OL Organic Letters

pubs.acs.org/OrgLett Letter

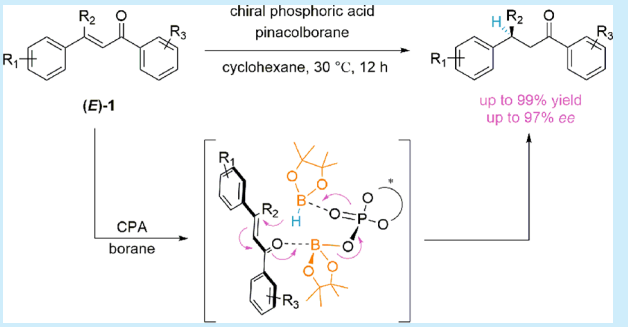
Catalytic Asymmetric Transfer Hydrogenation of *trans*-Chalcone Derivatives Using BINOL-derived Boro-phosphates

Fei Na,[§] Susana S. Lopez,[§] Alice Beauseigneur, Lucas W. Hernandez, Zhuoxin Sun, and Jon C. Antilla*

Cite This: https://dx.doi.org/10.1021/acs.orglett.0c02042 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: Chiral phosphoric-acid-catalyzed asymmetric reductions of *trans*-chalcones have been investigated in this work. A BINOL-derived boro-phosphate-catalyzed asymmetric transfer hydrogenation of the carbon−carbon double bond of *trans*-chalcone derivatives employing borane as a hydride source was realized. This methodology provides a convenient procedure to access chiral dihydrochalone derivatives in high yields and with high enantioselectivities under mild conditions.



Many noteworthy achievements have been made in the field of asymmetric transfer hydrogenation (ATH).[1] To date, a plethora of ATH methodologies have been reported that depend mostly on transition-metal catalysis (e.g., Ir,[2] Ru,[3] Rh,[4] and Fe[5]). Organocatalysts, those catalysts derived from small chiral organic molecules, have become an attractive alternative to metal/chiral ligand-based catalysts for ATH reactions in recent years. Examples of these organocatalysts include chiral Brønsted acids, iminiums, and imidazolidinones.[6]

Chiral phosphoric acids (CPAs) have shown potential in rendering a number of interesting transformations into catalytic and stereoselective variants.[7] When one looks at the ATH methods, CPAs have been widely employed in the hydrogenation of C═O,[8] C═N,[9] and C═C[10] bonds, although the selective hydrogenation of carbon−carbon double bonds of α,β-unsaturated ketones with organocatalysts is still rare, especially with acyclic unsaturated ketone substrates.[6] In 2006, MacMillan and List revealed the hydrogenation of unsaturated cyclic ketones by imidazolidinone or counterion catalysts with Hantzsch ester as the hydride source, respectively (Scheme 1a).[11] In List's work, the enantioselectivity of acyclic unsaturated ketones was distinctly lower than that with cyclic ketones.[11a] Additionally, in 2018, Cramer and coworkers demonstrated a valuable stereoselective 1,4-reduction of acyl pyrrole using chiral diazaphospholenes as the catalyst.[12] In this work, several unsaturated ketones were demonstrated to be viable substrates with moderate enantioselectivities. Compared with these two methods, the reactions that obtained the corresponding products from acyclic ketones are undoubtedly more challenging.

In recent studies, Nakajima and coworkers reported the ATH of β,β-disubstituted α,β-unsaturated ketones employing (*S*)-BINAPO as an organocatalyst to form related products with excellent enantioselectivities and a broad scope (Scheme 1b).[13] Conventional ATH reactions catalyzed by CPAs have mostly utilized Hantzsch esters as the hydride source. Benzothiazolines could also be used as another efficient hydride donor.[9−11] Our group observed that the BINOL-derived CPA forms a new phosphoryl boronate catalyst *in situ* in the presence of catecholborane (Figure 1) to reduce ketones (Scheme 1c).[8a] In this previous work, a plausible mechanism suggested that the boro-phosphate could behave as a chiral bifunctional activator. There have been several additional asymmetric hydrogenation reactions utilizing the combination of CPAs and boranes.[8,14] On the basis of these successes, in this study, we describe the asymmetric hydrogenation of the C═C bonds of *trans*-chalcone derivatives by chiral boro-phosphate catalysts (Scheme 1d).

