OL | Organic Letters

pubs.acs.org/OrgLett Letter

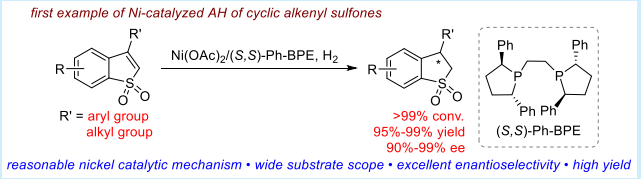
Nickel-Catalyzed Asymmetric Hydrogenation of Cyclic Alkenyl Sulfones, Benzo[*b*]thiophene 1,1-Dioxides, with Mechanistic Studies

Gongyi Liu, Kui Tian, Chenzong Li, Cai You, Xuefeng Tan, Heng Zhang,* Xumu Zhang,* and Xiu-Qin Dong*

Cite This: *Org. Lett.* 2021, 23, 668–675 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: A highly efficient catalytic system based on the cheap transition metal nickel for the asymmetric hydrogenation of challenging cyclic alkenyl sulfones, 3-substituted benzo[*b*]-thiophene 1,1-dioxides, was first successfully developed. A series of hydrogenation products, chiral 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxides, were obtained in high yields (95−99%) with excellent enantioselectivities (90−99% ee). According to the results of nonlinear effect studies, deuterium-labeling experiments, and DFT calculation investigations, a reasonable catalytic mechanism for this nickel-catalyzed asymmetric hydrogenation was provided, which displayed that the two added hydrogen atoms of the hydrogenation products could be from H_2 through the insertion of Ni−H and subsequent hydrogenolysis.



Asymmetric hydrogenation of prochiral unsaturated compounds has been regarded as a powerful and straightforward synthetic method to access chiral compounds that has been widely applied in the fields of agrochemicals and pharmaceuticals.[1] Most well-established asymmetric hydrogenation methods are based on heavy noble transition metal catalytic systems, mainly focused on ruthenium,[2] iridium,[3] rhodium,[4] and palladium.[5] However, these precious metal catalysts could suffer from the difficulties of high costs, limited resources, strong toxicity, and negative environmental impact. Therefore, great attention has been devoted to the development of cheap, sustainable, earth-abundant transition metal catalytic systems for asymmetric hydrogenation.[6] In recent years, some iron-, cobalt-, and nickel-catalyzed asymmetric (transfer) hydrogenation reactions of prochiral unsaturated compounds with C=C, C=O, or C=N bonds were reported[7−9] that demonstrated the great potential advantages of the cheap first-row transition metals in asymmetric hydrogenation. Among these asymmetric catalytic systems, Ni-catalyzed asymmetric hydrogenation was relatively less investigated. Some pioneering and important research works on Ni-catalyzed asymmetric (transfer) hydrogenation of prochiral ketones, alkenes, ketimines, and enamides were developed by Hamada,[9a,b] Chirik,[9c] Zhou,[9d−i] Zhang,[9j] and our group.[9k−p] In 2016, Chirik and co-workers developed the Ni-catalyzed asymmetric hydrogenation of *α*,*β*-unsaturated esters and performed deep research on the catalytic mechanism, proposing conjugate addition of the Ni−H species and nonselective protonation to release the product.[9c] In 2017, our group realized Ni-catalyzed asymmetric hydrogenation of *β*-acylamino nitroolefins, and experimental and DFT computational investigations revealed that it also involved 1,4-hydride addition of Ni−H and subsequent protonation to generate the desired product.[9k] In addition, these Ni-catalyzed asymmetric hydrogenation reactions were mainly focused on acyclic functionalized olefins and imines as substrates, which were always in accordance with this catalytic mechanism. In contrast, cyclic functionalized olefin substrates have rarely been investigated.

Chiral cyclic sulfone scaffolds are widely distributed in many biologically active compounds and natural products with important applications.[10] Because of the rigidity of cyclic functionalized olefins, the asymmetric hydrogenation of unsaturated cyclic sulfones to access these motifs is still in an early stage, and just a few examples involving unsaturated cyclic sulfones have been developed.[2l,3o,p,4k] In 2012, Andersson and co-workers described Ir-catalyzed enantioselective hydrogenation of prochiral cyclic and acyclic unsaturated sulfones with excellent results.[3o] In 2017, Pfaltz and co-workers successfully developed Ir-catalyzed asymmetric hydrogenation of cyclic alkenyl sulfones, benzo[*b*]thiophene 1,1-dioxides.[3p] Recently, our group realized Rh/*N*-methylated bisphosphine−thiourea ZhaoPhos-catalyzed asymmetric hydrogenation of these cyclic alkenyl sulfones with excellent results by the assistance of the possible hydrogen-bonding interaction between the substrate and the ligand.[4k] However, cheap transition metals have never been applied to catalyze the asymmetric hydrogenation of cyclic alkenyl sulfones. On the

Received: November 8, 2020
Published: January 20, 2021

https://dx.doi.org/10.1021/acs.orglett.0c03723
Org. Lett. 2021, 23, 668–675

basis of our long-standing efforts in asymmetric hydrogenation, we are interested in the development of cheap transition metal catalytic systems for the asymmetric hydrogenation of cyclic alkenyl sulfones. As a continuation of our investigations, in this work we successfully developed the first asymmetric hydrogenation of 3-substituted benzo[*b*]thiophene 1,1-dioxides catalyzed by the cheap transition metal Ni, affording a series of enantioenriched hydrogenation products with >99% conversion, 95−99% yield, and 90−99% ee (Scheme 1). Importantly, a reasonable catalytic mechanism was proposed for this hydrogenation on the basis of deuterium-labeling experiments and DFT calculations.

Scheme 1. First Asymmetric Hydrogenation of Cyclic Alkenyl Sulfones Catalyzed by the Cheap Transition Metal Ni

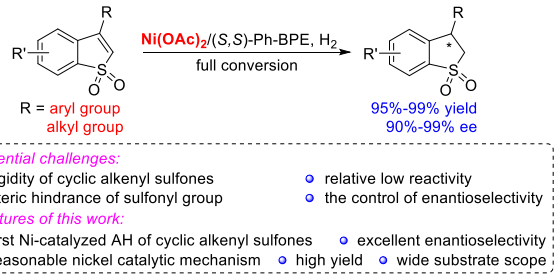
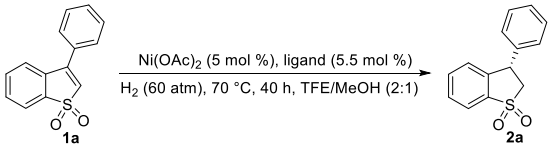


Table 1. Ligand Screening for Ni-Catalyzed Asymmetric Hydrogenation of 3-Phenylbenzo[*b*]thiophene 1,1-Dioxide (1a)[a]



entry	ligand	conv. (%)[b]	ee (%)[c]
1	(*S*,*S*)-Me-DuPhos	8	30
2	(*S*,*S*)-Ph-BPE	25	95
3	JosiPhos	50	59
4	(*S*)-SegPhos	NR	NA
5	(*Rc*,*Sp*)-DuanPhos	NR	NA
6	(*S*)-BINAP	NR	NA
7	WalPhos	83	56
8	ZhaoPhos	NR	NA

[a]Conditions: 0.1 mmol of **1a**, **1a**:Ni(OAc)$_2$:ligand = 1:0.05:0.055 in 1.0 mL of CF_3CH_2OH (TFE) under 60 atm H_2 for 40 h. The catalyst was precomplexed in MeOH (0.5 mL for each reaction vial). [b]Determined by ^{1}H NMR analysis. NR = no reaction. [c]The ee values were determined by HPLC on a chiral phase. NA = not available.

