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1,2,3-Triazole-linked dendrimers as a support for functionalized and recoverable catalysts for asymmetric borane reduction of prochiral ketones

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Abstract—A series of new, functionalized, and chiral catalysts have been synthesized based on 1,2,3-triazole-linked dendrimers. It has been found that dendrimer **7f** is an efficient catalyst for the enantioselective borane reduction of both electron-deficient and electron-rich ketones, and high enantioselectivities were obtained (up to 96%). The catalyst can be recovered and reused four times without a significant loss of catalytic activity.

1. Introduction

The development of well-defined dendritic catalysts that can efficiently catalyze asymmetric organic reactions and be separated completely from the product, still remains a challenge. The very first attempt to carry out asymmetric reaction using chiral dendritic ligand was reported by Brunner et al.[1] Since then, dendritic catalysts have been attracting much attention in asymmetric organic synthesis.[2] Recently, Bolm et al. reported optically active dendritic amino alcohols, while Zhao et al. reported supported-dendrimer prolinols for the asymmetric reduction of ketones with borane.[3] On the other hand, C_3-symmetry is also interesting in organic chemistry, and many C_3-symmetric compounds and their applications in asymmetric catalysis being reported in the literature.[4] The C_3-symmetric trisoxazoline compounds as chiral auxiliaries and ligands have been successfully applied in asymmetric synthesis and molecular recognition by Katsuki,[5] Ahn,[6] and Gade.[7] As an early example, Burns performed the enantioselective borane reduction of ketones using C_3-symmetric phosphoramide, although only 20% ee was obtained.[8] Recently, Du et al. also reported that chiral C_3-symmetric tris(β-hydroxy amide) ligands could be applied in the asymmetric addition of aryl alkynes to various aldehydes (up to 92% ee) and the asymmetric borane reduction of prochiral ketones with high enantioselectivities (up to 98% ee).[9]

The enantioselective reduction of prochiral ketones with borane in the presence of a chiral ligand leading to enantiomerically pure secondary alcohols plays an important role in asymmetric synthesis.[10] One of the most active research fields of reduction of prochiral ketones to optically active alcohols is to employ chiral oxaza-borolidine ligands as catalysts. This method known as CBS reduction was pioneered by Itsuno et al.[11] and further developed by Corey, Bakshi, and Shibata.[12] In order to find more effective catalysts, a large number of studies have been reported with many new ligands being prepared in the past few years.[13] Recently, the study of chiral amino alcohols based on prolinol has become an interesting research area with new derivatives such as sulfonyl prolinol,[14] polymer-supported sulfonamide,[15] chiral phosphinamides,[16] and chiral squaric prolinols[17] being reported and with high yields and with good enantioselectivities being obtained. However, the development of efficient methods to synthesize new

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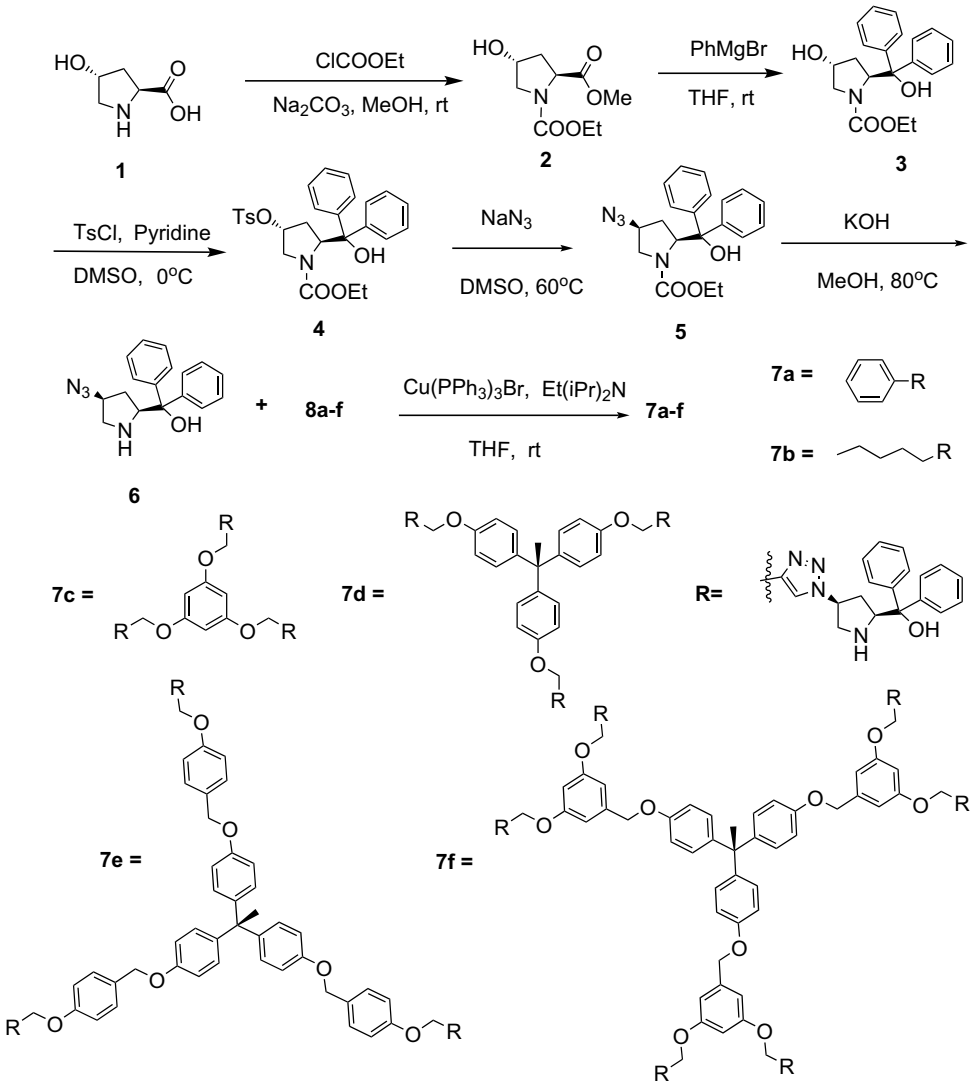
recoverable catalysts still remains a challenging research field.

