Rhodium-Catalyzed Ring-Opening Reactions of *N*-Boc-azabenzonorbornadiene with Chiral Amine Nucleophiles Derived from Amino Acids

Yong-Hwan Cho, Nai-Wen Tseng, Hisanori Senboku, Mark Lautens*

Davenport Laboratories, Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, ON, M5S 3H6, Canada
Fax +1(416)9468185; E-mail: mlautens@chem.utoronto.ca

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Abstract: The rhodium-catalyzed ring-opening of azabenzonorbornadienes with chiral amino nucleophiles derived from amino acids such as (*S*)-proline and (*R*)-phenylglycine is reported. The desired products were obtained as a mixture of diastereomers, which could be easily separated in high yield. Enantiomerically pure ring-fused nitrogen heterocycles and 1,2-diamines were also obtained by further transformation of the ring-opened products.

Key words: rhodium, ring-opening, diamines, heterocycles, diastereoselective

Chiral vicinal 1,2-diamines and their derivatives have extensively been used as chiral auxiliaries and chiral ligands for a variety of asymmetric reactions in the field of organic synthesis.[1–5] In addition, 1,2-diamine scaffolds have also been recognized as privileged structures in many biologically active compounds.[6–12] For example, *trans*-1,2-diaminotetrahydronaphthalenes such as DuP 747 and its analogues have been identified as potent κ-opioid receptor agonists.[9] Due to the versatile nature of the 1,2-diamine scaffold, considerable attention has been paid to their preparation and development of useful synthetic methods giving high diastereoselectivity and enantioselectivity.[13]

We have previously reported the catalytic asymmetric ring-opening reactions of azabenzonorbornadienes with various aliphatic and aromatic amines to give optically active 1,2-diamines with high yield and excellent enantioselectivity.[14,15] We have subsequently applied this methodology towards the total synthesis of an analgesic compound[14b] and the preparation of new chiral ligands.[15] In previous reports,[14a,16,17a] high levels of asymmetric induction have been observed, however, the use of large amounts of a tediously prepared chiral ligand[14a,15,18] was required.[19] To date, a high yielding, diastereoselective ring-opening of *N*-Boc-azabenzonorbornadiene (**1**) with amine nucleophiles containing an α-functional group still remains unexplored. We envisioned that by using our previously well-established procedures for ring-opening reactions, the use of chiral amine nucleophiles would provide a rapid diastereoselective route to *trans*-1,2-diaminotetrahydronaphthalene derivatives. We also sought to determine if the presence of functionality in the α-position in the amino nucleophile would have any influence on the diastereoselectivity. In addition, we investigated the chemoselectivity between two nucleophilic centers using substrates bearing amino and hydroxy functional groups.

Herein we report an expedient method to generate enantiomerically pure 1,2-diamine scaffolds by the catalytic ring-opening of *N*-Boc-azabenzonorbornadiene (**1**) using chiral amino nucleophiles easily derived from amino acids such as (*S*)-proline and (*R*)-phenylglycine in the presence of a readily available achiral rhodium-phosphine catalyst. We also demonstrate the preparation of optically active ring-fused nitrogen heterocyclic compounds and 1,2-diaminotetrahydronaphthalene[20] using this methodology.

Initial studies were conducted using proline derivatives in order to probe the influence of the α-stereocenter, which exists on its pyrrolidine ring in the catalytic asymmetric ring-opening reaction. Initial conditions with catalytic amounts of Et_3NHI (20 mol%) were chosen based on our previous reports[15] of the catalytic ring opening of **1** with amine nucleophiles. We found that the addition of the salts could prevent catalyst poisoning, thereby leading to dramatically lower catalyst loading for the efficient ring opening of **1** and decrease equivalents of amine nucleophile as well. It is noteworthy that proper selection of the ammonium halide salt for a given reaction is crucial since a dramatic halide effect on the reaction yield and enantioselectivity was noted.[14,15,17,21]

Hydrogen iodide of (*S*)-proline methyl ester (**2a**)[22] was prepared and used as the amine nucleophile to optimize the ring-opening reaction of **1**. Preliminary screening using 2.0 equivalents of **2a** and 3.0 equivalents of *i*-Pr_2NEt in the presence of 1.0 mol% of $[Rh(cod)Cl]_2$ and 3.0 mol% of dppf gave the corresponding ring-opening products **3a** and **3a′** in 42% yield in 1:1.5 ratio (Table 1, entry 1). Increasing the catalytic loading from 1.0 mol% to 2.5 mol% (entry 2) as well as increasing the amount of nucleophile and base improved the yield of the products **3a** and **3a′** in 73% yield (entry 3).

Each of the diastereomers **3a** and **3a′** could easily be isolated as the enantiomerically pure product (>99% ee) by conventional column chromatography. The absolute configuration of **3a** was determined to be *S*,*R*,*R* by X-ray crystal structure analysis of the cyclic derivative **4** (Figure 1),[23] which could be obtained in good yield by a TFA-mediated Boc-deprotection and subsequent intramolecular cyclization (Scheme 1).

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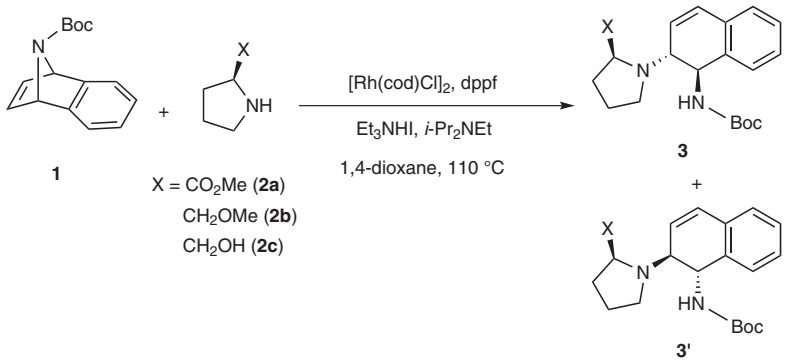
Table 1 Catalytic Ring-Opening Reaction of *N*-Boc-azabenzonorbornadiene (**1**) with (*S*)-Proline Derivatives (**2**)[a]



Entry	Nucleophile (equiv)	*i*-Pr_2NEt (equiv)	Time (h)	Product X	dr[b] **3**:**3′**	Yield (%)[c]
1[d]	**2a**·HI (2.0)	3.0	72	CO_2Me	1.0:1.5	42
2	**2a**·HI (2.0)	3.0	72	CO_2Me	1.0:1.5	54
3	**2a**·HI (3.0)	5.0	72	CO_2Me	1.0:1.5	73
4	**2b** (3.0)	5.0	36	CH_2OMe	1.0:1.0	88
5	**2c** (3.0)	6.0	72	CH_2OH	1.7:1.0	54
6	**2c** (5.0)	10.0	72	CH_2OH	1.7:1.0	70

[a] The reaction was carried out with **1** (0.25 mmol), nucleophile, Et_3NHI (20 equiv to Rh), and *i*-Pr_2NEt in dioxane (0.4 M) at 110 °C in the presence of $[Rh(cod)Cl]_2$ (2.5 mol%) and dppf (7.5 mol%).
[b] Diastereomeric ratio was measured by ^{1}H NMR spectroscopy.
[c] Combined yield of **3** and **3′**.
[d] The reactions were performed with $[Rh(cod)Cl]_2$ (1.0 mol%) and dppf (3.0 mol%).

