# Palladium-Catalyzed Negishi Cross-Coupling of Arylzinc Reagents with Functionalized Vinylic Tellurides

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**Abstract:** The Negishi cross-coupling reaction of arylzinc chlorides and bromides with functionalized vinylic tellurides in the presence of a catalytic amount of  $PdCl_2$  in THF at room temperature is described. This cross-coupling reaction is general and permits the synthesis of functionalized substituted alkenes in good yields and high stereoselectivity.

Key words: palladium, vinylic tellurides, organozinc, tellurium, Negishi

Transition-metal-catalyzed cross-coupling reactions between C<sub>sp2</sub>-centers have been extensively used for preparing pharmaceuticals and agrochemical intermediates.<sup>1</sup> Conversely in the last decade, there have been developments of coupling substrates that are more economic, more easily accessible and reactive even under mild conditions. Whereas Suzuki cross-coupling reactions have found many applications due to the high functional group compatibility of boronic acids and esters,<sup>2</sup> the Negishi cross-coupling reaction has found decidedly less applications due to the water and air instability of most organozinc species.<sup>3</sup> However, the excellent ability of organozinc species for undergoing transmetallation reactions allows one often to perform Negishi cross-coupling reactions, a powerful and versatile method for the construction of new carbon-carbon bonds, that can be applied to alkyl, alkenyl and alkynyl substrates.<sup>4</sup>

In addition, the application of vinylic tellurides utilizing palladium-catalyzed cross-coupling has been described. In this case, they behave as aryl or vinyl carbocation equivalents. They react in a manner similar to vinylic halides or triflates in the Sonogashira,<sup>5</sup> Heck,<sup>6</sup> Suzuki,<sup>7</sup> and Stille<sup>8</sup> cross-coupling reactions with palladium as a catalyst. In this way, there are some advantages to use vinylic tellurides instead of the other methods, such as the easy access by stereoselective reactions to either (*Z*)- or (*E*)-vinylic tellurides, no isomerization of the double bond and the enhanced stability of these compounds. Besides, the use of vinylic tellurides in cross-coupling reactions tolerates many sensitive functional groups and mild reaction conditions. We have described the synthesis of polyacetylenic acids isolated from *Heisteria acuminata* by us-

SYNLETT 2006, No. 7, pp 1035–1038 Advanced online publication: 24.04.2006 DOI: 10.1055/s-2006-939065; Art ID: S00306ST © Georg Thieme Verlag Stuttgart · New York ing a vinylic telluride coupling reaction<sup>9</sup> to demonstrate the great applicability of these compounds in organic synthesis.

We have reported the reaction of non-functionalized vinylic tellurides with heteroarylzinc chlorides catalyzed by palladium salts,<sup>10</sup> however, to the best of our knowledge, no Negishi cross-coupling reaction using functionalized vinylic tellurides as substrate in the preparation of  $sp^2-sp^2$ carbon–carbon bond has been described so far.<sup>11</sup> Hence, we assume that the use of functionalized vinylic tellurides would expand the scope of the Negishi cross-coupling reaction. Thus, our continuing interest in the palladiumcatalyzed cross-coupling of vinylic tellurides<sup>12</sup> prompted us to examine the cross-coupling reaction of functionalized vinylic tellurides **1a–f** with arylzinc reagents to obtain functionalized alkenes **3a–m** (Scheme 1).



Ar = aryl, heteroaryl; X = Cl, Br; Y = S, P;  $R^1 = R^2$ = alkyl, aryl, benzyl

### Scheme 1

Our initial efforts were devoted to the selection of a suitable catalyst system for efficient Negishi cross-coupling reaction between 1,2-bis(organoylchalcogeno)alkenes **1** with arylzinc chlorides **2** (3 mmol).<sup>13</sup> Thus, 1,2-bis(organoylchalcogeno)alkene **1a** (1 mmol) and phenylzinc chloride **2a** (3 mmol) were treated in THF (1 mL) at room temperature with Pd(0) and Pd(II) catalysts, in the presence and absence of CuI (Table 1).

As shown in Table 1, all Pd(0) and Pd(II) with different ligands tested exhibit a moderate to good catalytic activity, but the best result was obtained using PdCl<sub>2</sub> (20 mol%, Table 1, entry 7). It is important to note that when the amount of catalyst is reduced from 20 mol% to 1 mol% a decrease in the yield was observed (Table 1, entries 7–10). We also investigated the CuI influence in this coupling. We found that when the reaction was achieved with a catalytic amount (Table 2, entry 2) or in the absence of CuI (Table 2, entry 1), the desired product **3a** was obtained in an unsatisfactory yield.