Recently, Sharpless introduced 'click chemistry' as a new way of categorizing organic reactions.[18] In the past few years, these reactions have been used in organic synthesis, biological studies, material science, and so on,[19] since the special feature of this reaction is that it is completely specific, has quantitative yields, and almost perfect fidelity in the presence of a wide variety of functional groups.[20] We were especially interested in the Cu(I)-catalyzed 1,3-dipolar 'click' azide–alkyne cyclo-addition for the construction of 1,2,3-triazoles.[21] Very recently, we successfully prepared pyrrolidine-based triazole derivatives via 'click chemistry', which proved to be efficient catalysts for the highly diastereoselective and enantioselective Michael addition of ketones to nitroalkenes.[22] As an ongoing study in 'click chemistry', we herein report the utility of 'click chemistry' as a modular approach for the construction of C_3-symmetric 1,2,3-triazole-linked dendritic organocatalysts for the asymmetric borane reduction of prochiral ketones.

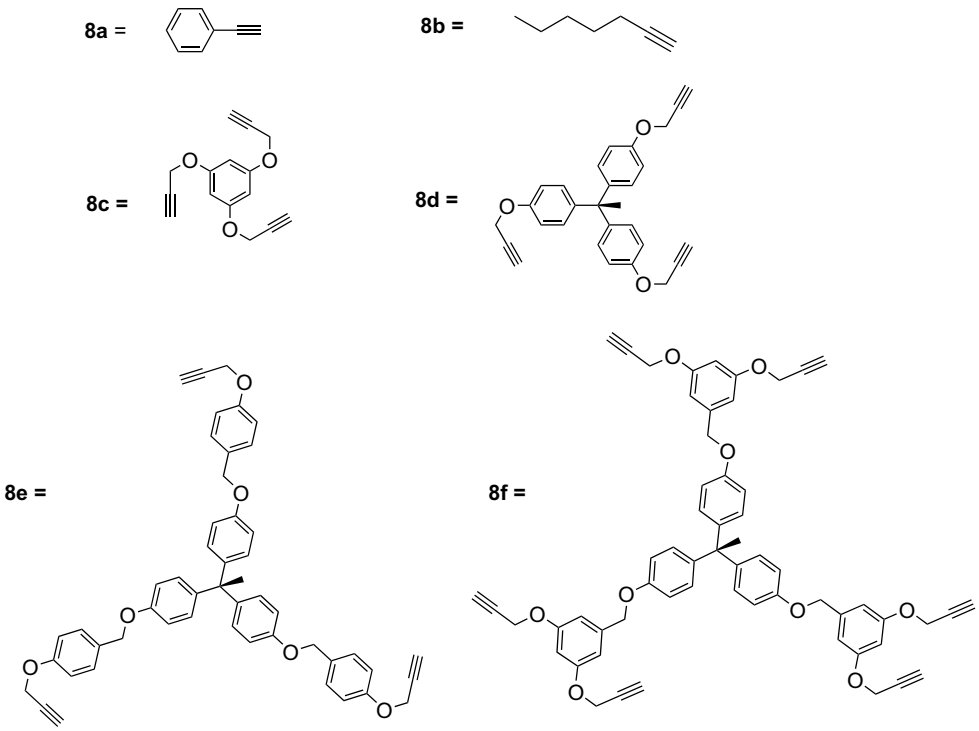
2. Results and discussion

A series of new ligands **7a–f** were synthesized from commercially available *trans*-4-hydroxyl-L-proline as depicted in Scheme 1. First, chiral *trans*-4-hydroxyl-L-proline **1** was reacted with ethyl chloroformate to give mixture **2**. The treatment of mixture **2** (without further purification) with phenyl magnesium bromide furnished tertiary alcohol **3**.[23] Compound **3** was reacted with 4-toluenesulfonyl chloride in pyridine to give tosylate **4**. Dis-placing the tosylate with sodium azide in dry DMSO gave compound **5**. The hydrolysis of compound **5** resulted in the formation of ((2*R*,4*S*)-4-azidopyrrolidine-2-yl)diphenylmethanol **6**. Various terminal alkynes **8a–f** (Scheme 2) reacted with **6** using Cu(I)-catalyzed 1,3-dipolar 'click' azide–alkyne cycloaddition condition to give the desired catalysts **7a–f**.

It is well known that the enantioselectivity of borane reduction is greatly affected by solvent, temperature, and the amount of catalyst.[24] In order to evaluate the efficiency of these ligands in the catalytic asymmetric reduction, in



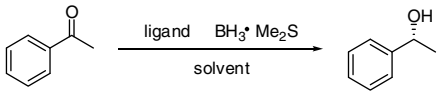
Scheme 1. Synthesis of new ligands.



Scheme 2. Various terminal alkynes.

preliminary experiments, we attempted to perform the enantioselective reduction of acetophenone with BH_3–Me_2S to explore the optimum reaction conditions. As shown in Table 1, when the reaction was carried out at the room temperature in THF, ligands **7a** (Table 1, entry 1) and **7c** (Table 1, entry 4) gave only very low enantioselectivity, less than 15% ee. This may be due to the dimerization of the catalysts at the lower temperature.[24e] When the reaction was carried out in refluxing THF (70 °C) (Table 1, entries 2 and 5), the corresponding (*R*)-1-phenylethanol was obtained in high enantioselectivities (up to 90%). To our delight, all the ligands from **7a** to **7f** gave excellent yields and high ee values (Table 1, entries 2, 3, and 5–8). In view of the slightly higher reactivity and enantioselectivity of **7f**, dendrimer **7f** was chosen for the following investigation (Table 1, entries 8–13). With

Table 1. Enantioselective borane reduction of acetophenone[a]



Entry	Ligand (mol %)	Solvent	*T* (°C)	Yield[b] (%)	ee[c] (%)	Config[d]
1	**7a** (15)	THF	rt	92	5	—
2	**7a** (15)	THF	70	98	89	(*R*)
3	**7b** (15)	THF	70	95	90	(*R*)
4	**7c** (5.0)	THF	rt	94	13	—
5	**7c** (5.0)	THF	70	96	90	(*R*)
6	**7d** (5.0)	THF	70	97	91	(*R*)
7	**7e** (5.0)	THF	70	96	92	(*R*)
8	**7f** (2.5)	THF	70	98	94	(*R*)
9	**7f** (2.5)	Toluene	70	92	86	(*R*)
10	**7f** (2.5)	Toluene	90	93	85	(*R*)
11	**7f** (1.25)	THF	70	94	87	(*R*)
12	**7f** (0.65)	THF	70	92	84	(*R*)
13	**7f** (4.0)	THF	70	97	95	(*R*)

[a] Reaction was carried out on a 0.5 mmol scale in 5 mL of solvent, molar ratio of $PhCOCH_3/BH_3$–$Me_2S = 1:1.5$.
[b] Isolated yields by column chromatography.
[c] Ee determined by HPLC analysis using a Daicel Chiralcel OJ column.
[d] The absolute configuration was assigned by comparison of the sign of the specific rotation with that in the literature.

the exception of the reaction temperature and catalysts, the reactivity and enantioselectivity were also affected by the solvent. An attempt to employ the reduction in toluene at 70 °C caused a lower yield and the enantioselectivity to be obtained. When the temperature was raised from 70 °C to 90 °C in toluene (Table 1, entries 9 and 10), the enantioselectivity and yield had only a negligible change. It was observed that a decrease in the catalyst loading from 2.5 mol % to 0.65 mol % using **7f** resulted in a dramatic decrease in the enantioselectivity and a slight loss of the yield (Table 1, entries 8, 11 and 12). Increasing the amount of the catalyst further to 4.0 mol % (Table 1, entry 13) resulted in a slight increase in the enantioselectivity.