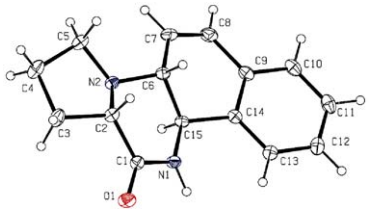
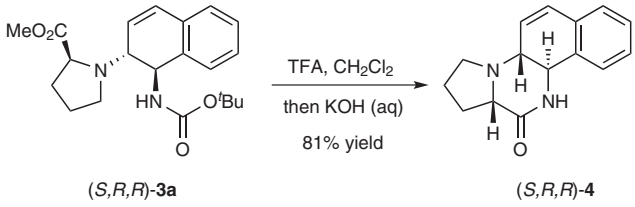


Figure 1 Crystal structure of cyclic **4**



Scheme 1 Preparation of benzopyrroloquinoxalinone **4**

Next, the ring-opening of **1** was carried out using (*S*)-2-(methoxymethyl)pyrrolidine (**2b**) to give the enantiomerically pure products **3b** and **3b′** in 88% yield as a 1:1 mixture (entry 4). The enantiomeric purity of **3b** and **3b′** were determined (>99% ee) by HPLC analysis,[24] and the absolute configuration of **3b** was determined to be *S*,*R*,*R* by X-ray analysis (Figure 2).[25] Changing the functionality on the pyrrolidine ring from an ester group (CO_2Me) into methoxymethyl group (CH_2OMe) showed an increase in reactivity.

Compared to **2b**, (*S*)-prolinol (**2c**) reacts more slowly. In the presence of 2.5 mol% of $[Rh(cod)Cl]_2$ and 7.5 mol% of dppf, the reaction of **1** with 3.0 equivalents of **2c** and 6.0 equivalents of *i*-Pr_2NEt at 110 °C for 72 hours gave the corresponding products **3c** and **3c′** in 54% yield (entry 5). An increase in the yield (70%) was observed in the reaction using 5.0 equivalents of **2c** and 10.0 equivalents of *i*-Pr_2NEt (entry 6) and a slightly higher selectivity on the formation of **3c** (**3c**:**3c′** = 1.7:1.0) was obtained (entry 6). The absolute configuration of ring-opened product **3c** was assigned to be *S*,*R*,*R* by correlation with the authentic sample, (*S*,*R*,*R*)-**3b** (vide infra),[25] after transformation of the hydroxy group in **3c** into methoxy group by treatment with dimethyl sulfate (Scheme 2).

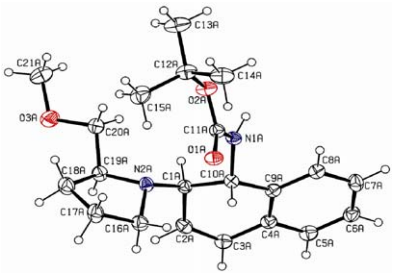
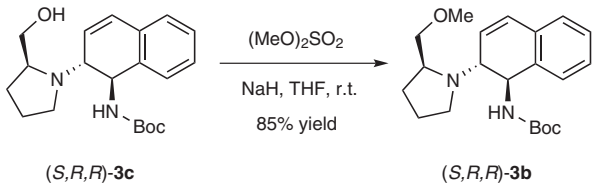


Figure 2 Crystal structure of **3b**



(*S,R,R*)-**3c** (*S,R,R*)-**3b**

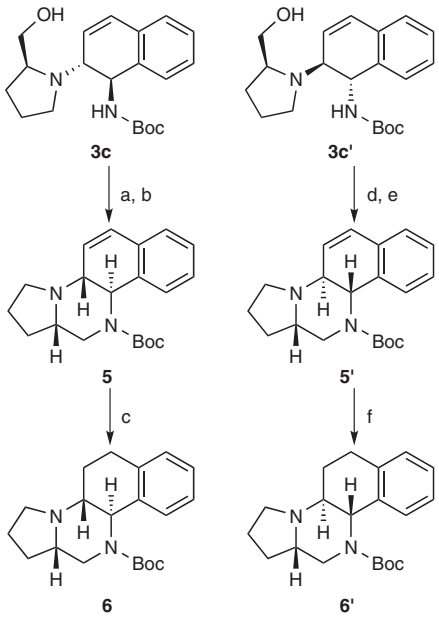
Scheme 2 Preparation of (*S,R,R*)-**3b** from **3c**

The difference in selectivity observed for (*S*)-prolinol (**2c**) compared to **2a** and **2b** is likely due to a catalyst-nucleophile interaction, which results in an increase of the selectivity for **3c**. Although, the specifics of this interaction still remain to be studied, it has been reported that amine nucleophile can affect the stereoselectivity of metal-catalyzed reactions by binding to the metal center of the catalyst.[14a,17b] Also, this strong interaction could explain the sluggish result of the reaction using **2c**. The ring-opening of **1** with amines such as pyrrolidines known to bind strongly to the metal catalyst typically showed slower reaction rates than reactions using other nucleophiles.[14a] Similarly, it is likely that (*S*)-proline methyl ester (**2a**) also interacts with the catalyst, but in a different manner. While the reaction using **2c** has a preference for the formation of the product **3c** with *S,R,R*-configuration, the ring-opening of **1** with **2a** showed the selective formation of the product **3a′** with *S,S,S*-configuration (entries 1, 2, and 3).

In contrast, the reaction using (*S*)-2-(methoxymethyl)pyrrolidine (**2b**) showed the best reactivity (entry 4), but had no selectivity for either **3b** or **3b′** (**3b**:**3b′** = 1:1), suggesting that the nature of the functionality on the α-position on the pyrrolidine ring plays a significant role in the reaction outcome.

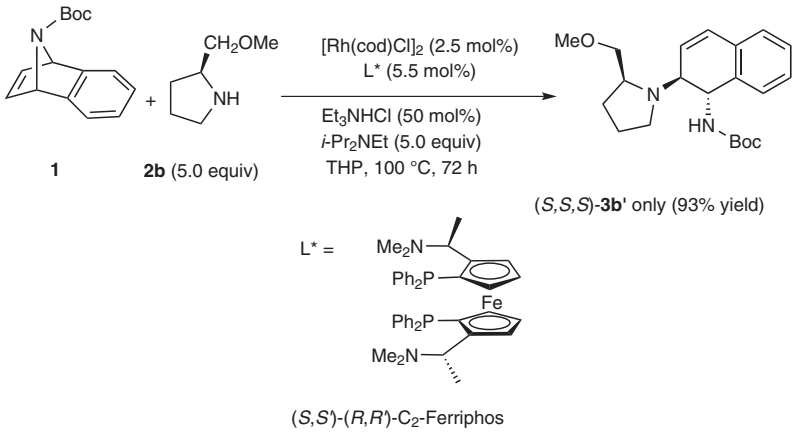
It is also found that carrying out the reaction using the enantiomerically pure ligand gave a single isomer. In the presence of 2.5 mol% of $[Rh(cod)Cl]_2$, 5.5 mol% of (*S,S′*)-(*R,R′*)-C_2-ferriphos,[18] and 50 mol% of Et_3NHCl, the ring-opening of **1** with 5.0 equivalents of (*S*)-**3b** and 5.0 equivalents of *i*-Pr_2NEt proceeded in tetrahydropyran at 100 °C for 96 hours to give only the product (*S,S,S*)-**3b′** in 93% yield (Scheme 3). Formation of the opposite diastereomer (*S,R,R*)-**3b** was not observed in this reaction.

The ring-opened products **3c** and **3c′** are also easily converted into unique cyclic compounds **6** and **6′** (Scheme 4). The key compounds are cyclic (*S,R,R*)-**5** and (*S,S,S*)-**5′**, obtained by the reaction of the hydroxy groups of **3c** and **3c′** with methanesulfonyl chloride followed by treatment of the mesylate with NaH at 55 °C for 12 hours. Catalytic hydrogenation of **5** and **5′** in the presence of Degussa E1 Pd catalyst under hydrogen atmosphere gave the corresponding cyclic products **6** and **6′** in 61 and 65% yield, respectively.

