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Combinatorial Design of Simplified High-Performance Chiral Phase-Transfer Catalysts for Practical Asymmetric Synthesis of α-Alkyl- and α,α-Dialkyl-α-Amino Acids

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Dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday

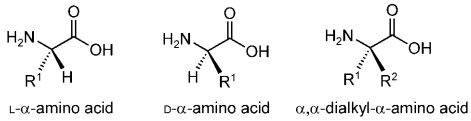
Abstract: A very efficient, chiral phase-transfer catalyst, (*S*)-**2Db**, was prepared by taking advantage of the combinatorial approach from the readily available (*S*)-1,1′-binaphthyl-2,2′-dicarboxylic acid. This catalyst exhibited high catalytic performance (0.01–0.1 mol%) in the asymmetric alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester and *N*-(*p*-chlorophenylmethylene)alanine *tert*-butyl ester relative to other chiral phase-transfer catalysts in current use. This has created a general and highly practical procedure for the enantioselective synthesis of structurally diverse natural and unnatural α-alkyl-α-amino acids as well as α,α-dialkyl-α-amino acids. A similar simplified catalyst, (*S*)-**2Fb**, is also applicable to the direct asymmetric aldol reaction between glycine Schiff base and aldehydes with moderate *syn* selectivity and high enantioselectivity.

Keywords: aldol reaction · alkylation · amino acids · asymmetric catalysis · phase-transfer catalysis

Introduction

The α-alkyl-α-amino acids are by far the most important, numerous, and diverse family of the naturally occurring amino acids. Although only 20 amino acids constitute polypeptide chains under genetic control, the total number of α-amino acids identified as occurring free or incorporated in the natural products of animals, plants, and microorganisms is estimated to be in the hundreds, and the list of such α-amino acids continues to grow. The majority of these naturally found α-alkyl-α-amino acids have the L configuration at the α-carbon atom. Many natural α-alkyl-α-amino acids of the D series are also found in non-protein compounds of plants, fungi, and microorganisms, but generally not in animals, and never in proteins.

In contrast to α-alkyl-α-amino acids, non-proteinogenic α,α-dialkyl-α-amino acids play a special role in the design of peptides with enhanced properties.[1] This is not only because they possess stereochemically stable quaternary carbon centers, but their incorporation into peptides imparts a significant influence on conformational preferences.[2] Furthermore, α,α-dialkyl-α-amino acids themselves are often effective enzyme inhibitors[3] and constitute a series of interesting building blocks for the synthesis of various biologically active compounds.[4] Accordingly, the development of truly efficient methods for their preparation, including α-alkyl-α-amino acid synthesis, especially in an enantiomerically pure form, has become of great importance.[5] However, despite numerous studies, only a few catalytic systems have been reported in asymmetric phase-transfer chemistry, with limited general applicability.[6–10] In this context, although we recently designed new, chiral spiro-type (*R*,*R*)- or (*S*,*S*)-3,4,5-trifluorophenyl-NAS bromide (*S*,*S*)-**1** (Ar = 3,4,5-F_3-C_6H_2) for effecting asymmetric alkylation of α-amino acid derivatives,[10f] the multi-step preparation (5 steps for right-hand (*S*)-3,5-dihydro-4*H*-dinaphth[2,1-*c*:1′2′-*e*]azepine from (*S*)-binaphthol; 11 more steps from (*S*)-binaphthol) of



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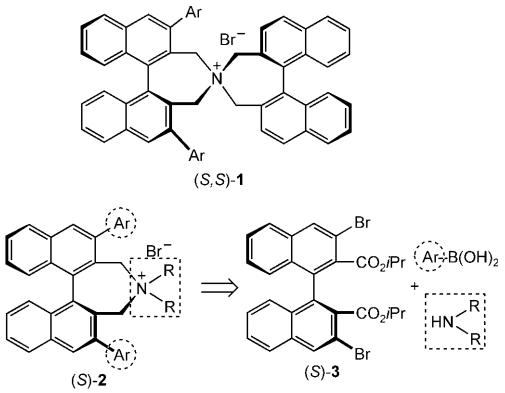
catalyst **1** constitutes a severe drawback. Simplification of catalyst **1** is therefore crucial for overcoming this intrinsic problem in chiral phase-transfer process chemistry.

Results and Discussion

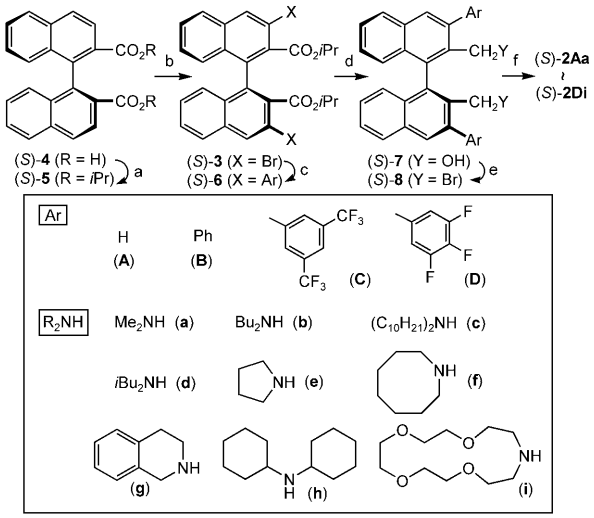
Combinatorial Design of Simplified Phase-Transfer Catalysts for Asymmetric α-Alkyl-α-Amino Acid Synthesis

To simplify the structure of the original catalyst (*S*,*S*)-**1**, we chose the fundamental structure **2** as a simplified chiral phase-transfer catalyst. Because the catalyst (*S*)-**2** can be readily prepared from three components, a chiral binaphthyl part (*S*)-**3**, an arylboronic acid ($ArB(OH)_2$), and a secondary amine (R_2NH) as described previously,[11] the appropriate modification of the $ArB(OH)_2$ and R_2NH portions should give a series of newly designed catalysts. Hence, we studied the substituent effects of Ar and R moieties in detail by using combinatorial chemistry, as variation of the substituents Ar and R would allow facile generation of large libraries of structures.



Abstract in Japanese:
従来のスピロ型キラル相間移動触媒(*S*,*S*)-**1**の片方のビナフチル基をアルキル基で置換した簡素化触媒(*S*)-**2**を新たにデザインした。これらの触媒活性をグリシン誘導体**9**の不斉ベンジル化反応によって評価したところ、ジブチル基を有する触媒(*S*)-**2Db**が最も良好な結果を与えた。触媒量の下限や基質の適用範囲などに関する検討を行ったところ、本触媒をわずか0.05mol%用いた系でも各種のα-アルキル-α-アミノ酸誘導体が高収率かつ高エナンチオ選択的に得られることを見いだした。また、グリシン誘導体**9**の不斉アルドール反応においては、触媒(*S*)-**2Fb**が良好な結果を与え、望みのアルドール体が高エナンチオ選択的かつ中程度の*syn*-選択性で得られることも見いだした。

The requisite catalyst (*S*)-**2** can be easily prepared from the known and readily available (*S*)-1,1′-binaphthyl-2,2′-dicarboxylic acid (*S*)-**4**[12] in the six-step sequence illustrated in Scheme 1.[13] Thus, dicarboxylic acid (*S*)-**4** was transformed



Scheme 1. Synthesis of various chiral phase-transfer catalysts (*S*)-**2Aa**–**Di**. Reaction conditions: a) *i*PrBr (10 equiv), $Bu_4N{\cdot}HSO_4$ (20 mol%), $KF{\cdot}2H_2O$ (10 equiv), THF, reflux (95%); b) 1) $Mg(TMP)_2$ (4 equiv), THF, room temperature, 2) Br_2 (8 equiv), −78°C→room temperature (91%); c) $ArB(OH)_2$ (2.4 equiv), $Pd(OAc)_2$ (5 mol%), PPh_3 (15 mol%), K_2CO_3 (3 equiv), DMF, 90°C (57–68%); d) $LiAlH_4$ (3 equiv), THF, 0°C→room temperature (59–82%); e) PBr_3 (1 equiv), THF, 0°C (65–87%); f) R_2NH (2 equiv), K_2CO_3 (1.5 equiv), CH_3CN, reflux (34–88%).

with *i*PrBr, catalytic $Bu_4N{\cdot}HSO_4$ and $KF{\cdot}2H_2O$ into the corresponding diisopropyl ester (*S*)-**5** in 95% yield. Treatment of (*S*)-**5** with freshly prepared $Mg(TMP)_2$ in THF and subsequent addition of Br_2 gave rise to (*S*)-3,3′-dibromo-1,1′-binaphthyl-2,2′-dicarboxylic ester (*S*)-**3** in 91% yield. Suzuki–Miyaura cross-coupling of (*S*)-**3** with arylboronic acid, $ArB(OH)_2$ (Ar = Ph, 3,5-$(CF_3)_2$-C_6H_3, 3,4,5-F_3-C_6H_2) in the presence of catalytic $Pd(OAc)_2$, PPh_3, and K_2CO_3 in DMF afforded (*S*)-3,3′-diaryl-1,1′-binaphthyl-2,2′-dicarboxylic ester (*S*)-**6** in 57–68% yield. Reduction of (*S*)-**6** with $LiAlH_4$ in THF and subsequent treatment of the resulting crude alcohol (*S*)-**7** with PBr_3 in THF furnished (*S*)-dibromide (*S*)-**8** in moderate to high yields. Reaction of (*S*)-**8** with dialkylamine and K_2CO_3 in acetonitrile led to the formation of catalysts (*S*)-**2Aa**–**Di** in high yields.

To examine the substituent effect of catalyst (*S*)-**2** on the variation of the substituents Ar and R, we first prepared a library of quaternary ammonium salts (*S*)-**2Aa**–**Di** by combining four aryl substituents with nine different dialkylamines. The chiral amplitude of these simplified phase-transfer catalysts (*S*)-**2Aa**–**Di** was screened efficiently by using an in situ generated method from 3,3′-diaryl (*S*)-binaphthyl dibromide (*S*)-**8** (Ar = H, Ph, 3,5-$(CF_3)_2$-C_6H_3, 3,4,5-F_3-C_6H_2) in the asymmetric alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **9** (Scheme 2). Thus, reaction of **9** with benzyl bromide (1.2 equiv) and 50% aqueous KOH in tolu-

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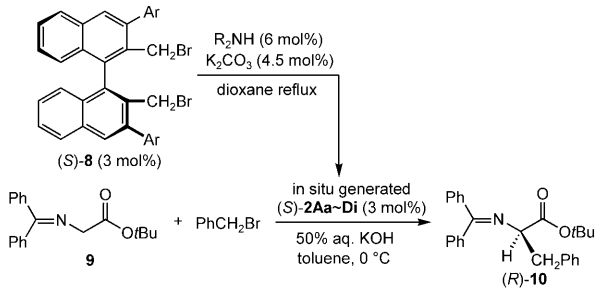

Scheme 2. Evaluation of in situ generated catalysts (*S*)-**2Aa**–**Di** by the asymmetric alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **9**.

ene was carried out in the presence of 3 mol% in situ generated catalysts (*S*)-**2Aa**–**Di** under argon atmosphere at 0°C to furnish benzylation product **10**. The results are shown in Table 1, which also includes selected results from the use of isolated, optically pure catalyst (*S*)-**2** for comparison.

Table 1. Screening of in situ generated catalysts (*S*)-**2Aa**–**Di** in the enantioselective phase-transfer benzylation of glycine derivative **9**.[a]

Amine (R_2NH)	Ar = H **A**	Ar = Ph **B**	Ar = 3,5-$(CF_3)_2$-C_6H_3 **C**	Ar = 3,4,5-F_3-C_6H_2 **D**
a	12	26	1	7
b	−27	43	93	97
	(−13)	(60)	(91)	(99)
c	−17	58	96	97
			(93)	(99)
d	−9	22	44	7
e	−7	5	31	43
f	−23	33	41	20
g	−19	26	78	81
		(28)		
h	22	3	2	6
i	15	41	75	83
				(87)

[a] All values reported as % *ee*; enantioselectivity values in parentheses were obtained with isolated, optically pure (*S*)-**2**.

Several characteristic features of the asymmetric alkylation on the screening of these in situ generated catalysts (*S*)-**2Aa**–**Di** are as follows: 1) The observed enantioselectivities vary from −27 to 97% *ee* with the majority of quaternary ammonium salts giving the preferential formation of the *R* isomer **10**. 2) Both the chiral binaphthol and dialkylamine units appear to play important roles in determining the overall enantioselectivity; in general, the choice of dialkylamines is more sensitive to the degree of enantioselectivity. 3) Combination of 3,5-bis(trifluoromethyl)phenyl and 3,4,5-trifluorophenyl groups with dialkylamines having straight alkyl chains exhibited excellent enantioselectivities (93–97% *ee* with (*S*)-**2Cb**, (*S*)-**2Cc**, (*S*)-**2Db**, and (*S*)-**2Dc**).

Effect of Alkyl Chains in (*S*)-2D on Enantioselectivity

With bis(3,4,5-trifluorophenyl)-substituted catalyst (*S*)-**2D**, we examined the substituent effect of R by changing the number of straight alkyl chains, as shown in Figure 1. In the

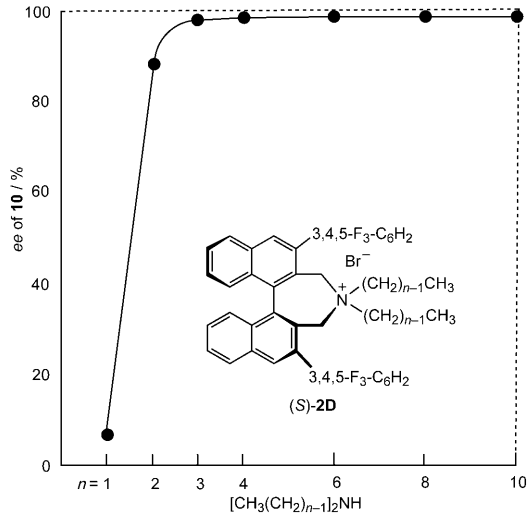

Figure 1. Effect of the number of straight alkyl chains in (*S*)-**2D** on enantioselectivity in the asymmetric benzylation of **9**.

asymmetric benzylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **9**, dimethylammonium salt (*S*)-**2Da** exhibited very low enantioselectivity, and the use of $(CH_3(CH_2)_{n-1})_2NH$ ($n \geq 4$) gave uniformly high asymmetric induction.

