Synthetic Studies on *d*-Biotin, Part 9.[1] An Improved Asymmetric Synthetic Route to *d*-Biotin *via* Hoffmann–Roche Lactone–Thiolactone Approach

Fen-Er CHEN,*[,a] Hui-Qing JIA,[a] Xu-Xiang CHEN,[b] Hui-Fang DAI,[a] Bin XIE,[a] Yun-Yan KUANG,[a] and Jian-Feng ZHAO[a]

[a] *Department of Chemistry, Fudan University; Shanghai, 200433, People's Republic of China: and* [b] *School of Pharmaceutical Engineering, Shenyang Pharmaceutical University; 110016, People's Republic of China.*

Received November 8, 2004; accepted February 28, 2005

An efficient and highly stereoselective total synthesis of *d*-biotin has been achieved starting from *cis*-1,3-dibenzyl-2-imidazolidone-4,5-dicarboxylic acid (2) with an overall yield of 33%. Polymer-supported oxazaborolidine-catalyzed asymmetric reduction of *meso*-cyclic imide 4 constitutes the key synthetic step in introducing stereogenic centers into the *d*-biotin molecule.

Key words *d*-biotin; vitamin H; polymer-supported oxazaborolidine; asymmetric reduction; Wittig reaction; desymmetrization

The development of efficient processes for the total synthesis of *d*-biotin (**1**), continues to be an attractive goal in synthetic organic chemistry, because of its unique structural features, significant biological properties and commercial importance.[2—8] Despite great advances[9—21] in total synthesis over the past 55 years, large-scale preparation of this vitamin employing the F. Hoffmann–La Roche lactone–thiolactone approach, developed by Goldberg and Sternbach in 1949, still retains technically and economic advantages.[22] However, a long-standing problem in this synthesis has been the lack of an efficient and convenient procedure for the desymmetrization of dicarboxylic acid **2** to form (3a*S*,6a*R*)-lactone (**6**). Our recent strategy, using a polymer-supported oxazaborolidine catalyzed enantioselective reduction of *meso*-cyclic imide approach, allowed us to prepare (3a*S*,6*R*,6a*R*)-hydroxylactam **5** from **2** in high yield and excellent enantiomeric excess.[23] However, this procedure is impractical for large-scale synthesis due to the use of expensive and toxic $BF_3 \cdot Me_2S$ as the reducing agent which requires a lot of precautions, and lack of a stable polymer-supported chiral ligand.[24] These obstacles prompted us, as part of our strategy to develop a new oxazaborolidine-catalyzed reducing system that can easily be employed and that gives high enantiomeric excess for a large-scale conversion of **4** into **5** as a precursor for the formation of **6**, to complete the asymmetric synthesis of **1**.

In the present paper, we describe an efficient and practical asymmetric total synthesis of **1** starting from commercially available dicarboxylic acid **2** through an improved enantioselective reduction of *meso*-cyclic imide **4** with the use of recoverable chiral polymer-supported oxazaborolidine as a catalyst.

Results and Discussion

The asymmetric synthesis of **1** is presented in Chart 1. The known *meso*-cyclic-1,2-dicarboxylic anhydride **3** was prepared in almost quantitative yield by heating **2** in xylene with a catalytic amount of Ac_2O with azeotropic removal of H_2O for 13 h. Treatment of **3** with benzylamine in toluene under reflux for 6 h afforded the *meso*-cyclic imide **4** in a 90% yield.

