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Communication

Gold Nanoparticle Supported on Ionic Liquid-modified Graphene Oxide as an Efficient and Recyclable Catalyst for One-Pot Oxidative A^3-coupling reaction of benzyl alcohols

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A novel gold nanoparticle supported on graphene oxide with ionic liquid framework (Au@GO-IL) was shown to be a highly active and recyclable catalyst for novel domino oxidative A^3-coupling reaction that has been successfully developed with benzyl alcohols instead of their corresponding aldehydes in aqueous media.

Multicomponent reactions (MCRs) have been proved to be very influential and efficient bond-forming tools in organic, combinatorial and medicinal chemistry.[1] In addition to the fundamental atom economy and selectivity underlying such reactions, simpler procedures, equipment, time, and energy savings, as well as environmental friendliness have all led to a sizable effort to design and execute MCRs in both academia and industry.[2] The three-component coupling of an aldehyde, an alkyne and an amine, commonly called an A^3-coupling as MCR has received much attention in recent years.[3] The resulting propargylamine derivatives are interesting molecules for drug screening, useful intermediates for heterocycle synthesis, and are involved in many different synthetic strategies.[4] For this reason, much effort has been devoted to the development of new alternatives of this extremely useful transformation. However, in the reported A^3-coupling reaction, commercially available aldehydes constitute the main starting materials. This is unfortunate since the use of aldehydes as the main reaction partner limits the versatility of this reaction. To address this issue, very recently it has been shown that replacing aldehydes with alcohols could significantly widen the versatility and the scope of well-known aldehyde-based multicomponent reactions.[5]

During recent years, substantial progress has been made in A^3-coupling reaction. Several transition-metal catalysts have been employed to assist the A^3 coupling reaction by C-H activation of the terminal alkyne.[6] Recent progress in this area has been reported using catalysts such as Fe, Cu, Ag, and Au, as well as Ir, In, and Zn compounds, among which the cationic gold species showed the highest catalytic activity.[7] 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 the chemistry and catalytic performance of this metal. Its ability to behave as a soft Lewis acid has only been recognized recently. Such a property allows gold to activate unsaturated functionalities such as alkynes, alkenes, and allenes, to create carbon–carbon and carbon–heteroatom bonds under extremely mild conditions. Moreover, by pre-coordination gold may activate sp, sp^2, and sp^3 carbon–hydrogen bonds efficiently. This may provide new opportunities in organic chemistry using gold as catalyst.[8] Additionally, supported gold nanoparticles have attracted considerable attention for oxidation of alcohols in aqueous media because of their extraordinarily high activity and selectivity.[9] High selectivity and stability of gold catalysts could be related to weak adsorption of reactants and products on gold particles as metallic gold is known to bind weakly with most molecules including water.[10]

To the best of our knowledge, there is currently no report of employing alcohols instead aldehyde in A^3-coupling reactions. Herein, we report that a novel gold nanoparticle supported on GO with ionic liquid framework is an efficient and highly selective catalyst in the novel domino oxidative A^3-coupling reactions of benzyl alcohols, terminal alkynes and secondary amines at very low catalyst loading and under aerobic conditions in aqueous media. Additionally, the effects of solvent polarity, and temperature on yield, and recycling potential of the catalyst have all been assessed. The synthesis of GO with ionic liquid framework is done by silylation modification technique on GO. Considering the ionic nature of ionic liquid groups in GO-IL, the materials can be utilized to support anionic gold species such as $AuCl_4^-$ *via* a simple ion exchange reaction. Therefore, the simple ion exchange with $AuCl_4^-$ provides the corresponding catalyst (Au@GO-IL).

Raman spectroscopy is a very useful tool for investigating the electronic and phonon structure graphene-based materials.[11] The Raman spectra of GO, GO-IL and Au@GO-IL (Fig. 1) show an obvious and step-by-step blue shift of the G band from 1571.27 to 1596.55 and 1600.29 cm^{-1}, probably due to the gradually increased compressive local stress induced by the attached IL groups and $AuCl_4^-$ on GO.[12] As shown, after the silylation of GO with IL, the ID/IG was 1.33 for the resulting GO-IL, while the ID/IG of GO was 1.59. Considering the G band and D band that represent the sp^2 C atoms and defects,[13] respectively, it can be anticipated that the increasing of the sp^2 hybridization structure (imidazolium ring) are raised from the successful silylation modification. The ID/IG decreases to 1.13 for the Au@GO-IL, possibly as a result of the Au NPs growth at the defective regions of the GO-IL surface.[14]

