Organic LETTERS

Letter

pubs.acs.org/OrgLett

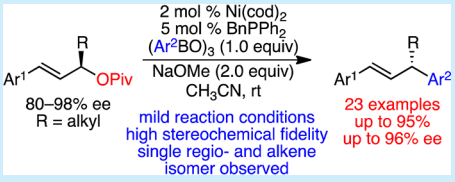
Enantiospecific, Nickel-Catalyzed Cross-Couplings of Allylic Pivalates and Arylboroxines

Harathi D. Srinivas,‡ Qi Zhou,‡ and Mary P. Watson*

Department of Chemistry and Biochemistry, University of Delaware, Newark, Delaware 19716, United States

Supporting Information

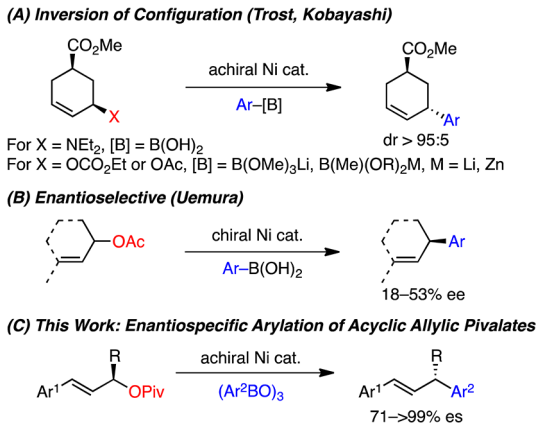
ABSTRACT: We have developed an enantiospecific, nickel-catalyzed cross-coupling of unsymmetric 1,3-disubstituted allylic pivalates with arylboroxines. The success of this reaction relies on the use of $BnPPh_2$ as a supporting ligand for the nickel(0) catalyst and NaOMe as a base. This method shows excellent functional group tolerance and broad scope in both the allylic pivalate and arylboroxine, enabling the preparation of 1,3-diaryl allylic products in high yields with excellent levels of regioselectivity and stereochemical fidelity.



Transition-metal-catalyzed allylic substitution provides an important method of C−C bond formation.[1] In particular, enantioselective or -specific arylation of readily accessible 1,3-disubstituted secondary allylic electrophiles enables facile construction of enantioenriched products equipped with vinyl-substituted benzylic carbon stereocenters. These products are useful both as synthetic intermediates and for their potential biological activity.[2] An ideal cross-coupling method to deliver these valuable enantioenriched products would enable high levels of enantiospecificity (or enantioselectivity) and regioselectivity, wide functional group tolerance, and the use of an air-stable coupling partner (such as an arylboronic reagent).[3,4] Toward these goals, Rh- and Pd-catalyzed cross-couplings of allylic electrophiles and arylboronic acids have been developed to deliver highly enantioenriched products.[5−10] However, the additional goal of developing nonprecious metal catalysts is also important in lowering the cost, ensuring adequate supplies of catalysts for large-scale applications, and reducing the environmental impact of this chemistry.[11] In contrast to the methods developed with precious metal catalysts, the use of nonprecious metal catalysts for enantiospecific or -selective allylic arylations is less developed and often requires use of air-sensitive aryl nucleophiles that may have incompatibilities with some functional groups. For example, formation of enantioenriched products via Cu-catalyzed allylic arylations largely relies on the use of Grignard, organozinc, or organoaluminum reagents;[12−16] only a limited number of methods allow the use of arylboronates.[17−19]

