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On the regioselectivity of palladium catalyzed cross-coupling reactions of alkenylsilanes: participation of β-cationic organosilicate-palladium species during the transmetallation

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Abstract

The cross-coupling reaction promoted by a palladium catalyst and fluoride salt of 1-[(fluoro)(dimethyl)silyl]-1-phenylethene (**1**) with substituted aryl iodides gave the unexpected *cine*-substitution products (*E*)-1-aryl-2-phenylethenes (**3**) along with the normal *ipso*-substitution product 1-aryl-1-phenylethene (**2**). The product ratios were strongly dependent on the electronic nature of the substituent on aryl iodides: *ipso*-substitution products (**2**) were favoured by an electron-withdrawing substituent, and *cine*-substitution products (**3**) by an electron-donating substituent. On the basis of these observations, the following mechanism of transmetallation of alkenyl(fluoro)silicates with arylpalladium is proposed: electrophilic attack of an arylpalladium complex on the olefinic α-carbon of an alkenyl(fluoro)silicate produces a β-cationic organosilicate-palladium species which then transfers the alkenyl group from silicon to the palladium complex.

Key words: Silane; Palladium; Transmetallation; Regioselectivity

1. Introduction

The cross-coupling reaction promoted by a palladium catalyst and fluoride salt of organosilicon compounds with organic electrophiles has proved useful for selective carbon–carbon bond formation [1]. A plausible mechanism for this reaction involves oxidative addition of an electrophile to a palladium(0) catalyst, followed by transmetallation with an anionic pentacoordinate organo(fluoro)silicate [2] which is formed by nucleophilic attack of fluoride ion on an organosilicon compound. A resulting bis(organo)palladium(II) complex undergoes rapid reductive elimination to give a coupled product and to regenerate the palladium(0) catalyst. Although the mechanisms of oxidative addition and reductive elimination have been well established [3], difficulties in stereochemical and kinetic studies of the transmetallation of transition metal complexes with main group organometallics have severely limited the mechanistic understanding of this reaction [4*].

We have demonstrated that the cross-coupling of alkenyl(fluoro)silanes with aryl halides or alkenyl halides is a reliable method for the synthesis of stereodefined conjugated polyenes [5]. However, the desired *ipso*-substitution reaction is sometimes accompanied by an unexpected *cine*-substitution, *i.e.*, the cross-coupling reaction taking place at the olefinic β-carbon of the alkenyl(fluoro)silanes [6]. For example, the cross coupling of 1-[(fluoro)(methyl)silyl]-1-phenylethene (**1**) with aryl iodide gives a mixture of 1-aryl-1-phenylethene (**2**) and (*E*)-1-aryl-2-phenylethene (**3**). We have studied the effect of substituent on the regioselectivity of the cross-coupling reaction with **1** and proposed that

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* Reference number with an asterisk indicates a note in the list of references.

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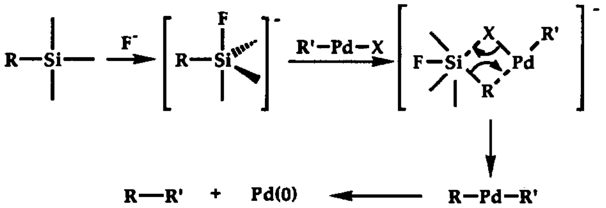


Scheme 1.

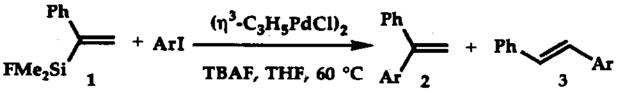
transmetallation of alkenyl(fluoro)silicates with arylpalladium(II) complexes should involve a β-cationic organosilicate-palladium species (5) during alkenyl transfer from silicon to palladium [7].

2. Results and discussion

A series of reactions of **1** with 4-substituted aryl iodides was carried out in the presence of a palladium catalyst and fluoride salt to evaluate the effect of substituent on the regiochemistry of cross-coupling reactions.

