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Enantioselective Synthesis of Boryl Tetrahydroquinolines via Cu-Catalyzed Hydroboration

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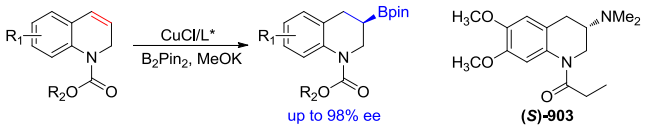


ABSTRACT: A Cu-catalyzed regio- and enantioselective hydroboration of 1,2-dihydroquinolines with high yields and excellent enantioselectivities (up to 98% ee) was presented. This method could be applied in the asymmetric synthesis of the important intermediates used in the enantioselective synthesis of the potential agent Sumanirole for the treatment of Parkinson's disease and potentially interesting positive inotropic agent (*S*)-903.

INTRODUCTION

Chiral 1,2,3,4-tetrahydroquinolines, particularly 3-substituted tetrahydroquinolines, are an important class of compounds widely present in natural products, pharmaceuticals and biologically active compounds, such as Sumanirole, Duocarmycin D_1 and (*S*)-903 (**Figure 1**). [1-3] Owing to their significance, there are great interests and efforts in the development of convenient and general approaches to construct the optically active tetrahydroquinoline. [4-6]

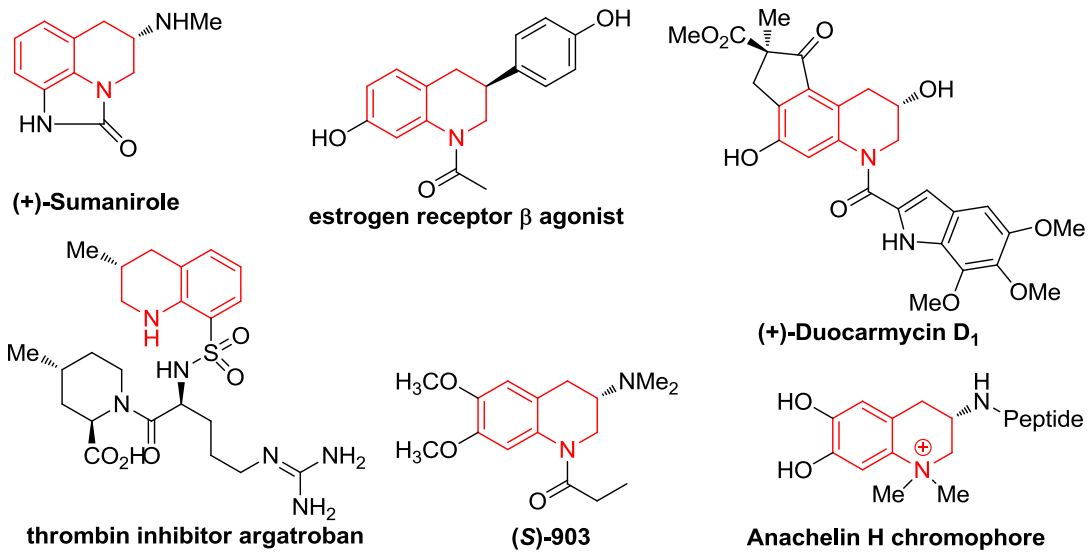
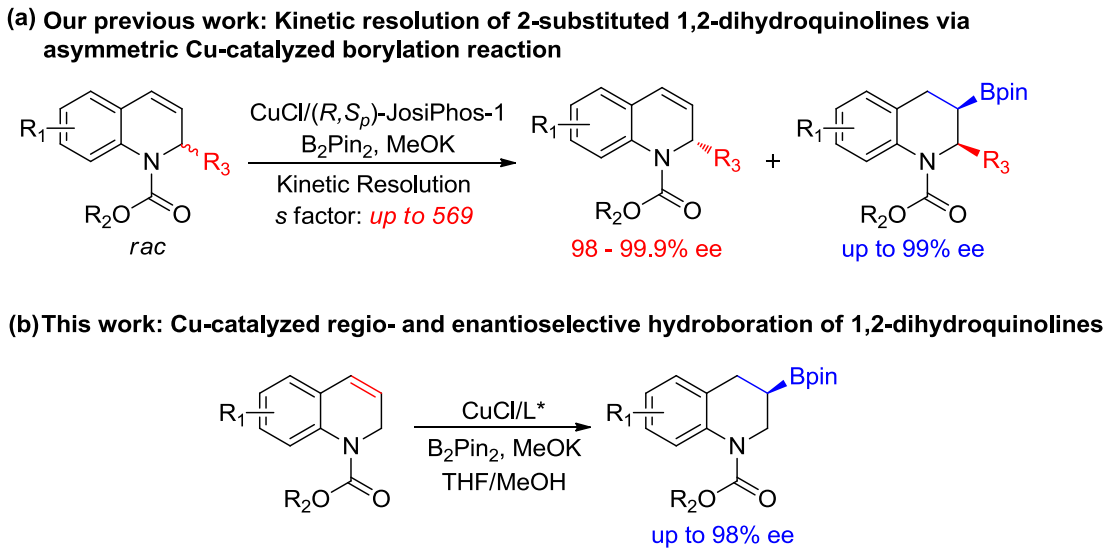


Figure 1. Selected bioactive compounds containing tetrahydroquinolines.

In addition, the synthesis of chiral organoboron compounds has been more and more attractive because of their wide application as key intermediates in versatile transformations including C-C and C-heteroatom bond formation. Over the past few decades, a large number of hydroboration reactions of alkenes have been developed by Cu, [7] Co, [8] Rh, [9] Ir [10] and NHC catalysis, [11] and some excellent results have also been achieved. Thereinto, Cu catalysts have received considerable attention due to their low cost, high earth abundance, and environmentally benign nature. Cu-catalyzed hydroboration of unsaturated C-C bonds provides an expedient access to organoboron compounds, [12-14] which can offer enabling platforms for chemical synthesis and functional-group transformations. [15] On the other hand, notwithstanding lots of examples on asymmetric hydroboration, the range of substrates involved is mainly non-cyclic alkenes. In sharp contrast, there are few reports on the hydroboration of cyclic substrates. At this regard, the Yun and Tortosa groups independently reported Cu-catalyzed hydroboration of bicyclic alkenes [13c] and cyclobutenes [12b] respectively. Ito and co-workers made outstanding contribution on the hydroboration of *N*-hetero cyclic substrates and reported Cu-catalyzed asymmetric hydroboration

of indoles, [13a] pyridines [13b] and dihydroquinolines derivatives [16] with high enantioselectivities via the strategy of sequential dearomatization/borylation. More recently, we have presented the first kinetic resolution of *N*-CO_2R-2-substituted 1,2-dihydroquinolines by asymmetric Cu-catalyzed borylation reaction under mild conditions achieving excellent kinetic resolution efficiency (**Scheme 1a**), which the *N*-CO_2R-protected group is widely used in organic synthesis and can be readily removed for synthetic purposes.[17] Considering the great utility of chiral organoboron compounds and tetrahydroquinolines in organic and pharmaceutical synthesis and as part of our continuous work, we attempted to conduct the enantioselective hydroboration of 1,2-dihydroquinolines. Herein, we present an approach to the synthesis of chiral 3-boryl-tetrahydroquinolines with up to 98% ee via Cu-catalyzed enantioselective hydroboration of *N*-CO_2R-protected 1,2-dihydroquinolines, which are readily prepared by the partial reduction of quinolines **(Scheme 1b**). Moreover, chiral 3-boryl-tetrahydroquinolines can be readily converted into other useful molecules.

Scheme 1. Cu-catalyzed hydroboration of 1,2-dihydroquinolines.

