Silver-Catalyzed Intermolecular Hydroamination of Alkenes and 1,3-Dienes

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Abstract: Silver triflate is used as efficient catalyst for the intermolecular addition of 4-toluenesulfonamide to alkenes under thermal or microwave heating. The hydroamination of 1,3-dienes can be performed at 85 °C with low catalyst loading (0.1–5 mol%) or at room temperature using 1 mol% of AgOTf, the use of HOTf affording similar results.

Key words: alkenes, conjugated dienes, hydroamination, sulfonamides, silver catalysts

Inter- and intramolecular hydroamination reactions of alkenes, allenes, and alkynes have been extensively used for the synthesis of acyclic and heterocyclic amines, respectively.¹ Alkenes showed a much lower reactivity specially in the case of intermolecular hydroamination processes. Recent advances in this field showed that Brønsted² and Lewis³ acids, mainly metal complexes, have been employed to promote this reaction. Electrophilic gold(I) complexes have shown high efficiency for the intermolecular hydroamination of alkenes and 1,3dienes with carbamates and sulfonamides.⁴ The active catalyst is prepared in situ by reaction of phosphanes or phosphites, gold(I) chloride complexes and a silver salt, mainly AgOTf, in order to generate cationic gold(I) complexes. Intramolecular hydroamination of alkynes from in situ generated imines to give pyrroles,⁵ oximes to give isoquinolinones,⁶ and from primary amines affording pyrrolines⁷ have been performed using silver salts. However, the electrophilic AgOTf has not been used as catalyst in the hydroamination of alkenes. The attempting addition of benzyl carbamate to dienes such as 3-methyl-1,3-pentadiene failed.^{4b} In spite of this unsuccessful precedents, and related to our studies on gold(I)-catalyzed hydroamination reactions of alkenes and 1,3-dienes, we carried out control experiments to study if silver salts can be used as catalysts. Herein, we report the first silvercatalyzed hydroamination of alkenes and 1,3-dienes with sulfonamides.

Hydroamination of norbornene (1a) with 4-toluenesulfonamide was performed in toluene at 90 °C under microwave heating during 15 minutes using 1 mol% loading of different silver salts (Table 1). No reaction was observed when silver chloride, nitrate, acetate, and fluoride were used as catalysts (Table 1, entries 1–4). Silver tetrafluoroborate and perclorate gave product **2a** in only 5% and 22% yield, respectively (Table 1, entries 5 and 6). However, silver triflate and hexafluoroantimoniate behave similarly giving rise to high yields (Table 1, entries 7 and 8). Silver triflate afforded higher yield (82%) than hexafluoroantimoniate (62%) when lowering the catalyst loading to 0.05 mol% (Table 1, entries 9 and 10). Under the same conditions, the use of triflic acid (0.05 mol%) gave only 18% yield in this hydroamination. In the presence of triphenylphosphane and silver triflate (1 mol%) the reaction failed (Table 1, entry 11). On the other hand, a 88% yield was obtained by using triphenylphosphite as additive (Table 1, entry 12).

 Table 1
 Hydroamination of Norbornene with 4-Toluenesulfonamide^a

	+ TsNH ₂ HMe, 90 °C (MW)	NHTs			
1a	30 min	2a			
Entry	Cat. (mol%)	Yield (%) ^b			
1	AgCl (1)	0			
2	$\operatorname{AgNO}_{3}(1)$	0			
3	AgOAc (1)	0			
4	AgF (1)	0			
5	$AgBF_4(1)$	5			
6	$AgClO_4(1)$	22			
7	AgOTf (1)	98			
8	$AgSbF_{6}(1)$	99			
9	AgOTf (0.05)	82			
10	$AgSbF_{6}(0.05)$	62			
11	Ph ₃ P (1)/AgOTf (1)	0			
12	[(PhO) ₃ P](1)/AgOTf (1)	88			

^a Reactions were performed with TsNH₂ (171 mg, 1 mmol), norbornene (376 mg, 4 mmol), AgX (see column) in dry toluene (2 mL) under Ar in a microwave reactor (70 W, 0.69 bar) with air stream cooling.

^b Isolated crude yield determined by GLC, based on TsNH₂.

