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The pentafluorophenyl group as a module for the direct modification of chiral diamines for asymmetric catalysis

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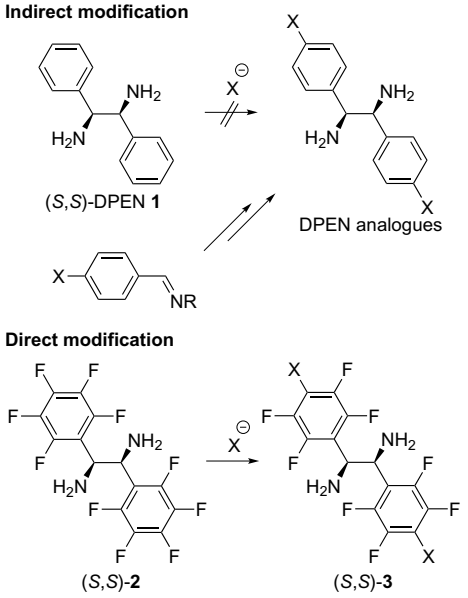
Abstract—A pentafluorophenyl group embedded in a chiral diamine allows the direct modification of an aryl group. The diamine is readily converted into *para*-disubstituted diamines. Although the electronic effect of the modified diamine somewhat lowers the catalytic activity of BINAP–Ru–diamine-catalyzed asymmetric hydrogenation, the enantioselectivity of the product is higher than that obtained by using a typical chiral diamine. Such an easy and direct modification of the chiral ligand has the potential to facilitate the optimization of the steric effect of chiral ligands in asymmetric catalysis.

1. Introduction

Asymmetric catalysts are crucial to the synthesis of useful chiral compounds. Typically, a homogeneous asymmetric catalyst is a metal complex containing one or more organic chiral ligands, which control the electronic and steric (chiral) environment of the metal catalyst.[1] Therefore, the development of the chiral ligand plays an important role in the development of an asymmetric catalyst. In many cases, many chiral ligands are screened in order to achieve high activity with high enantioselectivity in asymmetric catalysis. Although the electronic effect of the ligand often influences the enantioselectivity, stereo-regulation is mainly achieved by utilizing the repulsive interactions between the ligand and the reactive substrate. Accordingly, partial modification of chiral ligands to tune the steric effect is required in order to improve the enantioselectivity in asymmetric catalysis. However, the preparation of the modified ligands is often complicated and hinders research. For example, 1,2-diphenylethylenediamine (DPEN **1**, Scheme 1) is one of the most useful chiral ligands for asymmetric catalysis. However, DPEN analogues bearing substituted aryl groups cannot be prepared directly from **1** (Scheme 1). Instead, they must be synthesized via inconvenient asymmetric synthesis using individual starting materials, such as imines.[2] If a direct modification of the original chiral ligand is possible, optimization of the chiral ligand in asymmetric catalysis will be facilitated. For this reason, we have focused on a pentafluorophenyl (C_6F_5) group as a modifiable module in a chiral ligand, because this group is readily attacked by various nucleophiles to afford the *para*-substituted tetrafluorophenyl group (Scheme 1).[3]



Scheme 1. Direct modification of diamines bearing the C_6F_5 group.

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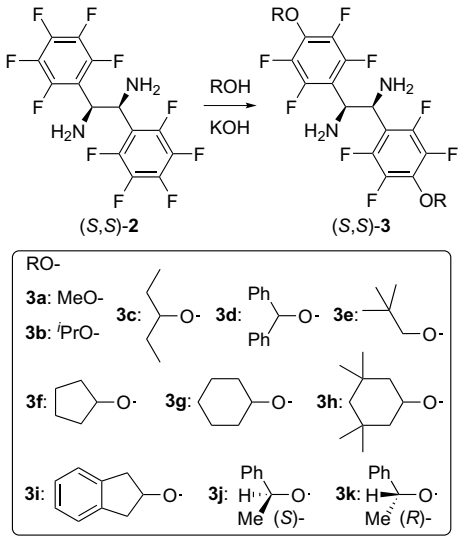
Herein, we report the effectiveness of the C_6F_5 group embedded in the chiral ligand as a modifiable unit. The chiral diamine **2** bearing two C_6F_5 groups[4] is used as the original ligand for self-modification at the *para*-position. The modified diamines **3** are used as ligands for Noyori–Ohkuma's asymmetric hydrogenation catalyst[5] to find the diamine ligand that exhibits an effective steric environment at the *para*-positions of the aryl groups.[6]

