Pergamon

Tetrahedron 54 (1998) 14465–14476

TETRAHEDRON

Synthesis of Novel Chiral Quaternary Phosphonium Salts with a Multiple Hydrogen-Bonding Site, and Their Application to Asymmetric Phase-Transfer Alkylation

Kei Manabe

Graduate School of Pharmaceutical Sciences, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Received 3 September 1998; accepted 24 September 1998

Abstract

Chiral phosphonium salts having two NH and two OH groups as hydrogen-bond donors have been synthesized as novel phase-transfer catalysts, and used for asymmetric alkylation of β-keto esters to give the corresponding products with up to 50% ee.

Keywords: asymmetric reactions; hydrogen bonding; phase transfer; phosphonium salts

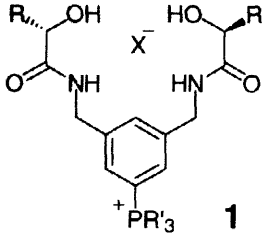
Phase-transfer catalysis (PTC) is a very important and practical tool in synthetic organic chemistry.[1-4] Common cases of its use are in two-phase reactions between solid or aqueous salts and substrates in organic solvents in the presence of catalysts. There are many advantages in PTC over conventional, homogeneous reaction procedures, particularly as there is no need for expensive or polar aprotic solvents. Onium salts such as quaternary ammonium or phosphonium salts are widely used as phase-transfer catalysts. Although enantioselective phase-transfer reactions by using chiral onium salts as catalysts should offer attractive methods to obtain optically active compounds, there have been so far only a limited number of successful examples,[5-21] most of which use quaternary ammonium salts derived from cinchona alkaloids. In enantioselective phase-transfer reactions, it is essential to control the ion-pair structure composed of a chiral onium cation and the counteranion which is a substrate or a reagent. However, work on methodology for controlling the ion-pair structure is still in a preliminary stage. It should be desirable, therefore, to develop chiral catalysts based on a new structural concept to expand the applicability of enantioselective phase-transfer reactions.

In the course of the research on artificial receptor molecules for oxo acids in this laboratory,[22-24] a multiple hydrogen-bonding strategy has been used for the complexation of the receptor molecules with oxo acids. In this strategy, hydrogen bonds between hydrogen-bond donor groups on the receptor molecules and the conjugate bases of oxo acids play a critical role in attaining strong complexation and geometry fixation. The application of this strategy to the design of chiral phase-transfer catalysts would lead to a new methodology to control the ion-pair structure which should affect the enantiomeric excess of reaction products. This paper describes the synthetic details of novel chiral phosphonium salts which have been designed based on the hydrogen-bonding strategy, and the application of the salts to asymmetric phase-transfer alkylation of β-keto esters.[25]

0040-4020/98/$ - see front matter
PII: S0040-4020(98)00899-0

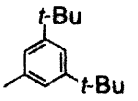
Results and Discussion

As a novel chiral phase-transfer catalyst, phosphonium salt **1** was designed. Two NH and two OH groups are introduced as hydrogen-bond donors to create a multiple hydrogen-bonding site. This multiple hydrogen-bonding site would interact with a counteranion (X^-) through the hydrogen bonds and keep the anion within the asymmetric environment created by the two asymmetric carbon atoms.



1

1a : X = Br, R = R' = Ph

1b : X = Br, R = Ph, R' = 

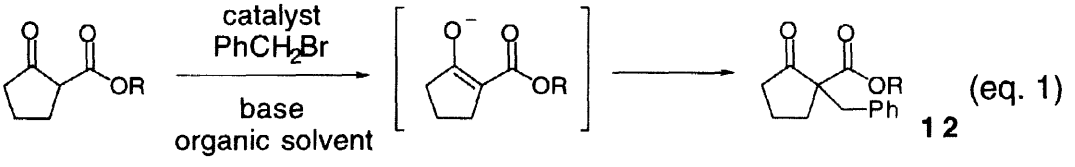
1c: X = Br, R = Ph, R' = $-(CH_2)_7CH_3$

1d : X = Br, R = *t*-Bu, R' = Ph

Phosphonium salts **1a–d** were synthesized as shown in Scheme 1. Tribromide **2**[26] was converted to diamine dihydrochloride **4** by a modified Gabriel synthesis.[27] The condensation of **4** with (*S*)-mandelic acid afforded diamide **5**. The quaternization of various phosphines with **5** was carried out in the presence of $Ni(cod)_2$ as a catalyst to give **1a–c**. This quaternization method is more useful than the reported procedure[28] because isolation of a Ni-phosphine complex prior to the quaternization reaction is not necessary. Phosphonium salts **1d** was similarly prepared from **4** via diamide **6**. Phosphonium salts **8** and **11** (Scheme 1) were also synthesized for comparison.

In order to show the presence of hydrogen bonds between the OH and NH groups of **1a** and the counteranion, ^1H NMR experiments were carried out. The ^1H NMR signal of the OH protons of diamide **5** in $CDCl_3$ at 30 °C (5.0 mM) is observed at 3.64 ppm, and that of phosphonium salt **1a** at 5.05 ppm. This downfield shift of 1.41 ppm is attributable to the hydrogen bonding between the OH groups and the bromide anion of **1a**. Similarly, the NH protons of **1a** show a downfield shift of 1.79 ppm (6.66 ppm for **5**, 8.45 ppm for **1a**). Although these results do not necessarily indicate the simultaneous participation of the OH and NH groups in the hydrogen bonding, it is clear that these groups act as hydrogen-bond donors to the counteranion.

