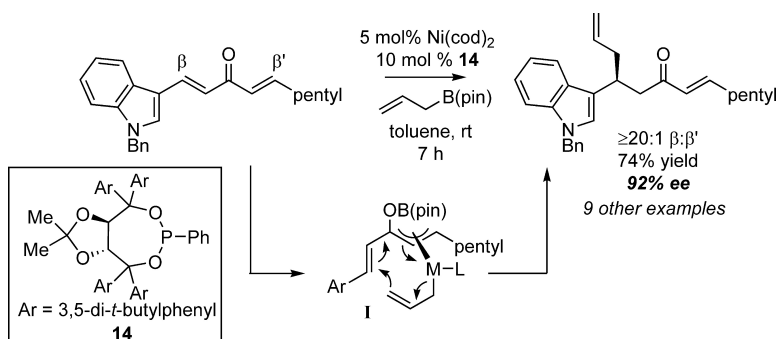


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## Asymmetric Ni-Catalyzed Conjugate Allylation of Activated Enones

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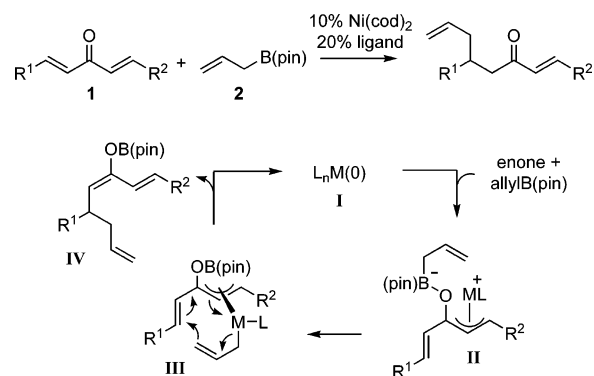
**Abstract:** The nickel-catalyzed enantioselective addition of allylboronic acid pinacol ester, allylB(pin), is described. This reaction is highly effective with dialkylidene ketones and favors the allylation of the benzylidene site in nonsymmetric substrates. The reaction appears to proceed by conversion of the dialkylidene ketone substrate to an unsaturated  $\pi$ -allyl complex (I), followed by reductive elimination. Enantioselectivities range from 91 to 94% ee for a range of substrates when chiral ligand **14** is employed.

## 1. Introduction

Conjugate addition of allyl groups to activated alkenes is an important method for the construction of organic compounds. Not only does this transformation establish a new carbon–carbon bond and result in the creation of a new stereocenter, it also provides a malleable product that contains carbonyl and olefin functional groups. The conjugate addition of allyl nucleophiles is a well-known process that can be accomplished with silicon,<sup>1</sup> tin,<sup>2</sup> and copper reagents.<sup>3</sup> More recently, the synthetic utility of allyltantalum,<sup>4</sup> allylbarium,<sup>5</sup> and allylindium<sup>6</sup> reagents in conjugate allylation has been recognized. However, asymmetric variants of these processes have not been achieved. For control of absolute facial selectivity, chiral auxiliaries are required, and this approach has been examined with allyltributylstannane,<sup>7</sup> allyltrimethylsilane,<sup>8</sup> and allyl Grignard reagents,<sup>9</sup> in conjunction with stoichiometric amounts of copper or a Lewis acid. Significantly, despite intense research focused toward enantioselective metal-catalyzed conjugate addition processes,<sup>10</sup> a catalytic asymmetric conjugate addition of allyl nucleophiles to  $\alpha,\beta$ -unsaturated carbonyl electrophiles has yet to emerge.

In a previous communication, we reported that Ni and Pd complexes can catalyze the addition of allylboronic acid pinacol

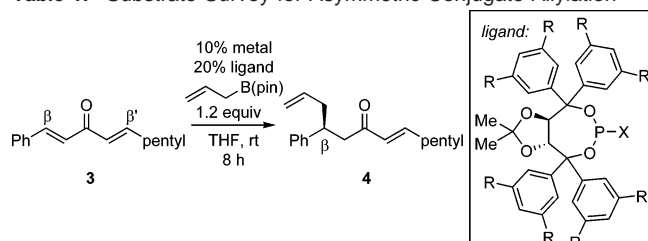
## Scheme 1



ester (allylB(pin), **2**, Scheme 1) to dialkylidene ketones (i.e., **1**, Scheme 1).<sup>11</sup> While allylboronates typically undergo 1,2-allylation reactions with carbonyl electrophiles, in the presence of a transition metal catalyst, dialkylidene ketones participate in 1,4-conjugate addition reactions. Preliminary studies suggest that this reaction proceeds by a mechanism involving oxidative addition of a Lewis acid activated enone to the transition metal catalyst (to provide **II**, Scheme 1),<sup>12</sup> followed by transmetalation (**II**→**III**) and 3,3' reductive elimination<sup>13,14</sup> from unsaturated  $\pi$ -allyl complex **III**; the latter elementary process was calculated to proceed with an extremely small activation barrier (for M = Pd,  $\Delta G^\ddagger = 1.52$  kcal/mol). These preliminary studies also documented an example of asymmetric catalysis with dibenzylidene acetone as substrate and a phosphoramidite-derived Pd complex as catalyst. Herein, we describe an effective Ni(0) catalyst system that allows enantioselective and chemoselective

