Heterogeneous intermolecular hydroamination of terminal alkynes with aromatic amines

Ganapati V. Shanbhag, Suresh M. Kumbar, Trissa Joseph and Shivappa B. Halligudi*

*Inorganic Chemistry and Catalysis Division, National Chemical Laboratory, Pune 411008, India*

Abstract—Heterogeneous intermolecular hydroamination of alkynes with aromatic amines using inexpensive transition metal-exchanged clay catalysts was investigated. Reaction of terminal alkynes with aromatic amines gave higher yields of imines.
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The direct addition of N–H bonds of ammonia or amines to alkenes and alkynes (hydroamination reaction) offers a very attractive straightforward approach for the synthesis of substituted amines and their derivatives without any by-product formation.[1] One such class of compounds is aromatic imines, which are used in the preparation of nitrogen-containing compounds such as secondary,[2a,b] and tertiary amines,[2c] nitrogen heterocycles,[2d,e] carboxylic amides,[2f,g] β-enamino esters[2h] and amino alcohols.[2i] The classical method for imine synthesis is amination of aldehydes or ketones, but direct hydroamination of alkynes is 100% atom efficient and can be used in domino reactions, where water as a side product must be avoided.

Initially the catalytic intermolecular hydroamination of alkynes was carried out in the presence of Hg and Tl salts.[3] Later, alkali metals,[4a] metallocenes of Zr[4b] and complexes of lanthanides and actinides,[5] have been designed to promote these reactions. In recent studies moisture- and air-sensitive titanium complexes,[6] and more expensive metal complexes of Ru,[7] Rh,[8] Ir,[8c] Pd[9] and Au[10] have been the most widely used catalysts for hydroamination of alkynes.

However, homogeneous methods suffer from tedious work-ups and low recyclability of the catalyst. There are a few reports available on the use of heterogeneous catalysts for hydroamination of alkynes. Müller and co-workers have developed metal-exchanged zeolites for alkyne hydroamination, which favoured Markovnikov addition products (Scheme 1).[11] Also, Pd complexes immobilized on a silica support were reported for intramolecular cyclization of amino-alkynes.[12]
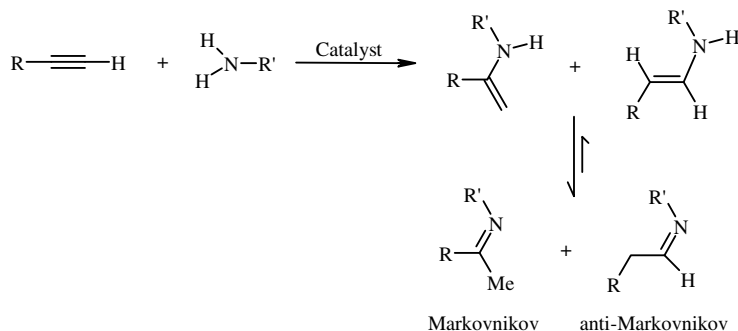
Scheme 1. Possible imine products from hydroamination of terminal alkynes.

Montmorillonite K-10 (hereafter K-10) is an acid-activated clay with an octahedral layer of alumina sandwiched between two tetrahedral silica layers.[13] The interlamellar space contains layer charge compensating cations like K^+, Na^+ and Ca^+, which can be exchanged easily with transition metal cations by a normal ion exchange method. In our earlier studies, we reported metal-exchanged clay for intermolecular hydroamination of phenylacetylene with aniline.[14] Therein, the effect of different substituents on aromatic amines and the efficiency of the catalyst for the hydroamination of different alkynes are discussed.

All catalysts were prepared by ion exchange of K-10 with aqueous metal acetate solutions under identical conditions.[15] Reactions were conducted in a round bottom flask with toluene as the solvent unless otherwise stated.[16] Among the different M^{2+} exchanged K-10 clays, Cu^{2+} gave the highest yields for the hydroamination of **1a** with *p*-toluidine (Table 1) and hence was used as the catalyst in further studies. The higher activity of Cu^{2+} and Zn^{2+} in hydroamination is due to their moderately hard Lewis acidity.[11c] The reaction proceeded with high regeoselectivity, only the Markovnikov addition product being observed in all cases.

To gain a greater insight into the scope and limitations of our method we examined the reactions of different alkynes with aniline (Table 2). Aromatic alkynes were more reactive than aliphatic alkynes[17] while terminal alkynes gave the highest yields. Internal alkynes (entries 4 and 6) did not undergo the reaction probably due to the steric hindrance by the bulky groups attached to the triple bond. The activated alkynes with electron-donating substituents, CH_3– and CH_3O– gave better yields (entries 7 and 8) whereas the alkyne with the electron-withdrawing NO_2 substituent was least reactive (entry 9).

The nature of the substituents on the anilines had a significant effect on the hydroamination reaction (Table 3). The aniline derivatives with electron-donating groups at the *ortho* and *para* positions reacted smoothly with **1a** (>90% yield) to give the corresponding imines. Interestingly, sterically demanding amines like 2,4,6-trimethylaniline and 2-isopropylaniline (entries 5 and 6), gave higher imine yields indicating that bulkier groups

Table 1. Intermolecular hydroamination of phenylacetylene with *p*-toluidine[a]

$$Ph{\equiv}H + p\text{-}CH_3C_6H_4NH_2 \xrightarrow[\text{toluene, 110 °C}]{\text{Catalyst}} \underset{Ph}{\overset{N{-}p\text{-}Tol}{\|}}$$

1a Markovnikov product

Entry	Catalyst	Yield (%)
1	Cu-K-10	64
2	Zn-K-10	52
3	Pd-K-10	8
4	Co-K-10	5
5	Ni-K-10	3
6	Mn-K-10	3
7[b]	H$^+$-K-10	2

[a] Conditions: Amine/alkyne 2:1, 4 ml toluene, 110 °C, 10 wt % catalyst, 4 h. All yields were determined by GC analysis and are referred to the alkyne. 100% selectivity for the Markovnikov product was observed in each case.
[b] Unexchanged clay.

