

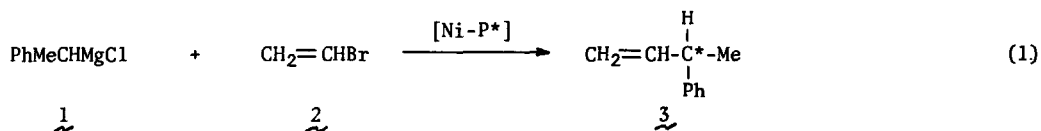
A NEW ASYMMETRIC GRIGNARD CROSS-COUPLING REACTION VIA AN ALKYL GROUP ISOMERIZATION CATALYZED BY CHIRAL PHOSPHINE-NICKEL COMPLEXES

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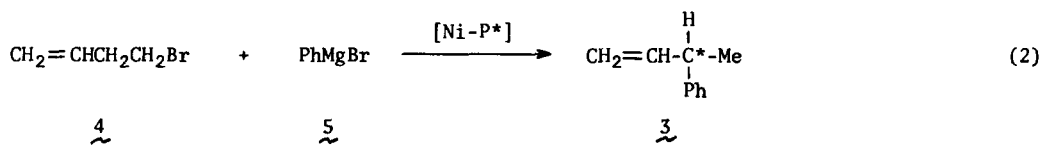
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We have previously reported that sec-alkyl Grignard reagents react with aryl and alkenyl halides to give optically active hydrocarbons in the presence of chiral phosphine-nickel complexes as catalysts, as exemplified by the following reaction.^{1,2}



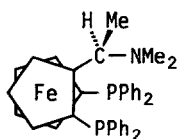
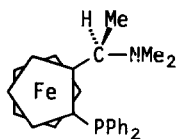
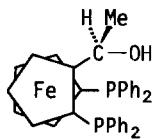
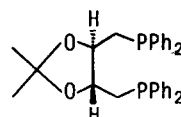
This asymmetric coupling reaction is classified not as a true asymmetric synthesis but as a kinetic resolution of racemic sec-alkyl Grignard reagents.

Recently we have found that a nickel-phosphine complex-catalyzed coupling reaction³ of 3-alkenyl halides with a phenyl Grignard reagent gave secondary alkenyl benzenes predominantly, as a result of alkyl group isomerization from primary to secondary.⁴ For example, 4-bromo-1-butene reacts with phenylmagnesium bromide in the presence of [Ni(dppp)Cl₂]⁵ as a catalyst to give 3-phenyl-1-butene in 48% yield, together with other possible isomeric butenylbenzenes.⁶ It was therefore anticipated that such a coupling reaction in the presence of any chiral phosphine-nickel complex as catalyst should afford optically active 3-phenyl-1-butene.



This reaction provides a new type of asymmetric synthesis in which the achiral halide is converted into a chiral moiety by the action of a chiral catalyst. It should be also noted that these two different types of asymmetric reaction, (1) and (2), give the same chiral product, which allows us to evaluate stereochemistry of the reaction intermediates more precisely.

The asymmetric synthesis could actually be achieved by the use of the following chiral phosphines as ligands.

 $(R)-(S)$ -BPPFA⁷ $(R)-(S)$ -PPFA⁷ $(R)-(S)$ -BPPFOH⁸(-)-DIOP⁹

Typical procedure is as follows. An ethereal solution of phenylmagnesium bromide (1.2 equiv) was added to an ethereal solution of 4-bromo-1-butene (4) (1 equiv) in the presence of an equimolar mixture of NiCl₂ and $(R)-(S)$ -BPPFA (0.5 mol %). The mixture was refluxed for 46 hr. Glc analysis after usual work-up showed that 3-phenyl-1-butene (3) was formed in 58% yield based on 4, along with 17% yield of (Z) -1-phenyl-2-butene and trace amounts of 4-phenyl-1-butene and (E) -1-phenyl-2-butene. 3 was isolated by preparative glc and was found to be optically active, $[\alpha]_D^{22} -2.16^\circ$ (neat), corresponding to 33.8% optical yield of the *R* isomer. Results are summarized in Table 1.

It seems of interest to compare the present results with those obtained from reaction (1). Firstly, optical yields attained by the present reaction are about one half or less of those obtained by reaction (1) for each chiral phosphine ligand.^{1,2,10} With respect to stereoselectivity, ferrocenylphosphines are much more effective ligands than DIOP. Secondly, these two types of asymmetric coupling reaction give the enantiomeric products in the presence of the same chiral phosphine ligand; *e.g.*, with $(S)-(R)$ -BPPFA as a ligand $(R)-(-)$ -3 is obtained from reaction (1), while reaction (2) forms $(S)-(+)$ -3.