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**Table 1.** Substrate Survey for Asymmetric Conjugate Allylation


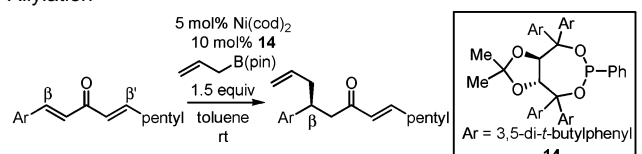
entry	metal	ligand	R	X	$\beta$ : $\beta'$ <sup>a</sup>	% yield <sup>b</sup>	% ee <sup>c</sup>
1	Ni(cod) <sub>2</sub>	PCy <sub>3</sub>			1:7.5	82	
2 <sup>d</sup>	Pd <sub>2</sub> (dba) <sub>3</sub>	<b>5</b>	<i>t</i> -Bu	NMe <sub>2</sub>	1:1.6	74	33(96)
3	Ni(cod) <sub>2</sub>	<b>6</b>	H	NMe <sub>2</sub>	3.8:1	36	44(75)
4	Ni(cod) <sub>2</sub>	<b>7</b>	H	N(CH <sub>2</sub> ) <sub>4</sub>	4.3:1	31	14
5	Ni(cod) <sub>2</sub>	<b>8</b>	H	N(CH <sub>2</sub> ) <sub>5</sub>	2.2:1	57	-3
6	Ni(cod) <sub>2</sub>	<b>9</b>	Me	NMe <sub>2</sub>	>20:1	53	44
7	Ni(cod) <sub>2</sub>	<b>5</b>	<i>t</i> -Bu	NMe <sub>2</sub>	4.7:1	29	69
8	Ni(cod) <sub>2</sub>	<b>10</b>	<i>t</i> -Bu	N(CH <sub>2</sub> ) <sub>5</sub>	2.5:1	24	47
9	Ni(cod) <sub>2</sub>	<b>11</b>	<i>t</i> -Bu	OEt	16:1	62	-3
10	Ni(cod) <sub>2</sub>	<b>12</b>	H	Ph	3.6:1	49	28
11	Ni(cod) <sub>2</sub>	<b>13</b>	Me	Ph	>20:1	50	-15
<b>12</b>	<b>Ni(cod)<sub>2</sub></b>	<b>14</b>	<b><i>t</i>-Bu</b>	<b>Ph</b>	<b>20:1</b>	<b>69</b>	<b>88</b>

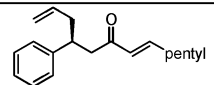
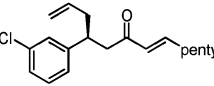
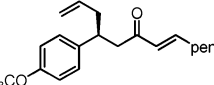
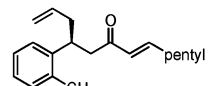
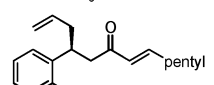
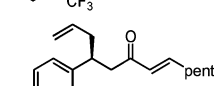
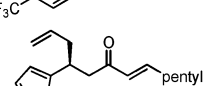
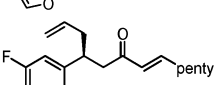
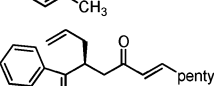
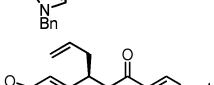
<sup>a</sup> Chemoselectivity determined by <sup>1</sup>H NMR. <sup>b</sup> Yield of conjugate addition product after silica gel chromatography. <sup>c</sup> Enantioselectivity of  $\beta$  isomer; number in parentheses is for the  $\beta'$  isomer. <sup>d</sup> 2.5 mol % of Pd<sub>2</sub>(dba)<sub>3</sub>, 6 mol % of ligand **5**, and reaction for 24 h.

conjugate allylation of *nonsymmetric* diallylidene ketones. Also described are a model for chemoselectivity and mechanistic aspects of this reaction process.

