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Design of Chiral Phase Transfer Catalyst with Conformationally Fixed Biphenyl Core: Application to Asymmetric Alkylation of Glycine Derivatives

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Abstract:

Chiral phase transfer catalysts (*S*)-1a and (*S*)-1b with a conformationally fixed biphenyl core were conveniently prepared from the known (*S*)-6,6′-dimethylbiphenyl-2,2′-diol 2 in five steps. These catalysts, (*S*)-1a and (*S*)-1b, are readily applicable to asymmetric alkylation of glycine derivatives with excellent enantioselectivity. In particular, catalyst (*S*)-1b was found to exhibit a unique temperature effect on the enantioselectivity, and asymmetric alkylation of glycine derivatives at room temperature gave a higher ee than that at 0 °C.

Phase transfer catalysis (PTC) has been recognized as a convenient and highly useful synthetic tool in both academia and industry because of several advantages of PTC (operational simplicity, mild reaction conditions with aqueous media and environmental consciousness, suitability for large-scale reactions, etc.), which meet the current requirement for practical organic synthesis.[1,2] Accordingly, various types of chiral phase transfer catalysts have been developed in recent years, and the chiral efficiency of such phase transfer catalysts was examined by the application to the development of new methodologies for the asymmetric synthesis of both natural and unnatural α-alkyl- and α,α-dialkyl-α-amino acids, especially in enantiomerically pure form.[3,4] However, despite numerous studies on asymmetric amino acid syntheses, practical catalytic systems using the easily available catalysts with high enantioselection at low catalyst loading (e.g., <1 mol %) are still rare in asymmetric carbon−carbon bond formation. Major progress in terms of catalyst loading as well as the easy availability of catalysts is still most desirable for practical asymmetric synthesis.[5] Herein we wish to report the synthesis of new phase transfer catalysts with a chiral biphenyl backbone and their application to asymmetric alkylation of glycine derivatives with excellent enantioselectivity.

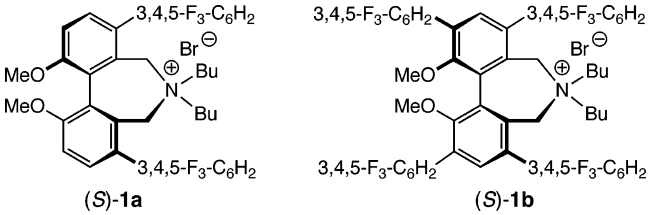

Figure 1.

The requisite catalysts (*S*)-**1a** and (*S*)-**1b** (Figure 1) can be easily prepared from the known (*S*)-6,6′-dimethylbiphenyl-2,2′-diol (*S*)-**2** (>99% ee), which is conveniently derived from commercially available 4,6-di-*tert*-butyl-*m*-cresol according to the reported procedure.[6] Methylation of (*S*)-**2** and

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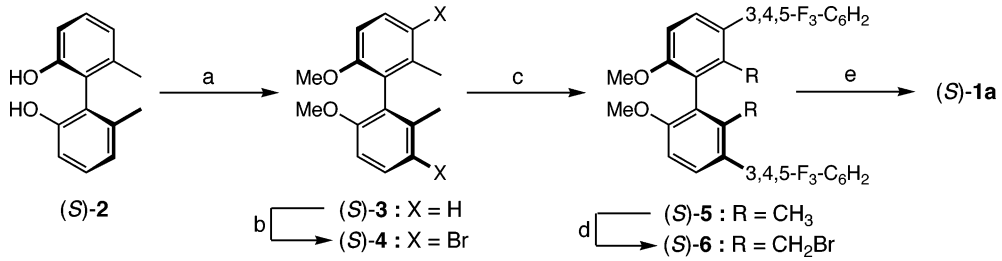
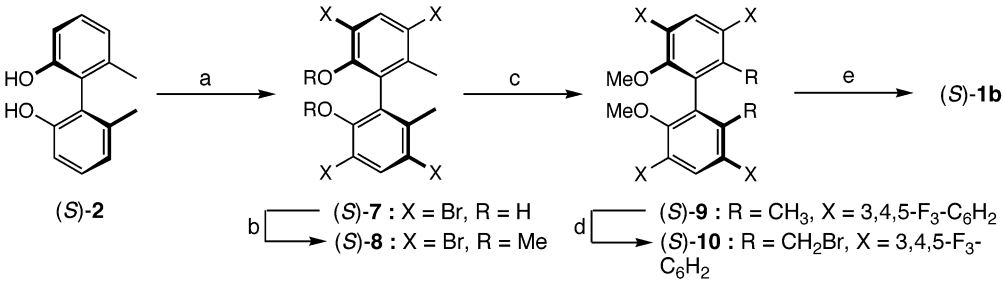
Scheme 1[a]



