A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition GDCh Chemie

www.angewandte.org

Accepted Article

Title: Ligand-Controlled Regiodivergent Enantioselective Rhodium-Catalyzed Alkene Hydroboration

Authors: Andrew J. Bochat, Veronika M. Shoba, and James M Takacs

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.201903308
Angew. Chem. 10.1002/ange.201903308

Link to VoR: http://dx.doi.org/10.1002/anie.201903308
http://dx.doi.org/10.1002/ange.201903308

WILEY-VCH

10.1002/anie.201903308

WILEY-VCH

COMMUNICATION

Ligand-Controlled Regiodivergent Enantioselective Rhodium-Catalyzed Alkene Hydroboration

*Andrew J. Bochat, Veronika M. Shoba, and James M. Takacs**

Dedicated to Professor David A. Evans

Abstract: *Regiocontrol in the rhodium-catalyzed boration of vinyl arenes is typically dominated by the presence of the conjugated aryl substituent. However, small differences in TADDOL-derived chiral monophosphite ligands can override this effect and direct rhodium-catalyzed hydroboration of β-aryl and -heteroaryl methylidenes by pinacolborane to produce either chiral primary or tertiary borated products selectively. The regiodivergent behavior is coupled with enantiodivergent addition of the borane. The nature of the TADDOL backbone substituents and that of the phosphite moiety function synergistically to direct the sense and extent of regioselectivity and enantioinduction. Twenty substrates undergo each reaction mode with regioselectivities reaching greater than 20:1 and enantiomer ratios reaching up to 98:2. A variety of subsequent transformations illustrate the potential utility of each product.*

The enantioselective preparation of chiral boronic esters is of current interest due to their synthetic utility through a diverse set of stereospecific transformations[1] and the growing appreciation that boronic acid derivatives may hold significant potential in medicinal chemistry.[2] Considerable progress has been realized in the development of regioselective asymmetric hydroboration[3],[4] and asymmetric borometallation[5] reactions, most exploiting substrate control through use of activated alkenes or directing groups. Catalysts that override inherent substrate bias to selectively produce either of two regioisomers offer greater synthetic utility. In addition to several recent examples of non-stereocontrolled borylative difunctionalizations via regiodivergent borocupration,[6] the ligand-controlled regiodivergent palladium-catalyzed hydroboration of terminal alkynes serves to illustrate the potential. Prabhu[7] reported a bulky *N*-heterocyclic carbene ligand promotes regioselective boropalladation to deliver boron to the terminus; protonolysis leads to **1** (Figure 1). In contrast, tricyclohexylphosphine effects delivery of boron to the internal position leading to the regioisomeric product **2**.

Examples of chiral catalyst-controlled regiodivergent and enantioselective reactions are less common.[8],[9] Herein, we report that relatively modest structural changes to a chiral TADDOL-monophosphite ligand results in a switch in both regioselectivity and the sense of enantioselectivity in the catalytic asymmetric hydroboration (CAHB) of β-aryl methylidene

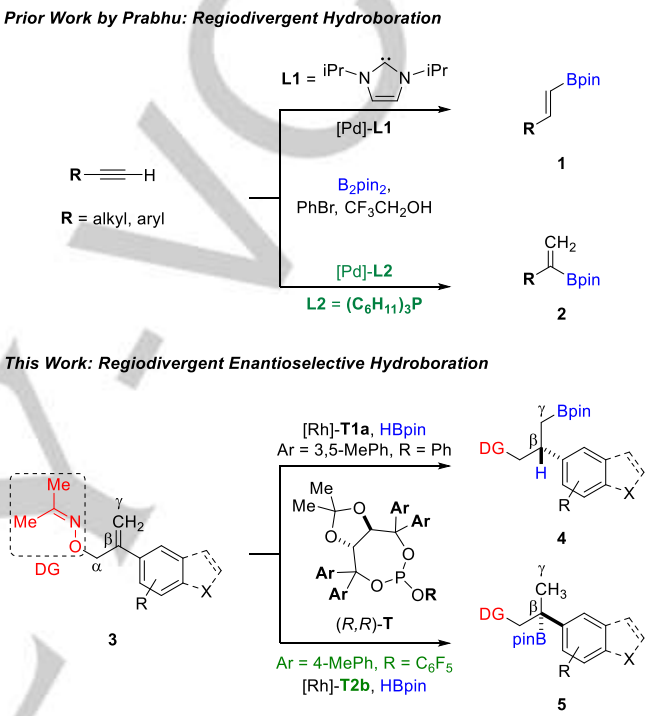


Figure 1. Regiodivergent hydroboration of alkenes.

substrates **3** by pinacolborane (pinBH). This methodology provides access to either rhodium-catalyzed γ-boration at the unsubstituted terminus leading to the primary organoboronic ester **4** (*si*-face addition favored)[10] or β-boration leading to the tertiary organoboronic ester **5** (*re*-face addition favored)[11] using ligands (*R*,*R*)-**T1a** or (*R*,*R*)-**T2b**, respectively.

