A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition

GDCh

Chemie

www.angewandte.org

Accepted Article

Title: Pd-Senphos Catalyzed trans-Selective Cyanoboration of 1,3-Enynes

Authors: Yuanzhe Zhang, Bo Li, and Shih-Yuan Liu

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.202005882

Link to VoR: https://doi.org/10.1002/anie.202005882

WILEY-VCH

10.1002/anie.202005882

WILEY-VCH

COMMUNICATION

Pd-Senphos Catalyzed *trans*-Selective Cyanoboration of 1,3-Enynes

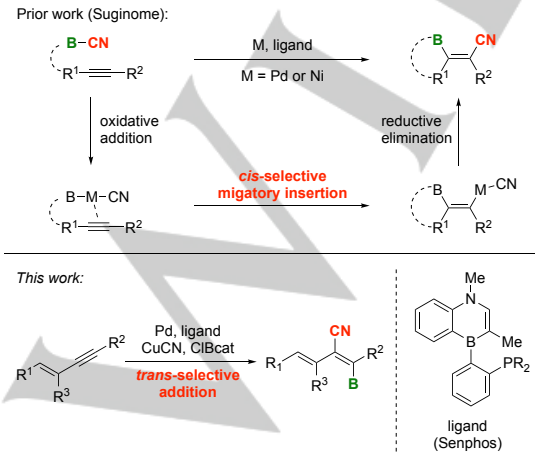
Yuanzhe Zhang[a], Bo Li[a], and Shih-Yuan Liu*[a]

[a] Y. Zhang, Dr. B. Li, Prof. Dr. S.-Y. Liu
Department of Chemistry, Boston College
Chestnut Hill, MA 02467-3860 (USA)
E-mail: shihyuan.liu@bc.edu

Supporting information for this article is given via a link at the end of the document.

Abstract: The first *trans*-selective cyanoboration reaction of an alkyne, specifically a 1,3-enyne, is described. The reported palladium-catalyzed cyanoboration of 1,3-enynes is site-, regio-, and diastereoselective, and is uniquely enabled by the 1,4-azaborine-based Senphos ligand structure. Tetra-substituted alkenyl nitriles are obtained providing useful boron-dienenitrile building blocks that can be further functionalized. The utility of our method has been demonstrated with the synthesis of Satigrel, an anti-platelet aggregating agent

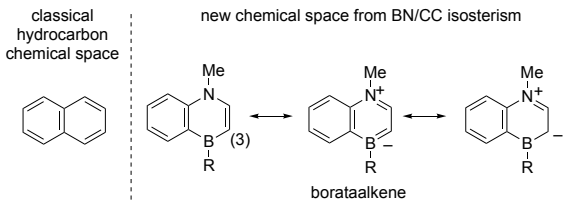
The alkenyl nitrile motif plays an important role in the field of polymers,[1] pharmaceutics,[2] and agrochemistry.[3] Thus, versatile and stereoselective synthetic approaches to substituted alkenyl nitriles has attracted significant attention. To date, a number of methods have been reported that involve alkyne X-CN difunctionalization (X = B,[4] C,[5] N,[6] O,[7] halogen,[5d, 8] Ge,[9] S,[10] Se,[10e] Si[11] and Sn[12]). The difunctionalization approach is attractive because the additionally installed functional group X provides a handle for possible structural diversification. Among the difunctionalization methods, the cyanoboration of alkynes[4] is particularly appealing due to the rich functionalization chemistry of organoboron derivatives.[13] Suginome reported the first intra- and intermolecular cyanoboration of alkynes catalyzed by Pd and Ni complexes (Scheme 1, top).[4] The working mechanistic hypothesis suggests initial oxidative addition of the B–CN bond to the metal followed by *cis*-selective *β*-migratory insertion into the alkyne and C–C reductive elimination, furnishing the *cis*-cyanoboration product.[14] The *trans*-selective X-CN



Scheme 1. Cyanoboration of alkynes.

difunctionalization of alkynes has significantly less precedent.[5b-d, 10b,12] For example, no *trans*-selective cyanoboration reaction of an alkyne has been reported to date. Herein we describe the *trans*-cyanoboration of 1,3-enynes catalyzed by a Pd complex supported by a 1,4-azaborine-based biaryl phosphine (Senphos) ligand (Scheme 1, bottom). Highly substituted alkenyl nitriles, including tetra-substituted derivatives are obtained in a site-, regio- and diastereoselective fashion, providing boron-dienenitrile building blocks that cannot be readily accessed by other synthetic methods.

