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Ziyong Wang, Jason Wu, Walid Lamine, Bo Li, Jean-Marc Sotiropoulos, et al.. C–Boron Enolates Enable Palladium Catalyzed Carboboration of Internal 1,3-Enynes. *Angewandte Chemie International Edition*, 2021, 60 (39), pp.21231-21236. 10.1002/anie.202108534 . hal-03351154

HAL Id: hal-03351154

<https://univ-pau.hal.science/hal-03351154v1>

Submitted on 22 Sep 2021

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C-Boron Enolates Enable Catalyzed Carboboration of Internal 1,3-Enynes

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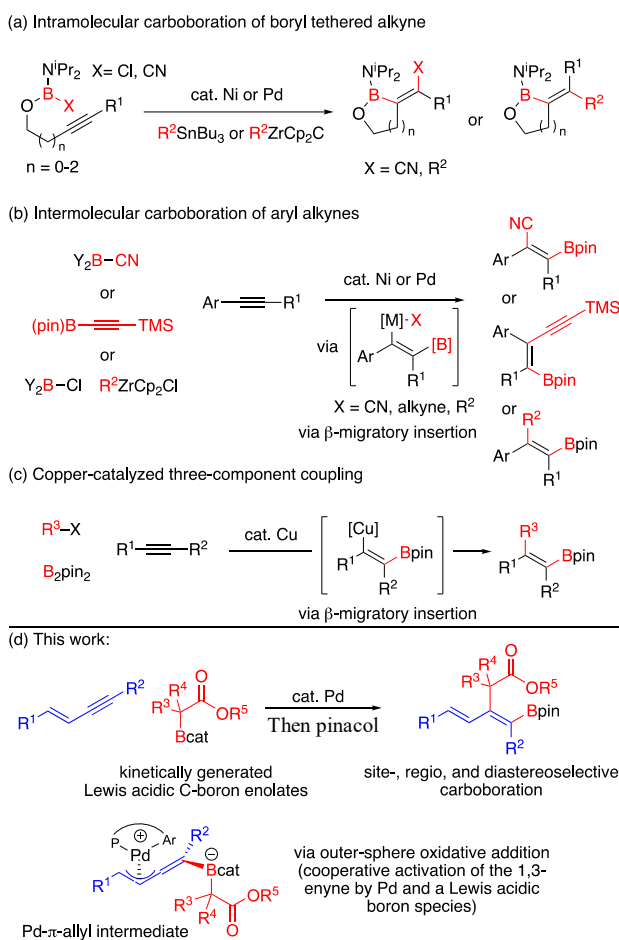
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ABSTRACT: A new family of carbon-bound boron enolates, generated by a kinetically controlled halogen exchange between chlorocatecholborane and silylketene acetals, is described. These C-boron enolates are demonstrated to activate 1,3-enyne substrates in the presence of a Pd(0)/Senphos ligand complex, resulting in the first examples of a carboboration reaction of an alkyne with enolate-equivalent nucleophiles. Highly substituted dienyl boron building blocks are produced in excellent site-, regio-, and diastereoselectivity by the described catalytic cis-carboboration reaction.

Alkenyl boronates are versatile building blocks in synthetic chemistry.¹ The ability of organoboron compounds to engage in Suzuki-Miyaura cross couplings² and to transform into various derivatives³ have made alkenyl boronates highly appealing in organic synthesis. In this context, numerous approaches⁴ have been developed to synthesize di-⁵ and tri-⁶ substituted alkenyl boronates. The synthesis of tetrasubstituted alkenyl⁷ boronates on the other hand, particularly in regioselective and stereoselective fashion, has been more challenging.⁸ Pioneering work by Suginome et al. (Scheme 1, a) established the nickel- or palladium catalyzed *intramolecular* boryl migration approach using alkyne substrates tethered with boryl moiety.⁹ Similarly, nickel and palladium catalyzed *intermolecular* carboboration of alkynes with various carbon sources (Scheme 1b) was reported.¹⁰ More recently, copper-catalyzed three-component coupling of an alkyne, B₂pin₂, and an electrophile (Scheme 1c) has received attention.¹¹ Despite these advances, carboboration reactions are still relatively limited in substrate scope and generality. In particular, stereoselective carboborations to produce tetra-substituted alkenes often face regio- and dia-stereoselectivity issues for internal unsymmetrical alkynes.^{11a-e} We recently reported the *trans*-hydroboration and *trans*-cyanoboration of 1,3-enynes catalyzed by a 1,4-azaborine biaryl phosphine (Senphos)-Pd complex.¹² The distinguishing feature of the Pd-Senphos catalyst system is the proposed unusual outer-sphere oxidative addition mechanism¹³ (a cooperative activation of the 1,3-enyne by LPd(0) and a Lewis acidic boron species) that introduces the boron group into the alkyne substrate with concomitant formation of a Pd- π -allyl species (vs. a more conventional β -migratory insertion pathway by reactions illustrated in Scheme 1, a-c). Given the known versatility of Pd π -allyl intermediate to achieve diverse functionalizations,¹⁴ we envisioned that new bond connections can be

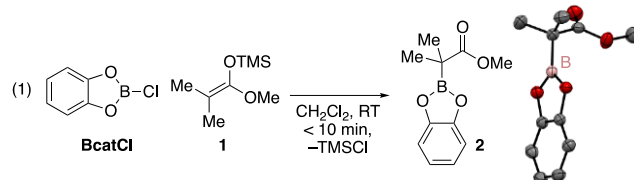
achieved with a variety of nucleophilic boron reagents. In this communication, we report the first carboboration reaction of an alkyne with a boron enolate, thus expanding the scope of carboboration reactions to include the ubiquitous family of enolate nucleophiles.¹⁵ The highly substituted dienyl boronates (containing a tetra-substituted alkene unit) are produced with exquisite site-, regio-, and diastereo-selectivity (Scheme 1d). Senphos ligand type structures are demonstrated to be uniquely enabling in achieving high catalytic efficiency and selectivity in this transformation.

