Catalytic self-assembled monolayers on gold nanoparticles

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This review describes the attractiveness of catalytic self-assembled monolayers (SAMs) on gold nanoparticles as catalytic systems. The hybrid inorganic–organic catalytic systems combine the advantages of homogeneous and heterogeneous catalysis (higher activity and catalyst recycling, respectively). The high fidelity process of SAM formation on gold nanoparticles, together with the possibility of making mixed SAMs composed of different thiols, provides an unprecedented route to stable, complex catalytic systems. Insertion of catalysts in a mixed monolayer can improve the catalytic performances, due to catalyst orientation, changes in the local chemical environment, or through the steering effect of neighbouring thiols. Alternatively, insertion of catalytic units in a monolayer may be an essential prerequisite in the case when catalysis requires cooperation between two catalytic units (for instance two metal ions). Finally, the multivalent nature of these systems is an important feature especially in the case when the substrate contains multiple reactive sites. Catalytic SAMs on gold nanoparticles also find applications beyond the field of catalysis, for instance in diagnostics and nanotechnology.

Introduction

The demand for atom-efficient chemical transformations with a low environmental impact makes catalyst development one of the main challenges for chemists. A wide variety of innovative approaches are being developed aimed either at a rapid identification and screening of new catalysts or at a facilitated use of established catalysts. Examples include combinatorial high-throughput screening protocols,1,2 supramolecular catalysis,3 directed evolution approaches4 and the use of supported homogeneous catalysts.5 Within this general framework, this review focuses on a sub-topic which is the application of monolayer protected gold clusters (Au MPCs) for catalysis.6–8 Several reasons exist for why these systems are of particular interest for application in catalysis. The main interest arises from the possibility of combining the advantages of heterogeneous and homogeneous catalysts in a single hybrid system. Anchoring of a catalyst on a solid support creates the possibility of catalyst recycling by filtration, which in the case of nanoparticles is typically preceded by solvent-induced aggregation. Simultaneously, the systems are homogeneously dissolved in the reaction medium and the catalysts localized at the periphery of the self-assembled monolayer (SAM) behave as if molecularly dissolved. An additional advantage of using nanoparticles with nanometer-size dimensions is their high organic–inorganic ratio, which limits the amount of required supporting material. Evidently, these...
advantages are not specific for gold nanoparticles. Indeed, the use of gold nanoparticles as a mere supporting material is more and more surpassed by other metals (like Fe2O3 or coated Fe, Co, etc.). This trend is mainly driven by the facilitated recycling of the (magnetic) catalytic material. This type of hybrid catalytic system has recently been extensively discussed in excellent reviews. However, there is a second major reason why monolayer protected gold nanoparticles are attractive systems for catalysis, which is directly related to the organic monolayer covering the gold nucleus. A monolayer is obtained through a self-assembly process driven by the formation of (most frequently) a stable Au–S bond. The result is the straightforward formation of a multivalent system similar to micelles, but with a significant higher stability. The use of self-assembly marks a difference compared to catalytic dendrimers which are typically obtained through covalent synthesis. Anchoring of thiols on the gold surface induces a unidirectional orientation of these molecules, which means that the self-assembly process contains an element of topological control. This positions the peripheral groups in close proximity exposed to the bulk solvent. Furthermore, the composition of the organic monolayer can be controlled in a highly predictable manner through synthetic protocols (e.g. by using multiple thiols for coverage or through place-exchange reactions on pre-formed monolayers). From the examples discussed in this review (with a full surface coverage of the gold nanoparticles by thiols) it will emerge that the SAM can play a crucial role in determining the catalytic properties of the system. In mixed monolayers thiols surrounding the catalyst may affect the efficiency and selectivity of the catalyst. This may occur through general effects (pH, polarity) originating from a micro-environment surrounding the SAM which is different from the bulk. Alternatively, embedding the catalyst within the SAM rather than at the periphery may create an enzyme-like catalytic cleft which may affect substrate orientation and thus the selectivity of product formation. Finally, the multivalency of the catalytic system may be exploited to induce substrate selectivity, in particular in the case when the substrate itself contains multiple reactive sites. The catalytic systems treated in the review are divided depending on the type of catalyst used (metal-based catalysis or organocatalysis).

