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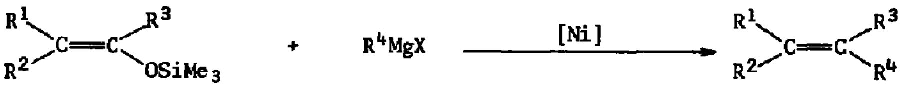
NICKEL-CATALYZED CROSS-COUPLING OF SILYL ENOL ETHERS WITH GRIGNARD REAGENTS. REGIO- AND STEREOCONTROLLED SYNTHESIS OF OLEFINS

Tamio Hayashi, Yoshio Katsuro, and Makoto Kumada*
Department of Synthetic Chemistry, Kyoto University, Kyoto 606, Japan

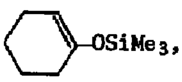
Summary: The substitution of the siloxy group in silyl enol ethers with Grignard reagents to form olefins is accomplished by use of nickel acetylacetonate or phosphine-nickel complexes as catalysts, the stereo- and regiochemistry of coupled olefins depending upon the nature of the catalyst and reaction conditions employed.

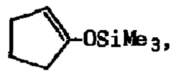
Although stereospecific cross-coupling of alkenyl halides with organometallic compounds such as Grignard reagents in the presence of transition metal complexes is one of the most useful pathways for the formation of the carbon-carbon bond,[1] no general method has been established for the selective preparation of the desired alkenyl halides, and limitations of the cross-coupling have been encountered in the synthesis of olefins. Recent studies have shown that alkenyl ethers,[2] sulfides,[3] and selenides[4] also enter into the catalytic cross-coupling. A method for the cross-coupling of silyl enol ethers with organometallics[5] would provide a new efficient route to selective formation of the carbon skeleton of various olefins, since there have been developed a wide variety of synthetic procedures for silyl enol ethers in a regio- and stereoselective manner,[6] with their versatility noted.

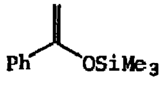
Silyl enol ethers are usually inert toward Grignard reagents and under drastic conditions such as reflux in dimethoxyethane the silicon-oxygen bond is cleaved slowly to form magnesium enolates.[7] We now find that the addition of a nickel catalyst brings about the conversion of the carbon-oxygen bond in silyl enol ethers into a carbon-carbon bond with Grignard reagents. Table 1 summarizes the reaction conditions and representative results.



1 2 3

1a: 

1b: 

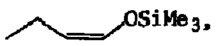
1c: 

1d: 

1e: 

1f: 

(E)-1g: 

(Z)-1g: 

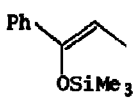
1h: 

Table 1. Coupling Reaction of Silyl Enol Ethers 1 with Grignard Reagents 2 Catalyzed by Nickel Complexes

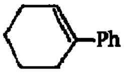
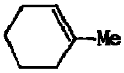
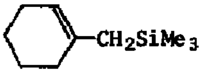
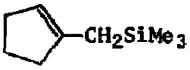
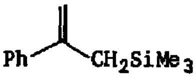
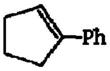
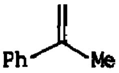
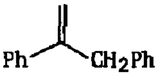
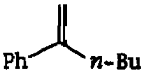
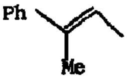
Entry	Silyl enol ether 1[a]	Grignard reagent 2	Reaction conditions[b]	Product 3[c]	Yield[d] (%)
1	1a	PhMgBr	A		73 (84)
2	1a	MeMgBr	A[e]		(87)
3	1a	Me_3SiCH_2MgCl	A		71
4	1b	Me_3SiCH_2MgCl	A		71 (91)
5	1c	Me_3SiCH_2MgCl	A		85
6	1d (37/63)[f]	PhMgBr	A	 (93/7)[f]	59
7	1e (9/91)[g]	PhMgBr	A	 (97/3)[g]	80
8	1e (9/91)[g]	Me_3SiCH_2MgCl	A	 (90/10)[g]	84
9	1f (92/8)[g]	Me_3SiCH_2MgCl	A	 (90/10)[g]	62
10	1b	PhMgBr	B		58[h]
11	1c	MeMgBr	B		(97)
12	1c	$PhCH_2MgCl$	B		75
13	1c	*n*-BuMgCl	C		53 (68)
14	1e (9/91)[g]	PhMgBr	B	 (7/93)[g]	71 (83)
15	1f (92/8)[g]	PhMgBr	B[i]	 (82/18)[g]	41[j]
16	(*E*)-1g	PhMgBr	B	 (100/0)[f]	(100)
17	(*Z*)-1g	PhMgBr	B	 (8/92)[f]	(98)
18	1h	MeMgBr	B		59

