Mini-account

How I came across the silicon-based cross-coupling reaction

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Abstract

Briefly reviewed are the historical background, motivation for invention, and salient features of the silicon-based cross-coupling reaction, now simply called Hiyama Coupling, in addition to recent progress. © 2002 Elsevier Science B.V. All rights reserved.

1. Background

In 1981, I started my research group at Sagami Chemical Research Center, focusing on the activation of C–Si and Si–Si bonds using a fluoride ion to generate the corresponding naked anionic species that were otherwise destabilized by metallic counter ions. Typical examples are synthetic reactions of Me_3Si–$SiMe_3$ [1] with 1,3-butadienes, reduction of ketones with $HSiMe_2Ph$ [2], and carbonyl addition of carbenoid-type carbanions $^-CX_nR_{3-n}$ [3], all mediated at room temperature by TBAF (n-Bu_4NF) or TASF $\{(Et_2N)_3S^+ (Me_3SiF_2^-)\}$, as summarized in Scheme 1.

2. Invention of organosilicon-based cross-coupling reaction

During the course of these studies, we envisaged what would happen if a Pd complex was present in the reaction mixture. Does a fluoride ion simply attack Pd(II) to deactivate the catalyst? Fortunately, this was not the case. Even in the presence of a Pd complex, a fluoride ion was found to preferentially attack Si to generate anionic species that were later proved to be pentacoordinated silicates, and involvement of this species was shown to be essential for smooth transmetalation of organosilicon reagents to complete the catalytic cycle of the cross-coupling reaction [4–7]. On the basis
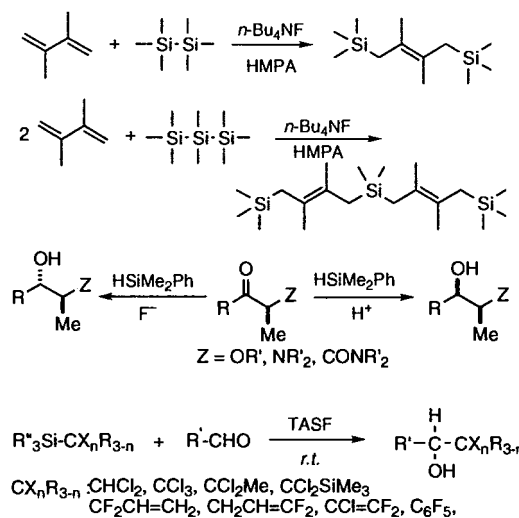
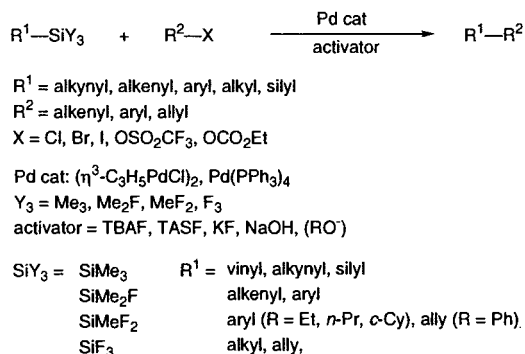Scheme 1. Fluoride ion-mediated synthetic reactions.

of substituent effect on silicon, we considered that the transmetalation should proceed via a 4-centered transition state, in which the pentacoordinated silicate is fully coordinated to become hexacoordinated. Scheme 2 summarizes the silicon-based cross coupling reaction and demonstrates that a variety of organic groups on Si are applicable to the reaction.

3. Attempts prior to ours

Prior to our findings, there were a few examples of desilylative coupling of organosilanes with aryl halides

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$$R^1-SiY_3 \quad + \quad R^2-X \quad \xrightarrow[\text{activator}]{\text{Pd cat}} \quad R^1-R^2$$

R^1 = alkynyl, alkenyl, aryl, alkyl, silyl
R^2 = alkenyl, aryl, allyl
X = Cl, Br, I, OSO_2CF_3, OCO_2Et

Pd cat: $(\eta^3\text{-}C_3H_5PdCl)_2$, $Pd(PPh_3)_4$
Y_3 = Me_3, Me_2F, MeF_2, F_3
activator = TBAF, TASF, KF, NaOH, (RO^-)

SiY_3 =	$SiMe_3$	R^1 =	vinyl, alkynyl, silyl
	$SiMe_2F$		alkenyl, aryl
	$SiMeF_2$		aryl (R = Et, n-Pr, c-Cy), ally (R = Ph)
	SiF_3		alkyl, ally,

Scheme 2. Summary of the silicon-based cross-coupling reaction (Hiyama coupling).

with the aid of a pallaidum catalyst. Kumada, Tamao, and their coworkers [8] as well as Hallberg et al. [9] reported that organo(pentafluoro)silicate and trimethyl-(vinyl)silane, respectively, coupled with iodobenzene to afford products. Later, Kikukawa and his coworkers revealed that arenediazonium tetrafluoroborates were a good coupling partner for α- and β-trimethylsilyl-substituted styrenes [10–12]. These reactions can be now considered to involve carbopalladation toward the C–C bond of alkenylsilanes in sharp contrast to the one involving pentacoordinated species.

4. Importance of pentacoordinated silicate

To facilitate the transmetalation, or to assist the formation of pentacoordinated silicates, we introduced fluorine(s) onto Si, depending on the organic group to be transmetalated [13]. The fluorine substituent may be replaced by an alkoxy, hydroxyl, or any other heteroatom substituents, as demonstrated later by us [14] and others [15].

When allylic carbonates or vinyloxiranes were employed as the substrate, the reaction proceeded without any activator, because p-allylic palladium complexes formed by the reaction of Pd(0) with the substrate generated oxygenic nucleophilic species that could attack the Si of the coupling partners to give rise to pentacoordinated species [16].

