Surface-Confined Single Molecules: Assembly and Disassembly of Nanosize Coordination Cages on Gold (111)

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Abstract: A cavitand functionalized with four alkylthioether groups at the lower rim, and four tolylpyridine groups on the upper rim is able to bind to a gold surface by its thioether groups, and forms a coordination cage with $[Pd(dppp)(CF_3SO_3)_2]$ by its pyridine groups. The cavitand or the cage complex can be inserted from solution into a self-assembled monolayer (SAM) of 11-mercaptoundecanol on gold. The inserted molecules can be individually detected as they protrude from the SAM by atomic force microscopy (AFM). The cages can be reversibly assembled and disassembled on the gold surface. AFM can distinguish between single cavitand and cage molecules of 2.5 nm and 5.8 nm height, respectively.

Keywords: cage compounds · cavitands · scanning probe microscopy · self-assembly · single-molecule studies

Introduction

Self-assembly, in its various forms, is emerging as a key technology for the formation of two- and three-dimensional structures.[1] The appeal of self-assembly resides in the thermodynamic control of the process, which leads to the exclusive formation of the desired molecular architecture under a given set of conditions. The reversibility of self-assembly conveys interesting properties, such as self-repairing ability and responsiveness to external stimuli. Of the various self-assembly protocols, metal-directed self-assembly is particularly appealing, because of the large number of different structural motifs and bond energies that are available through coordination chemistry.[2] There are relatively few publications that describe the transfer of self-assembly protocols from the solution phase to surfaces.[3] Our groups have recently reported on the attachment of thioether-functionalized coordination cages to gold substrates in micrometer-size patterned self-assembled monolayers (SAMs),[4] which were prepared by soft lithographic techniques.[5] The attachment of single molecular containers able to encapsulate ions and neutral molecules on solid surfaces is attractive for single-molecule addressing.[6]

Here we report on the synthesis of a cavitand, functionalized with four alkylthioether groups at the lower rim, and four tolylpyridine groups at the upper rim. We describe the self-assembly of coordination cages from the cavitands with $[Pd(dppp)(CF_3SO_3)_2]$ both in solution[7] and immobilized on gold surfaces. For the formation of coordination cages on gold, two different strategies leading to homocages and heterocages have been explored. Immobilized homocages result from the direct insertion of cages formed in solution into an SAM of 11-mercaptoundecanol (MU) on gold. Immobilized heterocages result from the insertion of the thioether-footed cavitand into an MU SAM, followed by assembly of cages by complexation of a different cavitand from solution. The insertion and assembly processes were monitored by atomic force microscopy (AFM) by measuring the height of individual cavitands and cages.

Results and Discussion

Synthesis: At the upper rim of cavitand **6** (Scheme 2) there are four phenylpyridine groups as bridging units between the phenolic OHs, and four alkylthioether chains at the lower rim. The presence of four outward oriented phenylpyridine groups is pivotal for cage self-assembly (CSA) by

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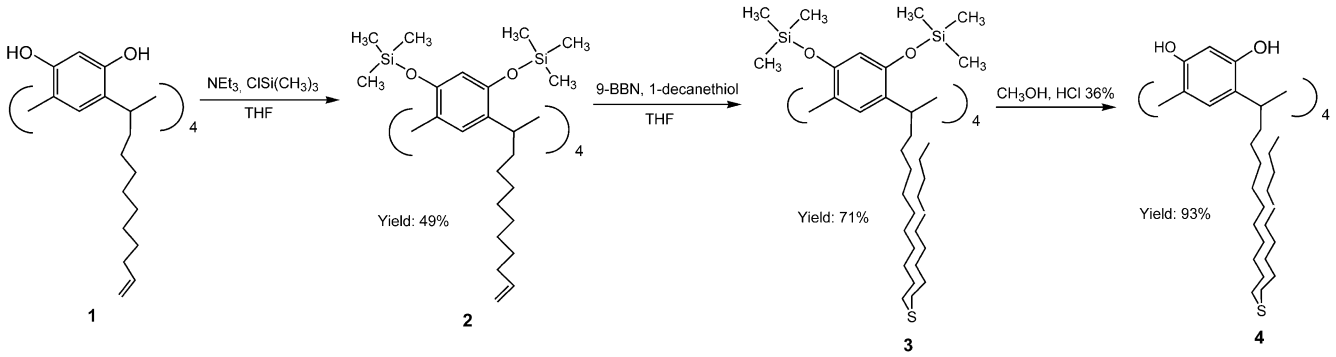
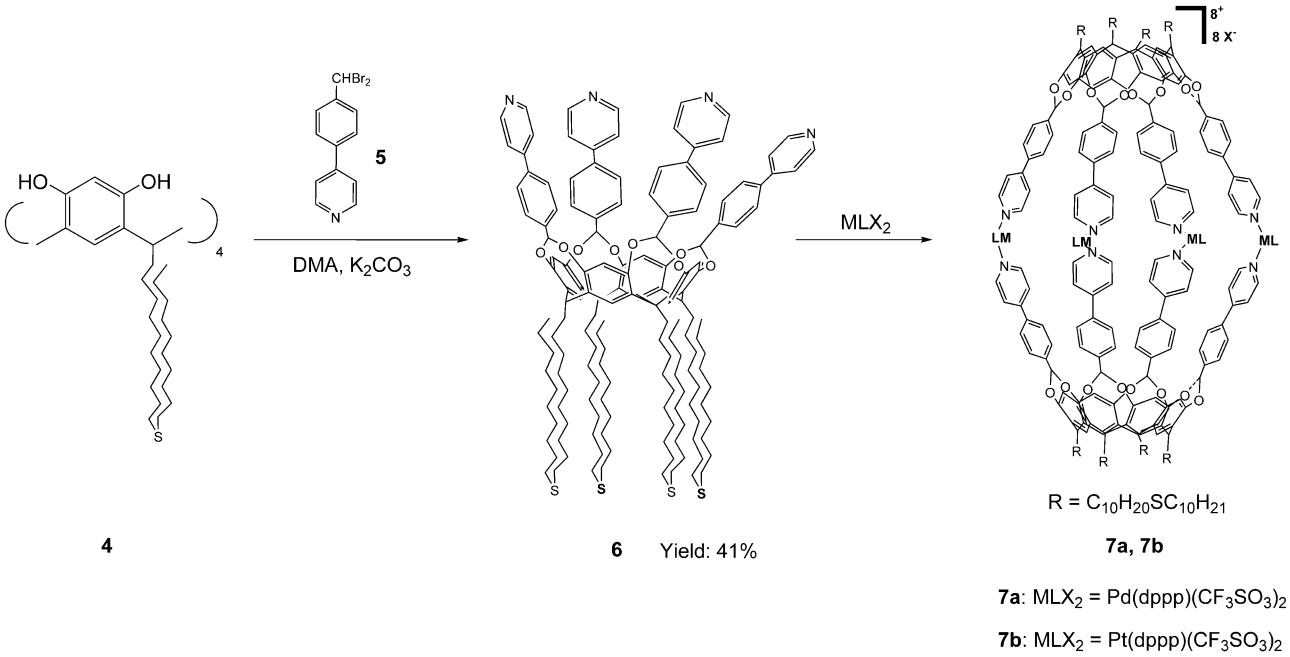


