Advanced Synthesis & Catalysis

Accepted Article

Title: Enantioselective Isoprenylboration Reaction of Aldehydes Catalyzed by a Chiral Phosphoric Acid

Authors: Yiyong Huang, Yulong Zhang, Bojun He, Yiwen Xie, Yuhao Wang, Yongcun Shen, and Yilong Wang

To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201900203

Link to VoR: http://dx.doi.org/10.1002/adsc.201900203

10.1002/adsc.201900203

COMMUNICATION

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

Enantioselective Isoprenylboration Reaction of Aldehydes Catalyzed by a Chiral Phosphoric Acid

Yu-Long Zhang,[†] Bo-Jun He,[†] Yi-Wen Xie, Yu-Hao Wang, Yi-Long Wang, Yong-Cun Shen, and Yi-Yong Huang*

Department of Chemistry, School of Chemistry, Chemical Engineering and Life Science, Wuhan University of Technology, Wuhan 430070, China
E-mail: huangyy@whut.edu.cn

[†]These authors contributed equally to this work.

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract. The BINOL-derived chiral phosphoric acid (*R*)-TRIP is utilized as an organocatalyst in the asymmetric isoprenylboration reaction of aldehydes, wherein hydrogen-bond interactions play a key role in the control of enantioselectivity. A wide arrays of enantioenriched dienyl homoallyl alcohols, including two natural products (-)-Ipsdienol and (-)-Ipsenol, have been successfully constituted. The synthetic application to chiral isoprenylated isobenzofuranone, vinyloxirane and cyclohexene derivatives has also been disclosed.

Keywords: Allylation; Chiral phosphoric acid; Boron reagent; Isoprenylation; Phthalide

Dienyl homoallyl alcohols (DHAs) represent an important family of compounds, not only because they are ubiquitous structural units embedded in naturally occurring products, but also serve as versatile synthetic intermediates for the conjugated diene and hydroxy functional groups.[1] As shown in Figure 1, (-)-Ipsdienol and (-)-Ipsenol are two natural products of the aggregation pheromones isolated from the bark beetle *Ips. paraconfusus*.[2] Vital nutrient Vitamin D3,[3] Calcipotriol (treatment of psoriasis)[4] and natural product Brassicicene D[5] all share the key DHA-fragment. In 2012, the Leighton group applied chiral DHAs into the total synthesis of polyketide natural products.[6] In 2015, the Song group showcased the synthetic utility of DHAs by the sequential hydrohalogenation/prins cyclization for the synthesis of multisubstituted tetrahydropyrans inculding natural product (-)-Exiguolide.[7] Accordingly, the development of efficient synthetic approaches to such type of molecules, both racemic or enantioenriched, remains highly desirable.[8] Especially, the catalytic asymmetric synthesis of chiral DHAs represents a challenging work, and only two reports have thus far been documented by using different organometallic catalysts. For example, the Yu group reported a chiral BINOL/Ti^{IV}-promoted asymmetric isoprenylation of aldehydes with an isoprenylstannane reagent (Scheme 1a).[9] During our manuscript preparation, the Krische group accomplished an elegant iridium-catalyzed asymmetric reductive coupling of isoprenyl carbonate and primary alcohols (or aldehydes) (Scheme 1b).[10] Therefore, we commence this study to devise new catalytic approach to implement the task of obtaining optically pure DHAs efficiently.

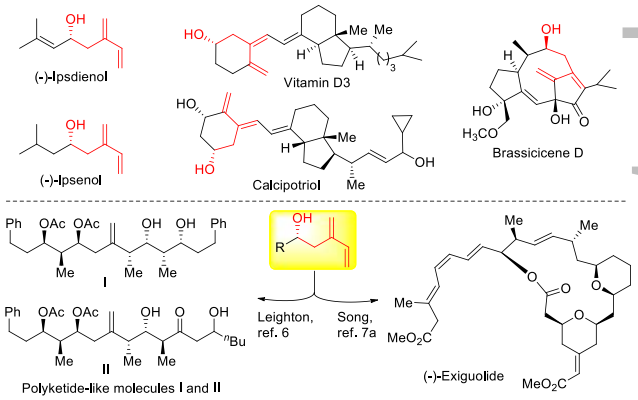
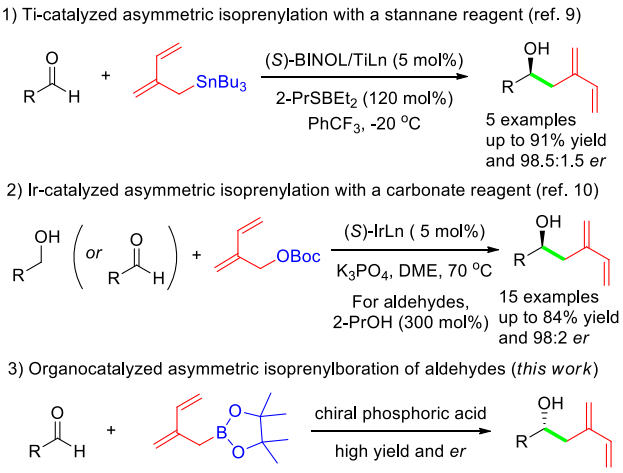


