Tetrabutylammonium Fluoride-Assisted Cross-Coupling Reaction Between Organic Halides and Tetraorganotin Reagents Catalyzed by Palladium

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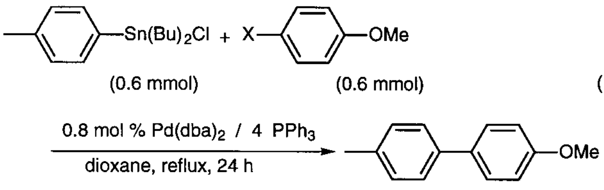
Abstract: Palladium-catalyzed cross-coupling reaction between organostannanes and organic halides are much facilitated by an addition of tetrabutylammonium fluoride (TBAF). All four substituents on tin can take part in the carbon-carbon bond formation. A butyl moiety of tetrabutyltin could also take part in the reaction.

Key words: fluoride, palladium(II) catalyst, tetraorganotin, hypercoordination, cross-coupling

It is well established that the palladium-catalyzed cross-coupling reaction between organic halides and organotins is a useful synthetic reaction.[1] The employment of highly coordinated organotin reagents has widened the scope of the reaction.[2,3] Although organotin molecules can carry four carbon functionalities on a tin atom, only one has been utilized, probably due to the deactivating nature of halogen in the haloorganotin reagents.[1] Therefore, activation of the organotin reagent would be necessary in order to utilize the second or more carbon functionalities.[4] Like in the case of the organosilicon chemistry,[5] generation of a highly coordinated organotin species appears promising. Recently, hyper-valent organotin species were suggested as the active species in the palladium-catalyzed cross-coupling reaction of organotin trichlorides with organic halides in aqueous base.[6] Moreover, highly active organotin reagents were developed by treatment of hetero-substituted organotin species with TBAF.[2] But previous methods require manipulation of labile reagents and/or synthesis of a special reagent. We report here that commercially abundant TBAF highly activates haloorganotin reagents and made it possible to utilize more than one functionality of tetraorganotin reagents for the palladium-catalyzed cross-coupling reaction with aryl halides.

To assess the reactivity of the second functionality, the reaction of *p*-tolyldibutyltin chloride was first examined (eq 1). A typical procedure is as follows: To a dioxane (5 mL) solution of bis(dibenzylideneacetone)palladium (0.01 mmol) and triphenylphosphine (0.04 mmol) was added the halide (1.2 mmol), *p*-tolyldibutyltin chloride (0.6 mmol), and TBAF (an amount indicated in Table 1), successively. The resulting yellow homogeneous solution was refluxed for 24 h. The reaction was cooled to rt and submitted to a VPC analysis to determine the yields of the products after an addition of decane as an internal standard. Isolated yields were obtained by silica-gel column chromatography of the reaction mixture after the evaporation of volatiles.



(1)

As shown in Table 1, the reaction produced the coupling product in the presence of TBAF (runs 3-6), while it did not in the absence of TBAF, at all (runs 1,2). The use of 2 mol equivs of TBAF to the tin reagent gave better results (runs 5,6) than that of 1 mol equiv (runs 3,4). This could be attributed to the consumption of the first equivalent in substitution for chloride on tin. Thus the second equivalent would be necessary to obtain a sufficient reactivity.[2a]

Table 1. The Effect of TBAF on the Reaction of *p*-Tolyldibutyltin Chloride with Haloanisoles

Run	TBAF (mol equiv)	X	Yield (%)[a]
1	0	Br	0
2	0	I	0
3	1	Br	18
4	1	I	41
5	2	Br	48
6	2	I	72

[a] VPC yields

These results encouraged us to investigate the use of tetraorganotins as reagents that supply more than one functionality per one tin. For the reaction of dibutyldi(*p*-tolyl)tin, 2 mol equivs of a halide was used, and 4 mol equivs for a tetraorganotin. The results are summarized in Table 2. A yield is given as the molar ratio between the product and the tin reagent. Both iodo- and bromoanisole reacted with aryltin reagents in the presence of TBAF, though chloroanisole did not (run 11). The larger was the amount of TBAF added, the higher was the number of the functionalities that took part in the reaction (runs 3-10). The highest yields were obtained with 3 mol equivs of TBAF to the tin reagent for the reaction with *p*-bromoanisole and with 4 mol equivs for that with *p*-iodoanisole.

Table 2. The TBAF Assisted Cross-Coupling of Tetraorganotin Reagents

Run	Tin Reagent	X (mol equiv)	TBAF (mol equiv)	Yield[a] (%)
1	$(p\text{-Tol})_2SnBu_2$	Br (2)	0	< 1
2	$(p\text{-Tol})_2SnBu_2$	I (2)	0	0
3	$(p\text{-Tol})_2SnBu_2$	Br (2)	1	96
4	$(p\text{-Tol})_2SnBu_2$	I (2)	1	93
5	$(p\text{-Tol})_2SnBu_2$	Br (2)	2	147 (120)
6	$(p\text{-Tol})_2SnBu_2$	I (2)	2	153
7	$(p\text{-Tol})_2SnBu_2$	Br (2)	3	185 (175)
8	$(p\text{-Tol})_2SnBu_2$	I (2)	3	160 (152)
9	$(p\text{-Tol})_2SnBu_2$	Br (2)	4	188 (174)
10	$(p\text{-Tol})_2SnBu_2$	I (2)	4	181
11	$(p\text{-Tol})_2SnBu_2$	Cl (2)	3	0
12	$(p\text{-Tol})_4Sn$	Br (4)	4	300
13	$(p\text{-Tol})_4Sn$	Br (4)	6	374
14	Bu_4Sn	I (4)	6	(106)

[a] VPC yields. Isolated yields are indicated in parentheses

These results might suggest that bromide ion is more efficacious than iodide in involving the haloorganotin into the reaction, although not so much as fluoride ion is. Indeed, for the reaction between di(*p*-tolyl)dibutyltin and *p*-bromoanisole, the use of three mol equivs of tetrabutylammonium chloride and bromide in place of TBAF (185 %, run 7) resulted in the formations of the coupling product in 135 and 92 % yields, respectively. To our surprise, in this condition, the reaction did not give the desired product in the absence of TBAF, at all (runs 1 and 2). On the other hand, it is now obvious that tetra(*p*-tolyl)tin can provide all four *p*-tolyl groups under the coexistence of 6 mol equivs of TBAF (run 13). The effect of TBAF would be further emphasized with the result obtained with tetrabutyltin of which otherwise inert butyl group could take part in the reaction (run 14).

In comparison with the widely used organotributyltin reagents, the use of tetraorganotins would be advantageous, giving less hazardous inorganic tin waste instead of tributyltin halides that are recently suspected as a kind of endocrine disrupters, and required tin reagents being only a quarter of the halide substrate.

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