Enantiospecific and diastereoselective synthesis of *syn*-β-amino-α-hydroxy acids

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Abstract: The reaction of chiral α-hydroxy β,γ-unsaturated esters with tosyl isocyanate followed by cyclization of the resulting allylic carbamates with iodine in the presence of sodium carbonate provided *trans*-4,5-disubstituted 2-oxazolidinone derivatives in a highly diastereoselective manner. The subsequent removal of the iodo group and the protective functionality afforded the *syn*-β-amino-α-hydroxy acids. Using the reaction sequence, (2R,3S)- and (2S,3R)-3-amino-2-hydroxy acids were synthesized with high enantioselectivity. © 1997 Elsevier Science Ltd. All rights reserved.

In recent years, *syn*-β-amino-α-hydroxy acids have received considerable attention as the crucial component of peptidomimetic protease inhibitors. For instance, this moiety occurs in important renin inhibitors such as KRI-1230[1] and KRI-1314,[2] in which the absolute stereochemistry of the corresponding acid parts is 2R,3S. On the other hand, an antipode of the stereochemistry, a (2S,3R)-β-amino-α-hydroxy acid unit, has also been found in amastatin[3] and a marine natural product, microginin,[4] which was recently isolated from the cultured fresh water blue–green algae *Microcystis aeruginosa* and exhibits an inhibitory activity toward the angiotensin-converting enzyme (Figure 1). Many methods have already been developed for the synthesis of these β-amino-α-hydroxy acid units. Most of the early studies that used chiral natural products as starting materials[5–9] were limited in their flexibility of structural modification. Although, more recently, several methods that are applicable to the synthesis of derivatives bearing a variety of side chains have been reported,[10,11] practical routes for the construction of both their enantiomers starting with common frameworks are still desirable. In this report, we describe the enantiospecific synthesis of *syn*-β-amino-α-hydroxy acids employing the prochiral β,γ-unsaturated α-oxo ester.

In earlier reports,[12,13] we disclosed an efficient route to chiral β,γ-unsaturated α-hydroxy esters via the chiral auxiliary-assisted enantioselective reduction of β,γ-unsaturated α-oxo esters that were prepared by the BF₃-promoted aldol-type reaction of acetals with 2-(trimethylsiloxy)acrylates. Our plan for the transformation of the β,γ-unsaturated α-hydroxy ester to the β-amino-α-hydroxy ester is shown in Scheme 1. According to Hirama's protocol,[14] the β,γ-unsaturated α-hydroxy ester **1** would be converted into allylic carbamate by treatment with tosyl isocyanate, and then the resulting

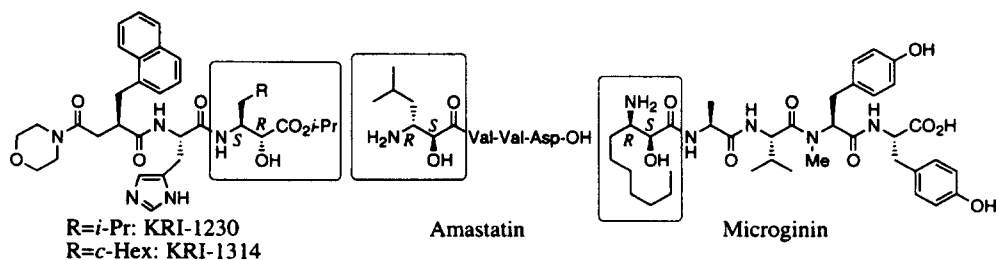R=*i*-Pr: KRI-1230
R=*c*-Hex: KRI-1314

Amastatin

Microginin

**Figure 1.**

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carbamate 2 would undergo intramolecular cyclization with iodine in the presence of base to provide the 2-oxazolidinone derivative 3. Removal of the iodo group and the protective functionality would lead to the desired β-amino-α-hydroxy acid 4. We began with an investigation of the construction of the 2-oxazolidinone using a racemic β,γ-unsaturated α-hydroxy ester.

Scheme 1.
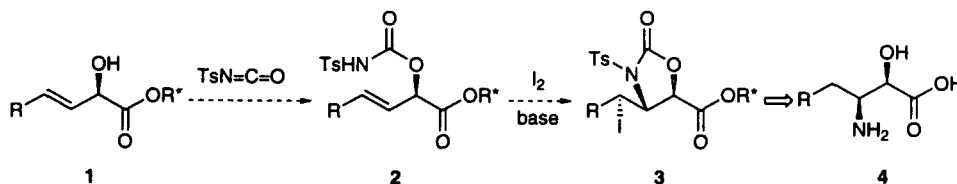
Results and discussion

Iodine-promoted cyclization of allylic carbamate

The β,γ-unsaturated α-hydroxy ester 5, which was prepared in a similar way as later described in part of the synthesis of cyclohexylnorstatine, was simply treated with tosyl isocyanate in dichloromethane to afford the allylic carbamate 6. Although Hirama et al. have disclosed that α-substituted allyl carbamates are easily cyclized to 2-oxazolidinone by treatment with iodine and potassium carbonate in ether as the solvent,[14] an initial attempt to apply this procedure to the allylic carbamate 6 failed due to separation of tarry matter. Therefore, further investigation of the reaction conditions regarding the base and solvent was undertaken. The results are summarized in Table 1.

$$(1)$$
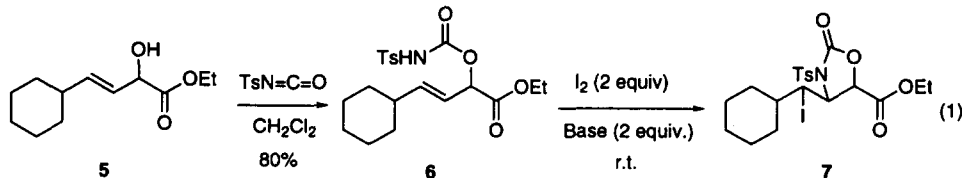
When dichloromethane was used as the solvent, the tarry material did not appear and the desired 2-oxazolidinone 7 was obtained in 24% yield along with a significant amount of recovery of the carbamate 6 (run 1). A prolonged reaction time did not lead to an improvement in the yield. However, the use of collidine instead of the heterogeneous inorganic base improved the yield of 7 to 47% (run 2). Further, by using acetonitrile as the solvent, the carbamate 6 was totally consumed to provide 7 in 61% yield (run 3). Other polar solvents such as dimethylformamide and nitromethane were less satisfactory than acetonitrile. Interestingly, when the carbonate salts were used as the base in this solvent system, the yields of 7 varied from poor to good depending on the kind of metal species (runs

Table 1. Iodonium ion promoted cyclization of carbamate 6

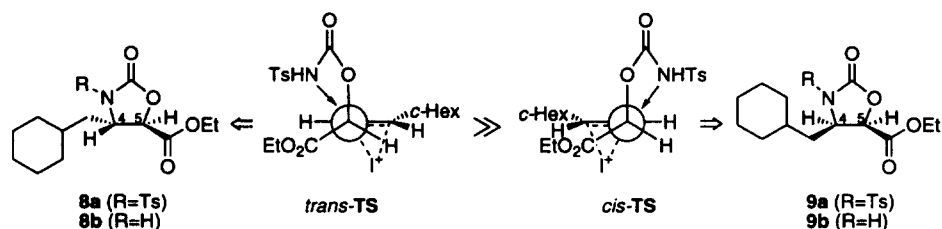| Run	Base	Solvent	Time/h	Yield of 7/%	Recovery of 6/%
1	K_2CO_3	CH_2Cl_2	30	24	38
2	collidine	CH_2Cl_2	24	47	8
3	collidine	MeCN	24	61	trace
4	K_2CO_3	MeCN	24	38	24
5	$KHCO_3$	MeCN	24	61	6
6	$NaHCO_3$	MeCN	24	55	12
7	Na_2CO_3	MeCN	24	70	5
8	Na_2CO_3[a]	MeCN	24	73	0

[a] 5 equiv. was used.