## 2. Results and Discussion

**2.1. Reaction Development and Substrate Scope.** With the goal of developing a general catalytic enantioselective conjugate allylation, a collection of chiral phosphorus ligands was surveyed in the conjugate allylation of nonsymmetric diallylidene ketone **3** (Table 1). TADDOL-derived phosphoramidites,<sup>15</sup> phosphonites, and phosphites were initially explored. For comparison purposes, the reaction with Ni(cod)<sub>2</sub> and PCy<sub>3</sub> is presented in entry 1; this catalyst favors allylation at the alkyldiene site. The catalyst derived from Pd<sub>2</sub>(dba)<sub>3</sub> and phosphoramidite **5**, an effective combination with dba as substrate, displayed low chemoselectivity with nonsymmetric substrate **3** (entry 2). Alternatively, moderate chemoselectivity was observed with Ni(cod)<sub>2</sub> and

**Table 2.** Scope of Ni-Catalyzed Enantioselective Conjugate Allylation


entry	product	time (h)	$\beta$ : $\beta'$ <sup>a</sup>	yield (%) <sup>b</sup>	% ee <sup>c</sup>
1		7	17:1	77	93
2		7	6.5:1	81	93
3		12	20:1	66	91
4		12	≥20:1	66	93
5		48	32:1	45	94
6		7	7.0:1	78	94
7		12	5.1:1	52	93
8		12	49:1	81	92
9		12	≥20:1	74	92
10		12	21:1	60	92

<sup>a</sup> Determined by GC or <sup>1</sup>H NMR analysis of the unpurified reaction mixture. <sup>b</sup> Isolated yield of purified material. Value is an average of two experiments. <sup>c</sup> Determined by chiral GC or SFC analysis.

phosphoramidite **5** (entry 7), an observation which stimulated further investigation of related ligands. While a variety of TADDOL-derived phosphoramidites and phosphites furnished moderate enantioselection and/or chemoselection, phosphonite ligand **14** (entry 12) provided a unique combination of high enantioselection and high chemoselectivity with nonsymmetric substrate **3**. Notably, the sense of chemoselectivity with all the heteroatom-derived phosphorus ligands, including **14**, was opposite to that observed with PCy<sub>3</sub> (entry 1). Thus, the present catalyst system provides a means for construction of benzylic hydrocarbon stereocenters through catalytic asymmetric conjugate allylation.

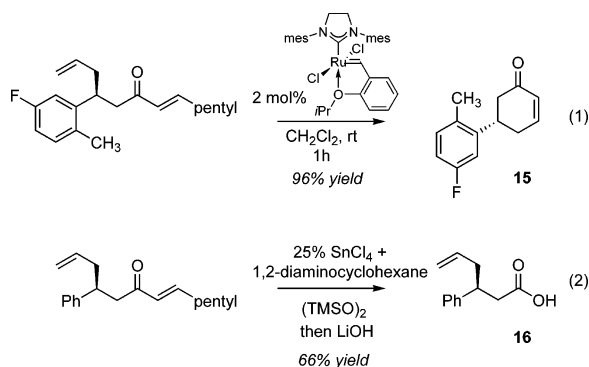
After further optimization of the reaction conditions (decreased catalyst loading, solvent optimization), an analysis of the substrate scope for the Ni-catalyzed asymmetric conjugate allylation was undertaken. As shown in Table 2, the reaction

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- (14) For Ni- and Pd-catalyzed conjugate additions that operate by oxidative addition/transmetalation/reductive elimination, as opposed to transmetalation/migratory insertion, see: (a) Refs 12c,e. (b) Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2007**, 1541.
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exhibits high enantioselection regardless of the nature of the arylidene group and generally favors chemoselective allylation at the arylidene site with  $\text{Ni}(\text{cod})_2$  and phosphonite **14**. Electron-deficient arenes were efficient in terms of reaction rate; however, chemoselectivity was lower for these substrates (entries 2 and 6). Electron-rich arenes reacted slower and therefore required longer reaction times; however, chemoselectivities were better for these substrates (entries 3, 9, and 10). Substitution at the *ortho* position of the substrate dramatically increased the chemoselectivity, but these substrates were allylated more slowly (entries 4, 5, and 8). In addition, substrates bearing functionalized aromatic groups common in natural products and drug targets were effective in the reaction (entries 9 and 10).

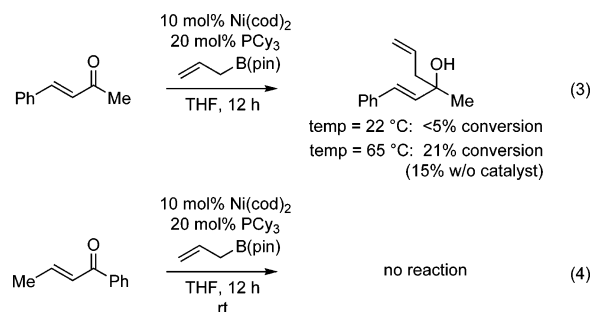
Manipulation and cleavage processes of the activating alkylidene auxiliary merit mention. As depicted in Scheme 2, the alkylidene unit provides a convenient handle for alkene metathesis,<sup>16</sup> and a ring-closing version was readily accomplished with the NHC-derived Hoveyda–Grubbs catalyst<sup>17</sup> to give cyclohexenone **15**. Alternatively, regioselective Baeyer–Villiger oxidation was accomplished by treatment of the conjugate allylation product with bis(trimethylsilyl)peroxide in the presence of Lewis acid.<sup>18</sup> This transformation selectively provided an intermediate enol ester which might be readily converted to a variety of functional groups including the derived carboxylic acid **16** as is shown.