Table 1. (Continued)

[a] Silyl enol ethers except for **1e** were prepared according to House's procedure (Et_3N/DMF/Me_3SiCl) (ref. 6b). Stereoisomers of **1g** were isolated by preparative GLC. **1e** was prepared from the kinetically controlled enolate (ref. 6c). [b] Procedure A: To a mixture of a Grignard reagent **2** (2.0 mmol) and $Ni(acac)_2$ (0.05-0.10 mmol) in ether (2-5 ml) was added a silyl enol ether **1** (1.0 mmol) at room temperature under nitrogen. The resulting black mixture was heated to reflux for 3-6 h. Procedure B: An ethereal solution of a Grignard reagent **2** (2-3 mmol) was added to $NiCl_2(PPh_3)_2$ (0.05-0.10 mmol), and the ether was then removed under reduced pressure. To the residue was added 2-4 ml of benzene and then a silyl enol ether **1** (1.0 mmol). The solution was refluxed in an oil bath at 90-100°C for 3-5 h. Procedure C: $NiCl_2$(dppf) (0.05 mmol) was used instead of $NiCl_2(PPh_3)_2$ in procedure B. [c] Isolated by preparative TLC or distillation under reduced pressure after hydrolysis with diluted hydrochloric acid. All products exhibited satisfactory spectral and analytical data. Isomeric purity was determined by NMR and GLC analysis. [d] Isolated yields based on the amount of silyl enol ether used. Yields determined by GLC are given in parentheses. [e] Reaction at room temperature for 20 h. [f] *E*/*Z* ratio. [g] Ratio of 2-olefin/1-olefin. [h] 1,1'-Bicyclopentenyl was also formed in 28% yield. [i] Refluxed for 23 h. [j] Recovered silyl enol ether ether contained no 1-isomer.

Nickel acetylacetonate [$Ni(acac)_2$] was the most active catalyst to complete the coupling reaction under mild conditions (ether reflux) in 3-6 h. Nickel chloride was also an active catalyst, but the activity did not last long. Silyl enol ethers **1a-c**, derived from cyclohexanone, cyclopentanone and acetophenone, were allowed to react with phenyl, methyl, and trimethylsilylmethyl Grignard reagents in the presence of $Ni(acac)_2$ to give the corresponding coupling products, olefins and allylsilanes, in high yields (entries 1-5). In the reaction of silyl enol ethers **1d**, **1e** and **1f**, the $Ni(acac)_2$ catalyst gave preferentially isomers of greater thermodynamic stability. Thus, the reaction of phenylmagnesium bromide with 1-trimethylsiloxy-1-octene (**1d**), consisting of *E* and *Z* isomers (*E*/*Z* = 37/63), gave mainly 1-phenyl-1-octene with *E* configuration (*E*/*Z* = 93/7) (entry 6). The ratio of 1- to 2-olefin in 2-trimethylsilylmethyloctenes obtained by the trimethylsilylmethylation of 2-trimethylsiloxy-1-octene (**1e**) and 2-trimethylsiloxy-2-octene (**1f**) was 10/90 in both cases (entries 8 and 9). The phenylation of **1e** catalyzed by $Ni(acac)_2$ resulted in the formation of 2-phenyl-2-octene as a main product (entry 7).

The loss of stereo- and regioisomeric purity during the $Ni(acac)_2$ catalyzed coupling reaction may be ascribed to the isomerization of the coupling product under the reaction conditions. 2-Phenyl-1-octene, prepared using a phosphine-nickel catalyst (*vide infra*), was found to isomerize into 2-phenyl-2-octene (95% isomeric purity) in 10 min under the conditions of the cross-coupling ($Ni(acac)_2$, Grignard reagent, reflux in ether).[8]

