

MOLECULAR ARCHITECTURE VIA METAL COORDINATION

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INTRODUCTION

Recently, there has been a rapid growth and widespread interest in the field of supramolecular architectures because of their potential to perform functions such as molecular recognition and catalysis,¹ and to function as molecular machines.² Therefore, efficient synthetic approaches to organized molecular structures is highly desirable. In the last decade, it has been found that controlled use of non-covalent forces provides an efficient method for creating large, well-defined supramolecular systems through self-assembly. “Self-assembly” was defined by Whitesides as “the spontaneous assembly of molecules into structured, stable, non-covalently joined aggregates”.³ The formation of such aggregates can be accomplished through various types of bonds and interactions, such as van der Waals, π - π stacking, hydrogen bonding and metal coordination. Compared with other types of interactions, metal-ligand interactions are much stronger and highly directional. Hence, they can be used in place of many weak interactions to direct the formation of multi-metal coordination structures.

Self-assembly via metal coordination offers significant advantages over traditional stepwise synthetic methods. Because metal coordination proceeds via the simultaneous assembly of predesigned building blocks, the resulting synthesis is highly convergent and thus more efficient than the corresponding covalent synthesis. Additionally, the kinetically labile non-covalent interactions among the self-assembling components provide relatively defect-free assemblies with self-maintained integrity. This feature comes as a result of the equilibria between the constituents and the products, which contributes to the rearrangement of components and correction of defects.⁴ This report will focus on the existing strategies for construction of supramolecular structures via metal coordination and investigations on the mechanism of self-assemblies in various supramolecular systems.

DESIGN STRATEGIES AND REPRESENTATIVE MOLECULAR STRUCTURES

The shape of the self-assembled supramolecular structures depends not only on the metal coordination geometry, but on the orientation of the binding sites in a given ligand. Based on these geometric requirements, three design strategies have been developed for constructing various supramolecules. All these concepts require the use of labile metal-ligand bonds, so “mistakes” from the initial formation of kinetic product can be repaired to give the thermodynamically favored product.

“Symmetry Interaction” Strategy

The “symmetry interaction” model is widely used by Saalfrank,⁵ Lehn⁶ and Raymond⁷ to assemble

various macrocyclic structures which contain main group or transition metals. This strategy emphasizes the importance of the symmetry elements of a particular point group.

One of the simplest multimetal aggregates incorporates two metal atoms linked by one or more ligands. When these two metal ions are linked by three identical, C_2 -symmetric ligand strands, the resulting aggregate is called a triple helicate. To design such a structure with D_3 symmetry, both the C_2 and C_3 axes of the point group must be taken into account. A C_2 -symmetric bis(bidentate) ligand can provide the 2-fold axis and a metal ion with pseudo-octahedral coordination by three bidentate chelators can provide the 3-fold axis. These symmetry axes must be oriented 90° to one another. Since the two metal centers share the same C_3 helical axis, the two coordination planes which are orthogonal to the C_3 axis must be parallel. This requires that the angle between two coordinate vectors (bisecting the

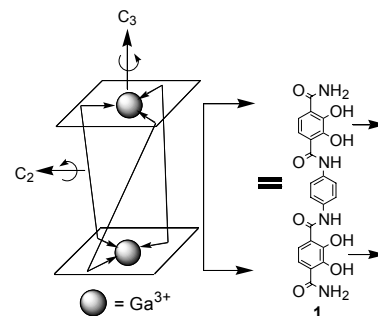


Figure 1. Triple helicate structure

chelating group and directed toward the metal ion) within a ligand be 0° (Figure 1). An M_4L_6 tetrahedral structure can also be constructed with the same combination of these symmetry elements. However, in this type of complex, the C_2 and C_3 axes must be oriented 54.7° from one another, which requires an angle of 70.6° between two coordinate vectors within a ligand (Figure 2).