### Scheme 2



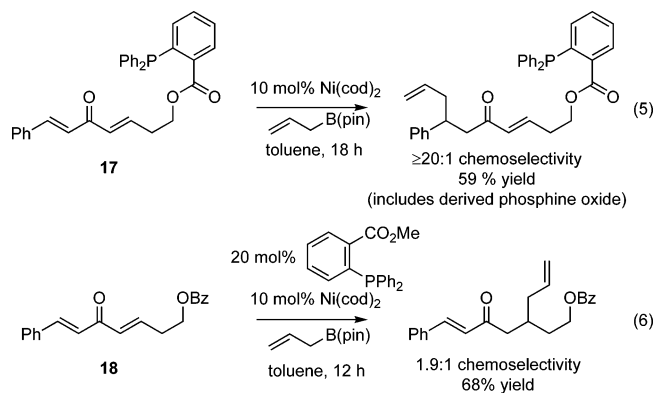
**2.2. Mechanistic Aspects. (a) Probe Substrates.** The nickel-catalyzed conjugate addition of allylB(pin) to enones requires alkylidene activation. As depicted in Scheme 3 (eq 3), there was <5% conversion when benzylidene acetone was used as the substrate in the reaction. Even when the reaction with benzylidene acetone was carried out at higher temperature, the 1,4-allylation product was not observed, the only product being that derived from 1,2-allylation of the ketone. Notably, the rate and chemoselectivity of the benzylidene acetone allylation reaction at high temperature were nearly identical in the presence or absence of catalyst, further suggesting the requirement for alkylidene activation of the catalytic reaction. Considering that the catalyst derived from  $\text{Ni}(\text{cod})_2$  and  $\text{PCy}_3$  favors allylation at the alkylidene site (Table 1, entry 1), the substrate in eq 4 was examined; again, no reaction occurred without benzylidene activation.

### Scheme 3



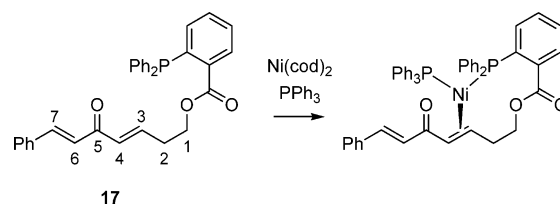
The enhanced reactivity of dialkylidene ketones relative to simple enones is consistent with the proposed requirement that the reaction proceed by 3,3' reductive elimination of an unsaturated Ni bis(allyl) complex (**III**, Scheme 1). As mentioned in the Introduction, DFT calculations are consistent with this conjecture. To experimentally substantiate the relevance of this elementary step, the experiments in eqs 5 and 6 (Scheme 4) were undertaken. When substrate **17**, possessing an internal phosphine ligand, was treated with allylB(pin) and 10 mol % of  $\text{Ni}(\text{cod})_2$ , the conjugate allylation product was isolated as a single constitutional isomer wherein allyl addition occurred distal to the phosphine directing group. The control experiment with substrate **18** (eq 6) highlights the significant enhancement in chemoselectivity that the tethered phosphine imparts on the catalytic allylation; in its absence a 1.9:1 mixture of constitutional isomers—favoring allylation proximal to the benzoate—was observed.

### Scheme 4



To verify whether the tethered phosphine in compound **17** directs the metal to the proximal or distal site in derived  $\pi$  complexes, the structure of a 1:1:1 mixture comprising **17**,  $\text{Ni}(\text{cod})_2$ , and  $\text{PPh}_3$  was examined (Scheme 5). While X-ray quality

### Scheme 5



crystals could not be obtained, NMR analysis of the mixture in solution was informative. Proton and carbon assignments were made by  $^1\text{H}$ ,  $^{13}\text{C}$ , COSY, NOESY, and HSQC spectroscopic

(16) *Handbook of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH: Weinheim, Germany, 2003.

(17) Garber, S. B.; Kingbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168.

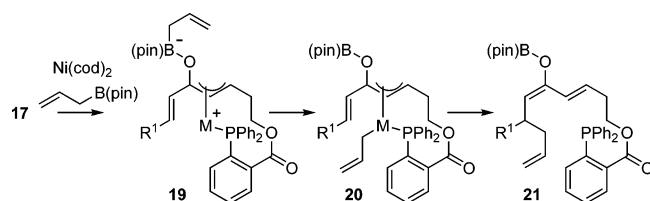
(18) Göttlich, R.; Yamakoshi, K.; Sasai, H.; Shibasaki, M. *Synlett* **1997**, 971.



