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# Catalyst-Free and Solvent-Controlled Reductive Coupling of Activated Vinyl Triflates with Chlorotrimethylsilane by Magnesium Metal and Its Synthetic Application

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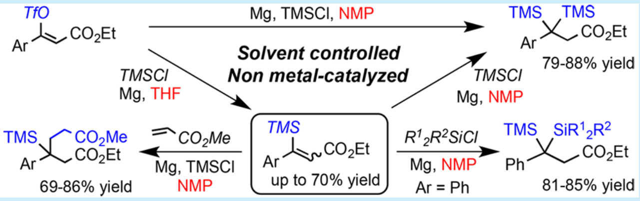
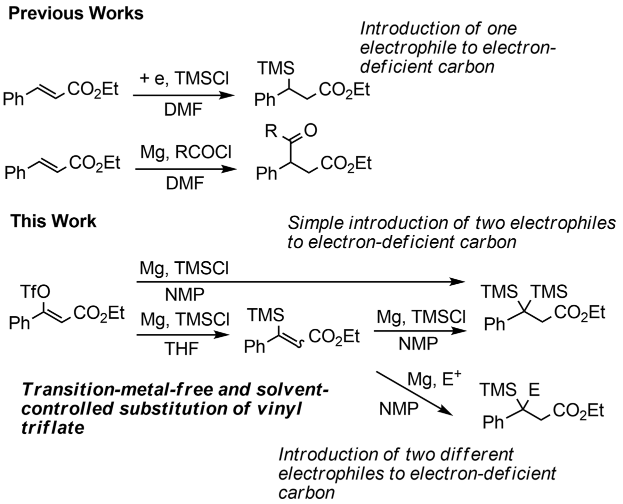
*Supporting Information*

**ABSTRACT:** Vinylsilanes were directly prepared from the corresponding vinyl triflates under magnesium-promoted reductive conditions in THF with no transition metal catalyst, and *gem*-bis-silylated compounds were obtained in NMP. Investigation of the redox potential of starting materials and products suggested that reductive coupling reactions of vinyl triflates might be controlled by the reduction potential. A variety of *gem*-bis-silylated compounds and 3-silyladipic acid esters were easily synthesized in only two steps from vinyl triflates in high yields.



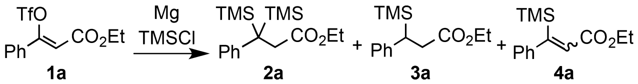
Alkyl triflates are typical reagents for substitution reactions with a good leaving group in synthetic organic chemistry, whereas vinyl triflates can be usually used for substitution only in the presence of a transition metal catalyst.[1] Many examples of transition-metal-catalyzed coupling reactions of vinyl triflates,[1] aryl triflates,[2] vinyl tosylates,[3] aryl tosylates,[4] and aryl mesylates[5] can be found in organic synthesis; however, there are few catalyst-free coupling reactions, which have been required for a synthetic process. To our best knowledge, only substitution reactions of vinyl triflates by nucleophilic attack of thiophenol[6] and electrochemical carboxylation of vinyl triflates[7] were reported with no transition metal catalyst.



We already reported reductive coupling reactions between electron-deficient atoms and developed carbon−carbon bond or carbon−silicon bond formation reactions by eco-friendly magnesium metal as a reductant.[8] Ethyl cinnamates can be acylated and silylated at the *β*-carbon atom of the carbonyl group under reductive reaction conditions.[9] In this study, we prepared ethyl cinnamates with a triflate at the *β*-position of the carbonyl group as starting vinyl triflates from easily available ethyl benzoylacetates[10] and investigated their coupling reactions. In our previous results,[8] aprotic polar solvents, such as DMF or NMP, were required for magnesium-promoted reductive coupling reactions of aromatic carbonyl compounds or aromatic conjugated carbonyl compounds, whereas reductive coupling did not occur in THF and acetonitrile.

Our first attempt to reduce **1a** in NMP, DMF, and DMA succeeded to give *gem*-bis-silylated compound **2a** as a main product with elimination of the triflate, and a reaction in acetonitrile failed as we predicted (Table 1). Surprisingly,

**Table 1. Solvent Effects of Magnesium-Promoted Reductive Silylation of 1a**[a]



| entry | solvent | GC yield (%) | | |
|---|---|---|---|---|
| | | 2a | 3a | 4a |
| 1 | DMF | 44 | 14 | 0 |
| 2 | NMP | 63 | 21 | 0 |
| 3 | DMA | 51 | 36 | 0 |
| 4 | MeCN | complex mixture | | |
| 5 | THF | 0 | 3[b] | 61[b,c] |

[a]Mg (6 equiv), TMSCl (8 equiv), rt, 8 h. [b]Isolated yield. [c]*Z*/*E* = 5/4.