[a] Reagents and conditions: (a) MeI (20 equiv), K_2CO_3(10 equiv), acetone, quant; (b) Br_2 (2.1 equiv), AcOH (0.2 equiv), CH_2Cl_2, 97%; (c) (3,4,5-F_3−C_6H_2)$B(OH)_2$ (4 equiv), $Pd(OAc)_2$ (0.2 equiv), P(*o*-Tol)$_3$ (0.8 equiv), K_3PO_4•*n*H_2O (10 equiv), DMF, reflux, quant; (d) AIBN (0.1 equiv), NBS (2.1 equiv), benzene, 91%; (e) Bu_2NH (0.9 equiv), K_2CO_3 (10 equiv), MeCN, reflux, 94%.

Scheme 2[a]



[a] Reagents and conditions: (a) Br_2 (4.1 equiv), AcOH (0.2 equiv), CH_2Cl_2, 87%; (b) MeI (20 equiv), K_2CO_3(10 equiv), acetone, 98%; (c) (3,4,5-F_3−C_6H_2)$B(OH)_2$ (8 equiv), $Pd(OAc)_2$ (0.2 equiv), P(*o*-Tol)$_3$ (0.8 equiv), K_3PO_4•*n*H_2O (10 equiv), DMF, reflux, 65%; (d) AIBN (0.1 equiv), NBS (2.1 equiv), benzene; (e) Bu_2NH (0.9 equiv), K_2CO_3 (10 equiv), MeCN, reflux, 53% for two steps.

Table 1. **Catalytic enantioselective phase transfer alkylation of glycine derivative 11**

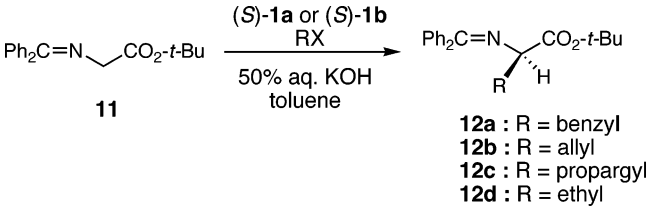
entry	PTC (mol %)	RX (equiv)	conditions	yield[a] (%)	ee[b] (%) (config)
1	**(*S*)-1a** (1)	BnBr (3)	0 °C, 5 h	97	96 (*R*)
2	**(*S*)-1a** (1)	BnBr (3)	rt, 3 h	quant.	91 (*R*)
3	**(*S*)-1a** (1)	EtI (8)	0 °C, 8 h	92	81 (*R*)
4	**(*S*)-1a** (1)	CH_2═$CHCH_2Br$ (3)	0 °C, 2.5 h	90	93 (*R*)
5	**(*S*)-1a** (1)	HC≡CCH_2Br (3)	0 °C, 4 h	95	86 (*R*)
6	**(*S*)-1b** (1)	BnBr (1.5)	0 °C, 4 h	94	86 (*R*)
7	**(*S*)-1b** (1)	BnBr (1.5)	rt, 2.5 h	96	98 (*R*)
8	**(*S*)-1b** (1)	HC≡CCH_2Br (1.5)	0 °C, 3 h	94	87 (*R*)
9	**(*S*)-1b** (1)	CH_2═$CHCH_2Br$ (1.5)	0 °C, 3.5 h	92	88 (*R*)
10	**(*S*)-1b** (1)	EtI (8)	0 °C, 10 h	86	90 (*R*)
11	**(*S*)-1b** (0.5)	HC≡CCH_2Br (2)	20 °C, 6 h	92	91 (*R*)
12	**(*S*)-1b** (0.5)	CH_2═$CHCH_2Br$ (1.5)	20 °C, 5 h	95	93 (*R*)
13	**(*S*)-1b** (1)	EtI (8)	20 °C, 10 h	81	90 (*R*)
14	**(*S*)-1b** (0.5)	BnBr (1.2)	20 °C, 5 h	93	95 (*R*)
15[c]	**(*S*)-1b** (0.1)	BnBr (1.5)	20 °C, 12 h	94	95 (*R*)

