Cite this paper: Li, B.; Xu, C.; He, Y.-M.; Deng, G.-J.; Fan, Q.-H. *Chin. J. Chem.* **2018**, *36*, 1169—1173.

Concise Report

DOI: 10.1002/cjoc.201800363

Asymmetric Hydrogenation of Bis(quinolin-2-yl)methanes: A Direct Access to Chiral 1,3-Diamines†

Bin Li,[a,b,‡] Cong Xu,[a,‡] Yan-Mei He,*[,a] Guo-Jun Deng,[b] and Qing-Hua Fan*[,a,c]

ABSTRACT The asymmetric hydrogenation of bis(quinolin-2-yl)methanes was described, using chiral cationic ruthenium/monosulfonated diamine complexes to afford chiral bis(tetrahydroquinolin-2-yl)methanes in high yield with excellent enantioselectivity and diastereoselectivity. The subsequent transformation of these 1,3-diamines to a new class of chiral 6-membered *N*-heterocyclic carbenes was also developed, which is important but difficult to access.

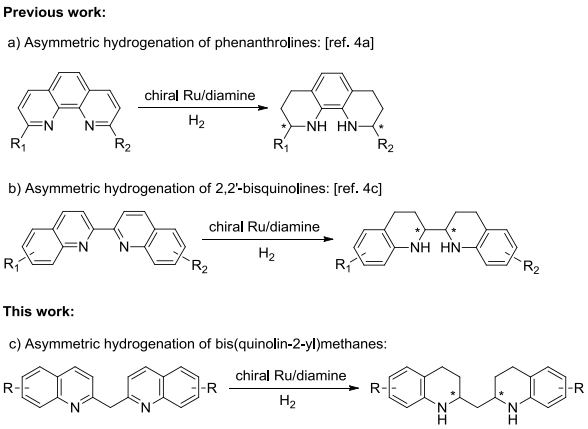
KEYWORDS asymmetric catalysis, hydrogenation, chiral 1,3-diamines, heterocycles, ruthenium

Introduction

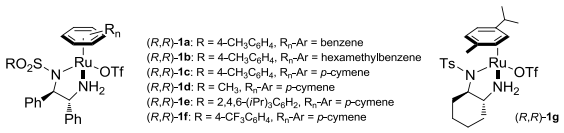
Chiral diamines are of great importance for their wide applications in both laboratory studies and industry manufacture, and they have gained extensive attention.[1,2] Compared with the extensively studied vicinal diamines,[1a] 1,3-diamines are less investigated. Enantiomerically enriched 1,3-diamines are important compounds or key structure units in natural products, pharmacologically active compounds, and chiral ligands.[2] Many methods have been developed for the effective preparation of these chiral diamine compounds.[3,4] However, the direct asymmetric syntheses of chiral 1,3-diamines are rarely reported.[3e-3l,4]

Transition-metal-catalyzed asymmetric hydrogenation (AH) of imines and *N*-containing heteroaromatic compounds is one of the most efficient methods for the synthesis of optically active amines.[5] Despite great progress made in this field, only a few examples about the synthesis of chiral diamines were reported.[4] Recently, we found that the cationic ruthenium complexes of chiral monosulfonated diamines are very efficient catalysts for AH of quinolines[6] as well as the more challenging substrates of phenanthroline[4a] and 2,2′-bisquinoline[4c] derivatives, providing a direct access to chiral vicinal diamines (Scheme 1). Encouraged by these results and given the importance of chiral 1,3-diamines, we herein describe the ruthenium-catalyzed AH of a new type of easily available but challenging substrate of bis(quinoline-2-yl)-methanes. To the best of our knowledge, this is the first example for the enantioselective synthesis of chiral bis(tetrahydroquinolin-2-yl)methanes, which could be easily derived to give a new class of chiral *N*-heterocyclic carbenes (NHCs) ligands.[7] These NHCs are difficult to access through other methods.

Scheme 1 Enantioselective syntheses of chiral diamines *via* asymmetric hydrogenation by Fan group



Scheme 2 The chiral ruthenium-diamine catalysts used in this work



Results and Discussion

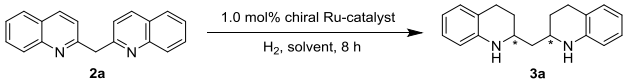
To start our initial investigations, several chiral ruthenium/monosulfonated diamine complexes (Scheme 2) were prepared according to the well-established method.[6b]

