Crystallization-Induced Asymmetric Transformations. Enantiomerically pure (−)-(*R*)- and (+)-(*S*)-2,3-Dibromopropan-1-ol and Epibromohydrins. A Study of Dynamic Resolution *via* the Formation of Diastereoisomeric Esters

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Dedicated to Professor *Dieter Seebach* on the occasion of his 65th birthday

(*S*)-2,3-Dibromopropan-1-ol of high enantiomer excess was obtained by crystallization-induced asymmetric transformations of racemic 2,3-dibromopropan-1-ol esterified with *N*-([1,1′-biphenyl]-4-ylcarbonyl-L-alanine; in particular, an asymmetric transformation of the first type (involving bromide exchange to equilibrate the diastereoisomeric esters) and an asymmetric transformation of the second type (involving a transesterification of diastereoisomeric esters with excess racemic alcohol) were devised.

Introduction. – The 2,3-dibromopropan-1-ol (**1**) is an obvious and attractive reagent for the generation of the dication 1-(hydroxymethyl)ethan-1,2-diylium (**2**); also, it can be an effective precursor to epibromohydrin (**3**), which is itself a reagent for either **2** or the dication 2-hydroxypropane-1,3-diylium (**4**). Most common reagents for the enantiomerically pure C_3 acceptor synthons **2** or **4** are glycidol or glycerol derivatives that have been obtained by enantioselective epoxidation or dihydroxylation of allyl alcohol derivatives [1], by stereoselective elaboration starting from D-mannitol or serine [2], or by elaboration of halo-hydroxy-propane derivatives kinetically resolved by means of chemical or enzymatic methods [3][4]. The enantiomerically enriched dibromo alcohol **1** has been obtained from the corresponding dibromoamine partially resolved by optical resolution [5] or by enantioselective addition of bromine to allyl glycosides [6]. These methods are, however, inefficient and lead to poor enantiomer excesses. As part of a program of systematic search for novel resolving agents suitable for use in dynamic resolutions [7–9], we wish to report here a productive approach to enantiomerically pure (*R*)- and (*S*)-**1** based on asymmetric transformation of appropriate ester derivatives.

Results and Discussion. – *Synthesis of Diastereoisomeric Esters* **9** *and* **10**. We set out by tayloring the homochiral acid to be conjugated with racemic 2,3-dibromopropan-1-ol. We adopted amino acids as the chiral source, because of some attractive features of this class of compounds as chiral auxiliaries: amino acids are often inexpensive, available in both chiral forms, and, as bifunctional substances, they allow easy conjugation with the racemic substrate to be resolved as well as with other groups by means of which the solubility properties of the diastereoisomeric conjugates can be

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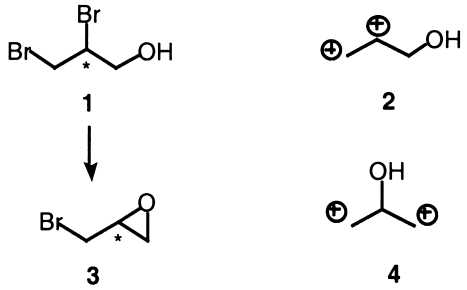


tuned and optimized. The control of the solubility of derivatized racemates is particularly important in consideration of a possible dynamic resolution: the two conjugates must not form a solid solution, and their solubility must be low under the conditions under which their equilibration occurs efficiently. Among the *N*-acyl-substituted amino acids tested (see **5** and **6**, *Fig.*), we found that *N*-([1,1′-biphenyl]-4-ylcarbonyl)-L-alanine provides esters (see **9** and **10**) that do not co-crystallize and exhibit appreciably different solubilities in various solvents such as toluene, MeCN, and MeOH.

