Pergamon

Tetrahedron 58 (2002) 4655–4663

TETRAHEDRON

Catalytic enantioselective rearrangement of *meso*-epoxides mediated by chiral lithium amides in the presence of excess cross-linked polymer-bound lithium amides

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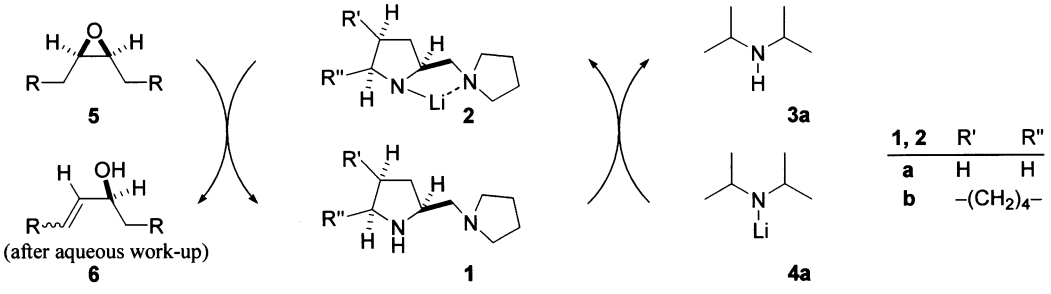
Received 4 January 2002; accepted 27 February 2002

Abstract—Insoluble polymer-bound achiral lithium dialkylamides were prepared from the corresponding cross-linked polymer-bound amines and butyllithium. The polymer-bound achiral reagent was applied to a catalytic enantioselective rearrangement of *meso*-epoxides as an in situ regenerating agent of a chiral lithium amide. The efficiency of the catalytic system was improved, and chiral allylic alcohol derivatives were obtained in high enantiomeric excesses by using excess polymer-bound reagents and a sub-stoichiometric amount of chiral lithium amide, prepared from (2*S*,3a*S*,7a*S*)-2-(pyrrolidin-1-ylmethyl)octahydroindole. The reaction was successfully applied in the synthesis of (1*S*,4*R*)-4-benzoylamino-2-cyclopentenol, a useful chiral synthetic intermediate for carbocyclic nucleosides, in 97% ee.

1. Introduction

Asymmetric transformations mediated by optically pure chiral lithium amides have received much attention as a useful method for the preparation of non-racemic compounds from prochiral compounds in recent years.[1–12] Among various synthetic reactions using lithium amide bases, we have been studying enantioselective rearrangement of epoxides to allylic alcohol derivatives by using chiral lithium pyrrolidides[6,13] and shown some applications in the syntheses of chiral natural products or useful chiral intermediates,[14–19] as well as other groups.[20–28] Although more than a stoichiometric amount of chiral bases were employed in those syntheses, a catalytic asymmetric reaction has advantages that it can produce a large amount of chiral products with only a small investment of chiral material, and is of great importance.[12] Therefore, we have also investigated an effective catalytic system using a chiral lithium amide.

As we had observed in our earlier work, a chiral lithium amide, lithium (*S*)-2-(pyrrolidin-1-ylmethyl)pyrrolidide (**2a**), was more reactive toward epoxides than usual lithium amides such as lithium diethylamide or lithium diisopropylamide (**4a**), we examined the catalytic cycle shown in Scheme 1.[29,30] The catalytic cycle was realized by using 0.2 equiv. of **2a** and 1.0 equiv. of **4a** in the presence of 6.0 equiv. of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) without significant decrease of the enantioselectivity of the reaction.[29] The catalytic system was more effectively



Scheme 1. Catalytic cycle of the enantioselective rearrangement of *meso*-epoxides using chiral lithium amide.

Keywords: supported reagents; asymmetric reactions; rearrangements; alcohols; epoxides; enantioselection; catalysis.
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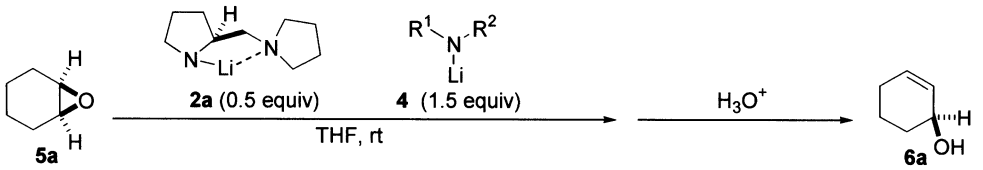
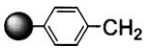
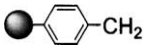
0040–4020/02/$ - see front matter
PII: S0040-4020(02)00371-X

Table 1. Effect of in situ regenerating agent in enantioselective deprotonation of cyclohexene oxide (**5a**) using 0.5 equiv. of **2a**



Entry	4	R^1	R^2	Time (h)	Yield (%)[a]	ee (%)[b]
1[c]	**a**	*i*-Pr	*i*-Pr	12	63	48
2	**b**	*i*-Pr	$PhCH_2$	24	86	64
3	**c**	*c*-C_6H_{11}	$PhCH_2$	24	87	65
4	**d**	*i*-Pr		24	84	73
5	**e**	*c*-C_6H_{11}		24	89	73

[a] Isolated yield after benzoylation.
[b] Determined by HPLC analysis (Opti-pak TA) of the benzoate.
[c] The result was taken from the literature.[29]

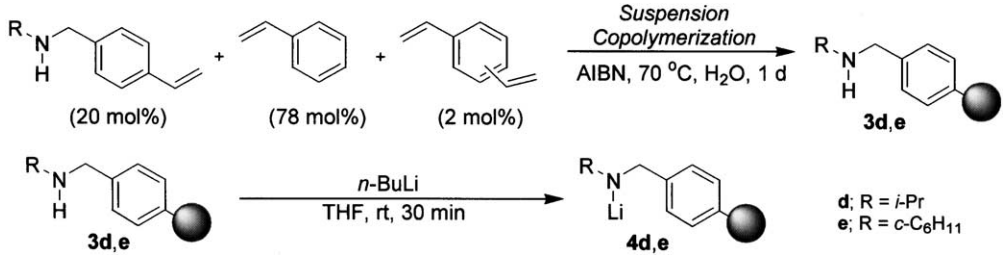
employed in the reaction using a chiral lithium amide **2b**, prepared from (2*S*,3a*S*,7a*S*)-2-(pyrrolidin-1-ylmethyl)octahydroindole (**1b**) and butyllithium, and the chiral allylic alcohol derivatives were obtained in high ees without DBU.[30] However, it was desirable to use a less reactive in situ regenerating agent[31,32] to effect the catalytic reaction with smaller amounts of the chiral reagent **2**, because **4a** reacted with the epoxide to a certain extent.

