OL | Organic Letters

pubs.acs.org/OrgLett

Letter

Enantioselective Hydroarylation or Hydroalkenylation of Benzo[*b*]thiophene 1,1-Dioxides with Organoboranes

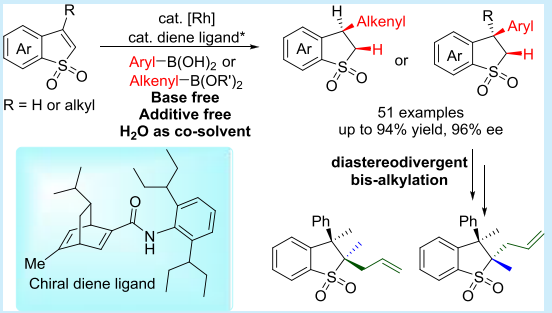
Fangdong Hu,[§] Jie Jia,[§] Ximing Li, and Ying Xia*

Cite This: *Org. Lett.* 2021, 23, 896–901

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

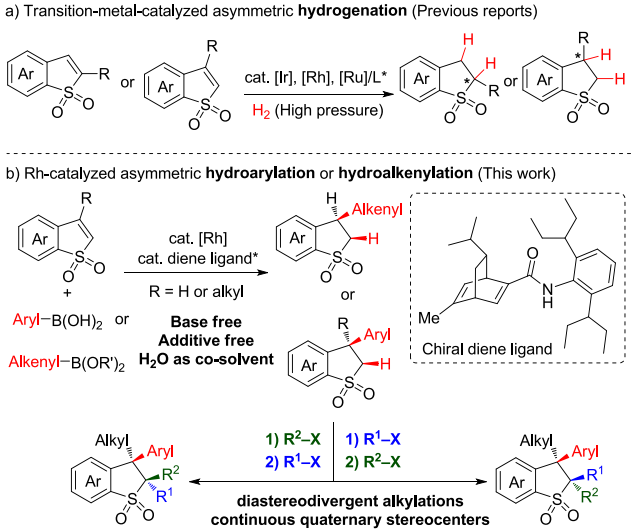
ABSTRACT: An efficient protocol for the asymmetric hydroarylation and hydroalkenylation of benzo[*b*]thiophene 1,1-dioxides with organoboranes has been developed. The combination of a rhodium(I) precatalyst and a chiral diene ligand constitutes the catalytic system, which enables the facile synthesis of 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxides in good yields with high enantioselectivities. The merging of this asymmetric hydroarylation with the downstream alkylations delivers 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxides that contain two continuous quaternary stereocenters with high enantioselectivities in a diastereodivergent manner.



Chiral heterocycles are of significant importance, being frequently encountered in numerous medicines and natural products and serving as useful and versatile building blocks for drug discovery.[1] Of such compounds, chiral 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxides constitute structurally unique compounds with interesting biological activity.[2] Accordingly, the development of efficient protocols for the stereocontrolled synthesis of these frameworks has therefore attracted a great deal of attention.

The transition-metal-catalyzed asymmetric hydrogenation of prochiral heteroarenes has been widely explored in the last several years and is deemed to be a versatile and straightforward method for the construction of chiral heterocycles.[3] In this regard, asymmetric hydrogenation has been developed as an important access to chiral 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxides (Scheme 1a). In 2017, Pfaltz and coworkers first achieved the enantioselective hydrogenation of substituted benzo[*b*]thiophene 1,1-dioxides catalyzed by iridium N,P-ligand complexes.[4,5] Zhang, Dong, and coworkers subsequently revealed a new catalytic system that involves a combination of $Rh(NBD)_2BF_4$ and ZhaoPhos, which improves the efficiency of this transformation and gives high yields and excellent enantioselectivities.[6] Recently, the groups of Hou[7] and Glorius[8] also reported the asymmetric hydrogenation of 2-alkyl-substituted dihydrobenzo[*b*]thiophene 1,1-dioxides, achieving good to excellent enantioselectivities with Rh-(*R*,*R*)-f-spiroPhos and Ru(II)-NHC-diamine complex, respectively. Whereas the asymmetric hydrogenation protocol provides a powerful tool for the construction of chiral 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxides, its inherent limitations, including the necessity of high-pressure hydrogen gas, the incapability of introducing an all-carbon quaternary stereocenter,[9] and the incompatibility of olefin moiety, hamper the access to such compounds with more diversity to some extent. Therefore, the development of a new catalytic system to address those issues is highly desirable.

Scheme 1. Strategy for the Enantioselective Synthesis of 2,3-Dihydrobenzo[*b*]thiophene 1,1-Dioxides



Received: December 13, 2020
Published: January 12, 2021

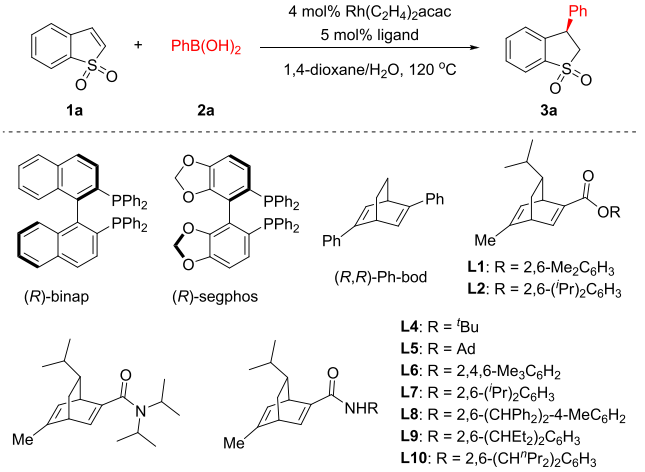
https://dx.doi.org/10.1021/acs.orglett.0c04114
Org. Lett. 2021, 23, 896–901

