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Development of axially chiral bis(arylthiourea)-based organocatalysts and their application in the enantioselective Henry reaction

Xu-Guang Liu,[a] Jia-Jun Jiang[a] and Min Shi[a,b,*]

[a]*School of Chemistry and Molecular Engineering, East China University of Science and Technology, 130 Mei Long Lu, Shanghai 200237, China*

[b]*State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China*

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Abstract—Axially chiral bis(arylthiourea)-based organocatalyst **6b**, prepared from (*R*)-(+)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine, was found to be an effective chiral organocatalyst for the enantioselective Henry reaction of arylaldehydes with nitromethane to give the corresponding adducts in moderate enantioselectivities and good yields.

1. Introduction

The reaction of a carbonyl compound and a nitroalkane, known as the Henry (or nitroaldol) reaction,[1] is a useful synthetic method in the formation of compounds containing a β-nitroalcohol.[2] Since the nitro group can be easily transformed into an amino group, as well as into carbonyl or carboxylic compounds via a Nef oxidation, the asymmetric Henry reaction has attracted much attention thus far. In recent years, several efficient catalytic enantioselective methods for performing this reaction have been described.[3] For example, an aldehyde (or an activated ketone) can be treated with a nitroalkane (mainly nitromethane or nitroethane) in the presence of a chiral metal complex and other additives, such as tertiary amines or molecular sieves, to afford nitroalcohols in good yields along with good to excellent enantiomeric purities. Over the last decade, asymmetric organocatalysis has emerged as a powerful and effective alternative to traditional metal-based catalysis for a variety of reactions.[4] High enantiomeric excesses have been achieved in the reaction between nitroalkanes and imines (aza-Henry reaction) using chiral, enantiopure organocatalysts. Good results have been obtained in particular by Takemoto et al,[5] and Yoon and Jacobsen.[6] However, to the best of our knowledge, only one remarkable result has been reported by Hiemstra et al. to date with regards to the traditional nitroaldol reaction of aldehyde with nitromethane under metal-free conditions, using Cinchona-thioureas as the chiral organocatalysts.[7]

Recently, thiourea-based organocatalysts have been widely used in the effective activation of carbonyl, imino, and nitro groups through double hydrogen-bonding interactions.[8,9] Herein, we report that several bis(thio)urea organocatalysts, derived from (*R*)-(+)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine, are fairly effective chiral catalysts for the enantioselective Henry reaction of arylaldehydes with nitromethane to give the corresponding adducts in moderate enantioselectivities and moderate to good yields under mild conditions.[10] The obvious advantage of these bis(thio)urea catalysts is their easily accessible structural diversity by condensation of a chiral diamine (1 equiv) with an iso(thio)cyanate (2 equiv).

2. Results and discussion

Chiral organocatalysts **2a**–**2c** and **6a**–**6b** were easily synthesized by condensation of axially chiral (*R*)-(+)-binaphthalenediamine (BINAM) **1** and (*R*)-(−)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine **3** with 2.0 equiv of iso(thio)cyanates in dichloromethane (DCM) at room temperature, respectively (Scheme 1). The axially chiral (*R*)-(+)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine **3** was prepared in 94% yield

* Corresponding author. E-mail: Mshi@mail.sioc.ac.cn

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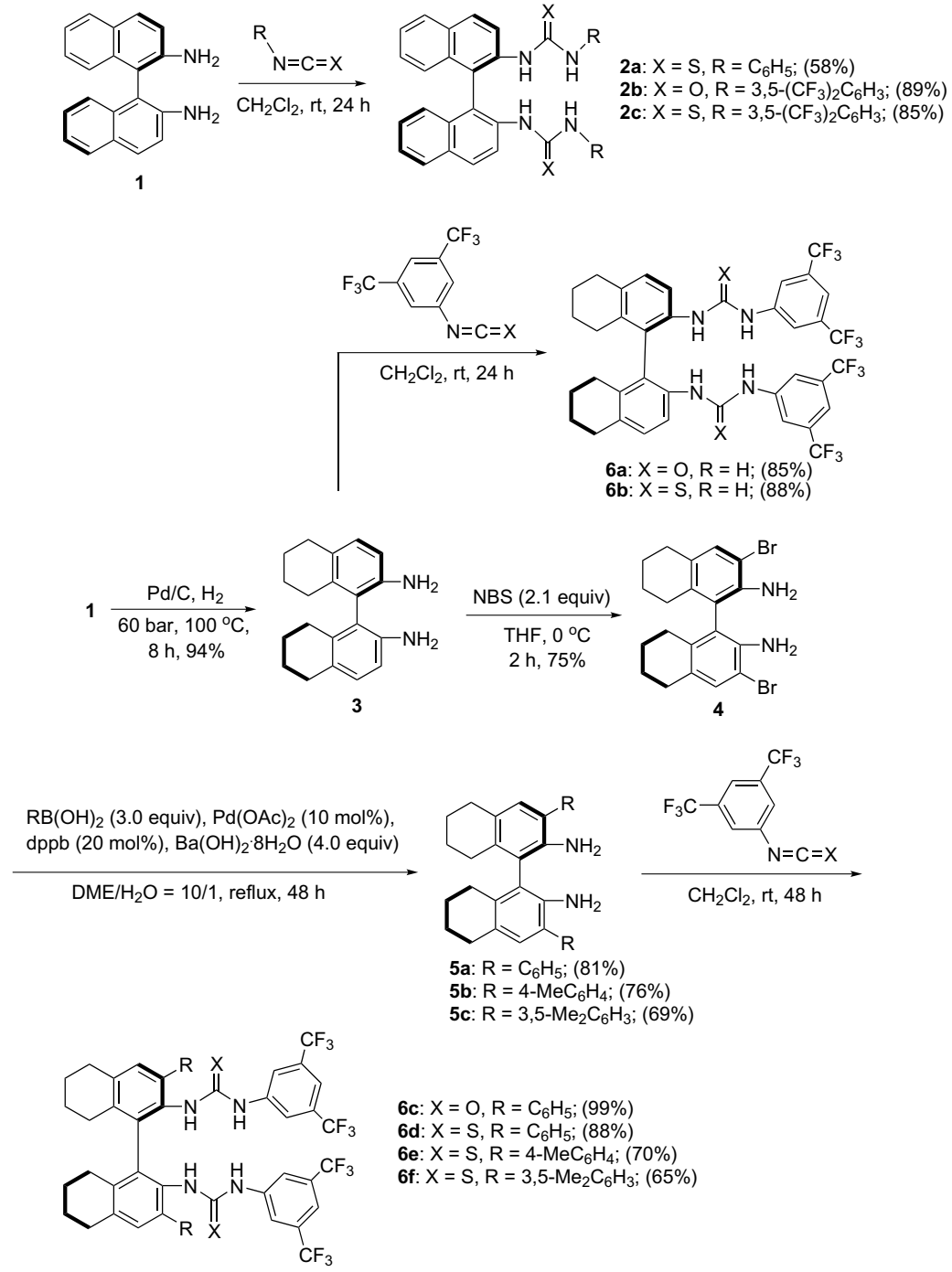
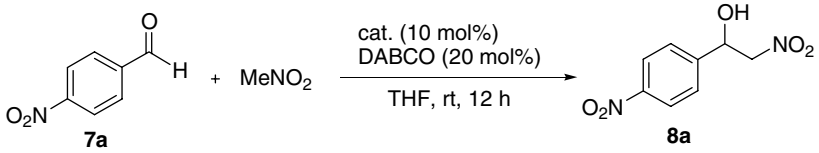