Although much attention has been directed to polymer-bound reagents recently because insoluble polymer-bound reagents have the advantages that they are removed from reaction mixtures by simple filtration and can be recycled,[33–36] lower reactivity of the cross-linked polymer-bound reagents in comparison with the corresponding monomeric reagents is often a drawback. We anticipated that this drawback would become an advantage provided the polymer-bound lithium amide is employed as an in situ regenerating agent of the chiral lithium amide in the above-mentioned catalytic reaction, because the non-enantioselective reaction with achiral lithium amide is diminished. Furthermore, the polymer-bound amine was expected to be recovered easily and used repeatedly. Thus, we started an investigation of a catalytic enantioselective rearrangement of *meso*-epoxides by combined use of chiral lithium amide and excess polymer-bound lithium amide. Herein we wish to report the results in detail.[37]

2. Results and discussion

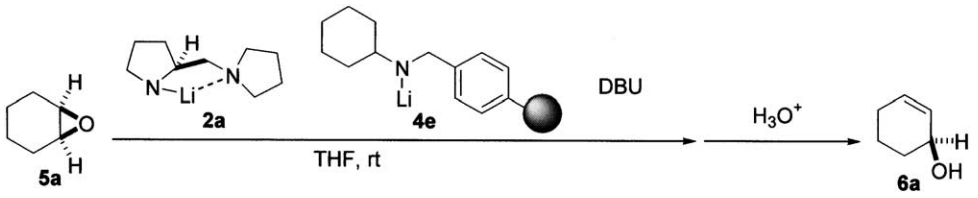
We first examined enantioselective rearrangement of cyclohexene oxide (**5a**) using 0.5 equiv. of lithium (*S*)-2-(pyrrolidin-1-ylmethyl)pyrrolidide (**2a**) and 1.5 equiv. of lithium *N*-isopropylbenzylamide (**4b**) or lithium *N*-cyclohexylbenzylamide (**4c**) in THF at room temperature (rt) for 24 h. As the lithium *N*-alkylbenzylamides **4b** and **c** gave better selectivities than **4a** (Table 1, entries 1–3), the corresponding cross-linked polymer-bound amines **3d** and **e** were prepared by suspension copolymerization of *N*-isopropyl-*p*-vinylbenzylamine (20 mol%) or *N*-cyclohexyl-*p*-vinylbenzylamine (20 mol%) with styrene (78 mol%) and divinylbenzene (2 mol%) in the presence of a catalytic amount of 2,2′-azobisisobutyronitrile (AIBN).[38,39] Then the reaction conditions to convert amines **3d** and **e** to the corresponding lithium amides **4d** and **e** were examined, because little was known for the generation and utilization of polymer-bound lithium amides.[40,41] After several experiments it was found that most of polymer-bound amine was lithiated with butyllithium in THF at rt for 30 min (Scheme 2).

As the reaction conditions for the preparation of polymer-bound lithium amide **4d** and **e** were settled, the reaction was examined using **4d**. To a mixture of polymer-bound *N*-isopropyl-*p*-vinylbenzylamine **3d** (amine content: 1.68 mmol/g; cross-linked with 2 mol% of divinylbenzene, 889 mg,



Scheme 2. Preparation of polymer-bound amines **3d**, **3e** and the corresponding lithium amides **4d**, **4e**.

Table 2. The catalytic enantioselective rearrangement of **5a** using **2a** and **4e**



Entry	**2a** (equiv.)	**4e** (equiv.)	DBU (equiv.)	Time (h)	Yield (%)[a]	ee (%)[b]
1	0.5	1.5	0	24	89	73
2	0.2	1.8	0	40	87	64
3	0.1	1.9	0	96	88	51
4	0.1	1.9	2.0	72	82	63
5	0.1	1.9	6.0	24	91	71
6	0.1	1.9	10	24	88	71
7	0.1	1.4	6.0	36	71	75

[a] Isolated yield after benzoylation.
[b] Determined by HPLC analysis (Opti-pak TA) of the benzoate.

1.5 mmol) and (*S*)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**1a**) (77 mg, 0.5 mmol) in THF (7 mL) was added butyllithium in hexane (1.61 M solution, 1.24 mL, 2.0 mmol) at rt. The color of the polymer changed immediately to red. After stirring was continued at rt for 30 min, cyclohexene oxide (**5a**) (98 mg, 1.0 mmol) in THF (3 mL) was added to the reaction mixture at rt. After being stirred for 24 h at rt the color of the polymer changed to pale yellow, and saturated aqueous NH_4Cl was added to the reaction mixture. The resin was removed by filtration and washed well with CH_2Cl_2. After usual work-up (see Experimental section), the crude product was benzoylated with benzoyl chloride, pyridine, and a catalytic amount of 4-*N*,*N*-dimethylaminopyridine. Then the resulting benzoate was purified by preparative TLC followed by bulb-to-bulb distillation to afford pure (*S*)-2-cyclohexenyl benzoate (170 mg, 84%). The ee was determined by HPLC analysis using a chiral column (73% ee, Table 1, entry 4). The product was obtained in the same ee in slightly better yield by using polymer-bound *N*-cyclohexyl-*p*-vinylbenzylamine **3e** (89%, 73% ee, Table 1, entry 5). It was noteworthy that the enatioselectivity of the reaction was improved by using polymer-bound reagents in place of the corresponding monomeric reagents (Table 1, entry 2 vs. entry 4, entry 3 vs. entry 5) as expected.

Next, we examined the reaction using a smaller amount of chiral lithium amide **2a** keeping the total amount of lithium amide reagents (**2a**+**4e**) to be 2.0 equiv. The ee of the resulting 2-cyclohexenol (**6a**) was gradually decreased to 64% ee (87% yield) and 51% ee (88% yield), respectively, as the amount of **2a** was reduced to 0.2 and 0.1 equiv. (Table 2, entries 2 and 3). The results meant that the difference in reactivity between **2a** and **4e** toward **5a** was not sufficient, and some part of **5a** reacted with **4e** to afford racemic **6a**. Then, the reaction was carried out using DBU as an additive to obtain better enantioselectivity by increasing the reactivity of **2a**. The effect of DBU was known in our previous work[29] and others.[31] The ee of the product was increased to 71% when using 0.1 equiv. of **2a** and 1.9 equiv. of **4e** in the presence of more than 6 equiv. of DBU (Table 2, entries 4–6). The enantioselectivity was further increased to 75% ee (71% yield) by decreasing the amount of **4e** to 1.4 equiv. (Table 2, entry 7). This result was identical to that obtained using 0.2 equiv. of **2a** and 1.0 equiv. of LDA (71% yield, 75% ee).[29]

At this stage, we examined the time-conversion relationship of the reaction of epoxide **5a** with some lithium amides by GC to confirm the effect of polymer-bound lithium amide **4e** as the less reactive in situ regenerating agent of chiral lithium amide **2**. A considerable amount of **5a** remained unreacted (84%) and only a little **6a** (7%) was detected even after 24 h at 0°C in the presence of 1.5 equiv. of **4e** in THF. Under the same reaction conditions, **4a** gave **6a** in 17% with unreacted epoxide **5a** (75%). On the other hand, the reaction was almost complete using chiral lithium amide **2a** in 24 h at 0°C and **6a** was detected in 89%. The effect of DBU was also confirmed as the reaction was complete more rapidly by using DBU as an additive. These results were in agreement with our assumption. Surprisingly, the reaction using chiral lithium amide **2b**, prepared from (2*S*,3a*S*,7a*S*)-2-(pyrrolidin-1-ylmethyl)octahydroindole (**1b**), took place very rapidly and was complete within only 1 h at 0°C. The results are depicted in Fig. 1.