[a] Isolated yield. [b] Enantiopurity of **12** was determined by HPLC analysis using a chiral column (DAICEL Chiralcel OD) with hexane/2-propanol as solvent. [c] A 5-g scale of **11** was used.

subsequent selective *para*-bromination of the resulting (*S*)-**3** afforded (*S*)-5,5′-dibromo-2,2′-dimethoxy-6,6′-dimethylbiphenyl (*S*)-**4** in 97% combined yield. Suzuki−Miyaura coupling of dibromide (*S*)-**4** and radical bromination of the resulting coupling product (*S*)-**5** gave dibromide (*S*)-**6** in 91% combined yield. Treatment of (*S*)-**6** with Bu_2NH furnished chiral quaternary ammonium salt (*S*)-**1a** in 83% overall yield from the known (*S*)-**2** (Scheme 1). In a similar manner, chiral quaternary ammonium salt (*S*)-**1b** was prepared from the known (*S*)-**2** in moderate overall yield except the use of the initial bromination and subsequent methylation as shown in Scheme 2.

The chiral efficiency of these chiral phase-transfer catalysts (*S*)-**1a** and (*S*)-**1b** was examined by carrying out asymmetric alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **11**, and the selected data are listed in Table 1. Thus, reaction of **11** with benzyl bromide (3 equiv) and 50% aqueous KOH in toluene was effected in the presence of 1 mol % of catalyst (*S*)-**1** under argon atmosphere at 0 °C for 5 h to furnish benzylation product **12a** (R = CH_2Ph, Scheme 3) in 97% yield with excellent enantioselectivity (96% ee) (Table 1, entry 1). As expected, the enantioselectivity is decreased upon warming to room temperature (entry 2). Asymmetric ethylation, allylation, and propargylation also proceeded smoothly at 0 °C with high enantioselectivity (entries 3, 4, and 5). Based on these results, asymmetric benzylation of **11** with catalyst (*S*)-**1b** was carried out at both 0 °C and room temperature (entries 6 and 7). Surprisingly, the room temperature reaction was found to exhibit higher enantioselectivity. This unique temperature effect on the

Scheme 3



enantioselectivity was also observed in asymmetric propargylation and allylation reactions (entries 8 and 9 vs 11 and 12). The catalytic amount of (*S*)-**1b** can be reduced to 0.5 mol % (entries 11, 12, and 14). In particular, in a 5-g scale reaction, the catalyst loading can be further reduced to 0.1 mol % without decreasing the enantioselectivity (entry 15).

In conclusion, new, efficient phase transfer catalysts of type **1** can be readily prepared in a five-step sequence from the known (*S*)-6,6′-dimethylbiphenyl-2,2′-diol and are successfully applied to a scalable asymmetric alkylation of glycine derivatives, implying the practicality of the catalyst **1** in asymmetric synthesis. The unique chemical behavior of catalyst (*S*)-**1b**, giving higher enantioselectivity at higher temperature, will be further studied in our laboratory.

