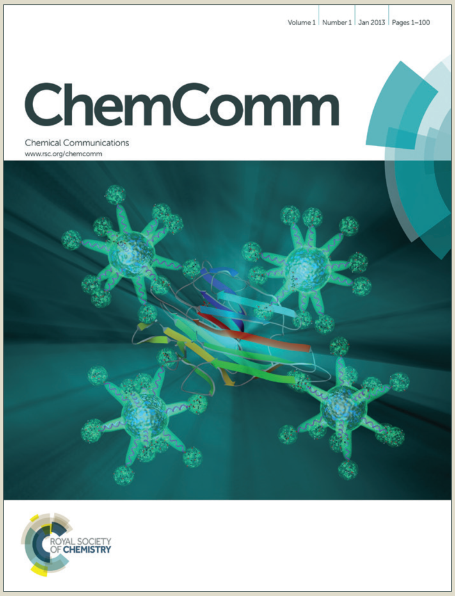
ChemComm

Accepted Manuscript



www.rsc.org/chemcomm

Journal Name RSCPublishing

COMMUNICATION

Differential reactivity of the *inner* and *outer* positions of $Au_{25}(SCH_2CH_2Ph)_{18}$ dimeric staples under place exchange conditions

Paolo Pengo,* Cristian Bazzo, Mariangela Boccalon and Lucia Pasquato*

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

The kinetic analysis of the place exchange reaction on the neutral $Au_{25}(SCH_2CH_2Ph)_{18}$ cluster by using 4-fluorobenzylthiol and a series of substituted arylthiols allowed us to establish, for the first time, that the selectivity for the *inner* and *outer* positions of the dimeric staples of the cluster can be modulated by using incoming thiols with different structures.

The self-assembly of nanosized materials into higher order structures with control over the resulting topology requires the development of anisotropic building blocks[1] capable of responding to directional forces[2] or displaying functional groups in well-defined relative positions.[3] As far as quasi spherical thiolate protected gold nanoparticles are concerned, anisotropy or symmetry breaking may be achieved by careful monolayer design by using blends of ligands.[3,4-6] This requires control over the mixed-monolayer stoichiometry and topology of the ligands responsible for the inter-particle interactions. On the other hand, at the lower bound of these nanosystems, the structural information available for atomically precise gold clusters offer an additional and complementary approach to building blocks with a well-defined number of functional groups in predetermined relative positions. At the core-shell interface of these systems, encompassing "staple" motifs of general formula $SR(AuSR)_n$ (n = 1-4),[7-11] the ligands are sorted in symmetry-inequivalent groups for which different reactivity under place exchange can be foreseen. Understanding the factors affecting the selectivity of the place exchange process at the different exchangeable sites of the staples is a key point in devising gold cluster-based building blocks that, presently, remains largely unaddressed.

Here we present a kinetic study on the neutral $Au_{25}(SCH_2CH_2Ph)_{18}$ cluster[12] specifically addressing this point. This cluster, in analogy with anionic $Au_{25}(SCH_2CH_2Ph)_{18}$ displays six dimeric staples in the ligand shell; the structure of a staple installed on two facets of the Au_{13} kernel is reported as **1** in Figure 1. In the following, the ligands found at the inequivalent positions of the staple will be dubbed *inner* (in) and *outer* (out). Among the plurality of structures identified so far, the dimeric staples -SR-Au-SR-Au-SR- found as the exclusive components of the $Au_{25}(SR)_{18}$ ligand shell, are the smallest structural units displaying inherently inequivalent thiolate ligands. The Au_{25} clusters are ideal models to interrogate the chemistry of the dimeric staples because they are reactive under place exchange conditions[13-18] and the six structural units are symmetry equivalent. Therefore, any differences in the site-selectivity will not be biased by the different electronic properties of the gold atoms of the underlying kernel. As incoming thiols we selected the 4-fluorobenzylthiol **2** and the arylthiols **3**-**5** to preliminarily explore the effect of the thiols structure on the reactivity of the inequivalent sites of **1**. The kinetic experiments were performed by ^1H NMR in benzene-d_6 at 25 °C on a 1.5 mM solution of clusters, corresponding to a 27 mM concentration of bound ligands, in the presence of 1.5 molar excess of thiols **2**-**5**. The kinetic profiles were built by monitoring the time evolution of the integrals of the signals pertaining to the protons β-H_{out}, the isochronous *o*-H_{in}, Figure 1, and the integrals of the β-H of the 2-phenylethanethiol (**6**) formed during the reaction.[§] The experimental data obtained by using **2** in three independent runs are reported in Figure 2A. Figure 2B reports the integral ratios I/I_0 for the β-H_{out} and *o*-H_{in} as a function of time.

