Kinetic Control of Self-Assembly

Pd^{II}-Directed Dynamic Assembly of a Dodecapyridine Ligand into End-Capped and Open Tubes: The Importance of Kinetic Control in Self-Assembly**

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Dynamic assembly deals with two or more self-assembled units, which are on a relatively flat potential energy surface and are interconverted into each other by the re-sorting or reorganization of the component species.[1–3] When dynamic structures have a cavity suitable for recognizing a guest, the predominant assembly of one particular host structure is induced by adding an appropriate guest. Such a guest-induced assembly of a specific host framework is often seen in biological events, and has been actively studied in both hydrogen-bonded and coordination assembly systems.[2] Here we report a unique dynamic assembly where, under a set of identical thermodynamic conditions, the same guest induces the formation of two different assemblies depending on whether the assembly process experiences crystallization or not.

The dynamic assembly discussed here stems from the {(en)Pd^{II}} coordination block **1** (en = 1,2-ethanediamine) and ligand **2**, which has four tripyridine podands on a benzenetetracarboxylate scaffold.[4] In an analogy with the guest-induced assembly of coordination nanotubes obtained from oligo(3,5-pyridine) ligands and Pd units,[5] ligand **2** is expected to yield the mono-end-capped coordination tube $\mathbf{3}^{12+}$ upon complexation with **1** in the presence of an appropriate guest (Scheme 1a).[6] This tube is designed to differentiate between the ends of symmetrical rodlike molecules; namely, the end that is accommodated at the bottom of the tube should show different properties from the other end. We have found that, in addition to expected structure $\mathbf{3}^{12+}$, the complexation of **1** and **2** also gives rise to the double open tube, $\mathbf{4}^{24+}$, in which ligand **2** adopts an extended conformation (Scheme 1b). This open tube is observed only at higher concentrations as a

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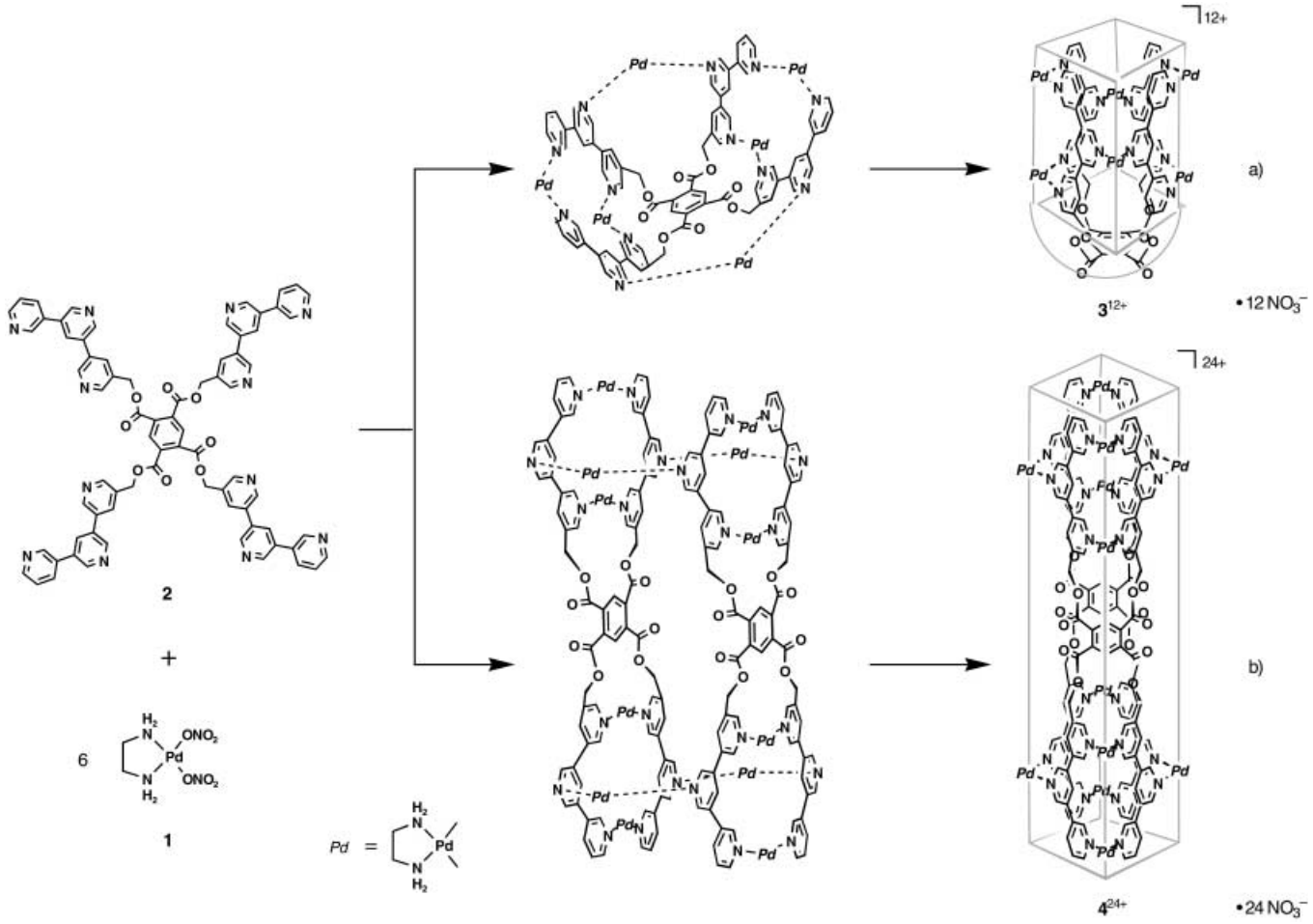