Figure 1. Structural importance and synthetic application of dienyl homoallyl alcohols.

Organoboronate reagents have emerged as indispensable tools since most of them are readily available, non-toxic, air and water stable, and tolerant to many functional groups. Various activation strategies assisted by chiral organo- or organometallic catalysts have been established to transfer functional groups–like allyl, allenyl, propargyl and aryl–in an asymmetric manner. Since the seminal work of chiral phosphoric acid catalyzed asymmetric

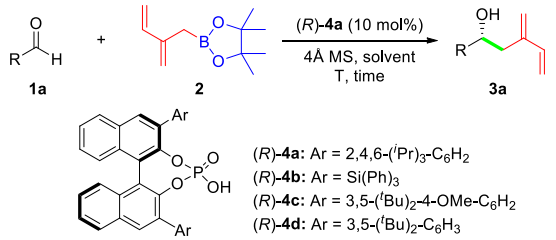
allylboronation of aldehydes was reported by the Antilla group,[11] the extensive exploration of using other types of unsaturated boronate reagents and related computational studies have been further compiled.[12] Such synthetic tactic features easy operation, exclusive γ-selective addition and high level of enantioselectivities. We reasoned that pinacolyl isoprenylboronate can be potentially employed to the asymmetric nucleophilic addition reaction of aldehydes to install chiral DHAs including natural products of (-)-Ipsdienol and (-)-Ipsenol (Scheme 1c), although pinacolyl isoprenylboronate was solely utilized in Diels-Alder and 1,4-hydrovinylation reactions in previous work.[13] In this context, we herein introduce an unprecedented asymmetric isoprenylboronation of aldehydes in the presence of a chiral Brønsted acid catalyst.[14]



Scheme 1. Catalytic asymmetric entries to chiral dienyl homoallyl alcohols.

In order to obtain the optimal reaction conditions to get chiral isoprenylated products with satisfactory yields and enantioselectivities, the model reaction using benzaldehyde **1a** and pinacolyl isoprenylboronate **2** was firstly carried out. As shown in Table 1, the background reaction without the assistance of any catalysts proceeded smoothly in toluene at room temperature (rt), and racemate **3a** was provided in 88% yield after 3 h (entry 1). In order to suppress the background reaction and achieve excellent enantio-induction, the reaction temperature was decreased along with using a chiral Brønsted acid (10 mol%) to activate the boronate reagent. The commonly used BINOL-derived chiral phosphoric acid (*R*)-**4a** ((*R*)-TRIP) was firstly selected. Initial temperature screening in toluene revealed that -40 °C was the best choice in terms of efficiency and enantioselectivity (entries 2-5), and (*R*)-**3a** was delivered in 89% yield with 93.1:6.9 enantiomeric ratio (*er*) (entry 4). Under the same temperature, CH_2Cl_2 slovent was unable to improve the enantioselectivity (entry 6). The solvent mixture toluene and cyclohexane gave the same enantioselectivity (entry 7 vs entry 4). To our delight, a significant increase in *er* (96.7:3.3) was observed in the solvent mixture toluene and CCl_4 (1:1) (entry 8). The use of other BINOL-derived chiral phosphoric acids with various substituents at the 3,3'-positions ((*R*)-**4b**, (*R*)-**4c**, (*R*)-**4d**) (entries 9-11), further increasing the volume ratio of CCl_4, or bringing down the temperature with (*R*)-**4a** afforded inferior results (entries 12-13). Control experiment in the absence of 4Å MS resulted in a much lower *er*, which suggested that trace amount of water has a detrimental effect on the enantioselectivity through affecting the interaction between catalyst and substrates (entry 14). The comparison study of catalyst loading indicated that 10 mol% was the most suitable amount for the transformation (entries 15-16).