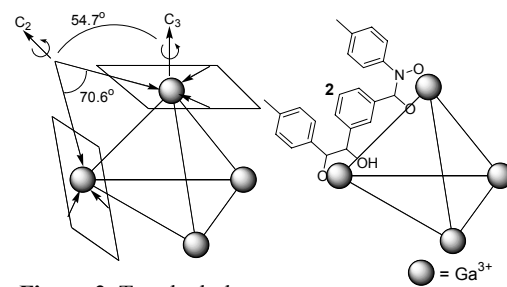


Figure 2. Tetrahedral structure

Catecholamide and hydroxamate ligands are excellent choices for binding units in these supramolecular complexes because they form highly stable octahedral coordination complexes with +3 metal ions (Al^{3+} , Ga^{3+} and Fe^{3+}). The feasibility for the proposed metal-ligand system has been explored prior to ligand synthesis using molecular mechanics calculations.⁸ Based on the strategy discussed above, Ga^{3+} and catecholamide **1** were used to synthesize triple helicate $[Ga_2\mathbf{1}_3]^{6-}$ (Figure 1),⁹ whereas hydroxamate ligand **2** was used in the synthesis of tetrahedral structure $[Ga_4\mathbf{2}_6]^{12-}$ (Figure 2).¹⁰

Although this design strategy is very useful for the synthesis of triple helicates and tetrahedral structures, there has been no report of its application to construct more complex systems. Nevertheless, this design principle is a sophisticated one.

“Molecular Library” Strategy

Another strategy for design of superamolecular structures is the “molecular library” model that was first applied by Verkade,¹¹ later improved by Fujita,¹² and systematized by Stang.¹³ Different from “symmetry interaction” model, which is focused on symmetry elements in a certain structure, this strategy considers which types of building blocks (ditopic units as edges, tritopic units as vertices) and how many of them are necessary for construction of a certain superamolecular structure.

This method implements binding of rigid, highly directional, multibranching monodentate ligands to coordinatively unsaturated transition-metal complexes through dative bond interactions. Therefore, construction of various macrocyclic structures, both two- and three-dimensional, can be achieved by assessing the appropriate angles between the binding sites of the donor and acceptor subunits. Based on the binding angle, the subunits can be classified into two types— linear rodlike subunits (abbreviated as **L**) with two opposite reactive sites (i.e., $\sim 180^\circ$) and angular subunits (**A**) with angles between 0° and 180° . When suitably rigid, complementary donor (ligand-based) and acceptor (metal-based) building blocks in the molecular library are combined, the highly directional formation of coordination bonds between them can generate a variety of secondary or polyhedral geometric structures (Figure 3).

ditopic units	60°	90°	109.5°	120°	180°	ditopic units	$90^\circ-90^\circ$	109°	180°
60°						60°			
90°						90°			
109.5°						109.5°	"double square"	adamantoid	dodecahedron
120°						120°	truncated tetrahedron	truncated tetrahedron	
180°									

Figure 3. "Molecular Library" for the construction of 2D and 3D assemblies.

The assembly of a molecular square can be achieved in various ways. One combination is four linear ditopic building units (abbreviated as L^2_4) with four monodentate angular (90°) ditopic ones (A^2_4). Alternatively, the combination of two different angular (90°) subunits can also provide a molecular square. Self-assembly of **6** was achieved by combining building blocks **4** and **5** in 1:1 ratio (Figure 4A).¹⁴ Based on the same strategy, molecular hexagon **9** was built via a combination of six linear ditopic subunits (L^2_6) **8** with six angular (120°) ones (A^2_6) **7** (Figure 4B).¹⁵ A much more complex two-dimensional lattice structure was also achieved via self-assembly using this strategy.¹⁶