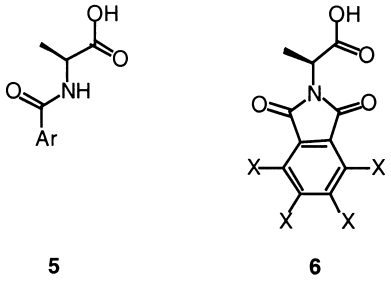
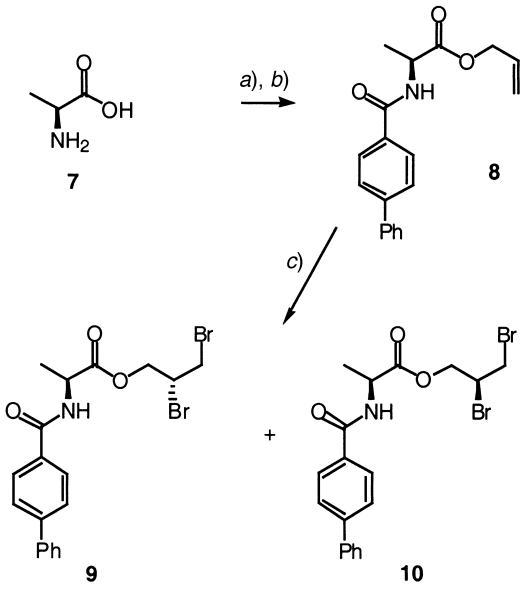


Figure. *Resolving agents tested for the separation of 2,3-dibromopropan-1-ol* (Ar = 3,4,5-triiodophenyl, 3,5-dinitrophenyl, [1,1′-biphenyl]-4-yl; X = Cl, Br)

The details of the protocol by which racemic 2,3-dibromopropan-1-ol conjugates with the resolving agent were obtained is shown in *Scheme 1*. Rather than preparing the mixture of diastereoisomers **9** and **10** by condensation of *N*-([1,1′-biphenyl]-4-ylcarbonyl)-L-alanine with racemic 2,3-dibromopropan-1-ol (which is commercially available but somewhat expensive), we found it more practical to get the mixture by bromination of allyl ester **8**. For the first preparation of allyl ester **8**, we condensed alanine allyl ester *p*-toluenesulfonate (obtained from **7**) with [1,1′-biphenyl]-4-carbonyl chloride. Addition of Br_2 to **8** gave a 1:1 mixture (HPLC and ^{13}C-NMR) of diastereoisomeric esters **9** and **10**; as expected, no asymmetric induction was observed in the bromination step (stereocontrol in the Br_2 addition to allyl alcohol derivatives has proved quite difficult, indeed [6]).

As mentioned above, rather than conducting the separation of the two diastereoisomeric esters **9** and **10** as a traditional fractional crystallization, we were aiming to devise conditions for dynamic resolution; this would require equilibration of **9** and **10** parallel to their precipitation as solids and would result in the conversion of the more-

Scheme 1. *Preparation of Diastereoisomeric Esters* **9** *and* **10**



a) Allyl alcohol, TsOH, hexane, reflux under continuous removal of H_2O. *b*) [1,1′-Biphenyl]-4-carbonyl chloride, Et_3N, CH_2Cl_2. *c*) Br_2, $CHCl_3$.

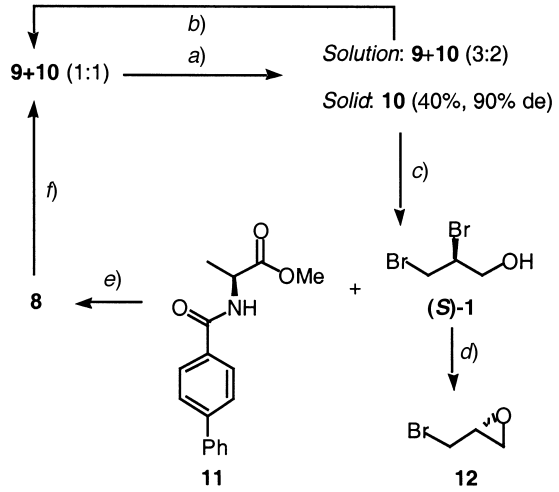
soluble of the stereoisomers to the less-soluble one to be isolated as a virtually single product. We attempted to accomplish this goal following two approaches that differ for the kind of process involved in the equilibration of the two esters, *i.e.*, *via* epimerization by bromide exchange or *via* epimerization by transesterification in the presence of an excess of racemic 2,3-dibromopropan-1-ol.