The new catalytic system was then applied to chiral lithium amide **2b**, which showed much higher enantioselectivity than **2a** in the reaction.[30] It was expected that the characteristic feature of the new system would be more successfully exploited in the reaction using **2b** due to its rapid reaction with epoxides. The reaction was carried out using 0.2 equiv. of **2b** and 1.8 equiv. of **4e**, and (*S*)-2-cyclohexenol (**6a**) was obtained in good yield with very high ee (94% ee) (Table 3, entry 1). The selectivity was slightly decreased by reducing the amount of **2b** to 0.1 and 0.05 equiv. (Table 3, entries 2 and 3). The alcohol **6a** in as high as 92% ee was obtained with 0.05 equiv. of **2b** by decreasing the amount of achiral reagent **4e** to 1.45 equiv. (Table 3, entry 4). It is of interest that the enatioselectivity of the reaction was enhanced using a catalytic amount of **2b** and excess **4e** as compared with that using stoichiometric amount (1.5 equiv.) of **2b** (89% ee) by the reaction at rt (Table 3, entries 1, 2, 4, and 5). We assume that the effect was attributed to the reduction of

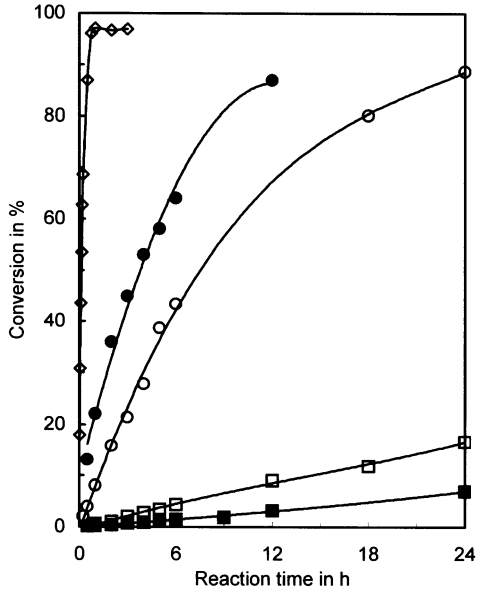
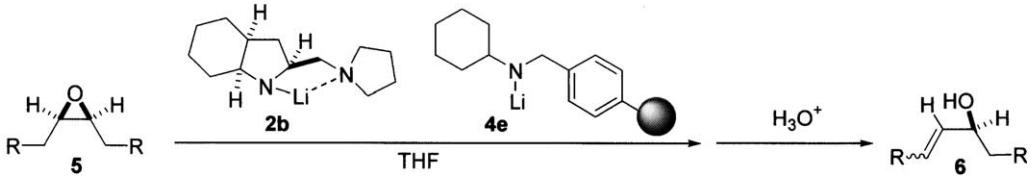


Figure 1. Time-conversion relationship of the isomerization reaction of cyclohexene oxide by lithium amide (1.5 equiv.). (◇): Chiral lithium amide **2b**, (○): Chiral lithium amide **2a**, (●): Chiral lithium amide **2a** in the presence of DBU, (□): LDA **4a**, (■): Polymer-bound lithium amide **4e**.

aggregation of **2b** in the solution by using insoluble polymer-bound lithium amide, which resulted in improvement of the enantioselectivity. As good results were obtained for cyclohexene oxide (**5a**), the reaction was applied to cyclopentene oxide (**5b**), cycloheptene oxide (**5c**), cyclooctene oxide (**5d**), *cis*-4-octene oxide (**5e**), and *cis*-5-decene oxide (**5f**) using **2b** as catalyst. High enantioselectivity was achieved in the reactions of **5c**, **e**, and **f**, and the corresponding (*S*)-alcohols **6c**,**e**,**f**[42] were obtained in high ee (>91% ee). Good enantioselectivity was obtained in the reaction with cyclopentene oxide (**5b**) (50, 77% ee, Table 3, entry 6), for which only moderate ees were reported by a stoichiometric[13] or a catalytic reaction.[31] The selectivity of the reaction of cyclooctene oxide (**5c**) was not improved by using the new system, probably because the reaction using **4e** was carried out at higher temperature (55°C) as compared to the reaction using **4a** (73% yield, 53% ee, at rt).[30]

Although it should be noted that the polymer-bound reagent was effective to improve the enantioselectivity of the reaction compared with that obtained using LDA, we examined another practical advantage of using polymer-bound reagent, namely, recovery and repeated use of **4e**. As mentioned above, **3e** was easily removed from the reaction

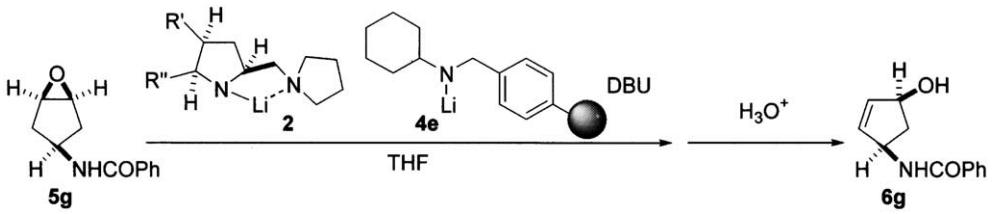
Table 3. Catalytic enantioselective rearrangement of *meso*-epoxides **5a**–**f** using **2b** and **4e**



Entry	Epoxide	**2b** (equiv.)	**4e** (equiv.)	Reaction conditions	Yield (%)[a]	ee (%)[b]
1[c]		0.2 (0.2)	1.8 (1.8)	rt, 12 h (rt, 6 h)	89 (95)	94[d] (88)[d]
2		0.1	1.9	rt, 24 h	91 (86)[e]	91[d] (87)[d,e]
3[c]		0.05 (0.05)	1.95 (1.95)	rt, 36 h (rt, 12 h)	89 (93)	89[d] (85)[d]
4		0.05	1.45	rt, 36 h	91	92[d]
5	**5a**	0.05	1.3	rt, 72 h	76	91[d]
6		0.2	1.8	rt, 24 h	50	77[d]
7	**5b**	0.05	1.45	rt, 2 h, then 55°C, 48 h	48	69[d]
8	**5c**	0.05	1.45	rt, 72 h	54	94[d]
9	**5d**	0.2	1.8	55°C, 12 h	87	52[d]
10[c]	C_3H_7 C_3H_7 **5e**	0.05 (0.2)	1.45 (1.8)	rt, 48 h (rt, 24 h)	90 (85)	93[f] (83)[f]
11	C_4H_9 C_4H_9 **5f**	0.05	1.45	rt, 72 h	93	95[f]

[a] Isolated yield after benzoylation.
[b] The absolute configurations of the alcohols were determined to be *S* by the comparison of the specific rotation with the reported values except for **6f**.[13,42,43]
[c] The figures in parentheses are the results obtained by using LDA **4a** in place of **4e**.[30]
[d] Determined by HPLC analysis (Opti-pak TA, Chiralcel OD–H) of the benzoate ester.
[e] The figures in parentheses are the results obtained by using recovered **4e**.
[f] Determined by ^{1}H NMR of the corresponding acetate in the presence of Eu(hfc)$_3$.