Our laboratory has been investigating BN/CC isosterism[15] (substitution of a CC bond unit with a BN bond unit) as a strategy to create structural, and as a consequence, functional diversity. To date, BN/CC isosterism has been successfully applied to create new properties and functions in biomedical research,[16] materials science,[17] and organic synthesis.[18] Somewhat surprisingly, the application of BN/CC isosterism to the ligand space has attracted less attention.[19] To this end, we recently reported a ligand family based on the biaryl 1,4-azaborine scaffold.[20] Electronic structure elucidation revealed a strong borataalkene character (Scheme 2) which renders the C(3) carbon significantly more nucleophilic/electron rich than the corresponding carbonaceous arene. The access to the new ligand space from BN/CC isosterism has resulted in new reaction selectivity, specifically the *trans*-selective hydroboration of 1,3-enynes.[21] In our continued efforts to expand the utility of Senphos-type ligands in metal-catalyzed transformations we are addressing in this work the outstanding problem of *trans*-selective cyanoboration reaction.



Scheme 2. Electronic structure of 1,4-azaborines.

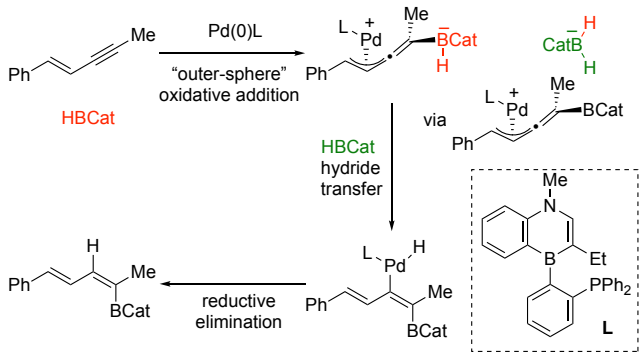
DFT calculations for the reported *trans*-hydroboration reaction predict a reaction pathway that involves an outer-sphere oxidative addition with catecholborane that is then followed by hydride transfer and reductive elimination (Scheme 3).[22] We envisioned that chlorocatecholborane (Cl-BCat) could serve as a potential boron source capable of facilitating the outersphere oxidative

10.1002/anie.202005882

WILEY-VCH

COMMUNICATION

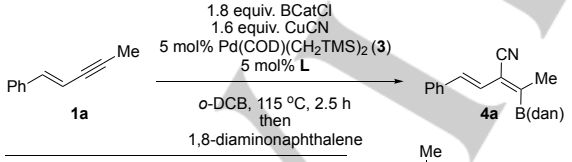
addition step and that a cyanide anion[23] (instead of a hydride) would attack the resulting Pd complex to furnish the cyanoboration product.



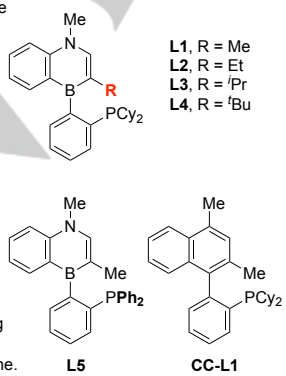
Scheme 3. Mechanism of the *trans*-hydroboration of 1, 3-enynes predicted by DFT calculations.

Thus, with Cl-BCat as the boron source,[24] copper(I) cyanide as the cyanide source,[25] Pd complex **3** as the precatalyst, and enyne **1a** as the initial substrate, we evaluated the effects of the ligand structure on the cyanoboration reactivity and selectivity. As can be seen from Table 1, the absence of a supporting ligand does not lead to an efficient productive reaction (entry 1). The presence of monodentate phosphine ligands promotes the product formation, albeit in low yield (entries 2 and 3). On the other hand, the bidentate phosphine ligand dppe is completely ineffective (entry 4). Gratifyingly, the use of Senphos-type ligands results in a substantial increase in the product yield while also achieving greater than 95:5 *trans* addition selectivity (entries 5-9). The substituent R at the C(3) position of the ligand has a profound influence on the product yield but not on the diastereoselectivity. For example, when **L1**, which bears the methyl group at the C(3) position, is used as the ligand, the reaction gives the product in superior yield (Table 1, entry 5) compared to those with bigger R substituents (entries 6-8). Switching the boron substituent from the *o*-dicyclohexyl-phosphinophenyl to *o*-diphenyl-phosphinophenyl group results in diminished reactivity for the model

Table 1. Pd-catalyzed *trans*-cyanoboration as a function of the ligand structure



entry	L	4a yield (*trans*:*cis*)[a]
1	none	3% (89:11)
2	$PhPCy_2$	13% (95:5)
3	XPhos	10% (90:10)
4	dppe	<1% (N/A)
5	**L1**	**92% (96:4)**
6	**L2**	69% (95:5)
7	**L3**	48% (95:5)
8	**L4**	24% (95:5)
9	**L5**	46% (96:4)
10	**CC-L1**	6% (89:11)

