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Semiconductor-Gold Nanocomposite Catalysts for the Efficient Three-Component Coupling of Aldehyde, Amine and Alkyne in Water

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Abstract: An efficient heterogeneous lead sulfide-gold catalyst has been successfully developed for the synthesis of propargylic amines *via* a three-component coupling reaction of aldehyde, amine and alkyne in water. The process is simple and applicable to a diverse range of aromatic and aliphatic aldehydes, amines and alkynes. Furthermore, the catalyst is stable to air and water, and can be easily recovered and reused.

Keywords: alkynes; gold; heterogeneous catalysis; multicomponent reactions; nanocomposite catalysts

Introduction

Supported transition metal nanoparticles have attracted much attention in recent years due to their interesting structure and high catalytic activities.[1] These heterogeneous catalysts offer the advantage of ease of separation from the media after completion of the reaction. They could be recovered and reused multiple times, making them attractive for applications in green and sustainable chemistry. Nanoparticles of many transition metals (e.g., Fe,[1b,2] Ru,[1b,3] Rh,[1b,3a,4] Pd,[1b,5] Pt,[1b,6] Cu,[1b,7] Ag[1b,8] and Au[1b,9]) have been prepared and investigated in various catalytic reactions. Au nanoparticles, in particular, have received widespread attention as catalysts over the past decade. Au was originally considered to be chemically inert and hence a poor catalyst. However, upon reduction of the particle size to the nanometer length scale and upon dispersion on a suitable support, Au could become a highly active catalyst in many reactions including hydrogenation,[10] oxidation,[11] hydroamination[12] and coupling reactions.[13]

Propargylic amines are useful and versatile precursors for the synthesis of various nitrogen-containing biologically active compounds, such as natural products and therapeutic drug molecules.[14] These compounds could be synthesized by classical methods involving the nucleophilic addition of an alkynyl-Li or Mg reagent to an imine or other similar C=N electrophiles.[15] The alkynyl-Li or Mg reagents were generated in a separate step, and used in stoichiometric amounts. Furthermore, these reagents were moisture-sensitive and incompatible with sensitive substrates. A more attractive and atom-efficient strategy to propargylic amine synthesis is through a one-pot, three-component coupling reaction of aldehyde, amine and alkyne *via* a C–H activation catalyzed by a transition metal. Catalytic multicomponent reactions are highly atom-efficient processes that would enable the implementation of several transformations in a single manipulation. These reactions also produce less side products as compared to classical stepwise methodologies. A number of homogeneous systems such as iron salts,[16] copper salts[17a] and their complexes,[17b] silver salts,[18] gold salts[19a,b] and their complexes,[19c,d] iridium complexes,[20] Hg_2Cl_2,[21] and a Cu/Ru[22] bimetallic system have been reported for the preparation of propargylic amines *via* this three-component coupling protocol. Although these catalysts were highly effective, the homogeneous systems could not be recovered for reuse.

Heterogeneous catalysts, on the other hand, would be able to overcome this recyclability issue. Heterogeneous systems such as silica-immobilized and hydroxyapatite-supported Cu(I) complexes,[17b,c,23] CuO nanoparticles,[24] Ag(I) salts in ionic liquids,[25] unsupported[13a] and supported gold nanoparticles on CeO_2 and ZrO_2,[13b] and layered double hydroxide[13d] have been reported to display high activities for the three-component coupling reaction of aldehyde,

amine and alkyne. In these reports, some of the heterogeneous catalysts have been recovered and reused for a number of cycles with nearly consistent activity. Our group has recently developed new synthetic methodologies for the preparation of various transition metal nanoparticles.[26] In this paper, we report our results on the efficient three-component coupling reaction of aldehyde, amine and alkyne catalyzed by semiconductor-gold nanocomposites in water.

Results and Discussion

Three different types of quantum dots (QDs) were prepared as hybrids with Au nanoparticles *via* solution methods. Figure 1 shows the transmission electron microscopy (TEM) images of the CdS, CdSe and PbS QDs and their nanocomposites with Au. Since Au has a strong imaging contrast, it was easily identified in the semiconductor-Au nanocomposites. Au was deposited at multiple sites on each QD. Energy dispersive X-ray (EDX) analysis (Supporting Information, Figure S1) further confirmed that the heterogeneous structure was composed of the semiconductor and Au components. The Au loading on the QDs ranged from 17.1 to 25.4 wt%, and the Au nanoparticles were 1–2 nm in diameter (Figure 1).