Then, bis(quinolin-2-yl)methane **2a** was selected as the model substrate for the screening of catalysts and the optimization of reaction conditions (Table 1). Generally, under the reaction conditions checked, full conversions and > 99% enantiomeric excesses were obtained, while the diastereoselectivity varied greatly. The screen of ruthenium catalysts was carried out in isopropanol under 50 atm of H_2 at room temperature. It was noted that the catalyst performance was affected by the substituents on the η^6–arene ligand (entries 1—3). Catalyst (*R*,*R*)-**1c** bearing a *p*-cymene co-ligand gave the best diastereoselectivity (> 20 : 1 *dr*). The substituent on the *N*-monosulfonate group also influenced the diastereoselectivity (entries 3—6). When tosyl group was replaced by 2,4,6-triisopropylphenyl or electron-withdrawing 4-trifluoromethylphenyl groups (entries 5 and 6), low *dr* values were obtained. The use of (*R*,*R*)-1,2-cyclohexyl diamine ligand also led to the decrease of diastereoselectivity (entry 7). From all the results obtained, **1c** was selected as the optimal catalyst for this study. Subsequently, isopropanol was proved to be optimal after the solvent screen (entries 8—15). The variation of reaction temperature and/or H_2 pressure did not affect the reaction outcome (entries 16—

[a] Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences (CAS), and University of Chinese Academy of Sciences, Beijing 100190, China
[b] Key Laboratory of Environmentally Friendly Chemistry of the Ministry of Education, College of Chemistry, Xiangtan University, Xiangtan, Hunan 411105, China
[c] Collaborative Innovation Center of Chemical Science and Engineering (Tianjin), Tianjin 300071, China
*E-mail: heym@iccas.ac.cn; fanqh@iccas.ac.cn
‡ These authors contributed equally to this work.
† Dedicated to Professor Xiyan Lu on the occasion of his 90th birthday.

18).

Table 1 Optimization of reaction conditions for the AH of **2a**[a]



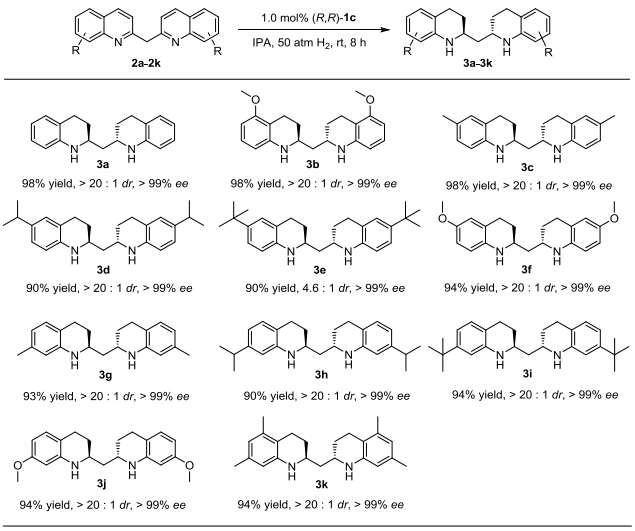
Entry	Catalyst	Solvent	H_2/atm; T/°C	Conv.[b]/%	*dr*[b]	*ee*[c]/%
1	(*R*,*R*)-**1a**	IPA	50; 25	> 95	5.1 : 1	> 99
2	(*R*,*R*)-**1b**	IPA	50; 25	> 95	15.8 : 1	> 99
3	**(*R*,*R*)-1c**	**IPA**	**50; 25**	**> 95**	**> 20 : 1**	**> 99**
4	(*R*,*R*)-**1d**	IPA	50; 25	> 95	> 20 : 1	> 99
5	(*R*,*R*)-**1e**	IPA	50; 25	> 95	11.6 : 1	> 99
6	(*R*,*R*)-**1f**	IPA	50; 25	> 95	18.8 : 1	> 99
7	(*R*,*R*)-**1g**	IPA	50; 25	> 95	8.0 : 1	> 99
8	(*R*,*R*)-**1c**	THF	50; 25	> 95	7.3 : 1	> 99
9	(*R*,*R*)-**1c**	toluene	50; 25	> 95	3.2 : 1	95
10	(*R*,*R*)-**1c**	DCM	50; 25	> 95	5.6 : 1	> 99
11	(*R*,*R*)-**1c**	MeOH	50; 25	> 95	4.6 : 1	> 99
12	(*R*,*R*)-**1c**	EtOH	50; 25	> 95	7.3 : 1	> 99
13	(*R*,*R*)-**1c**	*n*-BuOH	50; 25	> 95	3.5 : 1	96
14	(*R*,*R*)-**1c**	*t*-BuOH	50; 25	> 95	13.1 : 1	> 99
15	(*R*,*R*)-**1c**	amylene alcohol	50; 25	> 95	9.8 : 1	> 99
16	(*R*,*R*)-**1c**	IPA	50; 50	> 95	> 20 : 1	> 99
17	(*R*,*R*)-**1c**	IPA	80; 25	> 95	> 20 : 1	> 99
18	(*R*,*R*)-**1c**	IPA	10; 25	> 95	> 20 : 1	> 99

[a] Reaction conditions: 0.2 mmol **2a** in 1.0 mL solvent, 1.0 mol% Ru-cat, 50 atm H_2, rt, stirred for 8 h. [b] The conversions and diastereoselectivities were determined by ^{1}H NMR spectroscopy and/or HPLC analysis of the crude reaction mixture. [c] The enantiomeric excesses were determined by HPLC with a chiral AS-H column. IPA＝isopropanol, THF＝tetrahydrofuran, DCM ＝dichloromethane.