We began this investigation by optimizing the reaction conditions. First, a series of CPA catalysts were screened with (*E*)-**1a** and pinacolborane (**B1**) in toluene at 50 °C (Table 1, entries 1−5). Catalysts **PA1** and **PA2** could allow for preliminary enantioselectivity (entries 1 and 2, 68% *ee* and 52% *ee*). On the basis of these results, some solvents were also screened in efforts to improve the enantioselectivity. Full conversion and an obvious increase in enantioselectivity were obtained with cyclohexane (entry 6, 74% *ee*). In addition, when

Received: June 20, 2020

https://dx.doi.org/10.1021/acs.orglett.0c02042
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 1. Transfer Hydrogenations of Ketones

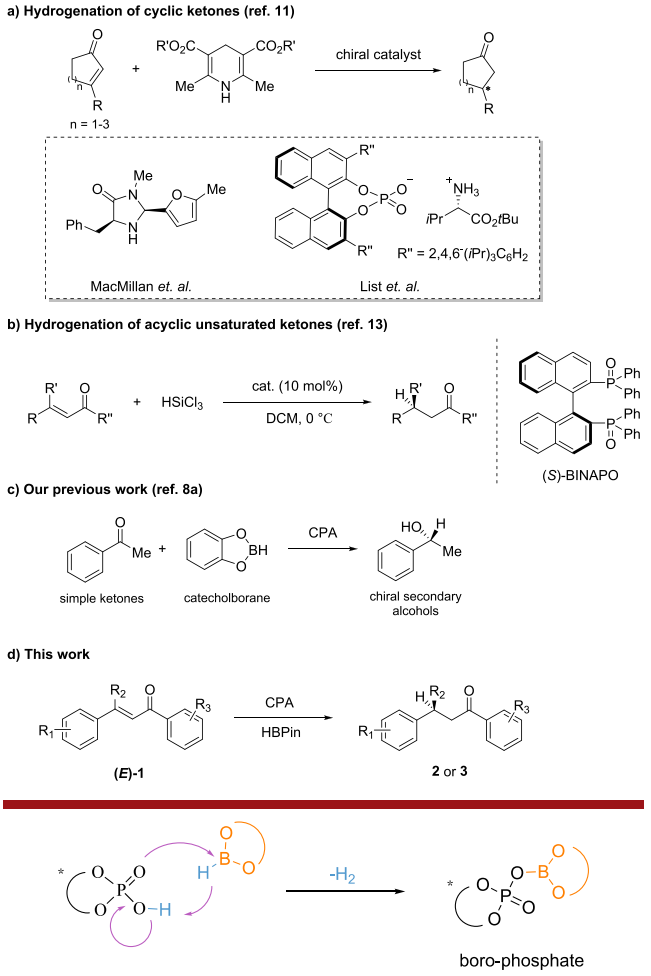
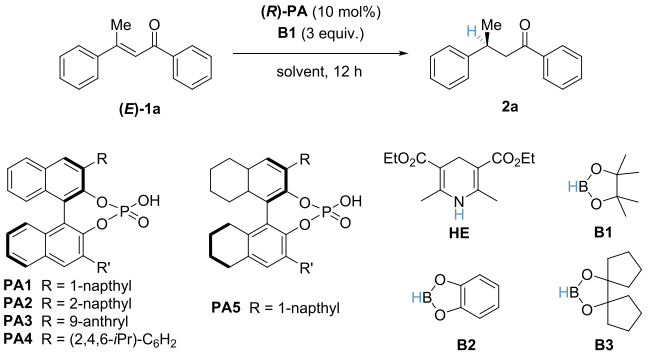


Figure 1. Proposed formation of a boro-phosphate catalyst.

Table 1. Screening of Transfer Hydrogenation[a]



entry	catalyst	solvent	temp. (°C)	conversion (%)[b]	*ee* (%)[c]
1	**PA1**	toluene	50	90	68
2	**PA2**	toluene	50	92	52
3	**PA3**	toluene	50	50	12
4	**PA4**	toluene	50	21	17
5	**PA5**	toluene	50	53	41
6	**PA1**	cyclohexane	50	100	74
7	**PA1**	cyclohexane	30	100	87
8	**PA1**	methylcyclohexane	30	100	72
9	**PA1**	cyclopentane	30	100	70
10	**PA2**	cyclohexane	30	100	91
11[d]	**PA2**	**cyclohexane**	**30**	**100**	**94**
12[e]	**PA2**	cyclohexane	30	100	88
13[f]	**PA2**	cyclohexane	30	n.d.	
14[g]	**PA2**	cyclohexane	30	n.d.	
15[h]	**PA2**	cyclohexane	30	50	91
16[i]	**PA2**	cyclohexane	30	50	70
17[j]	**PA2**	cyclohexane	30	21	39

[a]Reaction conditions: (*E*)-**1a** (1.0 equiv), borane (3.0 equiv), 10 mol % CPA with solvent indicated 0.10 M at temperature. [b]Determined by ^{1}H NMR. [c]*ee* was determined by HPLC analysis. [d]Reaction performed with 5 mol % catalyst. [e]Reaction performed with 1 mol % catalyst. [f]**HE** instead of **B1**. [g]**B2** instead of **B1**. [h]**B3** instead of **B1**. [i]E/Z isomers (1:1) instead of (*E*)-**1a**. [j](*Z*)-**1a** instead of (*E*)-**1a**. n.d. = not determined.