Based on our studies of enantiospecific, Ni-catalyzed couplings of benzylic pivalates and arylboroxines,[20] we envisioned that Ni-based catalysts may also serve as efficient, nonprecious metal catalysts for highly enantiospecific and regioselective couplings of 1,3-disubstituted allylic pivalates with aryl boroxines. Prior art in this area has indeed demonstrated that nickel catalysts efficiently catalyze the cross-coupling of allylic electrophiles with aryl Grignard reagents, with both diastereo- and enantioselective variants reported.[21−23] Trost and Kobayashi have also shown that more functional group tolerant borate and boronic acid nucleophiles can be used in cross-couplings with allylic amines and carbonates, respectively.[24,25] With respect to the stereochemical outcome of these reactions, they have demonstrated that the arylation of *cyclic* allylic electrophiles occurs with inversion of configuration, and Kobayashi has exploited this in the arylation of cyclopentene diol derivatives to deliver enantioenriched products (Scheme 1A).[24a−e,25] In addition,

Scheme 1. Enantioselective and Enantiospecific Nickel-Catalyzed Allylic Arylation with Arylboron Reagents



Uemura has reported a moderately enantioselective, Ni-catalyzed coupling of symmetric and terminal allylic acetates with arylboronic acids (Scheme 1B).[26] However, to our knowledge, there are no reports of enantiospecific, Ni-catalyzed cross-couplings of *acyclic* allylic electrophiles and arylboron reagents to deliver highly enantioenriched products.

Herein we report the first enantiospecific, Ni-catalyzed cross-coupling of acyclic, 1,3-disubstituted allylic pivalates and arylboroxines (Scheme 1C). This method enables efficient transformation of readily available, highly enantioenriched allylic

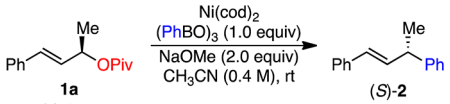
Received: June 10, 2014
Published: June 13, 2014

   dx.doi.org/10.1021/ol5016724 | *Org. Lett.* 2014, 16, 3596−3599

pivalates to valuable 1,3-diaryl allylic products in good yields with excellent regioselectivities and levels of stereochemical fidelity.

Our initial investigations focused on the coupling of pivalate **1a**, easily prepared in 96% ee via a CBS reduction/pivalation sequence, with phenylboroxine (Table 1). Under optimal

Table 1. Optimization of Reaction Conditions[a]



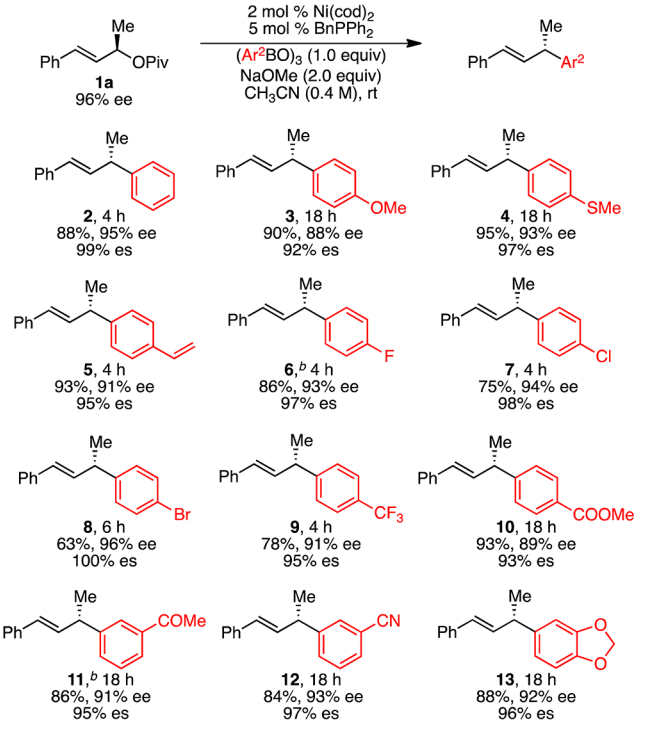
entry	mol % [Ni]	ligand (mol %)	temp (°C)	yield[b] (%)	ee[c] (%)
1[d]	10	none	50	95	18
2	10	none	50	96	57
3	10	dppp (11)[e]	50	90	57
4	10	XantPhos (11)[e]	50	30	27
5	10	PCy_3 (22)	50	80	84
6	10	$CyPPh_2$ (22)	50	83	85
7	10	$BnPPh_2$ (22)	50	85	87
8	10	$BnPPh_2$ (22)	rt	90	87
9	5	$BnPPh_2$ (11)	rt	90	92
10	2	$BnPPh_2$ (5)	rt	92	94
11[f]	2	$BnPPh_2$ (5)	rt	72	93
12[g]	2	$BnPPh_2$ (5)	rt	86	94