Effect of Aryl Substituents in (*S*)-2b on Enantioselectivity

With this information in hand, we further screened the substituent effect of various Ar groups by preparing (*S*)-**2b** catalysts derived from dibutylamine and various 3,3′-diarylated (*S*)-binaphthyl dibromide (*S*)-**8** as shown in Figure 2. Among monosubstituted phenyl derivatives, *p*-substituted

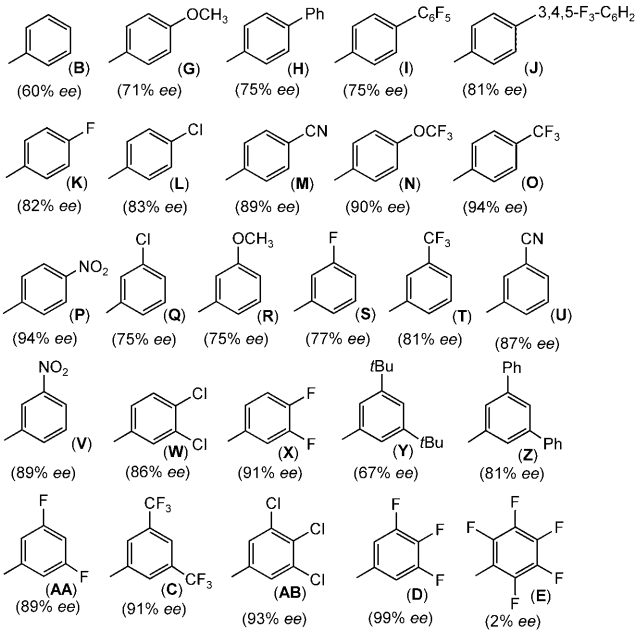

Figure 2. Effect of aryl substituents of (*S*)-**2b** (R = Bu) on enantioselectivity in the asymmetric benzylation of **9**.

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phenyl derivatives generally gave higher enantioselectivity than the corresponding *m*-substituted phenyl analogues in the asymmetric benzylation of **9**. In particular, *p*-(trifluoromethyl)phenyl and *p*-nitrophenyl derivatives exhibited high enantioselectivity (94% *ee*). These catalysts are more selective than various disubstituted phenyl derivatives. Among a variety of aryl substituents, catalyst (*S*)-**2Db** possessing 3,4,5-trifluorophenyl substituents was found to give the best result in terms of enantioselectivity (99% *ee*). Notably, bispentafluorophenyl catalyst (*S*)-**2Eb** exhibited dramatically low enantioselectivity (only 2% *ee*).

X-ray Crystal Structures of Catalyst (*S*)-2b

Although indirect evidence for the role of the aryl substituents (Ar) in (*S*)-**2b** was strong at this point, additional insight was provided by the X-ray crystal structures of catalysts (*S*)-**2Bb**, (*S*)-**2Db**, and (*S*)-**2Eb** (Figure 3). Interestingly, the dihedral angles between aryl and naphthyl groups are different among these three catalysts (46.6°/58.8°, 52.3°/59.8°, and 60.1°/72.0° for (*S*)-**2Bb**, (*S*)-**2Db**, and (*S*)-**2Eb**, respectively). The conformation of two fluxional butyl moieties are also different. These data may provide useful information to deduce possible structures of chiral phase-transfer catalysts in solution.

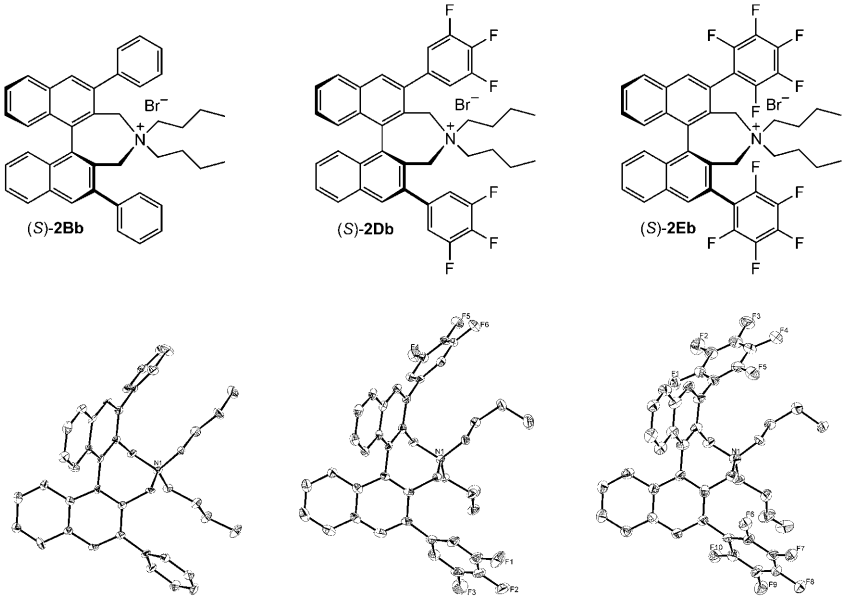

Figure 3. ORTEP diagram of catalysts (*S*)-**2Bb**, (*S*)-**2Db**, and (*S*)-**2Eb** (probability chosen for the ellipsoids is 50, 50, and 30%, respectively). All hydrogen atoms, solvents, and counter-anions are omitted for clarity.

Catalyst Loading Study

The chemical behavior of the simplified phase-transfer catalysts (*S*)-**2Cb**, (*S*)-**2Cc**, (*S*)-**2Db**, and (*S*)-**2Dc** was examined by carrying out asymmetric alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **9**, and quite surprisingly these types of catalysts were found to be by far the most active catalysts among existing chiral phase-transfer catalysts. Indeed, asymmetric reaction of **9** with benzyl bromide (1.2 equiv) and 50% aqueous KOH in toluene was effected in the presence of just 0.01–0.1 mol% chiral catalyst (*S*)-**2Db** under argon atmosphere at 0°C for 2–9 h to furnish benzylation product **10** almost quantitatively with excellent enantioselectivity (98–99% *ee*, Table 2, Entries 1–3).[14] However, the use of 0.005 mol% (*S*)-**2Db** lowered both the chemical yield and enantioselectivity (Entry 4). A similar trend was also observed in the case of catalyst (*S*)-**2Dc** (Entries 5 and 6).

Other selected examples are listed in Table 2. Several characteristic features of the present alkylations are as follows: 1) In contrast to existing chiral phase-transfer catalysts, the chiral phase-transfer catalysts (*S*)-**2Cb**, (*S*)-**2Cc**, (*S*)-**2Db**, and (*S*)-**2Dc** exhibited high catalytic performance (0.05–0.1 mol%), demonstrating the remarkable efficiency and practicability of the present approach for the enantioselective synthesis of α-alkyl-α-amino acids. 2) By using $CsOH·H_2O$ in place of 50% KOH, asymmetric alkylation of **9** with simple alkyl halides such as ethyl iodide proceeded smoothly at −20°C to furnish the corresponding α-alkyl-α-amino acids in good yield with high enantioselectivity (Entry 24 versus 23). It should be noted that monoalkylated products do not racemize under the phase-transfer conditions.

Asymmetric Synthesis of α,α-Dialkyl-α-Amino Acids

The simplified catalyst (*S*)-**2Db** can, of course, be applied to the asymmetric alkylation of aldimine Schiff base **11** derived from D,L-alanine *tert*-butyl ester (Scheme 3). Thus, reaction of **11** with benzyl bromide (1.2 equiv) and $CsOH·H_2O$ (5 equiv) in toluene in the presence of 1 mol% catalyst (*S*)-**2Db** under argon atmosphere at 0°C for 3 h gave rise to benzylation product **12** in 82% yield with 97% *ee*. Here, an aldimine Schiff base **11** and the stronger base $CsOH·H_2O$ are required in place of the corresponding benzophenone imine Schiff base and KOH to effect a smooth alkylation reaction. The virtually complete enantioselectivity (99% *ee*) was attained by lowering the reaction

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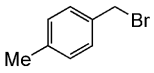
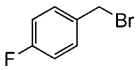
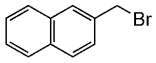
Table 2. Catalytic enantioselective phase-transfer alkylation of glycine derivative **9** catalyzed by (*S*)-**2Cb**, (*S*)-**2Cc**, (*S*)-**2Db**, and (*S*)-**2Dc**.[a]

Entry	Catalyst (*c* [mol%])	RX	*T* [°C]	*t* [h]	Yield [%][b]	*ee* [%][c]
1	(*S*)-**2Db** (0.1)	$PhCH_2Br$	0	2	99	99
2	(*S*)-**2Db** (0.05)		0	2	98	99
3	(*S*)-**2Db** (0.01)		0	9	92	98
4	(*S*)-**2Db** (0.005)		0	48	51	57
5	(*S*)-**2Dc** (0.05)		0	4	94	99
6	(*S*)-**2Dc** (0.01)		0	24	79	98
7	(*S*)-**2Cb** (0.1)		0	4	89	91
8	(*S*)-**2Cb** (0.05)		0	5	87	91
9	(*S*)-**2Cb** (0.01)		0	48	9	90
10	(*S*)-**2Cc** (0.05)		0	48	85	93
11	(*S*)-**2Cc** (0.01)		0	48	51	77
12	(*S*)-**2Db** (0.05)		0	4	99	98
13	(*S*)-**2Db** (0.05)		0	5	99	98
14	(*S*)-**2Db** (0.05)	$CH_2{=}CHCH_2Br$	0	3	87	98
15	(*S*)-**2Db** (0.01)		0	48	62	82
16	(*S*)-**2Dc** (0.05)		0	5	99	97
17	(*S*)-**2Cb** (0.01)		0	48	60	83
18	(*S*)-**2Cc** (0.05)		0	48	59	91
19	(*S*)-**2Db** (0.05)	$HC{\equiv}CCH_2Br$	0	4	88	98
20	(*S*)-**2Db** (0.01)		0	48	28	88
21	(*S*)-**2Cb** (0.05)		0	46	80	88
22	(*S*)-**2Db** (0.05)		0	64	84	97
23	(*S*)-**2Db** (0.1)	CH_3CH_2I[d]	0	72	12	91
24	(*S*)-**2Db** (0.1)	CH_3CH_2I[d,e]	−20	1	67	99

[a] Unless otherwise specified, the reaction was carried out with 1.2 equiv RX in the presence of (*S*)-**2** (cat.) in 50% aqueous KOH/toluene (1:1 *v*/*v*) under the given reaction conditions. [b] Isolated yield. [c] Enantiomeric purity of **10** was determined by HPLC analysis of the alkylated imine using a chiral column (Daicel Chiralcel OD) with hexane/isopropanol as solvent; absolute configuration in each case is *R*, and was determined by comparison of the HPLC retention time with the authentic sample independently synthesized by the reported procedure.[9d,10f] [d] Use of 5 equiv alkyl halide. [e] Use of $CsOH{\cdot}H_2O$ as base.

temperature to −20 °C. The catalyst loading can be decreased to 0.05 mol% (98% *ee* (63%) at −20 °C).

Other selected examples of several α-alkyl-α-amino acid derivatives in combination with alkyl halides under the influence of (*S*)-**2Db** (1 mol%) are listed below, for which exceedingly high enantioselectivity was observed in the catalytic enantioselective synthesis of α,α-dialkyl-α-amino acids.

Asymmetric Synthesis of β-Hydroxy-α-Amino Acids

The simplified catalyst (*S*)-**2** is also applicable toward the direct asymmetric aldol reaction between glycine Schiff base and aldehydes with moderate *syn* selectivity and high enantioselectivity. This approach is complementary to the *anti*-selective asymmetric aldol reaction between glycine Schiff base and aldehydes with chiral spiro-type (*S*,*S*)-3,5-bis[3,5-bis(trifluoromethyl)phenyl]phenyl-NAS bromide (*S*,*S*)-**1** (Ar = 3,5-bis-[3,5-$(CF_3)_2$-$C_6H_3]_2C_6H_3$), as reported previously.[15] At first, we initiated an examination of the direct asymmetric aldol reaction of *N*-(diphenylmethylene)glycine *tert*-butyl ester **9** with 3-phenylpropanal as a representative acceptor under phase-transfer conditions. Thus, treatment of **9** with 3-phenylpropanal (2 equiv) in a solution of toluene (0.1 M) and NaOH (1% aq) (2.5:1 *v*/*v*; 1 equiv base for **9**) in the presence of chiral quaternary ammonium salt (*S*)-**2Cb** (1 mol%) at 0 °C for 1.5 h and subsequent hydrolysis with 1 N HCl in THF resulted in the formation of the corresponding β-hydroxy-α-amino ester **13** ($R = CH_2CH_2Ph$) in 84% yield with a *syn*/*anti* ratio of 66:34 (Entry 1 in Table 3). The enantiomeric excess of the major *syn* isomer *syn*-**13** ($R = CH_2CH_2Ph$) and minor *anti*-**13** ($R = CH_2CH_2Ph$) was determined to be 56 and 71% *ee*, respectively, by HPLC analysis after transformation into the corresponding oxazolidine-2-thione derivatives **14** using thiocarbonyl diimidazole (Scheme 4). Significantly, the use of (*S*)-**2Fb** possessing a 3,5-bis[3,5-bis(trifluoromethyl)-phenyl]phenyl substituent as catalyst enhanced both diaster-

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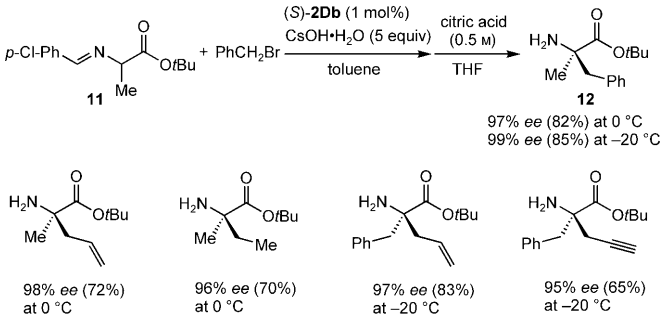


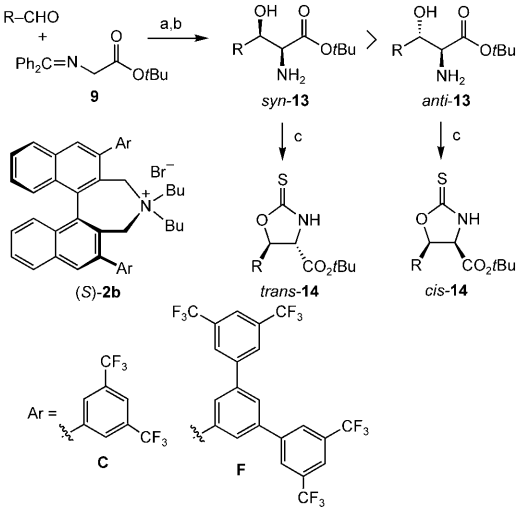
Scheme 3. Asymmetric synthesis of α,α-dialkyl-α-amino acids.

