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Novel cross-coupling reactions between organotellurides and Grignard

reagents employing a MnCl₂/CuI catalytic system

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ABSTRACT

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Introduction

Over the past two decades, organotellurium compounds have been the focus of a large number of studies. Some of these compounds have proven to be valuable synthetic intermediates.^{1,2} Most of the methods that lead to the formation of carbon–carbon bonds from organotellurium compounds are stoichiometric processes and involve Te/metal exchange reactions,³ leading to a reactive organometallic intermediate, like organolithium⁴ or organocopper⁵ reagents. Recently, the use of iron salts to replace palladium or nickel complexes as catalysts has emerged as a very promising area for sustainable development. From both economic and environmental standpoints, manganese salts can be a valuable alternative in metallic catalysis.⁶

From the perspective of green chemistry, the development of catalytic methods to promote carbon–carbon bond formation is not only environmentally friendly but also of great importance for synthetic methods. In this context, manganese salts are relatively cheap and nontoxic and can be used as an alternative catalyst to replace or complement the well established palladium or nickel complexes.^{6,7} However, the chemistry of manganese-catalyzed cross-coupling reactions is still in its early stage of

development and the synergism between $MnCl_2$ and CuI remains unclear.^{7,8}

Results and discussion

We present a general protocol for the cross-coupling reaction of Grignard reagents and organic tellurides.

Aryl Grignard reagents react stereospecifically with vinyl tellurides in the presence of a catalytic amount

of manganese (II) chloride and copper (I) iodide to produce good yields of the corresponding cross-cou-

We report here the cuprous iodide/manganese chloride catalyzed cross-coupling reaction of vinyl tellurides with aryl Grignard reagents. Initially, we screened different reaction conditions to evaluate the influence of the corresponding salts in the catalytic system. The use of CuI in this system is empirical, since the mechanism of the reaction is not known and Cu(I) salts are known as good co-catalytic reducing agents in metal-catalyzed reactions. The solvent and the temperature remained the same, and the amounts of MnCl₂ and CuI were varied as described in Table 1 (entries 1–9).

Searching for better conditions to perform the coupling reaction, we then tested several different compositions of the MnCl₂/ Cul catalytic system and PhMgCl. Initially the reaction was performed in the absence of MnCl₂ and subsequently in the absence of Cul (Table 1, entries 2 and 3). The results showed that MnCl₂ has a small influence in the conversion of **1** into **2** while copper salt appears have an important role in this reaction, leading to a higher yield. When 20 mol % of both salts were employed, the resulting conversion was acceptable but still inconclusive about the effect of the combination of both salts (entry 4). In comparison to entry 4, the yield was slightly increased when 1 equiv of each salt was used (entry 1).





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The O $Hint Cl_2 / Cul$ Z 1 $Hint Cl_2 / Cul$ Ph MgCl $Ph MgCl$ $Ph MgCl$ $Ph MgCl$ 2 Q					
Entry	MnCl ₂ (mol %)	CuI (mol %)	PhMgCl (mmol)	<i>T</i> (°C)	Yield of 2 ^a (%)
1	100	100	2.0	0	65
2	20	_	2.0	0	10
3	_	20	2.0	0	30
4	20	20	2.0	0	45
5	10	10	2.0	0	50
6	10	10	1.5	0	55
7	5	5	1.5	0	51
8	5	5	1.1	0	78
9	5	5	1.1	rt	48

^a All the reactions were conducted under anhydrous nitrogen atmosphere.

a for the resting and time

The decrease in the amount of salts and of the Grignard reagent (Table 1, entries 5, 6 and 7) resulted in a small increment in the yield. Reduction of the amount of the Grignard reagent was the most important parameter (Table 1, entries 5 and 6). The next experiment was designed based on a nearly equimolar addition (1.1 equiv) relative to substrate 1 (entry 8). This experiment again provided a significant yield increment, showing that the most important parameter in the reaction is the molarity of the Grignard reagent.

However, the highest yields were obtained when smaller amounts of both salts were employed. More specifically, the best result was achieved when 5 mol % of both salts were used at 0 °C, and with a smaller excess of the Grignard reagent (entry 8). There is also no increase in the conversion when the reaction was conducted at room temperature (entry 9). Coupling of **1** with PhMgCl gave the expected product **2**, but the reaction was not stereoretentive, leading to the total inversion of the double bond configuration to the *E* isomer, a fact that was also observed by Uemura.⁹

The homo-coupling by-product (Ph–Ph) was also observed, and despite the impairment, no bad smelling compounds were involved during the workup, even with the presence of butyl(phenyl)tellane or any other organic telluride that might be formed in small amounts.

The developed strategy was applied to the coupling of telluride **3**, in which the double bond was not capable of isomerization, leading to the formation of the coupling product **4** in a modest yield (Table 2, entry 2). On the other hand, when the alcohol **5** was submitted to the same conditions, the expected coupling product **6** was not observed.