2. Results and discussion

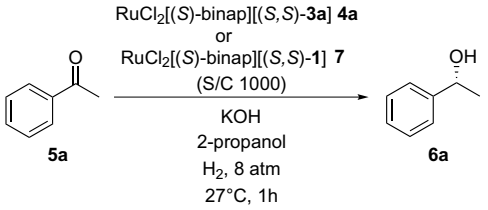
Chiral diamine **2** was readily converted into *para*-disubstituted (*S*,*S*)-**3**. The modification of **2** was performed using an alkoxide to avert the necessity of protection of the amino groups of **2**.[7] For example, (*S*,*S*)-**2** was exposed to KOH/methanol at room temperature for 3 h to afford (*S*,*S*)-**3a** in a quantitative yield. The modification of (*S*,*S*)-**2** afforded 11 types of *para*-disubstituted diamines **3a**–**k** (Scheme 2). However, substitution with *tert*-butoxy group was unsuccessful. The direct modification of **2** with alkoxide was found to be limited to primary or secondary alkoxides. Consequently, we could obtain a series of diamines **3** for screening the ligands in asymmetric catalysis within a short period of time.



Scheme 2. Easy modification of the diamine at the *para*-position of the C_6F_5 group.

Before screening the ligands for asymmetric hydrogenation, we verified the electronic influence of the fluorinated diamine **3** on the Ru catalyst.[8,9] Diamine **3a** was complexed with $RuCl_2$[(*S*)-binap](dmf)$_n$ in $CDCl_3$ to afford $RuCl_2$[(*S*)-binap][(*S*,*S*)-**3a**] **4a** quantitatively,[10] although **3a** had a weak electron-donating ability. Unfortunately, the hydrogenation of acetophenone **5a** using **4a** with 2 equiv of KOH with respect to the Ru complex in 2-propanol under 8 atm of H_2 at 27 °C for 1 h afforded alcohol **6a** in a low yield (39%), although the reaction using $RuCl_2$[(*S*)-binap]-[(*S*,*S*)-**1**] **7** afforded **6a** in a quantitative yield under the same conditions (Table 1, entry 1 vs 5). However, the yield of **6a** was improved when increasing the amount of KOH (Table 1, entries 2–4).[11] As a result, when **4a** with 8 equiv of KOH for the Ru complex was used for the hydrogenation of **5a**, **6a** was obtained in 95% yield (Table 1, entry 4). Although a marginal negative phenomenon was caused by the electronic effect of **3a**, the catalytic system of **4a** with KOH acted as a suitable hydrogenation catalyst.

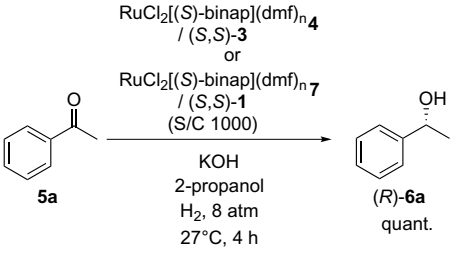
Table 1. Catalytic activities of catalysts **4a** and **7**



Entry	Catalysts	KOH (equiv)	Yield (%)
1	**4a**	2	39
2	**4a**	4	79
3	**4a**	6	89
4	**4a**	8	95
5	**7**	2	>99

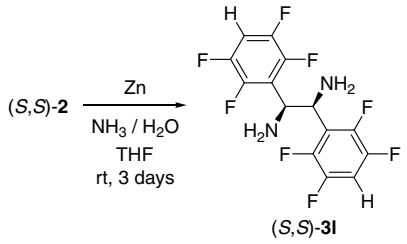
Asymmetric hydrogenations of **5a** were studied by using $RuCl_2$[(*S*)-binap](dmf)$_n$ and (*S*,*S*)-**3a**–**k**, which afforded $RuCl_2$[(*S*)-binap][(*S*,*S*)-**3a**–**k**] **4a**–**k** in situ, to explore the most sterically favored substituent at the *para*-position of the aryl groups in **3**, affording the highest enantioselectivity in the product. All the reactions were performed with 8 equiv of KOH for the Ru complex in 2-propanol under H_2 (8 atm) at 27 °C for 4 h to afford **6a** in a quantitative yield. All the products showed higher enantioselectivities than those obtained by using **7**, which afforded **6a** in 82% ee (Table 2, entries 1–11 vs 13). Even the use of **4a**, which

