ROYAL SOCIETY
OF CHEMISTRY

COMMUNICATION

Catalyzed formation of α,β-unsaturated ketones or aldehydes from propargylic acetates by a recoverable and recyclable nanocluster catalyst†

Man-Bo Li,[a] Shi-Kai Tian[b] and Zhikun Wu*[a]

An active, recoverable, and recyclable nanocluster catalyst, $Au_{25}(SR)_{18}^-$, has been developed to catalyze the formation of α,β-unsaturated ketones or aldehydes from propargylic acetates. The catalytic process has been proposed to be initialized by an S_N2' addition of OH^-. Moreover, a dramatic solvent effect was observed, for which a rational explanation was provided.

Bulk gold is catalytically inert in most organic reactions; however, it turns to be active in catalyzing certain reactions when the size of gold is reduced to less than 100 nm.[1] Recently, ultra-small gold nanoparticles (<3 nm, so-called nanoclusters) as catalysts have received extensive attention, which can be explained by at least two reasons.[2] One reason is the enhancement of catalytic activities of gold nanoparticles with decrease in size. The other reason is that the ultra-small nanoparticles with defined compositions and structures make it possible for structure-property correlation and in-depth investigation of catalytic mechanism. To date, it has been reported that gold nanoclusters can catalyze a few organic reactions, including selective oxidation and hydrogenation,[3,4] cross-coupling reactions,[5] C–H activation,[6] and electron transfer reactions.[7] However, there are no reports on gold nanocluster-catalyzed formation of α,β-unsaturated ketones or aldehydes from propargylic acetates as far as we know. α,β-Unsaturated ketones or aldehydes are one of the most important building blocks for complex compounds in some typical reactions like 1,4-addition and Diels–Alder reaction.[8] They are usually obtained by aldol condensation or HWE reaction suffering from harsh conditions (e.g. strong base).[9] The recent advances in gold salt catalyst

researches make their preparation possible in rather mild conditions.[10] However, the successful recovery and recycling of such catalysts has not been reported until now. Interestingly, we found a well-defined nanocluster, $Au_{25}(SR)_{18}^-$, (where SR = SCH_2CH_2Ph)[11] can also catalyze the formation of α,β-unsaturated ketones or aldehydes from propargylic acetates. More importantly, $Au_{25}(SR)_{18}^-$ can be readily isolated from the reaction system and reused with no further treatment in the subsequent catalysis without the loss of catalytic activity. This is greatly beneficial in practical applications and gives $Au_{25}(SR)_{18}^-$ a remarkable advantage over some existing catalysts. This reaction is proposed to be initialized by an S_N2' addition of OH^-, and it is found that the solvent plays an important role during the catalytic process. Herein we present some experimental results and our discussion.

In a typical experiment (details in the ESI†), 1,3-diphenyl-prop-2-ynyl acetate was mixed with $Au_{25}(SR)_{18}^-$ and K_2CO_3 in DMSO (containing water) with continuous stirring, and then heated to a preset temperature. After 2 h, the reaction was quenched by the addition of excessive water. The desired product (E)-chalcone was obtained in high isolated yield (84% under the optimized reaction conditions) after extraction with ethyl acetate and subsequent purification by preparative thin layer chromatography (PTLC) (Table 1, entry 20). The reaction temperature obviously influences the yield of (E)-chalcone, i.e. at low temperature (e.g. 25 °C), the reaction could not proceed smoothly (Table 1, entry 4), and when the temperature was increased to 60 °C a yield of 62% was obtained (Table 1, entry 5), and the highest yield was achieved at 100 °C (Table 1, entry 17). (Note that higher temperatures were not tested, and all the following experiments were conducted at 80 °C.) Indeed, the size of gold matters in this catalysis because when $Au_{25}(SR)_{18}^-$ was replaced by $Au_{38}(SR)_{24}$, $Au_{144}(SR)_{60}$, ~3 nm gold nanoparticles (with or without protecting by ligands) and bigger nanoparticles (~23 nm) under identical conditions, only trace amount of product (even no product for ~23 nm gold) was detected (see Table 1 (entries 9–13)).