Scheme 1. Regio- and Stereoselective Synthesis of Tetrasubstituted Alkenyl boronates



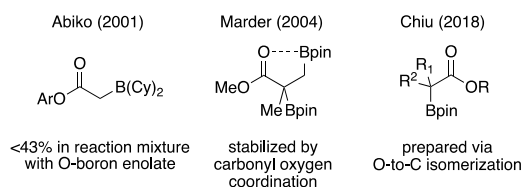
Key to successful development is the discovery of a new family of C-boron enolates as a suitably activating carboboration reagent. Treatment of a silylketene acetal **1** with catecholborane **BcatCl** cleanly furnishes C-catecholboron enolate **2**, which we have unambiguously structurally characterized by single crystal X-ray diffraction analysis (eq. 1). Compound **2** represents a rare example of a C-boron enolate without boron quaternization. The boron atom is completely planar (sum of bond angles = 360°), and the C=O bond is pointed in a direction relative to the C–B bond ($\angle\text{B-C-C=O} = -124.4(2)^\circ$) that is inconsistent with intramolecular coordination. The ^1H (*gem*-dimethyl signal at δ 1.5 ppm, ^{13}C (carbonyl carbon signal at δ 177.0 ppm), and ^{11}B NMR (signal at δ 34 ppm) of a CDCl_3 solution of **2** are also fully consistent with the C-boron enolate structure vs. O-boron enolate *in solution*.

Figure 1. Generation of C-boron enolates



To date, only few examples of unquaternized C-boron enolates have been reported.¹⁶ Abiko et al. reported the first C-boron enolates derived from carboxylic esters in their double aldol reaction study, which exists as equilibrium with the corresponding O-boron enolates.¹⁷ Marder's group observed C-boron enolates in a diborylation reaction, the stability of which was attributed to carbonyl oxygen coordination to β -boryl group.¹⁸ Recently, Chiu group synthesized C-pinacolboron enolates through alkenyl ester 1,4-hydroboration followed by a thermodynamically driven O-to-C isomerization.¹⁹

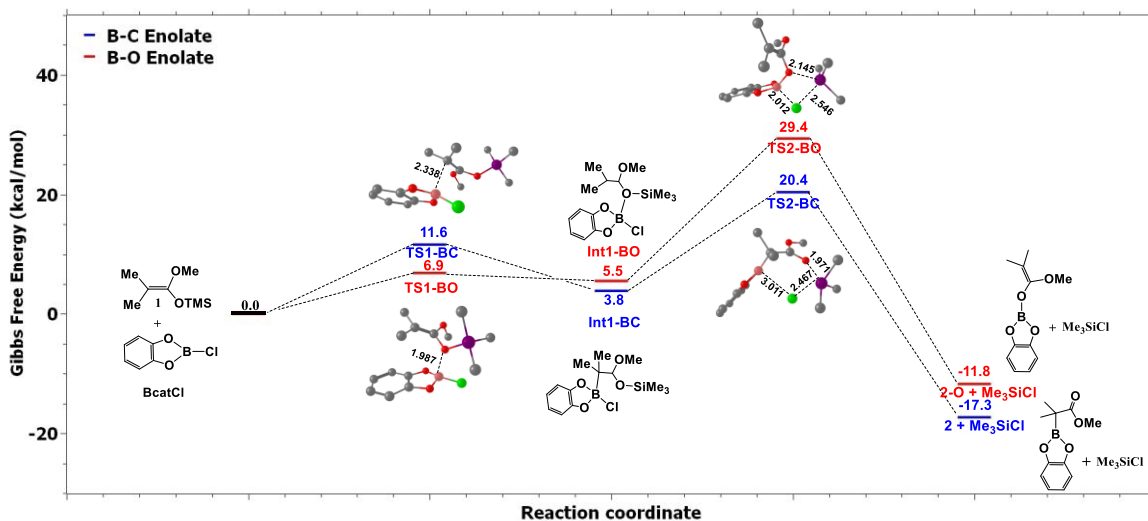
Scheme 2. C-Boron Enolates without Boron Quaternization accessed via thermodynamic control



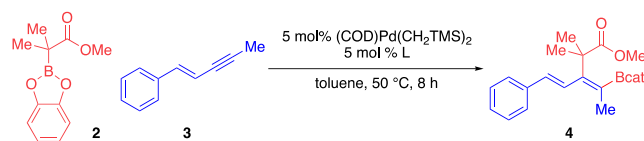
The distinguishing feature of our method illustrated in eq 1 is that the C-boron enolate is formed under kinetically controlled conditions. The reaction between **BcatCl** and silylketene acetal **1** does not lead to an observable built up of O-boron enolate by NMR. Furthermore, DFT calculations (see ESI for computational details) for the reaction between **BcatCl** and silylketene acetal **1**, performed at the SMD(CH_2Cl_2)-W97XD/6-31G(d,p) level of theory (Scheme 3),^{20,21} evidence a two-step mechanism (scheme 3) and predict that the rate-determining TMSCl elimination step is significantly more energetically unfavorable for the O-boron enolate pathway ($\Delta G^\ddagger = 29.4$ kcal/mol, red color) than for the C-boron enolate pathway ($\Delta G^\ddagger = 20.4$ kcal/mol,

blue color). DFT calculations also predict that the kinetically favored C-boron enolate product is also more stable than the O-boron enolate by 5.7 kcal/mol.