The electronic properties of nanocomposite were probed by X-ray photoelectron spectroscopy (XPS) analysis. As shown in Fig. 2, the peaks corresponding to Au 4f, C 1s, Cl 2s, N 1s, O 1s, and Si 2p & 2s are clearly observed in the XPS full spectrum. The XPS spectrum of N 1s core level region for Au@GO-IL shows a peak at 401.20 eV which corresponds to the bonding energy of quaternary nitrogen of IL that is clearly observed.[15] High-resolution Si 2p XPS spectrum of the Au@GO-IL hybrids can be split into two sublevels. The first one at 101.25 eV is attributed to the Si–O–C bonds, while the other one at 103.52 eV corresponding to the silicon participant from the siloxane network (Si–O–Si) resulting from the condensation of silane molecules.[16] The Au 4f core level region for Au@GO-IL nanocomposite includes two components. The first one is constituted by two doublets, situated at 83.47 and 88.27 eV, respectively, attributable to Au^0 that which arises due to the reduction of Au^{3+} by GO.[17] The second component located at 86.84 and 90.83 eV is attributable to the Au^{3+} as active catalytic spices in A^3 coupling reaction.[18] By integrating the area in the XPS has been found the ratio of Au^0:Au^{3+} to be 4:6.

TEM image also indicated no detectable aggregation or agglomeration of Au nanoparticles (NPs) in the fresh Au@GO-IL nanoconposite (Fig 3a).

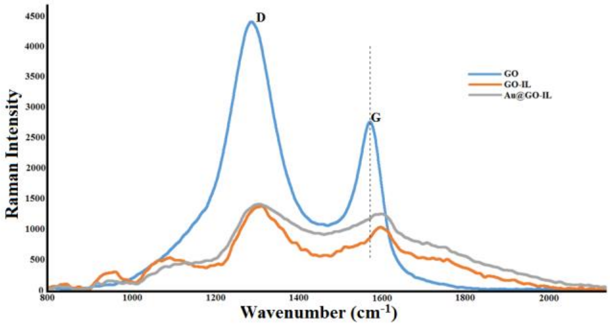


Fig. 1 Raman spectra GO, GO-IL and Au@GO-IL nanocomposites.

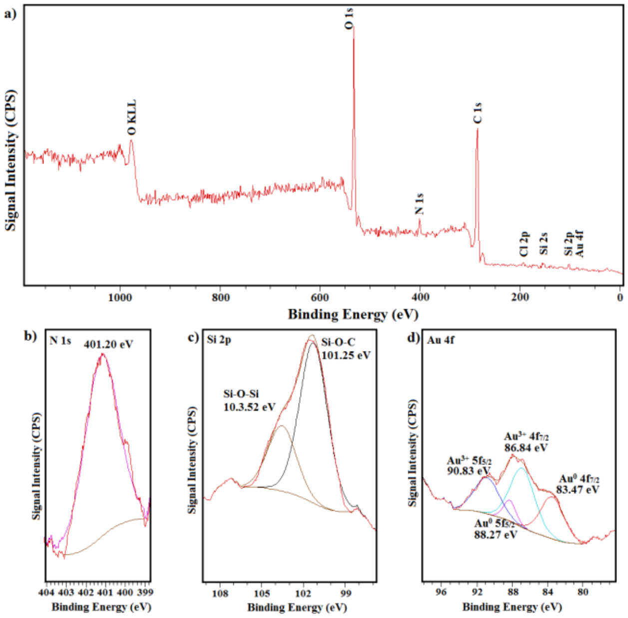


Fig. 2 Full range XPS spectrum (a), and the N 1s (b), Si 2p (c), Au 4f (d) core level regions XPS spectra of Au@GO-IL nanocopmosite, respectively.

The catalytic activity of the Au@GO-IL nanocomposite as catalyst was then tested in oxidative A^3-coupling. To optimize the reaction conditions benzyl alcohol, morpholine and phenylacetylene as model substrates in the presence of various solvents (Table 1). The results indicate that both reaction temperature and solvent significantly influence the product yield in the coupling reaction. After several screening experiments with different combinations the best conditions proved to be Au@GO-IL (1 mol% of Au), benzyl alcohol, (1 mmol), morpholine (1.2 mmol), phenylacetylene (1.3 mmol), H_2O (3 ml) at 100 ºC for 18 h.

