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Review

A historical note of the Stille reaction

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Abstract

This is a historical note of our early works, but not a comprehensive story. Starting from free radical allylation of organic halide with allyltributyltin, we found palladium-catalyzed cross-coupling reactions of organic halides with organotin compounds and developed their scope. Subsequently, we worked on palladium-catalyzed ternary coupling reactions of organic halides, olefins, and organotin compounds. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Palladium and compounds; Cross-coupling; Organic halides; Tin and compounds

1. Introduction

Transition metal-catalyzed reaction of organo-electrophiles with organotin compounds is one of the most useful and efficient carbon–carbon bond forming reactions and now called the Stille reaction. We would like to give a historical note on mainly what we have done in early days.

In the late 1960s, we were interested in the free radical dehalogenation (reduction) of organic halides using tributyltin hydride [1]. The reaction was very characteristic compared with chlorination, but it was not economical, we thought, because chemical prices were determined by their weights, and only a hydrogen atom, the lightest element of tributyltin hydride, was introduced to the product (Scheme 1).

So we devised the reaction in which heavier group than hydrogen atom could be utilized. Published in 1973 was the free radical allylation of organic halides with allyltributyltin. This was our first report using an organotin compound [2]. A similar reaction was also reported in the same year and the same journal by Pereyre and his coworker in France [3] (Scheme 2).

It took time until the reaction was recognized as an important free radical carbon–carbon bond forming reaction by the Keck's reports [4]. The reaction was limited, however, acid chloride and aryl iodide could not be allylated under free radical conditions, while they could be reduced by tributyltin hydride. At that time, we were impressed with Kharasch type reactions, which use inorganic salt and sometimes improves product yields. The first palladium-catalyzed reaction of organotin compounds was published in 1976 by Eaborn and coworkers [5] and was also considered as a Kharasch type reaction. Subsequently, the reaction turned out to be a general method for the preparation of organotin compounds as described later (Scheme 3).

During the investigation of our free radical allylation, we found that some of the reaction proceeded well in the presence of a catalytic amount of transition metal complexes. In 1977, we published three papers as shown later. Fortunately, these were recognized as the first reports of transition metal-catalyzed carbon–carbon bond-forming reactions using organotin compounds [6–8] (Scheme 4).

Initial Stille's report using organotin compounds was published in 1978 [9], dealing with a ketone synthesis. They used a $BnPdCl(PPh_3)_2$ catalyst and an HMPA solvent under reaction conditions much milder than ours, and yields were also significantly improved. A major difference from our results was a selection of solvent. Negishi reported the coupling reaction of ethynyltin with aryl iodide in the same year [10].

In 1979, Cacchi et al. reported a Michael addition using tetraphenyltin under two phase system [11]. Stille's full paper of ketone synthesis [12], the coupling of

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$$RX + Bu_3SnH \xrightarrow{\text{Initiator}} RH + Bu_3SnX$$

Scheme 1.

$$RX + CH_2{=}CHCH_2SnBu_3 \xrightarrow{\text{Initiator}} RCH_2CH{=}CH_2 + Bu_3SnX$$

Scheme 2.

$$Bu_3SnSnBu_3 + ArBr \xrightarrow{Pd(PPh_3)_4} ArSnBu_3 + ArAr + Bu_3SnBr$$

Scheme 3.

$$RCOCl + CH_2{=}CHCH_2SnBu_3 \xrightarrow{RhCl(PPh_3)_3} RCOCH_2CH{=}CH_2 + Bu_3SnCl$$

$$RCOCl + R'SnBu_3 \xrightarrow{Pd(PPh_3)_4} RCOR' + Bu_3SnCl$$

$$ArX + CH_2{=}CHCH_2SnBu_3 \xrightarrow{Pd(PPh_3)_4} ArCH_2CH{=}CH_2 + Bu_3SnX$$

Scheme 4.

tetraorganotin with aryl and benzyl halides [13], and the mechanistic investigation [14] appeared at the same time, followed by the first report of carbonylative coupling using organotin compounds as disclosed by Tanaka [15].