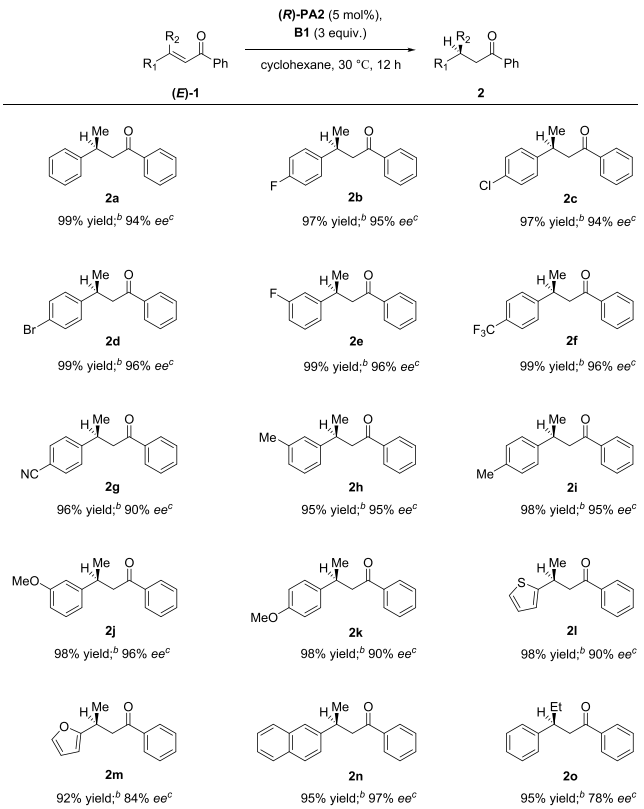
the temperature was lowered, a higher *ee* was obtained at 30 °C (entry 7, 87% *ee*). Additional cycloalkanes were explored as solvents, but no improvements were found (entries 8 and 9). Subsequently, **PA2** was utilized, and a 91% *ee* was found for the reaction product (entry 10). We were pleased to see that when the catalyst loading was lowered to 5 mol %, the reaction proceeded to full conversion, and a 94% *ee* was obtained (entry 11). Moreover, a full conversion was achieved using a 1 mol % catalyst loading, albeit with a moderate drop to 88% *ee* (entry 12). Notably, the hydrogenated compound was not detected when using Hantzsch ester (entry 13). Different boranes were also used to evaluate the *ee* value (entries 14 and 15). However, the desired product was not observed using **B2**. The use of **B3** allowed for an outstanding result in the enantiocontrol, but the conversion declined precipitously. When the substrates with a mixture of E/Z isomers (entry 16) or the pure Z-isomer (entry 17) were used in this transformation, the enantioselectivity decreased. These results indicated that the Z-isomer has a negative effect on the yield and enantioselectivity.

Inspired by our preliminary findings, various *trans*-chalcone derivatives were subjected to the optimized reaction conditions (Scheme 2), and substitutions of the R_1 group were examined. Phenyl derivatives bearing halogens at the para and meta positions could give the corresponding products in good yield with excellent enantioselectivity (Scheme 2, **2b**−**e**, 94−96% *ee*). With strong electron-withdrawing groups (EWGs) such as trifluoromethyl and cyano in the para position, the related chiral products were obtained in high yield with excellent enantioselectivity (Scheme 2, **2f**,**g**, 96 and 90% *ee*). Phenyl derivatives bearing electron-donating groups (EDGs) like methyl and methoxy in the para and meta positions also showed excellent results (Scheme 2, **2h**−**k**, 90−96% *ee*). In addition, other aromatic groups (2-thienyl, 2-naphthyl) were tried for this hydrogenation. The corresponding products **2l** and **2n** were formed with 90 and 97% *ee*. Only a slight decrease in the *ee* value was found with the use of a furan group (Scheme 2, **2m**, 84% *ee*). We also attempted to modify the R_2 group and used ethyl instead of methyl (Scheme 2, **2o**). The desired product was obtained, and the yield was still high, but an obvious drop to 78% *ee* was found. Larger groups at R_2 had adverse effects on the enantiocontrol.

