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Au₂₅ Clusters as Electron-Transfer Catalysts Induced the Intramolecular Cascade Reaction of 2-nitrobenzonitrile

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Design of atomically precise metal nanocluster catalysts is of great importance in understanding the essence of the catalytic reactions at the atomic level. Here, for the first time, Au₂₅^z nanoclusters were employed as electron transfer catalysts to induce an intramolecular cascade reaction at ambient conditions and gave rise to high conversion (87%) and selectivity (96%). Electron spin-resonance spectra indeed confirmed the consecutive electron transfer process and the formation of N radical. UV-vis absorption spectra also verified Au₂₅^z was intact after the catalytic cycle. Our research may open up wide opportunities for extensive organic reactions catalyzed by Au₂₅^z.

Atomically precise Au nanoclusters (NCs) serving as effective catalysts have been widely explored for a variety of organic reactions¹, such as the oxidation^{2–5}, hydrogenation^{6–8}, C-C coupling reactions⁹ and even C-H activation¹⁰. Among them, as homogeneous or heterogeneous catalysts, Au₂₅ NCs have attracted particular attention due to their precise number of atoms and stable structure, which is important to understand the catalytic mechanism at the atomic and molecular level^{4,11,12}. To our knowledge, there are three stable charge states (−1, 0, +1) for Au₂₅ NCs¹³. It is notable that the charge states (−1, 0) have been further confirmed by the corresponding single-crystal structures^{14,15}. Besides, the three different states are reciprocally transformed by oxidation and reduction¹⁶. Our previous results also indicated the single electron of Au₂₅[−] was capable to be transferred to organic molecule¹⁷. Notably, Au₂₅^z NCs employed as ET mediators, which provide electrons or deliver electrons, may offer novel insights into the mechanism of Au-catalyzed chemical reactions and the correlation between structure and catalytic property. The electron transfer (ET) reactions of the Au₂₅ NCs have been discussed by nuclear magnetic resonance¹⁸, electrochemistry and thermochemical calculations¹⁹. However, to date, there are no reports of Au₂₅ NCs functioning as ET catalysts in solution-phase organic reactions. Herein, we first demonstrate the ET catalysis of Au₂₅ in intramolecular cascade reaction of 2-nitrobenzonitrile, from which 2-amniobenzamide (a precursor of significant pharmaceuticals^{20,21}) is produced with high yield.

Results

The synthesis protocol of Au₂₅(SR)₁₈[−]TOA⁺ (abbreviation as Au₂₅[−], SR = SCH₂CH₂Ph) was referred to the previous literature²². The ultraviolet-visible (UV-vis) spectrum of the obtained NCs is shown in Supplementary Fig. S1. The composition of the as-prepared NCs is further verified by matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF-MS, see Supplementary Fig. S2). In this work, the intramolecular cascade reaction of 2-nitrobenzonitrile (abbreviated as **1a**) for 2-amniobenzamide (**2a**) was investigated using Au₂₅[−] as ET catalysts (See Fig. 1).

Cyclic voltammograms of **1a** and Au₂₅[−] in 0.1 M Bu₄NClO₄/CH₂Cl₂ solution are shown in Fig. 2 and Supplementary Table S1. It is obvious that half-wave potential of **1a** is positive than that of Au₂₅^{0/−1}, suggesting **1a** is capable to grab the electron from Au₂₅[−]. In the ET mediated system, Au₂₅[−] is susceptible to the substrate (**1a**) and easily oxidized into Au₂₅⁰. Meanwhile, N free radicals can be formed after **1a** getting electrons from Au₂₅[−] clusters, proceeding with an intramolecular cascade reaction. Additionally, while treated with NaBH₄, Au₂₅⁰ could be reduced back to Au₂₅[−], indicating Au₂₅ functioned as an electron bridge and excess NaBH₄ provided continual electron source. The electron transfer reactions are presented as follows (Fig. 3), which are indeed established by our investigation.

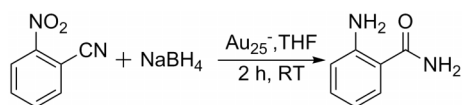


Figure 1 | Au_{25}^z catalyzed intramolecular cascade reaction of 2-nitrobenzonitrile.