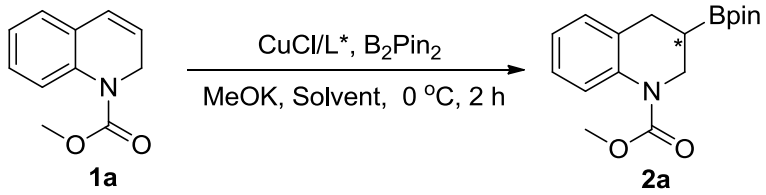


RESULTS AND DISCUSSION

We initially started our study with the evaluation of (*S,R*)-DuanPhos in the hydroboration of methyl quinoline-1(2*H*)-carboxylate **1a** with B_2pin_2 in the presence of catalytic amounts of CuCl and ^{t}BuOK at 0 ^{o}C affording the desired chiral 3-boryl-tetrahydroquinoline **2a** with good yield and enantioselectivity, 87% ee (**Table 1, entry 1**). Using ^{t}BuONa as the base, a moderate yield was observed albeit similar enantioselectivity obtained (**entry 2**). It was demonstrated that MeOK could provide higher yield with the same enantioselectivity (**entry 3**). Changing the metal precursor with $Cu(CH_3CN)PF_4$ which often exhibited good performance in hydroboration reactions, a little lower yield was provided without any erosion of enantioselectivity (**entry 4**). To our delight, when we used the JosiPhos type ligand (*R,S$_p$*)-JosiPhos-1 (**L2**), both higher yield (92%) and enantioselectivity (94% ee) were achieved (**entry 5**). Some other JosiPhos derivatives were also evaluated in this transformation. It was found that moderate enantioselectivities (63% ee and 77% ee) were afforded by (*S,R$_p$*)-JosiPhos-2 (**L3**) and (*R,S$_p$*)-JosiPhos-3 (**L4**) with poor yields (**entries 6 and 7**). Likewise, a similar yield and racemic product were observed when (*R,S$_p$*)-JosiPhos-4 (**L5**) was used in the reaction **(entry 8**). A variety of commercial available chiral bisphosphine ligands (**L6-L9**) were also screened. The use of (*S*)-Binap and (*R,R*)-Me-Duphos gave product **2a** with lower yields albeit comparable enantioselectivities obtained (**entries 9 and 11**). The ligand (*R*)-DM-SEGPHOS which exhibited excellent performance in the hydroboration of various non-cyclic alkenes only achieved very poor yield in the hydroboration of **1a**, (**entry 10**). Notably, (*R,R*)-QuinoxP* was the ligand of better choice, providing hydroboration product **2a** in 93% isolated yield and with outstanding enantioselectivity, 96% ee (**entry 12**). Then, we examined the effect of solvents including toluene, DME (1,2-dimethoxyethane) and DCE (1,2-dichloroethane) with the ligand (*R,R*)-QuinoxP* (**L9**) (**entries 13-15**). Although the

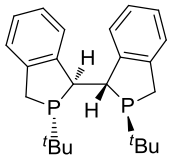
hydroboration products could be obtained with comparably high enantioselectivities (91-94% ee), the yields were dramatically decreased (27-44%). Finally, the optimal reaction conditions of CuCl/(*R*,*R*)-QuinoxP*/MeOK/THF were established.

Table 1. Reaction optimization.[a]

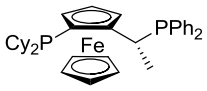


Entry	Ligand	Solvent	Base	Yield (%)[b]	ee (%)[c]
1	**L1**	THF	^{t}BuOK	71	87
2	**L1**	THF	^{t}BuONa	58	86
3	**L1**	THF	MeOK	76	87
4[d]	**L1**	THF	MeOK	65	87
5	**L2**	THF	MeOK	92	94
6	**L3**	THF	MeOK	32	63
7	**L4**	THF	MeOK	13	77
8	**L5**	THF	MeOK	15	0
9	**L6**	THF	MeOK	30	82
10	**L7**	THF	MeOK	8[e]	NA
11	**L8**	THF	MeOK	58	86
12	**L9**	THF	MeOK	93	96
13	**L9**	toluene	MeOK	36	94
14	**L9**	DME	MeOK	44	94

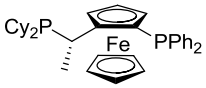
15	**L9**	DCE	MeOK	27	91



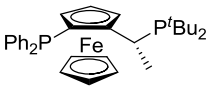
(*S*,*R*)-DuanPhos
(L1)



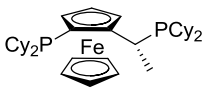
(*R*,S_p)-JosiPhos-1
(L2)



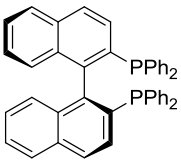
(*S*,R_p)-JosiPhos-2
(L3)



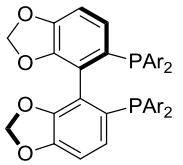
(*R*,S_p)-JosiPhos-3
(L4)



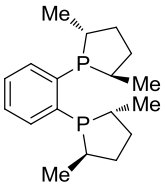
(*R*,S_p)-JosiPhos-4
(L5)



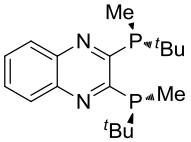
(*S*)-Binap
(L6)



Ar = 3,5-$(Me)_2C_6H_3$
(*R*)-DM-SEGPHOS
(L7)



(*R*,*R*)-Me-DuPhos
(L8)



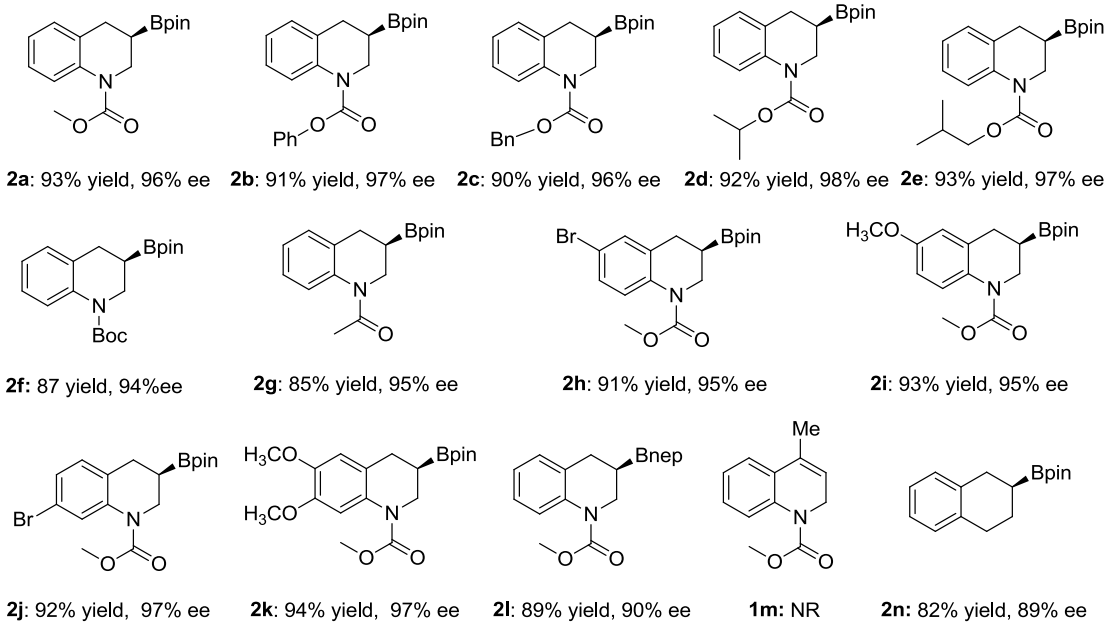
(*R*,*R*)-QuinoxP*
(L9)

[a] Reaction conditions: CuCl (0.025 mmol), ligand (0.025 mmol), **1a** (0.5 mmol), B_2Pin_2 (0.6 mmol), base (0.1 mmol), solvent (1.5 mL), MeOH (1.0 mmol), 0 ^oC, 2 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] $Cu(CH_3CN)PF_4$. [e] NMR yield.

Encouraged by the promising result obtained in the hydroboration of the substrate **1a**, we next subjected a variety of *N*-protected 1,2-dihydroquinolines (**Tabel 2**, **1b-1l**) to the hydroboration under the optimized conditions and all of them gave the corresponding products in satisfactory yields and with excellent enantioselectivities. Worth to note, 1, 2-dihydroquinolines bearing various -CO_2R protecting group on the nitrogen atom were suitable for the hydroboration affording the desired products **2a-2f** with excellent enantioselectivities of 94-98% ee and high yields, which demonstrated that the protecting group of substrates had no obvious influence on this transformation. For example, changing the R group of carbamates with methyl (**2a**), phenyl (**2b**), benzyl (**2c**), isopropyl (**2d**), isobutyl (**2e**), and ^{t}butyl (**2f**) similar results were achieved. *N*-Ac-protected 1,2-dihydroquinolines **1g** could also be hydroborylated with high enantioselectivity of 95% ee albeit a slightly decreased yield (85%). Furthermore, 1,2-dihydroquinolines bearing a Br or MeO group at 6- or 7-position (**1h-1k**) were smoothly

converted to the desired products with high yields (91-94%) and enantioselectivities (95-97% ee). Even the substrate with two MeO substituents at 6- and 7-position of the phenyl moiety could provide the product **2k** with 94% yield and excellent enantioselectivity, 96% ee. These results indicated that the electronic properties of the substituents on the phenyl moiety of the substrates had no apparent effect on the yield and enantioselectivity of the reaction. In addition, instead of B_2Pin_2, the substrate **1a** was also hydroborylated with B_2nep_2 under the optimized conditions to afford the corresponding 3-boryl-tetrahydroquinoline **2k** with high enantioselectivity, 90% ee. To be notable, this catalyst system was not effective for substrates bearing a substituent at 4-position. For example, attaching a methyl group at 4-position of the substrate as **1m** resulted in extremely poor reactivity. Finally, we also evaluated this catalyst in the hydroboration of 1,2-dihydronaphthalene (**1n**) and the corresponding desired product **2n** was also provided with good yield and enantioselectivity.

