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Rhodium-Catalyzed Dynamic Kinetic Asymmetric Transformations of Racemic Tertiary Allylic Trichloroacetimidates with Anilines

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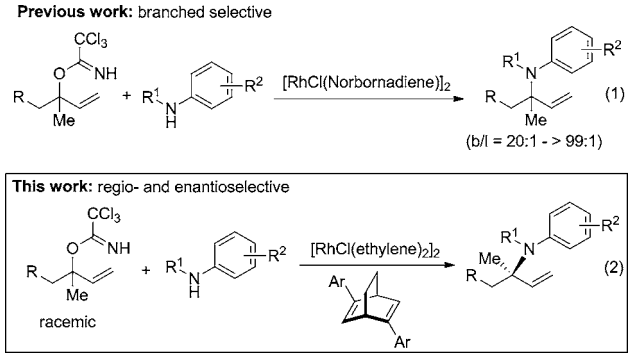
Supporting Information

ABSTRACT: The rhodium-catalyzed regio- and enantioselective amination of racemic tertiary allylic trichloroacetimidates with a variety of aniline nucleophiles is a direct and efficient route to chiral α,α-disubstituted allylic *N*-arylamines. We describe the first dynamic kinetic asymmetric transformations of racemic tertiary allylic electrophiles with anilines utilizing a chiral diene-ligated rhodium catalyst. The method allows for the formation of α,α-disubstituted allylic *N*-arylamines in moderate to good yields with good to excellent levels of regio- and enantioselectivity.

The prevalence of chiral amines in bioactive natural and non-natural products has stimulated numerous efforts toward their construction.[1] Although a variety of methods are available for the preparation of optically active amines,[2] the catalytic asymmetric synthesis of α,α-disubstituted amines remains relatively underdeveloped. A new approach to the asymmetric formation of α,α-disubstituted amines via palladium-catalyzed aza-Claisen rearrangements of linear allylic trihaloacetimidates has recently been reported.[3] Although allylic amines are formed in good yield and enantioselectivity, full conversion necessitates high temperatures over a period of days.[3] A more common approach to α,α-disubstituted amines involves the addition of organometallic reagents to ketimines.[4−7] Several challenges could potentially emerge using this approach. First, the addition to ketimines containing an α-hydrogen is problematic because imines have a propensity to enolize.[4b,7a] Second, stereoselectivity is often moderate with ketimines because they can exist as *E* and *Z* isomers, and differentiation of the enantiotopic faces is often limited.[5b] Third, ketimines are significantly less reactive than aldimines and require activation by a Lewis acid.[7a] In response to these challenges, Hayashi reported that rhodium−chiral diene complexes effectively catalyze the addition of sodium tetraarylborates to *N*-tosyl ketimines at 60−80 °C for 20 h.[8]

Transition-metal-catalyzed substitution of primary and racemic secondary allylic carbonates or acetates has been utilized for the regio- and enantioselective preparation of α-substituted *N*-arylamines.[9,10] However, only the regioselective synthesis of α,α-disubstituted *N*-arylamines via substitution of primary and racemic tertiary allylic acetates and carbonates catalyzed by palladium,[11a,b] iridium,[10c] and iron complexes[11c] has been described. We recently reported the rhodium-catalyzed regioselective amination of tertiary allylic imidates with aniline nucleophiles (eq 1).[13] Our method is applicable to a wide range of substrates, affording the amination products in excellent yields and regioselectivity. Herein we disclose the first rhodium-catalyzed regio- and enantioselective amination of racemic tertiary allylic trichloroacetimidates with anilines to provide α,α-disubstituted allylic *N*-arylamines (eq 2).[15,16]