In order to extend this methodology, different tellurides were prepared and submitted to the optimal condition found in Table 1, leading to the expected coupling products in a single isomer Z (except for Table 2, entry 1), in good yields.

As reported in the literature, halogenoenynes have also been studied as substrates for Mn-catalyzed cross-coupling reactions.¹⁰

Table 2

Table 1

Cross coupling reaction of tellurides with PhMgCl





All the reactions were performed in a 1 mmol scale, under anhydrous nitrogen atmosphere and at the same temperature (see Experimental Section/Supplementary data). * Yield determined by GC.

Table 3





In this context, we decided to employ equivalent tellurides (**9** and **11**) in this protocol. As can be seen in Table 2, entries 5 and 6, the tellurides **9** and **11**, respectively, led to the expected cross-coupling products in reasonable yields.

It is also important to comment on the stereochemistry of this reaction. Since the telluride **1** was the only substrate that leads to a total inversion of the configuration on the double bond geometry, a different mechanistic pathway shall not be discarded. One possibility is that this specific reaction proceeds through a conjugate addition of the corresponding organocopper reagent, followed by elimination of the butyltellanyl moiety. On the other hand, the same reaction conditions also lead to the same average yields when employing non-activated olefins (**7** and **11**, for example). However, these observations are not conclusive and mechanistic studies are necessary.

As can be seen in Table 2, a considerable number of tellurides containing different functional groups were tested and most of them were tolerated. Apparently this reaction is not very sensitive to the steric environment, since the coupling product can be obtained even from tetra-substituted sp^2 hybridized tellurides (Table 2, entry 12).

The following Figure 1 shows the key NOE enhancements observed for the compounds *Z*-**22** and *Z*-**24**, both obtained as single isomers.

It is possible to observe a strong NOE for both the methine aldol and the β -methyl protons, providing unquestionable proof of the Z



Figure 1. Key NOE enhancements observed for compounds 22 and 24 in the double bond geometry elucidation.

double bond geometry for compound **24**. Likewise, a strong NOE between the β -proton and the methine aldol **22** was also observed.

We also evaluated the scope of the corresponding catalyzed cross-coupling reaction in the presence of Grignard reagents bearing a methoxyl as an electron donating group (EDG) and a fluoro as an electron withdrawing group (EWG), employing both tellurides **1** and **23**, as shown in Table 3.

The results in Table 3 above show that both electron withdrawing and electron donating groups can be employed in this methodology, leading to the expected products in reasonable yields. However, for a detailed discussion of the influence of these substituents, a mechanistic approach should be considered.

Conclusions

In conclusion, the reaction of vinyl tellurides with organomagnesium compounds catalyzed by MnCl₂/Cul provides a reasonable alternative to coupling reactions that makes use of the more expensive and toxic palladium and nickel compounds as catalysts. Further studies of the presented cross-coupling reaction promoted by MnCl₂ will be reported in due course.

Experimental section

Typical procedure for coupling reaction: (E)-ethyl cinnamate (2). To a suspension of MnCl₂ (6.3 mg, 0.05 mmol) and CuI (9.5 mg, 0.05 mmol) in THF (3 mL) and (*Z*)-1 (284 mg, 1 mmol), a solution of phenylmagnesium chloride (1.2 mmol, 2 mol L^{-1} in THF) was added dropwise at 0 °C. After the completion of the Grignard addition, the mixture was warmed to room temperature and kept under stirring for an additional 20 min. The reaction mixture was washed with ammonium chloride (10 mL) and extracted with ethyl acetate (3 $\times\,5$ mL). The combined organic layers were washed with brine (10 mL), dried over MgSO₄, and concentrated under vacuum. Purification by chromatography on silica gel, eluent hexane : ethyl acetate (9:1), gave 0.137 g (78%) of 2 as a colorless oil. ¹H NMR: (300 MHz, CDCl₃, ppm) δ 7.69 (d, J = 16.2 Hz, 1H); 7.50–7.54 (m, 2H); 7.36–7.40 (m, 3H); 6.44 (d, J = 16.2 Hz, 1H); 4.27 (q, J = 7.2 Hz, 2H); 1.34 (t, J = 7.2 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃, ppm) δ 167.0; 144.6; 134.5; 130.2; 128.9; 128.5; 128.0; 127.7; 118.3; 60.5; 14.3. LREIMS m/z (rel. int.) 176 (M⁺,63); 148 (33); 130 (100); 104 (73); 77 (61); 51 (46). IRv_{max} , neat (cm⁻¹): 3053, 2957, 1646, 1370.

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Supplementary data

Supplementary data (The experimental procedure and NMR spectra of all the products are available free of charge via the Internet at www.journals.elsevier.com.) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.04.134.

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