

Enantioconvergent Cross-Couplings of Racemic Alkylmetal Reagents with Unactivated Secondary Alkyl Electrophiles: Catalytic Asymmetric Negishi α -Alkylations of *N*-Boc-pyrrolidineChristopher J. Cordier,^{†,‡} Rylan J. Lundgren,[†] and Gregory C. Fu^{†,‡,*}[†]Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, United States[‡]Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States

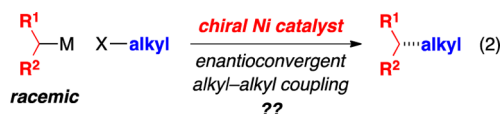
S Supporting Information

ABSTRACT: Although enantioconvergent alkyl–alkyl couplings of racemic electrophiles have been developed, there have been no reports of the corresponding reactions of racemic nucleophiles. Herein we describe Negishi cross-couplings of racemic α -zincated *N*-Boc-pyrrolidine with unactivated secondary halides, thus providing a one-pot, catalytic asymmetric method for the synthesis of a range of 2-alkylpyrrolidines (an important family of target molecules) from *N*-Boc-pyrrolidine, a commercially available precursor. Preliminary mechanistic studies indicated that two of the most straightforward mechanisms for enantioconvergence (dynamic kinetic resolution of the organometallic coupling partner and a simple β -hydride elimination/ β -migratory insertion pathway) are unlikely to be operative.

Recently we have been pursuing the development of an array of metal-catalyzed alkyl–alkyl cross-coupling processes.^{1–3} As part of this program, we have described several Ni-catalyzed methods for the enantioconvergent coupling of achiral alkylmetal reagents with racemic secondary alkyl electrophiles (eq 1).^{4,5}



The reversed-polarity process, wherein a racemic alkyl nucleophile is coupled with an alkyl electrophile (eq 2), has

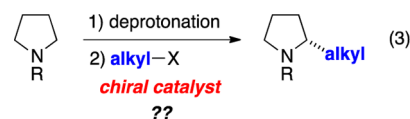


remained an unsolved challenge. However, Kumada has described a Ni-catalyzed enantioconvergent coupling of a racemic benzylic Grignard reagent (PhCHMeMgCl) with an alkenyl halide (bromoethylene) to generate an enantioenriched allylbenzene.^{6,7}

Pyrrolidines bearing an alkyl substituent at the 2-position are important across many areas of chemistry and biology. For example, they are present as subunits in bioactive natural⁸ and non-natural⁹ products, function as versatile intermediates in the synthesis of other useful classes of compounds,¹⁰ and serve as

effective chiral organocatalysts and ligands in asymmetric catalysis.¹¹ Because of this wide-ranging significance, the development of efficient methods for the enantioselective synthesis of 2-alkylpyrrolidines has been the target of substantial effort, and a broad array of approaches have been described, ranging from chiral-pool strategies to asymmetric synthesis.^{12,13}

The catalytic enantioselective 2-alkylation of pyrrolidine (or a readily available protected derivative) via deprotonation/electrophile-trapping represents an attractive, direct approach to the asymmetric synthesis of 2-alkylpyrrolidines (eq 3); to the best of