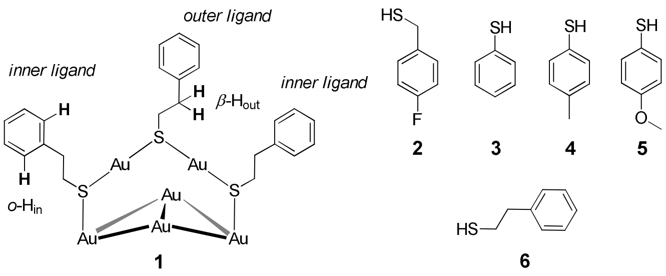


Figure 1 Structure of the dimeric staple motif with indication of the protons monitored in the kinetic analysis of the place exchange reaction and structure of the incoming and exiting thiols used in this study.

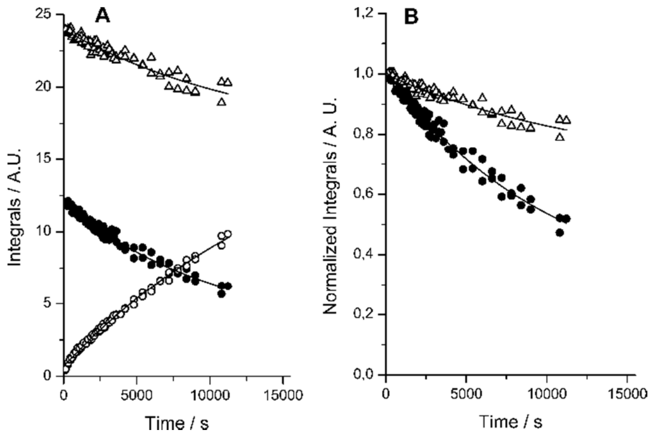


Figure 2 Kinetic profiles for the place exchange reaction on the neutral cluster $Au_{25}(SCH_2CH_2Ph)_{18}$ with 4-fluorobenzylthiol: solid circles β-H_{out}, open triangles *o*-H_{in}, open circles β-H of the released 2-phenylethanethiol. B) Time dependence of the β-H_{out} and *o*-H_{in} integrals normalized for the total number of *inner* and *outer* positions in the cluster. Trend lines are drawn to lead the eye.