[a]Conditions: pivalate **1a** (96% ee, 0.1 mmol, 1.0 equiv), $(PhBO)_3$ (1.0 equiv), $Ni(cod)_2$, ligand, NaOMe (2.0 equiv), CH_3CN (0.25 mL, 0.4 M), 4 h, unless otherwise noted. [b]Determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as internal standard. [c]Determined by HPLC analysis using a chiral stationary phase. [d]PhMe instead of CH_3CN. [e]dppp = 1,3-bis(diphenylphosphino)propane. XantPhos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene. [f]$PhB(OH)_2$ (3.0 equiv). [g]H_2O (1.5 equiv) added.

conditions for the coupling of benzylic pivalates [$Ni(cod)_2$, no additional phosphine ligand, PhMe], desired coupling product **2** was obtained in excellent yield. However, only 18% ee of product was observed (entry 1). Changing the solvent to MeCN resulted in higher enantiomeric excess (ee) of the product (57% ee) in similar yield (entry 2). In an effort to improve the stereochemical fidelity further, we investigated phosphine ligands to support the Ni catalyst. Although bidentate phosphine ligands led to poor ee's of product (entries 3, 4), the use of monodentate phosphine ligands resulted in significant improvement (entries 5–7). Among the ligands examined, benzyl diphenyl phosphine ($BnPPh_2$) proved to be the best (entry 7). Reducing the reaction temperature gave an increased yield (entry 8). Further increases in yield and ee were obtained when the catalyst loading was lowered to 2 mol % (entries 9, 10). The observation of higher levels of stereochemical fidelity at lower catalyst loadings may suggest a Ni-mediated epimerization pathway.[27] Under these optimized conditions, the use of phenylboronic acid in place of phenylboroxine led to a lower yield but with the same ee (entry 11). The reason for this difference is currently unclear, but does not seem to be due to the reaction's sensitivity to water. Addition of water to the reaction resulted in only a slightly reduced yield (entry 12).

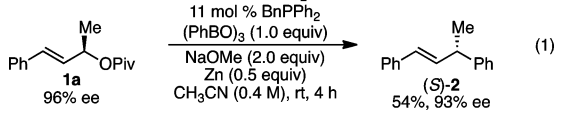
Under our optimized conditions (Table 1, entry 10), we observed a broad scope with respect to the arylboroxine (Scheme 2).[28] In all cases in Schemes 2 and 3, excellent regioselectivity and E/Z selectivity were observed; only α-aryl products with E-olefins were formed. High yields and excellent levels of stereochemical fidelity were obtained with arylboroxines bearing

Scheme 2. Scope of Arylboroxine[a]



[a]Conditions: pivalate **1a** (96% ee, 0.3 mmol, 1.0 equiv), $(PhBO)_3$ (1.0 equiv), $Ni(cod)_2$ (2 mol %), $BnPPh_2$ (5 mol %), NaOMe (2.0 equiv), CH_3CN (0.75 mL, 0.4 M), rt, unless otherwise noted. Average yields (±3%) and ee's (±1%) of isolated products of duplicate reactions. Ee determined by HPLC analysis using a chiral stationary phase. es = (ee of product)/(ee of starting material). [b] **1a** (95% ee).