Table 2. Asymmetric hydrogenation of acetophenone



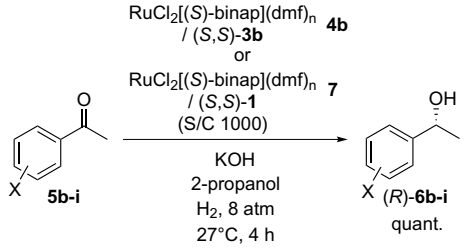
Entry	Catalysts (diamine)	ee of **6a** (%)
1	**4a** [(*S*,*S*)-**3a**]	87
2	**4b** [(*S*,*S*)-**3b**]	92
3	**4c** [(*S*,*S*)-**3c**]	90
4	**4d** [(*S*,*S*)-**3d**]	89
5	**4e** [(*S*,*S*)-**3e**]	90
6	**4f** [(*S*,*S*)-**3f**]	91
7	**4g** [(*S*,*S*)-**3g**]	91
8	**4h** [(*S*,*S*)-**3h**]	89
9	**4i** [(*S*,*S*)-**3i**]	90
10	**4j** [(*S*,*S*,*S*)-**3j**]	88
11	**4k** [(*S*,*S*,*R*)-**3k**]	90
12	**4l** [(*S*,*S*)-**3l**]	84
13	**7** [(*S*,*S*)-**1**]	82

had the smallest alkoxy substituents, afforded **6a** with 87% ee (Table 2, entry 1). The reason for the high enantioselectivity obtained when using **4** as compared with that obtained when using **7** is assumed to be the steric effect of the *para*-substituent of **3**, because the hydrogenation using **4l** included 2,3,5,6-tetrafluorophenyl analogue **3l**, which was synthesized by the reductive defluorination of **2** (Scheme 3),[12] gave only 84% ee of **6a** (Table 2, entry 12). Among diamines **3**, the hydrogenation using **4b**, which included **3b** bearing an isopropoxy substituent, showed the highest enantioselectivity of 92% ee (Table 2, entry 2). Therefore, we performed the hydrogenation of the other ketones **5b–i** using **4b** (Table 3). The enantioselectivities of **6**, excluding those of the *ortho*-substituted aromatics **6h** and **6i**, were higher than that using **7**. The results indicated that we could easily find out the generally effective ligand whose ability is greater than that of DPEN **1**.



Scheme 3. Synthesis of (*S*,*S*)-**3l** by reductive defluorination of (*S*,*S*)-**2**.

Table 3. Asymmetric hydrogenation of aromatic ketones



Entry	X	Catalysts	ee (%)
1	4-Me (**5b**)	**4b**	84 (**6b**)
2	4-Me (**5b**)	**7**	79 (**6b**)
3	4-MeO (**5c**)	**4b**	87 (**6c**)
4	4-MeO (**5c**)	**7**	80 (**6c**)
5	4-F (**5d**)	**4b**	73 (**6d**)
6	4-F (**5d**)	**7**	73 (**6d**)
7	3-Me (**5e**)	**4b**	91 (**6e**)
8	3-Me (**5e**)	**7**	88 (**6e**)
9	3-MeO (**5f**)	**4b**	87 (**6f**)
10	3-MeO (**5f**)	**7**	84 (**6f**)
11	3-F (**5g**)	**4b**	81 (**6g**)
12	3-F (**5g**)	**7**	70 (**6g**)
13	2-Me (**5h**)	**4b**	92 (**6h**)
14	2-Me (**5h**)	**7**	93 (**6h**)
15	2-MeO (**5i**)	**4b**	42 (**6i**)
16	2-MeO (**5i**)	**7**	77 (**6i**)

3. Conclusion

Herein, we have demonstrated that (*S*,*S*)-**2** was readily converted into 11 types of *para*-disubstituted (*S*,*S*)-**3**, and then diamine (*S*,*S*)-**3b**, which has an influential steric effect for the Noyori–Ohkuma asymmetric hydrogenation, can be easily found after the screening reaction using $RuCl_2$[(*S*)-binap][(*S*,*S*)-**3**]. The pentafluorophenyl group in the chiral diamine facilitated the ligand screening process in the asymmetric hydrogenation. Although the electronic effect of the *para*-substituted tetrafluorophenyl group in the ligand must be considered, the introduction of a pentafluorophenyl group as a modifiable module into other chiral ligands may turn into one method for avoiding the complicated screening required for tuning the steric effect of the chiral ligands for asymmetric catalyses.

4. Experimental

Asymmetric hydrogenations were carried out with degassed solvents under an argon atmosphere. Dehydrated 2-propanol was purchased from Kanto Chemical Co. and stored in Schlenk tubes under an argon atmosphere after degassing via freeze–thaw cycles. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Preparative column chromatography was carried out by using silica gel (Fuji Silysia BW-127 ZH, 100–270 mesh) or neutral silica gel (nacalai tesque Silica Gel 60, spherical, neutrality). HPLC analysis was carried out by using Daicel CHIRALCEL OD-H, Φ 4.6 mm × 25 cm, with the mixed solvent indicated. ^{1}H and ^{13}C NMR spectra were measured at 300 MHz and 75 MHz, respectively, and chemical shifts are given relative to tetramethylsilane (TMS). ^{19}F NMR spectra were measured at 282 MHz, and chemical shifts are given relative to CCl_3F using C_6F_6 as a secondary reference (−162.9 ppm). ^{31}P NMR spectra were measured at 121 MHz, and chemical shifts are given relative to H_3PO_4 as an external standard.

