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Efficient double bond migration of allylbenzenes catalyzed by $Pd(OAc)_2$–HFIP system with unique substituent effect

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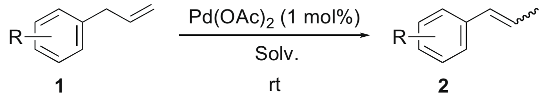
ABSTRACT

A novel catalyst system of $Pd(OAc)_2$–HFIP induces double-bond migration of allylbenzenes under mild conditions with low catalytic loading to afford 1-propenylbenzenes. The reaction shows a unique substituent effect that is highly dependent on the distance of substituents from the allylic moiety. Thus, the reactivity of substrates bearing a methyl group is ordered in *para* > *meta* > *ortho*, whereas it is entirely reversed as *ortho* > *meta* > *para* for methoxy and chloro substituents.

1,1,1,3,3,3-Hexafluoro-2-propanol (hexafluoroisopropanol), an alcohol bearing two CF_3 groups, has withdrawn much attention of synthetic chemists in the past decade.[1,2] The alcohol being abbreviated as HFIP is widely used as solvent, co-solvent, and additive in order to modify the characteristics of reactions owing to its unique properties. HFIP is a very strong hydrogen bond donor, and a highly polar solvent with an ionizing power. It is neither a nucleophile nor a hydrogen bonding acceptor. Moreover, the low boiling point of HFIP enables its easy recovery from the reaction mixture, overcoming the disadvantage of expensiveness. Such features of HFIP have led to the realization of remarkable outcomes not observed in usual systems.[3–12] Especially, HFIP exhibits a variety of reactivity in metal-catalyzed reactions because of the stabilizing ability of cationic species.[3–8] Among catalytic reactions using transition metal-HFIP system so far studied, a combination of Pd complex and HFIP has not been well investigated except for a few examples.[3–5] This fact prompted us to survey Pd(II)-catalyzed reactions in HFIP with focus on the double bond migration of terminal alkenes, which is one of the important protocols in elaborate synthetic sequences.[13–30] For such reactions, applicability of Ru,[20–26] Rh,[27,28] and Ir[29,30] complexes is still one of the recent concerns. In the present letter, we report a novel catalyst system of $Pd(OAc)_2$–HFIP, which converts allylbenzenes (3-propenylbenzenes) **1** into 1-propenylbenzenes **2** with unique reactivity toward the substituents on the benzene ring.

To a solution of $Pd(OAc)_2$ (0.01 mmol, 1 mol %) in HFIP (0.5 mL), a solution of allylbenzene **1a** (1.0 mmol) in HFIP (0.5 mL) was added under nitrogen, and the resultant mixture was stirred at room temperature for 9 h, monitoring the progress of reaction by gas chromatography. After consumption of **1a**, diethyl ether (1 mL) was added for quenching the reaction, and the mixture was filtered through a florisil column (0.5 g) and concentrated. The residue was subjected to measurement of ^{1}H NMR by which the yield of **2a** was determined to be 81% (0.81 mmol) (Table 1, run 1). Employment of *i*-PrOH instead of HFIP caused no reaction. A small amount of **2a** was formed when a mixed solvent (toluene or DME with HFIP) and longer reaction time were used (runs 2–4).

Table 1
Pd-Catalyzed double bond migration of substituted allylbenzenes **1** in HFIP