Table 3. Direct asymmetric aldol reactions of **9** with aldehydes (RCHO) by chiral phase-transfer catalysis in the presence of (*S*)-**2b**.[a]

Entry	R	Catalyst	*T* [°C]	*t* [h]	Yield [%][b]	*syn*/*anti*[c]	*ee* [%] (*syn*/*anti*)[d]
1	$PhCH_2CH_2$	(*S*)-**2Cb**	0	1.5	84	66:34	56/71
2		(*S*)-**2Fb**	0	1.5	79	78:22	92/96
3	$CH_3(CH_2)_3CH_2$	(*S*)-**2Cb**	0	1.5	84	70:30	40/64
4		(*S*)-**2Fb**[e]	0	2	68	66:34	92/91
5	$CH_2=CH(CH_2)_2$	(*S*)-**2Fb**[e]	0	2	68	85:15	93/92
6	CH_3[f]	(*S*)-**2Fb**[e]	0	2	60	53:47	94/99
7	$(CH_3)_2CH$	(*S*)-**2Fb**[e]	0	2	57	63:37	61/75

[a] Unless otherwise noted, the direct aldol reaction of **9** (0.2 mmol) was carried out with 2 equiv aldehyde in the presence of (*S*)-**2b** (1 mol%) in toluene (2 mL)/1% NaOH aqueous solution (0.8 mL) at 0°C. [b] Isolated yield. [c] Determined by ^{1}H NMR analysis. [d] Enantiomeric excess of *anti*-**13**, which was determined, after conversion into the corresponding oxazolidine-2-thione **14**, by HPLC analysis using a chiral column (DAICEL Chiralpak AD-H) with hexane/2-propanol as solvent. [e] Use of 2 mol% catalyst. [f] With 5 equiv aldehyde.

eo- and enantioselectivities in this reaction system (*syn*/*anti* = 78:22; 92 and 96% *ee* for *syn* and *anti* isomers, respectively; Entry 2). Other selected examples are listed in Table 3.



Scheme 4. Direct asymmetric aldol reaction of glycine Schiff base **9** with aldehydes in the presence of (*S*)-**2b** under phase-transfer conditions. Reaction conditions: a) (*S*)-**2Cb** or (*S*)-**2Fb** (1–2 mol%), toluene/NaOH (1% aq), 0°C, 1.5–2 h; b) HCl (1N)/THF, 0°C; c) thiocarbonyl diimidazole, CH_2Cl_2, room temperature.

Conclusions

We have developed a highly efficient, general, and useful procedure for the practical enantioselective synthesis of α-alkyl- and α,α-dialkyl-α-amino acids by asymmetric phase-transfer catalysis. By introducing the combinatorial design of catalysts (*S*)-**2**, a very active, chiral phase-transfer catalyst (*S*)-**2Db** has been devised. In particular, the catalyst loading of (*S*)-**2Db** has reached 0.01 mol% for the asymmetric alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **9**; this offers a powerful method for the synthesis of stereochemically homogeneous α-alkyl-α-amino acids in a totally predictable manner. Of course, this reaction is applicable toward the asymmetric alkylation of aldimine Schiff base **11** derived from several D,L-α-alkyl-α-amino acid *tert*-butyl esters. A similar simplified catalyst (*S*)-**2Fb** is also applicable toward the direct asymmetric aldol reaction between glycine Schiff base and aldehydes with moderate *syn* selectivity and high enantioselectivity, and complements the *anti*-selective asymmetric aldol reaction between glycine Schiff base and aldehydes with chiral spiro-type (*S*,*S*)-3,5-bis[3,5-bis(trifluoromethyl)phenyl]phenyl-NAS bromide (*S*,*S*)-**1** (Ar = 3,5-bis[3,5-$(CF_3)_2$-$C_6H_3]_2C_6H_3$). Therefore, the system presented herein has a distinct advantage in terms of operational simplicity, environmentally friendly conditions, and suitability for large-scale reactions for practical industrial applications.

Experimental Section

1. General

Infrared (IR) spectra were recorded on a Shimadzu IR Prestige-21 instrument. ^{1}H NMR and ^{13}C NMR spectra were measured on a Jeol JNM-FX400 (400 MHz) spectrometer, and a JMTC-400/54/SS (400 MHz) spectrometer. High-performance liquid chromatography (HPLC) was performed on Shimadzu 10A instruments using 4.6×250 mm Daicel Chiralcel OD, OD-H, and Chiralpak AD-H. Optical rotations were measured on a Jasco DIP-1000 digital polarimeter. High-resolution mass spectrometry (HRMS) data were collected on an Applied Biosystems Mariner API-TOF workstation and a Bruker micrOTOF focus-KR instrument. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used.

Dry THF was purchased from Kanto Chemical Co., Inc. as "dehydrated". CH_3CN, CH_2Cl_2, and dioxane were stored over molecular sieves (4 Å). Toluene was dried over Na. *N*,*N*-Dimethylformamide (DMF) was degassed before use. (*S*)-1,1′-binaphtyl-2,2′-dicarboxylic acid [(*S*)-**4**] was kindly supplied by Tanabe Seiyaku Co., Ltd. (*S*)-Dibromides **8A** and **8B** and their analytical data have been reported previously.[10f] (*S*)-Dibromide **8D** was synthesized from (*S*)-**3** according to the published methods.[13] *tert*-Butyl glycinate benzophenone Schiff base was prepared from

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tert-butyl bromoacetate and benzophenone imine[16] according to reported methods.[17] Other simple reagents were purchased and used without further purification, unless otherwise specified.

2. Screening of In Situ Generated Catalysts

*2.1. Preparation of Diester (S)-**5** by the Esterification[18] of (S)-1,1′-Binaphtyl-2,2′-dicarboxylic Acid (S)-**4***

(*S*)-2,2′-Bis(isopropoxycarbonyl)-1,1′-binaphtyl (*S*)-5: A mixture of tetrabutylammonium hydrogen sulfate ($Bu_4N{\cdot}HSO_4$, 14 mg, 0.040 mmol) and potassium fluoride dihydrate ($KF{\cdot}2H_2O$, 188 mg, 2.0 mmol) in THF (2.0 mL) was stirred at room temperature for 1 h. After the addition of binaphthyldicarboxylic acid (*S*)-**4** (69 mg, 0.20 mmol) and *i*PrBr (188 μL, 2.0 mmol), the mixture was held at reflux for 24 h. The resulting mixture was poured into H_2O and extracted with CH_2Cl_2. The organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (Et_2O/hexane = 1:3 as eluent) to furnish (*S*)-2,2′-bis(isopropoxycarbonyl)-1,1′-binaphtyl (*S*)-**5** (81 mg, 0.19 mmol, 95% yield): The ^1H NMR spectrum was consistent with reported data.[13]

*2.2. Syntheses of Diol (S)-**7C** by Sequential o-Magnesiation/Bromination, Suzuki–Miyaura Cross-Coupling Reaction and Reduction with $LiAlH_4$*

(*S*)-3,3′-Bis{3,5-bis(trifluoromethyl)phenyl}-2,2′-bis(hydroxymethyl)-1,1′-binaphthyl (*S*)-7C: (*S*)-3,3′-Dibromo-2,2′-bis(isopropoxycarbonyl)-1,1′-binaphtyl (*S*)-**3** was prepared from diester (*S*)-**5** by the *o*-magnesiation/bromination sequence according to published procedures.[13] A mixture of dibromide (*S*)-**3** (400 mg, 0.68 mmol), 3,5-bis(trifluoromethyl)phenylboronic acid (424 mg, 1.6 mmol), $Pd(OAc)_2$ (7.6 mg, 0.034 mmol), triphenylphosphine (27 mg, 0.10 mmol), and K_2CO_3 (282 mg, 2.0 mmol) in DMF (5.0 mL) was heated at 90 °C and stirred for 14 h under argon atmosphere. The mixture was poured into saturated NH_4Cl, and filtered with a Celite pad to remove the catalyst. The filtrate was extracted with EtOAc. The extracts were washed with brine and dried over Na_2SO_4. Evaporation of solvents and purification by column chromatography on silica gel (EtOAc/hexane = 1:20 as eluent) afforded (*S*)-3,3′-bis{3,5-bis(trifluoromethyl)phenyl}-2,2′-bis(isopropoxycarbonyl)-1,1′-binaphthyl (*S*)-**6C** (380 mg, 0.44 mmol, 65%): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.02–7.98 (8H, m, Ar-H), 7.91 (2H, s, Ar-H), 7.60 (2H, t, J = 7.4 Hz, Ar-H), 7.44 (2H, t, J = 7.5 Hz, Ar-H), 7.37 (2H, d, J = 8.5 Hz, Ar-H), 4.55–4.49 (2H, m, -C*H*Me_2), 0.56 (6H, d, J = 6.3 Hz, -CH_3), 0.51 ppm (6H, d, J = 6.3 Hz, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.78, 143.21, 135.35, 134.50, 133.09, 132.56, 131.96, 131.75 (q, J_{C-F} = 33.3 Hz), 129.90, 128.86, 128.82, 128.12, 127.87, 127.53, 123.30 (q, J_{C-F} = 273 Hz), 121.29–121.14 (m), 68.75, 20.60, 20.42 ppm; IR (neat): $\tilde{\nu}$ = 2982, 2941, 2878, 1719, 1470, 1377, 1315, 1277, 1229, 1179, 1130, 1098, 1015, 893, 876, 847, 835, 707, 667 cm^{-1}. HRMS (APCI-TOF) calcd for $C_{44}H_{31}F_{12}O_4$, 851.2025 $[M+H]^+$; found, 851.2016 $[M+H]^+$. $[\alpha]_D^{29} = -53.6°$ (c = 1.00, $CHCl_3$).

(*S*)-**6C** (43 mg, 0.051 mmol) in THF (0.5 mL) was added to a suspension of $LiAlH_4$ (6.0 mg, 0.15 mmol) in THF (0.5 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 5 h. The mixture was quenched with H_2O carefully and acidified with 1 N HCl. The mixture was extracted with CH_2Cl_2. The extracts were washed with brine and dried over Na_2SO_4. Concentration followed by column chromatography on silica gel (EtOAc/hexane = 1:20 as eluent) gave (*S*)-3,3′-bis{3,5-bis(trifluoromethyl)phenyl}-2,2′-bis(hydroxymethyl)-1,1′-binaphthyl (*S*)-**7C** (29 mg, 0.039 mmol, 77%): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.23 (4H, s, Ar-H), 7.98 (2H, d, J = 9.4 Hz, Ar-H), 7.97 (2H, s, Ar-H), 7.88 (2H, s, Ar-H), 7.57–7.53 (2H, m, Ar-H), 7.34–7.30 (2H, m, Ar-H), 7.02 (2H, d, J = 8.2 Hz, Ar-H), 4.17 (2H, d, J = 11.5 Hz, -C*H*H-), 4.12 (2H, d, J = 11.5 Hz, -C*H*H-), 3.56 (2H, s, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.96, 138.62, 136.92, 134.68, 132.81, 132.78, 131.31 (q, J_{C-F} = 33.3 Hz), 130.47, 130.27–130.15 (m), 128.30, 127.60, 127.32, 123.38 (q, J_{C-F} = 273 Hz), 121.37–121.21 (m), 59.69; IR (neat): $\tilde{\nu}$ = 3291, 3059, 2949, 2895, 1618, 1470, 1377, 1319, 1274, 1175, 1126, 1105, 1016, 902, 844, 735, 710, 696, 683 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{38}H_{22}F_{12}NaO_2$, 761.1320 $[M+Na]^+$; found, 761.1319 $[M+Na]^+$. $[\alpha]_D^{26} = -21.4°$ (c = 0.80, $CHCl_3$).