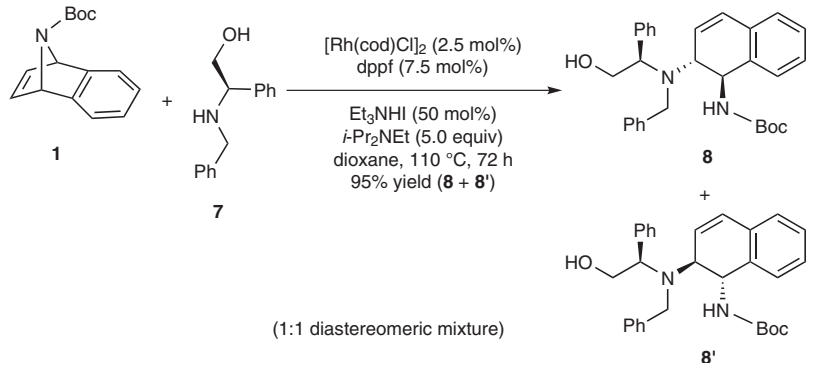


Scheme 4 Preparation of cyclic compounds **6** and **6′**. *Reagents and conditions*: a) $MeSO_2Cl$, Et_3N, 0 °C to r.t.; b) NaH, 55 °C, 82%; c) H_2 (1 atm), 10% Pd/C, MeOH–EtOAc, 61%; d) $MeSO_2Cl$, Et_3N, 0 °C to r.t.; e) NaH, 55 °C, 75%; f) H_2 (1 atm), 10% Pd/C, MeOH–EtOAc, 65%.

In our previous work, we reported that the synthesis of the enantiomerically pure free 1,2-diaminotetrahydronaphthalenes from the corresponding ring-opening products

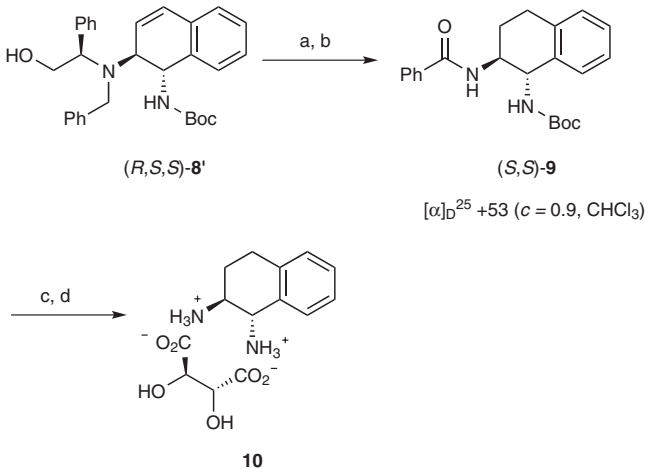


Scheme 3 Catalytic ring opening of **1** with (*S*)-**2b** in the presence of the rhodium catalyst coordinated with (*S,S′*)-(*R,R′*)-C_2-ferriphos



Scheme 5 Catalytic ring opening of **1** with (*R*)-2-benzylamino-2-phenylethanol (**7**)

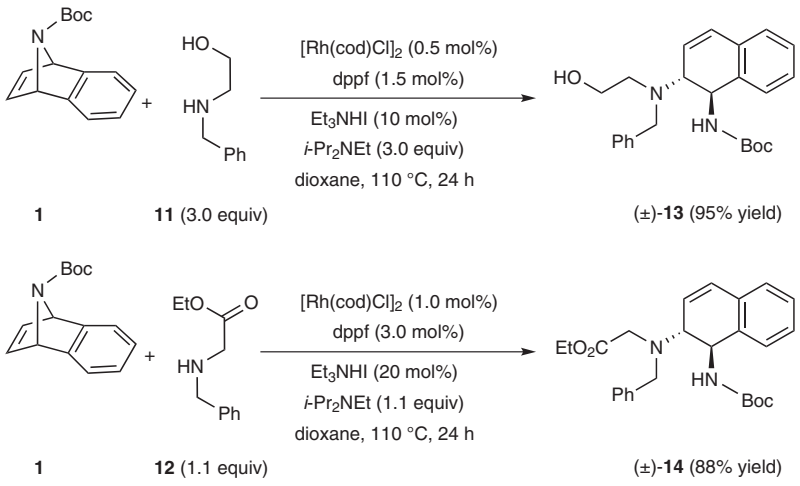
prepared by the asymmetric ring-opening of **1** using *N,N*-dibenzylamine as a nucleophile, by a sequential deprotection.[15] In a similar manner, we chose (*R*)-2-benzylamino-2-phenylethanol[26] (**7**) in order to prepare the enantiomerically pure 1,2-diaminonaphthalene following deprotection. In the presence of 2.5 mol% of $[Rh(cod)Cl]_2$, 7.5 mol% of dppf, and 50 mol% of Et_3NHI, the ring-opening of **1** using 3.0 equivalents of **7** and 5.0 equivalents of *i*-Pr_2NEt gave the corresponding products **8** and **8′** in 95% yield (**8**:**8′** = 1:1) (Scheme 5). It is very interesting that the reaction using **7** does not show any diastereoselectivity while the reaction of **1** with **2c** gave a modest dr (1.7:1).



Scheme 6 Preparation of diamine scaffold **10**. *Reagents and conditions*: a) 10% Pd/C, HCO_2NH_4, EtOAc, MeOH; b) benzoyl chloride, pyridine, THF, 55% (2 steps); c) aq 50% HCl; d) L-tartaric acid, EtOH–H_2O, 72% (2 steps).

The ring-opened product **8′** was subsequently converted into the versatile compound **10** (Scheme 6). Reduction of the double bond and debenzylation of the benzylphenylglycinol moiety[27] were carried out by catalytic hydrogenation of **8′** with HCO_2NH_4 in the presence of Pd/C.[28] Acylation of the resulting debenzylated product with benzoyl chloride gave **9** in 55% yield and the configuration of **9** was assigned to be 1*S*,2*S* by comparison of its specific rotation, $[\alpha]_D^{25}$ +53 (*c* 0.9, $CHCl_3$), with the previously reported value, $[\alpha]_D^{25}$ +58 (*c* 1.0, $CHCl_3$), for (1*S*,2*S*)-**9**.[15] The enantiomeric purity of **9** was also determined (>99% ee) by HPLC analysis.[29] Finally, diamide **9** was deprotected by treatment of 50% aqueous HCl and was converted into the 1,2-diaminonaphthalene tartrate **10** according to the reported procedure.[15]

The catalytic ring-opening reactions of **1** using *N*-benzylethanolamine (**11**) and *N*-benzylglycine ethyl ester (**12**) were also examined. The results revealed that the presence or absence of functionalities at the α-position in



Scheme 7 Catalytic ring opening of **1** with *N*-benzylethanolamine (**11**) and *N*-benzylglycine ethyl ester (**12**)

amine nucleophiles has a strong influence to the reaction rate (Scheme 7). The reactions using **11** and **12** proceeded much faster than with **7**, even with lower catalyst loadings. In the presence of 0.5 mol% of $[Rh(cod)Cl]_2$, 1.5 mol% of dppf, and 10 mol% of Et_3NHI, the ring-opening of **1** with 3.0 equivalents of **11** and 3.0 equivalents of *i*-Pr_2NEt at 110 °C for 24 hours gave the corresponding product **13** in 95% yield. Furthermore, in the presence of 1.0 mol% of $[Rh(cod)Cl]_2$, 3.0 mol% of dppf, and 20 mol% of Et_3NHI, the reaction of **1** with **12** at 110 °C for 24 hours gave the ring-opened product **14** in 88% yield.

