Supporting Information for

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Guest-controlled aggregation of cavitand gold nanoparticles and N-methyl pyridinium-terminated PEG.

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General Methods.

All reagents and chemicals were obtained from commercial sources and used without further purification. Dry pyridine was distilled from KOH before use. Column chromatography was performed using silica gel 60 (MERCK 70-230 mesh). Electrospray ionization ESI-MS experiments were performed on a Waters ZMD spectrometer equipped with an electrospray interface. Exact masses were determined using a LTQ ORBITRAP XL Thermo spectrometer equipped with an electrospray interface. ^{1}H NMR spectra were obtained using a Bruker AVANCE-300 (300 MHz) or a Bruker AVANCE 400 (400 MHz). All chemical shifts (δ) were reported in ppm relative to the proton resonances resulting from incomplete deuteration of the NMR solvents. ^{31}P NMR spectra were obtained using a Bruker AVANCE-400 (162 MHz) spectrometer. All chemical shifts (δ) were recorded in ppm relative to external 85% H_3PO_4 at 0.00 ppm.

Fluorescence spectra in solution were obtained with a modular UV/visible NIR spectrofluorimeter, Edinburgh, equipped with a 450 W Xe lamp. All solvents employed are CHROMASOLV, for HPLC grade.

Gold Nanoparticles TEM analysis

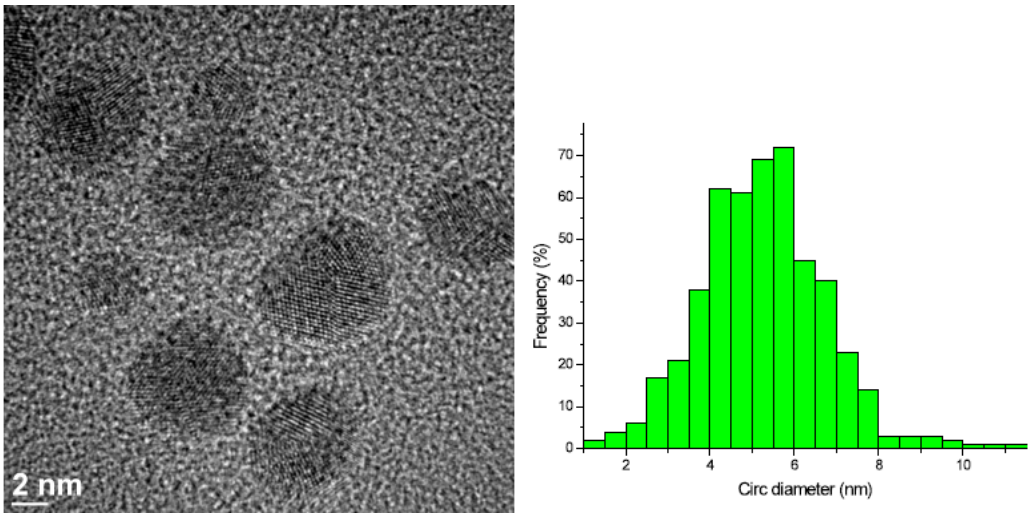
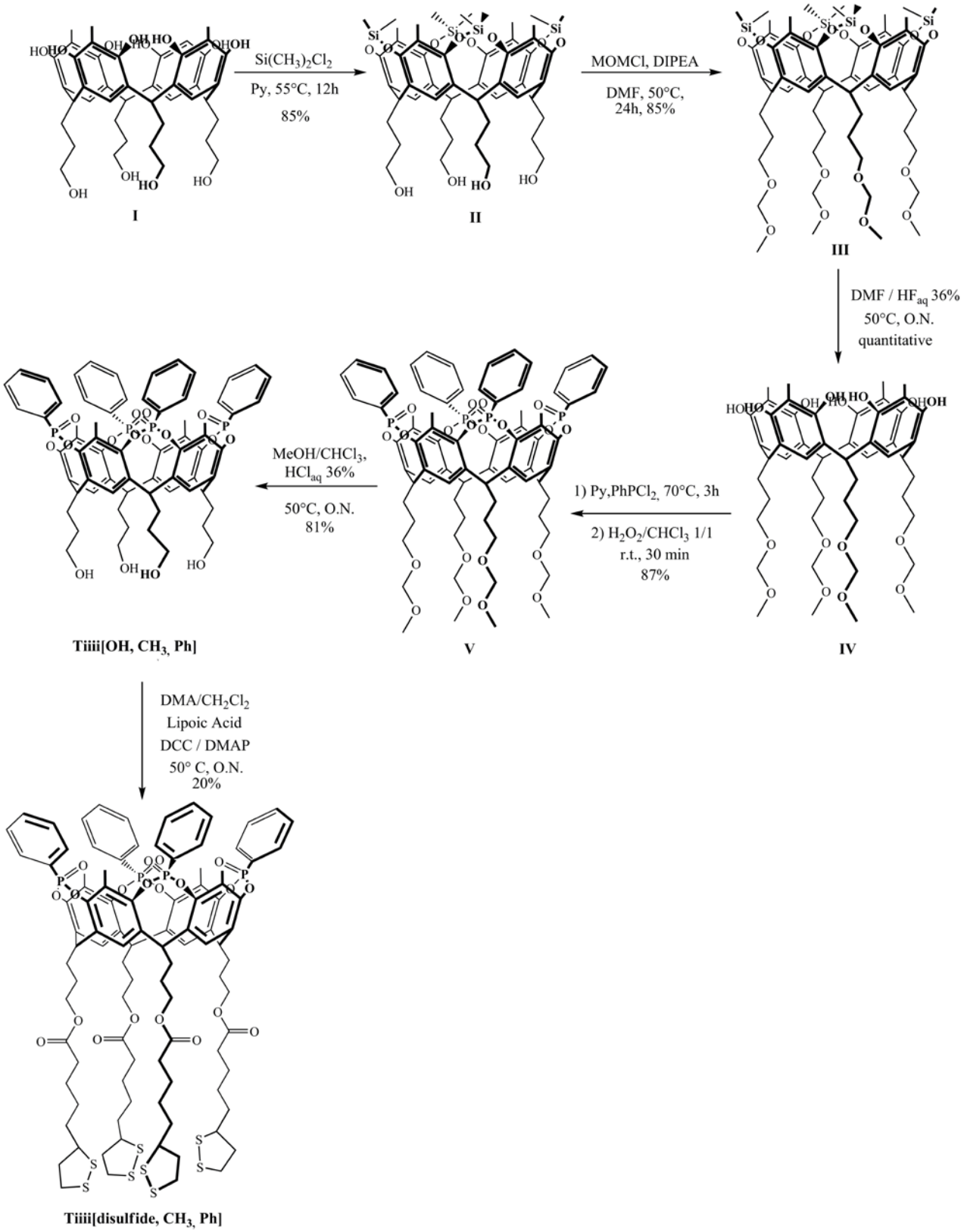


Figure S1 HR TEM image of the dodecanthiol AuNPs.