To probe the influence of structural changes in the ligand on the γ- to β-boration ratio (i.e., **4**:**5**) and the levels of asymmetric induction (i.e., *re*:*si* face addition), a series of TADDOL-derived phosphite ligands were evaluated under a standard set of screening conditions for the CAHB of **3a** (Figure 2). The selected TADDOL-derived ligands varied in the substituents at two positions. The **T1**-**T6** series of phosphites differ with respect to the aryl appendages on the TADDOL backbone; for example, the aryl appendages are 3,5-dimethylphenyl groups in the **T1** series, 4-methylphenyl groups in **T2**, etc. Next, each TADDOL backbone was evaluated as its phenyl phosphite (i.e., **T1a**-**T6a**, R = C_6H_5) and as its pentafluorophenyl phosphite (i.e., **T1b**-**T6b**, R = C_6F_5); for example, **T1a** is the TADDOL-phenylphosphite bearing 3,5-dimethylphenyl appendages and **T1b** is the corresponding pentafluorophenyl phosphite.

[*] Andrew J. Bochat, Dr. Veronika M. Shoba, Dr. James M. Takacs
Department of Chemistry and Nebraska Center for Integrated Biomolecular Communication, University of Nebraska-Lincoln
807 Hamilton Hall, Lincoln, NE, 68588-0304 (USA)
E-mail: jtakacs1@unl.edu

Supporting information and the ORCHID identification number(s) for the author(s) of this article can be found under:

10.1002/anie.201903308

WILEY-VCH

COMMUNICATION

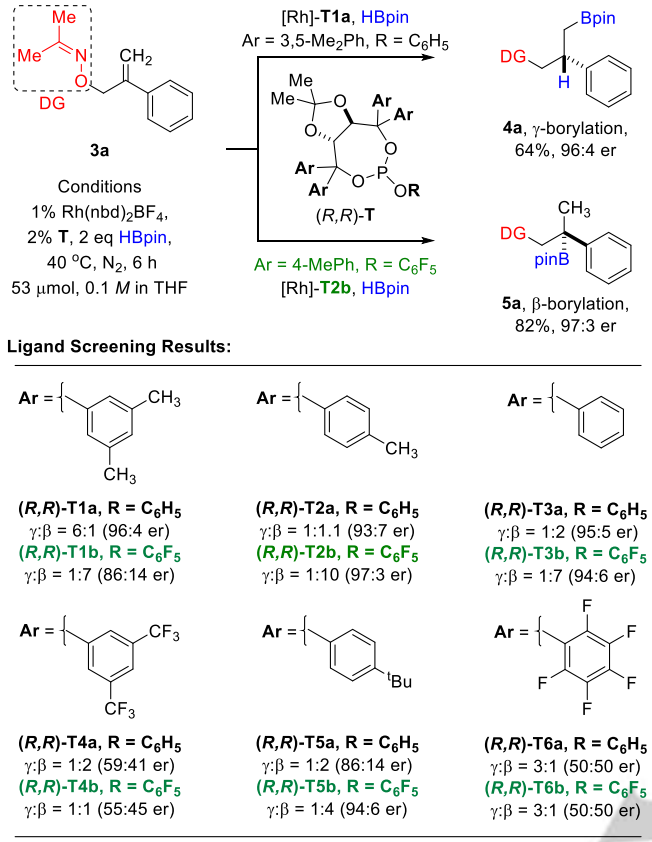


Figure 2. Comparison of phenyl and pentafluorophenyl phosphites for a series of TADDOL backbone derivatives. Notes: the structures shown correlate to the major enantiomer from HPLC, except the product from **T5b** which arises from the opposite sense of π-facial selectivity.

Phenylphosphite **T1a** (Ar = 3,5-$Me_2C_6H_3$) displays a significant preference for enantioselective γ-boration giving predominantly **4a** (6:1 γ:β); the major product reflects addition of pinBH to the *si*-face of the substrate (96:4 er). In contrast, the reaction run using phenylphosphite **T2a** (Ar = 4-MeC_6H_4) shows a slight preference for β-boration (1:1.1 γ:β), and the major regioisomer **5a** arises via predominant addition of pinBH to the *re*-face (93:7 er). The results show that the aryl substituents appended to the TADDOL backbone have a significant effect on the sense of enantioinduction and regioselectivity. The nature of the phosphite substituent also plays a significant role. Compared to the phenylphosphites **T1a**-**T3a**, the corresponding pentafluorophenyl phosphites **T1b**-**T3b** give enhanced levels of β-boration. Among the latter, **T2b** (Ar = 4-MeC_6H_4) gives the highest level (1:10 γ:β) and enantioselectivity favoring *re*-face addition (97:3 er).[12] Ligands **T4**-**T6** generally are less selective than the other structural analogs examined. The 4-^{t}BuC_6H_4-TADDOL derivative **T5b** is a curious case. It affords the β-boration product **5a** with moderate regioselectivity (1:4 γ:β), but in contrast to other β-selective ligands (e.g., **T2b**), pinBH adds to the *si*-face of the alkene (96:4 er).

