

Supporting Information

Molar Excess of Coordinating N-Heterocyclic Carbene Ligands Triggers Kinetic Digestion of Gold Nanocrystals

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Materials

Imidazole (99%) was purchased from Acros Organics (Morris Plains, NJ). Poly(ethylene glycol) methyl ether (average MW: ~ 750 Da), poly(isobutylene-*alt*-maleic anhydride) (PIMA) (average MW: ~6000 Da), 1-(3-aminopropyl)imidazole ($\geq 97.0\%$), potassium *tert*-butoxide ($\geq 98\%$), sodium bicarbonate, sodium azide ($\geq 99.5\%$), methanesulfonyl chloride ($\geq 99.7\%$), bromoethane ($\geq 99\%$), gold(III) chloride trihydrate ($> 99.9\%$), chloro(dimethylsulfide)gold(I) (Au(SMe₂)Cl), oleylamine (70%), sodium hydroxide, filter agent Celite 545, lipoic acid (LA, $> 98.0\%$) along with solvents used were purchased from Sigma Aldrich (St Louis, MO). Deuterated solvents used for NMR experiments were purchased from Cambridge Isotope Laboratories (Andover, MA). The chemicals and solvents were used as received unless otherwise specified. Column purification chromatography was performed using silica gel (60 Å, 230–400 mesh, purchased from Bodman Industries, Aston, PA).

Syntheses were carried out under N₂ passed through an O₂ scrubbing tower, unless otherwise stated. Air sensitive materials were handled in an Mbraun Labmaster glovebox, and standard Schlenk techniques were used when handling air-sensitive materials.

Instrumentation

The optical absorption spectra were acquired using a UV-vis spectrophotometer (UV 2450 model, Shimadzu, Columbia, MD). The photoligation experiments were carried out using a UV photoreactor (Model LZC-4V, Luzchem Research, Inc., Ottawa, Canada), equipped with a total of 14 lamps, 6 lamps installed on top and 4 lamps on each side. This reactor provides ultraviolet light (i.e., a band centered at $\lambda \sim 350$ nm) with a power of 4.5 mW/cm^2 .¹ The solution phase ^1H and ^{13}C NMR spectra, measured for the ligand solutions and AuNP dispersions, were collected using a 400/600 MHz NMR spectrometer (Bruker SpectroSpin, Billerica, MA). The 2D Heteronuclear Multiple Bond Correlation (HMBC) NMR spectra were collected using a standard Bruker pulse sequence “hmbcgp1pndqf” with 5s recycle delay, a cnst13 (J) = 5 Hz, 16 dummy scans, 8 scans, acquisition of 4096 data points, and 128 increments. Heteronuclear zero and double quantum coherence is applied to optimize on long-range couplings, and low-pass J-filter to gradient pulses are used for selection. The mass spectrometry data were obtained using a matrix-assisted laser-desorption/ionization time-of-flight (MALDI-TOF) spectrometer equipped with a 337 nm N_2 laser (MALDI, Bruker Daltonics, Auto Flex III L200, Bremen, Germany), and 4000 Q TRAP LC/MS/MS system (Applied Biosystem, MDS Sciex, Toronto, Canada). The MALDI matrix was prepared by dissolving 4-cyanohydroxysuccinic acid (10 mg) in a mixture of 75% acetonitrile and 25% water containing 0.1% TFA (v/v). The TEM images of gold nanoparticles were obtained using a JEOL JEM-ARM200cF (a cold field emission probe Cs-Corrected Transmission Electron Microscope, Peabody, MA) operated at 200 kV. The high angle annular dark field scanning transmission electron microscopy (HAADF-STEM) images were collected with a JEOL HAADF detector using the following experimental conditions: probe size 0.78 nm, scan speed 32 ms per pixel, and camera length 8 cm. These correspond to a probe convergence angle of 21 mrad and inner collection angle of 76 mrad. The TEM samples were prepared by drop casting dilute dispersions of either OLA-capped AuNPs in hexane, or the NHC-PEG-Au etched dispersions in THF onto a TEM grid (200 Cu mesh, Ted Pella, INC, CA), followed by slow drying under a mild vacuum overnight.