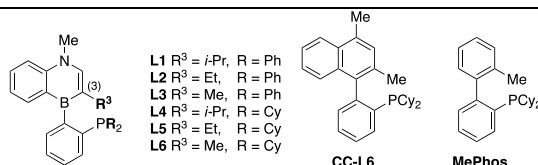
Scheme 3. Energy profiles for the reaction between BcatCl and **1** computed at SMD(CH₂Cl₂)-W97XD/6-31G(d,p) level of theory (ΔG in kcal/mol).



With a C-boron enolate in hand that is sufficiently Lewis acidic to possibly activate the 1,3-ene substrate in an outer-sphere oxidative addition fashion, we surveyed a series of ligands to optimize the carboboration reaction. In the presence of 5 mol% (COD)Pd(CH₂TMS)₂/ Senphos **L1**, reaction of 1,3-ene **3** with C-boron enolate **2** (generated from 2 equiv. BcatCl and 3 equiv. silyl ketene acetal **1**, see Supporting Information for experimental details) in toluene at 50 °C affords the corresponding *cis*-carboration product **4** in 10% yield with >98:2 *cis*-addition selectivity (Table 1, entry 1). In the absence of the catalyst under otherwise identical reaction conditions, no background reaction is observed. Switching the C(3) substituent R³ = *i*-Pr on the ligand to a sterically less demanding Et group improves the product yield (entry 2). A further decrease in the steric demand at the C(3) ligand position does not lead to further improvement in yield (entry 3, R³ = Me). Interestingly, changing the R group on the phosphorous atom from R = Ph to Cy improves the product yield significantly when R³ = Me (entry 6). However, the corresponding R³ = *i*-Pr ligand **L4** remains ineffective in supporting the Pd catalysis (entry 4). Moderate yield was achieved with ligand **L5** (R³ = Et, R = Cy, entry 5). Having established the optimal ligand structure as **L6**, we determined that the corresponding carbonaceous ligand **CC-L6** (entry 7) and the commercially available, structurally related **MePhos**²² (entry 8) are inferior ligands in terms of both efficiency and selectivity, highlighting the importance of the electronic structure provided by the BN heterocyclic Senphos ligands.²³ We also note that elevating the temperature from 50 °C to 60 °C results in a significant decrease in yield, presumably due to the competing decomposition of the reactive C-boron enolate **2** (entry 6 vs entry 9).²⁴

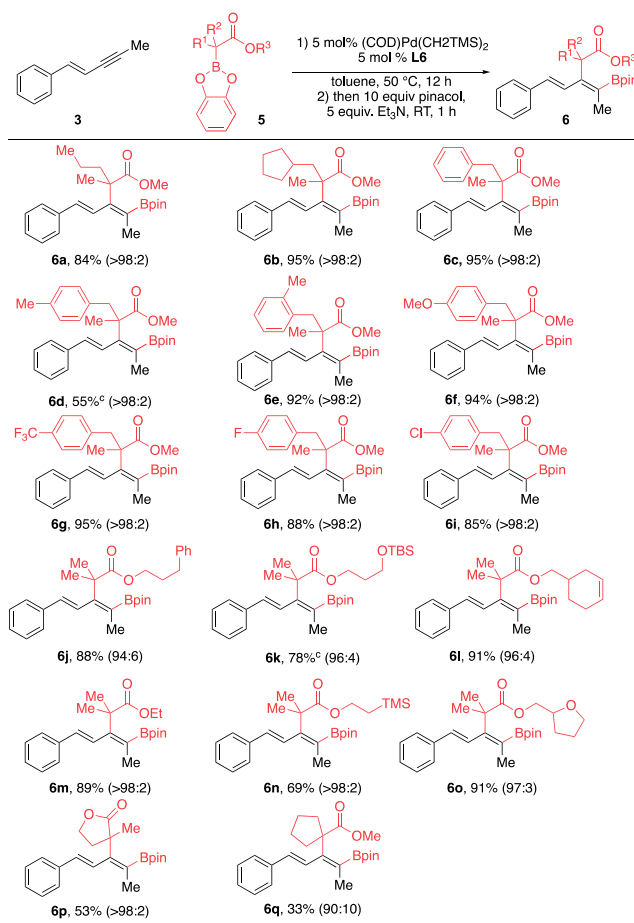
Table 1. Ligand Survey of Internal 1,3-enyne *cis*-Carboboration^a

entry	L	Yield (%) ^b	Selectivity ^b
1	L1	10	> 98:2 <i>cis</i> addition
2	L2	45	> 98:2 <i>cis</i> addition
3	L3	43	> 98:2 <i>cis</i> addition
4	L4	5	N.D.
5	L5	72	> 98:2 <i>cis</i> addition
6	L6	90(88)^c	> 98:2 <i>cis</i> addition
7	CC-L6	48	88:12 <i>cis</i> addition
8	MePhos	30	88:12 <i>cis</i> addition
9	L6	30 ^d	> 98:12 <i>cis</i> addition