Table 4. Catalytic asymmetric synthesis of (1*S*,4*R*)-4-benzoylamino-2-cyclopentenol



Entry	Chiral base **2**	**2** (equiv.)	**4e** (equiv.)	DBU (equiv.)	Temp. (°C)	Time (h)	Yield (%)	ee (%)[a]
1[b]	**a**	0.2 (3.0)	2.8 (0)	3.3 (3.3)	20 (20)	16 (4)	83 (53)	81 (83)
2[b]	**b**	0.2 (3.0)	2.8 (0)	0 (0)	0 (0)	12 (20)	87 (82)	94 (90)
3	**b**	0.2	2.8	0	−15	16	89	97
4	**b**	0.2	2.8	0	−30	48	86	97
5	**b**	0.15	2.85	0	−15	24	81	95
6	**b**	0.1	2.9	0	−15	36	84	94
7[c]	**b**	0.1	2.9	0	−15	12	87	67

[a] Determined by HPLC analysis (Chiralcel OD–H).
[b] The figures in parentheses are the results obtained by using 3.0 equiv. of **2a** or **2b**.[18]
[c] Achiral lithium amide **4c** was used in place of the corresponding polymer-bound lithium amide **4e**.

mixture by filtration. After washing with CH_2Cl_2, the polymer was further washed with 1,4-dioxane/water, 1,4-dioxane/2 M HCl, 1,4-dioxane/water, 1,4-dioxane/2 M NaOH, 1,4-dioxane/water, acetone, THF, and CH_2Cl_2, successively. Then, the solvent was removed at 90°C under reduced pressure (<1 mmHg) for 16 h. The recovered reagent could be employed in the reaction without significant loss of reactivity and enantioselectivity (Table 3, in parentheses of entry 2).

As high enantioselectivities were achieved in the reaction with various simple *meso*-epoxides, we next applied the catalytic system to enantioselective synthesis of 4-benzoylamino-2-cyclopentenol (**6g**), a useful intermediate for the syntheses of carbocyclic nucleosides and their analogues.[18,25–27]

In the first place, the reaction of *cis*-4-benzoylaminocyclopentene oxide (**5g**)[18,27] was examined using 0.2 equiv. of **2a** and 2.8 equiv. of **4e** in the presence of DBU (3.3 equiv.) in THF at 20°C for 16 h. The corresponding alcohol (1*S*,4*R*)-**6g**[18,27] was obtained in better yield with almost the same enantioselectivity (83% yield, 81% ee, Table 4, entry 1) as those obtained using 3.0 equiv. of **2a** (53% yield, 83% ee, Table 4, parentheses in entry 1). Next, the reaction was carried out using 0.2 equiv. of **2b** and 2.8 equiv. of **4e** in THF at 0°C. The reaction was almost complete in 12 h, and the alcohol (1*S*,4*R*)-**6g** was obtained in good yield with high ee (87% yield, 94% ee, Table 4, entry 2). The ee of the product (1*S*,4*R*)-**6g**, was further enhanced to 97% when the reaction was conducted at −15°C (Table 4, entry 3), however, lower temperature (−30°C) did not change the enantioselectivity (Table 4, entry 4). Good yield and high enantioselectivity were essentially maintained even by decreasing the amount of **2b** to 0.1 equiv. (Table 4, entries 5 and 6). The enantioselectivity dropped to 67% ee by using the corresponding soluble monomeric reagent **4c** with 0.1 equiv. of **2b** −15°C (Table 4, entry 7). It should be noted that the enantioselectivity of the reaction was enhanced exceedingly in the catalytic reaction comparing with the stoichiometric reaction in this case, too.

3. Conclusion

In conclusion, we have prepared cross-linked polymer-bound lithium amides **4d** and **e**, and employed them as a superior reagent to regenerate chiral lithium amide in situ in the catalytic enantioselective deprotonation of *meso*-epoxides. The characteristic feature of the new system is the utilization of lower reactivity of the polymer-bound reagent compared to the corresponding monomeric reagent. The effect of the polymer-bound reagents **4d** and **e** was also realized in the enhancement of enantioselectivity in the catalytic reaction compared to the stoichiometric reaction. The usefulness of the reaction was demonstrated by the preparation of (1*S*,4*R*)-4-benzoylamino-2-cyclopentenol (**6g**), a useful chiral synthetic intermediate for carbocyclic nucleosides and their analogues, in 97% ee using 0.2 equiv. of chiral lithium amide **2b** in the presence of 2.8 equiv. of **4e**.

4. Experimental

4.1. General

Most manipulations were carried out under an atmosphere of argon. Solvents were dried and purified in the usual manner. Melting points were obtained on a Büchi 535 apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer Paragon 1000. Proton (270 MHz) and carbon (67.9 MHz) NMR spectra were measured with a JEOL JNM-EX-270 spectrometer, using tetramethylsilane (TMS) as the internal standard for ^1H, chloroform as the internal standard for ^{13}C. The chemical shifts are given in δ (ppm). Coupling constants (J) are given in hertz. Specific rotations were measured on a Horiba SEPA-200 digital polarimeter using 1-dm cell at 20°C at sodium D line (589 nm) in the indicated solvent. Elemental analyses were carried out on a Perkin–Elmer 2400 CHN Elemental Analyzer. Mass spectra were obtained on a JEOL JMS SX102QQ mass spectometer. HPLC analyses were carried out with Tosoh instruments (pump, CCPS;

detector, UV-8020). GC analyses were carried out with Shimadzu GC 14 A. TLC analyses were done on silica-gel 60 F_{254}-coated plates (E. Merck). Column chromatography was carried out with Wakogel C-200 gel with indicated eluent unless otherwise described. Preparative TLC was performed on silica-gel-coated plates (Wakogel B-5F, 20 cm×20 cm).

