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Heterodimerization of Olefins. 1. Hydrovinylation Reactions of Olefins That Are Amenable to Asymmetric Catalysis

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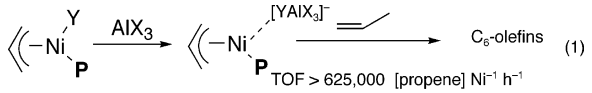
Received August 9, 2003

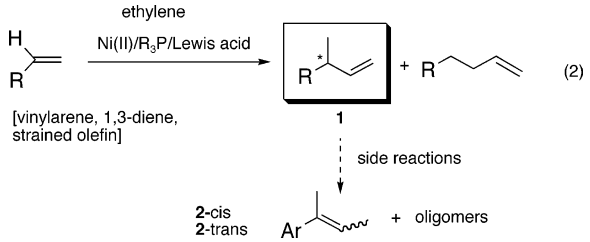
Through a systematic examination of ligand and counterion effects, new protocols for a nearly quantitative and highly selective codimerization of ethylene and various functionalized vinylarenes have been discovered. In a typical reaction, 4-bromostyrene and ethylene undergo codimerization in the presence of 0.0035 equiv each of $[(allyl)NiBr]_2$, triphenylphosphine, and AgOTf in CH_2Cl_2 at −56 °C to give 3-(4-bromophenyl)-1-butene in >98% yield and selectivity. Corresponding reactions with $[(allyl)PdX]_2$ are much less efficient and less selective and may require further optimization before a viable system can be identified. Another useful protocol that gives comparable yield and selectivity involves the use of a single-component catalyst prepared from allyl 2-diphenylphosphinobenzoate, $Ni(COD)_2$, and $(C_6F_5)_3B$. Recognition of a synergistic relationship between a chiral hemilabile ligand (for example, (*R*)-2-methoxy-2′-diphenylphosphino-1,1′-binaphthyl, MOP) and a highly dissociated counteranion (BARF or SbF_6) in an enantioselective version of the Ni-catalyzed reaction raises the prospects of developing a practical route for the synthesis of 3-arylbutenes. Several pharmaceutically relevant compounds, including widely used 2-arylpropionic acids, can be synthesized from these key intermediates. This reaction appears to be quite general. Synthesis of several new 2-diphenylphosphino-1,1-binaphthyl derivatives, prepared to probe the effect of hemilabile coordination on the efficiency and selectivity of the reaction, are also described.

Introduction

Among transition-metal-catalyzed carbon−carbon bond-forming processes, cationic nickel hydride-catalyzed homodimerization of propene, which forms the basis of the Dimersol technology (eq 1), is one of the most efficient



homogeneous catalyzed reactions.[1] The active catalyst, generated from $[\eta^3$-(allyl)$NiX]_2$, a trivalent phosphorus ligand and a Lewis acid, produces a mixture of C_6-olefins from propene with rates in excess of 625 000 [propene]-$[Ni]^{-1}[h]^{-1}$.[2] Applications of this and of other related heterodimerization reactions for the synthesis of fine chemicals have been the subject of much research since its discovery.[3] Among these, the hydrovinylation reaction, viz., the addition of a vinyl group and a hydrogen across a double bond (eq 2), has attracted the most attention.



Since the branched product **1** is chiral, a regio- and stereoselective version of this reaction could provide easy access to variety of olefin-derived products, including carboxylic acid derivatives. Thus hydrovinylation of vinylarene derivatives that leads to 3-arylbutenes could be used for the synthesis widely used antiinflammatory 2-arylpropionic acids (eq 3).[4] One of the hydrovinylation products of styrene, (*R*)-3-phenyl-1-butene, has been reported to give a very high melting (>400 °C) isotactic polymer under Ziegler conditions.[2a]

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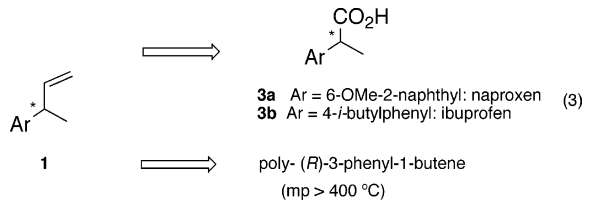
10.1021/jo035171b CCC: $25.00
Published on Web 10/02/2003



The hydrovinylation reaction has a long history dating back to 1965, when Alderson, Jenner, and Lindsey first reported the use of hydrated Rh and Ru chlorides to effect the codimerization of ethylene at high pressures (1000 psi) with a variety of olefins, including styrene and butadiene.[5a] Styrene has served as a prototypical test case for most investigations reported to date. In early studies, in addition to Rh,[5] other metals such as Ru,[5a,6] Co,[7] Pd,[8] and Ni[9] were also used, and in most instances, the reactions were complicated by isomerization of the initially formed 3-arylbutenes and oligomerization of the starting olefins (eq 2). Notable among the early studies are also the first examples of the asymmetric hydrovinylation of 1,3-cyclooctadiene, norbornene, and norbornadiene and a codimerization of propene and 2-butene using a combination of $[\eta^3\text{-}C_3H_5)NiCl]_2/Et_3Al_2Cl_3$ and a monoterpene-derived chiral phosphine, even though the selectivities were unacceptably poor.[10]

In more recent studies, the yield and selectivity of the Pd- and Ni-catalyzed hydrovinylation reactions have been improved considerably by varying the ligands and reaction conditions. Even though some initial reports[8,11] seemed to indicate that the Pd-catalyzed reactions gave

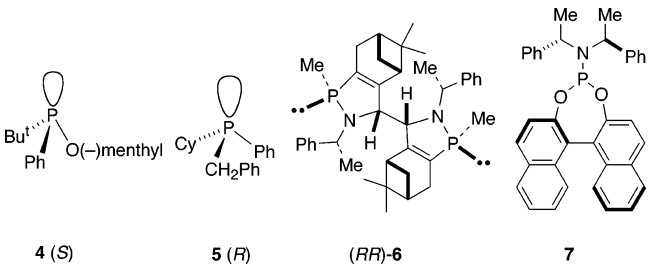
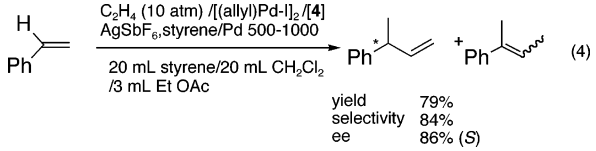
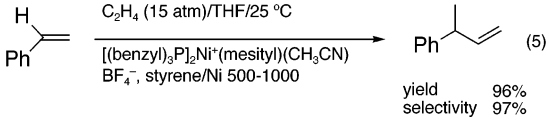


FIGURE 1. Assorted ligands used in hydrovinylation reactions.

mostly linear products and/or extensive isomerization, subsequent studies have shown that use of ligands such as Cy_3P,[12] **4**,[13] and **5**[14] (Figure 1) and carefully chosen reaction conditions permit the isolation of the branched product. Acceptable yields and best selectivities are achieved under low conversions, since isomerization of the primary product is a persistent problem with many of these reactions. Among these ligands, the phosphinite **4** is particularly noteworthy (eq 4).[13] With the appropriate counterion (SbF_6^-), 3-phenyl-1-butene can be synthesized in a moderate yield and in ee's up to 86% (*S*).



Recent improvements in the Ni-catalyzed heterodimerization reaction includes the use of $[ArNi(PR_3)(MeCN)]^+ BF_4^-$ (Ar = mesityl, R = benzyl), which served as an efficient catalyst for hydrovinylation of styrene (eq 5).[15]



High turnover numbers (up to 1915 h^{-1}) and selectivities for the 3-arylbutenes can be achieved for a variety of styrenes at 15 bar ethylene pressure. Heteroatom substituents are tolerated, but ring-alkylated styrenes give poor yields. The reaction rates fall unacceptably low below 20 °C, and as the temperature is increased, isomerization of the initially formed product is seen. Substitution of tribenzylphosphine with *cis*-myrtanyldiphenylphosphine gives high selectivity toward 3-phenylbutene, albeit with a disappointing enantioselectivity

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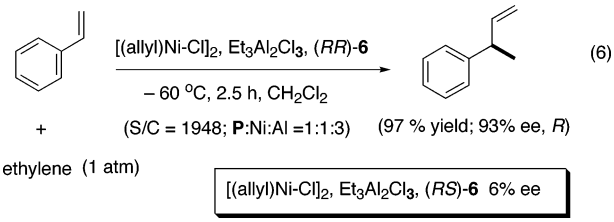
(~7% ee). Since there is an exothermic polymerization of ethylene at the end of the relatively more facile heterodimerization, control of temperature is crucial to get good selectivities under these reaction conditions. Monteiro et al.[16] reported the use of dicationic nickel complexes ($[Ni(CH_3CN)_6]^{2+}\cdot 2[BF_4]^-/Ph_3P/Et_2AlCl$) at room temperature and 10 bar pressure of ethylene to get yields of 68−87% of various hydrovinylation products. Isomerization of the primary product can be prevented by maintaining a high pressure of ethylene (>10 bar). A unique feature of this catalyst system that is not seen in any other Ni-catalyzed reactions is that chelating phosphines [e.g., diphenylphosphinoethane (dppe) or *N*,*N*-dimethyl-1-[2-(diphenylphosphino)ferrocen-yl]ethylamine (dppfa)] do not inhibit the reaction.

A careful examination of the work prior to our first initial report[17] on a new protocol for the Ni-catalyzed hydrovinylation of vinylarenes shows that the best catalyst reported for this reaction is also the one that gives the best enantioselectivity. This is the Wilke system that uses $[\eta^3-allyl)NiCl]_2/[(RR)$-**6**$]/Et_3Al_2Cl_3]$.[3b,18,19] With this catalyst, varying ee's are obtained, depending on the reaction conditions. The azaphospholene (*RR*)-**6** is a very special ligand for the hydrovinylation of vinylarenes and 1,3-dienes, and the Ni complexes derived from this ligand have been claimed[18] to give the highest ee recorded to date for many of these substrates (eqs 6 and 7). A variety



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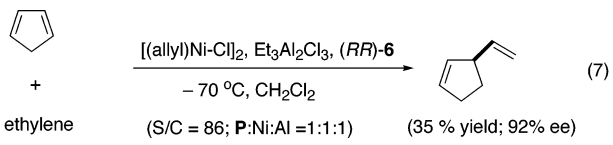
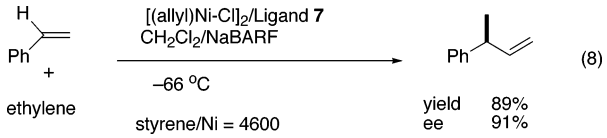


(7)

of vinylarenes, including 4-chlorostyrene, 4-isobutylstyrene, 2-methylstyrene, and 6-methoxy-2-vinylnaphthalene, gave very high ee's in the hydrovinylation reaction. The ligand (*RR*)-**6** is prepared from (−)(*R*)-myrtenal and (+)(*R*)-1-phenylethylamine in a multistep process.[3b] One other congener of this compound, the diastereomer (*RS*)-**6** (prepared from (−)(*R*)-myrtenal and (−)(*S*)-1-phenylethylamine), is much less active and selective for the hydrovinylation of styrene. Monomeric and structurally related versions of this ligand have been prepared[3b,20] in an attempt to simplify the synthesis, and it has been found that catalytic activity and enantioselectivity invariably fall below useful levels. These reports suggest that the azaphospholene ligand class has a narrow scope and are possibly of limited value for the development of a broadly applicable hydrovinylation reaction, especially for a *practical* enantioselective version. The use of pyrophoric aluminum alkyl Lewis acids is another major distraction of this protocol. We have since found that sodium tetrakis[3,5-bis(trifluoromethyl)phenylborate] (NaBARF) is a suitable replacement for the Lewis acids in the hydrovinylation reaction run in CH_2Cl_2 (vide infra). Leitner has extended the use of this salt for reactions in supercooled CO_2 with the ligand (*RR*)-**6**.[19]

In a very important recent development, Leitner et al. reported[21] that Feringa's phosphoramidite ligand **7** gave very high enantioselectivities in the hydrovinylation of a number of styrene derivatives (eq 8). Another signifi-



(8)

cant result in this area is the use of $(PCy_3)_2(CO)Ru(Cl)H$ in conjunction with $HBF_4\cdot Et_2O$.[22a] Use of silver salts in place of the acid gives a more active hydrovinylation catalyst (vide infra).