Various R_3 groups were subsequently explored, and this included phenyl derivatives with EWGs and EDGs. These substrates were excellent, with high yields and good enantioselectivities found for the reduction (Scheme 3, **3a**−**g**). The use of a 4-*t*Bu phenyl group resulted in a corresponding product with a moderate decline in *ee* probably

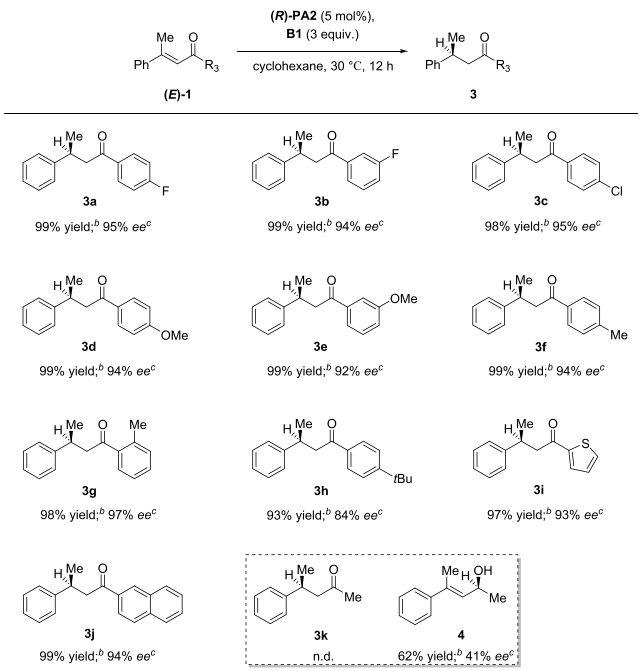
https://dx.doi.org/10.1021/acs.orglett.0c02042
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 2. Scope of Three-Substitutents[a]



[a]Reaction conditions: (*E*)-**1a** (1.0 equiv), **B1** (3.0 equiv), 5 mol % (*R*)-**PA2** with solvent indicated 0.10 M at 30 °C. [b]Isolated yield. [c]*ee* was determined by HPLC analysis.

Scheme 3. Scope of 1-Substitutents[a]

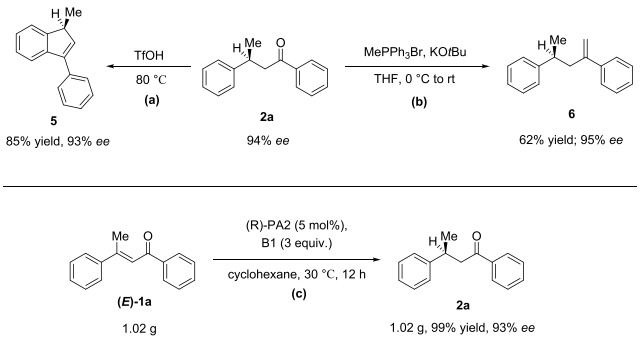


[a]Reaction conditions: (*E*)-**1a** (1.0 equiv), **B1** (3.0 equiv), 5 mol % (*R*)-**PA2** with solvent indicated 0.10 M at 30 °C. [b]Isolated yield. [c]*ee* was determined by HPLC analysis.

due to the steric hindrance of the *tert*-butyl group (Scheme 3, **3h**, 84% *ee*). Both 2-thienyl and 2-naphthyl group substitutions led to excellent yields and *ee* values for the reaction (Scheme 3, **3i,j**). However, in the case of an alkyl substitution at the one-position of the ketone, the desired reduction was not found (Scheme 3, **3k**), but rather the carbonyl was reduced to give chiral alcohol **4**. This example illustrated the significance of aromatic groups in the one-position for the chemoselective hydrogenation of the C=C moiety. The absolute configurations of **2**−**4** were confirmed by the comparison of the optical rotations of known compounds in the reported literature.[13,15,16]

After successfully expanding the scope of the substrates for the methodology, we sought to explore the subsequent transformation of interest utilizing the chiral products. A Friedel−Crafts-type reaction (Scheme 4a) and a Wittig

Scheme 4. Derivative Formation and Gram-Scale Reactions



reaction (Scheme 4b) were attempted with **2a** as a substrate under typical conditions, and the products **5** and **6** were obtained in good yields and high *ee* values were retained. We were satisfied that the yield and *ee* value of the model reaction were also maintained at a high level of efficiency operating on a 1 g scale (Scheme 4c).

