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ARTICLE TYPE

Highly Efficient Three-Component Coupling Reaction Catalyzed by Gold Nanoparticles Supported on Periodic Mesoporous Organosilica with Ionic Liquid Framework[†]

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A novel gold nanoparticles supported on periodic mesoporous organosilica with alkylimidazolium framework, Au@PMO-IL, was shown to be highly active, and recyclable catalyst for three-component coupling reaction of aldehyde, alkynes and 10 amines to give the corresponding propargylilc amine.

In the past few years, an increasing number of multicomponent reactions (MCRs) have developed for the synthesis of diverse complex molecules through a combination of three or more starting material in one-pot operation, while keeping reduced ¹⁵ waste and increased safety.¹ Among MCRs, the catalytic coupling reaction of aldehyde, amine, and alkyne (A³ coupling) is one of the best example, where propargylamine is obtained as the major product. Propargylamines are valuable synthetic building blocks in synthesis of varied natural products and biologically active ²⁰ compounds.²⁻³ Numerous method typically involve C-H bond activation of terminal alkynes using a wide range of transition-metal catalyst such as copper,⁴ iridium,⁵ nickel,⁶ iron,⁷ and indium⁸ have been well explored for the synthesis of propargylamines. ²⁵

Although for a long time gold has been regarded as a poor or even inactive catalyst, during the past decade increasing attentions have been directed toward both chemistry and catalytic performance of this metal. A major driving force for this interest is owing to the fact that gold have demonstrated unusual and 30 somewhat unexpected catalytic properties in many chemical transformations as underscored by appearing several excellent reviews in this field.9 Quite recently, surface structures and electronic properties of various gold single-crystal surfaces¹⁰ and different application of gold as a catalyst were studied.¹¹ In this 35 regards, oxidation of alcohols and carbon monoxide under mild conditions,¹² hydrogenation of olefins,¹³ Suzuki,¹⁴ Sonogashira¹⁵ and Ullman¹⁶ coupling reactions, etc. are some of the most important applications of gold catalysts. Meanwhile, it was also found that Lewis acid character and unique property of gold in 40 activating sp and (even sp^2 and sp^3) C-H bonds make it as a promising catalyst in three-component condensation reaction of terminal alkynes with aldehydes and amines.¹⁷ Nevertheless, reports of using gold as a catalyst are still very limited. Quite

recently, Vinu and co-workers reported a new promising catalyst ⁴⁵ system comprising gold nanoparticles embedded in mesoporous carbon nitride for the synthesis of propargylamines through A³ coupling reaction.^{17g} While this method provide an excellent approach in preventing the agglomeration of Au nanoparticles during the A³ coupling reaction, low selectivity of the products ⁵⁰ considerably limits the versatility of this catalytic system. Therefore, it seems that quest for novel, efficient and recoverable Au-based catalysts for A³ coupling reactions with appropriate selectivity remains a great challenge.

Herein, we report that a novel gold nanoparticles supported on 55 periodic mesoporous organosilica with imidazolium ionic liquid framework having 2D-hexagonal structure is an efficient and highly selective catalyst in the three-component coupling reactions of aldehydes, terminal alkynes, and amines at very low catalyst loading and under mild reaction conditions. Synthesis of 60 periodic mesoporous organosilica containing ionic liquid (PMO-IL) has been introduced recently by our research group.¹⁸ In this hydrolysis and co-condensation 1.3regard. of bis(trimethoxysilylpropyl) imidazolium chloride and tetra methoxysilane in the presence of P123 as structure directing 65 agent under acidic conditions afforded the corresponding PMO-IL. We also investigated the ability of the obtained mesoporous organosilicas to actually use as a support for the immobilization and stabilization of Pd-nanoparticles in the Suzuki-coupling reaction of aryl halides with arylboronic acids and aerobic 70 oxidation of alcohols under mild reaction conditions. Considering the ionic nature of bridge organic group in our PMO-IL, we reasoned that the materials might be indeed utilized to support anionic gold species like AuCl₄ via a simple ion exchange reaction. To verify our hypothesis, a dispersion of PMO-IL (0.5 75 g, 0.5 mmol imidazolium g⁻¹) was sonicated in deionized water (10 ml) for 10 minutes. A solution of NaAuCl₄ (0.034 g, 0.085 mmol) in deionized water was gradually added to the suspension while stirring at the room temperature for 4 hours. Assuming that all AuCl₄ were exchanged with the available amount of Cl⁻ in the 80 original PMO-IL, one would expect an Au content of approximate 0.16 mmol g⁻¹ in the resulting hybrid materials, a value which was confirmed by atomic adsorption spectroscopy.