In this paper we report the details of our investigations from which emerged a versatile and generally useful protocol for the hydrovinylation of vinylarenes. As a result, very high yields (>95%) and selectivities (>99% for the 3-arylbutenes) for several vinylarenes at one atmosphere of ethylene pressure and −55 °C have been achieved. In addition, the protocol is amenable to asymmetric catalysis by chiral phosphines. Two preliminary reports dealing with the early parts of this investigation have appeared.[17,23]

Results and Discussion

Mechanism of Ni-Catalyzed Hydrovinylation. Even though much of the early studies of hydrovinylation of styrene are characterized by a lack of any selectivity, many of them provide significant mechanistic insights into the reaction. For example, kinetic and solvent effect studies of hydrovinylation with $NiX_2/AlEt_3/BF_3\cdot OEt_2/P(OPh)_3$[9e−g] provided some early indications of the $[Ni-H]^+$ coordination to a styrene and subsequent addition. The deactivating effect of a solvent was found to increase in the order CH_2Cl_2, PhF, PhCl, PhMe, $PhNO_2$, Et_2O, consistent with an inhibitory effect of a coordinating Lewis base. Studies of D-distribution in the product when the hydrovinylation was carried out with $D_2C{=}CD_2$ provide further evidence for the involvement of a cationic nickel hydride intermediate.[9f] Even though a catalytically active $L_n[Ni-H]^+$ has not been isolated, its generation

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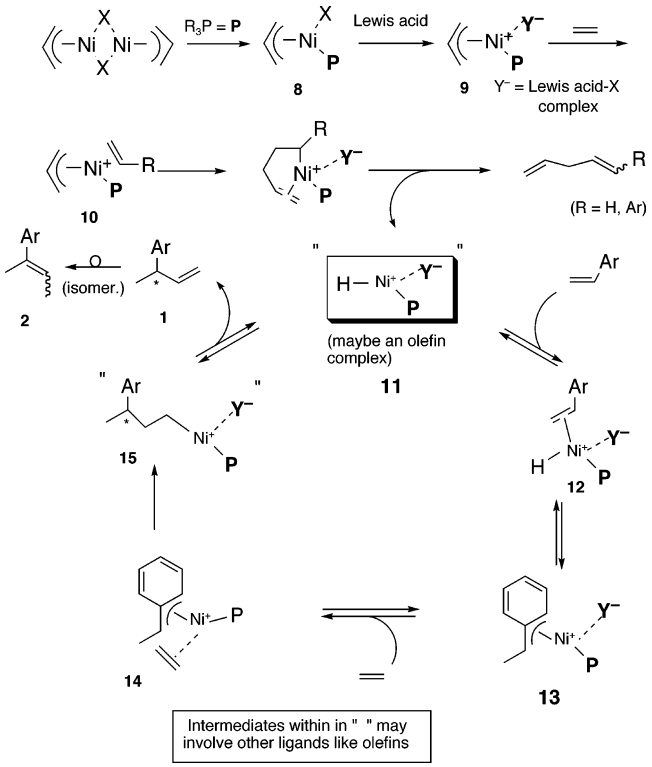
SCHEME 1. Proposed Mechanism for the Heterodimerization of Ethylene and Styrene



and inter-[2a] and intramolecular[24] additions have been documented. Since these early studies, Brookhart and DiRenzo have provided more details of their mechanistic study of the closely related Pd-catalyzed codimerization of styrene and ethylene.[12] On the basis of all the available evidence and our own initial observations, a hypothetical mechanism, shown in Scheme 1, can be proposed for this reaction. The functional equivalent of a catalyst can be represented by **11**, a cationic metal hydride intermediate associated with a weakly coordinated counteranion and a phosphine. This species is formed by the Lewis acid-assisted dissociation of the Ni−X bond from the 16-electron phosphine complex **8**, coordination of ethylene (or styrene) to form **10**, and insertion into the allyl Ni-bond followed by subsequent β-hydride elimination. Several crystal structures of complexes related to Ni-allyl compounds **8** and **9** are known with Cy_3P [X = $MeAlCl_3$],[10b] P(menthyl)(Me)(Bu^t) [X = Cl],[25a] and P(menthyl)$_2$(Me)[X = Me].[25b] Addition of the metal hydride to the vinylarene would lead to the benzyl complex **13**, which is shown as a 16-electron η^3-structure. Ligand substitution with ethylene leads to **14**. At higher concentrations of ethylene and styrene this species could serve as a catalyst resting state. Strong evidence for such a situation has been provided by Brookhart and DiRenzo[12] in the mechanistically related [(allyl)Pd(Cy_3P)]$^+$[BARF]$^-$-mediated dimerization of styrene. Insertion of ethylene followed by β-hydride elimination from **15** regenerates the metal hydride catalyst and the product **1**. A number of anecdotal observations reported in the literature and some made during this study can be accommodated by this mechanism.

(a) The diminished reactivity of electron-deficient vinylarenes might arise from the low rate of metal hydride addition (**11** → **13**).

(b) The apparent poor reactivity of substrates carrying heteroatoms when R_2AlX-type Lewis acids are employed could be the result of the coordination of these atoms to aluminum.

(c) The coordinating solvents show deactivating effects.

(d) The isomerization of the initially formed 3-aryl-1-butene to 2-aryl-2-butens (**1** → **2**) could be mediated by the metal hydride via sequential addition−elimination reactions.

(e) Chelating phosphines totally inhibit the reaction (vide infra).

An Improved Protocol for the Hydrovinylation of Vinylarenes. We have already alluded to the fact that when we started this work the only ligand that gave a satisfactory yield and selectivity for this reaction was Wilke's azaphospholene ligand **6** (eq 6). Several structural modifications of this ligand lead to inferior ligands. We concluded that the scope and selectivity of hydrovinylation could be significantly expanded by a careful study of the reaction in the presence of other phosphine ligands and what appeared to be the other important component of the catalyst, viz., the counteranion **Y** (see **11**, in Scheme 1). In this connection, we wondered whether with appropriately chosen counteranions of other metal salts could serve as an effective replacement for the troublesome Lewis acid in the traditional Wilke dimerization catalyst. In this context, readily available silver salts, with anions of varying donor abilities, could be explored. Previous studies had indicated that while the counteranion (**Y** in Scheme 1) played a significant role in various olefin dimerization and related reactions,[3a] the catalytic activity and selectivity varied considerably with the ligand used. For example, while weakly coordinating anions ($Et_2AlCl_2^-$, OTf^-, BF_4^-) give best selectivities with ligand (*RR*)-**6**,[3b] for other ligands such as (menthyl)$_2$P(Pr^i), more dissociating anions such as PF_6^- and SbF_6^- appear to be the best.[3a] Another parameter that could be explored in a new protocol might be the use of complexes of other metals such as Ru, Pd, and Rh. It was our expectation that with the correct synergy between the metal, the phosphine, and the counteranion we would be able to achieve a more *selective* reaction by affecting several individual steps in the catalytic cycle. For example, selectivity in the first step would arise from the metal hydride adding to the more reactive olefin (**11** → **13**). In the other key step, the smaller olefin can be expected to undergo insertion into the metal−benzyl bond (**13** → **15**), especially with a relatively bulky phosphine, which would increase steric crowding around Ni. Steric and/or electronic effects would prevent metal hydride-mediated isomerization (**1** → **2**) of the relatively hindered (and *unactivated*) primary product. After an extensive scouting program in which we systematically investigated the effect of varying the ligands, counterions, and metals, most of these expectations have been borne out. The full details of this study are disclosed here.

Ligand and Counteranion Effects. The initial scouting of ligands and various silver salts was conducted as

(24) Muller, U.; Keim, W.; Krüger, C.; Betz, P. *Angew. Chem., Int. Ed.* **1989**, *28*, 1011.

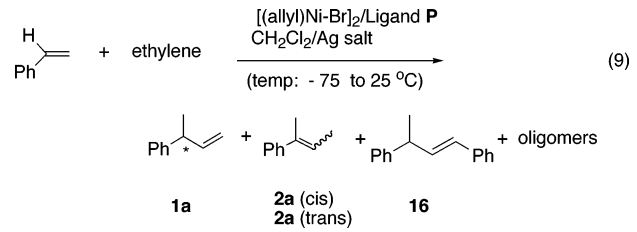
(25) (a) Brandes, H.; Goddard, R.; Jolly, P. W.; Krüger, C.; Mynott, R.; Wilke, G. *Z. Naturforsch.* **1984**, *39B*, 1139. (b) Barnett, B. L.; Krüger, C. *J. Organomet. Chem.* **1974**, *77*, 407.

TABLE 1. Ni-Catalyzed Hydrovinylation of Styrene Ligand and Counterion Effects

entry	P	AgX	conditions	conversion (**1a**:**2**:**16**)
1	Ph_3P	$AgSbF_6$	−78 °C, 7.5 h	low (**1a** + **16**)
2	Ph_3P	$AgSbF_6$	−78 to 25 °C, 14 h	100% (**1a** + **2** (maj) + **16**)
3	Ph_3P	$AgBF_4$	−78 to 25 °C,	no reaction
4	Ph_3P	$AgBPh_4$	−78 or −56 °C	no reaction
5	Ph_3P	AgOTf	25 °C, 5 min	100% [mix. **1a** + **2** (maj)]
6	Ph_3P	AgOTf	−45 to −37 °C, 2 h	100% (68:1:trace)
7	Ph_3P	AgOTf	−78 to 25 °C, 14 h	100% (5:1:0)
8	Ph_3P	AgOTf	−78 °C, 6 h	trace
9	**Ph_3P**	**AgOTf**	**−55 °C, 2 h**	**100% (100:0:0)**
10	Cy_3P	AgOTf	−56 °C, 2 h	11% (11:0:0), rest st mat.
11	Cy_3P	AgOTf	−35 °C, 0.5 h	11% (11:0:0), rest st mat.
12	Cy_3P	AgOTf	0 °C, 45 min	54% (50:0:4)

[a] See eq 9.

follows: in a nitrogen-filled drybox, stoichiometric amounts of $[(allyl)NiBr]_2$ and the phosphine (Ni:P = 1:1) were mixed in CH_2Cl_2 at room temperature and the mixture was added to a suspension of the silver salt in CH_2Cl_2. The precipitated salts were removed by filtration through a pad of Celite and the yellow solution was collected in a Schlenk flask. The flask was taken outside the drybox, and after adjusting the reaction mixture to the appropriate temperature, oxygen-free ethylene was introduced. A solution of the vinylarene in CH_2Cl_2 was then added and the mixture was stirred as noted. The reaction was quenched by adding half-saturated ammonium chloride solution. The *crude product* was analyzed by NMR, gas chromatography, and/or HPLC to ascertain the composition of the mixture (eq 9).



An initial survey of the most commonly available phosphines and silver salts quickly revealed that tricyclohexylphosphine and triphenylphosphine gave the best results. For initial studies, we chose AgOTf, $AgBF_4$, $AgBPh_4$, and $AgSbF_6$, which represent a spectrum of counteranions with varying donor abilities. Typical results obtained in these studies are shown in Table 1.

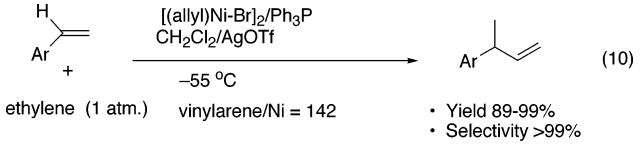
As can be seen in Table 1, $AgSbF_6$, $AgBF_4$, and $AgBPh_4$ are poor additives for the reaction done with Ph_3P at low temperatures (entries 1−4). Upon warming to higher temperatures (∼25 °C), $AgSbF_6$ shows some reactivity. However, the reaction gives a mixture of products that include the isomerized butenes and dimers of styrene. Silver triflate, on the other hand, is a superior additive for the reaction (entries 5−9). At 25 °C, a mixture of the desired product **1a** and the isomerization product **2** is obtained, depending on the length of time the reaction is maintained at higher temperatures (entries 5 and 7). Between −45 and −37 °C, the proportion of the isomerization is reduced considerably (entry 6). The most optimum condition for the reaction is to carry out the dimerization at −55 °C using 0.0035 equiv of $[(allyl)NiBr]_2$ and a ratio of P/Ni/AgOTf = 1:1:1. Under these conditions, neither the isomerization of the double bond nor oligomerization of styrene is observed. As determined by gas chromatography and ^1H NMR spectroscopy, the yield and selectivity of 3-phenyl-1-butene exceed 98% in repeated runs. Isolation usually involved filtration through a small plug of silica and evaporation of the solvent (ether/pentane). For the less volatile 3-arylbutenes, nearly quantitative recovery of the product is possible. Aliphatic phosphines represented by tricyclohexylphosphine are much less reactive under these reaction conditions. At room temperature, nearly quantitative conversion to the product is observed along with some dimerization of styrene.

TABLE 2. Scope of Substrates in Hydrovinylation of Vinylarenes (Eq 10)

entry	vinylarene	% yield[a]	conditions[b]
1	styrene	>95 (>99)	i
2	3-Me-styrene	(98)	i
3	4-Me-styrene	(>99)	i
4	2-chlorostyrene	30	i
5	4-chlorostyrene	(>99)	i
6	4-methoxystyrene	>95 (>99)	i
7	4-bromostyrene	>95 (98)	i
8	2-vinylnaphthalene	(>99)	i
9	6-MeO-2-vinyl-naphthalene (MVN)	94 (>99)	i, 1.4 mol % [Ni]
10	4-*i*-Bu-styrene	>90 (99) >97 (99)	i, 1 mol % [Ni] ii
11	3-F-4-C_6H_5-styrene	88	i
12	3-bromostyrene	(99)	i
13	3-Ph-C(O)-styrene	(99)	i

[a] In parentheses are yields based on gas chromatography. Selectivity >98% in all cases. [b] (i) 0.7 mol % [Ni], CH_2Cl_2/−55 °C/2 h. (ii) (*R*)-MOP/$Ar_4B^-Na^+$/CH_2Cl_2/−56 °C/2 h.