Table 3. Hydroamination of phenylacetylene with aromatic amines[a]

$$Ph{\equiv}H + RNH_2 \xrightarrow[\text{toluene, 110 °C}]{\text{Cu-K-10}} \underset{Ph}{\overset{N{-}R}{\|}}$$

Markovnikov

Entry	R	Time (h)	Yield (%)
1	C_6H_5	10	93
		20	99
2	$2\text{-}CH_3C_6H_4$	10	84
		20	99
3	$4\text{-}CH_3C_6H_4$	20	98
4	$2,4\text{-}(CH_3)_2C_6H_3$	20	99
5	$2,4,6\text{-}(CH_3)_3C_6H_2$	20	95
		20[b]	91
6	$2\text{-}i\text{-}PrC_6H_4$	20	99
7	$4\text{-}i\text{-}PrC_6H_4$	20	99
8	$4\text{-}CH_3OC_6H_4$	20	95
9	$2\text{-}ClC_6H_4$	20	32
10	$4\text{-}BrC_6H_4$	20	68
11[c]	$4\text{-}O_2NC_6H_4$	48	NR
12[c]	$4\text{-}HOCC_6H_4$	48	NR
13	1-Naphthyl	20	88

[a] Conditions: Amine/alkyne 2:1, 4 ml toluene, 110 °C, 10 wt % catalyst, NR = no reaction. Yields were determined by GC analysis and are referred to the alkyne. Reaction conditions are not optimized. 100% selectivity for the Markovnikov product was observed in each case.
[b] Isolated yield.
[c] Solvent was 1,4-dioxane, reaction at 100 °C.

Table 2. Hydroamination of alkynes with aniline[a]

Entry	Alkynes	Temp (°C)	Time (h)	Yield (%)
1	1-Hexyne	80	20	5
2[b]	1-Hexyne	110	20	45
3[b]	1-Heptyne	110	20	55
4[b]	3-Hexyne	110	48	NR
5	Phenylacetylene	110	10	93
6	Diphenylacetylene	110	48	NR
7	4-Ethynyltoluene	110	10	87
8	4-Ethynylanisole	110	10	84
9	1-Ethynyl-2-nitrobenzene	110	20	32

[a] Conditions: Amine/alkyne 2:1, 4 ml toluene, 10 wt % catalyst. Yields were determined by GC analysis and are referred to the alkyne. Reaction conditions are not optimized, NR = no reaction, 100% selectivity for the Markovnikov product was observed in each case.
[b] Reaction was carried out in a Parr autoclave under N_2.

around the NH_2- group do not affect the reactivity of the amine. The amines with electron-withdrawing substituents, Cl– and Br– were less reactive (entries 9 and 10), whereas amines with stronger electron-withdrawing substituents, NO_2 and CHO, did not undergo the hydroamination reaction at all (entries 11 and 12). This reaction also took place smoothly with 1-naphthylamine (entry 13).

In conclusion, we have demonstrated that an environmentally friendly, inexpensive and reusable transition metal ion exchanged montmorillonite K-10 can be used efficiently for intermolecular hydroamination of terminal alkynes with aromatic amines.

Acknowledgements

References and notes

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15. Typical procedure for catalyst preparation: Montmorillonite K-10 (Aldrich) (10 g) was stirred in an aqueous solution of $Cu(CH_3CO_2)_2$ (0.05 mol dm^{-3}) at 80 °C for 12 h. The clay was separated by filtration and washed repeatedly with distilled water. To ensure complete ion exchange, the procedure was repeated followed by drying at 120 °C and calcination at 250 °C. The Cu^{2+} content in the clay was found to be 0.4 mmol/g (AAS).
16. Typical procedure for the M^{2+}-K-10 catalyzed hydroamination reaction: Synthesis of *N*-(1-phenylethylidene)-2,4,6-trimethylaniline (entry 5, Table 3): phenylacetylene (5.37 mmol, 0.55 g) and 2,4,6-trimethylaniline (10.73 mmol, 1.45 g) were added to a stirred mixture of Cu-K-10 (0.2 g) in toluene (4 mL). The reaction mixture was stirred at 110 °C for 20 h under a N_2 atmosphere in an oil bath. The mixture was then cooled and filtered to remove the catalyst and the solvent was removed by distillation. The mixture was dried in vacuo and purified by column chromatography on neutral alumina as the stationary phase (petroleum ether/ethyl acetate, 200/1). Yield: 91%, light brown oil: ^{1}H NMR (CDCl$_3$, 200 MHz): $\delta = 7.86$–8.01 (m, 2H), 7.31–7.48 (m, 3H), 6.80 (s, 2H), 2.21 (s, 3H), 1.99 (s, 3H), 1.92 (s, 6H). ^{13}C NMR (CDCl$_3$): $\delta = 165.57$ (C), 146.50 (C), 139.33 (C), 131.96 (C), 130.43 (CH), 128.56 (CH), 128.43 (CH), 127.12 (CH), 125.63 (C), 20.81 (CH$_3$), 17.96 (CH$_3$), 17.48 (CH$_3$). FT IR (neat, cm^{-1}): 3025, 2940, 1638, 1207, 1025, 856, 762, 629. GCMS *m/z* (relative intensity): 237 (64) [M$^+$], 222 (100), 207 (47), 103 (52), 91 (55), 77 (40).
17. The reactions involving aliphatic alkynes were carried out in a Parr autoclave under N_2.