In summary, we have developed a rhodium-catalyzed ring-opening of azabenzonorbornadiene **1** with chiral amine nucleophiles derived from commercially available amino acids such as (*S*)-proline and (*R*)-phenylglycine. The reactions gave the desired products as a mixture of separable diastereomers. The use of both Et_3NHI and *i*-Pr_2NEt improved the reaction rate and yield in the present reaction. In addition, studies on the scope of reaction revealed that functionality at the α-position of the amine nucleophile has a strong influence on the reaction rate and the diastereoselectivity.

All moisture and air sensitive manipulations were carried out under dry N_2. NMR spectra were recorded on a Varian Mercury 300 MHz or 400 MHz NMR spectrometer. Chemical shifts are reported in δ (ppm) relative to TMS. IR spectra were obtained using a Perkin-Elmer Spectrum 1000 FT-IR spectrometer as neat films on NaCl plates. High-resolution mass spectra were obtained from a Micromass 70S-250 mass spectrometer (EI) or an ABI/Sciex Qstar mass spectrometer (ESI). Optical rotations were measured on a Perkin-Elmer Model 243 Polarimeter and melting points were taken on a Fisher-Johns melting point apparatus. HPLC analysis was performed on an Agilent 1100 Series HPLC with Chiralcel AD or AS columns. Dioxane and THF were distilled from sodium benzophenone ketyl immediately prior to use. CH_2Cl_2 was distilled from CaH_2. Degussa E1 catalyst (Pd, 5% on activated carbon, uniform, oxidic), $[Rh(cod)Cl]_2$ and dppf were acquired from Strem Chemicals Co. Ltd. Amine nucleophiles (*S*)-**2b** and (*S*)-**2c** were acquired from Alfa Aesar®. (*S*)-Proline, **11**, and **12** were acquired from Aldrich Chemical Co., Ltd. Azabenzonorbornadiene **1**[15] and (*R*)-**7**[26] were prepared according to the reported procedures.

Ring Opening of Azabenzonorbornadiene 1 with (*S*)-Proline Methyl Ester Hydroiodide (2a)

To a stirred solution of **1** (100 mg, 0.4 mmol), $[Rh(cod)Cl]_2$ (5.1 mg, 10 μmol), and dppf (17 mg, 31 μmol) in anhyd 1,4-dioxane (1.0 mL) was added the hydrogen iodide salt of (*S*)-proline methyl ester (**2a**) (317 mg, 1.23 mmol) and *i*-Pr_2NEt (0.4 mL, 2.1 mmol) under N_2. The mixture was allowed to stir at 110 °C for 72 h. The resulting mixture was cooled to r.t. and quenched with aq 1 N NaOH. The mixture was extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic extracts were dried ($MgSO_4$), and filtered. After evaporation under reduced pressure, the residue was purified by flash column chromatography (hexane–EtOAc, 70:30) to give 46 mg (30%) of **3a** and 66 mg (43%) of **3a′**.

(1*R*,2*R*)-{2-[(*S*)-2′-(Methoxycarbonyl)pyrrolidin-1′-yl]-1,2-dihydronaphthalen-1-yl}carbamic Acid *tert*-Butyl Ester (3a)

R_f = 0.55 (SiO_2, hexanes–EtOAc, 7:3); $[\alpha]_D^{25}$ –177.8 (*c* 1.00, $CHCl_3$).

IR (film): 3360, 1714, 1504, 1454, 1391, 1365, 1250, 1171, 1045, 1021, 861, 781 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.46 (s, 9 H), 1.74–2.05 (m, 4 H), 2.82–2.88 (m, 1 H), 3.05 (br s, 1 H), 3.51 (dd, *J* = 8.4, 4.8 Hz, 1 H), 3.65–3.70 (m, 1 H), 3.68 (s, 3 H), 4.90 (br s, 2 H), 5.96 (dd, *J* = 9.9, 3.6 Hz, 1 H), 6.59 (d, *J* = 9.9 Hz, 1 H), 7.06–7.09 (m, 1 H), 7.21–7.24 (m, 2 H), 7.35–7.38 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.19, 155.92, 135.47, 132.29, 129.80, 127.92, 127.74, 127.10, 126.47, 79.22, 61.57, 59.63, 51.71, 51.39, 48.40, 29.72, 28.33.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{29}N_2O_4$ [M + H^+]: 373.2121; found: 373.2117.

(1*S*,2*S*)-{2-[(*S*)-2′-(Methoxycarbonyl)pyrrolidin-1′-yl]-1,2-dihydronaphthalen-1-yl}carbamic Acid *tert*-Butyl Ester (3a′)

R_f = 0.45 (SiO_2, hexanes–EtOAc, 7:3); $[\alpha]_D^{25}$ +142.4 (*c* 1.00, $CHCl_3$).

IR (film): 3360, 1713, 1514, 1505, 1487, 1455, 1391, 1366, 1249, 1170, 1045, 1022, 863, 782 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.43 (s, 9 H), 1.61–1.83 (m, 3 H), 1.86–1.95 (m, 1 H), 2.06 (ddd, *J* = 17.1, 12.6, 8.4 Hz, 1 H), 2.48 (q, *J* = 7.8 Hz, 1 H), 3.00–3.06 (m, 1 H), 3.63 (s, 3 H), 3.65–3.69 (m, 1 H), 3.77–3.61 (m, 1 H), 4.65 (br d, *J* = 7.8 Hz, 1 H), 4.90 (br d, *J* = 7.8 Hz, 1 H), 5.98 (dd, *J* = 9.6, 5.1 Hz, 1 H), 6.62 (d, *J* = 9.6 Hz, 1 H), 7.08–7.11 (m, 1 H), 7.19–7.30 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.35, 154.86, 134.42, 132.20, 129.16, 128.53, 128.17, 126.74, 126.21, 79.49, 61.36, 59.02, 51.74, 49.45, 49.06, 29.98, 28.35, 23.63.

HRMS (ESI): *m*/*z* [M + H^+] calcd for $C_{21}H_{29}N_2O_4$: 373.2121; found: 373.2114.

Ring Opening of 1 with (*S*)-2-(Methoxymethyl)pyrrolidine (2b) in the Presence of Triethylamine Hydroiodide; (1*R*,2*R*)-{2-[(*S*)-2′-(Methoxymethyl)pyrrolidin-1′-yl]-1,2-dihydronaphthalen-1-yl}carbamic Acid *tert*-Butyl Ester (3b) and (1*S*,2*S*)-{2-[(*S*)-2′-(Methoxymethyl)pyrrolidin-1′-yl]-1,2-dihydronaphthalen-1-yl}carbamic Acid *tert*-Butyl Ester (3b′); Typical Procedure

To a stirred solution of **1** (100 mg, 0.4 mmol), $[Rh(cod)Cl]_2$ (5.1 mg, 10 μmol), dppf (17 mg, 31 μmol), and Et_3NHI (47 mg, 0.2 mmol) in anhyd 1,4-dioxane (1.0 mL) was added *i*-Pr_2NEt (0.4 mL, 2.1 mmol) and (*S*)-2-(methoxymethyl)pyrrolidine (**2b**; 142 mg, 1.23 mmol) under N_2. The mixture was allowed to stir at 110 ° C for 36 h. The resulting mixture was cooled to r.t. and quenched with aq 1 N NaOH. The mixture was extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic extracts were dried ($MgSO_4$). After evaporation under reduced pressure, the residue was purified by flash column chromatography (hexane–EtOAc, 70:30) to give 66 mg (45%) of **3b** and 63 mg of (43%) **3b′**.

3b

More than 99% ee by HPLC analysis with a chiral column (Chiralcel AS, hexane–propan-2-ol, 99:1, 0.5 mL/min), t_R (*S*,*R*,*R*)-(–)-, 14.5 min (major); (*R*,*S*,*S*)-(+)-, 17.6 min (minor); R_f = 0.41 (SiO_2, hexanes–EtOAc, 7:3); mp 90–92 °C; $[\alpha]_D^{25}$ –287.8 (*c* 1.00, $CHCl_3$).