[a]Key Laboratory of Materials Physics, Anhui Key Laboratory of Nanomaterials and Nanostructures, Institute of Solid State Physics, Chinese Academy of Sciences, Hefei, 230031, China. E-mail: zkwu@issp. ac.cn

[b]Department of Chemistry, University of Science and Technology of China, Hefei, Anhui 230026, China

† Electronic supplementary information (ESI) available: Experimental procedures, UV-Vis spectra and fluorescence spectra of catalysts, characterization data, and copies of MS spectra. See DOI: 10.1039/c4nr00658e

Table 1 The isolated yields of (E)-chalcone under various conditions[a]

Entry	Catalyst	Additive	Temp. (°C)	Yield[b] (%)
1	$Au_{25}(SR)_{18}^{-}$	None	80	0
2	None	K_2CO_3	80	0
3	$Au_{25}(SR)_{18}^{-}$	K_2CO_3	80	76
4	$Au_{25}(SR)_{18}^{-}$	K_2CO_3	25	0
5	$Au_{25}(SR)_{18}^{-}$	K_2CO_3	60	62
6	$Au_{25}(SR)_{18}^{-}$	KOH	80	40[c]
7	$Au_{25}(SR)_{18}^{-}$	CH_3COOH	80	Trace
8	$Au_{25}(SR)_{18}^{0}$	K_2CO_3	80	75[d]
9	$Au_{38}(SR)_{24}$	K_2CO_3	80	Trace
10	$Au_{144}(SR)_{60}$	K_2CO_3	80	Trace
11	~3 nm Au NP[e]	K_2CO_3	80	Trace
12	~3 nm Au NP[f]	K_2CO_3	80	Trace
13	~23 nm Au NP	K_2CO_3	80	0
14	$Au_{25}(SR)_{18}^{-}$	K_2CO_3	80	48[g]
15[g]	$Au_{25}(SR)_{18}^{0}$	K_2CO_3	80	48[d,g]
16[g]	$Au_{25}(SR)_{18}^{-}$	K_2CO_3	80	Trace[h]
17	$Au_{25}(SR)_{18}^{-}$	K_2CO_3	100	78
18	$Au_{25}(SR)_{18}^{-}$	K_2CO_3	100	78[i]
19	$Au_{25}(SR)_{18}^{-}$	K_2CO_3	100	80[j]
20	$Au_{25}(SR)_{18}^{-}$	K_2CO_3	100	84[j,k]

[a] Reaction conditions: 1,3-diphenylprop-2-ynyl acetate (0.20 mmol), catalyst (if any, 3.0 mg), additive (if any, 0.20 mmol), DMF (2.0 mL), H_2O (0.2 mL). [b] Isolated yield. [c] Hydrolysis product (1,3-diphenylprop-2-yn-1-ol) was obtained in 52% yield. [d] $Au_{25}(SR)_{18}^{0}$ was reduced to $Au_{25}(SR)_{18}^{-}$ after reaction (see Fig. S7). [e] Au NP was protected by phenylethanethiolate. [f] Au NP was not protected by ligands. [g] DMF was used as solvent. [h] Water was not added. [i] Reaction time was prolonged to 5 h. [j] Solvent: 0.5 mL DMF and 0.05 mL H_2O. [k] 10.0 mg catalyst was added.

Table 2 Recyclability of $Au_{25}(SR)_{18}^{-a,b}$

Entry	Number of cycles	Yield[c] (%)
1	1	76
2	2	76
3	3	72
4	4	70

[a] Reaction conditions: 1,3-diphenylprop-2-ynyl acetate (0.20 mmol), $Au_{25}(SR)_{18}^{-}$ (3.0 mg), K_2CO_3 (0.20 mmol), DMSO (2.0 mL), H_2O (0.2 mL), 80 °C, 2 h. [b] The catalyst was purified and recovered by column chromatography on silica gel with dichloromethane as eluent. [c] Isolated yield.
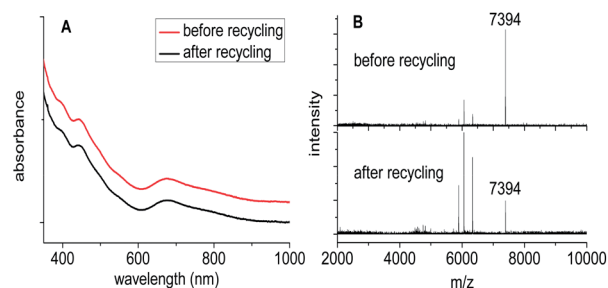

Fig. 1 UV-Vis spectra (A) and MALDI-TOF-MS spectra (the mole ratio of DCTB/$Au_{25}(SR)_{18}^{-}$ is 500/1) (B) of catalyst before and after recycling with DMSO as solvent.

