ORGANIC LETTERS

2006
Vol. 8, No. 18
3991−3994

Self-Assembly of Three-Dimensional M_3L_2 Cages via a New Flexible Organometallic Clip

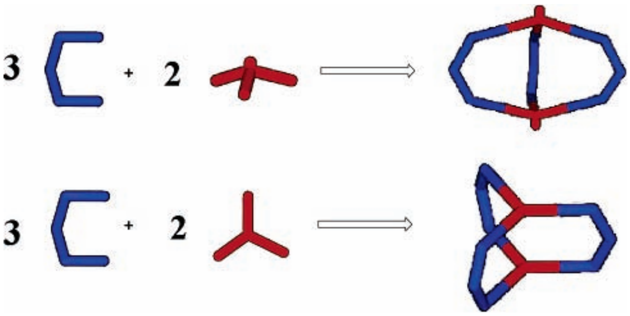
Hai-Bo Yang, Koushik Ghosh, Neeladri Das, and Peter J. Stang*

Department of Chemistry, University of Utah, 315 South 1400 East, RM 2020,
Salt Lake City, Utah 84112

stang@chem.utah.edu

Received June 14, 2006

ABSTRACT



The simple combination of tritopic pyridine donor linkers with a new flexible acceptor "clip" in a 2:3 stoichiometric ratio generates three-dimensional M_3L_2 cages which possess large cavities in essentially quantitative yields.

The protein coats of most viruses possess an icosahedral or dodecahedral shape.[1,2] Mimicking these biological processes intrigues and inspires people to fabricate elaborate three-dimensional (3D) architectures.[3−6] Among various strategies to build 3D cages having well-defined cavities, coordination-driven self-assembly has proven to be a highly effective approach.[7−12] Recently, a large number of 3D cages with potential applications in host−guest chemistry[13−17] and catalysis[18−20] have been reported. Among these elegant 3D supramolecular structures, M_3L_2-type cages[21−26] represent the

---

(1) Horne, R. W. *Virus Structure*; Academic Press: New York, 1974.

(2) Cann, A. J. *Principles of Molecular Virology*; Academic Press: San Diego, 1993; pp 1−234.

(3) Conn, M. M.; Rebek, J., Jr. *Chem. Rev.* **1997**, *97*, 1647−1668.

(4) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853−908.

(5) Seidel, S. R.; Stang, P. J. *Acc. Chem. Res.* **2002**, *35*, 972−983.

(6) Fujita, M.; Tominaga, M.; Hori, A.; Therrien, B. *Acc. Chem. Res.* **2005**, *38*, 371−380.

(7) Fujita, M. *Chem. Soc. Rev.* **1998**, *6*, 417−425.

(8) Caulder, D. L.; Raymond, K. N. *Acc. Chem. Res.* **1999**, *32*, 975−982.

(9) Holliday, B. J.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 2022−2043.

(10) Cotton, F. A.; Lin, C.; Murillo, C. A. *Acc. Chem. Res.* **2001**, *34*, 759−771.

(11) Fujita, M.; Umemoto, K.; Yoshizawa, M.; Fujita, N.; Kusukawa, T.; Biradha, K. *Chem. Commun.* **2001**, 509−518.

(12) Moon, D.; Kang, S.; Park, J.; Lee, K.; John, R. P.; Won, H.; Seong, G. H.; Kim, Y. S.; Kim, G. H.; Rhee, H.; Lah, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 3530−3531.

(13) Kusukawa, T.; Fujita, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 3142−3144.

(14) Ikeda, A.; Udzu, H.; Zhong, Z.; Shinkai, S.; Sakamoto, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **2001**, *123*, 3872−3877.

(15) Kuehl, C. J.; Kryschenko, Y. K.; Radhakrishnan, U.; Seidel, S. R.; Huang, S. D.; Stang, P. J. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4932−4936.

(16) Davis, A. V.; Raymond, K. N. *J. Am. Chem. Soc.* **2005**, *127*, 7912−7919.

(17) Crowley, D. J.; Gosche, J. A.; Bosnich, B. *Chem. Commun.* **2003**, 2824−2825.

