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Rhodium/Chiral Diene Complexes in the Catalytic Asymmetric Arylation of β-Pyrazol-1-yl Acrylates

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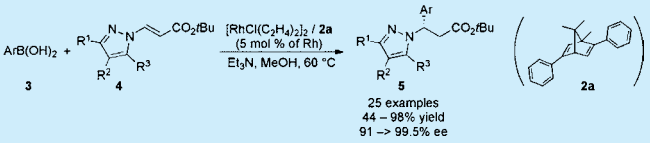
Supporting Information

ABSTRACT: The asymmetric conjugate addition of arylboronic acids to substituted and unsubstituted β-pyrazol-1-yl (*E*)-*tert*-butyl acrylates **4** catalyzed by 5 mol % of the Rh(I)/diene **2a** catalyst provided the corresponding addition products in 44−98% yield and 91−>99.5% ee. The method was applied to the formal synthesis of (3*S*)-3-aryl-3-(pyrazol-1-yl)propanoic acid **1b** with agonistic activity toward the human GPR40 G-protein coupled receptor.



Optically active N-containing heterocyclic compounds are commonly found in natural products, biologically active compounds, and pharmaceuticals.[1] Among these, chiral *N*-alkylpyrazoles have received significant attention due to their ubiquity in compounds with biological activity.[2] For example, pyridine *N*-oxide **1a**[2a] (Figure 1) that bears a pyrazole moiety

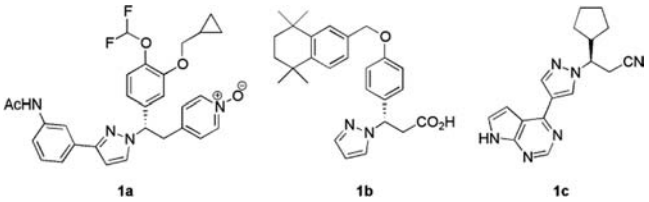


Figure 1. Biologically active chiral pyrazole compounds.

appended adjacent to a stereogenic center is a potent PDE4 (PhosphoDiEsterase type 4) inhibitor (IC_{50} = 0.5 nM) that is potentially useful for targeting inflammatory diseases.[3] Other examples include the β-pyrazol-1-yl acid **1b** that has activity ($EC_{50} \leq 10$ μM) toward human GPR40 G-protein coupled receptor[2b] and ruxolitinib (**1c**; INCB018424),[2c] a Janus kinase (JAK) inhibitor that is used in the treatment of myelofibrosis.

Chiral compounds such as **1a**−**1c** can be accessed by the asymmetric aza-Michael reaction: the organocatalytic enantioselective conjugate addition of N-containing heterocyclic nucleophiles to α,β-unsaturated carbonyl compounds. Although this has seen wide application in the synthesis of a diverse range of biologically active natural products,[4,5] only a limited number of examples utilizing pyrazole nucleophiles exist that have been accomplished with a good degree of enantioselectivity.[5d−f] As a result, when access to enantiopure pyrazoles is required, separation of racemic or enantioenriched aza-Michael product mixtures by chiral preparative HPLC or classical chiral salt resolution may be required. Moreover, the organocatalyzed asymmetric aza-Michael reaction benefits from Michael acceptors that can form hydrogen bonds and/or are able to form iminium ions. Therefore, while α,β-unsaturated aldehydes and ketones work well, α,β-unsaturated esters do not make good substrates. Given our own need to access β-pyrazol-1-yl substituted esters with a stereogenic center directly adjacent to the pyrazole moiety, and with further structural diversification of the addition products in mind, we sought to develop an efficient method that offered higher levels of stereocontrol than the corresponding asymmetric aza-Michael reaction could achieve.

In recent years the Rh-catalyzed enantioselective conjugate addition of organoboron reagents to electron-deficient olefins has experienced significant development, ultimately allowing for the formation of C−C bonds under relatively mild conditions.[6,7] The use of boronic acids and α,β-unsaturated carbonyl compounds is known as the Hayashi−Miyaura reaction and offers benefits over the analogous asymmetric cuprate 1,4-conjugate addition including not requiring low temperature, moisture- and air-free conditions, being catalytic, and not requiring the in situ preparation of the nucleophiles. Recently we have reported a series of variants of the Hayashi−Miyaura reaction utilizing highly reactive and enantioselective chiral Rh(I)-catalysts comprising a novel family of 2,5-diaryl substituted bicyclo[2.2.1]heptadiene ligands **2** and various Michael acceptors.[8,9] Building upon these results we herein report the rhodium-catalyzed asymmetric conjugate addition of arylboronic acids to β-pyrazol-1-yl acrylate esters employing novel chiral diene ligands furnishing β-aryl-β-pyrazol-1-yl esters in high yield and enantioselectivity.[10]

