Magnesium Catalyzed Stereoselective Hydrostannylation of Internal and Terminal Alkynes

Marc Magre,† Marcin Szewczyk,‡ and Magnus Rueping*,†,‡

†Institute of Organic Chemistry, RWTH Aachen University, Landoltweg 1, 52074 Aachen, Germany
‡KAUST Catalysis Center (KCC), King Abdullah University of Science and Technology (KAUST), Thuwal 23955-6900, Saudi Arabia

ABSTRACT: A regio- and stereoselective magnesium catalyzed hydrostannylation of internal and terminal alkynes has been developed. Excellent yields and selectivities are obtained for a wide range of terminal and internal symmetrical and unsymmetrical alkynes by using this alkaline earth metal catalyst as effective alternative to transition metal catalysts.

KEYWORDS: magnesium, alkynes, hydrostannylation, alkaline base earth-abundant metal

Organostannanes are important organometallic reagents in organic synthesis due to their versatile transformations including C-C cross-coupling reaction. Thus, the development of efficient methods for the preparation of organostannanes has attracted considerable attention. Despite the challenge of selectivity control, the hydrostannylation of alkynes is one of the most efficient and economic routes to vinyl stannanes which are relevant synthetic intermediates in organic synthesis. Regarding their stereoselective synthesis, radical type hydrostannylation, strong Lewis acid mediated as well as transition metal catalyzed protocols have been developed to provide (Z)- or (E)-vinyl stannanes, respectively. Examples for the latter are Pd, Mo or Cu-catalyzed syn-addition which may require laborious and/or bulky ligands to achieve good regio- and stereoselectivities. Nevertheless, these transition-metal catalyzed protocols paved the way for achieving hydrofunctionalizations of unsaturated bonds. Alkaline and in particular alkaline earth metal based catalysts have attracted increasing attention in recent years as an alternative to transition metal catalysts. Whereas more reactive Ca, Sr, and Ba catalysts have been widely applied, the use of Mg catalysts has been mostly focused on hydroboration of unsaturated bonds. In this respect and based on our interest in the further development of magnesium catalysis as an alternative to late transition metal catalysis, we decided to explore a magnesium catalyzed hydrostannylation of internal and terminal alkynes (Scheme 1).

We began our investigations of the magnesium catalyzed hydrostannylation using a symmetrical internal alkyne 1a in the presence of readily available MgBu2 (Table 1).

This work: Readily available alkaline earth-abundant metal

Scheme 1. MgBu2-catalyzed hydrostannylation of terminal and internal alkynes.

MgBu2 showed to be active at relatively mild reaction temperature (Table 1, entry 1), providing excellent yields and stereoselectivities towards product (Z)-2a. The change of reaction solvent resulted in lower yields and...
MgBu₂ was established as the optimal solvent (Table 1, entries 2-3). By decreasing the temperature or the catalyst loadings, we found out that MgBu₂ catalytic system is less active, but the excellent stereoselectivities were maintained (Table 1, entries 4 and 5). When we tested Mg-L1 as catalyst (Table 1 entry 6), it turned out to show similar activity and selectivity as readily available MgBu₂. Although the β-diketiminate Mg complex could also be used, we decided to proceed with amine ligand-free MgBu₂ as catalyst as it is as easy to handle but allows for a faster and simpler purification after the reaction.

Table 1. Optimization of MgBu₂-catalyzed hydrostannlation of alkyne 1a.[a]

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>temp. (°C)</th>
<th>selectivity[β] (Z)-2a : (E)-2a</th>
<th>yield [%][d]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>toluene</td>
<td>50</td>
<td>&gt;95:5</td>
<td>&gt;99 (98)</td>
</tr>
<tr>
<td>2</td>
<td>THF</td>
<td>50</td>
<td>&gt;95:5</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>CHCl₃</td>
<td>50</td>
<td>n.d.</td>
<td>&gt;5</td>
</tr>
<tr>
<td>4</td>
<td>toluene</td>
<td>23</td>
<td>&gt;95:5</td>
<td>90</td>
</tr>
<tr>
<td>5[b]</td>
<td>toluene</td>
<td>50</td>
<td>&gt;95:5</td>
<td>91</td>
</tr>
<tr>
<td>6[e]</td>
<td>toluene</td>
<td>50</td>
<td>&gt;95:5</td>
<td>&gt;99</td>
</tr>
<tr>
<td>7[f]</td>
<td>toluene</td>
<td>50</td>
<td>n.d.</td>
<td>&gt;5</td>
</tr>
</tbody>
</table>

[a] MgBu₂ (1 M in heptane, 10 mol%), alkyne (1a, 1.0 mmol), 1.1 equiv. of HSnBu₃, solvent (1.5 mL, 0.7 M), for 24 h. [b] Determined by ¹H NMR spectroscopy. [c] Determined by ¹H NMR using 1,3,5-trimethoxybenzene as internal standard. Isolated yields in parenthesis. [d] 5 mol% of MgBu₂ were used. [e] Using Mg-L1 (10 mol%) as catalyst. [f] No catalyst was used.