Figure 2.

4–7). The optimum condition for this cyclization was found to lie with the use of 5 equiv. of sodium carbonate in acetonitrile at room temperature for 24 h (run 8).[15]

In every case, 2-oxazolidinone **7** was produced as an almost single diastereomer (>90%), which was assigned to have a 4,5-*trans* relationship, after removal of the γ-iodo group, by comparison of the chemical shifts and coupling constants of the ^{1}H NMR with those of analogous structures, **8b** and **9b**. Accordingly, the reported ^{1}H NMR data[16] of H-5 in **8b** and **9b** are 4.55 ppm (J=5.1 Hz) and 5.04 ppm (J=8.5 Hz), respectively. The major peak of H-5 in the deiodinated product from **7** appeared at 4.57 ppm (J=2.0 Hz), whereas a minor signal was detected at 4.99 ppm (J=7.0 Hz). Since the chemical shift as well as the coupling constant of the major isomer was in good agreement with that of **8b**, the relative stereochemistry should be 4,5-*trans*.[17]

The stereoselective formation of the *trans*-2-oxazolidinone can be explained by the transition state models depicted in Figure 2. Compared to the *trans*-TS model, the *cis*-TS model is obviously unfavorable for the cyclization due to steric interaction between the ester moiety and the alkenyl side chain. Hence, the cyclization is thought to preferentially proceed through the *trans*-TS model in order to provide the 4,5-*trans*-isomer of the 2-oxazolidinone **7**.

Synthesis of norstatine and cyclohexylnorstatine as representatives of (2R,3S)-3-amino-2-hydroxy acids

With the diastereoselective cyclization procedure for the allylic carbamate in hand, we next turned our attention to its application for the synthesis of norstatine (**17a**) and cyclohexylnorstatine (**17b**) in combination with the method for preparing chiral α-hydroxy β,γ-unsaturated esters.[12] We have already disclosed that the Mukaiyama aldol-type reaction of a silylated pyruvic ester, 2-(trimethylsiloxy)acrylate ester, with acetals is best promoted by a boron trifluoride–ether complex.[18] Subsequent β-elimination of the alcohol provides the β,γ-unsaturated α-oxo esters,[13] which are used for the enantioselective reduction of the α-carbonyl, affording the desired β,γ-unsaturated α-hydroxy esters. Recently, Watanabe *et al.* have modified the above aldol reaction for direct use of aldehydes as a starting material instead of acetals.[19] Therefore, we adopted this modification for the preparation of β,γ-unsaturated α-oxo esters.

The BF₃-promoted aldol-type reaction of methyl 2-(trimethylsiloxy)acrylate (**11**) with isobutyralde-hyde (**10a**) and cyclohexanecarboxaldehyde (**10b**) in the presence of trimethyl orthoformate, followed by the elimination of methanol using silica gel under refluxing benzene produced the β,γ-unsaturated α-oxo esters **12a** and **12b** in 74% and 79% yields, respectively (Scheme 2). After introduction of the (−)-*trans*-2-phenylcyclohexyl moiety as a chiral auxiliary via transesterification, the α-carbonyls were reduced with L-Selectride® in ether at −78°C, affording (*R*)-α-hydroxy-β,γ-unsaturated esters **13a** and **13b** with a high diastereoisomeric purity (>97% d.e. by ^{1}H NMR). The addition of tosyl isocyanate to the hydroxyl group and the subsequent cyclization of the resulting crude carbamates under the previously established conditions (I₂, Na₂CO₃ in MeCN) provided the 2-oxazolidinones **14a** and **14b** in reasonable yields with high diastereoselectivity. The iodo group was removed by radical reduction using Bu₃SnH–AIBN (cat.) producing **15a** and **15b**, whose cyclic carbonate and 2-phenylcyclohexyl groups were removed by treatment with potassium carbonate in methanol leading to the methyl esters. Subsequent hydrolysis with lithium hydroxide yielded acids **16a** and **16b**, which could be purified by

recrystallization providing the enantiomerically pure acids. Finally, the tosyl group was removed by sodium–naphthalenide reduction to afford (2R,3S)-3-amino-2-hydroxy acids **17a** and **17b**. The spectral and physical properties of **17a**, **17b** and their hydrochloride salts were identical in every respect with those reported in the literature[20–23] (^{1}H and ^{13}C NMR, IR, $[\alpha]_D$, see Experimental Section).
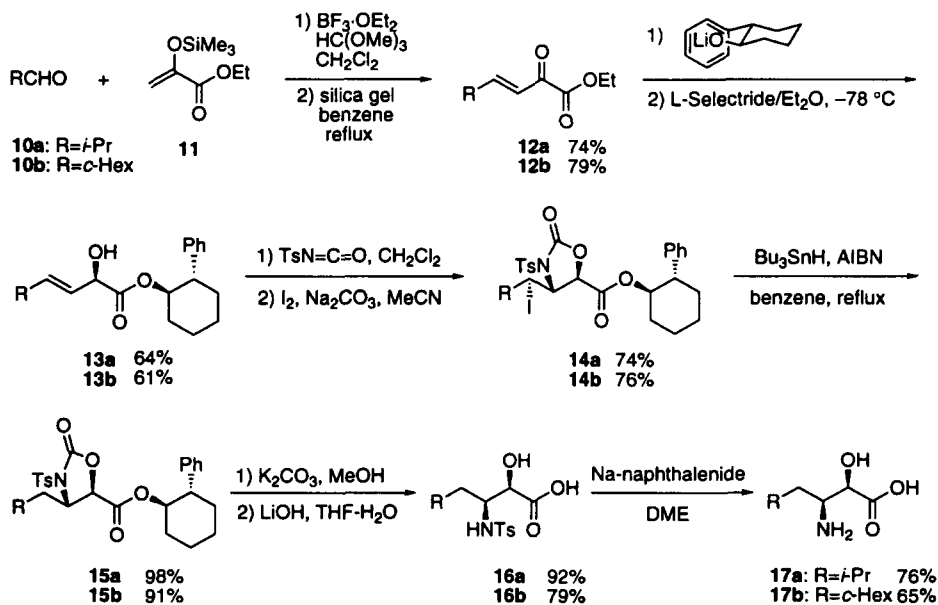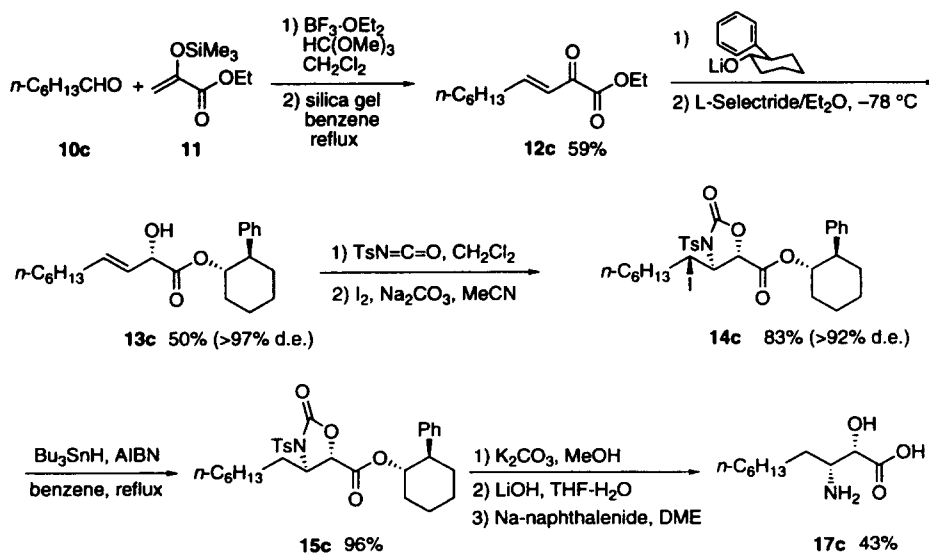