Synthesis



Scheme S1 Synthesis of the molecular receptor **Tiiii[disulfide,CH_3,Ph]**.

Tetrahydroxy sylilcavitand (II)

To a solution of **I** (2.5 g, 3.27 mmol) in pyridine (20 mL) dimethyldichlorosilane was added (4.13g, 3.85 mL, 32,7 mmol) at once. The resulting mixture was heated to 55°C for 12 hours. The solvent was removed under vacuum and the resulting residue was suspended in water. After filtration compound **II** was obtained in pure form as a white solid (2.46 g, 2.45 mmol, 84% yield). **^{1}H NMR ($CDCl_3$, CD_3OD, 400 MHz):** δ (ppm) 7.11 (s, 4H, Ar**H**); 4.45 (t, 4H, ArC**H**, ^{3}J = 7.8 Hz); 3.51 (t, 8H, $CH_2C\mathbf{H_2}OH$, ^{3}J = 5.7 Hz); 3.21 (s, 4H, $CH_2CH_2CH_2O\mathbf{H}$); 2.14 (bs, 8H, ArCHC$\mathbf{H_2}$); 1.77 (s, 12H, ArC$\mathbf{H_3}$); 1.38 (bs, 8H, $CH_2C\mathbf{H_2}CH_2OH$); 0.37 (s, 12H, SiC$\mathbf{H_{3out}}$); -0.70 (s, 12H, SiC$\mathbf{H_{3in}}$); **ESI-MS**: calculated. for $C_{52}H_{72}O_{12}Si_4$: 1001.46. Found: 1024.5. $[M+Na]^+$.

MOM-protected sylilcavitand (III)

To a solution of **II** (2.021 g, 2.02 mmol) in DMF (20 mL), diisopropilethylammine (5.30 mL, 30.3 mmol) and chloromethyl methyl ether (1.54 mL, 20.2 mmol) were added. The resulting mixture was heated a 50°C for 24 hours. The solvent was removed under vacuum and the resulting residue was suspended in water. After filtration compound **III** was obtained in pure form as white solid (2.01 g, 1.70 mmol, 85% yield). **^{1}H NMR ($CDCl_3$, 300 MHz):** δ (ppm) 7.17 (s, 4H, Ar**H**); 4.59 (s, 8H, OC$\mathbf{H_2}$O); 4.58 (t, 4H, ArC**H**, ^{3}J = 7.8 Hz); 3.51 (t, 8H, $CH_2CH_2C\mathbf{H_2}O$, ^{3}J = 5.7 Hz); 3.34 (s, 12H, OC$\mathbf{H_3}$); 2.30 (q, 8H, C$\mathbf{H_2}CH_2CH_2O$, ^{3}J = 7.5 Hz); 1.87 (s, 12H, ArC$\mathbf{H_3}$); 1.58 (q, 8H, $CH_2C\mathbf{H_2}CH_2OH$, ^{3}J = 7.5 Hz); 0.47 (s, 12H, SiC$\mathbf{H_{3out}}$); -0.72 (s, 12H, SiC$\mathbf{H_{3in}}$); **ESI-MS**: calculated for $C_{60}H_{88}O_{16}Si_4$: 1177.67. Found: 1200.12 $[M+Na]^+$.

MOM-protected resorcinare (IV)

An aqueous 36% HF solution (0.65 mL) was added to **III** (1.6 gr., 1.36 mmol) dissolved in DMF (20 mL). The mixture was heated at 50°C overnight. The solvent was removed in vacuo and the product was washed with water. Vacuum filtration afforded pure **IV** (1.30 g, 1.36 mmol, quantitative yield). **^{1}H NMR (DMSO-D_6 , 300 MHz):** δ (ppm) 8.68 (s, 8H, ArO**H**); 7.29 (s, 4H, Ar**H**); 4.53 (s, 8H, OC$\mathbf{H_2}$O); 4.22 (t, 4H, ArC**H**, ^{3}J = 7.8 Hz); 3.48 (t, 8H, $CH_2CH_2C\mathbf{H_2}O$, ^{3}J = 6.0 Hz); 3.24 (s, 12H, OC$\mathbf{H_3}$); 2.27 (m, 8H, C$\mathbf{H_2}CH_2CH_2O$); 1.94 (s, 12H, ArC$\mathbf{H_3}$); 1.58 (m, 8H, $CH_2C\mathbf{H_2}CH_2OH$); **ESI-MS**: calculated. for $C_{52}H_{72}O_{16}$: 953.12. Found: 976.2 $[M+Na]^+$.

