Mg-Promoted Regioselective Carbon-Silylation of α-Phosphorylacrylate Derivatives

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Treatment of aromatic α-phosphorylacrylate derivatives **1a-h** with Mg turnings in the presence of trimethylsilyl chloride brought about facile and regioselective C-silylation to give the corresponding β-silylated phosphonates **2a-h** in excellent yields. The reaction took place smoothly for activated olefins possessing appropriate reduction potentials and may be initiated by electron transfer from Mg to **1a-h.**

Regioselective introduction of a silyl group to a desired position of organic compounds may be one of challenging subjects in organic synthesis because of increasing interests in specific and valuable functions of organosilicon compounds.[1–3] It has been reported by us and Calas's group that electrochemical[4] and Mg-promoted reduction[5,6] of aromatic α,β-unsaturated esters such as ethyl cinnamate in the presence of trimethylsilyl chloride(TMSCl) affords β-trimethylsilyl-β-arylpropionates in moderate to good yields.[7,8] A regioselective carbon-silicon bond formation proceeds at the β-position of the ester groups through electron transfer from a cathode or Mg metal to the substrates. On the other hand, phosphorus-containing organic compounds are of much use as a variety of speciality chemicals such as agrochemicals, pharmaceutical drugs, flame retardants, metal-extraction agents and electronics materials.

In this study, we wish to report facile and efficient regioselective carbon-silylation of aromatic α-phosphorylacrylate derivatives **1a-h** to give the corresponding β-silylated phosphonates **2a-h** in excellent yields. Synthesis of these specific compounds bearing both of a phosphonate group and a silyl group in a same molecule may be interesting in material science as well as in organic chemistry.
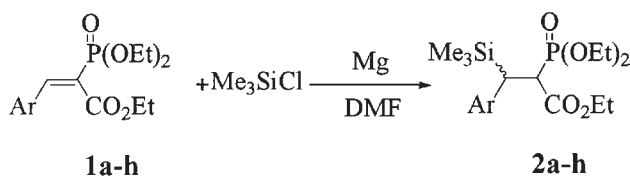

Scheme 1.

The starting α-phosphorylacrylates **1a-h** were prepared according to the reported literatures.[9–11] The typical procedure of the present Mg-promoted reductive silylation is as follows: Into a solution of *N,N*-dimethylformamide (DMF) containing TMSCl (15 equiv) and Mg turnings (6 equiv) for Grignard reaction without any pre-treatment was added a DMF solution of α-phosphorylacrylates **1a-h** dropwise at −10 °C under nitrogen atmosphere and the solution was continued to stir for 9 h at room temperature (15–20 °C). After the usual work-up of the reaction mixture, the products were isolated by flash column chromatography on silica gel. The corresponding β-silylated phosphonates **2a-h**[12] were obtained in 84–97% yields as mixtures of the

diastereoisomers, as shown in Table 1. The diastereoisomer ratios of the products **2a-h** were approximately 1 to 2, but their structures have not been determined as yet. Large excess amount of TMSCl must be required for smooth reaction because it was assumed that TMSCl did not only work as an electrophilic agent but also played a critical role of continuous activation of Mg metal surface as a weak Lewis acid. The similar silylation of ethyl α-phosphoryl-β-thienylacrylates **1h** having a heteroaromatic ring also successfully took place with a similar diastereoisomer ratio of **2h**. The yields of the products **2a-h** were little influenced by the nature of substituents on the benzene rings of the substrates **1a-h**.

Table 1. Mg-Promoted β-silylation of aromatic α-phosphorylacrylate derivatives **1a-h**

Entry	Substrate	Ar	Product	Yield / %	Ratio
1	**1a**	H	**2a**	95	1 : 1.8
2	**1b**	*p*-Me-C$_6$H$_4$	**2b**	91	1 : 2.7
3	**1c**	*m*-MeO-C$_6$H$_4$	**2c**	95	1 : 1.5
4	**1d**	*p*-MeO-C$_6$H$_4$	**2d**	97	1 : 1.7
5	**1e**	*m*-Cl-C$_6$H$_4$	**2e**	88	1 : 1.8
6	**1f**	*p*-F-C$_6$H$_4$	**2f**	88	1 : 1.8
7	**1g**	*p*-CF$_3$-C$_6$H$_4$	**2g**	88	1 : 1.1
8	**1h**		**2h**	84	1 : 1.3

Reaction Conditions: Substrate (4 mmol), TMSCl (60 mmol), Mg (24 mmol), DMF (50 ml), Temp. -10 °C to r.t., 9 h, under nitrogen atmosphere.