 Table 1
 Influence of Catalyst in the Reaction<sup>a</sup>

| Entry | Catalyst (mol%)                         | Yield of <b>3a</b> (%) |  |
|-------|---|------------------------|--|
| 1     | $Pd(OAc)_2(20)$                         | 65                     |  |
| 2     | $Pd(PPh_3)_2Cl_2(20)$                   | 49                     |  |
| 3     | $Pd(PhCN)_2Cl_2(20)$                    | 57                     |  |
| 4     | $Pd(dppe)_2$ (20)                       | 67                     |  |
| 5     | $Pd(dba)_2(20)$                         | 55                     |  |
| 6     | Pd(PPh <sub>3</sub> ) <sub>4</sub> (20) | 50                     |  |
| 7     | PdCl <sub>2</sub> (20)                  | 82                     |  |
| 8     | $PdCl_2(1)$                             | 51                     |  |
| 9     | $PdCl_2(5)$                             | 54                     |  |
| 10    | PdCl <sub>2</sub> (10)                  | 60                     |  |

<sup>a</sup> Reactions were performed in the presence of **1a** (1 mmol), **2a** (3 mmol), CuI (1 mmol), using THF as solvent at r.t. for 28 h.

Thus, the careful analysis of the optimized reactions revealed that the optimum condition for this coupling reaction was found to be the use of 1,2-bis(organoyl-chalcogeno)alkene **1a** (1 mmol), phenylzinc chloride **2a** (3 mmol), PdCl<sub>2</sub> (20 mol%), CuI (1 mmol) in THF (1 mL) at room temperature giving the corresponding vinyl sulfide **3a** in 82% yield (Scheme 2).<sup>14</sup>



#### Scheme 2

In order to demonstrate the efficiency of this reaction, we explored the generality of our method extending the conditions to other arylzinc halides and the results are summarized in Table 3.

Inspection of Table 3 shows that the reaction worked well for a variety of arylzinc chloride. A closer inspection of the results revealed that the reaction is not sensitive to the steric effect of an aromatic ring attached in the arylzinc chloride.

For example, arylzinc chloride bearing a Me substituent at the *o*-, *m*-, *p*-position gave the similar yield to the no substituted phenylzinc chloride (Table 3, entries 3 and 1, re-

| Entry | Condition            | Yield of <b>3a</b> (%) |
|-------|----------------------|------------------------|
| 1     | PhZnCl               | 17                     |
| 2     | PhZnCl/CuI (20%)     | 60                     |
| 3     | PhZnCl/CuI (1 equiv) | 82                     |
| 4     | PhZnBr               | 15                     |
| 5     | PhZnBr/CuI (20%)     | 54                     |
| 6     | PhZnBr/CuI (1 equiv) | 61                     |

<sup>a</sup> Reactions were performed in the presence of **1a** (1 mmol), **2a** (3 mmol), PdCl<sub>2</sub> (20 mol%), using THF as solvent, at r.t. for 28 h.

spectively). We also observed that electronic effects have no influence on the coupling reaction. A wide range of groups attached in the arylzinc chloride such as, electronrich, -neutral and -poor were cross-coupled efficiently under these conditions and produced the functionalized alkenes in good yields. It is interesting to note that *O*-, *S*-, *Se*-heteroarylzinc chloride underwent smooth coupling reaction with 1,2-bis(organoylchalcogeno)alkene **1a** (Table 3, entries 6–8). Differentiation in the reactivity between chlorine and bromine atoms from arylzinc reagents can be seen by coupling of arylzinc chloride or bromide with **1a** and the results demonstrated that arylzinc chlorides gave the desired product in higher yields than arylzinc bromides.

In an attempt to broaden the scope of our methodology, the possibility of performing the reaction with 1,2-bis(organoylchalcogeno)alkenes **1b**–**d** and other functionalized vinylic tellurides such as  $\beta$ -butyltelluro vinylphosphonate **1e** and  $\beta$ -butyltelluro vinylphosphine oxide **1f** instead of **1a**, were also investigated. As illustrated in Table 4, the cross-coupling reaction of **1b**–**f** and phenylzinc chloride **2a**, under the same reaction conditions described in Table 3, led to the corresponding coupling products **3i**–**m** in excellent yields (Table 4).

In summary, we have explored the Negishi cross-coupling reaction of aryl- or heteroarylzinc reagents with functionalized vinylic tellurides in the presence of a catalytic amount of  $PdCl_2$  under mild reaction conditions (r.t.) and established a new route to the synthesis of functionalized alkenes in good yields. The pharmacological activities of these compounds are under study in our laboratory. Analysis of the <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra showed that all the obtained products presented data in full agreement with their assigned structures.