On the basis of our previous published work with this catalytic system, we hypothesized a plausible mechanism for this transformation (Figure 2). Previous ^{11}B NMR studies already indicated the formation of a boro-phosphate from the reaction of CPA and borane.[8a] We assumed a similar catalyst for this methodology. For the reaction, the boron Lewis acid could be envisioned to activate the carbonyl oxygen of **1a** via

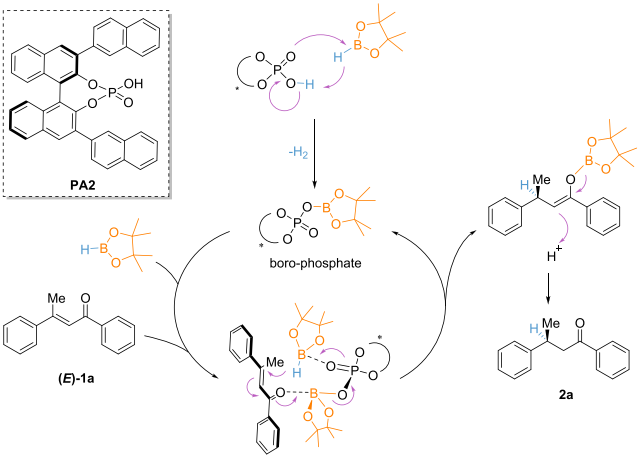


Figure 2. Proposed mechanism.

https://dx.doi.org/10.1021/acs.orglett.0c02042
Org. Lett. XXXX, XXX, XXX−XXX

an Lewis acid/Lewis base (LA/LB) interaction. Simultaneously, the oxygen of the phosphoryl group acts as a Lewis base to coordinate with another molecule of pinacolborane, and this activated borane provides a hydride to attack the β-position of unsaturated ketone **1a**. The resulting boron enolate would then pick up a proton, providing the chiral ketone **2a**.

In conclusion, we have described the ATH of *trans*-chalcone derivatives with unique BINOL-derived boro-phosphate catalysts. We realized this reaction using relatively mild conditions and readily accessible or commercially available materials, hydrides, and catalysts. Meanwhile, excellent yields, high enantioselectivities, and also an extensive substrate scope were exhibited.[17] According to our previous efforts, we speculate on the mechanism of this reaction. Other meaningful reactions with boro-phosphates are currently in progress in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c02042.

General procedure and ^{1}H and ^{13}C NMR and HPLC spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Jon C. Antilla − *Institute for Molecular Design and Synthesis, School of Pharmaceutical Science and Technology, Tianjin University, Tianjin 300072, China;* orcid.org/0000-0002-8471-3387; Email: jantilla@tju.edu.cn

Authors

Fei Na − *Institute for Molecular Design and Synthesis, School of Pharmaceutical Science and Technology, Tianjin University, Tianjin 300072, China*

Susana S. Lopez − *Department of Chemistry, University of South Florida, Tampa, Florida 33620, United States*

Alice Beauseigneur − *Department of Chemistry, University of South Florida, Tampa, Florida 33620, United States*

Lucas W. Hernandez − *Department of Chemistry, University of South Florida, Tampa, Florida 33620, United States;* orcid.org/0000-0001-9530-0927

Zhuoxin Sun − *Institute for Molecular Design and Synthesis, School of Pharmaceutical Science and Technology, Tianjin University, Tianjin 300072, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c02042

Author Contributions

[§]F.N. and S.S.L. contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support was provided by the National 1000 Talent Plan of China. We thank Tianjin University for start-up funds. We are also grateful to all members of the Instrumental Analysis Center of the School of Pharmaceutical Science and Technology.

■ REFERENCES

(1) For main reviews, see: (a) Gladiali, S.; Alberico, E. Asymmetric Transfer Hydrogenation: Chiral Ligands and Applications. *Chem. Soc. Rev.* **2006**, *35*, 226. (b) Ikariya, T.; Blacker, A. J. Asymmetric Transfer Hydrogenation of Ketones with Bifunctional Transition Metal-Based Molecular Catalysts. *Acc. Chem. Res.* **2007**, *40*, 1300. (c) Wang, D.; Astruc, D. The Golden Age of Transfer Hydrogenation. *Chem. Rev.* **2015**, *115*, 6621.

(2) For selected examples of Ir, see: (a) Saidi, O.; Williams, J. M. J. Iridium Catalysis. *Top. Organomet. Chem.* **2011**, *34*, 77. (b) Soltani, O.; Ariger, M. A.; Carreira, E. M. Transfer Hydrogenation in Water: Enantioselective, Catalytic Reduction of (*E*)-β,β-Disubstituted Nitroalkenes. *Org. Lett.* **2009**, *11*, 4196.

