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Gold Functionalized Platinum M₁₂L₂₄-Nanospheres and Their Application in Cyclization Reactions

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Abstract: Nanospheres can be formed by combining 24 bispyridinyl building blocks with a palladium or platinum precursor. These spheres can be functionalized on the inside with a gold(I) chloride complex leading to a high local concentration of gold(I) complexes. The high local concentration makes the neutral gold species an active catalyst. Furthermore, the platinum-gold spheres can be post-modified with a silver(I) salt to form cationic gold(I) catalysts. The platinum assemblies are demonstrated to be stable in the presence of various substrates and as a result several cyclization reactions have been carried out using these new spheres as catalysts. Higher conversions in

a [4+2] cycloaddition are observed for the sphere catalyst compared to the mono-nuclear analogues. Also the cyclization of 1,6-enynes can be facilitated by the confined gold catalyst and high activity is observed in the activation of allenes. For the lactonization of alkynoic acids, a different selectivity is observed compared to a standard gold(I) complex, demonstrating that the high local concentration due to a confined space can induce other selectivity in catalysis.

Keywords: cyclization reactions; gold catalysis; local concentration; nanospheres; supramolecular catalysis

Introduction

Transition metal catalysis continues to play an important role for the sustainable fabrication of chemical products relevant to society. Complex pharmaceutical molecules can be created *via* shortcuts in synthetic routes with the help of new catalysts. Furthermore, waste-forming stoichiometric reactions can be avoided by using a catalyst. The field of transition metal catalysis has been dominated by rhodium, cobalt, palladium but recently, gold catalysis has gained increased interest in homogeneous and heterogeneous catalysis as it has been demonstrated to facilitate a large variety of cyclization, hydration and oxidation reactions,^[1,2] relevant for the formation of valuable compounds. Due to the soft and carbon coordinating character of gold it can be used to activate allenes,^[3] alkenes^[4] and alkynes.^[5] Recent studies have also shown that dual gold catalysis can occur, in which two gold atoms are active in the catalytic cycle.^[6,7] All these examples demonstrate that, by enabling carbon-

carbon or carbon-heteroatom bond formation, gold catalysts can be used to form a broad array of cyclic products. One of the challenges in gold catalysis is to control the selectivity of the reaction as different products can be formed due to the attack of the nucleophile on different positions. Traditional means to control the properties of a catalyst involve changing the ligands in the first coordination sphere of the active gold species. More recently it has been demonstrated that supramolecular chemistry allows the construction of a second coordination sphere around the catalyst as a new means to control the properties of the metal complex by placing it in confined space.^[8–12] To form a confined space around a metal complex, either a template-ligand approach can be used,^[13] or a catalyst can be encapsulated in a known preformed cage. For example, it has been demonstrated that a gold carbene complex confined in a hexameric capsule^[14] leads to a different product distribution and also the encapsulation of gold phosphine complexes in tetrahedral molecular containers led to enhanced

reactivity.^[15] In these examples, the capsule around the catalyst impedes a different selectivity, hence resulting in a new product distribution. Noticeably, only one catalytic center is isolated in these molecular cages. We recently communicated our strategy to organize up to 24 gold complexes in a confined space by applying the $M_{12}L_{24}$ nanospheres pioneered by the group of Fujita. Bent bispyridinyl building blocks (L) self-assemble in the presence of square planar palladium(II) complexes (M) to form large $M_{12}L_{24}$ spheres.^[16] By synthetic modification of the building block the spheres can be functionalized on the outside or inside.^[17] For example, Fujita et al. decorated the inside of these spheres with polyethylene glycol, fluororous or coronene groups.

We demonstrated that functionalization of the building block with a phosphine gold(I) chloride moiety results in the encapsulation of 24 gold species inside these $M_{12}L_{24}$ spheres. The confinement of multiple gold species gives rise to a high local gold concentration^[18] and leads to *aurophilic* d^{10} – d^{10} interactions, as evidenced by a change in the UV-Vis spectra. This results, in contrast to the monomeric gold, in an active gold catalyst although the complex remains in the neutral form (Au–Cl). The local average concentration of gold could be controlled by using mixtures of gold-containing and non-functionalized building blocks for the sphere assembly process. This gives the opportunity to study the effect of the local concentration of the gold complexes on the catalytic performance. In this contribution we will report the molecular sphere assembly of bispyridyl functionalized gold phosphine building blocks using a platinum precursor. This results in the formation of more stable spheres and as a consequence it broadens the potential scope of catalytic applications, which is demonstrated by the use of the spheres in different gold-catalyzed intramolecular cyclization reactions.