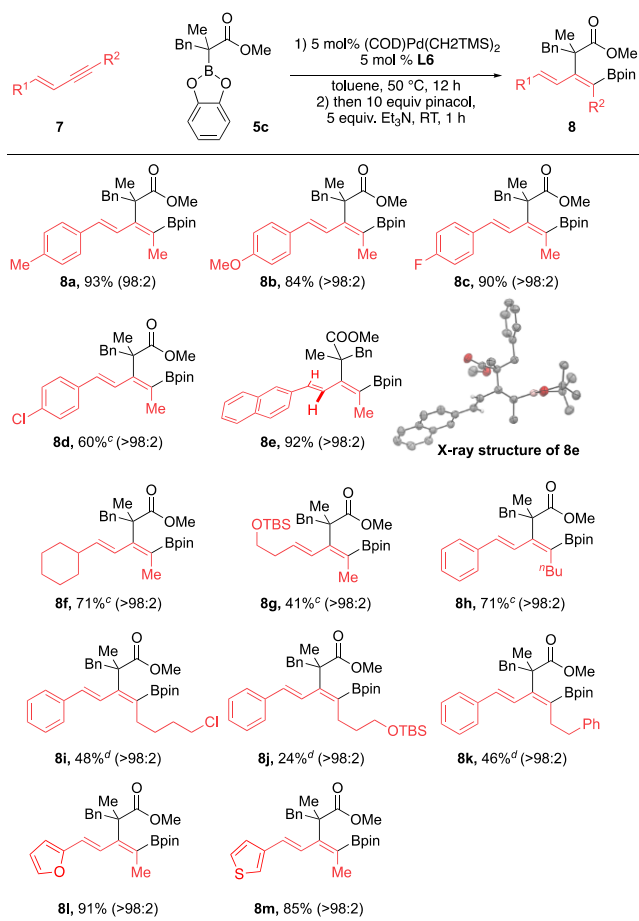
^a See SI for detailed procedure. ^b Yield and selectivity were determined by ¹H NMR analysis of unpurified reaction mixtures with CH₂Br₂ as the internal standard. ^c Isolated yield (in parenthesis) of the Bpin adduct. ^d Reaction performed at 60 °C.

Having identified optimal conditions, we next explored the scope of this transformation with different C-boron enolates (**Table 2**). Aryl substituents such as methoxy (entry **6f**), trifluoromethyl (entry **6g**), and aryl halides (entries **6h** and **6i**) are well tolerated. For as of yet to be determined reasons, a lower yield was observed for the *para*-methyl substituted aryl C-boron enolate (**6d**) while the *ortho*-methyl substituted C-boron enolate (entry **6e**) performed with high efficiency. Silyl ether (entry **6k**) and cyclic alkene (entry **6l**) functional groups are also tolerated. Sterically demanding cyclic C-boron enolates (entries **6p** and **6q**) are also suitable substrates, albeit a lower yield was observed.

Table 2. Reaction Scope of C-Boron Enolates^{a,b}

^a See SI for detailed procedure. Selectivity was determined by ¹H NMR analysis of the purified product. ^b Isolated yields are reported as the average of two runs. ^c 18 h reaction time.

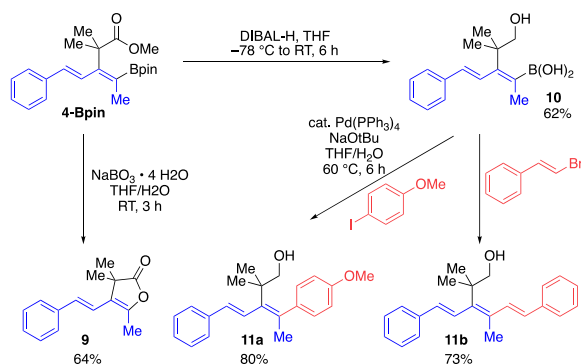
We then evaluated the generality of this method with respect to the internal 1,3-enyne (**Table 3**). 1,3-Enynes bearing an aryl group at the **R**¹ position generally give higher yields than alkyl groups (entry **6c**, **8a-c** vs. **8f-g**). When the steric demand at the **R**² position increases (**R**² > Me), the reaction becomes more sluggish (entries **8h-k**), however, the high diastereoselectivity is maintained. We are pleased to determine that heteroaryl derived enynes (furan: entry **8l**, and thiophene: entry **8m**) are excellent substrates for the carboboration reaction. We have obtained the X-ray crystal structure of product **8e**,²⁵ thus unambiguously establishing the connectivity and the diastereoselectivity of the reaction. Notably, the solid structure of compound **8e** shows an almost perpendicular diene structure with a C=C-C=C dihedral angle of -69.4(2)°, which highlights the steric demand imposed by the highly substituted alkene.²⁶ Overall, Table 3 illustrates that across all surveyed 1,3-enynes high site-, regio- and diastereoselectivity can be achieved for the carboboration.

Table 3. Reaction Scope of Internal 1,3-Enynes^{a,b}

^a See SI for detailed procedure. Selectivity was determined by ¹H NMR analysis of the purified product. ^b Isolated yields are reported as the average of two runs. ^c 18 h reaction time. ^d 18 h reaction time with 10 mol% [Pd]/**L6**.

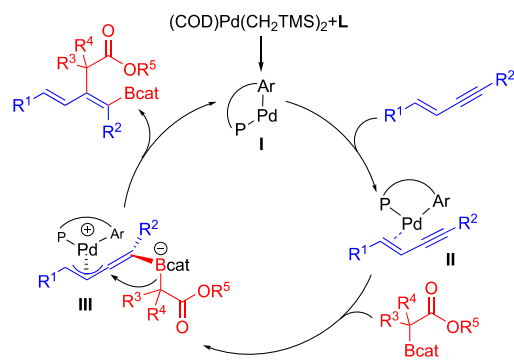
The highly substituted dienyl Bpin products can serve as useful intermediates in subsequent stereospecific transformations. For example, **4-Bpin** can be readily oxidized to afford the 2-furanone scaffold **9**, which comprises an important class of heterocyclic compounds in fragrances²⁷ and biologically active molecules.²⁸ Reduction of **4-Bpin** produces the dienyl boronic acid **10** which can further undergo Suzuki-Miyaura cross coupling with aryl or alkenyl halides to furnish the corresponding bis-aryl conjugated diene (**11a**) and triene (**11b**), respectively.