During our previous regioselective studies,[12] control experiments with an enantiopure starting imidate[14] (98% ee) resulted in a nearly racemic branched amination product (<7% ee). On the basis of this result, we hypothesized that if isomerization of the diastereomeric π-allylrhodium intermediates[17] occurs faster than attack by the aniline nucleophile (Figure 1), the dynamic kinetic asymmetric transformation (DYKAT) of tertiary allylic trichloroacetimidates could be feasible.[18] Ionization of the activated rhodium−alkene complexes **1** and *ent*-**1** (Figure 1)[19] with the chiral rhodium catalyst would provide the corresponding diastereomeric π-allylrhodium complexes **2** and *ent*-**2**, respectively. We reasoned that an asymmetric environment about the rhodium center could decrease the rate of nucleophilic attack by anilines and increase the time allowed for rapid $\pi-\sigma-\pi$ interconversion. An unfavorable interaction

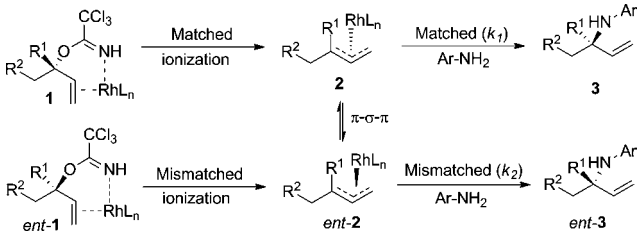


Figure 1. Strategy for DYKAT of tertiary allylic imidates.

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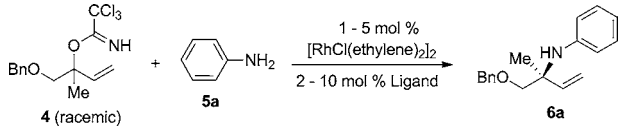
between one of the two π-allylrhodium intermediates would determine which enantiomer of the amination product **3** ($k_1 \gg k_2$) is preferentially formed.

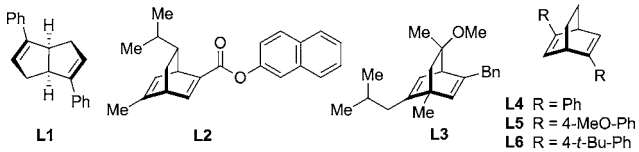
To test our hypothesis, we set out to explore the effects of the chiral diene ligands[20] **L1**–**L4** (Table 1) on the enantioselectivity

Table 1. Optimization Studies[a]



entry	ligand	Rh loading (mol%)	aniline (equiv)	solvent	temp (°C)	time (h)	yield (%)	% ee
1	**L1**	5	3	THF	40	4	14	-2
2	**L2**	5	3	THF	40	1	59	-1
3	**L3**	5	3	THF	40	1	71	-26
4	**L4**	5	3	THF	40	1	72	73
5	**L4**	5	3	THF	25	1	77	84
6	**L4**	5	3	THF	0	1	77	83
7	**L4**	1	3	THF	25	4	41	77
8	**L4**	5	3	Et_2O	25	1	72	76
9	**L4**	5	3	Dioxane	25	1	73	78
10	**L4**	5	3	Toluene	25	1	71	82
11	**L4**	5	3	MTBE	25	1	78	86
12	**L4**	5	1.5	MTBE	25	1	69	89
13	**L5**	5	1.5	MTBE	25	1	60	71
14	**L6**	5	1.5	MTBE	25	1	64	84
15	**L7**	**5**	**1.5**	**MTBE**	**25**	**1**	**85**	**94**
16	**L8**	5	1.5	MTBE	25	1	74	90

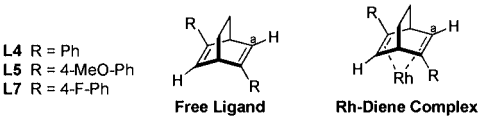
[a]All of the reactions were conducted at 0.2 M with 1 equiv of **4**. Isolated yields are shown; ee's were determined by chiral HPLC.



