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Simple and efficient Au^{I}-based catalyst for hydroamination of alkynes

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Hydroamination of terminal alkynes with anilines in the presence of $(C_6F_5)_3PAuNTf_2$ catalyst affords 2-aryliminoalkanes whose reduction *in situ* with sodium borohydride gives the corresponding secondary amines in high yields.

The establishment of an important fact that gold nanoparticles (AuNPs) possess unique properties which are quite different from those of bulk gold encouraged many researchers to investigate catalytic properties of nano-gold. The majority of works dealing with AuNPs study oxidation[1] and reduction processes,[2] making an emphasis on the molecular structure of the gold clusters.[3,4] There are some publications considering other reactions, usually catalyzed by the complexes of Pd, Pt, *etc*. Among such works a special place is occupied by the investigations dedicated to the C–N bond formation in the course of hydroamination of alkynes.[5] Other Au-catalyzed processes include the addition of HX to carbon–carbon multiple bonds,[6–8] however, hydroamination was found to be most problematic[9] but simultaneously one of the most important in the atom-economy synthesis. Such processes are attractive when the catalyst can be recycled, what depends not only on the size and structure of AuNPs but also on the support nature. The drawbacks of this approach include the unclear reaction mechanism and the possibility of its different interpretation when changing the reaction conditions and support nature.[10]

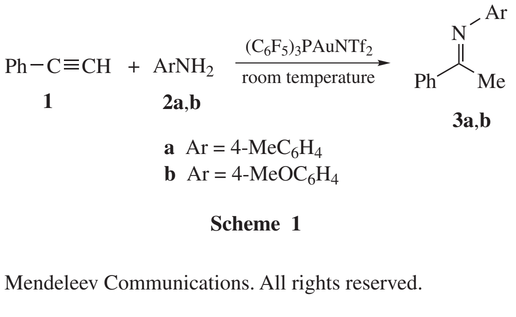
The attractiveness of gold as a catalyst evoked serious interest in Au^{I} and Au^{III} salts as Lewis acids. The first homogeneous intermolecular hydroamination of alkynes was carried out by Tanaka *et al.*[11] who used aromatic amines in the presence of $(Ph_3P)AuMe$ complex and acidic promoter like $H_3PW_{12}O_{40}$. High efficiency was manifested by Au complexes with N-heterocyclic carbenes[12–14] as well as $AuNTf_2$ complexes with triphenylphosphine and 2-(dicyclohexylphosphino)-2′,6′-dimethoxybiphenyl ligands.[15] In that study, 1-octyne was coupled with aliphatic amines and chiral α-phenylethylamine which are usually less active than aromatic ones. Supposing that the reaction proceeds due to the activation of the triple bond with $LAuNTf_2$, we have chosen the complex of Au^{I} with a weak donor ligand $(C_6F_5)_3P$. The complex was obtained from $HAuCl_4$ and $(C_6F_5)_3P$ *via* intermediate $(C_6F_5)_3PAuCl$ which was then subjected to the anion exchange with $AgNTf_2$.[16,17] The reaction conditions were optimized on coupling of phenylacetylene **1** with *p*-toluidine **2a** and 4-methoxyaniline **2b** (Scheme 1, Table 1).

Reactions were run at ambient temperature using 20% excess of alkyne. The reaction with **2a** in the presence of 2.5 mol% catalyst in CH_2Cl_2 provided 84% yield of the corresponding ketimine **3a** (entry 1), while on application of 1 mol% catalyst under neat conditions this product was obtained in 88% yield (entry 2). The reaction of a more donor *p*-methoxyaniline **2b** resulted in 80% yield of **3b** (entry 3). Note that we succeeded to use fivefold lower quantity of catalyst at room temperature than described in literature.[15]

Table 1 Optimization of the Au^{I}-catalyzed hydroamination conditions.

