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Regioselective synthesis of bis(silyl enol ethers) and bis(conjugated enones) through electron transfer from Mg metal

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Abstract—Treatment of α,β-unsaturated ketones with Mg metal in the presence of trimethylsilyl choride (TMSCl) brought about facile and regioselective reductive dimerization to give the corresponding bis(silyl enol ethers), 1,6-bis(trimethylsilyloxy)-1,5-dienes. Similar Mg-promoted reductive dimerization of 1,3-cyclic diketones in the presence of TMSCl followed by acid-catalyzed hydrolysis led to selective formation of the corresponding 1,6-diketo-2,4-dienes in moderate to good yields.

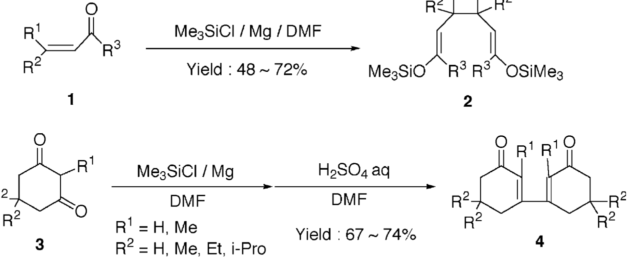
Much attention has been focused on reductive hydro dimerization of α,β-unsaturated carbonyl compounds to the corresponding useful 1,6-dicarbonyl compounds by electron transfer type of reactions. Electroreduction[1–9] and metal-promoted reactions[10–12] have been well known as the typical methods. However, little successful trapping of a dimeric anionic (or dianion) species generated with an electrophile has been reported.

In this study, we wish to report Mg-promoted facile and regioselective dimerization of α,β-unsaturated carbonyl compounds (**1**) at the β-carbons in the presence of trimethylsilyl chloride (TMSCl) in *N*,*N*,dimethylformamide (DMF) to give the corresponding 1,6-bis(trimethylsilyloxy)-1,5-dienes (**2**) in satisfactory yields.

Furthermore, 1,6-diketo-2,4-dienes (**4**) were selectively obtained in good yields through the similar Mg-promoted reductive dimerization of 1,3-diones (**3**) in the presence of TMSCl followed by acid-catalyzed hydrolysis. These reactions may be characterized by simple procedure, mild conditions, high regioselectivity, good yield and unique structure of the products, and environmental priority of Mg metal.

The typical procedure is as follows: Into an anhydrous DMF (40 mL) solution containing α,β-unsaturated ketones (**1**) (10 mmol) and Mg turning (50 mmol) for Grignard reaction (Nacalai tesque, purity: 99.5%) without any pre-treatment, was added TMSCl (100 mmol) dissolved in an hydrous DMF (10 mL) dropwise at 5 °C (Scheme 1).

After the addition, the solution was stirred at room temperature for 24 h, and then the reaction mixture was subjected to usual work-up. Silica gel (Merck, silica gel 60, 70–230 mesh) column chromatography of the crude products (eluent; hexane/EtOAc = 5:1) gave the corresponding 1,6-bis(trimethylsilyloxy)-1,5-dienes (**2**) in 48–72% yields, as shown in Table 1. Use of Ca and Zn instead of Mg led to some decrease in product yield (yield of **2f**: Mg; 51%, Ca; 50%, Zn; 32%) while the reaction did not take place either in THF or CH_3CN



Scheme 1.

Keywords: Dimerization; Electron transfer; Enol ethers; Magnesium and compounds.

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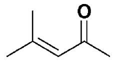
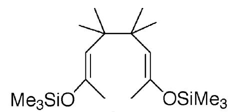
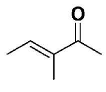
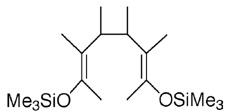
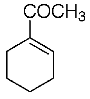
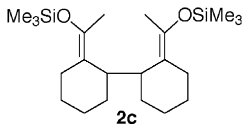
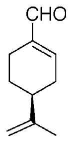
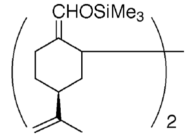
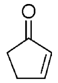
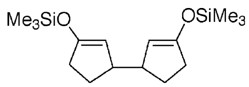
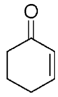
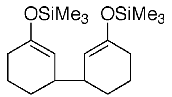
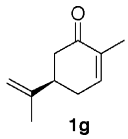
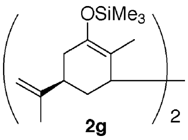
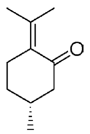
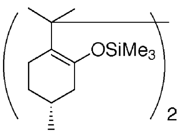
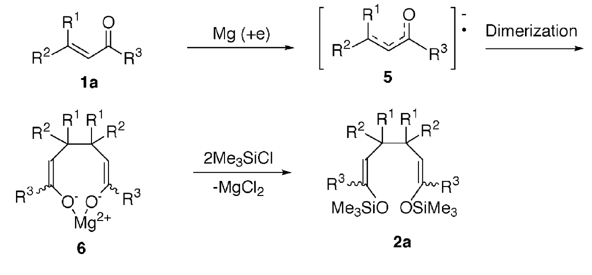
Table 1. Mg-Promotedbis(silyl enolization) of α,β-unsaturated ketones