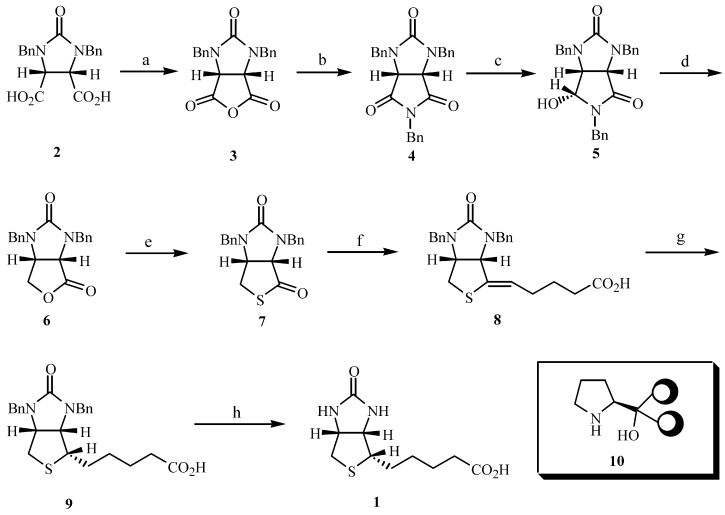
Next, we embarked upon the development of an efficient and convenient strategy for the large-scale asymmetric borane reduction of **4** into (3a*S*,6*R*,6a*R*)-hydroxylactam **5** using a chiral polymer-supported oxazaborolidine derived from polymer-supported ligand **10**[25] (containing 0.39 mmol of diaryprolinol function units/g of polymer by elemental analysis) with *in situ* generated borane from cheap and convenient hydritic reagents and boron halide etherates. Thus, the *meso*-cyclic imide **4** was treated with 80% NaH and $BF_3 \cdot Et_2O$ in the presence of **10** under reflux in anhydrous THF to afford **5** in 82% yield. The enantiomeric excess of **5** was measured to be >98% by HPLC analysis using a Chiralcel OD column (eluent : hexane/2-propanol, 6 : 4, 0.7 ml/min).

As pointed out in a number of studies,[26—32] one of the major advantages of a polymer reagent is the ease with which it can be worked up and recycled. The polymer-supported ligand **10** could be conveniently recovered from the reaction mixture by simple filtration followed by washing with hot H_2O, and EtOH after the reduction was completed. To demonstrate that the ligand **10** can be recycled a number of times, the enantioselective reduction of **4** was repeated fourteen times under the same reaction conditions. As shown in Table 1, the reached enantioselectivities remained around 98% ee, clearly illustrating the reusability of the polymer-supported ligand **10**.

The reduction of **5** by $NaBH_4$ in EtOH at 50 °C for 4 h and subsequent hydrolysis with 2N aq. H_2SO_4 at 80 °C for 1 h afforded the (3a*S*,6a*R*)-lactone **6** in 90% yield. Comparison of its specific optical rotation $\{[\alpha]_D^{20} +57.3°$ (c=2.0, $CHCl_3$)$\}$ with the literature value $\{[\alpha]_D^{20} +59.8°$ (c=2, $CHCl_3$)$\}$[33] for **6** implied an enantiomeric purity of 95.8%, which was then upgraded to 98.6% ee by recrystallization from EtOH. Treatment of **6** with potassium butylthioxanthogenate (*n*-BuSC(S)SK) in DMA at 125 °C for 6 h effected the thiolactonization to form the (3a*S*,6a*R*)-thiolactone **7** in 82% yield.

From a practical point of view, a one-step introduction of the carboxybutyl chain to **7** based on a Wittig reaction to form (*Z*)-configurated unsaturated acid **8** seemed to be very attractive. Following the published conditions,[34] Wittig olefination of **7** with the ylide, derived from 4-carboxybutyltriphenylphosphonium bromide ($BrPh_3PCH_2CH_2CH_2CH_2CO_2H$)

* To whom correspondence should be addressed. e-mail: rfchen@fudan.edu.cn



Reagents and conditions (a) Ac_2O, xylene, 13 h, 98%; (b) benzylamine, toluene, reflux, 3 h, 90%; (c) 80% NaH, $BF_3{\cdot}Et_2O$, **10**, THF, reflux, 5.5 h, 82%; (d) $NaBH_4$, EtOH, 50 ℃, r.t., 4 h, then 2N H_2SO_4, 80 ℃, 1 h, 90%; (e) *n*-BuSC(S)SK, DMA, 125 ℃, 6 h, 82%; (f) $Ph_3P{=}CHCH_2CH_2CH_2CO_2H$, toluene, 135 ℃, 7 h, 81%; (g) H_2, $Pd(OAc)_2$, AcOEt, r.t., 4 h, 95%; (h) CH_3SO_3H, AcOH, H_2O, reflux, 10 h, 80%.