4.1. Preparation of diamine 3

4.1.1. (1*S*,2*S*)-1,2-Bis(4-methoxy-2,3,5,6-tetrafluorophenyl)-ethane-1,2-diamine (*S*,*S*)-3a. A mixture of (*S*,*S*)-**2** (19.6 mg, 0.0500 mmol) and KOH (28.2 mg, 0.500 mmol) in methanol (1.0 mL) was stirred at room temperature for 3 h. The solvent was removed under reduced pressure. The residue was poured into water (5 mL) and extracted with Et_2O (3 × 5 mL). The combined organic extract was washed with brine. The organic layer was dried over $MgSO_4$, and concentrated under reduced pressure to afford a crude oil, which was purified by column chromatography (neutral SiO_2, CH_2Cl_2/MeOH, 30:1) to give (*S*,*S*)-**3a** (20.8 mg, 0.0500 mmol) in 100% yield: white solid; mp 56–58 °C; $[\alpha]_D^{20} = -85.8$ (*c* 0.50, MeOH); IR (KBr, cm^{-1}) 3371, 2957, 1651, 1495, 1196, 1128, 978; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.45 (s, 2H), 4.02 (t, $J = 1.5$ Hz, 6H), 2.03 (br, 4H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 62.0, 52.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ −145.7 to −145.6 (m, 4F), −158.7 to −158.6 (m, 4F); Anal. Calcd for $C_{16}H_{12}F_8N_2O_2$: C, 46.17; H, 2.91; N, 6.73; Found: C, 46.27; H, 3.04; N, 6.70. HLPC analysis: hexane/*i*-PrOH/Et_2NH (70:30:0.2), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3a**: 22.3 min (>99%), (*R*,*R*)-**3a**: 36.1 min (0%).

4.1.2. (1*S*,2*S*)-1,2-Bis(4-isopropoxy-2,3,5,6-tetrafluorophenyl)ethane-1,2-diamine (*S*,*S*)-3b. Compound (*S*,*S*)-**3b** was prepared from (*S*,*S*)-**2** (19.6 mg, 0.0500 mmol), KOH (56.1 mg, 1.00 mmol), and 2-propanol (1.0 mL) in 98% yield (23.2 mg, 0.0491 mmol) by the procedure described for (*S*,*S*)-**3a**: colorless oil; $[\alpha]_D^{30} = -92.5$ (*c* 0.21, MeOH); IR (neat, NaCl plate, cm^{-1}) 3387, 3325, 2986, 1651, 1489, 1381, 1242, 1103, 980; ^1H NMR (300 MHz, $CDCl_3$) δ 4.47 (m, 2H), 4.42 (s, 2H), 2.03 (br, 4H), 1.29 (d, $J = 6.2$ Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 78.0, 52.8, 22.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ −145.9 to −145.8 (m, 4F), −157.0 to −156.9 (m, 4F); Anal. Calcd for $C_{20}H_{20}F_8N_2O_2$: C, 50.85; H, 4.27; N, 5.93; Found: C, 50.58; H, 4.26; N, 5.75. HLPC analysis: hexane/*i*-PrOH/Et_2NH (70:30:0.2), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3b**: 18.1 min (>99%), (*R*,*R*)-**3b**: 32.6 min (0%).

4.1.3. (1*S*,2*S*)-1,2-Bis(4-(pentan-3-yloxy)-2,3,5,6-tetrafluorophenyl)ethane-1,2-diamine (*S*,*S*)-3c. Compound (*S*,*S*)-**3c** was prepared from (*S*,*S*)-**2** (19.6 mg, 0.0500 mmol), KOH (56.1 mg, 1.00 mmol), and 3-pentanol (1.0 mL) in 97% yield (25.5 mg, 0.0483 mmol) by the procedure described for (*S*,*S*)-**3a** at 50 °C for 6 h: yellow oil; $[\alpha]_D^{16} = -51.4$ (*c* 1.6, MeOH); IR (neat, NaCl plate, cm^{-1}) 3387, 3302, 2970, 1651, 1489, 1381, 1242, 1134, 980; ^1H NMR (300 MHz, $CDCl_3$) δ 4.41 (s, 2H), 4.13 (quint, $J = 5.7$ Hz, 2H), 2.07 (br, 4H), 1.57–1.61 (m, 8H), 0.91–0.97 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 87.8, 52.8, 26.2, 9.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ −146.0 to −145.9 (m 4F), −156.9 to −156.8 (m, 4F); Anal. Calcd for $C_{24}H_{28}F_8N_2O_2$: C, 54.54; H, 5.34; N, 5.30; Found: C, 54.41; H, 5.47; N, 5.07. HLPC analysis: hexane/*i*-PrOH/Et_2NH (70:30:0.4), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3c**: 18.1 min (>99%), (*R*,*R*)-**3c**: 31.0 min (0%).