IR (film): 3321, 2961, 1688, 1528, 1449, 1365, 1317, 1255, 1169, 1117, 1044, 1021, 780, 748 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.47 (s, 9 H), 1.51–1.57 (m, 1 H), 1.64–1.73 (m, 2 H), 1.76–1.88 (m, 1 H), 2.62 (q, *J* = 8.0 Hz, 1 H), 2.80 (br s, 1 H), 3.04–3.12 (m, 1 H), 3.22 (dd, *J* = 9.0, 6.0 Hz, 1 H), 3.29–3.35 (m, 4 H), 3.74–3.77 (m, 1 H), 4.80–4.95 (m, 1 H), 4.72 (br s, 1 H), 6.01 (dd, *J* = 9.9, 3.6 Hz, 1 H), 6.60 (d, *J* = 9.9 Hz, 1 H), 7.04–7.07 (m, 1 H), 7.18–7.22 (m, 2 H), 7.36–7.40 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.45, 136.18, 132.95, 129.78, 127.92, 127.81, 127.72, 126.99, 126.58, 78.12, 60.62, 59.44, 59.15, 53.62, 53.29, 48.40, 29.07, 28.65, 24.26.

Anal. Calcd for $C_{21}H_{30}N_2O_3$: C, 70.36; H, 8.44; N, 7.81. Found: C, 70.62; H, 8.78; N, 7.89.

3b′

More than 99% ee by HPLC analysis with a chiral column (Chiralcel AD, hexane–propan-2-ol, 98:2, 1.0 mL/min), t_R (*R*,*R*,*R*)-(–)-, 13.0 min (minor); (*S*,*S*,*S*)-(+)-, 19.7 min (major); R_f = 0.37 (SiO_2, hexanes–EtOAc, 7:3); $[\alpha]_D^{25}$ +218.6 (*c* 1.00, $CHCl_3$).

IR (film): 3332, 2972, 2927, 2823, 1709, 1489, 1454, 1390, 1365, 1249, 1170, 1112, 1045, 1023, 780, 748 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.44 (s, 9 H), 1.53–1.70 (m, 3 H), 1.72–1.88 (m, 1 H), 2.23 (q, *J* = 8.7 Hz, 1 H), 2.74–2.82 (m, 1 H), 3.20–3.38 (m, 6 H), 3.69 (t, *J* = 3.8 Hz, 1 H), 4.66–4.78 (m, 1 H), 4.94 (br s, 1 H), 5.96 (dd, *J* = 9.9, 4.8 Hz, 1 H), 6.60 (d, *J* = 9.0 Hz, 1 H), 7.07–7.10 (m, 1 H), 7.19–7.24 (m, 2 H), 7.31–7.34 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.18, 135.47, 132.59, 128.73, 128.28, 128.13, 128.01, 126.79, 79.55, 76.44, 59.09, 59.04, 58.12, 49.57, 49.26, 28.83, 28.58, 23.57.

Anal. Calcd for $C_{21}H_{30}N_2O_3$: C, 70.36; H, 8.44; N, 7.81. Found: C, 70.45; H, 8.48; N, 7.83.

(1*R*,2*R*)-{2-[(*S*)-2′-(Hydroxymethyl)pyrrolidin-1′-yl]-1,2-dihydronaphthalen-1-yl}carbamic Acid *tert*-Butyl Ester (3c) and (1*S*,2*S*)-{2-[(*S*)-2′-(Hydroxymethyl)pyrrolidin-1′-yl]-1,2-dihydronaphthalen-1-yl}carbamic Acid *tert*-Butyl Ester (3c′)

Prepared by following the above typical procedure using (*S*)-prolinol (**2c**) as the nucleophile to give the corresponding products **3c** and **3c′** in 70% yield (**3c**:**3c′** = 1.7:1) (Table 1, entry 6).

3c

R_f = 0.53 (SiO_2, hexanes–EtOAc, 1:1); $[\alpha]_D^{25}$ –139.2 (*c* 1.00, $CHCl_3$).

IR (film): 3334, 2971, 2869, 1699, 1505, 1451, 1391, 1366, 1250, 1169, 1145, 1023, 782, 747 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.48 (s, 9 H), 1.67–1.89 (m, 4 H), 2.67 (q, *J* = 8.4 Hz, 1 H), 2.85–3.00 (m, 1 H), 3.05–3.11 (m, 1 H), 3.36 (dd, *J* = 11.0, 3.3 Hz, 1 H), 3.56–3.63 (m, 2 H), 4.58 (d, *J* = 9.0 Hz, 1 H), 5.02 (t, *J* = 9.0 Hz, 1 H), 5.97 (dd, *J* = 9.6, 3.0 Hz, 1 H), 6.63 (dd, *J* = 9.9, 1.8 Hz, 1 H), 7.07–7.10 (m, 1 H), 7.20–7.25 (m, 2 H), 7.37–7.40 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.16, 135.27, 132.96, 130.19, 128.04, 128.00, 126.67, 126.61, 126.56, 79.84, 62.84, 60.66, 59.95, 53.47, 48.29, 28.48, 28.39, 24.55.

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{29}N_2O_3$ [M + H$^+$]: 345.2172; found: 345.2174.

3c′

R_f = 0.30 (SiO_2, hexanes–EtOAc, 1:1); $[\alpha]_D^{25}$ +89.8 (*c* 1.00, $CHCl_3$).

IR (film): 3331, 2970, 1699, 1489, 1391, 1366, 1251, 1169, 1045, 781, 747 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.43 (s, 9 H), 1.48–1.73 (m, 4 H), 1.83–1.96 (m, 1 H), 2.30 (q, *J* = 8.4 Hz, 1 H), 2.74–2.81 (m, 1 H), 3.36–3.45 (m, 2 H), 3.62–3.66 (m, 2 H), 4.60 (d, *J* = 7.2 Hz, 1 H), 4.93 (d, *J* = 7.2 Hz, 1 H), 5.92 (dd, *J* = 9.6, 5.4 Hz, 1 H), 6.62 (d, *J* = 9.9 Hz, 1 H), 7.10–7.13 (m, 1 H), 7.23–7.27 (m, 2 H), 7.29–7.33 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.22, 134.52, 132.51, 128.68, 128.63, 124.46, 127.19, 127.00, 79.85, 63.76, 59.61, 58.24, 49.38, 49.11, 28.96, 28.53, 24.20.

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{29}N_2O_3$ [M + H$^+$]: 345.2172; found: 345.2169.

(1*R*,2*R*)-{2-[*N*-(*R*)-2′-Hydroxy-1′-phenylethyl-*N*-benzyl]amino-1,2-dihydronaphthalen-1-yl}carbamic Acid *tert*-Butyl Ester (8) and (1*S*,2*S*)-{2-[*N*-(*R*)-2′-Hydroxy-1′-phenylethyl-*N*-benzyl]amino-1,2-dihydronaphthalen-1-yl}carbamic Acid *tert*-Butyl Ester (8′) (Scheme 5)

Prepared by following the above typical procedure using (*R*)-2-benzylamino-2-phenylethanol (**7**)[26] as the nucleophile to give the corresponding products **8** and **8′** in 95% yield (**8**:**8′** = 1:1).

8

R_f = 0.72 (SiO_2, hexanes–EtOAc, 7:3); $[\alpha]_D^{25}$ –267.6 (*c* 1.00, $CHCl_3$).