4.1.1. (2*S*,3a*S*,7a*S*)-*N*-Benzyloxycarbonyloctahydroindole-2-carboxylic acid. To (2*S*,3a*S*,7a*S*)-octahydroindole-2-carboxylic acid[44,45] (5.0 g, 30 mmol) in water (45 mL) was added sodium hydrogencarbonate (6.0 g, 60 mmol) and the mixture was stirred vigorously at 0°C. After addition of benzyloxycarbonyl chloride (2.8 g, 16 mmol) in toluene (7.5 mL) at 0°C, stirring was continued at rt for 2 h. Then benzyloxycarbonyl chloride (2.8 g, 16 mmol) in toluene (7.5 mL) was again added to the mixture at 0°C and the mixture was stirred overnight at rt. The aqueous layer was washed several times with ether, acidified with 6 M HCl, and extracted with ethyl acetate. The organic layer was washed with water and brine, and dried over anhyd Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica-gel, ether) to give (2*S*,3a*S*,7a*S*)-*N*-benzyloxycarbonyloctahydroindole-2-carboxylic acid[46] (8.46 g, 95%) as colorless solid (mp 41–44°C). $[\alpha]_D^{20}=-43.8$ (*c* 0.98, $CHCl_3$); IR (neat) ν: 2950, 1710, 1430, 1370, 1300, 1250, 1180, 1120, 1100, 1050, 1010, 790, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.14–2.32 (m, 11H), 3.88 (s, 1H), 5.11–5.15 (m, 2H), 7.29–7.36 (m, 5H), 10.9 (s, 1H). Found: *m*/*z* 303.1463. Calcd for $C_{17}H_{21}NO_4$: M, 303.1471.

4.1.2. 1-[(2*S*,3a*S*,7a*S*)-*N*-Benzyloxycarbonyloctahydroindole-2-carbonyl]pyrrolidine. To a dichloromethane solution (35 mL) of (2*S*,3a*S*,7a*S*)-*N*-benzyloxycarbonyloctahydroindole-2-carboxylic acid (8.5 g, 28 mmol) was added a dichloromethane solution (35 mL) of *N*,*N*′-dicyclohexylcarbodiimide (5.8 g, 28 mmol) at 0°C under argon atmosphere. After being stirred for 30 min dichloromethane solution (35 mL) of pyrrolidine (2.0 g, 28 mmol) was slowly added to the reaction mixture at 0°C. The temperature was then gradually warmed to rt and stirring was continued overnight at the temperature. After removal of precipitates, the filtrate was washed successively with 2% HCl, 4% sodium hydrogencarbonate, water, and brine. The organic layer was dried over anhyd Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica-gel, hexane/ethyl acetate=1/2) to give 1-[(2*S*,3a*S*,7a*S*)-*N*-benzyloxycarbonyloctahydroindole-2-carbonyl]pyrrolidine (5.5 g, 56%) as colorless crystals (mp 95–98°C). $[\alpha]_D^{20}=+5.42$ (*c* 1.62, CH_3OH); IR (neat) ν: 3050, 2950, 1690, 1650, 1440, 1410, 1350, 1180, 1110, 980, 920, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.04–2.33 (m, 15H), 3.21–3.97 (m, 5H), 4.43–4.52 (m, 1H), 4.93–5.19 (m, 2H), 7.27–7.39 (m, 5H). Anal. Calcd for $C_{21}H_{28}N_2O_3$: C, 70.76; H, 7.92; N, 7.86. Found: C, 70.67; H, 7.96; N, 7.87.

4.1.3. 1-[(2*S*,3a*S*,7a*S*)-Octahydroindole-2-carbonyl]pyrrolidine. Under hydrogen atmosphere a mixture of 1-[(2*S*,3a*S*,7a*S*)-*N*-benzyloxycarbonyloctahydroindole-2-carbonyl]pyrrolidine (5.5 g, 16 mmol) and 5% Pd–C (0.17 g) in methanol (20 mL) was stirred vigorously overnight at rt. After removal of catalyst by filtration, the filtrate was concentrated in vacuo. The crude product was recrystallized from ethyl acetate to give 1-[(2*S*,3a*S*,7a*S*)-octahydroindole-2-carbonyl]pyrrolidine (3.4 g, 94%) as colorless crystals (mp 68–71°C). $[\alpha]_D^{20}=-78.0$ (*c* 1.61, CH_3OH); IR (KBr) ν: 3300, 2950, 2850, 1630, 1450, 1410, 1340, 1220, 1190, 1120, 1100, 1040, 1000, 960, 900, 800, 740, 700, 660 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.14–2.25 (m, 16H), 3.07 (dd, *J*=9.6, 5.0 Hz, 1H), 3.31–3.60 (m, 4H), 3.82 (dd, *J*=9.9, 5.6 Hz, 1H). Found: *m*/*z* 222.1733. Calcd for $C_{13}H_{22}N_2O$: M, 222.1732.

4.1.4. (2*S*,3a*S*,7a*S*)-2-(Pyrrolidin-1-ylmethyl)octahydroindole (1b). To a THF suspension of lithium aluminum hydride (1.7 g, 46 mmol) was added a THF solution (40 mL) of 1-[(2*S*,3a*S*,7a*S*)-octahydroindole-2-carbonyl]-pyrrolidine (3.4 g, 15 mmol) at 0°C under argon atmosphere, and the reaction mixture was refluxed for 18 h. Then saturated sodium sulfate solution was added to the reaction mixture. After removal of the inorganic material the organic layer was concentrated in vacuo. Fractional distillation of the resulting oil afforded (2*S*,3a*S*,7a*S*)-2-(pyrrolidin-1-ylmethyl)octahydroindole (**1b**) (2.6 g, 83%, bp 190–195°C/2.0 mmHg by bulb-to-bulb distillation). $[\alpha]_D^{20}=+2.09$ (*c* 2.39, C_2H_5OH); IR (neat) ν: 2900, 2775, 1650, 1440, 1140, 870, 790 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.19–2.08 (m, 17H), 2.40–2.65 (m, 5H), 3.05 (dt, *J*=5.3, 5.3 Hz, 1H), 3.31 (m, 1H); ^{13}C NMR ($CDCl_3$) δ: 64.5, 57.5, 56.6, 54.6, 38.0, 36.2, 29.6, 28.6, 23.6, 23.4, 22.2; Anal. Calcd for $C_{25}H_{30}N_8O_{14}$ (dipicrate of **1b**; mp 170.6–171.8°C): C, 45.05; H, 4.54; N, 16.81. Found: C, 44.83; H, 4.54; N, 16.59.

4.1.5. Poly(styrene-*co*-*N*-isopropyl-*p*-vinylbenzylamine), 2% divinylbenzene cross-linked 3d. A solution of gelatin (0.26 g), poly(diallyldimethylammonium chloride-*co*-sulfur dioxide) (2.6 g, from Nittobo, Japan), boric acid (0.96 g, 15.5 mmol), and sodium nitrate (54 mg, 0.078 mmol) in water (85 mL) was adjusted to pH 9.5 with 25 wt% aqueous sodium hydroxide and was placed in a 200 mL round-bottom flask fitted with a reflux condenser and a mechanical stirrer. To the solution was added a mixture of *N*-isopropyl-*p*-vinylbenzylamine (5.0 g, 28 mmol), styrene (11.4 g, 109 mmol), divinylbenzene (0.36 g, 2.8 mmol), and 2,2′-azobisisobutyronitrile (0.14 g, 0.85 mmol). The flask was purged with nitrogen for 40 min, and a nitrogen atmosphere was maintained throughout polymerization. The mixture was stirred at 70°C for 1 d keeping the stirring speed in this preparation of 310 rpm. The insoluble polymer was obtained by filtration with a glass funnel (G1), and it was washed thoroughly with hot water, acetone, THF, and CH_2Cl_2. Cross-linked polymer-bound *N*-isoprpopyl-*p*-vinylbenzylamine **3d** (13.7 g, 80%) was obtained as beads after removal of the solvent under reduced pressure (<1 mmHg) at 90°C for 16 h. IR (KBr): ν 3319, 3026, 2923, 2849, 1602, 1494, 1453, 758, 698 cm^{-1}. Anal. Calcd for $(C_8H_8)_{0.78}\cdot(C_{12}H_{17}N)_{0.2}\cdot(C_{10}H_{10})_{0.02}$: C, 89.30; H, 8.34; N, 2.36. Found: C, 88.90; H, 8.58; N, 2.52.