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To initiate the study, the addition of phenylboronic acid (**3a**) to (*E*)-*tert*-butyl 3-(1H-pyrazol-1-yl)acrylate (**4a**) was tested in the presence of 2.5 mol % of $[RhCl(COD)_2]_2$ (Scheme 1 and

Scheme 1. Conjugate Addition of Phenylboronic Acid (3a) to (*E*)-3-(1*H*-Pyrazol-1-yl)acrylates

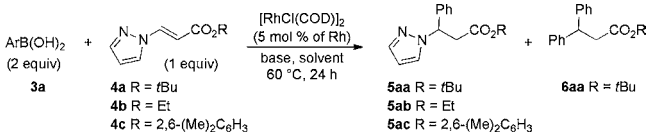
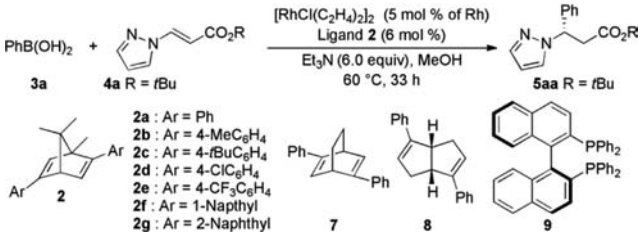


Table S1 in the Supporting Information). With a lack of precedent for the addition to *β*-pyrazol-1-yl acrylates, it was unclear whether the Rh(I) catalyst would tolerate the pyrazole moiety.[11] Although very commonly used in the Hayashi–Miyaura reaction using RhCl precatalysts in aqueous dioxane,[12] 0.5 equiv of KOH, NaOH, or K_2CO_3 proved ineffective at 60 °C providing the addition product **5aa** in only 6–17% along with the double addition product **6aa**, formed via elimination of pyrazole, in 3–9%. $NaHCO_3$, KHF_2, K_2HPO_4, and Et_3N proved equally ineffective (0–14% **5aa**; 0–10% **6aa**) under the same conditions, and although K_2CO_3, $NaHCO_3$, or K_2HPO_4 provided poor results in MeOH (5–12% **5aa**; 0–3% **6aa**), however, it was encouraging to find that the reaction of **4a** in the presence of KOH, NaOH, or KHF_2 in MeOH furnished the desired product **5aa** in much improved yields (65–88%) with none or only small amounts of side product **6aa**. To our delight, when the reaction in MeOH was conducted in the presence of 6 equiv of Et_3N, adduct **5aa** was produced in a 91% isolated yield within only 4 h. Interestingly, however, when alcohol homologues EtOH, *i*-PrOH, or *t*-BuOH were used in place of MeOH in conjunction with Et_3N, inferior results were observed (0–44% **5aa**; 0–21% **6aa**). Similarly DMF, THF, MeCN, or PhMe also gave disappointing results (0–16% **5aa**; 0–1% **6aa**). Using MeOH as solvent, an extensive screen of primary, secondary, and tertiary amines was conducted, and while most amines resulted in low to moderate yields (0–65% **5aa**; 0–5% **6aa**), *t*-$BuNH_2$ was most promising giving an 88% yield of **5aa** accompanied by 12% of double addition product **6aa**. In all, however, MeOH, which is preferred in industry to dioxane due to the toxicity of the latter, in conjunction with Et_3N proved the best and all subsequent tests therefore utilized this combination. Finally, both acrylates **4b** and **4c** proved not to be useful; ethyl acrylate **4b** underwent decomposition and provided no **5aa**, whereas no reaction occurred when using **4c**, presumably owing to steric hindrance provided by the bulky aryl ester functionality.