IR (film): 3319, 3026, 2975, 2927, 1691, 1494, 1452, 1391, 1366, 1250, 1170, 1044, 1027, 864, 782, 758, 701 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.57 (s, 9 H), 3.00 (d, *J* = 6.0 Hz, 1 H), 3.56–3.63 (m, 1 H), 3.64 (d, *J* = 13.8 Hz, 1 H), 3.89–4.00 (m, 3 H), 4.08 (t, *J* = 10.2 Hz, 1 H), 4.79 (d, *J* = 8.4 Hz, 1 H), 5.12 (dd, *J* = 9.9, 3.0 Hz, 1 H), 5.22 (d, *J* = 9.0 Hz, 1 H), 6.28 (dd, *J* = 9.9, 1.8 Hz, 1 H), 6.97–6.99 (m, 1 H), 7.18–7.21 (m, 2 H), 7.22–7.37 (m, 9 H), 7.42 (d, *J* = 6.9 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.48, 139.81, 138.03, 135.27, 132.81, 129.42, 128.96, 128.80, 128.74, 128.67, 128.58, 128.45, 128.25, 128.09, 127.84, 127.40, 127.17, 126.76, 126.66, 80.16, 68.84, 62.76, 61.39, 57.41, 53.48, 51.88, 28.65.

HRMS (EI): *m*/*z* calcd for $C_{30}H_{34}N_2O_3$ [M$^+$]: 470.2569; found: 470.2567.

8′

R_f = 0.40 (SiO_2, hexanes–EtOAc, 7:3); $[\alpha]_D^{25}$ +94.6 (*c* 1.00, $CHCl_3$).

IR (film): 3415, 3027, 2975, 2927, 1710, 1494, 1452, 1390, 1365, 1250, 1169, 1046, 1027, 781, 751, 699 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.45 (s, 9 H), 2.38 (br s, 1 H), 3.48–3.60 (m, 1 H), 3.64–3.74 (m, 1 H), 3.80–4.06 (m, 4 H), 4.43 (d, *J* = 9.0 Hz, 1 H), 4.85 (dd, *J* = 8.7, 4.5 Hz, 1 H), 5.81 (dd, *J* = 9.6, 4.5 Hz, 1 H), 6.63 (dd, *J* = 9.6, 1.5 Hz, 1 H), 7.00 (d, *J* = 7.5 Hz, 3 H), 7.06 (d, *J* = 7.5 Hz, 1 H), 7.13 (dt, *J* = 7.5, 1.5 Hz, 1 H), 7.18–7.33 (m, 7 H), 7.40 (d, *J* = 6.9 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.09, 140.71, 139.26, 135.20, 132.07, 130.02, 129.18, 129.05, 128.92, 128.61, 128.53, 128.42, 128.14, 128.71, 127.40, 127.23, 126.92, 79.59, 64.23, 62.52, 59.79, 50.46, 49.69, 28.61.

HRMS (EI): *m*/*z* calcd for $C_{30}H_{34}N_2O_3$ [M$^+$]: 470.2569; found: 470.2573.

(4a*R*,10b*R*,12a*S*)-1,2,3,10b,11,12a-Hexahydro-4a*H*-benzo[*f*]pyrrolo[1,2-*a*]quinoxalin-12-one (4)

To a stirred solution of **3a** (130 mg, 0.35 mmol) in anhyd CH_2Cl_2 (5.0 mL) was slowly added trifluoroacetic acid (0.5 mL, 6.98 mmol) at 0 °C over 5 min. The mixture was allowed to stir at r.t. for 18 h and the resulting mixture was carefully quenched with aq 4 N KOH at 0 °C. The mixture was extracted with CH_2Cl_2 (3 × 15 mL) and the separated organic layer was dried ($MgSO_4$) and filtered. After concentration under reduced pressure, the residue was purified by flash column chromatography (hexane–EtOAc, 50:50) to give 68 mg (81%) of **4**; mp 242–245 °C; $[\alpha]_D^{25}$ –127.5 (*c* 1.01, $CHCl_3$).

IR (film): 3208, 3058, 1660, 1459, 1416, 1311, 1229, 1187, 1136, 1004, 960, 780 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.84–2.00 (m, 2 H), 2.05–2.19 (m, 1 H), 2.27–2.38 (m, 1 H), 2.80–2.87 (m, 1 H), 2.99 (dd, *J* = 16.2, 7.7 Hz, 1 H), 3.63 (dd, *J* = 8.6, 6.0 Hz, 1 H), 3.80 (dt, *J* = 13.6, 2.3 Hz, 1 H), 4.84 (d, *J* = 13.6 Hz, 1 H), 6.11 (dd, *J* = 9.8, 1.5 Hz, 1 H), 6.56

(dd, *J* = 9.8, 3.0 Hz, 1 H), 6.79 (br s, 1 H), 7.16–7.19 (m, 1 H), 7.24–7.32 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.39, 133.91, 132.27, 128.61, 127.95, 127.52, 126.82, 121.68, 63.17, 58.27, 51.48, 47.01, 27.35, 23.29.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{17}N_2O$ [M + H$^+$]: 241.1335; found: 241.1342.

(4a*R*,10b*R*,12a*S*)-2,3,4a,10b,12,12a-Hexahydro-1*H*-benzo[*f*]pyrrolo[1,2-*a*]quinoxalin-11-carboxylic Acid *tert*-Butyl Ester (5); Typical Procedure

To a solution of **3c** (1.0 g, 2.90 mmol) and Et_3N (1.2 mL, 8.71 mmol) in anhyd THF (30 mL) was added $MeSO_2Cl$ (0.3 mL, 3.48 mmol) dropwise at 0 °C over 5 min. The mixture was then stirred at 0 °C for 1 h under N_2. NaH (60% oil dispersion) (174 mg, 4.35 mmol) was then added at 0 °C and the mixture heated to 55 °C for 5 h. The resulting mixture was quenched with H_2O (20 mL) and extracted with Et_2O (3 × 25 mL). The combined organic extracts were dried ($MgSO_4$) and filtered. After concentration under reduced pressure, the residue was purified by flash column chromatography (hexane–EtOAc, 90:10) to give 780 mg (82%) of **5**; mp 176–178 °C; $[\alpha]_D^{25}$ –254.0 (*c* 1.00, $CHCl_3$).

IR (film): 3240, 2958, 1682, 1524, 1455, 1366, 1250, 1162, 1074, 1045, 1019, 876, 815, 750 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.46 (s, 9 H), 1.50–1.56 (m, 1 H), 1.66–1.75 (m, 1 H), 2.02–2.11 (m, 1 H), 2.24–2.36 (m, 1 H), 2.65 (dd, *J* = 11.1, 8.7 Hz, 2 H), 3.06 (d, *J* = 10.2 Hz, 1 H), 3.41–3.45 (m, 1 H), 3.88–3.95 (m, 1 H), 4.56 (br s, 1 H), 5.01 (br s, 1 H), 5.91 (dd, *J* = 9.9, 4.2 Hz, 1 H), 6.61 (dd, *J* = 9.6, 1.5 Hz, 1 H), 7.07–7.10 (m, 1 H), 7.22–7.25 (m, 2 H), 7.33–7.36 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.41, 135.55, 132.60, 129.75, 128.43, 128.28, 127.62, 126.96, 126.61, 79.79, 64.79, 57.91, 56.83, 49.11, 48.85, 35.14, 28.66, 25.32.

HRMS (EI): *m*/*z* calcd for $C_{20}H_{27}N_2O_2$ [M + H$^+$]: 327.2072; found: 327.2070.

(4a*S*,10b*S*,12a*S*)-2,3,4a,10b,12,12a-Hexahydro-1*H*-benzo[*f*]pyrrolo[1,2-*a*]quinoxalin-11-carboxylic Acid *tert*-Butyl Ester (5′)

The cyclic compound **5′** was prepared from **3c′** following the same procedure as above for the preparation of **5** from **3c**; yield: 210 mg (75%); $[\alpha]_D^{25}$ +315.6 (*c* 1.00, $CHCl_3$); mp 141–143 °C.