In 1980, Beletskaya and coworkers came to this area to report the syntheses of aryl and allyltins using ditins [16] and the coupling of aryl halides with some tin compounds [17]. She published many papers focusing on the use of ligandless palladium. Her review appeared in 1983 [18]. Guibe et al. reported palladium-catalyzed reaction of acyl chlorides with tin hydride [19]. Trost and Keinan reported allylic alkylation using enoltins and allyltins [20]. At this stage, available groups on organotin compounds were alkyl, aryl, allyl, alkenyl, alkynyl, and even hydride groups. The three-step catalytic cycle that involves oxidative addition, transmetalation and reductive elimination proposed by Stille was a guide to the subsequent works.

From the viewpoints of aromatic substitution, a pioneering work of Eaborn's and coworkers [5] was useful under controlled conditions for the synthesis of aryltributylstannanes bearing a reactive functional group. The stannanes were difficult to prepare by conventional Grignard methods. The reaction was investigated by many groups and became a useful synthetic procedure for the preparation of tin compounds in general [16,20–23] (Scheme 5).

$$ArX + Bu_3SnSnBu_3 \xrightarrow{Pd(PPh_3)_4} ArSnBu_3 + Bu_3SnX$$

$$Ar = NO_2C_6H_4\text{-}, NCC_6H_4\text{-}, MeCOC_6H_4\text{-}$$

Scheme 5.

From the structural analogy of allylation, aromatic acetonylation was investigated and could be achieved using acetonyltributyltin prepared in situ from isopropenyl acetate and methoxytributyltin [24a]. The reaction was, for example, applied to the synthesis of functionalized nucleosides [24b]. Dichlorobis(tri-*o*-tolylphosphine)palladium was used as a catalyst for the first time in this protocol. This catalyst was originally used by Heck and Ziegler [25] (Scheme 6).

It was found that aromatic amination was also possible using this catalyst [26] owing to serendipity. Our intention was to prepare α-tributylstannylacetate in situ by the reaction of acetate with stannylamine as a base, followed by the palladium-catalyzed reaction of α-tributylstannylacetate with aryl bromide, and found that an aniline derivative was produced unexpectedly.

Quite recently (in 1995), the reaction has entered a second stage, that is, the tin-free reaction (amine and sodium *t*-butoxide instead of stannylamine) as developed by Hartwig [27] and Buchwald [28] group, independently. Preparation of an arylacetate was possible using a tributylstannylacetate which was prepared by the reaction of ketone with ethoxytributyltin. In this case, zinc halide as an additive was necessary to get good yields of products [29] (Scheme 7).

Methoxymethylation [30], hydroxymethylation [31a] applied to the synthesis of carbapenem derivatives quite recently [31b], and cyanomethylation [32] are also possible using the corresponding tin compounds, though thiomethylation and aminomethylation failed (Scheme 8).

Aromatic thiolation is possible [33], but this is not useful, because tin free system has already been developed [34] (Scheme 9).

Vinyl triflates instead of halides were introduced by Stille and coworkers 35. Triflates are quite useful and now widely accepted in organic synthesis (Scheme 10).

In 1986, the famous Stille's review was published [36]. Mitchell also reviewed in the same year [37]. The monograph 'Tin in Organic Synthesis' appeared next year [38]. Since then it has been recognized that the organotin protocol is useful for organic synthesis. Mitchell's second review covered literature from 1985 to 1990 [39]. A number of synthetic applications were introduced in his review. Among them, a quite impressive work was published in 1988 by Farina et al. who developed new ligands on palladium such as tri(2-furyl)phosphine or triphenylarsine [40,41]. Use of these ligands makes the reaction conditions much milder to allow the synthesis of unstable natural products. Activa-

$$\begin{tikzcd}[column sep=small]
 & & Bu_3SnOMe + CH_2{=}C(OAc)CH_3 \arrow[d] & & \\
ArX & + & {[Bu_3SnCH_2COCH_3]} \arrow[rr, "PdCl_2(Po\text{-}tol_3)_2"] & & ArCH_2COCH_3 + Bu_3SnX
\end{tikzcd}$$

Scheme 6.

