



## Novel and general cross-coupling reactions of alkynylzinc reagents and organotellurium compounds

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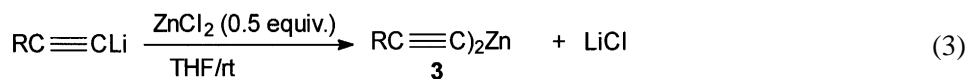
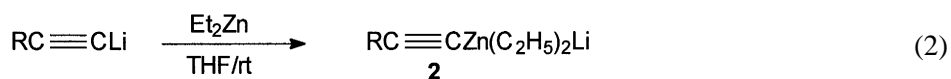
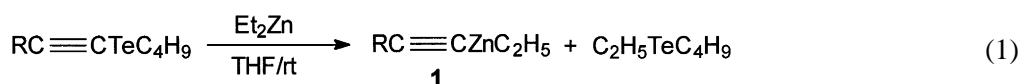
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### Abstract

The efficient cross-coupling reactions of different alkynyl organozinc reagents with unsaturated organotellurium species catalyzed by Pd(PPh<sub>3</sub>)<sub>4</sub>/CuI and using THF/DMF systems are described. These cross-coupling reactions are general and permit the formation of new *sp*–*sp*<sup>2</sup> carbon–carbon bonds. New reactions to reach the necessary alkynylzinc intermediates were also developed from terminal alkynes or using acetylenic tellurides as starting materials. © 2000 Elsevier Science Ltd. All rights reserved.

The ability of organozinc reagents to promote carbon–carbon bond formation by reaction with electrophiles is a well-recognized process.<sup>1</sup> However, the limited availability of alkynylzinc reagents has restricted their applications in organic synthesis.<sup>1c,2,3</sup> Herein, we wish to report three new and convenient routes to access a range of functionalized and nonfunctionalized alkynylzinc reagents of types **1**–**3**.

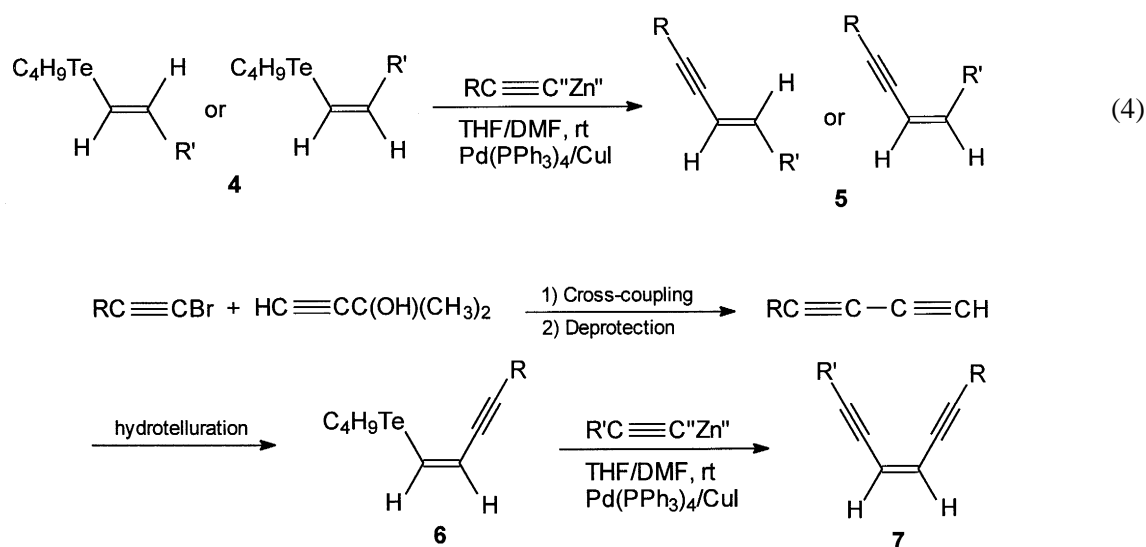


The first method involved the formation of ethylalkynylzinc compounds **1** under halide-free conditions by the Te/Zn-exchange reaction employing diethylzinc<sup>4</sup> (1.5 equiv., solution 1.0 M, in hexanes) in THF at room temperature. Treatment of lithium acetylides (generated in THF at 0°C) with diethylzinc