analysis. Upon treatment with Ni(cod)<sub>2</sub> and PPh<sub>3</sub>, the hydrogens at C3 and C4 exhibit an upfield shift of  $\Delta\delta$  3.01 and 2.45 ppm, respectively. Likewise the carbon resonances for C3 and C4 move to higher field by  $\Delta\delta$  71.6 and 60.2 ppm. In contrast, the hydrogens at C6 and C7 exhibit less substantial perturbation ( $\Delta\delta$  1.01 and <0.05 ppm). Similarly, the carbon resonances for C6 and C7 are relatively unaffected, showing  $\Delta\delta$  0.6 and 1.8 ppm, respectively. In addition to its effect on the alkene hydrogens, the metal association affects the chemical shift of the hydrogens at C2 and C1. The proton resonance at C2 experiences a substantial upfield shift ( $\Delta\delta$  0.76 ppm), and the protons at C1 in the metal complex have clearly become diastereotopic, one moving 0.72 ppm downfield and the other 0.44 ppm upfield. Collectively, the spectroscopic changes observed in substrate **17**, upon addition of nickel and PPh<sub>3</sub>, are consistent with the Ni binding to the alkene adjacent to the directing group. Other spectroscopic features are also consistent with the formulation in Scheme 5; the <sup>31</sup>P NMR shows two doublet resonances at 41.21 and 28.59 ppm ( $J = 32$  Hz).

The propensity for the phosphine in **17** to direct Ni coordination to the adjacent alkene, combined with the chemoselectivity observed for the Ni-catalyzed allylation of **17**, is highly suggestive of a reaction that proceeds by the proposed 3,3' reductive elimination process. As shown in Scheme 6, it is tenable that, upon directed oxidative formation of  $\pi$ -allyl **19**, transmetalation occurs to give **20**. Consistent with the proposed low-energy barrier for 3,3' reductive elimination, **20** transfers the allyl group to the olefin that is distal to the phosphine directing group providing **21**.

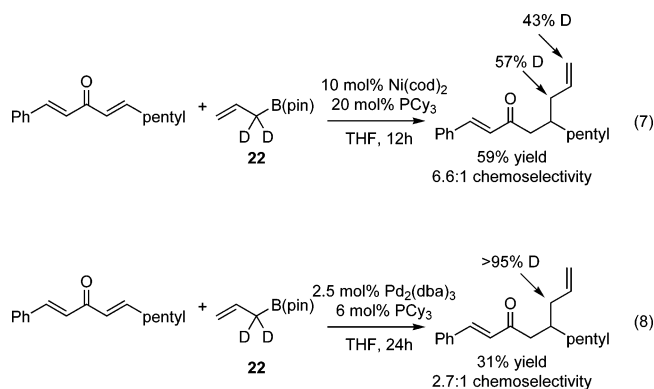
Scheme 6



Experiments undertaken with isotopically labeled boronate **22** were also revealing. As depicted in eqs 7 and 8 (Scheme 7), the isotope label in **22** was scrambled between the internal and terminal allyl sites when the reaction was carried out with Ni(cod)<sub>2</sub>/PCy<sub>3</sub> catalyst but was retained at the internal site when Pd<sub>2</sub>(dba)<sub>3</sub>/PCy<sub>3</sub> was employed. Considering that transmetalation of allyl groups is known to proceed by an S<sub>E'</sub>-type mechanism,<sup>19</sup> it stands to reason that, with Pd as catalyst, a rapid 3,3' reductive elimination leads to the product which is deuterated at the internal site (Scheme 8). The isotope scrambling observed with Ni catalysts can be ascribed to isomerization of the intermediate allyl complex **24**, perhaps through a structure such as **26** (Scheme 8).

**(b) Chemoselectivity.** As noted above, the hexylidene substituent activates the adjacent arylidene for conjugate allylation. Examination of other alkylidene groups revealed a correlation between alkylidene size and both stereo- and chemoselectivity. When the pentyl group of the alkylidene was

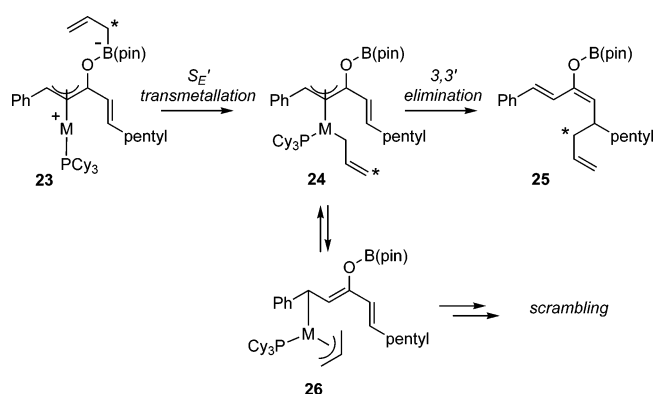
Scheme 7



\* note: **22** contaminated with 9% vinylB(pin)

replaced with a methyl group (Table 3, entry 1), the chemoselectivity for arylidene allylation increased (17:1  $\rightarrow$   $\geq$ 20:1); however, a corresponding decrease in reaction enantioselectivity was noted. When the pentyl group was replaced with a larger cyclohexyl substituent (entry 4), the opposite outcome was observed: chemoselectivity was diminished and the enantioselectivity was enhanced. This outcome is consistent with the above mechanistic hypothesis: enlarging the alkylidene substituent causes increased  $\pi$ -allyl formation at the arylidene site, which leads to more alkylidene allylation product. The same

Scheme 8



outcome was observed as the size of the arylidene substituent was enhanced: in the series 2-furyl, phenyl, *ortho*-tolyl, and *ortho*-trifluoromethylphenyl, the selectivity for arylidene allylation increased from 5.1:1 to 32:1 (Table 1, entries 5, 3, 6, and 7, respectively).

