Electronic Supplementary Information (ESI)

An Imine-Based Approach to Prepare Amine-Functionalized Janus Gold Nanoparticles

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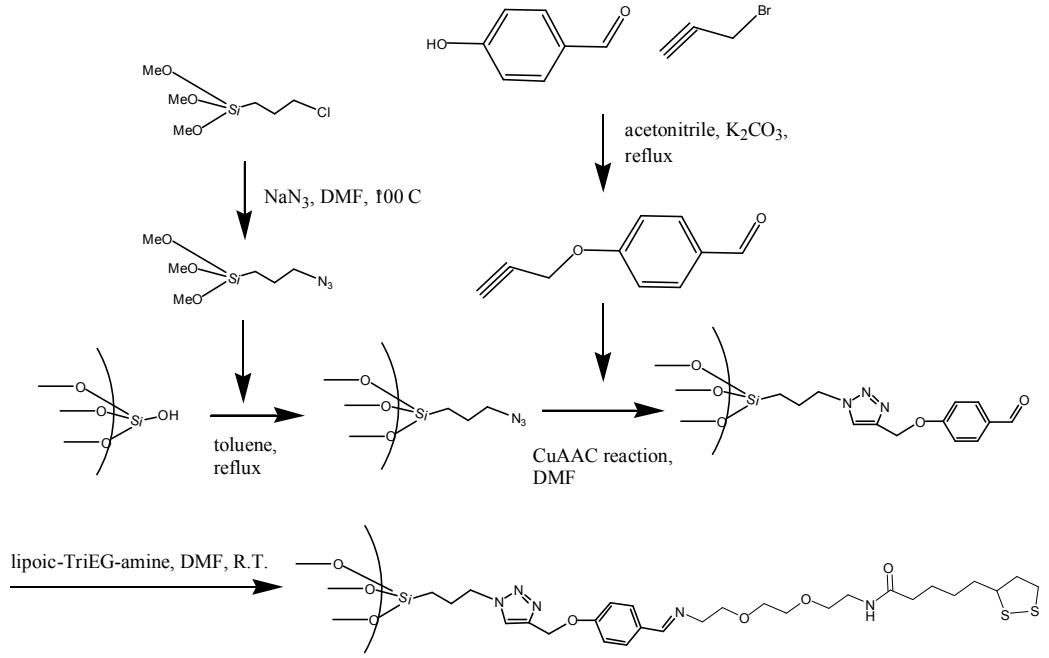
Materials and instruments

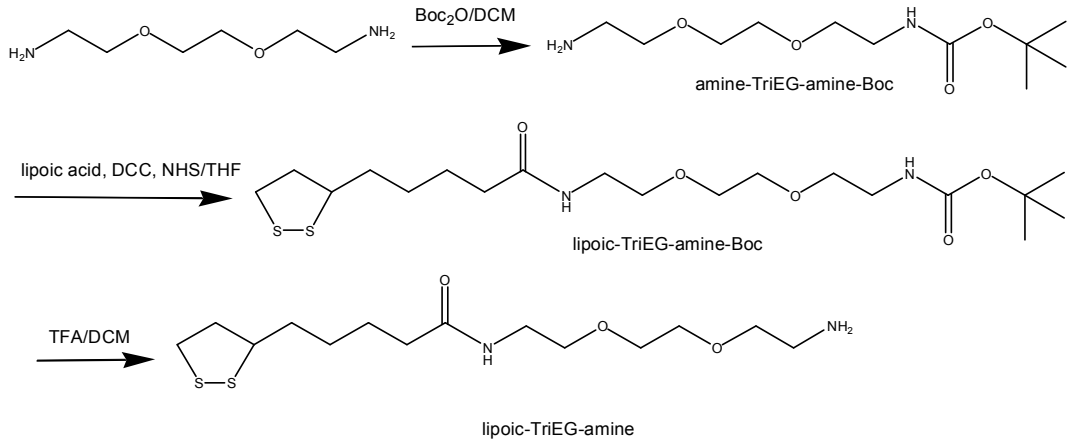
$AgNO_3$, 3-chloropropyltrimethoxysilane, 4-(dimethylamino)pyridine, dodecylamine, 2,2'-(ethylenedioxy)bis(ethylamine), 4-hydroxybenzaldehyde, poly(ethylene glycol) methyl ether (average M_n 750), (+)-sodium L-ascorbate, sodium citrate dihydrate, and tetraethyl orthosilicate (TEOS) were purchased from Sigma Aldrich. $CuSO_4{\cdot}5H_2O$, di-*tert*-butyl dicarbonate, $HAuCl_4{\cdot}3H_2O$, N-hydroxysuccinimide (NHS, >98%), lipoic acid, propargyl bromide solution, sodium azide, sodium borohydride, tetraoctylammonium bromide (TOAB), and trifluoroacetic acid were purchased from Alfa Aesar. N,N'-dicyclohexylcarbodiimide (DCC) was purchased from Merck. All chemicals were used as received.

