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Chemoselective cross-coupling Suzuki–Miyaura reaction of (*Z*)-(2-chlorovinyl)tellurides and potassium aryltrifluoroborate salts

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ABSTRACT

An ultrasound-assisted synthesis of functionalized vinylic chlorides is described by palladium-catalyzed cross-coupling reaction of potassium aryltrifluoroborate salts and (*Z*)-2-chloro vinylic tellurides. This procedure offers easy access to vinylic chlorides architecture that contains sterically demanding groups in good yields.

The main target of transition metal-catalyzed organic synthesis is carbon–carbon bond formation, being the Suzuki–Miyaura reaction one of the most efficient methods for construction of C–C bonds.[1] Organotellurium compounds have attained remarkable development as synthons and intermediates in synthetic organic chemistry.[2] In current decade, the organotellurium compounds have been identified as alternative to halogens as electrophilic partners in some palladium-catalyzed cross-coupling reactions, among these reactions we can mention the Heck,[3] Negishi,[4] Sonogashira[5] and Suzuki–Miyaura.[6] Recently, we have demonstrated the use of some organotellurium compounds in Suzuki–Miyaura reaction using potassium organotrifluoroborate salts as a nucleophilic partners.[6]

Chemoselectivity was observed during the palladium-catalyzed cross-coupling reactions of aryl tellurium compounds containing halide moiety with potassium organotrifluoroborate salts.[6a] The reaction was observed exclusively at the tellurium moiety, and none at the halide.

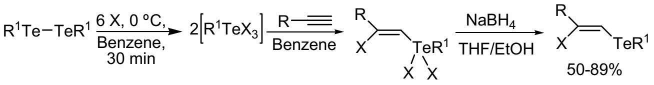
Molander[7] and his research group introduced potassium organotrifluoroborate salts as a nucleophilic partner in the Suzuki–Miyaura reaction instead of unstable organoborons. These reagents are readily prepared by addition of KHF_2 salt to organoboron intermediates,[8] and are crystalline solids indefinitely stable in the air.

Our recent efforts[9] indicated that the metal-assisted cross-coupling reaction of potassium organotrifluoroborate salts and organotellurium compounds can be successfully achieved in few minutes by using ultrasonic waves as a source of energy. The ultrasound effects are attributed to a physical process called cavitation.[10]

Herein, we report the palladium-catalyzed cross-coupling reactions of (*Z*)-butyl(2-chlorovinyl)tellurides with potassium aryltrifluoroborate salts and the chemoselectivity of these reactions. The novelty of this cross-coupling reaction is that of the (*Z*)-2-chloro vinylic tellurides containing two electrophilic centers, C-2 connected with a chloro atom and C-1 having aryl/butyltellurium groups, only tellurium moiety takes part in the cross-coupling reaction and chloro atom remain intact during the process.

In order to explore the organotellurium chemistry, the starting materials were prepared through the addition reaction of organotellurium trihalides, generated from the corresponding diaryl/dibutyl ditelluride, to alkynes to produce 2-halovinyl tellurium dihalides containing chloro, bromo, and iodo atoms using sufuryl chloride, molecular bromine, and iodine as halide sources, followed by reduction with sodium borohydride leading to (*Z*)-aryl/butyl-(2-halovinyl)tellurides (Scheme 1).[11,12]

Next, with the starting materials in hand we started the cross-coupling reactions that worked nicely only with those tellurium compounds which had chlorine atom while the vinylic telluride containing bromine and iodine led to the formation of several undesired byproducts. The difference in the electronegativity of the halides may be an explanation for this behavior with different halogens in the reaction (Scheme 2).



R= Ph, C_5H_{11}, C_3H_7, CH_3OCH_2, $(CH_3)_3C$, $CH_3(CH_2{=})C$, 1-cyclohexenyl
R^1=Ph, C_4H_9, (*p*-CH_3O)Ph,
X=Cl, Br, I (of SO_2Cl_2, Br_2 and I_2)

Scheme 1.

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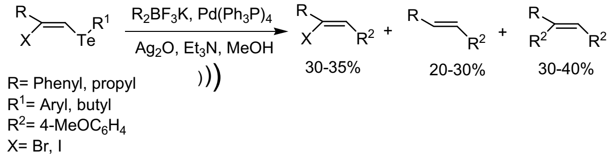


Scheme 2.