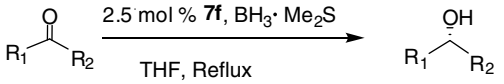
Under the optimum reaction conditions, using a catalytic amount (2.5 mol %) of ligand **7f** in refluxing THF, the reduction of other prochiral ketones was investigated. The results are summarized in Table 2. It has been shown that both electron-deficient and electron-rich ketones and all the reductions gave excellent yields and high ee values. Comparison of the results (Table 2, entries 1–10) indicated that electron-withdrawing groups were relatively beneficial to the enantioselectivity. In order to understand the generality of this catalytic system, we also investigated the borane reduction of representative prochiral α-halo ketones under the same conditions. High enantioselectivities were thus obtained (Table 2, entries 11 and 12). The results demonstrated that the steric effects had a significant impact on the enantioselectivity, for example, the reactions of 3,4-dihydronaphthalen-1(2*H*)-one (Table 2, entry 13) and propiophenone (Table 2, entry 14) were completed in moderate enantioselectivity due to the steric effect.

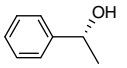
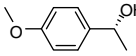
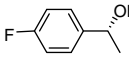
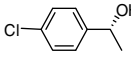
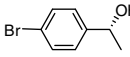
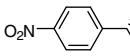
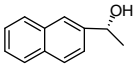
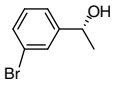
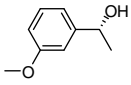
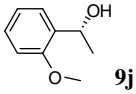
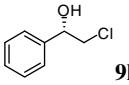
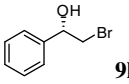
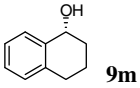
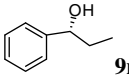
The recyclability and reusability of catalyst **7f** were also investigated (Table 3). The reduction of acetophenone was chosen as a model study. When the first run of the reduction was completed, the reaction was quenched with water and extracted with CH_2Cl_2. After the removal of the solvent under reduced pressure, diethyl ether was added. The product was re-dissolved in ether, and catalyst **7f** was precipitated. After removing the ether phase, the catalyst was dried under vacuum for 12 h, and then reused for the next cycle of the reaction. As can be seen from Table 3, good enantioselectivities and yields were obtained for four consecutive cycles with little to no loss of performance.

3. Conclusion

In conclusion, a series of new chiral catalysts have been synthesized from commercially available *trans*-4-hydroxyl-L-proline based on dendrimers as a support using 'click chemistry'. The catalytic borane reduction of ketones with these new chiral catalysts was investigated, and high enantioselectivities were obtained (up to 96%). The results showed that dendrimer **7f** is an efficient catalyst for the enantioselective borane reduction of ketones. Meanwhile, catalyst **7f** can be recovered and reused four times without any significant loss of activity. The development of other asymmetric reactions using these C_3-symmetric ligands is currently ongoing in our group.

Table 2. Catalytic asymmetric reduction of ketones[a]



Entry	Product	Yield[b] (%)	ee[c] (%)	Config[d]
1	 **9a**	95	94	(*R*)
2	 **9b**	91	90	(*R*)
3	 **9c**	98	96	(*R*)
4	 **9d**	97	92	(*R*)
5	 **9e**	93	94	(*R*)
6	 **9f**	99	93	(*R*)
7	 **9g**	95	87	(*R*)
8	 **9h**	90	89	(*R*)
9	 **9i**	95	92	(*R*)
10	 **9j**	96	93	(*R*)
11	 **9k**	95	87	(*S*)
12	 **9l**	93	92	(*S*)
13	 **9m**	98	81	(*R*)
14	 **9n**	95	71	(*R*)

[a] Reaction was carried out on a 0.5 mmol scale in 5 mL of solvent, molar ratio of ketone/BH_3–Me_2S = 1:1.5.
[b] Isolated yield by column chromatography.
[c] Ee determined by HPLC analysis using a Daicel Chiralcel OJ column.
[d] The absolute configuration assigned by comparison with the literature.

Table 3. Recycling of catalyst **7f** (reduction of acetophenone)[a]

Cycle	Yield[b] (%)	ee[c] (%)
1	97	94
2	95	92
3	96	90
4	93	90

[a] Reaction was carried out on a 1 mmol scale in 10 mL of solvent, molar ratio of $PhCOCH_3/BH_3$–$Me_2S = 1:1.5$.
[b] Isolated yield by column chromatography.
[c] Ee determined by HPLC analysis using a Daicel Chiralcel OJ column.

4. Experimental

4.1. General

Column chromatography was carried out on silica gel (200–300 mesh). ^{1}H NMR spectra were recorded on 300 MHz or 400 MHz in $CDCl_3$, chemical shifts are reported in ppm using TMS as the internal standard. ^{13}C NMR spectra were recorded on a Varian 75 MHz or Varian 100 MHz spectrometers with complete proton decoupling. IR spectra were recorded on a FT-IR spectrometer and only major peaks are reported in cm^{-1}. High resolution mass spectra (HRMS) were obtained by the ESI ionization sources. Melting points were determined on a microscopic apparatus and are uncorrected. All new compounds were further characterized by elemental analysis or HRMS. HPLC analysis was performed on Varian-Pro-Star using a ChiralPak OJ columns purchased from Daicel Chemical Industries, Ltd. Optical rotations were measured using a 1 mL cell with a 1 dm path length on a digital polarimeter and are reported as follows: $[\alpha]_D^{20}$ (c in g per 100 mL of solvent). Commercially available reagents and solvents were used without further purification. Toluene and tetrahydrofuran were distilled with sodium under nitrogen. Other solvents used were purified and dried by standard procedures. Borane-dimethyl sulfide complex was purchased from Aldrich.