Initially, a variety of readily available chiral diphosphine ligands (Figure 1) were applied for the Ni(OAc)$_2$-catalyzed asymmetric hydrogenation of the model substrate 3-phenylbenzo[*b*]thiophene 1,1-dioxide (**1a**) under 60 atm H_2 at 70 °C for 40 h. The Ni(OAc)$_2$/chiral diphosphine ligand catalyst was generated in situ in MeOH to achieve good solubility. (*S*,*S*)-Me-DuPhos and JosiPhos displayed poor reactivitites and enantioselectivities (8−50% conversion and 30−59% ee; Table 1, entries 1 and 3). Although 25% conversion was realized in the presence of (*S*,*S*)-Ph-BPE, excellent enantioselectivity of 95% ee was obtained (Table 1, entry 2). In addition, some other important chiral diphosphine ligands, such as (*S*)-SegPhos, (*Rc*,*Sp*)-DuanPhos, (*S*)-BINAP, and ZhaoPhos could not promote this Ni-catalyzed asymmetric hydrogenation, and no desired hydrogenation product **2a** was detected (Table 1, entries 4−6 and 8). WalPhos provided good conversion (83%) with moderate enantioselectivity (56% ee) (Table 1, entry 7).

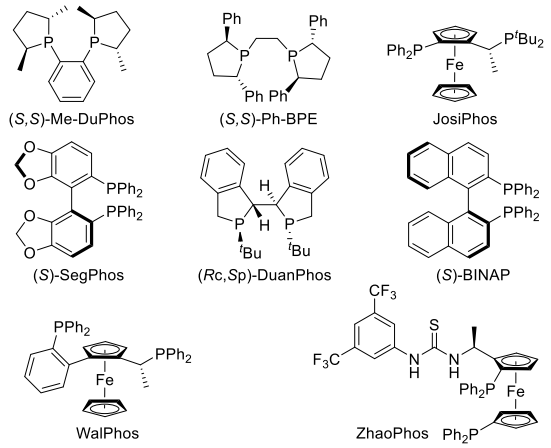
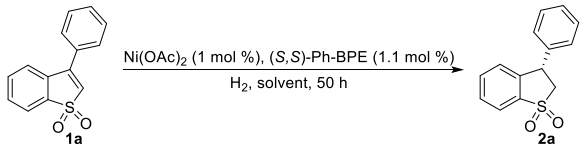


Figure 1. Structures of chiral diphosphine ligands.

Table 2. Optimization of the Reaction Conditions for Ni-Catalyzed Asymmetric Hydrogenation of 3-Phenylbenzo[*b*]thiophene 1,1-Dioxide (1a)[a]



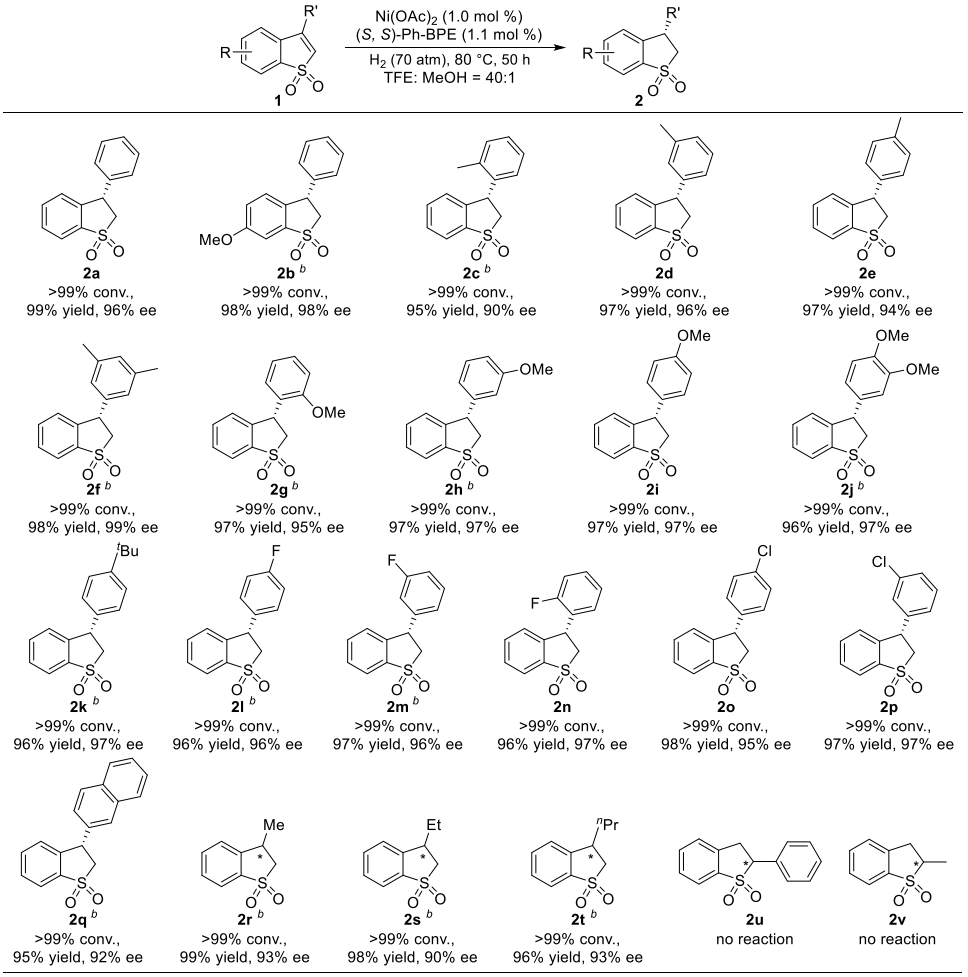
entry	solvent	P_{H_2} (atm)	T (°C)	conv. (%)[b]	ee (%)[c]
1[d]	MeOH	60	70	NR	NA
2	TFE:MeOH = 10:1	60	70	58	94
3	EtOH:MeOH = 10:1	60	70	NR	NA
4	CH_2Cl_2:MeOH = 10:1	60	70	NR	NA
5	THF:MeOH = 10:1	60	70	NR	NA
6	toluene:MeOH = 10:1	60	70	NR	NA
7	TFE:MeOH = 40:1	60	70	72	95
8[e]	TFE:MeOH = 40:1	60	80	82	96
9[e]	TFE:MeOH = 40:1	70	80	>99	96

[a]Conditions: 0.1 mmol of **1a**, **1a**:Ni(OAc)$_2$:(*S*,*S*)-Ph-BPE = 1:0.01:0.011 in 1.0 mL of TFE for 50 h. The catalyst was precomplexed in MeOH (0.1 mL for each reaction vial). THF is tetrahydrofuran. Solvent:MeOH ratios are v/v. [b]Determined by ^{1}H NMR analysis. [c]The ee values were determined by HPLC on a chiral phase. [d]0.1 mmol of **1a**, **1a**:Ni(OAc)$_2$:(*S*,*S*)-Ph-BPE = 1:0.05:0.055 in 1.0 mL of MeOH for 50 h. [e]0.1 mmol of **1a**, **1a**:Ni(OAc)$_2$:(*S*,*S*)-Ph-BPE = 1:0.01:0.011 in 2.0 mL of TFE for 50 h. The catalyst was precomplexed in MeOH (50 μL for each reaction vial).

In order to improve the conversion of this Ni/(*S*,*S*)-Ph-BPE-catalyzed asymmetric hydrogenation of **1a**, the reaction conditions were further optimized in various solvents. It was found that there was no conversion in MeOH, which was an unfavorable solvent for this Ni-catalyzed asymmetric hydrogenation (Table 2, entry 1). The Ni(OAc)$_2$/(*S*,*S*)-Ph-BPE catalytic system was dissolved well in MeOH, and it was better to investigate other solvents in the presence of MeOH. Then the catalyst solution was decreased to a catalyst loading of 1.0 mol % to reduce the negative effect of MeOH, and the

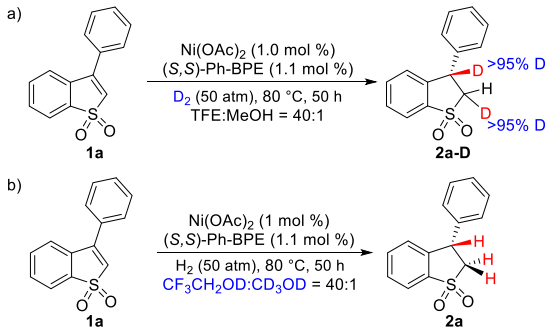
https://dx.doi.org/10.1021/acs.orglett.0c03723
Org. Lett. 2021, 23, 668−675

Scheme 2. Scope Study for the Ni-Catalyzed Asymmetric Hydrogenation of 3-Substituted Benzo[*b*]thiophene 1,1-Dioxides[a]



[a]Conditions: 0.1 mmol of substrate, substrate **1**:Ni(OAc)$_2$:(*S*,*S*)-Ph-BPE = 1:0.01:0.011 in 2.0 mL of CF_3CH_2OH for 50 h. The catalyst was precomplexed in MeOH (50 μL for each reaction vial). Isolated yields are shown. The ee values were determined by HPLC on a chiral phase. [b]S:C = 50, 60 h.