With the optimized reaction conditions, we explored the scope and limitations of the MgBu₂-catalyzed hydrostannlation of different internal alkynes (Scheme 2). For both symmetrical internal alkynes 1a and 1b, the major stereoisomer obtained was (Z)-2a and (Z)-2b, respectively. We could observe that the presence of O-protected groups on the alkyl substituent did not influence the stereochemistry of the product. Subsequently, we tested more challenging unsymmetrical alkynes 1c-1m, which are known to cause problems of regioselectivity.[5-6] We were delighted to see that MgBu₂ catalyst can successfully catalyze the hydrostannlation of internal aryl-alkyl alkynes (1c-1f), not only stereoselectively but also regioselectively, achieving in all cases the β-(Z)-isomer. Depending on the size of the alkyl substituent, the stereoselectivity slightly varies while maintaining the excellent levels of regioselectivity.

We were pleased to see that the presence of O-protected groups on the alkyl chain (1g-1i) did not have an influence on either activities or selectivities, achieving in all cases excellent yields and regio- and stereoselectivities. Surprisingly, when the internal alkyne bearing an N-protected group (1j) was tested, opposite regio- and stereoselectivities were achieved, affording the corresponding α-(E)-2j.

We attribute this behavior to the stronger coordinative effect of the NMe₃-group compared to the bulky OTIPS-group. The good catalytic performance of MgBu₂ for the hydrostannlation of internal aryl-alkyl alkynes was further extended to internal alkyl-alkyl alkynes 1k-1m, achieving excellent yields and stereoselectivities. Similar to the hydrostannlation of symmetrical internal alkynes (1a-1b), the major stereoisomer for the unsymmetrical internal alkynes (1c-1i, 1k-1m) was found to be (Z)-vinyl stannane, indicating that the hydrostannlation occurs in a trans-fashion.[i]

Scheme 2. MgBu₂-catalyzed hydrostannlation of internal alkynes.[a]

[a] Reaction conditions: 1a-1m (1.0 mmol), 1.1 mmol. HSnBu₃, MgBu₂ (10 mol%), toluene (1.5 mL), 50 °C for 24 h. Yields after purification. [b] Neat, 23 °C, 72 h. [c] 48 h. [d] 23 °C, 24 h. [e] ¹H NMR yield. [f] 40% of β-regioisomer. [g] 7% of...
β-regioisomer. For detailed information, see Supporting Information.

Finally, in order to expand the substrate scope, we tested several terminal alkynes (Scheme 3). When applying the same conditions to the terminal alkyne 3a we observed poor stereoselectivity towards (E)-4a. We could solve this selectivity problem by increasing the temperature (for details, see Supporting Information) while maintaining the excellent yields and regioselectivities.

With the optimized reaction conditions, we investigated the scope and limitations of our catalytic system. First, we tested various phenylacetylene derivatives with different electronic properties (3a-3e) and we were pleased to see that there was no influence on the catalytic activity, achieving in all cases excellent yields and regio- and stereoselectivities towards β-(E)-vinyl stannanes 4a-4e.

Scheme 3. MgBu₂-catalyzed hydrostannylation of internal alkynes.[a]

<table>
<thead>
<tr>
<th>R</th>
<th>3a-3r</th>
<th>HSnBu₃</th>
<th>MgBu₂ (7 mol%)</th>
<th>Toluene, 70 °C, 16 h</th>
<th>4a-4r</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>4a</td>
<td>89%</td>
<td>(99:1)</td>
<td>4b</td>
<td>91%</td>
</tr>
<tr>
<td>F</td>
<td>4c</td>
<td>93%</td>
<td>(99:1)</td>
<td>4d</td>
<td>95%</td>
</tr>
<tr>
<td>C</td>
<td>4e</td>
<td>92%</td>
<td>(99:1)</td>
<td>4f</td>
<td>90%</td>
</tr>
<tr>
<td>O</td>
<td>4g</td>
<td>89%</td>
<td>(97:3)</td>
<td>4h</td>
<td>91%</td>
</tr>
<tr>
<td>F</td>
<td>4i</td>
<td>93%</td>
<td>(99:1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Remarkably, these excellent selectivities are superior to those obtained using transition-metal catalysts, for which the regioselectivities showed to be electronically dependent.[5c-5d] Moreover, this good performance was also observed for sterically differentiated phenylacetylene derivatives 4f-4k.

Regarding terminal aliphatic alkynes, we observed that our MgBu₂ catalytic system is able to hydrostannylate terminal alkynes containing cyclic (4l), and linear (4m) alkyl substituents with excellent regio- and stereoselectivities, competing favorably with the best reports in the literature.[5-6]

Propargylic alcohols 3n-3q were also tested. However, MgBu₂ was not able to provide the corresponding β-(E)-vinyl stannane with acceptable regioselectivity. To solve this regioselectivity problem, sterically hindered Mg-L₁ catalyst was now used in order to diminish the ability of the hydroxyl moiety as a directing group.[5f] We were delighted to see that vinylstannes 4n-4q could now be isolated in excellent regio- and stereoselectivities, albeit in moderate-to-good yields. Finally, we studied O-protected propargylic alcohol 3r. In contrast to its respective unprotected alkynol (4o), excellent yields and regioselectivities were obtained with MaBu₂.

