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Ru-Catalyzed Asymmetric Transfer Hydrogenation of α-Trifluoromethylimines

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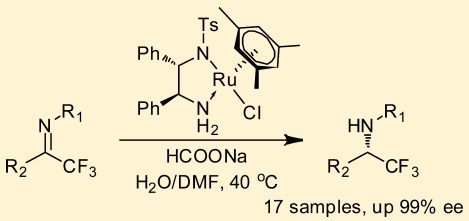
Supporting Information

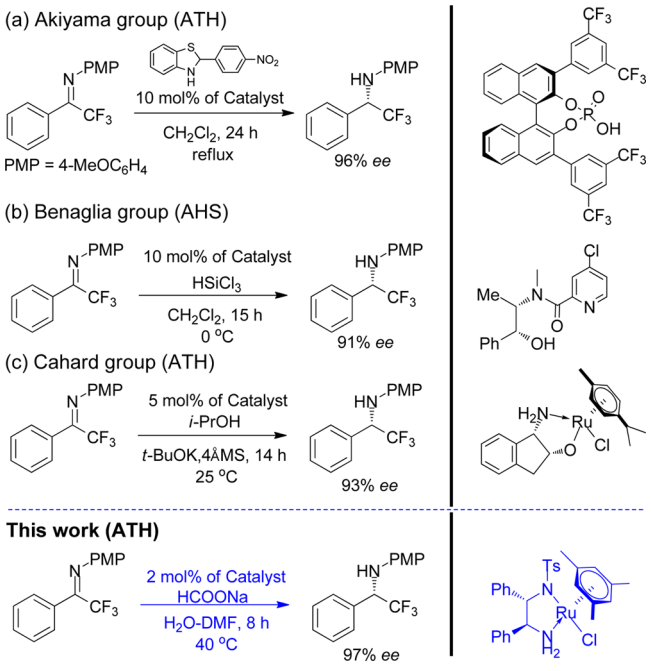
ABSTRACT: Enantioselective transformation of strong electron-withdrawing acyclic α-trifluoromethylimines to α-trifluoromethylamines through a ruthenium-catalyzed asymmetric transfer hydrogenation has been developed. The method described here is a facile catalytic process with sodium formate as a hydrogen resource and water−dimethylformamide as a cosolvent. The benefit of this enantioselective transformation affords a series of chiral α-trifluoromethylamines with high yields and excellent enantioselectivities (93−99% *ee*) under mild reaction conditions.



Since the pioneering works reported by Noyori, Ikariya, and co-workers on ruthenium(II)(diphosphine)(diamine) dichloride complexes for asymmetric hydrogenation of ketones and imines,[1] a large number of reviews and researches involving in *N*-sulfonylated 1,2-diamines as chiral ligands both in asymmetric hydrogenation and in asymmetric transfer hydrogenation of ketones and imines are well-documented theoretically and practically.[2] Also, various catalytic reaction systems covering 2-propanol, formic acid−triethylamine, formic acid, and sodium formate as hydrogen resources have been explored in asymmetric transfer hydrogenation of ketones and imines.[3] Most prominent examples employ chiral *N*-sulfonylated diamine-based η^5-Cp*−M complexes (η^5-Cp* = pentamethyl cyclopentadiene series) and η^6-arene−M complexes (η^6-arene = aromatic ring series) (M = Ru, Rh, and Ir), which have been applied extensively to various asymmetric transfer hydrogenation of ketones and imine.[4] Although these fruitful achievements have been obtained, their applications in enantioselective transformation of trifluoromethylimines remain an unmet challenge.

Optically pure α-trifluoromethylamine, as an important number of biologically active motifs, has been attracting much interest in medical and fluorine chemistry.[5] Recently, besides the methods of diastereoselective reductive aminations and asymmetric addition,[6] the construction of chiral α-trifluoromethylamines through enantioselective reduction of achiral α-trifluoromethylimines had been explored by a few groups.[7] The first two successful examples utilized an asymmetric hydrogenation method reported by the Uneyama and Zhou groups,[7b−d] in which Pd-catalyzed asymmetric reactions could afford chiral α-trifluoromethylamines with up to 94% enantioselectivity. However, high pressures of hydrogen and sensitive chiral diphosphine ligands still limited their practical applications. Interestingly, the latter three examples employed asymmetric transfer hydrogenation and asymmetric hydrosilylation methods to prepare chiral α-trifluoromethylamines.[7e−g] As shown in Scheme 1, the Akiyama group[7e] used an asymmetric transfer hydrogenation method through the use of a chiral phosphoric acid as a catalyst and benzothiazoline as a hydrogen resource to provide chiral 4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethyl)aniline with 96% *ee*, while the Benaglia group[7f] utilized an asymmetric hydrosilylation method through the use of a chiral organocatalyst (picolinamide) as a catalyst to

