



Sonogashira cross-coupling reaction of organotellurium dichlorides with terminal alkynes

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Abstract—The Sonogashira cross-coupling reaction of vinylic and heteroaromatic tellurium dichlorides has been explored, yielding the corresponding enynes and 2-alkynyl substituted heteroaromatic compounds. The reaction was carried out with PdCl₂/CuI as catalysts and triethylamine as base, using methanol as solvent. The reaction proceeded under mild conditions and the cross-coupled products were obtained in good yields and in a stereoconservative manner. © 2003 Elsevier Science Ltd. All rights reserved.

The chemistry of organotellurium compounds has increased in the past years, being the subject of many review articles¹ as well as books.² From the many classes of tellurium compounds, vinylic tellurides constitute one of the most useful. Several methods have been developed for their preparation,^{1,2} and among them, one of the most important is the hydrotelluration reaction of alkynes,³ which furnishes exclusively the (*Z*)-vinylic telluride. These species can be transmetalated with many organometallic reagents to generate the corresponding (*Z*)-vinyl organometallics with retention of the double bond geometry, which can react with several electrophiles like carbonyl compounds,⁴ enones⁵ and epoxides.⁶

On the other hand, the palladium-catalyzed cross-coupling reaction of vinylic tellurides with terminal alkynes was also previously described⁷ and has been subject of our research program.⁸ The symmetrical diorganotellurium dichlorides have also been used in cross-coupling reactions with organostannanes,⁹ organoboron¹⁰ compounds and iodonium salts.¹¹

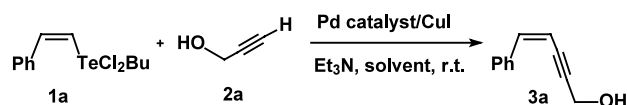
In order to extend the scope of the palladium catalyzed reaction of organic tellurides, we decided to investigate the Sonogashira type reaction of several vinylic and heteroaromatic tellurium dichlorides, since they are eas-

ily prepared^{2a} and much more stable to air oxidation than the corresponding vinylic and heteroaromatic tellurides. We used in all cases unsymmetrical diorganotellurium dichlorides in which one of the organic moieties attached to the tellurium atom is always a butyl group.

Our initial efforts were made in the direction to determine the optimum conditions to perform the cross-coupling reaction. To that end we have chosen the tellurium dichloride **1a** and the alkyne **2a** to establish the best conditions for the reaction (Scheme 1).

In our first trial we have performed the reaction using the protocol already described in our previous work.⁸ Thus, the reaction was carried out using 20 mol% of PdCl₂ as the palladium catalyst, 20 mol% of CuI, Et₃N as base in MeOH. Under these conditions the enyne **3a** was isolated in 82% yield after 6h (entry 1, Table 1).

We have then tried to conduct the reaction reducing the loading of the catalyst. So we used 10 mol% of PdCl₂ and the desired product was obtained in only 55% yield in a longer reaction time (entry 2, Table 1). Changing the solvent from MeOH to THF we have observed that



Scheme 1.

Keywords: cross-coupling; organotellurium dichlorides; palladium; tellurides.

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Table 1. Optimization of the Sonogashira coupling reaction of tellurium dichloride **1a** with propargyl alcohol **2a**

Entry	Pd Catalyst (20 mol%)	Solvent	Time (h)	Yield (%)
1	PdCl ₂	MeOH	6	82
2 ^a	PdCl ₂	MeOH	12	55
3	PdCl ₂	THF	6	27
4	Pd(OAc) ₂	MeOH	6	68
5	Pd(OAc) ₂	THF	6	18
6	Pd(PPh ₃) ₂ Cl ₂	MeOH	6	0
7	Pd(PPh ₃) ₂ Cl ₂	THF	6	0

^a 10 mol% of PdCl₂ was used.

many by-products were formed and the yield decreases to 27% (entry 3, Table 1). In order to evaluate the possibility to use another palladium(II) catalysts, we used Pd(OAc)₂ and Pd(PPh₃)₂Cl₂ as catalyst in our test system. Although we obtained the enyne **3a** using Pd(OAc)₂ in the loading of 20 mol%, the conversion to the desired product was still less than that observed with PdCl₂ (entries 4 and 6, Table 1). With Pd(PPh₃)₂Cl₂ none of the product was observed. These catalysts were also used with THF as solvent instead of MeOH, but again many by-products were observed at the end of the reaction and just a small amount of **3a** was obtained (entries 5 and 7, Table 1).

Analysis of the results of the test reactions revealed that the best conditions were using the organotellurium dichloride (1 mmol), the appropriated 1-alkyne (2 mmol), PdCl₂ (20 mol%), CuI (20 mol%), methanol as solvent in the presence of triethylamine as base.¹² Thus the reaction of the organotellurium dichloride **1a** was extended to other terminal acetylenes **2b**, and **2c** and the corresponding enynes were obtained in good yields showing that our protocol could be extended to other alkynes (entries 2–5, Table 2).