Growth of Oleylamine-capped AuNPs (OLA–AuNPs). The oleylamine-coated AuNPs (~10 nm diameter) were synthesized using a high temperature growth method, following the protocol reported in reference.² First, 4 mL of oleylamine was loaded into a 50 mL three-neck round-bottom flask and heated to 150 °C under N_2 flow. Separately, 119 mg of gold precursor ($\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$, tetrachloroauric (III) acid) was dissolved in 2 mL of oleylamine, and then rapidly injected into the above flask (pre-heated oleylamine solution). The reaction mixture was further heated at 150 °C for 40 min, then letting it cool to room temperature. The growth dispersion was diluted by adding hexane (~ 10-15 mL) followed by one round of centrifugation (at 3,700 RPM for 15 min); this removes unreacted precursors. The supernatant containing AuNPs dispersed in hexane was collected and stored until further use.

Top-down Etching of AuNPs using NHC-PEG Ligands. The etching experiments described in this study were performed using large molar excesses of NHC-PEG ligands with respect to AuNPs, namely, [NHC-PEG]:[AuNP] = 100,000:1, 300,000:1, 500,000:1 and 700,000:1. Here, we briefly detail conditions using 300,000-fold molar excess of NHC-PEG generated in the presence of the AuNPs (i.e., under in-situ conditions). The concentration of AuNPs was 5.6 nM for all samples. The same chemical approach was employed for the other molar ratios. An aliquot of hydrophobic stock dispersion of OLA-AuNPs (20.2 μ L, 0.56 μ M) in hexane was first mixed with excess ethanol yielding a precipitate. One round of centrifugation (3500 RPM, 5 min) was applied, the supernatant was discarded and the pellet was redispersed in THF (500 μ L). This step removes excess native ligands from the dispersion. A solution of PEG-EIm-ium (3 mg in 500 μ L of THF) was added and the mixture was sonicated for \sim 1 min yielding a homogeneous phase. The vial was sealed with a rubber septum and the atmosphere in the vial was switched to nitrogen by applying 3 rounds of vacuum, followed by purging with N₂. Then, a solution of KOtBu (1 mg in 1000 μ L THF) was added to the above mixture and left stirring at room temperature for the full duration of the experiment (i.e., the time required to achieve loss of SPR feature and loss of color). We note that three-fold molar excess of KOtBu with respect to PEG-EIm-ium was used to ensure complete carbene generation. The PEG-imidazolium salt (PEG-EIm-ium) was prepared from poly(ethylene glycol) methyl ether (average MW 750 Da) following a procedure reported by our group.³⁻⁴

Synthesis of NHC-PEG-Au-Cl Complex. PEG-EIm-ium (0.20 g, 0.22 mmol), Me₂S-Au-Cl (0.07 g, 0.22 mmol) and K₂CO₃ (0.091 g, 4.3 mmol) were mixed in acetone (3 mL) using a 20 mL scintillation vial and stirred at 60°C for 5 hours. The resulting reddish-brown mixture was filtered through a pad of Celite and the solvent was removed using a rotary evaporator. Purification of the compound was accomplished via silica gel column chromatography using DCM:MeOH mixtures (95:5 in volume) as eluent to afford the NHC-PEG-Au-Cl complex as a yellow oil. The overall yield of the reaction was \sim 70%.

Digestion Kinetic Studies

Digestion experiments implemented using excess NHC-PEG. In a typical digestion experiment, an aliquot of OLA-AuNPs dispersed in THF (20.2 μ L, 0.56 μ M) was mixed with a solution of PEG-EIm-ium in THF using a 7 mL Scintillation Vial. Then, KOtBu was added followed by sonication for \sim 1 min. The total volume of the dispersion was adjusted to 2 mL using THF, yielding a final AuNP concentration of 5.6 nM. A 400 μ L aliquot of the above gold colloid dispersion was retrieved, subjected to a round of centrifugation (3000 RPM, 2 min), and the supernatant was transferred to a 0.5 cm optical path quartz cuvette. The first absorption spectrum was recorded approx. 3 min after the addition of base, then several absorption profiles were collected, with a first set measured at 15 min intervals, followed by second set measured at 30 min intervals then 1 h intervals until the changes in the SPR absorbance peak reached saturation (i.e., anywhere between \sim 8 h and 3 days, depending on the concentration). Summary of the excess

molar ratios of PEG-EIm-ium and corresponding ratios of KOtBu used for digestion experiments are listed in Table S1.