Chart 1. Synthetic Route to *d*-Biotin (**1**)

Table 1. Recycling of the Chiral Polymer-Supported Ligand **10** in the Asymmetric Reduction of **4** in THF Under Reflux

Entry	Yield (%)[a)]	ee (%)[b)]
1	80.5	97.8
2	81	98.1
3	80	98.2
4	81	97.6
5	81	98.09
6	80.5	98
7	80.7	98
8	81	98.2
9	87	98.1
10	81	98.3
11	79.5	98.3
12	80	98
13	81.3	98.1
14	80.5	98.1

a) Yields of isolated pure products. *b*) Determined by chiral HPLC analysis.

provided the (*Z*)-configurated unsaturated acid **8** with low yield (max. 40%). Attempts to treat 4-carboxybutyltriphenylphosphonium bromide with freshly sublimed *t*-BuOK with **7** at reflux in anhydrous toluene failed completely. However, heating a toluene solution of these compounds at 135 °C in a sealed vessel for 7 h gave the desired **8** exclusively as a single (*Z*)-isomer in 81% yield. The (*Z*)-configuration of **8** was unequivocally ascertained by NOE experiments (Fig. 1). A 10.1% enhancement of the signal of H-C_{3a} at δ=4.62 was observed on irradiation of the signal at δ=5.53, which belongs to the olefinic H-atom of the side chain.

Stereospecific hydrogenation of **8** was carried out under 4 atm of H_2 in the presence of $Pd(OH)_2$ over charcoal to give the *N*,*N*-dibenzylbiotin **9** in 95% yield. Removal of the *N*-benzyl group was conducted with CH_3SO_3H–AcOH–H_2O (1.5 : 1.5 : 1) under reflux for 10 h to afford *d*-biotin (**1**) in 80% yield.

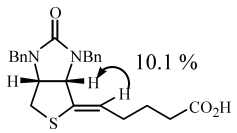


Fig. 1. ^{1}H-NMR Studies of NOE for Compound **8**

Conclusion

We have developed a very efficient route for the highly stereoselective synthesis of *d*-biotin in a 33% overall yield starting from readily accessible *cis*-1,3-dibenzyl-2-imidazolidione-4,5-dicarboxylic acid (**2**), *via* Hoffmann–Roche's lactone–thiolactone approach. The short steps, high yield, simple work-up, and ready availability of the reagents should provide a practical means with which to obtain *d*-biotin.

Experimental

General Procedure Melting points (mp) were measured using a WRS-1B digital melting point apparatus and are uncorrected. ^{1}H-NMR was recorded on Bruker DMX500 (500 MHz) spectrometer. Chemical shifts (δ) are expressed in ppm with TMS as an internal standard. Optical rotations were measured on a WZZ-2S digital automatic polarimeter. IR spetra were measured using a Nicolet FI-IR 360 Spectrometer. Mass spectra (MS) were recorded on HP-5988 Å mass spectrometer. THF was distilled from sodium benzo phenone ketyl and DMA was distilled from CaH_2 before use. Routine monitoring of reaction was carried out using Merck 60 GF_{254} silica gel, glass-supported plates (TLC). Polymer-supported chiral ligand **10** was prepared according to a literature method.[25)]

***cis*-1,3-Dibenzyl-tetrahydro-2*H*-furo[3,4-*d*]imidazole-2,4,6-trione (3)** A mixture of **2** (17.7 g, 50 mmol), acetic anhydride (0.94 ml, 0.01 mol), and xylene (100 ml) was stirred under reflux for 13 h and fixed with a Dean-Stark apparatus. The solid precipitate was cooled to r.t., filtered and washed with H_2O (100 ml) until acid-free. The solid product was dried to give **3** as a white solid (16.5 g, 98%), mp 237—239 °C (lit.[35)]: mp 236—238 °C). IR (KBr) ν_{max} 1800, 1738, 1686, 1226 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 4.20 (s, 2H), 4.18 (2H, d, *J*=15.0 Hz), 5.10 (2H, d, *J*=15.0 Hz), 7.24—7.37 (10H, m); EI-MS *m*/*z*: 336 ($14M^+$), 264 (16), 173 (6), 132 (112), 91 (100).

***N*-Benzyl-*cis*-1,3-dibenzyl-2-imidazolidone-4,5-dicarboximide (4)** A stirred mixture of **3** (60 g, 0.178 mol), benzylamine (19.2 g, 0.18 mol), and

toluene (280 ml) was heated under reflux for 5 h. The reaction mixture was cooled to r.t. and the precipitate was filtered, and dried to afford **4** as a white solid (68 g, 90%), mp 115—117 °C (lit.[23]: mp 114—116 °C). IR (KBr) ν_{max} 3435, 1712, 1688, 1647 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 4.24 (s, 2H), 4.27, 4.28, 4.71, 4.79 (4H, 4d, J=15.38, 15.42 Hz), 4.54 (2H, s), 7.20—7.38 (15H, m); EI-MS m/z: 425 (28, M^+), 334 (6), 237 (6), 132 (11), 91 (100).