The asymmetric addition of phenylboronic acid (**3a**) to compound **4a** was examined next, using 5 mol % of chiral Rh(I) precatalysts prepared *in situ* from $[RhCl(C_2H_4)_2]_2$ and a family of novel 2,5-diaryl-substituted chiral diene ligands **2a**–**2g**. Although proceeding more slowly than the achiral mode of the reaction, the *β*-pyrazol-1-yl substituted ester **5aa** was obtained in isolated yields of 51–90% (Table 1, entries 1–7). While the reaction proceeded less selectively in the presence of tolyl (**2b**, entry 2) or bulky 4-*tert*-butylphenyl (**2c**, entry 3) substituted ligands, good to comparable asymmetric induction (93–96% ee) was observed when *para*-electron-withdrawing substituted aryl containing ligands were used, such as **2d** (with a 4-Cl-phenyl substituent, entry 4) and **2e** (with a 4-CF_3-phenyl substituent, entry 5), or ligands substituted with 1-naphthyl (**2f**, entry 6) or 2-naphthyl groups (**2g**, entry 7). Next, several commercially available dienes and a phosphine ligand were compared under conditions

Table 1. Asymmetric Conjugate Addition of Phenylboronic Acid (3a) to *tert*-Butyl-*β*-Pyrazol-1-yl Acrylate (4a)[a]



entry	ligand	yield[b] (%)	ee[c] (%)
1	**2a**	80	97
2	**2b**	90	91
3	**2c**	80	90
4	**2d**	73	96
5	**2e**	80	94
6	**2f**	51	95
7	**2g**	76	93
8	**7**	25	−97
9	**8**	trace	N.D.[d]
10	**9**	trace	N.D.[d]

[a]Reaction conditions: compound **4a** (0.1 mmol), **3a** (0.2 mmol), Rh(I) catalyst (5 mol % of Rh), Et_3N (0.6 mmol). [b]Isolated yield. [c]Determined by chiral HPLC on a Chiracel OD-H column. [d]N.D. = not determined.

identical to those described above. Although the bicyclo[2.2.2]-based ligand **7** provided good asymmetric induction (−97% ee), the isolated product yield (25%) was unsatisfactory (entry 8).[12] Using chiral bicyclo[3.3.0]diene ligand **8**[8e,13] (entry 9) or (*S*)-BINAP (**9**, entry 10),[14] which are known for producing high catalytic activity and enantioselectivity in the Rh(I)-catalyzed asymmetric conjugate addition to *α*,*β*-unsaturated carbonyl compounds, furnished only trace amounts of the desired product **5aa** with undetermined ee's. The above results showed that the bicyclo[2.2.1]heptadiene ligand family **2** was well suited to this asymmetric transformation and, in terms of a compromise between yield and selectivity, that ligand **2a** was the optimal chiral modifier.

The scope of the reaction was investigated next through the enantioselective addition of a large number of arylboronic acids to *tert*-butyl *β*-pyrazol-1-yl acrylate (**4a**) (Table 2) under the optimized reaction conditions identified in Table 1, entry 1. Arylboronic acids bearing alkyl and electron-donating substituents gave the corresponding arylation products **5ba**–**5ia** in 48–90% yield and in 92–99% ee (entries 2–9). The stereochemical center of compound **5ia** was unequivocally determined by X-ray crystallography to be (*S*)-configured (Figure 2) indicating that conjugate addition to the *α*-*Re* face of compound **4a** was favored using Rh(I)/**2a**, consistent with that which we have reported previously.[9a] While achieving high asymmetric induction (99% ee), the addition of 2-tolylboronic acid (**3b**) provided a low chemical yield (48%), presumably as a result of steric hindrance (entry 2). Esters **5ea**, **5fa**, and **5ga** were targeted because their methyl and benzyl ethers offer potential for further functionalization by ether cleavage following conjugate addition, as was demonstrated for **5ga** (see below). Arylboronic acids substituted with electron-withdrawing groups were tolerated offering the addition products **5ja**–**5qa** in 54–88% yield and 96–99% ee (entries 10–17). When 2-naphthylboronic acid (**3r**) was used, pyrazole **5ra** was isolated in a high 98% yield with 94% ee (entry 18). The generality of the reaction