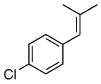
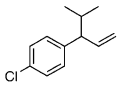
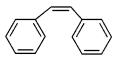
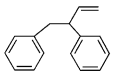
The scope of the new protocol (eq 10) is shown in Table 2. In all cases the chemo- and regioselectivity of the codimerization with respect to the desired product reaches nearly 100%. Lewis basic groups such as OMe and



carbonyl group are tolerated (entries 6, 9, and 13). It appears that the reactivity of the ortho derivative is less compared to the corresponding para analogue (entries 4 and 5), this difference arising from the steric effect that hinders the approach of the $[Ni-H]^+$ to the double bond. Note that excellent yields of hydrovinylation products are obtained from a variety of precursors appropriate for the synthesis of antiinflammatory 2-arylpropionic acids (entries 9−13). The product of hydrovinylation of 4-bromostyrene (entry 7) is another potentially important precursor that may be transformed into a number of 4-substituted analogues via organometallic cross-coupling reactions. In most instances, the crude product is exceptionally clean, as indicated by gas chromatography, and no further purification of the product is warranted.

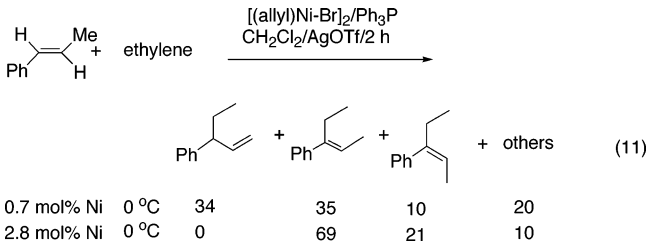
Under conditions where styrene gives a quantitative yield of the product, its derivatives substituted in the vinyl fragment show negligible reactivity (Table 3). Compared to α-methylstyrene, *β*-methylstyrene gave higher conversions (entries 1−3). At higher temperatures,

TABLE 3. Hydrovinylation of Side-Chain-Substituted Styrenes

entry	vinylarene	temp. (°C)	conver.(%)[a]	product	yield (%)
1.	α-methyl styrene	-56	no reaction		0
		0	46		42
2.	*trans*–β-methyl styrene 	-55	11		10
		-20	86		54[b]
		0	>99		34[c]
3.	*cis*–β-methyl styrene 	-55	8		8
4.		-55	no reaction		0
		0	6		<2
5.		-60	no reaction		0
		0	38[d]		13[e]

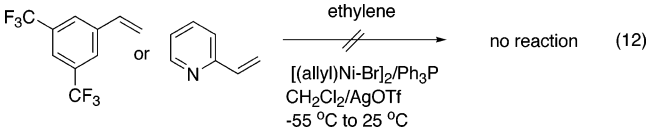
[a] Typical conditions: (i) 0.35 mol % $[(allyl)_2NiBr]_2$, Ph_3P, AgOTf, CH_2Cl_2/−55 °C/2 h. [b] Rest *cis*- and *trans*-3-phenylpentenes (15%:4%). [c] Rest *cis*- and *trans*-3-phenylpentenes (35%:10%) and unidentified products (20%). [d] 2.0 mol % catalyst. [e] Mixture of olefins.

up to 34% yield of the primary product is formed from *E*-*β*-methylstyrene in a reaction that proceeds with excellent conversion (entry 2 and eq 11). The isomers



(11)

were fully characterized by NMR experiments including NOE studies. Trisubstituted styrene derivatives react sluggishly. *Z*-Stilbene gives a mixture of olefinic products in low yields. Not unexpectedly, the recovered stilbene is a mixture of *Z*- and *E*-isomers, providing further support for a $[(\mathbf{L})Ni-H]^+$ intermediate in these reactions. Other related substrates that fail to undergo the hydrovinylation reaction under a variety of conditions include 3,5-bis(trifluromethyl)styrene, 2-vinylpyridine, and *N*-vinylcarbazole (eq 12). While the electron-deficient nature



(12)

of the styrene may preclude Ni-coordination, the lack of reactivity of vinylpyridine may have its origin in the formation of stable intermediates assisted by the pyridine nitrogen. Vinylcarbazole gives a polymer that is insoluble in most organic solvents. No further characterization of this material was undertaken.

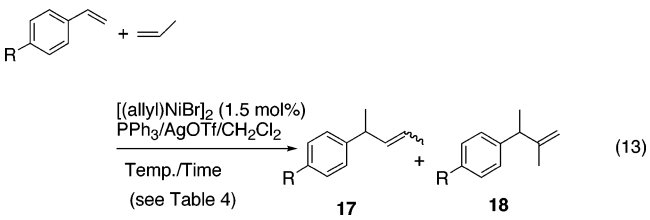
Heterodimerization of Styrene with Other Olefins. Unlike heterodimerization reactions of ethylene, no synthetically useful heterodimerization reaction using propene was known before our work. We find that

TABLE 4. Heterodimerization of Propene and Vinylarenes (Eq 13)

no.	R	temp, °C	time, min	% yield[a]	17:18
1	*i*-Bu	-15	15	96	3:1
2	OMe	-15	60	86	4:1
3	Cl	0	15	94	4:1
4	Br	0	10	95	4:1
5	OAc	−10	30	93	4:1
	OAc	−55 to −40	30	98[b]	5:1
6	PhC(O)[c]	10	15	94	4:1
7	NTs_2[c]	10	25	92	2:1
8	MVN[c,d]	−5	60	88	10:1

[a] Isolated yield. [b] 1.4 mol % Ni used. [c] 3 mol % Ni used. [d] 2-Methoxy-6-vinylnaphthelene.

propene reacts with styrene and substituted styrenes under conditions slightly modified from what was previously described for ethylene, giving excellent yields of the expected products (eq 13, Table 4). The reaction with



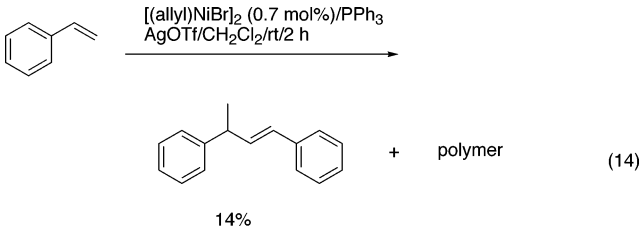
(13)

propene proceeds at a higher temperature (−15 to 10 °C vs −56 °C for ethylene), especially in the case of the more electron-deficient styrene derivatives. As expected, a mixture of regioisomeric products (with propene-C_1 addition to the benzylic position, **17**, as the major one) is obtained. Details of this reaction have since been published.[26]

Reaction of styrene alone with $[(allyl)_2NiBr]_2$ and Ph_3P at room temperature in the presence of AgOTf leads to the formation of 14% styrene dimer along with extensive

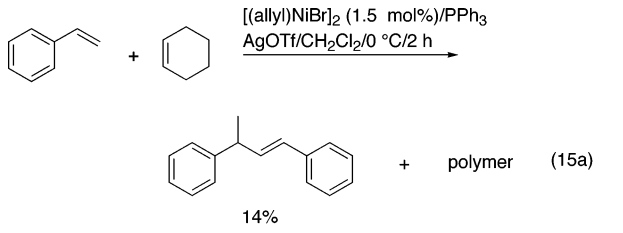
(26) Jin, J.; RajanBabu, T. V. *Tetrahedron* **2000**, *56*, 2145.

polymerization (eq 14). Attempts to effect heterodimer-

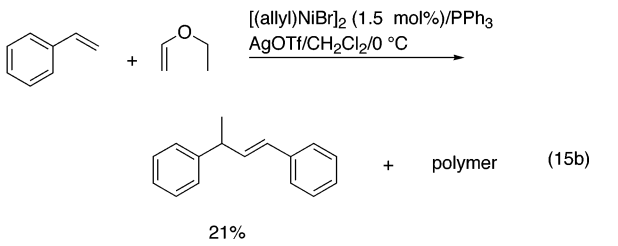


(14)

ization of styrene and cylohexene or ethyl vinyl ether also lead to polymer formation. Varying amounts of styrene dimer can be detected in gas chromatography (eq 15)

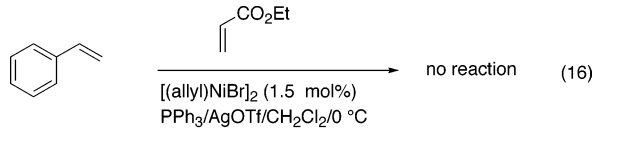


(15a)



(15b)

under these conditions. Codimerization of styrene and ethyl acrylate does not proceed under the standard hydrovinylation conditions (eq 16) using Ph_3P and AgOTf,



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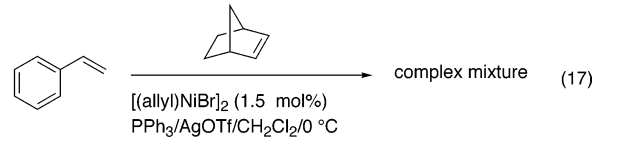
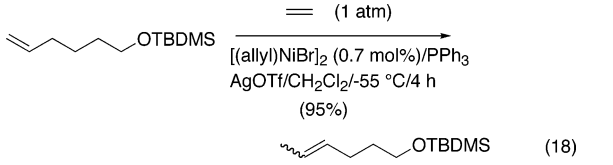


(17)

whereas with norbornene a complex mixture of hydrocarbons is obtained (eq 17). Treatment of a typical terminal olefin, 1-*tert*-butyldimethylsiloxy-5-hexene, with ethylene under hydrovinylation conditions leads to clean isomerization of the double bond to give a mixture of *Z*- and *E*-1-*tert*-butyldimethylsiloxy 4-hexenes (eq 18). No trace of dimerization products could be detected under these conditions.



(18)

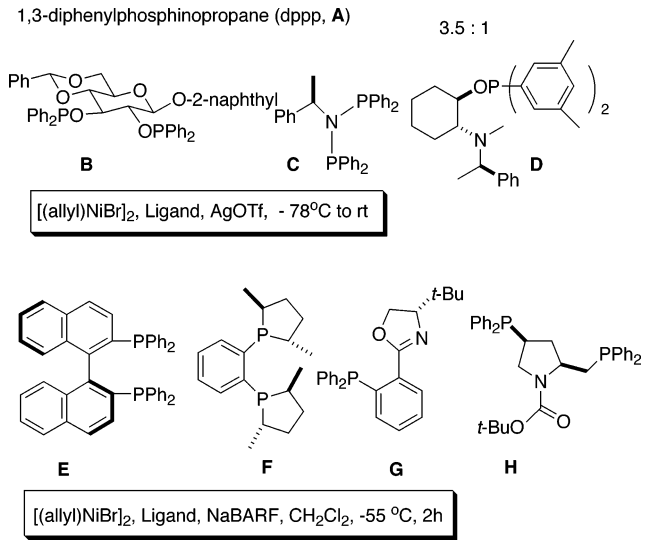
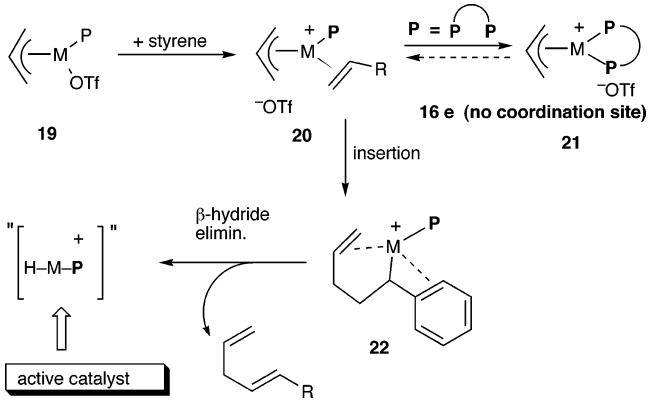


FIGURE 2. Chelating ligands used for the Ni-catalyzed hydrovinylation reactions.

SCHEME 2. Why a Chelating Ligand May Not Work in Hydrovinylation of a Vinylarene



Reactions Using Chelated Phosphines. If the proposed mechanism (Scheme 1) has any validity, there is only one ligand per metal in the catalytically active species. A number of studies have indicated that the Ni-catalyzed hydrovinylation reaction might be inhibited by chelating phosphines, even when the reactions are carried out under widely different conditions.[3b,15a] Nonetheless, we investigated the viability of different classes of chelating phosphines under the newly discovered protocol (eq 10). A list of ligands and some typical reaction conditions tested are listed in Figure 2. Careful examination of the crude reaction products by gas chromatography and NMR spectroscopy revealed that no C−C coupling products (oligomers, hetero- or homodimers) were formed under these reaction conditions, even when the reaction is run at higher temperatures.

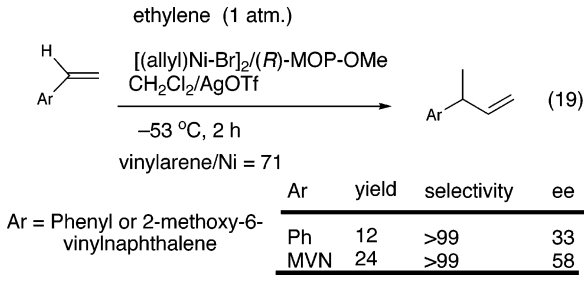
In retrospect, the conspicuous lack of activity of chelated phosphines in the hydrovinylation is not surprising. As shown in Scheme 2, the generation of the active catalyst is possible only if the OTf in the initially formed complex **19** is efficiently displaced by one of the olefins (ethylene or styrene), and this event is followed by an insertion (e.g., to form **22**) and a *β*-hydride elimination. A strongly chelating bis-phosphine would either prevent

the formation of **20** or effectively reduce its concentration such that the insertion pathway is no longer available.