in the amination reaction of racemic tertiary allylic trichloroacetimidate **4** with aniline (**5a**) (Table 1). Lin ligand **L1**[21] (entry 1) and Hayashi ligand **L2**[22] (entry 2) afforded nearly racemic α,α-disubstituted *N*-arylamine **6a**. Use of Carreira ligand **L3**[23] (entry 3) provided a measurable enantioselectivity (26% ee) for the process. Hayashi ligand **L4**[24] (entry 4) was the most enantioselective at 40 °C, providing **6a** as a single regioisomer in 72% yield with 73% ee. Lowering the reaction temperature to 25 °C (entry 5) resulted in a significant enhancement of the enantioselectivity of **6a** (84% ee). Lowering the temperature further to 0 °C (entry 6) did not impact the results. Lowering the metal and ligand loadings to 1 mol % (entry 7) decreased both the yield and the enantioselectivity. A number of solvents (entries 8–11) were then investigated, and *tert*-butyl methyl ether (MTBE) induced the highest enantioselectivity, providing **6a** with 86% ee (entry 11). Further optimization by lowering the equivalents of **5a** resulted in a system that afforded 89% ee with a good yield (69%) and complete regioselectivity (entry 12).

Having established bicyclo[2.2.2]octadiene ligand **L4** as the optimal chiral ligand, we next examined the steric and electronic nature of the substituents on the phenyl ring (**L5**–**L8**, Table 1). While the use of electron-rich 4-methoxyphenyl-substituted diene **L5** resulted in a decrease in the enantioselectivity (71% ee; entry 13), changing the diene substituent to the electron-poor 4-fluorophenyl group (ligand **L7**, entry 15) significantly improved both the yield (85%) and the enantioselectivity (94% ee).

To rationalize the improved enantioselectivity with an electron-withdrawing chiral diene ligand (**L7** vs **L5**, Table 1), the ligation of the diene ligands to rhodium was monitored by ^{13}C NMR spectroscopy (Figure 2). It was determined that the



Ligand	$^{13}C_a$free δ(ppm)	$^{13}C_a$ complex δ(ppm)	$\Delta\delta = (\delta_{complex}-\delta_{free})$ $^{13}C_a$	$J(^{103}Rh\text{-}^{13}C_a)$ (Hz)
L4	129.7772	45.3250	-84.4522	10.8
L5	127.3815	44.0943	-83.2872	12.0
L7	129.5563	45.4043	-84.1520	10.6

Figure 2. Studies of the stabilities of Rh–diene complexes.

electron density of the diene ligand significantly influences the coordination shift ($\Delta\delta = \delta_{complex} - \delta_{free\ ligand}$)[20a,25] as a result of increasing back-donation from the rhodium metal center.[26] For example, electron-withdrawing ligand **L7** has a larger coordination shift than electron-donating diene ligand **L5**. This result suggests that the presence of the electron-withdrawing group on the chiral diene **L7** shifts the hybridization of the coordinated olefinic carbon from sp^2 toward more sp^3 character, making the diene bind more strongly to rhodium than electron-rich **L5**.[26] The magnitude of the $^{103}Rh-^{13}C$ coupling constant of 10.6–12 Hz (Figure 2) suggests that there is considerable s character in the rhodium–chiral diene complexes.[27]

Under these optimized conditions, the scope of the allylic amination reaction with respect to aniline nucleophiles **5b**–**i** (Table 2) was explored. Electron-rich and electron-deficient para-substituted anilines **5b**–**f** (entries 1–5) were found to be suitable nucleophiles, giving rise to α,α-disubstituted allylic *N*-arylamines **6b**–**f** in moderate to good yields (51–86%) with good to high enantioselectivity (85–96% ee). In addition, all of the reactions proceeded with excellent regioselectivity. The amination reactions of anilines **5c** (entry 2) and **5e** (entry 4) bearing the *p*-bromo and *p*-boronic acid ester substituents, respectively, are noteworthy because the corresponding allylic *N*-arylamines **6c** and **6e** could be amenable to subsequent cross-coupling reactions.[28] Aniline **5g** containing ester functionality at the meta position provided product **6g** (entry 6) as a single regioisomer in good yield (79%) with high levels of enantioselectivity (94% ee). This method also worked well with ortho-substituted anilines **5h** and **5i** (entries 7 and 8), and the allylic amines were isolated with high enantioselectivity (89–94% ee) and regioselectivity [branched/linear (b/l) ratio = 48:1–51:1]. This suggests that the system is tolerant of sterically demanding anilines. As a result, we sought to extend this catalytic method to the challenging acyclic secondary aniline **5j** (entry 9), which is known to provide amination products with poor regioselectivity.[10a,c] The reaction proceeded smoothly under our optimal conditions, and *N*-arylamine **6j** was isolated in 70% yield with excellent selectivities (b/l = 30:1, 93% ee).