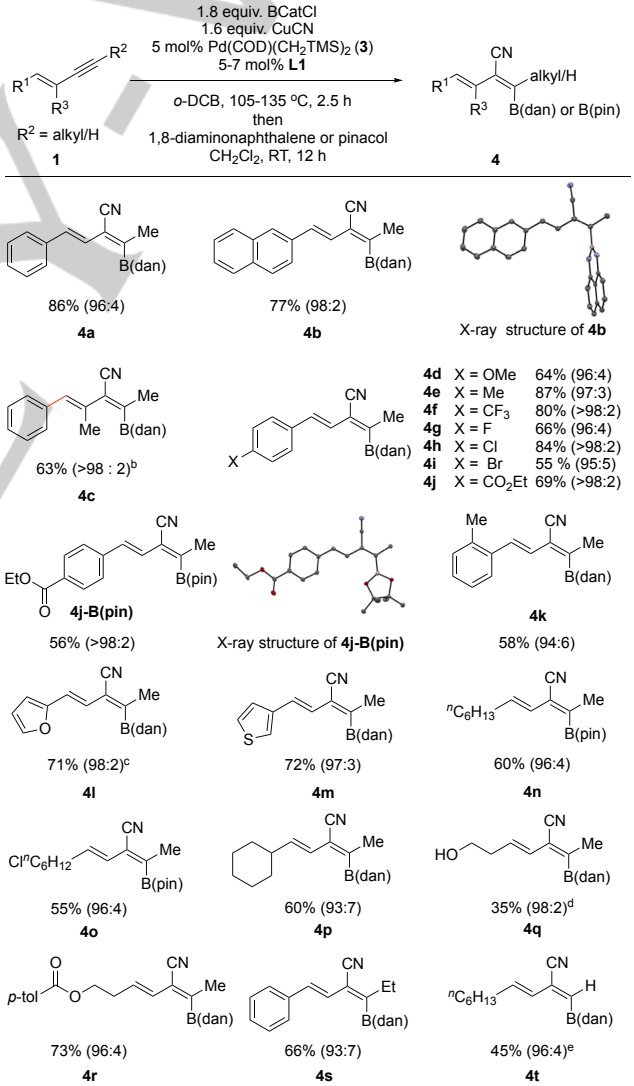


[a] Determined by ^{1}H NMR of the crude mixture *vs.* a calibrated internal standard after quenching with dan. dan: 1,8-diaminonaphthalene, COD: cyclooctadiene, *o*-DCB: *ortho*dichlobenzene.

substrate **1a** (Table 1, entry 5 vs. 9). Lastly, we determined that **CC-L1**, the carbonaceous analogue of the best performing Senphos ligand, is inferior to **L1** with regard to reaction efficiency and selectivity (entry 10 vs. entry 5), highlighting the importance of the unique electronic structure of the 1,4-azaborine motif in promoting the reaction.[26]

Under optimized reaction conditions, various alkyl/terminal (*E*)-1,3-enynes **1** were subjected to the *trans*-selective cyanoboration followed by quench with 1,8-diaminonaphthalene (dan)[27] or pinacol (pin), and the results are summarized in Table 2. High *trans*-selectivity was observed consistently with an array of electronically (e.g., entries **4d-4j**) and sterically different (e.g., entries **4c** and **4k**) substituents on the alkene. In addition to arenes, the R^1 position also tolerates heteroarenes (entries **4l** and **4m**) and alkyl groups (entries **4n-4r**). Functional groups such as aryl-halide (entries **4g-4i**), alkyl chloride (entry **4o**), esters (entries **4j** and **4r**), methoxy (entry **4d**), and alcohol (with pre-treatment

Table 2. Pd-catalyzed trans-cyanoboration of alkyl/terminal 1,3-enynes (R^2 = alkyl/H)[a]



