

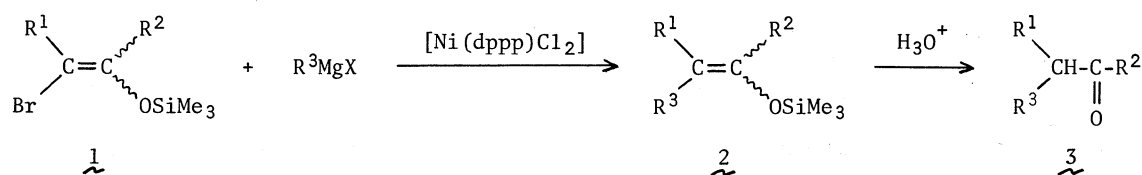
α-ALKYLATION AND α-ARYLATION OF CARBONYL GROUPS: NICKEL-PHOSPHINE
COMPLEX-CATALYZED GRIGNARD COUPLING OF *vic*-BROMOTRIMETHYLSILOXYALKENES

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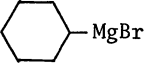
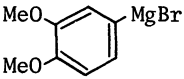
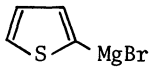
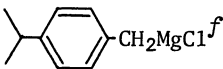
In the presence of [Ni(dppp)Cl₂] as a catalyst, *vic*-bromotrimethylsiloxy-alkenes (1) couple with Grignard reagents to produce alkylated and arylated silyl enol ethers, or, after acid hydrolysis, the corresponding α-alkylated and α-arylated carbonyl compounds. In these reactions, 1 can be regarded as an enolonium equivalent.

In the preceding communication,¹ we reported the nickel-phosphine catalyzed Grignard coupling² of β-bromovinyl ethyl ether to give the corresponding homologated vinyl ethers in one step. This was a step toward the functionalized carbon chain homologation by the nickel-phosphine complex catalyzed Grignard cross-coupling. In this paper we describe the Grignard coupling of *vic*-bromotrimethylsiloxyalkenes (brominated silyl enol ethers) (1). There are some advantages of 1 as the substrates in this reaction. (1) It has been reported that silyl enol ethers are almost reluctant to react with Grignard reagents under usual conditions.³ (2) Silyl enol ethers are readily hydrolyzed under mild conditions to give the corresponding carbonyl compounds.⁴ (3) A new route to the halogenated silyl enol ethers 1 starting with the corresponding, readily available silyl enol ethers⁵ have recently been developed by us.⁶



- a, R¹ = H, R² = Ph
b, R¹ = H, R² = Me
c, R¹ = Me, R² = H
d, R¹ = Et, R² = H
e, R¹ = R² = -(CH₂)₃-

Table. Grignard Coupling of *vic*-Bromotrimethylsiloxyalkenes (1) in the Presence of [Ni(dppp)Cl₂] as a Catalyst^a

Entry	R ¹	R ²	R ³ MgX	Conditions	Yield (%) ^b
1	H	Ph	<i>n</i> -BuMgBr	r.t., 20 h	70
2	H	Ph	<i>i</i> -PrMgBr	r.t., 20 h	64 ^c
3	H	Ph	PhMgBr	r.t., 20 h	94
4	H	Ph	Me ₃ SiCH ₂ MgCl	35°, 10 h	82 ^d
5	H	Me	<i>n</i> -BuMgBr	80°, ^e 20 h	78
6	H	Me	 MgBr	80°, ^e 20 h	45
7	H	Me	PhMgBr	80°, ^e 20 h	75
8	H	Me	 MgBr	80°, ^e 20 h	49
9	H	Me	 MgBr	80°, ^e 20 h	27
10	Et	H	PhMgBr	35°, 20 h	73 ^d
11	Me	H	 CH ₂ MgCl ^f	40°, 10 h	58 ^g
12	-(CH ₂) ₃ -		PhMgBr	35°, 40 h	33

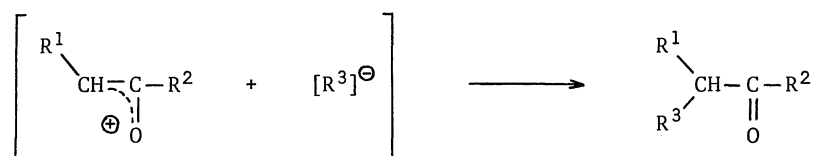
^a Halide : Grignard reagent : catalyst ≈ 1 : 1.2 : 0.01. Unless otherwise noted, the solvent was diethyl ether and the reactions were carried out in essentially the same manner as described in ref. 2. ^b Yields of the hydrolyzed carbonyl compounds 3 are given, unless otherwise noted. ^c *n*-Pr- : *i*-Pr- = 65 : 35 (see Text). ^d Isolated yield of the silyl enol ether 2. ^e Carried out in a glass sealed tube: To a nitrogen-filled glass tube were added successively the catalyst, 1b, and the Grignard solution at -78°. The tube was sealed under reduced pressure and heated at 80°. ^f A THF solution. ^g The product is cyclamen aldehyde.

Results summarized in Table were obtained using [Ni(dppp)Cl₂] as a catalyst.⁷ Several notable trends deserve comment. While the phenyl-substituted bromo enol ether 1a reacts readily at room temperature with various Grignard reagents (entries 1 - 4), the methyl analog 1b is less reactive and the satisfactory yields were obtained after rather prolonged heating at 80° in a sealed tube (entries 5 - 9). Silyl bromo enol ethers in which R² is hydrogen (1c, 1d) exhibited the intermediate reactivity (entries 10 and 11). Bromosiloxycycloalkene 1e also showed the relatively low reactivity. The

observed low reactivity of 1b and 1e may be due to the electron-donating nature of the methyl and methylene groups. The isopropyl Grignard reagent coupled with 1a to give a 65 : 35 mixture of *n*-propyl and isopropyl coupling products, owing to the concomitant alkyl group isomerization characteristic of the nickel-phosphine catalyzed Grignard coupling.⁸ The result indicates that the trimethylsiloxyalkenyl groups are among the electron-donating groups.

The coupling products can be isolated either as the corresponding silyl enol ethers by hydrolysis of the reaction mixture with neutral water, or as the corresponding carbonyl compounds by acid hydrolysis using dilute hydrochloric acid. In this manner, cyclamen aldehyde could be prepared in satisfactory yield (entry 11).

Thus, the present coupling reaction provides not only a novel method of the homologation of silyl enol ethers, which receive currently much attention in that they serve as versatile synthetic intermediates,⁹ but also a new type of selective mono α -alkylation and α -arylation of carbonyl compounds. Noteworthy, the overall result of the present coupling reaction can be regarded as the reaction between a nucleophilic organic moiety (Grignard reagent) and an enolonium (α -keto cation) equivalent (*vic*-bromotrimethylsiloxyalkene).



While α -alkylation of carbonyl groups has usually been accomplished by the reaction of the corresponding enolate anions or enols with electrophiles,¹⁰ the similar reaction cannot simply be applied to the α -arylation, unless the aryl groups are converted to the electron-deficient species.¹¹ Reactions of anionic alkylating and arylating agents with an appropriate enolonium synthon are much more limiting in number.¹¹ Under these circumstances, the α -arylation of carbonyl groups by the present nickel-catalyzed Grignard coupling is particularly interesting and should be useful.

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