Metal-chelating SAMs for catalysis

Hybrid homogeneous–heterogeneous catalytic systems

A first example of a transition-metal complex immobilized on gold nanoparticles was reported in 1998 by Tremel et al. Catalytic Au MPC 1 was prepared by mixing 4-methylhexa-3,5-diene-1-thiolated gold nanoparticles with RuCl3 and used as such for the ring-opening metathesis polymerization (ROMP) of norbornene (Scheme 1). Although not soluble in the reaction medium (dichloromethane), the obtained system showed an impressive increase in the TOF compared to the molecular catalyst (16 000 h−1 against 3000 h−1). The authors tentatively ascribed this effect to the orientation of the catalyst on the surface, which favours its interaction with the monomer and the growing polymer chain.

In another pioneering example, Mrksich et al. immobilized a dihydroquinone ligand on gold nanoparticles of around 2.5 nm and used the obtained Au MPC 2 in the presence of OsO4 for the asymmetric dihydroxylation of β-substituted styrene (Scheme 2). In all cases, the corresponding diols were obtained with yields of around 80% and enantiomeric excesses (ee’s) of 85–90%. Recycling of the catalyst resulted in a small drop in both the yield and ee to 72 and 79%, respectively, when β-methyl styrene was used. This was ascribed to the desorption of alkanethiols from the colloids.

In an analogous manner, Sasai et al. covered 5 nm sized gold nanoparticles with a homogeneous monolayer terminated with (R)-1,1-bi-2-naphthol ((R)-BINOL) moieties. The catalytic activity of system 3, after in situ formation of the Ti-BINOL, was tested on the asymmetric alyklation of benzaldehyde with Et2Zn (Scheme 3). Also in this case the catalytic system displayed activities comparable to the isolated catalyst both in terms of yield (＞95%) and ee (80–90%). Interestingly, however, it was observed that the obtained ee was dependent on the length of the alkyl chain of the used thiol with a maximum for an intermediate length of 5 carbons. Although not further investigated, this observation was a first clue suggesting that the SAM may be more than just an innocent organic support.

This point was effectively made by Pfaltz et al. who distinguished two different situations for catalytic SAMs (Fig. 1). A convex catalytic site is formed in the case when the metal center extends out of the SAM. In this case, it can be expected that the catalyst behaves most closely as a homogenously solubilized catalyst. In this case, the SAM may serve to physically separate...
catalysts and thus prevent de-activation through catalyst aggregation or may indirectly affect the catalytic parameters through additional interactions with the substrate. Alternatively, in the case when the metal center is embedded in the monolayer (for example, by using a shorter alkyl spacer), a concave active site is formed resembling the active site of an enzyme. This would give the perspective of modulating the catalytic parameters by changing the neighbouring thiols. So, mixed monolayers were prepared on 2.3–3.5 nanometer-sized gold nanoparticles from thiols terminating with chiral rhodium catalysts in combination with thiols of different length (C₆–C₁₀) and head group polarity (CH₃ vs. OH, NH₂). For the apolar systems conversions (>99%) and ee’s (93%) were obtained in the hydrogenation of methyl α-acetamidocinnamate, which were nearly identical to the monomeric reference catalyst. However, the polar colloids appeared to perform less, both in terms of reactivity (between 32 and 94%) and ee (between 68 and 86%). Although the reason for this observation was not clear, it illustrates well the importance of the surrounding thiols in controlling the activity of the embedded catalysts.

