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Enantioselective Construction of Carbocyclic and Heterocyclic Tertiary Boronic Esters by Conjunctive Cross-Coupling Reaction

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ABSTRACT: Synthesis of stereodefined carbocyclic and heterocyclic tertiary boronic esters is accomplished by performing a conjunctive cross-coupling reaction on preformed cyclic boron ate complexes. Boronates bearing spirocyclic and aryl bicyclic skeletons can be synthesized enantioselectively using a chiral PHOX-ligated Pd catalyst with achiral starting material, while substrates bearing continuous stereogenic centers can be generated diastereoselectively. A variety of aryl and alkenyl electrophiles are incorporated.

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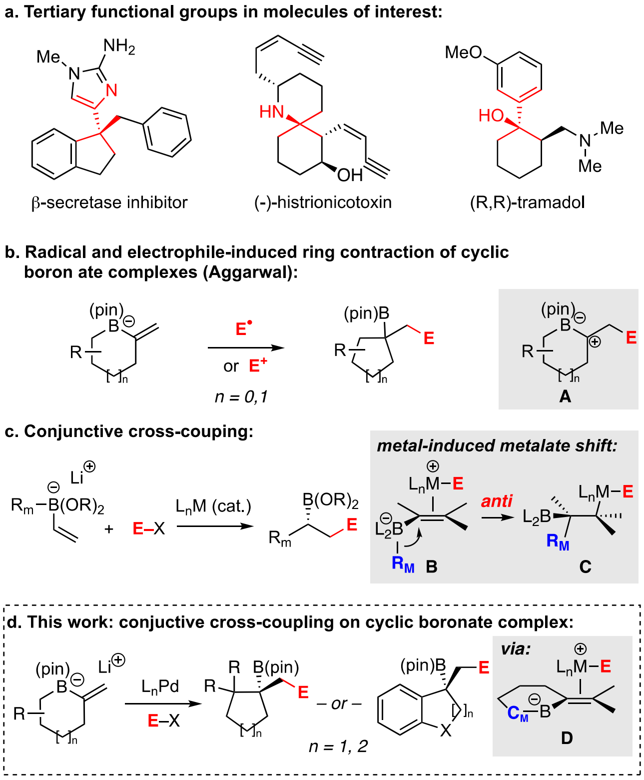
Tertiary functional groups attached to carbocycles are ubiquitous in natural products and therapeutic agents (Scheme 1a),[1] and the development of strategies to construct such stereogenic centers has been a focus in synthetic chemistry.[2] Among methods for accomplishing this objective, the stereospecific transformation of tertiary alkyl boronic esters has been established as a versatile tool for the construction of tertiary alcohols and amines as well as quaternary carbon centers.[3] To construct tertiary boronates, a number of stoichiometric and catalytic processes have been introduced,[4] with metalate shift-based reactions of α-substituted alkenyl boronate complexes being notable for their ability to effect new C−C and C−electrophile bond formation.[5] In this connection, Aggarwal and Studer's group have demonstrated that a variety of electrophiles can induce such rearrangement through radical or radical-polar crossover pathways.[6] Recently, Aggarwal reported that electrophile-induced 1,2-migration can apply to cyclic boron ate complexes (Scheme 1b), resulting in ring contraction and construction of cyclobutanes and cyclopentanes bearing tertiary boronic esters.[7] Analysis of the stereochemical outcome of these reactions (stereospecific at the migrating carbon and stereoselective at the emerging stereocenter) suggests the reactions may occur through the intermediacy of an α-boryl carbocation (**A**, inset).

Scheme 1. Conjunctive Coupling with Cyclic Boron Ate Complexes and Its Applications



As a catalytic enantioselective method to construct chiral secondary and tertiary organoboronic esters, our group has employed chiral palladium- and nickel-based complexes to effect conjunctive coupling of alkenyl boron ate complexes (Scheme 1c).[8,9] The stereochemical outcome of these reactions indicates that they occur by a concerted *anti* addition of the migrating carbon atom (R_M) and the metal complex to the alkene (**B** → **C**, inset). In contrast, Ready has demonstrated that Ir(allyl)-induced metalate shift may occur by *syn* addition across alkene.[10] To extend the metal-catalyzed conjunctive coupling reaction to the construction of intricate cyclic motifs, we considered reactions of cyclic boron ate complexes (Scheme 1d). In addition to enantiodiscrimination, a critical concern that arises is whether the cyclic constraint of substrates precludes necessary alignment of the participating