Along with a correlation between substrate steric properties and chemoselectivity, a rough correlation between ligand basicity and chemoselectivity was observed. As depicted in Table 4, the Lewis basic phosphine PCy<sub>3</sub> favors allylation of the alkylidene site of nonsymmetric substrate **3**. With achiral ligands, when the basicity of the ligand structure decreased, as measured by the CO stretching frequency of derived *trans*-L<sub>2</sub>-Rh(CO)Cl complex,<sup>20,21</sup> the selectivity for alkylidene allylation decreased (Table 4). Comparing entries 4 and 5 suggests that steric effects may be less important than electronic effects: the Tolman cone angles of P(*O*-*o*-*t*-BuPh)<sub>3</sub> and P(OPh)<sub>3</sub> are 175 and 128°, respectively,<sup>22</sup> yet the chemoselectivity was almost

(19) (a) Hayashi, T.; Konishi, M.; Kumada, M. *J. Chem. Soc., Chem. Commun.* **1983**, 736. (b) Hatanaka, Y.; Goda, K.; Hiyama, T. *Tetrahedron Lett.* **1994**, 35, 1279. (c) Hiyama, T.; Matsuhashi, H.; Fujita, A.; Tanaka, M.; Hirabayashi, K.; Shimizu, M.; Mori, A. *Organometallics* **1996**, 15, 5762. (d) Yamamoto, Y.; Takada, S.; Miyaura, N. *Chem. Lett.* **2006**, 35, 704.

(20) (a) Vastag, S.; Heil, B.; Markó, L. *J. Mol. Catal.* **1979**, 5, 189. (b) Ohgomori, Y.; Yoshida, S.-I.; Watanabe, Y. *J. Chem. Soc., Dalton Trans.* **1987**, 2969.

**Table 3.** Correlation between Substrate Structure and Chemoselectivity

entry	Ar	R	$\beta:\beta'$ <sup>a</sup>	% yield <sup>b</sup>	% ee <sup>c</sup>
1	Ph	Me	$\geq 20:1$	60	67
2	Ph	Et	$\geq 20:1$	82	83
3	Ph	<i>n</i> -pentyl	17:1	77	93
4	Ph	Cy	7:1	76	96
5	2-furyl	<i>n</i> -pentyl	5.1:1	52	93
6	<i>o</i> -tol	<i>n</i> -pentyl	$\geq 20:1$	66	93
7	<i>o</i> -CF <sub>3</sub> Ph	<i>n</i> -pentyl	32:1	45	94

<sup>a</sup> Chemoselectivity determined by <sup>1</sup>H NMR or GC analysis of the unpurified reaction mixture. <sup>b</sup> Yield of conjugate addition product after silica gel chromatography. Value is an average of two experiments in each case. <sup>c</sup> Enantioselectivity of major isomer.

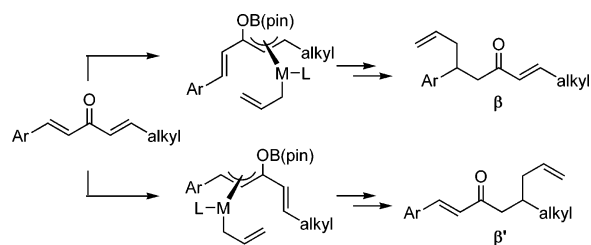
identical and appears to better follow the ligand basicity correlation. Notably, these generalizations do not appear to apply to chiral ligands, where chemoselectivity is not clearly related to either electronic or steric features. For instance, ligand **9** gives predominant addition to the arylidene, whereas the reaction employing electronically similar ligand PPh<sub>3</sub> is relatively nonselective. The fact that there is a nonlinear correlation between the size of remote ligand substituents and chemoselectivity (compare entries 3, 6, and 7 in Table 1) suggests that catalyst–substrate interactions, distant from the metal center, can have a significant effect on selectivity.