Under the optimized reaction conditions (Table 1, entry 3), the substrate scope of various substituted bis(quinolin-2-yl)methanes was then explored (Scheme 3). For all the symmetric substrates bearing electron-donating groups, such as alkyls and methoxy group, excellent isolated yields (better than 90%) and enantioselectivities (> 99% *ee*) were achieved. For most chiral bis(tetraquinolin-2-yl)methanes products, *dr* values are excellent (*dr* > 20 : 1). Only the substrate **3e** bearing *tert*-butyl group at C6-position gave a low diastereoselectivity. The absolute configuration of **3a** was determined to be (*S*,*S*) based on the single-crystal X-ray analysis of the corresponding derivative **4** (see Scheme S1 in the Supporting Information).[8] The configurations of the other chiral products were assigned by analogy. To expand the substrate scope, we also tried to synthesize some bis(quinolin-2-yl)methanes bearing electron-withdrawing groups, but we failed.[9]

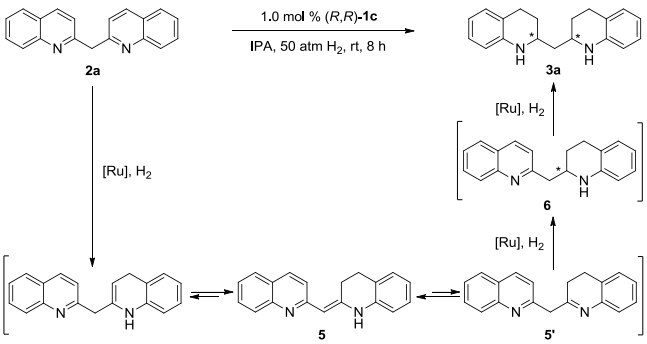
To gain further understanding of this catalytic process, several control experiments were carried out with **2a**. When the reaction temperature was lowered to 20 °C and H_2 pressure to 20 atm, only 74% conversion was observed, and a dihydro-intermediate **5** was mainly obtained. Compound **5** was then isolated and well characterized (Scheme S2). Further hydrogenation of **5** under the optimal reaction conditions offered the final product **3a** in similar diastereoselectivity and enantioselectivity with comparison to those obtained from the direct hydrogenation of **2a** (Scheme S3). Furthermore, the ESI-HRMS spectrum of the reaction mixture demonstrated the formation of not only the dihydro-intermediate **5** (*m*/*z* 273.13806) but also a tetrahydro-intermediate **6** (*m*/*z* 275.15369) (Scheme S4). On the basis of these experimental results and our previous study on the reaction mechanism of the Ru/diamine-catalyzed asymmetric hydrogenation of quinolines,[6b] we proposed a catalytic reaction pathway (Scheme 4).

Scheme 3 Scope of the asymmetric hydrogenation[a]



[a] Reaction conditions: 0.2 mmol **2** in 1.0 mL isopropanol, 1.0 mol% (*R*,*R*)-**1c**, 50 atm H_2, rt, stirred for 8 h. The yields are isolated yields. The diastereoselectivities were determined by ^{1}H NMR spectroscopy of the crude reaction mixture. The enantiomeric excesses were determined by HPLC with a chiral AS-H column.

