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Facile synthesis of multifunctionalized allenes by magnesium-promoted reductive silylation of aromatic conjugated ynones

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ABSTRACT

Mg-promoted reductive silylation of 4-phenyl-3-butyn-2-one in *N*,*N*-dimethylformamide (DMF) in the presence of chlorotrimethylsilane brought about double silylation at the β-carbon and oxygen atoms of the carbonyl group to give a multifunctionalized allene with a vinylsilane moiety and a silyl enol ether moiety. A variety of allenes can be synthesized through this simple methodology. Acid-catalyzed hydrolysis of an allene derived from the trimethylsilylation of 4-phenyl-3-butyn-2-one resulted in the formation of the corresponding benzalacetone with a trimethylsilyl group at the β-position of the carbonyl group in high yield.

Allenes are well known as an isomerized structure of acetylene and in recent years, some researchers have focused on allenes as attractive targets in axial asymmetric synthesis.[1–6] However, the selective synthesis of allenes is not necessarily easy because of their high reactivity. As a result, the exploration of novel synthetic methods for allene synthesis,[7–16] especially multi-functionalized allenes, remains an important topic in organic synthesis.[16–25] Chemical reactions to utilize allenes as organic fine-chemical intermediates are also a topic of investigation.

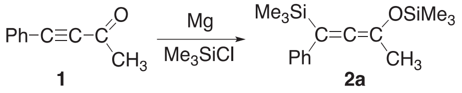
Silicone-containing organic compounds such as vinylsilanes, allylsilanes, or silyl enol ethers, are used as important intermediates, and the efficient introduction of a silyl group has been exclusively researched in the field of organic synthesis. Although the introduction of a silyl group onto the β-carbon atom of α,β-unsaturated carbonyl compounds generally requires the Michael addition of a silyl anion species at low temperature, reductive silylation can resolve the problems with this approach, such as the severe reaction conditions required and the generation of an unstable silyl anion during its nucleophilic addition. For example, electrochemical and magnesium-promoted silylation of ethyl cinnamate at room temperature produces β-silylated compounds in high yields.[26,27]

However, in the previous study on the reductive silylation of aromatic conjugated ynones, the potential formation of aromatic allenes under similar reaction conditions was indicated by Merault and co-workers, although the suspected carcinogen HMPA was used as the solvent and the isolation of multifunctionalized aromatic allenes was not reported.[28] In this study, the reductive coupling of aromatic conjugated ynones with chlorotrialkylsilane in the presence of magnesium metal in *N*,*N*-dimethylformamide (DMF) led to the successful synthesis of various silylated multifunctionalized allenes in good to excellent yields.

Commercially available 4-phenyl-3-butyn-2-one (**1**) was chosen as an aromatic conjugated ynone and optimized reaction conditions for the silylation of **1** were investigated as shown in Scheme 1 and Table 1.

Tetrahydrofuran is not a suitable solvent for this trimethylsilylation and an aprotic polar solvent such as DMF or *N*-methyl-2-pyrrolidinone is required to obtain the allene derivative in good yield.[29]

The combination of more than 4 equiv of magnesium and 4 equiv of chlorotrimethylsilane is sufficient for this coupling



Scheme 1.

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Table 1
Mg-promoted silylation of 4-phenyl-3-butyn-2-one (**1**) in the presence of chlorotrimethylsilane

Entry	Solvent	Mg (equiv mol)	TMSCl (equiv mol)	Isolated yield (%) **2a**
1	THF	6	8	0
2	NMP	6	8	67
3	DMF	6	8	91
4	DMF	6	7	82
5	DMF	6	6	79
6	DMF	6	4	77
7	DMF	4	8	80
8	DMF	4	6	80

Solvent (30 mL), 25 °C, **1** (5 mmol), 5 h, nitrogen atmosphere.

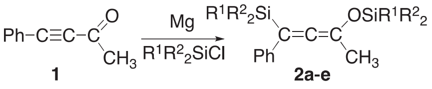
reaction to produce the unstable allene **2a** (entries 3–8), and 6 equiv of magnesium and 8 equiv of chlorotrimethylsilane gave the best result in 91% yield (entry 3).

Various silylating agents were used in this coupling reaction; the results are summarized in Scheme 2 and Table 2.[30]

Reactions of **1** with chlorotrialkylsilane afforded the corresponding allenes (entries 1–4 and 6), whereas application of chlorochloromethyldimethylsilane (entry 5) or dichlorodimethylsilane (entry 7) failed, probably because of the reduction of highly reactive silanes. The silane with a long alkyl group (entry 4) and the bulky silanes (entries 3 and 6) gave the decreased yields of **2**.