Scheme 4. Control experiments.

a) Formation of BuMgH active species

<table>
<thead>
<tr>
<th>HSnBu₃ + MgBu₂ (1 equiv.)</th>
<th>H₂, toluene</th>
<th>BuMgH</th>
<th>Bu₂SnBu₃</th>
<th>Bu₂SnSnBu₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 equiv.</td>
<td>1 equiv.</td>
<td>traces</td>
<td>traces</td>
<td>not formed</td>
</tr>
</tbody>
</table>

b) Stoichiometric experiment

1g → SnBu₃

Toluene, 23 °C, 20 h

2g; >99% yield; 95:5 Z:E

c) Lewis acid SnBu₃ as catalyst

1g → SnBu₃

Toluene, 23 °C, 20 h

2g; 8% yield

d) MgBu₂-promoted isomerization

5 → SnBu₃

Toluene, 23 °C, 20 h

5; 75:25 (Z : E)
Evidencing Mg/B exchange, (E)-vinyl borane products are achieved. Herein we report that for the MgBu₄-catalyzed hydrostannylation of alkynes the stereochemical outcome is, however, opposite.

In order to get more information on the reaction mechanism, we decided to perform several control experiments (Scheme 4). First, due to the trans-stereoselectivity observed, we confirmed our hypothesis that the MgBu₄-catalyzed hydrostannylation of alkynes does not take place through active species BuMgH. When MgBu₄ was mixed with stoichiometric excess of HSnBu₃, only traces of SnBu₃ were observed (for details, see Supporting Information). This finding agrees with the different hydride reactivity that HBpin and HSnBu₃ present. Whereas hydridic B-H bond undergoes σ-bond metathesis with MgBu₄ to provide active species BuMgH, Sn-H bond does not.[5] We also conducted stoichiometric experiments (Scheme 4b) and observed that only one molecule of HSnBu₃ is necessary to obtain the corresponding vinylstannane product in quantitative yield. This result discards the possibility of a mechanism that involves the formation of active BuMgH species, therefore MgBu₄ activates HSnBu₃ through a different pathway.[6] Given that traces of SnBu₃ were formed when catalyst and tri-n-butylin hydride were mixed, we tested if Lewis acidic SnBu₄ could potentially catalyze the transformation (Scheme 4c). In this case, only traces of product 2g could be observed, discarding the possibility that Lewis acidic SnBu₄ acts as a catalyst. By additional control experiments (Scheme 4d), we have proven that MgBu₄ is able to isomerize (Z)-vinylstannanes to (E)-vinylstannanes. Depending on the size of the R² substituent, the isomerization is more favored, which explains the isomerization observed when terminal alkynes were studied.

In agreement with Weiner and Still et al.[7] who reported that organotin/organolithium exchange occurs in equilibrium, we believe that organomagnesium can also undergo exchange with the vinylstannane, providing the more thermodynamically stable (E)-stereoisomer.

Regarding the mechanism and catalytic cycle of the MgBu₄-catalyzed hydrostannylation of alkynes we can only postulate that it may be similar to those reported using strong Lewis acids and the recently reported trans-hydrophosphination reaction.[8] In line with all experimental data we propose that the stereoselective trans-hydrostannylation takes place through a carbocationic intermediate in which either the stannane or alkyne is activated by the Mg-catalyst (Scheme 5a, b). Moreover, we have observed that (Z)-vinylstannanes (Scheme 4d and Supporting Information) isomerize to more thermodynamically stable (E)-products in the presence of MgBu₂. Although there is no relevant data in the literature which support this isomerization, our findings led us to propose that Mg-catalyst isomerizes vinylstannane species via carbanion species, as Mitchell and coworkers reported when vinylstannanes are mixed with organolithium species.[9, 7] In summary, we report the first active and selective catalytic system based on inexpensive and readily available magnesium catalyst for the hydrostannylation of terminal and internal alkynes. Under relatively mild reaction conditions and low catalysts loadings, excellent yields and regio- and stereoselectivities have been achieved for a wide range of terminal and internal alkynes, even for challenging unsymmetrical substrates. Moreover, mechanistic studies suggest that hydrostannylation may occur through Lewis acidic activation either of HSnBu₃ or C=C bond, providing the corresponding vinylstannanes. Finally, we have proven that MgBu₄ can also isomerize (Z)-vinylstannanes to more stable (E)-stereoisomer.

**Scheme 5.** Proposed mechanisms for MgBu₄-catalyzed isomerization of vinylstannanes (Scheme 5a and b). The Supporting Information is available free of charge on the