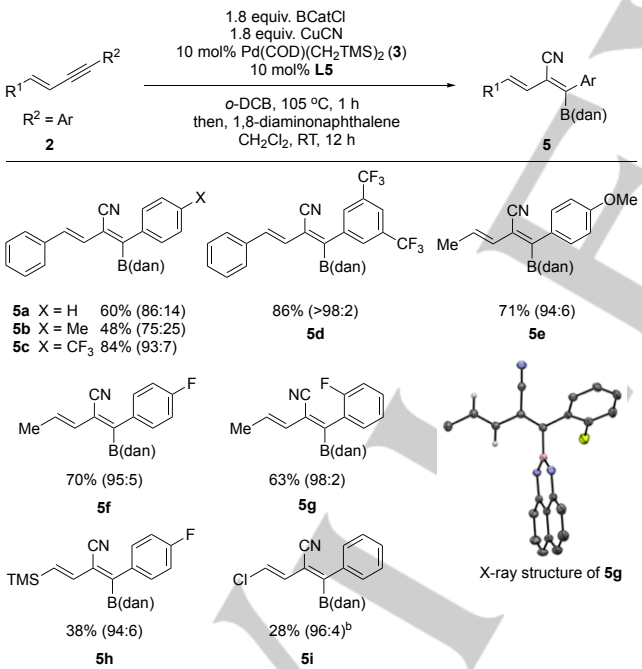
[a] Yields of isolated isomerically pure *trans* product (average of 2 runs), based on **1**. The diastereomeric ratio in parenthesis (*trans*:*cis*) was determined by ^{1}H NMR of the crude material after addition of 1,8-diaminonaphthalene or pinacol. [b] Isomerization occured at the highlighted position. E/Z ratio of the crude material is 5:1. Yield is of isolated pure E isomer. [c] **L5** was used instead of **L1**. [d] The substrate was first pre-treated with HBCat before subjecting it to the reaction conditions. [e] 10 mol% catalyst loading, 90 °C, 40 min reaction time.

10.1002/anie.202005882

with H-BCat; entry **4q**) are also tolerated. When the steric demand of the R^2 substituent is increased from Me to Et, a slight decrease in diastereoselectivity was observed (**4s** vs. **4a**). For the furyl substrate **1l**, **L5** was a superior ligand compared to **L1** with regard to reaction selectivity.[28] The terminal enyne substrate **1t** required higher catalyst loading at a lower reaction temperature and reaction time (entry **4t**). The bond connectivity and stereochemistry of two *trans*-cyanoboration products, **4b** and **4j-B(pin)** was confirmed by single crystal X-ray diffraction analysis (Table 2).

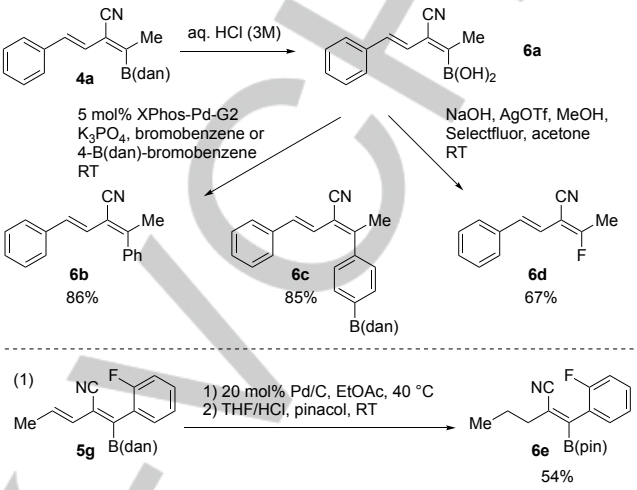
For aryl (*E*)-1,3-enynes (R^2 = Ar) **2**, we determined that **L5** was a superior ligand compared to **L1**.[29] The diastereoselectivity of the reaction for diaryl 1,3-enynes (R^1 = Ar, R^2 = Ar) substrates **2a-d** is dependent on the electronic nature of the R^2 substituent, with electron-deficient R^2 groups resulting in higher *trans*-cyanoboration selectivity (entry **5c** and **5d** vs. **5b** and **5a**). On the other hand, for monoaryl 1,3-enynes (R^2 = Ar, $R^1 \neq$ Ar) the observed *trans*-cyanoboration selectivity remains excellent (>94:6) regardless of the electronic nature of the R^2 substituent (entries **5e-i**). Good diastereoselectivity was also observed for the alkenyl silane and alkenyl chloride substrates **2h** and **2i**, albeit with diminished yields. We have obtained the X-ray crystal structure of product **5g**, thus unambiguously establishing connectivity and diastereoselectivity.