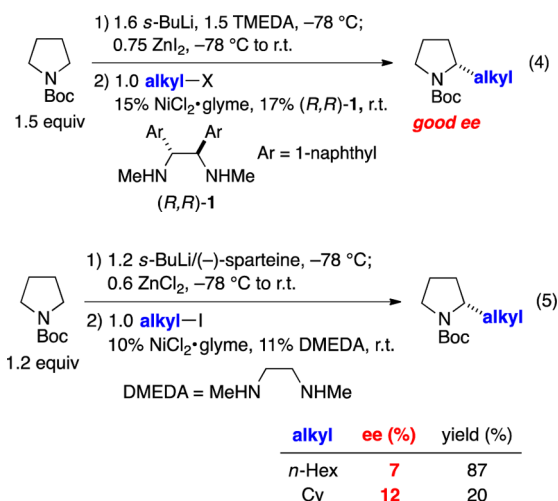
our knowledge, such a process has not been reported to date. On the other hand, pioneering studies by Beak established that deprotonation of *N*-Boc-pyrrolidine in the presence of a stoichiometric quantity of (–)-sparteine¹⁴ followed by trapping with any of a wide range of electrophiles (e.g., *n*-Bu₃SnCl, Me₃SiCl, benzophenone, CO₂) can furnish 2-substituted pyrrolidines with high enantioselectivity; among unactivated alkyl electrophiles, only dimethyl sulfate and methyl iodide have been shown to serve as suitable coupling partners.¹⁵ Building on these key observations, O'Brien developed a method that employs a substoichiometric quantity (20 mol %) of a chiral amine and provides 2-functionalized (although not 2-alkyl) *N*-Boc-pyrrolidines with up to 88% ee.¹⁶

In view of the potential utility of the transformation outlined in eq 3, we pursued the development of the first enantioconvergent alkyl–alkyl cross-coupling wherein a racemic alkyl nucleophile is employed as a reaction partner. In particular, we found that, in the presence of a chiral Ni catalyst, racemic α -zincated *N*-Boc-pyrrolidine (prepared in situ from commercially available *N*-Boc-pyrrolidine) can be coupled with unactivated alkyl electrophiles to generate 2-alkylpyrrolidines with good ee (eq 4).¹⁷

Initially, in view of recent reports by Campos of stoichiometric asymmetric α -lithiation/transmetalation/Pd-catalyzed Negishi arylation of *N*-Boc-pyrrolidine,¹⁸ we examined the cross-coupling of enantioenriched α -zincated *N*-Boc-pyrrolidine (>90% ee)¹⁹ with *n*-hexyl iodide and cyclohexyl iodide in the presence of an achiral Ni–1,2-diamine catalyst (eq 5). In both

Received: May 30, 2013

Published: July 19, 2013



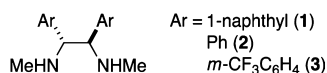
cases, the alkyl–alkyl coupling product was formed with low ee (<15% ee).²⁰ Because the organozinc reagent is configurationally stable at room temperature, these observations suggest that stereochemical scrambling occurs during the Ni-catalyzed cross-coupling process.

Because the use of an achiral catalyst for the cross-coupling of a highly enantioenriched nucleophile provided almost racemic product, we decided to examine the stereochemically converse transformation: the use of a chiral catalyst for the cross-coupling of a racemic nucleophile to generate enantioenriched product. In view of the paucity of asymmetric metal-catalyzed alkyl–alkyl couplings of secondary nucleophiles with secondary electrophiles,²¹ we chose to employ cyclohexyl iodide as the electrophilic coupling partner. Investigation of a range of parameters showed that the desired enantioconvergent coupling of racemic α -zincated *N*-Boc-pyrrolidine with cyclohexyl iodide can be achieved using a combination of $\text{NiCl}_2\cdot\text{glyme}$ and chiral 1,2-diamine ligand **1**²² in good yield (86%) with high ee (93% ee) at room temperature (Table 1, entry 1). In the absence of either $\text{NiCl}_2\cdot\text{glyme}$ or **1**, essentially no alkyl–alkyl cross-coupling product was observed (entries 2 and 3); similarly, α -lithiated *N*-

Table 1. Enantioconvergent Cross-Coupling of a Racemic Nucleophile: Effect of the Reaction Parameters^a