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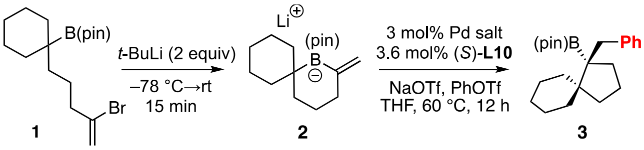
B−C$_M$ bond and the alkene π system (**D**, inset). If these two features are too far out of alignment, the activation barrier for the metalate shift may be raised sufficiently that direct Suzuki−Miyaura reaction becomes the predominant reaction pathway.[11] In this Letter, we demonstrate that Pd-catalyzed conjunctive coupling can indeed operate efficiently on cyclic boron ate complexes (Scheme 1d) and provides access to a range of enantiomerically enriched spirocycles and benzo-fused carbocycles and heterocycles in an efficient fashion.

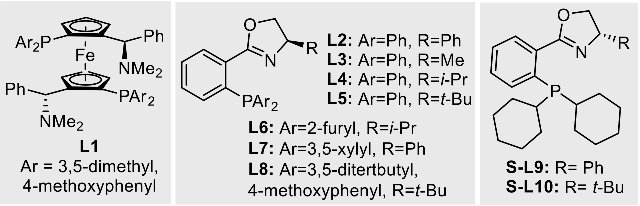
To examine the prospects for ring-contracting conjunctive coupling of cyclic ate complexes, tertiary alkylboronate **1** (Table 1) was treated with *t*-butyllithium at −78 °C, warmed to room temperature, and then employed in couplings with PhOTf, palladium complexes, and a series of ligands (Note: NaOTf was employed as bromide scavenger[12]). As shown in Table 1, when the reaction was conducted with Pd(OAc)$_2$ and Mandyphos[13] (**L1**), a ligand that has consistently proven effective across a broad range of acyclic substrates, ring contraction product **3** was generated in 75% isolated yield, but with minimal enantioselectivity (72:28 er, entry 1). Examination of tunable phosphino-oxazoline ligands that have proven effective in recent conjunctive couplings[14] was undertaken, and it was found that analogs bearing large oxazoline substituents and electron-rich phosphines provided notably improved results (cf. entries 2−9). When dibenzylideneacetone, a presumed inhibitor of the reaction, was avoided by the use of Pd(PPh$_3$)$_4$ as the palladium source, consistently high yields and high selectivity were observed with ligands **L9** (91:9 er, entry 11) and **L10** (95:5 er, entry 12).

Table 1. Survey of Catalysts for the Enantioselective Conjunctive Coupling of Cyclic Carbonates



entry	Pd source	ligand	yield **3** (%)[a]	er[b]
1	Pd(OAc)$_2$	**L1**	75	72:28
2	Pd$_2$(dba)$_3$	**L2**	83	65:35
3	Pd$_2$(dba)$_3$	**L3**	79	55:45
4	Pd$_2$(dba)$_3$	**L4**	86	65:35
5	Pd$_2$(dba)$_3$	**L5**	69	72:28
6	Pd$_2$(dba)$_3$	**L6**	77	52:48
7	Pd$_2$(dba)$_3$	**L7**	80	72:28
8	Pd$_2$(dba)$_3$	**L8**	55	80:20
9	Pd$_2$(dba)$_3$	**L9**	30	90:10
10	Pd(ACN)$_2$Cl$_2$	**L9**	72	86:14
11	Pd(PPh$_3$)$_4$	**L9**	77	91:9
12	Pd(PPh$_3$)$_4$	**L10**	72	95:5

[a]Yield determined by ^{1}H NMR versus an internal standard. [b]Enantiomer ratios determined by chiral SFC analysis and have an error of ±1%.



With effective conditions identified for reactions of cyclic tertiary boron ate complexes, a variety of substrates were examined in the coupling reaction. Carbocyclic boronic esters bearing a number of spirocyclic skeletons were successfully prepared by a conjunctive cross-coupling reaction. Migrating groups bearing different ring sizes are readily accommodated, allowing access to enantiomerically enriched spirocycles with 4- to 7-membered rings in good yield and selectivity (Figure 1, products **4**−**7**). Heteroatoms are also tolerated, thereby providing access to spirocyclic piperidine and tetrahydropyran motifs (**8** and **9**) as well as products with ketal units (**10**). With a longer tether connecting the bromoalkene to the boronate in the substrate, the reaction furnishes 6,6-spirocyclic boronic ester **12**; however, 7-membered ring closure could not be realized with this method and only delivered Suzuki−Miyaura coupling product (data not shown). Heteroarenes were also found to be suitable electrophiles for the reaction, allowing the introduction of pyridine (**13**), pyrazine (**14**), pyrimidine (**15**),