*2.3. Preparation of Dibromide (S)-**8C** by Bromination of Diol (S)-**7C***

(*S*)-3,3′-Bis{3,5-bis(trifluoromethyl)phenyl}-2,2′-bis(bromomethyl)-1,1′-binaphthyl (*S*)-8C: PBr_3 (7 μL, 0.074 mmol) was added dropwise to a solution of (*S*)-**7C** (1.0 mL, 55 mg, 0.074 mmol) in THF at 0 °C. The reaction mixture was stirred at same temperature for 0.5 h and poured into H_2O. Extractive workup was performed with Et_2O, and combined extracts were dried over Na_2SO_4. Evaporation of volatiles and purification of the residue by column chromatography on silica gel (EtOAc/hexane = 1:40 as eluent) furnished (*S*)-3,3′-bis{3,5-bis(trifluoromethyl)phenyl}-2,2′-bis(bromomethyl)-1,1′-binaphthyl (*S*)-**8C** (45 mg, 0.052 mmol, 70%): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.15 (4H, br, Ar-H), 8.00–7.95 (6H, m, Ar-H), 7.59 (2H, t, J = 7.5 Hz, Ar-H), 7.38 (2H, t, J = 7.5 Hz, Ar-H), 7.20 (2H, d, J = 8.5 Hz, Ar-H), 4.15 ppm (4H, s, -CH_2-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.26, 137.82, 136.46, 133.00, 132.21, 131.63 (q, J_{C-F} = 33.6 Hz), 131.57, 130.99, 129.85 (br s), 128.17, 128.01, 127.64, 127.19, 123.30 (q, J_{C-F} = 273 Hz), 121.85–121.69 (m), 30.88 ppm; IR (neat): $\tilde{\nu}$ = 1618, 1470, 1375, 1319, 1275, 1171, 1128, 1024, 899, 847, 795, 735, 710, 696, 683 cm^{-1}. HRMS (APCI-TOF) calcd for $C_{38}H_{20}Br_2F_{12}$, 861.9735 $[M]^+$; found, 861.9733 $[M]^+$. $[\alpha]_D^{29} = -48.5°$ (c = 1.00, $CHCl_3$).

*2.4. Representative Procedure for Screening of In Situ Generated Catalyst (S)-**2***

A mixture of (*S*)-**8D** (10.5 mg, 0.015 mmol), Bu_2NH (5 μL, 0.03 mmol), K_2CO_3 (3.1 mg, 0.023 mmol), and dioxane (3.0 mL) in a reaction vessel was held at reflux for 3 h. After cooling to room temperature, toluene (3.0 mL) and glycine derivative **9** (148 mg, 0.50 mmol) were added. The vessel was replaced with argon gas. Continuous addition of 50% aqueous KOH (1.0 mL) and benzyl bromide (73 μL, 0.60 mmol) was performed at 0 °C. The reaction mixture was stirred vigorously at the same temperature for 24 h. The mixture was then poured into H_2O and extracted with ether. The organic extracts were washed with brine and dried over Na_2SO_4. Evaporation of solvents and purification of the residual oil by column chromatography on silica gel (ether/hexane = 1:10 as eluent) gave *tert*-butyl (*R*)-*N*-(diphenylmethylene)phenylalaninate (*R*)-**10** (146 mg, 0.38 mmol, 76% yield). The enantiomeric excess (97% *ee*) was determined by HPLC analysis (Daicel Chiralcel OD, hexane/2-propanol = 100:1, flow rate 0.5 mL min^{-1}, t_R: 14.8 min (*R*) and 28.2 min (*S*)).

2.5. Preparation of Isolated Pure Catalysts

Several catalysts were prepared from corresponding dibromide (*S*)-**8A**, (*S*)-**8B**, (*S*)-**8C**, and (*S*)-**8D**, and purified by column chromatography.[11]

Chiral ammonium salt (*S*)-2Ab: A mixture of dibromide (*S*)-**8A** (220 mg, 0.50 mmol), dibutylamine (169 μL, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in acetonitrile (5.0 mL) was heated at reflux and stirred for 10 h. The resulting mixture was poured into H_2O and extracted with CH_2Cl_2. The organic extracts were washed with brine and dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (MeOH/CH_2Cl_2 = 1:20 as eluent) to furnish (*S*)-**2Ab** (84 mg, 0.17 mmol, 34% yield): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (2H, d, J = 8.2 Hz, Ar-H), 8.08 (2H, d, J = 8.2 Hz, Ar-H), 8.00 (2H, d, J = 8.2 Hz, Ar-H), 7.58 (2H, t, J = 7.5 Hz, Ar-H), 7.41 (2H, d, J = 8.5 Hz, Ar-H), 7.34 (2H, t, J = 7.7 Hz, Ar-H), 5.23 (2H, d, J = 12.9 Hz, Ar-C*H*H-N), 3.85 (2H, td, J = 13.0, 4.3 Hz, N-C*H*H-CH_2), 3.63 (2H, d, J = 12.9 Hz, Ar-C*H*H-N), 3.28 (2H, td, J = 13.0, 4.3 Hz, N-C*H*H-CH_2), 2.08–1.99 (2H, m, -CH_2-), 1.91–1.83 (2H, m, -CH_2-), 1.50–1.34 (4H, m, -CH_2-), 0.97 ppm (6H, t, J = 7.4 Hz, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.45, 134.26, 131.08, 130.03, 128.53, 128.25, 127.41, 126.99, 126.68, 62.96, 58.84, 24.42, 19.92, 13.55 ppm; IR (neat): $\tilde{\nu}$ = 2963, 2933, 2874, 1595, 1508, 1466, 1368, 1030, 923, 874, 828, 727, 640 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{30}H_{34}N$, 408.2686 $[M-Br]^+$; found, 408.2684 $[M-Br]^+$. $[\alpha]_D^{29} = +221.6°$ (c = 0.61, $CHCl_3$).

Chiral ammonium salt (*S*)-2Bb: (66% yield): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.08 (2H, s, Ar-H), 8.02 (2H, d, J = 8.5 Hz, Ar-H), 7.64–7.34 (16H, m, Ar-H), 5.05 (2H, d, J = 13.8 Hz, Ar-C*H*H-N), 3.64 (2H, d, J = 13.8 Hz, Ar-C*H*H-N), 3.04 (2H, t, J = 12.9 Hz, N-C*H*H-CH_2), 2.54 (2H, t, J = 12.6 Hz, N-C*H*H-CH_2), 0.99–0.86 (6H, m, -CH_2-), 0.61 (6H, t, J = 6.5 Hz, -CH_3), 0.09 ppm (2H, br s, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.53, 138.18, 137.88, 133.43, 130.60, 130.19, 129.70 (br),

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129.10 (brs), 128.04, 127.80, 127.76, 127.07, 126.94, 123.24, 56.87, 56.66, 23.53, 19.00, 12.81 ppm; IR (neat): $\tilde{\nu}$ = 2963, 2934, 2874, 1589, 1493, 1469, 1451, 1377, 1029, 923, 878, 852, 723, 704, 637 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{42}H_{42}N$, 560.3312 $[M-Br]^+$; found, 560.3306 $[M-Br]^+$. $[\alpha]_D^{28}$ = +38.9° (c = 1.04, $CHCl_3$).

Chiral ammonium salt (*S*)-2Bg: (63% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (1H, s, Ar-H), 8.09 (1H, s, Ar-H), 8.07 (1H, d, J = 8.2 Hz, Ar-H), 8.06 (1H, d, J = 8.2 Hz, Ar-H), 7.68–7.64 (2H, m, Ar-H), 7.58–7.33 (12H, m, Ar-H), 7.27 (1H, brs, Ar-H), 7.21 (1H, t, J = 7.5 Hz, Ar-H), 7.04 (1H, t, J = 7.4 Hz, Ar-H), 6.93 (1H, t, J = 7.6 Hz, Ar-H), 6.78 (1H, d, J = 7.7 Hz, Ar-H), 6.55 (1H, d, J = 7.7 Hz, Ar-H), 5.21 (1H, d, J = 13.8 Hz, N-C*H*H-), 5.14 (1H, d, J = 13.1 Hz, N-C*H*H-), 4.81 (1H, d, J = 15.5 Hz, N-C*H*H-), 3.94–3.78 (4H, m, -CH_2-), 3.06–2.99 (1H, m, -C*H*H-), 2.91–2.83 (1H, m, -C*H*H-), 2.21–2.14 ppm (1H, m, -C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.84, 139.69, 138.26, 137.97, 137.83, 137.64, 133.65, 133.63, 130.88, 130.77, 130.36, 129.99, 129.50, 129.10, 128.73 (br), 128.28, 128.22, 127.94, 127.90, 127.79, 127.54, 127.16, 127.10, 127.06, 126.72, 124.59, 123.34, 123.20, 59.24, 59.09, 55.70, 55.00, 22.72 ppm; IR (neat): $\tilde{\nu}$ = 3055, 1589, 1495, 1451, 1031, 924, 907, 723, 704, 636 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{43}H_{34}N$, 564.2686 $[M-Br]^+$; found 564.2683 $[M-Br]^+$. $[\alpha]_D^{31}$ = +177.9° (c = 1.01, $CHCl_3$).

Chiral ammonium salt (*S*)-2Cb: (88% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (2H, brs, Ar-H), 8.09 (2H, s, Ar-H), 8.09 (2H, d, J = 7.7 Hz, Ar-H), 8.03 (4H, brs, Ar-H), 7.70 (2H, t, J = 7.4 Hz, Ar-H), 7.45 (2H, t, J = 7.5 Hz, Ar-H), 7.38 (2H, d, J = 8.5 Hz, Ar-H), 4.79 (2H, d, J = 13.8 Hz, Ar-C*H*H-N), 4.02 (2H, d, J = 13.8 Hz, Ar-C*H*H-N), 3.29 (2H, t, J = 12.6 Hz, N-C*H*H-CH_2), 2.65 (2H, td, J = 13.3, 4.6 Hz, N-C*H*H-CH_2), 1.07 (4H, brs, -CH_2-), 0.86 (2H, brs, -CH_2-), 0.61 (6H, t, J = 7.0 Hz, -CH_3), 0.28 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.23, 138.68, 136.71, 133.78, 132.95 (br), 132.54, 131.24, 130.14 (d, J_{C-F} = 53.3 Hz), 128.94, 128.73, 128.42, 127.62, 122.84 (q, J_{C-F} = 274 Hz), 122.74, 122.31, 57.71, 57.57, 24.51, 19.06, 13.35 ppm; IR (neat): $\tilde{\nu}$ = 2967, 2937, 2878, 1618, 1470, 1369, 1279, 1175, 1134, 925, 897, 847, 729, 683 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{46}H_{38}F_{12}N$, 832.2807 $[M-Br]^+$; found, 832.2797 $[M-Br]^+$. $[\alpha]_D^{31}$ = +22.2° (c = 1.04, $CHCl_3$).

Chiral ammonium salt (*S*)-2Cc: (50% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (2H, br, Ar-H), 8.10–8.03 (8H, m, Ar-H), 7.72–7.68 (2H, m, Ar-H), 7.48–7.44 (2H, m, Ar-H), 7.39 (2H, d, J = 8.5 Hz, Ar-H), 4.83 (2H, d, J = 13.8 Hz, Ar-C*H*H-N), 4.04 (2H, d, J = 13.8 Hz, Ar-C*H*H-N), 3.23 (2H, t, J = 12.6 Hz, N-C*H*H-CH_2), 2.68 (2H, td, J = 13.0, 5.3 Hz, N-C*H*H-CH_2), 1.27–0.80 (30H, m, -CH_2-), 0.86 (6H, t, J = 7.0 Hz, -CH_3), 0.30 ppm (2H, br, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.29, 138.64, 136.73, 133.72, 132.44, 131.24, 130.48–129.94 (m), 128.84, 128.66, 128.32, 127.61, 122.85, 122.80 (q, J_{C-F} = 274 Hz), 122.22–122.15 (m), 57.70, 57.60, 31.63, 29.17, 29.03, 28.95, 25.70, 22.47, 13.90 ppm; IR (neat): $\tilde{\nu}$ = 2955, 2926, 2857, 1618, 1470, 1371, 1276, 1179, 1136, 1024, 897, 847, 683 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{58}H_{62}F_{12}N$, 1000.4685 $[M-Br]^+$; found, 1000.4655 $[M-Br]^+$. $[\alpha]_D^{31}$ = +15.4° (c = 1.04, $CHCl_3$).

Chiral ammonium salt (*S*)-2Di: (69% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (2H, d, J = 8.2 Hz, Ar-H), 8.04 (2H, s, Ar-H), 7.65 (2H, t, J = 7.5 Hz, Ar-H), 7.43–7.31 (8H, m, Ar-H), 4.92 (2H, d, J = 13.7 Hz, Ar-C*H*H-N), 4.03 (2H, br, N-C*H*H-CH_2), 3.98 (2H, d, J = 13.7 Hz, Ar-C*H*H-N), 3.69 (2H, br, N-C*H*H-CH_2), 3.56–3.35 (14H, m, -CH_2-), 3.09–3.04 ppm (2H, m, -CH_2-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.08 (d, J_{C-F} = 255 Hz), 139.74 (d, J_{C-F} = 253 Hz), 138.20, 136.92, 134.97–134.82 (m), 133.52, 131.46, 130.86, 128.59, 128.47, 127.84, 127.29, 123.21, 114.67 (d, J_{C-F} = 21.3 Hz), 69.98, 69.25, 69.10, 64.40, 59.97, 59.73 ppm; IR (neat): $\tilde{\nu}$ = 2943, 2901, 2868, 1614, 1526, 1447, 1360, 1242, 1126, 1045, 923, 894, 729 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{44}H_{38}F_6NO_4$, 758.2700 $[M-Br]^+$; found, 758.2696$[M-Br]^+$. $[\alpha]_D^{30}$ = +17.7° (c 1.04, $CHCl_3$).

*3. Preparation of Chiral Ammonium Salts (S)-**2** for the Study of Substituent Effects of R (Alkyl Groups)*

Catalysts having the different number of straight alkyl chains were prepared from dibromide (*S*)-**8D** and commercially available dialkylamines in a manner similar to that described above.