In a related approach, Tanaka et al. prepared mixed monolayers of thiols terminating with a chiral bisoxazoline-copper(II) complex but with different spacer length (C₄–C₁₀) and hexanethiol. Differences between the various systems only emerged after catalyst recycling with large drops in yield observed for those systems with the longest spacers. It was postulated that embedding the catalyst in the SAM protected the system from aggregation. Although the above results are interesting, they do not provide unequivocal evidence that the SAM is indeed able to affect intrinsic catalytic parameters such as rate or enantioselectivity. From this perspective, the most promising results have been reported by Paluti and Gawalt and for their importance will be treated here, even though the studies have been performed on flat gold surfaces rather than on nanoparticles.²⁰,²¹ Aza-bis(oxazoline) copper complexes were immobilized in 2D SAMs with three different surface orientations: above (4), even (5), and below (6) the head groups of the surrounding alkanethiols (Fig. 2a). The obtained systems were tested in the cyclopropanation reaction of ethyl diazoacetate and styrene (Fig. 2b). This reaction gives a trans- and cis-product, both as a couple of enantiomers. As a reference, the monomeric catalyst gave a cis/trans ratio of 20/80 with respective ee’s of 80 and 87%. Nearly identical results were obtained in the case when the catalyst was positioned well above the surrounding monolayer (cis/trans 23/77; eeₜ₇₇ = 81; eeₐ₈₅ = 85) indicating that this construction provides supported catalysts with homogeneous-like properties (Fig. 2c). Changes were observed upon positioning the catalyst even with the monolayer surface. The cis/trans ratio changed slightly to 16/84, but a significant increase in the ee of the trans-product was observed (from 87 to 93%). For the cis-isomer no change in enantioselectivity was reported (82 vs. 80), but, remarkably, the opposite enantiomer was favoured. Finally, embedding the catalyst within the monolayer caused a drop both in the cis/trans ratios (36/64), but also in the ee’s of both products (eeᵃᵩ = 37; eeᵄᵣᵩ = 45). The latter results were tentatively ascribed to the occurrence of steric interactions between the alkyl chains and the catalysts. From this comparative study emerges that the most advantageous situation occurs when the catalyst is levelled with the monolayer surface. This was even better evidenced with a modified catalyst containing methyl substituents rather than the bulky tert-butyl substituents. This system showed an increase in the cis/trans ratio

![Fig. 1 Schematic representations of concave and convex catalytic sites in monolayers on Au nanoparticles. In addition, also the intermediate situation with the catalysts positioned on the periphery of the monolayer is depicted.](image1)

![Fig. 2 (a) Catalytic monolayers formed on flat Au surfaces. (b) Cyclopropanation reaction of ethyl diazoacetate and styrene, (c) product ratios for the different catalytic monolayers.](image2)
from 34/68 to 9/91 with a concomitant increase in the ee’s from 62 to 86% for the trans-product and from 58 to 89% for the cis-product (with inversion). As such, this is one of a few examples in which the parameters of the catalyst have actually improved upon immobilization in a SAM. This study also clearly evidences the importance of the surface position of the catalyst.

In this context, a final example by Yu and co-workers is worth mentioning. They immobilized Pd-complexes on the surface of gold nanoparticles for use in the Heck coupling reaction between iodo-benzene and a series of acrylates. The ligand for Pd was inserted in a C8 apolar monolayer through the place-exchange protocol arriving at a 40–60% loading. Importantly, a sub-stoichiometric amount of Pd(CH3CN)2Cl2 precursor was added with respect to the ligand in order to generate the active catalyst. This suppressed leaching of Pd from the support, which is a well-known problem for supported Pd catalysts. A remarkably high catalytic activity was reported for both the fully and partially palladated catalysts reaching TOFs up to $4.87 \times 10^4 \text{ h}^{-1}$, which was even higher than that of the monomeric reference catalyst. The catalytic system could be quantitatively recovered as a black solid upon centrifugation and recycled. Conversions higher than 90% were obtained in the first 11 cycles after which it dropped gradually to 82% at the 15th cycle. For the fully palladated system a more rapid decrease in yield was observed, ascribed to a leaching of Pd.