Use of Hemilabile Ligands. An attractive solution to such a problem would be to use a chelating ligand with one strongly coordinating group and one weakly coordinating group.[27] The strength of the bond between this latter group and the metal would be a critical element in the successful execution of this idea. A number of "hemilabile" groups, including carboxylate (anionic), ester carbonyl, triarylphosphonoyl, and sufur (from a thiophene) moiety, have been investigated in a variety of reactions, including oligomerization of ethylene,[28a−d] codimerization ethylene and styrene,[28e] and ethylene/CO oligomerization.[28f] Since our eventual goal was to develop an asymmetric version of the hydrovinylation reaction, we decided to explore the use of a hemilabile ligand in the context of a chiral ligand. In the absence of any clear lead, an ether-oxygen was chosen as the hemilabile group in the first ligands we investigated. This choice was not entirely arbitrary, since phosphino−ether systems have been extensively investigated,[27] starting with the initial *o*-diphenylphosphinoanisole, which was the first hemilabile ligand to be so named.[27a]

In the event, (*R*)-2-diphenylphosphino-2′-methoxy-1,1′-binaphthyl (MOP),[29] in which the methoxy moiety would play the role of the hemilabile ligand, was chosen for the initial study. The BINAP structural motif was considered especially attractive, since it allowed considerable flexibility in ligand tuning, including variations of the 2′-substituents, which would allow further explorations of the hemilabile ligand concept.

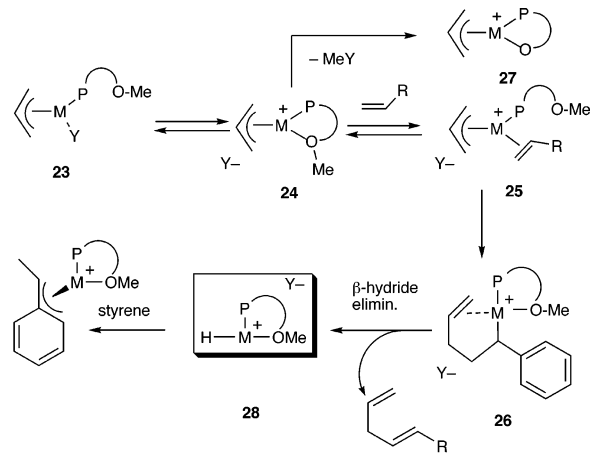
Hydrovinylation of styrene and 2-methoxy-6-vinylnaphthalene (MVN) was carried out using the MOP ligand under the standard protocol described earlier (eq 10) using AgOTf, and the results are shown in eq 19. A



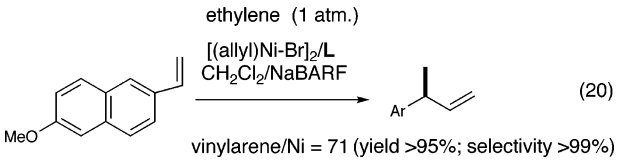
Ar = Phenyl or 2-methoxy-6-vinylnaphthalene	Ar	yield	selectivity	ee
	Ph	12	>99	33
	MVN	24	>99	58

highly selective reaction ensues, yielding the expected product, albeit in disappointingly low conversion (12% and 24% yield) and enantioselectivity (33% and 58% ee). The conversions were of special concern, since nearly *quantitative* reactions were routinely observed in reactions reported earlier (Table 2). Even though the exact origin of the diminished activity of a Ni-catalyst with a hemilabile ligand under these conditions remains unknown, further development of the reaction would rely upon the following rationale (Scheme 3).

SCHEME 3. Effect of Counteranion Y on Catalyst Generation



The initially formed complex **23** could be in equilibrium with a chelated complex **24**. The generation of the catalyst is possible only if the hemilabile ligand is successfully displaced by an olefin to form **25**. The relative concentrations of **23**−**25** thus become an important factor in the catalyst turnover. Low concentrations of the catalytically competent species **25** and/or side reactions, which remove the catalyst (for example, by methylation of the triflate to give catalytically inactive[30] **27**), may account for the poor reactivity under these reaction conditions. Support for this conjecture comes from the fact that upon replacement of the triflate by a totally dissociated, nonnucleophilic counteranion, BARF ($B[(3,5\text{-}(CF_3)_2C_6H_3)]_4^-$),[31] the activity of the catalyst system is completely restored. The primary products from 4-isobutylstyrene and MVN are formed in more than 95% yields with enantioselectivities of 40% and 62% (eq 20), respectively.



Effect of Various Hemilabile Groups. To probe the effect of the hemilabile atom, we prepared a number of 2′-derivatives of BINAP (Figure 3) and examined the hydrovinylation of MVN. The results are summarized in Table 5. Increasing the steric bulk of the 2′-*O*-alkyl substituent has little effect on the enantioselectivity of the MVN reaction, but the yield of the product is reduced.

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(28) (a) Keim, W. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 235. (b) Bonnet, M. C.; Dahan, F.; Ecke, A.; Keim, W.; Schulz, R. P.; Tkatchenko, I. *Chem. Commun.* **1994**, 615. (c) Meking, S.; Keim, W. *Organometallics* **1996**, *15*, 2650. (d) Komon, Z. J. A.; Bu, X.; Bazan, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 1830. (e) Britovsek, G. J. P.; Cavell, K. J.; Keim, W. *J. Mol. Catal. A, Chemical* **1996**, *110*, 77. (f) Keim, W.; Maas, H.; Mecking, S. *Z. Naturforsch.* **1995**, *50B*, 430.

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(30) For structurally related, unreactive, neutral Pd-complexes see, ref 28e.

(31) (a) Nishida, H.; Takada, N.; Yoshimura, M.; Sonoda, T.; Kobayashi, H. *Bull. Chem. Soc. Jpn.* **1984,** *57*, 2600. (b) Brookhart, M.; Grant, B.; Volpe, A. *Organometallics*, **1992**, *11*, 3920. For the use of Ar_4B^- in related reactions, see: DiRenzo, G. M.; White, P. S.; Brookhart, M. *J. Am. Chem. Soc.* **1996**, *118*, 6225.

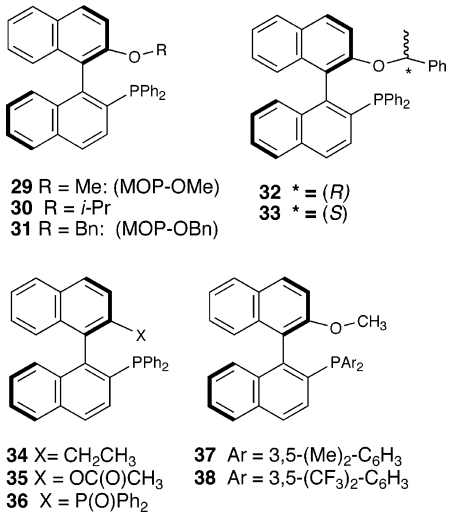


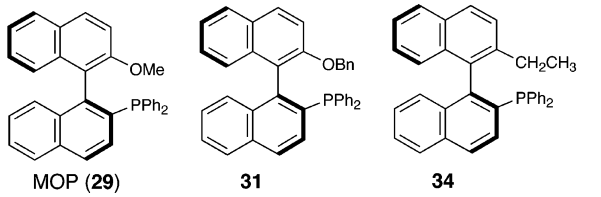
FIGURE 3. BINAP ligands for hydrovinylation.

TABLE 5. Effects of BINAP 2′-Substituents on the Hydrovinylation of 2-Methoxy-6-vinylnaphthalene (MVN)[a]

entry	ligand	(2 group, Figure 4)	% yield	% ee[b]	remarks
1	(*R*)-BINAP	Ph_2P	0		
2	**29**	OCH_3	>98	62	
3	**30**	i-Pr	69	69	
4	**31**	OCH_2Ph	97	73	−55 °C; $AgNTf_2$ 87%
5	**31**	OCH_2Ph	93	80	at −70 °C
6	**32** (*aRR*)	$OC(H)(Ph)(CH_3)$	>98	71	
7	**33** (*aRS*)	$OC(H)(Ph)(CH_3)$	79	65	
8	**34**	CH_2CH_3	12	<3	styrene 13%
9	**35**	$OC(O)CH_3$	0		
10	**36**	$P(O)Ph_2$	0		
11	**37**	OMe	94	63	
12	**38**	OMe	93	63	

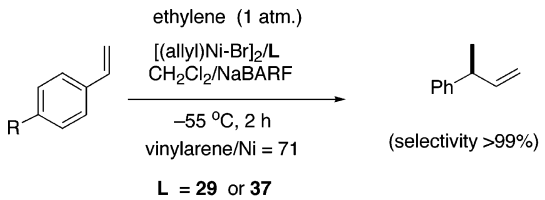
[a] See eq 20 for a typical procedure. [b] Ee determined by HPLC.

Thus *O*-*i*-Pr derivative **30** under identical conditions gave 69% yield and 70% ee. For MVN, a benzyloxy analogue of MOP (**31**) gave 80% ee when the reaction was carried



out at −70 °C. Evidence of the involvement of hemilabile oxygen may also be inferred from the different activities of catalysts prepared from BINAP derivatives with (*R*)- and (*S*)-phenethyl ether side chains (**32** and **33**). While the former gave an excellent yield (96%) (71% ee) of the product, the latter gave only 79% yield (65% ee). In an attempt to probe the effect of the hemilabile ligand, we prepared the 2′-ethyl analogue **34** and tested this ligand under both sets of conditions, viz., using AgOTf and NaBARF as additives. For the hydrovinylation of MVN using BARF counteranion, 12% yield and 3% ee of the product were obtained, whereas AgOTf gave less than 2% conversion. If the hemilabile ligation is important, one should expect different reactivities from ligands with varying donor properties.[27,28] Allyl(Ni) complexes of 2′-acetoxy (**35**) and diphenylphosphosphoryl (**36**) analogues failed to produce any hydrovinylation products under the standard reaction conditions (entries 9 and 10). Phosphinoxide is known to be a strongly coordinating group[28c] and it is not surprising if the catalyst generation is prevented due to the inability of an olefin to displace this group. As for the acetoxy derivative **35**, the carbonyl oxygen is known to be a strongly coordinating atom as compared to an ether-oxygen in a variety of metal complexes.[32] Finally, the electronic effect of ligands on the hydrovinylation selectivity was examined by comparison of ee's obtained using ligands **37** and **38** with that from **29** (entries 2, 11, and 12). In sharp contrast to the Ni(0)-catalyzed hydrocyanation, Rh(I)-catalyzed hydrogenation, or the Pd(0)-catalyzed allylation,[33] ligand electronic properties appear to have little effect on hydrovinylation; in each case, the chemical yield and ee were almost identical. Note that a significant difference between these reactions and the hydrovinylation is that there is no change in the oxidation state of the metal in the catalytic cycle of the hydrovinylation reaction. Nickel(II) with its ligands plays the role of a complex Lewis acid!

Hydrovinylation of styrene using the ligands **29** and **37** gave >80% yield 25−27% ee at −55 °C (eq 21). The



L = 29 or 37

Substrate	Ligand	Yield	ee
styrene	**29**	80	25
styrene	**37**	85	27
4-*t*-Bu-styrene	**29**	93	40

reactions are exceptionally clean as judged by gas chromatographic and NMR analysis of the product, and the observed low yield of the product is most likely a result of its high volatility.

As expected from the proposed mechanism, the reaction shows pronounced solvent effects (Table 6). Under conditions described in eq 20 (−55 °C, 0.7 mol % [(allyl)-$NiBr]_2$, NaBARF, 2 h), the following yields and enantioselectivities were observed for the solvents indicated: CH_2Cl_2 (97, 73); ether (87, 77); toluene (88, 74); THF (0,

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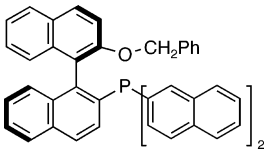
(33) Examination of electronic effects has become a common practice in asymmetric catalysis. For some of the early examples of electronic tuning of asymmetric catalysts, see: (a) Inoguchi, K.; Sakuraba, S.; Achiwa, K. *Synlett* **1992**, 169. (b) Jacobsen, E. N.; Zhang, W.; Guler, M. L. *J. Am. Chem. Soc.* **1991**, *113*, 6703. (c) RajanBabu, T. V.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1992**, *114*, 6265. (d) RajanBabu, T. V.; Ayers, T. A.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1994**, *116*, 4101. (e) Schnyder, A.; Hintermann, L.; Togni, A. *Angew. Chem., Int. Ed.* **1995**, *34*, 931. Other examples from our work: Casalnuovo, A. L.; RajanBabu, T. V.; Ayers, T. A.; Warren, T. H. *J. Am. Chem. Soc.* **1994**, *116*, 9869.; RajanBabu, T. V.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 6325.; RajanBabu, T. V.; Ayers, T. A.; Halliday, G. A.; You, K. K.; Calabrese, J. C. *J. Org. Chem.* **1997**, *62*, 6012.; Clyne, D. S.; Mermet-Bouvier, Y. C.; Nomura, N.; RajanBabu, T. V. *J. Org. Chem.* **1999**, *64*, 7601.; Yan, Y.; RajanBabu, T. V. *Org. Lett.* **2000**, *2*, 4137.