4.2. Synthesis of catalysts 7a–7f

4.2.1. Synthesis of *trans*-4-hydroxyl-α,α-bisphenyl-L-prolinol carbamate ester 3.[23] To a solution of *trans*-4-hydroxyl-L-proline **1** in methanol was slowly added ethyl chloroformate. The reaction mixture was stirred for 24 h at room temperature, and then filtered. The filtrate was extracted with ethyl acetate and concentrated to give product **2** as a colorless oil. To a solution of **2** (5.0 g, 23.0 mmol) in dry THF (100 mL) was added phenyl magnesium bromide (1 M in THF, 138 mL, 138.0 mmol) at 0 °C under an argon atmosphere. After being stirred for 5 h, the reaction solution was diluted with saturated aqueous NH_4Cl and extracted with CH_2Cl_2 (2 × 50 mL). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to give a residue, which was chromatographed on silica gel (eluent: hexanes/EtOA = 2:1) to give the product as a white foam (4.55 g, 58% yield). White solid, mp 174–176 °C, $[\alpha]_D^{20} = -43.2$ (c 1.1, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.40$–7.20 (m, 10H), 5.06 (t, $J = 7.2$ Hz, 1H), 4.03–3.86 (m, 3H), 3.52–3.48 (m, 1H), 2.97–2.94 (m, 1H), 2.19–1.97 (m, 3H), 1.12 (t, $J = 6.3$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 158.0$, 145.2, 143.1, 127.8, 127.6, 127.3, 127.2, 127.1, 81.4, 69.5, 65.4, 61.9, 56.0, 39.0, 14.4. IR (KBr, cm^{-1}) 3417, 2950, 1682, 1416, 1198, 1107, 984, 700. Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.32; H, 6.78; N, 4.12.

4.2.2. Synthesis of (2*S*,4*R*)-ethyl-2-(hydroxydiphenylmethyl)-4-(tosyloxy)pyrrolidine-1-carboxylate 4. To an ice-cold solution of **3** (3.41 g, 10.0 mmol) in pyridine (20 mL) was added 4-toluenesulfonyl chloride (2.29 g, 12.0 mmol). The reaction mixture was stirred for 6 h and then diluted with ethyl acetate (100 mL). The organic phase was washed with 10% HCl (3 × 50 mL), saturated $NaHCO_3$ solution (3 × 50 mL), and saturated NaCl solution (2 × 50 mL). The organic phase was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was subjected to flash chromatography on silica gel (eluent: pentane/EtOAc 1:1). Yield: 4.36 g (88%). White solid, mp 77–79 °C, $[\alpha]_D^{20} = +46.5$ (c 1.0, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.63$ (d, $J = 8.1$ Hz, 2H), 7.29–7.20 (m, 12H), 5.00 (dd, $J = 6.3$ Hz, 8.1 Hz, 1H), 4.42 (br, 1H), 4.09–3.96 (m, 1H), 3.68–3.64 (m, 1H), 3.07 (br, 1H), 2.40 (s, 3H), 2.22–2.12 (m, 2H), 1.16 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 155.7$, 144.9, 144.8, 133.4, 129.8, 127.9, 127.8, 127.7, 127.4, 127.1, 81.3, 79.3, 64.5, 62.0, 53.1, 36.2, 21.6, 14.3. IR (KBr, cm^{-1}) 3446, 2921, 1688, 1416, 1371, 1342, 1175, 1096, 887, 746, 649. Anal. Calcd for $C_{27}H_{29}NO_6S$: C, 65.44; H, 5.90; N, 2.83. Found: C, 65.40; H, 5.94; N, 2.80.

4.2.3. Synthesis of (2*S*,4*S*)-ethyl-4-azido-2-(hydroxydiphenyl-methyl)pyrrolidine-1-carboxylate 5. Compound **4** (4.1 g, 8.4 mmol) was dissolved in dry DMSO (50 mL), and sodium azide (1.63 g, 25.2 mmol) was added. The reaction mixture was heated to 60 °C for 20 h, allowed to cool to room temperature and diluted with ethyl acetate (100 mL). The organic phase was washed with H_2O (3 × 100 mL) and saturated brine (2 × 50 mL), dried with Na_2SO_4, and the solvent was evaporated. The crude product was subjected to flash chromatography using 2:1 hexanes/EtOAc to afford 2.77 g (90% yield) of the indicated compound **5** as a white solid. White solid, mp 116–118 °C, $[\alpha]_D^{20} = +87.6$ (c 1.2, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.50$ (d, $J = 7.8$ Hz, 2H), 7.39–7.19 (m, 8H), 4.94 (dd, $J = 6.6$ Hz, 8.1 Hz, 1H), 4.09–3.90 (m, 3H), 3.75 (br, 1H), 2.93 (br, 1H), 2.47–2.39 (m, 1H), 1.96–1.87 (m, 1H), 1.04 (t, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 156.0$, 144.5, 143.3, 127.8, 127.7, 127.2, 127.1, 127.1, 127.0, 127.1, 81.4, 65.1, 61.7, 57.8, 51.6, 35.2, 14.2. IR (KBr, cm^{-1}) 3379, 2981, 2104, 1667, 1439, 1343, 1229, 761, 700. Anal. Calcd for $C_{20}H_{22}N_4O_3$: C, 65.56; H, 6.05; N, 15.29. Found: C, 65.52; H, 6.04; N, 15.32.

4.2.4. Synthesis of ((2*S*,4*S*)-4-azidopyrrolidin-2-yl)diphenylmethanol 6. Compound **5** (2.5 g, 6.8 mmol) and KOH (3.0 g, 53.5 mmol) in methanol (25 mL) were heated at 80 °C for 8 h. After the reaction was complete, and cooled to room temperature, the methanol was removed under reduced pressure. Water (50 mL) was added to the reaction mixtures, the mixtures were extracted with CH_2Cl_2

(3 × 20 mL). The organic layer was washed with saturated NaCl solution (2 × 30 mL), dried with Na_2SO_4, and the solvent was evaporated and the residue was chromatographed using 4:1 hexanes/EtOAc to afford 1.72 g (86% yield) of the indicated compound **6** as a white solid. White solid, mp 82–84 °C, $[\alpha]_D^{20} = -62.7$ (*c* 1.5, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.57–7.47$ (m, 4H), 7.30–7.24 (m, 4 H), 7.22–7.13 (m, 2H), 4.28 (t, $J = 7.5$ Hz, 1H), 3.97–3.90 (m, 1H), 3.09–2.97 (m, 2H), 1.97–1.76 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 147.1$, 144.6, 128.3, 128.0, 126.6, 126.5, 125.7, 125.3, 76.5.0, 63.8, 60.3, 51.9, 32.3. IR (KBr, cm^{-1}) 3345, 2938, 2100, 1267, 703. Anal. Calcd for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.16; N, 19.03. Found: C, 69.40; H, 6.12; N, 19.01.

