Homogeneous Silver(I) Salts and Heterogeneous Ag₃PW₁₂O₄₀-Catalyzed Intermolecular Allylation of Arenes with Allylic Alcohols

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Received 31 July 2011

Abstract: AgOTf is an effective catalyst for intermolecular allylation of aromatic and heteroaromatic compounds with allylic alcohols affording allylated arenes in up to 99% yields. Heterogeneous allylation of arenes catalyzed by $Ag_3PW_{12}O_{40}$ gave comparable product yields to those obtained by AgOTf. $Ag_3PW_{12}O_{40}$ could be reused five times with slightly decreased activity.

Key words: allylation, allylic alcohols, silver catalysis, Friedel–Crafts alkylation, recyclable

Friedel–Crafts allylation is a useful tool for the synthesis of aromatic compounds.¹ The most widely used allylation reagents are allylic acetates, carbonates, and halides. With the increasing demand of environmentally benign reactions for chemical synthesis, Friedel–Crafts allylation with allylic alcohol has been attracting considerable attention as water is the only by-product of this reaction. The complexes of scandium,² iron,³ molybdenum,⁴ ruthenium,^{5–7} palladium,^{8,9} indium,¹⁰ and gold,¹¹ and Brønsted acids¹² have been demonstrated to be effective to catalyze intermolecular Friedel–Crafts allylation of arenes^{2,5,6,11} and heteroaromatic compounds^{3,4,5b,7–11} (particularly indoles^{3,7,8a,9,10}) with allylic alcohols.

We have been interested in the use of silver(I) compounds to mediate organic reactions owing to the inexpensiveness, stability towards air and moisture, and easy handling and storage, of silver(I) compounds. In literature, a variety of organic reactions mediated by silver compounds have been demonstrated to have useful applications in organic synthesis.¹³ Herein we report homogeneous and heterogeneous intermolecular Friedel–Crafts allylic alkylation of arenes with allylic alcohols catalyzed by AgOTf and Ag₃PW₁₂O₄₀, respectively.

At the outset, we examined intermolecular Friedel–Crafts allylic alkylation by using *p*-xylene (**1a**) and (*E*)-cinnamyl alcohol (**2a**) at 140 °C (Scheme 1). A panel of metal catalysts were screened including Au(PR₃)Cl–AgOTf, AuCl₃, Au(SMe₂)Cl, PtCl₂, AgX (X = OTf⁻, SbF₆⁻, BF₄⁻, PF₆⁻, ClO₄⁻), and Cu(OTf)₂. The results are depicted in Table

SYNLETT 2011, No. 18, pp 2713–2718 Advanced online publication: 19.10.2011 DOI: 10.1055/s-0031-1289548; Art ID: W17011ST © Georg Thieme Verlag Stuttgart · New York S1 in the supporting information. AgOTf displayed the best performance affording the allylated product **3a** in 40% yield. No reaction was observed when AuCl₃ or Au(SMe₂)Cl was used as the catalyst. The Brønsted acid, HOTf and Lewis acid BF₃·Et₂O, led to **3a** in 15% and 10% yields, respectively (entries 11 and 18, Table S1). Using AgOTf as catalyst, the reaction conditions were examined. The use of excessive **1a** (20 mL, 162 mmol) and increasing catalyst loading (15 mol% based on allylic alcohol) improved the product yield to 83% and the reaction was completed in two hours (entry 15, Table S2 in the Supporting Information). Lowering temperature to 80 °C led to a long reaction time (3 d) and a slightly lower product yield of 79% (entry 6, Table S2).



Scheme 1 Friedel–Crafts allylation with cinnamyl alcohol

With the optimal conditions, the scope of allylic alcohols for the AgOTf-catalyzed allylation of 1a was examined. As depicted in Table 1, a variety of allylic alcohols were found to react with 1a in the presence of AgOTf to afford allylation products in good to high product yields. The reactions of (E)-cinnamyl alcohol derivatives bearing electron-withdrawing substituent(s) on the phenyl ring gave high product yields (entries 2-7, Table 1), whereas the relatively more electron-donating *p*-methyl substituent rendered the reaction less efficient giving 40% yield of allylation product (entry 8). Trisubstituted (E)-cinnamyl alcohol 2i reacted with 1a to give the allylated product 3i in 88% yield (entry 9). Terminal allylic alcohol 2j reacted with **1a** to give **3a** in 89% yield (entry 10). Aliphatic allylic alcohols were less reactive than cinnamyl alcohol giving the products in moderate yields (entries 11 and 12). The propargylic alcohol 2n gave the propargylated product **3n** in 27% yield (entry 13).