The slopes of the initial parts of these decay curves are a direct measure of the observed first order rate constant for the place exchange at the *outer* and *inner* sites, k_{out} and k_{in} respectively. Since the place exchange reaction is an equilibrium process, the kinetic parameters of the reactions at the *outer* and *inner* sites were conveniently determined under initial rate conditions (see ESI†). The observed first order rate constants k_{in} and k_{out} and the selectivity ratios k_{out}/k_{in} of the place exchange reaction of neutral $Au_{25}(SCH_2CH_2Ph)_{18}$ with **2** are reported in Table 1. The selectivity of the reaction is k_{out}/k_{in} = 2.7 ± 0.4 or k_{out}:k_{in} = 1:0.37; the *outer* positions are almost three times more reactive than the *inner* ones. This selectivity should result in a site occupancy ratio *outer:inner* = 1:0.74 for **2** in the ligand shell of the cluster. From Figure 2A, after 180 minutes of exchange, the presence of 2 units of **2** at the *inner* and 3 units of **2** at the *outer* sites can be inferred, with a calculated *outer:inner* occupancy ratio equal to 3:2 or 1:0.7 in agreement with the values determined by the kinetic analyses under initial rate conditions. To confirm the introduction of 5 units of **2** in the exchange product, the composition of the ligand shell was assessed by ^1H NMR analysis of the mixture of disulfides obtained by iodine decomposition of the cluster. From this analysis the **6**:**2** ratio was calculated to be 1:0.4 corresponding to 13 residual units of **6** and 5 units of **2**. The *outer:inner* site occupancy ratio 1:0.74 is also supported by the observation of two distinct signals at -117.9 and -119.2 ppm integrating 1:0.76 in the ^{19}F NMR spectrum of the exchange product, Figure 3. On the basis of the kinetic and ^1H NMR evidences, these signals are tentatively assigned to the 4-fluorobenzylthiol bound at the *outer* and *inner* positions respectively. The good agreement between the site occupancy determined under initial rate conditions and by analysis of the composition of the exchange product suggests that selectivity remains constant throughout the reaction and that ligand hopping between the inequivalent sites of **1** is probably not relevant under the conditions employed.

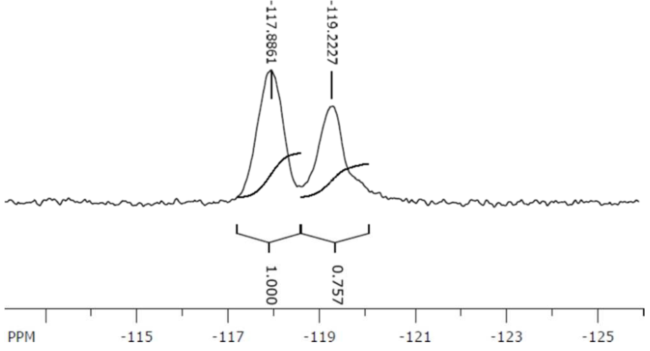


Figure 3 ^{19}F NMR spectrum in benzene-d_6 of the exchange products formed in the reaction between the cluster $Au_{25}(SCH_2CH_2Ph)_{18}^0$ and 4-fluorobenzylthiol.

The place exchange of thiophenol **3** with neutral $Au_{25}(SCH_2CH_2Ph)_{18}$ was carried out as described for **2**, except for a longer monitoring, up to 375 minutes. The experimental data obtained in three independent runs are reported in Figure 4A. The I/I_o ratios for the β-H_{out} and *o*-H_{in} as a function of time are reported in Figure 4B and 4C. In this case, the release of **6** is clearly biphasic[18] and our analysis was restricted to the first fast process. The observed rate constants for the place exchange at the *inner* and *outer* positions are reported in Table 1. In this case the selectivity ratio was k_{out}/k_{in} = 1.1 ± 0.3 or k_{out}:k_{in} = 1:0.9; at variance with **2**, the place exchange by **3** proved to be essentially non-selective. Overall, the reaction with **2** is faster than the reaction with **3**; comparison of the second order rate constants (k''), Table 1, for the exchange at the *inner* and *outer* sites by thiols **2** and **3** is indeed more intriguing. While the k''_{in} for the place exchange by **2**, is only 1.7-fold higher than the rate constant measured for **3**; the k''_{out} values are considerably different, with the k''_{out} for the exchange by **2** 4.3 times larger than the rate constant measured for **3**.

Table 1 Observed first order and second order rate constants for the place exchange reaction at the *inner* and *outer* sites of the dimeric staples of the neutral cluster $Au_{25}(SCH_2CH_2Ph)_{18}$ with 4-fluorobenzylthiol **2** and arylthiols **3-5**.