Table 3. Pd-catalyzed trans-cyanoboration of aryl 1,3-enynes (R^2 = Ar)[a]



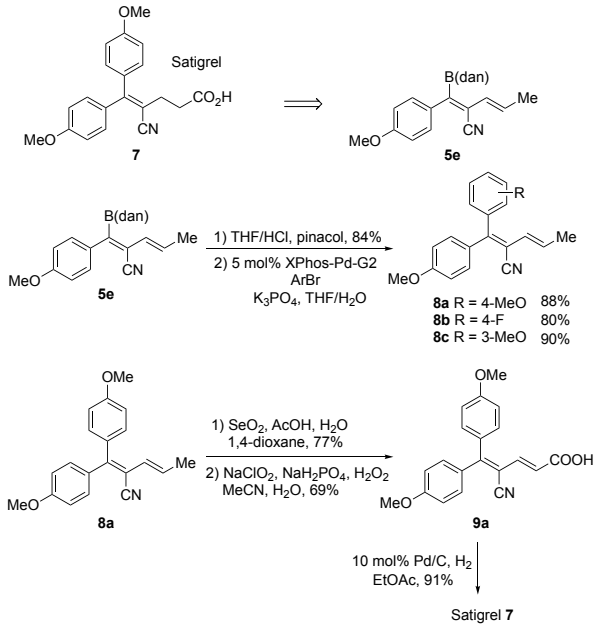
[a] Yields of isolated isomerically pure *trans* product (average of 2 runs), based on **2**. The diastereomeric ratio in parenthesis (*trans*:*cis*) was determined by ^{1}H NMR of the crude material after addition of 1,8-diaminonaphthalene. [b] 15 mol% catalyst loading, 1.2 equiv. CuCN, 1.6 equiv. BCatCl, 90 °C, 25 min.

Vicinal boron-substituted alkenylnitrile derivatives are versatile synthetic building blocks. For example, Scheme 4 illustrates that cyanoboration product **4a** undergoes hydrolysis (to form boronic acid derivative **6a**) and subsequent Pd-catalyzed Suzuki-Miyaura coupling with bromobenzene or 4-*B*(dan)-bromobenzene to furnish **6b** and **6c** in 86% and 85% yield, respectively, with complete retention of olefin stereochemistry. Furthermore, fluorination of **6a** with Selectfluor[30] produces a novel (*E*)-2-nitrile-fluorodiene motif **6d**. We also determined that our borylated dienylnitriles can be hydrogenated regioselectively. For example, when diene **5g** is subjected to Pd/C catalyzed hydrogenation, tetra-substituted borylated alkenylnitrile **6e** is obtained after transesterification with pinacol (eq 1).



Scheme 4. Functionalization of cyanoboration products.

Finally, we applied our *trans*-selective cyanoboration reaction to the synthesis of Satigrel **7**, an anti-platelet aggregating agent that contains a tetra-substituted acrylonitrile core.[31] With a stereoselective method for the construction of tetra-substituted acrylonitrile now at our disposal, we reasoned that Satigrel could be synthesized from **5e** in a straight forward fashion (Scheme 5). We commenced first with the transesterification of **5e** followed by Suzuki-Miyaura coupling to produce a variety of bis-aryl substituted dienenitriles **8a-c** in a stereospecific manner. The bis-4-methoxy-phenyl derivative **8a** was then subjected to oxidation[32] to yield the carboxylic acid **9a**. Finally, catalytic hydrogenation[33]



Scheme 5. Synthesis of Satigrel.

selectively reduced the more accessible alkene to furnish Satigrel. The synthesis described in Scheme 5 offers a modular and stereoselective synthetic approach toward bis-aryl substituted dienenitriles, taking advantage of the versatile boron functional handle.

In summary, we have developed the first *trans*-selective cyanoboration reaction of an alkyne. The described palladium-catalyzed cyanoboration of 1,3-enynes is site-, regio-, and diastereoselective, and we have determined that our 1,4-azaborine-based Senphos ligand structure is uniquely suited to support the Pd catalysis. The described method provides access to the important tetra-substituted alkenyl nitrile motif in a straightforward fashion, and we demonstrated the utility of our method with the synthesis of Satigrel. Future efforts will be directed at developing additional stereoselective difunctionalization reactions of alkynes employing the Senphos ligand framework.

Acknowledgements

Research reported in this publication was supported by the National Institute of General Medical Sciences of the National Institutes of Health under Award Number R01GM094541 and by Boston College start-up funds.

Keywords: *trans*-cyanoboration • azaborine • enyne

[1] J. F. Brazdil, Acrylonitrile in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, **2012**.

[2] a) F. F. Fleming, *Nat. Prod. Rep.* **1999**, *16*, 597-606; b) F. F. Fleming, L. Yao, P. C. Ravikumar, L. Funk, B. C. Shook, *J. Med. Chem.* **2010**, *53*, 7902-7917.

[3] M. Van Boven, N. Blaton, M. Cokelaere, P. Daenens, *J. Agric. Food. Chem.* **1993**, *41*, 1605-1607.