Results and Discussion

Assembly and Characterization of the Gold Functionalized Spheres

The group of Fujita has already demonstrated that the platinum sphere analogues are more stable to acidic and basic conditions due to the stronger platinum–pyridine bond.^[19] The more stable and robust platinum spheres that are decorated on the inside with gold complexes would therefore be better suitable for catalysis, as harsher reaction conditions can be employed compared to the palladium analogues. To investigate the formation of the platinum spheres, the previously reported bispyridyl functionalized gold phosphine building block was used. It was synthesized from 2,6-dibromophenol in four steps yielding com-

plex **A** (depicted in Figure 1a). The large $Pd_{12}A_{24}(BF_4)_{24}$ spheres were formed by adding a solution containing 0.5 equivalent of $[Pd(MeCN)_4](BF_4)_2$ complex to a CD_3CN solution of gold complex **A**. After stirring for one hour at 70 °C, a similar coordination was observed as in our previously reported palladium triflate spheres, according to 1H NMR spectroscopy (Figure 1b and c).^[18] For the formation of the platinum analogue of these spheres, the assembly was formed by stirring **A** with a solution of $[Pt(MeCN)_4](PF_6)_2$ for 24 h at 70 °C. After the reaction, a typical shift of pyridine signals in the 1H NMR spectrum is observed, confirming the formation of the sphere in solution. As reported in the literature, the 1H NMR peaks of the deshielded pyridine protons are broadened due to the restricted motion of the building blocks on the NMR timescale, which is caused by the strong pyridine–platinum bond.^[19,20] Further indication of the formation of spheres was given by *diffusion ordered NMR spectroscopy* (DOSY), displayed in Figure 1e. This reveals a diffusion constant of log *D* of $-9.51\text{ m}^2\text{ s}^{-1}$ and corresponds with the formation of a large species that has a diameter of 3.9 nm.

Activity of the Neutral Gold Assemblies in Cyclization Reactions

To explore the reactivity of the gold-containing platinum spheres, they were used in the intramolecular hydroalkoxylation of allenol **1**.^[21,22] The palladium spheres with 24 neutral gold chloride complexes were previously demonstrated to be active catalysts for this reaction, in contrast to the mono-gold chloride complexes (**A**), which show no conversion of **1**. It was demonstrated that the local high concentration of gold inside the nanosphere facilitates gold–gold interactions and results in an active catalyst. In the current experiments a different palladium salt as precursor for the synthesis of the supramolecular spheres was used leading to palladium spheres with different counter anions (BF_4 vs. OTf). Also for these spheres the neutral gold complexes inside the palladium sphere become active as a result of the high local concentration, yielding the five-membered ring as sole product (Table 1). Remarkably, we observed an effect of the counter anion as the current palladium sphere (BF_4) results in lower conversion of **1** compared to the previously reported sphere that has triflate anions (51% after 24 h vs. 90% yield after 12 h). As the inside of both spheres are functionalized with the same neutral gold complex, this indicates that the anions of the sphere itself also influences the cyclization of **1**, hence the reactivity of the gold complex is influenced by the palladium precursor that is used in the formation of the assembly. Importantly, the analogous gold-containing spheres based on platinum also

Figure 1. a) Synthesis and PM3 calculated structure of (Pt)₁₂(A)₂₄(PF₆)₂₄ spheres. ¹H NMR spectra of b) free building block A, c) (Pd)₁₂(A)₂₄(BF₄)₂₄ spheres and d) (Pt)₁₂(A)₂₄(PF₆)₂₄ spheres in CD₃CN. Protons indicated in the spectra display the shift of the pyridine signals due to metal-pyridine coordination. e) DOSY of (Pt)₁₂(A)₂₄(PF₆)₂₄ spheres showing a band corresponding with a size of 3.9 nm.

Table 1. Cyclization of allenol **1** into five membered ring **2**, catalyzed by the neutral gold chloride spheres.^[a]

Entry	Catalyst	Conversion [%] ^[b] 24 h	72 h
1	(Pd) ₁₂ (A) ₂₄ (BF ₄) ₂₄	51	83
2	(Pt) ₁₂ (A) ₂₄ (PF ₆) ₂₄	39	68
3	A	0	—

^[a] Reaction conditions: 8 μmol of substrate, 0.11 μmol of sphere. Total reaction volume contains 0.3 mL of CD₃CN and 0.5 mL of CD₂Cl₂.