Having identified the γ, *si*-face selective ligand **T1a** and β, *re*-face selective ligand **T2b**, a series of methylidenes were examined to probe the substrate scope of each.[13] Figure 3A summarizes the results obtained using each ligand for CAHB/oxidation of 4-substituted aryl methylidene derivatives **3b**-**j**. Halogenated derivatives generally work well affording predominantly **4b**-**d** using **T1a** and predominantly **5b**-**d** using **T2b**. Yields are in the range of 64-76% after oxidation with enantiomer ratios (er) up to 98:2. The methyl benzoate derivative **3e**, 4-trifluoromethylphenyl derivative **3f**, and 4-methylphenyl derivative **3g** undergo γ-boration using the Rh-**T1a** catalyst to afford **4e** (70%, 94:6 er), **4f** (76%, 94:6 er), and **4g** (63%, 98:2 er), respectively. The more electron rich aromatic derivatives, 4-methoxyphenyl **3h** and 4-(dimethylamino)phenyl **3i**, afford their respective γ-borylated products **4h** (57%, 95:5 er) and **4i** (57%, 94:6 er) albeit with lower regiocontrol. The Boc-protected 4-aminophenyl derivative **3j** exhibits good regioselectivity, but the yield of **4j** (52%, 93:7 er) is again moderate.

The β-boration results obtained using the **T2b** catalyst for substrates **3b**-**f** are like those described above for the **T1a** γ-boration catalyst; yields for **5b**-**f** range from 64-78% with enantiomer ratios from 96:4 to 98:2 er. The two catalyst systems differ to a greater extent with substrates bearing electron donating substituents. In contrast to the moderate yields but good enantioselectivity using the **T1a** catalyst, **3g**-**i** (especially the 4-methoxyphenyl and 4-(dimethylamino)phenyl derivatives **3h** and **3i**) give somewhat higher yields but exhibit attenuated enantioselectivity for β-borated **5g** (66%, 91:9 er), **5h** (76%, 86:14 er) and **5i** (60%, 80:20 er) using **T2b**.

Figure 3B illustrates the results obtained with several more highly functionalized aryl derivatives including several methylidenes bearing heteroaryl substituents. Using the **T1a**-catalyst, the 3-methoxyphenyl (**3k**), 3-chlorotolyl (**3l**), 3,4-methylenedioxyphenyl (**3m**), and indole derivative (**3n**) afford **4k**-**n** in 60-75% yield and up to 97:3 er. The thienyl and benzofuran derivatives **3o**-**q** give γ-borylated products in more moderate yields (50-59%) due to higher levels of β-boration for **4o** and **4q**, and higher levels of the reduction product for **4p**. The enantioselectivity is also lower for these substrates, ranging from 90:10 er for **4o** to 65:35 er for **4q**. In contrast, the 3- and 2-thienyl derivatives are efficient substrates in the **T2b**-catalyzed reaction affording **5o** (85%, 98:2 er) and **5p** (71%, 96:4 er), respectively. The benzofuran derivative **3q** provides good regio- and enantioselectivity for **5q** (40%, 94:6 er); the moderate yield reflects competing reduction in this case.[4a, 14] The yields, regio- and enantioselectivities obtained for **5k** (60%, 94:6) and **5l** (65%, 95:5) are similar to those observed for the corresponding γ-borated products. However, substrates bearing multiple donor groups can give surprising results; **5k** and **5l**, for example, form with the opposite sense of stereoinduction (see SI).

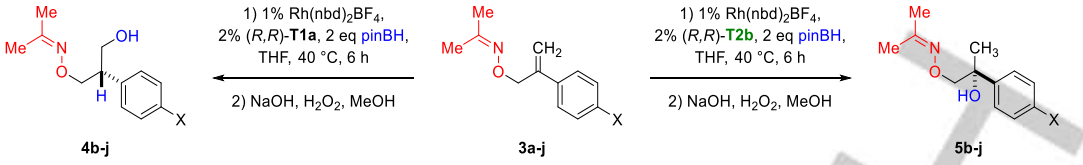
Several other limitations are found (Figure 3C). Substrates bearing *ortho*-substituted aryl groups (e.g., **3r** and **3s**) do not exhibit regio- or enantioswitching. Both catalyst systems provide almost exclusively γ-borated products with little asymmetric induction. Unlike aryl substituted methylidenes **3a**-**s**, the alkyl-substituted methylidene **3t** undergoes β-boration using the **T1a**-catalyst to give **5t** (85%, 95:5 er);[4a] less than 5% of the γ-borylated product is formed. β-Boration of **3t** giving **5t** (58%, 92:8 er) remains the major pathway using ligand **T2b**, although the percentage of γ-boration increases to 32%.