(3) For selected examples of Ru, see: (a) Touge, T.; Hakamata, T.; Nara, H.; Kobayashi, T.; Sayo, N.; Saito, T.; Kayaki, Y.; Ikariya, T. Oxo-Tethered Ruthenium(II) Complex as a Bifunctional Catalyst for Asymmetric Transfer Hydrogenation and H_2 Hydrogenation. *J. Am. Chem. Soc.* **2011**, *133*, 14960. (b) Touge, T.; Sakaguchi, K.; Tamaki, N.; Nara, H.; Yokozawa, T.; Matsumura, K.; Kayaki, Y. Multiple Absolute Stereocontrol in Cascade Lactone Formation via Dynamic Kinetic Resolution Driven by the Asymmetric Transfer Hydrogenation of Keto Acids with Oxo-Tethered Ruthenium Catalysts. *J. Am. Chem. Soc.* **2019**, *141*, 16354. (c) Zhao, Z.; Bagdi, P. R.; Yang, S.; Liu, J.; Xu, W.; Fang, X. Stereodivergent Access to Enantioenriched Epoxy Alcohols with Three Stereogenic Centers via Ruthenium-Catalyzed Transfer Hydrogenation. *Org. Lett.* **2019**, *21*, 5491.

(4) For selected examples of Rh, see: (a) Albrecht, M.; Crabtree, R. H.; Mata, J.; Peris, E. Chelating Bis-Carbene Rhodium(III) Complexes in Transfer Hydrogenation of Ketones and Imines. *Chem. Commun.* **2002**, 32. (b) McSkimming, A.; Bhadbhade, M. M.; Colbran, S. B. Bio-Inspired Catalytic Imine Reduction by Rhodium Complexes with Tethered Hantzsch Pyridinium Groups: Evidence for Direct Hydride Transfer from Dihydropyridine to Metal-Activated Substrate. *Angew. Chem., Int. Ed.* **2013**, *52*, 3411. (c) Kang, S.; Han, J.; Lee, E. S.; Choi, E. B.; Lee, H.-K. Enantioselective Synthesis of Cyclic Sulfamidates by Using Chiral Rhodium-Catalyzed Asymmetric Transfer Hydrogenation. *Org. Lett.* **2010**, *12*, 4184.

(5) For selected examples of Fe, see: (a) Morris, R. H. Asymmetric Hydrogenation, Transfer Hydrogenation and Hydrosilylation of Ketones Catalyzed by Iron Complexes. *Chem. Soc. Rev.* **2009**, *38*, 2282. (b) Wei, D.; Darcel, C. Iron Catalysis in Reduction and Hydrometalation Reactions. *Chem. Rev.* **2019**, *119*, 2550. (c) Li, Y.; Yu, S.; Shen, W.; Gao, J. Iron-, Cobalt-, and Nickel-Catalyzed Asymmetric Transfer Hydrogenation and Asymmetric Hydrogenation of Ketones. *Acc. Chem. Res.* **2015**, *48*, 2587.

(6) For related reviews, see: (a) Rossi, S.; Benaglia, M.; Massolo, E.; Raimondi, L. Organocatalytic Strategies for Enantioselective Metal-Free Reductions. *Catal. Sci. Technol.* **2014**, *4*, 2708. (b) Faísca Phillips, A. M.; Pombeiro, A. J. L. Recent Advances in Organocatalytic Enantioselective Transfer Hydrogenation. *Org. Biomol. Chem.* **2017**, *15*, 2307. (c) You, S.-L. Recent Developments in Asymmetric Transfer Hydrogenation with Hantzsch Esters: A Biomimetic Approach. *Chem. - Asian J.* **2007**, *2*, 820. (d) Zheng, C.; You, S.-L. Transfer Hydrogenation with Hantzsch Esters and Related Organic Hydride Donors. *Chem. Soc. Rev.* **2012**, *41*, 2498.

(7) For reviews and selected recent examples of CPA, see: (a) Parmar, D.; Sugiono, E.; Raja, S.; Rueping, M. Complete Field Guide to Asymmetric BINOL-Phosphate Derived Brønsted Acid and Metal Catalysis: History and Classification by Mode of Activation; Brønsted Acidity, Hydrogen Bonding, Ion Pairing, and Metal Phosphates. *Chem. Rev.* **2014**, *114*, 9047. (b) Rueping, M.; Sugiono, E.; Schoepke, F. R. Thieme Chemistry Journal Awardees - Where Are They Now? Asymmetric Brønsted Acid Catalyzed Transfer Hydrogenations. *Synlett* **2010**, *6*, 852. (c) Akiyama, T. Stronger Brønsted Acids. *Chem. Rev.* **2007**, *107*, 5744. (d) Terada, M. Chiral Phosphoric Acids as Versatile Catalysts for Enantioselective Transformations. *Synthesis* **2010**, *12*, 1929. (e) Yue, C.; Na, F.; Fang, X.; Cao, Y.; Antilla, J. C. Chiral Phosphoric Acid Catalyzed Asymmetric Synthesis of Heterotriarylmethanes from Racemic Indolyl Alcohols. *Angew.*

