Pure Appl. Chem., Vol. 77, No. 7, pp. 1285–1296, 2005.
DOI: 10.1351/pac200577071285

Chiral designer phase-transfer catalysts for practical asymmetric synthesis*

Keiji Maruoka

Department of Chemistry, Graduate School of Sciece, Kyoto University, Kyoto 606-8502, Japan

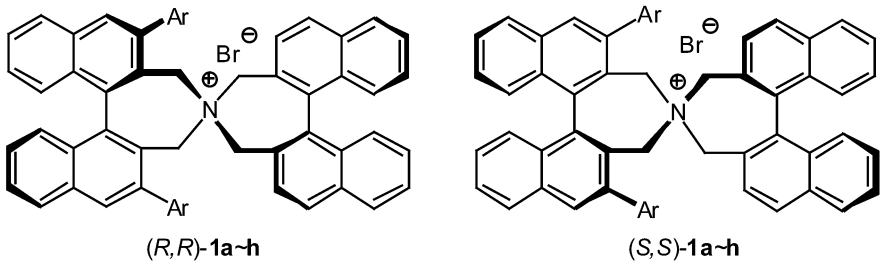
Abstract: A series of C_2-symmetric, spiro-type chiral quaternary ammonium bromides have been designed as new, purely synthetic chiral phase-transfer catalysts, and readily prepared from commercially available optically pure (*R*)- or (*S*)-1,1'-bi-2-naphthol as a basic chiral unit. The structures of the assembled *N*-spiro chiral quaternary ammonium bromides were unequivocally determined by single-crystal X-ray diffraction analysis. The reactivity and selectivity of these chiral ammonium bromides as chiral phase-transfer catalysts have been evaluated in the asymmetric alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester under mild liquid–liquid phase-transfer conditions, and the optimization of the reaction variables (solvent, base, and temperature) has also been conducted. Furthermore, the scope and limitations of other asymmetric transformations have been thoroughly investigated with a variety of substrates, in which the advantage of the unique *N*-spiro structure of our chiral phase-transfer catalysts and dramatic effect of the steric as well as the electronic properties of the aromatic substituents on the 3,3'-position of one binaphthyl moiety have been particularly emphasized.

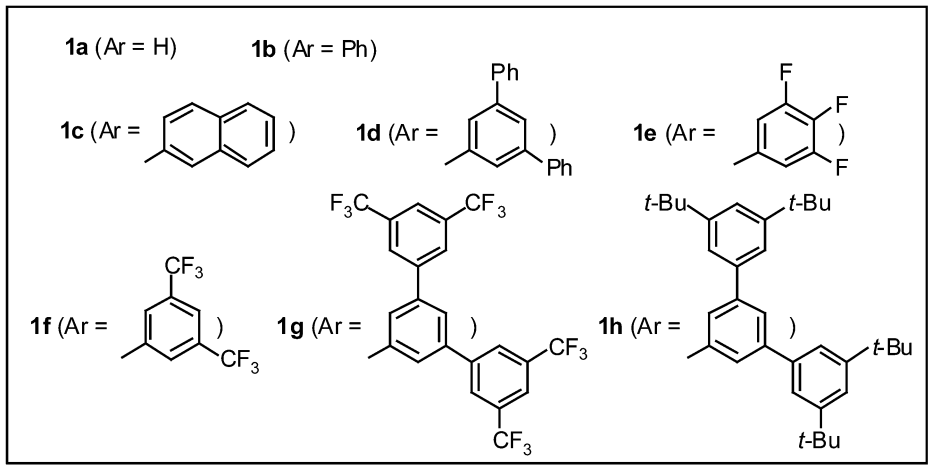
Keywords: phase-transfer catalysts; asymmetric synthesis; amino acids; aldol reactions; peptides.

INTRODUCTION

Since the pioneering work of O'Donnell et al. in 1989, asymmetric synthesis of α-amino acids by phase-transfer enantioselective alkylation of a prochiral protected glycine derivative using a chiral catalyst has provided an attractive method for the preparation of both natural and unnatural amino acids [1,2]. After eight years, the Corey and Lygo groups independently reported an impressive departure from the previous results in terms of enantioselectivity and general applicability [3]. More recently, Jew and Najera prepared several new dimeric and trimeric cinchonidine- and cinchonine-derived chiral phase-transfer catalysts [4]. However, almost all of the elaborated chiral phase-transfer catalysts reported so far have been restricted to *cinchona* alkaloid derivatives, which unfortunately constitute a major difficulty in rationally designing and fine-tuning of catalysts to attain sufficient reactivity and selectivity for various chemical transformations under phase-transfer-catalyzed conditions [5]. Accordingly, structurally rigid, chiral spiro ammonium salts of type **1** derived from commercially available (*S*)- or (*R*)-1,1'-bi-2-naphthol have been designed as a new C_2-symmetric chiral phase-transfer catalyst and successfully applied to the highly efficient, catalytic enantioselective alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester under mild phase-transfer conditions [6].

Pure Appl. Chem.* **77, 1087–1296. An issue of reviews and research papers based on lectures presented at the 15th International Conference on Organic Synthesis (ICOS-15), held in Nagoya, Japan, 1–6 August 2004, on the theme of organic synthesis. This paper is based on the acceptance lecture for the Nagoya Silver Medal.