either electron-donating or -withdrawing groups (**2**–**13**). A wide range of functional groups were tolerated including ether (**3**), thioether (**4**), vinyl (**5**), halide (**6**–**8**), trifluoromethyl (**9**), ester (**10**), ketone (**11**), nitrile (**12**), and acetal (**13**) groups. In particular, the vinyl, bromide, chloride, and thioether groups highlight the mildness of these reaction conditions; undesired Ni-catalyzed reactions of these groups do not occur under our conditions. Notably, the Ni(0) catalyst generated in situ from $NiBr_2$, $BnPPh_2$, and Zn was also effective in this arylation, providing product **2** in the same ee as with $Ni(cod)_2$, albeit in somewhat reduced yield (eq 1). These conditions enable a benchtop setup of the arylation reaction.

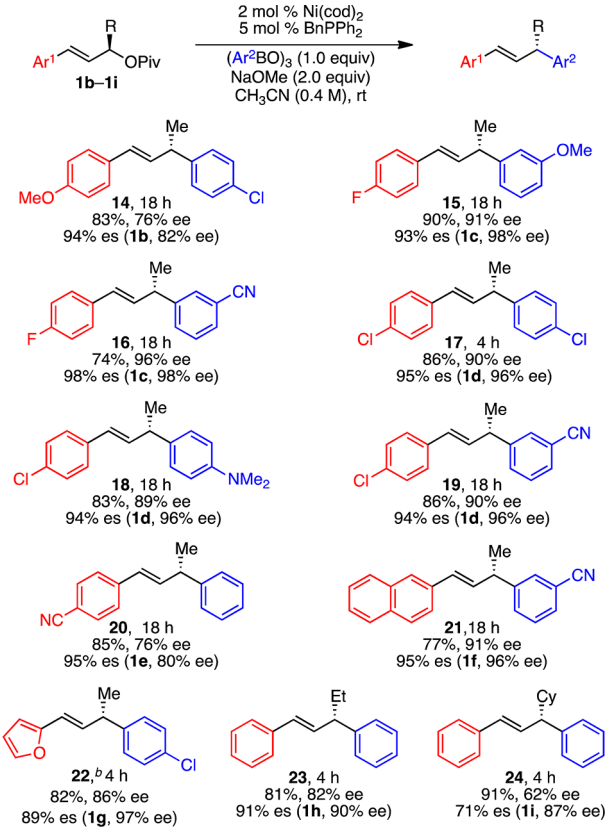


(1)

With respect to the allylic pivalate, pivalates with both electron-rich and -deficient aryl substituents efficiently underwent arylation (Scheme 3, **14**–**20**). As had been true of the arylboroxine, aryl chlorides are also well tolerated on the allylic pivalate, again highlighting the orthogonality of this reaction to aryl chlorides (**17**–**19**). In addition to the functional groups already demonstrated on the arylboroxine, a tertiary amine was well tolerated (**18**). Allylic pivalates with naphthyl and heteroaryl substituents were also successfully coupled (**21**, **22**). In terms of the alkyl substituent (R) on the allylic pivalate, increased steric hindrance did not diminish reactivity, but lower levels of

dx.doi.org/10.1021/ol5016724 | Org. Lett. 2014, 16, 3596–3599

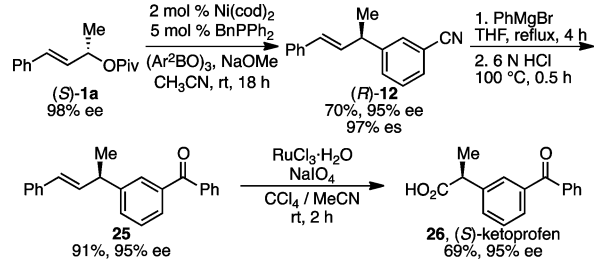
Scheme 3. Scope of Pivalates[a]



[a]Conditions: pivalates **1b−1i** (0.3 mmol, 1.0 equiv), $(PhBO)_3$ (1.0 equiv), $Ni(cod)_2$ (2 mol %), $BnPPh_2$ (5 mol %), NaOMe (2.0 equiv), CH_3CN (0.75 mL, 0.4 M), rt, unless otherwise noted. Average yields (±3%) and ee's (±1%) of isolated products of duplicate reactions. Ee determined by HPLC analysis using a chiral stationary phase. es = (ee of product)/(ee of starting material); corresponding starting materials and their ee's in parentheses. [b] Single experiment.