Scheme 1. Asymmetric Transfer Hydrogenation (ATH) and Asymmetric Hydrosilylation (AHS) of 4-Methoxy-*N*-(2,2,2-trifluoro-1-phenylethylidene)aniline



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obtain 91% *ee* of chiral 4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethyl)aniline. In particular, the Cahard group[7g] took advantage of the η^6-arene−Ru complex (chiral aminoalcohol/$[RuCl_2(p\text{-cymene})]_2$) as a catalyst and 2-propanol as a hydrogen resource to enable enantioselective reduction of achiral 4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethylidene)aniline to chiral 4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethyl)aniline (93% *ee*) through an asymmetric transfer hydrogenation method. Although the above three examples had been presented successfully, the first two examples needed 10 mol % of catalyst to reach their enantioselective performances, while *ee* values in Ru-catalyzed asymmetric transfer hydrogenation with 5 mol % of catalyst in the last example needed to be further enhanced. Therefore, by utilizing chiral N-sulfonylated diamine-based catalysts, realization of highly efficient asymmetric transfer hydrogenation of α-trifluoromethylimines with a low catalyst's amount under mild reaction conditions is high desirable.

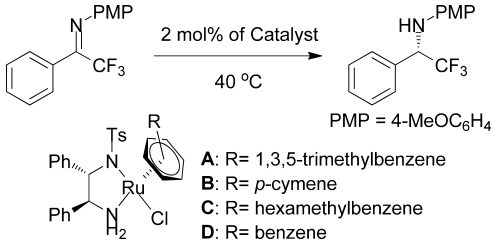
As an effort to develop highly efficient catalysts for asymmetric transfer hydrogenation,[8] we herein screen a series of *N*-(4-methyl)benzenesulfonylated 1,2-diphenylethylenediamine (TsDPEN)-based η^6-arene−M complexes to identify a TsDPEN-based η^6-mesitylene−Ru complex as an optimal catalyst, realizing an efficiently ruthenium-catalyzed asymmetric transfer hydrogenation of achiral aryltrifluoromethylimines to chiral aryltrifluoromethylamines with 2 mol % of catalyst under mild reaction conditions.

On the basis of the idea in further development of chiral N-sulfonylated diamine-based η^6-arene−M complexes for asymmetric transfer hydrogenation of trifluoromethylimines, the η^6-arene−Ru complex was investigated in asymmetric transfer hydrogenation of 4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethylidene)aniline under different reaction conditions, respectively. According to four common hydrogen resources, formic acid−triethylamine, formic acid, 2-propanol, and sodium formate, we screened its catalytic performance at first. As shown in Table 1, it was found that, in the case of HCOOH−NEt_3 cosolvent as a hydrogen resource, poor yield and medium enantioselectivity were obtained because the decomposition of 4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethylidene)aniline produced the side product of 2,2,2-trifluoro-1-phenylethanol (Table 1, entry 1).[7g] Similarly, the decomposition also existed in the case of HCOOH as a hydrogen resource (Table 1, entry 2). Differing from the above hydrogen resources, the asymmetric reaction with *i*-PrOH as a hydrogen resource had a high enantioselectivity (86% *ee*), but the yield was poor (Table 1, entry 3). To our delight, in the case of HCOONa as a hydrogen resource and water as a solvent that was inspired by the works of the Xiao and Deng groups on asymmetric transfer hydrogenation of quinolines and *N*-sulfonylimines,[9] we found that catalyst **A** could produce the desirable (*S*)-4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethyl)aniline with 86% yield and 89% *ee* (Table 1, entry 4).

On the basis of this finding, we further investigated the different η^6-arene−Ru complexes in the asymmetric transfer hydrogenation of 4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethylidene)aniline using HCOONa as a hydrogen resource and water as a solvent. As shown in entries 5−7 of Table 1, it was found that catalyst **A** afforded the desirable products slightly higher than that of catalyst **B** (Table 1, entries 4−5), and markedly better than those of catalysts **C** and **D** (Table 1, entry 4 versus entries 6−7). Therefore, (*S*,*S*)-TsPDEN/$[RuCl_2(\text{mesitylene})]_2$ (**A**) was identified as an optimal catalyst through the use of HCOONa as a hydrogen resource and water as a solvent.