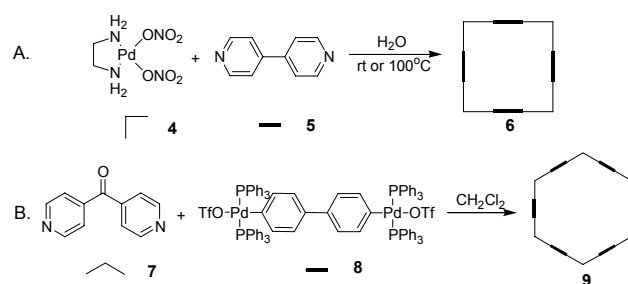


Figure 4. Construction of polygons

The dodecahedron, consisting of 12 regular pentagonal faces, represents the second largest of the Platonic solids. The synthesis of a macromolecular dodecahedral cage was accomplished through the self-assembly of 50 building blocks, 30 of which have ditopic, $\sim 180^\circ$ edges and the other 20 comprise tritopic, $\sim 108^\circ$ vertices. The reaction of **10** with either **11** or **12** yields dodecahedra **13** and **14**, respectively (Figure 5).¹⁷ Both **13** and **14** were characterized by multinuclear NMR showing the overall entities of high symmetry. The data of ESI-MS, Pulsed gradient Spin Echo (PGSE) NMR and transmission electron

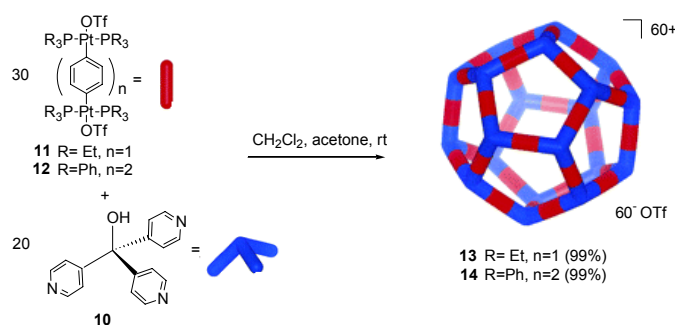


Figure 5. Construction of Dodecahedron

microscopy (TEM) also confirmed the product structures. With their molecular masses of ca.41kDa for **13** and ca.62kDa for **14**, these two organic-soluble dodecahedra are among the largest, highly-symmetrical, transition-metal-based assemblies that have been artificially constructed to date. Their nanoscopic void spaces, occupied by solvents and/or anions, are potentially able to host large guests. The size of these entities falls within the domain of proteins.

The major advantage of this “molecular library” strategy is its “combinatorial” capability; different polygons or polyhedra can be constructed through different combinations of the same angular and linear subunits. Compared with “symmetry interaction” strategy, this design principle is easier to understand.

“Molecular Paneling” Strategy

In 2001 Fujita reported “molecular paneling”—another strategy for construction of organized molecular structures.¹⁸ Different from the first two strategies, which choose the right building blocks as vertices or edges for construction of superamolecules, this molecular design involves linking two-dimensional (2D) planar organic components via metal coordination to construct three-dimensional (3D) structures. This idea comes from the fact that 3D-molecular structures can be well designed by deducing the molecular components from polyhedra. For instance, equilateral triangles, squares and pentagons are the basic components for construction of Platonic solids. The common feature of these solids is that they consist of regular polygons which are arranged in space to make sure that the edges, vertices and three coordinate directions of each solid are equivalent. For application of this strategy, several molecular panels with the basic shapes of triangles, squares and rectangles (Figure 6) have been synthesized. The *cis*-protected square planar metals, (en)Pd²⁺ and (en)Pt²⁺ (en= ethylenediamine), are found to be very useful to panel the molecules. The assembling of these panels with the *cis*-protected coordination unit can be considered as “molecular paneling”.

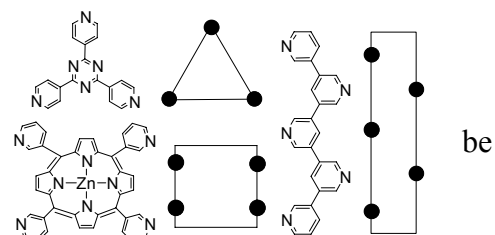


Figure 6. Structural and cartoon representation of molecular panels.

