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α–Selective Cross-coupling Reaction of Allyltrifluorosilanes: Remarkable Ligand Effect on the Regiochemistry

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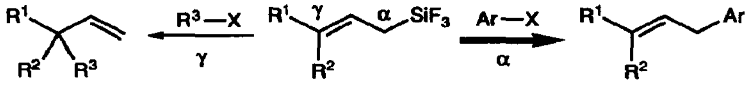
Abstract: The cross-coupling reaction of allyltrifluorosilanes with aryl halides or aryl triflates promoted by a fluoride salt takes place at the α-carbon of the allyltrifluorosilanes in the presence of a catalytic amount of $PdCl_2[Ph_2P(CH_2)_nPPh_2]$ (n = 2, 3), giving allylic arenes with high regioselectivity.

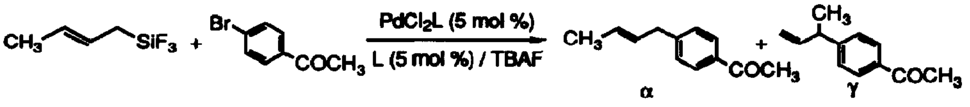
Electrophilic substitution of allylsilanes has been well-established to proceed through S_E' mechanism with γ-selectivity.[1] The γ-selectivity is also observed in the cross-coupling reaction of allyltrifluorosilanes with organic halides or triflates in the presence of a fluoride salt and a catalytic amount of $Pd(PPh_3)_4$.[2] We have found that the regioselectivity of this reaction is strongly influenced by the nature of a palladium catalyst and report herein that high degree of *α-selectivity* can be realized by using an appropriate diphosphine ligand.



R^1, R^2 = H, Me; R^3 = aryl, alkenyl, Ar = aryl, X = OTf, Br, I

In order to evaluate the effect of a phosphine ligand (L) on the regioselectivity of the cross-coupling reaction, (*E*)-crotyltrifluorosilane[3] was allowed to react with 4-bromoacetophenone in a sealed tube at 120 °C in the presence of $n\text{-}Bu_4N^+F^-$ (TBAF), $PdCl_2L$ (5.0 mol %), and L (5.0 mol %) in tetrahydrofuran (THF). The reaction gave a mixture of 1-(4-acetylphenyl)-2-butene (α-coupled product) and 1-(4-acetylphenyl)-1-methyl-2-propene (γ-coupled product) in moderate to good yields. The results summarized in **Table 1** apparently show that the length of the methylene chain (n) of chelating diphosphines $Ph_2P(CH_2)_nPPh_2$ significantly affects the regioselectivity. Thus, the α/γ ratio decreases in the order n = 2 (dppe) $\sim$ n = 3 (dppp) >> n = 1 (dppm) > n = 4 (dppb) > n = 5 (dppent) > PPh_3. High α-selectivity of the cross-coupling reaction was achieved by using $PdCl_2(dppe)$ or $PdCl_2(dppp)$ as a catalyst (α : γ = 97 : 1 and 99 : 1, respectively) (entries 2 and 3). In contrast, palladium catalysts such as $PdCl_2(dppb)$, $PdCl_2(dppent)$ and $PdCl_2(PPh_3)_2$ preferentially gave the γ-coupled product (entries 4, 5 and 6).[2a] Low regioselectivity was observed in the reaction catalyzed by $PdCl_2$(dppm) (entry 1).[4]

Table 1. Ligand Effect on the Regioselectivity of the Cross-coupling Reaction of (*E*)-crotyltrifluorosilane with 4-Bromoacetophenone Promoted by $PdCl_2L$ and TBAF[a]



Entry	L	Reaction time / h	Product ratio		Yield / %[b]
			α (*E*:*Z*) :	γ	
1	$Ph_2PCH_2PPh_2$ (dppm)	23	55 (4.6 : 1) :	45	85
2	$Ph_2P(CH_2)_2PPh_2$ (dppe)	18	97 (8.1 : 1) :	1	86
3	$Ph_2P(CH_2)_3PPh_2$ (dppp)	15	99 (7.2 : 1) :	1	92
4	$Ph_2P(CH_2)_4PPh_2$ (dppb)	6	16 (4.3 : 1) :	84	57
5	$Ph_2P(CH_2)_5PPh_2$ (dppent)	41	6 (4.8 : 1) :	94	77
6	Ph_3P [c]	12	0 :	100	97