^{1}H-NMR and ^{13}C-NMR spectra were measured on a Bruker BBFO-400 spectrometer. Mass spectrometry was measured on a ThermoFinnigan LCQ Fleet MS spectrometer. Transmission electron microscopy (TEM) characterization was carried out on a JEM-1400 (JEOL) operating at 100kV. Scanning electron microscopy (SEM) characterization and energy dispersive X-ray spectroscopy were carried out on a field emission JSM-6700F (JEOL). X-ray photoelectron spectroscopy (XPS) analysis was carried out on a SPECS HSA3500 plus spectrometer with Mg X-ray source. FT-IR spectra were recorded using Perkin-Elmer 1760X FT-IR spectrometer with SiO_2 powder diluted in KBr. UV-vis spectra were recorded using a Shimadzu UV-3600 UV–vis–NIR spectrophotometer. Zeta-potential value was measured by Mavern Nanosizer.

Synthesis of organic compounds and nanoparticles



Scheme S1. Preparation procedure of SiO_2 NPs functionalized with lipoyl ligand bridged via imine bond.



Scheme S2. Preparation of the ligand lipoic-TriEG-amine.

1. Synthesis of 3-azidopropyltrimethoxysilane

   3-Chloropropyltrimethoxysilane (0.86g, 4.3mmol) and sodium azide (1.10g, 17mmol) were loaded into anhydrous DMF (10 mL). The reaction was carried out at 90 °C under nitrogen atmosphere for 24h. Then, the reaction solution was cooled to room temperature and filtered quickly to remove any solids. The filtrate was subjected to vacuum at 40 °C to remove all DMF solvent, affording the product. Yield: 69.2%. ^{1}H-NMR (400MHz, $CDCl_3$): δ 3.55 (s, 9H), 3.25 (t, J=8Hz, 2H), 1.69 (m, 2H), 0.68(t, J=8Hz, 2H). ^{13}C-NMR (100MHz, $CDCl_3$): δ 53.69, 50.29, 22.42, 6.30.
2. Synthesis of 4-(propargyloxy)-benzaldehyde[1]

   4-Hydroxybenzaldehyde (3.05g, 25mmol) was dissolved in acetone (125 mL). Potassium

carbonate (4.85g, 35mmol) was then added and the mixture was refluxed under N_2 for 30min. Thereafter, propargylbromide (5.55mL, 50mmol) was added and the mixture was further refluxed for 2h. After cooling, acetone was removed under reduced pressure and the residue was dissolved in ethyl acetate (150mL). The solution was washed with water and brine, dried over $MgSO_4$. After filtration, it was concentrated under reduced pressure. The crude mixture was purified through chromatography (hexane: EtOAc, 5:1) to obtain product as white solids. Yield: 90.3%. ^{1}H-NMR (400MHz, $CDCl_3$): δ 9.90 (s, 1H), 7.86 (t, 2H), 7.10 (t, 2H), 4.78 (s, 2H), 2,59 (s, 1H). ^{13}C-NMR (100MHz, $CDCl_3$): 190.75, 162.37, 131.88, 130.60, 115.19, 77.58, 76.41, 55.95. ESI-MS: m/z calcd for $C_{10}H_8O_2$:160.05, found: 160.98 $[M+H]^+$.

3. Synthesis of lipoic-TriEG-amine-Boc

   Lipoic acid (0.74g, 3.6mmol) and N-hydroxysuccinimide (0.46g, 3.96mmol) were dissolved in tetrahydrofuran (14mL). N,N'-Dicyclohexylcarbodiimide (0.82g, 3.96mmol) dissolved in tetrahydrofuran (7mL) was then added. The mixture was stirred for 4h and the generated precipitate was removed by filtration. The filtrate was then added into tetrahydrofuran solution (14mL) of {2-[2-(2-amino-ethoxy)-ethoxy]-ethyl}-carbamic acid tert-butyl ester[2] (amine-TriEG-amine-Boc in Scheme S2, 0.90g, 3.60mmol). The mixture was stirred overnight at room temperature. After removing the generated solids, the crude product was purified through chromatography (hexane: EtOAc, 1:1 and then EtOAc: MeOH, 10:1) to obtain yellow viscous oil. Yield: 88.1%. ^{1}H-NMR (400MHz, MeOH-D_4): δ 3.53-3.65 (m, 9H), 3.38 (t, 2H), 3.11-3.26 (m, 4H), 2.45-2.53 (m, 1H), 2.24 (t, 2H), 1.88-1.96 (m, 1H), 1.60-1.80 (m, 4H), 1.46 (s, 11H). ^{13}C-NMR (100MHz, MeOH-D_4): δ 174.62, 156.94, 78.73, 69.95, 69.75, 69.41, 56.29, 40.03, 38.98, 38.09, 35.50, 34.41, 33.44, 28.54, 27.75, 25.44, 25.38. ESI-MS: m/z calcd for $C_{19}H_{36}N_2O_5S_2$: 436.21, found: 437.28 $[M+H]^+$.

