ACS Catalysis

pubs.acs.org/acscatalysis

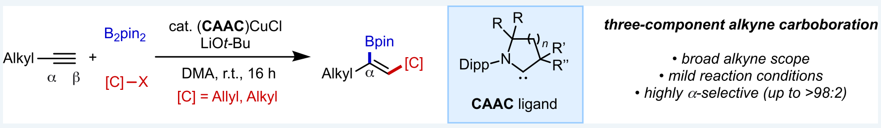
Letter

(CAAC)Copper Catalysis Enables Regioselective Three-Component Carboboration of Terminal Alkynes

Yang Gao, Nana Kim,‡ Skyler D. Mendoza,‡ Sima Yazdani, Andre Faria Vieira, Mingyu Liu, Aaron Kendrick, IV, Douglas B. Grotjahn, Guy Bertrand,* Rodolphe Jazzar,* and Keary M. Engle*

Cite This: *ACS Catal.* 2022, 12, 7243−7247

Read Online



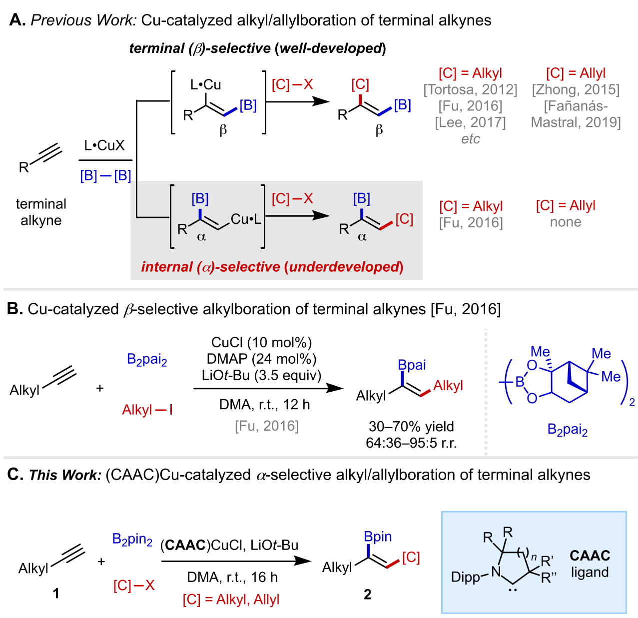
ABSTRACT: Cyclic(alkyl)(amino)carbene (CAAC) ligands are found to perturb regioselectivity of the copper-catalyzed carboboration of terminal alkynes, favoring the less commonly observed internal alkenylboron regiosomer through an α-selective borylcupration step. A variety of carbon electrophiles participate in the reaction, including allyl alcohol derivatives and alkyl halides. The method provides a straightforward and selective route to versatile trisubstituted alkenylboron compounds that are otherwise challenging to access.

KEYWORDS: *organoboron, copper, carboboration, CAAC ligand, regioselectivity*

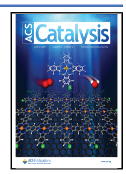
Organoboron compounds play a unique role in the chemical sciences. Carbon−boron bonds can readily be converted into a diverse array of carbon−carbon and carbon−heteroatom linkages via an ever-expanding battery of methods,[1−4] and organoboron molecules themselves possess a myriad of functions in the context of biology[5,6] and materials science.[7−9] The invention of new methods to assemble organoboron compounds from simple chemical inputs streamlines access to important families of molecules. Multicomponent catalytic couplings, in which three or more building blocks are united in a single reaction, hold tremendous promise in enabling direct synthesis of densely functionalized organoboron compounds. In this context, copper-catalyzed borylative 1,2-difunctionalization of alkynes is an established means of preparing tri- and tetrasubstituted alkenylboron targets via a mechanism involving migratory insertion of an alkyne into a L_n·Cu^I−boryl intermediate, followed by coupling of the resulting L_n·Cu^I(alkenyl) species with an electrophile.[10−13] Controlling the regioselectivity of these processes to access either regioisomer in a predictable manner remains challenging (Scheme 1). With terminal alkynes, the vast majority of catalytic systems deliver the boryl group to the terminal (β) position, restricting access to the opposite alkenylboron regioisomers (Scheme 1A). Here, we demonstrate that appropriately tuned cyclic(alkyl)(amino)-carbene (CAAC)-ligated copper catalysts enable regioselective carboboration to give internal (α) alkenylboron compounds with a broad collection of carbon electrophiles (Scheme 1C).