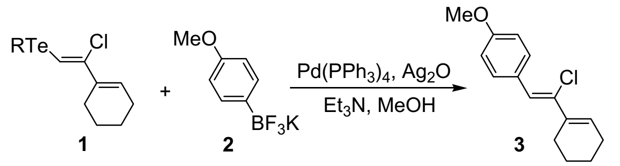
After we have selected chlorine containing aryl/butyl vinylic tellurides for the study as electrophilic partners in the Suzuki–Miyaura cross-coupling reaction, we investigate the best transfer group connected to tellurium atom preparing (*Z*)-butyl(2-chloro-2-cyclohexenylvinyl)telluride, (*Z*)-phenyl(2-chloro-2-cyclohexenylvinyl)telluride, and (*Z*)-4-methoxyphenyl(2-chloro-2-cyclohexenylvinyl)telluride.

The cross-coupling reaction was performed using potassium 4-methoxyphenyltrifluoroborate salt as nucleophilic partner leading to the coupling product **3** in 85%, 72%, and 65% yield, respectively (Table 1). The ^{1}H NMR of isolated compound **3** showed one singlet at 3.75 and 6.13 ppm due to 4-methoxyl group hydrogens and one vinylic hydrogen, respectively. Two doublets appeared at 6.78 and 7.32 ppm due to aromatic ring hydrogens, one triplet at 7.50 ppm and two multiplets at 1.54–1.65 and 2.07–2.33 ppm due to cyclohexene ring hydrogens. Further the *m*/*z* peak at 248 (M^+) and 250 (M^++2) in GC–MS confirmed the structure of compound **3a** as (*Z*)-1-(2-chloro-2-cyclohexenylvinyl)-4-methoxybenzene and presence of chlorine atom in the product.

With the collected information about the halogen and that butyltellurium group is more reactive in cross-coupling reaction with potassium organotrifluoroborate salts, the next step was the screening of several common catalyst/additive combinations, bases, and solvents (Tables 2 and 3) to try find the best cross-coupling reaction conditions.

Toward this end, potassium 4-methoxyphenyltrifluoroborate salt (**2**) and (*Z*)-butyl(2-chloro-2-phenylvinyl)telluride **1d** were chosen as model substrates and a variety of conditions were screened (Tables 2 and 3). All reactions were monitored by TLC or GC.

Table 1
Study of the best transfer tellurium group



Entry	R (1)	Yield (%) (3)
1	*n*-Bu	85
2	C_6H_5	72
3	4-$MeOC_6H_4$	65

Table 2
Study of catalyst effect using potassium 4-methoxyphenyltrifluoroborate salt **2** and (*Z*)-butyl(2-chloro-2-phenylvinyl)telluride **1d**

Entry	Catalyst[a]	Yield[b] (%)
1	$PdCl_2$	5
2	$Pd(acac)_2$	18
3	$Pd_2(dba)_3$	40
4	$Pd(AcO)_2$	44
5	$PdCl_2(dppf)·CH_2Cl_2$	41
6	$Pd(PPh_3)_4$	60

[a] 10 mol % of catalyst was used.
[b] Isolated yields.

Table 3
Study of additive and base effect using potassium 4-methoxyphenyltrifluoroborate salt **2** and (*Z*)-butyl(2-chloro-2-phenylvinyl)telluride **1d**

Entry	Base (equiv)	Additive (equiv)	$Pd(PPh_3)_4$ (mol %)	Yield[a] (%)
1	K_2CO_3	Ag_2O (1)	$Pd(PPh_3)_4$ (10)	60
2	Cs_2CO_3	Ag_2O (1)	$Pd(PPh_3)_4$ (10)	66
3	Et_3N (1)	Ag_2O (1)	$Pd(PPh_3)_4$ (10)	73
4	—	Ag_2O (1)	$Pd(PPh_3)_4$ (10)	nr
5	Et_3N (1)	AgOAc (1)	$Pd(PPh_3)_4$ (10)	55
6	Et_3N (1)	Ag_2CO_3 (1)	$Pd(PPh_3)_4$ (10)	22
7	Et_3N (2)	AgOAc (2)	$Pd(PPh_3)_4$ (10)	60
8	Et_3N (3)	AgOAc (4)	$Pd(PPh_3)_4$ (10)	40
9	Et_3N (2)	Ag_2O (2)	$Pd(PPh_3)_4$ (10)	80
10	Et_3N (3)	Ag_2O (4)	$Pd(PPh_3)_4$ (10)	64
11	Et_3N (2)	Ag_2O (2)	$Pd(PPh_3)_4$ (10)	58[b]

[a] Isolated yields.
[b] Conventional condition.

First of all, the palladium catalyst was determinated and Pd(II) or (0) species were used in the coupling reactions and the best result was reached with $Pd(PPh_3)_4$ (Table 2, entry 6). AgOAc was used as additive, K_2CO_3 as base, and methanol as solvent, and the reaction was irradiated for 30 min in ultrasound bath. The product was obtained in 60% isolated yield.