Scheme 3. Deuterium-Labeling Experiments



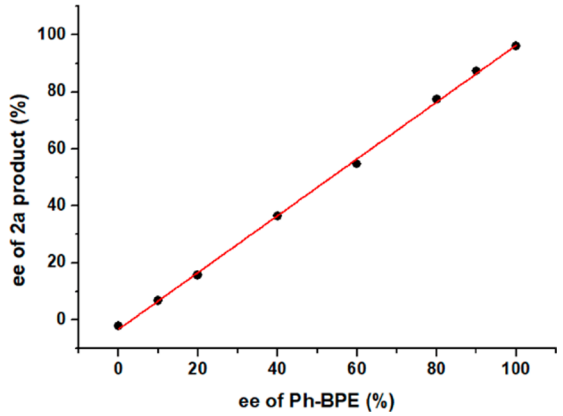


Figure 2. Linear effect study of the hydrogenation of model substrate **1a** using (*S*,*S*)-Ph-BPE with different ee values.

conversion was greatly increased to 58% (Table 2, entry 2). Some other solvents were then examined, but no hydrogenation product was detected in EtOH, CH_2Cl_2, THF, or toluene (Table 2, entries 3−6). The conversion was increased to 72% with 95% ee when the ratio of TFE was increased to TFE:MeOH = 40:1 (Table 2, entry 7). TFE may help to accelerate the addition of the Ni−H active species to the C═C bond. Good conversion (82%) and excellent enantioselectivity (96% ee) could be achieved at a higher reaction temperature of 80 °C (Table 2, entry 8). To our delight, >99% conversion with 96% ee was obtained when the pressure of H_2 was increased to 70 atm (Table 2, entry 9).

Under the optimized reaction conditions, we began to explore the substrate generality of this Ni/(*S*,*S*)-Ph-BPE-catalyzed asymmetric hydrogenation of 3-substitued benzo[*b*]-thiophene 1,1-dioxides. These results are summarized in

https://dx.doi.org/10.1021/acs.orglett.0c03723
Org. Lett. 2021, 23, 668−675

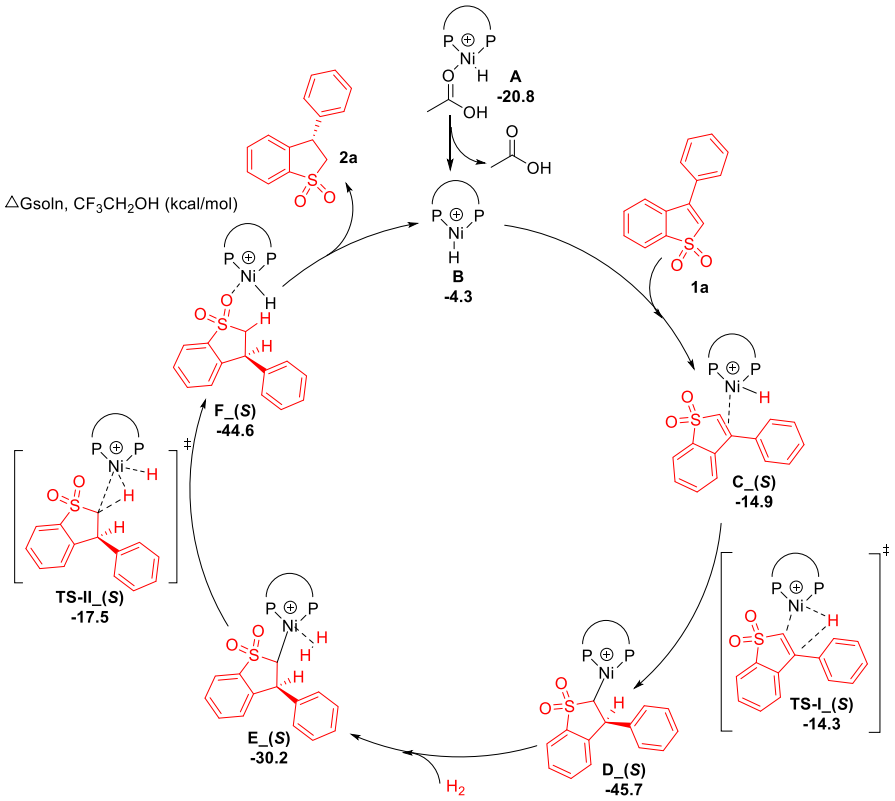
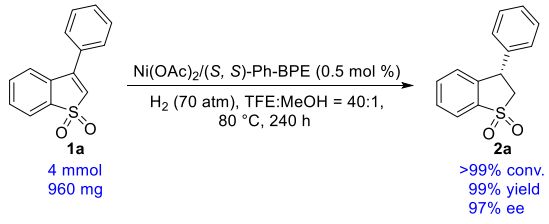


Figure 3. DFT-calculated free energy profile for the proposed catalytic cycle of the Ni-catalyzed asymmetric hydrogenation.

Scheme 4. Gram-Scale Asymmetric Hydrogenation



Scheme 2. Substrates with electron-netural groups (**1a** and **1b**), electron-donating groups (**1c**–**k**), and electron-withdrawing groups (**1l**–**p**) on the phenyl ring reacted well, affording the corresponding hydrogenation products (**2a**–**p**) with excellent results (>99% conversion, 95–99% yields, 90–99% ee). In addition, the position of substituents on the phenyl ring had little influence on the reactivity and enantioselectivity. Remarkably, the challenging substrates **1c**, **1d**, **1f**–**h**, **1j**, **1m**, **1n**, and **1p** bearing steric hindrance from the *ortho* and *meta* substituents on the phenyl ring were hydrogenated smoothly in 95–98% yield with 90–99% ee. Furthermore, the asymmetric hydrogenation of substrate **1q** with a bulky 2-naphthyl group also proceeded smoothly to afford product **2q** with full conversion in 95% yield with 92% ee. To our delight, the alkyl substrates with a 3-methyl group (**1r**), an ethyl group (**1s**), and an *n*-propyl group (**1t**) also worked well to provide the hydrogenation products **2r**–**t** with excellent results (96–99% yield with 90–93% ee). In addition, the 2-substitued benzo[*b*]thiophene 1,1-dioxide substrates containing a phenyl group (**1u**) or methyl group (**1v**) were then hydrogenated, but unfortunately, there was no reaction in this Ni-catalyzed system.

In order to explore the possible mechanism, deuterium-labeling experiments were carried out. The Ni-catalyzed asymmetric hydrogenation of model substrate **1a** was conducted under 50 atm D_2. Interestingly, we found that the deuterium atoms of the product **2a-D** were attached at both the α- and β-positions (Scheme 3a). In addition, this hydrogenation was conducted in the presence of H_2 with CF_3CH_2OD and CD_3OD as the reaction solvents, and no deuterium atoms were found in the hydrogenation product (Scheme 3b). These observations are quite different from the previous research work,[9c,k] indicating that this Ni-catalyzed asymmetric hydrogenation may go through a different catalytic pathway.

In addition, a nonlinear effect study of this Ni-catalyzed asymmetric hydrogenation was performed. A series of hydrogenations of model substrate **1a** were carried out with ligand (*S*,*S*)-Ph-BPE with different ee values. As shown in Figure 2, a linear effect could be observed in this asymmetric transformation, and it is possible that there is no catalyst self-aggregation or ligand–substrate agglomeration in this catalytic system.[11]

According to these above reaction results, DFT calculations were performed to further reveal the possible catalytic mechanism of this hydrogenation. Our favored computed catalytic cycle (Figure 3) starts with the formation of Ni–H complex **B** through hydrogenolysis of the coordinated Ni(II) complex, which can be deemed as the active catalyst. Subsequent coordination of **B** with substrate **1a** and then insertion of Ni–H into the double bond gives Ni–C complex **D**_(*S*). The second hydrogenolysis delivers the desired *S*-configured hydrogenated product **2a** and regenerates the active catalyst **B**. This catalytic process is quite different from the previously reported 1,4-hydride addition and subsequent

https://dx.doi.org/10.1021/acs.orglett.0c03723
Org. Lett. 2021, 23, 668–675

protonation to give the desired product.[9c,k] In addition, the computational details of other catalytic pathways are provided in the Supporting Information.

