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Contrast performance in catalytic ability—new cinchona phase transfer catalysts for asymmetric synthesis of α-amino acids

Shanmugam Elango,* Murugapillai Venugopal, P. S. Suresh and Eni

Institute of Chemical and Engineering Sciences, 1 Pesek road, Jurong Island 627833, Singapore

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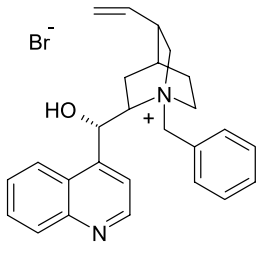
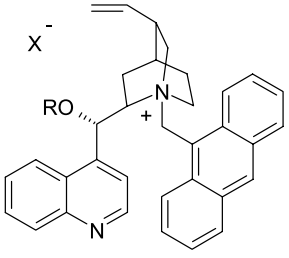
Abstract—Two new cinchona phase transfer catalysts are prepared from dihydrocinchonidine using 13-picenylmethyl bromide and 1-pyrenylmethyl bromide, respectively. A total contrast in catalytic efficiency is observed during the asymmetric alkylation of glycinate esters; with one catalyst, the reaction is either incomplete or the enantioselectivity is very poor (15% ee) while the other catalyst afforded high selectivity up to 94% ee.

1. Introduction

The growing importance of enantiomerically pure compounds for life-science applications has fueled a wealth of research in asymmetric synthesis. In particular, since the pioneering work by O'Donnell[1] et al. in 1989 on asymmetric alkylation of glycinate esters using the benzylammonium salt of cinchona alkaloid **1**, there has been tremendous achievements over the development of novel chiral phase transfer catalysts. Lygo[2] and Corey[3] independently reported an improved version by introducing a 9-anthracenylmethyl group onto the nitrogen of the quinuclidine ring in cinchonidine (CD) **2**.



1. R= H, Allyl, benzyl



2. R= H, Allyl
X= Cl, Br

Further modifications of the above system include dimeric[4,5] and trimeric[6] phase transfer catalysts (PTCs) Maruoka[7] reported chiral binol-based versatile C_2-symmetric spiral ammonium salts, which allow many options for rational design and fine-tuning for improving greater reactivity and selectivity. The unusual aromatic-F effect in cinchona based PTCs on the selectivity was also demonstrated by Park et al.[8] Furthermore, non-cinchona chiral catalysts, such as phosphonium salts,[9] TADDOL,[10] and salen–metal complexes[11] have also been introduced for asymmetric PTC reactions. However, there has been little understanding over the arylmethyl groups employed for the quaternization of cinchonidine and their influence on asymmetric induction. Here we wish to report the total contrast in the performance of two cinchona PTCs and the reasons for the difference in catalytic ability are analyzed.

2. Results and discussions

Prompted by the successful results from anthracenylmethyl and naphthylmethyl groups employed for the formation of PTCs, we envisioned that 13-picenylmethyl and 1-pyrenylemethyl groups having additional benzene ring(s) but fused in a different manner could be beneficial for the exploration of efficient chiral PTCs due to extended planarity of the aromatics and the steric bulkiness. Thus, dihydrocinchonidine (CDH2) was reacted with 13-picenylmethyl bromide or 1-pyrenylmethyl bromide at 100 °C in toluene for 6 h to provide **5** or **6**, respectively (91 or 92% yield). 13-Picenylmethyl bromide **3** was prepared from LAH reduction of the picene-13-carboxylic acid methyl ester[12] group and then bromination of the resulting alcohol. 1-Pyrenylmethyl bromide[13] **4** was prepared from 1-pyrenecarboxaldehyde through a sequence of reduction and bromination by conventional methods. Both the catalysts **5** and **6** were

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* Corresponding author. Tel.: +65 67963912; fax: +65 63166184; e-mail: s_elango@ices.a-star.edu.sg

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thoroughly characterized by ^{1}H and ^{13}C NMR spectroscopic studies. The impact of the bulky unit on the hydroxyl group in **6** was also studied by alkylating with allyl bromide and 9-anthracenylmethyl bromide in aq NaOH to obtain **7** and **10**, respectively, following the literature method (Scheme 1).[4b]