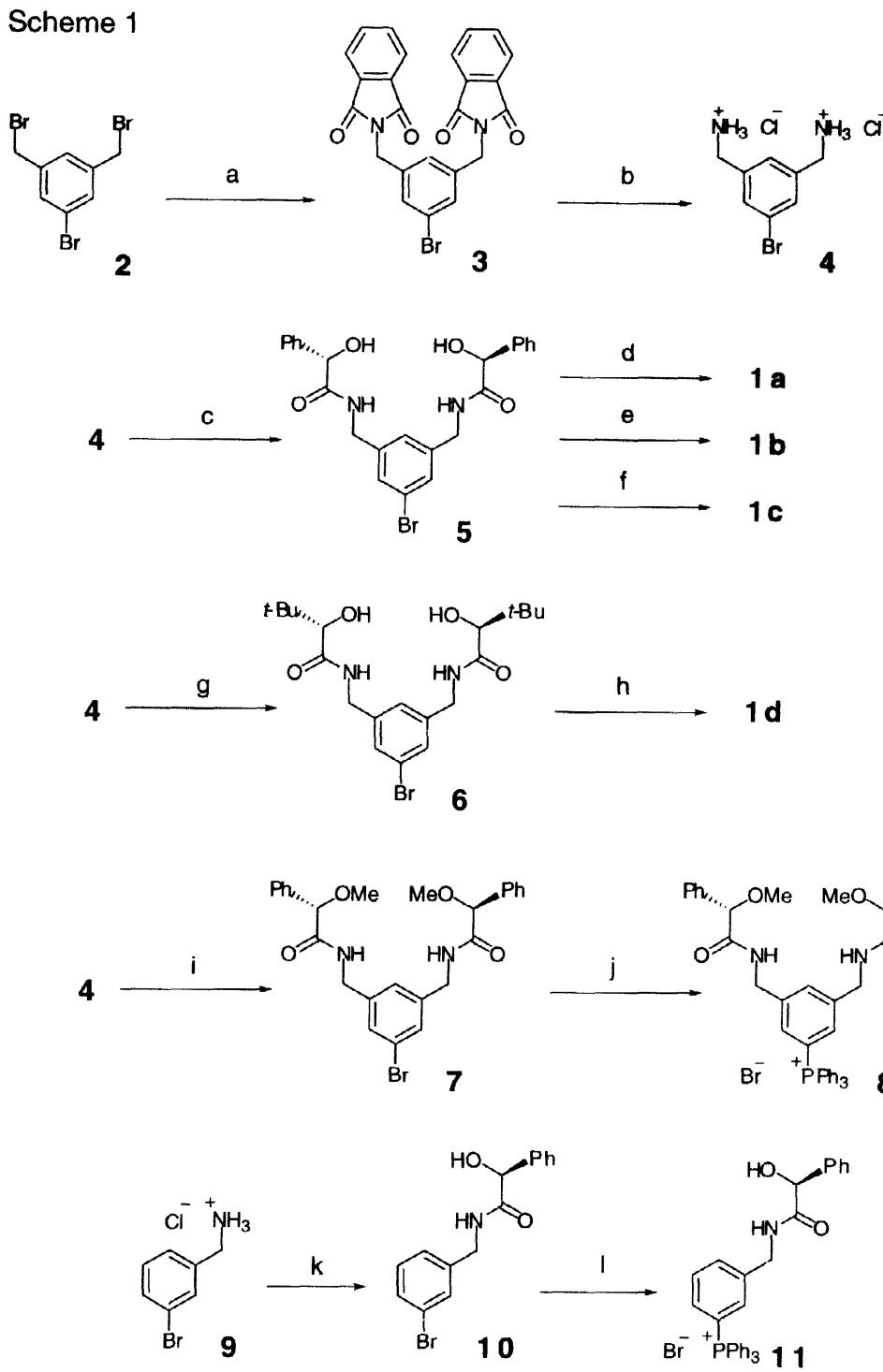
Phosphonium salts **1a–d**, **8**, and **11** were applied to asymmetric benzylation reactions of alkyl 2-oxocyclopentanecarboxylates as shown in eq. 1. The results under various conditions are shown in Table 1.



12 (eq. 1)

The phosphonium salts accelerated the reaction, and showed moderate enantioselectivities. For example, in the presence of 1 mol % of phosphonium salt **1a** as a catalyst, a saturated aqueous solution of K_2CO_3 as a base, and toluene as an organic solvent, the *t*-butyl ester gave the benzylated product **12** (R = *t*-Bu) with 39% ee in 43% yield (Table 1, entry 3). Benzylation of the methyl and the benzyl esters resulted in very low enantioselectivities (entry 1, 2). Use of other aqueous bases and other organic solvents did not improve the ee (entry 4–13). Without an organic solvent, the ee decreased (entry 14). Diluting the K_2CO_3 solution from 53% (saturated) to 40% and 10% reduced not only the yields but also the enantioselectivities (entry 15, 16). Although

Scheme 1



(a) Potassium phthalimide, hexadecyltri-*n*-butylphosphonium bromide (cat.), toluene, reflux, 80%; (b) (1) hydrazine monohydrate, EtOH, reflux; (2) conc. HCl, MeOH, 80%; (c) (*S*)-mandelic acid, DEPC, Et_3N, DMF, rt, 77%; (d) PPh_3, $Ni(cod)_2$ (cat.), EtOH, 110 °C in a sealed tube, 43%; (e) Tris(3,5-di-*t*-butylphenyl)phosphine, $Ni(cod)_2$ (cat.), EtOH, 110 °C in a sealed tube, 66%; (f) trioctylphosphine, $Ni(cod)_2$ (cat.), EtOH, 110 °C in a sealed tube, 24%; (g) (1) NaOH, (2) (*S*)-2-hydroxy-3,3-dimethylbutyric acid, HOOBt, WSCI•HCl, CH_2Cl_2, DMF, 67%; (h) PPh_3, $Ni(cod)_2$ (cat.), EtOH, 110 °C in a sealed tube, 42%; (i) (1) NaOH, (2) (*S*)-α-methoxyphenylacetic acid, HOOBt, WSCI•HCl, DMF, 78%; (j) PPh_3, $Ni(cod)_2$ (cat.), EtOH, 110 °C in a sealed tube, 45%; (k) (1) NaOH, (2) (*S*)- mandelic acid, HOOBt, WSCI•HCl, DMF, 83%; (l) PPh_3, $Ni(cod)_2$ (cat.), EtOH, 110 °C in a sealed tube, 32%.
HOOBt: 3-hydroxy-1,2,3-benzotriazin-4(3*H*)-one. WSCI•HCl: 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride.

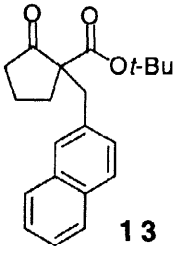
Table 1.
Asymmetric benzylation of alkyl 2-oxocyclopentanecarboxylates with benzyl bromide.

Entry	R	Catalyst (mol %)	Base	Organic solvent	Temp. (°C)	Reaction time (h)	Yield (%)	ee(%)
1	Me	**1a** (1.0)	satd. aq. K_2CO_3	toluene	20	24	50	1 (*R*)
2	Bn	**1a** (1.0)	satd. aq. K_2CO_3	toluene	20	24	88	4
3	*t*-Bu	**1a** (1.0)	satd. aq. K_2CO_3	toluene	20	24	43	39 (*R*)
4	-Bu	**1a** (1.0)	satd. aq. Na_2CO_3	toluene	20	24	7	25 (*R*)
5	*t*-Bu	**1a** (1.0)	satd. aq. Rb_2CO_3	toluene	20	24	56	29 (*R*)
6	*t*-Bu	**1a** (1.0)	satd. aq. Cs_2CO_3	toluene	20	24	49	20 (*R*)
7	*t*-Bu	**1a** (1.0)	50% aq. NaOH	toluene	20	6	8	3 (*S*)
8	*t*-Bu	**1a** (1.0)	10% aq. NaOH	toluene	20	6	75	4 (*R*)
9	*t*-Bu	**1a** (5.0)	satd. aq. K_2CO_3	hexane	20	24	17	2 (*R*)
10	*t*-Bu	**1a** (1.0)	satd. aq. K_2CO_3	CH_2Cl_2	20	24	65	7 (*R*)
11	*t*-Bu	**1a** (1.0)	satd. aq. K_2CO_3	Et_2O	20	24	30	14 (*R*)
12	*t*-Bu	**1a** (1.0)	satd. aq. K_2CO_3	benzene	20	24	59	34 (*R*)
13	*t*-Bu	**1a** (1.0)	satd. aq. K_2CO_3	PhEt	20	24	28	36 (*R*)
14	*t*-Bu	**1a** (1.0)	satd. aq. K_2CO_3	-	20	24	93	10 (*R*)
15	*t*-Bu	**1a** (1.0)	10%. aq. K_2CO_3	toluene	20	24	5	20 (*R*)
16	*t*-Bu	**1a** (1.0)	40% aq. K_2CO_3	toluene	20	24	21	32 (*R*)
17	*t*-Bu	**1a** (1.0)	K_2CO_3 (solid)	toluene	20	24	67	1 (*S*)
18	*t*-Bu	**1a** (5.0)	satd. aq. K_2CO_3	toluene	20	24	47	38 (*R*)
19	*t*-Bu	**1a** (0.2)	satd. aq. K_2CO_3	toluene	20	24	37	40 (*R*)
20	*t*-Bu	**1a** (1.0)	satd. aq. K_2CO_3	toluene	20	168	80	38 (*R*)
21	*t*-Bu	**1a** (1.0)	satd. aq. K_2CO_3	toluene	0	168	44	50 (*R*)
22	*t*-Bu	**1b** (1.0)	satd. aq. K_2CO_3	toluene	20	24	92	13 (*R*)
23	*t*-Bu	**1c** (1.0)	satd. aq. K_2CO_3	toluene	20	24	90	5 (*R*)
24	*t*-Bu	**1d** (1.0)	satd. aq. K_2CO_3	toluene	20	24	85	21 (*R*)
25	*t*-Bu	**8** (1.0)	satd. aq. K_2CO_3	toluene	20	24	50	10 (*S*)
26	*t*-Bu	**11** (1.0)	satd. aq. K_2CO_3	toluene	20	24	63	1 (*S*)