Due to poor solubility of substrates, optimization of cosolvent using **A** as a catalyst was further attempted. As shown Table 2, it was found that the enantioselectivity of the asymmetric reaction with H_2O/DMF (v/v = 1:1) as a cosolvent could further enhance from 89% to 97% *ee*, where the reaction time could be decreased to 8 h because of the good-solubility of the substrate in the mixed H_2O/DMF cosolvent system (Table 2, entry 6). As compared with the other cosolvents, such an *ee* value was obviously higher than those obtained with the mixed H_2O/THF and H_2O/dioxane as cosolvents (Table 2, entry 6 versus entries 1−2), and slightly higher than those obtained with the others (Table 2, entry 6 versus entries 3−5). Therefore, the mixed H_2O/DMF (v/v = 1:1) was identified as an optimal cosolvent. As a comprehensive result, the

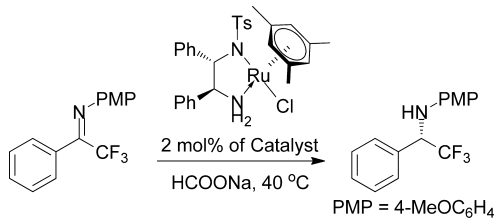
Table 1. Optimization of H Resource and Catalysts for Asymmetric Transfer Hydrogenation[a]



entry	cat.	solvent and/or H resource	time (h)	yield (%)	*ee* (%)[b]
1	**A**	HCOOH−NEt_3	24	49	78
2	**A**	HCOOH	24	43	68
3	**A**	*i*-PrOH	24	38	86
4	**A**	H_2O−HCOONa	24	86	89
5	**B**	H_2O−HCOONa	24	83	86
6	**C**	H_2O−HCOONa	24	50	70
7	**D**	H_2O−HCOONa	24	10	57

[a]Reactions were performed with 4.0 μmol of catalyst, 0.20 mmol of 4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethylidene)aniline in 2.0 mL of solvent at 40 °C. [b]Determined by HPLC.

Table 2. Optimization of Cosolvent for Asymmetric Transfer Hydrogenation[a]



entry	cat.	cosolvent	time (h)	yield (%)	*ee* (%)[b]
1	**A**	H_2O/THF (1:1)	24	70	54
2	**A**	H_2O/dioxane (1:1)	24	88	nd
3	**A**	H_2O/*i*-PrOH (1:1)	24	40	96
4	**A**	H_2O/DMA (1:1)	8	91	93
5	**A**	H_2O/DMSO (1:1)	8	92	96
6	**A**	H_2O/DMF (1:1)	8	93	97

[a]Reactions were performed with 4.0 μmol of catalyst, 0.20 mmol of 4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethylidene)aniline, 1.0 mmol of HCOONa in 2.0 mL of cosolvent at 40 °C. [b]Determined by HPLC.

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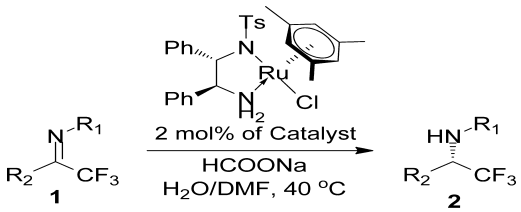
asymmetric reaction with 2.0 mmol % of **A** as a catalyst, HCOONa as a hydrogen resource, and H_2O/DMF (v/v = 1:1) as a cosolvent at 40 °C was determined as the optimal reaction condition.

Having established that catalyst **A** enabled a highly efficient asymmetric transfer hydrogenation of 4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethylidene)aniline, we further investigated its general applicability to prepare chiral aryltrifluoromethylamines with a series of aryl-substituted substrates. As shown in Table 3,

Table 3. Substrate Scope for Ru-Catalyzed Asymmetric Transfer Hydrogenation of α-Trifluoromethylimines[a]