Resolution Involving Epimerization by Bromide Ion Exchange. As the most obvious approach, we hoped to accomplish the dynamic resolution of **9** and **10** by digestion or recrystallization of the two solids from a solution containing free bromide ion to induce epimerization at the secondary bromide centers. So, when a 1:1 mixture of stereoisomers **9** and **10** was allowed to recrystallize from 3.5 parts of a 33% solution of Bu_4NBr in MeCN, ester **10** was obtained in 25% yield and 75% de; however, analysis of the mother liquors showed that the more-soluble diastereoisomer was prevailing and little or no epimerization had occurred during the separation of **10**. The high salt concentration, although ineffective in producing a rapid bromide exchange at the epimeric center, was, however, essential for differentiating the solubility of the two stereoisomers to the extent that the less-soluble isomer could be obtained in reasonable yield from a single recrystallization. The reasons for this result are not apparent but might suggest another important use of concentrated salts solutions known as ionic liquids [10][2]). The dynamic resolution of **9** and **10** proved unpractical as a second-order

[2]) The specific features of concentrated salt solutions in differentiating isomer solubility is under investigation.

asymmetric transformation because, under the conditions of an effective bromide exchange (higher salt concentration and temperature), the solubility of the two esters was too high. Taking advantage of the substantially different solubilities of the two diastereoisomers, we were able, however, to devise conditions for a practical asymmetric transformation of the first type, whose net result is the clean conversion of the 1:1 diastereoisomeric mixture to an equivalent amount of the single, less-soluble diastereoisomer (*Scheme 2*). Thus, the relative amounts of solvent, salt, and esters were adjusted to obtain the maximum amount of the less-soluble diastereoisomer of acceptable purity from a single recrystallization: for example, the recrystallization of **9** and **10** from a solution of Bu_4NBr (5 parts) in MeCN (5 parts) afforded **10** (0.2 part, 40%) of 90% de. The mother liquors of this recrystallization (in which the more-soluble stereoisomer was prevailing) were converted to a solution virtually identical to that of the first recrystallization by adding **9** and **10** (1:1 mixture; 0.2 part, same as the amount of **10** obtained as the first crop) and heating for a time long enough to allow the bromide exchange to bring about complete equilibration. Upon cooling, a second crop of pure diastereoisomer **10** was obtained as from the first recrystallization and the cycle could be repeated. The mother liquors could be used to process more samples of the mixture **9**/**10** with a constant yield of pure **10** at each step and without apparent loss of diastereoisomer purity of the resolving agent.

Scheme 2. *Production of Enantiomerically pure (2*S*)-2,3-Dibromopropan-1-ol* ((*S*)-**1**) *and* D*-Epibromohydrin* (**12**) *Involving Bromide Exchange*



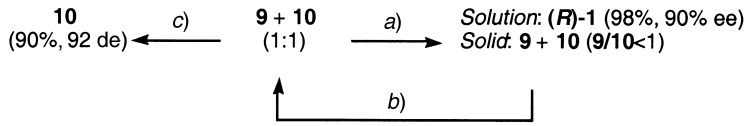
a) Recrystallization from 45% Bu_4NBr solution in MeCN. *b*) Addition of **9** + **10**, 90°, 6 h. *c*) MeOH, HCl. *d*) Aq. NaOH soln. *e*) Allyl alcohol, hexane, *p*-toluenesulfonic acid, continuous removal of H_2O. *f*) Br_2, $CDCl_3$.

Acid-catalyzed methanolysis of the single diastereoisomer **10** afforded enantiomerically pure 2,3-dibromopropan-1-ol (*S*)-**1** along with methyl ester **11**, which were cleanly separated and quantitatively recovered. Dibromide (*S*)-**1** was converted quantitatively to epibromohydrine (**12**), whose enantiimer purity turned out to be $>95\%$ by gas chromatography (chiral column). Methyl ester **11** was recycled to give more diastereoisomeric dibromo esters **9** and **10**, by a quantitative transesterification

with allyl alcohol followed by bromination of the intermediate allyl ester **8**. No detectable racemization of the resolving agent was produced when the above process was repeated 5 times.