4. Synthesis of lipoic-TriEG-amine

   Lipoic-TriEG-amine-Boc (6.46g, 14.8mmol) was dissolved in DCM (50mL). Then, trifluoroacetic acid (TFA, 15mL) was added under stirring for overnight. Both DCM and TFA were removed under vacuum. The crude product was purified via chromatography (hexane: EtOAc, 1:1 to 1:10) to obtain yellow viscous oil. Yield: 60.0%. ^{1}H-NMR (400MHz, MeOH-D_4): δ 3.66-3.75 (m, 9H), 3.38-3.41 (m, 2H), 3.13-3.18 (m, 4H), 2.45-2.50 (m, 1H), 2.21-2.28 (m, 2H), 2.00-2.10 (m, 2H), 1.85-1.95 (m, 1H), 1.63-1.72 (m, 4H), 1.47-1.55 (m, 2H). ^{13}C-NMR (100MHz, MeOH-D_4): δ 174.83, 70.00, 69.32, 66.56, 56.23, 39.95, 39.27, 38.87, 37.96, 35.59, 34.33, 28.46, 25.49, 25.02. ESI-MS: m/z calcd for $C_{14}H_{28}N_2O_3S_2$: 336.15, found: 337.21 $[M+H]^+$.

5. Synthesis of lipoic-mPEG$_{750}$

   Lipoic acid (3.10g, 15.0mmol), mPEG$_{750}$ (13.50g, 18.0mmol), 4-(dimethylamino)pyridine (0.55g, 4.5mmol) were dissolved in DCM (120mL). Then, N,N'-dicyclohexylcarbodiimide (3.40g, 16.5mmol) dissolved in DCM (30mL) was added. After stirring at room temperature overnight, the generated solids were removed by filtration. The filtrate was then wash with dilute HCl aqueous solution, brine and water, dried over $MgSO_4$. After concentrating under reduced pressure, the crude product was purified through chromatography (hexane: EtOAc, 1:1, then EtOAc: MeOH,

6:1) to obtain yellow viscous oil. Yield: 72.4%. ^{1}H-NMR (400MHz, $CDCl_3$): δ 3.98 (t, 2H), 3.30-3.58 (m, 57H), 2.84-2.97 (m, 2H), 2.19-2.27 (m, 1H), 2.10-2.13 (m, 2H), 1.63-1.71 (m, 1H), 1.39-1.49 (m, 4H), 1.21-1.32 (m, 2H). ^{13}C-NMR (100MHz, $CDCl_3$): δ 173.00, 71.74, 70.38, 68.93, 63.22, 58.77, 56.08, 40.02, 38.29, 34.41, 33.70, 28.49, 24.43.

6. Synthesis of pristine SiO_2 NPs

   Under vigorous stirring, TEOS (9mL) was added dropwise into ethanol (300mL) containing ammonia aqueous solution (ca. 25%, 21mL). The reaction was stirred overnight. Thereafter, the generated SiO_2 NPs were washed with ethanol for 5 times and finally dispersed in ethanol for storage.

7. Preparation of azide functionalized SiO_2 NPs

   Pristine SiO_2 NPs (ca. 1g) were dispersed in toluene (100mL) and the mixture was then heated to 100 °C under N_2 atmosphere and with vigorous stirring. Then, 3-azidopropyltrimethoxysilane (1mL) was injected. The reaction was maintained at 110 °C for 24h. After cooling the reaction solution to room temperature, SiO_2 NPs were purified via repeated centrifugation-washing process with the use of ethanol to finally obtain azide functionalized SiO_2 NPs.

8. Preparation of benzaldehyde functionalized SiO_2 NPs

   Azide functionalized SiO_2 NPs (0.16g) and 4-(propargyloxy)-benzaldehyde (0.14g, 0.88mmol) were loaded into DMF (5mL). The mixture was ultrasonicated to make a clear suspension. Then, $CuSO_4{\cdot}5H_2O$ (0.32g, 1.29mmol) and (+)-sodium L-ascorbate (1.28g, 6.45mmol) were added successively. The mixture was stirred at room temperature for 24h. After that, a proper amount of HCl aqueous solution was added to make insoluble organic by-products dissolved, before the mixture was subjected to centrifugation to obtain benzaldehyde functionalized SiO_2 NPs. The obtained SiO_2 NPs were washed few times with DMF and water, and finally stored in DMF.