^[b] Reaction was followed by ¹H NMR spectroscopy.

facilitate the cyclization and convert the substrate solely into the five-membered ring product with 39% conversion after 24 h. The reaction continues to proceed as after 72 h (room temperature) 68% of the product is formed.

To further look into the reactivity of the spheres, functionalized at the inside with gold complexes, we investigated their activity in the [4+2] cycloaddition of **3**, which is reported to be catalyzed by cationic gold(I) complexes.^[23,24] The palladium-based sphere containing the neutral gold chloride complexes proved to be almost inactive in the cyclization of substrate **3** (Table 2, entry 1). Furthermore, the same catalyst based on the building block (A) showed a negligible activity as only 3% conversion to product **4** is observed after 24 h. Interestingly, using the same conditions with the platinum sphere showed a conversion of 15% to exclusively form product **4** (entry 3). We in-

Table 2. [4+2] Cycloaddition of substrate **3** to product **4**, catalyzed by neutral gold(I) species.^[a]

Entry	Catalyst	Conv. [%] after 24 h ^[b]
1	(Pd) ₁₂ (A) ₂₄ (BF ₄) ₂₄	3
2	A	4
3	(Pt) ₁₂ (A) ₂₄ (PF ₆) ₂₄	15
4	Ph ₃ PAuCl	6
5	[Pt(MeCN) ₄](PF ₆) ₂	6
6 ^[c]	(Pt) ₁₂ (B) ₂₄ (PF ₆) ₂₄	3

^[a] Reaction conditions: 30 μmol of substrate, catalyst, based on 1.5 μmol of Au or 0.75 μmol of Pt. Total reaction volume contains 0.3 mL of CD₃CN and 0.2 mL of CD₂Cl₂.

^[b] Reaction was followed by ¹H NMR spectroscopy, depicted conversion is an average of two reactions.

^[c] Pt₁₂B₂₄(PF₆)₂₄ (entry 6), is a platinum sphere made of a building block functionalized with a methoxy group (B) of which the structure is depicted in Figure 2.

investigated the reaction mixture during catalysis and observed by NMR spectroscopy that the palladium-based sphere disassembles during the reaction. In the ¹H NMR spectra, the formation of the free building block with a chemical shift around 8.5 ppm is observed (see the Supporting Information, S4). This indicates that under the reaction conditions the alkyne destabilizes the sphere, possibly by coordination to the palladium atoms that hold the sphere together. Interestingly, the platinum-based assembly showed no formation of the free building block under these reaction conditions, and the broad singlet indicative for the sphere remains visible in the ¹H NMR spectrum during the reaction. This corresponds with the expected higher stability of these spheres, which is based on the stronger pyridine–platinum bond, making the assemblies resistant to substrates that can also bind to the metals that are used for the sphere formation.

The reactivity of the platinum-based sphere containing the 24 gold complexes was higher than the neutral triphenylphosphine gold(I) chloride catalyst (entry 4). The higher conversion with the neutral gold catalyst inside the platinum spheres demonstrates that the high local concentration of metal complexes can yield a more active catalyst. Control experiments using the platinum(II) building block or a platinum sphere that was functionalized with a methoxy group at the inside (entry 5 and 6), showed in both cases lower conversion, indicating that the gold species are responsible for the activity as the platinum plays no role in the conversion to product **4**.

Application of Cationic Gold Complexes inside the Spheres

With the known higher activity of cationic gold complexes we wondered if the stability of the platinum-based sphere is sufficient to allow the formation of cationic gold complexes inside such spheres. Therefore, the assembled sphere, Pt₁₂A₂₄(PF₆)₂₄ was mixed with a solution of AgPF₆ to form the cationic gold species. We confirmed by NMR spectroscopy that the platinum sphere remains stable in the presence of AgPF₆ and substrate (see the Supporting Information, S4) and no free building block was observed over time. The activity of the cationic gold complexes was higher than that of the neutral analogue as full conversion of the substrate was observed after 24 h at room temperature (Table 3, entry 1). The activity of the cationic gold sphere is more active than that of the cationic gold complex A (entry 2), which shows significantly lower conversion compared to the sphere (22%). Similar to previous observations with the neutral gold species, the palladium-based sphere shows similar reactivity as the free building block (17% conversion, entry 3), caused by the decomposition of the spheres under these conditions due to the weaker palladium–pyridine interactions. As another control experiment, we also evaluated a standard catalyst, (triphenylphosphine gold chloride with AgPF₆) under these conditions (entry 4). Although the conversion