4.2.5. Synthesis of diphenyl((2*S*,4*S*)-4-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pyrrolidin-2-yl)methanol 7a. A solution of ethynylbenzene (122 mg, 1.2 mmol), compound **6** (294 mg, 1 mmol), *N*,*N*-diisopropylethyl-amine (51.6 mg, 0.4 mmol), and $Cu(PPh_3)_3Br$ (92.8 mg, 0.1 mmol) was prepared in tetrahydrofuran (5 mL). The reaction mixture was then stirred at room temperature for ca. 48 h. The solvent was removed under reduced pressure. The crude product was purified by column chromatography, eluting with EtOAc to give **7a** as a white solid (380 mg, 96% yield). White solid, mp 157–158 °C, $[\alpha]_D^{20} = -150.2$ (*c* 1.2, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.94$ (s, 1H), 7.80 (d, $J = 8.1$ Hz, 2H), 7.60–7.57 (m, 2H), 7.48 (d, $J = 7.8$ Hz, 2H), 7.41–7.13 (m, 11H), 5.14 (br, 1H), 4.42 (t, $J = 7.5$ Hz, 1H), 3.48 (m, 1H), 3.30 (m, 1H), 2.31–2.12 (m, 2H), 2.01 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 147.7$, 146.5, 144.3, 130.5, 128.7, 128.4, 128.1, 128.0, 126.9, 126.7, 125.7, 125.6, 125.1, 117.8, 76.5, 64.5, 59.6, 53.1, 33.5. IR (KBr, cm^{-1}) 3418, 3083, 1442, 1256, 972, 694. Anal. Calcd for $C_{25}H_{24}N_4O$: C, 75.73; H, 6.10; N, 14.13. Found: C, 75.70; H, 6.07; N, 14.15. HRMS (ESI, $M+H^+$), calcd, 397.2023; found 397.2021.

4.2.6. Synthesis of ((2*S*,4*S*)-4-(4-pentyl-1*H*-1,2,3-triazol-1-yl)pyrrolidin-2-yl)diphenylmethanol 7b. A solution of hept-1-yne (115 mg, 1.2 mmol), compound **6** (294 mg, 1 mmol), *N*,*N*-diisopropylethylamine (51.6 mg, 0.4 mmol), and $Cu(PPh_3)_3Br$ (92.8 mg, 0.1 mmol) was prepared in tetrahydrofuran (5 mL). The reaction mixture was then stirred at room temperature for ca. 48 h. The solvent was removed under reduced pressure. The crude product was purified by column chromatography (eluent: pentane/EtOAc = 1:2) to give **7b** as a white solid (359 mg, 92% yield). White solid, mp 100–102 °C, $[\alpha]_D^{20} = -103.9$ (*c* 1.2, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.67–7.58$ (m, 2H), 7.55–7.43 (m, 4H), 7.33–7.14 (m, 5H), 5.13–5.10 (m, 1H), 4.45 (d, $J = 8.8$ Hz, 1H), 3.48 (dd, $J = 7.2$ Hz, 10.8 Hz, 1H), 3.25 (dd, $J = 3.6$ Hz, 10.8 Hz, 1H), 2.69 (t, $J = 7.6$ Hz, 1H), 2.26–2.09 (m, 2H), 1.94 (s, 1H), 1.69–1.61 (m, 2H), 1.35–1.31 (m, 4H), 0.90 (t, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 148.5$, 146.6, 144.4, 132.0, 131.9, 131.8, 128.3, 128.1, 126.8, 126.7, 125.7, 125.1, 118.6, 76.6, 64.5, 59.4, 53.0, 33.5, 31.4, 29.0, 25.6, 22.3, 13.9. IR (KBr, cm^{-1}) 3447, 3119, 2926, 2858, 1443, 1173, 1119, 973, 697. Anal. Calcd for $C_{24}H_{30}N_4O$: C, 73.81; H, 7.74; N, 14.35. Found: C, 73.85; H, 7.71; N, 14.32. HRMS (ESI, $M+H^+$), calcd, 391.2492; found 391.2490.

4.2.7. Synthesis of (2*S*,2′*S*,2″*S*,4*S*,4′*S*,4″*S*)-4,4′,4″-(4,4′,4″-(benzene-1,3,5-triyltris(oxy))tris(methylene)tris(1*H*-1,2,3-triazole-4,1-diyl))tris(pyrrolidine-4,2-diyl)tris(diphenyl methanol) 7c. A solution of **8c** (120 mg, 0.5 mmol),[25a] compound **6** (529 mg, 1.8 mmol), *N*,*N*-diisopropylethylamine (516 mg, 4.0 mmol), and $Cu(PPh_3)_3Br$ (139.2 mg, 0.15 mmol) was prepared in tetrahydrofuran (10 mL). The reaction mixture was then stirred at room temperature for ca. 72 h. The solvent was removed under reduced pressure. The crude product was purified by column chromatography, eluting with a 30:1 mixture of dichloromethane and methanol to give **7c** as a white solid (527 mg, 94% yield). White solid, mp 135–136 °C, $[\alpha]_D^{20} = -160.7$ (*c* 1.0, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.80$ (s, 3H), 7.55 (d, $J = 6.9$ Hz, 6H), 7.46–7.43 (m, 6H), 7.28–7.10 (m, 18H), 6.28 (s, 1H), 5.07 (s, 9H), 4.38 (t, $J = 7.8$ Hz, 3H), 3.42 (dd, $J = 7.2$ Hz, 10.5 Hz, 3H), 3.22 (dd, $J = 3.6$ Hz, 11.1 Hz, 3H), 2.24–2.05 (m, 6H), 1.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 160.0$, 146.5, 144.4, 143.6, 128.3, 128.1, 126.8, 126.6, 125.7, 125.1, 121.3, 95.0, 76.5, 64.4, 61.9, 59.7, 52.9, 33.6. IR (KBr, cm^{-1}) 3338, 2869, 1596, 1447, 1151, 1054, 749, 700. Anal. Calcd for $C_{66}H_{66}N_{12}O_6$: C, 70.57; H, 5.92; N, 14.96. Found: C, 70.53; H, 5.94; N, 14.99. HRMS (ESI, $M+H^+$), calcd, 1123.5031; found 1123.5031.