For the purpose of evaluation of the catalysts, the conventional alkylation reaction of *t*-butylglycine ester was studied. Initially, when the *N*-picenylmethyl hydrocinchonidinium bromide **5** was employed, it surprisingly resulted in disappointing results. Not only that did it provide low optical purity but the catalytic efficiency was also sluggish. Thus, reactions did not go to completion even with reactive alkylating agents. With allyl bromide, it took 19 h to consume the starting material and the reaction proceeded with poor selectivity of only 10% ee (entry 1). The possible reason could be, due to rigid transition state formed through hydrogen bonding and π-stacking between the glycine enolate and PTC **5**, the glycine moiety is sandwiched between linearly fused picene aromatics and the cinchonidine moiety and consequently the electrophile is hampered from approaching the enolate. This is further substantiated by the increase in reaction time observed as the size of the alkylating agent increases from allyl bromide to benzyl bromide. There was no product formation with piperonyl bromide at 0 °C for 24 h. This observation indicates that although the cinchona alkaloid is the best template for making chiral PTCs, it may not be a better performer when sterically overcrowded with the quaternizing group.

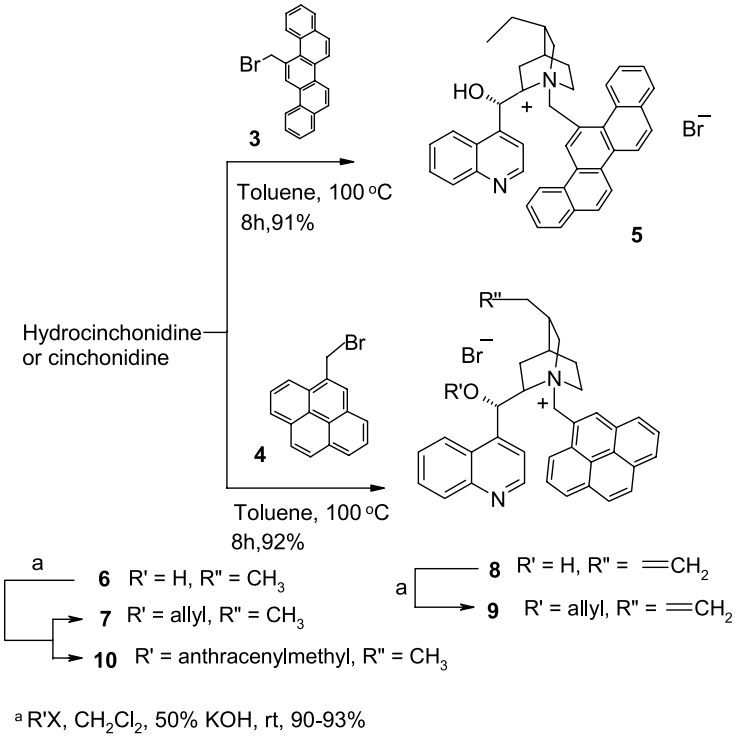
Then, we decided to introduce an optimal group using 1-pyrenylmethyl bromide and thus prepared **6**–**9**. With this system, CDH2 derived PTC **6** was a better template, exhibiting enhanced enantioselectivity of about 13% compared to cinchonidine derived PTC **8** (entries 4 and 9) CD. As endorsed previously, low temperature reactions favored mild improvement in asymmetric induction compared to the room temperature reactions (entries 4 and 5). Despite the fact that by switching over the solvent system from toluene to a mixture of toluene: $CHCl_3$ (7:3) there was substantial increase in selectivity (~8%), it led to simultaneous retardation of the reaction rate remarkably (entries 4 and 8); the reaction time increased from 8 to 14 h. With our catalyst, the enantioselectivity obtainable in toluene (83%) is nearer to that in a mixture of toluene and $CHCl_3$ (91%). There was little preference between the bases NaOH and KOH (entries 7 and 8). We introduced a more bulky anthracenylmethyl group on the hydroxyl (**10**) but there was a drop in ee about 10% (entries 8 and 13). The *N*-pyrenyl-1-methyl hydrocinchonidinium bromide **6** proved to be most efficient of all other catalysts (**7**–**9**) providing up to ~94% ee under reasonably moderate conditions (entry 7) with reproducibility of ±5% ee.