[4] a) M. Suginome, A. Yamamoto, M. Murakami, *J. Am. Chem. Soc.* **2003**, *125*, 6358-6359; b) M. Suginome, A. Yamamoto, M. Murakami, *Angew. Chem.* **2005**, *117*, 2432-2434; *Angew. Chem. Int. Ed.* **2005**, *44*, 2380-2382; c) M. Suginome, A. Yamamoto, M. Murakami, *J. Organomet. Chem.* **2005**, *690*, 5300-5308; d) T. Ohmura, T. Awano, M. Suginome, H. Yorimitsu, K. Oshima, *Synlett* **2008**, 423-427.

[5] a) B. Liu, Y. Wang, Y. Chen, Q. Wu, J. Zhao, J. Sun, *Org. Lett.* **2018,** *20*, 3465-3468; b) H. Murayama, K. Nagao, H. Ohmiya, M. Sawamura, *Org. Lett.* **2016**, *18*, 1706-1709; c) Y.-T. He, L.-H. Li, Q. Wang, W. Wu, Y.-M. Liang, *Org. Lett.* **2016**, *18*, 5158-5161; d) N. Sakata, K. Sasakura, G. Matsushita, K. Okamoto, K. Ohe, *Org. Lett.* **2017**, *19*, 3422-3425; e) S. Arai, T. Sato, Y. Koike, M. Hayashi, A. Nishida, *Angew. Chem.* **2009**, *121*, 4598-4601; *Angew. Chem. Int. Ed.* **2009**, *48*, 4528-4531; f) S. Arai, Y. Koike, A. Nishida, *Adv. Synth. Catal.* **2010**, *352*, 893-900; g) S. Arai, T. Sato, A. Nishida, *Adv. Synth. Catal.* **2009**, *351*, 1897-1904; h) T. Igarashi, S. Arai, A. Nishida, *J. Org. Chem.* **2013**, *78*, 4366-4372. For reviews, see: i) P.-H. Chen, B. A. Billett, T. Tsukamoto, G. Dong, *ACS Catal.* **2017**, *7*, 1340-1360; j) Q. Wen, P. Lu, Y. Wang, *RSC Adv.* **2014**, *4*, 47806-47826; k) X. Kou, J. Fan, X. Tong, Z. Shen, *Chin. J. Org. Chem.* **2013**, *33*, 1407-1422; l) M. Tobisu, N. Chatani, *Chem. Soc. Rev.* **2008**, *37*, 300-307.

[6] a) L. Chen, S. Cao, J. Zhang, Z. Wang, *Tetrahedron Lett.* **2019,** *60*, 1678-1681, b) Z.-Y. Liao, P.-Y. Liao, T.-C. Chien, *Chem. Commun.* **2016,** *52*, 14404-14407; c) G. Qiu, X. Qiu, J. Liu, J. Wu, *Adv. Synth. Catal.* **2013,** *355*, 2441-2446.

[7] a) X. Wang, A. Studer, *J. Am. Chem. Soc.* **2016,** *138*, 2977-2980; b) Y. Zhu, Z. Shen, *Adv. Synth. Catal.* **2017,** *359*, 3515-3519.

[8] a) P. Moreau, A. Commeyras, *J. Chem. Soc., Chem. Commun.* **1985**, 817-818; b) M. Murai, R. Hatano, S. Kitabata, K. Ohe, *Chem. Commun.* **2011**, *47*, 2375-2377; c) A. G. Barrado, A. Zielinski, R. Goddard, M. Alcarazo, *Angew. Chem.* **2017**, *129*, 13586-13590; *Angew. Chem. Int. Ed.* **2017**, *56*, 13401-13405; e) N. V. Lukashev, A. V. Kazantsev, A. A. Borisenko, I. P. Beletskaya, *Tetrahedron* **2001,** *57*, 10309-10317.

[9] N. Chatani, N. Horiuchi, T. Hanafusa, *J. Org. Chem.* **1990,** *55*, 3393-3395.

[10] a) I. Kamiya, J. Kawakami, S. Yano, A. Nomoto, A. Ogawa, *Organometallics* **2006**, *25*, 3562-3564; b) S. Higashimae, D. Kurata, S. I. Kawaguchi, S. Kodama, M. Sonoda, A. Nomoto, A. Ogawa, *J. Org. Chem.* **2018**, *83*, 5267-5273; c) Y. T. Lee, S. Y. Choi, Y. K. Chung, *Tetrahedron Lett.* **2007**, *48*, 5673-5677; d) M. Bürger, M. N. Loch, P. G. Jones, . B. Werz, *Chem. Sci.* **2020**, 11, 1912-1917; e) T. Ozaki, A. Nomoto, I. Kamiya, J. Kawakami, A. Ogawa, *Bull. Chem. Soc. Jpn.* **2011**, *84*, 155-163.