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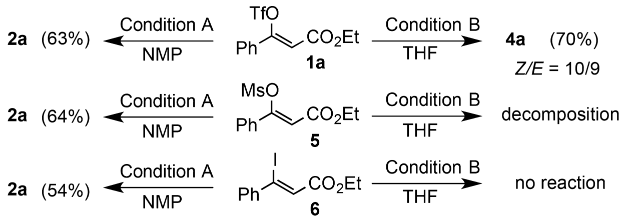
reductive C−Si bond formation of **1a** occurred, accompanied by elimination of the triflate group in THF to afford *Z*/*E* isomers of the corresponding vinylsilane selectively. As an example of magnesium-promoted reaction in THF, reductive elimination of a fluorine atom of the trifluoroacetyl group has been reported by Uneyama and co-workers, and there is no direct formation of carbon−carbon and carbon−silicon bonds at the $sp^2$ carbon atom.[11] The leaving group is one of the most important factors in this coupling reaction in THF, and only triflate gave the substituted compound **4a**; mesylate **5** was decomposed in situ, and iodinated compound **6** was recovered quantitatively (Scheme 1). Compounds **1a**, **5**, and **6** were converted into **2a** in good yields in NMP.

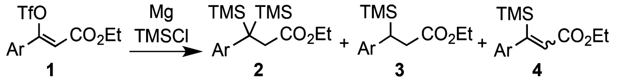
### Scheme 1. Effects of the Leaving Group in Reductive Substitution of Ethyl Cinnamate Derivatives



Condition A: Mg (6 equiv), TMSCl (6 equiv), rt, 5 h, GC yield
Condition B: Mg (3 equiv), TMSCl (3 equiv), rt, 5 h, isolated yield

After the optimization of reaction conditions in THF and NMP, the general tendency of the reactions was examined, and the results are shown in Table 2. In NMP, about 20% of saturated monosilylation product **3** was detected as a byproduct, which could be directly prepared from reductive silylation of ethyl cinnamate **7** in previous results.[9a,b] In THF, vinylsilane **4** was obtained as a sole product in good to moderate yield.

### Table 2. Reductive Silylation of 1 by Magnesium Metal in NMP[a] and THF[a]

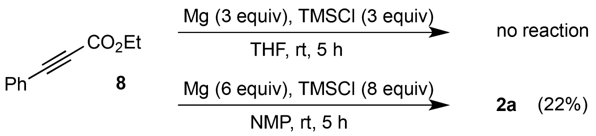


| entry | Ar (1) | solvent | isolated yield (%) 2 | | 3 | | 4 | |
|---|---|---|---|---|---|---|---|---|
| 1 | Ph | NMP | 57 | **2a** | 20 | **3a** | | |
| 2 | (**1a**) | THF | | | | | 70 | **4a**[c] |
| 3 | 4-$ClC_6H_4$ | NMP | 50 | **2b** | 17 | **3b** | | |
| 4 | (**1b**) | THF | | | | | 64 | **4b**[c] |
| 5 | 4-$CH_3C_6H_4$ | NMP | 58 | **2c** | 21 | **3c** | | |
| 6 | (**1c**) | THF | | | | | 50 | **4c**[d] |
| 7 | 3-$FC_6H_4$ | NMP | 42 | **2d** | 22 | **3d** | | |
| 8 | (**1d**) | THF | | | | | 64 | **4d**[c] |
| 9 | 3-$CH_3OC_6H_4$ | NMP | 49 | **2e** | 27 | **3e** | | |
| 10 | (**1e**) | THF | | | | | 43 | **4e**[e] |
| 11 | 2-naphthyl | NMP | 47 | **2f** | 25 | **3f** | | |
| 12 | (**1f**) | THF | | | | | 69 | **4f**[f] |

[a] Mg (6 equiv), TMSCl (6 equiv), rt, 5 h. [b] Mg (3 equiv), TMSCl (3 equiv), rt, 5 h. [c] *Z*/*E* = 10/9. [d] *Z*/*E* = 1/1. [e] *Z*/*E* = 10/7. [f] *Z*/*E* = 5/4.