Reaction scheme: 1.5 equiv <i>N</i>-Boc-pyrrolidine reacts with 1) 1.6 <i>s</i>-BuLi, 1.5 TMEDA, -78°C, 3.5 h; 0.75 ZnI_2, -78°C to r.t., 1.5 h; 2) 1.0 Cy-I, 15% $\text{NiCl}_2\cdot\text{glyme}$, 17% (<i>R,R</i>)-1, r.t., 60 h "standard" conditions to form product with Cy substituent.			
entry	variation from the "standard" conditions	ee (%)	yield (%) ^b
1	none	93	86
2	no $\text{NiCl}_2\cdot\text{glyme}$	–	<2
3	no 1	–	2
4	no ZnI_2	–	<2
5	2 , instead of 1	82	80
6	3 , instead of 1	75	76
7	10% $\text{NiCl}_2\cdot\text{glyme}$, 12% 1	92	53
8	$\text{Ni}(\text{cod})_2$, instead of $\text{NiCl}_2\cdot\text{glyme}$	93	61
9	$\text{NiBr}_2\cdot\text{glyme}$, instead of $\text{NiCl}_2\cdot\text{glyme}$	92	38
10	0.5, instead of 0.75, ZnI_2 (R = <i>N</i> -Boc-pyrrolidinyl)	90	74

^aAll data are averages of two experiments. ^bDetermined by GC analysis vs a calibrated internal standard.



N-Boc-pyrrolidine was not a suitable coupling partner (entry 4). Under the same conditions, related C₂-symmetric 1,2-diamines furnished somewhat lower ee and yield (entries 5 and 6). Using less catalyst (entry 7) or another Ni source (entries 8 and 9) led to comparable ee but reduced yield. Our observation that 2-cyclohexyl-*N*-Boc-pyrrolidine formed in 74% yield with 90% ee in the presence of 0.5 equiv of the diorganozinc reagent (entry 10) provides strong evidence that the cross-coupling is an enantioconvergent process, not a simple kinetic resolution.

The catalytic asymmetric synthesis of an array of 2-alkylpyrrolidines can be achieved via the coupling of a single precursor (*N*-Boc-pyrrolidine) with a variety of readily available, unactivated alkyl iodides (Table 2).²³ Three parent cycloalkyl

Table 2. Enantioconvergent Negishi Reactions of Racemic α -Zincated *N*-Boc-pyrrolidine with Unactivated Alkyl Iodides^a

entry	electrophile	ee, yield (%) ^b	entry	electrophile	ee, yield (%) ^b
1		93, 80	5		94, 96
2		82, 91	6		91, 94
3		84, 50	7		90, 85
4		92, 96	8		58, 85

^aFor the reaction conditions, see eq 4. All data are averages of two experiments. ^bYields of purified products (reaction scale: 1.0 mmol of the electrophile).

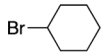
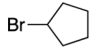
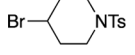
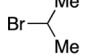
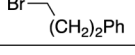
iodides underwent enantioconvergent alkyl–alkyl cross-coupling with racemic α -zincated *N*-Boc-pyrrolidine with good enantioselectivity (entries 1–3); the process could be conducted on a gram scale with comparable efficiency [performing entry 1 on a 6.0 mmol scale gave 1.12 g of product (74% yield) with 94% ee]. Heterocyclic electrophiles coupled with high ee (entries 4–6), as did an acyclic secondary alkyl iodide (entry 7). In contrast, moderate ee was observed for the asymmetric Negishi reaction of a primary alkyl iodide (entry 8).

This method thus complements other catalytic enantioselective approaches to the synthesis of 2-alkylpyrrolidines, which are typically only effective for the incorporation of a primary alkyl group.²⁴ Pyrrolidines bearing a secondary alkyl substituent at the 2-position are found in a wide variety of compounds, including an array of pyrrolizidine (e.g., heliotridane), indolizidine (e.g., tashiromine, grandisine A²⁵), and crambescidin²⁶ alkaloids.

Alkyl bromides can also be employed as electrophiles in these Ni-catalyzed enantioconvergent cross-couplings of a racemic nucleophile (Table 3).²⁷ Under the same conditions as for iodides (except for the temperature, in a few cases), alkyl–alkyl bond formation between α -zincated *N*-Boc-pyrrolidine and a range of cyclic and acyclic unactivated secondary alkyl bromides proceeded with good ee's but generally modest yields (entries 1–4). As in the case of a primary alkyl iodide, a primary bromide cross-coupled with lower ee (entry 5).