Scheme 2.

Synthesis of (2S,3R)-3-amino-2-hydroxydecanoic acid (AHDA)

The absolute stereochemistry of AHDA, the *N*-terminal moiety of microginin, has been unambiguously established as 2S,3R by synthetic approaches.[24,25] Also, thereafter, its asymmetric synthesis has been reported by several groups.[26,27] Our synthetic route is outlined in Scheme 3. Starting with heptanal, the same sequence of the reactions (**10c**→**12c**→**13**→**14c**→**15c**→**17c**) described above, except using the (+)-enantiomer of the chiral auxiliary, provided the desired AHDA, **17c**. A highly stereochemical outcome was again observed in both the reduction and the cyclization steps.

In conclusion, we have developed a novel enantiospecific and stereoselective route to *syn*-β-amino-α-hydroxy acids employing the combination of the diastereoselective reduction of chiral β,γ-unsaturated α-oxo esters and the cyclization of allylic carbamates derived from the resulting α-hydroxy β,γ-unsaturated esters as key steps. The feasibility of this approach was demonstrated by synthesizing both enantiomers of the biologically important β-amino-α-hydroxy acids. This method will be applicable to the synthesis of a wide range of *syn*-β-amino-α-hydroxy acids.

Experimental

All melting points are uncorrected. Optical rotations were determined using a JASCO DIP-360 polarimeter. ^{1}H and ^{13}C NMR spectra were obtained on a JEOL JNM-EX400 spectrometer with Me$_4$Si as the internal standard. *J* values are given in Hz. IR spectra were recorded on a Perkin–Elmer Model 1600 spectrophotometer. TLC was performed on plates coated with silica gel 60 F$_{254}$ (Merck). For column chromatography, Wakogel C-300 (Wako Chemicals) was used. THF and ether were freshly distilled from sodium–benzophenone ketyl under Ar prior to use. Other solvents were distilled from the appropriate drying agent and stored over molecular sieves.

Scheme 3.

Methyl (E)-5-methyl-2-oxo-3-hexenoate 12a

To a solution of isobutyraldehyde (10a) (18.7 mL, 206 mmol) and HC(OMe)$_3$ (24.8 mL, 226 mmol) in CH$_2$Cl$_2$ (500 mL) was added BF$_3$·OEt$_2$ (27.8 mL, 226 mmol) under Ar at −78°C. After 20 min, a solution of 11[13] (35.8 g, 206 mmol) in CH$_2$Cl$_2$ (60 mL) was added dropwise into the mixture at the same temperature with stirring. After 30 min, the reaction mixture was warmed to −30°C over 1 h and stirred for an additional 1 h at 0°C. The reaction was then quenched with saturated aqueous NaHCO$_3$. The mixture was extracted with CH$_2$Cl$_2$. The organic layer was dried over MgSO$_4$ and concentrated under reduced pressure. The residue was dissolved in benzene (1 L). Silica gel for chromatography (Wakogel C-300, 310 g) was added to the solution, and then the mixture was heated at reflux with vigorous stirring for 16 h. After being cooled to room temperature, the silica gel was filtered off and washed with ether several times. The filtrate was combined and concentrated. The residue was purified by distillation to give 12a (23.8 g, 152 mmol, 74%) as a yellow oil. Bp 76–78°C/5 Torr; ^{1}H NMR (CDCl$_3$) δ 1.11 (d, J=6.8, 6H), 2.51–2.62 (m, 1H), 3.89 (s, 3H), 6.62 (dd, J=1.5, 16.0, 1H), 7.17 (dd, J=6.6, 16.0, 1H); ^{13}C NMR (CDCl$_3$) δ 20.9 (×2), 31.8, 52.8, 122.3, 160.9, 162.8, 183.3.

(1R,2S)-2-Phenylcyclohexyl (2R,3E)-2-hydroxy-5-methyl-3-hexenoate 13a

To a solution of (1R,2S)-(−)-2-phenylcyclohexanol (1.27 g, 7.20 mmol) in THF (60 mL) was added BuLi (1.66 M in hexane, 4.0 mL, 6.60 mmol) dropwise at 0°C under Ar. After 15 min, the reaction mixture was cooled to −30°C and diluted with THF (170 mL). A solution of 12a (936 mg, 6.00 mmol) in THF (50 mL) was then added dropwise to the mixture. After 40 min, saturated aqueous NH$_4$Cl was added to the reaction mixture and the aqueous layer was extracted three times with ether. The organic layer was dried over MgSO$_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane:AcOEt=15:1) to give (1R,2S)-2-phenylcyclohexyl (E)-5-methyl-2-oxo-3-hexenoate (1.18 g, 3.91 mmol, 65%) as a yellow oil. ^{1}H NMR (CDCl$_3$) δ 0.95 (d, J=6.4, 3H), 0.96 (d, J=6.4, 3H), 1.36–1.66 (m, 4H), 1.80–1.83 (m, 1H), 1.90–2.00 (m, 2H), 2.16–2.20 (m, 1H), 2.30–2.36 (m, 1H), 2.78 (dt, J=4.4, 11.6, 1H), 5.20 (dt, J=4.4, 10.7, 1H), 6.11 (dd, J=1.2, 16.1, 1H), 6.45 (dd, J=6.4, 16.1, 1H), 7.17–7.30 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 20.5, 20.9, 24.7, 25.6, 31.6, 32.0, 33.8, 49.6, 78.2, 122.9, 126.7, 127.6 (×2), 128.4 (×2), 142.6, 160.8, 162.3, 185.5.