Regioselectivity trends in L_n·Cu−boryl alkyne addition processes are complex and reflect an interplay between the steric and electronic properties of the ligand, the identity of the boryl group, and the substituent(s) on the alkyne substrate.[14−16] N-Heterocyclic carbene (NHC) ligands[17,18] have been widely

Scheme 1. Overview of Cu-Catalyzed Regioselective Carboboration of Terminal Alkynes



Received: February 4, 2022
Revised: May 25, 2022
Published: June 2, 2022



https://doi.org/10.1021/acscatal.2c00614
ACS Catal. 2022, 12, 7243−7247

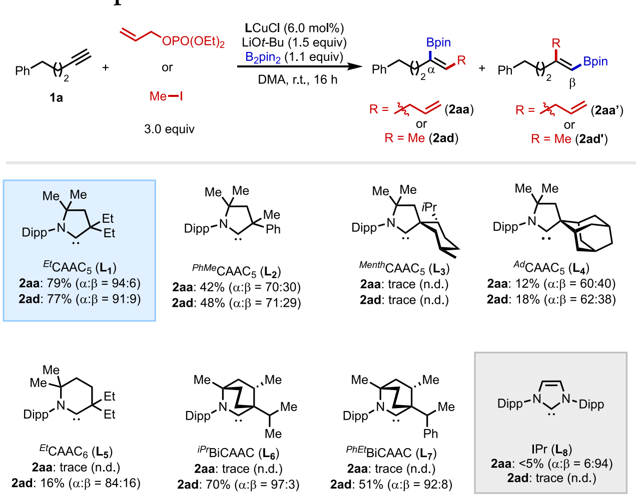
used in catalytic L_n·Cu−boryl catalysis and generally favor boryl transfer to the terminal position of terminal alkynes with Bpin and related boryl groups, though either position can predominate depending on the nature of substrate and the ligand environment around boron. We recently demonstrated that strongly σ-donating CAAC ligands[19−21] override substituent effects of the boryl group and the alkyne, allowing for reliably Markovnikov (α-selective) protoboration of diverse terminal alkynes with a variety of bis-boron nucleophiles.[22] On the basis of this result, we questioned whether it would be possible to employ C(sp^3)-based electrophiles in lieu of a proton to develop a three-component carboboration, with regioselectivity and product substitution patterns that would complement existing methodology.[23−32] Of relevance to this proposal, Xiao and Fu disclosed an important study in which the combination of CuCl (10 mol %) as the precatalyst, DMAP (24 mol %) as the ligand, and B_2pai_2 (pai = (+)-pinanediolato) as the bis-boron reagent led to branched-selective carboboration, though in this case yields and regioselectivities were variable (30−70% yield, 64:36−95:5 r.r.) (Scheme 1B). The less common and more expensive B_2pai_2 nucleophile was employed to maximize regioselectivity, and some synthetically useful carbogenic groups were incompatible with this protocol (e.g., allyl electrophiles).[33]

To reduce our idea to practice, we examined carboboration of model terminal alkyne **1a** with two representative carbon electrophiles, allyl diethyl phosphate and methyl iodide. The former was selected because allyl electrophiles have not been previously employed in α-selective carboboration of alkynes, despite being used in several reports of linear selectivity.[30−32,34] The latter was selected because it was found to be low-yielding under previously published conditions (one example, 87:13 r.r., 32% yield).[33]