(18) Fiedler, D.; Leung, D. H.; Bergman, R. G.; Raymond, K. N. *Acc. Chem. Res.* **2005**, *38*, 351−360.

(19) Yoshizawa, M.; Takeyama, Y.; Kusukawa, T.; Fujita, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 1347−1349.

(20) Yoshizawa, M.; Miyagi, S.; Kawano, M.; Ishiguro, K.; Fujita, M. *J. Am. Chem. Soc.* **2004**, *126*, 9172−9173.

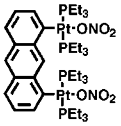
(21) Fujita, M.; Nagao, S.; Ogura, K. *J. Am. Chem. Soc.* **1995**, *117*, 1649−1650.

(22) Ikeda, A.; Yoshimura, M.; Udzu, H.; Fukuhara, C.; Shinkai, S. *J. Am. Chem. Soc.* **1999**, *121*, 4296−4297.

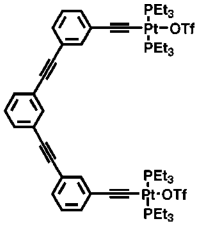
10.1021/ol0614626 CCC: $33.50

simplest constructions and some of them exhibit unusual properties. One noteworthy example is that of a trigonal bipyramidal structure,[22] synthesized from Pd(II) ions and calix[3]arene subunits, that was able to reversibly encapsulate a molecule of C_{60}.

Recently, the self-assembly of a molecular "clip" (**1**) (Figure 1) as an efficient unit into highly symmetric trigonal prismatic cages has been reported by our group.[15,23,24] X-ray crystallography of **1** showed that this linker possesses the necessary two labile coordination sites directed into a parallel arrangement, like a molecular clip.[27] The distance between the two Pt centers in **1** is 5.6 Å. We consider this to be a limitation in size because upon self-assembly with organic donor subunit **8a** the cavity of the resulting 3D cage is small and can accommodate only one nitrate anion. Hence, it is important to design and synthesize a new molecular clip with a larger Pt−Pt distance so that the new D_{3h}-cages based on a bigger clip would have larger cavities.



1



7

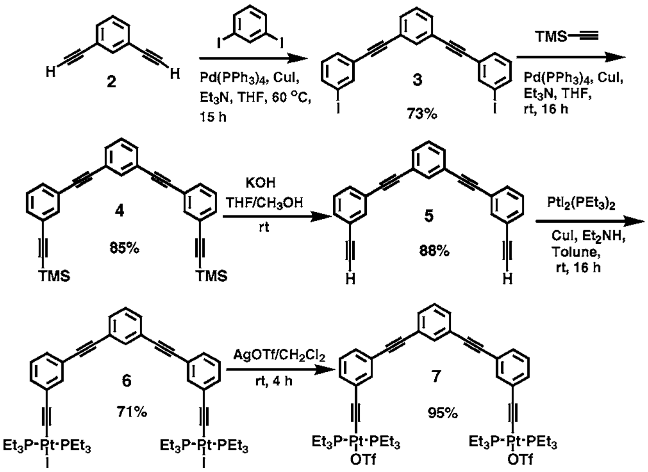
Figure 1. Structures of clips **1** and **7**.

In recent years, the design of oligomeric and polymeric transition-metal complexes containing σ-bonded acetylene units has received considerable attention because of significant variation in their physical properties compared to conjugated organic oligomers and polymers.[28−32] In this area, the diethynylbenzene unit ($-C\equiv CC_6H_4C\equiv C-$) has proven to be a very useful tecton to build oligomeric and polymeric materials with potential applications in the field of molecular-scale electronic devices.[33−38]

Herein, we report the synthesis of a new molecular clip (**7**) (Figure 1) with multiple diethynylbenzene units and its use in the self-assembly of several nanoscalar cages, with pyridine-based tritopic donor ligands, resulting in a bigger cavity. Because these new cages possess larger cavities, they may provide some interesting applications in host−guest chemistry. Likewise, the presence of multiple diethynylbenzene units may provide these 3D cages with new and interesting electronic and photonic properties. The structures of these 3D supramolecular cages were characterized by multinuclear NMR (^1H and ^{31}P), ESI/mass spectrometry, and elemental analysis.