Table 3. [4+2] Cycloaddition of substrate **3** to product **4**, catalyzed by cationic gold(I) species.^[a]

Entry	Catalyst	Conv. [%] after 24 h ^[b]
1	(Pt) ₁₂ (A) ₂₄ (PF ₆) ₂₄	97
2	A	22
3 ^[c]	(Pd) ₁₂ (A) ₂₄ (BF ₄) ₂₄	17
4	Ph ₃ PAuCl	54
5	AgPF ₆	3
6 ^[d]	(Pt) ₁₂ (B) ₂₄ (PF ₆) ₂₄	3

^[a] Reaction conditions: 30 μmol of substrate, catalyst, based on 1.5 μmol of Au and 1.5 μmol of AgPF₆. Total reaction volume contains 0.3 mL of CD₃CN and 0.2 mL of CD₂Cl₂.

^[b] Reaction was monitored by ¹H NMR spectroscopy, conversion is an average of two reactions.

^[c] Based on ¹H NMR spectroscopy the sphere decomposes and free building block A is observed (see the Supporting Information, S4).

^[d] Pt₁₂B₂₄(PF₆)₂₄ (entry 6), is a platinum sphere made of a building block functionalized with a methoxy group (B) of which the structure is depicted in Figure 2.

observed is higher than that in the experiment with the free building block **A** (54% conversion vs. 22%), it does not reach full conversion as observed with the platinum spheres after 24 h. In the final control experiments, we excluded that any of the other metals (Ag/Pt) present in the solution acts as a catalyst for

this reaction (entry 5 and 6). With the $Pt_{12}A_{24}(PF_6)_{48}$ species being the best catalyst under these conditions, we demonstrated that also for this reaction the high local concentration of cationic gold species inside the sphere is beneficial for the conversion of **3** into **4**.

Figure 2. Effect of the local concentration of the catalyst on the cyclization of **3** when 1% of gold complex is used. The conversion of the product is plotted in time. *Reaction conditions:* 150 μ mol of substrate, catalyst, based on 1.5 μ mol of Au and 1.5 μ mol of $AgPF_6$. Total reaction volume contains 0.3 mL of CD_3CN and 0.2 mL of CD_2Cl_2 . Reaction was monitored by 1H NMR spectroscopy, conversion is an average of two runs.

The higher stability of the cationic gold complexes inside the sphere was further demonstrated when a lower catalyst loading (1% of gold) was utilized for the [4+2] cycloaddition. Monitoring the cyclization in time with 1% of sphere gold(I) complex yielded 41% conversion to the product **4** after one day and the reaction still proceeds (see Figure 2). The activity is considerably higher when compared to the achieved conversion of the free building block (5% yield of **4**) or Ph_3PAu^+ (19% yield) under the same conditions, also depicted in Figure 2. Again, these experiments demonstrate the effect of the local high concentration of gold complex on the activity of the catalyst. To further investigate if we can control the reactivity of the system by changing only the local concentration of cationic gold(I) complexes, we investigated the effect of local dilution of the gold complex by using mixtures of functionalized/non-functionalized building blocks (**A** and **B**) in different ratios during the sphere assembly. This leads to statistical mixtures in which the local concentration decreases with increasing amount of **B**, a strategy that previously was demonstrated with the palladium-based spheres.^[18] For the catalysis experiments, solutions of spheres were prepared with building block ratios of 18:6 and 6:18 (**A**:**B**), while keeping the overall concentration of gold (building block **A**) the same. Hence, we diluted the effective local concentration of the gold complex. The conversion of substrate **3** with these diluted gold complexes was monitored in time and is plotted in Figure 2. The results clearly demonstrate that the highest activity is obtained in the experiment with a higher local gold concentration, which gradually de-

creases with the lower local concentration of the gold complex. This correlation between the local catalyst concentration and activity demonstrates that the high local concentration of the gold species inside the sphere enhances the activity of the catalyst.