9. Conjugation of lipoic-TriEG-amine onto SiO_2 NPs

   For the conjugation of lipoic-TriEG-amine onto SiO_2 NPs, the obtained benzaldehyde functionalized SiO_2 NPs (ca. 0.1g) were dispersed in DMF (4mL), to which a methanol solution of lipoic-TriEG-amine (0.5M, 1mL) was then added. The reaction mixture was stirred at room temperature overnight. After that, SiO_2 NPs were washed with DMF for three times to remove the excess lipoic-TriEG-amine, which were finally dispersed in DMF. For XPS analysis, ethanol was used as solvent in place of DMF to avoid interference on nitrogen analysis.

10. Synthesis of AuNPs

    Citrate stabilized AuNPs with a size of 14nm were synthesized as follows. $HAuCl_4{\cdot}3H_2O$ (0.07g, 0.17mmol) was dissolved in deionized water (386mL). The solution was heated to about 140 °C. Under vigorous stirring, sodium citrate dihydrate (0.23g, 0.79mmol) dissolved in deionized water (4mL) was injected. The reaction was maintained at 140 °C for 15min before it was slowly cooled down to room temperature.

    Citrate stabilized AuNPs with a size of 40nm were synthesized under a similar process. $HAuCl_4{\cdot}3H_2O$ (0.05g, 0.12mmol) was dissolved in deionized water (400mL) and the mixture was heated to 140 °C. Under vigorous stirring, sodium citrate dihydrate (0.05g, 0.15mmol) dissolved

in deionized water (4mL) was injected. The reaction was kept for 5min before cooling to room temperature.

Dodecylamine capped AuNPs were synthesized as follows. $HAuCl_4 \cdot 3H_2O$ (0.06g, 0.15mmol) was dissolved in deionized water (6mL), to which a toluene solution (16mL) of tetraoctylammonium bromide (0.43g, 0.79mmol) was then added. The two-phase mixture was vigorously stirred at 0 °C for 10min before a freshly prepared water solution of sodium borohydride (0.07g, 1.78mmol) was added dropwise. After 2h, the toluene phase was separated and washed with H_2SO_4 water solution (1M) and water successively. Thereafter, dodecylamine (0.15g, 0.79mmol) was added into the toluene solution and the mixture was stirred at room temperature overnight. After that, methanol was added to precipitate these dodecylamine capped AuNPs. These AuNPs were collected after centrifugation and re-dispersed in toluene for storage.

11. Synthesis of citrate stabilized AgNPs

    $AgNO_3$ (90.5mg, 0.53mmol) was dissolved in deionized water (500mL) and the mixture was heated to 140°C. Sodium citrate dihydrate (0.1g, 0.34mmol) dissolved in water (10mL) was then injected to the reaction mixture. The reaction was kept at 140°C for 1h before it was cooled to room temperature. The obtained AgNPs were polydisperse, including some non-spherical crystals such as rods, triangular bricks and long wires. After standing for a few days, some large crystals were settled down and thereafter, AgNPs on the uppermost level were collected for further use.

12. Preparation of Janus AuNPs

    Under vigorous stirring, the lipoic-TriEG-amine conjugated SiO_2 NPs in DMF were added into water solution (50mL) of as-prepared citrate stabilized AuNPs. The density of AuNPs on SiO_2 NPs surface could be adjusted by changing the quantity of SiO_2 NPs added. Similarly, for adsorption of dodecylamine capped AuNPs, SiO_2 NPs in DMF was added into toluene or DMF solution of dodecylamine capped AuNPs. To passivate the external surface of the adsorbed AuNPs, an excess amount of lipoic-$mPEG_{750}$ dissolved in MeOH was added to the above NPs dispersions, and the reaction was kept overnight. Thereafter, the obtained SiO_2NPs@AuNPs were isolated through centrifugation by removing the excess lipoic-$mPEG_{750}$. The obtained SiO_2NPs@AuNPs were then washed with water for three times before they were dispersed in 2% HF water solution (pH~1). After a few hours, the adsorbed AuNPs were released completely, while the solution was further kept in the acidic solution overnight. Finally, the obtained AuNPs were purified by either the centrifugation-washing process or dialysis against water.

References:

1. S. Hoogendoorn, A. E. M. Blom, L. I. Willems, G. A. van der Marel and H. S. Overkleeft, *Org. Lett.*, 2011, **13**, 5656–5659.
2. G. Pastorin, W. Wu, S. Wieckowski, J.-P. Briand, K. Kostarelos, M. Prato and A. Bianco, *Chem. Commun.*, 2006, 1182-1184.