Dynamic Resolution Involving Transesterification. The equilibration of two diastereoisomers (such as **9** and **10**), which is necessary to obtain the selective precipitation of the less-soluble one in a dynamic resolution, does not necessarily require that the chiral center of the species to be resolved is directly involved in the epimerization process. In the specific case of **9** and **10**, we thought that equilibration could also be accomplished by digesting the solid mixture **9**/**10** in the presence of an excess of racemic alcohol under conditions in which the small portion of dissolved esters can undergo transesterification with the free alcohol. Because of the rules involved in the equilibration of two species forming separate solid phases, one would expect to see a progressive increase of the less-soluble diastereoisomeric ester in the solid at the expense of the more-soluble one, paralleled by a deracemization of the free alcohol in solution. This result, perhaps surprising at first sight, is actually what would be obtained by the resolution of the alcohol with a substoichiometric amount of resolving agent; this method is frequently employed in the resolution of organic acids and bases by formation of insoluble salts with enantiomerically pure bases or acids, respectively, but it has never been adopted in resolutions with covalently bound chiral auxiliary reagents. This technique proved quite successful in our case. Indeed, by digesting a mixture **9/10** in an Et_2O solution containing an excess (1.5- to 2.5-fold) of racemic 2,3-dibromopropan-1-ol in the presence of an acid catalyst, an increase of the portion of more insoluble **10** to up to 92% de in the solid phase was observed; the most-practical conditions to accomplish equilibration turned out to be the use of Et_2O as the solvent and methanesulfonic acid as the transesterification catalyst. Other catalysts, such as BF_3, $AlMe_3$ (added to the alcohol to form the trialkoxide), or $ZnCl_2$, although effective as well, made the final isolation of **10** unnecessarily more complicated. Alternatively, we envisaged that the equilibration of solid esters **9** and **10** with a deficiency of free dibromo alcohol would lead to enantiomerically pure free alcohol in solution and to a mixture of stereoisomeric esters that, rather than being decomposed to obtain an enantiomerically enriched alcohol, could be epimerized to a 1:1 mixture by bromide exchange (as seen in the previous section) and used to treat another batch of racemic alcohol in a cyclic process made by alternating steps of transesterification and bromide exchange. One interesting feature of this approach is that the enantiomerically pure alcohol is produced directly free from any derivatization. According to our expectation, (*S*)-**1** of 90% ee resulted by equilibrating a solution of racemic alcohol with a four-fold excess of the diastereoisomer mixture **9**/**10** in Et_2O containing methanesulfonic acid.

Scheme 3. *Enantioselective Transformation Involving Transesterification*



a) Racemic 2,3-dibromopropan-1-ol (0.25 mol), Et_2O, methanesulfonic acid. *b*) 45% Bu_4NBr in MeCN, 90°, 6 h. *c*) Racemic 2,3-dibromopropan-1-ol (2 mol), Et_2O, methanesulfonic acid.

Conclusions. – Two effective preparations of the hitherto elusive enantiomerically pure 2,3-dibromopropan-1-ol were devised *via* crystallinity-induced asymmetric transformations of diastereoisomeric esters. A suitable chiral auxiliary reagent, *N*-([1,1′-biphenyl]-4-ylcarbonyl)-L-alanine, was found among five alanine derivatives designed for this purpose. An asymmetric transformation of the first type involving bromide exchange for the equilibration of the two diastereoisomeric conjugates was possible because of their unexpectedly high difference in solubility in the concentrated solution of Bu_4NBr originally meant to induce epimerization. In a successful asymmetric transformation of the second type, equilibration of **9** and **10** was obtained by transesterification with an excess of racemic alcohol; conceptually related to an optical resolution with a substoichiometric amount of resolving agent (which allows only the pure enantiomer giving rise to the less-soluble derivative to separate as a conjugate), this technique of asymmetric transformation (or optical resolution) has never been adopted before in cases in which the resolving agent and the racemic compound are covalently bound. With the above results, we have demonstrated that, by a systematic search of the resolving agent, enantiomer separation *via* diastereoisomer formation can be efficiently applied to a preselected target.

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Experimental Part

1. *General*. M.p.: uncorrected. B.p.: oven temp. of the bulb-to-bulb distillation apparatus (*Buki KR200*). Gas chromatography: enantiomer-excess evaluation of **12** with an *Astec Chiraldex GTA* column (trifluoroacetylated cyclodextrins, 20 m, i.d. 0.25 mm). HPLC: *Nucleosil-100* silica-gel column, 5 μm, 25 cm, i.d. 4.6 mm). NMR Spectra: ^{1}H at 200 MHz and ^{13}C at 50 MHz; $CHCl_3$ solns., unless otherwise stated; δ in ppm, J in Hz.