Chiral ammonium salt (*S*)-2Da (R = Me): (88% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (2H, d, J = 8.0 Hz, Ar-H), 8.03 (2H, s, Ar-H), 7.66 (2H, t, J = 7.3 Hz, Ar-H), 7.42 (2H, t, J = 7.5 Hz, Ar-H), 7.38 (2H, d, J = 8.8 Hz, Ar-H), 7.11 (4H, brs, Ar-H), 4.94 (2H, d, J = 13.9 Hz, Ar-C*H*H-N), 3.74 (2H, d, J = 13.5 Hz, Ar-C*H*H-N), 2.99 ppm (6H, s, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.39 (ddd, J_{C-F} = 254, 10.0, 3.9 Hz), 140.07 (dt, J_{C-F} = 254, 15.0 Hz), 137.96, 137.10, 134.36–134.17 (m), 133.71, 131.33, 131.01, 128.71, 128.68, 128.08, 127.37, 123.92, 114.84–114.59 (m), 61.11, 51.06 ppm; IR (neat): $\tilde{\nu}$ = 2961, 2928, 1614, 1528, 1447, 1423, 1362, 1242, 1045, 907, 856, 727, 640 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{36}H_{24}F_6N$, 584.1807 $[M-Br]^+$; found, 584.1806 $[M-Br]^+$. $[\alpha]_D^{30}$ = +31.1° (c = 0.50, $CHCl_3$).

Chiral ammonium salt (*S*)-2Dj (R = Et): (87% yield): ^{1}H NMR (400 MHz, $CDCl_3$/CD_3OD = 4:1): δ = 8.10 (2H, s, Ar-H), 8.09 (2H, d, J = 8.2 Hz, Ar-H), 7.70 (2H, t, J = 7.3 Hz, Ar-H), 7.47–7.38 (6H, m, Ar-H), 7.20 (2H, brs, Ar-H), 4.76 (2H, d, J = 13.8 Hz, Ar-C*H*H-N), 3.65 (2H, d, J = 13.8 Hz, Ar-C*H*H-N), 3.17–3.12 (2H, m, N-C*H*H-CH_2), 2.79–2.74 (2H, m, N-C*H*H-CH_2), 0.64 ppm (6H, t, J = 6.9 Hz, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$/CD_3OD = 4:1): δ = 151.25 (d, J_{C-F} = 264 Hz), 139.59 (dt, J_{C-F} = 255, 15.0 Hz), 138.08, 136.68, 134.73–134.52 (m), 133.46, 131.28, 130.64, 128.44, 128.41, 127.84, 127.10, 122.82, 114.54 (br), 55.78, 51.76, 7.43 ppm; IR (neat): $\tilde{\nu}$ = 2980, 2913, 1614, 1528, 1472, 1449, 1418, 1362, 1242, 1047, 895, 858, 810, 679 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{38}H_{28}F_6N$, 612.2120 $[M-Br]^+$; found, 612.2125 $[M-Br]^+$. $[\alpha]_D^{33}$ = +16.5° (c = 0.40, $CHCl_3$).

Chiral ammonium salt (*S*)-2Db (R = Bu): Prepared as described in the Supporting Information in reference [11a].

Chiral ammonium salt (*S*)-2Dk (R = hexyl): (79% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (2H, s, Ar-H), 7.98 (2H, d, J = 8.2 Hz, Ar-H), 7.58–7.54 (2H, m, Ar-H), 7.34–7.25 (8H, m, Ar-H), 5.01 (2H, d, J = 14.0 Hz, Ar-C*H*H-N), 3.75 (2H, d, J = 14.0 Hz, Ar-C*H*H-N), 3.29 (2H, t, J = 12.7 Hz, N-C*H*H-CH_2), 2.60 (2H, td, J = 13.0, 4.4 Hz, N-C*H*H-CH_2), 1.21–0.98 (10H, m, -CH_2-), 0.95–0.88 (4H, m, -CH_2-), 0.83 (6H, t, J = 7.3 Hz, -CH_3), 0.35 ppm (2H, br, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.22 (d, J_{C-F} = 252 Hz), 139.86 (dt, J_{C-F} = 256, 14.5 Hz), 138.49, 137.01, 134.84–134.64 (m), 133.61, 131.39, 130.97, 128.53, 128.50, 127.91, 127.53, 123.37, 114.78 (d, J_{C-F} = 157 Hz), 57.52, 57.46, 31.22, 25.76, 22.85, 22.39, 13.67 ppm; IR (neat): $\tilde{\nu}$ = 2957, 2928, 2860, 1614, 1585, 1526, 1470, 1449, 1425, 1362, 1242, 1047, 893, 860, 845, 708 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{46}H_{44}F_6N$, 724.3372 $[M-Br]^+$; found, 724.3376 $[M-Br]^+$. $[\alpha]_D^{27}$ = +7.5° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Dl (R = octyl): (83% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (2H, s, Ar-H), 7.97 (2H, d, J = 7.3 Hz, Ar-H), 7.57–7.52 (2H, m, Ar-H), 7.32–7.26 (8H, m, Ar-H), 4.99 (2H, d, J = 14.3 Hz, Ar-C*H*H-N), 3.76 (2H, d, J = 14.3 Hz, Ar-C*H*H-N), 3.20 (2H, t, J = 12.5 Hz, N-C*H*H-CH_2), 2.60 (2H, t, J = 12.5 Hz, N-C*H*H-CH_2), 1.28–0.90 (22H, m, -CH_2-), 0.86 (6H, t, J = 7.0 Hz, -CH_3), 0.32 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.12 (d, J_{C-F} = 254 Hz), 139.75 (dt, J_{C-F} = 255, 15.2 Hz), 138.47, 137.02, 134.86–134.66 (m), 133.53, 131.26, 130.96, 128.42, 127.81, 127.49, 123.41, 114.78 (d, J_{C-F} = 157 Hz), 57.33, 57.27, 31.44, 29.08, 28.94, 26.06, 22.76, 22.37, 13.87 ppm; IR (neat): <Gn 2955, 2926, 2857, 1614, 1585, 1526, 1470, 1447, 1425, 1360, 1258, 1242, 1213, 1047, 895, 858, 727, 710 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{50}H_{52}F_6N$, 780.3998 $[M-Br]^+$; found, 780.4000 $[M-Br]^+$. $[\alpha]_D^{26}$ = +2.8° (c = 1.00, $CHCl_3$).

*4. Synthesis of C_2-Symmetric Chiral Ammonium Salts (S)-**2** with Various Aryl Groups: Representative Procedure for the Synthesis of Chiral Ammonium Salts (S)-**2Gb**–(S)-**2ABb***

(*S*)-2,2′-Bis(isopropoxycarbonyl)-3,3′-bis(4-methoxyphenyl)-1,1′-binaphthyl [(*S*)-6G (Ar = 4-methoxyphenyl)]: A mixture of dibromide (*S*)-**3** (1.42 g, 2.44 mmol), 4-methoxyphenylboronic acid (0.890 g, 5.86 mmol), $Pd(OAc)_2$ (27 mg, 0.12 mmol) triphenylphosphine (96 mg, 0.37 mmol), and K_2CO_3 (1.01 g, 7.32 mmol) in DMF (10 mL) was degassed and backfilled with argon gas, and heated at 90 °C for 16 h. The mixture was poured into saturated NH_4Cl and filtered to remove the catalyst. The filtrate was extracted with EtOAc. The extracts were washed with brine and dried over Na_2SO_4. Evaporation of solvents and purification by column chromatography on silica gel (EtOAc/hexane = 1:5 as eluent) afforded (*S*)-2,2′-bis(isopropoxycarbonyl)-3,3′-bis(4-methoxyphenyl)-1,1′-bi-

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naphthyl (*S*)-**6G** (895 mg, 1.40 mmol, 57% yield) as a pale yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.92 (2H, s, Ar-H), 7.89 (2H, d, J=8.2 Hz, Ar-H), 7.52–7.48 (2H, m, Ar-H), 7.46 (4H, d, J=8.7 Hz, Ar-H), 7.34–7.29 (4H, m, Ar-H), 6.94 (4H, d, J=8.7 Hz, Ar-H), 4.56–4.46 (2H, m, -CHMe$_2$), 3.84 (6H, s, -OCH_3), 0.55 (6H, d, J=7.7 Hz, -CH_3), 0.54 ppm (6H, d, J=7.7 Hz, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=167.36, 158.92, 136.79, 134.25, 133.38, 133.04, 132.89, 131.69, 129.66, 128.76, 127.53, 127.45, 127.03, 126.29, 113.53, 67.62, 55.05, 20.69, 20.53 ppm; IR (neat): $\tilde{\nu}$=3061, 2978, 2934, 2835, 1717, 1609, 1514, 1464, 1271, 1246, 1177, 1140, 1100, 1034, 907, 829, 731 cm^{-1}. HRMS (APCI-TOF) calcd for $C_{42}H_{39}O_6$, 639.2741 [M+H]$^+$; found, 639.2736 [M+H]$^+$. $[\alpha]_D^{30}$=−53.1° (c=1.15, $CHCl_3$).

(*S*)-2,2′-Bis(hydroxymethyl)-3,3′-bis(4-methoxyphenyl)-1,1′-binaphthyl [(*S*)-7G (Ar=4-methoxyphenyl)]: (*S*)-**6G** (319 mg, 0.50 mmol) in THF (5.0 mL) was added to a suspension of $LiAlH_4$ (114 mg, 3.0 mmol) in THF (5 mL) at 0°C and the reaction mixture was stirred at room temperature for 1 h. The mixture was quenched with H_2O carefully and acidified with 1N HCl. The resulting mixture was extracted with CH_2Cl_2. The extracts were washed with brine and dried over Na_2SO_4. Concentration followed by column chromatography on silica gel (EtOAc/CH_2Cl_2/hexane=1:2:4 as eluent) gave (*S*)-2,2′-bis(hydroxymethyl)-3,3′-bis(4-methoxyphenyl)-1,1′-binaphthyl (*S*)-**7G** (216 mg, 0.41 mmol, 82% yield) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.94 (2H, s, Ar-H), 7.92 (2H, d, J=8.2 Hz, Ar-H), 7.65 (4H, d, J=8.0 Hz, Ar-H), 7.47 (2H, t, J=7.5 Hz, Ar-H), 7.24–7.22 (2H, m, Ar-H), 7.03–7.00 (6H, m, Ar-H), 4.42 (2H, d, J=11.4 Hz, Ar-C*H*H-), 4.17 (2H, d, J=11.4 Hz, Ar-C*H*H-), 3.88 (3H, s, -OCH_3), 3.88 (3H, s, -OCH_3), 3.20 ppm (2H, brs, -OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=158.79, 141.13, 136.65, 135.92, 133.32, 132.95, 132.19, 130.87, 129.62, 127.98, 126.45, 126.31, 126.14, 113.34, 59.72, 55.16 ppm; IR (neat): $\tilde{\nu}$=3287, 3057, 2955, 2899, 2835, 1609, 1512, 1285, 1244, 1177, 1028, 981, 907, 831, 727, 648, 617 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{36}H_{30}NaO_4$, 549.2036 [M+Na]$^+$; found, 549.2044 [M+Na]$^+$. $[\alpha]_D^{30}$=−21.1° (c=0.96, $CHCl_3$).

(*S*)-2,2′-Bis(bromomethyl)-3,3′-bis(4-methoxyphenyl)-1,1′-binaphthyl (*S*)-8G: PBr_3 (28 μL, 0.30 mmol) was added dropwise to a solution of (*S*)-**7G** (1.0 mL, 158 mg, 0.30 mmol) in THF at 0°C. The reaction mixture was stirred at the same temperature for 1 h and poured into H_2O. Extractive workup was performed with CH_2Cl_2, and combined extracts were dried over Na_2SO_4. Evaporation of solvents and purification of the residue by column chromatography on silica gel (EtOAc/CH_2Cl_2/hexane=1:1:10 as eluent) afforded (*S*)-2,2′-bis(bromomethyl)-3,3′-bis(4-methoxyphenyl)-1,1′-binaphthyl (*S*)-**8G** (127 mg, 0.19 mmol, 65%) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.88 (2H, s, Ar-H), 7.87 (2H, d, J=8.9 Hz, Ar-H), 7.54 (4H, d, J=8.7 Hz, Ar-H), 7.47 (2H, t, J=7.4 Hz, Ar-H), 7.24 (2H, t, J=7.6 Hz, Ar-H), 7.15 (2H, d, J=8.5 Hz, Ar-H), 7.01 (4H, d, J=8.7 Hz, Ar-H), 4.29 (4H, s, Ar-CH_2-), 3.85 ppm (6H, s, -OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.03, 140.63, 136.36, 133.17, 132.78, 132.54, 131.71, 130.60, 130.44, 127.78, 127.26, 127.13, 126.35, 113.57, 55.24, 32.29 ppm; IR (neat): $\tilde{\nu}$=3055, 2999, 2955, 2932, 2911, 1609, 1512, 1464, 1437, 1287, 1177, 1107, 1034, 907, 866, 839, 727, 650, 617 cm^{-1}. HRMS (APCI-TOF) calcd for $C_{36}H_{28}Br_2O_2$, 650.0451 [M]$^+$; found, 650.0443 [M]$^+$. $[\alpha]_D^{30}$=−5.9° (c=1.10, $CHCl_3$).