IR (film): 3241, 2957, 2935, 2804, 1693, 1675, 1550, 1327, 1309, 1250, 1183, 1169, 1047, 977, 877, 776, 758, 746 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.46 (s, 9 H), 1.47–1.53 (m, 1 H), 1.70–1.77 (m, 1 H), 2.05–2.18 (m, 1 H), 2.32 (t, *J* = 10.2 Hz, 1 H), 2.49 (dt, *J* = 10.8, 2.7 Hz, 1 H), 2.75 (d, *J* = 11.7 Hz, 1 H), 2.97 (d, *J* = 11.7 Hz, 1 H), 3.41–3.45 (m, 1 H), 3.82–3.90 (m, 1 H), 4.57 (br s, 1 H), 4.98 (br s, 1 H), 5.93 (dd, *J* = 9.6, 4.5 Hz, 1 H), 6.63 (d, *J* = 10.8 Hz, 1 H), 7.08–7.10 (m, 1 H), 7.22–7.25 (m, 2 H), 7.33–7.36 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.48, 135.37, 132.54, 129.85, 128.47, 128.32, 127.71, 126.99, 125.73, 79.71, 64.63, 57.50, 56.80, 49.15, 48.91, 35.40, 28.64, 25.52.

HRMS (EI): *m*/*z* calcd for $C_{20}H_{27}N_2O_2$ [M + H$^+$]: 327.2072; found: 327.2077.

Catalytic Hydrogenation of 5 and 5′

To a solution of **5** (80 mg, 0.25 mmol) in EtOAc (10 mL) and MeOH (30 mL) was added Degussa E1 catalyst (53 mg, 0.025 mmol). The mixture was allowed to stir at r.t. for 1 h under 1 atm of H_2 in a Parr hydrogenation apparatus. The resulting mixture was then filtered through Celite. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexane–EtOAc, 90:10) to give 49 mg (61%) of (*S*,*R*,*R*)-**6**; R_f = 0.34 (SiO_2, hexanes–EtOAc, 9:1); mp 167–169 °C; $[\alpha]_D^{25}$ –35.9 (*c* 1.01, $CHCl_3$).

(*S*,*R*,*R*)-6

IR (film): 3289, 2934, 2790, 1671, 1539, 1437, 1362, 1330, 1252, 1180, 1072, 1016, 912, 841, 741 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 (s, 9 H), 1.65–1.83 (m, 3 H), 1.97–2.06 (m, 1 H), 2.10–2.20 (m, 1 H), 2.38 (t, *J* = 10.0 Hz, 1 H), 2.52–2.66 (m, 3 H), 2.75–2.94 (m, 2 H), 3.23–3.30 (m, 1 H), 3.89–3.98 (m, 1 H), 4.55–4.65 (m, 1 H), 4.87 (t, *J* = 8.9 Hz, 1 H), 7.03–7.07 (m, 1 H), 7.11–7.19 (m, 2 H), 7.36–7.40 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.5, 137.7, 136.3, 128.3, 128.1, 126.8, 126.1, 79.1, 66.7, 56.8, 56.4, 51.1, 50.4, 35.4, 29.1, 28.5, 25.6, 22.6.

HRMS (EI): *m*/*z* calcd for $C_{20}H_{28}N_2O_2$ [M $^+$]: 328.2151; found: 328.2146.

(*S*,*S*,*S*)-6′

The compound (*S*,*S*,*S*)-**6′** was prepared from **5′** following the same procedure as above for the preparation of (*S*,*R*,*R*)-**6** from **5**; yield: 65%; R_f = 0.24 (SiO_2, hexanes–EtOAc, 9:1); mp 185–187 °C; $[\alpha]_D^{25}$ +10.2 (*c* 1.00, $CHCl_3$).

IR (film): 3239, 2935, 2797, 1689, 1673, 1558, 1451, 1317, 1266, 1248, 1172, 1067, 757, 741 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (s, 9 H), 1.52–1.57 (m, 1 H), 1.64–1.79 (m, 2 H), 1.99–2.08 (m, 1 H), 2.09–2.23 (m, 2 H), 2.55 (t, *J* = 10.2 Hz, 1 H), 2.68 (t, *J* = 10.2 Hz, 1 H), 2.75–3.05 (m, 4 H), 3.90–4.00 (m, 1 H), 4.56–4.64 (m, 1 H), 4.86 (t, *J* = 9.7 Hz, 1 H), 7.03–7.07 (m, 1 H), 7.11–7.20 (m, 2 H), 7.36–7.41 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.7, 137.8, 136.2, 128.3, 128.0, 126.8, 126.1, 79.0, 66.9, 60.6, 56.9, 51.2, 45.8, 35.7, 29.2, 28.5, 25.6, 21.8.

HRMS (EI): *m*/*z* calcd for $C_{20}H_{28}N_2O_2$ [M $^+$]: 328.2151; found: 328.2146.

(1*S*,2*S*)-(2-Benzoylamino-1,2,3,4-tetrahydronaphthalen-1-yl)carbamic Acid *tert*-Butyl Ester (9)

To a stirred solution of (*R*,*S*,*S*)- **8′** (200 mg, 0.42 mmol) in EtOAc (10 mL) and MeOH (20 mL) was added ammonium formate (268 mg, 4.25 mmol) and 30 mol% of Pd/C (10 wt%, 136 mg, 0.13 mmol). The mixture was heated at reflux for 25 min and was cooled to r.t. The resulting black suspension was filtered through Celite and the cake was washed with Et_3N–MeOH (1:1, v/v, 2 × 15 mL). The filtrate was concentrated under reduced pressure and the residue was dissolved in anhyd THF (5.0 mL), and pyridine (0.1 mL, 1.27 mmol) was added. Benzoyl chloride (60 μL, 0.50 mmol) was then slowly added at 0 ° C and the mixture was stirred at r.t. for 15 h under N_2. The resulting mixture was quenched with aq 1 N NaOH (20 mL) and extracted with Et_2O (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated under reduced pressure. Flash column chromatography on silica gel (hexane–EtOAc, 70:30) gave 75 mg (55%) of (1*S*,2*S*)-**9**;

>99% ee by HPLC analysis with a chiral column (Chiralcel AD, hexane–propan-2-ol, 90:10, 1.0 mL/min): t_R (*R*,*R*)-(–)-, 9.4 min (minor); (*S*,*S*)-(+)-, 11.5 min (major); $[\alpha]_D^{25}$ +53.1 (*c* 0.90, $CHCl_3$) {Lit.[15] $[\alpha]_D^{25}$ +58.2 (*c* 1.00, $CHCl_3$) for (1*S*,2*S*)-**9** of >99% ee}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38 (s, 9 H), 1.80 (dq, *J* = 12.3, 5.1 Hz, 1 H), 2.43–2.49 (m, 1 H), 2.87 (dd, *J* = 17.3, 3.2 Hz, 1 H), 3.07 (ddd, *J* = 17.3, 12.3, 5.1 Hz, 1 H), 4.11–4.22 (m, 1 H), 4.97–5.02 (m, 2 H), 7.10–7.13 (m, 1 H), 7.18–7.25 (m, 3 H), 7.38–7.50 (m, 4 H), 7.88 (d, *J* = 6.9 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.5, 28.7, 29.0, 54.3, 55.0, 80.5, 126.5, 127.1, 127.3, 127.7, 128.6, 129.1, 131.6, 134.3, 135.4, 136.9, 158.0, 167.5.