Incoming thiol	10^5 x k_{out}^{a} / s^{-1}	10^5 x k_{in}^{a}/ s^{-1}	k_{out}/k_{in}^{a}	**[incoming thiol]**$_0$ / mM	10^3 x k''_{out}^{a} / $M^{-1}s^{-1}$	10^3 x k''_{in}^{a} / $M^{-1}s^{-1}$
2	7.0 ± 1.0	2.6 ± 0.3	2.7 ± 0.4	40.0	1.77 ± 0.2	0.66 ± 0.08
3	2.0 ± 0.2	1.8 ± 0.3	1.1 ± 0.3	48.0	0.41 ± 0.04^b	0.38 ± 0.07^b
4	2.9 ± 0.4	1.7 ± 0.4	1.7 ± 0.6	42.4	0.68 ± 0.1^c	0.4 ± 0.08^c
5	4.2 ± 0.3	1.2 ± 0.1	3.5 ± 0.5	40.0	1.0±0.1^c	0.28 ± 0.02^c

[a] average of three independent runs for thiols **2** and **3** and of two independent runs for thiols **4** and **5**. [b] These values are in good agreement with the most recent value of the second order rate constant for the release of **4-6** reported in the reaction of the cluster $Au_{25}(SCH_2CH_2Ph)_{18}^-$ TOA^+ with a series of 4-substituted arylthiols.[15]

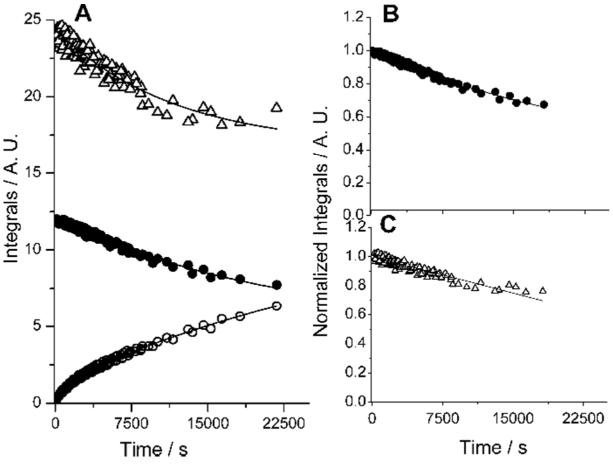


Figure 4 A) Kinetic profiles for the place exchange reaction of the neutral cluster $Au_{25}(SCH_2CH_2Ph)_{18}$ with thiophenol: solid circles β-H_{out}, open triangles *o*-H_{in}, open circles β-H of the released 2-phenylethanethiol. B) Time dependence of the normalized β-H_{out} integrals. C) Time dependence of the normalized *o*-H_{in} integrals. Trend lines are drawn to lead the eye.

Therefore, the *outer* sites display a higher sensitivity to the structure of the incoming thiol than the *inner* ones. Since the *inner* sites are likely more sterically hindered than the *outer* positions, the higher sensitivity of the latter to the structure of the incoming thiol can only be partly rationalized on the basis of sole steric considerations.[¶] We reasoned that the different reactivity and selectivity scored with **2** and **3**, may probably reflect the different electronic properties of the incoming thiols and/or the different electronic properties of the bound thiolates at the *inner* and *outer* sites as suggested in previous studies.[19] To confirm this hypothesis, the kinetic analysis was extended to 4-methylbenzenethiol **4** and 4-methoxybenzenethiol **5**. In the series of thiophenols **3**-**5**, the selectivity ratio k_{out}/k_{in} increases by increasing the electron donating properties of the substituent at the *para* position, Table 1. The observed second order rate constants for the place exchange at the *outer* sites increase with increasing the electron donating properties of the substituent of the incoming thiol; an opposite, although less pronounced, effect was observed for the place exchange at the *inner* sites. Overall, the *outer* positions proved to be more sensitive to the structure of the incoming thiol than the *inner* ones, confirming the behaviour observed with 4-fluorobenzylthiol **2** and thiophenol **3**. However, the comparison of the electronic effect of substituted arylthiols 3-5 and of benzyl thiol 2 on the selectivity is not straightforward because of their different structures. The decreased selectivity for the *outer* sites observed with less electron donating substituents at the *para* position, is also in line with the recent report by Ackerson and coworkers that proved selective exchange at the *inner* positions of the neutral $Au_{25}(SCH_2CH_2Ph)_{18}$ cluster in the presence of 4-bromobenzethiol[17] by blocking the reaction shortly afterwards the addition of thiol.[#]

