Dynamics of Place-Exchange Reactions on Monolayer-Protected Gold Cluster Molecules

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Monolayer-protected gold clusters (Au MPCs) are stable, easily synthesized, organic solvent-soluble, nanoscale materials. MPCs with protecting monolayers composed of alkanethiolate ligands (RS) can be functionalized (R′S) by ligand place-exchange reactions, i.e., $x(R'SH) + (RS)_mMPC \rightarrow x(RSH) + (R'S)_m(RS)_{m-x}MPC$, where x is the number of ligands place-exchanged (1 to 108) and m is the original number (ca. 108) of alkanethiolate ligands per Au_{314} cluster. The dynamics and mechanism of this reaction were probed by determining its kinetic order and final equilibrium position relative to incoming (R′S) and initial (RS) protecting thiolate ligands. The reactions were characterized by ^{1}H NMR and IR spectroscopy, and the dispersity of place-exchange reaction products was preliminarily inspected by chromatography. The results of these experiments show that ligand exchange is an associative reaction and that the displaced thiolate becomes a thiol solution product. Disulfides and oxidized sulfur species are not involved in the reaction. Cluster-bound thiolate ligands differ widely in susceptibility to place-exchange, presumably owing to differences in binding sites (Au core edge and vertice sites are presumably more reactive than terrace sites). The rate of place-exchange decreases as the chain length and/or steric bulk of the initial protecting ligand shell is increased. The exchange results and proposed mechanism are compared to those for place-exchange reactions on self-assembled monolayers confined to flat gold surfaces.

The development of versatile strategies to functionalize alkanethiolate monolayer-protected gold clusters (Au MPCs)[1] is vital in contemplating these materials as potential chemical reagents and catalysts. Reactions developed to this end include ligand place-exchange (forming poly-homo-[2,3] and poly-hetero-functionalized[4] MPCs), the nucleophilic substitution of ω-bromoalkanethiolate clusters with primary amines to form clusters with ω-(RNH)-alkanethiolate ligands,[5] and the formation of cluster-bound esters and amides.[6] By combining these simple transformations in a serial fashion, complex polyfunctional ligand shells can be generated, thereby minimizing the variety of functionalized thiols that must be prepared and purified. Rationally designed poly-functionalized gold clusters have potential for performing multistep catalysis within the space of a single cluster and in water-soluble forms, mimicking enzymatic functions.

In the place-exchange reaction, a new thiolate ligand (R′S) is incorporated into a cluster monolayer by mixing its thiol (R′SH) and the alkanethiolate (RS) Au MPC in solution. This reaction represents the most elemental of cluster functionalizations and has also been reported on CdS nanoparticles protected by arylthiolates[7] and on Au clusters protected by triphenylphosphine.[8] To better understand this important reaction, we initiated and report here a study of the dynamics and mechanism of place-exchange and the factors which enhance or inhibit this process. Such knowledge will improve the design of synthetic routes to complex cluster monolayers.

This study also addresses, by analogy, the currently debated mechanism by which ligand place-exchange occurs on self-assembled monolayers[9] on flat gold surfaces (2-D SAMs).[10] Evidence has appeared supporting both rate-determining dissociative pathways[11−13] and associative pathways.[14−17] Another important issue is whether place-exchange reactions occur predominantly at surface defects, such as terrace edges and corners, or at terrace surface sites. Studies of ligand place-exchange on 2D-SAMs are complicated by the small quantities of material (< nanomole) present in a monolayer, and the associated difficulty in unambiguously identifying the progress of the reaction and its products. An advantage of gold MPCs in the latter regard is the ease of making them in large

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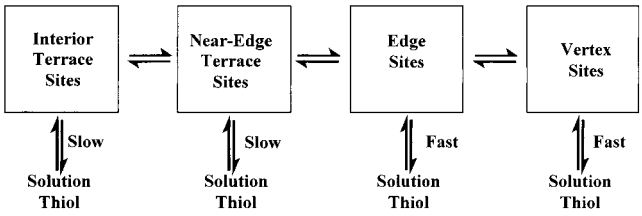
Scheme 1. Model of Processes in Place-Exchange Reactions on AuMPCs



quantities (> mmol) that are readily characterized with standard spectroscopic methods (such as transmission FTIR and NMR).

Several important differences between monolayers on MPCs and flat surfaces should be noted. Whereas terrace sites are the dominant motif on a flat gold surface, the core surfaces of nanoclusters[18,19] contain a large fraction of classically defined defect sites (up to 45% of all surface sites are edges and vertexes).[20] Additionally, the high radius of curvature of MPC surfaces produces a gradient in ligand packing density; in contrast, the packing density on a 2D-SAM terrace is nearly uniform over the chain-length of an alkanethiolate ligand. Another notable difference between the two is monolayer ordering. IR spectroscopic studies[5] of the Au MPCs in solution find that the alkanethiolate ligands are highly vagile, with a methylene disorder approaching that of liquid alkane. In contrast, the methylene chains on 2-D SAMs are highly ordered, nearly identical to that of crystalline polyethylene,[10] and the semicrystallinity[18c] of methylene chains on calculated nonsolvated MPCs is diminished in their solutions.[5] However, if the mechanism of place-exchange depends directly on the strength and nature of the Au−S bond, the aforementioned structural differences may be in degree and not in type; i.e., reaction rates may differ, but mechanistic pathways remain the same.

The results presented here support an associative pathway for place-exchange on Au MPCs and are consistent with widely differing core site reactivities as proposed in Scheme 1: fast place-exchange at edge and vertice thiolate sites on the cluster core, slower exchange at near-edge and interior terrace sites, and (probable) migration between the surface sites.