Different alkenes and 1,3-dienes were hydroaminated with 4-toluenesulfonamide and AgOTf as catalyst and were compared with HOTf (Table 2).⁸ Norbornene af-

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forded product 2a in 96% yield under conventional heating at 85 °C during 4 hours using 0.5 mol% of AgOTf (Table 2, entry 1). Alternatively, this hydroamination can be performed at room temperature using CH₂Cl₂ as solvent and 5 mol% of AgOTf affording 2a in 97% yield (Table 2, entry 2). This process has been also described using 1 mol% of HOTf in 1,2-dichloroethane, yielding 2a in 91% yield (Table 2, entry 3).^{2d} In the case of cyclohexene (1b) the addition took place in toluene at 85 °C in low yield (38%) using 2 mol% of AgOTf (Table 2, entry 4), whereas a higher 58% yield has been obtained using 1 mol% HOTf^{2d} (Table 2, entry 5). However, when this reaction was performed using solvent-free conditions at 90 °C under MW heating a higher 71% yield of product **2b** was obtained (Table 2, entry 6). In the case of α -pinene (1c), the hydroamination took place only without solvent with concomitant rearrangement to provide N-tosylisobornylamine (2c), structure being confirmed by X-ray analysis (Figure 1), using 5 mol% of AgOTf in 79% yield (Table 2, entry 7). However, using 5 mol% of HOTf, crude product **2c** was obtained in 66% yield impurified by secondary products from α -pinene isomerization and dimerization (Table 2, entry 8). Styrene (**1d**) was regioselectively transformed into sulfonamide **2d** using 5 mol% of AgOTf either under conventional or microwave heating in toluene at 85 °C in 64% or 58% yield, respectively (Table 2, entries 9 and 11), a slight better 70% yield being described using HOTf at 85 °C^{2c} (Table 2, entry 10). Attempted hydroaminated by Au(I)^{4g} failed when using AgOTf. In general, the use of AgOTf gave cleaner transformations than HOTf, which in our hands afforded mixtures of alkenes dimeric products.

Conjugated dienes showed a higher reactivity than alkenes, the addition of 4-toluenesulfonamide being carried out under heating and at room temperature. In the case of cyclohexa-1,3-diene (**1e**), *N*-tosylcyclohex-2-enylamine (**2e**) was obtained in 76% or 49% yield using 0.1 mol% or

 Table 2
 Hydroamination of Alkenes and Dienes with 4-Toluenesulfonamide Catalyzed by AgOTf or HOTf^a

Entry	Alkene or diene	Compd	Solvent	Cat. (mol%)	Temp (°C)	Time (h)	Product ^b	Compd	Yield (%) ^c
1 2 3		1a 1a 1a	PhMe CH ₂ Cl ₂ DCE	AgOTf (0.5) AgOTf (5) HOTf (1)	85 25 25	4 24 6	NHTS	2a 2a 2a	96 (99) 97 (99) 91 ^d
4 5 6	\bigcirc	1b 1b 1b	PhMe PhMe neat	AgOTf (2) HOTf (1) AgOTf (5)	85 85 90 ^e	14 22 0.5	NHTs	2b 2b 2b	38 (50) 58 ^d 71 (88)
7 8	$\langle \! / \! \rangle$	1c 1c	neat neat	AgOTf (5) HOTf (1)	85 85	14 14	NHTs	2c 2c	79 (98) (66)
9 10 11		1d 1d 1d	PhMe PhMe PhMe	AgOTf (5) HOTf (5) AgOTf (5)	85 85 90°	14 14 0.5	NHTs	2d 2d 2d	64 (72) 70 ^f 58 (76)
12 13 14		1e 1e 1e	PhMe DCE CH ₂ Cl ₂	AgOTf (0.1) HOTf (1) AgOTf (1)	85 50 25	14 25 24	NHTs	2e 2e 2e	76 (87) 63 ^d 49 (58)
15 16 17	m.//	1f ^g 1f ^g 1f ^g	$\begin{array}{c} PhMe\\ CH_2Cl_2\\ CH_2Cl_2 \end{array}$	AgOTf (0.1) AgOTf (1) HOTf (1)	85 25 25	14 24 24	www.NHTs	2f ^h 2f ⁱ 2f ⁱ	73 (88) 53 (66) 55
18 19 20	multi //	1g ^j 1g ^j 1g ^j	$\begin{array}{l} PhMe\\ CH_2Cl_2\\ CH_2Cl_2 \end{array}$	AgOTf (0.1) AgOTf (1) HOTf (1)	85 25 25	14 24 24	What NHTs	$\begin{array}{l} \mathbf{2g}^k\\ \mathbf{2g}^l\\ \mathbf{2g}^l\\ \mathbf{2g}^l\end{array}$	78 (95) 51 (69) 59