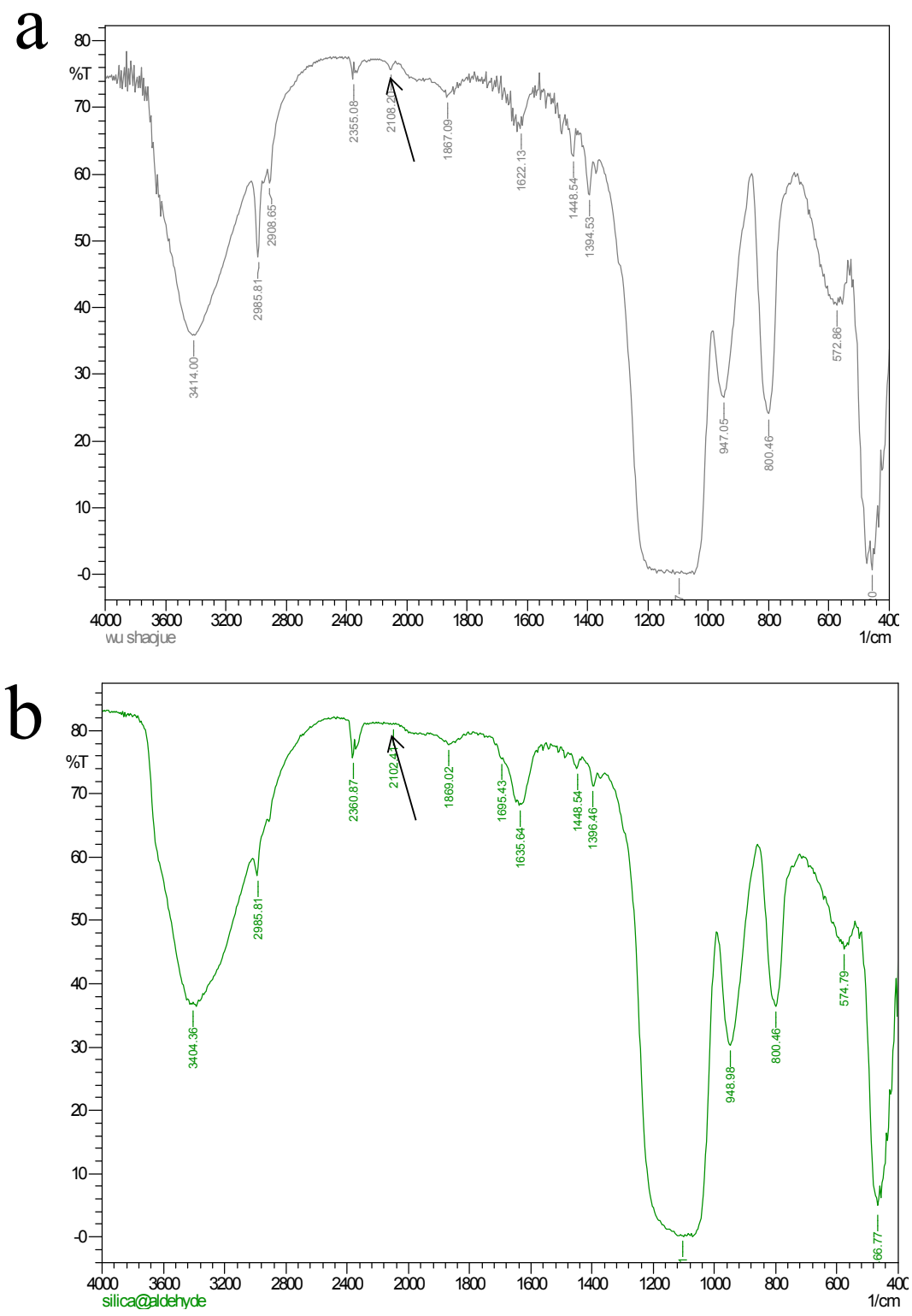


Fig. S1. (a) FTIR spectrum of SiO_2 NPs grafted with 3-azidopropyltrimethoxysilane. The absorption band at 2108 cm^{-1} (as indicated by the black arrow) proves successful grafting of azide onto the SiO_2 NPs. (b) FTIR spectrum of azide functionalized SiO_2 NPs after reacting with 4-(propargyloxy)-benzaldehyde. The band at 2108 cm^{-1} disappeared (as indicated by the black arrow) after the reaction, confirming that the azide functionality reacted with the alkyne group successfully.