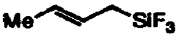
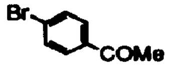
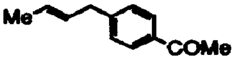
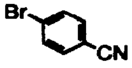
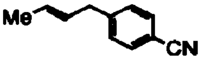
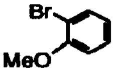
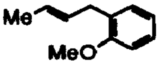
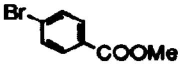
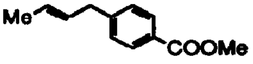
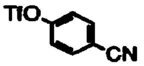
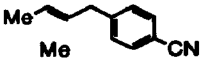
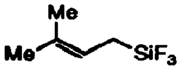
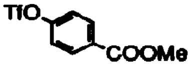
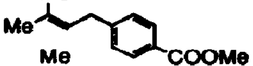
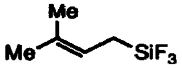
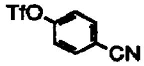
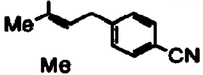
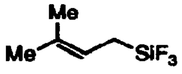
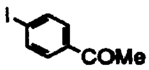
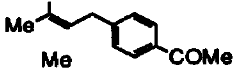
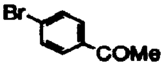
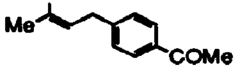
[a] All reactions were carried out in a sealed tube with (*E*)-crotyltrifluorosilane (0.60 mmol) with 4-bromoacetophenone (0.15 mmol) in the presence of a palladium catalyst (7.5×10^{-3} mmol), a ligand (7.5×10^{-3} mmol) and TBAF (0.45 mmol) in THF at 120 °C unless otherwise noted. [b] Isolated yields. [c] Phosphine (1.5×10^{-2} mmol) was used.

The optimized conditions were applied to the reaction of various aryl halides and triflates (**Table 2**).[5] (*E*)-Crotyltrifluorosilane smoothly reacted with aryl bromides or triflates to give the corresponding α-coupled product selectively ($\alpha : \gamma = > 99 : 1$) in good yields (entries 1-5). It should be noted that these are the first successful examples of the highly α-selective cross-coupling reaction of crotylmetal reagents with organic halides or triflates.[6] The cross-coupling reaction of (3-methyl-2-butenyl)trifluorosilane with aryl triflates also smoothly proceeded, affording the α-coupled product with high selectivity (entries 6 and 7),[7] whereas the reaction with aryl halides led to the low regioselectivity (entries 8 and 9).

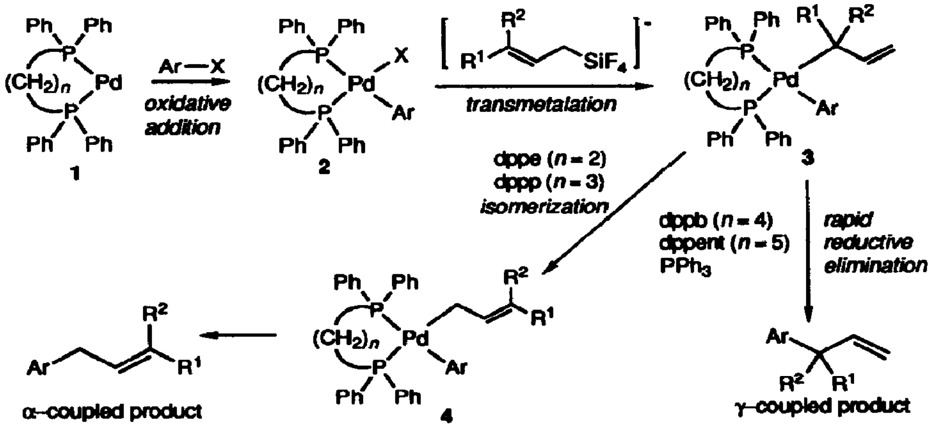
Functional groups such as ester and ketone carbonyls, and cyano group were tolerated under the reaction conditions. Thus, these results demonstrated that the α-selective cross-coupling reaction of allyltrifluorosilanes is one of the most reliable and straightforward route to a wide range of allylic arenes with these functional groups.