Table 1. Screening of solvents and temperature.[a]



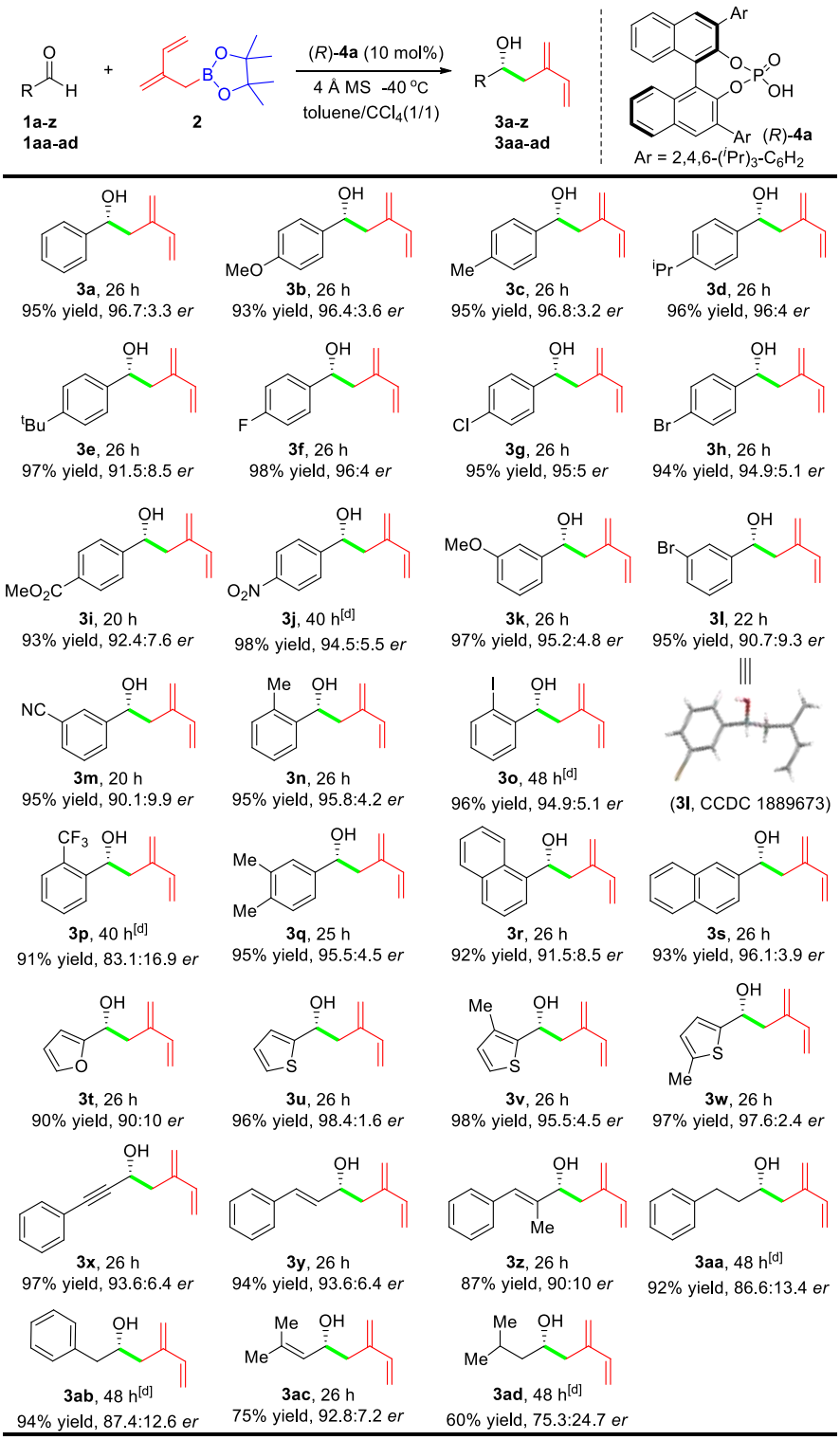
entry	catalyst	solvent	T/°C	time/h	yield/%[b]	*er*[c]
1	**4a**	toluene	rt	3	88	50:50
2	**4a**	toluene	0	10	86	59.8:40.2
3	**4a**	toluene	-20	20	84	85.5:14.5
4	**4a**	toluene	-40	26	89	93.1:6.9
5	**4a**	toluene	-50	36	94	92.8:7.2
6	**4a**	CH_2Cl_2	-40	24	85	83.9:16.1
7	**4a**	toluene/cyclohexane (1/1)	-40	26	76	93.6:6.4
8	**4a**	toluene/CCl_4 (1/1)	-40	26	95	96.7:3.3
9	**4b**	toluene/CCl_4 (1/1)	-40	24	89	77.4:22.6
10	**4c**	toluene/CCl_4 (1/1)	-40	26	94	70.1:29.9
11	**4d**	toluene/CCl_4 (1/1)	-40	20	90	85.3:14.7
12	**4a**	toluene/CCl_4 (1/2)	-40	26	90	93.6:6.4
13	**4a**	toluene/CCl_4 (1/1)	-50	36	93	95.8:4.2
14[d]	**4a**	toluene/CCl_4 (1/1)	-40	26	92	85.7:14.3
15[e]	**4a**	toluene/CCl_4 (1/1)	-40	30	94	86.9:13.1
16[f]	**4a**	toluene/CCl_4 (1/1)	-40	20	92	96.8:3.2