Digestion experiments implemented using excess NHC-PIMA-PEG. The samples were prepared following the steps described above except that the NHC-PEG was substituted with NHC-polymer. We modified the excess molar concentration of NHC-PIMA-PEG to be one-twentieth of the NHC-PEG concentration to account for the difference in coordination numbers between the two ligands, i.e., the final molar excess is calculated with respect to the concentration of NHC groups. To maintain a consistent AuNP concentration of 5.6 nM across all digestion experiments, the dispersion's overall volume was adjusted to 1.8 mL. NHC-PIMA-PEG was prepared following the details provided in a previous protocol.⁴

Digestion experiments implemented using thiol-appended ligands (LA-PEG and SH-PEG). We followed the steps described above but substituted the NHC-PEG with either LA-PEG or SH-PEG ligands.^{3,5} Typically, a dispersion of OLA-AuNPs in THF (16.6 μ L, 0.61 μ M) was mixed with a solution of LA-PEG in THF using a 1 cm optical path quartz cuvette. Similarly, a AuNP dispersion in THF (20 μ L, 0.5 μ M) was mixed with SH-PEG. The molar concentration of LA-PEG/SH-PEG in each solution was adjusted, according to their associated molecular weights, to achieve the desired molar excess with respect to AuNPs. Varying amounts of THF were added to each dispersion to yield a final volume of 1.8 mL, a final AuNP concentration of 5.6 nM, but a varying concentration of ligands to achieve the desired molar excess of LA or SH (see Figure 7 and Tables 2 and 3). The cuvette was sealed using a screw cap and placed inside the UV-vis cell holder fitted with an electronic cell stirrer. The initial absorption spectrum was recorded immediately (\sim 30 s after mixing). Subsequently, sets of absorption profiles were measured at 15 min, 30 min, 1 h and 4 h intervals until the SPR absorbance peak reached saturation. LA-PEG and SH-PEG ligands were synthesized following protocols reported by our group.^{3,5-6} In particular, the SH-PEG ligand was synthesized by appending the same PEG₇₅₀ block onto 11-(Acetylthio)undecanoic acid, following the protocol described in our recent report.⁵ It is the same PEG block employed for preparing PEG-EIm-ium described above.

NMR Sample Preparation. To prepare final (etched) samples of the NHC-PEG-Au to acquire 1D ¹H and 2D (HMBC) NMR measurements, the reaction product after incubation was first centrifuged to remove excess KOtBu or/and potassium salts. Then, the supernatant containing NHC-PEG-Au complexes was collected and washed two times with hexane, followed by centrifugation (5 min at 3,500 RPM). The retrieved pellet was gently dried under nitrogen flow, dispersed in D₂O (500 μ L), and then loaded into an NMR tube for data collection. The 1D ¹³C NMR sample of NHC-PEG-Au (500 μ L volume) was prepared following the same steps described above, except that DMSO-d₆ was used (instead of D₂O) to disperse the AuNPs and acquire the spectra. We found that the downfield resonance ascribed to the metallated carbene carbon is more readily detectable when DMSO-d₆ was used as the NMR solvent.