Scheme 1. Self-assembly of a) the mono-end-capped tube $\mathbf{3}^{12+}$, and b) the double open tube $\mathbf{4}^{24+}$. The template molecules necessary for the formation of $\mathbf{3}^{12+}$ and $\mathbf{4}^{24+}$ are omitted for clarity.

minor component, but is isolated in a pure form through slow crystallization. Interestingly, once isolated, $\mathbf{4}^{24+}$ is not converted into $\mathbf{3}^{12+}$ at lower concentrations, which indicates that both structures are kinetically trapped at local minima of the potential surface. Accordingly, we discuss here the self-assembly and the host–guest behavior of the end-capped tube $\mathbf{3}^{12+}$ and the open tube $\mathbf{4}^{24+}$, as well as the importance of kinetic effects in their self-assembly processes.

The quantitative assembly of **2** into end-capped tube $\mathbf{3}^{12+}$ was, in fact, accomplished by the template effect of rodlike guests such as 4,4′-dimethylbiphenyl (**5**).[7] Without the template, the complexation of ligand **2** with [(en)Pd(NO_3)$_2$] (**1**) in D_2O resulted in a complex mixture (Figure 1a). The addition of **5** to the solution, however, induced the assembly of a single product within 3 h at 70 °C (Figure 1b). In the tube structure, the side arms of **2** are equivalent whereas the methylene protons on each side arm are diastereotopic and thus observed as an AB quartet. In addition to satisfactory NMR, the formation of complex ion $\mathbf{3}^{12+}$ was strongly supported by cold-spray ionization mass spectrometry (CSI-MS).[8,9]

Observation by ^{1}H NMR spectroscopy yielded some structural aspects of the inclusion complex. As expected, the