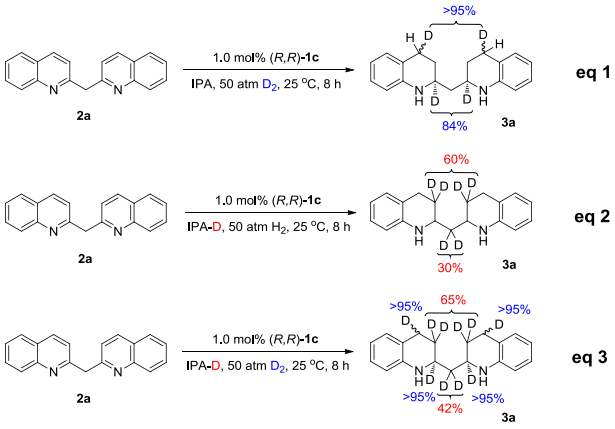
Scheme 4 A proposed catalytic pathway



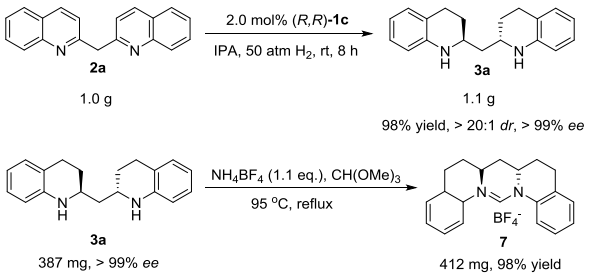
In the deuterium labeling study of the asymmetric hydrogenation with **2a** (Scheme 5), 84% and 95% deuterium incorporation was observed at the C2- and C4-positions, respectively, when deuterated gas was used (Scheme 5, eq 1). Instead, when hydrogenation was carried out in isopropanol-d8 under 50 atm H_2, the deuterium atoms were found at the C3-position of tetrahydroquinoline ring and the bridged methylene group (Scheme 5, eq 2). Expectedly, hydrogenation proceeded smoothly with both deuterated gas and solvent, providing **3a** with high deuterium incorporations at all the C1-, C2-, C3-, and C4-positions of tetrahydroquinoline ring and the bridged methylene group (Scheme 5, eq 3). All these results agree with the proposed catalytic pathway.

The potential application of this new method was demonstrated by a scale-up synthesis of (*S*,*S*)-**3a** and the preparation of a chiral 6-membered *N*-heterocyclic carbene precursor (Scheme 6). The asymmetric hydrogenation of **2a** on a gram scale gave (*S*,*S*)-**3a** in 98% isolated yield with > 20 : 1 *dr* and > 99% *ee*. Subsequent treatment of (*S*,*S*)-**3a** with trimethyl orthoformate and NH_4BF_4 offered the key NHC precursor **7** in 98% yield, providing a facile and practical approach to a new class of 6-membered rigid NHC ligands, which might be useful for asymmetric catalysis.[7]

Scheme 5 Deuterium-labeling studies



Scheme 6 Scale-up reaction and product transformation



Conclusions

In conclusion, the first asymmetric hydrogenation of bis(quinolin-2-yl)methanes by using chiral cationic ruthenium diamine catalysts was developed with up to 96% isolated yield, > 20 : 1 *dr*, and > 99% *ee*. This new protocol provides not only a practical and facile approach to the synthesis of optically pure chiral 1,3-diamines, but also a straight-forward and effective way to derive a novel class of 6-membered chiral NHC ligands, which are difficult to access through other methods. We believe this work will stimulate future study on the applications of these new chiral 1,3-diamines and NHC ligands in asymmetric catalysis.

Experimental

General procedure for the synthesis of bis(tetrahydroquinolin-2-yl)methanes

A 30 mL glass-lined stainless-steel reactor equipped with a magnetic stirrer bar was charged with Ru-catalyst (*R*,*R*)-**1c** (0.002 mmol), the corresponding bis(quinolin-2-yl)methanes **2** (0.2 mmol) in IPA (1.0 mL) under nitrogen atmosphere in a glove box. The autoclave was closed, and the final pressure of the hydrogen gas was adjusted to 50 atm after purging the autoclave with hydrogen gas several times. The reaction mixture was stirred at room temperature for 8 h. Then the hydrogen gas was carefully released and the conversion was determined by ^{1}H NMR. The reaction mixture was filtered through a short pad of silica (ethyl acetate/petroleum ether, 1/100, *V*/*V*) to give the pure products. The diastereoselectivities were determined by ^{1}H NMR spectroscopy or HPLC analysis, and the enantiomeric excess of the product was determined by HPLC with a chiral AS-H column.

(*S*,*S*)-**3a**: (New compound). Light yellow solid, m.p. 125—126 °C, isolated yield 98%, *dr* > 20 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+6.4 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.00—6.97 (m, 4H), 6.65 (t, *J*=7.4 Hz, 2H), 6.52 (d, *J*=8.0 Hz, 2H), 3.56—3.55 (m, 2H), 2.93—2.76 (m, 4H), 1.98—1.95 (m, 2H), 1.81—1.72 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 144.4, 129.5, 126.9, 121.6, 117.7, 114.8, 48.8, 42.4, 28.6, 26.6. HRMS-ESI exact mass calcd. for $C_{19}H_{23}N_2^+$ ($[M+H]^+$) requires *m*/*z* 279.18558, found *m*/*z* 279.18521. The enantiomeric excess was determined by HPLC on Chiralcel AS-H column (hexane : isopropanol=95 : 5, flowing rate=1 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=9.0 min (major), t_{R2}=11.3 min (minor).

