$(PPh_3)AuCl/AgOTf$-Catalyzed Intermolecular Hydroamination of Alkynes with Sulfonamides To Form *N*-Sulfonyl Imines

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Abstract: In the presence of a catalytic amount of $(PPh_3)AuCl$ and AgOTf, intermolecular hydroamination of unactivated alkynes with sulfonamides has been shown to proceed and give *N*-sulfonyl ketimines in medium to excellent yields.

Key words: hydroamination, *N*-sulfonyl ketimines, sulfonamide, alkyne, gold catalysis

N-Sulfonyl imines are useful building blocks in organic and medicinal chemistry.[1] The most common method reported in the literature for synthesis of these compounds involves the condensation of carbonyl compounds with sulfonamides.[2] Syntheses of *N*-sulfonyl imines have also been reported using other approaches, including the condensation of oximes with sulfinyl chlorides[3] or sulfonyl cyanides,[4] isomerization of aziridines,[5] reaction of the carbonyl compounds with sulfinamides and following oxidation.[6] Despite these advantages, several drawbacks remain associated with such reactions, including the use of harsh acids and generating toxic byproducts in a multistep process. Thus, development of new methods for their synthesis is still needed.

Gold salts are powerful soft Lewis acids and readily promote reaction of unsaturated C–C bonds with a variety of nucleophiles for the formation of carbon–carbon and carbon–heteroatom bonds.[7,8] In the literature, a wide range of metal-catalyzed inter- and intramolecular hydroamination of alkynes are known, but the intermolecular hydroamination of alkynes with sulfonamides has not been reported previously.[9–16] On the basis of some recent studies,[17] herein we describe an efficient gold-catalyzed intermolecular hydroamination of unactivated alkynes with sulfonamides to afford *N*-sulfonyl imines.

The reaction of 4-methoxyphenylacetylene (**1a**, 1.5 mmol) with 4-methylbenzenesufonamide (**2a**, 0.5 mmol) in the presence of 2 mol% of $(PPh_3)AuCl$ and 8 mol% of AgOTf in toluene at 100 °C proceeded efficiently to form **3a** in 97% yield with perfect regioselectivity (Table 1, entry 1). Efficient hydroamination was realized with significantly lower catalyst loading (entry 2). Investigation of molar ratio of the starting materials revealed that an excess of alkynes (2–3 equiv) was necessary to drive the alkynes to full conversion (entry 3). Decreasing the amount of AgOTf resulted in lower yields (entries 4 and 5). Using either gold or silver precatalyst alone gave lower yields (entries 6 and 7). These results indicated that both Au source and AgOTf played a crucial role in this hydroamination. The superior efficiency of trifluoromethanesulfonate anion through a comparison with other weakly or noncoordinating counteranion was demonstrated. While methanesulfonate and tetrafluoroborate as counteranions were ineffective, change of counteranion to hexafluroantimonate led to 73% yield of **3a** (entries 8–10). Only trace of **3a** was formed by using $Cu(OTf)_2$ which was a robust catalyst in intramolecular hydroamination of alkynylsulfonamides (entry 11).[11b] Other metal catalysts such as $(PPh_3)_2NiCl_2$, $(PPh_3)_2PdCl_2$, and $(cod)PtCl_2$ were ineffective (entries 12–14). Different solvents were screened and toluene was found to be the most suitable one. Other solvents, such as chloroform, THF, and dioxane were compatible to the hydroamination. In all case, 1-(4-methoxyphenyl)ethanone as the hydration product could be detected due to water present in small amounts in the reaction solution. In addition, the reaction of 1-(4-methoxyphenyl)ethanone, instead of **1a**, with **2a** did not proceed at all under the same conditions.