Rhodium-catalyzed asymmetric hydroarylation of electron-deficient double bonds (C=C, C=O, or C=N) with organoboronic acids or their derivatives represents one of the most reliable and straightforward approaches to enantioenriched compounds.[10] Chiral diene ligands have played a central role in the control of the enantioselectivity, and Rh(I)/diene was discovered as a useful catalytic system in these transformations.[11,12] Recently, the hydroarylation of C=N bonds in N-containing arenes has been developed as an important route to chiral N-containing heterocycles.[13] Taking advantage of the fact that benzo[*b*]thiophene 1,1-dioxides can be regarded as containing a special type of electron-deficient C=C double bonds, we envisioned that chiral 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxides could be constructed through the rhodium-catalyzed asymmetric hydroarylation/hydroalkenylation of benzo[*b*]thiophene 1,1-dioxides with organoboranes.[14,15] Herein we describe that the Rh/diene catalytic system is competent in the asymmetric hydroarylation/hydroalkenylation of benzo[*b*]thiophene 1,1-dioxides, and the merging with downstream diastereodivergent alkylations enables the introduction of two continuous quaternary stereocenters (Scheme 1b).

Our investigation started with the reaction between benzo[*b*]thiophene 1,1-dioxides **1a** and phenylboronic acid **2a** using rhodium(I) precatalysts and chiral ligands (Table 1). The chiral diphosphine ligands (*R*)-binap and (*R*)-segphos were initially tested with 1,4-dioxane/H_2O as the solvent at 120 °C, affording the desired product **3a** in 66% yield with 36% ee and in 72% yield with 61% ee, respectively (entries 1 and 2). Although the reaction was sluggish with the simple C_2-symmetric chiral diene ligand (*R*,*R*)-Ph-bod, the enantioselectivity was elevated to 83% (entry 3). Encouraged by this result, a series of reported chiral diene ligands **L1**−**L7**, were evaluated in this transformation (entries 4−10).[16,17] As for the enantioselectivity of the reaction, it was found that the amide diene ligands were superior to the ester ligands (entries 4 and 5 vs entries 9 and 10). The bulkier diene ligands generally expressed better enantioselectivity (entry 4 vs entry 5; entries 6−9 vs entry 10), providing the hydroarylation product in 68% yield with 88% ee when using **L7** as the ligand (entry 10). Inspired by this observation, the sterically bulkier chiral diene ligands **L8**−**L10** were designed and synthesized according to a similar procedure.[17g] Whereas **L8** failed to improve the enantioselectivity of this transformation (entry 10 vs entry 11), both **L9** and **L10** showed an improved ee value (entry 10 vs entries 12 and 13). In this stage, the desired product can be obtained in 75% yield with 92% ee (entry 12). Further optimization of the reaction temperature (entry 14), the ratio of the solvent mixture (entries 15−17), and the concentration (entries 18, 19) were conducted, and it was found that slightly decreasing the reaction concentration was beneficial to the efficiency, providing the product in 81% yield with 93% ee (entry 18). The absolute configuration of **3a** was determined by referring to its optical rotation of the literature.[6]

With the optimized conditions, the scope of this transformation was then investigated. A wide variety of benzo[*b*]-thiophene 1,1-dioxides were readily arylated with high yields and enantioselectivities, as depicted in Table 2. First, numerous five-substituted benzo[*b*]thiophene 1,1-dioxides were tested. Electron-donating or -withdrawing substrates with different functional groups, including methyl (**1b**), methoxyl (**1c**), free hydroxy (**1d**), halogen (**1e**, **1f**), and phenyl (**1g**), were tolerated in the reaction, which provided the hydroarylation

Table 1. Optimization of the Reaction Conditions[a]



entry	ligand	1,4-dioxane (mL)/H_2O (mL)	yield (%)[b]	ee (%)[c]
1	(*R*)-binap	0.5/0.5	66	36
2	(*R*)-segphos	0.5/0.5	72	61
3	(*R*,*R*)-Ph-bod	0.5/0.5	34	83
4	L1	0.5/0.5	70	65
5	L2	0.5/0.5	80	76
6	L3	0.5/0.5	68	84
7	L4	0.5/0.5	58	82
8	L5	0.5/0.5	66	83
9	L6	0.5/0.5	62	84
10	L7	0.5/0.5	68	88
11	L8	0.5/0.5	77	51
12	L9	0.5/0.5	75	92
13	L10	0.5/0.5	65	90
14[d]	L9	0.5/0.5	51	93
15	L9	0.66/0.33	73	93
16	L9	0.8/0.2	50	93
17	L9	0.3/0.3	63	92
18	L9	0.75/0.75	81	93
19	L9	1.0/1.0	77	93

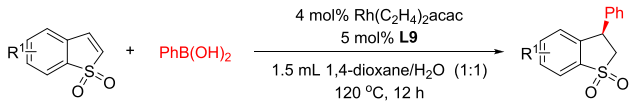
[a]Reaction conditions: **1a** (0.10 mmol), **2a** (0.15 mmol), Rh-$(C_2H_4)_2$acac (4 mol %), ligand (5 mol %) in 1,4-dioxane/H_2O at 120 °C for 12 h. [b]Isolated yield. [c]ee value was determined by HPLC using a chiral stationary phase column. [d]Reaction was run at 100 °C. Ad = 1-adamantyl.

products (**3b**−**3g**) in yields of 64−76% with high enantioselectivities (entries 2−7). Remarkably, the strained cyclopropane ring remained intact during the reaction (entry 8). The catalytic system was competent for alkenyl substrates **1i** and **1j**, affording the desired products in satisfactory yields with satisfactory enantioselectivities (entries 9 and 10). Benzo[*b*]-thiophene 1,1-dioxides bearing methyl (**1k**), methoxyl (**1l**), and sulfonamide (**1m**) at the six-position exhibited similar reactivities, yielding the corresponding products **3k**−**3m** in 63−74% yield with 88−93% ee (entries 11−13). In addition, a substrate bearing a seven-substituent was also tolerated under the optimized reaction conditions (entry 14).