2. *Allyl* N-*([1,1′-Biphenyl]-4-ylcarbonyl)*-L-*alaninate* (**8**). A mixture of L-alanine (30 g, 0.34 mol), allyl alcohol (230 ml, 3.4 mol), and $TsOH \cdot H_2O$ (77.5 g, 0.4 mol) was heated to reflux in hexane (300 ml) under continuous removal of H_2O. The resulting homogeneous mixture was evaporated and the residue triturated in Et_2O: *alanine allyl ester p-toluenesulfonate salt* (96 g, 94%). Crystalline solid. M.p. 89° ([11]: 84–85°).

To a mixture of the above ester (41.5 g, 0.14 mol), and [1,1′biphenyl]-4-carbonyl chloride (30 g, 0.14 mol) in CH_2Cl_2 (300 ml), while cooled in an ice bath Et_3N (70 ml, 51 g, 0.505 mol) was added dropwise, and the reaction was allowed to proceed overnight. The mixture was washed with sat. $NaHCO_3$ soln., dried, and evaporated to afford a residue from which **8** (32.1 g, 75%) was obtained by trituration in Et_2O. The anal. sample was recrystallized from hexane. M.p. 118–120°. ^{1}H-NMR: 1.53 (*d*, *J* = 7.3, 3 H); 4.64 (*d*, *J* = 5.4, 2 H); 4.80 (*q*, *J* = 7.3, 1 H); 5.21–5.36 (*m*, 2 H); 5.80–5.99 (*m*, 1 H); 6.96 (*d*, *J* = 7.3, 1 H); 7.33–7.45 (*m*, 3 H); 7.55–7.63 (*m*, 4 H); 7.86 (*d*, *J* = 8.3, 2 H). ^{13}C-NMR: 19.2; 46.4; 49.2; 66.6; 119.4; 127.8; 128.2; 128.6; 129.5; 132.1; 133.2; 140.6; 173.6. Anal. calc. for $C_{19}H_{19}NO_3$: C 73.77, H 6.19, N 4.53; found: C 73.2, H 6.5, N 4.5.

3. *(2*R*)- and (2S)-2,3-Dibromopropyl* N-*([1,1′-Biphenyl]-4-ylcarbonyl)*-L-*alaninate* (**9** and **10**, resp.). To a soln. of allyl ester **8** (27.5 g, 0.09 mol) in $CHCl_3$ (200 ml), magnetically stirred and cooled in an ice bath, Br_2 (5 ml) was added dropwise, and the mixture was further stirred for 2 h at r.t. The mixture was washed with 10% sodium thiosulfate soln., dried ($MgSO_4$), and evaporated to afford a residue from which **9**/**10** (38.5 g, 94%) was obtained after trituration in cold Et_2O. M.p. 138–140°. ^{1}H-NMR: 1.58 (*d*, *J* = 7.3, 3 H); 3.71–3.85 (*m*, 2 H); 4.36 (*m*, 1 H); 4.56–4.66 (m, 2 H); 4.88 (*m*, 1 H); 6.74 (*d*, *J* = 7.3, 1 H); 7.37–7.49 (*m*, 3 H); 7.58–7.68 (*m*, 4 H); 7.87 (*d*, *J* = 8.3, 2 H). ^{13}C-NMR: 19.2; 32.4; 32.6; 47.1; 49.2; 66.3; 66.7; 127.9; 128.2; 128.7; 129.6; 133.0; 140.6; 145.3; 167.4; 173.2. Anal. calc. for $C_{19}H_{19}Br_2NO_3$: C 48.64, H 4.18, Br 34.06, N 2.99; found: C 48.4, H 4.3, Br 34.0, N 2.9.