To demonstrate the potential synthetic application of this Ni-catalyzed transformation, the gram-scale asymmetric hydrogenation on 4 mmol of model substrate **1a** was conducted in the presence of just 0.5 mol % catalyst. The desired product **2a** was obtained in full conversion and 99% yield with 97% ee, showing the potential synthetic importance of our catalytic system (Scheme 4).

In summary, we successfully developed the first asymmetric hydrogenation of challenging cyclic alkenyl sulfones, 3-substituted benzo[*b*]thiophene 1,1-dioxides, catalyzed by the cheap transition metal Ni. A series of hydrogenation products, chiral 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxides, were obtained in 95−99% yield with 90−99% ee. A reasonable catalytic cycle was proposed for this Ni-catalyzed hydrogenation on the basis of combined deuterium-labeling experiments and DFT calculations. Also, we found that the two added hydrogen atoms in the hydrogenation product could be from H_2 through insertion of Ni−H and subsequent hydrogenolysis, which is different from the previously reported 1,4-hydride addition and subsequent protonation.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c03723.

Experimental procedures and compound characterization (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

Xiu-Qin Dong − *Engineering Research Center of Organosilicon Compounds & Materials, Ministry of Education, College of Chemistry and Molecular Sciences, Wuhan University, Wuhan, Hubei 430072, China; Suzhou Institute of Wuhan University, Suzhou, Jiangsu 215123, China;* orcid.org/0000-0002-5045-1198; Email: xiuqindong@whu.edu.cn

Xumu Zhang − *Engineering Research Center of Organosilicon Compounds & Materials, Ministry of Education, College of Chemistry and Molecular Sciences, Wuhan University, Wuhan, Hubei 430072, China; Shenzhen Grubbs Institute, Southern University of Science and Technology, Shenzhen, Guangdong 518055, China;* orcid.org/0000-0001-5700-0608; Email: zhangxm@sustech.edu.cn

Heng Zhang − *Engineering Research Center of Organosilicon Compounds & Materials, Ministry of Education, College of Chemistry and Molecular Sciences, Wuhan University, Wuhan, Hubei 430072, China;* orcid.org/0000-0003-4823-4167; Email: hengzhang@whu.edu.cn

Authors

Gongyi Liu − *Engineering Research Center of Organosilicon Compounds & Materials, Ministry of Education, College of Chemistry and Molecular Sciences, Wuhan University, Wuhan, Hubei 430072, China; Pharmaceutical Research Institute, Wuhan Institute of Technology, Wuhan, Hubei 430205, China*

Kui Tian − *Engineering Research Center of Organosilicon Compounds & Materials, Ministry of Education, College of Chemistry and Molecular Sciences, Wuhan University, Wuhan, Hubei 430072, China*

Chenzong Li − *Engineering Research Center of Organosilicon Compounds & Materials, Ministry of Education, College of Chemistry and Molecular Sciences, Wuhan University, Wuhan, Hubei 430072, China; Pharmaceutical Research Institute, Wuhan Institute of Technology, Wuhan, Hubei 430205, China*

Cai You − *Shenzhen Grubbs Institute, Southern University of Science and Technology, Shenzhen, Guangdong 518055, China*

Xuefeng Tan − *Shenzhen Grubbs Institute, Southern University of Science and Technology, Shenzhen, Guangdong 518055, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c03723

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for financial support from the National Natural Science Foundation of China (Grant 22071187), the Natural Science Foundation of Jiangsu Province (Grant BK20190213), and the Shenzhen Science and Technology Innovation Committee (Grant KQTD20150717103157174). The Program of Introducing Talents of Discipline to Universities of China (111 Project) is also appreciated. The numerical calculations in this paper were done on the supercomputing system in the Supercomputing Center of Wuhan University.

■ REFERENCES

(1) (a) Knowles, W. S. Asymmetric Hydrogenations (Nobel Lecture). *Angew. Chem., Int. Ed.* **2002**, *41*, 1998−2007. (b) Noyori, R. Asymmetric Catalysis: Science and Opportunities (Nobel Lecture 2001). *Adv. Synth. Catal.* **2003**, *345*, 15−32. (c) Tang, W.; Zhang, X. New Chiral Phosphorus Ligands for Enantioselective Hydrogenation. *Chem. Rev.* **2003**, *103*, 3029−3070. (d) Gridnev, I. D.; Imamoto, T. On the Mechanism of Stereoselection in Rh-Catalyzed Asymmetric Hydrogenation: A General Approach for Predicting the Sense of Enantioselectivity. *Acc. Chem. Res.* **2004**, *37*, 633−644. (e) Cui, X.; Burgess, K. Catalytic Homogeneous Asymmetric Hydrogenations of Largely Unfunctionalized Alkenes. *Chem. Rev.* **2005**, *105*, 3272−3296. (f) Farina, V.; Reeves, J. T.; Senanayake, C. H.; Song, J. J. Asymmetric Synthesis of Active Pharmaceutical Ingredients. *Chem. Rev.* **2006**, *106*, 2734−2793. (g) Johnson, N. B.; Lennon, I. C.; Moran, P. H.; Ramsden, J. A. Industrial-Scale Synthesis and Applications of Asymmetric Hydrogenation Catalysts. *Acc. Chem. Res.* **2007**, *40*, 1291−1299. (h) Minnaard, A. J.; Feringa, B. L.; Lefort, L.; De Vries, J. G. Asymmetric Hydrogenation Using Monodentate Phosphoramidite Ligands. *Acc. Chem. Res.* **2007**, *40*, 1267−1277. (i) Roseblade, S. J.; Pfaltz, A. Iridium-Catalyzed Asymmetric Hydrogenation of Olefins. *Acc. Chem. Res.* **2007**, *40*, 1402−1411. (j) Saudan, L. A. Hydrogenation Processes in the Synthesis of Perfumery Ingredients. *Acc. Chem. Res.* **2007**, *40*, 1309−1319. (k) Shimizu, H.; Nagasaki, I.; Matsumura, K.; Sayo, N.; Saito, T. Developments in Asymmetric Hydrogenation from an Industrial Perspective. *Acc. Chem. Res.* **2007**, *40*, 1385−1393. (l) Zhang, W.; Chi, Y.; Zhang, X. Developing Chiral Ligands for Asymmetric Hydrogenation. *Acc. Chem. Res.* **2007**, *40*, 1278−1290. (m) Xie, J.-H.; Zhu, S.-F.; Zhou, Q.-L. Transition Metal-Catalyzed Enantioselective Hydrogenation of Enamines and Imines. *Chem. Rev.* **2011**, *111*, 1713−1760. (n) Ager, D. J.; de Vries, A. H. M.; de Vries, J. G. Asymmetric homogeneous hydrogenations at scale. *Chem. Soc. Rev.* **2012**, *41*, 3340−3380. (o) Blaser, H.-U.; Pugin, B.; Spindler, F. Asymmetric Hydrogenation. In *Organometallics as*

Catalysts in the Fine Chemical Industry; Beller, M., Blaser, H.-U.; Eds.; Springer: Berlin, 2012; pp 65−102. (p) Xie, J.-H.; Zhou, Q.-L. New Progress and Prospects of Transition Metal-Catalyzed Asymmetric Hydrogenation. *Huaxue Xuebao* **2012**, *70*, 1427−1438. (q) Wang, D.-S.; Chen, Q.-A.; Lu, S.-M.; Zhou, Y.-G. Asymmetric Hydrogenation of Heteroarenes and Arenes. *Chem. Rev.* **2012**, *112*, 2557−2590. (r) Chen, Q.-A.; Ye, Z.-S.; Duan, Y.; Zhou, Y.-G. Homogeneous palladium-catalyzed asymmetric hydrogenation. *Chem. Soc. Rev.* **2013**, *42*, 497−511. (s) Verendel, J. J.; Pamies, O.; Diéguez, M.; Andersson, P. G. Asymmetric Hydrogenation of Olefins Using Chiral Crabtree-type Catalysts: Scope and Limitations. *Chem. Rev.* **2014**, *114*, 2130−2169. (t) Genet, J.-P.; Ayad, T.; Ratovelomanana-Vidal, V. Electron-Deficient Diphosphines: The Impact of DIFLUORPHOS in Asymmetric Catalysis. *Chem. Rev.* **2014**, *114*, 2824−2880. (u) Zhang, Z.; Butt, N. A.; Zhang, W. Asymmetric Hydrogenation of Nonaromatic Cyclic Substrates. *Chem. Rev.* **2016**, *116*, 14769−14827. (v) Zhu, S.-F.; Zhou, Q.-L. Iridium-Catalyzed Asymmetric Hydrogenation of Unsaturated Carboxylic Acids. *Acc. Chem. Res.* **2017**, *50*, 988−1001. (w) Wang, Z.; Zhang, Z.; Liu, Y.; Zhang, W. Development of the Asymmetric Hydrogenation of Enol Esters. *Youji Huaxue* **2016**, *36*, 447−459.