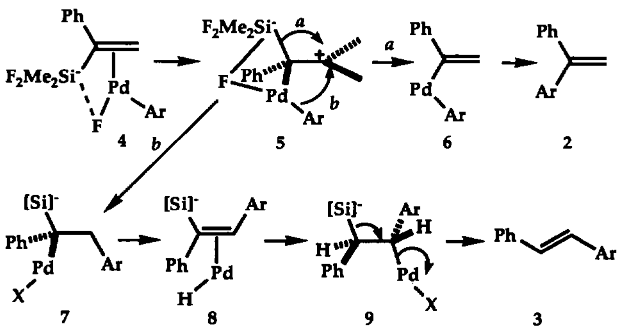
2.1. Substituent effect on the cross-coupling of 1-fluoro(dimethyl)silyl-1-phenylethene (1) with aryl iodides

The cross-coupling of **1** with 4-substituted aryl iodides in the presence of $(\eta^3\text{-}C_3H_5PdCl)_2$ (2.5 mol%) and tetrabutylammonium fluoride (TBAF) (1.1 equiv) in tetrahydrofuran (THF) at 60°C afforded a mixture of an *ipso*-substitution product (**2**) and a *cine*-substitution product (**3**). The ratio **2**/**3** varied depending on the electronic nature of the 4-substituent. The formation of the *ipso*-substitution product (**2**) was favoured by electron-withdrawing groups like trifluoromethyl and acetyl. The relative amount of *ipso*-substitution product (**2**) decreased in step with the decrease of substituent constant σ_p. Thus, the reaction of **1** with 4-(trifluoromethyl)-1-iodobenzene (CF_3, $\sigma_p = +0.54$) gave a mixture of **2** and **3** with a ratio of 93:7, while the reaction with 4-acetyl-1-iodobenzene (CH_3CO, $\sigma_p = +0.50$) and 4-fluoro-1-iodobenzene (F, $\sigma_p = +0.34$) gave the products with ratios of 88:12 and 79:21 respectively. In contrast, the *cine*-substitution was induced by electron-donating groups like methyl and ethoxy, with the corresponding coupled products **2** and **3** being produced in ratios of 59:41 and 60:40 respectively. In addition to electronic effects, steric attributes of the substituents also affected product selectivity. For example, the cross-coupling of bulky 1-iodonaphthalene with **1** gave the *ipso*-substituted product **2** exclusively. These observations led us to propose a mechanism for the transmetallation of alkenylsilanes with palladium complexes as depicted in Scheme 3.



Ar					
4-$CF_3C_6H_4$	24 h	93	:	7	72%
4-AcC_6H_4	20 h	88	:	12	73%
4-FC_6H_4	4 h	79	:	21	80%
C_6H_5	4 h	75	:	25	69%
4-$CH_3C_6H_4$	14 h	59	:	41	84%
4-$C_2H_5OC_6H_4$	20 h	60	:	40	63%
1-naphtyl	21 h	100	:	0	74%

Scheme 2.



Scheme 3. Proposed mechanism for the transmetallation of an alkenylsilane with a palladium complex.

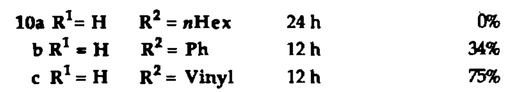
An anionic pentacoordinate silicate, formed by nucleophilic attack of fluoride ion on **1**, can coordinate to an arylpalladium species through a fluoride bridge [4] to form a π-complex (**4**). Subsequent bond formation between the palladium and the olefinic α-carbon of the coordinated alkenylsilicate gives a β-cationic organosilicate-palladium complex (**5**) [8*], whose partial positive charge can be stabilized effectively by the anionic silyl moiety [9*]. Subsequent desilylation (path a) leads to an *ipso*-substitution product (**2**). On the other hand, the presence of an electron-donating substituent on Ar enhances the nucleophilicity of the aryl group to promote intramolecular nucleophilic attack of Ar to the cationic β-carbon (path b). The resulting σ-organopalladium complex (**7**) undergoes β-hydride elimination to give **8**, re-addition of H–Pd–X to produce **9**, and a final desilyl-depalladation to afford a *cine*-substitution product (**3**). The selective formation of the *ipso*-substitution product (**2**) from the coupling of **1** with 1-iodonaphthalene can be explained by the same scheme. Since the nucleophilic attack of bulky naphthyl group to the cationic centre is sterically retarded, desilylation (path a) may well take place preferentially to yield **2**.