4.1.6. Poly(styrene-*co*-*N*-cyclohexyl-*p*-vinylbenzylamine), 2% divinylbenzene cross-linked 3e. According to the similar procedure for the preparation of **3d** as described above, cross-linked polymer-bound *N*-cyclohexyl-*p*-vinyl-

benzylamine (**3e**) (12.5 g, 73%) was obtained from *N*-cyclohexyl-*p*-vinylbenzylamine (5.8 g, 27 mmol), styrene (11.0 g, 106 mmol), divinylbenzene (0.35 g, 2.7 mmol), and 2,2′-azobisisobutyronitrile (0.14 g, 0.85 mmol). IR (KBr): ν 3315, 3026, 2942, 2903, 2846, 1602, 1511, 1493, 1452, 758, 702 cm^{-1}. Anal. Calcd for $(C_8H_8)_{0.78}\cdot(C_{15}H_{21}N)_{0.2}\cdot(C_{10}H_{10})_{0.02}$: C, 89.34; H, 8.45; N, 2.21. Found: C, 89.25; H, 8.22; N, 2.16.

4.1.7. Catalytic enantioselective rearrangement of cyclohexene oxide (5a) using 2a (0.5 equiv.) and 4a–e (1.5 equiv.) (representative procedure; Table 1, entry 4). To a mixture of polymer-bound *N*-isopropyl-*p*-vinylbenzylamine **3d** (amine content: 1.68 mmol/g; cross-linked with 2 mol% of divinylbenzene, 889 mg, 1.5 mmol) and (*S*)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**1a**)[13] (77 mg, 0.5 mmol) in THF (7 mL) was added butyllithium in hexane (1.61 M solution, 1.24 mL, 2.0 mmol) at rt. After the reaction mixture was stirred for 30 min at rt, cyclohexene oxide (**5a**) (98 mg, 1.0 mmol) in THF (3 mL) was added to the reaction mixture at rt. After being stirred for 24 h at rt, saturated aqueous ammonium chloride was added to the reaction mixture. The resin was removed by filtration with a glass filter (G1) and washed well with CH_2Cl_2. The aqueous solution was extracted with CH_2Cl_2. The combined organic layer was washed with 1 M HCl and brine, and dried over anhyd Na_2SO_4. After removal of the solvent at atmospheric pressure, the resulting crude product was benzoylated with benzoyl chloride (0.30 mL, 2.6 mmol), pyridine (0.40 mL, 4.9 mmol), and a catalytic amount of 4-*N*,*N*-dimethylaminopyridine in dichloromethane (5 mL). After treatment with 3-dimethylaminopropylamine (0.5 mL, 4.0 mmol), water was added to the mixture and the aqueous phase was extracted with CH_2Cl_2. The organic layer was washed with 1 M HCl and brine, and dried over anhyd Na_2SO_4 and then concentrated in vacuo. The crude product was purified by preparative thin-layer chromatography (silica-gel, hexane/ether=10/1), followed by bulb-to-bulb distillation (120°C/0.65 mmHg) to give (*S*)-2-cyclohexenyl benzoate (170 mg, 84%, $[\alpha]_D^{20}=-165.2$ (*c* 1.00, $CHCl_3$)). The ee was determined to be 73% by HPLC analysis using a chiral column (Waters Opti-pak TA (30 cm×0.39 cm i.d.); 254 nm UV detector; eluent, 0.1% 2-propanol in hexane; flow rate, 0.5 mL/min; t_R, 16.0 min for minor peak, t_s, 17.3 min for major peak).

4.1.8. Catalytic enantioselective rearrangement of cyclohexene oxide (5a) using 2a and 4e in the presence of DBU (representative procedure; Table 2, entry 7). To a mixture of polymer-bound *N*-cyclohexyl-*p*-vinylbenzylamine **3e** (864 mg, 1.4 mmol) and **1a** (16 mg, 0.1 mmol) in THF (6 mL) was added butyllithium in hexane (1.57 M solution, 0.96 mL, 1.5 mmol) at rt. After the reaction mixture was stirred for 30 min at rt, DBU (913 mg, 6.0 mmol) in THF (2 mL) was added to the reaction mixture at rt. After being stirred for 30 min, **5a** (98 mg, 1.0 mmol) in THF (2 mL) was added to the reaction mixture at rt and the reaction mixture was stirred for 24 h at the temperature. After a similar treatment of the reaction mixture as described above, (*S*)-2-cyclohexenyl benzoate was obtained in 71% yield based on **5a**. $[\alpha]_D^{20}=-173.3$ (*c* 1.08, $CHCl_3$). The ee was determined to be 75% by HPLC analysis using a chiral column.

4.1.9. Catalytic enantioselective rearrangement of cyclohexene oxide (5a) using 2b and 4e (representative procedure; Table 3, entry 1). To a mixture of **3e** (1.17 g, 1.8 mmol) and (2*S*,3a*S*,7a*S*)-2-(pyrrolidin-1-ylmethyl)octahydroindole (**1b**) (42 mg, 0.2 mmol) in THF (9 mL) was added butyllithium (1.61 M hexane solution, 1.24 ml, 2.0 mmol) at rt and the reaction mixture was stirred for 30 min at rt. Cyclohexene oxide (**5a**) (98 mg, 1 mmol) in THF (1 mL) was added to the mixture and stirring was continued for 12 h at rt. After a similar treatment of the reaction mixture as described above, (*S*)-2-cyclohexenyl benzoate (180 mg, 89%, $[\alpha]_D^{20}=-210.2$ (*c* 1.00, $CHCl_3$)) was obtained. The ee was determined to be 94% by HPLC analysis using a chiral column.

4.1.10. Enantioselective rearrangement of cyclopentene oxide (5b) (Table 3, entry 6). The reaction was carried out in a similar manner as described for **5a** using **2b** (0.2 equiv.) and **4e** (1.8 equiv.), and the reaction mixture was stirred for 24 h at rt. After similar work-up described above for **5a**, the crude product was purified by preparative thin-layer chromatography (silica-gel, hexane/ether=9/1), followed by bulb-to-bulb distillation (100°C/0.8 mmHg) to give (*S*)-2-cyclopentenyl benzoate (94 mg, 50%, $[\alpha]_D^{20}=-169.5$ (*c* 1.01, $CHCl_3$)). The ee was determined to be 77% by HPLC analysis using a chiral column (Waters Opti-pak TA (30 cm×0.39 cm i.d.); 254 nm UV detector; eluent, 0.1% 2-propanol in hexane; flow rate, 0.5 mL/min; t_R, 21.5 min for minor peak, t_s, 23.0 min for major peak).