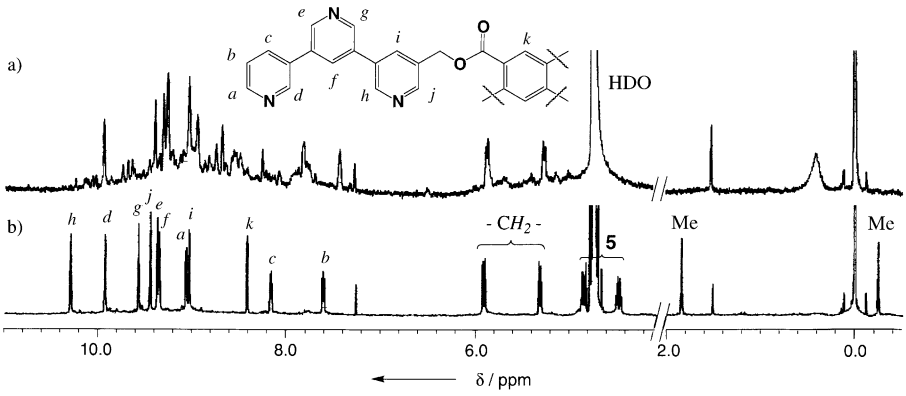

Figure 1. ^{1}H NMR spectroscopic observation of the guest-templated formation of $\mathbf{5}\subset\mathbf{3}^{12+}$ (500 MHz, D_2O, 25 °C, TMS). a) An oligomeric mixture obtained from **2** (1.7 μmol) and [(en)Pd(NO_3)$_2$] (10.2 μmol) in D_2O (0.8 mL); b) the $\mathbf{5}\subset\mathbf{3}^{12+}$ complex assembled after the addition of **5** (1.7 μmol).

two methyl groups of guest **5** accommodated in $\mathbf{3}^{12+}$ were clearly discriminated, and were observed at $\delta = -0.25$ and 1.83 ppm (Figure 1b). The significant upfield shift of one methyl group (approximately −2.6 ppm shifted from ordinary chemical-shift region) suggests that this methyl group is located on the benzene scaffold and surrounded by four pyridine rings. Below 60 °C, these two methyl resonances did not coalesce, which indicates that the guest is strongly bound within the deep cavity of $\mathbf{3}^{12+}$, and the flipping of the guest along its long axis is suppressed.[10] Aromatic protons of **5** were also shifted upfield, being observed at $\delta = 4.47$–4.86 ppm.

Asymmetric guests, such as sodium biphenylcarboxylate ($Na^+\mathbf{6}^-$) could be efficiently accommodated in a unidirectional fashion.[7] Only one isomer was formed in which the hydrophobic biphenyl group was included deep within the tube and the hydrophilic carboxylate group was exposed outside, as indicated by ^{1}H NMR spectroscopy (Figure 2a). Interestingly, disodium biphenyldicarboxylate ($2Na^+\mathbf{7}^{2-}$), which was bound in an open tube in our previous study,[5] was not included in $\mathbf{3}^{12+}$, which shows that the end-capped site of $\mathbf{3}^{12+}$ provides an efficient hydrophobic pocket that cannot bind the hydrophilic portion of the guest.

The self-assembly of inclusion complex $\mathbf{6}^-\subset\mathbf{3}^{12+}$ was concomitant with the formation of a minor component at high concentrations ($[\mathbf{2}]_0 > 8$ mM; Figure 2b). Fortunately, this minor product was isolated as single crystals by slow evaporation (over more than two weeks) of the solution. X-ray crystallographic analysis showed that this product ($\mathbf{4}^{24+}$) is a double open tube, which consists of two molecules of ligand **2** that are held together by twelve {(en)Pd} units (Figure 3).[7,11] Open tube $\mathbf{4}^{24+}$ accommodates two molecules of $\mathbf{6}^-$, each of which is oriented so that its carboxylate group is exposed outside the tube. An important feature is that the 16-component self-assembled structure (two ligands, twelve metals, and two guests) possesses a 3.0 nm molecular tube, which is one of the longest among those structurally defined by crystallography. The biphenyl moiety is surrounded by a hydrophobic framework through efficient π–π and CH–π interactions. The elemental analysis was consistent with a formula of $(Na\mathbf{6})_2\subset\mathbf{4}(NO_3)_{24}\cdot 45\,H_2O$.

The stability of the isolated $(\mathbf{6}^-)_2\subset\mathbf{4}^{24+}$ complex requires special attention. When crystals of $(\mathbf{6}^-)_2\subset\mathbf{4}^{24+}$ were dissolved in D_2O at room temperature, we observed the $(\mathbf{6}^-)_2\subset\mathbf{4}^{24+}$ complex in a pure form (Figure 2c) although the $\mathbf{6}^-\subset\mathbf{3}^{12+}$ complex was the major product before isolation. More surprisingly, the $(\mathbf{6}^-)_2\subset\mathbf{4}^{24+}$ complex remained unchanged in solution, even after one month. These results clearly show that the $\mathbf{6}^-\subset\mathbf{3}^{12+}$ and $(\mathbf{6}^-)_2\subset\mathbf{4}^{24+}$ complexes are not in equilibrium despite the labile nature of Pd^{II}–pyridine coordination bonds. Slow conversion to the $(\mathbf{6}^-)_2\subset\mathbf{4}^{24+}$ complex only occurs when $\mathbf{6}^-\subset\mathbf{3}^{12+}$ is crystallized at high concentrations.