M₆L₄ octahedral assembly **17** was achieved in quantitative yield by treating **15** with **16** in 2:3 ratio (Figure 7A).¹⁹ In this complex, the four triangle panels are linked together at the corners of the triangles so that every other face of the octahedron contains either a molecular panel or a portal. It has been found that an excess of **16** does not destabilize the formation of the product, so complex **17** is thermodynamically stable. This octahedral cage has a very large cavity, having a diameter of 1 nm, and it exhibits a remarkable ability to encapsulate large and neutral molecules. Based on the same strategy, rectangular

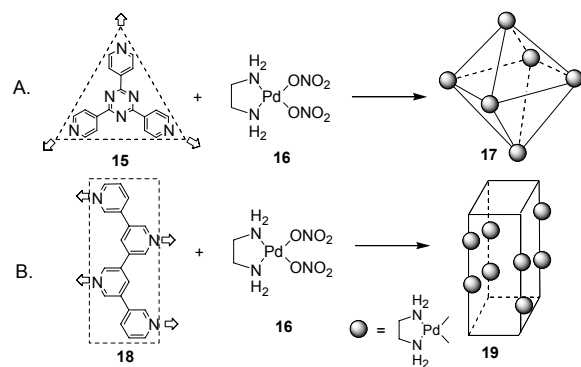
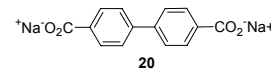


Figure 7. Molecular structures via molecular paneling

panel **18** was employed in construction of nanotube **19** (Figure 7B).²⁰ However, the formation of complex **19** was only observed in the presence of a rod-like guest molecule such as sodium 4,4'-biphenyldicarboxylate **20**. The encapsulation of **20** in the nanotube was verified by NMR data, which showed the protons of **20** were shifted up-field by as much as 2.6 ppm. Interestingly, the tube dissociates into its components upon removal of the guest molecule and reassociates upon the addition of guest molecule, which indicates that the formation of these tubes is reversible.



Remarkable progress has been made using the “molecular paneling” strategy, and this method enables the construction of large cage-like molecules having large cavities. These large cavities represent isolated spaces which are potentially useful for molecular recognition and catalysis.

All three of the strategies discussed above have been used effectively for the construction of more complex nanoscopic structures with predefined shapes and sizes, and the scope of these approaches is still under investigation.

MECHANISM OF MULTI-COMPONENT ASSEMBLY

To achieve better design and construction of complex supermolecular structures, it is crucial to understand the mechanism of the self-organization process. Few such studies have been reported, but it is, nevertheless, known that various factors may affect the formation of desired complex, such as metal-to-ligand ratio, reaction temperature and presence of guest molecules. All these factors complicate the self-assembly process.

Mechanism of self-assembly of grid-type complex

The self-assembly of the [3×3]-grid-type complex $L_6Ag^+_9$ (**22**; Figure 8) from the tritopic ligand **21** and Ag^+ ions was reported before.²¹ Recently, Lehn and co-workers have investigated the nature of the intermediates, which are progressively generated as the amount of metal ions added to a solution of the ligand increases. The evolution of intermediates in the reaction mixtures was monitored by 1H and ^{109}Ag NMR spectroscopy. It is proposed that triangular $L_3Ag^+_3$ **23** or square $L_4Ag^+_3$ **24** species (Figure 9) could form at a low Ag^+/L ratio. As the Ag^+/L ratio increases, the complex $L_5Ag^+_6$ **25** begins to form. The formation of complex **26** is proposed as the prerequisite for the generation of the final grid $L_6Ag^+_9$. When Ag^+/L ratio reaches 9:6, the complex **22** forms quantitatively. It has also been found that complex **22** is stable in the presence of a large excess of Ag^+ ions (4 equiv), which indicates that the $L+Ag^+$

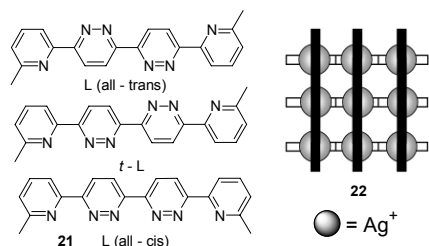


Figure 8. Schematic representation of the grid complex; the white bars denote parts of ligands “behind” the silver cations while the black bars represent those “in front”.