(1*S*,2*S*)-1,2,3,4-Tetrahydronaphthalen-1,2-diamine (*R*,*R*)-Tartrate (10)

Diamide **9** (1.0 g, 2.7 mmol, >99% ee) was treated with 50% HCl (80 mL) at 100 °C for 48 h. The mixture was cooled to r.t. and the acidic solution was washed with Et_2O (3 × 20 mL). To the combined aqueous solution was slowly added aq 4 N NaOH at 0 °C over 30 min and its pH was adjusted to approximately pH 11. The mixture was extracted with CH_2Cl_2 (3 × 20 mL) and the combined CH_2Cl_2 layers were dried ($MgSO_4$). After concentration under reduced pressure, the residue was dissolved in EtOH (40 mL) and H_2O (5 mL), and a solution of L-(+)-tartaric acid (0.3 g, 1.82 mmol) in EtOH (10 mL) was added. The mixture was heated at reflux for 12 h and was cooled to r.t. The precipitate was collected by filtration and the collected solid was dried under vacuum. The enantiomerically pure diamine tartrate **10**[15] (1.7 g) was obtained in 72% yield (2 steps); $[\alpha]_D^{25}$ +27.0 (*c* = 1.00, H_2O).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.70–1.82 (m, 1 H), 2.05–2.13 (m, 1 H), 2.80–2.86 (m, 2 H), 2.98–3.05 (m, 1 H), 3.70 (d, *J* = 9.4 Hz, 1 H), 3.76 (s, 2 H), 7.09 (d, *J* = 7.4 Hz, 1 H), 7.18 (td, *J* = 7.2, 1.6 Hz, 1 H), 7.22 (td, *J* = 7.4, 1.6 Hz, 1 H), 7.59 (d, *J* = 7.4 Hz, 1 H).

***trans*-{2-[*N*-Benzyl-*N*-(2-hydroxyethyl)amino]-1,2-dihydronaphthalen-1-yl}carbamic Acid *tert*-Butyl Ester (13) (Scheme 7)**

Prepared by the asymmetric ring-opening of **1** (1 equiv) using *N*-benzylethanolamine (**11**, 3 equiv) in the presence of $[Rh(cod)Cl]_2$ (0.5 mol%), dppf (1.5 mol%), Et_3NHI (10 mol%), and *i*-Pr_2NEt (3.0 equiv) to give **13** in 95% yield in a similar manner as described in our previous work.[15]

IR (film): 3401, 3337, 1694, 1514, 1454, 1391, 1366, 1251, 1170, 1045, 1021, 782, 747 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.51 (s, 9 H), 2.65 (dt, *J* = 13.5, 4.5 Hz, 1 H), 2.90 (dt, *J* = 13.5, 4.5 Hz, 1 H), 3.17 (br s, 1 H), 3.52–3.59 (m, 4 H), 3.81 (d, *J* = 12.3 Hz, 1 H), 4.53 (d, *J* = 8.7 Hz, 1 H), 5.12 (t, *J* = 8.7 Hz, 1 H), 5.96 (dd, *J* = 9.9, 3.6 Hz, 1 H), 6.57 (dd, *J* = 9.9, 1.5 Hz, 1 H), 7.03–7.05 (m, 1 H), 7.18–7.34 (m, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.01, 139.40, 134.72, 132.47, 129.52, 129.10, 128.25, 128.09, 127.97, 127.10, 126.71, 126.15, 79.79, 60.95, 59.19, 54.85, 52.09, 50.16, 28.42.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{30}N_2O_3$ [M$^+$]: 394.2256; found: 394.2257.

***trans*-{2-[*N*-Benzyl-*N*-(ethoxycarbonylmethyl)amino]-1,2-dihydronaphthalen-1-yl}carbamic Acid *tert*-Butyl Ester (14) (Scheme 7)**

Prepared by the asymmetric ring-opening of **1** (1 equiv) using *N*-benzylglycine ethyl ester (**12**, 1.1 equiv) in the presence of $[Rh(cod)Cl]_2$ (1 mol%), dppf (3 mol%), Et_3NHI (20 mol%), and *i*-Pr_2NEt (1.1 equiv) to give **14** in 88% yield in a similar manner as described in our previous work.[15]

IR (film): 3358, 1731, 1713, 1505, 1454, 1391, 1366, 1250, 1171, 1046, 1028, 976 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (t, *J* = 7.2 Hz, 3 H), 1.48 (s, 9 H), 3.31 (s, 2 H), 3.65 (br s, 1 H), 3.82 (d, *J* = 13.9 Hz, 1 H), 3.97 (d, *J* = 13.9 Hz, 1 H), 4.06 (q, *J* = 7.6 Hz, 2 H), 4.91 (d, *J* = 7.6 Hz, 1 H), 5.07 (t, *J* = 7.6 Hz, 1 H), 6.04 (dd, *J* = 9.8, 4.2 Hz, 1 H), 6.61 (dd, *J* = 9.8, 1.5 Hz, 1 H), 7.05–7.18 (m, 1 H), 7.18–7.29 (m, 5 H), 7.33–7.38 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.01, 155.57, 139.28, 135.19, 132.20, 129.73, 128.79, 128.10, 128.05, 127.79, 127.69, 126.94, 126.60, 126.50, 79.23, 60.66, 60.29, 54.51, 51.21, 50.29, 28.38, 14.07.

HRMS (EI): *m*/*z* calcd for $C_{26}H_{32}N_2O_4$ [M$^+$]: 436.2362; found: 436.2354.

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(19) For the preparation of 15.0 g of the ring-opened product **3** from 8.0 g of the starting material **1**, 2.7 g of (*S*,*S*′)-(*R*,*R*′)-C_2-Ferriphos would be required to ensure high enantioselectivity in the catalytic ring-opening reaction.

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(22) To a solution of (*S*)-proline methyl ester hydrochloride in MeOH (0.5–1.0 M) was added 1.0 equiv of NaI solution in MeOH dropwise at r.t. The mixture was stirred at r.t. for an additional 1 h. After filtration to remove the NaCl, the solution was concentrated and the residue was dissolved in CH_2Cl_2 and the insoluble precipitate was filtered off again. After removal of all volatile substrates, the corresponding iodide (quantitative yield) was obtained.

(23) Crystal data for **4**: $C_{15}H_{16}N_2O$, M = 240.30, orthorhombic, space group $P2_12_12_1$, a = 7.3032 (2) Å, b = 12.2966 (6) Å, c = 13.5897 (6) Å, α = 90°, β = 90°, γ = 90°, V = 1220.42 (9) Å^3, Z = 4, Dc = 1.308 Mg/m^3, μ(Cu-Kα) = 0.083 mm^{-1}, F(000) = 512 reflections were collected, of which 9593 were considered to be observed with $I > 2\sigma(I)$. The structure was determined by direct methods using the SHELXTLTM suite of programs. Hydrogen atoms were placed in calculated positions. Full-matrix least squares refinement based on F^2 with anisotropic thermal parameters for the non-hydrogen atoms led to agreement factors $R1$ = 0.0360 and $wR2$ = 0.0887. Crystallographic data for the structure **4** reported in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary material No. CCDC-639749. Copies of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 33603 or e-mail: deposit@ccdc.cam.ac.uk).

(24) Chiral stationary phase columns (Chiralcel AS for **3b** and AD for **3b′**).

(25) Crystal data for **3b**: $C_{21}H_{30}N_2O_3$, M = 358.47, monoclinic, space group $P2_1$, a = 9.4130 (4) Å, b = 19.6173 (12) Å, c = 11.8127 (7) Å, α = 90°, β = 110.225 (3)°, γ = 90°, V = 2046.81 (19) Å^3, Z = 4, Dc = 1.163 Mg/m^3, μ(Cu-Kα) = 0.078 mm^{-1}, F(000) = 776 reflections were collected, of which 111510 were considered to be observed with $I > 2\sigma(I)$. Full-matrix least squares refinement based on F^2 with anisotropic thermal parameters for the nonhydrogen atoms led to agreement factors $R1$ = 0.0491 and $wR2$ = 0.1115. Crystallographic data for the structure **3b** reported in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary material No. CCDC-639748. Copies of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 33603 or e-mail: deposit@ccdc.cam.ac.uk).

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