(*S*,*S*)-**3b**: (New compound). Light yellow solid, m.p. 117—119 °C, isolated yield 98%, *dr* > 20 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+26.8 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 6.95 (t, *J*=8.0 Hz, 2H), 6.25 (d, *J*=8.0 Hz, 2H), 6.20 (d, *J*=8.0 Hz, 2H), 3.80 (s, 6H), 3.51—3.46 (m, 2H), 2.85—2.80 (m, 2H), 2.63—2.56 (m, 2H), 2.00—1.95 (m, 2H), 1.76—1.67 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 158.1, 145.4, 127.0, 110.2, 108.2, 99.9, 55.4, 48.3, 41.8, 28.3, 20.5. HRMS-ESI exact mass calcd. for $C_{21}H_{27}N_2O_2^+$ ($[M+H]^+$) requires *m*/*z* 339.20670, found *m*/*z* 339.20667. The enantiomeric excess was determined by HPLC on Chiralcel AS-H column (hexane : isopropanol=95 : 5, flowing rate=1.0 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=12.5 min (major), t_{R2}=18.7 min (minor).

(*S*,*S*)-**3c**: (New compound). Light yellow solid, m.p. 124—126 °C, isolated yield 98%, *dr* > 20 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+42.0 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 6.82—6.80 (m, 4H), 6.46 (d, *J*=8.8 Hz, 2H), 3.97 (br, s, 2H), 3.55—3.49 (m, 2H), 2.91—2.72 (m, 4H), 2.23 (s, 6H), 1.98—1.93 (m, 2H), 1.80—1.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 142.1, 130.0, 127.5, 127.0, 121.7, 115.0, 49.0, 42.4, 28.9, 26.6, 20.5. HRMS-ESI exact mass calcd. for $C_{21}H_{27}N_2^+$ ($[M+H]^+$) requires *m*/*z* 307.21688, found *m*/*z* 307.21634. The enantiomeric excess was determined by HPLC on Chiralcel As-H column (hexane : isopropanol=99 : 1, flowing rate=0.8 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=12.0 min (major), t_{R2}=15.2 min (minor).

(*S*,*S*)-**3d**: (New compound). Light yellow oil, isolated yield 90%, *dr* 20 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+35.6 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 6.88—6.86 (m, 4H), 6.48 (d, *J*=7.6 Hz, 2H), 4.15 (br, s, 2H), 3.53—3.51 (m, 2H), 2.93—2.75 (m, 6H), 1.97—1.93 (m, 2H), 1.80—1.71 (m, 4H), 1.21 (d, *J*=6.4 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 142.4, 138.4, 127.4, 124.9, 121.5, 115.0, 48.9, 42.4, 33.4, 28.9, 26.8, 24.4, 24.4. HRMS-ESI exact mass calcd. For $C_{25}H_{35}N_2^+$ ($[M+H]^+$) requires *m*/*z* 363.27948, found *m*/*z* 363.27917. The enantiomeric excess was determined by HPLC on Chiralcel AS-H column (hexane : isopropanol=99 : 1, flowing rate=1.0 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=8.7 min (major), t_{R2}=12.9 min (minor).

(*S*,*S*)-**3e**: (New compound). Light yellow oil, isolated yield 90%, *dr* 4 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+35.6 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.07—7.05 (m, 4H), 6.52 (d, *J*=8.0 Hz, 2H), 3.82 (br, s, 2H), 3.57—3.56 (m, 2H), 2.97—2.90 (m, 2H), 2.82—2.79 (m, 2H), 2.00—1.98 (m, 2H), 1.83—1.77 (m, 4H), 1.33 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 142.2, 140.6, 126.3, 123.9, 121.0, 114.6, 48.9, 42.5, 34.0, 31.7, 29.0, 26.9. HRMS-ESI exact mass calcd. for $C_{27}H_{39}N_2^+$ ($[M+H]^+$) requires *m*/*z* 391.31078, found *m*/*z* 391.31014. The enantiomeric excess was determined by HPLC on Chiralcel AS-H column (hexane : isopropanol=95 : 5, flowing rate=1.0 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=19.1 min (major), t_{R2}=26.7 min (minor).

(*S*,*S*)-**3f**: (New compound). Light yellow solid, m.p. 194—195 °C, isolated yield 94%, *dr* > 20 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+6.4 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 6.61—6.58 (m, 4H), 6.48 (d, *J*=8.4 Hz, 2H), 3.73 (s, 6H), 3.48—3.47 (m, 2H), 2.92—2.84 (m, 2H), 2.77—2.72 (m, 2H), 1.95—1.92 (m, 2H), 1.78—1.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 152.4, 138.5, 123.0, 116.1, 114.9, 113.1, 56.0, 49.2, 42.4, 28.9, 27.0. HRMS-ESI exact mass calcd. for $C_{21}H_{27}O_2N_2^+$ ($[M+H]^+$) requires *m*/*z* 339.20670, found *m*/*z* 339.20688. The enantiomeric excess was determined by HPLC on Chiralcel AS-H column (hexane : isopropanol=95 : 5, flowing rate=1.0 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=10.1 min

(major), t_{R2}=13.4 min (minor).