More importantly, $Au_{25}(SR)_{18}^{-}$ was readily isolated by column chromatography on silica gel with dichloromethane as eluent. After evaporating the solvent, the remaining solid was reused in the reaction without any further treatment (e.g. calcinations). The isolated yield of (E)-chalcone had no obvious drop even after four cycles (the slight decrease is due to the partial loss of catalyst in recycling), which indicates that the catalyst is rather stable under the given conditions (Table 2). To confirm this, spectrophotometry and mass spectrometry were used to monitor the change of Au_{25} after the reaction. No obvious spectral changes in absorption were found after four cycles of catalysis (Fig. 1A). The identical signals in the MS spectrum at 7394 Da and similar fragment mode further support that the $Au_{25}(SR)_{18}^{-}$ catalyst did not change during the catalysis process (Fig. 1B). Taken together, these results unambiguously demonstrate that $Au_{25}(SR)_{18}^{-}$ is ultra-robust and can be recovered and reused for catalysis, which imparts a special merit to $Au_{25}(SR)_{18}^{-}$ as catalyst for practical applications.

As for the formation mechanism of α,β-unsaturated ketones from propargylic acetates,[10,12] two dominant pathways were put forward: pathway I and pathway II. In pathway I (Tandem hydrolysis–Meyer–Schuster rearrangement),[12] (E)-chalcone is produced through proton-promoted Meyer–Schuster rearrangement of 1,3-diphenylprop-2-yn-1-ol formed from the starting material by hydrolysis. In pathway II (S_N2' addition),[10] the reaction is initialized by the S_N2' addition of nucleophile (OH⁻ or H_2O) to the alkyne activated by the catalyst, and (E)-chalcone is finally obtained through keto–enol tautomerization of the intermediate, which is formed after extrusion of the acetyl group (or CH_3COOH molecule) following the S_N2' addition (see Fig. 2). Given that our reaction was conducted under basic conditions in the whole process, it is not rational to conclude that the reaction proceeds by pathway I due to the known fact that the Meyer–Schuster rearrangement of 1,3-diphenylprop-2-yn-1-ol can only occur under acidic conditions.[12] Thus, pathway II[10] seems to fit our case and the nucleophile is OH⁻, due to the following facts: (1) the reaction fails to proceed under either neutral or acidic conditions (Table 1, entries 1 and 7); (2) water is necessary for the catalysis (Table 1, entry 16); and (3) a strong base is not beneficial to the desired reaction owing to hydrolysis of the starting material (Table 1, entry 6). Herein, $Au_{25}(SR)_{18}^{-}$ facilitates the S_N2' addition by attracting the conjugated electrons of alkynyl[13] and provides suitable location for the reaction. The detailed process is illustrated in Fig. 3.
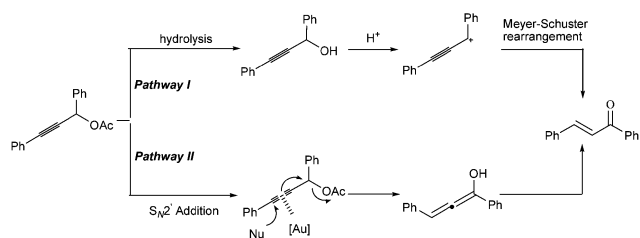
Fig. 2 Two possible pathways to form (*E*)-chalcone (Nu represents H_2O or OH^-).

