Rhodium- and Iridium-Catalyzed Allylation of Electron-Rich Arenes with Allyl Tosylate

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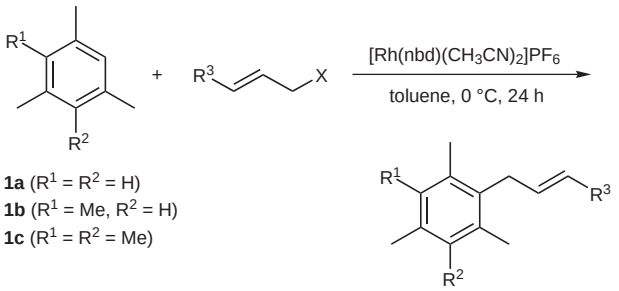
Received 20 March 2003

Abstract: The allylation of electron-rich arenes with allyl tosylate proceeded at 0 °C in the presence of $[Rh(nbd)(CH_3CN)_2]PF_6$. Various oxygenated arenes were allylated with high *para*-selectivity in almost all cases. Especially in the reaction of anisoles, the tendency was remarkable.

Key words: allylations, arenes, catalysis, iridium, rhodium

Allyl- or prenyl-substituted arenes, especially phenolic compounds, constitute an important class of biologically active natural products and drugs.[1] Aromatic electrophilic substitution with alkyl halides, namely the Friedel–Crafts reaction, is one of the most simple and general methods for the synthesis of substituted arenes.[2,3] However, in the reaction using allyl halide or allyl alcohol, a classical metal halide catalyst such as $AlCl_3$ brings about the addition to the double bond and/or various side reactions.[2,3] Thus, the yield of the desired allylated product is generally low. In contrast, scandium(III) triflate[4] or transition metal complexes such as $Pd(OAc)_2$/dppf[5] and $[(C_5Me_5)RuCl(SPr^i)_2Ru(OH_2)\text{-}(C_5Me_5)]OTf$[6] were recently reported to catalyze the allylation with allylic alcohols to afford allylated products in high yields without the side reactions. Molybdenum and tungsten complexes are also efficient for the allylation of arenes with allylic esters,[7] and, furthermore, the allylation catalyzed by $[Mo(CO)_4Br_2]_2$ or $(acac)_2Mo(SbF_6)_2$ with allylic compounds such as allylic esters and alcohols proceeds even at room temperature.[8] In our previous study utilizing allyl tosylate as an allylating agent,[9] we found that cationic rhodium complexes were efficient for the allylation of alkenes with allyl tosylate.[9b] We report here that the allylation of electron-rich arenes with allyl tosylate proceeds smoothly at 0 °C in the presence of rhodium or iridium complexes.

The reaction of mesitylene (**1a**) with allyl tosylate (Scheme 1) at 0 °C in the presence of $[Rh(nbd)(CH_3CN)_2]PF_6$ (5 mol%) afforded the allylated product **2a** in 71% yield (Table 1, entry 1). Other rhodium complexes such as $[Rh(nbd)Cl]_2$, $[Rh(nbd)_2]BF_4$ and $RhCl(PPh_3)_3$ were less effective, and no reaction occurred using several palladium and molybdenum complexes, which are known to be efficient for various allylic substitution reactions. Although by using allyl mesylate as an allylating reagent a trace amount of **2a** was obtained (entry 2), the reaction with other allylic compounds such as allyl acetate, allyl trifluoroacetate, allyl methyl carbonate, allyl alcohol, allyl iodide, and allyl bromide did not give any product. More electron-rich arenes, such as 1,2,3,5-tetramethylbenzene (**1b**) and pentamethylbenzene (**1c**), reacted with allyl tosylate, affording the allylated product **2b** and **2c** in good yields, respectively (entries 3 and 4). However, no reaction occurred when xylene, 1,2,3-trimethylbenzene, 1,2,4-trimethylbenzene, and 1,2,4,5-tetramethylbenzene were used. These results indicate that the allylation occurs only on an aromatic carbon that has more than three methyl substituents on its *ortho*- and *para*-positions. Crotyl tosylate also reacted with **1a**, giving the linear product **2d** selectively (entry 5).