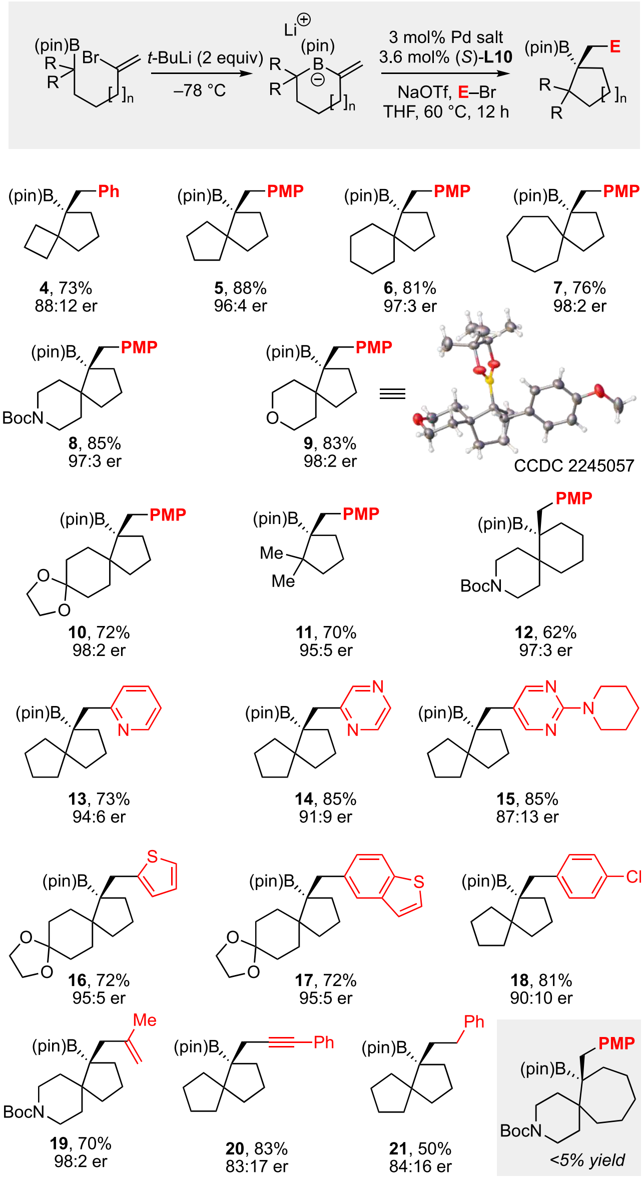


Figure 1. Substrate survey of enantioselective conjunctive coupling of cyclic boron ate complexes. PMP = *p*-methoxyphenyl.

thiophene (**16**), and benzothiophene (**17**) products. Of note, preparation of compounds **20** and **21** represents the first successful use of alkynyl and benzyl electrophiles in metal-catalyzed enantioselective conjunctive couplings. Lastly, configuration assignment of product **9** was accomplished by X-ray crystallographic analysis of the product.

Considering the efficiency observed in the coupling of heteroatom-containing aliphatic boronic ester substrates in Figure 1, it was of interest to learn whether reactions of aryl boron ate complexes might provide a useful route to substituted tetrahydroquinoline and chromane reaction products. For effective preparation of ate complexes, substrate selection proved to be critical: while treatment of **22** with *t*-butyllithium cleanly provides ate complex **23** when the positions of the Br and B(pin) groups are reversed, the addition of *t*-BuLi to the B(pin) group is competitive with Li—halogen exchange. Therefore, a series of alkenyl boronic esters were examined as conjunctive cross-coupling candidates. As depicted in Figure 2, an ether-tethered substrate participates in ring-contracting coupling with substituted arenes, heteroarenes, and an alkenyl electrophile (**24**−**28**). Though reactions with an aryl migrating group tend to be slower than with alkyl migrating groups and require longer reaction times, the coupling products were often delivered in good yield and high enantioselectivity. Methoxy groups (**29**, **31**) and halogen atoms (**30**, **32**) could be installed on the migrating arene. Moreover, the structure of the tether that connects the alkenyl boron and the bromoarene can include a Boc-protected amine and, in this case, furnishes a tetrahydroquinoline skeleton (**33**). Similarly, if the heteroatom linker is removed from the substrate, then boronate-containing indane skeletons can be constructed efficiently (**34**−**37**). Aryl bromides bearing a protected catechol (**38**) or B(pin) functional group (**39**) can be used as electrophiles to access more complex structures.