4.1.4. (1*S*,2*S*)-1,2-Bis(4-benzhydryloxy-2,3,5,6-tetrafluorophenyl)ethane-1,2-diamine (*S*,*S*)-3d. A mixture of (*S*,*S*)-**2** (4.9 mg, 0.0125 mmol), KOH (14.0 mg, 0.250), and benzhydrol (0.500 g, 2.71 mmol) in DMF (0.10 mL) was stirred at 50 °C for 24 h. To the reaction mixture was added water, and the organic layer was extracted with Et_2O (3 × 2 mL). The combined organic extract was washed with brine. The organic layer was dried over $MgSO_4$, and concentrated under reduced pressure to afford a crude oil, which was purified by column chromatography (neutral SiO_2, CH_2Cl_2/MeOH, 30:1) to give (*S*,*S*)-**3d** (8.10 mg, 0.0112 mmol) in 90% yield: yellow oil; $[\alpha]_D^{32} = -41.9$ (*c* 0.19, MeOH); IR (neat, NaCl plate, cm^{-1}) 3395, 3325, 3031, 2962, 1651, 1489, 1265, 1126, 988; ^1H NMR (300 MHz, $CDCl_3$) δ 7.28–7.42 (m, 20H), 6.35 (s, 2H), 4.31 (s, 2H), 1.94 (br, 4H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 139.4, 128.5, 127.0, 86.8, 52.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ −145.9 to −145.8 (m, 4F), −155.1 to −155.0 (m, 4F); Anal. Calcd for $C_{40}H_{28}F_8N_2O_2$: C, 66.67; H, 3.92; N, 3.89; Found: C, 66.87; H, 4.23; N, 3.79. HLPC analysis: hexane/*i*-PrOH/Et_2NH (60:40:0.1), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3d**: 14.8 min (>99%), (*R*,*R*)-**3d**: 21.9 min (0%).

4.1.5. (1*S*,2*S*)-1,2-Bis(4-neopentyloxy-2,3,5,6-tetrafluorophenyl)ethane-1,2-diamine (*S*,*S*)-3e. Compound (*S*,*S*)-**3e** was prepared from (*S*,*S*)-**2** (19.6 mg, 0.0500 mmol), KOH (56.1 mg, 1.00 mmol), and 2,2-dimethyl-1-propanol (2.00 g, 22.7 mmol) in 91% yield (24.0 mg, 0.0454 mmol) by the procedure described for (*S*,*S*)-**3a** at 55 °C for 18 h: yellow oil; $[\alpha]_D^{30} = -89.2$ (*c* 0.45, MeOH); IR (neat, NaCl plate, cm^{-1}) 3387, 3310, 2962, 1651, 1504, 1366, 1265, 1134, 986; ^1H NMR (300 MHz, $CDCl_3$) δ 4.45 (s, 2H), 3.79 (s, 4H), 2.08 (br, 4H), 1.01 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 84.9, 52.6, 32.7, 26.0; ^{19}F NMR (282 MHz, $CDCl_3$) δ −145.9 to −145.8 (m, 4F), −157.9 to −157.8 (m, 4F); Anal. Calcd for $C_{24}H_{28}F_8N_2O_2$: C, 54.54; H, 5.34; N, 5.30; Found: C, 54.76; H, 5.54; N, 4.97. HLPC analysis: hexane/*i*-PrOH/Et_2NH (70:30:0.4), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3e**: 16.1 min (>99%), (*R*,*R*)-**3e**: 24.5 min (0%).

