N-Methylimidazole-functionalized gold nanoparticles as catalysts for cleavage of a carboxylic acid ester

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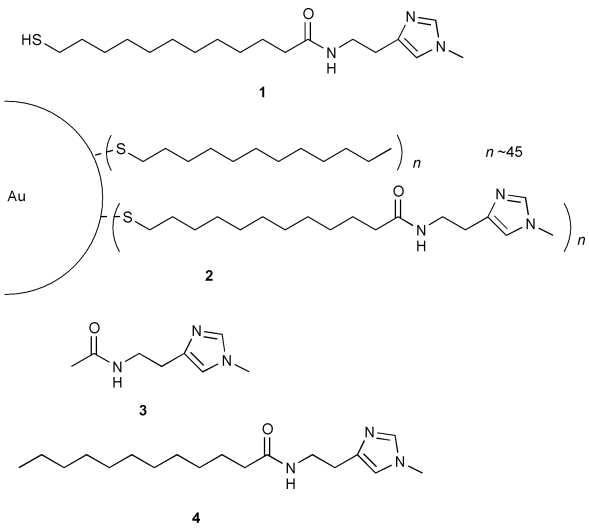
New *N*-methylimidazole-functionalized gold clusters 2 catalyze, in 6:4 methanol–water solution, the cleavage of 2,4-dinitrophenyl acetate with more than an order of magnitude rate acceleration with respect to acetyl-*N*-methylhistamine 3; comparison with dodecanoyl-*N*-methylhistamine 4 comicellized with Brij 35 reveals that 2 is still a better catalyst than the comicellar system and highlights analogies and differences between the two systems.

The last few years have witnessed a growing interest in nanomaterials for their potential applications ranging from catalysis to technology. Among them monolayer-protected gold clusters (Au-MPCs) appear particularly promising. Since the seminal work by Brust, Schiffrin *et al.*[1] these materials can be easily obtained as systems which are stable,[2] soluble in organic solvents (according to the properties of the protecting monolayer) and rather monodisperse in size. However, in spite of these interesting properties, reports concerning applications of Au-MPCs in catalysis are rather limited. In particular, the potential for cooperativity between several functional groups assembled on gold nanoclusters has not been specifically exploited so far. This communication addresses these aspects of Au-MPCs.

The conventional preparation procedure of the nanoparticles calls for the synthesis *in situ* by reduction of an Au(III) salt in the presence of the functional thiol derivative, followed, when required, by further derivatization[3] or by solution exchange of hydrocarbon-protected Au-MPC with a suitable functional thiol.[4] Following this latter approach we have first prepared gold nanoparticles protected with a monolayer of dodecanthiolates (C12) according to the detailed protocol reported by Murray and coworkers.[5] The resulting Au-MPC-C12 proved to be rather monodisperse by transmission electron microscopy (TEM) with an average core diameter of 2.2 ± 1.0 nm. This result, combined with the elemental analysis, indicates that the clusters are composed mainly of $Au_{225}(C12)_{90}$. Subsequently, we accomplished the place-exchange reaction[4,6] by codissolving MPC-C12 and thiol **1**† in dichloromethane–methanol (1:1) under an entering:exiting ligand ratio of 1:1.5. The resulting material was purified by exclusion chromatography [Sephadex LH-60, CH_2Cl_2–MeOH (1:1)]. Proton NMR spectra‡ reveal that the obtained Au-MPC comprises a 1:1 mixture of dodecane- and *N*-methylimidazole-functionalized thiolates. TEM measurements show that during the place-exchange process the average dimension of the gold core remains unchanged while the size distribution becomes slightly larger. The presence of a 1:1 mixture does not necessarily mean a random distribution. As recently reported,[7] in solution there may be rearrangement of thiols on the Au surface.

In the design of **2** our specific goal was the realization of a catalytically active Au-MPC for the cleavage of a carboxylate ester. Furthermore we wanted to verify the possibility of cooperativity of the active functional groups because of their confinement on the surface of Au-MPC **2**. For this purpose imidazole (or *N*-methylimidazole) appeared to be a suitable



candidate because of its key role as a catalyst in many hydrolytic systems where cooperativity between two such units has been reported.[8,9]

Cleavage of 2,4-dinitrophenyl acetate (DNPA), as a model ester, was studied in a methanol–water (6:4) solution, in which the new MPCs **2** are fully soluble, in the pH range 4.5–7.2. The reactions were monitored by UV–VIS following the formation of the 2,4-dinitrophenolate at 400 nm and 25 °C. For comparison purposes acetyl-*N*-methylhistamine **3** was also used as a reference monomeric catalyst.