Interestingly, a dramatic solvent effect was observed in the catalytic reaction. The highest isolated yield (76%) was achieved in DMSO, whereas in DMF the yield was decreased to 48%, and only trace amount of product was detected in other common solvents (such as toluene, tetrahydrofuran, 1,4-dioxane, 1,2-dichloroethane, acetone and water) with other conditions identical (see Table 3), which can be explained by the following two reasons. One reason is that reductive and affinitive DMSO and DMF can protect $Au_{25}(SR)_{18}^-$ from oxidation or decomposition during the reaction, whereas other examined solvents cannot effectively protect Au_{25} from damage. This is illustrated in the UV/Vis/NIR spectra change of $Au_{25}(SR)_{18}^-$ before and after the reaction (see Fig. S1–8† for comparison). The instability of $Au_{25}(SR)_{18}^-$ in the reaction system with toluene, tetrahydrofuran, 1,4-dioxane, 1,2-dichloroethane, acetone or water as solvent leads to the loss of catalytic activity of $Au_{25}(SR)_{18}^-$. Neutral Au_{25} can be reduced to anion Au_{25} in both DMF and DMSO, and neutral Au_{25} exhibits identical catalytic activity with anion Au_{25} in the above two solvents also support our opinion (Table 1, entry 8, 15, see Fig. S9†). The second possible reason is the affinity of DMSO and DMF to the catalyst and reactants (including OH^- and the substrate). DMSO and DMF can act as a glue to link $Au_{25}(SR)_{18}^-$, OH^- and substrate adequately (illustrated in Fig. 3), whereas other examined solvents do not have such affinity (*e.g.* 1,2-dichloroethane does not have good affinity
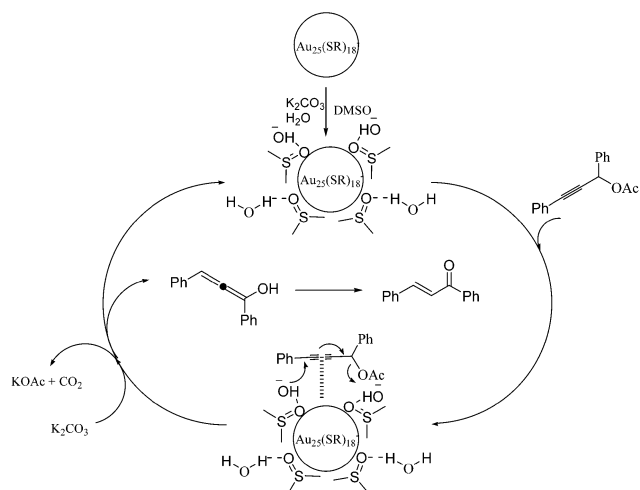
to OH^-). Of course, too strong an affinity to $Au_{25}(SR)_{18}^-$ surely has an adverse effect on the catalytic activity due to the competition between the solvent and the substrate. This may explain why the yield of (*E*)-chalcone is higher in DMSO than that in DMF (76% *vs.* 48%) under identical conditions. One clue for the strong affinity of DMF to $Au_{25}(SR)_{18}^-$ is that the DMF-stabilized gold nanocluster has been isolated and identified, while the DMSO-stabilized gold nanocluster has not been obtained until now as far as we know.[4c,14] Another reason is that the emission of $Au_{25}(SR)_{18}^-$ in DMF is clearly stronger than that in DMSO (see Fig. S10† for comparison). In a previous work, it was found that the fluorescence of gold clusters is notably influenced by the surface.[11c] Thus, the distinct enhancement of fluorescence of $Au_{25}(SR)_{18}^-$ in DMF indicates the strong interaction of DMF and $Au_{25}(SR)_{18}^-$.

Note that a dramatic substitution effect of the substrates on the yield was not observed. Moreover, the catalytic activity of $Au_{25}(SR)_{18}^-$ for a few more substrates with alkynyl were investigated and comparable yields were obtained (see Table 4).

Table 3 Effect of solvents on the $Au_{25}(SR)_{18}^-$ cluster-catalyzed formation of α,β-unsaturated ketones from propargylic acetates[a]

Entry	Solvent	Yield[b] (%)
1	DMF	48
2	DMSO	76
3	Toluene	Trace
4	THF	Trace
5	1,4-Dioxane	Trace
6	1,2-Dichloroethane	Trace
7	Acetone	Trace
8[c]	H_2O	Trace

[a] Reaction conditions: 1,3-diphenylprop-2-ynyl acetate (0.20 mmol), $Au_{25}(SR)_{18}^-$ (3.0 mg), K_2CO_3 (0.20 mmol), solvent (2.0 mL), H_2O (0.2 mL), 80 °C, 2 h. [b] Isolated yield. [c] $Au_{25}(SG)_{18}$ was used as catalyst.