Run	R		Solv.	Time (h)	Yield[a] (%)	*E*/*Z*
1	H	**a**	HFIP	9	81	98/2
2	H	**a**	*i*-PrOH	9	0	–
3	H	**a**	HFIP/PhMe (1/1)	27	1	–
4	H	**a**	HFIP/DME (1/8)	27	36	95/5
5[b]	H	**a**	HFIP	9	83	97/3
6	H	**a**	HFIP	1	69	98/2
7	*p*-Me	**b**	HFIP	1	59	98/2
8	*m*-Me	**c**	HFIP	1	29	98/2
9	*o*-Me	**d**	HFIP	1	15	94/6
10	*p*-MeO	**e**	HFIP	1	37	93/7
11	*m*-MeO	**f**	HFIP	1	65	93/7
12	*o*-MeO	**g**	HFIP	1	86	96/4
13	*p*-Cl	**h**	HFIP	1	Trace	–
14	*m*-Cl	**i**	HFIP	1	10	97/3
15	*o*-Cl	**j**	HFIP	1	31	95/5
16	*p*-Cl	**h**	HFIP	24	17	95/5
17	*o*-Cl	**j**	HFIP	24	60	96/4

[a] Determined by ^{1}H NMR.
[b] 0.05 mol % of $Pd(OAc)_2$ was used.

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Under the same conditions as above, no significant change was observed in the yield of **2a** by decreasing the catalyst concentration down to 0.1 mol %. Moreover, the catalyst loading could be reduced to 0.05 mol % by keeping a high catalytic activity, in which **2a** was formed in 83% in 9 h (run 5). It corresponds to 1660 turnover number (TON). High efficiency of the catalyst is environmentally acceptable.

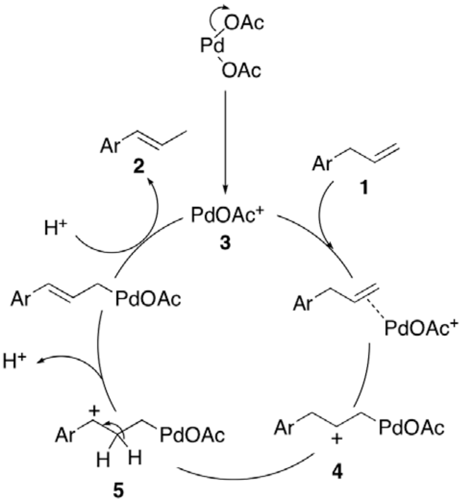
The present catalyst system was applied to allylbenzenes[31] having a series of substituents such as methyl (**1b–d**), methoxy (**1e–g**), and chloro (**1h–j**) groups. Each substrate underwent the double bond migration to afford their corresponding propenylbenzenes **2b–j**[31] with high *E*/*Z* ratios; however, the reactivity was sensitive to the nature of substituents. In order to estimate the influence of the substituent, the yield of **2** was compared in an early stage of the reaction (1 h) (runs 6–17).

Among methyl-substituted allylbenzenes **1b–d**, the reactivity of *para*-methyl derivative **1b** was almost comparable to that of allylbenzene **1a** (runs 6 and 7) itself . However, approaching the methyl group to allyl moiety enforced the reaction to be highly sluggish. Consequently, the order of reactivity in terms of the substituent position for the methyl group was *para* > *meta* > *ortho*.

In contrast, the opposite tendency was observed in reactions of methoxy-substituted allylbenzenes **1e**–**g**, in which *ortho*-methoxy derivative **1e** exhibited the highest reactivity (run 12). The longer a distance between methoxy and allyl moieties was, the lower reactivity of allylbenzene was resulted. Thus, the order of reactivity in the position of methoxy group was *ortho* > *meta* > *para*.

Although chloro-substituted allylbenzenes **1h–j** (runs 13–15) were generally inactive, the tendency was similar to that of methoxy derivatives **1e–g**. In the case of *para*-chloro derivative **1h**, only a trace amount of propenylbenzene **2h** (run 13) was detected; however, approaching the chloro group to allyl moiety resulted in a relatively higher yield of **2i** or **2j** (runs 14 and 15). Even in a prolonged reaction (24 h), the catalyst was continuously active to afford 60% yield of **2j** (run 17). In the case of less reactive *para*-chloro derivative **1h**, a 17% yield of **2h** was formed in 24 h (run 16).