**Table 4.** Correlation between Ligand Basicity and Chemoselectivity

entry	L	$\nu_{\text{CO}}$ (cm <sup>-1</sup> ) <sup>a</sup>	$\beta:\beta'$ <sup>b</sup>	% yield <sup>c</sup>
1	PCy <sub>3</sub>	1943	1:7.5	82
2	P(NMe <sub>2</sub> ) <sub>3</sub>	1964	1:2.5	82
3	PPh <sub>3</sub>	1979	1:2.4	49
4	P( <i>o</i> - <i>t</i> BuPh) <sub>3</sub>	2012	1:1.5	40
5	P(OPh) <sub>3</sub>	2016	1:1.1	55
6 <sup>c</sup>	<b>9</b>	1984	$\geq 20:1$	53

<sup>a</sup> Values are for the derived *trans*-L<sub>2</sub>Rh(CO)Cl complex in CH<sub>2</sub>Cl<sub>2</sub> solvent. See ref 21 for values. <sup>b</sup> Chemoselectivity determined by <sup>1</sup>H NMR analysis of the unpurified reaction mixture. <sup>c</sup> Yield of conjugate addition product after silica gel chromatography. Value is an average of two experiments in each case.

A working model for chemoselectivity is depicted in Scheme 9. The data above are most readily accommodated by considering the stability of the  $\pi$ -allyl complexes: both small alkylidene substituents and large arylidene groups enhance the amount of

**Scheme 9**

$\pi$ -allyl complex at the alkylidene site. Subsequent 3,3' elimination transfers the allyl group to the arylidene unit and leads to an enhanced  $\beta:\beta'$  ratio. The opposite outcome is observed with large alkylidene groups and small arylidene groups. Additionally, alkylidene allylation is increasingly favored with electron-rich ligands. This outcome may be rationalized by assuming again that  $\pi$ -allyl stability is product-determining and that, with an electron-rich metal, the  $\pi$ -allyl bearing the electron-accepting aryl ring is favored. Arguably, the aryl group may facilitate  $d\pi-\pi^*$  donation in the precursor L<sub>n</sub>Ni  $\pi$  complex, similar to the dba effect<sup>23</sup> recognized in cross-coupling reactions, and thereby favor  $\pi$ -allyl formation at the arylidene site. This contention is supported by observations with electronically modified substrates in the presence of chiral ligand **14**: the *para*-methoxy phenyl substituent provides more arylidene allylation (Table 2, entry 3) relative to the electron-withdrawing *para*-trifluoroethyl phenyl derivative (Table 2, entry 6).

**(c) Catalyst Composition.** The concentration of ligand relative to the metal catalyst has a significant impact on the reaction outcome. As depicted in Table 5, in the absence of ligand, 1,2-allylation of the enone was the predominant product, and the 1,4-addition occurred exclusively at the alkylidene site (entry 1). Addition of 0.5 equiv of ligand, relative to nickel, was sufficient to reverse the 1,2-/1,4-selectivity, providing a 5:1 ratio favoring conjugate allylation; further, the addition of ligand reversed the chemoselectivity of the conjugate addition product and favored the arylidene site by 6.6:1. The fact that pronounced ligand acceleration<sup>24</sup> operates was revealed by noting a significant enhancement in extent of reaction (82 versus 38% conversion) and high enantioselection for the arylidene allylation product (95% ee), even in the presence of excess Ni(cod)<sub>2</sub> relative to ligand. A further increase in ligand/metal ratio (1:1) embellished the trend initiated by the first data point, and a ligand/metal ratio > 1:1 did not offer any additional improvement.

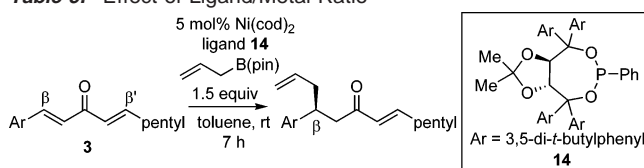
To learn more about the nature of the catalytic reaction, nonlinear effects were examined. As depicted in Figure 1, there was a subtle negative nonlinear effect when the reaction enantioselectivity and ligand enantiopurity were compared. Importantly, the *chemoselectivity* also changed in this series of experiments, decreasing from 27:1  $\beta:\beta'$  when racemic **14** was used to 17:1  $\beta:\beta'$  when ligand **14** of >99% ee was employed. Along with a change in selectivity, it was also determined that

(21) For the values in Table 3, see (entries 1–3): (a) Otto, S.; Roodt, A. *Inorg. Chim. Acta* **2004**, *357*, 1. Entry 4: (b) Fernández, E.; Ruiz, A.; Claver, C.; Castillón, S.; Polo, A. *Organometallics* **1998**, *17*, 2857. Entry 5: Ref 20a. Entry 6: (c) Burks, H. E.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 8766.