Similar regiochemical scrambling during the palladium catalyzed cross-coupling reactions has been reported for the arylation of 1-deuterio-1-(trimethylsilyl)ethene [6c, d] and 1-trimethylsilyl-1-phenylethene

[6e], which afforded *cine*-substitution products predominantly. A mechanism proposed for the preferential *cine*-substitution involves (1) 1,2-addition of Ar–Pd–X to CH_2=C(Y)$SiMe_3$ (Y = Ph, D) to form Ar–CH_2–CY($SiMe_3$)–Pd–X, (2) β-elimination of H–Pd–X and its re-addition to give Ar–CH(PdX)–CHY($SiMe_3$), (3) desilyl-depalladation of which to yield ArCH=CHY. This mechanism, however, apparently does not apply to the Pd catalyst/F^- promoted cross coupling of **1**, wherein *ipso*-substitution predominated and the regioselectivity was strongly influenced by the nature of substituents. In contrast, the mechanism we propose above can consistently explain the *cine*-substitution observed in these palladium catalyzed coupling reactions. Namely, the cross coupling of alkenyl(trimethyl)silanes in the absence of fluoride salt does not produce the pentacoordinate silicate intermediates, hereby the desilylation akin to path a being markedly slower than aryl migration (similar to path b), leading to the selective formation of the *cine*-substitution product [10*].

2.2. *Substituent effect on the cross-coupling of alkenyl(trimethyl)silanes with aryl iodide*

Participation of a β-cationic organosilicate-palladium species during the transmetallation step is also supported by the following observations. Though (*E*)-1-(trimethylsilyl)-1-octene (**10a**) failed to react with phenyl iodide ((η^3-$C_3H_5PdCl)_2$ (2.5 mol%), TBAF (1.1 equiv), THF, 60°C, 24 h), (*E*)-1-trimethylsilyl-2-phenylethene (**10b**) and 1-(trimethylsilyl)-1,3-butadiene (**10c**) effectively coupled with phenyl iodide under the same conditions to give (*E*)-1,2-diphenylethene (**11b**) and (*E*)-1-phenyl-1,3-butadiene (**11c**) respectively. In contrast, 1-trimethylsilyl-1-phenylethene (**10d**) did not give any coupled products [11*]. The success of the coupling reactions of **10b** and **10c** is apparently due to the nature of the substituent at the olefinic β-carbon; a cation-stabilizing group like phenyl or vinyl remarkably accelerates the coupling reaction. These observations are completely consistent with the mechanism described in Scheme 3.



10a R^1 = H	R^2 = *n*Hex	24 h	0%
b R^1 = H	R^2 = Ph	12 h	34%
c R^1 = H	R^2 = Vinyl	12 h	75%
d R^1 = Ph	R^2 = H	24 h	0%

Scheme 4.

3. Conclusion

The transmetallation of an alkenylsilane with an arylpalladium catalyst was shown to proceed through a β-cationic alkenylsilicate-palladium species, which gives either an *ipso*-substitution product by desilylation or a *cine*-substitution product by aryl ligand migration from Pd to the β-carbon of the alkenylsilicate, depending on the degree of the stabilization of the cationic centre, the ease of desilylation, and the nucleophilicity of the aryl ligand. It can be assumed that this mechanism applies to all types of transition metal catalyzed cross-coupling reactions of alkenylmetal reagents.

4. Experimental details

The ^1H NMR spectra were recorded on a Hitachi R-90 (90 MHz) spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Infrared spectra were obtained on a JASCO A-202 spectrometer. Elemental analyses were carried out with a Perkin Elmer Model 240. Product ratios of coupling reactions were estimated by GC analyses using a Shimadzu GC-14A equipped with a 0.25 mm × 50 m OV-1 capillary column and a flame ionization detector.

THF was freshly distilled from sodium-benzophenone. TBAF (THF solution, 1.1 M) was obtained commercially (Aldrich). (*E*)-1-(Trimethyl)silyl-1-octene (**10a**) was prepared in 92% yield by the reaction of methylmagnesium bromide with (*E*)-1-(trichloro)silyl-1-octene [12] in THF. 2-(3-Iodophenyl)ethyl acetate was synthesized by the reaction of 2-(3-iodophenyl)ethanol with acetyl chloride in the presence of triethylamine in dichloromethane. 4-Ethoxy-1-iodobenzene was prepared by treatment of 4-iodophenol with ethyl bromide in aqueous sodium hydroxide solution. The other aryl iodides used in this work were obtained commercially. The spectra and physical properties of the following products were consistent with the reported data: (*E*)-1-phenyl-1,3-butadiene [13], 1-[4-(trifluoromethyl)phenyl]-1-phenylethene [14], (*E*)-1-[4-(trifluoromethyl)phenyl]-2-phenylethene [15], 1-(4-acetylphenyl)-1-phenylethene [16], (*E*)-1-(4-acetylphenyl)-2-phenylethene [17], 1-(4-methylphenyl)-1-phenylethene [18], (*E*)-1-(4-methylphenyl)-2-phenylethene [15], 1-(4-fluorophenyl)-1-phenylethene [19], (*E*)-1-(4-fluorophenyl)-2-phenylethene [20], 1-(1-naphthyl)-1-phenylethene [21].