[a] Reaction conditions unless otherwise specified: **1a** (0.10 mmol), **2** (0.15 mmol), solvent (0.3 mL), (*R*)-**4** (10 mol%), and 4 Å MS (25 mg). [b] Isolated yield. [c] The enantiomeric ratio (*er*) was determined by HPLC with a chiral stationary phase. [d] No 4 Å MS. [e] The reaction was conducted with 5 mol% of catalyst. [f] The reaction was conducted with 15 mol% of catalyst.

With the optimized reaction conditions in hand, we next examined the scope of this enantioselective isoprenylation by using a wide array of commercially available aldehydes. The results were summarized in Scheme 2. Initially, the substituent effects including diverse electronic, steric and position of substituted groups on the benzene ring were checked. Comparing with the catalytic results obtained from benzylaldehyde **1a** to product **3a** (95% yield and 96.7:3.3 *er*), the incorporation of electron-donating groups (MeO-, Me- and ^{i}Pr-) at the *para*-position provided identical level of yields and enantiomeric ratios, albeit the bulky ^{t}Bu group resulted in a lower *er* (**3e**, 91.5:8.5 *er*). Similar reactivities and >94.9:5.1 *er* were found when using arylaldehydes containing

10.1002/adsc.201900203

halogen groups (F-, Cl- and Br-). The presence of electron-withdrawing groups (-CO_2Me and -NO_2) seemed more challenging. Chiral adduct **3i** was obtained under the standard reaction conditions, whereas **3j** was achieved with a satisfactory *er* under newly optimized reaction conditions (CH_2Cl_2, -60 °C). In the case of substituents at the *meta*-position, selected groups including MeO-, Br- and -CN exhibiting various electronic properties were surveyed with high enantioselective outcome (**3k**, **3l** and **3m**). Substituents at the *ortho*-position impose higher steric congestion than other positions, which may has a serious effect on the enantioinduction. For instance, high *er* value (95.8:4.2) was observed for the Me-substitued aldehyde under the standard conditions, whereas the CF_3- and iodo-substituted aldehydes were transformed with satisfactory results under a set of reaction conditions like aldehyde **1j**. The asymmetric isoprenylboration of 3,4-dimethylbenzaldehyde **1q** was also performed in 95% yield with 95.5:4.5 *er*. 2-Naphthyl aldehyde **1s** converted to compound **3s** with a higher *er* comparing with the 1-naphthyl aldehyde **1r** probably due to the negative steric hindrance effect (96.1:3.9 *er* vs 91.5:8.5 *er*). The asymmetric transformation of heteroaromatic aldehydes was exemplified with furyl and thienyl derivatives. 2-Furyl-derived DHA **3t** was delivered with 90% yield and 90:10 *er*. Gratifyingly, 2-thienyl adduct **3u** was formed with a perfect *er* of 98.4:1.6, and other two products with an additional methyl substituent **3v** and **3w** were also installed with slightly lower enantioselectivities. Furthermore, arylalkynyl and arylalkenyl aldehydes (**1x** and **1y**) underwent the asymmetric isoprenylation with an identical *er* (93.6:6.4), and the incorporation of a methyl group at the α-position of **1y** was detrimental to the yield and enantio-induction (**3y**, 87% yield and 90:10 *er*). Aliphatic aldehydes remain more challenging than the above aromatic cases in terms of reactivity and enantiofacial discrimination. Comparable results were achieved for two arylalkynyl products **3aa** and **3ab** in CH_2Cl_2 at -60 °C. (-)-Ipsdienol **3ac** was generated in 75% yield and 92.8:7.2 *er* under the standard contions, and (-)-Ipsenol **3ad** was accessed with an improvable yield and *er* under the revised reaction conditions (CH_2Cl_2, -60 °C).