MOM-protected tetraphosphonate cavitand (V)

To a solution of **IV** (1.345 g, 1.41 mmol) in freshly distilled pyridine (15 mL), dichlorophenylphosphine (0.8 mL, 5.9 mmol) was added slowly, at room temperature. After 3 hours of stirring at 70 °C, the solution was allowed to cool at room temperature and 10 mL of a mixture of aqueous 35% H_2O_2 and $CHCl_3$ (1:1) was added. The resulting mixture was stirred for 30 minutes at room temperature, then the solvent was removed in vacuo. Addition of water resulted in the precipitation of a white powder, which is filtered to give pure **V** (1.77 g, 1.23 mmol, 87% yield). **^{1}H NMR ($CDCl_3$, 300 MHz):** δ (ppm) 8.06 (m, 8H, P(O)Ar$\mathbf{H_{ORTO}}$); 7.56 (m, 4H+8H,P(O)Ar$\mathbf{H_{PARA}}$ + P(O)Ar$\mathbf{H_{META}}$); 7.17(s, 2H, Ar$\mathbf{H_{DOWN}}$); 4.82 (bt, 4H, ArC**H**,); 4.62 (s, 8H, OC$\mathbf{H_2}$O); 3.62 (t, 8H, $CH_2CH_2C\mathbf{H_2}O$, ^{3}J = 6.0 Hz); 3.35 (s, 12H, OC$\mathbf{H_3}$); 2.56 (m, 8H, C$\mathbf{H_2}CH_2CH_2O$); 2.10 (s, 12H, ArC$\mathbf{H_3}$); 1.60 (m, 8H, $CH_2C\mathbf{H_2}CH_2OH$);**^{31}P NMR** (**CDCl3**, 161 MHz)**:** δ (ppm) 8.58 (s, P(O)); **ESI-MS**: calculated for $C_{70}H_{72}O_{14}P_4$: 1441.36. Found: 1464.36.$[M+Na]^+$.

Tetrahydroxy-footed tetraphosphonate cavitand (Tiiii[OH, CH_3, Ph])

To a solution of **V** (1.77 g, 1.22 mmol) in $CHCl_3$(15 mL) and methanol (32mL) an aqueous 36% HCl solution was added. The resulting suspension was heated at 50°C overnight and the resulting residue was suspended in water. After filtration, pure compound **VI** was obtained as yellow light solid (1.26 g, 0.99 mmol, 81% yield). **^{1}H NMR (Acetone-D_6, 300 MHz):** δ (ppm) 8.29 (s, 2H, Ar$\mathbf{H_{DOWN}}$); 8.20 (m, 8H, P(O)Ar$\mathbf{H_{ORTO}}$); 7.73 (m, 4H+8H,P(O)Ar$\mathbf{H_{PARA}}$ + P(O)Ar$\mathbf{H_{META}}$); 4.81 (t, 4H, ArC**H**, ^{3}J = 7.6 Hz); 3.69 (t, 8H, $CH_2CH_2C\mathbf{H_2}OH$, ^{3}J = 5.3 Hz); 2.91 (m, 8H, C$\mathbf{H_2}CH_2CH_2O$); 2.16 (s, 12H, ArC$\mathbf{H_3}$); 1.60 (m, 8H, $CH_2C\mathbf{H_2}CH_2OH$); **^{31}P NMR** (**Acetone-**

D6, 161 MHz): δ (ppm) 9.32 (s, P(O)); **ESI-MS**: calculated for $C_{70}H_{72}O_{14}P_4$: 1264.36. Found: 1287.49 $[M+Na]^+$.

Tetralipoic ester-footed tetraphosphonate cavitand (Tiiii[disulfide, CH_3, Ph])

To a solution of **Tiiii[OH, CH_3, Ph]** (395 mg., 0.312 mmol) in CH_2Cl_2 (2 mL), DCC (546 mg, 2.65 mmol), DMAP (95 mg, 0.78 mmol), and lipoic acid (514mg, 2.49 mmol) were added. The resulting suspension was heated at 50°C overnight. The solvent was removed in vacuo and a 3 : 1 dichloromethane / ether solution was added. The white solid was filtrated and washed with 2 : 1 dichloromethane / ether solution. The filtrate was collected and the solvent was evaporated in vacuo. The resulting solid was washed with ether (2 x 20 mL). The crude was purified by column chromatography (0.1-10% MeOH / CH_2Cl_2) (127 mg, 0.062 mmol, 20% yield). **^{1}H NMR ($CDCl_3$, 300 MHz)**: δ (ppm) 8.08 (m, 8H, P(O)Ar**H_{ORTO}**); 7.73 (m, 4H+8H+4H, P(O)Ar**H_{PARA}** + P(O)Ar**H_{META}** + Ar**H_{DOWN}**); 4.81 (t, 4H, ArC**H**, ^3J = 7.6 Hz); 4.25 (t, 8H, $CH_2CH_2C\mathbf{H_2}O$, ^3J = 6.2 Hz); 3.52 (m, 4H, $CH_2(S)CH_2C\mathbf{H}(S)$), 3.13 (m, 8H, $C\mathbf{H_2}(S)CH_2CH(S)$), 2.42 (m, 8H, $CH_2(S)C\mathbf{H_2}CH(S)$); 2.40 (m, 8H, $C\mathbf{H_2}CH_2CH_2O$); 2.11 (s, 12H, ArC**H_3**); 1.94-1.57 (m, 32H, $CH_2C\mathbf{H_2}CH_2O$ + $O(CO)C\mathbf{H_2}CH_2CH_2CH_2$+$O(CO)CH_2C\mathbf{H_2}CH_2$ CH_2 + $O(CO)CH_2CH_2C\mathbf{H_2}CH_2$), 1.40 (m, 8, $O(CO)CH_2CH_2CH_2C\mathbf{H_2}$); **^{31}P NMR ($CDCl_3$, 161 MHz**): δ (ppm) 7.31 (s, P(O)); **HR ESI-MS**: calculated. for the complex **Tiiii[disulfide, CH_3, Ph]**•N-methylbutyl ammonium iodide $C_{105}H_{130}N_1O_{20}P_4S_8$ $[M+C_5H_{14}N]^+$:2104.58968. Found: 2104.60183.

Preparation of AuNPs

AuNPs were synthesised by a two-phase method: nanoparticles were prepared by dissolving 0.400 g (1.02 mmol) of hydrogen tetrachloro-aurate(III) trihydrate in 30 mL of deionized water. The solution was then shaken in a separatory funnel with 80 mL of toluene solution containing 2.00 g (3.56 mmol) of tetra-n-octylammonium bromide (TOAB). The toluene phase was then recovered and combined with 0.018 mL (0.015 g, 0.07 mmol) of dodecyl mercaptane. A freshly prepared aqueous solution of sodium borohydride (25 mL, 0.386 g) was slowly added under vigorous stirring. After further stirring for 3 h, the organic phase was separated, concentrated to 10 mL and mixed with 70 mL of ethanol. The mixture was cooled overnight at -20°C and the dark precipitate was then recovered by filtration. The crude product was then purified by soxhlet extraction with acetone as cleansing solvent to remove all the unbound free thiol and residual TOAB impurities.
Elemental analysis: found (%) C = 24.7; H = 4.2; N = 0.0.