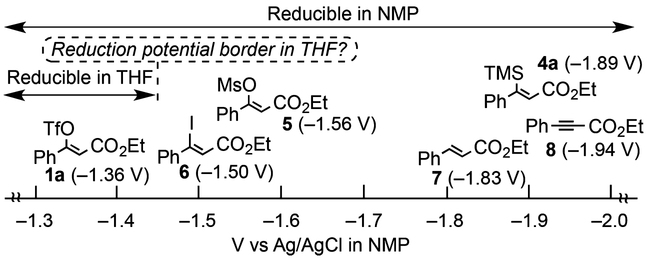
Reduction of phenylacetylene derivative **8** was carried out because **1a** was regarded as an equivalent of **8**; however, it was inert under the same reaction conditions in THF, and a low yield of **2a** was obtained in NMP and DMF after complete consumption of **8** (Scheme 2).[12]

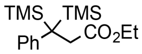
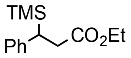
### Scheme 2. Reaction of Phenylacetylene Derivative under the Same Reduction Conditions



From a total view of the results shown in Table 2 and Schemes 1 and 2, we measured the reduction potential of some starting materials and products in NMP and THF; however, significant peaks could not be detected in THF (Table 3). Reduction of **1a** was possible in THF and NMP, and all of the conjugated carbonyl compounds, except **1a**, could not be reduced in THF. Product **4a** was also inert in THF. Therefore, a hypothesis on the magnesium-promoted reduction in THF is proposed from these results; namely, there may be a reduction potential border for the magnesium-promoted reduction in THF, and its value will be around −1.40 V in NMP.[13] In NMP and DMF, our previous results suggested that the reduction potential limit of magnesium-promoted reduction would be about −2.40 V.[8] The approximately estimated value on the reduction potential border enabled us to explore a simple way to prepare various functionalized compounds.

### Table 3. Hypothesis on the Reduction Potential Border of Magnesium-Promoted Reduction in THF Estimated from the Reduction Potential of Some Compounds in NMP[a]



| compound | potential (V) | compound | potential (V) |
|---|---|---|---|
| **1a** | -1.36 | **5** | -1.56 |
|  **2a** | - | **6** | -1.50 |
|  **3a** | - | **7** | -1.83 |
| **4a** | -1.89 | **8** | -1.94 |

[a] Cyclic voltammetry; Pt as working electrode, Pt as counter electrode, Ag/AgCl as reference electrode, NMP as solvent, $n\mathrm{Bu}_4\mathrm{NClO}_4$ as supporting electrolyte; scan rate = 0.2 V $s^{-1}$, scan range = 0 to − 3.00 V.

First, selective synthesis of **2** from **4** was investigated, and the results are summarized in Table 4. Both *Z* and *E* isomers of **4a** were converted into the same *gem*-bis-silylated compound in excellent yield with less monosilylated compound **3a** (entries 1 and 2). The other *gem*-bis-silylated compounds were easily synthesized from compounds **4** (entries 3−7).

Furthermore, application of a two-step strategy to **1** led to the synthetic possibility of compounds attacked by two different electrophiles at the electron-deficient *β*-carbon atom of the

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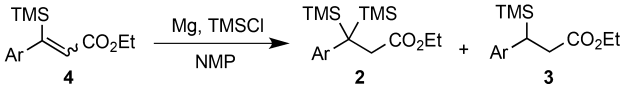
*Org. Lett.* XXXX, XXX, XXX−XXX

Table 4. Reductive Synthesis of *gem*-Bis-silylated Compounds 2 from Vinylsilanes 4 in NMP[a]



| | Ar | isolated yield (%) | | | |
|---|---|---|---|---|---|
| entry | 4 | 2 | | 3 | |
| 1 | Ph (**4a**-*Z*) | 84 | **2a** | 12 | **3a** |
| 2 | Ph (**4a**-*E*) | 80 | **2a** | 17 | **3a** |
| 3 | 4-ClC$_6$H$_4$ (**4b**-*Z*) | 86 | **2b** | 10 | **3b** |
| 4 | 4-CH$_3$C$_6$H$_4$ (**4c**-*Z*) | 88 | **2c** | 8 | **3c** |
| 5 | 3-FC$_6$H$_4$ (**4d**-*Z*) | 85 | **2d** | 11 | **3d** |
| 6 | 3-CH$_3$OC$_6$H$_4$ (**4e**-*Z*) | 86 | **2e** | 9 | **3e** |
| 7 | 2-naphthyl (**4f**-*Z*) | 79 | **2f** | 10 | **3f** |