(3a*S*,6*R*,6a*R*)-1,3,5-Tribenzyl-6-hydroxy-tetrahedro-4*H*-pyrolo[3,4-*d*]imidazole-2,4(1*H*)-dione (5) $BF_3\cdot Et_2O$ (35.7 ml, 0.28 mol) was added dropwise to a suspension of 80% NaH (5.85 g, 0.2 mol) in THF (45 ml) and the suspension was stirred at r.t for 25 min under N_2. Polymer-supported ligand **10** (15 g) was added, and the reaction mixture was heated at reflux for an additional 25 min. A solution of **4** (27.4 g, 60 mmol) in THF (185 ml) was added dropwise over 2.5 h. Stirring was continued under reflux until the TLC showed complete disappearance of compound **4** (3 h). After cooling to r.t., the mixture was filtered, and the polymer-supported catalyst was washed with EtOAc (3×50 ml) and H_2O (3×40 ml). The organic layers were separated, and the aqueous layers were extracted with EtOAc (3×50 ml). The combined organic layers were washed with sat. aq. $NaHCO_3$ (3×30 ml), H_2O (3×40 ml), and sat. aq. NaCl (3×30 ml), and dried over Na_2SO_4. The solvent was evaporated under reduced pressure. The residue was purified by CC (silica gel, hexane/EtOAc 2 : 1) to afford **5** as a white solid (21 g, 82%), mp 127—130 °C, $[\alpha]_D^{20}$ +69.1° (c=0.1, CH_2Cl_2) {lit.[23]: mp 128—131 °C, $[\alpha]_D^{20}$ +69.2° (c=0.1, CH_2Cl_2)}. IR (KBr) ν_{max} 3315, 2930, 1703, 1451, 1235, 1079, 739, 700 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 3.76—3.78 (m, 2H), 4.11, 4.40, 5.03, 5.10 (4H, 4d, J=14.9 Hz), 4.20, 4.93 (2H, 2d, J=13.7 Hz), 4.91 (1H, dd, J<1, 5.1 Hz), 7.21—7.40 (15H, m), EI-MS m/z: 427 (13, M^+), 264 (21), 106 (6), 91 (100).

(3a*S*,6a*R*)-1,3-Dibenzyl-tetrahydro-4*H*-furo[3,4-*d*]imidazole-2.4(1*H*)-dione (6) Compound **5** (128.25 g, 0.30 mol) in anhydrous EtOH (460 ml) was added dropwise at 0—5 °C to a stirred mixture of $NaBH_4$ (22.7 g, 0.60 mol) and anhydrous EtOH (100 ml). After stirring at 50 °C for 4 h. 2 N H_2SO_4 (245 ml) was added dropwise to the reaction mixture. The reaction mixture was allowed to warm to 80 °C and stirring for a further 1 h. After cooling to r.t., the mixture was extracted with EtOAc (4×80 ml). The combined org. layers were washed successively with sat. aq. NaCl (3×35 ml) and H_2O (3×40 ml), and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to give the crude product, which was recrystallized from EtOH to afford **6** as a white solid (86.9 g, 90%), mp 118—120 °C, $[\alpha]_D^{25}$ +61.5° (c=2, $CHCl_3$) {lit.[36]: mp 120—121 °C, $[\alpha]_D^{25}$ +61.4° (c=2, $CHCl_3$)}. IR (KBr) ν_{max} 1776, 1705, 1210, 1185, 1028, 970 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.25 (1H, dd, J=2.3, 12.8 Hz), 3.35 (1H, dd, J=5.6, 12.8 Hz), 3.96 (1H, d, J=8.8 Hz), 4.20 (1H, ddd, J=2.3, 5.4, 8.0 Hz), 4.24, 4.32, 4.46, 4.95 (4H, 4d, J=14 Hz), 7.27—7.38 (10H, m); EI-MS m/z: 322 (25, M^+), 265 (58), 245 (78), 187 (62), 91 (100).