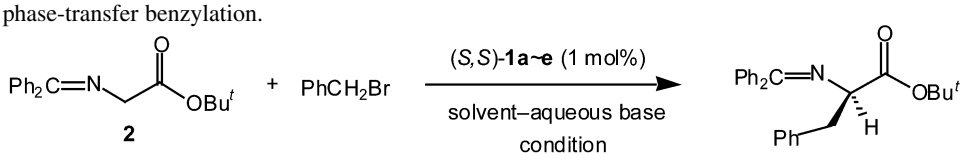




ASYMMETRIC ALKYLATION OF GLYCINE DERIVATIVES

With a series of C_2-symmetric chiral, spiro-type ammonium salts (*R,R*)-**1a~h** and (*S,S*)-**1a~h**, we set out to evaluate these C_2-symmetric quaternary ammonium salts as chiral phase-transfer catalyst in the alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **2**. We chose benzylation as a benchmark reaction and first tested the quaternary ammonium salt (*S,S*)-**1a**. Thus, treatment of *N*-(diphenylmethylene)glycine *tert*-butyl ester **2** with 1 mol % of symmetric (*S*,*S*)-**1a** in 50 % aqueous NaOH–benzene (volume ratio = 1:3) at room temperature gave rise to the corresponding benzylation product in 76 % yield with 73 % ee (*R*) (entry 1 in Table 1). Introduction of an aromatic substituent on the 3,3'-position of one binaphthyl subunit of the catalyst (Ar) afforded a beneficial effect on the enantiofacial discrimination as the reaction with (*S*,*S*)-**1b** resulted in formation of the product in 43 % yield with 81 % ee (entry 2). The use of toluene as organic solvent at lower reaction temperature (0 °C) led to even higher enantioselectivity (88 % ee) (entry 3). Moreover, the reaction under the influence of (*S*,*S*)-**1b** was completed within 30 min at 0 °C with 50 % KOH as an aqueous base giving the product in 81 % yield with 89 % ee (entry 4). Switching the catalyst to (*S*,*S*)-**1c** and sterically more hindered (*S*,*S*)-**1d** further increased the enantioselectivity to 96 and 98 % ee, respectively (entries 5 and 6), and virtually complete stereochemical control was achieved using (*S*,*S*)-**1e** as catalyst (entry 7) [6b]. The lower chemical yield of the benzylation with (*S*,*S*)-**1e** was ascribed to the intervention of enolate oxidation by aerobic oxygen, and this problem was overcome by simply performing the reaction under argon atmosphere (entry 8).

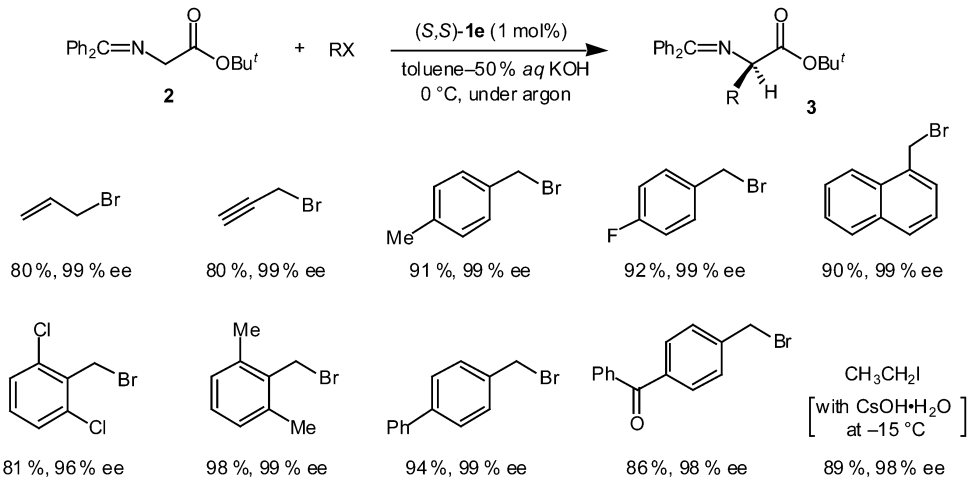
Table 1 Effect of catalyst structure, solvent, and aqueous base on the reactivity and selectivity of phase-transfer benzylation.



Entry	Catalyst	Solvent	Base	Condition (°C; h)	% Yield	% ee (config.)
1	(*S,S*)-**1a**	Benzene	50 % NaOH	r.t.; 10	76	73 (*R*)
2	(*S,S*)-**1b**			r.t.; 10	43	81 (*R*)
3		Toluene		0; 5	62	88 (*R*)
4			50 % KOH	0; 0.5	82	89 (*R*)
5	(*S,S*)-**1c**			0; 0.5	95	96 (*R*)
6	(*S,S*)-**1d**			0; 0.5	91	98 (*R*)
7	(*S,S*)-**1e**			0; 2	79	99 (*R*)
8	(*S,S*)-**1e**			0; 12	90	99 (*R*)*

*Under argon atmosphere.