3. Conclusion

We have developed a new cinchona based chiral PTC and established its efficacy. This new catalyst provides high enantioselectivity (86–94% ee) at either 0 °C or room temperature. At the same time, we have also shown the contrasting behavior towards asymmetric induction in two PTCs (**5** and **6**) due to the influence of the arylmethyl group.

4. General

All the chemicals were used as received. The NMR spectra



Scheme 1.

were recorded on a Bruker Avance 400 instrument, operating at 400 and 100.1 MHz for ^{1}H and ^{13}C nuclei, respectively. IR spectra were recorded for KBr pellets on Biorad FTS3000MX spectrometer. Low and high-resolution EI mass spectra (MS and HRMS) were taken on a Finnigan MAT 95 XP spectrometer. Melting points were determined (uncorrected) on a Buchi (B-540) apparatus. Column chromatography was carried out using silica gel (Merck 400–230 mm).

5. Experimental

5.1. General

5.1.1. Preparation of 13-bromomethyl-picene (3). Picene-13-carboxylic acid methyl ester[12] (1.18 g, 3.5 mmol) was dissolved in dry THF (25 mL) under argon atmosphere and LAH (250 mg) was added in portion over the period of 15 min at room temperature. After the addition, the reaction mixture was stirred for another 15 min and then quenched with water (2 mL) by slow addition. The reaction mixture was then acidified with 1 N HCl and extracted with ethyl acetate (3×50 mL). The combined organic layer washed with water, dried over magnesium sulfate and removal of the solvent in vacuo gave picen-13-ol (1.04 g, 97%) as off-white solid; mp 189.4 °C; IR (KBr) 3485, 1460 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (1H, s), 8.93 (d, $J=8.0$ Hz, 1H), 8.84 (d, $J=8.0$ Hz, 1H), 8.75 (d, $J=9.20$ Hz, 1H), 8.69 (d, $J=9.20$ Hz, 1H), 8.0–7.90 (m, 4H), 7.72–7.63 (m, 4H), 5.52 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.73, 132.99, 131.97, 130.21, 130.13 (2C), 128.87, 128.50, 128.42, 127.91, 127.82, 126.91, 126.75 (2C), 126.37, 126.30, 123.36, 124.35, 123.13, 121.96, 121.90, 121.55, 67.17. MS *m/e* (%) 308 (M^+, 45), 291 (40), 289 (20), 136 (65), 107 (20), 89 (20), 77 (20); HRMS (EI) calcd for $C_{23}H_{16}O$ 308.1204, found 308.1233.

Picen-13-ol obtained above (678 mg, 2.2 mmol) was dissolved in chloroform (5 mL) and HBr (48% aq solution, 4 mL) was added to it and stirred for 4 h at room temperature. The reaction mixture was diluted with chloroform (20 mL) and organic layer separated, washed with water (2×30 mL), dried over magnesium sulfate and concentrated. The crude product was crystallized in CH_2Cl_2–hexane mixture as yellow solid **3**. (710 mg, 87%); mp 169–172 °C (decomp); IR (KBr) 1210, 797, 732 cm^{-1}. ^{1}H NMR: (400 MHz, $CDCl_3$) δ 9.05 (d, $J=8.4$ Hz, 1H), 9.00 (s, 1H), 8.82 (d, $J=8.4$ Hz, 1H), 8.71 (d, $J=8.8$ Hz, 1H), 8.65 (d, $J=9.2$ Hz, 1H), 7.99 (m, 2H), 7.75 (m, 2H), 7.66 (m, 2H), 5.4 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.1, 132.8, 131.9, 130.4, 129.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0 (2C), 127.9, 127.8, 127.1, 126.9, 126.5, 126.4, 123.1, 121.9, 121.5, 38.8. MS (EI) 370; HRMS (EI) calcd for $[C_{23}H_{15}Br]+$ 370.0357, found 370.0375.