TABLE 6. Solvent Effects on the Ni-catalyzed Hydrovinylation of MVN using 31 as a Ligand

entry	solvent	selectivity	% yield	% ee[b]
1	CH_2Cl_2	>99	>98	73
2	ether	>99	87	77
3	toluene	>99	88	74
4	THF		0	0

[a] See eq 20 for a typical procedure (−55 °C). [b] Ee determined by HPLC.

TABLE 7. Hydrovinylation Using Di(2-naphthyl)-MOP-OBn (39)



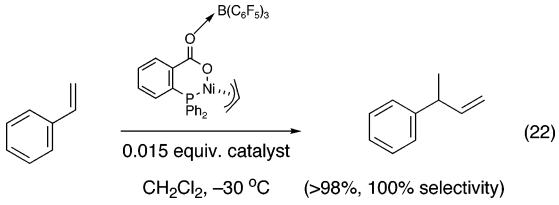
entry	vinylarene	additive	temp (°C)/ time (h)	% yield[b]	% ee (*S*)[c]
1	styrene	NaBARF	−35/2	73	32
2	styrene	$AgSbF_6$	−25/3	76	28
3	styrene	$AgNTf_2$	−25/2.5	57	27
4	4-*i*-Bu-styrene	NaBARF	−20/3	99	40

[a] See eq 20 for typical procedure. [b] The rest was starting material. [c] Ee determined by HPLC.

0). Tetrahydrofuran is a strongly coordinating solvent and it is no surprise that under these conditions no hydrovinylation is observed.

A limited effort was made to modify the diaryl substituents of BINAP to examine the effect of this structural variation on the selectivity in the hydrovinylation reactions. The results are shown in Table 7. Increasing the size of the aryl units from phenyl to 2-naphthyl affects the overall rate of the reaction. The overall yield and enantioselectivity remains the same when the reaction is carried out at −20 °C. The experiments using styrene also showed for the first time that other dissociated silver salts ($AgSbF_6$ and $AgNTf_2$) could effectively replace NaBARF in these reactions.

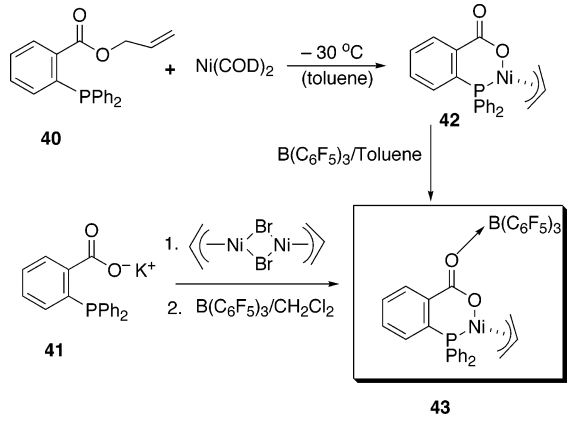
Other Protocols for Nickel-Catalyzed Hydrovinylation Reactions. During the course of these investigations, we have uncovered a number of other viable procedures for this exacting reaction. Thus, a catalyst prepared from allyl 2-diphenylphosphinobenzoate **40** and $Ni(COD)_2$ or the corresponding potassium salt of the acid (**41**) and allyl nickel bromide (Scheme 4) shows very good activity and excellent selectivity in the hydrovinylation reactions of styrene when activated with $(C_6F_5)_3B$[28d] (eq 22). Structurally related catalysts have been used for



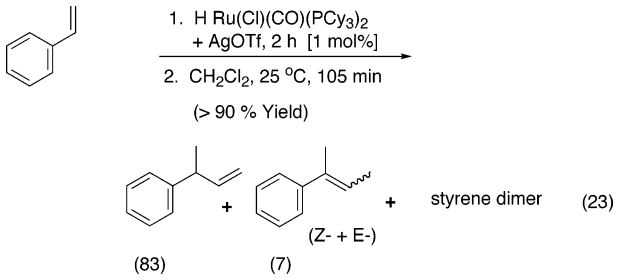
(22)

oligomerization of ethylene.[28a−d] These novel methods (Scheme 4) for the preparation of the neutral carboxylate complexes (e.g., **43**) from the allyl ester or the acid might find other applications.

SCHEME 4. A Single-Component Catalysts for Hydrovinylation of Styrene

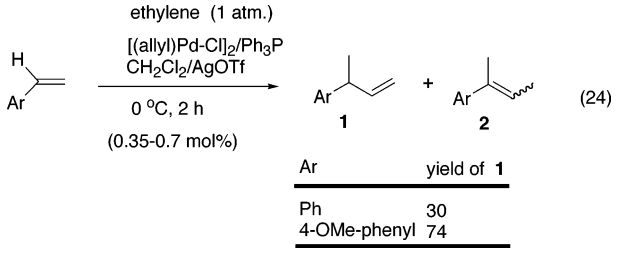


Ruthenium-Catalyzed Reactions. In a modern version of the Ru-catalyzed hydrovinylation,[5a,6] Yi et al. has recently reported that $(Cy_3P)_2Ru(CO)(H)(Cl)$ in the presence of $HBF_4{\cdot}Et_2O$ effects hydrovinylation of vinylarenes and dienes.[22] We have examined this reaction under activation of this Ru-catalyst using AgOTf instead of $HBF_4{\cdot}OEt_2$ and find that nearly quantitative conversion of styrene maybe achieved. However, competitive formation of the isomerization products, (*Z*)- and (*E*)-2-phenyl-3-butenes, and the formation of head-to-tail styrene dimer could not be avoided under a variety of conditions (eq 23). Further optimization of this system might yield a catalyst that works at or near room temperature.



(23)

Palladium-Catalyzed Reactions. As noted earlier, several studies in the literature indicate that the formation of isomerization products seriously limits the Pd-catalyzed hydrovinylation reactions, especially when the reactions are carried to completion. We find that the use of $[(allyl)PdCl]_2$ in the place of $[(allyl)NiCl]_2$ in our protocol leads to similar results. For a given ligand and counterion, the catalyst is noticeably less active vis-à-vis the corresponding Ni-analogue. As represented in the eq 24, at low conversions, the primary product, 3-phenyl-

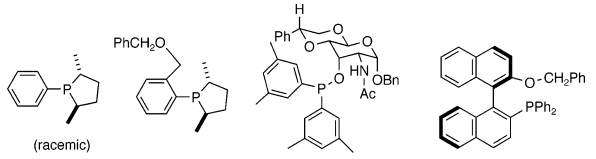


Ar	yield of **1**
Ph	30
4-OMe-phenyl	74

(24)

1-butene, is formed with excellent isomeric purity. Asymmetric hydrovinylation reactions have been much less

TABLE 8. Pd-Catalyzed Hydrovinylation of Styrene[a]

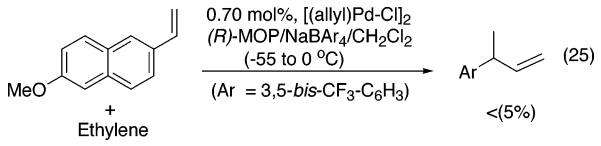


44 **45** **46** **31**

entry	ligand	additive	temp (°C)/ time (h)	st mat. (%)	3-Ph-bute (%)	(*Z*+*E*)-2-Ph-2-butenes(%)
1	**44**	AgOTf[b]	−55/3	100	0	0
2	**44**	AgOTf[b]	−5/3	61	27	11
3	**44**	AgOTf[b]	25/3	41	39	18
4	**45**	NaBARF[b]	−20/3	0	65	32
5	**29**	NaBARF[c]	−55/2	100	<5	
6	**46**	NaBARF[c]	0−10/2	30	57	13

[a] See eq 21/25 for typical procedures. [b] [(allyl)PdBr]$_2$ used. [c] [(allyl)PdI]$_2$ used.

successful (eq 25). Attempts to circumvent this problem



with alternate ligands (**31**, **44**−**46**, Table 8) and counterions have not yet been successful. Recall that *all* of these ligands give excellent yield and selectivities (>95%) for the 3-arylbutenes in the Ni-catalyzed reactions at low temperature.[34,35]

A Model Transition State for the Asymmetric Induction in the Hydrovinylation Catalyzed by (*R*)-MOP-Ni(allyl)-BARF. Even though the details of the mechanism of asymmetric hydrovinylation including the nature of the rate- and enantioselectivity-determining steps remain unknown, a useful, working model for the transition state maybe constructed based on reasonable assumptions derived from experimental observations. Addition of a chelated metal hydride through one of the four possible square planar Ni(II) complexes (**47**−**50**) is shown in Figure 4. In this preferred transition state, the olefin is coordinated trans to the phosphine (sterically less encumbered compared to the corresponding *cis*-olefin/PAr$_2$ structures) and the metal-hydride addition takes place from the *re*-face of the olefin (e.g., through the transition state **51**), eventually leading to the observed major product. In this orientation, the interaction between the hydrogen ortho to the OR group and the aromatic moiety of the vinylarene is minimized as the distance between the Ni-atom and the benzylic carbon is reduced during the bond-formation. Such interaction would retard addition to the *si*-face. In partial support of this argument, the observed ee for a bulky vinylarene (2-methoxy-3-vinylnaphthalene) is significantly higher than that for simple styrene derivatives (80% vs <30%) under identical conditions. We have since found this

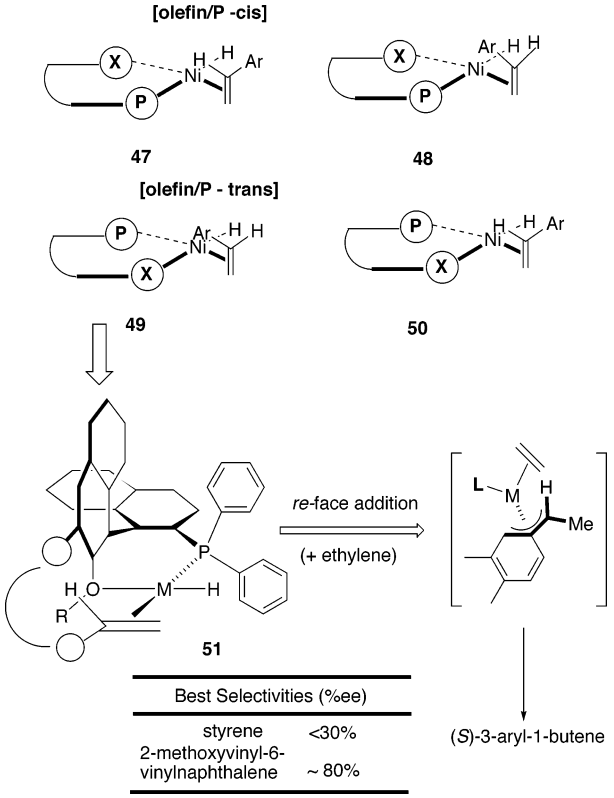


FIGURE 4. A model TS for the addition of a chelated metal hydride to the vinylarene in [(*R*)-MOP)] M(H)(vinylarene).

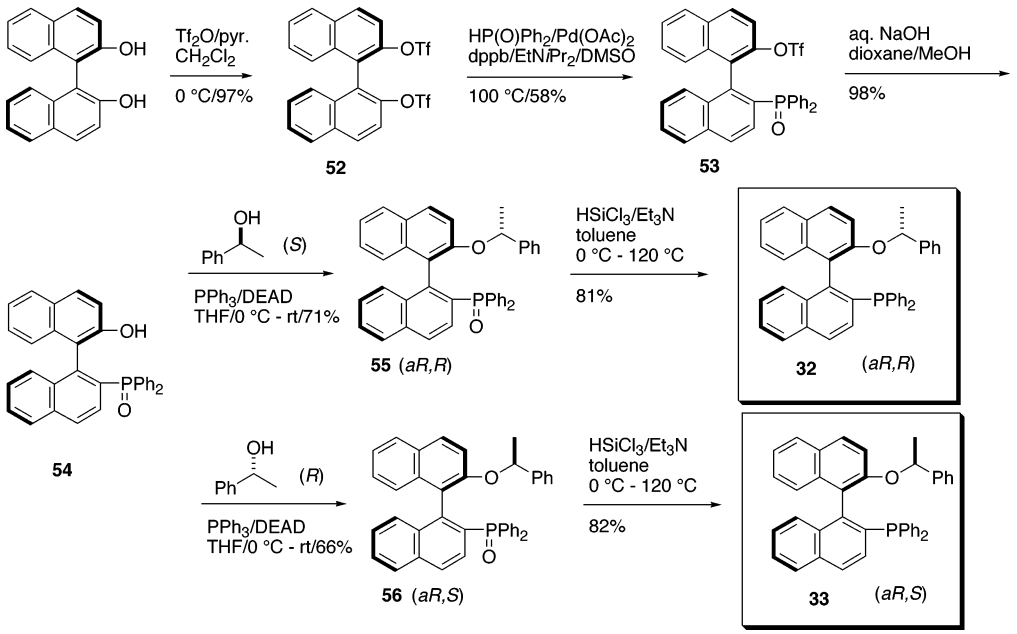
working model to be applicable for other asymmetric catalysts with different ligands.[23,34]

Synthesis of Ligands. Synthesis of ligands with specific electronic and steric requirements is an essential, often tedious, part of any asymmetric catalysis program that relies on ligand tuning to bring about optimum results, and the present case is no exception. Syntheses of a number of ligands used during this study have been described in the literature, while several others are new. Ligands **29**−**31**, **34** (Figure 3) were prepared via procedures described by Hayashi[29] using 2,2′-trifluromethylsulfonyloxy-1,1-binaphthyl (**52**)[38] as a starting material (Scheme 5). The ligands **32** and **33** were prepared by Mitsunobu reaction of 2-diphenylphosphinoyl-2′-hydroxy-1,1′-binaphthyl (**54**) with either (*S*)- or (*R*)-2-phenylethanol (Scheme 5), respectively. Acetylation of **57** with acetic anhydride in the presence of Et$_3$N and DMAP gave **35** (Scheme 6).