Preparation and characterization of Tiiii Au NPs[1]

Dodecanthiol stabilized gold nanoparticles (20 mg)[2] were mixed in dry chloroform with tetraphosphonate cavitand (13.52 mg 0.0067 mmol) at room temperature, for 5 days. The solvent was evaporated under N_2 flux and the resulting solid was suspended in a toluene / ethanol mixture (2:1). The suspension was then ultracentrifugated at 15000 rpm (2 runs of 15 minutes each). The supernatant was decanted off, the solid was collected and dried under vacuum. The washing procedure was repeated twice.

[1] Beer, P. D.; Cormode, D. P.; Davis, J. J., *J. Chem. Soc., Chem. Commun.* ,**2004**, 414-415

[2] a)Brust , M.; Walker, M.; Bethell, D.; Schiffrin,D.J.; Whyman, R., *J. Chem. Soc., Chem. Commun.*, **1994**, 801 – 802;b) Waters, C.A.; Mills, A.J.; Johnson, K.A.; Schiffrin,D.J., *J. Chem. Soc., Chem. Commun.*, **2003**, 540 – 541.

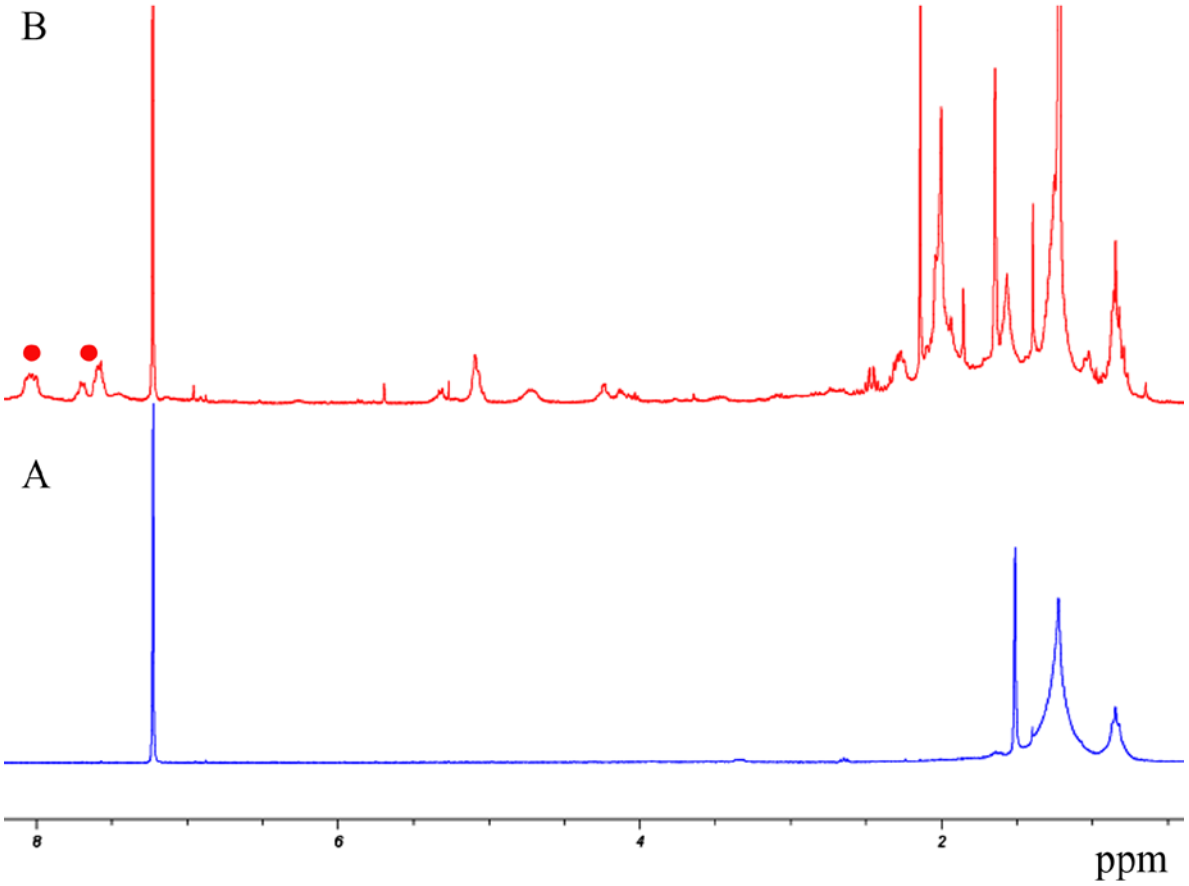


Figure S2 A) ^{1}H NMR of dodecanthiol-stabilized gold nanoparticles in $CDCl_3$; B)^{1}H NMR of **Tiiii-AuNPs** in $CDCl_3$ ● diagnostic cavitand signals)