The synthesis of linker **7** is very conveniently realized in five steps from the commercially available 1,3-diethynylbenzene (Scheme 1). The Sonogashira coupling reaction of 1,3-diethynylbenzene with 4 equiv of 1,3-diiodobenzene in a mixture of THF and triethylamine generated 1,3-bis(1-iodo-3-ethynylphenyl)benzene **3**, in the presence of cuprous iodide/Pd(0) catalysts, in good yield. 1,3-Bis(1,3-diethynylphenyl)benzene **5** was synthesized by the coupling reaction of compound **3** with (trimethylsilyl)acetylene under the same conditions as those in step 1, followed by deprotection with KOH in a mixture of methanol and THF. Compound **5** was then reacted with 4 equiv of *trans*-$PtI_2(Et_3)_2$ to give diiodometal complex **6**, as reported in the literature.[39] Subsequent halogen abstraction with AgOTf resulted in the isolation of the bistriflate salt **7** in high yield.

Scheme 1. Synthesis of Acceptor Clip **7**



This diplatinum linker **7** displayed a singlet at 24.7 ppm accompanied by concomitant ^{195}Pt satellites. Attempts to grow single crystals for X-ray diffraction studies of **7** failed,

---

(23) Schweiger, M.; Seidel, S. R.; Schmitz, M.; Stang, P. J. *Org. Lett.* **2000**, *2*, 1255−1257.

(24) Kuehl, C. J.; Yamamoto, T.; Seidel, S. R.; Stang, P. J. *Org. Lett.* **2002**, *4*, 913−915.

(25) Kryschenko, Y. K.; Seidel, S. R.; Muddiman, D. C.; Nepomuceno, A. I.; Stang, P. J. *J. Am. Chem. Soc.* **2003**, *125*, 9647−9652.

(26) Kim, D.; Paek, J. H.; Jun, M.-J.; Lee, J. Y.; Kang, S. O.; Ko, J. *Inorg. Chem.* **2005**, *44*, 7886−7894.

(27) Kuehl, C. J.; Huang, S. D.; Stang, P. J. *J. Am. Chem. Soc.* **2001**, *123*, 9634−9641.

(28) Paul, F.; Lapinte, C. *Coord. Chem. Rev.* **1998**, *178−180*, 431−509.

(29) Ziessel, R.; Hissler, M.; El-ghayoury, A.; Harriman, A. *Coord. Chem. Rev.* **1998**, *178−180*, 1251−1298.

(30) Nguyen, P.; Gómez-Elipe, P.; Manners, I. *Chem. Rev.* **1999**, *99*, 1515−1548.

(31) Dembinski, R.; Bartik, T.; Bartik, B.; Jaeger, M.; Gladysz, J. A. *J. Am. Chem. Soc.* **2000**, *122*, 810−822.

(32) Long, N. J.; Williams, C. K. *Angew. Chem., Int. Ed.* **2003**, *42*, 2586−2617.

(33) Werner, H.; Bachmann P.; Martin, M. *Can. J. Chem.* **2001**, *79*, 519−524.

(34) John, K. D.; Hopkins, M. D. *Chem. Commun.* **1999**, 589−590.

(35) Werner, H.; Bachmann, P.; Laubender, M.; Gevert, O. *Eur. J. Inorg. Chem.* **1998**, 1217−1224.

(36) Wong, W.-Y.; Wong, C.-K.; Lu, G.-L.; Lee, A. W.-M.; Cheah, K.-W.; Shi, J.-X. *Macromolecules* **2003**, *36*, 983−990.

(37) Berenguer, J. R.; Bernechea, M.; Fornies, J.; Lalinde, E.; Torroba, J. *Organometallics* **2005**, *24*, 431−438.