[a] Reaction conditions unless otherwise specified: **1** (0.10 mmol), **2** (0.15 mmol), solvent (0.3 mL), (*R*)-**4** (10 mol%), and 4Å MS (25 mg). [b] Yield of isolated product. [c] The *er* value was determined by HPLC analysis on a chiral stationary phase. [d] CH_2Cl_2, -60 °C.

Scheme 2. Aldehyde scope in the asymmetric isoprenylboration.[a,b,c]

The absolute configuration of the chiral isoprenylated products including (-)-Ipsdienol and (-)-Ipsenol was assigned by comparing with the optical rotation of known compounds,[10] and the X-ray crystal structure of compound **3l** was also determined to verify the stereochemical results.[15] Therefore, the chiral carbon atom of compound **3a** is determined as *R*-configuration, which suggests that the asymmetric isoprenylboration across the *Re*-face of benzylaldehyde mediated by the chiral phosphoric acid (*R*)-**4**. The stereochemistry can be explained by using the transition model

proposed by Goodman,[12g] and already used in our pr evious work.[12q] As shown in Figure 2, the molecular recognition between chiral phosphoric acid and the six-membered cyclic chair-like transition state assembled from benzylaldehyde and isoprenylboronate is based on hydrogen bonding. The protonation of boronate oxygen atom can efficiently increase the Lewis acidity of boron atom and enhance the electrophilicity of aldehyde,[16] thus accomplish an enantioselective reaction pathway by suppressing the competitive racemic background process at low temperature. In terms of enantiofacial discrimination, the favorable *Re*-face nucleophilic attack probably results from the minimized steric repulsion between catalyst and substrates in TS-*Re* instead of TS-*Si*.

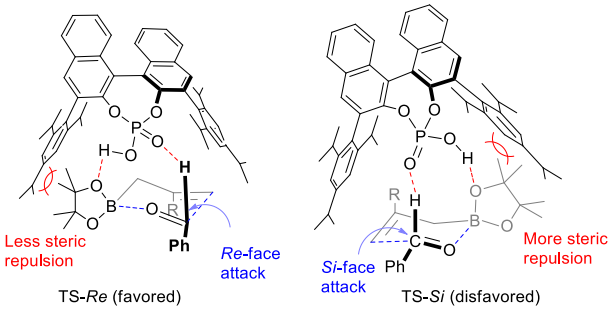
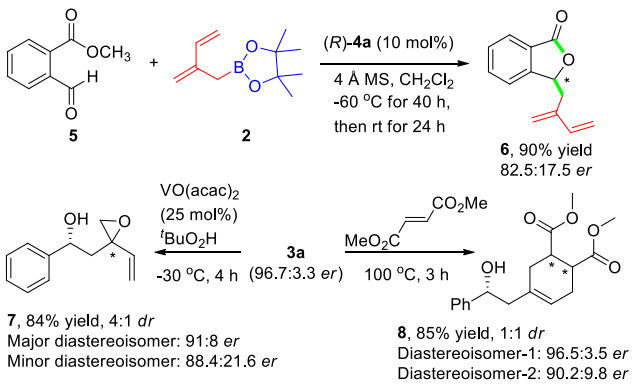


Figure 2. Proposed transition states.

In order to construct chiral *O*-containing heterocycle fameworks, we then turned our attention to apply such catalytic protocol into the asymmetric tandem isoprenylboration/cyclization reaction.[17] Chiral isobenzofuranones (or called "phthalides") are important compounds possessing a broad range of biological activities, and the exploration of catalytic asymmetric approaches to the entities has drawn great interest.[18] Methyl 2-formylbenzoate **5** and **2** underwent the initial asymmetric isoprenylboration at -60 °C for 40 h and sequential intramolecular transesterification at rt for 24 h to afford the desired enantioenriched isoprenyl-substituted phthalide **6** in 90% yield with 82.5:17.5 *er*. Furthermore, the synthetic utility of chiral adduct (*R*)-**3a** involving $^{t}BuO_2H$-mediated asymmetric epoxidation and Diels-Alder reaction was displayed, and chiral vinyloxirane **7** and cyclohexene **8** were prepared with good results (Scheme 3).