5.1.2. Preparation of *N*-13-picenylmethylhydrocinchonidinium bromide 5. A mixture of (−)-hydrocinchonidine (1 g, 3.39 mmol) with 13-picenylmethy l bromide (1.26 g, 3.39 mmol) in toluene (40 mL) was stirred at 100 °C for 8 h. After cooling the reaction mixture to room temperature, the suspension was filtered off and the solid dissolved in MeOH (30 mL) and the turbid solution filtered over celite pad, partly concentrated and crystallized along with ether to afford **5** as a pale yellow solid in 91% yield. $[\alpha]_{23}^{D}=-383.23$ ($c=2.0$, DMSO); mp 180.3–182.1 °C (decomp); IR (KBr) 3327, 3192, 3050, 2951, 1591, 1509, 1458, 808 cm^{-1}. δ_H ^{1}H NMR (400 MHz, MeOH-d4) 9.36 (s, 1H), 8.97 (d, $J=8.0$ Hz, 1H), 8.89 (d, $J=8.1$ Hz), 8.82 (d, $J=4.4$ Hz, 1H), 8.75–8.66 (m, 2H), 8.44 (d, $J=8.5$ Hz, 1H), 8.1 (d, $J=8.5$ Hz, 1H), 8.0–7.93 (m, 3H), 7.90–7.80 (m, 2H), 7.78 (d, $J=4.2$ Hz, 1H), 7.7 (q, $J=8.6$ Hz, 2H), 7.62 (t, $J=8.4$ Hz, 2H), 6.82 (s, 1H), 6.72 (d, $J=12.1$ Hz, 1H), 5.87 (d, $J=12.2$ Hz, 1H), 4.0–3.89 (m, 1H), 3.83 (t, $J=9.3$ Hz, 1H), 2.78 (d, $J=12.8$ Hz, 1H), 2.40 (t, $J=12.6$ Hz, 1H), 2.35–2.67 (m, 1H), 1.97 (t, $J=12.4$ Hz, 1H), 1.75–1.56 (m, 2H), 1.32–1.05 (m, 3H); ^{13}C NMR ($J=100$ Hz, MeOH-d4): 151.0, 148.8, 147.6, 134.6, 133.6, 133.6, 132.1, 131.6, 131.2, 131.2, 131.1, 131.0, 130.4, 130.3, 129.9, 129.7, 129.4, 129.3, 129.1, 128.8, 128.7, 128.5, 128.4, 127.7, 126.2, 124.8, 124.5, 122.9, 122.8, 122.2, 121.2. MS (EI) 587; HRMS (EI) calcd for $[C_{42}H_{39}N_2O]+$ 587.3053, found 587.3055.

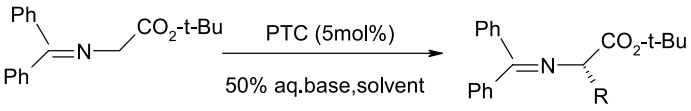
5.1.3. *N*-1-Pyrenylmethylhydrocinchonidinium bromide 6. The same procedure as above was followed to obtain **6** as a off-white solid (92%, 1.84 g). $[\alpha]_{D}^{23}=-243$ ($c=2$, MeOH); mp 186.5–188 °C (decomp); IR (KBr) 3420, 3195, 1590, 1459, 855 cm^{-1}. δ_H ^{1}H NMR (400 MHz, MeOH-d4) 8.61 (d, $J=4.6$ Hz, 1H), 8.56 (d, $J=9.4$ Hz, 1H), 8.39–8.36 (m, 1H), 8.34–8.32 (m, 3H), 8.31–8.28 (m, 2H), 8.20 (d, $J=9.20$ Hz, 1H), 8.12 (d, $J=9.20$ Hz, 1H), 8.10–8.04 (m, 2H), 7.99 (d, $J=7.8$ Hz, 1H), 7.84–7.76 (m, 2H), 6.87 (bs, 1H), 6.04 (d, $J=13.2$ Hz, 1H), 5.49 (d, $J=13.2$ Hz, 1H), 4.76–4.73 (m, 1H), 4.21 (t, $J=8.4$ Hz, 1H), 3.61–3.55 (m, 1H), 3.46–3.40 (m, 1H), 3.14–3.07 (m, 1H), 2.29–2.22 (m, 1H), 2.18–2.10 (m, 1H), 1.93–1.86 (m, 1H), 1.70–1.61 (m, 1H), 1.59–1.50 (m, 1H), 1.42–1.33 (m, 1H), 1.30–1.13 (m, 2H), 0.67 (t, $J=7.4$ Hz, 3H); ^{13}C NMR (100 MHz, MeOH-d4): δ 151.2, 148.9, 147.9, 134.7, 134.0, 133.6, 132.7, 131.8, 131.3, 130.8, 130.5, 130.5, 129.4, 128.4, 128.0, 127.9, 127.4, 126.3, 126.3, 126.0, 125.5, 124.5, 124.0, 121.7, 121.6, 69.67, 67.0, 64.6, 61.8, 53.3, 37.7, 27.6, 26.7, 25.5, 22.6, 11.8. MS (EI) 511; HRMS (EI) calcd for $[C_{36}H_{35}N_2O]+$ 511.2741, found 511.2709.