Chem., Int. Ed. **2018**, *57*, 11004. (f) Bai, Y.; Yuan, J.; Hu, X.; Antilla, J. C. Catalytic Enantioselective Diels−Alder Reactions of Benzoquinones and Vinylindoles with Chiral Magnesium Phosphate Complexes. *Org. Lett.* **2019**, *21*, 4549. (g) Fang, X.; Deng, Z.; Zheng, W.; Antilla, J. C. Catalytic One-Pot Double Asymmetric Cascade Reaction: Synthesis of Chlorinated Oxindoles and Geminal Diamines. *ACS Catal.* **2019**, *9*, 1748. (h) Mori, K.; Isogai, R.; Kamei, Y.; Yamanaka, M.; Akiyama, T. Chiral Magnesium Bisphosphate-Catalyzed Asymmetric Double C(sp^3)-H Bond Functionalization Based on Sequential Hydride Shift/ Cyclization Process. *J. Am. Chem. Soc.* **2018**, *140*, 6203. (i) Jiang, F.; Chen, K.-W.; Wu, P.; Zhang, Y.-C.; Jiao, Y.; Shi, F. A Strategy for Synthesizing Axially Chiral Naphthyl-Indoles: Catalytic Asymmetric Addition Reactions of Racemic Substrates. *Angew. Chem., Int. Ed.* **2019**, *58*, 15104. (j) Ouyang, J.; Kennemur, J. L.; De, C. K.; Farès, C.; List, B. Strong and Confined Acids Enable a Catalytic Asymmetric Nazarov Cyclization of Simple Divinyl Ketones. *J. Am. Chem. Soc.* **2019**, *141*, 3414. (k) Tsuji, N.; Kennemur, J. L.; Buyck, T.; Lee, S.; Prévost, S.; Kaib, P. S. J.; Bykov, D.; Farès, C.; List, B. Activation of Olefins via Asymmetric Brønsted Acid Catalysis. *Science* **2018**, *359*, 1501. (l) Zhang, J.; Yu, P.; Li, S.-Y.; Sun, H.; Xiang, S.-H.; Wang, J.; Houk, K. N.; Tan, B. Asymmetric Phosphoric Acid-Catalyzed Four-Component Ugi Reaction. *Science* **2018**, *361*, eaas8707. (m) Ma, D.; Miao, C.-B.; Sun, J. Catalytic Enantioselective House-Meinwald Rearrangement: Efficient Construction of All-Carbon Quaternary Stereocenters. *J. Am. Chem. Soc.* **2019**, *141*, 13783.

(8) For selected ATH of C═O, see: (a) Zhang, Z.; Jain, P.; Antilla, J. C. Asymmetric Reduction of Ketones by Phosphoric Acid Derived Catalysts. *Angew. Chem., Int. Ed.* **2011**, *50*, 10961. (b) Enders, D.; Stöckel, B. A.; Rembiak, A. Enantio- and chemoselective Brønsted-acid/Mg(^{n}Bu)$_2$ catalysed reduction of α-keto esters with catecholborane. *Chem. Commun.* **2014**, *50*, 4489.

(9) For selected ATH of C═N, see: (a) Li, G.; Liang, Y.; Antilla, J. C. A Vaulted Biaryl Phosphoric Acid-Catalyzed Reduction of α-Imino Esters:The Highly Enantioselective Preparation of α-Amino Esters. *J. Am. Chem. Soc.* **2007**, *129*, 5830. (b) Li, G.; Antilla, J. C. Highly Enantioselective Hydrogenation of Enamides Catalyzed by Chiral Phosphoric Acids. *Org. Lett.* **2009**, *11*, 1075. (c) Rueping, M.; Sugiono, E.; Azap, C.; Theissmann, T.; Bolte, M. Enantioselective Brønsted Acid Catalyzed Transfer Hydrogenation: Organocatalytic Reduction of Imines. *Org. Lett.* **2005**, *7*, 3781. (d) Henseler, A.; Kato, M.; Mori, K.; Akiyama, T. Chiral Phosphoric Acid Catalyzed Transfer Hydrogenation: Facile Synthetic Access to Highly Optically Active Trifluoromethylated Amines. *Angew. Chem., Int. Ed.* **2011**, *50*, 8180. (e) Sakamoto, T.; Mori, K.; Akiyama, T. Chiral Phosphoric Acid Catalyzed Enantioselective Transfer Deuteration of Ketimines by Use of Benzothiazoline As a Deuterium Donor: Synthesis of Optically Active Deuterated Amines. *Org. Lett.* **2012**, *14*, 3312. (f) Rueping, M.; Antonchick, A. P.; Theissmann, T. A Highly Enantioselective Brønsted Acid Catalyzed Cascade Reaction: Organocatalytic Transfer Hydrogenation of Quinolines and their Application in the Synthesis of Alkaloids. *Angew. Chem., Int. Ed.* **2006**, *45*, 3683. (g) Rueping, M.; Antonchick, A. P. Organocatalytic Enantioselective Reduction of Pyridines. *Angew. Chem., Int. Ed.* **2007**, *46*, 4562.