Scheme 4. Derivatization of Reaction Products



A plausible reaction mechanism is illustrated in Scheme 5. In the presence of Senphos ligand **L** the (COD)Pd(CH₂TMS)₂ precatalyst reductively eliminates 1,2-bis(trimethylsilyl)ethane to form the active LPd(0) species **I**,²⁹ which then subsequently binds to the 1,3-enyne. The LPd(0)-enyne complex **II** is then activated by the Lewis acidic C-boron enolate to furnish the outer-sphere oxidative adduct **III**. The Pd π -allyl is then attacked by an enolate equivalent to yield the product with concomitant regeneration of LPd(0) species **I**.¹⁴ C-Boron enolates are uniquely effective for this coupling reaction due to its more Lewis acidic boron center (vs. O-boron enolate) that can help activate the enyne substrate via an outer-sphere oxidation mechanism.³⁰ The stronger Lewis acidic character of the C-boron enolate versus O-boron enolate is corroborated by the electronic structure calculations where an analysis of LUMOs with a strong boron contribution reveals a significant lower energy for C-boron enolate (see ESI).

Scheme 5. Proposed Catalytic Cycle



In summary, we discovered a new class of C-boron enolates via a kinetically controlled halogen exchange between chlorocatecholborane and silylketene acetals. These C-boron enolates are uniquely capable

in activating 1,3-enyne substrates in the presence of a Pd(0)/Senphos ligand complex via a proposed outer-sphere oxidative addition reaction mechanism, resulting in the first examples of a carboboration reaction of an alkyne with enolate-equivalent nucleophiles. The described catalytic *cis*-carboboration reaction produces highly substituted dienyl boron building blocks in high site-, regio-, and diastereoselectivity under mild conditions. Current efforts are directed toward developing new metal/Senphos-catalyzed processes as well as a better understanding of the underlying reaction mechanisms.

ACKNOWLEDGMENT

Research reported in this publication was supported by the National Institute of General Medical Sciences of the National Institutes of Health under Award Number R01GM136920, the Excellence Initiative of Université de Pau et des Pays de l'Adour I-Site E2S UPPA, and by Boston College start-up funds. The "Direction du Numérique" of the Université de Pau et des Pays de l'Adour, CINES under allocation A009080045 made by Grand Equipement National de Calcul Intensif (GENCI) and Mésocentre de Calcul Intensif Aquitain (MCIA) are acknowledged for computational facilities.

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REFERENCE

- (1) For leading references, see: (a) Reid, W. B.; Spillane, J. J.; Krause, S. B.; Watson, D. A., Direct Synthesis of Alkenyl Boronic Esters from Unfunctionalized Alkenes: A Boryl-Heck Reaction. *J Am Chem Soc* **2016**, *138*, 5539-5542. (b) Hall, D. G., *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials*. John Wiley & Sons: 2012.
- (2) Miyaura, N.; Suzuki, A., Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds. *Chem. Rev.* **1995**, *95*, 2457-2483.
- (3) Fawcett, A.; Biberger, T.; Aggarwal, V. K., Carbopalladation of C–C σ -bonds enabled by strained boronate complexes. *Nat. Chem.* **2019**, *11*, 117-122.
- (4) For select reviews, see: (a) Takaya, J.; Iwasawa, N., Catalytic, Direct Synthesis of Bis(boronate) Compounds. *ACS Catal.* **2012**, *2*, 1993-2006. (b) Yoshida, H., Borylation of Alkynes under Base/Coinage Metal Catalysis: Some Recent Developments. *ACS Catal.* **2016**, *6*, 1799-1811. (c) Hemming, D.; Fritzscheier, R.; Westcott, S. A.; Santos, W. L.; Steel, P. G., Copper-boryl mediated organic synthesis. *Chem. Soc. Rev.* **2018**, *47*, 7477-7494. (d) Royes, J.; Cuenca, A. B.; Fernández, E., Access to 1,1-Diborylalkenes and Concomitant Stereoselective Reactivity. *Eur. J. Org. Chem.* **2018**, *2018*, 2728-2739. (e) Carreras, J.; Caballero, A.; Pérez, P. J., Alkenyl Boronates: Synthesis and Applications. *Chem. Asian J.* **2019**, *14*, 329-343. (f) Whyte, A.; Torelli, A.; Mirabi, B.; Zhang, A.; Lautens, M., Copper-Catalyzed Borylative Difunctionalization of π -Systems. *ACS Catal.* **2020**, *10*, 11578-11622.
- (5) For select examples, see: (a) Ojha, D. P.; Prabhu, K. R., Pd-Catalyzed Hydroborylation of Alkynes: A Ligand Controlled Regioselectivity Switch for the Synthesis of α - or β -Vinylboronates. *Org. Lett.* **2016**, *18*, 432-435. (b) Aparece, M. D.; Gao, C.; Lovinger, G. J.; Morken, J. P., Vinylidenation of Organoboronic Esters Enabled by a Pd-Catalyzed Metallate Shift. *Angew. Chem., Int. Ed.* **2019**, *58*, 592-595. (c) Lu, W.; Shen, Z., Direct Synthesis of Alkenylboronates from Alkenes and Pinacol Diboron via Copper Catalysis. *Org. Lett.* **2019**, *21*, 142-146. (d)

Wang, Y.; Guan, R.; Sivaguru, P.; Cong, X.; Bi, X., Silver-Catalyzed anti-Markovnikov Hydroboration of C–C Multiple Bonds. *Org. Lett.* **2019**, *21*, 4035-4038. (e) Bhattacharjee, J.; Harinath, A.; Bano, K.; Panda, T. K., Highly Chemoselective Hydroboration of Alkynes and Nitriles Catalyzed by Group 4 Metal Amidophosphine–Borane Complexes. *ACS Omega* **2020**, *5*, 1595-1606.