(*S*,*S*)-**3g**: (New compound). Light yellow solid, m.p. 107—108 °C, isolated yield 93%, *dr* > 20 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+44.4 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 6.88 (d, *J*=7.5 Hz, 2H), 6.49 (d, *J*=7.5 Hz, 2H), 6.36 (s, 2H), 4.09 (br, s, 2H), 3.55—3.51 (m, 2H), 2.88—2.82 (m, 2H), 2.77—2.72 (m, 2H), 2.25 (s, 6H), 1.97—1.94 (m, 2H), 1.79—1.71 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 144.3, 136.6, 129.4, 118.6, 115.3, 48.8, 42.4, 28.8, 26.2, 21.2. HRMS-ESI exact mass calcd. for $C_{21}H_{27}N_2^+$ ($[M+H]^+$) requires *m/z* 307.21688, found *m/z* 307.21686. The enantiomeric excess was determined by HPLC on Chiralcel AS-H column (hexane : isopropanol=95 : 5, flowing rate=1 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=10.7 min (minor), t_{R2}=13.6 min (major).

(*S*,*S*)-**3h**: (New compound). Light yellow oil, isolated yield 90%, *dr* > 20 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+86.4 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.03 (d, *J*=7.5 Hz, 2H), 6.66 (d, *J*=7.5 Hz, 2H), 6.52 (s, 2H), 4.14 (br, s, 2H), 3.64—3.61 (m, 2H), 3.00—2.83 (m, 6H), 2.07—2.03 (m, 2H), 1.89—1.81 (m, 4H), 1.34 (d, *J*=7.0 Hz, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 147.8, 144.3, 129.4, 119.0, 116.0, 112.7, 48.7, 42.5, 33.9, 28.8, 26.3, 24.1. HRMS-ESI exact mass calcd. for $C_{25}H_{35}N_2^+$ ($[M+H]^+$) requires *m/z* 363.27948, found *m/z* 363.27879. The enantiomeric excess was determined by HPLC on Chiralcel AS-H column (hexane : isopropanol=99 : 1, flowing rate=0.5 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=13.2 min (major), t_{R2}=18.2 min (minor).

(*S*,*S*)-**3i**: (New compound). Light yellow solid, m.p. 194—195 °C, isolated yield 94%, *dr* > 20 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+30.8 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 6.96 (d, *J*=8.0 Hz, 2H), 6.74 (dd, J_1=7.8 Hz, J_2=1.8 Hz, 2H), 6.59 (d, *J*=2.0 Hz, 2H), 4.19 (br, s, 2H), 3.59—3.53 (m, 2H), 2.93—2.74 (m, 4H), 2.01—1.95 (m, 2H), 1.82—1.72 (m, 4H), 1.30 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 150.2, 144.1, 129.2, 118.9, 115.1, 112.0, 48.8, 42.6, 34.4, 31.5, 29.0, 26.2. HRMS-ESI exact mass calcd. for $C_{21}H_{26}N_2^+$ ($[M+H]^+$) requires *m/z* 391.31078, found *m/z* 391.31074. The enantiomeric excess was determined by HPLC on Chiralcel AS-H column (hexane : isopropanol=95 : 5, flowing rate=1 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=15.8 min (minor), t_{R2}=19.6 min (major).

(*S*,*S*)-**3j**: (New compound). Light yellow solid, m.p. 177—178 °C, isolated yield 94%, *d.r.* > 20 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+40.4 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 6.89 (d, *J*=8.4 Hz, 2H), 6.26 (dd, J_1=8.2 Hz, J_2=2.6 Hz, 2H), 6.09 (d, *J*=2.4 Hz, 2H), 4.15 (br, s, 2H), 3.75 (s, 6H), 3.57—3.50 (m, 2H), 2.86—2.69 (m, 4H), 1.99—1.92 (m, 2H), 1.78—1.69 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 159.0, 145.3, 130.1, 114.1, 103.7, 99.9, 55.3, 48.7, 42.4, 28.9, 25.8. HRMS-ESI exact mass calcd. for $C_{21}H_{27}O_2N_2^+$ ($[M+H]^+$) requires *m/z* 339.20670, found *m/z* 339.20712. The enantiomeric excess was determined by HPLC on Chiralcel AS-H column (hexane : isopropanol=95 : 5, flowing rate=1 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=17.9 min (major), t_{R2}=33.3 min (minor).