Experimental Section

(*S*)-2,2′-Dimethoxy-6,6′-dimethylbiphenyl (*S*)-3: To a solution of (*S*)-2,2′-dihydroxy-6,6′-dimethylbiphenyl (*S*)-**2** (89 mg, 0.42 mmol) in acetone (5.0 mL) at room temperature were added MeI (0.52 mL, 8.3 mmol) and K_2CO_3 (0.57 g, 4.2 mmol). After being stirred at room temperature for 5 h, the resulting mixture was filtered through a pad of Celite with EtOAc. The filtrate was concentrated to yield a residue, which was purified by column chromatography on silica gel (hexane/EtOAc) to furnish (*S*)-2,2′-dimethoxy-6,6′-dimethylbiphenyl (*S*)-**3** (105 mg, quantitative): $[\alpha]^{32}_D$ −38° (*c* 0.60, $CHCl_3$); ^{1}H NMR δ 7.21 (t, J = 8 Hz, 2 H), 6.89 (d, J = 8 Hz, 2 H), 6.79 (d, J = 8 Hz, 2 H), 3.65 (s, 6 H), 1.93 (s, 6 H); ^{13}C NMR δ 156.9, 138.1, 127.8, 126.1, 122.1, 108.2, 55.6, 19.5; IR (neat) 2941, 1579, 1466, 1252, 1080, 777, 743 cm^{-1}; HRMS (ESI) Calcd for $C_{16}H_{19}O_2$: 243.1380 ([M + H]$^+$), Found: 243.1383 ([M + H]$^+$).

(*S*)-5,5′-Dibromo-2,2′-dimethoxy-6,6′-dimethylbiphenyl (*S*)-4: To a solution of (*S*)-2,2′-dimethoxy-6,6′-dimethylbiphenyl (*S*)-**3** (105 mg, 0.42 mmol) in CH_2Cl_2 (4.0 mL) at room temperature were added AcOH (0.005 mL, 0.083 mmol) and Br_2 (0.45 mL, 0.87 mmol) successively. The resulting solution was stirred at room temperature for 1 h and poured into an ice-cold saturated $NaHCO_3$. The organic phase was separated, and the aqueous phase was extracted with EtOAc twice. The combined extracts were dried over Na_2SO_4 and concentrated to provide a residual oil, which was purified by column chromatography on silica gel (hexane/EtOAc) to afford (*S*)-5,5′-dibromo-2,2′-dimethoxy-6,6′-dimethylbiphenyl (*S*)-**4** (161 mg, 97%): $[\alpha]^{32}_D$ −36° (*c* 0.68, $CHCl_3$); ^{1}H NMR δ 7.49 (d, J = 9 Hz, 2 H), 6.68 (d, J = 8 Hz, 2 H), 3.63 (s, 6 H), 1.99 (s, 6 H); ^{13}C NMR δ 156.0, 137.3, 131.9, 127.6, 116.3, 109.9, 55.8, 20.0; IR (neat) 2934, 2359, 1566, 146, 1429, 1281, 1254, 1080, 1230,799 cm^{-1}; HRMS (ESI) Calcd for $C_{16}H_{16}Br_2O_2$: 397.9512 ([M]$^+$), Found: 397.9500 ([M]$^+$).