Scheme 1. Preparation of chiral bis(arylthiourea)-based organocatalysts **2a**–**2c** and **6a**–**6f**.

from the hydrogenation of BINAM **1** in the presence of Pd/C at 100 °C under 60 bar of H_2 for 8 h (Scheme 1). Dibromination of **3** with NBS in THF at 0 °C afforded (*R*)-(+)-3,3′-dibromo-5,6,7,8,5′,6′,7′,8′-octahydro-[1,1′]binaphthalenyl-2,2′-diamine **4** in 75% yield.[11] The subsequent Suzuki-coupling reaction using $Pd(OAc)_2$ (10 mol %) as catalyst and dppb (20 mol %) as a ligand produced the corresponding (*R*)-(−)-3,3′-disubstituted-5,6,7,8,5′,6′,7′,8′-octahydro-[1,1′]binaphthalenyl-2,2′-diamines **5a**–**5c** in good yields in the presence of $Ba(OH)_2{\cdot}8H_2O$ (4.0 equiv) in DME/H_2O (10:1) at reflux (Scheme 1). The condensation of **5a**–**5c** with 2.0 equiv of 3,5-bis(trifluoromethyl)phenyl iso(thio)cyanate gave the corresponding chiral organocatalysts **6c**–**6f** in good yields (Scheme 1).

Our initial experiments were performed using 4-nitrobenzaldehyde **7a** as a model substrate and DABCO (20 mol %) as a base with 10 equiv of nitromethane at room temperature in THF in the presence of various organocatalysts (10 mol %). Organocatalysts **2a**–**2c** and **6a**–**6f** were first examined and the results of these experiments are summarized in Table 1. It was found that the structure of these

Table 1. Optimization of the reaction conditions in the asymmetric Henry reaction of 4-nitrobenzaldehyde and nitromethane[a]

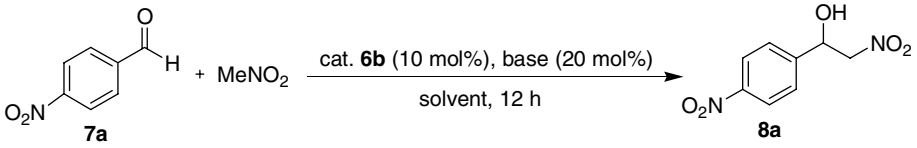


Entry	Cat.	Yield[b] (%) **8a**	ee[c] (%) **8a**
1	**2a**	99	7
2	**2b**	99	12
3	**2c**	99	17
4	**6a**	99	15
5	***6b***	***83***	***33***
6	**6c**	99	11
7	**6d**	99	16
8	**6e**	99	11
9	**6f**	99	5

[a] Reactions were carried out with **3** (0.3 mmol), $MeNO_2$ (3.0 mmol), cat. (0.03 mmol), DABCO (0.06 mmol) in 0.3 mL of THF at rt.
[b] Yield of isolated product.
[c] Determined by HPLC analysis using a Chiralcel column.

organocatalysts marginally affects the enantioselectivity of **8a**, although the chemical yields achieved are very similar (Table 1, entries 1–9). As can be seen from Table 1, bis(thio)ureas **2c**, **6b**, and **6d** are slightly more effective than those of bisureas **2b**, **6a**, and **6c** under identical conditions, presumably due to the stronger H-bonding ability of thioureas than that of ureas, which makes them more effectively to interact with the substrates (Table 1, entries 2–7). Under the standard conditions, catalyst **2c** was found to be better than catalyst **2a**, suggesting that the H-bonding interaction of the thiourea group with the carbonyl group of 4-nitrobenzaldehyde **7a** could be indeed imposed by 3,5-bis(trifluoromethyl)phenyl in **2c** over the phenyl group in **2a**.[12] Therefore, bis(thio)urea **2c** was the better catalyst for this reaction, providing **8a** in 99% yield and 17% ee after 12 h while the corresponding bisurea organocatalyst **2a** showed a lower enantioselectivity under identical conditions (Table 1, entries 1 and 3). In addition, similar results were obtained using **2b** and **6a** as well as **2c** and **6b**, suggesting that the chiral backbone skeleton did not significantly affect the enantioselectivity in this reaction (Table 1, entries 2–5). Using **6b** as a catalyst, **8a** was obtained in 83% yield and 33% ee (Table 1, entry 5). Moreover, since sterically more congested catalysts will in general improve the enantioselectivity, we utilized bis(thio)ureas **6c**–**6f** into the reaction. Unfortunately, sterically more hindered diamine-(thio)urea catalyst **6c**–**6f** showed poor enantioselectivities under identical conditions to give **8a** in 5–16% ees (Table 1, entries 6–9). This may be due to the fact that the dihedral angle of **6b** is superior to others. As

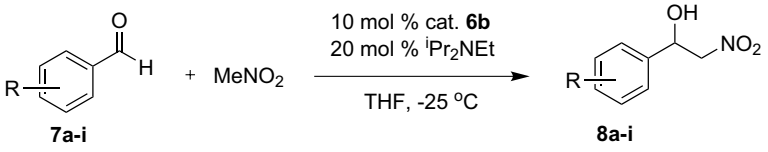
Table 2. Optimization of the reaction conditions in the asymmetric Henry reaction of 4-nitrobenzaldehyde and nitromethane[a]



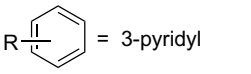
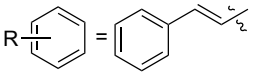
Entry	Base	Solvent	*T* (°C)	Yield[b] (%) **8a**	ee[c] (%) **8a**
1	DABCO	THF	rt	83	33
2	DABCO	MeOH	rt	99	8
3	DABCO	DMF	rt	99	47
4	DABCO	MeCN	rt	99	25
5[d]	DABCO	DMF	−25	99	65
6[d]	DABCO	THF	−25	65	66
7[d]	Et_3N	DMF	−25	99	57
8[d]	Et_3N	THF	−25	50	71
9[d]	***$^iPr_2Et$***	***THF***	***−25***	***99***	***72***
10[d]	DMAP	THF	−25	84	65
11[d]	DBU	THF	−25	78	21
12[d]	Et_2NH	THF	−25	78	50

[a] Reactions were carried out with **7a** (0.15 mmol), $MeNO_2$ (1.5 mmol), cat. **6b** (0.015 mmol), base (0.03 mmol) in 0.15 mL of solvent.
[b] Yield of isolated product.
[c] Determined by HPLC analysis using a Chiralcel column.
[d] The reaction was carried out for 24 h.