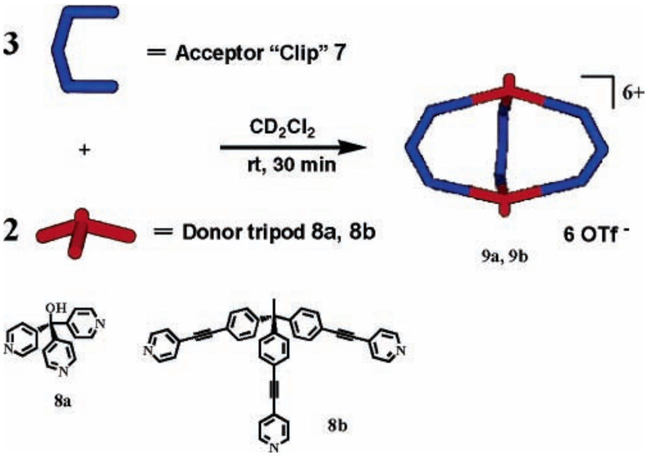
(38) Vicente, J.; Chicote, M.-T.; Alvarez-Falcon, M. M.; Jones, P. G. *Organometallics* **2005**, *24*, 2764−2772.

(39) Leininger, S.; Stang, P. J.; Huang, S. *Organometallics* **1998**, *17*, 3981−3987.

so the distance between the two Pt centers (14.45 Å) was estimated using MM2 force-field stimulations. There are two significant differences between **1** and **7**. First, the distance between the two Pt centers is larger in **7** compared to that in **1**. Second, the clip **1** is rigid and the dihedral angle between the two Pt centers is 0°, while the clip **7** is quite flexible. The two Pt centers of **7** are able to adopt any dihedral angle between 0° and 120° by rotation around the central acetylene bonds. A similar arrangement is observed in polymers of 1,2-bis(3-pyridyl)ethyne and the analogue with relative metal salts.[40,41] Flexible components are generally less predictable during self-assembly and have a tendency to generate catenanes, helicates, or oligomeric products.[42−46] Hence, there are fewer examples of assemblies, especially 3D cages, derived from flexible building blocks.[12,21,47,48] Herein, we report the facile self-assembly of three-dimensional M_3L_2 cages via the flexible organometallic clip **7**.

3D cages **9a** and **9b** can be prepared by combination of acceptor clip **7** and the tetrahedral donor tripods **8a** and **8b** in a 3:2 ratio, respectively (Scheme 2). The self-assembly of the 3D cages can be verified by ^{31}P{^{1}H} and ^{1}H NMR. The ^{31}P spectrum of each cage displayed a sharp singlet (ca. 18.5 ppm, **9a**; 16.0 ppm, **9b**) shifted upfield from the starting platinum donor **7** by 6.2 and 8.7 ppm, respectively, which suggests the formation of a discrete, highly symmetric assembly. This change, as well as the decrease in coupling of the flanking ^{195}Pt satellites ($\Delta^1 J_{\mathrm{PPt}}$ = ca. −75 Hz, **9a**; $\Delta^1 J_{\mathrm{PPt}}$ = ca. −60 Hz, **9b**), is consistent with back-donation from the platinum atoms. In the ^{1}H NMR, the β-protons displayed a more dramatic downfield shift (0.4−0.6 ppm) with respect to **8**, and the α-protons shifted only slightly (0.1−0.2 ppm).

Scheme 2. Self-Assembly of 3D Cages **9a** and **9b**



The structures of the 3D cages **9a** and **9b** have also been confirmed by ESI/MS and elemental analysis. The ESI/MS peaks of cages **9a** and **9b** (Figure 2) are attributable to the loss of triflate counterions $[M - 3OTf]^{3+}$ (m/z = 1511.4, **9a**; m/z = 1709.6, **9b**) and $[M - 4OTf]^{4+}$(m/z = 1096.3, **9a**; m/z = 1245.0, **9b**), where M represents the intact assemblies. These peaks were isotopically resolved, and they agree very well with the theoretical distribution as shown in Figure 2.