The three semiconductor-Au nanocomposites were tested for their catalytic activities in the three-component coupling reaction of the model substrates benzaldehyde, piperidine and phenylacetylene in water at 100 °C (Table 1, entries 1–11). These initial screening experiments showed that with a catalyst loading of 0.3 mol% Au and a reaction time of 6 h at 100 °C in air, PbS-Au nanocomposite provided the highest activity, giving the desired propargylic amine product in 76% isolated yield (Table 1, entry 7). The CdS-Au and CdSe-Au nanocomposites gave lower isolated yields of 43% and 53%, respectively (Table 1, entries 1 and 4). Recycling of the catalysts was investigated by recovering the three semiconductor-Au nanocomposites *via* centrifugation of the reaction mixture after the addition of a non-polar solvent (i.e., hexane), followed by three more hexane washes. The aqueous layer containing the recovered catalyst was then used in the subsequent run without further addition of the solvent (i.e., water). As shown in Table 1 (entries 2, 5 and 8), the catalytic activities of the three semiconductor-Au nanocomposites decreased upon recycling. Note that the Au content in these nanocomposite catalysts was quite high (17.1–25.4 wt%), and since these experiments were performed on a 1 mmol scale, the catalyst loading (0.3 mol% Au) for each experiment was small (2.3–3.5 mg). Hence, some of the materials might be lost in handling during the catalyst recovery process, leading to a decrease in the isolated yield of the propargylic amine product.

All three semiconductor-Au nanocomposites showed an improved yield of the propargylamine product (Table 1, entries 3, 6 and 9) when a higher catalyst loading (0.5 mol% Au instead of 0.3 mol% Au) and a longer reaction time (12 h instead of 6 h) were used. The PbS-Au nanocomposite was again the most active catalyst, producing the desired product in 85% isolated yield. Comparable yields of 86–87% were obtained when even higher PbS-Au catalyst loadings (0.8–1.0 mol% Au) were used (Table 1, entries 10 and 11).

The differences in the catalytic activities of the CdS-Au, CdSe-Au and PbS-Au nanocomposites could not be due to the size of the Au nanoparticles as their diameters were similar (1–2 nm). The CdS-Au, CdSe-Au and PbS-Au nanocomposites have different Au contents (25.4, 20.5 and 17.1 wt%, respectively). To investigate the possibility of the Au content affecting the catalytic activities of the nanocomposites, two additional samples of the PbS-Au nanocomposites with a lower and higher Au content of 10.0 and 45.0 wt% were synthesized. The Au nanoparticles on these two PbS-Au nanocomposites were similar in size (Supporting Information, Figure S2). Both catalysts gave comparable yields of the propargylic amine product (Table 1, entries 12 and 13). Hence, the different Au contents in the semiconductor-Au nanocomposites did not affect the catalytic activities of these materials.

The surface chemistry of Au nanoparticles on the three QDs was subjected to X-ray photoelectron spectroscopy (XPS) analysis. As shown in Figure 2, for PbS-Au nanocomposite (with 17.1 wt% Au), the Au 4*f* XPS spectra could be deconvoluted into two pairs of doublets. The more intense doublet (at 84.1 and 87.8 eV) was attributed to Au(0). The second and weaker doublet (at 84.7 and 88.4 eV) could be assigned to Au(I).[27,28] The PbS-Au nanocomposites with Au contents of 10.0 and 45.0 wt% also showed similar XPS spectra with two pairs of doublets (Supporting Information, Figure S3). On the other hand, the Au 4*f* XPS spectra of CdS-Au and CdSe-Au exhibited mainly one set of doublets associated with Au(0).

In the three-component coupling reaction of aldehyde, amine and alkyne catalyzed by gold salts, it was proposed that a Au(I) species was the active catalyst.[19a,b] For heterogeneous Au/CeO_2 and Au/ZrO_2 catalysts, Au(III) was considered to be the most active catalytic species [as compared to Au(I) and Au(0)].[13b] In our studies, although the exact nature of the active Au species in the coupling reaction remained unknown, the improved catalytic activity of the PbS-Au nanocomposite as compared to the CdS-Au and CdSe-Au nanocomposites could nevertheless be attributed to the presence of the oxidized Au(I) species in the former. Au(0) species would be expected to be less active than Au(I) as evidenced by the re-