Applying an identical catalytic system, a series of arylboronic acids were investigated in this reaction with benzo[*b*]-thiophene 1,1-dioxide **1a** (Table 3). As depicted in entries 1−8, a range of arylboronic acids with different para-substituted functional groups, including alkyl (**2b**, **2c**), methoxyl (**2d**), halogen (**2e**, **2f**), trifluoromethyl (**2g**), ester

https://dx.doi.org/10.1021/acs.orglett.0c04114
Org. Lett. 2021, 23, 896−901

Table 2. Rh-Catalyzed Asymmetric Hydroarylation of Various Substituted Benzo[*b*]thiophene 1,1-Dioxides with Phenylboronic Acid[a]

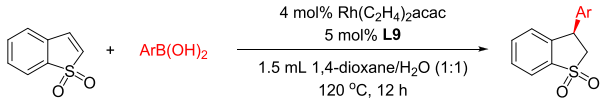


1a-1n 2a 3a-3n

entry	R	product	yield (%)[b]	ee (%)[c]
1	H (**1a**)	**3a**	81	93
2	5-Me (**1b**)	**3b**	72	93
3	5-OMe (**1c**)	**3c**	70	92
4	5-OH (**1d**)	**3d**	76	93
5	5-F (**1e**)	**3e**	66	90
6	5-Cl (**1f**)	**3f**	64	90
7	5-Ph (**1g**)	**3g**	74	91
8	5-cyclopropyl (**1h**)	**3h**	71	91
9	5-isopropenyl (**1i**)	**3i**	73	92
10	5-styryl (**1j**)	**3j**	70	91
11	6-Me (**1k**)	**3k**	70	93
12	6-OMe (**1l**)	**3l**	63	91
13	6-NHTs (**1m**)	**3m**	74	88
14	7-Me (**1n**)	**3n**	70	93

[a]All reactions were run on a 0.1 mmol scale under standard conditions. [b]Isolated yield. [c]ee value was determined by HPLC using a chiral stationary phase column.

Table 3. Rh-Catalyzed Asymmetric Hydroarylation of Benzo[*b*]thiophene 1,1-Dioxides with Various Arylboronic Acids[a]



1a 2b-2q 4b-4q

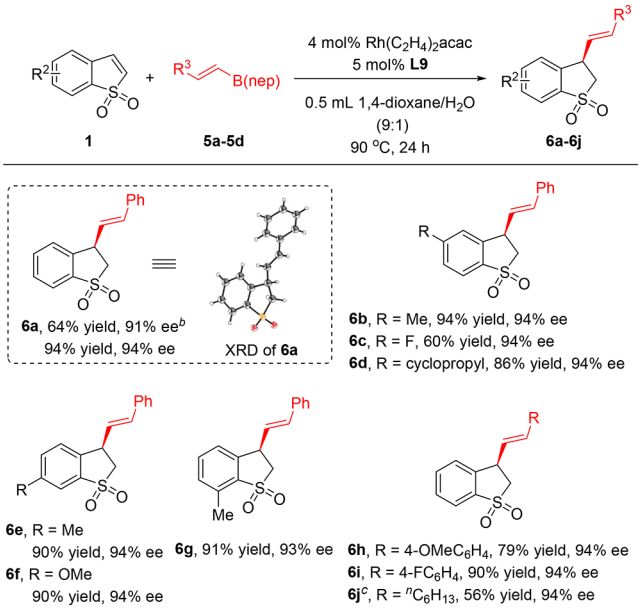
entry	Ar	product	yield (%)[b]	ee (%)[c]
1	4-MeC_6H_4 (**2b**)	**4b**	74	92
2	4-$^tBuC_6H_4$ (**2c**)	**4c**	78	90
3	4-$OMeC_6H_4$ (**2d**)	**4d**	80	89
4	4-FC_6H_4 (**2e**)	**4e**	79	90
5	4-ClC_6H_4 (**2f**)	**4f**	73	93
6	4-$CF_3C_6H_4$ (**2g**)	**4g**	71	92
7	4-$CO_2MeC_6H_4$ (**2h**)	**4h**	79	95
8	4-$COMeC_6H_4$ (**2i**)	**4i**	74	93
9	4-CH_2=CHC_6H_4 (**2j**)	**4j**	44	91
10	3-MeC_6H_4 (**2k**)	**4k**	82	93
11	3-$OMeC_6H_4$ (**2l**)	**4l**	82	92
12	3-ClC_6H_4 (**2m**)	**4m**	69	91
13	2-FC_6H_4 (**2n**)	**4n**	77	96
14	2-$OMeC_6H_4$ (**2o**)	**4o**	70	89
15	2-naphthyl (**2p**)	**4p**	90	92
16	3-thienyl (**2q**)	**4q**	65	93

[a]All of the reactions were run on a 0.1 mmol scale under the standard conditions. [b]Isolated yield. [c]ee value was determined by HPLC using a chiral stationary phase column.