In addition to facilitating [4+2] cycloadditions and the cyclization of allene functionalities into heterocycles, we were also interested in the effect of the local high concentration on the cyclization of 1,6-enynes. As a model substrate, 1,6-enyne **5** was used. It has been reported in literature^[5,25,26] that this substrate can give multiple products depending on the gold(I) catalyst that is used. A 6-*endo*-dig reaction leads to the formation of the 6-membered ring product **6** whereas a 5-*exo*-dig cyclization results in the formation of a 5-membered ring intermediate. This intermediate, known to be a gold(I) carbene,^[25,26] can then undergo proto-deauration to form product **7** or it can be attacked by a nucleophile (like water) to give product **8** (see Table 4). Interested in the effect of the high local concentration, this cyclization was carried out with our gold functionalized nanosphere. When we added the silver additive (AgPF_6) and subsequent 1,6-enyne **5** in CD_3CN to a solution of $\text{Pt}_{12}\text{A}_{24}(\text{PF}_6)_{24}$ we observed no conversion of the starting material after 24 h at room temperature. Acetonitrile is an uncommon solvent in gold catalysis, as the coordinating character of this solvent hampers the reaction by competing for the vacant site. Therefore, other solvents for the assembly of the spheres and subsequent catalytic reactions were explored. The insolubility of the building blocks hampered the formation of the spheres in various standard solvents like dichlorome-

Table 4. Gold(I)-catalyzed cyclization of 1,6-enyne **5** into 6-, 5-membered ring or hydrolyzed product **6**, **7** and **8** in nitromethane- d_3 at room temperature.^[a]

Entry	Catalyst	Conv. [%] ^[b]	6	7	8	Ratio 6 : 7
1 ^[c]	(Pt) ₁₂ (A) ₂₄ (PF_6) ₂₄	0	0	0	0	
2 ^[c]	A	0	0	0	0	
3	(Pt) ₁₂ (A) ₂₄ (PF_6) ₂₄	100	38 (39)	56 (55)	6 (7)	0.68 (0.70)
4	A	0	0	0	0	
5	(Pt) ₁₂ (B) ₂₄ (PF_6) ₂₄	0	0	0	0	
6 ^[d]	[Pt (MeCN) ₄](PF_6) ₂	0	0	0	0	
7	AgPF_6	0	0	0	0	
8	Ph_3PAuCl	100	40 (39)	58 (51)	2	0.69 (0.76)

^[a] Reaction conditions: 30 μmol of substrate, catalyst, based on 1.5 μmol of Au and AgPF_6 . Total reaction volume contains 0.5 mL of CD_3NO_2 .

^[b] Conversion is based on ^1H NMR spectroscopy and is an average of two runs; numbers in parentheses are isolated yields.

^[c] Reaction was performed in ACN/DCM mixture (3:2) for 24 h.

^[d] 0.75 μmol of Pt was used.

thane, toluene or methanol (see the Supporting Information, S9). One of the solvents that is able to solubilize both building blocks is nitromethane. Thus, a combination of the gold chloride building block **A** with a platinum precursor in nitromethane- d_3 resulted in a clear solution. The typically shift of the pyridine protons and DOSY experiments confirm the smooth formation of the spheres also in this solvent. For the catalysis experiments, this nanosphere pre-catalyst was treated with $AgPF_6$ after which the substrate was added. As the reaction was carried out in nitromethane- d_3 , the reaction progress could be monitored by 1H NMR spectroscopy.

The use of the gold complexes in this less coordinating solvent resulted in the rapid formation of a mixture of 5- and 6-membered products (see Table 4, entry 3), with full conversion of the starting material within 30 min. Due to the presence of small amounts of water in the solvent, also some hydrolyzed product (**8**) is observed. The mononuclear complex **A** showed no conversion at all under these conditions (entry 4). It is likely that the free pyridine moieties of **A** inhibit the cationic gold(I) complex through coordination, thus preventing catalysis. Control experiments confirmed that the other metals present (Pt, Ag), which can form these products at elevated temperatures,^[27–31] are not active under these conditions at room temperature (Table 4, entries 5–7).

To compare our system to a mononuclear gold complex, we utilized triphenylphosphine gold(I) under the same reaction conditions (entry 8). Cyclization of substrate **5** by Ph_3PAu^+ gave also full conversion within half an hour (entry 8). As both reactions went to full completion after 30 min, no information is available of the sphere effect on the activity in this reaction. Based on the 1H NMR spectra, a similar ratio of the products with the five- and six-membered ring is obtained, which indicates that the high local concentration of catalyst does not lead to a different product distribution in this reaction.

Next, we studied the gold-catalyzed conversion of enyne **9**.^[32–34] The gold catalysts inside the sphere rapidly converted **9** into the 5-membered product (**12**) as the major compound (Table 5, entry 1). In addition, small amounts of the six-membered ring **10** and hydrolyzed product (**13**) are also formed.