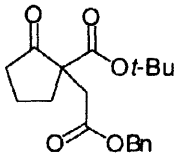
there is no conclusive explanation for the effect of base concentration on the enantioselectivity, the amount of water in the organic solvent may affect the ion-pair structure and, consequently, the enantioselectivity. Use of solid K_2CO_3 as a base drastically reduced the ee (entry 17). Surprisingly, the amount of the catalyst does not significantly affect the yields (entry 18, 19). This is probably due to the very low solubility of **1a** in toluene; only a small portion of the catalyst molecules exists in the toluene solution and participates in the catalytic cycle. Elongation of the reaction time from 24 h to 168 h led to an increase of the yield up to 80% with practically unchanged ee (entry 20). Finally, lowering the reaction temperature to 0 °C improved the selectivity up to 50% ee (entry 21). This is so far the best result as far as the ee is concerned. Phosphonium salts **1b**, **1c**, and **1d** significantly improved the yields, although they showed poorer enantioselectivities (entry 22–24). The phosphonium salts **8**, which has methoxy groups instead of hydroxy groups, gave the product with opposite configuration (entry 25). Furthermore, phosphonium salt **11**, which has only one mandelamide unit, afforded the product in almost racemic form (entry 26). This result suggests that two mandelamide units of **1a** are necessary to create an effective chiral environment for the substrate anion.

Other alkylating agents were tested for the asymmetric reaction under the same conditions as those of Table 1, entry 3. Benzyl iodide gave almost the same result (41% ee (*R*), 42% yield) as benzyl bromide did, although benzyl chloride did not afford the product. 2-(Bromomethyl)naphthalene gave **13** with 31% ee (the absolute configuration has not been determined) in 45% yield. However, benzyl 2-bromoacetate gave **14** in almost racemic form (4% ee, 93% yield), although the phosphonium salt accelerated the reaction. The reason for the low enantioselectivity has not been identified. These results show that the structure of the alkylating agents also affects the enantioselectivity.

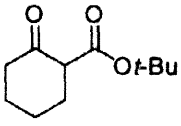
Unfortunately, *t*-butyl 2-oxocyclohexanecarboxylate **15** did not react with benzyl bromide under the conditions shown in Table 1.



13

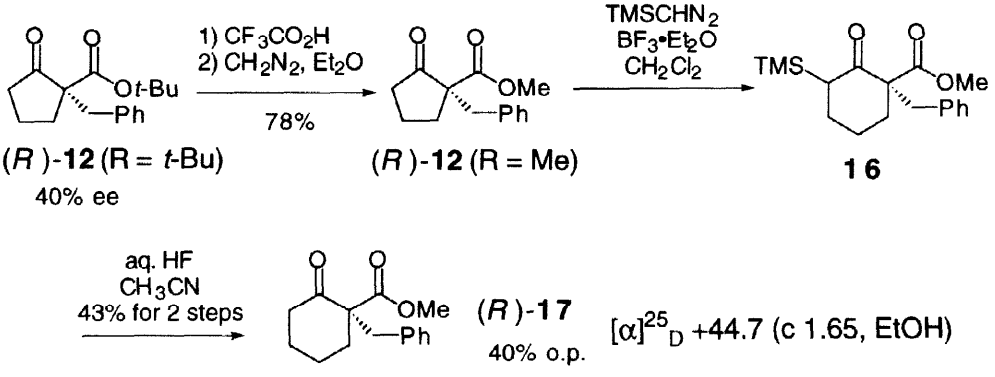


14



15

The absolute configuration of **12** (R = *t*-Bu) was determined as shown below. The benzylated compound **12** (R = *t*-Bu) with 40% ee was converted to methyl ester **12** (R = Me). The ring expansion with (trimethylsilyl)diazomethane[29] gave cyclohexanone derivative **16**, which unexpectedly has a trimethylsilyl group even after aqueous quenching of the reaction mixture. Finally, the conversion of **16** to the known compound **17**[30] was done with aqueous HF. The comparison of the specific rotation with the reported one[30] revealed the absolute configuration.



(*R*)-**12** (R = *t*-Bu)
40% ee

(*R*)-**12** (R = Me)

16

(*R*)-**17**
40% o.p.

$[\alpha]^{25}_{D}$ +44.7 (c 1.65, EtOH)

Conclusion

Phosphonium salts with a multiple hydrogen-bonding site were synthesized through the route including quaternization of a phosphine in the presence of $Ni(cod)_2$, and used as new phase-transfer catalysts for alkylation of alkyl 2-oxocyclopentanecarboxylates. Although the yields and enantioselectivities still remain to be improved further, this research provides a new concept for the designing of chiral phase-transfer catalysts.

Experimental

Phthalimide 3. A suspension of 1-bromo-3,5-bis(bromomethyl)benzene (**2**) (364 mg, 1.06 mmol), potassium phthalide (496 mg, 2.68 mmol), and hexadecyltributylphosphonium bromide (54.4 mg, 0.107 mmol) in toluene (5mL) was stirred under reflux for 1 h. CH_2Cl_2 (30 mL) was added at room temperature, and then the mixture was filtered and evaporated to give a white solid. This was recrystallized from toluene to give the product as colorless fine needles (352 mg, 80%). mp 240 °C; ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 4.79 (s, 4H), 7.44 (s, 3H), 7.73 (dd, J = 5.6, 3.0 Hz, 4H), 7.86 (dd, J = 5.6, 3.0 Hz, 4H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 40.79, 122.95, 123.50, 127.51, 130.82, 131.97, 134.11, 138.74, 167.80; IR (KBr) 1770, 1710 cm^{-1}; MS *m/z* 476, 474 (M^+); Anal. Calcd for $C_{24}H_{15}BrN_2O_4$: C, 60.65; H, 3.18; N, 5.89. Found: C, 60.45; H, 2.93; N, 5.99.