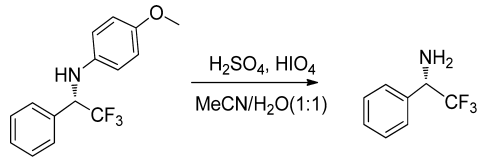
entry	R_1, R_2	2	time (h)	yield (%)	*ee* (%)[b]
1	PMP, Ph	**2a**	8	93	97
2	PMP, 4-FC_6H_4	**2b**	8	91	97
3	PMP, 4-ClC_6H_4	**2c**	8	90	99
4	PMP, 4-BrC_6H_4	**2d**	8	88	95
5	PMP, 3-BrC_6H_4	**2e**	8	94	95
6	PMP, 4-$CF_3C_6H_4$	**2f**	5	93	97
7	PMP, 4-MeC_6H_4	**2g**	17	75	96
8	PMP, 4-$MeOC_6H_4$	**2h**	9	87	98
9	PMP, 2-$MeOC_6H_4$	**2i**	8	82	93
10	PMP, 2-thienyl	**2j**	20	70	97
11	4-MeC_6H_4, Ph	**2k**	8	88	95
12	4-MeC_6H_4, 4-FC_6H_4	**2l**	8	93	94
13	4-MeC_6H_4, 4-BrC_6H_4	**2m**	8	89	95
14	Ph, Ph	**2n**	8	94	96
15	4-ClPh, Ph	**2o**	8	91	95
16	1-naphthyl, Ph	**2p**	12	89	96
17	2-naphthyl, Ph	**2q**	9	90	99

[a]Reactions were performed with 4.0 μmol of catalyst D, 0.20 mmol of α-trifluoromethylimines, 1.0 mmol of HCOONa in 2.0 mL of water/DMF (v/v = 1/1) at 40 °C. [b]Determined by HPLC.

in general, high yields, no intermediate products, and excellent enantioselectivities were obtained under the optimal reaction conditions for all tested substrates. It is noteworthy that the structures and electronic properties of substituents in the aromatic ring at the R_2 group did not affect significantly their enantioselectivities; that is, various electron-withdrawing and electron-donating substituents in the Ar moiety at the R_2 group were equally efficient (entries 2−9). However, the slight effects on yields could be observed, in which electron-withdrawing substituents in the Ar moiety at the R_2 group had slightly higher yields than those of electron-donating substituents (entries 2−6 versus entries 7−9). In addition, the thienyl-substituted substrate could be also converted to the corresponding chiral products with excellent enantioselectivity (Table 2, entry 10). Moreover, besides the general *p*-methoxyphenyl (PMP) protection group, other protection groups, such as *p*-tolyl, Ph, and naphthyl, could also be expanded to the asymmetric transfer hydrogenation, providing the desirable chiral aryltrifluoromethylamines with high enantioselectivities (entries 11−17).

As mentioned in the part of the Introduction, chiral 2,2,2-trifluoro-1-phenylethanamine as an important synthetic motif could be converted to various optically pure biologically active molecules in medical and fluorine chemistry.[5] In this case, in order to obtain optically pure 2,2,2-trifluoro-1-phenylethanamine, we attempted to remove the PMP protection group of the hydrogenated product (*S*)-4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethyl)aniline. Among those reported methods,[6c,7d,g,10] it was found that the use of an equivalent of HIO_4 and H_2SO_4 in the cosolvent of MeCN/H_2O (v:v = 1:1) as a reaction condition could afford the best result,[7g] where the PMP protection group of (*S*)-4-methoxy-*N*-(2,2,2-trifluoro-1-phenylethyl)aniline could be removed readily to give (*S*)-2,2,2-trifluoro-1-phenylethanamine with the slightly decreased enantioselectivity in 72% isolated yield, as shown in Scheme 2.

Scheme 2. Removal of the PMP Protection Group



In conclusion, by the further investigation of Noyori's catalysts, we find that RuCl[(*S*,*S*)-TsDPEN)](mesitylene) is an efficient catalyst in the asymmetric transfer hydrogenation of acyclic α-trifluoromethylimines with sodium formate as a hydrogen resource and water−dimethylformamide as a cosolvent, which produces various chiral aryl-substituted α-trifluoromethylamines in high yields and enantioselectivities (93−99% *ee*). Furthermore, the mild reaction conditions make this asymmetric reaction an attractive character for the construction of valuable α-trifluoromethylamines through the transformations of strong electron-withdrawing α-trifluoromethylimines.