A library of CAAC·CuCl precatalysts with different steric and electronic properties was tested, and a summary of the data is shown in Table 1. To our delight, ^{Et}CAAC$_5$-ligated Cu complex ($\mathbf{L_1}$CuCl) promoted both transformations with high conversion and high α-selectivity. Replacement of the ethyl groups on the α-carbon of $\mathbf{L_1}$[35] with either an electron-withdrawing group ($\mathbf{L_2}$)[36] or more sterically bulky groups ($\mathbf{L_3}$,$\mathbf{L_4}$)[35,37] led to decreased yield and α:β ratio. ^{Et}CAAC$_6$ ligand ($\mathbf{L_5}$),[38] a much stronger electron-donor than $\mathbf{L_1}$, gave poor yields in both transformations, though high α:β ratio (84:16) was observed in the methylboration reaction. Interestingly, BiCAAC ligands,[39] $^{i\text{-}Pr}$BiCAAC ($\mathbf{L_6}$) and ^{PhEt}BiCAAC ($\mathbf{L_7}$), which are also strong electron-donors, furnished the desired methylborylated product **2ad** with high α-selectivity (97% and 92%, respectively). However, neither $\mathbf{L_6}$ or $\mathbf{L_7}$ could deliver any desired allylborylated product **2aa**. Moreover, further exploration of substrate scope for methylboration using $\mathbf{L_6}$ suggested that this ligand could not tolerate the presence of Lewis basic functional groups. For example, when an ether-containing substrate was attempted (see **2kd** below, Table 3), only 23% yield and 47% α-selectivity were observed. A control experiment with IPr ($\mathbf{L_8}$), a representative N-heterocyclic carbene ligand commonly used in copper−boryl chemistry,[10−13] led to low yield with both electrophiles.

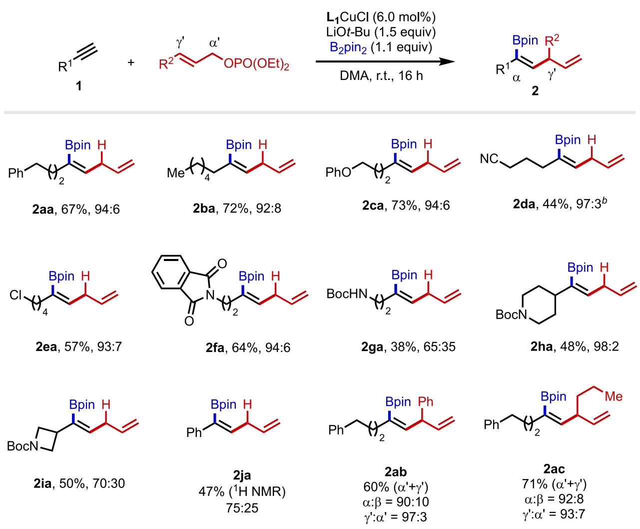
With the optimized conditions in hand, we examined the scope of the allylboration reaction (Table 2). Terminal alkynes bearing primary alkyl groups provided the corresponding products in excellent yields with high levels of regioselectivity (**2aa** and **2ba**). In addition, functional groups such as ether (**2ca**), cyano (**2da**), halogen (**2ea**), protected amines (**2fa** and **2ga**), pendant piperidine (**2ha**) and azetidine (**2ia**) were well tolerated, furnishing desired products in good yields and high α-selectivity, except in the case of **2ga** and **2ia**, where moderate α-selectivity (65% and 70%, respectively) was observed. Notably, when phenylacetylene was subjected to the optimal reaction conditions, the desired product **2ja** was generated with 75% α-selectivity. Allyl electrophiles with phenyl and n-propyl groups at the γ-position were also compatible under the reaction conditions, furnishing the desired products in high yields (60−71%) and excellent regioselectivity (>90% α-borylation, 93−97% S_N2' allylation) (**2ab** and **2ac**).

Table 1. Optimization of Reaction Conditions[a]