A mechanism for the present reaction most likely involves oxidative addition of Ar-X (X = Br, I, OTf) to a palladium(0)-phosphine complex **1** and transmetalation of the resulting arylpalladium(II) **2** with an anionic pentacoordinate allyltetrafluorosilicate[2c] which is formed by the reaction of fluoride ion and allyltrifluorosilanes (**Scheme 1**). Our recent study on transmetalation revealed that electrophilic attack of the arylpalladium(II) complex **2** on the double bond of an allylsilicate takes place exclusively at the γ-carbon so as to yield a σ-allyl(aryl)palladium complexes **3**.[2b] Rapid reductive elimination of **3** should selectively give the γ-coupled product. Diphosphine ligands such as dppb, dppent and PPh_3, which render a wide P-Pd-P bite angle, are considered to sterically accelerate the reductive elimination of **3** ($n = 4, 5$ or PPh_3), thereby favoring predominant formation of the γ-coupled product.[8] On the other hand, the α-selectivity observed in the reaction catalyzed by $PdCl_2$(dppp) or $PdCl_2$(dppe) can be explained in terms of slow reductive elimination of less bulky dppe- or

Table 2. The Cross-coupling Reaction of allyltrifluorosilanes with aryl halides and aryl triflates Promoted by $PdCl_2(dppp)$ and TBAF[a]

Entry	allylsilane	Substrate	Reaction time / h	Product	E / Z	Yield / %[b]
1			12		7.2	92
2			12		5.7	88
3			12		6.5	58
4			12		7.2	95
5			12		5.7	100
6			48		-	60
7			48		-	49
8			50		-	38[c]
9			50		-	35[d]

[a] All reactions were carried out in a sealed tube with allyltrifluorosilane (0.60 mmol) with aryl halides or triflates (0.15 mmol) in the presence of $PdCl_2(dppp)$ (7.5×10^{-3} mmol), dppp (7.5×10^{-3} mmol) and TBAF (0.45 mmol) in THF at 120 °C. [b] Isolated yields. [c] A mixture of regioisomers ($\alpha : \gamma = 73 : 27$) was obtained in 38% yield. [d] A mixture of regioisomers ($\alpha : \gamma = 1 : 1$) was obtained in 35% yield.



Scheme 1

dppp-coordinated **3** (n = 2, 3);[9] these long-lived species can allow isomerization to sterically less crowded σ-allyl(aryl)palladium complexes **4** which give the α-coupled product via reductive elimination.[10]

In conclusion, we have found remarkable ligand effect on the regioselectivity of the palladium catalyzed cross-coupling reaction of allyltrifluorosilanes. The present results should provide an insight into the long-standing problem whether the intermediate in the palladium catalyzed cross-coupling reaction of allylic substrates is a σ-allylpalladium or a π-allylpalladium complex.[10, 11]

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5. The following procedure is representative (**Table 2**, entry 1). To a THF solution of n-Bu$_4$NF 3H$_2$O (1.0 M, 0.45 ml, 0.45 mmol) was added (E)-crotyltrifluorosilane (84 mg, 0.60 mmol) at 0 °C. After stirring at room temperature for 1 h, the THF was removed under reduced pressure, and dry benzene (5 ml) was added to the reaction mixture. Bulk of the benzene was distilled away to remove water as benzene azeotrope. To the resulting mixture was added a THF (1 ml) solution of 4-bromoacetophenone (30 mg, 0.15 mmol), PdCl$_2$(dppp) (4.4 mg, 7.5 x 10^{-3} mmol), and dppp (3.1 mg, 7.5 x 10^{-3} mmol). The reaction mixture was heated at 120 °C in a sealed tube for 15 h. Concentration and purification by silica gel column chromatography using hexane/ethyl acetate (10 : 1) gave a mixture of (E)-4-(4-acetylphenyl)-2-butene and (Z)-4-(4-acetylphenyl)-2-butene in 92% (24 mg, E : Z = 7.2 : 1). The E/Z ratio was determined by ^{1}H NMR. The assignment of each product was based on the comparison with the published spectral data: Echavarren, A. M.; Stille, J. K. *J. Am. Chem, Soc.* **1987**, *109*, 5478.
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