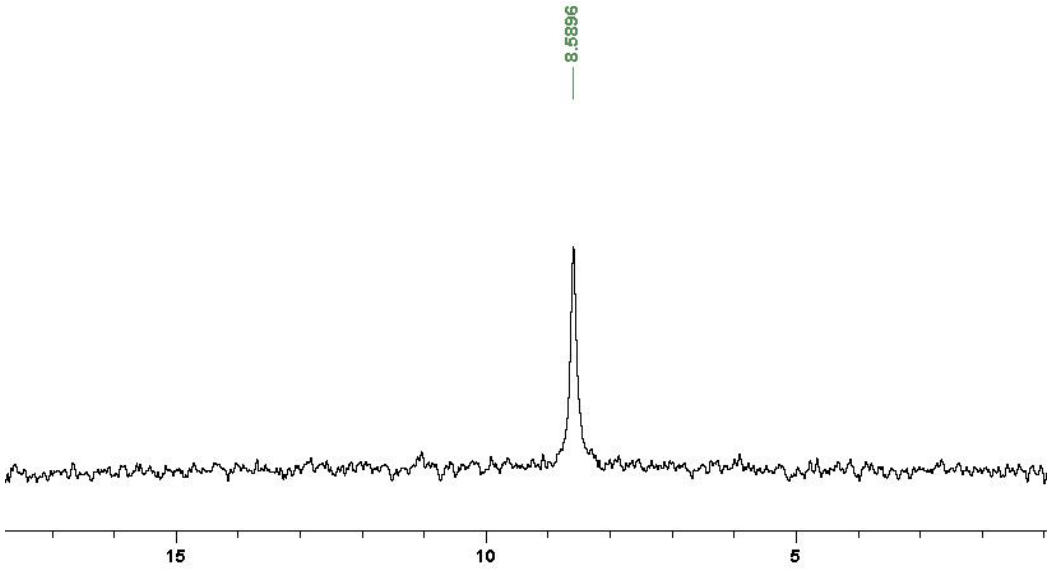


Figure S3 ^{31}P NMR of **Tiiii Au NPs** in $CDCl_3$

Fluorimetric Titration

3 mL of a $1x10^{-6}$ M solution of fluorescent pyrene guest derivative **2** in dichloromethane were prepared by repeated dilution of a concentrated mother solution ($1x10^{-3}$ M) and a starting point spectra (blue line of Figure 1 in the text) was recorded. This solution was then titrated adding 10 µl aliquots of a dichloromethane solution of **Tiiii-AuNPs** prepared dissolving 1.5 mg of **Tiiii-AuNPs** in 1 mL of dichloromethane. The solution was left without any agitation for 5 minutes after each addition in order to achieve the equilibrium, then an emission spectra was recorded (λ exc = 345 nm). The aliquots were added until no more changes in the spectrum were observed, i.e. until the achievement of the equivalent point. This required the addition of 130 µl of **Tiiii-AuNPs** solution corresponding to the addition of 0.2 mg of **Tiiii-AuNPs**. The experiment was repeated three times. The **Tiiii-AuNPs** aliquots added ranged between 130 and 140 µl.

To a saturated solution of **Tiiii-AuNPs • 2 complex** increasing amount of competitive guest **3** were added, as 10 µl aliquots (0 -1.3 eq. of a solution $1x10^{-5}$ M). In this case the solution was left with any further agitation for 30 minutes after each addition before acquiring the spectra. The competitor guest **3** was added until no further change was visible, i.e., until all the **Tiiii** present on the nanoparticles was complexed.

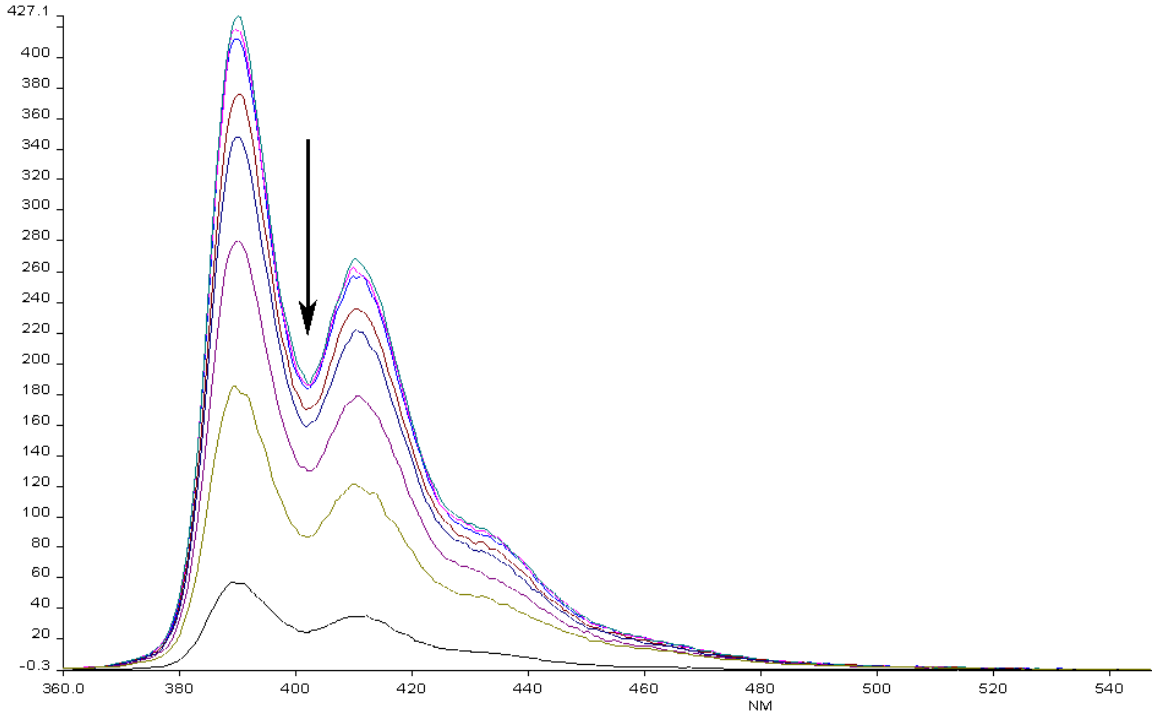


Figure S4 Fluorescence spectra (λ exc =345 nm) of a CH_2Cl_2 solution of **Tiiii-AuNPs•2 complex** upon addition of an increasing (0–1.3 eq.) amount of competitive guest **3**.