(**2h**), and ketone (**2i**), smoothly afforded the expected product in acceptable yields with high enantioselectivities. Nevertheless, 4-vinylphenylboronic acid delivered the desired product **4j** in low yield (entry 9), which was most likely caused by the coordination effect of the terminal olefin moiety to the rhodium center. As expected, arylboronic acids bearing a meta-substituent were proved to be competent reaction partners (entries 10−12). Electron-rich and electron-deficient ortho-substituted substrates afforded the desired products in comparable yields (entries 13 and 14), and an electron-deficient substrate resulted in a higher ee value (entries 13). Notably, 2-naphthaleneboronic acid **2p** and 3-thiophenebornic acid **2q** could also be tolerated, affording **4p** and **4q** in 90% yield with 92% ee and in 65% yield with 93% ee, respectively (entries 15 and 16).

In addition to arylboronic acids, alkenylboronic acid was used in this reaction under slightly modified conditions, which gave the hydroalkenylation product **6a** in 64% yield with 91% ee. A further screening of the reaction conditions revealed that a higher yield and ee value were obtained with alkenylboronates as the coupling partner. (See Tables S1−S3 in the Supporting Information.) The scope of benzo[*b*]thiophene 1,1-dioxides and alkenylboronates was explored (Scheme 2).

Scheme 2. Rh-Catalyzed Asymmetric Hydroalkenylation of Benzo[*b*]thiophene 1,1-Dioxides with Alkenylboronates[a]



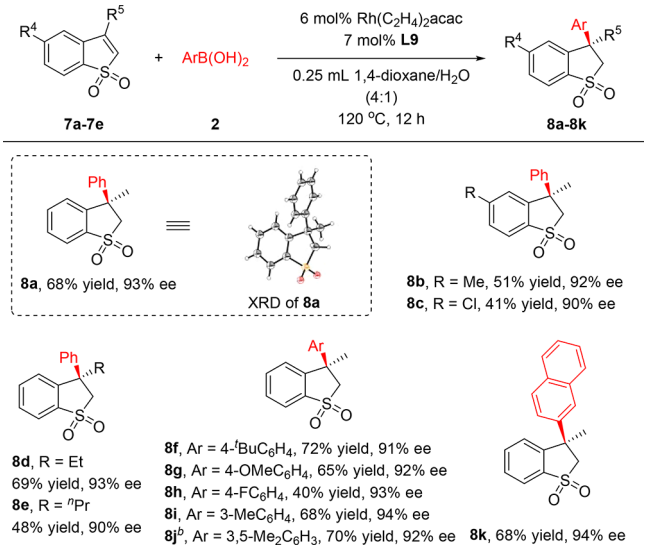
[a]Reaction conditions: **1** (0.10 mmol), **5** (0.12 mmol), $Rh(C_2H_4)_2acac$ (4 mol %), ligand (5 mol %) in 1,4-dioxane/H_2O (0.5 mL, 9/1) at 90 °C for 24 h. [b]Result was obtained using the corresponding boronic acid under the above conditions. [c](*E*)-5,5-Dimethyl-2-(oct-1-en-1-yl)-1,3,2-dioxaborinane **5d** (0.20 mmol) was used. nep = neopentylglycolato. ORTEP representation with 50% probability thermal ellipsoids.

Benzo[*b*]thiophene 1,1-dioxides bearing electron-donating groups at different positions were successfully coupled to alkenylboronates in good results (**6b**, **6d**−**g**). The electron-deficient substrate **1e** was a suitable reactant, and a high ee value was obtained in a moderate yield (**6c**). In addition, *β*-aryl alkenylboronates with a para-substituent were similarly reactive, furnishing **6h** and **6i** in 79% and 90% yield with the same ee value. Moreover, the methodology could also be extended to aliphatic alkenylboronates (**6j**), although in moderate yield. It should be noted that this series of products cannot be obtained by transition-metal-catalyzed asymmetric hydrogenation,[4−8] thus demonstrating the merits of our protocol. The absolute configuration of the desired product **6a** was unambiguously characterized by X-ray crystallography.

https://dx.doi.org/10.1021/acs.orglett.0c04114
Org. Lett. 2021, 23, 896−901

The substrates scope was further expanded with 3-alkyl benzo[*b*]thiophene 1,1-dioxides, which could result in the formation of chiral quaternary centers. It is worth noting that chiral all-carbon quaternary centers are challenging to construct via rhodium-catalyzed asymmetric hydroarylations, which generally require the use of specific aryl organometal reagents rather than simple arylboronic acids.[18] Because of the low conversion of the substrates, further optimization of the reaction conditions was conducted. (See Table S4 in the Supporting Information.) The substrates installed with methyl or chlorine at the five-position served as suitable reaction partners, delivering products in moderate yields with high enantioselectivities (**8b**, **8c**). Ethyl and propyl substituents did not hamper the reaction, which afforded the expected products **8d** and **8e** in 69% yield with 93% ee and in 48% yield with 90% ee, respectively. The reactions can be successfully carried out with several arylboronic acids containing different functional groups (**8f**–**8k**). The electronic property had a marginal influence on the enantioselectivities, whereas the electron-deficient arylboronic acids (**8h**) gave lower conversion compared with electron-rich ones (**8f**, **8g**, **8i**, **8j**). In addition, polyaromatic substrate **2p** could be utilized as well, resulting in an equally good yield and high enantioselectivity (**8k**). Note that 3-aryl and 2-alkyl/aryl benzo[*b*]thiophene 1,1-dioxides were unable to give the corresponding products under our reaction conditions. As shown in Scheme 3, the absolute