To further assess the scope of this process, we have examined the hydroamination of different alkynes with sulfonamides using the optimized reaction conditions as described in entry 1 of Table 1. The results are summarized in Table 2. Alkynes with an electron-donating group on the benzene ring all gave higher the yields (entries 1–4). In sharp contrast, with an electron-withdrawing substituent on the aromatic ring, the corresponding adduct **3g** was obtained in 40% yield (entry 6). Various aryl sulfonamides were then examined, not only electron-donating but also electron-withdrawing groups on benzene ring of phenylsulfonamide gave excellent yields (entries 1 and 7–10). Under the same reaction conditions, hydroamination of aliphatic sulfonamides took place smoothly to afford the corresponding *N*-sulfonyl ketimine **3l** with 72% yield (entry 11). In addition, *p*-$TolSO_2NHNH_2$ was also an efficient substrate for hydroamination (entry 12). Furthermore, in striking contrast to aromatic alkynes, aliphatic alkynes, such as 1-octyne and internal alkynes, such as diphenylacetylene, failed to undergo Au-catalyzed hydroamination under the same conditions.

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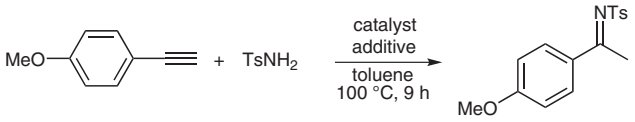
Table 1 Hydroamination of **1a** with **2a**[a]



1a **2a** **3a**

Entry	Cat. (mol%)	Additive (mol%)	Yield of **3a** (%)[b]
1	$(PPh_3)AuCl$ (2)	AgOTf (8)	97
2	$(PPh_3)AuCl$ (1)	AgOTf (8)	96
3[c]	$(PPh_3)AuCl$ (2)	AgOTf (8)	88
4	$(PPh_3)AuCl$ (2)	AgOTf (6)	66
5	$(PPh_3)AuCl$ (2)	AgOTf (4)	50
6	$(PPh_3)AuCl$ (2)	–	10
7	–	AgOTf (8)	35
8	$(PPh_3)AuCl$ (2)	AgOMs (8)	11
9	$(PPh_3)AuCl$ (2)	$AgBF_4$ (8)	trace
10	$(PPh_3)AuCl$ (2)	$AgSbF_6$ (8)	73
11	$Cu(OTf)_2$ (2)	–	trace
12	$(PPh_3)_2NiCl_2$ (2)	–	0
13	$(PPh_3)_2PdCl_2$ (2)	–	0
14	$(cod)PtCl_2$ (2)	–	0
15[d]	$(PPh_3)AuCl$ (2)	AgOTf (8)	78
16[d]	$(PPh_3)AuCl$ (2)	TfOH (8)	0
17[d]	–	TfOH (8)	0

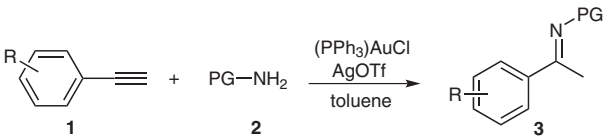
[a] Conditions: **1a** (1.5 mmol), **2a** (0.5 mmol), cat. (0–2 mol%), silver salt (0–8 mol%), toluene (2 mL), 100 °C, 9 h.
[b] Isolated yields.
[c] Using 1.0 mmol of **2a**.
[d] At r.t.

On the basis of the experiments and precedent reports,[8g,18] a plausible mechanism is shown in Scheme 1. We proposed that $(PPh_3)Au^+$, generated in situ from $(PPh_3)AuCl$ and Ag^+, coordinated to the alkyne to form a cationic M(I)–alkyne complex. Then the complex underwent an intermolecular nucleophilic attack by sulfonamide to finish the reaction.

