Differential reactivity of the *inner* and *outer* positions of \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0 \) dimeric staples under place exchange conditions

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Electronic Supplementary Information

**Table of contents**

Experimental section, general .................................................. Page S2  
Synthesis of \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^- \text{TOA}^+ \) cluster .................................................. Page S2  
Synthesis of \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0 \) .................................................. Page S3  
Procedure for the kinetic runs .................................................. Page S4  
Kinetic Analysis ................................................................... Page S5  
Figure S1. \(^1\text{H} \) NMR of \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^- \text{TOA}^+ \) .................................................. Page S6  
Figure S2. UV-Vis spectrum of the cluster \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^- \text{TOA}^+ \) .................................................. Page S6  
Figure S3. \(^1\text{H} \) NMR of \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0 \) .................................................. Page S7  
Figure S4. UV-Vis spectrum of the cluster \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0 \) .................................................. Page S7  
Figure S5. \(^1\text{H} \) NMR spectrum of the exchange product obtained in the reaction of the cluster \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0 \) with 4-fluorobenzylthiol .................................................. Page S8  
Figure S6. UV-Vis spectrum of the exchange product obtained in the reaction of the cluster \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0 \) with 4-fluorobenzylthiol .................................................. Page S8  
Figure S7. \(^1\text{H} \) NMR spectrum of the exchange product obtained in the reaction of the cluster \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0 \) with thiophenol .................................................. Page S9  
Figure S8. UV-Vis spectrum of the exchange product obtained in the reaction of the cluster \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0 \) with thiophenol .................................................. Page S9  
Figure S9. \(^1\text{H} \) NMR spectrum of disulfides obtained by decomposition of the exchange product of the cluster \( \text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0 \) with 4-fluorobenzylthiol .................................................. Page S10  
References ...................................................................... Page S10
Experimental section

General

All commercially available reagents were from Aldrich, and used without purification unless otherwise mentioned. Solvents were purchased from Aldrich, or VWR and deuterated solvents from Cambridge Isotope Laboratories. Chlorinated solvents were kept over K₂CO₃ for at least 24 h prior to use. NMR spectra were recorded on a Jeol JNM-EX-400 spectrometer (operating at 400 MHz for proton) or a Varian 500 spectrometer (operating at 500 MHz for proton, and 470.13 MHz for \(^{19}\)F). \(^1\)H NMR spectra were referenced to the residual protons in the deuterated solvent. \(^{19}\)F NMR spectra were referenced to CFCl₃ as external standard. Chemical shifts (\(\delta\)) are reported in ppm and the multiplicity of each signal is designated by the conventional abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; dd, doublet of doublets. UV-Visible spectra were recorded on a Perkin Elmer Lambda 35 spectrophotometer. Fitting of the kinetic data were performed by using Origin 8.

Representative small scale synthesis of the Au\(_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^+\) TOA\(^+\) cluster.\(^1\)

In a three neck 25 mL round bottom flask were introduced 61 mg of HAuCl₄-3H₂O (0.15 mmol) and 4.3 mL of deossigenated THF. Under argon atmosphere, 102 mg (0.19 mmol) of tetraoctylammonium bromide (TOAB) were added obtaining a deep orange solution. The mixture was cooled at 0 °C by aid of a melting ice bath and kept under stirring for 30 minutes. 2-phenylethanethiol, 100 \(\mu\)L (0.75 mmol) was added slowly to the reaction mixture and the stirring was reduced to a low speed (ca. 60 rpm), after addition of the thiol fading of the solution colour was observed. After 1 hour the ice bath was removed, after two hours from the addition of 2-phenylethanethiol complete disappearing of the original coloration was observed; the mixture was left stirring overnight at room temperature. The mixture was brought at 0 °C with a melting ice bath and kept at this temperature for 1 hour. The stirring rate was increased to a fast regime and a freshly prepared solution of NaBH₄ prepared by dissolving 58 mg of NaBH₄ (1.5 mmol, 10 eq) in 1.5 mL of milliQ water previously chilled in an ice bath was quickly added to the reaction mixture. The solution turned immediately deep brown, after three hours the ice bath was removed and the mixture allowed to react at room temperature. The mixture was left under stirring for 27 hours, monitoring the formation of the Au\(_{25}\) clusters by periodic UV-Vis analysis of the reaction mixture. When no further variations in the UV-Vis spectrum were observed, the reaction mixture was transferred into a stoppered
centrifuge tube and centrifuged at 4000 rpm for 10 minutes operating at 4 °C to remove any solid materials. The supernatant was transferred into a 25 mL round bottom flask and the solvent removed under a gentle argon stream leaving an orange oily residue and a clear aqueous layer. The most of the aqueous solution was pipetted off and the remaining residue was washed with a 70:30 methanol:water mixture (3 x 10 mL) and with a 80:20 methanol:water mixture (3 x 10 mL). The residue was serially treated with 2 mL of methanol and 2 mL of water obtaining a milky white emulsion, the emulsion was pipetted off paying attention to not remove the brown oily residue. This process was repeated until no further formation of the white emulsion could be observed. The residue was washed with water (2 mL) and methanol (2 mL) and dried under vacuum obtaining 26 mg of crude product. H NMR analysis displayed the residual presence of tetraoctylammonium, see Figure S1. The residue was treated several times with acetonitrile (2 mL) each to dissolve the Au25 clusters until no further materials could be collected. The organic phases were combined and the solvent evaporated under reduced pressure obtaining 20 mg of material (yield 42% based on Au).