The dependence of the second order rate constant, k_2,§ with pH for Au-MPC **2** and monomeric catalyst **3** is shown in Fig. 1 where the remarkable rate acceleration exerted by the nano-

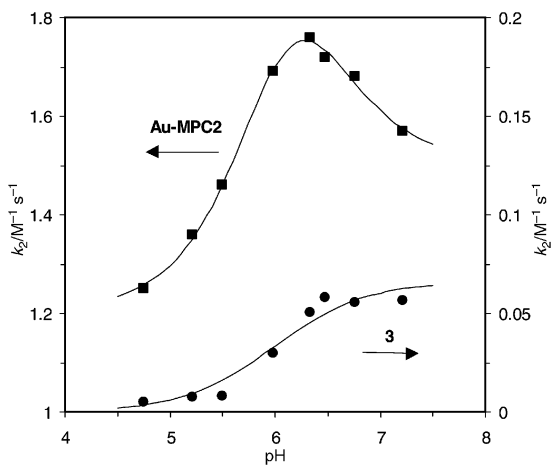


Fig. 1 pH dependence of the second order rate constants for the hydrolysis of 2,4-dinitrophenyl acetate in MeOH–H_2O (6:4) in the presence of Au-MPC **2** (■) or of the model system **3** (●). The solid curves are the best fitting of the experimental points.

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particles relative to **3** can be readily appreciated. Although the pK_a of *N*-methylimidazole of **2** could not be determined because of its insolubility at the high concentration required for the potentiometric titration, it is likely to be similar to the value (6.2) determined for **3** in the solvent mixture employed for the kinetic experiments. The low dependence of k_2 from pH in the pH range 5–7, with a small maximum in the proximity of the pK_a, supports cooperativity between two methylimidazoles in the DNPA cleavage by the nanocluster (general acid/general base or nucleophilic catalysis). The solid curves of Fig. 1 represent the computer-generated best fitting of the experimental points assuming a cooperative process (Au-MPC) and nucleophilic catalysis (**3**). A fair comparison between the two systems can be made at the pH values of the maxima of the two curves (pH 7.2 for **3** and 6.1 for **2**). Under these conditions the nanoclusters-catalyzed process is *ca.* 30 times faster than that using monomeric **3**. The kinetic behavior is very similar to that reported by the group of Baltzer[8] who studied four helix bundle-forming hydrolytic peptides bearing multiple imidazole side arms where cooperativity had been clearly demonstrated.

We note here that the system is really catalytic as all kinetic reactions were performed using an excess substrate (up to 7 : 1) over catalyst and the kinetic profile followed, in all cases, a well behaved pseudo-first-order process accounting for all added substrate.

Because gold nanoclusters **2** present structural analogies with a micellar aggregate we also tested the lipophilic *N*-methylhistamine derivative **4** in Brij 35 comicelles. As expected, micellar aggregates exist only in aqueous solution and not in the methanol–water mixture used for the study of **2**, as the hydrophobic effect that is at the basis of monomer aggregation vanishes in this solvent. Consequently, the catalytic efficiency in the mixed solvent is rather poor and similar to that of **3**. Comicellar **4**/Brij 35, however, binds DNPA in water (pH 6.3) with $K_b = 40\ M^{-1}$ and, in this solvent, accelerates the rate of its cleavage with k_{lim}, the pseudo-first-order rate constant for the fully bound substrate, of $2.5 \times 10^{-2}\ s^{-1}$. The comparison between the two systems is complicated by the fact that, because of the mixed solvent and the very low concentration of **2** used, the Au-MPCs are not expected to significantly bind the substrate. For this reason we have determined the second-order rate constant for the micellar system at very low surfactant concentration in the linear part of the rate *vs.* concentration profile above the critical aggregate concentration. At pH 6.2 the rate acceleration over that of the monomeric catalyst **3** is 35 for **2** and 22 for the comicelles indicating a slightly better efficiency of the Au-MPCs.

In conclusion we have reported the very first example of functional gold nanoclusters which are catalytically active in the hydrolysis of an activated ester. These systems present analogies with micellar aggregates although they exist under solvent conditions where micelles do not survive. Furthermore, the cooperative effects of the functional moieties may be exploited at very low concentration of the catalyst because the nanocluster does not require the critical aggregate concentration necessary for the formation of micelles. As for these properties, Au-MPCs resemble dendrimers, although the synthetic effort required for their formation is much less demanding. We believe that these systems present great potentialities as catalysts, and work aimed at the realization of new Au-MPCs bearing different functional groups, as well as small peptides, is in progress in our laboratory.