Scheme 3. Rh-Catalyzed Asymmetric Hydroarylation of 3-Alkyl Benzo[*b*]thiophene 1,1-Dioxides with Arylboronic Acid[a]

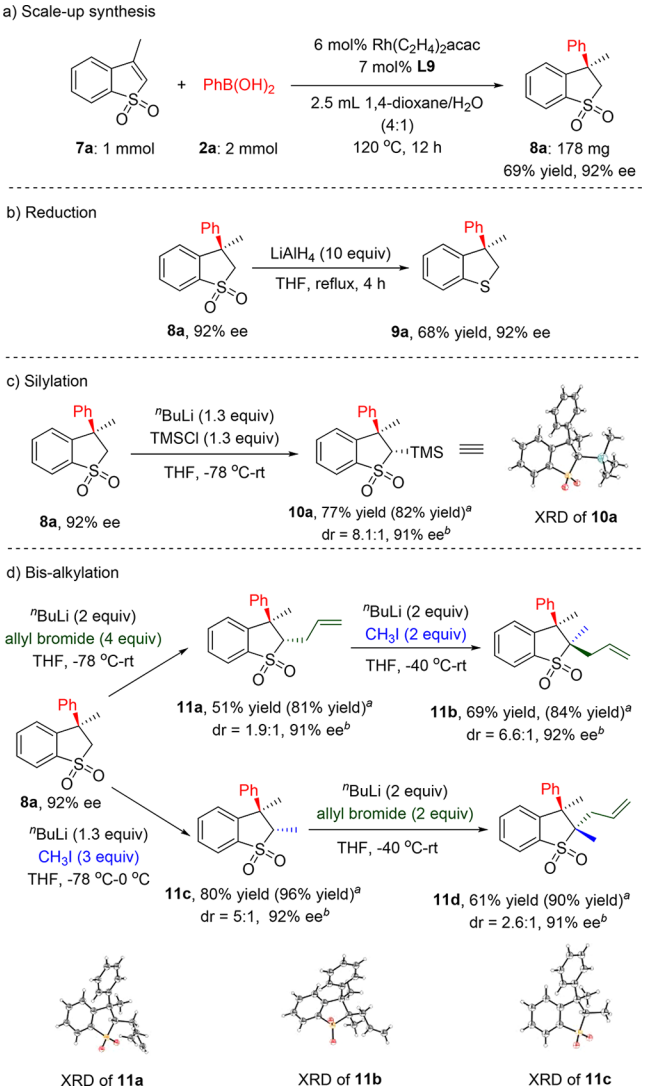


[a]Reaction conditions: **7** (0.10 mmol), **2** (0.20 mmol), $Rh(C_2H_4)_2acac$ (6 mol %), ligand (7 mol %) in 1,4-dioxane/H_2O (0.25 mL, 4:1) at 120 °C for 12 h. [b]1,4-Dioxane/H_2O (0.50 mL, 4/1) was used. ORTEP representation with 50% probability thermal ellipsoids.

configuration of **8a** was ascertained by X-ray crystallography. The stereochemical induction model as well as the deuterium-labeling experiments are detailed in the Supporting Information.

The synthetic potentials of this transformation are demonstrated in Scheme 4. First, the reaction can be carried out on a 10-fold scale with no significant influence on either the yield or the ee value (Scheme 4a). Second, the product **8a**

Scheme 4. Synthetic Applications



[a]Number in parentheses is the total yield determined by ^1H NMR using 1,1,2,2-tetrachloroethane as an internal standard. [b]ee value referred to the major product. ORTEP representation with 50% probability thermal ellipsoids.

was treated with $LiAlH_4$ in THF at reflux to afford 3-methyl-3-phenyl-2,3-dihydrobenzo[*b*]thiophene **9a** in 68% yield with no erosion of the optical purity (Scheme 4b). Third, the product **8a** was lithiated in the presence of *n*BuLi and subsequently quenched with TMSCl to give the silylated product **10a** in 77% isolated yield with 8.1:1 dr and 91% ee, in which the structure of the major product was determined by X-ray crystallography (Scheme 4c). Furthermore, the desired product **8a** could be sequentially alkylated with different carbon electrophiles, which paved the way to constructing vicinal quaternary stereocenters (Scheme 4d). For example, the product **8a** can be initially allylated with allyl bromide (**11a**) and methylated with iodomethane (**11b**) successively. Under similar conditions, the diastereoisomer (**11d**) of **11b** can be conveniently obtained when the reaction sequence is exchanged with carbon electrophiles. The alkylation transformations gave the products **11a**–**d** with a moderate to good diastereoselective ratio. As expected, the derivation had no influence on the enantioselectivity. In particular, the absolute

https://dx.doi.org/10.1021/acs.orglett.0c04114
Org. Lett. 2021, 23, 896–901

configuration of the major products (**11a**–**c**) was unambiguously confirmed by X-ray crystallography. Note that the newly installed alkyl moieties were all cis to the methyl group in the major products. The observed regioselectivity may be attributed to the diastereotopic oxygen atoms of the sulfonyl group, which may coordinate to the organolithium with a preference for the methyl face of the substrate, leading to a configurationally stable carbanion that gives the observed syn stereochemistry in the products.

In summary, we have developed a rhodium-catalyzed hydroarylation or hydroalkenylation of benzo[*b*]thiophene 1,1-dioxides with arylboronic acids or alkenylboronates, in which a modified chiral diene ligand enables the reaction occurring with high efficiency and enantioselectivity. This synthetic method is complementary to the established asymmetric hydrogenation, which has been demonstrated by the facile introduction of an olefin moiety and an all-carbon quaternary stereocenter. It is particularly noteworthy that the downstream bis-alkylation can be used to prepare heterocycles that contain two continuous quaternary stereocenters with high enantioselectivities in a diastereodivergent manner. We expect that this strategy can be utilized as a general protocol for the synthesis of chiral heterocycles.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c04114.