4.1.6. (1*S*,2*S*)-1,2-Bis(4-cyclopentyloxy-2,3,5,6-tetrafluorophenyl)ethane-1,2-diamine (*S*,*S*)-3f. Compound (*S*,*S*)-**3f** was prepared from (*S*,*S*)-**2** (9.8 mg, 0.0250 mmol), KOH (28.1 mg, 0.500 mmol), and cyclopentanol (0.70 mL) in 82% yield (10.7 mg, 0.0204 mmol) by the procedure described for (*S*,*S*)-**3a** at 50 °C for 6 h: yellow oil; $[\alpha]_D^{31} = -77.2$ (*c* 0.54, MeOH); IR (neat, NaCl plate, cm^{-1}) 3387, 3310, 2939, 1651, 1489, 1373, 1242, 1134, 980; ^1H NMR (300 MHz, $CDCl_3$) δ 4.78–4.84 (m, 2H), 4.41 (s, 2H), 2.08 (br, 4H), 1.61–1.83 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 87.1, 52.8, 32.7, 23.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ −146.0 to −145.9 (m, 4F), −157.2 to −157.1 (m, 4F); Anal. Calcd for $C_{24}H_{24}F_8N_2O_2$: C, 54.96; H, 4.61; N, 5.34; Found: C, 55.14; H, 4.91; N, 4.98. HLPC analysis: hexane/*i*-PrOH/Et_2NH (70:30:0.4), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3f**: 21.7 min (>99%), (*R*,*R*)-**3f**: 37.0 min (0%).

4.1.7. (1*S*,2*S*)-1,2-Bis(4-cyclohexyloxy-2,3,5,6-tetrafluorophenyl)ethane-1,2-diamine (*S*,*S*)-3g. Compound (*S*,*S*)-**3g** was prepared from (*S*,*S*)-**2** (19.6 mg, 0.0500 mmol), KOH (56.1 mg, 1.00 mmol), and cyclohexanol (1.4 mL) in 77% yield (21.2 mg, 0.0384 mmol) by the procedure described for (*S*,*S*)-**3a** at 50 °C for 6 h: yellowish oil; $[\alpha]_D^{32} = -80.2$ (*c* 0.13, MeOH); IR (neat, NaCl plate, cm^{-1}) 3389, 3317, 2939, 1651, 1489, 1373, 1242, 1134, 980; ^1H NMR (300 MHz, $CDCl_3$) δ 4.41 (s, 2H), 4.14–4.21 (m, 2H), 1.98 (br, 4H), 1.57–1.88 (m, 8H), 1.51–1.57 (m, 6H), 1.25–1.35 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 82.9, 52.9, 32.0, 25.3, 23.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ −146.0 to −145.9 (m, 4F), −156.9 to −156.8 (m, 4F); Anal. Calcd for $C_{26}H_{28}F_8N_2O_2$: C, 56.52; H, 5.11; N, 5.07; Found: C, 56.91; H, 5.32; N, 4.71. HLPC analysis: hexane/*i*-PrOH/Et_2NH (70:30:0.4), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3g**: 21.4 min (>99%), (*R*,*R*)-**3g**: 39.4 min (0%).

4.1.8. (1*S*,2*S*)-1,2-Bis(2,3,5,6-tetrafluoro-4-(3,3,5,5-tetramethylcyclohexyloxy)phenyl)ethane-1,2-diamine (*S*,*S*)-3h. Compound (*S*,*S*)-**3h** was prepared from (*S*,*S*)-**2** (19.6 mg, 0.0500 mmol), KOH (56.1 mg, 1.00 mmol), 3,3,5,5-tetramethylcyclohexanol (2.00 g, 12.8 mmol), and DMF (0.40 mL) in 58% yield (19.4 mg, 0.0292 mmol) by the procedure described for (*S*,*S*)-**3d** at 50 °C for 24 h: yellow oil;

$[\alpha]_D^{32} = -95.8$ (*c* 0.78, MeOH); IR (neat, NaCl plate, cm^{-1}) 3402, 3317, 2954, 1651, 1489, 1366, 1242, 1134, 988; ^1H NMR (300 MHz, $CDCl_3$) δ 4.39–4.44 (m, 2H), 4.41 (s, 2H), 1.93 (br, 4H), 1.72–1.80 (m, 4H), 1.07–1.27 (m, 8H), 0.98 (s, 12H), 0.95 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 80.3, 52.9, 51.3, 45.0, 35.0, 32.6, 27.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ −146.0 to −145.9 (m, 4F), −156.9 to −156.8 (m, 4F); Anal. Calcd for $C_{34}H_{44}F_8N_2O_2$: C, 61.43; H, 6.67; N, 4.21; Found: C, 61.82; H, 6.82; N, 4.08. HLPC analysis: hexane/*i*-PrOH/Et_2NH (70:30:0.4), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3h**: 12.4 min (>99%), (*R*,*R*)-**3h**: 17.0 min (0%).