(3a*S*,6a*R*)-1,3-Dibenzyl-tetrahydro-4*H*-thieno[3.4-*d*]imidazole-2.4(1*H*)-dione (7) Potassium butylthioxanthogerate (30.7 g, 0.15 mol) was added to a stirred solution of **6** (48.3 g, 0.15 mol) in DMA (125 ml) and the mixture was heated at 125 °C for 6 h under N_2. After cooling to r.t., H_2O (250 ml) was added. The mixture was extracted with toluene (4×60 ml); the combined organic layers were washed with sat. aq. NaCl (3×45 ml) and H_2O (3×40 ml), and then dried over Na_2SO_4. The solvent was evaporated under reduced pressure to give the crude product, which was recrystallized from EtOAc to afford **7** as colorless crystals (41.6 g, 82%), mp 125—126 °C, $[\alpha]_D^{20}$ +90.8° (c=1, $CHCl_3$) {lit.[37]: mp 125—128 °C, $[\alpha]_D^{20}$ +90.5° (c=1.0, $CHCl_3$)}. IR (KBr) ν_{max} 1705, 1695, 1424, 1225 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.24 (1H, dd, J=2.2, 12.8 Hz), 3.35 (1H, dd, J=5.5, 12.8 Hz), 3.82 (1H, d, J=8.0 Hz), 4.14 (1H, ddd, J=2.2, 5.5, 8.0 Hz), 4.35, 4.38, 4.67, 5.00 (4H, 4d, J=15.2 Hz), 7.27—7.35 (10H, m); EI-MS m/z: 338 (5, M^+), 310 (25), 277 (8), 264 (66), 91 (100).

(3a*S*,4*S*,6a*R*)-1,3-Dibenzyl-tetrahydro-1*H*-thieno[3,4-*d*]imidazole-2(3*H*)-one-4-yl-pentanoic Acid (8) *t*-BuOK (10.8 g, 90 mmol) was added to a suspension of 4-carboxybutyltriphenylphosphonium bromide (19.95 g, 45 mmol) in anhydrous toluene (100 ml) at 10 °C and the reaction mixture was stirred at 25 °C for 45 min. A solution of **7** (13.5 g, 40 mmol) in anhydrous toluene (100 ml) was added, and the resulting mixture was placed in a standard stainless steel vessel under a nitrogen atmosphere and stirred at 135 °C for 7 h. After cooling to r.t., H_2O (150 ml) was added. The organic layer was separated and the aqueous layer was extracted with toluene (3×35 ml). The combined organic layers were washed with sat. aq. NaCl (3×40 ml) and H_2O (3×40 ml), dried over Na_2SO_4, and concentrated under reduced pressure to give the crude product, which was purified by column chromatography (silica gel, benzene/EtOAc 4 : 1) to afford **8** as a white solid (13.7 g, 81%), mp 84—85 °C, $[\alpha]_D^{20}$ +236° (c=1.0, 0.1 N NaOH) {lit.[38] mp 84—85 °C, $[\alpha]_D^{20}$ +236.2° (c=1, 0.1 N NaOH)}. IR (KBr) ν_{max} 3432, 1725, 1662, 1485, 1452 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.39—1.93 (4H, m, 2×CH_2), 2.00 (2H, t, J=7.4 Hz), 2.81 (1H, dd, J=5.5, 12.1 Hz), 2.95 (1H, d, J=12.3 Hz), 4.16 (1H, m), 4.62 (1H, d, J=7.9 Hz), 4.05, 4.34, 4.52, 4.97 (4H, 4d, J=15.5, 16.8 Hz), 5.53 (1H, t, J=7.8 Hz), 7.24—7.40 (10H, m); EI-MS m/z: 422 (6, M^+), 311 (6), 289 (20), 238 (12), 106 (48), 91 (100).