Detailed experimental procedures, characterization data, copies of ^{1}H and ^{13}C NMR spectra, HPLC spectra, and X-ray crystal structures of **6a**, **8a**, **10a**, **11a**, **11b**, and **11c** (PDF)

Accession Codes

CCDC 2039125–2039130 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Ying Xia − *West China School of Public Health and West China Fourth Hospital and State Key Laboratory of Biotherapy, Sichuan University, Chengdu 610041, China;* orcid.org/0000-0002-4803-8599; Email: xiayingscu@scu.edu.cn

Authors

Fangdong Hu − *West China School of Public Health and West China Fourth Hospital and State Key Laboratory of Biotherapy, Sichuan University, Chengdu 610041, China; School of Chemistry and Chemical Engineering, Linyi University, Linyi 276005, China*

Jie Jia − *West China School of Public Health and West China Fourth Hospital and State Key Laboratory of Biotherapy, Sichuan University, Chengdu 610041, China*

Ximing Li − *West China School of Public Health and West China Fourth Hospital and State Key Laboratory of Biotherapy, Sichuan University, Chengdu 610041, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c04114

Author Contributions

§F.H. and J.J. contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work is supported by the "Thousand Youth Talents Plan" and the start-up funding from Sichuan University. The Public Health and Preventive Medicine Provincial Experiment Teaching Center at Sichuan University and Food Safety Monitoring and Risk Assessment Key Laboratory of Sichuan Province are acknowledged for the support. F.H. acknowledges the National Natural Science Foundation (grant 21801109), the Natural Science Foundation of Shandong Province (grant ZR2018BB019), and the Higher Educational Science and Technology Program of Shandong Province (grant J17KA099) for their financial support.

■ REFERENCES

(1) (a) Corey, E. J.; Czakó, B.; Kürti, L. *Molecules and Medicine*; Wiley: Hoboken, NJ, 2007. (b) Majumdar, K. C.; Chattopadhyay, S. K. *Heterocycles in Natural Product Synthesis*; Wiley: Weinheim, Germany, 2011. (c) Li, J. J. *Heterocyclic Chemistry in Drug Discovery*; Wiley: Hoboken, NJ, 2013. (d) Andrushko, V.; Andrushko, N. *Stereoselective Synthesis of Drugs and Natural Products*; Wiley: Karlsruhe, Germany, 2013.

(2) (a) Rempfler, H.; Edmunds, A.; De Mesmaeker, A.; Seckinger, K. Patent WO9909023, 1999. (b) Saitou, M.; Sekiguchi, H.; Ogawa, S. Patent WO2000069853, 2000. (c) Saitou, M.; Sekiguchi, H.; Ogawa, S. Patent WO2000020408, 2000. (d) Hall, R. G.; Loiseleur, O.; Pabba, J.; Pal, S.; Jeanguenat, A.; Edmunds, A.; Stoller, A. Patent WO2009010260, 2009. (e) Edmunds, A.; Mghlebach, M.; Stoller, A.; Loiseleur, O.; Buchholz, A.; Hueter, O. F.; Bigot, A.; Hall, R. G.; Emery, D.; Jung, P. J. M.; Lu, L.; Wu, Y.; Chen, R. Patent WO2015000715, 2015. (f) Wehn, P.; Yang, H. U.S. Patent US20160362390, 2016.

(3) (a) Zhou, Y.-G. Asymmetric Hydrogenation of Heteroaromatic Compounds. *Acc. Chem. Res.* **2007**, *40*, 1357–1366. (b) Wang, D.-S.; Chen, Q.-A.; Lu, S.-M.; Zhou, Y.-G. Asymmetric Hydrogenation of Heteroarenes and Arenes. *Chem. Rev.* **2012**, *112*, 2557–2590. (c) Chen, Q.-A.; Ye, Z.-S.; Duan, Y.; Zhou, Y.-G. Homogeneous Palladium-Catalyzed Asymmetric Hydrogenation. *Chem. Soc. Rev.* **2013**, *42*, 497–511. (d) Kim, A. N.; Stoltz, B. M. Recent Advances in Homogeneous Catalysts for the Asymmetric Hydrogenation of Heteroarenes. *ACS Catal.* **2020**, *10*, 13834–13851.

(4) Tosatti, P.; Pfaltz, A. Iridium-Catalyzed Asymmetric Hydrogenation of Benzo[b]thiophene 1,1-Dioxides. *Angew. Chem., Int. Ed.* **2017**, *56*, 4579–4582.

(5) For a recent iridium-catalyzed asymmetric hydrogenation of benzoheterocycles, see: Ge, Y.; Wang, Z.; Han, Z.; Ding, K. Iridium-Catalyzed Enantioselective Hydrogenation of Indole and Benzofuran Derivatives. *Chem. - Eur. J.* **2020**, *26*, 15482–15486.

(6) 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.

(7) Yan, Q.; Xiao, G.; Wang, Y.; Zi, G.; Zhang, Z.; Hou, G. Highly Efficient Enantioselective Synthesis of Chiral Sulfones by Rh-Catalyzed Asymmetric Hydrogenation. *J. Am. Chem. Soc.* **2019**, *141*, 1749–1756.

(8) 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.