Next, the scope of arenes was examined by using (E)-cinnamyl alcohol (**2a**) as allylation reagent. As depicted in

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Table 2, all of the monosubstituted, disubstituted and trisubstituted arenes underwent Ag(I)-catalyzed allylation with **2a** to give corresponding products in good to high yields (entries 1–5, Table 2). When **1b**, **1c**, or **1e** was used, a mixture of regioisomers in each case with ratios of

o/m = 20:80, o/o'/m = 11:0:89, and o/m/p = 12:0:88, respectively was obtained (entries 1, 2 and 4, Table 2). Toluene was allylated in a lower yield (entry 5, Table 2). In contrast to electron-rich arenes, the reactions of benzene, chlorobenzene and nitrobenzene were sluggish.

 Table 1
 Allylation of p-Xylene (1a) with Allylic Alcohols Catalyzed by AgOTf

Entry ^a	Alcohol	Product	Yield (%) ^b
1	ОН 2а		83
2	F 2b	Ja F	71
3	Br OH 2c		82
4	F ₃ C OH 2d	F ₃ C	92
5	O ₂ N 2e	0 ₂ N 3e	82
6	CI 2f	G CI CI	88
7	CI OH	CI 3g	84
8	он 2h	3h	40



Entry ^a	Alcohol	Product	Yield (%) ¹
9	2і		88
10	OH V	3i	89
11°	2 ј Он 2 k	3j	53
12°	он 21	3k	60
13	OH		27
	2n	3n	

 Table 1
 Allylation of p-Xylene (1a) with Allylic Alcohols Catalyzed by AgOTf (continued)

^a Reaction conditions: arene (20 mL), (E)-cinnamyl alcohol (0.5 mmol), AgOTf (15 mol%), 140 °C, 2 h.

^b Isolated yield.

^c Reaction time was 5 h.

After achieving allylation of arenes with allylic alcohols, we extended this protocol to heteroaromatic compounds. Treatment of furan with **2a** in toluene at 100 °C gave the allylation product **5a** in 21% yield (entry 1, Table 3). Under the same conditions, 2-methylfuran (**4b**) gave a better result than furan affording a mixture of two regioisomers **5b** and **7b** with a ratio of 82:18 in overall 79% yield (entry 2). When thiophene (**4c**) was used, regioisomers **5c** and **6c** were obtained in 94% yield with a ratio of 77:23. No isomer **7c** was observed (entry 3). In contrast, three regioisomers were obtained in a ratio of **5d/6d/7d** = 79:2:19 when 2-methylthiophene (**4d**) was used (entry 4). Pyrrole (**4e**) was also reactive to undergo allylation giving **5e** as the major product (entry 5).

This AgOTf-catalyzed intermolecular allylation protocol can be scaled up. Treatment of **1a** (150 mL) with **2a** (1.34 g) in the presence of AgOTf (15 mol%) at 140 °C for four hours gave **3a** (1.66 g) in 75% yield.

To gain insight into the reaction mechanism, we monitored the AgOTf-catalyzed allylation of **1a** with **2a** by ¹H NMR spectroscopy (see SI for the time course). Dicinnamyl ether (8) was observed to develop at the beginning of the reaction and was subsequently consumed at the end of the reaction. Treatment of 8 with 1a in the presence of AgOTf (15 mol%) at 140 °C for two hours afforded 3a in 80% yield. With these findings, we propose that allylation



Scheme 2 Proposed pathways in AgOTf-catalyzed allylation of 1a with 2a

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 Table 2
 Allylation of Arenes with (E)-Cinnamyl Alcohol (2a) Catalyzed by AgOTf



 $^{\rm a}$ Reaction conditions: arene (20 mL), (*E*)-cinnamyl alcohol (0.5 mmol), AgOTf (15 mol%), 140 °C, 2 h.

^b Isolated yield.

^c Reaction time was 5 h.

^d Isomer ratio o/o'/m.

^e Isomer ratio *o/m/p*.

