

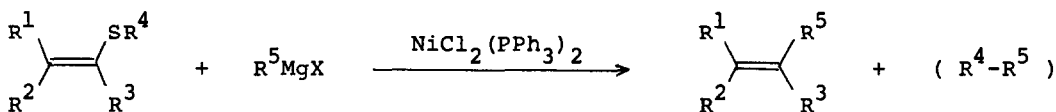
NICKEL-PHOSPHINE COMPLEX CATALYZED COUPLING REACTION OF
GRIGNARD REAGENTS WITH ALKENYL OR ARYL SULFIDES

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Recently Kumada and his coworkers¹⁾ have found that Grignard reagents can couple stereospecifically with alkenyl or aryl halides (C_{sp^2} -halogen) in the presence of nickel-phosphine complex. The coupling reaction of organometallic compounds with organic halides is now well recognized to be one of the most useful methods for the formation of carbon-carbon bond, and a variety of organometallic compounds were tested. As to the substrate of the coupling reaction, most of the previous investigations have been confined to the cases of organic halides,²⁾ and little attention has been paid to sulfides.³⁾

We now found that alkenyl or aryl sulfides^{4,5)} (C_{sp^2} -S) could be used as substrates of the nickel promoted coupling reaction.



Thus, phenylmagnesium bromide reacted with phenyl styryl sulfide^{5a)} in the presence of $NiCl_2(PPh_3)_2$ ⁶⁾ to give stilbene and biphenyl. The formation of hydrogen sulfide was also confirmed after quenching the reaction with dilute acid. The results under various reaction conditions were summarized in Table 1.

As shown in Table 1, the use of stoichiometric amount of Ni-complex caused a significant formation of homo-coupled product, biphenyl, (run 1-3), but a satisfactory result was obtained when catalytic amount (3 mole%) of Ni-complex was used (run 5). It was also confirmed that, without Ni-catalyst, the reaction did not occur (run 7) and the organolithium compound was not suitable for this reaction (run 8).

Table 1. Coupling Reaction of PhMgBr with Phenyl Styryl Sulfide
in the Presence of $\text{NiCl}_2(\text{PPh}_3)_2$ ^{a)}

$$\text{Ph} \begin{array}{c} \diagup \\ \diagdown \end{array} \text{SPh} + 2 \text{ PhMgBr} \xrightarrow[\text{THF, reflux}]{\text{NiCl}_2(\text{PPh}_3)_2} \text{Ph} \begin{array}{c} \diagup \\ \diagdown \end{array} \text{Ph} + \text{Ph-Ph}$$

Run	PhMgBr (eq.)	$\text{NiCl}_2(\text{PPh}_3)_2$ (eq.)	time (h)	$\text{Ph} \begin{array}{c} \diagup \\ \diagdown \end{array} \text{Ph}$ (%) ^{b)}	Ph-Ph (%) ^{b)}
1	2.35	1.02	9	47	78 ^{c)}
2	4.4	1.02	5	72	200
3	4.0	1.02	1	60	172
4	4.0	0.98	20 ^{d)}	trace	trace ^{e)}
5	2.1	0.03	5.5	90	64
6	1.2	0.03	6	48	23 ^{f)}
7	2.3	0	5	trace	trace ^{e)}
8	2.3 ^{g)}	0.03	5	0	trace ^{h)}





















a) The reactions were carried out in THF at a refluxing temperature, unless otherwise noted. b) The yields were determined by glpc and calculated based on phenyl styryl sulfide. c) The sulfide (25%) was recovered. d) The reaction was carried out at a room temperature. e) Large amount of the sulfide was recovered. f) The sulfide (23%) was recovered. g) PhLi was used instead of PhMgBr. h) The starting sulfide was not recovered.

The results of the coupling reaction between a variety of sulfides and Grignard reagents were shown in Table 2.

The following observation and interpretations may be worth noting. (1) The Ni-catalyzed reaction in each case is highly stereospecific (>94%), supporting an assumption that all steps proceed with retention of configurations similar to the case of alkenyl halides.^{1,7)} (2) This coupling reactions only occur between alkenyl or aryl sulfides ($\text{C}_{\text{sp}^2}\text{-S}$) and Grignard reagents. In the case of alkyl sulfide ($\text{C}_{\text{sp}^3}\text{-S}$), the cleavage of carbon-sulfur bond does not occur. So alkenyl aryl sulfides require 2 equiv. of Grignard reagents, and then alkenyl alkyl sulfides require 1 equiv., while excess amount of Grignard reagents gave the products in higher yields.

Table 2. Cross Coupling of Sulfides with Grignard Reagents

Catalyzed by $\text{NiCl}_2(\text{PPh}_3)_2^{\text{a}}$

Sulfide	RMgX (eq.)	solvent	time(h)	Product ^{b)}	Yield(%) ^{c)}	E/Z
PhS  Ph (Z) ^{5b)}	PhMgBr (2.4)	THF	6	Ph  Ph	97	6/94
	BuMgBr (2.4)	Et ₂ O	8	Ph  Ph	45	6/94
MeS  Ph (E) ^{5c)}	PhMgBr (1.2)	THF	6	Ph  Ph	80	97/3
	PhMgBr (1.5)	THF	6	Ph  Ph	85	95/5
	BuMgBr (1.2)	THF	6	Ph  Ph	44	98/2
	BuMgBr (1.2)	Et ₂ O	8	Ph  Ph	53	95/5
	BuMgBr (1.5)	Et ₂ O	8	Ph  Ph	64	95/5
EtS  Ph (Z) ^{5b)}	PhMgBr (1.5)	THF	8	Ph  Ph	96	5/95
PhS 	PhMgBr (2.4)	THF	6	Ph 	60	--
PhS  Ph ^{5d)}	PhMgBr (2.2)	THF	6	Ph  Ph	81 (64)	mixt.
PhSMe	BuMgBr (1.5)	Et ₂ O	14	Ph-Bu	29	--
MeS  Ph	PhMgBr (2.4)	THF	6	Ph  Ph	0 ^{d)}	--
EtS  ^{5e)}	PhMgBr (1.5)	THF	20	Ph- 	38 ^{e)}	--
	PhMgBr (2.0)	THF	20	Ph- 	56 ^{f,g)}	--