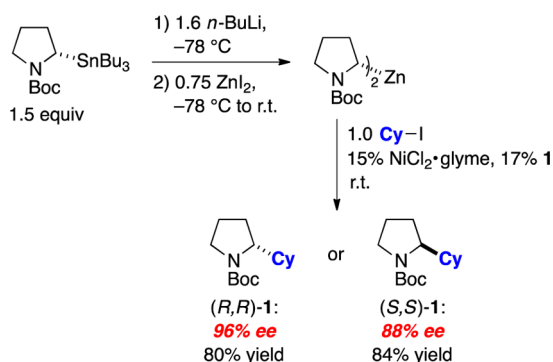
We next focused on gaining insight into the origin of the stereoconvergence in these asymmetric Negishi reactions of α -zincated *N*-Boc-pyrrolidine.²⁸ In Kumada's earlier study of the enantioselective cross-coupling of racemic PhCHMeMgCl with bromoethylene to form an allylbenzene, it was postulated that stereoconvergence arose from a dynamic kinetic resolution of a

Table 3. Enantioconvergent Negishi Reactions of Racemic α -Zincated *N*-Boc-pyrrolidine with Unactivated Alkyl Bromides^a

entry	electrophile	ee (%)	yield (%) ^b
1 ^c		92	41
2		88	80
3 ^c		88	44
4 ^c		90	51
5		58	61

^aFor the reaction conditions, see eq 4. All data are averages of two experiments. ^bYields of purified products. ^cReaction temperature: 35 °C.

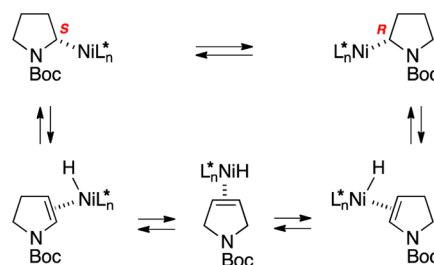
rapidly racemizing benzylic nucleophile by the chiral Ni catalyst.⁶ In contrast, our nucleophile, α -zincated *N*-Boc-pyrrolidine, is configurationally stable under our reaction conditions in the absence of Ni. Thus, an enantioenriched organozinc reagent was prepared from the corresponding stannane through Sn–Li exchange followed by transmetalation to zinc (Figure 1).²⁹ When

**Figure 1.** The product stereochemistry is controlled predominantly by the stereochemistry of the chiral Ni catalyst, not that of the nucleophile, in a Negishi reaction of α -zincated *N*-Boc-pyrrolidine.

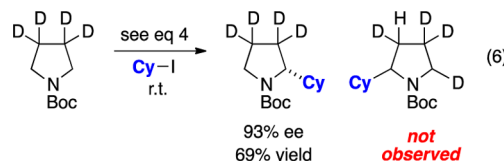
this nucleophile was cross-coupled with bromobenzene under the Campos conditions,¹⁸ (*R*)-2-phenyl-*N*-Boc-pyrrolidine was generated in 95% yield with 90% ee, thereby establishing the stereochemical integrity of the organozinc reagent. When this enantioenriched nucleophile was reacted with cyclohexyl iodide under our standard conditions using either (*R,R*)- or (*S,S*)-1, the stereochemistry of the cross-coupling product was dependent primarily on the stereochemistry of the ligand rather than of the organozinc nucleophile.