Table 2. Substrate scope. [a, b, c]



2a: 93% yield, 96% ee **2b**: 91% yield, 97% ee **2c**: 90% yield, 96% ee **2d**: 92% yield, 98% ee **2e**: 93% yield, 97% ee

2f: 87 yield, 94%ee **2g**: 85% yield, 95% ee **2h**: 91% yield, 95% ee **2i**: 93% yield, 95% ee

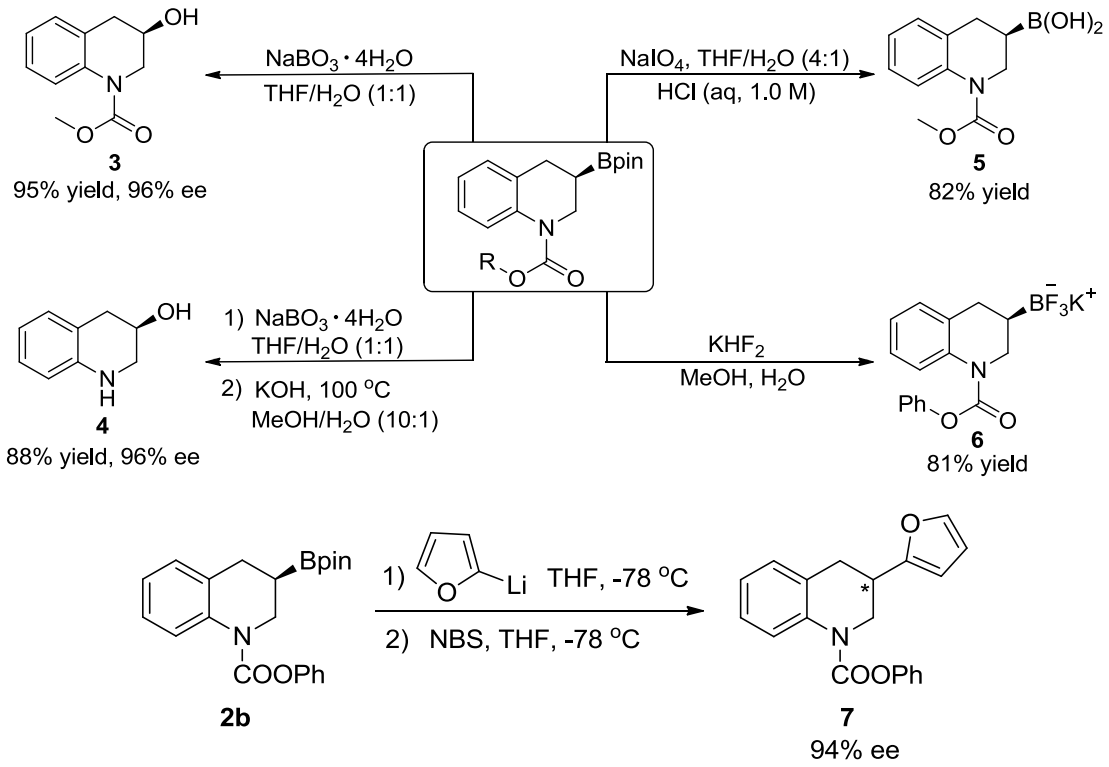
2j: 92% yield, 97% ee **2k**: 94% yield, 97% ee **2l**: 89% yield, 90% ee **1m:** NR **2n:** 82% yield, 89% ee

[a] Unless otherwise mentioned, all reaction were carried out with CuCl (0.025 mmol),

(*R*,*R*)-QuinoxP* (0.025 mmol), **1** (0.5 mmol), B_2Pin_2 or B_2nep_2 (0.6 mmol), MeOK (0.1 mmol), THF (1.5 mL), MeOH (1.0 mmol), 0 ^oC, 2 h. [b] Isolated yield. [c] Determined by chiral HPLC and SFC analysis, and the absolute configuration of the products **2** were assigned by comparison with the reported optical rotation of the corresponding hydroxyl compounds obtained by oxidation of products **2**. [12h, 16]

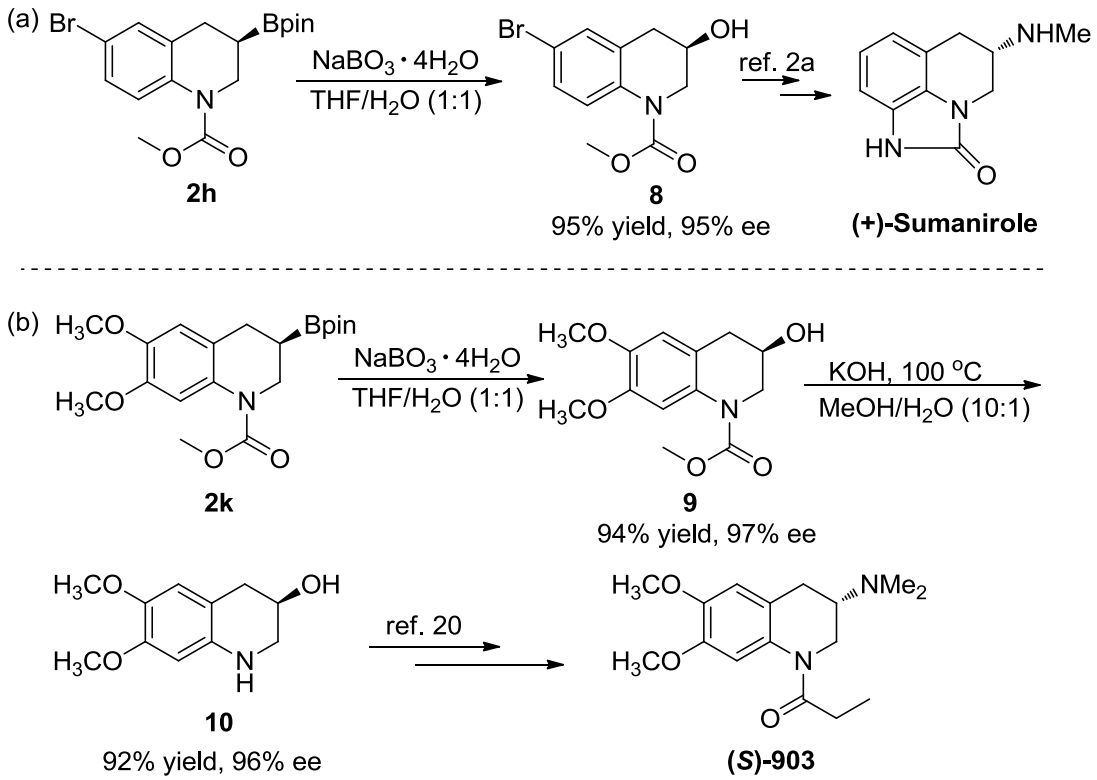
The chiral 3-boryl-tetrahydroquinolines **2** are versatile synthetic intermediates that can be easily converted to numerous other derivatives (**Scheme 2**). [12a, 18] For example, the product **2a** could be converted into the chiral 3-hydroxyl tetrahydroquinoline **3** in 95% yield without any loss of enantioslectivity by the oxidation of $NaBO_3$. The oxidation of the **2a** with $NaBO_3$ and followed by deprotection of the ester moiety afforded the chiral 3-hydroxyl tetrahydroquinoline **4** without the loss of optical activity, 96% ee. The **2a** could also be converted into the boronic acid **5** in the presence of $NaIO_4$ and HCl (aq). In addition, the **2b** was smoothly transformed into trifluoroborate salt **6** in the presence of KHF_2 (aq) with MeOH in good yield. As the important coupling reagent, the chiral boronate ester **2b** could be used to construct C-C bond for synthesis of **7** by coupling reaction. To demonstrate the potential application of this reaction, the hydroboration of **1a** was also carried out on a gram scale (6 mmol, 1.14g) under a lower catalyst loading of 1 mol% CuCl/(*R*,*R*)-QuinoxP*. Satisfyingly, both the high yield of 94% and excellent enantioselectivity, 96% ee, were still maintained.

