Selective Allylation of Arenethiols Using Water-soluble Palladium Complex Catalyst in Recyclable Water/Hexane Biphasic Media

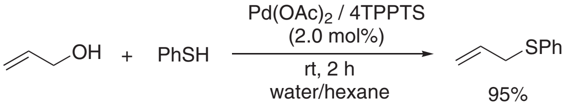
Nobuyuki Komine, Akari Sako, Shin-ya Hirahara, Masafumi Hirano, and Sanshiro Komiya*
Department of Applied Chemistry, Graduate School of Engineering, Tokyo University of Agriculture and Technology,
2-24-16 Nakacho, Koganei, Tokyo 184-8588

(Received November 19, 2004; CL-041398)

Allylation of arenethiols by allylic alcohol with sterically hindered carbon of the allylic moiety is smoothly catalyzed by $Pd(OAc)_2$/TPPTS in biphasic water/hexane media under ambient conditions. The catalyst water layer can be repeatedly reused without catalytic activity loss.

Aqueous/organic biphasic catalyses attract growing interests in relation to environmentally friendly chemical processes, due to easy separation of products and catalysts, multiple use of catalysts, and reduction of organic solvents.[1] We recently reported the synthesis and some organometallic reactions of water-soluble alkyltransition metal complexes[2] and biphasic carbonyl-selective hydrogenation of unsaturated carbonyl compounds.[3] Allylation reactions represented as Tsuji–Trost reaction are regarded as one of the most important chemical processes in organic synthesis.[4] Among them, Pd-catalyzed allylation of thiols are still exceptionally rare,[5] probably because of possible catalyst poisoning by sulfur coordination, though Ru-catalyzed allylation was recently reported by Mitsudo.[6] We now report novel allylation of arenethiols with allylic alcohols catalyzed by $Pd(OAc)_2$/TPPTS in aqueous/organic biphasic media.[7,8] Success in using allylic alcohols as allyl source is also an important value added in this reaction,[6,9] since allylic alcohols are easily accessible and believed to be a poor inlet to η^3-allylpalladium intermediates in comparison with other allyl sources such as allylic halides, carbonates, esters, and ethers.

Treatment of benzenethiol with allyl alcohol in the presence of 2 mol% $Pd(OAc)_2$ and 4 equiv. of TPPTS [TPPTS $=$ $P\{C_6H_4(SO_3Na)\text{-}3\}_3$] at room temperature for 2 h under nitrogen atmosphere in biphasic water/hexane media gave allyl phenyl sulfide quantitatively (Eq 1).



(1)

Catalytic activity of several palladium catalytic systems was examined in the reaction of benzenethiol with allyl alcohol (Table 1). Water/benzene or AcOEt system or only water can also be used, but the yield of allyl phenyl sulfide decreased under the comparable conditions (Entries 2–4). No allylation product was obtained when the reaction was carried out in only organic solvents such as dimethyl sulfoxide, methanol, benzene and acetonitrile in the presence of $Pd(OAc)_2$/4 TPPTS or the corresponding palladium catalysts with triphenylphosphine ligand ($Pd(OAc)_2$/4 PPh_3) (Entries 5–10). It is interesting to note that use of biphasic water/hexane media is critically important for this success. $Pd(TPPTS)_3$ also shows catalytic activity for allylation of benzenethiol in biphasic water/hexane media (Entry 11).

Table 1. Allylation of thiol using allyl alcohol by palladium catalyst[a]

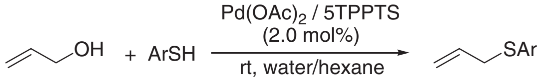
Entry	Catalyst	Solvent	Time /h	Yield /%
1	$Pd(OAc)_2$/4TPPTS	water/hexane[b]	2	95
2	$Pd(OAc)_2$/4TPPTS	water/benzene[b]	2	52
3	$Pd(OAc)_2$/4TPPTS	water/AcOEt[b]	2	64
4	$Pd(OAc)_2$/4TPPTS	water	3	25
5	$Pd(OAc)_2$/4TPPTS	dimethyl sulfoxide	6	0
6	$Pd(OAc)_2$/4TPPTS	methanol	6	0
7	$Pd(OAc)_2$/4PPh_3	benzene	6	0
8	$Pd(OAc)_2$/4PPh_3	acetonitrile	6	0
9	$Pd(PPh_3)_4$[c]	benzene	6	0
10	$Pd(PPh_3)_4$[c]	acetonitrile	6	0
11	$Pd(TPPTS)_3$[c]	water/hexane[b]	2	96

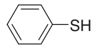
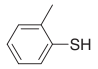
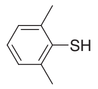
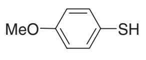
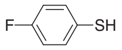
[a]Reaction conditions: $Pd(OAc)_2$ (0.02 mmol), phosphine ligand (0.08 mmol), allyl alcohol (1.0 mmol), benzenethiol (1.0 mmol), solvent = 8 mL, room temperature. [b]solvent = water 4.0 mL, organic solvent 4.0 mL. [c]Pd(0) complex (0.02 mmol).