To establish the absolute stereochemistry of the amination products, allylic *N*-arylamine **6c** was converted to the trifluoroacetate (TFA) salt and shown by X-ray crystallographic analysis to be *S*-configured. The solid-state structure of the

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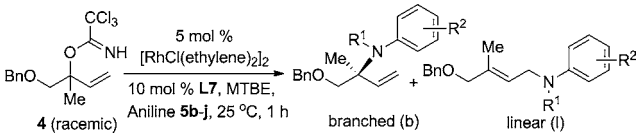
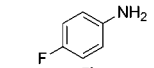
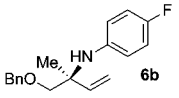
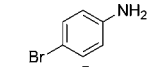
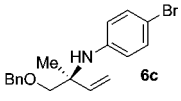
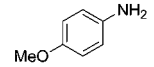
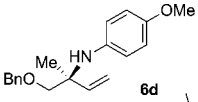
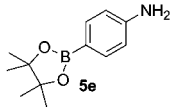
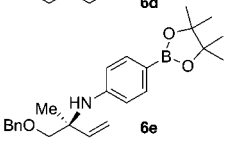
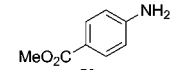
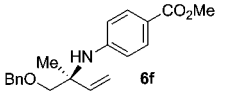
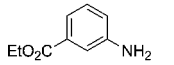
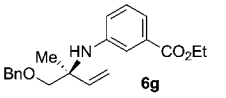
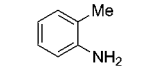
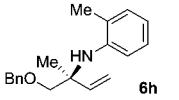
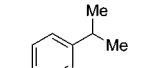
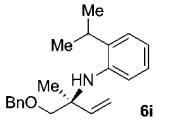
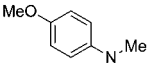
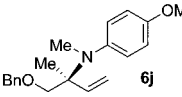
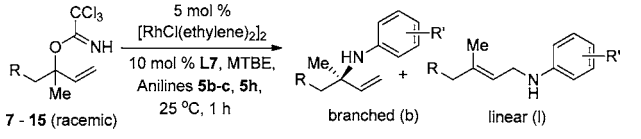
Table 2. Survey of Aniline Nucleophiles[a]

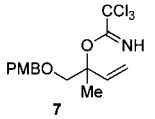
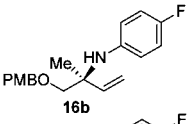
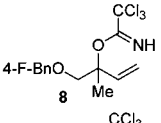
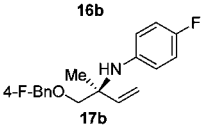
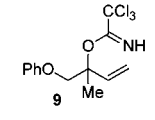
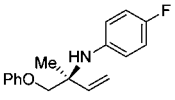
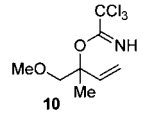
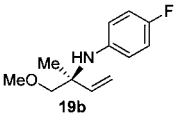
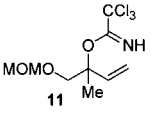
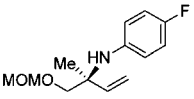
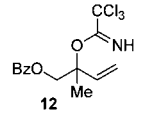
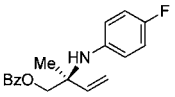
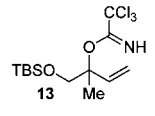
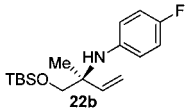
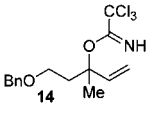
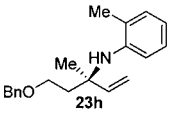
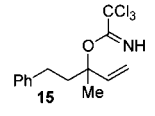
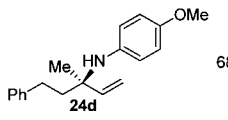