^f The reaction was carried out at 110 °C for 10 h.

^g Isomer ratio could not be determined by ¹H NMR.

products were formed directly from allylic alcohols and via intermediate **8** (Scheme 2). A similar mechanism was previously reported in a diruthenium complex catalyzed allylation.^{5b}

 Table 3
 Allylation of Heteroaromatic Compounds with (E)-Cinnamyl Alcohol (2a) Catalyzed by AgOTf



^a Reaction conditions: heteroarene (0.05 mol), (*E*)-cinnamyl alcohol (0.5 mmol), toluene (5 mL), AgOTf (15 mol%), 100 °C, 2 h.
^b Isolated yield.

Catalyst reusability in metal-catalyzed allylation of aromatic and heteroaromatic compounds with allylic alcohols has not been addressed in previous examples,^{2–11,14} except for the reaction catalyzed by Sc(OTf)₃, in which case Sc(OTf)₃ was reused after evaporating the aqueous mixture followed by subsequent heating in vacuo at 180 °C.^{2b}

Table 4 Allylation of Arenes with Allylic Alcohols Catalyzed by Ag₃PW₁₂O₄₀^a



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Entry ^a	Allylic alcohol	Product	Yield (%) ^b
3	Br 2c	Br C C C C C C C C C C C C C C C C C C C	92
4	F ₃ C 2d	F ₃ C	82
5	CI CI 2f		88
6	CI OH		84
7	OH 2k		57
8	OH 2i		89
9°	он 2a	3a	97
10 ^d	ОН 2а	Sq Sc Sc	96 ^e

 Table 4
 Allylation of Arenes with Allylic Alcohols Catalyzed by Ag₃PW₁₂O₄₀^a (continued)

^a Reaction conditions: *p*-xylene (20 mL), allylic alcohol (0.5 mmol), $Ag_3PW_{12}O_{40}$ (15 mol%), 140 °C, 2 h.

^b Isolated yield.

^c Reaction was performed with.1,3,5-trimethylbenzene (20 mL).

^d Thiophene (0.05 mol) in toluene (5 mL), 100 °C, 2 h.

^e A regioisomeric ratio of 5:6:7 = 87:11:2 was determined by ¹H NMR.

To address this issue, we synthesized a heterogeneous silver(I) catalyst $Ag_3PW_{12}O_{40}$ according to the literature.¹⁵ This silver(I) compound was characterized by PXRD, SEM, and EDAX (see the Supporting Information). Then we used this compound to catalyze the intermolecular allylation reaction. To our delight, this heterogeneous silver compound $Ag_3PW_{12}O_{40}$ showed high activity towards the

allylation giving comparable product yields as those obtained in the homogenous Ag(I) catalysis (Table 4).

Importantly, $Ag_3PW_{12}O_{40}$ could be easily recovered and reused by simple filtration of the reaction mixture after the reaction. As depicted in Table 5, after five recycles, the catalyst $Ag_3PW_{12}O_{40}$ was still active (Table 5).

Table 5Reuse of $Ag_3PW_{12}O_{40}$ in Allylation of 1a with 2a

Run ^a	1	2	3	4	5
Yield (%) ^b	84	81	77	71	62

^a Reaction conditions: *p*-xylene (20 mL), allylic alcohol (0.5 mmol), $Ag_3PW_{12}O_{40}$ (15 mol%), 140 °C, 2 h.

^b Isolated yield.

In conclusion, we have demonstrated that AgOTf is an efficient catalyst for the intermolecular allylation of aromatic and heteroaromatic compounds with allylic alcohols. This method can be applied to a gram-scale synthesis. We have also found that $Ag_3PW_{12}O_{40}$ is an active and recyclable heterogeneous catalyst for the allylation reaction.

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

Acknowledgment

We are thankful for the financial support of The University of Hong Kong (University Development Fund), Hong Kong Research Grant Council (HKU 7052/07P), Research Grants Council (CityU 2/06C and HKU1/CRF/08), CAS-GJHZ200816 and CAS-Croucher Funding Scheme for Joint Laboratory and the Areas of Excellence Scheme established under the University Grants Committee of the Hong Kong SAR, China (AoE/P- 10/01). G.-Q. Chen thanks the Croucher Foundation of Hong Kong for the postgraduate studentship.

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