EXPERIMENTAL SECTION

General Methods. All manipulations were carried out under an inert atmosphere using a nitrogen-filled glovebox or Schlenk techniques. Deuterated solvents were purchased commercially and were degassed and stored over activated 4 Å molecular sieves. The α-trifluoromethylimines and (*S*)-2,2,2-trifluoro-1-phenylethanamine were prepared according to the published procedures.[7d−g,11] All other reagents were obtained from commercial sources and used without further purification. The ^1H, ^{19}F, and $^{13}C\{1H\}$NMR spectra were recorded at 400, 376, and 101 MHz, respectively. ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the outside standard and low field is positive. Mass spectrometry was performed on a GC/MS spectrometer with the electron impact (EI) ionization technique. HRMS data were recorded on a GC-TOF instrument using the EI technique. The enantiomeric excesses (*ee*) were determined by an HPLC analysis with a UV−vis detector using a Daicel OD-H or OB-H or AD-H Chiralcel column (Φ 0.46 × 25 cm).

Typical Procedure for Asymmetric Transfer Hydrogenation of α-Trifluoromethylimines. The catalyst (2.49 mg, 4.0 μmol, 2.0 mol %), α-trifluoromethylimines (0.20 mmol), HCOONa (68.0 mg, 1.0 mmol, 5.0 equiv) and 2.0 mL of H_2O/DMF (v/v = 1/1) were added sequentially to a 5.0 mL round−bottom flask. The mixture was then stirred at 40 °C for 5−12 h. During this period, the reaction was monitored constantly by TLC. After completion of the reaction, the aqueous solution was extracted with ethyl ether (3 × 3.0 mL). The combined ethyl ether extracts were washed with $NaHCO_3$ and brine, and then dehydrated with Na_2SO_4. After evaporation of ethyl ether,

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the residue was purified by silica gel flash column chromatography to afford the desired product. The yields were determined by ^{1}H NMR, and the *ee* values were determined by a HPLC analysis using a UV−vis detector and a Daicel chiralcel column (Φ 0.46 × 25 cm).[7d−g,10]

2a:.[7d,e] 52.266 mg, 0.186 mmol, 93% yield, 97% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.47 (m, 2H), 7.44−7.39 (m, 3H), 6.79−6.75 (m, 2H), 6.66−6.62 (m, 2H), 4.87−4.81(m, 1H), 3.74 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.7, 139.9, 134.7, 129.4, 129.2, 128.3, 125.6 (q, J_{C-F} = 280 Hz), 118.3, 116.1, 115.2, 60.7 (q, J_{C-F} = 30 Hz), 55.8; GC/MS (*m*/*z*): 281; HPLC (OD-H, elute: Hexanes/*i*-PrOH = 95/5, detector: 254 nm, flow rate: 0.5 mL/min, 25 °C), t_1 = 16.5 min (major), t_2 = 18.9 min.

2b:[7f] 54.418 mg, 0.182 mmol, 91% yield, 97% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47−7.43 (m, 2H), 7.12−7.07 (m, 2H), 6.77−6.74 (m, 2H), 6.60−6.59 (m, 2H), 4.85−4.79(m, 1H), 4.07 (s, 1H), 3.74 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.6, 162.1, 153.7, 139.5, 130.3, 130.0, 130.0, 125.3 (q, J_{C-F} = 279 Hz), 116.0, 115.1, 61.3 (q, J_{C-F} = 29 Hz), 55.8; GC/MS (*m*/*z*): 299; HPLC (OD-H, elute: Hexanes/*i*-PrOH = 95/5, detector: 254 nm, flow rate: 0.5 mL/min, 25 °C), t_1 = 21.94 min (major), t_2 = 26.1 min.

2c:.[7e,g] 56.700 mg, 0.180 mmol, 90% yield, 99% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.33 (m, 4H), 6.75−6.71 (m, 2H), 6.58−6.54 (m, 2H), 4.76−4.86 (m, 1H), 4.09 (s, 1H), 3.72 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.7, 139.3, 135.3, 133.0, 129.6, 129.4, 125.1 (q, J_{C-F} = 280 Hz), 116.1, 115.1, 61.3 (q, J_{C-F} = 29 Hz), 55.9. GC/MS (*m*/*z*): 315; HPLC (AD-H, elute: Hexanes/*i*-PrOH = 90/10, detector: 254 nm, flow rate: 0.8 mL/min, 25 °C), t_1 = 12.0 min (major), t_2 = 14.9 min.