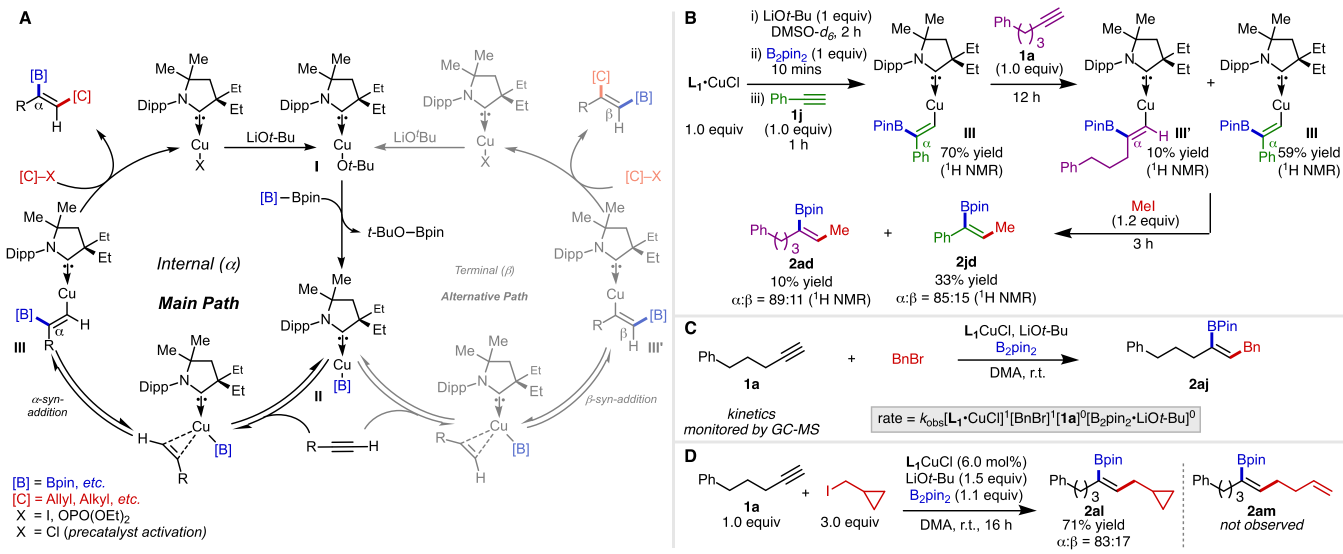
[a]Yields of products (**2aa** or **3aa**) and regioselectivity (±2%) were determined by ^{1}H NMR spectroscopy (600 MHz) using CH_2Br_2 as the internal standard. n.d. = not determined.

Table 2. Scope of α-Selective Allylboration of Terminal Alkynes[a]



[a]Conditions: **1** (0.10 mmol), B_2pin_2 (0.11 mmol), allyl electrophile (0.30 mmol), $\mathbf{L_1}$CuCl (0.006 mmol), LiO*t*-Bu (0.15 mmol), and DMA (0.60 mL), r.t. Ratios of α:β (±2) were determined via ^{1}H NMR spectroscopy (600 MHz) of the crude reaction mixtures. Percentages represent isolated yields of the α-borylated product. [b]The corresponding protoboration side product (23%) was observed by ^{1}H NMR analysis of the crude reaction mixture.