Diamine dihydrochloride 4. To a suspension of **3** (12.6 g, 26.5 mmol) in EtOH (260 mL) was added NH_2NH_2•H_2O (80%, 4.8 mL). The mixture was refluxed for 3 h. At room temperature 2 N HCl (120 mL) was added, and the mixture was filtered and rinsed with water (500 mL). The filtrate was evaporated to about 300 mL and filtered again. After addition of 2 N NaOH (120 mL), the filtrate was extracted with CH_2Cl_2 (100 mL x 4). The combined extracts were washed with brine, dried over K_2CO_3, and concentrated to give a mixture of a colorless solid and a colorless oil. MeOH (100 mL) and conc.HCl (40 mL) were added and evaporated to afford crude material as a white solid. Reprecipitation from MeOH–Et_2O yielded the product (6.11 g, 80%) as colorless fine needles. mp 282–283 °C; ^{1}H NMR (D_2O, DSS, 270 MHz) δ 4.20 (s, 4H), 7.46 (s, 1H), 7.71 (s, 2H); ^{13}C NMR (D_2O, DSS, 67.8 MHz) δ 44.91, 125.55, 130.87, 135.20, 138.26; IR (KBr) 2910 cm^{-1}; Anal. Calcd for $C_8H_{13}BrCl_2N_2$: C, 33.36; H, 4.55; N, 9.73. Found: C, 33.14; H, 4.27; N, 9.55.

Diamide 5. A solution of DEPC (90%, 1.02 g, 5.63 mmol) in DMF (1 mL) was added to a suspension of (*S*)-mandelic acid (845 mg, 5.56 mmol), **4** (763 mg, 2.65 mmol), and triethylamine (0.74 mL, 5.31 mmol) at 0 °C under Ar, and then the flask used for the DEPC solution was rinsed with DMF (1 mL). After 15 min, triethylamine (0.78 mL, 5.60 mmol) was added for 7 min. The whole was stirred for 12 h at room temperature. The mixture was diluted with AcOEt (50 mL), washed with satd. $NaHCO_3$ (20 mL x 2), 10% HCl (20 mL), satd. $NaHCO_3$ (20 mL), and brine (20 mL), dried over $MgSO_4$, and concentrated to afford a colorless amorphous solid. Silica gel column chromatography (AcOEt–CH_2Cl_2) gave the product (986 mg, 77%) as a colorless amorphous solid. mp 69–77 °C; $[\alpha]^{25}_D$ +25.2 (c 0.656, EtOH); ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 3.64 (brs, 2H), 4.30 (dd, J = 15.5, 5.9 Hz, 2H), 4.39 (dd, J = 15.5, 5.9 Hz, 2H), 5.08 (s, 2H), 6.66 (brt, J = 5.9 Hz, 2H), 6.92 (s, 1H), 7.19 (s, 2H), 7.32–7.42 (m, 10H); ^{13}C NMR (acetone-d_6, 67.8 MHz) δ 42.95, 75.22, 123.22, 126.56, 127.93, 128.95, 129.42, 129.89, 142.34, 143.52, 173.78; IR (KBr) 3320, 1660, 1530 cm^{-1}; MS *m/z* 485, 483 (M^++1); Anal. Calcd for $C_{24}H_{23}BrN_2O_4$: C, 59.64; H, 4.80; N, 5.80. Found: C, 59.36; H, 4.89; N, 5.77.

Phosphonium salt 1a. Under Ar, **5** (96.1 mg, 0.199 mmol), PPh_3 (70.9 mg, 0.270 mmol), $Ni(cod)_2$ (11.3 mg, 0.0411 mmol), and dry EtOH (2 mL, bubbled with Ar for 30 min) were charged into a sealed tube, and heated at 110 °C. After 20 h, the mixture was cooled to room temperature, filtered, and concentrated. The resulting green amorphous solid was purified by silica gel column chromatography (CH_2Cl_2–AcOEt, AcOEt, then MeOH–CH_2Cl_2), and the resulting colorless amorphous solid was dissolved in CH_2Cl_2, washed with saturated

aq. NaBr (10 mL X 2) and water (10 mL X 3), and concentrated. After drying *in vacuo* (0.1 mmHg, 100 °C, overnight), the product (63.8 mg, 43%) was obtained as a colorless powder. mp 118–122 °C; $[\alpha]^{27}_{D}$ +27.7 (c 0.448, EtOH); ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 4.26 (dd, J = 15.2, 5.3 Hz, 2H), 4.50 (dd, J = 15.2, 6.9 Hz, 2H), 5.05 (d, J = 5.9 Hz, 2H), 5.22 (d, J = 5.9 Hz, 2H), 7.13–7.74 (m, 24H), 7.85 (td, J = 7.6, 2.0 Hz, 3H), 7.98 (s, 1H), 8.45 (dd, J = 6.9, 5.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 42.21, 73.44, 116.40 (d, J = 89.0 Hz), 117.55 (d, J = 89.0 Hz), 126.65, 127.53, 128.09, 130.53 (d, J = 12.2 Hz), 130.84, 132.03 (d, J = 10.9 Hz), 134.34 (d, J = 9.7 Hz), 135.40, 139.96, 142.11 (d, J = 13.4 Hz), 173.80; IR (KBr) 3270, 1660, 1520, 1440, 1110 cm^{-1}; Anal. Calcd for $C_{42}H_{38}BrN_2O_4P$: C, 67.65; H, 5.14; N, 3.76. Found: C, 67.42; H, 5.25; N, 3.67.

Tris(3,5-di-*t*-butylphenyl)phosphine. Under Ar, BuLi (1.57 N in hexanes, 9.40 mL, 14.8 mmol) was added to a solution of 3,5-di-*t*-butylbromobenzene[31] (3.80 g, 14.1 mmol) in THF (14.0 mL) at -78 °C during 5 min. After 5 min, PCl_3 (0.410 mL, 4.70 mmol) was added during 5 min. After 5 min, the reaction mixture was warmed to 0 °C, and then stirred for 30 min. Brine (50 mL), water (10 mL), and Et_2O (100 mL) were added, and the organic layer was dried over $MgSO_4$, and concentrated. The resulting crude mixture was purified by recrystallization (EtOH, 5mL) to give the product (1.67 g, 59%) as colorless fine needles. mp 145.5–146.0 °C; ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 1.22 (s, 18H), 7.08 (dd, J = 7.9, 1.7 Hz, 2H), 7.36 (s, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 31.36, 34.83, 122.19, 127.94 (d, J = 19.5 Hz), 136.96 (d, J = 9.7 Hz), 150.33 (d, J = 7.3 Hz); IR (KBr) 2950, 1575, 1475 cm^{-1}; MS *m/z*: 598 (M^+); Anal. Calcd for $C_{42}H_{63}P$: C, 84.23; H, 10.60. Found: C, 83.95; H, 10.80.

Phosphonium salt 1b. Under Ar, the suspension of **5** (283 mg, 0.585 mmol), tris(3,5-di-*t*-butylphenyl)phosphine (423 mg, 0.706 mmol), and $Ni(cod)_2$ (32.9 mg, 0.120 mmol) in EtOH (6 mL, distd. from CaH_2, then bubbled with Ar for 30 min) was placed in a sealed tube, then heated at 110 °C. After 14 h, the mixture was cooled to room temperature, filtered, and concentrated to give a pale green amorphous solid. Silica gel column chromatography (CH_2Cl_2/MeOH) afforded the desired phosphonium salt (497 mg) as a colorless amorphous solid. This was dissolved in CH_2Cl_2 (30 mL), washed with saturated aqueous NaBr (10 mL X 2) and distd. water (10 mL X 3), filtered through filter paper, and concentrated to give the product (415 mg, 66%) as a colorless amorphous solid. mp 98.0–105.0 °C; $[\alpha]^{22}_{D}$ -4.77 (c 0.986, EtOH); ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 1.28 (s, 54H), 4.19 (dd, J = 15.5, 5.6 Hz, 2H), 4.55 (dd, J = 15.5, 7.3 Hz, 2H), 5.17 (br, 2H), 5.33 (s, 2H), 7.22–7.36 (m, 14H), 7.61 (d, J = 7.3 Hz, 4H), 7.87 (d, J = 1.7 Hz, 3H), 8.19 (s, 1H), 8.51 (dd, J = 7.3, 5.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 30.95, 35.20, 42.03, 73.19, 117.10 (d, J = 86.5 Hz), 117.20 (d, J = 87.7 Hz), 126.69, 127.33, 127.96, 128.11 (d, J = 11.0 Hz), 129.51, 131.42 (d, J = 10.9 Hz), 133.78, 139.82, 142.01 (d, J = 12.2 Hz), 153.46, (d, J = 12.1 Hz), 173.75; IR (KBr) 3400, 2960, 1670 cm^{-1}; Anal. Calcd for $C_{66}H_{86}BrN_2O_4P$: C, 73.24; H, 8.01; N, 2.59. Found: C, 73.18; H, 8.17; N, 2.69.