(*S*)-2,2′-Dimethoxy-6,6′-dimethyl-5,5′-bis(3,4,5-trifluorophenyl)biphenyl (*S*)-5: To a solution of (*S*)-5,5′-dibromo-2,2′-dimethoxy-6,6′-dimethylbiphenyl (*S*)-**4** (550 mg, 1.37 mmol) in dry DMF (15 mL) at room temperarure were added 3,4,5-trifluorophenylboronic acid (868 mg, 5.50 mmol), $Pd(OAc)_2$ (62 mg, 0.28 mmol), P(*o*-tol)$_3$ (335 mg, 1.10 mmol), and $K_3PO_4 \cdot nH_2O$ (3.93 g, 13.8 mmol) sequentially. After being refluxed under argon atmosphere overnight, the resulting mixture was filtered through a pad of Celite with Et_2O. The filtrate was poured into a mixture of H_2O and Et_2O with vigorous stirring. The organic phase was separated, and the aqueous phase was extracted with Et_2O twice. The combined extracts were dried over Na_2SO_4 and concentrated to furnish a residue, which was purified by column chromatography on silica gel (hexane/EtOAc) to afford (*S*)-2,2′-dimethoxy-6,6′-dimethyl-5,5′-bis(3,4,5-trifluorophenyl)biphenyl (*S*)-**5** in quantitative yield: $[\alpha]^{32}_D$ −8° (*c* 0.43, $CHCl_3$); ^{1}H NMR δ 7.18 (d, J = 8 Hz, 2 H), 6.97 (t, J = 8 Hz, 4 H), 6.90 (d, J = 8 Hz, 2 H), 3.76 (s, 6 H), 1.86 (s, 6 H); ^{13}C NMR δ 156.7, 150.7 (ddd, J_{C-F} = 250, 10, 4 Hz), 138.6 (dt, J_{C-F} = 251, 5 Hz), 138.2−138.5 (m), 135.2, 132.2, 129.6, 126.9, 113.82, 113.76, 113.67, 113.6, 108.4, 55.7, 17.4; IR (neat) 2940, 1614, 1516, 1477, 1261, 1244, 1084, 1042, 806, 754 cm^{-1}; HRMS (ESI) Calcd for $C_{28}H_{20}F_6O_2$: 502.1362 ([M]$^+$), Found: 502.1381([M]$^+$).

(*S*)-6,6′-Bis(bromomethyl)-2,2′-dimethoxy-5,5′-bis(3,4,5-trifluorophenyl)biphenyl (*S*)-6: To a solution of (*S*)-2,2′-dimethoxy-6,6′-dimethyl-5,5′-bis(3,4,5-trifluorophenyl)biphenyl (*S*)-**5** (690 mg, 1.37 mmol) in benzene (10 mL) at room temperature were added *N*-bromosuccinimide (611 mg, 3.43 mmol) and AIBN (23 mg, 0.14 mmol) successively. After being refluxed for 1.5 h, the mixture was cooled to room temperature and filtered through a pad of Celite with Et_2O. The filtrate was concentrated to afford a residue, which was purified by column chromatography on silica gel (hexane/Et_2O) to provide (*S*)-6,6′-bis(bromomethyl)-2,2′-dimethoxy-5,5′-bis(3,4,5-trifluorophenyl)biphenyl (*S*)-**6** (820 mg, 91%): $[\alpha]^{33}_D$ +51° (*c* 0.40, $CHCl_3$); ^{1}H NMR δ 7.26 (d, J = 9 Hz, 2 H), 7.16 (d, J = 8 Hz, 4 H), 7.04 (d, J = 8 Hz, 2 H), 4.08 (s, 4 H), 3.77 (s, 6 H); ^{13}C NMR δ 157.0, 150.7 (ddd, J_{C-F} = 251, 10, 5 Hz), 139.1 (dt, J_{C-F} = 253, 15 Hz), 136.2−136.5 (m), 132.8, 131.3, 125.5, 113.9, 113.8, 113.74, 113.69, 111.2, 55.7, 30.1; IR (neat) 2940, 1614, 1526, 1477, 1435, 1271, 1043, 816, 758 cm^{-1}; HRMS (ESI) Calcd for $C_{28}H_{18}Br_2F_6O_2$: 657.9572 ([M]$^+$), Found: 657.9571 ([M]$^+$).