To achieve the essential understanding, UV-vis and electron spin-resonance (ESR) spectra were initially employed to investigate the electron transfer process. The distinguished UV-vis absorption characters of Au_{25}^z ($z = -1, 0$) can indeed serve as spectroscopic fingerprints and be capable for ready determination of the negative and neutral states¹⁵. When increased amounts of **1a** were added to Au_{25}^- in tetrahydrofuran, the UV-vis spectra showed obvious changes, in contrast to pure Au_{25}^- . As shown in Fig. 4a, the shoulder peak at 800 nm, the fine spectral peak of Au_{25}^- , successively declined and eventually disappeared. Simultaneously, a new shoulder dominated at ~ 620 nm emerged and gradually enhanced, indicating the progressive formation of Au_{25}^0 from Au_{25}^- . On the other hand, after excess addition of sodium borohydride, the 800 nm absorption shoulder arised again (Fig. 4b), suggesting the recovery of Au_{25}^- . The above spectroscopic evidence confirmed that Au_{25}^z was an electron mediator and it kept delivering electrons from NaBH_4 to substrate. After a circle, a molecule of **1a** gained an electron from Au_{25}^- to form a radical anion and further converted into 2-aminoacetophenone. More significantly, we achieved ESR data to further confirm the occurrence of the initial ET process. Pure Au_{25}^- shows no signal while the mixture of Au_{25}^- and **1a** displays a triplet peaks, suggesting the formation of N radical (Fig. 4c). In addition, more complicated radical was formed with the addition of NaBH_4 (Supplementary Fig. S3), indicating the N radical proceeded with further reaction.

To get a deep insight into the catalytic reaction, a range of control experiments were carried out, the conversion was determined by GC. The catalytic reduction was operated in THF at 20 °C for 2 h. Au_{25}^- could achieve high conversion (87%) and selectivity (96%) (Entry 10, table 1), which was considered as highly efficient at ambient condition. For comparison, a range of functionalities like nitro, amino, nitrile groups were introduced to assess the electronic effects. Comparing with **1a**, solo-functionalized nitrobenzene was reduced to azoxybenzene in relatively low yield in the presence of Au_{25}^- (Entry 1, table 1). It is worth mentioning that no reductive or additive product of cyanobenzene was detected even through the prolonged reaction time, neither did the substituted cyanobenzene with an electron-donating group or an electron-withdrawing group

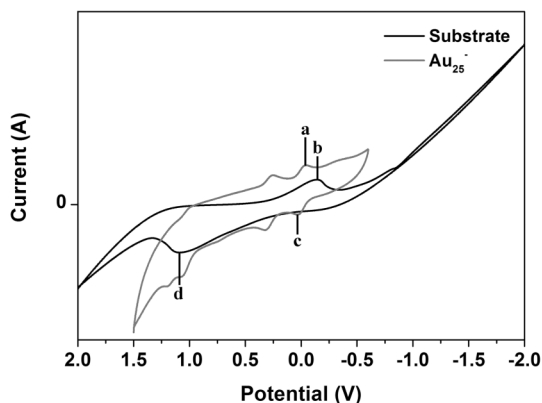


Figure 2 | The cyclic voltammograms of $\text{Au}_{25}^- \text{TOA}^+$ and 2-nitrobenzonitrile in 0.1 M $\text{Bu}_4\text{NClO}_4/\text{CH}_2\text{Cl}_2$ at 298 K (degassed by N_2 , scan speed: 0.05 $\text{V}\cdot\text{s}^{-1}$). (a), (b) The reduction peaks of Au_{25}^- (0/−1) and substrate, respectively; (c), (d) the oxidation peaks of Au_{25}^- (0/−1) and substrate, respectively.

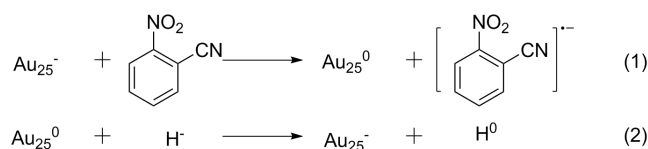


Figure 3 | The electron transfer process.

(Entry 3, 4, 5, table 1), indicating the reaction of **1a** was not originated from electron effects. Moreover, para-substituted 4-nitrobenzonitrile was selectively reduced (Entry 2, table 1) and partially reduced products of **1a** gave no conversion (Entry 6, 7, table 1). Hence, only when nitro group and nitrile group were placed at ortho positions could both of them be reduced in high yields. When the H_2O in THF was replaced by D_2O , two more Daltons (138 Da vs 136 Da, see Supplementary Fig. S4, S5) of the molecule mass for the products were detected, implying water involved in the transformation. In contrast, few products were achieved without any catalysts (Entry 8, table 1). When Au NPs were employed as catalysts in the system, a few products could be achieved either. The occurrence may be ascribed to the charge transfer from the surface of Au NPs. However, this kind of effect is too weak and Au NPs can't deliver electrons efficiently from NaBH_4 to substrates. As a result, low yield is doomed (Entry 9, table 1, TEM image of Au NPs was presented in Supplementary Fig. S6). Limited to their uncertain and complicated structure, it is difficult to get deep in understanding the mechanism of Au NPs catalyzed reactions. Notably, Au_{25} is a great candidate to