4. *(2*S*)-2,3-Dibromopropyl* N-*([1,1′-Biphenyl]-4-ylcarbonyl)*-L-*alaninate* (**10**). 4.1. *By Bromide Exchange.* A mixture **9/10** (8 g) was recrystallized from a hot soln. of Bu_4NBr (20 g) in MeCN (20 ml). The precipitate was collected by filtration, washed with MeCN (2 × 5 ml), and dried: **10** (1.5 g, 90% de). A sample was recrystallized from MeOH. M.p. 160°. ^{1}H-NMR: 1.58 (*d*, *J* = 7.3, 3 H); 3.71–3.85 (*m*, 2 H); 4.36 (*m*, 1 H); 4.56–4.66 (*m*, 2 H); 4.88 (*m*, 1 H); 6.74 (*d*, *J* = 7.3, 1 H); 7.37–7.49 (*m*, 3 H); 7.58–7.68 (*m*, 4 H); 7.87 (*d*, *J* = 8.3, 2 H). ^{13}C-NMR:

19.2; 32.4; 47.1; 49.2; 66.3; 127.9; 128.2; 128.7; 129.6; 133.0; 140.6; 145.3; 167.4; 173.2. Recrystallization afforded **10** of 100% de.

A mixture **9**/**10** (1.5 g) was added to the filtrate which was heated under reflux for 6 h, while allowing *ca.* 10 ml of solvent to evaporate. Upon cooling, a second crop of **10** separated; the filtrate was processed as above and the cycle repeated up to 5 times.

4.2. *By Transesterification*. A suspension of **9/10** (3.0 g, 6.4 mmol) in a soln. containing racemic 2,3-dibromopropan-1-ol (2.8 g, 12.8 mmol) and methanesulfonic acid (0.50 ml, 7.7 mmol) in Et_2O (15 ml) was stirred at 40° in a screw-cap glass tube for 15 d. The solid phase was collected by filtration (2.7 g) and, upon analysis, was discovered to be 92% pure (HPLC) ester **10**.

5. *(2*R*)- or (2*S*)-2,3-Dibromopropan-1-ol* ((*R*)-or (*S*)-**1**, resp.) 5.1. *By Bromide Exchange*. Pure dibromopropyl ester **10** (obtained as described in *Exper. 4.1*; 1.5 g, 3.2 mmol) was added in a soln. obtained by dissolving AcCl (0.75 ml, 81 mmol) in MeOH (15 ml) and the mixture was heated to reflux until **10** was totally consumed (*ca.* 3 h, TLC monitoring; silica-gel; hexane/AcOEt 7:3). The mixture was cooled in a refrigerator to produce the precipitation of *methyl* N-*([1,1′-bipheny]-4-ylcarbonyl)*-L-*alaninate* (**11**), which was filtered off; H_2O (15 ml) was added to the filtrate, an additional crop of ester **11** was collected. Total yield: 0.88 g (98%): M.p. 160°. ^{1}H-NMR: 1.52 (*d*, *J* = 7.3, 3 H); 3.78 (*s*, 3 H); 4.82 (*q*, 1 H); 6.87 (*d*, *J* = 7.3, 1 H); 7.36–7.47 (*m*, 3 H); 7.57–7.65 (*m*, 4 H); 7.87 (*d*, *J* = 8.3, 2 H). ^{13}C-NMR: 19.3; 49.2; 53.2; 127.9; 128.2; 128.7; 129.6; 133.2; 140.6; 145.2; 167.2; 173.4. Anal. calc. for $C_{17}H_{17}NO_3$: C 72.07, H 6.05, N 4.94; found: C 71.6, H 6.3, N 4.8.

The clear filtrate was saturated with NaCl and extracted with Et_2O; the extract was dried ($CaCl_2$) and evaporated to afford crude (*S*)-**1** as a light tan oil (0.68 g, 95%). The anal. sample was purified by bulb-to-bulb distillation at 100°/10 Torr. $[\alpha]_D = -7.6$ (*c* = 0.316, MeOH). ^{1}H-NMR: 2.37 (*s*, 1 H); 3.77 (*d*, *J* = 7.8, 2 H); 3.98 (*d*, *J* = 4.4, 2 H); 4.22–4.33 (*m*, 1 H). ^{13}C-NMR: 32.3; 54.1; 64.8.