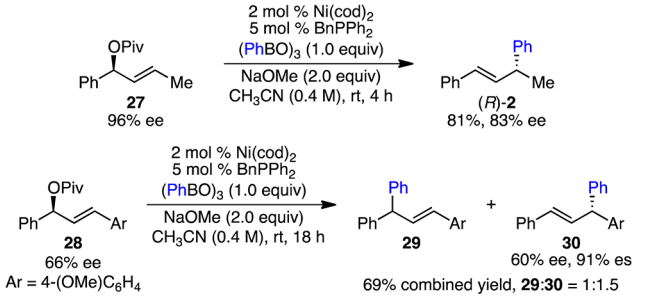
stereochemical fidelity were observed with cyclohexyl-substituted **1i** (**23**, **24**). The X-ray crystallographic analysis of product **17** shows that its absolute configuration is *S*,[29] which indicates that the reaction proceeds with inversion of configuration. To confirm further the stereochemical outcome and demonstrate the utility of this arylation method, compound (*R*)-**12**, prepared in 95% ee via the arylation of (*S*)-**1a**, was converted to (*S*)-ketoprofen (**26**), an anti-inflammatory drug, via a two-step manipulation (Scheme 4). Comparison of the optical rotation of **26** to previously reported values confirms its absolute configuration is *S*.[30] The absolute configurations of other products were assigned by analogy.

Scheme 4. Synthesis of (*S*)-Ketoprofen



Consistent with previous Ni-catalyzed allylations, we propose that this reaction proceeds through a π-allylnickel intermediate.[21−26,31] To test this hypothesis, we subjected pivalate **27** (96% ee), a regioisomer of **1a**, to the reaction conditions. Product (*R*)-**2** was formed in 81% yield and 83% ee with inversion of the absolute stereochemistry (Scheme 5). The

Scheme 5. Regioselectivity Studies



reason for the mild erosion of ee is unclear, but may be due to epimerization of a faster formed π-allylnickel intermediate. The observation that both regioisomers of starting material (**1a** and **27**) lead to the same product (**2**) supports the intermediacy of an η^3-allylnickel complex. Also consistent with an η^3-allylnickel intermediate, the arylation of 1,3-diaryl-substituted **28** resulted in a 1:1.5 ratio of regioisomers **29** and **30** (Scheme 5). Despite the modest regioselectivity, it is notable that **30** was obtained with 91% es.

In conclusion, we have developed an enantiospecific, Ni-catalyzed cross-coupling of enantioenriched secondary allylic pivalates and arylboroxines to deliver 1,3-diaryl allyl products. The method features mild conditions that allow broad functional group tolerance on both the allylic pivalate and arylboroxine. In all cases, good yields and excellent levels of regioselectivity, *E*/*Z* selectivity, and stereochemical fidelity were observed. In addition, air-stable, less expensive $NiBr_2$ can be used as an alternative to $Ni(cod)_2$. Studies exploring other substrate classes as well as details of the mechanism are currently ongoing and will be reported in due course.

■ ASSOCIATED CONTENT

Supporting Information

Full experimental data, details on methods and starting materials, and copies of spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: mpwatson@udel.edu.