(2) (a) Uematsu, N.; Fujii, A.; Hashiguchi, S.; Ikariya, T.; Noyori, R. Asymmetric Transfer Hydrogenation of Imines. *J. Am. Chem. Soc.* **1996**, *118*, 4916−4917. (b) Noyori, R.; Hashiguchi, S. Asymmetric Transfer Hydrogenation Catalyzed by Chiral Ruthenium Complexes. *Acc. Chem. Res.* **1997**, *30*, 97−102. (c) Ohta, T.; Takaya, H.; Kitamura, M.; Nagai, K.; Noyori, R. Asymmetric hydrogenation of unsaturated carboxylic acids catalyzed by BINAP-ruthenium(II) complexes. *J. Org. Chem.* **1987**, *52*, 3174−3176. (d) Uemura, T.; Zhang, X.; Matsumura, K.; Sayo, N.; Kumobayashi, H.; Ohta, T.; Nozaki, K.; Takaya, H. Highly Efficient Enantioselective Synthesis of Optically Active Carboxylic Acids by $Ru(OCOCH_3)_2[(S)\text{-}H_8\text{-}BINAP]$. *J. Org. Chem.* **1996**, *61*, 5510−5516. (e) Cheng, X.; Zhang, Q.; Xie, J.-H.; Wang, L.-X.; Zhou, Q.-L. Highly Rigid Diphosphane Ligands with a Large Dihedral Angle Based on a Chiral Spirobifluorene Backbone. *Angew. Chem., Int. Ed.* **2005**, *44*, 1118−1121. (f) Yan, Z.; Xie, H.-P.; Shen, H.-Q.; Zhou, Y.-G. Ruthenium-Catalyzed Hydrogenation of Carbocyclic Aromatic Amines: Access to Chiral Exocyclic Amines. *Org. Lett.* **2018**, *20*, 1094−1097. (g) Li, J.; Zhu, Y.; Lu, Y.; Wang, Y.; Liu, Y.; Liu, D.; Zhang, W. RuPHOX-Ru-Catalyzed Selective Asymmetric Hydrogenation of Exocyclic α,β-Unsaturated Pentanones. *Organometallics* **2019**, *38*, 3970−3978. (h) Li, J.; Lu, Y.; Zhu, Y.; Nie, Y.; Shen, J.; Liu, Y.; Liu, D.; Zhang, W. Selective Asymmetric Hydrogenation of Four-Membered Exo-α,β-Unsaturated Cyclobutanones Using RuPHOX-Ru as a Catalyst. *Org. Lett.* **2019**, *21*, 4331−4335. (i) Li, J.; Ma, Y.; Lu, Y.; Liu, Y.; Liu, D.; Zhang, W. Synthesis of Enantiopure γ-Lactones via a RuPHOX-Ru Catalyzed Asymmetric Hydrogenation of γ-Keto Acids. *Adv. Synth. Catal.* **2019**, *361*, 1146−1153. (j) Li, W.; Schlepphorst, C.; Daniliuc, C.; Glorius, F. Asymmetric Hydrogenation of Vinylthioethers: Access to Optically Active 1,5-Benzothiazepine Derivatives. *Angew. Chem., Int. Ed.* **2016**, *55*, 3300−3303. (k) Paul, D.; Beiring, B.; Plois, M.; Ortega, N.; Kock, S.; Schlüns, D.; Neugebauer, J.; Wolf, R.; Glorius, F. A Cyclometalated Ruthenium-NHC Precatalyst for the Asymmetric Hydrogenation of (Hetero)arenes and Its Activation Pathway. *Organometallics* **2016**, *35*, 3641−3646. (l) Li, W.; Wagener, T.; Hellmann, L.; Daniliuc, C. G.; Mück-Lichtenfeld, C.; Neugebauer, J.; Glorius, F. Design of Ru(II)-NHC-Diamine Precatalysts Directed by Ligand Cooperation: Applications and Mechanistic Investigations for Asymmetric Hydrogenation. *J. Am. Chem. Soc.* **2020**, *142*, 7100−7107.

(3) (a) Tang, W.; Wang, W.; Zhang, X. Phospholane-Oxazoline Ligands for Ir-Catalyzed Asymmetric Hydrogenation. *Angew. Chem., Int. Ed.* **2003**, *42*, 943−946. (b) Li, S.; Zhu, S.-F.; Zhang, C.-M.; Song, S.; Zhou, Q.-L. Iridium-Catalyzed Enantioselective Hydrogenation of α,β-Unsaturated Carboxylic Acids. *J. Am. Chem. Soc.* **2008**, *130*, 8584−8585. (c) Lu, W.-J.; Chen, Y.-W.; Hou, X.-L. Iridium-Catalyzed Highly Enantioselective Hydrogenation of the C═C Bond of α, β-Unsaturated Ketones. *Angew. Chem., Int. Ed.* **2008**, *47*, 10133−10136. (d) Zhao, J.; Burgess, K. Synthesis of Vicinal Dimethyl Chirons by Asymmetric Hydrogenation of Trisubstituted Alkenes. *J. Am. Chem. Soc.* **2009**, *131*, 13236−13237. (e) Rageot, D.; Woodmansee, D. H.; Pugin, B.; Pfaltz, A. Proline-Based P,O Ligand/Iridium Complexes as Highly Selective Catalysts: Asymmetric Hydrogenation of Trisubstituted Alkenes. *Angew. Chem., Int. Ed.* **2011**, *50*, 9598−9601. (f) Zhu, S.-F.; Yu, Y.-B.; Li, S.; Wang, L.-X.; Zhou, Q.-L. Enantioselective Hydrogenation of α-Substituted Acrylic Acids Catalyzed by Iridium Complexes with Chiral Spiro Aminophosphine Ligands. *Angew. Chem., Int. Ed.* **2012**, *51*, 8872−8875. (g) Bernasconi, M.; Müller, M.-A.; Pfaltz, A. Asymmetric Hydrogenation of Maleic Acid Diesters and Anhydrides. *Angew. Chem., Int. Ed.* **2014**, *53*, 5385−5388. (h) Liu, Y.; Gridnev, I. D.; Zhang, W. Mechanism of the Asymmetric Hydrogenation of Exocyclic α,β-Unsaturated Carbonyl Compounds with an Iridium/BiphPhox Catalyst: NMR and DFT Studies. *Angew. Chem., Int. Ed.* **2014**, *53*, 1901−1905. (i) Feng, G.-S.; Zhao, Z.-B.; Shi, L.; Zhou, Y.-G. Iridium-catalyzed asymmetric hydrogenation of quinazolinones. *Org. Chem. Front.* **2019**, *6*, 2250−2253. (j) Hu, S.-B.; Zhai, X.-Y.; Shen, H.-Q.; Zhou, Y.-G. Iridium-catalyzed Asymmetric Hydrogenation of Polycyclic Pyrrolo/Indolo-[1,2-*a*]quinoxalines and Phenanthridines. *Adv. Synth. Catal.* **2018**, *360*, 1334−1339. (k) Hu, S.-B.; Chen, M.-W.; Zhai, X.-Y.; Zhou, Y.-G. Synthesis of Tetrahydropyrrolo/ indolo[1,2-a]pyrazines by Enantioselective Hydrogenation of Heterocyclic Imines. *Huaxue Xuebao* **2018**, *76*, 103−106. (l) Ji, Y.; Wang, J.; Chen, M.-W.; Shi, L.; Zhou, Y.-G. Dual Stereocontrol for Enantio-selective Hydrogenation of Dihydroisoquinolines Induced by Tuning the Amount of N-Bromosuccinimide. *Chin. J. Chem.* **2018**, *36*, 139−142. (m) Chen, M.-W.; Ji, Y.; Wang, J.; Chen, Q.-A.; Shi, L.; Zhou, Y.-G. Asymmetric Hydrogenation of Isoquinolines and Pyridines Using Hydrogen Halide Generated in Situ as Activator. *Org. Lett.* **2017**, *19*, 4988−4991. (n) Wang, Y.; Yang, G.; Xie, F.; Zhang, W. A Ferrocene-Based NH-Free Phosphine-Oxazoline Ligand for Iridium-Catalyzed Asymmetric Hydrogenation of Ketones. *Org. Lett.* **2018**, *20*, 6135−6139. (o) Zhou, T.; Peters, B.; Maldonado, M. F.; Govender, T.; Andersson, P. G. Enantioselective Synthesis of Chiral Sulfones by Ir-Catalyzed Asymmetric Hydrogenation: A Facile Approach to the Preparation of Chiral Allylic and Homoallylic Compounds. *J. Am. Chem. Soc.* **2012**, *134*, 13592−13595. (p) Tosatti, P.; Pfaltz, A. Iridium-Catalyzed Asymmetric Hydrogenation of Benzo[b]thiophene 1,1-Dioxides. *Angew. Chem., Int. Ed.* **2017**, *56*, 4579−4582. (q) Peters, B. K.; Zhou, T.; Rujirawanich, J.; Cadu, A.; Singh, T.; Rabten, W.; Kerdphon, S.; Andersson, P. G. An Enantioselective Approach to the Preparation of Chiral Sulfones by Ir-Catalyzed Asymmetric Hydrogenation. *J. Am. Chem. Soc.* **2014**, *136*, 16557−16562. (r) Feng, G.-S.; Shi, L.; Meng, F.-J.; Chen, M.-W.; Zhou, Y.-G. Iridium-Catalyzed Asymmetric Hydrogenation of 4,6-Disubstituted 2-Hydroxypyrimidines. *Org. Lett.* **2018**, *20*, 6415−6419.