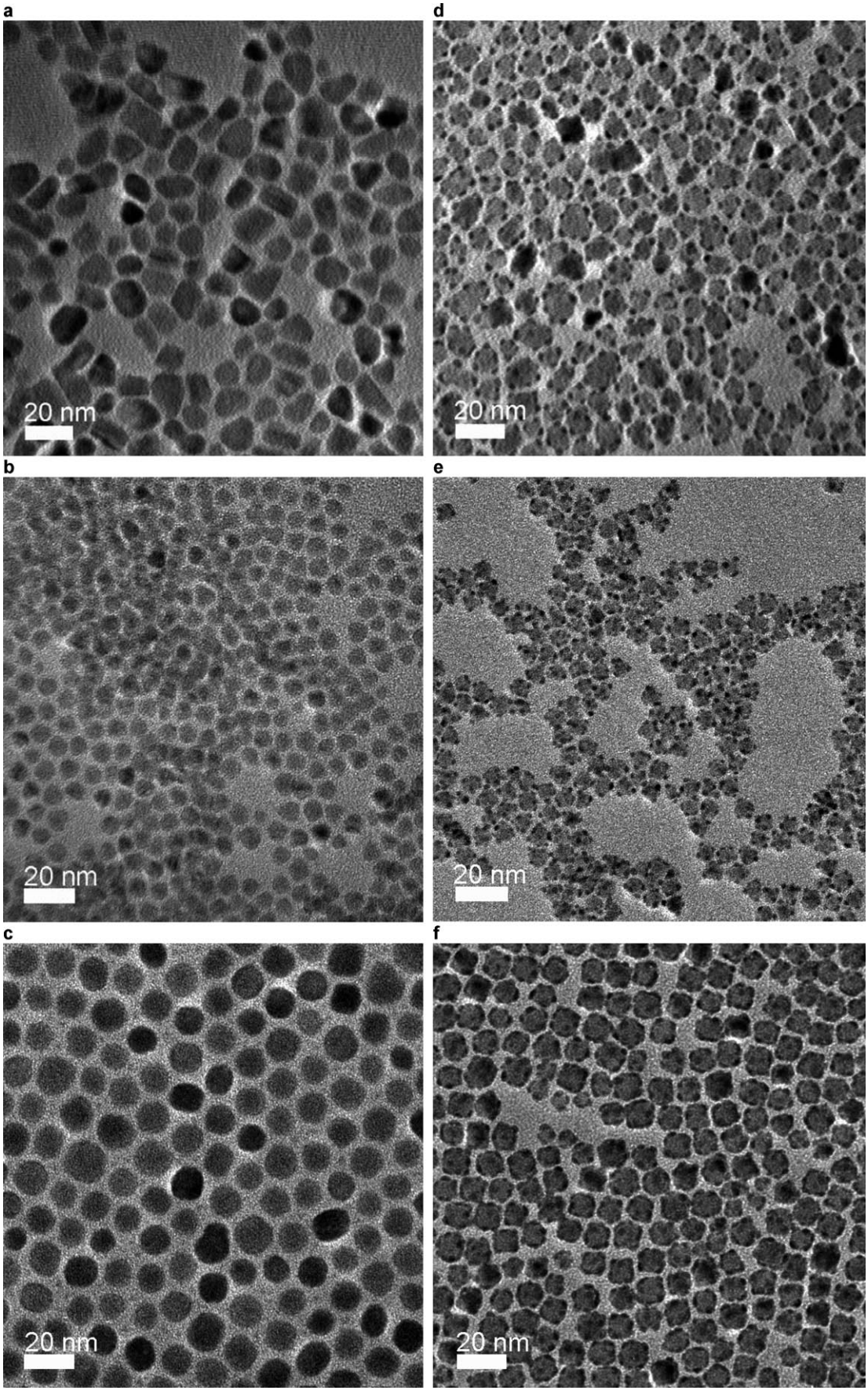
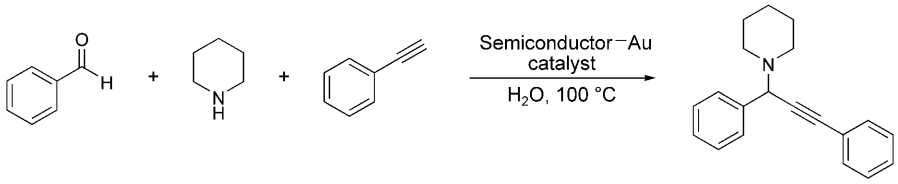


Figure 1. TEM images of (**a**) CdS, (**b**) CdSe and (**c**) PbS QDs, and (**d**) CdS-Au, (**e**) CdSe-Au and (**f**) PbS-Au nanocomposites.

Table 1. Three-component coupling of benzaldehyde, piperidine and phenylacetylene catalyzed by semiconductor-Au nanocomposites.[a]



Entry	Catalyst	Au content [wt%]	Au [mol%]	Time [h]	Yield [%][b]	TON[c]	TOF[d]
1	CdS-Au	25.4	0.3	6	43	143	24
2[e]	CdS-Au	25.4	0.3	6	33	110	18
3	CdS-Au	25.4	0.5	12	77	154	13
4	CdSe-Au	20.5	0.3	6	53	177	30
5[f]	CdSe-Au	20.5	0.3	6	29	97	16
6	CdSe-Au	20.5	0.5	12	62	124	10
7	PbS-Au	17.1	0.3	6	76	253	42
8[g]	PbS-Au	17.1	0.3	6	61	203	34
9	PbS-Au	17.1	0.5	12	85	170	14
10	PbS-Au	17.1	0.8	12	87	109	9
11	PbS-Au	17.1	1.0	12	86	86	7
12	PbS-Au	10.0	0.5	12	87	174	15
13	PbS-Au	45.0	0.5	12	87	174	15

[a] *Reaction conditions:* benzaldehyde (1.0 mmol), piperidine (1.2 mmol) and phenylacetylene (1.3 mmol), H_2O (HPLC grade, 1.0 mL), 100 °C, 1000 rpm, under air.
[b] Isolated and unoptimized yield based on benzaldehyde.
[c] Number of moles of product per mole of catalyst.
[d] Number of moles of product per mole of catalyst per hour.
[e] The recycled CdS-Au catalyst from entry 1 was used in this experiment.
[f] The recycled CdSe-Au catalyst from entry 4 was used in this experiment.
[g] The recycled PbS-Au catalyst from entry 7 was used in this experiment.

duced activities of CdS-Au and CdSe-Au as compared to PbS-Au. The validity of this hypothesis was further supported by numerous examples of the activation of alkynes by cationic gold species in the literature.[29]