Derivatives of **1** were also silylated with chlorotrimethylsilane under the same reaction conditions to give the corresponding allenes **4** (Scheme 3, Table 3).

Compared with the results in Table 2, the yields hardly depended on the bulkiness of the substituent of the starting materials **3** (entries 1–4). Note that a ketone with a *tert*-butyl group bonded to the carbonyl group was also transformed into the corresponding allene in high yield (entry 3). However, an ester could not be used in this reaction instead of a ketone and a complex mixture was obtained, probably because the product from the ester would include a structure of the ketene silyl acetal from the ester that was unstable and reactive (entry 6). Reductive silylation of an aliphatic α,β-ynone with no aromatic conjugation system also gave no functionalized allene because the active anionic species derived from the reduction of the aliphatic species would not be stabilized by conjugation (entry 7).

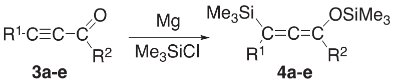


Scheme 2.

Table 2
Mg-promoted silylation of 4-phenyl-3-butyn-2-one (**1**) with various silylating agents

Entry	R^1	R^2		Isolated yield (%)
1	CH_3	CH_3	**2a**	91
2	CH_3CH_2	CH_3	**2b**	80
3	$(CH_3)_2CH$	CH_3	**2c**	76
4	$CH_3CH_2CH_2CH_2$	CH_3	**2d**	41[a]
5	$ClCH_2$	CH_3		Complex mixture
6	CH_3CH_2	CH_3CH_2	**2e**	67
7	Cl	CH_3		Complex mixture

Compound **1** (5 mmol), Mg (6 equiv mol), silylating agent (8 equiv mol), DMF (30 mL), 25 °C, 5 h, nitrogen atmosphere.
[a] NMR yield.

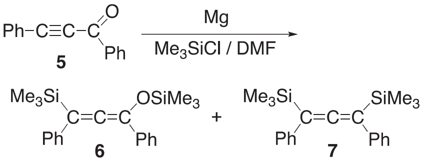


Scheme 3.

Table 3
Mg-promoted silylation of ynone derivatives (**3**) with chlorotrimethylsilane

Entry	R^1	R^2		Isolated yield (%) **4**
1	Ph	Bu	**4a**	81
2	Ph	*cyclo*C_6H_{11}	**4b**	83
3	Ph	*tert*Bu	**4c**	80
4	Ph	$C_6H_5CH_2CH_2$	**4d**	75
5	*p*-$CH_3C_6H_4$	CH_3	**4e**	66
6	Ph	OCH_3		Complex mixture
7	Bu	CH_3		Complex mixture

Compound **3** (5 mmol), Mg (6 equiv mol), chlorotrimethylsilane (8 equiv mol), DMF (30 mL), 25 °C, 5 h, nitrogen atmosphere.



Scheme 4.

The reductive silylation of an aromatic ketone (**5**) was also investigated under the similar reaction conditions, and a mixture of two allenes was obtained; the corresponding allene (**6**) and a symmetrical deoxyallene (**7**) (Scheme 4). The reaction at −15 °C or 45 °C also afforded a mixture of **6** and **7**; however, under a higher concentration of **5**, only **6** was formed in 62% yield (Table 4). In the presence of an excess amount of magnesium, we conducted the reaction for one day; however, the ratio of the product was unchanged. This result suggests that the product **7** was independently obtained, which may indicate that **7** is not the reduced compound of **6**. Although the reason why compound **6** was selectively obtained is not clear, the silylation at the β-carbon atom of the carbonyl group may be kinetically accelerated under high concentration because the anion at the carbonyl carbon atom will be stabilized by conjugation with the benzene ring and acetylenic moiety to be less reactive, which will be shown in the reaction mechanism. However, selective synthesis of deoxyallene **7** could not be attained in this reaction.

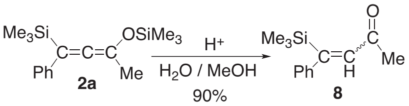
Hydrolysis of the product **2a** was conducted under acidic reaction conditions by sulfuric acid and exclusively formed β-silylated benzalacetone **8** in high yield as shown in Scheme 5, which was isolated as a single isomer, although its absolute structure has not been identified yet.[31]

The reduction potential of some starting materials and products was measured using cyclic voltammetry, as shown in Table 5. The voltammograms of compounds **1** and **5** showed a reduction peak at

Table 4
Optimized reaction conditions for the synthesis of **6**

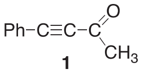
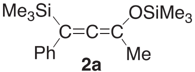
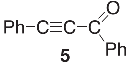
Entry	Temperature (°C)	Concentration (mol L^{-1})	Yield[b] (%)	
			6	**7**
1	−15	0.10	38	10
2	25	0.10	51	15
3	45	0.10	17	27
4	25	0.50[a]	62[c]	Trace

Compound **5** (5 mmol), Mg (6 equiv mol), chlorotrimethylsilane (8 equiv mol), DMF (50 mL), 5 h, nitrogen atmosphere.
[a] DMF (10 mL).
[b] NMR yield.
[c] Isolated yield.