2d:.[7e,g] 63.184 mg, 0.176 mmol, 88% yield, 95% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 8.8 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 6.78−6.73 (m, 2H), 6.01−6.56 (m, 2 H), 4.82−4.77 (m, 1H), 3.73 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.7, 139.3, 133.5, 132.3, 129.9, 125.0 (q, J_{C-F} = 281 Hz), 123.5, 116.0, 115.1, 61.5 (q, J_{C-F} = 30 Hz), 55.9; GC/MS (*m*/*z*): 359; HPLC (OD-H, elute: Hexanes/*i*-PrOH = 95/5, detector: 254 nm, flow rate: 0.5 mL/min, 25 °C), t_1 = 23.4 min (major), t_2 = 30.2 min.

2e: 67.492 mg, 0.188 mmol, 94% yield, 95% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (s, 1H), 7.55−7.53 (m, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.31−7.27 (m, 1H), 6.80−6.76 (m, 2H), 6.63−6.59 (m, 2H), 4.85−4.79 (m 1H), 3.75 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.8, 139.3, 136.9, 132.6, 131.3, 130.7, 126.9, 125.1 (q, J_{C-F} = 281 Hz), 123.5, 116.0, 115.2, 61.5 (q, J_{C-F} = 30 Hz), 55.9; ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.80 (d, *J* = 7.5 Hz); GC/MS (*m*/*z*): 359; HR-MS (ESI) $[M + H]^+$ (*m*/*z*): calcd for $C_{15}H_{13}BrF_3NO$, 360.0205, found 360.0196. HPLC (OD-H, elute: Hexanes/*i*-PrOH = 95/5, detector: 254 nm, flow rate: 0.5 mL/min, 25 °C), t_1 = 24.5 min (major), t_2 = 29.9 min.

2f:.[7d,e,g] 64.914 mg, 0.186 mmol, 93% yield, 97% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 6.77−6.75 (m, 2H), 6.58 (d, *J* = 8.4 Hz, 2H), 4.94−4.88 (m, 1H), 3.74 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.9, 139.3, 138.6, 131.7, 131.5, 128.7, 126.1, 125.0 (q, J_{C-F} = 280 Hz), 116.1, 115.2, 61.6 (q, J_{C-F} = 30 Hz), 55.8; GC/MS (*m*/*z*): 349; HPLC (OB-H, elute: Hexanes/*i*-PrOH = 90/10, detector: 254 nm, flow rate: 0.5 mL/min, 25 °C), t_1 = 26.7 min, t_2 = 33.3 min (major).

2g:.[7d,e] 44.250 mg, 0.150 mmol, 75% yield, 93% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.66−6.63 (m, 3H), 6.54−6.50 (m, 2H), 4.72−7.66 (m, 1H), 3.62 (s, 3H), 3.39 (s, 1H), 2.26 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.5, 139.8, 139.2, 131.5, 129.8, 128.0, 125.4 (q, J_{C-F} = 280 Hz), 116.0, 115.1, 61.7 (q, J_{C-F} = 29 Hz), 55.9, 21.4; GC/MS (*m*/*z*): 295; HPLC (AD-H, elute: Hexanes/*i*-PrOH = 90/10, detector: 254 nm, flow rate: 0.8 mL/min, 25 °C), t_1 = 10.1 min (major), t_2 = 14.2 min.

2h:.[7d,e] 54.114 mg, 0.174 mmol, 87% yield, 98% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.4 Hz, 2H), 6.96−6.93 (m, 2H), 6.78−6.75 (m, 2H), 6.65−6.62 (m, 2H), 4.82−4.77 (m, 1H), 4.01 (bar, 1H), 3.83 (s, 3H), 3.74 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 160.3, 153.5, 139.9, 129.3, 126.5, 125.5 (q, J_{C-F} = 280 Hz), 116.0, 115.1, 114.5, 61.4 (q, J_{C-F} = 30 Hz), 55.9, 55.5; GC/MS (*m*/*z*): 311; HPLC (AD-H, elute: Hexanes/*i*-PrOH = 90/10, detector: 254 nm, flow rate: 0.8 mL/min, 25 °C), t_1 = 15.4 min (major), t_2 = 22.8 min.