Under the same reaction conditions the mononuclear complex, triphenylphosphinegold(I), also converted the substrate within 30 min. The mononuclear complex appears less selective for the formation of **12** (Table 5, entry 2). While the amount of six-membered ring (**10**) is the same as with the gold-functionalized spheres when Ph_3PAuCl is used, also the isomerized five-membered ring product (**11**) is observed. This product **11** is not formed at all under the same conditions after 30 min when $Pt_{12}A_{24}(PF_6)_{24}$ is used as catalyst. As compound **11** could be formed from **12** by

Table 5. Cyclization of 1,6-enyne **9**.^[a]

Entry	Catalyst	Conv. [%] ^[b]	10	11	12	13
1	$(Pt)_{12}(A)_{24}(PF_6)_{24}$	100	9	0	79	12
2	Ph_3PAuCl	100	13	23	63	0
3 ^[c]	$(Pt)_{12}(A)_{24}(PF_6)_{24}$	100	11	28	55	7
4 ^[c]	Ph_3PAuCl	100	15	53	32	0

^[a] Reaction conditions: 30 μ mol of substrate, catalyst, based on 1.5 μ mol of Au and $AgPF_6$. Total reaction volume was 0.5 mL of CD_3NO_2 .

^[b] Conversion and ratio is based on 1H NMR spectroscopy and is an average of two runs.

^[c] Ratio of products after 24 h.

isomerization, we investigated the product distribution after a prolonged reaction time. As displayed in entries 3 and 4, more of **11** is formed after 24 h, also in the catalytic experiment where $Pt_{12}A_{24}(PF_6)_{24}$ is applied, suggesting that the high local concentration of gold complexes has a slower isomerization rate and therefore yields a higher selectivity.

To further explore the scope of the possible transformations by the cationic gold complexes inside the sphere we utilized them in the cyclization of allenol **1**.^[21,22] High selectivity with the stable spheres with cationic gold complexes, which were generated *in situ* by the addition of $AgPF_6$, is obtained and full conversion to product **2** is observed within two hours at room temperature.

Compared to the neutral gold complexes in the sphere (see Scheme 1 and Table 1) faster and higher conversion to the product is obtained, which is expected for the generally more active cationic gold complexes. The higher stability of the platinum-based spheres allows the use of an acid as nucleophile and thus allenic acid **14** could also be cyclized, yielding lactone **15** as the sole product.^[35]

As a final case study for our stable assemblies with confined gold complexes we investigated the lactonization of alkynoic acids. Again the assembly remained stable when either 4-pentynoic acid (see the Supporting Information, S8) or hex-4-ynoic acid (**16**) was used as the substrate, demonstrating the stability in the presence of acids (see Table 6). Control experi-

Scheme 1. Cyclization of allenes **1** and **14**, catalyzed by the platinum-based gold sphere. Conversions are given based on ^1H NMR spectroscopy. The numbers in parentheses are isolated yields. *Reaction conditions:* 30 μmol of substrate, catalyst, based on 1.5 μmol of Au and AgPF_6 . Reaction volume is 0.5 mL of CD_3NO_2 .

Table 6. Gold(I)-catalyzed lactonization of hex-4-ynoic acid.^[a]

Entry	Catalyst	Conv. [%] ^[b]	17	18	Ratio 17:18
1	(Pt) ₁₂ (A) ₂₄ (PF ₆) ₂₄	100	67	33	2.0
2	Ph ₃ PAuCl	100	92	8	11.5
3	(Pt) ₁₂ (B) ₂₄ (PF ₆) ₂₄	0	–	–	–

^[a] *Reaction conditions:* 60 μmol of substrate, catalyst, based on 1.5 μmol of Au and AgPF_6 . Reaction volume was a total of 0.5 mL CD_3NO_2 .

^[b] Conversions are based on ^1H NMR spectroscopy and is an average of two independent runs.

ments showed that the spheres that have no gold are not active in this transformation (entry 3). Interestingly, the cationic gold complexes in the sphere give rise to a different product distribution compared to the control experiment with Ph_3PAu^+ as catalyst, indicated by the ^1H NMR spectra. The spheres with the embedded high local concentration of gold complexes $\text{Pt}_{12}\text{A}_{24}(\text{PF}_6)_{24}$ form the 6-membered ring **17** and 5-membered ring **18** in a 2:1 ratio (see Table 6, entry 1), whereas the mononuclear Ph_3PAu^+ catalyst gives a ratio of 11:1. The clear difference in product ratio of the different catalysts shows that the high local concentration of gold complexes influences the selectivity of the reaction, resulting in more formation of the 5-membered ring **18**.