Experimental Section

Chemicals. ω-Ferrocenyloctanethiol (FcC8SH), ω-methylester-hexadecanethiol ($MeO_2CC15SH$), ω-methylester-undecanethiol ($MeO_2CC11SH$), ω-hydroxydodecanethiol (HOC12SH), ω-phenyl-butanethiol (PhC4SH), dibenzyl disulfide (BzSSBz), and the monolayer-protected gold clusters were prepared as previously described.[2−4,15] The cluster preparation used had an *average*[21] composition of $(RS)_{108}$ Au_{314} from TEM and thermogravimetric analysis results. Perdeuterated octanethiolate-protected gold clusters were synthesized from $C_8D_{17}SH$, which was in turn synthesized[15] from $C_8D_{17}Br$ (Cambridge Isotope Labs). Benzylthiol (BzSH), butanethiol (C4SH), octanethiol (C8SH), dodecanethiol (C12SH), and hexadecanethiol (C16SH) were purchased from Aldrich. The above parenthetical abbreviations are used throughout the report. Other chemicals were purchased from standard sources and used as received.

Spectroscopy. ^{1}H NMR spectra of C_6D_6, toluene-d_8, $CDCl_3$, and CD_2Cl_2 Au MPC solutions were collected at 200 MHz on a Bruker AC200 spectrometer using a sufficient relaxation delay to ensure accurate integration (5 s or $6T_1$). The data were processed using a line broadening factor of 1 Hz in order to improve the S/N ratio. Infrared spectra (dropcast cluster thin films on a KBr plate) were collected on a Bio-Rad 6000 FTIR spectrometer (256 scans), using a spectrum of a clean KBr plate for background subtraction.

Stoichiometric and Thermodynamic Studies. A 1:1 product molar relationship between the number of ligands entering and exiting a cluster monolayer during ligand place-exchange was established in the following experiments. Approximately 10 mg of cluster (C4S, C8S, C12S, or C16S MPC) and 1 mg of ferrocene as an internal NMR reference (controls show that ferrocene has no effect on ligand exchange or cluster stability) were co-dissolved in *ca.* 0.7 mL of C_6D_6 and added to an NMR tube. After 2 μL of BzSH was added and the tube sealed, the ^{1}H NMR spectrum was obtained immediately, after 7 h, and after 24 h. Reactions were stored at ambient temperature between data acquisitions. The 1:1 molar relationship was determined using the following peaks as diagnostics: (a) BzSH, doublet at 3.72 ppm corresponding to $BzCH_2SH$; (b) BzSSBz, singlet at 3.59 ppm corresponding to $BzCH_2SSCH_2Bz$; (c) alkanethiol, quartet at 2.50 ppm corresponding to RCH_2SH; and (d) dialkyl disulfide, triplet at 2.60 ppm corresponding to RCH_2SSCH_2R.

Equilibrium place-exchange reactions were performed between MPCs and solution thiols as a function of the chain length of both MPC (protecting) and exchanging (incoming) ligands. Approximately 50 mg of Au MPC (either C4, C8, C12, or C16) was co-dissolved in toluene (~ 3 mg MPC/mL) with the ω-methylester-alkanethiolate of selected chain length (Table 2) at 1:20, 1:2, 2:1, or 20:1 reactant mole ratios of exchanging thiol to cluster-bound thiolate. The solutions were stirred for 96 h (a time judged sufficient to approach equilibrium) at room temperature, after which the solvent was removed under vacuum. The exchange product was collected on a frit and thoroughly rinsed with acetonitrile to remove any unreacted ω-methylester-alkanethiolate ligands. ^{1}H NMR was then used to measure the ratio of nonexchanged alkanethiolate ligands (methyl resonance, broad peak at 0.9 ppm) to exchanged ω-methylester-alkanethiolate (methyl resonance, broad peak at 3.7 ppm). The ratio was converted into numbers of ligands exchanged based on the average cluster composition noted above.[21]

Kinetic Studies. Approximately 80 mg of alkanethiolate cluster and the desired amount of ω-ferrocenyloctanethiol (FcC8SH; i.e., R′SH) were co-dissolved in 60 mL of toluene at room temperature. The reaction was periodically quenched, precipitating the cluster from 5 mL reaction aliquots (usually in < 3 min) by addition of 100 mL of a 1:1 EtOH:CH_3CN mixture. The quenched aliquots were passed through a Celite layer and washed serially with 30 mL of EtOH and 30 mL of acetone. Each precipitated cluster aliquot was washed from the Celite with 20 mL of tetrahydrofuran, rotovaped to dryness, and the amount of FcC8SH that had exchanged onto the cluster up to the quenching time measured using ^{1}H NMR spectroscopy. The integrated intensity ratios of cluster-bound ferrocene (broad, *ca.* 4.0 ppm) and methyl peaks (broad, ca. 0.9 ppm, of the nonexchanged alkanethiolate ligands) were converted into numbers of ligands exchanged based on an average initial cluster composition of $(RS)_{108}Au_{314}$.[21]

The place-exchange results obtained over the entire reaction course were fit to numerous rate expressions without success.

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(20) The average diameter of the clusters used in this study is 2.1 nm; this comprises ca. 314 atoms in the gold core and 108 RS groups in the monolayer.

(21) The cluster preparation used in this study typically has a core size dispersity of ± 20%; however, because the clusters prefer certain "magic numbers" (closed shell structures) this relatively small dispersity still represents a large variation in the number of gold atoms per individual cluster (and hence the molecular weight). For example, besides the Au_{314} cluster, significant amounts of Au_{459} and Au_{225} clusters were present. Because all samples were synthesized by identical procedures, we consider the reported rate differences to be real. Fractional precipitation can give monodisperse clusters, but obtaining large amounts of material is difficult. Work is in progress to isolate sufficient quantities of monodisperse clusters to explore the sensitivity of the rate of exchange to the size (and number of defects) of the gold core. For a more complete discussion of dispersity issues in MPC samples, see: Green, S. J.; Pietron, J. J.; Stokes, J. J.; Hostetler, M. J.; Vu, H.; Wuelfing, W. P.; Murray, R. W. *Langmuir* **1998**, *14*, 5612−5619.