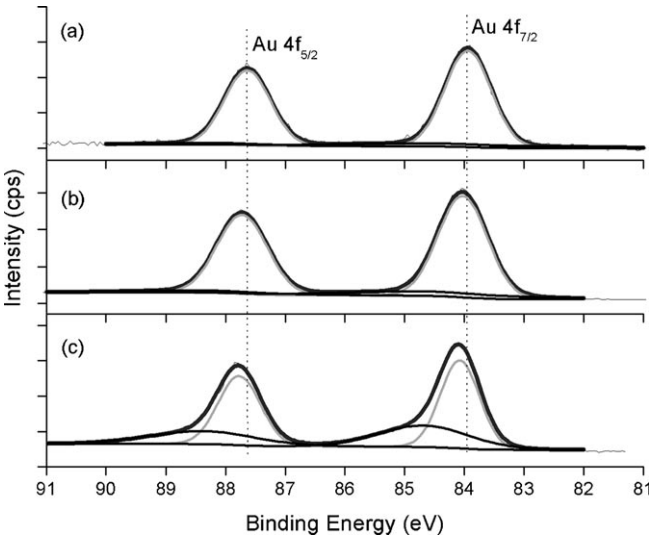


Figure 2. Au 4*f* XPS spectra of (**a**) CdS-Au, (**b**) CdSe-Au and (**c**) PbS-Au. Approximately 34% of Au in PbS-Au nanocomposite is in the Au(I) oxidation state.

The PbS-Au nanocomposite powder was not very easy to handle due to its sticky nature from the use of oleylamine surfactants in its synthesis. To facilitate its handling and recycling, PbS-Au was supported on carbon. Two samples of PbS-Au/C catalysts, both with a low Au content of 4.4 wt% were prepared; they were non-sticky black solids. One of the samples was subjected to an acetic acid reflux (120 °C for 3 h) to remove the oleylamine surfactants from the Au surface. There was no aggregation of the nanocomposite particles in both samples as confirmed by their TEM images (Figure 3).

The two PbS-Au/C catalysts were tested in the model three-component coupling reaction of benzaldehyde, piperidine and phenylacetylene (Table 2, entries 1 and 2). At a catalyst loading of 0.5 mol% Au in the solvent water at 100 °C, the two samples gave comparable results after 12 h in air (85–88% isolated yield). There were no significant differences between the two PbS-Au/C samples, although the sample subjected to an acetic acid reflux appeared to stick less to the walls of the glass vial. The effect of solvent on the standard three-component coupling reaction was

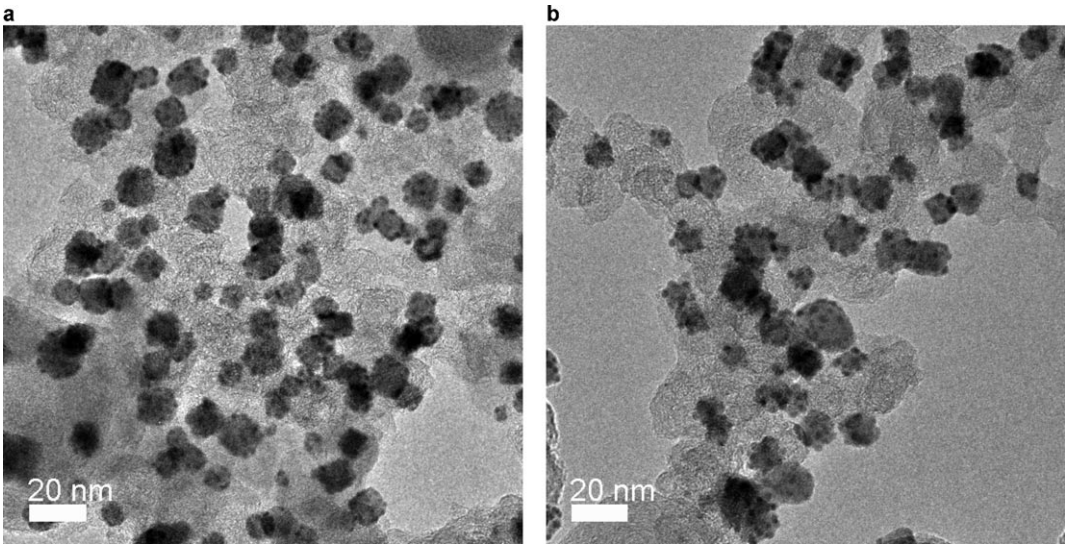
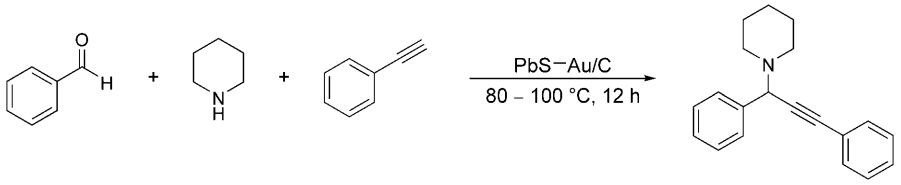


Figure 3. TEM images of PbS-Au/C powders (**a**) before and (**b**) after reflux in acetic acid at 120 °C for 3 h.