**Oxidation of Au25(SCH2CH2Ph)18− TOA+ to the Au25(SCH2CH2Ph)180 cluster.**

The oxidation was carried out as described in the literature. In a typical preparation 20 mg of Au25(SCH2CH2Ph)18− TOA+ (2.5 x 10⁻³ mmol) were dissolved in DCM and the solution was permeated under air pressure through a short silica gel plug previously equilibrated with DCM. The grey-green effluent solution was collected and the solvent evaporated. The residue was washed with acetonitrile (1 x 3 mL), hexane (3 x 3 mL) and dried under vacuum obtaining 17 mg (2.3 x10⁻³ mmol) of Au25(SCH2CH2Ph)180 in 92% yield (38% with respect to Au over the two steps). UV-Vis and H NMR confirmed the successful oxidation and the absence of residual tetraoctylammonium salts. H NMR: (400 MHz, benzene-d6) δ: 7.46 (br, 24 H, o-Hα); 7.25-7.0 (m, 66H, m-Hm + p-Hm + o-Hout + m-Hout + p-Hout); 5.47-5.13 (br, 28H (77% with respect to theoretical 36H), α-CH2out + β-CH2in); 2.83 (br, 12H, β-CH2out). UV-Vis: (DCM) λmax: 325, 400, 460, 641, 687 nm.
Procedure for the kinetic runs

The kinetic analyses were performed by $^1$H NMR (400 MHz) in benzene-$d_6$ at 25 °C on a 1.5 mM solution of clusters, corresponding to a 27 mM concentration of the bound thiolates. A 1.5 mM solution of the cluster was prepared in a 1 mL volumetric flask, 600 µL of this solution were then introduced into a 5 mm NMR tube. The sample was allowed to equilibrate at 25 °C into the NMR magnet and the shims were optimized. To the NMR tube 25 µL of a concentrated solution of the incoming thiol (1.0 M for 2, 1.2 M for 3, 1.06 M for 4 and 1.0 M for 5) in benzene-$d_6$ were quickly added to initiate the reaction and the NMR tube was reinserted into the pre-shimmed thermostated NMR magnet. The $^1$H NMR spectra were recorded at given time intervals, each experiment required the acquisition of 8 transients with a relaxation delay of 5 seconds. The NMR spectra were apodized using an exponential window function with a line broadening of 1 Hz.

The kinetic profiles were built by monitoring the time evolution of the integrals of the signals pertaining to the protons $\beta$-H$_{\text{out}}$ (2.83 ppm), the isochronous $\alpha$-H$_{\text{in}}$ (7.46 ppm) and the integrals of the $\beta$-H (2.54 ppm) of the 2-phenylethanethiol formed during the reaction.