Author Contributions

‡These authors contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

NSF (CAREER CHE 1151364) is gratefully acknowledged. We thank AstraZeneca for donated boronic acids. Data were acquired at UD on instruments obtained with the assistance of NSF and NIH funding (NSF CHE0421224, CHE 1229234, and CHE0840401; NIH P20 GM103541 and S10 RR02692).

dx.doi.org/10.1021/ol5016724 | *Org. Lett.* 2014, 16, 3596−3599

REFERENCES

(1) (a) Tsuji, J. *Acc. Chem. Res.* **1969**, *2*, 144. (b) Trost, B. M. *Tetrahedron* **1977**, *33*, 2615. (c) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (d) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921. (e) Kazmaier, U.; Pohlman, M. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; de Meijere, A., Diederich, F., Eds; Wiley-VCH: Weinheim, 2004; Vol. *2*, pp 531−583. (f) Helmchen, G.; Kazmaier, U.; Forster, S. In *Catalytic Asymmetric Synthesis*, 3rd ed.; Ojima, I., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, 2010.

(2) (a) Belloni, P. N.; Jolidon, S.; Klaus, M.; Lapierre, J.-M. Rar Selective Retinoid Agonists. U.S. Patent 2002/0026060 A1, Feb. 28, 2002. (b) Klaus, M.; Lapierre, J.-M. Heterocyclic Retinoid Compounds. U.S. Patent 2003/0158178A1, Aug. 21, 2003. (c) Horibe, H.; Fukuda, Y.; Kondo, K.; Okuno, H.; Murakami, Y.; Aoyama, T. *Tetrahedron* **2004**, *60*, 10701.

(3) Pigge, F. C. *Synthesis* **2010**, 1745.

(4) For representative reviews of Suzuki cross-couplings, see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147. (c) Suzuki, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 6722.

(5) For rhodium-catalyzed desymmetrizations of allylic diol derivatives, see: (a) Lautens, M.; Dockendorff, C.; Fagnou, K.; Malicki, A. *Org. Lett.* **2002**, *4*, 1311. (b) Menard, F.; Chapman, T. M.; Dockendorff, C.; Lautens, M. *Org. Lett.* **2006**, *8*, 4569. (c) Menard, F.; Perez, D.; Sustac Roman, D.; Chapman, T. M.; Lautens, M. *J. Org. Chem.* **2010**, *75*, 4056. (d) Miura, T.; Takahashi, Y.; Murakami, M. *Chem. Commun.* **2007**, 595. (e) Yu, B.; Menard, F.; Isono, N.; Lautens, M. *Synthesis* **2009**, 853.

(6) For enantioselective, rhodium-catalyzed arylations of nitroallyl acetates, see: (a) Dong, L.; Xu, Y.-J.; Cun, L.-F.; Cui, X.; Mi, A.-Q.; Jiang, Y.-Z.; Gong, L.-Z. *Org. Lett.* **2005**, *7*, 4285. (b) Dong, L.; Xu, Y.-J.; Yuan, W.-C.; Cui, X.; Cun, L.-F.; Gong, L.-Z. *Eur. J. Org. Chem.* **2006**, 4093.

(7) Enantioselective, rhodium-catalyzed arylations have also been accomplished with arylzinc reagents. See: Evans, P. A.; Uraguchi, D. *J. Am. Chem. Soc.* **2003**, *125*, 7158.

(8) For enantiospecific, palladium-catalyzed arylations of allylic alcohols and derivatives, see: (a) Ohmiya, H.; Makida, Y.; Tanaka, T.; Sawamura, M. *J. Am. Chem. Soc.* **2008**, *130*, 17276. (b) Li, D.; Tanaka, T.; Ohmiya, H.; Sawamura, M. *Org. Lett.* **2010**, *12*, 3344. (c) Ohmiya, H.; Makida, Y.; Li, D.; Tanabe, M.; Sawamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 879. (d) Makida, Y.; Ohmiya, H.; Sawamura, M. *Chem.—Asian J.* **2011**, *6*, 410. (e) Li, C.-G.; Xing, J.-X.; Zhao, J.-M.; Huynh, P.; Zhang, W.-B.; Jiang, P.-K.; Zhang, Y.-J. *Org. Lett.* **2012**, *14*, 390. (f) Zhao, J.-M.; Ye, J.; Zhang, Y.-J. *Adv. Synth. Catal.* **2013**, *355*, 491. (g) Wu, H.-B.; Ma, X.-T.; Tian, S.-K. *Chem. Commun.* **2014**, *50*, 219.