We therefore considered only the early stages of the reaction, where depletion of exchanging thiol and the reverse reaction (FcC8SAu displaced by a previously displaced $CH_3(CH_2)_nSH$ ligand) can be ignored, and the rate, k_{OBS}, at which the population of alkanethiolate ligands on MPCs decreased could be modeled as a reaction pseudo first-order in FcC8SH. Values for k_{OBS} were determined from the slope of plots of ln $\{[(CH_3(CH_2)_NS)_{m-x}Au]_{TIME}/[(CH_3(CH_2)_nS)_mAu]_{INIT}\}$ vs time and was found to depend linearly on [FcC8SH].

Exchange Product Dispersity. A 2 cm diameter column packed with 35 cm of dry Celite was conditioned with 500 mL of hexane, under pressure (N_2 @ 5 psi). Samples of cluster that had been place-exchanged for various periods of time were added onto the top of the wet column as a slurry in a minimum amount of hexane (typically 200 mg of MPC in 5 mL of hexane). The column was then washed with solvent mixtures of increasing polarity and the cluster dissolved at each polarity was collected (MPCs are highly colored; the column was washed with each mixture until its eluant was clear). The solvent mixtures used (and amounts), in order, were: (a) hexane, 300 mL; (b) 2:1 (v:v) hexane/ethanol, 350 mL; (c) 1:2 (v:v) hexane/ethanol, 200 mL; and (d) ethanol, 200 mL. After the solvents were removed, the cluster fractions were decomposed with I_2 in hexane as described previously,[5] which quantitatively liberates the MPC monolayer as the corresponding mixed dialkyl disulfides. The product molar ratio of R′S:RS was analyzed using ^{1}H NMR spectroscopy.

Reversed-phase thin-layer chromatography (TLC) of C12S MPCs that had been place-exchanged with HOC12SH for periods of 1, 3, 5, and 7 days was performed on glass plates coated with C18-modified silica gel (Whatman, 250 μm stationary phase thickness). One to two μL of a $\sim 10^{-5}$ M solution of each of the place-exchanged cluster products was spotted near the bottom edge of the 10 × 20 cm plate, allowed to dry, then placed into a small covered chamber containing a shallow pool of mobile phase consisting of 60% hexane/40% ethanol. After allowing the mobile phase to migrate to near the top of plates, the plates were removed from the solvent chamber and allowed to dry. The MPCs were visualized based on their strong coloration (dark brown in color). Two well-separated spots were observed on each TLC track. The width (band spreading) of each spot noticeably narrowed for MPC samples taken progressively at reaction times from 1 to 7 days.

Results and Discussion

This section presents a background of potential place-exchange reaction mechanisms, followed by data describing the identity of ligands entering and exiting MPC monolayers, observations on factors favoring and inhibiting ligand place-exchange, kinetic results, and finally a preliminary analysis of the per-cluster dispersity in number of incorporated ligands. The combined evidence presented in this report argues that the place-exchange reaction stoichiometry is

$$x(\mathrm{R'SH}) + (\mathrm{RS})_m\mathrm{MPC} \rightarrow x(\mathrm{RSH}) + (\mathrm{RS})_{m-x}(\mathrm{R'S})_x\mathrm{MPC} \quad (1)$$

where the displaced thiolate appears in solution as a thiol (RSH), and the entering R′S group disappears from the R′SH solution population in a 1:1 product stoichiometry relative to displaced RS.

General Mechanistic Pathways. We begin with a survey of mechanistic studies on flat gold surfaces, which offer analogies and differences to Au MPCs, as noted earlier. Nearly every report of ligand exchange on 2D-SAMs on Au surfaces observes that many sites exchange extremely slowly or not at all, whereas others are relatively reactive.[8,10,14,17] Although the microscopic details remain uncertain, these observations invite speculation that exchange occurs preferentially at minority sites such as defects (terrace edges) and grain boundaries, and that terrace-bound ligands are both less reactive and, at best, only slightly mobile (ligands lying well within an ordered section of the monolayer on a terrace do not appear to exchange). Two quite different exchange mechanism pathways could rationalize such a site preference: (a) the incoming ligand penetrates the monolayer in order to undergo place-exchange (which would favor less crowded, nonterrace sites),[8,14,17] or (b) ligands undergo desorption (preferentially at defect sites) followed by incoming thiol attachment to the newly created surface vacancy.[11−13]

Schlenoff et al. found[11] kinetic similarities (order, rate) for place-exchange and thermal desorption on 2-D SAMs, which were interpreted as pointing to a common mechanism involving rate-limiting disulfide surface detachment. While the quantities of disulfides generated were too small to be detected in solution, this mechanism is consistent with an X-ray structural analysis indicating that the surface ligands are bound as disulfides.[22] These reports contradicted, on the other hand, an earlier one which supplied strong evidence that the S−S bond of a disulfide is cleaved upon adsorption to a clean gold surface.[16] Another study suggests that oxidized sulfur ligands are readily generated on 2D-SAM surfaces and might be the species which participate in exchange and control the extent to which it occurs.[17] Later, careful studies showed that such oxidized states result from ozone exposure.[23] Ligand exchange on 2D-SAMs remains an unclarified topic; do Au MPCs provide useful insights? Vital points to hammer out in the present study of ligand place-exchange reactions on Au MPCs are the role of surface defect sites, the identity and stoichiometry of exchanging and departing ligands, and whether the rate-determining step in exchange is associative or dissociative.

The Identity of Ligands Entering and Exiting MPC Monolayers. The ready solubility of Au MPCs in nonpolar organic solvents makes it a straightforward task, using ^{1}H NMR spectroscopy, to monitor MPC reactions as they progress. Table 1 displays results for a series of place-exchange reactions of alkanethiolate MPCs with benzylthiol (BzSH).