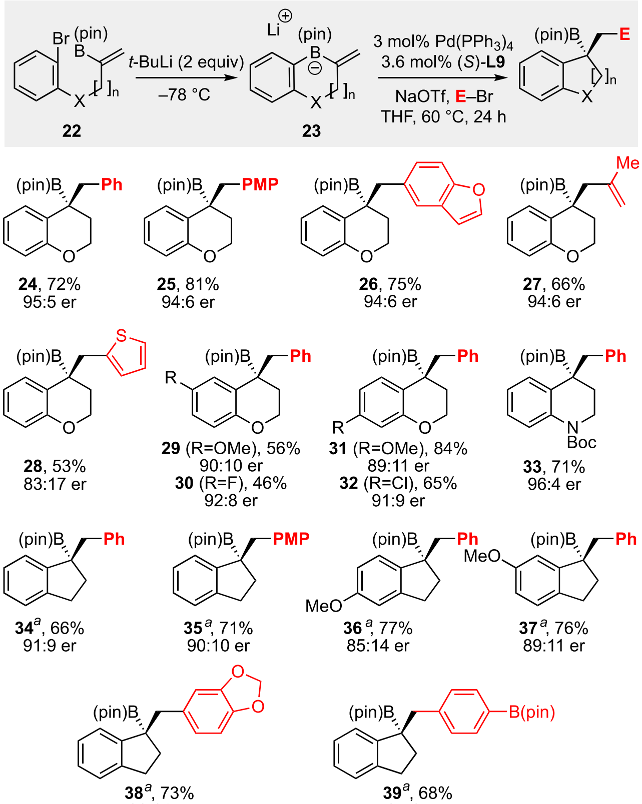


Figure 2. Enantioselective conjunctive coupling of cyclic aromatic boron ate complexes. [a]Reaction conducted at 40 °C for 24 h.

With efficient and selective strategies for conjunctive couplings with cyclic boron ate complexes established, aspects of synthesis utility were examined. In one experiment, we conducted a preparative scale reaction. As depicted in Figure 3a, substrate **42** was prepared by copper-catalyzed coupling between benzyl bromide **40** and allylboron reagent **41**.[15] Subsequent conjunctive coupling with bromobenzene in the presence of Pd/**L9** provided **34** with good and slightly improved selectivity compared to smaller scale reactions. Given that transformations of hindered tertiary benzylic boronates can be challenging, reactions of **34** were probed. As shown in Figure 3b, subjection of **34** to conditions for