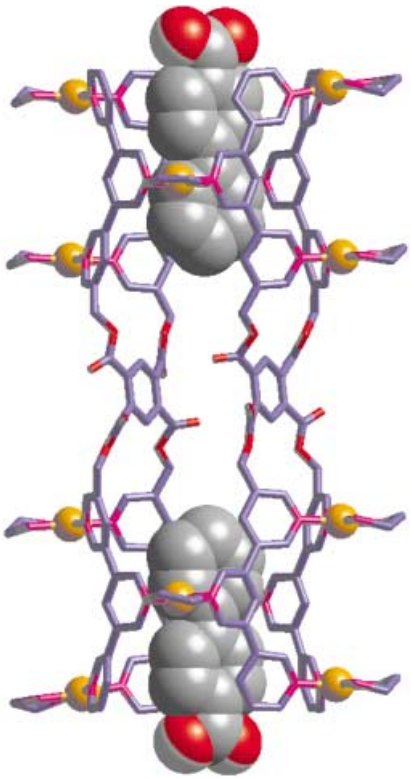

Figure 3. Crystal structure of $(\mathbf{6}^-)_2\subset\mathbf{4}^{24+}$. For clarity, H atoms, water molecules, and NO_3^- ions are omitted.

It is noteworthy that two different assemblies ($\mathbf{6}^-\subset\mathbf{3}^{12+}$ and $(\mathbf{6}^-)_2\subset\mathbf{4}^{24+}$) were obtained under a set of identical thermodynamic conditions, dependent only on whether the assembly process involved crystallization or not. We thus

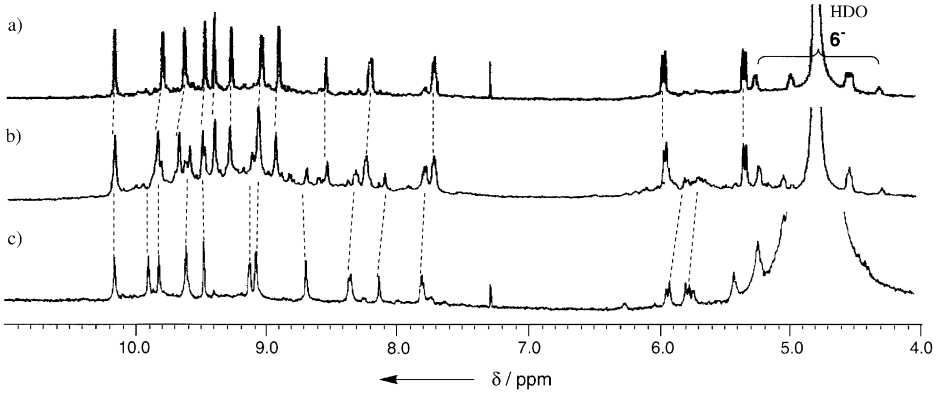

Figure 2. ^{1}H NMR spectra showing the conversion of $\mathbf{6}^-\subset\mathbf{3}^{12+}$ into $(\mathbf{6}^-)_2\subset\mathbf{4}^{24+}$ (500 MHz, D_2O, 25 °C, TMS). a) $[\mathbf{2}]_0 = 2.1$ mM; b) $[\mathbf{2}]_0 = 8.5$ mM; c) complex $(\mathbf{6}^-)_2\subset\mathbf{4}^{24+}$ isolated as crystals.

suggest the following: a) Complexes $\mathbf{6}^{-}\subset\mathbf{3}^{12+}$ and $(\mathbf{6}^{-})_2\subset\mathbf{4}^{24+}$, which are sustained by 12 and 24 Pd^{II}–pyridine interactions, respectively, are not thermodynamically trapped, but rather kinetically trapped structures; b) complex $\mathbf{6}^{-}\subset\mathbf{3}^{12+}$ is kinetically formed and trapped through intramolecular complexation, although the more stable $(\mathbf{6}^{-})_2\subset\mathbf{4}^{24+}$ complex also exists on a potential energy surface; c) the interconversion of $\mathbf{6}^{-}\subset\mathbf{3}^{12+}$ into $(\mathbf{6}^{-})_2\subset\mathbf{4}^{24+}$ does not occur at low concentrations, but is slowly promoted at high concentrations, and much more strongly facilitated by removing the $(\mathbf{6}^{-})_2\subset\mathbf{4}^{24+}$ complex through crystallization.