A primary question concerns the propensity of cluster-bound ligands to desorb into solution. At 60 °C, there was no detectable desorption of C8S, or its disulfide (entry 1); heating the cluster solution at 100 °C for 30 min (entry 2) caused ca. 15% of the C8S ligands to desorb from the MPC into solution as disulfide. Prolonged (24 h) thermolysis at 100 °C did not provoke further desorption, indicating that the MPC monolayer contains only a limited number of ligands that are bound weakly enough to be lost as disulfides at these temperatures. Importantly, this ligand loss does not occur at levels which can be detected at room temperature (entry 1), except for long times and very short alkanethiolate chains (entry 3). Thermolysis at higher temperatures causes irreversible loss of large amounts of disulfide, leaving behind insoluble clusters.[24] Interestingly, a 2D-SAM heated to 100 °C can lose 20% of its ligands while the remaining surface remains well ordered by STM.[25] Monolayers on 2D-SAMs (and presumably MPCs) can adjust to compensate for empty spots, but in the MPC case, if ligand loss makes Au−Au contact between clusters possible, irreversible cluster core aggregation occurs.

What kind of sulfur species undergo ligand place-exchange? Dialkyl disulfides can be used[26] to form

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Table 1. Place-Exchange Experiments

entry	reaction design[a]	reaction result[b]
1	C8S MPC; 60 °C; 30 min	no sign of C8SH or C8S−SC8 in solution
2	C8S MPC; 100 °C; 30 min	~ 15% of the ligands desorb as C8S−SC8
3	BzS−SBz + C4S MPC; rt; 5 d	no exchange of BzS− onto MPC; some desorption (observe ~ 5% C4S−SC4)
4	BzS−SBz + C8S, C12S, or C16S MPC; rt; 5 d	no exchange; no desorption products
5	BzSH + C4S MPC; rt; 5 d	products were: 10% in BzS−SBz, 6% in C4S−SC4, 84% C4SH
6	BzSH + C8S MPC; rt; 5 d	products were: 4% in BzS−SBz; 3% in C8S−SC8; 93% C8SH
7	BzSH + C12S or C16S MPC; rt; 5 d	1:1 molar exchange of BzSH for either C12SH or C16SH; no disulfides detected
8	BzSH + C8S MPC; 60 °C; 30 min	1:1 molar exchange of BzSH for C8SH; no disulfides detected
9	BzSH + C8S MPC; 100 °C; 30 min	product was: C8SH ~10× more than any disulfide

[a] Reagents; temperature; reaction time. All reactions performed in toluene-d_8 with a ferrocene standard. [b] Place-exchange reactions (#5−9) were performed at a 50:1 mole ratio of exchanging thiol to cluster-bound thiolate. The reactions were performed in sealed NMR tubes without isolation of the final exchanged Au MPC product. Hence, the extent of place-exchange on each of the reactions was not followed in these cases, but prior experience indicates that exchange should be close to 100%. Byproducts detected by ^{1}H NMR spectroscopy.

monolayers *in the synthesis* of Au MPCs. However benzyl disulfide does not place-exchange into monolayers of already-formed MPCs (entries 3−4). Under identical conditions, benzyl (and other[2−4]) alkanethiols readily participate in place-exchange (entries 5−9).

^{1}H NMR was used to establish the 1:1 product stoichiometry (entries 7, 8, Experimental and Supporting Information) of the place-exchange reaction (1) on MPCs. Immediately after BzSH was added to an NMR tube containing 10 mg of Au MPC (C8S, C12S, C16S), the NMR spectrum shows only signals corresponding to the two as-yet-unreacted materials: broad peaks for the methyl (0.9 ppm) and methylene (1.5 ppm) of the cluster-bound alkanethiolate and sharp peaks corresponding to BzCH_2-SH methylene (3.72 ppm) and benzyl ring (7.3 ppm). After reacting for 24 h, the spectrum was markedly changed; the benzylthiol peaks described above are now superimposed broad and sharp peaks, indicating a mixture of cluster-bound benzylthiolate and free benzylthiol species. Most notable, however, is a new, sharp (i.e., not cluster-bound) peak at 2.5 ppm corresponding to the α-methylene (RCH_2SH) of the alkanethiol that has been liberated from the cluster as a result of place-exchange. The corresponding α-methylene peak for alkanethiolate bound to cluster is broadened into the baseline. The increase in integrated NMR intensity of the new alkanethiol species at 2.5 ppm is identical to the decreases in intensity of BzCH_2SH peak (± 5%), and is taken as proof of a 1:1 place-exchange reaction stoichiometry.

During place-exchange reactions with clusters bearing short-chain alkanethiolate monolayers, a small amount of disulfide does appear (entries 5, 6, 9), but this occurs only at long times or elevated temperatures. We interpret this behavior as strong evidence that disulfides are formed by thermal decomposition side-reactions, not as a result of place-exchange. For example, in the reaction of entry 5, after 1 h at room temperature the only displaced C4 species was C4SH, whereas after 24 h, the products contained 3% dibutyl disulfide, after 48 h, 6% disulfide, and after 5 days, 10% disulfide. For the more thermally stable, long chain alkanethiolate MPCs (e.g., C12S and C16S MPCs), disulfides were never observed in the reaction mixture under the same conditions. In fact, the rate at which dialkyl disulfide appears during place-exchange resembles that for cluster decomposition under exchange-free conditions (entries 1, 2). In conclusion, no evidence has appeared that points to ligand place-exchange occurring by other than a simple 1:1 incoming thiol/bound MPC thiolate interchange.

Infrared spectroscopy of solid exchange product provides evidence that the average conformational ordering of a place-exchanged ligand monolayer changes with the extent of exchange.[27,28] The position of the d^- band (CH_2 antisymmetric stretching vibration) is a well-known indicator of methylene chain conformation; values around 2920 cm^{-1} signal an all-*trans* zigzag conformation (as in crystalline polyethylene[9]), whereas a value around 2924 cm^{-1} reflects a highly disordered methylene chain, such as found for a liquid hydrocarbon.[29] A place-exchange reaction was designed to probe changes in conformational ordering with the extent of exchange, by reacting perdeutero-C8S MPC with a C12SH thiol. The solid product of this exchange reaction showed that the d^- band for C12S ligands exchanged onto the MPC lies at 2924.6 ± 0.1 cm^{-1} for an exchange reaction conducted for 90 min, and at 2923.1 ± 0.1 cm^{-1} after 240 min. The average C12S MPC ligand thus becomes more ordered as more C12S ligands become exchanged onto the MPC. Similar results were observed for exchange of other ligands (FcC8SH, $MeCO_2$C11SH, see Experimental Section) onto perdeutero-C8S MPCs. Improved ordering of newly incorporated ligands has no analogue in the 2D-SAM literature, and multiple explanations are possible, including formation of domains of the longer chain alkanethiolate, migration away from defect sites into more ordered regions (i.e., terraces), and even annealing of the Au core structure. Additional study will be required to determine which, among any, of these explanations is correct.