In conclusion, we have demonstrated an efficient $(PPh_3)AuCl$/AgOTf-catalyzed intermolecular hydroamination of unactivated alkynes with sulfonamides to produce *N*-sulfonyl ketimines under mild conditions with perfect regioselectivity.[19] Further efforts to expand the scope of the chemistry and studies of the detailed mechanism are currently under way in our laboratories.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

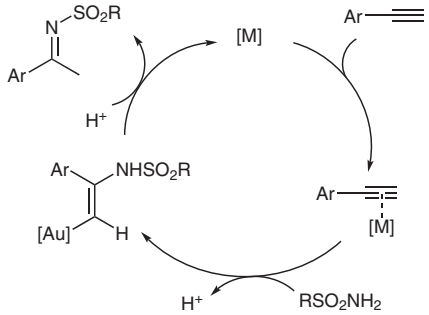
Table 2 Reaction Scope for the Hydroamination of Alkynes with Sulfonamides[a]



1 **2** **3**

Entry	PG	R	Product	Yield (%)[b]
1	4-$TolSO_2$	4-EtO	**3b**	99
2[c]	4-$TolSO_2$	4-n-C_5H_{11}	**3c**	77
3[c]	4-$TolSO_2$	4-n-Bu	**3d**	80
4[c]	4-$TolSO_2$	4-Et	**3e**	78
5[c]	4-$TolSO_2$	H	**3f**	91
6[c]	4-$TolSO_2$	3-F	**3g**	40
7	2-$TolSO_2$	4-EtO	**3h**	98
8	$PhSO_2$	4-MeO	**3i**	91
9	4-$BrPhSO_2$	4-MeO	**3j**	96
10	4-$IPhSO_2$	4-MeO	**3k**	99
11[c]	$MeSO_2$	4-MeO	**3l**	72
12[c]	4-$TolSO_2NH$	4-EtO	**3m**	63

[a] Reaction conditions: **1** (1.5 mmol), **2** (0.5 mmol), $(PPh_3)AuCl$ (0.01 mmol), AgOTf (0.04 mmol), toluene (2 mL), 100 °C, 9 h.
[b] Isolated yields.
[c] Using 2 mL of THF as solvent.



Scheme 1 Proposed mechanism for hydroamination

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(19) **Typical Experimental Procedure**
To a reactor containing sulfonamide (0.5 mmol), $(PPh_3)AuCl$ (0.01 mmol), AgOTf (0.04 mmol), and anhyd toluene (2 mL), was added alkyne (1.5 mmol). The mixture was then sealed and stirred at 100 °C. After 9 h, it was quenched with sat. soln of $NaHCO_3$ and then with EtOAc (3 × 10 mL), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash chromatography to give the pure product.

***N*-[1-(4-Ethoxyphenyl)ethylidene]-4-methylbenzenesulfonamide (3b)**
Yellow solid; mp 103–105 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.92–7.88 (m, 4 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 6.86 (d, *J* = 9.0 Hz, 2 H), 4.06 (q, *J* = 7.0 Hz, 2 H), 2.92 (s, 3 H), 2.43 (s, 3 H), 1.41 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.7, 163.4, 143.3, 139.1, 130.7, 129.7, 129.4, 127.0, 114.3, 63.9, 21.6, 20.7, 14.6. IR (KBr): 2980, 2936, 2884, 1607, 1578, 1557, 1385, 1173, 1150 cm^{-1}. HRMS (CI): *m/z* calcd for $C_{17}H_{19}NO_3S$ $[M + H]^+$: 318.1164; found: 318.1164.

***N*-[1-(4-Methoxyphenyl)ethylidene]methanesulfonamide (3l)**
Pale yellow solid; mp 107–108 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 9.0 Hz, 2 H), 6.93 (d, *J* = 9.0 Hz, 2 H), 3.88 (s, 3 H), 3.22 (s, 3 H), 2.86 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.9, 163.9, 130.5, 129.6, 114.0, 55.6, 43.2, 20.8. IR (KBr): 3032, 2937, 1635, 1609, 1595, 1384, 1182, 1143 cm^{-1}. HRMS (EI): *m/z* calcd for $C_{10}H_{13}NO_3S$ $[M]^+$: 227.0616; found: 227.0612.