(4) (a) Reetz, M. T.; Mehler, G. Highly Enantioselective Rh-Catalyzed Hydrogenation Reactions Based on Chiral Monophosphite Ligands. *Angew. Chem., Int. Ed.* **2000**, *39*, 3889−3890. (b) van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. Highly Enantioselective Rhodium-Catalyzed Hydrogenation with Monodentate Ligands. *J. Am. Chem. Soc.* **2000**, *122*, 11539−11540. (c) Li, C.; Xiao, J. Asymmetric Hydrogenation of Cyclic Imines with an Ionic Cp*Rh(III) Catalyst. *J. Am. Chem. Soc.* **2008**, *130*, 13208−13209. (d) Chen, J.; Zhang, W.; Geng, H.; Li, W.; Hou, G.; Lei, A.; Zhang, X. Efficient Synthesis of Chiral β-Arylisopropylamines by Using Catalytic Asymmetric Hydrogenation. *Angew. Chem., Int. Ed.* **2009**, *48*, 800−802. (e) Imamoto, T.; Tamura, K.; Zhang, Z.; Horiuchi, Y.; Sugiya, M.; Yoshida, K.; Yanagisawa, A.; Gridnev, I. D. Rigid P-Chiral Phosphine Ligands with tert-Butylmethylphosphino Groups for Rhodium-Catalyzed Asymmetric Hydrogenation of Functionalized Alkenes. *J. Am. Chem. Soc.* **2012**, *134*, 1754−1769. (f) Liu, G.; Liu, X.; Cai, Z.; Jiao, G.; Xu, G.; Tang, W. Design of Phosphorus Ligands with Deep Chiral Pockets: Practical Synthesis of Chiral β-Arylamines by Asymmetric Hydrogenation. *Angew. Chem., Int. Ed.* **2013**, *52*, 4235−4238. (g) Liu, T.-L.; Wang, C.-J.; Zhang, X. Synthesis of Chiral Aliphatic Amines through

https://dx.doi.org/10.1021/acs.orglett.0c03723
Org. Lett. 2021, 23, 668−675

Asymmetric Hydrogenation. *Angew. Chem., Int. Ed.* **2013**, *52*, 8416−8419. (h) Shang, G.; Yang, Q.; Zhang, X. Rh-Catalyzed Asymmetric Hydrogenation of α-Aryl Imino Esters: An Efficient Enantioselective Synthesis of Aryl Glycine Derivatives. *Angew. Chem., Int. Ed.* **2006**, *45*, 6360−6362. (i) Zhang, J.; Jia, J.; Zeng, X.; Wang, Y.; Zhang, Z.; Gridnev, I. D.; Zhang, W. Chemo- and Enantioselective Hydrogenation of α-Formyl Enamides: An Efficient Access to Chiral α-Amido Aldehydes. *Angew. Chem., Int. Ed.* **2019**, *58*, 11505−11512. (j) Zhang, J.; Liu, C.; Wang, X.; Chen, J.; Zhang, Z.; Zhang, W. Rhodium-catalyzed asymmetric hydrogenation of β-branched enamides for the synthesis of β-stereogenic amines. *Chem. Commun.* **2018**, *54*, 6024−6027. (k) Liu, G.; Zhang, H.; Huang, Y.; Han, Z.; Liu, G.; Liu, Y.; Dong, X.-Q.; Zhang, X. Efficient synthesis of chiral 2,3-dihydro-benzo[b]thiophene 1,1-dioxides via Rh-catalyzed hydrogenation. *Chem. Sci.* **2019**, *10*, 2507−2512.

(5) (a) Abe, H.; Amii, H.; Uneyama, K. Pd-Catalyzed Asymmetric Hydrogenation of α-Fluorinated Iminoesters in Fluorinated Alcohol: A New and Catalytic Enantioselective Synthesis of Fluoro α-Amino Acid Derivatives. *Org. Lett.* **2001**, *3*, 313−315. (b) Yu, C.-B.; Wang, J.; Zhou, Y.-G. Facile synthesis of chiral indolines through asymmetric hydrogenation of in situ generated indoles. *Org. Chem. Front.* **2018**, *5*, 2805−2809. (c) Xie, H.-P.; Yan, Z.; Wu, B.; Hu, S.-B.; Zhou, Y.-G. Synthesis of electron-deficient (Sa,R,R)-$(CF_3)_2$-C_3-TunePhos and its applications in asymmetric hydrogenation of α-iminophosphonates. *Tetrahedron Lett.* **2018**, *59*, 2960−2964. (d) Feng, G.-S.; Chen, M.-W.; Shi, L.; Zhou, Y.-G. Facile Synthesis of Chiral Cyclic Ureas through Hydrogenation of 2-Hydroxypyrimidine/Pyrimidin-2(1H)-one Tautomers. *Angew. Chem., Int. Ed.* **2018**, *57*, 5853−5857. (e) Song, B.; Chen, M.-W.; Zhou, Y.-G. Synthesis of chiral sultams with two adjacent stereocenters via palladium-catalyzed dynamic kinetic resolution. *Org. Chem. Front.* **2018**, *5*, 1113−1117. (f) Chen, Z.-P.; Hu, S.-B.; Chen, M.-W.; Zhou, Y.-G. Synthesis of Chiral Fluorinated Hydrazines via Pd-Catalyzed Asymmetric Hydrogenation. *Org. Lett.* **2016**, *18*, 2676−2679. (g) Yan, Z.; Wu, B.; Gao, X.; Chen, M.-W.; Zhou, Y.-G. Enantioselective Synthesis of α-Amino Phosphonates via Pd-Catalyzed Asymmetric Hydrogenation. *Org. Lett.* **2016**, *18*, 692−695. (h) Chen, Z.-P.; Chen, M.-W.; Shi, L.; Yu, C.-B.; Zhou, Y.-G. Pd-catalyzed asymmetric hydrogenation of fluorinated aromatic pyrazol-5-ols via capture of active tautomers. *Chem. Sci.* **2015**, *6*, 3415−3419. (i) Yu, C.-B.; Huang, W.-X.; Shi, L.; Chen, M.-W.; Wu, B.; Zhou, Y.-G. Asymmetric Hydrogenation via Capture of Active Intermediates Generated from Aza-Pinacol Rearrangement. *J. Am. Chem. Soc.* **2014**, *136*, 15837−15840. (j) Cai, X.-F.; Huang, W.-X.; Chen, Z.-P.; Zhou, Y.-G. Palladium-catalyzed asymmetric hydrogenation of 3-phthalimido substituted quinolones. *Chem. Commun.* **2014**, *50*, 9588−9590. (k) Duan, Y.; Li, L.; Chen, M.-W.; Yu, C.-B.; Fan, H.-J.; Zhou, Y.-G. Homogenous Pd-Catalyzed Asymmetric Hydrogenation of Unprotected Indoles: Scope and Mechanistic Studies. *J. Am. Chem. Soc.* **2014**, *136*, 7688−7700. (l) Fan, D.; Liu, Y.; Jia, J.; Zhang, Z.; Liu, Y.; Zhang, W. Synthesis of Chiral α-Aminosilanes through Palladium-Catalyzed Asymmetric Hydrogenation of Silylimines. *Org. Lett.* **2019**, *21*, 1042−1045. (m) Chen, J.; Zhang, Z.; Li, B.; Li, F.; Wang, Y.; Zhao, M.; Gridnev, I. D.; Imamoto, T.; Zhang, W. $Pd(OAc)_2$-catalyzed asymmetric hydrogenation of sterically hindered N-tosylimines. *Nat. Commun.* **2018**, *9*, 5000.