The use of dichlorobis(triphenylphosphine)nickel(II), $NiCl_2(PPh_3)_2$, as a catalyst enabled the cross-coupling to proceed in a regio- and stereospecific manner. The phosphine-nickel catalyst was less active than $Ni(acac)_2$ and the cross-coupling was best effected in refluxing benzene. Use of ethereal solvents, tetrahydrofuran, dimethoxyethane and dioxane, resulted in very low yields (<5%) of coupling products and cleavage of the oxygen-silicon bond as a main reaction. The reaction of **1e** with phenylmagnesium bromide in the presence of $NiCl_2(PPh_3)_2$ in refluxing benzene led to 2-phenyl-1-octene selectively, while the reaction of **1f** to 2-phenyl-2-octene selectively (entries 14 and 15). Phenylation of (*E*)- and (*Z*)-1-trimethylsiloxy-1-butene (**1g**) gave stereoselectively (*E*)- and (*Z*)-1-phenyl-1-butene, respectively (entries 16 and 17). Entry 18 shows that the stereoselective alkylation also occurred in the reaction of a trisubstituted siloxyalkene **1h**.

The *n*-butyl group was introduced into **1c** by use of NiCl$_2$(dppf), where dppf stands for 1,1'-bis(diphenylphosphino)ferrocene and has been found to be one of the best ligands for the nickel- or palladium-catalyzed cross-coupling of alkyl Grignard reagents bearing β-hydrogens.[9]

The present reaction provides the first general and practical method for replacing the siloxy group on silyl enol ethers by an alkyl or aryl group to form a new carbon-carbon bond. We are continuing to explore the scope, mechanism, and synthetic applications of this coupling reaction.

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REFERRENCES AND NOTES

(1) For a pertinent review, see K. Tamao and M. Kumada, "Organometallic Reactions and Syntheses", E. I. Becker, M. Tsutsui, Ed., Plenum, New York, in press.

(2) (a) E. Wenkert, E. L. Michelotti, and C. S. Swindell, *J. Am. Chem. Soc.*, **101**, 2246 (1979); (b) Reaction of diketene with Me$_3$SiCH$_2$MgCl has been reported, K. Itoh, T. Yogo, and Y. Ishii, *Chem. Lett.*, 103 (1977); (c) For related reactions, see also L. Blaszczak, J. Winkler, and S. O'Kuhn, *Tetrahedron Lett.*, 4405 (1976); I. Arai and G. D. Daves, Jr., *J. Am. Chem. Soc.*, **100**, 287 (1978).

(3) (a) H. Okamura, M. Miura, and H. Takei, *Tetrahedron Lett.*, 43 (1979); (b) E. Wenkert, T. W. Ferreira, and E. L. Michelotti, *J. C. S. Chem. Comm.*, 637 (1979); (c) B. M. Trost and Y. Tanigawa, *J. Am. Chem. Soc.*, **101**, 4743 (1979).

(4) H. Okamura, M. Miura, K. Kosugi, and H. Takei, *Tetrahedron Lett.*, **21**, 87 (1980).

(5) Wenkert et al. described very briefly a nickel-catalyzed coupling of a silyl enol ether with PhMgBr, which gave an olefin only in a low yield (ref. 2a).

(6) (a) J. K. Rasmussen, *Synthesis*, 91 (1977); (b) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969); (c) R. D. Clark and C. H. Heathcock, *J. Org. Chem.*, **41**, 1396 (1976); (d) I. Kuwajima and M. Kato, *J. C. S. Chem. Comm.*, 708 (1979); (e) H. J. Reich, J. J. Rusek, and R. E. Olson, *J. Am. Chem. Soc.*,, **101**, 2225 (1979); (f) H. Suzuki, Y. Koyama, Y. Moro-oka, and T. Ikawa, *Tetrahedron Lett.*, 1415 (1979); (g) S. Murai and N. Sonoda, *Angew. Chem. Int. Ed.*, **18**, 837 (1979).

(7) (a) G. Stork and P. F. Hudrlik, *J. Am. Chem. Soc.*, **90**, 4464 (1968); (b) P. F. Hudrlik and C. N. Wan, *J. Org. Chem.*, **40**, 2963 (1975).

(8) For a pertinent book concerning nickel-catalyzed isomerization of olefins, see P. W. Jolly and G. Wilke, "The Organic Chemistry of Nickel", Vol. II, Academic Press, New York, 1975, Chapter 1.

(9) (a) T. Hayashi, M. Konishi, and M. Kumada, *Tetrahedron Lett.*, 1871 (1979); (b) T. Hayashi, M. Konishi, and M. Kumada, *J. Organomet. Chem.*, **186**, C1 (1980); (c) T. Hayashi, M. Konishi, K. Yokota, and M. Kumada, *Chem. Lett.*, 767 (1980).

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