Scheme 2. Catalytic Cycle and Mechanistic Studies

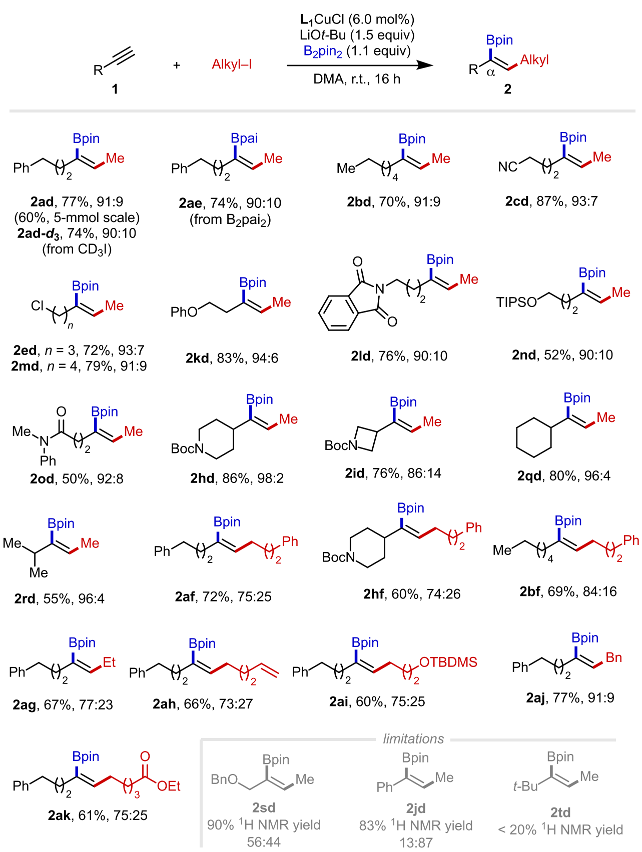


We next explored the scope of terminal alkynes for alkylboration. Alkynes containing different primary alkyl chains readily underwent efficient methylboration with high α-selectivity (**2ad** and **2bd**). In addition, a range of functional groups, including ether (**2kd**), chloro (**2ed**, **2md**), cyano (**2 cd**), amide (**2od**), and protected amino group (**2ld**), were tolerated, furnishing the desired products in good yields and high regioselectivity. The reactions of alkynes bearing secondary alkyl groups at the α-position (**2qd** and **2rd**) gave high α-selectivity as well. However, like in the previously reported (CAAC)Cu-catalyzed protoboration reaction,[22] *tert*-butyl acetylene (**2td**) has very low reactivity under the optimal conditions. Alkynes with medicinally relevant functional groups, such as pendant piperidine and azetidine moieties, were both competent coupling partners (**2hd** and **2id**). Unfortunately, poor α-selectivity was observed when benzyl-protected propargyl alcohol (**2sd**) or phenylacetylene (**2jd**) were used as substrates.

The scope of the alkyl electrophile was then examined. Deuterated methyl iodide works well, showing the ability of this method to assemble isotopically labeled compounds efficiently. The reactions of primary alkyl electrophiles with **1a** afforded the α-selective alkylboration products with high yield, though relatively lower α:β ratios were observed compared to the reaction using methyl iodide (**2af**, **2ag**). Notably, alkyl electrophiles containing functional groups, such as terminal alkene, silyl ether, and ester, were compatible under our reaction conditions, giving 60−66% yield and 73−75% α-selectivity (**2ah**−**2aj**). Using benzyl bromide as the electrophile, the desired product (**2ak**) was generated in excellent yield and high α-selectivity. A similar α:β ratio was observed when an alkyne bearing secondary alkyl groups at the α-position was applied (**2hf**).

A plausible catalytic cycle for this reaction is depicted in Scheme 2A. One possible explanation for the observation that regioselectivity varies across the different C(sp^3) electrophiles tested in Table 3 is that the borylcupration step could be reversible. Under such a scenario, the nature of the C(sp^3) electrophile and the rate of C−C bond formation may influence regioselectivity. To test this hypothesis, we performed a crossover experiment between alkynes **1a** and **1j**. In this

Table 3. Scope of α-Selective Alkylboration of Terminal Alkynes[a]



[a]Conditions: **1** (0.10 mmol), B_2pin_2 (0.11 mmol), alkyl iodide (0.30 mmol), $\mathbf{L_1}$CuCl (0.006 mmol), LiO*t*-Bu (0.15 mmol), and DMA (0.60 mL), r.t. Ratios of α:β (±2) were determined via ^{1}H NMR spectroscopy (600 MHz) of the crude reaction mixtures. Percentages represent isolated yields of the α-borylated products.

experiment, $\mathbf{L_1}$·CuCl was reacted with LiO*t*-Bu, then B_2pin_2, followed by alkyne **1j** in a J. Young tube and monitored by NMR spectroscopy to show a 70% yield of the *in situ*-generated complex **III** (Scheme 2B). Subsequent addition of alkyne **1a**

https://doi.org/10.1021/acscatal.2c00614
ACS Catal. 2022, 12, 7243−7247

afforded a mixture of borylcuprated species **III** and **III′**, as observed by ^{1}H and ^{13}C NMR spectroscopies. These results support a reversible borylcupration in which complex **III** reverts to boryl complex **II** (Scheme 2A) followed by reinsertion with alkyne **1a** to afford the observed mixture. In parallel, we also performed kinetic studies of the reaction of alkyne **1a** and BnBr and found a first-order rate dependence in catalyst [$\mathbf{L_1}$·CuCl] and electrophile [BnBr]. Meanwhile, a zeroth-order rate dependence was observed from the alkyne [**1a**] and the borane/base combination [B_2pin_2·LiO*t*-Bu] (Scheme 2C). The resulting rate law is consistent with the mechanism proposed in Scheme 2A, wherein a reversible borylcupration precedes the regio- and rate-determining reaction with the electrophile. These studies taken together support the proposed mechanism wherein a reversible borylcupration would account for the change in regioselectivity as a function of electrophile identity. To investigate the mechanism of the alkylation step, we performed a radical clock experiment with cyclopropylmethyl iodide (Scheme 2D). The results of this study show exclusive formation of the ring-intact product (**2al**) with no detectable quantity of ring-opened product (**2am**) observed. This indicates that the alkylation step likely does not proceed through a radical-based mechanism.