UV/Vis spectra

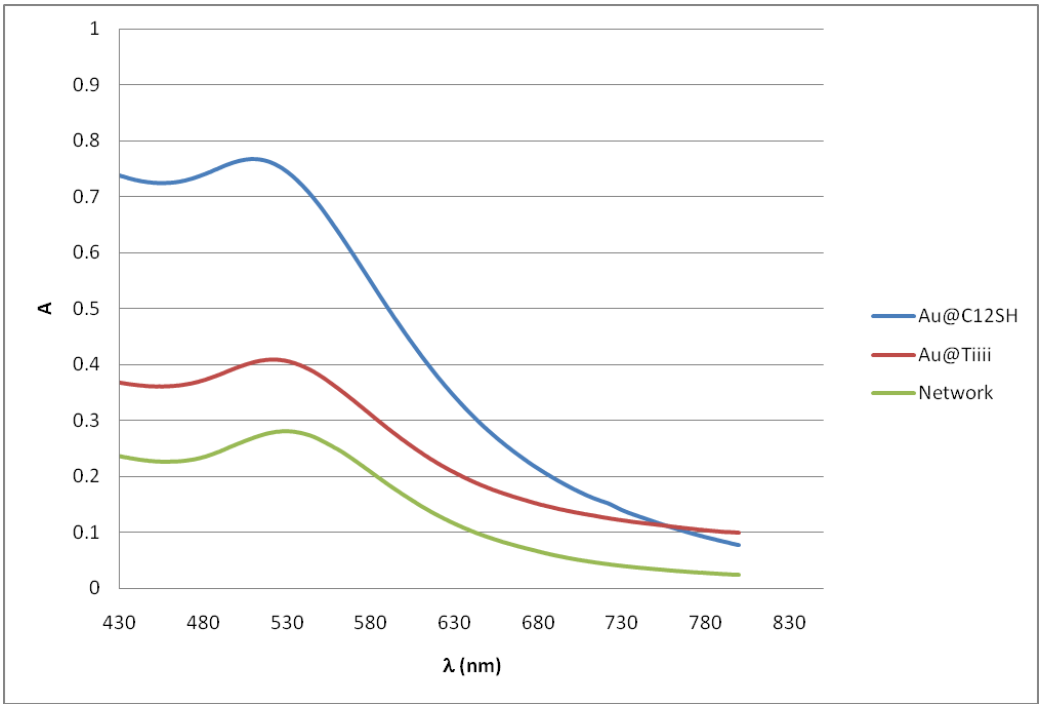


Figure S5: Plasmon Band Resonance shift of Dodecanthiol AuNPs (blue line); **Tiiii Au NPs** (red line); **Tiiii-AuNPs•1** network (green line).

DLS and UV-Vis measurements

Nanoparticles hydrodynamic diameter distributions were obtained through Dynamic Light Scattering measurements employing a Malvern Nano ZS instrument with a 633 nm laser diode. Samples were housed in semi-micro (1400 µL volume) quartz cells of 1cm optical path length, using chloroform as solvent (CHROMASOLV® Plus, for HPLC,≥99.9%, amylene stabilized) . All DLS measurements were carried on 400 µL solutions. NPs suspensions were prepared through sonication in chloroform at room temperature (10 min). Solvent and suspensions used were thoroughly filtered (PTFE membrane syringe filter, 0.20 µm) before any DLS measurement.

The width of DLS hydrodynamic diameter distribution is indicated by PdI (Polydispersion Index). In case of a mono-modal distribution (gaussian) calculated by means of cumulant analysis, $PdI=(\sigma/Z_{avg})^2$, where σ is the width of the distribution and Z_{avg} is average diameter of the particles population respectively.

The hydrodynamic diameter values determined during the titrations with ditopic guest **1** (concentration of nanoparticle bound **Tiiii** ≈ $5x10^{-5}$ M) are mediated upon three different measurements, while the hydrodynamic diameter of the assembly-disassembly experiments with guest **1** and **3** (d_H Volume Mean, Table 1) are the mean values (± standard deviation) of ten measurements of the same suspension.

The concentration of nanoparticle bound **Tiiii (**≈ $5x10^{-5}$ M) was selected to make the system suitable for DLS measurements, to be fairly close to the one used in the NMR experiments and to promote an almost quantitative **Tiiii- AuNPs•1** network formation during the titration.

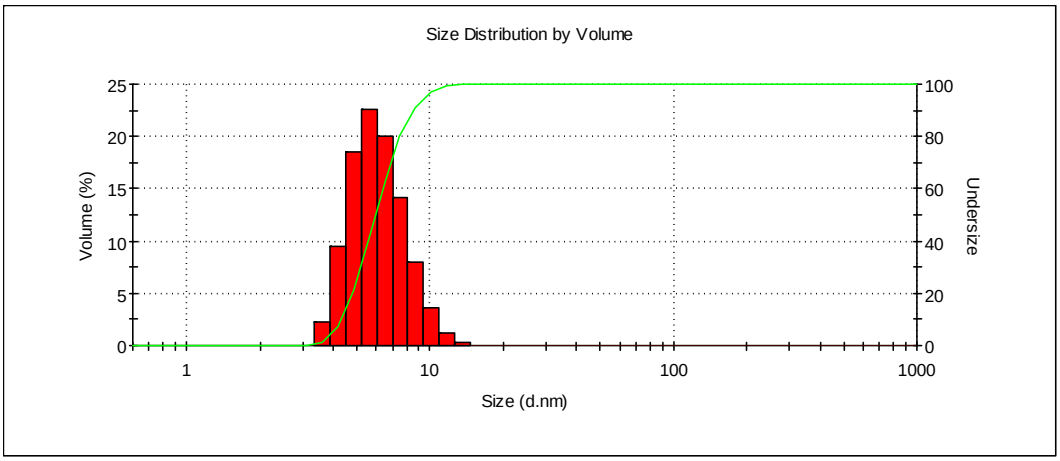


Figure S6: Size volume distribution of dodecanthiol coated Au nanoparticles, d_H = (8 ± 1) nm, (chloroform, 20°C).