10.1002/anie.201903308

WILEY-VCH

COMMUNICATION

Figure 3A



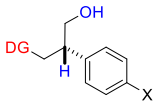
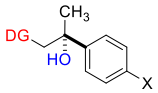
X =	F	Cl[a]	Br[a]	CO_2Me[b]	CF_3[a]	CH_3	OMe	NMe_2	N(H)Boc
	**4b** 74%, 97:3 er (<5% β)	**4c** 65% 98:2 er (<5% β)	**4d** 75% 97:3 er (<5% β)	**4e** 70% 94:6 er (<5% β)	**4f** 76% 94:6 er (<5% β)	**4g** 63% 98:2 er (8% β)	**4h** 57% 95:5 er (19% β)	**4i** 57% 94:6 er (14% β)	**4j** 52% 93:7 er (5% β)
	**5b** 73%, 96:4 er (13% γ)	**5c** 64% 98:2 er (<5% γ)	**5d** 76% 96:4 er (8% γ)	**5e** 78% 96:4 er (<5% γ)	**5f** 75% 98:2 er (7% γ)	**5g** 66% 91:9 er (18% γ)	**5h** 76% 86:14 er (5% γ)	**5i**[c] 60% 80:20 er (5% γ)	**5j** 65% 94:6 er (5% γ)

Figure 3B

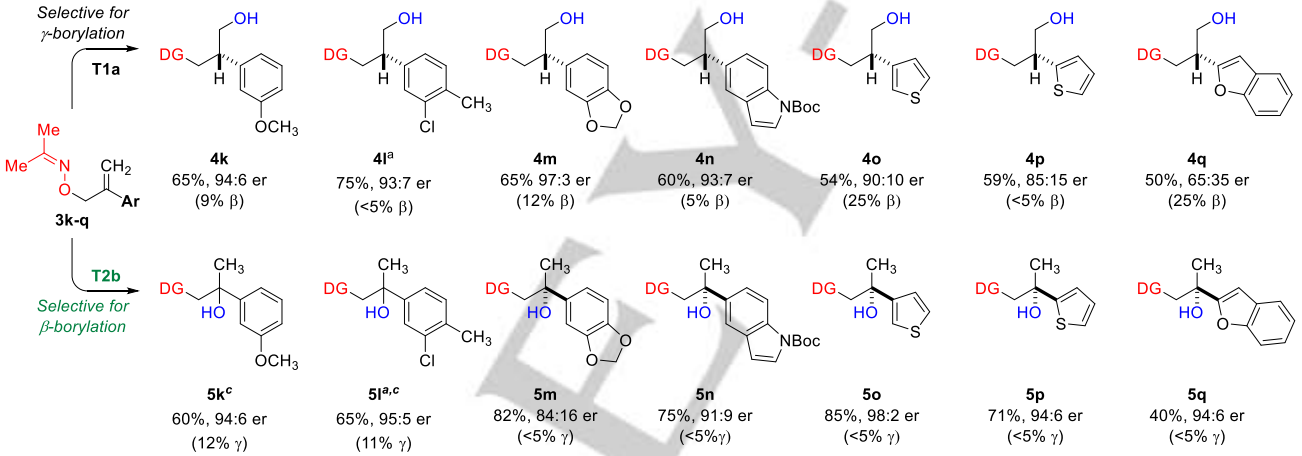


Figure 3C

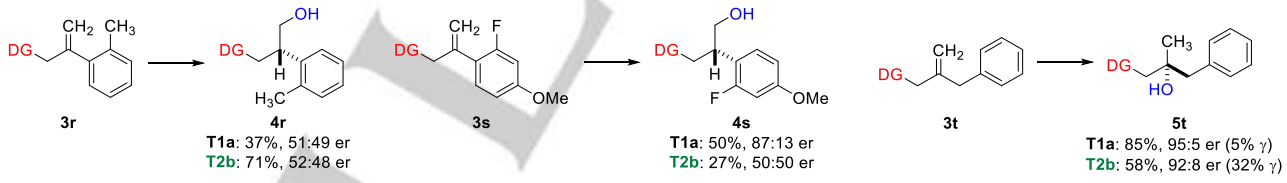


Figure 3A-C. Substrate scope: **A**. 4-Substituted phenyl derivatives; **B**. 3-Substituted phenyl and heteroaromatic derivatives; **C**. *ortho*-Substituted aryl and alkyl derivatives. Reported yields and enantiomer ratios are for the isolated alcohol after oxidation. **DG** = (Me_2C=N-O). Notes: [a] used 1:1 Rh:L ratio; [b] yield of boronic ester before oxidation with $NaBO_3$-H_2O; [c] Compounds **5i**, **5k**, and **5l** exhibited an opposite sign of optical rotation and order of elution on chiral HPLC; see SI.