Scheme 2. Representative transformations of products 2.



Notably, the oxidation of the product **2h** with 95% ee by $NaBO_3$ afforded the 3-hydroxyl tetrahydroquinoline **8** with unchanged ee value which could be subsequently applied to the enantioselective synthesis of Sumanirole.[2a, 19] Besides, the oxidation of the boronate ester **2k** with $NaBO_3$ and followed by deprotection of the carbonate moiety provided the chiral 3-hydroxyl tetrahydroquinoline **10** without any loss of enantioselectivity, which could be used as the important intermediate to the synthesis of potentially interesting positive inotropic agent (*S*)-903 (**Scheme 3**) according to the literature.[20]

Scheme 3. Applications of chiral products 2.



CONCLUSIONS

In summary, we have demonstrated Cu-catalyzed regio- and enantioselective hydroboration of 1,2-dihydroquinolines with high yield and excellent enantioselectivities. This protocol could be successfully applied in the asymmetric synthesis of the important intermediates used in the enantioselective synthesis of the potential agent Sumanirole for the treatment of Parkinson's disease and potentially interesting positive inotropic agent (*S*)-903.

EXPERIMENTAL SECTION

General Information: All the air or moisture sensitive reactions and manipulations were performed by using standard Schlenk techniques and in a nitrogen-filled glovebox. DME, THF and toluene were distilled from sodium benzophenone ketyl. DCE was distilled from calcium hydride. Anhydrous MeOH was distilled from magnesium. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AV (400 MHz) spectrometers and JEOL JNM-ECX600P and JNM-ECS600

(600 MHz) spectrometers ($CDC1_3$ was the solvent used for the NMR analysis, with TMS as the internal standard. Chemical shifts were reported upfield to TMS (0.00 ppm) for ^1H NMR. Data is represented as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, dd = double of doublets, t = triplet, q = quartet, m = multiplet) and coupling constants (*J*) in Hertz (Hz). Optical rotation was determined using Autopol III Automatic polarimeter. HPLC and SFC analysis were conducted on 1260 series instrument. HRMS were recorded on a Waters LCT Premier XE mass spectrometer with APCI or ESI.

Preparation and Analytical Data of Substrates 1: To a solution of quinoline or substituted quinoline (20 mmol) in MeOH (30.0 mL) was added dropwise $ClCO_2R$ (24 mmol) at 0 ^oC under a nitrogen atmosphere, then $NaBH_4$ (20 mmol) was added portionwise at 0 ^oC over 1 h. The reaction mixture was then allowed to warm to room temperature. After 2-3 h, the solution was carefully quenched with H_2O and extracted with EtOAc. The organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was purified by silica gel column chromatography using petroleum ether/ EtOAc as an eluent (PE/EA/ = 4/1 to 30/1) to give the corresponding 1,2-dihydroquinoline (**1a-1e** and **1g-1j**) as light yellow oil, which was immediately used and stored at -30 ^oC under an nitrogen atmosphere in order to prevent decomposition. [13b]

To a mixture of quinoline (10 mmol), acetic anhydride (12 mL) and acetic acid (40 mL) was gradually added $NaBH_4$ (40 mmol) at 0 ^oC over 1.5 h. After the addition was complete, the reaction mixture was then allowed to warm to room temperature. After 1 h, the reaction mixture was concentrated under vacuum, diluted with H_2O, neutralized with sodium carbonate and extracted with DCM. The organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was purified by silica gel column chromatography using petroleum ether/EtOAc as an

eluent (PE/EA/ = 5/1) to give the corresponding 1,2-dihydroquinoline **1f** as a light yellow oil. [21]

Methyl quinoline-1(2*H*)-carboxylate (1a): 0.65 g, yield: 17%; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 7.57 (d, J = 7.2 Hz, 1H), 7.26-7.18 (m, 1H), 7.09-7.05 (m, 2H), 6.49 (d, J = 9.6 Hz, 1H), 6.02-5.98 (m, 1H), 4.41 (dd, J = 4.2 Hz, 1.8 Hz, 2H), 3.79 (s, 3H). ^{13}C{^{1}H}NMR ($CDCl_3$, 150 MHz) δ: 154.8, 136.4, 128.1, 127.5, 126.5, 126.4, 125.6, 124.5, 123.7, 53.1, 43.6. TOF-HRMS Calcd. for $C_{11}H_{12}NO_2$ [M+H$^+$]: 190.0862, found 190.0861.

Phenyl quinoline-1(2*H*)-carboxylate (1b): 2.3 g, yield: 46%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.72 (s, 1H), 7.42-7.38 (m, 2H), 7.26-7.12 (m, 6H), 6.58 (dd, J = 9.6 Hz, 1.3 Hz, 1H), 6.11-6.06 (m, 1H), 4.56 (s, 2H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 153.2, 151.6, 136.5, 129.9, 128.8, 128.1, 127.1, 127.0, 126.2, 125.5, 124.3, 122.2, 44.4. TOF-HRMS Calcd. for $C_{16}H_{13}NO_2Na$ [M+Na$^+$]: 274.0838, found 274.0838.

Benzyl quinoline-1(2*H*)-carboxylate (1c): 1.65 g, yield: 31%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.68 (d, J = 6.6 Hz, 1H), 7.45-7.34 (m, 5H), 7.26-7.21 (m, 1H), 7.13-7.08 (m, 2H), 6.52 (d, J = 9.6 Hz, 1H), 6.03-5.99 (m, 1H), 5.29 (s, 2H), 4.47 (dd, J = 4.2 Hz, 1.8 Hz, 2H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 154.7, 136.9, 136.8, 129.2, 128.8, 128.7, 128.6, 128.0, 127.0, 126.9, 126.0, 125.1, 124.3, 68.3, 44.2. TOF-HRMS Calcd. for $C_{17}H_{15}NO_2Na$ [M+Na$^+$]: 288.0995, found 288.0994.

Isopropyl quinoline-1(2*H*)-carboxylate (1d): 0.61 g, yield: 14%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.60 (d, J = 8.1 Hz, 1H), 7.26-7.15 (m, 1H), 7.04 (d, J = 4.1 Hz, 2H), 6.47 (dd, J = 9.4, 1.4 Hz, 1H), 6.01-5.96 (m, 1H), 5.08-5.02 (m, 1H), 4.42-4.39 (m, 2H), 1.31 (d, J = 6.3 Hz, 6H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 154.4, 137.1, 128.5, 127.8, 127.0, 126.8, 126.1, 124.7, 124.1, 70.3, 43.8, 22.6. TOF-HRMS Calcd. for $C_{13}H_{16}NO_2$ [M+H$^+$]: 218.1175, found 218.1177.

Isobutyl quinoline-1(2*H*)-carboxylate (1e): 0.51 g, yield: 11%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ:

7.59 (d, *J* = 8.0 Hz, 1H), 7.21-7.17 (m, 1H), 7.08-7.04 (m, 2H), 6.48 (dt, *J* = 9.5 Hz, 1.4 Hz, 1H), 6.02-5.98 (m, 1H), 4.42 (dd, *J* = 4.2 Hz, 1.8 Hz, 2H), 3.98 (d, *J* = 6.6 Hz, 2H), 2.03-1.93 (m, 1H), 0.95 (d, *J* = 6.7 Hz, 6H). $^{13}C\{^{1}H\}$NMR ($CDCl_3$, 100 MHz) *δ*: 154.9, 137.0, 128.5, 127.8, 127.0, 126.8, 126.1, 124.8, 124.2, 72.8, 43.9, 28.4, 19.7. TOF-HRMS Calcd. for $C_{14}H_{18}NO_2$ [M+H$^+$]: 232.1332, found 232.1332.