4.1.11. Enantioselective rearrangement of cycloheptene oxide (5c) (Table 3, entry 8). The reaction was carried out in a similar manner as described for **5a** using **2b** (0.05 equiv.) and **4e** (1.45 equiv.), and the reaction mixture was stirred for 72 h at rt. After a similar treatment as described for **5a**, (*S*)-2-cycloheptenyl benzoate (120°C/0.9 mmHg by bulb-to-bulb distillation) was obtained in 54% based on cycloheptene oxide (**5c**). $[\alpha]_D^{20}=-52.2$ (*c* 1.02, $CHCl_3$). The ee was determined to be 94% by HPLC analysis using a chiral column (Daicel Chiralcel OD-H (25 cm×0.46 cm i.d.); 254 nm UV detector; eluent, 0.1% 2-propanol in hexane; flow rate, 0.5 mL/min; t_R, 21.5 min for minor peak, t_s, 23.5 min for major peak).

4.1.12. Enantioselective rearrangement of cyclooctene oxide (5d) (Table 3, entry 9). The reaction was carried out in a similar manner as described for **5a** using **2b** (0.2 equiv.) and **4e** (1.8 equiv.), and the reaction mixture was stirred for 12 h at 55°C. After a similar treatment as described for **5a**, (*S*)-2-cyclooctenyl benzoate (200°C/2 mmHg by bulb-to-bulb distillation) was obtained in 87% based on cyclooctene oxide (**5d**). $[\alpha]_D^{20}=+52.2$ (*c* 1.01, $CHCl_3$). The ee was determined to be 52% by HPLC analysis using a chiral column (Waters Opti-pak TA (30 cm×0.39 cm i.d.); 254 nm UV detector; eluent, 0.1% 2-propanol in hexane; flow rate, 0.5 mL/min; t_R, 19.5 min for minor peak, t_s, 22.0 min for major peak).

4.1.13. Enantioselective rearrangement of *cis*-4-octene oxide (5e) (Table 3, entry 10). The reaction was carried out in a similar manner as described for **5a** using **2b** (0.05 equiv.) and **4e** (1.45 equiv.), and the reaction mixture was stirred for 48 h at rt. After a similar treatment as

described for **5a**, (*S*)-1-propyl-2-pentenyl benzoate (180°C/1.4 mmHg by bulb-to-bulb distillation) was obtained in 90% based on *cis*-4-octene oxide (**5e**). $[\alpha]_D^{20}=+16.7$(*c* 1.05, $CHCl_3$). After hydrolysis of the benzoate with sodium hydroxide,[13] resulting crude (*E*)-5-octen-4-ol (**6e**) was acetylated with acetic anhydride (2.4 mL), pyridine (0.4 mL), and a catalytic amount of 4-*N*,*N*-dimethylaminopyridine in dichloromethane (5 mL) at rt to give (*E*)-(*S*)-1-propyl-2-pentenyl acetate (170°C/2 mmHg by bulb-to-bulb distillation, $[\alpha]_D^{20}=-52.1$ (*c* 0.61, $CHCl_3$)) after usual work-up. The ee was determined by ^{1}H NMR using chiral shift reagent, Eu(hfc)$_3$.[13]

4.1.14. Enantioselective rearrangement of *cis*-5-decene oxide (5f) (Table 3, entry 11). The reaction was carried out in a similar manner as described for **5a** using **2b** (0.05 equiv.) and **4e** (1.45 equiv.) and the reaction mixture was stirred for 72 h at rt. After a similar treatment as described for **5a**, 1-butyl-2-hexenyl benzoate (120°C/0.4 mmHg by bulb-to-bulb distillation) was obtained in 93% based on *cis*-5-decene oxide (**5f**). $[\alpha]_D^{20}=+12.5$ (*c* 0.97, $CHCl_3$); IR (neat) ν: 2930, 2858, 1718, 1451, 1351, 1113, 1026, 950, 755, 711 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 0.85–0.93 (m, 6H), 1.33–1.47 (m, 6H), 1.55–1.80 (m, 2H), 1.98–2.06 (m, 2H), 5.41–5.54 (m, 2H), 5.73–5.83 (m, 1H), 7.41–7.56 (m, 3H), 8.03–8.07 (m, 2H). After hydrolysis of the benzoate with sodium hydroxide,[13] resulting crude (*E*)-6-decen-5-ol (**6f**) was converted to the corresponding acetate in a similar manner as described for **6e**. $[\alpha]_D^{20}=-48.0$ (*c* 1.07, $CHCl_3$). The ee was determined by ^{1}H NMR using chiral shift reagent, Eu(hfc)$_3$. Pure (−)-(*E*)-6-decen-5-ol[47] was obtained by hydrolysis of the acetate with sodium hydroxide followed by column chromatography (silica-gel, hexane/ether=5/1) and bulb-to-bulb distillation (120°C/16 mmHg). $[\alpha]_D^{20}=-7.42$ (*c* 0.98, $CHCl_3$); IR (neat) ν: 3355, 2958, 2930, 2873, 1466, 1379, 969 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 0.90 (t, 6H, *J*=7.3 Hz), 1.23–1.60 (m, 11H), 2.01 (q, 2H, *J*=6.9 Hz), 4.04 (q, 1H, *J*=6.7 Hz), 5.46 (ddt, 1H, *J*=15.5, 6.7, 1.3 Hz), 5.63 (dt, 1H, *J*=15.5, 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ: 133.2, 132.0, 73.2, 37.0, 34.3, 27.7, 22.6, 22.3, 14.1, 13.6.

4.1.15. Catalytic enantioselective rearrangement of *cis*-4-benzoylaminocyclopentene oxide (5g) (Table 4, entry 3). To a mixture of **3e** (864 mg, 1.4 mmol) and **2a** (21 mg, 0.1 mmol) in THF (6 mL) was added butyllithium in hexane (1.50 M solution, 1.0 mL, 1.5 mmol) at rt. After stirring was continued at rt for 30 min, *cis*-4-benzoylaminocyclopentene oxide (**5g**)[18,27] (102 mg, 0.5 mmol) in THF (3 mL) was added to the reaction mixture at rt. After being stirred for 16 h at −15°C, saturated aqueous ammonium chloride was added to the reaction mixture. The resin was removed by filtration with a glass filter (G1) and washed well with CH_2Cl_2. The aqueous solution was extracted with CH_2Cl_2. The combined organic layer was washed with 1 M HCl and brine, and dried over anhyd Na_2SO_4. The organic solvent was removed under reduced pressure. The crude product was purified by preparative thin-layer chromatography (silica-gel, ether/ethyl acetate=4/1) to give (1*S*,4*R*)-*cis*-4-benzoylamino-2-cyclopentenol[18,27] (90 mg, 89%). $[\alpha]_D^{20}=-144.5$ (*c* 1.01, $CHCl_3$). The ee was determined to be 97% by HPLC analysis using a chiral column (Daicel Chiralcel OD–H (25 cm×0.46 cm i.d.); 254 nm UV detector; eluent, 5% 2-propanol in hexane; flow rate, 0.5 mL/min; t_R, 43.0 min for minor peak, t_s, 48.5 min for major peak).