To a solution of the above ester (1.05 g, 3.50 mmol) in ether (70 mL) was added L-Selectride® (1.0 M in THF, 4.2 mL, 4.2 mmol) dropwise at −78°C under Ar. After 1 h, MeOH (14 mL), 10% aqueous

NaOH (18 mL) and 30% aqueous H_2O_2 (18 mL) were successively added, and then the reaction mixture was allowed to warm to room temperature for over 1 h. After 20 mL of water has been added, the aqueous layer was separated and washed three times with ether. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane:AcOEt=8:1) to give **13a** (1.05 g, 3.47 mmol, 99%, >97% de) as a colorless oil. $[\alpha]_D^{28}$ −50.2 (*c* 0.948, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.81 (d, *J*=6.8, 3H), 0.83 (d, *J*=6.8, 3H), 1.26–1.60 (m, 4H), 1.76–1.81 (m, 1H), 1.86–2.06 (m, 3H), 2.16–2.22 (m, 1H), 2.69 (dt, *J*=4.4, 11.5, 1H), 2.71 (d, *J*=6.4, 1H), 4.36 (dd, *J*=6.4, 6.4, 1H), 4.75 (ddd, *J*=1.5, 5.6, 15.6, 1H), 5.06 (dt, *J*=4.4, 10.7, 1H), 5.56 (ddd, *J*=1.5, 6.4, 15.6, 1H), 7.14–7.18 (m, 3H), 7.23–7.27 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.8 (×2), 24.7, 25.7, 30.4, 32.2, 34.2, 49.7, 71.1, 77.8, 122.9, 126.6, 127.4 (×2), 128.3 (×2), 140.4, 142.7, 173.3; IR (neat) 3511, 3029, 2935, 2863, 1729, 1450, 1262, 1203, 1147, 1111, 1012 cm^{-1}. Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.55; H, 8.65.

(4R,5R)-4-[(1S)-1-Iodo-2-methylpropyl)]-5-[(1R,2S)-2-phenylcyclohex-1-yloxycarbonyl]-3-tosyl-2-oxazolidinone 14a

To a solution of **13a** (1.98 g, 6.56 mmol) in CH_2Cl_2 (22 mL) was added TsNCO (1.09 mL, 7.22 mmol) dropwise at room temperature under Ar. After 1 h, the solvent was removed under reduced pressure. The residue was dissolved in acetonitrile (170 mL), and then Na_2CO_3 (3.48 g, 32.8 mmol) and I_2 (3.33 g, 13.1 mmol) were added to the solution. The reaction mixture was stirred at room temperature for 24 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$. The mixture was extracted four times with ether. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane:ethyl acetate=8:1) to give **14a** (3.02 g, 4.82 mmol, 74%, >93% de). Recrystallization from hexane:ether (5:1) afforded colorless needles. Mp 132–133°C; $[\alpha]_D^{28}$ −1.3 (*c* 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (d, *J*=6.8, 3H), 0.93 (d, *J*=6.8, 3H), 1.23–1.61 (m, 5H), 1.79–2.08 (m, 4H), 2.46 (s, 3H), 2.68 (dt, *J*=4.0, 16.3, 1H), 3.83 (dd, *J*=2.6, 2.8, 1H), 4.40 (dd, *J*=2.8, 5.9, 1H), 4.49 (d, *J*=2.6, 1H), 5.11 (dt, *J*=4.0, 15.6, 1H), 7.18–7.34 (m, 5H), 7.36 (d, *J*=8.3, 2H), 7.83 (d, *J*=8.3, 2H); ^{13}C NMR ($CDCl_3$) δ 21.8, 22.2, 22.6, 24.6, 25.5, 32.0, 32.4, 34.0, 49.1, 49.6, 62.8, 75.4, 78.8, 127.1, 127.4 (×2), 128.7 (×4), 129.7 (×2), 134.3, 142.2, 145.9, 150.4, 166.6; IR (neat) 3058, 2938, 2861, 1799, 1752, 1450, 1597, 1370, 1266, 1174, 1089, 1005 cm^{-1}. Anal. Calcd for $C_{27}H_{32}INO_6S$: C, 51.84; H, 5.16; N, 2.24; S, 5.13. Found: C, 51.58; H, 5.15; N, 2.26; S, 5.25.

(4S,5R)-4-(2-Methylpropyl)-5-[(1R,2S)-2-phenylcyclohex-1-yloxycarbonyl]-3-tosyl-2-oxazolidinone 15a

To a solution of **14a** (611 mg, 0.980 mmol) and AIBN (41.1 mg, 0.245 mmol) in benzene (15 mL) was added Bu_3SnH (0.33 mL, 1.18 mmol), and the mixture was heated at reflux for 1 h. After being cooled to room temperature, the mixture was evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:AcOEt=9:1) to give **15a** (478 mg, 0.956 mmol, 98%) as a viscous oil. $[\alpha]_D^{28}$ +17.5 (*c* 1.50, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.82 (d, *J*=6.8, 3H), 0.91 (d, *J*=6.8, 3H), 1.29–1.69 (m, 7H), 1.74–2.05 (m, 4H), 2.46 (s, 3H), 2.66 (dt, *J*=3.8, 16.3, 1H), 3.82 (ddd, *J*=2.0, 3.4, 10.3, 1H), 4.29 (d, *J*=2.0 Hz, 1H), 5.08 (dt, *J*=3.8, 10.7, 1H), 7.27–7.36 (m, 5H), 7.33 (d, *J*=8.3, 2H), 7.77 (d, *J*=8.3, 2H); ^{13}C NMR ($CDCl_3$) δ 21.5, 21.8, 23.3, 24.4, 24.6, 25.6, 32.0, 34.0, 43.3, 49.5, 59.7, 75.0, 78.4, 127.2, 127.3 (×2), 128.5 (×2), 128.7 (×2), 129.6 (×2), 134.8, 142.2, 145.5, 150.7, 167.0; IR (neat) 3030, 2956, 1790, 1748, 1597, 1454, 1372, 1164, 970 cm^{-1}. Anal. Calcd for $C_{27}H_{33}NO_6S$: C, 64.91; H, 6.66; N, 2.80. Found: C, 64.65; H, 6.87; N, 2.62.