Scheme 3. Synthetic utility.

In summary, we have demonstrated a novel, useful and easily-handled approach to build enantioenriched dienyl homoallyl alcohols comprising two nature products (-)-Ipsdienol and (-)-Ipsenol through the chiral phosphoric acid-catalyzed asymmetric isoprenylboration of aldehydes. Wide substrate scope as exemplified by aryl, heteroaryl, arylalkynyl, arylalkenyl, and aliphatic aldehydes were observed with up to 98% yield and 98.4:1.6 *er*. A cyclic transition state model involving the chiral phosphoric acid activation through the double hydrogen-bond formation was proposed to understand the enantiotopic face differentiation. Notably, the synthetic application of such reaction protocol for the facile access to chiral isobenzofuranone, vinyloxirane and cyclohexene frameworks has been finally presented. Further study on the asymmetric isoprenylboration of other electrophiles is ongoing in our lab.

Experimental Section

General procedure for the asymmetric isoprenylboration of aldehydes: To an oven dried 2 mL test tube with a stir bar was added catalyst (*R*)-**4** (10 mol%) and 4 Å MS (25.0 mg). In nitrogen atmosphere, aldehyde **1** (0.10 mmol) and anhydrous solvent (0.2 mL) were added at rt. The reaction mixture was then cooled to the temperature indicated in the main text, followed by the addition of a solution of pinacolyl isoprenylboronate **2** (0.15 mmol) (0.1 mL of solvent) over 20 minutes. The mixture was stirred for the time indicated in Scheme 2, then subjected to preparative thin layer chromatography to get the target isoprenylated products **3**.

Acknowledgements

We gratefully thank the financial support of this investigation by the National Natural Science Foundation of China (21573169, 21772151), Natural Science Foundation of Hubei Province (2018CFA084), and Wuhan Morning Light Plan of Youth Science and Technology (2017050304010314).

References

[1] a) N. C. Yang, D. D. H. Yang, C. B. Ross, *J. Am. Chem. Soc.* **1959**, *81*, 133-136; b) A. T. Blomquist, R. J.

Himics, *J. Org. Chem.* **1968**, *33*, 1156-1159; c) B. B. Snider, D. J. Rodini, *Tetrahedron Lett*. **1980**, *21*, 1815-1818; d) B. B. Snider, D. J. Rodini, T. C. Kirk, R. Cordova, *J. Am. Chem. Soc.* **1982**, *104*, 555-563; e) C. P. Cartaya-Marin, A. C. Jackson, B. B. Snider, *J. Org. Chem.* **1984**, *49*, 2443-2446; f) H. T. Dang, V. T. Nguyen, V. D. Nguyen, H. D. Arman, O. V. Larionov, *Org. Biomol. Chem.* **2018**, *16*, 3605-3609.

[2] a) M. Terada, K. Mikami, *J. Chem. Soc. Chem. Commun.* **1995**, 2391-2392; b) K. Mori, H. Takikawa, *Tetrahedron* **1991**, *47*, 2163-2168; c) H. C. Brown, R. S. Randad, *Tetrahedron Lett.* **1990**, *31*, 455-458; d) H. C. Brown, R. S. Randad, *Tetrahedron* **1990**, *46*, 4463-4472; e) N. Ikeda, I. Arai, H. Yamamoto, *J. Am. Chem. Soc.* **1986**, *108*, 483-486.

[3] a) H. Nemoto, H. Kurobe, K. Fukumoto, T. Kametani, *Heterocycles* **1985**, *23*, 567-569; b) H. Nemoto, H. Kurobe, K. Fukumoto, T. Kametani, *J. Org. Chem.* **1986**, *51*, 5311-5320; c) T. Hanazawa, A. Koyama, T. Wada, E. Morishige, S. Okamoto, F. Sato, *Org. Lett.* **2003**, *5*, 523-525.

[4] M. J. Calverley, *Tetrahedron* **1987**, *43*, 4609-4619.