Scheme 1. Protection/deprotection scheme for the synthesis of resorcinarene **4**.



Scheme 2. Synthesis of the cavitand ligand **6,** and self-assembly of nanosize coordination cages **7a** and **7b**.

coordination to Pd or Pt metal precursors,[8] while the four thioether chains at the lower rim are necessary to attach the compound to a gold surface.[9] In order to obtain cavitand **6**, the thioether-footed resorcinarene **4** was synthesized and then bridged with 4,4′-(α,α′-dibromotolyl)pyridine (**5**).

The bridging group **5** was obtained by radical bromination of the methyl group of tolylpyridine,[10] by using *N*-bromosuccinimide (NBS) in the presence of benzoyl peroxide as an initiator. By mixing tolylpyridine, NBS, and benzoyl peroxide in a suitable ratio, the reaction gave 4-(α,α′-dibromotolyl)pyridine as a major product with traces of tribrominated tolylpyridine as a byproduct. The reaction was carried out in the presence of a large amount of radical initiator to prevent attack at the aromatic rings, and to favor the bromination of the methyl group.

The thioether footed resorcinarene **4** was synthesized following a protection/deprotection scheme (Scheme 1).[11] The first step was the protection of the hydroxyl moieties of resorcinarene **1** by trimethylsilane groups to avoid reaction with 9-BBN; this was achieved by using chlorotrimethylsilane as a reagent and triethylamine as a base at room temperature in THF. Resorcinarene **2** was obtained in a 49% yield. The second step was the anti-Markovnikov addition of 1-decanethiol to the double bonds of **2** in presence of a stoichiometric quantity of 9-BBN in THF as a solvent at room temperature. Resorcinarene **3** with four sulfide chains at the lower rim, was obtained in 71% yield. Finally, the silane groups in **3** were removed with HCl (36% in methanol), and the desired resorcinarene **4** was obtained in 32% overall yield starting from **1**. This synthetic procedure represents a general route to thioether-footed cavitands in all cases in which the bridging units at the upper rim are BBN-sensitive.

This molecule was used for the preparation of the phenylpyridine functionalized thioether-footed cavitand (**6**) (*oooo* isomer). The synthesis of this deep-cavity cavitand[12] was performed by bridging the resorcinarene **4** with 4,4′-(α,α′-dibromotolyl)pyridine (**5**) in the presence of K_2CO_3 as a base. The reaction gave the desired *oooo* isomer (41% yield) as the only product with four tolylpyridyl groups

pointing outwards from the cavity (Scheme 2).[13] The stereochemical control of the reaction is assured by the bulkiness of the bridging units, which can be accommodated only in the outward orientation.

General procedure for the self-assembly of the thioether-functionalized coordination cages 7a and 7b: Before engaging in surface-confined self-assembly, cage self-assembly (CSA) of cavitand **6** was tested in solution with $[M(dppp)(OTf)_2]$ (M = Pt, Pd) as metal precursors to verify that the thioether chains do not interfere with the cage formation by complexing the metal centres (Figure 1). The self-assembly of cages **7a** and **7b** was monitored by ^{1}H NMR spectroscopy (Figure 1). Mixing the two components in a 1:2 molar ratio at room temperature in acetone gave cages **7a** and **7b**, which were obtained in quantitative yields. Therefore, the thioether chains at the lower rim do not interfere with CSA. In all cases ^{1}H NMR spectra clearly showed the formation of a new set of signals indicative of the presence of only one highly symmetric compound (D_{2h} symmetry). The signals corresponding to the CH_2 α of sulfur in the thioether chains, were not shifted by the addition of the metal complex to a solution of cavitand **6**. The only shifts recorded are those of the hydrogens, which correspond to the phenylpyridine groups, which are shifted downfield as a consequence of the coordination to the metal. The coordination cage was the only product observed and intermediates in the self-assembly process were not detected. Addition of one equivalent of $[Pt(dppp)(CF_3SO_3)_2]$ to a solution of cavitand **6** (spectrum a) in $[D_6]$acetone (1:1 ratio) showed that the only species present in solution are the free cavitand and the cage (labeled by colored dots); there was no evidence of oligomers or partial complexation products (spectrum b). When a second equivalent of metal complex was added to the same solution (final ratio 1:2 ligand/metal complex), the cage was the only product present in solution (spectrum c). This is consistent with the rapid formation of the thermodynamically favored cage with respect to other species. ^{31}P NMR spectra exhibited a sharp singlet, with appropriate Pt coupling satellites for cage **7b**, which indicates that all the DPPP phosphorus atoms are equivalent; this therefore confirms the symmetry of the cage. Further evidence of cage formation was given by MALDI analysis, which contained a prominent peak at $m/z = [M-CF_3SO_3^-]^+$ for both cages.

