APPLIED ORGANOMETALLIC CHEMISTRY
*Appl. Organometal. Chem.* 2004; **18**: 83–85
Published online in Wiley InterScience (www.interscience.wiley.com). DOI:10.1002/aoc.585

*Short communication*

# Stille coupling reactions of functionalized triorganotin halides

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Received 7 November 2003; Revised 12 November 2003; Accepted 13 November 2003

**Convenient conditions for the Stille coupling of halide-bearing triorganotin compounds, which do not normally react under typical Stille reaction conditions, are presented. The coupling of vinylstannanes with allyl bromide using palladium(II) catalysis is accomplished under fluoride assistance to give the substituted 2,5-hexadien-1-ols in *Z*-configuration. Copyright © 2004 John Wiley & Sons, Ltd.**

**KEYWORDS:** Stille coupling; triorganotin halides; allylic alcohols; fluoride assistance

Metal-catalyzed cross-coupling reactions are very important tools for the formation of C–C bonds. The Stille reaction[1] of organotin compounds with organic halides under palladium catalysis is undoubtedly one of the most important ones. To be able to transfer a vinylic residue with defined stereochemistry is one of the most significant features of the Stille reaction.[2]

Historically, the Stille cross-coupling reaction suffered from the disadvantage that only one residue of a compound $R_4Sn$ could be transferred from tin to carbon; the triorganotin halide (later triflate, etc.) formed in the initial transfer reaction was too unreactive to be able to supply other groups. This situation was, however, made use of, as *selective* transfer of the required group R′ starting from $R_3SnR'$ was no problem.

Techniques involving the expansion of the coordination sphere at tin have altered this situation completely. Thus, Fugami *et al.*[3] showed that it is possible to transfer up to two butyl or four aryl groups starting from tetraorganotin using tetra-*n*-butylammonium fluoride (TBAF) as a fluoride donor. Perhaps more importantly, they showed that it is possible starting from *p*-tolyldi-*n*-butyltin chloride to transfer the *p*-tolyl group selectively in a coupling with an aryl chloride to yield a biaryl in moderate to good yields using two equivalents of TBAF. In related work Garcia Martinez *et al.*[4] carried out coupling reactions between vinyl or aryl triflates and triphenyl or tribenzyltin fluoride with the help of TBAF.

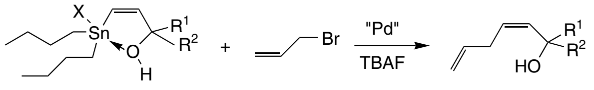
We have recently carried out a detailed study on hydrostannylation of propargylic alcohols using mixed tin hydrides of the type $Bu_2SnHX$ (X = Cl, Br),[5] compounds that have recently exchanged their previous role of laboratory curiosities for one of synthetically valuable reagents, thanks in particular to the work of Shibata and co-workers.[6,7]

These reactions lead, for example, to allylic alcohols bearing a terminal halodibutylstannyl group. The products show intramolecular coordination of the alcohol oxygen with the tin,[5,8] and, as expected, the products do not undergo Stille couplings under standard conditions (data not shown).

We felt, however, that the use of TBAF should make it possible to carry out what is effectively the transfer of a functionalized vinyl group with retention of the configuration of the double bond. Thus, starting from a *Z*-alkene (substituted by $Bu_2SnX$), a *Z*-diene was formed as expected.

Two model systems were chosen for study and were allowed to react with allyl bromide under a variety of conditions (Scheme 1).

The results are shown in Table 1. In all cases, equimolar amounts (2.0 to 2.5 mmol) of both starting materials were used, together with the amounts of catalyst and TBAF indicated in the Experimental section.



X = Cl, Br
$R^1$, $R^2$ = H,H (**A**) or -$(CH_2)_5$- (**B**)

**Scheme 1.** Stille coupling of triorganotin halides with allyl bromide.

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**Table 1.** Reactions of the dibutylhalogenostannylalkenes with allyl bromide and TBAF