Chiral Ammonium Salt (*S*)-1a: To a solution of dibromide (*S*)-**6** (316 mg, 0.48 mmol) in CH_3CN (5 mL) at room temperature were added Bu_2NH (0.74 mL, 0.43mmol) and K_2CO_3 (0.60 mg, 4.4 mmol). After being stirred at 85 °C overnight, the resulting mixture was cooled to room temperature and filtered through a pad of Celite with CH_2Cl_2. The filtrate was concentrated to leave a residue which was purified by column chromatography on silica gel (CH_2Cl_2/MeOH) to furnish chiral ammonium salt (*S*)-**1a** (290 mg, 94%) as a white solid: $[\alpha]^{32}_D$ −63° (*c* 0.37, $CHCl_3$); ^{1}H

NMR δ 7.41 (d, J = 9 Hz, 2 H), 7.23 (d, J = 9 Hz, 2 H), 7.14 (br s, 4 H), 4.74 (d, J = 14 Hz, 2 H), 3.90 (s, 6 H), 3.66 (d, J = 14 Hz, 2 H), 3.18 (t, J = 13 Hz, 2 H), 2.65−2.80 (m, 2 H), 0.90−1.18 (m, 6 H), 0.73 (t, J = 7 Hz, 6 H), 0.20−0.38 (m, 2 H); ^{13}C NMR δ 156.9, 151.6−152.4 (m), 149.2−149.8(m), 139.3 (dt, J_{C-F} = 255, 16 Hz), 134.7−135.0 (dt, J_{C-F} = 16, 4 Hz), 132.5, 131.9, 126.3, 125.0, 113.5−115.5 (m), 113.3, 57.1, 56.9, 55.8, 24.2, 19.0, 12.9; IR (neat) 3400, 2965, 1614, 1528, 1489, 1287, 1045, 733 cm^{-1}; HRMS (ESI) Calcd for $C_{36}H_{36}F_6NO_2$: 628.2645 ([M]$^+$), Found: 628.2642 ([M]$^+$).

(*S*)-3,3′,5,5′-Tetrabromo-2,2′-dihydroxy-6,6′-dimethylbiphenyl (*S*)-7: To a solution of (*S*)-2,2′-dihydroxy-6,6′-dimethylbiphenyl (*S*)-**2** (110 mg, 0.51 mmol) in CH_2Cl_2 (5.0 mL) at ambient temperature were added AcOH (0.006 mL, 0.10 mmol) and Br_2 (0.11 mL, 2.10 mmol) successively. After being stirred at ambient temperature for 40 min, the resulting solution was poured into a mixture of H_2O and CH_2Cl_2 with vigorous stirring. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 twice. The combined extracts were dried over Na_2SO_4 and concentrated to afford a residual solid, which was purified by column chromatography on silica gel (hexane/EtOAc) to furnish (*S*)-3,3′,5,5′-tetrabromo-2,2′-dihydroxy-6,6′-dimethylbiphenyl (*S*)-**7** (236 mg, 87%): $[\alpha]^{32}_D$ −38° (*c* 0.50, $CHCl_3$); ^{1}H NMR δ 7.75 (s, 2 H), 5.35 (s, 2 H), 2.03 (s, 6 H); ^{13}C NMR δ 149.0, 137.8, 134.7, 124.5, 116.1, 107.9, 20.0; IR (neat) 3501, 1425, 1287, 1211, 1061, 1032, 758, 675 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_9Br_4O_2$: 524.7331 ([M − H]$^-$), Found: 524.7337 ([M − H]$^-$).