The synthetic versatility of enantioselective, regiodivergent CAHB is demonstrated by the selected conversions of **4a** and **5a** to **6**-**21** (Figure 4).[15] Both the primary and tertiary pinacol boronic esters are converted to the corresponding cesium[16] or potassium[17] trifluoroborate salts, **6a** and **7a** respectively, in 97-98% yield. Similarly, boronic acids **6b** and **7b** and the corresponding *N*-methyliminodiacetic acid (MIDA) esters[18] **6c** and **7c** are readily accessible (62-72%). The one-carbon homologated boronic esters **8** (75%) and **9** (55%) are obtained via the Matteson protocol.[19] In the case of the tertiary boronic ester **5a**, the reaction proceeds with stereoretention to afford (*R*)-**9** (98:2 er). Hydrolysis of the primary boronic ester **4a** to the boronic acid, followed by Raney Nickel cleavage of N-O bond affords chiral oxaborolane **10** (71%). Reduction of the oxime C-N double bond in **5a** with $NaCNBH_3$ affords **11** (77%); the reduction works equally as well for **4a** (results not shown, see SI).

10.1002/anie.201903308

WILEY-VCH

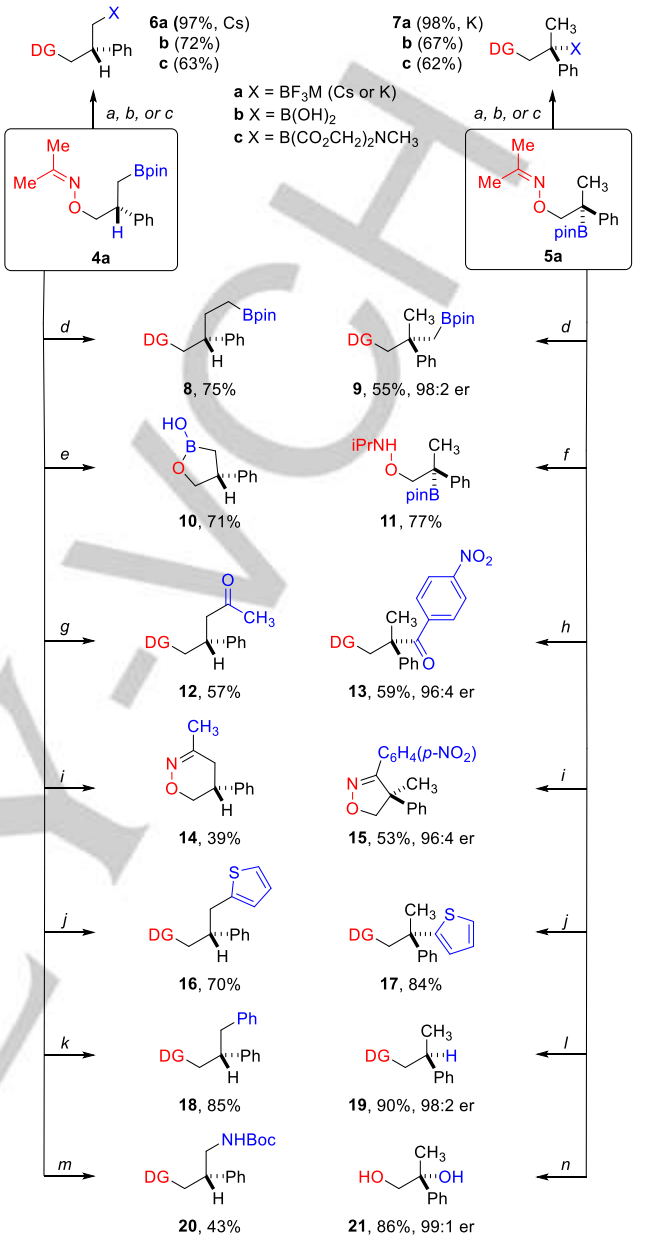
COMMUNICATION

In addition to forming boron derivatives **6–11**, other transformations highlight the flexible and diverse ways in which **4a** and **5a** can be elaborated. Using Aggarwal's modification of the Zweifel olefination,[20] the primary boronic ester **4a** is converted to ketone **12** (57%). For the tertiary boronic ester **5a**, rhodium-catalyzed 1,2-addition to 4-nitrobenzaldehyde followed by DMP oxidation affords ketone **13** (59%, 96:4 er).[21] Ketones **12** and **13** undergo acid-catalyzed cyclizations to the chiral dihydrooxazine **14** (39%) and chiral isoxazoline **15** (53%, 96:4 er), respectively.