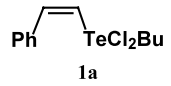
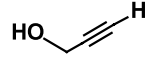
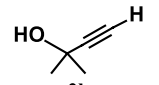
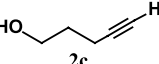
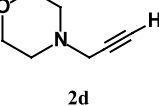
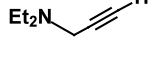
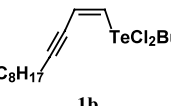
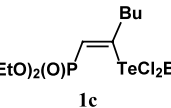
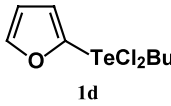
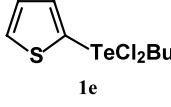
Moreover, several organotellurium dichlorides were prepared and tested under our cross-coupling conditions (Table 2). They act as an equivalent of an vinyl carbocation, reacting in a similar way to the vinylic halides or triflates in the Sonogashira coupling reaction.¹³ The reaction was performed using vinylic derivatives containing a triple bond (**1b**), phosphonates (**1c**) and also heteroaromatic systems derived from furan (**1d**) and thiophene (**1e**). In all cases, the reaction proceeded smoothly and the cross-coupled products were obtained in good yields. As shown, the reaction conditions tolerate many functionalities like alcohols, amines, phosphonates and triple bonds. Also just a small amount of the alkyne homocoupling was observed. This suggests that the *sp*²–*sp* σ-bond formation is faster than homocoupling at these conditions.

All compounds have had their structure confirmed by NMR analysis and are in accordance with those already described in the literature.^{7,8} The stereochemical outcome of the reaction shows that it proceeds in a stereoselective way, resulting in only the (*Z*)-enyne. The stereochemistry was easily established by measuring the

coupling constants of the vinylic hydrogens, showing a *cis* relationship between them.

In summary, we have described the Sonogashira type cross-coupling reaction of unsymmetrical organotellurium dichlorides with terminal alkynes in a stereoselective manner. The reaction proceeds with good yields under mild conditions using palladium dichloride and copper iodide as catalysts. The present procedure nicely improves the methods recently described,^{9–11}

Table 2. Cross-coupling reaction of several organotellurium dichlorides **1** with terminal alkynes **2**

#	Organotellurium Dichloride 1	Alkyne 2	Time (h)	Yield (%)
1	 1a	 2a	6	82
2	1a	 2b	6	73
3	1a	 2c	6	79
4	1a	 2d	6	87
5	1a	 2e	6	84
6	 1b	2a	6	75
7	1b	2b	6	77
8	 1c	2a	6	64
9	1c	2b	6	61
10	 1d	2a	6	83
11	1d	2b	6	81
12	 1e	2a	6	79
13	1e	2b	6	77

offering several advantages such as the compatibility with many functionalities and avoidance of losing one of the vinylic moieties when divinyl tellurides were used as starting materials.

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- Representative procedure for the Sonogashira cross-coupling reaction:** To a two-necked 25 mL round-bottomed flask under an argon atmosphere containing PdCl₂ (0.035 g, 20 mol%), CuI (0.038 g, 20 mol%) and dry methanol (5 mL) was added **1a** (0.358 g, 1 mmol). After stirring the mixture for 5 minutes at room temperature, propargyl alcohol **2a** (0.112 g, 2 mmol) and Et₃N (0.8 mL) were added. The reaction was stirred at room temperature for 6 h. After this time the solid part was filtered under vacuum. To the filtrate brine was added and extracted with dichloromethane (3×25 mL). The combined organic layers were dried over MgSO₄ and concentrated under vacuum. The residue was purified by flash chromatography eluting with hexane/ethyl acetate (80:20). **Selected spectral and analytical data for 3a:** Yield 0.13g (82%); ¹H NMR (CDCl₃, 200 MHz, δ ppm) 7.83–7.27 (m, 5H), 6.63 (d, J =12 Hz, 1H), 5.74 (dt, J^1 =12, J^2 =2 Hz, 1H), 4.46 (d, J =2 Hz, 2H), 2.10 (s, 1H); ¹³C NMR (CDCl₃, 50 MHz, δ ppm) 139.10, 136.15, 132.55, 128.55, 128.25, 106.70, 93.80, 84.00, 51.70; IR (neat, cm⁻¹) ν 3370, 3060, 2200, 1660, 786; LRMS m/z (rel. int.) 158 (15), 140 (19), 102 (100), 77 (30). All compounds have had their analytical data compared with literature data and are in agreement with those already reported (see Ref. 8).
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