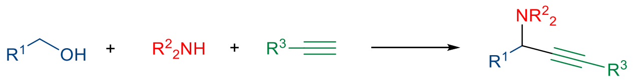
Table 1. Screening of the reaction conditions[a]

Entry	Solvent	Temp (ºC)	Yield (%)[b]
1	H_2O	60	78
2	MeOH	60	72
3	CH_3CN	60	60
4	$PhCH_3$	60	15
5	$CHCl_3$	60	65
6	H_2O	100	90

[a] benzyl alcohol, (1 mmol), morpholine (1.2 mmol), phenylacetylene (1.3 mmol), solvent (3 ml), Au@GO-IL (1 mol% of Au), 18 h, Air.[b] Isolated yield

Using the optimized reaction conditions, it was then attempted to expand the scope of benzyl alcoholes secondary amines, and terminal alkynes applicable to the present oxidative A^3 coupling reaction (Table 2). The benzyl alcohol bearing electron-withdrawing groups (*p*-Cl and *p*-NO_2) led to higher yield compared to the benzyl alcohol bearing electron-donating group (*p*-Me) (Table 2, entries 2-4). Additionally, the other benzylic alcohols were used in A^3-coupling with piperidine or pyrollidine and phenylacetylene (Table 2, entries 5-8). Furthermore, by using various substituted phenylacetylenes with substituents that have different electronic properties, different yields of the final products were achieved. The aryl acetylene bearing electron-donating group (*p*-Me) were more reactive compared to the aryl acetylene bearing electron-withdrawing group (*p*-CF_3) (Table 2, entries 9 and 10), which could be a reflection of the reduced nucleophilicity of the acetylide anion. Alkyl acetylene shows low reactivity under the optimized conditions, probably due to their lower acidity (Table 2, entry 11).

Table 2. Oxidative Three-component reaction of various benzyl alcohols, secondary amines and acethylenes catalyzed by Au@GO-IL[a]



Entry	R^1	$R_2{}^2NH$	R^3	Yield (%)[b]
1	Ph	morpholine	Ph	90
2	4-MeC_6H_4	morpholine	Ph	64
3	4-ClC_6H_4	morpholine	Ph	91
4	4-$NO_2C_6H_4$	morpholine	Ph	98
5	4-ClC_6H_4	piperidine	Ph	93
6	4-ClC_6H_4	pyrollidine	Ph	67
7	3-$NO_2C_6H_4$	pyrollidine	Ph	73
8	4-MeC_6H_4	piperidine	Ph	68
9	4-ClC_6H_4	morpholine	4-MeC_6H_4	89
10	4-ClC_6H_4	morpholine	4-$CF_3C_6H_4$	81
11	4-ClC_6H_4	morpholine	*n*-C_6H_{13}	70

[a] Alcohols, (1 mmol), amine (1.2 mmol), phenylacetylene (1.3 mmol), H_2O (3 ml), Au@GO-IL (1 mol% of Au), 18 h, 100 °C, Air.[b] Isolated yield.

The heterogeneous nature of the catalysis was proved using a hot filtration test and AAS analysis. To determine whether the catalyst is actually functioning in a heterogeneous manner or whether it is merely a reservoir for more active soluble gold species, we performed a hot filtration test in the oxidative A^3 coupling reaction of benzyl alcohol, morpholine and phenylacetylene after ~50% of the coupling reaction is completed. The hot filtrates were then transferred to another flask containing H_2O at 100 °C. Upon the further heating of catalyst-free solution for 24 h, no considerable progress (~6% by GC analysis) was observed. Moreover, using AAS of the same reaction solution at the midpoint of completion indicated that no significant quantities of gold are lost to the reaction liquors during the process.

The recyclability of the Au@GO-IL nanocomposite was also examined by the one-pot oxidative A^3-coupling reaction. It was found that the recovery can be successfully achieved in five successive reaction runs (Table. 3).

Table 3. Reusability of the Au@GO-IL nanocomposite in One-Pot Oxidative A^3-coupling reaction[a]

Reaction cycle	1st	2nd	3rd	4th	5th
Yield[b] (%)	90	90	89	87	84

benzyl alcohol, (1 mmol), morpholine (1.2 mmol), phenylacetylene (1.3 mmol), water (3 ml), Au@GO-IL (1 mol% of Au), 18 h, 100 °C.[b] Isolated yield .

Although the recovered catalyst exhibited very slowly decreasing activity in several consecutive runs, in each cycle the metal leaching was negligible. Moreover, no appreciable changes in textural properties after five reactions cycles was detected, as clearly evidenced from TEM analysis of the recycled catalyst (Fig. 3). TEM image also indicated no detectable aggregation or agglomeration of Au nanoparticles (NPs) in the recovered Au@GO-IL after the 5rd reaction run. The imidazolium IL plays an important role in improving the dispersibility of Au NPs on the GO-IL sheets.[19] As Fig. 3b shows, the surfaces of graphene are covered by distributed Au NPs with an average size of 20–30 nm.