Catalysis through induced cooperativity

A particularly interesting situation arises in the case when catalysis originates from the cooperative action between neighbouring thiols. Here, SAM formation by the thiols is a prerequisite in order to obtain a catalytically active system, since the isolated thiols are catalytically inactive. The first example was reported by Scrimin et al. and involved catalytic Au MPCs for the transphosphorylation of 2-hydroxypropyl-$\beta$-nitrophenyl phosphate (HPNPP), which is an RNA model compound (Fig. 3a). The catalytic units were composed of 1,4,9-triazacyclonanone (TACN)-Zn(n) complexes obtained in situ upon the addition of Zn(n) nitrate to 2 nm sized Au nanoparticles covered with TACN-terminating thiols. This system was coined a nanozyme for the analogy with enzymes in displaying Michaelis-Menten like substrate saturation behaviour. The system displayed a rate acceleration of over 40,000 ($k_{\text{cat}}/k_{\text{uncat}}$) compared to the background reaction ranking it among the best-performing Zn(n)-based catalysts for this reaction.

Remarkably, much lower rate accelerations were observed for analogous systems under identical conditions (pH, temperature, buffer) in which the identical complex was inserted in dendrimers or tripodal ligands, which demonstrates the effectiveness of the SAM in orienting two TACN-Zn(n) complexes to form a catalytic pocket. Evidence that the catalytic site was formed between two neighbouring TACN-Zn(n) complexes came from measurements of the initial rate of reaction as a function of the concentration of Zn(n) present (Fig. 3b). The observed sigmoidal profile indicates that catalytic activity is only present in the case when the amount of TACN-Zn(n) complexes on the surface is high enough so that neighbouring complexes are present in the monolayer.

At low ratios of Zn(n) only isolated complexes are present that are not catalytically active. In fact, subsequent studies on mixed monolayers composed of TACN Zn(n) and triethyleneglycol terminating thiols showed a strong decrease in catalytic activity ($k_{\text{cat}}$) for systems with a low molar fraction ($\chi < 0.4$) of TACN-Zn(n). This observation also provided evidence that the two thiols were randomly distributed on the surface. In addition, these studies pointed also to another intrinsic advantage of using multivalent scaffolds for the formation of catalytic pockets, in particular when a substrate pre-binding event occurs. Clustering of catalytic units in a SAM causes the formation of a large number of potential catalytic sites, since a catalytic unit can pick many neighboring units with whom to form a catalytic site. Effectively this increases the apparent concentration of catalytic sites compared to the same number of units organized in, for example, a dimeric system. Consequently, the multivalent system will display a much higher apparent binding constant. Although this has no effect on the efficiency of the catalytic site itself (which is determined by $k_{\text{cat}}$), it implies that the system will perform intrinsically better at lower concentrations.

Subsequent studies revealed a very high affinity of the cationic multivalent surface for oligoanions, such as ATP, ADP and Ac-DDD-OH. A systematic study of a series of phosphates and carboxylates revealed that the affinity of the oligoanions for the catalytic monolayer surface was strictly related to the number of negative charges of the probe. This characteristic was used for setting up an assay for the detection of enzyme activity, taking advantage of the catalytic activity of the monolayer. The enzyme assay relies on the use of an enzyme substrate $S_1$ that also functions as an inhibitor for the catalysis by the nanoparticles (Fig. 4). Upon hydrolysis by the enzyme, the substrate/inhibitor $S_1$ is fragmented and loses affinity for the monolayer surface. As a consequence, catalytic
activity of the monolayer is restored, resulting in the production of the p-nitrophenolate anion $P_2$ as a reporter molecule. An attractive feature of catalytic signal amplification is that the amount of produced signal depends on the turn-over number of the catalyst. This permits a much higher sensitivity compared to classical assays relying on the production of a single reporter for each substrate molecule cleaved.