2i: 51.004 mg, 0.164 mmol, 82% yield, 93% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 1H), 7.33−7.29 (m, 1H), 6.98−6.92 (m, 2H), 6.76−6.71 (m, 2H), 6.64−6.60 (m, 2H), 5.45−5.39 (m, 1H), 4.23 (bar, 1H), 3.88 (s, 3H), 3.70 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 158.0, 153.5, 134.0, 130.4, 128.4, 126.0 (q, J_{C-F} = 281 Hz), 123.1, 121.3, 116.0, 115.8, 115.2, 111.5, 56.0, 55.8, 55.0(q, J_{C-F} = 30 Hz); GC/MS (*m*/*z*): 311; ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.74 (d, *J* = 7.4 Hz); HR-MS (ESI) $[M + H]^+$ (*m*/*z*): calcd for $C_{16}H_{16}F_3NO_2$, 312.1206, found 312.1209. HPLC (AD-H, elute: Hexanes/*i*-PrOH = 90/10, detector: 254 nm, flow rate: 0.8 mL/min, 25 °C), t_1 = 5.6 min (major), t_2 = 11.2 min.

2j:[7e] 40.180 mg, 0.140 mmol, 70% yield, 97% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (dd, *J* = 1.2 Hz, 1.2 Hz, 2H), 7.19 (d, *J* = 3.2 Hz, 2H), 7.05 (dd, *J* = 3.6, 3.6 Hz, 1H), 6.83−6.79 (m, 1H), 6.72−6.68 (m, 1H), 5.16−5.11 (m, 1H), 3.94 (bar, 1H), 3.76 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 154.0, 139.5, 137.6, 127.5, 127.3, 126.5, 125.0 (q, J_{C-F} = 280 Hz), 116.4, 115.2, 58.3 (q, J_{C-F} = 29 Hz), 55.8; GC/MS (*m*/*z*): 287; HPLC (AD-H, elute: Hexanes/*i*-PrOH = 97/3, detector: 254 nm, flow rate: 1.0 mL/min, 25 °C), t_1 = 12.0 min (major), t_2 = 14.6 min.

2k:[7d] 46.640 mg, 0.176 mmol, 88% yield, 95% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 6.0 Hz, 2H), 7.44−7.38 (m, 3H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.58 (d, *J* = 8.4 Hz, 2H), 4.93−4.86 (m, 1H), 4.23 (d, J = 7.2 Hz, 1H), 2.24 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 143.5, 134.6, 130.1, 129.3, 129.2, 128.9, 128.2, 125.5(q, J_{C-F} = 280 Hz), 114.5, 61.2 (q, J_{C-F} = 30 Hz), 20.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.90 (d, *J* = 7.0 Hz); GC/MS (*m*/*z*): 265; HPLC (OD-H, elute: Hexanes/*i*-PrOH = 97/3, detector: 254 nm, flow rate: 1.0 mL/min, 25 °C), t_1 = 8.5 min (major), t_2 = 9.5 min.

2l: 52.638 mg, 0.186 mmol, 93% yield, 94% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (dd, *J* = 6.4, 5.2 Hz, 2H), 7.13−7.07 (m, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.56 (d, *J* = 8.4 Hz, 2H), 4.93−4.86 (m, 1H), 4.22 (d, *J* = 6.8 Hz, 1H), 2.25 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.3, 162.06, 143.15, 130.1, 130.0, 129.0, 125.2(q, J_{C-F} = 280 Hz), 116.2, 116.0, 114.4, 60.5 (q, J_{C-F} = 29 Hz), 20.6; GC/MS (*m*/*z*): 283; HR-MS (ESI) $[M + H]^+$ (*m*/*z*): calcd for $C_{15}H_{13}F_4N$, 284.1057, found 284.1055. HPLC (OD-H, elute: Hexanes/*i*-PrOH = 97/3, detector: 254 nm, flow rate: 1.0 mL/min, 25 °C, t_1 = 12.9 min (major), t_2 = 17.6 min.

2m: 61.232 mg, 0.178 mmol, 89% yield, 95% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56−7.53 (m, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.54 (d, *J* = 7.6 Hz, 2H), 4.90−4.83 (m, 1H), 4.22 (d, *J* = 6.0 Hz, 1H), 2.24 (s, 3H).; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 143.0, 133.5, 132.3, 130.1, 129.8, 129.1, 128.2, 125.0(q, J_{C-F} = 280 Hz), 114.4, 60.8 (q, J_{C-F} = 30 Hz), 20.6; GC/MS (*m*/*z*): 343; HR-MS (ESI) $[M + H]^+$ (*m*/*z*): calcd for $C_{15}H_{13}BrF_3N$, 344.0256, found 344.0254. HPLC (OD-H, elute: Hexanes/*i*-PrOH = 95/5, detector: 254 nm, flow rate: 1.0 mL/min, 25 °C), t_1 = 14.0 min (major), t_2 = 19.8 min.