In conclusion, we have extended our investigations of (CAAC)Cu−boryl catalysis to the three-component carboboration of terminal alkynes and have found that high levels of α-selectivity are maintained across different carbon electrophiles, including allyl electrophiles, which have not been previously employed in an α-selective reaction system. The generality of the method across different alkyne substrates offers a convenient means of preparing trisubstituted alkenylboron compounds with established utility in organic synthesis.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscatal.2c00614.

Experimental procedures and spectral data (PDF)

NMR data (MNova format) (ZIP)

■ AUTHOR INFORMATION

Corresponding Authors

Guy Bertrand − *UCSD-CNRS Joint Research Laboratory (IRL 3555), Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States*; Email: gbertrand@ucsd.edu

Rodolphe Jazzar − *UCSD-CNRS Joint Research Laboratory (IRL 3555), Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States*; orcid.org/0000-0002-4156-7826; Email: rjazzar@ucsd.edu

Keary M. Engle − *Department of Chemistry, The Scripps Research Institute, La Jolla, California 92037, United States*; orcid.org/0000-0003-2767-6556; Email: keary@scripps.edu

Authors

Yang Gao − *Department of Chemistry, The Scripps Research Institute, La Jolla, California 92037, United States*; orcid.org/0000-0001-9270-6251

Nana Kim − *Department of Chemistry, The Scripps Research Institute, La Jolla, California 92037, United States*

Skyler D. Mendoza − *Department of Chemistry, The Scripps Research Institute, La Jolla, California 92037, United States*; orcid.org/0000-0003-1939-1884

Sima Yazdani − *UCSD-CNRS Joint Research Laboratory (IRL 3555), Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States; Department of Chemistry and Biochemistry, San Diego State University, San Diego, California 92182, United States*

Andre Faria Vieira − *UCSD-CNRS Joint Research Laboratory (IRL 3555), Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States*

Mingyu Liu − *Department of Chemistry, The Scripps Research Institute, La Jolla, California 92037, United States*

Aaron Kendrick, IV − *Department of Chemistry, The Scripps Research Institute, La Jolla, California 92037, United States*

Douglas B. Grotjahn − *Department of Chemistry and Biochemistry, San Diego State University, San Diego, California 92182, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/acscatal.2c00614

Author Contributions

‡(N.K., S.D.M.) These authors contributed equally to this manuscript.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was financially supported by the National Institutes of Health (5R35GM125052-04 and diversity supplement, 5R35GM125052-04S1) and an ACS PRF Doctoral New Investigator Grant (K.M.E.). This work was also supported by the U.S. Department of Energy, Office of Science, Basic Energy Sciences, Catalysis Science Program, under Award No. DE-SC0009376 (G.B.), National Science Foundation Award No. CHE-1800598 (D.B.G.), and the Agence Nationale de la Recherche Award No. ANR-19-276CE07-0017 (R.J). Individual fellowships were provided by National Science Foundation Award No. CHE-2213302 (S.D.M.) and an SDSU University Graduate Fellowship (S.Y.).

■ REFERENCES

(1) Miyaura, N.; Suzuki, A. Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds. *Chem. Rev.* **1995**, *95*, 2457−2483.

(2) Scott, H. K.; Aggarwal, V. K. Highly Enantioselective Synthesis of Tertiary Boronic Esters and their Stereospecific Conversion to Other Functional Groups and Quaternary Stereocentres. *Chem.—Eur. J.* **2011**, *17*, 13124−13132.

(3) Lennox, A. J. J.; Lloyd-Jones, G. C. Selection of Boron Reagents for Suzuki−Miyaura Coupling. *Chem. Soc. Rev.* **2014**, *43*, 412−443.

(4) West, M. J.; Fyfe, J. W. B.; Vantourout, J. C.; Watson, A. J. B. Mechanistic Development and Recent Applications of the Chan−Lam Amination. *Chem. Rev.* **2019**, *119*, 12491−12523.

(5) António, J. P. M.; Russo, R.; Carvalho, C. P.; Cal, P. M. S. D.; Gois, P. M. P. Boronic Acids as Building Blocks for the Construction of Therapeutically Useful Bioconjugates. *Chem. Soc. Rev.* **2019**, *48*, 3513−3536.