After finding the appropriate Pd catalyst, we turned our attention to search an appropriate solvent. In order to select the best solvent we checked the reaction with several polar and non-polar solvents such as methanol, ethanol, DMF, DME, isopropyl alcohol, and THF, but the desired compound was isolated in best yield (60%) with methanol.

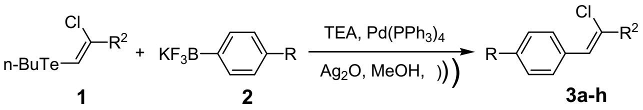
The next step was the determination of the best base and the necessity of an additive in the reaction (Table 3). Initially we used inorganic bases, like potassium and cesium carbonates (Table 3, entries 1 and 2), in presence of Ag_2O and cesium carbonate afforded the best result, 66% isolated yield. When the organic base, triethylamine, (1 equiv) was used, the desired compound was isolated in 73% yield (Table 3, entry 3). No reaction was observed in the absence of base (Table 3, entry 4).

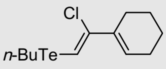
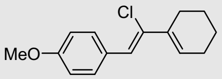
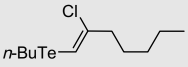
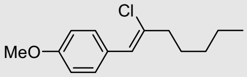
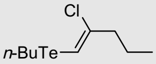
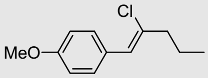
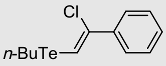
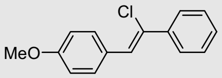
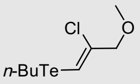
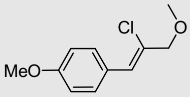
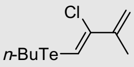
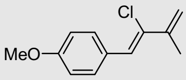
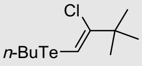
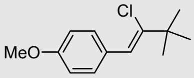
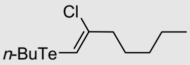
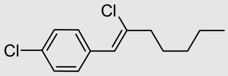
Further to check the effect of additive, we performed the same reaction with different additives, such as Ag_2O, AgOAc, and Ag_2CO_3, and isolated desired product in 73%, 55% and 22% yields, respectively (Table 3, entries 3, 5, and 6). No reaction was observed in the absence of additive.

The reaction stoichiometry was checked using different equivalents of triethylamine with different amounts of Ag_2O and AgOAc (Table 3, entry 8–11) and the best result (80%) was obtained with 2 equiv of triethylamine and Ag_2O (Table 3, entry 9). Further to obtain more appropriate conditions we attempted the same reaction under conventional condition (stirring at room temperature for 2 h), but the desired compound was isolated in 58% yield (Table 3, entry 11).

During the optimization studies for (*Z*)-vinylic chlorides **3**, it was observed that the reaction mixture of 1.1 equiv of potassium aryltrifluoroborate salt **2**, 1 equiv of (*Z*)-butyl-(2-chloro-2-phenylvinyl) telluride **1d**, 2 equiv Ag_2O, 2 equiv of triethylamine, and 10 mol % of $Pd(PPh_3)_4$ in methanol irradiated under ultrasonic waves for 20 min, was the best reaction condition for the synthesis of (*Z*)-1-(2-chloro-2-phenylvinyl)-4-methoxybenzene **3d**. After achieving the best condition for the synthesis of **3**, we synthesized a series of these (*Z*)-vinylic chlorides **3a–h** using the optimized condition in 58–85% yields (see Table 4).[13] After completion the reaction mixture was poured into water and neutralized with ammonium chloride solution followed by extraction with ethyl acetate. The crude product was purified by flash column chroma-

Table 4
Suzuki–Miyaura reaction of (Z)-*n*-butyl(2-chloro-2-organovinyl)telluride and potassium 4-aryltrifluoroborate salt



Entry	Vinyl tellurides (1)	Products	Reaction time (min)	Yields (%)
1	 **1a**	 **3a**	30	85
2	 **1b**	 **3b**	30	82
3	 **1c**	 **3c**	60	58
4	 **1d**	 **3d**	20	80
5	 **1e**	 **3e**	40	73
6	 **1f**	 **3f**	40	82
7	 **1g**	 **3g**	60	74
8	 **1h**	 **3h**	60	69

tography using hexane as eluent. The reaction was monitored by TLC and GC. All the synthesized compounds were characterized by spectroscopic analysis.

In summary, we have shown that tellurium moiety can be a good electrophile alternative to the traditional halides in cross-coupling Suzuki–Miyaura reaction. Further studies associated with the bromine and iodide containing tellurides as electrophilic partners in the Suzuki–Miyaura reaction are currently in progress.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.05.129.

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