Substrate 1	Products 2	Yield (%)[a]
 **1a**	 **2a** (EE:ZZ:EZ=20:44:36)	65
 **1b**	 **2b**	62[b]
 **1c**	 **2c**	72[b]
 **1d**	 **2d**	53[b]
 **1e**	 **2e**	61[c]
 **1f**	 **2f**	51[c]
 **1g**	 **2g**	72[c]
 **1h**	 **2h**	48

[a] Total yield stereoisomers.

[b] *dl*/*meso*, *E*/*Z* isomers.

[c] *dl*/*meso*-1/1 mixture.



Scheme 2.

and the starting substrate was recovered quantitatively. The reaction proceeded smoothly whether a substrate was cyclic or acyclic compound to afford an expected product in satisfactory yield.

It may be noteworthy that bis(silyl enolization) took place in a regioselective manner. The following scheme may be postulated as one of the most plausible reaction mechanisms, as shown in Scheme 2. The first electron transfer from Mg metal to α,β-unsaturated ketones (**1**) may generate the corresponding radical anions (**5**), which were subjected to dimerization to form the bis(enolate anions) (**6**). These dianions may be coordinated with Mg^{2+} to be trapped by TMSCl, giving the bis(silyl enol ethers) (**2**).[†]

Treatment of cyclic 1,3-diones (**3**) with Mg metal in the presence of TMSCl under the similar conditions to that for α,β-unsaturated ketones (**1**) followed by acid-catalyzed hydrolysis brought about specific dimerization and elimination of two silyloxyl groups to afford the corresponding 1,6-diketo-2,4-dienes (**4**) in good yields. Product yield and selectivity were found to be influenced by molar ratios of Mg metal and TMSCl based on a starting substrate. Thus, use of 5 equiv mol of Mg metal and 10 equiv mol of TMSCl led to an optimum result. Under these conditions, a variety of bis(conjugated enones) (**4**) were obtained in 67–74% yields, as shown in Table 2.[‡]

In order to get some information for reaction mechanism, the dimerization product, 1,6-bis(trimethylsilyloxy)-1,3,5-triene derivative (**7a**), from a substrate **3a** was isolated prior to acid-catalyzed hydrolysis in a 54% yield, and was characterized by spectroscopic methods ^1H and ^{13}C NMR, IR, MS).[§] Subsequent acid-catalyzed hydrolysis of **7a** under an air atmosphere gave the oxidation product **4a** in a quantitative yield. Interestingly, unstable 1,6-diketo-2-hexene (**8a**) could be obtained from the same treatment of **7a** under nitrogen atmosphere.

[†] All of the products **2a–h** and **4a–d** were characterized by spectroscopic methods ^1H and ^{13}C NMR, IR, Mass, and/or elemental analysis. For example, analytical data for **2f** as a *dl* and *meso* mixture and **2h** were shown as follows. **2f**: ^1H NMR ($CDCl_3$, 400 MHz) δ 0.18 (s 18H), 1.14–1.23 (m 2H), 1.49–1.63 (m 4H), 1.76–1.82 (m 2H), 1.91–2.03 (m 4H), 2.10–2.18 (m 2H), 4.73 (s 1H), 4.82 (s 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 0.38, 22.27, 22.54, 25.59, 26.67, 30.04, 30.11, 40.06, 40.11, 107.91, 108.14, 150.86, 151.18 ppm. IR (neat) 2920, 1680, 1250, 1185, 840 cm^{-1}. MS m/z 338 (M^+), Anal. calcd for $C_{18}H_{34}O_2Si_2$: C, 63.84; H, 10.12. Found: C, 64.01; H, 10.20.