Table 2. Three-component coupling of benzaldehyde, piperidine and phenylacetylene catalyzed by PbS-Au/C.[a]



Entry	Catalyst	Solvent[b]	Temperature [°C]	Yield [%][c]	TON[d]	TOF[e]
1	PbS-Au/C[f]	Water	100	85	170	14
2	PbS-Au/C[g]	Water	100	88	176	15
3	PbS-Au/C[g]	Acetonitrile	100	8	16	1
4	PbS-Au/C[g]	1,4-Dioxane	100	10	20	2
5	PbS-Au/C[g]	Methanol	80	26	52	4

[a] *Reaction conditions:* PbS-Au/C catalyst (0.5 mol% Au), benzaldehyde (1.0 mmol), piperidine (1.2 mmol) and phenylacetylene (1.3 mmol), solvent (1.0 mL), 80–100 °C, 12 h.
[b] Reaction mixture was heated under air for the solvent water (1000 rpm), and under argon for the solvents acetonitrile, 1,4-dioxane and methanol (500 rpm).
[c] Isolated and unoptimized yield based on benzaldehyde.
[d] Number of moles of product per mole of catalyst.
[e] Number of moles of product per mole of catalyst per hour.
[f] This PbS-Au/C sample (with 17.1 wt% Au content in PbS-Au and 4.4 wt% Au content in PbS-Au/C) was not subjected to an acetic acid reflux.
[g] This PbS-Au/C sample (with 17.1 wt% Au content in PbS-Au and 4.4 wt% Au content in PbS-Au/C) was subjected to an acetic acid reflux to remove the oleylamine surfactants.

further investigated using the sample subjected to an acetic acid reflux. As shown in Table 2 (entries 2–5), water was found to be the best solvent for this reaction. The use of other polar solvents, for example, acetonitrile, 1,4-dioxane and methanol, led to a significant decrease in the yield of the propargylamine product (8–26% isolated yields). The PbS-Au/C catalyst could be recovered and reused easily when the reaction was performed in water. For the recyclability study (Table 3), the catalyst was recovered in the aqueous layer after centrifugation and separation from the organic layer containing the product and the hexane washes. The recovered PbS-Au/C catalyst in the aqueous layer was then used in the subsequent run without the addition of more water. This catalyst could be recycled and reused three times (Table 3, up to run #4) without a significant reduction in catalytic activity. The catalytic activity decreased by 1%, 10% and 18% after the first, second and third consecutive cycles, respectively. The slight decrease in the isolated

Table 3. Recycling of PbS-Au/C catalyst for the three-component coupling reaction of benzaldehyde, piperidine and phenylacetylene.[a]

Run #	1	2	3	4	5
Yield [%][b]	88	87	79	72	23
TON[c]	176	174	158	144	46
TOF[d]	15	15	13	12	4

[a] *Reaction conditions:* PbS-Au/C catalyst (0.5 mol% Au), benzaldehyde (1.0 mmol), piperidine (1.2 mmol) and phenylacetylene (1.3 mmol), H_2O (HPLC grade, 1.0 mL), 100 °C, 12 h, 1000 rpm. This PbS-Au/C sample (with 17.1 wt% Au content in PbS-Au and 4.4 wt% Au content in PbS-Au/C) was subjected to an acetic acid reflux prior to catalytic studies. For the recycling experiments (runs #2–5), the aqueous layer containing the recovered catalyst was used in the subsequent run without the addition of more water.

[b] Isolated and unoptimized yield based on benzaldehyde.

[c] Number of moles of product per mole of catalyst.

[d] Number of moles of product per mole of catalyst per hour.

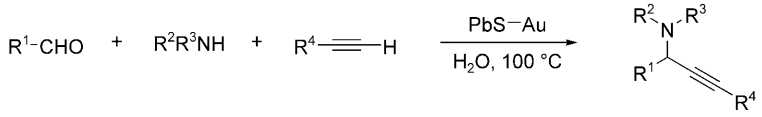
yield of the product was probably due to some loss of the nanocomposite catalysts during the recovery process.

The PbS-Au nanocomposite system offered certain advantages over other reported heterogeneous gold catalysts such as unsupported gold nanoparticles[13a] and supported gold nanoparticles on CeO_2 and ZrO_2,[13b] and layered double hydroxide.[13d] Compared to the unsupported gold nanoparticles (TON $\leq$ 10) and supported gold nanoparticles on layered double hydroxide (TON $\leq$ 33), the catalytic activity of the PbS-Au nanocomposite (TON $\leq$ 253) was higher. Although the supported gold nanoparticles on CeO_2 and ZrO_2 displayed higher catalytic activities (TON $\leq$ 788), these catalysts showed a greater decrease in their activity upon recycling (a decrease of 13%, 22% and 25% after the first, second and third successive cycles, respectively). Furthermore, the synthetic route for the semiconductor-Au nanocomposites was simple and flexible, and could be easily extended to the fabrication of other types of semiconductor-Au nanocomposites. Thus, the catalytic activity of these nanocomposites could be further modified by varying the structure and composition of the nanocomposites.