Computational Details. Orca package was used to carry out the density functional theory (DFT) calculations.⁷ The binding energy was computed (equation S1) for several NHC-Au and Thiol-Au complexes in gas phase, for both edge and face of a gold crystal. The number of gold atoms in the clusters are 20, 23, 26, 32, 36 and 42, where the number of gold atoms in the first layer was kept constant comprising 12 atoms while the second and the third layer were changed to observe how the energy converges. For each system, geometry optimization was done employing LANL2DZ basis set for all atoms, plus Hay-Wadt pseudopotential for gold atoms. For modeling the long-range interactions, the D3⁸ dispersion correction was added to the DFT energies (using B3LYP functional). To model the bulk gold crystal behavior their coordinates were kept constant (2.8838 Å). Following geometry optimization two single point calculations were performed, one for the gold clusters and one for the NHC/thiol molecule.

$$\Delta E = E(\text{Au-NHC/thiol}) - E(\text{NHC}) - E(\text{thiol}) \quad (\text{S1})$$

Table S1. Summary of the various molar ratios of PEG-EIm-ium ligands and K₂OtBu used for the digestion experiments.

Fold excess ligand ^a	PEG-EIm-ium (mg)	Excess K ₂ OtBu (eq)	K ₂ OtBu amount (mg)
100,000	1	3	0.4
300,000	3	3	1
500,000	5	3	1.6
700,000	7	3	3

^a Equal to [NHC-PEG]/[OLA-AuNPs].

Table S2. Binding energies (kcal/mol) and bond distances (Å) of NHC- or S-bound gold predicted for nanoclusters of 20, 23, 26, 32, 36 and 42 Au atoms, respectively.

Nanocluster Size	Binding Energy (kcal/mol)		Bond Distance (Å)	
	NHC-bound Au	S-bound Au	NHC-Au	S-Au
Au ₂₀	52.75	33.22	2.32	2.69
Au ₂₃	51.94	33.41	2.32	2.71
Au ₂₆	52.04	33.03	2.33	2.71
Au ₃₂	55.67	35.95	2.30	2.66
Au ₃₆	58.10	36.42	2.30	2.65
Au ₄₂	55.91	35.28	2.30	2.68

