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Synthesis of new dimeric-PEG-supported cinchona ammonium salts as chiral phase transfer catalysts for the alkylation of Schiff bases with water as the solvent

Xin Wang, Liang Yin, Ting Yang and Yongmei Wang*

Department of Chemistry, NanKai University, 300071 Tianjin, China

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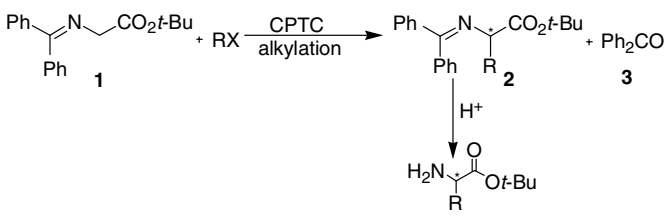
Abstract—The water-soluble PEG-supported cinchona ammonium salts were successfully synthesized and used as chiral phase transfer catalysts for the asymmetric alkylation of *tert*-butyl benzophenone Schiff base derivatives with high chemical yields (up to 98%) and enantioselectivities (up to 97%) in aqueous media. The recycling results showed that the polymers were stable and rarely lost activities.

1. Introduction

Chiral phase transfer catalysis (CPTC) is a very useful approach that typically involves simple experimental operations, mild reaction conditions, inexpensive, environmentally benign reagents and large-scale reactions.[1] The CPTC methodology has been applied to the Michael addition,[2a,b] Darzen reaction,[2c–h] cyclopropanation,[2i] aldol condensation,[2j–l] fluorination,[2m–o] epoxidation,[2p–r] and alkylation, reactions amongst others.

Among these, asymmetric alkylation of *tert*-butyl benzophenone Schiff base derivatives **1** has received much attention and been successfully applied to the enantioselective synthesis of natural and unnatural amino acids (Scheme 1).[3] In 1989, O'Donnell reported[4] that *N*-benzyl derivatives of the cinchona alkaloids could catalyze the process, typically leading to enantioselectivities in the range of 42–66% ee. Later, the same group[5] demonstrated that *N*-benzyl-*O*-alkyl *cinchona* alkaloids derivatives generated in the reactions could lead to remarkably higher enantiomeric excess.[6] Finally, the third generation of catalysts, cinchona alkaloids with the bulky group *N*-anthracenylmethyl instead of the benzyl group, was reported in 1997 independently by Lygo[6a] and Corey.[6b] Recently, dimeric[7] and trimeric[8] cinchona alkaloid derivatives, guanidinium salts,[9] C_2-symmetric ammonium salts derived from BINOL,[10] phosphonium salts,[11] TADDOL,[12] tartaric derivatives,[13] and other metal catalysts[14] have emerged as powerful variants.



Scheme 1.

With the aim of improving the efficiency of these catalytic processes and making the ligands and catalysts readily recoverable and recyclable,[15] considerable effort has been devoted to the immobilization of cinchona alkaloids on polymers.

Our group is one of the pioneers in this research field. We have anchored cinchona alkaloids to cross-linked polystyrene and used them for the asymmetric alkylation of *tert*-butyl benzophenone Schiff base derivative,[16] although the enantioselectivity was not satisfactory. Subsequently, many scientists had synthesized multifarious polymer-supported chiral phase-transfer catalysts, and investigated their applications for the alkylation of *tert*-butyl benzophenone Schiff's base. For these systems, the catalytic reactions

* Corresponding author. Tel./fax: +86 22 2350 2654; e-mail: wangxinadv@yahoo.com.cn

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could not proceed in aqueous media. Neither the yield nor the ee were very satisfactory, and furthermore, the recycled polymers lost activities due to saponification. Moreover, stringent reaction condition and the instability of the PS-PTC were difficult problems to overcome.[17]

For the purpose of increasing the enantiomeric excess and carrying out the reaction in aqueous media without any organic solvent, we successfully synthesized the dimeric cinchonine, which had been N-anchored to a long linear PEG chain, and investigated asymmetric epoxidation of chalcones catalyzed by this novel PS-PTC (the highest ee was 86%).[18] Unfortunately, since the reaction cannot proceed in water, the advantage of this catalyst could not be revealed. Therefore, herein we report the asymmetric alkylation of *tert*-butyl benzophenone Schiff base derivative catalyzed by the PEG supported cinchona alkaloids in aqueous media.