(9) For enantiospecific, palladium-catalyzed coupling of allylic boronates with aryl iodides, see: Chausset-Boissari, L.; Ghozati, K.; LaBine, E.; Chen, J. L.-Y.; Aggarwal, V. K.; Crudden, C. M. *Chem.—Eur. J.* **2013**, *19*, 17698.

(10) For an enantioselective, iridium-catalyzed arylation with an organozinc, see: Polet, D.; Rathgeb, X.; Falciola, C. A.; Langlois, J.-B.; El Hajjaji, S.; Alexakis, A. *Chem.—Eur. J.* **2009**, *15*, 1205.

(11) For the importance of developing nonprecious metal catalysts, see: (a) Bullock, R. M. *Catalysis without Precious Metals*; Wiley-VCH: Weinheim, 2010. (b) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. *Chem. Rev.* **2011**, *111*, 1346. (c) Han, F.-S. *Chem. Soc. Rev.* **2013**, *42*, 5270. (d) Yamaguchi, J.; Muto, K.; Itami, K. *Eur. J. Org. Chem.* **2013**, 19.

(12) Falciola, C. A.; Alexakis, A. *Eur. J. Org. Chem.* **2008**, *2008*, 3765.

(13) For enantioselective, copper-catalyzed arylations with Grignard reagents, see: (a) Selim, K. B.; Yamada, K.-i.; Tomioka, K. *Chem. Commun.* **2008**, 5140. (b) Selim, K. B.; Matsumoto, Y.; Yamada, K.-i.; Tomioka, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 8733. (c) Lopez, F.; van Zijl, A. W.; Minnaard, A. J.; Feringa, B. L. *Chem. Commun.* **2006**, 409.

(14) For enantiospecific, copper-catalyzed arylations with Grignard reagents, see: (a) Norinder, J.; Bäckvall, J.-E. *Chem.—Eur. J.* **2007**, *13*, 4094. (b) Norinder, J.; Bogár, K.; Kanupp, L.; Bäckvall, J.-E. *Org. Lett.* **2007**, *9*, 5095. (c) Thalén, L. K.; Sumic, A.; Bogár, K.; Norinder, J.; Persson, A. K. Å.; Bäckvall, J.-E. *J. Org. Chem.* **2010**, *75*, 6842. (d) Li, M.-B.; Tang, X.-L.; Tian, S.-K. *Adv. Synth. Catal.* **2011**, *353*, 1980. (e) See also: Lauer, A. M.; Mahmud, F.; Wu, J. *J. Am. Chem. Soc.* **2011**, *133*, 9119.

(15) For enantioselective, copper-catalyzed arylations using organozinc reagents, see: Kacprzynski, M. A.; May, T. L.; Kazane, S. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 4554.

(16) For enantioselective, copper-catalyzed arylations and vinylations using organoaluminum reagents, see: (a) Gao, F.; Lee, Y.-M.; Mandai, K.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 8370. (b) Lee, Y.; Akiyama, K.; Gillingham, D. G.; Brown, M. K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 446.

(17) For enantioselective, copper-catalyzed arylations with arylboronates, see: Shintani, R.; Takatsu, K.; Takeda, M.; Hayashi, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 8656.

(18) For enantiospecific, copper-catalyzed arylations with arylboronates, see: Ohmiya, H.; Yokokawa, N.; Sawamura, M. *Org. Lett.* **2010**, *12*, 2438.

(19) See also: Whittaker, A. M.; Rucker, R. P.; Lalic, G. *Org. Lett.* **2010**, *12*, 3216.