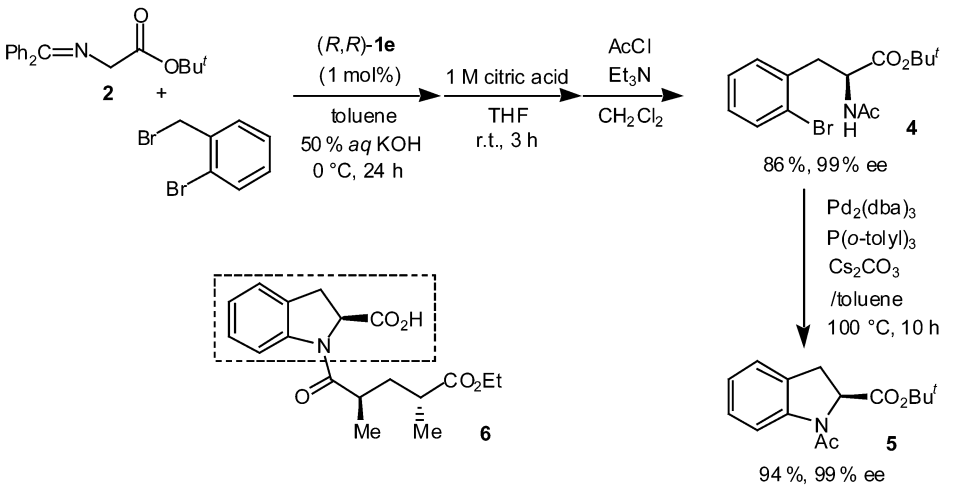
(*S,S*)-**1e** is the catalyst of choice for the preparation of a variety of essentially enantiopure α-amino acids by this transformation as shown in eq. 1. Facile asymmetric synthesis of α-amino acids usually inaccessible by enzymatic processes becomes feasible by employing appropriate electrophiles such as *ortho*-disubstituted benzyl bromides. In the reaction with the simple alkyl halides such as ethyl iodide, use of aqueous cesium hydroxide (CsOH) as a basic phase at lower reaction temperature is generally recommended [6b].



(1)

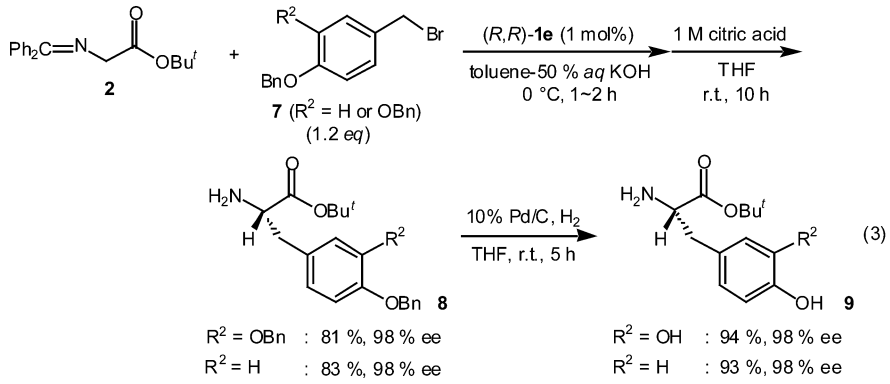
Since both enantiomers of the catalyst of type **1** can be readily assembled in exactly the same manner starting from either (*R*)- or (*S*)-1,1'-bi-2-naphthol, a wide variety of natural and unnatural α-amino acids can be synthesized in an enantiomerically pure form by the phase-transfer catalytic alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **2**. The utility of such advantage has been demonstrated by asymmetric synthesis of (*S*)-*N*-acetylindoline-2-carboxylate **5**, a key intermediate in the synthesis of the ACE inhibitor **6**. The structure and stereochemical integrity of **4** was simultaneously constructed by the asymmetric alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **2** with *o*-bromobenzyl bromide in the presence of the catalyst (*R,R*)-**1e**, and subsequent hydrolysis with citric

acid and *N*-acetylation afforded **4** in 86 % yield with 99 % ee (*S*). According to Buchwald's procedure [7], almost enantiopure **4** was efficiently converted to **5** (94 %, 99 % ee) (eq. 2) [6b].



(2)

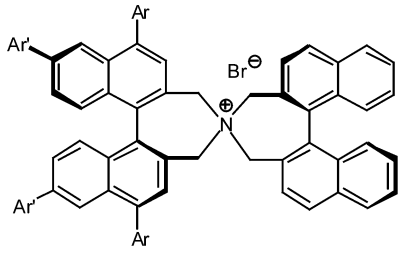
The synthetic utility of chiral phase-transfer catalysis of **1** was further highlighted by the facile synthesis of L-Dopa ester and its analog, which have usually been prepared by either asymmetric hydrogenation of eneamides or enzymatic processes and tested as potential drugs for the treatment of Parkinson's disease. Catalytic phase-transfer alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **2** with the requisite benzyl bromide **7** (R^2 = OBn) in toluene–50 % KOH aqueous solution proceeded smoothly at 0 °C under the influence of (*R*,*R*)-**1e** (1 mol %) to furnish fully protected L-Dopa *tert*-butyl ester, which was subsequently hydrolyzed with a 1 M citric acid in THF at room temperature for 10 h to afford the corresponding amino ester **8** (R^2 = OBn) in 80 % yield with 98 % ee. Debenzylation of **8** (R^2 = OBn) under catalytic hydrogenation conditions produced the desired L-Dopa *tert*-butyl ester (**9**; R^2 = OH) in 93 % yield. The successful asymmetric synthesis of natural tyrosine *tert*-butyl ester (**9**; R^2 = H) in a similar manner strongly implies the feasibility of highly enantioselective synthesis of various L-Dopa analogs (eq. 3). Furthermore, a "scale–up" experiment with 5.00 g of the starting Schiff's base and 7.77 g of **7** (R^2 = OBn) was performed to provide 3.37 g of the desired L-Dopa *tert*-butyl ester (**9**; R^2 = OH) [8].



