Facile Synthesis of Trifluoromethyl-substituted Enynes: Remarkable Reactivity and Stereoselectivity of Tributyl(3,3,3-trifluoropropynyl)stannane in Carbostannylation of Alkynes

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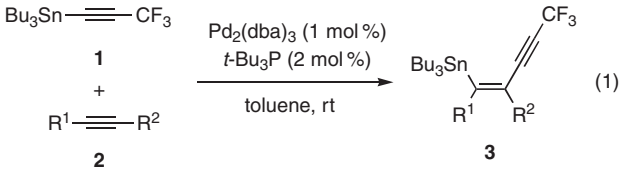
Carbostannylation of alkynes with tributyl(3,3,3-trifluoropropynyl)stannane is found to proceed at *room temperature* in a syn-manner, giving rise to the corresponding CF_3-substituted enynes as *a single stereoisomer* in good yields. Both terminal and, CF_3- or RO_2C-substituted internal alkynes are applicable to the addition reaction. Synthetic applications of the adduct are also demonstrated.

Since carbon–carbon triple bonds can undergo various kinds of transformations, 3,3,3-trifluoropropynyl-containing compounds[1] serve as versatile building blocks for the preparation of trifluoromethylated molecules, to which much attention has been paid in the fields of pharmaceuticals, agrochemicals, and organic materials.[2] Hence, generation and reactions of 3,3,3-trifluoropropynyllithium, -magnesium, -silyl, and -zinc reagents have been studied well.[3] Meanwhile, transition metal-catalyzed carbostannylation of alkynes with alkynylstannanes has emerged as a powerful synthetic tool because an alkynyl and stannyl groups are simultaneously incorporated into alkynes in a syn-manner to afford stereodefined alkenyltins, which can further be transformed into a variety of alkenes via stereospecific carbon–carbon and carbon–heteroatom bond formations with the aid of the tin functionality.[4] Therefore, carbostannylation of alkynes with 3,3,3-trifluoropropynylstannanes is highly attractive for the preparation of diverse trifluoromethylated enynes. We report here palladium-catalyzed carbostannylation of alkynes with tributyl(3,3,3-trifluoropropynyl)stannane (**1**),[5] which proceeds smoothly at room temperature to give CF_3-substituted enynes **3** as a single stereoisomer in good yields (Eq 1).



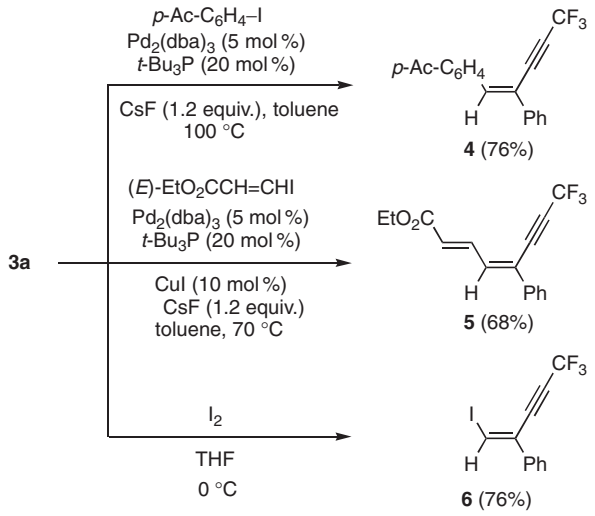
In the course of our synthetic study utilizing **1**, we attempted cross-coupling reaction of **1** with iodobenzene to prepare 3,3,3-trifluoro-1-phenylpropyne. Thus, a toluene solution of **1** and iodobenzene in the presence of $Pd_2(dba)_3$ (1 mol %) and t-Bu_3P (2 mol %) was stirred at room temperature.[6] The isolated product unexpectedly turned out to be alkenylstannane **3** ($R^1 = CF_3$, $R^2 = Ph$) as a single stereoisomer in 40% yield, which was considered to form via carbostannylation of the cross-coupled product with **1**. This result prompted us to investigate generality of the carbostannylation with **1**. The results are summarized in Table 1. Under the same conditions, aryl acetylenes **2a**–**2d** were carbostannylated with **1** at room temperature to give **3a**–**3d** as a stereochemically pure form in good yields (Entries 1–4),[7] respectively. *Z*-Stereochemistry of **3b** determined by NOE data of the vinyl hydrogen and protonolysis of the C–Sn bond[8] indicated that the reaction proceeded via syn-addition and the Bu_3Sn group that was bulkier than a CF_3CC group added to the less hindered sp carbon. Methyl propiolate (**2e**) and *N*,*N*-dimethyl propiolamide (**2f**) also reacted with **1** to afford stereochemically pure **3e** and **3f**, whose stereochemistries were deduced by protonolysis, with the opposite regioselectivity (Entries 5 and 6).[8] Since these stereochemical outcome is consistent with typical carbostannylation, the present reaction is considered to proceed via the well-accepted reaction mechanism,[4] which involves oxidative addition of **1** to the Pd(0) complex and successive insertion of an alkyne to the Pd–C bond followed by reductive elimination, resulting in production of **3** and regeneration of the Pd(0) complex.