entry	anilines	products	% yield	b/l ratio	% *ee*
1	 **5b**	 **6b**	82	>99:1	96
2	 **5c**	 **6c**	86	>99:1	91
3	 **5d**	 **6d**	77	33:1	90
4	 **5e**	 **6e**	54	>99:1	91
5	 **5f**	 **6f**	51	>99:1	85
6	 **5g**	 **6g**	79	>99:1	94
7	 **5h**	 **6h**	69	51:1	89
8	 **5i**	 **6i**	74	48:1	94
9	 **5j**	 **6j**	70	30:1	93

[a]All of the reactions were conducted with 1 equiv of **4** and 1.5 equiv of the aniline. Isolated yields are shown; ee's were determined by chiral HPLC and b/l ratios by GC.

Table 3. Survey of Tertiary Allylic Imidates[a]



entry	imidates	products	% yield	b/l ratio	% *ee*
1	 **7**	 **16b**	76	>99:1	93
2	 **8**	 **17b**	61	>99:1	92
3	 **9**	 **18b**	84	>99:1	80
4	 **10**	 **19b**	57	>99:1	86
5	 **11**	 **20b**	62	>99:1	89
6	 **12**	 **21b**	53	>99:1	59
7	 **13**	 **22b**	92	90:1	76
8	 **14**	 **23h**	70	5:1	56
9	 **15**	 **24d**	68	7:1	52

[a]All of the reactions were conducted with 1 equiv of the allylic imidate and 1.5 equiv of the aniline. Isolated yields are shown; ee's were determined by chiral HPLC and b/l ratios by GC.

amine–TFA salt shows that it exists as two independent cation–anion pairs through hydrogen bonding. The ammonium cations have the same configuration but different conformations.[29]

In addition to tertiary allylic imidate **4**, the functional-group tolerance of the present catalysis was evaluated with a number of branched imidates (Table 3). Both electron-rich and electron-deficient benzyl ether derivatives (**7** and **8**, entries 1 and 2) provided the amination products **16b** and **17b** with an enantioselectivity (~93% ee) comparable to that of benzyl ether **4** (96% ee; Table 2). The ester group, however, was not suitable for this system, and allylic amine **21b** (entry 6) was isolated with 59% ee. As the functional group became more bulky (entry 7), a significant reduction in enantioselectivity was also observed (76% ee). These results suggests that tertiary allylic imidates having benzyl, phenyl, and methyl ether groups at the β-position (entries 1–5) provide additional chelation control on the rhodium center,[10a,30] whereas ester and silyl protecting groups (entries 6 and 7) reduce the ligation of the ether oxygen to the metal center. Reductions in regio- and enantioselectivity were also observed in the reactions of tertiary allylic imidates **14** and **15** lacking an oxygen substituent at the β-position (entries 8 and 9). We further examined the limitation of the current method with ethyl- and aryl-substituted imidates. Although we were able to prepare trichloroacetimidates having an aryl group at the α-position, these substrates rapidly underwent [3,3]-sigmatropic rearrangement.[31] We were unable to prepare allylic imidates bearing an ethyl group at the α-position, presumably because their tertiary alcohol precursors were too sterically hindered to react with trichloroacetonitrile.

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In summary, we have reported the first dynamic kinetic asymmetric transformation of racemic tertiary allylic acetimidates with aniline nucleophiles using a rhodium−diene ligand complex, providing α,α-disubstituted allylic *N*-arylamines in moderate to good yields with good to excellent regio- and enantioselectivity. Investigations into the full racemic tertiary allylic trichloroacetimidate scope and further transformations are ongoing and will be reported in due course.