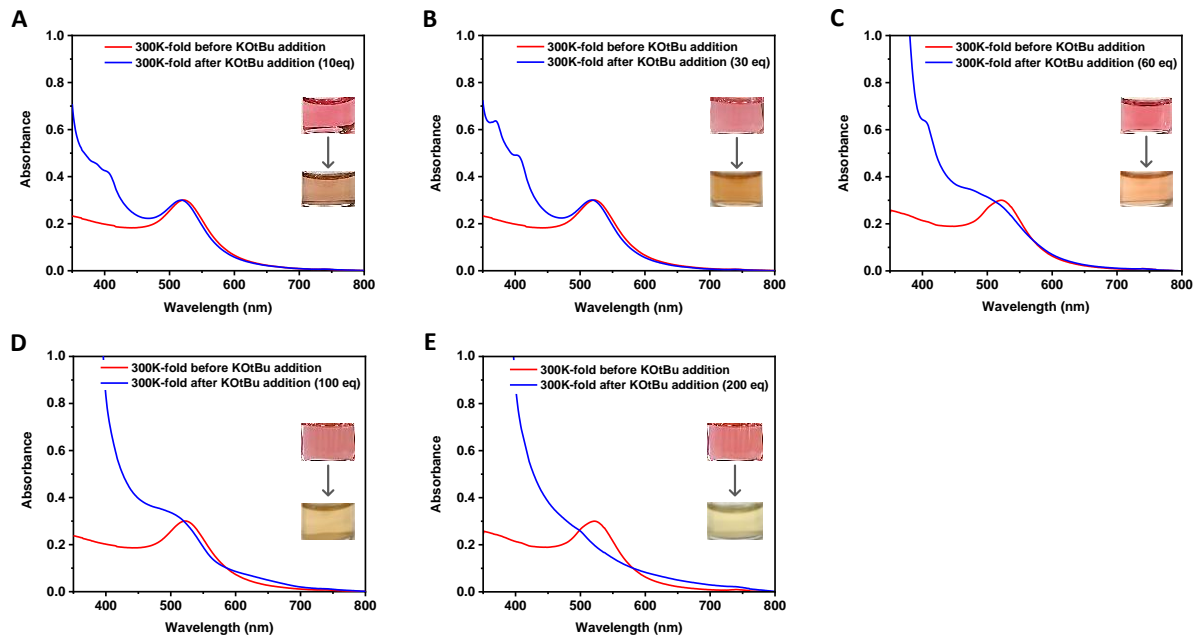


Figure S1. Effect of varying the molar equivalent of KOtBu with respect to the molar concentration of the PEG-EIm-ium used during the etching experiments. (A-E) Side-by-side UV-vis spectra collected from the AuNP dispersion (before, red lines) and right after KOtBu addition (blue lines). Data clearly indicate that using higher molar equivalent of base leads to faster changes in the SPR signature. The insets show white light images of AuNP dispersions in THF before (top) and after KOtBu addition (bottom). Experiments were carried out using approx. 300-fold excess NHC-PEG ligand with respect to the molar concentration of AuNPs.

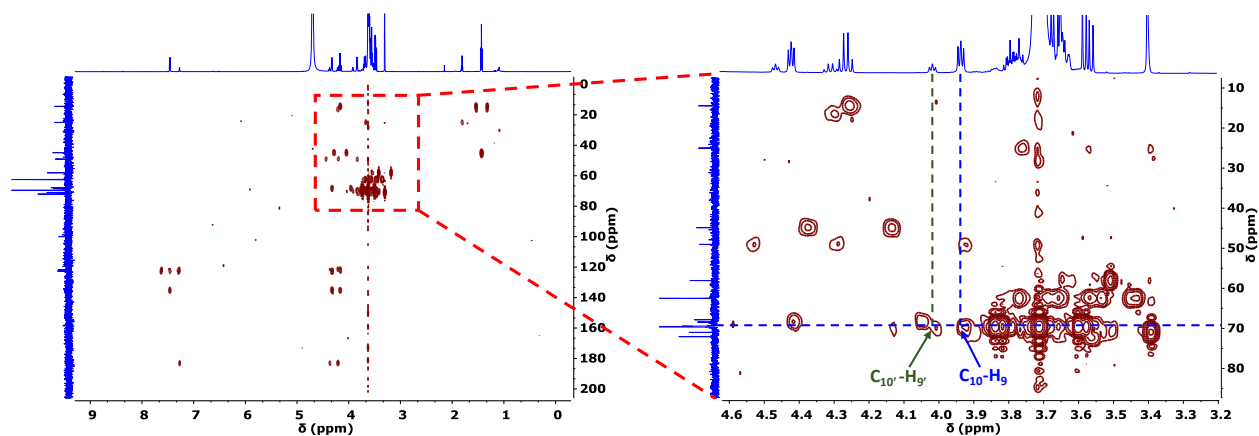


Figure S2. Expanded 2D HMBC spectrum covering the upfield chemical shift.