***tert*-butyl quinoline-1(2*H*)-carboxylate (1f):** 1.1 g, 60 % yield; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.26 -7.04 (4H, m), 6.52 (1H, d, *J* = 9.6 Hz), 6.03 (1H, s), 4.44- 4.36 (2H, m), 1.49 (9H, s). The analytical data are consistent with the literature.[21]

1-(Quinolin-1(2*H*)-yl)ethanone (1g): 1.02 g, yield: 59%; ^{1}H NMR ($CDCl_3$, 600 MHz) *δ*: 7.28-7.11 (m, 4H), 6.53 (d, *J* = 9.5 Hz, 1H), 6.10-6.09 (m, 1H), 4.47 (s, 2H), 2.21 (s, 3H). $^{13}C\{^{1}H\}$NMR ($CDCl_3$, 150 MHz) *δ*: 170.1, 137.1, 129.4, 128.3, 127.2, 126.5, 126.2, 125.7, 123.9, 41.4, 22.5. [21]

Methyl 6-bromoquinoline-1(2*H*)-carboxylate (1h): 0.54 g, yield: 10%; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.46 (d, *J* = 8.0 Hz, 1H), 7.27 (dd, *J* = 8.7 Hz, 2.3 Hz, 1H), 7.16 (d, *J* = 2.3 Hz, 1H), 6.38 (d, *J* = 9.6 Hz, 1H), 6.03-5.98 (m, 1H), 4.38 (dd, *J* = 4.2 Hz, 1.8 Hz, 2H), 3.78 (s, 3H). $^{13}C\{^{1}H\}$NMR ($CDCl_3$, 100 MHz) *δ*: 155.0, 135.8, 130.6, 130.3, 129.4, 127.4, 125.9, 125.7, 117.7, 53.7, 44.0. TOF-HRMS Calcd. for $C_{11}H_{10}NBrO_2Na$ [M+Na$^+$]: 289.9787, found 289.9791.

Methyl 6-methoxyquinoline-1(2*H*)-carboxylate (1i): 0.92g, yield: 21%; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.46 (s, 1H), 6.75 (dd, *J* = 11.8 Hz, 2.9 Hz, 1H), 6.60 (d, *J* = 2.9 Hz, 1H), 6.44 (d, *J* = 9.6 Hz, 1H), 6.04-5.99 (m, 1H), 4.37 (dd, *J* = 4.1 Hz, 1.7 Hz, 2H), 3.77 (d, *J* = 5.2 Hz, 6H). $^{13}C\{^{1}H\}$NMR ($CDCl_3$, 100 MHz) *δ*: 156.9, 155.4, 130.0, 129.7, 127.0, 125.3, 113.3, 111.7, 56.0, 53.5, 44.0. TOF-HRMS Calcd. for $C_{12}H_{14}NO_3$ [M+H$^+$]: 220.0968, found 220.0966.

Methyl 7-bromoquinoline-1(2*H*)-carboxylate (1j): 0.97 g, yield: 18%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.78 (s, 1H), 7.16 (dd, J = 8.1 Hz, 2.0 Hz, 1H), 6.88 (d, J = 8.1 Hz, 1H), 6.41 (d, J = 9.6 Hz, 1H), 6.00-5.95 (m, 1H), 4.37 (dd, J = 4.2 Hz, 1.8 Hz, 2H), 3.79 (s, 3H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 154.9, 137.9, 128.0, 127.9, 127.2, 126.9, 126.2, 121.2, 53.8, 44.1. TOF-HRMS Calcd. for $C_{11}H_{10}NBrO_2Na$ [M+Na^{+}]: 289.9787, found 289.9791.

Methyl 6,7-dimethoxyquinoline-1(2*H*)-carboxylate (1k): 0.80 g, yield: 16%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.25 (s, 1H), 6.56 (s, 1H), 6.39 (d, J = 9.5 Hz, 1H), 5.89-5.84 (m, 1H), 4.35 (dd, J = 4.1 Hz, 1.5 Hz, 2H), 3.85 (d, J = 10.2 Hz, 6H), 3.77 (s, 3H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 155.3, 148.5, 146.5, 130.5, 126.6, 123.6, 121.5, 109.7, 108.7, 56.7, 56.6, 53.5, 43.9. TOF-HRMS Calcd. for $C_{13}H_{16}NO_4$ [M+H^{+}]: 250.1073, found 250.1069.

methyl 4-methylquinoline-1(2*H*)-carboxylate (1m): 1.75 g, yield: 43%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.57-7.56 (m, 1H), 7.27-7.21 (m, 2H), 7.15-7.11 (m, 1H), 5.80 (s, 1H), 4.33-4.31 (m, 2H), 3.77 (s, 3H), 2.05 (d, J = 1.5 Hz, 3H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 155.2, 136.9, 132.2, 130.4, 127.7, 124.9, 124.3, 123.8, 122.7, 53.5, 43.7, 18.9. TOF-HRMS Calcd. for $C_{12}H_{14}NO_2$ [M+H^{+}]: 204.1019, found 204.1025.

1,2-dihydronaphthalene (1n) : 760 mg, 80% yield; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 7.31-7.22 (3H, m), 7.16 (1H, t, J = 10.7 Hz), 6.61-6.60 (1H, m), 6.18-6.14 (1 H, m), 2.95-2.92 (2H, m), 2.45 (2H, t, J = 2.4 Hz). ^{13}C{^{1}H}NMR ($CDCl_3$, 150 MHz) δ: 135.7, 134.4, 128.8, 128.1, 127.8, 127.1, 126.7, 126.1, 27.8, 23.5. The analytical data are consistent with the literature. [22]

General procedure of Cu-catalyzed enantioselective hydroboration of 1,2-dihydroquinolines 2: In a nitrogen-filled glovebox, CuCl (0.025 mmol), (*R*,*R*)-QuinoxP* (0.025 mmol), B_2pin_2 or B_2nep_2 (0.6 mmol) and KOMe (0.1 mmol) were placed in an oven-dried Schleck reaction vial,

which was sealed with a rubber plug. The Schleck reaction vial was then removed from glovebox. THF (1.5 mL) was added to the Schleck vial through the rubber plug. After **1** (0.50 mmol) was added to the mixture at 0 ℃, MeOH (1.0 mmol) was added dropwise. Upon completion of the reaction, the reaction mixture was passed through a short silica gel column eluting with Et_2O. The crude mixture was purified by chromatography on silica gel using petroleum ether/EtOAc as an eluent (PE/EA/ = 3/1 to 20/1) to give the corresponding borylation product **2**. The ee values of **2** were determined by HPLC or SFC analysis on a chiral stationary phase.

(*R*)-methyl

3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (2a): 147.5 mg, yield: 93%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.68 (d, J = 8.1 Hz, 1H), 7.26-7.06 (m, 2H), 6.98-6.94 (m, 1H), 4.11-4.06 (m, 1H), 3.78 (s, 3H), 3.59-3.48 (m, 1H), 2.87-2.70 (m, 2H), 1.59-1.51 (m, 1H), 1.21 (s, 12H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 155.9, 138.6, 130.9, 128.9, 126.4, 124.2, 123.9, 84.1, 53.3, 46.9, 30.2, 29.6, 25.3. TOF-HRMS Calcd. for $C_{17}H_{25}BNO_4$ [M+H$^+$]: 318.1874, found 318.1873. 96% ee; $[\alpha]_D^{25}$ = -30.2 (c = 1.0, $CHCl_3$); Enantiomeric excess of the corresponding hydroxyl compound obtained by oxidation with $NaBO_3$ in THF/H_2O (1:1); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 20:80, 1.0 mL/min, 254 nm; t_A = 11.8 min (minor), t_B = 15.2 min (major).

(*R*)-phenyl

3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (2b): 172.6 mg, yield: 91%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.83 (d, J = 7.1 Hz, 1H), 7.39 (t, J = 8.2 Hz, 2H), 7.26-7.13 (m, 5H), 7.03 (t, J = 7.3 Hz, 1H), 4.27 (dd, J = 12.7 Hz, 4.7 Hz, 1H), 3.73 (t, J = 11.4 Hz, 1H), 2.97-2.81 (m, 2H), 1.73-1.65 (m, 1H), 1.24 (s, 12H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100

MHz) δ: 153.8, 151.9, 138.3, 131.3, 129.8, 129.0, 126.6, 125.9, 124.3, 122.4, 84.3, 47.5, 30.3, 29.7, 25.3. TOF-HRMS Calcd. for $C_{22}H_{27}BNO_4$ [M+H$^+$]: 380.2032, found 380.2033. 97% ee; $[\alpha]_D^{25}$ = -41.4 (c = 1.0, $CHCl_3$); SFC condition: Lux 5u Cellulose-1 (250 × 4.60 mm), CO_2 : ipa = 95:5, 2.5 mL/min, 230 nm; t_A = 12.0 min (minor), t_B = 12.8 min (major).