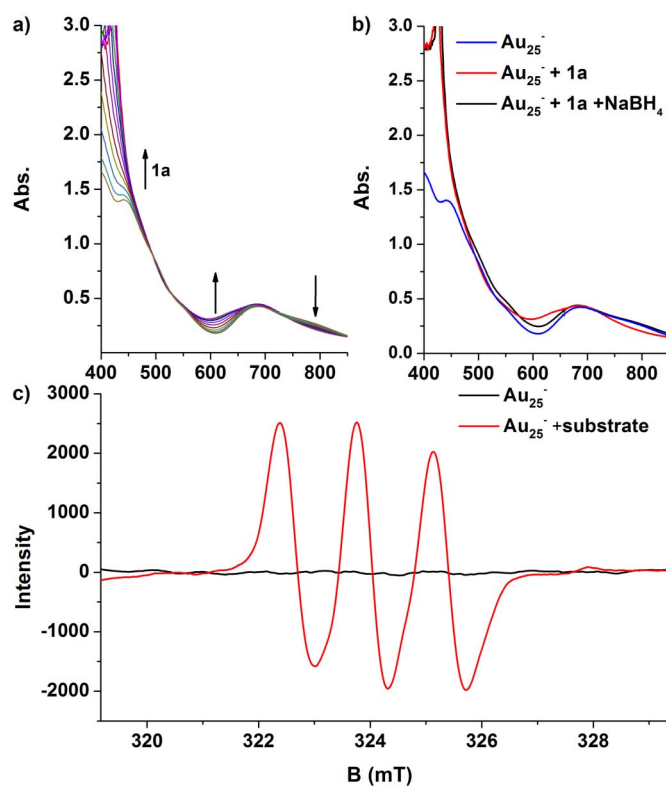


Figure 4 | UV-vis and ESR monitoring spectra of Au_{25}^- mixed with **1a** and/or NaBH_4 (single crystals of Au_{25}^- dissolved in tetrahydrofuran). (a): Only **1a** was added into Au_{25}^- (The spectra gradually changed on addition of **1a** as the arrows showed); (b): blue line is UV-vis spectrum of pure Au_{25}^- , red line is UV-vis spectrum of mixed Au_{25}^- and **1a**, black line displays the UV-vis spectrum of mixed Au_{25}^- and **1a** after NaBH_4 added; (c): ESR signals of pure Au_{25}^- (black line) and the reaction mixture of Au_{25}^- and **1a** (red line) (0.8 mg **1a** dissolved in 0.55 mL THF added to 0.55 mL THF of 1 mg Au_{25}^- clusters).



Entry	Substrate	Product	Time (h)	Conversion (%) ^b	Selectivity (%) ^b
1			20	53.8	98
2			16	91.1	3 97
3		-----	20	-----	-----
4		-----	20	-----	-----
5		-----	20	-----	-----
6		-----	20	-----	-----
7		-----	20	-----	-----
8 ^c			2	3.7	96
9 ^d			2	18.7	95
9 ^e			2	87	96

^aAll the reaction was conducted in 10 ml THF at 20°C, loading of Au was 1 wt% of substrate, sodium borohydride was 2.0 equiv. of substrate.
^bDetermined by GC.
^cCatalyst blank.
^dCatalyzed by Au NP (~2 nm).
^eCatalyzed by Au₂₅.

make up the deficiency due to its well-defined structure and properties, for which is easy to shift between negative and neutral states.

Given nitrile group and nitro group coexist in **1a** and they were both reduced, three possible paths were postulated to further probe the reaction route (see Supplementary Fig. S7): (1) 2-aminobenzotrile (**4a**; Supplementary Fig. S7) acted as intermediate; (2) a five-member ring intermediate was formed; (3) nitrile group was reduced at the beginning (**5a**; Supplementary Fig. S7). The transforming process was supposed to follow one of the three paths. Given the whole reaction was conducted in strong reducing environment (excessive NaBH₄ present), oxidative addition to form carbonyl bond from **4a** to **2a**, or from **1a** to **5a** was clearly impossible, which meant both path 1 and 3 were implausible. Hence, path 2 was considered to be the plausible route. The two-step reaction proceeded as an intramolecular cascade reaction. As nitro group was sensitive to the catalyst, after the nitrile group at ortho position was reduced, they were supposed to form a five-member heteroring (**3a**; Supplementary Fig. S7). Similar theories were previously reported by Baker's yeast catalysis²³ and transition metal catalysis^{24,25}.