(9) For selected reviews, see: (a) Douglas, C. J.; Overman, L. E. Catalytic Asymmetric Synthesis of All-Carbon Quaternary Stereocenters. *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5363−5367. (b) Quasdorf, K. W.; Overman, L. E. Catalytic Enantioselective Synthesis of Quaternary Carbon Stereocentres. *Nature* **2014**, *516*, 181−191. (c) Liu, Y.; Han, S.-J.; Liu, W.-B.; Stoltz, B. M. Catalytic Enantioselective Construction of Quaternary Stereocenters: Assembly of Key Building Blocks for the Synthesis of Biologically Active Molecules. *Acc. Chem. Res.* **2015**, *48*, 740−751. (d) Feng, J.; Holmes, M.; Krische, M. J. Acyclic Quaternary Carbon Stereocenters via Enantioselective Transition Metal Catalysis. *Chem. Rev.* **2017**, *117*, 12564−12580.

(10) For reviews, see: (a) Fagnou, K.; Lautens, M. Rhodium-Catalyzed Carbon-Carbon Bond Forming Reactions of Organometallic Compounds. *Chem. Rev.* **2003**, *103*, 169−196. (b) Hayashi, T.; Yamasaki, K. Rhodium-Catalyzed Asymmetric 1,4-Addition and Its Related Asymmetric Reactions. *Chem. Rev.* **2003**, *103*, 2829−2844. (c) Edwards, H. J.; Hargrave, J. D.; Penrose, S. D.; Frost, C. G. Synthetic Applications of Rhodium Catalysed Conjugate Addition. *Chem. Soc. Rev.* **2010**, *39*, 2093−2105. (d) Tian, P.; Dong, H.-Q.; Lin, G.-Q. Rhodium-Catalyzed Asymmetric Arylation. *ACS Catal.* **2012**, *2*, 95−119. (e) Jia, T.; Cao, P.; Liao, J. Enantioselective Synthesis of Gem-Diarylalkanes by Transition Metal-Catalyzed Asymmetric Arylations (TMCAAr). *Chem. Sci.* **2018**, *9*, 546−559.

(11) For seminal references, see: (a) Hayashi, T.; Ueyama, N.; Tokunaga, N.; Yoshida, K. A Chiral Chelating Diene as a New Type of Chiral Ligand for Transition Metal Catalysts: Its Preparation and Use for the Rhodium-Catalyzed Asymmetric 1,4-Addition. *J. Am. Chem. Soc.* **2003**, *125*, 11508−11509. (b) Fischer, C.; Defieber, C.; Suzuki, T.; Carreira, E. M. Readily Available [2.2.2]-Bicyclooctadienes as New Chiral Ligands for Ir(I): Catalytic, Kinetic Resolution of Allyl Carbonates. *J. Am. Chem. Soc.* **2004**, *126*, 1628−1629.

(12) For reviews, see: (a) Defieber, C.; Grützmacher, H.; Carreira, E. M. Chiral Olefins as Steering Ligands in Asymmetric Catalysis. *Angew. Chem., Int. Ed.* **2008**, *47*, 4482−4502. (b) Shintani, R.; Hayashi, T. Chiral Diene Ligands for Asymmetric Catalysis. *Aldrichimica Acta* **2009**, *42*, 31−38. (c) Feng, C.-G.; Xu, M.-H.; Lin, G.-Q. Development of Bicyclo[3.3.0]octadiene- or Dicyclopentadiene-Based Chiral Diene Ligands for Transition-Metal-Catalyzed Reactions. *Synlett* **2011**, *2011*, 1345−1356. (d) Feng, X.; Du, H. Synthesis of Chiral Olefin Ligands and their Application in Asymmetric Catalysis. *Asian J. Org. Chem.* **2012**, *1*, 204−213.

(13) (a) Wang, Y.; Liu, Y.; Zhang, D.; Wei, H.; Shi, M.; Wang, F. Enantioselective Rhodium-Catalyzed Dearomative Arylation or Alkenylation of Quinolinium Salts. *Angew. Chem., Int. Ed.* **2016**, *55*, 3776−3780. (b) Robinson, D. J.; Spurlin, S. P.; Gorden, J. D.; Karimov, R. R. Enantioselective Synthesis of Dihydropyridines Containing Quaternary Stereocenters Through Dearomatization of Pyridinium Salts. *ACS Catal.* **2020**, *10*, 51−55.

(14) For the rhodium-catalyzed asymmetric hydroarylation or hydroalkenylation of sulfonyl-containing olefins, see: (a) Mauleón, P.; Carretero, J. C. Rhodium-Catalyzed Enantioselective Conjugate Addition of Organoboronic Acids to α,β-Unsaturated Sulfones. *Org. Lett.* **2004**, *6*, 3195−3198. (b) Mauleón, P.; Carretero, J. C. Enantioselective Construction of Stereogenic Quaternary Centres via Rh-Catalyzed Asymmetric Addition of Alkenylboronic Acids to α,β-Unsaturated Pyridylsulfones. *Chem. Commun.* **2005**, 4961−4963. (c) Mauleón, P.; Alonso, I.; Rivero, M. R.; Carretero, J. C. Enantioselective Synthesis of Chiral Sulfones by Rh-Catalyzed Asymmetric Addition of Boronic Acids to α,β-Unsaturated 2-Pyridyl Sulfones. *J. Org. Chem.* **2007**, *72*, 9924−9935. (d) Nishimura, T.; Takiguchi, Y.; Hayashi, T. Effect of Chiral Diene Ligands in Rhodium-Catalyzed Asymmetric Addition of Arylboronic Acids to α,β-Unsaturated Sulfonyl Compounds. *J. Am. Chem. Soc.* **2012**, *134*, 9086−9089.