(10) For selected ATH of C═C, see: (a) Wang, Z.; Ai, F.; Wang, Z.; Zhao, W.; Zhu, G.; Lin, Z.; Sun, J. Organocatalytic Asymmetric Synthesis of 1,1-Diarylethanes by Transfer Hydrogenation. *J. Am. Chem. Soc.* **2015**, *137*, 383. (b) Mayer, S.; List, B. Asymmetric Counteranion-Directed Catalysis. *Angew. Chem., Int. Ed.* **2006**, *45*, 4193.

(11) (a) Martin, N. J. A.; List, B. Highly Enantioselective Transfer Hydrogenation of α,β-Unsaturated Ketones. *J. Am. Chem. Soc.* **2006**, *128*, 13368. (b) Tuttle, J. B.; Ouellet, S. G.; MacMillan, D. W. C. Organocatalytic Transfer Hydrogenation of Cyclic Enones. *J. Am. Chem. Soc.* **2006**, *128*, 12662. (c) Gutierrez, O.; Iafe, R. G.; Houk, K. N. Origin of Stereoselectivity in the Imidazolidinone-Catalyzed Reductions of Cyclic α,β-Unsaturated Ketones. *Org. Lett.* **2009**, *11*, 4298.

(12) Miaskiewicz, S.; Reed, J. H.; Donets, P. A.; Oliveira, C. C.; Cramer, N. Chiral 1,3,2-Diazaphospholenes as Catalytic Molecular Hydrides for Enantioselective Conjugate Reductions. *Angew. Chem., Int. Ed.* **2018**, *57*, 4039.

(13) Sugiura, M.; Ashikari, Y.; Takahashi, Y.; Yamaguchi, K.; Kotani, S.; Nakajima, M. Lewis Base-Catalyzed Enantioselective Conjugate Reduction of β,β-Disubstituted α,β-unsaturated ketones with Trichlorosilane: *E*/*Z*-Isomerization, Regioselectivity, and Synthetic Applications. *J. Org. Chem.* **2019**, *84*, 11458.

(14) (a) Enders, D.; Rembiak, A.; Seppelt, M. Asymmetric Organocatalytic Reduction of Ketimines with Catecholborane Employing a N-Triflyl Phosphoramide Brønsted Acid as Catalyst. *Tetrahedron Lett.* **2013**, *54*, 470. (b) Enders, D.; Rembiak, A.; Stoeckel, B. A. Chemo- and Enantioselective Brønsted Acid-Catalyzed Reduction of α-Imino Esters with Catecholborane. *Adv. Synth. Catal.* **2013**, *355*, 1937. (c) Zhou, Q.; Meng, W.; Yang, J.; Du, H. A Continuously Regenerable Chiral Ammonia Borane for Asymmetric Transfer Hydrogenations. *Angew. Chem., Int. Ed.* **2018**, *57*, 12111. (d) Yang, K.; Lou, Y.; Wang, C.; Qi, L.-W.; Fang, T.; Zhang, F.; Xu, H.; Zhou, L.; Li, W.; Zhang, G.; Yu, P.; Song, Q. Chiral Brønsted Acid from Chiral Phosphoric Acid Boron Complex and Water: Asymmetric Reduction of Indole. *Angew. Chem., Int. Ed.* **2020**, *59*, 3294.

(15) (a) Lu, S.-M.; Bolm, C. Highly Chemo- and Enantioselective Hydrogenation of Linear α,β-Unsaturated Ketones. *Chem. - Eur. J.* **2008**, *14*, 7513. (b) Chen, X.; Zhou, H.; Zhang, K.; Li, J.; Huang, H. Highly Enantioselective Hydrogenation of Steric Hindrance Enones Catalyzed by Ru Complexes with Chiral Diamine and Achiral Phosphane. *Org. Lett.* **2014**, *16*, 3912.

(16) On the basis of reported literature, the absolute configuration of **2a** was assigned as (S) by a comparison of the optical rotation value with that of known absolute stereochemistry. (See the Supporting Information.)

(17) The ortho-substituted phenyl substrates of R_1 (2-Me and 2-F) were also explored. Unfortunately, low conversions (<10%) were observed under the optimal conditions.

https://dx.doi.org/10.1021/acs.orglett.0c02042
Org. Lett. XXXX, XXX, XXX−XXX