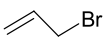
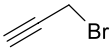
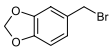
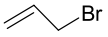
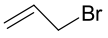
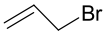
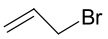
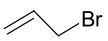
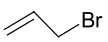
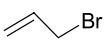
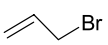
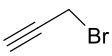
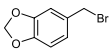
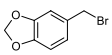
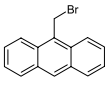
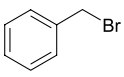
5.1.4. *N*-1-Pyrenylmethyl-O(9)-allylhydrocinchonidinium bromide 7. Pale yellow solid. $[\alpha]_{D}^{23}=-185.34$ ($c=2.0$, DMSO); mp 166.9–169.0 °C (decomp); IR (KBr) 3375, 2947, 1458, 852 cm^{-1}. δ_H ^{1}H NMR (400 MHz, MeOH-d4) 8.94 (d, $J=4.6$ Hz, 1H), 8.49–8.41 (m, 1H), 8.38–8.32 (m, 2H), 8.31–8.26 (m, 1H), 8.25–8.18 (m, 1H), 8.17–8.05 (m, 3H), 8.0 (t, $J=7.3$ Hz, 1H), 7.97–7.87 (m, 3H), 6.63 (bs, 1H), 6.36–6.23 (m, 1H), 5.78 (d, $J=12.9$ Hz, 1H), 5.58–5.49 (m, 2H), 5.44 (d, $J=11.9$ Hz, 1H), 4.47–4.19 (m, 4H), 3.69–3.59 (m, 1H), 3.37 (t, $J=11.9$ Hz, 1H), 3.17–3.02 (m, 1H), 2.39–2.27 (m, 1H), 2.17–2.05 (m, 1H), 1.93–1.83 (bs, 1H), 1.66–1.37 (m, 3H), 1.30–1.02 (m, 2H), 0.66 (t, $J=7.3$ Hz, 3H); ^{13}C NMR (100 MHz, MeOH-d4): δ 151.1, 149.3, 143.2, 134.8, 134.7, 133.9, 133.5, 132.6, 131.7, 131.5, 130.8, 130.6, 130.5, 129.5, 128.3, 127.9, 127.8, 127.4, 127.0, 126.3, 126.0, 125.5, 124.2, 123.7, 121.6, 121.1, 119.4, 71.5. MS (EI) 551; HRMS (EI) calcd for $[C_{39}H_{39}N_2O]+$ 551.3053, found 551.3035.