As showed in Fig. 5, the possible reaction mechanism was speculated to disclose the process. The single electron was first transferred from Au₂₅⁻ to **1a** with the formation of N radical. Importantly, this

electron transfer step and the formation of N radical were supported by ESR spectra. Then, the radical could be readily transformed into the intermediate of 2-(hydroxyamino) benzotrile. Before the final product (**2a**) was eventually formed, a five-member heterocyclic intermediate emerged to grab another electron from Au₂₅⁻. Meanwhile, one molecule of water was generated after a circle which could be involved in the intramolecular cascade reaction. Notably, solo-functionalized and para-substituted substrates were not capable to attain the active intermediate five-member ring. When reacted with NaBH₄, Au₂₅⁰ could be reduced to Au₂₅⁻, suggesting Au₂₅ served as the ET mediator and NaBH₄ provided consequent electron source. UV-vis spectra also confirmed the circle of catalytic species. After the reaction reached a chemical equilibrium, the mixture was centrifugated to test the supernate for UV-vis spectrum and MALDI-TOF-MS. Typical absorption bands centered at 670 nm and 450 nm were observed (See Supplementary Fig. S8). Besides, molecular ion peak of 7391 (See Supplementary Fig. S9) further verified that the Au₂₅ remained after catalyzing the intramolecular cascade reaction, which was consistent with our hypothesis.

Discussion

In summary, we have demonstrated an intramolecular cascade reaction catalyzed by Au₂₅^z which served as electron mediators. It was worth noting that this reaction achieved high conversion (87%) and selectivity (96%) with Au₂₅^z NCs as ET catalysts at ambient conditions. Furthermore, the catalytic mechanism was systematically investigated. Au₂₅^z shifted between Au₂₅⁻ and Au₂₅⁰ in order to ensure the intermolecular electron flow. Excess NaBH₄ provided hydrogen source and kept Au₂₅ at negative state. More importantly, the catalytic species Au₂₅^z was proved to be still existed after the reaction finished, which meant it could be recovered and recycled. It is believed that our research may open up wide opportunities for ET catalysis of Au₂₅ in extensive organic reactions.

Methods

General experimental detail. All the chemicals and reagents are commercially available. TLC plates (Merck Silica Gel 60 F254) were used for analytical TLC and Merck Kieselgel 200–300 was used for preparative column chromatography. ¹H NMR spectra were acquired on a Bruker AM 400 operating at 400 MHz. ¹³C NMR spectra were acquired on a Bruker AM 400 operating at 100 MHz. Conversion and selectivity was measured with Shimadzu GC 2010 plus. UV tests were conducted with a Hewlett-Packard (HP) 8453 diode array spectrophotometer. TEM images were obtained by JEM 2100. Room temperature electron spin resonance (ESR) was conducted on JEOL JES-FA200 EPR spectrometer (300 K, 9048 MHz, X-band). Cyclic voltammetric measurements (CV) were performed on an electrochemical workstation (CHI 660D) at a scan rate of 0.05 V·s⁻¹ under ambient conditions.