(3)

In the series of this work, introduction of 3,3'-diaryl substituents to the parent symmetrical ammonium bromide **1a** is found to be crucially important for obtaining high enantioselectivity. During the course of this study, we have been interested in the possibility of examining the effect of adjacent 4,4'-substituents of the catalyst rather than 3,3'-substituents in the asymmetric phase-transfer alkyla-

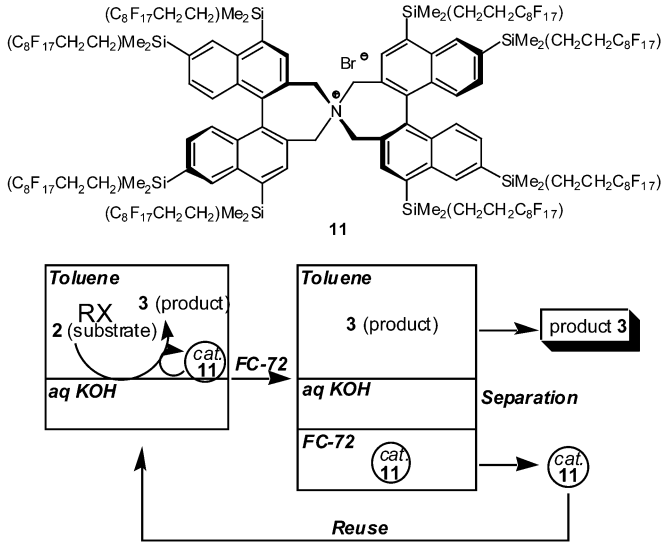
tions. Interestingly, even 4,4'-diaryl substituents of the catalysts of type **10** exhibited unexpectedly high asymmetric induction on such asymmetric phase-transfer alkylations. For example, reaction of **2** with benzyl bromide in toluene/50 % *aqueous* KOH under the influence of 1 mol % of catalyst **10a** at 0 °C for 7 h gave rise to benzylation product **9** (R = CH_2Ph) in 90 % yield with 91 % ee [9]. The observed enantioselectivity is rather surprising compared to that (89 % ee) using 3,3'-diphenyl-substituted **1d** under similar reaction conditions.



10a (Ar = Ar' = Ph)
10b (Ar = Ph; Ar' = H))
10c (Ar = Ar' = 3,5-diphenylphenyl)

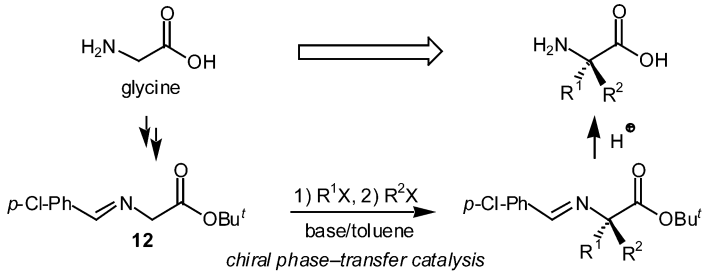
The (*S,S*)-4,4'-diphenylbinaphthyl derivative **10b** was found to exhibit similar reactivity and a little bit lower selectivity compared to **10a** in the asymmetric alkylation of glycine derivative **2**. We also prepared sterically more hindered (*S,S*)-4,4',6,6'-tetrakis(3,5-diphenylphenyl)binaphthyl analog **10c** and applied it to the asymmetric alkylation of glycine derivative **2** to furnish the alkylation product **3** with slightly higher enantioselectivity and shorter reaction time. However, the observed enantioselectivity is not as appealing as that with 3,3'-bis(3,5-diphenylphenyl) analog **1d** (e.g., 98 % ee in the asymmetric benzylation of **2** with **1d** under similar phase-transfer conditions).

A further useful advance in the field of chiral phase-transfer chemistry would involve the design of easily recyclable catalysts. Few examples of polymer-supported chiral phase-transfer catalysts derived from *cinchona* alkaloid have been reported for this purpose, however, and unfortunately almost all of these systems seriously reduced the enantioselection of the product compared with nonsupported catalyst systems. In this context, we are interested in the development of fluorous chiral phase-transfer catalyst **11** as a recyclable catalyst, since fluorous phase-separation techniques for the recovery of fluorinated catalyst have been found a most useful method in recently advanced catalyst recovery techniques. Such recyclable fluorous chiral phase-transfer catalyst can be designed and successfully applied to the catalytic asymmetric synthesis of both natural and unnatural α-amino acids based on the asymmetric alkylation of glycine derivative followed by extractive recovery of chiral phase-transfer catalyst by using fluorous solvent [10].



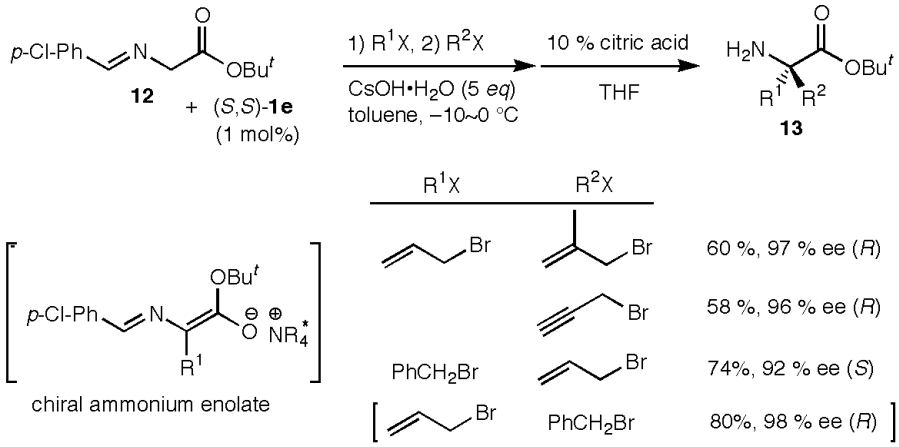
ASYMMETRIC DIALKYLATION OF GLYCINE DERIVATIVES

With this basic information at hand, our attention has now been focused on the α,α-dialkyl-α-amino acid synthesis. Such nonproteinogenic α,α-dialkyl-α-amino acids have played a special role in the design of peptides with enhanced properties. Furthermore, α,α-dialkyl-α-amino acids themselves are often effective enzyme inhibitors and also constitute a series of interesting building blocks for the synthesis of various biologically active compounds. Accordingly, development of truly efficient methods for their preparation, especially in an enantiomerically pure form, has become of great importance. In this context, we envisioned that two different side chains could be introduced directly to the aldimine Schiff's base **12** derived from glycine in a highly enantioselective manner by appropriate chiral phase-transfer catalysis. This possibility of the one-pot asymmetric double alkylation has been realized by using C_2-symmetric chiral quaternary ammonium bromide (*S*,*S*)-**1** whose effectiveness for the asymmetric synthesis of α-alkylamino acids has already been demonstrated in the previous section [6].