5.1.5. *N*-1-Pyrenylmethylcinchonidinium bromide 8. Off-white white solid. $[\alpha]_D^{23} = -290.01$ ($c = 2.2$, CH_2Cl_2); mp 184.7–185.9 °C (decomp); IR (KBr) 3632, 3180, 1585, 1459, 848 cm^{-1}. δ_H ^1H NMR (400 MHz, MeOH-d4) 8.87 (d, $J = 4.6$ Hz, 1H), 8.47 (d, $J = 10.1$ Hz, 1H), 8.42–8.37 (m, 2H), 8.35 (t, $J = 8.30$ Hz, 3H), 8.23–8.16 (m, 2H), 8.10–7.92 (m, 3H), 7.88 (d, $J = 9.20$ Hz, 1H), 7.70–7.62 (m, 2H), 6.84 (s, 1H), 6.06 (d, $J = 12.8$ Hz, 1H), 5.66 (d, $J = 12.8$ Hz, 1H), 5.63–5.51 (m, 1H), 5.39 (s, 1H), 5.06 (d, $J = 17.5$ Hz, 1H), 4.86 (d, $J = 11.0$ Hz, 1H), 4.67–4.56 (m, 1H), 4.24 (t, $J = 8.3$ Hz, 1H), 3.97–3.88 (m, 1H), 3.36 (t, $J = 11.9$ Hz, 1H), 3.06–2.94 (m, 1H), 2.48–2.37 (m, 1H), 2.19–2.09 (m, 1H), 2.05–1.96 (m, 1H), 1.56–1.43 (m, 1H), 1.32–1.16 (m, 1H), 0.67 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (100 MHz, MeOH-d4): δ 150.9, 148.8, 147.8, 138.9, 134.5, 134.0, 133.5, 132.7, 131.8, 131.2, 130.8, 130.5, 130.4, 130.23, 129.3, 128.3, 128.0, 127.9, 127.4, 126.2, 126.0, 125.5, 124.5, 124.0, 121.6, 121.4, 117.7, 68.6, 67.1, 62.54, 61.6, 53.1, 39.4, 27.8, 26.2, 23.1. MS (EI) 509; HRMS (EI) calcd for $[C_{36}H_{33}N_2O]+$ 509.2585, found 509.2560.

5.1.6. *N*-1-Pyrenylmethyl-O(9)-allylcinchonidinium bromide 9. Yellow solid. $[\alpha]_D^{23} = -199.61$ ($c = 2$, DMSO); mp 164.5–165.1 °C (decomp). IR (KBr) 3383,

Table 1. Enantioselective alkylation of glycinate ester



Entry	RX	Catalyst	T (°C)	Time (h)	Yield[a] %	ee %[b] (config.)[c]
1		**5**	25	19	89	10% (*S*)
2		**5**	25	22	78	10% (*S*)
3		**5**	0	24	No reaction	
4		**6**	25	8	91	83% (*S*)
5		**6**	0	10	94	89% (*S*)
6		**6**	0	15	93[d]	93% (*S*)
7		**6**	0	15	91[e]	94% (*S*)
8		**6**	25	14	91[d]	91% (*S*)
9		**8**	25	13	91	69% (*S*)
10		**9**	25	13	93	74% (*S*)
11		**7**	0	21	89[d]	93% (*S*)
12		**7**	25	12	91	84% (*S*)
13		**10**	25	15	91	80% (*S*)
14		**6**	25	8	90	84% (*S*)
15	CH_3I	**6**	25	48	94	52% (*S*)
16	CH_3CH_2I	**6**	25	48	88	79% (*S*)
17		**6**	25	7	89	88% (*S*)
18		**6**	0	10	89	87% (*S*)
19		**6**	25	12	86	90% (*S*)
20		**6**	25	9	91	88% (*S*)

The reaction was carried out with RX (5 equiv for entries 1–2 and 4–13 and more than 10 equiv for entries 15 and 16; 1.1 equiv for entries 3 and 17–20) and aq NaOH (50%, 13 equiv) in the presence of catalyst (5 mol%) in toluene unless otherwise mentioned.

[a] Yields of isolated product.

[b] Determined by HPLC analysis using a chiral column (DAICEL, Chiralcel OD-H) with hexane/2-propanol (500:0.5 to 500:1) as solvent.

[c] The absolute configuration was determined by comparison of its optical rotation with that of an authentic sample, which was independently synthesized by the reported procedure.[2a]

[d] KOH is the base.

[e] Solvent is toluene/chloroform (7:3).