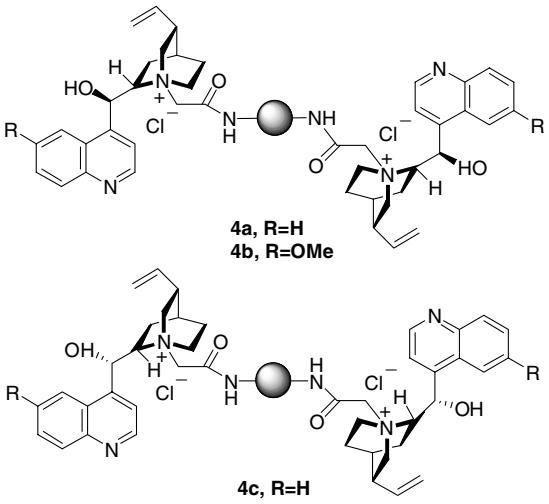


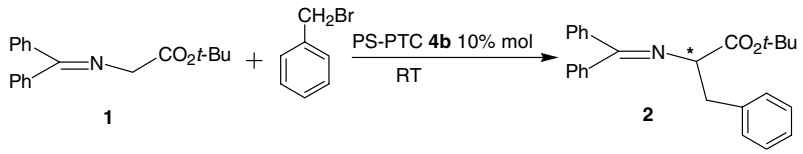
Figure 1.

2. Results and discussion

The polymers were prepared by the following method: resin-supported ammonium salts **4a** and **4b** (Fig. 1) were obtained by the reactions of diacetamido-PEG2000 chloride[19] with an excess (2 equiv) of cinchonidine and quinine, respectively, in refluxing chloroform. After filtration and washing thoroughly with diethyl ether, polymer-supported quaternary ammonium chlorides **4a** and **4b** were obtained. Moreover, the cinchonine-derived PEG-supported ammonium salt **4c** (Fig. 1) was also obtained. As cinchonine has been considered as a pseudoenantiomer of cinchonidine, its use offers a simple way of achieving opposite enantioselection.

The polymer supported dimeric CPTCs were tested as water-soluble catalysts in the asymmetric alkylation of the *tert*-butyl benzophenone Schiff base **1** with PEG-supported quinine **4b**. Various factors that may affect the reaction were examined, such as the temperature, the solvent, the concentration and species of the inorganic base, the amounts of the benzyl bromide and CPTC. It was found that the reaction proceeded best in 1 M aqueous solution of KOH (10 equiv, 2 mL) at room temperature, with benzyl bromide (2.4 equiv) and PS-PTC (10 mol %). We also attempted to perform the reaction at 0 °C (Table 1, entry 9). However, the result was unsatisfactory since the PS-PTC was deposited when the temperature was low. As shown in Table 1, both the chemical and enantiomeric excesses are higher when the solvent is water rather than classical organic solvents. The amount of benzophenone **3** is

Table 1. Asymmetric alkylation of **1** in the presence of catalyst **4b** with different solvents



Entry	Solvent	BnBr (equiv)	Yield[c] (%)	ee[d] (%) Config[e]
1[a]	Toluene	2.4	73	65(*S*)
2[a]	CH_2Cl_2	2.4	54	48(*S*)
3[a]	Toluene/CH_2Cl_2 7:3	2.4	59	54(*S*)
4[a]	Toluene/$CHCl_3$ 7:3	2.4	74	71(*S*)
5	1 M KOH	1.2	86	79(*S*)
6	1 M KOH	2.4	98	83(*S*)
7	1 M KOH	5.0	97	81(*S*)
8	1 M KOH	10.0	95	82(*S*)
9[b]	1 M KOH	2.4	78	55(*S*)
10	1 M NaOH	2.4	93	72(*S*)
11	10 M KOH	2.4	89	72(*S*)