■ ASSOCIATED CONTENT

Supporting Information

Complete experimental details and spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For a review, see: *Chiral Amine Synthesis*; Nugent, T. C., Ed.; Wiley-VCH: New York, 2008.

(2) For representative examples, see: (a) Brown, S. P.; Goodwin, N. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 1192. (b) Ooi, T.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **2003**, *125*, 5139. (c) Saaby, S.; Bella, M.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 8120. (d) Kano, T.; Hashimoto, T.; Maruoka, K. *J. Am. Chem. Soc.* **2006**, *128*, 2174. (e) Balskus, E. P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2006**, *128*, 6810. (f) Terada, M.; Nakano, M.; Ube, H. *J. Am. Chem. Soc.* **2006**, *128*, 16044. (g) Mashiko, T.; Hara, K.; Tanaka, D.; Fujiwara, Y.; Kumagai, N.; Shbasaki, M. *J. Am. Chem. Soc.* **2007**, *129*, 11342. (h) Clayden, J.; Donnard, M.; Lefrance, J.; Minassi, A.; Tetlow, D. J. *J. Am. Chem. Soc.* **2010**, *132*, 6624.

(3) (a) Fischer, D. F.; Xin, Z. Q.; Peters, R. *Angew. Chem., Int. Ed.* **2007**, *46*, 7704. (b) Fischer, D. F.; Barakat, A.; Xin, Z. Q.; Weiss, M. E.; Peters, R. *Chem.—Eur. J.* **2009**, *15*, 8722.

(4) (a) Shibasaki, M.; Kanai, M. *Chem. Rev.* **2008**, *108*, 2853. (b) Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 3600. (c) Hannedouche, J.; Riant, O. *Org. Biomol. Chem.* **2007**, *5*, 873.

(5) (a) Jacobsen, E. N.; Vachal, P. *Org. Lett.* **2000**, *2*, 867. (b) Connon, S. J. *Angew. Chem., Int. Ed.* **2008**, *47*, 1176. (c) Enders, D.; Gottfried, K.; Raabe, G. *Adv. Synth. Catal.* **2010**, *352*, 3147.

(6) Suto, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2007**, *129*, 500.

(7) (a) Spero, D. M.; Kapadia, S. R. *J. Org. Chem.* **1997**, *62*, 5537. (b) Cogan, D. A.; Ellman, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 268. (c) Enders, D.; Reinhold, U. *Tetrahedron: Asymmetry* **1997**, *8*, 1895. (d) Lauzon, C.; Charette, A. *Org. Lett.* **2006**, *8*, 2743. (e) Wada, R.; Shibuguchi, T.; Makino, S.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 7687.

(8) Shintani, R.; Takeda, M.; Tsuji, T.; Hayashi, T. *J. Am. Chem. Soc.* **2010**, *132*, 13168.

(9) For a review, see: Trost, B. M.; Zhang, T.; Sieber, J. D. *Chem. Sci.* **2010**, *1*, 427.

(10) (a) Evans, P. A.; Robinson, J. E.; Moffett, K. K. *Org. Lett.* **2001**, *3*, 3269. (b) Takeuchi, R.; Ue, N.; Tanabe, Y.; Yamashita, K.; Shiga, N. *J. Am. Chem. Soc.* **2001**, *123*, 9525. (c) Shu, C.; Leitner, A.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2004**, *43*, 4797. (d) Stanley, L. M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 8971.

(11) (a) Watson, I. D. G.; Yudin, A. K. *J. Am. Chem. Soc.* **2005**, *127*, 17156. (b) Dubovyk, I.; Watson, I. D. G.; Yudin, A. K. *J. Am. Chem. Soc.* **2007**, *129*, 14172. (c) Plietker, B. *Angew. Chem., Int. Ed.* **2006**, *45*, 6053.

(12) Arnold, J. S.; Stone, R. F.; Nguyen, H. M. *Org. Lett.* **2010**, *12*, 4580.