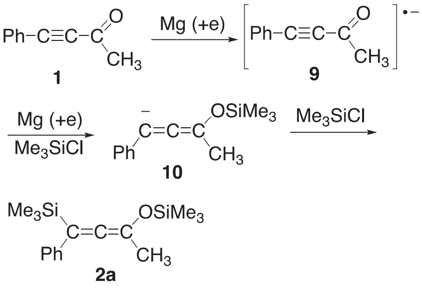


Scheme 5.

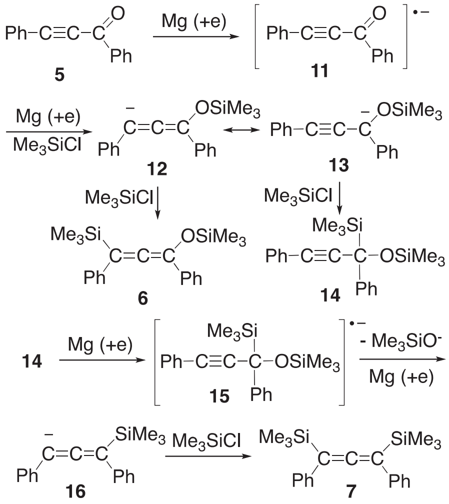
Table 5
Reduction potentials of some starting materials and a product

Reagent	Potential V *vs* Ag/AgCl
 **1**	-1.69
 **2a**	No peak
 **5**	-1.38
Me_3SiCl	No peak

Working electrode Pt, counter electrode Pt, reference electrode Ag/AgCl solvent DMF, supporting electrode Bu_4NClO_4, scan rate 200 mVs^{-1}.



Scheme 6.



Scheme 7.

−1.69 V and −1.38 V versus Ag/AgCl, respectively, while chlorotrimethylsilane showed no significant peak in the range between −3 V and 0 V. Therefore, this result suggests that the reductive coupling may be initiated by a single electron transfer from magnesium metal to **1** or **5**. Because the product **2a** showed no significant peak in the range between −3 V and 0 V, the allenes **2** and **4** were selectively synthesized in these coupling reactions with no further reduction. The proposed reaction mechanism is shown in Scheme 6.

The reduction can be initiated by a single electron transfer from magnesium to aromatic ynone **1**. An anion radical species **9** may be formed, followed by the attack of chlorotrimethylsilane and the second electron transfer to give an unstable anion **10**. Exclusive silylation of **10** at the benzylic position resulted in the formation of **2a** as a single product.

However, the reaction mechanism of the compound **5** is somewhat different because **5** comprises two phenyl groups (Scheme 7). An anion radical species **11** will be silylated and reduced to give the corresponding resonance structures **12** and **13**. The anionic species **12** will be transformed into the normal allene **6** through silylation, whereas **13** will be stabilized by the neighboring phenyl group and react with chlorotrimethylsilane to give **14**. We could not isolate the compound **14**, which might undergo further reduction and silylation to produce an anion **16**, followed by final silylation to give the deoxyallene **7**. Under the higher concentration of chlorotrimethylsilane, the generated intermediate **12** will be attacked by chlorotrimethylsilane immediately to give the exclusive formation of **6**.

In summary, the reductive coupling of aromatic conjugated ynones with chlorotrialkylsilane in the presence of magnesium metal in DMF brought about the selective formation of multifunctionalized aromatic allenes in good to excellent yields. Note that selective double silylation of the β-position and the oxygen atoms of the carbonyl group occurred, and unstable multifunctionalized allenes were successfully isolated, which might be useful as silicone-containing intermediates in organic syntheses.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.09.066.

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29. The solvent effects cannot be clearly explained, but it may be related with the reduction potential of the starting material.
30. In most of the cases, magnesium was completely consumed, which would show chlorotrimethylsilane might be reduced by the activated magnesium throughout the reaction.
31. The NOE experiments for the compound **8** did not give an absolute confidence for the identification of the structure to us.