To investigate the scope and generality of the three-component coupling reaction with the PbS-Au/C catalyst, a variety of different aldehydes, amines and alkynes were examined (see Table 4). The aldehydes selected for this investigation included aliphatic as well as aromatic compounds with different functional groups. Aryl aldehydes with electron-donating groups (Table 4, entries 2–4 and 6) gave good to excellent yields of 70–95%. Some steric hindrance was tolerated in this coupling reaction as shown by the equivalent yields (95%) attained when the methyl group was at either the *ortho* or *para* position of the benzaldehyde (Table 4, entries 3 and 4). However, when the aryl aldehyde became too bulky (with two methyl substituents at the *ortho* positions), there was no coupling reaction (Table 4, entry 5). Benzaldehydes with electron-withdrawing substituents, such as chloro or bromo at the *para* position, also coupled smoothly with piperidine and phenylacetylene to give their respective propargylic amine products in good yields (88–89%, Table 4, entries 7 and 8). However, with stronger electron-withdrawing groups such as 4-cyanobenzaldehyde and pentafluorobenzaldehyde (Table 4, entries 9 and 10), no coupling reaction occurred. Aliphatic aldehydes such as cyclohexanecarboxaldehyde (Table 4, entry 15) also showed high reactivity with a good yield of 84%. However, with valeraldehyde, octylaldehyde and pivalaldehyde (Table 4, entries 11, 12 and 16), moderate to low yields of 40%, 36% and 8% were achieved, respectively. In the case of pivalaldehyde, the low yield could be due to the lower boiling point of the aldehyde substrate (74–76 °C). As the coupling reaction was performed at 100 °C, most of the pivalaldehyde substrate could exist in the vapor phase, thus, there would be less of the substrate for reaction. For valeraldehyde and octylaldehyde, the low yields could be attributed to the formation of an unwanted side-product. These two aldehydes contained an α-hydrogen, and in the presence of a catalytic amount of acid (present in the PbS-Au/C that was subjected to an acetic acid reflux), the aldol condensation could occur, resulting in the formation of the α,β-unsaturated carbonyl side-product after a dehydration step. This was further confirmed with two more coupling reactions with the octylaldehyde substrate. Using a PbS-Au/C catalyst that was not subjected to an acetic acid reflux (Table 4, entry 13), a higher isolated yield of 49% was achieved. In this case, although the catalyst was not subjected to an acetic acid reflux, the carbon support contained some carboxylic acid functional groups that could act as a catalyst in the aldol condensation side reaction. When the coupling reaction was performed with a PbS-Au catalyst that was not supported on carbon (Table 4, entry 14), the yield improved to 79%, and very little of the unwanted α,β-unsaturated carbonyl by-product was detected in the gas chromatography-mass spectrometry (GC-MS) analysis of the reaction mixture.

Heterocyclic aldehydes (Table 4, entries 17–22) generally did not participate in the three-component coupling reaction catalyzed by PbS-Au nanocomposite. With the exception of 3-thiophenecarboxaldehyde (Table 4, entry 22), which gave an isolated yield of 68%, the heterocyclic aldehydes (2-pyridyl, 2-furfuryl, 3-furfuryl and 2-thiophenyl) displayed either no reac-

Table 4. Coupling of aldehyde, amine and alkyne by PbS-Au/C in water.[a]