Furthermore, the reaction of internal alkynes, which was usually difficult to achieve in the typical alkynylstannylation chemistry,[4] was scrutinized. The results are shown in entries 7–17 in Table 1. To our delight, the addition to CF_3-substituted aryl acetylenes **2g**–**2n** occurred also at room temperature under the same conditions to give **3g**–**3n** as a sole product (Entries 7–14). Various functional groups were tolerant under the conditions. Phenyl- and methyl-substituted propiolate derivatives **2o** and **2p** as well as dimethyl acetylenic dicarboxylate (**2q**) reacted

Table 1. Carbostannylation of alkynes **2** with **1**[a]

Entry	**2**	R^1	R^2	**3**	Yield/%
1	**2a**	H	C_6H_5	**3a**	79
2	**2b**	H	p-MeO-C_6H_4	**3b**	73
3	**2c**	H	p-C_6H_5-C_6H_4	**3c**	82
4	**2d**	H	p-CF_3-C_6H_4	**3d**	79
5	**2e**	CO_2Me	H	**3e**	78
6	**2f**	$CONMe_2$	H	**3f**	58
7	**2g**	CF_3	Ph	**3g**	76
8	**2h**	CF_3	p-Me-C_6H_4	**3h**	52
9	**2i**	CF_3	p-MeO-C_6H_4	**3i**	67
10	**2j**	CF_3	p-Cl-C_6H_4	**3j**	62
11	**2k**	CF_3	p-Ac-C_6H_4	**3k**	68
12	**2l**	CF_3	p-EtO_2C-C_6H_4	**3l**	57
13	**2m**	CF_3	p-O_2N-C_6H_4	**3m**	58
14	**2n**	CF_3	p-CF_3-C_6H_4	**3n**	67
15	**2o**	CO_2Et	Ph	**3o**	87
16	**2p**	CO_2Et	Me	**3p**	77
17	**2q**	CO_2Me	CO_2Me	**3q**	71

[a]Reagents and conditions: **1** (0.6 mmol), **2** (0.9 mmol), $Pd_2(dba)_3$ (6.0 μmol), t-Bu_3P (12 μmol), toluene (1.6 mL), and rt.



Scheme 1. Synthetic application of **3a**.

in a Michael fashion to afford **3o–3q** as a single stereoisomer in good yields, respectively (Entries 15–17). Since diphenylacetylene and 4-octyne did not react with **1** at all, the presence of such an electron-withdrawing group as CF_3 and CO_2R appears to be essential for the realization.

The fact that all the reactions took place at *room temperature* definitely shows remarkably higher reactivity of **1** than those of common alkynyltins which require heating at 50 or 90 °C to effect the carbostannylation reaction.[4] Strong electron-withdrawing effect by a CF_3 group may induce acceleration of the oxidative addition step to undergo the reaction at room temperature, which lead to perfect stereoselectivity.[9]

Alkenyltin functionality of **3** can be readily utilized for further transformation.[10] Representative examples with **3a** are demonstrated in Scheme 1. Pd-catalyzed cross-coupling reaction with aryl and alkenyl iodides gave CF_3-substituted enyne **4** and dienyne **5**, while iodinated enyne **6** was prepared in good yield by treatment with I_2 in THF.

In summary, we have demonstrated that carbostannylation of alkynes with tributyl(3,3,3-trifluoropropynyl)stannane constitutes facile and stereoselective synthesis of 1-tributylstannyl-5,5,5-trifluoropent-1-en-3-ynes. Both terminal and internal alkynes are applicable to the reaction. Synthetic application of the CF_3-substituted enynes is in progress in our laboratory.

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6 No carbostannylated product formed when *N*-[2-(diphenylphosphino)benzylidene]cyclohexylamine, which was essential for conventional carbostannylation of alkynes, or PPh_3 was employed as a phosphine ligand with $Pd_2(dba)_3$ complex.

7 Reaction of alkyl acetylenes with **1** failed to give the carbostannylation products under the conditions.

8 See Supporting Information.

9 In marked contrast, no reaction took place with tributylpropynylstannane under the same conditions, suggesting that the fluorine atoms played a crucial role in the reaction of **1**.

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