(6) For selected examples, see: (a) Wang, C.; Wu, C.; Ge, S., Iron-Catalyzed E-Selective Dehydrogenative Borylation of Vinylarenes with Pinacolborane. *ACS Catal.* **2016**, *6*, 7585-7589. (b) Wen, H.; Zhang, L.; Zhu, S.; Liu, G.; Huang, Z., Stereoselective Synthesis of Trisubstituted Alkenes via Cobalt-Catalyzed Double Dehydrogenative Borylations of 1-Alkenes. *ACS Catal.* **2017**, *7*, 6419-6425. (c) Tanaka, S.; Saito, Y.; Yamamoto, T.; Hattori, T., Electrophilic Borylation of Terminal Alkenes with BBr₃/2,6-Disubstituted Pyridines. *Org. Lett.* **2018**, *20*, 1828-1831. (d) Grams, R. J.; Fritzemeier, R. G.; Slebodnick, C.; Santos, W. L., trans-Hydroboration of Propiolamides: Access to Primary and Secondary (E)-β-Borylacrylamides. *Org. Lett.* **2019**, *21*, 6795-6799. (e) Meng, F.-F.; Xue, Q.-Y.; Jiang, B.; Zhao, M.; Xie, J.-H.; Xu, Y.-H.; Loh, T.-P., Divergent Protosilylation and Protoborylation of Polar Enynes. *Org. Lett.* **2019**, *21*, 2932-2936. (f) Yoshii, D.; Jin, X.; Mizuno, N.; Yamaguchi, K., Selective Dehydrogenative Mono- or Diborylation of Styrenes by Supported Copper Catalysts. *ACS Catal.* **2019**, *9*, 3011-3016. (g) Gao, Y.; Wu, Z.-Q.; Engle, K. M., Synthesis of Stereodefined 1,1-Diborylalkenes via Copper-Catalyzed Diboration of Terminal Alkynes. *Org. Lett.* **2020**, *22*, 5235-5239. (h) Liu, X.; Ming, W.; Friedrich, A.; Kerner, F.; Marder, T. B., Copper-Catalyzed Triboration of Terminal Alkynes Using B₂pin₂: Efficient Synthesis of 1,1,2-Triborylalkenes. *Angew. Chem., Int. Ed.* **2020**, *59*, 304-309. (i) Molloy, J. J.; Schäfer, M.; Wienhold, M.; Morack, T.; Daniliuc, C. G.; Gilmour, R., Boron-enabled geometric isomerization of alkenes via selective energy-transfer catalysis. *Science* **2020**, *369*, 302-306.

(7) For a recent overview of stereoselective synthesis of tetrasubstituted alkenes, see: Buttard, F.; Sharma, J.; Champagne, P. A., Recent advances in the stereoselective synthesis of acyclic all-carbon tetrasubstituted alkenes. *Chem. Commun.* **2021**, *57*, 4071-4088.

(8) For selected examples, see: (a) Itami, K.; Kamei, T.; Yoshida, J., Diversity-oriented synthesis of tamoxifen-type tetrasubstituted olefins. *J. Am. Chem. Soc.* **2003**, *125*, 14670-14671. (b) Shimizu, M.; Nakamaki, C.; Shimono, K.; Schelper, M.; Kurahashi, T.; Hiyama, T., Stereoselective cross-coupling reaction of 1,1-diboryl-1-alkenes with electrophiles: A highly stereocontrolled approach to 1,1,2-triaryl-1-alkenes. *J. Am. Chem. Soc.* **2005**, *127*, 12506-12507. (c) Mannathan, S.; Jeganmohan, M.; Cheng, C.-H., Nickel-Catalyzed Borylative Coupling of Alkynes, Enones, and Bis(pinacolato)diboron as a Route to Substituted Alkenyl Boronates. *Angew. Chem., Int. Ed.* **2009**, *48*, 2192-2195. (d) Endo, K.; Hirokami, M.; Shibata, T., Stereoselective Synthesis of Tetrasubstituted Alkenylboronates via 1,1-Organodiboronates. *J. Org. Chem.* **2010**, *75*, 3469-3472. (e) Kuang, Z.; Chen, H.; Yan, J.; Yang, K.; Lan, Y.; Song, Q., Base-Catalyzed Borylation/B–O Elimination of Propynols and B₂pin₂ Delivering Tetrasubstituted Alkenylboronates. *Org. Lett.* **2018**, *20*, 5153-5157. (f) Cabrera-Lobera, N.; Quirós, M. T.; Brennessel, W. W.; Neidig, M. L.; Buñuel, E.; Cárdenas, D. J., Atom-Economical Ni-Catalyzed Diborylative Cyclization of Enynes: Preparation of Unsymmetrical Diboronates. *Org. Lett.* **2019**, *21*, 6552-6556. (g) Guo, W.-H.; Zhao, H.-Y.; Luo, Z.-J.; Zhang, S.; Zhang, X., Fluoroalkylation-Borylation of Alkynes: An Efficient Method To Obtain (Z)-Tri- and Tetrasubstituted Fluoroalkylated Alkenylboronates. *ACS Catal.* **2019**, *9*, 38-43.

(9) (a) Suginome, M.; Yamamoto, A.; Murakami, M., Palladium- and Nickel-Catalyzed Intramolecular Cyanoboration of Alkynes. *J. Am. Chem. Soc.* **2003**, *125*, 6358-6359. (b) Yamamoto, A.; Suginome, M., Nickel-Catalyzed trans-Alkynylboration of Alkynes via Activation of a Boron-Chlorine Bond. *J. Am. Chem. Soc.* **2005**, *127*, 15706-15707. (c) Daini, M.; Yamamoto, A.; Suginome, M., Palladium-Catalyzed trans- and cis-Carboboration of Alkynes Tethered to Chloroborane with Organozirconium Reagents: Ligand-Dependent Complementary Stereoselectivity. *J. Am. Chem. Soc.* **2008**, *130*, 2918-2919.