Chiral ammonium salt (*S*)-2Gb (Ar=4-methoxyphenyl, R=Bu): A mixture of (*S*)-**8G** (66 mg, 0.10 mmol), dibutylamine (34 μL, 0.20 mmol), and K_2CO_3 (21 mg, 0.15 mmol) in acetonitrile (3.0 mL) was heated at reflux and stirred for 3 h. The resulting mixture was poured into H_2O and extracted with CH_2Cl_2. The organic extracts were washed with brine and dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (MeOH/CH_2Cl_2=1:20 as eluent) to furnish (*S*)-**2Gb** (60 mg, 0.086 mmol, 86% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.05 (2H, s, Ar-H), 8.01 (2H, d, J=8.2 Hz, Ar-H), 7.64–7.60 (2H, m, Ar-H), 7.50 (4H, d, J=7.7 Hz, Ar-H), 7.36–7.33 (4H, m, Ar-H), 7.12 (4H, d, J=7.7 Hz, Ar-H), 5.13 (2H, d, J=13.5 Hz, Ar-C*H*H-N), 3.88 (6H, s, -OCH_3), 3.60 (2H, d, J=13.5 Hz, Ar-C*H*H-N), 3.15 (2H, t, J=13.1 Hz, N-C*H*H-CH_2), 2.55 (2H, td, J=12.6, 4.5 Hz, N-C*H*H-CH_2), 1.01–0.88 (6H, m, -CH_2-), 0.65 (6H, t, J=7.0 Hz, -CH_3), 0.23 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.54, 139.70, 138.27, 133.88, 131.28, 130.77, 130.74, 130.43, 128.31, 128.05, 127.51, 127.07, 124.06, 114.99, 57.52, 57.14, 55.58, 24.37, 19.76, 13.47 ppm; IR (neat): $\tilde{\nu}$=2960, 2934, 1606, 1510, 1468, 1440, 1288, 1248, 1177, 1030, 912, 908, 831, 638 cm^{-1}. HRMS calcd for $C_{44}H_{46}NO_2$, 620.3523 [M−Br]$^+$; found, 620.3524 [M−Br]$^+$. $[\alpha]_D^{23}$=−9.9° (c=0.50, $CHCl_3$).

Chiral ammonium salt (*S*)-2Hb (Ar=4-biphenylyl, R=Bu): (72% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.14 (2H, s, Ar-H), 8.05 (2H, d, J=8.2 Hz, Ar-H), 7.85–7.83 (4H, m, Ar-H), 7.69–7.63 (10H, m, Ar-H), 7.46 (4H, t, J=7.5 Hz, Ar-H), 7.40–7.36 (6H, m, Ar-H), 5.20 (2H, d, J=13.8 Hz, Ar-C*H*H-N), 3.70 (2H, d, J=13.8 Hz, Ar-C*H*H-N), 3.19 (2H, t, J=13.1 Hz, N-C*H*H-CH_2), 2.61 (2H, td, J=12.6, 4.5 Hz, N-C*H*H-CH_2), 0.99–0.87 (6H, m, -CH_2-), 0.55 (6H, t, J=6.9 Hz, -CH_3), 0.28 ppm (2H, br, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ=141.12, 139.76, 139.71, 138.46, 137.47, 133.95, 131.10, 130.76, 130.70, 128.91, 128.51, 128.27, 128.14, 127.78, 127.61, 127.43, 127.07, 123.88, 57.43, 57.16, 24.34, 19.59, 13.36 ppm; IR (neat): $\tilde{\nu}$=2961, 2918, 1599, 1487, 1470, 1244, 1028, 852, 696, 658 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{54}H_{50}N$, 712.3938 [M−Br]$^+$; found, 712.3934 [M−Br]$^+$. $[\alpha]_D^{32}$=+10.7° (c=0.30, $CHCl_3$).

Chiral ammonium salt (*S*)-2Ib (Ar=4-(pentafluorophenyl)phenyl, R=Bu): (70% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.15 (2H, s, Ar-H), 8.07 (2H, d, J=8.2 Hz, Ar-H), 7.77 (4H, brs, Ar-H), 7.70–7.65 (6H, m, Ar-H), 7.44–7.37 (4H, m, Ar-H), 5.20 (2H, d, J=13.7 Hz, Ar-C*H*H-N), 3.76 (2H, d, J=13.7 Hz, Ar-C*H*H-N), 3.27 (2H, t, J=12.8 Hz, N-C*H*H-CH_2), 2.64 (2H, td, J=13.1, 4.5 Hz, N-C*H*H-CH_2), 1.04–0.96 (6H, m, -CH_2-), 0.63 (6H, t, J=7.0 Hz, -CH_3), 0.39 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ=143.92 (d, J_{C-F}=244 Hz), 140.58 (d, J_{C-F}=255 Hz), 139.53, 138.98, 138.47, 137.82 (d, J_{C-F}=255 Hz), 133.83, 131.80–129.90 (m), 131.44, 131.29, 130.78, 128.52, 128.39, 127.66, 127.51, 126.55, 123.50, 114.83, 57.51, 57.43, 24.29, 19.51, 13.25 ppm; IR (neat): $\tilde{\nu}$=2964, 2926, 1653, 1508, 1493, 1471, 1261, 1223, 1153, 1063, 1030, 988, 849, 637, 573 cm^{-1}. HRMS calcd for $C_{54}H_{40}F_{10}N$, 892.2996 [M−Br]$^+$; found, 892.3001 [M−Br]$^+$. $[\alpha]_D^{23}$=+8.1° (c=0.6, $CHCl_3$).

Chiral ammonium salt (*S*)-2Jb (Ar=4-(3,4,5-trifluorophenyl)phenyl, R=Bu): (98% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.13 (2H, s, Ar-H), 8.07 (2H, d, J=8.2 Hz, Ar-H), 7.77–7.65 (10H, m, Ar-H), 7.44–7.37 (4H, m, Ar-H), 7.31 (2H, d, J=8.2 Hz, Ar-H), 7.29 (2H, d, J=8.2 Hz, Ar-H), 5.19 (2H, d, J=13.5 Hz, Ar-C*H*H-N), 3.70 (2H, d, J=13.5 Hz, Ar-C*H*H-N), 3.26 (2H, t, J=13.1 Hz, N-C*H*H-CH_2), 2.59 (2H, td, J=12.6, 4.2 Hz, N-C*H*H-CH_2), 1.02–0.94 (4H, m, -CH_2-), 0.88–0.81 (2H, m, -CH_2-), 0.55 (6H, t, J=7.0 Hz, -CH_3), 0.27–0.24 ppm (2H, brm, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ=151.44 (ddd, J_{C-F}=250, 9.5, 4.5 Hz), 139.48 (d, J_{C-F}=256 Hz), 139.12, 138.55, 138.46, 137.95, 135.94–135.78 (m), 133.85, 131.09, 130.92 (brs), 130.72, 128.49, 128.37, 127.90, 127.59, 127.52, 123.65, 111.04 (dd, J_{C-F}=16.0, 6.2 Hz), 57.53, 57.31, 24.59, 19.70, 13.53 ppm; IR (neat): $\tilde{\nu}$=2960, 2924, 1616, 1535, 1508, 1437, 1364, 1246, 1041, 1013, 897, 852 cm^{-1}. HRMS calcd for $C_{54}H_{44}F_6N$, 820.3372 [M−Br]$^+$; found, 820.3376 [M−Br]$^+$. $[\alpha]_D^{23}$=+13.3° (c=0.7, $CHCl_3$).

Chiral ammonium salt (*S*)-2Kb (Ar=4-fluorophenyl, R=Bu): (84% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.06 (2H, s, Ar-H), 8.03 (2H, d, J=8.2 Hz, Ar-H), 7.66–7.62 (2H, m, Ar-H), 7.59 (4H, brs, Ar-H), 7.41–7.28 (8H, m, Ar-H), 5.10 (2H, d, J=13.7 Hz, Ar-C*H*H-N), 3.67 (2H, d, J=13.7 Hz, Ar-C*H*H-N), 3.22 (2H, t, J=13.2 Hz, N-C*H*H-CH_2), 2.56 (2H, td, J=12.4, 4.4 Hz, N-C*H*H-CH_2), 1.05–0.98 (4H, m, -CH_2-), 0.92–0.85 (2H, m, -CH_2-), 0.68 (6H, t, J=7.0 Hz, -CH_3), 0.24–0.21 ppm (2H, brm, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.28 (d, J_{C-F}=249 Hz), 138.54, 138.11, 134.41 (d, J_{C-F}=3.3 Hz), 133.55, 131.71 (brs), 130.87, 130.42, 128.17, 128.03, 127.23, 127.19, 123.46, 116.32 (d, J_{C-F}=21.3 Hz), 57.20, 57.08, 24.11, 19.41, 13.18 ppm; IR (neat): $\tilde{\nu}$=2962, 2873, 1603, 1508, 1470, 1159, 922, 907, 877, 856, 833, 823, 638, 609, 569 cm^{-1}. HRMS calcd for $C_{42}H_{40}F_2N$, 596.3123 [M−Br]$^+$; found, 596.3122 [M−Br]$^+$. $[\alpha]_D^{30}$=+33.1° (c=1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Lb (Ar=4-chlorophenyl, R=Bu): (91% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.05 (2H, s, Ar-H), 8.03 (2H, d, J=8.2 Hz, Ar-H), 7.65–7.61 (2H, m, Ar-H), 7.56 (8H, brs, Ar-H), 7.39–7.32 (4H, m, Ar-H), 5.02 (2H, d, J=13.9 Hz, Ar-C*H*H-N), 3.67 (2H, d, J=13.9 Hz, Ar-C*H*H-N), 3.12 (2H, t, J=12.9 Hz, N-C*H*H-CH_2), 2.55 (2H, td, J=13.0, 4.4 Hz, N-C*H*H-CH_2), 1.04–0.96 (4H, m, -CH_2-), 0.90–0.83 (2H, m, -CH_2-), 0.68 (6H, t, J=7.0 Hz, -CH_3), 0.21–0.18 ppm (2H, brm, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ=138.52, 138.23,

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136.84, 134.55, 133.66, 131.35, 130.98, 130.57, 129.58, 128.33, 128.22, 127.43, 127.36, 123.39, 57.35, 57.14, 24.35, 19.62, 13.29 ppm; IR (neat): $\tilde{\nu}$ = 2963, 2874, 1620, 1595, 1491, 1470, 1364, 1269, 1092, 1028, 1015, 922, 903, 878, 853, 826 cm^{-1}. HRMS calcd for $C_{42}H_{40}Cl_2N$, 628.2532 $[M-Br]^+$; found, 628.2532 $[M-Br]^+$. $[\alpha]_D^{23}$ = +27.6° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Mb (Ar = 4-cyanophenyl, R = Bu): (82% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (2H, s, Ar-H), 8.07 (2H, d, J = 8.2 Hz, Ar-H), 7.91 (4H, d, J = 8.2 Hz, Ar-H), 7.78 (4H, d, J = 8.2 Hz, Ar-H), 7.69 (2H, t, J = 7.5 Hz, Ar-H), 7.44 (2H, t, J = 7.7 Hz, Ar-H), 7.35 (2H, d, J = 8.5 Hz, Ar-H), 5.04 (2H, d, J = 14.0 Hz, Ar-C*H*H-N), 3.74 (2H, d, J = 14.0 Hz, Ar-C*H*H-N), 3.23 (2H, t, J = 12.8 Hz, N-C*H*H-CH_2), 2.54 (2H, td, J = 13.1, 4.4 Hz, N-C*H*H-CH_2), 1.05–0.95 (4H, m, -CH_2-), 0.89–0.81 (2H, m, -CH_2-), 0.67 (6H, t, J = 7.0 Hz, -CH_3), 0.19 ppm (2H, br, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.13, 138.65, 138.12, 133.84, 133.28, 131.61, 131.07, 128.83, 128.75, 128.25, 127.57, 123.08, 117.99, 112.46, 57.49, 57.45, 24.41, 19.50, 13.36 ppm; IR (neat): $\tilde{\nu}$ = 2961, 2924, 2228, 1605, 1470, 1366, 1248, 1026, 901, 854, 660, 606, 577 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{44}H_{40}N_3$, 610.3217 ($[M-Br]^+$); found, 610.3222 $[M-Br]^+$. $[\alpha]_D^{29}$ = +22.8° (c = 0.60, $CHCl_3$).