Thermodynamics: Place-Exchange Reactions at Equilibrium. On a 2D-SAM, the thermodynamics that govern mixed monolayer formation are complex, but generally reflect the relative solubilities of the components in solution as well as chain−chain interactions in the monolayer.[15] The situation is somewhat different for Au MPCs, since the cluster *and* the thiol ligands presented for exchange are *dissolved* in the same solution. The similarity between a thiolate ligand in a cluster monolayer and its thiol monomer analogue in solution is most clearly shown by the nearly identical reactivities of ω-functional groups on the two.[5]

We have recently reported cluster place-exchange reactions that involve as many as five different types of ligands,[4] where all of the ligands were either exchanged simultaneously with a Au MPC, or in a stepwise fashion (isolating and characterizing products after each step). In stepwise exchanges done in order of increasing and

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Table 2. Equilibrium Results for Place-Exchange Reactions between Cluster Ligands and Solution Thiols

expt. #	cluster/ligand	Reactant Mole Ratio: Thiol/Cluster Ligand 1:20	Reactant Mole Ratio: Thiol/Cluster Ligand 1:2	Reactant Mole Ratio: Thiol/Cluster Ligand 2:1	Reactant Mole Ratio: Thiol/Cluster Ligand 20:1
1	C4S MPC/MeO_2CC11SH				
	ligand exch: #expected[a]	2	16	77	102
	#observed[b]	6	31	86	100
	obs/expected[c]	3.0	2.0	1.1	1.0
2	C8S MPC/MeO_2CC11SH				
	ligand exch: #expected	3	27	80	104
	#Observed	3	16	51	75
	obs/expected	1.0	0.60	0.64	0.72
3	C12S MPC/MeO_2CC11SH				
	ligand exch: #expected	4	25	72	105
	#observed	4	18	34	77
	obs/expected	1.0	0.72	0.47	0.73
4	C16S MPC/MeO_2CC11SH				
	ligand exch: #expected	3	26	84	104
	#observed	4	20	42	73
	obs/expected	1.3	0.76	0.50	0.70
5	C16S MPC/MeO_2CC15SH				
	ligand exch: #expected	2	22	75	104
	#observed	3	14	42	42
	obs/expected	1.5	0.64	0.56	0.40

[a] Number of thiols expected to place-exchange from solution onto the cluster (within the total of 106 ligands per cluster), assuming nonselective exchange (no preference for exchange among the various cluster sites) between the initial mixture of free thiols and thiolate cluster ligands. [b] Number of thiols (average, per cluster) experimentally observed (^{1}H NMR) after 96 h of reaction to have place-exchanged from the solution onto the cluster (within the total of 106 per cluster). [c] The ratio of experimental observation to expectation, assuming nonselective place-exchange.

decreasing alkanethiol chain lengths, thiols with long-chain ligands (such as BrC12SH, HOC12SH, and MeO_2-CC15SH) readily displaced MPC thiolate ligands with short-chain, bulky groups, PhC4SH (Ph = phenyl) and FcC8SH (Fc = ferrocene), *but not vice versa*. It was proposed that this trend is related to the energetic cost of disturbing chain packing density, which, for a 2 nm diameter cluster protected by C12S monolayer, is ca. 9 times greater near the cluster surface relative to the chain termini.

In the present study, the effect of the relative thiol/thiolate chain lengths and reaction proportions on the final (apparent equilibrium) place-exchange product was examined (Table 2). Five place-exchange reactions, in which the entering ligand chain length ranged from shorter to substantially longer than the original monolayer, were set up at four different (thiol):(bound cluster thiolate) reactant mole ratios: 1:20, 1:2, 2:1, and 20:1. The 1:20 reaction probed for the most easily exchanged (presumably defect) sites, whereas the large molar-excess 20:1 reaction probes sites that are more difficult to exchange (presumably terrace). For the purposes of discussing the products of these experiments, we have defined the thiolates bound to Au atoms on the flat faces of the proposed MPC truncoctahedral core morphology[18a−c] as terrace sites. Those thiolates bound to Au atoms lying at the intersection of two flat faces we denote as edge sites, while those thiolates bound to Au atoms lying at the intersection of three flat faces are denoted as vertice sites. Our general terminology differs from that of Luedtke et al. for the different MPC thiolate sites,[18c] who discuss calculated equilibrium, nonsolvated structures in more detail. MPCs are studied here as solutes, the monolayers are not so regularly organized, and some fraction of the core shapes may be kinetic, not equilibrium forms.

Reactions were run for 5 days, which appeared to be at or near equilibrium (± 5%). Table 2 indicates, for each reaction, the number of entering ligands that would be expected from the given reaction proportions ("# Expected"), provided the reaction were to show *no selectivity* between entering and exiting ligands. Table 2 also shows the observed number of exchanged ligands ("# Observed"), and the ratio of observed-to-expected exchanged ligands. Recall that the MPCs used in this study contain an *average* of 108 ligands/cluster.[21]

Under 1:20 reaction proportions (dilute in exchanging thiol R′SH, Expt. #1−5), the observed/expected product mole ratio is near unity even with ligands of disparate chain lengths, indicating a nonselective exchange. This is evidence that the reaction under dilute conditions indeed probes the most readily exchangeable and sterically indifferent sites; to a first order the affinity of ligands for these sites involves the Au−S bond energy and little else. Crudely, it appears that ca. 4 of these sites are available on each cluster. Of the sites on an MPC, those at vertexes are both of smallest population and least sterically crowded, relative to edge or terrace sites. Estimates of the average number of occupied vertice sites (the actual core shape is uncertain) on clusters of the size used here vary from 4 to 12. The experimental observations are consistent with the low end of this average.