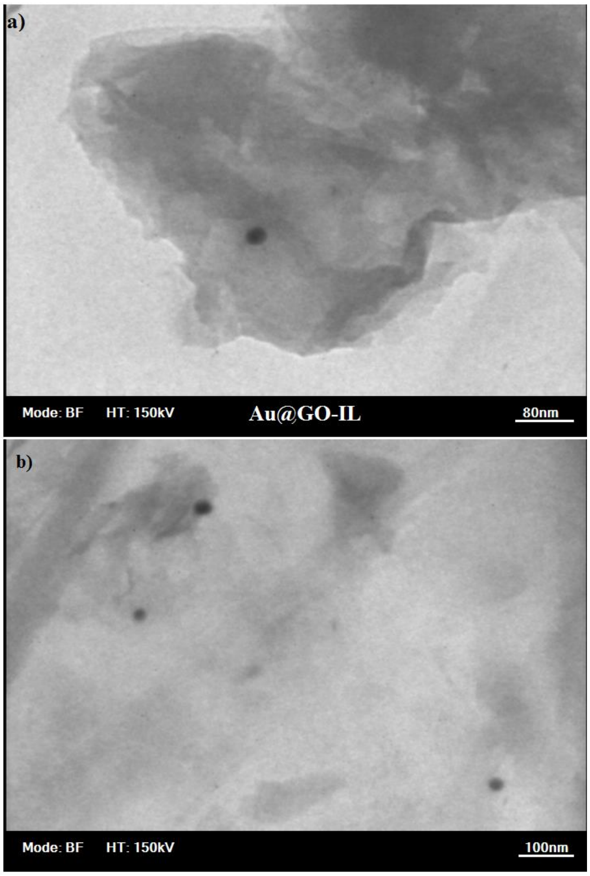


Fig. 3 TEM image of Au@GO-IL a) fresh and b) reused after five run.

The Au 4f core level region for the reused Au@GO-IL nanocomposite after three runs includes two components (Fig. 4). The first one is constituted by two doublets, situated at 82.83 and 88.14 eV, respectively, attributable to Au^0. The second component located at 86.39 and 90.96 eV is attributable to the Au^{3+}. By integrating the area in the XPS has been found the ratio of Au^0:Au^{3+} to be 5.7:4.3 (than this ratio for fresh nanocomposite 4:6) that indicated more reduction of Au^{3+} by GO.

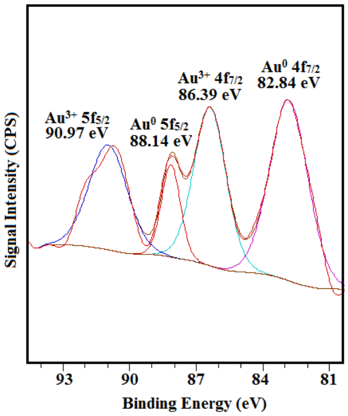


Fig. 4 XPS spectrum of the Au 4f core level region the reused Au@GO-IL nanocopmosite after three runs.

Conclusions

In conclusion, we have developed a novel domino, aerobic, oxidative A^3 -coupling reaction of benzyl alcohols by Au@GO-IL nanocomposite. This catalyst system shows excellent selectivity and good to excellent yields for a range of propargylamine through domino aerobic oxidation of benzyl alcohols followed by A^3-coupling using different combinations of secondary amines and terminal alkynes. Leaching tests such as hot filtration test and AAS analysis indicate that the catalytic reaction is mainly heterogeneous in nature. The reusability of this catalyst is high and the catalyst can be reused five times without significant decrease in its catalytic activity. Furthermore, the TEM image of the recovered catalyst showed the presence of well-distributed Au NPs on the GO-IL sheets without any aggregation.

Notes and references

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† Electronic Supplementary Information (ESI) available: [Experimental details for the preparation of catalyst, EDX mapping of Au@GO-IL, FT-IR spectra for GO, GO-IL and Au@GO-IL, XRD patterns of GO and Au@GO-IL, SEM image of Au@GO-IL, TEM images of GO and GO-IL, TGA plots of GO, GO-IL and Au@GO-IL and ^{1}H NMR for products]. See DOI: 10.1039/b000000x/

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