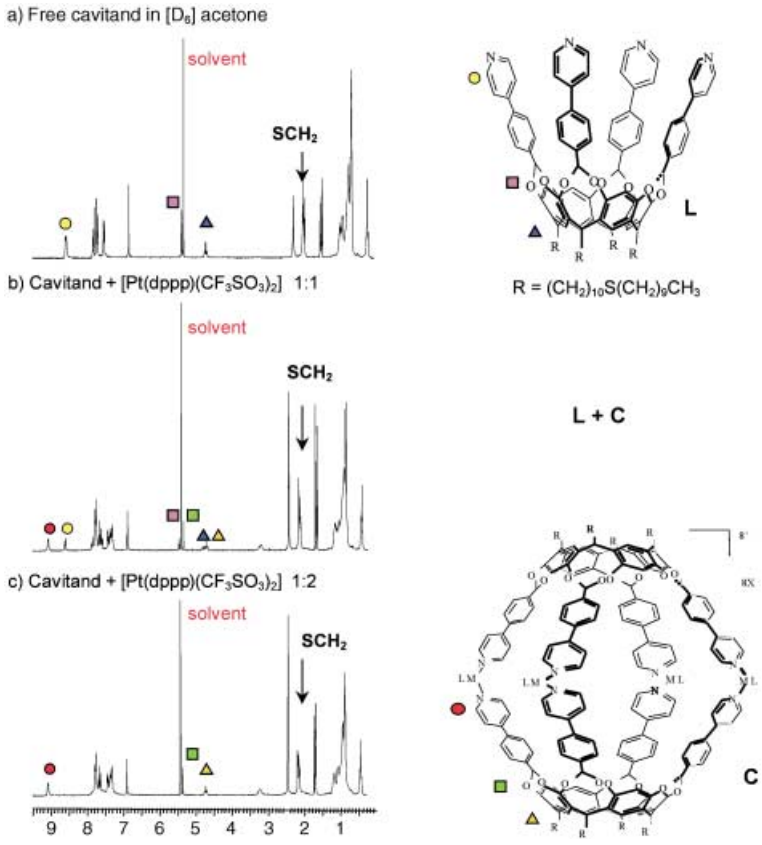


Figure 1. Self-assembly of cage **7b** in solution monitored by ^{1}H NMR spectroscopy.

Surface assembly: Having established CSA of **7a and 7b** in solution, we extended this protocol to surface-directed CSA. Two different approaches have been followed. First, the direct insertion of the preformed cage **7a** into a monolayer of thiols (homocages insertion), and second the insertion of cavitand **6** into a monolayer of thiols followed by cage self-assembly on the preformed SAM (surface self-assembly of heterocages). Insertion or assembly of immobilized individual cages was monitored by tapping-mode atomic force microscopy (TM-AFM). Self-assembled monolayers of MU were prepared on flame-annealed gold surfaces. These hydroxy-terminated SAMs are favored over methyl-terminated alkylthiolate SAMs, because they cause less physisorption of cavitand molecules.[4] The monolayers were analyzed by TM-AFM before being used for insertion experiments to ensure that no undefined features were present on the surface. Insertion experiments were performed according to procedures previously used in our groups,[14] although solvents and insertion times had to be adjusted for the adsorbate molecules. The insertion of molecules occurs at random, and this method is an excellent and easy strategy to perform scanning probe microscopy on immobilized single molecules and assemblies.[15]

In order to verify the correctness of the experimental data, X-ray data from alkyl-footed cavitands were used to

estimate the height of cavitand **6** (2.5 nm) and cage **7a** (5.8 nm) considering the contribution of the thioether chains in a backfolded conformation to the total length (see Table 1).[8] The MU molecules in the SAM are tilted to optimize the van der Waals interactions and the packing stability. The thickness of the MU monolayer is about 0.8 nm, due to this tilted orientation.[16] On the basis of these considerations, **7a** is expected to protrude beyond the OH-terminated surface by at least 5.0 nm, and about 1.7 nm for **6**.

Table 1. Theoretical and experimental heights of cavitand and cages.[a]

Cavitand and cages	Height from X-ray data[8]	Protrusion height[b]	Measured height (AFM)
cavitand **6**	2.5	1.7	1.87 ± 0.18
homocage **7a**	5.8[c]	5.0	5.27 ± 0.59
heterocage **8**	4.8[d]	4.0	3.96 ± 0.32

[a] All heights in nm. [b] Protrusion heights are calculated by subtracting the thickness of the MU SAM (0.8 nm) from the X-ray data. [c] Value calculated for the upper thioether chains in the backfolded conformation (1.8 nm). [d] Value calculated for the hexyl chains in the all-*trans* conformation (0.8 nm).

The homocages insertion process of thioether-footed cage **7a** is schematically shown in Figure 2a. A clean MU SAM is soaked into a solution of cage **7a** (0.25 mM) in dichloromethane for one hour at room temperature. After extensive rinsing with dichloromethane, ethanol, and water, the sample surface was analysed by AFM (Figure 2b). The 3D image shows the presence of objects protruding from the MU SAM. The section analysis shows some variation in the height of these objects (Figure 2b). We conclude that these objects are individual cages inserted into, and protruding from the SAM. The average height of the cage is 5.27 ± 0.59 nm (average of 22 measurements), which is consistent with the dimensions obtained from the X-ray structure of an identical cage with C_6H_{13} alkyl feet.[8] The variation in height can be attributed to the flexible conformation of the sulfide chains at the lower rim of the cages, which can lead to variation in protrusion length of the cages from the SAM, and also to the measurement technique (note that the AFM tip is very large compared to the molecule).

The surface self-assembly of heterocages was achieved by inserting cavitand **6** into a MU SAM, and performing CSA on the immobilized cavitand (schematically shown in Figure 3a and 4). The insertion into a MU SAM was achieved by soaking the SAMs for one hour into a solution (0.25 mM) of cavitand molecules **6** in dichloromethane. Extensive washing (dichloromethane, ethanol, and water) ensured the removal of all physisorbed material. TM-AFM experiments and section analysis showed the presence of objects protruding from the monolayer (Figure 3b). Section analysis revealed that these entities had a height of 1.87 ± 0.18 nm (average of 25 measurements). From X-ray and CPK models, the total height of cavitand **6** is about 2.5 nm (Table 1). Since the molecules are inserted into a SAM of