The clustering of catalytic units in a SAM is appealing in all cases where the reaction is second order in the catalyst concentration. One such example is the hydrolytic kinetic resolution (HKR) of epoxides by chiral [salen]Co(III) complexes developed by Jacobsen et al.\textsuperscript{30} For that reason, the covalent connection of two catalysts or the immobilization of multiple copies on a multivalent scaffold has attracted an enormous interest, also driven by the industrial relevance of this chemical conversion. With the aim of combining highly active catalysts with an easy recovery and recycling, Jacobsen and Belser immobilized salen-terminated thiols on the surface of 3.4 nm-sized gold nanoparticles through place-exchange reactions with n-octane thiol (Scheme 4).\textsuperscript{31} A final ratio of 3 : 1 of catalytic and inactive thiolates was obtained after 36 hours, which is more than sufficient for guaranteeing the formation of dimeric catalytic pockets. The functionalized nanoparticles 8 were highly active in the HKR of racemic hexane-1-oxide, exhibiting complete kinetic resolution (>99.9% ee of recovered epoxide) within 5 h. The fact that similar results using a monomeric equivalent of the catalyst (at the same 0.01 mol% loading) required 52 hours illustrates the effectiveness of the system. Recycling of the system through centrifugal filtration did not affect the ee during seven cycles, but caused a 50% reduction in reactivity after the sixth recycling step. The original reactivity could be regenerated by reoxidation using TIOH and air.

**Multivalency**

Another attractive feature of catalytic SAMs originates from their multivalent nature, in particular when multivalent substrates are targeted. This is nicely illustrated by an example of Mancin, Scrimin et al. in which thiolated BAPA-Zn(II) complexes were immobilized on gold nanoparticles together with triethylene glycol-terminated thiols (Scheme 5).\textsuperscript{32} The obtained system Au MPC \textsuperscript{9} showed an extraordinary activity in the cleavage of the DNA model substrate bis-p-nitrophenylphosphate (BNP) with a rate acceleration of over 5 orders of magnitude over the background. Importantly, comparison with the monomeric complex BAPA-Zn(II) showed that insertion in the SAM caused a 100-fold gain in reactivity. Similarly to that observed in the system discussed above (Au MPC \textsuperscript{7}), the major source for this rate acceleration originates from the formation of dinuclear catalytic sites in the SAM. Nonetheless, the most intriguing aspect of this system appeared when DNA was used as a substrate. Incubation of pBR 322 plasmid DNA with the catalytic system resulted in a significant phosphodiester cleavage. Under the same conditions, the monomeric catalyst showed no activity at all. Remarkably, the amount of linear DNA formed was 50% larger than that of nicked DNA, the formation of which is statistically much more favourable. This result indicates that the multivalent system preferably performs double strand cleavage. This seems to be a consequence of the multivalency of the system, which generates multiple contacts between catalyst and cleavable bonds upon formation of the catalyst–substrate complex.

**Organocatalytic SAMs on gold nanoparticles**

Contrary to transition-metal based catalysts, the relatively low cost of organocatalysts makes that catalyst recovery is less an issue from an economic point of view. On the other hand, the typically high catalyst loadings required in organocatalysis may complicate product isolation. Catalyst immobilization alleviates this problem. Nonetheless, the main reason for the preparation of organocatalytic SAMs on gold nanoparticles is the interest in improving the intrinsic catalytic parameters of the catalyst through changes in the local chemical environment or cooperative effects.
Reinhoudt, Huskens et al. prepared sulfonic acid derivatized Au MPCs 10 for the hydrolysis of trimethylsilyl protected ethers (Scheme 6).35 Although at first sight gold nanoparticles may appear an odd (and expensive) choice as supporting material, this system served as a homogeneous model system for similar catalytic monolayers on AFM tips. The acidic nanoparticles indeed catalyzed in solution the hydrolysis of a TMS protected substrate (containing a disulfide bond for immobilization on a flat Au surface). Subsequently, it was shown by means of contact angle measurements, grazing incidence angle FT-IR and XPS that the TMS group was also effectively removed from a 2D SAM of the substrate on flat Au. This opened up the possibility of catalytic probe lithography in which a gold coated AFM tip covered with the catalytic thiols was used to write on a flat reactive SAM-covered Au surface.34 Here, the physical contact between the AFM tip and the surface creates a localized position where catalysis takes place. This results in the liberation of the hydroxyl-group which can then be further functionalized. Lines down to 25 nm were drawn on the surface, the resolution of which was only limited by the actual contact area between the AFM tip and the substrate and the instrumental drift.