Table 3. Henry reaction of a variety of arylaldehydes with $MeNO_2$[a]



7a-i 8a-i

Entry	Substrate	R	Time (h)	Yield[b] (%) **8a–g**	ee[c,d] (%) **8a–g**
1	**7a**	4-NO_2	24	**8a**, 99	**8a**, 72 (*S*)
2	**7b**	3-NO_2	12	**8b**, 82	**8b**, 68 (*S*)
3	**7c**	2-NO_2	12	**8c**, 99	**8c**, 71 (*S*)
4	**7d**	H	96	**8d**, 80	**8d**, 64 (*S*)
5	**7e**	2-Cl	24	**8e**, 83	**8e**, 75 (*S*)
6	**7f**	4-Cl	48	**8f**, 99[e]	**8f**, 46 (*S*)
7	**7g**	4-Me	120	**8g**, 65	**8g**, 69 (*S*)
8	**7h**		48	**8h**, 76	**8h**, 22 (*S*)
9	**7i**		120	**8i**, 75[e]	**8i**, 50 (+)

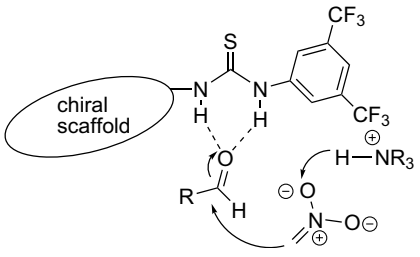
[a] Reactions were carried out with **3** (0.3 mmol), $MeNO_2$ (3.0 mmol), cat. **6b** (0.03 mmol), $^iPr_2NEt$ (0.06 mmol) in 0.3 mL of THF at −25 °C.
[b] Yield of isolated product.
[c] Determined by HPLC analysis using a Chiralcel column.
[d] The absolute configurations for compounds **8** were assigned by comparison of their specific rotations with those literature values.
[e] Conversion (based on the recovered starting materials).

bis(thio)urea **6b** is the best catalyst examined above, further optimization of the reaction conditions was performed by using it as the organocatalyst.

During the second step on the optimization of the reaction conditions, the solvent effect and the reaction temperatures were examined and the results of these experiments are summarized in Table 2. We were delighted to observe that in *N*,*N*-dimethylformamide (DMF) at room temperature, **8a** was obtained in 47% ee after 12 h (Table 2, entry 3). When the reaction was carried out in methanol, **8a** was obtained in 8% ee (Table 2, entry 2). Lowering the reaction temperature to −25 °C provided synthetically useful levels of asymmetric induction at a still reasonable reaction rate in DMF and THF (Table 2, entries 5 and 6). The nature of the nucleophilic base is known to have a pronounced influence on the Henry reaction.[13] Therefore various tertiary amines were screened in combination with catalyst **6b** for the reaction (Table 2, entries 8–12). In the case of Et_3N or $^iPr_2NEt$, the enantioselectivity of **8a** can reach 71% or 72% in THF (Table 2, entries 8 and 9). Other bases are less effective than Et_3N or $^iPr_2NEt$ under identical conditions (Table 2, entries 10–12). Therefore, the best conditions are to carry out the reaction in THF at −25 °C with **6b** (10 mol %) as a catalyst in the presence of $^iPr_2NEt$ (20 mol %).

With these optimized conditions in hand, we next examined this asymmetric Henry reaction using a variety of arylaldehydes **7** with nitromethane and the results are summarized in Table 3. As can be seen from Table 3, a variety of arylaldehydes could be transformed into the corresponding nitroalcohols in consistently high yields and moderate enantiomeric excesses (Table 3, entries 1–8). As for the unsubstituted aromatic aldehyde (phenylaldehyde) or 4-methylbenzaldehyde, a prolonged reaction time is required to give the corresponding nitroalkane **8d** or **8g** in good yield and 64% or 69% ee, suggesting that electron-deficient arylaldehydes accelerate the reaction rate (Table 3, entries 4 and 7). 3-Pyridinecarboxaldehyde could also react with nitromethane to give **8h** in 76% yield under standard conditions, but in a lower enantioselectivity (Table 3, entry 7). These reaction conditions are also suitable for the reaction of a non-aromatic aldehyde, cinnamaldehyde, with nitromethane to give the corresponding adduct **8i** in 50% ee and good yield (Table 3, entry 9).

Although the reason for the observed enantioselectivity is still unclear, we believe that the aldehyde is activated by a thiourea moiety through double hydrogen-bonding, and the nitromethane is activated by the basic nitrogen atom (Scheme 2). These interactions control the stereochemical outcome of the reaction and accelerate the reaction rate.[7]



Scheme 2. Proposed mode of the interaction of catalyst bis(thio)urea and base with substrates.

3. Conclusion

In conclusion, chiral bis(arylthiourea)-based organocatalyst **6b**, prepared from (*R*)-(+)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine, was found to be a fairly effective chiral catalyst for the enantioselective Henry reaction of arylaldehydes with nitromethane to give the corresponding adducts in moderate enantioselectivities and good yields under mild conditions. These results help promote us design and synthesize new effective chiral bis(arylthiourea)-based organocatalysts for asymmetric reactions. Further efforts are currently underway with a focus on improving the catalyst activity and reaction enantioselectivity, as well as to elucidate the mechanistic details of this asymmetric Henry reaction.

4. Experimental

4.1. General methods

Melting points were obtained with a Yanagimoto micro-melting point apparatus and are uncorrected. Optical rotations were determined in a solution of $CHCl_3$ or CH_2Cl_2 at 20 °C by using a Perkin–Elmer-241 MC polarimeter; $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. Infrared spectra were measured on a spectrometer. Unless noted, ^{1}H NMR spectra were recorded for solution in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard; ^{19}F NMR spectra were recorded at 282 MHz for a solution in $CDCl_3$ with $CFCl_3$ as the external reference. *J*-values are in Hertz. Mass spectra were recorded with a HP-5989 instrument and HRMS was measured by a Finnigan MA+ mass spectrometer. The organic solvents used were dried by standard methods when necessary. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai $60F_{254}$ Silica Gel coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel at an increased pressure. All Henry reactions were performed under argon using standard Schlenk techniques. The enantiomeric purities of the adducts were determined by HPLC analysis using a chiral stationary phase column (column, Daicel Co. Chiralcel AD and OD) and the absolute configuration of the major enantiomer was assigned according to the sign of the specific rotation.

4.2. Representative procedure for the synthesis of diamines 3, 4, 5a, 5b and 5c

4.2.1. (*R*)-5,6,7,8,5′,6′,7′,8′-Octahydro-[1,1′]binaphthalenyl-2,2′-diamine 3. This is a known compound.[14] BINAM (284 mg, 1.0 mmol), 5% Pd/C (142 mg) and 50 mL of EtOAc were placed in a 100 mL autoclave and the reaction mixture was stirred under 60 bar H_2 at 100 °C for 8 h. After no more hydrogen consuming was detected, the reaction mixtures were cooled to room temperature and Pd/C metal catalyst was filtered off, and then washed with CH_2Cl_2 (3×25 mL). The combined filtrates were concentrated in vacuum to give 275 mg of **3**, which is a pure product on the basis of ^{1}H NMR and ^{13}C NMR spectra (94% yield). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.65–1.75 (8H, m, CH_2), 2.11–2.32 (4H, m, CH_2), 2.69–2.73 (4H, m, CH_2), 3.23 (4H, s, NH_2), 6.60 (2H, d, $J = 8.1$ Hz, Ar), 6.91 (4H, d, $J = 8.1$ Hz, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.1, 23.4, 26.9, 29.3, 113.0, 121.9, 127.6, 129.2, 136.1, 141.4.