It may be noteworthy that Mg-promoted reduction of diethyl 2-phenylethenylphosphonate (**3**)[13] under the similar conditions led to formation of the hydrodimerization product **3C** (19% yield)[14] as the main product accompanying with formation of a small amount of the β-silylated product **3A** (10% yield) and much tarry material. On the other hand, the reaction of diethyl benzylidenmalonate (**4**) and ethyl benzylideneacetoacetate (**5**) resulted in considerable decrease in the yield of the corresponding β-silylated products **4A** and **5A** (70–67% yield) , and considerable amounts (23–24 yield) of simply hydrogenated products **4B** and **5B** were obtained as the by-products. Also, from the reaction of ethyl benzylidenecyanoacetate (**6**), only some of a simply hydrogenated products **6B** (23% yield) and a small amount of the

Table 2. Reduction Potentials and Products of Aromatic Active Olefins[a]

	Substrate			Product yield / %		
	Ar	R^1	R^2	R.P. / V^b	A	B	C
1a	Ph	COOEt	O=P(OEt)$_2$	-1.75	95	2	-[c]
1e	m-ClPh	COOEt	O=P(OEt)$_2$	-1.72	88	4	-[c]
1h	[thiophene]	COOEt	O=P(OEt)$_2$	-1.76	84	-[c]	4
3	Ph	H	O=P(OEt)$_2$	-2.33	10	-[c]	19
4	Ph	COOEt	COOEt	-1.68	70	23	-[c]
5	Ph	COMe	COOEt	-.1,60	67	24	-[c]
6	Ph	CN	COOEt	-1.40	9	23	-[c]

[a]Reaction conditions: Substrate (4 mmol), TMSCl (60 mmol), Mg (24 mmol), DMF (50 ml), Temp. -10 °C to r.t., 9 h, under nitrogen atmosphere. [b]Reduction potential:10%Bu$_4$NClO$_4$ / DMF, room temp., sweep rate 200 mV/s, working electrode: Pt, counter electrode: Pt, reference electrode: Ag/AgCl. [c]A trace amount.

β-silylated product **6A** (9% yield) were obtained accompanying with formation of much tarry material, as shown in Table 2.

Cyclic voltammetry of these aromatic α-phosphorylacrylates **1a**, **1e**, **1h**, **3** and the related compounds **4-6** may provide some significant informations for elucidation of remarkable differences in their reaction behaviors, as shown in Table 2. There seems a tendency in the present reactions that the reaction of a substrate possessing more negative reduction potential gives a hydro-dimerzation product (type C) while a simply hydrogenated product (type B) is obtained to some extent from that of a substrate possessing a less negative reduction potential. A substrate such as α-phosphorylacrylates **1a-h**, whose reduction potential are $-1.70-$-1.80 V, are most suitable for the present Mg-promoted regioselective C-silylation, giving a type A product predominantly.

The present Mg-promoted reductive silylation may proceed through electron transfer from Mg metal to activated electron–difficient olefins **1a-h** to give the corresponding radical anions, which are successively subjected to electrophlic attack of TMSCl, second electron transfer and protonation. Different reaction behaviors of a variety of activated olefins, depending upon their reduction potentials, may be attributed to stability and reactivity of the corresponding radical anions.[15]

As a conclusion, efficient and facile regioselective formation of C-Si bond was successfully accomplished through electron transfer from Mg metal to appropriately activated aromatic α-phosphorylacrylates, which might be of much use in organic synthesis and material science.

References and Notes
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7 Calas et al. represented the used solvent, hexamethylphosphortriamide ((Me$_2$N)$_3$PO) as the abbreviation HMPT in their series of Mg-promoted reactions. However, the solvent, (Me$_2$N)$_3$PO, is represented as carcinogenic hexamethylphosphoric triamide (HMPA) and should be different from hexamethylphosphorous triamide ((Me$_2$N)$_3$P) (HMPT) which may be too reactive to use as a solvent.[8]
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12 All the products **2a-h**, **3A**, **3C**, **4A-C**, **5A-B**, **6A-B**, and **7A-B** were characterized by spectroscopic methods (^{1}H- and ^{13}C-NMR, IR, Mass), and elementary analysis.
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14 Use of 0.5 eq of TMSCl in the reaction of **3** resulted in some increase in the yield of the hydrodimerization product **3C** to 39%, and formation of a trace amount of the silylated product **3A**.
15 It may be one of plausible explanation that a less stable radical anion from **3** is apt to dimerize at a proximity to Mg metal surface while a more stable one form **4-6** has enough life-time to diffuse into a bulk solution and to catch a proton rather than reactive TMSCl.