A plausible mechanism for the present double bond migration is illustrated in Scheme 1 in which cationic species participate as intermediates that are stabilized by HFIP.[3] The double bond of **1** coordinates to cationic PdOAc$^+$ **3**[32] derived via elimination of acetate ion from $Pd(OAc)_2$. The step is followed by the formation of carbonium cation **4**,[33] from which benzyl cation **5** is resulted by hydride transfer. The double bond formation and protonation lead to propenylbenzene **2** together with the regeneration of **3**.[34]



Scheme 1. A plausible mechanism for the present double bond migration with $Pd(OAc)_2$–HFIP system.

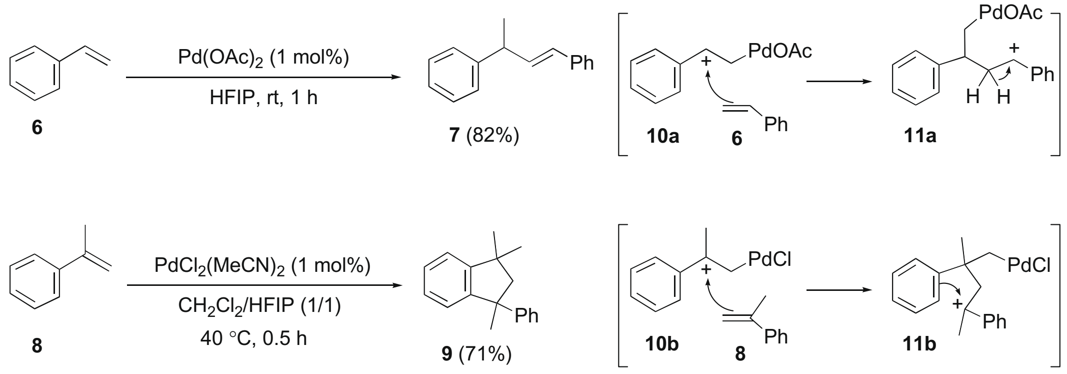
The plausibility of this mechanism must be supported by the following observations. As shown in Scheme 2, the catalyst system of $Pd(OAc)_2$–HFIP induced dimerization of styrene **6** to give an 82% yield of head-to-tail dimer **7**[35,36] (1 mol % of Pd, 1 h). Although α-methylstyrene **8** was inactive in this system, the use of $PdCl_2(MeCN)_2$ with HFIP in CH_2Cl_2 produced cyclic dimer (indane derivative) **9**[37,38] in 71% yield.[39] The dimerization proceeds via palladation of **6** or **8** leading to benzyl cation **10a** or **10b** which is attacked by another alkene. The intramolecular Friedel–Crafts reaction of **11b** constructs a condensed ring[33,40] to give **9**. While Doherty et al. show that palladium complex does not catalyze well the dimerization of alkenes,[40] our reaction efficiently proceeds with $PdCl_2$. This is presumably due to the stabilizing ability of HFIP for cationic intermediates.[3]

The difference in reactivity observed in the present study is apparently dependent on the distance between the substituent and allylic alkene. Such an intriguing outcome could be interpreted by a combination of steric and electronic factors of the substituents. Since the reaction proceeds via coordination of allylic alkene to palladium species, the reactivity of substrate is largely determined by its prevention or acceleration. With *ortho*-methyl group (Fig. 1), this coordination is obviously prevented by its steric hindrance. Therefore, *ortho*-isomer **1d** is less reactive compared to either **1b** or **1c** in which the methyl group is located successively far from the reaction site. In the case of *para*-methyl group, electronic effect becomes more influential. Electronically more stabilized cationic intermediate **5b**, as shown in Figure 1, undergoes the reaction more rapidly than the corresponding *meta*-methyl derivative **5c**. Consequently, the order of reactivity becomes *para* > *meta* > *ortho* for the methyl derivatives.