(*S*,*S*)-**3k**: (New compound). Light yellow solid, m.p. 136—137 °C, isolated yield 94%, *dr* > 20 : 1, > 99% *ee*. $[\alpha]_D^{20}$=+26.4 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 6.40 (s, 2H), 6.24 (s, 2H), 3.49—3.45 (m, 2H), 2.71—2.59 (m, 4H), 2.20 (s, 6H), 2.15 (s, 6H), 2.02—1.98 (m, 2H), 1.79—1.72 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 144.5, 137.2, 136.1, 120.7, 117.4, 113.5, 48.4, 41.9, 29.0, 23.7, 21.1, 19.4. HRMS-ESI exact mass calcd. for $C_{23}H_{31}N_2^+$ ($[M+H]^+$) requires *m/z* 335.24818, found *m/z* 335.24776. The enantiomeric excess was determined by HPLC on Chiralcel AS-H olumn (hexane : isopropanol=99 : 1, flowing rate=0.8 mL/min, 25 °C, UV detection at *λ*=250 nm), t_{R1}=6.9 min (major), t_{R2}=8.3 min (minor).

(*S*,*S*)-**7**: (New compound). White solid, isolated yield 98%; m.p. 260—262 °C; $[\alpha]_D^{20}$=−197.6 (*c*=0.25, CH_2Cl_2); ^{1}H NMR (500 MHz, DMSO) *δ*: 9.23 (s, 1H), 7.90 (d, *J*=8.5 Hz, 2H), 7.39—7.29 (m, 6H), 4.08—4.05 (m, 2H), 3.06—2.93 (m, 4H), 2.41 (t, *J*=5.5 Hz, 2H), 2.21—2.17 (m, 2H), 2.04—1.96 (m, 2H); ^{13}C NMR (125 MHz, DMSO) *δ*: 148.5, 136.4, 130.0, 130.0, 127.2, 126.9, 118.4, 51.4, 30.4, 27.7, 25.7. HRMS-ESI exact mass calcd. for $C_{20}H_{21}N_2^+$ ($[M\text{-}BF_4]^+$) requires *m/z* 289.16993, found *m/z* 289.16977.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.201800363.

Acknowledgement

Financial supports from the National Natural Science Foundation of China (Nos. 21473216, 21521002 and 21790332) and CAS (QYZDJSSW-SLH023) are gratefully acknowledged.

References

[1] (a) Lucet, D.; Gall, T. L.; Mioskowski, C. *Angew. Chem. Int. Ed*. **1998**, *37*, 2580; (b) Kizirian, J.-C. *Chem. Rev*. **2008**, *108*, 140; (c) Hems, W. P.; Groarke, M.; Zanotti-Gerosa, A.; Grasa, G. A. *Acc. Chem. Res.* **2007**, *40,* 1340; (d) Kotti, S. R. S. S.; Timmons, C.; Li, G. *Chem. Biol. Drug Des.* **2006**, *67*, 101.

[2] (a) Busscher, G. F.; Rutjes, F. P. J. T.; van Delft, F. L. *Chem. Rev*. **2005**, *105*, 775; (b) Erickson, J.; Neidhart, D. J.; VanDrie, J.; Kempf, D. J.; Wang, X. C.; Norbeck, D. W.; Plattner, J. J.; Rittenhouse, J. W.; Turon, M.; Wideburg, N.; Kohlbrenner, W. E.; Simmer, R.; Helfrich, R.; Paul, D. A.; Knigge, M. *Science* **1990**, *249*, 527; (c) Franklin, A. S.; Ly, S. K.; Mackin, G. H.; Overman, L. E.; Shaka, A. J. *J. Org. Chem.* **1999**, *64*, 1512; (d) Cohen, F.; Overman, L. E. *J. Am. Chem. Soc.* **2001**, *123*, 10782; (e) Kodama, K.; Sugawara, K.; Hirose, T. *Chem. Eur. J*. **2011**, *17*, 13584; (f) Csillag, K.; Szakonyi, Z.; Fülöp, F. *Tetrahedron*: *Asymmetry* **2013**, *24*, 553; (g) Serra, M. E. S.; Murtinho, D.; Paz, V. *Tetrahedron*: *Asymmetry* **2017**, *28*, 381.