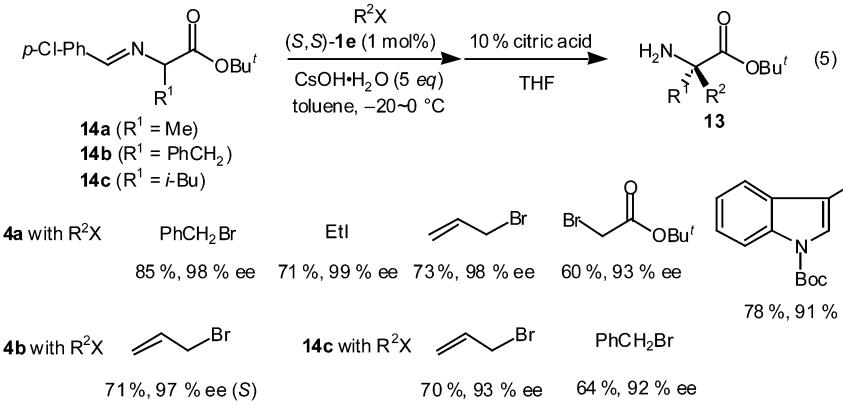
Initial treatment of the toluene solution of **12** and (*S*,*S*)-**1c** (1 mol %) with allyl bromide (1 equiv) and $CsOH{\cdot}H_2O$ (5 equiv) at –10 °C for 3.5 h and the subsequent reaction with benzyl bromide (1.2 equiv) at 0 °C for 30 min resulted in formation of the double alkylation product **13** ($R^1 = CH_2CH{=}CH_2$, $R^2 = CH_2Ph$) in 61 % yield with 87 % ee after hydrolysis. It is of interest that the use of (*S*,*S*)-**1e** as catalyst under similar conditions enhanced both chemical yield and the enantioselectivity to 80 % and 98 % ee, respectively [11]. The distinct feature of this procedure is that it enables straightforward asymmetric synthesis of various α,α-dialkyl-α-amino acids including those otherwise inaccessible from the

naturally occurring amino acids as exemplified in eq. 4. Notably, in the double alkylation of **12** by the addition of the halides in a reverse order, the absolute configuration of the product **13** was confirmed to be opposite, indicating the intervention of the expected chiral ammonium enolate in the second alkylation stage.



(4)

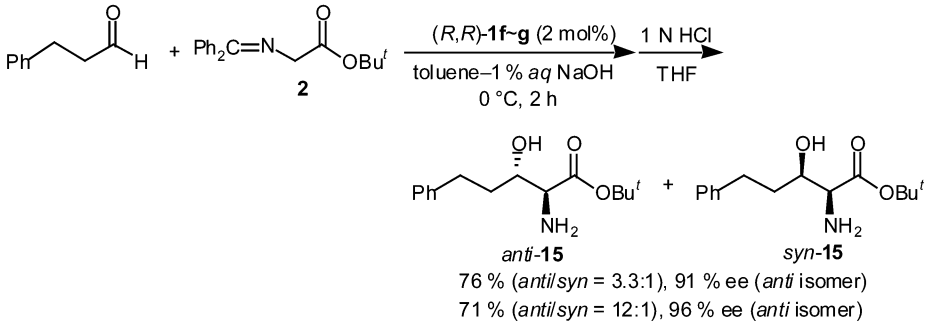
Since the stereochemistry of the newly created quaternary carbon center was apparently determined in the second alkylation process, the core of this method should be applicable to the asymmetric alkylation of aldimine Schiff's base **14** derived from the corresponding α-amino acids. Indeed, rapid benzylation of *dl*-alanine-derived imine **14a** occurred at 0 °C in toluene with benzyl bromide ($R^2 = CH_2Ph$) (1.2 equiv) and $CsOH{\cdot}H_2O$ (5 equiv) using (*S*,*S*)-**1e** (1 mol %) as a catalyst, giving the alkylation product **13** (R^1 = Me, $R^2 = CH_2Ph$; 85 %) in an almost enantiomerically pure form (98 % ee). Other selected results illustrated in eq. 5 demonstrate the remarkable efficiency and generality of this method [11]. Use of *tert*-butyl α-bromoacetate as an alkylating agent allows facile enantioselective access to α-methyl aspartic acid and asymmetric synthesis of α-methyl tryptophan, an important amino acid for the design of dipeptoid with high affinity for the central cholecystokinin receptor, can also be realized. In addition, the phase-transfer catalytic alkylation of aldimine Schiff's base derived from other α-amino acids such as *dl*-phenylalanine (**14b**) and *dl*-leucine (**14c**) also appeared to be feasible with high efficiency, providing the desired noncoded amino acid esters **13** with excellent asymmetric induction (eq. 5).