The transition-metal-free sp^2-sp^3 cross-couplings of electron-rich aromatic systems convert **4a** and **5a** to the thienyl derivatives **16** (70%) and **17** (84%), respectively.[22] Treatment of the primary boronic ester **4a** with bromobenzene under typical palladium-catalyzed Suzuki cross-coupling conditions[5c] affords **18**, a product that is not readily accessible using the transition-metal-free procedure employed for thienylation. Protodeboronation of the tertiary boronic ester **5a** affords **19** (90%, 98:2 er).[23] In our hands, the common amination procedure[24] is only successful for the primary boronic ester **4a**; a moderate yield of the chiral 1,3-aminoalcohol derivative **20** (43%) is obtained. Oxidation of C-B bond in the tertiary boronic ester **5a** followed by N-O bond cleavage gives chiral 1,2-diol **21** (86%, 99:1 er).

In summary, the CAHB of styrene and related vinyl arenes (e.g., β-methylstyrene or indene derivatives) often leads to formation of the chiral secondary benzylic borated products. The observed regioselectivity is usually attributed to the formation of an intermediate η^3-complex with the aryl substituent.[25] However, aryl methylidenes (e.g., α-methylstyrene) generally give the primary boronic ester. The chiral, tertiary benzylic regioisomer is not formed, presumably due to hindrance in forming the corresponding η^3-complexed intermediate. We find that rhodium-catalyzed hydroboration of β-aryl methylidenes affords either the chiral primary or tertiary boronic ester depending on the TADDOL-derived phosphite ligand employed. Twenty substrates are shown to undergo regioselective reaction using each catalyst system. Regioselectivities reach levels greater than 20:1 and enantiomer ratios up to 98:2 are obtained. Conversions of **3a** to **6**-**21** illustrate the potential synthetic utility of regiodivergent CAHB.

In terms of the mechanism, the aryl substituents appended to the TADDOL backbone as well as the nature of the arylphosphite moiety act synergistically to affect the sense of regioselectivity and enantioinduction. This appears to be due, at least in part, to an electronic effect because the pentafluorophenyl substituent is not unique in promoting β-boration. For example, the corresponding **T2** ligand bearing either a (4-trifluoromethyl)phenyl or a 4-cyanophenyl phosphite substituent also exhibit regioswitching, although the levels of regio- and enantioselectivity are not as high. Deuterium labeling experiments with **T1a** and **T2b** show that addition of H (D) is rapid and reversible, leading to competitive H/D-exchange in the substrate using either regiodivergent catalyst.[26] Several hypotheses that might account for the coupled regio- and enantiodivergent CAHB, effected by ostensibly similar catalyst systems, are currently under investigation.



Reaction Conditions: (a) CsF or KF, MeCN/H_2O; (b) BCl_3, DCM; (c) BCl_3, DCM; MIDA, DMSO; (d) $LiCH_2Cl$, -78 °C Et_2O; (e) BCl_3, DCM; Raney Ni, H_2, MeOH/THF; (f) $NaBH_3CN$, MeOH/HCl; (g) $LiC(OEt)=CH_2$, THF, -78 °C; I_2; NaOMe, MeOH; (h) KF, MeCN/H_2O; $O_2NC_6H_4CHO$, 5 mol% $[Rh(cod)Cl]_2$, dioxane, 80 ℃; DMP, DCM; (i) **12** or **13**, HCl/H_2O/MeOH, 40 °C; (j) thiophene, nBuLi, THF, -78 °C; NBS; (k) PhBr, 15 mol% $Pd(OAc)_2$, 15 mol% BINAP, KOH, THF/H_2O, 100 °C; (l) TBAF, toluene; (m) MeON(H)Li, THF, 60 ℃; Boc_2O; (n) H_2O_2, NaOH, MeOH/H_2O; Raney Ni, H_2

Figure 4. Versatility of the primary and tertiary boronic esters **4a** and **5a** [DG = (Me_2C=N-O)].

Acknowledgements

Funding from the NIH National Institutes of General Medical Sciences (R01-GM100101) is gratefully acknowledged.

Keywords: regiodivergent • enantiodivergent • rhodium-catalyzed hydroboration • catalysis

[1] a) D. S. Matteson, *J. Org. Chem.* **2013**, *78*, 10009; b) C. Sandford, V. K. Aggarwal, *Chem. Commun.* **2017**, *53*, 5481.

[2] a) B. C. Das, P. Thapa, R. Karki, C. Schinke, S. Das, S. Kambhampati, S. K. Banerjee, P. V. Veldhuizen, A. Verma, L. M. Weiss, T. Evans, *Future Med. Chem.* **2013**, *5*, 653; b) D. B. Diaz, A. K. Yudin, *Nat. Chem.* **2017**, *9*, 731; c) G. Antonio Abad, R. Alexey, A.-J. Erik, G. T.-F. Jose, *Curr. Med. Chem.* **2018**, *25*, 1; d) G. R. Mereddy, A. Chakradhar, R. M. Rutkoski, S. C. Jonnalagadda, *J. Organomet. Chem.* **2018**, *865*, 12.

