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Insights into the Mechanism of Coordination-Directed Self-Assembly

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Coordination-directed self-assembly has become a powerful new technique for the preparation of large supramolecular structures of defined shapes and sizes.[1] Among the largest self-assembled discrete structures prepared are dodecahedra (**1**, Scheme 1).[2] The two structures reported to date have outer dimensions of ∼5 and ∼8 nm and molecular masses of ∼42 and ∼62 kDa, respectively.[2] However, very little is known at this time about the mechanism of formation of these large structures. In the present contribution we describe the chemical exchange in the reaction mixture of partially assembled structures and the analysis of their sizes by NMR methods and the concomitant mechanistic implications for coordination-directed self-assembly.

One of the most important questions is whether starting materials, intermediates, and final ensembles undergo chemical exchange on the time scale of the assembly. If such exchange occurs, the composition of the products depends primarily on the thermodynamic parameters of the possible products and intermediates. On one hand, such exchange provides a mechanism for "self-correction", which results in the conversion of all possible unfavorable products and intermediates into a single product.[3] On the other hand, thermodynamic control limits the formation of a single product unless it has a sufficient thermodynamic advantage. For large self-assembled polyhedra the energy difference between structures with different geometries may not be sufficient enough to provide for selective self-assembly. This is likely one of the reasons why only a few abiological self-assembled structures with well-defined shape and size larger than 1 nm have been reported.[1] Furthermore, thermodynamics favors structures with small or no cavities, and hence large polyhedra have little chance to be assembled under thermodynamic control, therefore interpenetrating structures[4] and networks[5] are usually preferentially formed.

We are not aware of studies focusing on the kinetic and mechanistic aspects of the self-assembly processes, although their importance is obvious. Yet, the quest for the synthesis of larger discrete self-assembled structures requires the use of stronger bonds for thermodynamic reasons.[6] Stronger bonds (e.g., coordination vs hydrogen bonds) are less prone to favor a facile chemical exchange between intermediates and the final ensembles, hence kinetically controlled processes become increasingly important.

Supramolecular structures held together by Pt−pyridine bonds present a good example of self-assembled molecules for which both thermodynamic and kinetic considerations appear to be very important. Such complexes can undergo a rapid chemical exchange with an excess of the pyridine-containing ligands or with coordinating solvents, such as DMF, DMSO, and acetonitrile.[7] Our results indicate that the preparation of molecular polygons and polyhedra requires the gradual addition of the pyridine containing donor unit to the Pt triflate acceptor unit.[2,8] Under these conditions the Pt triflate precursor is always present in excess, which precludes the nucleophilic attack of a free strongly coordinating ligand on a square-planar complex of Pt(II). The best results are usually achieved when the self-assembly is performed in weakly coordinating solvents, such as methylene chloride, acetone, chloroform, and nitromethane. All of these data indicate that kinetically controlled events play a significant role in the process of self-assembly.

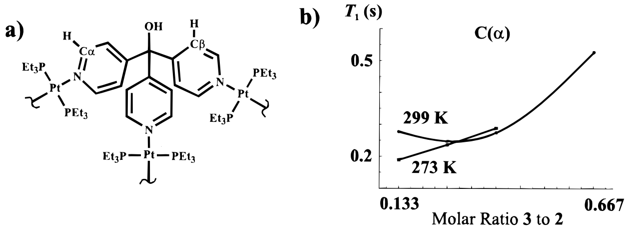
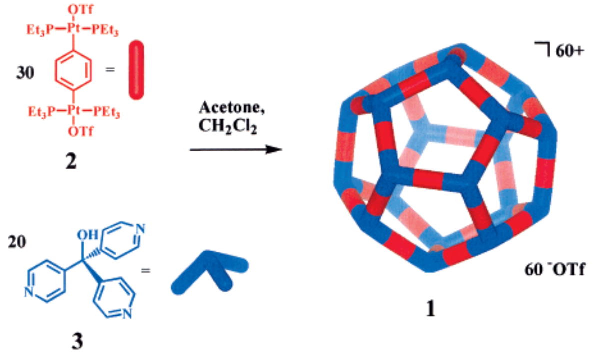


Figure 1. Measurement of longitudinal spin−spin relaxation rates. (a) Representation of the structure of self-assembled intermediates. (b) Relaxation rates of the α-pyridine carbons at various ratios of **3** to **2** and various temperatures.