[a] Mg (3 equiv), TMSCl (3 equiv), rt, 5 h.

carbonyl group. Different silylating agents were applied to this coupling reaction to give *gem*-bis-silylated compounds with different silyl groups (**9**) in high yields, accompanied by a small amount of **3a** as a byproduct (Scheme 3).[14]

Scheme 3. Synthesis of *gem*-Bis-silylated Compounds with Different Silyl Groups

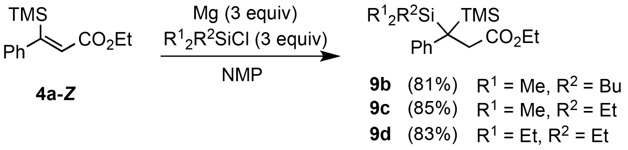
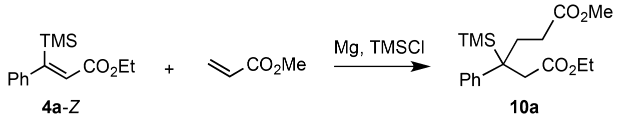


Table 5. Solvent Effects of Magnesium-Promoted Reductive and Unsymmetrical Carbon−Carbon Bond Formation between 4a and Methyl Acrylate[a]

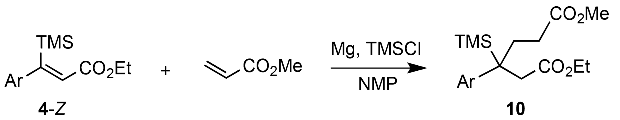


| entry | solvent | isolated yield (%) |
|---|---|---|
| 1 | DMF | 55 |
| 2 | NMP | 83 |
| 3 | THF | 0 |

[a] Mg (3 equiv), TMSCl (3 equiv), methyl acrylate (4 equiv), −10 °C, 4 h.

Our next target to the coupling reaction of **4** was a new carbon−carbon bond formation at the benzylic position, and methyl acrylate was chosen as a reagent. As shown in Table 5, unsymmetrical coupling between two different $\alpha,\beta$-unsaturated esters in DMF and NMP occurred at $\beta$-positions smoothly to give adipic acid ester (**10a**), and NMP was the best solvent.[15]

Table 6. Reductive Carbon−Carbon Bond Formation of Vinylsilane 4 in NMP[a]

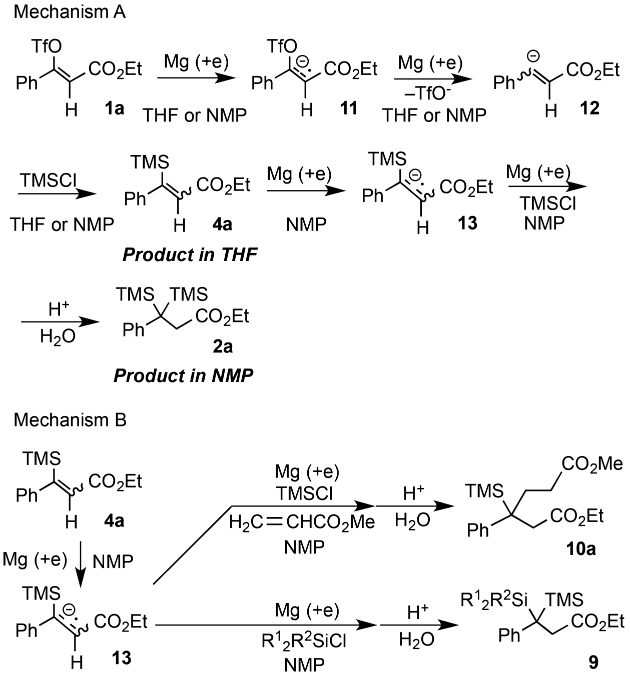


| entry | Ar (4) | isolated yield of **10** (%) | |
|---|---|---|---|
| 1 | 4-ClC$_6$H$_4$ (**4b**-*Z*) | 85 | **10b** |
| 2 | 4-CH$_3$C$_6$H$_4$ (**4c**-*Z*) | 77 | **10c** |
| 3 | 3-FC$_6$H$_4$ (**4d**-*Z*) | 69 | **10d** |
| 4 | 3-CH$_3$OC$_6$H$_4$ (**4e**-*Z*) | 80 | **10e** |
| 5 | 2-naphthyl (**4f**-*Z*) | 86 | **10f** |
| 6 | 4-FC$_6$H$_4$ (**4g**-*Z*) | 75 | **10g** |

[a] Mg (3 equiv), TMSCl (3 equiv), methyl acrylate (4 equiv), −10 °C, 4 h.