Chiral ammonium salt (*S*)-2Nb (Ar = 4-(trifluoromethoxy)phenyl, R = Bu): (80% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (2H, s, Ar-H), 8.03 (2H, d, J = 8.2 Hz, Ar-H), 7.66–7.62 (6H, m, Ar-H), 7.46–7.33 (8H, m, Ar-H), 5.04 (2H, d, J = 13.8 Hz, Ar-C*H*H-), 3.72 (2H, d, J = 13.8 Hz, Ar-C*H*H-), 3.16 (2H, t, J = 12.7 Hz, N-C*H*H-CH_2), 2.59 (2H, td, J = 12.7, 4.7 Hz, N-C*H*H-CH_2), 1.01–0.83 (6H, m, -CH_2-), 0.65 (6H, t, J = 7.0 Hz, -CH_3), 0.25–0.22 ppm (2H, brm, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.18–149.12 (m), 138.36, 138.35, 137.12, 133.72, 131.57, 131.33, 130.70, 128.42, 128.36, 127.59, 127.45, 123.38, 121.68, 120.29 (q, J_{C-F} = 257 Hz), 57.39, 57.34, 24.34, 19.52, 13.21 ppm; IR (neat): $\tilde{\nu}$ = 2964, 2876, 1612, 1508, 1470, 1256, 1165, 1030, 922, 854, 584 cm^{-1}. HRMS calcd for $C_{44}H_{40}F_6NO_2$, 728.2958 $[M-Br]^+$; found, 728.2960 $[M-Br]^+$. $[\alpha]_D^{23}$ = +29.9° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Ob (Ar = 4-(trifluoromethyl)phenyl, R = Bu): (80% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (2H, s, Ar-H), 8.03 (2H, d, J = 8.2 Hz, Ar-H), 7.84 (4H, d, J = 8.5 Hz, Ar-H), 7.79 (4H, d, J = 8.5 Hz, Ar-H), 7.65–7.61 (2H, m, Ar-H), 7.40–7.33 (4H, m, Ar-H), 5.04 (2H, d, J = 13.8 Hz, Ar-C*H*H-N), 3.74 (2H, d, J = 13.8 Hz, Ar-C*H*H-N), 3.15 (2H, t, J = 12.8 Hz, N-C*H*H-CH_2), 2.55 (2H, td, J = 12.8, 4.5 Hz, N-C*H*H-CH_2), 0.98–0.86 (4H, m, -CH_2-), 0.82–0.79 (2H, m, -CH_2-), 0.58 (6H, t, J = 7.1 Hz, -CH_3), 0.10 (2H, br, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.37, 138.60, 138.52, 133.88, 131.60, 131.02, 130.83, 130.42 (q, J_{C-F} = 32.8 Hz), 128.68, 128.60, 127.93, 127.64, 126.49 (q, J_{C-F} = 3.6 Hz), 123.96 (q, J_{C-F} = 273 Hz), 123.42, 57.36, 24.41, 19.41, 13.08; IR (neat): $\tilde{\nu}$ = 2965, 2910, 1616, 1470, 1321, 1167, 1125, 1109, 1067, 1016, 901, 854 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{44}H_{40}F_6N$, 696.3059 $[M-Br]^+$; found, 696.3052 $[M-Br]^+$. $[\alpha]_D^{29}$ = +33.4° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Pb (Ar = 4-nitrophenyl, R = Bu): (64% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (4H, d, J = 8.3 Hz, Ar-H), 8.11 (2H, s, Ar-H), 8.06 (2H, d, J = 8.2 Hz, Ar-H), 7.85 (4H, d, J = 8.3 Hz, Ar-H), 7.68–7.64 (2H, m, Ar-H), 7.43–7.39 (2H, m, Ar-H), 7.35 (2H, d, J = 8.2 Hz, Ar-H), 5.01 (2H, d, J = 14.0 Hz, Ar-C*H*H-N), 3.78 (2H, d, J = 14.0 Hz, Ar-C*H*H-N), 3.20 (2H, t, J = 12.6 Hz, N-C*H*H-CH_2), 2.56 (2H, td, J = 12.9, 4.2 Hz, N-C*H*H-CH_2), 0.99–0.90 (4H, m, -CH_2-), 0.88–0.78 (2H, m, -CH_2-), 0.56 (6H, t, J = 7.1 Hz, -CH_3), 0.17 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.55, 145.07, 138.64, 137.71, 133.74, 131.59, 131.49 (br), 131.12, 128.77, 128.73, 128.24, 127.57, 124.59, 123.11, 57.46, 57.37, 24.37, 19.39, 13.22 ppm; IR (neat): $\tilde{\nu}$ = 2961, 2928, 2874, 1597, 1516, 1472, 1344, 1265, 1105, 1015, 901, 847, 704, 660 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{42}H_{40}N_3O_4$, 650.3013 $[M-Br]^+$; found 650.3012 $[M-Br]^+$. $[\alpha]_D^{30}$ = −8.6° (c = 0.80, $CHCl_3$).

Chiral ammonium salt (*S*)-2Qb (Ar = 3-chlorophenyl, R = Bu): (76% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (2H, s, Ar-H), 8.04 (2H, d, J = 8.2 Hz, Ar-H), 7.65 (2H, t, J = 7.4 Hz, Ar-H), 7.60 (6H, brs, Ar-H), 7.48 (2H, d, J = 7.5 Hz, Ar-H), 7.40 (2H, t, J = 7.6 Hz, Ar-H), 7.35 (2H, d, J = 8.5 Hz, Ar-H), 5.35–4.69 (2H, brm, N-CH_2-), 3.64 (2H, brs, N-CH_2-), 3.40–3.22 (2H, brm, N-CH_2-), 2.55 (2H, brs, N-CH_2-), 1.13–0.94 (6H, m, -CH_2-), 0.69 (6H, t, J = 6.5 Hz, -CH_3), 0.19 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.24 (brs), 138.50 (brs), 138.29, 135.13 (brs), 133.69, 131.11, 130.70, 129.45 (brs), 128.46, 128.38, 128.33, 127.66, 127.41, 123.58 (brs), 57.51, 57.20, 24.51, 19.53, 13.51 ppm; IR (neat): $\tilde{\nu}$ = 2962, 2874, 1587, 1562, 1470, 922, 907, 638 cm^{-1}. HRMS calcd for $C_{42}H_{40}Cl_2N$, 628.2532 $[M-Br]^+$; found, 628.2533 $[M-Br]^+$. $[\alpha]_D^{23}$ = +13.9° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Rb (Ar = 3-methoxyphenyl, R = Bu): (67% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (2H, brs, Ar-H), 8.04 (2H, d, J = 8.2 Hz, Ar-H), 7.66–7.62 (2H, m, Ar-H), 7.52 (2H, brs, Ar-H), 7.41–7.38 (4H, m, Ar-H), 7.18 (2H, br, Ar-H), 7.04–7.02 (4H, m, Ar-H), 5.13 (2H, br, Ar-C*H*H-N), 3.92 (6H, s, -OCH_3), 3.65 (2H, brs, Ar-C*H*H-N), 3.15 (2H, t, J = 12.6 Hz, N-C*H*H-CH_2), 2.61 (2H, td, J = 12.3, 3.6 Hz, N-C*H*H-CH_2), 1.07–0.93 (6H, m, -CH_2-), 0.66 (6H, t, J = 6.9 Hz, -CH_3), 0.20 (2H, br, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.13 (brs), 140.05, 138.32, 133.89, 131.02, 130.71, 128.53, 128.24, 127.64, 127.41, 123.85, 122.97 (brs), 115.67 (brs), 112.97 (brs), 57.52, 57.20, 55.41, 24.29, 19.54, 13.32; IR (neat): $\tilde{\nu}$ = 2961, 2930, 2874, 1593, 1487, 1468, 1331, 1287, 1256, 1229, 1169, 1042, 883, 710 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{44}H_{46}NO_2$, 620.3523 $[M-Br]^+$; found, 620.3529 $[M-Br]^+$. $[\alpha]_D^{32}$ = +2.3° (c = 0.20, $CHCl_3$).

Chiral ammonium salt (*S*)-2Sb (Ar = 3-fluorophenyl, R = Bu): (85% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (2H, s, Ar-H), 8.03 (2H, d, J = 8.2 Hz, Ar-H), 7.63 (2H, t, J = 7.3 Hz, Ar-H), 7.60 (2H, brs, Ar-H), 7.40–7.30 (8H, m, Ar-H), 7.17 (2H, d, J = 8.5 Hz, Ar-H), 5.06 (2H, brs, N-CH_2-), 3.66 (2H, d, J = 13.5 Hz, N-C*H*H-CH_2), 3.19–2.26 (2H, brm, N-CH_2-), 2.57 (2H, t, J = 11.4 Hz, N-CH_2-), 1.03–0.83 (6H, m, -CH_2-), 0.66 (6H, t, J = 6.9 Hz, -CH_3), 0.18 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$) 162.62 (d, J_{C-F} = 249 Hz), 140.42 (d, J_{C-F} = 7.4 Hz), 138.36, 138.08, 133.48, 131.28 (d, J_{C-F} = 8.2 Hz), 130.86, 130.49, 128.25, 128.14, 127.40, 127.21, 126.49 (br), 123.21, 116.38 (br), 114.93 (d, J_{C-F} = 20.5 Hz), 57.26, 57.04, 24.15, 19.27, 13.15 ppm; IR (neat): $\tilde{\nu}$ = 2963, 2876, 1610, 1581, 1450, 1252, 1211, 1157, 1130, 1030, 887, 849, 658 cm^{-1}. HRMS calcd for $C_{42}H_{40}F_2N$, 596.3123 $[M-Br]^+$; found, 596.3128 $[M-Br]^+$. $[\alpha]_D^{21}$ = +22.1° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Tb (Ar = 3-(trifluoromethyl)phenyl, R = Bu): (88% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (2H, s, Ar-H), 8.07 (2H, d, J = 8.2 Hz, Ar-H), 7.90–7.75 (8H, m, Ar-H), 7.67 (2H, t, J = 7.5 Hz, Ar-H), 7.41 (2H, t, J = 7.6 Hz, Ar-H), 7.35 (2H, d, J = 8.5 Hz, Ar-H), 5.46–4.57 (2H, m, N-CH_2-), 3.70 (2H, brs, N-CH_2-), 3.28 (1H, brs, N-CH_2-), 2.53 (2H, brs, N-CH_2-), 2.09 (1H, brs, N-CH_2-), 0.94–0.80 (6H, m, -CH_2-), 0.59 (6H, t, J = 6.4 Hz, -CH_3), 0.17 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MH, $CDCl_3$): δ = 139.24 (br), 138.51, 134.65 (br), 133.75, 131.78 (br), 131.53, 130.81, 130.60 (brs), 128.51, 127.84, 127.43, 125.88 (brs), 125.00–124.88 (m), 123.41 (br), 122.29, 119.57, 57.26, 24.23, 19.12, 13.22 ppm; IR (neat): $\tilde{\nu}$ = 2965, 2876, 1584, 1472, 1339, 1321, 1312, 1273, 1167, 1125, 1074, 924, 806, 729, 710 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{44}H_{40}F_6N$, 696.3059 $[M-Br]^+$; found, 696.3052 $[M-Br]^+$. $[\alpha]_D^{28}$ = +42.1° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Ub (Ar = 3-cyanophenyl, R = Bu): (89% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (2H, s, Ar-H), 8.06 (2H, d, J = 8.9 Hz, Ar-H), 7.96–7.77 (8H, m, Ar-H), 7.69–7.65 (2H, m, Ar-H), 7.43–7.39 (2H, m, Ar-H), 7.34 (2H, d, J = 8.5 Hz, Ar-H), 5.35–4.65 (2H, m, N-CH_2-), 3.69 (2H, brs, N-CH_2-), 3.25–2.13 (2H, brm, N-CH_2-), 2.52 (2H, brs, N-CH_2-), 0.99 (4H, brs, -CH_2-), 0.87 (2H, brs, -CH_2-), 0.66 (6H, t, J = 6.7 Hz, -CH_3), 0.10 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MH, $CDCl_3$): δ = 139.93 (brs), 138.52, 137.57 (brs), 135.64 (brs), 133.71, 132.59 (brs), 131.63, 131.50, 130.93, 128.66, 128.57, 128.03, 127.46, 123.34 (brs), 117.89, 113.34 (brs), 57.16 (brs), 24.28, 19.34, 13.28 ppm; IR (neat): $\tilde{\nu}$ = 2962, 2873, 2229, 1616, 1472, 922, 804, 702 cm^{-1}. HRMS calcd for $C_{44}H_{40}N_3$, 610.3217 $[M-Br]^+$; found, 610.3216 $[M-Br]^+$. $[\alpha]_D^{23}$ = +21.0° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Vb (Ar = 3-nitrophenyl, R = Bu): (85% yield): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44 (1H, brs, Ar-H), 8.37 (2H, d, J = 8.5 Hz, Ar-H), 8.14 (6H, brs, Ar-H), 8.09 (2H, d, J = 8.2 Hz, Ar-H), 7.92 (1H, brs, Ar-H), 7.71 (2H, t, J = 7.1 Hz, Ar-H), 7.46 (2H, t, J = 7.3 Hz, Ar-H), 7.39 (2H, d, J = 8.5 Hz, Ar-H), 5.51–4.59 (2H, brm, N-CH_2-), 3.72 (2H, brs, N-CH_2-), 3.23 (2H, brs, N-CH_2-), 2.57 (2H, brs, N-CH_2-), 0.99–0.78 (6H, m, -CH_2-), 0.57 (6H, brs, -CH_3), 0.15 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.50, 140.12,