Fig. 3 Proposed mechanism of $Au_{25}(SR)_{18}^-$ cluster catalyzed formation of α,β-unsaturated ketones from propargylic acetates.

Table 4 Formation of α,β-unsaturated ketones or aldehydes from propargylic acetates catalyzed by $Au_{25}(SR)_{18}^{-a}$

Entry	R^1	R^2	Yield[b] (%)
1	Ph	Ph	76
2	Ph	Me	78
3	H	Ph	75
4	H	Me	70

[a] Reaction conditions: propargylic acetate (0.20 mmol), $Au_{25}(SR)_{18}^-$ (3.0 mg), K_2CO_3 (0.20 mmol), DMSO (2.0 mL), H_2O (0.2 mL), 80 °C, 2 h. [b] Isolated yield.

Conclusions

In summary, for the first time, we have demonstrated $Au_{25}(SR)_{18}{}^{-}$-catalyzed formation of α,β-unsaturated ketones and aldehydes from propargylic acetates in high isolated yields. More importantly, our catalyst is recoverable and recyclable, which is greatly beneficial to practical applications, and gives $Au_{25}(SR)_{18}{}^{-}$ a remarkable advantage over some existing catalysts. The catalysis has been proposed to be initialized by an S_N2' addition of OH^-. Interestingly, a dramatic solvent effect for the catalysis was observed, for which a rational explanation was provided. Thus, our research has extended the catalytic properties of gold nanoclusters and demonstrated the potential use of gold nanoclusters as a novel type of catalyst. The study on the reaction mechanism and the solvent effect could be of help to understand gold nanocluster catalysis. Moreover, it is expected that our work may spur more research and open up novel opportunities for the transformation of alkynes to other functional compounds.

Acknowledgements

Notes and references

1 For selected reviews on catalytic activities of gold nanoparticles, see: (a) Y. Zhang, X. Cui, F. Shi and Y. Deng, *Chem. Rev.*, 2012, **112**, 2467; (b) M. Stratakis and H. Garcia, *Chem. Rev.*, 2012, **112**, 4469.

2 For selected reviews on catalytic activities of gold nanoclusters, see: (a) Y. Lu and W. Chen, *Chem. Soc. Rev.*, 2012, **41**, 3594; (b) H. Qian, M. Zhu, Z. Wu and R. Jin, *Acc. Chem. Res.*, 2012, **45**, 1470; (c) G. Li and R. Jin, *Acc. Chem. Res.*, 2013, **46**, 1749.

3 For selective oxidation catalyzed by gold nanoclusters, see: (a) M. Haruta, *Nature*, 2005, **437**, 1098; (b) M. Turner, V. B. Golovko, O. P. H. Vaughan, P. Abdulkin, A. Berenguer-Murcia, M. S. Tikhov, B. F. G. Johnson and R. M. Lambert, *Nature*, 2008, **454**, 981; (c) Y. Liu, H. Tsunoyama, T. Akita and T. Tsukuda, *J. Phys. Chem. C*, 2009, **113**, 13457; (d) Y. Liu, H. Tsunoyama, T. Akita and T. Tsukuda, *Chem. Commun.*, 2010, **46**, 550; (e) Y. Liu, H. Tsunoyama, T. Akita, S. Xie and T. Tsukuda, *ACS Catal.*, 2011, **1**, 2; (f) S. Xie, H. Tsunoyama, W. Kurashige, Y. Negishi and T. Tsukuda, *ACS Catal.*, 2012, **2**, 1519; (g) X. Nie, H. Qian, Q. Ge, H. Xu and R. Jin, *ACS Nano*, 2012, **6**, 6014; (h) G. Li, H. Qian and R. Jin, *Nanoscale*, 2012, **4**, 6714.

4 For selective hydrogenation catalyzed by gold nanoclusters, see: (a) Y. Zhu, H. Qian, B. A. Drake and R. Jin, *Angew. Chem., Int. Ed.*, 2010, **49**, 1295; (b) Y. Zhu, Z. Wu, C. Gayathri, H. Qian, R. R. Gil and R. Jin, *J. Catal.*, 2010, **271**, 155; (c) H. Yamamoto, H. Yano, H. Kouchi, Y. Obora, R. Arakawa and H. Kawasaki, *Nanoscale*, 2012, **4**, 4148; (d) A. Shivhare, S. J. Ambrose, H. Zhang, R. W. Purves and R. W. J. Scott, *Chem. Commun.*, 2013, **49**, 276.