4.2.8. Synthesis of (2*S*,2′*S*,2″*S*,4*S*,4′*S*,4″*S*)-4,4′,4″-(4,4′,4″-(4,4′,4″-(ethane-1,1,1-triyl)tris(benzene-4,1-diyl))tris(oxy)tris(methylene)tris(1*H*-1,2,3-triazole-4,1-diyl))tris(pyrrolidine-4,2-diyl)tris(diphenylmethanol) 7d. A solution of **8d** (210 mg, 0.5 mmol),[25a,b] compound **6** (529 mg, 1.8 mmol), *N*,*N*-diisopropylethylamine (516 mg, 4.0 mmol), and $Cu(PPh_3)_3Br$ (139.2 mg, 0.15 mmol) was prepared in tetrahydrofuran (10 mL). The reaction mixture was then stirred at room temperature for ca. 72 h. The solvent was removed under the reduced pressure. The crude product was purified by column chromatography, eluting with a 20:1 mixture of dichloromethane and methanol to give **7d** as a white solid (592 mg, 91% yield). White solid, mp 145–146 °C, $[\alpha]_D^{20} = -92.1$ (*c* 1.0, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.78$ (s, 3H), 7.56 (d, $J = 7.5$ Hz, 6H), 7.46 (d, $J = 7.5$ Hz, 6H), 7.31–7.11 (m, 18H), 7.11–7.00 (d, $J = 9.0$ Hz, 6H), 6.97–6.84 (d, $J = 9.0$ Hz, 6H), 5.11–5.07 (d, 9H), 4.41 (t, $J = 8.1$ Hz, 3H), 3.44 (dd, $J = 7.2$ Hz, 11.1 Hz, 3H), 3.25 (dd, $J = 3.6$ Hz, 11.1 Hz, 3H), 2.27–2.10 (m, 9H), 1.95 (br, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 156.2$, 146.5, 144.3, 144.0, 142.1, 129.5, 128.3, 128.1, 126.8, 126.7, 125.6, 125.1, 121.0, 113.8, 76.5, 64.4, 61.8, 59.6, 52.9, 50.5, 33.5, 30.6. IR (KBr, cm^{-1}) 3362, 3055, 1503, 1180, 1006, 829, 698. Anal. Calcd for $C_{80}H_{78}N_{12}O_6$: C, 73.71; H, 6.03; N, 12.89. Found: C, 73.74; H, 6.04; N, 12.92. HRMS (ESI, $M+H^+$), calcd, 1303.6240; found 1303.6229.

4.2.9. Synthesis of (2*S*,2′*S*,2″*S*,4*S*,4′*S*,4″*S*)-4,4′,4″-(4,4′,4″-(4,4′,4″-(4,4′,4″-(ethane-1,1,1-triyl)tris(benzene-4,1-diyl))tris(oxy)tris(methylene)tris(benzene-4,1-diyl))tris(oxy)tris(methylene)tris(1*H*-1,2,3-triazole-4,1-diyl))tris(pyrrolidine-4,2-diyl)tris(diphenylmethanol) 7e. To a stirred solution of 1-(bromomethyl)-4-(prop-2-ynloxy)benzene (742 mg 3.3 mmol)[25c] and 1,1,1-tris(4-hydroxyphenyl)ethane (306 mg, 1 mmol) in acetone (20 mL) added potassium carbonate (450 mg,

3.3 mmol) and 18-crown-6 (10 mg, 0.04 mmol). The reaction mixture was stirred in refluxing acetone under a nitrogen atmosphere for 36 h, filtered, and evaporated to dryness. The crude material was then as purified by column chromatography, eluting with dichloromethane to give compound **8e** as a white solid (612 mg, yield 83%). White solid, White solid, mp 70–72 °C, ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.34$ (d, $J = 8.7$ Hz, 6H), 6.98 (t, $J = 7.5$ Hz, 12H), 6.83 (d, $J = 8.7$ Hz, 6H), 4.92 (s, 6H), 4.66 (d, $J = 2.4$ Hz, 6H), 2.51 (t, $J = 2.4$ Hz, 3H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 157.2$, 156.7, 141.8, 129.9, 129.5, 129.1, 114.8, 113.8, 78.4, 75.5, 69.4, 55.6, 50.5, 30.6. IR (KBr, cm^{-1}) 1607, 1509, 1238, 1220, 1175, 1007, 823, 683. Anal. Calcd for $C_{50}H_{42}O_6$: C, 81.28; H, 5.73. Found: C, 81.26; H, 5.72.

A solution of **8e** (369 mg, 0.5 mmol), compound **6** (529 mg, 1.8 mmol), *N*,*N*-diisopropylethylamine (516 mg, 4.0 mmol), and $Cu(PPh_3)_3Br$ (139.2 mg, 0.15 mmol) was prepared in tetrahydrofuran (10 mL). The reaction mixture was then stirred at room temperature for ca. 72 h. The solvent was removed under the reduced pressure. The crude product was purified by column chromatography, eluting with a 10:1 mixture of dichloromethane and methanol to give **7e** as a white solid (712 mg, 88% yield). White solid, mp 121–123 °C, $[\alpha]_D^{20} = -105.6$ (*c* 1.3, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.78$ (s, 3H), 7.56 (d, $J = 8.1$ Hz, 6H), 7.45 (d, $J = 8.4$ Hz, 6H), 7.34–7.13 (m, 24H), 6.99–6.95 (m, 12H), 6.85–6.82 (m, 6H), 5.13–5.06 (m, 9H), 4.92 (s, 3H), 4.39 (t, $J = 7.5$ Hz, 3H), 3.46–3.39 (m, 3H), 3.27–3.22 (m, 3H), 2.21–2.01 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 157.9$, 156.7, 146.5, 144.3, 143.8, 141.8, 129.6, 129.5, 129.1, 128.3, 128.1, 126.8, 126.7, 125.6, 125.1, 121.1, 114.7, 113.8, 76.5, 69.5, 64.4, 61.9, 59.6, 52.8, 50.5, 33.5, 30.6. IR (KBr, cm^{-1}) 3414, 2926, 1613, 1508, 1236, 1174, 1005, 823, 699. Anal. Calcd for $C_{101}H_{96}N_{12}O_9$: C, 74.79; H, 5.79; N, 10.36. Found: C, 74.83; H, 5.78; N, 10.37. HRMS (ESI, M+H$^+$), calcd, 1621.7496; found 1621.7491.