(6) Baker, S. J.; Ding, C. Z.; Akama, T.; Zhang, Y.-K.; Hernandez, V.; Xia, Y. Therapeutic Potential of Boron-Containing Compounds. *Future Med. Chem.* **2009**, *1*, 1275−1288.

(7) Jäkle, F. Lewis Acidic Organoboron Polymers. *Coord. Chem. Rev.* **2006**, *250*, 1107−1121.

(8) Mellerup, S. K.; Wang, S. Boron-Based Stimuli Responsive Materials. *Chem. Soc. Rev.* **2019**, *48*, 3537−3549.

(9) Miao, J.; Wang, Y.; Liu, J.; Wang, L. Organoboron Molecules and Polymers for Organic Solar Cell Applications. *Chem. Soc. Rev.* **2022**, *51*, 153−187.

(10) Yoshida, H. Borylation of Alkynes under Base/Coinage Metal Catalysis: Some Recent Developments. *ACS Catal.* **2016**, *6*, 1799−1811.

(11) Hemming, D.; Fritzemeier, R.; Westcott, S. A.; Santos, W. L.; Steel, P. G. Copper-Boryl Mediated Organic Synthesis. *Chem. Soc. Rev.* **2018**, *47*, 7477−7494.

(12) Carreras, J.; Caballero, A.; Pérez, P. J. Alkenyl Boronates: Synthesis and Applications. *Chem.—Asian J.* **2019**, *14*, 329−343.

(13) Whyte, A.; Torelli, A.; Mirabi, B.; Zhang, A.; Lautens, M. Copper-Catalyzed Borylative Difunctionalization of π-Systems. *ACS Catal.* **2020**, *10*, 11578−11622.

(14) Tsushima, T.; Tanaka, H.; Nakanishi, K.; Nakamoto, M.; Yoshida, H. Origins of Internal Regioselectivity in Copper-Catalyzed Borylation of Terminal Alkynes. *ACS Catal.* **2021**, *11*, 14381−14387.

(15) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. Highly Selective Methods for Synthesis of Internal (α-) Vinylboronates through Efficient NHC−Cu-Catalyzed Hydroboration of Terminal Alkynes. Utility in Chemical Synthesis and Mechanistic Basis for Selectivity. *J. Am. Chem. Soc.* **2011**, *133*, 7859−7871.

(16) Moure, A. L.; Mauleón, P.; Gómez Arrayás, R.; Carretero, J. C. Formal Regiocontrolled Hydroboration of Unbiased Internal Alkynes via Borylation/Allylic Alkylation of Terminal Alkynes. *Org. Lett.* **2013**, *15*, 2054−2057.

(17) Bellotti, P.; Koy, M.; Hopkinson, M. N.; Glorius, F. Recent Advances in the Chemistry and Applications of N-Heterocyclic Carbenes. *Nat. Rev. Chem.* **2021**, *5*, 711−725.

(18) Díez-González, S.; Marion, N.; Nolan, S. P. N-Heterocyclic Carbenes in Late Transition Metal Catalysis. *Chem. Rev.* **2009**, *109*, 3612−3676.

(19) Jazzar, R.; Soleilhavoup, M.; Bertrand, G. Cyclic (Alkyl)- and (Aryl)-(amino)carbene Coinage Metal Complexes and Their Applications. *Chem. Rev.* **2020**, *120*, 4141−4168.

(20) Morvan, J.; Mauduit, M.; Bertrand, G.; Jazzar, R. Cyclic (Alkyl)(amino)carbenes (CAACs) in Ruthenium Olefin Metathesis. *ACS Catal.* **2021**, *11*, 1714−1748.

(21) Melaimi, M.; Jazzar, R.; Soleilhavoup, M.; Bertrand, G. Cyclic (Alkyl)(amino)carbenes (CAACs): Recent Developments. *Angew. Chem., Int. Ed.* **2017**, *56*, 10046−10068.

(22) Gao, Y.; Yazdani, S.; Kendrick IV, A.; Junor, G. P.; Kang, T.; Grotjahn, D. B.; Bertrand, G.; Jazzar, R.; Engle, K. M. Cyclic (Alkyl)(amino)carbene Ligands Enable Cu-Catalyzed Markovnikov Protoboration and Protosilylation of Terminal Alkynes: A Versatile Portal to Functionalized Alkenes. *Angew. Chem., Int. Ed.* **2021**, *60*, 19871−19878.