For the 1:2 reaction proportion, ca. 60−75% of the expected number of ligands exchange. That these results are <100% indicates a mild selectivity disfavoring the entering ligand. (Expt. #1 was an exception; the MeO_2-CC11SH ligand place-exchanged onto the cluster at nearly twice the proportion expected on the basis of a nonselective exchange reaction with the C4S MPC.) The 1:2 results were generally similar to those for the 2:1 and 20:1 reaction proportions. (Expt. #1 again showed a higher degree of exchange.) Other subtle effects appear in the results of Expts. #3−5 as the reaction proportions move from 1:2 to 20:1, that may reflect the steric consequences of exchanging large proportions of the ester linkages onto the MPC being counterbalanced by forcing reaction conditions.

The central conclusions drawn from the Table 2 data are: (a) As the reaction proportion increases above mole ratios of 1:20 and readily exchanging sites become exhausted, on average, the thiol ligand prefers to remain in the solvent relative to the cluster monolayer. This result, plus the observation that the thiol ligand is more polar (ester) than the MPC thiolate that it displaces, in a reaction

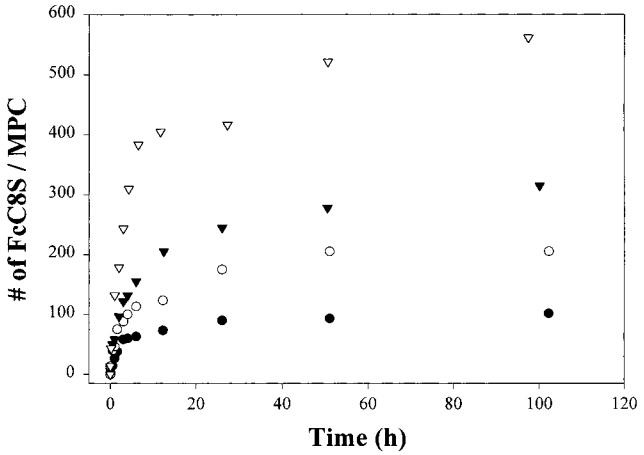


Figure 1. Plot of #Fc/cluster exchanged on a C8S MPC vs time for various concentrations of FcC8SH. From top to bottom: 1.7×10^{-3} M (open triangle); 1.2×10^{-3} M (closed triangle); 4.1×10^{-4} M (open circle); 1.6×10^{-4} M (closed circle).

occurring in a nonpolar solvent, argues that a *strong* gradation of surface site reactivity must exist. Even at 5 days, the place-exchange may not lie at true equilibrium.[30] (b) Except for Expt. #1, the number of thiolate ligands that become exchanged under nonforcing reaction conditions (i.e., mole ratio of 1:2) is 34 to 51. This number is crudely consistent with the total number of vertice plus edge sites on various assumed cluster shapes. (c) even under forcing (20:1) reaction conditions, not all sites are place-exchanged (except again for Expt. #1). For clusters with short-chain ligands, vigorous conditions (high temperature or repeatedly renewing the amount of free ligand in solution)[31] can force full exchange, but on the C12S MPC and C16S MPC clusters, nearly 20% of the ligands would not exchange. This is an important result, as it suggests that exchange of ligands on terrace sites, (or perhaps more likely, migration[30] of terrace site ligands to more reactive vertice/edge sites), can be very slow. (d) Longer chain lengths are preferred in the product cluster monolayer, which indicates that chain−chain interactions are significant factors in the stabilization of the monolayer. That they would be so is not as obvious as in reactions forming 2D-SAMs, which typically occur from a polar solvent. The MPC place-exchange reactions described here take place in a very nonpolar solvent, so the expected energetic differences between hydrophobic chain−chain monolayer and thiol solution are less obvious.

Kinetic Studies. The major question of whether the rate-determining step in MPC place-exchange reaction is associative (first order in both reagents) or dissociative (first order only in cluster concentration; desorption as disulfides) was addressed by monitoring the incorporation of FcC8SH (Fc = ferrocene) into several different types of cluster monolayers (Figure 1 and Table 3). Figure 1 shows

Table 3. Rate Data for Ligand Exchange Studies

cluster	[RSAu],[a] M	[FcC8SH], M	rate constant,[b] s^{-1}	rate constant,[c] $M^{-1}\ s^{-1}$
C8	1.2×10^{-3}	1.6×10^{-4}	5×10^{-6}	3×10^{-2}
C8	1.3×10^{-3}	4.1×10^{-4}	8×10^{-6}	2×10^{-2}
C8	1.2×10^{-3}	8.1×10^{-4}	1.0×10^{-5}	1×10^{-2}
C8	1.4×10^{-3}	1.7×10^{-3}	1.6×10^{-5}	9×10^{-3}
C12	1.1×10^{-3}	7.1×10^{-4}	6×10^{-6}	8×10^{-3}
C16	1.1×10^{-3}	8.0×10^{-4}	4×10^{-6}	6×10^{-3}

[a] Initial concentration of C8S MPC, C12S MPC, or C16S MPC sites. [b] Pseudo first-order rate constant. [c] Second-order rate constant.