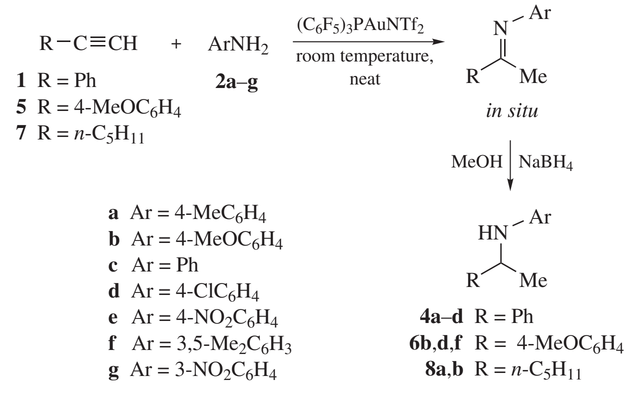
Entry	Amine	Catalyst (mol%)	Solvent	Imine	Yield^a (%)
1	**2a**	2.5	CH_2Cl_2	**3a**	84
2	**2a**	1	neat	**3a**	88
3	**2b**	1	neat	**3b**	80

^{a}Yields after chromatographic isolation.



Scheme 1

As ketimines may always contain admixtures of the relative ketones due to easy hydrolysis, further we reduced them *in situ* with $NaBH_4$ (Scheme 2, Table 2).† Intermediate imines were synthesized under the optimized conditions, and the yields of the secondary amines **4a**,**b** were high enough (entries 1, 2). The highest yield (98%) was achieved with the simplest aniline **3c**



Scheme 2

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† *Catalytic hydroamination of alkynes (general procedure).* Alkyne **1**, **5** or **7** (1.2 mmol), aniline derivative **2a**–**g** (1 mmol) and $(C_6F_5)_3PAuNTf_2$ catalyst (10 mg, 1 mol%) were placed into a vial and stirred at ambient temperature for *ca.* 24 h until the reaction was complete (TLC control). The mixture was diluted with 3 ml MeOH, followed by addition of $NaBH_4$ (2 mmol, 76 mg) and stirring for 3 h (TLC control). The mixture was diluted with CH_2Cl_2 (15 ml), washed with water (15 ml) and saturated NaCl aqueous solution (15 ml). The organic layer was separated, dried over anhydrous Na_2SO_4, evaporated *in vacuo* and the residue was chromatographed on silica gel using 3–5% EtOAc in light petroleum. ^1H and ^{13}C NMR spectroscopic data of compounds **3a**,[15] **3b**,[18] **4a–c**,[19] **4d**,[20] **6b**,[21] **6d**,[22] **6f**,[23] **8a**,[24] **8b**[25] are consistent with those described in the literature.

Table 2 Synthesis of secondary amines *via* Au^I-catalyzed hydroamination.

Entry	Alkyne	Amine	Product	Yield[a] (%)
1	**1**	**2a**	**4a**	78
2	**1**	**2b**	**4b**	81
3	**1**	**2c**	**4c**	98
4	**1**	**2d**	**4d**	88
5	**1**	**2e**	No reaction	—
6	**5**	**2b**	**6b**	82
7	**5**	**2d**	**6d**	70
8	**5**	**2f**	**6f**	75
9	**5**	**2g**	No reaction	—
10	**7**	**2a**	**8a**	61
11	**7**	**2b**	**8b**	56

[a] Yields after chromatographic isolation.

(entry 3), the use of a weak electron-withdrawing *p*-chloroaniline **2d** also resulted in a high yield of product **4d** (88%, entry 4). However, in the case of stronger electron-withdrawing nitro-substituted reactant the reaction was completely cancelled (entry 5). The presence of electron-donating methoxy group in alkyne **5** did not decrease its reactivity and amines **6b**,**d**,**f** were isolated in 70–82% yields (entries 6–8). 3-Nitroaniline was essentially unreactive (entry 9). Aliphatic 1-heptyne **7** gave amines **8a**,**b** in lower yields, what is in good agreement with published data.[15]

The catalyst can be easily separated from product **4c** by adding hexane and can be used at least three times without substantial loss in activity.

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