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(solution 1.0 M, in hexanes) or with 0.5 equiv. of zinc chloride at room temperature afforded the desired alkynylzinc reagents **2** and **3**, respectively. They were used immediately in situ in subsequent reactions. All the alkynylzinc reagents **1–3** obtained here are shown to promote the highly efficient formation of  $sp-sp^2$  carbon–carbon bonds by the cross-coupling with unsaturated organotellurium (or iodo) compounds such as vinyl tellurides<sup>5</sup> (Eq. (4)), tellurobutenyne<sup>6</sup> (Scheme 1) and aryl tellurides<sup>7</sup> or also with aryl iodides<sup>8</sup> (Eq. (5)).  $\text{Pd}(\text{PPh}_3)_4$  proved to be an efficient catalyst (5% mol) and the optimal conditions were achieved by the addition of  $\text{CuI}$  as a promotor. The reactions were conveniently carried out<sup>9</sup> at room temperature exclusively affording the cross-coupling product in good yield. Different alkynylzinc compounds (1.5 equiv.) by reaction with *E*- or *Z*-vinylic tellurides **4** were transformed into the corresponding enynes **5** with total retention of configuration (Table 1).



Scheme 1.

The same approach using the butyltellurobutenyne **6** of *Z* configuration as the electrophilic partners was applied to the synthesis of the (*Z*)-enediynes **7** in excellent yields.<sup>9</sup> These enediyne substructures are present in a broad series of the powerful antitumor and anticancer antibiotics isolated from natural sources.<sup>10</sup> In combination with our previous methodology to obtain the unsymmetrical tellurobutenyne,<sup>6</sup> enediynes can be built from three different terminal acetylenes in a cross-coupling/hydrotelluration/cross-coupling sequential protocol (Scheme 1).

The arylation of alkynylzinc reagents was also achieved in moderated yields by reaction with phenylbutyl telluride as electrophile<sup>9</sup> (entries 5 and 6, Table 1). The reaction described in entry 6 (Table 1) was very slow, then the homocoupling reaction was observed as a side reaction, and the corresponding diyne was isolated in a considerable amount (42%). However, a better yield was obtained when the cross-coupling of the same alkynylzinc reagent was carried out with an aryl iodide (entry 7, Table 1). In the last case, the homocoupling product was not observed. It should be pointed out that the reaction time was shorter, accompanied by a higher yield than when phenylbutyl telluride was used.

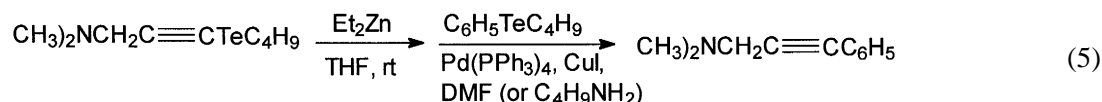
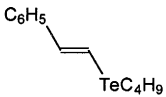
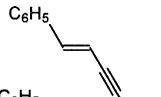
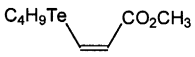
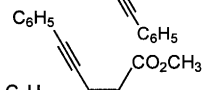
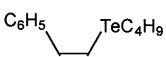
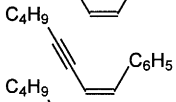
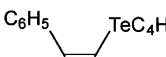
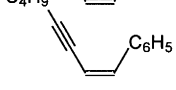
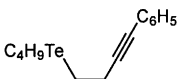
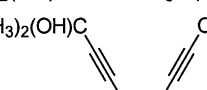
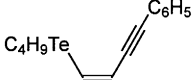
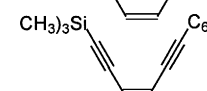
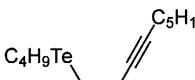
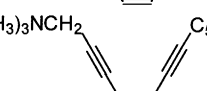

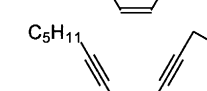
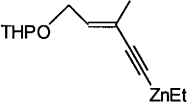
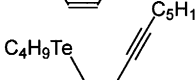
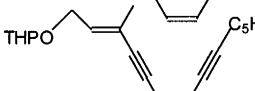
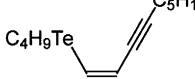
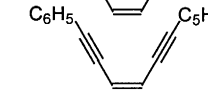