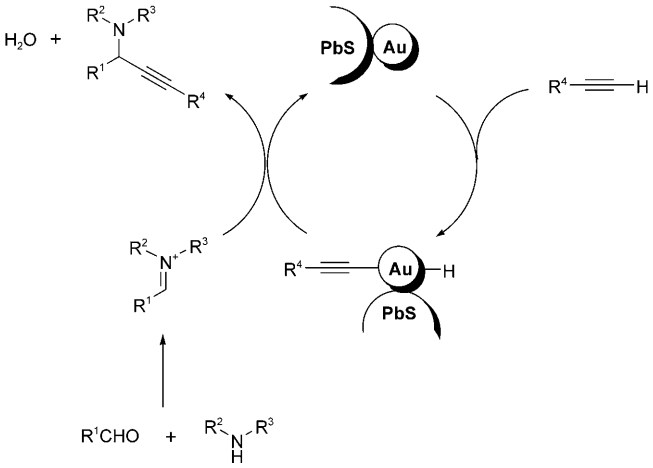


Entry	R^1	R^2R^3NH	R^4	Time [h]	Yield [%][b]	TON[c]	TOF[d]
1	Ph	Piperidine	Ph	12	88	176	15
2	1-Naphthyl	Piperidine	Ph	12	91	182	15
3	4-MeC_6H_4	Piperidine	Ph	12.5	95	190	15
4	2-MeC_6H_4	Piperidine	Ph	12.5	95	190	15
5	2,6-$Me_2C_6H_3$	Piperidine	Ph	12.5	0	0	0
6	4-$MeOC_6H_4$	Piperidine	Ph	12	70	140	12
7	4-ClC_6H_4	Piperidine	Ph	13	88	176	14
8	4-BrC_6H_4	Piperidine	Ph	12	89	178	15
9	4-NCC_6H_4	Piperidine	Ph	12	0	0	0
10	C_6F_5	Piperidine	Ph	12	0	0	0
11	Butyl	Piperidine	Ph	12	40	80	7
12	Heptyl	Piperidine	Ph	12.5	36	72	6
13[e]	Heptyl	Piperidine	Ph	12.5	49	98	8
14[f]	Heptyl	Piperidine	Ph	12.5	79	158	13
15[e]	Cyclohexyl	Piperidine	Ph	12.5	84	168	13
16	$(CH_3)_3C$	Piperidine	Ph	12.5	8	16	1
17	2-Pyridyl	Piperidine	Ph	12	0	0	0
18	2-Furfuryl	Piperidine	Ph	12	0	0	0
19[e]	3- Furfuryl	Piperidine	Ph	12.5	0	0	0
20[e]	2-Thiophenyl	Piperidine	Ph	12.5	1	2	<1
21[f]	2-Thiophenyl	Piperidine	Ph	12.5	8	16	1
22[e]	3-Thiophenyl	Piperidine	Ph	12.5	68	136	11
23	Ph	Morpholine	Ph	13	62	124	10
24	Ph	$R^2=R^3=PhCH_2$	Ph	12.5	28	56	4
25[e]	Ph	$R^2=R^3=PhCH_2$	Ph	12.5	26	52	4
26[f]	Ph	$R^2=R^3=PhCH_2$	Ph	12.5	32	64	5
27	Ph	$R^2=R^3=$Allyl	Ph	12.5	63	126	10
28	Ph	*cis*-2,6-Dimethylpiperidine	Ph	12.5	0	0	0
29	Ph	Piperidine	4-$MeOC_6H_4$	12.5	77	154	12
30	Ph	Piperidine	4-FC_6H_4	13	90	180	14
31	Ph	Piperidine	4-ClC_6H_4	12.5	90	180	14
32	Ph	Piperidine	4-BrC_6H_4	12.5	86	172	14
33	Ph	Piperidine	Cyclohexyl	13	50	100	8
34	Ph	Piperidine	$(CH_3)_3C$	12.5	10	20	2
35	Ph	Piperidine	Butyl	12	13	26	2
36	Ph	Piperidine	3-Thiophenyl	13	92	184	14
37	Ph	Piperidine	2-Pyridyl	12	0	0	0

[a] *Reaction conditions:* PbS-Au/C catalyst (0.5 mol% Au), aldehyde (1.0 mmol), amine (1.2 mmol) and alkyne (1.3 mmol), H_2O (HPLC grade, 1.0 mL), 100 °C, 1000 rpm, unless otherwise specified. The PbS-Au/C sample (with 17.1 wt% Au content in PbS-Au and 4.4 wt% Au content in PbS-Au/C) was subjected to an acetic acid reflux prior to catalytic studies.
[b] Isolated and unoptimized yield based on aldehyde.
[c] Number of moles of product per mole of catalyst.
[d] Number of moles of product per mole of catalyst per hour.
[e] PbS-Au/C catalyst (0.5 mol% Au) was used. This PbS-Au/C sample (with 17.1 wt% Au content in PbS-Au and 4.4 wt% Au content in PbS-Au/C) was not subjected to an acetic acid reflux prior to catalytic studies.
[f] PbS-Au catalyst (0.5 mol% Au) was used. This PbS-Au sample (with 17.1 wt% Au content in PbS-Au) was not supported on C.

tivity or very low yields of 1–8% (Table 4, entries 17–21).

Different types of secondary amines (cyclic and acyclic) were also studied with the PbS-Au catalyst (Table 4, entries 23–28). With morpholine and diallylamine (Table 4, entries 23 and 27), moderate yields of 62% and 63% were attained, respectively. Dibenzylamine, on the other hand, gave lower yields of 26–



Scheme 1. Tentative mechanism for the PbS-Au catalyzed three-component coupling of aldehyde, amine and alkyne in water.

32% (Table 4, entries 24–26). No coupling reaction occurred with a sterically hindered cyclic secondary amine, such as *cis*-2,6-dimethylpiperidine (Table 4, entry 28).

A variety of different alkyl- and arylalkynes were also tested (Table 4, entries 29–37) with the PbS-Au nanocomposite. In general, the arylalkynes gave better yields than the alkylalkynes. Arylalkynes with electron-withdrawing substituents (F, Cl, Br) displayed higher reactivities with good yields of 86–90% (Table 4, entries 30–32), while the electron-donating substituents led to a slightly lower yield of 77% for 4-methoxyphenylacetylene (Table 4, entry 29). For the aliphatic alkynes (Table 4, entries 33–35), the reactivities correlated to the boiling points of the substrates. A higher boiling substrate (130–132 °C for cyclohexylacetylene) would result in a higher yield of the desired propargylamine product (50% isolated yield) (Table 4, entry 33). Alkyne substrates with lower boiling points (33–35 °C for 3,3-dimethyl-1-butyne and 71–72 °C for 1-hexyne) gave lower yields of the coupled products (10–13%) (Table 4, entries 34 and 35). Heterocyclic alkyne, such as 3-ethynylthiophene, produced an excellent yield of 92% (Table 4, entry 36). However, for 2-ethynylpyridine (Table 4, entry 37), no coupling reaction was observed.