(5)

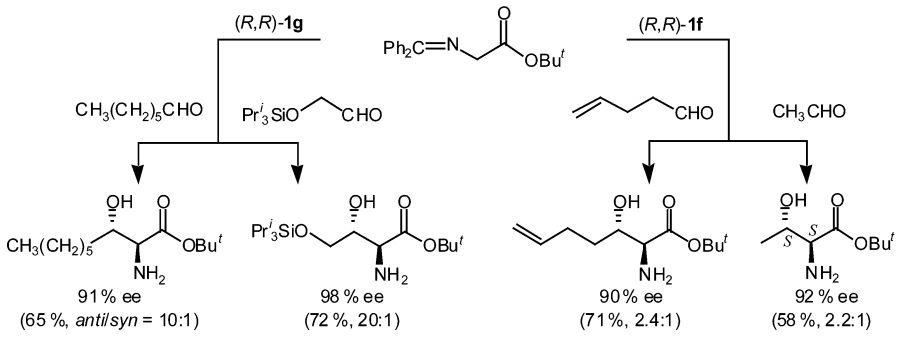
ASYMMETRIC DIRECT ALDOL REACTION OF GLYCINE DERIVATIVES

Although phase-transfer catalytic enantioselective direct aldol reactions of glycine donor with aldehyde acceptors could provide an ideal method for the simultaneous construction of the primary structure and stereochemical integrity of β-hydroxy-α-amino acids, extremely important chiral units, especially from the pharmaceutical viewpoint, the examples reported to date are very limited. In this context, we were successfully able to realize an efficient, highly enantioselective direct aldol reaction of glycine Schiff's base with aldehydes under phase-transfer conditions using C_2-symmetric chiral quaternary ammonium salt **1**. Treatment of *N*-(diphenylmethylene)glycine *tert*-butyl ester **2** with 3-phenylpropanal (2 equiv) in toluene–1 % NaOH aqueous solution (volume ratio = 1.25:1; 2 equiv of base for Schiff's base) in the presence of (*R*,*R*)-**1f** (2 mol % at 0 °C for 2 h and subsequent hydrolysis with 1 N HCl in the THF resulted in the formation of the corresponding β-hydroxy-α-amino ester **15** in 76 % isolated yield with the *anti*/*syn* ratio of 3.3:1, and the enantiomeric excess of the major *anti*-isomer was determined to be 91 % ee. Interestingly, use of (*R*,*R*)-**1g** possessing 3,5-bis[3,5-bis(trifluoromethyl)phenyl]phenyl substituent as a catalyst enhanced both diastereo- and enantioselectivities (*anti*/*syn* = 12:1, 96 % ee for *anti*-isomer) (eq. 6) [12a].



(6)

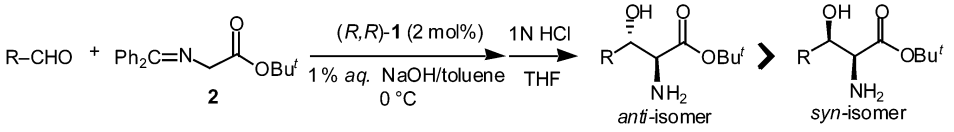
The potential synthetic utility of this procedure has been demonstrated by the direct asymmetric synthesis of various useful β-hydroxy-α-amino esters (eq. 7). Heptanal was found to be a good candidate, indicating the feasibility of direct asymmetric synthesis of a variety of lipo β-hydroxy-α-amino acids, a useful component for the preparation of lipophilic peptides and glycopeptides possessing the characteristic properties of high enzymatic stability and enhanced drug transport activity. The reaction with α-triisopropylsiloxyacetaldehyde cleanly produced the desired β-hydroxy-α-amino ester in 72 % yield with virtually complete stereochemical control (98 % ee, *anti*/*syn* = 20:1), which parallels the L-threonine aldolase-catalyzed aldol reaction utilized for the synthesis of monobactam antibiotic Carunoman and analogs. A key building block for the synthesis of carbacephem antibiotic Loracarbef, previously prepared by a chemo-enzymatic process with serine hydroxymethyltransferase (SHMT), was readily assembled with 4-pentenal as acceptor, where (*R*,*R*)-**1f** was rather beneficial than (*R*,*R*)-**1g** to obtain higher enantioselectivity. It was also found that L-*allo*-threonine ester can be obtained by the reaction with acetaldehyde using (*R*,*R*)-**1f**, confirming that the absolute configuration of the α-stereocenter newly created in this transformation is (*S*). Notably, this method allows a facile preparation of unnatural D-*allo*-threonine because of the ready availability of the enantiomeric catalyst (*S*,*S*)-**1f** [12a].



(7)

The initially developed reaction conditions using 2 equiv of aqueous base (1 % NaOH aq) exhibited inexplicably limited general applicability in terms of aldehyde acceptors. For example, reaction of glycine derivative **2** with 4-benzyloxybutanal gave the aldol product with low diastereoselectivity (*anti*/*syn* = 58:42; 82 % ee for *anti*-isomer). The mechanistic investigation revealed the intervention of an unfavorable, yet inevitable retro aldol process involving chiral catalyst **1**. Based on this information, a reliable procedure has been established by use of a catalytic amount of 1 % NaOH and ammonium chloride, which tolerates a wide range of aldehydes to afford the corresponding *anti*-β-hydroxy-α-amino esters almost exclusively in an essentially optically pure form [12b].