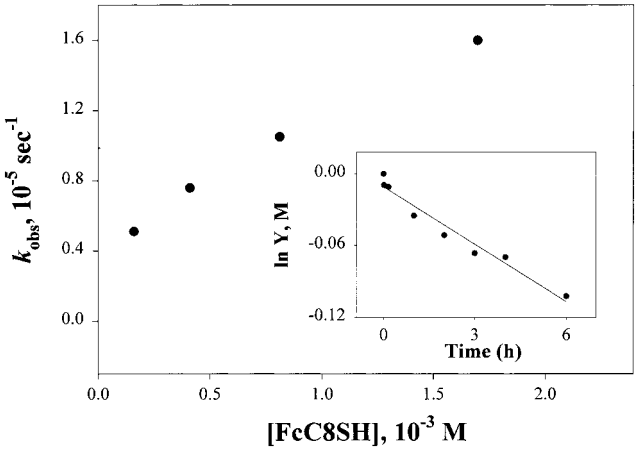


Figure 2. Plot of k_{OBS} vs $[FcC8SH]_{INIT}$ for the ligand exchange reaction (initial rate). Inset: Plot of ln Y [$Y = (RS)_{m-x}MPC]_{TIME}/[(RS)_mMPC]_{INIT}$ vs time.

that the rate of place-exchange on MPCs is initially rapid but then slows dramatically.

The rate equation for an equilibrium reaction featuring two reactants and two products is complicated. We chose to focus on the first 10% of the reaction[32] so that the reverse reaction (displacing a Au−SC8Fc by a C8SH) is negligible; pseudo first-order kinetic behavior, $k_{OBS} = k[FcC8SH]_{INIT}$, can be assumed. This also focuses on the reactivity of the most exchangeable MPC sites, the gradation of which appears to be more important than reverse reactions.

Figure 2 (inset) shows an example of a plot of ln $[(RS)_{m-x}MPC]_{TIME}/[(RS)_mMPC]_{INIT}$ vs time, the linearity indicating a first order dependence on the population of the ligand originally present on the MPC. Figure 2 presents a plot of the pseudo first-order rate constants (k_{OBS}, from slopes of Figure 2 inset) vs $[FcC8SH]_{INIT}$ and shows that the rate of place-exchange depends in a roughly linear manner on the concentration of entering ligand but that the first-order behavior in $[FcC8SH]_{INIT}$ is not ideal. The drift in k_{OBS} can be rationalized by examining how many sites per cluster become place-exchanged at each [FcC8SH] over the course of the reaction followed.[32] At the lowest FcC8SH concentration, at the end of the monitored reaction period,[32] only ~3% of the surface sites had become exchanged, whereas at the highest incoming FcC8SH ligand concentration, ~25% of the sites undergo place-exchange.[33] The thermodynamic study (Table 2) has shown that reactivity differs with the number of sites exchanged (i.e., vertexes, edges terrace sites next to edges, interior terrace sites, and so on). Thus, the apparent second-order rate constants at *high* FcC8SH concentrations seem to

(30) There is other evidence for slow surface migration of ligands exchanged onto a cluster away from these most reactive sites. Thus, following exchange (and isolation/cleanup) of $MeO_2CC11SH$ onto a C12S Au cluster to form a 4:1 $C12SMeO_2CC11S$ monolayer, the cluster was exposed to an amount of C12SH that should have been sufficient to exchange off most of the bound $C11CO_2Me$ ligands. Only about 50% of these ligands exchanged off within 48 h; if $MeO_2CC11SH$ had entered and remained at reactive vertice and edge sites, then it would be reasonable to expect these ligands to be most susceptible to subsequent exchange. This was not observed. One explanation is that cluster-bound ligands can slowly migrate onto the terrace surfaces; experiments are in progress that should help verify this hypothesis.

(31) It is possible to fully exchange off all of the original ligands when the reaction is performed at room temperature; however, this was only observed with the C4 MPC. Longer protecting ligands proved highly resistant to full exchange.

(32) The concentration of the desorbing ligand was no more than 10% of the concentration of the remaining original incoming ligand.

(33) These values differ significantly as the rate data are plotted just until $[RSH] \sim 0.1[FcC8SH]_{INIT}$. Thus, at low $[FcC8SH]_{INIT}$, only a few ligands need to exchange in order to satisfy this condition.

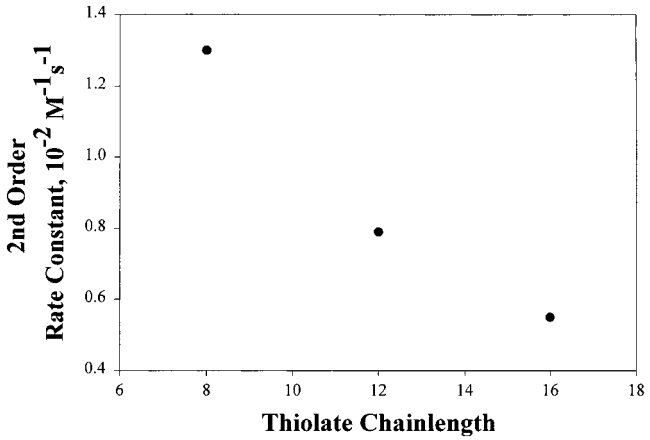


Figure 3. Plot of the second-order rate constant, k_{second} (= k_{OBS}/[RSAu]$_{INIT}$; k_{OBS} is the rate constant derived from the first 10% of exchange of FcC8SH) vs the chain length of the ligand surrounding the original Au MPC.

reflect exchange of a site population that is thermodynamically, and apparently kinetically, less reactive.[34] The gradation of site reactivity does not, however, obscure the fact that the rate of ligand exchange depends on the concentration of *both* entering and exiting ligand. This behavior is not expected for exchange controlled by the rate of ligand desorption (dissociative pathway).

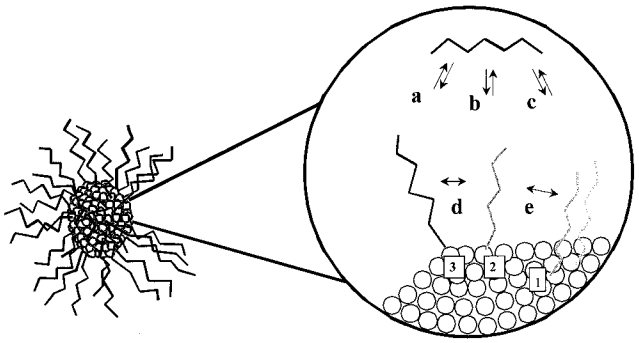
Kinetic studies (Table 3) were also performed for FcC8SH exchange as a function of monolayer chain length (C8, C12, C16). Figure 3 shows that exchange occurs more rapidly (range of ca. 3-fold) onto clusters that have shorter chain length alkanethiolate monolayers. This is consistent with a reaction in which an incoming thiol must penetrate to within some proximity of the core in order for place-exchange to occur, and/or where surface thiolate migration (Scheme 1) influences the rate. Figure 3 is also consistent with an increased stability of long chain alkanethiolate ligands due to increased chain−chain interactions within the cluster monolayer.