(*R*)-benzyl

3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (2c): 177.0 mg, yield: 90%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.75 (d, *J* = 8.0 Hz, 1H), 7.45-7.31 (m, 5H), 7.17-7.09 (m, 2H), 7.01-6.98 (m, 1H), 5.31-5.24 (m, 2H), 4.16 (dd, *J* = 12.6 Hz, 4.8 Hz, 1H), 3.66-3.61 (m, 1H), 2.92-2.76 (m, 2H), 1.65-1.57 (m, 1H), 1.23 (s, 12H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 155.3, 138.6, 137.2, 131.0, 129.1, 129.0, 128.6, 128.5, 126.5, 124.4, 124.0, 84.1, 67.9, 47.0, 29.7, 25.3. TOF-HRMS Calcd. for $C_{23}H_{29}BNO_4$ [M+H$^+$]: 394.2188, found 394.2186. 96% ee; $[\alpha]_D^{25}$ = -32.5 (c = 1.0, $CHCl_3$); Enantiomeric excess of the corresponding hydroxyl compound obtained by oxidation with $NaBO_3$ in THF/H_2O (1:1); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 30:70, 1.0 mL/min, 254 nm; t_A = 9.8 min (minor), t_B = 10.8 min (major).

(*R*)-isopropyl

3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (2d): 158.8 mg, yield: 92%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.67 (d, *J* = 8.2 Hz, 1H), 7.12-7.04 (m, 2H), 6.95-6.91 (m, 1H), 5.07-4.98 (m, 1H), 4.06 (dd, *J* = 12.7 Hz, 4.8 Hz, 1H), 3.52-3.46 (m, 1H), 2.86-2.69 (m, 2H), 1.58-1.50 (m, 1H), 1.30 (dd, *J* = 6.3 Hz, 1.8 Hz, 6H), 1.19 (s, 12H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 155.1, 138.8, 130.9, 128.9, 126.3, 124.4, 123.6, 84.0, 69.8, 46.7, 29.8, 25.2, 22.7. TOF-HRMS Calcd. for $C_{19}H_{29}BNO_4$ [M+H$^+$]: 346.2188, found 346.2187.

98% ee; $[\alpha]_D^{25}$ = -38.4 (c = 1.0, $CHCl_3$); Enantiomeric excess of the corresponding hydroxyl compound obtained by oxidation with $NaBO_3$ in THF/H_2O (1:1); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 30:70, 1.0 mL/min, 254 nm; t_A = 5.6 min (minor), t_B = 6.9 min (major).

(*R*)-isobutyl

3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (2e): 167.1 mg, yield: 93%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.67 (d, J = 8.2 Hz, 1H), 7.13-7.05 (m, 2H), 6.97-6.93 (m, 1H), 4.08 (dd, J = 12.7 Hz, 4.7 Hz, 1H), 4.00-3.92 (m, 2H), 3.55-3.49 (m, 1H), 2.87-2.71 (m, 2H), 2.02-1.94 (m, 1H), 1.59-1.52 (m, 1H), 1.19 (s, 12H), 0.96 (d, J = 6.7 Hz, 6H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 155.5, 138.7, 130.9, 128.9, 126.3, 124.4, 123.7, 84.1, 72.4, 46.8, 29.7, 28.5, 25.2, 19.8. TOF-HRMS Calcd. for $C_{20}H_{31}BNO_4$ [M+H$^+$]: 360.2344, found 360.2347. 97% ee; $[\alpha]_D^{25}$ = -29.8 (c = 1.0, $CHCl_3$); Enantiomeric excess of the corresponding hydroxyl compound obtained by oxidation with $NaBO_3$ in THF/H_2O (1:1); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 30:70, 1.0 mL/min, 254 nm; t_A = 5.6 min (minor), t_B = 6.9 min (major).

(*R*)-*tert*-butyl

3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (2f): 312 mg, 87% yield; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 7.22-6.88 (4H, m), 4.08 (1H, s), 3.59-3.54 (1H, m), 2.86 (1H, dd, J = 16.0 Hz, 5.4 Hz), 2.74 (1H, t, J = 15.8 Hz), 1.62 (1H, m), 1.49 (9H, s), 1.20 (12H, s). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 148.8, 147.6, 137.0, 128.5, 126.3, 124.7, 123.9, 85.1, 83.8, 47.3, 28.5, 27.5, 24.8. TOF-HRMS Calcd. for $C_{20}H_{30}NO_4Na$ [M+Na$^+$]: 382.2164, found 382.2167. 94% ee; $[\alpha]^D_{20}$ = -0.018 (c = 1.0, $CHCl_3$); Enantiomeric excess of the corresponding

hydroxyl compound was obtained by the oxidation with $NaBO_3$ in THF/H_2O (1:1); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 20:80, 0.7 mL/min, 254 nm; t_A = 13.6 min (major), t_B = 14.3 min (minor).

(*R*)-1-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinolin-1(2*H*)-yl)ethanone (2g): 128 mg, yield: 85%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.07-6.95 (m, 4H), 3.88 (s, 1H), 3.62-3.56 (m, 1H), 2.75-2.70 (m, 1H), 2.63-2.57 (m, 1H), 2.14 (m, 3H), 1.47 (s, 1H), 1.11 (s, 12H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 170.7, 139.3, 128.7, 126.4, 125.3, 125.1, 84.1, 83.0, 75.4, 29.2, 25.3, 25.2, 25.1. TOF-HRMS Calcd. for $C_{17}H_{25}BNO_3$ [M+H$^+$]: 302.1925, found 302.1923. 95% ee; $[\alpha]_D^{25}$ = -20.2 (c = 1.0, $CHCl_3$); Enantiomeric excess of the corresponding hydroxyl compound obtained by oxidation with $NaBO_3$ in THF/H_2O (1:1); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 30:70, 1.0 mL/min, 254 nm; t_A = 9.9 min (minor), t_B = 12.1 min (major).

(*R*)-methyl 6-bromo-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquino-line-1(2*H*)-carboxylate (2h): 180.2 mg, yield: 91%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.60 (d, *J* = 8.6 Hz, 1H), 7.26-7.19 (m, 2H), 4.05-4.01 (m, 1H), 3.78 (s, 3H), 3.54-3.48 (m, 1H), 2.83-2.67 (m, 2H), 1.56-1.49 (m, 1H), 1.20 (s, 12H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 155.7, 137.7, 133.0, 131.5, 129.4, 125.8, 116.6, 84.3, 53.4, 46.9, 29.6, 25.3, 25.2. TOF-HRMS Calcd. for $C_{17}H_{24}BBrNO_4$ [M+H$^+$]: 396.0979, found 396.0983. 95% ee; $[\alpha]_D^{25}$ = -35.7 (c = 1.0, $CHCl_3$); Enantiomeric excess of the corresponding hydroxyl compound obtained by oxidation with $NaBO_3$ in THF/H_2O (1:1); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 30:70, 1.0 mL/min, 254 nm; t_A = 7.2 min (minor), t_B = 7.8 min (major).

(*R*)-methyl

6-methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (2i): 161.5 mg, yield: 93%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.55 (d, J = 8.6 Hz, 1H), 6.68 (dd, J = 9.0 Hz, 2.6 Hz, 1H), 6.60-6.59 (m, 1H), 4.04 (dd, J = 12.7 Hz, 4.7 Hz, 1H), 3.73 (d, J = 7.6 Hz, 6H), 3.49-3.43 (m, 1H), 2.83-2.67 (m, 2H), 1.56-1.48 (m, 1H), 1.19 (s, 12H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 156.1, 155.9, 132.2, 132.0, 125.4, 113.6, 112.2, 84.1, 55.9, 53.1, 46.7, 29.8, 25.2. TOF-HRMS Calcd. for $C_{18}H_{27}BNO_5$ [M+H$^+$]: 348.1980, found 348.1981. 98% ee; $[\alpha]_D^{25}$ = -31.9 (c = 1.0, $CHCl_3$); SFC condition: Lux 5u Cellulose-1 (250 × 4.60 mm), CO_2 : ipa = 95:5, 2.5 mL/min, 230 nm; t_A = 6.9 min (major), t_B = 7.5 min (minor).