Phosphonium salt 1c. Under Ar, a suspension of **5** (345 mg, 0.715 mmol), trioctylphosphine (0.35 mL, 0.785 mmol), and $Ni(cod)_2$ (39.1 mg, 0.142 mmol) in EtOH (2 mL, distd. from CaH_2, then bubbled with Ar for 30 min) was placed in a sealed tube, then heated at 110 °C. After 46 h, CH_2Cl_2 (5 mL) was added at room temperature. The mixture was filtered, and concentrated to give a brown oil. Silica gel column chromatography (CH_2Cl_2/MeOH) afforded the desired phosphonium salt (148 mg, 24%) as a colorless oil. $[\alpha]^{22}_{D}$ +16.1 (c 0.995, EtOH); $[\alpha]^{22}_{435}$ +31.4 (c 0.995, EtOH); ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 0.87 (t, J = 6.9 Hz, 9H), 1.2–1.5 (brm, 36H), 2.48 (br, 6H), 4.25 (dd, J = 15.5, 5.3 Hz, 2H), 4.46 (dd, J = 15.5, 6.3 Hz, 2H), 5.19 (d, J = 4.6

Hz, 2H), 5.30 (d, J = 4.6 Hz, 2H, OH), 7.25–7.28 (m, 6H), 7.43–7.48 (m, 5H), 7.74 (d, J = 12.2 Hz, 2H), 8.10 (brt, J = 6.3, 5.3 Hz, 2H, NH); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 13.96, 19.47 (d, J = 47.6 Hz), 21.49 (d, J = 4.9 Hz), 22.48, 28.77, 28.86, 30.41 (d, J = 14.6 Hz), 31.59, 42.10, 73.42, 117.38 (d, J = 80.6 Hz), 126.47, 127.64, 128.12, 129.02 (d, J = 9.8 Hz), 132.76, 139.75, 141.38 (d, J = 12.3 Hz), 173.80; IR ($CHCl_3$) 3400, 3250, 1670, 1520 cm^{-1}; Elemental analysis could not be successfully done because of the hygroscopic nature of **1c**.

Diamide 6. Compound **4** (501 mg, 1.74 mmol) was neutralized with 2 N NaOH (20 mL), and extracted with CH_2Cl_2 (30, 10, 10 mL). The combined extracts were dried over K_2CO_3, and concentrated. To this free diamine were added (*S*)-2-hydroxy-3,3-dimethylbutyric acid (478 mg, 3.62 mmol), HOObt (598 mg, 3.67 mmol), CH_2Cl_2 (5 mL), and DMF (5 mL). To the resulting yellow suspension was added WSCI•HCl (701 mg, 3.66 mmol), and the whole was stirred at room temperature. After 37 h, the reaction mixture was diluted with AcOEt (50 mL), washed with 1 N HCl (20 mL), water (20 mL), satd. $NaHCO_3$ (20 mL X 2), and brine (20 mL), dried over $MgSO_4$, and concentrated. The resulting crude mixture was purified by silica gel column chromatography (AcOEt/hexanes) to give the product (514 mg, 67%) as a colorless amorphous solid. mp 62.0–70.0 °C; $[\alpha]^{23}_D$ –61.9 (c 0.446, EtOH); ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 1.00 (s, 18H), 3.01 (br, 2H), 3.75 (d, J = 5.3 Hz, 2H), 4.32 (dd, J = 15.2, 5.9 Hz, 2H), 4.48 (15.2, 6.6 Hz, 2H), 6.80 (br, 2H), 7.14 (s, 1H), 7.32 (s, 2H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 26.02, 34.99, 42.09, 79.55, 122.57, 124.94, 129.36, 140.93, 173.53; IR (KBr) 3400, 2960, 1650, 1530 cm^{-1}; MS *m/z*: 445, 443(M^++1), 444, 442 (M^+); Anal. Calcd for $C_{20}H_{31}BrN_2O_4$: C, 54.18; H, 7.05; N, 6.32. Found: C, 54.05; H, 7.01; N, 6.18.

Phosphonium salt 1d. Under Ar, a suspension of **6** (291 mg, 0.656 mmol), triphenylphosphine (230 mg, 0.877 mmol), and $Ni(cod)_2$ (58.3 mg, 0.212 mmol) in EtOH (6.5 mL, distd. from CaH_2, then bubbled with Ar for 30 min) was placed in a sealed tube, then heated at 110 °C. After 14 h, the mixture was cooled to room temperature, filtered, and concentrated to give a green oil. Silica gel column chromatography (CH_2Cl_2/MeOH) afforded the desired phosphonium salt (263 mg) as a pale green amorphous solid. This was dissolved in CH_2Cl_2 (30 mL), washed with saturated aqueous NaBr (10 mL X 2) and distd. water (20 mL X 2), filtered through filter paper, concentrated, and dried at 100 °C under 0.08 mmHg to give the product (192 mg, 42%) as a colorless powder. mp 121.0–125.0 °C; $[\alpha]^{23}_D$ –14.0 (c 0.454, EtOH); ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 0.955 (s, 18H), 3.85 (d, J = 6.3 Hz, 2H), 4.20 (d, J = 6.3 Hz, 2H), 4.33 (dd, J = 14.8, 5.6 Hz, 2H), 4.59 (dd, J = 14.8, 6.6 Hz, 2H), 7.43 (d, J = 13.2 Hz, 2H), 7.58–7.66 (m, 6H), 7.71–7.78 (m, 6H), 7.85–7.91 (m, 3H), 8.25–8.29 (m, 3H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 26.29, 34.88, 42.18, 78.78, 116.25 (d, J = 88.9 Hz), 117.73 (d, J = 89.0 Hz), 130.64 (d, J = 12.2 Hz), 132.22 (d, J = 9.8 Hz), 134.45 (d, J = 9.8 Hz), 135.15, 135.53 (d, J = 2.4 Hz), 142.58 (d, J = 13.4 Hz), 174.11; IR (KBr) 3360, 1655, 1520, 1440, 1110 cm^{-1}; Elemental analysis could not be successfully done because of the hygroscopic nature of **1d**.