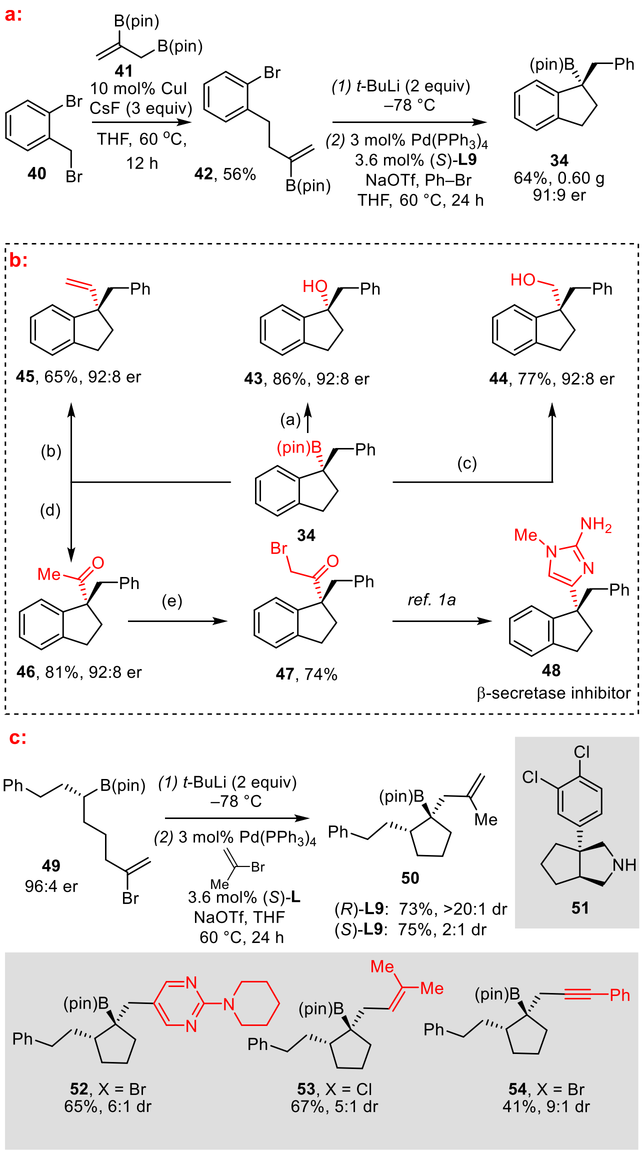


Figure 3. Practical aspects of conjunctive coupling of cyclic aromatic boron ate complexes. [a]NaOH, H_2O_2, THF, rt, 1 h. [b]Vinyl magnesium bromide, then I_2, $LiOCH_3$, CH_3OH/THF, −78 °C to rt. [c]CH_2Br_2, *n*-BuLi, −78 °C to rt, 2 h; then NaOH, H_2O_2. [d]Ethyl vinyl ether, *t*-BuLi, then I_2, $LiOCH_3$, CH_3OH/THF, and then 3 M HCl. [e]Br_2, MeOH, 0 °C to rt, 3 h.

Matteson homologation,[16] oxidation, and Evans−Zweifel olefination[17] furnished the corresponding products (**43−45**) efficiently. Moreover, modified Zweifel olefination[18] to an enol ether followed by hydrolysis was found to deliver **46** in good yield. Intermediate **46** was easily brominated to generate **47**, which is a known intermediate in the synthesis of β-secretase inhibitor **48**.[1a] In a last set of experiments, we examined the prospect for reactions of secondary boronates to provide trisubstituted ring systems that might be relevant for the construction of tramadol (Figure 1), the promising triple reuptake inhibitor **51**,[19] or other motifs. Since the requisite substrates to address these compounds are chiral, the issue of double asymmetric induction arises. In this event, enantiomerically enriched **49** was prepared and subjected to conjunctive coupling. When the reaction was conducted in the presence of the (*S*) enantiomer of **L9** the reaction occurred with low selectivity; however, when (*R*)-**L9** was employed, cyclic boronic ester **50** was generated in good yield and with excellent diastereoselectivity. Thus, with appropriate matching of catalyst chirality and substrate chirality, trisubstituted cyclopentanes should be readily available, and this process was examined with aryl, alkenyl, and alkynyl electrophiles to deliver corresponding compounds **52−54**.

As the examples above indicate, ring-contracting conjunctive couplings to provide five- and six-membered rings proceed with good efficiency, thereby suggesting that the cyclic nature of the substrate does not prohibit alignment of the migrating carbon atom with the reacting alkene. However, when the analogous process was applied to a substrate that would deliver a four-membered carbocycle (**55**, Figure 4a), the reaction did not furnish any of the conjunctive coupling product **56** and instead generated Suzuki−Miyaura coupling product **57**. To determine whether this alternate outcome arises from strain that develops during the 1,2-boronate shift (i.e., energetically disfavored metalate shift) or is due to misaligned reaction components (increased barrier to metalate shift), computational analysis of the rearrangement was undertaken for model systems of both ring sizes. As the data in Figure 4b indicates, the 1,2-boronate rearrangement to form both four- and five-membered rings are exergonic reactions; however, the activation barrier to form the four-membered ring is 2.2 kcal/mol higher than the barrier for cyclopentane ring formation. Presumably this increased barrier provides an opportunity for direct transmetalation to be competitive, and hence the Suzuki−Miyaura pathway becomes favored for smaller cyclic boronates. Of note, the overall exergonic nature of the reaction suggests that boron or palladium ligand designs that inherently preclude direct transmetalation might prove effective for contraction to form smaller cyclic boronic esters. Studies in this connection are in progress.