1a ($R^1 = R^2 = H$)
1b ($R^1 = Me$, $R^2 = H$)
1c ($R^1 = R^2 = Me$)

2a ($R^1 = R^2 = R^3 = H$)
2b ($R^1 = Me$, $R^2 = R^3 = H$)
2c ($R^1 = R^2 = Me$, $R^3 = H$)
2d ($R^1 = R^2 = H$, $R^3 = Me$)

Scheme 1

Since polymethyl-substituted electron-rich arenes are reactive in the present allylation, we next examined the reaction of electron-rich oxygenated arenes. Some of the allylated products obtained are naturally occurring materials, and serve as perfumes, agrochemicals, and pharmaceuticals and their synthetic intermediates. Table 1 shows the results of the allylation of alkoxy-substituted arenes with allyl tosylate. The reaction of anisole (**3a**) was highly selective to give estragole (**4a**) in 54% yield, without the formation of *o*- and *m*-isomers (entry 1). The reaction of arenes which have two or three methoxy groups also proceeded smoothly at 0 °C with high regioselectivity. Methyl eugenol (**4b**) was obtained by the allylation of 1,2-dimethoxybenzene (**3b**) (entry 2). 1,3-Dimethoxybenzene (**3c**) and 1,3,5-trimethoxybenzene (**3e**) were also reacted

Synlett 2003, No. 10, Print: 05 08 2003.
Art Id.1437-2096,E;2003,0,10,1431,1434,ftx,en;U08703ST.pdf.

Table 1 Rhodium-Catalyzed Allylation of Arenes with Allylic Compounds[a]

Entry	Arene	X	R^3	Product	Yield[b] (%)
1	**1a**	OTs	H	**2a**	71
2	**1a**	OMs	H	**2a**	trace
3	**1b**	OTs	H	**2b**	64
4[c]	**1c**	OTs	H	**2c**	80[d]
5	**1a**	OTs	Me	**2d**	45[d]

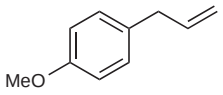
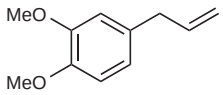
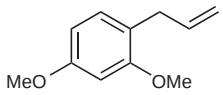
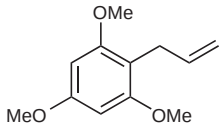
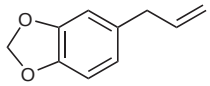
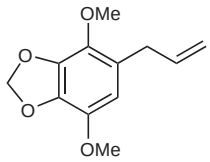
[a] Reaction conditions: **1** (5.0 mmol), an allylic compound (0.5 mmol), $[Rh(nbd)(CH_3CN)_2]PF_6$ (0.025 mmol), and toluene (1 mL), 0 °C, 24 h.
[b] Determined by GC.
[c] 0.5 mmol of **1c** and 1.0 mmol of allyl tosylate were used.
[d] Isolated yields.

with allyl tosylate, giving the allylation products **4c** and **4d** in good to high yields (entries 3 and 5, respectively). In all the reactions, the allylation occurred on the *para*-position of the methoxy group. No product was obtained using *para*-substituted anisoles like 1,4-dimethoxybenzene (**3d**) under the same conditions (entry 4). Safrole (**4e**) and apiole (**4f**) can be readily prepared in one step from 1,3-benzodioxoles **3f** and **3g**, respectively (entries 5 and 6).

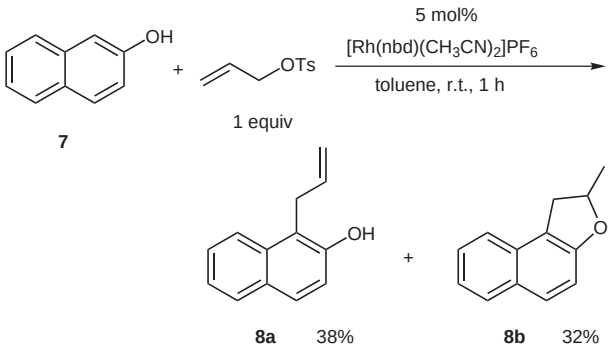
This method is also applicable to the allylation of phenols. Table 2 shows the results of the allylation of various phenols with allyl tosylate. Although the reaction of phenol (**5a**) proceeded with high *para*-selectivity (entry 1), in the allylation of *o*-cresol (**5b**) and *m*-cresol (**5c**), a small amount of *ortho*-isomers such as **6c** were also obtained in addition to the *para*-allylated products (**6b** and **6d**). Furthermore, unlike the case of the *para*-substituted anisole **3d** (Table 1, entry 4), the allylation occurred even using *para*-substituted phenols such as *p*-cresol (**5d**) and *p*-methoxyphenol (**5g**), giving the *ortho*-allylated products **6e** and **6h**, respectively (entries 6 and 10). The reaction of *o*-methoxyphenol (**5f**) afforded eugenol (**6g**) in 64% yield selectively, without the formation of other regioisomers (entry 9). The iridium complex, $[Ir(cod)(CH_3CN)_2]PF_6$, was also effective for the reaction of phenols, giving the allylation products in higher yields than those using the rhodium catalyst with similar regioselectivities (entries 2, 4, 8 and 11).