(23) Alfaro, R.; Parra, A.; Alemán, J.; García 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.

(24) Zhang, L.; Cheng, J.; Carry, B.; Hou, Z. Catalytic Boracarboxylation of Alkynes with Diborane and Carbon Dioxide by an N-Heterocyclic Carbene Copper Catalyst. *J. Am. Chem. Soc.* **2012**, *134*, 14314−14317.

(25) Yoshida, H.; Kageyuki, I.; Takaki, K. Copper-Catalyzed Three-Component Carboboration of Alkynes and Alkenes. *Org. Lett.* **2013**, *15*, 952−955.

(26) 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.

(27) 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.

(28) Cheng, L.-J.; Mankad, N. P. Copper-Catalyzed Borocarbonylative Coupling of Internal Alkynes with Unactivated Alkyl Halides: Modular Synthesis of Tetrasubstituted β-Borylenones. *Angew. Chem., Int. Ed.* **2018**, *57*, 10328−10332.

(29) Zhurakovskyi, O.; Dias, R. M. P.; Noble, A.; Aggarwal, V. K. Stereo- and Regiocontrolled Methylboration of Terminal Alkynes. *Org. Lett.* **2018**, *20*, 3136−3139.

(30) 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.

(31) Mateos, J.; Rivera-Chao, E.; Fañanás-Mastral, M. Synergistic Copper/Palladium Catalysis for the Regio- and Stereoselective Synthesis of Borylated Skipped Dienes. *ACS Catal.* **2017**, *7*, 5340−5344.

(32) 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.

(33) 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.

(34) Control experiments revealed that the α-selective reaction conditions from ref 33 did not lead to appreciable product formation (<5%) when allyl electrophiles were employed.

(35) (a) Lavallo, V.; Canac, Y.; Präsang, C.; Donnadieu, B.; Bertrand, G. Stable Cyclic (Alkyl)(Amino)Carbenes as Rigid or Flexible, Bulky, Electron-Rich Ligands for Transition-Metal Catalysts: A Quaternary Carbon Atom Makes the Difference. *Angew. Chem., Int. Ed.* **2005**, *44*, 5705−5709. (b) Vermersch, F.; Oliveira, L.; Hunter, J.; Soleilhavoup, M.; Jazzar, R.; Bertrand, G. Cyclic (Alkyl)(amino)carbenes: Synthesis of Iminium Precursors and Structural Properties. *J. Org. Chem.* **2022**, *87*, 3511−3518.

(36) Morvan, J.; Vermersch, F.; Zhang, Z.; Falivene, L.; Vives, T.; Dorcet, V.; Roisnel, T.; Crévisy, C.; Cavallo, L.; Vanthuyne, N.; Bertrand, G.; Jazzar, R.; Mauduit, M. Optically Pure C_1-Symmetric Cyclic(alkyl)(amino)carbene Ruthenium Complexes for Asymmetric Olefin Metathesis. *J. Am. Chem. Soc.* **2020**, *142*, 19895−19901.

(37) Lavallo, V.; Frey, G. D.; Kousar, S.; Donnadieu, B.; Bertrand, G. Allene Formation by Gold Catalyzed Cross-Coupling of Masked Carbenes and Vinylidenes. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 13569−13573.

(38) Weinstein, C. M.; Junor, G. P.; Tolentino, D. R.; Jazzar, R.; Melaimi, M.; Bertrand, G. Highly Ambiphilic Room Temperature Stable Six-Membered Cyclic (Alkyl)(amino)carbenes. *J. Am. Chem. Soc.* **2018**, *140*, 9255−9260.

(39) Tomás-Mendivil, E.; Hansmann, M. M.; Weinstein, C. M.; Jazzar, R.; Melaimi, M.; Bertrand, G. Bicyclic (Alkyl)(amino)carbenes (BICAACs): Stable Carbenes More Ambiphilic than CAACs. *J. Am. Chem. Soc.* **2017**, *139*, 7753−7756.

https://doi.org/10.1021/acscatal.2c00614
ACS Catal. 2022, 12, 7243−7247