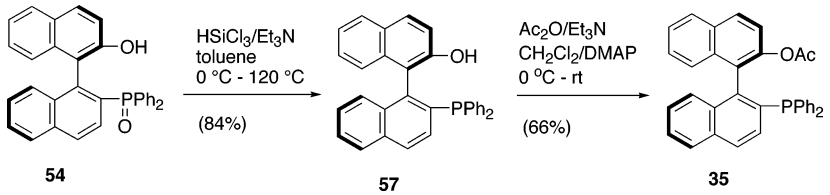
While the synthesis of the bis-3,5-dimethylphenyl derivative **37** posed no problem (Scheme 7), the corresponding bis(3,5-bis(trifluoromethyl)phenyl) derivative **38** could not be synthesized by the standard protocol (Scheme 8). The diarylphosphonous acid failed to react with the bis-triflate **52** under catalysis by Pd(OAc)$_2$/dppb/EtN(*i*-Pr)$_2$. The problem was overcome by Pd-catalyzed coupling of **52** with diethyl phosphite, followed by conversion of the resulting phosphonate **61** to a dichloride, which was

(34) Kumareswaran, R.; Nandi, M.; Park, H.; Jin, J.; RajanBabu, T. V. (unpublished results).
(35) For ligands **44**, **45** and **46**, see ref 23 and 36. For the use of a phosphinite ligand see also, Bayersdörfer, R.; Ganter, B.; Englert, U.; Keim, W.; Vogt, D. *J. Organomet. Chem.* **1998**, *552*, 187.
(36) Park, H.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2002**, *124*, 734.
(37) Hayashi, T.; Konishi, M.; Fukushima, M.; Kanehira, K.; Hioki, T.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 2195.
(38) Kurz, L.; Lee, G.; Morgans, D., Jr.; Waldyke, M. J.; Ward, T. *Tetrahedron Lett.* **1990**, *31*, 6321.

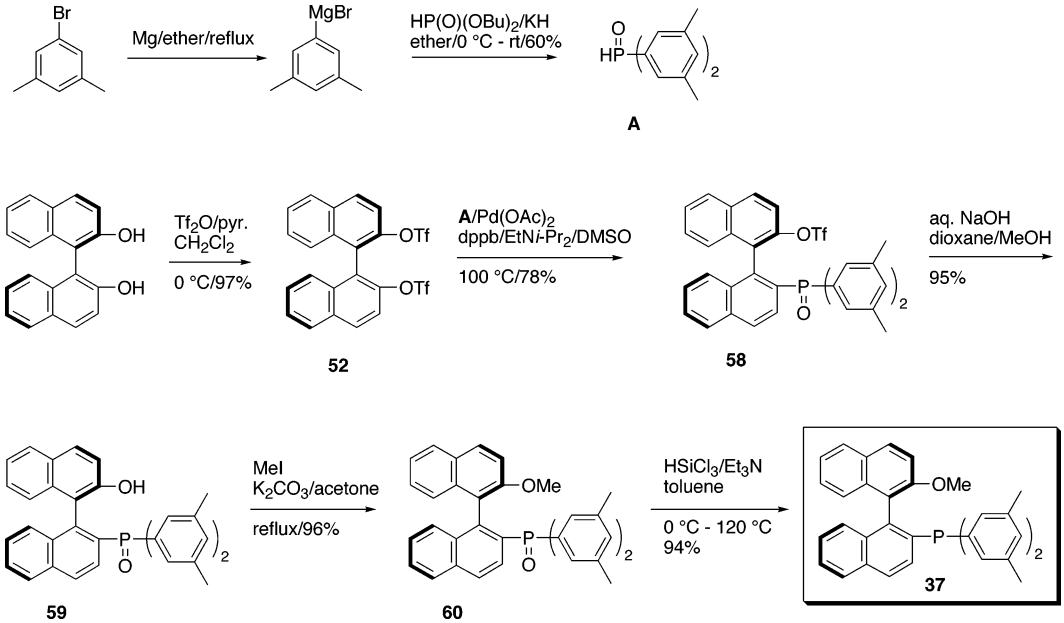
SCHEME 5. Synthesis of Ligands 32 and 33



SCHEME 6. Synthesis of Ligand 35

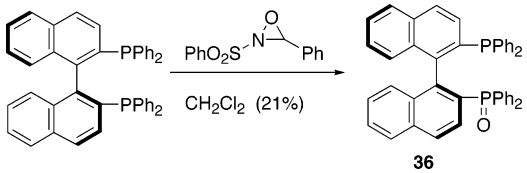


SCHEME 7. Synthesis of Ligand 37



subsequently treated with an excess of the Grignard reagent. The phosphine oxide **63** was reduced under the standard conditions using $HSiCl_3/Et_3N$ to get a modest overall yield of the ligand **38**. Incidentally, the diethylphosphonate **61** failed to react with the Grignard reagent at 0 °C in ether.

The BINAP-monophosphine oxide **36** is prepared by selective oxidation of (*S*)-BINAP with oxaziridine (eq 26).[39] A mixture of mono- and diphosphineoxides are



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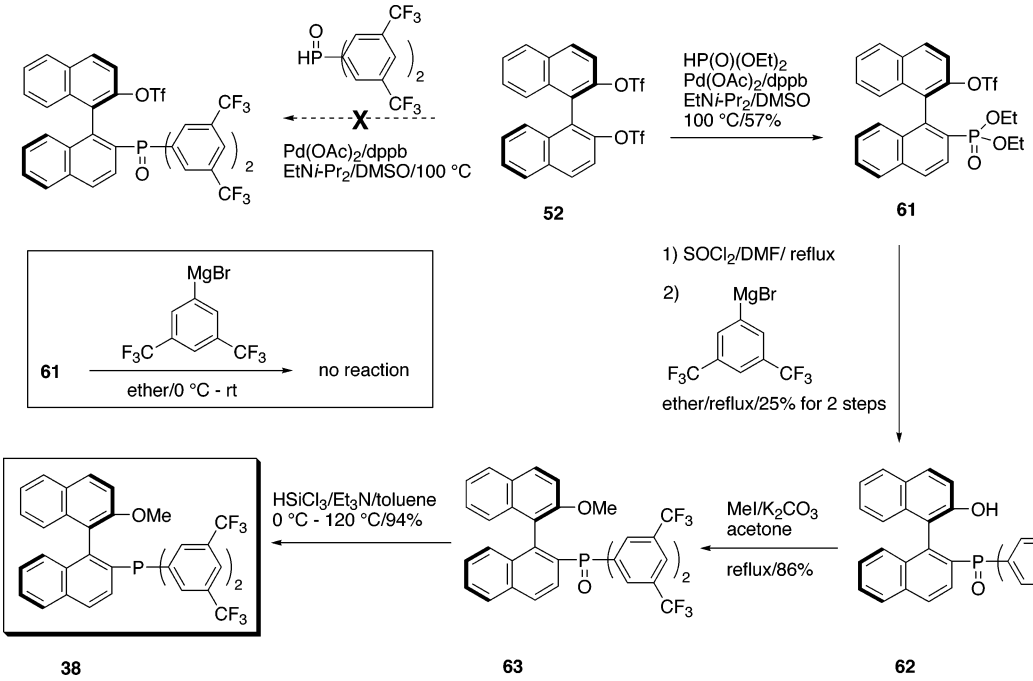
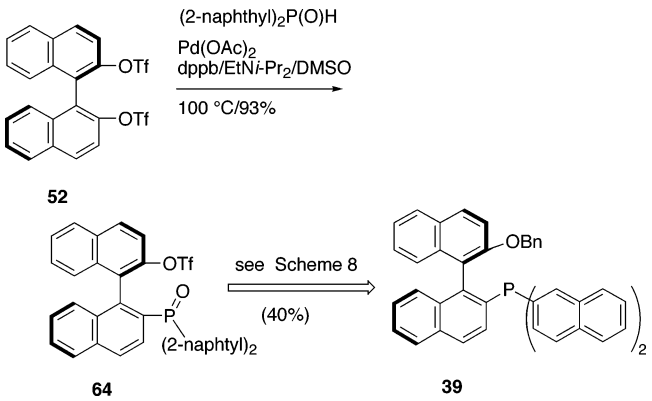
SCHEME 8. Synthesis of Ligand 38



SCHEME 9. Synthesis of Ligand 39



formed even at low temperatures, from which the monooxide is isolated by column chromatography.

The ligand **39** was prepared along the lines outlined in Scheme 7,[29] starting with the coupling of bis(2-naphthyl)P(O)H with the bis-triflate **52** to form **64**, followed by the same reactions used in the preparation of **37** (Scheme 9).

Summary and Conclusions

New protocols for nearly quantitative and highly selective codimerization of ethylene and various functionalized vinylarenes are described. Excellent functional group tolerance and high turnover numbers in the Ni-catalyzed reaction have been demonstrated. Reactions using Pd and Ru catalysts appear to be much less efficient and less selective and may require further development before a viable system can be identified. Recognition of a synergistic relationship between a chiral hemilabile ligand (MOP) and a highly dissociated counteranion (BARF or SbF_6) in an enantioselective version of the Ni-catalyzed reaction raises the prospects of developing a practical route for the synthesis of 3-arylbutenes. Several pharmaceutically relevant compounds, including widely used 2-arylpropionic acids, can be synthesized from these key intermediates.

(39) Davis, F. A.; Ray, J. K.; Kasperowicz, S.; Preslawski, R. M.; Durst, H. D. *J. Org. Chem.* **1992**, *57*, 2594.

Experimental Section

For general methods and details of experimental procedures for items listed in the tables see the Supporting Information. Only preparatively useful typical procedures, and synthesis and characterization of key compounds are described below.

Ni-Catalyzed Hydrovinylation Using 1,3-Bis(Diphenylphosphino)propane (dppp) Ligand (with Added Silver Salt). Typical Run for Reactions Using Chelated Phosphines (Figure 2 A−D) and Those Shown in Entries 1−8, Table 1. This is a typical procedure for all hydrovinylation reactions with added silver salts when a chelated ligand was used. To [(allyl)NiBr]$_2$ (3.4 mg, 9.5 μmol; 1.0 mol % Ni) in CH_2Cl_2 (0.5 mL) was added dppp (7.8 mg, 19 μmol) in CH_2Cl_2 (1.5 mL) at 25 °C. The mixture was cooled at −30 °C and it was transferred into AgOTf (5.2 mg, 20 μmol) in CH_2Cl_2 (2 mL), which was also precooled at −30 °C. The mixture was stirred for 2 h at 25 °C. The resulting suspension was filtered through a plug of Celite in a disposable pipet. The precipitate was rinsed with CH_2Cl_2 (1 mL). The filtrate was collected in a Schlenk flask, and it was taken out of the drybox. The mixture was cooled at −78 °C, and N_2-evacuation and ethlene-purge were repeated several times, carefully avoiding oxygen. Under an ethylene atmosphere (∼1 atm), styrene (0.230 mL, 2.01 mmol) was added drop by drop at −78 °C. The reaction mixture was slowly warmed to 25 °C in 12 h, and it was stirred for an additional 12 h at 25 °C. GC analysis indicated no reaction.

Preparative Runs Using Triphenylphosphine and AgOTf (Procedure i, Table 2). The following is a typical procedure for the Ni-catalyzed hydrovinylation reactions. To a red solution of 0.0035 equiv of [Ni(allyl)Br]$_2$ in dichlo-

romethane (1.5 mL) was added a solution of 0.0070 equiv of triphenylphosphine in dichloromethane (1.5 mL) in a nitrogen-filled drybox. Then, the resulting yellow solution was added to a suspension of 0.0080 equiv of silver triflate in dichloromethane (2 mL). After 1.5 h of stirring at room temperature, the brown suspension was filtered through a short pad of Celite into a Schlenk flask, removed from the drybox, and cooled to −55 °C. Oxygen-free ethylene (~1 atm) was then introduced into the yellow catalyst solution, and 1.0 equiv of a hydrovinylation substrate was added dropwise through a rubber septum with a syringe. The resulting reaction mixture was stirred for 2 h at −55 °C under an ethylene atmosphere (~1 atm) and was then quenched with half-saturated aqueous ammonium chloride solution (5 mL). The product was extracted with diethyl ether or dichloromethane (50 mL). The organic phase was dried over magnesium sulfate and analyzed by GC to determine the conversion of the substrate. The solution was concentrated under reduced pressure to isolate the corresponding hydrovinylation product. The isomeric purity was determined by NMR and further confirmed by gas chromatographic analysis, where the limits of detection were established as >0.2%.