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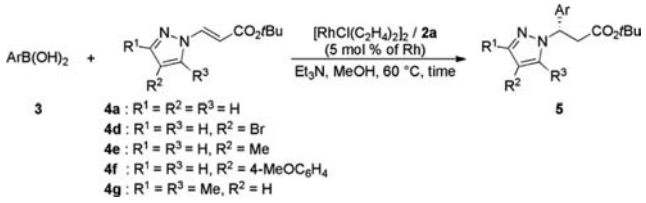
Table 2. Asymmetric Conjugate Addition of Arylboronic Acids to β-Pyrazol-1-yl Acrylates[a]



entry	Ar	substrate	time (h)	yield[b] (%)	ee[c] (%)
1	Ph (**3a**)	**4a**	33	80 (**5aa**)	97
2	2-MeC_6H_4 (**3b**)	**4a**	48	48 (**5ba**)	99
3	3-MeC_6H_4 (**3c**)	**4a**	33	85 (**5ca**)	96
4	4-MeC_6H_4 (**3d**)	**4a**	33	88 (**5da**)	96
5	3-MeOC_6H_4 (**3e**)	**4a**	25	90 (**5ea**)	93
6	4-MeOC_6H_4 (**3f**)	**4a**	25	78 (**5fa**)	96
7	4-BnOC_6H_4 (**3g**)	**4a**	60	48[d] (**5ga**)	97
8	4-*t*BuC_6H_4 (**3h**)	**4a**	33	86 (**5ha**)	92
9	4-PhC_6H_4 (**3i**)	**4a**	24	71 (**5ia**)	98
10	4-FC_6H_4 (**3j**)	**4a**	28	73 (**5ja**)	98
11	4-ClC_6H_4 (**3k**)	**4a**	24	83 (**5ka**)	98
12	3,4-$Cl_2C_6H_3$ (**3l**)	**4a**	24	70 (**5la**)	96
13	3-$CF_3C_6H_4$ (**3m**)	**4a**	26	88 (**5ma**)	98
14	4-$CF_3C_6H_4$ (**3n**)	**4a**	26	87 (**5na**)	98
15	3-$NO_2C_6H_4$ (**3o**)	**4a**	28	54 (**5oa**)	97
16	4-$NO_2C_6H_4$ (**3p**)	**4a**	26	79 (**5pa**)	98
17	4-CNC_6H_4 (**3q**)	**4a**	26	76 (**5qa**)	97
18	2-Naphthyl (**3r**)	**4a**	24	98 (**5ra**)	94
19	Ph (**3a**)	**4d**	24	55 (**5ad**)	99
20	4-PhC_6H_4 (**3h**)	**4d**	24	62 (**5hd**)	97
21	4-$NO_2C_6H_4$ (**3p**)	**4d**	24	44 (**5pd**)	91
22	2-Naphthyl (**3r**)	**4d**	24	60 (**5 rd**)	97
23	Ph (**3a**)	**4e**	32	82 (**5ae**)	96
24	Ph (**3a**)	**4f**	36	90 (**5af**)	99
25	Ph (**3a**)	**4g**	44	70 (**5ag**)	>99.5

[a]Reaction conditions: compound **4** (0.1 mmol), **3** (0.2 mmol), Rh(I) catalyst (5 mol % of Rh), and Et_3N (0.6 mmol). [b]Isolated yield. [c]Determined by chiral HPLC. [d]80% yield based on recovered **4a**.

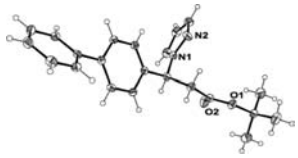
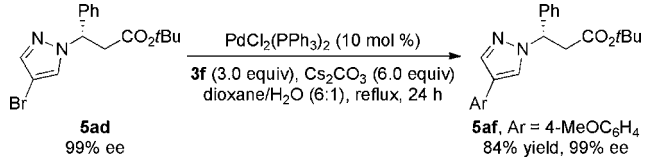


Figure 2. ORTEP illustration of compound **5ia** with thermal ellipsoid drawn at 30% probability level.

was further extended to the arylation of substituted β-pyrazol-1-yl acrylates. Reaction of acrylate **4d** with phenylboronic acid (**3a**), 4-biphenylboronic acid (**3h**), 4-nitrophenylboronic acid (**3p**), or 2-naphthylboronic acid (**3r**) provided a 44−62% yield of the corresponding addition products **5ad**, **5hd**, **5pd**, or **5rd**, respectively, in 91−99% ee (entries 19−22). Methyl and aryl substituted pyrazoles **4e**−**4g** were well tolerated, giving rise to desired products **5ae**, **5af**, and **5ad** in 70−90% yield and with up to greater than 99.5% ee (entries 23−25).