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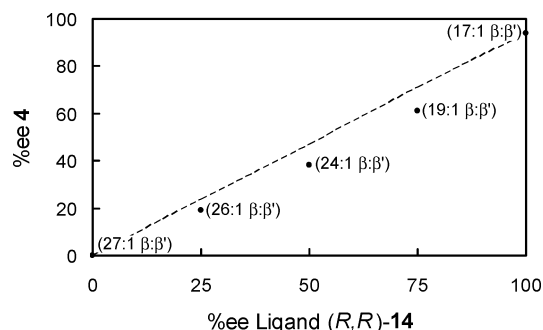
(23) (a) Mace, Y.; Kapdi, A. R.; Fairlamb, J. S.; Jutand, A. *Organometallics* **2006**, *25*, 1795. (b) Fairlamb, I. J. S.; Kapdi, A. R.; Lee, A. F. *Org. Lett.* **2004**, *6*, 4435.

(24) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1059.

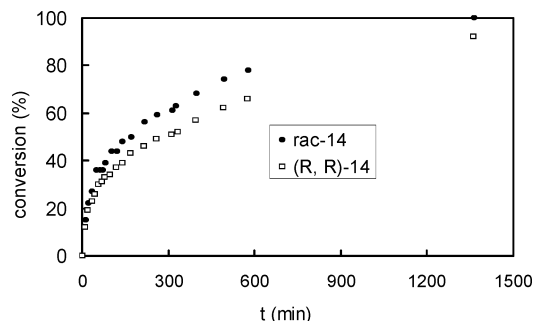
**Table 5.** Effect of Ligand/Metal Ratio


entry	mol % ( <i>R,R</i> )-14	1,4:1,2	$\beta$ : $\beta'$ <sup>a</sup>	% conv <sup>b</sup>	% ee ( $\beta$ ) <sup>c</sup>
1	0	1:1.4	1:>50	38	
2	2.5	5:1	6.6:1	82	95
3	5	>20:1	17:1	>95	95
4	7.5	>20:1	17:1	>95	94
5	10	>20:1	17:1	>95	93

<sup>a</sup> Chemoselectivity determined by GC analysis of the unpurified reaction mixture. <sup>b</sup> Percent conversion determined by NMR analysis. Value is an average of two experiments in each case. <sup>c</sup> Enantioselectivity of major isomer.



**Figure 1.** Correlation between product enantiomeric purity, chemoselectivity, and ligand enantiomeric purity. Dashed line is for a linear correlation between % ee product and % ee ligand.



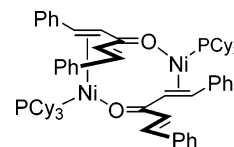
**Figure 2.** Comparison of reaction rates in the presence of enantiomerically enriched ligand and racemic ligand.

the reaction with racemic catalyst is faster than the reaction with enantiopure catalyst (Figure 2).

Given the propensity for Pd to bind two monodentate phosphines when bound to dibenzylideneacetone,<sup>25</sup> it is conceivable that the nonlinear effects described above might arise

(25) (a) Amatore, C.; Jutland, A. *Coord. Chem. Rev.* **1998**, 178–180, 511. (b) Amatore, C.; Jutland, A.; Meyer, G. *Inorg. Chim. Acta* **1998**, 273, 76.

due to the intermediacy of a (substrate)ML<sub>2</sub> complex. Examination of the catalyst structure by NMR provided an alternate rationale for the effect of catalyst enantiomeric purity on reaction outcome. When PCy<sub>3</sub> was added to Ni(cod)<sub>2</sub> in a 1:1 ratio in THF-*d*<sub>8</sub>, no observable reaction occurs. However, when dibenzylidene acetone was added in an equimolar proportion, <sup>31</sup>P NMR indicated clean formation of a new complex characterized by a singlet resonance at 38.19 ppm. Importantly, when 2 equiv of PCy<sub>3</sub> was employed, only 1 equiv of the ligand was incorporated into the new structure, the remainder was uncomplexed as determined by <sup>31</sup>P NMR. The <sup>1</sup>H NMR spectrum of the 1:1:1 complex revealed upfield-shifted olefinic resonances. Integration was consistent with only one alkene participating in coordination to the metal but not the other. A structural formulation, such as that in Scheme 10, may account for the spectral properties of the complex. Similar dimeric Ni–enone complexes have recently been isolated by Kurosawa as a product of the reaction between Ni(0), PCy<sub>3</sub>, and cyclopropyl ketones, and they are spectroscopically similar to the 1:1:1 complex described above.<sup>26</sup> Thus, in the case of substrate **3** and chiral ligand **14** of varying enantiomeric purity, it is tenable that dimeric [(**14**)Ni–enone]<sub>2</sub> structures are involved; either allylB–(pin) induced oxidative addition or dimer dissociation occurs at different rates and with different chemoselectivity for the heterochiral versus the homochiral complexes.

**Scheme 10**

### 3. Conclusion

In conclusion, we have documented the first catalytic enantioselective conjugate allylation reactions that may be applied to a range of activated aromatic enones. Experiments implicate the intermediacy of dimeric metal–ligand–substrate complexes and a catalytic cycle that operates by oxidative  $\pi$ -allyl formation, followed by 3,3' reductive elimination. Studies that focus on the application of these concepts to related reactions are in progress.

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**Supporting Information Available:** Characterization and procedures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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