[3] For selected examples, see: (a) Kaiser, A.; Balbi, M. *Tetrahedron*: *Asymmetry* **1999**, *10*, 1001; (b) Yao, Q. J.; Judeh, Z. M. A. *Tetrahedron* **2011**, *67*, 4086; (c) Zhao, C.-H.; Liu, L.; Wang, D.; Chen, Y.-J. *Eur. J. Org. Chem.* **2006**, 2977; (d) Braun, W.; Calmuschi-Cula, B.; Englert, U.; Höfener, K.; Alberico, E.; Salzer, A. *Eur. J. Org. Chem.* **2008**, 2065; (e) Matsubara, R.; Nakamura, Y.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2004**, *43*, 1679; (f) Terada, M.; Machioka, K.; Sorimachi, K. *Angew. Chem. Int. Ed.* **2006**, *45*, 2254; (g) Lu, S.-F.; Du, D.-M.; Xu, J.; Zhang, S.-W. *J. Am. Chem. Soc.* **2006**, *128*, 7418; (h) Yang, X.; Zhou, X.; Lin, L.; Chang, L.; Liu, X.; Feng, X. *Angew. Chem. Int. Ed*. **2008**, *47*, 7079; (i) Rabalakos, C.; Wulff, W. D. *J. Am. Chem. Soc.* **2008**, *130*, 13524; (j) Trost, B. M.; Malhotra, S.; Olson, D. E.; Maruniak, A.; Bois, J. D. *J. Am. Chem. Soc.* **2009**, *131*, 4190; (k) Dagousset, G.; Drouet, F.; Masson, G.; Zhu, J. *Org. Lett.* **2009**, *11*, 5546; (l) Kumar, P.; Jha, V.; Gonnade, R. *J. Org. Chem*. **2013**, *78*, 11756.

[4] Recent examples of chiral diamines obtained by asymmetric hydrogenation: (a) Wang, T.; Chen, F.; Qin, J.; He, Y.-M.; Fan, Q.-H. *Angew. Chem. Int. Ed*. **2013**, *52*, 7172; (b) Zhang, J.; Chen, F.; He, Y.-M.; Fan, Q.-H. *Angew. Chem. Int. Ed.* **2015**, *54*, 4622; (c) Ma, W.; Zhang, J.; Xu, C.; Chen, F.; He, Y.-M.; Fan, Q.-H. *Angew. Chem. Int. Ed*. **2016**, *55*, 12891; (d) Feng, G.-S.; Chen, M.-W.; Shi, L.; Zhou, Y.-G. *Angew. Chem. Int. Ed*. **2018**, *57*, 5853; (e) Zhu, X.; Du, H. *Org. Lett*. **2015**, *17*, 3106.

[5] (a) Nugent, T. C.; El-Shazly, M. *Adv. Synth. Catal.* **2010**, *352*, 753; (b) Xie, J.-H.; Zhu, S.-F.; Zhou, Q.-L. *Chem. Rev.* **2011**, *111*, 1713; (c) Glorius, F. *Org. Biomol. Chem*. **2005**, *3*, 4171; (d) Wang, D.-S.; Chen, Q.-A.; Lu, S.-M.; Zhou, Y.-G. *Chem. Rev.* **2012**, *112*, 2557; (e) He, Y.-M.; Song, F.-T.; Fan, Q.-H. T*op. Curr. Chem.* **2014**, *343*, 145; (f) Zhang, Z.; Butt, N. A.; Zhou, M.; Liu, D.; Zhang, W. *Chin. J. Chem.* **2018**, *36*, 443; (g) Ji, Y.; Wang, J.; Chen, M.; Shi, L.; Zhou, Y. *Chin. J. Chem.* **2018**, *36*, 139; (h) Hu, S.-B.; Chen, M.-W.; Zhai, X.-Y.; Zhou, Y.-G. *Acta Chim. Sinica* **2018**, *76*, 103.

[6] (a) Zhou, H.; Li, Z.; Wang, Z.; Wang, T.; Xu, L.; He, Y.; Fan, Q.-H.; Pan, J.; Gu, L.; Chan, A. S. C. *Angew. Chem. Int. Ed*. **2008**, *47*, 8464; (b) Wang, T.; Zhuo, L.-G.; Li, Z.; Chen, F.; Ding, Z.; He, Y.; Fan, Q.-H.; Xiang, J.; Yu,

Z.-X.; Chan, A. S. C. *J. Am. Chem. Soc*. **2011**, *133*, 9878.
[7] (a) César, V.; Bellemin-Laponnaz, S.; Gade, L. H. *Chem. Soc. Rev.* **2004**, *33*, 619; (b) Park, J. K.; Lackey, H. H.; Rexford, M. D.; Kovnir, K.; Shatruk, M.; McQuade, D. T. *Org. Lett.* **2010**, *12*, 5008; (c) Huang, L.; Cao, Y.; Zhao, M.; Tang, Z.; Sun, Z. *Org. Biomol. Chem*. **2014**, *12*, 6554.
[8] CCDC-1856538 for (*S*,*S*)-**4** contains the supplementary crystallographic data for this paper. Data are provided free of charge by The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.
[9] At present, this methodology has not been applied to the asymmetric hydrogenation of symmetric bis(quinolin-2-yl)methanes bearing electron-withdrawing groups and other asymmetric bis(quinolin-2-yl)methanes substrates.

Manuscript received: July 27, 2018
Manuscript revised: September 20, 2018
Manuscript accepted: September 20, 2018
Accepted manuscript online: September 25, 2018
Version of record online: October 5, 2018