A possible mechanism for enantioconvergence in the Ni-catalyzed asymmetric Negishi reactions described herein is a series of β -hydride eliminations/ β -migratory insertions of an organonickel intermediate, without dissociation of the olefin from Ni (Figure 2). We have in fact observed such an isomerization process in an enantioselective Negishi cross-coupling of a racemic electrophile with an achiral cyclopentylzinc reagent.²¹

To assess the viability of the pathway outlined in Figure 2, we investigated the Negishi reaction of a deuterium-labeled *N*-Boc-

**Figure 2.** A hypothetical pathway for stereomutation of an α -metalated *N*-Boc-pyrrolidine: β -hydride elimination and β -migratory insertion without olefin dissociation.

pyrrolidine (eq 6). Essentially no deuterium incorporation (<5%) α to nitrogen in the cross-coupling product was observed,



indicating that the β -hydride elimination/ β -migratory insertion pathway for stereomutation depicted in Figure 2 is not the mechanism by which stereoconvergence is achieved.³⁰

In summary, we have developed the first enantioconvergent alkyl–alkyl cross-coupling of a racemic nucleophile, specifically, the asymmetric Negishi reaction of α -zincated *N*-Boc-pyrrolidine with unactivated secondary iodides and bromides, providing a one-pot route to an array of 2-alkylpyrrolidines from a single, readily available precursor (*N*-Boc-pyrrolidine). Because the highest enantioselectivity was obtained for the incorporation of secondary alkyl substituents, this method complements existing catalytic asymmetric approaches to the synthesis of 2-alkylpyrrolidines, which are generally most effective for primary alkyl groups. The pathway for stereoconvergence in the present method does not involve a dynamic kinetic resolution of the organometallic coupling partner, in contrast to a previous report of an enantioconvergent alkyl–alkenyl cross-coupling. Furthermore, a deuterium-labeling study ruled out stereomutation via a simple β -hydride elimination/ β -migratory insertion pathway that we had observed in another Ni-catalyzed alkyl–alkyl coupling. Additional investigations to elucidate the mechanism of this unusual enantioconvergent cross-coupling and to expand the range of racemic nucleophiles that can be employed in such alkyl–alkyl coupling processes are underway.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author

gcfu@caltech.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the NIH NIGMS (R01-GM62871) for support and Dr. Scott C. Virgil (Caltech Center for Catalysis and Chemical

Synthesis) and Dr. David G. VanderVelde (Caltech NMR facility) for assistance.