4.1.9. (1*S*,2*S*)-1,2-Bis(4-(2,3-dihydro-1*H*-inden-2-yloxy)-2,3,5,6-tetrafluorophenyl)ethane-1,2-diamine (*S*,*S*)-3i. Compound (*S*,*S*)-**3i** was prepared from (*S*,*S*)-**2** (19.6 mg, 0.0500 mmol), KOH (56.1 mg, 1.00 mmol), 2-indanol (2.00 g, 14.9 mmol), and DMF (0.40 mL) in 71% yield (22.0 mg, 0.0355 mmol) by the procedure described for (*S*,*S*)-**3d** at 50 °C for 24 h: yellowish oil; $[\alpha]_D^{32} = -72.8$ (*c* 0.18, MeOH); IR (neat, NaCl plate, cm^{-1}) 3395, 3317, 3024, 2954, 1651, 1489, 1358, 1134, 980; ^1H NMR (300 MHz, $CDCl_3$) δ 7.15–7.44 (m, 8H), 5.17–5.22 (m, 2H), 4.44 (s, 2H), 3.09–3.23 (m, 8H), 1.74 (br, 4H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 139.7, 126.9, 124.7, 85.3, 52.8, 40.0, 39.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ −145.5 to −145.4 (m, 4F), −157.0 to −156.8 (m, 4F); Anal. Calcd for $C_{32}H_{24}F_8N_2O_2$: C, 61.94; H, 3.90; N, 4.51; Found: C, 61.75; H, 4.28; N, 4.15. HLPC analysis: hexane/*i*-PrOH/Et_2NH (60:40:0.1), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3i**: 26.9 min (>99%), (*R*,*R*)-**3i**: 48.4 min (0%).

4.1.10. (1*S*,2*S*)-1,2-Bis(4-((*S*)-1-phenylethoxy)-2,3,5,6-tetrafluorophenyl)ethane-1,2-diamine (*S*,*S*,*S*)-3j. Compound (*S*,*S*)-**3j** was prepared from (*S*,*S*)-**2** (15.7 mg, 0.0400 mmol), KOH (44.9 mg, 0.800 mmol), and (*S*)-1-phenylethanol (1.0 mL) in 86% yield (20.4 mg, 0.0342 mmol) by the procedure described for (*S*,*S*)-**3a** at 50 °C for 24 h: yellowish oil; $[\alpha]_D^{32} = -177.3$ (*c* 0.23, MeOH); IR (neat, NaCl plate, cm^{-1}) 3395, 3317, 3032, 2986, 1651, 1489, 1381, 1211, 1134, 980; ^1H NMR (300 MHz, $CDCl_3$) δ 7.28–7.35 (m, 10H), 5.38 (q, $J = 6.6$ Hz, 2H), 4.31 (s, 2H), 1.71 (br, 4H), 1.66 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 140.4, 128.7, 128.5, 126.2, 82.5, 52.5, 22.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ −146.1 to −146.0 (m, 4F), −156.0 to −155.9 (m, 4F); Anal. Calcd for $C_{30}H_{24}F_8N_2O_2$: C, 60.40; H, 4.06; N, 4.70; Found: C, 60.72; H, 4.19; N, 4.82. HLPC analysis: hexane/*i*-PrOH/Et_2NH (60:40:0.1), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3j**: 13.5 min (>99%), (*R*,*R*)-**3j**: 20.9 min (0%).

4.1.11. (1*S*,2*S*)-1,2-Bis(4-((*R*)-1-phenylethoxy)-2,3,5,6-tetrafluorophenyl)ethane-1,2-diamine (*S*,*S*,*R*)-3k. Compound (*S*,*S*)-**3k** was prepared from (*S*,*S*)-**2** (15.7 mg, 0.0400 mmol), KOH (44.9 mg, 0.800 mmol), and (*R*)-1-phenylethanol (1.0 mL) in 93% yield (22.1 mg, 0.0370 mmol) by the procedure described for (*S*,*S*)-**3a** at 50 °C for 24 h: yellowish oil; $[\alpha]_D^{32} = +63.9$ (*c* 0.55, MeOH); IR (neat, NaCl plate, cm^{-1}) 3402, 3310, 3031, 2986, 1651, 1489, 1242, 1134, 980; ^1H NMR (300 MHz, $CDCl_3$) δ 7.28–7.34 (m, 10H), 5.39 (q, $J = 6.3$ Hz, 2H), 4.32 (s, 2H), 1.93 (s, 4H), 1.65 (d, $J = 6.3$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 140.5, 128.6, 128.5, 126.2, 82.5, 52.5, 22.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ −146.1 to −146.0 (m, 4F), −156.0 to −155.9 (m, 4F); Anal. Calcd for $C_{30}H_{24}F_8N_2O_2$: C, 60.40; H, 4.06; N, 4.70; Found: C, 60.47; H, 4.13; N, 4.37. HLPC analysis: hexane/*i*-PrOH/Et_2NH (60:40:0.1), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3k**: 15.0 min (>99%), (*R*,*R*)-**3k**: 21.9 min (0%).