4.2.2. (*R*)-3,3′-Dibromo-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]-binaphthalenyl-2,2′-diamine 4. To a stirred solution of (*R*)-**3** (292 mg, 1.0 mmol) in anhydrous THF (3.0 mL) was added NBS (374 mg, 2.1 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h. Then, the reaction was quenched with saturated $NaHCO_3$ aqueous solution and saturated Na_2SO_3 aqueous solution at 0 °C, and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/EA = 4:1) to afford (*R*)-**4** (337.65 mg, 0.75 mmol, 75% yield). Mp 170–172 °C; $[\alpha]_D^{20} = +40.0$ (*c* 0.94, $CHCl_3$). IR (CH_2Cl_2) *v* 3468, 3376, 2926, 2854, 1602, 1457, 1276, 1260, 762, 751 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.64–1.71 (8H, m, CH_2), 2.03–2.26 (4H, m, CH_2), 2.67–2.71 (4H, m, CH_2), 3.52 (4H, s, NH_2), 7.21 (2H, s, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.9, 23.1, 26.7, 29.0, 107.0, 122.3, 129.0, 132.3, 135.6, 139.1. MS (EI) *m*/*z* 450 (M+2H$^+$, 100.0), 449 (M+H$^+$, 13.2), 448 (M$^+$, 46.1), 407 (M$^+$−41, 4.4), 405 (M$^+$−43, 3.4), 371 (M$^+$−77, 4.1), 369 (M$^+$−79, 5.8), 354 (M$^+$−94, 5.3), 290 (M$^+$−158, 12.3), 289 (M$^+$−159, 5.0), 272 (M$^+$−176, 3.3). HRMS (EI): (M+2H$^+$) calcd for $C_{20}H_{22}Br_2N_2$, 450.0150; found, 450.0159.

4.2.3. (*R*)-3,3′-Diphenyl-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]-binaphthalenyl-2,2′-diamine 5a. A mixture of (*R*)-**4** (450 mg, 1.0 mmol), $Pd(OAc)_2$ (22 mg, 0.1 mmol), dppb (85 mg, 0.2 mmol), $Ba(OH)_2{\cdot}8H_2O$ (1.26 g, 4.0 mmol) and phenylboronic acid (366 mg, 3.0 mmol) in degassed DME (4 mL) and H_2O (400 μL) was refluxed for 48 h. After cooling to room temperature, the resulting mixture was poured into water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/EA = 80:1) to afford (*R*)-**5** (360 mg, 0.81 mmol, 81% yield). Mp 228–230 °C; $[\alpha]_D^{20} = -27.4$ (*c* 1.13, CH_2Cl_2). IR (CH_2Cl_2) *v* 3469, 3374, 3055, 2927, 2854, 2834, 1606, 1495, 1458, 1414, 1264, 776, 738, 703 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.66–1.74 (8H, m, CH_2), 2.23–2.41 (4H, m, CH_2), 2.74–2.76 (4H, m, CH_2), 3.53 (4H, s, NH_2), 6.92 (2H, s, Ar), 7.31 (2H, t, $J = 6.9$ Hz, Ar), 7.42 (4H, t, $J = 7.5$ Hz, Ar), 7.50 (4H, d, $J = 6.9$ Hz, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.3, 23.5, 27.0, 29.3, 122.3, 125.6, 126.8, 127.3, 128.6, 129.1, 130.3, 135.5, 138.7, 140.0. MS (EI) *m*/*z* 444 (M$^+$, 100.0), 443 (M$^+$−1, 10.6), 442 (M$^+$−2, 6.9), 441 (M$^+$−3, 4.9), 440 (M$^+$−4, 6.0), 428 (M$^+$−16, 2.9), 427 (M$^+$−17, 3.3), 426 (M$^+$−18, 2.6), 401 (M$^+$−43, 6.7), 399 (M$^+$−45, 3.9), 222 (M$^+$−222, 2.9). HRMS (EI): (M$^+$) calcd for $C_{32}H_{32}N_2$, 444.2565; found, 444.2566.

4.2.4. (*R*)-3,3′-Di-*p*-tolyl-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]-binaphthalenyl-2,2′-diamine 5b. Diamine **5b** was prepared in a similar manner as that described above using *p*-tolylboronic acid instead of phenylboronic acid (76% yield).

Mp 198–200 °C; $[\alpha]_D^{20} = -19.5$ (c 1.01, CH_2Cl_2). IR (CH_2Cl_2) ν 3469, 3374, 3021, 2925, 2855, 2835, 1605, 1513, 1457, 1264, 1110, 823, 738 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.67–1.73 (8H, m, CH_2), 2.22–2.40 (4H, m, CH_2), 2.37 (6H, s, CH_3), 2.73–2.75 (4H, m, CH_2), 3.51 (4H, s, NH_2), 6.90 (2H, s, Ar), 7.22 (4H, d, $J = 7.8$ Hz, Ar), 7.38 (4H, d, $J = 7.8$ Hz, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.1, 23.3, 23.5, 27.0, 29.3, 122.3, 125.5, 127.2, 129.0, 129.3, 130.2, 135.3, 136.4, 137.0, 138.8. MS (EI) m/z 472 (M^+, 100.0), 471 (M^+-1, 9.6), 470 (M^+-2, 6.2), 469 (M^+-3, 5.3), 468 (M^+-4, 6.7), 455 (M^+-17, 2.8), 429 (M^+-43, 5.4), 427 (M^+-45, 2.9), 236 (M^+-236, 2.7). HRMS (EI): (M^+) calcd for $C_{34}H_{36}N_2$, 472.2878; found, 472.2884.

4.2.5. (*R*)-3,3′-Bis(3,5-dimethylphenyl)-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]binaphthalenyl-2,2′-diamine 5c. Product **5c** was prepared in a similar manner as that described above using 3,5-dimethylphenylboronic acid instead of phenylboronic acid (69% yield). Mp 124–126 °C; $[\alpha]_D^{20} = -37.9$ (c 0.96, CH_2Cl_2). IR (CH_2Cl_2) ν 3471, 3375, 3019, 2925, 2855, 2835, 1602, 1458, 1314, 1265, 1217, 1100, 851, 738, 711 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.61–1.71 (8H, m, CH_2), 2.13–2.38 (4H, m, CH_2), 2.34 (12H, s, CH_3), 2.69–2.74 (4H, m, CH_2), 3.48 (4H, s, NH_2), 6.89 (2H, s, Ar), 6.95 (2H, s, Ar), 7.11 (4H, s, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.3, 23.3, 23.5, 27.0, 29.3, 122.2, 125.8, 126.9, 127.1, 128.4, 130.1, 135.2, 138.1, 138.7, 140.0. MS (EI) m/z 500 (M^+, 100.0), 499 (M^+-1, 8.4), 498 (M^+-2, 4.1), 497 (M^+-3, 3.4), 496 (M^+-4, 3.5), 428 (M^+-72, 2.9), 484 (M^+-16, 2.8), 483 (M^+-17, 3.9), 476 (M^+-24, 2.8), 457 (M^+-43, 4.4), 250 (M^+-250, 2.6). HRMS (EI): (M^+) calcd for $C_{36}H_{40}N_2$, 500.3191; found, 500.3191.