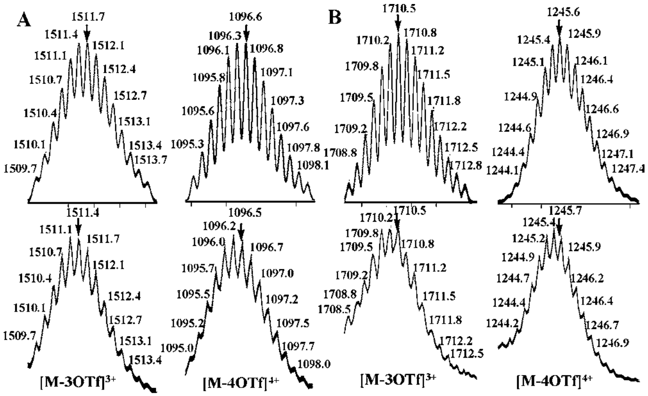
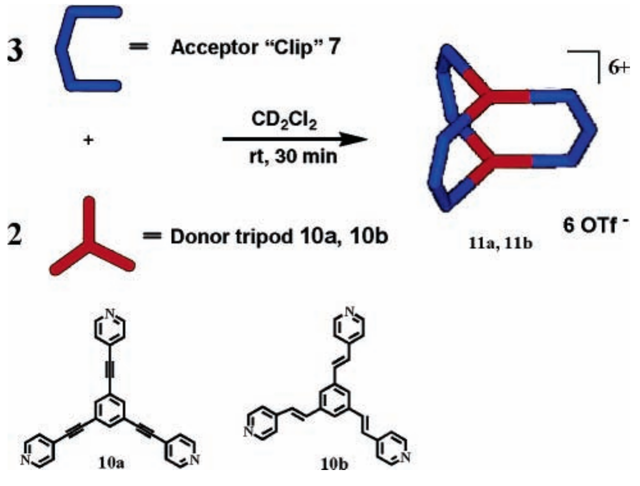


Figure 2. Calculated (top) and experimental (bottom) ESI/MS spectra of 3D cages **9a** (A) and **9b** (B).

When clip **7** was reacted with the planar tripod donors **10a** and **10b**, respectively, in CD_2Cl_2 at room temperature, different kinds of 3D cages **11a** and **11b** were formed (Scheme 3). ^{31}P{^{1}H} NMR analysis of the reaction mixture

Scheme 3. Self-Assembly of 3D Cages **11a** and **11b**



---

(40) Zaman, M. B.; Smith, M. D.; Ciurtin, D. M.; Zur Loye, H. C. *Inorg. Chem.* **2002**, *41*, 4895−4903.

(41) Zaman, M. B.; Udachin, K.; Akhtaruzzaman, M.; Yamashita, Y.; Ripmeester, J. A. *Chem. Commun.* **2002**, 2322−2323.

(42) Fujita, M.; Ibukuro, F.; Seki, H.; Kamo, O.; Imanari, M.; Ogura, K. *J. Am. Chem. Soc.* **1996**, *118*, 899−900.

(43) Fujita, M.; Aoyagi, M.; Ibukuro, F.; Ogura, K.; Yamaguchi, K. *J. Am. Chem. Soc.* **1998**, *120*, 611−612.

(44) Hiraoka, S.; Fujita, M. *J. Am. Chem. Soc.* **1999**, *121*, 10239−10240.

(45) Fujita, M.; Kwon, Y. J.; Sasaki, O.; Yamaguchi, K.; Ogura, K. *J. Am. Chem. Soc.* **1995**, *117*, 7287−7288.

(46) Bowyer, P. K.; Cook, V. C.; Naseri, N. G.; Gugger, P. A.; Rae, D. A.; Swiegers, G. F.; Willis, A. C.; Zank, J.; Wild, S. B. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4877−4882.

(47) Mukherjee, P. S.; Das, N.; Stang, P. J. *J. Org. Chem.* **2004**, *69*, 3526−3529.