Naphthols reacted with allyl tosylate at a higher temperature. The allylation of 2-naphthol (**7**) occurred, as expected, only at the C-1 position, giving the allylated product **8a** along with the dihydronaphthofuran **8b** (Scheme 2), which was generated by the cyclization of **8a**.[10] The reaction of 1-naphthol (**9**) afforded only the corresponding cyclized product **10** in a lower yield (Scheme 3).

Table 2 Rhodium-Catalyzed Allylation of Methoxy-Substituted Arenes with Allyl Tosylate[a]

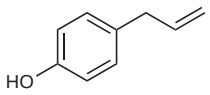
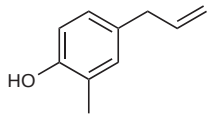
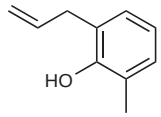
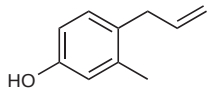
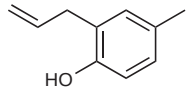
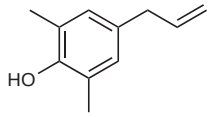
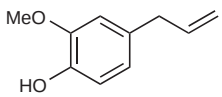
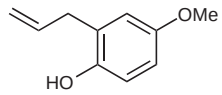
Entry	Arene	Product	Yield[b] (%)
1	anisole (**3a**)	 **4a**	63
2	1,2-dimethoxybenzene (**3b**)	 **4b**	67
3	1,3-dimethoxybenzene (**3c**)	 **4c**	59[c]
4	1,4-dimethoxybenzene (**3d**)		0
5	1,3,5-trimethoxybenzene (**3e**)	 **4d**	96
6	1,3-benzodioxole (**3f**)	 **4e**	45
7[d]	4,7-dimethoxy-1,3-benzodioxole (**3g**)	 **4f**	68[c]

[a] Reaction conditions: **3** (5.0 mmol), allyl tosylate (0.5 mmol), $[Rh(nbd)(CH_3CN)_2]PF_6$ (0.025 mmol), and toluene (1 mL), 0 °C, 15 h.
[b] Determined by GC.
[c] Isolated yields.
[d] 2.0 mmol of **3g** was used.

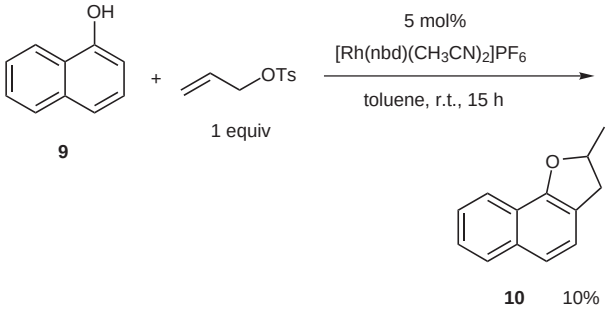


Scheme 2

Table 3 Rhodium- and Iridium-Catalyzed Allylation of Phenol Derivatives with Allyl Tosylate[a]

Entry	Arene	Product	Yield[b] (%)
1	phenol (**5a**)	 **6a**	54[c]
2[d,e]	**5c**	**6a**	79
3	*o*-cresol (**5b**)	 **6b**  **6c**	76 (**6b**/**6c** = 81/19)
4[d,e]	**5b**	**6b**, **6c**	82 (**6b**/**6c** = 74/26)
5[e]	*m*-cresol (**5c**)	 **6d**	59[f]
6	*p*-cresol (**5d**)	 **6e**	61[c]
7[e]	2,6-dimethylphenol (**5e**)	 **6f**	38[c]
8[d,e]	**5e**	**6f**	100[c]
9[e]	*o*-methoxyphenol (**5f**)	 **6g**	70
10[e]	*p*-methoxyphenol (**5g**)	 **6h**	37[c]
11[d,e]	**5g**	**6h**	68[c]

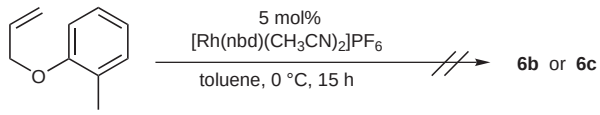
[a] Reaction conditions: **5** (5.0 mmol), allyl tosylate (0.5 mmol), $[Rh(nbd)(CH_3CN)_2]PF_6$ (0.025 mmol), and toluene (1 mL), 0 °C, 24 h.
[b] Determined by GC.
[c] Isolated yields.
[d] $[Ir(cod)(CH_3CN)_2]PF_6$ (0.025 mmol) was used as catalyst.
[e] Reaction time; 15 h.
[f] Contaminated with a small amount of isomers.