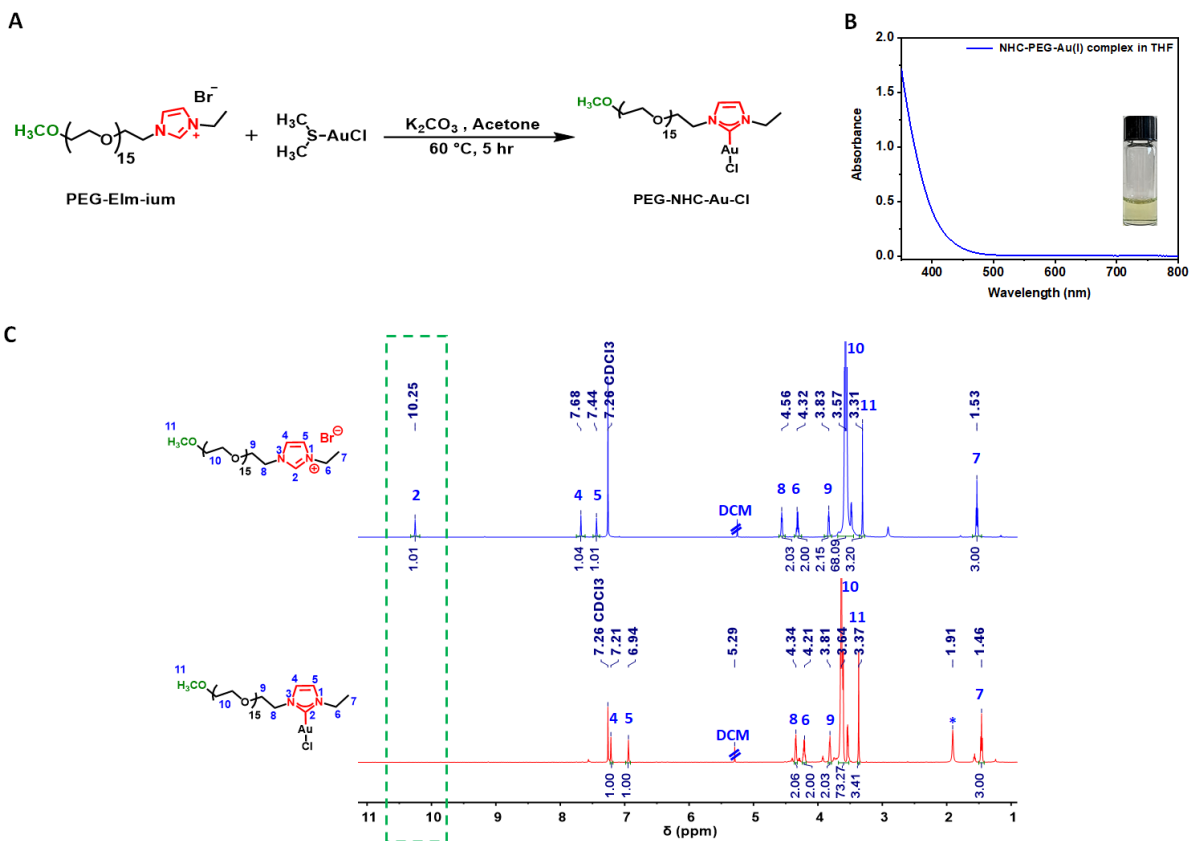


Figure S3. (A) One-step synthesis of NHC-PEG-Au-Cl complex via reaction of Me₂S-Au-Cl with PEG-Elm-ium in the presence of K₂CO₃ (weak base) at 60 °C. (B) The UV-vis spectrum collected from the NHC-PEG-Au-Cl complex in THF clearly indicates that the complex has no SPR absorption feature. Inset shows white light image of NHC-PEG-Au-Cl complex in THF. (C) Stacked ¹H NMR spectra of PEG-Elm-ium salt precursor (top) and NHC-PEG-Au-Cl complex (bottom). All samples were prepared in CDCl₃. Absence of the acidic proton peak (C₂) at 10.25 ppm confirms NHC-Au complexation.