Previous kinetic studies have addressed in different ways the effect of incoming ligand bulk.[4] Five different thiols, PhC4SH, FcC8SH, HOC8SH, BrC8SH, MeO_2-CC15SH, were simultaneously[4] mixed with a C12S protected gold cluster (for coding see Experimental Section). Consistent with an associative reaction, the extent of exchange of each thiol indicated that the rate of exchange decreases as the bulk of the terminal group increases and the length of the connecting chain decreases. Interestingly, the relative product mole ratios of the functionalized ligands exchanged onto the cluster remained constant (and different from the free ligand ratio), even though the total number of exchanged ligands increased. Thus, small, fast exchanging ligands do not bind to the cluster in the early stages of exchange only to be displaced by more stable ligands.[30]

Exchange Product Dispersity. There have been substantial discussions elsewhere about the compositional dispersity present in MPC samples.[21] Besides the known dispersity in the cluster core size (and speculation about dispersity in monolayer coverage), one can expect some dispersity in the number of ligands place-exchanged into monolayers of different clusters. Importantly, the dynamics of the MPC place-exchange reaction may have direct bearing on the type and extent of dispersity observed in

(34) The quenching process took about 8 min, so it was not possible to take a satisfactory number of time points at the early stages of the reaction for the fastest reactions. It is sufficiently clear, however, that the exchange rate depends on the concentration of the incoming ligand.

Scheme 2. A Cartoon Illustration of the Proposed Processes Involved in Ligand Place-Exchange Reactions on Au MPCs[a]



[a] (a) Exchange of vertice thiolates (3) with solution thiol; (b) Exchange of edge and near-edge thiolates (2) with solution thiol; (c) Exchange of terrace thiolates (1) with solution thiol; (d) Surface migration among vertice and edge thiolates; (e) Surface migration among edge (and near-edge) and terrace thiolates. The gold sites are labeled as: (1) terrace core sites, (2) edge and near-edge core sites; and (3) vertice sites.

place-exchanged products. Experimental tools are sorely needed that will allow for dispersity in place-exchanged MPC reaction products to be analyzed and results correlated to knowledge of the reaction dynamics.

We present as part of this study a promising new tool to investigate dispersity in the place-exchanged MPC reaction products. The utility of the new method has been preliminarily explored by subjecting samples of place-exchanged clusters to separation by solubility properties and C18 thin-layer chromatography. In the former, (see Experimental) cluster was eluted at different levels of solvent polarity and then analyzed. Using this procedure, a place-exchanged sample which had an average content of 10 HOC11S ligands per cluster (on a C12S MPC), became separated into two major fractions that contained 6 exchanged ligands (∼37%, by weight) and 17 exchanged ligands (52%). Ten percent of the sample did not elute and was not characterized. Interestingly, the dispersity in exchange number roughly matches the dispersity in core size (TEM and MALDI reveal that a similarly prepared sample consists of 2−3 major species).

Similar, although less quantitative, results were obtained by thin-layer chromatography (C18 plates) in which, by judicious choice of solvent (60% hexane/40% ethanol), the exchange dispersity can be quickly visualized. For example, the exchange of HOC12SH onto a C12S MPC, monitored at periods of 1, 3, 5, and 7 days, exhibited two major TLC spots at all time points. The width (band spreading) of each spot noticeably narrowed as the exchange reaction progressed. The latter observation is consistent with the existence of secondary levels of dispersity around each major fraction and is currently being probed further to relate the extent of ligand place-exchange with different core sizes.

Conclusions. The kinetic results show that the rates of ligand exchange on Au MPCs depend on the concentrations of entering and exiting ligand. The most straightforward explanation is that an R′SH ligand enters the monolayer and protonates a bound thiolate ligand in an associative rate-determining step. (The present experiments do not provide details of the reaction at the microscopic level.) The rate of place-exchange decreases with an increase in the size of the entering ligand and the chain length of the protecting monolayer. There is a substantial gradation in reactivity of surface sites on the cluster. Some sites are significantly easy to exchange

(likely the vertexes of the cluster); others are nearly nonexchangeable sites (likely to be interior terrace sites). Importantly, the easy-to-exchange sites are not a static population, as demonstrated by serial exchange experiments.[4,30] On the basis of all of these observations, we suggest Scheme 2 to represent the processes occurring. A significant aspect of the scheme is surface migration of thiolate ligands, and the implication that the migration depends on the presence of sites that are either vacancies or that exhibit a variable thiolate coordination number.

By analogy, a similar mechanism can be suggested for place-exchange reactions on 2D-SAMs: exchange at defect sites leading to the incorporation of a new surface-bound thiolate. The rate determining step, after exchange at these minority sites, is either the slow migration of other thiolates to the defect sites (which implies migration in their terraces) or the very slow exchange of thiol directly with terrace sites. In the case of the former, the exchange reaction would have the appearance of being independent of the concentration of thiol (entering ligand) and, further, would have the same rate as ligand desorption (which occurs via disulfide formation). Consistent with this idea are the STM observations of Allara[35] in which the domain boundaries of mixed 2D-SAMs on Au were shown to change with time; the migrating species was proposed to be an entire RSAu unit.

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Supporting Information Available: Example NMR spectra of C12 MPC place-exchange reaction with BzSH, both immediately upon addition of reagents and at 24 h. This material is available free of charge via the Internet at http://pubs.acs.org.

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