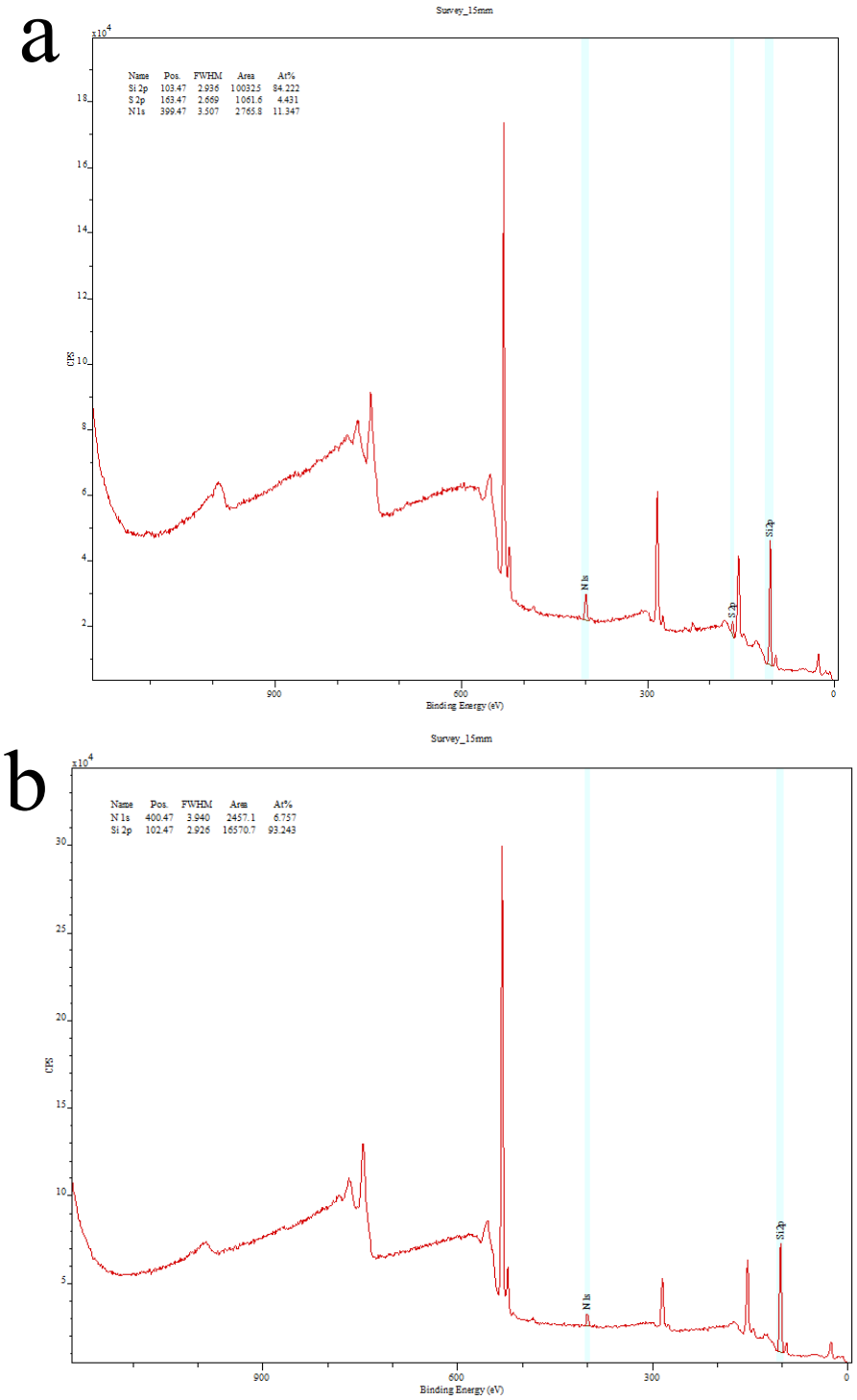


Fig. S2. (a) XPS spectrum of SiO_2 NPs functionalized with lipoic-TriEG-amine via imine bond as the linkage. The theoretical quantity ratio between S and N is 0.400. Experimental obtained ratio is 0.389, showing a reaction efficiency of 97.2%. (b) XPS spectrum of these SiO_2 NPs after treatment with HCl aqueous solution. The signal corresponding to sulfur element disappeared, while the signal of nitrogen element still existed, confirming that the imine bond was cleaved upon the acid treatment.