4.2.10. Synthesis of (2*S*,2′*S*,2″*S*,2‴*S*,2⁗*S*,2⁗′*S*,4*S*,4′*S*,4″*S*,4‴*S*,4⁗*S*,4⁗′*S*)-4,4′,4″,4‴,4⁗,4⁗′-(4,4′,4″,4‴,4⁗,4⁗′-(5,5′,5″-(4,4′,4″-(ethane-1,1,1-triyl)tris(benzene-4,1-diyl))tris(oxy)tris(methylene)tris(benzene-5,3,1-triyl))hexakis(oxy)hexakis(methylene)hexakis(1*H*-1,2,3-triazole-4,1-diyl))hexakis(pyrrolidine-4,2-diyl)hexakis (diphenyl methanol) 7f. To a solution of **8f** (225 mg, 0.25 mmol),[25b] compound **6** (529 mg, 1.8 mmol), *N*,*N*-diisopropylethylamine (516 mg, 4.0 mmol), and $Cu(PPh_3)_3Br$ (139.2 mg, 0.15 mmol) in tetrahydrofuran (10 mL) were added. The reaction mixture was then stirred at room temperature for ca. 72 h. The solvent was removed under reduced pressure. The crude product was purified by column chromatography, eluting with a 10:1 mixture of dichloromethane and methanol to give **7f** as a white solid (566 mg, 85% yield). White solid, mp 124–126 °C, $[\alpha]_D^{20} = -54.8$ (*c* 1.2, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.77$ (s, 6H), 7.54 (d, $J = 7.6$ Hz, 12H), 7.48–7.42 (m, 12H), 7.26–7.10 (m, 36H), 6.96–6.93 (m, 6H), 6.81–6.79 (m, 6H), 6.67 (d, $J = 8.4$ Hz, 6H), 6.59 (s, 3H), 5.15–5.05 (m, 18H), 4.95 (s, 6H), 4.37 (t, $J = 8.8$ Hz, 6H), 3.41–3.40 (m, 6H), 3.23–3.20 (m, 6H), 2.18–2.06 (m, 15H), 1.91 (br, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.5$, 156.5, 146.5, 144.4, 143.5, 141.9, 139.7, 129.5, 128.2, 128.0, 126.7, 126.6, 125.7, 125.1, 121.3, 113.9, 106.5, 101.3, 76.6, 69.6, 64.3, 61.9, 59.6, 52.7, 50.5, 33.5, 30.6. IR (KBr, cm^{-1}) 3416, 2925, 1598, 1449, 1241, 1155, 1049, 1009, 832, 700. Anal. Calcd for $C_{161}H_{156}N_{24}O_{15}$: C, 72.50; H, 5.90; N, 12.60. Found: C, 72.52; H, 5.88; N, 12.64.

4.3. General procedure for asymmetric borane reduction of prochiral ketones

Under an argon atmosphere, BH_3–Me_2S (0.75 mmol) was added to a solution of catalyst **7f** (0.025 mmol) in dry THF (5 mL). The suspension was stirred and refluxed for 1 h. Then, a THF (2 mL) solution of ketone (0.5 mmol) was added by syringe pump over a period of 1 h, and the reaction mixture stirred for an additional 1 h. The reaction mixture was cooled and quenched by the dropwise addition of water (5 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The organic layer was treated with saturated brine, and then dried over anhydrous Mg_2SO_4. After concentration by rotatory evaporation, diethyl ether was added. The product was dissolved in the ether, and catalyst **7f** was precipitated. After removing the ether phase, the catalyst was dried under vacuum for 12 h, and then reused for the next cycle of the reaction. After the solvent was removed from the ether phase under the reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 8:1) to afford the corresponding secondary alcohol. The ee value was determined by Chiralcel OJ column (eluent: hexane/2-propanol = 90/10).

4.3.1. (*R*)-1-Phenyl-ethanol 9a.[26a] Colorless oil; 95% yield. 94% ee. Determined by HPLC analysis (Daicel Chiralcel OB column, hexane/isopropanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 16.04$ and $t_{minor} = 14.64$ min. $[\alpha]_D^{20} = +29.6$ (*c* 1.3, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.33$–7.21 (m, 5H), 4.82 (q, $J = 6.3$ Hz, 1H), 2.27 (br, 1H), 1.45 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 145.7$, 128.3, 127.3 125.3, 70.2, 25.0. lit.[26a] $[\alpha]_D^{20} = +28.4$ (*c* 1.2, MeOH); 97% ee.

4.3.2. (*R*)-1-(4-Methoxy-phenyl)-ethanol 9b.[9b] Colorless oil; 91% yield. 90% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/isopropanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 29.36$ and $t_{minor} = 27.54$ min. $[\alpha]_D^{20} = +37.9$ (*c* 1.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.26$ (d, $J = 8.4$ Hz, 2H), 6.87–6.84 (m, 3H), 4.81 (q, $J = 6.6$ Hz, 1H), 3.77 (s, 1H), 2.15 (br, 1H), 1.46 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 158.7$, 138.0, 126.6, 113.6, 69.6, 55.1, 24.8. lit.[9b] $[\alpha]_D^{20} = +49.4$ (*c* 2.3, CH_2Cl_2); 93% ee.

4.3.3. (*R*)-1-(4-Fluoro-phenyl)-ethanol 9c.[9b] Colorless oil; 98% yield. 96% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 95:5, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 15.82$ and $t_{minor} = 15.18$ min. $[\alpha]_D^{20} = +39.8$ (*c* 1.0, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.36$–7.32 (m, 2H), 7.06–7.00 (m, 2H), 4.89 (q, $J = 6.6$ Hz, 1H), 1.74 (br, 1H), 1.48 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 162.0$,

141.5, 127.0, 126.9, 114.9, 69.3, 24.9. lit.[9b] $[\alpha]_D^{20} = +34.1$ (*c* 2.0, CH_2Cl_2); 95% ee.

4.3.4. (*R*)-1-(4-Chloro-phenyl)-ethanol 9d.[9b] Colorless oil; 97% yield. 92% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 14.53$ and $t_{minor} = 13.61$ min. $[\alpha]_D^{20} = +39.5$ (*c* 1.2, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.32–7.26$ (m, 4H), 4.85 (q, $J = 6.8$ Hz, 1H), 2.10 (br, 1H), 1.45 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 144.4$, 133.2, 128.8, 126.0, 69.9 25.4. lit.[9b] $[\alpha]_D^{20} = +47.2$ (*c* 1.8, CH_2Cl_2); 94% ee.

4.3.5. (*R*)-1-(4-Bromophenyl)-ethanol 9e.[9b] Colorless oil; 93% yield. 94% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 15.52$ and $t_{minor} = 14.49$ min. $[\alpha]_D^{20} = +17.6$ (*c* 1.4, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.47–7.43$ (m, 2H), 7.26–7.21 (m, 2H), 4.83 (q, $J = 6.3$ Hz, 1H), 2.16 (br, 1H), 1.44 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 144.7$, 131.3, 127.0, 121.0, 69.4, 25.0. lit.[9b] $[\alpha]_D^{20} = +16.8$ (*c* 2.1, CH_2Cl_2); 91% ee.