(6) (a) Morris, R. H. Asymmetric hydrogenation, transfer hydrogenation and hydrosilylation of ketones catalyzed by iron complexes. *Chem. Soc. Rev.* **2009**, *38*, 2282−2291. (b) Li, Y. Y.; Yu, S. L.; Shen, W. Y.; Gao, J. X. Iron-, Cobalt-, and Nickel-Catalyzed Asymmetric Transfer Hydrogenation and Asymmetric Hydrogenation of Ketones. *Acc. Chem. Res.* **2015**, *48*, 2587−2598. (c) Morris, R. H. Exploiting Metal−Ligand Bifunctional Reactions in the Design of Iron Asymmetric Hydrogenation Catalysts. *Acc. Chem. Res.* **2015**, *48*, 1494−1502. (d) Chirik, P. J. Iron- and Cobalt-Catalyzed Alkene Hydrogenation: Catalysis with Both Redox-Active and Strong Field Ligands. *Acc. Chem. Res.* **2015**, *48*, 1687−1695.

(7) (a) Zhou, S.; Fleischer, S.; Junge, K.; Das, S.; Addis, D.; Beller, M. Enantioselective Synthesis of Amines: General, Efficient Iron-Catalyzed Asymmetric Transfer Hydrogenation of Imines. *Angew. Chem., Int. Ed.* **2010**, *49*, 8121−8125. (b) Mikhailine, A. A.; Maishan, M. I.; Morris, R. H. Asymmetric Transfer Hydrogenation of Ketimines Using Well-Defined Iron(II)-Based Precatalysts Containing a PNNP Ligand. *Org. Lett.* **2012**, *14*, 4638−4641. (c) Zuo, W.; Lough, A. J.; Li, Y. F.; Morris, R. H. Amine(imine)diphosphine Iron Catalysts for Asymmetric Transfer Hydrogenation of Ketones and Imines. *Science* **2013**, *342*, 1080−1083. (d) Lagaditis, P. O.; Sues, P. E.; Sonnenberg, J. F.; Wan, K. Y.; Lough, A. J.; Morris, R. H. Iron(II) Complexes Containing Unsymmetrical P-N-P' Pincer Ligands for the Catalytic Asymmetric Hydrogenation of Ketones and Imines. *J. Am. Chem. Soc.* **2014**, *136*, 1367−1380. (e) Lu, L.-Q.; Li, Y.; Junge, K.; Beller, M. Relay Iron/Chiral Brønsted Acid Catalysis: Enantioselective Hydrogenation of Benzoxazinones. *J. Am. Chem. Soc.* **2015**, *137*, 2763−2768. (f) Li, Y. Y.; Yu, S. L.; Wu, X. F.; Xiao, J. L.; Shen, W. Y.; Dong, Z. R.; Gao, J. X. Iron Catalyzed Asymmetric Hydrogenation of Ketones. *J. Am. Chem. Soc.* **2014**, *136*, 4031−4039. (g) Bigler, R.; Huber, R.; Mezzetti, A. Highly Enantioselective Transfer Hydrogenation of Ketones with Chiral $(NH)_2P_2$ Macrocyclic Iron(II) Complexes. *Angew. Chem., Int. Ed.* **2015**, *54*, 5171−5174. (h) Lagaditis, P. O.; Lough, A. J.; Morris, R. H. Low-Valent Ene-Amido Iron Complexes for the Asymmetric Transfer Hydrogenation of Acetophenone without Base. *J. Am. Chem. Soc.* **2011**, *133*, 9662−9665. (i) Zhou, S. L.; Fleischer, S.; Junge, K.; Das, S.; Addis, D.; Beller, M. Enantioselective Synthesis of Amines: General, Efficient Iron-Catalyzed Asymmetric Transfer Hydrogenation of Imines. *Angew. Chem., Int. Ed.* **2010**, *49*, 8121−8125. (j) Mikhailine, A.; Lough, A. J.; Morris, R. H. Efficient Asymmetric Transfer Hydrogenation of Ketones Catalyzed by an Iron Complex Containing a P−N−N−P Tetradentate Ligand Formed by Template Synthesis. *J. Am. Chem. Soc.* **2009**, *131*, 1394−1395. (k) Sui-Seng, C.; Freutel, F.; Lough, A. J.; Morris, R. H. Highly Efficient Catalyst Systems Using Iron Complexes with a Tetradentate PNNP Ligand for the Asymmetric Hydrogenation of Polar Bonds. *Angew. Chem., Int. Ed.* **2008**, *47*, 940−943. (l) Sonnenberg, J. F.; Coombs, N.; Dube, P. A.; Morris, R. H. Iron Nanoparticles Catalyzing the Asymmetric Transfer Hydrogenation of Ketones. *J. Am. Chem. Soc.* **2012**, *134*, 5893−5899. (m) Mikhailine, A. A.; Maishan, M. I.; Lough, A. J.; Morris, R. H. The Mechanism of Efficient Asymmetric Transfer Hydrogenation of Acetophenone Using an Iron(II) Complex Containing an (*S*,*S*)-$Ph_2PCH_2CH{=}NCHPhCHPhN{=}CHCH_2PPh_2$ Ligand: Partial Ligand Reduction Is the Key. *J. Am. Chem. Soc.* **2012**, *134*, 12266−12280.

(8) (a) Friedfeld, M. R.; Shevlin, M.; Hoyt, J. M.; Krska, S. W.; Tudge, M. T.; Chirik, P. J. Cobalt Precursors for High-Throughput Discovery of Base Metal Asymmetric Alkene Hydrogenation Catalysts. *Science* **2013**, *342*, 1076−1080. (b) Monfette, S.; Turner, Z. R.; Semproni, S. P.; Chirik, P. J. Enantiopure C1-Symmetric Bis(imino)pyridine Cobalt Complexes for Asymmetric Alkene Hydrogenation. *J. Am. Chem. Soc.* **2012**, *134*, 4561−4564. (c) Hu, Y.; Zhang, Z.; Zhang, J.; Liu, Y.; Gridnev, I. D.; Zhang, W. Cobalt-Catalyzed Asymmetric Hydrogenation of C═N Bonds Enabled by Assisted Coordination and Nonbonding Interactions. *Angew. Chem., Int. Ed.* **2019**, *58*, 15767−15771. (d) Friedfeld, M. R.; Shevlin, M.; Margulieux, G. W.; Campeau, L.; Chirik, P. J. Cobalt-Catalyzed Enantioselective Hydrogenation of Minimally Functionalized Alkenes: Isotopic Labeling Provides Insight into the Origin of Stereoselectivity and Alkene Insertion Preferences. *J. Am. Chem. Soc.* **2016**, *138*, 3314−3324. (e) Chen, J. H.; Chen, C. H.; Ji, C. L.; Lu, Z. Cobalt-Catalyzed Asymmetric Hydrogenation of 1,1-Diarylethenes. *Org. Lett.* **2016**, *18*, 1594−1597.

