN): δ 7.93–7.60 (m, bpy), 7.30 (s, bpy), 6.93 (br d, bpy), 4.0 (m, CH_2OCH_2), 3.1–2.4 (m, $\text{CH}_2\text{CH}_2\text{CO}_2\text{tBu}$), 2.07 (s, $\text{CH}_2\text{CH}_2\text{CO}_2\text{tBu}$), 1.41 (s, *tBu*), 1.35 (s, *tBu*). FAB-MS (NBA): *m/z* 2807 [$\text{Ag}_3(3)_2(\text{CF}_3\text{SO}_3)_2$]⁺.

Physico-chemical measurements. Spectrophotometric titrations (Figure 1) were performed on a Kontron Uvikon 860 apparatus, thermostated at 25 °C. The solvent system was acetonitrile–chloroform (1:1, v/v). The ligand concentration was 0.03 mM and the silver concentration was varied from 0.003 to 0.05 mM by addition of AgCF_3SO_3 with a calibrated Gilmot pipette. Data refinement was performed on an IBM-AT equivalent computer with the REFSPEC nonlinear least-squares program.¹⁸ Variable-tempreture NMR was performed on a 200 MHz Bruker instrument in CD_3CN – CDCl_3 (2:1, v/v).

Potentiometric titrations of the silver ion were performed on a custom-built apparatus of the type described by Gustowski *et al.*¹⁹ The electrodes were solid silver wires. Data were collected on a Metrohm Model 636 potentiometer. Electrodes were calibrated in $\text{p}[\text{Ag}] = -\log [\text{Ag}^+]$ and checked for linearity in the region from $\text{p}[\text{Ag}]$ 3 to 8.1. The supporting electrolyte was 0.1 M $\text{NBu}_4\text{CF}_3\text{SO}_3$. The apparatus was thermostated at 25 °C. The solvent was acetonitrile–chlorobenzene (1:1, v/v). The ligand concentration was 0.4 mM and the silver concentration was varied from 0.04 to 0.8 mM.

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