$$\mathrm{ArBr} + \mathrm{Bu_3SnNEt_2} \xrightarrow{\mathrm{PdCl_2(P}o\text{-}\mathrm{tol_3)_2}} \mathrm{ArNEt_2} + \mathrm{Bu_3SnBr}$$

$$\mathrm{ArBr} + \mathrm{Bu_3SnCH_2CO_2Et} \xrightarrow[\mathrm{ZnBr_2\ in\ DMF}]{\mathrm{PdCl_2(P}o\text{-}\mathrm{tol_3)_2}} \mathrm{ArCH_2CO_2Et} + \mathrm{Bu_3SnBr}$$

Scheme 7.

$$\mathrm{ArBr} + \mathrm{Bu_3SnCH_2OMe} \xrightarrow[\mathrm{HMPA}]{\mathrm{PdCl_2(PPh_3)_2}} \mathrm{ArCH_2OMe} + \mathrm{Bu_3SnBr}$$

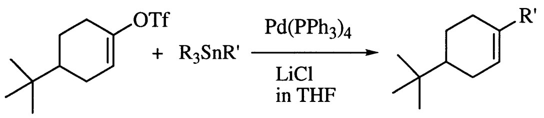
$$\mathrm{ArBr} + \mathrm{Bu_3SnCH_2OH} \xrightarrow[\text{1,4-dioxane}]{\mathrm{Pd(PPh_3)_4}} \mathrm{ArCH_2OH} + \mathrm{Bu_3SnBr}$$

$$\mathrm{ArBr} + \mathrm{Bu_3SnCH_2CN} \xrightarrow[\mathrm{xylene}]{\mathrm{PdCl_2(P}o\text{-}\mathrm{tol_3)_2}} \mathrm{ArCH_2CN} + \mathrm{Bu_3SnBr}$$

Scheme 8.

$$\mathrm{ArBr} + \mathrm{Bu_3SnSR} \xrightarrow{\mathrm{Pd(PPh_3)_4}} \mathrm{ArSR} + \mathrm{Bu_3SnBr}$$

Scheme 9.



Scheme 10.

tion of the reaction by intramolecular coordination is also noteworthy [42] (Schemes 11 and 12).

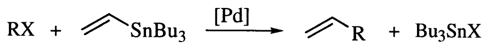
After the Stille's review was published, we started trials to combine the Stille reaction and Mizoroki–Heck reaction [43], that is, the palladium-catalyzed ternary coupling of organic halides, olefins, and organotin compounds (Scheme 13).

Unfortunately, utilizable olefins were quite limited, however, only norbornene and related compounds and 1,3-dioxole were found to be useful [44,45] (Scheme 14).

In 1997, Farina et al. published a comprehensive survey of the Stille reaction from the beginning to 1995 [46]. Mitchell's review published in 1998 covered the references from 1991 to 1996 [47].

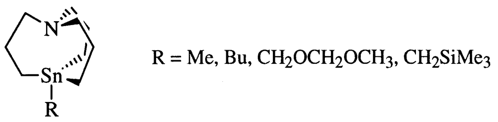
2. Summary

Starting from free radical allylation of organic halide with allyltributyltin, we found palladium-catalyzed cross-coupling reactions of organic halides with organotin compounds and developed their scope. Subsequently, we worked on palladium-catalyzed ternary coupling reactions of organic halides, olefins, and organotin compounds. Today a variety of synthetic chemists use organotin compounds in the presence of palladium complexes. One of the major problems is the toxicity of organotin compounds. To avoid this drawback, several trials gradually appeared recently, for example, fluorous tin [48], polymer-supported tin [49], reactions catalytic in tin [50], monoorganotin [51] etc. We are very happy to be able to contribute some works in this fascinating area.

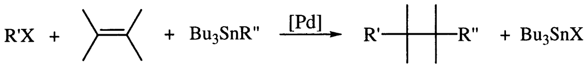


[Pd] = $\mathrm{Pd_2(dba)_3}$ + P(2-furyl)$_3$ or $\mathrm{AsPh_3}$

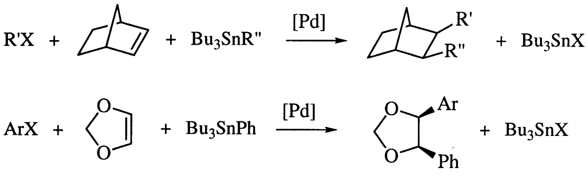
Scheme 11.



Scheme 12.



Scheme 13.



Scheme 14.

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