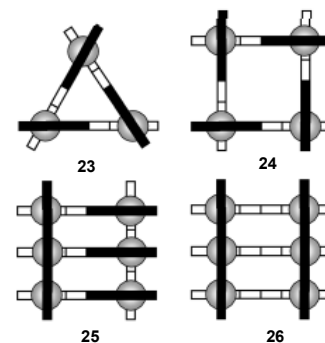


Figure 9. Intermediate structures 69

system displays high robustness with respect to formation of $L_6Ag^+_9$.²²

Mechanism of self-assembly of Dodecahedron

The mechanism of the formation of large molecular cages is also of great interest. Stang and co-workers studied the formation of dodecahedra.²³ The rates of longitudinal relaxation of nuclei, which correspond to the rates of rotational diffusion, were measured to evaluate the size of these intermediates at different ratios of **11** and **10**. The α - and β -pyridyl ^{13}C nuclei are considered to be characteristic of the rate of the tumbling of the whole complex, because they are located close to the vertices of the self-assembled polyhedra (Figure 10A). The measured T_1 values for the α - and β -pyridyl ^{13}C nuclei decrease as a solution of **10** is added to the solution of **11**, pass through a minimum and then start increasing at high ratios of **10** to **11**. The dependence of T_1 on the ratio of **10** to **11** is very similar to its dependence on the logarithm of the rate of tumbling when the dipole-dipole relaxation mechanism is applied. T_1 also showed a strong dependence on temperature (Figure 10B). Hence, the minimum on the T_1 curve at lower temperatures correspond to structures formed at lower ratios of **10** to **11**.

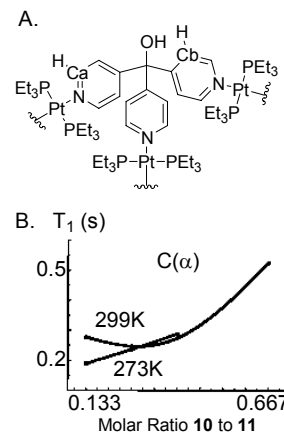


Figure 10. Measurement of T_1 of the C_a in the intermediates.

From these data, it is concluded that the average size of the intermediates grows as more **10** is added to the mixture and the ratio of **10** and **11** approaches the stoichiometric ratio for the dodecahedron. In order to explain the selective assembly of convex supramolecular polyhedra, a self-correction pathway involving a concerted sequence of ring formation and breaking was proposed. If the stereochemistry of the two neighboring sites on the first pentagon **A** is in syn configuration, a new ring **B** can close without correction (Figure 11A); However, if the configuration is anti, to form the new ring **B**, the original pentagon **A** has to reopen, followed by cyclization to form **B**, and finally recyclization of the open chain onto the correct face to reform pentagon **A** (Figure 11B).

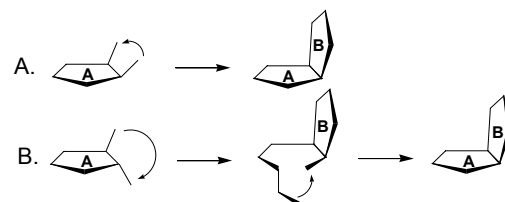


Figure 11. Self-correction process: (a) syn configuration; (b) anti configuration