(20) (a) Zhou, Q.; Srinivas, H. D.; Dasgupta, S.; Watson, M. P. *J. Am. Chem. Soc.* **2013**, *135*, 3307. (b) See also: Harris, M. R.; Hanna, L. E.; Greene, M. A.; Moore, C. E.; Jarvo, E. R. *J. Am. Chem. Soc.* **2013**, *135*, 3303.

(21) For a phosphine-directed, diastereoselective arylation of allylic ethers with Grignard reagents, see: Didiuk, M. T.; Morken, J. P.; Hoveyda, A. H. *Tetrahedron* **1998**, *54*, 1117.

(22) For seminal work in enantioselective, nickel-catalyzed arylations using aryl Grignard reagents, see: (a) Consiglio, G.; Morandini, F.; Piccolo, O. *J. Chem. Soc., Chem. Commun.* **1983**, 112. (b) Hiyama, T.; Wakasa, N. *Tetrahedron Lett.* **1985**, *26*, 3259. (c) Consiglio, G.; Piccolo, O.; Roncetti, L.; Morandini, F. *Tetrahedron* **1986**, *42*, 2043. (d) Consiglio, G.; Waymouth, R. M. *Chem. Rev.* **1989**, *89*, 257.

(23) Hayashi, T.; Konishi, M.; Yokota, K.-I.; Kumada, M. *J. Organomet. Chem.* **1985**, *285*, 359.

(24) (a) Kobayashi, Y.; Tokoro, Y.; Watatani, K. *Tetrahedron Lett.* **1998**, *39*, 7537. (b) Kobayashi, Y.; Mizojiri, R.; Ikeda, E. *J. Org. Chem.* **1996**, *61*, 5391. (c) Kobayashi, Y.; Watatani, K.; Kikori, Y.; Mizojiri, R. *Tetrahedron Lett.* **1996**, *37*, 6125. (d) Kobayashi, Y.; Takahisa, E.; Usmani, S. B. *Tetrahedron Lett.* **1998**, *39*, 597. (e) Kobayashi, Y.; Tokoro, Y.; Watatani, K. *Eur. J. Org. Chem.* **2000**, 3825. (f) For the related coupling of allylic acetates with vinyl borates, see: Usmani, S. B.; Takahisa, E.; Kobayashi, Y. *Tetrahedron Lett.* **1998**, *39*, 601.

(25) Trost, B. M.; Spagnol, M. D. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2083.

(26) (a) Chung, K.-G.; Miyake, Y.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 15. (b) For the related coupling of alkynyl borates with allylic carbonates, including a modestly enantioselective example, see: Chen, H.; Deng, M.-Z. *J. Organomet. Chem.* **2000**, *603*, 189.

(27) A similar effect was observed in the nickel-catalyzed coupling of benzylic ammonium triflates; see: Maity, P.; Shacklady-McAtee, D. M.; Yap, G. P. A.; Sirianni, E. R.; Watson, M. P. *J. Am. Chem. Soc.* **2013**, *135*, 280.

(28) We use "% es" (or % enantiospecificity) to indicate the percentage of the reaction that proceeds via the enantiospecific pathway. es = (ee of product)/(ee of starting material).

(29) CCDC 973168 contains the supplementary crystallographic data for **17**. The data can be obtained from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif free of charge. These data are also included in the Supporting Information.

(30) (a) Allen, A. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2011**, *133*, 4260. (b) Shiina, I.; Nakata, K.; Onda, Y. *Eur. J. Org. Chem.* **2008**, 5887. (c) Fadel, A. *Synlett* **1992**, *1992*, 48.

(31) (a) Felkin, H.; Swierczewski, G. *Tetrahedron Lett.* **1972**, *13*, 1433. (b) Consiglio, G.; Morandini, F.; Piccolo, O. *J. Am. Chem. Soc.* **1981**, *103*, 1846. (c) Kochi, J. K. *Organometallic Mechanisms and Catalysis*; Academic Press: New York, 1978; p 404.