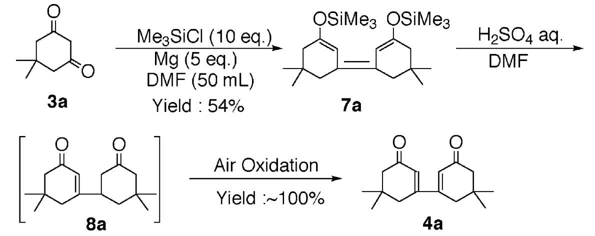
[‡] **2h**: ^1H NMR ($CDCl_3$, 400 MHz) δ 0.18 (s 18H), 0.92 (d 6H, $J = 6.4$ Hz), 1.05 (s 6H), 1.22 (s 6H), 1.53–1.61 (m 5H), 1.73–1.80 (m 3H), 1.94–1.97 (m 4H), 2.08 (dd 2H, $J = 5.0$ Hz, 15.8 Hz) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 1.73, 22.01, 26.31, 28.46, 29.54, 32.21, 41.01, 45.93, 119.08, 143.04 ppm. IR (neat) 2950, 1640, 1250, 840 cm^{-1}. MS m/z 450 (M^+).

[§] **7a** (single isomer, not clear for the geometry): ^1H NMR ($CDCl_3$, 400 MHz) δ 0.19 (s 18H), 0.93 (s 12H), 1.96 (s 4H), 2.02 (s 4H), 5.80 (s 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 0.47, 28.48, 30.92, 39.11, 44.52, 106.81, 125.08, 151.16 ppm. IR (KBr) 2950, 1620, 1380, 1260, 1230, 1160, 950, 870, 840 cm^{-1}. MS m/z 392 (M^+), mp 114–116 °C.

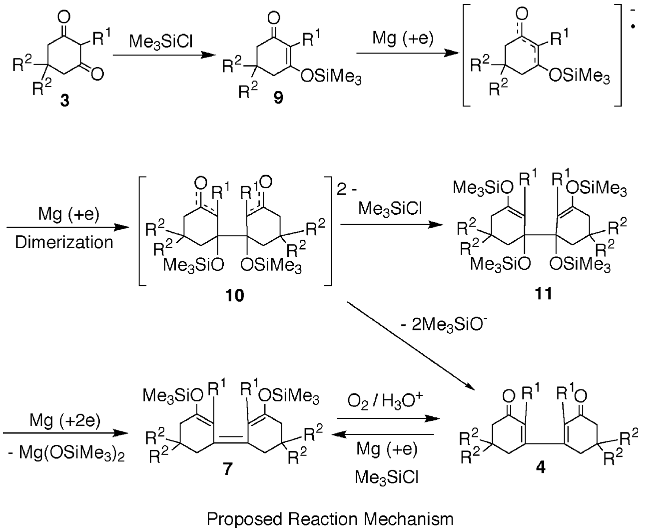
Table 2. Selective synthesis of bis-conjugated enones by Mg-promoted dimerization of cyclic 1,3-diones

Substrate **3**	R	Yield of **4**/%	
3a	H	**4a**	73
3b	Me	**4b**	67
3c	Et	**4c**	74
3d	$CH(CH_3)_2$	**4d**	67

Mg 5 equiv, Me_3SiCl 10 equiv, DMF 50 mL, 5 °C, 24 h.



Scheme 3.



Scheme 4. Proposed reaction mechanism.

From these experimental results, the following scheme may be proposed as a reaction mechanism for the present specific dimerization of cyclic 1,3-diones (**3**). Starting substrates, cyclohexa-1,3-diones (**3**), are easily transformed to 3-trimethylsilyloxy-2-cyclohexenone (**9**) from Mg-promoted *O*-silylation with TMSCl.[13] The first electron transfer from Mg metal to **9** may afford the corresponding anion radicals, which are subjected to dimerization at the β-carbon followed by double *O*-silylation of the dianions generated, giving the 1,3,4,6-tetrasilyloxy-1,5-dienes (**11**) (Scheme 3).

Subsequent reductive elimination of the two silyloxy groups from the bis(silyl ethers) of 1,2-diols (**11**) may take place forming 1,6-bis(trimethylsilyloxy)-1,3,5-trienes (**7**), which were subjected to oxidative hydrolysis to give the products (**4**).[14–17]

As a conclusion, a simple and efficient method for synthesis of 1,6-trimethylsilyloxy-1,5-dienes (**2**) and 1,6-diketo-2,4-dienes (**4**), possibly useful synthetic intermediates, was successfully developed by treatment of α,β-unsaturated enones and 1,3-diones, respectively, with easily available Mg metal in the presence of TMSCl (Scheme 4).

Acknowledgements

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17. It may be proposed as another possibility that **7** was formed by elimination of $TMSO^-$ from the dimerized dianion intermediate, followed by further reduction of the produced diene–dione **4** by Mg in the presence of TMSCl.