(48) Chi, K.-W.; Addicott, C.; Kryschenko, Y. K.; Stang, P. J. *J. Org. Chem.* **2004**, *69*, 964−966.

is consistent with the formation of a single, highly symmetrical species by the appearance of a sharp singlet (ca. 18.4 ppm, **10a**; 16.2 ppm, **10b**) with concomitant ^{195}Pt satellites, shifted upfield by 6.3 and 8.5 ppm, respectively, as compared to **7**. As expected, a decrease in coupling of the flanking ^{195}Pt satellites was also observed ($\Delta^1J_{\mathrm{PPt}} = -$ 64 Hz, **10a**; $\Delta^1J_{\mathrm{PPt}} = -$ 45 Hz, **10b**). As expected, in the ^{1}H NMR spectrum of cages **11a** and **11b**, the β-hydrogen nuclei of the pyridine rings exhibited 0.4−0.6 ppm downfield shifts.

The ESI/MS spectra of **11a** and **11b** exhibited characteristics very similar to those of the spectra of **9a** and **9b** (Figure 3). The ESI/MS spectra showed two charged states at m/z = 1589.6 (**11a**) and m/z = 1593.6 (**11b**) and m/z = 1154.8 (**11a**) and m/z = 1157.9 (**11b**), corresponding to the [M − 3OTf]$^{3+}$ and [M − 4OTf]$^{4+}$ species, respectively, and their isotopic resolution is in excellent agreement with the theoretical distribution.

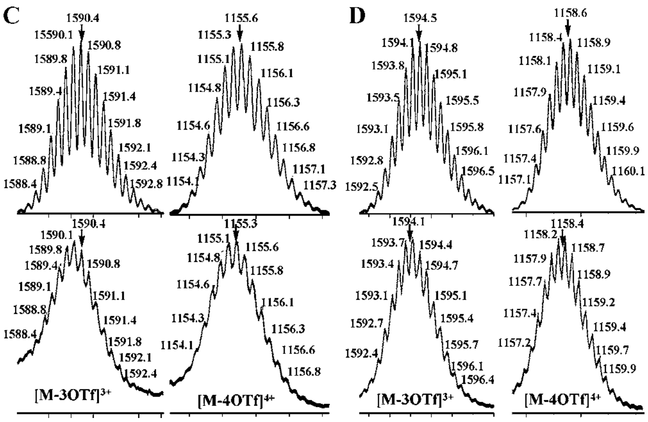


Figure 3. Calculated (top) and experimental (bottom) ESI/MS spectra of 3D cages **11a** (C) and **11b** (D).

Unfortunately, all attempts to grow X-ray quality single crystals failed. Hence, a simple molecular model was obtained using MM2 force-field simulation to visualize the size and shape of the 3D cage **9a** (Figure 4). The diameter of the inner cavity of this cage (**9a**) is about 3.2 nm, whereas the same for the cage derived from the tritopic linker **8a** and clip **1** is ca. 2.0 nm.[15] This suggests that our cage **9a** possesses a bigger cavity, and this can be attributed to the larger size of our newly designed molecular clip **7**.

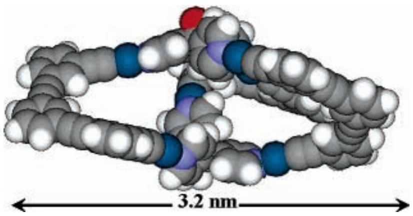


Figure 4. Space-filling model of 3D cage **9a** optimized with the MM2 force-field simulation (triethylphosphine ligands have been removed after the optimization for clarity).

In summary, we report the design of supramolecular cages **9a**, **9b**, **11a**, and **11b** based on a flexble clip **7** with multiple diethynylbenzene units as a modular subunit synthesized by means of coordination-driven self-assembly. This enriches the library of three-dimensional architectures. Despite its ability to form oligomeric products considering its flexible nature, clip **7** prefers to self-assemble into closed, discrete ensembles. This provides further evidence of thermodynamic control favoring formation of discrete entities over oligomeric networks. The structure of these 3D cages which possess large cavities was established by multinuclear NMR and ESI/MS spectral data along with elemental analysis.

Acknowledgment. P.J.S. thanks the NIH (GM-57052) and the NSF (CHE-0306720) for financial support. We also thank the NSF (CHE-9708413) and the University of Utah Institutional Funds Committee for funding the Micromass Quattro II mass spectrometer.

Supporting Information Available: Experimental procedures and characterization data including multinuclear NMR and ESI/MS spectra of all 3D cages. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0614626