(2R,3S)-2-Hydroxy-5-methyl-3-(tosylamino)hexanoic acid 16a

Compound **15a** (1.31 g, 2.62 mmol) was dissolved in a 0.3 M K_2CO_3 solution of MeOH (15 mL) and the reaction mixture was stirred at room temperature for 6 h. After being neutralized with 0.2 M HCl, the mixture was extracted five times with chloroform. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel

(hexane:AcOEt=3:1) to give methyl (2R,3S)-2-hydroxy-5-methyl-3-(tosylamino)hexanoate (830 mg, 2.52 mmol, 96%) as a colorless oil. $[\alpha]_D^{27}$ −39.0 (c 0.840, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 0.75 (d, J=6.4, 3H), 0.81 (d, J=6.4, 3H), 1.12–1.21 (m, 1H), 1.43–1.55 (m, 2H), 2.42 (s, 3H), 3.15 (d, J=4.4, 1H), 3.67–3.74 (m, 1H), 3.68 (s, 3H), 4.10 (dd, J=2.0, 4.4, 1H), 4.78 (d, J=9.8, 1H), 7.30 (d, J=8.3, 2H), 7.73 (d, J=8.3, 2H); ^{13}C NMR (CDCl$_3$) δ 21.4, 22.1, 22.4, 24.3, 41.2, 52.8, 54.1, 71.4, 127.0 (×2), 129.5 (×2), 138.2, 143.2, 173.5; IR (neat) 3486, 3286, 2957, 1732, 1598, 1434, 1333, 1160, 1092 cm^{-1}. Anal. Calcd for C$_{15}$H$_{23}$NO$_5$S: C, 54.69; H, 7.04; N, 4.25. Found: C, 54.44; H, 7.16; N, 4.04.

The methyl ester (4.76 g, 14.5 mmol) was dissolved in 0.3 M LiOH solution in THF:H$_2$O (3:1, 14 mL), and the solution was stirred at room temperature for 4 h. The reaction mixture was neutralized using an ion-exchange resin (H$^+$-form) and then filtered. The residual resin was washed with acetone several times. The filtrates were combined and concentrated. The residue was purified by recrystallization from CHCl$_3$:MeOH (4:1) to give **16a** (4.39 g, 13.9 mmol, 96%) as colorless needles. Mp 143–144°C; $[\alpha]_D^{28}$ −35.3 (c 0.904, acetone); ^{1}H NMR (acetone-d_6) δ 0.70 (d, J=6.4, 3H), 0.79 (d, J=6.4, 3H), 1.12–1.18 (m, 1H), 1.41–1.59 (m, 2H), 2.41 (s, 3H), 3.69–3.71 (m, 1H), 4.12 (d, J=2.4, 1H), 6.17 (br, 1H), 7.37 (d, J=7.3, 2H), 7.76 (d, J=7.3, 2H); ^{13}C NMR (CD$_3$CN) δ 20.2, 21.2, 21.2, 23.7, 39.8, 53.9, 70.7, 126.5 (×2), 129.2 (×2), 138.4, 143.2, 172.7; IR (KBr) 3400, 3253, 2956, 1747, 1599, 1444, 1323, 1151, 1090, 1040 cm^{-1}. Anal. Calcd for C$_{14}$H$_{21}$NO$_5$S: C, 53.32; H, 6.71; N, 4.44. Found: C, 53.12; H, 6.61; N, 4.32.

(2R,3S)-3-Amino-2-hydroxy-5-methylhexanoic acid 17a

To a sodium naphthalenide solution, prepared from naphthalene (10.9 g, 84.7 mmol) and Na (1.77 g, 77.0 mmol) in DME (96 mL) with stirring for 1 h at room temperature, was added a solution of **16a** (4.76 g, 14.5 mmol) in DME (30 mL) at 0°C under Ar. After 1 h, 150 mL of water was added to the reaction mixture. The organic layer was separated and washed twice with water. The aqueous layer was acidified with an ion-exchange resin (H$^+$-form) to pH 4 and filtered. The residual resin was washed with water several times until the washings became pH 7. The resin was eluted with 7% aqueous NH$_3$, and then the eluent was concentrated under reduced pressure. The residue was purified by recrystallization from EtOH:H$_2$O (4:1) to give **17a** as a white solid (1.58 g, 9.80 mmol, 76%). $[\alpha]_D^{28}$ +28.4 (c 0.45, AcOH) [lit.[20] $[\alpha]_D^{25}$ +26.9 (c 0.32, AcOH)]; ^{1}H NMR (D$_2$O) δ 0.92 (d, J=6.4, 3H), 0.94 (d, J=6.8, 3H), 1.31–1.45 (m, 2H), 1.65–1.75 (m, 1H), 3.19–3.24 (m, 1H), 3.95 (d, J=2.9, 1H); ^{13}C NMR (D$_2$O) δ 22.2, 22.8, 24.7, 41.1, 52.2, 74.3, 179.3.

(2R,3S)-3-Amino-2-hydroxy-5-methylhexanoic acid hydrochloride

Compound **17a** (110 mg) was dissolved in 25% HCl (4 mL) and heated at 80°C for 12 h. The mixture was concentrated to ca 1 mL. After standing overnight at room temperature, **17a**·HCl was collected by filtration as white crystals.[21] ^{1}H NMR (D$_2$O) δ 1.01 (d, J=6.4, 3H), 1.02 (d, J=6.4, 3H), 1.57–1.64 (m, 1H), 1.67–1.82 (m, 2H), 3.75 (m, 1H), 4.45 (d, J=3.4, 1H); ^{13}C NMR (D$_2$O) δ 22.0 22.4, 24.5, 38.6, 52.4, 70.3, 175.7.

Methyl (E)-4-cyclohexyl-2-oxo-3-butenoate 12b

According to the procedure described for **12a**, starting with **10b** (16.0 mL, 132 mmol), HC(OMe)$_3$ (15.8 mL, 145 mmol), BF$_3$·OEt$_2$ (17.8 mL, 145 mmol) and **11** (22.9 g, 132 mmol), **12b** (20.3 g, 104 mmol, 79%) was obtained as a yellow oil. Bp 114°C/1.5 Torr; ^{1}H NMR (CDCl$_3$) δ 1.15–1.38 (m, 5H), 1.68–1.82 (m, 5H), 2.22–2.26 (m, 1H), 3.89 (s, 3H), 6.61 (d, J=16.0, 1H), 7.13 (dd, J=6.8, 16.0, 1H); ^{13}C NMR (CDCl$_3$) δ 25.6 (×2), 25.8, 31.3 (×2), 41.3, 52.8, 122.6, 159.9, 162.8, 183.4.

(1R,2S)-2-Phenylcyclohexyl (2R,3E)-4-cyclohexyl-2-hydroxy-3-butenoate 13b

According to the procedure for **13a**, starting with (1R,2S)-(−)-2-phenylcyclohexanol (2.19 g, 12.4 mmol), BuLi (1.66 M in hexane, 6.87 mL, 11.4 mmol) and **12b** (2.03 g, 10.4 mmol), (1R,2S)-2-phenylcyclohexyl (E)-4-cyclohexyl-2-oxo-3-butenoate (2.33 g, 6.84 mmol, 66%) was obtained as a yellow oil. ^{1}H NMR (CDCl$_3$) δ 0.94–1.83 (m, 15H), 1.89–2.04 (m, 3H), 2.13–2.21 (m, 1H), 2.77 (dt,

J=4.4, 11.7, 1H), 5.19 (dt, J=4.4, 10.7, 1H), 6.11 (dd, J=1.0, 16.1, 1H), 6.43 (dd, J=6.6, 16.1, 1H), 7.15–7.32 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 24.6, 25.5, 25.6, 25.6, 25.8, 30.9, 31.2, 31.9, 33.8, 41.0, 49.5, 78.2, 123.1, 126.6, 127.5 (×2), 128.4 (×2), 142.5, 159.6, 162.3, 185.3.