The absolute configuration of (*S*)-3-phenyl-1-butene was determined by GC analysis using a 50 m Lipodex C capillary column [conditions: 1.5 mL helium/min, 35 °C (50 min), 0.1 °C/min (60 min), 41 °C (30 min); retention times: *R*-isomer 95.8 min, *S*-isomer 97.2 min]. The configurations were confirmed by measurement of optical rotation measurements.[37]

Hydrovinylation of 3-Bromostyrene. 2-(3-Bromophenyl)-1-butene. To a solution of allylnickel bromide (2.2 mg, 0.0061 mmol) in CH_2Cl_2 (1.0 mL) was added a solution of triphenylphosphine (3.2 mg, 0.0122 mmol) in CH_2Cl_2 (2.0 mL). The resulting orange solution was added to a suspension of silver triflate (3.8 mg, 0.015 mmol) in CH_2Cl_2 (1.0 mL) and the resulting mixture was stirred at room temperature for 1.5 h. The mixture was filtered through Celite to get a clear yellow solution that was subsequently cooled to −52 °C. Ethylene was introduced to the reaction followed by addition of 3-bromostyrene (148 mg, 0.86 mmol) in 1 mL CH_2Cl_2. The reaction was stirred at −52 °C for 3 h and was quenched by adding saturated NH_4Cl aqueous solution (5 mL). The mixture was extracted twice with ether. Gas chromatographic analysis showed >99% conversion and >99% selectivity for the 3-arylbutene. The dried organic layer was evaporated to afford the crude product (170 mg, 99%, 99% pure by GC, >95% pure by NMR): ^{1}H NMR (400 MHz, $CDCl_3$) 1.35 (d, J = 7.0, 3 H), 3.45 (q, J = 6.8, 1 H), 5.03−5.13 (m, 2 H), 5.93−6.08 (m, 1 H), 7.10−7.21 (m, 2 H), 7.31−7.42 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 20.8, 43.1, 114.0, 112.7, 126.2, 129.4, 130.2, 130.6, 142.6, 148.2.

Heterodimerization of Styrene and Propene. To a solution of [(allyl)NiBr]$_2$ (10.8 mg, 30.1 μmol) in 1 mL of CH_2Cl_2 under nitrogen at room temperature was added a solution of triphenylphosphine (15.8 mg, 60.2 μmol) in 4 mL of CH_2Cl_2. The resulting brown solution was added to a mixture of AgOTf (21.6 mg, 84.1 μmol) in 5 mL of CH_2Cl_2. After stirring for 1.5 h at room temperature, the mixture was filtered through a small plug of Celite, and the precipitate was rinsed with 5 mL of CH_2Cl_2. The filtrate was collected in a Schlenk flask and was taken out of the drybox. The catalyst solution was cooled to −20 °C. Under one atmosphere of propene, 0.23 mL (2.00 mmol) of styrene was added dropwise to the catalyst solution. After stirring at −20 °C for 35 min, the mixture was quenched with saturated aqueous NH_4Cl solution and extracted three times with 10 mL portions of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash chromatograghy on silica gel, eluting with hexanes to give an inseparable mixture of alkenes **17** and **18** as a clear oil (275 mg, 94%). Alkene **17**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.35 (d, J = 7.0 Hz, 3 H), 1.66−1.71 (m, 3 H), 3.35−3.49 (m, 1 H), 5.41−5.70 (m, 2 H), 7.16−7.37 (m, 5 H); EI MS m/z (relative intensity) 146 (M^+, 7), 105 (100); HRMS calcd for $C_{11}H_{14}$ 146.1096, found 146.1106. Alkene **18**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.39 (d, J = 7.1 Hz, 3 H), 1.61 (s, 3 H), 3.35−3.49 (m, 1 H), 4.86 (s, 1 H), 4.87 (s, 1 H), 7.16−7.37 (m, 5 H); EI MS m/z (relative intensity) 146 (M^+, 7), 105 (100); HRMS calcd for $C_{11}H_{14}$ 146.1096, found 146.1106. Ratio of **17** to **18**, 4.2:1.0. Ratio of (*E*)- to (*Z*)-phenyl-2-pentene by GC, 8:1; by NMR, 7.3:1.

Attempted Cross-Dimerization of Ethylene with 6-*tert*-Butyldimethylsiloxy-1-hexene, a Typical Terminal Olefin (Eq 18). To a solution of [(allyl)NiBr]$_2$ (5.2 mg, 14.4 μmol) in 1 mL of CH_2Cl_2 under nitrogen at room temperature was added a solution of triphenylphosphine (7.6 mg, 28.8 μmol) in 1 mL of CH_2Cl_2. The resulting brown solution was added to a mixture of AgOTf (10.3 mg, 40.0 μmol) in 1 mL of CH_2Cl_2. After stirring for 1.5 h at room temperature, the mixture was filtered through a small plug of Celite, and the precipitate was rinsed with 2 mL of CH_2Cl_2. The filtrate was collected in a Schlenk flask, and was taken out of the drybox. The catalyst solution was cooled to −55 °C. Under one atmosphere of ethylene, 0.428 g (2.00 mmol) of 6-*tert*-butyldimethylsiloxy-1-hexene was added dropwise to the catalyst solution. After stirring at −55 °C for 4 h, the mixture was quenched with saturated aqueous NH_4Cl solution and extracted three times with 10 mL portions of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was analyzed by GC, which indicated that two olefins were produced in a ratio of 3.5:1.0 (*E:Z*) with no starting material left. The crude product was purified by flash chromatograghy on silica gel, eluting with hexanes/ethyl acetate (98:2), to give the product as a clear oil (406 mg, 95%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.05 (s, 6 H), 0.90 (s, 9 H), 1.54−1.67 (m, 5 H), 1.97−2.10 (m, 2 H), 3.57−3.65 (m, 2 H), 5.40−5.46 (m, 2 H).

Single-Component Catalysts for Hydrovinylation (Scheme 4). Allyl 2-Diphenylphosphinobenzoate (40). To a mixture of 2-diphenylphosphinobenzoic acid (205 mg, 0.67 mmol), K_2CO_3 (185 mg, 1.33 mmol), and Bu_4NCl (8.4 mg, 0.003 mmol) was added THF (3 mL). After stirring at room temperature for 5 h, a solution of allyl bromide in THF (1.0 mL) was added, and the resulting mixture was stirred for 4 days in glovebox. The reaction was quenched by degassed, saturated NH_4Cl aqueous solution and extracted with ether three times. The dried organic layer was evaporated and chromatographed to get the desired product (170 mg, 74%): ^{1}H NMR (250 MHz, $CDCl_3$) 4.91 (d, 2 H), 5.35 (d, 1 H), 5.45 (d, 1 H), 5.98−6.15 (m, 1 H), 7.32−7.45 (m, 12 H), 8.04 (d, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 65.8, 118.5, 128.9, 128.9, 129.4, 129.5, 129.6, 130.3, 132.4, 133.3, 133.5, 134.1, 134.3, 136.3, 136.5, 144.3, 144.5, 166.2; ^{31}P NMR (162 MHz, $CDCl_3$) −3.71 (s).

Hydrovinylation (Eq 22, Method A) Using Allyl 2-Diphenylphosphinobenzoic Acid (40) as a Ligand Precursor (Scheme 4). To a solution of Ni(COD)$_2$ (5.4 mg, 0.020 mmol) in toluene (1.0 mL) at −30 °C was added a solution of the allyl ester **40** (7.1 mg, 0.020 mmol) in toluene (1.5 mL). The resulting mixture was stirred for 1 h at room temperature and was concentrated to dryness over 2 h to get a yellow residue. To the residue was added toluene (2.0 mL) and tris(pentafluorophenyl)borane (10.2 mg, 0.020 mmol) solution in toluene (1.0 mL). The resulting mixture was stirred for 15 min as it became a homogeneous solution. The solvent was evaporated in vacuo, and the residue was dissolved in CH_2Cl_2 (3.0 mL). The resulting solution was filtered through a pad of Celite and washed with CH_2Cl_2 (2.0 mL). The filtrate was cooled to −32 °C and was placed under ethylene atmosphere in a Schlenk flask. Into this flask was added styrene (0.15 mL, 1.3 mmol) dropwise. The reaction mixture was stirred for 1 h and then quenched by adding aqueous $NaHCO_3$ solution. The product was extracted with ether. Gas chromatographic analysis showed >99% conversion with 88% of the desired product.

Hydrovinylation (Eq 22, Method B) Using the Potassium Salt of 2-Diphenylphosphinobenzoic Acid (41) as a Ligand Precursor (Scheme 4). To a solution of 2-diphenylphosphinobenzoic acid (4.6 mg, 0.015 mmol) in CH_2Cl_2 (1.0

mL) was added a suspension of KH (0.8 mg, 0.020 mmol) in CH_2Cl_2 (1.0 mL). The resulting mixture was stirred for 10 min at room temperature before it was filtered through Celite. To the filtrate was added a solution of allylnickel bromide (2.7 mg, 0.0075 mmol) in CH_2Cl_2 (1.5 mL). The resulting solution was stirred at room temperature for 1.5 h and was then filtered through Celite. To the filtrate was added a solution of tris(pentafluorophenyl)borane (8.4 mg, 0.016 mmol) in CH_2Cl_2 (1.5 mL). The resulting solution was stirred for 5 min before it was taken out of the drybox and cooled to −30 °C. The flask was connected to a ballon containing ethylene, and to the catalyst solution was added styrene (0.13 mL, 1.1 mmol) in a dropwise fashion. The reaction was stirred for 110 min before it was quenched by adding aqueous $NaHCO_3$. The product was extracted with ether. Gas chromatographic analysis showed 99% conversion with 97% selectivity. The dried organic layer was carefully evaporated to get the crude product (143 mg, 97% yield).

Asymmetric Hydrovinylation of Styrene Using 29 and AgOTf (Eq 19). In a drybox, to $[(allyl)NiBr]_2$ (2.6 mg, 0.0072 mmol) in CH_2Cl_2 (0.5 mL) was added (*R*)-MOP-OMe (**29**, 7.3 mg, 0.016 mmol) in CH_2Cl_2 (1.5 mL) at 25 °C. The brown solution was transferred into AgOTf (5.3 mg, 0.021 mmol) in 2 mL of CH_2Cl_2 at 25 °C. The mixture was stirred for 1.5 h at 25 °C. The resulting suspension was filtered through Celite in a disposable pipet, and the precipitate was rinsed with CH_2Cl_2 (1 mL). The filtrate was collected in a Schlenk flask, and it was taken out of the drybox. The catalyst solution was cooled to −54 °C and the nitrogen in the Schlenk flask was evacuated and replaced by ethylene. Under an ethylene atmosphere was added styrene (0.230 mL, 2.01 mmol). After 2 h, the reaction was quenched with aqueous NH_4Cl solution. The crude product was analyzed by GC and ^1H NMR. The crude mixture contained the desired product (12%) and styrene (72%) by ^1H NMR. The enantiomeric excess of the product was 33% ee. The ee was determined by HPLC analysis using a CHIRALCEL OB column (Daicel) (hexane/*i*-PrOH = 95:5, 0.5 mL/min), after the mixture was converted to the corresponding acetate of the alcohols obtained by a hydroboration/oxidation sequence as described; see below.

(*R*)- and (*S*)-3-Phenyl-1-butanol and 3-Phenyl-1-butyl Acetate (for HPLC Analysis). To 9-BBN (0.5M, 3 mL, 1.5 mmol) in THF (2 mL) was added the 3-phenyl-1-butene (133 mg, 1.01 mmol) at 0 °C. The mixture was stirred for 15 min at 0 °C and 16 h at 25 °C. After the mixture was cooled at 0 °C, 2 N NaOH (3 mL, 6 mmol) and 30% H_2O_2 (1 mL) were added to this mixture. Stirring was continued for 16 h at 25 °C. The mixture was diluted with aqueous NH_4Cl, and the organic compounds were extracted with ether. The organic layer was dried over $MgSO_4$, and the crude material was purified by flash column chromatography to afford 2-phenylbutan-4-ol (124 mg, 82% yield); TLC R_f = 0.33 (hexane/EtOAc = 3:1); ^1H NMR (250 MHz) δ 7.15−7.35 (m, 5H), 3.57 (m, 2H), 2.89 (sextet, J = 7.1 Hz, 1H), 1.86 (q, J = 6.9, 2H), 1.28 (d, J = 6.9 Hz, 3H).

To the alcohol (13 mg, 0.087 mmol) dissolved in 2 mL of CH_2Cl_2 were added Ac_2O (4 drops by pipet), Et_3N (50 μL), and DMAP (catalytic amount) at 25 °C. The mixture was stirred for 2 h. Then aqueous NH_4Cl was added to this mixture. The organic compounds were extracted with ether. The crude compound was purified by column chromatography to afford the acetylated product: TLC R_f = 0.69 (hexane/EtOAc = 3:1); ^1H NMR (250 MHz) 7.05−7.25 (m, 5 H), 3.91 (dt, J = 11.1, 6.7 Hz, 1 H), 3.85 (dt, J = 11.2, 7.2 Hz, 2 H), 2.74 (sextet, J = 7.1 Hz, 1 H), 1.90 (s, 3 H), 1.82 (q, J = 7.0 Hz, 1 H), 1.19 (d, J = 7.0 Hz, 3 H). This product was analyzed by HPLC on a Chriracel OB column using 95:5 hexane/*i*-PrOH as solvent (0.0.5 mL/min).