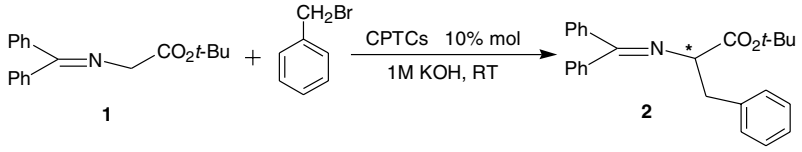
[a] The reaction was carried out in organic solvent (2 mL) and 13 equiv 9 M aqueous solution of KOH (0.3 mL).
[b] The reaction was performed at 0 °C.
[c] Isolated yield.
[d] Enantiomeric excess was determined by HPLC analysis using a chiral column (DAICEL Chiralcel OD-H) with hexane–isopropanol as an eluent.
[e] The absolute configuration was confirmed by comparison of the HPLC retention time of an authentic sample, which was synthesized independently by reported procedures.[6b]

also decreased in aqueous media. It indicated that the best way to prevent the decomposition of **2** was to use water as the solvent.[20a]

After optimizing the reaction condition with PS-PTC **4b**, we were also interested in the effects of other CPTCs including PEG-supported cinchonine **4c** and cinchonidine **4a**, CPTC **5** reported by Thierry,[17d] and catalysts **6a**, **6b** prepared by O'Donnell's method (Fig. 2).[4] As shown in Table 2, the reaction afforded the best results with PS-PTC **4b**. The desired product **2** was obtained in 98% yield and 83% ee. Under the same reaction condition, the polymer **5** and catalysts **6a**, **6b** seemed to give a notable decrease in both the chemical yield and enantioselectivity. We were also interested in the recovery and recycling of the polymers. Fortunately, satisfactory ee and yields were obtained using the recovered catalysts **4b** (Table 2, entries 4–6). This reproducibility showed that the catalyst is much more stable than other PEG-supported cinchona alkaloids that had been reported previously,[17e] since the acetamido-group, which connected cinchona and PEG, is hardly disintegrated under the mild reaction conditions.

Encouraged by these preliminary results, different benzyl bromides and other alkyl halides were tested as electrophiles (Table 3). Satisfactory ees and yields were obtained under the conditions above by alkylation with a substituted benzyl bromide, allylic bromide, and alkyl iodide. The solid or liquid state, and amounts of the electrophiles, which have been reported[20] to affect the result substantially, showed no significant influence on the enantioselectivity and yield in this current system. The difference may be related to the structure of our catalyst. The linking PEG group is a high-powered surfactant, which can mix the organic compound with water, resulting in a homogeneous reaction system, and therefore no obvious difference was observed between solid and liquid halides. The alkylated product could be obtained in good yields and ee with a small quantity of electrophiles.

Table 2. Asymmetric alkylation of **1** with different catalysts in aqueous media



Entry	Catalyst	Catalyst (equiv)	Yield (%)[e]	ee[f] (%) Config.[g]
1	**4b**	0.1	98	83(*S*)
2	**4b**	0.05	90	73(*S*)
3	**4b**	0.01	73	57(*S*)
4[a]	**4b**	0.1	94	82(*S*)
5[b]	**4b**	0.1	92	80(*S*)
6[c]	**4b**	0.1	88	80(*S*)
7	**4c**	0.1	97	80(*R*)
8	**4c**	0.05	92	69(*R*)
9[d]	**4c**	0.1	76	74(*R*)
10	**4a**	0.1	95	75(*S*)
11	**5**	0.1	76	38(*S*)
12	**6a**	0.1	81	61(*S*)
13	**6b**	0.1	85	68(*S*)

[a] Recycled catalyst for the first run.
[b] Recycled catalyst for the second run.
[c] Recycled catalyst for the third run.
[d] The reaction was performed with toluene/$CHCl_3$ 7:3 as the solvent.
[e] Isolated yield.
[f] Enantiomeric excess was determined by HPLC analysis using a chiral column (DAICEL Chiralcel OD-H) with hexane–isopropanol as an eluent.
[g] The absolute configuration was confirmed by comparison of the HPLC retention time of an authentic sample, which was synthesized independently by reported procedures.[6b]

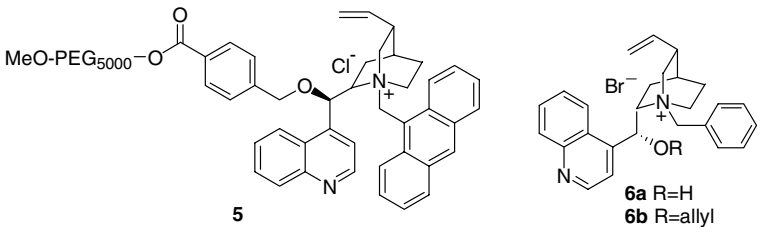
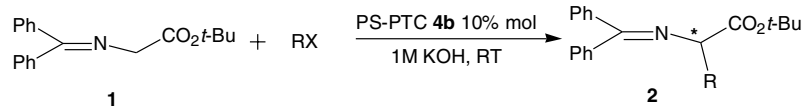


Figure 2.