Conclusions

We had previously studied gold-catalyzed transformations at extremely high local concentrations by using self-assembled nanospheres using palladium coordination chemistry. The number of transformations that were catalyzed by these systems was limited due to the instability of the spheres in the presence of substrates with certain functional groups, and also the cationic gold complexes could not be generated within these spheres. In this paper we report platinum-based assemblies using similar ditopic pyridine (gold-containing) ligands. Also within these assemblies, a high local concentration of gold(I) is obtained. The platinum-based spheres show a higher tolerance for functional groups, enabling a broader scope in catalysis, which is demonstrated by their use in various gold-catalyzed cyclization reactions. We demonstrate that the high local concentration of gold complexes can give a higher conversion in [4+2] cycloadditions. The platinum-based spheres are sufficiently stable to generate the cationic gold complexes, which are known to be more reactive than the neutral analogues, *via* post modification by reaction with silver salts. The high local concentration of cationic gold complex has a positive effect on the activity of the gold catalyst in the [4+2] cycloaddition. Furthermore, 5-*exo*-dig and 6-*endo*-dig reactions are possible within the spheres containing cationic gold complexes in a polar but less-coordinating solvent (nitromethane). We observed that the catalyst in the sphere has a lower rate for the isomerization of the product compared to an electronically similar, but mononuclear free catalyst (Ph_3PAu^+), and as a result the sphere catalyst displays a higher selectivity. The lactonization of hex-4-ynoic acid also resulted in a different product distribution with sphere catalyst and a higher selectivity for the five-membered ring is observed. In this paper we have shown that the platinum-based spheres remain stable under various conditions, extending the possibilities to study catalytic reactions at extremely high local concentrations. The observation of a higher reactivity and different selectivity of these stable spheres is encouraging, and as such we will explore their application in other transformations.

Experimental Section

(Pd)₁₂(A)₂₄(BF₄)₂₄

A vial was charged with **A** (8.6 mg, 10 μmol , 1 equiv.) and dissolved in 0.3 mL of CD_3CN . A separate vial was charged with $[\text{Pd}(\text{MeCN})_4](\text{BF}_4)_2$ (2.44 mg, 5.5 μmol , 0.55 equiv.), dissolved in 0.2 mL of CD_3CN and transferred to the first vial. The resulting yellow solution was stirred at 70 °C for 1 hour after which NMR spectroscopy showed full conversion towards the sphere. ^1H NMR (300 MHz, CD_3CN): $\delta =$

9.01 (d, $J=4.8$ Hz, 4H), 7.64 (d, $J=7.9$ Hz, 2H), 7.57 (d, $J=5.9$ Hz, 4H), 7.47–7.10 (m, 10H), 7.15–6.82 (m, 2H), 6.83–6.46 (m, 1H), 4.14 (s, 2H), 3.94 (s, 2H), 1.82 (s, 4H); ^{31}P NMR (121 MHz, CD_3CN): $\delta=32.84$ (s); HR-MS (ESI+): $m/z=2316.0786$, calcd. for $[(\text{Pd})_{12}(\text{A})_{24}(\text{BF}_4)_{14}]^{10+}$; 2316.0837, $m/z=2097.5266$, calcd. for $[(\text{Pd})_{12}(\text{A})_{24}(\text{BF}_4)_{13}]^{11+}$; 2097.5302, $m/z=1915.4827$, calcd. for $[(\text{Pd})_{12}(\text{A})_{24}(\text{BF}_4)_{12}]^{12+}$; 1915.4857, $m/z=1761.44520$, calcd. for $[(\text{Pd})_{12}(\text{A})_{24}(\text{BF}_4)_{11}]^{13+}$; 1761.4480, $m/z=1629.4126$, calcd. for $[(\text{Pd})_{12}(\text{A})_{24}(\text{BF}_4)_{10}]^{14+}$; 1629.4157, $m/z=1514.9854$, calcd. for $[(\text{Pd})_{12}(\text{A})_{24}(\text{BF}_4)_9]^{15+}$; 1514.9877.