| Entry | $R^1$ | $R^2$ | X | TBAF amount | Catalyst | Solvent | Consumption organotin (%)[a] | Isolated yield (%) |
|---|---|---|---|---|---|---|---|---|
| 1 | H | H | Cl | 5% | 1% $Pd(OAc)_2$ | None | 0 | – |
| 2 | H | H | Cl | 5% | 1% $Pd(OAc)_2$ | NMP | 0 | – |
| 3 | H | H | Cl | 3 equiv. | 1% $Pd(OAc)_2$ | NMP | <10 | – |
| 4 | H | H | Br | 3 equiv. | 3% $Pd(OAc)_2$ | NMP | ~70 | – |
| 5 | H | H | Br | 3 equiv. | 5% $Pd(OAc)_2$ | NMP | 100[b] | – |
| 6 | H | H | Br | 3 equiv. | 3% $Pd_2(dba)_3$ | NMP | 100[b] | – |
| 7 | H | H | Br | 3 equiv. | 5% $Pd_2(dba)_3$ | NMP | 100[b] | – |
| 8 | $-(CH_2)_5-$ | | Cl | 1 equiv. | 5% $Pd(OAc)_2$ | None | 0 | – |
| 9 | $-(CH_2)_5-$ | | Cl | 1 equiv. | 5% $Pd(OAc)_2$ | NMP | ~5 | – |
| 10 | $-(CH_2)_5-$ | | Cl | 3 equiv. | 5% $Pd(OAc)_2$ | None | 100 | 31[c] |
| 11 | $-(CH_2)_5-$ | | Cl | 3 equiv. | 5% $Pd(OAc)_2$ | NMP | 100 | 54[c] |
| 12 | $-(CH_2)_5-$ | | Cl | 3 equiv. | 3% $Pd_2(dba)_3$ | NMP | 100 | 26[c] |
| 13 | $-(CH_2)_5-$ | | Cl | 3 equiv. | 3% $BzPdCl(PPh_3)_2$ | NMP | ~5 | – |
| 14 | $-(CH_2)_5-$ | | Cl | 3 equiv. | 3% $Pd(PPh_3)_4$ | NMP | 0 | – |
| 15 | $-(CH_2)_5-$ | | Br | 3 equiv. | 3% $Pd(OAc)_2$ | NMP | 100 | 24[d] |
| 16 | $-(CH_2)_5-$ | | Br | 3 equiv. | 3% $Pd_2(dba)_3$ | NMP | 100 | 27[d] |

[a] As estimated from $^{119}$Sn and $^1$H NMR spectra.
[b] Product not isolable, polymerization and/or rearrangement occurs during purification.
[c] After column chromatography.
[d] After Kugelrohr distillation.

Attempts to work without solvent were unsuccessful except in one case (Table 1, entry 10). A catalytic amount of TBAF or only one equivalent was not sufficient (Table 1, entries 1, 2, 8, 9). Even using three equivalents of TBAF, 1% palladium(II) acetate $Pd(OAc)_2$ did not suffice (Table 1, entry 3), while benzylbis(triphenylphosphine)palladium chloride, $BzPdCl(PPh_3)_2$, and tetrakis(triphenylphosphine)palladium, $Pd(PPh_3)_4$, did not catalyse the reaction (Table 1, entries 13, 14). Thus, we elected to use 3–5% of the palladium catalyst and three equivalents of TBAF.

However, isolation of the 2,5-hexadien-1-ol formed from model system A was unsuccessful in spite of quantitative conversion of the starting material, as seen by $^{119}$Sn NMR (consumption of starting material) and $^1$H NMR spectra. Before purification, the NMR spectra of the oil were consistent with the formation of the required alcohol;[9] column chromatography, however, led to an unidentifiable polymerization and/or rearrangement product with molecular weight (MS) 279.

System B did afford the required alcohol, which was completely characterized by NMR spectroscopy (see Spectroscopic data section), via either column chromatography or Kugelrohr distillation, though isolated yields were, unfortunately, only moderate.

This is partly due to the aqueous workup needed to remove the TBAF. We are confident that further optimization of the reaction conditions (perhaps two equivalents of TBAF would suffice, *vide infra*) and workup procedures will significantly improve isolated yields.

Nevertheless, it has been demonstrated that a vinyl transfer is possible even when starting from the chlorostannyl compound, in which the intramolecular coordination is stronger than in the bromostannyl compound.[10]

In order to obtain some insight into the role of TBAF, a mixture of the bromostannyl compound of system A and one, two or three equivalents of TBAF in $CDCl_3$ was prepared and studied by $^{119}$Sn NMR: the tin chemical shifts were as shown in Table 2 (a glass capillary containing $Me_4Sn$ and $C_6D_6$ was introduced into the sample tube prior to the measurement to provide a lock substance and a reference substance for tin ($\delta(Me_4Sn) = 0$ ppm)).

No Sn–F coupling was observed. The lines are (except when adding only one equivalent of TBAF) not exceedingly broad and the solution stays colourless. The same procedure was followed using *N*-methylpyrrolidin-2-one (NMP) as the solvent (see Table 3). Again, no Sn–F coupling was observed in all cases, so that we have no clear evidence of replacement

**Table 2.** $^{119}$Sn NMR chemical shifts of *Z*-3-bromodi-*n*-butylstannyl-2-propene-1-ol in $CDCl_3$ with varying amounts of TBAF

| TBAF (equiv.) | $\delta_{Sn}$ (112 MHz, $CDCl_3$) (ppm) | Line width (Hz) |
|---|---|---|
| 0 | −1.4 | 7 |
| 1 | −26.5 | 1471 |
| 2 | −61.5 | 296 |
| 3 | −71.0 | 216 |

