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An efficient reusable silver-exchanged tungstophosphoric acid heterogeneous catalyst for solvent-free intermolecular hydroamination of alkynes†

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Hydroamination of alkynes with both aromatic and aliphatic amines proceeds efficiently in the presence of silver-exchanged tungstophosphoric acid (AgTPA) catalyst under solvent-free conditions to afford ketimines in excellent yields.

In recent years the search for environmentally benign chemical processes or methodologies has received much attention from chemists, because they are essential for the conservation of global ecosystems. The development of heterogeneous catalysts for specialty chemical synthesis has become a major area of research, as the potential advantage of these materials (simplified recovery and reusability) over homogeneous systems can lead to environmentally benign chemical procedures for academia and industry.

The addition of ammonia or primary and secondary amines to alkenes and alkynes, known as hydroamination[1] is one of the most efficient approaches for the synthesis of higher substituted amines and their derivatives, which are important bulk and fine chemicals or building blocks in organic chemistry. A wide range of transition-metal based catalysts such as of zinc, cadmium[2] mercury, thallium,[3] zirconium,[4] titanium,[5] lanthanides,[6] ruthenium[7] and palladium[8] have been examined for catalytic hydroamination. However, for practical exploitation, the results are not satisfactory in terms of yield, catalytic efficiency and simplicity of procedure. Of late, several homogeneous catalysts have been studied for the intermolecular solvent-free hydroamination of alkynes. Eiichiro *et al.*[9] have examined successfully homogeneous Au(I)-catalyzed solvent-free hydroamination of alkynes. With the usage of Au(I) catalyst hydroamination proceeds smoothly in the presence of an acidic promoter. Coexistence of both metal and acidic promoter is mandatory in order to obtain the desired hydroamination product. The authors also concluded that among the various acidic promoters, heteropolyacids (HPAs) effectively promote intermolecular hydroamination of alkynes. Moreover the catalysts are ineffective for the hydroamination of alkynes with aliphatic amines under the specified conditions. Recently silver-catalyzed hydroamination of siloxyalkynes has been reported by Sun *et al.*[10] The authors studied the ability of a silver-based catalyst to promote a *syn*-selective hydroamination of electron-rich alkynes with either secondary amides or carbamates. All these homogeneous methods suffer from tedious workups and low recyclability of the catalyst. Thus development of novel and cheaper new heterogeneous catalytic systems remains an intriguing challenge.

Heterogeneous catalysts such as zeolites, metal-exchanged zeolites and clays have been examined for intermolecular hydroamination of alkynes. However their overall activity is not satisfactory, as they require more than 20 h of reaction time.[11]

In the present communication, we report an efficient and reusable silver metal exchanged tungstophosphoric acid‡ (AgTPA) heterogeneous catalyst for the solvent-free intermolecular hydroamination of various alkynes with both aliphatic and aromatic amines.§

The reactions between alkynes and amines using the present protocol are highly regioselective, only Markownikoff addition product is observed and there is no formation of anti-Markownikoff product. All the reactions with different substrates of alkynes and amines carried out under solvent-free conditions at 70 °C using AgTPA catalyst are shown in Table 1. The schematic hydroamination reaction is illustrated in Scheme 1.

The hydroamination of aniline with phenylacetylene using AgTPA gave *N*-(α-methylbenzylidene)aniline in 96% yield within 2 h reaction time (Table 1, entry 1). Anilines with strong electron-withdrawing groups such as 4-nitroaniline also give the corresponding hydroamination product with relatively high yields within the same reaction time (entry 5).

Table 1 AgTPA-catalyzed intermolecular hydroamination of alkynes with amines

Entry	R^1	R^2	R^3	Time/h	Yield of A (%)
1	Ph	H	Ph	2	95
2	Ph	H	2-ClC_6H_4	2	98
3	Ph	H	3-ClC_6H_4	2	98
4	Ph	H	4-FC_6H_4	2	99, 94[a]
5	Ph	H	4-$NO_2C_6H_4$	2	97
6	Ph	H	3-Cl-4-$NO_2C_6H_3$	2.5	93
7	Ph	H	2,3-$F_2C_6H_3$	2	97
8	Ph	H	C_8H_{17}	4	83
9	$C_{10}H_{18}$	H	4-FC_6H_4	2	96
10	$C_{10}H_{18}$	H	C_7H_{15}	4	79
11	$(CH_3)_2CH$	H	4-FC_6H_4	3	92
12	*n*-C_2H_5	*n*-C_2H_5	4-FC_6H_4	5	56,47[a]
13	*n*-C_3H_7	*n*-C_3H_7	4-FC_6H_4	5	52
14	Ph	H	Naphthyl	2	97
15	Ph	H	4-$CH_3C_6H_4$	2	96
16	Ph	H	4-$CH_3OC_6H_4$	2	95

[a] Yield obtained after fourth recycle. *Reaction conditions*: 1.0 mmol of alkyne, 1.2 mmol of amine, AgTPA: 50 mg, 70 °C. Yields were determined by ^1H NMR spectroscopy.