(10) (a) Suginome, M.; Yamamoto, A.; Murakami, M., Palladium-Catalyzed Addition of Cyanoboranes to Alkynes: Regio- and Stereoselective Synthesis of α,β-Unsaturated β-Boryl Nitriles. *Angew. Chem., Int. Ed.* **2005**, *44*, 2380-2382. (b) Suginome, M.; Shirakura, M.; Yamamoto, A., Nickel-Catalyzed Addition of Alkynylboranes to Alkynes. *J. Am. Chem. Soc.* **2006**, *128*, 14438-14439. (c) Daini, M.; Suginome, M., Palladium-catalyzed carboboration of alkynes using chloroborane and organozirconium reagents. *Chem. Commun.* **2008**, 5224-5226.

(11) For selected examples, see: (a) Alfaro, R.; Parra, A.; Aleman, J.; Garcia Ruano, J. L.; Tortosa, M., Copper(I)-Catalyzed Formal Carboboration of Alkynes: Synthesis of Tri- and Tetrasubstituted Vinylboronates. *J. Am. Chem. Soc.* **2012**, *134*, 15165-15168. (b) Yoshida, H.; Kageyuki, I.; Takaki, K., Copper-catalyzed three-component carboboration of alkynes and alkenes. *Org. Lett.* **2013**, *15*, 952-955. (c) Zhou, Y.; You, W.; Smith, K. B.; Brown, M. K., Copper-Catalyzed Cross-Coupling of Boronic Esters with Aryl Iodides and Application to the Carboboration of Alkynes and Allenes. *Angew. Chem., Int. Ed.* **2014**, *53*, 3475-3479. (d) Bin, H.-Y.; Wei, X.; Zi, J.; Zuo, Y.-J.; Wang, T.-C.; Zhong, C.-M., Substrate-Controlled Regio- and Stereoselective Synthesis of Boron-Substituted 1,4-

Dienes via Copper-Catalyzed Boryl-Allylation of Alkynes with Allyl Phosphates and Bis(pinacolato)diboron. *ACS Catal.* **2015**, *5*, 6670-6679. (e) Itoh, T.; Shimizu, Y.; Kanai, M., Ligand-Enabled, Copper-Catalyzed Regio- and Stereoselective Synthesis of Trialkylsubstituted Alkenylboronates from Unactivated Internal Alkynes. *J. Am. Chem. Soc.* **2016**, *138*, 7528-7531. (f) Su, W.; Gong, T.-J.; Zhang, Q.; Zhang, Q.; Xiao, B.; Fu, Y., Ligand-Controlled Regiodivergent Copper-Catalyzed Alkylboration of Unactivated Terminal Alkynes. *ACS Catal.* **2016**, *6*, 6417-6421. (g) Zhao, J.; Szabo, K. J., Catalytic Borylative Opening of Propargyl Cyclopropane, Epoxide, Aziridine, and Oxetane Substrates: Ligand Controlled Synthesis of Allenyl Boronates and Alkenyl Diboronates. *Angew. Chem., Int. Ed.* **2016**, *55*, 1502-1506. (h) Boreux, A.; Indukuri, K.; Gagosz, F.; Riant, O., Acyl Fluorides as Efficient Electrophiles for the Copper-Catalyzed Boroacylation of Allenes. *ACS Catal.* **2017**, *7*, 8200-8204. (i) Fujihara, T.; Sawada, A.; Yamaguchi, T.; Tani, Y.; Terao, J.; Tsuji, Y., Boraformylation and Silaformylation of Allenes. *Angew. Chem., Int. Ed.* **2017**, *56*, 1539-1543. (j) Mateos, J.; Rivera-Chao, E.; Fananas-Mastral, M., Synergistic Copper/Palladium Catalysis for the Regio- and Stereoselective Synthesis of Borylated Skipped Dienes. *ACS Catal.* **2017**, *7*, 5340-5344. (k) Mun, B.; Kim, S.; Yoon, H.; Kim, K. H.; Lee, Y., Total Synthesis of Isohericerin, Isohericenone, and Erinacerin A: Development of a Copper-Catalyzed Methylboration of Terminal Alkynes. *J. Org. Chem.* **2017**, *82*, 6349-6357. (l) Rivera-Chao, E.; Fananas-Mastral, M., Synthesis of Stereodefined Borylated Dendralenes through Copper-Catalyzed Allylboration of Alkynes. *Angew. Chem., Int. Ed.* **2018**, *57*, 9945-9949. (m) Rivera-Chao, E.; Mitxelena, M.; Varela, J. A.; Fañanás-Mastral, M., Copper-Catalyzed Enantioselective Allylboration of Alkynes: Synthesis of Highly Versatile Multifunctional Building Blocks. *Angew. Chem., Int. Ed.* **2019**, *58*, 18230-18234. (n) Li, Z.; Zhang, L.; Nishiura, M.; Luo, G.; Luo, Y.; Hou, Z., Enantioselective Cyanoborylation of Allenes by N-Heterocyclic Carbene-Copper Catalysts. *ACS Catal.* **2020**, *10*, 11685-11692. (o) Pozo, J. d.; Zhang, S.; Romiti, F.; Xu, S.; Conger, R. P.; Hoveyda, A. H., Streamlined Catalytic Enantioselective Synthesis of α -Substituted β,γ -Unsaturated Ketones and Either of the Corresponding Tertiary Homoallylic Alcohol Diastereomers. *J. Am. Chem. Soc.* **2020**, *142*, 18200-18212.