(*S*)-3,3′,5,5′-Tetrabromo-2,2′-dimethoxy-6,6′-dimethylbiphenyl (*S*)-8: To a solution of (*S*)-3,3′,5,5′-tetrabromo-2,2′-dihydroxy-6,6′-dimethylbiphenyl (*S*)-**7** (236 mg, 0.45 mmol) in acetone (10 mL) at room temperature were added MeI (0.56 mL, 8.9 mmol) and K_2CO_3 (0.62 g, 4.45 mmol). After being stirred at room temperature for 2 h, the resulting mixture was filtered through a pad of Celite with EtOAc. The filtrate was concentrated to yield a residue, which was purified by column chromatography on silica gel (hexane/EtOAc) to furnish (*S*)-3,3′,5,5′-tetrabromo-2,2′-dimethoxy-6,6′-dimethylbiphenyl (*S*)-**8** (246 mg, 98%): $[\alpha]^{32}_D$ +7° (*c* 0.64, $CHCl_3$); ^{1}H NMR δ 7.84 (s, 2 H), 3.54 (s, 6 H), 2.03 (s, 6 H); ^{13}C NMR δ 153.8, 136.8, 136.0, 133.6, 120.3, 115.0, 60.5, 20.5; IR (neat) 2938, 1452, 1406, 1350, 1260, 1063, 930, 866 cm^{-1}; HRMS (ESI) Calcd for $C_{16}H_{14}Br_4O_2$: 553.7722 ([M]$^+$), Found: 553.7718 ([M]$^+$).

(*S*)-2,2′-Dimethoxy-6,6′-dimethyl-3,3′,5,5′-tetrakis(3,4,5-trifluorophenyl)biphenyl (*S*)-9: To a solution of (*S*)-3,3′,5,5′-tetrabromo-2,2′-dimethoxy-6,6′-dimethylbiphenyl (*S*)-**8** (423 mg, 0.76 mmol) in dry DMF (10 mL) at room temperature were added 3,4,5-trifluorophenylboronic acid (718 mg, 4.55 mmol), $Pd(OAc)_2$ (34 mg, 0.15 mmol), P(*o*-tol)$_3$ (185 mg, 0.61 mmol), and $K_3PO_4 \cdot nH_2O$ (2.17 g, 7.58 mmol) sequentially. After being refluxed under an argon atmosphere for 20 h, the resulting mixture was filtered through a pad of Celite with Et_2O. The filtrate was poured into a mixture of H_2O and Et_2O with vigorous stirring. The organic phase was separated, and the aqueous phase was extracted with Et_2O twice. The combined extracts were dried over Na_2SO_4 and concentrated to furnish a residue, which was purified by column chromatography on silica gel (hexane/Et_2O) to yield (*S*)-2,2′-dimethoxy-6,6′-dimethyl-3,3′,5,5′-tetrakis(3,4,5-trifluorophenyl)biphenyl (*S*)-**9** (377 mg, 65%) : $[\alpha]^{34}_D$ +17° (*c* 0.15, $CHCl_3$); ^{1}H NMR δ 7.28 (d, J = 8 Hz, 2 H), 7.29 (d, J = 9 Hz, 2 H), 7.20 (s, 2 H), 7.00 (d, J = 8 Hz, 2 H), 6.98 (d, J = 8 Hz, 2 H), 3.31 (s, 6 H), 1.98 (s, 6 H); ^{13}C NMR δ 154.8, 151.1 (ddd, J_{C-F} = 251, 10, 4 Hz), 138.8 (ddt, J_{C-F} = 254, 16, 4 Hz), 136.1, 135.65, 135.56 (ddt, J_{C-F} = 316, 8, 5 Hz), 132.8, 131.2, 129.4, 113.8, 113.7, 113.61, 113.55, 113.2, 113.1, 113.02, 112.97, 60.4, 18.1; IR (neat) 2930, 2359, 1614, 1526, 1470, 1418, 1395, 1258, 1098, 860, 732 cm^{-1}; HRMS (ESI) Calcd for $C_{40}H_{22}F_{12}O_2$: 762.1423 ([M]$^+$), Found: 762.1424 ([M]$^+$).

Chiral Ammonium Salt (*S*)-1b: To a solution of biphenyl compound (*S*)-**9** (377 mg, 0.49 mmol) in benzene (5.0 mL) at room temperature were added *N*-bromosuccinimide (203 mg, 1.14 mmol) and AIBN (8 mg, 0.049 mmol) successively. After being refluxed for 30 min, the mixture was cooled to room temperature and filtered through a pad of Celite with Et_2O. The filtrate was concentrated to afford a residual solid, which was used for the next reaction without further purification.