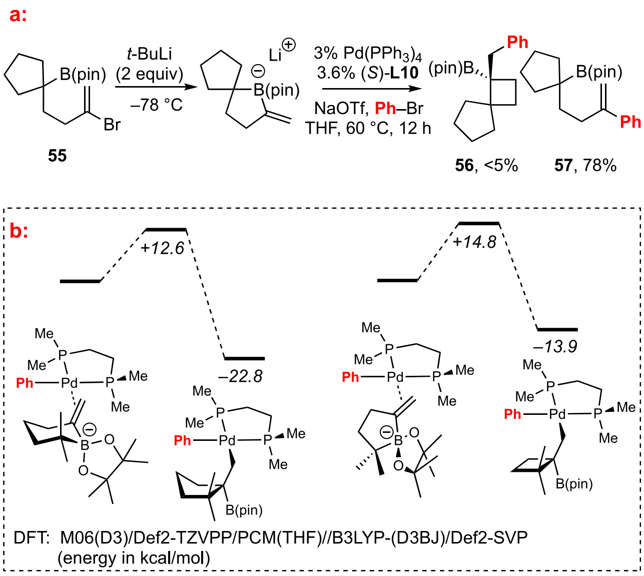


Figure 4. Analysis of coupling reactions with smaller ring sizes. (a) Reaction of a cyclic five-membered ring boronate. (b) DFT analysis of barriers for the metalate shift involving six-membered and five-membered cyclic boronates.

In summary, the synthesis of stereodefined carbocyclic tertiary boronic esters is accomplished by performing a conjunctive cross-coupling reaction on preformed cyclic boron ate complexes. Boronates bearing spirocyclic and benzo-fused bicyclic skeletons can be synthesized selectively using a phosphino-oxazoline-ligated Pd catalyst with achiral starting material, while substrates bearing continuous stereogenic centers can be generated diastereoselectively.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.3c05815.

Procedures, characterization, and spectral data (PDF)

Accession Codes

CCDC 2245057 and 2245059 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

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■ REFERENCES

(1) For β-secretase inhibitor: (a) Merck & Co Inc. WO2009/108550 A1, 2009. For total synthesis of histrionicotoxin: (b) Sinclair, A.; Stockman, R. A. Thirty-five Years of Synthetic Studies Directed Towards the Histrionicotoxin Family of Alkaloids. *Nat. Prod. Rep.* **2007**, *24*, 298−326. For recent total synthesis of Tramadol: (c) Monos, T. M.; Jaworski, J. N.; Stephens, J. C.; Jamison, T. F. Continuous-Flow Synthesis of Tramadol from Cyclohexanone. *Synlett.* **2020**, *31*, 1888−1893.

(2) For recent advances in catalytic asymmetric synthesis of carbocyclic tertiary alcohols, α-tertiary amines, and quaternary carbon centers, see: (a) Liu, Y. L.; Lin, X. T. Recent Advances in Catalytic Asymmetric Synthesis of Tertiary Alcohols via Nucleophilic Addition to Ketones. *Adv. Synth. Catal.* **2019**, *361*, 876−918. (b) Liu, H. C.; Lau, V. H.; Xu, M. P.; Chan, T. H.; Huang, Z. X. Diverse Synthesis of α-Tertiary Amines and Tertiary Alcohols via Desymmetric Reduction of Malonic Esters. *Nat. Commun.* **2022**, *13*, 4759. (c) Qiao, Y.; Bai, S. M.; Wu, X. F.; Yang, Y. Y.; Meng, H.; Ming, J. L. Rhodium-Catalyzed Desymmetric Arylation of γ,γ-Disubsituted Cyclohexadienones: Asymmetric Synthesis of Chiral All-Carbon Quaternary Centers. *Org. Lett.* **2022**, *24*, 1556−1560.

(3) For stereospecific amination of tertiary alkylboronates: (a) Edelstein, E. K.; Grote, A. C.; Palkowitz, M. D.; Morken, J. P. A Protocol for Direct Stereospecific Amination of Primary, Secondary, and Tertiary Alkylboronic Esters. *Synlett.* **2018**, *29*, 1749−1752. (b) Liu, X. X.; Zhu, Q.; Chen, D.; Wang, L.; Jin, L. Q.; Liu, C. Aminoazanium of DABCO: An Amination Reagent for Alkyl and Aryl Pinacol Boronates. *Angew. Chem., Int. Ed.* **2020**, *59*, 2745−2749. For stereospecific construction of quaternary carbon centers from tertiary boronic esters: (c) Mykura, R. C.; Songara, P.; Luc, E.; Rogers, J.; Stammers, E.; Aggarwal, V. K. Studies on the Lithiation, Borylation, and 1,2-Metalate Rearrangement of O-Cycloalkyl 2,4,6-Triisopropylbenzoates. *Angew. Chem., Int. Ed.* **2021**, *60*, 11436−11441. (d) Odachowski, M.; Bonet, A.; Essafi, S.; Conti-Ramsden, P.; Harvey, J. N.; Leonori, D.; Aggarwal, V. K. Development of Enantiospecific Coupling of Secondary and Tertiary Boronic Esters with Aromatic Compounds. *J. Am. Chem. Soc.* **2016**, *138*, 9521−9532. (e) Sandford, C.; Aggarwal, V. K. Stereospecific Functionalizations and Transformations of Secondary and Tertiary Boronic Esters. *Chem. Commun.* **2017**, *53*, 5481−5494.