Also the group of Stellacci reported on the immobilization of sulfonic acids on Au nanoparticles, in this case as acidic catalysts for the esterification of carboxylic acids.35 This study was aimed at investigating to which extent the catalytic parameters were influenced by the composition and morphology of the monolayer. A series of Au MPCs were prepared with mixed SAMs composed of the sulfonic acid derivatized thiol and phenyl-terminated alkane thiols of different length (C4–C8) and tested in the acetylation reaction of benzyl thiol and phenyl-terminated alkane thiols of different length with mixed SAMs composed of the sulfonic acid derivatized Au MPCs. Owing to the presence of a short C4-chain in the surrounding thiols gave better results compared to the C8-chains, which is in line with observations made earlier in other systems (see above). The catalytic systems were isolated from the reaction medium simply by centrifugation and reused without further purification. While the 2nd and 3rd run gave essentially the same results as the original catalyst, a significant deterioration of the ee was observed in the 4th run (68%). This was ascribed to a partial desorption of the catalytic thiols from the nanoparticles, thus favouring the background reaction catalysed by C4-functionalized nanoparticles.

The cooperative action of imidazoles in catalyzing trans-esterification reactions through a combination of nucleophilic and general acid–base catalysis renders the insertion of multiple imidazoles in multivalent scaffolds highly attractive. In an early example, Scrimin, Pasquato and co-workers demonstrated the effectiveness of imidazole-functionalized gold nanoparticles 12 in cleaving carboxylate esters (Fig. 5a).39 These studies not only clearly illustrated cooperative effects between neighbouring imidazoles on the surface, but also the induction of different mechanistic pathways compared to the same reaction in bulk solvent. Cooperativity between two 2-methylimidazoles on the surface of an Au MPC in the hydrolysis of 2,4-dinitrophenylacetate emerged from the profile of the second-order rate constant, k2, as a function of pH (Fig. 5b). The bell-shaped curve indicated that both protonated and free base (nucleophilic) imidazole are involved in the catalytic pathway. The monomeric catalyst 13 showed a typical decrease in k2 upon lowering the pH correspondingly resulting from a decrease in the concentration of free base imidazole (Fig. 5b).

The particular ability of Au MPCs to create a local chemical environment that is different from the bulk emerged from the study of Au MPC 14 that had the SAM terminating with a HisPhe-OH dipeptide (Fig. 6a).40 Compared to the reference
dipeptide Ac-HisPhe-OH (16), containing the same functional groups but unable to assemble, for all pH values studied the nanoparticle system was at least one order of magnitude more effective in catalyzing the hydrolysis of 2,4-dinitrophenylbutanoate (DNPB) (Fig. 6b). More importantly, though, the nanoparticle-based catalyst showed a much different behavior as a function of pH. The monomeric catalyst behaved as a system in which a catalytically relevant nucleophile is generated with \( pK_a \) 6.6, which is consistent with the basicity of the imidazole. On the other hand, the profile observed for the nanoparticle system indicated the formation of first nucleophilic species with \( pK_a \) 4.2, and a second one with \( pK_a \) 8.1. These \( pK_a \) values were assigned to the carboxylic acid and the imidazolium, respectively. The reason for the higher value of the \( pK_a \) of the imidazolium in the nanoparticle is due to the anionic nature of the nanoparticle that disfavors the deprotonation of the imidazolium cation. The confinement of the catalytic units in the monolayer covering the nanoparticles triggers a cooperative hydrolytic mechanism operative at pH < 7 in which a carboxylate ion and an imidazolium ion act as general base and general acid, respectively. The absence of this mechanism in the monomeric catalyst results in a 300-fold rate acceleration at acidic pH for the nanoparticle-based catalyst. Finally, it was shown that these systems can be developed into hybrid organic–inorganic structures of higher complexity by grafting catalytic dodecapeptides on the surface of Au nanoparticles.41 The observed catalytic activity of this system illustrates that this kind of system may in fact yield synthetic catalytic systems that can match up to the complexity of enzymes.

