Gold-catalyzed addition of sulfonic acids to alkynes to form vinyl sulfonates†

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In the presence of a catalytic amount of $(Ph_3P)AuNO_3$ and phthalimide, the addition of toluenesulfonic acid or methanesulfonic acid to alkynes has been shown to proceed and gives vinyl tosylates and vinyl mesylates in good yields and regioselectivity.

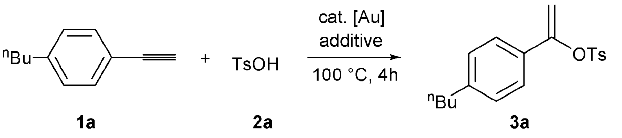
During the past ten years, several research groups have developed gold-catalyzed homogeneous catalytic reactions.[1] A variety of organic transformations have been shown to be mediated by gold(I) or gold(III) complexes in solution.[2] In addition to its ability to activate alkynes and related substrates, the catalysis of nucleophilic addition by gold complexes for the formation of carbon–carbon and carbon–heteroatom bonds has been one of the most investigated reactions in modern organometallic catalysis.[3] Various nucleophilic reagents, such as water,[4] alcohols,[1g] amines,[5] acetic acid[4e] *etc*., have been used in the intermolecular addition to alkynes. As part of our ongoing studies on metal-catalyzed atom-economical reactions, we have been interested in the use of gold for simple and highly efficient transformations.[6] On the other hand, vinyl sulfonates are important building blocks in organic synthesis, especially as electrophiles for cross-coupling chemistry.[7] Further, vinyl tosylates and vinyl mesylates are more convenient to use because they are more stable to water than triflates. Surprisingly few vinyl tosylates and vinyl mesylates have been documented in the literature, and the majority of methods for their synthesis are the sulfonylation of the ketone with sulfonic anhydride by base.[7d,8] In contrast to the sometimes-difficult synthesis and protection of carbonyls, alkynes are known to be synthetically robust, and the synthesis of substituted alkynes can be quite simple. Hirsch and co-workers reported the addition of methanesulfonic acid to *tert*-butylacetylene catalyzed by HgO, but only with one example.[9] In this paper, we wish to develop a gold(I) complex catalyzed addition of sulfonic acids to alkynes to synthesize vinyl tosylates and vinyl mesylates.

The reaction of 4-butylphenylacetylene (**1a**) (1.0 mmol) with toluenesulfonic acid (**2a**) (0.5 mmol) in the presence of a catalytic amount of $(Ph_3P)AuNO_3$ (2 mol%) and phthalimide (PhthNH) (4 mol%) in dichloroethane (2 mL) at 100 °C proceeded efficiently to form the Markovnikov adduct **3a** in 74% isolated yield with perfect regioselectivity (Table 1, entry 3). Other possible isomers could be hardly detected. Decreasing the amount or the absence of PhthNH resulted in lower yield, and the addition of a large amount of PhthNH did not affect the reaction (Table 1, entries 1, 2, 4 and 5).

Different solvents were screened, and dichloroethane was found to be the most suitable one (Table 1, entries 6–8). The superior efficiency of the weakly coordinating anion nitrate was demonstrated through a comparison with other weakly or non-coordinating anions trifluoromethanesulfonate, tetrafluoroborate, and hexafluoroantimonate under the same conditions. While treatment of **1a** and **2a** with $(Ph_3P)AuCl$ and $AgBF_4$ resulted in only trace formation of **3a**, use of $(Ph_3P)AuCl$ and $AgSbF_6$ produced **3a** in lower yields, $(Ph_3P)AuCl$ and AgOTf provided no catalytic activity (Table 1, entries 11–14). The reaction did not proceed in the absence of the Au catalyst (Table 1, entries 9 and 10). In all case, 1-(4-butylphenyl)ethanone as the hydration product could be detected due to water that was present in small amounts in the reaction solution. In addition, the reaction of 1-(4-butylphenyl)ethanone, instead of **1a**, with **2a** did not proceed at all under the same conditions.

In order to assess the scope of this process, we have examined the addition to several alkynes with aliphatic and aromatic sulfonic acids under the optimized conditions

Table 1 Au-catalyzed addition of toluenesulfonic acid (**2a**) to *p*-butylphenylacetylene (**1a**) to form **3a**[a]