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1565 cm ⁻¹ and 1633cm ⁻¹ in the spectrum of the initial PMO-IL is
attribute to C=C and C=N stretching bonds of imidazolium ring,
respectively. ¹⁷ This indicates that ionic liquid precursor was
incorporated into the PMO-IL material and remains intact into 5
PMO matrix after both sol-gel process and surfactant extraction.
The nitrogen adsorption-desorption isotherm of both PMO-IL and
Au@PMO-IL exhibited type-IV curves with sharp type H1
hysteresis loop, thus implying the cylindrical mesoporous with
relatively uniform pore size distribution (Figure 2S). The BET 10
surface area, as well as mesoporous volume of Au@PMO-IL was
calculated to be 516 m ² g ⁻¹ and 1.00 cm ³ g ⁻¹ , respectively. The
values were lower than that calculated for PMO-IL (S_{BET} = 554
m^2 g ⁻¹ , V _p = 1.06 cm ³ g ⁻¹), which highlight the notion that
exchange of AuCl ₄ ⁻ with Cl ⁻ might be significantly accrued into 15
the nanosized pores of the mesoporous materials. The average
pore size diameter of PMO-IL and Au@PMO-IL were calculated
be 5.29 nm using BJH methods, which furthermore affirm the
narrow pore size distributions in the samples. The TEM images
of both samples also revealed regular arrangements of hexagonal 20
tubules having channel dimension of ~ 5 nm, which is in good
agreement with the results obtained by N2 adsorption-desorption
analysis. We were next very interested to examine the catalytic
efficiency of the as-synthesized Au@PMO-IL in A ³ coupling
reaction of phenyl acetylene with varied aldehyde and amines. 25

The FT-IR of the catalyst was studied (Figure 1S). The peaks at

Table 1. The effects of various variables on $[A^3]$ three-component of 4methylbenzaldehyde, piperidine, and phenylacetylene using Au@PMO-IL^{a)}

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Me		Au@PMO-IL Solvent Me	
Entry	Solvent	T (°C)	Isolated Yield
1	Toluene	60	45
2	Water	60	55
3	CHCl ₃	60	88
4	Solvent-free	60	50
5	PEG (200)	60	Trace
6	CH ₃ CN	60	trace
7	Toluene	100	65
8	Water	100	70
9	CHCl ₃	25	30

^{a)}Condition: aldehyde (1 eq.), amine (1.2 eq.), alkyne (1.3eq) and ₃₀ Au@PMO-IL (12 mg, 0.2 mol% Au) in 5 mL solvent for 11 h.

We focused our initial investigation on the effect of various types of solvents on the reaction of *p*-tolualdehyde, piperidine, and phenyl acetylene at different temperatures (Table 1).The results ³⁵ indicate that both reaction temperature, type of solvent used significantly influence the product yields in the described coupling reaction (Table 1). After several screening experiment with different combinations of the above-mentioned variable, the best condition was proved to be Au@PMO-IL (12 mg, 0.2 mol% ⁴⁰ of Au), *p*-tolualdehyde (1mmol), piperidine (1.2 mmol), phenylacetylene (1.3mmol), CH₃Cl (5 ml) at 60 °C during 11 h.

Table 2. Three-component	eaction of various aldehyde, secondary						
amines and terminal alkynes catalyzed by Au@PMO-IL ^a							
	2						
$R^1CHO + R^2_2NH + R^3 =$	$= \frac{\text{Au@PMO-IL}}{\text{CHCl}_{3}.60 ^{\circ}\text{C}} R^{1}$						

			CHCl₃, 60 °C	R' R3	
Entry	\mathbf{R}^1	R ² ₂ NH	R ³	Time(h)	Yield
1	Ph	Piperidine	Ph	12	87
2	Ph	Morpholine	Ph	12	86
3	4-Me-C ₆ H ₄	Piperidine	Ph	11	88
4	4-Me-C ₆ H ₄	Morpholine	Ph	15	82
5	2-Thiophenyl	Morpholine	Ph	20	87
6	2-Thiophenyl	Piperidine	Ph	20	82
7	1-Naphthyl	Piperidine	Ph	20	83
8	3-Me-C ₆ H ₄	Piperidine	Ph	15	78
9	2-Cl-C ₆ H ₄	Piperidine	Ph	7	86
10	2-Cl-C ₆ H ₄	Morpholine	Ph	10	84
11	2-Furfuryl	Piperidine	Ph	17	85
12	2-Furfuryl	Morpholine	Ph	20	85
13	Heptyl	Morpholine	Ph	10	75
14	Ph	Piperidine	4-OMe-C ₆ H ₄	10	88
15	4-Me-C ₆ H ₄	Piperidine	4-OMe-C ₆ H ₄	11	83
16	Ph	Morpholine	4-OMe-C ₆ H ₄	10	84
17	1-Naphthyl	Piperidine	4-OMe-C ₆ H ₄	20	81
18	Heptyl	Morpholine	4-OMe-C ₆ H ₄	12	77
19	2-pheny ethyl	Morpholine	4-OMe-C ₆ H ₄	12	80

^{a)} Condition: aldehyde (1 eq.), amine (1.2 eq.), alkyne (1.3eq) and Au@PMO-IL (12 mg, 0.2 mol% Au) in 5 ml CHCl₃ at 60 °C[.]