[11] a) N. Chatani, T. Hanafusa, *J. Chem. Soc., Chem. Commun.* **1985**, 838-839; b) N. Chatani, T. Takeyasu, N. Horiuchi, T. Hanafusa, *J. Org. Chem.* **1988**, *53*, 3539-3548; c) M. Suginome, H. Kinugasa, Y. Ito *Tetrahedron Lett.* **1994**, *35*, 8635-8638.

[12] Y. Obora, A. S. Baleta, M. Tokunaga, Y. Tsuji, *J. Organomet. Chem.* **2002**, 660, 173-177.

[13] a) J. W. B. Fyfe, A. J. B. Watson, *Chem.* **2017**, *3*, 31-55; b) G. Pattison, *Org. Biomol. Chem.* **2019**, *17*, 5651-5660; c) X. Yang, S. J. Kalita, S. Maheshuni, Y.-Y. Huang, *Chem. Rev.* **2019**, *392*, 35-48.

[14] M. Suginome, A. Yamamoto, T. Sasaki, M. Murakami, *Organometallics* **2006**, *25*, 2911-2913.

[15] a) Z. Liu, T. B. Marder, *Angew. Chem.* **2007**, *120*, 248-250; *Angew. Chem. Int. Ed.* **2008**, *47*, 242-244; b) M. J. D. Bosdet, W. E. Piers, *Can. J. Chem.* **2009**, *87*, 8-29; c) P. G. Campbell, A. J. Marwitz, S.-Y. Liu, *Angew. Chem.* **2012**, *124*, 6178-6197; *Angew. Chem. Int. Ed.* **2012**, *51*, 6074-6092; d) Z. X. Giustra, S.-Y. Liu, *J. Am. Chem. Soc.* **2018**, *140*, 1184-1194; e) c. R. McConnell, S.-Y. Liu, *Chem. Soc. Rev.* **2019**, *48*, 3436-3453.

[16] a) D. H. Knack, J. L. Marshall, G. P. Harlow, A. Dudzik, M. Szaleniec, S.-Y. Liu, J. Heider, *Angew. Chem.* 2013, 125, 2660-2662; *Angew. Chem. Int. Ed.* **2013**, *52*, 2599-2601; b) H. Lee, M. Fischer, B. K. Shoichet, S.-Y. Liu, *J. Am. Chem. Soc.* **2016**, *138*, 12021-12024; c) P. Zhao, D. O. Nettleton, R. G. Karki, F. J. Zecri, S.-Y. Liu, *ChemMedChem* **2017**, *12*, 358-361; d) K. Boknevitz, J. S. Italia, B. Li, A. Chatterjee, S.-Y. Liu, *Chem. Sci.* **2019**, *10*, 4994-4998; e) Y. Liu, S.-Y. Liu, *Org. Biomol. Chem.* **2019**, *17*, 7002-7006.

[17] a) X.-Y. Wang, J.-Y. Wang, J. Pei, *Chem. Eur. J.* **2015,** *21*, 3528-3539; b) Z. Liu, J. S. A. Ishibashi, C. Darrigan, A. Dargelos, A. Chrostowska, B. Li, M. Vasiliu, D. A. Dixon, S.-Y. Liu, *J. Am. Chem. Soc.* **2017**, *139*, 6082-6085.

[18] a) A. W. Baggett, M. Vasiliu, B. Li, D. A. Dixon, S.-Y. Liu, *J. Am. Chem. Soc.* **2015,** *137*, 5536-5541; b) A. N. Brown, B. Li, S.-Y. Liu, *J. Am. Chem. Soc.* **2015,** *137*, 8932-8935; c) R. J. Burford, B. Li, M. Vasiliu, D. A. Dixon, S.-Y. Liu, *Angew. Chem.* **2015**, *127*, 7934-7938; *Angew. Chem. Int. Ed.* **2015,** *54*, 7823-7827; d) Z. X. Giustra, X. Yang, M. Chen, H. F. Bettinger, S.-Y. Liu, *Angew. Chem.* **2019**, *131*, 19094-19098; *Angew. Chem. Int. Ed.* **2019**, *58*, 18918-18922.

[19] a) J. A. Bailey, M. F. Haddow, P. G. Pringle, *Chem. Commun.* **2014,** *50*, 1432-1434; b) A. D. Gorman, J. A. Bailey, N. Fey, T. A. Young, H. A. Sparkes, P. G. Pringle, *Angew. Chem.* **2018**, *130*, 16028-16032; *Angew. Chem. Int. Ed.* **2018,** *57*, 15802-15806.