The subsequent reduction was performed using the above ester (1.17 g, 3.44 mmol) and L-Selectride® (1.0 M in THF, 4.1 mL, 4.13 mmol) to give **13b** (1.10 g, 3.20 mmol, 93%, >97% de) as a colorless oil. [α]$_D^{28}$ −53.0 (*c* 1.08, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 0.77–0.95 (m, 2H), 1.09–2.00 (m, 16H), 2.08–2.23 (m, 1H), 2.66–2.89 (m, 1H), 2.72 (d, J=5.9, 1H), 4.36 (dd, J=5.9, 5.9, 1H), 4.72 (ddd, J=1.5, 5.9, 15.6, 1H), 5.06 (dt, J=4.4, 10.7, 1H), 5.53 (ddd, J=1.5, 6.8, 15.6, 1H), 7.14–7.27(m, 5H); ^{13}C NMR (CDCl$_3$) δ 24.7, 25.7, 25.9, 26.0, 26.1, 32.2, 32.3, 32.3, 34.2, 40.0, 49.7, 71.2, 77.8, 123.3, 126.5, 127.4 (×2), 128.3 (×2), 139.0, 142.7, 173.3; IR (neat) 3510, 3029, 2925, 2852, 1731, 1449, 1262, 1207, 1121, 1058 cm^{-1}. Anal. Calcd for C$_{22}$H$_{30}$O$_3$: C, 77.16; H, 8.83. Found: C, 76.90; H, 9.09.

(4R,5R)-4-[(1S)-1-Iodocyclohexylmethyl]-5-[(1R,2S)-2-phenylcyclohex-1-yloxycarbonyl]-3-tosyl-2-oxazolidinone 14b

According to the procedure described for **14a**, starting with **13b** (7.47 g, 21.9 mmol) and TsNCO (3.65 ml, 24.1 mmol), then Na$_2$CO$_3$ (11.6 g, 110 mmol) and I$_2$ (11.1 g, 43.9 mmol), **14b** (11.1 g, 16.7 mmol, 76%, >92% de) was obtained as colorless needles. [α]$_D^{28}$ −20.6 (*c* 1.00, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 0.99–2.05 (m, 19H), 2.46 (s, 3H), 2.66 (dt, J=4.4, 11.7, 1H), 3.96 (dd, J=2.4, 2.4, 1H), 4.43 (dd, J=2.4, 6.8, 1H), 4.48 (d, J=2.4, 1H), 5.15 (dt, J=4.4, 10.7, 1H), 7.19 (d, J=7.3, 2H), 7.24–7.36 (m, 5H), 7.83 (d, J=8.3, 2H); ^{13}C NMR (CDCl$_3$) δ 21.8, 24.7 25.6, 25.8, 25.8, 26.0, 32.0, 32.1, 33.8, 33.9, 41.3, 48.1, 49.6, 61.9, 75.3, 78.5, 127.2, 127.3 (×2), 128.7 (×4), 129.7 (×2), 134.4, 142.0, 145.8, 150.3, 166.5; IR (neat) 3058, 2935, 2857, 1797, 1752, 1450, 1376, 1266, 1175, 1137, 1089 cm^{-1}. Anal. Calcd for C$_{30}$H$_{36}$INO$_6$S: C, 54.14; H, 5.45; N, 2.10. Found: C, 53.95; H, 5.53; N, 2.01.

(4S,5R)-4-(Cyclohexylmethyl)-5-[(1R,2S)-2-phenylcyclohex-1-yloxycarbonyl]-3-tosyl-2-oxazolidinone 15b

According to the procedure described for **15a**, starting with **14b** (10.4 g, 15.7 mmol), AIBN (514 mg, 3.13 mmol) and Bu$_3$SnH (5.1 mL, 18.8 mmol), **15b** (7.70 g, 14.3 mmol, 91%) was obtained as a colorless viscous oil. [α]$_D^{26}$ +11.5 (*c* 1.50, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 0.78–0.99 (m, 5H), 1.11–1.89 (m, 14H), 1.95–2.12 (m, 2H), 2.46 (s, 3H), 2.65 (dt, J=4.4, 10.0, 1H), 3.81 (ddd, J=1.5, 2.9, 10.3, 1H), 4.29 (d, J=1.5, 1H), 5.10 (dt, J=4.4, 10.7, 1H), 7.17 (d, J=6.8, 2H), 7.21–7.37 (m, 5H), 7.77 (d, J=8.3, 2H); ^{13}C NMR (CDCl$_3$) δ 21.7, 24.6, 25.1, 25.3, 25.9, 26.0, 32.0, 32.0, 33.6, 33.6, 34.1, 41.9, 49.5, 59.3, 75.0, 78.1, 127.1 (×4), 128.4, 128.7 (×2), 129.6 (×2), 134.8, 142.2, 145.4, 150.7, 166.9; IR (neat) 3029, 2922, 1732, 1597, 1495, 1456, 965 cm^{-1}. Anal. Calcd for C$_{30}$H$_{37}$NO$_6$S: C, 66.77; H, 6.91; N, 2.60; S, 5.94. Found: C, 66.57; H, 7.02; N, 2.44; S, 5.92.

(2R,3S)-4-Cyclohexyl-2-hydroxy-3-(tosylamino)butanoic acid 16b

According to the procedure described for **16a**, starting with **15b** (7.22 g, 13.4 mmol) and a 0.3 M methanolic solution of K$_2$CO$_3$, methyl (2*R*,3*S*)-4-cyclohexyl-2-hydroxy-3-(tosylamimo)butanoate (3.96 g, 10.7 mmol, 80%) was obtained as a colorless oil. [α]$_D^{27}$ −49.1 (*c* 1.36, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 0.66–0.82 (m, 2H), 0.88–1.13 (m, 4H), 1.16–1.25 (m, 1H), 1.39–1.65 (m, 6H), 2.43 (s, 3H), 3.20 (d, J=4.4, 1H), 3.67–3.77 (m, 1H), 3.71 (s, 3H), 4.11 (dd, J=2.0, 4.4, 1H), 4.80 (d, J=9.8, 1H), 7.30 (d, J=8.3, 2H), 7.74 (d, J=8.3, 2H); ^{13}C NMR (CDCl$_3$) δ 21.5, 25.9, 26.1, 26.3, 33.0 (×2), 33.6, 40.1, 53.0, 53.3, 71.7, 127.1 (×2), 129.6 (×2), 138.2, 143.4, 173.5; IR (neat) 3490, 3279, 2926, 2853, 1740, 1448, 1327, 1266, 1160, 1094 cm^{-1}. Anal. Calcd for C$_{18}$H$_{27}$NO$_5$S: C, 58.51; H, 7.37; N, 3.79. Found: C, 58.31; H, 7.43; N, 3.89.