Having the optimized reaction condition, it was then attempted to expand the scope of amines, aldehydes and terminal alkynes ⁵⁰ applicable to the present A³ coupling reaction as demonstrated in Table 2. From these results we found that the conditions were equally applicable to the coupling a variety of aromatic aldehydes including heterocyclic aldehydes as well as 1-naphtaldehyde with either morpholine or piperidine utilizing phenyl acetylene, giving ⁵⁵ the corresponding propargylamines in high yields (Scheme 1, Table 2, entries 1-13). As demonstrated in Table 2, this reaction successfully works for coupling of of aromatic aldehydes with both piperidine and morpholine by 4-methoxy phenyl acetylene as carbon nucleophile partner, affording 4-methoxy propargylic ⁶⁰ amines in excellent as well (Table 2, entries 14-19).

In order to show the practical applicability of the Au@PMO-IL, we have scaled up the reaction of benzaldehayde to 10 mmol with 12 mmol of piperidine and 13 mmol of phenyl acetylene under similar optimized reaction conditions. The reaction proceeds well 65 with 92 isolated yields at 11 h.

Furthermore, the Au@PMO-IL is stable and reusable up to three reaction runs, giving an average of 83% isolated yields under the described conditions. Our investigation showed that although the recovered catalyst exhibited very slowly decreasing activity in 70 several consecutive runs, in each cycle the metal leaching was negligible. Moreover, no appreciable changes in textural properties after three reactions cycle has been detected as clearly evidenced from N₂ adsorption-desorption (Figure 2S) and TEM analysis of the recycled catalyst (Figure 1). TEM images also 75 indicate no detectable Au nanoparticles aggregation in the recovered Au@PMO-IL after the 3rd reaction run. Based on TEM images it is believe that integrated ionic liquid units (imidazolium units) incorporated in the mesochannels of PMO-IL may indeed

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provide a means of generating and stabilizing active catalytic AuNPs species during the described reaction.



Figure 1. TEM image of Au@PMO-IL after the 3rd reaction cycle (Scale s bar: 100 nm).

It has been well-documented that cationic gold species in the form of either Au^I or Au^{III} exhibit higher catalytic performance than metallic gold in the A³ coupling reactions. To assess whether 10 the cationic gold species are functioning as actual catalyst in our system or not, we have prepared a reduced Au@PMO-IL sample by treating the pristine catalyst with an excess of NaBH₄. We interestingly found that this catalyst system provided significantly decreased conversion (<15%) as compared to untreated 15 Au@PMO-IL (88 %) when using in the A^3 Coupling of ptolualdehyde with piperidine and phenyl acetylene under essentially identical conditions. To gain more insight into the exact gold oxidation state in our catalyst, we have studied both the pristine Au@PMO-IL and the reduced catalyst by employing 20 X-ray photoelectron spectroscopy (XPS) analysis. XPS spectra of the region corresponding to the binding energy range of 80-90 eV for both materials were recorded, which include Au 4f_{5/2}, and Au 4f_{7/2} peaks. The peaks located around 83.0/86.8 eV and 85.2/88.9 eV were assigned to the spin-orbit splitted components of the Au 25 4f level in the pure Au metalic form (84 eV for pure bulk metallic Au) and cationic Au(III) species, respectively.¹⁹ This spectrum clearly indicates the reduced samples (inactive catalyst) contained only Au⁰ species, whereas the pristine catalyst is only comprising ionic Au(III) species. In the basis of this observation it is very 30 likely that ionic gold species most probably in the form of Au(III) is the active component in our active catalyst system, while we could not exclude some catalysis by metallic gold.

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Notes and References

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[†] Electronic Supplementary Information (ESI) available: [The experimental details for the preparation of catalyst, TEM images, FT-IR spectrum for PMO-IL and Au@PMO-IL, XPS spectra, nitrogen ⁴⁵ adsorption-desorption isotherms, ¹H- and ¹³C-NMR for products] See DOI: 10.1039/b000000x/

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