[5] a) A. Tazawa, Y. Ye, T. Ozaki, C. Liu, Y. Ogasawara, T. Dairi, Y. Higuchi, N. Kato, K. Gomi, A. Minami, H. Oikawa, *Org. Lett.* **2018**, *20*, 6178-6182; b) Y. Tang, Y. Xue, G. Du, J. Wang, J. Liu, B. Sun, X. Li, G. Yao, Z. Luo, Y. Zhang, *Angew. Chem.* **2016**, *128*, 4137-4141; *Angew. Chem. Int. Ed.* **2016**, *55*, 4069-4073.

[6] S. K. Reznik, B. S. Marcus, J. L. Leighton, *Chem. Sci.* **2012**, *3*, 3326-3330.

[7] a) Y. Xu, Z. Yin, X. Lin, Z. Gan, Y. He, L. Gao, Z. Song, *Org. Lett.* **2015**, *17*, 1846-1849; b) L. Li, X. Sun, Y. He, L. Gao, Z. Song, *Chem. Commun.* **2015**, *51*, 14925-14928.

[8] a) M. Tokuda, N. Mimura, K. Yoshioka, T. Karasawa, H. Fujita, H. Suginome, *Synthesis* **1993**, 1086-1088; b) Y. Masuyama, M. Fuse, Y. Kurusu, *Chem. Lett.* **1993**, 1199-1202; c) M. Kimura, M. Fukushima, D. Takushima, *J. Am. Chem. Soc.* **2010**, *132*, 16346-16348.

[9] C. M. Yu, M. Jeon, J. Y. Lee, J. Jeon, *Eur. J. Org. Chem.* **2001**, 1143-1148.

[10] M. Xiang, G. Luo, Y. Wang, M. J. Krische, *Chem. Commun.* **2019**, *55*, 981-984.

[11] P. Jain, J. C. Antilla, *J. Am. Chem. Soc.* **2010**, *132*, 11884-11886.

[12] For reviews, see: a) D. G. Hall, *Synlett* **2007**, 1644-1655; b) P. Barrio, E. Rodríguez, S. Fustero, *Chem. Rec*. **2016**, *16*, 2046-2060; c) D. M. Sedgwick, M. N. Grayson, S. Fustero, P. Barrio, *Synthesis* **2018**, *50*, 1935-1957; For selected examples, see: d) M. Z. Wang, S. Khan, E. Miliordos, M. Chen, *Adv. Syn. Catal.* **2018**, *360*, 4634-4639; e) M. Wang, S. Khan, E. Miliordos, M. Chen, *Org. Lett.* **2018**, *20*, 6174-6177; f) H. Wang, P, Jain, J. C. Antilla, K. N. Houk, *J. Org. Chem.* **2013**, *78*, 1208-1215; g) M. N. Grayson, S. C. Pellegrinet, J. M. Goodman, *J. Am. Chem. Soc.* **2012**, *134*, 2716-2722; h) C. H. Xing, Y. X. Liao, Y. Zhang, D. Sabarova, M. Bassous, Q. S. Hu, *Eur. J. Org. Chem.* **2012**, 1115-1118; i) C. A. Incerti-Pradillos, M. A. Kabeshov, A. V. Malkov, *Angew. Chem.* **2013**, *125*, 5446-5449; *Angew. Chem. Int. Ed.* **2013**, *52*, 5338-5341; j) T. Miura, Y. Nishida, M. Morimoto, M. Murakami, *J. Am. Chem. Soc.* **2013**, *135*, 11497-11500; k) S. Fustero, E. Rodríguez, R. Lázaro, L. Herrera, S. Catalán, P. Barrio, *Adv. Synth. Catal.* **2013**, *355*, 1058-1064; l) P. Barrio, E. Rodriguez, K. Saito, S. Fustero, T. Akiyama, *Chem. Commun.* **2015**, *51*, 5246-5249; m) E. Rodríguez, M. N. Grayson, A. Asensio, P. Barrio, K. N. Houk, S. Fustero, *ACS Catal.* **2016**, *6*, 2506-2514; n) M. N. Grayson, Z. Yang, K. N. Houk, *J. Am. Chem. Soc.* **2017**, *139*, 7717-7720; o) M. N. Grayson, J. M. Goodman, *J. Am. Chem. Soc.* **2013**, *135*, 6142-6148; p) L. R. Reddy, *Org. Lett.* **2012**, *14*, 1142-1145; q) Y. Y. Huang, X. Yang, Z. Lv, C. Cai, C. Kai, Y. Pei, Y. Feng, *Angew. Chem.* **2015**, *127*, 7407-7410; *Angew. Chem. Int. Ed*. **2015**, *54*, 7299-7302; r) T. Miura, J. Nakahashi, M. Murakami, *Angew. Chem.* **2017**, *129*, 7093-7097; *Angew. Chem. Int. Ed*. **2017**, *56*, 6989-6993; s) T. Miura, J. Nakahashi, W. Zhou, Y. Shiratori, S. G. Stewart, M. Murakami, *J. Am. Chem. Soc.* **2017**, *139*, 10903-10908; t) M. Chen, W. R. Roush, *J. Am. Chem. Soc.* **2012**, *134*, 10947-10952; u) A. S. Tsai, M. Chen, W. R. Roush, *Org. Lett.* **2013**, *15*, 1568-1571; v) L. R. Reddy, *Chem. Commun.* **2012**, *48*, 9189-9191; w) P. Jain, H. Wang, K. N. Houk, J. C. Antilla, *Angew. Chem.* **2012**, *124*, 1420-1423; *Angew. Chem. Int. Ed.* **2012**, *51*, 1391-1394.