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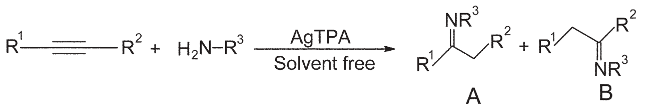


Scheme 1

Among the various substituted amines, 4-fluoroaniline reacted more smoothly with phenylacetylene in the presence of AgTPA catalyst and the reaction also proceeded with 2-fluoro- and 3-chloroaniline. This indicates that substituent groups present on the aromatic group of aniline react smoothly, irrespective of their nature or position, and the resulting corresponding hydroamination products are obtained in good yields (entries 2–4). Interestingly, sterically hindered disubstituted amines such as 2,3-difluoro- and 3-chloro-4-nitroaniline also gave their corresponding imines in high yields, inferring that groups around the $-NH_2$ group do not affect the reactivity of the amine (entries 6 and 7). Aromatic amines such as naphthylamine also react smoothly with alkyne affording high yields (entry 14).

Another observation that can be made here is that hydroamination of an aromatic alkyne with electron-donating aniline derivatives is as rapid as that of electron-withdrawing aniline derivatives (entries 15 and 16). The corresponding ketimine yields are similar to those of electron-withdrawing aniline derivatives.

The nature of substituents on the anilines had no significant effect on the hydroamination reaction. The aniline derivatives with electron-withdrawing groups at *ortho*, *meta* and *para* positions reacted smoothly to give their corresponding imines. The presence of electron-donating substituents on aniline also led to smooth reaction.

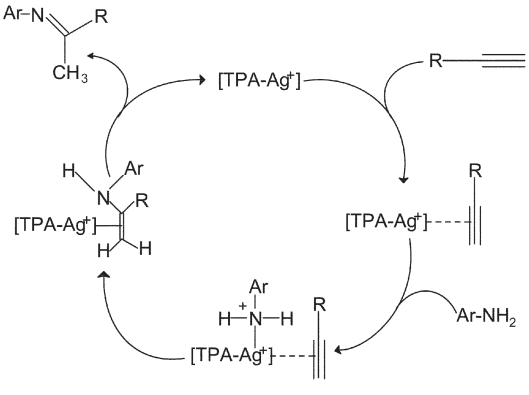
In addition, it is interesting to note that long-chain aliphatic terminal alkynes such as 1-decyne react smoothly, similarly to aromatic alkynes, with aromatic amine to obtain the corresponding ketimines with good yields (entry 9). 3-Methylbut-1-yne also reacts effectively with aromatic amine to yield the corresponding imine (entry 11).

Among the various catalysts reported so far for hydroamination, no catalyst was successful, despite tremendous effort made for the addition of aliphatic amines to alkynes.[9] It is noteworthy to mention here that by using AgTPA, aliphatic amines such as heptylamine and octylamine are successfully reacted with both aliphatic and aromatic alkynes smoothly affording high yields of the corresponding imine product (entries 8 and 10).

An interesting observation that can be made is that the hydroamination of internal alkynes such as 3-hexyne and 4-octyne affords relatively lower yields of the corresponding imine (entries 12 and 13). The lower yield is presumably due to the steric hindrance of the internal alkyne.

Separate experiments were performed using the Ag-free pure acid form of TPA and also without using any catalyst. The reaction did not proceed in the absence of catalyst and produced only very low yields (<10%) with TPA under the stated conditions.

The reusability of the catalyst was tested after recovering it by simple filtration and using for the hydroamination of phenylacetylene and 4-fluoroaniline (entry 4). The recycling experiments were also carried for the hydroamination of an internal alkyne (3-hexyne) and 4-fluoroaniline (entry 12). The same procedure was continued four times and no appreciable change in the catalyst activity was observed.



Scheme 2

The reactivity trend can be rationalized by the plausible mechanism illustrated in Scheme 2. The Ag(I) cationic species are envisaged to interact with an alkyne forming a cationic Ag(I)–alkyne complex. Then coordination of an amine to the Ag center occurs prior to the C–N bond formation.

In summary, it is demonstrated that an environmentally friendly, inexpensive and reusable AgTPA catalyst can be used efficiently for intermolecular hydroamination of both terminal and internal alkynes with either aromatic and aliphatic amines affording excellent yields of ketimines under solvent-free conditions in short reaction times.

Notes and references

‡ *Catalyst preparation*: AgTPA was prepared by adding an aqueous solution of silver nitrate to an aqueous solution of 12-tungstophosphoric acid. The excess water was removed on a water-bath and the resultant salt was dried in an oven at 120 °C for 12 h and finally calcined at 300 °C for 2 h in air. Retention of the HPA Keggin structure after modification with silver was confirmed by FT-IR and X-ray diffraction.

§ *Experimental procedure*: Synthesis of 4-fluoro-*N*-(α-methylbenzylidene) aniline. Under a nitrogen atmosphere, a mixture of phenyl acetylene (1 mmol), 4-fluoroaniline (1.2 mmol) and AgTPA (50 mg) was stirred at 70 °C for 2 h. The progress of the reaction was monitored by TLC and on completion, the mixture was cooled and hexane (10 mL) was added to precipitate the corresponding product. The product was recrystallized from hexane–dichloromethane to give 4-fluoro-*N*-(α-methylbenzylidene)aniline (99% yield).

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