The following hydrolysis of the above methyl ester (3.72 g, 10.1 mmol) gave **16b** (3.54 g, 10.0 mmol, 99%) as colorless needles. Mp 159–160°C; [α]$_D^{28}$ −47.7 (*c* 1.00, acetone); ^{1}H NMR (acetone-d_6) δ 0.64–0.81 (m, 2H), 0.93–1.35 (m, 5H), 1.41–1.69 (m, 6H), 2.41 (s, 3H), 3.70–3.72 (m, 1H), 4.17 (d, J=2.4, 1H), 6.19 (d, J=8.8, 1H), 7.37 (d, J=8.1, 2H), 7.77 (d, J=8.1, 2H); ^{13}C NMR (acetone-d_6) δ 21.4, 26,5, 26.7, 27.0, 33.4, 33.9, 34.1, 39.4, 54.3, 72.5, 127.8 (×2), 130.2 (×2), 140.2, 143.6, 174.2;

IR (KBr) 3542, 2926, 1753, 1451, 1326, 1245, 1196, 1140, 1091 cm^{-1}. Anal. Calcd for $C_{17}H_{25}NO_5S$: C, 57.44; H, 7.09; N, 3.94. Found: C, 57.28; H, 7.14; N, 3.74.

(2R,3S)-3-Amino-4-cyclohexyl-2-hydroxybutanoic acid 17b

According to the procedure described for **17a**, starting with **16b** (3.63 g, 10.2 mmol) and sodium naphthalenide solution (71.5 mmol), **17b** (1.33 g, 6.61 mmol, 65%) was obtained as a white solid. ^{1}H NMR (D$_2$O) δ 0.98–1.10 (m, 2H), 1.25–1.48 (m, 7H), 1.59–2.02 (m, 4H), 3.28 (br, 1H), 4.02 (d, J=2.9, 1H); ^{13}C NMR (D$_2$O) δ 26.6, 26.7, 27.1, 33.4, 34.1, 34.4, 40.8, 51.3, 75.5, 180.4.

(2R,3S)-3-Amino-4-cyclohexyl-2-hydroxybutanoic acid hydrochloride

According to the procedure described for **17a·HCl**, starting with **17b**, **17b·HCl**[21–23] was obtained as white solid. ^{1}H NMR (D$_2$O) δ 0.9–1.1 (m, 2H), 1.15–1.35 (m, 3H), 1.4–1.8 (m, 8H), 3.7 (m, 1H), 4.28 (br, 1H).

Methyl (E)-2-oxo-3-decenoate 12c

According to the procedure described for **12a**, starting with **10c** (23.0 mL, 165 mmol), HC(OMe)$_3$ (19.8 mL, 181 mmol), BF$_3$·OEt$_2$ (22.3 mL, 181 mmol) and **11** (31.6 g, 181 mmol), **12c** (19.2 g, 97.0 mmol, 59%) was obtained as a yellow oil. Bp 96–100°C/2 Torr; ^{1}H NMR (CDCl$_3$) δ 0.88 (dd, J=6.8, 6.8, 3H), 1.30–1.54 (m, 8H), 2.30 (dt, J=7.3, 7.3, 1H), 3.89 (s, 3H), 6.65 (d, J=15.6, 1H), 7.21 (dt, J=6.8, 15.6, 1H); ^{13}C NMR (CDCl$_3$) δ 14.0, 22.5, 27.7, 28.8, 31.5, 33.1, 52.8, 125.0, 155.4, 162.8, 183.0.

(1S,2R)-2-Phenylcyclohexyl (2S,3E)-2-hydroxy-3-decenoate 13c

According to the procedure described for **13a**, starting with (1S,2R)-(+)-2-phenylcyclohexanol (4.48 g, 25.4 mmol), BuLi (1.68 M in hexane, 15.1 mL, 25.4 mmol) and **12c** (4.73 g, 23.9 mmol), (1S,2R)-2-phenylcyclohexyl (E)-2-oxo-3-decenoate (4.54 g, 13.3 mmol, 56%) was obtained as a yellow oil. ^{1}H NMR (CDCl$_3$) δ 0.89 (t, J=7.1, 3H), 1.24–1.66 (m, 13H), 1.80–2.19 (m, 5H), 2.76 (dt, J=4.4, 11.7, 1H), 5.20 (dt, J=4.4, 10.7, 1H), 6.11 (d, J=16.1, 1H), 6.33 (dt, J=6.7, 16.1, 1H), 7.17–7.31 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 14.0, 22.5, 24.7, 25.6, 27.4, 28.8, 31.5, 32.0, 33.1, 33.8, 49.6, 78.2, 125.7, 126.7, 127.6 (×2), 128.4 (×2), 142.6, 155.5, 162.5, 185.3.

The following reduction was performed using the above ester (2.08 g, 6.07 mmol) and L-Selectride® (1.0 M in THF, 7.28 mL, 7.28 mmol) to give **13c** (1.89 g, 5.49 mmol, 90%, >97% de) as a colorless oil. [α]$_D^{28}$ +51.8 (c 0.583, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 0.90 (t, J=7.1, 3H), 1.18–1.61 (m, 13H), 1.74–1.97 (m, 4H), 2.12–2.19 (m, 1H), 2.67 (d, J=5.9, 1H), 2.68 (dt, J=4.4, 11.5, 1H), 4.35 (dd, J=5.9, 5.9, 1H), 4.73 (dd, J=5.9, 15.6, 1H), 5.04 (dt, J=4.4, 10.7, 1H), 5.54 (ddt, J=1.5, 6.8, 15.6, 1H), 7.14–7.27 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 14.1, 22.6, 24.7, 25.7, 28.8, 28.9, 31.7, 32.1, 32.2, 34.0, 49.8, 71.1, 78.0, 125.7, 126.6, 127.5 (×2), 128.3 (×2), 133.8, 142.6, 173.3; IR (neat) 3510, 2929, 2857, 1734, 1450, 1262, 1203, 1140, 1113, 1011 cm^{-1}. Anal. Calcd for $C_{22}H_{30}O_3$: C, 76.70; H, 9.36. Found: C, 76.56; H, 9.53.