These features may be rationalized by Scheme 1. Thus, according to the mechanism proposed for the nickel-phosphine complex-catalyzed Grignard cross-coupling reaction,³ chiral diorganonickel complexes 6 and 7 are believed to be involved as crucial intermediates in the reactions (1) and (2), respectively. The fact that these two reactions give enantiomeric coupling products clearly indicates that both the intermediates contain the chiral carbon center of the same

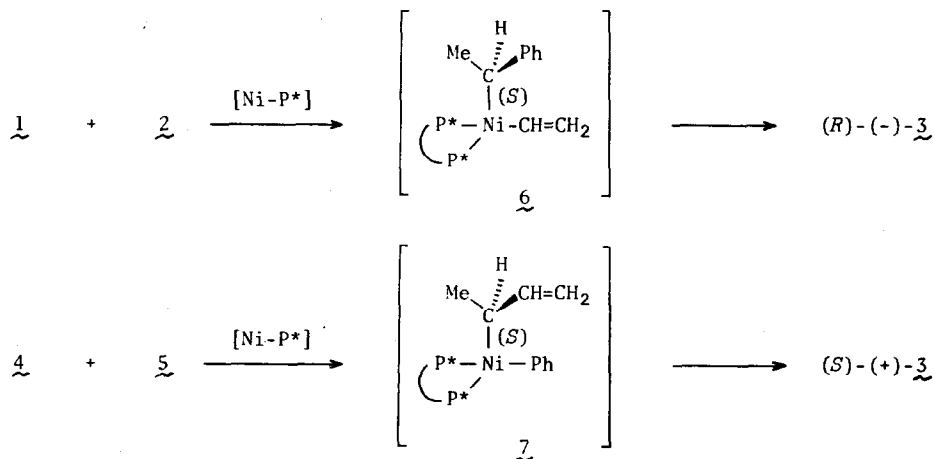
Table 1. Asymmetric Cross-Coupling Reaction of 4-Bromo-1-butene with Phenylmagnesium Bromide in the Presence of Chiral Phosphine-Nickel Complexes as Catalysts^a

Ni catalyst ^b	3-Phenyl-1-butene (3)		
	Yield (%) ^c	$[\alpha]_D^{22}$ (neat)	Predominant configuration (% ee) ^d
[Ni((-)-DIOP)Cl ₂]	28	-0.69 ^e	R (5.7)
NiCl ₂ -(R)-(S)-BPPFA	58	-2.16	R (33.8)
NiCl ₂ -(S)-(R)-BPPFA	58	+2.14	S (33.4)
NiCl ₂ -(R)-(S)-BPPFOH	24	-0.91	R (14.2)
NiCl ₂ -2(S)-(R)-PPFA	16	+1.21	S (18.8)

^a Catalyst/4-bromo-1-butene/PhMgBr = $5 \times 10^{-3}/1/1.2$. Refluxed for 46 hr. ^b For the abbreviation of the ligands, see the text. ^c Yields were determined by glc based on the organic halide (4). ^d Maximum rotation of (R)-(-)-3-phenyl-1-butene; $[\alpha]_D^{22}$ -6.39° (neat): D. J. Cram, *J. Amer. Chem. Soc.*, **74**, 2141 (1952). ee = Enantiomeric excess. ^e Benzene solution (c 2.9).

absolute configuration. The major part of the observed differences in stereoselectivity between these two reactions may be attributable to the different bulkiness between the phenyl group on the one hand and the vinyl group on the other, attached to the chiral carbon center.

Scheme 1



A mechanism for the isomerization is briefly discussed here. An initially formed 3-butenyl-nickel intermediate arising from the oxidative addition of 4 to a low valent nickel species isomerizes to a chiral σ -1-methyl-2-propenyl-nickel intermediate (cf. 7), possibly via transient formation of a butadiene-hydrido-nickel complex. The predominant formation of the chiral coupling product 3 demonstrates that the coupling of the two organic moieties in the intermediate 7 proceeds faster than the isomerization of the butenyl group via π -allylic nickel intermediates, because the latter would give achiral non-branched coupling products predominantly, as observed in, e.g., coupling of butadiene and ethylene catalyzed by nickel-hydride complexes.¹¹

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4. This reaction is the first example of the alkyl group isomerization from primary to secondary in the nickel-phosphine complex-catalyzed Grignard coupling, while the isomerization from secondary to primary has been observed: K. Tamao, Y. Kiso, K. Sumitani and M. Kumada, *J. Amer. Chem. Soc.*, 94, 9268 (1972); Y. Kiso, K. Tamao and M. Kumada, *J. Organometal. Chem.*, 50, C12 (1973).
5. dppp = $\text{Ph}_2\text{P}(\text{CH}_2)_3\text{PPh}_2$.
6. Yields of the isomeric products are as follows: $\text{CH}_2=\text{CHCH}_2\text{CH}_2\text{Ph}$ (1.5%), (*Z*)- $\text{CH}_3\text{CH}=\text{CHCH}_2\text{Ph}$ (1.5%), and (*E*)- $\text{CH}_3\text{CH}=\text{CHCH}_2\text{Ph}$ (12%).
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