Scheme 1. Self-assembly of an Supramolecular Dodecahedron



A 2D $^{31}P\{^1H\}$ EXSY NMR spectrum of a mixture containing 1,4-bis[*trans*-bis(triethylphosphine)platinum(II)triflate]benzene (2) in methylene chloride and tris(4-pyridyl)methanol (**3**) in acetone in a 5:2 ratio revealed no exchange between the signals assigned to Pt triflate and Pt−pyridine moieties at mixing times as long as 1 s.[9] This suggests that intermediates do not exchange with the starting bistriflate **2.** To evaluate the size of these intermediates at different ratios of **2** and **3**, we measured the rates of longitudinal relaxation of nuclei which correspond to rates of rotational diffusion.[10] Examination of the structure of possible assemblies reveals that the rates of longitudinal relaxation of the α- and *β*-pyridyl ^{13}C nuclei can be characteristic of the rate of tumbling of the whole assembly since they are located close to the vertexes of the self-assembled polyhedra (Figure 1a). Moreover, these ^{13}C nuclei are not present in the starting bistriflate **2**; thus, an excess of this reagent will not contribute to the measured average tumbling rates of the assembled intermediates and polyhedra.

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(1) (a) *Comprehensive Supramolecular Chemistry*; Lehn, J.-M., Chair Ed.; Atwood, J. L., Davis, J. E. D., MacNicol, D. D., Vögtle, F., Exec. Eds.; Pergamon: Oxford, UK, 1987−1996; Vols. 1−11. (b) Fujita, M. *Acc. Chem. Res.* **1999**, *32*, 53. (c) Caulder, D. L.; Raymond, K. N. *Acc. Chem. Res.* **1999**, *32*, 975. (d) Saalfrank, R. W.; Demleitner, B. In *Transition Metals in Supramolecular Chemistry*; Sauvage, J. P., Ed.; John Wiley & Sons Ltd.: NY.; 1999; pp 1−51. (e) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853.

(2) Olenyuk, B.; Levin, M. D.; Whiteford, J. A.; Shield, J. E.; Stang, P. J. *J. Am. Chem. Soc.* **1999**, *121*, 10434.

(3) Whitesides, G. M.; Mathias, J. P.; Seto, C. T. *Science* **1991**, *271*, 1312.

(4) (a) Raymo, F. M.; Stoddart, J. F. *Chem. Rev.* **1999**, *99*, 1643. (b) Fujita, M.; Fujita, N.; Ogura, K.; Yamaguchill, K. *Nature* (London) **1999**, *400*, 52.

(5) Yaghi, O. M.; Li, H.; Davis, C.; Richardson, D.; Groy, T. L. *Acc. Chem. Res.* **1998**, *31*, 474.

(6) Ercolani, G. *J. Phys. Chem. B* **1998**, *102*, 5699.

(7) (a) Fuss, M.; Siehl, H.-U.; Olenyuk, B.; Stang, P. J. *Organometallics* **1999**, *18*, 758−769. (b) Stang, P. J.; Olenyuk, B.; Arif, A. *Organometallics* **1995**, *14*, 5281−5289.

(8) Fan, J.; Whiteford, J. A.; Olenyuk, B.; Levin, M. D.; Stang, P. J.; Fleischer, E. B. *J. Am. Chem. Soc.* **1999**, *121*, 2741.

(9) See Supporting Information.

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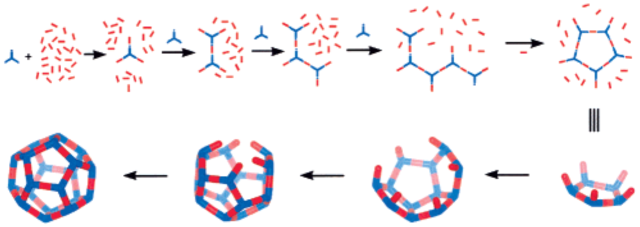
Scheme 2. Growth of Intermediates as the Ratio of Donor Unit **3** (blue triangles) to the Acceptor Unit **2** (red rods) Grows

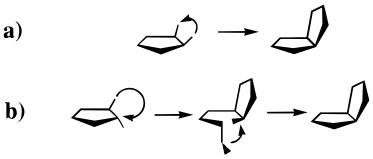


The measured T_1 for the α-pyridyl (Figure 1b) and β-pyridyl[9] ^{13}C nuclei are decreasing as a solution of **3** is added to a solution of **2**, pass through a minimum, and start increasing at high ratios of **3** to **2**. The dependence of T_1 on the ratio of **3** to **2** is very similar to the dependence of T_1 on the logarithm of the rate of tumbling when the dipole−dipole relaxation mechanism is the predominant one.[10] T_1 also showed a strong dependence on temperature (Figure 1b); hence, the minimum on the T_1 curve at lower temperature corresponds to structures formed at lower ratios of **3** to **2**.