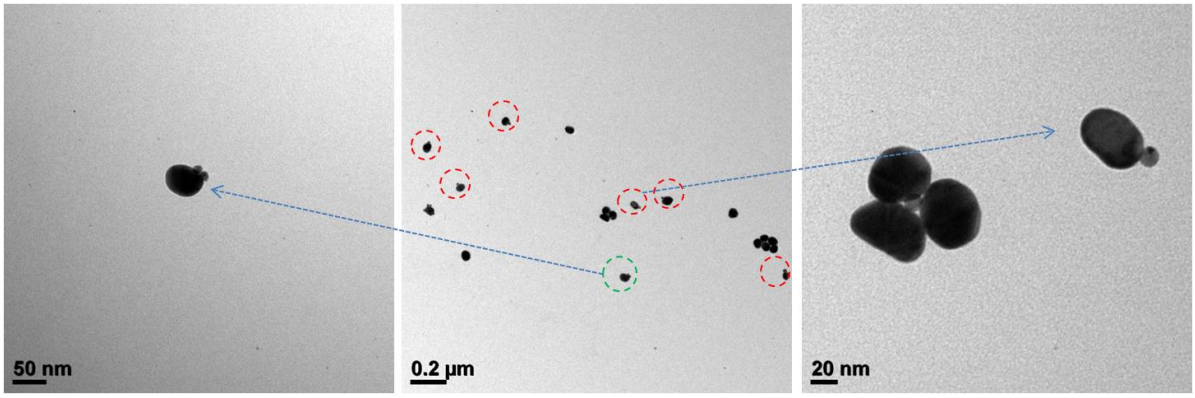


Fig. S3. TEM images of nanoparticle clusters assembled from 40nm Janus AuNPs and 14nm citrate stabilized AuNPs. Red circles are dimers consisting of Janus AuNPs and citrate stabilized AuNPs.

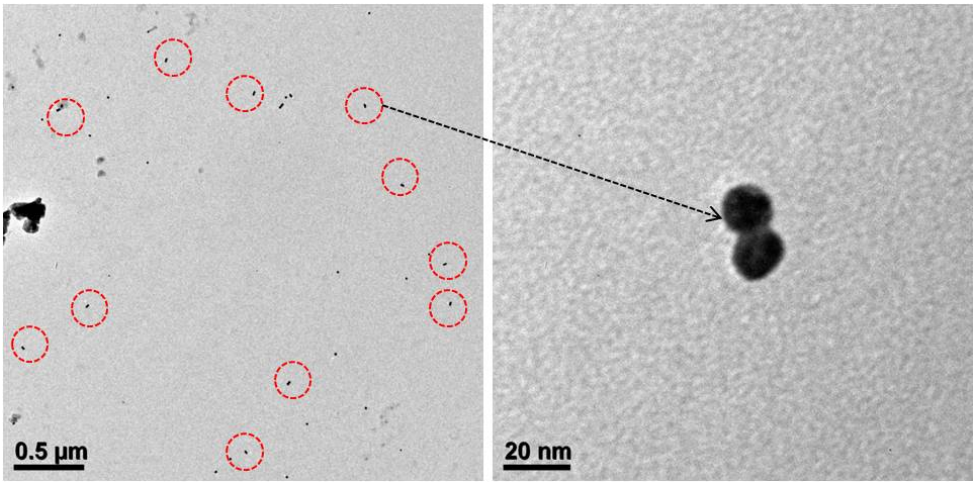


Fig. S4. TEM images of nanoparticle clusters assembled from 14nm Janus AuNPs and 14nm citrate stabilized AuNPs. Red circles are dimers of such AuNPs.

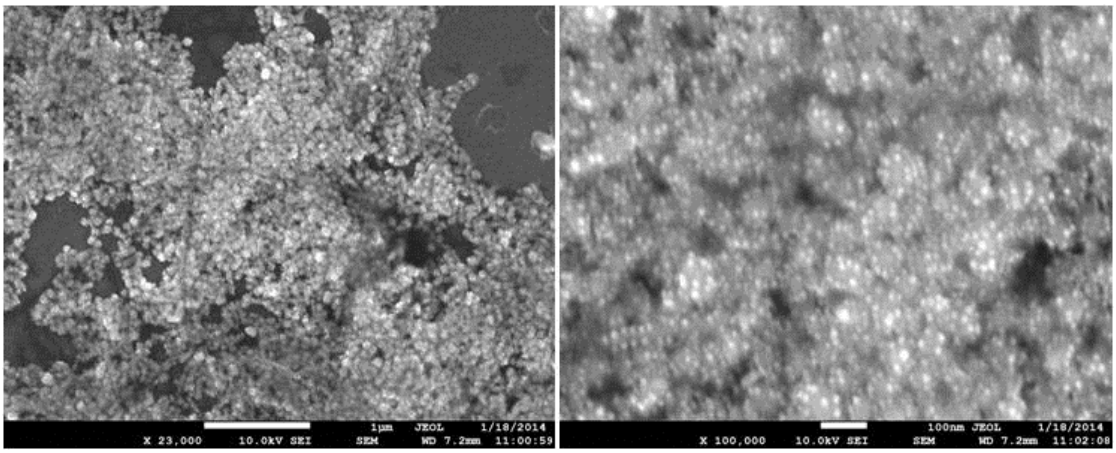


Fig. S5. SEM images of core-satellite structures assembled from 14nm Janus AuNPs and AgNPs (average size 56nm). The structures have AgNPs as cores and AuNPs as satellites covered on AgNPs surfaces.