(4S,5S)-4-[(1R)-1-Iodoheptyl)]-5-[(1S,2R)-2-phenylcyclohex-1-yloxycarbonyl]-3-tosyl-2-oxazolidinone 14c

According to the procedure described for **14a**, starting with **13c** (1.52 g, 4.41 mmol) and TsNCO (0.87 mL, 5.74 mmol), then Na$_2$CO$_3$ (2.34 g, 22.1 mmol) and I$_2$ (2.24 g, 8.82 mmol), **14c** (2.45 g, 3.67 mmol, 83%, >92% de) was obtained as colorless needles. [α]$_D^{28}$ +23.1 (c 0.872, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 0.95 (t, J=6.8, 3H), 1.09–1.60 (m, 14H), 1.78–1.82 (m, 1H), 1.88–1.99 (m, 2H), 2.04–2.21 (m, 1H), 2.45 (s, 3H), 2.67 (dt, J=3.9, 11.6, 1H), 3.38 (dd, J=2.9, 2.9, 1H), 4.39 (d, J=2.9, 1H), 4.40–4.42 (m, 1H), 5.15 (dt, J=3.9, 10.7, 1H), 7.18 (d, J=6.8, 2H), 7.22–7.37 (m, 5H), 7.83 (d, J=8.3, 2H); ^{13}C NMR (CDCl$_3$) δ 14.1, 21.8, 22.6, 24.7, 25.6, 28.2, 29.2, 31.5, 32.1, 34.2, 34.7, 39.0, 49.8, 63.8, 74.1, 78.4, 127.3 (×3), 128.7 (×2), 128.8 (×2), 129.7 (×2), 134.3, 142.2, 145.9, 150.2, 166.5; IR (neat) 3029, 2926, 2857, 1790, 1756, 1713, 1597, 1454, 1372, 1172, 1006 cm^{-1}. Anal. Calcd for $C_{30}H_{38}INO_6S$: C, 53.97; H, 5.74; N, 2.10. Found: C, 52.78; H, 5.55; N, 2.21.

(4R,5S)-4-Heptyl-5-[(1S,2R)-2-phenylcyclohex-1-yloxycarbonyl]-3-tosyl-2-oxazolidinone 15c

According to the procedure described for **15a**, starting with **14c** (2.28 g, 3.42 mmol), AIBN (113 mg, 0.685 mmol) and Bu₃SnH (1.10 mL, 4.1 mmol), **15c** (1.77 g, 3.27 mmol, 96%) was obtained as colorless needles. Mp 102–103°C; $[\alpha]_D{}^{27}$ −7.1 (*c* 0.608, CHCl₃); ¹H NMR (CDCl₃) δ 0.91 (t, *J*=7.1, 3H), 1.07–1.61 (m, 14H), 1.64–1.71 (m, 2H), 1.79–1.89 (m, 2H), 1.95–1.98 (m, 1H), 2.04–2.07 (m, 1H), 2.45 (s, 3H), 2.65 (dt, *J*=4.4, 12.1, 1H), 3.46–3.49 (m, 1H), 4.24 (d, *J*=2.4, 1H), 5.01 (dt, *J*=4.4, 10.7, 1H), 7.18 (d, *J*=6.8, 2H), 7.20–7.38 (m, 5H), 7.75 (d, *J*=8.3, 2H); ¹³C NMR (CDCl₃) δ 14.1, 21.7, 22.6, 23.2, 24.6, 25.5, 29.0, 31.6, 32.1, 33.5, 34.3, 49.8, 60.7, 74.3, 78.5, 127.3, 127.4 (×2), 128.4 (×2), 128.6 (×2), 129.6 (×2), 134.7, 142.2, 145.5, 150.8, 167.0; IR (KBr) 2931, 1803, 1598, 1496, 1451, 1374, 1183, 934 cm⁻¹. Anal. Calcd for C₃₀H₃₉NO₆S: C, 66.52; H, 7.26; N, 2.59. Found: C, 66.57; H, 7.25; N, 2.58.

(2S,3R)-2-Hydroxy-3-(tosylamino)decanoic acid 16c

According to the procedure described for **16a**, starting with **15c** (1.67 g, 3.09 mmol) and 0.3 M methanolic solution of K₂CO₃, methyl (2S,3R)-2-hydroxy-3-(tosylamino)decanoate (802 mg, 2.16 mmol, 70%) was obtained as a colorless oil. $[\alpha]_D{}^{28}$ +42.0 (*c* 0.50, CHCl₃); ¹H NMR (CDCl₃) δ 0.86 (t, *J*=7.3, 3H), 1.12–1.28 (m, 10H), 1.31–1.39 (m, 1H), 1.55–1.60 (m, 1H), 2.42 (s, 3H), 3.27 (d, *J*=4.9, 1H), 3.63 (dtd, *J*=1.5, 7.3, 9.8, 1H), 3.68 (s, 3H), 4.14 (dd, *J*=1.5, 4.9, 1H), 4.96 (d, *J*=9.8, 1H), 7.29 (d, *J*=8.3, 2H), 7.73 (d, *J*=8.3, 2H); ¹³C NMR (CDCl₃) δ 14.1, 21.5, 22.6, 25.8, 29.0 (×2), 31.6, 32.5, 52.9, 55.9, 71.6, 127.0 (×2), 129.6 (×2), 138.3, 143.3, 173.5; IR (neat) 3488, 3282, 2927, 2857, 1740, 1598, 1441, 1331, 1160, 1094 cm⁻¹. Anal. Calcd for C₁₈H₂₉NO₅S: C, 58.20; H, 7.87; N, 3.77. Found: C, 58.13; H, 8.12; N, 3.48.

Hydrolysis of the methyl ester (684 mg, 1.84 mmol) gave **16c** (657 mg, 1.84 mmol, 100%) as colorless needles. Mp 111–113°C; $[\alpha]_D{}^{28}$ +39.5 (*c* 0.60, acetone); ¹H NMR (acetone-d_6) δ 0.87 (t, *J*=7.1, 3H), 1.11–1.31 (m, 11H), 1.60–1.63 (m, 1H), 2.42 (s, 3H), 3.60–3.62 (m, 1H), 4.16 (d, *J*=2.9, 1H), 6.19 (d, *J*=9.3, 1H), 7.37 (d, *J*=8.3, 2H), 7.76 (d, *J*=8.3, 2H); ¹³C NMR (CD₃CN) δ 13.1, 20.2, 22.1, 25.1, 28.4 (×2), 30.9, 31.1, 55.8, 70.9, 126.6 (×2), 129.3 (×2), 138.5, 143.1, 172.7; IR (KBr) 3480, 3250, 2929, 1750, 1439, 1154 cm⁻¹. Anal. Calcd for C₁₇H₂₇NO₅S: C, 57.12; H, 7.61; N, 3.92. Found: C, 57.31; H, 7.69; N, 3.66.

(2S,3R)-3-Amino-2-hydroxydecanoic acid 17c

According to the procedure described for **17a**, starting with **16c** (577 mg, 1.61 mmol) and sodium naphthalenide solution (9.68 mmol), **17c**[24] (202 mg, 0.995 mmol, 62%) was obtained as a white solid. ¹H NMR (D₂O) δ 0.92 (t, *J*=6.8, 3H), 1.34–1.65 (m, 12H), 3.13–3.16 (m, 1H), 4.02 (d, *J*=3.4, 1H); ¹³C NMR (D₂O) δ 13.9, 22.6, 26.0, 28.9, 29.2, 31.6, 32.8, 53.8, 74.8, 180.1.

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