4.1. *1-Phenyl-1-[fluoro(dimethyl)silyl]ethene (1)*

To a solution of dichloro(dimethyl)silane (12.8 g, 99 mmol) in THF (40 ml) was added at 0°C (1-phenylethenyl)magnesium bromide prepared from 1-bromo-

1-phenylethene (6.0 g, 33 mmol) and magnesium (1.04 g, 43 mmol) in THF (15 ml). After stirring at room temperature, the bulk of the solvent was removed under reduced pressure, and dry hexane was added to the reaction mixture. The resulting slurry was filtered, and the filtrate was concentrated to give a brown oil. Distillation of this oil at 100°C (22 mmHg) afforded 1-[chloro(dimethyl)silyl]-1-phenylethene as a colourless oil (3.6 g, 18 mmol, 56%): IR (neat) 3060, 2960, 1400, 1260, 845, 790 cm^{-1}; ^1H NMR (90 MHz): δ 0.30 (s, 6H), 5.68 (d, $J = 2.0$ Hz, 1H), 5.82 (d, $J = 2.0$ Hz, 1H), 7.00–7.30 (m, 5H). This chlorosilane was converted to the corresponding fluorosilane. A solution of 1-[chloro(dimethyl)silyl]-1-phenylethene (1.8 g, 9.0 mmol) in ether (5 ml) was added to a suspension of $CuF_2 \cdot 2H_2O$ (0.62 g, 4.5 mmol) in ether (5 ml) at 0°C, and the resulting reaction mixture was stirred at room temperature for 8 h. The mixture was diluted with pentane (50 ml), and filtered. The filtrate was dried over $MgSO_4$, and concentrated to give 1-[fluoro(dimethyl)silyl]-1-phenylethene (**1**) (1.2 g, 6.6 mmol, 73%): bp (bulb-to-bulb) 130°C (14 mmHg); IR (neat) 3050, 2950, 1255, 850, 790 cm^{-1}; ^1H NMR (90 MHz): δ 0.38 (d, $J = 7.5$ Hz, 6H), 5.76 (d, $J = 3.0$ Hz, 3H), 6.00 (d, $J = 3.0$, 3H), 7.20–7.45 (m, 5H). Anal. Calcd. for $C_{10}H_{13}SiF$: C, 66.62; H, 7.27. Found: C, 66.51; H, 7.33%.

4.2. Representative procedure for cross-coupling reaction; reaction of 1-fluoro(dimethyl)silyl-1-phenylethene (1) with 4-ethoxy-1-iodobenzene

A THF solution of TBAF (1.1 M solution, 0.23 ml, 0.25 mmol) was added to 1-[(fluoro)(dimethyl)silyl]-1-phenylethene (**1**) (45 mg, 0.25 mmol), 4-ethoxy-1-iodobenzene (55 mg, 0.20 mmol) and $(\eta^3\text{-}C_3H_5PdCl)_2$ (2.3 mg, 0.0050 mmol) dissolved in THF (1.5 ml) at 0°C under argon atmosphere. The reaction mixture was stirred at 60°C for 4 h. Concentration and purification by column chromatography (silica gel) using hexane gave (E)-1-(4-ethoxyphenyl)-2-phenylethene (11 mg, 25%) and 1-(4-ethoxyphenyl)-1-phenylethene (17 mg, 38%). The ^1H NMR spectrum of (E)-1-(4-ethoxyphenyl)-2-phenylethene was consistent with that reported [22].

1-(4-Ethoxyphenyl)-1-phenylethene: colourless solid, mp 77.0–77.8°C; IR (KBr) 3100, 3000, 1610, 1510, 1245, 845, 790, 710 cm^{-1}; ^1H NMR (90 MHz): δ 1.43 (t, $J = 7$ Hz, 3H), 4.05 (q, $J = 7$ Hz, 2H), 5.33–5.68 (m, 2H), 6.88 (d, $J = 9$ Hz, 2H), 7.30 (d, $J = 9$ Hz, 2H), 7.33 (s, 5H). Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.44; H, 7.38%.