Table 3. Asymmetric alkylation of **1** in the presence of catalyst **4b** with various electrophiles in aqueous media



1 **2**

Entry	RX	No.	Yield[a] (%)	ee[b] (%) Config.[c]
1	$PhCH_2Br$	**2a**	98	83(*S*)
2	*o*-CH_3PhCH_2Br	**2b**	84	82(*S*)
3	*m*-CH_3PhCH_2Br	**2c**	86	90(*S*)
4	*p*-CH_3PhCH_2Br	**2d**	91	85(*S*)
5	*o*-$ClPhCH_2Br$	**2e**	94	97(*S*)
6	*m*-$ClPhCH_2Br$	**2f**	83	92(*S*)
7	*p*-$ClPhCH_2Br$	**2g**	82	91(*S*)
8	$CH_2{=}CHCH_2Br$	**2h**	77	86(*S*)
9	C_2H_5I	**2i**	82	90(*S*)
10	CH_3I	**2j**	79	83(*S*)

[a] Isolated yield.
[b] Enantiomeric excess was determined by HPLC analysis using a chiral column (DAICEL Chiralcel OD-H) with hexane–isopropanol as an eluent.
[c] The absolute configuration was confirmed by comparison of the HPLC retention time of an authentic sample, which was synthesized independently by reported procedures.[3a,6a,b,11a,8]

3. Conclusion

In summary, we have successfully synthesized the water-soluble PS-PTC, which can catalyze the asymmetric alkylation of *tert*-butyl benzophenone Schiff base derivatives with high chemical yields and enantioselectivities in aqueous media. In addition, due to the stability of the catalyst, we obtained steady yield and ee with the recycled PS-PTC. Further research focusing on the application of PS-PTC is under investigation in our laboratory.

4. Experimental

All the reagents and solvents employed the best grade available and were used without further purification. The ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-P300 instrument in $CDCl_3$. Melting points were determined using an electrothermal apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 341 Polarimeter at 20 °C. Enantiomeric excesses were determined by HPLC using Daicel Chiralcel OD-H columns with racemic products as standards.

4.1. General procedure for the synthesis of PEG-supported ammonium salts 4a, 4b, and 4c

To a suspension of cinchonine, cinchonidine, or quinine (2 mmol) in chloroform (20 mL) was added diacetamido-PEG2000 chloride (0.5 equiv), and the mixture was stirred at reflux for 100 h. The reaction mixture was cooled to room temperature and the solid was filtered, evaporated in vacuo. Diethyl ether (25 mL) was added to the residue, frozen, and the solid was filtered. The crude product thus obtained was crystallized from dichloromethane–diethyl ether mixture to afford the polymer-supported ammonium salts.

4.1.1. Characterization of PS-PTC ammonium salts 4a. A light yellow solid, mp 48–50 °C; $[\alpha]_D^{20} = -15.6$ (*c* 0.4, CH_2Cl_2); solubility in water: 175 mg/mL (stable for several days at 20 °C); IR (KBr) *v*: 3422, 3218, 3068, 2885, 1678, 1590, 1510, 1467, 1360, 1344, 1281, 1242, 1112, 1061, 963, 842, 779 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 9.37–9.34 (m, 2H), 8.92 (d, 2H, $J = 4.5$ Hz), 8.10 (d, 2H, $J = 8.4$ Hz), 7.97 (d, 2H, $J = 7.5$ Hz), 7.83 (d, 2H, $J = 4.5$ Hz), 7.66 (d, 2H, $J = 8.1$ Hz), 7.59 (d, 2H, $J = 6.9$ Hz), 5.58–5.44 (m, 2H), 5.24 (d, 2H, $J = 17.1$ Hz), 5.00 (d, 2H, $J = 10.2$ Hz), 4.92–4.89 (m, 2H), 4.79–4.71 (m, 2H), 4.42–4.27 (m, 4H), 3.89–3.71 (m, 2H, PEG), 3.66–3.53 (m, PEG), 3.41–3.37 (m, 2H, PEG), 2.77–2.76 (m, 2H), 2.26–1.92 (m, 16H), 1.15–1.07 (m, 2H), 0.81–0.76 (m, 2H); ^{13}C NMR: δ 164.6, 139.1, 136.9, 136.8, 130.3, 128.1, 124.8, 123.6, 123.1, 117.4, 110.0, 106.4, 70.7, 69.0, 65.7, 65.0, 61.8, 59.8, 56.4, 38.0, 26.3, 25.7, 21.9.