4.3. General procedure for the preparation of chiral bis(arylthiourea)-based organocatalysts 2a–2c and their derivatives 6a–6h

To a solution of (*R*)-(+)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine (292 mg, 1.0 mmol) in dichloromethane (DCM) (4.0 mL) was added 1-isothiocyanato-3,5-bis(trifluoromethyl)benzene (543 mg, 2.0 mmol) at room temperature and the reaction mixture was stirred for the required time. After the reaction was complete, the reaction solution was concentrated under reduced pressure and the residue purified by flash chromatography on silica gel to afford the pure product.

4.3.1. (*R*)-1-Phenyl-3-[2′-(3-phenylthioureido)-[1,1′]binaphthalenyl-2-yl]thiourea 2a. Mp 148–150 °C; $[\alpha]_D^{20} = +60.0$ (c 1.00, CH_2Cl_2). IR (CH_2Cl_2) ν 3176, 2953, 2925, 2853, 1592, 1522, 1497, 1277, 1180, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 6.02 (4H, d, $J = 7.5$ Hz, Ar), 6.85 (4H, t, $J = 7.2$ Hz, Ar), 6.96 (2H, t, $J = 7.2$ Hz, Ar), 7.21–7.30 (4H, m, Ar), 7.51 (2H, s, NH), 7.50–7.53 (2H, m, Ar), 7.80 (2H, d, $J = 8.7$ Hz, Ar), 7.96–8.00 (4H, m, Ar), 8.44 (2H, s, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 125.3, 126.4, 127.1, 127.2, 127.3, 128.0, 128.1, 129.3, 129.5, 132.2, 132.3, 135.0, 135.5, 179.4. MS (ESI) m/z 555.2 ($M+H^+$, 100). HRMS (ESI): (M^++H) calcd for $C_{34}H_{26}N_4S_2$, 555.1599; found, 555.1678.

4.3.2. (*R*)-1-(3,5-Bis-trifluoromethylphenyl)-3-{2′-[3-(3,5-bis-trifluoromethylphenyl)ureido]-[1,1′]binaphthalenyl-2-yl}-urea 2b. Mp 166–168 °C; $[\alpha]_D^{20} = +79.9$ (c 1.02, CH_2Cl_2). IR (CH_2Cl_2) ν 3331, 2956, 2925, 2854, 1664, 1572, 1508, 1474, 1386, 1277, 1180, 1132, 884, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 6.96–7.02 (4H, m, Ar), 7.16 (2H, t, $J = 8.1$ Hz, Ar), 7.33 (2H, s, NH), 7.36 (2H, t, $J = 8.1$ Hz, Ar), 7.46 (4H, s, Ar), 7.74 (2H, s, NH), 7.81 (2H, d, $J = 8.4$ Hz, Ar), 7.90 (2H, d, $J = 8.4$ Hz, Ar), 8.00 (2H, d, $J = 8.4$ Hz, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 116.2, 118.3, 122.8 (q, $J = 270.7$ Hz), 122.9, 123.4, 125.2, 125.7, 127.3, 128.3, 129.7, 131.3, 131.9 (q, $J = 33.1$ Hz), 132.7, 134.6, 139.4, 153.5. ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$): δ −63.72. MS (ESI) m/z 795.2 ($M+H^+$, 100). HRMS (ESI): (M^++H) calcd for $C_{38}H_{22}F_{12}N_4O_2$, 795.1551; found, 795.1600.

4.3.3. (*R*)-1-(3,5-Bis-trifluoromethylphenyl)-3-{2′-[3-(3,5-bis-trifluoromethylphenyl)thioureido]-[1,1′]binaphthalenyl-2-yl}thiourea 2c. This is a known compound.[10] Mp 132–134 °C; $[\alpha]_D^{20} = +169.7$ (c 1.00, CH_2Cl_2). IR (CH_2Cl_2) ν 3247, 2955, 2926, 2854, 1507, 1471, 1380, 1277, 1179, 1135, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 7.12 (2H, d, $J = 8.4$ Hz, Ar), 7.29 (2H, t, $J = 7.2$ Hz, Ar), 7.51 (2H, t, $J = 7.2$ Hz, Ar), 7.57 (2H, s, NH), 7.64 (2H, s, Ar), 7.70 (4H, s, Ar), 7.86 (2H, d, $J = 8.7$ Hz, Ar), 7.97 (2H, d, $J = 8.7$ Hz, Ar), 8.05 (2H, s, NH), 8.12 (2H, d, $J = 9.0$ Hz, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 119.5 (q, $J = 3.1$ Hz), 122.6 (q, $J = 271.2$ Hz), 124.7, 125.3, 126.8, 127.5, 127.8, 128.6, 130.2, 131.8 (q, $J = 34.1$ Hz), 132.2, 132.6, 133.7, 138.5, 180.0. ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$): δ −63.45. MS (ESI) m/z 827.1 ($M+H^+$, 100). HRMS (ESI): (M^++H) calcd for $C_{38}H_{22}F_{12}N_4S_2$, 827.1094; found, 827.1180.

4.3.4. (*R*)-1-(3,5-Bis-trifluoromethylphenyl)-3-{2′-[3-(3,5-bis-trifluoromethylphenyl)ureido]-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]binaphthalenyl-2-yl}urea 6a. Mp 164–166 °C; $[\alpha]_D^{20} = +48.5$ (c 0.50, CH_2Cl_2). IR (CH_2Cl_2) ν 3331, 2927, 2858, 1664, 1570, 1526, 1472, 1386, 1278, 1180, 1133, 882, 751 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.51–1.69 (8H, m, CH_2), 2.11–2.12 (4H, m, CH_2), 2.63–2.76 (4H, m, CH_2), 6.92 (2H, s, Ar), 7.03 (2H, d, $J = 8.1$ Hz, Ar), 7.36 (2H, s, NH), 7.39 (2H, d, $J = 8.1$ Hz, Ar), 7.56 (4H, s, Ar), 7.75 (2H, s, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.5, 22.8, 27.4, 29.4, 116.0, 118.4, 121.7 (q, $J = 3.8$ Hz), 122.9 (q, $J = 270.8$ Hz), 129.7, 130.2, 132.0 (q, $J = 33.3$ Hz), 132.2, 135.7, 136.3, 139.8, 154.2. ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$): δ −63.79. MS (ESI) m/z 803.2 ($M+H^+$, 100). HRMS (ESI): (M^++H) calcd for $C_{38}H_{30}F_{12}N_4O_2$, 803.2177; found, 803.2255.