References and notes

1 Y. Hatanaka and T. Hiyama, *Synlett*, (1991) 845.
2 R.J.P. Corriu and J.C. Young, in S. Patai (ed.), *The Chemistry of Organic Silicon Compounds*, Chap. 20, Wiley, New York, 1989.
3 J.P. Collmann, L.S. Hegedus, J.R. Norton and R.G. Finke, *Principles and Applications of Organotransition Metal Chemistry*, Chap. 5, University Science Books, Mill Valley, 1987.
4 Recently, we reported that the transition states of the transmetallation of alkyl(fluoro)silicates with arylpalladium(II) complexes depend on reaction temperature and solvent polarity: (a) Y. Hatanaka and T. Hiyama, *J. Am. Chem., Soc., 112* (1990) 7793; see also: (b) J.W. Labadie and J.K. Stille, *J. Am. Chem. Soc., 105* (1983) 669.
5 Y. Hatanaka and T. Hiyama, *J. Org. Chem., 54* (1989) 268.
6 (a) G. Stork and R.C. Isaacs, *J. Am. Chem., Soc., 112* (1990) 7399; (b) N. Miyaura and A. Suzuki, *J. Organomet. Chem., 213* (1981) C53; (c) K. Karabelas and A. Hallberg, *J. Org. Chem., 51* (1986) 5286; (d) G.D. Daves and A. Hallberg, *Chem. Rev., 89* (1989) 1433; (e) K. Ikenaga, S. Matsumoto, K. Kikukawa and T. Matsuda, *Chem. Lett.*, (1988) 873.
7 Part of this work has been reported [1].
8 It was recently reported that 1,2-addition of a cationic pyridylzirconium complex to vinyl(trimethyl)silane selectively occurred so as to form the Zr–C bond on the α-carbon of vinyl(trimethyl)silane due to the electronic influence of trimethylsilyl group: A.S. Guram and R.F. Jordan, *Organometallics, 9* (1990) 2190.
9 It can be assumed that positive charge stabilization is enhanced by an anionic silicate: H. Sakurai, *Synlett*, (1989) 1.
10 Aryl bromides substituted by an electron-withdrawing group also favoured the *ipso*-substitution in palladium catalyzed cross-coupling with vinylstannanes [6a]. This suggests the participation of a β-stannyl cationic species (E. Negishi, *Organometallics in Organic Synthesis*, Wiley, New York, 1980, p. 416) during the transmetallation with the arylpalladium species.
11 In the cross-coupling with organic halides, 1-fluoro(dimethyl)silyl-1-phenyl-1-ethene is much more reactive than 1-trimethylsilyl-1-phenylethene, since the fluoro(dimethyl)silyl group can effectively stabilize the negative charge of the pentacoordinate silicate intermediates to promote the cross-coupling, whereas the trimethylsilyl group cannot do so: Y. Hatanaka and T. Hiyama, *J. Org. Chem., 54* (1989) 268.
12 K. Tamao, H. Yamamoto, M. Kakui, M. Akita, M. Ishikawa, J. Yoshida and M. Kumada, *Organometallics, 1* (1982) 355.
13 E.J. Corey and D.E. Cane, *J. Org. Chem., 34* (1969) 3053.
14 M.F. Ruasse and E. Lefebvre, *J. Org. Chem., 49* (1984) 3210.
15 W.J. Bard and W.E. McEwen, *J. Org. Chem., 55* (1990) 493.
16 Z. Xu, C.R. McArthur and C.C. Leznoff, *Can. J. Chem., 61* (1983) 1405.
17 A. Altomare, C. Carlini, M. Panattoni and R. Salano, *Macromolecules, 17* (1984) 2207.
18 K. Kikukawa, M. Naritomi, G.X. He, F. Wada and T. Matsuda, *J. Org. Chem., 50* (1985) 299.
19 F. Bergmann and J. Szmuszkowicz, *J. Am. Chem. Soc., 70* (1984) 2748.
20 J.M. Gascoyne, P.J. Mitchell and L. Phillips, *J. Chem. Soc., Perkin Trans., 2* (1977) 1051.
21 K. Maruyama, T. Otsuki and K. Mitsui, *J. Org. Chem. 45* (1980) 1424.
22 K. Sugioka, M. Uchiyama, T. Suzuki and Y. Yanagi, *Nippon Kagaku Kaishi*, (1985) 527.