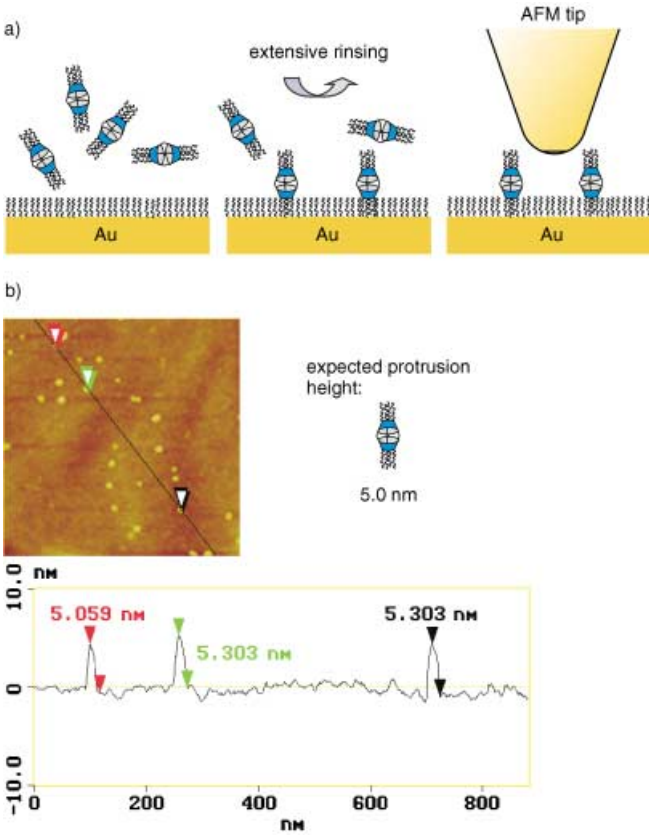


Figure 2. a) Schematic representation of the insertion of homocage **7a** in a MU SAM; b) TM-AFM height image and section analysis of a MU SAM with inserted homocages **7a**.

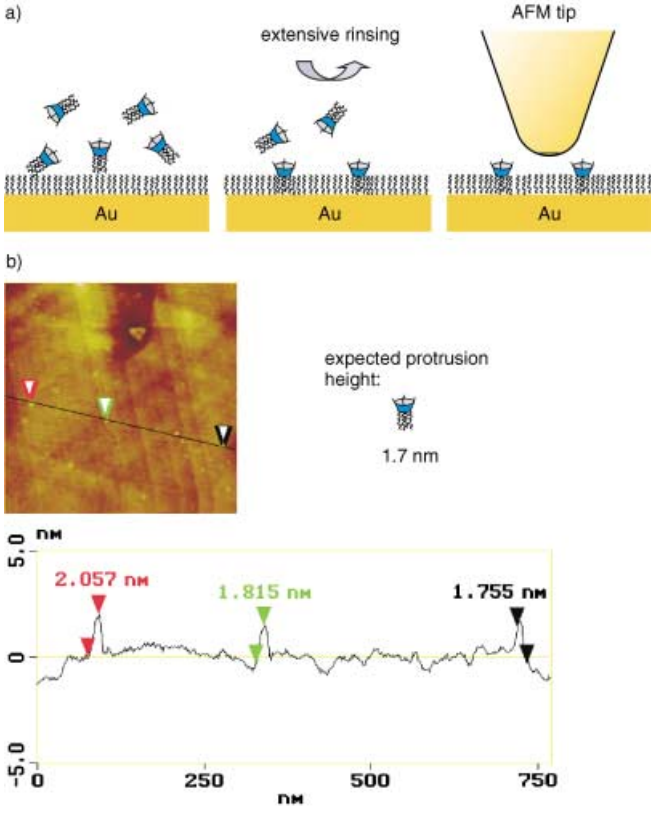


Figure 3. a) Schematic representation of cavitand **6** insertion and AFM analysis on MU SAM; b) TM-AFM image and section analysis of a MU SAM with inserted phenylpyridine functionalized thioether-footed cavitand **6**.