[3] For recent examples, see a) J. Chen, T. Xi, Z. Lu, *Org. Lett.* **2014**, *16*, 6452; b) J. Chen, T. Xi, X. Ren, B. Cheng, J. Guo, Z. Lu, *Org. Chem. Front.* **2014**, *1*, 1306; c) L. Zhang, Z. Zuo, X. Wan, Z. Huang, *J. Am. Chem. Soc.* **2014**, *136*, 15501; d) N. Hu, G. Zhao, Y. Zhang, X. Liu, G. Li, W. Tang, *J. Am. Chem. Soc.* **2015**, *137*, 6746; e) Z. Wang, X. He, R. Zhang, G. Zhang, G. Xu, Q. Zhang, T. Xiong, Q. Zhang, *Org. Lett.* **2017**, *19*, 3067.

[4] For related publications, see a) V. M. Shoba, N. C. Thacker, A. J. Bochat, J. M. Takacs, *Angew. Chem. Int. Ed.* **2016**, *55*, 1465; *Angew. Chem.* **2016**, *128*, 1487; b) S. Chakrabarty, J. M. Takacs, *J. Am. Chem. Soc.* **2017**, *139*, 6066; c) S. Chakrabarty, J. M. Takacs, *ACS Catal.* **2018**, *8*, 10530.

[5] a) N. Matsuda, K. Hirano, T. Satoh, M. Miura, *J. Am. Chem. Soc.* **2013**, *135*, 4934; b) T. Jia, P. Cao, B. Wang, Y. Lou, X. Yin, M. Wang, J. Liao, *J. Am. Chem. Soc.* **2015**, *137*, 13760; c) B. Chen, P. Cao, X. Yin, Y. Liao, L. Jiang, J. Ye, M. Wang, J. Liao, *ACS Catal.* **2017**, *7*, 2425; d) K. M. Logan, M. K. Brown, *Angew. Chem. Int. Ed.* **2017**, *56*, 851; *Angew. Chem.* **2017**, *129*, 869.

[6] a) R. Sakae, K. Hirano, M. Miura, *J. Am. Chem. Soc.* **2015**, *137*, 6460; b) W. Su, T.-J. Gong, X. Lu, M.-Y. Xu, C.-G. Yu, Z.-Y. Xu, H.-Z. Yu, B. Xiao, Y. Fu, *Angew. Chem. Int. Ed.* **2015**, *54*, 12957; *Angew. Chem.* **2015**, *127*, 13149; c) W. Su, T.-J. Gong, Q. Zhang, Q. Zhang, B. Xiao, Y. Fu, *ACS Catal.* **2016**, *6*, 6417; d) S. R. Sardini, M. K. Brown, *J. Am. Chem. Soc.* **2017**, *139*, 9823; e) K. B. Smith, M. K. Brown, *J. Am. Chem. Soc.* **2017**, *139*, 7721; f) T. Jia, Q. He, R. E. Ruscoe, A. P. Pulis, D. J. Procter, *Angew. Chem. Int. Ed.* **2018**, *57*, 11305; *Angew. Chem.* **2018**, *130*, 11475.

[7] D. P. Ojha, K. R. Prabhu, *Org. Lett.* **2016**, *18*, 432.

[8] For the use of enantiomeric catalysts with chiral substrates to effect regiodivergent catalytic reactions, see: N. Funken, Y.-Q. Zhang, A. Gansäuer, *Chem. - Eur. J.* **2017**, *23*, 19.

[9] For examples of regiodivergent, enantioselective, metal-catalyzed reactions, see a) D. M. Dalton, A. K. Rappé, T. Rovis, *Chem. Sci.* **2013**, *4*, 2062; b) E. Cahard, H. P. J. Male, M. Tissot, M. J. Gaunt, *J. Am. Chem. Soc.* **2015**, *137*, 7986; c) E. Richmond, I. U. Khan, J. Moran, *Chem. - Eur. J.* **2016**, *22*, 12274; d) G. Xu, H. Zhao, B. Fu, A. Cang, G. Zhang, Q. Zhang, T. Xiong, Q. Zhang, *Angew. Chem. Int. Ed.* **2017**, *56*, 13130; *Angew. Chem.* **2017**, *129*, 13310; e) H. Zhou, Z. Wei, J. Zhang, H. Yang, C. Xia, G. Jiang, *Angew. Chem. Int. Ed.* **2017**, *56*, 1077; *Angew. Chem.* **2017**, *129*, 1097; f) L. Liang, H.-Y. Niu, M.-S. Xie, G.-R. Qu, H.-M. Guo, *Org. Chem. Front.* **2018**, *5*, 3148; g) S. Xu, Z.-M. Zhang, B. Xu, B. Liu, Y. Liu, J. Zhang, *J. Am. Chem. Soc.* **2018**, *140*, 2272.