(12) (a) Xu, S.; Zhang, Y.; Li, B.; Liu, S.-Y., Site-Selective and Stereoselective trans-Hydroboration of 1,3-Enynes Catalyzed by 1,4-Azaborine-Based Phosphine-Pd Complex. *J. Am. Chem. Soc.* **2016**, *138*, 14566-14569. (b) Zhang, Y.; Li, B.; Liu, S.-Y., Pd-Senphos Catalyzed trans-Selective Cyanoboration of 1,3-Enynes. *Angew. Chem., Int. Ed.* **2020**, *59*, 15928-15932.

(13) Yang, Y.; Jiang, J.; Yu, H.; Shi, J., Mechanism and Origin of the Stereoselectivity in the Palladium-Catalyzed trans Hydroboration of Internal 1,3-Enynes with an Azaborine-Based Phosphine Ligand. *Chem. Eur. J.* **2018**, *24*, 178-186.

(14) (a) Trost, B. M.; Van Vranken, D. L., Asymmetric Transition Metal-Catalyzed Allylic Alkylations. *Chem. Rev.* **1996**, *96*, 395-422. (b) Trost, B. M.; Crawley, M. L., Asymmetric Transition-Metal-Catalyzed Allylic Alkylations: Applications in Total Synthesis. *Chem. Rev.* **2003**, *103*, 2921-2944.

(15) Braun, M., *Modern Enolate Chemistry: From Preparation to Applications in Asymmetric Synthesis*. John Wiley & Sons: 2015.

(16) For an overview of C-boron enolates, see: He, Z.; Zajdlík, A.; Yudin, A. K., α -Borylcarbonyl compounds: from transient intermediates to robust building blocks. *Dalton Trans.* **2014**, *43*, 11434-11451.

(17) Abiko, A.; Inoue, T.; Masamune, S., Mechanism of the Double Aldol Reaction: The First Spectroscopic Characterization of a Carbon-Bound Boron Enolate Derived from Carboxylic Esters. *J. Am. Chem. Soc.* **2002**, *124*, 10759-10764.

(18) Bell, N. J.; Cox, A. J.; Cameron, N. R.; Evans, J. S. O.; Marder, T. B.; Duin, M. A.; Elsevier, C. J.; Baucherel, X.; Tulloch, A. A. D.; Tooze, R. P., Platinum catalysed 3,4- and 1,4-diboration of α,β -unsaturated carbonyl compounds using bis-pinacolatodiboron. *Chem. Commun.* **2004**, 1854-1855.

(19) Ng, E. W. H.; Low, K.-H.; Chiu, P., Synthesis and Applications of Unquaternized C-Bound Boron Enolates. *J. Am. Chem. Soc.* **2018**, *140*, 3537-3541.

(20) (a) Chai, J.-D.; Head-Gordon, M., Long-range corrected hybrid density functionals with damped atom-atom dispersion corrections. *Phys. Chem. Chem. Phys.* **2008**, *10*, 6615-6620. (b) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378-6396.

(21) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J.

- E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, Revision D.01; Gaussian Inc.: Wallingford, CT, 2009.
- (22) Surry, D. S.; Buchwald, S. L., Biaryl Phosphane Ligands in Palladium-Catalyzed Amination. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338-6361.
- (23) Xu, S.; Haeffner, F.; Li, B.; Zakharov, L. N.; Liu, S.-Y., Monobenzofused 1,4-Azaborines: Synthesis, Characterization, and Discovery of a Unique Coordination Mode. *Angew. Chem., Int. Ed.* **2014**, *53*, 6795-6799.
- (24) At elevated temperatures, C-boron enolate **2** begins to decompose to dimethyl ketene and methoxycatecholborane.
- (25) Deposition Numbers 2091128 (for **2**) and 2091129 (for **8e**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.
- (26) (a) Mori, H.; Ikoma, K.; Masui, Y.; Isoe, S.; Kitaura, K.; Katsumura, S., Abnormally high reactivity of the vinyl hydrogen toward singlet oxygen in twisted 1,3-diene. *Tetrahedron Lett.* **1996**, *37*, 7771-7774. (b) Mori, H.; Ikoma, K.; Isoe, S.; Kitaura, K.; Katsumura, S., Photosensitized Oxygenation of Twisted 1,3-Dienes: Abnormally Higher Reactivity of Vinyl Hydrogen Rather than Allyl Hydrogen toward Singlet Oxygen. *J. Org. Chem.* **1998**, *63*, 8704-8718. (c) Mori, H.; Katsumura, S., Unique Reactivity of Twisted 1, 3-Diene. *J. Syn. Org. Chem. Jpn.* **2003**, *61*, 857-867.
- (27) (a) Miyazawa, Y.; Ohashi, T.; Kawaguchi, K.; Tanaka, N.; Katsuta R.; Yajima, A.; Nukada T.; Ishigami, K., Synthesis and odour evaluation of double-bond isomers of Damascenolide, 4-(4-methylpent-3-en-1-yl)-2(5H)-furanone, which has a citrus-like odour. *Flavour Fragr. J.* **2020**, *35*, 341-349. (b) Berger, R. G., *Flavours and fragrances: chemistry, bioprocessing and sustainability*. Springer Science & Business Media: 2007.
- (28) Husain, A.; Khan, S. A.; Iram, F.; Iqbal, M. A.; Asif, M., Insights into the chemistry and therapeutic potential of furanones: A versatile pharmacophore. *Eur. J. Med. Chem.* **2019**, *171*, 66-92.
- (29) Takahashi, R.; Kubota, K.; Ito, H., Air- and moisture-stable Xantphos-ligated palladium dialkyl complex as a precatalyst for cross-coupling reactions. *Chem. Commun.* **2020**, *56*, 407-410.
- (30) We have determined that O-boron enolates (e.g., derived from an amide rather than an ester) do not react under our currently optimized reaction conditions. See Supporting Information for experimental details.