^a Reactions were performed with TsNH₂ (171 mg, 1 mmol), alkene or diene (4 mmol), AgOTf (see column) in dry solvent (2 mL) under Ar. ^b All products have been identified by ¹H and ¹³C NMR and compare with the previously described in ref. 4g. The new product **2c** has been characterized also by X-ray diffraction analysis (Figure 1).⁹ All isolated purified products were >95% pure by GLC and/or ¹H NMR. ^c Isolated yield after flash chromatography or recrystallization. In parentheses, isolated crude yields determined by GLC, based on TsNH₂.

^e In a microwave reactor (70 W, 0.69 bar) with air stream cooling.

^f Ref. 2c.

 $^{g}Z/E = 1:1.8.$

 $^{h}Z/E = 1:4.3.$

ⁱ Z/E = 1:26. ^j Z/E = 1:2.5.

k Z/E = 1.2.5.

 $^{1}Z/E = 1:99.$

d Ref. 2d.



Figure 1 Crystal structure of 2c⁹

1 mol% catalyst loading either in toluene at 85 °C or at room temperature in CH₂Cl₂, respectively (Table 2, entries 12 and 14). When HOTf (1 mol%) was employed at 50 °C in 1,2-dichloroethane as solvent, product 2e was obtained in 63% yield^{2d} (Table 2, entry 13). Penta-1,3-diene (1f) was used as a mixture Z/E (1:1.8), affording product 2f as a Z/E mixture of 1:4.3 at 85 °C and 1:26 at room temperature (Table 2, entries 15 and 16). Similar results have been observed when HOTf (1 mol%) was used as catalyst at room temperature, giving product 2f in 55% yield as a 1:26 Z/E mixture (Table 2, compare entries 16 and 17). In the case of 3-methylpenta-1,3-diene (1g), which was purchased as a 1:2.5 Z/E mixture, product 2g was obtained as a 1/8 Z/E mixture when the hydroamination was carried out in toluene at 85 °C in 78% yield (Table 2, entry 18), whereas >99% of the *E*-diasteromer 2g was isolated at room temperature in 51% yield (Table 2, entry 19). Using HOTf as catalysts at room temperature, a similar 59% yield of (E)-2g was isolated (Table 2, compare entries 19 and 20).

In summary, it has been shown that AgOTf is a good catalysts to perform the hydroamination of alkenes and dienes with 4-toluenesulfonamide, affording similar results than when using HOTf. This methodology competes with the gold(I) complexes–silver triflate combination used for the intermolecular hydroamination of the same substrates with sulfonamides with the only exception of terminal alkenes.

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- (8) General Procedure for the Hydroamination of Alkenes and Dienes

To a mixture of silver salt (see Tables 1 and 2) and sulfonamide (171 mg, 1 mmol) in dry solvent (2 mL, see Tables 1 and 2) was added the alkene or 1,3-diene (4 mmol) with magnetic stirring in a sealed tube under argon atmosphere in the dark. For neat experiments (see Table 2, entries 6-8) no solvent was added. After the corresponding reaction time under the conditions indicated in Tables 1 and 2 (for microwave heating the vessel was sealed with a pressure lock, and the mixture was heated at 90 °C in a CEM Discover MW reactor at 70 W, 0.69 bar with air stream cooling during 30 min), to the reaction mixture cooled at r.t. was added H₂O (2 mL) and brine (2 drops). The organic layer was separated, and the aqueous phase was extracted with EtOAc (2×10 mL). All organic phases were mixed, dried with MgSO₄, and evaporated. Pure products were obtained by recrystallization or by flash chromatography.

(9) Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk./data_request/cif as supplementary publication no. CCDC 748465 [unit cell parameters: *a* 12.2371 (16), *b* 17.627 (2), *c* 7.9272 (11), *β* 105.117 (3), space group P21/c].

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