Table 1  
Cross-coupling products obtained using alkynylzinc reagents

Entry	Alkynylzinc reagent <sup>a</sup>	Electrophile	Product	Yield (%) <sup>b</sup>
1	$\text{C}_6\text{H}_5\text{C}\equiv\text{C}_2\text{Zn}$			89
2	$\text{C}_6\text{H}_5\text{C}\equiv\text{C}_2\text{Zn}$			78
3	$\text{C}_4\text{H}_9\text{C}\equiv\text{CZnEt}$			92
4	$\text{C}_4\text{H}_9\text{C}\equiv\text{CZnEt}_2\text{Li}$			91
5	$\text{CH}_3)_2\text{NCH}_2\text{C}\equiv\text{CZnEt}$	$\text{C}_6\text{H}_5\text{TeC}_4\text{H}_9$	$\text{CH}_3)_2\text{NCH}_2\text{C}\equiv\text{CC}_6\text{H}_5$	65
6	$\text{CH}_3)_2\text{C}(\text{OH})\text{CC}\equiv\text{C}_2\text{Zn}$	$\text{C}_6\text{H}_5\text{TeC}_4\text{H}_9$	$\text{CH}_3)_2\text{C}(\text{OH})\text{CC}\equiv\text{CC}_6\text{H}_5$	50 <sup>c</sup>
7	$\text{CH}_3)_2\text{C}(\text{OH})\text{CC}\equiv\text{C}_2\text{Zn}$	$\text{CH}_3\text{OC}_6\text{H}_4\text{I}$	$\text{CH}_3)_2\text{C}(\text{OH})\text{CC}\equiv\text{CC}_6\text{H}_4\text{OCH}_3$	79
8	$\text{CH}_3)_2\text{C}(\text{OH})\text{CC}\equiv\text{C}_2\text{Zn}$			83
9	$\text{CH}_3)_3\text{SiC}\equiv\text{C}_2\text{Zn}$			93
10	$\text{CH}_3)_2\text{NCH}_2\text{C}\equiv\text{C}_2\text{Zn}$			84
11	$\text{C}_5\text{H}_{11}\text{C}\equiv\text{C}_2\text{Zn}$			88
12				80
13	$\text{C}_6\text{H}_5\text{C}\equiv\text{CZnEt}_2\text{Li}$			86

<sup>a</sup>1.5 Equivalents of the alkynylzinc reagents were used. <sup>b</sup>Isolated yields. <sup>c</sup>The homocoupling product  $(\text{CH}_3)_2(\text{OH})\text{CC}\equiv\text{C}-\text{C}\equiv\text{C}(\text{OH})(\text{CH}_3)_2$  was isolated in 42% yield.

We had observed that the solvent affected the overall rate of the cross-coupling reaction; using THF as solvent the conversion of the organo tellurides was incomplete. However, the use of DMF as a co-solvent dramatically enhances the rate resulting in a complete conversion to the product.

As shown in Table 1, a range of functionalized alkynylzinc reagents can be used including those bearing either an unprotected hydroxy group (entries 6–8) or an amino group (entries 5 and 10). The organotellurium compounds employed could also incorporate different functionalities. It is noteworthy to mention that the unsymmetrical (mixed) alkynyldialkylzincates **2** exhibited a considerable selectivity for the transfer of only the alkynyl group.

In conclusion, by using our new cross-coupling reaction, a new carbon–carbon bond can be formed with a range of functionalized alkynylzinc reagents and unsaturated organotellurium (or iodo)

compounds, leading to polyfunctional unsaturated compounds such as arylalkynes, enynes, enediynes, alcohols, ethers, esters or amino compounds. The compatible functionalities present in these molecules can be submitted to further useful conversions.

## Acknowledgements

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9. To a flask containing the appropriate organotellurium compound (2.0 mmol) in THF (20 mL),  $\text{Pd}(\text{PPh}_3)_4$  (0.11 g, 0.2 mmol),  $\text{CuI}$  (0.38 g, 2.0 mmol) and DMF (15 mL) were added at room temperature under  $\text{N}_2$ . Then, the alkynyl zinc reagent **1**, **2** or **3** (3.0 mmol) previously prepared in another flask (see items a, b and c in this procedure) was transferred dropwise via syringe. The dark brown mixture was stirred at rt and the reaction time was determined monitoring the reaction by TLC. The mixture was extracted with diethyl ether, washed with water, dried over  $\text{MgSO}_4$  and the solvent removed under vacuum. The product was purified by column chromatography. a) Ethyl alkynylzinc reagents of type **1** were obtained by adding diethylzinc (4.5 mmol, 4.5 mL, 1.0 M in hexanes) to a solution of an acetylenic telluride<sup>4</sup> (3.0 mmol) in THF (12 mL) and stirred for 30 min at rt. b) The lithium diethyl alkynyl zincates of type **2** were prepared by the addition of diethylzinc (3.0 mmol, 3.0 mL, 1.0 M in hexanes) at rt to a solution of a lithium acetylide (3.0 mmol) in THF (12 mL). c) Dialkynylzinc reagents of type **3** were prepared by the addition of anhydrous  $\text{ZnCl}_2$  (0.408 g, 3.0 mmol) to a solution of a lithium acetylide generated by treating a terminal alkyne (6.0 mmol) in THF at 0°C with  $\text{BuLi}$  (6.0 mmol). After stirring for 20 min at rt, compounds **3** were used in situ.
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