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138.61, 137.58, 133.79, 131.66, 131.43, 131.03, 128.80, 128.67, 128.21, 127.48, 124.08, 123.03, 57.37, 24.47, 19.26, 13.20 ppm; IR (neat): $\tilde{\nu}$ = 2961, 2876, 1614, 1527, 1470, 1344, 1426, 1028, 897, 810, 694, 657 cm^{-1}. HRMS calcd for $C_{42}H_{40}N_3O_4$, 650.3013 $[M-Br]^+$; found, 650.3012 $[M-Br]^+$. $[\alpha]_D^{23}$ = +36.4° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Wb (Ar = 3,4-dichlorophenyl, R = Bu): (88% yield): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (2H, s, Ar-H), 8.03 (2H, d, J = 11.1 Hz, Ar-H), 7.71 (2H, d, J = 8.0 Hz, Ar-H), 7.64 (2H, t, J = 7.4 Hz, Ar-H), 7.55 (2H, brs, Ar-H), 7.55–7.46 (2H, m, Ar-H), 7.38 (2H, t, J = 7.7 Hz, Ar-H), 7.31 (2H, d, J = 10.9 Hz, Ar-H), 5.08 (2H, br, N-CH_2-), 3.65 (2H, brs, N-CH_2-), 3.26 (1H, br, N-CH_2-), 2.54 (2H, brs, N-CH_2-), 1.95 (1H, brs, N-CH_2-), 1.02–0.88 (6H, m, -CH_2-), 0.68 (6H, t, J = 6.5 Hz, -CH_3), 0.24 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.61, 138.55, 137.57, 133.81, 133.55, 133.01, 131.83, 131.41, 131.33, 130.95, 130.58, 128.64, 128.62, 127.96, 127.59, 123.53, 57.47, 57.31, 24.64, 19.55, 13.42 ppm; IR (neat): $\tilde{\nu}$ = 2963, 2913, 1620, 1585, 1549, 1472, 1443, 1327, 1246, 1130, 887, 827, 715, 658 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{42}H_{38}Cl_4N$, 696.1753 $[M-Br]^+$; found, 696.1759 $[M-Br]^+$. $[\alpha]_D^{32}$ = +1.6° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Xb (Ar = 3,4-difluorophenyl, R = Bu): (35% yield): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (2H, s, Ar-H), 8.03 (2H, d, J = 8.7 Hz, Ar-H), 7.65 (2H, t, J = 7.5 Hz, Ar-H), 7.43 (6H, brs, Ar-H), 7.39 (2H, t, J = 7.6 Hz, Ar-H), 7.32 (2H, d, J = 8.5 Hz, Ar-H), 5.07 (2H, brs, N-CH_2-), 3.68 (2H, brs, N-CH_2-), 3.20 (2H, brs, N-CH_2-), 2.58 (2H, brs, N-CH_2-), 1.06 (4H, brs, -CH_2-), 0.95 (2H, brs, -CH_2-), 0.72 (6H, t, J = 6.6 Hz, -CH_3), 0.28 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.25 (dd, J_{C-F} = 252, 12.3 Hz), 138.37, 137.72, 135.41, 133.67, 131.21, 130.74, 128.45, 127.75, 127.42, 123.41, 118.98, 118.82, 57.50, 57.32, 24.55, 19.57, 13.37 ppm; IR (neat): $\tilde{\nu}$ = 2962, 2876, 1603, 1516, 1470, 1416, 1273, 1117, 1030, 920, 878, 638 cm^{-1}. HRMS calcd for $C_{42}H_{38}F_4N$, 632.2935 $[M-Br]^+$; found, 632.2929 $[M-Br]^+$. $[\alpha]_D^{23}$ = +28.6° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Yb (Ar = 3,5-di-*tert*-butylphenyl, R = Bu): (81% yield): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.10 (2H, s, Ar-H), 8.06 (2H, d, J = 8.2 Hz, Ar-H), 7.65 (2H, t, J = 6.2 Hz, Ar-H), 7.57 (2H, s, Ar-H), 7.48 (2H, s, Ar-H), 7.42–7.37 (4H, m, Ar-H), 7.21 (2H, brs, Ar-H), 5.08 (2H, d, J = 13.3 Hz, Ar-C*H*H-N), 3.80 (2H, d, J = 13.3 Hz, Ar-C*H*H-N), 3.15 (2H, t, J = 13.3 Hz, N-C*H*H-CH_2), 2.53 (2H, td, J = 13.3, 6.0 Hz, N-C*H*H-CH_2), 1.43 (18H, s, -$C(CH_3)_3$), 1.37 (18H, s, -$C(CH_3)_3$), 1.04 (4H, brs, -CH_2-), 0.85 (2H, brs, -CH_2-), 0.63 (6H, t, J = 6.9 Hz, -CH_3), 0.55 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.48, 151.66, 140.84, 138.41, 137.95, 133.98, 131.49, 130.56, 128.45, 128.13, 127.69, 127.19, 124.36, 124.21, 123.57, 122.53, 57.66, 57.50, 35.23, 31.62, 24.36, 19.67, 14.01 ppm; IR (neat): $\tilde{\nu}$ = 2960, 2872, 1620, 1593, 1471, 1363, 1248, 1181, 921, 885, 860 cm^{-1}. HRMS calcd for $C_{58}H_{74}N$, 784.5816 $[M-Br]^+$; found, 784.5816 $[M-Br]^+$. $[\alpha]_D^{23}$ = +43.9° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2Zb (Ar = 3,5-diphenylphenyl, R = Bu): (60% yield): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.21 (2H, s, Ar-H), 8.08 (2H, d, J = 8.2 Hz, Ar-H), 7.99 (2H, s, Ar-H), 7.95 (2H, s, Ar-H), 7.82–7.78 (8H, m, Ar-H), 7.68–7.63 (4H, m, Ar-H), 7.53–7.43 (14H, m, Ar-H), 7.35 (2H, t, J = 7.0 Hz, Ar-H), 5.15 (2H, d, J = 13.5 Hz, Ar-C*H*H-N), 3.87 (2H, d, J = 13.5 Hz, Ar-C*H*H-N), 3.21 (2H, t, J = 13.1 Hz, N-C*H*H-CH_2), 2.78 (2H, td, J = 12.7, 4.2 Hz, N-C*H*H-CH_2), 1.01–0.91 (4H, m, -CH_2-), 0.82–0.79 (2H, m, -CH_2-), 0.45 (6H, t, J = 7.01 Hz, -CH_3), 0.45 ppm (2H, brs, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.03, 142.66, 139.92, 139.73, 139.62, 139.37, 138.38, 133.86, 131.69, 130.70, 128.94, 128.48, 128.30, 128.05, 127.91, 127.61, 127.58, 127.49, 127.12, 126.88, 125.55, 123.51, 57.67, 57.39, 24.72, 19.54, 13.72 ppm; IR (neat): $\tilde{\nu}$ = 3055, 2960, 2872, 1591, 1468, 1408, 1361, 1028, 921, 908, 885, 698 cm^{-1}. HRMS calcd for $C_{66}H_{58}N$, 864.4564 $[M-Br]^+$; found, 864.4560 $[M-Br]^+$. $[\alpha]_D^{23}$ = +6.6° (c = 1.00, $CHCl_3$).

Chiral ammonium salt (*S*)-2AAb (Ar = 3,5-difluorophenyl, R = Bu): (90% yield): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07 (2H, s, Ar-H), 8.05 (2H, d, J = 8.5 Hz, Ar-H), 7.66 (2H, t, J = 7.5 Hz, Ar-H), 7.41 (2H, t, J = 7.7 Hz, Ar-H), 7.34 (2H, d, J = 8.5 Hz, Ar-H), 7.20–7.11 (4H, m, Ar-H), 6.96 (2H, tt, J = 8.7, 2.3 Hz, Ar-H), 5.01 (2H, d, J = 14.0 Hz, Ar-C*H*H-N), 3.75 (2H, d, J = 14.0 Hz, Ar-C*H*H-N), 3.27 (2H, t, J = 12.9 Hz, N-C*H*H-CH_2), 2.67 (2H, td, J = 12.6, 4.4 Hz, N-C*H*H-CH_2), 1.15–1.00 (6H, m, -CH_2-), 0.73 (6H, t, J = 7.0 Hz, -CH_3), 0.37–0.33 ppm (2H, m, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.16 (d, J_{C-F} = 252 Hz), 141.93 (t, J_{C-F} = 9.4 Hz), 138.43, 137.71 (t, J_{C-F} = 2.5 Hz), 133.71, 131.35, 130.96, 128.64, 128.00, 127.52, 123.20, 113.47 (d, J_{C-F} = 101 Hz), 103.97 (t, J_{C-F} = 25.0 Hz), 57.58, 57.35, 24.57, 19.35, 13.28 ppm; IR (neat): $\tilde{\nu}$ = 2963, 2876, 1620, 1593, 1470, 1449, 1429, 1344, 1256, 1119, 989, 887, 862, 847, 702 cm^{-1}. HRMS (ESI-TOF) calcd for $C_{42}H_{38}F_4N$, 632.2935 $[M-Br]^+$; found, 632.2933 $[M-Br]^+$. $[\alpha]_D^{31}$ = +3.9° (c = 0.50, $CHCl_3$).

Chiral ammonium salt (*S*)-2ABb (Ar = 3,4,5-trichlorophenyl, R = Bu): (72% yield): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (2H, s, Ar-H), 8.05 (2H, d, J = 8.0 Hz, Ar-H), 7.73 (2H, brs, Ar-H), 7.70–7.66 (2H, m, Ar-H), 7.63 (2H, brs, Ar-H), 7.45–7.40 (2H, m, Ar-H), 7.33 (2H, d, J = 8.5 Hz, Ar-H), 4.99 (2H, d, J = 13.9 Hz, Ar-C*H*H-N), 3.78 (2H, d, J = 13.9 Hz, Ar-C*H*H-N), 3.33 (2H, t, J = 13.1 Hz, N-C*H*H-CH_2), 2.67 (2H, td, J = 13.0, 4.4 Hz, N-C*H*H-CH_2), 1.16–0.85 (6H, m, -CH_2-), 0.73 (6H, t, J = 7.1 Hz, -CH_3), 0.39–0.35 ppm (2H, brm, NCH_2-C*H*H-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.71, 138.39, 136.45, 135.26 (brs), 133.63, 132.28, 132.06, 131.59, 130.98, 130.20 (brs), 129.92, 129.69 (brs), 128.71, 128.59, 128.15, 128.13, 127.49, 123.06, 57.61, 57.48, 25.01, 19.63, 13.66 ppm; IR (neat): $\tilde{\nu}$ = 2962, 2874, 1580, 1537, 1470, 1423, 1373, 1325, 1277, 1250, 1163, 923, 887, 866, 844, 810, 611 cm^{-1}. HRMS calcd for $C_{42}H_{36}Cl_6N$, 764.0973 $[M-Br]^+$; found, 764.0968 $[M-Br]^+$. $[\alpha]_D^{30}$ = −4.6° (c = 1.00, $CHCl_3$).

*5. General Procedure for Catalytic Enantioselective Alkylation of tert-Butyl Glycine Benzophenone Schiff Base **9** (Benzylation)*

A CH_2Cl_2 solution of chiral catalyst (*S*)-2Db (50 μL, 3×10^{-3} M, 0.05 mol%) was added to a reaction vessel, and the solvent was completely evaporated off in vacuo. After addition of glycine derivative **9** (89 mg, 0.30 mmol), the reaction vessel was flushed with argon gas, and toluene was added (1.0 mL). A continuous addition of KOH (50% aq, 1.0 mL) and benzyl bromide (43 μL, 0.36 mmol) was carried out at 0 °C. The reaction mixture was stirred vigorously at the same temperature for 2 h. The mixture was then poured into H_2O and extracted with ether. The organic extracts were washed with brine and dried over Na_2SO_4. Evaporation of solvents and purification of the residual oil by column chromatography on silica gel (ether/hexane = 1:10 as eluent) gave *tert*-butyl (*R*)-*N*-(diphenylmethylene)phenylalaninate (*R*)-**10** (113 mg, 0.29 mmol, 98% yield).

*6. Representative Procedure for Catalytic Enantioselective Alkylation of α-Alkyl-α-Amino Acid tert-Butyl Ester Aldimine Schiff Base **11** (Benzylation)*

Chiral catalyst (*S*)-**2Db** (2.2 mg, 1 mol%) and alanine derivative **11** (80.3 mg, 0.30 mmol) were added to a reaction vessel, and the reaction vessel was flushed with argon gas before toluene was added (2.0 mL). A continuous addition of benzyl bromide (43 μL, 0.36 mmol) and $CsOH\cdot H_2O$ (252 mg, 1.5 mmol) was carried out at −20 °C. The reaction mixture was stirred vigorously at the same temperature for 3 h. The mixture was then poured into H_2O and extracted with CH_2Cl_2. Solvents were evaporated, and the residue was dissolved in THF (5.0 mL). Citric acid (0.5 M, 5.0 mL) was added, and the mixture was stirred at room temperature for 1 h. After evaporation to remove THF, the aqueous phase was washed with hexane. It was then made basic by the addition of solid $NaHCO_3$ and extracted with CH_2Cl_2. The organic extracts were dried over Na_2SO_4. Evaporation of solvents and purification of the residual oil by column chromatography on silica gel (EtOAc/hexane = 1:2 as eluent) gave the benzylation product **12** (60 mg, 0.25 mmol, 85% yield). The enantiomeric excess was determined by HPLC analysis (Daicel Chiralcel AD-H, hexane/2-propanol = 30:1, flow rate 0.5 mL min^{-1}, t_R: 12.6 min (*R*) and 19.4 min (*S*)).

*7. Representative Procedure for Direct Catalytic Asymmetric Aldol Reaction of Glycinate Schiff Base **9** with Aldehydes under Phase-Transfer Conditions*

An aqueous solution of NaOH (1%, 0.8 mL) was added to a solution of *tert*-butylglycinate benzophenone Schiff base **9** (59 mg, 0.20 mmol) and (*S*)-**2Fb** (3.0 mg, 1 mol%) in toluene (2.0 mL) at 0 °C under argon atmosphere; 3-phenylpropanal (53 μL, 0.40 mmol) was then introduced drop-

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wise. The whole mixture was stirred at 0 °C for 2 h. Saturated NH_4Cl and ether were added sequentially. The organic phase was separated, washed with brine, and dried over Na_2SO_4. After evaporation of solvents, THF (6.0 mL) and 1 N HCl (1.0 mL) were added at 0 °C. After the solution was stirred for 1 h, THF was removed in vacuo. The resulting aqueous solution was washed with ether three times and neutralized with K_2CO_3. The mixture was then extracted with CH_2Cl_2 three times. The combined extracts were dried over Na_2SO_4 and concentrated. Purification of the residue by column chromatography on silica gel ($MeOH/CH_2Cl_2 = 1:30$ as eluent) afforded *tert*-butyl 2-amino-3-hydroxy-5-phenylpentanoate (**13**) as a mixture of diastereomers (42 mg, 0.16 mmol, 79% yield, *syn*/*anti* = 78:22). The diastereomeric ratio was determined by ^1H NMR analysis. The enantiomeric excess was determined, after conversion into the corresponding oxazoline-2-thione **14** [thiocarbonyl diimidazole (1.0 equiv), CH_2Cl_2], by HPLC analysis. [*cis*-**14**: Daicel Chiralcel AD-H, hexane/2-propanol = 10:1, flow rate = 0.5 mL min^{-1}, t_R = 18.9 min (minor) and 28.7 min (major); *trans*-**14**: Daicel Chiralcel AD-H, hexane/2-propanol = 10:1, flow rate = 0.5 mL min^{-1}, t_R = 19.9 min (major) and 32.9 min (minor)].[14b]

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