4.3.5. (*R*)-1-(3,5-Bis-trifluoromethylphenyl)-3-{2′-[3-(3,5-bis-trifluoromethylphenyl)thioureido]-5,6,7,8,5′,6′,7′,8′-octahydro-[1,1′]binaphthalenyl-2-yl}thiourea 6b. Mp 170–172 °C; $[\alpha]_D^{20} = +209.3$ (c 0.50, CH_2Cl_2). IR (CH_2Cl_2) ν 3358, 3229, 2956, 2925, 2860, 1541, 1492, 1468, 1381, 1345, 1275, 1176, 1134, 1108, 751, 681 cm^{-1}; ^1H NMR ($(CD_3)_2SO$, 300 MHz, TMS): δ 1.62–1.67 (8H, m, CH_2), 2.02–2.07 (2H, m, CH_2), 2.03–2.40 (2H, m, CH_2), 2.78–2.80 (4H, m, CH_2), 7.16 (2H, d, $J = 8.4$ Hz, Ar), 7.46

(2H, d, $J = 8.4$ Hz, Ar), 7.65 (2H, s, Ar), 8.05 (4H, s, Ar), 8.99 (2H, s, NH), 9.84 (2H, s, NH). ^{13}C NMR ($(CD_3)_2SO$ 75 MHz): δ 22.2, 22.5, 27.0, 29.2, 116.7, 123.1 (q, $J = 270.8$ Hz), 123.6, 125.3, 128.8, 129.7 (q, $J = 32.6$ Hz), 132.5, 133.6, 135.5, 136.2, 141.4, 179.8. ^{19}F NMR ($(CD_3)_2SO$, 282 MHz, $CFCl_3$): δ 57.54. MS (ESI) m/z 835.2 ($M+H^+$, 100). HRMS: calcd for $C_{38}H_{30}F_{12}N_4S_2$, 835.1720; found, 835.1782.

4.3.6. (*R*)-1-(3,5-Bis-trifluoromethylphenyl)-3-{2′-[3-(3,5-bis-trifluoromethylphenyl)ureido]-3,3′-diphenyl-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]binaphthalenyl-2-yl}urea 6c. Mp 178–180 °C; $[\alpha]_D^{20} = -87.1$ (c 0.60, CH_2Cl_2). IR (CH_2Cl_2) ν 3321, 2928, 2859, 1653, 1549, 1472, 1437, 1385, 1278, 1180, 1134, 882, 701, 683 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.68–1.77 (8H, m, CH_2), 2.22–2.25 (4H, m, CH_2), 2.83–2.85 (4H, m, CH_2), 6.64 (4H, s, NH), 7.13–7.17 (4H, m, Ar), 7.24 (4H, t, $J = 7.2$ Hz, Ar), 7.32–7.41 (10H, m, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.6, 22.9, 27.5, 29.6, 116.4, 118.0, 119.2, 122.9 (q, $J = 271.6$ Hz), 127.4, 128.4 (q, $J = 3.1$ Hz), 131.2, 131.8 (q, $J = 32.6$ Hz), 135.5, 136.7, 137.4, 137.8, 139.3, 153.9. ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$): δ −63.69. MS (ESI) m/z 955.3 ($M+H^+$, 100). HRMS (ESI): (M^++H) calcd for $C_{50}H_{38}F_{12}N_4O_2$, 955.2803; found, 955.2883.

4.3.7. (*R*)-1-(3,5-Bis-trifluoromethylphenyl)-3-{2′-[3-(3,5-bis-trifluoromethylphenyl)thioureido]-3,3′-diphenyl-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]binaphthalenyl-2-yl}thiourea 6d. Mp 150–152 °C; $[\alpha]_D^{20} = +142.0$ (c 1.06, CH_2Cl_2). IR (CH_2Cl_2) ν 3160, 2930, 2846, 1541, 1497, 1471, 1382, 1343, 1277, 1178, 1135, 765, 751, 699, 682 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.78–1.91 (8H, m, CH_2), 2.30–2.34 (4H, m, CH_2), 2.86–2.94 (4H, m, CH_2), 7.12 (4H, s, NH), 7.23 (4H, s, Ar), 7.30 (2H, s, Ar), 7.37–7.47 (12H, m, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.3, 22.7, 27.7, 29.7, 119.3, 122.7 (q, $J = 272.3$ Hz), 126.4, 127.7, 128.2, 129.0, 130.9 (q, $J = 33.7$ Hz), 132.9, 134.1, 135.8, 136.0, 138.2, 138.9, 139.7, 179.4. ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$): δ −63.65. MS (ESI) m/z 987.2 ($M+H^+$, 100). HRMS (ESI): (M^++H) calcd for $C_{50}H_{38}F_{12}N_4S_2$, 987.2346; found, 987.2449.

4.3.8. (*R*)-1-(3,5-Bis-trifluoromethylphenyl)-3-{2′-[3-(3,5-bis-trifluoromethylphenyl)thioureido]-3,3′-di-*p*-tolyl-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]binaphthalenyl-2-yl}thiourea 6e. Mp 154–156 °C; $[\alpha]_D^{20} = +95.6$ (c 1.01, CH_2Cl_2). IR (CH_2Cl_2) ν 3168, 3025, 2934, 2862, 1709, 1621, 1533, 1472, 1451, 1382, 1279, 1178, 1133, 1108, 988, 887, 820, 701, 682 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.78–1.92 (8H, m, CH_2), 2.20–2.31 (4H, m, CH_2), 2.36 (6H, s, CH_3), 2.84–2.94 (4H, m, CH_2), 7.16–7.21 (12H, m, Ar), 7.27 (2H, s, NH), 7.35 (4H, d, $J = 7.8$ Hz, Ar), 7.41 (2H, s, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.8, 22.3, 22.8, 27.7, 29.7, 119.4, 122.7 (q, $J = 271.4$ Hz), 126.3 (q, $J = 4.3$ Hz), 127.5, 128.0, 129.7, 130.9 (q, $J = 33.8$ Hz), 133.0, 134.0, 135.2, 135.6, 135.7, 138.4, 138.9, 139.6, 179.2. ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$): δ −63.70. MS (ESI) m/z 1015.3 ($M+H^+$, 100). HRMS (ESI): (M^++H) calcd for $C_{52}H_{42}F_{12}N_4S_2$, 1015.2659; found, 1015.2740.

4.3.9. (*R*)-1-(3,5-Bis-trifluoromethylphenyl)-3-[2′-[3-(3,5-bis-trifluoromethylphenyl)thioureido]-3,3′-bis(3,5-dimethylphenyl)-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]binaphthalenyl-2-yl]thiourea 6f. Mp 174–176 °C; $[\alpha]_D^{20} = +84.1$ (c 1.10, CH_2Cl_2). IR (CH_2Cl_2) ν 3359, 3183, 3024, 2937, 2863, 1602, 1531, 1485, 1451, 1382, 1345, 1278, 1172, 1129, 987, 886, 852, 732, 701, 682 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.83–1.95 (8H, m, CH_2), 2.23 (12H, s, CH_3), 2.30–2.31 (4H, m, CH_2), 2.85–2.94 (4H, m, CH_2), 7.00 (2H, s, NH), 7.05 (4H, s, Ar), 7.10 (4H, s, Ar), 7.14 (4H, s, Ar), 7.30 (2H, s, Ar), 7.41 (2H, s, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.0, 22.4, 22.8, 26.9, 27.6, 29.7, 119.2, 122.7 (q, $J = 271.5$ Hz), 125.8, 126.1 (q, $J = 4.0$ Hz), 127.7, 130.0, 130.8 (q, $J = 33.6$ Hz), 132.9, 133.9, 135.5, 135.7, 138.0, 138.8, 139.0, 139.4, 179.1. ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$): δ −63.74. MS (ESI) m/z 1043.3 ($M+H^+$, 100). HRMS (ESI): (M^++H) calcd for $C_{54}H_{46}F_{12}N_4S_2$, 1043.2972; found, 1043.3069.