(3a*S*,4*S*,6a*R*)-1,3-Dibenzyl-tetrahydro-1*H*-thieno[3,4-*d*]imidazol-2(3*H*)-one-4-yl-pentanoic Acid (9) A suspension of $Pd(OH)_2$/C (1.7 g) in EtOAc (70 ml) was preactivated for 1 h under a H_2 pressure of 4 atm. A solution of **8** (21.1 g, 50 mmol) in EtOAc (130 ml) was added. The reaction mixture was shaken at r.t. under an atmosphere of H_2 (4 atm) for 4 h. The mixture was filtered through a pad of *Celite*. The filtrate was evaporated under reduced pressure to give the crude product, which was recrystallized from *iso*-PrOH/hexane to afford **9** as a white solid (20.2 g, 95%), mp 91—93 °C, $[\alpha]_D^{23}$ −26.6° (c=1.0, CH_3OH) {lit.[39]: mp 91—92 °C, $[\alpha]_D^{23}$ −26.7° (c=1.0, CH_3OH)}. IR (KBr) ν_{max} 2926, 1097, 1451, 1238, 703 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.39—1.69 (6H, m), 2.20 (2H, t, J=6.6 Hz), 2.70 (2H, 4d, J=2.35, 4.4 Hz), 3.08 (m, 1H), 3.90 (1H, dd, J=5.56 Hz), 3.97 (1H, m), 4.04, 4.16, 4.74, 5.02 (4H, 4d, J=15.1, 15 Hz), 7.22—7.37 (10H, m); EI-MS m/z: 423 (37, M^+), 289 (18), 238 (11), 106 (49), 91 (100).

***d*-Biotin (1)** A mixture of **9** (42.4 g, 0.1 mol), methanesulfonic acid (100 ml), AcOH (100 ml), and H_2O (50 ml) was stirred in xylene (200 ml) until all of compound **9** had been consumed (10 h, confirmed by TLC). After cooling to r.t., H_2O (200 ml) was added. The organic layer separated off the aqueous layer and was concentrated under reduced pressure to an approximate volume of 100 ml. The precipitated product was collected by filtration, and recrystallized from H_2O to afford **1** as a white crystalline powder (19.6 g, 80%), mp 231—232 °C, $[\alpha]_D^{22}$ +91° (c=1.0, 0.1 N NaOH) {lit.[23]: mp 232—233 °C, $[\alpha]_D^{22}$ +91.2° (c=1.0, 0.1 N NaOH)}. IR (KBr) ν_{max} 3311, 2933, 1705, 1665 cm^{-1}; ^{1}H-NMR δ: 1.31—1.62 (6H, m), 2.18 (2H, t, J=7.3 Hz), 2.57 (1H, dd, J=1.7, 12.5 Hz), 2.79 (1H, dd, J=4.7, 12.5 Hz), 3.15 (1H, m), 4.16 (1H, m), 4.36 (1H, m), 6.37 (1H, s), 6.47 (1H, s), 11.98 (1H, br s); EI-MS m/z: 245 (1.15, M^+), 227 (9), 184 (25), 112 (26), 97 (100), 85 (66).

Acknowledgements This work was partially supported by a Grant-in-Aid (96107) for Scientific Research from the Ministry of Chemical Industry of China.

References and Notes

1) Chen F. E., Chen X. X., Dai H. F., Kuang Y. Y., Xie B. Zhao J. F., *Adv. Synth. & Catal.*, **347**, 549—554 (2005).
2) Mistry P. S., Dakshinamurti K., *Vitam. Horm.*, **22**, 1—55 (1964).
3) Maebashi M., Makino Y., Furukawa Y., Ohinata K., Kimura S., Sato T., *J. Clin. Biochem, Nurt.*, **14**, 211—218 (1993).
4) Coggeshall C. J., Heggers J. P., Robson C. M., Baker H., *Ann. N.Y. Acad. Sci.*, **447**, 389—392 (1985).
5) Parry R. J., Naidu M. V., *Tetrahedron Lett.*, **21**, 4783—4786 (1980).
6) Trainor D. A., Parry R. J., Gitterman A., *J. Am. Chem. Soc.*, **102**, 1467—1468 (1980).
7) Ahler M., Muller W., Reichert A., Ringsdorf H., Venzmer J., *Angew. Chem., Int. Ed. Engl.*, **29**, 1269—1285 (1990).
8) Marquet A., Frappier F., Guillerm G., Azoulav M., Florentin D., *J. Am. Chem. Soc.*, **115**, 2139—2145 (1993).
9) De Clercq P. J., *Chem. Rev.*, **97**, 1755—1792 (1997).
10) Shimizu T., Seki M., *Tetrahedron Lett.*, **41**, 5099—5101 (2000).
11) Shimizu T., Seki M., *Tetrahedron Lett.*, **42**, 429—432 (2001).
12) Shimizu T., Seki M., *Tetrahedron Lett.*, **43**, 1039—1042 (2002).
13) Mori Y., Seki M., *Heterocycles*, **58**, 125—127 (2002).
14) Mori Y., Seki M., *J. Org. Chem.*, **68**, 1571—1574 (2003).
15) Seki M., Hatsuda M., Mori Y., Yamada S., *Tetrahedron Lett.*, **43**, 3269—3272 (2002).
16) Seki M., Mori Y., Hatsuda M., Yamada S., *J. Org. Chem.*, **67**, 5527—5536 (2002).
17) Seki M., Shimizu T., Inubushi K., *Synthesis*, **2003**, 361—364 (2003).
18) Mori Y., Kimura M., Seki M., *Synthesis*, **2003**, 2311—2316 (2003).
19) Seki M., Kimura M., Hatsuda M., Yoshida S., Shimizu T., *Tetrahedron Lett.*, **44**, 8905—8907 (2003).
20) Kimura M., Seki M., *Tetrahedron Lett.*, **45**, 1635—1637 (2004).
21) Kimura M., Seki M., *Tetrahedron Lett.*, **45**, 3219—3223 (2004).
22) Uskokovic M. R., "Encyclopedia of Chemical Technology," 3rd ed., Vol. 24, ed. by Kirk D. E., Othmer D. E., Wiley, New York, 1984, pp. 41—49.
23) Chen F. E., Yuan J. L., Dai H. F., Kuang Y. Y., Chu Y., *Synthesis*, **2003**, 2155—2160 (2003).