Diamide 7. Compound **4** (279 mg, 0.970 mmol) was neutralized with 2 N NaOH (20 mL), and extracted with CH_2Cl_2 (30, 10, 10 mL). The combined extracts were dried over K_2CO_3, and concentrated. To this free diamine were added (*S*)-α-methoxyphenylacetic acid (330 mg, 1.99 mmol), HOObt (334 mg, 2.04 mmol), and DMF (10 mL). To the resulting yellow suspension was added WSCI•HCl (391 mg, 2.04 mmol), and the whole was stirred at room temperature. After 30 h, the reaction mixture was diluted with AcOEt (50 mL), washed with 1 N HCl (20 mL), water (20 mL), satd. $NaHCO_3$ (20 mL X 2), and brine (20 mL), dried over $MgSO_4$, and concentrated. The resulting crude mixture was purified by silica gel column chromatography (AcOEt/hexanes) to

give the product (387 mg, 78%) as a colorless solid. mp 38.0–39.0 °C; $[\alpha]^{23}_{D}$ +48.9 (c 0.438, EtOH); ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 3.37 (s, 6H), 4.36 (dd, J = 15.2, 6.3 Hz, 2H), 4.40 (dd, J = 15.2, 6.3 Hz, 2H), 4.69 (s, 2H), 6.99 (s, 1H), 7.07 (brt, J = 6.3 Hz, 2H), 7.28 (s, 2H), 7.30–7.43 (m, 10H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 41.96, 57.05, 83.58, 122.77, 125.37, 126.85, 128.46, 128.52, 129.42, 136.75, 140.74, 170.60; IR (KBr) 3320, 1670, 1520, 1100 cm^{-1}; MS *m/z*: 512, 510 (M^+);Anal. Calcd for $C_{26}H_{27}BrN_2O_4$: C, 61.06; H, 5.32; N, 5.48. Found: C, 61.15; H, 5.37; N, 5.22.

Phosphonium salt 8. Under Ar, a suspension of **7** (180 mg, 0.352 mmol), triphenylphosphine (120 mg, 0.459 mmol), and $Ni(cod)_2$ (21.2 mg, 0.0771 mmol) in EtOH (3.5 mL, distd. from CaH_2, then bubbled with Ar for 30 min) was placed in a sealed tube, then heated at 110 °C. After 21 h, the mixture was cooled to room temperature, filtered, and concentrated to give a green oil. Silica gel column chromatography (CH_2Cl_2/MeOH) and preparative HPLC (JAIGEL-H, $CHCl_3$) afforded the desired phosphonium salt as a colorless oil. This was dissolved in CH_2Cl_2 (30 mL), washed with saturated aqueous NaBr (10 mL X 2) and distd. water (20 mL X 2), filtered through filter paper, concentrated, and dried at 100 °C under 0.1 mmHg to give the product (122 mg, 45%) as a colorless amorphous solid. mp 113–123 °C; $[\alpha]^{22}_{D}$ +42.5 (c 1.00, EtOH); ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 3.36 (s, 6H), 4.38 (dd, J = 15.2, 6.3 Hz, 2H), 4.52 (dd, J = 15.2, 6.3 Hz, 2H), 4.76 (s, 2H), 7.19–7.23 (m, 6H), 7.41–7.54 (m, 12H), 7.65–7.72 (m, 7H), 7.83 (dt, J = 1.7, 7.6 Hz, 3H), 8.33 (t, J = 6.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 42.05, 57.04, 83.24, 116.60 (d, J = 89.0 Hz), 117.55 (d, J = 89.0 Hz), 127.08, 128.03, 128.23, 130.53 (d, J = 12.2 Hz), 132.17 (d, J = 11.0 Hz), 134.34 (d, J = 9.7 Hz), 134.56 (d, J = 3.7 Hz), 135.29 (d, J = 2.4 Hz), 137.39, 142.23 (d, J = 12.2 Hz), 171.14; IR (KBr) 3420, 1670, 1110 cm^{-1}; Anal. Calcd for $C_{44}H_{42}BrN_2O_4P$: C, 68.31; H, 5.47; N, 3.62. Found: C, 68.11; H, 5.47; N, 3.66.

Amide 10. 3-Bromobenzylamine hydrochloride (191 mg, 0.859 mmol) was neutralized with 10% NaOH (10 mL), and extracted with CH_2Cl_2 (30, 10, 10 mL). The combined extracts were dried over K_2CO_3, and concentrated. To this free amine were added (*S*)-mandelic acid (144 mg, 0.945 mmol), HOObt (156 mg, 0.956 mmol), and DMF (4.0 mL). To the resulting yellow suspension was added WSCI•HCl (183 mg, 0.956 mmol), and the whole was stirred at room temperature. After 17 h, the reaction mixture was diluted with AcOEt (50 mL), washed with 1 N HCl (40 mL), water (40 mL), satd. $NaHCO_3$ (20 mL X 2), and brine (40 mL), dried over $MgSO_4$, and concentrated. The resulting crude mixture was purified by silica gel column chromatography (AcOEt/CH_2Cl_2) and subsequent recrystallization (toluene) to give the product (228 mg, 83%) as colorless plates. mp 91.5–93.5 °C; $[\alpha]^{22}_{D}$ +16.0 (c 1.06, EtOH); ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 3.39 (d, J = 3.6 Hz, 1H), 4.44 (d, J = 5.9 Hz, 2H), 5.12 (d, J = 3.6 Hz, 1H), 6.45 (br, 1H), 7.12 (d, J = 7.6 Hz, 1H), 7.17 (t, J = 7.6 Hz, 1H), 7.31 (s, 1H), 7.38–7.42 (m, 6H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 42.61, 74.16, 122.68, 126.04, 126.70, 128.72, 128.86, 130.21, 130.39, 130.60, 139.25, 140.04, 172.25; IR (KBr) 3400, 3290, 1660, 1620 cm^{-1}; MS *m/z*: 321, 319 (M^++1), 320, 318 (M^+);Anal. Calcd for $C_{15}H_{14}BrNO_2$: C, 56.27; H, 4.41; N, 4.37. Found: C, 56.28; H, 4.21; N, 4.44.

Phosphonium salt 11. Under Ar, a suspension of **10** (106 mg, 0.330 mmol), triphenylphosphine (113 mg, 0.432 mmol), and $Ni(cod)_2$ (10.6 mg, 0.0385 mmol) in EtOH (3.3 mL, distd. from CaH_2, then bubbled with Ar for 30 min) was placed in a sealed tube, then heated at 110 °C. After 25 h, the mixture was cooled to room temperature, filtered, and concentrated to give a green oil. Silica gel column chromatography (CH_2Cl_2/MeOH) afforded the desired phosphonium salt as a colorless amorphous solid. This was dissolved in

CH_2Cl_2 (30 mL), washed with saturated aqueous NaBr (10 mL X 2) and distd. water (10 mL X 3), filtered through filter paper, concentrated, and dried at 100 °C under 0.5 mmHg to give the product (62.0 mg, 32%) as a colorless amorphous solid. mp 85–95 °C; $[\alpha]^{21}_D$ +8.32 (c 0.580, EtOH); ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 4.54 (dd, J = 15.5, 6.3 Hz, 1H), 4.58 (dd, J = 15.5, 6.3 Hz, 1H), 4.63 (d, J = 5.9 Hz, 1H), 5.27 (d, J = 5.9 Hz, 1H), 7.10–7.31 (m, 4H), 7.52–7.91 (m, 20 H), 9.22 (t, J = 6.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 42.39, 73.26, 116.83 (d, J = 89 Hz), 117.58 (d, J = 89 Hz), 126.61, 127.33, 128.00, 130.34 (d, J = 13 Hz), 130.67 (d, J = 13 Hz), 132.39 (d, J = 11 Hz), 133.54 (d, J = 11 Hz), 134.40 (d, J = 11 Hz), 135.34 (d, J = 4 Hz), 135.51 (d, J = 3 Hz), 140.32, 142.48 (d, J = 12 Hz), 173.91; IR (KBr) 3400–3200, 1660, 1440, 1110 cm^{-1}; HRMS (EI$^+$). Calcd for $C_{33}H_{28}NO_2P$ (M-Br$^-$): 501.1858. Found: 501.1866.