5.2. *Transesterification*. A suspension of **9**/**10** (5.8 g, 12.4 mmol) in a soln. of racemic 2,3-dibromopropan-1-ol (0.7 g, 3.2 mmol) and methanesulfonic acid (0.5 ml, 7.7 mmol) in Et_2O (15 ml) was stirred in a screw-cap tube at 40° for 15 d. The soln. was diluted with hexane, filtered, and evaporated: crude (*R*)-**1** (0.7 g, 100%). Its enantiomer excess (90%) was established by GC analysis of the corresponding epibromohydrin (see below).

*(R)-Epibromohydrine (=(2*R*)-2-(Bromomethyl)oxirane* (**12**). A soln. of (*S*)-**1** (0.4 g, 1.82 mmol) in Et_2O (10 ml) was stirred in the presence of 30% aq. NaOH soln. for 45 min. The Et_2O phase was dried ($MgSO_4$) and evaporated to give a residue from which pure **12** (0.21 g, 85%) was obtained by bulb-to-bulb distillation. $[\alpha]_D = -15.0$ (*c* = 0.031, MeOH) [2b]. ^{1}H-NMR: 2.66 (*m*, 1 H); 2.93 (*m*, 1 H); 3.13–3.66 (*m*, 3 H). ^{13}C-NMR: 33.1; 49.2; 51.9.

REFERENCES

[1] R. M. Hanson, *Chem. Rev.* **1991**, *91*, 437.

[2] a) M. C. Pirrung, S. E. Dunlap, U. P. Trinks, *Helv. Chim. Acta* **1989**, *72*, 1301; b) Y. Kawakami, T. Asai, K. Umeyama, Y. Yamashita, *J. Org. Chem*. **1982**, *47*, 3581; c) M. Bols, 'Carbohydrate Building Blocks', Wiley, New York, 1996; J. J. Baldwin, A. W. Raab, K. Mensler, B. H. Arison, D. E. McLure, *J. Org. Chem*. **1978**, *43*, 4876.

[3] M. K. Ellis, B. T. Golding, A. B. Maude, W. P. Watson, *J. Chem. Soc., Perkin Trans. 1* **1991**, 747; M. E. Furrow, S. E. Schaus, E. N. Jacobsen, *J. Org. Chem*. **1998**, *63*, 6776; S. E. Schaus, J. Branalt, E. N. Jacobsen, *J. Org. Chem*. **1998**, *63*, 4876; D. A. Annis, E. N. Jacobsen, *J. Am. Chem. Soc.* **1999**, *121*, 4147.

[4] C. A. G. M. Weijers, *Tetrahedron: Asymmetry* **1997**, *8*, 639; T. Suzuki, N. Kasai, N. Minamiura, *Tetrahedron: Asymmetry* **1994**, *5*, 239; N. Kasai, K. Sakaguki, *Tetrahedron Lett.* **1992**, *33*, 1211; B. Cambou, A. M. Klibanov, *J. Am. Chem. Soc*. **1984**, *106*, 2687; C. S. Chen, Y. C. Liu, M. Marsella, *J. Chem. Soc., Perkin Trans. 1* **1990**, 2559.

[5] A. C. Huitrich, W. P. Gordon, S. D. Nelson, *J. Chem. Eng. Data* **1982**, *27*, 474.

[6] G. Bellucci, C. Chiappe, F. D'Andrea, *Tetrahedron Asymmetry* **1995**, *6*, 221.

[7] J. Jacques, A. Collet, S. H. Wilen, 'Enantiomers, Racemates, and Resolutions', Wiley, New York, 1981.

[8] E. L. Eliel, S. H. Wilen, L. N. Mander, 'Stereochemistry of Organic Compounds', Wiley, New York, 1994.

[9] E. J. Ebbers, G. J. A. Ariaans, J. P. M. Houbiers, A. Bruggink, B. Zwanenburg, *Tetrahedron* **1997**, *53*, 9417; S. Caddick, K. Jenkins, *Chem. Soc. Rev.* **1996**, 447.

[10] P. Wassersheid, W. Keim, *Angew. Chem*. **2000**, *112*, 3926; T. Welton, *Chem. Rev.* **1999**, *99*, 2071.

[11] H. Waldmann, H. Kunz, *Liebigs Ann. Chem*. **1983**, 1912.

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