a) All reactions were carried out at a refluxing temperature in the presence of $\text{NiCl}_2(\text{PPh}_3)_2$ (3 mole%), unless otherwise noted. b) The structure of the products was confirmed by comparison with authentic samples.⁸⁾ c) The yields were determined by glpc and the number in parentheses is isolated yield. d) The starting sulfide (97%) was recovered. e) The sulfide (31%) was recovered. f) The reaction was carried out in the presence of $\text{NiCl}_2(\text{PPh}_3)_2$ (15 mole%). g) The sulfide (24%) was recovered.

The following experiment provides a typical procedure for the cross coupling: To a mixture of 4-phenyl-1-phenylthio-1-butene (241 mg, 1.00 mmol) and $\text{NiCl}_2(\text{PPh}_3)_2$ (20 mg, 0.03 mmol) in THF (12 ml) was added phenylmagnesium bromide (2,2 mmol, 0.8M ether solution) at a room temperature with stirring. The resulting black mixture was heated to reflux for 6 h. After addition of 1N hydrochloric acid and ether, the mixture was filtered. The organic layer was separated, washed, and dried. In general, the amount of product was measured by glpc using a suitable internal standard (in this case, 1,2-diphenylethane was used). After removal of the solvent in vacuo, 1,4-diphenyl-1-butene was isolated by column chromatography purification (silica-gel, hexane). 134 mg, 64%.

References and Notes

- 1) K. Tamao, K. Sumitani, Y. Kiso, M. Zembayashi, A. Fujioka, S. Kodama, I. Nakajima, A. Minato, and M. Kumada, *Bull. Chem. Soc. Jpn.*, **49**, 1958 (1976); and references cited therein.
- 2) In some cases, sulfonates, phosphates, and carboxylates were used as substrates. In the case of organocopper reagents; e. g., G. H. Posner, *Org. React.*, **22**, 253 (1975).
- 3) Alkylthio or arylthio groups of β -alkylthio or arylthio α,β -unsaturated esters^{a,b)} and ketones^{b,c,d)} and methyl styryl sulfide^{e)} were reported to be replaced by alkyl group by the reaction with organocopper reagents. But the reactions were thought to proceed via addition-elimination mechanisms.
a) S. Kobayashi, H. Takei, and T. Mukaiyama, *Chem. Lett.*, **1973**, 1097. b) G. H. Posner and D. J. Brunelle, *J. Chem. Soc., Chem. Commun.*, **1973**, 907. c) E. J. Corey and R. H. K. Chen, *Tetrahedron Lett.*, **1973**, 3817. d) R. M. Coates and L. O. Sandfur, *J. Org. Chem.*, **39**, 275 (1974). e) G. H. Posner and D. J. Brunelle, *J. Org. Chem.*, **38**, 2747 (1973).
- 4) Alkenyl sulfides have lately attracted considerable attention in the field of synthetic organic chemistry because of their usefulness as intermediates. E. g., a) T. Mukaiyama, S. Fukuyama, and T. Kumamoto, *Tetrahedron Lett.*, **1968**, 3787; b) E. J. Corey and J. I. Shulman, *J. Org. Chem.*, **35**, 777 (1970); c) E. J. Corey and J. I. Shulman, *J. Am. Chem. Soc.*, **92**, 5522 (1970); d) K. Oshima, K. Shimoji, H. Takahashi, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **95**, 2694 (1973); e) T. Cohen, G. Herman, J. R. Falck, and A. J. Mura, Jr., *J. Org. Chem.*, **40**, 812 (1975); f) A. J. Mura, Jr., D. A. Bennett, and T. Cohen, *Tetrahedron Lett.*, **1975**, 4433.
- 5) Alkenyl sulfides are readily available,⁴⁾ and the sulfides used here were synthesized according to the following procedures; a) F. A. Carey and A. S. Court, *J. Org. Chem.*, **37**, 939 (1972). b) W. E. Truce and J. A. Simms, *J. Am. Chem. Soc.*, **78**, 2756 (1956). c) T. Kojima and T. Fujisawa, *Abstr.*, III-1257, 30th Annual Meeting of the Chemical Society of Japan, Osaka, 1974. d) H. Okamura, Y. Mitsuhiro, M. Miura, and H. Takei, *Chem. Lett.*, **1978**, 517. e) T. Mukaiyama and K. Saigo, *Chem. Lett.*, **1973**, 479.
- 6) F. A. Cotton, O. D. Faut, and D. M. L. Goodgame, *J. Am. Chem. Soc.*, **83**, 344 (1961).
- 7) S. Baba and E. Negishi, *J. Am. Chem. Soc.*, **98**, 6729 (1976).
- 8) Authentic samples were purchased from commercial sources or synthesized by the established manners.

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