Entry	2 mol% [Au]	Additive (mol%)	Solvent	Yield (%)[b]
1	$(Ph_3P)AuNO_3$	PhthNH (100)	$Cl(CH_2)_2Cl$	72
2	$(Ph_3P)AuNO_3$	PhthNH (50)	$Cl(CH_2)_2Cl$	74
3	$(Ph_3P)AuNO_3$	PhthNH (4)	$Cl(CH_2)_2Cl$	74
4	$(Ph_3P)AuNO_3$	PhthNH (2)	$Cl(CH_2)_2Cl$	59
5	$(Ph_3P)AuNO_3$	—	$Cl(CH_2)_2Cl$	58
6	$(Ph_3P)AuNO_3$	PhthNH (4)	Toluene	57
7	$(Ph_3P)AuNO_3$	PhthNH (4)	Dioxane	16
8	$(Ph_3P)AuNO_3$	PhthNH (4)	Chlorobenzene	0
9	—	PhthNH (4)	Toluene	0
10	—	—	$Cl(CH_2)_2Cl$	0
11	$(Ph_3P)AuCl$	$AgBF_4$ (4)	Toluene	Trace
12	$(Ph_3P)AuCl$	$AgSbF_6$ (4)	Toluene	24
13	$(Ph_3P)AuCl$	$AgSbF_6$ (4)	$Cl(CH_2)_2Cl$	40
14	$(Ph_3P)AuCl$	AgOTf (4)	Toluene	0

[a] The reactions were performed with 0.5 mmol of toluenesulfonic acid, 1.0 mmol of 4-butylphenylacetylene, [Au], and additive in 2 mL of solvent at 100 °C for 4 h. [b] Isolated yield.

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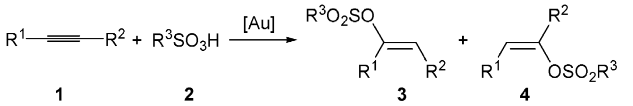
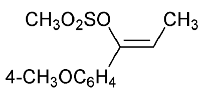
indicated in entry 3 of Table 1. The results are summarized in Table 2. Regarding the sulfonic acids, methanesulfonic acid was also converted into the expected addition products, the regioselectivity was higher under the same conditions (Table 2, entries 1–10). To further look at possible electronic effects and to expand the scope of this method, acetylenes bearing aromatic groups of various electron densities were also studied. Alkynes with an electron-donating alkyl group on the benzene ring with either methanesulfonic acid or toluenesulfonic acid all gave good isolated yields of the corresponding vinyl sulfonates with high regioselectivity (Table 2, entries 2–3, 12–13). With a more electron-donating alkoxy group, the expected adducts were obtained in excellent yields and regioselectivity (Table 2, entries 5 and 6). In sharp contrast, as an electron-withdrawing group, the *meta*-fluoro-substituted alkyne yielded the anti-Markovnikov adduct **4h** as the main product (Table 2, entry 7). Under the same reaction conditions, the addition to an alkyl alkyne with sulfonic acids also took place smoothly and showed similar reactivity and selectivity to the aryl alkynes (Table 2, entries 8 and 12). Furthermore, internal alkynes also worked well. Diphenylacetylene reacted with sulfonic acids to afford *cis*-adducts **3j** and **3p** with high selectivity (Table 2, entries 9 and 15). For the unsymmetrical internal alkyne, two adducts **3k1** and **3k2** were obtained in 82% yield with high regioselectivity (Table 2, entry 10). Single crystals of the compound **3p** suitable for X-ray crystallographic analysis were also obtained (Fig. 1). It shows that **3p** is the *E* isomer, the ester oxy link being *trans* to one of the phenyl groups (Fig. 1).

Table 2 Au-catalyzed addition of sulfonic acids to alkynes[a]

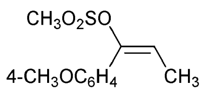


Entry	R^1	R^2	R^3	Yield of product (%)[b]
1	C_6H_5	H	CH_3	60 (**3b** : **4b** = 93 : 7)
2	4-$C_2H_5C_6H_4$	H	CH_3	82 (**3c** : **4c** = 100 : 0)
3	4-$^nC_4H_9C_6H_4$	H	CH_3	80 (**3d** : **4d** = 94 : 6)
4	4-$^nC_5H_{11}C_6H_4$	H	CH_3	78 (**3e** : **4e** = >99 : 1)
5	4-$CH_3OC_6H_4$	H	CH_3	95 (**3f** : **4f** = 100 : 0)
6	4-$C_2H_5OC_6H_4$	H	CH_3	94 (**3g** : **4g** = 100 : 0)
7	3-FC_6H_4	H	CH_3	60 (**3h** : **4h** = 7 : 93)
8	$^nC_8H_{17}$	H	CH_3	74 (**3i** : **4i** = 90 : 10)
9	C_6H_5	C_6H_5	CH_3	73 (**3j** : **4j** = 100 : 0)
10	4-$CH_3OC_6H_4$	CH_3	CH_3	82 (**3k** : **4k** = 100 : 0)[c]
11	C_6H_5	H	4-Tol	60 (**3l** : **4l** = 84 : 16)
12	$^nC_8H_{17}$	H	4-Tol	62 (**3m** : **4m** = 100 : 0)
13	4-$C_2H_5C_6H_4$	H	4-Tol	76 (**3n** : **4n** = 100 : 0)
14	4-$^nC_5H_{11}C_6H_4$	H	4-Tol	75 (**3o** : **4o** = 100 : 0)
15	C_6H_5	C_6H_5	4-Tol	50 (**3p** : **4p** = 100 : 0)