(9) (a) Hamada, Y.; Koseki, Y.; Fujii, T.; Maeda, T.; Hibino, T.; Makino, K. Catalytic asymmetric hydrogenation of α-amino-β-keto ester hydrochlorides using homogeneous chiral nickel-bisphosphine complexes through DKR. *Chem. Commun.* **2008**, 6206−6208. (b) Hibino, T.; Makino, K.; Sugiyama, T.; Hamada, Y. Homogeneous Chiral Nickel-Catalyzed Asymmetric Hydrogenation of Substituted Aromatic α-Aminoketone Hydrochlorides through Dynamic Kinetic Resolution. *ChemCatChem* **2009**, *1*, 237−240. (c) Shevlin, M.;

https://dx.doi.org/10.1021/acs.orglett.0c03723
Org. Lett. 2021, 23, 668−675

Friedfeld, M. R.; Sheng, H.; Pierson, N. A.; Hoyt, J. M.; Campeau, L.-C.; Chirik, P. J. Nickel-Catalyzed Asymmetric Alkene Hydrogenation of α,β-Unsaturated Esters: High-Throughput Experimentation-Enabled Reaction Discovery, Optimization, and Mechanistic Elucidation. *J. Am. Chem. Soc.* **2016**, *138*, 3562−3569. (d) Yang, P.; Xu, H. Y.; Zhou, J. Nickel-Catalyzed Asymmetric Transfer Hydrogenation of Olefins for the Synthesis of α- and β-Amino Acids. *Angew. Chem., Int. Ed.* **2014**, *53*, 12210−12213. (e) Guo, S. Y.; Yang, P.; Zhou, J. Nickel-catalyzed asymmetric transfer hydrogenation of conjugated olefins. *Chem. Commun.* **2015**, *51*, 12115−12117. (f) Xu, H. Y.; Yang, P.; Chuanprasit, P.; Hirao, H.; Zhou, J. Nickel-Catalyzed Asymmetric Transfer Hydrogenation of Hydrazones and Other Ketimines. *Angew. Chem., Int. Ed.* **2015**, *54*, 5112−5116. (g) Yang, P.; Lim, L. H.; Chuanprasit, P.; Hirao, H.; Zhou, J. Nickel-Catalyzed Enantioselective Reductive Amination of Ketones with Both Arylamines and Benzhydrazide. *Angew. Chem., Int. Ed.* **2016**, *55*, 12083−12087. (h) Guo, S.; Zhou, J. N. N-Dimethylformamide as Hydride Source in Nickel-Catalyzed Asymmetric Hydrogenation of α,β-Unsaturated Esters. *Org. Lett.* **2016**, *18*, 5344−5347. (i) Zhao, X.; Xu, H.; Huang, X.; Zhou, J. Asymmetric Stepwise Reductive Amination of Sulfonamides, Sulfamates, and a Phosphinamide by Nickel Catalysis. *Angew. Chem., Int. Ed.* **2019**, *58*, 292−296. (j) Li, B.; Chen, J.; Zhang, Z.; Gridnev, I. D.; Zhang, W. Nickel-Catalyzed Asymmetric Hydrogenation of N-Sulfonyl Imines. *Angew. Chem., Int. Ed.* **2019**, *58*, 7329−7334. (k) Gao, W.; Lv, H.; Zhang, T.; Yang, Y.; Chung, L. W.; Wu, Y.-D.; Zhang, X. Nickel-catalyzed asymmetric hydrogenation of β-acylamino nitroolefins: an efficient approach to chiral amines. *Chem. Sci.* **2017**, *8*, 6419−6422. (l) Li, X.; You, C.; Li, S.; Lv, H.; Zhang, X. Nickel-Catalyzed Enantioselective Hydrogenation of β-(Acylamino)acrylates: Synthesis of Chiral β-Amino Acid Derivatives. *Org. Lett.* **2017**, *19*, 5130−5133. (m) Long, J.; Gao, W.; Guan, Y.; Lv, H.; Zhang, X. Nickel-Catalyzed Highly Enantioselective Hydrogenation of β-Acetylamino Vinylsulfones: Access to Chiral β-Amido Sulfones. *Org. Lett.* **2018**, *20*, 5914−5917. (n) Guan, Y.-Q.; Han, Z.; Li, X.; You, C.; Tan, X.; Lv, H.; Zhang, X. A cheap metal for a challenging task: nickel-catalyzed highly diastereo- and enantioselective hydrogenation of tetrasubstituted fluorinated enamides. *Chem. Sci.* **2019**, *10*, 252−256. (o) Liu, Y.; Yi, Z.; Tan, X.; Dong, X.-Q.; Zhang, X. Nickel-Catalyzed Asymmetric Hydrogenation of Cyclic Sulfamidate Imines: Efficient Synthesis of Chiral Cyclic Sulfamidates. *iScience* **2019**, *19*, 63−73. (p) Han, Z.; Liu, G.; Zhang, X.; Li, A.; Dong, X.-Q.; Zhang, X. Synthesis of Chiral β-Borylated Carboxylic Esters via Nickel-Catalyzed Asymmetric Hydrogenation. *Org. Lett.* **2019**, *21*, 3923−3926. (q) Hu, Y.; Chen, J.; Li, B.; Zhang, Z.; Gridnev, I. D.; Zhang, W. Nickel-Catalyzed Asymmetric Hydrogenation of 2-Amidoacrylates. *Angew. Chem., Int. Ed.* **2020**, *59*, 5371−5375. (r) Liu, Y.; Dong, X.-Q.; Zhang, X. Recent Advances of Nickel-Catalyzed Homogeneous Asymmetric Hydrogenation. *Youji Huaxue* **2020**, *40*, 1096−1104.

(10) (a) Ghosh, A. K.; Liu, W. Chiral Auxiliary Mediated Conjugate Reduction and Asymmetric Protonation: Synthesis of High Affinity Ligands for HIV Protease Inhibitors. *J. Org. Chem.* **1995**, *60*, 6198−6201. (b) Velazquez, F.; Sannigrahi, M.; Bennett, F.; Lovey, R. G.; Arasappan, A.; Bogen, S.; Nair, L.; Venkatraman, S.; Blackman, M.; Hendrata, S.; Huang, Y.; Huelgas, R.; Pinto, P.; Cheng, K.-C.; Tong, X.; McPhail, A. T.; Njoroge, F. G. Cyclic Sulfones as Novel P3-Caps for Hepatitis C Virus NS3/4A (HCV NS3/4A) Protease Inhibitors: Synthesis and Evaluation of Inhibitors with Improved Potency and Pharmacokinetic Profiles. *J. Med. Chem.* **2010**, *53*, 3075−3085. (c) Kim, C. U.; McGee, L. R.; Krawczyk, S. H.; Harwood, E.; Harada, Y.; Swaminathan, S.; Bischofberger, N.; Chen, M. S.; Cherrington, J. M.; Xiong, S. F.; Griffin, L.; Cundy, K. C.; Lee, A.; Yu, B.; Gulnik, S.; Erickson, J. W. New Series of Potent, Orally Bioavailable, Non-Peptidic Cyclic Sulfones as HIV-1 Protease Inhibitors. *J. Med. Chem.* **1996**, *39*, 3431−3434.

(11) (a) Guillaneux, D.; Zhao, S.-H.; Samuel, O.; Rainford, D.; Kagan, H. B. Nonlinear Effects in Asymmetric Catalysis. *J. Am. Chem. Soc.* **1994**, *116*, 9430−9439. (b) Girard, C.; Kagan, H. B. Nonlinear Effects in Asymmetric Synthesis and Stereoselective Reactions: Ten Years of Investigation. *Angew. Chem., Int. Ed.* **1998**, *37*, 2922−2959.

https://dx.doi.org/10.1021/acs.orglett.0c03723
Org. Lett. 2021, 23, 668−675