4.1.2. Characterization of PS-PTC ammonium salts 4b. A light brown solid, mp 45–46 °C; $[\alpha]_D^{20} = -20.2$ (*c* 0.4, CH_2Cl_2); solubility in water: 245 mg/mL (stable for several days at 20 °C); IR (KBr) *v*: 3421, 3210, 3077, 2884, 1677, 1621, 1588, 1560, 1508, 1467, 1359, 1344, 1280, 1241, 1112, 963, 841, 779 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 9.26–9.20 (m, 2H), 8.77 (d, 2H, $J = 4.8$ Hz), 8.09 (d, 2H, $J = 9$ Hz), 7.96–7.87 (m, 4H), 7.41–7.37 (m, 2H), 5.62–5.52 (m, 2H), 5.29 (d, 2H, $J = 17$ Hz), 5.07 (d, 2H, $J = 12$ Hz), 4.95–4.84 (m, 2H), 4.57–4.51 (m, 2H), 4.09–4.06 (m, 4H), 3.89–3.80 (m, 4H, PEG), 3.66–3.51 (m, PEG), 3.47 (s, 6H), 2.80–2.70 (m, 4H), 2.18–1.81 (m, 14H), 1.11–0.95 (m, 4H); ^{13}C NMR: δ 164.8, 158.6, 137.4, 137.3, 137.0, 131.2, 126.2, 122.9, 120.5, 117.1, 110.0, 101.4, 70.7, 69.0, 66.2, 63.6, 61.7, 59.7, 57.5, 56.9, 37.9, 26.4, 25.8, 22.3.

4.1.3. Characterization of PS-PTC ammonium salts 4c. A red solid, mp 44–46 °C; $[\alpha]_D^{20} = +45.3$ (*c* 0.4, CH_2Cl_2); Solubility in water: 180 mg/mL (stable for several days at 20 °C); IR (KBr) *v*: 3404, 3210, 3040, 2956, 1690, 1637, 1590, 1510, 1462, 1425, 1386, 1310, 931, 855, 779 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 9.39–9.36 (m, 2H), 8.92 (d, 2H, $J = 4.5$ Hz), 8.07–7.92 (m, 4H), 7.85 (d, 2H, $J = 4.5$ Hz), 7.63–7.50 (m, 4H), 6.01–5.82 (m, 2H), 5.57

(d, 2H, $J = 14.7$ Hz), 5.31–5.25 (m, 4H), 4.77–4.64 (m, 4H), 4.46–4.41 (m, 2H), 4.17–4.06 (m, 4H), 3.90–3.86 (m, 2H, PEG), 3.65–3.54 (m, PEG), 3.45–3.39 (m, 2H, PEG), 2.78–2.46 (m, 6H), 2.27–2.19 (m, 2H), 1.97–1.77 (m, 6H), 0.96–0.85 (m, 4H); ^{13}C NMR: δ 163.9, 139.4, 138.6, 135.1, 131.8, 128.7, 124.8, 123.9, 123.8, 118.7, 110.0, 103.0, 70.8, 70.0, 65.9, 61.9, 59.6, 55.7, 38.3, 27.1, 24.1, 21.2.