A tentative mechanism for the three-component coupling reaction catalyzed by PbS-Au nanocomposites was proposed (Scheme 1). The reaction mechanism of the PbS-Au catalyst could proceed *via* the activation of the C_{sp}–H bond of the terminal alkyne by the PbS-Au nanocomposite. The alkynyl-Au intermediate generated would then react with the immonium ion generated *in situ* from the aldehyde and secondary amine to produce the corresponding propargylic amine product, and regenerate the active PbS-Au species for further reactions.

Conclusions

In conclusion, we have successfully developed an efficient heterogeneous PbS-Au catalyst for the synthesis of propargylic amines *via* a three-component coupling reaction of aldehyde, amine and alkyne in water. The process is simple and applicable to a diverse range of aromatic and aliphatic aldehydes, amines and alkynes. Furthermore, the catalyst is stable to air and water, and can be easily recovered and reused.

Experimental Section

Synthesis of QDs

CdS QDs were synthesized according to a published method.[30] In a three-neck flask equipped with a condenser and a magnetic stirring bar, 91.5 mg of $CdCl_2$ and 20 mL of oleylamine were heated to 90 °C with concurrent degassing with nitrogen for 30 min. In another flask, 16 mg of elemental sulfur and 2 mL of oleylamine were heated to 90 °C with concurrent degassing with nitrogen for 30 min. The sulfur precursor solution was injected rapidly into the three-neck flask containing the cadmium precursor at 160 °C. The solution was left at the growth temperature of 160 °C for 1 h, and then cooled down to room temperature. The CdS nanocrystals were purified by precipitation with ethanol, centrifuging, and re-dispersing in 20 mL of toluene.

CdSe QDs were prepared by a previously reported solution method.[31] In a typical synthesis of the CdSe cores, 65 mg of CdO, 400 mg of octadecylphosphonic acid (ODPA), and 25 mL of trioctylamine (TOA) were first placed in a four-neck round-bottom flask under an argon flow, and stirred at 300 °C until CdO was completely dissolved. Se powder (200 mg) was dissolved in 2.5 mL of trioctylphosphine (TOP). The TOPSe solution was then injected into the Cd solution with rapid stirring, and kept at 300 °C for 2 min, followed by cooling down to room temperature. 25 mL of chloroform and 50 mL of methanol were added to precipitate the CdSe nanocrystals. The product was then washed twice with copious methanol, and re-dispersed in 20 mL of toluene.

Synthesis of PbS QDs was achieved using an established solution method with some modification.[32] In brief, 190 mg of $Pb(OAc)_2$, 20 mL of oleylamine, and 2 mL of oleic acid were placed in a two-neck round-bottom flask, and the mixture was heated to 160 °C under an argon flow until all the solids were completely dissolved. S powder (16 mg) was dissolved in 2 mL of oleylamine. The S solution in oleylamine was then injected into the Pb(II) solution with rapid stirring, and kept at 160 °C for 5 min, followed by cooling down to room temperature. 10 mL of toluene and 60 mL of methanol were added to precipitate the PbS nanocrystals. The product was then washed twice with copious methanol, and re-dispersed in 20 mL of toluene.

Transfer of Au(III) into Toluene

The transfer of Au(III) from water to toluene was accomplished using a common method developed by Brust et al.[33]

30 mL of 20 mM of aqueous $HAuCl_4$ solution were mixed with 60 mL of 50 mM of toluene solution of tetraoctylammonium bromide. The mixture was stirred for 1 min, and settled for phase separation. The toluene layer containing the Au(III) species (10 mM) was separated, and used in the synthesis of the semiconductor-Au nanocomposites.

Synthesis of Semiconductor-Au Nanocomposites

The preparation of semiconductor-Au nanocomposites followed a method established for the synthesis of PbS-Au nanocomposites with slight modification.[34] Briefly, 12.5 mL of Au(III) in toluene were mixed with the QD organosol prepared above, followed by the addition of 2.5 mL of dodecylamine. The mixture was aged for 2 h under stirring at room temperature. 60 mL of methanol were added to precipitate the hybrid materials. The products were then washed twice with copious methanol, and dried under vacuum at room temperature.

Three-Component Coupling Reactions

General procedure for the three-component coupling reaction of aldehyde, amine and alkyne (Table 4, entries 1–37): A mixture of the PbS-Au nanocomposite catalyst (0.5 mol% Au), aldehyde (1.0 mmol), amine (1.2 mmol), alkyne (1.3 mmol) and water (HPLC grade, 1.0 mL) was heated at 100 °C (1000 rpm) in a closed 8 mL glass vial under air for 12–13 h. The reaction mixture was cooled to room temperature, and 3 mL of hexane were added. The mixture was centrifuged at 5000 rpm for 5 min. The upper organic layer containing the product was separated, and the lower aqueous layer containing the catalyst was washed with hexane (3 × 3 mL). The solvent was removed from the combined organic layers by rotary evaporation, followed by purification by column chromatography (silica gel, dichloromethane to 9/1 dichloromethane/ethyl acetate, unless noted otherwise).

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