After optimization of the reaction conditions, scope and limitation of this coupling reaction were investigated, as shown in Table 6. Simple and direct coupling reaction between aliphatic $\alpha,\beta$-unsaturated ester and aromatic $\alpha,\beta$-unsaturated ester **4** proceeded easily to give unsymmetrical adipic acid esters with both an aromatic ring and a silyl group at the 3-position in high yields. The reduction potential of methyl acrylate was measured by cyclic voltammetry, and methyl acrylate showed no significant reduction peak in NMP. This result indicates that methyl acrylate will be reduced neither in THF nor in NMP, and that the reductive coupling will start from the reduction of aromatic conjugated ester **4**.

Scheme 4. Plausible Reaction Mechanism for Reductive Coupling of Ethyl Cinnamate Derivatives



Plausible reaction mechanisms for a series of coupling reactions are shown in Scheme 4. The most important reaction is the reductive substitution reaction of **1a** by magnesium metal in the presence of chlorotrimethylsilane in THF and NMP (mechanism A). Single electron transfer from magnesium metal to vinyl triflate **1a** in the presence of chlorotrimethylsilane in THF or NMP, followed by elimination of the triflate as an anion and the second electron transfer, will give a vinyl anion (**12**).[16] Silylation of **12** afforded vinylsilane **4a** as *Z*/*E* isomers, and no further reaction occurred in THF. The second reductive silylation of **4a** proceeded in NMP to give *gem*-bis-silylated compound **2a** as a main product. Anion **12** will be stabilized by a magnesium ion in THF, such as a vinyl Grignard reagent, whereas **12** may be unstable in NMP and abstract a proton, for example, from solvent NMP to give monosilylated compound **3a** in part.[17]

Isolation of **4a** enabled us to explore novel synthetic processes (mechanism B). In NMP, **4a** could be reduced by magnesium metal to give an anion radical species (**13**). An anionic species derived from **13** or **13** itself will attack chlorotrialkylsilane, nucleophilically, or will be subjected to Michael addition to methyl acrylate, respectively.[18] Protonation after the reaction brought about selective formation of *gem*-bis-silylated compounds **9** and adipic acid derivatives **10** in high yields.

In conclusion, magnesium-promoted reductive silylation of aromatic vinyl triflates **1** proceeded with no transition metal catalyst. The reaction could be controlled by the choice of solvent, and this result suggested that the reduction by magnesium in THF would have a potential limit much more positive than that in NMP. Intermediates, vinylsilanes **4**, which would be generated in the reduction in NMP were trapped and isolated selectively in the reduction in THF. These phenomena were utilized in the selective introduction of two different electrophiles to the electron-deficient carbon, especially synthesis of *gem*-bis-silylated compounds **2**, **9**, and 3-silyladipic acid esters **10**. Related studies are in progress.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b00496.

$^{1}$H and $^{13}$C NMR spectra of **1b−f**, **2a−f**, **3d**, **3e**, (*Z*)-**4b−g**, (*E*)-**4b−f**, **5**, **9b−d**, and **10a−g**, and $^{19}$F NMR spectra of **2d**, **3d**, (*Z*)-**4d**, (*E*)-**4d**, (*Z*)-**4g**, **10d**, and **10g** (PDF)

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

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(12) The yield of **2a** in DMF was 18%.

(13) It is impossible to have a precise discussion on the reduction potential of the compounds treated in this reaction because our trial to measure the reduction potential in THF failed, and the reduction potentials of an organic compound in different solvents are not the same, in general. The reduction potential in NMP has been used as a standard to classify compounds.

(14) Monosilylated compound **3a** was obtained in 12−13% yield as a byproduct in all cases.

(15) Addition of chlorotrimethylsilane to this C−C bond formation reaction is probably essential to activate the surface of magnesium metal and to stabilize intermediates generated during the reaction. The typical additives for Grignard reactions, such as iodine, iodomethane, and 1,2-dibromoethane, were inappropriate for our magnesium-promoted reduction.

(16) In the electron transfer reaction, formation of dianionic species is thought to be unfavorable, and elimination of a triflate from **11** prior to the second electron transfer is adopted in Scheme 4.[7]

(17) In NMP, monosilylated compound **3a** may also be generated from an anion radical species **13**.

(18) Before hydrolysis, a ketene silyl acetal or a magnesium enolate may be formed in situ.