4.2. General procedure for asymmetric alkylation of *tert*-butyl benzophenone Schiff base derivatives with PS-PTC 4a, 4b, and 4c

Poly(ethylene glycol)-2000 supported cinchona alkaloid (0.02 mmol) and *N*-(diphenylmethylene)-glycine *tert*-butyl ester (59 mg, 0.2 mmol) dissolved in 2 mL of 1 M aqueous potassium hydroxide solution at room temperature. After the dropwise addition of benzyl bromide (0.48 mmol), the reaction mixture was further stirred for 6 h at room temperature (determined by TLC). Then 10 mL water was added, and the resulting mixture was extracted by CH_2Cl_2 (10 mL × 3). The combined organic phase was washed with water (10 mL × 2), dried over anhydrous sodium sulfate, filtered off, and evaporated in vacuo. Diethyl ether (15 mL) was added in the residue, shaken, and then stilled. The polymeric catalyst was filtered and reclaimed. The solution was concentrated under reduced pressure to give the crude product **2**. Further purification by column chromatography on silica gel (petroleum/ethyl acetate 30:1 as the eluent, neutralized with 1% Et_3N) afforded **2** as a colorless oil.

4.2.1. (*S*)-*tert*-Butyl-3-phenyl-2-diphenylmethylene amino propanoate 2a (Table 3, entry 1). Yield: 98%; $[\alpha]_D^{20} = -12.6$ (*c* 0.2, $CHCl_3$); ee = 83%; ^{1}HNMR (300 MHz, $CDCl_3$): δ 7.56–7.58 (m, 2H, Ph–H), 7.26–7.38 (m, 6H, Ph–H), 7.13–7.21 (m, 3H, Ph–H), 7.04–7.06 (m, 2H, Ph–H), 6.60 (br d, 2H, $J = 6.0$ Hz, Ph–H), 4.10 (dd, 1H, $J = 4.4$, 9.6 Hz, CHC=O), 3.23 (dd, 1H, $J = 4.4$, 13.6 Hz, $PhCH_2$), 3.15 (dd, 1H, $J = 9.6$, 13.6 Hz, $PhCH_2$), 1.44 (s, 9H, *t*-Bu) ppm; IR (neat): 2978, 1732, 1624, 1576, 1495, 1447, 1367, 1286, 1150, 1082, 1030, 849, 756, 696 cm^{-1}; HPLC analysis: DAICEL Chiralcel OD-H, hexane/isopropanol = 99.5:0.5, flow rate = 0.5 mL/min, retention time: 16.9 min (*R*) and 24.1 min (*S*).

4.2.2. (*S*)-*tert*-Butyl-3-(2-methylphenyl)-2-diphenylmethylene amino propanoate 2b (Table 3, entry 2). Yield: 84%; $[\alpha]_D^{20} = -14.1$ (*c* 0.2, $CHCl_3$); ee = 82%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72–7.69 (m, 3H, Ph–H), 7.59–7.50 (m, 3H, Ph–H), 7.32–7.29 (m, 4H, Ph–H), 7.08–6.63 (m, 4H, Ph–H), 4.08–3.19 (dd, 1H, $J = 9.2$, 4.4 Hz, CHC=O), 3.17 (dd, 2H, $J = 13.6$, 9.2 Hz, $PhCH_2$), 2.26 (s, 3H, CH_3), 1.44 (s, 9H, *t*-Bu) ppm; IR (neat) 2972, 2927, 1732, 1621, 1511, 1444, 1367, 1286, 1151, 894, 840, 762 cm^{-1}; HPLC analysis: DAICEL Chiralcel OD-H, hexane/isopropanol = 99.5:0.5, flow rate = 0.5 mL/min, retention time: 20.7 min (*R*) and 29.6 min (*S*).

4.2.3. (*S*)-*tert*-Butyl-3-(3-methylphenyl)-2-diphenylmethylene amino propanoate 2c (Table 3, entry 3). Yield: 86%; $[\alpha]_D^{20} = -13.7$ (*c* 0.2, $CHCl_3$); ee = 90%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72–7.69 (m, 3H, Ph–H), 7.58–7.50 (m, 5H, Ph–H), 7.30–7.26 (m, 2H, Ph–H), 7.06–7.03 (m, 2H, Ph–H), 6.61–6.56 (m, 2H, Ph–H), 4.24–4.09 (dd, 1H, $J = 9.2$, 4.4 Hz, CHC=O), 3.18–3.13 (dd, 2H, $J = 13.6$, 9.2 Hz, $PhCH_2$), 2.28 (s, 3H, CH_3), 1.44 (s, 9H, *t*-Bu) ppm; IR (neat) 2972, 2927, 1732, 1621, 1511, 1444, 1367, 1286, 1151, 894, 840, 762 cm^{-1}; HPLC analysis: DAICEL Chiralcel OD-H, hexane/isopropanol = 99.5:0.5, flow rate = 0.5 mL/min, retention time: 20.6 min (*R*) and 24.5 min (*S*).