In summary, here we reported, for the first time, that the site-selectivity of the place exchange reaction for the *inner* and *outer* positions of the dimeric staples of neutral $Au_{25}(SCH_2CH_2Ph)_{18}$ depends on the structure of the incoming thiol employed. With 4-fluorobenzylthiol the site-selectivity, measured by the k_{out}/k_{in} ratio was 2.7 while by using thiophenol as the incoming ligand no site-selectivity could be observed with a k_{out}/k_{in} = 1.1. In a series of 4-substituted arylthiols, the k_{out}/k_{in} selectivity ratio increases with increasing electron donating properties of the substituent. The observation of a differential selectivity for the two sites of the dimeric staples and its dependence on the electronic properties of the incoming ligands, or of the reactive sites, offers a structural basis for the rational design of functionalized Au_{25} gold clusters displaying well-defined functional groups in a strictly predetermined geometric arrangement. To this aim our group is further exploring thiols with different electronic properties to achieve complete selectivity. The achievement of these materials will represent a major step forward in the implementation of gold clusters as building blocks in nanotechnology and supramolecular chemistry.

This work was financially supported by the Italian Ministry of Education, University and Research, MIUR under project MULTINANOITA; the University of Trieste (FRA 2011, FRA 2012), and Beneficentia Stiftung. M.B. thanks the University of Trieste for a postdoctoral fellowship.

Notes and references

Department of Chemical and Pharmaceutical Sciences, University of Trieste, Via L. Giorgieri 1, I-34127 Trieste (Italy). e-mail: ppengo@units.it, lpasquato@units.it.

[§] At the end of the kinetic runs, the exchange products were purified and the isolated species displayed the UV-Vis absorption signatures of the neutral Au_{25} clusters, confirming the stability of the Au_{25} core under the conditions employed.

[¶] We consider the *inner* positions more sterically hindered because much closer to the gold surface than the *outer* sites which, in turn, considering the strong curvature of the cluster, are more exposed to external reagents.

[#] By considering the favourable crystal contacts observed, the author suggest that they may have crystallized a subset of the possible ligand-exchange products.

Electronic Supplementary Information (ESI) available: Synthetic details for the preparation of the clusters and their characterization; details for the kinetic runs and kinetic analysis. See DOI: 10.1039/c000000x/

1 (a) P. F. Damasceno, M. Engel and S. C. Glotzer, *Science*, 2012, **337**, 453-457; (b) S. C. Glotzer, and M. J. Solomon, *Nat. Mat.* 2007, **6**, 557-562.

2 (a) X. Ye, J. Chen, M. Engel, J. A. Millan, W. Li, L. Qi, G. Xing, J. E. Collins, C. R. Kagan, J. Li, S. C. Glotzer and C. B. Murray, *Nat. Chem*., 2013, **5**, 466-473; (b) J. A: Millan, D. Ortiz, G. van Anders and S. C. Glotzer, *ACS Nano,* 2014, **8**, 2918–2928. (c) K. Young, M. Personick, M. Engel, P. F. Damasceno, S. Barnaby, R. Bieher, T. Li, S. C. Glotzer, B. Lee and C. A. Mirkin, *Angew. Chem. Int. Ed*., 2013, **52**, 13980-13984.

3 (a) G. A. DeVries, M. Brunnbauer, Y. Hu, A. M. Jackson, B. Long, B. T. Neltner, O. Uzun, B. H. Wunsch and F. Stellacci, *Science,* 2007, **315**, 358-361; (b) R. P. Carney, G. A. DeVries, C. Dubois, H. Kim, J.-Y. Kim, C. Singh, P. K. Ghorai, J. B. Tracy, R. L. Stiles, R. W. Murray, S. C. Glotzer and F. Stellacci, *J. Am. Chem. Soc*., 2008, **130**, 798-799.