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**Table 3.** $^{119}$Sn NMR chemical shifts of *Z*-3-bromodi-*n*-butylstannyl-2-propene-1-ol in NMP with varying amounts of TBAF

| TBAF (equiv.) | $\delta_{Sn}$ (112 MHz, NMP) (ppm) | Line width (Hz) | Comments |
|---|---|---|---|
| 0 | −35.9 | 27 | – |
| 1 | −47.5 | 1200 | Green solution |
| 2 | −96.2 | 726 | Brown solution |
| 3 | −102.8 | 991 | Pink solution |

of bromine by fluorine on adding TBAF. It is obvious that NMP breaks down the intramolecular coordination in the organotin,[5] and that the largest high-field shift is observed on adding the second equivalent of TBAF in both solvents, whereas the third has little effect. Thus, it can be speculated that two fluorine atoms (and presumably one NMP, compare Tables 2 and 3) are involved in the reaction. We would have expected to see a clear splitting of the tin resonance with the corresponding multiplicity and $^1J_{Sn-F}$ coupling constants of around 2000 to 2500 Hz.[11] We observe very broad lines at room temperature (line width at half height of the signal: 700–1200 Hz), so that we cannot be sure whether a weak bonding is hidden under the line or not. Coupling constants as small as 780 Hz have been observed for bridging fluorine atoms in complexes with pentacoordinated tinatoms.[12] Variable-temperature NMR measurements would have to be conducted to clarify the binding situation and the number of fluorine atoms involved.

In conclusion, it can be stated that the Stille coupling of halide-bearing triorganotin compounds is possible under mild reaction conditions. The coupling of vinylstannanes with allyl bromide gives the substituted 2,5-hexadiene-1-ols in *Z*-configuration. After optimization of the workup procedures, this will certainly be an important tool for organic chemistry.

## EXPERIMENTAL

2.5 mmol of the di-*n*-butylhalogenovinylstannane (system A: 0.81 g of *Z*-3-di-*n*-butylchlorostannyl-2-propene-1-ol; system B: 0.98 g of *Z*-1-[2-(di-*n*-butylchlorostannyl)-ethenyl]-1-cyclohexanol or comparable amounts of the bromo-di-*n*-butylstannyl compounds, respectively) were placed in a flame dried apparatus under argon. If NMP was used as a solvent, then 10 ml of NMP was added, followed by an equimolar amount of allyl bromide (2.5 mmol, 0.30 g) and 1–5% of palladium catalyst ($2.5 \times 10^{-2}$ to $12.5 \times 10^{-2}$ mmol $Pd(OAc)_2$, $Pd(dba)_2$, $BzPd(PPh_3)_2Cl$ or $Pd(PPh_3)_4$. The appropriate amount of TBAF ($12.5 \times 10^{-2}$ to 7.5 mmol, 39 mg to 2.36 g) was added. After stirring for 12 h at room temperature, heating was applied to 40 to 50 °C for 1 to 3 days. After cooling down to room temperature the reaction mixture was diluted with 30 ml of diethyl ether and poured onto 20 ml of a 0.17 M potassium fluoride solution (10 g KF in 100 ml $H_2O$). After phase separation, the organic layer was washed with 20 ml of the KF solution (0.17 M) and 20 ml of $H_2O$. The solvent was dried and evaporated. Purification was achieved either via Kugelrohr distillation (system B: $4.7 \times 10^{-2}$ mbar, 100 °C) or column chromatography (on silica using *n*-hexane: diethyl ether = 9 : 1 as eluent).

### Spectroscopic data for *Z*-1-penta-1′,4′-dienyl-cyclohexanol

NMR: $\delta_H$ (400 MHz, $CDCl_3$, 23 °C) 5.88 (1H, ddt, 17.3 Hz, 10.5 Hz, 6.2 Hz, H4′), 5.44 (1H, dm, 11.6 Hz, H1′), 5.42 (1H, d, 11.6 Hz, H2′), 5.05 (1H, ddt, 17.3 Hz, 3.5 Hz, 1.7 Hz, $H5'_\beta$), 5.00 (1H, ddt, 10.5 Hz, 3.5 Hz, 1.7 Hz, $H5'_\alpha$), 3.15 (2H, tt, 6.2 Hz, 1.7 Hz, H3′), 1.62 (10H, m, H2–H4); $\delta_C$ (100 MHz, $CDCl_3$, 23 °C) 137.5 (d, C4′), 137.1 (d, C1′), 128.7 (d, C2′), 114.6 (t, C5′), 72.5 (s, C1), 39.2 (t, C2), 32.6 (t, C3′), 25.3 (t, C3), 22.3 (t, C4). IR: $\tilde{\nu}$/cm$^{-1}$ (neat), 3442 ($\nu$(O–H), s), 3078–3008 ($\nu(C-H_{unsat})$, m), 2933–2858 ($\nu(C-H_{sat})$, s), 1450 ($\delta$(C–H), w). MS (70 eV): $m/z$ 166 ($M^+$), 148 ($M^+ - H_2O$), 123 ($M^+$ − All), 109 ($M^+ - C_4H_9$), 96 ($M^+ - C_5H_{11}$), 81 ($M^+ - C_6H_{13}$), 67 ($M^+ - C_7H_{15}$), 55 ($C_4H_7$), 41 ($C_3H_5$). $R_f$ (*n*-hexane: diethyl ether = 9 : 1): 0.23.

## Acknowledgements

C.M.T. thanks the Land Nordrhein–Westfalen for a postgraduate scholarship. This work was supported by the Fonds der Chemischen Industrie.

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