The silicon-based coupling reaction was applied to the synthesis of HMG-CoA reductase inhibitor NK104 [17], biaryls and heterobiaryls [18]. A convenient one-pot synthesis is illustrated in Scheme 3 18c.

5. Silicon has advantages

What is the advantage of silicon? It would be safe to say that it is a comparably environmentally benign element, since organosilicon compounds are oxidized ultimately to biologically inactive silica gel. Various organosilicon reagents are now available owing to the growth of silicon industry. In addition, the configuration of a silyl-substituted carbon is stable and thus optically active organosilicon compounds are available via asymmetric reactions [19]. This character facilitated the stereochemical study of transmetalation step, which had remained relatively unexplored. In fact, we found that transmetalation in THF at low temperatures proceeded with retention of configuration, whereas at higher temperatures or in polar solvents, inversion became to prevail [20]. The data are shown in Fig. 1. We consider retention of configuration is attributable to a cyclic transition state in transmetalation like S_E2 (cyclic) illustrated in Scheme 4, whereas, inversion to S_E2 (open) transition state that lacks the interaction between Pd and F (or halogen) on silicon.
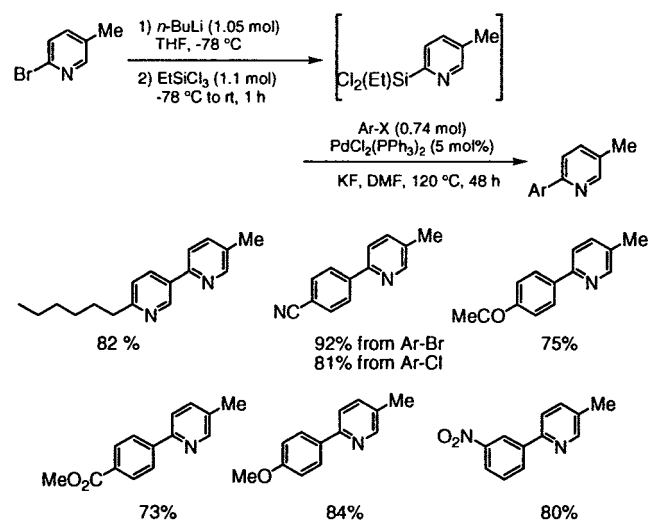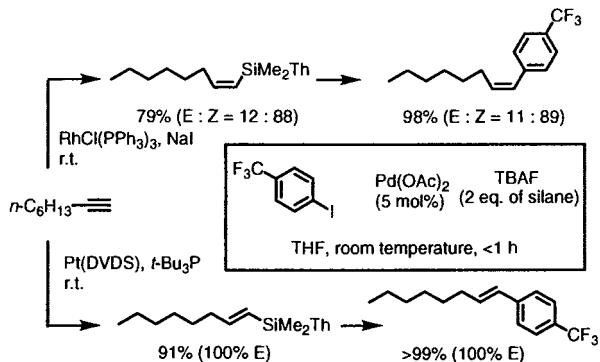
Scheme 3. Practical synthesis of 2-aryl-3-methylpyridines.
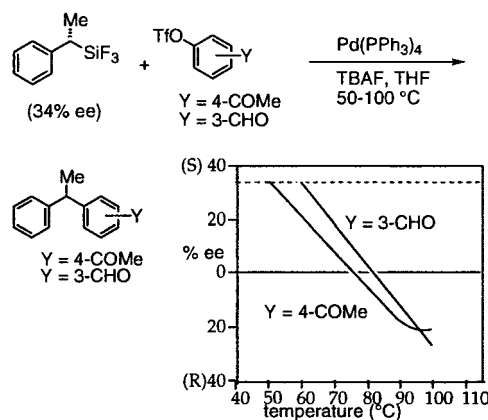
Fig. 1. Temperature vs. stereochemistry of cross-coupling of (S)-$PhCH(Me)SiF_3$ (34% ee) with substituted phenyl triflates.
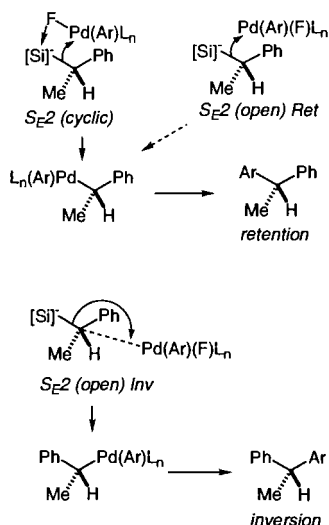
Scheme 4. Stereochemical course of transmetalation.

Scheme 5. Synthesis of (Z)- and (E)-1-octenyl(4-trifluoromethyl)-benzenes.

6. Recent progress

Recently, we have applied the reaction to polymer-supported coupling reaction to find that phenyl–phenyl coupling as well as phenyl-2-pyridyl coupling proceed as well [21], whereas, 2-furyl and 2-thienyl groups failed to give heterobiaryls. The negative results have led us to find 2-thienyl group (Th) is a nice activating group on Si. Typical examples starting with stereoselective hydrosilylation of 1-octyne with HSiMe$_2$Th followed by the stereospecific cross-coupling reaction are shown in Scheme 5 [22]. Salient features of a Th group are: (1) alkenyl(Th)silanes can be handled without any precautions and (2) an alkenyl–Si bond is appropriately activated to accept nucleophilic attack by a fluoride ion and thus to facilitate transmetalation. Accordingly, the silicon-based cross-coupling reaction is becoming much more accessible than before with the aid of a Th group on silicon.

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