4.4. Typical reaction procedure for the Henry reactions

To a mixture of arylaldehydes (0.30 mmol), ^{i}Pr$_2$NEt (0.06 mmol) and catalyst **6b** (0.03 mmol) in solvent was added $MeNO_2$ (3.0 mmol) under an argon atmosphere stirring at room temperature for the required time indicated in the Tables. After the reaction solution was concentrated under reduced pressure, the residue was purified by flash chromatography on silica gel (Eluent: EtOAc/petroleum = 1:8) to afford the pure product **8**.

4.4.1. 2-Nitro-1-(4-nitrophenyl)ethanol 8a. This is a known compound.[3j] $[\alpha]_D^{20} = +26.0$ (c 1.10, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 3.15 (1H, d, $J = 3.6$ Hz, OH), 4.55–4.66 (2H, m, CH_2), 5.59–5.64 (1H, m, CH), 7.63 (2H, d, $J = 9.0$ Hz, Ar), 8.28 (2H, d, $J = 9.0$ Hz, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (hexane/*i*PrOH = 65:35, 0.7 mL/min, 254 nm, $t_{minor} = 9.38$ min, $t_{major} = 11.56$ min; 72% ee).

4.4.2. 2-Nitro-1-(3-nitrophenyl)ethanol 8b. This is a known compound.[3h] $[\alpha]_D^{20} = +28.0$ (c 0.80, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 3.18 (1H, s, OH), 4.56–4.69 (2H, m, CH_2), 5.63 (1H, dd, $J_1 = 4.2$ Hz, $J_2 = 7.8$ Hz, CH), 7.63 (1H, t, $J = 8.4$ Hz, Ar), 7.78 (1H, d, $J = 7.8$ Hz, Ar), 8.25 (1H, d, $J = 8.4$ Hz, Ar), 8.34 (1H, s, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 90:10, 0.7 mL/min, 254 nm, $t_{minor} = 39.66$ min, $t_{major} = 44.53$ min; 68% ee).

4.4.3. 2-Nitro-1-(2-nitrophenyl)ethanol 8c. This is a known compound.[3j] $[\alpha]_D^{20} = +160.0$ (c 1.10, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 3.21 (1H, s, OH), 4.56 (1H, dd, $J_1 = 13.8$ Hz, $J_2 = 9.0$ Hz, CH_2), 4.88 (1H, dd, $J_1 = 13.8$ Hz, $J_2 = 2.0$ Hz, CH_2), 6.05 (1H, d, $J = 9.0$ Hz, CH), 7.56 (1H, dt, $J_1 = 8.1$ Hz, $J_2 = 1.2$ Hz, Ar), 7.75 (1H, t, $J = 7.5$ Hz, Ar), 7.96 (1H, d, $J = 7.8$ Hz, Ar), 8.08 (1H, d, $J = 7.8$ Hz, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 90:10, 0.7 mL/min, 230 nm, $t_{minor} = 20.83$ min, $t_{major} = 22.98$ min; 71% ee).

4.4.4. 2-Nitro-1-phenylethanol 8d. This is a known compound.[3m] $[\alpha]_D^{20} = +23.7$ (c 1.10, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 2.91 (1H, s, OH), 4.49 (1H, ddd, $J_1 = 13.5$ Hz, $J_2 = 3.0$ Hz, $J_3 = 0.9$ Hz, CH_2), 4.59 (1H, ddd, $J_1 = 13.2$ Hz, $J_2 = 9.6$ Hz, $J_3 = 0.9$ Hz, CH_2), 5.42 (1H, dd, $J_1 = 9.3$ Hz, $J_2 = 1.8$ Hz, CH), 7.34–7.43 (5H, m, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 95:5, 0.5 mL/min, 230 nm, $t_{minor} = 77.45$ min, $t_{major} = 91.64$ min; 64% ee).

4.4.5. 1-(2-Chlorophenyl)-2-nitroethanol 8e. This is a known compound.[3j] $[\alpha]_D^{20} = +42.0$ (c 1.10, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 3.25 (1H, s, OH), 4.44 (1H, dd, $J_1 = 13.5$ Hz, $J_2 = 9.6$ Hz, CH_2), 4.66 (1H, dd, $J_1 = 13.5$ Hz, $J_2 = 2.4$ Hz, CH_2), 5.83 (1H, d, $J = 9.6$ Hz, CH), 7.27–7.39 (3H, m, Ar), 7.65 (1H, d, $J = 7.2$ Hz, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 98:2, 0.7 mL/min, 214 nm, $t_{minor} = 42.29$ min, $t_{major} = 45.38$ min; 75% ee).

4.4.6. 1-(4-Chlorophenyl)-2-nitroethanol 8f. This is a known compound.[3h] $[\alpha]_D^{20} = +11.0$ (c 0.5, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 2.88 (1H, s, OH), 4.49 (1H, dd, $J_1 = 13.5$ Hz, $J_2 = 3.0$ Hz, CH_2), 4.58 (1H, dd, $J_1 = 13.5$ Hz, $J_2 = 9.0$ Hz, CH_2), 5.46 (1H, dd, $J_1 = 9.0$ Hz, $J_2 = 3.0$ Hz, CH), 7.34–7.41 (4H, m, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (hexane/*i*PrOH = 80:20, 0.7 mL/min, 254 nm, $t_{minor} = 10.61$ min, $t_{major} = 11.98$ min; 46% ee).

4.4.7. 2-Nitro-1-*p*-tolylethanol 8g. This is a known compound.[3h] $[\alpha]_D^{20} = +49.6$ (c 1.10, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 2.36 (3H, s, CH_3), 4.49 (1H, dd, $J_1 = 13.5$ Hz, $J_2 = 3.0$ Hz, CH_2), 4.61 (1H, dd, $J_1 = 13.5$ Hz, $J_2 = 9.6$ Hz, CH_2), 5.44 (1H, dd, $J_1 = 9.6$ Hz, $J_2 = 3.0$ Hz, CH), 7.21 (2H, d, $J = 7.8$ Hz, Ar), 7.29 (2H, d, $J = 7.8$ Hz, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel OJ-H column (hexane/*i*PrOH = 90:10, 0.7 mL/min, 230 nm, $t_{minor} = 19.03$ min, $t_{major} = 22.53$ min; 69% ee).

4.4.8. 2-Nitro-1-pyridin-3-yl-ethanol 8h. This is a known compound.[7] $[\alpha]_D^{20} = +5.0$ (c 1.10, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 4.54 (1H, dd, $J_1 = 12.9$ Hz, $J_2 = 3.3$ Hz, CH_2), 4.64 (1H, dd, $J_1 = 12.9$ Hz, $J_2 = 9.6$ Hz, CH_2), 5.53 (1H, dd, $J_1 = 9.6$ Hz, $J_2 = 3.3$ Hz, CH), 7.34–7.38 (1H, m, Ar), 7.83 (1H, d, $J = 7.8$ Hz, Ar), 8.46 (1H, d, $J = 4.2$ Hz, Ar), 8.52 (1H, s, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel OJ-H column (hexane/*i*PrOH = 75:25, 0.7 mL/min, 214 nm, $t_{minor} = 10.38$ min, $t_{major} = 12.96$ min; 22% ee).