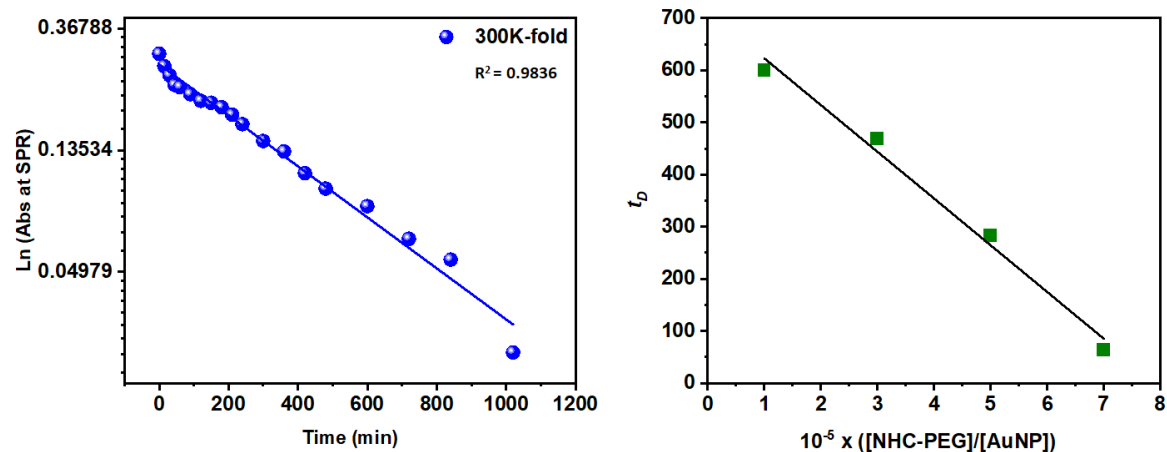


Figure S4. (left) Plot of $\ln(\text{Abs})$ vs time of reaction applied to the data acquired from a sample using 300-fold excess NHC-PEG. (right) Digestion time vs NHC-PEG molar excess deduced from the data shown in Figure 6 main text. The line is included to prove the linear progress of the digestion time with the ligand molar excess.

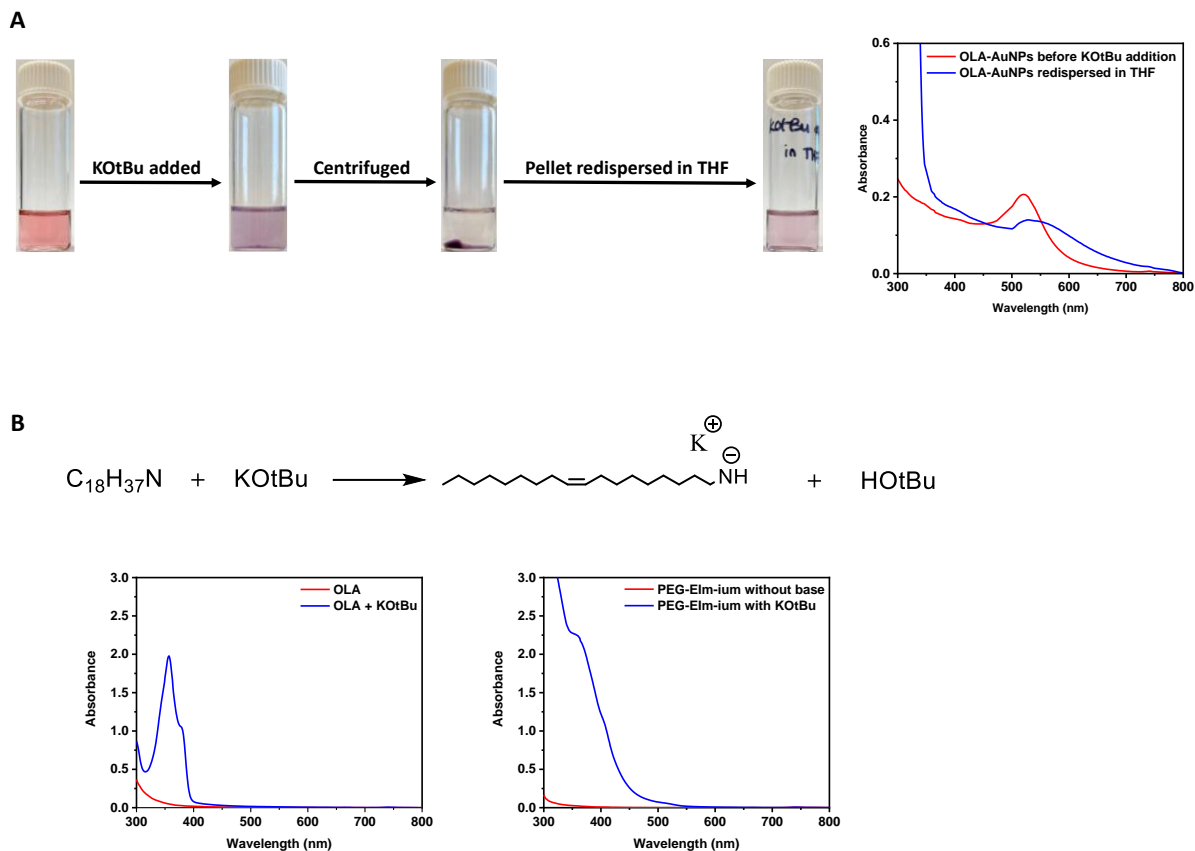


Figure S5. Effects of excess KOtBu. (A) White light images of AuNP dispersions subjected to the indicated steps, side-by-side with the UV-vis absorption spectra acquired from the starting OLA-AuNPs in THF and from the NPs after redispersing the pellet in THF. (B) UV-vis absorption spectra of OLA (left) and PEG-Elm-ium (right) before and after base treatment (both in THF). The addition of base alters the absorption profiles of OLA (at wavelengths below 400 nm) and PEG-Elm-ium (at wavelengths below 500 nm). A reaction between base and OLA is proposed.