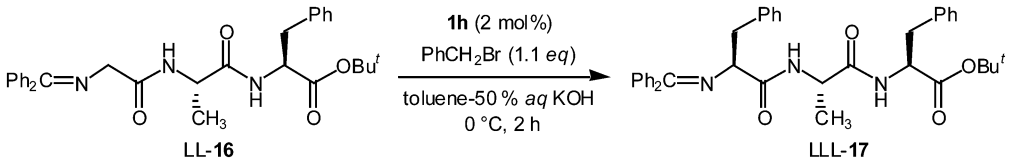
Table 2 Direct asymmetric aldol reaction of glycine derivative **2** and aldehyde.



Aldehyde	1 % NaOH (equiv)	Time (h)	NH_4Cl (equiv)	Catalyst	Yield (*anti*/*syn*)	*Anti*-isomer (% ee)
Cyclohexyl-CHO	2	2	–	(*R*,*R*)-**1f**	78 (1.2:1)	93
	0.2	24	–	(*R*,*R*)-**1g**	49 (>20:1)	95
	0.15	3	0.1	(*R*,*R*)-**1g**	83 (>24:1)	98
$CH_3(CH_2)_5CHO$	2	2	–	(*R*,*R*)-**1g**	65 (10:1)	91
	0.2	12	–	(*R*,*R*)-**1g**	47 (>20:1)	98
	0.15	10	0.1	(*R*,*R*)-**1g**	80 (>24:1)	97

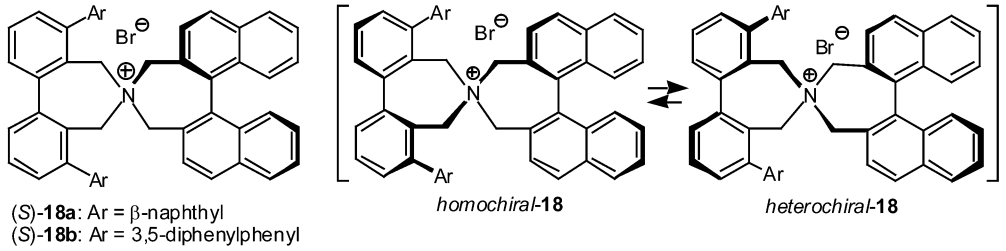
Diastereoselective peptide alkylation

Peptide modification is an essential yet flexible synthetic concept for efficient target screening and optimization of lead structures in the application of naturally occurring peptides as pharmaceuticals. The introduction of side chains directly to a peptide backbone represents a powerful method for the preparation of unnatural peptides. Achiral glycine subunit has generally been used for this purpose. However, the control of the stereochemical outcome of such a process in an absolute sense is a difficult task, especially in the modification of linear peptides, and, hence, development of an efficient and practical approach to establish sufficient stereoselectivity and general applicability has been an issue of central importance. Accordingly, the chiral phase-transfer catalysis with (*S*,*S*)-**1f** can be executed for the stereoselective *N*-terminal alkylation of Gly-Ala-Phe derivative LL-**16**, as tripeptide [13]. For example, stereoselective benzylation of LL-**16** with (*S*,*S*)-**1h** under the optimized conditions resulted in poor diastereoselectivity (20 % de) with LLL-**17** as a major product. In contrast, enantiomeric (*R*,*R*)-**1h** as catalyst turned out to be a matched catalyst in this benzylation, leading to preferential formation of LLL-**17** (93 % de) under similar conditions.



Simplification of chiral phase-transfer catalysts

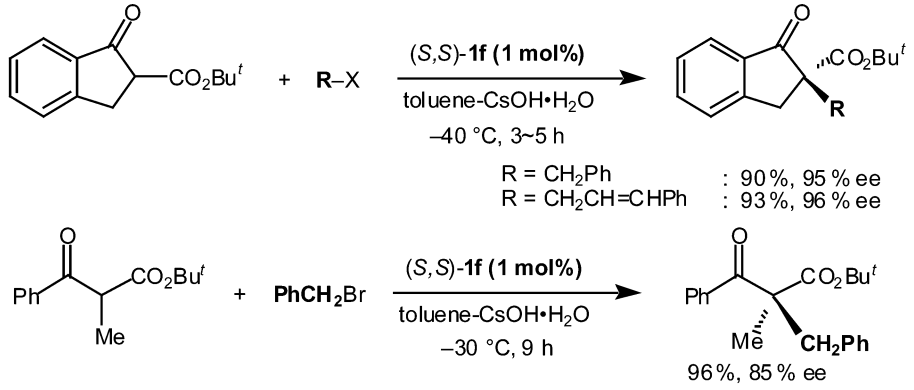
Although the conformationally rigid, *N*-spiro structure created by two chiral binaphthyl subunits represents a characteristic feature of **1** and seems essential for attaining sufficient reactivity and enantioselectivity, it also imposes limitations on the catalyst design due to the imperative use of the two chiral binaphthyl moieties. Accordingly, a new C_2-symmetric chiral quaternary ammonium bromide of type **18** possessing an achiral, conformationally flexible biphenyl subunit has been developed for the simplification of *N*-spiro-type chiral phase-transfer catalysts **1** [14]. Thus, the phase-transfer benzylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester **2** with the catalyst (*S*)-**18a** having β-naphthyl group on 3,3'-position of the flexible biphenyl moiety was found to proceed smoothly at 0 °C to afford the corresponding alkylation product in 85 % yield with 87 % ee (*R*) after 18 h. Switching Ar substituent from β-naphthyl to 3,5-diphenylphenyl group in (*S*)-**18** further enhanced the enantioselectivity to 92 % ee. The origin of the observed chiral efficiency could be ascribed to the considerable difference of catalytic activity between the rapidly equilibrated, diastereomeric homo- and heterochiral catalysts; namely, *homochiral*-**18** is primarily responsible for the efficient asymmetric phase-transfer catalysis to produce the alkylation product with high enantiomeric excess, whereas *heterochiral*-**18** displays very low reactivity and stereoselectivity.