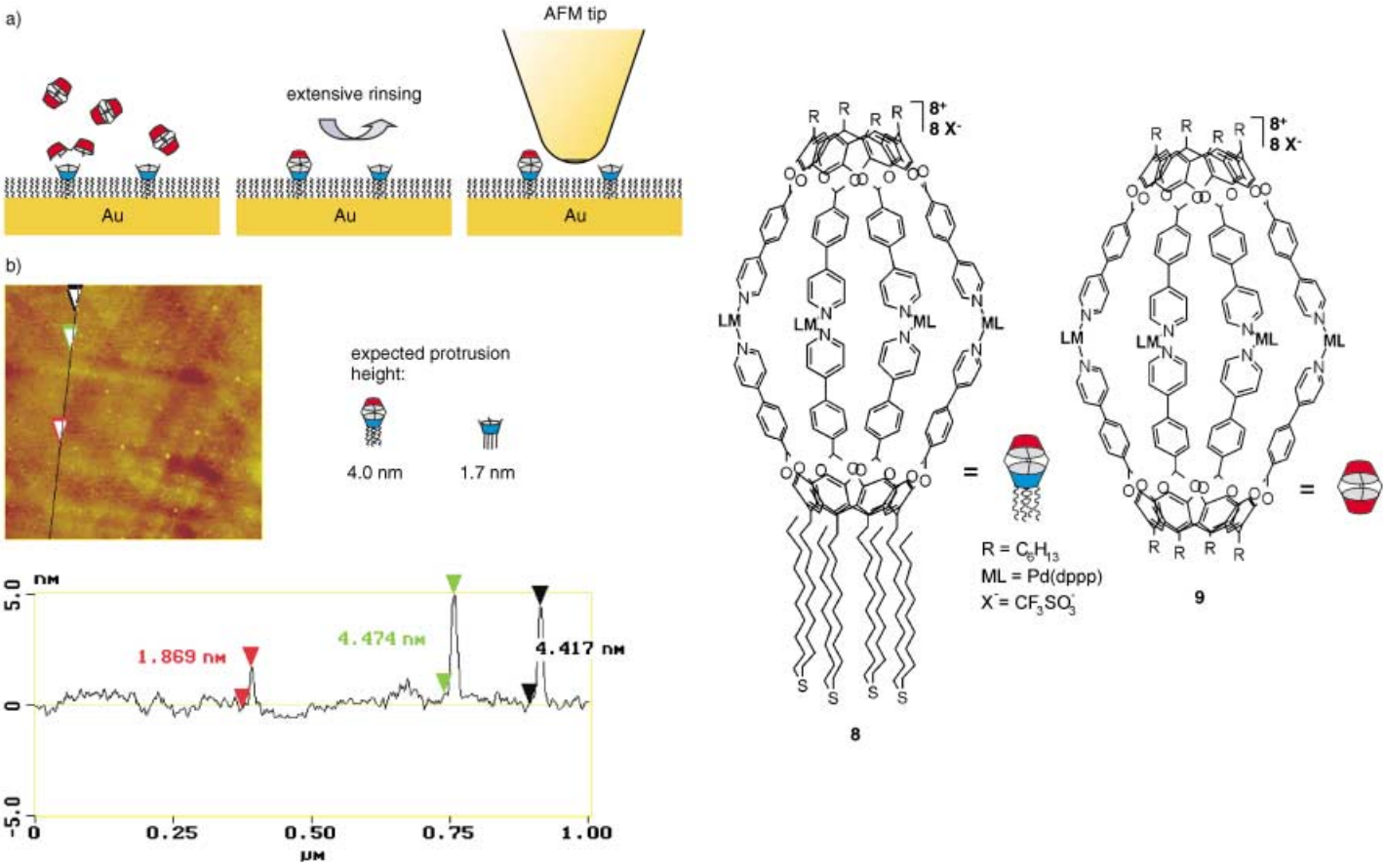


Figure 4. a) Schematic representation of the surface assembly of heterocages **8** from surface bound cavitands with cages in solution; b) TM-AFM image and section analysis of a MU SAM with heterocages **8** (green and black) and cavitands (red).

0.8 nm height, they are expected to protrude from the SAM by approximately 1.7 nm. Hence, we contend that we can observe individual cavitand molecules protruding from the SAM. The height differences which are measured for the cavitands on the surface can be caused by the factors discussed above.

The next step was the assembly of the heterocage **8** (Figure 4a). By using the cavitands already attached to the surface, nanosize cages could be assembled on the gold surface. Exposing an SAM of **6** to a solution (0.25 mM) of cage **9**,[8] with eight hexyl chains at the lower rim of the resorcinarene skeleton, the assembly of heterocage **8** on gold was obtained (Figure 4a). The formation of cages **8** on gold required ligand exchange with cages **9** present in solution. Ligand exchange between cages has already been proven in solution.[7g] These experiments were performed by using the cage of the cavitands without thioether-chains to make sure that the cages seen on the surface were assembled in two steps on the surface, and not directly inserted from solution (see control experiments). Rinsing with dichloromethane, ethanol, and water ensured the removal of all physisorbed material. AFM experiments and section analysis showed the presence of two different features: i) objects with a height of about 4–5 nm, and ii) objects with a height of about 2 nm (Figure 4b). The different heights of the objects suggest that both uncapped cavitands and heterocages are present. Partial success of the capping reaction is not surprising considering that very dilute conditions do not favor a complete ligand exchange.

Control experiments: Since we started from clean MU SAMs and used extensive rinsing to remove physisorbed material, we contend that the features observed in AFM are really inserted cavitands or cages. To confirm these results and to exclude artefacts, two control experiments have been carried out: a) insertion of molecules without interaction sites, and b) disassembly of the cages on gold.

The first control experiment was performed by using cavitand **10** and cage **9** with inert hexyl tails instead of thioethers at the lower rim . A full MU SAM was soaked into a solution (0.25 mM) of cavitand **10** or cage **9** for one hour. After successive rinsing with dichloromethane, ethanol, and water, the substrates were analyzed by TM-AFM (Figure 5). The analysis clearly shows that no detectable features are present on the gold surface. Hence, no insertion or absorption of molecules occurs in the absence of a functional group with affinity for gold, and the thioether functions in cavitand **6** and cage **7a** are required for binding to the gold substrate.

The second control experiment consisted of the disassembly of cage **7a** immobilized on gold. A gold substrate with inserted homocages (route 1) was exposed to a solution of triethylamine in ethanol (5 mM solution) for one hour (Fig-

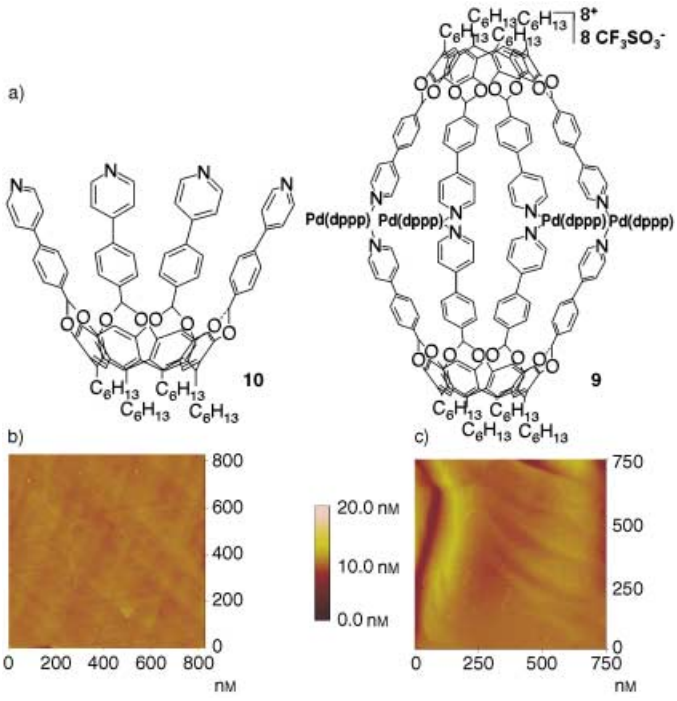


Figure 5. a) Cavitand **10** and cage **9** used for the control experiments; b) AFM image of 11-mercaptoundecanol monolayer after 1 h in a solution (0.25 mM) of cavitand **10**; c) AFM image of 11-mercaptoundecanol monolayer after 1 h in a solution (0.25 mM) of cage **9**.