By way of example of the diversification available with the products of this reaction, compound **5ad** was cross-coupled with 4-methoxyphenylboronic acid (**3f**) to produce compound **5af** (Scheme 2).[15] We envision that further diversification should be possible by functional transformation of aryl groups harboring

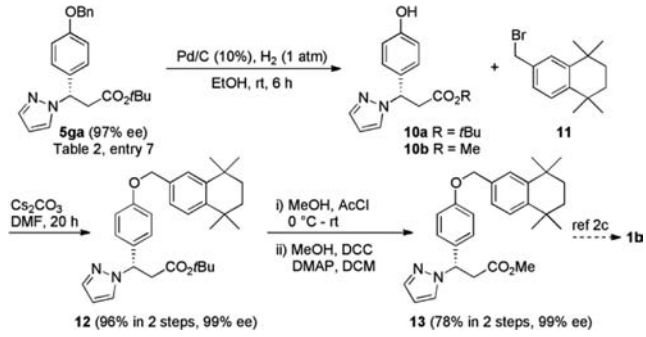
Scheme 2. Further Elaboration of the β-Pyrazol-1-yl Core to Provide Compound 5af



nitrile, methyl and benzyl ethers, or even chloride[16] which, for example, could be converted to amides, reverse amides, amines, sulfonamides, esters, biaryl ethers, or even biaryls, and this could prove useful for the generation of medicinal chemistry compound libraries.

Finally, to demonstrate the synthetic utility of this methodology the formal synthesis of bioactive compound **1b** was conducted (Scheme 3). Hydrogenolysis of enantioenriched

Scheme 3. Formal Synthesis of β-Aryl-β-pyrazol-1-yl Propanoic Acid Agonistic 1b



pyrazole **5ga** (Table 2, entry 7) offered phenol **10a** in quantitative yield, which was *O*-alkylated with commercially available benzyl bromide **11** to provide benzyl ether **12** in 96% yield over two steps without loss of enantiopurity. Transesterification using AcCl and MeOH followed by DCC promoted coupling with MeOH provided the reported β-pyrazolyl ester **13**. This precursor was prepared previously[2b] using a nonstereoselective double alkylation, oxidative double bond cleavage and esterification sequence that required chiral HPLC separation of the racemate of **10b** followed by alkylation with **11** to give **13**. Hydrolysis of **13** is known to furnish **1b**.[2b]

In conclusion, the first example of the asymmetric conjugate addition of arylboronic acids to β-pyrazol-1-yl acrylates, which are readily prepared by the 1,4-addition of the corresponding pyrazoles to *tert*-butyl propiolate, in the presence of a chiral Rh(I)-catalyst, generated *in situ* from $[RhCl(C_2H_4)_2]_2$ and chiral diene ligands, has been reported. This method affords the corresponding arylation products in good to high yields with high to excellent ee's and proceeds best in the industrially acceptable solvent MeOH using Et_3N as the base. The reaction generally provides higher ee's than does the corresponding aza-Michael reaction for similar compounds in the presence of chiral organocatalysts and, therefore, offers an alternative approach for the preparation of such compounds.[5d,f] The reaction is compatible with a range of aryl functionality as well as a range of substituted pyrazole derivatives, including 4-bromo-pyrazol-1-yl derivatives, that can be further functionalized subsequent to the conjugate addition step, as was demonstrated using a Pd-catalyzed cross-coupling reaction of **5ad** to afford **5af**. Further diversification useful for the generation of medicinal chemistry

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libraries should be possible by use of arylboronic acids with other reactive and functionalizable substituents such as nitrile, ether, or halide. By way of demonstration the formal synthesis of (3*S*)-*β*-aryl-*β*-pyrazol-1-yl propanoic acid **1b** was performed.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and complete characterization of addition products (NMR spectra, HPLC chromatograms). 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) (a) *Alkaloids, Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Elsevier Science, Ltd.: Oxford, 1999. (b) Dewick, P. M. *Medicinal Natural Products: A Biosynthetic Approach*, 3rd ed.; John Wiley & Sons, Ltd.: Chichester, 2009.

(2) (a) Park, C.-M.; Jeon, D.-J. *Org. Biomol. Chem.* **2012**, *10*, 2613. (b) Brown, S. P.; Dransfield, P.; Houze, J. B.; Liu, J.; Liu, J.; Ma, Z.; Medina, J. C.; Pattaropond, V.; Schmitt, M. J.; Sharma, R.; Wang, Y.; U.S. Patent 7,687,526, 2010. (c) Mesa, R. A.; Yasothan, U.; Kirkpatrick, P. *Nat. Rev. Drug Discovery* **2012**, *11*, 103.