Typical procedure for asymmetric alkylation: To a suspension of **1a** (3.7 mg, 0.0050 mmol) and *t*-butyl 2-oxocyclopentanecarboxylate (92.0 mg, 0.50 mmol) in toluene (5.0 mL) was added satd. K_2CO_3 (3.0 mL) at 20 °C. After 5 min, benzyl bromide (0.090 mL, 0.76 mmol) was added, and the whole was vigorously stirred for 24 h at 20 °C. The reaction mixture was diluted with H_2O (30 mL) and satd. NaBr (10 mL), and extracted with CH_2Cl_2 (30 mL, 10 mL, 10 mL). The combined extracts were dried over $MgSO_4$ and concentrated. The crude mixture was purified by silica gel column chromatography (hexanes–Et_2O 25:1) to give **12** (R = *t*-Bu) (59.5 mg, 43%) as a colorless oil. Its ee (39% ee (*R*)) was determined by HPLC analysis (CHIRALCEL OD-H (Daicel); haxanes–2-PrOH 1000:1; flow rate: 1 mL/min; the retention time of the major isomer: 20.1 min, that of the minor isomer: 15.9 min). $[\alpha]^{25}_D$ –41.3 (c 0.606, $CHCl_3$).

(±)-*t*-Butyl 1-benzyl-2-oxocyclopentanecarboxylate (12: R = *t*-Bu). ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 1.43 (s, 9H), 1.49–1.58 (m, 1H), 1.82–2.03 (m, 3H), 2.29–2.36 (m, 2H), 3.12 (s, 2H), 7.13–7.16 (m, 2H), 7.20–7.26 (m, 3H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 19.48, 27.83, 31.92, 38.30, 38.71, 61.89, 81.96, 126.65, 128.25, 130.30, 136.93, 170.33, 215.34; IR (KBr) 2980, 1750, 1725, 1140 cm^{-1}; HRMS calcd for $C_{17}H_{22}O_3$: 274.1569; found: 274.1613.

(±)-Benzyl 1-benzyl-2-oxocyclopentanecarboxylate (12: R = Bn). ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 1.54–1.60 (m, 1H), 1.80–2.09 (m, 3H), 2.29–2.46 (2H), 3.13 (d, J = 13.9 Hz, 1H), 3.23 (d, J = 13.9 Hz, 1H), 5.15 (s, 2H), 7.07–7.10 (m, 2H), 7.20–7.23 (m, 3H), 7.30–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 19.43, 31.65, 38.33, 39.01, 61.46, 67.15, 126.81, 128.01, 128.28, 128.36, 128.57, 130.15, 135.47, 136.44, 170.78, 214.64; IR (KBr) 1750, 1725, 1210, 1160, 1140 cm^{-1}; HRMS calcd for $C_{20}H_{20}O_3$: 308.1412. Found: 308.1448.

(±)-*t*-Butyl 1-(2-naphthyl)methyl-2-oxocyclopentanecarboxylate (13). ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 1.45 (s, 9H), 1.45–1.57 (m, 1H), 1.85–2.02 (m, 3H), 2.32–2.41 (m, 2H), 3.30 (s, 2H), 7.27 (dd, J = 8.6, 1.7 Hz, 1H), 7.40–7.48 (m, 2H), 7.60 (s, 1H), 7.71–7.81 (m, 3H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 19.52, 27.84, 31.86, 38.28, 38.73, 62.01, 82.01, 125.55, 125.97, 127.51, 127.58, 127.78, 128.52, 128.93, 132.20, 133.26, 134.50, 170.31, 215.42; IR (KBr) 2990, 1750, 1720, 1145 cm^{-1}; MS m/z: 324 (M$^+$); Anal Calcd for $C_{21}H_{24}O_3$: C, 77.25; H, 7.46. Found: C, 77.66; H, 7.45.

(±)-Benzyl 2-(1-((*t*-butyl)oxycarbonyl)-2-oxocyclopentyl)acetate (14). ^{1}H NMR ($CDCl_3$, TMS, 270 MHz) δ 1.40 (s, 9H), 1.94–2.14 (m, 3H), 2.31–2.52 (m, 3H), 2.84 (d, J = 7.2 Hz, 1H), 2.97 (d, J = 7.2 Hz, 1H), 5.10 (s, 2H), 7.31–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 19.59, 27.71, 33.41, 37.47,

38.10, 58.01, 66.49, 82.28, 128.21, 128.27, 128.52, 135.53, 169.38, 170.71, 214.46; IR (KBr) 2970, 1730, 1140 cm^{-1}; HRMS calcd for $C_{19}H_{24}O_5$: 332.1624. Found: 332.1612.

Methyl 1-benzyl-2-oxocyclopentanecarboxylate (12: R = Me). Trifluoroacetic acid (0.50 mL) was added to **12** (R = *t*-Bu) (40% ee, 151 mg, 0.552 mmol) at 0 °C, and the whole was stirred for 10 min. Et_2O (30 mL) and H_2O (10 mL) were added, and the organic layer was washed with H_2O (10 mL), dried over $MgSO_4$, and concentrated to give a yellow oil (167 mg). This oil was dissolved in Et_2O (5.0 mL). To this was added a solution of CH_2N_2 in Et_2O, prepared from *N*-methyl-*N*-nitrosourea and 8 N KOH, at 0 °C until the reaction mixture became yellow. The remaining CH_2N_2 was quenched with AcOH. The reaction mixture was diluted with Et_2O (30 mL), washed with satd. $NaHCO_3$ (10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated. The resulting crude mixture was purified by silica gel column chromatography (hexanes/Et_2O) to give the product (100 mg, 78%) as a colorless oil. The ee was found to be 39% by HPLC analysis (CHIRALCEL OD-H (Daicel), hexanes/2-PrOH 100/1). $[\alpha]^{24}_D$ -21.0 (c 1.00, EtOH); ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 1.57–1.64 (m, 1H), 1.83–2.11 (m, 3H), 2.31–2.47 (m, 2H), 3.12 (d, J = 13.5 Hz, 1H), 3.21 (d, J = 13.5 Hz, 1H), 3.73 (s, 3H), 7.11–7.14 (m, 2H), 7.18–7.30 (m, 3H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 19.37, 31.61, 38.32, 39.07, 52.58, 61.44, 126.81, 128.34, 130.06, 136.44, 171.30, 214.81; IR (neat) 2950, 1750, 1720 cm^{-1}; MS *m/z*: 232 (M^+).