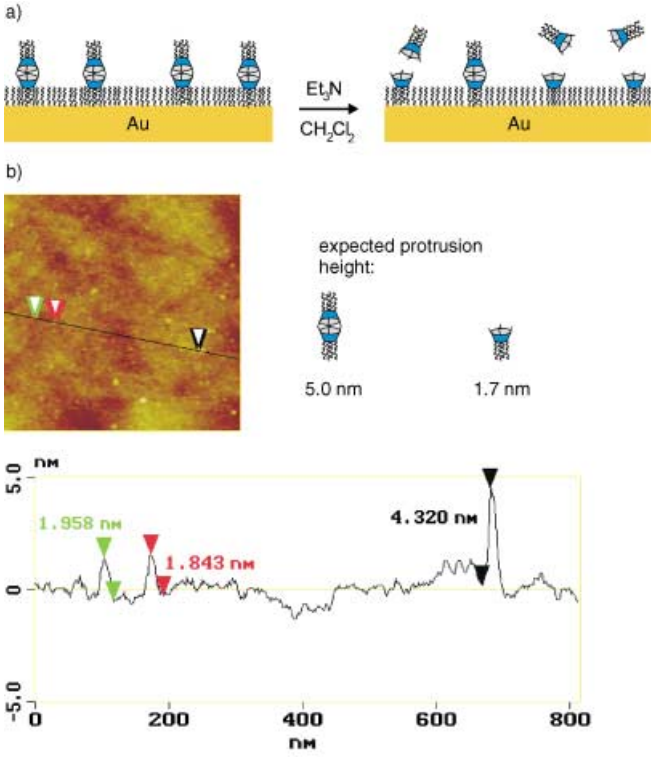


Figure 6. a) Schematic representation of the disassembly of the surface bound cages **7a**; b) TM-AFM height image of partly disassembled cages **7a** in a MU SAM.

ure 6a). Triethylamine was able to shift the equilibrium towards the formation of $[Pd(dppp)(NEt_3)_2(OTf)_2]$ plus free cavitand by competing with Pd coordination centres.[7g] AFM indicated that more than half of the cages were disassembled, leaving the free cavitand molecules as shown in Figure 6b. This experiment confirms that metal-directed self-assembly of cages is a reversible process, also on surfaces.

Conclusion

Molecular containers of nanosize dimensions have been assembled in a controlled fashion on gold. The assembly in two steps, and the disassembly of the Pd-coordinated cage compound were monitored by TM-AFM. We envisage that the reversibility of the system can be exploited to reversibly encapsulate guests in the cage on the surface. Also, the formation of heterocages with different substituents in the upper and lower part opens new possibilities. For example, the thioether chains on the top half of homocages might be used to attach gold colloids from solution and prepare'sandwich' structures that may find application in nanoscale electronic device preparation. Alternatively, the top half of heterocages might be equipped with further functionalities for specific interaction with molecules or nanoparticles in solution. Both approaches are currently being pursued in our laboratories.

Experimental Section

General methods: All commercial reagents were ACS reagent grade and used as received. All solvents were dried over 3 and 4 Å molecular sieves. ^{1}H NMR spectra were recorded on Bruker AC300 (300 MHz) spectrometer at 300 K, and all chemical shifts (δ) were reported in parts per million (ppm) relative to the proton resonances; this resulted from incomplete deuteration of the NMR solvents. ^{31}P NMR spectra were recorded on a Bruker AMX400 (162 MHz), and all chemical shifts were reported in ppm relative to external 85% H_3PO_3 at 0.00 ppm. Melting points were obtained with an electrothermal capillary apparatus and were uncorrected. Mass spectra of the organic compounds were measured with a Finningan-MAT SSQ 710 spectrometer by using CI (chemical ionization) technique. Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectra were obtained on a PerSeptive Biosystems Voyager DE-RP spectrometer equipped with delayed extraction. Column chromatography was performed by using silica gel 60 (Merck 70–230 mesh). 4-(4′-Tolyl)pyridine and resorcinarene **2** were prepared according to literature procedures.[10,17] Metal precursors were prepared from the corresponding dichlorobis derivatives following established procedures.[18]

For monolayer preparation and rinsing p.a. grade solvents were used as received. Water was purified by a Millipore (MilliQ, Q2) system. MU (97%, Aldrich) was used as received.

Gold substrates were obtained from Metallhandel Schroer GmbH, Lienen, Germany. Samples consisted of an 11×11 mm glass substrate with 5 nm chromium adhesion layer, and on top of that 200 nm gold. Prior to use, substrates were rinsed with dichloromethane, dried in N_2 flow, and annealed in a hydrogen (purity 6) flame. After annealing, the slightly cooled substrates were first immersed in ethanol. After five minutes, the substrates were rinsed with ethanol and immersed into the MU solution.

AFM-analyses were performed on a Nanoscope III multimode AFM (Digital Instruments, Santa Barbara, CA) in the tapping mode by using the E-scanner (~12 micron). Silicon cantilevers (nanosensors) with a stiff-

ness between 37 and 56 $N\,m^{-1}$ were used. Measurements were performed at frequencies slightly lower than the natural resonance frequency of the cantilever in air (~300 kHz). All AFM analyses were performed at room temperature and ambient pressure.

Trimethylsylane protected resorcinarene (2): NEt_3 (5.6 mL, 40.3 mmol) and $ClSi(CH_3)_3$ (3.2 g, 25.3 mmol) were added to a solution of resorcinarene **1** (3.0 g, 2.88 mmol) in dry THF (20 mL) cooled to −10 °C. The solution was stirred at 0 °C for 2 h and then at room temperature for 16 h. After evaporation of the solvent under vacuum, the brown crude product obtained was purified by flash column chromatography on silica by using CH_2Cl_2/hexane (8:2 v/v) as an eluent to give compound **2** as a white solid (2.3 g, 1.4 mmol, 49 %). R_f = 0.2; m.p. 80–83 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.39 (s, 72H; Si(CH_3)$_3$), 1.27 (m, 52H; R-(CH_2)$_6$), 1.72 and 1.83 (brm, 8H; R−CH_2CH=CH_2, diastereotopic protons), 2.04 (q, 8H; ArCH−CH_2), 4.41 (t, 4H; ArC*H*, *J* = 7.9 Hz), 4.97 (m, 8H; R−CH=CH_2), 5.83 (m, 4H; C*H*=CH_2−R), 6.02 (brs, 2H; Ar*H*), 6.20 (brs, 2H; Ar*H*), 6.30 (brs, 2H; Ar*H*), 7.18 ppm (brs, 2H; Ar*H*); MS (CI): *m*/*z* (%): 1620 [*M*H$^+$, (100)].