24) We noticed that the polymer-supported chiral sulfonamide was partially decomposed in the sixth cycle in the enantioselective reduction of **4** into **5**. This made the work-up procedure very difficult to carry out and recycling of the polymer inefficient.
25) Price M. O., Sui J. K., Kurth M. J., Schore N. E., *J. Org. Chem.*, **67**, 8086—8089 (2002).
26) Zhao G., Hu J. B., Qian Z. S., Yin W. X., *Tetrahedron: Asymmetry*, **13**, 2095—2098 (2002).
27) Itsuno S., Ito K., *J. Chem, Soc, Perkin Trans I*, **1984**, 2887—2893 (1984).
28) Brown H. C., Jadhav P. K., Mandal A. K., *Tetrahedron*, **37**, 3547—3587 (1981).
29) Apsimo J. W., Sequin R. P., *Tetrahedron*, **35**, 2797—2842 (1979).
30) Itsuno S., Matsumoto T., Sato D., Inoue T., *J. Org. Chem.*, **65**, 5879—5881 (2000).
31) Felder M., Giffels G., Wandrey C., *Tetrahedron: Asymmetry*, **8**, 1975—1977 (1997).
32) Itsuno S., Nakano M., Ito K., *J. Chem. Soc. Perkin Trans. I*, **1985**, 2615—2619 (1985).
33) Aoki Y., Suzuki H., Akiyama H., Akano S., U.S. Patent, 3 876 659 (1975) [*Chem. Abstr.* **80**, 95951*z* (1974)].
34) Ohashi N., Ikeda T., Shimage K., Takakashi T., Ishizumi K., Eur. Patent Appl., EP 84 377 (1983) [*Chem. Abstr.* **100**, 34338*q* (1983)].
35) Chen F. E., Huang Y. D., Fu H., Cheng Y., Zhang D. M., Li Y. Y., Peng Z. Z., *Synthesis*, **2000**, 2004—2008 (2000).
36) Chen F. E., Dai H. F., Kuang Y. Y., Jia H. Q., *Tetrahedron: Asymmetry*, **14**, 3667—3672 (2003).
37) Yamano T., Tokuyama S., Aoki I., Nishiguchi Y., Nakahama K., Takanohashi T., *Bull. Chem. Soc. Jpn.*, **66**, 1456—1460 (1993).
38) Hirata N., Miyamoto Y., Mizuno M., Takahashi T., Mizuno T., Jpn. Kokai Tokkyo Koho JP 188247 (1996) [*Chem. Abstr.* **124**, 8815*u* (1996)].
39) Takahash T., Minai M., Yamamoto T., Mizuno T., Miyamoto Y., Eur. Pat. Appl., EP 0633 263 (1995) [*Chem. Abstr.* **122**, 187270*r* (1995)].