4.3.6. (*R*)-1-(4-Nitro-phenyl)-ethanol 9f.[9b] Colorless oil; 99% yield. 93% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 38.04$ and $t_{minor} = 34.61$ min. $[\alpha]_D^{20} = +29.0$ (*c* 1.2, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.17$ (d, $J = 9.2$ Hz, 2H), 7.54 (d, $J = 8.4$ Hz, 2H), 5.01 (q, $J = 6.8$, 1H), 2.48 (br, 1H), 1.51 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 153.1$, 147.0, 126.0, 123.6, 69.3, 25.3. lit.[9b] $[\alpha]_D^{20} = +27.1$ (*c* 2.1, CH_2Cl_2); 98% ee.

4.3.7. (*R*)-1-Naphthalen-2-yl-ethanol 9g.[26a] White solid; 95% yield. 87% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 40.46$ and $t_{minor} = 31.05$ min. $[\alpha]_D^{20} = +29.8$ (*c* 1.3, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.83–7.79$ (m, 4H), 7.50–7.24 (m, 3H), 4.81 (q, $J = 6.6$ Hz, 1H), 2.06 (br, 1H), 1.45 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 143.4$. 133.5, 133.1, 128.5, 128.1, 127.8, 126.3, 126.0, 124.0, 70.7, 29.9. 25.3. lit.[26a] $[\alpha]_D^{20} = +30.4$ (*c*1.4, $CHCl_3$); 93% ee.

4.3.8. (*R*)-1-(3-Bromophenyl)-ethanol 9h.[26a] Colorless oil; 90% yield. 87% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 14.73$ and $t_{minor} = 13.22$ min. $[\alpha]_D^{20} = +39.2$ (*c* 1.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.53$ (s, 1H), 741–7.38 (m, 2H), 7.30–7.18 (m, 2H), 4.86 (q, $J = 6.3$ Hz, 1H), 1.90 (br, 1H), 1.48 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 148.0$, 130.3, 129.9, 128.4, 123.9, 122.4, 69.5, 25.1. lit.[26a] $[\alpha]_D^{20} = +45.4$ (*c* 1.0, $CHCl_3$); 96% ee.

4.3.9. (*R*)-1-(3-Methoxy-phenyl)-ethanol 9i.[26b] Colorless oil; 95% yield. 92% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 25.30$ and $t_{minor} = 23.51$ min. $[\alpha]_D^{20} = +38.5$ (*c* 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.26–7.20$ (m, 1H), 6.91 (m, 2H), 6.79–6.76 (m, 1H), 4.81 (q, $J = 6.6$ Hz, 1H), 3.77 (s, 3H), 2.34 (br, 1H), 1.45 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 159.6$, 147.5, 129.3, 117.6, 112.7, 110.8, 70.1, 55.1, 25.0. lit.[26b] $[\alpha]_D^{28} = +39$ (*c* 1.0, $CHCl_3$); 96% ee.

4.3.10. (*R*)-1-(2-Methoxy-phenyl)-ethanol 9j.[9b] Colorless oil; 96% yield. 93% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 20.65$ and $t_{minor} = 20.05$ min. $[\alpha]_D^{20} = +45.8$ (*c* 1.4 CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.33$ (d, $J = 7.2$ Hz, 1H), 7.26–7.20 (m, 1H), 6.97–6.92 (m, 1H), 6.88–6.85 (d, $J = 8.4$ Hz, 1H), 5.08 (q, $J = 6.3$ Hz, 1H), 3.84 (s, 3H), 2.72 (br, 1H), 1.49 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 156.4$, 133.3, 128.2, 126.0, 120.7, 110.3, 66.3, 55.1, 22.8. lit.[9b] $[\alpha]_D^{20} = +53.0$ (*c* 1.5, CH_2Cl_2); 87% ee.

4.3.11. (*S*)-2-Chloro-1-phenyl-ethanol 9k.[26c] Colorless oil; 95% yield. 87% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 28.79$ and $t_{minor} = 26.68$ min. $[\alpha]_D^{20} = +41.8$ (*c* 1.4, C_6H_{12}). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.36–7.22$ (m, 5H), 4.85 (dd, $J = 3.6$ Hz, 8.4 Hz, 1H), 3.73–3.58 (m, 2H), 2.82 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 139.8$, 128.5, 128.3, 125.9, 73.9, 50.7. lit.[26c] $[\alpha]_D^{25} = +42.8$ (*c* 1.5, C_6H_{12}); 87% ee.

4.3.12. (*S*)-2-Bromo-1-phenyl-ethanol 9l.[26c] Colorless oil; 93% yield. 92% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 28.40$ and $t_{minor} = 26.30$ min. $[\alpha]_D^{20} = +38.8$ (*c* 1.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.36–7.30$ (m, 5H), 4.87 (dd, $J = 3.2$ Hz, 6.4 Hz, 1H), 3.60–3.48 (m, 2H), 2.97 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 140.3$, 128.6, 128.3, 125.9, 73.7, 39.9. lit.[26d] $[\alpha]_D^{25} = +40.1$ (*c* 1.8, $CHCl_3$); 92% ee.

4.3.13. (*R*)-1,2,3,4-Tetrahydronaphthalen-1-ol 9m.[26e] Colorless oil; 98% yield. 81%, ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 14.64$ and $t_{minor} = 12.97$ min. $[\alpha]_D^{20} = -28.3$ (*c* 1.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.41–7.39$ (m, 1H), 7.38–7.15 (m, 2H), 7.08–7.06 (m, 1H), 4.72 (s, 1H), 2.76–2.65 (m, 2H), 2.13 (s, 1H); 1.99–1.71 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 138.7$, 137.0, 128.8, 128.5, 127.4, 126.0, 67.9, 32.1, 29.1, 18.7. lit.[26e] $[\alpha]_D^{20} = -28.6$ (*c* 0.5, $CHCl_3$); 82% ee.

4.3.14. (*R*)-1-Phenylpropan 9n.[26e] Colorless oil; 95%, yield. 71% ee. Determined by HPLC analysis (Daicel Chiralcel OJ column, hexane/2-propanol = 90:10, 0.5 mL/min, 254 nm). Retention time: $t_{major} = 14.49$ and $t_{minor} = 13.82$ min. $[\alpha]_D^{20} = +27.6$ (*c* 1.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.34–7.23$ (m, 5H), 4.53 (t, $J = 4.8$ Hz, 1H), 2.26 (br, 1H), 1.82–1.69 (m, 2H), 0.88 (t, $J = 6.6$ Hz, 3H);

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 144.5$, 128.3, 127.3, 125.9, 75.8, 31.7, 10.0. lit.[26e] $[\alpha]_D^{20} = +29.0$ (c 1.0, $CHCl_3$); 77% ee.

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