Thioether-footed trimethylsylane protected resorcinarene (3): 9-BBN (11.36 mL, 5.68 mmol; commercial solution 0.5 M in THF), and 1-decanethiol (11.8 mL, 56.8 mmol) were added to a solution of **2** (2.3 g, 1.42 mmol) in dry THF (15 mL) cooled to −10 °C. The solution was stirred at room temperature for 16 h. After evaporation of the solvent under vacuum, the crude product was dissolved in CH_2Cl_2 (20 mL), and washed with water (3×20 mL). The organic layer was dried on $MgSO_4$, filtered, and the solvent evaporated under vacuum. After recrystallization from ethanol, compound **3** was obtained as a white solid (2.3 g, 0.99 mmol, 70 %). M.p. 42 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.35 (s, 72H; Si(CH_3)$_3$), 0.88 (t, 12H; CH_3), 1.26 (m, 112H; (CH_2)$_{14}$), 1.55 (m, 16H; R−CH_2CH_2S), 1.78 (m, 8H; ArCH−CH_2), 2.50 (t, 16H; R−CH_2-S), 4.36 (t, 4H; ArC*H*, *J* = 7.7 Hz), 5.97 (brs, 2H; Ar*H*), 6.15 (brs, 2H; Ar*H*), 6.25 (brs, 2H; Ar*H*), 7.12 ppm (brs, 2H; Ar*H*); MS (CI): *m*/*z* (%): 2318 [*M*H$^+$, (100)], 2143 [*M*H$^+$-1-decanethiol, (30)].

Thioether-footed resorcinarene (4): HCl 36 % (2.0 mL) was added to a solution of **3** (2.3 g, 0.99 mmol) in methanol (40 mL). The pink solution was stirred at room temperature for 16 h. The reaction was quenched with water (15 mL), and the white solid formed was washed with water to neutrality. After drying at the vacuum pump, compound **4** was obtained in pure form as a white solid (1.6 g, 0.92 mmol, 93 %). M.p. 222–225 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.88 (t, 12H; R−CH_3), 1.28 (m, 112H; (CH_2)$_{14}$), 1.57 (m, 16H; R−CH_2CH_2S), 2.21 (brm, 8H; ArCH−CH_2), 2.49 (t, 16H; R−CH_2S), 4.3 (brt, 4H; ArC*H*), 6.09 (brs, 4H; Ar*H*), 7.21 (brs, 4H; Ar*H*), 9.28 (brs, 4H; O*H*), 9.58 ppm (brs, 4H; O*H*); MS (CI): *m*/*z* (%): 1737 [*M*H$^+$, (30)].

4,4′-(α,α′-Dibromotolyl)pyridine (5): 4-(4′-Tolyl)-pyridine (7.4 g, 44.0 mmol) and benzoyl peroxide (0.53 g, 2.0 mmol) were added under nitrogen to a suspension of *N*-bromosuccinimide (15.6 g, 87.0 mmol) in degassed CCl_4 (300 mL). The mixture was stirred under reflux in a nitrogen atmosphere for 16 h. The suspension was filtered, the solid was rinsed with CH_2Cl_2, and the resulting liquid was washed with saturated Na_2CO_3 solution. The liquid was then dried on K_2CO_3 and evaporated. The crude product was purified by column chromatography on silica by using ethyl acetate/hexane (8:2 v/v) as an eluant to give compound **5** as a yellow solid (5.9 g, 18.0 mmol, 41 %). R_f = 0.35; m.p. 100–101 C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.70 (s, 1H; C*H*Br$_2$), 7.74 (d (AA′ part of a AA′XX′system), 2H; Ph*H*, J_o = 6.5 Hz, J_m = 2.0 Hz), 7.80 (d (AA′ part of a AA′XX′ system), 2H; PyH_m, J_o = 6.6 Hz, J_m = 1.7 Hz), 8.00 (d (XX′ part of a AA′XX′ system), 2H; Ph*H*, J_o = 6.5 Hz, J_m = 2.0 Hz), 8.82 (d (XX′ part of a AA′XX′ system), 2H; PyH_o, J_o = 6.6 Hz, J_m = 1.7 Hz); MS (CI): *m*/*z* (%): 328 [*M*$^+$, (30)]; 248 [(*M*−Br)$^+$, (100)].

Phenylpyridine bridged thioether-footed cavitand (6) (*oooo* isomer): Compound **5** (0.23 g, 0.69 mmol) and K_2CO_3 (0.19 g, 1.38 mmol) were added under nitrogen to a solution of resorcinarene **4** (0.2 g, 0.11 mmol) dissolved in dry DMA (15 mL). The mixture was stirred in a sealed tube at 80 °C for 16 h. The reaction was quenched by the addition of water (10 mL), and the mixture was extracted with CH_2Cl_2 (15 mL). The organic layer was washed with water (3×15 mL), dried on K_2CO_3, and then the solvent evaporated. The black crude product obtained was purified by column chromatography on silica by using CH_2Cl_2/ethanol (9:1 v/v) as an eluent to give compound **6** (*oooo* isomer) as a yellow solid (0.11 g, 0.046 mmol, 41 %). R_f = 0.7; m.p. 243 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.87 (t, 12H; R−CH_3), 1.26 (m, 104H; (CH_2)$_{13}$), 1.48 (brm, 8H; CH_3−CH_2−R), 1.57 (m, 16H; R−CH_2CH_2S), 2.36 (brm, 8H; ArCH−CH_2), 2.50 (m, 16H; R−CH_2−S), 4.99 (t, 4H; ArC*H*, *J* = 8.0 Hz), 5.56 (s, 4H; ArC*H*), 6.74 (s, 4H; Ar*H*), 7.31 (s, 4H; Ar*H*), 7.51 [bd (AA′ part of a AA′XX′ system), 8H; PyH_m), 7.72 (d (AA′ part of a AA′BB′ system), 8H; Ph*H*, *J* = 8.3 Hz), 7.83 (d (BB′ part of a AA′BB′ system), 8H; Ph*H*, *J* = 8.3 Hz), 8.68 ppm (brd (XX′ part of a AA′XX′ system), 8H; PyH_o); ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 0.86 (t, 12H; R−CH_3), 1.28 (m, 104H; (CH_2)$_{13}$), 1.51 (brm, 8H; CH_3−CH_2−R), 1.57 (m, 16H; R−CH_2CH_2S), 2.50 (m, 24H; ArCH−CH_2+R−CH_2S), 5.03 (t, 4H; ArC*H*, *J* = 8.1 Hz), 5.65 (s, 4H; ArO-C*H*), 7.02 (s, 4H; Ar*H*), 7.65 (d (AA′ part of a AA′XX′ system), 8H; PyH_m, *J* = 4.6 Hz), 7.82 (m (AA′ part of a AA′BB′ system), 12H; Ph*H*+Ar*H*), 7.92 (d (BB′ part of a AA′BB′ system), 8H; Ph*H*, *J* = 8.2 Hz), 8.63 ppm (brd (XX′ part of a AA′XX′ system), 8H; PyH_o); MS (CI): *m*/*z* (%): 2401 [*M*H$^+$, (100)].