4.1.12. (1*S*,2*S*)-1,2-Bis(2,3,5,6-tetrafluorophenyl)ethane-1,2-diamine (*S*,*S*)-3l. To a solution of (*S*.*S*)-**2** (20.0 mg, 0.0510 mmol) in THF (0.21 mL) were added zinc powder (0.500 g, 7.65 mmol), NH_4Cl (0.206 g, 3.85 mmol), and 28% aqueous ammonia (2.1 mL). The resulting mixture was stirred at room temperature for 3 days. Unconsumed zinc was separated, and filtrate was extracted with ether (3 × 5 mL). The combined organic layer was dried over $MgSO_4$, and concentrated under reduced pressure to afford crude oil, which was purified by column chromatography (neutral SiO_2, CH_2Cl_2/MeOH, 30:1) to give (*S*,*S*)-**3l** (11.3 mg, 0.0317 mmol) in 62% yield: colorless oil; $[\alpha]_D^{18} = -61.9$ (*c* 1.8, MeOH); IR (neat, NaCl plate, cm^{-1}) 3387, 3306, 3084, 2974, 1616, 1502, 1387, 1254, 1175, 920, 851; ^1H NMR (300 MHz, $CDCl_3$) δ 6.83–6.94 (m, 2H), 4.53 (s, 2H), 2.07 (br, 4H); ^{13}C NMR (75 MHz, $CDCl_3$ (except for C_6F_4)) δ 105.3, 52.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ −139.6 to −139.5 (m, 4F), −144.5 to −144.4 (m, 4F); Anal. Calcd for $C_{14}H_8F_8N_2$: C, 47.20; H, 2.26; N, 7.86; Found: C, 47.23; H, 2.48; N, 7.67. HLPC analysis: hexane/*i*-PrOH/Et_2NH (60:40:0.1), 0.5 mL min^{-1}, UV 254 nm, retention time (t_R); (*S*,*S*)-**3l**: 13.8 min (>99%), (*R*,*R*)-**3l**: 21.3 min (0%).

4.2. General procedure for the asymmetric hydrogenation of ketones

$RuCl_2$[(*S*)-binap](dmf)$_n$ (7.5 mg, 8.0 μmol), (*S*,*S*)-diamine **3b** (3.8 mg, 8.0 μmol), 2-propanol (6.4 mL), and a solution of KOH/2-propanol (0.5 M, 128 μL, 64 μmol) were placed in an autoclave under a stream of argon. The mixture was stirred at room temperature for 30 min. Acetophenone **5a** (0.93 mL, 8.0 mmol) was added to the mixture at room temperature under a stream of argon, and then hydrogen was introduced at a pressure of 8 atm. After having vigorously stirred at 27 °C for 4 h, the solvent was removed under reduced pressure. The residue was filtered through a short column packed with silica gel. Chemical yield and enantiomeric ratio of phenethyl alcohol **6a** were determined by chiral GC (>99%, 92% ee (*R*)). GC (column CP-Cyclodextrin-β-2,3,6-M-19, i.d. 0.25 mm × 25 m, CHROMPACK; carrier gas, helium (80 KPa); column temperature, 100 °C; injection temp, 250 °C; split ratio, 50:1), retention time (t_R); (*R*)-(+)-**6a**: 23.4 min (96.1%), (*S*)-(−)-**6a**: 26.2 min (3.9%), **5a**: 13.2 min (0%).

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10. The formation of complex **4a** was confirmed by ^{1}H and ^{31}P NMR spectra without purification. In particular, **4a** is clearly identified as a single complex (δ 45.8, s) by ^{31}P NMR spectra.
11. KOH is used for the deprotonation of an amino proton of **4a** to give active species (Ref. 5c). The reason for the necessity of such a large amount of KOH in the case of **4a** is assumed to be due to a relatively weak coordination between Ru and **3a**, which prevents to increase the amino proton acidity by complexation (Ref. 5c). The distance between the Ru and N atoms of **4a** is longer than that of $RuCl_2$[(*S*)-binap][(*S*,*S*)-**1**] **7** (2.199 Å for **4a** vs 2.178 Å for **7**) by the DFT calculations at the B3LYP/6-31G* (LANL2DZ for Ru) using GAUSSIAN 03. In addition, N–H stretching vibration values of **4a** (3341, 3279 cm^{-1}) are larger than those of **7** (3335, 3260 cm^{-1}) by measurement of IR spectra (KBr), which indicates that the N–H bond of **4a** is stronger than that of **7**.
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