In the case of methoxy derivatives **1e**–**g**, coordination of methoxy group to PdOAc$^+$ species becomes crucial. The palladated methoxy group could serve as an electron-withdrawing group that destabilizes a benzyl cation as shown in intermediate **5e** (Fig. 2). Thus, *para*-methoxy derivative **1e** is less reactive than the *meta*-isomer **1f**. In the case of *ortho*-methoxy derivative **1g**, such an effect is also detrimental. However, since the methoxy group attracts PdOAc$^+$ species effectively, the double bond readily coordinates to PdOAc$^+$ under equilibrium because of its nearby position to the double bond (Fig. 2). In other words, the effective capturing of palladium species by methoxy group like a fishhook determines the reactivity. As a result, *ortho*-methoxy derivative **1g** is the most reactive among three isomeric methoxy-substituted allylbenzenes **1e**–**g**.

In the case of a chloro group, its electronegative property is disadvantageous for the present cationic reaction, resulting in the retardation of the reaction. In fact, the yields of chloropropenylbenzenes **2h–j** were lower than those of methoxy derivatives **2e–g**. However, the tendency of reactivity was identical between these cases. This must be also explained in a similar manner as shown in Figure 2. In this case, the chloro group at the *ortho*-position serves as a fishhook to the palladium species.

In summary, we demonstrate a novel catalyst system of $Pd(OAc)_2$–HFIP, which catalyzes the double bond migration under mild conditions. Simple experimental manipulations, easy treatability of the catalyst, and low catalytic loading are preferential in terms of practical use and environmental acceptability, and its application to other substrates such as *N*-allyl amines or amides is one of the future subjects. The present study discloses an intriguing substituent effect in which the reactivity depends on the distance from the reaction site. Namely, the reactivity is ranked in the order of *para* > *meta* > *ortho* for methyl group, whereas is *ortho* > *meta* > *para* for methoxy and chloro substituents. The opposite tendency of reactivity is reasonably interpreted by a combination of steric and electronic effects of substituents. A fishhook effect of *ortho*-substituents such as methoxy to palladium(II) species will be useful for designing elaborate synthetic sequences.



Scheme 2. Dimerization of styrene **6** and α-methylstyrene **8** using a catalyst system of Pd(II)–HFIP.

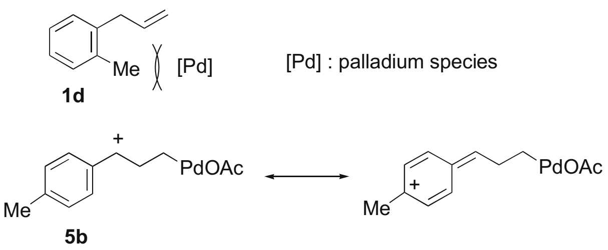


Figure 1. Substituent effect of a methyl group.

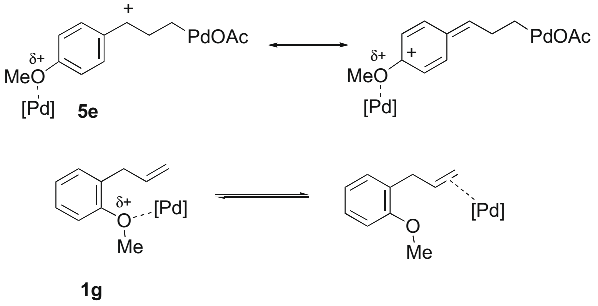


Figure 2. Substituent effect of a methoxy group.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.05.014.

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33. The carbonium cation **4** could be formed via coordination of Pd(OAc)$_2$ to the double bond of **1** and subsequent elimination of acetate ion. There is no reason to disregard this process; however, in order to emphasize the importance of cationic species in the present reaction, the pathway involving PdOAc$^+$ cation **3** is depicted in the light of references.[41,42]
34. The present isomerization is also accounted for by the pathway involving (π-allyl)PdOAc formed via coordination of Pd(OAc)$_2$ to the double bond of **1**. However, the substituent effects observed is not likely supported by this mechanism, because it does not lead to cationic species explicitly.
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