(3) (a) John, E. S.; David, A.; Carol, S. *Immunopharmacology* **2000**, *47*, 127. (b) Miles, D. H.; Peter, S.; Kam, Y. J. Z. *Drug Discovery Today* **2005**, *10*, 1503.

(4) For seminal reviews on enantioselective aza-Michael additions, see: (a) Vicario, J. L.; Badía, D.; Carrillo, L.; Etxebarria, J.; Reyes, E.; Ruiz, N. *Org. Prep. Proced. Int.* **2005**, *37*, 513. (b) Xu, L. W.; Xia, C. G. *Eur. J. Org. Chem.* **2005**, 633. (c) Vicario, J. L.; Badía, D.; Carrillo, L. *Synthesis* **2007**, 2065. (d) Enders, D.; Wang, C.; Liebich, J. X. *Chem.—Eur. J.* **2009**, *15*, 11058. (e) Krishna, P. R.; Sreeshailam, A.; Srinivas, R. *Tetrahedron* **2009**, *65*, 9657. (f) Wang, J.; Li, P.; Choy, P. Y.; Chan, A. S. C.; Kwong, F. Y. *ChemCatChem* **2012**, *4*, 917.

(5) (a) Dinér, P.; Nielsen, M.; Marigo, M.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 1983. (b) Wang, J.; Zu, L.; Li, H.; Xie, H.; Wang, W. *Synthesis* **2007**, 2576. (c) Uria, U.; Vicario, J. L.; Badia, D.; Carrillo, L. *Chem. Commun.* **2007**, 2509. (d) Lin, Q.; Meloni, D.; Xia, M.; Rodgers, J.; Shepard, S.; Li, M.; Galya, L.; Metcalf, B.; Yue, T.-Y.; Liu, P.; Zhou, J. *Org. Lett.* **2009**, *11*, 1999. (e) Gogoi, S.; Zhao, C.-G.; Ding, D. *Org. Lett.* **2009**, *11*, 2249. (f) Li, P.; Fang, F.; Chen, J.; Wang, J. *Tetrahedron: Asymmetry* **2014**, *25*, 98.

(6) (a) *Conjugate Addition Reactions in Organic Synthesis*; Perlmutter, P., Ed.; Pergamon Press: Oxford, UK, 1992. (b) Schmalz, H.-G. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, UK, 1991; Vol. 4, Chapter 1.5. (c) Rossiter, B. E.; Swingle, N. M. *Chem. Rev.* **1992**, *92*, 771. (d) Tomioka, K.; Nagaoka, Y. *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag: Berlin, 1999; Chapter 31.1. (e) Yamaguchi, M. *Comprehensive Asymmetric Synthesis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag: Berlin, 1999; Chapter 31.2. (f) Krause, N.; Hoffmann-Roder, A. *Synthesis* **2001**, 171.

(7) (a) Miyaura, N. *Organoboranes for Syntheses*; Ramachandran, P. V., Brown, H. C., Eds.; American Chemical Society: Washington, D.C., 2001; p 94. (b) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829. (c) Hayashi, T. *Pure. Appl. Chem.* **2004**, *76*, 465. (d) Edwards, H. J.; Hargrave, J. D.; Penrose, S. D.; Frost, C. G. *Chem. Soc. Rev.* **2010**, *39*, 2093.