(13) Arnold, J. S.; Cizio, G. T.; Nguyen, H. M *Org. Lett.* **2011**, *13*, 5576.

(14) (a) Bartels, B.; García-Yebra, C.; Rominger, F.; Helmchen, G. *Eur. J. Org. Chem.* **2002**, 2569. (b) Fischer, C.; Defieber, C.; Suzuki, T.; Carreira, E. M. *J. Am. Chem. Soc.* **2004**, *126*, 1628.

(15) For kinetic resolution of racemic secondary allylic electrophiles via transition-metal-catalyzed amination reactions, see: (a) Vrieze, D. C.; Hoge, G. S.; Hoerter, P. Z.; Van Haitsma, J. T. *Org. Lett.* **2009**, *11*, 3140. (b) Stanley, L. M.; Bai, C.; Ueda, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 8918.

(16) For dynamic kinetic resolution of racemic secondary allylic electrophiles via transition-metal-catalyzed amination, see: (a) You, S. L.; Zhu, X. Z.; Luo, Y. M.; Hou, X. L.; Dai, L. X. *J. Am. Chem. Soc.* **2001**, *123*, 7471. (b) Lafrance, M.; Roggen, M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *57*, 3470. (c) Defieber, C.; Ariger, M. A.; Moriel, P.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 3139−3143. (d) Rogen, M.; Carreira, E. M. *J. Am. Chem. Soc.* **2010**, *132*, 11917−11919.

(17) For an alternative enylrhodium intermediate, see: Evans, P. A.; Nelson, J. D. *J. Am. Chem. Soc.* **1998**, *120*, 5581.

(18) Trost, B. M.; Fandrick, D. R. *Aldrichimica Acta* **2007**, *40*, 59.

(19) (a) Kirsch, S. F.; Overman, L. E. *J. Am. Chem. Soc.* **2005**, *127*, 2866. (b) Kirsch, S. F.; Overman, L. E.; White, N. S. *Org. Lett.* **2007**, *9*, 911. (c) Cannon, J. S.; Kirsch, S. F.; Overman, L. E. *J. Am. Chem. Soc.* **2010**, *132*, 15185. (d) Topczewski, J. J.; Tewson, T. J.; Nguyen, H. M. *J. Am. Chem. Soc.* **2011**, *133*, 19318.

(20) (a) Defieber, C.; Grützmacher, H.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 4482. (b) Xu, M.-H.; Lin, G.-Q. *Synlett* **2011**, 1345.

(21) Wang, Z.-Q.; Feng, C.-G.; Xu, M.-H.; Lin, G.-Q. *J. Am. Chem. Soc.* **2007**, *129*, 5336.

(22) Okamoto, K.; Hayashi, T.; Rawal, V. H. *Org. Lett.* **2008**, *10*, 4387.

(23) Fischer, C.; Defieber, C.; Suzuki, T.; Carreira, E. M. *J. Am. Chem. Soc.* **2004**, *126*, 1628.

(24) Tokunaga, N.; Otomaru, Y.; Okamoto, K.; Ueyama, K.; Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2004**, *126*, 13584.

(25) Mann, B. E.; Taylor, B. F. In *^{13}C NMR Data for Organometallic Compounds*; Academic Press: London, 1981; p 16.

(26) Crabtree, R. H. In *The Organometallic Chemistry of the Transition Metals*, 4th ed.; Wiley-Interscience: Hoboken, NJ, 2005; pp 125−128.

(27) Bodner, G. M.; Storhoff, B. N.; Doddrell, D.; Todd, L. J. *Chem. Commun.* **1970**, 1530.

(28) Negishi, E. I. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E. I., Ed.; Wiley-Interscience: New York, 2002; Vol. *1*, p 1051.

(29) See the Supporting Information for details.

(30) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.

(31) (a) Overman, L. E. *J. Am. Chem. Soc.* **1974**, *96*, 597. (b) For a comprehensive review, see: Overman, L. E.; Carpenter, N. E. *Org. React.* **2005**, *66*, 1.