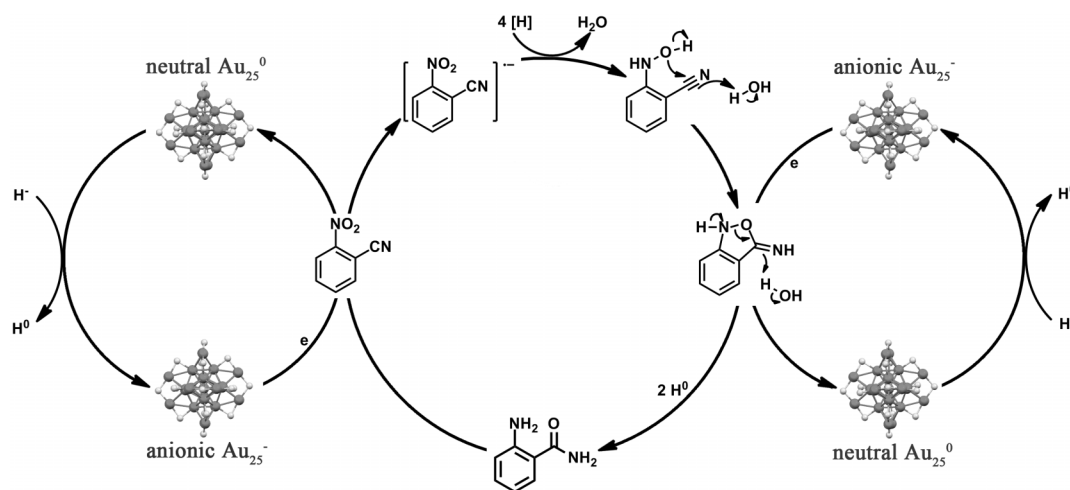


Figure 5 | Proposed mechanism of Au₂₅^z catalyzed intramolecular cascade reaction.



Preparation of $\text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}^- \text{TOA}^+$. Briefly, $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$ dissolved in deionized water along with TOAB dissolved in toluene, were combined in a 25 mL tri-neck round bottom flask. After stirring for ~ 15 min, the aqueous phase was excluded by syringe. The toluene solution was protected with N_2 and cooled down in an ice bath. Hereafter, $\text{PhCH}_2\text{CH}_2\text{SH}$ was added with a very low speed. 1 h later, the stirring speed was adjusted to fast stirring; an aqueous solution of NaBH_4 was quickly added all at once. The synthesis proceeded overnight. The final product was purified by precipitation with acetonitrile three times.

Typical procedure of reduction reaction. 0.2 g 2-nitrobenzonitrile (1.35 mmol), 0.102 g NaBH_4 (2.7 mmol) and 2 mg catalyst was added into 10 mL of THF in round-bottom flask. The mixture was stirred for 2 h at room temperature before being evaporated to dryness under vacuum. The crude product was dissolved in 8 mL methylene dichloride and washed by 3 mL deionized water. Finally the pure product was obtained by column chromatography.

- Li, G. & Jin, R. Atomically precise gold nanoclusters as new model catalysts. *Acc. Chem. Res.* **46**, 1749–1758 (2013).
- Liu, Y., Tsunoyama, H., Akita, T. & Tsukuda, T. Efficient and selective epoxidation of styrene with TBHP catalyzed by Au_{25} clusters on hydroxyapatite. *Chem. Commun.* **46**, 550–552 (2010).
- Zhang, Y., Cui, X., Shi, F. & Deng, Y. Nano-gold catalysis in fine chemical synthesis. *Chem. Rev.* **112**, 2467–2505 (2011).
- Liu, Y., Tsunoyama, H., Akita, T., Xie, S. & Tsukuda, T. Aerobic oxidation of cyclohexane catalyzed by size-controlled Au clusters on hydroxyapatite: size effect in the sub-2 nm regime. *ACS Catal.* **1**, 2–6 (2010).
- Liu, Y., Tsunoyama, H., Akita, T. & Tsukuda, T. Preparation of ~ 1 nm gold clusters confined within mesoporous silica and microwave-assisted catalytic application for alcohol oxidation. *J. Phys. Chem. C* **113**, 13457–13461 (2009).
- Zhu, Y., Qian, H., Drake, B. A. & Jin, R. Atomically precise $\text{Au}_{25}(\text{SR})_{18}$ nanoparticles as catalysts for the selective hydrogenation of α,β -unsaturated ketones and aldehydes. *Angew. Chem. Int. Ed.* **49**, 1295–1298 (2010).
- Zhu, Y. *et al.* Exploring stereoselectivity of Au_{25} nanoparticle catalyst for hydrogenation of cyclic ketone. *J. Catal.* **271**, 155–160 (2010).
- Yamamoto, H. *et al.* N,N-dimethylformamide-stabilized gold nanoclusters as a catalyst for the reduction of 4-nitrophenol. *Nanoscale* **4**, 4148–4154 (2012).
- Li, G., Liu, C., Lei, Y. & Jin, R. Au_{25} nanocluster-catalyzed Ullmann-type homocoupling reaction of aryl iodides. *Chem. Commun.* **48**, 12005–12007 (2012).
- Pei, X.-L., Yang, Y., Lei, Z. & Wang, Q.-M. Geminal tetraauration of acetonitrile: hemilabile-phosphine-stabilized Au_8Ag_4 cluster compounds. *J. Am. Chem. Soc.* **135**, 6435–6437 (2013).
- Nie, X., Qian, H., Ge, Q., Xu, H. & Jin, R. CO oxidation catalyzed by oxide-supported $\text{Au}_{25}(\text{SR})_{18}$ nanoclusters and identification of perimeter sites as active centers. *ACS Nano* **6**, 6014–6022 (2012).
- Kauffman, D. R., Alfonso, D., Matranga, C., Qian, H. & Jin, R. Experimental and computational investigation of Au_{25} clusters and CO_2 : a unique interaction and enhanced electrocatalytic activity. *J. Am. Chem. Soc.* **134**, 10237–10243 (2012).
- Negishi, Y., Chaki, N. K., Shichibu, Y., Whetten, R. L. & Tsukuda, T. Origin of magic stability of thiolated gold clusters: a case study on $\text{Au}_{25}(\text{SC}_6\text{H}_{13})_{18}$. *J. Am. Chem. Soc.* **129**, 11322–11323 (2007).
- Zhu, M., Aikens, C. M., Hollander, F. J., Schatz, G. C. & Jin, R. Correlating the crystal structure of a thiol-protected Au_{25} cluster and optical properties. *J. Am. Chem. Soc.* **130**, 5883–5885 (2008).
- Zhu, M., Eckenhoff, W. T., Pintauer, T. & Jin, R. Conversion of anionic $[\text{Au}_{25}(\text{SCH}_2\text{CH}_2\text{Ph})_{18}]^-$ cluster to charge neutral cluster via air oxidation. *J. Phys. Chem. C* **112**, 14221–14224 (2008).