4.4.9. 1-Nitro-4-phenyl-but-3-en-2-ol 8i. This is a known compound.[3i] $[\alpha]_D^{20} = +3.0$ (c 0.20, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 2.64 (1H, d, $J = 4.5$ Hz, OH), 4.47–4.56 (2H, m, CH_2), 5.03–5.10 (1H, m, CH), 6.15 (1H, dd, $J_1 = 15.9$ Hz, $J_2 = 6.6$ Hz, CH), 6.80 (1H, d, $J = 15.9$ Hz, CH), 7.27–7.47 (5H, m, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 90:10, 0.8 mL/min, 230 nm, $t_{major} = 34.46$ min, $t_{minor} = 38.71$ min; 50% ee).

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References

1. Henry, L. C. R. *Hebd. Seances. Acad. Sci.* **1895**, *120*, 1265.
2. For recent reviews, see: (a) Boruwa, J.; Gogoi, N.; Saikia, P. P.; Barua, N. C. *Tetrahedron: Asymmetry* **2006**, *17*, 3315–3326; (b) Palomo, C.; Oiarbide, M.; Laso, A. *Eur. J. Org. Chem.* **2007**, 2561–2574.
3. For related studies, see: (a) Marcelli, T.; van der Haas, R. N. S.; van Maarseveen, J. H.; Hiemstra, H. *Synlett* **2005**, 2817–2819; (b) Sohtome, Y.; Takemura, N.; Iguchi, T.; Hashimoto, Y.; Nagasawa, K. *Synlett* **2006**, 144–146; (c) Arai, T.; Watanabe, M.; Fujiwara, A.; Yokoyama, N.; Yanagisawa, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 5978–5981; (d) Palomo, C.; Oiarbide, M.; Mielgo, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 5442–5444; (e) Xiong, Y.; Wang, F.; Huang, X.; Wen, Y.-H.; Feng, X.-M. *Chem. Eur. J.* **2007**, *13*, 829–833; (f) Ooi, T.; Doda, K.; Maruoka, K. *J. Am. Chem. Soc.* **2003**, *125*, 2054–2055; (g) Bandini, M.; Piccinelli, F.; Tommasi, S.; Umani-Ronchi, A.; Ventrici, C. *Chem. Commun.* **2007**, 616–618; (h) Jiang, J. J.; Shi, M. *Tetrahedron: Asymmetry* **2007**, *18*, 1376–1382; (i) Saá, J. M.; Tur, F.; González, J.; Vega, M. *Tetrahedron: Asymmetry* **2006**, *17*, 99–106; (j) Evans, D. A.; Seidel, D.; Rueping, M.; Lam, H. W.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2003**, *125*, 12692–12693; (k) Sasai, H.; Suzuki, T.; Itoh, N.; Tanaka, K.; Date, T.; Okamura, K.; Shibasaki, M. *J. Am. Chem. Soc.* **1993**, *115*, 10372–10373; (l) Sasai, H.; Suzuki, T.; Arai, S.; Arai, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 4418–4420; (m) Palomo, C.; Oiarbide, M.; Laso, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 3881–3884; (n) Trost, B. M.; Yeh, V. S. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 861–863; (o) Du, D. M.; Lu, S. F.; Fang, T.; Xu, J. *J. Org. Chem.* **2005**, *70*, 3712–3715; (p) Lu, S. F.; Du, D. M.; Zhang, S. W.; Xu, J. *Tetrahedron: Asymmetry* **2004**, *15*, 3433–3441.
4. For comprehensive reviews regarding asymmetric organocatalysis, see: (a) Dalko, P. I.; Moisan, L. *Angew. Chem., Int. Ed.* **2001**, *40*, 3726–3748; (b) Dalko, P. I.; Moisan, L. *Angew. Chem., Int. Ed.* **2004**, *43*, 5138–5175.
5. (a) Okino, T.; Nakamura, S.; Furukawa, T.; Takemoto, Y. *Org. Lett.* **2004**, *6*, 625–627; (b) Xu, X.; Furukawa, T.; Okino, T.; Miyabe, H.; Takemoto, Y. *Chem. Eur. J.* **2006**, *12*, 466–476.
6. Yoon, T. P.; Jacobsen, E. N. *Angew. Chem.* **2005**, *117*, 470–472; Yoon, T. P.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2005**, *44*, 466–468.
7. Marcelli, M.; van der Haas, R. N. S.; van Maarseveen, J. H.; Hiemstra, H. *Angew. Chem., Int. Ed.* **2006**, *45*, 929–931.
8. For selected reviews on thio(urea)-catalyzed reactions, see: (a) Connon, S. J. *Chem. Eur. J.* **2006**, *12*, 5418–5427; (b) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520–1543.
9. For selected recent studies on thiourea catalyzed reactions, see: (a) McCooey, S. H.; Connon, S. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 6367–6370; (b) Berkessel, A.; Roland, K.; Neudörfl,

J. M. *Org. Lett.* **2006**, *8*, 4195–4198; (c) Sohtome, Y.; Tanatani, A.; Hashimoto, Y.; Nagasawa, K. *Tetrahedron Lett.* **2004**, *45*, 5589–5592; (d) Song, J.; Wang, Y.; Deng, L. *J. Am. Chem. Soc.* **2006**, *128*, 6048–6049; (e) Wang, J.; Li, H.; Zu, L. S.; Jiang, W.; Xie, H. X.; Duan, W. H.; Wang, W. *J. Am. Chem. Soc.* **2006**, *128*, 12652–12653; (f) Herrera, R. P.; Sgarzani, V.; Bernardi, L.; Ricci, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 6576–6579; (g) Taylor, M. S.; Tokunaga, N.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2005**, *44*, 6700–6704; (h) Lalonde, M. P.; Chen, Y. G.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 6366–6370; (i) Yalalov, D. A.; Tsogoeva, S. B.; Schmatz, S. *Adv. Synth. Catal.* **2006**, *348*, 826–832; (j) Ye, J. X.; Dixon, D. J.; Hynes, P. S. *Chem. Commun.* **2005**, 4481–4483; (k) Shi, Y. L.; Shi, M. *Adv. Synth. Catal.* **2007**, *349*, 2129–2135.

10. When we were carrying out this research, Connon et al. reported the chiral bis(arylthiourea)-based organocatalysts for asymmetric Friedel–Crafts type reactions: Fleming, E. M.; McCabe, T.; Connon, S. J. *Tetrahedron Lett.* **2006**, *47*, 7037–7042.
11. Kano, T.; Tanaka, Y.; Maruoka, K. *Org. Lett.* **2006**, *8*, 2687–2689.
12. Bordwell, F. G.; Algrim, D. J.; Harrelson, J. A. *J. Am. Chem. Soc.* **1988**, *110*, 5903–5904.
13. Ma, K. Y.; You, J. S. *Chem. Eur. J.* **2007**, *13*, 1863–1871.
14. Korostylev, A.; Tararov, V. I.; Fischer, C.; Monsees, A.; Börner, A. *J. Org. Chem.* **2004**, *69*, 3220–3221.