Allylation using several allylic alcohols and arenethiols also proceeded with $Pd(OAc)_2$/TPPTS catalyst in biphasic water/hexane media (Tables 2 and 3). Table 2 shows the results of allylation of arenethiol derivatives by allyl alcohol. Electron-donating substituent at *para*-position and *ortho*-substitutents in arenethiol discouraged the catalytic activity (Entries 2–4).

One notable fact observed in Table 3 is that more sterically hindered side of the allylic moiety is substituted by mercapto

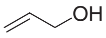
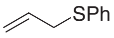
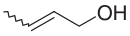
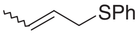
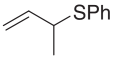
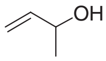
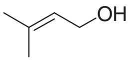
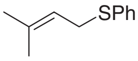
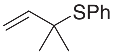
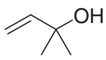
Table 2. Allylation of several arenethiol with allyl alcohol[a]



Entry	ArSH	Time/h	Conv./%	Yield/%
1		2	100	96
2		2 5	42 100	39 94
3		2 24	20 58	14 41
4		2 6	52 92	45 91
5		2	100	91

[a]Reaction conditions: $Pd(OAc)_2$ (0.02 mmol), TPPTS (0.10 mmol), allyl alcohol (1.0 mmol), thiol (1.0 mmol), solvent = water 4.0 mL, hexane 4.0 mL, room temperature.

Table 3. Allylation of benzenethiol with several allylic alcohols[a]

Entry	Allylic alcohol	Time/h	Conv./%	Product (yield/%)	
1		2	100		(95)
2	 (*E*/*Z* = 95/5)	3	45	 (18) (*E*/*Z* = 94/6)	 (24)
3		5	79	(32) (*E*/*Z* = 88/12)	(40)
4		9	100	(45) (*E*/*Z* = 81/19)	(56)
5		3	83	(29) (*E*/*Z* = 64/36)	(50)
6		5	98	(38) (*E*/*Z* = 65/35)	(59)
7		24	100	 (32)	 (61)
8		24	100	(35)	(65)

[a]Reaction conditions: Pd(OAc)$_2$ (0.02 mmol), TPPTS (0.10 mmol), allylic alcohol (1.0 mmol), benzenethiol (1.0 mmol), solvent = water 4.0 mL, hexane 4.0 mL, room temperature.

group regardless of the starting allylic alcohols.[8] E/Z ratio of the products in the reactions using crotyl alcohol and its regioisomer, 1-methylallyl alcohol was slightly different. In addition substituents at the 3-position of the allylic alcohol significantly suppressed the reaction rate (Entries 2–6). One possible mechanism is initial coordination of allylic alcohol via C=C double bond, followed by protonation of OH with thiol to give an η^1-allyl)palladium(II) intermediate having substituents at the terminal sp^2 carbon due to steric hindrance, to which the thiolato anion selectively attacks by an S$_N$2$'$ mechanism. Another possibility is formation of allylic cation coordinated complex which selectively reacts with thiolato anion at the substituted carbon, since the secondary and tertiary carbocation is more stable than the primary one. Such stabilization of these intermediates with increased nucleophilic reactivity of the thiolate could be assisted by water coordination and solvent effect, though further mechanistic studies including immiscible solvent interface problems are required.

Biphasic allylation can also be applied for amine and carbon nucleophile. Treatment of diethylamine with allyl alcohol in the presence of Pd(OAc)$_2$/5 TPPTS (0.4 mol %) at 110 °C for 2 h in water/pentane media gave allyldiethylamine quantitatively. Allylation of 2,4-pentanedione with allyl alcohol selectively gave monoallylation product in 73% yield in the presence of NaOH (8 mol %).

Table 4. Recycling of catalyst for allylation of benzenethiol[a]

Run	Conv./%	Yield/%
1	100	93
2	100	97
3	100	93
4	100	96

[a]Reaction conditions: Pd(OAc)$_2$ (0.02 mmol), TPPTS (0.10 mmol), allyl alcohol (1.0 mmol), benzenethiol (1.0 mmol), solvent = water 4.0 mL, hexane 4.0 mL, room temperature, 2 h.

In all catalytic allylations, the products were easily separated from the catalyst by simple decantation of the organic layer. Since the catalyst remained in the water layer, the allylation can be run again by simply adding the hexane solution of the reactants (Table 4). Four runs were performed without loss of catalytic activity for the reaction of benzenethiol with allyl alcohol, by using the recycled water layer containing the water-soluble catalyst.