(15) For the rhodium-catalyzed asymmetric hydroarylation of the C═C double bond in nonaromatic heterocycles, see: (a) So, C. M.; Kume, S.; Hayashi, T. Rhodium-Catalyzed Asymmetric Hydroarylation of 3-PyrrolinesGiving 3-Arylpyrrolidines: Protonation as a Key Step. *J. Am. Chem. Soc.* **2013**, *135*, 10990−10993. (b) Lim, K. M.-H.; Hayashi, T. Rhodium-Catalyzed Asymmetric Arylation of Allyl Sulfones under the Conditions of Isomerization into Alkenyl Sulfones. *J. Am. Chem. Soc.* **2015**, *137*, 3201−3204. (c) Lim, K. M.-H.; Hayashi, T. Dynamic Kinetic Resolution in Rhodium-Catalyzed Asymmetric Arylation of Phospholene Oxides. *J. Am. Chem. Soc.* **2017**, *139*, 8122−8125.

(16) Okamoto, K.; Hayashi, T.; Rawal, V. H. Simple Chiral Diene Ligands Provide High Enantioselectivities in Transition-Metal-Catalyzed Conjugate Addition Reactions. *Org. Lett.* **2008**, *10*, 4387−4389.

(17) For other related examples, see: (a) Okamoto, K.; Hayashi, T.; Rawal, V. H. Electronic and Steric Tuning of Chiral Diene Ligands for Rhodium-Catalyzed Asymmetric Arylation of Imines. *Chem. Commun.* **2009**, 4815−4817. (b) Pattison, G.; Piraux, G.; Lam, H. W. Enantioselective Rhodium-Catalyzed Addition of Arylboronic Acids to Alkenylheteroarenes. *J. Am. Chem. Soc.* **2010**, *132*, 14373−14375. (c) Sasaki, K.; Nishimura, T.; Shintani, R.; Kantchev, E. A. B.; Hayashi, T. Rhodium/Diene-Catalyzed Tandem 1,4-Shift/1,4-Addition of (E)-1,2-Diphenylethenylboronic Acid to Enones: Density Functional Theory Modeling and Asymmetric Catalysis. *Chem. Sci.* **2012**, *3*, 1278−1283. (d) Roy, I. D.; Burns, A. R.; Pattison, G.; Michel, B.; Parker, A. J.; Lam, H. W. A Second-Generation Ligand for the Enantioselective Rhodium-Catalyzed Addition of Arylboronic Acids to Alkenylazaarenes. *Chem. Commun.* **2014**, *50*, 2865−2868. (e) Yasukawa, T.; Suzuki, A.; Miyamura, H.; Nishino, K.; Kobayashi, S. Chiral Metal Nanoparticle Systems as Heterogeneous Catalysts beyond Homogeneous Metal Complex Catalysts for Asymmetric Addition of Arylboronic Acids to α,β-Unsaturated Carbonyl Compounds. *J. Am. Chem. Soc.* **2015**, *137*, 6616−6623. (f) Li, R.; Wen, Z.; Wu, N. A Nordehydroabietyl Amide-Containing Chiral Diene for Rhodium-Catalysed Asymmetric Arylation to Nitroolefins. *Org. Biomol. Chem.* **2016**, *14*, 11080−11084. (g) Okamoto, K.; Nanya, A.; Eguchi, A.; Ohe, K. Asymmetric Synthesis of 2H-Azirines with a Tetrasubstituted Stereocenter by Enantioselective Ring Contraction of Isoxazoles. *Angew. Chem., Int. Ed.* **2018**, *57*, 1039−1043. (h) Xue, F.; Hayashi, T. Asymmetric Synthesis of Axially Chiral 2-Aminobiaryls by Rhodium-Catalyzed Benzannulation of 1-Arylalkynes with 2-(Cyanomethyl)phenylboronates. *Angew. Chem., Int. Ed.* **2018**, *57*, 10368−10372.

(18) (a) Shintani, R.; Tsutsumi, Y.; Nagaosa, M.; Nishimura, T.; Hayashi, T. Sodium Tetraarylborates as Effective Nucleophiles in Rhodium/Diene-Catalyzed 1,4-Addition to β,β-Disubstituted α,β-Unsaturated Ketones: Catalytic Asymmetric Construction of Quaternary Carbon Stereocenters. *J. Am. Chem. Soc.* **2009**, *131*, 13588−13589. (b) Shintani, R.; Takeda, M.; Nishimura, T.; Hayashi, T. Chiral Tetrafluorobenzobarrelenes as Effective Ligands for Rhodium-Catalyzed Asymmetric 1,4-Addition of Arylboroxines to β,β-Disubstituted α,β-Unsaturated Ketones. *Angew. Chem., Int. Ed.* **2010**, *49*, 3969−3971. (c) Hawner, C.; Müller, D.; Gremaud, L.; Felouat, A.; Woodward, S.; Alexakis, A. Rhodium-Catalyzed Asymmetric 1,4-Addition of Aryl Alanes to Trisubstituted Enones: Binap as an Effective Ligand in the Formation of Quaternary Stereocenters. *Angew. Chem., Int. Ed.* **2010**, *49*, 7769−7772. (d) Shintani, R.; Hayashi, T. Rhodium-Catalyzed Asymmetric 1,4-Addition of Sodium Tetraarylborates to β,β-Disubstituted α,β-Unsaturated Esters. *Org. Lett.* **2011**, *13*, 350−352.

https://dx.doi.org/10.1021/acs.orglett.0c04114
Org. Lett. 2021, 23, 896−901