Acknowledgements

Financial support from the Fujisawa Foundation and the Japan Securities Scholarship Foundation, and a gift of (2*S*,3a*S*,7a*S*)-octahydroindole-2-carboxylic acid from Kawaken Fine Chemicals Co., Ltd are gratefully acknowledged. The authors thank Professor Masao Tomoi (Yokohama National University) for valuable discussions.

References

1. Koga, K. *J. Synth. Org. Chem. Jpn* **1990**, *48*, 463–475.
2. Cox, P. J.; Simpkins, N. S. *Tetrahedron: Asymmetry* **1991**, *2*, 1–26.
3. Koga, K. *Pure Appl. Chem.* **1994**, *66*, 1487–1492.
4. Koga, K.; Shindo, M. *J. Synth. Org. Chem. Jpn* **1995**, *53*, 1021–1032.
5. Simpkins, N. S. *Pure Appl. Chem.* **1996**, *68*, 691–694.
6. Asami, M. *J. Synth. Org. Chem. Jpn* **1996**, *54*, 188–199.
7. Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. *Tetrahedron* **1996**, *52*, 14361–14384.
8. O'Brien, P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1439–1458.
9. Willis, M. C. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1765–1784.
10. O'Brien, P. *J. Chem. Soc., Perkin Trans. 1* **2001**, *1*, 95–113.
11. Jones, S. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1–21.
12. Eames, J. *Eur. J. Org. Chem.* **2002**, 393–401.
13. Asami, M. *Bull. Chem. Soc. Jpn* **1990**, *63*, 721–727.
14. Asami, M. *Bull. Chem. Soc. Jpn* **1990**, *63*, 1402–1408.
15. Asami, M.; Inoue, S. *Tetrahedron* **1995**, *51*, 11725–11730.
16. Asami, M.; Takahashi, J.; Inoue, S. *Tetrahedron: Asymmetry* **1994**, *5*, 1649–1652.
17. Asami, M.; Ishizaki, T.; Inoue, S. *Tetrahedron Lett.* **1995**, *36*, 1893–1894.
18. Asami, M.; Ogawa, M.; Inoue, S. *Tetrahedron Lett.* **1999**, *40*, 1563–1564.
19. Asami, M.; Sato, S.; Honda, K.; Inoue, S. *Heterocycles* **2000**, *52*, 1029–1032.
20. Saravanan, P.; Singh, V. K. *Tetrahedron Lett.* **1998**, *39*, 167–170.
21. O'Brien, P.; Poumellec, P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2435–2442.
22. Colman, B.; de Sousa, S. E.; O'Brien, P.; Towers, T. D.; Watson, W. *Tetrahedron: Asymmetry* **1999**, *10*, 4175–4182.
23. Hodgson, D. M.; Gibbs, A. R.; Drew, M. G. B. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3579–3590.
24. O'Brien, P.; Pilgram, C. D. *Tetrahedron Lett.* **1999**, *40*, 8427–8430.
25. O'Brien, P.; Towers, T. D.; Voith, M. *Tetrahedron Lett.* **1998**, *39*, 8175–8178.
26. de Sousa, S. E.; O'Brien, P.; Steffens, H. C. *Tetrahedron Lett.* **1999**, *40*, 8423–8425.
27. Barrett, S.; O'Brien, P.; Steffens, H. C.; Towers, T. D.; Voith, M. *Tetrahedron* **2000**, *56*, 9633–9640.
28. Kee, A.; O'Brien, P.; Pilgram, C. D.; Watson, S. T. *Chem. Commun.* **2000**, 1521–1522.

29. Asami, M.; Ishizaki, T.; Inoue, S. *Tetrahedron: Asymmetry* **1994**, *5*, 793–796.
30. Asami, M.; Suga, T.; Honda, K.; Inoue, S. *Tetrahedron Lett.* **1997**, *38*, 6425–6428.
31. Södergren, M. J.; Bertilsson, S. K.; Andersson, P. G. *J. Am. Chem. Soc.* **2000**, *122*, 6610–6618.
32. During the preparation of this manuscript Ahlberg et al., reported a non-reactive bulk base for this type of reaction: Nilsson Lill, S. O.; Pettersen, D.; Amedjkouh, M.; Ahlberg, P. *J. Chem. Soc., Perkin Trans. 1* **2001**, 3054–3063.
33. Maud, J. M. Reactions involving polymeric resins—a survey. In *Solid Supports and Catalysts in Organic Synthesis*, Smith, K., Ed.; Ellis Horwood Ltd: West Sussex, 1992; pp 171–192.
34. Shuttleworth, S. J.; Allin, S. M.; Sharma, P. K. *Synthesis* **1997**, 1217–1239.
35. Shuttleworth, S. J.; Allin, S. M.; Wilson, R. D.; Nasturica, D. *Synthesis* **2000**, 1035–1074.
36. Clapham, B.; Reger, T. S.; Janda, K. D. *Tetrahedron* **2001**, *57*, 4637–4662.
37. A part of this work has been communicated: Asami, M.; Seki, A. *Chem. Lett.* **2002**, 160–161.
38. Tomoi, M.; Ford, W. T. *J. Am. Chem. Soc.* **1981**, *103*, 3821–3828.
39. Tomoi, M.; Akada, Y.; Kakiuchi, H. *Makromol. Chem., Rapid Commun.* **1982**, *3*, 537–542.
40. Majewski, M.; Ulaczyk, A.; Wang, F. *Tetrahedron Lett.* **1999**, *40*, 8755–8758.
41. Henderson, K. W.; Kerr, W. J.; Moir, J. H. *Chem. Commun.* **2001**, 1722–1723.
42. The absolute configuration of **6f** was not known but can be tentatively assigned by analogy with **6e**.[13]
43. Levina, A.; Muzart, J. *Tetrahedron: Asymmetry* **1995**, *6*, 147–156.
44. Vincent, M.; Baliarda, J.; Marchand, B.; Remond, G. Eur. Pat. Appl. EP 308,339, 1989; *Chem. Abstr.* **1989**, *111*, 77846y.
45. Maryanoff, C. A.; Fedde, C. L.; Stanzione, R. C.; Villani, F. J., Jr. US Patent 5,258,525, 1993; *Chem. Abstr.* **1994**, *120* 217275z.
46. Rose, C.; Vargas, F.; Bourgeat, P.; Schwartz, J.-C.; Bishop, P. B.; Bambal, R. B.; Ganellin, C. R.; Leblond, B.; Moore, A. N. J.; Chan, S.; Zhao, L. PCT Int. Appl. WO 96 35,805, 1996; *Chem. Abstr.* **1997**, *126*, 72042h.
47. Weber, B.; Seebach, D. *Tetrahedron* **1994**, *50*, 7473–7484.