(*R*)-methyl

7-bromo-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydro-quinoline-1(2*H*)-carboxylate (2j): 182.2 mg, yield: 92%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.93 (s, 1H), 7.07 (dd, J = 8.1 Hz, 1.8 Hz, 1H), 6.97-6.90 (m, 1H), 4.03 (dd, J = 12.8 Hz, 4.6 Hz, 1H), 3.79 (s, 3H), 3.52-3.47 (m, 1H), 2.81-2.62 (m, 2H), 1.53-1.48 (m, 1H), 1.20 (s, 12H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 155.6, 139.8, 130.2, 129.6, 126.8, 126.7, 119.6, 84.2, 53.5, 46.9, 30.2, 29.4, 25.3. TOF-HRMS Calcd. for $C_{17}H_{24}BBrNO_4$ [M+H$^+$]: 396.0979, found 396.0983. 97% ee; $[\alpha]_D^{25}$ = -37.2 (c = 1.0, $CHCl_3$); Enantiomeric excess of the corresponding hydroxyl compound obtained by oxidation with $NaBO_3$ in THF/H_2O (1:1); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 10:90, 1.0 mL/min, 254 nm; t_A = 19.1 min (minor), t_B = 20.2 min (major).

(*R*)-methyl

6,7-dimethoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (2k): 177.3 mg, yield: 94%; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 7.30 (1H, d, J = 44.3 Hz),

6.54 (1H, s), 4.07 (1H, dd, *J* = 12.7 Hz, 4.2 Hz), 3.83-3.75 (9H, m), 3.47-3.35 (1H, m), 2.73 (2H, dd, *J* = 16.1 Hz, 8.0 Hz), 1.56-1.49 (1H, m), 1.19 (12H, s). $^{13}C\{^{1}H\}$NMR ($CDCl_3$, 150 MHz) δ: 155.3, 146.7, 145.3, 131.2, 121.9, 111.1, 107.7, 100.0, 83.7, 56.0, 52.8, 46.2, 28.7, 24.8, 24.6. TOF-HRMS Calcd. for $C_{19}H_{29}BNO_6$ [M+H$^+$]: 378.2086, found 378.2081. 97% ee; $[\alpha]_D^{25}$ = -39.6 (c = 1.0, $CHCl_3$); Enantiomeric excess of the corresponding hydroxyl compound obtained by oxidation with $NaBO_3$ in THF/H_2O (1:1); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 30:70, 1.0 mL/min, 254 nm; t_A = 19.2 min (minor), t_B = 21.7 min (major).

(*R*)-methyl 3-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (2l): 134.9 mg, yield: 89%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.68 (d, *J* = 7.8 Hz, 1H), 7.15-7.06 (m, 2H), 6.99-6.95 (m, 1H), 4.10 (dd, *J* = 12.7 Hz, 4.7 Hz, 1H), 3.78 (s, 3H), 3.60 (s, 4H), 3.43 (t, *J* = 11.5 Hz, 1H), 2.85-2.67 (m, 2H), 1.49-1.41 (m, 1H), 0.93 (s, 6H). $^{13}C\{^{1}H\}$NMR ($CDCl_3$, 100 MHz) δ: 156.0, 138.7, 131.5, 128.9, 126.3, 124.2, 123.8, 53.3, 47.2, 32.2, 29.9, 22.3.TOF-HRMS Calcd. for $C_{16}H_{23}BNO_4$ [M+H$^+$]: 304.1718, found 304.1724. 90% ee; $[\alpha]_D^{25}$ = -21.4 (c = 1.0, $CHCl_3$); Enantiomeric excess of the corresponding hydroxyl compound obtained by oxidation with $NaBO_3$ in THF/H_2O (1:1); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 20:80, 1.0 mL/min, 254 nm; t_A = 12.2 min (minor), t_B = 15.6 min (major).

(*S*)-4,4,5,5-tetramethyl-2-(1,2,3,4-tetrahydronaphthalen-2-yl)-1,3,2-dioxaborolane (2n): 168 mg, 82% yield; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 7.10-6.96 (4H, m), 2.94-2.74 (4H, m), 2.08-1.98 (1H, m), 1.72-1.65 (1H, m), 1.36-1.34 (1H, m), 1.27 (12H, s). $^{13}C\{^{1}H\}$NMR ($CDCl_3$, 150 MHz) δ: 137.6, 137.1, 129.2, 129.0, 125.4, 83.2, 30.8, 29.8, 24.9. The analytical data are consistent with the literature.[12h] 89% ee; $[\alpha]^{D}_{20}$ = –0.415 (c = 1.0, $CHCl_3$). Enantiomeric excess of the corresponding hydroxyl compound was obtained by the oxidation with NaBO3 in THF/H_2O (1:1);

HPLC condition: Lux 5μm Amylose-1 (250 × 4.60 mm), ipa : hex = 10:90, 1.0 mL/min, 254 nm; t_A = 6.6 min (major), t_B = 7.2 min (minor).

Procedure for the synthesis of 3 [13a]: In a round bottom flask, **2a** (0.2 mmol) was dissolved in THF/H_2O (1:1, 4 mL). $NaBO_3$•$4H_2O$ (1.0 mmol) was added at room temperature. After stirred for 2 h, the reaction mixture was extracted with EtOAc, dried over Na_2SO_4, and filtered. The residue was purified by silica gel chromatography using petroleum ether/EtOAc as an eluent (PE/EA = 1/1) to afford **3**. 39.3 mg, yield: 95%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.61 (d, J = 8.0 Hz, 1H), 7.17-7.01 (m, 3H), 4.21-4.16 (m, 1H), 3.82-3.67 (m, 5H), 3.19 (s, 1H), 3.06-3.01 (m, 1H), 2.78-2.73 (m, 1H). ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ: 156.4, 138.0, 130.0, 127.6, 126.7, 124.8, 124.3, 65.3, 53.7, 51.0, 36.5. The analytical data are consistent with the literature. [2a] 96% ee; $[\alpha]_D^{25}$ = -38.4 (c = 1.0, $CHCl_3$); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 20:80, 1.0 mL/min, 254 nm; t_A = 11.8 min (minor), t_B = 15.2 min (major).

Procedure for the synthesis of 4 [13a, 23]: In a round bottom flask, **2a** (0.2 mmol) was dissolved in THF/H_2O (1:1, 4 mL). $NaBO_3$•$4H_2O$ (1.0 mmol) was added at room temperature. After stirred for 2 h, the reaction mixture was extracted with EtOAc, dried over Na_2SO_4, and filtered. The resulting crude material was used in the next reaction without further purification. To a solution of this intermediate in a mixture of MeOH and H_2O (1:1, 5.5 mL) was added KOH (9.0 mmol) at rt. The resulting mixture was heated to 100 ^{o}C. After the reaction was completed, and the reaction mixture was extracted with DCM, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/EtOAc as an eluent (PE/EA/ = 2/1) to afford **4**, 26.2 mg, yield: 88%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.03-7.68 (m, 2H), 6.69 (t, J = 7.4 Hz, 1H), 6.54 (d, J = 7.9 Hz, 1H), 4.25-4.23 (m, 1H), 3.35-3.32 (m, 1H), 3.26-3.22 (m, 1H),

3.07-3.02 (m, 1H), 2.81-2.76 (m, 1H). $^{13}C\{^{1}H\}$NMR ($CDCl_3$, 100 MHz) δ: 144.2, 131.1, 127.6, 119.2, 118.7, 114.7, 63.9, 48.2, 36.0. The analytical data are consistent with the literature.[5b] 96% ee. $[\alpha]_D^{25}$ = +12.6 (c = 1.0, $CHCl_3$); SFC condition: Lux 5u Cellulose-1 (250 × 4.60 mm), CO_2 : MeOH = 90:10, 2.5 mL/min, 210 nm; t_A = 8.2 min (minor), t_B = 8.6 min (major).

Procedure for the synthesis of 5 [17]: In a round bottom flask, **2a** (0.5 mmol) was dissolved in a THF and H_2O (4:1, 2 mL). $NaIO_4$ (0.75 mmol) was then added at rt, and the suspension was stirred for 15 min. HCl (aq, 1.0 M, 0.50 mL) was added. After the completion of the reaction, the reaction mixture was extracted with EtOAc. The combined organic layers were washed with H_2O and brine, dried with Na_2SO_4, filtered, and concentrated under vacuum to give the product **5**. 96.4 mg, yield: 82%; $[\alpha]_D^{25}$ = -32.2 (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 7.65 (1H, d, *J* = 7.3 Hz), 7.18 (1H, t, *J* = 7.8 Hz), 7.10 (1H, d, *J* = 7.6 Hz), 7.05 (1H, t, *J* = 7.4 Hz), 4.29 (1H, s), 3.81 (2H, d, *J* = 4.8 Hz), 3.79 (3H, d, *J* = 1.5 Hz), 3.09 (1H, dd, *J* = 16.5 Hz, 5.2 Hz), 2.81 (1H, dd, *J* = 16.4 Hz, 5.3 Hz), 1.88 (1H, s), 1.60 (1 H, s). $^{13}C\{^{1}H\}$NMR ($CDCl_3$, 150 MHz) δ: 155.8, 137.6, 129.6, 126.7, 126.5, 124.4, 123.9, 65.1, 53.2, 50.6, 36.1. TOF-HRMS Calcd. for $C_{11}H_{14}BNO_4Na$ $[M+Na^+]$: 258.0910, found 258.0912.