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| Table 3  | Cross-Coupling Products Using Vinylic Telluride 1a and |  |
|----------|--|--|
| Arylzinc | leagents 2a-h  |  |

| $H_{11}C_{5}$ |                    | P   | dCl <sub>2</sub> (20%), THF                                 | C <sub>5</sub> |
|---------------|--------------------|---|---|----------------|
| BuTe<br>1     | SMe + Ar-<br>SMe 2 | -ZnX ——<br><b>a-h</b>   | Cul (1 equiv) A<br>r.t., 28 h                               | SMe<br>3a–h    |
| Entry         | ArZnX              |   | Product <b>3</b>  | Yield (%)      |
| 1             |                    | $\begin{aligned} \mathbf{X} &= \mathbf{C}\mathbf{l}\\ \mathbf{X} &= \mathbf{B}\mathbf{r} \end{aligned}$ | MeS C5H11   | 82<br>66       |
|               | 2a                 |   | 3a  |                |
| 2             | No.                | $\begin{aligned} \mathbf{X} &= \mathbf{C}\mathbf{l}\\ \mathbf{X} &= \mathbf{B}\mathbf{r} \end{aligned}$ | MeS C5H11   | 76<br>60       |
|               | 2b                 |   | 3b  |                |
| 3             | 2                  | $\begin{aligned} \mathbf{X} &= \mathbf{C}\mathbf{l}\\ \mathbf{X} &= \mathbf{B}\mathbf{r} \end{aligned}$ | MeS   | 72<br>57       |
|               | 2c                 |   | 3c  |                |
| 4             |                    | $\begin{aligned} X &= Cl \\ X &= Br \end{aligned}$  | MeS C <sub>5</sub> H <sub>11</sub>                          | 67<br>50       |
|               | 2d                 |   | 3d  |                |
| 5             |                    | $\begin{aligned} \mathbf{X} &= \mathbf{C}\mathbf{l}\\ \mathbf{X} &= \mathbf{B}\mathbf{r} \end{aligned}$ |   | 74<br>52       |
|               | 2e <sup>a</sup>    |   | 3e  |                |
| 6             | رم<br>غ<br>2f      | $\begin{aligned} \mathbf{X} &= \mathbf{C}\mathbf{l}\\ \mathbf{X} &= \mathbf{B}\mathbf{r} \end{aligned}$ | MeS C5H11   | 71<br>60       |
| 7             | ر<br>ج<br>2 م      | $\begin{aligned} \mathbf{X} &= \mathbf{C}\mathbf{l}\\ \mathbf{X} &= \mathbf{B}\mathbf{r} \end{aligned}$ | MeS S   | 77<br>65       |
| 8             | $z_{s}$            | $\begin{aligned} \mathbf{X} &= \mathbf{C}\mathbf{l}\\ \mathbf{X} &= \mathbf{B}\mathbf{r} \end{aligned}$ | $MeS \xrightarrow{C_5H_{11}} Se \xrightarrow{C_5H_{3h}} 3h$ | 78<br>58       |

<sup>a</sup> Prepared by transmetallation from stoichiometric amount of Grignard reagent and  $ZnX_2$  (X = Cl, Br).

**Table 4**Cross-Coupling Products Using Functionalized VinylicTellurides**1b–f** and Phenylzinc Chloride**2a**<sup>a</sup>



<sup>a</sup> Reactions were performed in the presence of **1b–f** (1 mmol) and phenylzinc chloride (**2a**, 3 mmol).

<sup>b</sup> A mixture of isomers *Z*:*E* (75:25) of  $\beta$ -butyltelluro vinylphosphine oxide was utilized.

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- (13) The arylzinc reagents were prepared in situ by the reaction of aryl halides with *n*-BuLi in THF followed by addition of ZnCl<sub>2</sub>.
- (14) Typical Procedure for Cross-Coupling Reaction.
  A 25 mL, two-necked, round-bottom flask equipped with a magnetic stir bar, rubber septum and argon was charged sequentially with PdCl<sub>2</sub> (0.035 g, 0.2 mmol), CuI (0.19 g, 1 mmol), THF (1 mL) and 1,2-bis(organoylchalcogeno)alkene (1a, 0.328 g, 1 mmol). Then, phenylzinc chloride (2a, 3 mmol), previously prepared in another flask was transferred via cannula at r.t. The black mixture was stirred at r.t.

and the reaction time was determined monitoring the reaction by TLC. The reaction mixture was then quenched with aqueous NH<sub>4</sub>Cl (30 mL), washed with CH<sub>2</sub>Cl<sub>2</sub> (3 × 20 mL), dried with MgSO<sub>4</sub> and the solvent removed under vacuum. The products were purified by column chromatography. Selected spectral and analytical data for **3a**: yield: 0.180 g (82%). <sup>1</sup>H NMR: (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.39–7.24 (m, 5 H), 5.93 (s, 1 H), 2.43 (t, *J* = 6.76 Hz, 2 H), 2.22 (s, 3 H), 1.33–1.28 (m, 6 H), 0.85 (t, *J* = 6.32 Hz, 3 H) ppm. <sup>13</sup>C NMR: (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 140.05, 139.35, 128.05, 127.92, 127.01, 123.41, 38.66, 31.30, 28.13, 22.39, 17.85, 13.98 ppm.