Study on “guest-controlled” self-assembly

The study on an interesting mechanistic feature—“guest-controlled” assembly of open cones and tetrahedron structures—was reported by Fujita and co-workers using the molecular paneling design strategy (Figure 12).²⁴ The combination of ligand **27** and metal acceptor **16** in the presence of excess guest **28** resulted in the quantitative assembly of M_8L_4 open cone **29** accommodating one molecule of **28**. This structure was observed by NMR and ESI-MS. However, the presence of small guest molecules such as CBr_4 **30** lead to tetrahedral coordination assembly **30-31**, which was determined by NMR and X-ray crystallographic analysis. In the absence of guest molecules, the self-assembly of **27** and **16** gave a 3:2

mixture. The minor product was identified as **29**. The portion of the major product was found to increase at lower concentrations, which indicates this product consists of fewer components than **29**. Since its NMR is qualitatively the same as that of **29**, the major product was tentatively assigned as an M_6L_3 trimeric open cone structure **32**. It was also found by ^1H NMR kinetic studies that the three complexes **29**, **31** and **32** are interconvertible with one another through remarkably effective reorganization processes, which are induced by guest addition

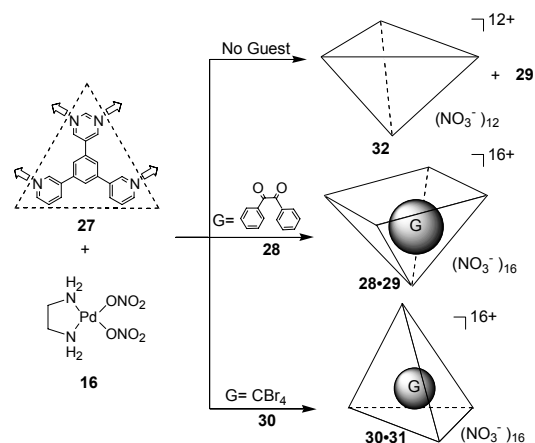


Figure 12. Guest-controlled assembly

or exchange. Complex **32** (in the mixture of **29** and **32**) was converted to **28·29** upon the addition of guest molecule **28**. The addition of **30** to the mixture of **29** and **32** resulted in the conversion of both **29** and **32** to complex **30·31**. The assembled open cone **28·29** was transformed into complex **30·31** upon addition of excess **30** via guest exchange.

Although great insight has been gained into the mechanism of some self-assembly processes, further understanding is required for the successful self-assembly of more complex objects.

CHALLENGES IN THE CHARACTERIZATION OF SUPRAMOLECULES

Among traditional characterization methods, multinuclear NMR spectroscopy gives some insight into supramolecular structures. However, it is often unable to provide adequate data because the nuclei in the highly symmetric complexes are magnetically equivalent. Mass spectrometry is another important tool, providing information on the molecular weight and confirming the empirical formula. But EI-, CI-, FAB-MS require harsh conditions and have limited mass detecting range, which greatly restricts their application in characterizing supramolecular structures. In some particular cases, even ESI-MS can only provide fragment ion peaks. The most unambiguous method for characterizing solid-state structures is single-crystal structure analysis, which has helped confirm the structures of many self-assemblies in small size. However, the larger the self-assembled structures are, the more difficult it becomes to grow crystals suitable for analysis. Moreover, the possibility always exists that the solid-state structure is different from the structure in solution. The application of determining molecular weight by colligative properties is limited by problems of solubility and precision of measurement.

Recently, CSI-MS (Coldspray Ionization Mass Spectrometry) has been developed and applied to characterize the solution structures of various organometallic compounds.²⁵ Using a very mild condition, this method allows for convenient and precise measurement of mass of molecular ions generated from labile self-assembling nano-sized complexes. Microscopic techniques such as scanning tunneling

microscopy (STM) and transmission electron microscopy (TEM) have also become useful in providing information on the size and shape of the self-assembled supramolecules. Nevertheless, there is a great demand for the development of more convenient and accurate characterization techniques.

CONCLUSION

Self-assembly via metal coordination processes have generated many novel molecular architectures with various functions, often in a rational and highly selective manner and by one-step, in-situ processes. The structural complexity of these products has been greatly enhanced in the last decade through better understanding of the nature of self-assembly process and improved characterization methods. Further advances involving the development of new self-assembly methodologies are anticipated. Seeking novel and complicated higher order structures represents an attractive area of research for organic chemists.