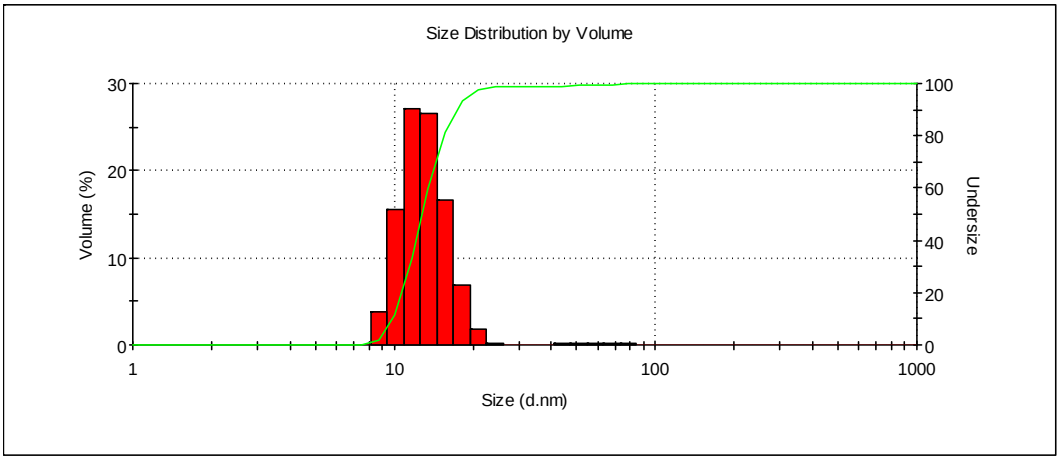


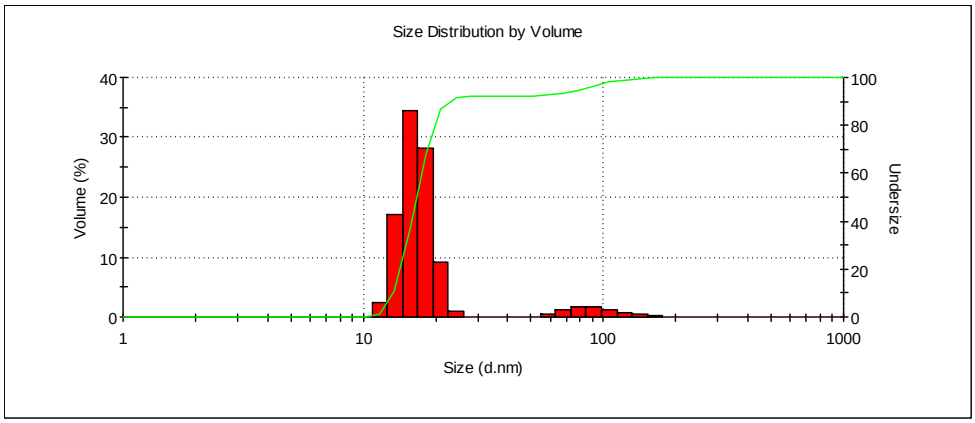
Figure S7: Size volume distribution of **Tiiii Au NPs**, d_H = (13 ± 3) nm, (chloroform, 20°C).

Table S1 Volume mean hydrodynamic diameter during the assembly-disassembly experiments of the system **Tiiii-AuNPs** with guest **1** and **3**. (concentration of nanoparticle bound **Tiiii** ≈ $5x10^{-5}$M, chloroform 20°C); [(a)] [**1**] = 150 μM; [(b)] [**1**] = 150 μM, [**3**] = 280 μM.

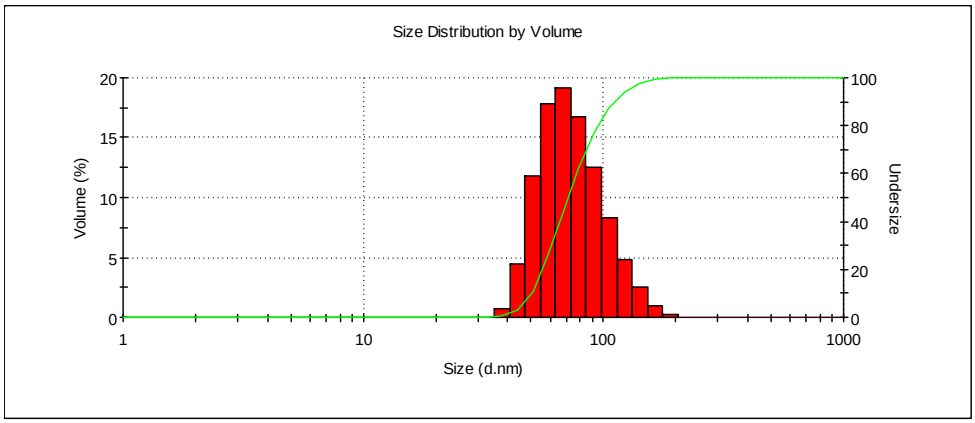
	d_H Volume Mean (nm)
Pristine	**25±3**
(a)	**75±15**
(b)	**29±5**

The measured size volume distribution for **Tiiii-AuNPs** (chloroform, 20°C) in diluted conditions (concentration of nanoparticle bound **Tiiii** ≅ $2x10^{-6}$ M) was d_H = (13 ± 3) nm, a value that is consistent with the presence of **Tiiii[disulfide,CH_3,Ph]** on the AuNPs surface (see Fig. S7†). The slight increase of d_H measured for **Tiiii-AuNPs** at higher concentration (concentration of nanoparticle bound **Tiiii** ≅ $5x10^{-5}$ M) during the pristine and final parts of the aggregation experiments carried out with guests **1** and **3**, are attributed to non-specific reversible interactions between nanoparticles.

Pristine



[**1**] = 150 µM;



[**1**] = 150 µM,

[**3**] = 280 µM;

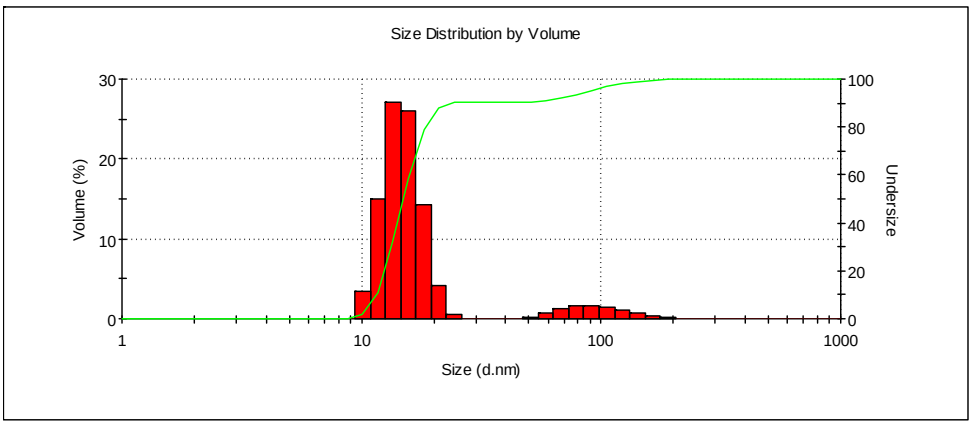


Figure S8: Sample size volume distributions during the assembly-disassembly experiments of **Tiiii-AuNPs** with guests **1** and **3.** (concentration of nanoparticle bound **Tiiii** ≈ $5x10^{-5}$ M, chloroform, 20°C).