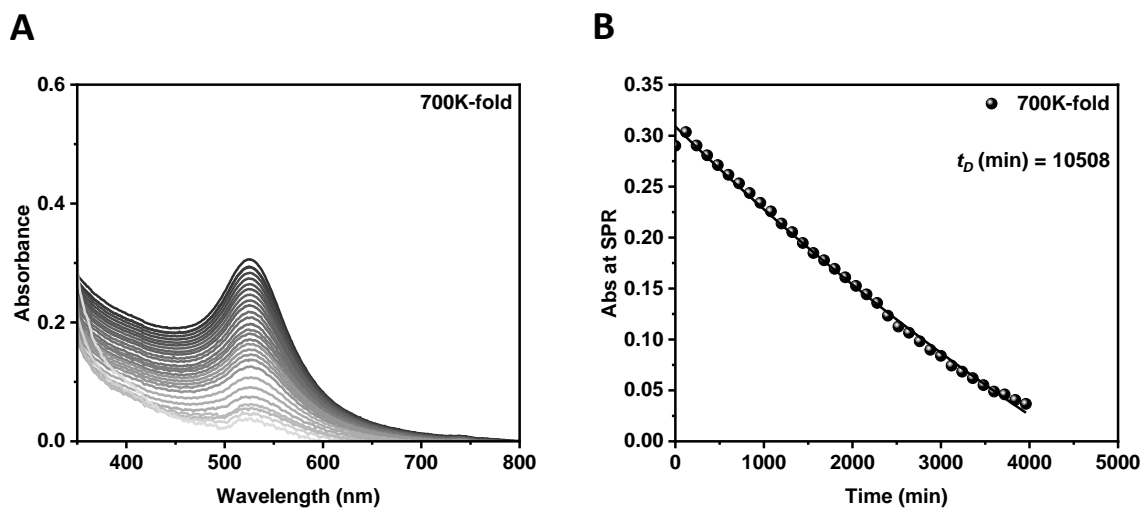


Figure S6. Digestion experiments using 700k-fold NHC-PIMA-PEG. (A) UV-vis absorption spectra acquired at varying time intervals. (B) Progression of the SPR peak value vs time extracted from the absorption data shown in (A). The molar excess is given for the overall concentration of NHC groups (not the polymer chains) with respect to AuNPs.

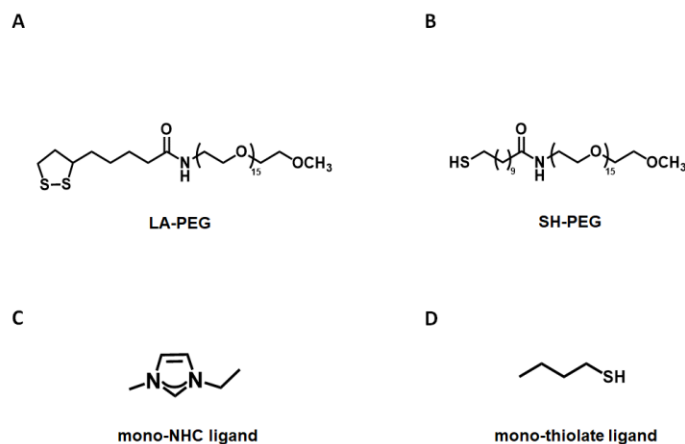


Figure S7. Chemical structures of (A) LA-PEG and (B) SH-PEG, along with the structures of monoNHC and thiolate ligands used for the DFT calculations (C, D).

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