Procedure for the synthesis of 6 [12b]: In a round bottom flask, **2b** (0.5 mmol) was dissolved in MeOH (2 mL), An aqueous solution of KHF_2 (4.5M, 2.5 mmol) was added to the flask. The solution was stirred at rt for 4 h. After the evaporation of the solvent under vacuum, the residual pinacol was removed by adding three portions of Et_2O, retiring the resulting solution. The solid that was obtained was triturated with acetone and filtered through a plug of Celite. The acetone solution was evaporated to yield the compound **6**, 120.3mg, yield: 81%; $[\alpha]_D^{25}$ = +24.8 (c = 0.5, CH_3COCH_3); ^{1}H NMR (DMSO, 600 MHz) δ: 7.68-6.96 (m, 9H), 4.02 (s, 1H), 2.61-2.39 (m,

4H). ^{13}C NMR (DMSO, 150 MHz) δ: 153.4, 151.8, 138.3, 135.2, 129.8, 128.5, 125.7, 125.5, 123.7, 123.6, 122.6, 50.7, 40.4, 40.3, 40.2, 40.0, 39.9, 39.8, 39.6. TOF-HRMS Calcd. for $C_{16}H_{14}BF_3NO_2$ [M-K^+]: 320.1078, found 320.1074.

Procedure for the synthesis of 7: To a solution of furan (22 μL, 0.3 mmol) in THF (1 mL) was added *n*-BuLi (2.5 M in hexane, 0.3 mmol) at -78 ^{o}C, and the reaction was stirred for 1h at -78 ^{o}C. Then the **2b** (75.9 mg, 0.2 mmol) in THF (0.5 mL) was added to the reaction mixture. After stirred for 1h at -78 ^{o}C, the solution of NBS (53.5 mg, 0.3 mmol) in THF (0.5 mL) was added dropwise. After stirred 1h at -78 ^{o}C, a saturated aqueous solution of $Na_2S_2O_3$ was added and the reaction mixture was then allowed to warm to room temperature. The reaction mixture was extracted with EtOAc. The organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was purified by silica gel column chromatography using petroleum ether/EtOAc as an eluent (PE/EA = 15/1) to give the corresponding product **7** as a light yellow oil.[24] 26 mg, 40 % yield; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 7.81 (1H, s), 7.39-7.33 (3H, m), 7.22 -7.18 (3H, m), 7.12-7.08 (3H, m), 6.32 (1H, dd, J = 3.2 Hz, 1.9 Hz), 6.12 (1H, dt, J = 3.2 Hz, 0.8 Hz), 4.38-4.32 (1H, m), 3.92-3.83 (1H, m), 3.48-3.39 (1H, m), 3.24 (1H, dd, J = 16.5 Hz, 6.1 Hz), 3.10 (1H, dd, J = 16.5 Hz, 8.9 Hz). ^{13}C{^{1}H}NMR ($CDCl_3$, 150 MHz) δ: 155.5, 153.2, 151.2, 147.4, 141.8, 137.6, 129.4, 129.1, 126.4, 125.6, 124.5, 121.8, 110.3, 105.5, 100.0, 48.6, 33.9, 32.1.TOF-HRMS Calcd. for $C_{20}H_{17}NO_3Na$ [M+Na^+]: 342.1100, found 342.1105. 94% ee; $[\alpha]^D_{20}$ = – 0.322 (c = 1.0, $CHCl_3$); HPLC condition: Lux 5u Cellulose-1 (250 × 4.60 mm), ipa : hex = 10:90, 1.0 mL/min, 210 nm; t_A = 12.2 min (major), t_B = 13.0 min (minor).

Procedure for the synthesis of 8 [13a]: In a round bottom flask, **2h** (0.2 mmol) was dissolved in THF/H_2O (1:1, 4 mL). $NaBO_3$•$4H_2O$ (1.0 mmol) was added at room temperature. After stirred for

2 h, the reaction mixture was extracted with EtOAc, dried over Na_2SO_4, and filtered. The residue was purified by silica gel chromatography using petroleum ether/EtOAc as an eluent (PE/EA/ = 2/1) to afford **8**, 57.2 mg, yield: 95%; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 7.53 (1H, d, J = 8.3 Hz), 7.30-7.19 (2H, m), 4.31-4.14 (1H, m), 3.78-3.70 (5H, m), 3.01 (1H, d, J = 16.3 Hz), 2.75 (1H, d, J = 15.6 Hz), 2.46 (1H, s). ^{13}C{^{1}H}NMR ($CDCl_3$, 150 MHz) δ: 155.7, 136.7, 132.1, 129.4, 129.0, 125.4, 117.2, 64.4, 53.4, 50.4, 35.8. The analytical data are consistent with the literature. [2a] 95% ee; $[\alpha]_D^{25}$ = +23.6 (c = 1.0, $CHCl_3$); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 30:70, 1.0 mL/min, 254 nm; t_A = 7.2 min (minor), t_B = 7.8 min (major).

Procedure for the synthesis of 9 [13a]: In a round bottom flask, **2k** (0.3 mmol) was dissolved in THF/H_2O (1:1, 6 mL). $NaBO_3$•$4H_2O$ (1.5 mmol) was added at room temperature. After stirred for 2 h, the reaction mixture was extracted with EtOAc, dried over Na_2SO_4, and filtered. The residue was purified by silica gel chromatography using petroleum ether/EtOAc as an eluent (PE/EA/ = 1/1) to afford **9**, 75.4 mg, yield: 94%; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 7.32-7.26 (m, 1H), 6.55 (s, 1H), 4.27-4.25 (m, 1H), 3.86-3.73 (m, 11H), 3.03 (dd, J = 16.5 Hz, 5.4 Hz, 1H), 2.73 (dd, J = 16.5 Hz, 5.2 Hz, 1H), 2.03-2.01 (m, 1H). ^{13}C{^{1}H}NMR ($CDCl_3$, 150 MHz) δ: 156.3, 147.6, 146.6, 131.1, 112.1, 108.2, 65.5, 56.6, 53.6, 50.9, 36.2. TOF-HRMS Calcd. for $C_{13}H_{18}NO_5$ [M+H$^+$]: 268.1179, found 268.1184. 97% ee; $[\alpha]_D^{25}$ = -29.8 (c = 1.0, $CHCl_3$); HPLC condition: Lux 5u Cellulose-4 (250 × 4.60 mm), ipa : hex = 30:70, 1.0 mL/min, 254 nm; t_A = 19.2 min (minor), t_B = 21.7 min (major).

Procedure for the synthesis of 10 [23]: To a solution of **9** (0.2 mmol) in a mixture of MeOH and H_2O (1:1, 5.5 mL) was added KOH (9.0 mmol) at rt. The resulting mixture was heated to 100 ^{o}C. After the reaction was completed, and the reaction mixture was extracted with DCM, dried over

Na_2SO_4 and evaporated under reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/EtOAc as an eluent (PE/EA = 1/2) to afford **10**, 38.5mg, yield: 92%; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 6.52 (1H, s), 6.15 (1H, s), 4.21 (1H, s), 3.79 (6H, d, *J* = 8.1 Hz), 3.25 (1H, d, *J* = 11.1 Hz), 3.20 (1H, dd, *J* = 11.2 Hz, 4.9 Hz), 2.98 (1H, dd, *J* = 16.3 Hz, 4.2 Hz), 2.69 (1H, dd, *J* = 15.9 Hz, 2.9 Hz), 2.71-2.67 (1H, m). ^{13}C{^{1}H}NMR ($CDCl_3$, 150 MHz) δ: 148.5, 142.3, 137.4, 114.5, 110.1, 99.6, 63.7, 56.7, 56.0, 47.9, 35.1. The analytical data are consistent with the literature.[5b] 96% ee; $[\alpha]_D^{25}$ = +19.2 (c = 1.0, $CHCl_3$); SFC condition: Lux 5u Cellulose-1 (250 × 4.60 mm), CO_2 : MeOH = 97:3, 2.5 mL/min, 210 nm; t_A = 8.7 min (major), t_B = 9.2 min (minor).

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SUPPORTING INFORMATION

NMR and HPLC spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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