(8) For seminal reviews on chiral ligands containing olefins, see: (a) Glorius, F. *Angew. Chem., Int. Ed.* **2004**, *43*, 3364. (b) Johnson, J. B.; Rovis, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 840. (c) Defieber, C.; Grützmacher, H.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 4482. (d) Shintani, R.; Hayashi, T. *Aldrichimica Acta* **2009**, *42*, 31. (e) Feng, C.-G.; Xu, M.-H.; Lin, G.-Q. *Synlett* **2011**, *10*, 1345. (f) Tian, P.; Dong, H.-Q.; Lin, G.-Q. *ACS Catal.* **2012**, *2*, 95. (g) Feng, X.; Du, H. *Asian J. Org. Chem.* **2012**, *1*, 204. For recent significant work, see: (h) Fischer, C.; Defieber, C.; Suzuki, T.; Carreira, E. M. *J. Am. Chem. Soc.* **2004**, *126*, 1628. (i) Defieber, C.; Paquin, J.-F.; Serna, S.; Carreira, E. M. *Org. Lett.* **2004**, *6*, 3873. (j) Paquin, J.-F.; Stephenson, C. R. J.; Defieber, C.; Carreira, E. M. *Org. Lett.* **2005**, *7*, 3821. (k) Paquin, J.-F.; Defieber, C.; Stephenson, C. R. J.; Carreira, E. M. *J. Am. Chem. Soc.* **2005**, *127*, 10850. (l) Gendrineau, T.; Genet, J.-P.; Darses, S. *Org. Lett.* **2009**, *11*, 3486. (m) Hu, X.; Zhuang, M.; Cao, Z.; Du, H. *Org. Lett.* **2009**, *11*, 4744. (n) Brown, M. K.; Corey, E. J. *Org. Lett.* **2010**, *12*, 172. (o) Gendrineau, T.; Genet, J.-P.; Darses, S. *Org. Lett.* **2010**, *12*, 308. (p) Wang, Y.; Hu, X.; Du, H. *Org. Lett.* **2010**, *12*, 5482. (q) Li, Q.; Dong, Z.; Yu, Z.-X. *Org. Lett.* **2011**, *13*, 1122. (r) Trost, B. M.; Burns, A. C.; Tautz, T. *Org. Lett.* **2011**, *13*, 4566. (s) Low, D. W.; Pattison, G.; Wieczysty, M. D.; Churchill, G. H.; Lam, H. W. *Org. Lett.* **2012**, *14*, 2548. (t) Chen, Y.-J.; Chen, Y.-H.; Feng, C.-G.; Lin, G.-Q. *Org. Lett.* **2014**, *16*, 3400.

(9) (a) Wei, W.-T.; Yeh, J.-Y.; Kuo, T.-S.; Wu, H.-L. *Chem.—Eur. J.* **2011**, *17*, 11405. (b) Liu, C.-C.; Janmanchi, D.; Chen, C.-C.; Wu, H.-L. *Eur. J. Org. Chem.* **2012**, 2503. (c) Chung, Y.-C.; Janmanchi, D.; Wu, H.-L. *Org. Lett.* **2012**, *14*, 2766. (d) Huang, K.-C.; Gopula, B.; Kuo, T.-S.; Chiang, C.-W.; Wu, P.-Y.; Henschke, J. P.; Wu, H.-L. *Org. Lett.* **2013**, *15*, 5730. (e) Gopula, B.; Chiang, C.-W.; Lee, W.-Z.; Kuo, T.-S.; Wu, P.-Y.; Henschke, J. P.; Wu, H.-L. *Org. Lett.* **2014**, *16*, 632. (f) Chen, C.-C.; Gopula, B.; Syu, J.-F.; Pan, J.-H.; Kuo, T.-S.; Wu, P.-Y.; Henschke, J. P.; Wu, H.-L. *J. Org. Chem.* **2014**, *79*, 8077. (g) Wu, H.-L, Chen C.-C., Liu, C.-C., Wei, W.-T., Fang, J.-H. U.S. Patent 8,586,810, 2013.

(10) See the only example of Rh(I)-catalyzed addition of boron compounds to acrylates with a nitrogen atom (phthaloyl protected) directly affixed to the *β*-position: Nishmura, T.; Wang, J.; Nagaosa, M.; Okamoto, K.; Shintani, R.; Kwong, F.-Y.; Yu, W.-Y.; Chan, A. S. C.; Hayashi, T. *J. Am. Chem. Soc.* **2010**, *132*, 464.

(11) Chen, L. Z.; Flammang, R.; Maquestiau, A.; Taft, R. W.; Catalan, J.; Cabildo, P.; Claramunt, R. M.; Elguero, J. *J. Org. Chem.* **1991**, *56*, 179.

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

(13) Helbig, S.; Sauer, S.; Cramer, N.; Laschat, S.; Baro, A.; Frey, W. *Adv. Synth. Catal.* **2007**, *349*, 2331.

(14) Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. *J. Am. Chem. Soc.* **1998**, *120*, 5579.

(15) Migliorini, A.; Oliviero, C.; Gasperi, T.; Loreto, M. A. *Molecules* **2012**, *17*, 4508.

(16) (a) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722. (b) Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 2719.

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