General procedure for cage formation (7a and 7b): Cages **7a** and **7b** were assembled by mixing cavitand **6** with different metal precursors [M(dppp)(OTf)$_2$] (M = Pt, Pd) in a 1:2 molar ratio at room temperature in acetone. In all cases, removal of the solvent in vacuum gave the desired cage in quantitative yields. Cage **7a** (M = Pd): ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 0.85 (t, 24H; R−CH_3), 1.26 (m, 224H; (CH_2)$_{14}$), 1.46 (m, 32H; R−CH_2CH_2S), 1.55 (m, 16H; ArCH−CH_2), 2.50 (m, 40H; R−CH_2S+PCH$_2$CH_2), 3.41 (brm, 16H; PCH_2CH$_2$), 4.93 (t, 8H; ArC*H*, J = 8.2 Hz), 5.53 (s, 8H; ArO−C*H*), 7.00 (s, 8H; Ar*H*), 7.38–7.43 (m, 48H; Ar$H_m$dppp+Ar$H_p$dppp), 7.47 (d (AA′ part of a AA′XX′ system), 16H; PyH_m, *J* = 5.8 Hz), 7.69 (d (AA′ part of a AA′BB′ system), 16H; Ph*H*Py, *J* = 8.5 Hz), 7.76–7.85 (m, 56H; Ar$H_o$dppp+Ar*H*+(BB′ part of a AA′BB′ system), Ph*H*Py), 9.06 ppm (brd (XX′ part of a AA′XX′ system), 16H; PyH_o); ^{31}P NMR ([D$_6$]acetone, 162 MHz): δ = 12.6 ppm; MALDI-TOF MS: *m*/*z* (%): found 7918 [*M*−CF_3SO_3, (100)]$^+$; calculated 7918.26, in which *M* = $C_{428}H_{528}O_{40}N_8Pd_4P_8S_{16}F_{24}$ (8067.32 amu). Cage **7b** (M = Pt): ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 0.85 (t, 24H; R−CH_3), 1.27 (m, 224H; (CH_2)$_{14}$), 1.46 (m, 32H; R−CH_2CH_2S), 1.55 (m, 16H; ArCH−CH_2), 2.48 (m, 40H; R−CH_2S+PCH$_2$CH_2), 3.51 (brm, 16H; PCH_2CH$_2$), 4.93 (t, 8H; ArC*H*, *J* = 8.0 Hz), 5.53 (s, 8H; ArO−C*H*), 7.00 (s, 8H; Ar*H*), 7.38–7.45 (m, 48H; Ar$H_m$dppp+Ar$H_p$dppp), 7.49 (d (AA′ part of a AA′XX′ system), 16H; PyH_m, *J* = 6.6 Hz), 7.71 (d (AA′ part of a AA′BB′ system), 16H; Ph*H*Py, *J* = 8.6 Hz), 7.76–7.85 (m, 56H; Ar-$H_o$dppp+Ar*H*+(BB′ part of a AA′BB′ system), Ph*H*Py), 9.09 ppm (brd (XX′ part of a AA′XX′ system), 16H; PyH_o); ^{31}P NMR ([D$_6$]acetone, 162 MHz): δ = −8.1 ppm (J_{P-Pt} = 3050 Hz); MALDI-TOF MS: *m*/*z* (%); found 8273 [M−CF_3SO_3 (100)]$^+$; calculated 8272.9, in which M = $C_{428}H_{528}O_{40}N_8Pt_4P_8S_{16}F_{24}$ (8421.96 amu).

SAM preparation: All glassware used was cleaned in piranha solution (3 parts concentrated sulphuric acid, 1 part 30 % hydrogen peroxide) for at least 15 minutes. *Warning: piranha solution should be handled with caution. It has been reported to detonate unexpectedly. Contact with organic solvents must be avoided.* After removing from piranha the glass was rinsed extensively with MilliQ water to remove all acid. Gold substrates for AFM measurements were flame-annealed with a hydrogen flame (grade 6), and after cooling the subtrates were kept in ethanol solution for five minutes. Substrates were immersed with minimal delay into a solution (1.0 mM) of MU in ethanol, and kept overnight at room temperature. The substrates were removed from the solution and extensively rinsed with pure water, ethanol, and dichloromethane. Before insertion experiments, the MU SAMs were checked for the presence of nanometer-sized features by TM-AFM. To ensure that pollution particles on the SAM were not mistaken for inserted cavitands, only SAMs with less than ~3 features per 1 μm^2 were used.

Insertion of cages and cavitands was obtained by soaking the 11-mercaptoundeacol monolayer into a solution (0.25 mM) of cage **7a** or cavitand **6** in dichloromethane for one hour at room temperature. Self-assembly of heterocage **8** was obtained by exposing a SAM of cavitand **6** to a solution (0.25 mM) of cage **9** in dichloromethane for one hour. Homocage disassembly was obtained by soaking the MU SAMs with inserted cage **7a** into a solution(~5 mM) of Et_3N in CH_2Cl_2 for one hour.

All monolayers were extensively rinsed with pure ethanol and dichloromethane, and dried in a nitrogen flow before the AFM analyses.

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