Scheme 3

The present allylation smoothly proceeded using electron-rich aromatics, and afforded only *ortho*- and/or *para*-isomers. These results indicate that the reaction proceeds via electrophilic aromatic substitution; however, it cannot be determined whether the free allyl cation or the allylrhodium intermediate generated from allyl tosylate really attacks arenes. Note that the reaction of the anisoles did not exhibit the classical distribution of *ortho*- and *para*-isomers, but exclusive regioselectivity for *para*-isomers, indicating some kind of participation of rhodium in the electrophilic attack of allyl moiety to the arenes.[11] Kočovský reported that the molybdenum-catalyzed allylation of anisole with allylic acetates proceeded via allylic cations with exclusive *para*-selectivity in almost all cases, and consistently accounted for the selectivity by the HOMO-LUMO interactions and the steric repulsions between the methoxy group of anisole and the substituents on the allylic cation.[8a] While the *para*-selectivity is extremely high in case where the repulsion is significant; both *para*- and *ortho*-isomers are obtained in cases in which the repulsion is small. In the present rhodium-catalyzed allylation, however, the reaction of anisoles with allyl tosylate afforded only the *para*-isomers, whereas the steric repulsion was extremely small in these cases. Further investigation is needed to elucidate the precise reaction mechanism and the reason for high regioselectivity.

Unlike the reaction of anisoles, the *ortho*-allylation products were obtained in some of the reactions of phenols. It is well known that the Claisen rearrangement of allyl aryl ethers affords allylphenols[12] and is accelerated in the presence of Lewis acids or transition metal complexes.[12d,13] It is possible that O-allylated products, allyl aryl ethers, are initially produced in the present rhodium-catalyzed allylation of phenols, and are then rearranged to allylphenols. The existence of two paths, the Claisen rearrangement and the direct C-allylation, to the allylphenols possibly causes the formation of both of the *ortho*- and *para*-isomers. To address this issue, the Claisen rearrangement of allyl *o*-tolyl ether (**11**) was attempted as shown in Scheme 4. Under the same reaction conditions, neither the allylphenols **6b** nor **6c** were obtained. This result indicates that the present allylation does not proceed via the Claisen rearrangement, but by direct C-allylation.



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Scheme 4

In summary, we have developed a new method for the allylation of electron-rich arenes, which proceeds at a low temperature (0 °C) with extremely high regioselectivity, especially using anisoles, and gives *para*-allylated products.[14]

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(10) The cyclization of **8a** catalyzed by TsOH, which generated from the reaction of allyl tosylate and **7**. Treatment of **8a** with 50 mol% of $TsOH \cdot H_2O$ for 15 h at room temperature in toluene afforded **8b** quantitively.

(11) Reactions with cotyl tosylate and 1-methyl-2-propenyl tosylate should provide some information about the mechanism. However, we were not able to prepare 1-methyl-2-propenyl tosylate because of its instability.

(12) For reviews, see: (a) Wipf, P. In *Comprehensive Organic Synthesis*, Vol. 5; Trost, B. M.; Fleming, I.; Paquette, L. A., Eds.; Pergamon Press: Oxford, UK, **1991**, 827. (b) Rhoads, S. J.; Raulins, N. R. *Org. React.* **1975**, *22*, 1. (c) Bennett, G. B. *Synthesis* **1977**, 589. (d) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205.

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(14) **Typical Procedure:** To a suspension of an arene (5.0 mmol) and $[Rh(nbd)(CH_3CN)_2]PF_6$ (0.025 mmol) in dry toluene (1 mL), allyl tosylate (0.5 mmol) was added at 0 °C under an N_2 atmosphere. After stirring for 15 h or 24 h, the mixture was filtered thorough a plug of silica, followed by washing with diethyl ether (ca. 30 mL). The solvent was removed under reduced pressure to give an oil that was further purified by flash column chromatography to yield an allylated product. The products obtained were identified by comparison of their ^1H NMR spectral data with those of commercial or reported samples.