Hydrovinylation of MVN with MOP(OMe) in the Presence of AgOTf (Eq 19). To $[(allyl)NiBr]_2$ (2.6 mg, 7.2 μmol; 0.7 mol % Ni) in CH_2Cl_2 (0.5 mL) was added (*R*)-MOP (7.3 mg, 16 μmol) in CH_2Cl_2 (1.5 mL) at 25 °C. The brown solution was transferred into AgOTf (4.3 mg, 17 μmol) in CH_2Cl_2 (2 mL) at 25 °C. The mixture was stirred for 1.5 h at 25 °C. The resulting mixture was filtered on Celite purged with glasswool in a pipet, and the precipitate was rinsed with CH_2Cl_2 (1 mL). The filtrate was collected in a Schlenk flask, and the flask was taken out of the drybox. The catalyst solution was cooled to −50 °C and the flask was connected to the ethylene line (∼1 atm). 6-Methoxy-2-vinylnaphthalene (0.368 g, 2.00 mmol) in CH_2Cl_2 (4 mL) was added to this mixture drop by drop. Soon the reaction mixture turned red. After 3 h at −50 °C, the reaction was quenched with aqueous NH_4Cl. The crude product was purified by flash column chromatography to afford a mixture (351 mg) of the desired product (24% yield) and MVN (68% yield). The enantiomeric excess of the product (58%) was determined by HPLC using Chiracel OJ column, where baseline separation of the two isomers was observed (see Supporting Information for a chromatogram).

Asymmetric Hydrovinylation of Styrene Using MOP-OMe Ligand and BARF as a Counteranion (Eq 21). To $[(allyl)NiBr]_2$ (2.5 mg, 7.0 μmol; 0.7 mol % Ni) in CH_2Cl_2 (0.5 mL) was added (*R*)-MOP-OMe (7.1 mg, 15 μmol) in CH_2Cl_2 (1.5 mL) at 25 °C. The brown solution was transferred into $NaBAr_4$ (20.0 mg, 23 μmol) in CH_2Cl_2 (2 mL) at 25 °C. The mixture was stirred for 1.5 h at 25 °C. The resulting mixture was filtered through Celite in a glass pipet, and the precipitate was rinsed with CH_2Cl_2 (1 mL). The filtrate was collected in a Schlenk flask and taken out of the drybox. The catalyst solution was cooled at −53 °C. N_2 in the Schlenk flask was evacuated and ethylene was purged at −53 °C, and under an ethylene atmosphere (∼1 atm), styrene (0.230 mL, 2.01 mmol) was added to this mixture drop by drop. After 2 h, the reaction was quenched with aqueous NH_4Cl. The crude product was analyzed by GC and ^1H NMR. The crude mixture contained the desired product (80%) and styrene (19%) by ^{1}NMR. The enantiomeric excess of the product was 25% ee by HPLC analysis.

Asymmetric Hydrovinylation of 6-Methoxy-2-vinylnaphthalene (MVN) Using 31 and $[3,5\text{-}(CF_3)_2C_6H_3]_4B]^-$ Counteranion: Synthesis of 3-(6-Methoxy-2-naphthyl)-1-butene (Eq 20 and Table 5). To a solution of $[(allyl)NiBr]_2$ (2.6 mg, 0.0072 mmol) in CH_2Cl_2 (0.5 mL) under nitrogen at room temperature was added a solution of (*R*)-MOP-OBn (31, 7.8 mg, 0.014 mmol) in CH_2Cl_2 (1.5 mL). The resulting brown solution was added to a solution of NaBARF (15.3 mg, 0.017 mmol) in CH_2Cl_2 (2 mL). After stirring for 1.5 h at room temperature, the mixture was filtered through a small plug of Celite, and the precipitate was rinsed with CH_2Cl_2 (1 mL). The filtrate was collected in a Schlenk flask and was taken out of the drybox. The catalyst solution was cooled to −55 °C. Under one atmosphere of ethylene, a solution of 2-methoxy-6-vinylnaphthalene (0.184 g, 1.00 mmol) in CH_2Cl_2 (1 mL) was added dropwise to the catalyst solution. After stirring at −55 °C for 2 h, the mixture was quenched with saturated aqueous NH_4Cl solution and extracted three times with 10 mL portions of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was analyzed by GC, which indicated that the alkene product was produced in >99% yield and selectivity with no starting material left. The crude product was purified by flash chromatograghy on silica gel, and eluting with hexanes/ethyl acetate (19:1) gave a clear oil (206 mg, 97%): ^1H NMR (250 MHz, $CDCl_3$) 7.10−7.75 (m, 6 H), 6.09 (ddd, J = 6.0, 10.0, 17.0 Hz, 1 H), 5.09 (dt, J = 1, 17.0 Hz, 1 H), 5.07 (dt, J = 1.0, 10.0 Hz, 1 H), 3.92 (s, 3 H), 3.61 (m, 1 H), 1.45 (d, J = 7.0 Hz, 3 H). The enantiomeric excess (ee) of product alkene was determined as 73% (*S*) by HPLC on Chiracel OJ column (hexane/*i*-PrOH = 95:5, 0.5 mL/min).

The same reaction carried out at −70 °C for 7 h gave an yield of 93% and ee of 80%.

Hydrovinylation of MVN using ligands **30** and **32**− **38** as well as those shown in Figure 2 **(E**−**H)** were carried out at

−55 °C using the above-described procedure and the results are shown in Table 5.

The same experiments with **36** at temperatures in the range of −55 to 25 °C did not yield any products.

Asymmetric Hydrovinylation of Styrene Using 34 and 37. Asymmetric hydrovinylation of styrene was examined using ligands **37** (89% yield and 27% ee) and **34** (17% yield and 0% ee) under the same conditions.

Solvent Effects on Ni-Catalyzed Asymmetric Hydrovinylation (Table 6). The same procedure as described in the previous experiment was used in examining the solvent effects shown in Table 6.

Procedure for the Use of [(Allyl)Pd(X)]$_2$ (Table 8). The following is a typical procedure for the Pd(II)-catalyzed asymmetric hydrovinylation reactions. A solution of 0.030 equiv of the phosphorus ligand (**L**) in dichloromethane (1.5 mL) was added to a solution of 0.015 equiv of [Pd(allyl)Cl]$_2$ or [Pd(allyl)I]$_2$ in dichloromethane (1.5 mL). The resulting yellow solution was added to a suspension of 0.031 equiv of NaBARF in dichloromethane (2 mL), stirred for 1.5 h at room temperature, filtered through a short pad of Celite into a Schlenk flask, and then taken out of the drybox. Oxygen-free ethylene (∼1 atm) was introduced into the yellow catalyst solution at 0 to −10 °C, and 1.0 equiv of styrene was added dropwise via a syringe. The resulting reaction mixture was stirred for 2 h at 0 to −10 °C under an ethylene atmosphere (∼1 atm), quenched with half-saturated aqueous ammonium chloride (5 mL), and extracted with diethyl ether (50 mL). The results are shown in Table 8.

Synthesis of Ligands. Preparation of Phenol 57. To a mixture of 220 mg (0.468 mmol) of **54**[38] and 2.6 mL (18.7 mmol) of Et_3N in 10 mL of toluene at 0 °C under nitrogen was added 0.47 mL (4.68 mmol) of $HSiCl_3$. After stirring at 0 °C for 10 min, the mixture was heated and refluxed at 120 °C for 23 h. After cooling to room temperature, the mixture was diluted with ether, quenched with 20 drops of saturated aqueous $NaHCO_3$ solution, and dried over $MgSO_4$. The resulting mixture was filtered through a small plug of Celite and the filtrate was concentrated in vacuo to produce **57** as a white solid (179 mg, 84%): ^{1}H NMR (250 MHz, $CDCl_3$) 6.70−7.98 (m, 22 H); ^{31}P NMR (101 MHz, $CDCl_3$) −14.4.

Preparation of 32. To a solution of 120 mg (0.689 mmol) of DEAD, 84 mg (0.689 mmol) of (*S*)-1-phenylethanol, and 181 mg (0.689 mmol) of PPh_3 in 5 mL of THF at 0 °C under nitrogen was added a solution of 108 mg (0.230 mmol) of phenol **54** in 2 mL of THF. The mixture was allowed to warm to room temperature and stirred for 20 h. The mixture was concentrated and the residue was purified by flash chromatograghy on silica gel, eluting with hexanes/ethyl acetate (1:1), to produce **55** as a white solid (93 mg, 71%): ^{1}H NMR (250 MHz, $CDCl_3$) 1.40 (d, J = 6.4 Hz, 3 H), 5.28 (q, J = 6.4 Hz, 1 H), 6.81−8.10 (m, 27 H); ^{31}P NMR (101 MHz, $CDCl_3$) 27.8.

To a mixture of 80 mg (0.139 mmol) of **55** and 0.8 mL (5.57 mmol) of Et_3N in 5 mL of toluene at 0 °C under nitrogen was added 0.14 mL (1.39 mmol) of $HSiCl_3$. After stirring at 0 °C for 10 min, the mixture was heated and refluxed at 120 °C for 23 h. After cooling to room temperature, the mixture was diluted with ether, quenched with 5 drops of saturated aqueous $NaHCO_3$ solution, and dried over $MgSO_4$. The resulting mixture was filtered through a small plug of Celite, the filtrate was concentrated, and residue was purified by flash chromatography on silica gel, eluting with hexanes/ethyl acetate (98:2), to produce **32** as a white solid (63 mg, 81%): ^{1}H NMR (250 MHz, $CDCl_3$) 1.16 (d, J = 6.4 Hz, 3 H), 5.34 (q, J = 6.4 Hz, 1 H), 6.76−7.98 (m, 27 H); ^{31}P NMR (101 MHz, $CDCl_3$) −14.2; HRMS (EI) calcd for $C_{40}H_{31}OP$ 558.2113, found 558.2118.

Ligand **33** was prepared by a similar procedure starting with (*R*)-1-phenylethanol and **54**.

Preparation of Ligand 36. To a solution of 99 mg (0.159 mmol) of (*R*)-BINAP in 5 mL of CH_2Cl_2 at room temperature under nitrogen was added 42 mg (0.161 mmol) of *N*-(phenylsulfonyl)-3-phenyloxaziridine.[39] The mixture was stirred at room temperature for 20 h and the concentrated residue was purified by flash chromatograghy on silica gel, eluting with hexanes/ethyl acetate (3:1), to produce **36** as a white solid (21 mg, 21%): ^{1}H NMR (250 MHz, $CDCl_3$) 6.62−7.96 (m, aromatic); ^{31}P NMR (101 MHz, $CDCl_3$) −15.8, 27.6.

Preparation of Phenol 62. To a solution of 292 mg (0.543 mmol) of **61**[38] in 2 mL of $SOCl_2$ under nitrogen was added 0.1 mL of DMF. The mixture was refluxed at 90 °C for 16 h. After cooling to room temperature, the mixture was concentrated in vacuo. The residue was used for the next step without further purification.

To a solution of the above residue in 2 mL of ether under nitrogen was added 5 mL (3.75 mmol) of a 0.75 M solution of 3,5-bis(trifluoromethyl)phenylmagnesium bromide in ether. The mixture was stirred at room temperature for 5 h and refluxed at 45 °C for 12 h. After cooling to room temperature, the mixture was quenched with 2 N aqueous HCl solution (10 mL). The aqueous layer was extracted three times with 10 mL portions of ether. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatograghy on silica gel, eluting with hexanes/ethyl acetate (3:1), to give phenol **62** as a white solid (100 mg, 25% from **61**). ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.85−8.38 (m, 18 H); ^{31}P NMR (101 MHz, $CDCl_3$) δ 23.5.

Preparation of Ether 63. To a solution of 100 mg (0.135 mmol) of **62** in 5 mL of acetone under nitrogen was added 94 mg (0.674 mmol) of K_2CO_3 and 0.086 mL (1.348 mmol) of MeI. The mixture was heated to reflux for 24 h. After cooling to room temperature, the mixture was filtered through a small plug of Celite and washed with 10 mL of CH_2Cl_2. The filtrate was concentrated in vacuo. The residue was purified by flash chromatograghy on silica gel, eluting with hexanes/ethyl acetate (6:1), to produce **63** as a white solid (87.6 mg, 86%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.75 (s, 3 H), 6.76−8.14 (m, 18 H); ^{31}P NMR (101 MHz, $CDCl_3$) δ 22.9.

Preparation of MOP Ligand 38. To a mixture of 47 mg (0.0622 mmol) of **63** and 0.35 mL (2.49 mmol) of Et_3N in 3 mL of toluene at 0 °C under nitrogen was added 0.063 mL (0.622 mmol) of $HSiCl_3$. After stirring at 0 °C for 10 min, the mixture was heated and refluxed at 120 °C for 17 h. After cooling to room temperature, the mixture was diluted with ether, quenched with 5 drops of saturated aqueous $NaHCO_3$ solution, and dried over $MgSO_4$. The resulting mixture was filtered through a small plug of Celite and the filtrate was concentrated in vacuo. The residue was purified by flash chromatograghy on silica gel, eluting with hexanes/ethyl acetate (9:1), to produce **38** (43.3 mg, 94%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.63 (s, 3 H), 6.75−8.08 (m, 18 H); ^{31}P NMR (101 MHz, $CDCl_3$) δ −11.5; FABMS m/z (relative intensity) 741 (M^++H, 52).

Acknowledgment. Financial assistance by the US National Science Foundation (CHE-0079948, CHE-0308378) and the Petroleum Research Fund administered by the ACS is also gratefully acknowledged.

Supporting Information Available: Full experimental details of entries listed in various tables and equations, synthesis and characterization of ligands not listed in the Experimental Section. This material is available free of charge via the Internet at http://pubs.acs.org.

JO035171B