4 C. Singh, P. K. Ghorai, M. A. Horsch, A. M. Jackson, R. G. Larson, F. Stellacci and S. C. Glotzer, *Phys. Rev. Lett*., 2007, **99**, 226106.

5 I. C. Pons-Siepermann and S. C. Glotzer, *Soft Matter,* 2012, **8**, 6226-6231.

6 I. C. Pons-Siepermann and S. C. Glotzer, *ACS Nano*, 2012, **6**, 3919-3924.

7 P. D. Jadzinsky, G. Calero, J. C. Ackerson, D. A. Bushnell and R. D. Kornberg, *Science,* 2007, **318**, 430−433.

8 (a) M. W. Heaven, A. Dass, P. S. White, K. M. Holt and R. W. Murray, *J. Am. Chem. Soc.,* 2008, **130**, 3754–3755; (b) J. F. Parker,C. A. Fields-Zinna and R. W. Murray, *Acc. Chem. Res*., 2010, **43**, 1289-1296.

9 (a) M. Zhu, C. M. Aikens, F. J. Hollander, G. C. Schatz and R. Jin, *J. Am. Chem. Soc*., 2008, **130**, 5883–5885; (b) M. A. McDonald, D. M. Chevrier, P. Zhang, H. Quian and R. Jin, *J. Phys. Chem. C,* 2011, **115**, 15282–15287.

10 C. Zeng, T. Li, A. Das, N. L. Rosi and R. Jin, *J. Am. Chem. Soc*. 2013, **135**, 10011−10013.

11 A. Das, T. Li, G. Li, K. Nobusada, C. Zeng, N. L. Rosi and R. Jin, *Nanoscale*, 2014, **6**, 6458-6462.

12 (a) M. Zhu, T. W. Eckenhoff, T. Pintauer and R. Jin, *J. Phys. Chem. C,* 2008, **112**, 14221−14224; (b) A. Venzo, S. Antonello, J. A. Gascón, I. Guryanov, R. D. Leapman, N. V. Perera, A. Sousa, M. Zamuner, A. Zanella and F. Maran, *Anal. Chem*. 2011, **83**, 6355–6362.

13 J. B. Tracy, M. C. Crowe, J. F. Parker, O. Hampe, C. A. Fields-Zinna, A. Dass and R. W. Murray, *J. Am. Chem. Soc*., 2007, **129**, 16209-16215.

14 R. Guo and R. W. Murray, *J. Am. Chem. Soc*., 2005, **127**, 12140-12143.

15 J. F. Parker, K. A. Kacprzak, O. Lopez-Acevedo, H. Häkkinen and R. W. Murray, *J. Phys Chem. C,* 2010, **114**, 8276-8281.

16 (a) C. A. Fields-Zinna, J. F. Parker and R. W. Murray, *J. Am. Chem. Soc*., 2010, **132**, 17193-17198; (b) S. Knoppe and T. Bürgi, *Phys. Chem. Chem. Phys*., 2013, **15**, 15816-15820; (c) S. Si, C. Gautier, J. Boudon, R. Taras, S. Gladiali and T. Bürgi, *J. Phys. Chem. C,* 2009, **113**, 12966–12969.

17 T. W. Ni, M. A. Tofanelli, B. D. Philips, C. J. Ackerson, *Inorg. Chem*., 2014, **53**, 6500-6502.

18 R. Guo, Y. Song, G. Wang and R. W. Murray, *J. Am. Chem. Soc*., 2005, **127**, 2752-2757.

19 (a) J. Akola, M. Walter, R. L. Whetten, H. Häkkinen and H. Grönbeck, *J. Am. Chem. Soc*., 2008, **130**, 3756–3757; (b) C. M. Aikens, *J. Phys. Chem. C,* 2008, **112**, 19797–19800; (c) Z. Wu and R. Jin, *ACS Nano*, 2009, **3**, 2036-2042.