(4) (a) Stymiest, J. L.; Bagutski, V.; French, R. M.; Aggarwal, V. K. Enantiodivergent Conversion of Chiral Secondary Alcohols into Tertiary Alcohols. *Nature* **2008**, *456*, 778−782. (b) O'Brien, J. M.; Lee, K.; Hoveyda, A. H. Enantioselective Synthesis of Boron-Substituted Quaternary Carbons by NHC-Cu-Catalyzed Boronate Conjugate Additions to Unsaturated Carboxylic Esters, Ketones, or Thioesters. *J. Am. Chem. Soc.* **2010**, *132*, 10630−10633. (c) Kubota, K.; Yamamoto, E.; Ito, H. Copper(I)-Catalyzed Enantioselective Nucleophilic Borylation of Aldehydes: An Efficient Route to Enantiomerically Enriched α-Alkoxyorganoboronate Esters. *J. Am. Chem. Soc.* **2015**, *137*, 420−424.

(5) Namirembe, S.; Morken, J. P. Reactions of Organoboron Compounds Enabled by Catalyst-Promoted Metalate Shifts. *Chem. Soc. Rev.* **2019**, *48*, 3464−3474.

(6) For 1,2-migration of α-substituted alkenyl boronate complex using radical-polar crossover strategies: (a) You, C.; Studer, A. Synthesis of 1,3-Bis-(boryl)alkanes Through Boronic Ester Induced Consecutive Double 1,2-Migration. *Angew. Chem., Int. Ed.* **2020**, *59*, 17245−17249. (b) Armstrong, R. J.; Niwetmarin, W.; Aggarwal, V. K. Synthesis of Functionalized Alkenes by a Transition-Metal-Free Zweifel Coupling. *Org. Lett.* **2017**, *19*, 2762−2765. (c) Silvi, M.; Sandford, C.; Aggarwal, V. K. Merging Photoredox with 1,2-Metallate Rearrangements: The Photochemical Alkylation of Vinyl Boronate Complexes. *J. Am. Chem. Soc.* **2017**, *139*, 5736−5739. (d) You, C.; Studer, A. Three-Component 1,2-Carboamination of Vinyl Boronic Esters via Amidyl Radical Induced 1,2-Migration. *Chem. Sci.* **2021**, *12*, 15765−15769. For a review, see: (e) Wang, H.; Jing, C. C.; Noble, A.; Aggarwal, V. K. Stereospecific 1,2-Migrations of Boronate Complexes Induced by Electrophiles. *Angew. Chem., Int. Ed.* **2020**, *59*, 16859−16872.

(7) (a) Davenport, R.; Silvi, M.; Noble, A.; Hosni, Z.; Fey, N.; Aggarwal, V. K. Visible-Light-Driven Strain-Increase Ring Contraction Allows the Synthesis of Cyclobutyl Boronic Esters. *Angew. Chem., Int. Ed.* **2020**, *59*, 6525−6528. (b) Fairchild, M. E.; Noble, A.; Aggarwal, V. K. Diastereodivergent Synthesis of Cyclopentyl Boronic Esters Bearing Contiguous Fully Substituted Stereocenters. *Angew. Chem., Int. Ed.* **2022**, *61*, e202205816.

(8) (a) Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. Catalytic Conjunctive Cross-Coupling Enabled by Metal-induced Metallate Rearrangement. *Science* **2016**, *351*, 70−74. (b) Myhill, J. A.; Zhang, L.; Lovinger, G. J.; Morken, J. P. Enantioselective Construction of Tertiary Boronic Esters by Conjunctive Cross-Coupling. *Angew. Chem., Int. Ed.* **2018**, *57*, 12799−12803. (c) Wilhelmsen, C. A.; Zhang, X. T.; Myhill, J. A.; Morken, J. P. Enantioselective Synthesis of Tertiary β-Boryl Amides by Conjunctive Cross-Coupling of Alkenyl Boronates and Carbamoyl Chlorides. *Angew. Chem., Int. Ed.* **2022**, *61*, e2021167.