4.2.4. (*S*)-*tert*-Butyl-3-(4-methylphenyl)-2-diphenylmethylene amino propanoate 2d (Table 3, entry 4). Yield: 91%; $[\alpha]_D^{20} = -15.7$ (*c* 0.2, $CHCl_3$); ee = 85%; ^{1}H NMR (300MHz, $CDCl_3$) δ: 7.72–7.69 (m, 1H, Ph–H), 7.60–7.50 (m, 3H, Ph–H), 7.32–7.29 (m, 4H, Ph–H), 7.05–7.03 (m, 4H, Ph–H), 6.64–6.62 (m, 2H, Ph–H), 4.13–4.07 (m, 1H, CHC=O), 3.19–3.18 (m, 2H, $PhCH_2$), 2.26 (s, 3H, CH_3),1.44 (s, 9H, *t*-Bu) ppm; IR (neat) 2978, 2928, 1735, 1624, 1516, 1447, 1367, 1286, 1151, 910, 845, 779, 696 cm^{-1}; HPLC analysis: DAICEL Chiralcel OD-H, hexane/isopropanol = 99.5:0.5, flow rate = 0.5 mL/min, retention time: 12.8 min (*S*) and 21.2 min (*R*).

4.2.5. (*S*)-*tert*-Butyl-3-(2-chlorophenyl)-2-diphenylmethylene amino propanoate 2e (Table 3, entry 5). Yield: 94%; $[\alpha]_D^{20} = -16.3$ (*c* 0.2, $CHCl_3$); ee = 97%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62–7.61 (m, 2H, Ph–H), 7.41–7.39 (m, 2H, Ph–H), 7.38–7.27 (m, 6H, Ph–H), 7.17–7.12 (t, 1H, $J = 7.2$ Hz, Ph–H), 7.06–7.04 (m, 3H, Ph–H), 4.39–4.38 (m, 1H, CHC=O), 3.48–3.47 (m, 2H, $PhCH_2$), 1.47 (s, 9H, *t*-Bu) ppm; IR (neat) 2978, 2928, 1728, 1626, 1508, 1447, 1369, 1285, 1221, 1148, 841, 781, 698 cm^{-1}; HPLC analysis: DAICEL Chiralcel OD-H, hexane/isopropanol = 99.5:0.5, flow rate = 0.5 mL/min, retention time: 15.6 min (*R*) and 17.8 min (*S*).

4.2.6. (*S*)-*tert*-Butyl-3-(3-chlorophenyl)-2-diphenylmethylene amino propanoate 2f (Table 3, entry 6). Yield: 83%; $[\alpha]_D^{20} = -16.6$ (*c* 0.2, $CHCl_3$); ee = 92%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60–7.57 (m, 2H, Ph–H), 7.57–7.36 (m, 6H, Ph–H), 7.14–7.12 (m, 2H, Ph–H), 7.07–6.91 (m, 2H, Ph–H), 6.68–6.66 (m, 2H, Ph–H), 4.13–4.11 (m, 1H, CHC=O), 3.21–3.19 (m, 2H, $PhCH_2$), 1.46 (s, 9H, *t*-Bu) ppm; IR (neat) 2974, 2921, 1726, 1624, 1506, 1447, 1369, 1286, 1148, 865, 787, 742 cm^{-1}; HPLC analysis: DAICEL Chiralcel OD-H, hexane/isopropanol = 99.5:0.5, flow rate = 0.5 mL/min, retention time: 14.8 min (*S*) and 21.8 min (*R*).