[20] S. Xu, F. Haeffner, B. Li, L. N. Zakharov, S.-Y. Liu, *Angew. Chem.* **2014***, 126,* 6913-6917; *Angew. Chem. Int. Ed.* **2014**, *53*, 6795-6799.

[21] S. Xu, Y. Zhang, B. Li, S.-Y. Liu, *J. Am. Chem. Soc.* **2016**, *138*, 14566-14569.

[22] Y. Yang, J. Jiang, H. Yu, J. Shi, *Chem. Eur. J.* **2018**, *24*, 178-186.

[23] a) G. P. Ellis, T. M. Romney-Alexander, *Chem. Rev.* **1987**, *87*, 779-794; b) T. Sakamoto, K. Ohsawa, *J. Chem. Soc., Perkin Trans. 1* **1999**, 2323-2326.

[24] The use of Cl-BCat is essential for the reaction. For example, the use of Cl-B(pin) under otherwise identical reaction conditions led to an intractable mixture.

[25] To the best of our knowledge, NC-BCat is an unknown compound. CuCN may react with Cl-BCat to form NC-BCat *in situ* during the cyanoboration reaction. Independent treatment of CuCN with Cl-BCat at room temperature results in slow formation of a new boron-containing species with a ^{11}B NMR chemical shift of 22 ppm in $CDCl_3$. For the synthesis of the related 2-cyano-2,3-dihydro-1,3-dimethyl-1H-1,3,2-benzodiazabolole, see reference 14.

[26] Under the optimized conditions, about 1% of chloroboration of substrate **1a** was observed in 78:22 *trans:cis* ratio.

[27] H. Noguchi, K. Hojo, M. Suginome, *J. Am. Chem. Soc.* **2007**, *129*, 758-759.

[28] When the reaction was performed with **L1** as the ligand, the product **4l** was obtained in 81% yield 94:6 (*trans*/*cis)* ratio.

[29] When the reaction was performed with **2f** as the substrate and **L1** as the ligand, the product **5f** was obtained in 46% yield with (91:9) *trans*/*cis* ratio.

[30] T. Furuya, T. Ritter, *Org. Lett.* **2009**, *11*, 2860-2863.

10.1002/anie.202005882

[31] a) T. Fujimori, K. Harada, T. Saeki, M. Kogushi, K. Akasaka, Y. Yamagishi, I. Yamatsu, *Arzneim.Forsch.* **1987**, *37*, 1143-1148; b) S. Hoshi, M. Goto, N. Koyama, K. Nomoto, H. Tanaka, *J. Biol. Chem.* **2000**, *275*, 883-889; c) T. Nakajima, I. Kitajima, H. Shin, H. W. Matsumoto, Y. Soejima, I. Maruyama, *Biochem. Biophys. Res. Commun.* **1994**, *203*, 1181-1187; d) T. Fujimori, K. Harada, T. Saeki, M. Kogushi, K. Katayama, M. Satoh, *Cardiovascular Drug Reviews* **1991**, *9*, 264-284.

[32] a) Y. Moazami, T. V. Gulledge, S. M. Laster, J. G. Pierce, *Bioorg. Med. Chem. Lett.* **2015**, *25*, 3091-3094; b) Q. Huang, J. D. Pennington, H. J. Williams, A. I. Scott, *Synth. Commun.* **2006**, *36*, 2577-2585; c) E. Dalcanale, F. Montanari, *J. Org. Chem.* **1986**, *51*, 567-569.

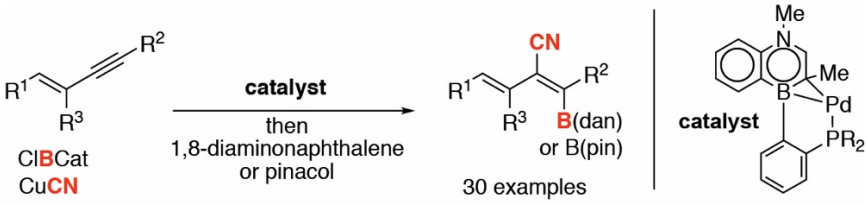
[33] G. Majetich, J. Yu, *Can. J. Chem.* **2012**, *90*, 75-84.

10.1002/anie.202005882

WILEY-VCH

COMMUNICATION

Entry for the Table of Contents



A *trans*-selective alkyne cyanoboration reaction debuts! A Pd complex supported by an 1,4-azaborine-derived phosphine ligand is uniquely capable in transforming 1,3-enynes into tetra-substituted borylated dienenitriles with high site-, regio- and *trans*-diastereoselectivity.