[a] Reaction conditions: alkyne (1.0 mmol), sulfonic acid (0.5 mmol), $(Ph_3P)AuNO_3$ (2 mol% based on sulfonic acid), phthalimide (4 mol% based on sulfonic acid) in $Cl(CH_2)_2Cl$ (2 mL) at 100 °C for 4 h. [b] Isolated yield; ratio was determined by ^1H NMR spectroscopy. [c] Ratio of **3k** (**3k1** and **3k2**) was 53 : 47.



3k1



3k2

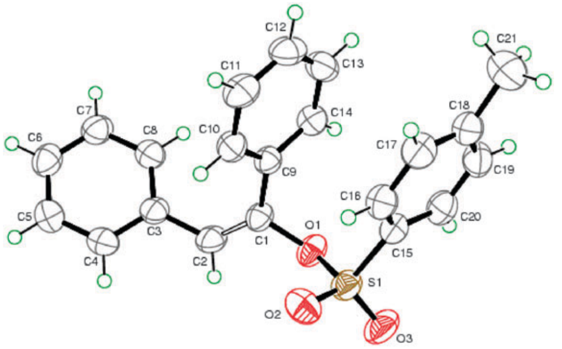
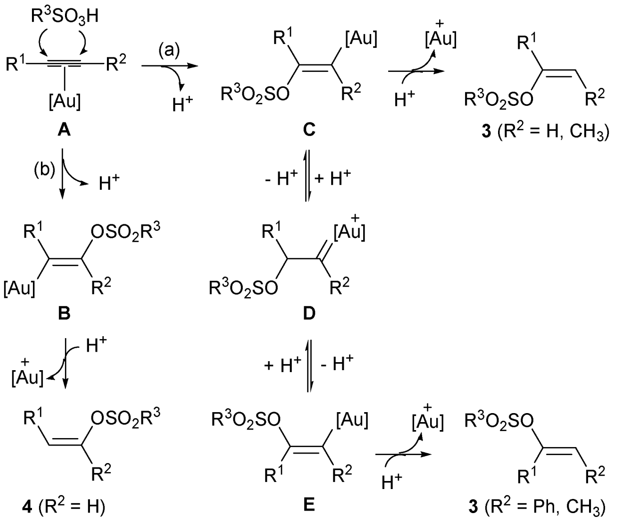


Fig. 1 X-Ray structure of **3p** (30% thermal ellipsoid).

The proposed catalytic cycle, which involves the *anti*-addition of gold and the sulfonic acid to mono- and disubstituted alkynes, is shown in Scheme 1. The gold cation coordinates to the alkyne to form an Au–π-alkyne complex **A**. The sulfonic acid as the nucleophile attacks the gold cation-coordinated C≡C bond to form a vinylgold species **B** or **C**. Then, the organogold intermediate **B** or **C** liberates the adduct **3** or **4** and the gold catalyst by protodemetallation. Regioselectivity is determined by electronic factors; attack of the sulfonic acid takes place at the electro-deficient alkynyl moiety, though almost all nucleophilic additions follow Markovnikov's rule.[10] Isomerization from the *Z*-isomer of **3** to the *E*-isomer of **3** can be envisaged through the protonation–deprotonation of intermediate **C** *via* the cationic gold carbene **D**. In comparison to forming **3k** as a mixture of *E* and *Z* isomers, for R^2 = Ph, **3j** and **3p** were produced with an exclusive *E* selectivity; perhaps due to steric hindrance, complete equilibration to the more favored intermediate **E** leads to the formation of a single isomer. On the other hand, although the source of the catalytic activity of PhthNH as an additive is unclear, a possible role for PhthNH is to stabilize the gold fragment forming $(Ph_3P)AuNPhth$. Furthermore, using 2 mol% of $(Ph_3P)AuNPhth$ synthesized[11] as the catalyst, addition of **2a** to **1a** could proceed to give **3a** in 52% yield under the same



Scheme 1 Proposed mechanism for the addition of sulfonic acids to alkynes.

conditions; this supports the feasibility of coordination of PhthNH to gold(I).

In summary, we have developed a new process of ionic gold-catalyzed addition of sulfonic acids to alkynes to provide vinyl sulfonates. This reaction takes place under mild conditions with effective and high regio- and stereoselectivity; the adducts are synthetically important as substrates for metal-catalyzed cross-coupling reactions. Detailed mechanistic studies and scope expansion work are currently underway in our laboratory.

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