Methyl 1-benzyl-2-oxo-3-trimethylsilylcyclohexanecarboxylate (16). A solution of **12** (R = Me) (97.3 mg, 0.419 mmol) in CH_2Cl_2 (8.0 mL) was cooled to –15 °C. BF_3•OEt_2 (0.080 mL, 0.631 mmol) was added. After 5 min, $TMSCHN_2$ (2.0 M in hexanes, 0.32 mL, 0.640 mmol) was added during 10 min, and then the mixture was stirred at between –15 and –10 °C. After 2 h 15 min, satd. $NaHCO_3$ (20 mL) and Et_2O (30 mL) were added. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The resulting orange oil was purified by silica gel column chromatography (hexanes/Et_2O) to give an almost pure product (63.8 mg, 48%) as a colorless oil. This was used for the subsequent reaction without further purification. ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 0.09 (s, 9H), 1.44–1.61 (m. 2H), 1.66–1.76 (m, 2H), 1.86 (dd, J = 12.9, 5.0 Hz, 1H), 2.02–2.07 (m, 1H), 2.41–2.47 (m, 1H), 2.88 (d, J = 14.0 Hz, 1H), 3.31 (d, J = 14.0 Hz, 1H), 3.68 (s, 3H), 7.07–7.10 (m, 2H), 7.20–7.27 (m, 3H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ –2.46, 23.65, 29.15, 35.71, 40.67, 41.82, 52.04, 62.57, 126.58, 127.98, 130.12, 136.71, 171.70; IR (neat) 2950, 1740, 1720, 1700, 1250 cm^{-1}; HRMS Calcd for $C_{18}H_{26}O_3Si$: 318.1651; found: 318.1647.

Methyl 1-benzyl-2-oxocyclohexanecarboxylate (17). A solution of **16** (63.8 mg, 0.200 mmol) in CH_3CN (2.0 mL) was cooled to 0 °C. Aqueous HF (46%, 0.1 mL) was added, and the whole was stirred at 0 °C. After 40 min, satd. $NaHCO_3$ (5 mL) was added slowly. The crude mixture was extracted with Et_2O (30 mL), washed with brine, dried over $MgSO_4$, and concentrated. The resulting oil was purified by silica gel column chromatography (hexanes/Et_2O) to give the product (44.6 mg, 90%) as a colorless oil. The ee was determined to be 38% by HPLC (CHIRALCEL OJ (Daicel), hexanes/2-PrOH 50/1) and 40% (*R*) by optical rotation. $[\alpha]^{25}_D$ +44.7 (c 1.65, EtOH). (lit. 100% ee (*S*): $[\alpha]^{25}_D$ –111 (c 1.63, EtOH)); ^1H NMR ($CDCl_3$, TMS, 270 MHz) δ 1.40–1.72 (m, 4H), 1.99–2.04 (m, 1H), 2.33–2.51 (m, 3H), 2.86 (d, J = 13.5 Hz, 1H), 3.32 (d, J = 13.5 Hz, 1H), 3.63 (s, 3H), 7.07–7.10 (m, 2H), 7.17–7.28 (m, 3H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 22.41, 27.51, 35.74, 40.40, 41.26, 52.10, 62.18, 126.63, 127.98, 130.15, 136.46, 171.36, 207.10; IR (neat) 2950, 1740, 1710 cm^{-1}; MS *m/z*: 246 (M^+).

Acknowledgments. The author is grateful to Professor Kenji Koga (Nara Institute of Science and Technology) for helpful discussions, and to the Ministry of Education, Science, Sports, and Culture, Japan for financial support.

References

(1) Dehmlow, E. V.; Dehmlow, S. S. *Phase transfer catalysis*; Third Edition ed.; VCH: Weinheim, 1993.

(2) Starks, C. M.; Liotta, C. L.; Halpern, M. *Phase-transfer catalysis: fundamentals, applications and industrial perspectives*; Chapman & Hall: New York, 1994.

(3) *Phase-transfer catalysis: mechanisms and syntheses*; Halpern, M. E., Ed.; American Chemical Society: Washington, DC, 1997.

(4) *Handbook of phase transfer catalysis*; Sasson, Y.; Neumann, R., Eds.; Chapman & Hall: London, 1997.

(5) O'Donnell, M. J. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH Publishers: New York, 1993, p 389-411.

(6) Shioiri, T. In *Handbook of phase transfer catalysis*; Sasson, Y., Neumann, R., Eds.; Chapman & Hall: London, 1997, p 462-479.

(7) Dolling, U.-H.; Davis, P.; Grabowski, E. J. J. *J. Am. Chem. Soc.* **1984**, *106*, 446-447.

(8) Bhattacharya, A.; Dolling, U.-H.; Grabowski, E. J. J.; Karady, S.; Ryan, K. M.; Weinstock, L. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 476-477.

(9) Conn, R. S. E.; Lovell, A. V.; Karady, S.; Weinstock, L. M. *J. Org. Chem.* **1986**, *51*, 4710-4711.

(10) Hughes, D. L.; Dolling, U.-H.; Ryan, K. M.; Schoenewaldt, E. F.; Grabowski, E. J. J. *J. Org. Chem.* **1987**, *52*, 4745-4752.

(11) Masui, M.; Ando, A.; Shioiri, T. *Tetrahedron Lett.* **1988**, *29*, 2835-2838.

(12) Arai, S.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 2145-2148.

(13) O'Donnell, M. J.; Bennett, W. D.; Wu, S. *J. Am. Chem. Soc.* **1989**, *111*, 2353-2355.

(14) O'Donnell, M. J.; Wu, S. *Tetrahedron: Asymmetry* **1992**, *3*, 591-594.

(15) O'Donnell, M. J.; Wu, S.; Huffman, J. C. *Tetrahedron* **1994**, *50*, 4507-4518.

(16) Nerinckx, W.; Vandewalle, M. *Tetrahedron: Asymmetry* **1990**, *1*, 265-276.

(17) Lee, T. B. K.; Wong, G. S. K. *J. Org. Chem.* **1991**, *56*, 872-875.

(18) Eddine, J. J.; Cherqaoui, M. *Tetrahedron: Asymmetry* **1995**, *6*, 1225-1228.

(19) Lygo, B.; Wainwright, P. G. *Tetrahedron Lett.* **1997**, *38*, 8595-8598.

(20) Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414-12415.

(21) Corey, E. J.; Noe, M. C.; Xu, F. *Tetrahedron Lett.* **1998**, *39*, 5347-5350.

(22) Manabe, K.; Okamura, K.; Date, T.; Koga, K. *J. Am. Chem. Soc.* **1992**, *114*, 6940-6941.

(23) Manabe, K.; Okamura, K.; Date, T.; Koga, K. *J. Org. Chem.* **1993**, *58*, 6692-6700.

(24) Manabe, K.; Okamura, K.; Date, T.; Koga, K. *Tetrahedron Lett.* **1994**, *35*, 2705-2708.

(25) For preliminary communication, see: Manabe, K. *Tetrahedron Lett.* **1998**, *39*, 5807-5810.

(26) Steenwinkel, P.; James, S. L.; Grove, D. M.; Veldman, N.; Spek, A. L.; vanKoten, G. *Chem. Eur. J.* **1996**, *2*, 1440-1445.

(27) Ciuffarin, E.; Isola, M.; Leoni, P. *J. Org. Chem.* **1981**, *46*, 3064-3070.

(28) Cassar, L.; Foa, M. *J. Organomet. Chem.* **1974**, *74*, 75-78.

(29) Hashimoto, N.; Aoyama, T.; Shioiri, T. *Tetrahedron Lett.* **1980**, *21*, 4619-4622.

(30) Tomioka, K.; Ando, K.; Takemasa, Y.; Koga, K. *J. Am. Chem. Soc.* **1984**, *106*, 2718-2719. The specific rotation reported for optically pure (*S*)-**17**: $[\alpha]^{25}_{D}$ −111 (c 1.63, EtOH).

(31) Komen, C. M. D.; Bickelhaupt, F. *Synth. Commun.* **1996**, *26*, 1693-1697.