[10] The absolute configuration for (*R*)-**4a** was determined by conversion to (*R*)-2,3-diphenylpropanol; see SI.

[11] The absolute configuration for (*R*)-**5a** was determined by conversion to (*R*)-2-phenylpropane-1,2-diol; see SI.

[12] Other phenyl phosphites also afford predominantly β-boration. For example, the (4-trifluoromethyl)phenyl phosphite **T2c** (Ar = 4-MeC_6H_4) gives (1:8 γ:β) with enantioselectivity favoring *re*-face addition (92:8 er), and the 4-cyanophenyl phosphite **T2d** (Ar = 4-MeC_6H_4) is similar.

[13] The metal-to-ligand ratio (Rh:L) employed varies on a case-by-case basis to maximize enantioselectivity, see SI.

[14] Competing alkene reduction typically accounts for low yields of boronic ester; see V. M. Shoba, J. M. Takacs, *J. Am. Chem. Soc.* **2017**, *139*, 5740.

[15] In scaling up to 2.65 mmol of **3a**, a reduced catalyst (0.5 mol%) and 1:1 Rh:L ratio afforded: **4a** (70%, 97:3 er) using **T1a** and **5a** (81% 93:7 er) using **T2b**.

[16] a) A. J. J. Lennox, G. C. Lloyd-Jones, *Angew. Chem. Int. Ed.* **2012**, *51*, 9385; *Angew. Chem.* **2012**, *124*, 9519.

[17] V. Bagutski, A. Ros, V. K. Aggarwal, *Tetrahedron* **2009**, *65*, 9956.

[18] S. J. Lee, K. C. Gray, J. S. Paek, M. D. Burke, *J. Am. Chem. Soc.* **2008**, *130*, 466.

[19] a) K. M. Sadhu, D. S. Matteson, *Organometallics* **1985**, *4*, 1687; b) S. P. Thomas, R. M. French, V. Jheengut, V. K. Aggarwal, *Chem. Rec.* **2009**, *9*, 24.

[20] a) R. P. Sonawane, V. Jheengut, C. Rabalakos, R. Larouche-Gauthier, H. K. Scott, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2011**, *50*, 3760; *Angew. Chem.* **2011**, *123*, 3844.

[21] a) A. Ros, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2009**, *48*, 6289; *Angew. Chem.* **2009**, *121*, 6407.

[22] A. Bonet, M. Odachowski, D. Leonori, S. Essafi, V. K. Aggarwal, *Nat. Chem.* **2014**, *6*, 584.

[23] S. Nave, R. P. Sonawane, T. G. Elford, V. K. Aggarwal, *J. Am. Chem. Soc.* **2010**, *132*, 17096.

[24] S. N. Mlynarski, A. S. Karns, J. P. Morken, *J. Am. Chem. Soc.* **2012**, *134*, 16449.

[25] a) B. S. L. Collins, C. M. Wilson, E. L. Myers, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2017**, *56*, 11700; *Angew. Chem*. **2017**, *129*, 11860.

[26] S. Chakrabarty, H. Palencia, M. D. Morton, R. O. Carr, J. M. Takacs, *Chem. Sci.* **2019**, DOI: 10.1039/c8sc05613g.

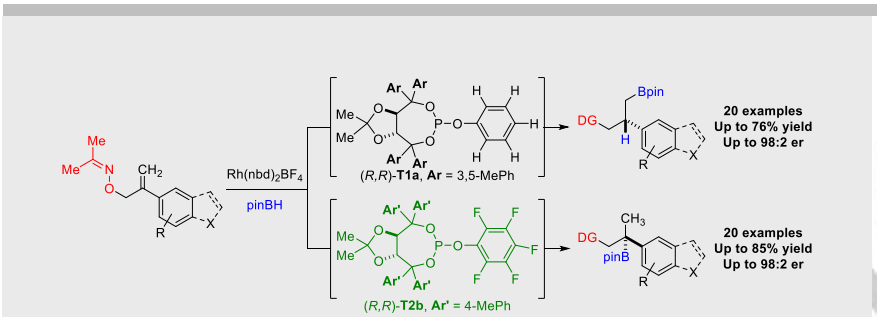
10.1002/anie.201903308

WILEY-VCH

Entry for the Table of Contents (Please choose one layout)

Layout 2:

COMMUNICATION



Regiodivergent with enantioselectivity included! Small changes in the structure of the TADDOL-derived chiral monophosphite ligand direct the rhodium-catalyzed hydroboration of methylidenes to give either primary or tertiary chiral boronic esters.

*Andrew J. Bochat, Veronika M. Shoba, James M. Takacs**

Page No. – Page No.

Ligand-Controlled Regiodivergent Enantioselective Rhodium-Catalysed Alkene Hydroboration