REFERENCES

- (1) (a) For a recent report of a Ni-catalyzed process, see: Wilsily, A.; Tramutola, F.; Owston, N. A.; Fu, G. C. *J. Am. Chem. Soc.* **2012**, *134*, 5794. (b) For an overview of Pd-catalyzed couplings, see: Netherton, M. R.; Fu, G. C. *Top. Organomet. Chem.* **2005**, *14*, 85.
- (2) For leading references, see: (a) Glasspoole, B. W.; Crudden, C. M. *Nat. Chem.* **2011**, *3*, 912. (b) Glorius, F. *Angew. Chem., Int. Ed.* **2008**, *47*, 8347. (c) Rudolph, A.; Lautens, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2656. (d) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417.
- (3) For examples of applications of Pd-catalyzed alkyl–alkyl cross-couplings in the total synthesis of natural products, see: (a) Griggs, N. D.; Phillips, A. J. *Org. Lett.* **2008**, *10*, 4955. (b) Keaton, K. A.; Phillips, A. J. *Org. Lett.* **2007**, *9*, 2717.
- (4) (a) For a recent report of a Suzuki reaction, see ref 1a. (b) For an example of a Negishi reaction, see: Son, S.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 2756.
- (5) For a recent application in the total synthesis of a natural product, see: Schmidt, T.; Kirschning, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 1063.
- (6) (a) Hayashi, T.; Tajika, M.; Tamao, K.; Kumada, M. *J. Am. Chem. Soc.* **1976**, *98*, 3718. (b) Hayashi, T.; Konishi, M.; Fukushima, M.; Mise, T.; Kagotani, M.; Tajika, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 180.
- (7) Other examples of the asymmetric cross-coupling of racemic nucleophiles with alkenyl electrophiles have been described, but the conversion of both enantiomers of the racemic nucleophile into the enantioenriched coupling product has generally not been clearly demonstrated (i.e., the ee of the product could in principle result from a simple kinetic resolution in which one enantiomer of the nucleophile is selectively cross-coupled).
- (8) For examples and leading references, see: (a) *Naturally Occurring Pyrrolizidine Alkaloids*; Rizk, A. F. M., Ed.; CRC Press: Boca Raton, FL, 1991. (b) Mattocks, A. R. *Chemistry and Toxicology of Pyrrolizidine Alkaloids*; Academic Press: London, 1986. (c) Bronner, S. M.; Im, G.-Y. J.; Garg, N. K. In *Heterocycles in Natural Product Synthesis*; Majumdar, K. C., Chattopadhyay, S. K., Eds.; Wiley-VCH: Weinheim, Germany, 2011; pp 221–265. (d) Michael, J. P. *Nat. Prod. Rep.* **2008**, *25*, 139. (e) Michael, J. P. *Alkaloids* **2001**, *55*, 91.
- (9) For reviews that include examples, see: (a) Table 6 in: Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451. (b) Li, X.; Li, J. *Mini-Rev. Med. Chem.* **2010**, *10*, 794. (c) Cheng, X.-C.; Wang, Q.; Fang, H.; Xu, W.-F. *Curr. Med. Chem.* **2008**, *15*, 374. (d) Karoyan, P.; Sagan, S.; Lequin, O.; Quancard, J.; Lavielle, S.; Chassaing, G. *Targets Heterocycl. Syst.* **2004**, *8*, 216.
- (10) For example, see: Blum, A.; Diederich, W. E. *Curr. Org. Synth.* **2009**, *6*, 38.
- (11) For example, see: Zhang, S.; Wang, W. *Privileged Chiral Ligands and Catalysts*; Zhou, Q.-L., Ed.; Wiley-VCH: Weinheim, Germany, 2011; Chapter 11.
- (12) For a review and leading references, see: Companyo, X.; Alba, A.-N.; Rios, R. *Targets Heterocycl. Syst.* **2009**, *13*, 147.
- (13) For recent reports of methods for the catalytic asymmetric synthesis of 2-alkylpyrrolidines, see: (a) Brown, A. R.; Uyeda, C.; Brotherton, C. A.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2013**, *135*, 6747. (b) Trost, B. M.; Lam, T. M.; Herbage, M. A. *J. Am. Chem. Soc.* **2013**, *135*, 2459.
- (14) Only the (–) enantiomer of sparteine is naturally occurring, and this compound is no longer available from suppliers such as Sigma-Aldrich. A surrogate of (+)-sparteine (see: Dearden, M. J.; Firkin, C. R.; Hermet, J.-P. R.; O'Brien, P. J. *Am. Chem. Soc.* **2002**, *124*, 11870) is commercially available.