To a solution of crude dibromide (*S*)-**10** in CH_3CN (5 mL) at room temperature were added Bu_2NH (0.051 mL, 0.30 mmol) and K_2CO_3 (410 mg, 2.96 mmol). After being stirred at 95 °C for 10 h, the resulting mixture was cooled to room temperature and filtered through a pad of Celite with CH_2Cl_2. The filtrate was concentrated to leave a residue which was purified by column chromatography on silica gel (CH_2Cl_2/MeOH) to furnish chiral ammonium salt (*S*)-**1b** (254 mg, 53% for two steps) as a white solid: $[\alpha]^{34}_D$ −34° (*c* 0.48, $CHCl_3$); ^{1}H NMR δ 7.20−7.60 (m, 10 H), 4.73 (d, J = 14 Hz, 2 H), 4.05 (d, J = 14 Hz, 2 H), 3.41 (s, 6 H), 3.08 (t, J = 12 Hz, 2 H), 2.85 (t, J = 12 Hz, 2 H), 0.85−1.20 (m, 6 H), 0.73 (t, J = 7 Hz, 6 H), 0.30 (br s, 2 H); ^{13}C NMR δ 156.0, 151.2 (ddd, J_{C-F} = 251, 9, 3 Hz), 139.8 (dq, J_{C-F} = 256, 15 Hz), 136.6, 134.7, 134.1−134.6 (m), 133.8, 132.5−133.0 (m), 113.6 (dd, J_{C-F} = 16, 6 Hz), 61.8, 57.5, 24.4, 19.4, 13.2; IR (neat) 3404, 2965, 2357, 1616, 1528, 1472, 1398, 1260, 1242, 1045, 862 cm^{-1}; HRMS (ESI) Calcd for $C_{48}H_{38}F_{12}NO_2$: 880.2705 ([M]$^+$), Found: 880.2703 ([M]$^+$).

Representative Procedure for Catalytic Asymmetric Alkylation of *tert*-Butyl *N*-(Diphenylmethylene)glycinate (11) under Phase Transfer Conditions (Benzylation). To a mixture of glycine derivative **11** (5 g, 16.93 mmol) and chiral phase transfer catalyst (*S*,*S*)-**1b** (17 mg, 0.017 mmol) in toluene (24 mL) were added KOH (50% aqueous, 16 mL) and benzyl bromide (3.02 mL, 24.43 mmol). After being stirred vigorously at 20 °C for 12 h, the starting material **11** was consumed. The mixture was poured into water and extracted with Et_2O twice. The combined organic layers were dried over Na_2SO_4 and concentrated to afford a residual oil, which was purified by flash column chromatography on silica gel with hexane/Et_2O (100:1 to 30:1) to furnish *tert*-butyl *N*-(diphenylmethylene)phenylalaninate **12a** (6.13 g, 94% yield). The enantiomeric excess was determined by chiral

HPLC analysis (Daicel Chiralcel OD, hexane/2-propanol = 100:1, flow rate = 0.5 mL/min, retention time 12.0 min (*R*) and 16.3 min (*S*)). The absolute configuration was determined by comparison of the HPLC retention time with the authentic sample independently synthesized by the reported procedure.[3b] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.58 (m, 2 H), 7.26−7.38 (m, 6 H), 7.13−7.21 (m, 3 H), 7.04−7.06 (m, 2 H), 6.60 (d, J = 6 Hz, 2 H), 4.10 (dd, J = 9.6, 4.4 Hz, 1 H), 3.23 (dd, J = 13.6, 4.4 Hz, 1 H), 3.15 (dd, J = 13.6, 9.6 Hz, 1 H), 1.44 (s, 9 H); IR (neat) 2978, 1732, 1624, 1576, 1495, 1447, 1367, 1286, 1150, 1082, 1030, 849, 756, 696 cm^{-1}.

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