3042, 2950, 1589, 852 cm^{-1}. δ_H ^1H NMR (400 MHz, MeOH-d4) 8.94 (d, $J=4.6$ Hz, 1H), 8.45–8.35 (m, 3H), 8.34–8.29 (m, 1H), 8.28–8.21 (m, 3H), 8.20–8.15 (m, 1H), 8.14–8.08 (m, 2H), 8.04 (t, $J=7.4$ Hz, 1H), 7.86–7.80 (m, 3H), 6.66 (bs, 1H), 6.38–6.25 (m, 1H), 5.86 (d, $J=13.8$ Hz, 1H), 5.63–5.52 (m, 3H), 5.47 (d, $J=10.1$ Hz, 1H), 5.03 (d, $J=18.4$ Hz, 1H), 4.90 (d, $J=11.0$ Hz, 1H), 4.48–4.18 (m, 4H), 3.93–3.84 (m, 1H), 3.46 (t, $J=12.8$ Hz, 1H), 3.20–3.10 (m, 1H), 2.52–2.42 (m, 1H), 2.40–2.30 (m, 1H), 2.17–2.05 (m, 1H), 1.98–1.90 (m, 1H), 1.68–1.55 (m, 1H), 1.51–1.40 (m, 1H); ^{13}C NMR (100 MHz, MeOH-d4): δ 151.1, 149.3, 143.1, 138.5, 134.8, 134.7, 133.9, 133.5, 132.6, 131.7, 131.5, 130.8, 130.6, 130.5, 129.5, 128.3, 127.9, 127.8, 127.4, 126.9, 126.3, 126.1, 125.5, 124.3, 123.6, 121.5, 121.1, 119.4, 117.7, 71.5 (2C), 69.6, 62.5, 62.2, 53.2, 39.16, 27.72, 26.1, 23.1. MS (EI) 549; HRMS (EI) calcd for $[C_{39}H_{37}N_2O]+$ 549.2887, found 549.2863.

5.1.7. *N*-1-Pyrenylmethyl-O(9)-9-anthracenylhydrocinchonidinium bromide 10. Yellow solid. $[\alpha]_D^{23}=-160.36$ ($c=2$, CH_2Cl_2); mp 178.9–180.3 °C (decomp); IR (KBr) 3379, 2957, 1457, 853 cm^{-1}. δ_H ^1H NMR (400 MHz, MeOH-d4) 9.19 (d, $J=4.6$ Hz, 1H), 8.70 (bs, 1H), 8.44–8.33 (m, 2H), 8.32–8.24 (m, 5H), 8.22–8.16 (m, 3H), 8.16–8.11 (m, 2H), 8.11–8.03 (m, 4H), 7.99 (t, $J=7.4$ Hz, 1H), 7.85 (t, $J=8.7$ Hz, 1H), 7.60 (t, $J=8.7$ Hz, 1H), 7.52 (t, $J=7.4$ Hz, 2H), 6.66–6.55 (m, 2H), 6.01 (d, $J=12.9$ Hz, 1H), 5.76 (d, $J=12.9$ Hz, 1H), 5.08 (d, $J=12.0$ Hz, 1H), 4.26, 4.20–4.01 (m, 1H), 3.84–3.72 (m, 1H), 3.30–3.23 (m, 1H) 2.99 (t, $J=11$ Hz, 1H), 2.81–2.69 (m, 1H), 2.61–2.50 (m, 1H), 2.21–2.08 (m, 1H), 1.97–1.89 (bs, 1H), 1.64 (t, $J=14$ Hz, 1H), 1.55–1.41 (m, 1H), 1.12–1.10 (m, 2H), 0.59 (t, $J=7.4$ Hz, 3H); ^{13}C NMR (100 MHz, MeOH-d4): δ 151.1, 149.3, 143.2, 134.8, 134.7, 133.9, 133.5, 132.6, 131.7, 131.5, 130.8, 130.6, 130.5, 129.5, 128.3, 127.9, 127.8, 127.4, 127.0, 126.3, 126.0, 125.5, 124.2, 123.7, 121.6, 121.1, 119.4, 71.5 (2C), 69.7, 64.5, 62.4, 53.3, 37.3, 27.3, 26.7, 25.4, 22.7, 11.6. MS (EI) 701; HRMS (EI) calcd for $[C_{51}H_{45}N_2O]+$ 701.3521, found 701.3495.

5.2. Representative procedure for enantioselective alkylation using chiral PTC

To a mixture of *N*-(diphenylmethylene) glycine *t*-butyl ester (30 mg, 0.1 mmol) and chiral PTC (5 mol%) in toluene/chloroform (1 mL, vol. ratio 7:3) or in toluene (1 mL) was added the alkyl halide. Then 50% aqueous base was added to the reaction mixture at the required temperature and stirred until the starting material had been consumed by TLC. The suspension was diluted with ethyl acetate (15 mL), washed with water (2×5 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was purified through flash column chromatography on silica gel (hexane–EtOAc = 30:1) to afford the desired product (Table 1).

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