These data allow us to conclude that the average size of the intermediates is growing as more **3** is added to the reaction mixture and the ratio of the two building blocks approaches the stoichiometric ratio for the dodecahedron. Furthermore, the lack of fast exchange in partially titrated mixtures suggests that the formation of intermediates occurs under primarily kinetic control. However, the growth of 3D supramolecular structures under kinetic control usually yields insoluble cross-linked polymers.[1b] For discrete convex structures to assemble, two other processes must take place in addition to the kinetically controlled growth: (a) ring formation and (b) self-correction of defective rings of the wrong size or stereochemistry. Both steps should be very efficient and selective such that only macrocyclic pentagons are formed with an all-*syn* stereochemistry. These two processes have to involve chemical exchange between the Pt triflate and Pt−pyridine moieties. The observed lack of experimental exchange can be accounted for by assuming that the processes of ring formation and self-correction occur rapidly and cease before the NMR data can be acquired. 2D-EXSY experiments are rather lengthy, and it is impossible to observe exchange if it happens for a short time and then stops. We propose that ring formation occurs as an oligomer chain curls as it grows and undergoes intramolecular ring closure (Scheme 2). As **3** is added, oligomer chains start growing statistically, but they form rings as they grow long enough. When there are no more chains long enough to cyclize and there is no more **3** to sustain the chain growth, exchange processes cease. This mechanism allows for ring formation with a concerted intramolecular breaking and formation of relatively strong Pt−pyridine bonds, thus it should have a low barrier and should proceed at a high rate. The process is also favorable entropically since it proceeds with the formation of two particles from one. Once a ring is formed, it is more stable kinetically, and no exchange is noticeable as NMR data is acquired.

The initially formed ring serves as a template for the creation of other rings, which then grow into a convex structure (Scheme 2). However, this is only possible if only all-*syn* pentagons are formed or if pentagons with other stereochemistries are converted into the all-*syn* ones along the reaction pathway. Following the same logic, we propose that a self-correction process involves a concerted sequence of ring formation and ring breaking via a similar exchange reaction (Scheme 3). These processes may proceed as **3** is added, oligomer chains attached to an existing pentagon grow larger and close in a new macrocycle. If the stereochemistry of two neighboring sites on the templating pentagon is *syn*, a new macrocycle can close without any correction. If the configuration is *anti*, the new ring can only form upon opening of the original templating pentagon. In this way, the newly formed macrocycle will serve as a template for the open chain formed from the initial templating ring. This chain can approach the cyclization point from a different face and form a new pentagon without opening of the templating one. This sequence of events effectively corrects the possible wrong *anti* stereochemistry of the original templating pentagon. Thus, we can arrive at a single “corrected” structure at the end of the self-assembly process.

Scheme 3. Formation of Macrocycle Pentagons[a]



[a] Templated by an original pentagon: (a) *syn* configuration of two neighboring growing groups; (b) *anti* configuration of two neighboring growing groups requires opening of the original pentagon to close the second pentagon, then the original pentagon closes.

However, several questions remain unanswered. It is not clear what a transition state for such a ring-closing reaction looks like. Even though the proposed mechanism can provide for the selective assembly of a single final structure, the reason for the high selectivity for the formation of a pentagon rather than macrocycles of other sizes is not completely clear.[1c] It is obvious however, that unless the selectivity of pentagon formation itself is high, no selective overall self-assembly is possible. We have shown[2] that dodecahedra do not assemble from flexible precursors, probably due to the lack of selectivity in the formation of pentagons (Scheme 2).

In conclusion, intermediates in the self-assembly of molecular dodecahedra held together by Pt−pyridine bonds do not undergo any noticeable chemical exchange in weakly coordinating solvents with excess Pt triflate acceptor moieties. The size of the intermediates grows steadily as more pyridine-containing reagent is added to a solution of a Pt triflate containing precursor. A mechanism is proposed which accounts for the observed data and allows for the selective assembly of convex supramolecular polyhedra.

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Supporting Information Available: Experimental details, 2D ^{31}P{^{1}H} EXSY NMR spectrum of a mixture containing the precursors **2** and **3** in a 5:2 ratio (Figure 1s) and a plot of the longitudinal relaxation rate of the β-pyridine carbon from the molar ration of **3** to **2** (Figure 2s, PDF). This material is available free of charge via the Iternet at http://pubs.acs.org.

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[10] Harris, R. K. *Nuclear Magnetic Resonance Spectroscopy: A Physicochemical View*; Longman Scientific & Technical: Essex, 1987.