[13] a) F. Erver, G. Hilt, *Org. Lett.* **2012**, *14*, 1884-1887; b) F. Erver, G. Hilt, *Org. Lett.* **2011**, *13*, 5700-5703; c) P. Raster, A. Schmidt, M. Rambow, N. Kuzmanovic, B. König, G. Hilt, *Chem. Commun.* **2014**, *50*, 1864-1866.

[14] a) D. Parmar, E. Sugiono, S. Raja, M. Rueping, *Chem. Rev*. **2017**, *117*, 10608-10620; b) T. Akiyama, J. Itoh, K. Yokota, K. Fuchibe, *Angew. Chem.* **2004**, *116*, 1592-1594; *Angew. Chem. Int. Ed.* **2004**, *43*, 1566-1568; c) D. Uraguchi, M. Terada, *J. Am. Chem. Soc.* **2004**, *126*, 5356-5357.

[15] CCDC 1889673 (**3l**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[16] Y. Li, K. N. Houk, *J. Am. Chem. Soc.* **1989**, *111*, 1236-1240.

[17] X. Yang, S. Pang, F. Cheng, Y. Zhang, Y. W. Lin, Q. Yuan, F. L. Zhang, Y. Y. Huang, *J. Org. Chem.* **2017**, *82*, 10388-10397.

[18] For a recent review on the synthesis of phthalides, see: a) R. Karmakar, P. Pahari, D. Mal, *Chem. Rev.* **2014**, *114*, 6213-6284; For selected examples on chiral phthalides, see: b) J. M. Cabrera, J. Tauber, M. J. Krische, *Angew. Chem.* **2018**, *130*, 1404-1407; *Angew. Chem. Int. Ed.* **2018**, *57*, 1390-1393; c) D. H. T. Phan, B. Kim, V. M. Dong, *J. Am. Chem. Soc.* **2009**, *131*, 15608-15609; d) B. Zhang, M. H. Xu, G. Q. Lin, *Org. Lett.* **2009**, *11*, 4712-4715; e) J. H. Xie, X. Y. Liu, J. B. Xie, L. X. Wang, Q. L. Zhou, *Angew. Chem.* **2011**, *123*,

10.1002/adsc.201900203

7467-7470; *Angew. Chem. Int. Ed.* **2011**, *50*, 7329-7332; f) H. Egami, J. Asada, K. Sato, D. Hashizume, Y. Kawato, Y. Hamashima, *J. Am. Chem. Soc.* **2015**, *137*, 10132-10135; g) F. Zhong, J. Luo, G. Y. Chen, X. Dou, Y. Lu, Y. Hamashima, *J. Am. Chem. Soc.* **2012**, *134*, 10222-10227; h) J. Yang, N. Yoshikai, *J. Am. Chem. Soc.* **2014**, *136*, 16748-16751.

10.1002/adsc.201900203

COMMUNICATION

Enantioselective Isoprenylboration Reaction of Aldehydes Catalyzed by a Chiral Phosphoric Acid

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Yu-Long Zhang,† Bo-Jun He,† Yi-Wen Xie, Yu-Hao Wang, Yi-Long Wang, Yong-Cun Shen, and Yi-Yong Huang*