$(\text{Pt})_{12}(\text{A})_{24}(\text{PF}_6)_{24}$

A vial was charged with **A** (8.6 mg, 10 μmol , 1 equiv-) and dissolved in 0.3 mL of CD_3CN . A separate vial was charged with $[\text{Pt}(\text{MeCN})_4](\text{PF}_6)_2$ (3.57 mg, 5.5 μmol , 0.55 equiv.), dissolved in 0.2 mL of CD_3CN and transferred to the first vial. The resulting solution was stirred at 70 °C for 24 h after which NMR spectroscopy showed full conversion towards the sphere. ^1H NMR (300 MHz, CD_3CN): $\delta=8.88$ (s br, 4H, Py), 7.56 [s br, 2H (Ar)+4H (Py)], 7.31 (s br, 10H, Ar), 6.98 (s br, 2H, Ar), 6.68 (s br, 1H, Ar), 4.20 (s br, 2H, CH_2), 3.92 (s br, 2H, CH_2), 1.83 (s br, 4H $2\times\text{CH}_2$); ^{31}P NMR (121 MHz, CD_3CN): $\delta=32.93$ (s), -141.59 (p); ^{19}F NMR (282 MHz, CD_3CN): $\delta=-72.40$ (d, $J=709.5$ Hz); DOSY (CD_3CN , 25 °C): $\log D=-9.51\text{ m}^2\text{ s}^{-1}$. Authors would like to note that, due to broadening of the peaks, no ^{13}C NMR is possible of this assembly. $(\text{Pt})_{12}(\text{A})_{24}(\text{PF}_6)_2$ in CD_3NO_2 : ^1H NMR (400 MHz, CD_3NO_2): $\delta=9.48$ –8.33 (m, 4H), 8.16–6.51 (m, 17H), 4.12 (s br, 4H), 1.99 (s br, 4H); ^{19}F NMR (282 MHz, CD_3NO_2): $\delta=-75.52$ (d, $J=707.6$ Hz); ^{31}P NMR (162 MHz, CD_3NO_2): $\delta=33.17$, -144.57 (hept, $J=708.1$ Hz); DOSY (CD_3NO_2 , 25 °C): $\log D=-9.82\text{ m}^2\text{ s}^{-1}$.

Standard Procedure for the Cyclization of **3** without Activation

A vial was charged with a stock solution of substrate **3** (30 μmol , 100 μL solution in CD_2Cl_2). Then, a solution of catalyst was added (1.5 μmol based on Au; solution of spheres was added in CD_3CN ; solution of building block **A** or Ph_3PAuCl was added in CD_2Cl_2). Then the solution was diluted to a total volume of 0.2 mL of CD_2Cl_2 and 0.3 mL of CD_3CN after which the reaction was followed by NMR spectroscopy over time.

Standard Procedure for the Cyclization of **3** with Activation

A vial was charged with a solution of AuCl complex (1.5 μmol based on Au, **A** or Ph_3PAuCl was added as a stock solution in CD_2Cl_2 , sphere was added as a solution in CD_3CN). A solution of 1.5 μmol AgPF_6 (in 75 μL CD_3CN) was added and left to stand for 15 min. Then, it was further diluted to a total volume of 0.1 mL CD_2Cl_2 and 0.3 mL CD_3CN . Finally a solution of substrate (30 μmol , in 100 μL CD_2Cl_2) was added and the reaction was followed by NMR spectroscopy.

Standard Procedure for the Cyclization Reactions in CD_3NO_2

A NMR tube with a screw cap was flushed 3 times with N_2 /vacuum. Then, under N_2 , the tube was charged with catalyst (1.5 μmol of Au, 150 μL of a sphere solution based on 10 μmol of **A** in 1 mL of CD_3NO_2 and pre-dried over 3 Å molecular sieves) and a solution of AgPF_6 [1.5 μmol in 50 μL , not(!) dried over 3 Å molecular sieves] was added. The solution was diluted with 250 μL of CD_3NO_2 (pre-dried over 3 Å molecular sieves), shaken and left to stand for 15 min at room temperature. Then a solution of 30 μmol of substrate in 100 μL of CD_3NO_2 (pre-dried over 3 Å molecular sieves) was added, the NMR tube was sealed, shaken again and measured after 30 min. For the isolation of the products, the crude reaction mixture was flushed over a plug of silica with ethyl acetate and concentrated. A mixture of the products was obtained after which the yield was determined with ^1H NMR spectroscopy. The spectral data of the products (**6**,^[25] **7**,^[36] **8**^[37]) corresponded with those reported in the literature and were confirmed with COSY. For the cyclization of enyne **9**, no isolation was performed but the spectral data of the products corresponded with those reported in the literature.^[34]

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