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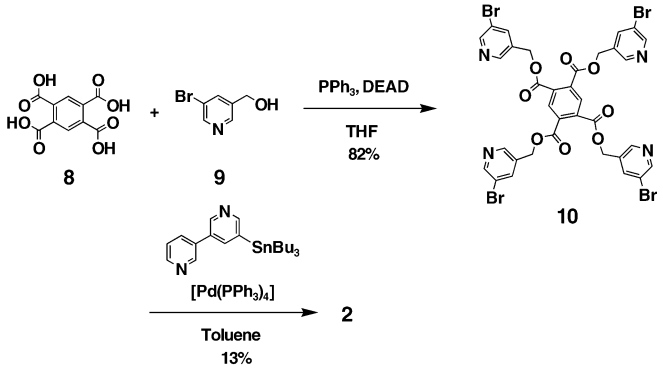
[1] For reviews: a) I. Huc, J.-M. Lehn, *Proc. Natl. Acad. Sci. USA* **1997**, *94*, 2106–2110; b) J.-M. Lehn, *Chem. Eur. J.* **1999**, *5*, 2455–2463; c) G. R. L. Cousins, S.-A. Poulsen, J. K. M. Sanders, *Curr. Opin. Chem. Biol.* **2000**, *4*, 270–279; d) S. J. Rowan, S. J. Cantrill, G. R. L. Cousins, J. K. M. Sanders, J. F. Stoddart, *Angew. Chem.* **2002**, *114*, 938–993; *Angew. Chem. Int. Ed.* **2002**, *41*, 898–952.

[2] a) M. Fujita, S. Nagao, K. Ogura, *J. Am. Chem. Soc.* **1995**, *117*, 1649–1650; b) B. Hasenknopf, J.-M. Lehn, N. Boumediene, A. Dupont-Gervais, A. V. Dorsselaer, B. Kneisel, D. Fenske, *J. Am. Chem. Soc.* **1997**, *119*, 10956–10962; c) B. Klekota, M. H. Hammond, B. L. Miller, *Tetrahedron Lett.* **1997**, *38*, 8639–8642; d) M. Scherer, D. L. Caulder, D. W. Johnson, K. N. Raymond, *Angew. Chem.* **1999**, *111*, 1690–1694; *Angew. Chem. Int. Ed.* **1999**, *38*, 1588–1592; e) M. Albrecht, O. Blau, R. Fröhlich, *Chem. Eur. J.* **1999**, *5*, 48–56; f) S. Hiraoka, M. Fujita, *J. Am. Chem. Soc.* **1999**, *121*, 10239–10240; g) Y. Kubota, S. Sakamoto, K. Yamaguchi, M. Fujita, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4854–4856; h) S. Otto, R. L. E. Furlan, J. K. M. Sanders, *Science* **2002**, *297*, 590–593.

[3] a) G. W. Orr, L. J. Barbour, J. L. Atwood, *Science* **1999**, *285*, 1049–1052; b) M. Ziegler, J. J. Miranda, U. N. Andersen, D. W. Johnson, J. A. Leary, K. N. Raymond, *Angew. Chem.* **2001**, *113*, 755–758; *Angew. Chem. Int. Ed.* **2001**, *40*, 733–736; c) S. Hiraoka, T. Yi, M. Shiro, M. Shionoya, *J. Am. Chem. Soc.* **2002**, *124*, 14510–14511; d) C.-Y. Su, Y.-P. Cai, C.-L. Chen, F. Lissner, B.-S. Kang, W. Kaim, *Angew. Chem.* **2002**, *114*, 3519–3523; *Angew. Chem. Int. Ed.* **2002**, *41*, 3371–3375.