2n:[7d] 47.188 mg, 0.188 mmol, 94% yield, 96% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.38 (m, 2H), 7.18 (t, *J* = 7.6 Hz, 2H), 6.80 (t, *J* = 7.6 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 2H), 4.97−4.91 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ145.7, 134.3, 128.1, 129.6, 129.4, 129.1, 128.1, 125.3 (q, J_{C-F} = 280 Hz), 119.5, 114.2, 60.8 (q, J_{C-F} = 30 Hz); GC/MS (*m*/*z*): 251; HPLC (AD-H, elute: Hexanes/*i*-PrOH = 95/5, detector: 254 nm, flow rate: 1.0 mL/min, 25 °C), t_1 = 7.7 min (major), t_2 = 10.0 min.

2o:[10] 51.870 mg, 0.182 mmol, 91% yield, 95% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54−7.47 (m, 5H), 7.22−7.18 (m, 2H), 6.67−6.63 (m, 2H), 5.00−4.93 (m, 1H), 4.47 (d, *J* = 5.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 144.4, 133.9, 129.6, 129.5, 129.3, 128.1, 125.3(q, J_{C-F} = 280 Hz), 124.3, 116.2, 116.0, 114.4, 61.0 (q, J_{C-F} = 30 Hz), 20.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.76 (d, *J* = 7.1 Hz); GC/MS (*m*/*z*): 285; HPLC (OD-H, elute: Hexanes/*i*-PrOH = 95/5, detector: 254 nm, flow rate: 0.5 mL/min, 25 °C), t_1 = 14.8 min (major), t_2 = 18.3 min.

2p:[7g] 53.578 mg, 0.178 mmol, 89% yield, 96% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H),

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7.59−7.52 (m, 4H), 7.47−7.43 (m, 3H), 7.36 (d, J = 8.4 Hz, 1H), 7.29−7.25 (m, 1H), 6.56 (d, J = 7.2 Hz, 1H), 5.20−5.07 (m, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 140.7, 134.6, 134.0, 129.5, 129.2, 129.1, 128.2, 126.3, 125.7, 124.3, 125.4 (q, J_{C-F} = 281 Hz), 120.0, 119.9, 107.4, 60.8 (q, J_{C-F} = 29 Hz); GC/MS (m/z): 301; HPLC (OD-H, elute: Hexanes/*i*-PrOH = 95/5, detector: 254 nm, flow rate: 0.5 mL/min, 25 °C), t_1 = 21.3 min, t_2 = 30.6 min(major).

2q:[7g] 54.180 mg, 0.180 mmol, 90% yield, 99% *ee*; ^1H NMR (400 MHz, $CDCl_3$): δ 7.71−7.68(m, 2H), 7.59−7.53(m, 3H), 7.43−7.36 (m, 4H), 7.28−7.24 (m, 1H), 6.99 (dd, J = 2.4, 2.4 Hz, 1H), 6.84 (d, J = 1.2 Hz, 1H), 5.12−5.07 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 143.3, 134.9, 134.1, 129.5, 129.4, 129.2, 128.5, 128.1, 127.8, 126.7, 126.5, 125.3 (q, J_{C-F} = 281 Hz), 123.2, 118.0, 107.1, 60.6 (q, J_{C-F} = 29 Hz); GC/MS (m/z): 301; HPLC (AD-H, elute: Hexanes/*i*-PrOH = 95/5, detector: 254 nm, flow rate: 0.5 mL/min, 25 °C), t_1 = 19.0 min (major), t_2 = 31.2 min.

(S)-2,2,2-Trifluoro-1-phenylethanamine:[7g] 25.20 mg, 0.144 mmol, 72% yield, 96% *ee*; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.33 (m, 5H), 4.31 (q, J = 7.6 Hz, 1H), 1.84 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 135.6, 131.4, 129.1, 128.8, 125.8 (q, J_{C-F} = 280 Hz), 58.1 (q, J_{C-F} = 30 Hz); HPLC (OD-H, elute: Hexanes/*i*-PrOH = 95/5, detector: 254 nm, flow rate: 0.5 mL/min, 25 °C), t_1 = 20.5 min (major), t_2 = 26.21 min.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Characterizations and chiral HPLC analysis of the catalytic enantioselective reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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