Absorption spectra of **Tiiii-AuNps**, during the aggregation experiments with ditopic guest **4** were measured using a 400 µL **Tiiii-AuNps** suspension housed in a micro quartz cuvette of 2 mm optical length. This experimental set up allowed to carry out DLS and UV-VIS experiments on identical solution at the same time.

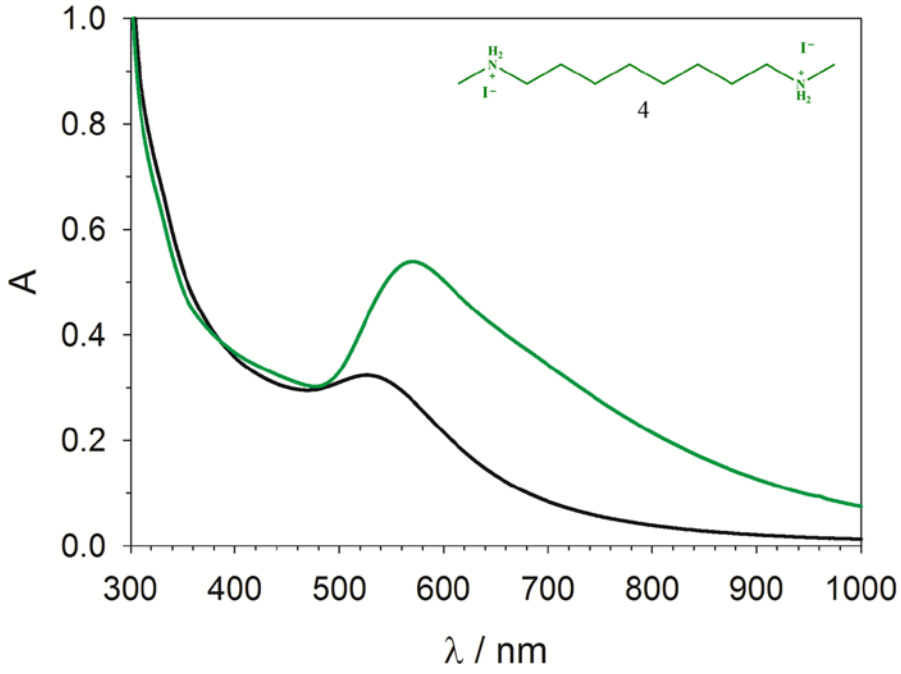


Figure S9 Absorption spectra of **Tiiii-AuNps** (concentration of nanoparticle bound **Tiiii** ≈ $1x10^{-5}$ M in $CHCl_3$, black line, λ_{max}=527nm), and of **Tiiii-AuNps** with ditopic guest **4** (**[4]**=$0.34x10^{-5}$ M, methanol, green line, λ_{max}=569nm, 1300 min.) showing a 42 nm plasmon band resonance red shift caused by the formation of NPs network.

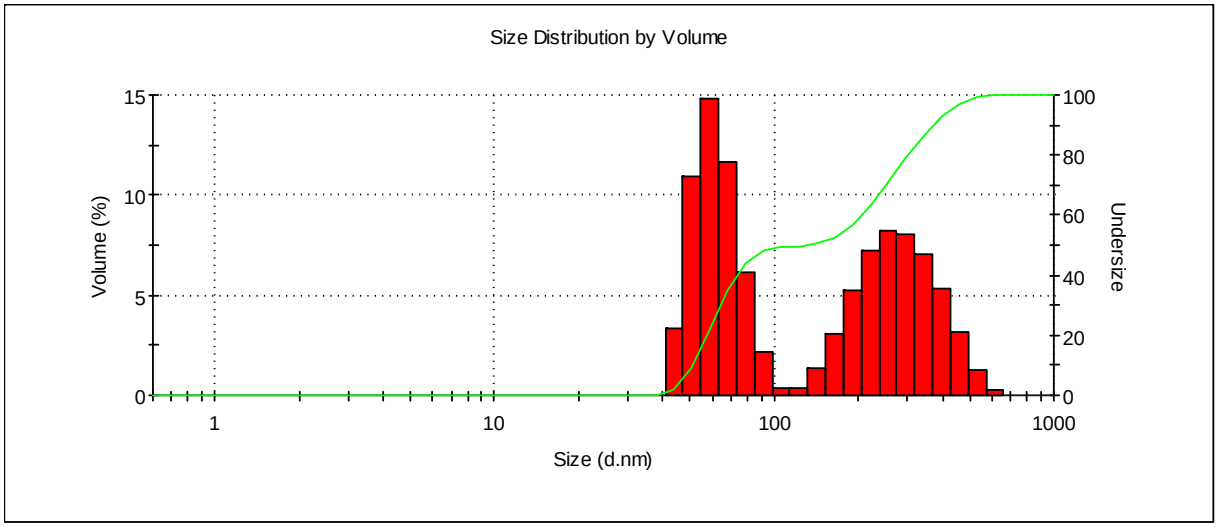


Figure S10: Sample size volume distribution during the assembly experiments of **Tiiii-AuNPs** in $CHCl_3$ with guest **4** (concentration of nanoparticle bound **Tiiii)** ≈ $1x10^{-5}$ M, [**4**]=$0.34x10^{-5}$ M, 1300 min., methanol, 20°C). Hydrodynamic diameters: d_H (average)=170 nm (PDI=0.29), single distributions d_H small=(64±10) nm, d_H large=(270±80) nm.