[4] Ligand **2** was synthesized as follows: The Mitsunobu esterification of tetracarboxylic acid **8** with alcohol **9** gave tetrabromide precursor **10** (82%), which is subsequently treated with tributyltin bipyridine under the Stille coupling conditions ($[Pd(PPh_3)_4]$ (10 mol%), toluene, reflux) to give **2** in 13% yield.



[5] a) M. Aoyagi, K. Biradha, M. Fujita, *J. Am. Chem. Soc.* **1999**, *121*, 7457–7458; b) M. Aoyagi, S. Tashiro, M. Tominaga, K. Biradha, M. Fujita, *Chem. Commun.* **2002**, 2036–2037; c) M. Tominaga, S. Tashiro, M. Aoyagi, M. Fujita, *Chem. Commun.* **2002**, 2038–2039.

[6] a) I. Tabushi, K. Shimokawa, N. Shimizu, H. Shirakata, K. Fujita, *J. Am. Chem. Soc.* **1976**, *98*, 7855–7856; b) S. Zhao, J. H. T. Luong, *J. Chem. Soc. Chem. Commun.* **1995**, 663–664; c) D. Whang, J. Heo, J. H. Park, K. Kim, *Angew. Chem.* **1998**, *110*, 83–85; *Angew. Chem. Int. Ed.* **1998**, *37*, 78–80; d) T. Heinz, D. M. Rudkevich, J. Rebek, Jr., *Nature* **1998**, *394*, 764–766; e) S. Saito, C. Nuckolls, J. Rebek, Jr., *J. Am. Chem. Soc.* **2000**, *122*, 9628–9630.

[7] For the physical properties of $\mathbf{5}\subset\mathbf{3}^{12+}$, $\mathbf{6}^{-}\subset\mathbf{3}^{12+}$, and $(\mathbf{6}^{-})_2\subset\mathbf{4}^{24+}$, see the Supporting Information.

[8] a) S. Sakamoto, M. Fujita, K. Kim, K. Yamaguchi, *Tetrahedron* **2000**, *56*, 955–964; b) Y. Yamanoi, Y. Sakamoto, T. Kusukawa, M. Fujita, S. Sakamoto, K. Yamaguchi, *J. Am. Chem. Soc.* **2001**, *123*, 980–981.

[9] Complex $\mathbf{3}^{12+}$ was analyzed by CSI-MS to investigate the accommodation of biphenylcarboxylate or naphthalene as a guest. A series of $[M-(NO_3)_n]^{n+}$ peaks were observed. See Supporting Information.

[10] At 80 °C, broad methyl signals were observed indicating that the coalescence temperature was being approached (see the Supporting Information).

[11] Crystal data for $(\mathbf{6}^{-})_2\subset\mathbf{4}^{24+}$ ($C_{202}H_{218}N_{72}O_{119}Pd_{14}$, $M_w = 7048.08$): crystal dimensions $0.40\times0.20\times0.20\ mm^3$, triclinic, $P\bar{1}$, $a = 16.494(4)$, $b = 16.610(4)$, $c = 31.977(8)$ Å, $\alpha = 78.438(5)$, $\beta = 86.281(5)$, $\gamma = 70.333(4)°$, $V = 8082(3)$ Å^3, $Z = 1$, $\rho_{calcd} = 1.438\ mg\,m^{-3}$, $F(000) = 3482$, radiation: $\lambda(Mo_{K\alpha}) = 0.71073$ Å, $T = 113(2)$ K, reflections collected/unique 51758/35688 ($R_{int} = 0.0585$). The structure was solved by direct methods (SHELXL-97) and refined by full-matrix least-squares methods on F^2 with 1658 parameters. $R_1 = 0.1255$ ($I > 2\sigma(I)$), $wR_2 = 0.3444$, GOF = 1.149, max./min. residual density 3.141/−3.798 e Å^{-3}. Several water molecules, nitrate molecules, and 1,2-ethanediamine ligands are disordered. Guest molecules sit on two positions (1:1 ratio) in the cavity of a host molecule. The thermal temperature factors of some disordered groups were constrained. The bond lengths of severely disordered molecules were chemically restrained. CCDC-204999 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).