5 G. Li, C. Liu, Y. Lei and R. Jin, *Chem. Commun.*, 2012, **48**, 12005.

6 X.-L. Pei, Y. Yang, Z. Lei and Q.-M. Wang, *J. Am. Chem. Soc.*, 2013, **135**, 6435.

7 H. Chong, P. Li, S. Wang, F. Fu, J. Xiang, M. Zhu and Y. Li, *Sci. Rep.*, 2013, **3**, 3214.

8 For selected reviews on 1,4-addition reactions, see: (a) N. Krause and A. Hoffmann-Röder, *Synthesis*, 2001, 171; (b) A. Alexakis and C. Benhaim, *Eur. J. Org. Chem.*, 2002, 3221; (c) T. Hayashi and K. Yamasaki, *Chem. Rev.*, 2003, **103**, 2829; (d) H.-C. Guo and J.-A. Ma, *Angew. Chem., Int. Ed.*, 2006, **45**, 354. For selected reviews onDiels–Alder reactions, see ; (e) K.-i. Takao, R. Munakata and K.-I. Tadano, *Chem. Rev.*, 2005, **105**, 4779; (f) W. Notz, F. Tanaka and C. F. Barbas III, *Acc. Chem. Res.*, 2004, **37**, 580.

9 For selected reviews, see:(a) G. Jones, *Org. React.*, 1967, **15**, 204; (b) W. S. Wadsworth, Jr, *Org. React.*, 1977, **25**, 73; (c) W. J. Stec, *Acc. Chem. Res.*, 1983, **16**, 411.

10 For selected examples of formation of α,β-unsaturated ketone from propargylic acetate, see: (a) N. Marion, P. Carlqvist, R. Gealageas, P. de Frémont, F. Maseras and S. P. Nolan, *Chem.–Eur. J.*, 2007, **13**, 6437; (b) M. Yu, G. Li, S. Wang and L. Zhang, *Adv. Synth. Catal.*, 2007, **349**, 871; (c) D. Wang, Y. Zhang, A. Harris, L. N. S. Gautam, Y. Chen and X. Shi, *Adv. Synth. Catal.*, 2011, **353**, 2584.

11 (a) Z. Wu, J. Suhan and R. Jin, *J. Mater. Chem.*, 2009, **19**, 622; (b) Z. Wu, C. Gayathri, R. R. Gil and R. Jin, *J. Am. Chem. Soc.*, 2009, **131**, 6535; (c) Z. Wu and R. Jin, *Nano Lett.*, 2010, **10**, 2568; (d) Z. Wu, J. Chen and R. Jin, *Adv. Funct. Mater.*, 2011, **21**, 177; (e) M. Wang, Z. Wu, J. Yang, G. Wang, H. Wang and W. Cai, *Nanoscle*, 2012, **4**, 2087; (f) Z. Wu, *Angew. Chem., Int. Ed.*, 2012, **51**, 2934.

12 (a) K. H. Meyer and K. Schuster, *Chem. Ber.*, 1922, **55**, 819; (b) E. T. Clapperton and W. S. MacGregor, *J. Am. Chem. Soc.*, 1950, **72**, 2501; (c) G. F. Hennion and B. R. Fleck, *J. Am. Chem. Soc.*, 1955, **77**, 3253; (d) M. Edens, D. Boerner, C. R. Chase, D. Nass and M. D. Schiavelli, *J. Org. Chem.*, 1977, **42**, 3403; (e) J. Andres, R. Cardenas, E. Silla and O. Tapia, *J. Am. Chem. Soc.*, 1988, **110**, 666; (f) M. Yoshimatsu, M. Naito, M. Kawahigashi, H. Shimizu and T. Kataoka, *J. Org. Chem.*, 1995, **60**, 4798.

13 P. Maity, H. Tsunoyama, M. Yamauchi, S. Xie and T. Tsukuda, *J. Am. Chem. Soc.*, 2011, **133**, 20123.

14 H. Kawasaki, H. Yamamoto, H. Fujimori, R. Arakawa, Y. Iwasaki and M. Inada, *Langmuir*, 2010, **26**, 5926.