REFERENCES

- (1) Ito, H.; Kusukawa, T.; Fujita, M. *Chem. Lett.* **2000**, 598.
- (2) Armaroli, N.; Balzani, V.; Collin, J.-P.; Gaviña, P.; Sauvage, J.-P.; Ventura, B. *J. Am. Chem. Soc.* **1999**, *121*, 4397.
- (3) Whitesides, G. M.; Mathias, J. P.; Seto, C. T. *Science* **1991**, *254*, 1312.
- (4) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853.
- (5) Saalfrank, R. W.; Bernt, I.; Uller, E.; Hampel, F. *Angew. Chem. Int. Ed.* **1997**, *36*, 2482.
- (6) Baxter, P. N. W.; Lehn, J.-M.; Kneisel, B. O.; Baum, G.; Fenske, D. *Chem. Eur. J.* **1999**, *5*, 113.
- (7) Caulder, D. L.; Raymond, K. N. *J. Chem. Soc., Dalton Trans.* **1999**, 1185.
- (8) CAChe 4.0, Oxford Molecular Group, Inc., USA, 1997.
- (9) Meyer, M.; Kersting, B.; Powers, R. E.; Raymond, K. N. *Inorg. Chem.* **1997**, *36*, 5179.
- (10) Beissel, T.; Powers, R. E.; Raymond, K. N. *Angew. Chem. Int. Ed.* **1996**, *35*, 1084.
- (11) Stricklen, P. M.; Volcko, E. J.; Verkade, J. G. *J. Am. Chem. Soc.* **1983**, *105*, 2494.
- (12) Fujita, M. *Chem. Soc. Rev.* **1998**, *27*, 417.
- (13) Olenyuk, B.; Fechtenkötter, A.; Stang, P. J. *J. Chem. Soc., Dalton Trans.* **1998**, 1707.
- (14) Fujita, M.; Yazaki, J.; Ogura, K. *J. Am. Chem. Soc.* **1990**, *112*, 5645.
- (15) Stang, P. J.; Persky, N.; Manna, J. *J. Am. Chem. Soc.* **1997**, *119*, 4777.
- (16) Drain, C. M.; Nifiatis, F.; Vasenko, A.; Batteas, J. D. *Angew. Chem. Int. Ed.* **1998**, *37*, 2344.
- (17) Olenyuk, B.; Levin, M.D.; Whiteford, J. A.; Shield, J. E.; Stang, P. J. *J. Am. Chem. Soc.* **1999**, *121*, 10434.
- (18) Fujita, M.; Umemoto, K.; Yoshizawa, M.; Fujita, N.; Kusukawa, T.; Biradha, K. *Chem. Commun.* **2001**, 509.
- (19) Fujita, M.; Oguro, D.; Miyazawa, M.; Oka, H.; Yamaguchi, K.; Ogura, K. *Nature*, **1995**, *378*, 469.
- (20) Aoyagi, M.; Biradha, K.; Fujita, M. *J. Am. Chem. Soc.* **1999**, *121*, 7457.
- (21) Baxter, P. N. W.; Lehn, J. -M.; Fischer, J.; Youinou, M. -T. *Angew. Chem. Int. Ed.* **1994**, *33*, 2284.
- (22) Marquis, A.; Kintzinger, J.-P.; Graff, R.; Baxter, P.N.W.; Lehn, J.-M. *Angew. Chem. Int. Ed.* **2002**, *41*, 2760.
- (23) Levin, M. D.; Stang, P. J. *J. Am. Chem. Soc.* **2000**, *122*, 7428.
- (24) Umemoto, K.; Yamaguchi, K.; Fujita, M. *J. Am. Chem. Soc.* **2000**, *122*, 7150.
- (25) Sakamoto, S.; Fujita, M.; Kim, K.; Yamaguchi, K. *Tetrahedron*, **2000**, *56*, 955.