With regard to generation of complexity, a key challenge is a straightforward synthetic access towards such systems.

Even though the self-assembly of catalytic SAMs on gold nanoparticles is evidently an attractive strategy, these are typically still of rather low complexity. This originates from the use of synthetic protocols for mixed SAM formation (for example place-exchange) which do not give a full control over the final composition, the need for purification of each single nanoparticle system and issues related to the characterization of mixed SAMs both in terms of composition and morphology. Recently, we have developed an alternative strategy, relying on the self-assembly of small catalytic peptides on the surface of cationic Au MPCs.42 These peptides contained a negatively charged patch of Asp-residues to ensure binding through electrostatic interactions, a fluorescent Trp-residue to detect binding, and one or more His-residues for catalytic cleavage of esters (Scheme 8). When bound to the surface, the peptides accelerated the cleavage of the \( p \)-nitrophenylester of N-Cbz phenylalanine by more than two orders of magnitude. Detailed studies showed that co-localization of substrate and catalyst on the multivalent surface was the main reason for
observing catalytic activity at μM concentrations in water. The catalysis was further enhanced by a local pH at the surface that was 0.7 units higher than the pH of the bulk solvent, caused by the cationic ammonium groups. This increases the concentration of the free-base imidazole which acts as the nucleophile during catalysis. These results indicate that it is possible to create complex catalytic systems through the self-assembly of small peptide sequences and gold nanoparticles, without the need for purification and characterization of a catalytic (hetero)SAM.

Perspectives

The use of monolayer protected Au nanoparticles as catalytic systems offers a series of advantages which emerge from the systems discussed in this review. The hybrid inorganic–organic systems combine the advantages of heterogeneous (recycling) and homogeneous (activity) catalysis. Arguably, this advantage is not exclusive for Au nanoparticles and, in fact, currently a series of other (magnetic) nanoparticles is being considered as alternative support. Nonetheless, the use of Au nanoparticles benefits from an advantage which is related to the SAM. The formation of SAMs by thiols in particular is a process that occurs with high fidelity and reproducibility. The strength of the Au–thiol bond ensures a high thermodynamic stability of the system and permits its use even at highly diluted conditions. Furthermore, systems are stable both in aqueous and organic phases, the solubility is determined by the peripheral groups of the monolayer. Mixed SAMs can be prepared in a controlled manner by synthetic protocols (upon SAM formation using a mixture of thiols or afterwards by place-exchange mechanisms). The resulting SAMs are highly regular and position the terminal groups in close proximity. It is in particular a combination of these ultimate aspects that render gold nanoparticles appealing supports for forming catalytic monolayers. It has been illustrated that cooperativity effects may arise from the close proximity of neighbouring catalytic units. The catalytic parameters are affected by the surface morphology of the monolayer and the local chemical environment may induce a higher activity or selectivity. In addition, the multivalent nature of the catalytic system can play a role in determining catalytic selectivity.

All these issues render catalytic Au MPCs a highly attractive class of catalysts for further exploration. Although initial results have shown that the catalytic parameters of an embedded catalyst can depend on neighbouring inert thiols, these studies are just in its infancy. In particular, it is expected that the enantio- and regioselectivity of the catalyzed reactions are highly amendable for fine tuning in mixed monolayer systems. The fact that catalytic Au MPCs are obtained through self-assembly protocols means that it would be in principle possible to exploit combinatorial high-throughput synthesis and screening protocols for catalyst development. The use of additives that interact in a noncovalent manner with the catalytic surface Au MPCs may be an alternative way to alter the catalytic properties. The use of self-assembly provides the additional prospect of creating complex synthetic systems that can match up to the size and complexity of enzymes. Finally, it is anticipated that catalytic Au MPCs will also find applications beyond the field of catalysis, such as in the development of enzyme assays relying on catalytic signal amplification and in nanotechnology.

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References