The integrals of the signals were referenced to the integral of the water peak that remains constant during the kinetics.
**Kinetic analysis**

Since the place exchange reaction is an equilibrium process, the rate of reaction at the *outer* and *inner* sites is described by equations 1a and 1b where $k''_{f,\text{out}}$, $k''_{b,\text{out}}$, and $k''_{f,\text{in}}$, $k''_{b,\text{in}}$ represent the second order rate constants for the forward and backward reaction at the *outer* and *inner* sites respectively; $[L]$ and $[L']$ represent the concentration of the bound ligands of the reagent and product.

\[ \frac{d[L^\text{out}]}{dt} = -k^*_{f,\text{out}}[L^\text{out}][2] + k^*_{b,\text{out}}[L'^\text{out}][6] \] \hspace{1cm} 1a

\[ \frac{d[L^\text{in}]}{dt} = -k^*_{f,\text{in}}[L^\text{in}][2] + k^*_{b,\text{in}}[L'^\text{in}][6] \] \hspace{1cm} 1b

Under initial rate analysis the backward reaction is negligible and the concentration of the bound ligands appearing at right hand side of equations 1a and 1b can be approximated to its initial value and substituted with the integral area measured at the beginning of the reaction obtaining equations 2a and 2b:

\[ \frac{d[L^\text{out}/L^\text{out}]}{dt} = -k_{f,\text{out}}[2]_0 = -k_{\text{out}} \] \hspace{1cm} 2a

\[ \frac{d[L^\text{in}/L^\text{in}]}{dt} = -k_{f,\text{in}}[2]_0 = -k_{\text{in}} \] \hspace{1cm} 2b

The same arguments apply to aryl thiols 3-5. In this case the integration of the $o$-$\text{H}_{\text{in}}$ signals is partially biased by the signals of thiophenol, and the rate constant for the reaction at these sites was calculated from the difference between the initial rate of formation of 2-phenylethanethiol and the initial rate for the exchange at the *outer* sites since the $\beta$-$\text{H}_{\text{out}}$ signal do not suffer of any overlaps with the signals of the incoming thiol.
Figure S1. $^1$H NMR spectrum (400 MHz) of the cluster Au$_{25}$(SCH$_2$CH$_2$Ph)$_{18}^-$ TOA$^+$ in benzene-$d_6$.

Figure S2. UV-Vis spectrum of the cluster Au$_{25}$(SCH$_2$CH$_2$Ph)$_{18}^-$ TOA$^+$ recorded in dichloromethane (DCM).
Figure S3. $^1$H NMR spectrum (400 MHz) of the cluster $\text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}$ in benzene-$d_6$. In the spectrum * and # denote DCM traces and hexane traces respectively.

Figure S4. UV-Vis spectrum of the cluster $\text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}$ recorded in DCM.
Figure S5. $^1$H NMR spectrum (400 MHz) in benzene-$d_6$ of the exchange product obtained in the reaction of the cluster Au$_{25}$(SCH$_2$CH$_2$Ph)$_{18}$ with 4-fluorobenzylthiol. In the spectrum * and # denote DCM traces and hexane traces respectively.

Figure S6. UV-Vis spectrum of the exchange product obtained in the reaction of the cluster Au$_{25}$(SCH$_2$CH$_2$Ph)$_{18}$ with 4-fluorobenzylthiol, the spectrum was recorded in DCM.
Figure S7. $^1$H NMR spectrum (400 MHz) in benzene-$d_6$ of the exchange product obtained in the reaction of the cluster $\text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0$ with thiophenol. In the spectrum * and # denote DCM traces and hexane traces respectively.

Figure S8. UV-Vis spectrum of the exchange product obtained in the reaction of the cluster $\text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^0$ with thiophenol, the spectrum was recorded in DCM.
Figure S9. Region 4.0-1.5 ppm of the $^1$H NMR spectrum (400 MHz) recorded in benzene-$d_6$ of the mixture of disulfides obtained by iodine decomposition of the exchange product obtained in the reaction of the cluster Au$_{25}$(SCH$_2$CH$_2$Ph)$_{18}^0$ with 4-fluorobenzylthiol. Letters in the spectrum have the following meaning: a: 4-fluorobenzyl disulfide (CH$_2$); b: mixed disulfide (CH$_2$); c: 2-phenylethyl disulfide (CH$_2$). Assignment was made by comparison with the $^1$H NMR spectra of authentic samples of 4-fluorobenzyl disulfide and 2-phenylethyl disulfide recorded in benzene-$d_6$.

Composition calculation:

2:4 = (a+b):c = 0.4:1

Units of 2 in the ligand shell (n2):
N2 = 18 x 0.40/(1.4) = 5

Units of 4 in the ligand shell (n4):
N4 = 18 x 1/(1.4) = 13

References