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Notes and references

† **1** was obtained by hydrolysis of the thioacetylated precursor: δ_H(250 MHz, $CDCl_3$) 1.20–1.40 (m, 14H), 1.43–1.65 (m, 4H), 2.15 (t, 2H, *J* 7.67), 2.52 (q, 2H, *J* 7.43), 2.72 (t, 2H, *J* 6.02), 3.52 (q, 2H, *J* 6.02), 3.64 (s, 3H), 6.5 (br, 1H, NH), 6.66 (s, 1H), 7.34 (s, 1H). δ_C(62.9 MHz, $CDCl_3$) 24.65, 25.71, 28.35, 29.04, 29.27, 29.37, 29.47, 34.03, 35.76, 36.52, 38.2, 118.19, 133.55, 134.75, 174.29. IR (film on KBr) ν/cm^{-1}: 3333, 2917, 2850, 2613, 1738, 1640, 1543, 1471, 1423, 1170, 717, 625.

‡ δ_H(250 MHz, CD_3OD) 0.96 (br s, 3H), 1.08–2.10 (br, 44H), 2.23 (br, 2H), 2.90 (br, 2H), 3.49 (br, 2H), 3.90 (br, 3H), 7.32 (br, 1H), 8.57 (br, 1H). δ_C[600 MHz HMQC (^{13}C–^1H), 400 MHz HMBC (^{13}C–^1H), CD_3OD] 15.01, 24.27, 26.91, 27.47, 29.79, 30.56, 31.27 (br), 33.59, 35.84, 37.56, 39.63, 121.27, (C5-Im, 7.32), 135.14 (C4-Im), 137.26 (C2-Im), 176.42 (C=O). IR (film on KBr), ν/cm^{-1}: 3467, 2919, 2849, 1644, 1465, 1415, 1261, 1167, 1021, 722, 624. Anal Calc. for $Au_{225}(C_{30}H_{57}N_3OS_2)_{45}$: C, 23.66; H, 3.77; N, 2.76; S, 4.21. Found: C, 23.57; H, 3.44; N, 2.50; S, 4.24.

§ Standard reaction conditions are: [DNPA] = $3.35–10.8 \times 10^{-5}$ M, [MI] = 1.54×10^{-5} M ([MI] is the molar concentration of methylimidazole or the methylimidazole head group in Au-MPC. The nanoparticle concentration is *ca.* [MI]/45), 25 °C in MeOH : H_2O (6 : 4). [Buffer] = 2×10^{-2} M. Buffers used were: AcO^-/AcOH pH 4.75, 5.21, 5.5; MES pH 5.98, 6.33, 6.47, 6.76 and HEPES pH 7.21; $k_2 = (k_{obs} - k_0)$/[MI]. For reference k_{obs}/k_0 (pH 6.5 at the above concentration) were *ca.* 1.3 and 10 for **3** and **2**, respectively, with $k_0 = 2 \times 10^{-5}\ s^{-1}$.

1 M. Brust, M. Walker, D. Bethell, D. J. Schiffrin and R. Whyman, *J. Chem. Soc., Chem. Commun.*, 1994, 801.
2 A. C. Templeton, W. P. Wuelfing and R. W. Murray, *Acc. Chem. Res.*, 2000, **33**, 27.
3 For example: A. C. Templeton, M. J. Hostetler, E. K. Warmoth, S. Chen, C. M. Hartshorn, V. M. Krishnamurthy, M. D. E. Forbes and R. W. Murray, *J. Am. Chem. Soc.*, 1998, **120**, 4845.
4 R. S. Ingram, M. J. Hostetler and R. W. Murray, *J. Am. Chem. Soc.*, 1997, **119**, 9175; M. J. Hostetler, A. C. Templeton and R. W. Murray, *Langmuir*, 1999, **15**, 3782.
5 M. J. Hostetler, J. E. Wingate, C.-J. Zhong, J. E. Harris, R. W. Vachet, M. R. Clark, J. D. Londono, S. J. Green, J. J. Stokes, G. D. Wignall, G. L. Glish, M. D. Porter, N. D. Evans and R. W. Murray, *Langmuir*, 1998, **14**, 17.
6 M. J. Hostetler, S. J. Green, J. J. Stokes and R. W. Murray, *J. Am. Chem. Soc.*, 1996, **118**, 4212.
7 A. K. Boal and V. M. Rotello, *J. Am. Chem. Soc.*, 2000, **122**, 734.
8 K. S. Broo, H. Nilsson, J. Nilsson, A. Flodberg and L. Baltzer, *J. Am. Chem. Soc.*, 1998, **120**, 4063.
9 R. Breslow, J. B. Doherty, G. Guillot and C. Lipsey, *J. Am. Chem. Soc.*, 1978, **100**, 3227; E. Anslyn and R. Breslow, *J. Am. Chem. Soc.*, 1989, **111**, 5972.