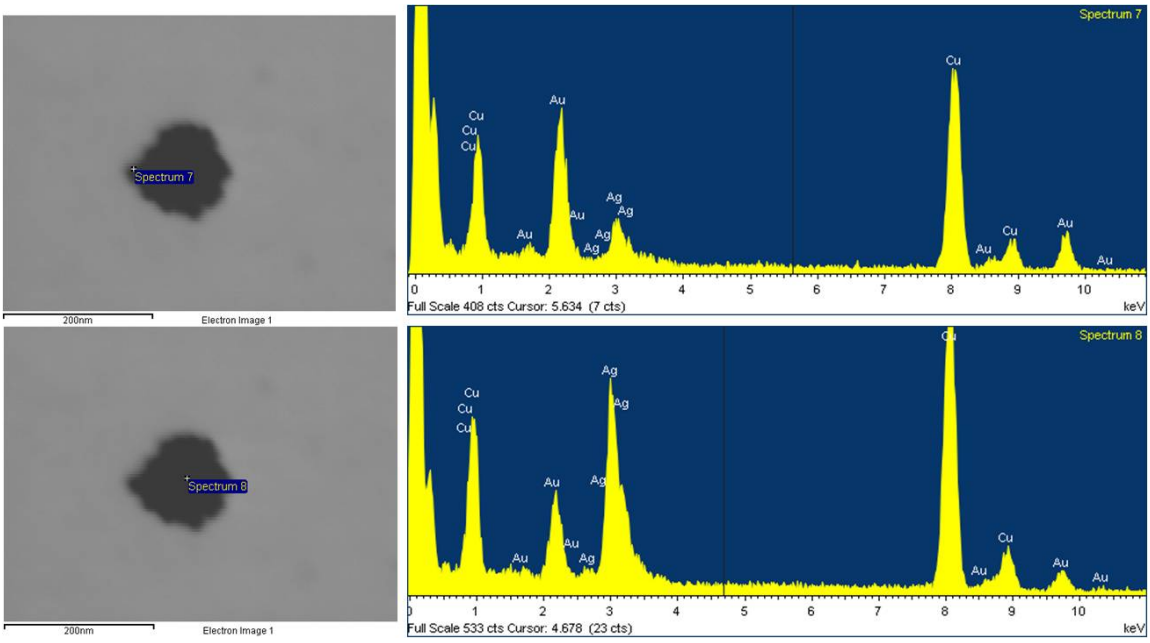


Fig. S6. SEM-EDS analysis showing both Au and Ag elements at the fringe (up) and central (down) sites, while the percentage of Ag is larger than Au at the central site, indicating that it is a satellite structure with an AgNP center surrounded by AuNPs.

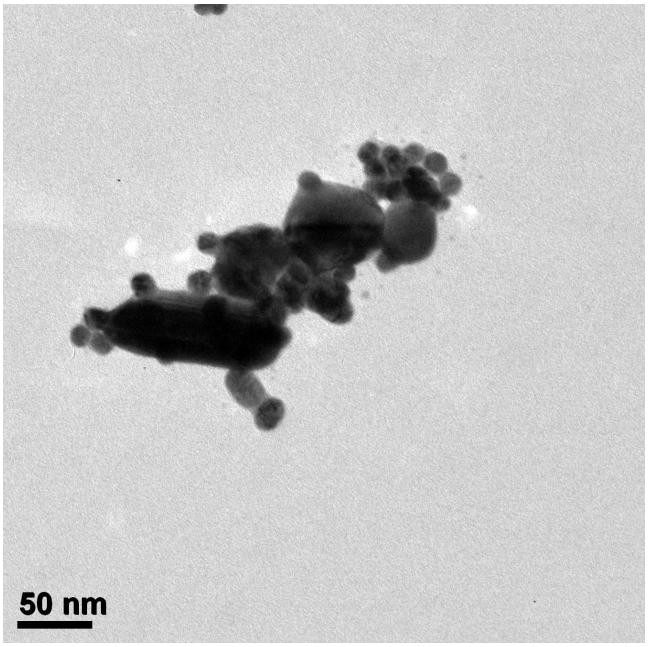


Fig. S7. TEM image of a large irregular aggregate by mixing citrate stabilized AgNPs and 14nm AuNPs stabilized only with lipoic-TriEG-amine. The concentrations of AgNPs and AuNPs were kept similar to those in Fig. 2g,h and Fig. S6 via the adjustment by UV-vis absorption intensity.