This work was partially supported by New Energy and Industrial Technology Development Organization (NEDO) and Japan Chemical Innovation Institute (JCII).

References and Notes

1 a) “Aqueous-Phase Organometallic Catalysis, Concepts and Applications,” ed. by B. Cornils and W. A. Herrmann, Wiley-VCH, Weinheim (1998) and references cited therein. b) “Applied Homogeneous Catalysis with Organometllic Compounds,” ed. by B. Cornils and W. A. Herrmann, VCH, Weinheim (1996), Vols. 1 and 2.

2 a) S. Komiya, M. Ikuine, N. Komine, and M. Hirano, *Chem. Lett.*, **2002**, 72. b) S. Komiya, M. Ikuine, N. Komine, and M. Hirano, *Bull. Chem. Soc. Jpn.*, **76**, 183 (2003).

3 A. Fukuoka, W. Kosugi, F. Morishita, M. Hirano, L. McCaffrey, W. Henderson, and S. Komiya, *Chem. Commun.*, **1999**, 489.

4 J. Tsuji, “Palladium Reagents and Catalysts,” Wiley, Chichester (1995).

5 a) C. Goux, P. Lhoste, and D. Sinou, *Tetrahedron Lett.*, **33**, 8099 (1992). b) M. Moreno-Mañas, R. Pleixats, and M. Villarroya, *Tetrahedron*, **49**, 1457 (1993). c) C. Goux, P. Lhoste, and D. Sinou, *Tetrahedron*, **50**, 10321 (1994). d) M. Frank and H.-J. Gais, *Tetrahedron: Asymmetry*, **9**, 3353 (1998). e) K. Tsutsumi, T. Yabukami, K. Fujimoto, T. Kawase, T. Morimoto, and K. Kakiuchi, *Organometallics*, **22**, 2996 (2003).

6 T. Kondo, Y. Morisaki, S. Uenoyama, K. Wada, and T. Mitsudo, *J. Am. Chem. Soc.*, **121**, 8657 (1999).

7 A number of examples of the Tsuji–Trost reaction with allylic acetates or carbonates in water are known. a) M. Safi and D. Sinou, *Tetrahedron Lett.*, **32**, 2025 (1991). b) J. P. Genêt, E. Blart, and M. Savignac, *Synlett*, **1992**, 715. c) E. Blart, J. P. Genêt, M. Safi, M. Savignac, and D. Sinou, *Tetrahedron*, **50**, 505 (1994). d) D. E. Bergbreiter and Y.-S. Liu, *Tetrahedron Lett.*, **38**, 7843 (1997). e) H. Danjo, D. Tanaka, T. Hayashi, and Y. Uozumi, *Tetrahedron*, **55**, 14341 (1999). f) S. Kobayashi, W. W.-L. Lam, and K. Manabe, *Tetrahedron Lett.*, **41**, 6115 (2000). g) Y. Uozumi and K. Shibatomi, *J. Am. Chem. Soc.*, **123**, 2919 (2001).

8 Very recently, Shinokubo and Oshima have reported analogous allylation of amine and 1,3-diketone by allylic alcohol catalyzed by [PdCl(η^3-C$_3$H$_5$)]$_2$ and TPPTS in an water/ethyl acetate biphasic system, where nucleophiles attack the possible η^3-allyl intermediate. H. Kinoshita, H. Shinokubo, and K. Oshima, *Org. Lett.*, **6**, 4085 (2004).

9 a) J. Qu, Y. Ishihara, T. Oe, and N. Nagato, *Nippon Kagaku Kaishi*, **1996**, 250. b) M. Sakamoto, I. Shimizu, and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **69**, 1065 (1996). c) Y. Masuyama, M. Kagawa, and Y. Kurusu, *Chem. Lett.*, **1995**, 1121. d) Y. Tamaru, Y. Horino, M. Araki, S. Tanaka, and M. Kimura, *Tetrahedron Lett.*, **41**, 5705 (2000). e) M. Kimura, Y. Horino, R. Mukai, S. Tanaka, and Y. Tamaru, *J. Am. Chem. Soc.*, **123**, 10401 (2001). f) S.-C. Yang and Y.-C. Tasai, *Organometallics*, **20**, 763 (2001). g) F. Ozawa, H. Okamoto, S. Kawagsi, S. Yamamoto, T. Minami, and M. Yoshifuji, *J. Am. Chem. Soc.*, **124**, 10968 (2002). h) Y. Kayaki, T. Koda, and T. Ikariya, *J. Org. Chem.*, **69**, 2595 (2004). i) K. Manabe and S. Kobayashi, *Org. Lett.*, **5**, 3241 (2004).

Published on the web (Advance View) January 22, 2005; DOI 10.1246/cl.2005.246