- (15) For reviews and leading references on enantioselective lithiations, see: (a) Beak, P.; Johnson, T. A.; Kim, D. D.; Lim, S. H. *Top. Organomet. Chem.* **2003**, *5*, 139. (b) Hoppe, D.; Christoph, G. In *Chemistry of Organolithium Compounds*; Rappoport, Z., Marek, I., Eds.; Wiley: Chichester, U.K., 2004; Vol. 2, pp 1055–1164. (c) Gawley, R. E. *Top. Stereochem.* **2010**, *26*, 93. (d) Mitchell, E. A.; Peschiulli, A.; Lefevre, N.; Meerpoel, L.; Maes, B. U. W. *Chem.—Eur. J.* **2012**, *18*, 10092.
- (16) McGrath, M. J.; O'Brien, P. J. *Am. Chem. Soc.* **2005**, *127*, 16378.
- (17) For recent reports of methods for the synthesis of racemic 2-alkylpyrrolidines, see: (a) Hennessy, E. T.; Betley, T. A. *Science* **2013**, *340*, 591. (b) Jurberg, I. D.; Peng, B.; Wöstefeld, E.; Wasserloos, M.; Maulide, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 1950. For enantioenriched 2-benzyl- and 2-methylpyrrolidines, see ref 13a.
- (18) (a) Campos, K. R.; Klapars, A.; Waldman, J. H.; Dormer, P. G.; Chen, C.-y. *J. Am. Chem. Soc.* **2006**, *128*, 3538. (b) Barker, G.; McGrath, J. L.; Klapars, A.; Stead, D.; Zhou, G.; Campos, K. R.; O'Brien, P. J. *Org. Chem.* **2011**, *76*, 5936.
- (19) A portion of the enantioenriched organozinc reagent (eq 5) was subjected to the Campos arylation procedure using bromobenzene as the electrophile, which afforded N-Boc-2-phenylpyrrolidine in 97% yield with 92% ee.
- (20) Our attempts to apply the Campos procedure [which employs a Pd/P(*t*-Bu)₃ catalyst] to cross-couplings of alkyl electrophiles were not successful.
- (21) For exceptions (couplings of achiral secondary nucleophiles with racemic secondary electrophiles), see: (a) Binder, J. T.; Cordier, C. J.; Fu, G. C. *J. Am. Chem. Soc.* **2012**, *134*, 17003. (b) Zultanski, S. L.; Fu, G. C. *J. Am. Chem. Soc.* **2011**, *133*, 15362.
- (22) All previous reports of enantioselective alkyl–alkyl Negishi cross-couplings (which employed racemic electrophiles rather than racemic nucleophiles) utilized Ni in combination with a pyridine–oxazoline-type ligand, never with a chiral diamine ligand. However, when such pyridine–oxazolines were applied to the coupling of α -zincated N-Boc-pyrrolidine with cyclohexyl iodide, the desired product was generated in <10% yield. For leading references, see refs 1a, 4b, and 21a.
- (23) Notes: (a) The product ee was essentially constant during the course of the reaction. (b) Under the standard cross-coupling conditions, 3-iodopentane and *tert*-butyl iodide reacted very slowly (<20% yield after 2.5 days), and the use of ZnCl₂ rather than ZnI₂ led to inferior results.
- (24) For example, for the hydroamination of olefins, see: Reznichenko, A. L.; Hultzsich, K. C. In *Chiral Amine Synthesis*; Nugent, T. C., Ed.; Wiley-VCH: Weinheim, Germany, 2011; pp 341–375.
- (25) For example, see: Maloney, D. J.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 7789.
- (26) For pioneering studies, see: Coffey, D. S.; McDonald, A. I.; Overman, L. E.; Rabinowitz, M. H.; Renhowe, P. A. *J. Am. Chem. Soc.* **2000**, *122*, 4893.
- (27) Under the standard cross-coupling conditions, cyclohexyl chloride reacted very slowly (<10% yield after 2.5 days).
- (28) For examples of and leading references to diastereoconvergent Pd-catalyzed Negishi reactions of cyclic organozinc reagents, see: Seel, S.; Thaler, T.; Takatsu, K.; Zhang, C.; Zipse, H.; Straub, B. F.; Mayer, P.; Knochel, P. *J. Am. Chem. Soc.* **2011**, *133*, 4774.
- (29) Gross, K. M. B.; Beak, P. J. *Am. Chem. Soc.* **2001**, *123*, 315. Notes: (a) Sn–Li exchange, rather than (–)-sparteine-mediated lithiation, was employed to avoid any complications in the Ni-catalyzed cross-coupling due to the presence of (–)-sparteine. (b) The absolute configuration of the stannane has been determined by X-ray crystallography. See: Gawley, R. E.; Narayan, S.; Vivic, D. A. *J. Org. Chem.* **2005**, *70*, 328.
- (30) In a preliminary study, when N-Boc-pyrrolidine-2,2-*d*₂ was subjected to the standard asymmetric cross-coupling conditions, no evidence of deuterium scrambling was observed.