(9) (a) Lovinger, G. J.; Morken, J. P. Ni-Catalyzed Enantioselective Conjunctive Coupling with C(sp^3) Electrophiles: A Radical-Ionic Mechanistic Dichotomy. *J. Am. Chem. Soc.* **2017**, *139*, 17293−17296. (b) Koo, S. M.; Vendola, A. J.; Momm, S. N.; Morken, J. P. Alkyl Group Migration in Ni-Catalyzed Conjunctive Coupling with C(sp^3) Electrophiles: Reaction Development and Application to Targets of Interest. *Org. Lett.* **2020**, *22*, 666−669.

(10) Davis, C. R.; Luvaga, I. K.; Ready, J. M. Enantioselective Allylation of Alkenyl Boronates Promotes a 1,2-Metalate Rearrangement with 1,3-Diastereocontrol. *J. Am. Chem. Soc.* **2021**, *143*, 4921−4927.

(11) Zou, G.; Falck, J. R. Suzuki-Miyaura Coss-Coupling of Lithium *n*-Alkylborates. *Tetrahedron Lett.* **2001**, *42*, 5817−5819.

(12) Lovinger, G. J.; Aparece, M. D.; Morken, J. P. Pd-Catalyzed Conjunctive Cross-Coupling between Grignard-Derived Boron "Ate" Complexes and C(sp^2) Halides or Triflates: NaOTf as a Grignard Activator and Halide Scavenger. *J. Am. Chem. Soc.* **2017**, *139*, 3153−3160.

(13) Schwink, L.; Knochel, P. Enantioselective Preparation of C_2-Symmetrical Ferrocenyl Ligands for Asymmetric Catalysis. *Chem. Eur. J.* **1998**, *4*, 950−968.

(14) Gao, C. P.; Wilhelmsen, C. A.; Morken, J. P. Palladium-Catalyzed Conjunctive Cross-Coupling with Electronically Asymmetric Ligands. *J. Org. Chem.* **2023**, *88*, 1828−1835.

(15) Wang, G. Z.; Jiang, J.; Bu, X. S.; Dai, J. J.; Xu, J.; Fu, Y.; Xu, H. J. Copper-Catalyzed Cross-Coupling Reaction of Allyl Boron Ester with 1°/2°/3°-Halogenated Alkanes. *Org. Lett.* **2015**, *17*, 3682−3685.

(16) (a) Matteson, D. S. α-Halo Boronic Esters: Intermediates for Stereodirected Synthesis. *Chem. Rev.* **1989**, *89*, 1535−1551. (b) Matteson, D. S.; Collins, B. S. L.; Aggarwal, V. K.; Ciganek, E. The Matteson Reaction. *Organic Reactions* **2021**, *105*, 427−860.

(17) (a) Zweifel, G.; Arzoumanian, H.; Whitney, C. C. A Convenient Stereoselective Synthesis of Substituted Alkenes via Hydroboration-iodination of Alkynes. *J. Am. Chem. Soc.* **1967**, *89*, 3652−3653. (b) Armstrong, R. J.; Garcia-Ruiz, C.; Myers, E. L.; Aggarwal, V. K. Stereodivergent Olefination of Enantioenriched Boronic Esters. *Angew. Chem., Int. Ed.* **2017**, *56*, 786−790.

(18) Sonawane, R. P.; Jheengut, V.; Rabalakos, C.; Larouche-Gauthier, R.; Scott, H. K.; Aggarwal, V. K. Enantioselective Construction of Quaternary Stereogenic Centers from Tertiary Boronic Esters: Methodology and Applications. *Angew. Chem., Int. Ed.* **2011**, *50*, 3760−3763.

(19) Shao, L. M.; Hewitt, M. C.; Malcolm, S. C.; Wang, F. J.; Ma, J. G.; Campbell, U. C.; Spicer, N. A.; Engel, S. R.; Hardy, L. W.; Jiang, Z. D.; Schreiber, R.; Spear, K. L.; Varney, M. A. Synthesis and Pharmacological Characterization of Bicyclic Triple Reuptake Inhibitor 3-Aryl Octahydrocyclopenta[c]pyrrole Analogues. *J. Med. Chem.* **2011**, *54*, 5283−5295.