4.2.7. (*S*)-*tert*-Butyl-3-(4-chlorophenyl)-2-diphenylmethylene amino propanoate 2g (Table 3, entry 7). Yield: 82%; $[\alpha]_D^{20} = -15.8$ (*c* 0.2, $CHCl_3$); ee = 91%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62–7.60 (m, 2H, Ph–H), 7.36–7.25 (m, 6H, Ph–H), 7.16 (d, 2H, $J = 8.0$ Hz, Ph–H), 7.04 (d, 1H, $J = 8.0$ Hz, Ph–H), 6.63 (m, 3H, Ph–H), 4.48 (m, 1H, CHC=O), 3.69–3.48 (m, 2H, $PhCH_2$), 1.45 (s, 9H, *t*-Bu) ppm; IR (neat) 2978, 1732, 1661, 1622, 1560, 1437, 1369, 1286, 1148, 841, 787, 698 cm^{-1}; HPLC analysis: DAICEL Chiralcel OD-H, hexane/isopropanol = 99.5:0.5, flow rate = 0.5 mL/min, retention time: 12.1 min (*S*) and 21.1 min (*R*).

4.2.8. (*S*)-*tert*-Butyl-3-(2-allyl)-2-diphenylmethylene amino propanoate 2h (Table 3, entry 8). Yield: 77%; $[\alpha]_D^{20} = -11.4$ (*c* 0.2, $CHCl_3$); ee = 86%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.65–7.62 (m, 2H, Ph–H), 7.47–7.29 (m, 6H, Ph–H), 7.20–7.16 (m, 2H, Ph–H), 5.62–5.60 (m, 1H, $CH{=}CH_2$), 5.03 (dd, 1H, $J = 17.2$, 1.5 Hz, $CH{=}CH_2$), 5.01 (dd, 1H, $J = 10.2$, 1.5 Hz, $CH{=}CH_2$), 4.00 (dd, 1H, $J = 7.6$, 5.6 Hz, CHC=O), 2.57–2.69 (m, 2H, CH_2–$CH{=}CH_2$), 1.44 (s, 9H, *t*-Bu) ppm; IR (neat) 2978, 1735, 1624, 1447, 1367, 1286, 1151, 916, 847, 781, 696 cm^{-1}; HPLC analysis: DAICEL Chiralcel OD-H, hexane/isopropanol = 99.5:0.5, flow rate = 0.5 mL/min, retention time: 9.3 min (*S*) and 10.9 min (*R*).

4.2.9. (*S*)-*tert*-Butyl-3-ethyl-2-diphenylmethylene amino propanoate 2i (Table 3, entry 9). Yield: 82%; $[\alpha]_D^{20} = -12.2$ (*c* 0.2, $CHCl_3$); ee = 90%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.62–7.65 (br m, 2H, Ph–H), 7.30–7.50 (m, 6H, Ph–H), 7.17–7.20 (m, 2H, Ph–H), 3.85 (dd, 1H, $J = 5.7$, 3.9 Hz, CHC=O), 1.86–1.95 (m, 2H, CH_2CH_3), 1.44 (s, 9H, *t*-Bu), 0.87 (t, 3H, $J = 5.4$ Hz, CH_3) ppm; IR (neat) 2978, 1735, 1624, 1447, 1367, 1279, 1153, 696 cm^{-1}; HPLC analysis: DAICEL Chiralcel OD-H, hexane/isopropanol = 99.5:0.5, flow rate = 0.5 mL/min, retention time: 11.6 min (*S*) and 13.3 min (*R*).

4.2.10. (*S*)-*tert*-Butyl-3-methyl-2-diphenylmethylene amino propanoate 2j (Table 3, entry 10). Yield: 79%; $[\alpha]_D^{20} = -10.8$ (*c* 0.2, $CHCl_3$); ee = 83%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.62–7.65 (m, 2H, Ph–H), 7.51–7.30 (m, 6H, Ph–H), 7.20–7.17 (m, 2H, Ph–H), 4.03 (q, 1H, $J = 6.8$ Hz, CHC=O), 1.46 (d, 3H, $J = 6.8$ Hz, CH_3), 1.44 (s, 9H, *t*-Bu) ppm; IR (neat) 2978, 1735, 1624, 1447, 1367, 1286, 1153, 1030, 849, 781, 696 cm^{-1}; HPLC analysis: DAICEL Chiralcel OD-H, hexane/isopropanol = 99.5:0.5, flow rate = 0.5 mL/min, retention time: 10.7 min (*S*) and 12.0 min (*R*).

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