- Zhu, M. *et al.* Reversible switching of magnetism in thiolate-protected Au_{25} superatoms. *J. Am. Chem. Soc.* **131**, 2490–2492 (2009).
- Liu, Z., Zhu, M., Meng, X., Xu, G. & Jin, R. Electron transfer between $[\text{Au}_{25}(\text{SC}_2\text{H}_4\text{Ph})_{18}]^- \text{TOA}^+$ and oxoammonium cations. *J. Phys. Chem. Lett.* **2**, 2104–2109 (2011).
- Venzo, A. *et al.* Effect of the charge state ($z = -1, 0, +1$) on the nuclear magnetic resonance of monodisperse $\text{Au}_{25}[\text{S}(\text{CH}_2)_2\text{Ph}]_{18}^z$ clusters. *Anal. Chem.* **83**, 6355–6362 (2011).
- Antonello, S., Hesari, M., Polo, F. & Maran, F. Electron transfer catalysis with monolayer protected Au_{25} clusters. *Nanoscale* **4**, 5333–5342 (2012).
- Zhou, J. & Fang, J. One-pot synthesis of quinazolinones via iridium-catalyzed hydrogen transfers. *J. Org. Chem.* **76**, 7730–7736 (2011).
- Mhaske, S. B. & Argade, N. P. Regioselective quinazolinone-directed ortho lithiation of quinazolinoylquinoline: practical synthesis of naturally occurring human DNA topoisomerase I poison luotonin A and luotonins B and E. *J. Org. Chem.* **69**, 4563–4566 (2004).
- Zhu, M., Lanni, E., Garg, N., Bier, M. E. & Jin, R. Kinetically controlled, high-yield synthesis of Au_{25} clusters. *J. Am. Chem. Soc.* **130**, 1138–1139 (2008).
- Amarasekara, A. S., Hernandez, W. & Bonham, P. Baker's yeast (*Saccharomyces cerevisiae*) mediated transformations of C-aryl-N-phenylnitrones. *Tetrahedron Lett.* **47**, 4893–4895 (2006).
- Chauhan, J. & Fletcher, S. One-pot synthesis of 2,1-benzisoxazoles (anthranils) by a stannous chloride-mediated tandem reduction–heterocyclization of 2-nitroacylbenzenes under neutral conditions. *Tetrahedron Lett.* **53**, 4951–4954 (2012).
- Koprivova, K. & Cerveny, L. Hydrogenation of nitrobenzonitriles using Raney nickel catalyst. *Res. Chem. Intermed.* **34**, 93–101 (2008).

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Author contributions

H.C. conducted most of the experiments, collected the data, and wrote the paper. S.W., F.F. and J.X. synthesized and characterized the $\text{Au}_{25}(\text{SR})_{18}$ NCs. M.Z., P.L. and Y.L. conceived the experiments and wrote the paper. All authors analyzed the data and discussed the results.

Additional information

Supplementary information accompanies this paper at <http://www.nature.com/scientificreports>

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