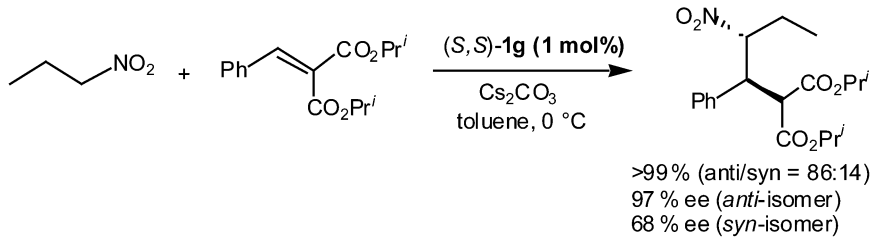
Application to other asymmetric transformations

In addition to the enantioselective synthesis of structurally diverse natural and unnatural α-alkyl-α-amino acid as well as α,α-dialkyl-α-amino acid derivatives, our *N*-spiro-type, chiral phase-transfer catalysts **1** can be successfully applied to the asymmetric alkylation of β-keto ester derivatives as well as asymmetric conjugate addition of nitroalkanes to alkylidenemalonates with excellent enantioselectivity [15,16].

Asymmetric Alkylation of β-Keto Esters



Asymmetric Conjugate Addition to Alkylidenemalonates



REFERENCES

1. Recent reviews: (a) M. J. O'Donnell. *Aldrichimica Acta* **34**, 3 (2001); (b) K. Maruoka and T. Ooi. *Chem. Rev.* **103**, 3013 (2003); (c) M. J. O'Donnell. *Acc. Chem. Res*. **37**, 506 (2004); (d) B. Lygo and B. I. Andrews. *Acc. Chem. Res*. **37**, 518 (2004).
2. M. J. O'Donnell, W. D. Bennett, S. Wu. *J. Am. Chem. Soc*. **111**, 2353 (1989).
3. (a) E. J. Corey, F. Xu, M. C. Noe. *J. Am. Chem. Soc*. **119**, 12414 (1997); (b) B. Lygo and P. G. Wainwright. *Tetrahedron Lett*. **38**, 8595 (1997).
4. (a) S.-s. Jew, B.-S. Jeong, M.-S. Yoo, H. Huh, H.-g. Park. *Chem. Commun*. 1244 (2001); (b) H.-g. Park, B.-S. Jeong, M.-S. Yoo, M.-k. Park, H. Huh, S.-s. Jew. *Tetrahedron Lett*. **42**, 4645 (2001); (c) H.-g. Park, B.-S. Jeong, M.-S. Yoo, J.-H. Lee, M.-k. Park, Y.-J. Lee, M.-J. Kim, S.-s. Jew. *Angew. Chem., Int. Ed.* **41**, 3036 (2002); (d) R. Chinchilla, P. Mazon, C. Najera. *Tetrahedron: Asymmetry* **13**, 927 (2002).
5. (a) T. Kita, A. Georgieva, U. Hashimoto, T. Nakata, K. Nagasawa. *Angew. Chem., Int. Ed.* **41**, 2832 (2002); (b) T. Shibuguchi, Y. Fukuta, Y. Akachi, A. Sekine, T. Ohshima, M. Shibasaki. *Tetrahedron Lett*. **43**, 9539 (2002); (c) B. Lygo, B. Allbutt, S. R. James. *Tetrahedron Lett.* **44**, 5629 (2003).
6. (a) T. Ooi, M. Takeuchi, M. Kameda, K. Maruoka. *J. Am. Chem. Soc*. **122**, 5228 (2000); (b) T. Ooi, M. Kameda, K. Maruoka. *J. Am. Chem. Soc*. **125**, 5139 (2003).
7. S. Wagaw, R. A. Rennels, S. L. Buchwald. *J. Am. Chem. Soc*. **119**, 8451 (1997).
8. T. Ooi, M. Kameda, H. Tannai, K. Maruoka. *Tetrahedron Lett*. **41**, 8339 (2000).
9. T. Hashimoto and K. Maruoka. *Tetrahedron Lett.* **44**, 3313 (2003).
10. S. Shirakawa, Y. Tanaka, K. Maruoka. *Org. Lett.* **6**, 1429 (2004).
11. T. Ooi, M. Takeuchi, M. Kameda, K. Maruoka. *J. Am. Chem. Soc.* **122**, 5228 (2000).

12. (a) T. Ooi, M. Taniguchi, M. Kameda, K. Maruoka. *Angew. Chem., Int. Ed.* **41**, 4542 (2002); (b) T. Ooi, M. Kameda, M. Taniguchi, K. Maruoka. *J. Am. Chem. Soc.* **126**, 9685 (2004).
13. (a) T. Ooi, E. Tayama, K. Maruoka. *Angew. Chem., Int. Ed.* **42**, 579 (2003); (b) T. Ooi, E. Tayama, K. Maruoka. *Proc. Nat. Acad. Sci.* **101**, 5824 (2004).
14. T. Ooi, Y. Uematsu, M. Kameda, K. Maruoka. *Angew. Chem., Int. Ed. Engl.* **41**, 1621 (2002).
15. T. Ooi, T. Miki, M. Taniguchi, M. Shiraishi, M. Takeuchi, K. Maruoka. *Angew. Chem., Int. Ed.* **42**, 3796 (2003).
16. T. Ooi, S. Fujioka, K. Maruoka. *J. Am. Chem. Soc.* **126**, 11790 (2004).